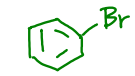
(F, Cl, Br, I)

Organic molecules containing halogen atoms (X) bonded to carbon are useful compounds in synthesis and on their own.

$-(CF_2CF_2)_n$ Teflon

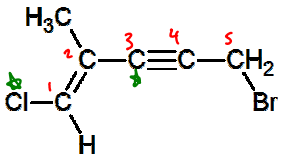
Trichloroethylene (a solvent) | Halothane (an inhaled anesthetic) | Dichlorodifluoromethane (a refrigerant) | Bromomethane (a fumigant)

A **vinyl halide** has X bonded to a C=C double bond.
An **aryl halide** has X bonded to a benzene ring.
An **alkyl halide** has X bonded to an sp^3 carbon



bromobenzene

Alkyl halide nomenclature follows normal IUPAC rules, with -fluoro, -chloro, -bromo, and -iodo taking alphabetical precedence with other numbered groups.



(1E)- 5-bromo-1-chloro-2-methyl pent-1-en-3-yne

	IUPAC	Common
CH_3Cl	chloromethane	methyl chloride
CH_2Cl_2	dichloromethane (DCM)	methylene chloride
$CHCl_3$	tri "	chloroform
CCl_4	tetra "	carbon tetrachloride

↖ (nonpolar) ↗

The C-X bond gets **longer** and **weaker** going down the periodic table.

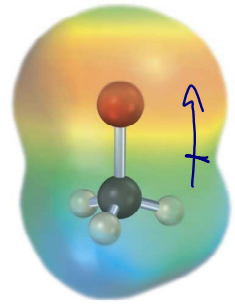
F
Cl
Br
I

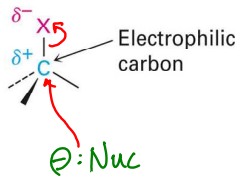
Table 10.1 A Comparison of the Halomethanes

Halomethane	Bond length (pm)	Bond strength (kJ/mol)	Bond strength (kcal/mol)	Dipole moment (*D*)
CH_3F	139	452	108	1.85
CH_3Cl	178	351	84	1.87
CH_3Br	193	293	70	1.81
CH_3I	214	234	56	1.62

The C-X bond is somewhat polar with halogens being more electronegative than carbon. This makes an electrophilic (δ+) carbon which can be attacked.

Halogen atoms Br and I are considered very **polarizable**, meaning their electron clouds will very easily respond to an approaching charge.



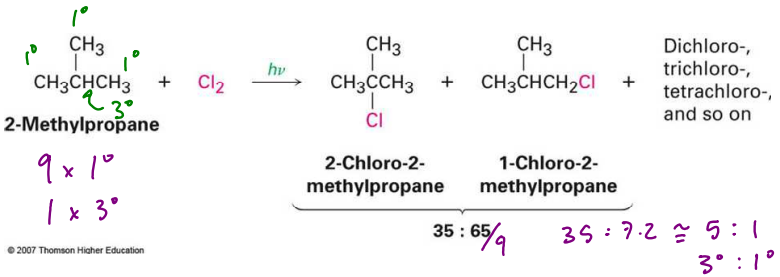


Radical chlorination makes a **mixture** of 1°, 2°, and 3° alkyl chlorides from alkanes. It has initiation, propagation, and termination steps like any radical reaction:

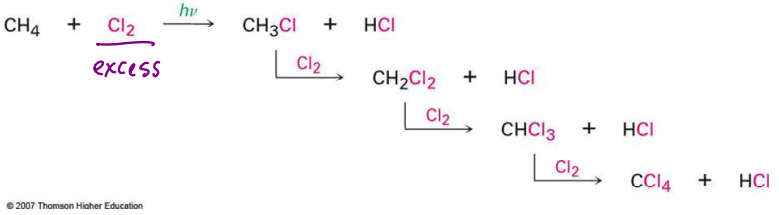
Initiation: $Cl_2 \xrightarrow{h\nu} 2\,Cl\cdot$

Propagation: $H_3C\cdot + Cl_2 \rightarrow H_3C{-}Cl + \cdot Cl$ (react w/ a new CH_4)

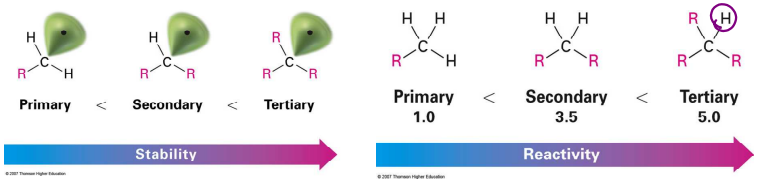
Termination: $H_3C\cdot + \cdot Cl \rightarrow H_3C{-}Cl$ or $2\,Cl\cdot \rightarrow Cl_2$ or $2\,CH_3\cdot \rightarrow CH_3CH_3$



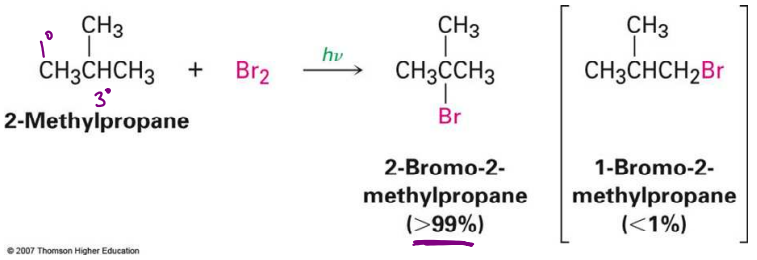
Multiple chlorinations are common:



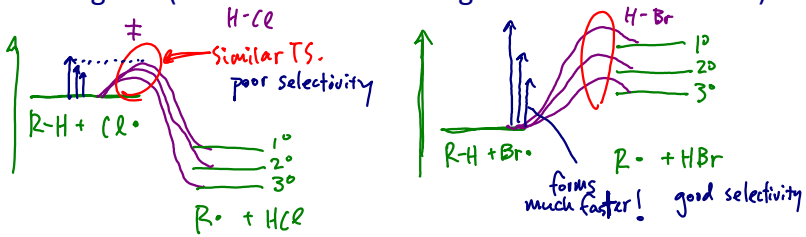
Careful analysis of chlorination product mixtures reveals a radical stability trend similar to carbocations:



While reaction of Cl_2/hv gives a mixture of products, Br_2/hv is much more selective:



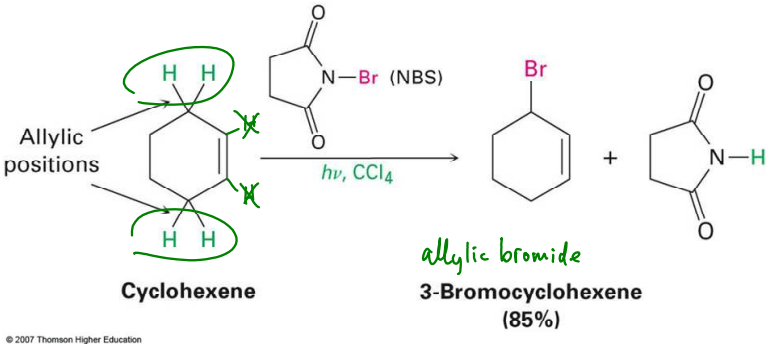
This is because the first propagation step of chlorination is exergonic while the first step of bromination is endergonic (the C-Cl bond is stronger than the C-Br bond)



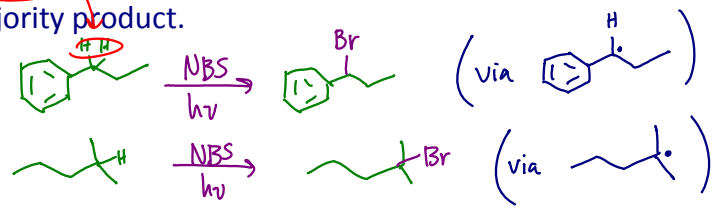
10.4 Allylic bromination

N-bromosuccinimide (NBS) can be used to very selectively replace an allylic hydrogen with a bromine. → makes Br_2 in situ

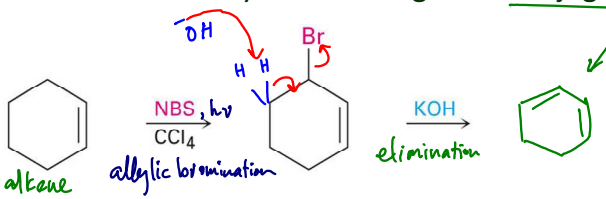
(**Allylic**: **next to** a double-bonded carbon)



It also gives exclusive products when there's a single type of benzylic hydrogen. A tertiary hydrogen will give a majority product.

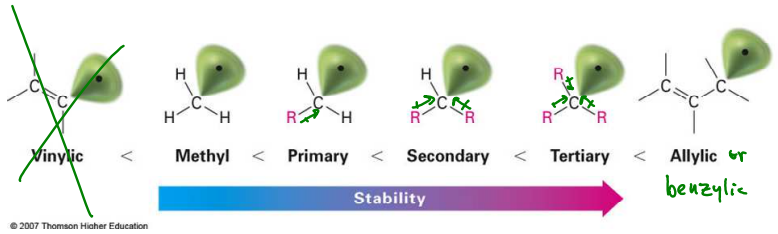


Elimination of an allylic bromide gives a conjugated diene.

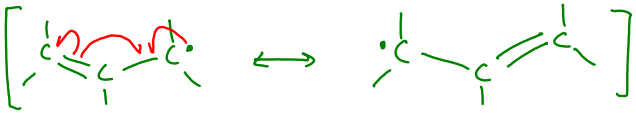


10.5 Stability of the allylic radical

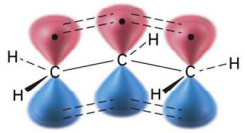
Allylic and benzylic radicals are more stable than their alkyl counterparts:



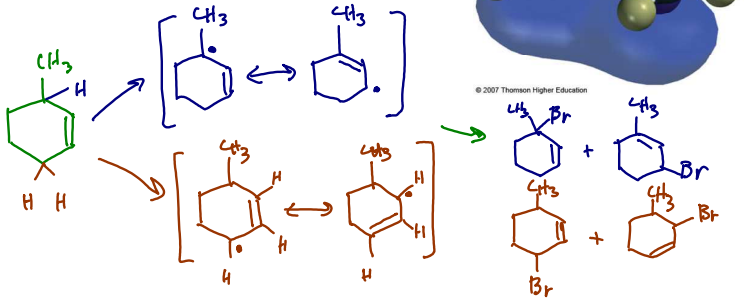
This is because the radical is resonance stabilized:



The resonance hybrid has half of the radical properties at each end of the three-carbon group.



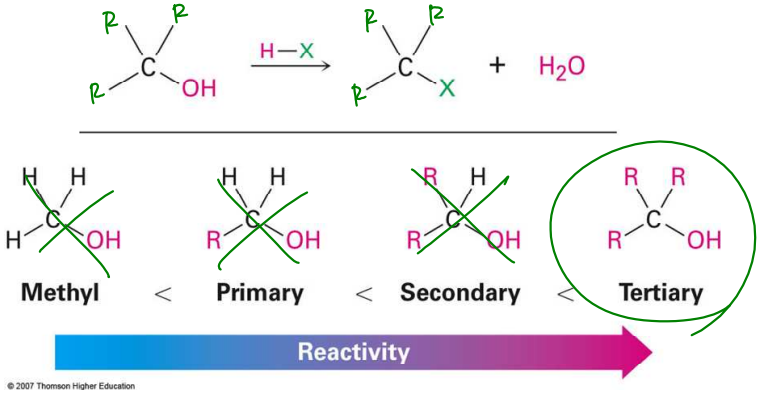
Non-symmetrical allylic systems will give a mixture of products:



10.6 Preparing alkyl halides from alcohols

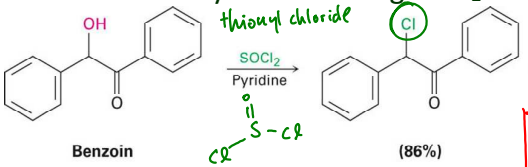
Tertiary alkyl halides can be formed from the corresponding tertiary alcohol by reacting it with H-X.

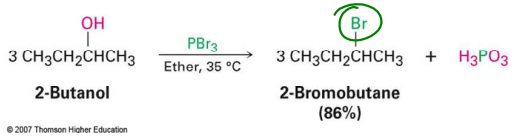
HCl
HBr, HI



(This reaction goes by way of the S_N1 mechanism which we will learn about in chapter 11.)

Primary and secondary alcohols can be efficiently converted to alkyl halides using $SOCl_2$ or PBr_3:

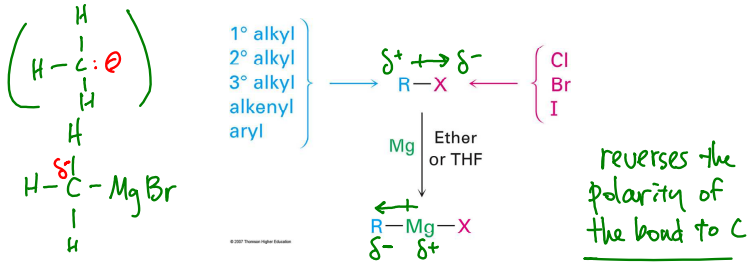




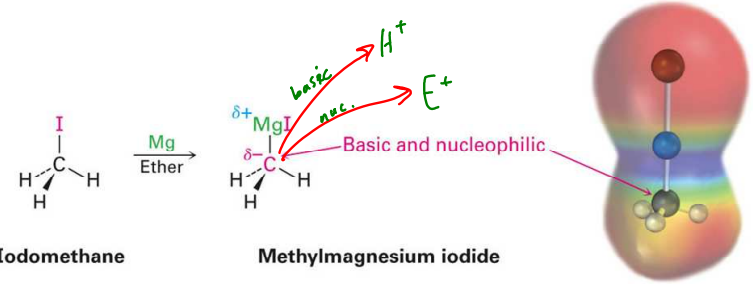
R-OH → R-Cl or R-Br
1° SOCl2 or PBr3
2° SOCl2 or PBr3
3° HCl or HBr

10.7 Reactions of alkyl halides: Grignard reagents

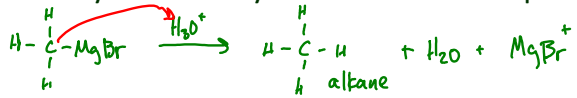
Almost any alkyl halide will react with magnesium metal to form an alkylmagnesium halide (RMgX) called a **Grignard reagent**.



Grignard reagents react like a carbanion ($C:^-$) paired with ^+MgX. Since hydrocarbons are among the weakest of acids, carbanions are tremendously strong bases and nucleophiles.

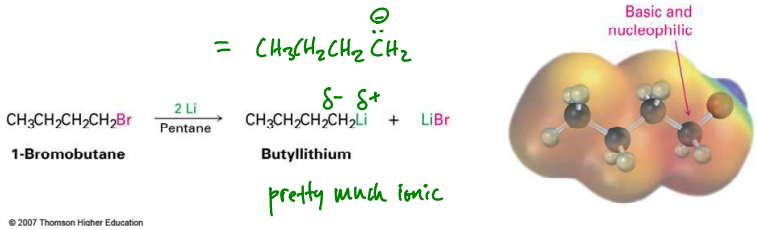


They will immediately react with any acidic H (H_3O^+, H_2O, ROH, RNH_2, etc) to form a new C-H bond. They will be very useful in synthesis in later chapters.

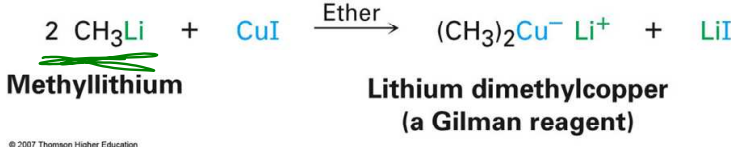


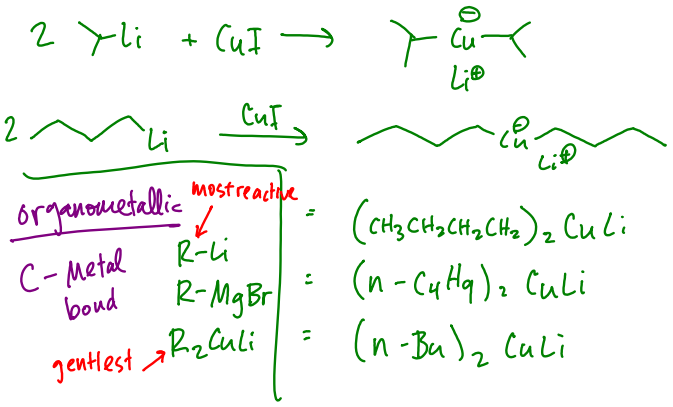
10.8 Organometallic coupling reagents

Lithium will replace a halogen to make an alkyllithium, similar to a Grignard reagent. These are the strongest bases routinely used in organic synthesis.



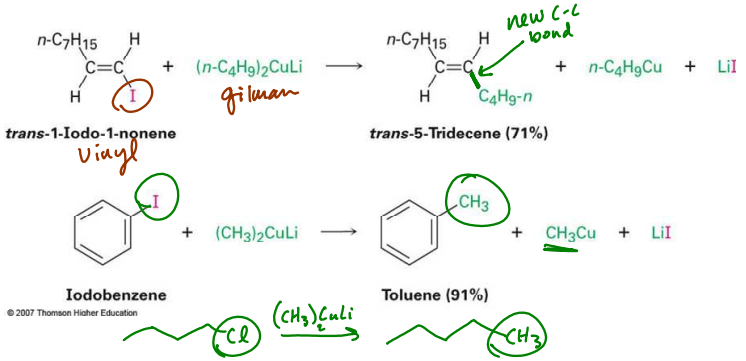
The resulting alkyllithium reagents can be converted to lithium dialkylcuprates by reaction with CuI. This produces a less reactive, gentler, carbon nucleophile called a **Gilman reagent.**





Gilman dialkylcuprate coupling

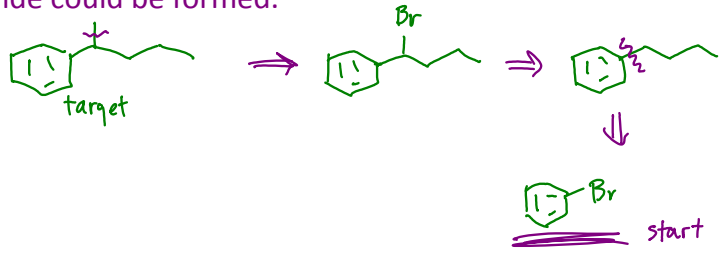
Gilman reagents will react with alkyl, vinyl, and aryl halides to perform our second important C-C bond-forming coupling reaction.



This is tremendously useful because it can make a carbon-carbon bond to an sp^3 or an sp^2 carbon. (Acetylide alkylation makes a bond to an sp carbon).

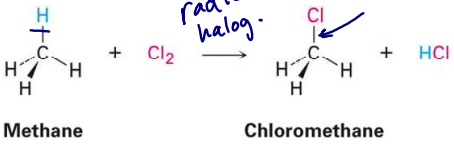
Use this in synthesis if you need to add a methyl, ethyl, propyl, butyl, etc. group to a molecule. Simple alkyl group

Retrosynthetically, look at where in the molecule an alkyl halide could be formed.

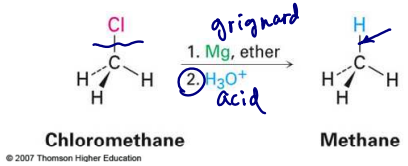


10.9 Oxidation and reduction

	Form	or	Break
Oxidation:	C-O, C-N, C-X		C-H
Reduction:	C-H		C-O, C-N, C-X



Oxidation: C–H bond broken and C–Cl bond formed



Reduction: C–Cl bond broken and C–H bond formed

form C-Br and C-H
neither ox nor red

Carbon's oxidation levels:

CH_3CH_3	$H_2C{=}CH_2$	$HC{\equiv}CH$		no H's on C
alkane	CH_3OH	$H_2C{=}O$	HCO_2H	CO_2
	CH_3Cl	CH_2Cl_2	$CHCl_3$	CCl_4
	CH_3NH_2	$H_2C{=}NH$	$HC{\equiv}N$	

Low oxidation level → High oxidation level

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