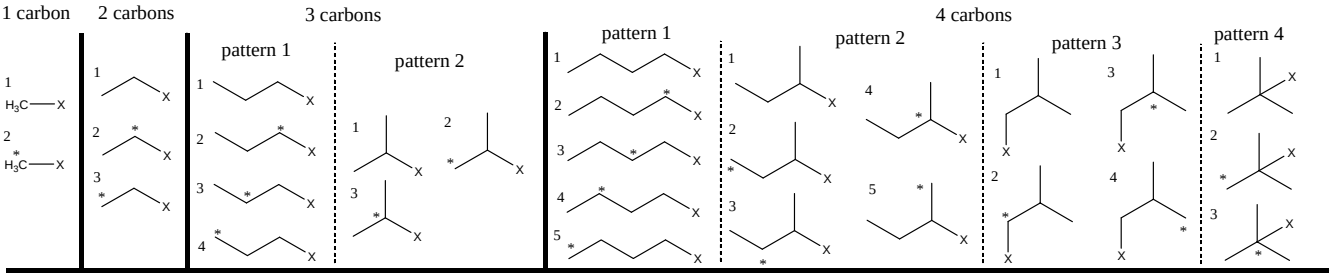
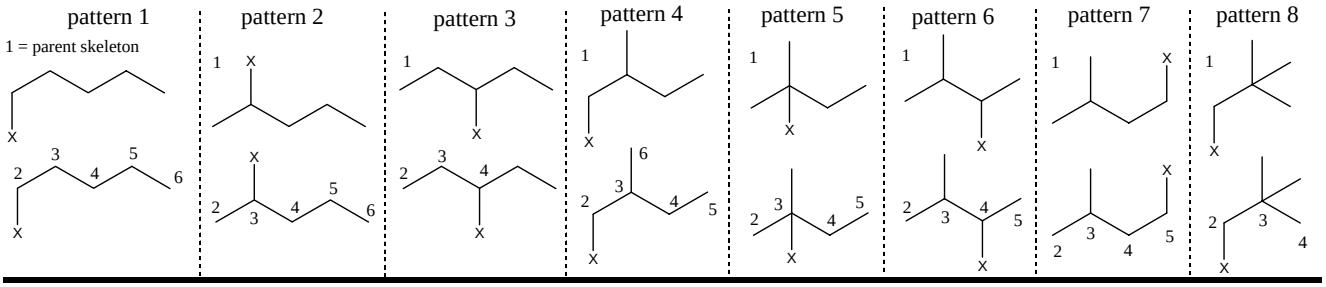
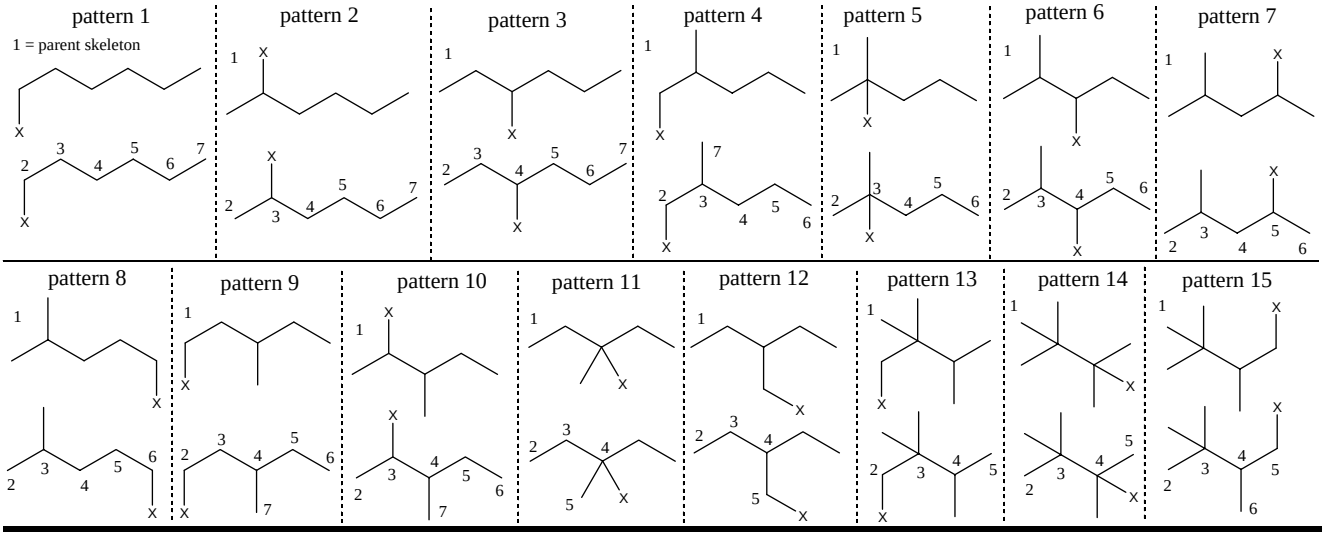
The following carbon skeletons represent parts of structures that can be made with or without ^{14}C labeled positions. C1 – C4 carbon skeletons are all shown, with "*" to indicate the location of any ^{14}C label. In structures with 5 carbon atoms, or more, the first structure drawn represents the parent skeleton and the second structure shows all of the different positions that a single ^{14}C label could be inserted (a number indicates each different possibility). "X" represents a simple functional group or a point of attachment in a functional group pattern that could have more than one carbon portion. (See the last page for several examples of functional group patterns that could have 2 or more branches.) Synthetic targets can be randomly generated by drawing out a number for the carbons in the skeleton (1-7), then picking a random pattern, then picking a random isomer with or without a ^{14}C label. This can be done once, twice or 3 times for each branch in the selected functional group pattern (which can also be picked at random). The possibilities are effectively endless for organic synthesis problems (there are about 420 skeletal patterns, including ^{14}C labels). These problems are relatively straight forward because there is only 1 functional group. More than one functional group may require protection/deprotection steps and the difficulty of such synthetic problems can rapidly go up. Some patterns may have limitations due to steric crowding.



5 carbons: 1 = parent skeleton without any ^{14}C label, numbers = skeleton location with a ^{14}C label at that position (for reference in synthesis problems)



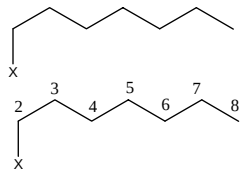
6 carbons: 1 = parent skeleton without any ^{14}C label, numbers = skeleton location with a ^{14}C label at that position (for reference in synthesis problems)



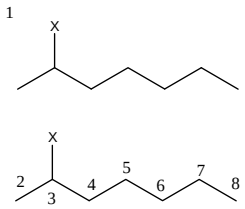
7 carbons: 1 = parent skeleton without any ^{14}C label, numbers = skeleton location with a ^{14}C label at that position (for reference in synthesis problems)

pattern 1

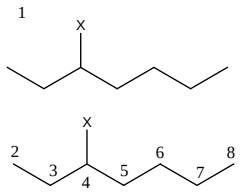
1 = parent skeleton



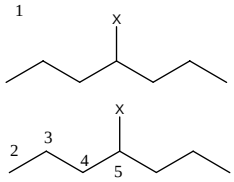
pattern 2



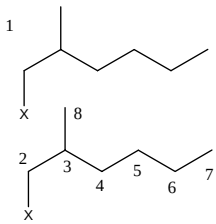
pattern 3



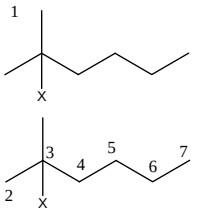
pattern 4



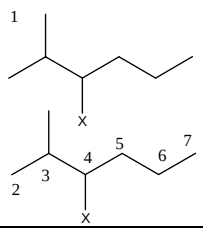
pattern 5



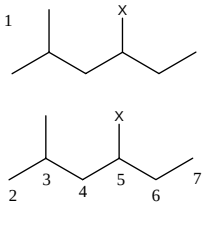
pattern 6



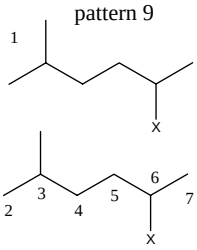
pattern 7



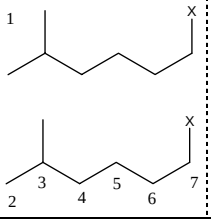
pattern 8



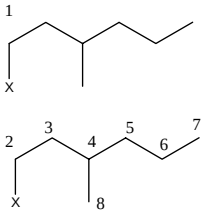
pattern 9



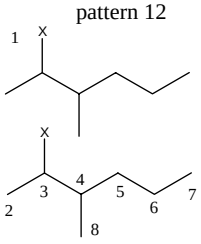
pattern 10



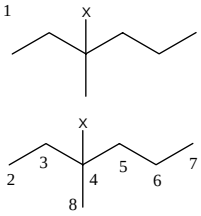
pattern 11



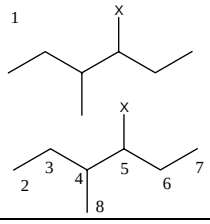
pattern 12



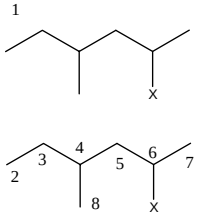
pattern 13



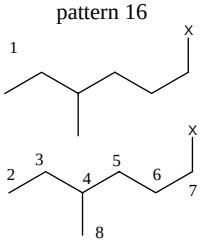
pattern 14



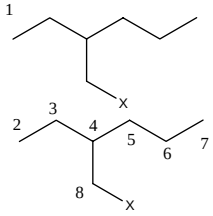
pattern 15



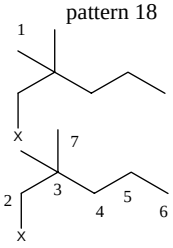
pattern 16



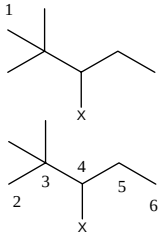
pattern 17



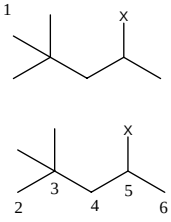
pattern 18



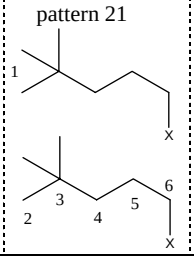
pattern 19



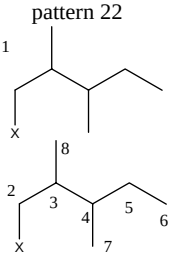
pattern 20



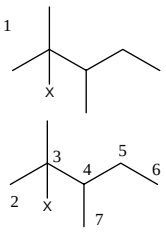
pattern 21



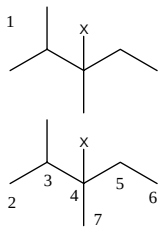
pattern 22



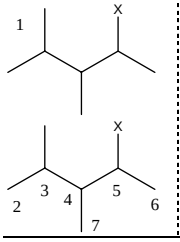
pattern 23



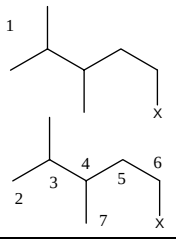
pattern 24



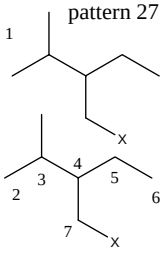
pattern 25



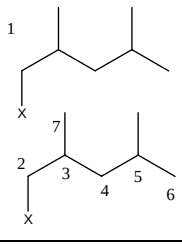
pattern 26



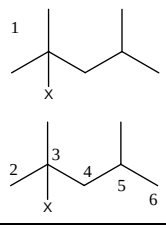
pattern 27



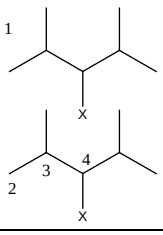
pattern 28



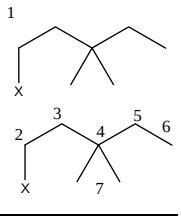
pattern 29



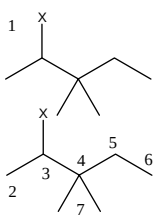
pattern 30



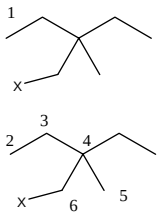
pattern 31



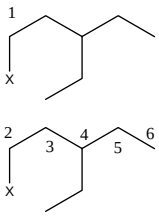
pattern 32



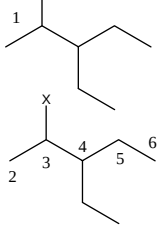
pattern 33



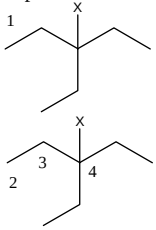
pattern 34



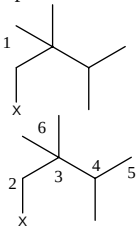
pattern 35



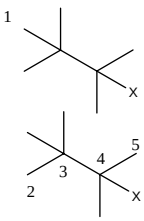
pattern 36



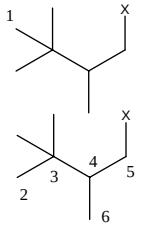
pattern 37



pattern 38

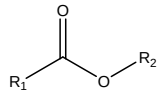


pattern 39

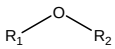


Connecting 2 or 3 patterns from above in the functional groups below.

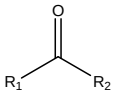
Several of the patterns below may require an additional 1 or 2 carbon atoms at the connecting point, in addition to the R_1 and R_2 patterns.



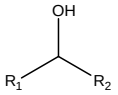
esters
carboxylate + RBr
acid chloride + ROH
Fischer ester synthesis



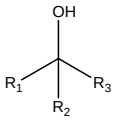
ethers
ROH + RBr (S_N1)
$RO^{\ominus}$ + RBr (S_N2)
alkene + ROH



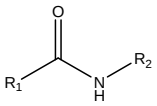
ketones
oxidation of 2^o ROH
nitrile + R-Li/R-MgBr
acid chloride + cuprate
3^o amide + R-Li/R-MgBr
carboxylic acid + 2 eqs. R-Li
alkyne hydrolysis
dithiane (react twice),
Friedel Crafts acylation



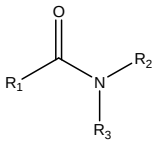
2^o alcohols
ketone + LAH
aldehyde + R-Li/R-MgBr
epoxide + LAH
epoxide + R-Li/R-MgBr
alkene hydrolysis,
S_N2, $S_N1$and more



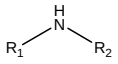
3^o alcohols
ketone + R-Li/R-MgBr
epoxide + LAH
epoxide + R-Li/R-MgBr
ester + R-Li/R-MgBr (2 eqs.)
alkene hydrolysis
S_N2, $S_N1$and more



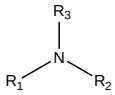
2^o amides
acid chlorides + 1^o amines



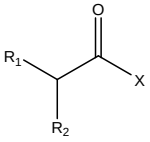
3^o amides
acid Cl + 2^o amines,



2^o amines
use ald / ket + 1^o amine, then
imine reduction with NaH_3BCN,
LAH reduction of 2^o amide

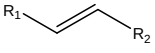


3^o amines
use ald / ket + 2^o amine, then
imine reduction with NaH_3BCN,
LAH reduction of 3^o amide

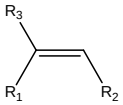


two couplings using
enolate chemistry of
various carbonyl patterns,
enamines or enol ethers too

cis disubstituted alkenes
using Wittig reaction
or reduction of alkyne (Lindlar's)
(alkynes have some limitations),
some E1 or E2 reactions



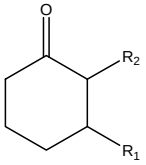
trans disubstituted alkenes
using reduction of alkyne (Na/NH_3)
(alkynes have some limitations),
some E1 or E2 reactions



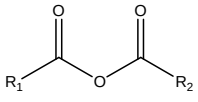
trisubstituted alkene
using Wittig reaction,
some E1 or E2 reactions

cuprate coupled sp^3/sp^3
all carbon linkagess,
reduction or other
functional groups
(aldehyde, ketone, alkene,
alkyne, etc.) (hard to see)

disubstituted alkynes
(R_1 and R_2 must be
primary or methyl
when RX = S_N2),
open epoxides,
or attack carbonyls



cuprate conjugate addition
followed by reaction
with enolate intermediate
(tandom reaction)

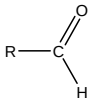


anhydrides from
acid chlorides
+ carboxylates

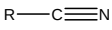
X = single groups (a few examples)

many possibilities
R-H + Br_2/hv;
S_N2, S_N1 at ROH + $HBr/PBr_3/SOBr_2$
a. TsCl/py, b. NaBr (avoids rearrangement)
HBr addition to alkenes
(Markovnikov, anti-Markovnikov)

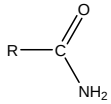
alcohols = many possibilities
S_N2, S_N1 at RX
addition to alkenes
(Markovnikov, anti-Markovnikov)
$LAlH_4$ or $NaBH_4$ reduction
of carbonyls and epoxides,
ozonolysis of alkenes
(WK = $NaBH_4$); etc.



aldehydes
oxidation of 1^o ROH
DIBAH reduction of
ester, nitrile, acid Cl,
anti-Markovnikov addition
to alkyne; dithianes (1x);
oxonolysis of alkenes
(WK = CH_3SCH_3); etc.

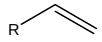


nitriles
RX + NaCN
S_N2 at Me, 1^o, 2^o RX
1^o amide + $SOCl_2$
Sandmeyer rxn
makes aromatic nitriles

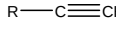


1^o amides
acid (HCl/H_2O) or
base hydrolysis
of nitriles;
acid Cl + NH_3

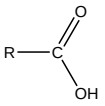
1^o amines
Gabriel amine syn (1^o)
use ald / ket + NH_3, then
imine reduction with NaH_3BCN,
LAH reduction of 1^o amide



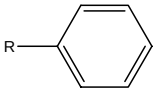
E2, E1 with RX
$ROH/H_2SO_4/\Delta$
reduction of alkynes
Wittig reactions



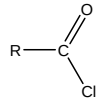
alkynes
RX + NaCCR (make)
(S_N2 at Me, 1^o RX)
zipper reaction
double elimination (E2)



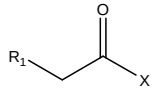
carboxylic acids
RMgBr or RLi + CO_2
Jones oxidation of 1^o ROH
acid or base hydrolysis of esters,
acid or base hydrolysis of nitriles
ozonolysis of alkenes
(WK = H_2O_2); etc.



aromatic derivatives
Friedel Crafts alkylation or
acylation; cuprate coupling;
Ar-MgBr or Ar-Li reactions,
and more



carboxylic acid +
$SOCl_2$ or PCl_3 or
oxalyl chloride



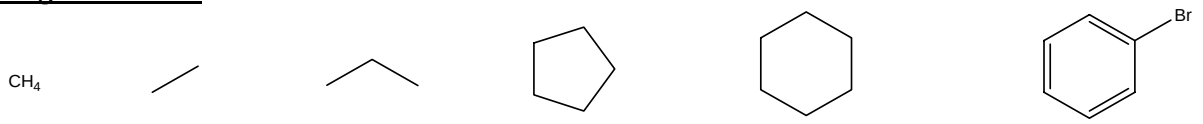
single coupling using
enolate chemistry of
various carbonyl patterns,
enamines or enol ethers too

thiols
RX + $HS^{\ominus}$

etc.

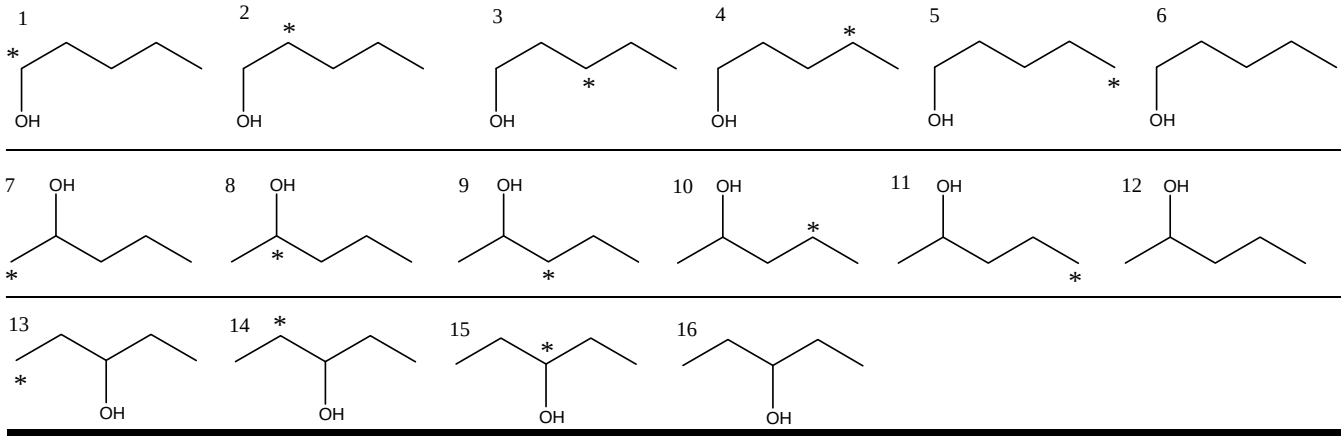
Use clues in the target molecule (TM) to determine what the last step could have been. Once you work back one step, use clues in that molecule (TM-1) to determine how you could work back one additional step (TM-2). Repeat this process until you get to the necessary starting conditions (TM-n), i.e. allowable ^{14}C starting units (*CH_4, *CO_2, Na*CN where "*" indicates a radioactive ^{14}C isotope) and other allowed starting materials. Until aromatic chemistry is covered bromobenzene is also available. You may use any reagents learned in our course. Many of the simpler starting structures below were prepared in the above reactions (1C, 2C and 3C examples).

Starting Structures:

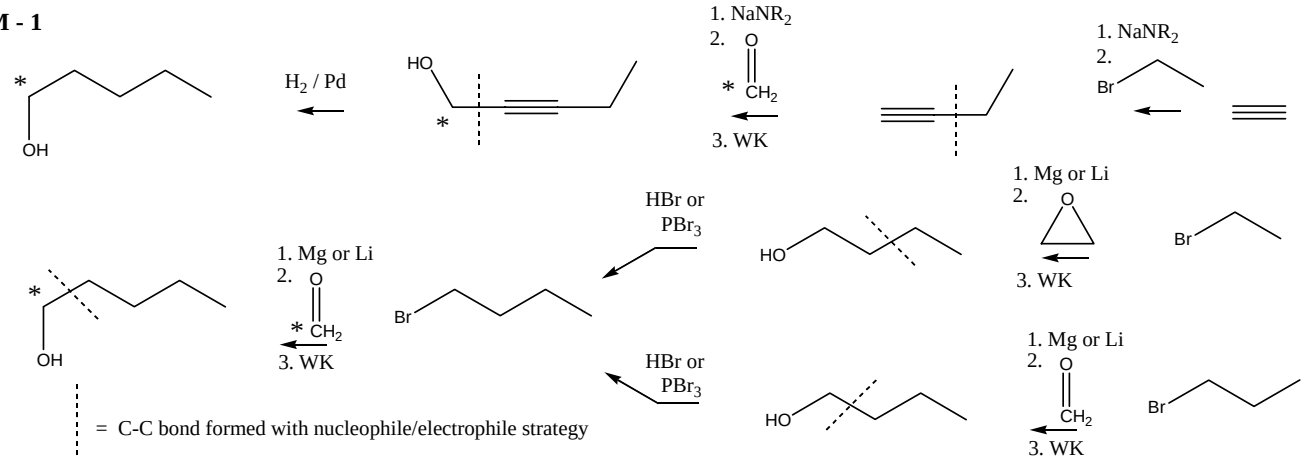


Examples – Target Molecules (TM - #)

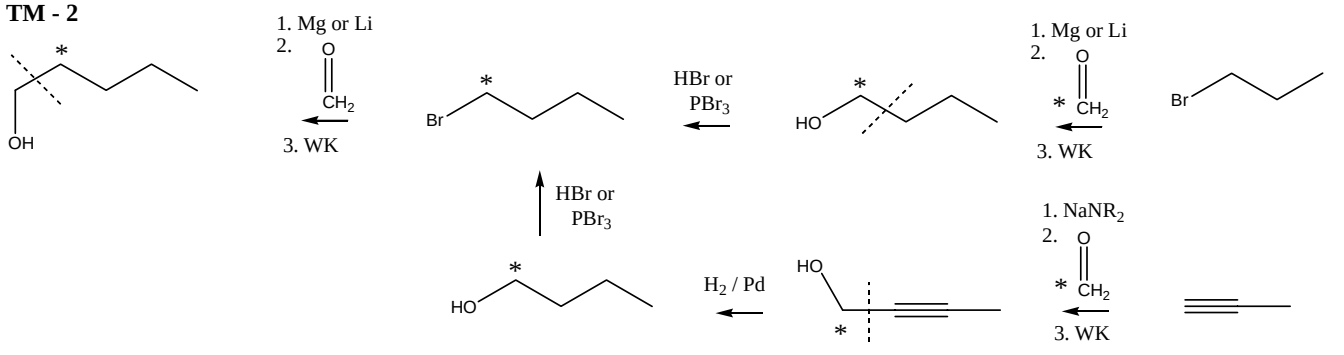
Straight chain C5 alcohols



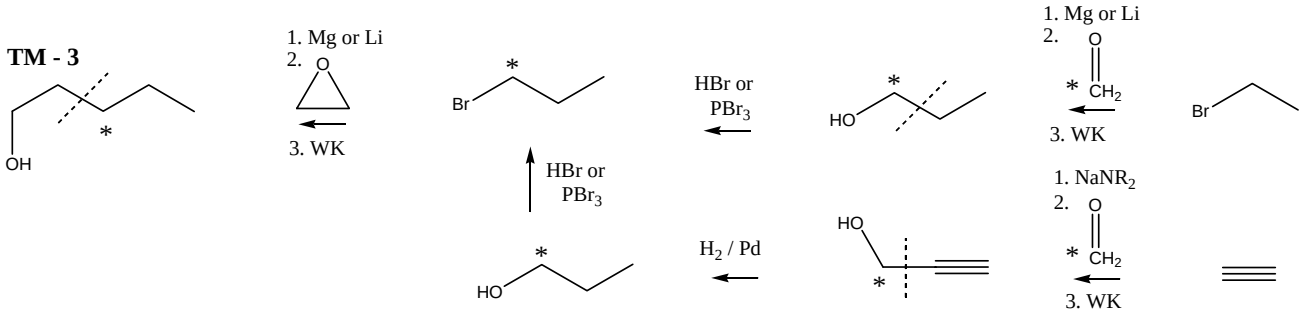
TM - 1



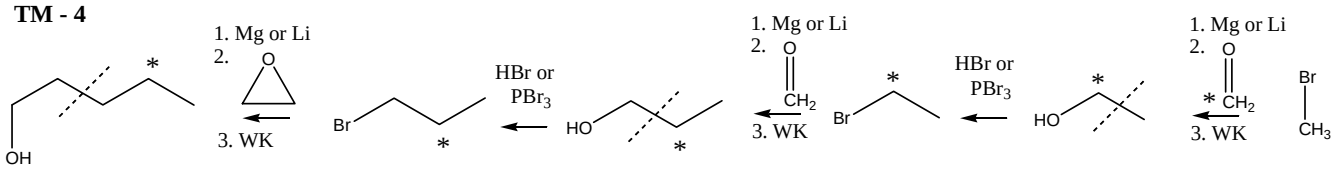
TM - 2



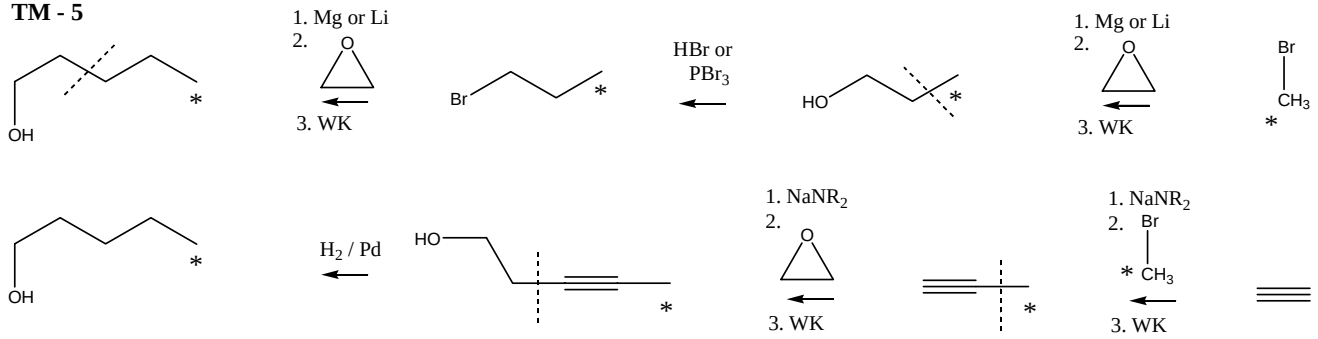
TM - 3



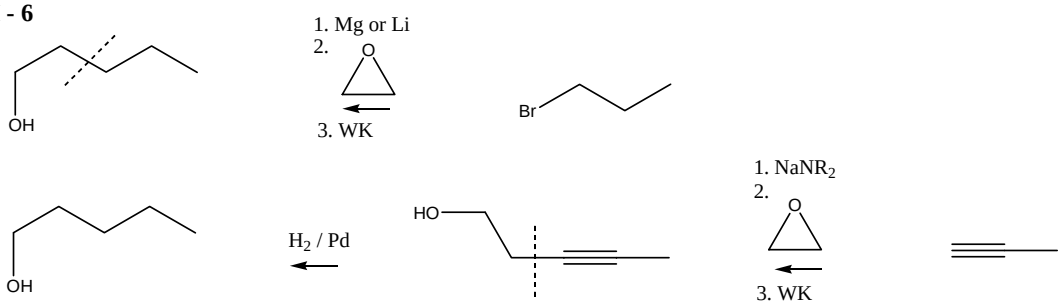
TM - 4



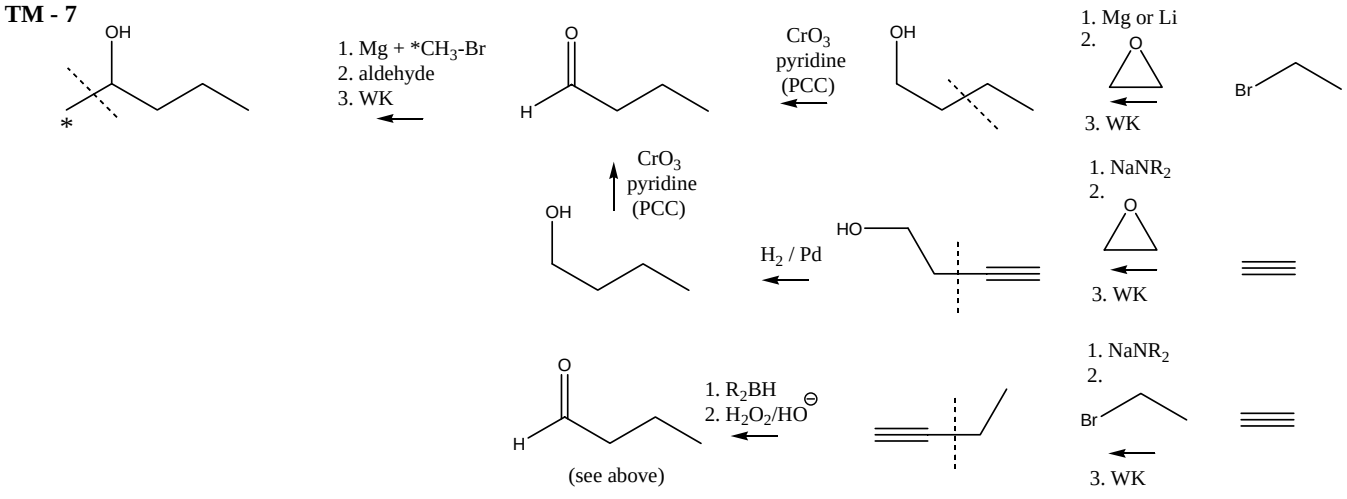
TM - 5



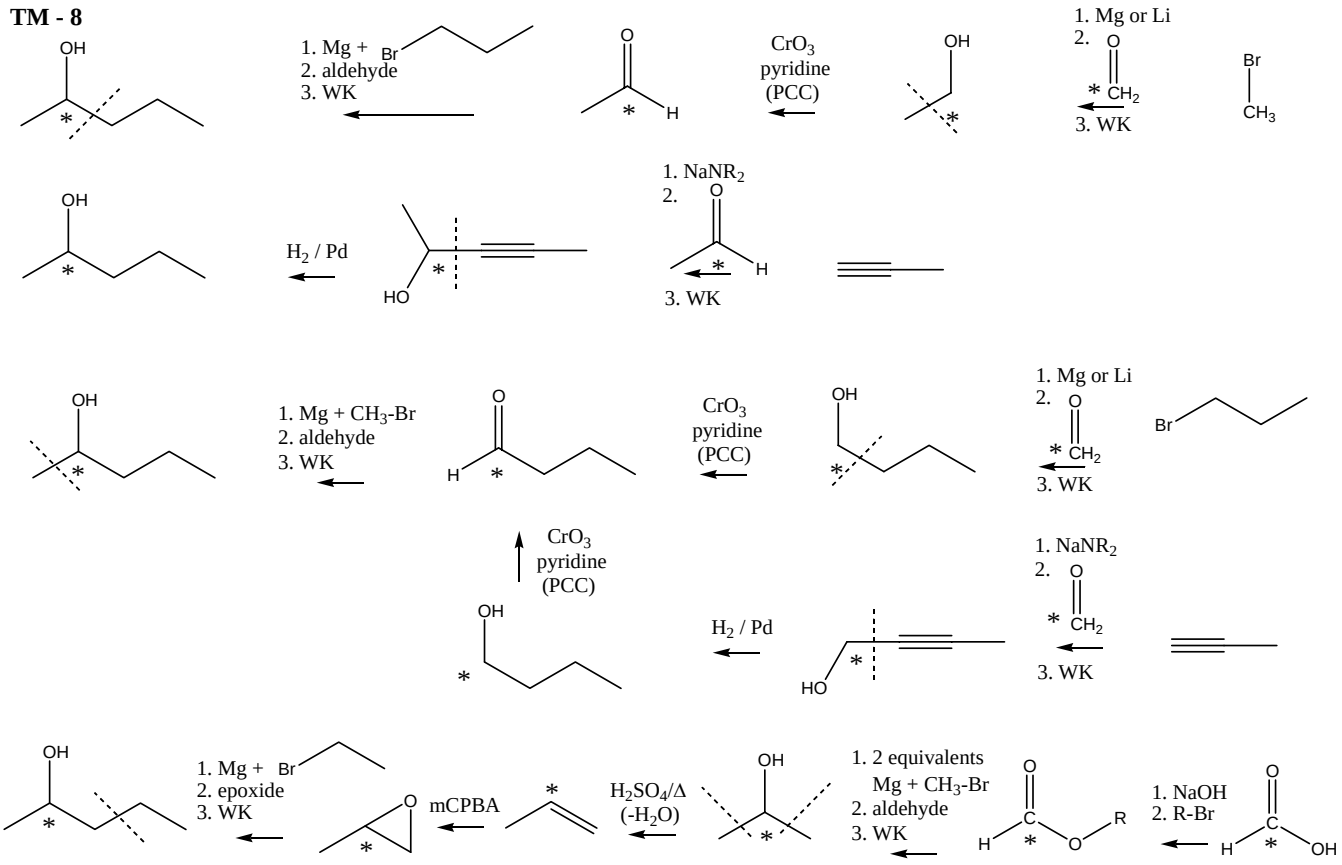
TM - 6



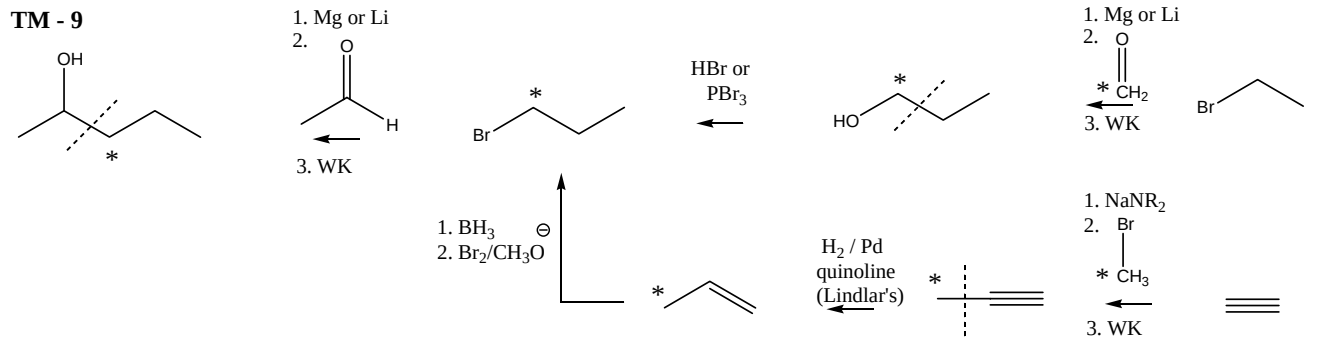
TM - 7



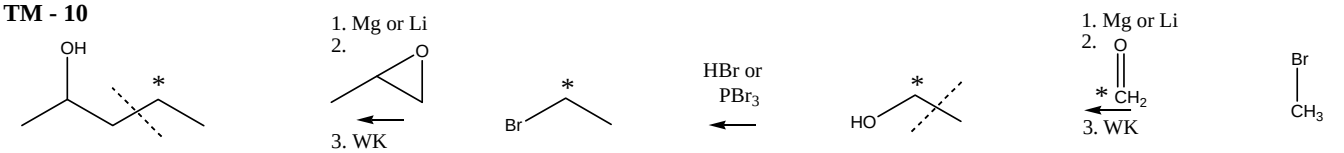
TM - 8



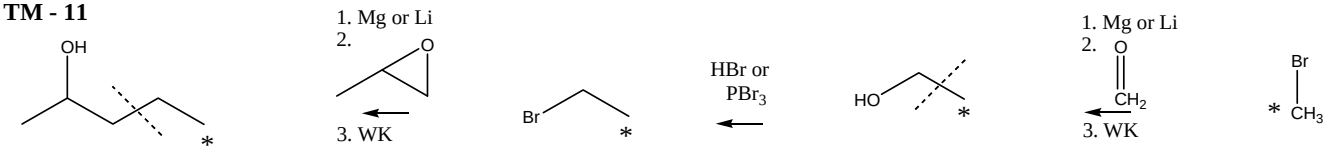
TM - 9



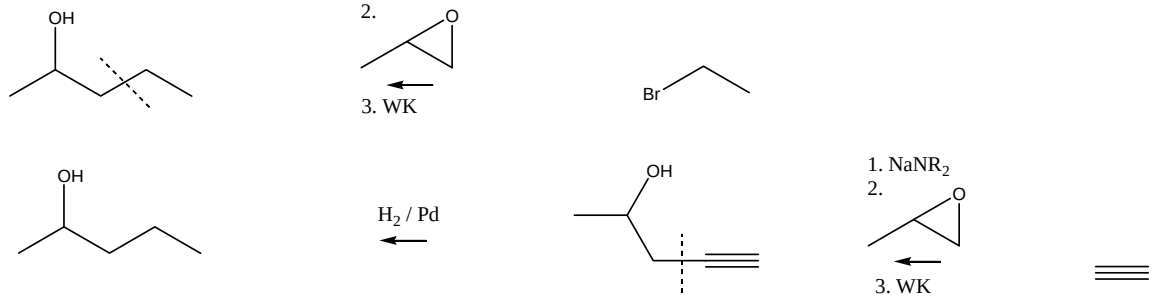
TM - 10



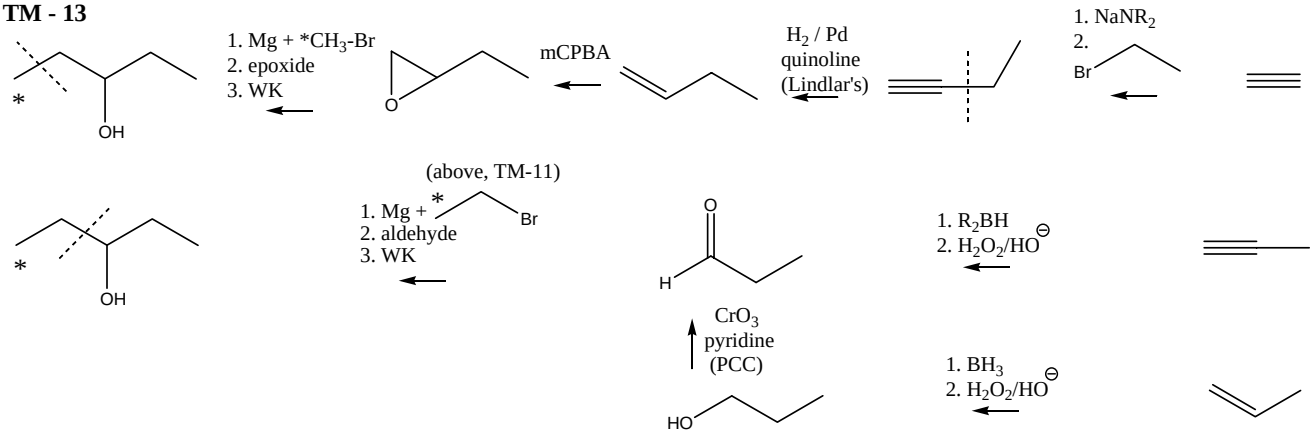
TM - 11



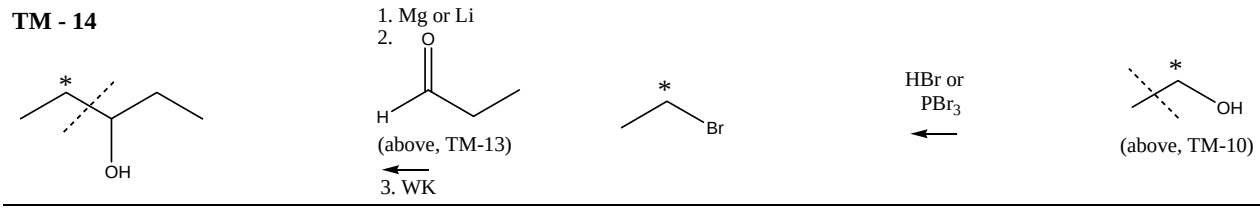
TM - 12



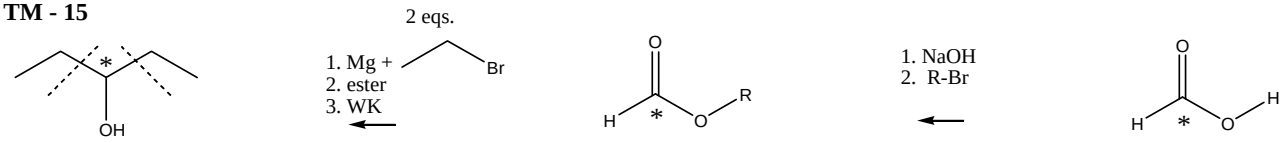
TM - 13



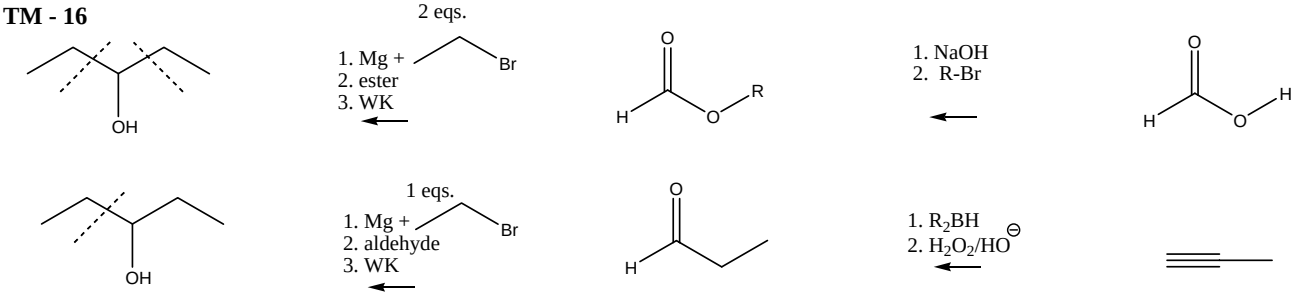
TM - 14



TM - 15

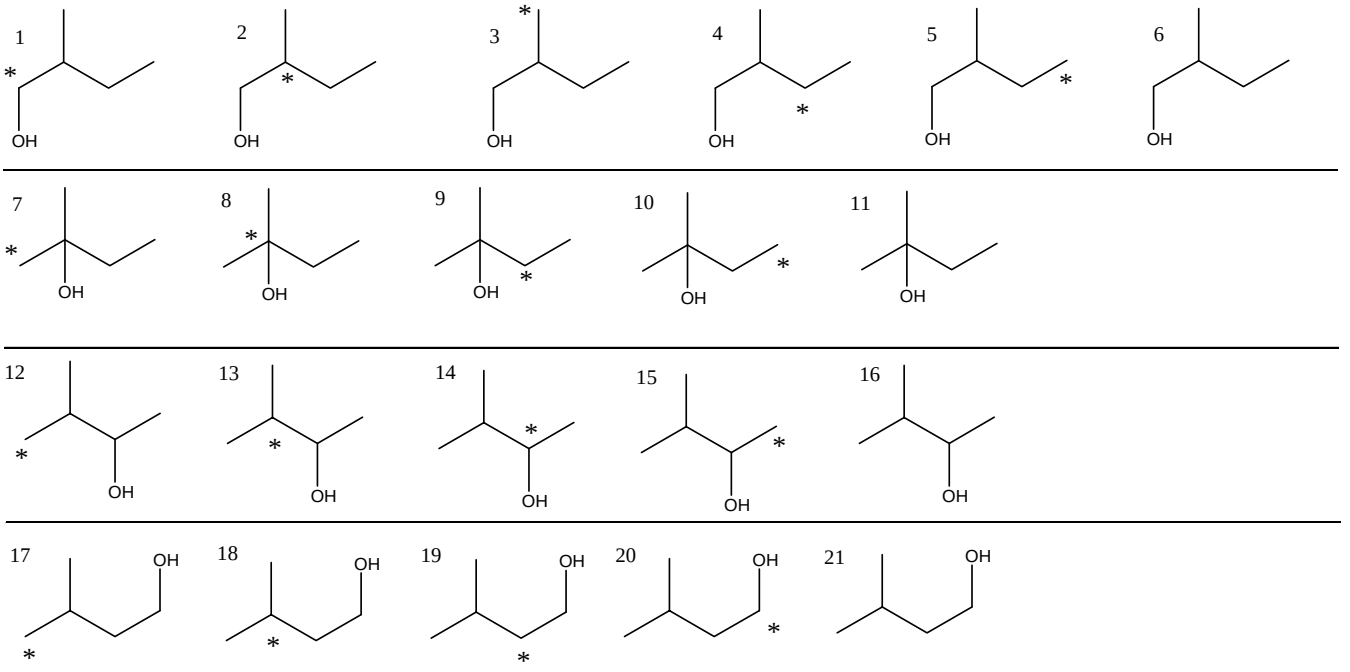


TM - 16

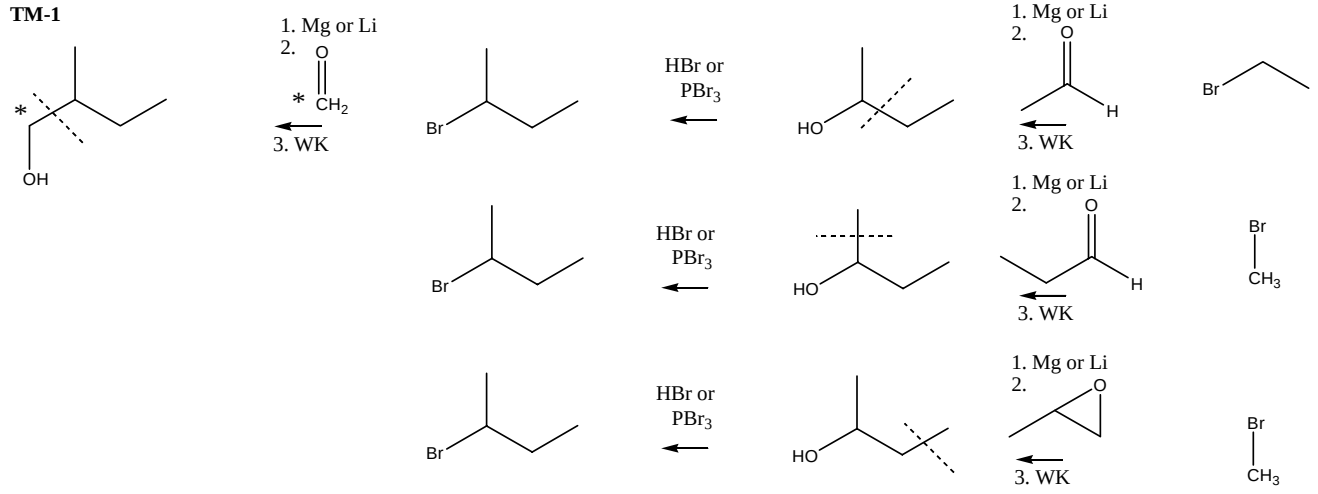


Examples – Target Molecules (TM - #)

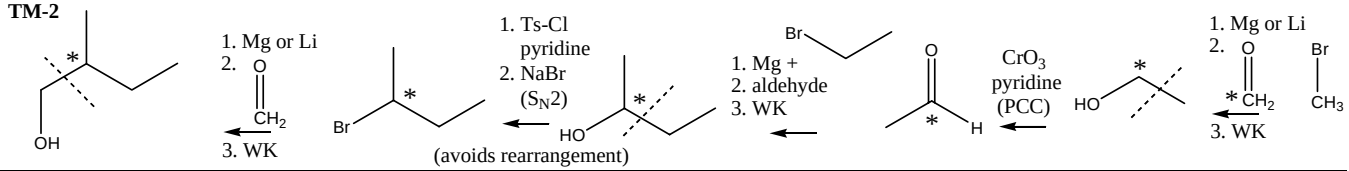
4C chain with methyl branch alcohols



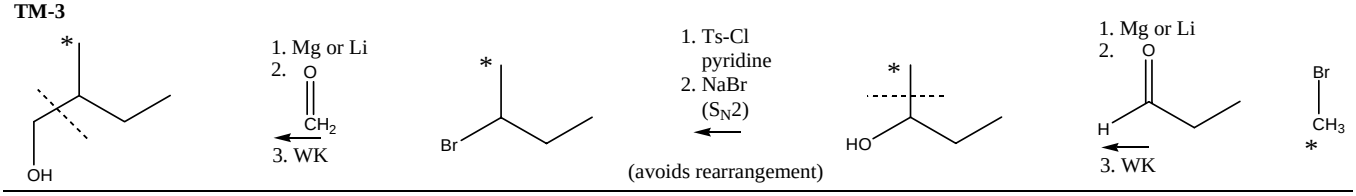
TM-1



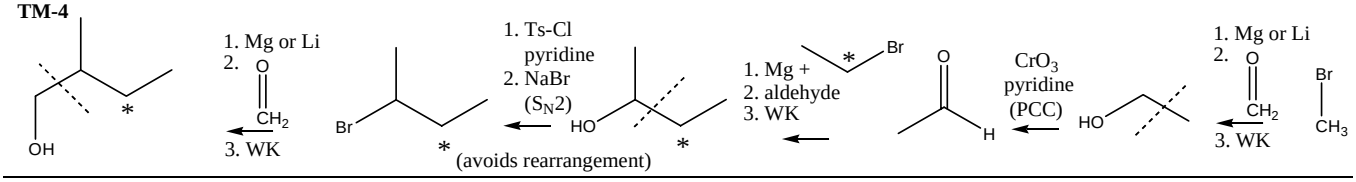
TM-2



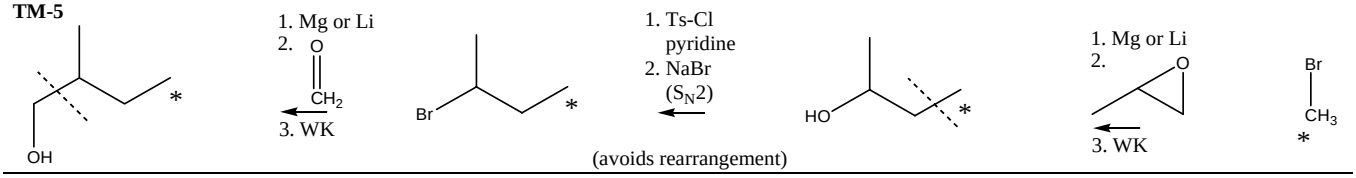
TM-3



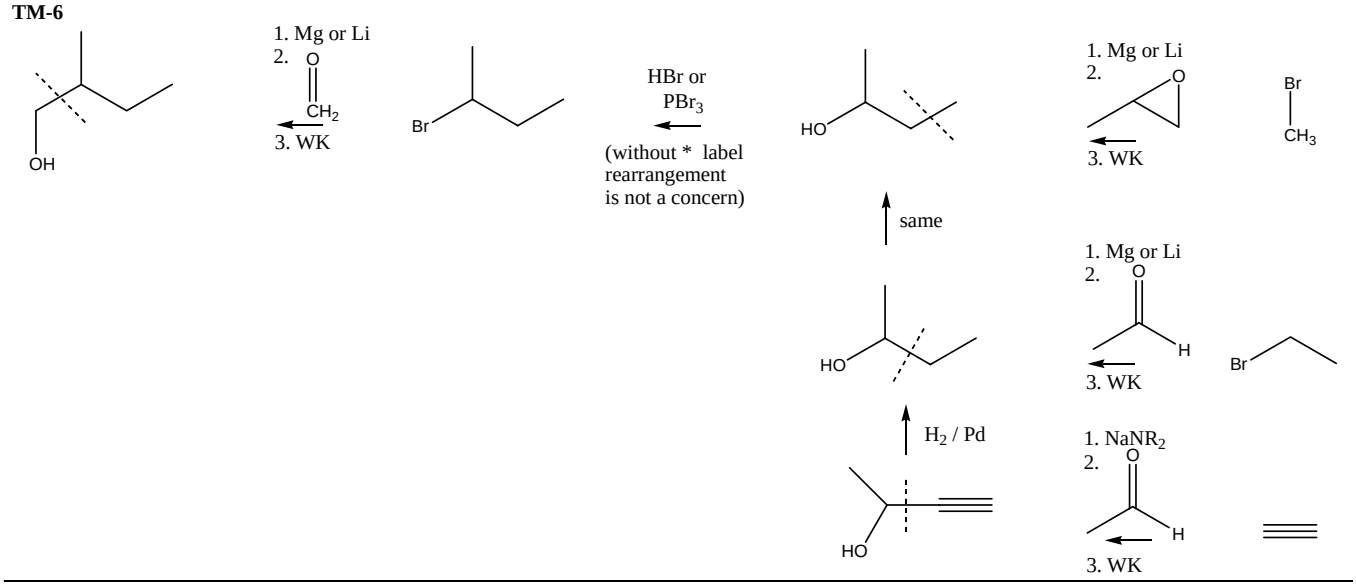
TM-4



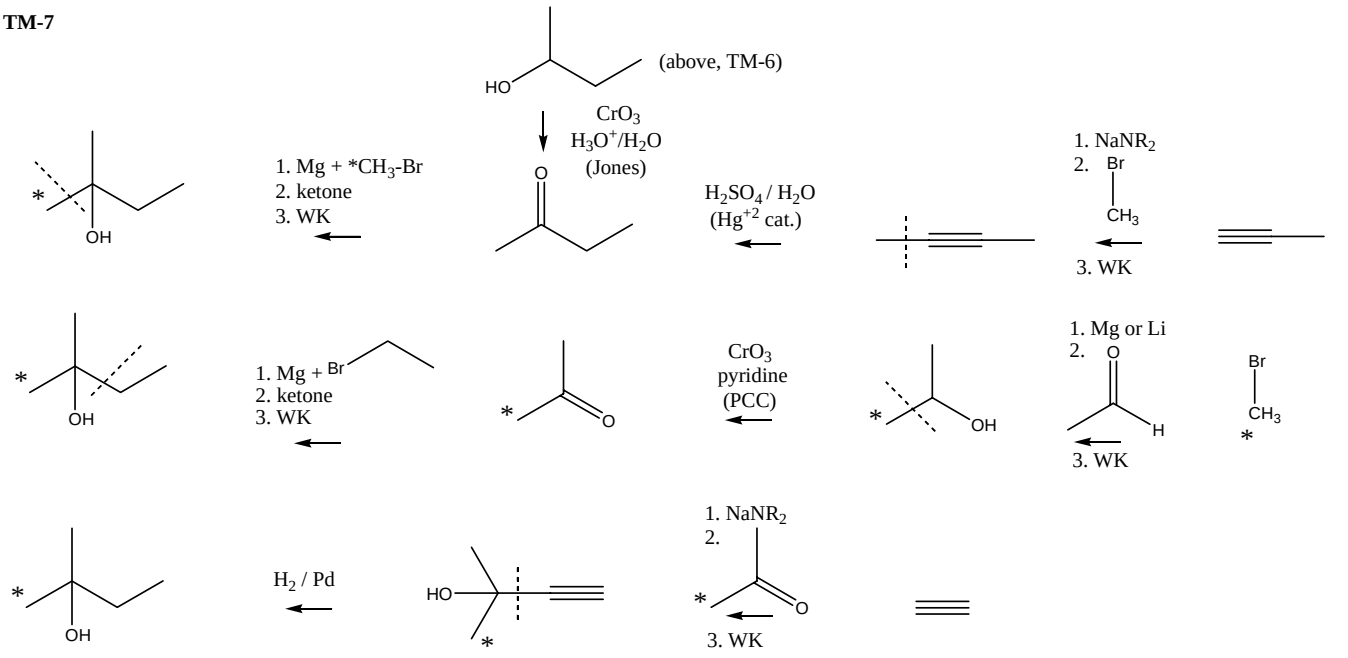
TM-5



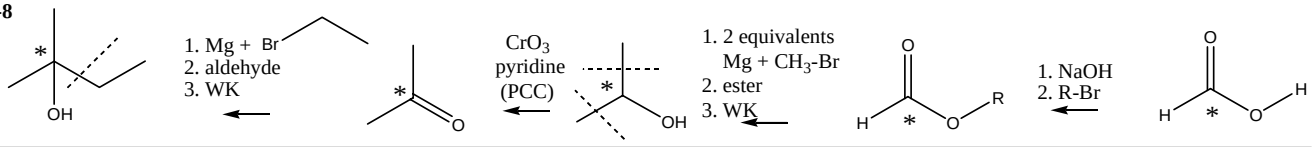
TM-6



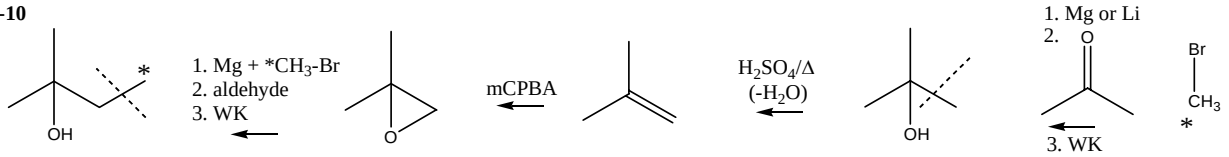
TM-7



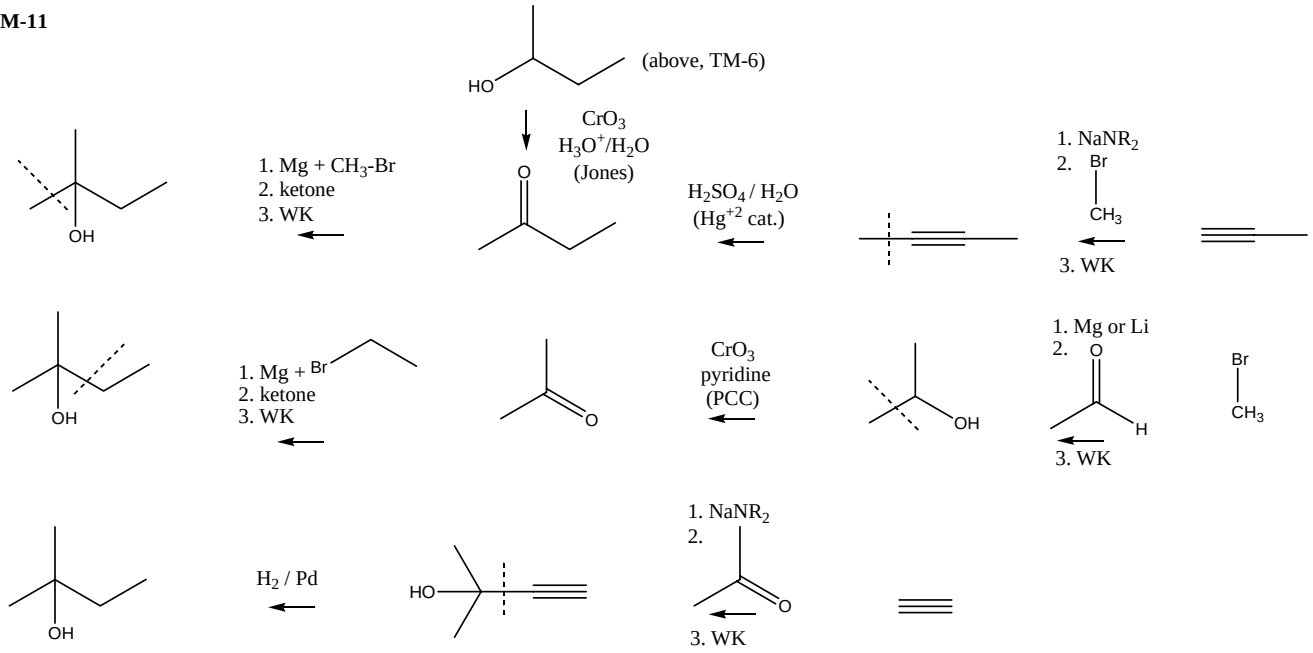
TM-8



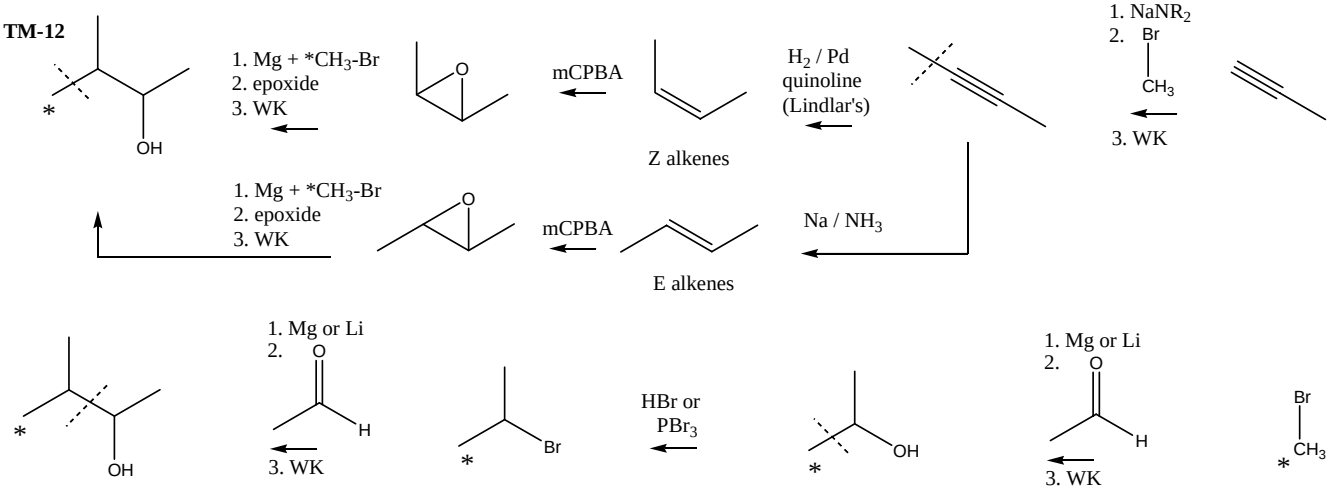
TM-10



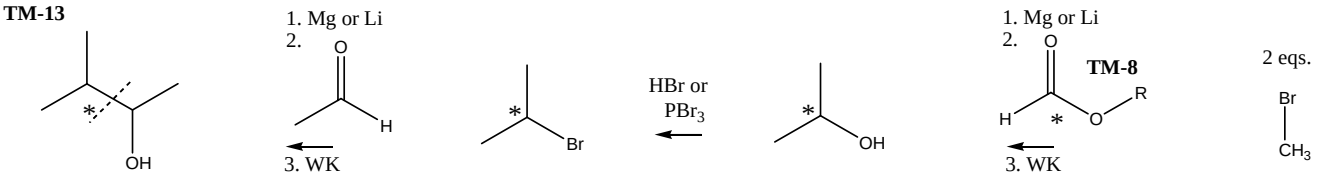
TM-11



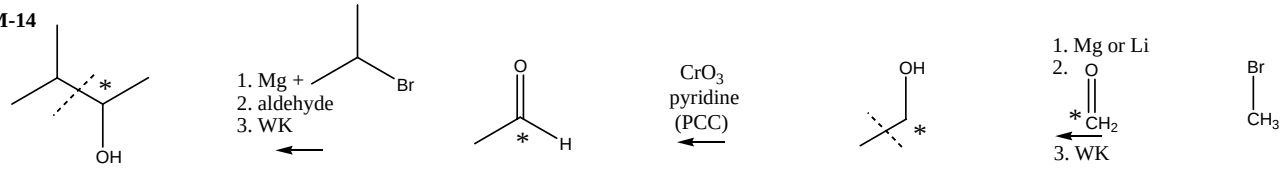
TM-12



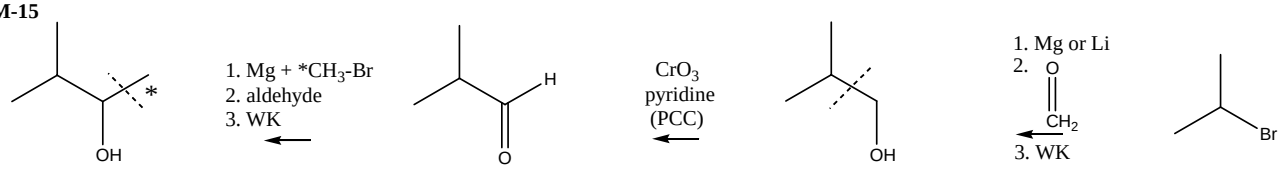
TM-13



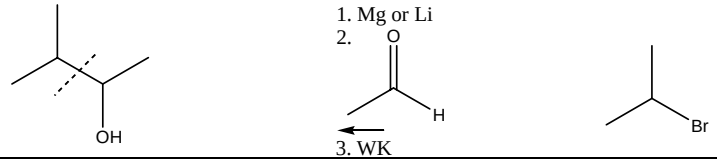
TM-14



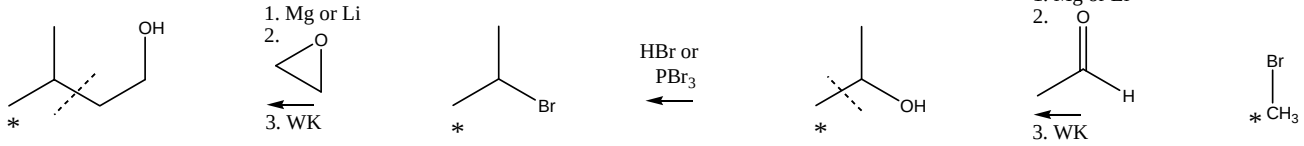
TM-15



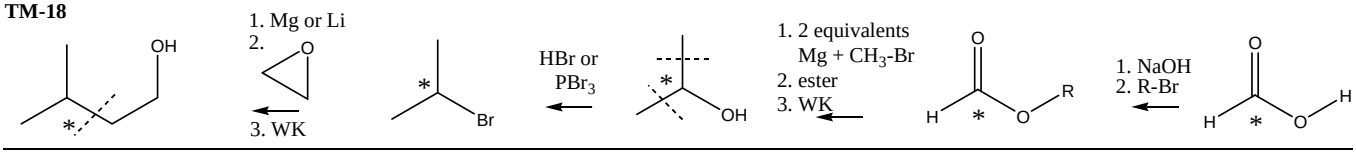
TM-16



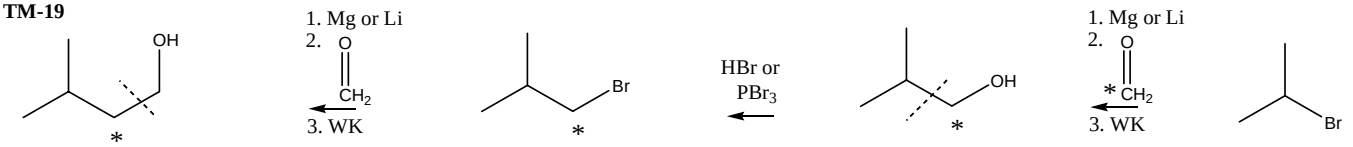
TM-17



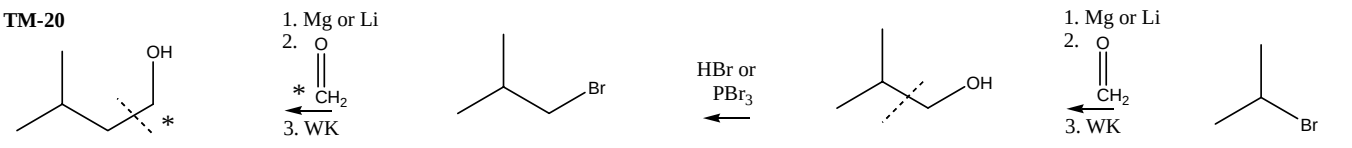
TM-18



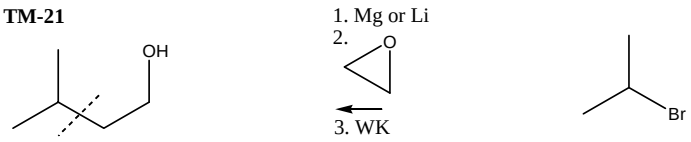
TM-19



TM-20

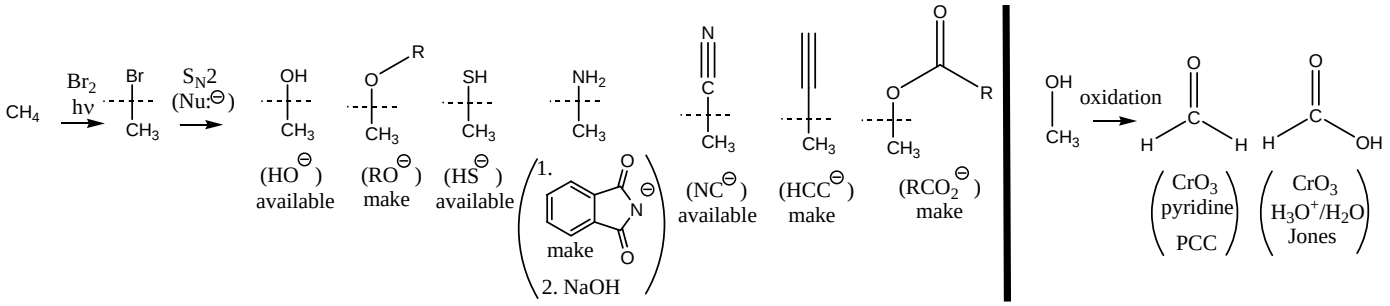


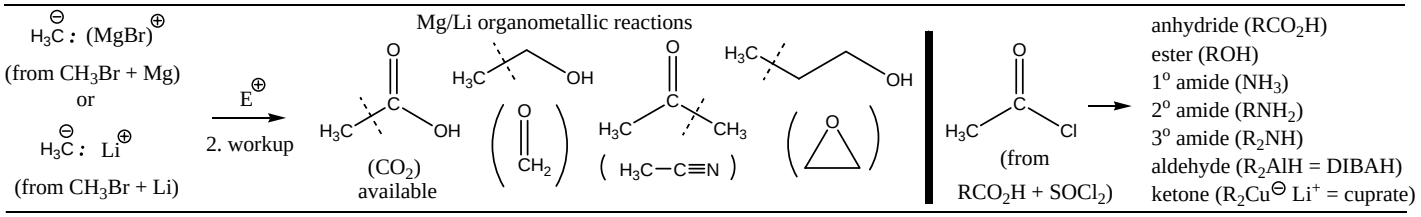
TM-21

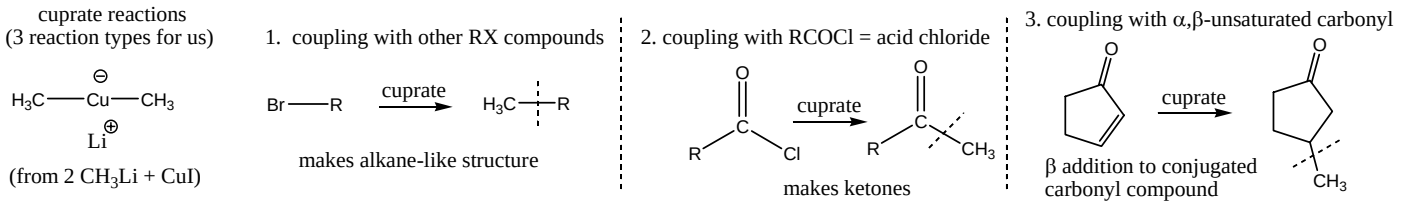


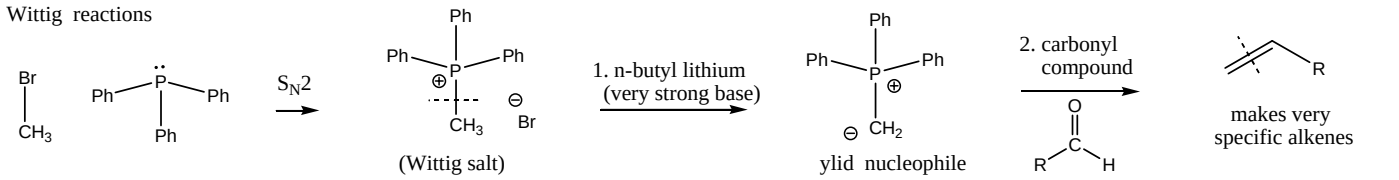
Some important 1C, 2C and 3C building blocks that are used in the C-14 syntheses that follow.

1 Carbon – some examples of reagents that allow synthetic transformations among these structures.

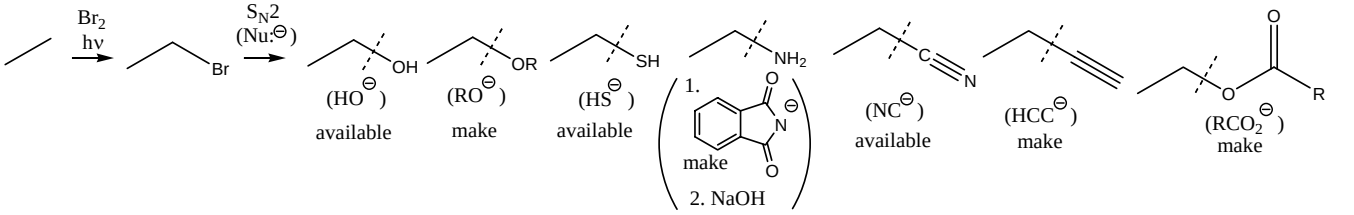


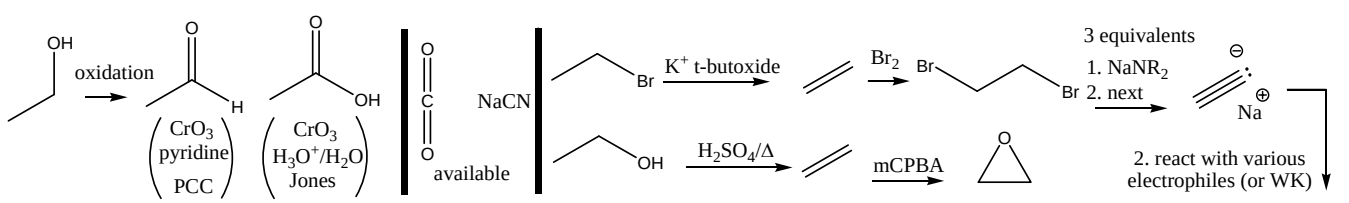


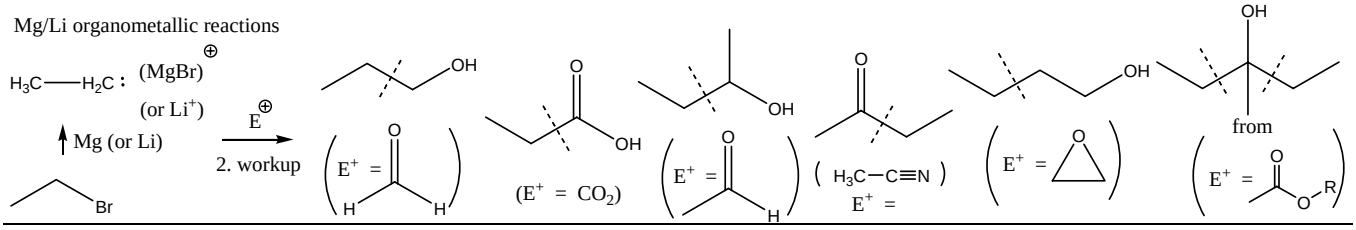


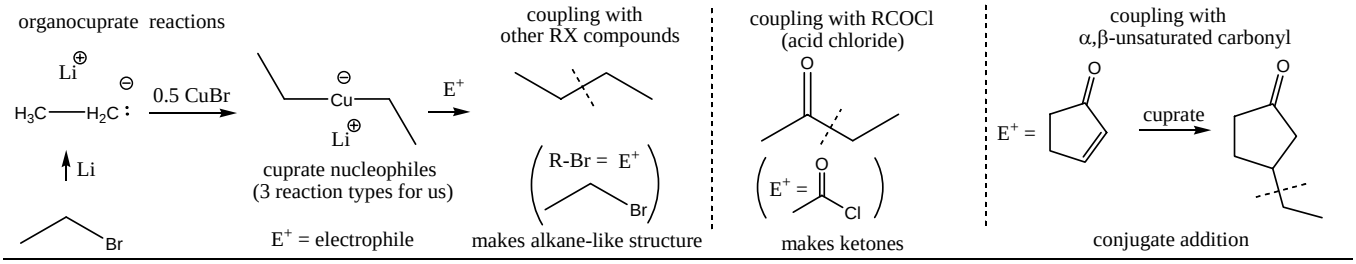


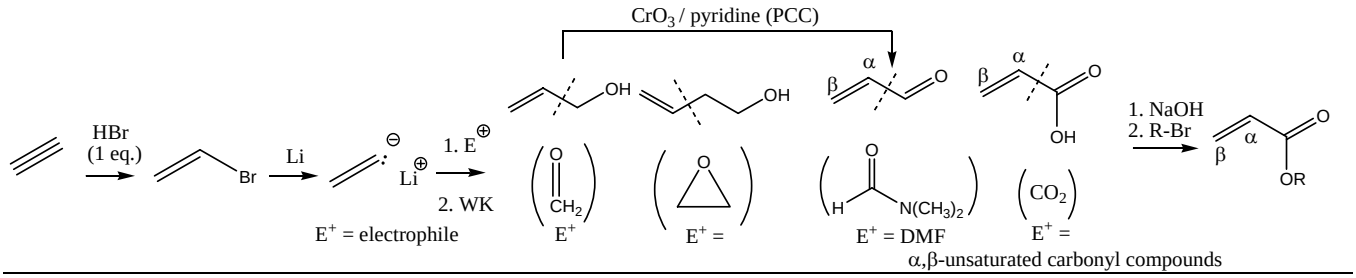
2 Carbons – some examples of reagents that allow synthetic transformations among these structures.

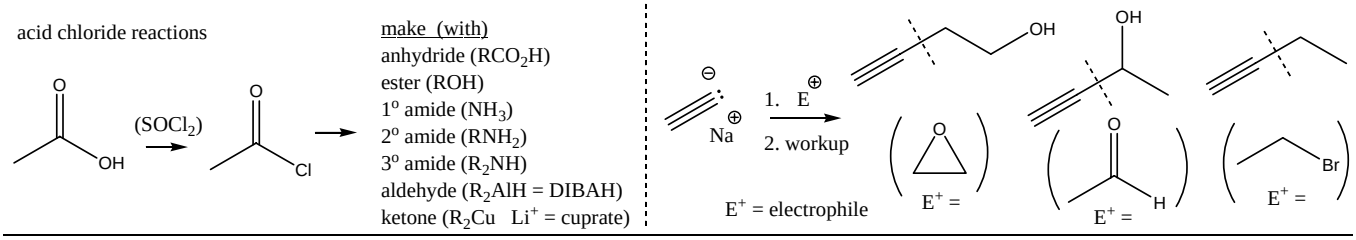


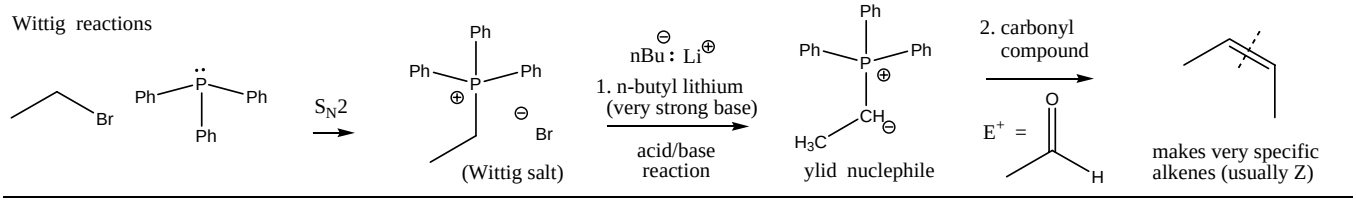


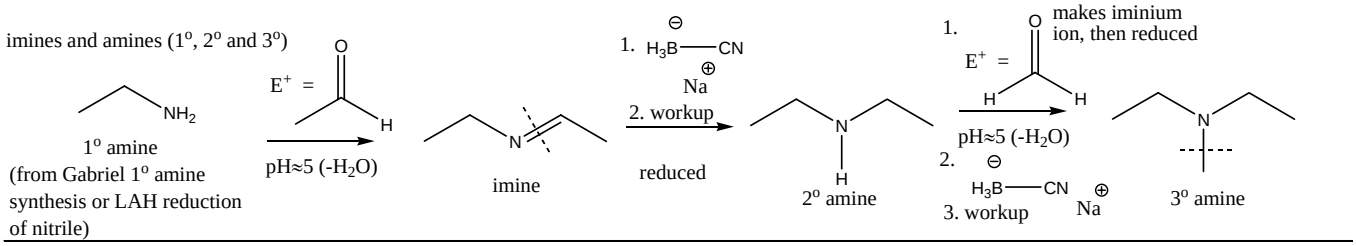


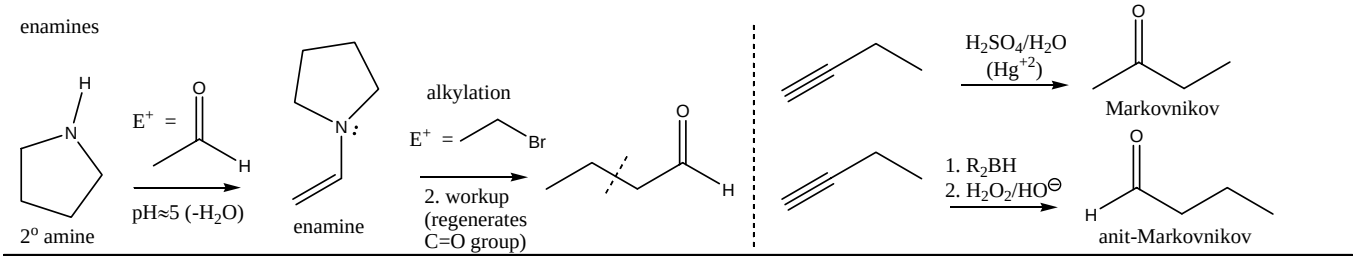

organocuprate reactions
0.5 CuBr
cuprate nucleophiles
(3 reaction types for us)
E+ = electrophile
coupling with
other RX compounds
R-Br = E+
makes alkane-like structure
coupling with RCOCl
(acid chloride)
makes ketones
coupling with
α,β-unsaturated carbonyl
cuprate
conjugate addition

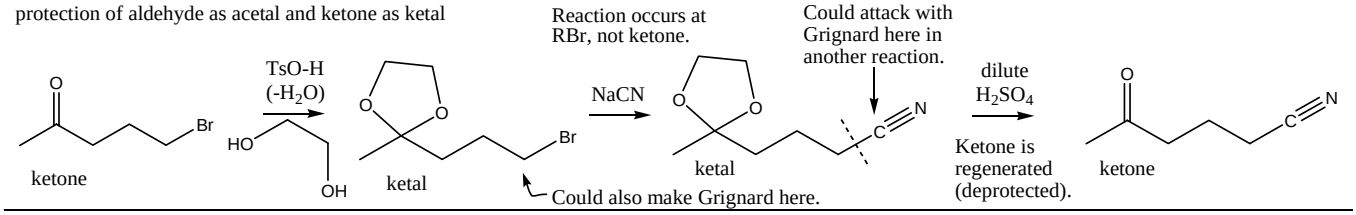

CrO3 / pyridine (PCC)
HBr
(1 eq.)
Li
1. E+
2. WK
E+ = electrophile
E+ = DMF
1. NaOH
2. R-Br
α,β-unsaturated carbonyl compounds

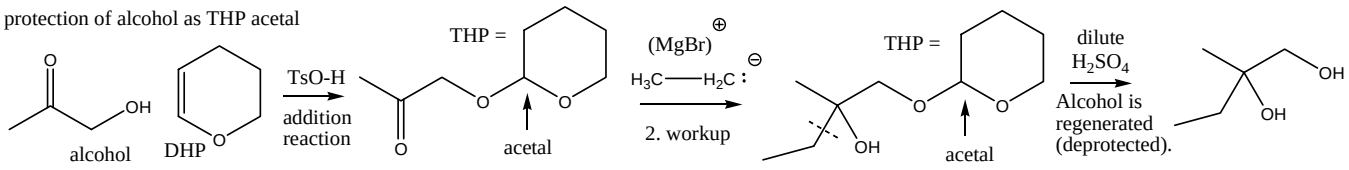

acid chloride reactions
(SOCl2)
make (with)
anhydride (RCO2H)
ester (ROH)
1° amide (NH3)
2° amide (RNH2)
3° amide (R2NH)
aldehyde (R2AlH = DIBAH)
ketone (R2Cu Li+ = cuprate)
1. E+
2. workup
E+ = electrophile


Wittig reactions
SN2
(Wittig salt)
nBu: Li+
1. n-butyl lithium
(very strong base)
acid/base
reaction
ylid nuclephile
2. carbonyl
compound
makes very specific
alkenes (usually Z)

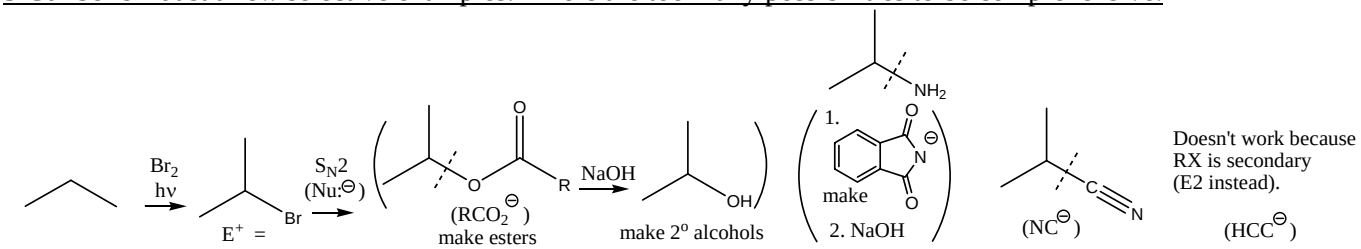

imines and amines (1°, 2° and 3°)
1° amine
(from Gabriel 1° amine
synthesis or LAH reduction
of nitrile)
pH≈5 (-H2O)
imine
reduced
2° amine
makes iminium
ion, then reduced
3. workup
3° amine

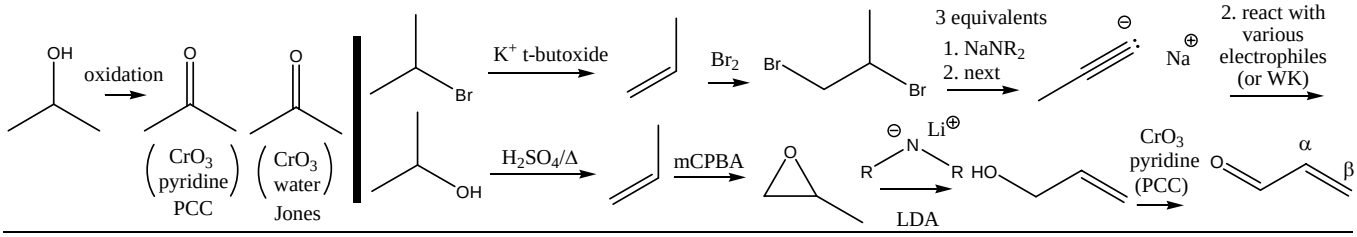

enamines
2° amine
pH≈5 (-H2O)
enamine
alkylation
2. workup
(regenerates
C=O group)
H2SO4/H2O
(Hg+2)
Markovnikov
1. R2BH
2. H2O2/HO-
anit-Markovnikov

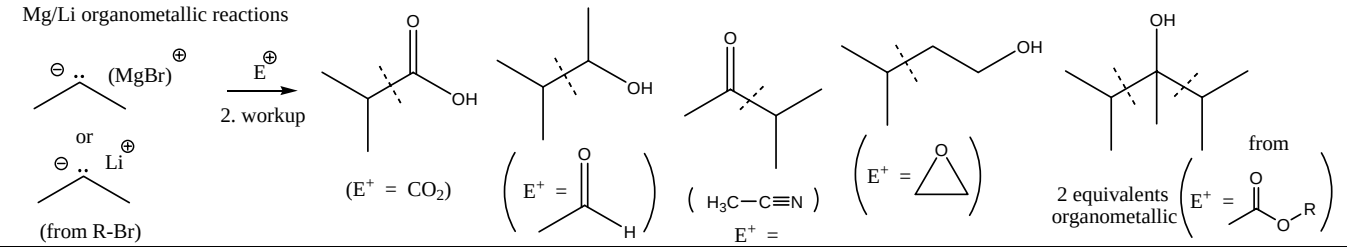


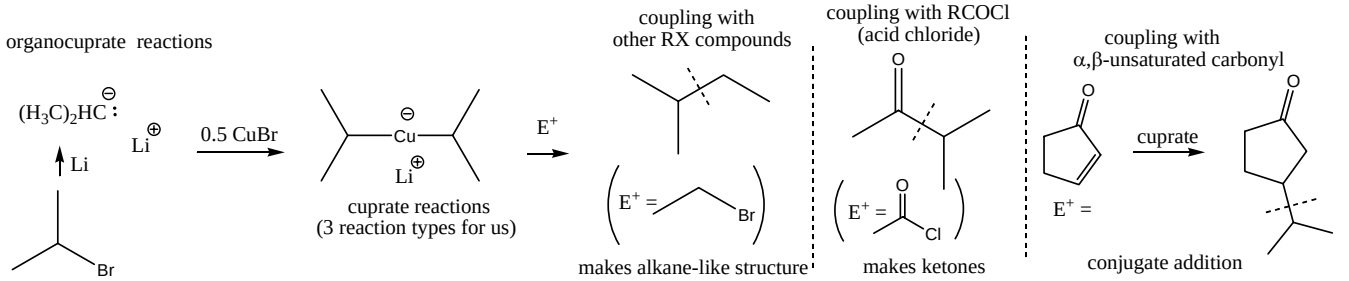


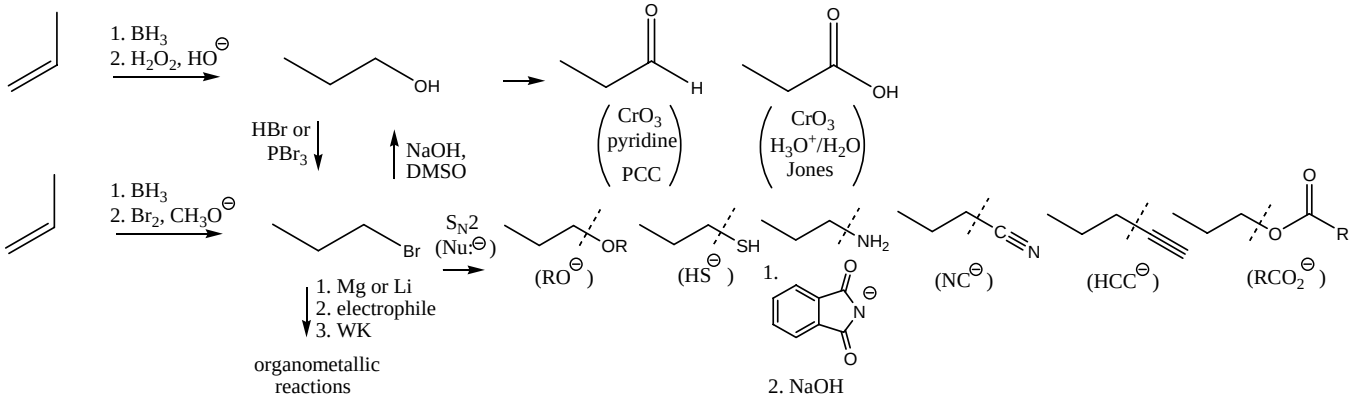
3 Carbons – Just a few selective examples. There are too many possibilities to be comprehensive.

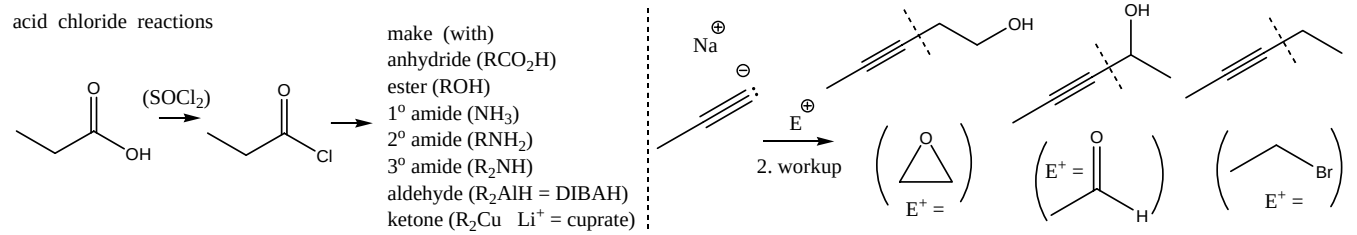


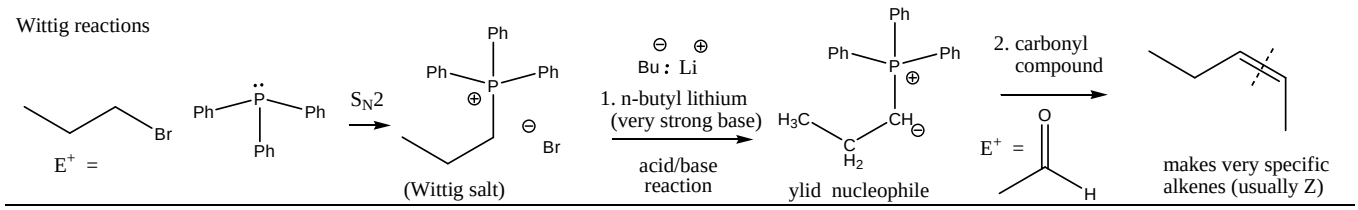


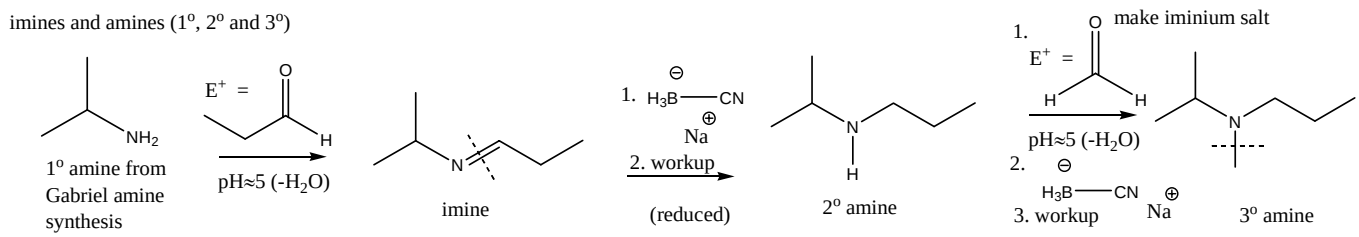


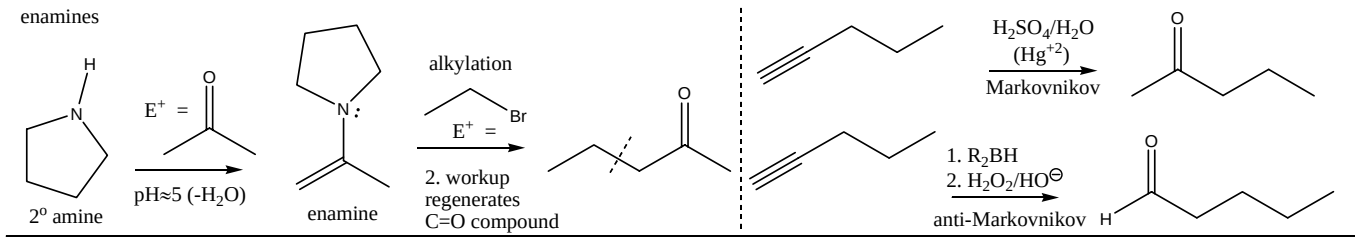



1. BH3
2. H2O2, HO⊖
HBr or PBr3
NaOH, DMSO
1. BH3
2. Br2, CH3O⊖
SN2 (Nu:⊖)
1. Mg or Li
2. electrophile
3. WK
organometallic reactions
CrO3 pyridine PCC
CrO3 H3O+/H2O Jones
(RO⊖)
(HS⊖)
1.
2. NaOH
(NC⊖)
(HCC⊖)
(RCO2⊖)


acid chloride reactions
(SOCl2)
make (with)
anhydride (RCO2H)
ester (ROH)
1° amide (NH3)
2° amide (RNH2)
3° amide (R2NH)
aldehyde (R2AlH = DIBAH)
ketone (R2Cu Li+ = cuprate)
2. workup
E+ =


Wittig reactions
SN2
(Wittig salt)
1. n-butyl lithium (very strong base)
acid/base reaction
ylid nucleophile
2. carbonyl compound
makes very specific alkenes (usually Z)
E+ =


imines and amines (1°, 2° and 3°)
1° amine from Gabriel amine synthesis
pH≈5 (-H2O)
imine
1.
2. workup
(reduced)
2° amine
make iminium salt
3. workup
3° amine

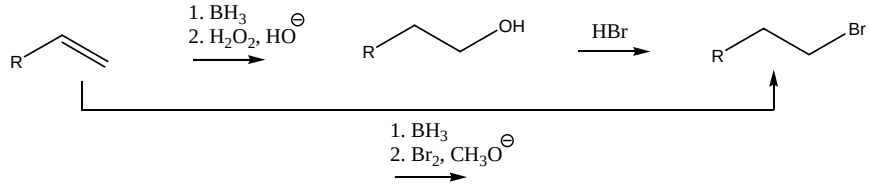

enamines
2° amine
pH≈5 (-H2O)
enamine
alkylation
2. workup regenerates C=O compound
H2SO4/H2O (Hg+2)
Markovnikov
1. R2BH
2. H2O2/HO⊖
anti-Markovnikov

Key strategies in a ^{14}C synthesis problem?

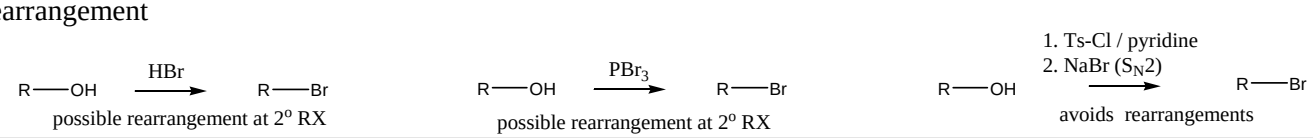
1. How do you prepare RX compounds? (Use bromides as a consistent, reliable target.)

   a. from alkenes (Markovnikov reaction)

   b. from alkenes (anti-Markovnikov reaction)



   c. from alcohols (HBr or PBr_3), S_N2 at 1° ROH and S_N1 at 2° ,3° ROH, use 1. make tosylate, 2. NaBr to avoid rearrangement

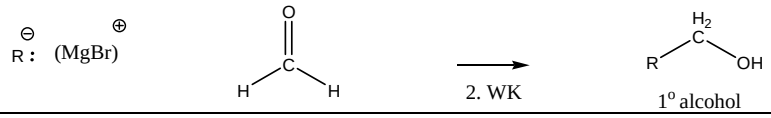


2. Generation of an organometallic carbanion nucleophile from an RX compound

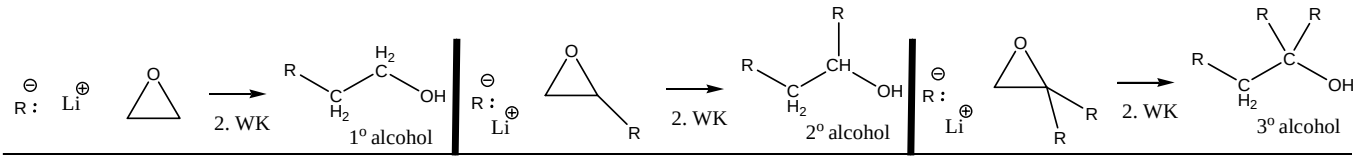
   a. organomagnesium reagents (Grignard reactions) and organolithium reagents (mostly interchangeable in our course).

3. Organometallic nucleophiles + organic electrophiles (e- pair acceptors), WK = work up = acidic neutralization

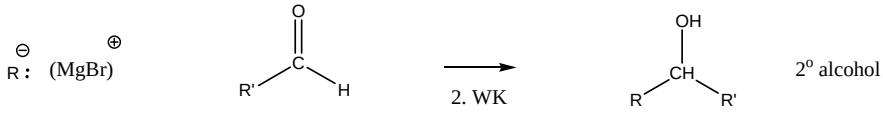
   a. formaldehyde (methanal) = 1C extension of $R:^{-}$ with 1° alcohol functionality at the end



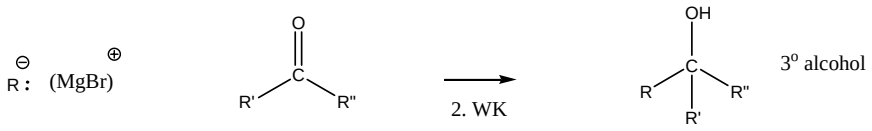
   b. ethylene oxide (epoxides) = 2C extension of $R:^{-}$ with alcohol functionality



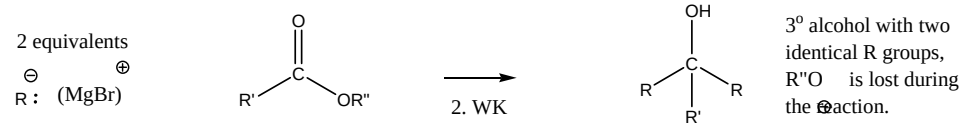
   c. general aldehydes = extension of $R:^{-}$ with 2° alcohol functionality



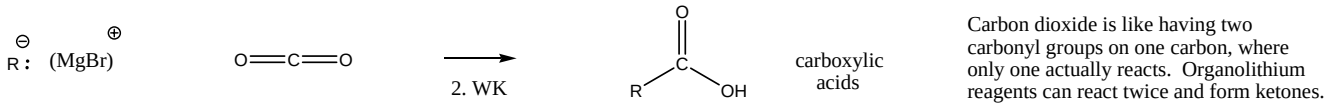
d. general ketone = extension of R:$^{--}$ with tertiary alcohol functionality



e. general ester = extension of R:$^{--}$ with tertiary alcohol functionality (at least two identical R' groups)

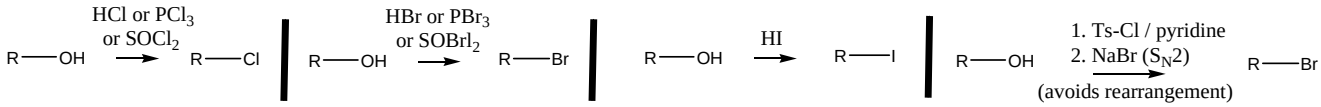


f. carbon dioxide = extension of R: $^{--}$ with carboxylic acid functionality (can be converted into ester with RX)



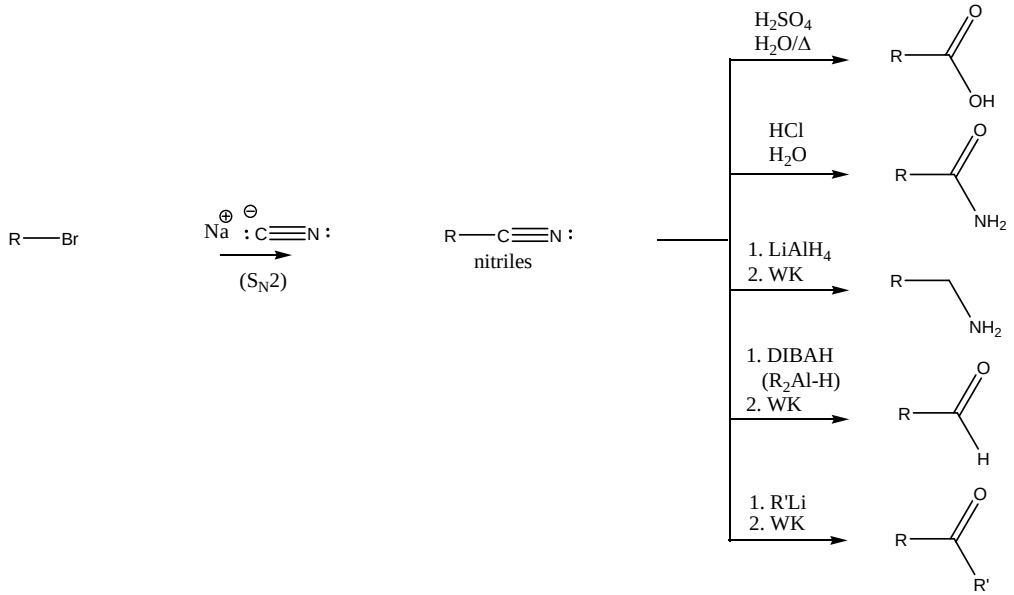
4. Remember additional reactions of alcohols, RX compounds, alkenes, alkynes, carbonyls (aldehydes, ketones, esters, acids and others will accumulate).

a. alcohols can be made into RX compounds (above, chlorides, bromides, iodides, tosylates). Reactions occur by S_N2 at methyl and primary and S_N1 at secondary and tertiary (with possibility of rearrangement) in our course.

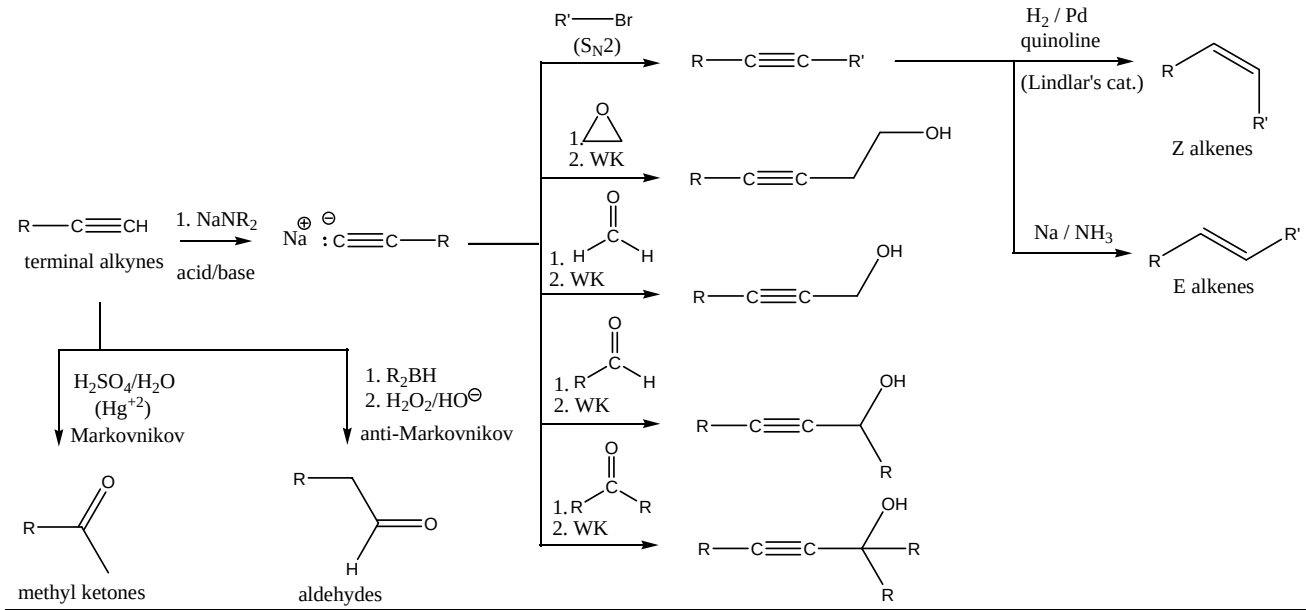


b. RX compounds can react with nucleophiles in S_N2 (methyl, 1° and 2°) and S_N1 (2° and 3°) reactions

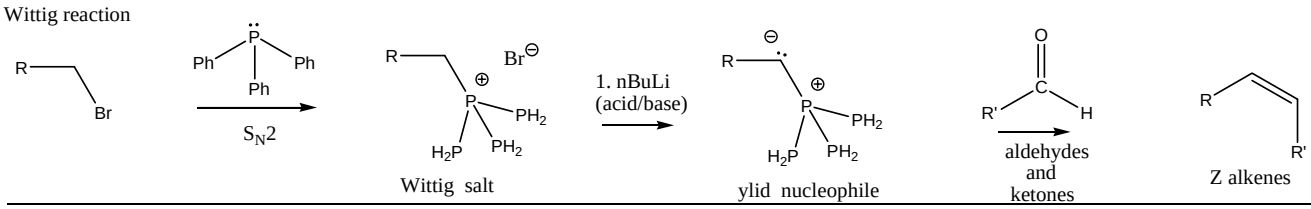
i. cyanide (nitriles at methyl, 1° and 2° RX)



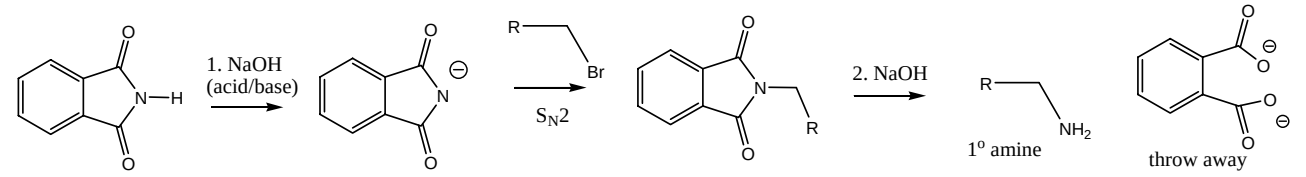
ii. terminal acetylides (react at methyl and 1° RX, epoxides, ketones and aldehydes), and can be converted into aldehydes, ketones, alkanes, and E/Z-alkenes.



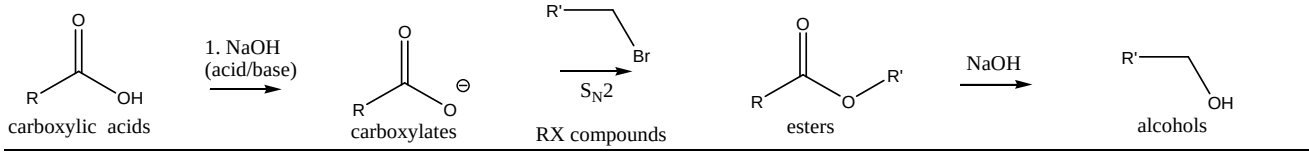
iii. triphenylphosphine (makes phosphonium salts, used in Wittig reactions with aldehydes/ketones to make alkenes)



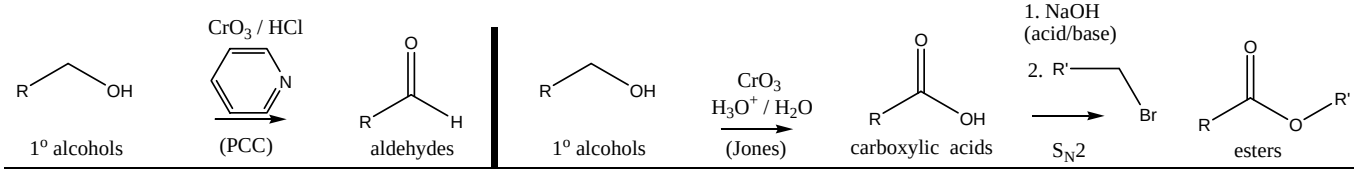
iv. phthalimide anion (make 1° amines after hydrolysis with aqueous hydroxide, or hydrazine, H_2NNH_2)



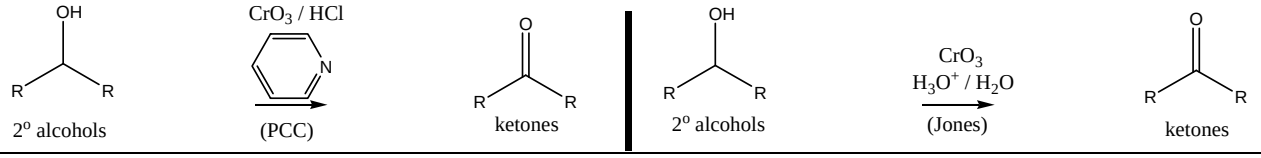
v. esters (acetates), then hydrolyze to form alcohols (most useful at 2° RX), additional chemistry is possible.



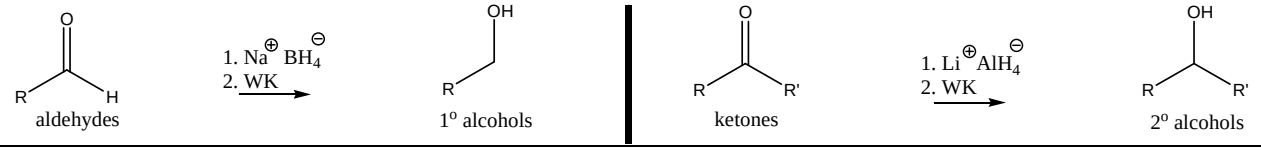
c. primary alcohols can be oxidized to aldehydes or carboxylic acids (…which can be made into esters, see above)



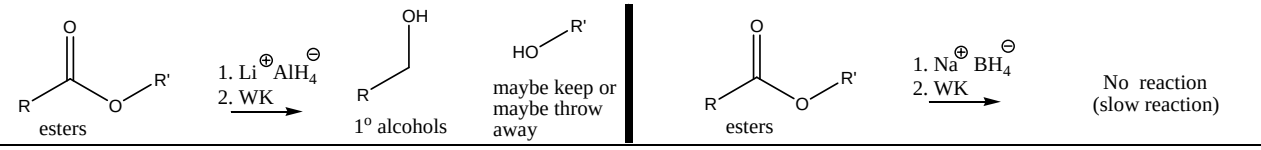
d. secondary alcohols can be oxidized to ketones with either of our "Cr^{+6}" oxidizing reagents



e. aldehydes/ketones reduced to alcohols (1^o and 2^o) by $LiAlH_4$ and $NaBH_4$ after acid workup



f. esters and acids are only reduced by $LiAlH_4$ (not $NaBH_4$), to primary alcohols after acid workup

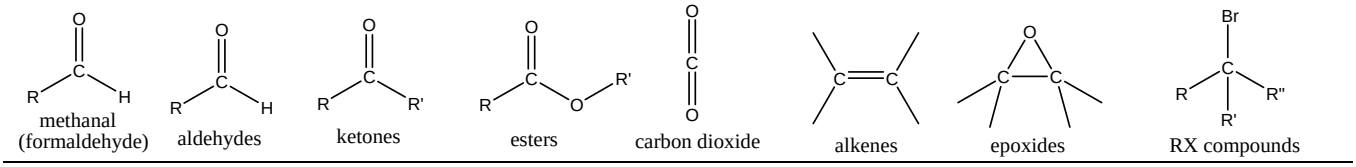


Obviously not ever reaction cannot be covered in this short handout, but this hopefully gives you a sample of reactions for approaching these kinds of problems.

Points to ponder when considering a retrosynthetic step.

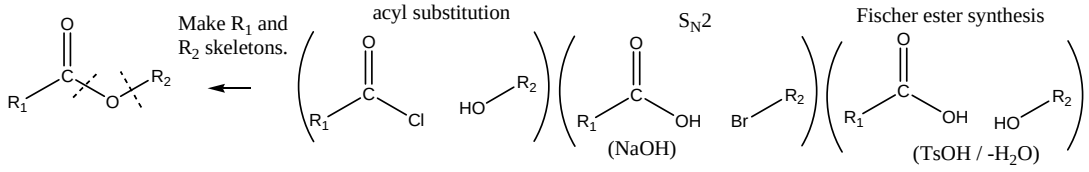
1. Which carbon could have been a carbonyl (C=O) functional group? (methanal, general aldehyde, ketone, ester, carbon dioxide)? Or, some other functional group (alkene, RX compound, epoxide)?
2. To start from some "functional group", what features (and skeletal parts) have to be retained from the target structure, or regenerated in the starting structure?
3. What features can be taken away from the target structure (that were originally in the starting structure, but are now lost)?
4. Draw a possible starting structure (or structures).
5. What portion has to be added and how can we do that (usually nucleophile/electrophile or functional group interconversion)
6. Is protection required to keep some part of the starting structure from reacting (often more advanced than we consider)?

Starting possibilities to produce alcohol OH or carboxylic acid OH (only CO_2).

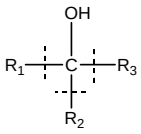


Combination Problems – Two (or more) ^{14}C structures in one target molecule.

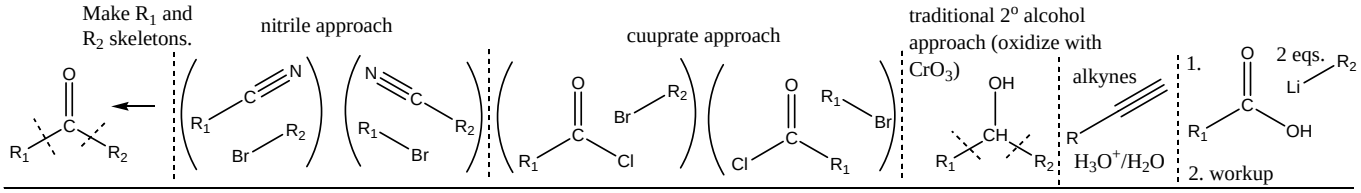
Esters



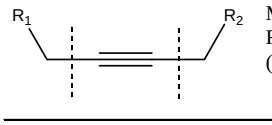
Alcohols



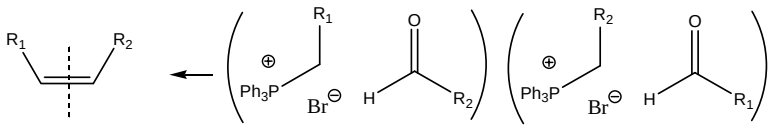
Ketones



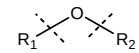
Alkynes



Wittig Reactions

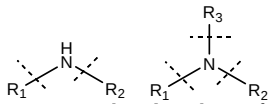


Ethers



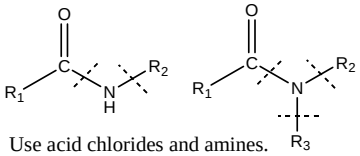
Join in S_N1, S_N2 and addition reactions to alkenes.

Amines



Use amine/carbonyl synthesis of imine and reduce with sodium cyanoborohydride.

Amides



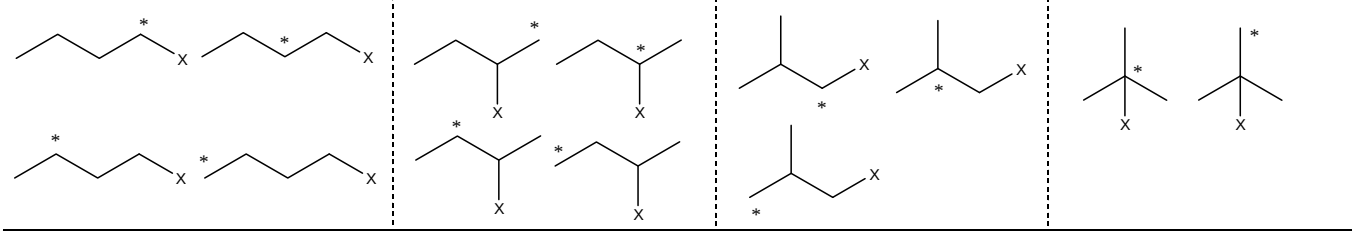
Use acid chlorides and amines.

Cuprate Couplings

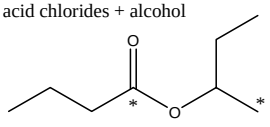
Both R_1 and R_2 come from R-Br compounds. One is made into lithium reagent to react with other as RBr. Hard to see, because there are no clues.

Generic examples of 4C patterns with one C-14 label and specific patterns using above functional groups

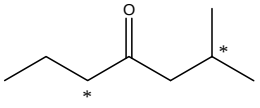
Example 4C patterns with C-14 labels



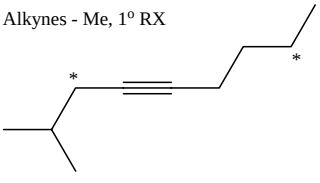
Esters - S_N2, Fischer syn, acid chlorides + alcohol



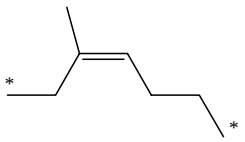
Ketones - from cuprates, nitriles, alcohols, carboxylic acids



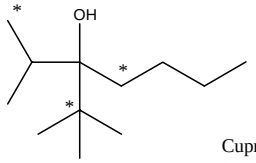
Alkynes - Me, 1° RX



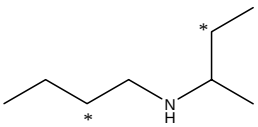
Alkenes (Wittig)



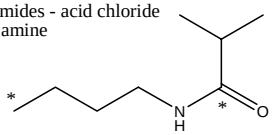
Alcohols - C=O + organometallic



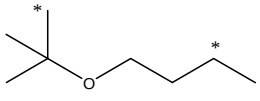
Amines - Gabriel, reductive amination



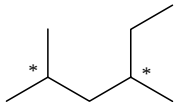
Amides - acid chloride + amine



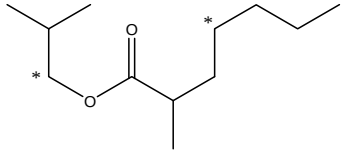
Ethers - S_N2, S_N1, alkene addition



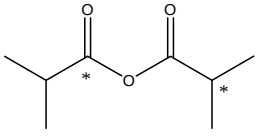
Cuprates - coupling (2 x RX)



Cuprates - conjugate addition



Anhydrides - use acid chloride



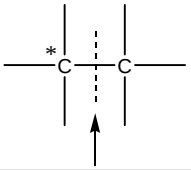
Construct two (or more) 4 carbon patterns, then join them together using one of the above functional groups.

Products from reactions of carbon nucleophiles and carbon electrophiles used in the ^{14}C Game and our course:

Carbon and hydrogen nucleophiles

Carbon electrophiles	R:⊖ Li⊕ organolithium reagents	R:⊖ (MgBr)⊕ organolithium reagents	RCC:⊖ Na⊕ acetylides	Na⊕ :CN:⊖ cyanide	$R_2Cu^{\ominus}$ $Li^{\oplus}$ cuprates	H_2C=P(Ph)(Ph)Ph ylid Wittig reagents	$Li^{\oplus}$ $AlH_4^{\ominus}$ (LAH)	$Na^{\oplus}$ $BH_4^{\ominus}$	R-Al(R)-H diisobutylaluminium hydride (DIBAH)
H_3C—Br methyl RX	not useful	not useful	alkynes	nitriles	2 RX coupling reaction	not useful	alkyls	alkyls	not useful
R(H)(H)C—Br primary RX	not useful	not useful	alkynes	nitriles	2 RX coupling reaction	not useful	alkyls	alkyls	not useful
R(R)CH—Br secondary RX	not useful	not useful	E2	nitriles	2 RX coupling reaction	not useful	alkyls	alkyls	not useful
ethylene oxide	1° ROH	1° ROH	1° ROH alkynes	1° ROH nitriles	1° ROH	not useful	1° ROH	1° ROH	not useful
propylene oxide	2° ROH	2° ROH	2° ROH alkynes	2° ROH nitriles	2° ROH	not useful	2° ROH	2° ROH	not useful
isobutylene oxide	3° ROH	3° ROH	3° ROH alkynes	3° ROH nitriles	3° ROH	not useful	3° ROH	3° ROH	not useful
methanal	1° ROH	1° ROH	1° ROH alkynes	cyanohydrin	not used in our course	specific alkenes	methanol	methanol	not useful
simple aldehydes	2° ROH	2° ROH	2° ROH alkynes	cyanohydrin	not useful	specific alkenes	1° ROH	1° ROH	not useful
simple ketones	3° ROH	3° ROH	3° ROH alkynes	cyanohydrin unless sterically hindered	not useful	specific alkenes	2° ROH	2° ROH	not useful
simple esters	3° ROH (Nu: twice)	3° ROH (Nu: twice)	not used in our course	not useful	not useful	not useful	1° ROH	not useful	aldehydes
simple carboxylic acids	ketones use 2 equivalents (B: once Nu: once)	acid/base no net rxn	acid/base no net rxn	acid/base no net rxn HCN = danger	acid/base no net rxn	not useful	acid/base no net rxn	acid/base no net rxn	acid/base no net rxn
simple acid chlorides	3° ROH (Nu: twice)	3° ROH (Nu: twice)	not useful	not useful	ketones	not useful	1° ROH	1° ROH	aldehydes
simple nitriles	ketones	ketones	not useful	not useful	not useful	not useful	1° amines	not useful	aldehydes
RCONR'$_2$ 3° amides	ketones	ketones					(also amines from amides)		(also aldehydes from 3° amides)
carbon dioxide	carboxylic acids	carboxylic acids	carboxylic acids	not useful	not useful	not useful	not useful	not useful	not useful
α,β-unsaturated ketones	3° ROH	3° ROH	not useful	conjugate addition	conjugate addition	not useful	alcohols	alcohols	not useful

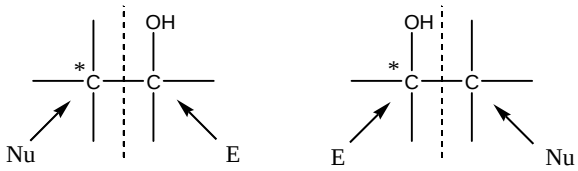
WK = normal workup to neutralize the reaction conditions. For the basic reactions (like above) above this would require mild acid neutralization (H_3O^+).
NR = no reaction or no productive result or not emphasized



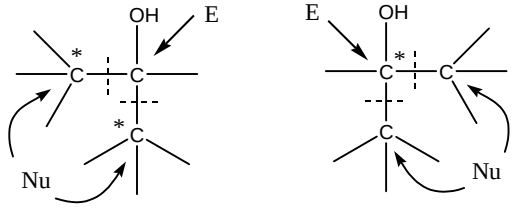
nucleophile (Nu) = ?

electrophile (E) = ?

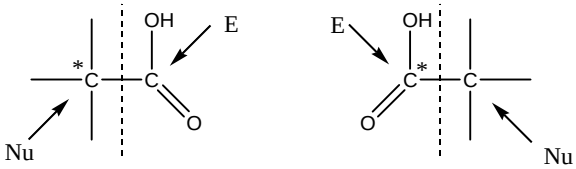
In our course every carbon-carbon bond made with asterisked carbon must be made with a nucleophile/electrophile reaction.



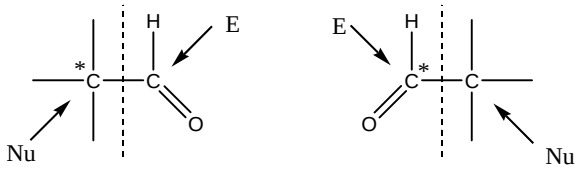
clue: COH group could have been an electrophilic C=O group (aldehyde or ketone) + nucleophilic Grignard or lithium reagent.



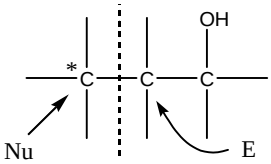
clue: COH group could have been an electrophilic C=O group (ester) + nucleophilic Grignard or lithium reagent (2x).



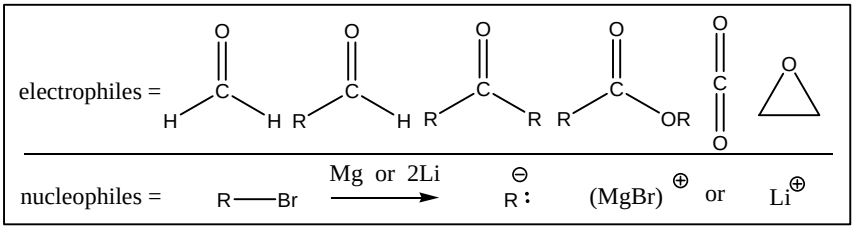
clue: COH group could have been an electrophilic C=O group (carbon dioxide) + nucleophilic Grignard or lithium reagent.

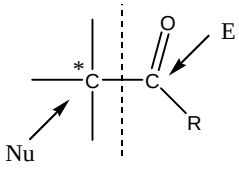


clue: CHO (aldehyde) group can be made from nucleophilic Grignard or lithium reagents + electrophilic dimethylformamide (DMF).

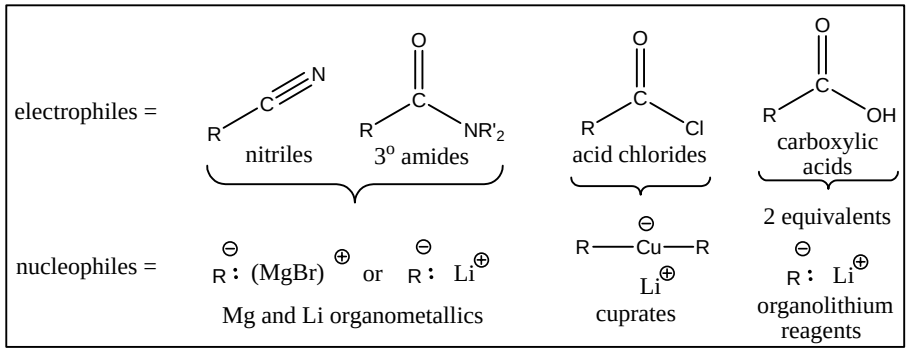


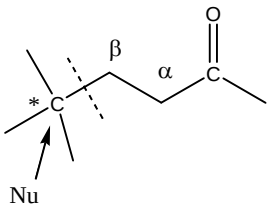
clue: COH group could have been an electrophilic epoxide group + nucleophilic Grignard or lithium reagent.





clue: C=O group could have been a nitrile (+ Grignard or lithium reagent), a 3^o amide (+ Grignard or lithium reagent), acid chloride (+ cuprate) or carboxylic acid (+ 2 eqs. of R-Li).





clue: C=O group could have been an electrophilic α,β-unsaturated C=O (+ nucleophilic cuprate = conjugate addition).