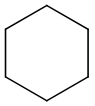
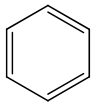
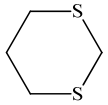
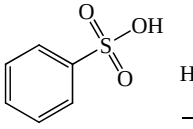
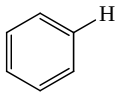
Functional Group Reactions

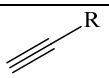
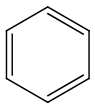
Given sources of carbon: CH_4      CO_2 NaCN 

Alkanes: Make from

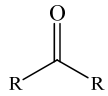
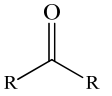
R—H ← alkenes (H_2 / Pd); alkynes (H_2 / Pd); R—Br haloalkanes (1. Mg 2. workup); R—Br haloalkanes (1. $LiAlH_4$ ($LiAlD_4$) 2. workup);  aldehydes & ketones (Wolff-Kishner NH_2NH_2 / ROH / Δ);  aldehydes & ketones (Clemmenson Zn / HCl)

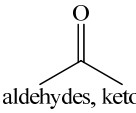
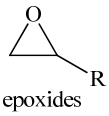
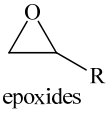
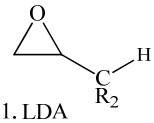
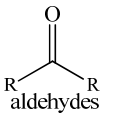
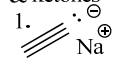
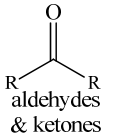
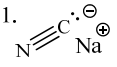
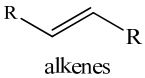
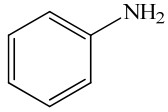
 aromatic sulfonic acids (H_2SO_4, H_2O) → 

Halo-organics: Make from

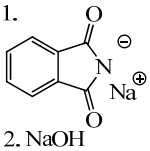
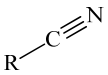
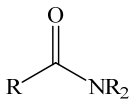
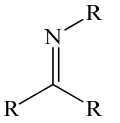
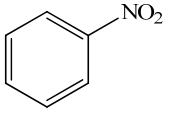
R—X ←  alkenes (HX Markovnikov);  alkenes (1. BH_3 2. Br_2 / CH_3O anti-Markovnikov);  alkenes (HBr / ROOR anti-Markovnikov);  alcohols (HBr or PBr_3 poss. rearranement); R—OH alcohols (1. TsCl/py 2. NaBr no rearranement);  alkynes (HX 1 or 2 eqs. Markovnikov); R—H alkanes (Br_2 / hν);  aromatic (Br_2 / $FeBr_3$)

Alcohols Make from

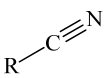
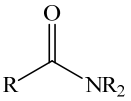
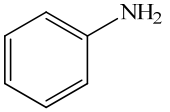
R—OH ←  alkenes (H_2SO_4 / H_2O Markovnikov poss. rearranement);  alkenes (1. BH_3 2. H_2O_2 / $HO^{\ominus}$ anti-Markovnikov); R—X haloalkanes (NaOH (Me,1° RX = S_N2)); R—X haloalkanes (H_2O (2°,3° RX = S_N1) poss. rearranement); R—X haloalkanes (a. $RCO_2^{\ominus}$ b. NaOH (Me,1°,2° RX = S_N2) no rearranement);  aldehydes & ketones (1. $NaBH_4$ or $LiAlH_4$ 2. workup);  acids / esters (1. $LiAlH_4$ 2. workup)

 aldehydes, ketones acids, esters (1. RMgBr or LiR 2. workup);  epoxides (1. $NaBH_4$ or $LiAlH_4$ 2. workup);  epoxides (1. RMgBr or LiR 2. workup);  (1. LDA 2. workup make allylic ROH);  aldehydes & ketones (1.  2. workup);  aldehydes & ketones (1.  2. workup);  alkenes (1. O_3, -78°C 2. $NaBH_4$);  aromatic amines (1. $NaNO_2$ / HCl (< 5°C) 2. H_2O (> 5°C))

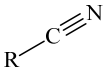
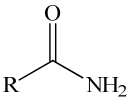
Amines Make from

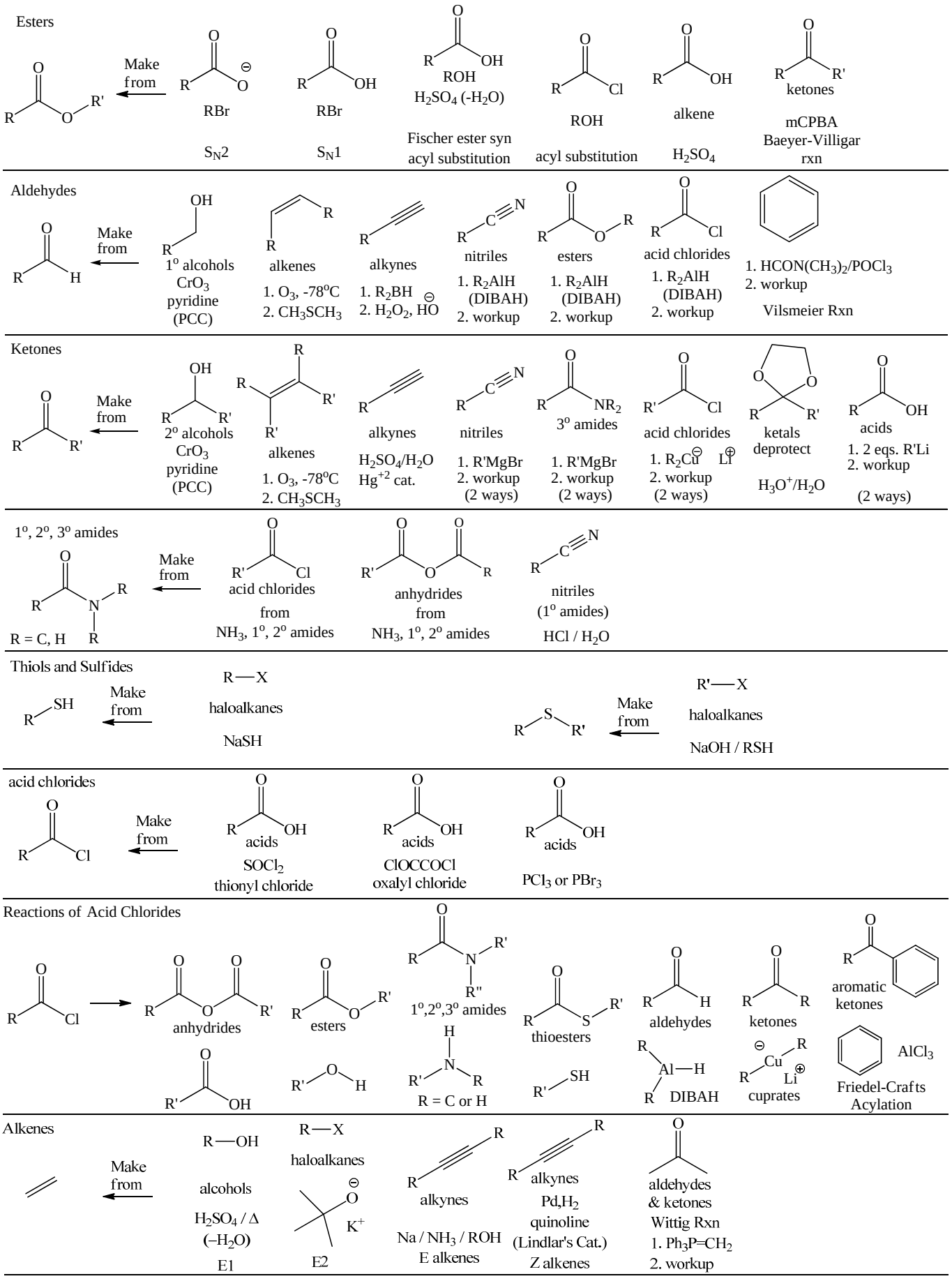
$R—NH_2$ ← R—X haloalkanes (1.  2. NaOH); R—X haloalkanes (1. NaN_3 2. $LiAlH_4$);  nitriles (1. $LiAlH_4$ 2. workup);  1°,2°,3° amides (1. $LiAlH_4$ 2. workup);  imines (1. $NaBH_3CN$ 2. workup);  nitroaromatics (Sn / HCl or Fe / HCl)

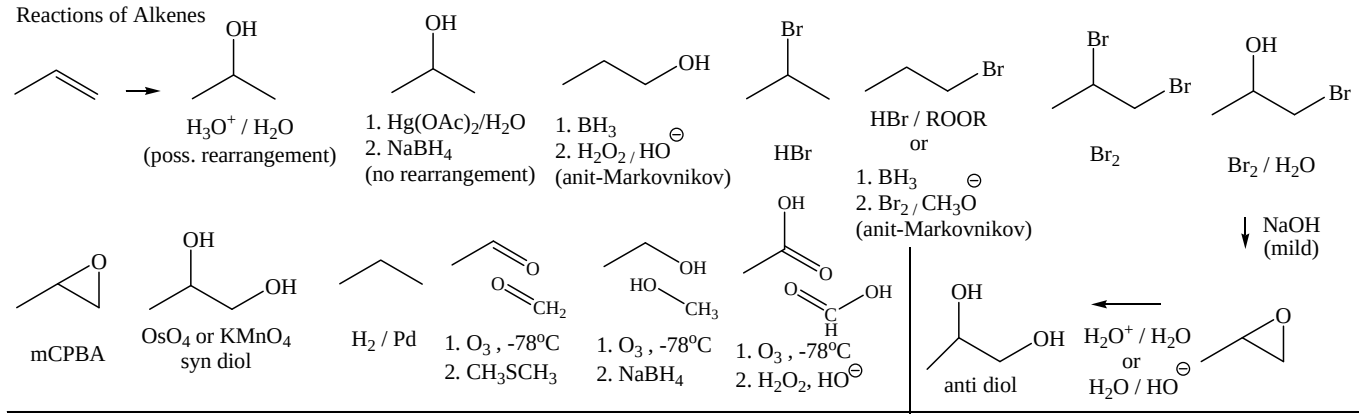
Nitriles Make from

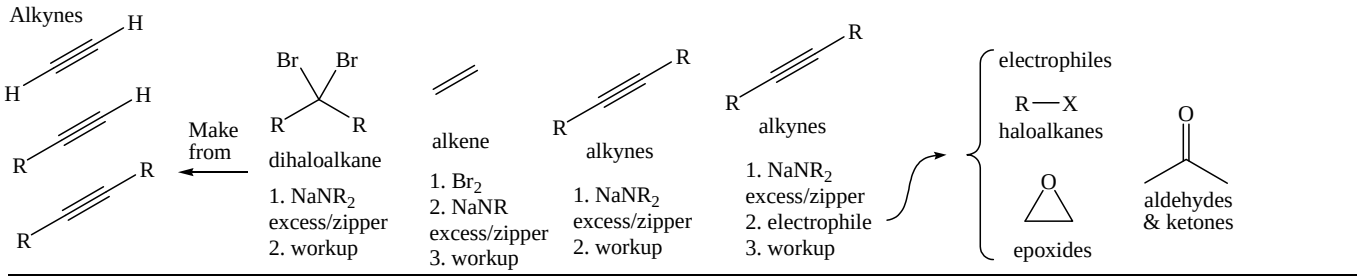
 ← R—Br haloalkanes (NaCN Me,1°,2° RX);  1° amides ($SOCl_2$);  aromatic amines (1. $NaNO_2$ / HCl (< 5°C) 2. CuCN (> 5°C))

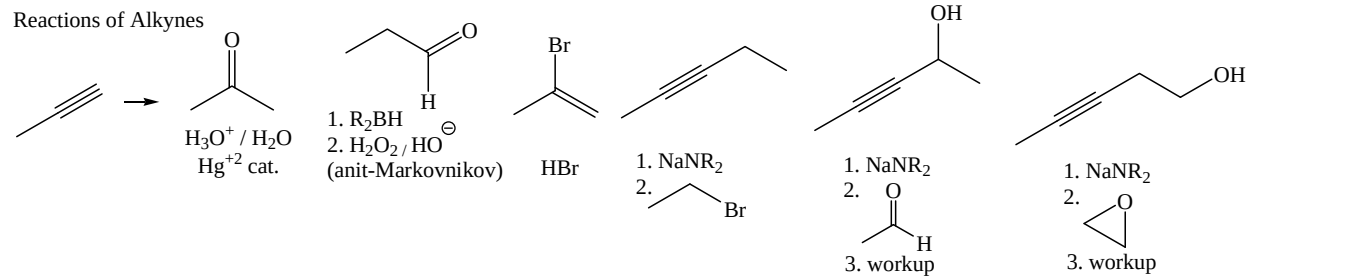
Reactions of Nitriles

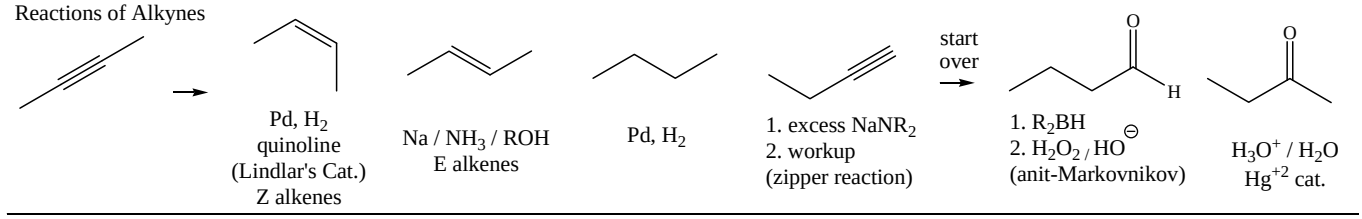
 →  1° amides (HCl / H_2O (milder)); acids (H_2SO_4 / H_2O Δ (harsher)); 1° amines (1. $LiAlH_4$ 2. workup); aldehydes (DIBAH); ketones (1. RMgBr 2. workup)

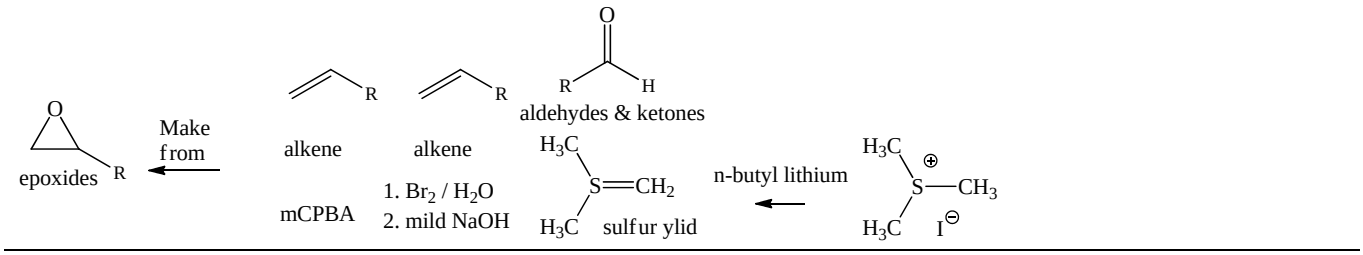

Esters
Make from
RBr
S_N2
RBr
S_N1
ROH
H_2SO_4 (-H_2O)
Fischer ester syn
acyl substitution
ROH
acyl substitution
alkene
H_2SO_4
ketones
mCPBA
Baeyer-Villigar
rxn
Aldehydes
Make from
1° alcohols
CrO_3
pyridine
(PCC)
alkenes
1. O_3, -78°C
2. CH_3SCH_3
alkynes
1. R_2BH
2. H_2O_2, HO^-
nitriles
1. R_2AlH
(DIBAH)
2. workup
esters
1. R_2AlH
(DIBAH)
2. workup
acid chlorides
1. R_2AlH
(DIBAH)
2. workup
1. $HCON(CH_3)_2/POCl_3$
2. workup
Vilsmeier Rxn
Ketones
Make from
2° alcohols
CrO_3
pyridine
(PCC)
alkenes
1. O_3, -78°C
2. CH_3SCH_3
alkynes
H_2SO_4/H_2O
Hg^{+2} cat.
nitriles
1. R'MgBr
2. workup
(2 ways)
3° amides
1. R'MgBr
2. workup
(2 ways)
acid chlorides
1. R_2Cu^- Li^+
2. workup
(2 ways)
ketals
deprotect
H_3O^+/H_2O
acids
1. 2 eqs. R'Li
2. workup
(2 ways)
1°, 2°, 3° amides
R = C, H
Make from
acid chlorides
from
NH_3, 1°, 2° amides
anhydrides
from
NH_3, 1°, 2° amides
nitriles
(1° amides)
HCl / H_2O
Thiols and Sulfides
Make from
haloalkanes
NaSH
haloalkanes
NaOH / RSH
acid chlorides
Make from
acids
$SOCl_2$
thionyl chloride
acids
ClOCCOCl
oxalyl chloride
acids
PCl_3 or PBr_3
Reactions of Acid Chlorides
anhydrides
esters
1°,2°,3° amides
R = C or H
thioesters
aldehydes
DIBAH
ketones
cuprates
aromatic
ketones
$AlCl_3$
Friedel-Crafts
Acylation
Alkenes
Make from
alcohols
H_2SO_4 / Δ
(–H_2O)
E1
haloalkanes
E2
alkynes
Na / NH_3 / ROH
E alkenes
alkynes
Pd,H_2
quinoline
(Lindlar's Cat.)
Z alkenes
aldehydes
& ketones
Wittig Rxn
1. $Ph_3P{=}CH_2$
2. workup

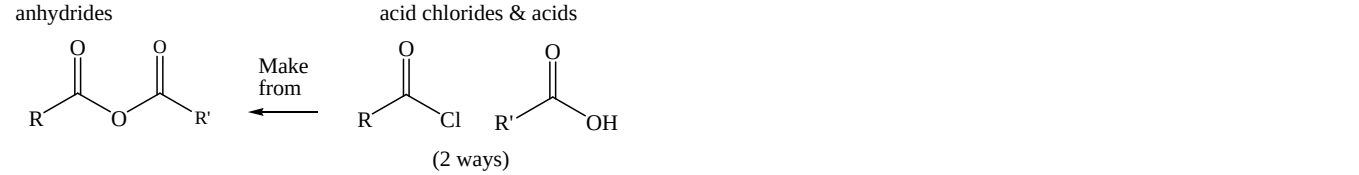

Reactions of Alkenes
H3O+ / H2O
(poss. rearrangement)
1. Hg(OAc)2/H2O
2. NaBH4
(no rearrangement)
1. BH3
2. H2O2 / HO⊖
(anit-Markovnikov)
HBr
HBr / ROOR
or
1. BH3
2. Br2 / CH3O⊖
(anit-Markovnikov)
Br2
Br2 / H2O
NaOH
(mild)
mCPBA
OsO4 or KMnO4
syn diol
H2 / Pd
1. O3 , -78°C
2. CH3SCH3
1. O3 , -78°C
2. NaBH4
1. O3 , -78°C
2. H2O2, HO⊖
anti diol
H2O+ / H2O
or
H2O / HO⊖

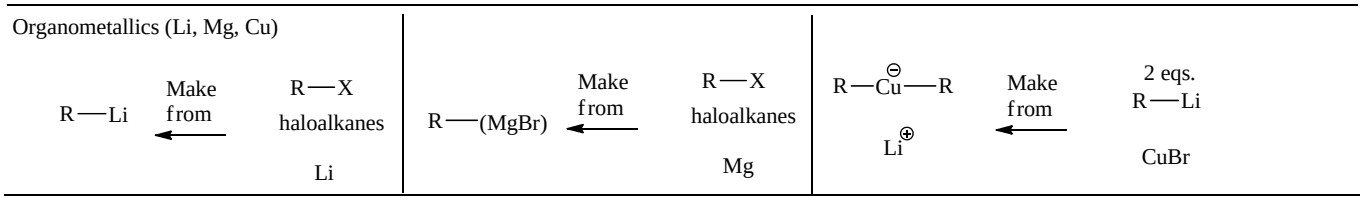

Alkynes
Make
from
dihaloalkane
1. NaNR2
excess/zipper
2. workup
alkene
1. Br2
2. NaNR
excess/zipper
3. workup
alkynes
1. NaNR2
excess/zipper
2. workup
alkynes
1. NaNR2
excess/zipper
2. electrophile
3. workup
electrophiles
R—X
haloalkanes
epoxides
aldehydes
& ketones


Reactions of Alkynes
H3O+ / H2O
Hg+2 cat.
1. R2BH
2. H2O2 / HO⊖
(anit-Markovnikov)
HBr
1. NaNR2
2.
1. NaNR2
2.
3. workup
1. NaNR2
2.
3. workup

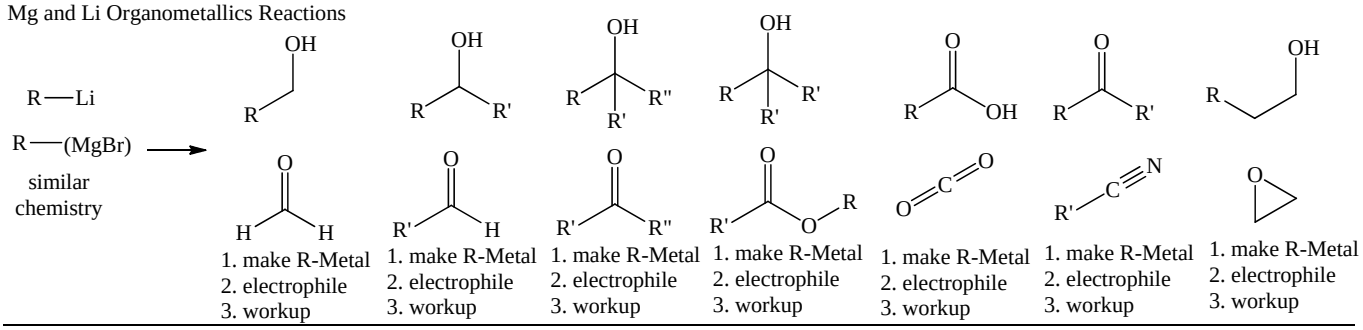

Reactions of Alkynes
Pd, H2
quinoline
(Lindlar's Cat.)
Z alkenes
Na / NH3 / ROH
E alkenes
Pd, H2
1. excess NaNR2
2. workup
(zipper reaction)
start
over
1. R2BH
2. H2O2 / HO⊖
(anit-Markovnikov)
H3O+ / H2O
Hg+2 cat.


epoxides
Make
from
alkene
alkene
1. Br2 / H2O
2. mild NaOH
mCPBA
aldehydes & ketones
n-butyl lithium
sulfur ylid

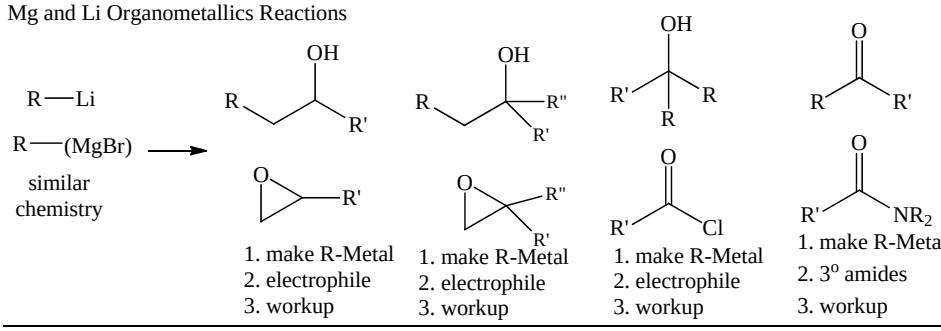

anhydrides
acid chlorides & acids
Make
from
(2 ways)


Organometallics (Li, Mg, Cu)
R—Li
Make
from
R—X
haloalkanes
Li
R—(MgBr)
Make
from
R—X
haloalkanes
Mg
R—Cu⊖—R
Li⊕
Make
from
2 eqs.
R—Li
CuBr

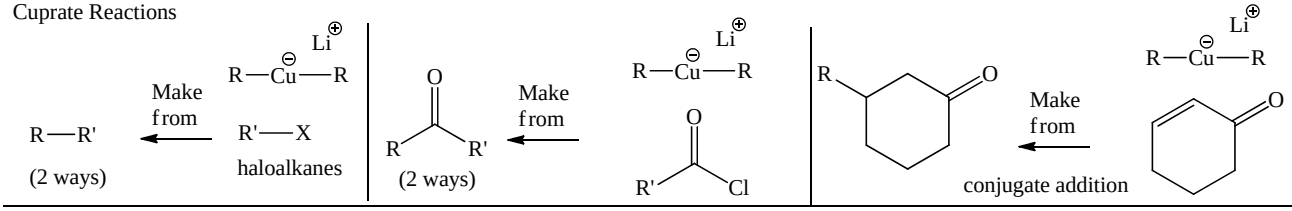
Mg and Li Organometallics Reactions



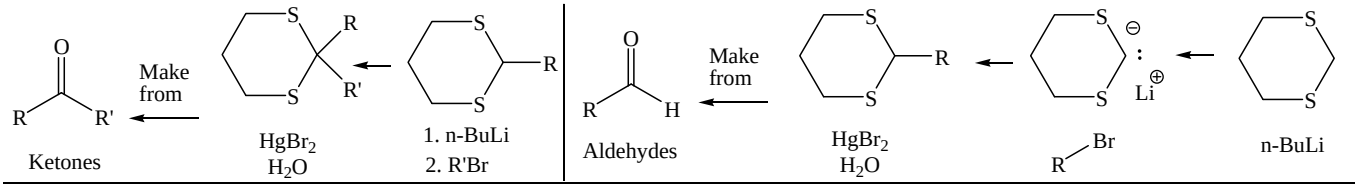
Mg and Li Organometallics Reactions



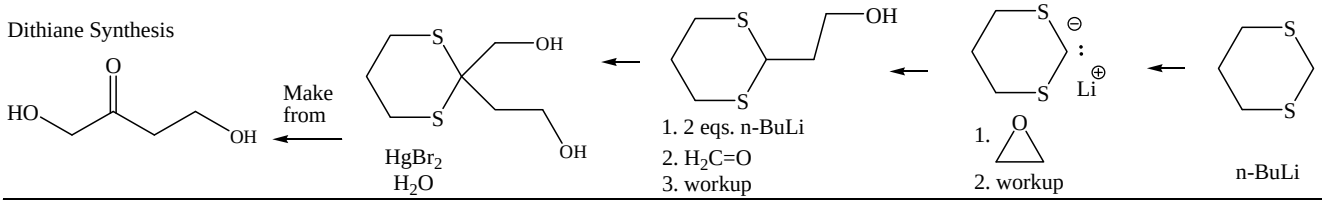
Cuprate Reactions



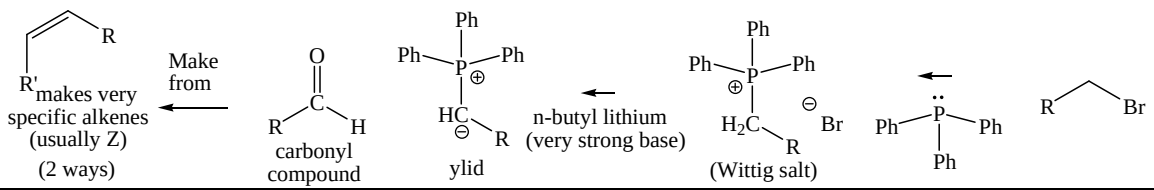
Dithiane Synthesis of Aldehydes and Ketones



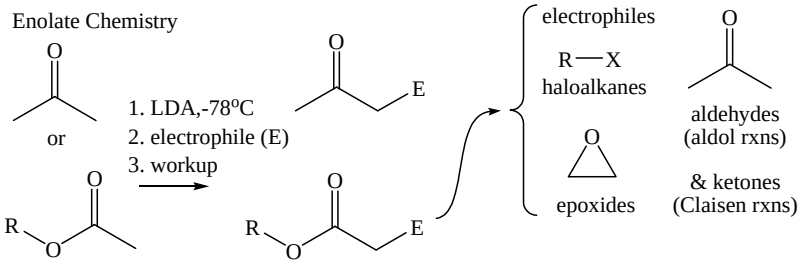
Dithiane Synthesis



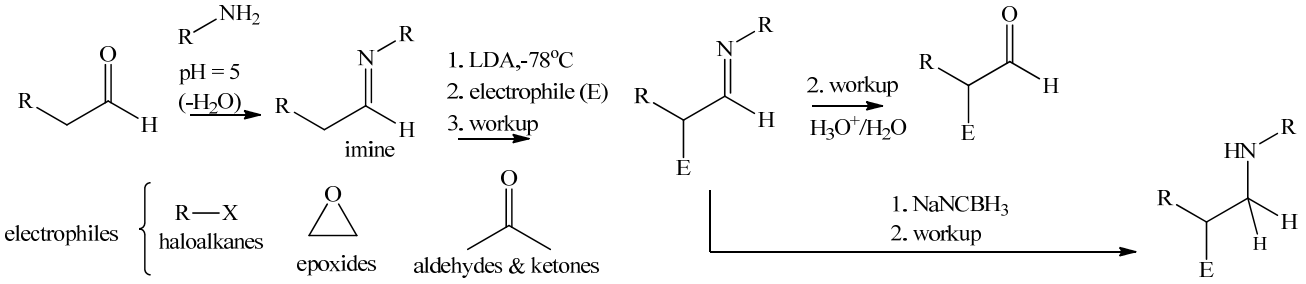
Wittig Reactions



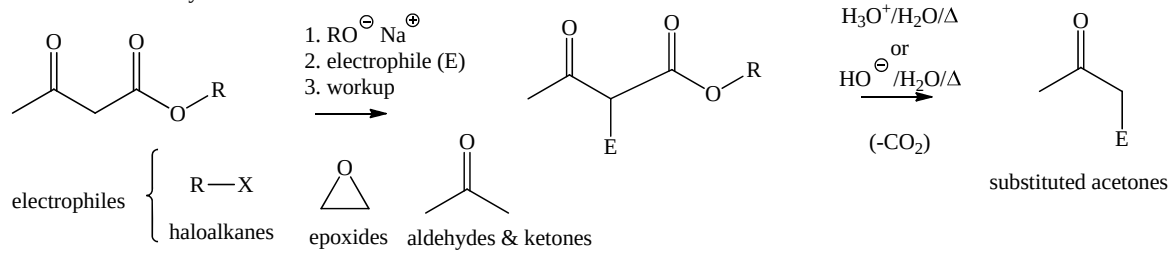
Enolate Chemistry



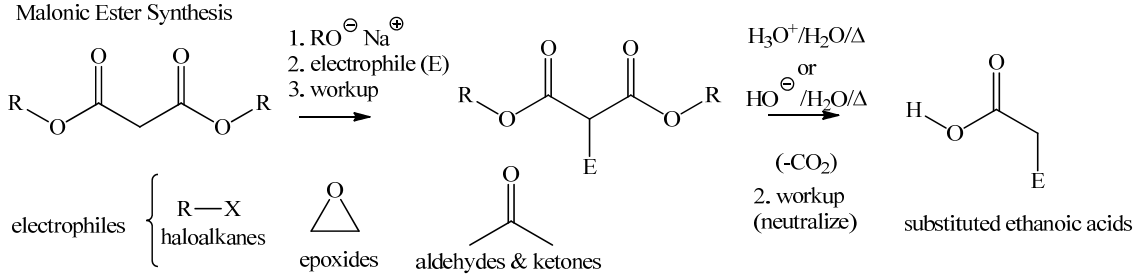
Imine Enolate Chemistry (aldehyde strategy when the aldehyde is too reactive)



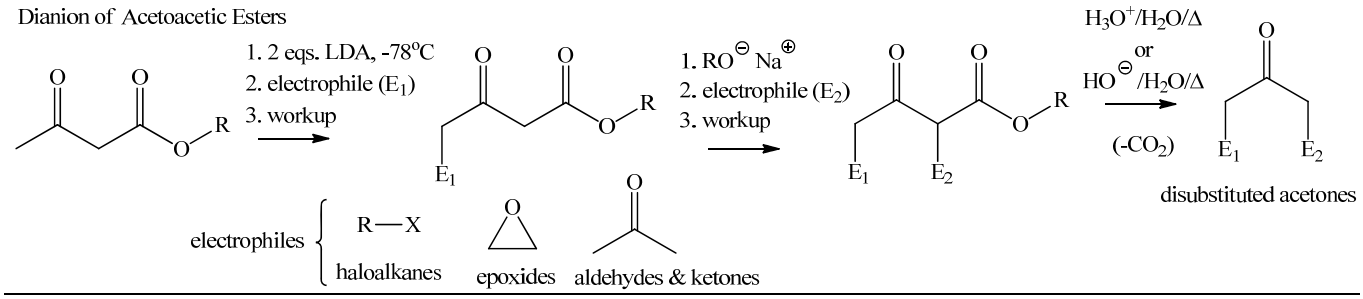
Acetoacetic Ester Synthesis



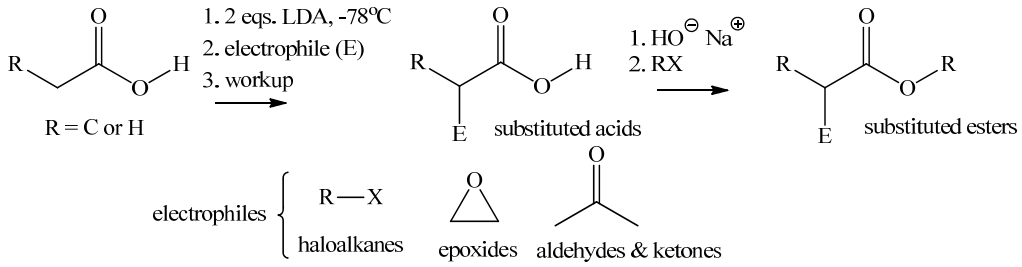
Malonic Ester Synthesis



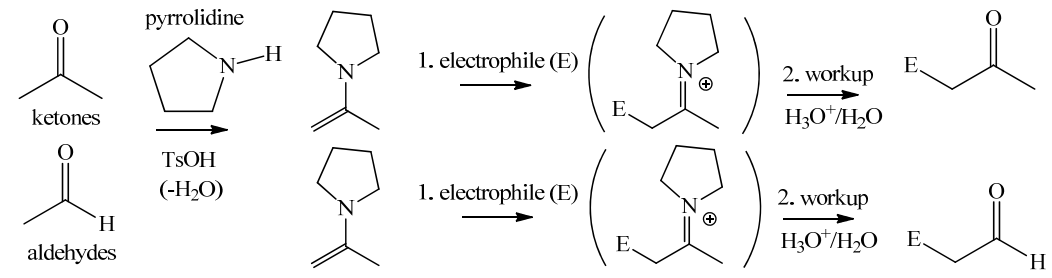
Dianion of Acetoacetic Esters



Dianions of Carboxylic Acids



Enamine Chemistry



Electrophilic Aromatic Substitution Reactions (aromatic ring is a π nucleophile)

second substituent

Reaction 1: Br_2, $FeBr_3$ → ortho/para director
1 o/p dibromo; 2 o/p bromo / alkyl; 3 o/p bromo / keto; 4 o/p bromo / nitro; 5 o/p bromo / sulfonic acid

Reaction 2: R–Cl, $AlCl_3$ → alkyl benzenes, ortho/para director
1 o/p alkyl / bromo; 2 o/p alkyl / alkyl; 3 o/p alkyl / keto; 4 o/p alkyl / nitro; 5 o/p alkyl / sulfonic acid

Reaction 3: RCOCl, $AlCl_3$ → aromatic ketones, meta director
1 meta keto / bromo; 2 poor reaction; 3 poor reaction; 4 meta keto / nitro; 5 meta keto / sulfonic acid

Reaction 4: HNO_3, H_2SO_4 → meta director
1 meta nitro / bromo; 2 poor reaction; 3 poor reaction; 4 meta dinitro; 5 meta nitro / sulfonic acid

Reaction 5: H_2SO_4 ⇌ meta director
1 meta sulfonic acid / bromo; 2 poor reaction; 3 poor reaction; 4 meta sulfonic acid / nitro; 5 meta disulfonic acid

benzene sulfonic acids and this reaction can be reversed with the addition of water.

Organometallic reactions

Br, Mg → $(MgBr)^{\oplus}$

the aromatic ring is a σ nuclephile, the electron donation comes from an sp^2 orbital not the π electrons

1. CO_2, 2. WK → NaOH, RX
1. $H_2C{=}O$, 2. WK → HBr → NaCN
1. RCHO, 2. WK
1. R(C=O)R, 2. WK
1. R(C=O)OR', 2. WK (reacts twice)
1. epoxide, 2. WK → HBr; CrO_3 (PCC); CrO_3, H_2O (Jones)
1. substituted epoxide, 2. WK → CrO_3 (PCC)
1. CuBr, 2. RX
1. CuBr, 2. RCOCl (compare to Friedel-Crafts reactions)
1. CuBr, 2. cyclohexenone (conjugate addition)

1. amine (1.LAH, 2. WK)
2. amide (HCl, H_2O)
3. acid (H_2SO_4, H_2O)
4. ketone (1.RMgBr, 2. WK)
5. aldehyde (1.DIBAH, 2. WK)

Diazonium chemistry

the aromatic ring is a σ electrophile

NO_2 → Fe / HCl or $SnCl_2$ / HCl reduction → aniline (NH_2) → $NaNO_2$, HCl, T > 5°C → diazonium chemistry

meta substitution

complete ortho/para substitution with some electophiles (NH_2 is too reactive) or the nitrogen complexes with acid becoming positively charged and a meta director; an alternative strategy forms the amide to make the substituent less reactive and then hydrolyze amide back to the amine (aniline) when done

acetanilide

controlled ortho/para substitution is possible and the amide can be cleaved in acid or base back to the amine (aniline derivative)

CuCl → Cl; CuBr → Br; CuCN → CN; KI → I; H_2O → OH; HF, BF_3 → F; H_3PO_2 → H

Diazonium chemistry provides our only route to some aromatic substituents: such as CN, I, OH and F. There are alternative options for Cl, Br and H. The polarity of the joining groups is completely backwards from the other aromatic reactions. The aromatic ring is the electrophile.

Side chain reactions

CrO_3, Δ → oxidation

at least one benzylic hydrogen

$NH_2NH_2^{\ominus}$ / RO / Δ, Wolff-Kishner Reduction

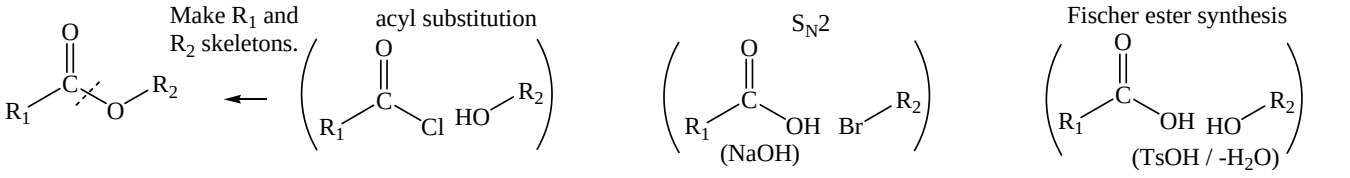
Clemmenson Reduction: Zn, HCl

Br_2 / hν → free radical substitution of sp^3 CH

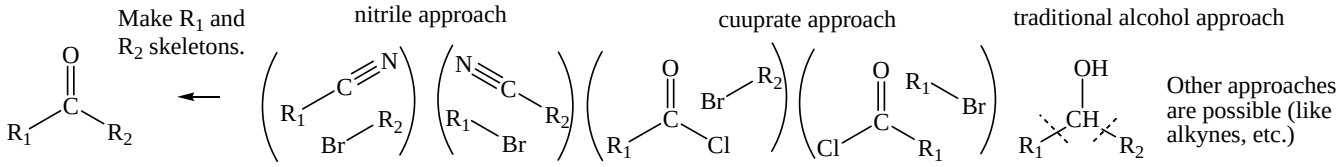
at least one benzylic hydrogen

Combination Problems – Two structures (or more) in one target molecule.

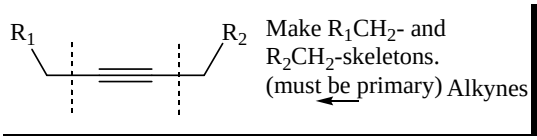
Esters



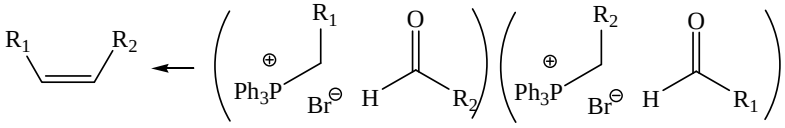
Ketones



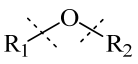
Alkynes



Wittig Reactions

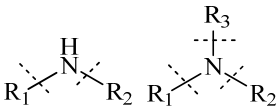


Ethers



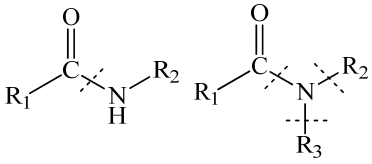
Join in S_N1, S_N2 and addition reactions to alkenes.

Amines



Use amine/carbonyl synthesis of imine and reduce with sodium cyanoborohydride. OR 1. $LiAlH_4$ 2. workup

Amides

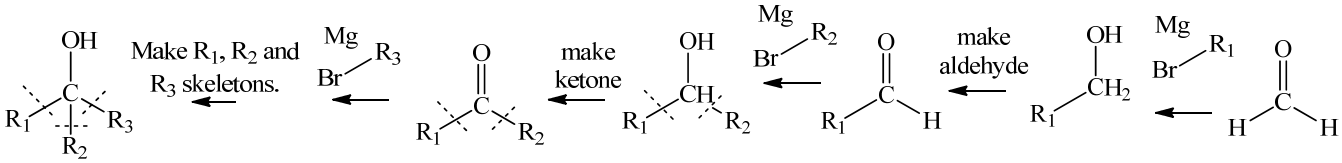


Use acid chlorides and amines.

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. Hardest to see, because there are no clues.

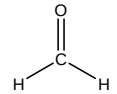
2^o and 3^o Alcohols

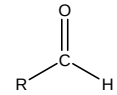


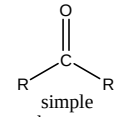
Other approaches to ketone are possible (like alkynes, nitriles, 3^o amides, acid chlorides, etc.)

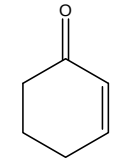
Electrophiles (Lewis acids)

aldehydes and ketones, carbonyl addition reactions

a  methanal

b  simple aldehydes

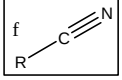
c  simple ketones

d  conjugated carbonyl compounds

carbon dioxide

e

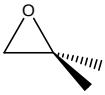
nitriles

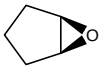
f 

epoxide derivatives

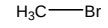
g 

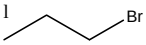
h 

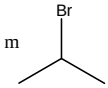
i 

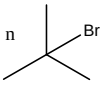
j 

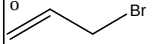
RX derivatives
S_N2 / E2 and S_N1 / E1

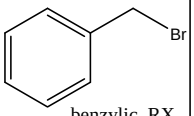
k  methyl RX

l  1° RX

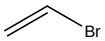
m  2° RX

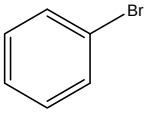
n  3° RX

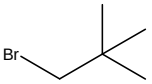
o  allylic RX

p  benzylic RX

unreactive RX patterns

 vinyl RX

 phenyl RX

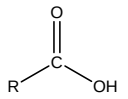
 neopentyl RX

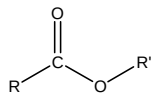
Other Lewis acids used: FeX_3, AlX_3, BH_3, BF_3, HgX_2, etc.

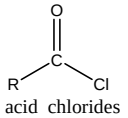
Occasional weak Lewis acids: Br_2, Cl_2, H_2O_2 (also react in free radical reactions)

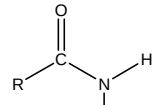
Strong Bronsted acids: H_2SO_4, H_3PO_4, HCl, HBr, HI

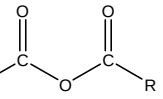
carboxylic acids and derivatives, carbonyl substitution reactions

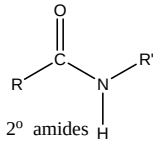
q  carboxylic acids

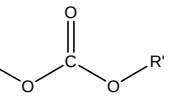
u  esters

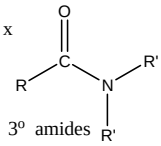
r  acid chlorides

v  1° amides

s  anhydrides

w  2° amides

t  dialkyl carbonates

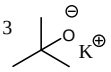
x  3° amides

Nucleophiles (Bases)

oxygen nucleophiles (and/or bases)

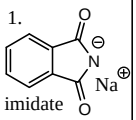
1  hydroxide

2  alkoxides

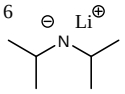
3  t-butoxide

4  carboxylates

nitrogen nucleophiles (and/or bases)

5  imidate

2. NaOH

6  lithium diisopropylamide (LDA)

always a base

7 1. $Na^{\oplus}$ $R_2N^{\ominus}$

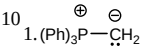
2. workup

sodium amide (always a base)

carbanion nucleophiles (and/or bases)

8  cyanide

9  acetylides

10  ylid (make)

2.WK

11 1. R-MgX

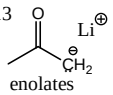
2. WK

Grignard reagents

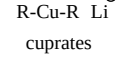
12 1. R-Li

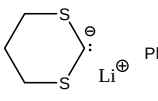
2. WK

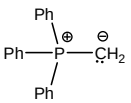
organolithium reagents

13  enolates

2. WK

14  cuprates

 dithiane carbanions

 Wittig ylid

hydride nucleophiles (and/or bases)

15 1. $LiAlH_4$ (LAH)

2. workup

16 1. $NaBH_4$

2. workup

17

DIBAH

2.WK

18 NaH

always a base

19 KH

always a base

weak nucleophiles (and/or bases)

20 H-O-H

21 R-O-H

22

And any functional group with a lone pair of electrons (e.g. oxygen and nitrogen)

neutral carbon nucleophiles

 alkenes

 alkynes

 aromatic comounds

 enamines

 enols and enol ethers

Occasional weak Lewis bases: R-Cl, R-Br, R-I, Br_2, Cl_2 with strong Lewis acids like: FeX_3, AlX_3, etc.

miscillaneous neutral nucleophiles (and/or bases)

NH_3 ammonia

R_3P phosphines

 1° amines

H_2S hydrogen sulfide

 2° amines

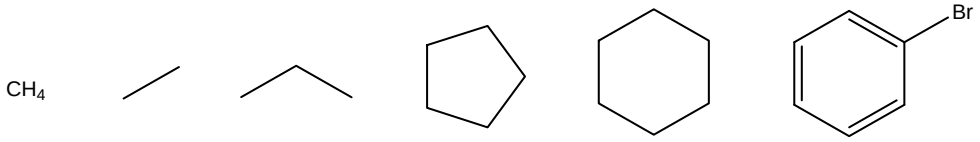
 thiols

 3° amines

 sulfides

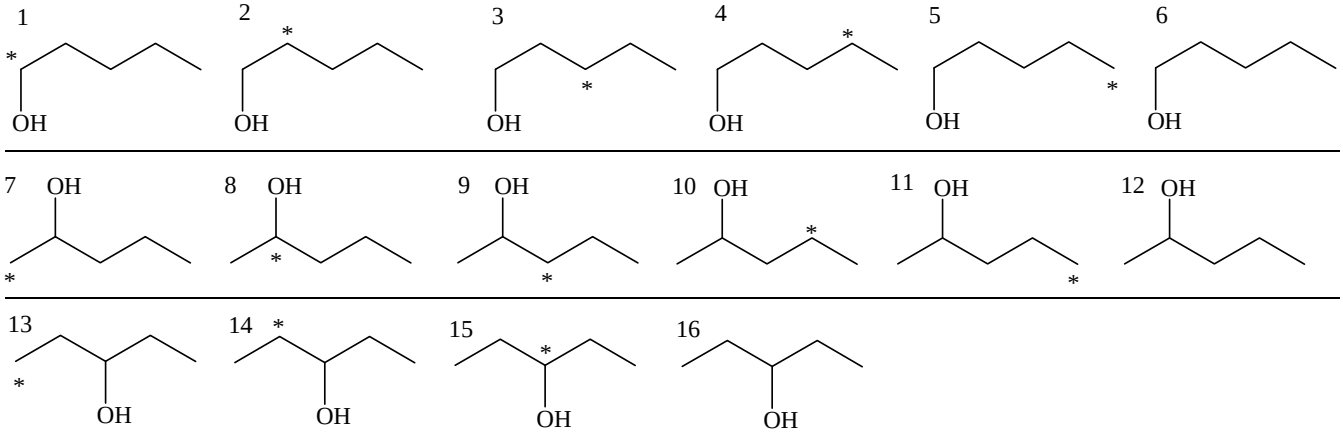
Use clues in the target molecule to determine what the last step could have been. Once you work back one step, use clues in that molecule to determine how you could work back one additional step. Repeat this process until you get to the necessary starting conditions, i.e. allowable ^{14}C starting units (*CH_4, *CO_2, Na*CN where "*" indicates a radioactive ^{14}C isotope). Until aromatic chemistry is covered bromobenzene is also available.

Starting Structures:

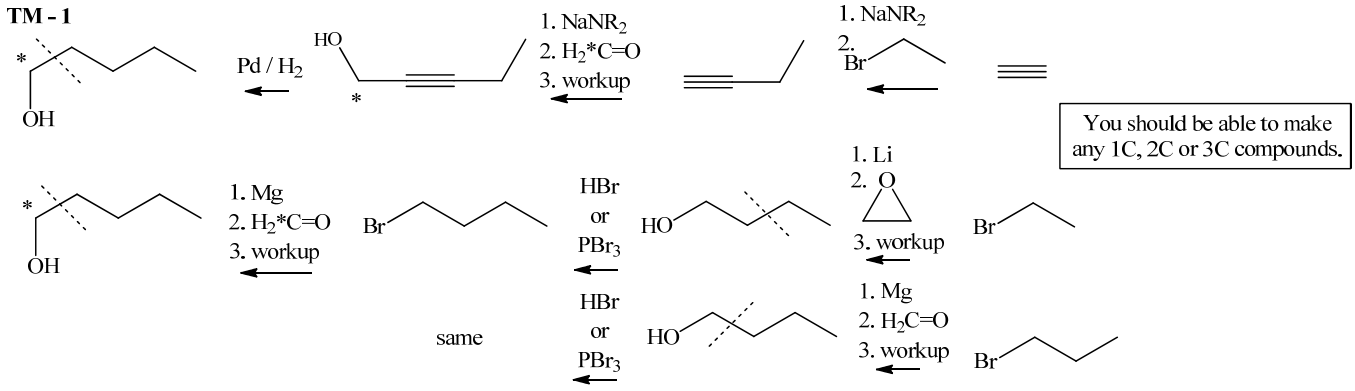


Examples – Target Molecules (TM - #)

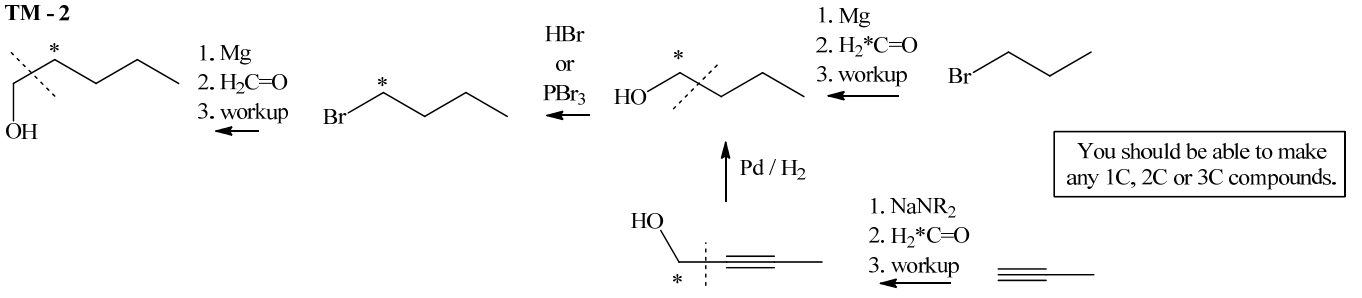
Straight chain C5 alcohols



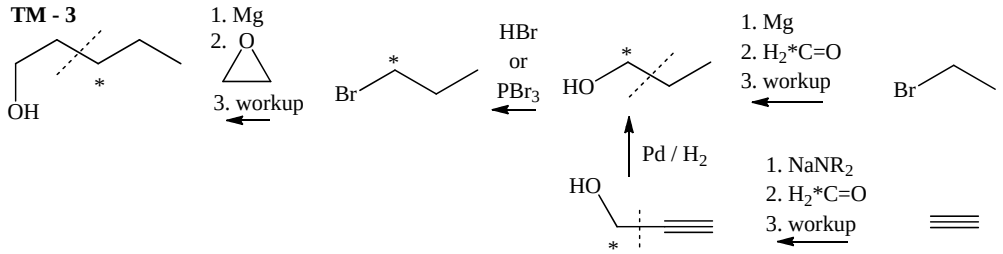
TM - 1



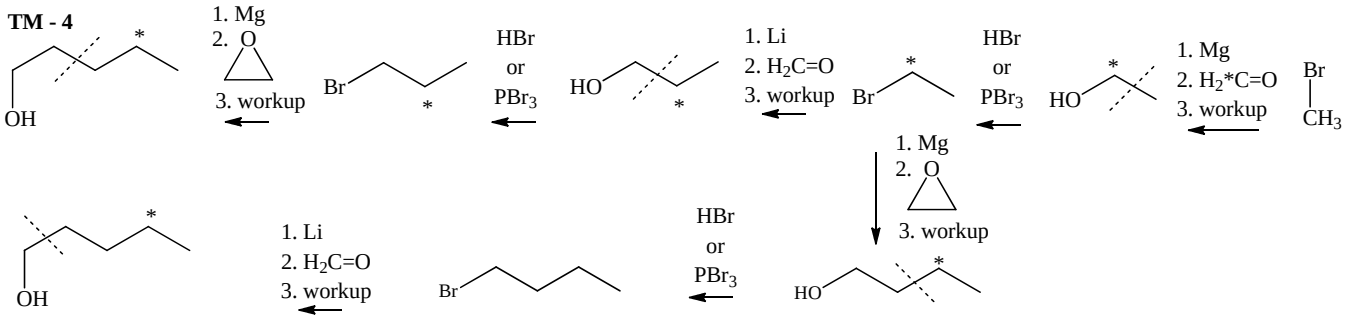
TM - 2



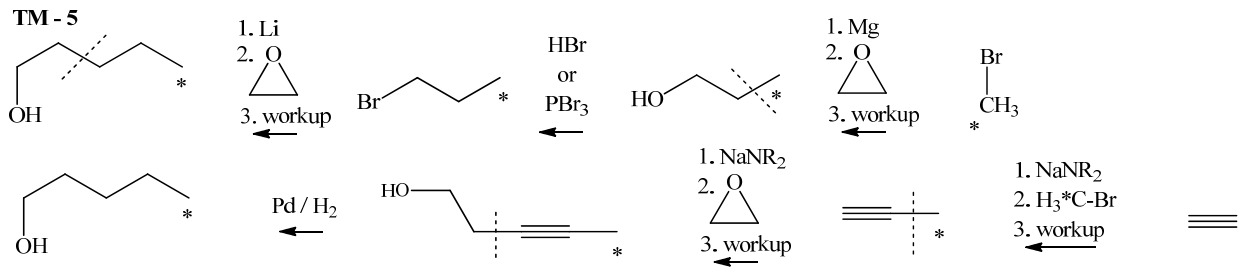
TM - 3



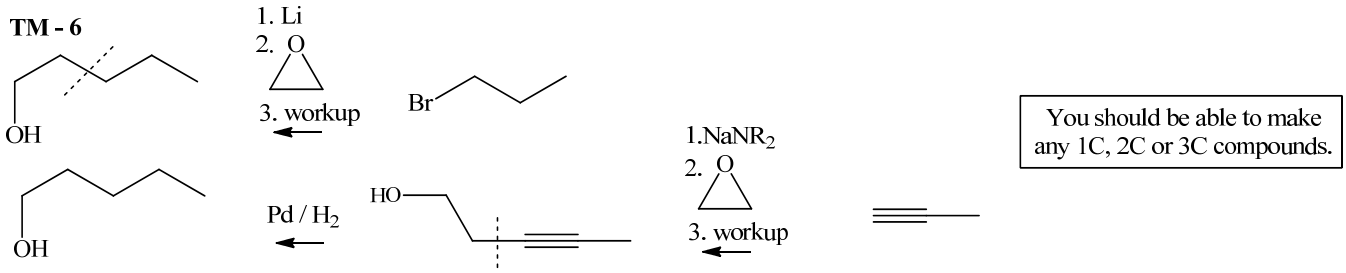
TM - 4



TM - 5

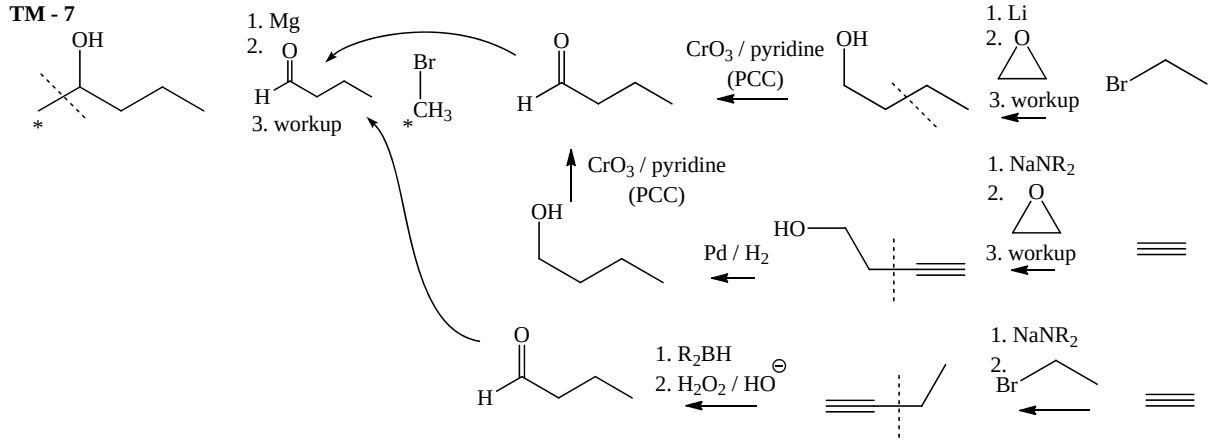


TM - 6

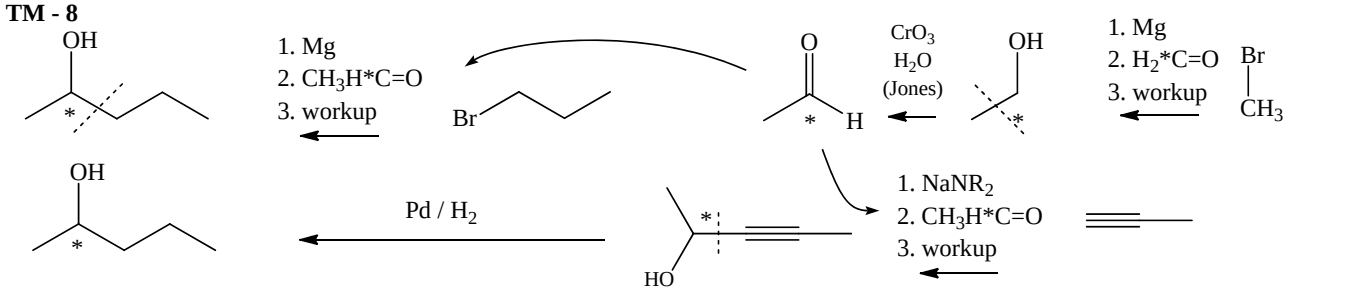


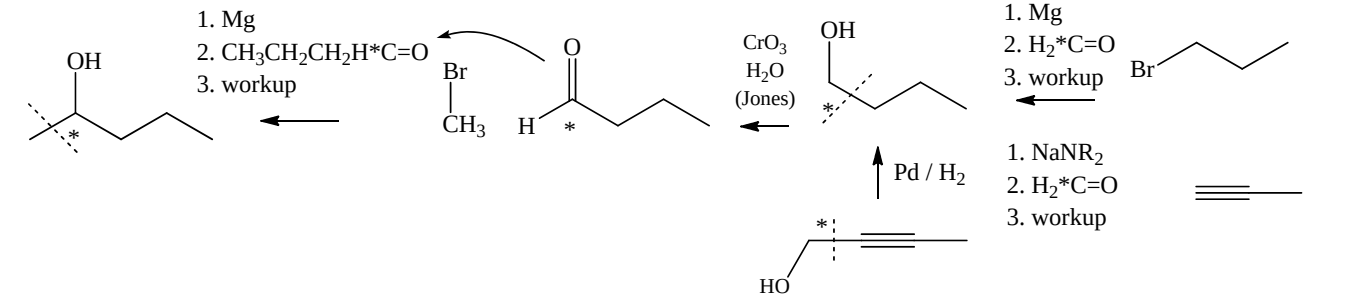
You should be able to make any 1C, 2C or 3C compounds.

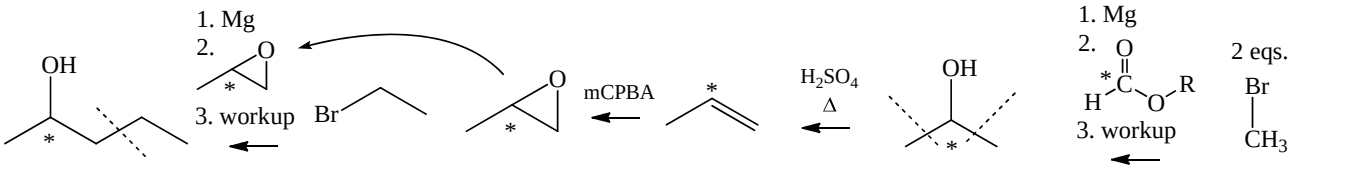
TM - 7



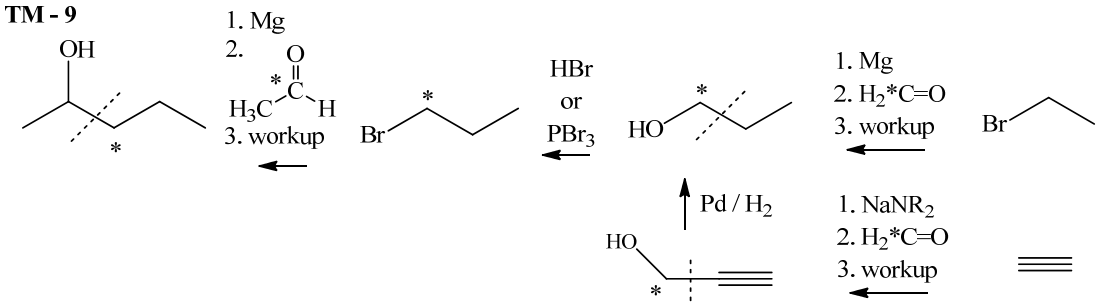
TM - 8



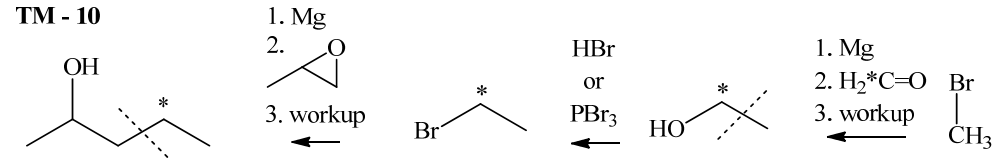




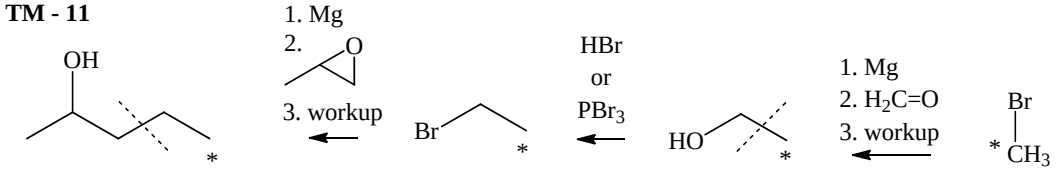
TM - 9



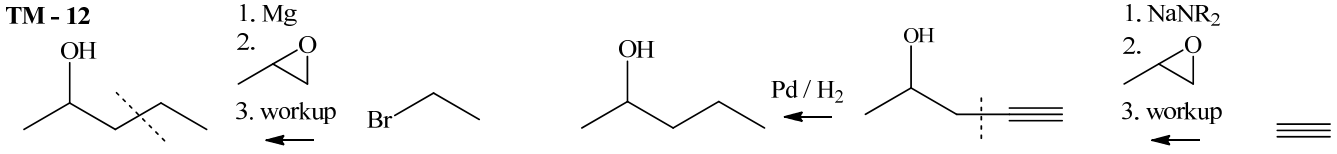
TM - 10



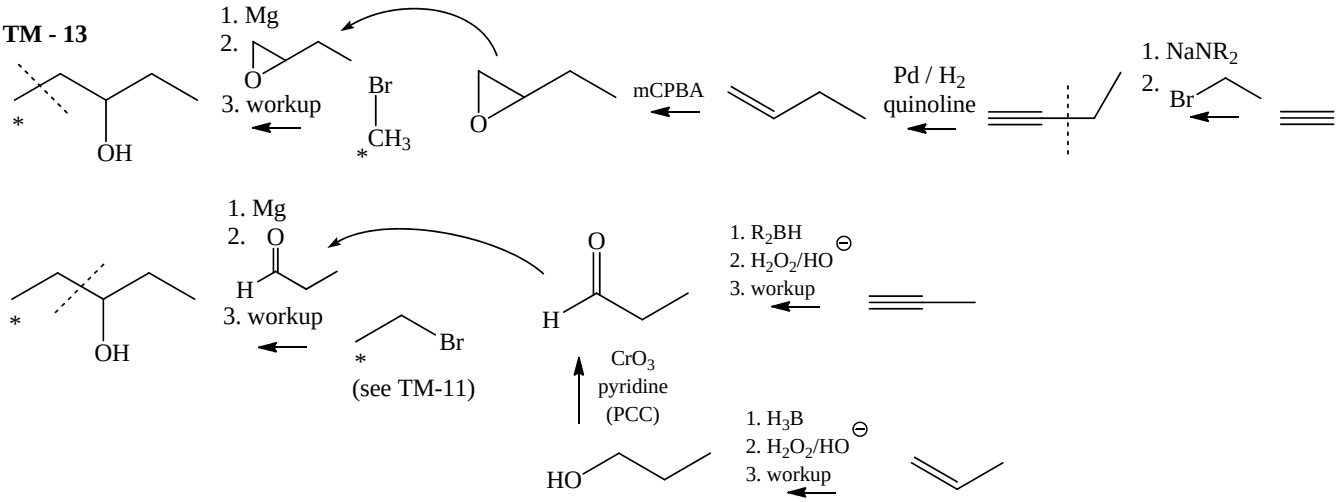
TM - 11



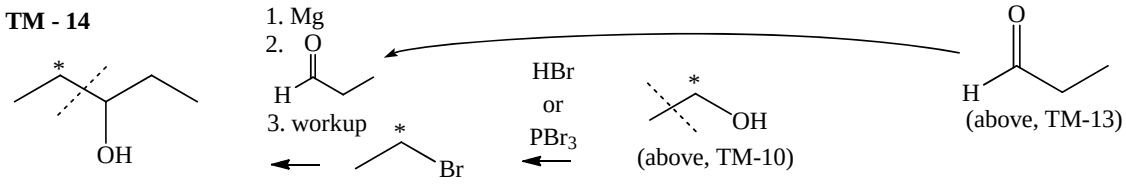
TM - 12



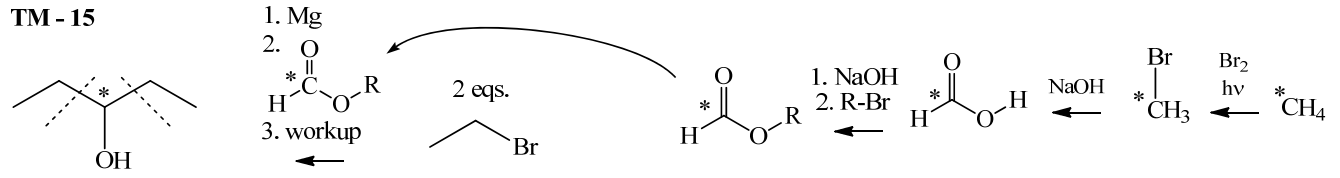
TM - 13



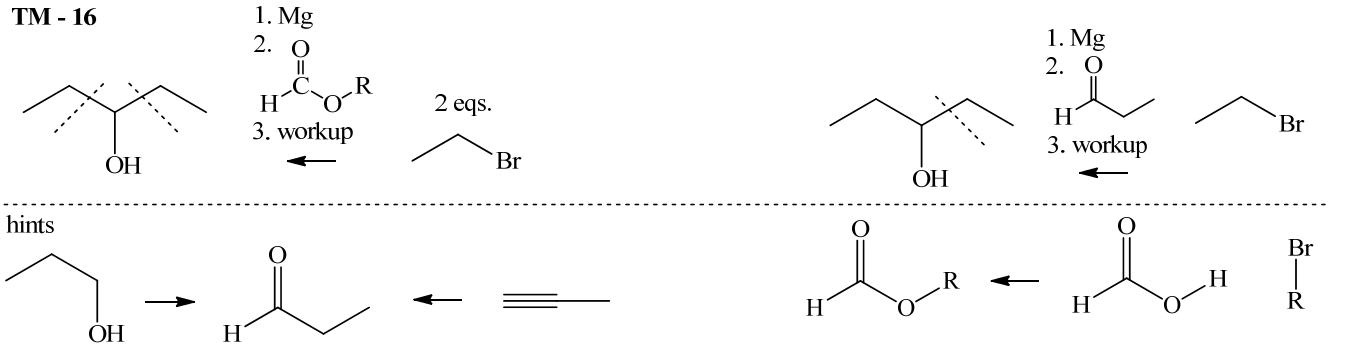
TM - 14



TM - 15

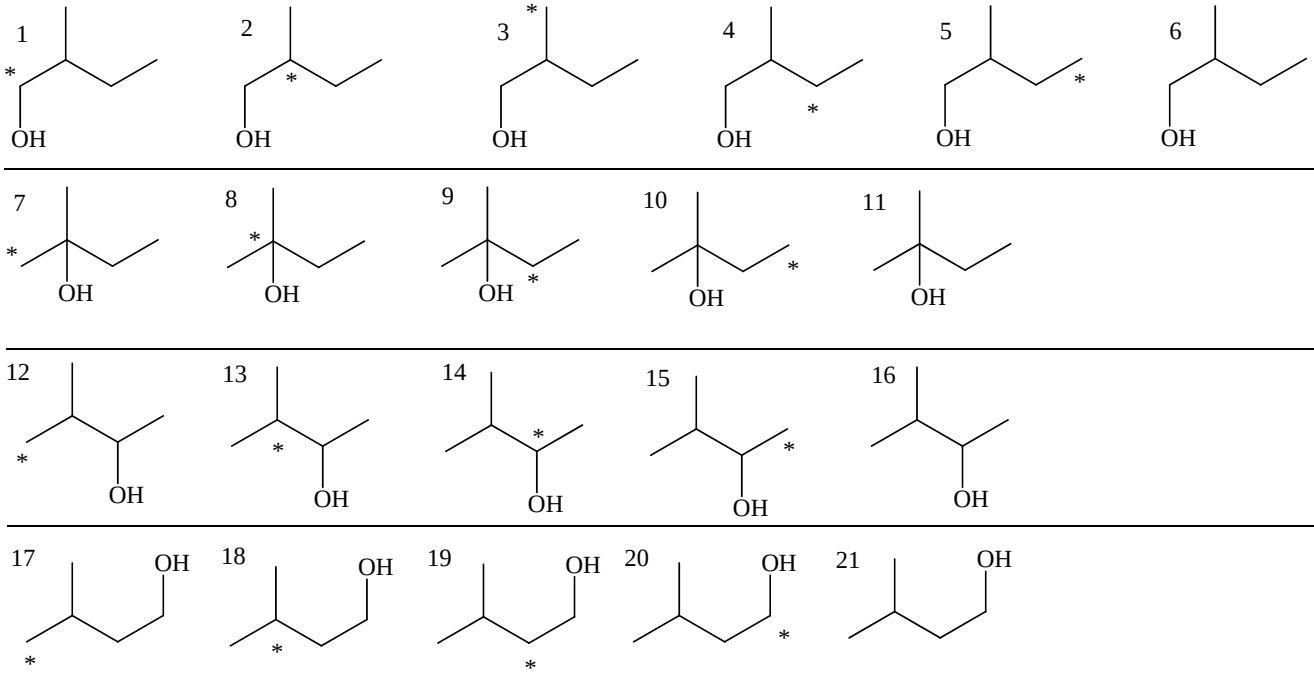


TM - 16

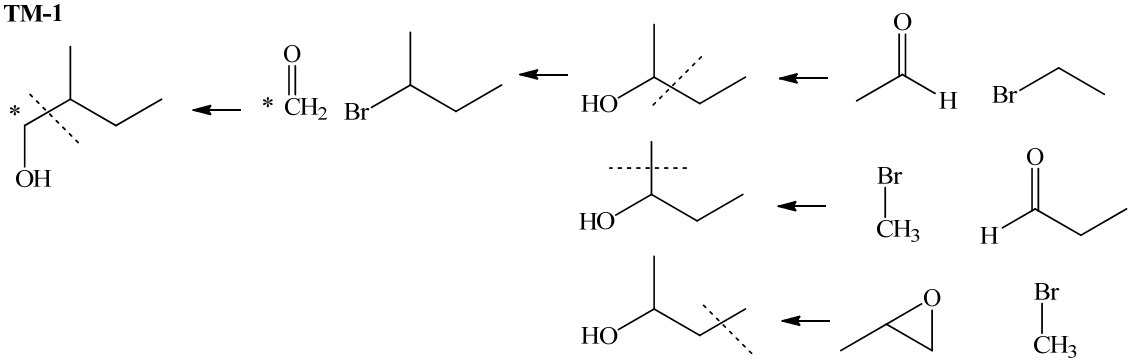


Examples – Target Molecules (TM - #)

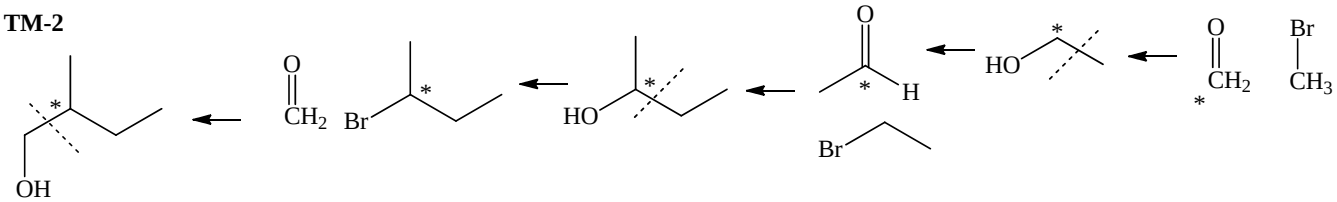
4C chain with methyl branch alcohols – Many approaches. Ran out of time to write them out. Ask, if questions. There are "hints" at possibilities that follow, but not ever step is shown.



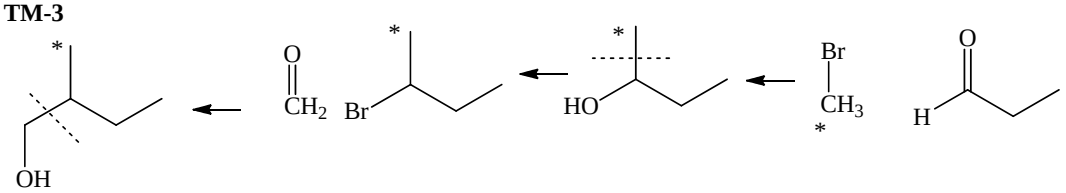
TM-1



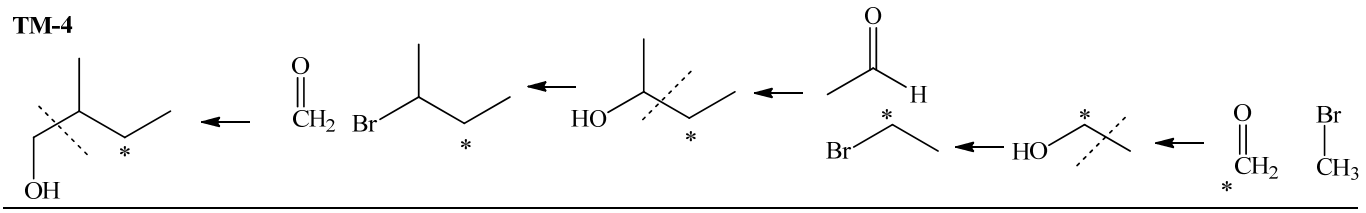
TM-2



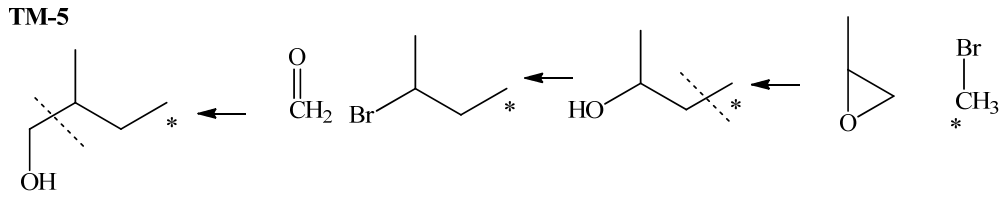
TM-3



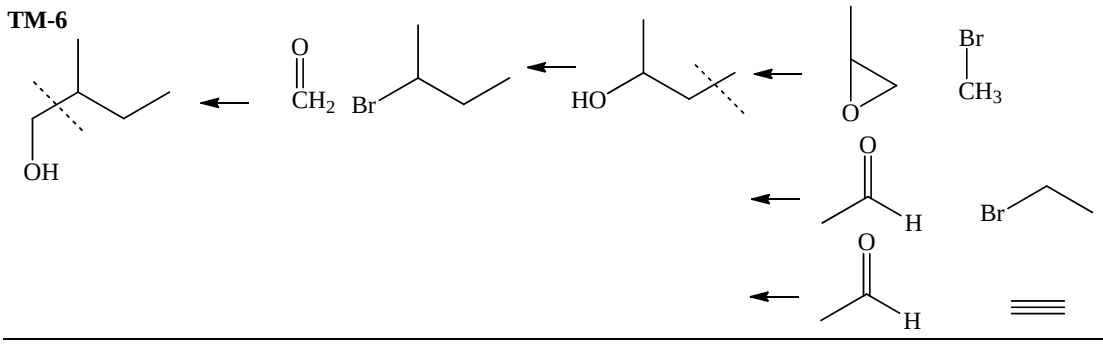
TM-4



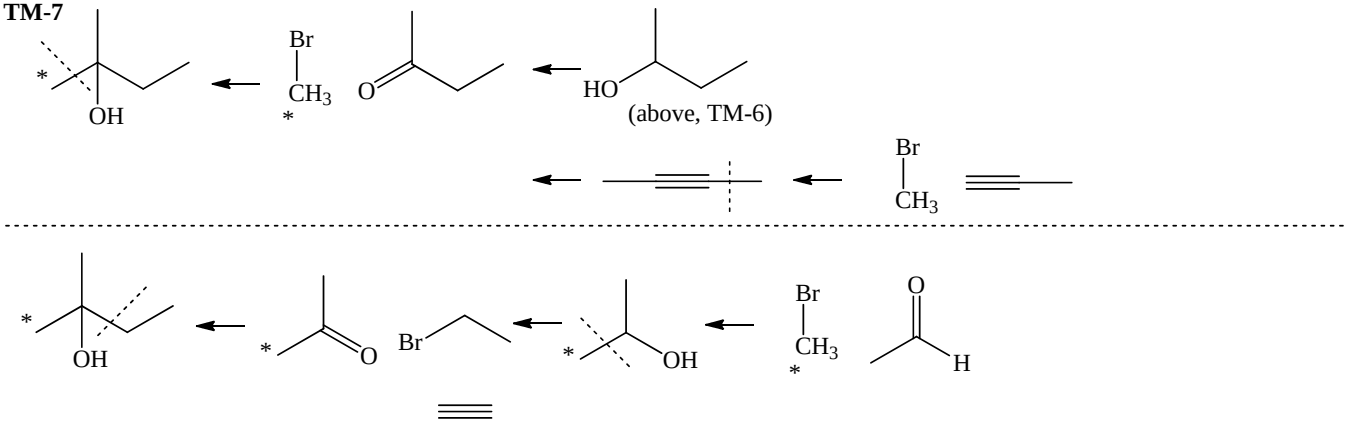
TM-5



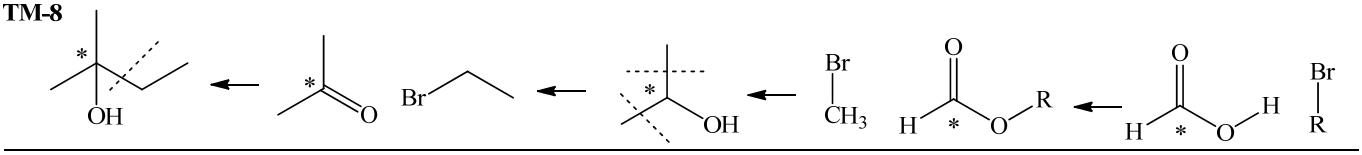
TM-6



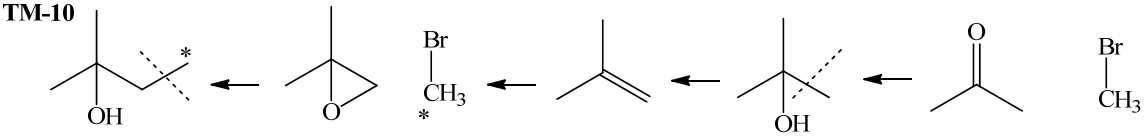
TM-7



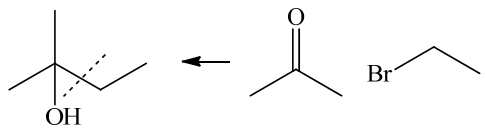
TM-8



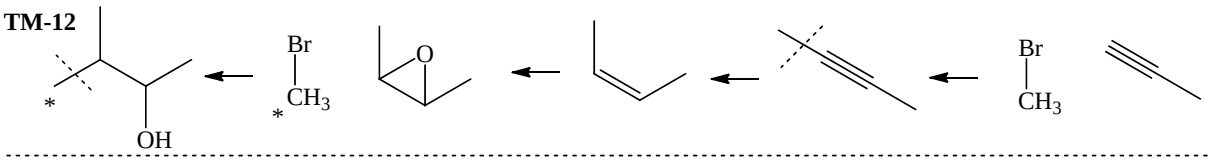
TM-10

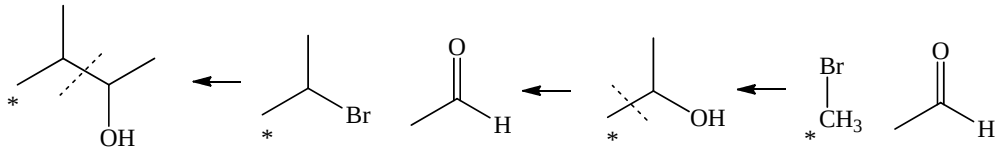


TM-11

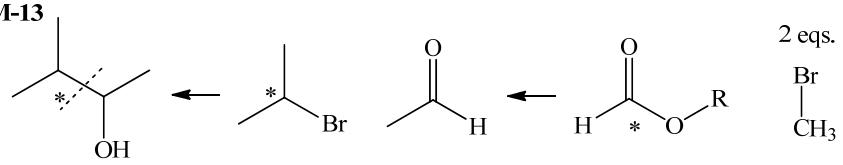


TM-12

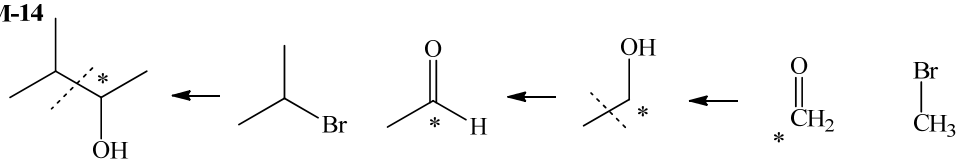




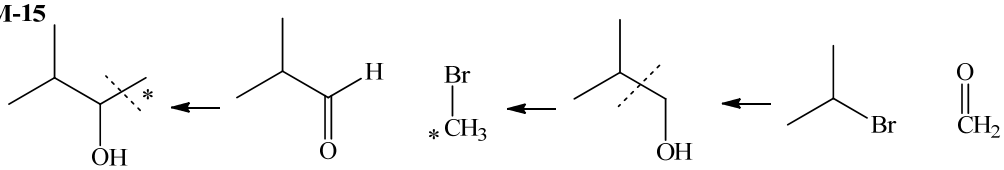
TM-13



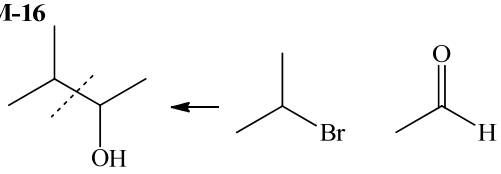
TM-14



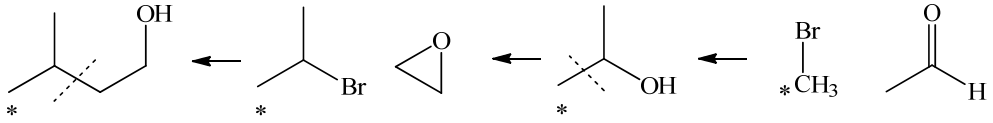
TM-15



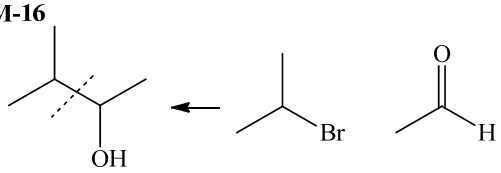
TM-16



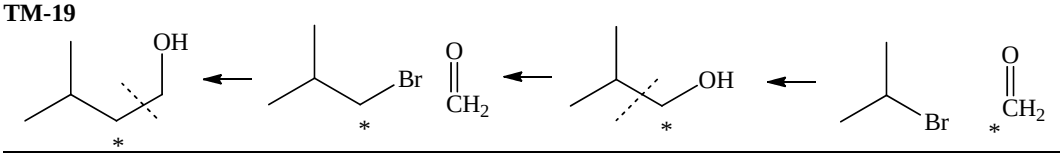
TM-17



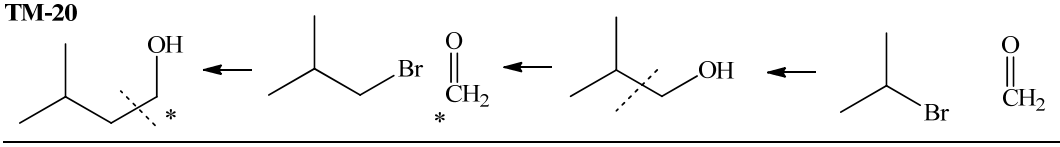
TM-16



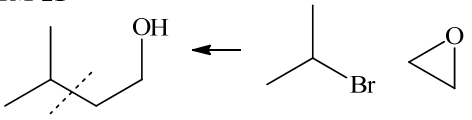
TM-19



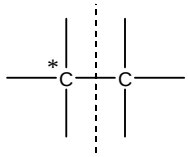
TM-20



TM-21

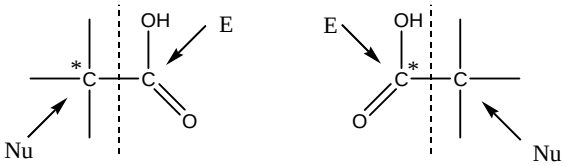


In our course every carbon-carbon bond made with asterisked carbon must be made with a nucleophile/electrophile reaction.

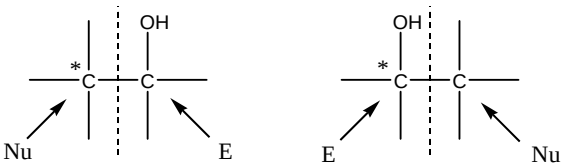


nucleophile (Nu) = ?

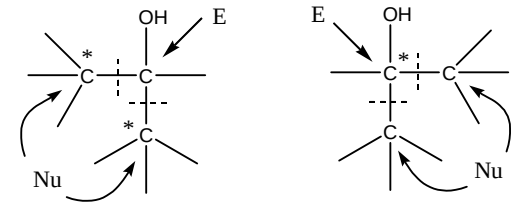
electrophile (E) = ?



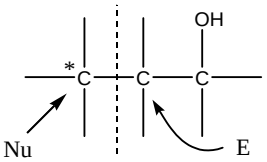
clue: COH group could have been C=O group (carbon dioxide).



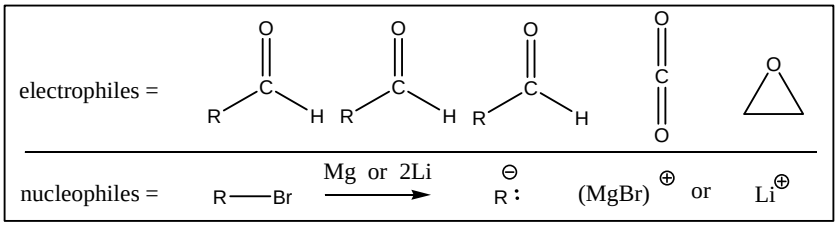
clue: COH group could have been C=O group (aldehyde or ketone).



clue: COH group could have been C=O group (ester).

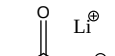
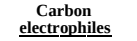
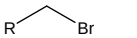
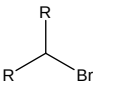
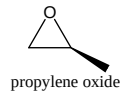
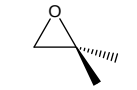
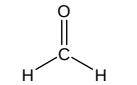
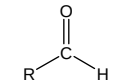
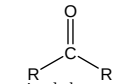
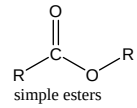
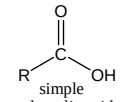
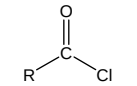
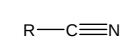
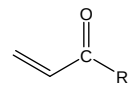


clue: COH group could have been an epoxide group.



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 Li cuprates	Li AlH_4 (LAH)	Na BH_4	diisobutylaluminium hydride (DIBAH)	 enolates
 methyl RX	NR	NR	alkynes	nitriles	2 RX coupling reaction	alkyls	alkyls	NR	S_N2 alkylation
 primary RX	NR	NR	alkynes	nitriles	2 RX coupling reaction	alkyls	alkyls	NR	S_N2 alkylation
 secondary RX	NR	NR	E2	nitriles	2 RX coupling reaction	alkyls	alkyls	NR	S_N2 alkylation
 ethylene oxide	1° ROH	1° ROH	1° ROH alkynes	1° ROH nitriles	1° ROH	1° ROH	1° ROH	NR	S_N2 - like opens epoxide
 propylene oxide	2° ROH	2° ROH	2° ROH alkynes	2° ROH nitriles	2° ROH	2° ROH	2° ROH	NR	S_N2 - like opens epoxide
 isobutylene oxide	3° ROH	3° ROH	3° ROH alkynes	3° ROH nitriles	3° ROH	3° ROH	3° ROH	NR	S_N2 - like opens epoxide
 methanal	1° ROH	1° ROH	1° ROH alkynes	cyanohydrin	NR	methanol	methanol	NR	acyl addition adds to C=O
 simple aldehydes	2° ROH	2° ROH	2° ROH alkynes	cyanohydrin	NR	1° ROH	1° ROH	NR	acyl addition adds to C=O
 simple ketones	3° ROH	3° ROH	3° ROH alkynes	cyanohydrin unless sterically hindered	NR	2° ROH	2° ROH	NR	acyl addition adds to C=O
 simple esters	3° ROH (Nu: twice)	3° ROH (Nu: twice)	NR	NR	1° ROH (Nu: twice)	1° ROH	NR	aldehydes	acyl substitution at C=O
 simple carboxylic acids	ketones (B: once Nu: once)	acid/base no net rxn	acid/base no net rxn	NR	acid/base no net rxn	acid/base no net rxn	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)	NR	NR	ketones	1° ROH	1° ROH	NR	acyl substitution at C=O
 simple nitriles	ketones	ketones	NR	NR	NR	1° amines (also amines from amides)	NR	aldehydes (also aldehydes from 3° amides)	ketones
carbon dioxide	carboxylic acids	carboxylic acids	carboxylic acids	NR	NR	NR	NR	NR	carboxylic acids
 α,β-unsaturated ketones	3° ROH	3° ROH	NR	NR	conjugate addition	alcohols	alcohols	NR	conjugate addition

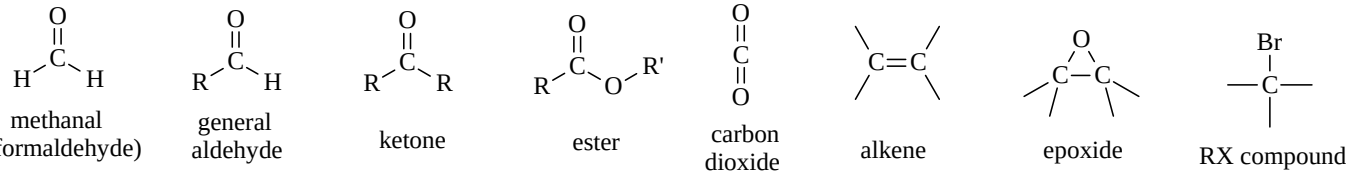
WK = normal workup to neutralize the reaction conditions. For the basic reactions (like above) above this would require mild acid neutralization (H_3O^+).
NR = no reaction or no productive result or not emphasized

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

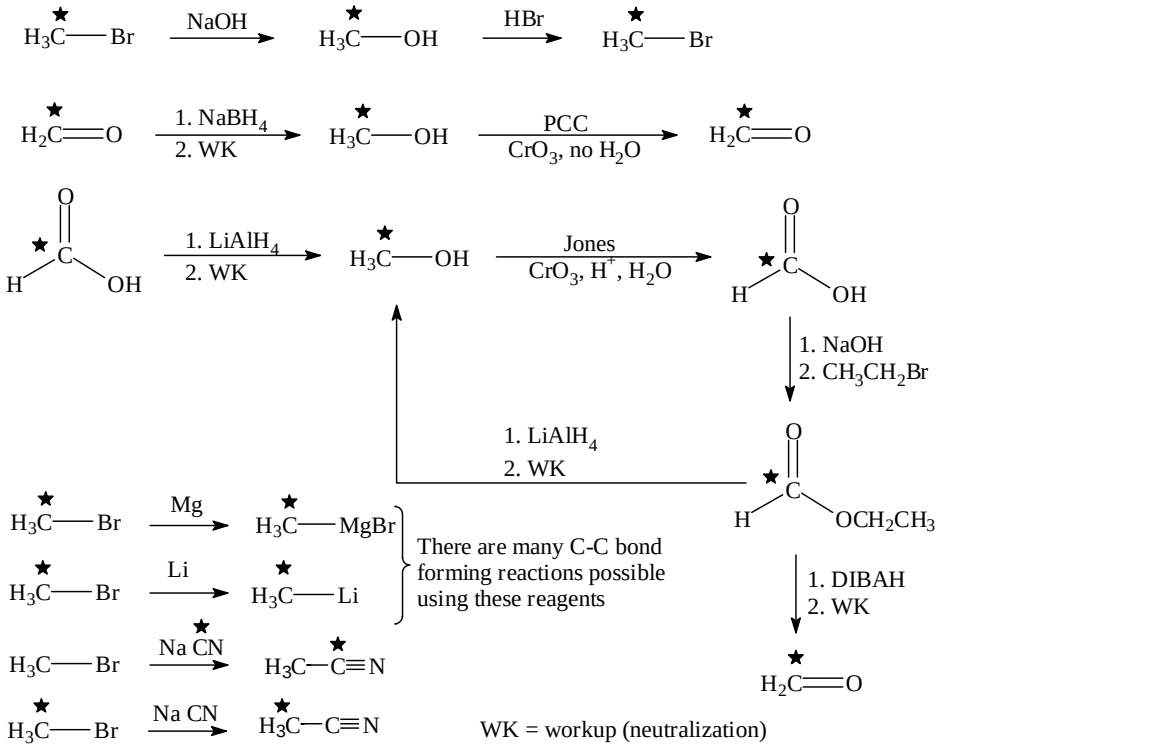
Use clues in the target molecule to determine what the last step could have been. Once you work back one step, use clues in that molecule to determine how you could work back one additional step. Repeat this process until you get to the necessary starting conditions, i.e. allowable ^{14}C starting units (*CH_4, *CO_2, Na*CN). These can be converted into other C1 molecules such as: *CH_3Br, *CH_3OH, *CH_2=O, H*CO_2H, H*CO_2R.. Until aromatic chemistry is covered bromobenzene is also available.

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 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.
5. What portion has to be added and how can we do that?

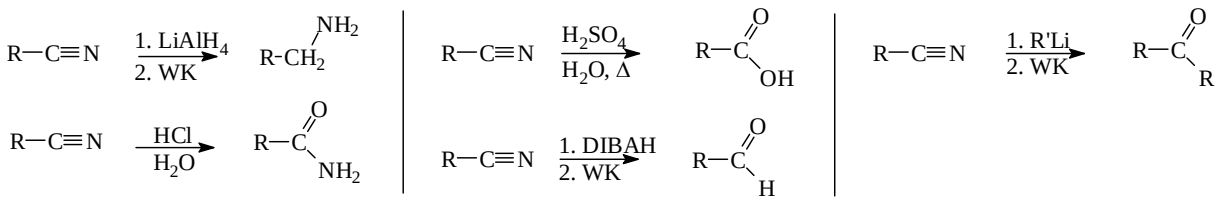
Starting possibilities to produce alcohols.



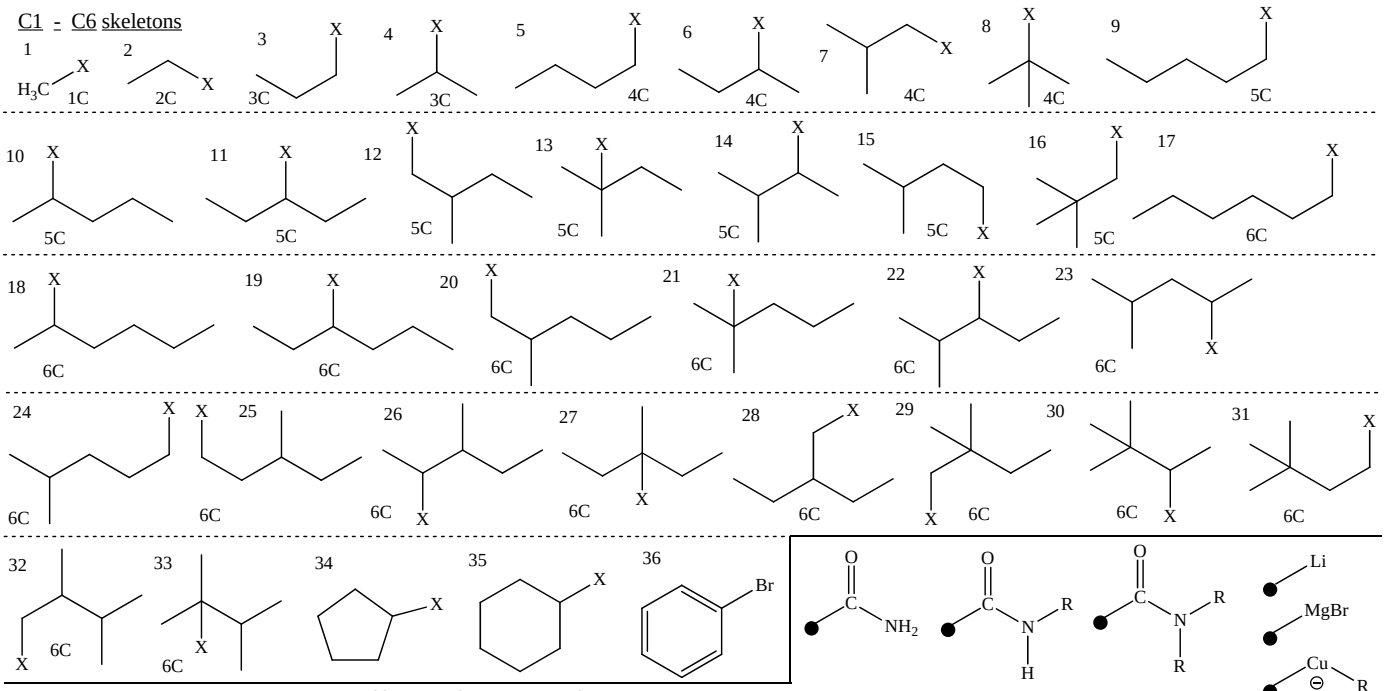
Some useful interconversions in ^{14}C syntheses (using 1C transformations).



Sample Reactions of Nitriles - further transformations to: amines, amides, carboxylic acids, aldehydes, ketones



C1 - C6 skeletons



Some skeletal patterns above are more difficult to fit with these functional group patterns than others.

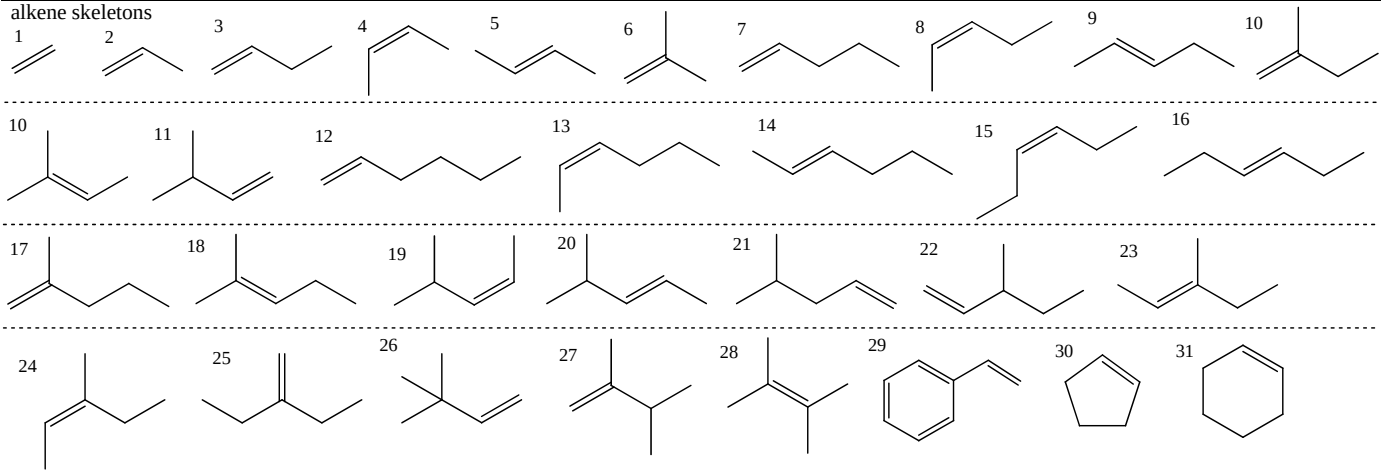
X = Br, OH, O–R, O(C=O)–R, NH_2, SH, S–R, C≡N, C≡C–R, C(=O)OH, C(=O)Cl, C(=O)O–R

ketone (C=O) - when in an internal position and not tertiary

aldehyde (-CH=O) - when X is on a terminal position

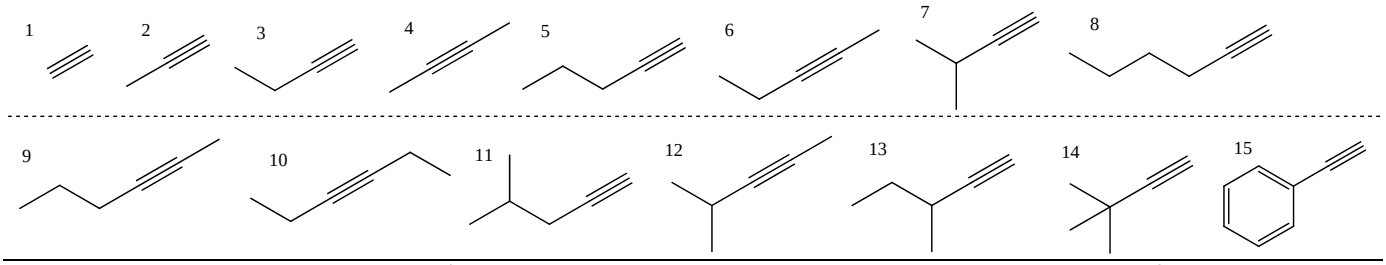
carboxylic acid (-CO_2H) - when X is on a terminal position

alkene skeletons



Every one of these alkenes could be transformed into epoxides, ROH and RBr (Markovnikov and anti-Markovnikov). Other typical alkene reactions conditions are listed in the first part of this document (along with many, many other reactions).

alkyne skeletons - remember that terminal acetylides do not react well with 2^o RX compounds



allylic alcohols ⟶ allylic carbonyls made from epoxides and LDA (can make α,β-unsaturated carbonyl compounds). Just a few examples are shown.