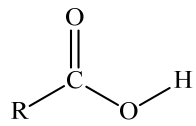
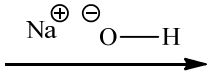
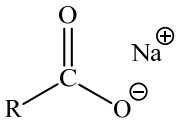
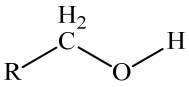
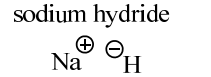
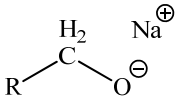
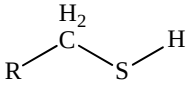
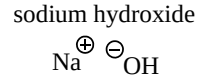
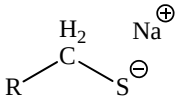
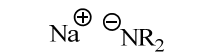
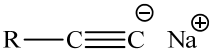
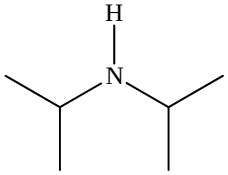
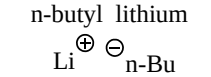
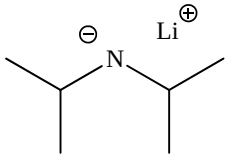
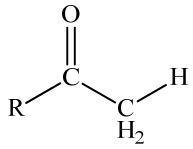
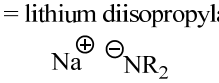
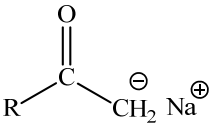
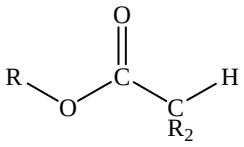
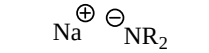
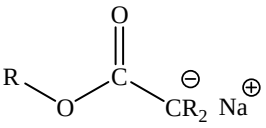
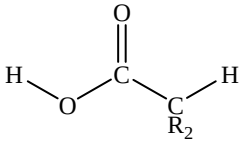
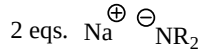
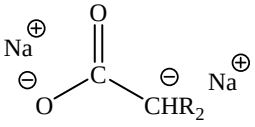
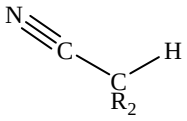
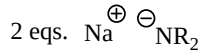
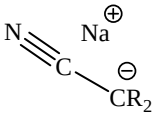
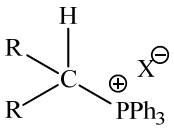
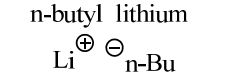
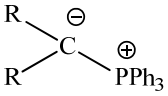
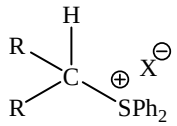
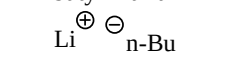
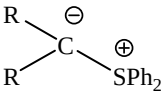
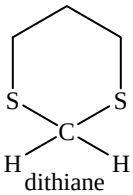
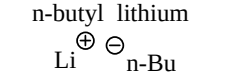
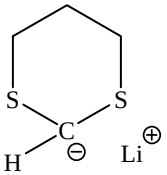
Organic Reactions Summary

For Use as a Study Guide

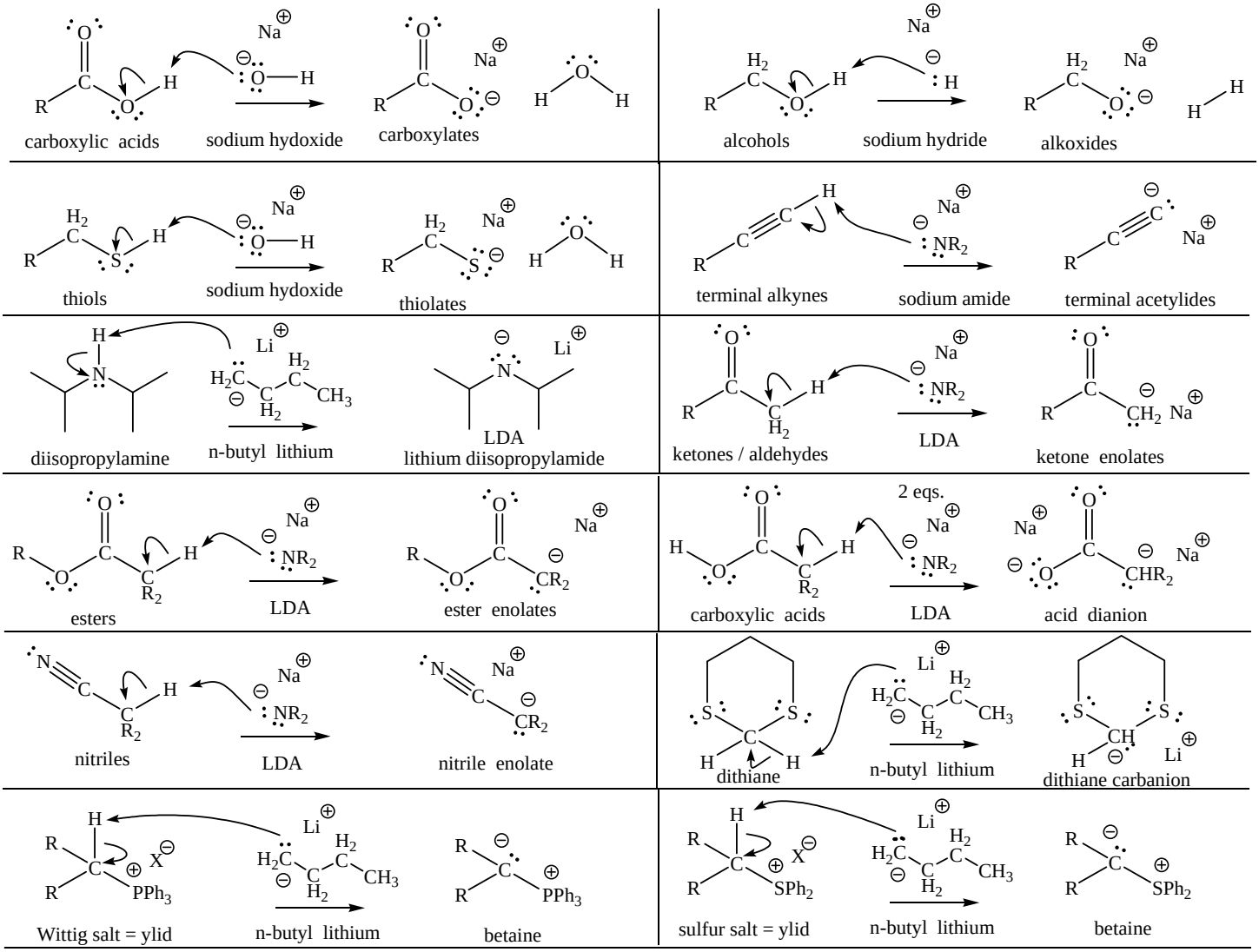
Beauchamp

Important acid/base reactions used in the examples below. Write out every one of these easy mechanisms.

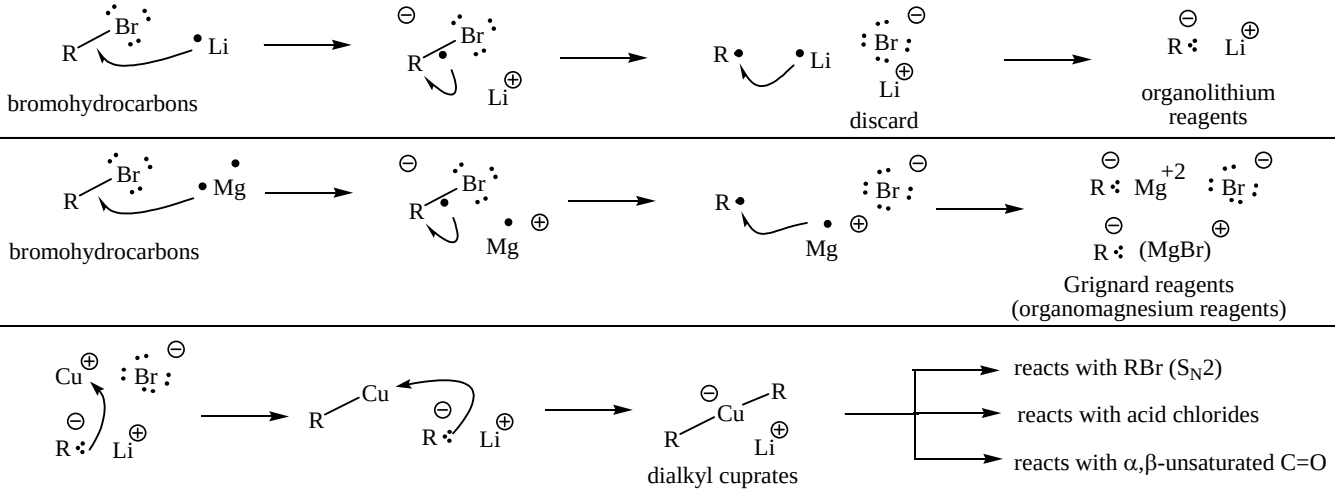
Acid	Base	New Base	Comments
 carboxylic acids	sodium hydroxide  $K_{eq} = \frac{K_a(RCO_2H)}{K_a(H_2O)}$ $K_{eq} = \frac{10^{-5}}{10^{-16}} = 10^{+11}$	 carboxylates	Carboxylates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX
 alcohols	sodium hydride  $K_{eq} = \frac{K_a(ROH)}{K_a(H_2)}$ $K_{eq} = \frac{10^{-17}}{10^{-35}} = 10^{+18}$	 alkoxides	alkoxides are OK nucleophiles, S_N2 > E2 at Me and 1° RX, and strong bases, E2 > S_N2 at 2° and 3°RX.
 thiols	sodium hydroxide  $K_{eq} = \frac{K_a(RSH)}{K_a(H_2O)}$ $K_{eq} = \frac{10^{-8}}{10^{-16}} = 10^{+8}$	 thiolates	thiolates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX, and strong bases, E2 > S_N2 at 3°RX.
 terminal alkynes	sodium amide  $K_{eq} = \frac{K_a(RCCH)}{K_a(HNR_2)}$ $K_{eq} = \frac{10^{-25}}{10^{-37}} = 10^{+12}$	 terminal acetylides	terminal acetylides are OK nucleophiles, S_N2 > E2 at Me and 1° RX, and strong bases, E2 > S_N2 at 2° and 3°RX.
 diisopropylamine	n-butyl lithium  $K_{eq} = \frac{K_a(HNR_2)}{K_a(H\text{-}C_4H_9)}$ $K_{eq} = \frac{10^{-37}}{10^{-50}} = 10^{+13}$	 LDA = lithium diisopropylamide	LDA is a very strong base that is also very sterically hindered, it always acts as a base in our course.
 ketones / aldehydes	LDA = lithium diisopropylamide  $K_{eq} = \frac{K_a(RCOCH_3)}{K_a(HNR_2)}$ $K_{eq} = \frac{10^{-20}}{10^{-37}} = 10^{+17}$	 ketone enolates	enolates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX, and strong bases, E2 > S_N2 at 3°RX.

 esters	LDA = lithium diisopropylamide  $K_{eq} = \frac{K_a(ROCOCH_3)}{K_a(HNR_2)}$ $K_{eq} = \frac{10^{-25}}{10^{-37}} = 10^{+12}$	 ester enolates	enolates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX, and strong bases, E2 > S_N2 at 3°RX.
 carboxylic acids	LDA = lithium diisopropylamide  $K_{eq} = \frac{K_a(^{\ominus}O_2CCH_3)}{K_a(HNR_2)}$ $K_{eq} = \frac{10^{-25}}{10^{-37}} = 10^{+12}$	 acid dianion	enolates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX, and strong bases, E2 > S_N2 at 3°RX.
 nitriles	LDA = lithium diisopropylamide  $K_{eq} = \frac{K_a(^{\ominus}O_2CCH_3)}{K_a(HNR_2)}$ $K_{eq} = \frac{10^{-30}}{10^{-37}} = 10^{+7}$	 nitrile enolate	enolates are good nucleophiles, S_N2 > E2 at Me, 1° and 2° RX, and strong bases, E2 > S_N2 at 3°RX.
 Wittig salt = ylid	n-butyl lithium  $K_{eq} = \frac{K_a(HCR_2PPh_3)}{K_a(H\text{-}C_4H_9)}$ $K_{eq} = \frac{10^{-33}}{10^{-50}} = 10^{+17}$	 betaine	n-butyl lithium removes proton from Wittig salt and makes a good nucleophile at ketones and aldehydes, forming alkenes.
 sulfur salt = ylid	n-butyl lithium  $K_{eq} = \frac{K_a(HCR_2SPh_2)}{K_a(H\text{-}C_4H_9)}$ $K_{eq} = \frac{10^{-33}}{10^{-50}} = 10^{+17}$	 betaine	n-butyl lithium removes proton from sulfur salt and makes a good nucleophile at ketones and aldehydes, forming epoxides.
 dithiane	n-butyl lithium  $K_{eq} = \frac{K_a(dithiane)}{K_a(H\text{-}C_4H_9)}$ $K_{eq} = \frac{10^{-33}}{10^{-50}} = 10^{+17}$	 dithiane carbanion	n-butyl lithium removes proton from dithiane and makes a good nucleophile at all of our electrophiles. It can react once or twice in S_N2 reactions. Sulfur acetal forms carbonyl group after hydrolysis using Hg^{+2}. Makes aldehydes and ketones.

Arrow-Pushing schemes for the above reactions



Organometallics used in our course (Mg, Li and Cu)



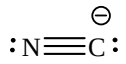
S_N2 versus E2 choices at 2^oRX.

At secondary RX (X= OTs, I, Br, Cl) S_N2 and E2 products are in close competition with each other. Anions whose conjugate acids have higher pK_a's (stronger bases have weaker acids) generally produce more E2 relative to S_N2. The examples that we will emphasize at 2^oRX centers are carboxlyates (S_N2 > E2) vs hydroxide and alkoxides (E2 > S_N2), and cyanide (S_N2 > E2) vs terminal acetylides (E2 > S_N2), azide (S_N2 > E2) vs dialkylamides (E2 > S_N2) and metal hydrides (S_N2 > E2) vs simple hydride (E2 > S_N2). Higher basicity and steric hindrance in either RX or the electron pair donor also favors E2 > S_N2.

The following examples show similar looking base/nucleophiles (used in our course) that react differently with 2^oRX structures. (They all react by S_N2 at methyl and 1^oRX and they all react by E2 at 3^oRX.) It is the reactions at 2^o RX centers that are ambiguous.

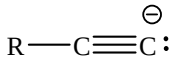
2^o RX structures are the most ambiguous.

Less basic, so S_N2 > E2.



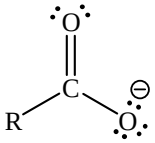
cyanide
pK_a of conjugate acid = 9

More basic, so E2 > S_N2.



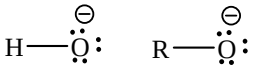
terminal acetylides
pK_a of conjugate acid = 25

Less basic, so S_N2 > E2.



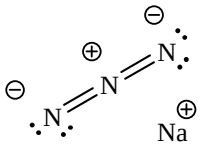
carboxylates
pK_a of conjugate acid = 5

More basic, so E2 > S_N2.



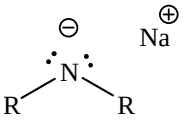
hydroxide and alkoxides
pK_a of conjugate acid = 16-19

Less basic, so S_N2 > E2.



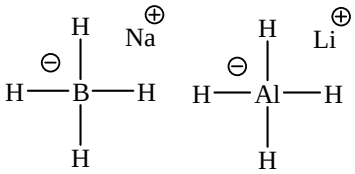
azide
pK_a of conjugate acid = 5

More basic, so E2 > S_N2.



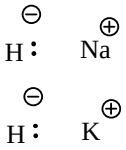
dialkyl amides
pK_a of conjugate acid = 37

Less basic, so S_N2 > E2.



sodium borohydride
lithium aluminum hydride
pK_a of conjugate acid = ?

More basic, so E2 > S_N2.

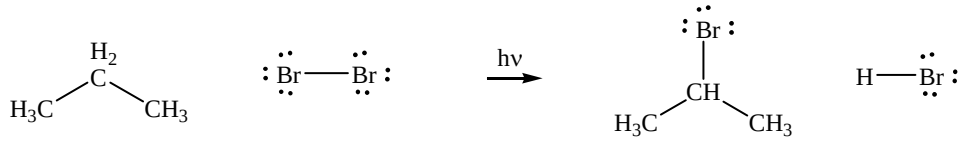


hydrides
pK_a of conjugate acid = 37

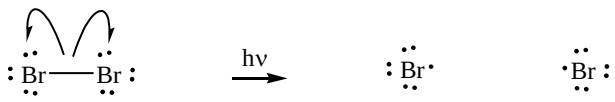
1. Making RBr from alkane and alkene hydrocarbons and alcohols

a. RBr from alkanes - mechanism using Br_2 / hν for free radical substitution of alkane sp^3 C-H bonds to form sp^3 C-Br bonds at the weakest C-H bond.

overall reaction



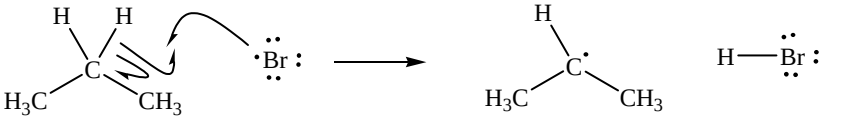
1. initiation



weakest bond ruptures first

ΔH = 46 kcal/mole

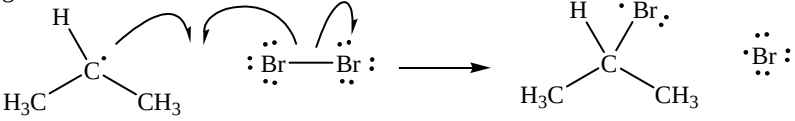
2a propagation



BE = +95 kcal/mole
BE = -88 kcal/mole

ΔH = +7 kcal/mole (overall)

2b propagation

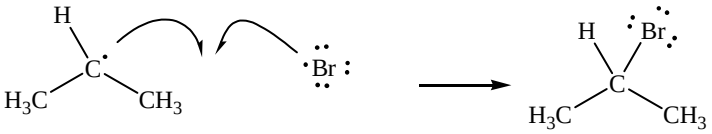


BE = +46 kcal/mole
BE = -68 kcal/mole

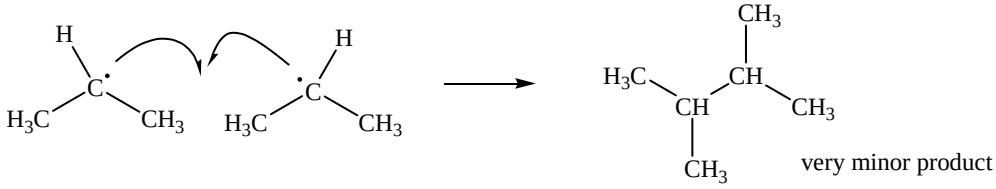
ΔH = -22 kcal/mole (overall)

ΔH = -15 both steps

3. termination = combination of two free radicals - relatively rare because free radicals are at low concentrations



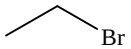
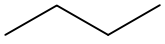
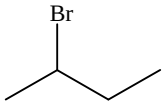
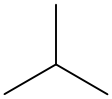
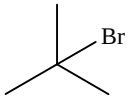
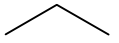
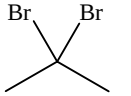
ΔH = -68 kcal/mole

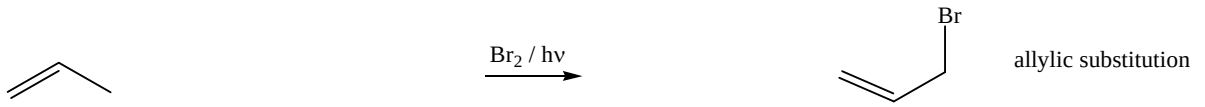


ΔH = -80 kcal/mole

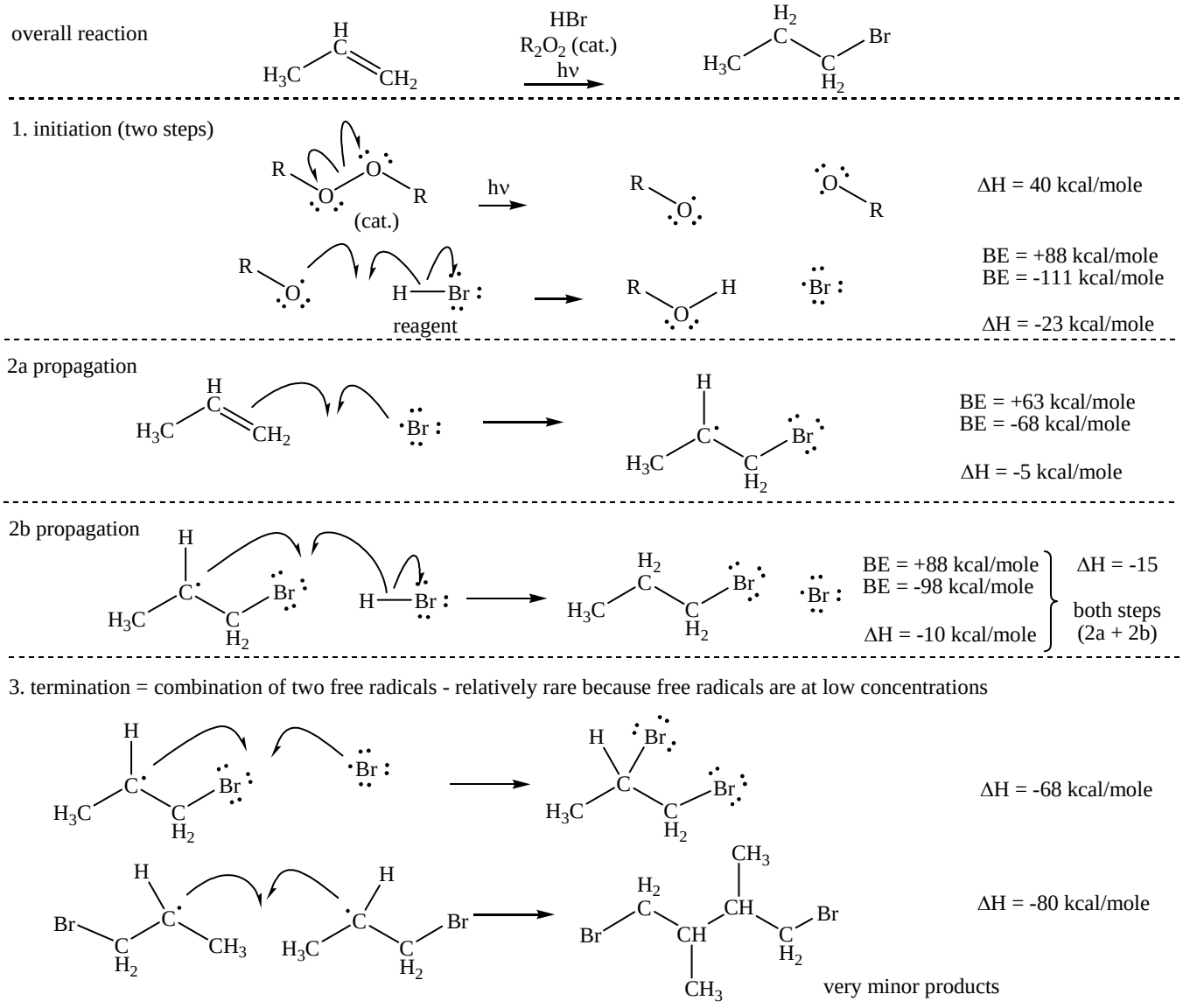
very minor product

Example reactions

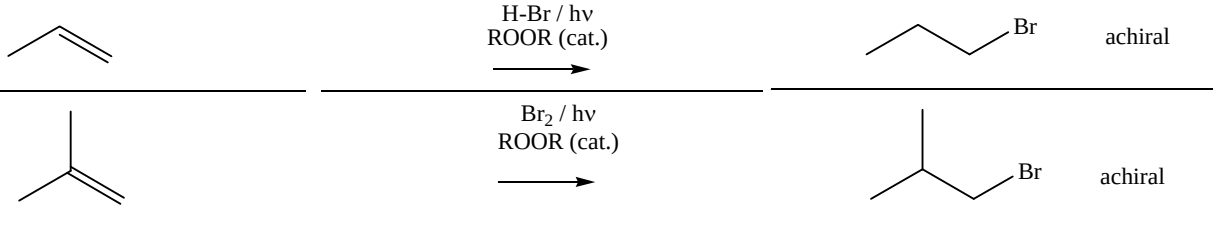
CH_4	Br_2 / hν	H_3C—Br	achiral
	Br_2 / hν		achiral
	Br_2 / hν		enantiomers (R and S)
	Br_2 / hν		achiral
	2 Br_2 / hν		can do E2 twice, to make alkynes

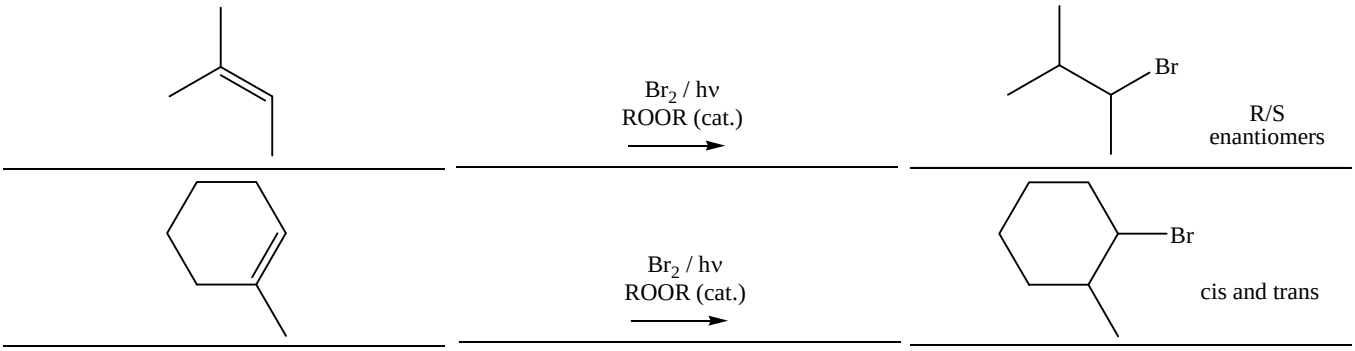


b. RBr from alkenes (anti-Markovnikov addition of HBr using free radical chemistry): mechanism using HBr / ROOR / hν for free radical addition to alkane pi bonds (anti-Markovnikov addition = Br adds to less substituted position to form most stable free radical intermediate, and then H adds to more substituted position)

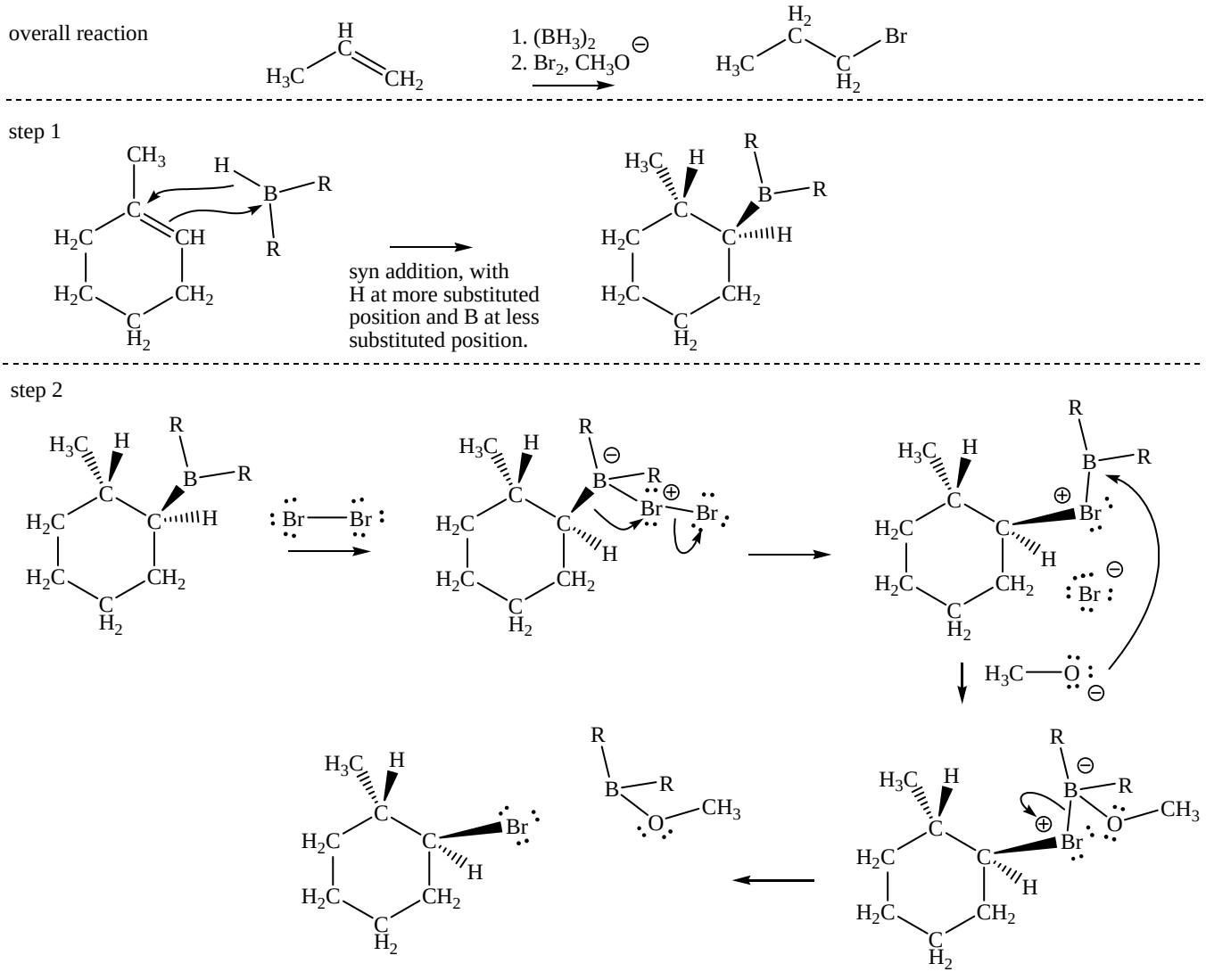


Example reactions

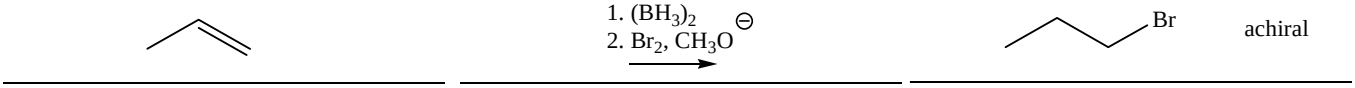


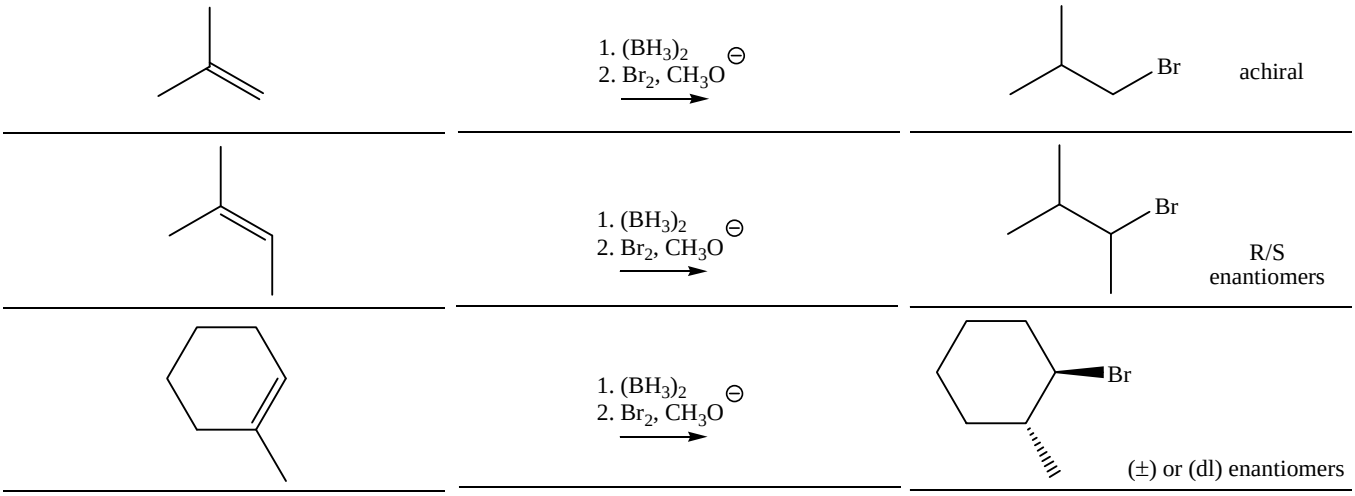


c. RBr from alkenes (anti-Markovnikov addition of HBr using borane chemistry): mechanism using 1. BH_3 2. Br_2 / CH_3O^- for anti-Markovnikov addition of H-Br to alkane pi bonds (concerted, syn addition of H-BH_2 to alkene pi bond, followed by complex with Br_2 and migration of R group to Br)



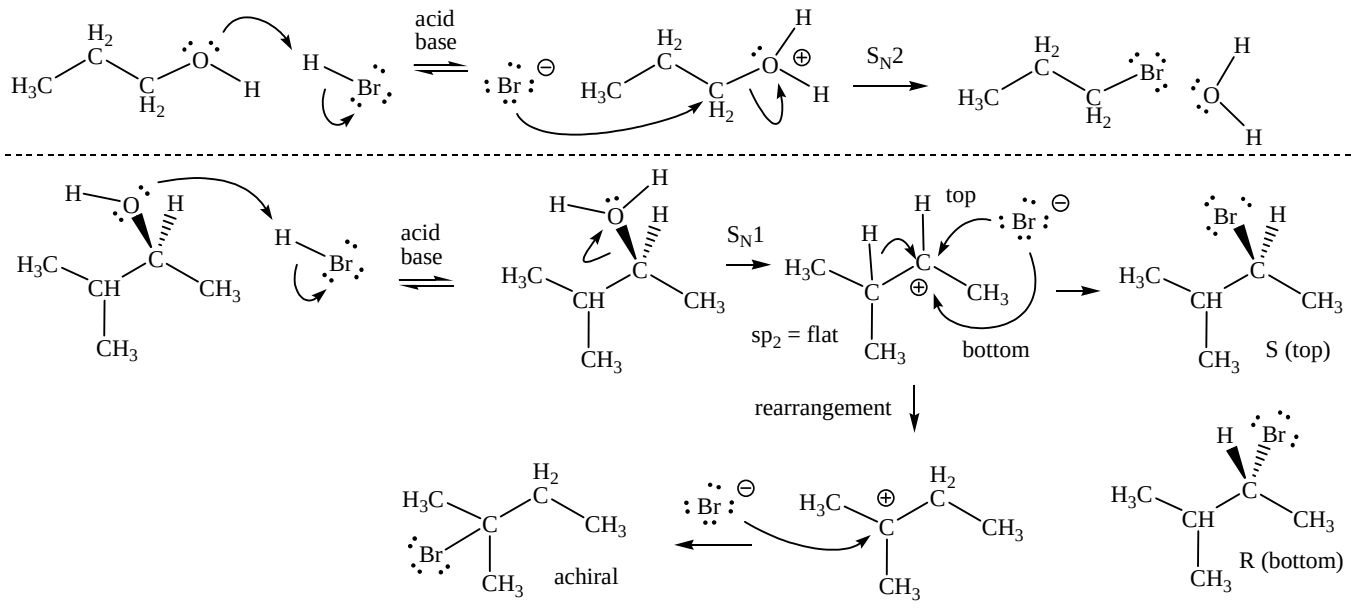
Example reactions



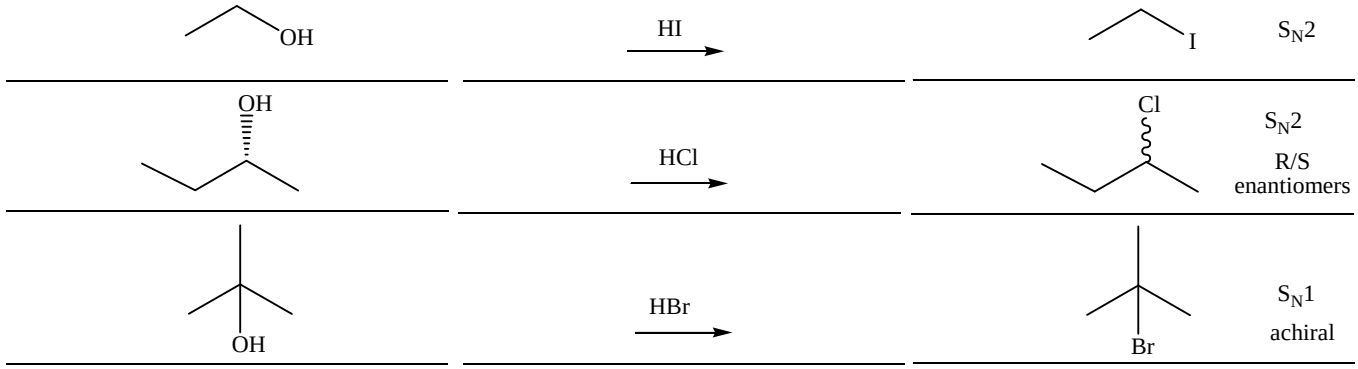


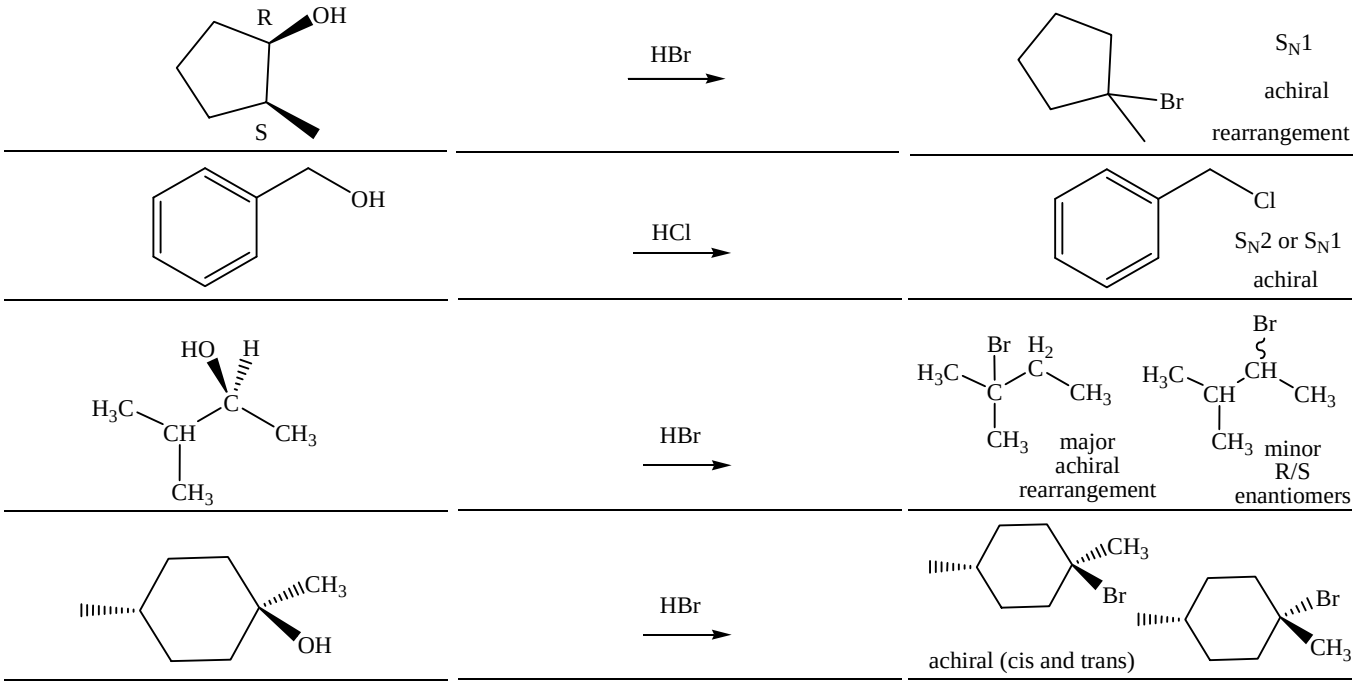
d. RBr from alcohols:

i. mechanism using HBr S_N2 at methyl and 1° ROH; S_N1 at 2° and 3° ROH, with possibility of rearrangements

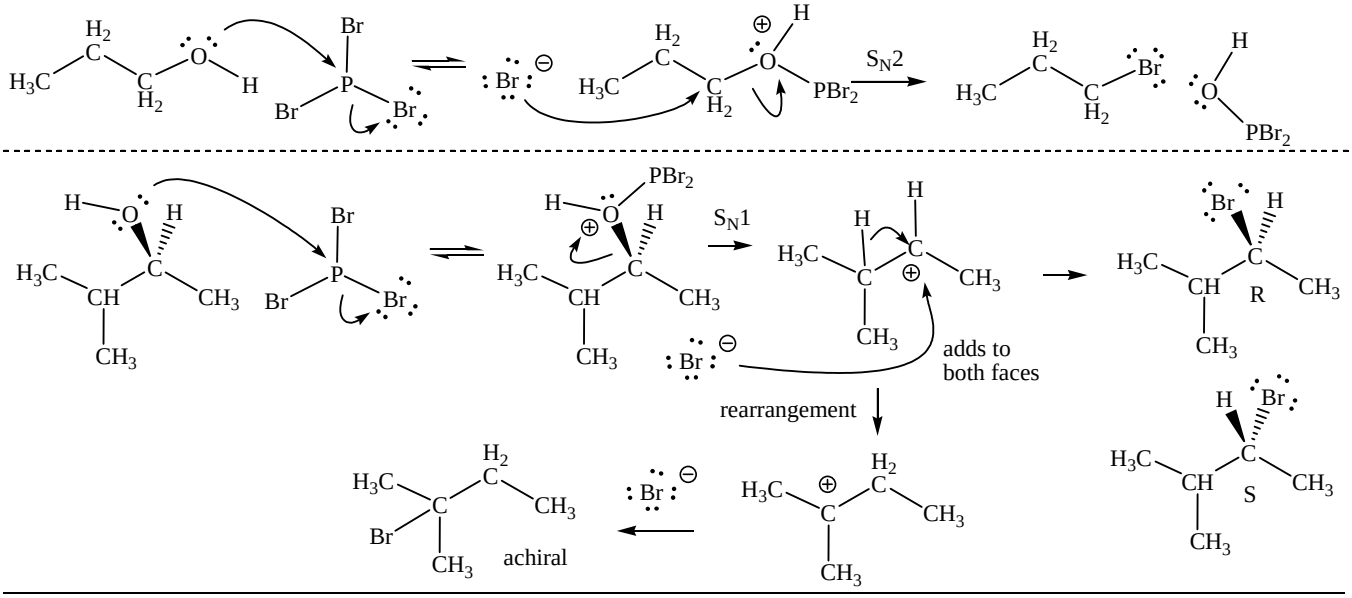


Example reactions

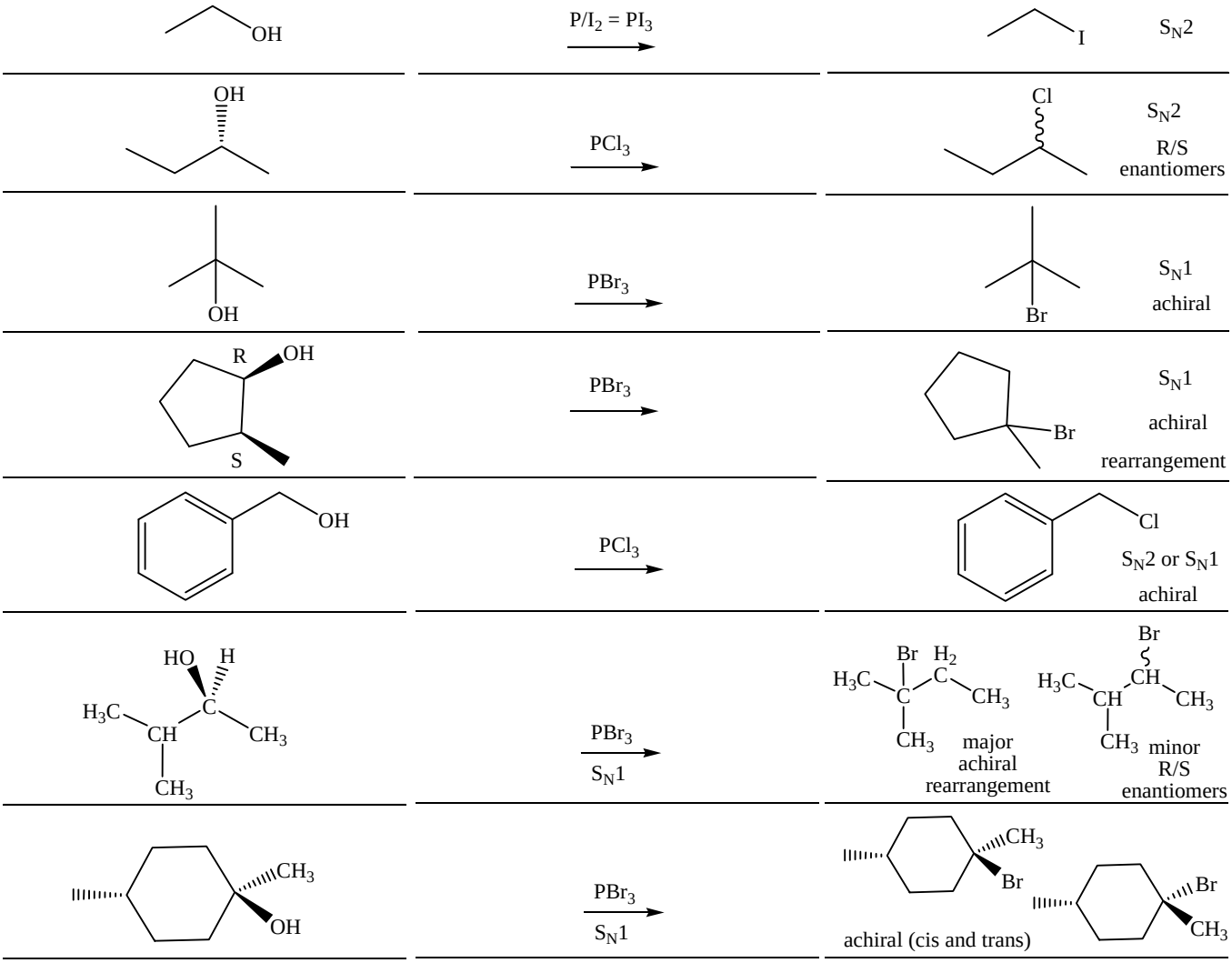




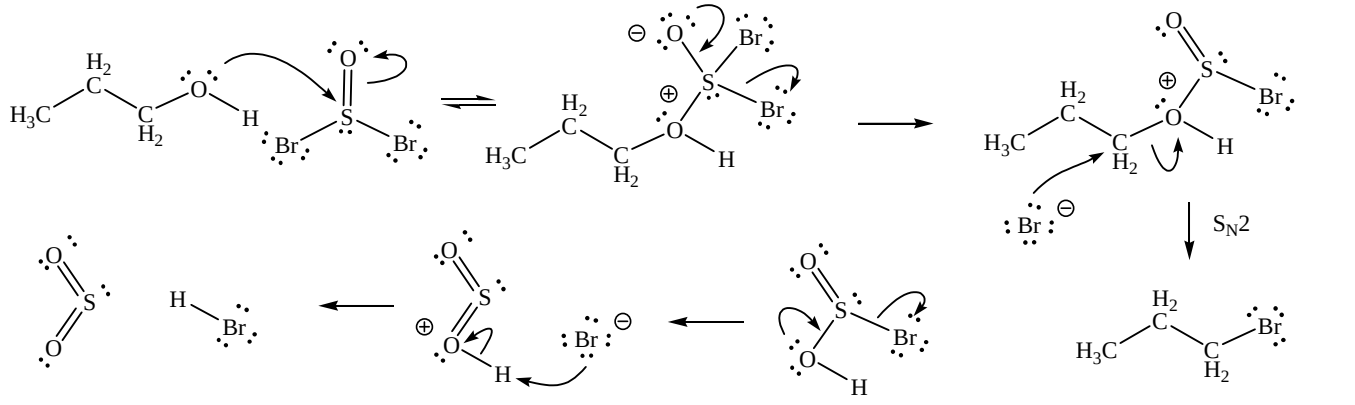
ii. mechanism using PBr_3 : S_N2 at methyl and 1° ROH; S_N1 at 2° and 3° ROH, with possibility of rearrangements

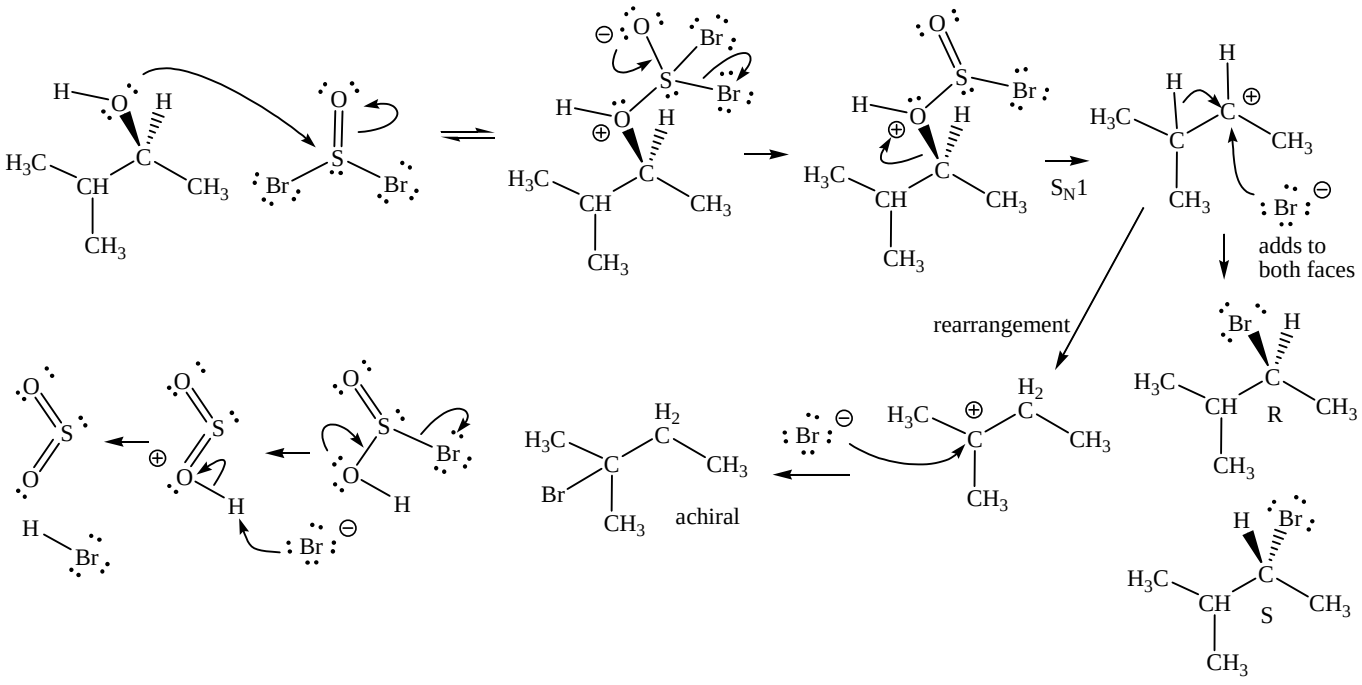


Example reactions

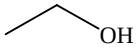
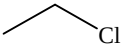
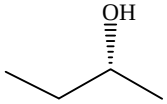
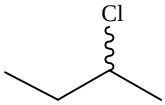
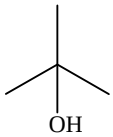
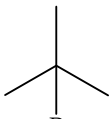
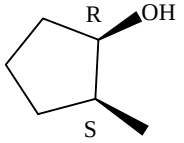
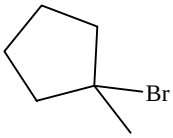
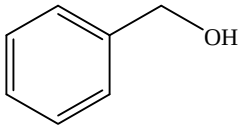
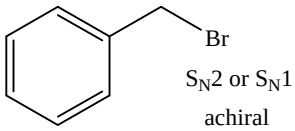
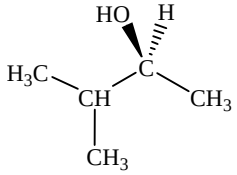
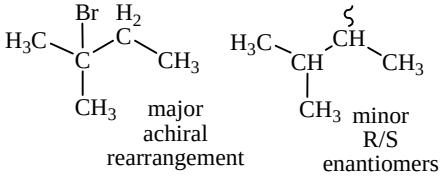


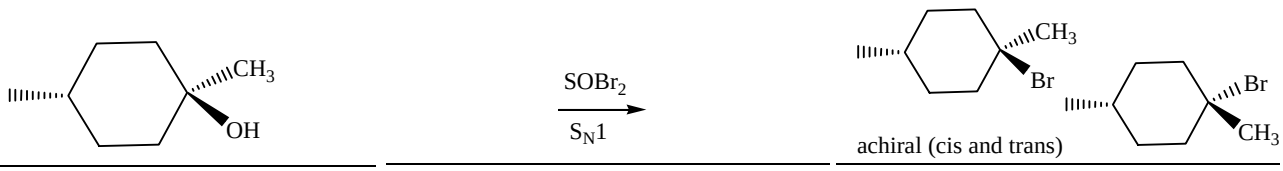
iii. mechanism using $SOBr_2$ S_N2 at methyl and 1° ROH; S_N1 at 2° and 3° ROH, with possibility of rearrangements



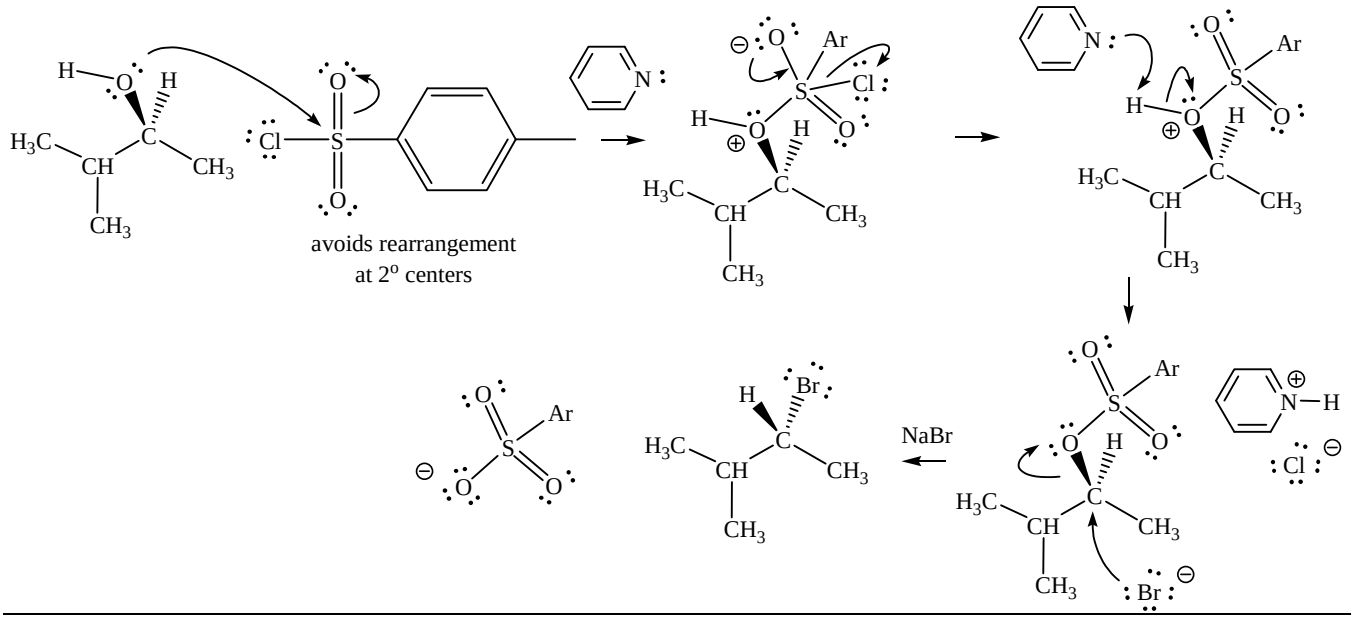


Example reactions

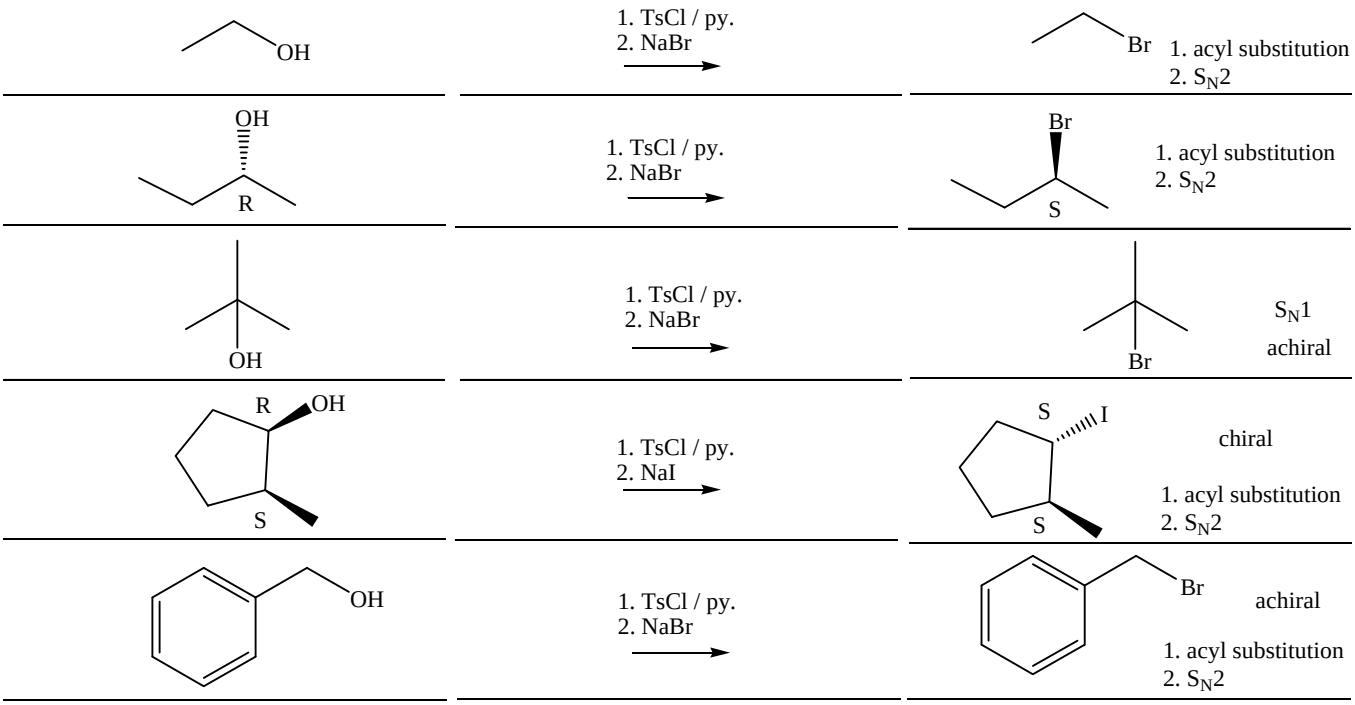
	$SOCl_2$	 S_N2
	$SOCl_2$	 S_N2 R/S enantiomers
	$SOBr_2$	 S_N1 achiral
	$SOBr_2$	 S_N1 achiral rearrangement
	$SOBr_2$	 S_N2 or S_N1 achiral
	$SOBr_2$ S_N1	 major achiral rearrangement; minor R/S enantiomers

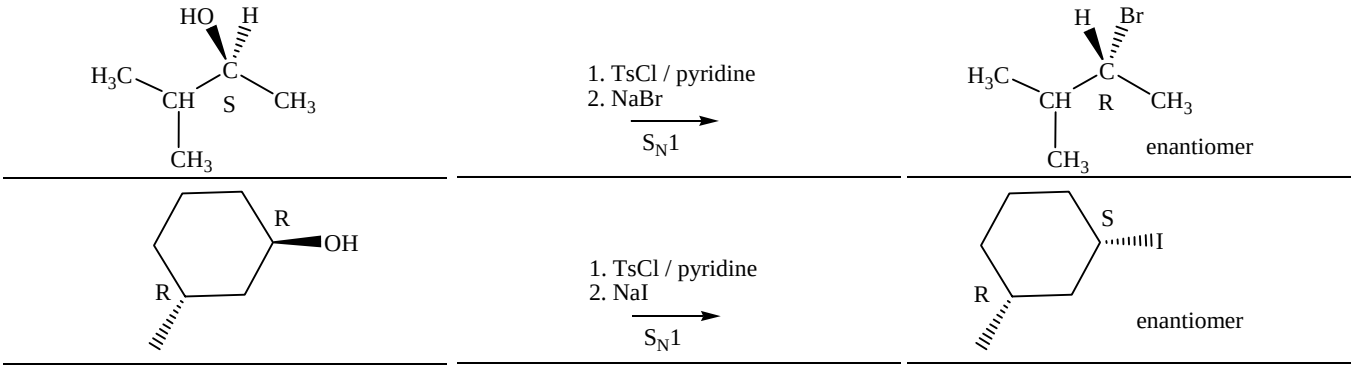


iv mechanism using 1. TsCl/pyridine 2. NaBr S_N2 at methyl, 1° and 2° ROH, avoids rearrangements



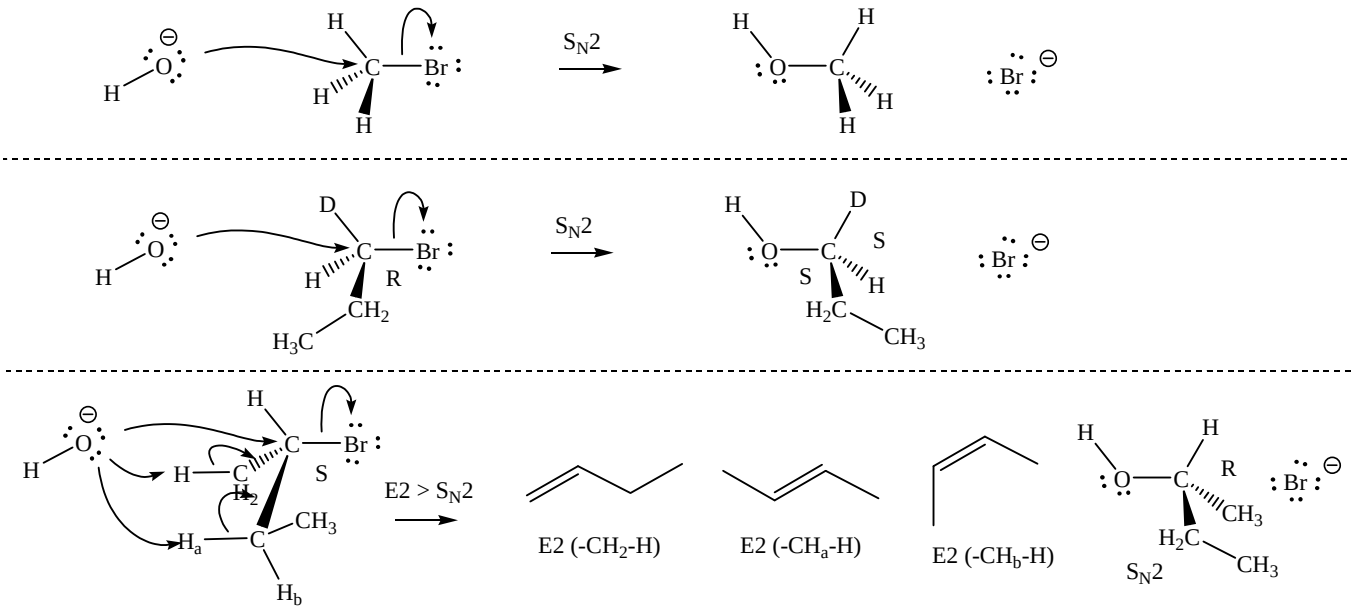
Example reactions



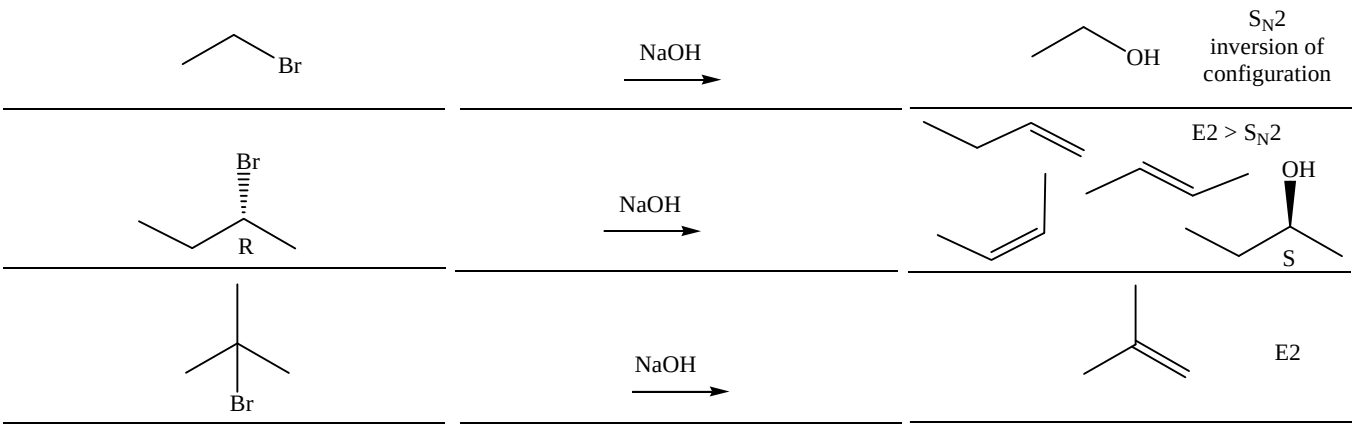


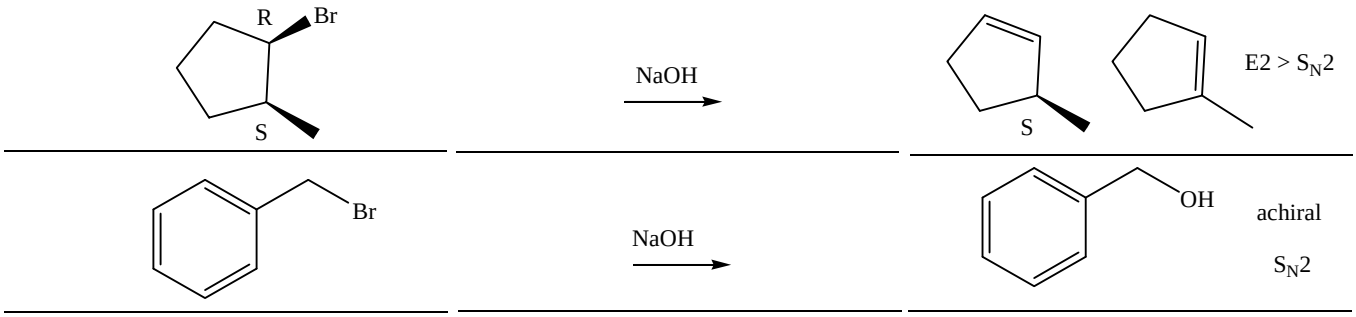
2. S_N2 reactions using RBr compounds:

a. mechanisms using NaOH, S_N2 at methyl and 1° RBr; E2 > S_N2 at 2° and only E2 at 3° RBr,

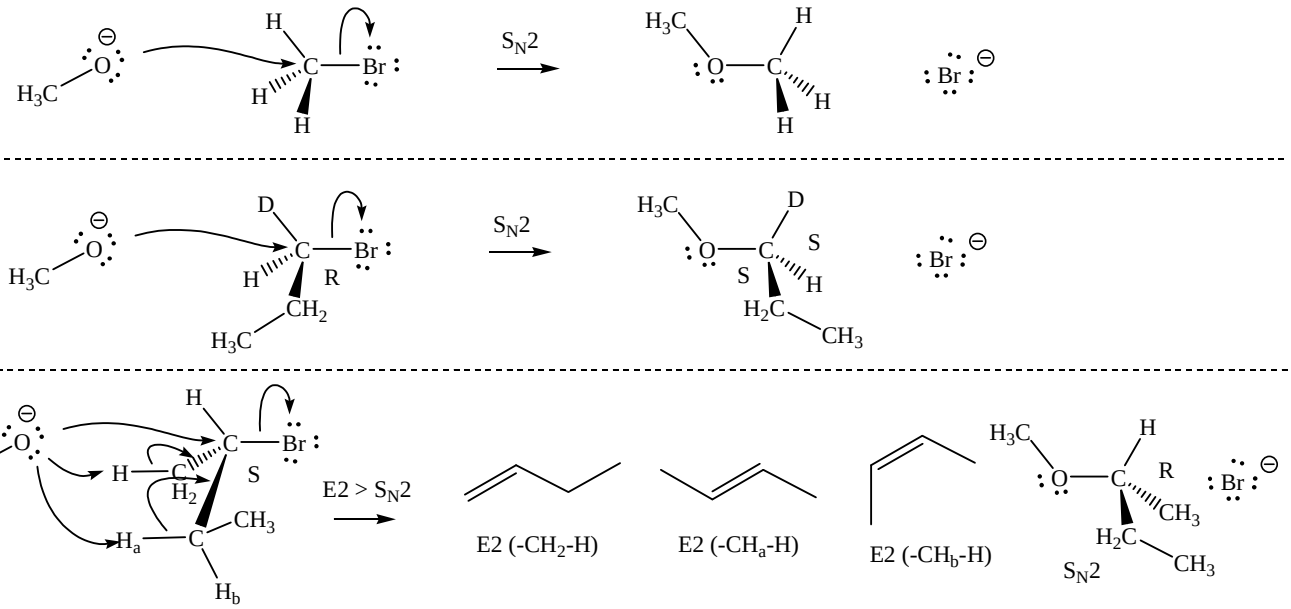


Example reactions

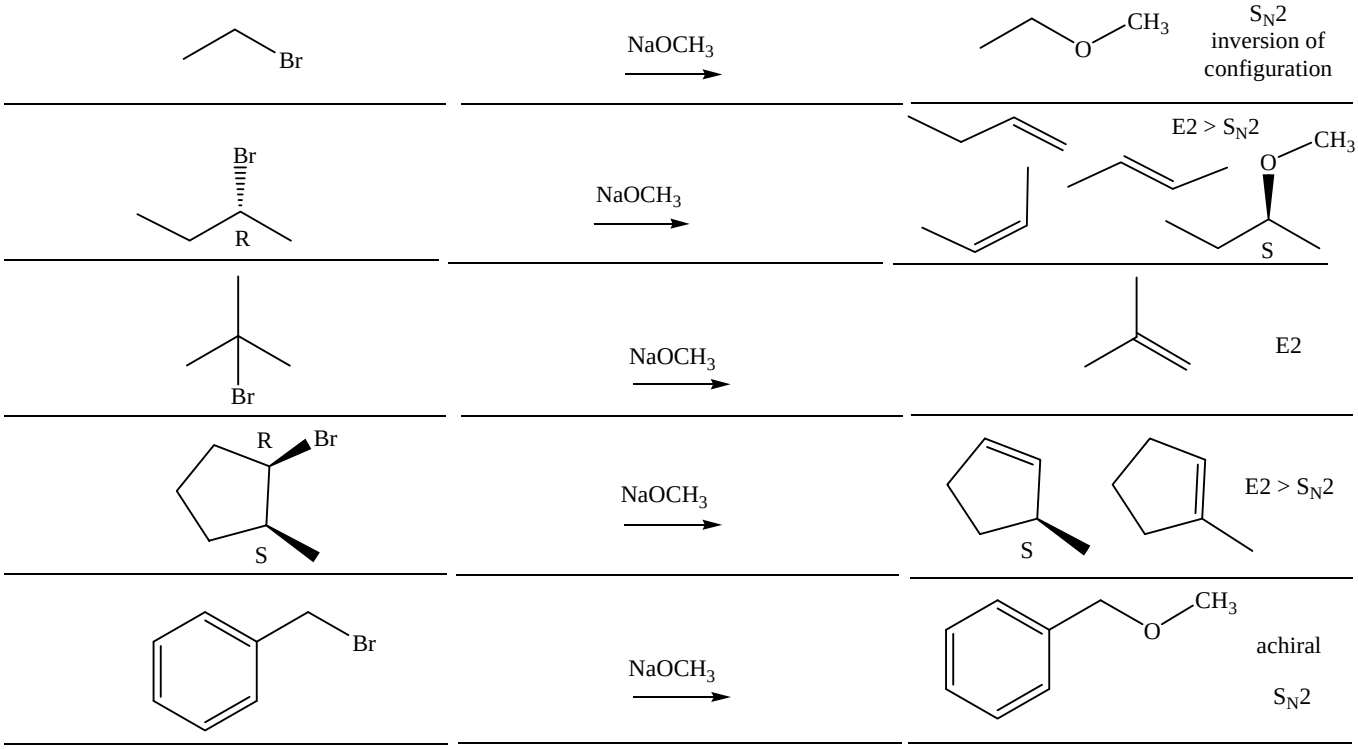




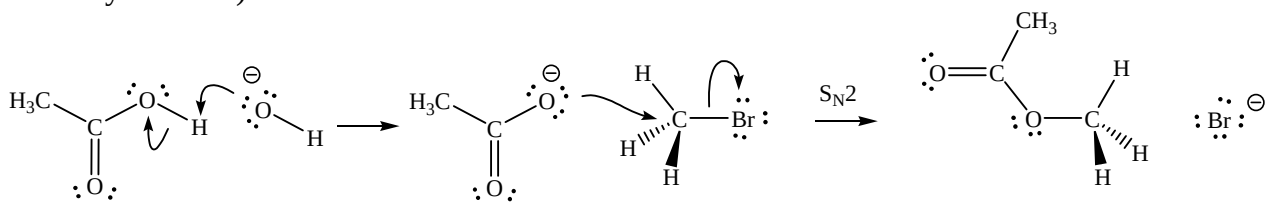
b. mechanisms using $NaOCH_3$, S_N2 at methyl and 1° RBr; E2 > S_N2 at 2° and only E2 at 3° RBr,

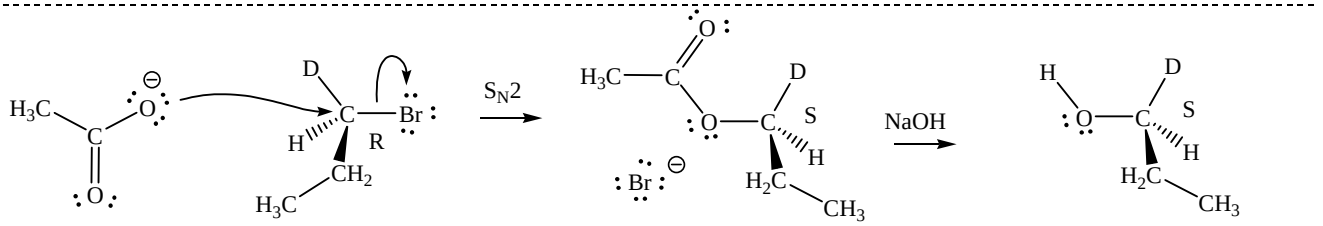


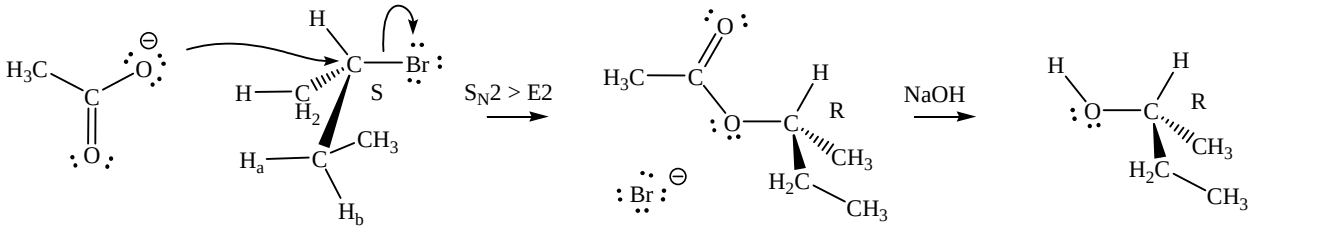
Example reactions



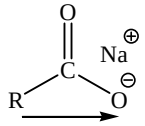
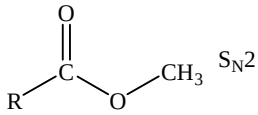
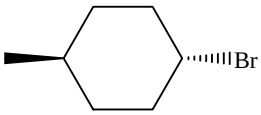
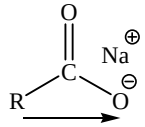
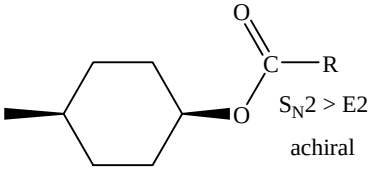
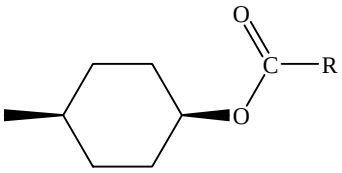
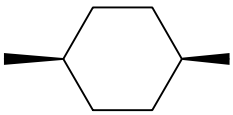
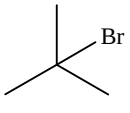
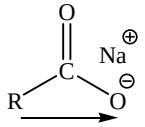
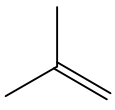
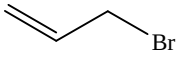
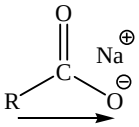
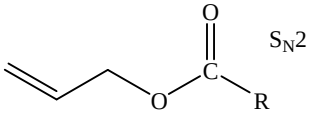
c. mechanisms using NaO_2CCH_3, sodium carboxylates, S_N2 at methyl 1° and 2° RBr; and only E2 at 3° RBr
Ester synthesis (can hydrolyze with NaOH (base) to ROH and RCO_2H, providing an alternate approach to secondary alcohols).

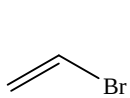


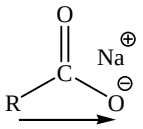




Example reactions

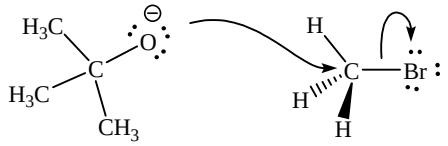
H_3C-Br		 S_N2
		 $S_N2 > E2$ achiral
	$NaOH / H_2O$	 2° alcohol; acyl substitution
		 E2
		 S_N2 allylic and benzylic, very fast S_N2 reactions



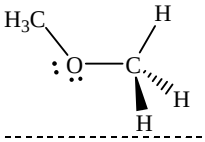


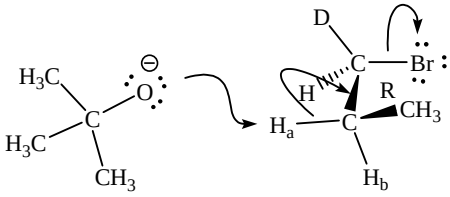
no reaction

d. mechanism using potassium t-butoxide, $KOC(CH_3)_3$, S_N2 at methyl and E2 at 1°, 2° and 3° RBr,

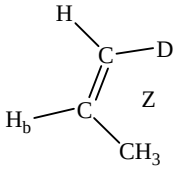


S_N2

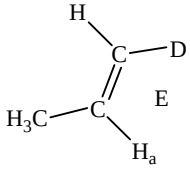




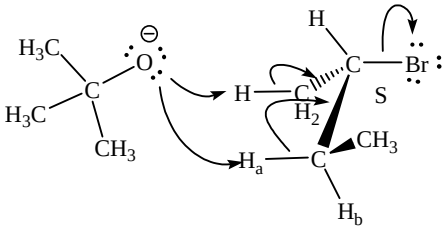
E2



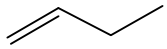
Z



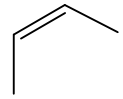
E



E2



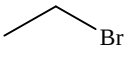
E2 (-CH_2-H)

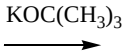


E2 (-CH_b-H)

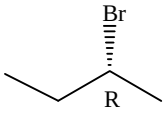
E2 (-CH_a-H)

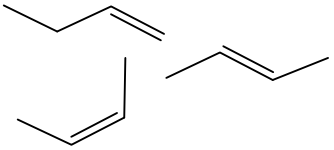
Example reactions



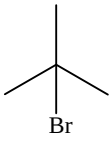


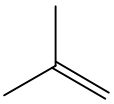
E2 > S_N2 anti elimination



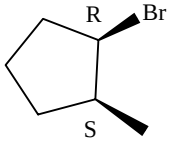


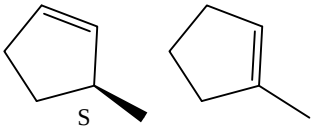
E2



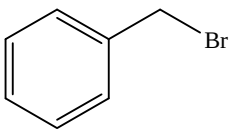


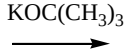
E2

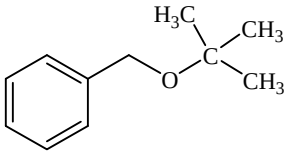




E2

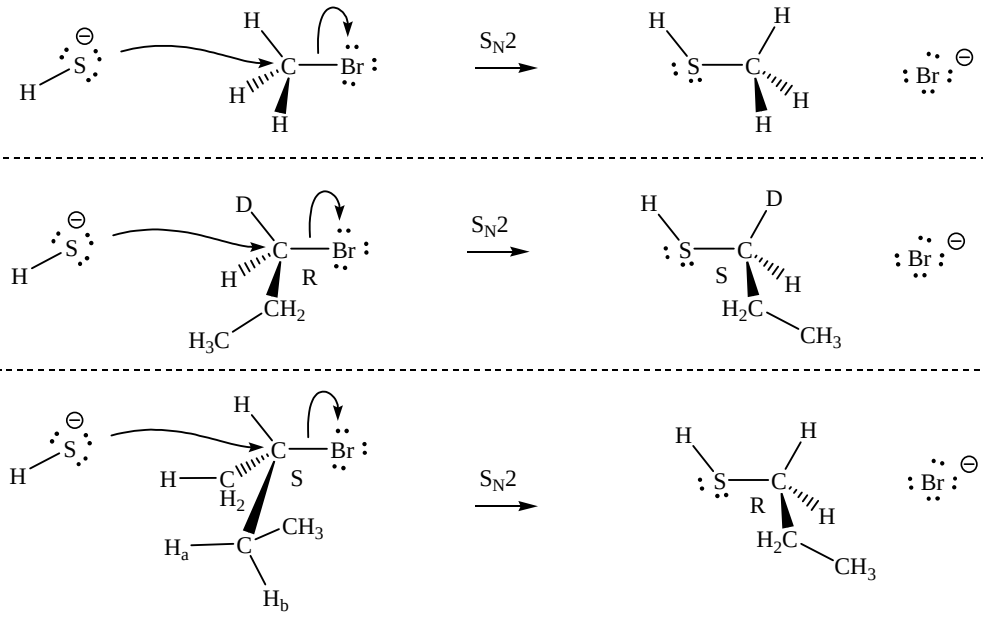




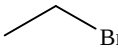
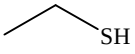
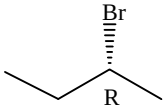
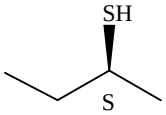
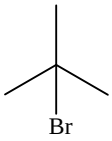
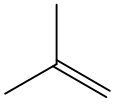
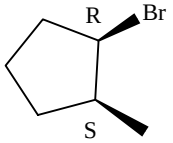
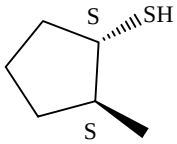
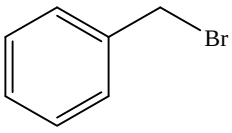
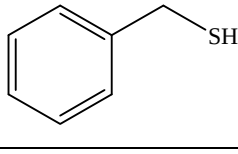


S_N2 no other option

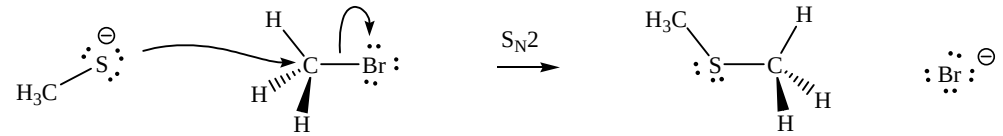
e. mechanism using NaSH, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,

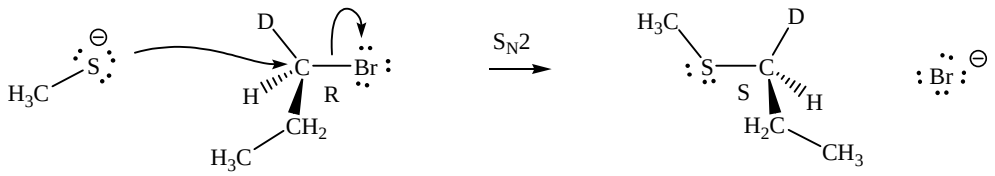


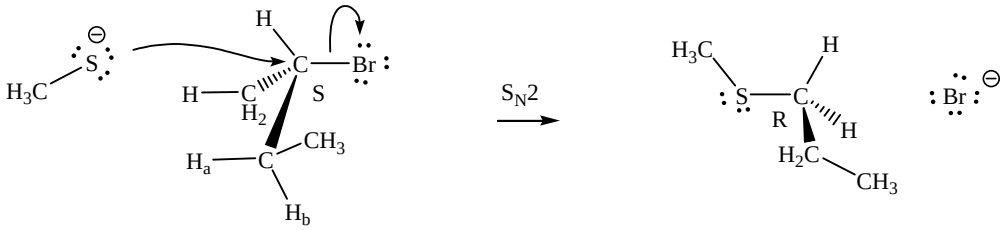
Example reactions

	NaSH →	 S_N2 inversion of configuration
	NaSH →	 S_N2
	NaSH →	 E2
	NaSH →	 S_N2
	NaSH →	 achiral S_N2

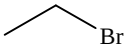
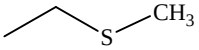
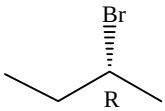
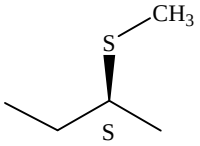
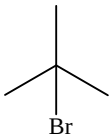
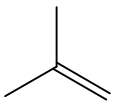
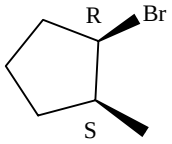
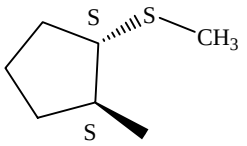
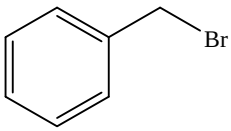
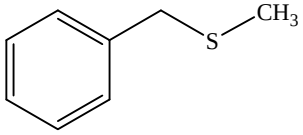
f. mechanism using $NaSCH_3$, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



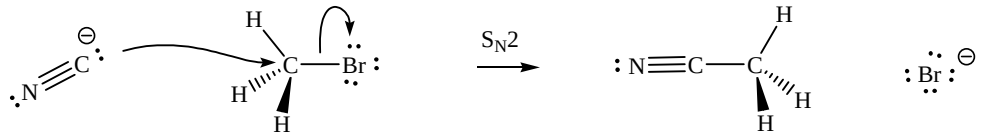


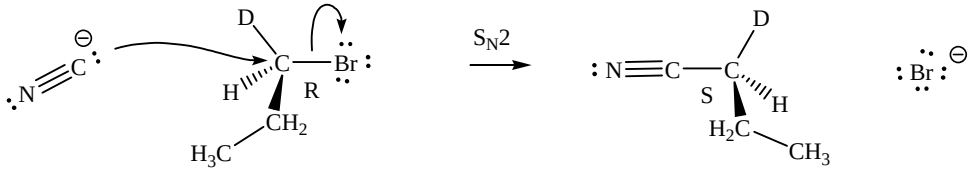


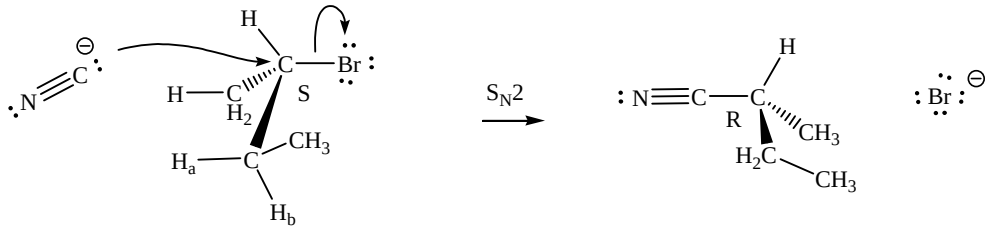
Example reactions

	$NaSCH_3$		S_N2 inversion of configuration
	$NaSCH_3$		S_N2
	$NaSCH_3$		E2
	$NaSCH_3$		S_N2
	$NaSCH_3$		achiral S_N2

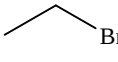
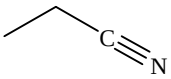
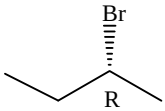
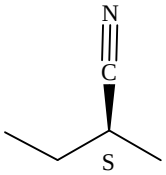
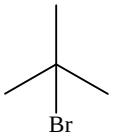
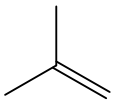
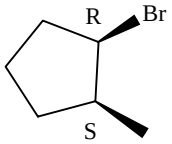
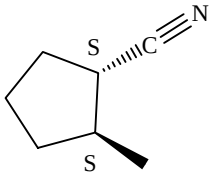
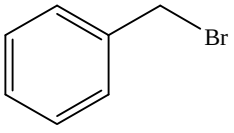
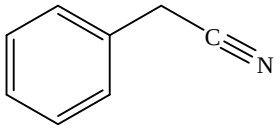
g. mechanism using NaCN, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



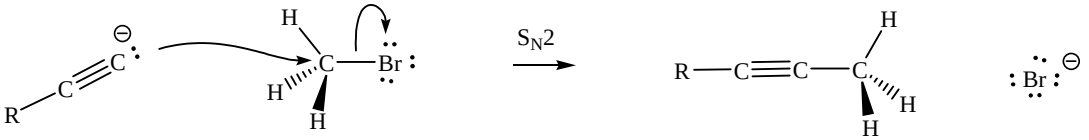


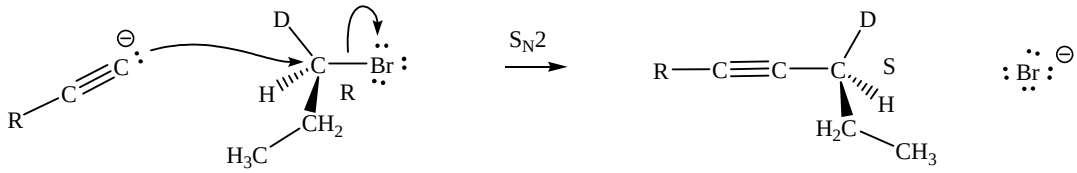


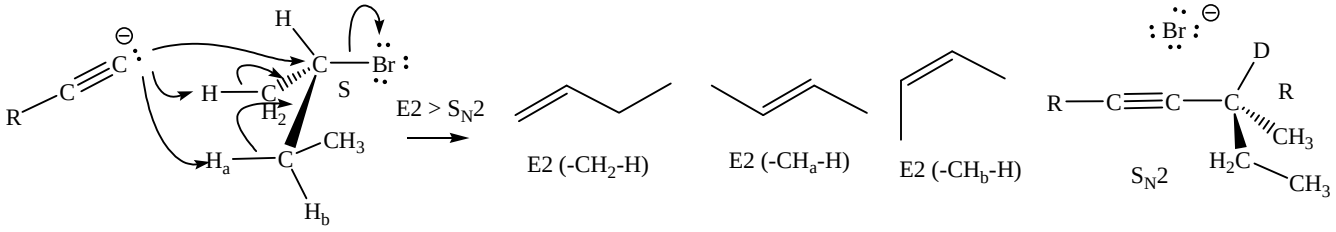
Example reactions

	NaCN →	 S_N2 inversion of configuration
	NaCN →	 S_N2
	NaCN →	 E2
	NaCN →	 S_N2
	NaCN →	 achiral S_N2

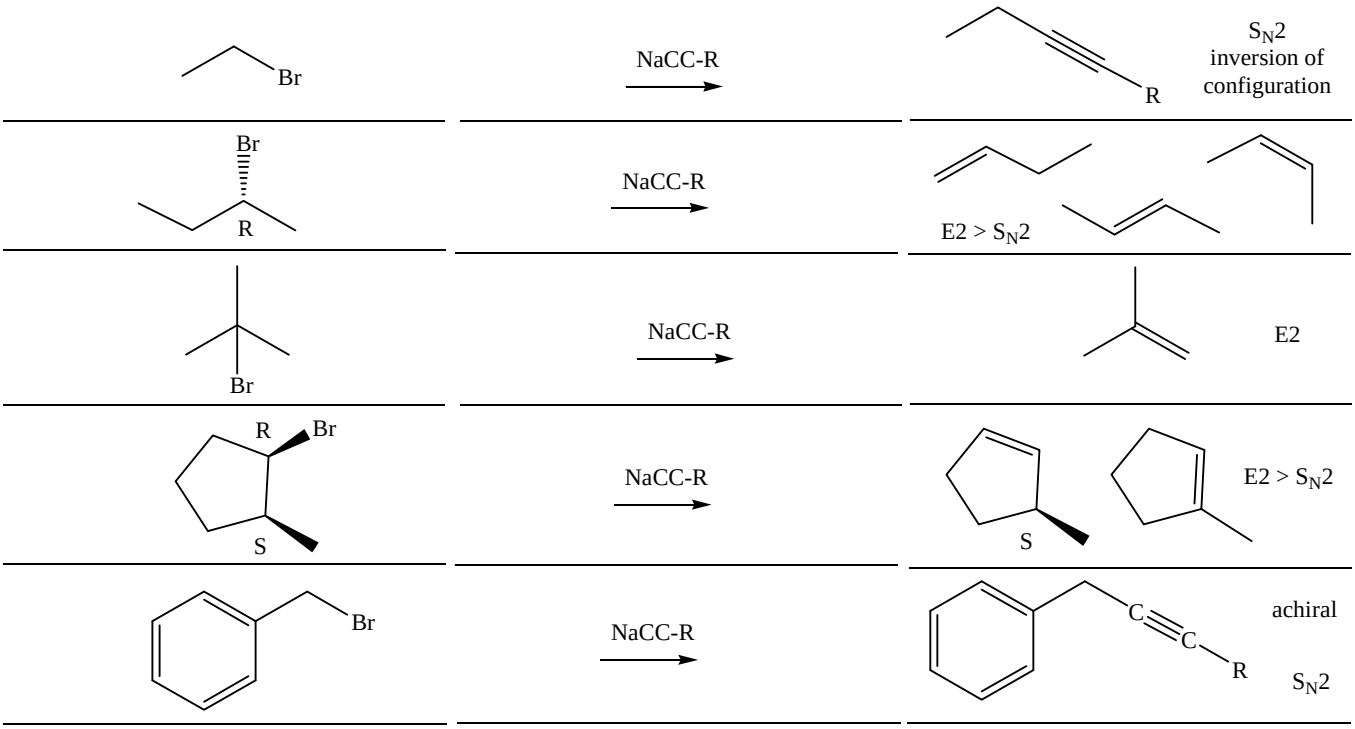
h. mechanism using NaCC-R, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



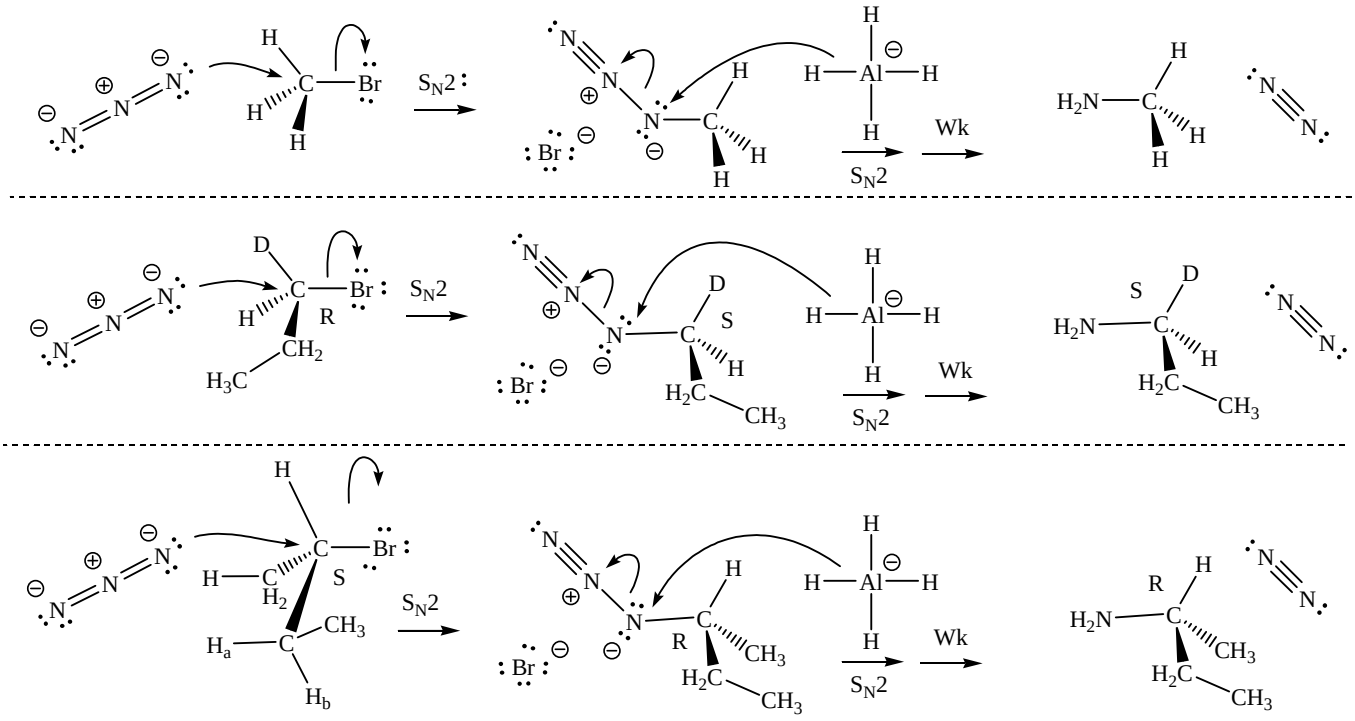




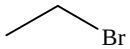
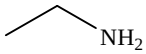
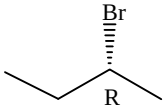
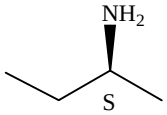
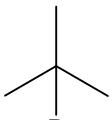
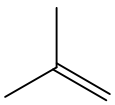
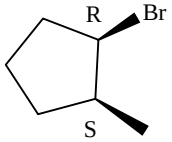
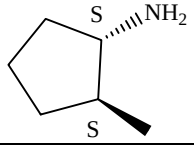
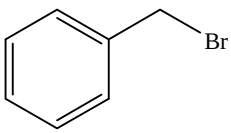
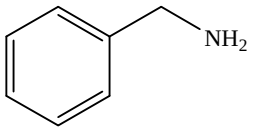
Example reactions



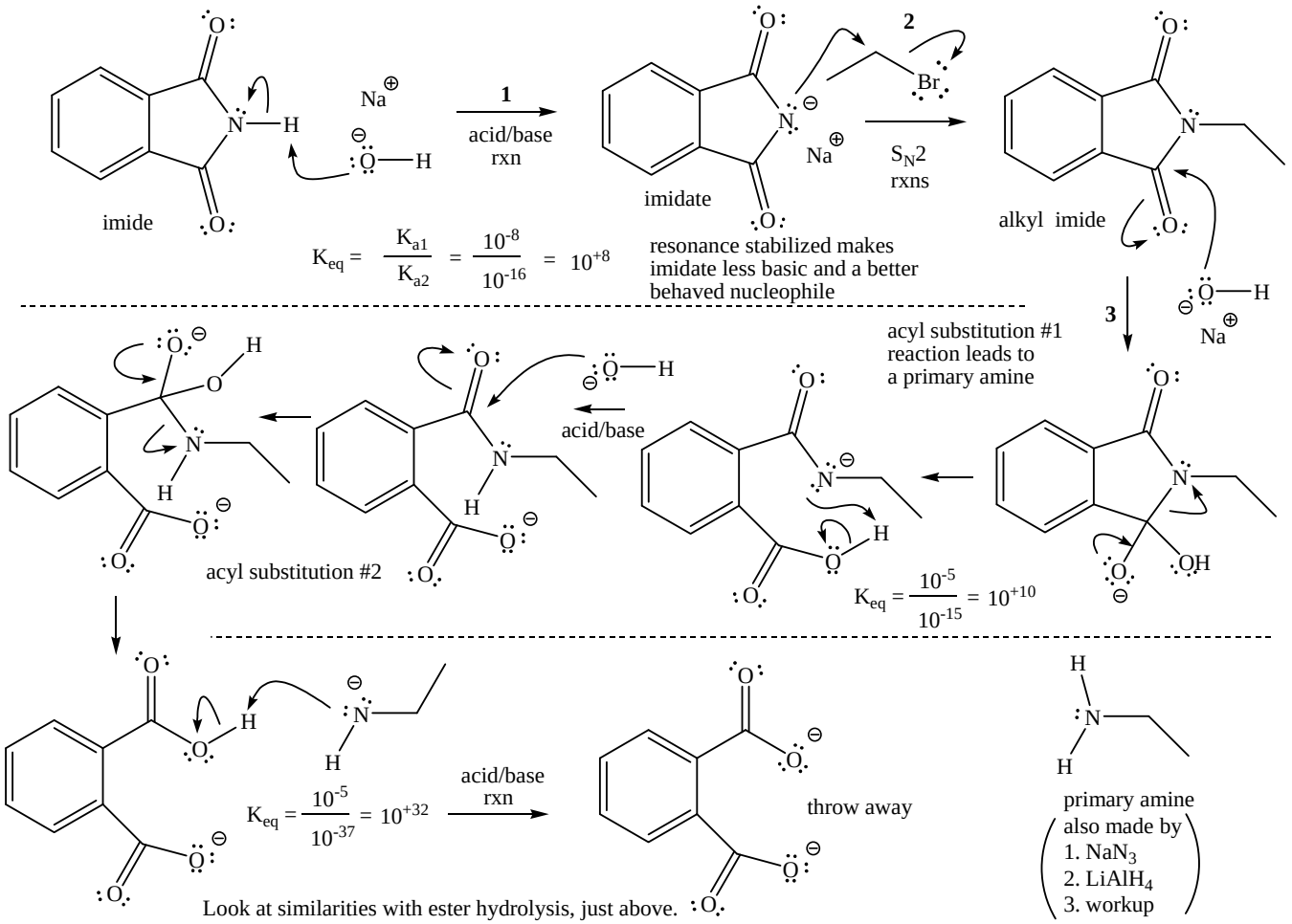
i. mechanism using 1. NaN_3, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr 2. $LiAlH_4$ 3. Workup, makes 1° amines (RNH_2)



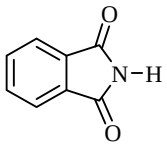
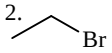
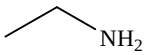
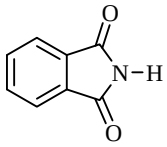
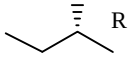
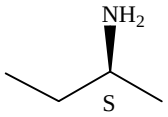
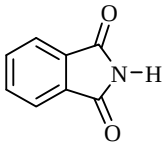
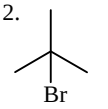
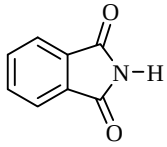
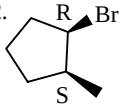
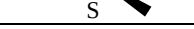
Example reactions

	1. NaN_3 2. $LiAlH_4$ 3. workup	 S_N2 twice
	1. NaN_3 2. $LiAlH_4$ 3. workup	 S_N2
	1. NaN_3 2. $LiAlH_4$ 3. workup	 E2
	1. NaN_3 2. $LiAlH_4$ 3. workup	 S_N2
	1. NaN_3 2. $LiAlH_4$ 3. workup	 achiral S_N2

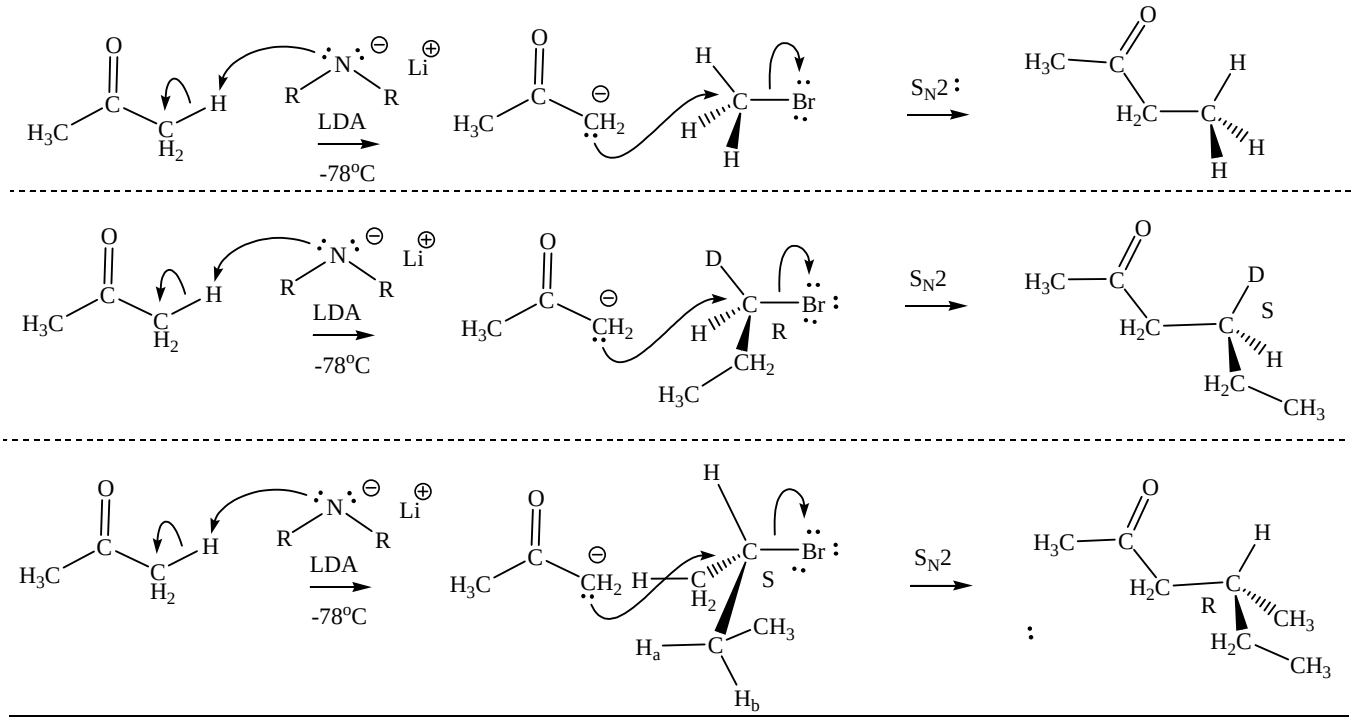
j. mechanism using 1. Na^+ imidate, S_N2 at methyl, 1^o and 2^o RBr and only E2 at 3^o RBr 2. NaOH



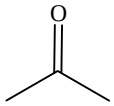
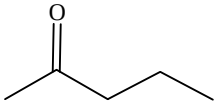
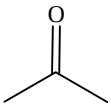
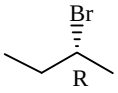
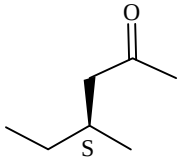
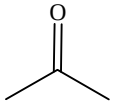
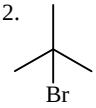
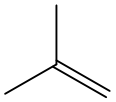
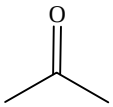
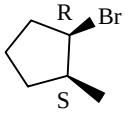
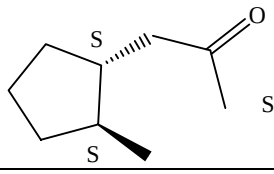
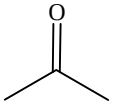
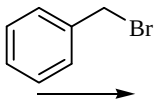
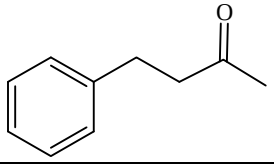
Example reactions

	1. NaOH 2.  3. NaOH	 1. S_N2 2. acyl substitution (2 times)
	1. NaOH 2.  3. NaOH	 S_N2
	1. NaOH 2.  3. NaOH	 E2
	1. NaOH 2.  3. NaOH	 S_N2

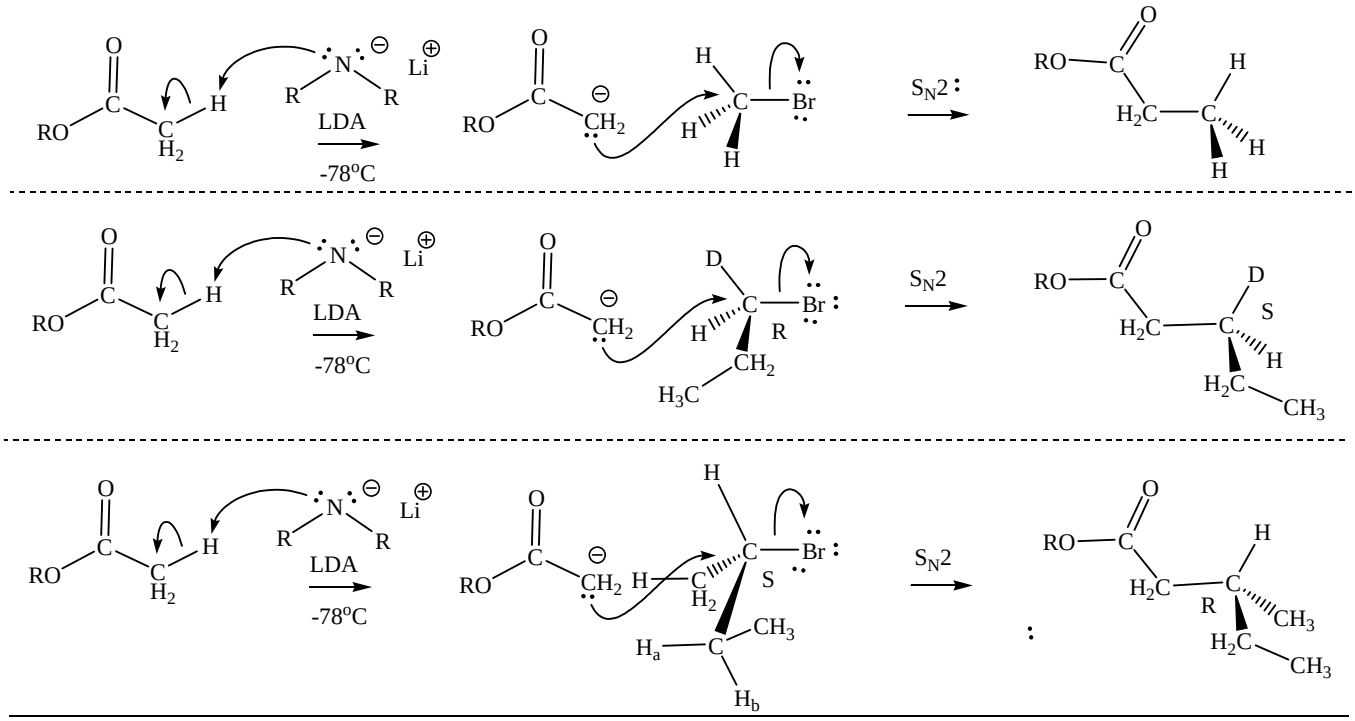
k. mechanism using ketone enolates, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr (See acid/base reactions at the beginning for synthesis of LDA.)



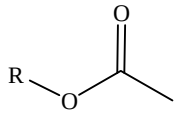
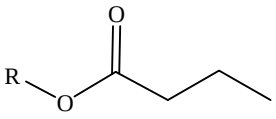
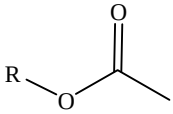
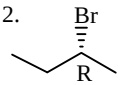
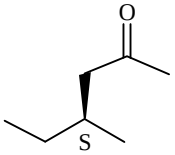
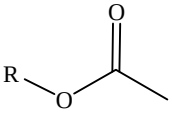
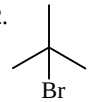
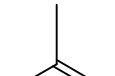
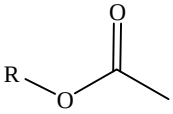
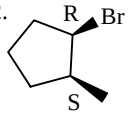
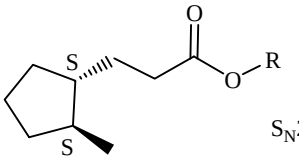
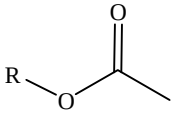
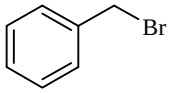
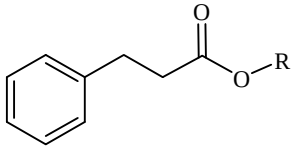
Example reactions

	1. LDA, -78°C 2. 	 S_N2 inversion of configuration
	1. LDA, -78°C 2. 	 S_N2
	1. LDA, -78°C 2. 	 E2
		 S_N2
	1. LDA, -78°C 2. 	 achiral S_N2

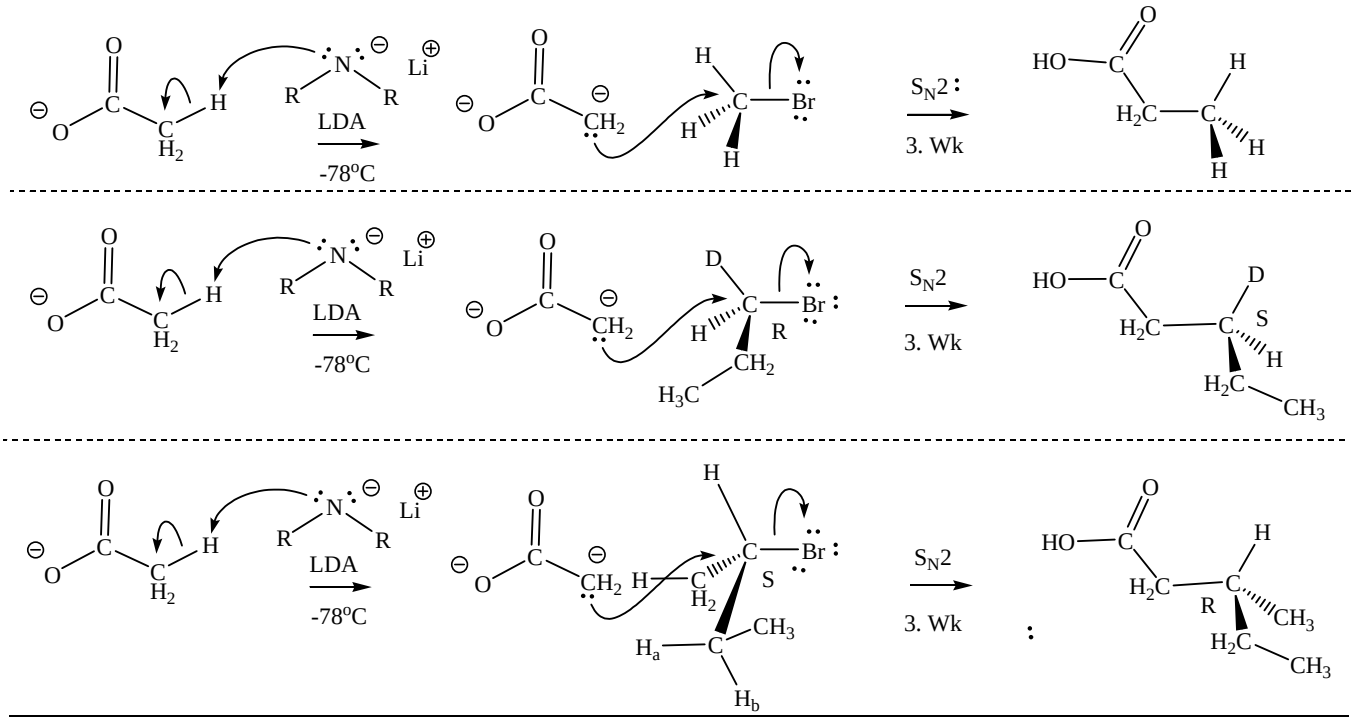
l. mechanism using ester enolates, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



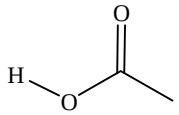
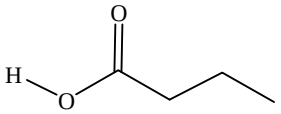
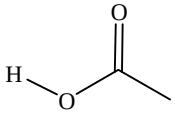
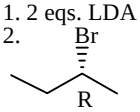
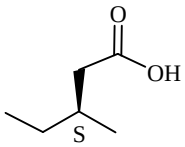
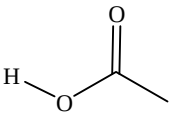
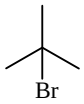
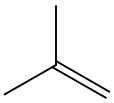
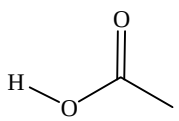
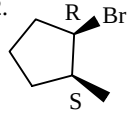
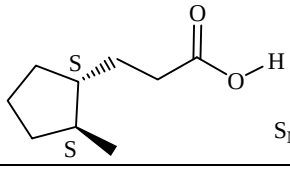
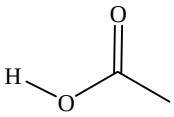
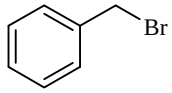
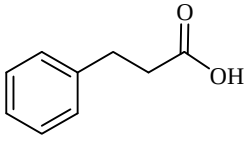
Example reactions

	1. LDA, -78°C 2. 	 S_N2 inversion of configuration
	1. LDA, -78°C 2. 	 S_N2
	1. LDA, -78°C 2. 	 E2
	1. LDA, -78°C 2. 	 S_N2
	1. LDA, -78°C 2. 	 achiral S_N2

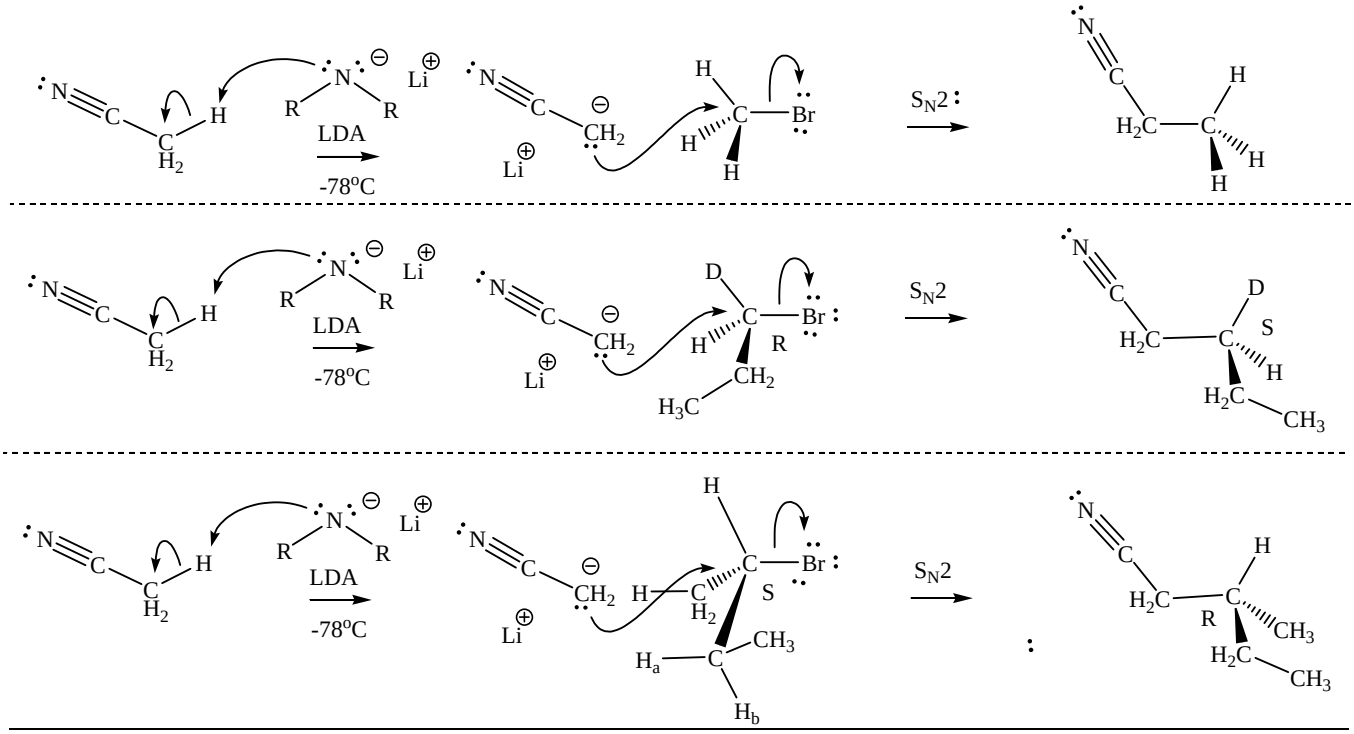
m. mechanism using acid dianion enolates, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



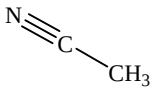
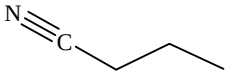
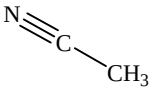
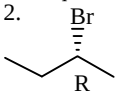
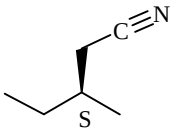
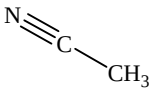
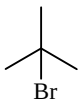
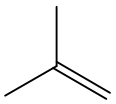
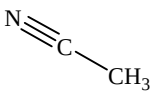
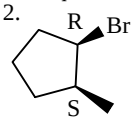
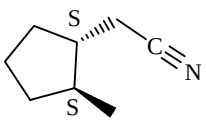
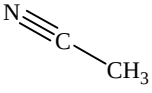
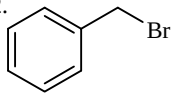
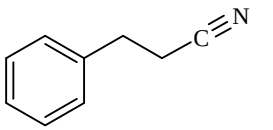
Example reactions

	1. 2 eqs. LDA 2.  3. workup	 S_N2
	1. 2 eqs. LDA 2.  3. workup	 S_N2
	1. 2 eqs. LDA 2.  3. workup	 E2
	1. 2 eqs. LDA 2.  3. workup	 S_N2
	1. 2 eqs. LDA 2.  3. workup	 achiral S_N2

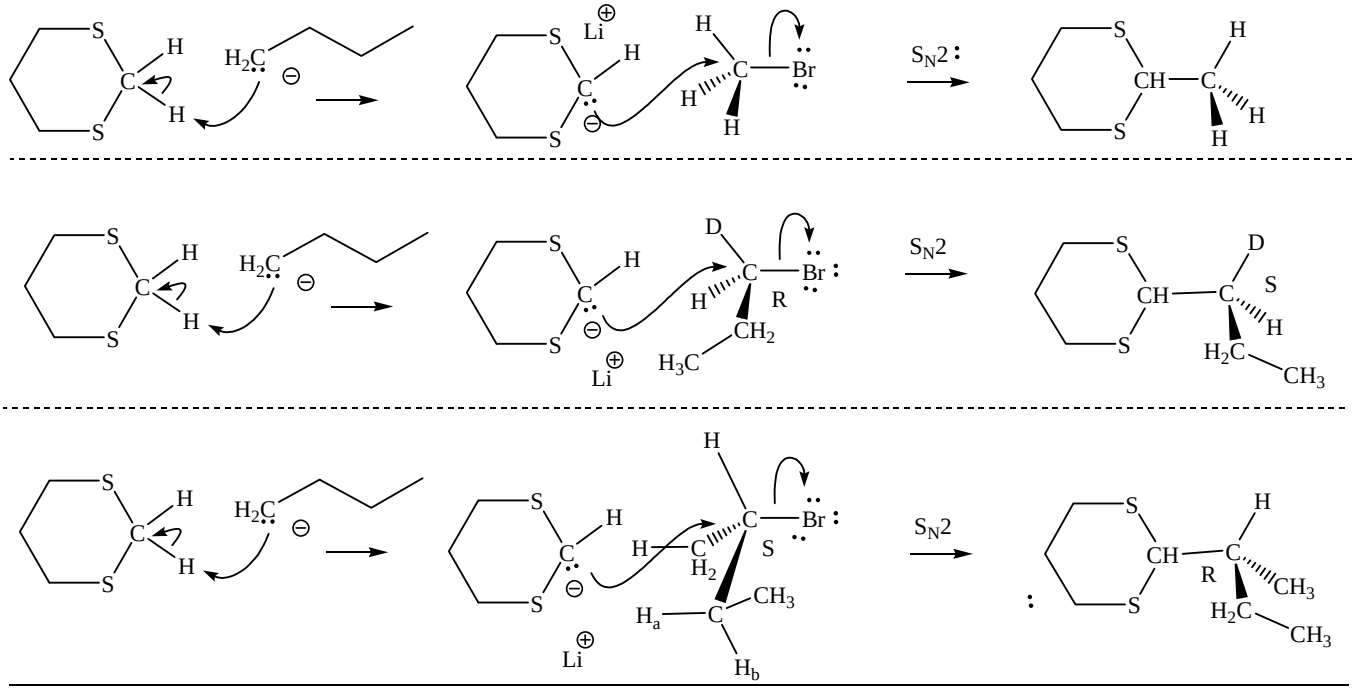
n. mechanism using nitrile enolates, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



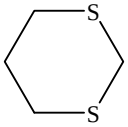
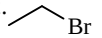
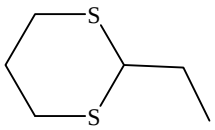
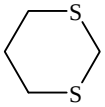
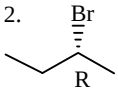
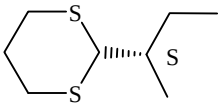
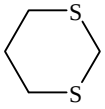
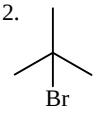
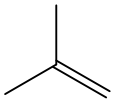
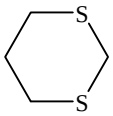
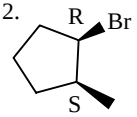
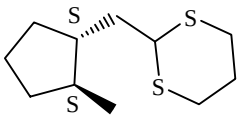
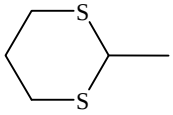
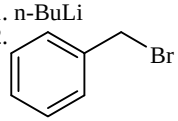
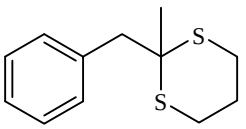
Example reactions

	1. 2 eqs. LDA 2.  3. workup	 S_N2 inversion of configuration
	1. 2 eqs. LDA 2.  3. workup	 S_N2
	1. 2 eqs. LDA 2.  3. workup	 E2
	1. 2 eqs. LDA 2.  3. workup	 S_N2
	1. 2 eqs. LDA 2.  3. workup	 achiral S_N2

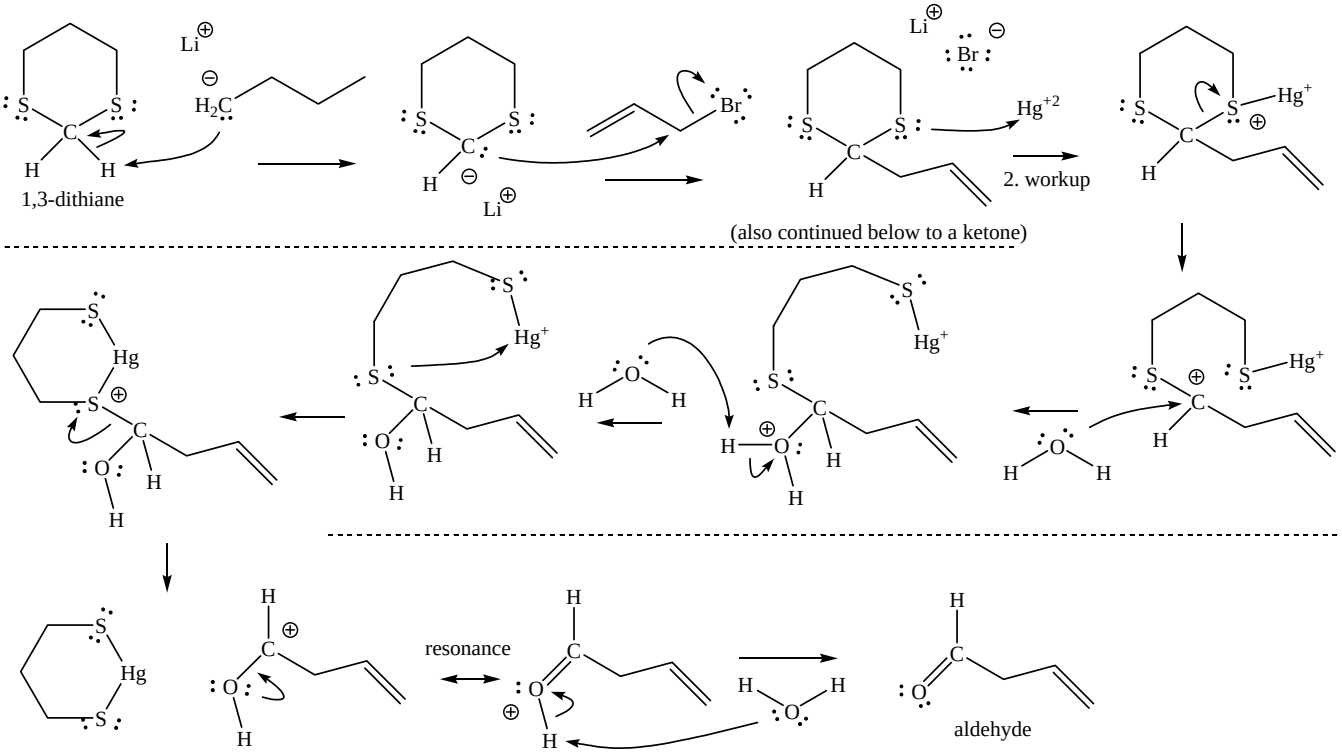
o. mechanism using dithiane anions, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,

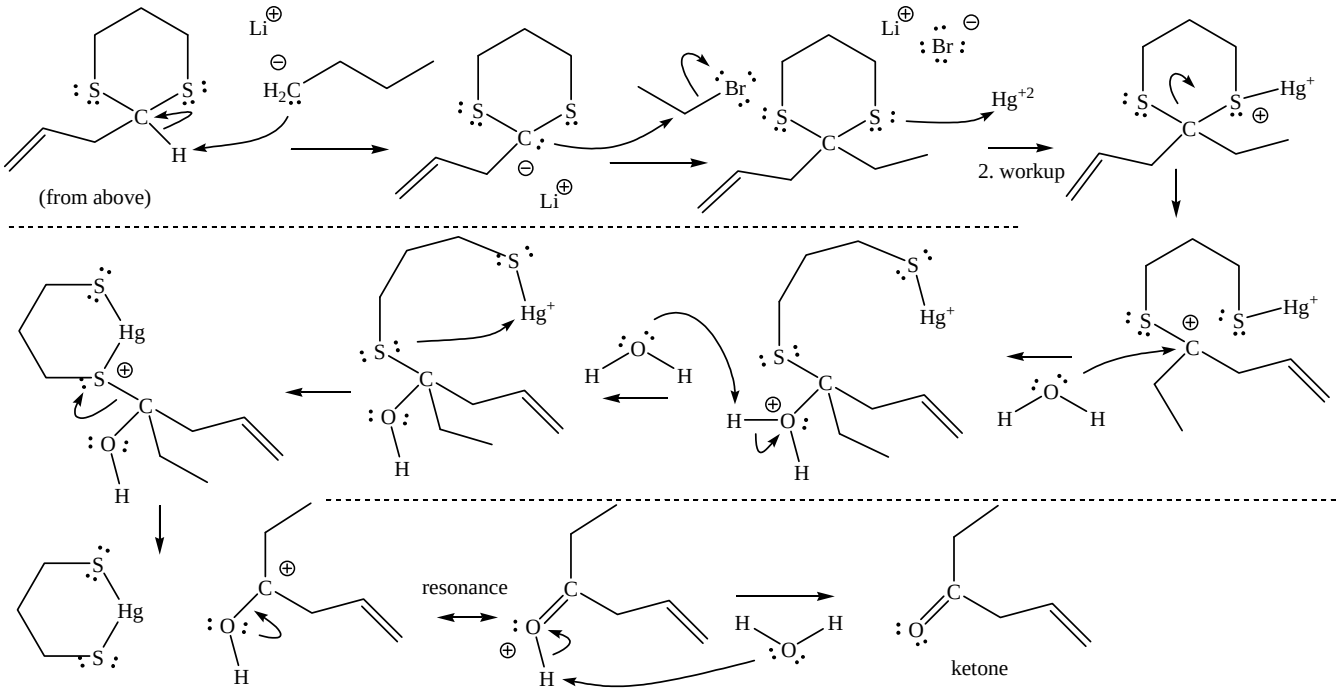


Example reactions

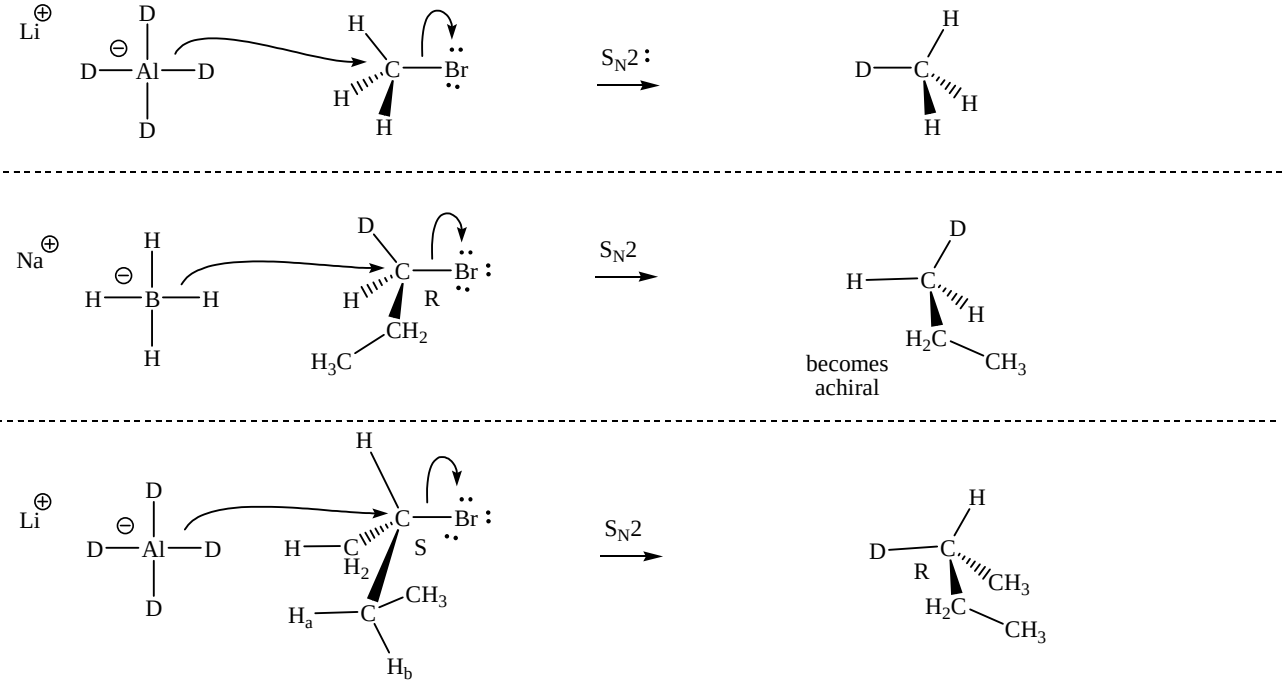
	1. n-BuLi 2. 	 S_N2 inversion of configuration
	1. n-BuLi 2. 	 S_N2
	1. n-BuLi 2. 	 E2
	1. n-BuLi 2. 	 S_N2
	1. n-BuLi 2. 	 achiral S_N2

Hydrolysis of thioacetals (one as aldehyde and one as ketone)

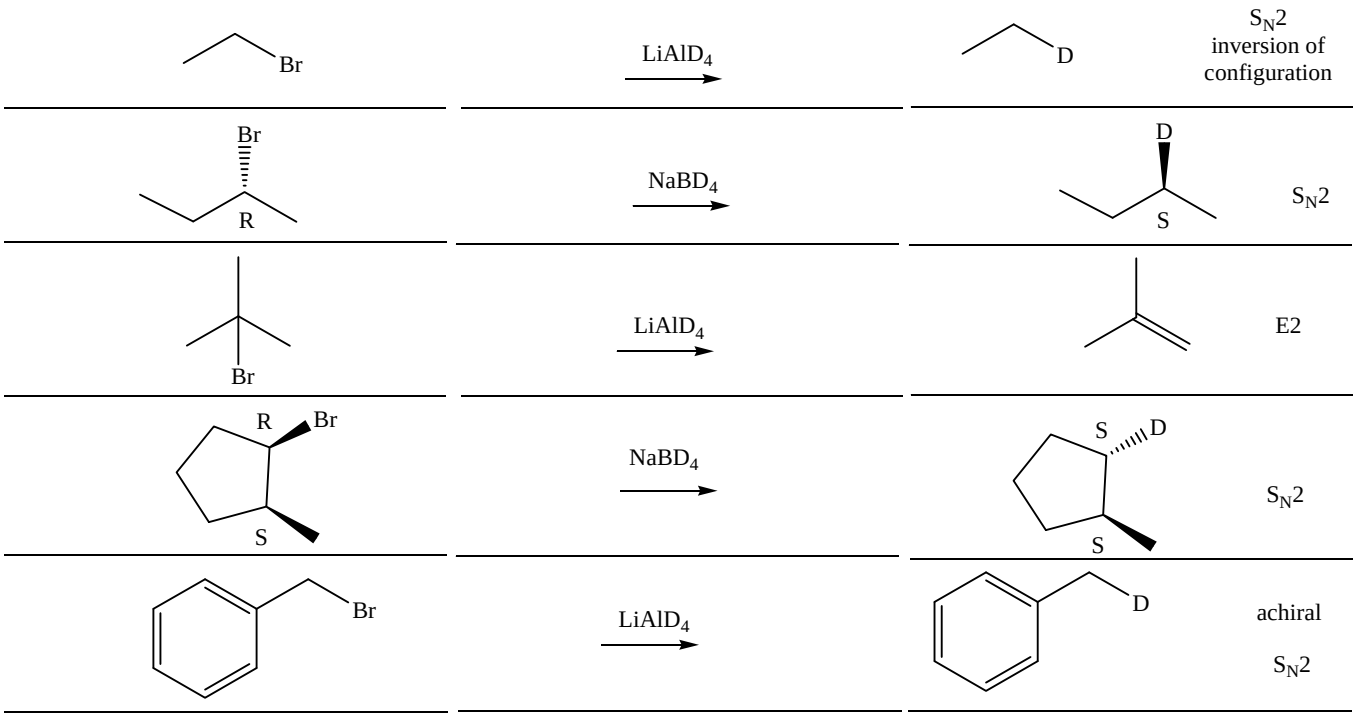




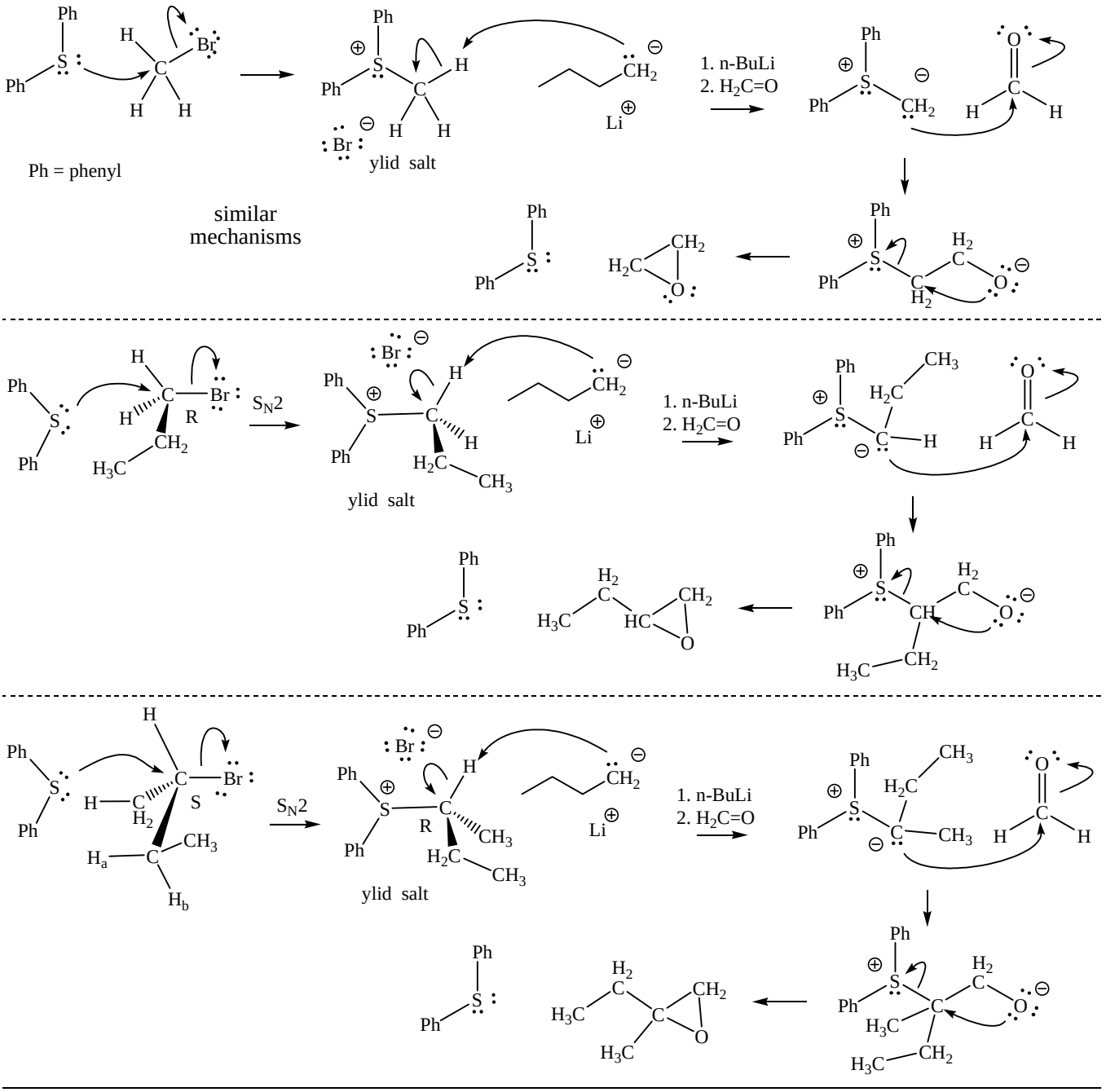
p. mechanism using $LiAlH_4$ or $NaBH_4$ (and deuterides), S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr,



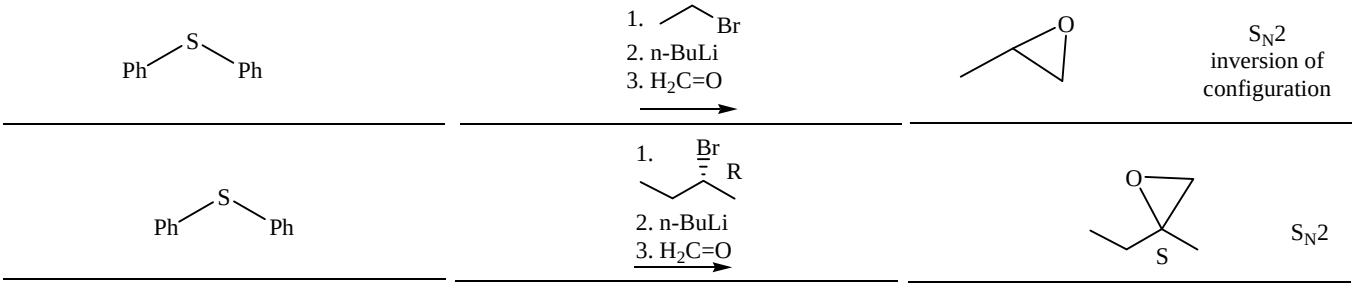
Example reactions

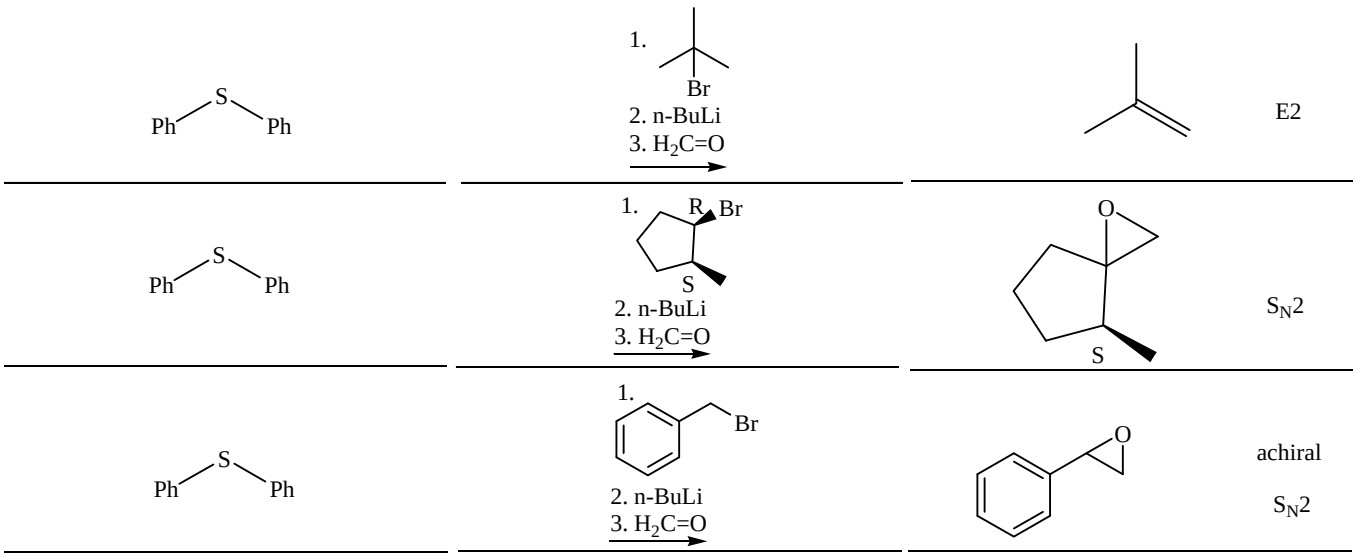


q. mechanism using diphenylsulfide to make diphenylsulfonium salt, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr, used to make a diphenylsulfonium ylids, which are used to make epoxides with aldehydes and ketones.

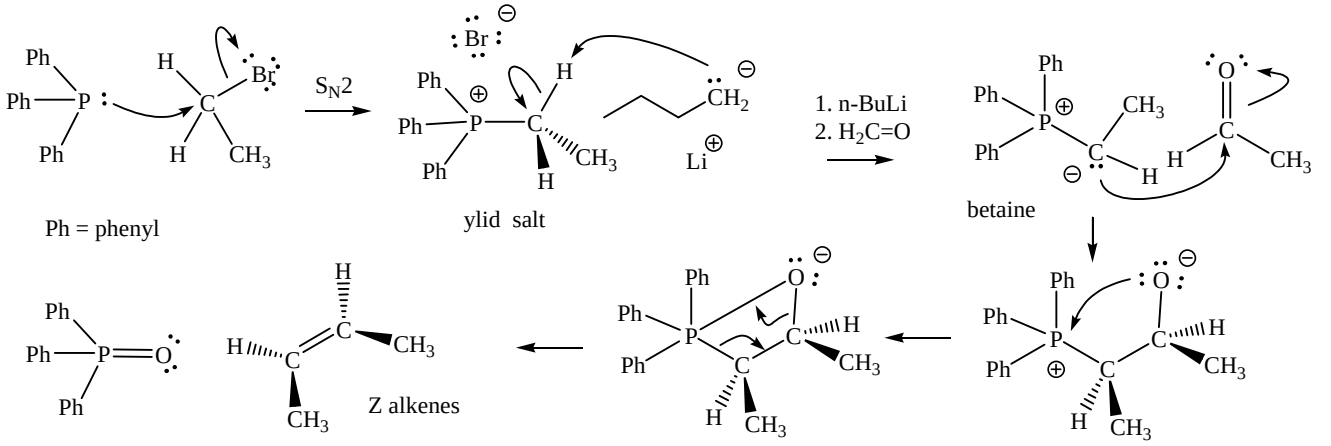


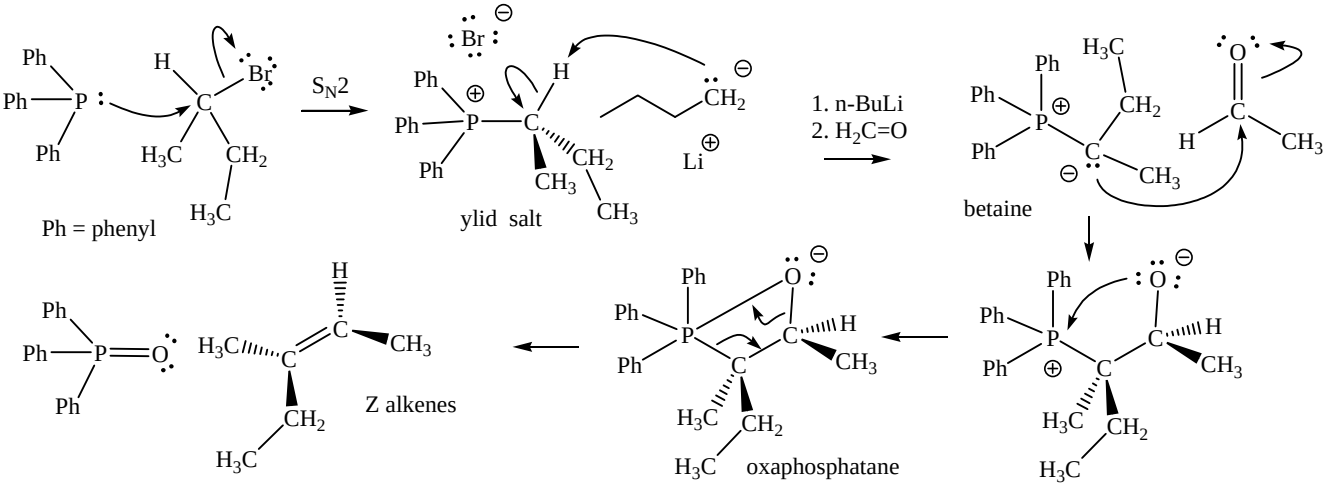
Example reactions



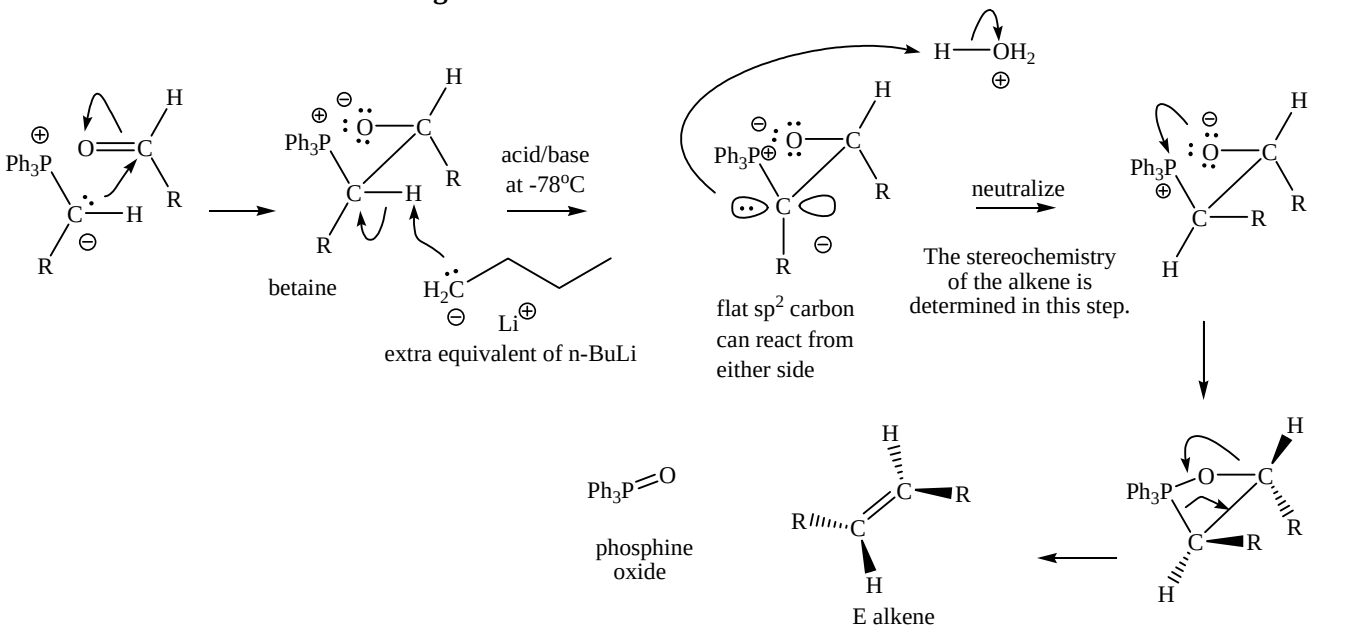


r. mechanism using triphenylphosphine to make triphenylphosphonium salt, S_N2 at methyl, 1° and 2° RBr and only E2 at 3° RBr, used to make a triphenylphosphonium ylid to make Z and E alkenes with aldehydes and ketones.

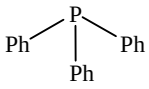
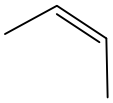
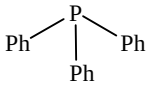
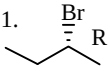
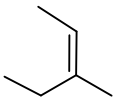
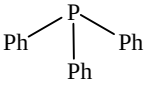
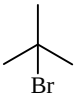
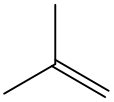
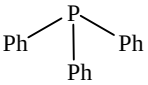
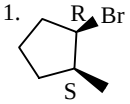
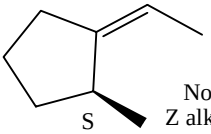
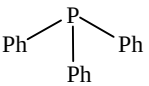
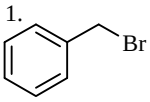
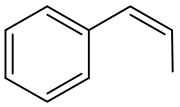
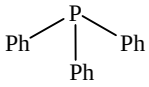
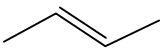




Schlosser Modification of the Wittig reaction to make E alkenes

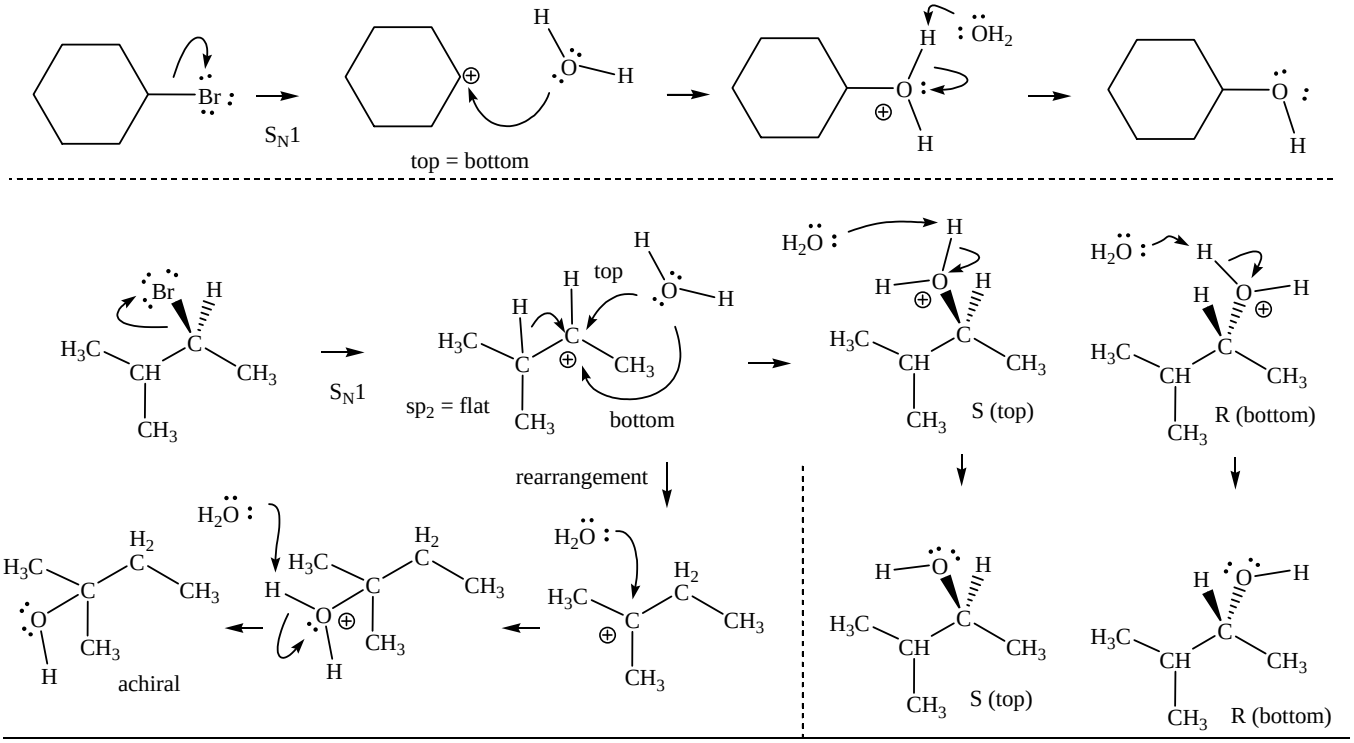


Example reactions

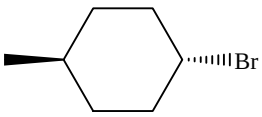
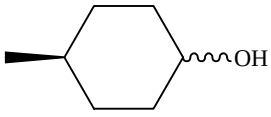
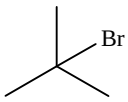
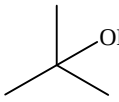
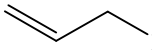
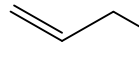
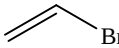
	1.  2. n-BuLi 3. $CH_3CH{=}O$	 Normal Wittig Z alkene preferred
	1.  2. n-BuLi 3. $CH_3CH{=}O$	 Normal Wittig Z alkene preferred
	1.  2. n-BuLi 3. $CH_3CH{=}O$	 E2
	1.  2. n-BuLi 3. $CH_3CH{=}O$	 Normal Wittig Z alkene preferred
	1.  2. n-BuLi 3. $CH_3CH{=}O$	 Normal Wittig Z alkene preferred
	1.  2. n-BuLi 3. $CH_3CH{=}O$ 4. -78°C, n-BuLi 5. HCl, warm	 Schlosser modification of the Wittig E alkenes preferred

3. S_N1 reactions using RBr compounds:

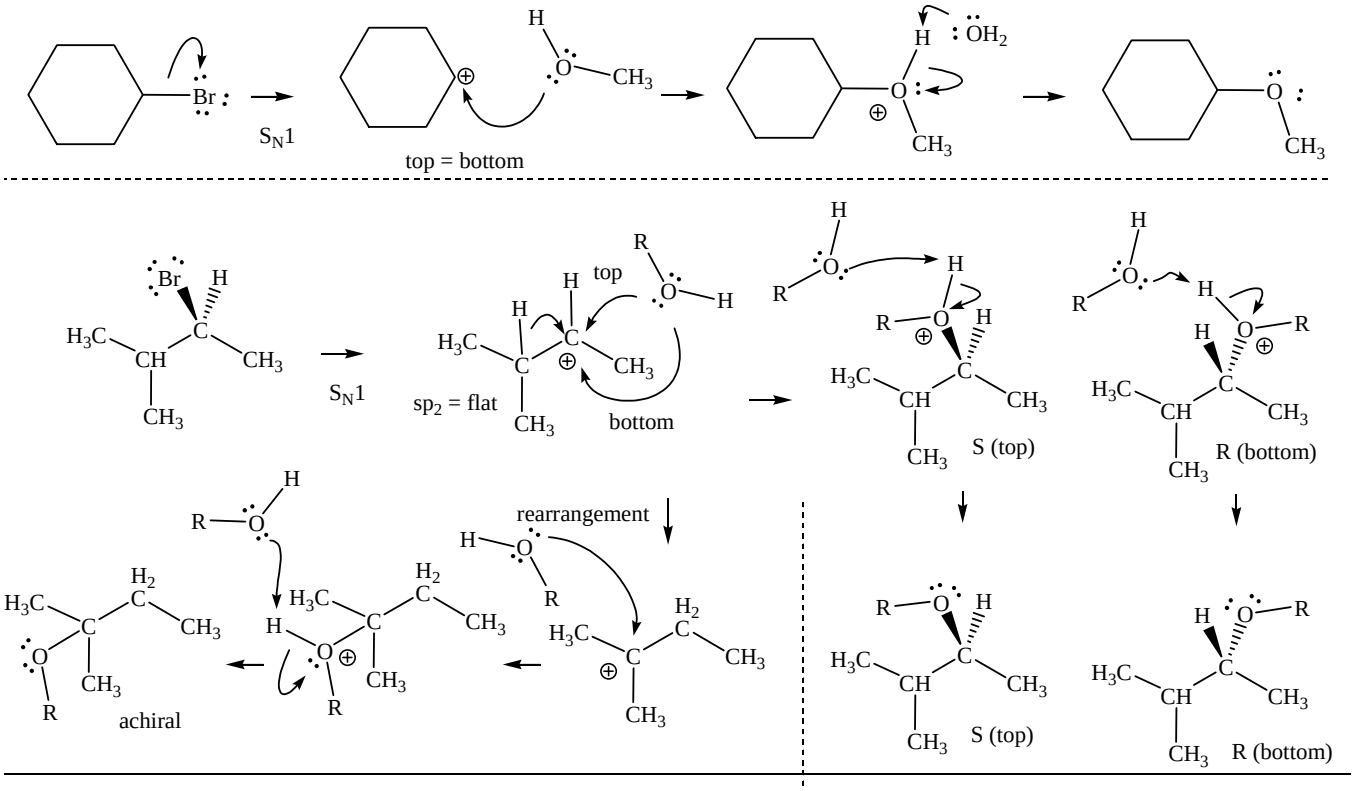
a. RX compounds with water. S_N1 conditions form carbocations with possible rearrangements. Alcohol synthesis is the major product with E1 as minor product (unless reaction is run at high temperature).



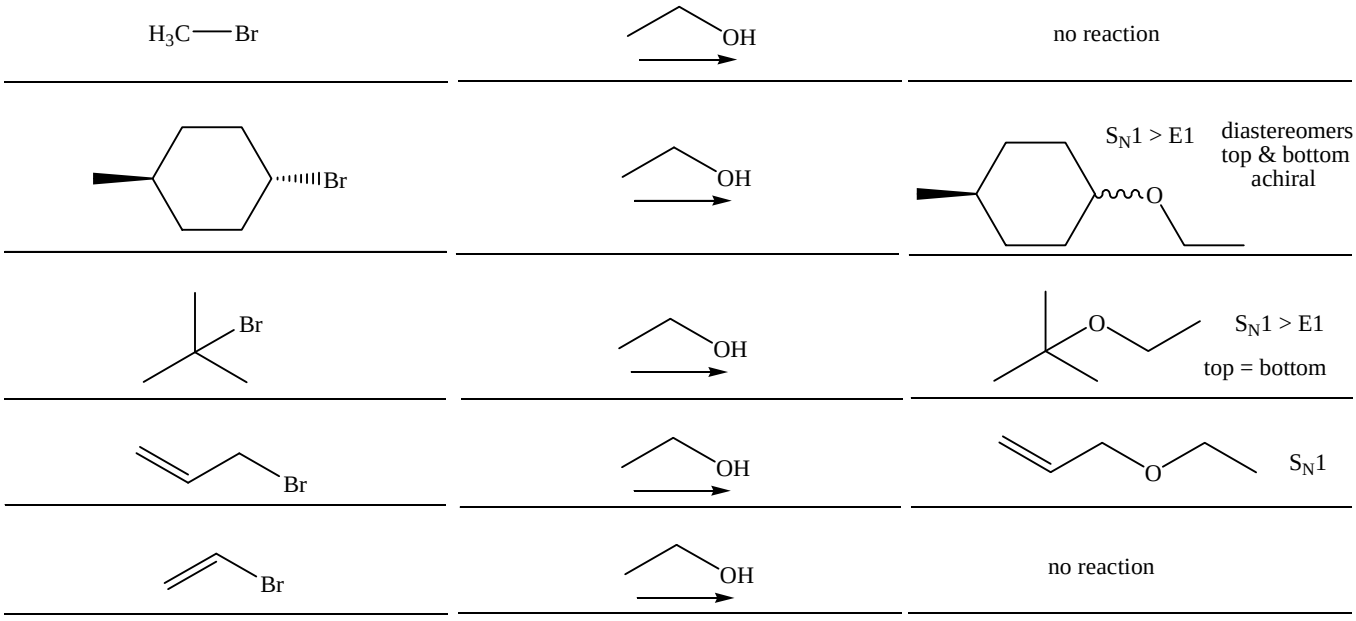
Example reactions

H_3C—Br	H_2O →	no reaction
	H_2O →	 S_N1 > E1 diastereomers top & bottom achiral
	H_2O →	 S_N1 > E1 top = bottom
	H_2O →	 S_N1 resonance stabilization of R^+
	H_2O →	no reaction, vinyl carbocation is too unstable

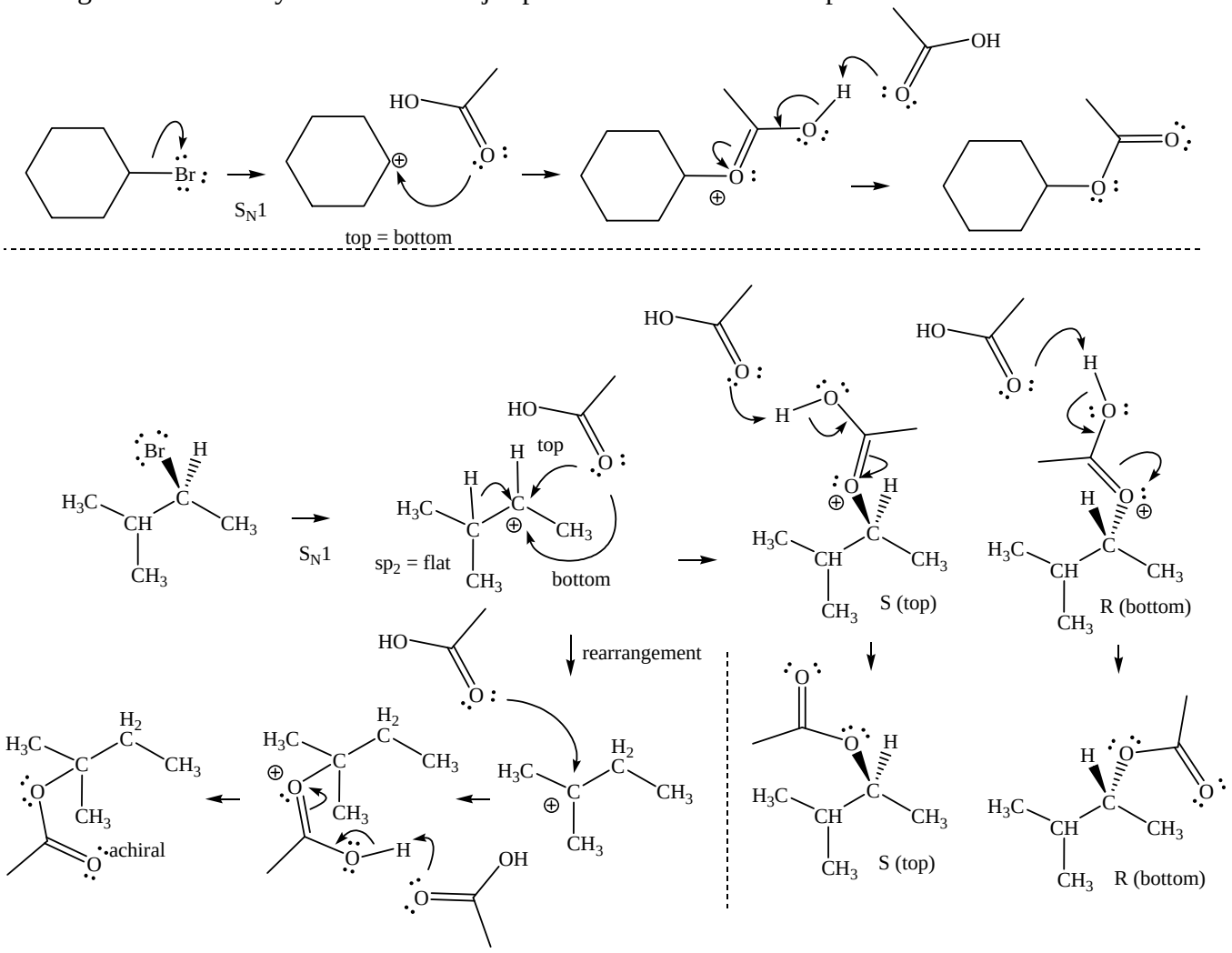
b. RX compounds with alcohols. S_N1 conditions form carbocations with possible rearrangements. Ether synthesis is the major product with E1 as minor product (unless reaction is run at high temperature).

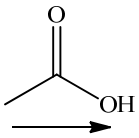
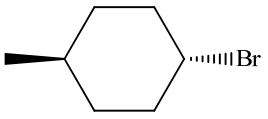
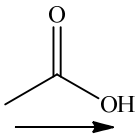
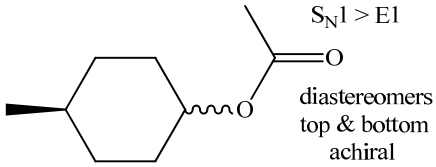
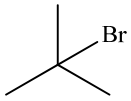
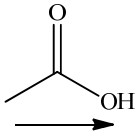
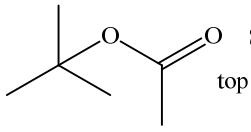
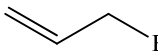
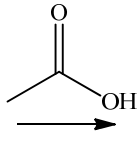
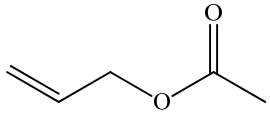


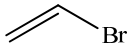
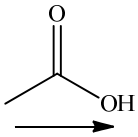
Example reactions



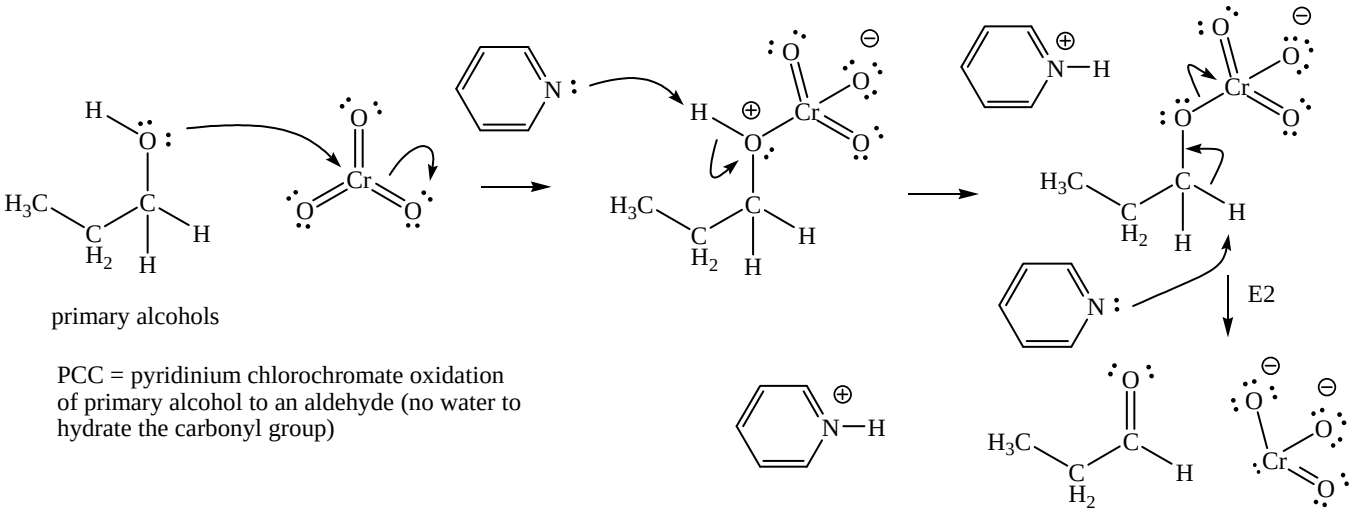
c. RX compounds with liquid carboxylic acids. S_N1 conditions form carbocations with possible rearrangements. Ester synthesis is the major product with E1 as minor product.

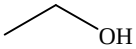
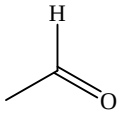
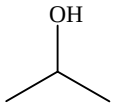
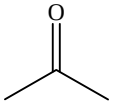
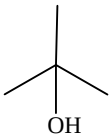
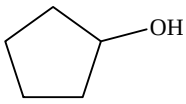
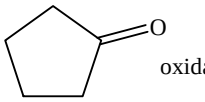
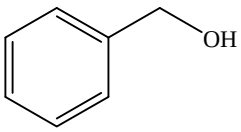
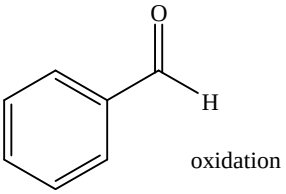


H_3C—Br		no reaction
		 $S_N1 > E1$ diastereomers top & bottom achiral
		 $S_N1 > E1$ top = bottom
		 S_N1

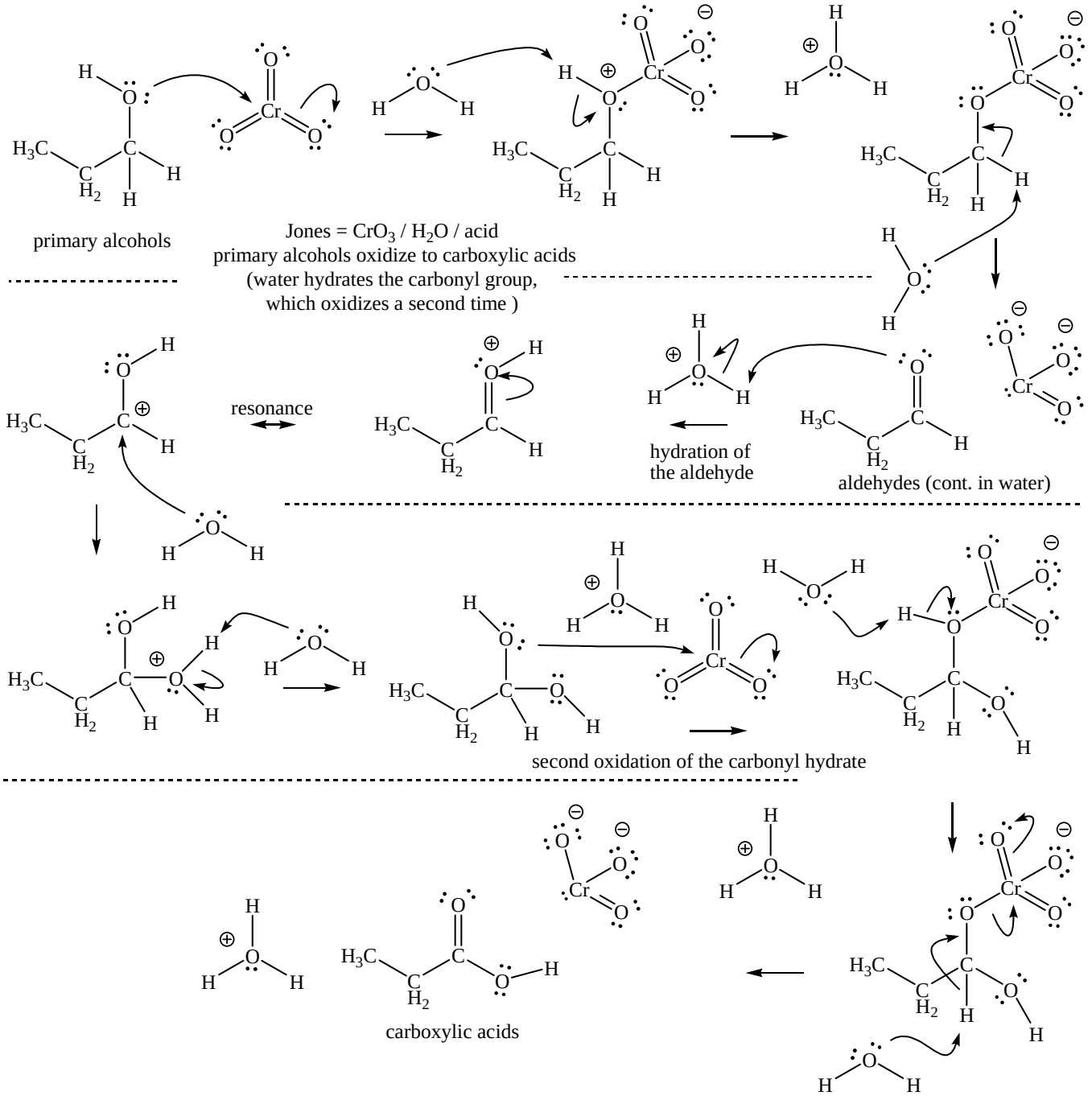
		no reaction

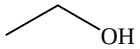
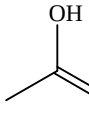
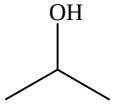
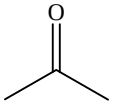
d. Oxidation of ROH with: CrO_3 / pyridine (PCC). Synthesis of aldehydes or ketones.

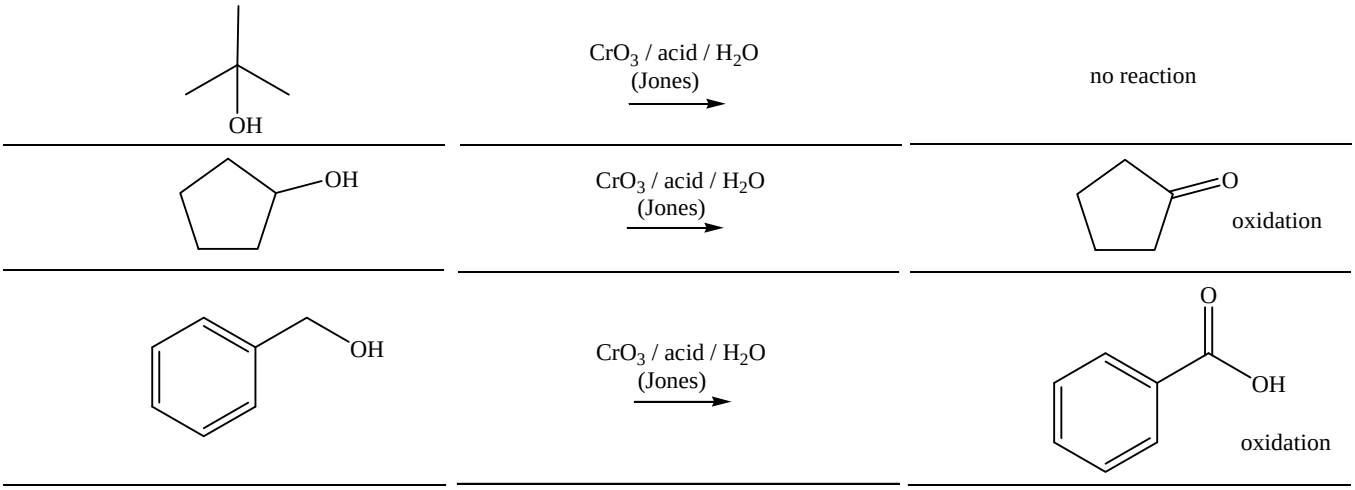


	CrO_3 / pyridine (PCC) →	 oxidation
	CrO_3 / pyridine (PCC) →	 oxidation
	CrO_3 / pyridine (PCC) →	no reaction
	CrO_3 / pyridine (PCC) →	 oxidation
	CrO_3 / pyridine (PCC) →	 oxidation

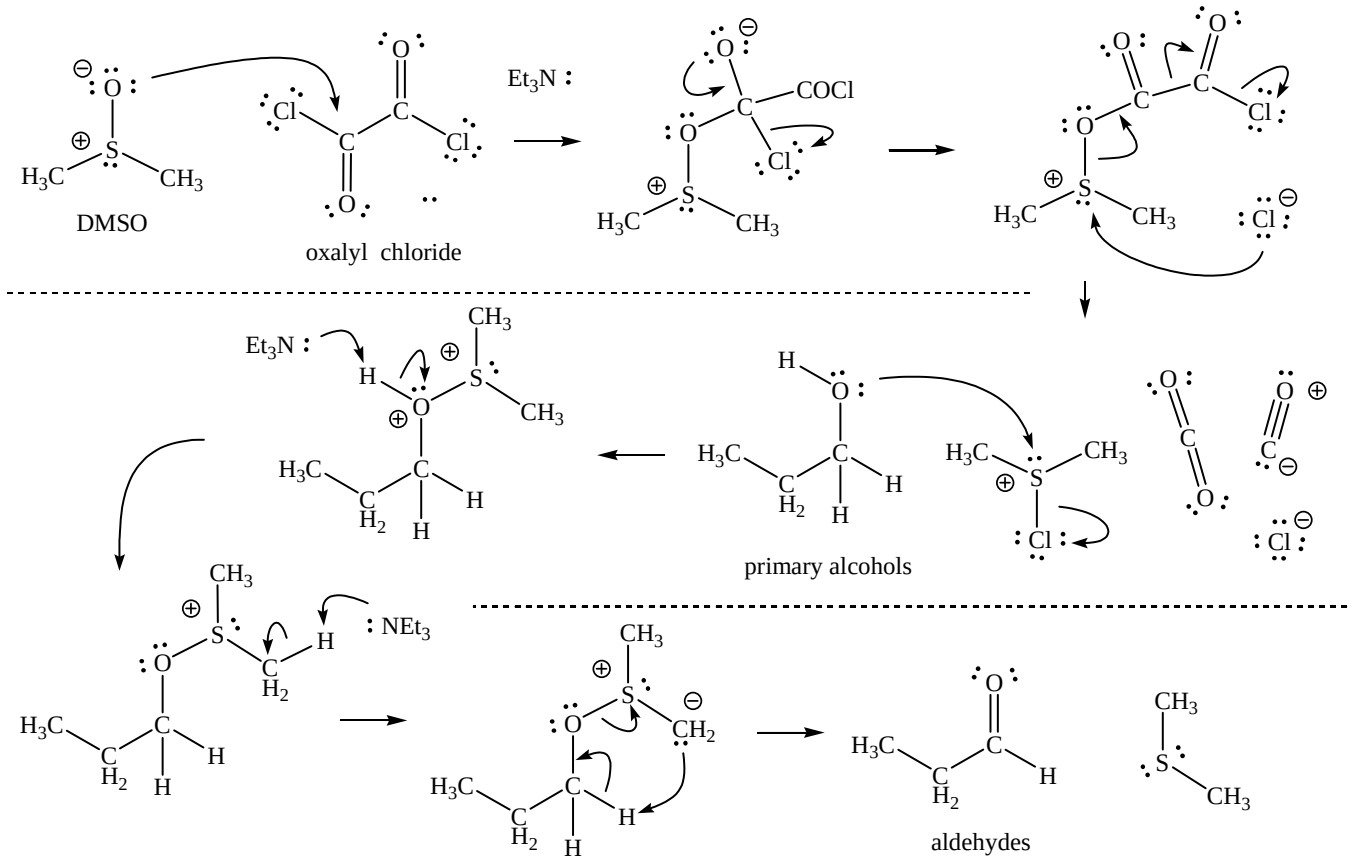
e. Oxidation of ROH with: CrO_3 / acid / water (Jones). Synthesis of carboxylic acids or ketones.

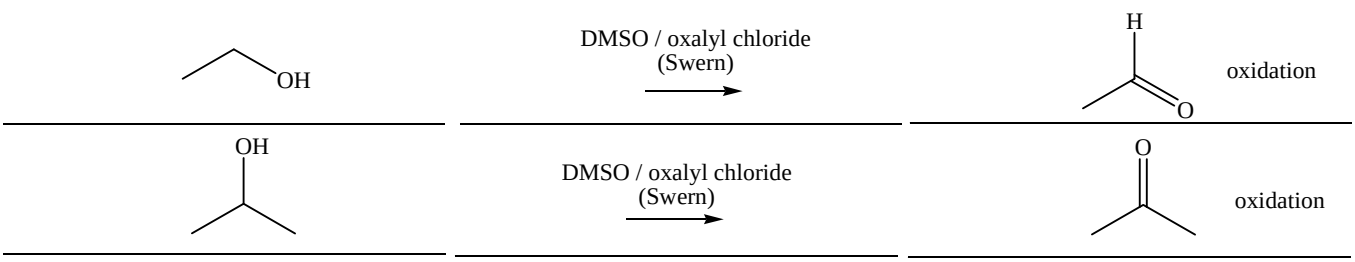


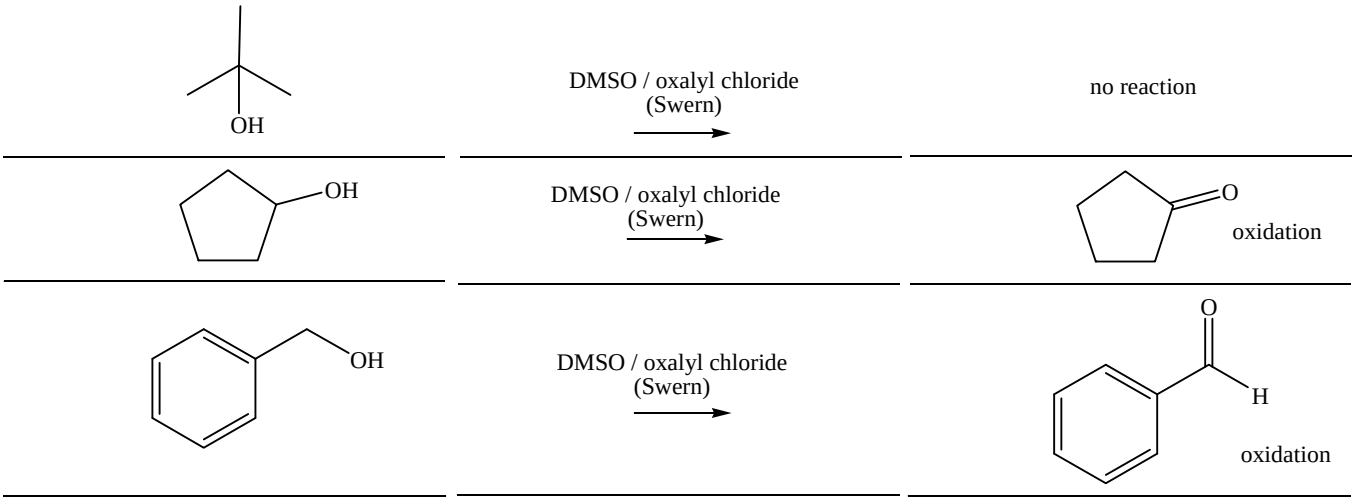
	CrO_3 / acid / H_2O (Jones) →	 oxidation
	CrO_3 / acid / H_2O (Jones) →	 oxidation



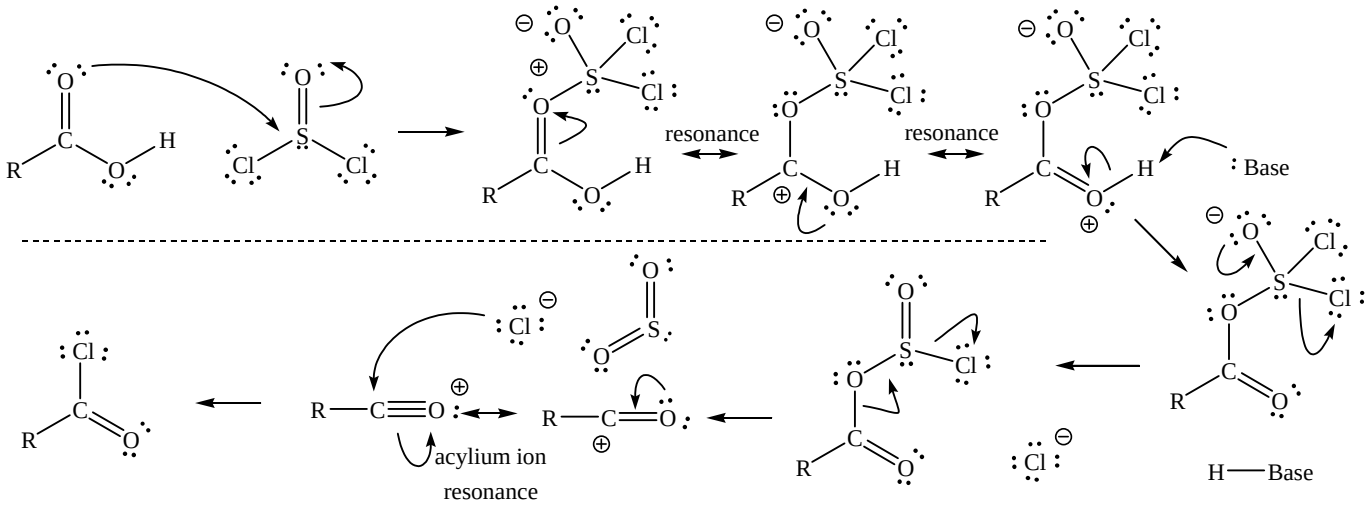
d. Oxidation of ROH with: DMSO / ClOCCOCl / Et_3N (Swern, many variations). Synthesis of aldehydes or ketones.



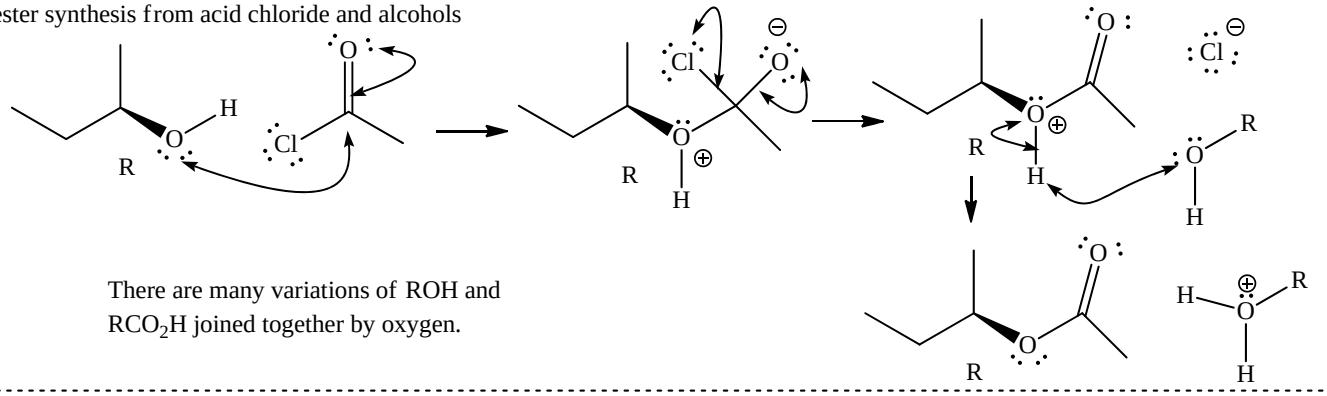




e. RCO_2H with thionyl chloride. Synthesis of esters. Amides, thioesters and anhydrides (Need to make RCOCl with $SOCl_2$ + acid.) There are a variety of approaches you could propose for this transformation.

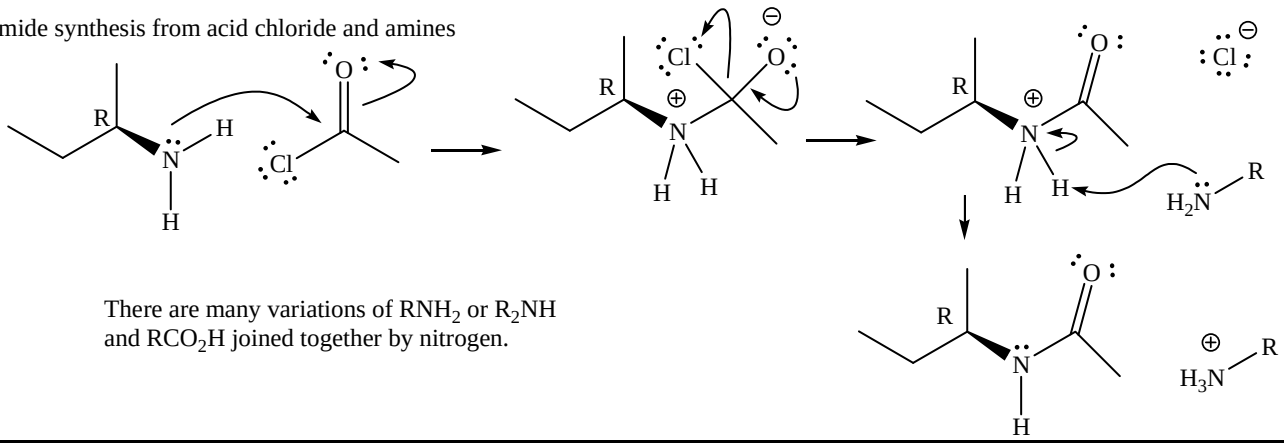


ester synthesis from acid chloride and alcohols



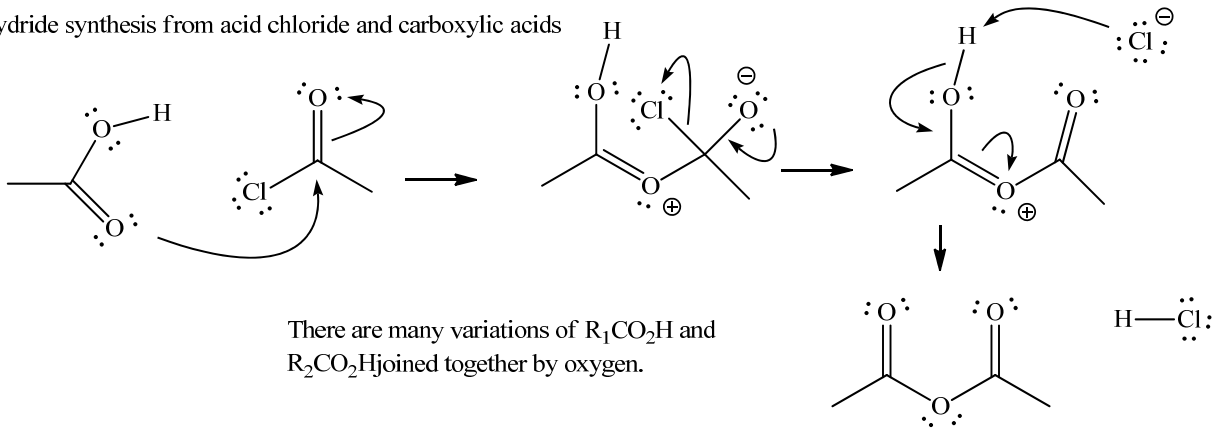
There are many variations of ROH and RCO_2H joined together by oxygen.

amide synthesis from acid chloride and amines

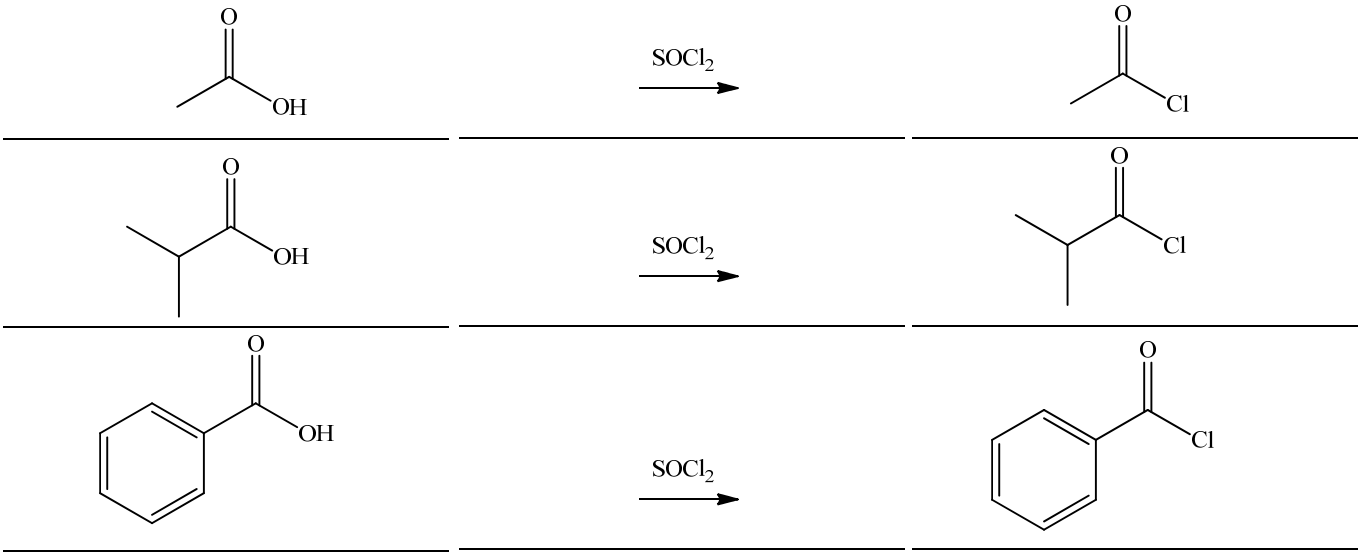


There are many variations of RNH_2 or R_2NH and RCO_2H joined together by nitrogen.

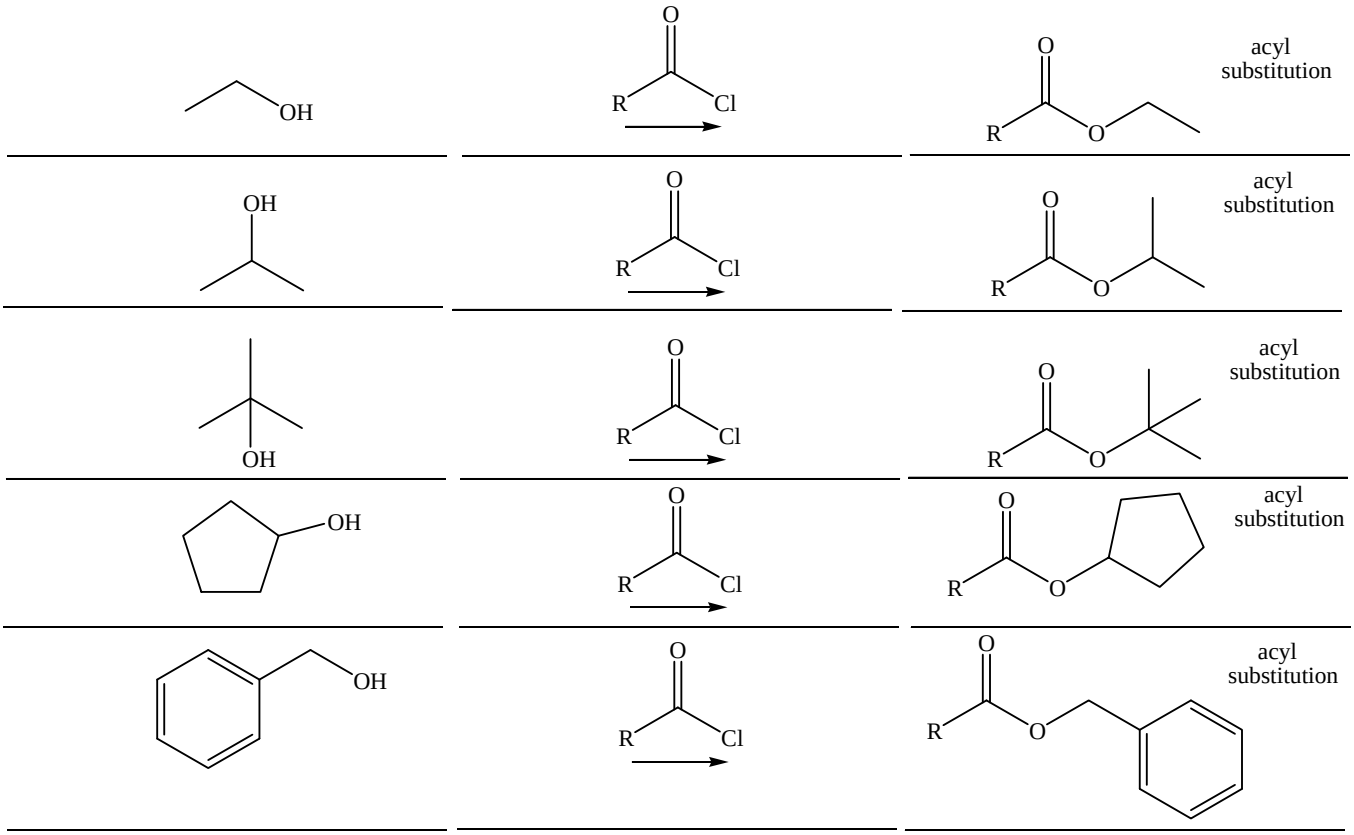
anhydride synthesis from acid chloride and carboxylic acids



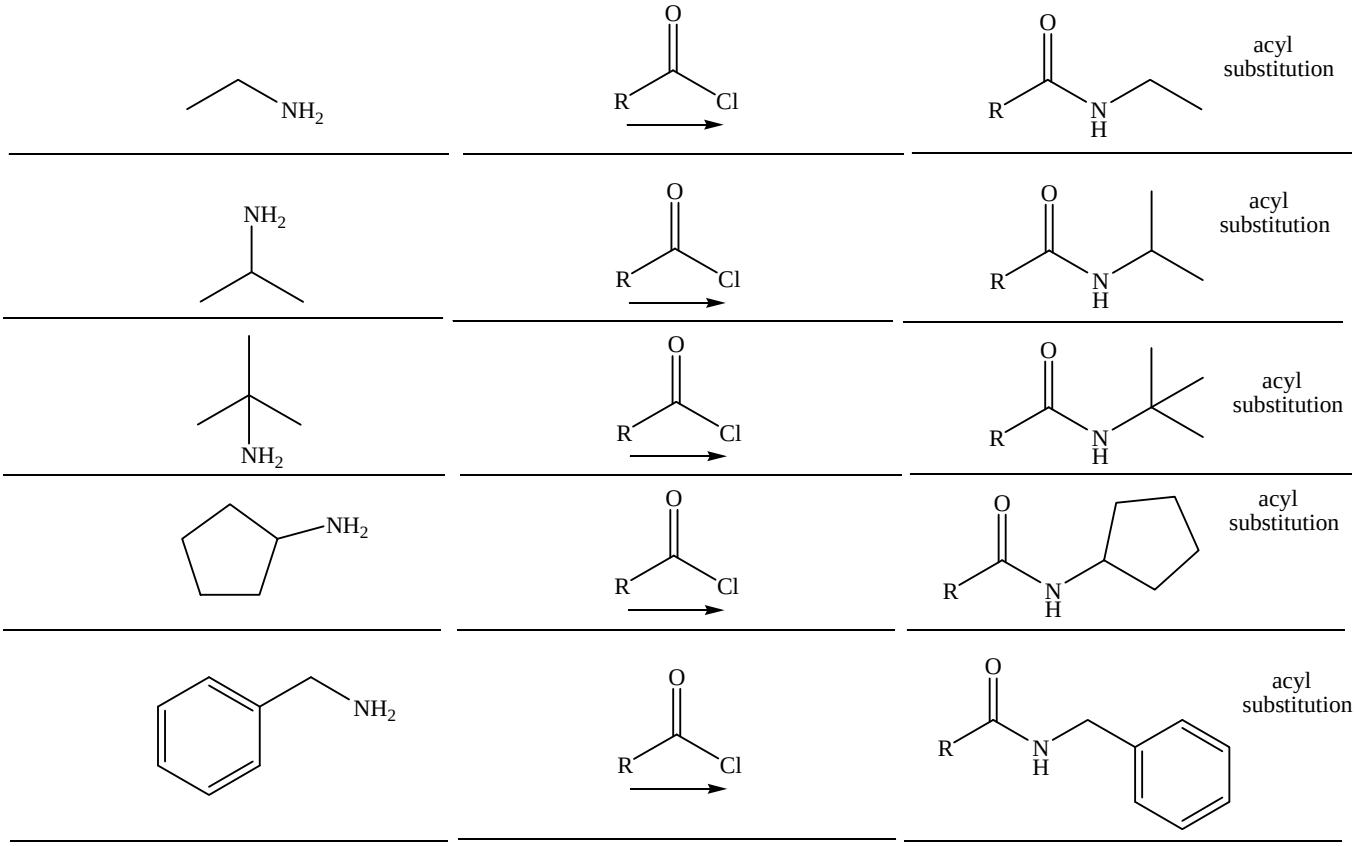
There are many variations of R_1CO_2H and R_2CO_2Hjoined together by oxygen.



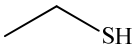
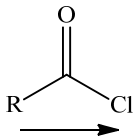
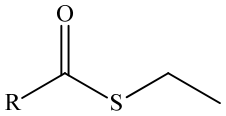
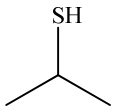
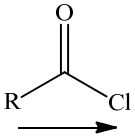
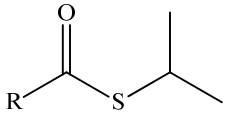
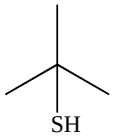
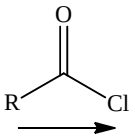
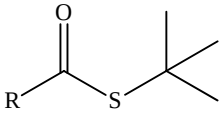
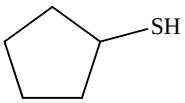
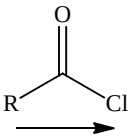
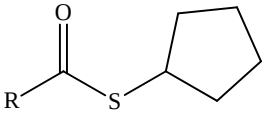
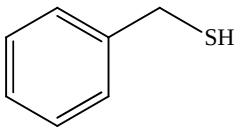
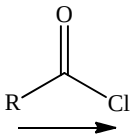
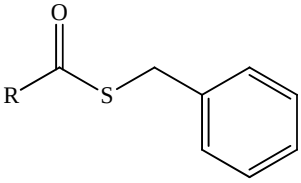
f. ROH with acid chlorides. Synthesis of esters. (Need to make RCOCl with $SOCl_2$ + acid.)



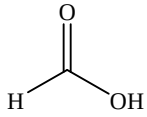
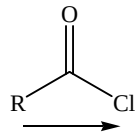
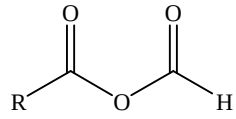
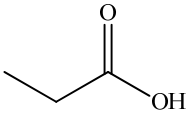
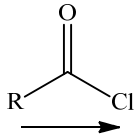
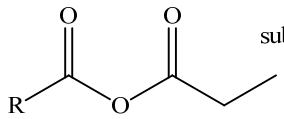
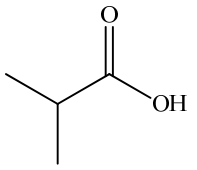
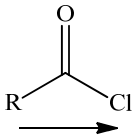
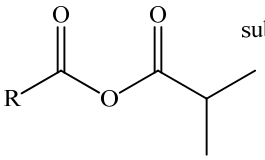
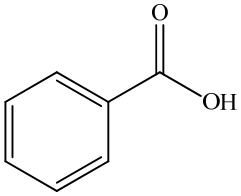
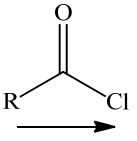
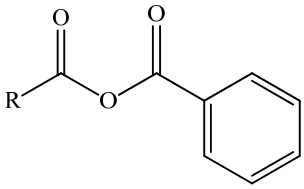
g. RNH_2 with acid chlorides. Synthesis of amides. (Need to make RCOCl with $SOCl_2$ + acid.)



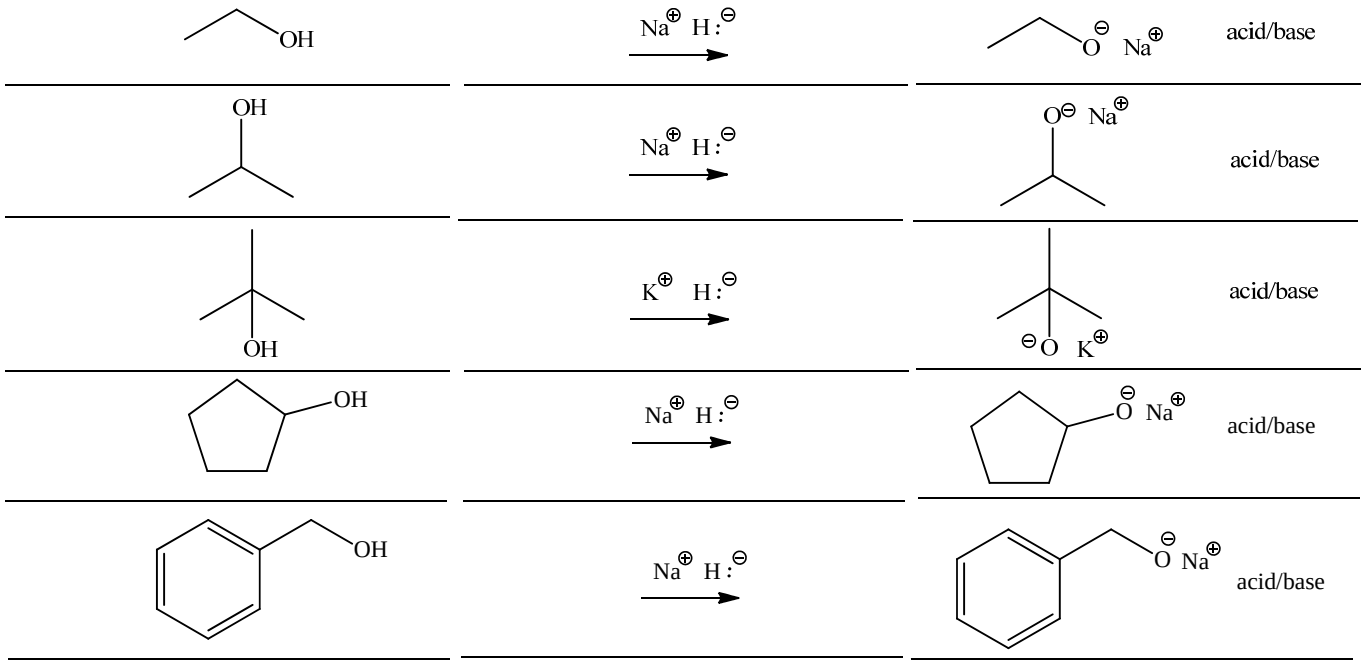
h. RSH with acid chlorides. Synthesis of thioesters. (Need to make RCOCl with $SOCl_2$ + acid.)

		 acyl substitution
		 acyl substitution
		 acyl substitution
		 acyl substitution
		 acyl substitution

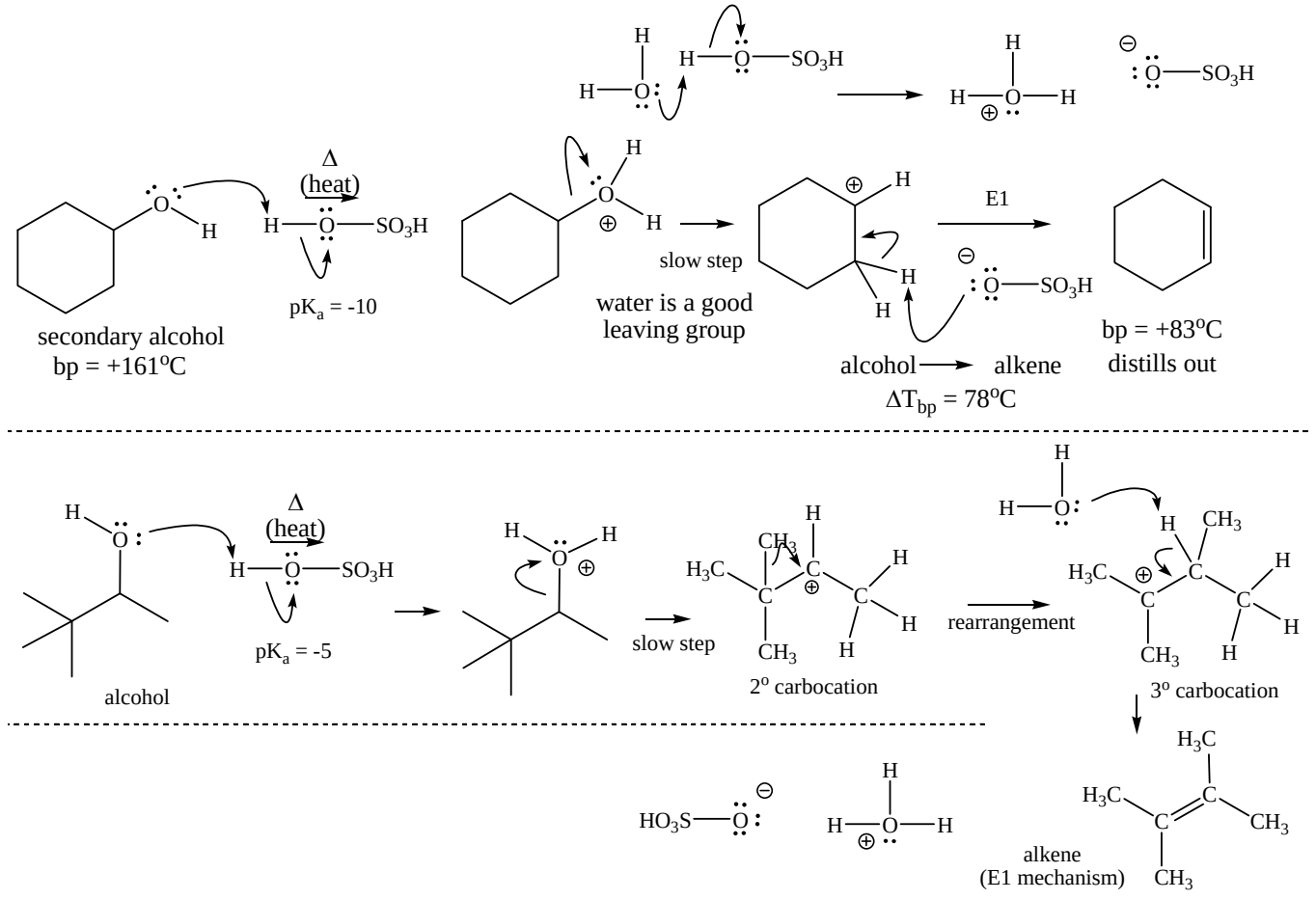
i. RCO_2H with acid chlorides. Synthesis of anhydrides. (Need to make RCOCl with $SOCl_2$ + acid.)

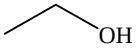
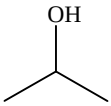
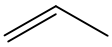
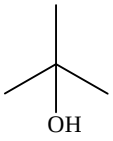
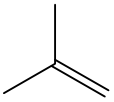
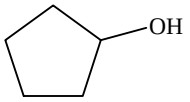
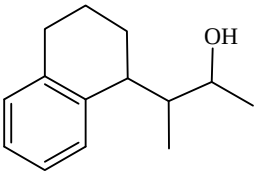
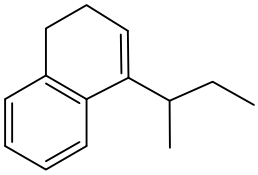
		 acyl substitution There is no 1C acid chloride, so the anhydride works as a substitute.
		 acyl substitution
		 acyl substitution
		 acyl substitution

j. ROH with sodium hydride, NaH. Synthesis of sodium alkoxides.

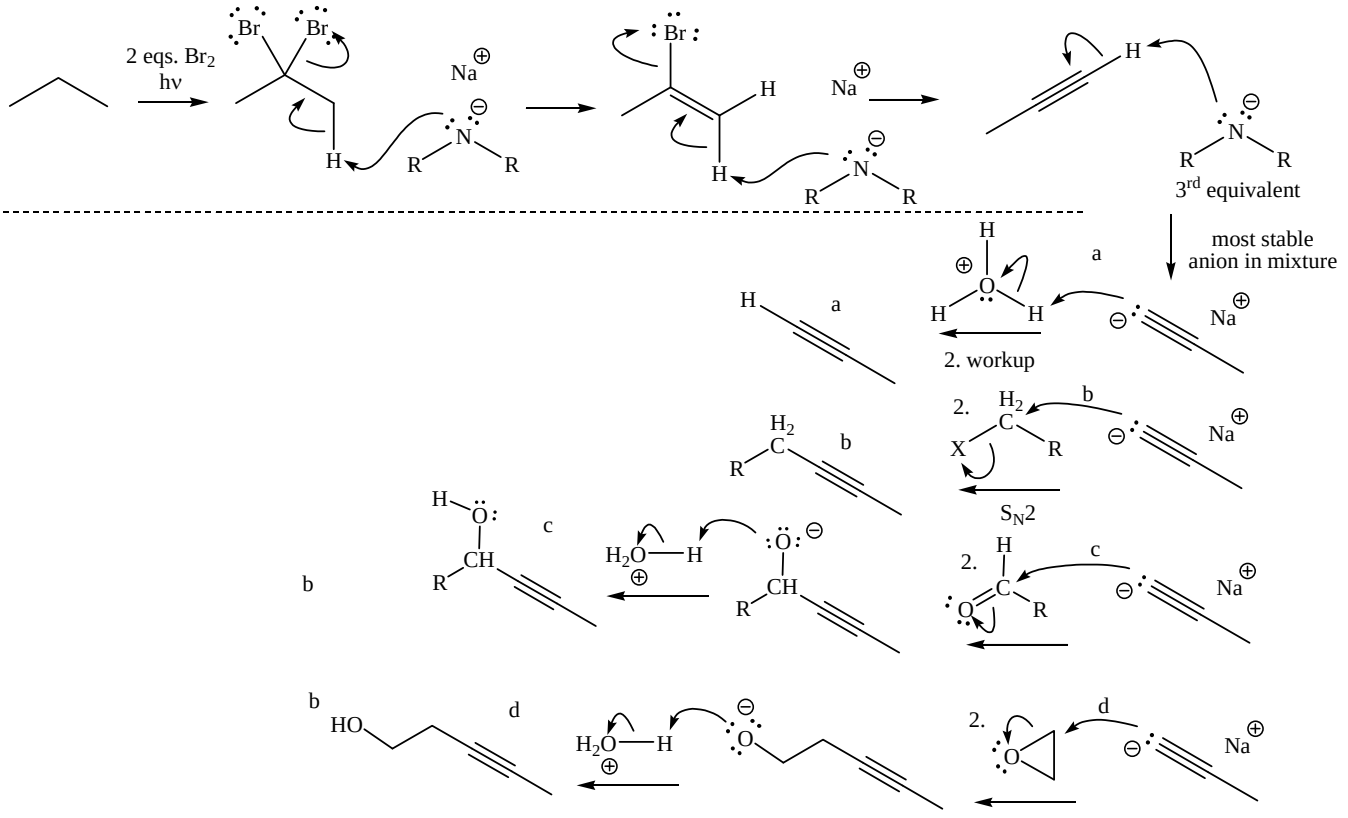


k. ROH with sulfuric acid / heat. Synthesis of alkenes (our only useful E1 reaction. Rearrangement is possible).

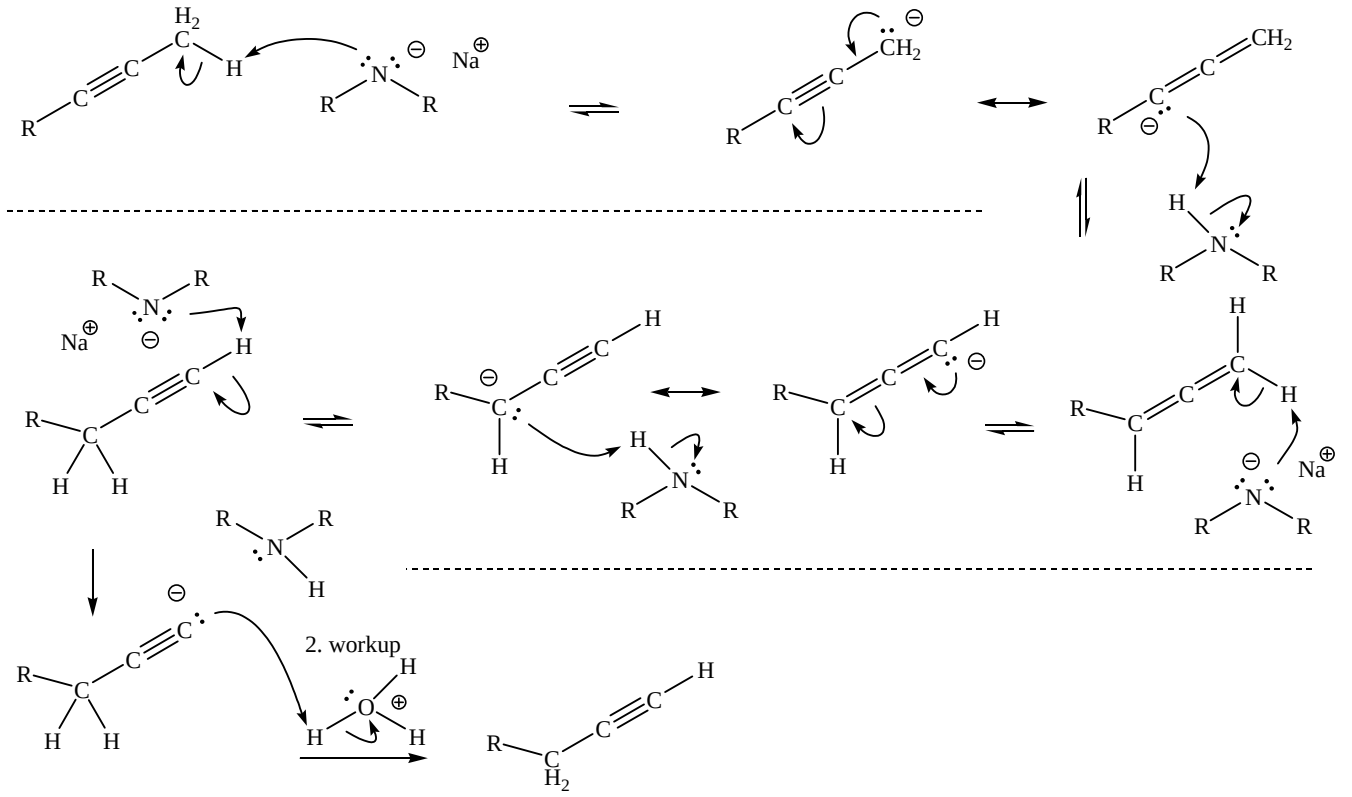


	H_2SO_4 / Δ →	 probably E2
	H_2SO_4 / Δ →	 E1
	H_2SO_4 / Δ →	 E1
	H_2SO_4 / Δ →	 E1
	H_2SO_4 / Δ →	 E1

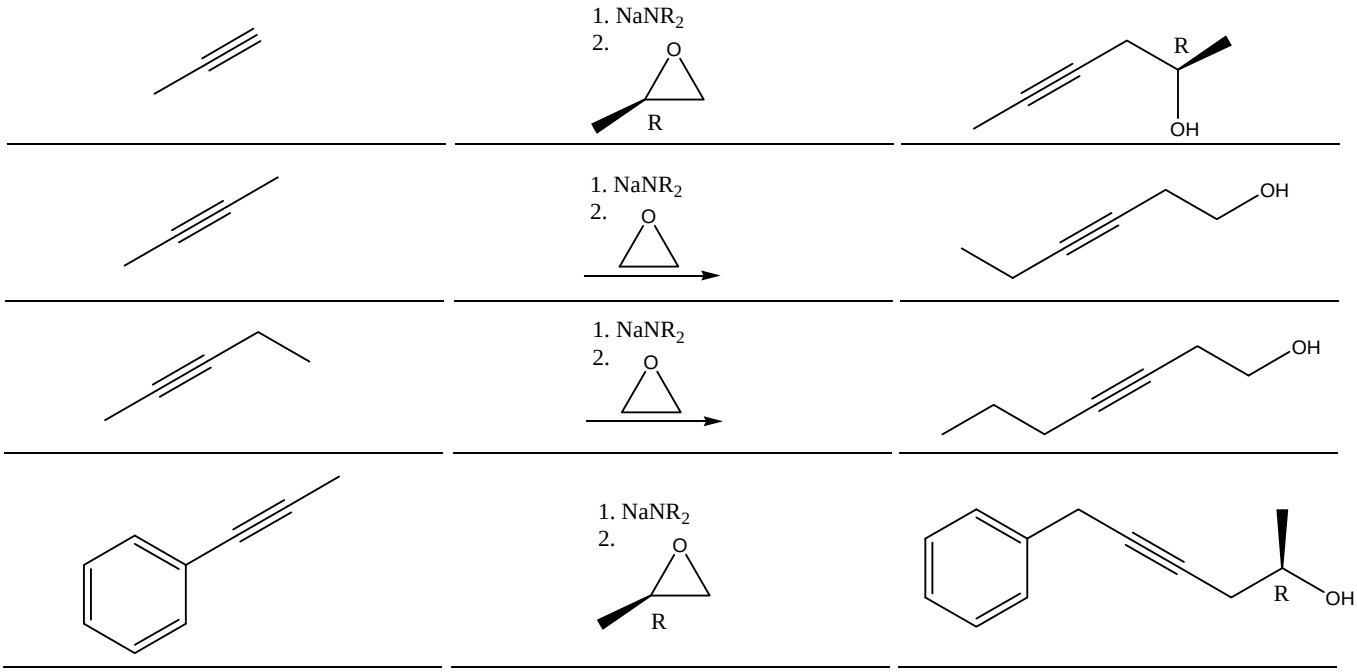
l. Double elimination from dibromoalkanes to form alkynes and terminal acetylides used in many additional reactions (S_N2 with RBr, C=O addition to aldehyses and ketones, and reaction with epoxides)



The zipper reaction moves a triple bond in an unbranched linear chain to the end and allows all of the above reactions.

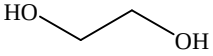
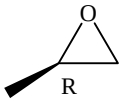
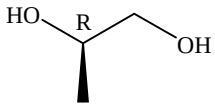
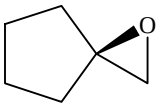
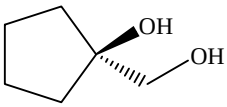
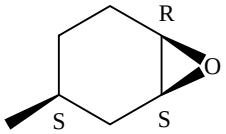
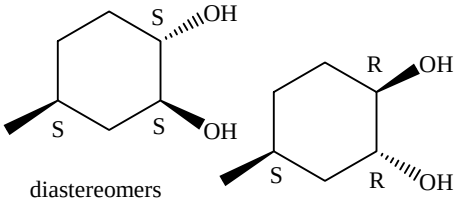


j. Formation of conjugate base + addition of epoxide electrophile forms an alkynyl alcohol via S_N2 reaction.

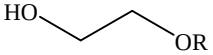
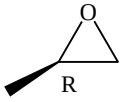
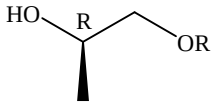
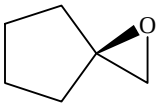
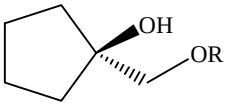
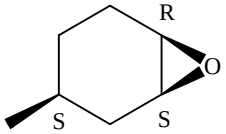
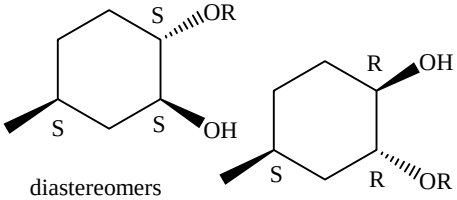


Epoxide chemistry

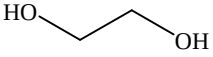
a. Epoxides with aqueous hydroxide (followed by workup = neutralization).

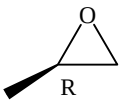
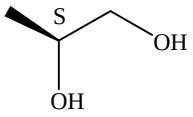
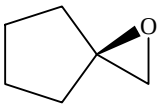
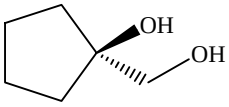
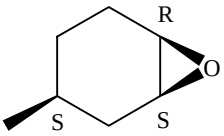
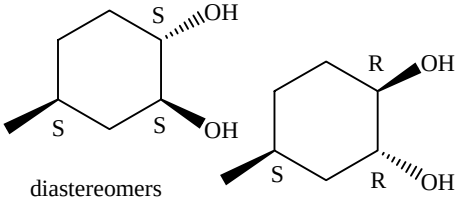
	NaOH, H_2O, 2. WK		achiral
	NaOH, H_2O, 2. WK		chiral
	NaOH, H_2O, 2. WK		achiral
	NaOH, H_2O, 2. WK	 diastereomers	

b. Epoxides with alcoholic alkoxide (followed by workup = neutralization).

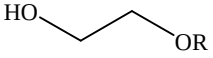
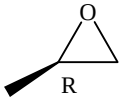
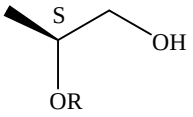
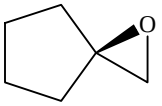
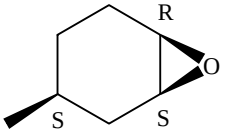
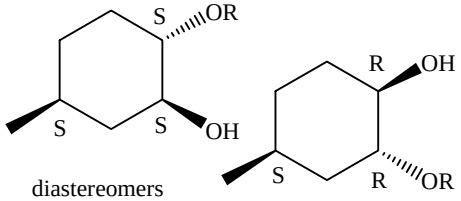
	$RO^{\ominus}$ / ROH, 2. WK		achiral
	$RO^{\ominus}$ / ROH, 2. WK		chiral
	$RO^{\ominus}$ / ROH, 2. WK		achiral
	$RO^{\ominus}$ / ROH, 2. WK	 diastereomers	

c. Epoxides with aqueous acid.

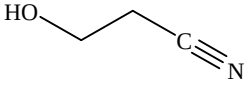
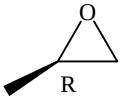
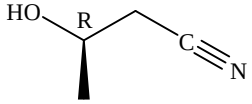
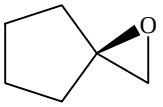
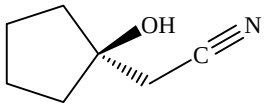
	H_2SO_4 / H_2O (H_3O^+), 2. WK		achiral

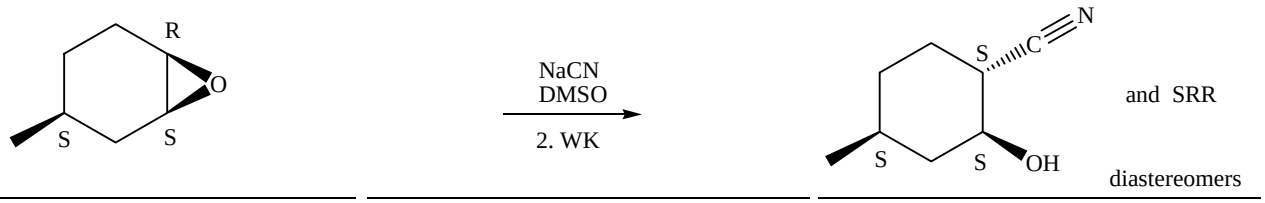
	H_2SO_4 / H_2O (H_3O^+) 2. WK		chiral (inversion)
	H_2SO_4 / H_2O (H_3O^+) 2. WK		achiral
	H_2SO_4 / H_2O (H_3O^+) 2. WK	 diastereomers	

d. Epoxides with alcoholic sulfuric acid.

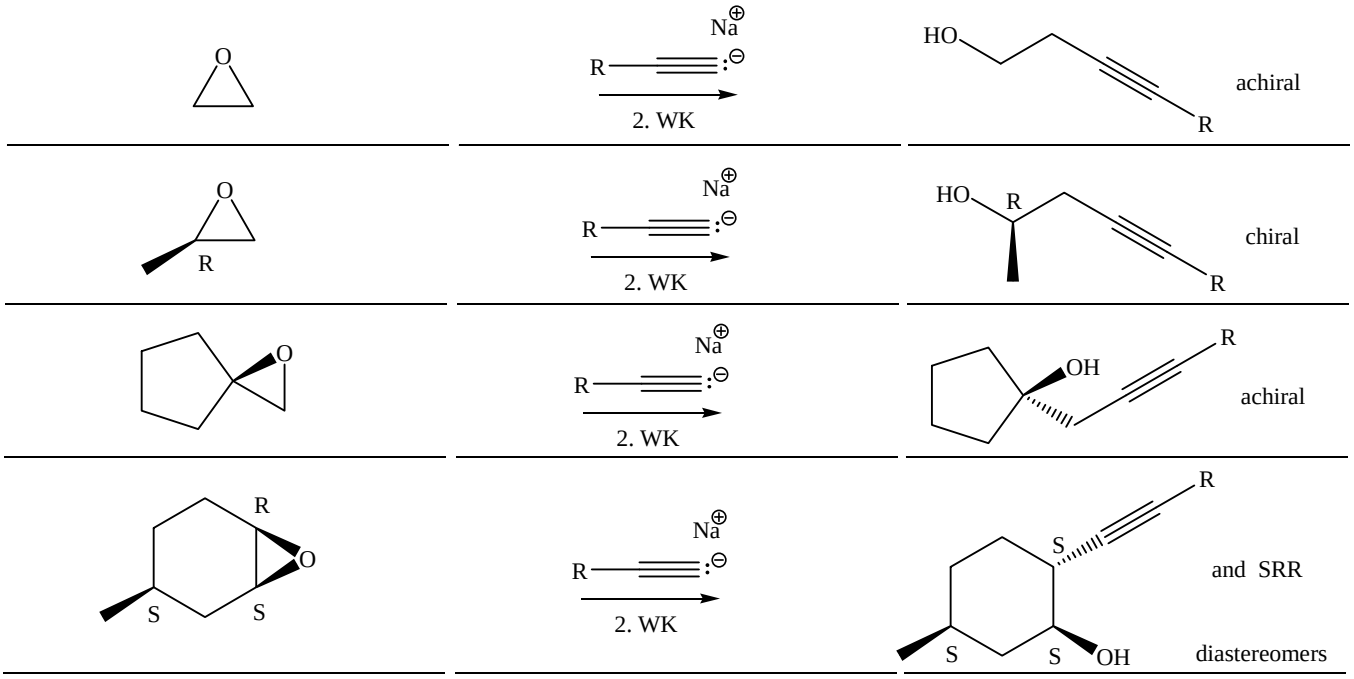
	H_2SO_4 / ROH (ROH_2^+) 2. WK		achiral
	H_2SO_4 / ROH (ROH_2^+) 2. WK		chiral (inversion)
	H_2SO_4 / ROH (ROH_2^+) 2. WK		achiral
	H_2SO_4 / ROH (ROH_2^+) 2. WK	 diastereomers	

e. Epoxides with cyanide (followed by workup = neutralization).

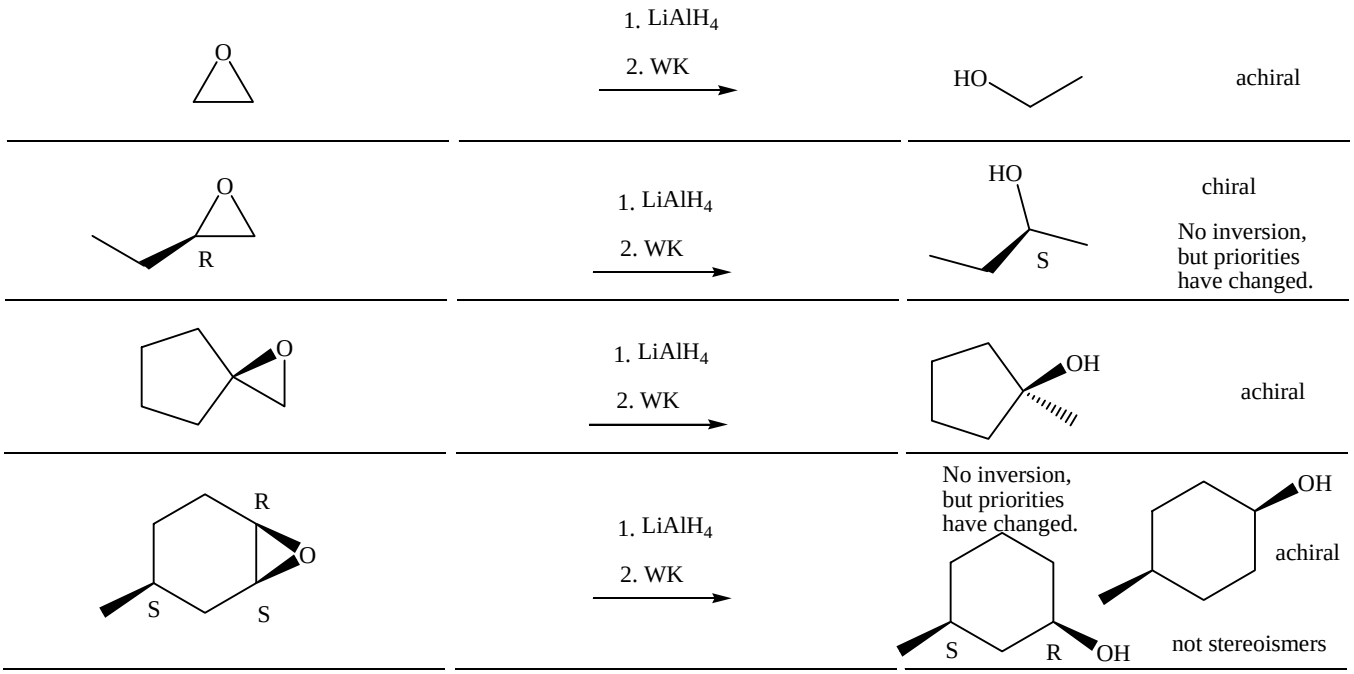
	NaCN DMSO 2. WK		achiral
	NaCN DMSO 2. WK		chiral
	NaCN DMSO 2. WK		achiral



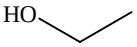
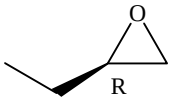
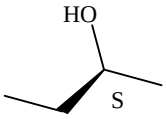
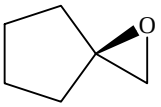
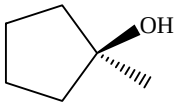
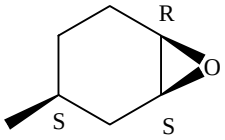
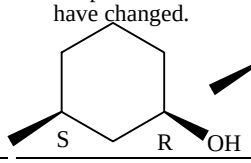
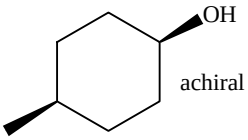
f. Epoxides with terminal acetylides (followed by workup = neutralization).



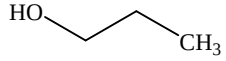
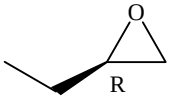
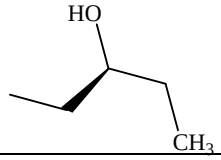
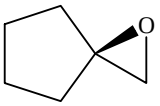
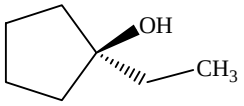
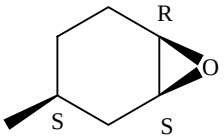
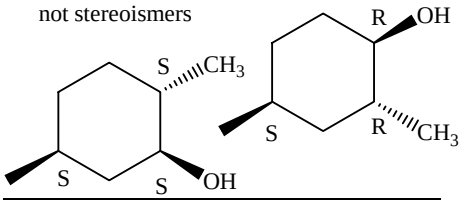
g. Epoxides with $LiAlH_4$ (LAH) (followed by workup = neutralization).



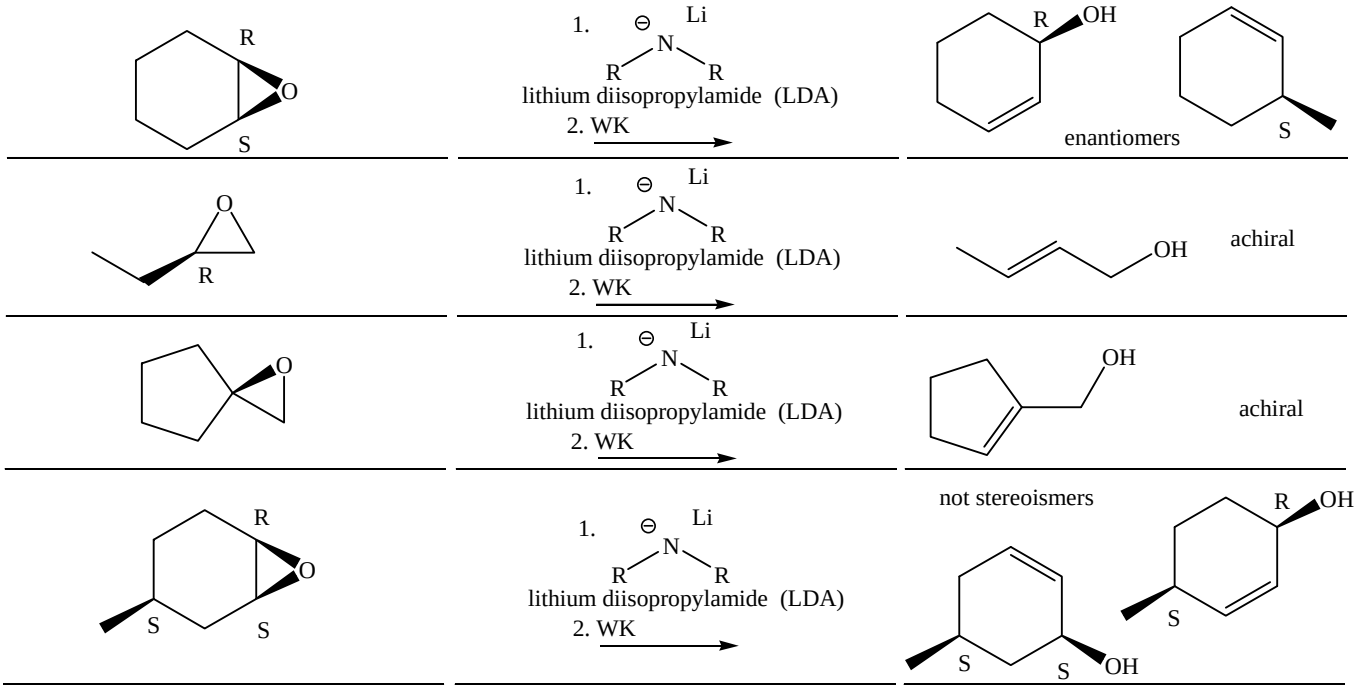
h. Epoxides with $NaBH_4$ (followed by workup = neutralization).

	1. $NaBH_4$ 2. WK		achiral
	1. $NaBH_4$ 2. WK		chiral No inversion, but priorities have changed.
	1. $NaBH_4$ 2. WK		achiral
	1. $NaBH_4$ 2. WK	No inversion, but priorities have changed.  	achiral not stereoismers

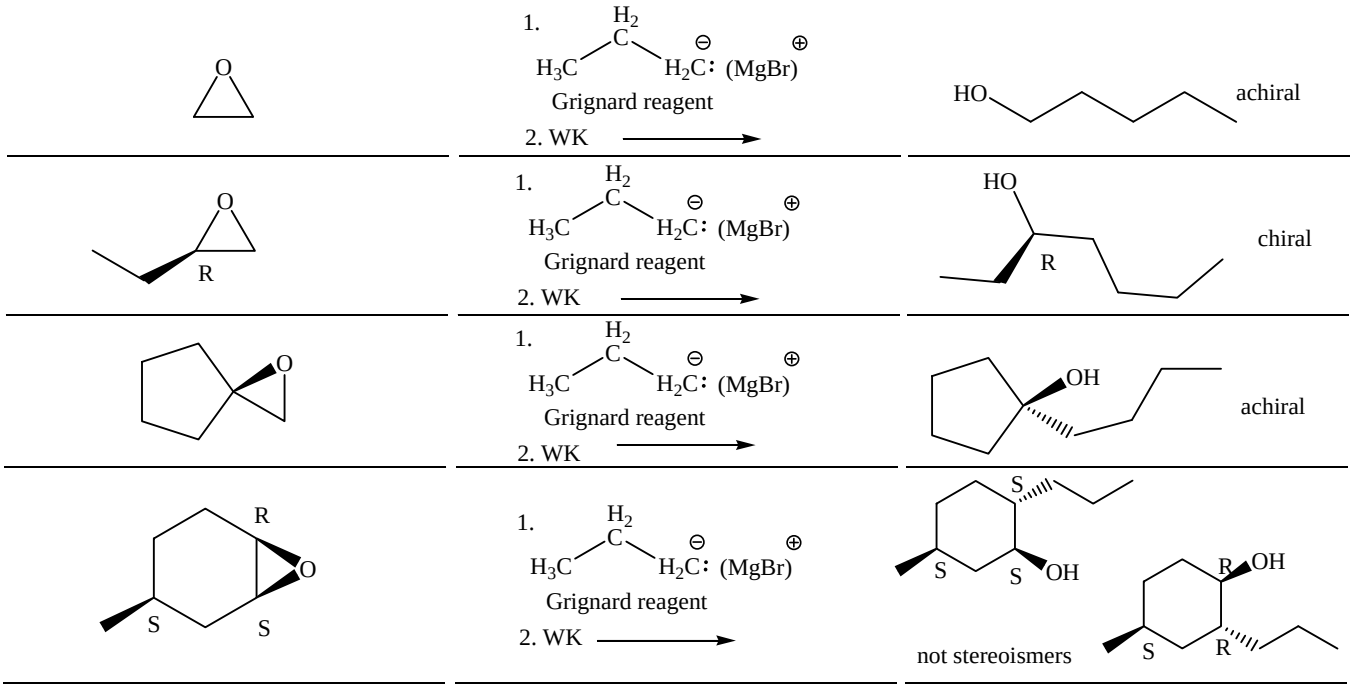
i. Epoxides with cuprates (followed by workup = neutralization).

	1. $(CH_3)_2Cu\ \ Li^{\oplus}$ cuprate reagent 2. WK		achiral
	1. $(CH_3)_2Cu\ \ Li^{\oplus}$ cuprate reagent 2. WK		achiral
	1. $(CH_3)_2Cu\ \ Li^{\oplus}$ cuprate reagent 2. WK		achiral
	1. $(CH_3)_2Cu\ \ Li^{\oplus}$ cuprate reagent 2. WK	not stereoismers 	

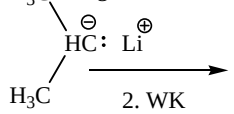
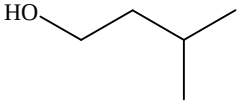
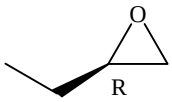
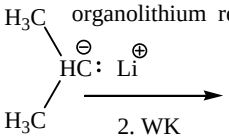
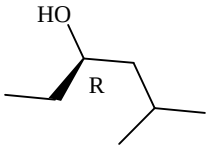
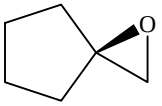
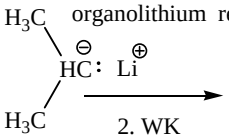
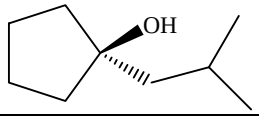
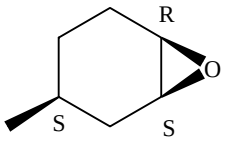
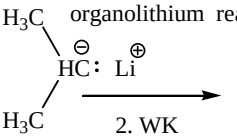
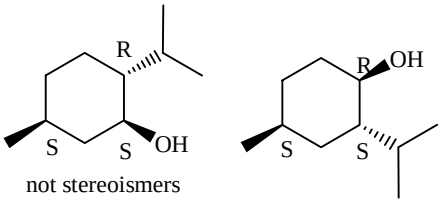
j. Epoxides with lithium diisopropyl amide (LDA, followed by workup = neutralization).



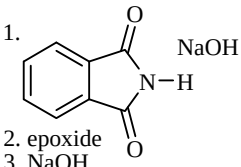
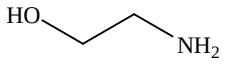
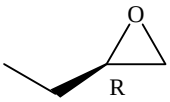
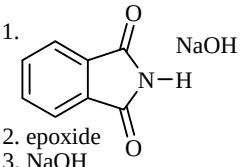
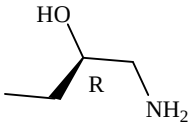
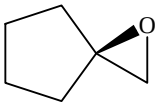
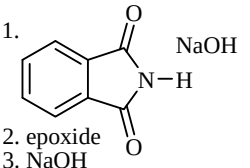
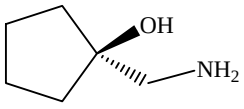
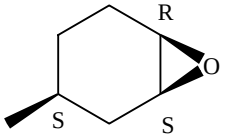
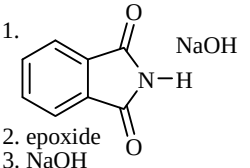
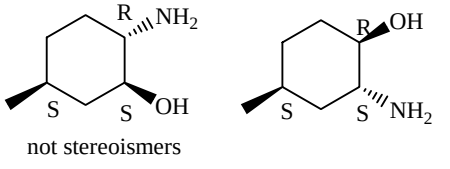
k. Epoxides with Grignard reagents (followed by workup = neutralization).



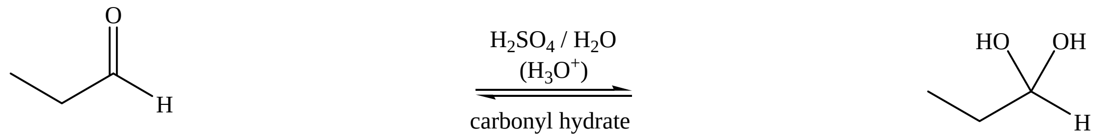
l. Epoxides with organolithium reagents (followed by workup = neutralization).

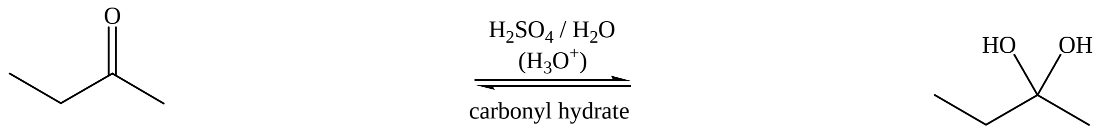
	1. H_3C organolithium reagent  2. WK	 achiral
	1. H_3C organolithium reagent  2. WK	 chiral
	1. H_3C organolithium reagent  2. WK	 achiral
	1. H_3C organolithium reagent  2. WK	 not stereoismers

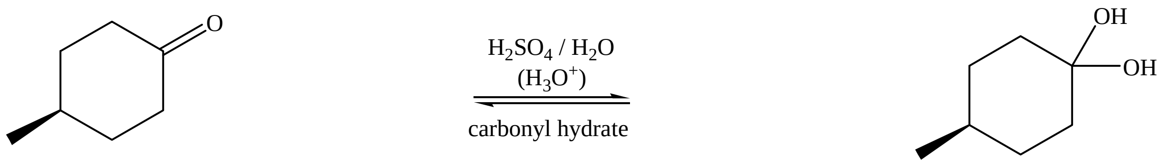
m. Epoxides with conjugate base of phthalimide (followed by hydrolysis and workup = neutralization).

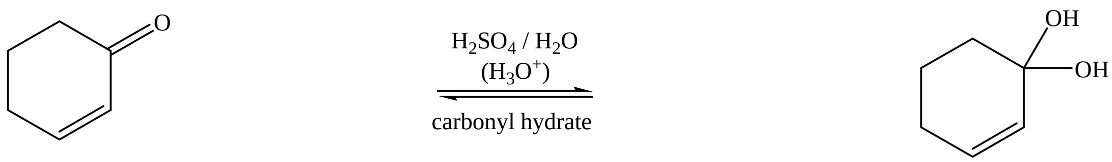
	1.  2. epoxide 3. NaOH 4. WK	 achiral
	1.  2. epoxide 3. NaOH 4. WK	 chiral
	1.  2. epoxide 3. NaOH 4. WK	 achiral
	1.  2. epoxide 3. NaOH 4. WK	 not stereoismers

a. Aldehydes and ketones in aqueous acid form carbonyl hydrates.

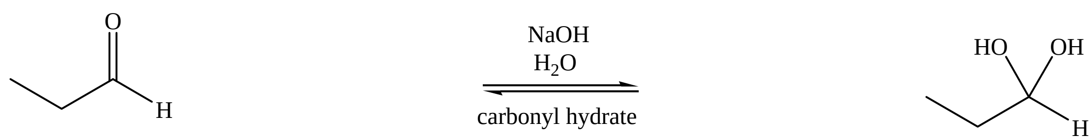


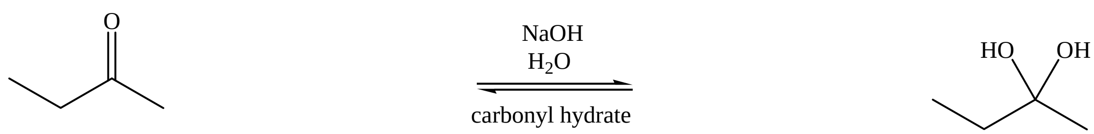


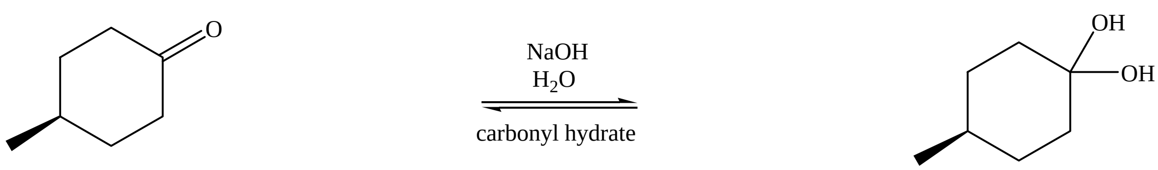


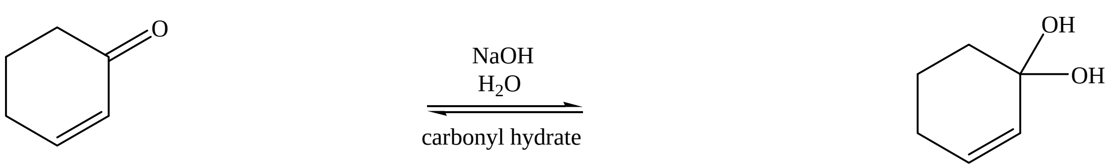


b. Aldehydes and ketones in aqueous base form carbonyl hydrates.

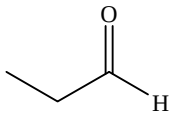
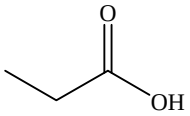
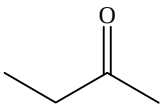




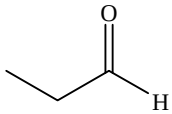
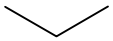
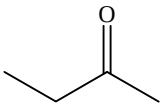
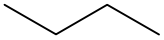
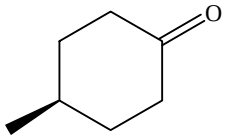
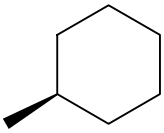
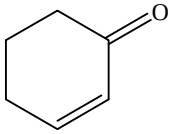
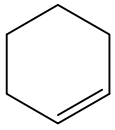




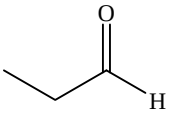
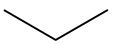
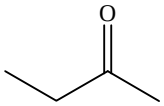
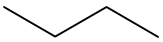
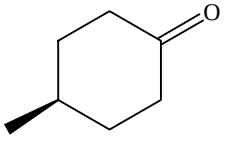
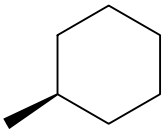
c. Aldehydes and ketones with Jones reagent. Converts aldehydes to carboxylic acids.

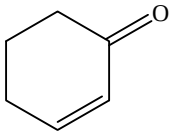
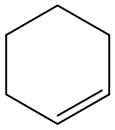
	CrO_3 acid / water Jones	
	CrO_3 acid / water Jones	No reaction with ketones.

d. Aldehydes and ketones with Zn/HCl (Clemmenson reduction).

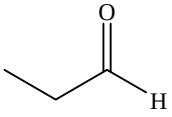
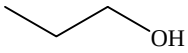
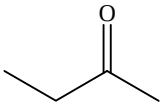
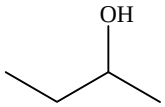
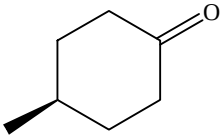
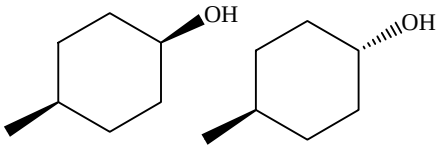
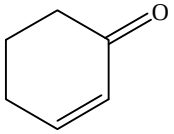
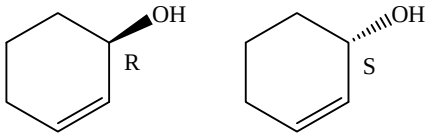
	Zn / HCl Clemmenson reduction	
	Zn / HCl Clemmenson reduction	
	Zn / HCl Clemmenson reduction	
	Zn / HCl Clemmenson reduction	

e. Aldehydes and ketones with hydrazine and base (Wolff-Kishner reduction).

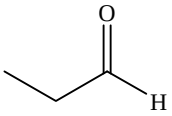
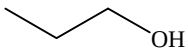
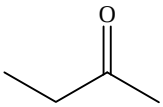
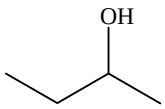
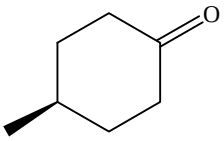
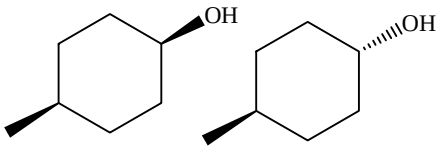
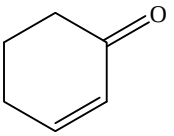
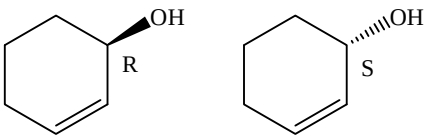
	H_2NNH_2 / $RO^{\ominus}$ / D Wolff-Kishner reduction	
	H_2NNH_2 / $RO^{\ominus}$ / D Wolff-Kishner reduction	
	H_2NNH_2 / $RO^{\ominus}$ / D Wolff-Kishner reduction	

	H_2NNH_2 / $RO^{\ominus}$ / D Wolff-Kishner reduction	

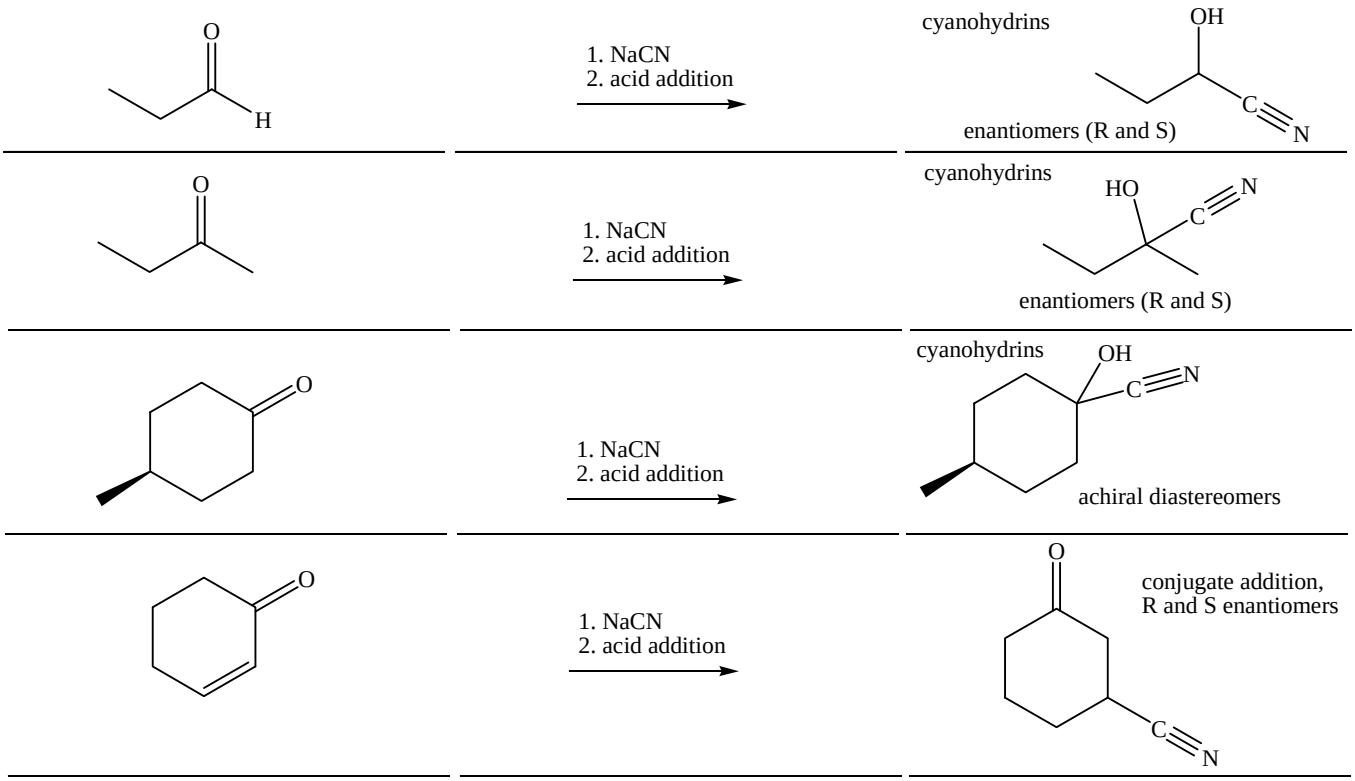
f. Aldehydes and ketones with $LiAlH_4$ (LAH).

	1. $LiAlH_4$ 2. WK	 achiral
	1. $LiAlH_4$ 2. WK	 enantiomers (R and S)
	1. $LiAlH_4$ 2. WK	 achiral diastereomers
	1. $LiAlH_4$ 2. WK	 chiral enantiomers

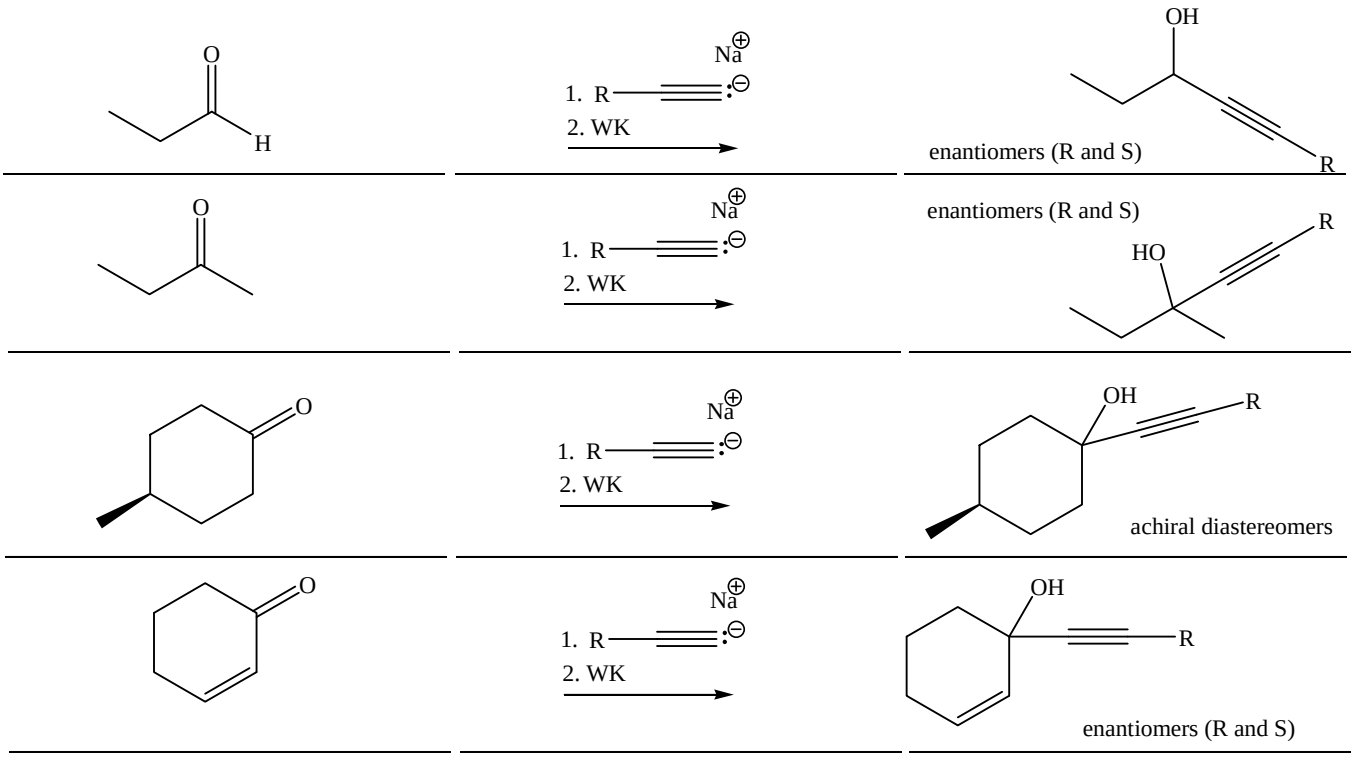
g. Aldehydes and ketones with $NaBH_4$.

	1. $NaBH_4$ 2. WK	 achiral
	1. $NaBH_4$ 2. WK	 enantiomers (R and S)
	1. $NaBH_4$ 2. WK	 achiral diastereomers
	1. $NaBH_4$ 2. WK	 chiral enantiomers

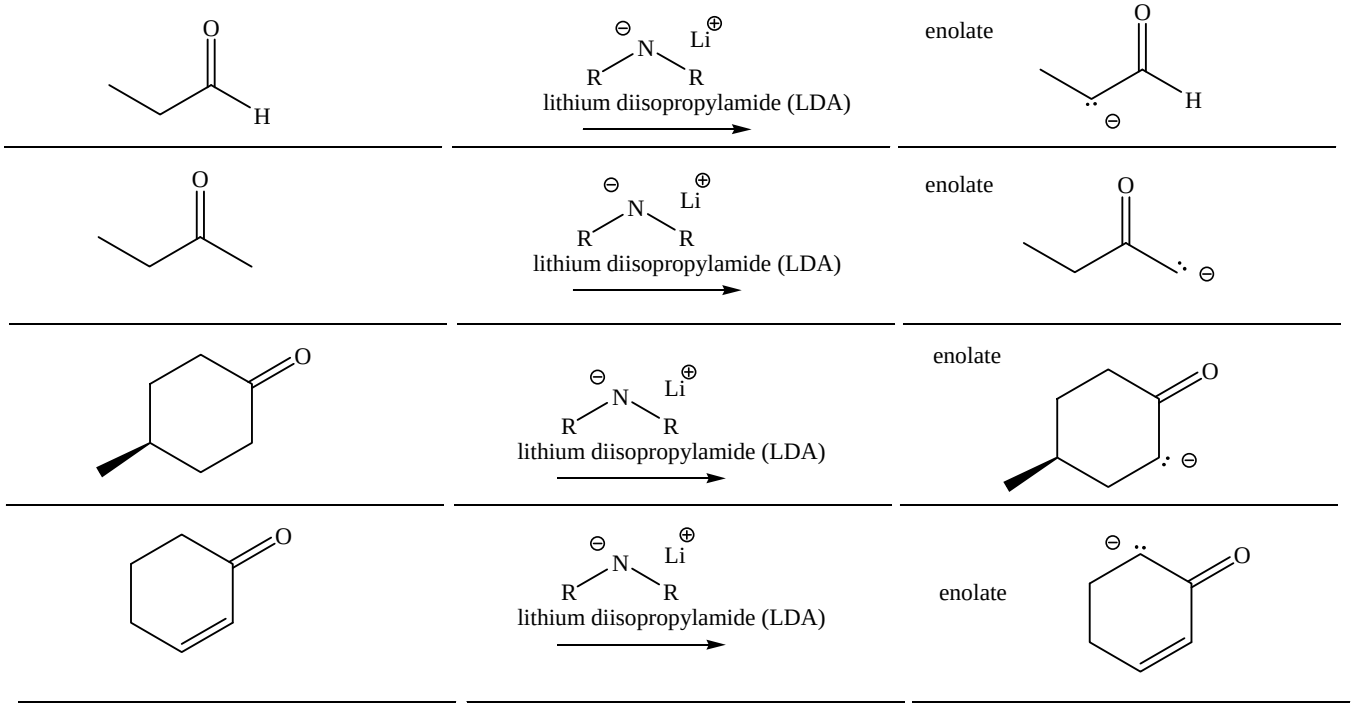
h. Aldehydes and ketones with cyanide, cyanohydrin synthesis or conjugate addition to alpha-beta unsaturated C=O.



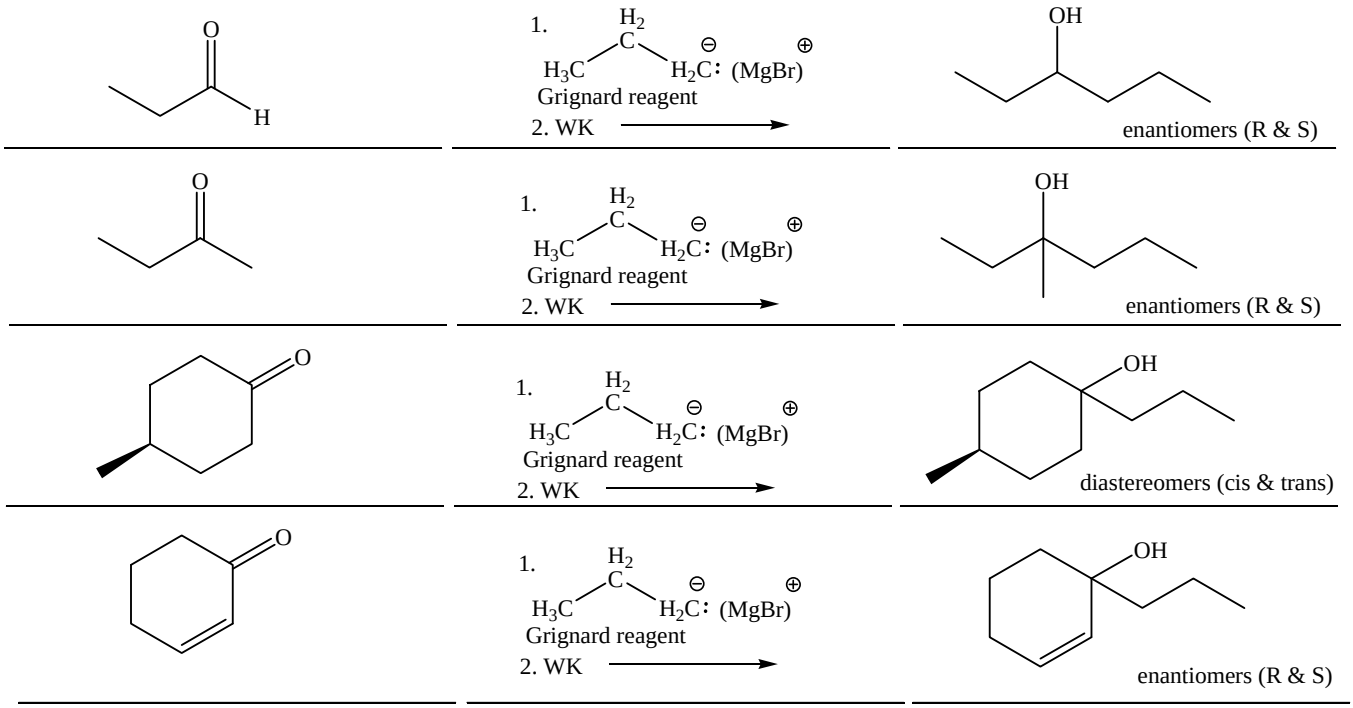
i. Aldehydes and ketones with terminal acetylides.



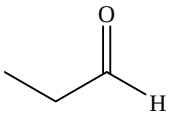
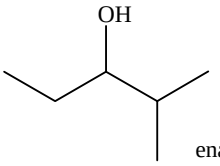
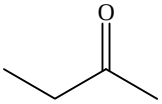
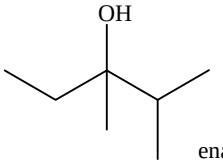
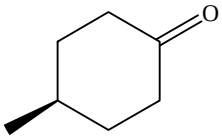
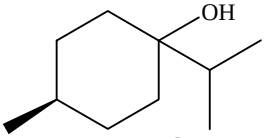
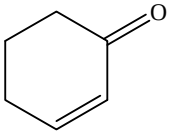
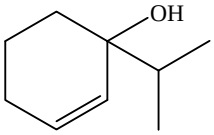
j. Aldehydes and ketones with LDA makes enolates (carbanion nucleophiles).



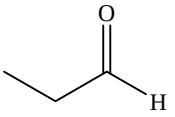
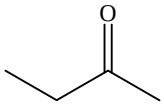
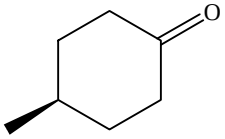
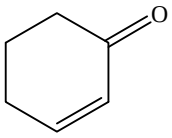
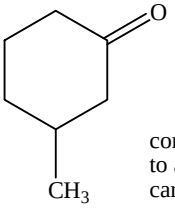
k. Aldehydes and ketones with Grignard (Mg) reagents.



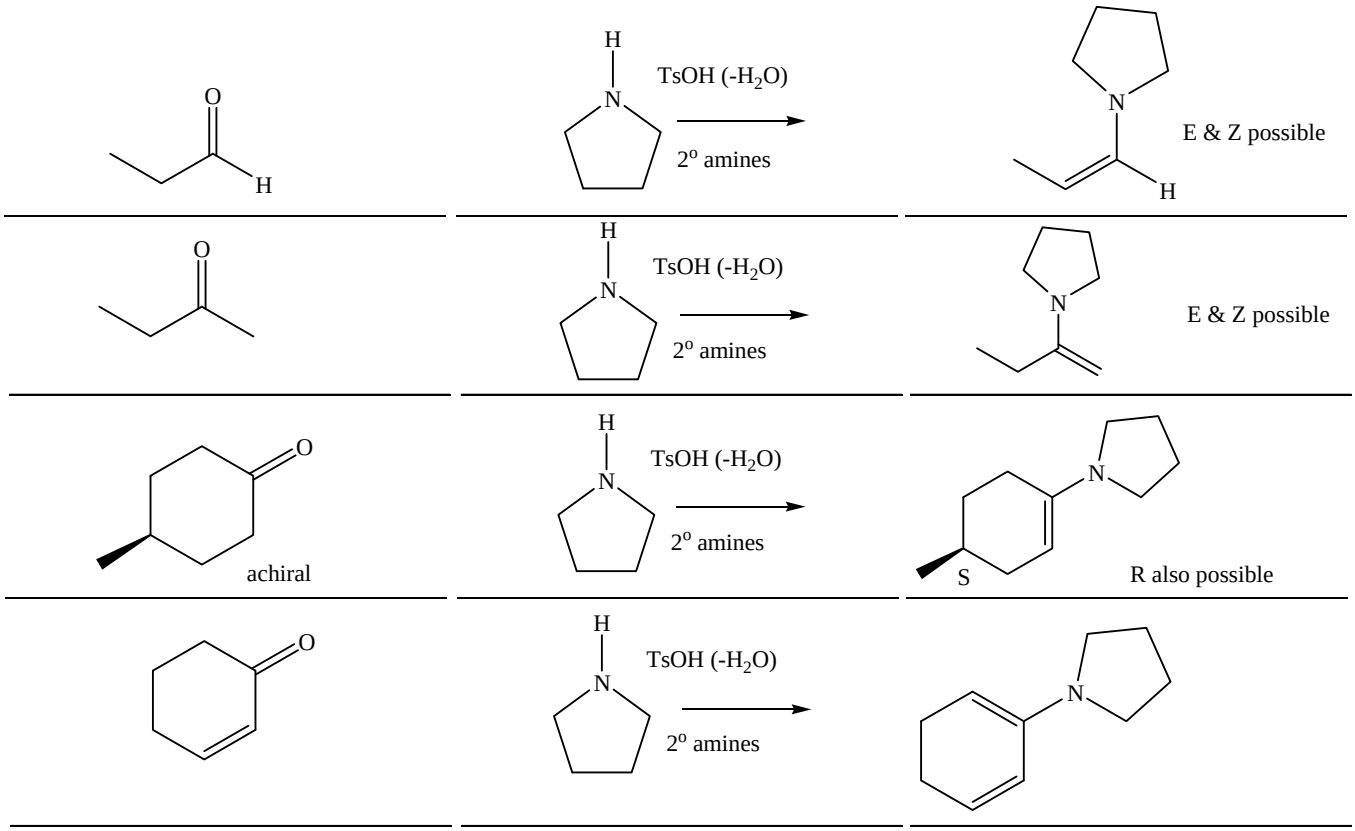
l. Aldehydes and ketones with organolithium reagents.

	1. H_3C $HC^{\ominus}$: $Li^{\oplus}$ H_3C 2. WK organolithium reagent	 enantiomers (R & S)
	1. H_3C $HC^{\ominus}$: $Li^{\oplus}$ H_3C 2. WK organolithium reagent	 enantiomers (R & S)
	1. H_3C $HC^{\ominus}$: $Li^{\oplus}$ H_3C 2. WK organolithium reagent	 diastereomers (cis & trans)
	1. H_3C $HC^{\ominus}$: $Li^{\oplus}$ H_3C 2. WK organolithium reagent	 enantiomers (R & S)

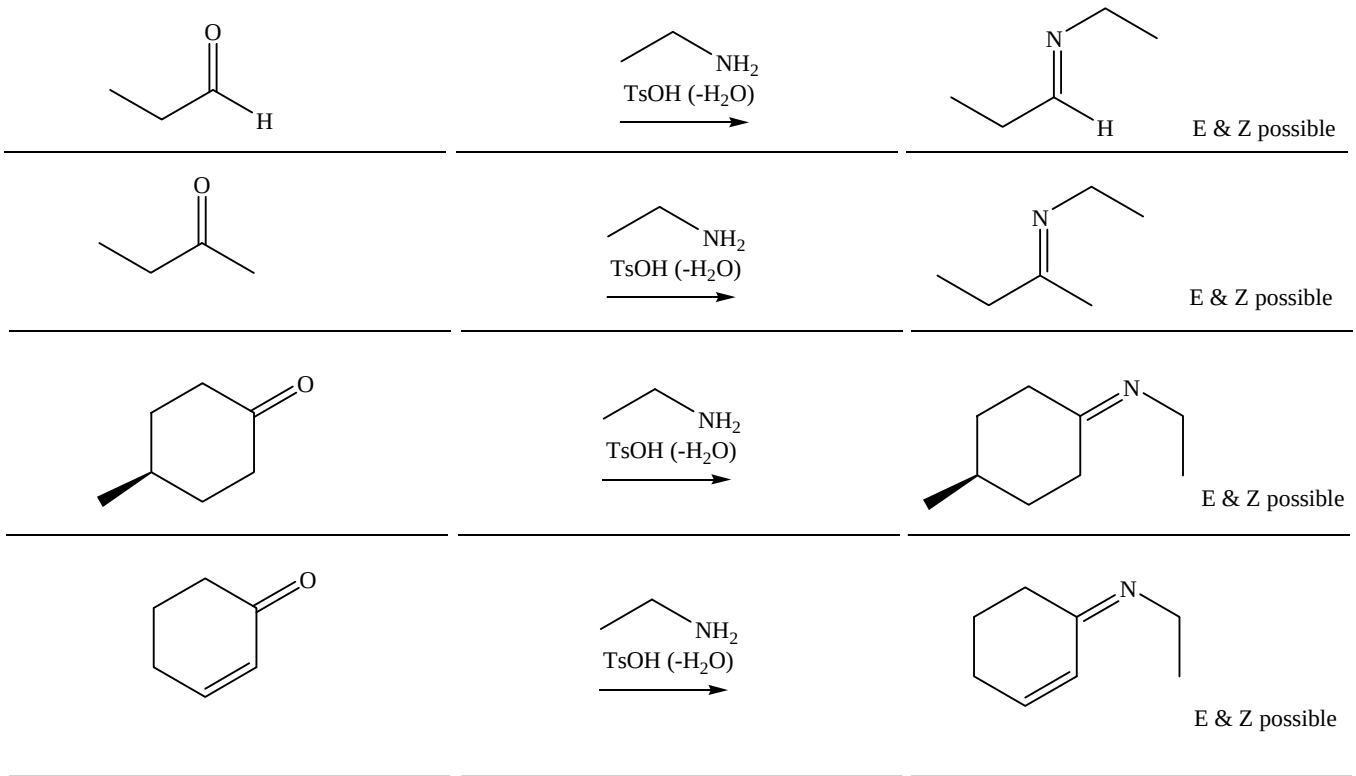
m. Aldehydes and ketones with cuprates.

	1. $(CH_3)_2Cu^{\ominus}$ $Li^{\oplus}$ cuprate reagent 2. WK	Cuprates react slowly with ketones, esters and aldehydes.
	1. $(CH_3)_2Cu^{\ominus}$ $Li^{\oplus}$ cuprate reagent 2. WK	Cuprates react slowly with ketones, esters and aldehydes.
	1. $(CH_3)_2Cu^{\ominus}$ $Li^{\oplus}$ cuprate reagent 2. WK	Cuprates react slowly with ketones, esters and aldehydes.
	1. $(CH_3)_2Cu^{\ominus}$ $Li^{\oplus}$ cuprate reagent 2. WK	 conjugate addition to a,b-unsaturated carbonyl compounds

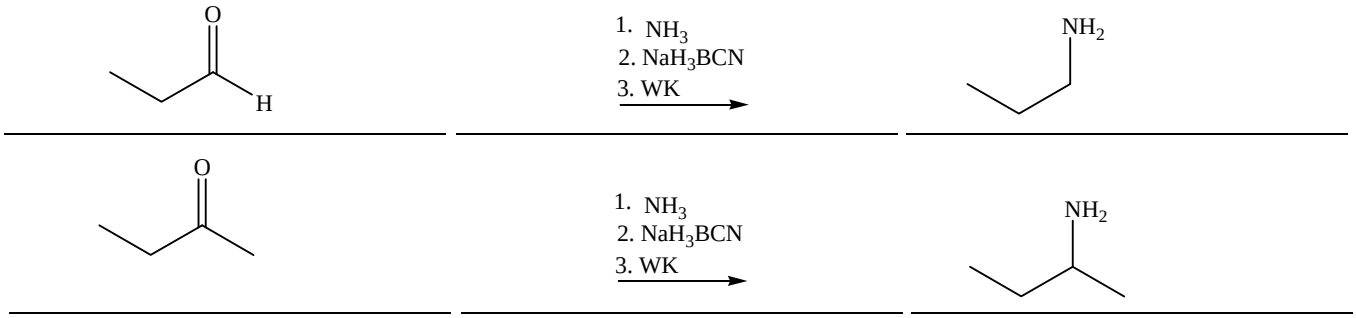
n. Aldehydes and ketones with secondary amines (enamine synthesis, alkylation, hydrolysis).



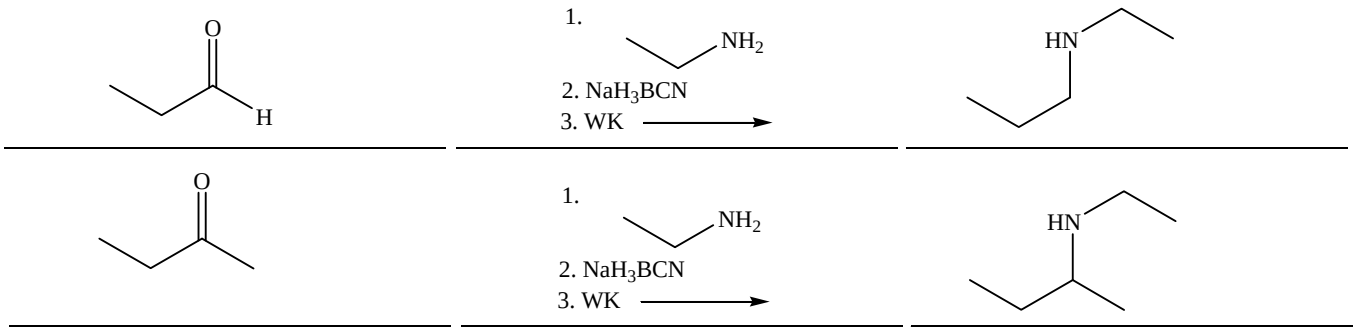
o. Aldehydes and ketones with primary amines (imine synthesis).



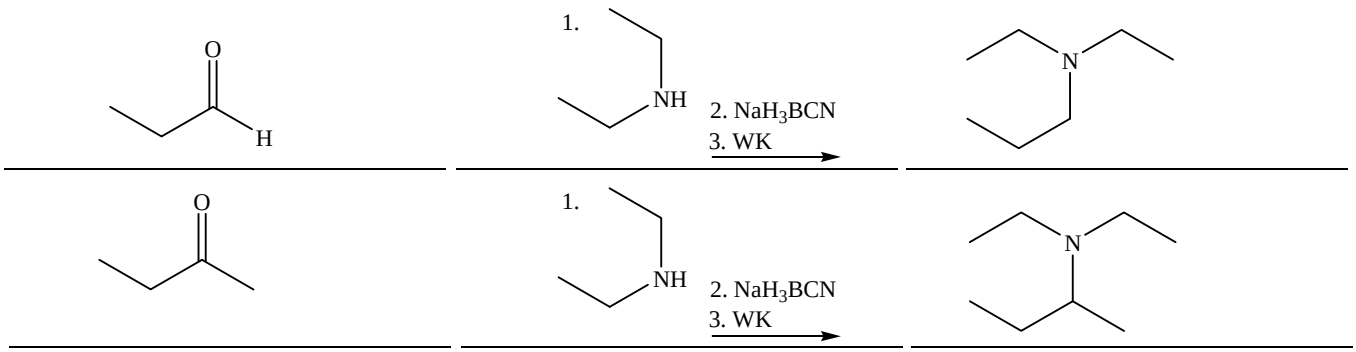
p. Aldehydes and ketones with ammonia + $NaBH_3CN$ = primary amine synthesis.



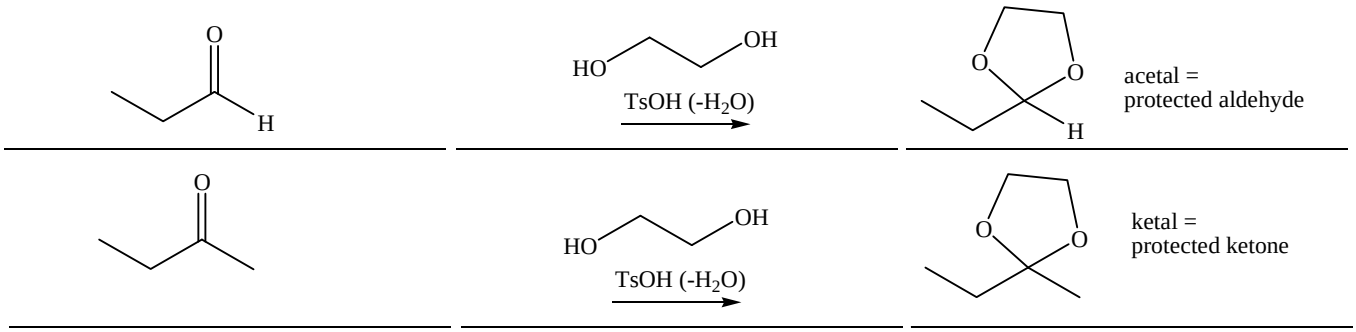
q. Aldehydes and ketones primary amine + $NaBH_3CN$ = secondary amine synthesis.

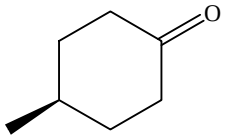
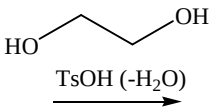


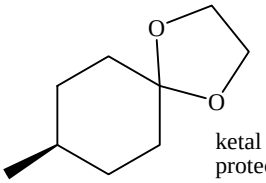
r. Aldehydes and ketones secondary amine + $NaBH_3CN$ = tertiary amine synthesis.

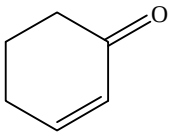
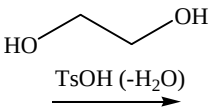


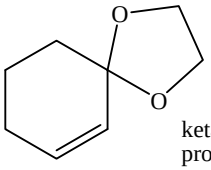
s. Aldehydes and ketones ethylene glycol, acid, dehydration: ketal and acetal synthesis = protection).



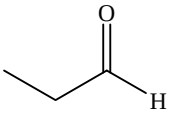
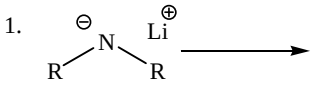



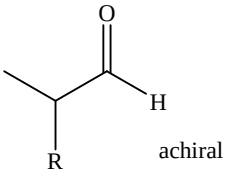


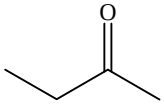
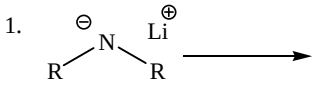



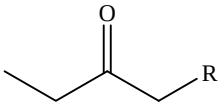


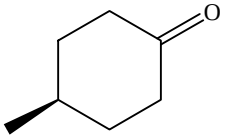
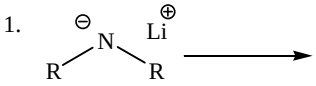
t. Aldehydes and ketones with 1. LDA 2. RX = alkylation of C=O.

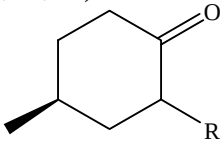



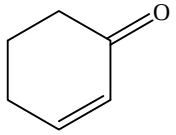
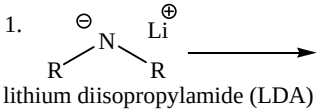


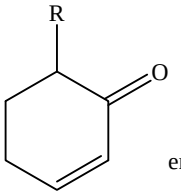





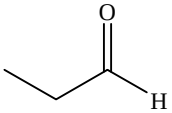
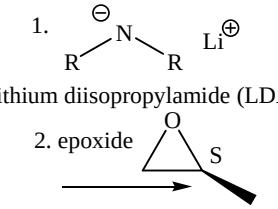
enantiomers and diastereomers
(RR, SS, RS, SR)


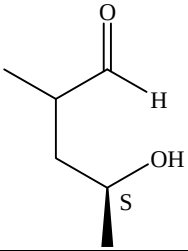



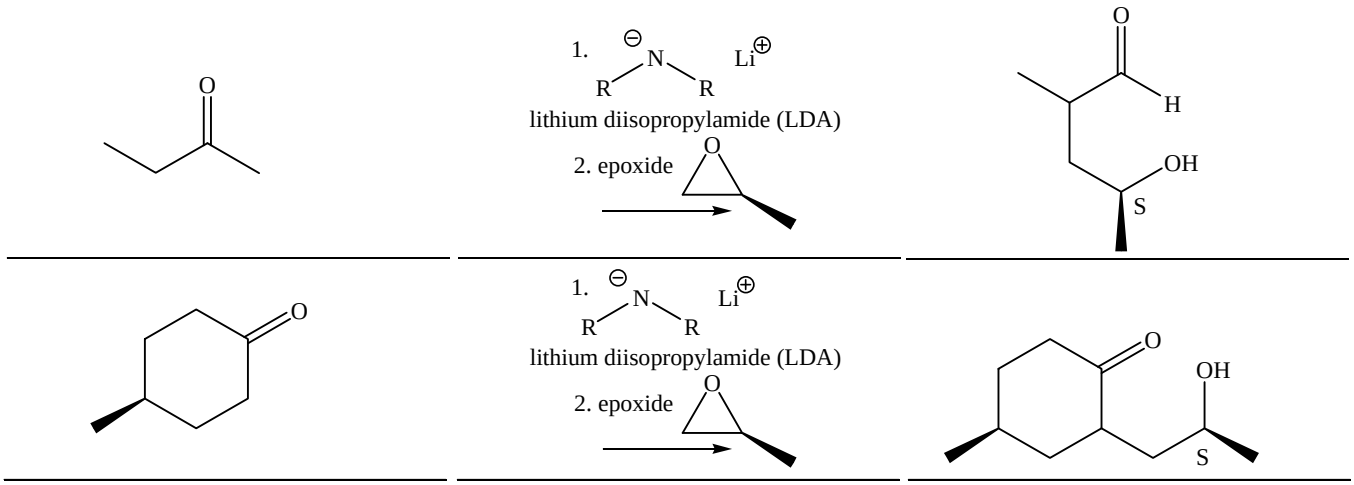


enantiomers (R and S)

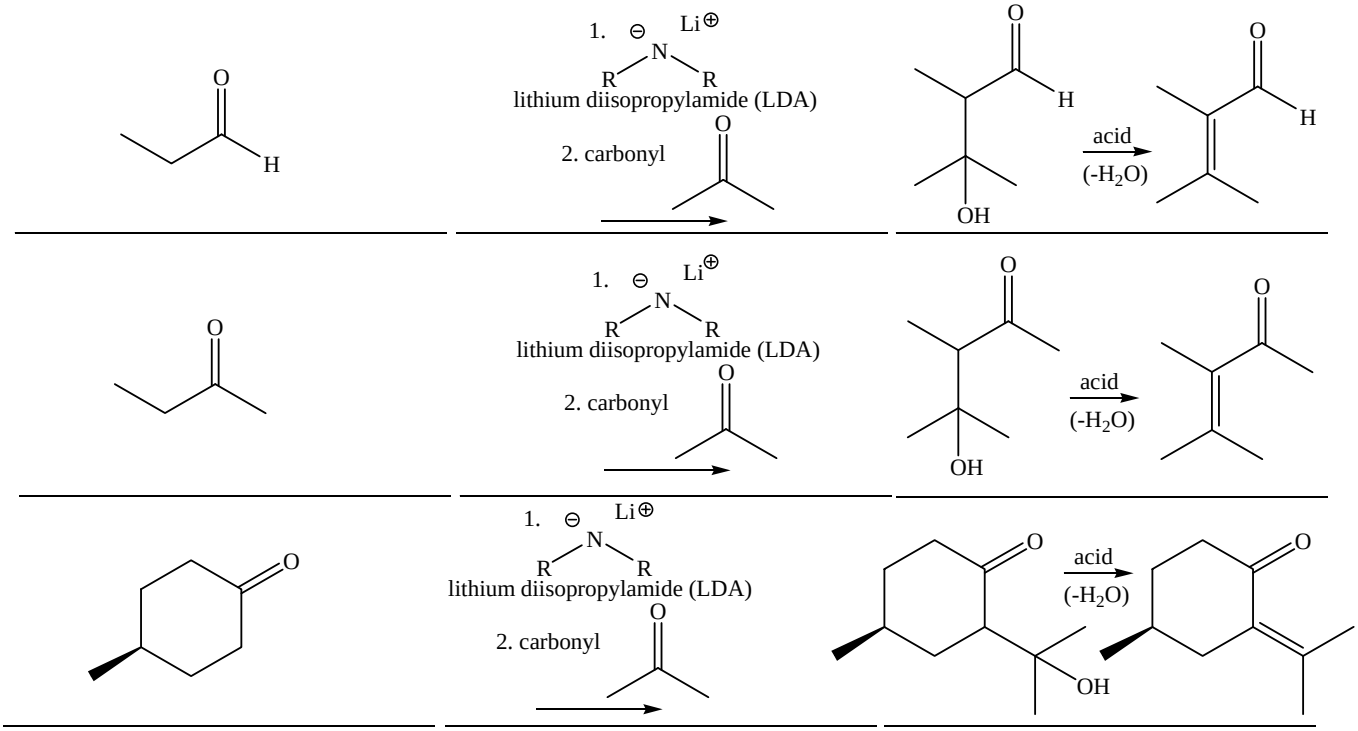
u. Aldehydes and ketones with 1. LDA 2. epoxide = alkylation of C=O.

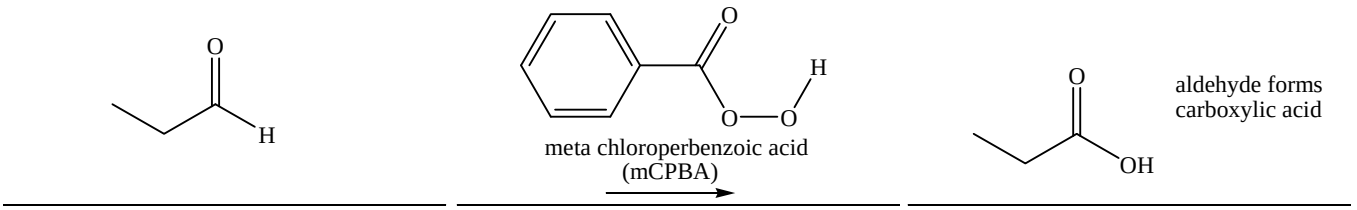


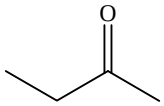


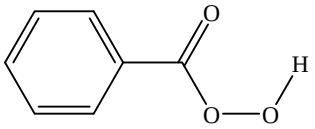
v. Aldehydes and ketones with 1. LDA 2. another C=O = addition to C=O. Forms a beta hydroxyl carbonyl, which can be dehydrated in acid or base (with heat) to an α,β-unsaturated carbonyl compound.

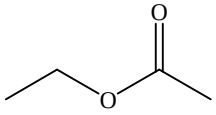


w. Aldehydes and ketones with mCPBA (Baeyer-Villigar oxidation) to form esters (cyclic = lactones).

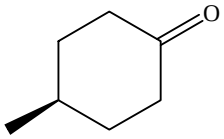


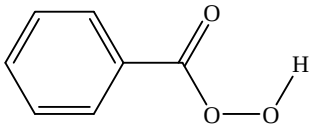


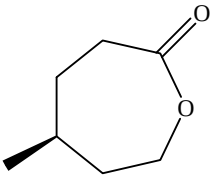




The better R_+ group migrates better.

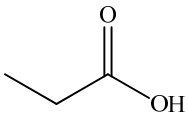




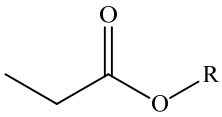


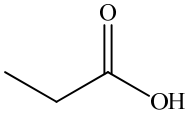
Cyclic esters are called lactones.

Show the products of the following miscellaneous reactions.

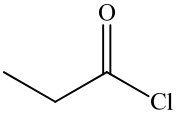


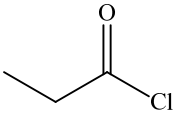
1. NaOH
2. RX (R = methyl, 1^o, 2^o)



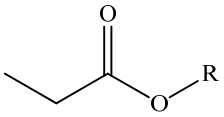


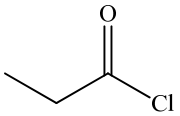
$SOCl_2$



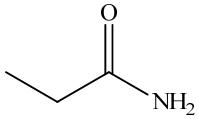


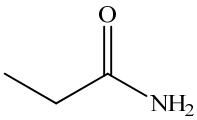
R—OH





NH_3





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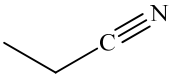
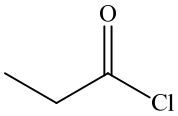
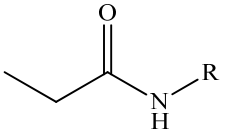
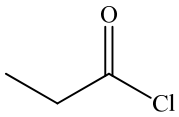
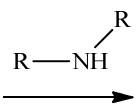


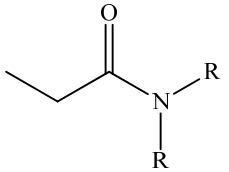


$R—NH_2$









other possible reactions

cuprates
Sulfur ylids
Phosphorous ylids (4 variations)
Ketals / acetals
Imines → amines → amides