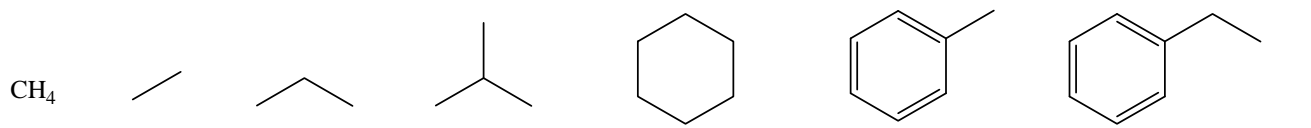


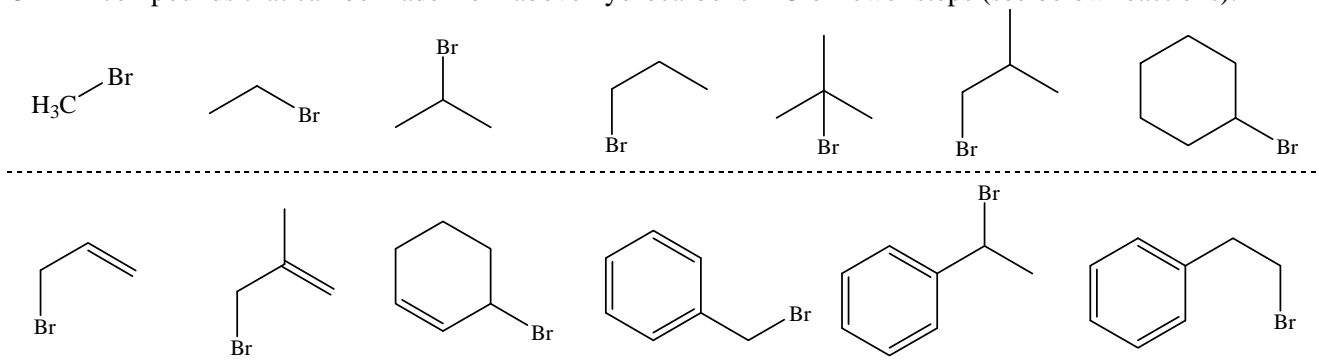
Whenever necessary, 'workup' is written as the last step. Essentially, this means that the reaction mixture is neutralized. Our topics studied this quarter (Chem 315):

1. Acid/Base Chemistry (34 pages)
2. SN/E Chemistry (72 pages)
3. Epoxide and Carbonyl Analogies (17 pages)
4. Synthesis and Intro to Organic Reactions Using Carbanion Chemistry (42 pages)
5. Alkene and Alkyne Chemistry (64 pages)

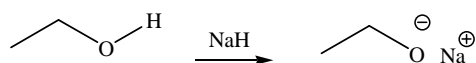
Our hydrocarbon starting points for reaction studied this quarter.



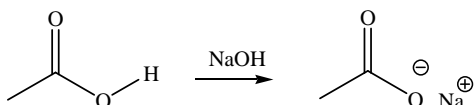
13 R-Br compounds that can be made from above hydrocarbons in 3 or fewer steps (see below reactions).



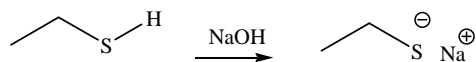
1. Various acid/base reactions necessary to do reactions in our course. Show a mechanism for each reaction. (p. 12, Acid/Base topic)



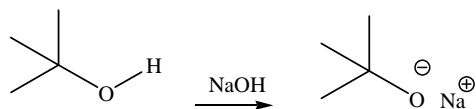
Alkoxides are good nucleophiles with Me and 1° RX, carbonyl compounds and epoxides.



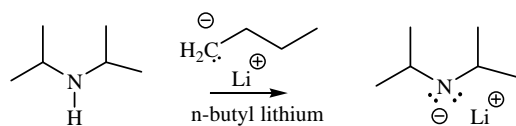
Alkoxides are good nucleophiles with Me and 1° RX, carbonyl compounds and epoxides.



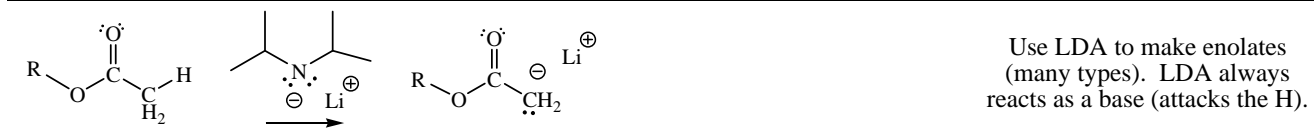
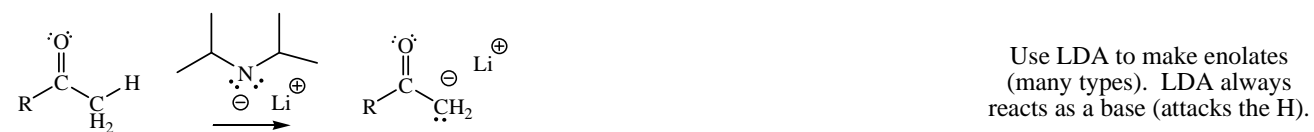
Thiolates are good nucleophiles with Me, 1° and 2° RX compounds.



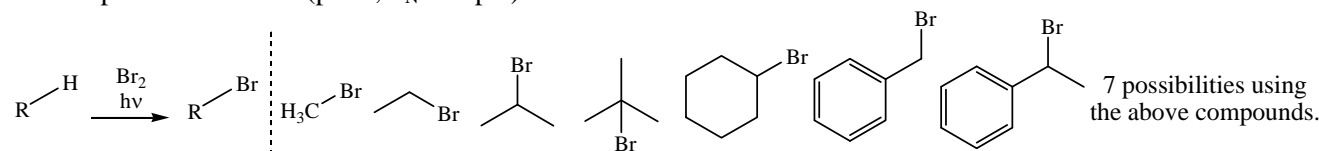
t-butoxide is big and bulky and forces E2 even at 1° and 2° RX compounds.



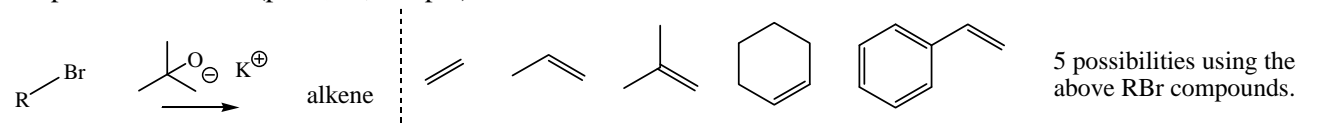
Formation of lithium diisopropyl amide (LDA), a very basic, sterically hindered base using n-butyl lithium.



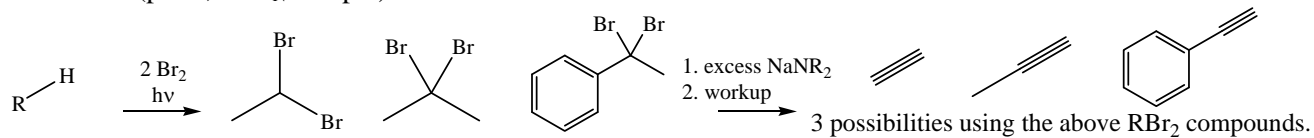
2. Free radical substitution used to make R-Br from (R-H + Br₂ + hv). The weakest C-H bond reacts first. Show one complete mechanism (p. 64, S_N/E topic)



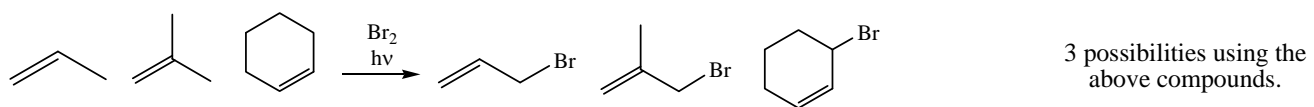
3. E2 reaction used to make alkenes from (R-Br + potassium t-butoxide). Requires 'anti' conformation. Show one complete mechanism (p. 11, S_N/E topic)



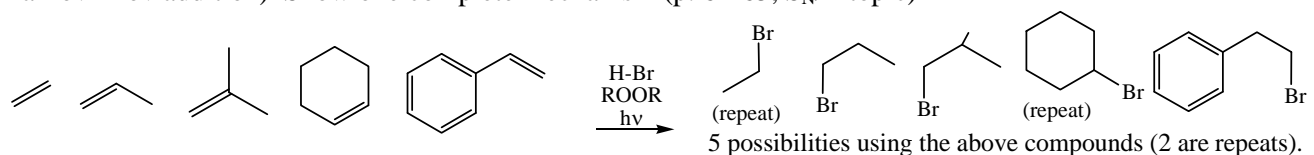
4. Free radical substitution (twice) used to make RBr_2 from $(R-H + 2 \text{ eqs. } Br_2 + hv)$. The weakest C-H bonds react first. The dibromoalkanes are used to make alkynes (double E2 with excess $NaNR_2$). Show one complete mechanism (p. 21, 64 S_N/E topic)



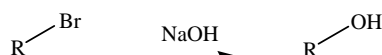
5. Free radical substitution used to make allylic RBr from $(\text{alkene} + Br_2 + hv)$. The weakest C-H bond reacts first. Show one complete mechanism (p. 64, S_N/E topic)



6. Free radical addition to a pi bond is used to make $1^\circ RBr$ from $(\text{alkene} + H-Br + ROOR + hv)$. (anti-Markovnikov addition) Show one complete mechanism (p. 64-65, S_N/E topic)

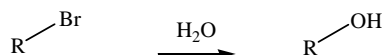


7. S_N2 reaction with hydroxide at methyl, primary and allylic or benzylic secondary RX is used to make alcohols. Similar to #11 (alkoxides). Show one complete mechanism (p. 6, S_N/E topic)



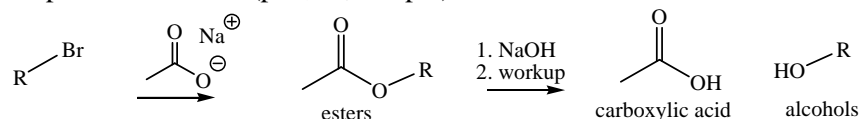
10 possibilities using Me, 1° , allylic and benzylic RBr .
(Not 2° and $3^\circ RBr$.)

8. S_N1 reaction with water at secondary or tertiary RX (only if rearrangement is not a problem) is used to make alcohols. Similar to #10 and #12 (alcohols make ethers). Show one complete mechanism (p. 39-41, S_N/E topic)



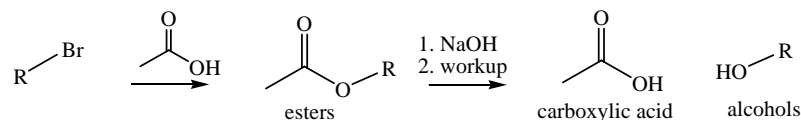
5 possibilities using Me, 1° , allylic and benzylic RBr .
(Not 2° and $3^\circ RBr$.)

9. S_N2 reaction with carboxylates at methyl, primary, secondary and allylic or benzylic RX is used to make esters. If desired, can be carried on step farther, reacting with hydroxide (acyl substitution), making ROH . Show one complete mechanism (p. 9, S_N/E topic)



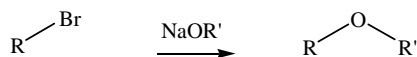
12 possibilities using the above RBr compounds.

10. S_N1 reaction with carboxylic acids at secondary and tertiary RX (only if rearrangement is not a possibility) is used to make esters. Similar to #8 and #12. If desired, can be carried on step farther, reacting with hydroxide (acyl substitution), making ROH . Show one complete mechanism (p. #, S_N/E topic, mechanism at end of this handout)



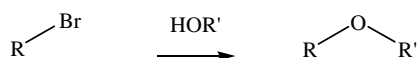
5 possibilities using the above RBr compounds (not counting 1° allylic, which could work too).

11. S_N2 reaction with alkoxide at methyl, primary and allylic or benzylic secondary RX is used to make ethers. Similar to #8. Show one complete mechanism (p. 4, S_N/E topic)



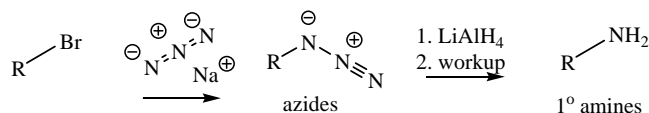
10 possibilities using RBr (Me, 1° , allylic and benzylic) and 12 possibilities using RO^\ominus (not t-butyl).

12. S_N1 reaction with alcohols at secondary or tertiary RX (only if rearrangement is not a problem) is used to make ethers. Similar to #8 and #10. Show one complete mechanism (p. 39-41, S_N1/E topic)



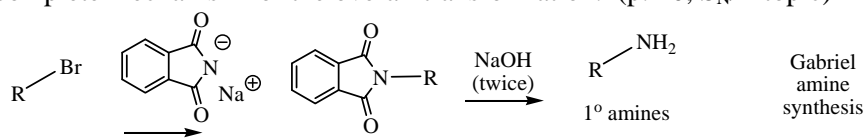
6 possibilities using RBr
(2° and 3°) and 13 possibilities
using ROH.

13. S_N2 reactions (twice = 1. azide, 2. LAH) with azides at methyl, primary, secondary and allylic or benzylic RX is used to make azidoalkanes. These are carried on step farther, reacting with lithium aluminum hydride (LAH = LiAlH_4), making RNH_2 . Show one complete mechanism for the overall transformation. (p. 10, S_N1/E topic)



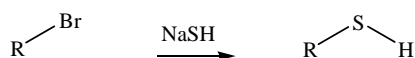
12 possibilities using the
above RBr compounds.

14. S_N2 reaction with imidate at methyl, primary, secondary and allylic or benzylic RX is used to make alkylimidate. These are carried on step farther, reacting with NaOH (acyl substitution twice) making RNH_2 . Show one complete mechanism for the overall transformation. (p. 10, S_N1/E topic)



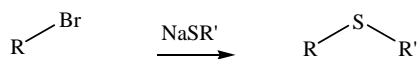
12 possibilities using the
above RBr compounds.

15. S_N2 reaction with NaSH at methyl, primary, secondary and allylic or benzylic RX is used to make thiols, RSH. Similar to #16. Show one complete mechanism for the overall transformation. (p. 11, S_N1/E topic)



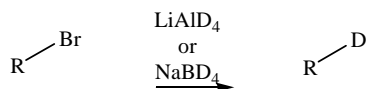
12 possibilities using the
above RBr compounds.

16. S_N2 reaction with NaSR' at methyl, primary, secondary and allylic or benzylic RX is used to make sulfides, RSR' . Similar to #15. Show one complete mechanism for the overall transformation. (p. 11, S_N1/E topic)

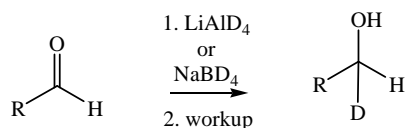


12 possibilities using RBr
(Me, 1°, allylic and benzylic)
and 12 possibilities using
 RS^- (not t-butyl).

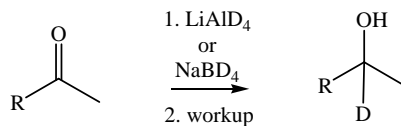
17. S_N2 reaction with LiAlH_4 (LiAlD_4) or NaBH_4 (NaBD_4) at methyl, primary, secondary and allylic or benzylic RX is used to make R-D (usually 'H', but D used to show reaction location). They also react with carbonyl and epoxide compounds. Show one complete mechanism for the overall transformation. (p. 14, S_N1/E topic, some mechanisms at the end of this topic.)



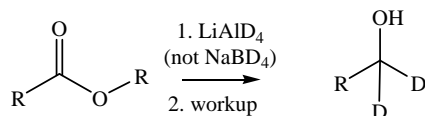
12 possibilities using
the above compounds.



Many possible
combinations.



Many possible
combinations.



Many possible
combinations.
Reacts twice.



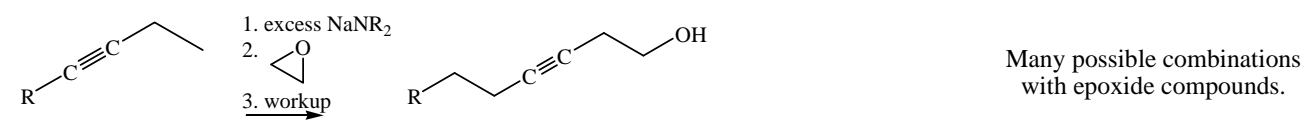
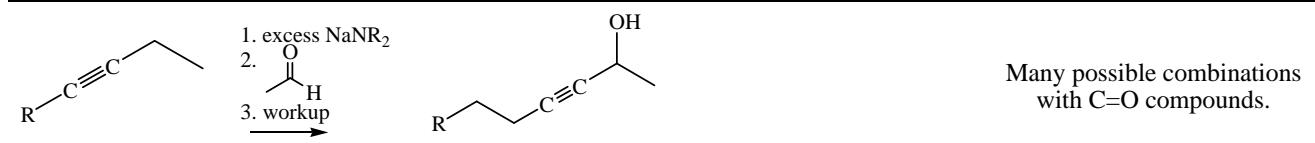
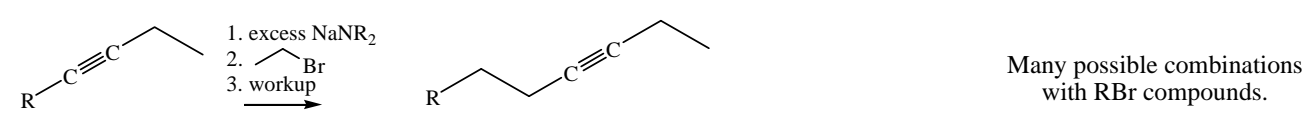
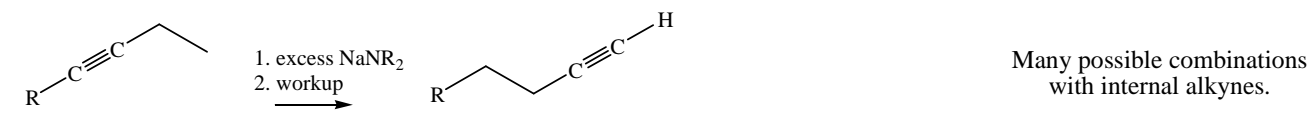
18. S_N2 reaction with NaCN at methyl, primary, secondary and allylic or benzylic RX is used to make nitriles, RCN. Show one complete mechanism for the overall transformation. (p. 1, 12, problem 3, Carbanion topic)



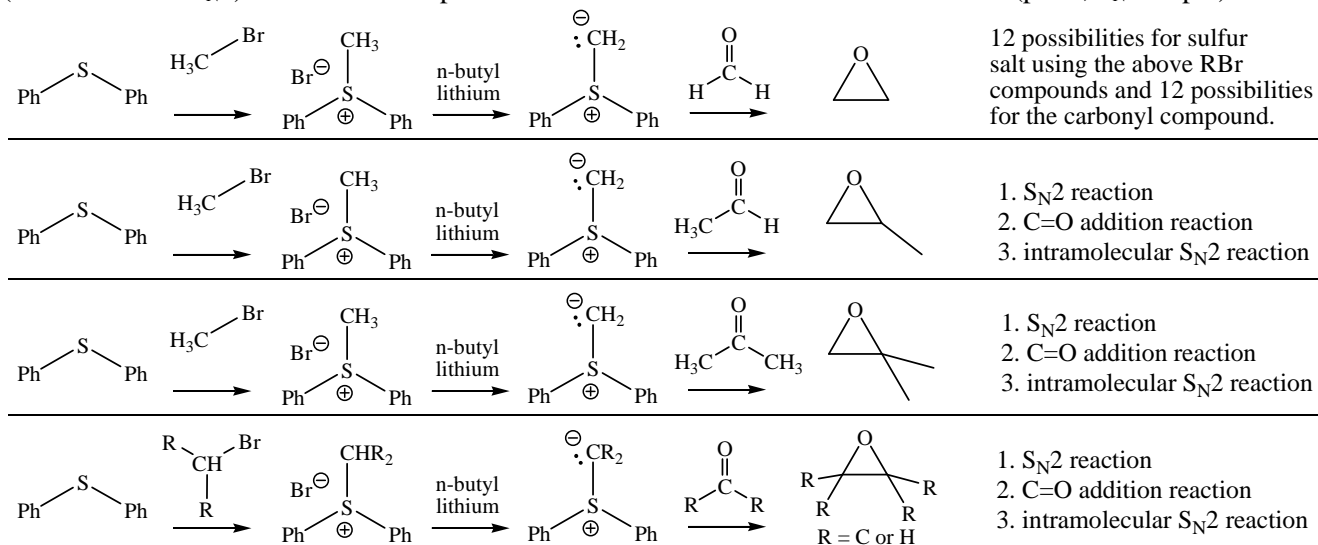
19. S_N2 reaction with terminal acetylide (see #3) at methyl, primary and allylic or benzylic secondary RX is used to make larger alkynes. Show one complete mechanism (p. 11, 21-22, S_N/E topic)



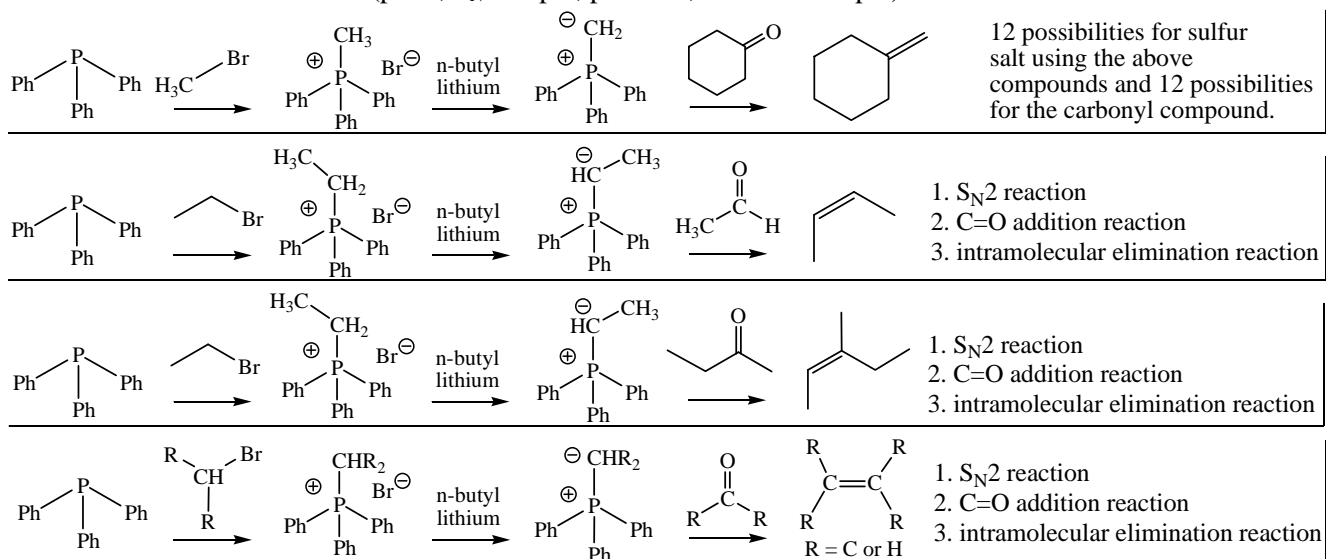
20. Use zipper reaction to move an internal alkyne bond to a terminal position and react with various end reactions. Many possibilities from alkynes generated in #19. Show one complete mechanism (p. 12, S_N/E topic)



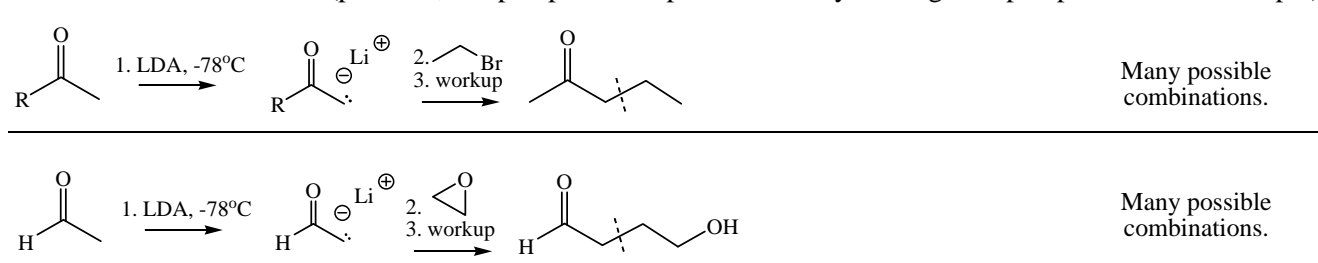
21. S_N2 reaction with Ph-S-Ph (diphenylsulfide) at methyl, primary, secondary and allylic or benzylic RX is used to make sulfur salts to make sulfur ylids, which react with C=O compounds (addition reaction) to make epoxides (intramolecular S_N2). Show one complete mechanism for the overall transformation. (p. 13, S_N/E topic)

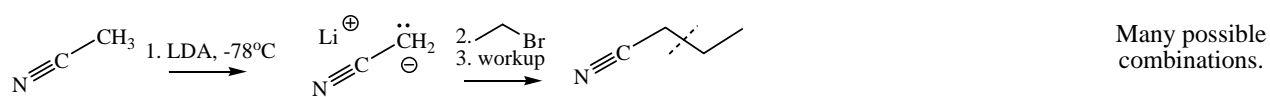
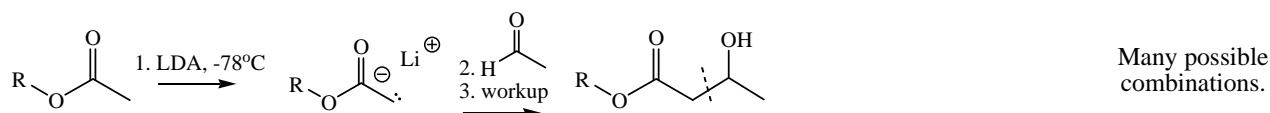


22. S_N2 reaction with Ph_3P (triphenylphosphine) at methyl, primary, secondary and allylic or benzylic RX is used to make phosphonium salts to make phosphorous ylids, which are reacted with aldehydes and ketones (C=O addition reaction) to make Z-alkenes (elimination reaction) (= Wittig reaction). Show one complete mechanism for the overall transformation. (p. 13, S_N/E topic, p. 34-36, Carbanion topic)

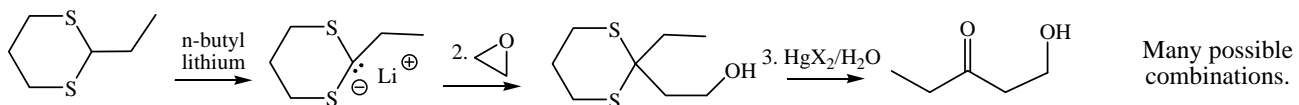
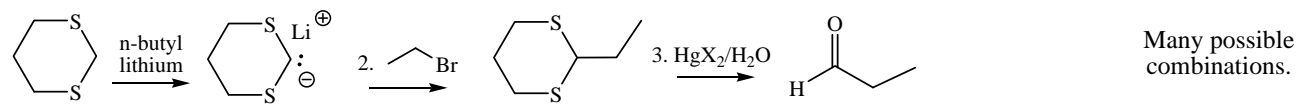


23. S_N2 reaction with carbonyl enoates (esters, ketones, aldehydes and nitriles) at methyl, primary, secondary and allylic or benzylic RX is used to make nitriles, larger carbonyl compounds. Show one complete mechanism for the overall transformation. (p. 12, S_N/E topic, p. 10-11 epoxide/carbonyl analogies topic, p. 13 Carbanion topic)

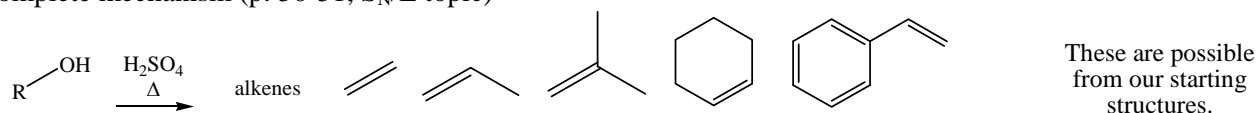




24. S_N2 reaction with dithiane anion at methyl, primary, secondary and allylic or benzylic RX. Can react once and then hydrolyze (add water) to make aldehydes or react twice, then hydrolyze to make ketones (extra mechanism at end of this topic). Show one complete mechanism for the overall transformation to a ketone. (p. 11, S_N/E topic, p. 33 Carbanion topic)



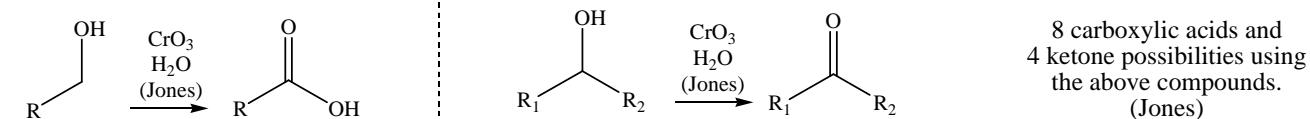
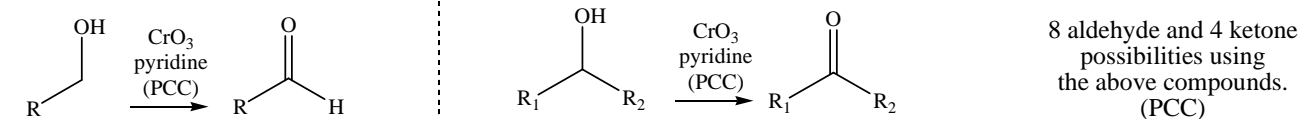
25. $E1$ reaction used to make alkenes from (R-OH + H_2SO_4/Δ). Only useful if no rearrangements occur. Show one complete mechanism (p. 50-51, S_N/E topic)



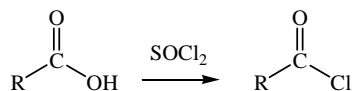
26. S_N2 and S_N1 reactions of ROH with HBr. S_N2 at Me and 1° RBr. S_N1 at 2° and 3° RBr if rearrangement is not a problem. Show one complete mechanism for each type. (p. 49-50, S_N/E topic)



27. Make aldehydes, ketones and carboxylic acids from alcohols and CrO_3 /pyridine (PCC) or CrO_3/H_2O (Jones). Show one complete mechanism (p. 67-70, S_N/E topic).

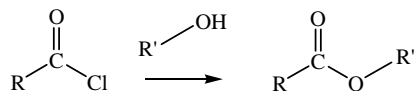


28. Make acid chlorides from carboxylic acids + $SOCl_2$. Show one complete mechanism (p. 55, S_N/E topic).



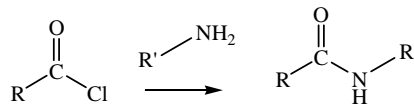
7 possibilities from our starting structures. The one carbon acid chloride is not stable (use an unsymmetrical anhydride as a substitute)

29. Make esters from acid chlorides + alcohols. Show one complete mechanism (p. 53, 55, S_N/E topic).



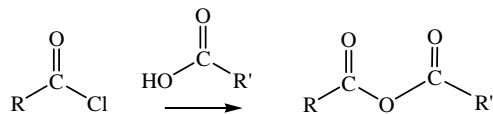
7 possibilities acid chlorides plus 13 possible alcohols can form many possible esters.

30. Make amides from acid chlorides + amines. Show one complete mechanism (p. 53, 55, S_N/E topic).



7 possibilities acid chlorides plus 12 possible amines can form many possible amides.

31. Make anhydrides from acid chlorides + acids. Show one complete mechanism (p. 56, S_N/E topic).



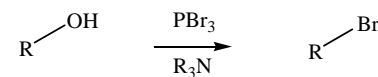
7 possibilities acid chlorides plus 8 possible acids can form many possible anhydrides. The one carbon version serves as a substitute for the one carbon acid chloride, which is unstable.

32. Make bromoalkanes from alcohols + SOBr₂ (also SOCl₂). S_N2 at Me and 1° ROH. S_N1 at 2° and 3° ROH. Show one complete mechanism of each type. (p. 54, S_N/E topic).



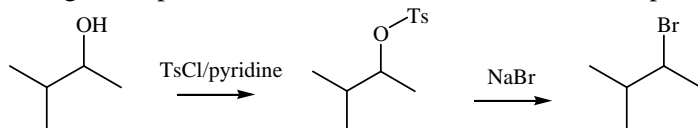
13 possibilities using the above compounds.

33. Make bromoalkanes from alcohols + PBr₃ (also PCl₃). Double S_N2 at Me and 1° ROH. S_N2/S_N1 at 2° and 3° ROH. Show one complete mechanism of each type. (p. 56, S_N/E topic).



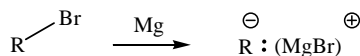
13 possibilities using the above compounds.

34. Make bromoalkanes from 1. ROH / TsCl / pyridine (acyl-like substitution) + 2. NaBr (S_N2). Avoids rearrangement problems of carbocations. Show one complete mechanism (p. 52-53, S_N/E topic).



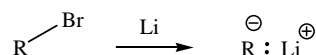
13 possibilities using the above compounds. No rearrangement in this example.

35. Make organomagnesium reagents (Grignard reagents) from Mg + R-Br. Can be used with many carbonyl and epoxide electrophiles and can be made into organocuprate reagents. Show one complete mechanism (p. 9, Carbanion topic).



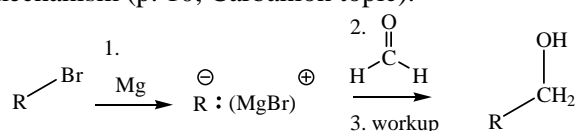
13 possibilities using the above compounds for Mg. Grignards react poorly with RBr which is good, otherwise they would react with themselves (which they do a little bit, but we ignore it). We use cuprates when we want to couple 2 RBr compounds (#45).

36. Make organolithium reagents from 2Li + R-Br. Can be used with many carbonyl and epoxide electrophiles and can be made into organocuprate reagents. Show one complete mechanism (p. 9, Carbanion topic).

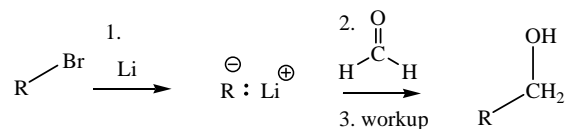


13 possibilities using the above compounds for Mg. Organolithiums react poorly with RBr which is good, otherwise they would react with themselves (which they do a little bit, but we ignore it). We use cuprates when we want to couple 2 RBr compounds (#45).

37. Make primary alcohols from 1. Mg or Li + RBr 2. H₂C=O (methanol) 3 workup. Show one complete mechanism (p. 10, Carbanion topic).

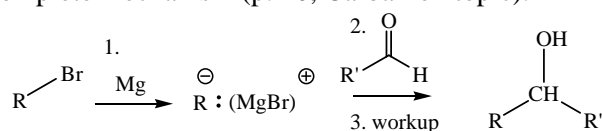


13 possibilities using the above compounds.

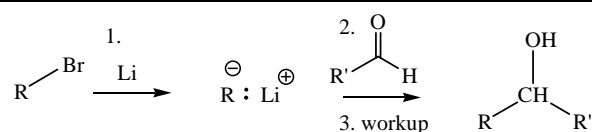


13 possibilities using the above compounds.

38. Make secondary alcohols from 1. Mg or Li + RBr 2. RCH=O (simple aldehydes) 3 workup. Show one complete mechanism (p. 10, Carbanion topic).

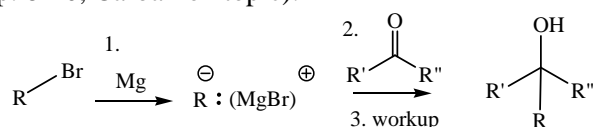


13 possibilities using the above compounds.

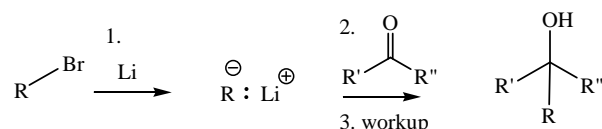


13 possibilities using the above compounds.

39. Make tertiary alcohols from 1. Mg or Li + RBr 2. R₂C=O (ketones) 3 workup. Show one complete mechanism (p. 8-10, Carbanion topic).

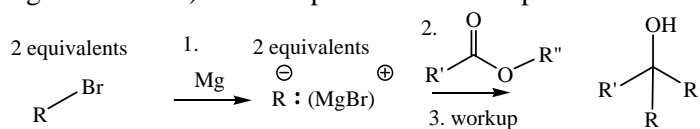


13 possibilities using the above compounds.

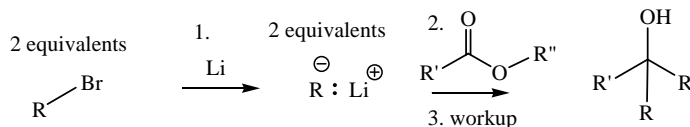


13 possibilities using the above compounds.

40. Make tertiary alcohols from 1. Mg or Li + RBr (two equivalents) 2. RCO₂R' (esters react twice with organometallics) 3 workup. Show one complete mechanism (p. 4, 6, SN/E topic, p. 2, 11 Carbanion topic).

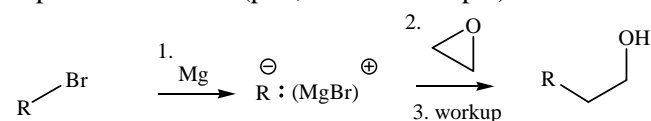


13 possibilities using the above compounds.

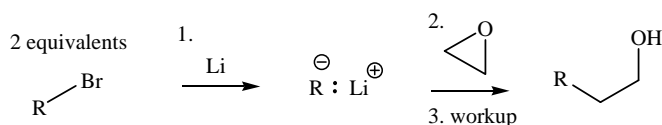


13 possibilities using the above compounds.

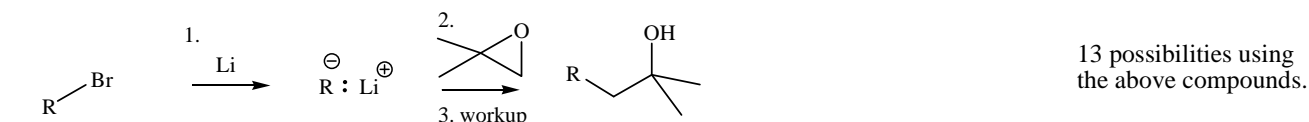
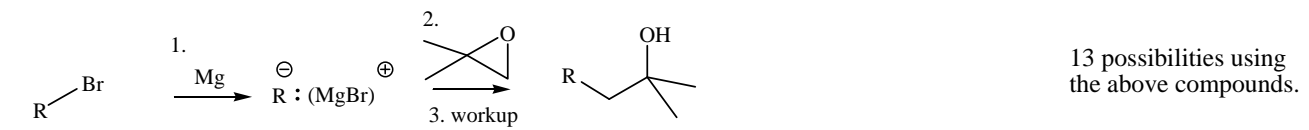
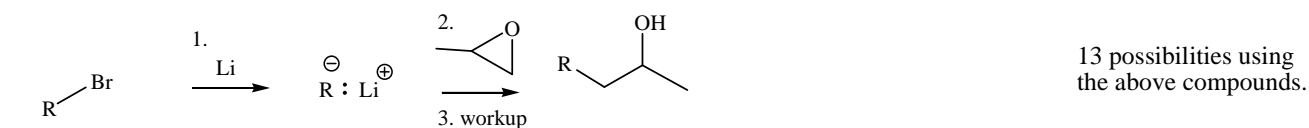
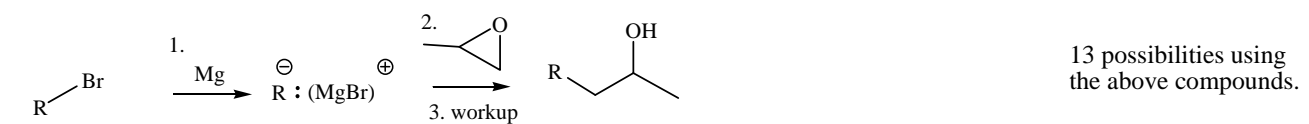
41. Make primary, secondary or tertiary alcohols from 1. Mg or Li + RBr 2. epoxides 3 workup. Show one complete mechanism (p. 2, Carbanion topic).



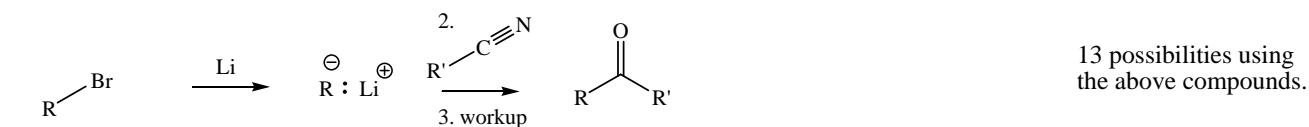
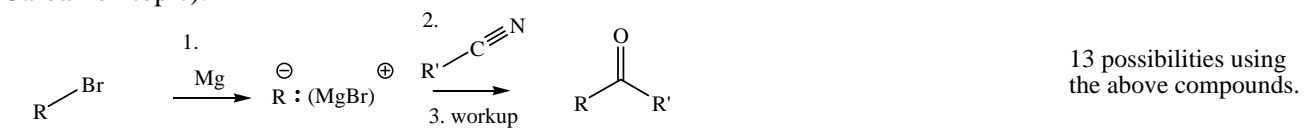
13 possibilities using the above compounds.



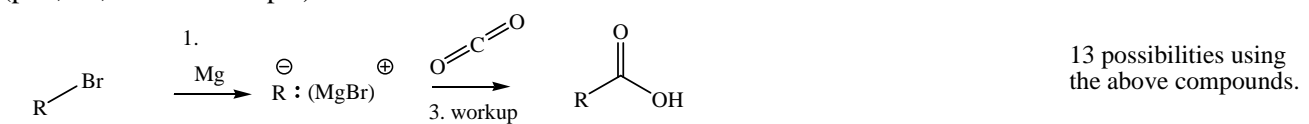
13 possibilities using the above compounds.



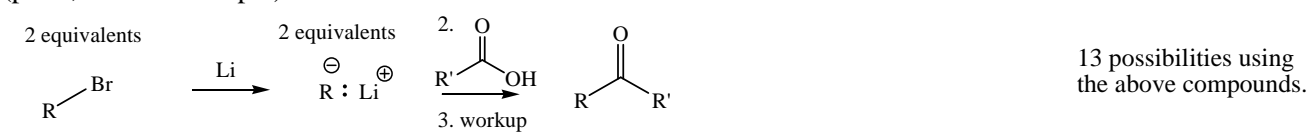
42. Make ketones from 1. Mg or Li + RBr 2. RCN (nitriles) 3 workup. Show one complete mechanism (p. 3, 11, Carbanion topic).



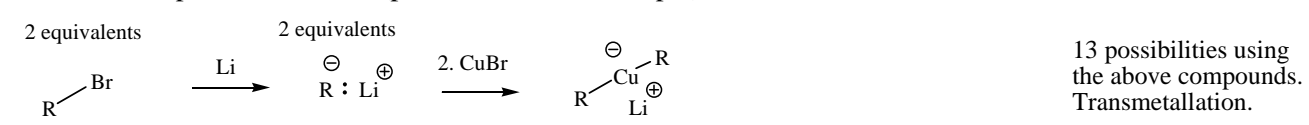
43. Make carboxylic acids from 1. Mg + RBr 2. CO₂ (carbon dioxide) 3 workup. Show one complete mechanism (p. 2, 11, Carbanion topic).

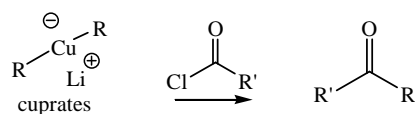


44. Make ketones from 1. Li (only) + RBr 2. RCO₂H (carboxylic acids) 3 workup. Show one complete mechanism (p. 12, Carbanion topic).

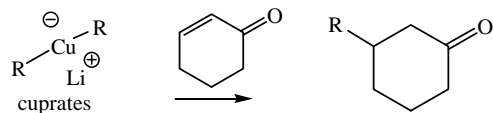


45. Make organocuprates from CuBr + organolithium reagents (transmetalation). React R₂Cu⁻ with 3 different classes of compounds that react differently with Mg and Li organometallics (RBr compounds → couples 2 RBr compounds or acid chlorides → makes ketones or conjugate addition to α,β-unsaturated carbonyl compounds). Show one complete mechanism (p. 14-16, Carbanion topic).



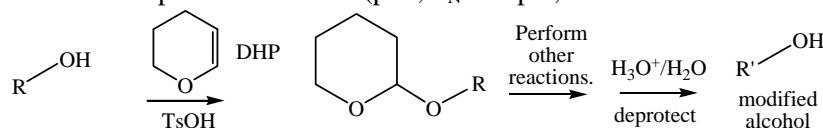


13 possibilities using the above compounds. Can reverse the reagents and get the same product. Two additions occur when Mg and Li reagents are used.



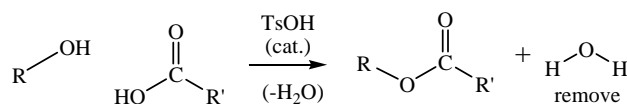
13 possibilities using the above compounds. Can reverse the reagents and get the same product. Attack occurs at the carbonyl carbon when Mg and Li reagents are used.

46. Protect alcohols as THP ethers. $\text{ROH} + \text{DHP} + \text{TsOH} \rightarrow \text{THP ethers}$. Deprotect THP ethers with aqueous acid. Show one complete mechanism (p. #, $\text{S}_{\text{N}}/\text{E}$ topic, mechanism is added at the end of this topic).



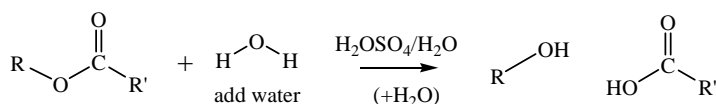
Many possibilities. THP ether protects alcohol during subsequent reactions. When finished deprotect alcohol.

47. Fischer esterification using RCO_2H (carboxylic acids) + $\text{R}'\text{OH}$ (alcohols) + TsOH (cat.) ($-\text{H}_2\text{O}$) \rightarrow esters. Show one complete mechanism (p. 15, Epoxide/carbonyl topic). This can be done using base conditions too (see #9).



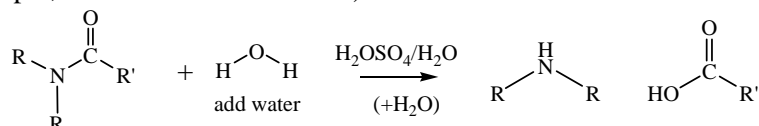
8 possible carboxylic acids plus 13 possible alcohols leads to many possible esters.

48. Hydrolyze esters to carboxylic acids + alcohols using $\text{H}_2\text{SO}_4/\text{H}_2\text{O}$ (acid hydrolysis). Similar reaction to #45, but run in reverse. Show one complete mechanism (p. 12-15, problem 12, $\text{S}_{\text{N}}/\text{E}$ topic). This can be done using base conditions too (see #9).



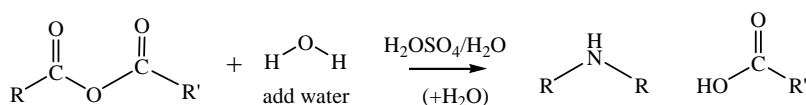
Acidic ester hydrolysis makes carboxylic acids and alcohols.

49. Hydrolyze amides to carboxylic acids + amines using $\text{H}_2\text{SO}_4/\text{H}_2\text{O}/\Delta$. Show one complete mechanism (p. #, $\text{S}_{\text{N}}/\text{E}$ topic, mechanism added at end).



Acidic ester hydrolysis makes amides and amines.

50. Hydrolyze anhydrides to 2 carboxylic acids using $\text{H}_2\text{SO}_4/\text{H}_2\text{O}$. Show one complete mechanism (p. #, $\text{S}_{\text{N}}/\text{E}$ topic, mechanism added at end).



Acidic anhydride hydrolysis makes 2 carboxylic acids.

51. Hydrolyze carboxyl groups (acid chlorides, anhydrides, esters, amides and nitriles) to carboxylic acids in aqueous acid.

That's all. Ran out of time.

52. Hydrolyze carboxyl groups (acid chlorides, anhydrides, esters, amides and nitriles) to carboxylic acids in aqueous base.

possibilities using the above compounds.

53. Make imines, hydrolyze imines, reactions of imines.

possibilities using
the above compounds.

54. Make enamines, hydrolyze enamines, reactions of enamines.

possibilities using
the above compounds.

55. Dicarbonyl and dianion chemistry.

possibilities using
the above compounds.

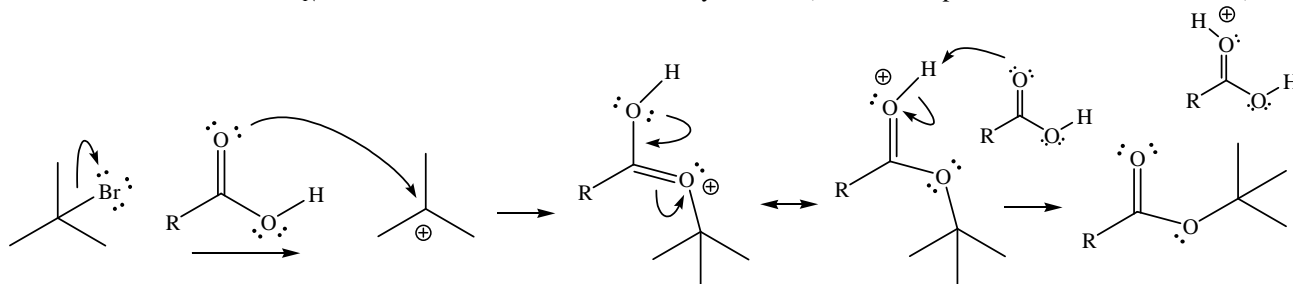
56. Alkene and alkyne chemistry.

possibilities using
the above compounds.

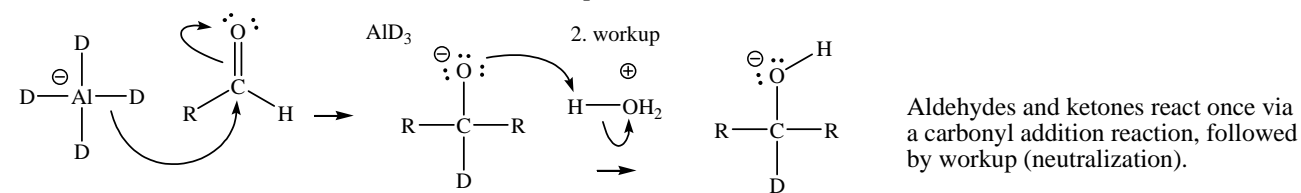
57. Aromatic chemistry.

possibilities using
the above compounds.

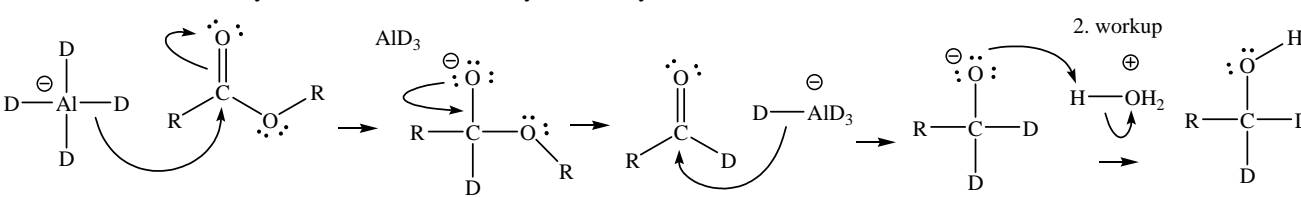
From #10: Mechanism for S_N1 reaction of RBr with neutral carboxylic acids (weak nucleophile, like water and alcohols)



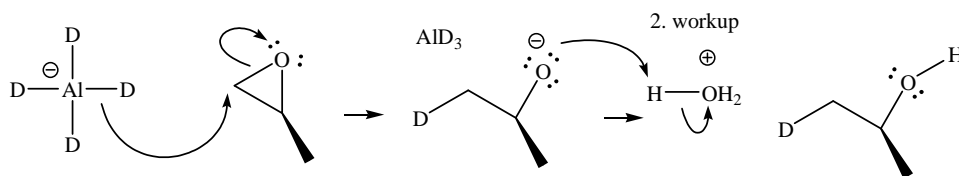
From #17: LAH/LAD mechanisms with various electrophiles.



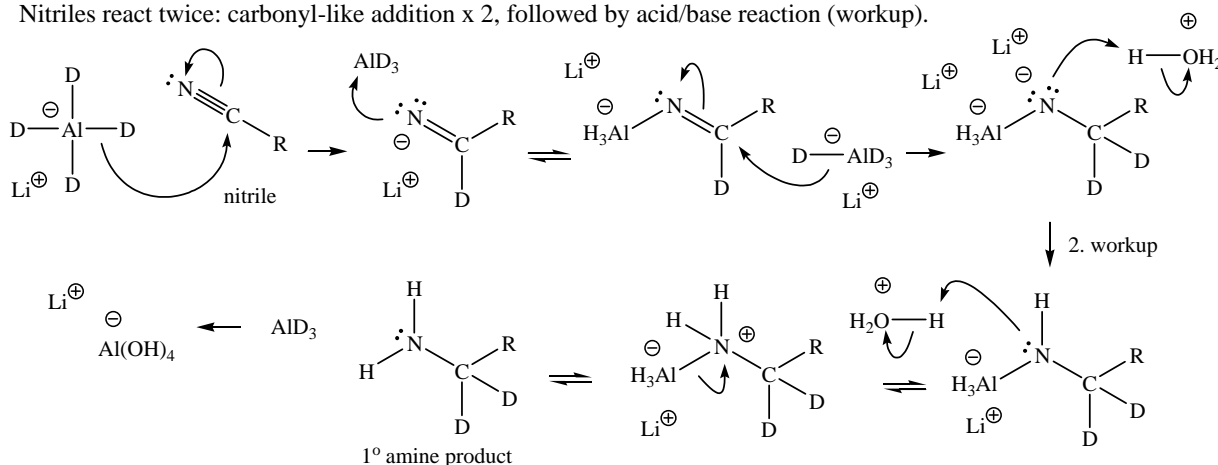
Esters react twice: a. acyl substitution, followed by b. carbonyl addition reaction.



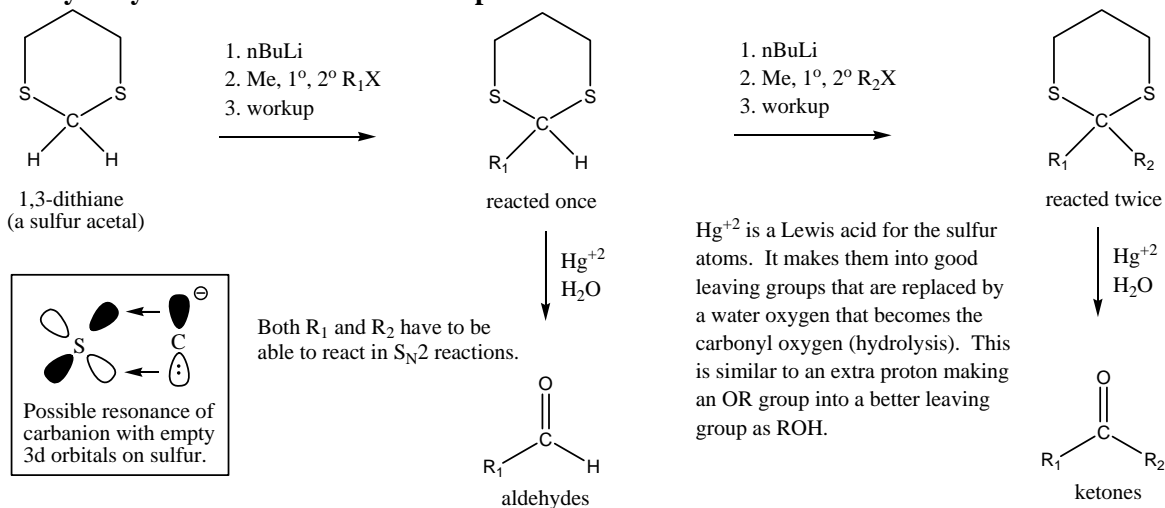
Epoxides react once. S_N2 -like substitution, followed by acid/base reaction (workup).

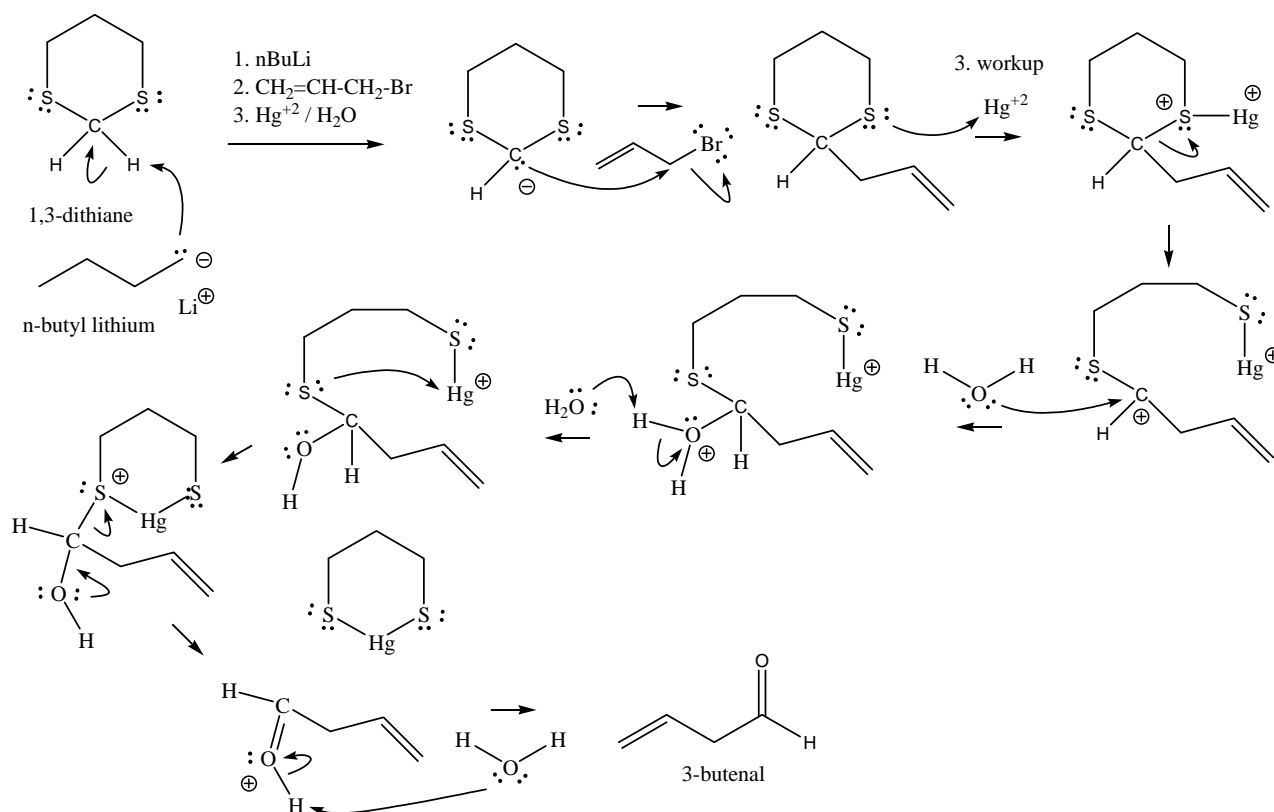


Nitriles react twice: carbonyl-like addition x 2, followed by acid/base reaction (workup).

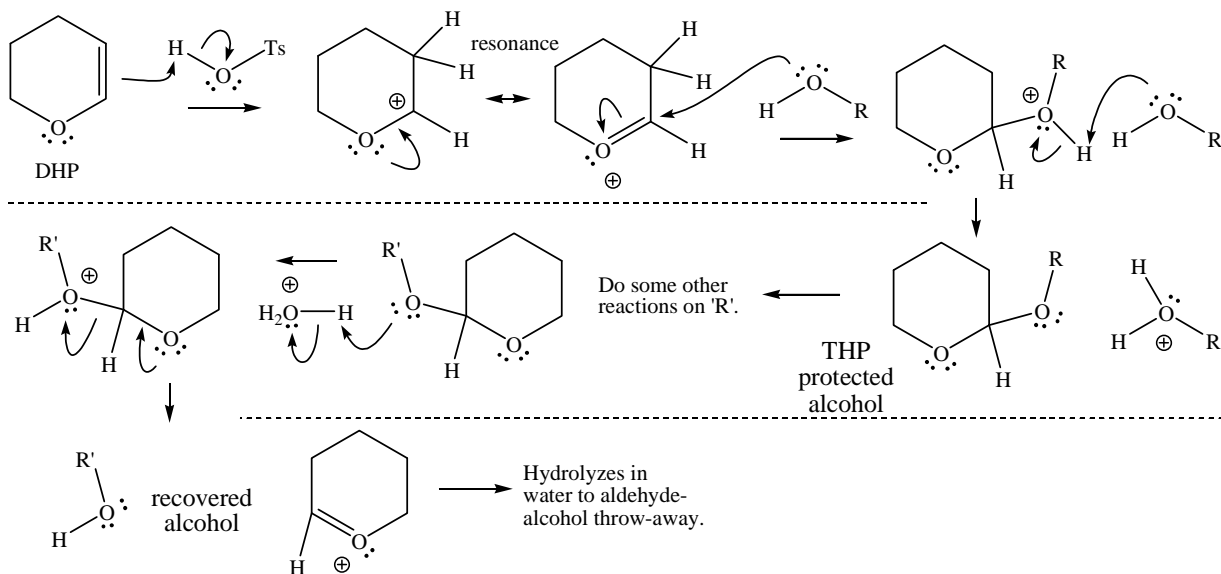


#24 hydrolysis mechanism of dithiane products





From #46: Protection of alcohol as THP ether. Do chemistry that would interfere with alcohol. Deprotect to release alcohol.



Ketals (forward and backward)

Imines, enamines

Hydrolysis of amides and anhydrides and acid chlorides