20. (25 pts.) For the reaction of this epoxide with methanol in acid, fill in the details of the mechanism. Draw the appropriate chemical structures and use arrows to show how pairs of electrons are moved to make and break bonds during the reaction. For this question, you must draw all molecules produced in each step (yes, these equations need to be balanced!). Finally, fill in the boxes adjacent to the arrows with the type of step involved, such as "Make a bond" or "Take a proton away". MAKE SURE TO NOTICE THE QUESTIONS AT THE BOTTOM. Use wedges and dashes to indicate stereochemistry where appropriate, BUT if an intermediate or product is really a racemic mixture, you only need to draw one enantiomer for this problem (we are making this easier for you).
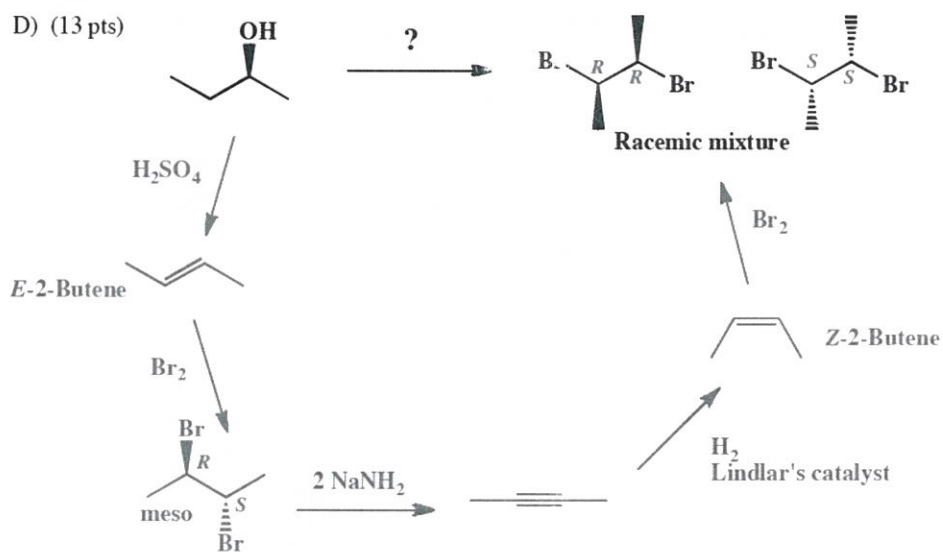
add a proton

make a bond between a nucleophile and electrophile

take a proton away
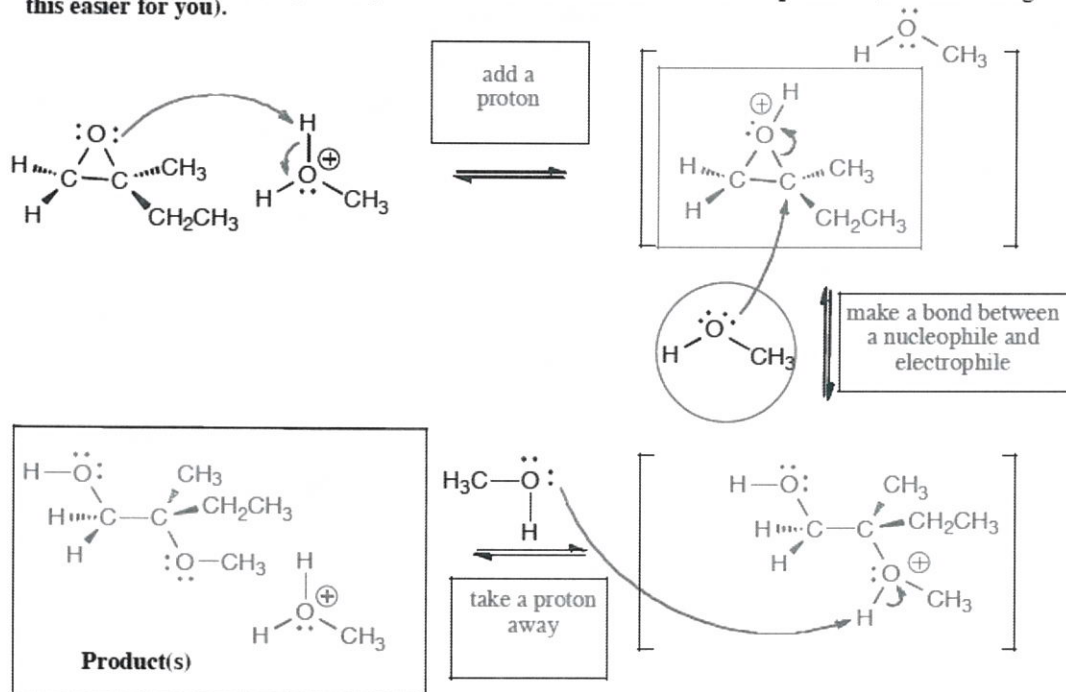
Product(s)

17. These are synthesis questions. You need to show how the starting material can be converted into the product(s) shown. You may use any reactions we have learned provided that the product(s) you draw for each step is/are the predominant one(s). Show all the reagents you need. Show each molecule synthesized along the way and be sure to pay attention to the regiochemistry and stereochemistry preferences for each reaction. You must draw all stereoisomers formed, and use wedges and dashes to indicate chirality at each chiral center. Write racemic when appropriate.

C) (18 pts) For this one, all of the carbon atoms of the product must come from the 1-propanol starting material.
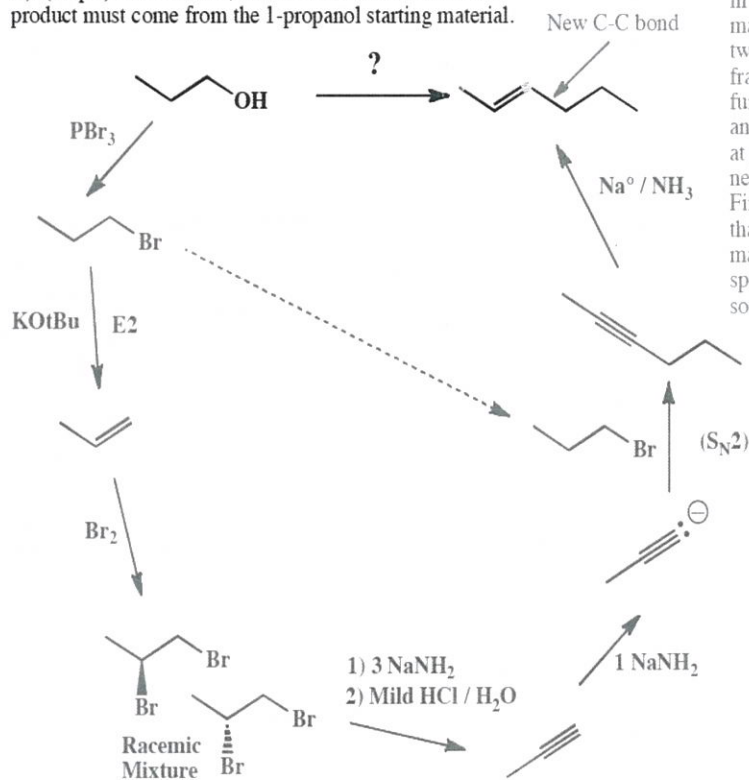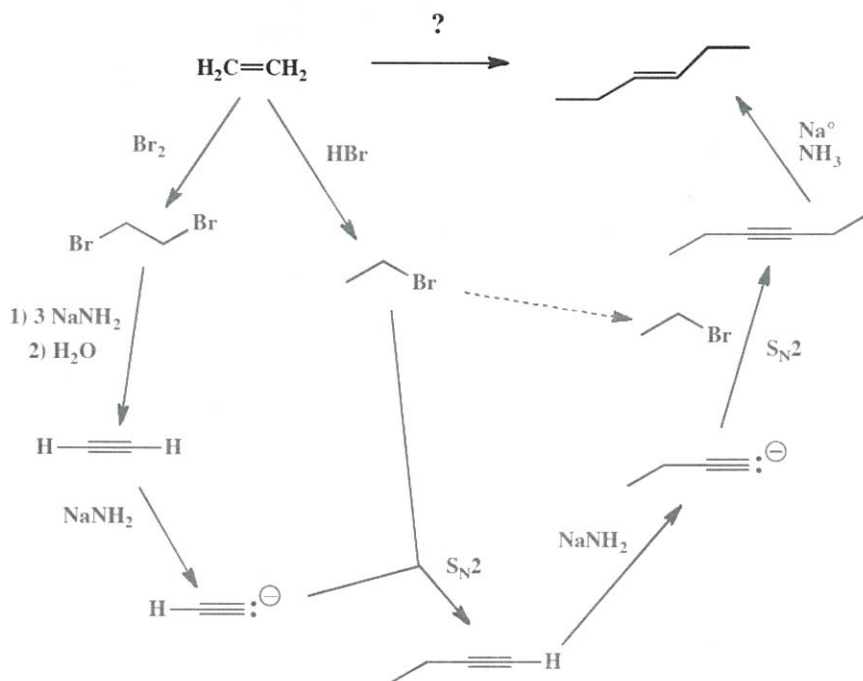
Recognize that the product has six carbons in a chain so you need to make a C-C bond from two three carbon fragments. **Recognize** further that an alkyne anion must be involved at precisely where the new C-C bond is formed. Finally, **recognize** also that the only way to make an *E* alkene at that spot from an alkyne uses sodium in ammonia

New C-C bond

?

$Na° / NH_3$

PBr₃

Br

KOtBu | E2

Br | (S_N2)

Br₂

⊖

Br

Racemic
Mixture   Br

Br

Br

1) 3 NaNH₂
2) Mild HCl / H₂O

1 NaNH₂

Recognize that the required alkyne (DFW) can be made from the starting alcohol by conversion to the haloalkane followed by an E2 to give the alkene (Austin) followed by reaction with X₂ to give the vicinal dihaloalkane (Waco) then elimination using NaNH₂ followed by a mild acid treatment. **Recognize** also that the 1-brompropane needed for the key C-C bond forming step (as well as the first step overall) can be made from 1-propanol by reaction with PBr₃

D) (13 pts)

OH

?

B. R R Br

Br S S Br

Racemic mixture

Br$_2$

H_2SO_4

E-2-Butene

Z-2-Butene

Br$_2$

Br R
meso S
Br

2 NaNH$_2$

H$_2$
Lindlar's catalyst

Recognize that the product vicinal dihaloalkane could only come from anti addition of Br$_2$ to Z-2-butene. **Recognize** further that the only way you know to make a Z alkene is through the syn addition of H$_2$ to an alkyne using H$_2$ and Lindlar's catalyst. **Recognize** therefore that you must get to the alkene from the starting alcohol. The most effecient way so do this is to start by dehydrating the alcohol as in part A), then follow I-35 to the meso vicinal dihaloakane (Waco) followed by reaction with NaNH$_2$ to give the alkyne (DFW).

C) (21 pts)

?

$H_2C{=}CH_2$ $\longrightarrow$

Br_2 HBr

Br Br

1) 3 NaNH$_2$
2) H$_2$O

H ——— H

NaNH$_2$

H ———:⊖

Br

S$_N$2

S$_N$2

NaNH$_2$

———:⊖

Br

Na°
NH$_3$

———H

Recognize that this molecule can be assembled from three different 2-carbon pieces, using the alkyne alkylation strategy each time. Therefore, an alkyne is required, so **recognize** that the last step must be the reduction of the alkyne group using Na° and NH$_3$ to give the E-alkene product. The rest is standard chemistry at this point.

D) (16 pts)
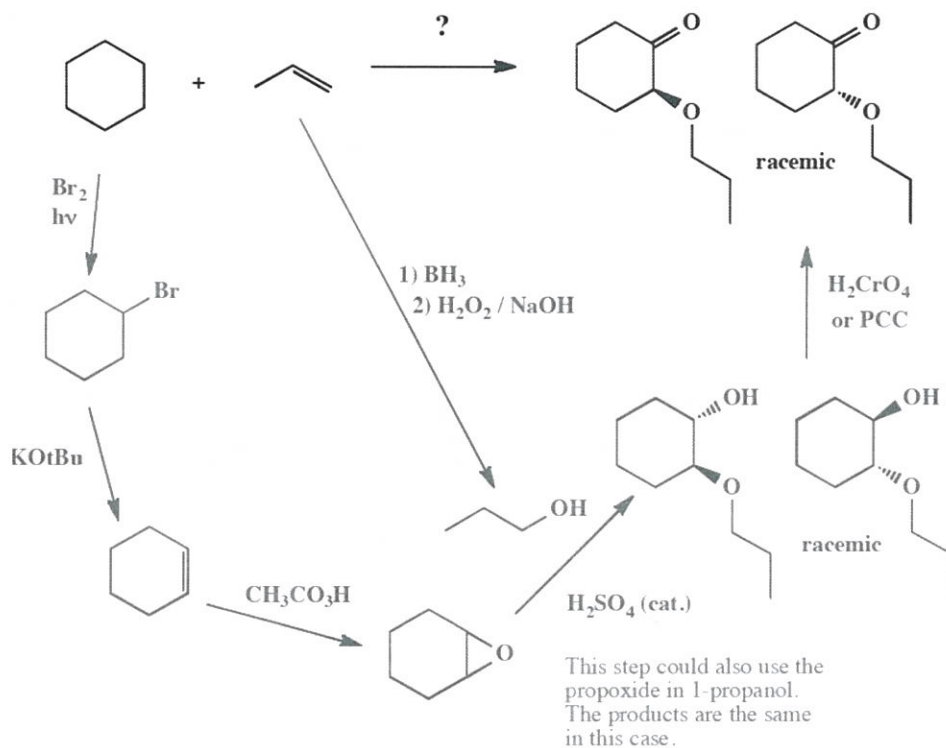
Recognize the product as having a ketone, which in this class can only be made through ozonolysis of an alkene or oxidation of an alcohol. We can rule out ozonolysis because counting carbons makes it clear there are no C-C bonds broken, thus propose the last step as an oxidation of the alcohol. The hard part of this synthesis is to **recognize** that to make the vicinal ether-alcohol in high yield you must use 1-propanol to open an epoxide in either acid (shown) or basic conditions. Alkylating a vicinal diol would not work for this because the yield would be seriously compromised by creating a statistical mixture of products. The rest of the required chemistry is fairly straightforward.
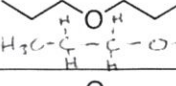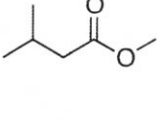
C) (15 pts)
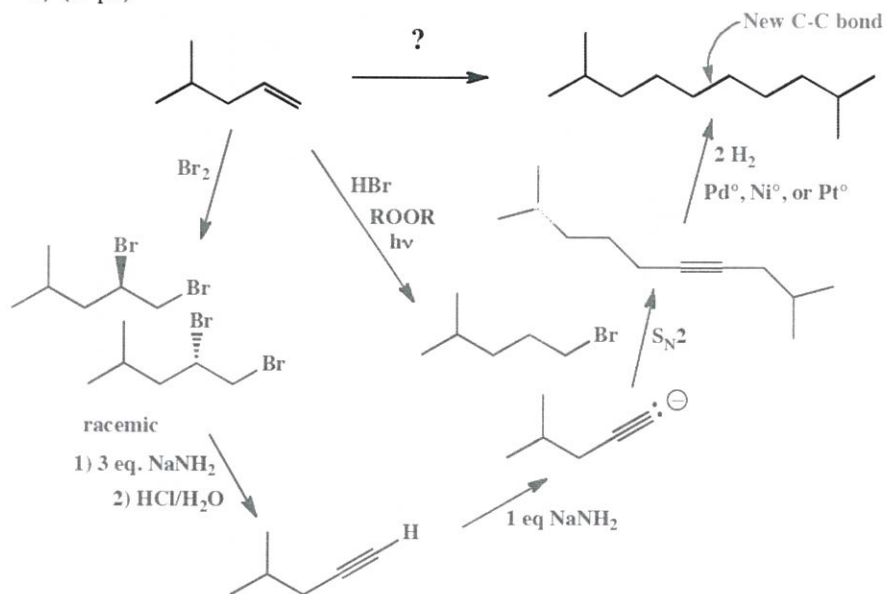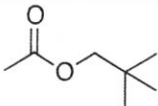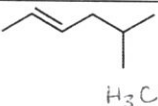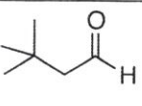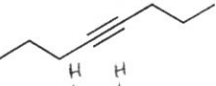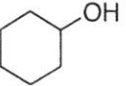
Recognize that there are 12 carbons in the product and 6 in the starting material. Assume you need to put two starting material molecules together at the central bond as shown. The only way this can be done using the reactions you know is to react the anion of a terminal alkyne with a primary haloalkane. Therefore, assume there was once an alkyne in the molecule so predict that the last step is the hydrogenation of the alkyne to give the alkane. Continuing to work backwards, the required 12 carbon alkyne can be derived from the reaction of the 6 carbon primary haloalkane shown and the corresponding 6 carbon terminal alkyne. The primary haloalkane can be made in a single step from the starting alkene by using HBr in the presence peroxide and light. The terminal alkyne can be made using the familiar "I-35" sequence of steps involving reaction with Br_2 followed by reaction with the strong base $NaNH_2$.

Splitting Key: s => singlet q => quartet
d => doublet m => multiplet (>4)
t => triplet

^{1}H NMR Problems

Molecule	# of Sets of Equivalent H Atoms (# of signals)	Ratio of Signal Integrations	Splitting Patterns	Other Notes
H₃C-C-C-OH	4	3:2:2:1	t, m, t, s	Alcohol => broad -OCH₂ 3-4 ppm
H₃C-C-O-C-C-CH₃	3	3:2:9	s, s, s	t-butyl group (large singlet) -OCH₂ 3-4 ppm
	1	—	s	symmetric
H₃C-C=C-C-C-CH₃	6	3:1:1:2:6:1	d,m,q t,m,d	Alkene Hs 5-5.7 ppm
H₃C-C-C-C-H	3	9:2:1	s, d, t	t-butyl group (large singlet) Aldehyde 9.5-10 ppm
H₃C-C-C-C≡C-C-C-CH₃	3	3:2:2 (6:4:4)	t, m, t	Symmetric alkyne
	5	1:1:4:4:2	s,m,q m,m	alcohol, broad -OCH- 3-4 ppm
H₃C-C-CH₃	3	1:1:6	s,m,d	alcohol broad -OCH- 3-4 ppm
H₃C-C-O-CH₃	3	3:2:3	t, q, s	-OCH₂ 3-4 ppm -OCH₃ 3-4 ppm
H₃C-C-C-O-C-C-CH₃	3	3:2:2 (6:4:4)	t, q, t	Symmetric -OCH₂ 3-4 ppm
H-C-C-C-OCH₃	4	6:1:2:3	d, m d, s	-OCH₃ 3-4 ppm

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