

EAS Synthesis Strategies

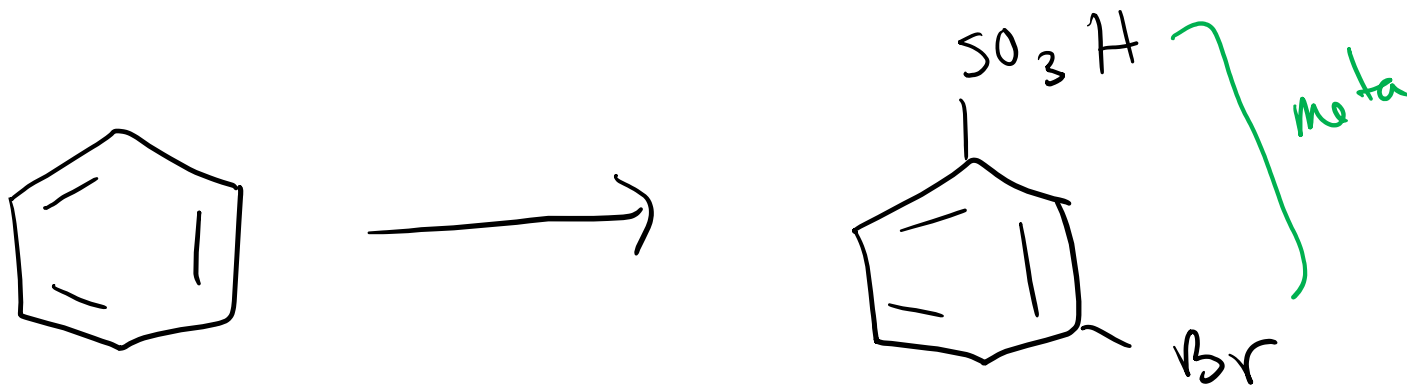
Nucleophilic Aromatic Substitution (S_NAr)

Alcohols

1/27/2023

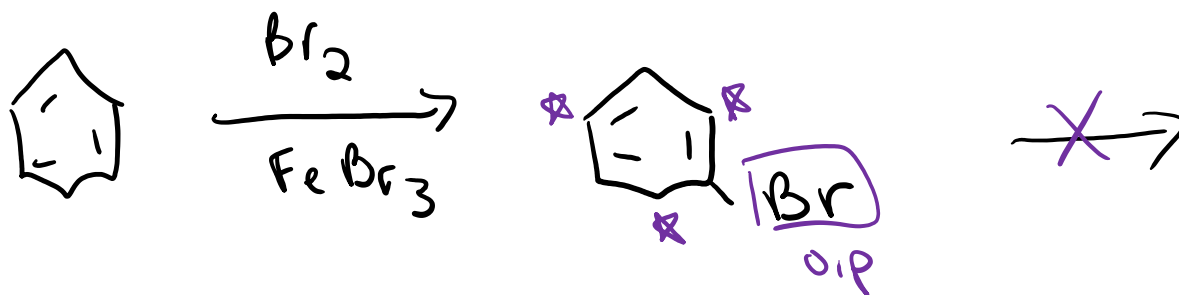
EAS Synthesis Strategies

(18.12)



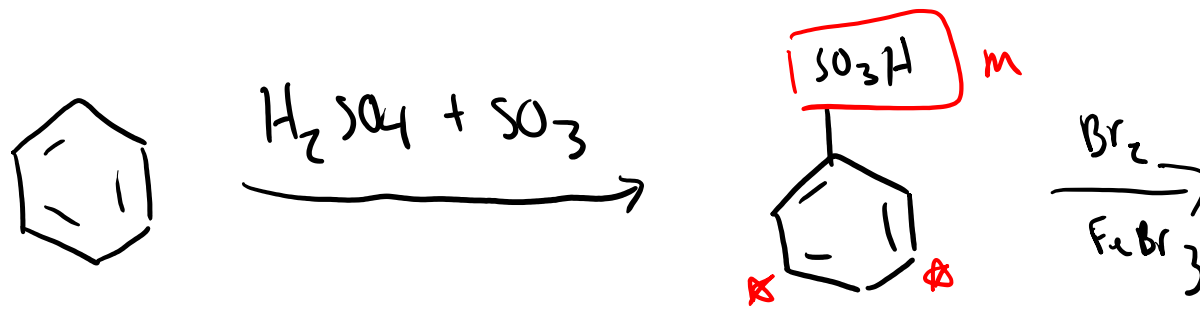
propose a synthesis!

~~option #1~~



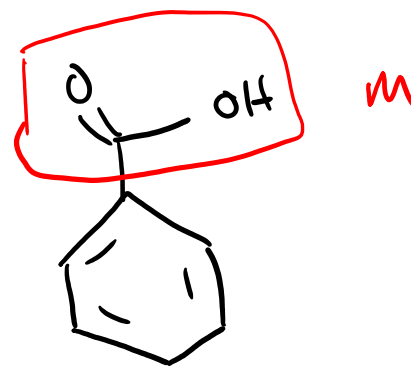
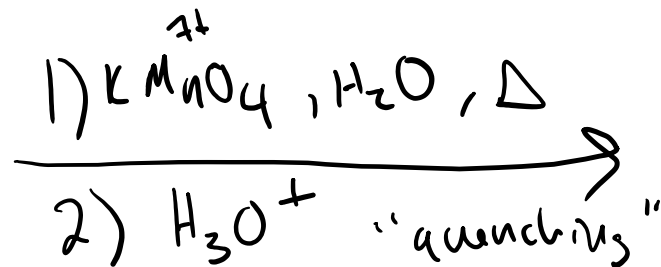
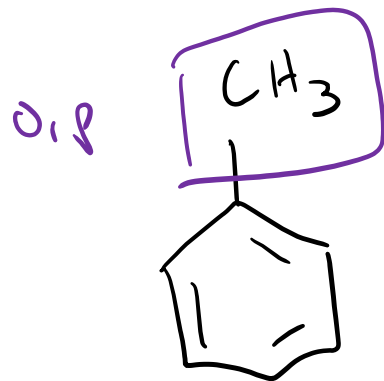
wrong directing effect!

#2

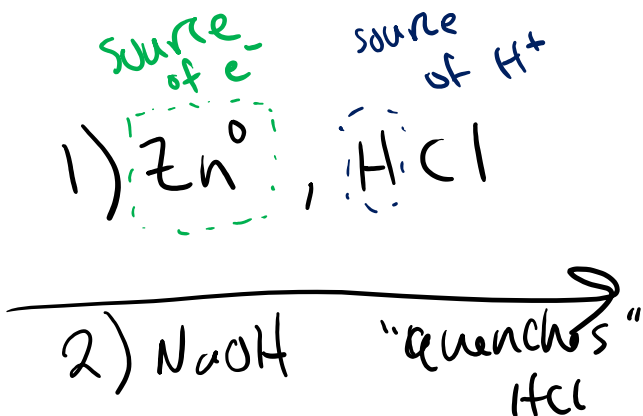
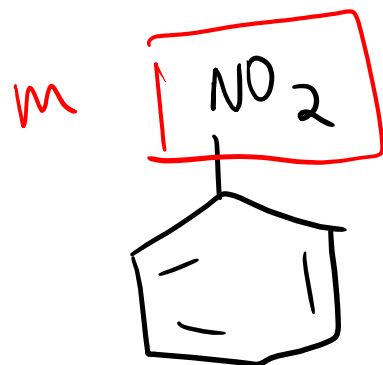
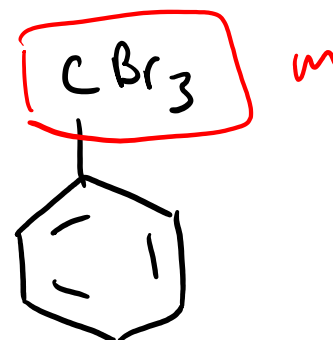
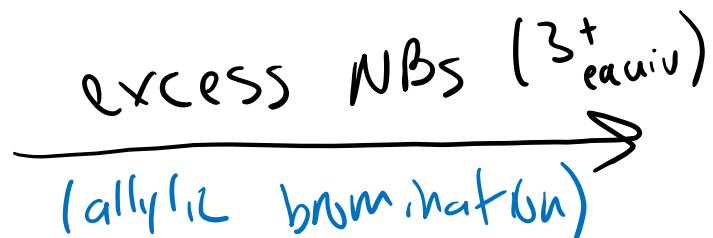
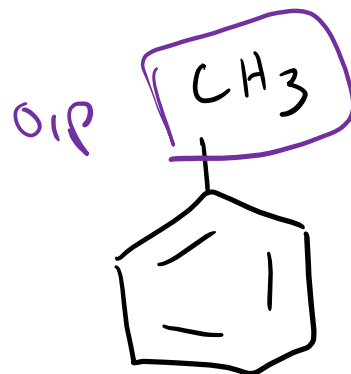


Some Useful Transformations

KNOW THESE RECIPES



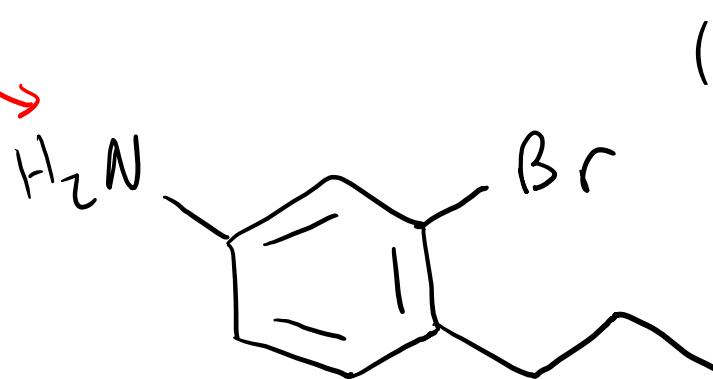
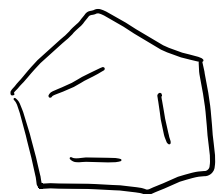
carboxylic acid



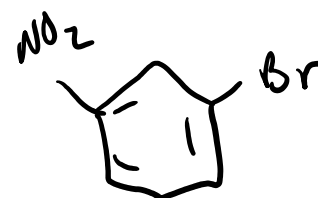
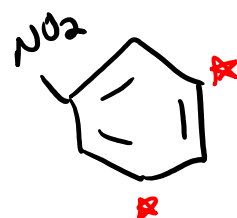
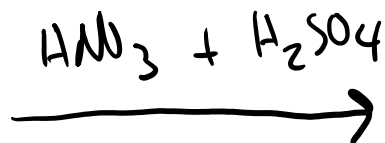
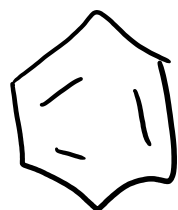
amine

EAS Synthesis Strategies

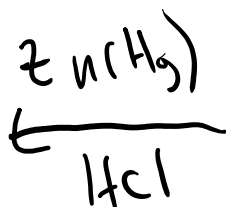
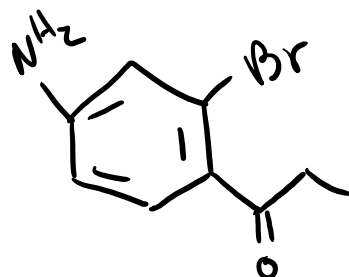
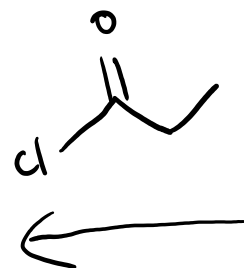
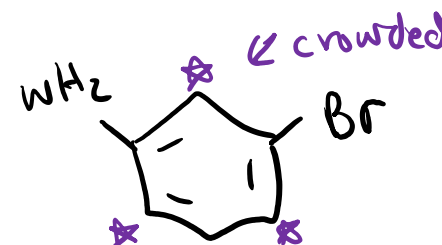
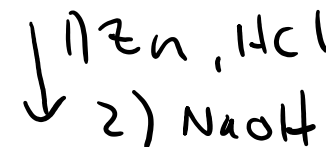
(18.12)



F-C, ring can't be more than weakly deactivated at that step



no F-C!



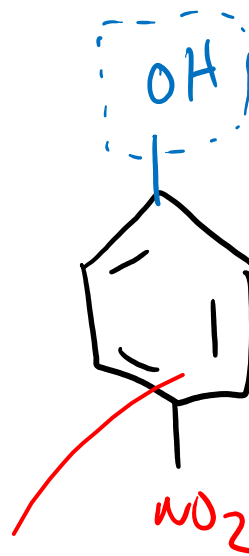
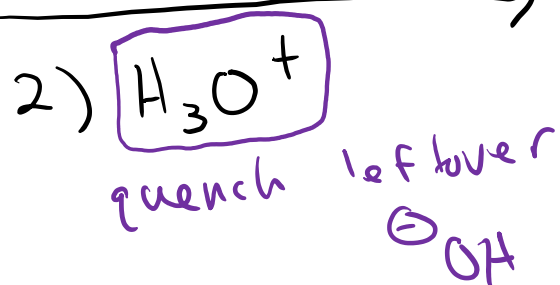
Nucleophilic Aromatic Substitution (S_NAr) (like S_N2 , kinda.) (18.13)

good leaving group



NO_2

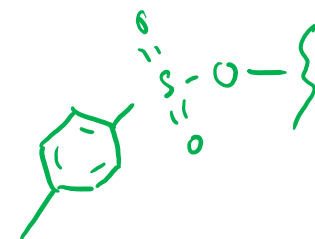
nucleophile



phenol $pK_a \sim 10$
leftover OH^- will deprotonate it if not "quenched"

3 requirements for S_NAr :

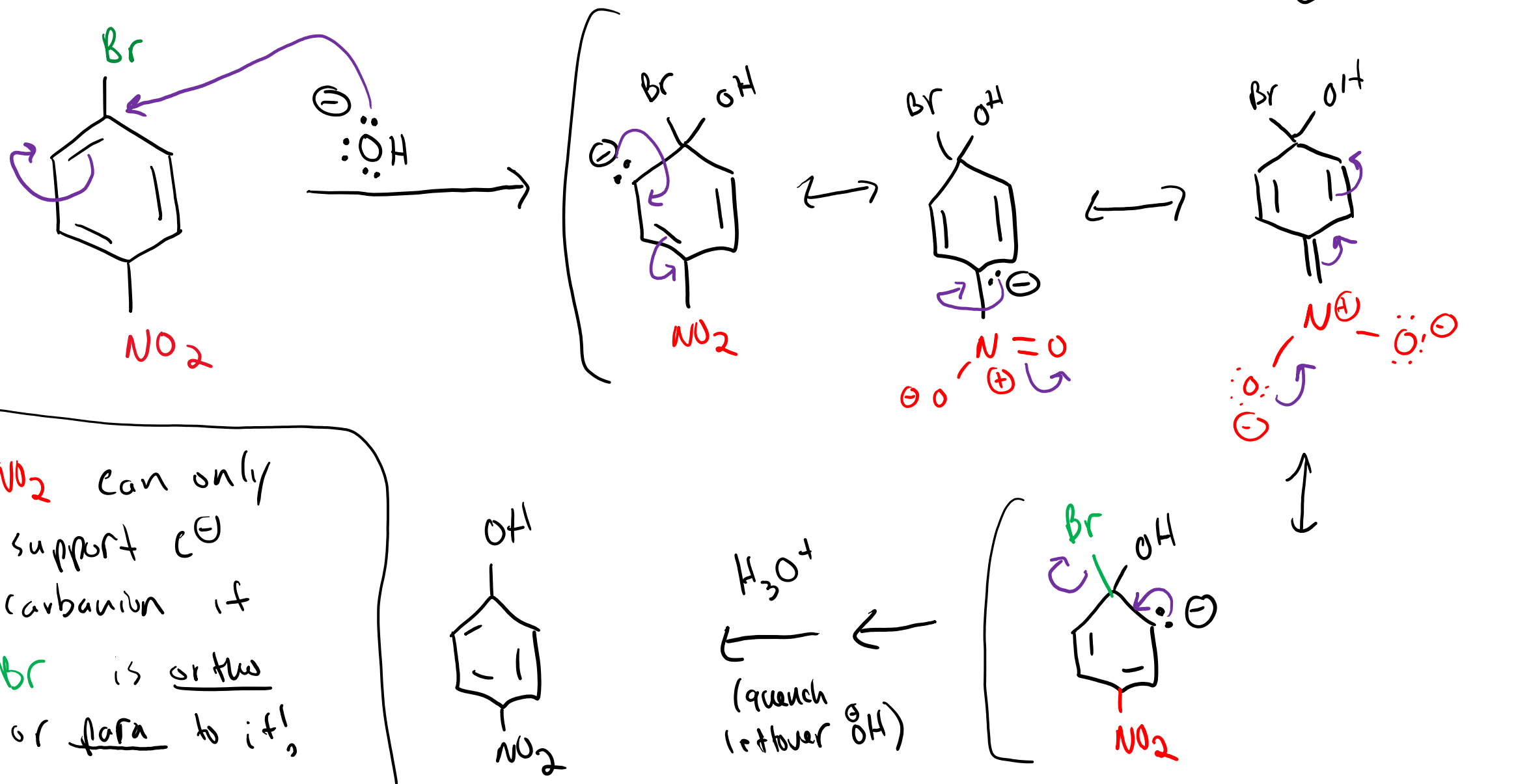
1. Ring must contain a strong EWG (typically NO_2)



2. Ring must contain a good leaving group (Cl , Br , I , $-OTs$ tosylate)

3. EWG and leaving group must be ortho or para to each other!

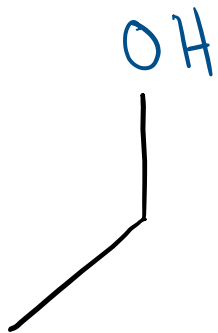
Nucleophilic Aromatic Substitution (S_NAr): Mechanism



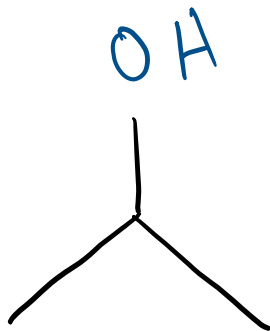
Chapter 12: Alcohols

R-OH

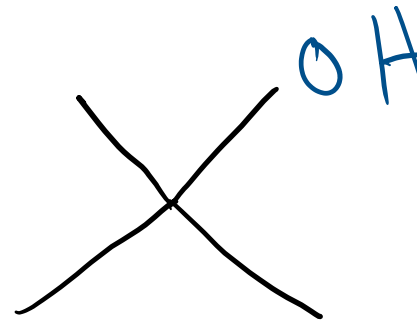
* water is pretty much an alcohol *



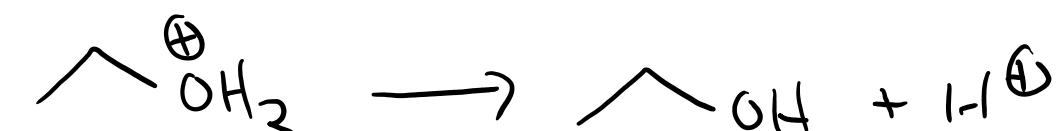
1° primary



2° secondary



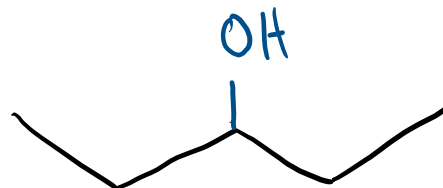
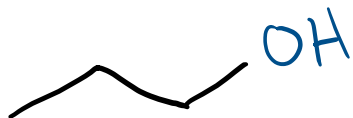
3° tertiary

- weak **acids** $pK_a \sim 16$ 
CCCO + [B] >> CCO[O-] + [H+]
- weak **bases** $pK_{aH} \sim -2$ 
CCCO + [H+] >> CCO[OH2+] + [H-]
- weak **nucleophile**, unless deprotonate first (use NaH, $pK_a \sim 35$)
- OH is poor **leaving group**, unless modified

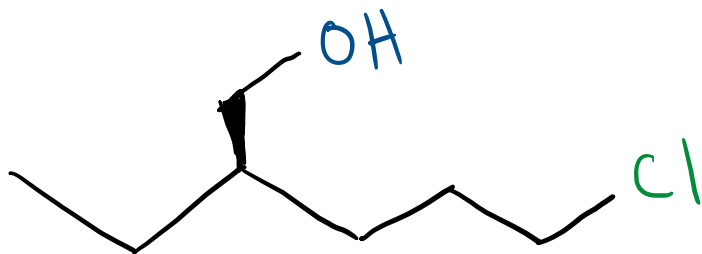
Alcohols: Naming

(12.1)

- Identify the **parent chain** – the longest carbon chain containing the –OH group as a substituent, and change the **suffix** from –ane to **-ol**



- Add the **locant #** of the carbon bearing the -OH before the **parent chain** name. Number the **chain** so that the **-OH locant # is as small as possible**.

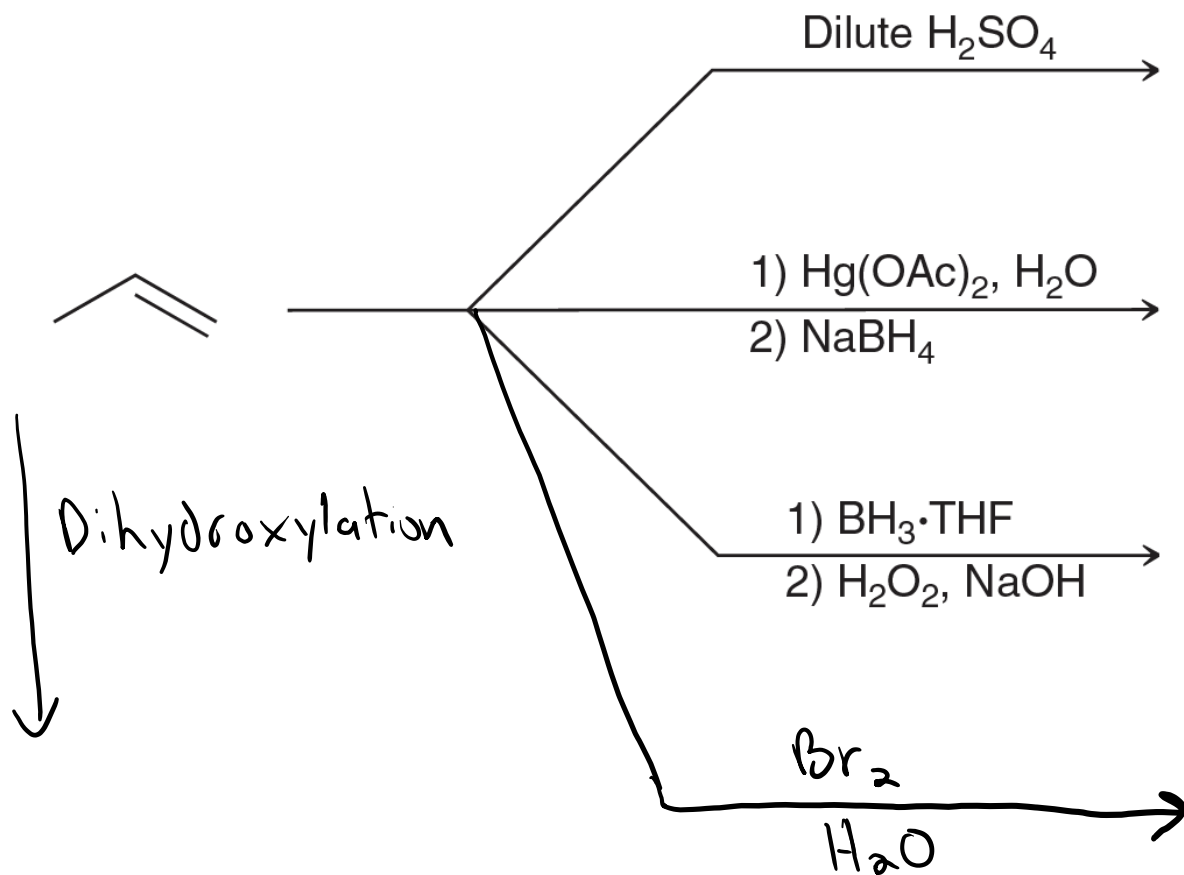


- Name the rest of the substituents, chiral centers, etc. as usual.

Preparation of Alcohols (Chapter 8, Che 211)

(12.3)

via alkene addition:



Or, via substitution:

