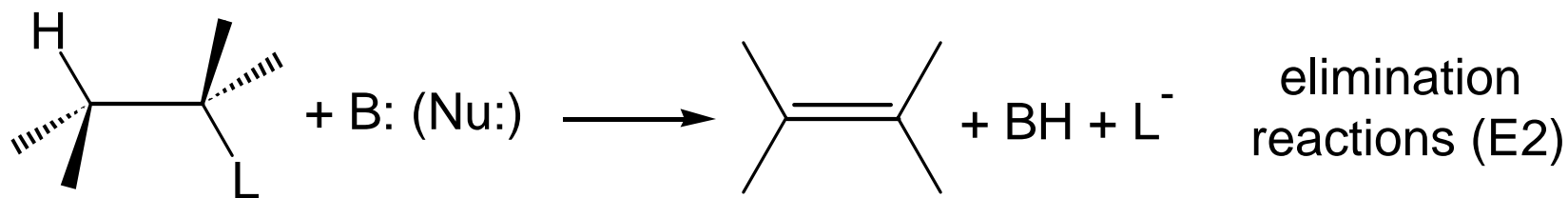
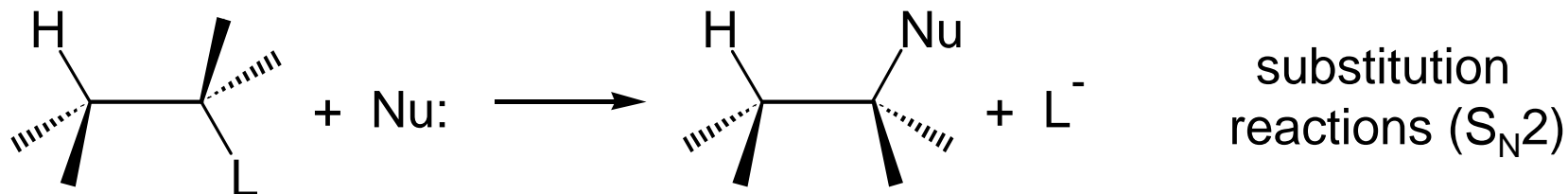


Chapter 10 Synthetic Applications

- What to master
 - ◆ Predicting the Major Products of Substitution and Elimination Reactions
 - ◆ Predicting the Stereochemistry of Substitution and Elimination Reactions
 - ◆ Writing the Mechanisms for Substitution and Elimination Reactions
 - ◆ Using Substitution and Elimination Reactions to Synthesize Target Compounds

Chapter 10 Syntheses: Principles



Preparation of Alcohols & Esters

- Alcohols, HO-R: substitution with alkyl halides (R-X)
 - ◆ HO⁻: S_N2 with 1° / reactive 2° halides; [📖 349 bottom](#)
 - ◆ H₂O: S_N1 (hydrolysis) with bulky (3°) halides; [📖 350 top](#)
 - ◆ CH₃C(O)O⁻: better Nu ([weak B:](#)) with [2° halides](#); [📖 351 bot](#)
 - a synthetic equivalent to HO⁻: ester hydrolysis
- Esters: R'CO₂-R, [📖 357 bottom](#)
 - ◆ *practice*: [📖 350 Problem 10.1](#), [📖 358 Problem 10.14](#)

Preparation of Ethers: R'O-R

- Williamson synthesis: RO^- ; [📖 352 bottom](#)
 - ◆ preparation of alkoxides: [📖 352](#), reactions: [📖 353](#)
 - ◆ synthetic design: $\text{CH}_3\text{CH}_2\text{-O-CH}(\text{CH}_3)_2$, [📖 354 Fig. 10.2](#)
 - 1° electrophiles: less elimination; [📖 355 Problem 10.7](#)
- $\text{S}_{\text{N}}1$ / acid-catalyzed ether synthesis: [📖 356 top](#)
 - ◆ 3° electrophiles & solvolysis conditions (weak Nu)
- Intramolecular reactions: cyclic ethers, [📖 356 bot](#)
 - ◆ *practice*: [📖 355-7 Problems 10.8, 10.9, 10.10-12](#)

Preparation of Alkyl Halides

□ Activation of alcohols into better leaving groups

◆ strong acids (H^+): $\text{R-OH} \rightarrow \text{R-}^+\text{OH}_2$; [📖 358 middle](#)

○ [HI, HBr, HCl & \$\text{ZnCl}_2\$ \(cat\)](#): [📖 359 top & 358 bottom](#)

◆ conversion to sulfonates: less rearrangement; [📖 359 bottom](#)

◆ one-step conversion: SOCl_2 / PBr_3 / PI_3






○ thionyl chloride: R-Cl ; [📖 360 Figure 10.3](#)

○ phosphorus tribromide / triiodide: R-Br / R-I ; [📖 361 top](#)

○ from halides: equilibrium-controlled in acetone; [📖 361 middle](#)

◆ *practice*: [📖 361-2, Problems 10.16 & 10.17](#)

Reaction of Ethers

- Cleavage of C-O bond in acid:  [372 bottom](#)
- Ring opening of epoxide (oxirane): **strained & reactive**
 - ◆ acidic conditions: intermediate between S_N1 and S_N2 ;
inversion at the more substituted carbon,  [373 bot](#) & [374](#)
 - ◆ basic conditions: S_N2 at the less hindered C;  [373](#) & [374](#)
 - ◆ industrial application: EO,  [375 Focus On](#)
 - ◆ *practice*:  [374 Problem 10.25](#)

Preparation of Amines

- Alkylation of 2° & 3° amines: [📖 362 bottom](#)
 - ◆ multiple alkylation with NH_3 & RNH_2 : [📖 363 Figure 10.4](#)
 - ◆ Gabriel synthesis: phthalimide ($\text{p}K_a$ 9.9); [📖 364 & Fig. 10.5](#)
 - ◆ Other alkylating agents: mace; [📖 366](#), SAM; [📖 367](#)
 - ◆ *practice*: [📖 363 Problem 10.18](#) & [📖 363 Problems 10.19-20](#)

Preparation of Hydrocarbons

- $\text{S}_{\text{N}}2$ reactions of R-L with H^- (Nu): [📖 368 bottom](#)
 - ◆ reduction with a hydride ion: $\text{LiAlH}_4 > \text{NaBH}_4$; [📖 369 top](#)

Formation of C-C Bonds

- Carbon nucleophiles: carbanions, [📖 369 middle](#)
 - ◆ $\text{N}\equiv\text{C}^-$: weak base & good nucleophile ($\text{S}_{\text{N}}2$), [📖 369-370](#)
 - ◆ $\text{R}-\text{C}\equiv\text{C}^-$: strong base & good nucleophile ($\text{S}_{\text{N}}2$)
 - preparation & reactions: [📖 370 middle & bottom](#)
 - ◆ *practice*: [📖 371 Problems 10.22-23](#)

Phosphorus & Sulfur Nucleophiles

- Better nucleophiles & weak bases: [📖 371-372](#)
 - ◆ *practice*: [📖 372 Problems 10.24](#)

Preparation of Alkenes & Alkynes

□ Limitations in elimination reactions

◆ competing S_N reactions, regioselectivity, stereoselectivity

□ Dehydrohalogenation: E2 with R-X, [📖 376 bottom](#)

◆ *practice*: [📖 376 Problem 10.26](#), [📖 377 10.27 & 10.28](#)

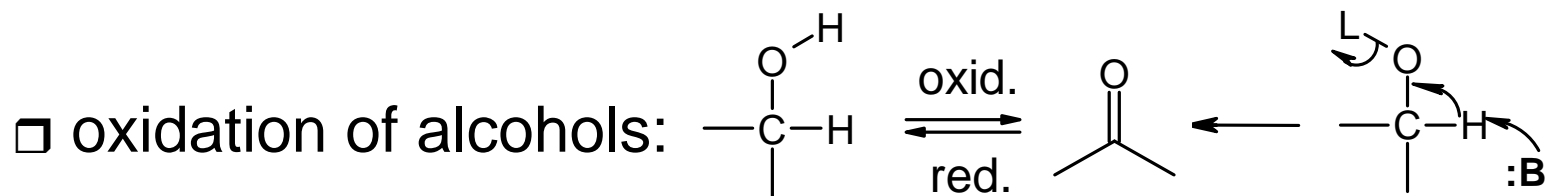
□ Dehydration: acid-catalyzed (E1), [📖 379 Fig. 10.6](#)

◆ side reactions: **rearrangement**; [📖 380 Figure 9.7](#)

□ Alkynes: E2 of vinyl halides, [📖 377 bot & 378 top](#)

◆ *practice*: [📖 380 Problem 10.30 & 378 10.29](#)

Preparation of Aldehydes & Ketones



◆ mechanism: CrO_3 , H_2CrO_4 ; [383 Figure 10.8](#)

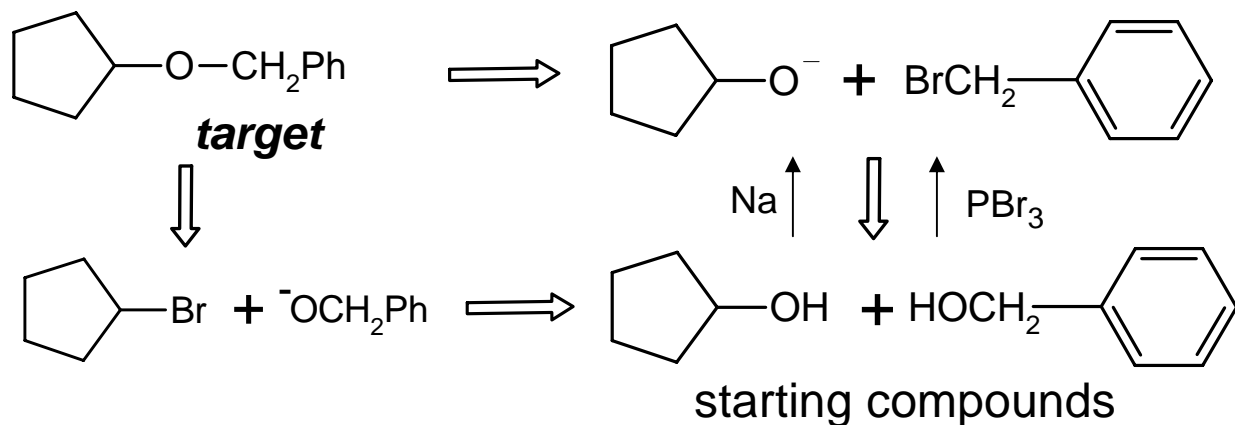
○ oxidants: [383 Table 10.1](#)

◆ types of alcohols & reactions: [381 middle](#) & [382](#)

◆ Green Chemistry: NaOCl in AcOH , [384-5 Focus On](#)

◆ *practice*: [383 Problem 10.31](#)

Synthetic Approach: Retrosynthetic Analysis



- How to prepare cyclopentanol: [📖 386 bottom](#)
 - ◆ from commercially available cyclopentyl halides
- Proposed synthesis: [📖 387 top](#)
 - ◆ *practice*: [📖 387 Practice 10.3](#) & [📖 389 Problem 10.32](#)