



### Roadmap Reaction Legend

#### Reaction 6.1

HX

- Markovnikov regiochemistry
- Mixed stereochemistry of addition
- Carbocation intermediate

#### Reaction 6.3

X<sub>2</sub>

- Anti addition
- Halonium ion intermediate

#### Reaction 6.2

H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub>

- Markovnikov regiochemistry
- Mixed stereochemistry of addition
- Carbocation intermediate

#### Reaction 6.4

X<sub>2</sub>, H<sub>2</sub>O

- Markovnikov regiochemistry (-OH on more substituted)
- Anti addition
- Halonium ion intermediate

### Reaction 6.5

1. Hg(OAc)<sub>2</sub>, H<sub>2</sub>O
  2. NaBH<sub>4</sub>
- Markovnikov regiochemistry
  - Mixed stereochemistry of addition
  - Mercurinium intermediate

### Reaction 6.7

1. OsO<sub>4</sub>
  2. NaHSO<sub>3</sub>, H<sub>2</sub>O
- Syn addition
  - Cyclic osmate ester intermediate

### Reaction 6.9

- H<sub>2</sub>, transition metal catalyst
- Syn addition

### Reaction 7.2

- RC≡C: <sup>-</sup>
- S<sub>N</sub>2 reaction (see Section 9.2)
  - Must be primary haloalkane to avoid E2
  - Makes a carbon-carbon bond

### Reaction 7.4

- 2 X<sub>2</sub>
- Adding only one equivalent of X<sub>2</sub> gives an (E)-dihaloalkene

### Reaction 7.7a

1. BH<sub>3</sub>
  2. H<sub>2</sub>O<sub>2</sub>, NaOH
- Little regiochemical preference
  - Reaction involves enol formation followed by keto-enol tautomerism

### Reaction 7.8

1. H<sub>2</sub>O, H<sub>2</sub>SO<sub>4</sub>, HgSO<sub>4</sub>
- Markovnikov regiochemistry for terminal alkynes
  - Reaction involves enol formation followed by keto-enol tautomerism

### Reaction 7.9b

- H<sub>2</sub>, Lindlar catalyst
- Syn addition
  - Great way to make (Z) alkene

### Reaction 7.11

- 2Na<sup>•</sup> or 2Li<sup>•</sup> in NH<sub>3</sub> (l)
- Radical mechanism involving two cycles of one electron reduction followed by protonation
  - Great way to make (E) alkene

### Reaction 8.1

- X<sub>2</sub> and light or heat
- X predominantly ends up on most substituted C atom, especially for Br<sub>2</sub> (Hammond's postulate)
  - Radical chain mechanism

### Reaction 8.4

- HBr and peroxides
- Non-Markovnikov regiochemistry
  - Mixed stereochemistry of addition
  - Radical chain mechanism

### Reaction 6.6

1. BH<sub>3</sub>
  2. H<sub>2</sub>O<sub>2</sub>, NaOH
- Non-Markovnikov regiochemistry
  - Syn addition
  - Four-membered ring transition state

### Reaction 6.8

1. O<sub>3</sub>
  2. (CH<sub>3</sub>)<sub>2</sub>S
- Complex mechanism involving malozonide and ozonide intermediates
  - Cleavage of C=C bond

### Reaction 7.3

- 2 NaNH<sub>2</sub> in NH<sub>3</sub> (l)
- Last step in converting an alkene into an alkyne through a vicinal dihaloalkane
  - 3 NaNH<sub>2</sub> followed by protonation for terminal alkyne

### Reaction 7.5

- 2 HX
- Markovnikov regiochemistry (with terminal alkynes)
  - Adding only one equivalent of HX gives a haloalkene

### Reaction 7.7b

1. (sia)<sub>2</sub>BH
  2. H<sub>2</sub>O<sub>2</sub>, NaOH
- Non-Markovnikov regiochemistry for terminal alkynes
  - Reaction involves enol formation followed by keto-enol tautomerism

### Reaction 7.9a

- 2H<sub>2</sub>, transition metal catalyst
- Reaction does not stop at the alkene but continues on to the alkane

### Reaction 7.10

1. R<sub>2</sub>BH
  2. Protonolysis (i.e. CH<sub>3</sub>CO<sub>2</sub>H)
- Can give Markovnikov regiochemistry depending on R
  - Syn addition
  - Alternative way to make (Z) alkene

### Reaction 8.2

- NBS and light or heat
- Br adds to any of the possible allylic C atoms to make the most stable alkene (most substituted alkene and trans if relevant)
  - Radical chain mechanism involving an allylic radical intermediate

### Reaction 9.1

#### Various nucleophiles

- Inversion of configuration of chiral haloalkanes
- $S_N2$  reaction mechanism in which the nucleophile attacks the backside of the carbon-leaving group bond
- $S_N1$  mechanism (reaction 9.2) involving a carbocation intermediate can occur with hindered starting materials and weakly basic nucleophiles, usually mixed with  $E1$

Reagents for individual substitution reactions:

Reaction 9.1a:  $H_2S, HS^-$

Reaction 9.1c:  $RC\equiv C:^-$  (new C-C bond)

Reaction 9.1e:  $R_2NH$  (R can be H)

Reaction 9.1g:  $H_2O, HO^-$

### Reaction 10.3

#### HX

- Mixed stereochemistry of substitution
- Primary alcohols react via  $S_N2$ , tertiary alcohols react via  $S_N1$  and secondary alcohols react via a combination of  $S_N2$  and  $S_N1$  mechanisms

### Reaction 10.5

#### $SOCl_2$ and $SOBr_2$

- Inversion of configuration at chiral alcohols
- Alkyl chlorosulfite or alkyl bromosulfite intermediate

### Reaction 10.8

#### $H_2CrO_4 / H_2O$

- Primary alcohols react to give carboxylic acids
- Aldehyde intermediate is formed that then adds water and the resulting geminal diol is oxidized further

### Reaction 10.10

#### PCC (pyridinium chlorochromate)

- Primary alcohols react to give aldehydes
- There is no water in the reagent so the aldehyde cannot hydrate
- Secondary alcohols react to give ketones

### Reaction 11.1

#### $RO^-$

- Williamson ether synthesis
- Primary alcohols react via  $S_N2$
- $E2$  reaction predominates for secondary or tertiary haloalkanes

### Reaction 11.4

#### HBr or HI

- Cleavage of primary or secondary alkyl ethers is by an  $S_N2$  pathway while tertiary alkyl ethers is by an  $S_N1$  pathway

### Reaction 11.6

#### $RCO_3H$ such as MCPBA

- Mechanism involves a single concerted step with a cyclic transition state

### Reaction 9.4

#### Base (Often $RO^-$ )

- Zaitsev's rule predicts the predominant product (most highly substituted favored, trans favored over cis)
- $E2$  reaction mechanism involving an anti and coplanar transition state
- $E1$  mechanism (reaction 9.3) involving a carbocation intermediate can occur with hindered starting materials and weakly basic nucleophiles, usually mixed with  $S_N1$

Reaction 9.1b:  $RSH, RS^-$

Reaction 9.1d:  $NC^-$  (new C-C bond)

Reaction 9.1f:  $N_3^-$

Reaction 9.1h:  $ROH, RO^-$

### Reaction 10.4

#### $PBr_3$

- Inversion of configuration at chiral alcohols
- Protonated dibromophosphite intermediate

### Reaction 10.6

#### $H_3PO_4$

- Usually follows Zaitsev's rule
- Mechanism is reverse of acid catalyzed hydration
- Rearrangements are common with secondary alcohols and primary alcohols with  $\beta$ -branching

### Reaction 10.9

#### $H_2CrO_4 / H_2O$

- Secondary alcohols react to give ketones

### Reaction 10.11

#### $HIO_4$

- Vicinal diols (glycols) react to cleave the carbon-carbon bond between the hydroxyl groups with oxidation to give aldehydes or ketones

### Reaction 11.3

#### $ROH$ , acid catalyst

- Markovnikov regiochemistry
- Carbocation intermediate

### Reaction 11.5

#### $t-BuMe_2SiCl$

- The tert-butyl dimethylsilyl ether is a hydroxyl protecting group cleaved with the fluoride anion

### Reaction 11.7

#### $NaOH / H_2O$

- Configuration of the halohydrin determines stereochemistry of the epoxide
- Mechanism involves deprotonation of the hydroxyl group followed by internal  $S_N2$  reaction on backside of C-X bond

### Reaction 11.9

$\text{H}_2\text{O}$  in acid or  $\text{HO}^-$

- $\text{H}_2\text{O}$  in acid reacts at more substituted carbon (Markovnikov regiochemistry) via an oxonium ion intermediate
- $\text{HO}^-$  reacts at the less hindered carbon via  $\text{S}_{\text{N}}2$
- Both reactions give exclusively trans diol products

### Reaction 11.11

1.  $\text{LiAlH}_4$  2.  $\text{H}_2\text{O}$

- Hydride transfers to the less hindered carbon atom via  $\text{S}_{\text{N}}2$
- The H atom and OH end up exclusively trans to each other

### Reaction 11.10

$\text{NH}_3$

- $\text{NH}_3$  reacts at the less hindered carbon via  $\text{S}_{\text{N}}2$
- Reaction gives exclusively trans aminoalcohol products