

# Ch 18 – college essay



**ASSIGN  
BUSTER**

Chapter 18 Ethers & Epoxides; Thiols and Sulfides Assigned Reading from McMurry: Read Sections 18. 1 through 18. 9; not responsible for “ Focus on ... Epoxy Resins & Adhesives, pp. 697-698). Recommended Problems from McMurry: 18. 1a-e; 18. 18. 2; 18. 3a-d; 18. 4; 18. 5a-d; 18. 6a-b; 18. 7a-b; 18. 8; 18. 9; 18. 10; 18. 11; 18. 12a, b; 18. 13a, b; 18. 14a-c; 18. 16a-f; 18. 17; 18. 18; 18. 19a-c; 18. 20; 18. 21; 18. 22; 18. 23a-e; 18. 24a-l; 18. 25a-f; 18. 26a-d; 18. 27; 18. 28; 18. 29ad; 18. 30a-e; 18. 31; 18. 32; 18. 33; 18. 34; 18. 35a-d; 18. 36; 18. 37; 18. 38; 18. 39; 18. 40a, b; 18. 41a-d; 18. 2; 18. 43; 18. 44; 18. 45; 18. 45; 18. 46; 18. 47; 18. 48; 18. 49; 18. 51; 18. 52; 18. 53; 18. 54; 18. 551-e; 18. 56; 18. 57; 18. 58a-b; 18. 59a-b; 18. 60; 18. 61. 18. 1

Names and Properties of Ethers Method A: Simple ethers; alphabetize if two organic substituents.  $\text{CH}_3\text{-CH}_2\text{-O-CH}_2\text{-CH}_3$  Diethyl ether Methyl propyl ether O  $\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-O-CH}_3$  CH<sub>3</sub> Methyl phenyl ether SP 18. 01 Provide systematic names for the following ethers.  $\text{CH}_3\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3$  O SP 18. 02 Provide structures for the following systematic names.

Systematic name: Isopropyl phenyl ether Systematic name: Cyclohexyl ethyl ether

Method B: Other functional groups present, ether component is an “ alkoxy” substituent. Alkoxy examples: methoxy -OCH<sub>3</sub>, ethoxy -OCH<sub>2</sub>CH<sub>3</sub>, propoxy -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, etc. O C H<sub>3</sub> O CH<sub>3</sub> O C H<sub>3</sub> para-Dimethoxybenzene 3-Methoxy-1-cyclopentene SP 18. 03 Provide systematic names for the following complex ethers. OCH<sub>3</sub> O CH<sub>2</sub>CH<sub>3</sub> Cl SP 18. 04 Provide structures for the following systematic names. Systematic name: meta-Bromopropoxybenzene Systematic name: 1-Isopropoxycyclopentene 18. 2

Synthesis of Ethers The Williamson Ether Synthesis  $R-O^- + C-X \rightarrow R-O-C + X^-$   
 $S_N2$  an alkyl halide methyl & 1° best;  $X = Cl, Br, I, OTos$   $O-C$  ether product

Example:  $\text{O}^- \text{Na}^+$  + Sodium phenoxide  $\text{CH}_3\text{Br}$   $\text{O}^- \text{CH}_3$  Phenyl methyl ether

(anisole) + Na Br + X SP 18. 05 Complete the following reactions. CH<sub>3</sub> CH<sub>3</sub> C

$$O Na + CH_3 I + Na I CH_3 CH_3 CH_3 C CH_3 I + Na O CH_3 + Na I$$
 SP 18. 06

Provide the suitable alkoxide and alkyl halide necessary to produce 2-ethoxy-

2-methyl butane in good yield.  $\text{CH}_3\text{CH}_2\text{CH}_2\text{C}(\text{OCH}_3)_2\text{CH}_3 + \text{NaBr} \xrightarrow{\text{H}^+} \text{CH}_3\text{CH}_2\text{CH}_2\text{C}(\text{OH})_2\text{CH}_3 + \text{HBr}$

### Oxymercuration Intermediates • For laboratory-scale hydration of an alkene

- Use mercuric acetate in THF followed by sodium borohydride

## Markovnikov orientation – via mercurinium ion Alkoxymercuration of Alkenes

General Reaction:  $R-C(=O)-C(=O)-R \xrightarrow[2) \text{NaBH}_4]{1) \text{H}^+/\text{H}_2\text{O}} R-CH_2-CH_2-R$  Ether

Alkene RO Step #1 RO C 1)  $\text{Hg}(\text{OAc})_2$ , ROH H g OA c C C Step #2 R + HOAc

Markovnikov addition SP 18. 07 Complete the following reactions by

displaying the final major organic product. H C 1)  $\text{Hg}(\text{OAc})_2$ ,  $\text{CH}_3\text{OH}$  H C 2)

NaBH<sub>4</sub> H CH<sub>3</sub> CH<sub>3</sub> C C H CH<sub>3</sub> 1) Hg(OAc)<sub>2</sub>, CH<sub>3</sub>OH 2) NaBH<sub>4</sub> SP 18. 08

Specify the alkene and alcohol needed to produce the following ether.

Alcohol  $\text{OCH}_2\text{CH}_3$  1)  $\text{Hg}(\text{OAc})_2$ ,  $\text{CH}_3$  2)  $\text{NaBH}_4$  Alkene 18. 3 Reactions of

Ethers: Acidic Ether Cleavage General Reaction:  $\text{HX} + \text{C}-\text{O}-\text{C} \rightarrow \text{C}-\text{OH} + \text{X}-\text{C}$  (strong)

acid) Ether Alcohol Alkyl halide SP 18. 09 Predict the product for the

following ether-cleavage reaction.  $\text{CH}_3\text{CH}_2\text{C}(\text{OCH}_3)_2 + \text{HBr} \rightarrow \text{CH}_3\text{CH}_2\text{C}(\text{OH})_2 + \text{CH}_3\text{Br}$  8. 4

Reactions of Ethers: Claisen Rearrangement

Thermodynamically more stable o 250 Allyl phenyl ether C<sub>9</sub>H<sub>10</sub>O ortho-Allyl

phenol C<sub>9</sub>H<sub>10</sub>O Mechanism (involves six-membered transition state): 1 O TS

2 3 1 O 2 H keto-enol tautomerization 3 O H SP 18. 10 Predict the structure

for the following Claisen rearrangement. O o 250 2-Butenyl phenyl ether

C<sub>10</sub>H<sub>12</sub>O 18. 5 Cyclic Ethers: Epoxides (2 methods) General Reaction 1: O C C + R Alkene C O O O O C H A peracid C An epoxide R C O A carboxylic acid Specific Example 1: O Cl C O O H m-CPBA o H O O + CH<sub>2</sub>Cl<sub>2</sub>, 25 C H 1, 2-Epoxycycloheptane Cl H C O H 18. Cyclic Ethers: Epoxides (2 methods) General Reaction 2: C OH X<sub>2</sub>, H<sub>2</sub>O C C C X A halohydrin Alkene O NaOH H<sub>2</sub>O C + H<sub>2</sub>O + NaX C An epoxide Review Section 7. 3 Specific Example 2: H CH<sub>3</sub> C C H CH<sub>3</sub> cis-2-Butene Br<sub>2</sub> H<sub>2</sub>O H CH<sub>3</sub> Br C OH C H CH<sub>3</sub> NaOH H<sub>2</sub>O O HC CH<sub>3</sub> C H + H<sub>2</sub>O + NaBr CH<sub>3</sub> meso-2, 3-Dimethyl-oxirane (or cis-2, 3-epoxybutane) SP 18. 11 Fill in the appropriate intermediates showing the correct stereochemistry. H CH<sub>3</sub> C C CH<sub>3</sub> Br<sub>2</sub> NaOH H H<sub>2</sub>O H<sub>2</sub>O trans-2-Butene + H<sub>2</sub>O + NaBr 18. 6 Reactions of Epoxides: Ring-Opening General epoxide structure: O C Since each atom is sp<sup>3</sup> there is considerable angle strain in the epoxide ring-system.

C Acidic Conditions: Epoxide opening under acidic conditions (aqueous acid) yields 1, 2-diols General Reaction: H H O O C H C HO C H<sub>2</sub>O An epoxide C OH A 1, 2-diol (glycol) H O C H C + O H H O C + C H O H H O H Specific Example (using symmetrical epoxide): H + H H<sub>3</sub>O OH H<sub>2</sub>O OH O H H trans-1, 2-Cyclohexanediol SP 18. 12 Predict the correct structure of the product diol showing the correct stereochemistry. O H CH<sub>3</sub> C C CH<sub>3</sub> H trans-2, 3-epoxybutane H<sub>3</sub>O<sup>+</sup> H<sub>2</sub>O Note: Epoxide opening under anhydrous acidic conditions yields halohydrins. Specific Example (2° and 1° carbons): o 1 carbon o 2 carbon O CH<sub>3</sub> H C C H H 1, 2-Epoxypropane

OH HCl Et<sub>2</sub>O CH<sub>3</sub> C Cl CH<sub>2</sub> Cl + CH<sub>3</sub> H 1-Chloro-2-propanol (90%) C CH<sub>2</sub> OH H 2-Chloro-1-propanol (10%) SP 18. 13 Using the above model predict the major halohydrin. O H C H C HCl H Et<sub>2</sub>O O H C C H H HCl OH C Et<sub>2</sub>O H Cl CH<sub>2</sub>

Cl + C CH<sub>2</sub> OH H Explanation: In cases where a 2° carbon and a 1° carbon form the epoxide ring, the major halohydrin product will be the one where the incipient alcohol is 2° and the halide is 1°. Upon protonation of the epoxide oxygen the halide ion simply attacks the less-hindered 1° carbon with a greater frequency to give the major regioisomer. Specific Example (3° and 1° carbons): SP 18. 4 Using the above model predict the major

halohydrin. Circle one. O C C H H HCl OH C Et<sub>2</sub>O + C H Cl Cl H C OH C H H

Explanation: In cases where a 3° carbon and a 1° carbon form the epoxide ring, the major halohydrin product will be the one where the incipient alcohol is 1° and the halide is 3°. Upon protonation of the epoxide oxygen the halogen attacks the more-stabilized (same as more substituted) carbon atom to give the major regioisomer described. Basic Conditions: Note: Nucleophile will always attack least-hindered position. Specific Example: o 3 carbon 1o carbon O CH<sub>3</sub> CH<sub>3</sub> C C H H OH NaOH H<sub>2</sub>O, ? CH<sub>3</sub> C CH<sub>2</sub> OH CH<sub>3</sub> -Methyl-1, 2-propanediol SP 18. 15 Predict the structure of the 1, 2-diol from the

following reaction. O C C H H NaOH H<sub>2</sub>O, ? Reaction with Grignard Reagents: O CH<sub>3</sub> CH<sub>3</sub> C C H H OH 1) CH<sub>3</sub>CH<sub>2</sub>MgBr, Et<sub>2</sub>O 2) (aq) NH<sub>4</sub>Cl CH<sub>3</sub> C CH<sub>2</sub> CH<sub>3</sub>

CH<sub>2</sub> CH<sub>3</sub> SP 18. 16 Predict the structure of the organic product from the

following Grignard epoxide reaction. O H C C H H 1) CH<sub>3</sub>MgBr, Et<sub>2</sub>O 2) (aq)

NH<sub>4</sub>Cl Reaction with a 1° amine: O H C OH CH<sub>2</sub> H H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> C CH<sub>2</sub> N

CH<sub>2</sub> CH<sub>2</sub> H Reaction with a 2° amine: O H C OH H H<sub>3</sub>C CH<sub>2</sub> + N H<sub>3</sub>C H C CH<sub>2</sub>

N CH<sub>3</sub> CH<sub>3</sub> CH<sub>3</sub> SP 18. 17 Predict the structure of the epoxide and amine needed to generate the amino alcohol shown to the right.

OH + CH<sub>3</sub> C CH<sub>3</sub> Epoxide Amine CH<sub>2</sub> N H 18. 7 Crown Ethers • Large rings consisting of repeating (-OCH<sub>2</sub>CH<sub>2</sub>-) or similar units • Named as x-crown-y –

x is the total number of atoms in the ring – y is the number of oxygen atoms  
– 18-crown-6 ether: 18-membered ring containing 6 oxygen atoms • Central cavity is electronegative and attracts cations

### 18. 8 Thiols and Sulfides •

Thiols (RSH), are sulfur analogues of alcohols – Named with the suffix -thiol – SH group is called “ mercapto group” (“ capturer of mercury”) Thiols:

Formation and Reaction • From alkyl halides by displacement with a sulfur nucleophile such as  $\text{HS}^-$  The alkylthiol product can undergo further reaction with the alkyl halide to give a symmetrical sulfide, giving a poorer yield of the thiol

### Sulfides •

Sulfides ( $\text{RSR}'$ ), are sulfur analogues of ethers – Named by rules used for ethers, with sulfide in place of ether for simple compounds and alkylthio in place of alkoxy

Using Thiourea to Form Alkylthiols • Thiols can undergo further reaction with the alkyl halide to give dialkyl sulfides • For a pure alkylthiol use thiourea ( $\text{NH}_2(\text{C}=\text{S})\text{NH}_2$ ) as the nucleophile • This gives an intermediate alkylisothiurea salt, which is hydrolyzed cleanly to the alkyl thiourea

### Oxidation of Thiols to Disulfides

Reaction of an alkyl thiol ( $\text{RSH}$ ) with bromine or iodine gives a disulfide ( $\text{RSSR}$ ) • The thiol is oxidized in the process and the halogen is reduced

### Sulfides •

Thiolates ( $\text{RS}^-$ ) are formed by the reaction of a thiol with a base • Thiolates react with primary or secondary alkyl halide to give sulfides ( $\text{RSR}'$ ) • Thiolates are excellent nucleophiles and react with many electrophiles

### Sulfides as Nucleophiles •

Sulfur compounds are more nucleophilic than their oxygen-compound analogues – 3p valence electrons (on S) are less tightly held than 2p electrons (on O) • Sulfides react with primary alkyl halides ( $\text{S}_\text{N}2$ ) to give dialkylsulfonium salts ( $\text{R}_3\text{S}^+$ )

### Oxidation of Sulfides •

Sulfides are easily oxidized with  $\text{H}_2\text{O}_2$  to the sulfoxide ( $\text{R}_2\text{SO}$ ) • Oxidation of a sulfoxide with a peroxyacid yields a sulfone ( $\text{R}_2\text{SO}_2$ ) • Dimethyl sulfoxide (DMSO) is often

used as a polar aprotic solvent

### 18. 9 Spectroscopy of Ethers

- Infrared: C–O single-bond stretching 1050 to 1150  $\text{cm}^{-1}$  overlaps many other absorptions.
- Proton NMR: H on a C next to ether O is shifted downfield to  $\delta$  3.4 to  $\delta$  4.5

– The  $^1\text{H}$  NMR spectrum of dipropyl ether shows this signal at  $\delta$  3.4 – In epoxides, these H's absorb at  $\delta$  2.5 to  $\delta$  3.5 in their  $^1\text{H}$  NMR spectra

Carbon NMR: C's in ethers exhibit a downfield shift to  $\delta$  50 to  $\delta$  80

### Let's Work a Problem

When 2-methyl-2, 5-pentanediol is treated with sulfuric acid, dehydration occurs and 2, 2-dimethyltetrahydrofuran is formed. Suggest a mechanism for this reaction. Which of the two oxygen atoms is most likely to be eliminated and why?

Answer First, there is protonation of the 3 $^\circ$  –OH group, then a 3 $^\circ$  carbocation is formed via loss of  $\text{H}_2\text{O}$ . Then there is a nucleophilic attack of the carbocation by the 2 $^\circ$  –OH group. The 3 $^\circ$  OH group is the one eliminated in all likelihood because its removal involves the formation of the more stable 3 $^\circ$  carbocation.