INTRODUCTION TO CHEM 2312
AND
REVIEW OF CHEM 2311

These class notes are designed to be incomplete - we will complete them in class. Reading sections (S #.#) and appropriate problems (P #.#) are listed in the top right-hand corner of some slides.

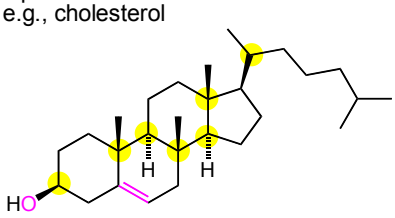
OBJECTIVES OF CHEM 2312

To build on the principles of Structure, Reactivity and Mechanism to:

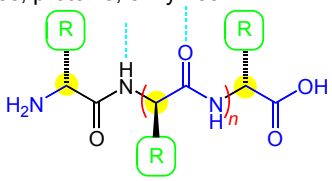
1. *Develop methods to prepare complex organic molecules from simple feedstocks.*
2. *Introduce topics of biological and industrial relevance.*
3. *Provide a foundation for the study of biochemistry and polymer science.*

BIOMOLECULES

Lipids
e.g., cholesterol



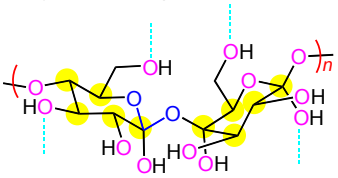
Peptides, proteins, enzymes



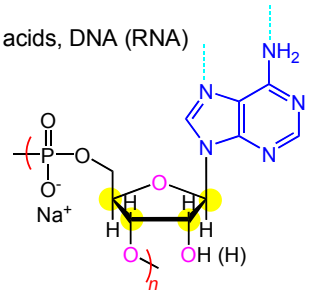
R = CH_3, $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, ...

R = $-CH_2OH$, $-(CH_2)_2NH_2$, $-(CH_2)_2COOH$, ...

Carbohydrates, Sugars



Nucleic acids, DNA (RNA)



Prob:3.20,31

ACIDS, BASES, ELECTROPHILES AND NUCLEOPHILES

Acids	**Bases**
Proton sources Loss of proton leads to conjugate base	Proton acceptors Donate pair of electrons to a proton
Electrophiles *Electron defficient species* δ+ end of polar bond Carbocations Lewis acids	**Nucleophiles** *Source of electrons* Neutral with lone pair Anion with lone pair Neutral with pi-bond

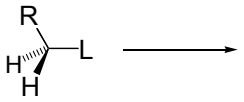
Curved Arrows

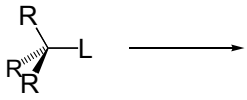
Show movement of electrons from "source" to "destination"

UNDERSTANDING MECHANISMS AND RATIONALIZING OBSERVATIONS

Nucleophilic Substitutions *S:6.1-14 Prob:6.14,16,17*

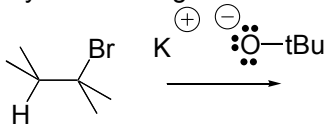
Nucleophilic substitutions at an sp^3 carbon may occur with inversion of stereochemistry or racemization. This, along with other pieces of evidence (kinetics, effect of substrate structure, etc), is taken to indicate two possible pathways (mechanisms).



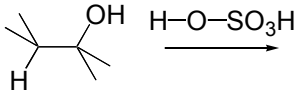


Eliminations *S:6.15-19 Prob:7.6-7,24a-i*

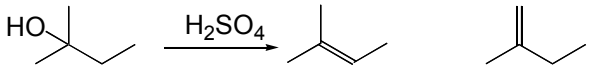
Bases promote dehydrohalogenation of alkyl halides to give alkenes



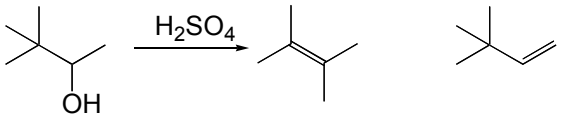
Acids promote dehydration of alcohols to form alkenes



Eliminations generally lead to more substituted alkenes (Zaitsev's rule)

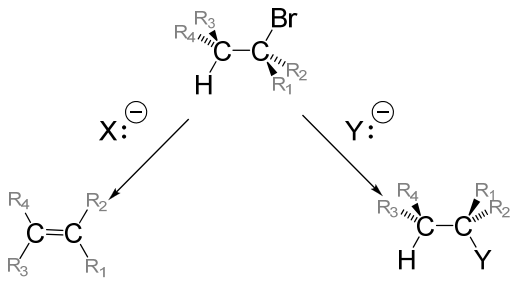


Carbocation intermediates (formed upon treatment of alcohols with strong acid) rearrange!



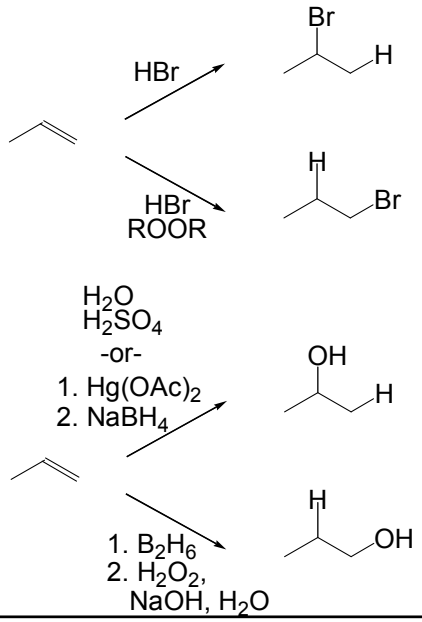
Elimination versus Substitution: Basicity versus Nucleophilicity

The structure of substrate and reagent effect the outcome of a reaction



Addition *S:7.14-15;8.2-13 Prob:18.28,29,31*

Regiochemistry: Reagents for Markovnikov and anti-Markovnikov additions to alkenes



Addition Reactions

Know the reagents and outcomes (stereochemistry, regiochemistry)

Rationalize outcomes through knowledge of reactive intermediates and reaction pathways (mechanism)

Addition of H_2
- H_2/Pd (alkene, alkyne)
- H_2/Lindlar catalyst (alkyne → cis alkene)
- dissolving metal reduction (alkyne → trans alkene)

Addition of H-Hal
- Markovnikov
- anti-Markovnikov

Addition of H_2O
- H_3O^+ (regiochemistry)
- Oxymercuration-demercuration (regiochemistry, stereochemistry)
- Hydroboration-oxidation (regiochemistry, stereochemistry)
- hydration of alkynes (regiochemistry)

Addition of Hal_2
- Hal_2 (regiochemistry, stereochemistry)
- Hal_2/H_2O (regiochemistry)

Addition of carbenes

Epoxidation

Ring opening reactions of epoxides (H_2O, ROH, HCN)

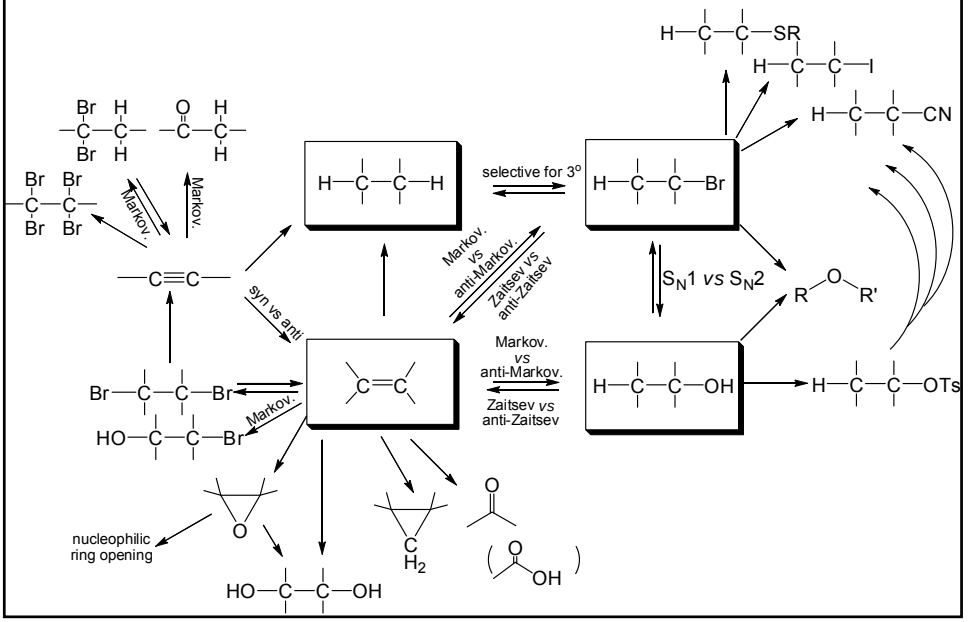
syn-Hydroxylation

Oxidative cleavage of alkenes and alkynes
- $KMnO_4$
- Ozonolysis

Radical Polymerization

REACTIONS

S:Chap 6,7,8,11



ALKANES ARE QUITE UNREACTIVE

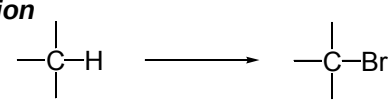
S:10.3

Two Reactions of Alkanes

Combustion

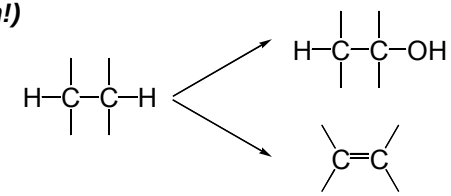
$$C_nH_{2n+2} + (3n+1)/2\ O_2 \longrightarrow n\ CO_2 + n+1\ H_2O$$

Radical Bromination

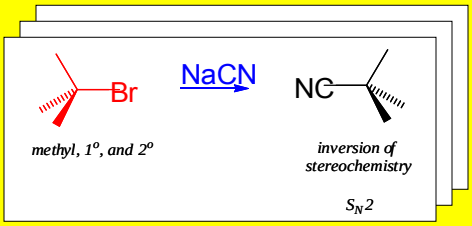


Very limited utility: this is only a useful process for substitution of hydrogens on 3° carbons (or 2° carbons if monosubstitution only leads to one possible product)

Two Reactions of Alkanes DO NOT Undergo (so do not even think of suggesting them!)



~ MAKE FLASHCARDS ~



front

Substrate + Reagent (and conditions)

back

Product

Substrate and Product

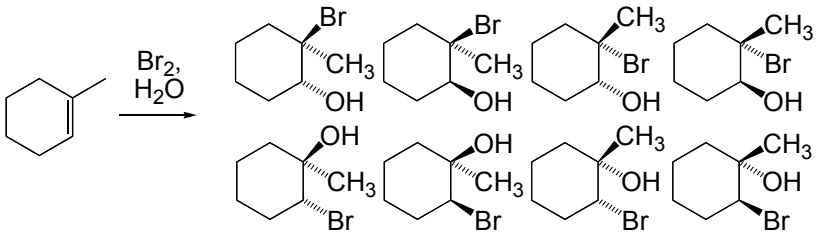
Reagent +Conditions

Reagent and Product

Substrate

UNDERSTANDING MECHANISMS AIDS LEARNING

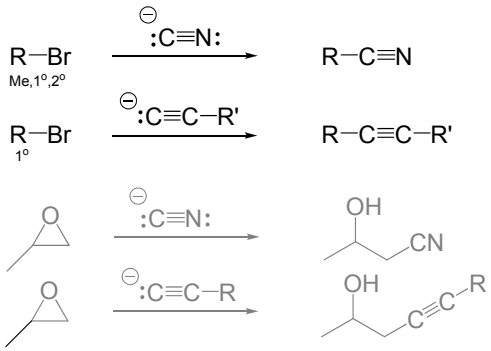
Which of the following is/are the product(s) of the reaction shown?



The *regiochemistry* and *stereochemistry* can be rationalized in terms of *MECHANISM:* The reaction proceeds by reaction of water with a cyclic bromonium ion….

CARBON-CARBON BOND-FORMING REACTIONS

To date, we have a very limited number of reactions to make C-C bonds.

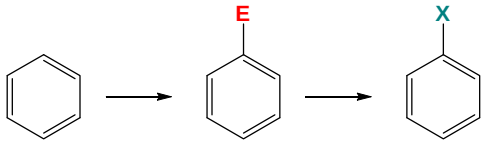


A focus of CHEM 2312 is the preparation of complex molecules through forming new C-C bonds.

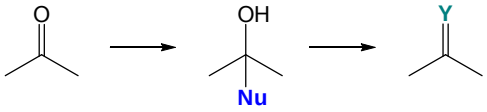
PREVIEW OF ORGANIC-II

Chemistry of…

Arenes

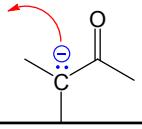


Carbonyls



Acid derivatives

Carbonyl α-carbanions



REVIEWING ORGANIC CHEMISTRY

-Make flash cards of reactions

-Work problems to become familiar with reactions and mechanisms

- Make an effort to understand the mechanistic principles rather than just trying to "learn reactions"

- Retake Organic 1?

MAKING PROGRESS IN ORGANIC CHEMISTRY

-Make flash cards and flow sheets of reactions – use them!

-Work problems to become familiar with reactions and mechanisms

- Make an effort to understand the mechanistic principles rather than just trying to "learn reactions"

- Develop regular study habits: Do the reading, HWebs, HWs….keep up-to-date

- Work in a group: discuss chemistry with your peers

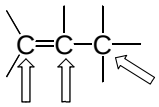
TOPIC 1. CONJUGATED SYSTEMS AND AROMATICITY (Chapters 13 and 14)

OBJECTIVES

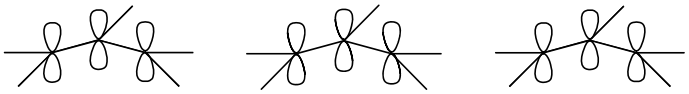
1. Describe the interaction of alkenes with adjacent p-orbitals.
2. Discuss the influence of this interaction on the chemistry of dienes (relative to alkenes)
3. Describe the influence of conjugation on the ease of formation of carbocations and radicals (relative to alkyl radicals) and carbocations
4. Contrast the structure and reactivity of alkenes and benzene
5. Provide a theoretical basis for aromaticity: the observation that compounds with a benzene ring are particularly stable
6. Recognize that antiaromatic compounds are unstable

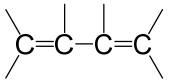
INTRODUCTION

Alkenes undergo addition chemistry. However, alkenes also influence the reactivity of adjacent sp^3 "allylic" carbons.



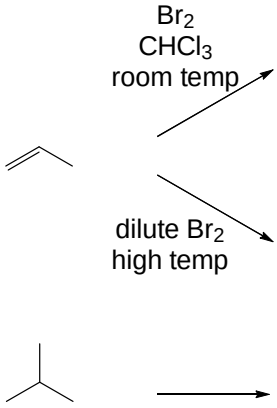
p-orbitals adjacent to a cation, anion, radical, or alkene influence each other and are said to be "conjugated" (*verb:* to join together, as in marriage)



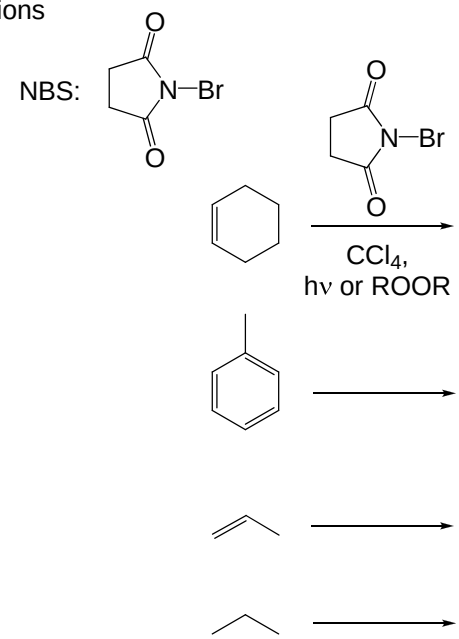


ALLYLIC AND BENZYLIC RADICALS

Bromination

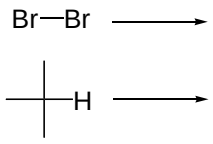


N-Bromosuccinimide (NBS) is a useful reagent for allylic and benzylic brominations

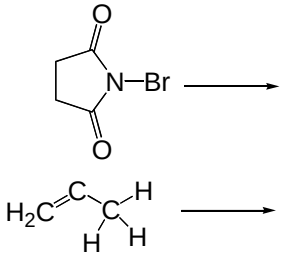


Mechanism

Review of Radical Bromination of Alkanes

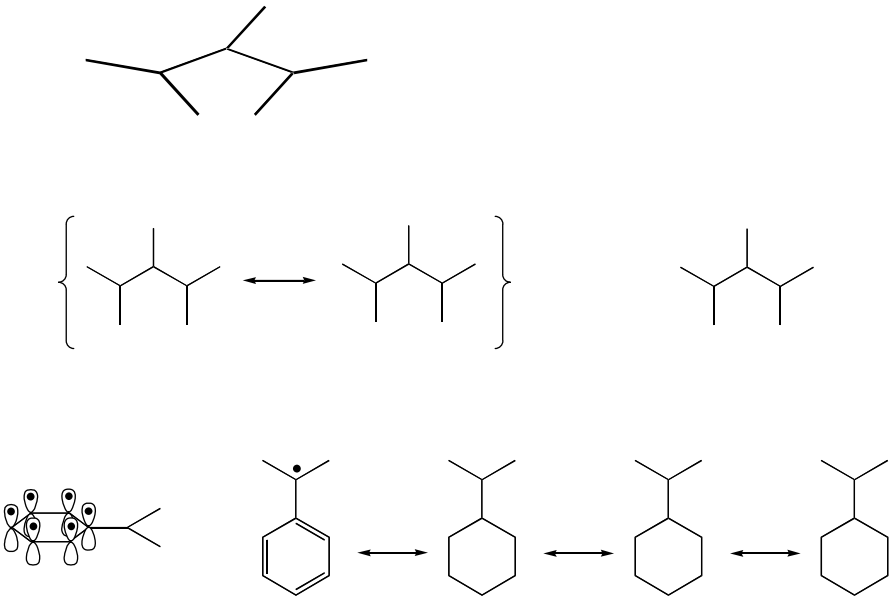


Bromination of Allylic and Benzylic Positions: Influence of a Double Bond

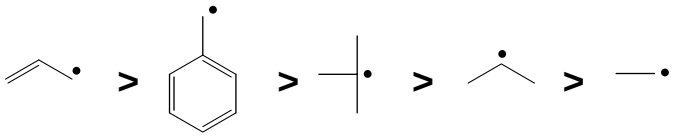


⇒

The Stability of the Allylic and Benzylic Radicals



Stability of radicals (and ease of formation)



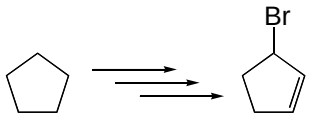
allylic benzylic 3° 2° 1°

Consequence of Resonance Stabilization of Intermediate Radicals – Formation of Regioisomers

Problem [Solomons 13.36] – What are the four isomers with formula C_5H_9Br formed by the reaction of 1-pentene with NBS?

?

[Solomons Problem 13.22e] - How would you carry out the following transformation? (several steps may be necessary)



?

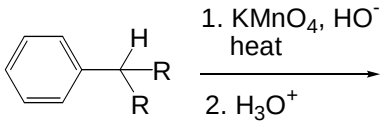
? *Prob:*13.1,22,36 ?

L3

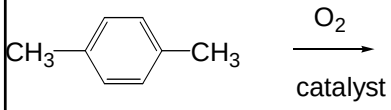
S:15.16;21.10

Oxidation of Benzylic Positions

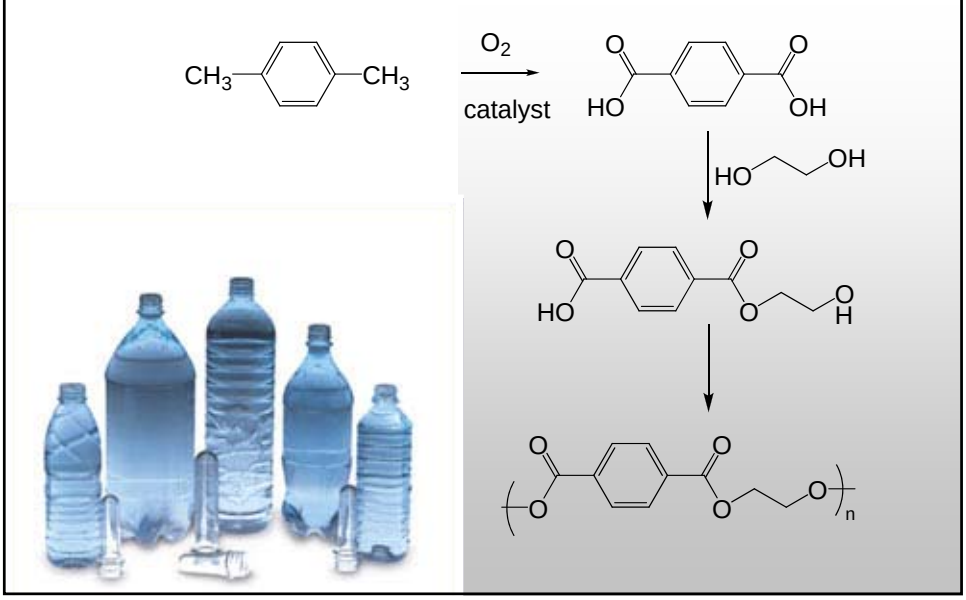
In laboratory



In industry



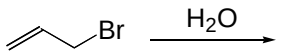
Oxidation of p-xylene to terephthalic acid
for production of polyester

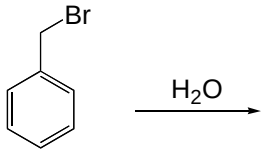


ALLYLIC AND BENZYLIC CARBOCATIONS

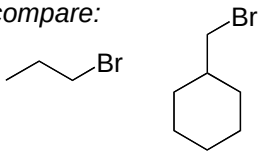
S:13.4; 15.15
*Prob:*13.33

Propenyl bromide (allyl bromide) and benzylic bromides undergoes rapid hydrolysis to form the corresponding alcohols





compare:

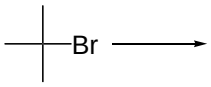


quite unreactive

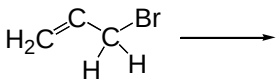
Previously we have seen that hydrolysis of tertiary alkyl bromides by an S_N1 mechanism via a tertiary carbocation

Mechanism

Review of Hydrolysis (S_N1 reaction with H_2O) of tert-Butyl Halides

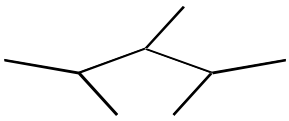


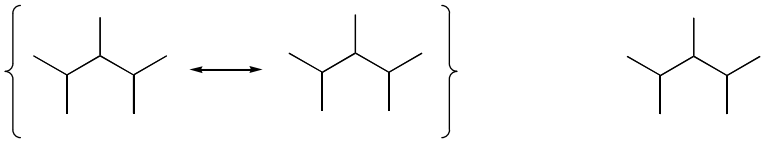
Hydrolysis Allylic and Benzylic Positions: Influence of a Double Bond

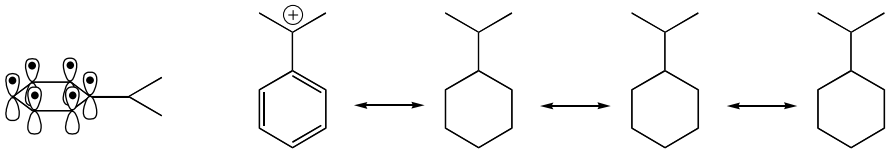


$\Rightarrow$

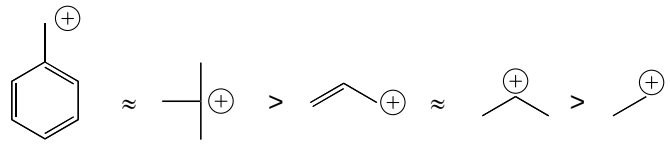
The Stability of the Allylic and Benzylic Carbocations





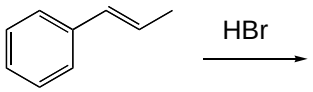


Stability (and ease of formation):



benzylic 3° allylic 2° 1°

Carbocations are also formed by the protonation of alkenes (e.g., in the addition of HBr and H_2O/H^+). The enhanced stability of allylic and benzylic cations can be used to explain the regiochemistry of addition reactions.



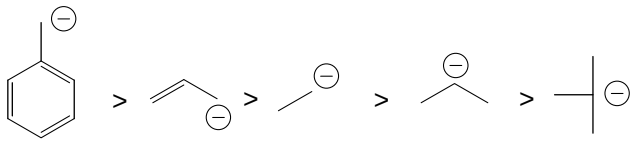
Consequences of the enhanced stability of allylic and benzylic cations by resonance include:

- Mild *nucleophilic substitution* reactions of allyl and benzyl halides (via more stable carbocation)

- Regiochemistry of *electrophilic addition* to alkenyl benzenes (via more stable carbocation)

A brief note about anions

Stability (ease of formation):

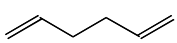


Problem [Solomons 13.33] – What are the ***four*** products with molecular formula C_4H_7Cl formed upon treatment of $CH_3CH{=}CHCH_2OH$ with HCl?

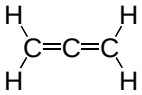
? *Prob:* 1.4,32 ?

ALKADIENES AND POLYUNSATURATED HYDROCARBONS

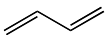
Classes of dienes



1,5-hexadiene
an isolated diene; the
alkenes react independently



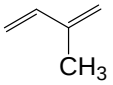
1,2-propadiene
a cumulated diene; not common



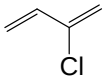
1,3-butadiene
a conjugated diene;
⇒ *alkenes influence one another*

CONJUGATED DIENES

Examples



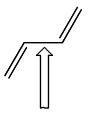
isoprene
monomer of natural rubber



chloroprene
monomer of neoprene

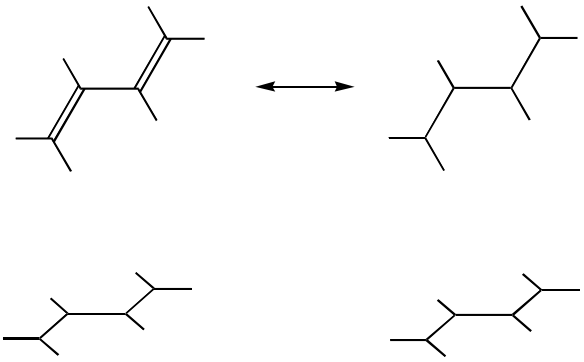
The effect of conjugation on the structure of dienes

$H_3C–CH_3$	1.54 Å
$H_2C=CH_2$	1.34 Å
HC≡CH	1.20 Å



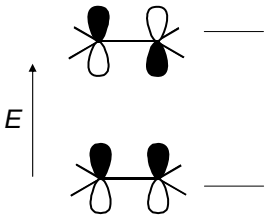
1.47 Å

Resonance in Conjugated Dienes

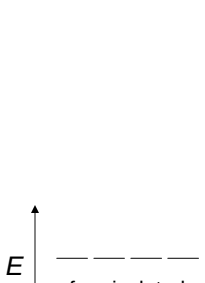


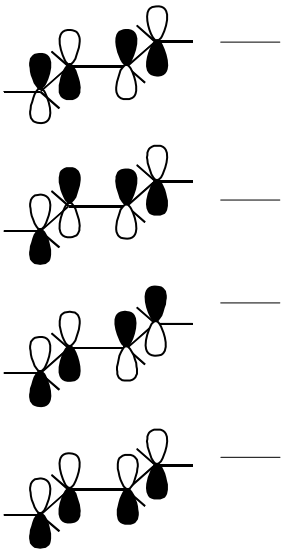
A Molecular Orbital Description of Butadiene

Ethene



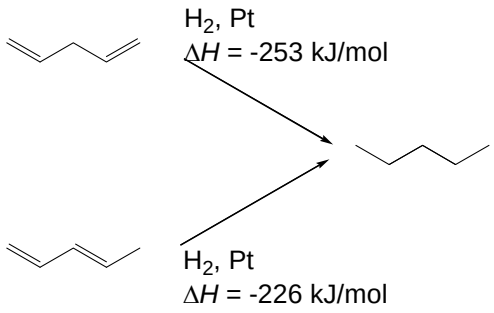
1,3-Butadiene

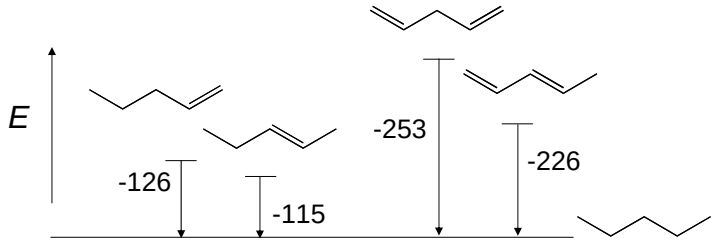




The Effect of Conjugation on the Stability of Dienes

Heats of Hydrogenation



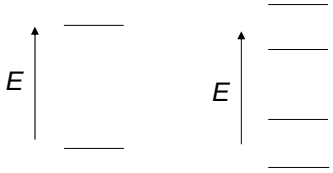


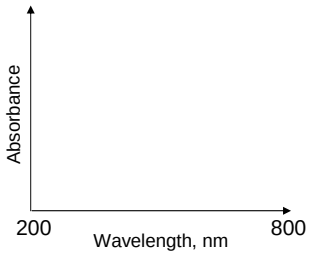
ULTRAVIOLET-VISIBLE SPECTROSCOPY

S:13.9

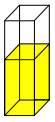
The energy required to promote electrons from π or n (non-bonding) orbitals to π^* corresponds to radiation in the ultraviolet-visible region of the electromagnetic spectrum (200-800 nm)

ethene *1,3-butadiene*





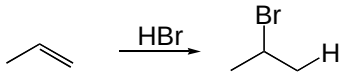
$$A = \varepsilon \, l \, c$$

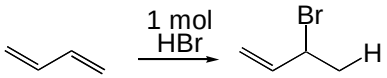


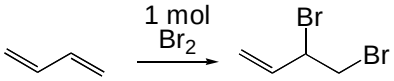
ELECTROPHILIC ADDITION TO CONJUGATED DIENES

S:13.10
*Prob:*13.20, 23,34

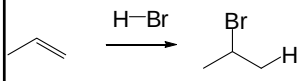
1,2- and 1,4- Addition

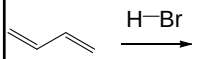


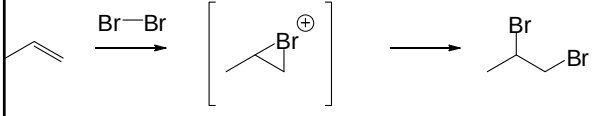


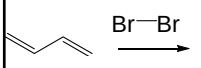


Mechanism

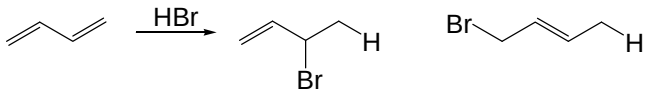






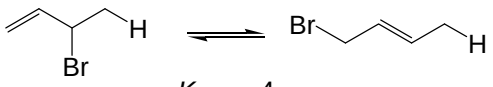


Kinetics versus Thermodynamics

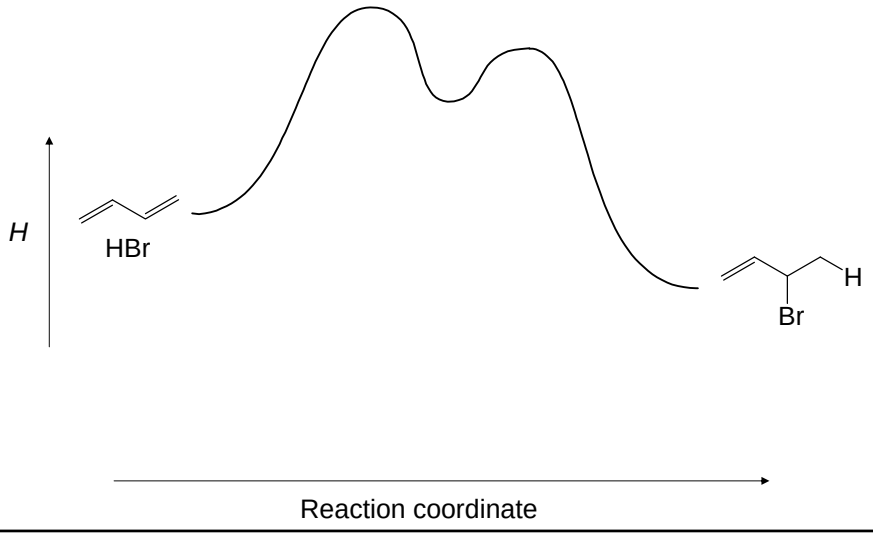


40 °C:	20%	80%
-15 °C:	54%	46%
-80 °C:	80%	20%

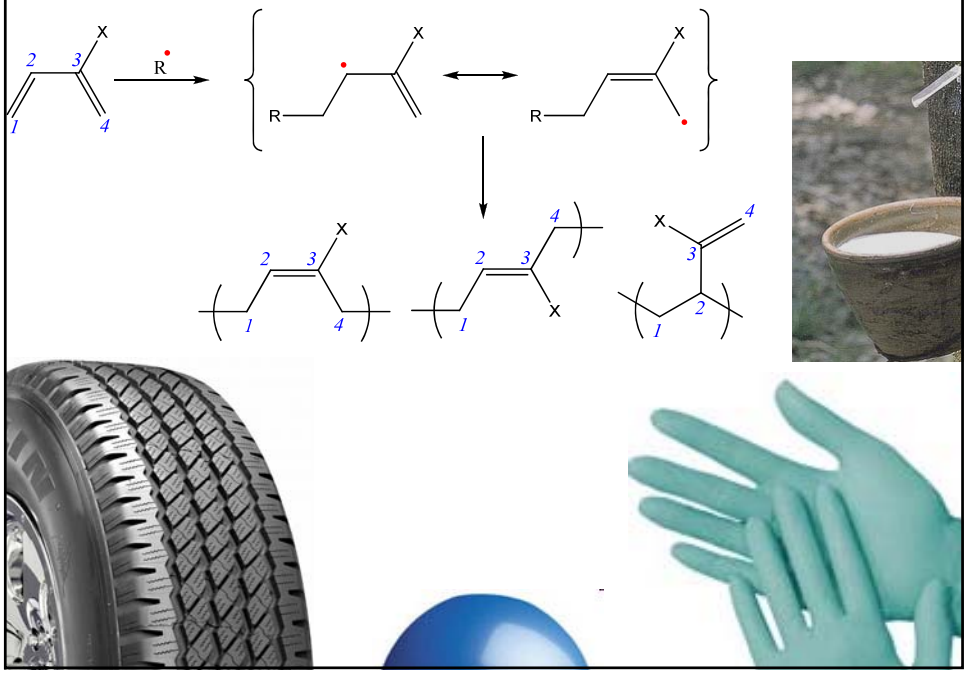
At 40 °C:



$K_{eqm} = 4$



Natural rubber (X=CH_3) and Neoprene (X=Cl)



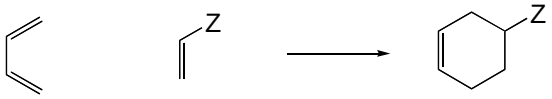
? *Prob:*13.20,23 ?

THE DIELS-ALDER REACTION: A 1,4-CYCLOADDITION REACTION OF DIENES

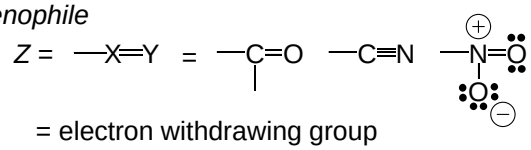
S:13.11
*Prob:*13.24,25, 28,40

1,3-Dienes Undergo Addition Reactions with Electron-poor Alkenes

Mechanism

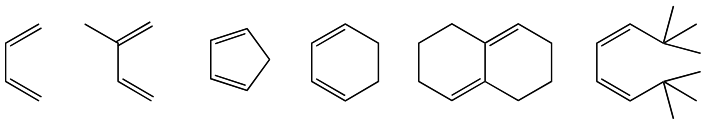


Dienophile



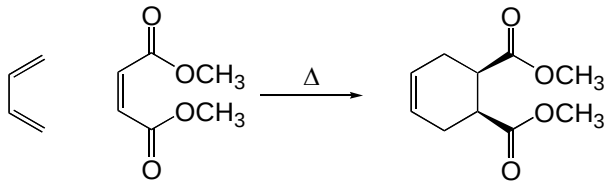
= electron withdrawing group

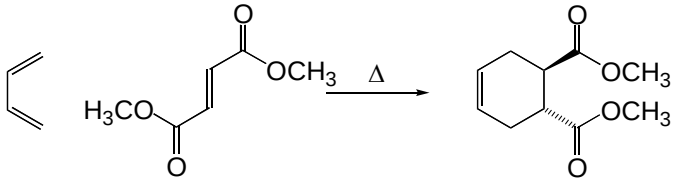
Diene – must be able to adopt an s-cis conformation



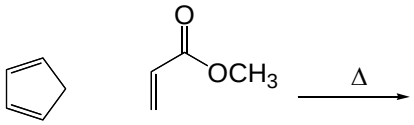
Product ("adduct")

The Reaction is Stereospecific





Addition to Cyclic Dienes Gives Bicyclic Products….



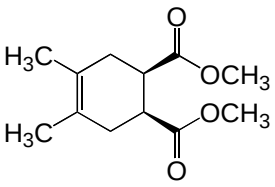
…with predominanty *endo* stereochemistry

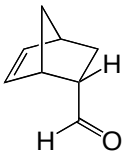
DESIGNING MULTISTEP SYNTHESIS

*Prob:*13.16, 18,19

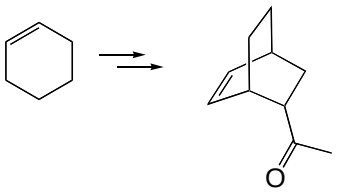
Diels-Alder reactions always provide a six-membered ring containing a pi-bond. To determine which diene and dienophile can be used to make a Diels-Alder aduct, push electrons around to account for a retro-Diels-Alder process.

Problem [Solomons 13.24b,f] – Which diene and dienophile are required to prepare the following compounds?



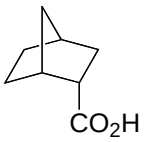


Problem - Provide a synthetic route to achieve the following transformation



?

Problem - Provide a synthetic route to make the following molecule from starting materials with ≤5 carbon atoms.



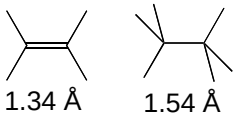
?

? *Prob:*13.16,18,19,24,25,28,40 ?

IT'S "*BENZENE*!": NOT CYCLOHEXATRIENE *S:14.1,3,10*

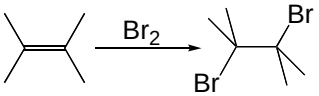
Benzene possesses different properties than alkenes

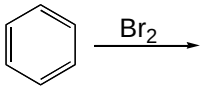
Structure

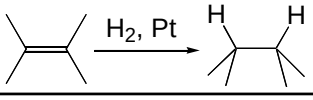


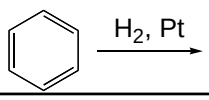
All carbon-carbon bonds: 1.42 Å

Reactivity



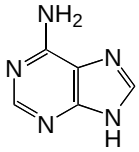




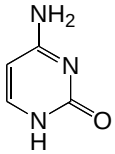


Aromatic Structures in Biology: DNA Bases

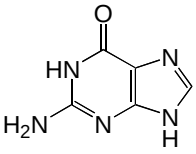
Adenine



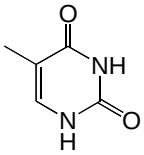
Cytosine

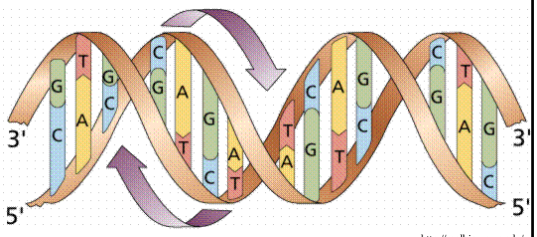


Guanine

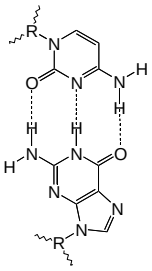


Tyrosine

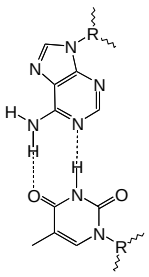




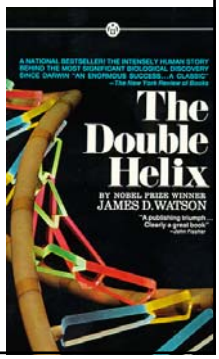
http://molbio.unmc.edu/



C-G



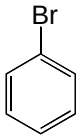
A-T

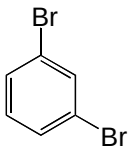


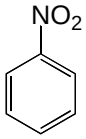
NOMENCLATURE OF BENZENE DERIVATIVES

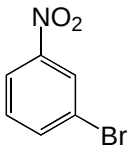
S:14.2
Prob:14.16,17

Substituted Benzene Nomenclature

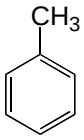




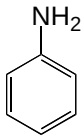




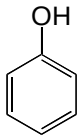
Trivial Base Names

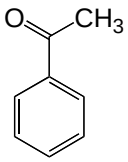


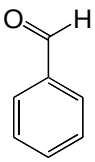
a common solvent



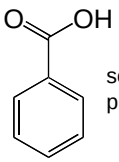
ingredient in dyes



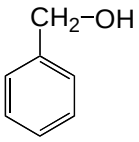


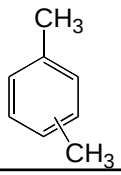


Almond flavor



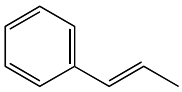
sodium salt: preservative

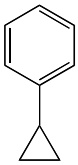




1,2-
1,3-
1,4-

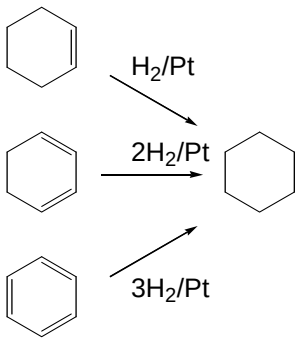
Phenyl Substituent Nomenclature





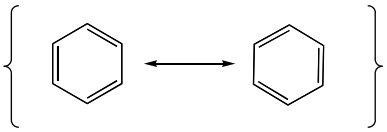
STABILITY OF BENZENE: EXPERIMENTAL OBSERVATIONS AND THEORY

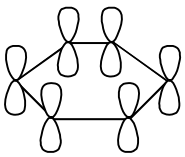
Heats of Hydrogenation as an Indication of Stability

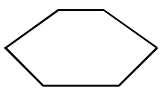


	ΔH (kJ/mol)	
	Predicted	Experimental
	-	-120
	-240	-232
	-360	-208

Resonance

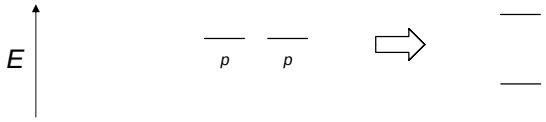




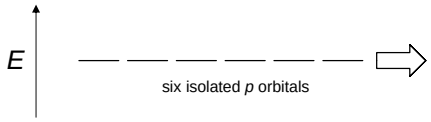


Combination of Atomic Orbitals

Alkenes:

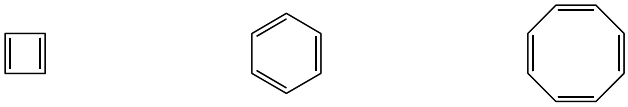


Benzene:



HÜCKEL'S RULE, AROMATIC IONS AND HETEROARENES

S:14.7-9
Prob: 14.21,22



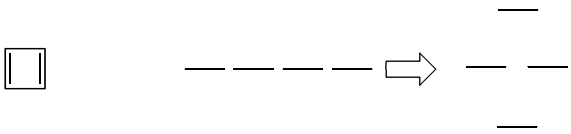
cyclobutadiene	benzene	cyclooctatetraene
very reactive	*different reactivity from alkenes*	*reacts like an alkene* (i.e., addition reactions)
unstable	***especially stable***	***stable***
isolated only at very low temperatures		

Huckel's rule: Compounds with (4*n*+2) π electrons (n=0,1,2…) in a planar cycle of p-orbitals are particularly stable ("aromatic").

Compounds with (4*n*) electrons in a planar cycle of p-orbitals are particularly unstable ("anti-aromatic").

Other compounds are non-aromatic

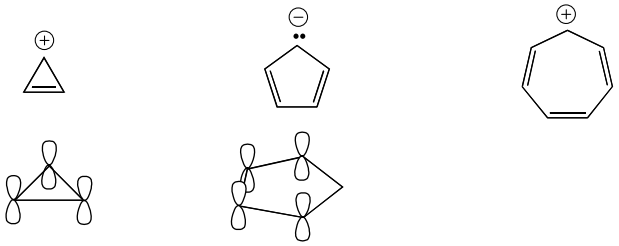
Why is Cyclobutadiene Unstable? The Origin of Anti-Aromaticity



Cyclooctatetraene has 8 π Electrons: Why is it Stable (*i.e.*, not antiaromatic)?

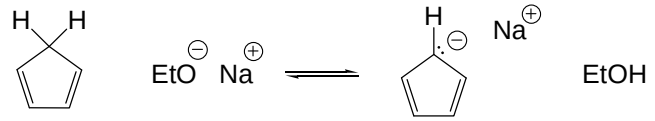
Aromatic and Antiaromatic Ions

*S:*14.8,9
Prob: 14.22



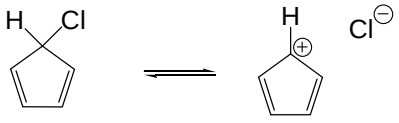
Consequences of Aromaticity on the Course of Reactions

1,3-Cyclopentadiene has a low pK_a relative to other hydrocarbons

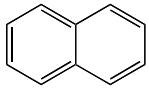


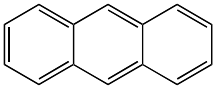
pK_a=16 pK_a=16

5-Chloro-1,3-cyclopentadiene does not undergo dissociation to form a resonance stabilized carbocation

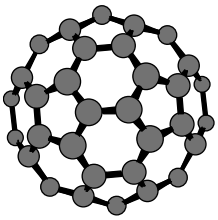


Fused Benzenes



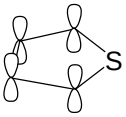


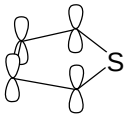
Buckminsterfullerene



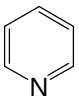
Heteroarenes

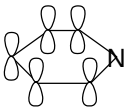
thiophene



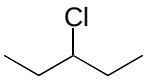


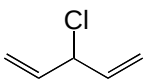
pyridine

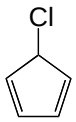




Problem [Solomons 4.22] – Why does 3-chloro-1,4-pentadiene undergo hydrolysis (S_N1 reaction with H_2O) much more rapidly than 3-chloropentane? Why does 5-Chloro-1,3-cyclopentadiene undergo hydrolysis much more slowly?







? *Prob:* 14.16,17,21 ?

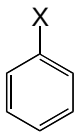
SPECTROSCOPY OF AROMATIC COMPOUNDS

S:14.11;12.12
*Prob: 14.*27-32

^{1}H NMR: Ar-H 6.5-9.0 ppm

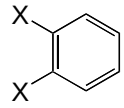
^{13}C NMR: C_{Ar} 135-175 ppm

IR: C_{Ar}-H, 3050 cm^{-1} (680-860 cm^{-1} used to characterize substitution pattern: CHEM2380)

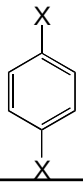


doublet (2H)
+ triplet (2H)
+ triplet (1H)
-or-
multiplet (5 H)
-or-
broad singlet (5H)

[^{13}C: 4 peaks]

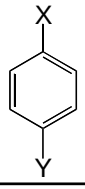


doublet (2H)
doublet (2H)
[^{13}C: peaks]



singlet (4H)

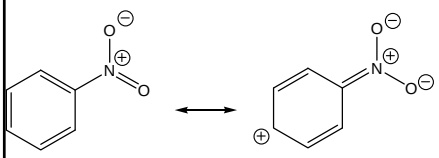
[^{13}C: peaks]



^{1}H NMR Chemical shift of aromatic H's have a large range, 6.5-9.0 ppm. Why?

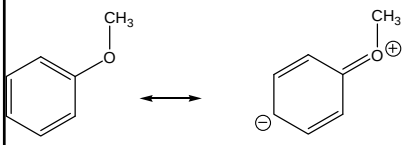
Depends very much on electronic nature of attached group.

Strongly electron withdrawing -<u>deshielding</u>



Typical chemical shift for -NO_2
δ (ppm)
ortho 8.2
meta 7.5
para 7.7

Strongly electron donating - <u>shielding</u>



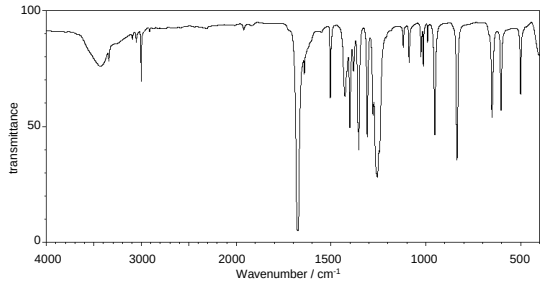
Typical chemical shift for -OCH_3
δ (ppm)
ortho 6.5
meta 7.0
para 6.6

Problem: Draw the other resonance structures that show electron delocalization in the *ortho* positions.

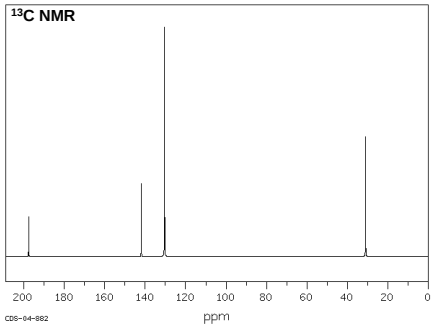
Empirical Formula: C_5H_5O

Mass Spec: M^+ *m/e*= 162

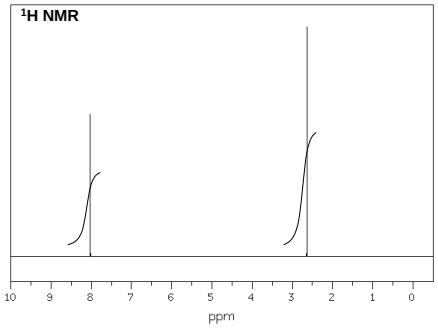
IR



^{13}C NMR



^{1}H NMR



L

REVIEW: CONCEPTS

Resonance

1,2- versus 1,4- electrophilic additions to conjugated dienes

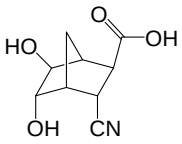
(e.g., $+Br_2$, $+H_2O/H^+$, $+Br_2,H_2O$)

Diels-Alder cycloadditions

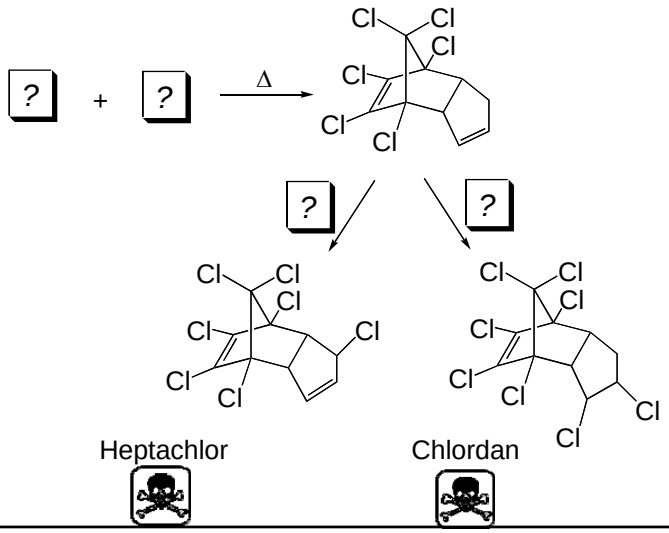
Aromaticity

REVIEW: PROBLEMS

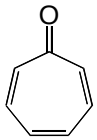
Problem. The following compound was prepared by a graduate student, Sahar Javanmard, as a potential therapeutic agent for treatment of drug abuse. How would you prepare this compound?

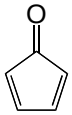


Problem [Solomons 13.31] – What are the substrates and reagents in the following scheme to prepare Heptchlor and Chlordan?

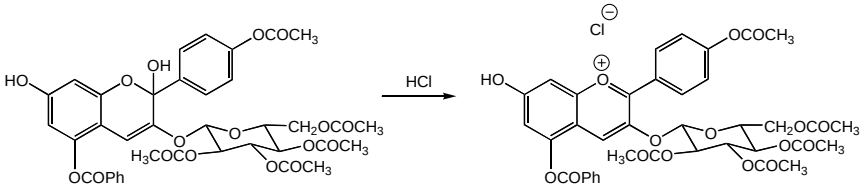


Problem [Solomons 14.21] - Cycloheptatrienone is very stable, whereas cyclopentadienone is unstable an undergoes Diel-Alder reaction with itself. Provide an explanation for these observations and provide the structure of the dimer of cyclopentadienone

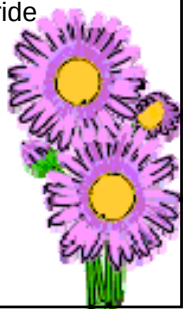




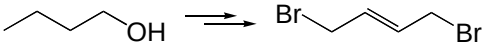
Problem [Solomons Learning Group Problem 14.1] – Callistephin chloride is a red pigment found in the purple-red aster. The last step in its synthesis is shown below. What kind of process is taking place? What is the mechanism? Why is this a reasonable mechanism?



Callistephin chloride



Problem [Solomons 13.19c] - How would you convert 1-butanol into 1,4-dibromo-2-butene?



?

Problem [Solomons Group Learning Problem 13.1] - What are the structures of **A**-**I**?

?

A (C_5H_8)

↓ Br_2, warm (1 equiv.)

F

↓ $NaOCH_3$ (2 equiv.)

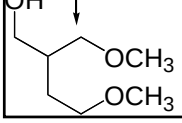
G

↓ HBr (no peroxides)

H

↓ tBuOK

I ($C_7H_{14}O_2$)



B (C_9H_{10})

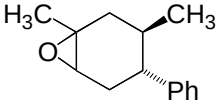
↑ NaOEt, heat

E

↑ NBS, ROOR, heat

D

A (C_5H_8) + **B** (C_9H_{10}) → **C** → CH_3CO_3H



TOPIC 1 ON EXAM 1

Types of Questions

- Predict the product of individual reactions (know the reagents!)
- Write a detailed mechanism for reactions (understand nucleophiles, electrophiles and radicals!)
- Provide IUPAC names for compounds (including common names for substituted benzenes; review rules from CHEM 2311)
- Assess stability of reactive intermediates and compounds (*i.e.*, resonance, aromatic versus anti-aromatic, Hückel's rule)
- Use spectra to identify compounds (use of NMR and IR!)

Do other problems in the book - they are great examples of the types of problems on the exam!

Preparing for Exam 1

- Get up-to-date *NOW!*
- Work as many problems as possible. Do the problems first, then consult the solutions manual
- Work in groups, discuss chemistry, teach and test each other
- Do the "Learning Group Problem" at the end of the chapter