JRG College of Pharmacy

JRG COLLEGE OF PHARMACY

UNIVERSITY SOLVED QUESTION WITH ANSWER

Year	:	**2019-20**
Subject	:	**Ph. Organic Chemistry-II**
Subject Code	:	**BP301T**
Subject In-Charge	:	**Mr. Biswajit Biswal**

Registration No : | | | | | | | | | | |

Total Number of Pages : 01

B.Pharm
BP301T

3rd Semester Regular/Back Examination 2019-20
PHARMACEUTICAL ORGANIC CHEMISTRY II
BRANCH : B.Pharma
Max Marks : 75
Time : 3 Hours
Q.CODE : HRB519

Answer Question No.1 (Part-A) and 02 (Part-B) which are compulsory and any TWO from Part-C.

The figures in the right hand margin indicate marks.

Part- A

Q1 **Only Short Answer Type Questions (Answer All-10)** **(2 x 10)**

a) Write the structure and use of BHC.
b) Define acid value. Mention its significance.
c) Why fats are solid and oils are liquid?
d) What is Kolbe's reaction?
e) Why '$-NO_2$' group acts as meta directing?
f) What happens when benzoic acid is heated with hydrazoic acid?
g) Why amines are basic in nature?
h) Phenol is an acid, but does not react with $NaHCO_3$. Why?
i) Write the structure and uses of saccharin.
j) What is Freund's method?

Part- B

Q2 **Only Focused-Short Answer Type Questions- (Answer Any FIVE out of SEVEN)** **(5 x 7)**

a) Explain Reimer-Tiemann's reaction.
b) Ammonia is stronger base than aniline. Give reason.
c) Write note on hydrogenation and hydrolysis of oil.
d) Briefly explain saponification value and RM value.
e) Discuss the effects of substituents on acidity of Phenol.
f) Discuss the various general methods of preparation of aromatic amines.
g) Write short note on the Kekule structure of benzene.
h) Mention the general method of preparation of cycloalkanes.
i) Explain the effect of substituents on electrophilic substitution reaction of benzene.

Part-C

Only Long Answer Type Questions (Answer Any TWO out of FOUR)

Q3 Discuss the mechanism of nitration reaction and Friedelcraft's acylation reaction of benzene. **(10)**

Q4 Write the important steps in Haworth's synthesis of naphthalene. Describe its important chemical reactions. **(10)**

Q5 Explain Bayer's strain theory. Mention its limitations. **(10)**

Q6 Write any five methods of preparation and five chemical reactions of phenol. **(10)**

3rd semester (2019-2020)

B. Pharm

Pharmaceutical organic chemistry

Q. 1. (a) Write the structure & use of BHC.

ANS →

BHC → Benzene Hexachloride ($C_6H_6Cl_6$).

Structure:- BHC consists of a cyclohexane ring with each carbon atom bonded to one hydrogen atom & one chlorine atom, totalling six hydrogens & six chlorines.

→ The structure is Not aromatic as it lacks a delocalized Pi-electron system.

Uses:- used as an agricultural insecticide.

→ used for seed treatment in agriculture.

(b) Define acid value. Mention its significance.

ANS → Acid value is the Number of Milligrams of KOH Needed to Neutralise the free fatty acids in 1g of fat or oil.

→ It's significance lies in indicating oil quality, as a high acid value signifies rancidity, decomposition, poor storage.

(c) Why fats are solid oils are liquid?

ANS → Fats are solid at room temp. due to their Saturated fatty acid content.

Straight chain → pack tightly → High Melting point → solids.

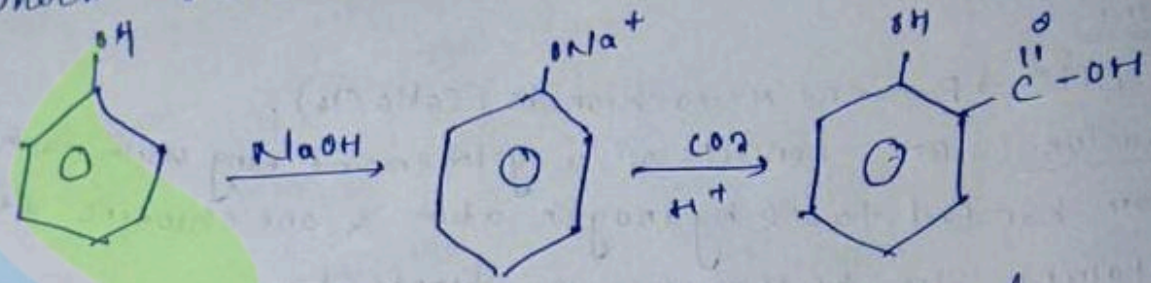
While oils are unsaturated fatty acids. (c=c double bonds).

loose packing → Low melting point → liquids.

q. What is Kolbe reaction?

Ans →

phenol react with NaOH to form sodium phenoxide. which react with CO_2 to form Salicylic acid.



Phenol · Sodium phenoxide Salicylic acid

Q. Why '$-NO_2$' group act as Meta directing?

→ $-NO_2$ is strongly electron withdrawing (-M, I effect).

→ It deactivates ortho & para positions due to instability of Carbocation intermediate.

→ Hence, electrophile attacks meta position.

(F) What happens when benzoic acid is heated with hydrazoic acid?

Ans Benzoic acid + Hydrazoic acid (HN_3)
→ phenyl isocyanate (via Curtius rearrangement).
- on hydrolysis → gives aniline.

(g) Why amines are basic in nature?

Ans) Amines have a lone pair of electrons on nitrogen → Can accept protons (Bronsted base).
- Greater electron density → higher basicity compared to ammonia (in aliphatic amines).

(h) phenol is an acid, but does not react with $NaHCO_3$ Why?

Ans) phenol ($pKa \sim 10$) is weaker acid than carbonic acid ($pKa \sim 6.4$).
- Therefore, phenol cannot liberate CO_2 from $NaHCO_3$ solution.

(i) Write the structure and uses of Saccharin?

Ans) Structure:
- Use: Artificial non-nutritive sweetner (300 × Sweeter than sucrose), used by diabetics.

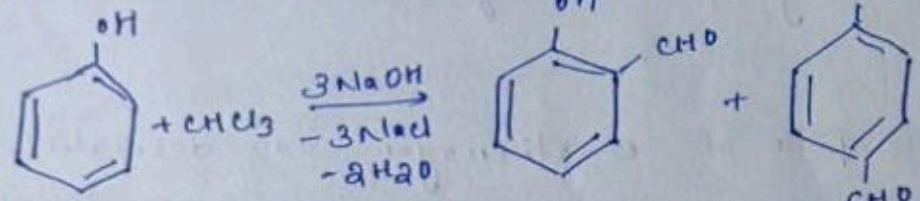
(j) What is freund's Method?

Ans) freund's Method: Industrial Method of preparing benzaldehyde.
- Toluene is oxidized by chromyl chloride (CrO_2Cl_2) → Benzaldehyde.

PART-B

Q.2. (a) Explain Reimer-Tiemann's reactions.

ANS: When phenols react with chloroform & NaOH solution it gives Hydroxyl aldehydes. this reaction is known as Reimer-Tiemann reaction.



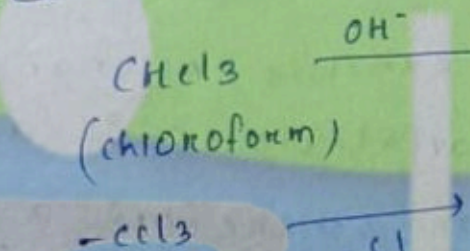
Phenol

Salicyldehyde

4-Hydroxy benzaldehyde.

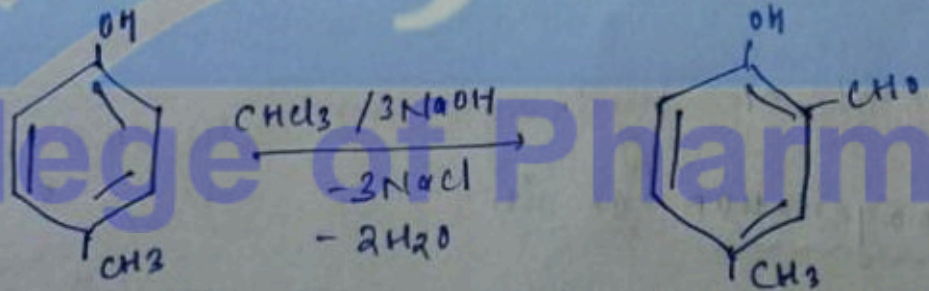
Mechanism

It involves the electrophilic substitution reaction & the electrophile in this reaction is dichlorocarbene ($:CCl_2$) which is produced by the α-elimination reaⁿ between chloroform & alkali.



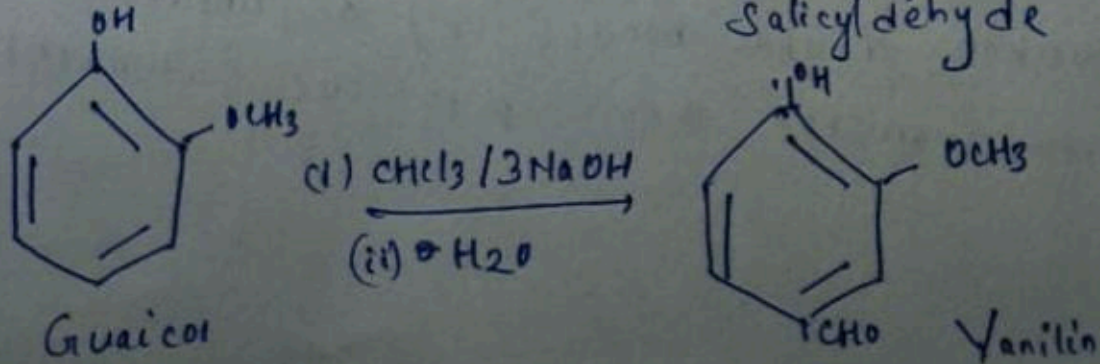
Dichlorocarbene.

Example



P-cresol

5-methyl Salicyldehyde



Guaicol

Vanilin

(b) Ammonia is stronger base than aniline. Give reason.

ANS→

Ammonia → It has alone pair of electrons at Nitrogen that is freely available for protonation.

Aniline → NH_2 group is directly attached to a benzene ring.

→ The lone pair of Nitrogen can delocalize into the aromatic ring through resonance, forming a conjugated structure.

→ Ammonia is a stronger base than aniline due to resonance effects in aniline.

→ in aniline, the lone pair of ~~electron~~ Nitrogen is delocalized into the aromatic ring, reducing its availability to accept protone & thus its basicity.

→ Ammonia doesnot exhibit resonance, leaving the lone pair fully available. So it acts as a better proton acceptor & therefore a Stronger base.

(c) White Note on Hydrogenation & Hydrolysis of oil.

ANS→ Hydrogenation of oil:-

→ It is the addition of Hydrogen across the carbon-carbon double bonds (C=C) of unsaturated triglycerides to convert them into More Saturated products.

Application

→ It convert liquid vegetable oils into solid or semi-solid fats.

→ It improve melting point.

Reactions

- Hydrogeneous catalysts such as Ni, Pd/C ore pt.

Mechanism

Adsorption of H_2 & alkene (C=C) on the catalyst surface → stepwise transfer of H atoms to double bond.

Hydrolysis of oil:-

→ Hydrolysis of triglycerides is clevage of ester bonds to yield glycerol & fatty acids.

Types

- Acidic hydrolysis: Heating oil with water & mineral acid.
- Alkaline Hydrolysis: Reaction with strong base producing Glycerol & soap.

Mechanism

The water molecules break the ester bonds that link the fatty acids to glycerol in a triglyceride molecule.

Uses

→ To obtain free fatty acid for industry.

→ classical soap manufacture, KOH gives softer soap.

(d) Briefly Explain saponification value & RM value.

ANS→ **saponification value (SV)** = Mg of KOH required to saponify 1g of fat/oil. it measures the total amount of free & bound acids.

Interpretation:-

High SV:- More KOH required per g → indicates shorter chain fatty acids.

Low SV:- Indicates Longer chain fatty acids.

Determination:-

→ Heat oil with excess alcoholic KOH to saponify.

→ Back-titrate the remaining KOH with standard HCl.

→ SV calculated from amount of KOH consumed.

&

RM value:-

Reichert - Meissl Value.

→ RM value measures the amount of short-chain volatile water-soluble fatty acids present in fat. it is defined as the Millilitres of 0.1 N NaOH required to neutralise Volatile fatty acids distilled from 5g of fat after saponification & acidification.

→ RM value is particularly important for identifying & assessing the quality of animal fats. which are rich in volatile acids.

Interpretation! -

High RM value indicates presence of short-chain fatty acids - characteristics of butter & milk fat.

→ Vegetable oils & fats with long chains have low RM values.

Applications! -

Differentiate butter from margarine, adulteration, tests, characterization of dairy fats.

(e) Discuss the effects of substituent on acidity of phenol.

ANS → The acidity of phenol is affected by the presence & Nature of substituents on its aromatic ring.

Electron - withdrawing groups such as nitro, cyano or halogens increases the acidity of phenol.

→ The stronger the EWG & closer its position to the -OH group, the greater the increase in acidity.

→ conversing, electron - donating groups like methyl, Methoxy or amino destabilise the phenoxide ion by increasing electron density, thereby decreasing phenol's acidity.

(1.) Electron withdrawing substituents:-

→ increase acidity because they stabilise the Negative charge on oxygen by inductive withdrawl.

(2) Electron donating substituents:-

→ Decrease acidity because they donate electron density to ring / oxygen & destabilise phenoxide anion.

(3.) Resonance donors:-

→ Donate electron density by resonance into the ring. which can delocalise Negative charge.

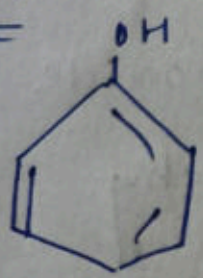
(4.) position dependence:-

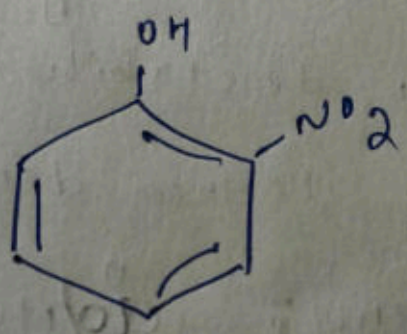
→ ortho & para substituents can exert resonance effects & inductive effects.

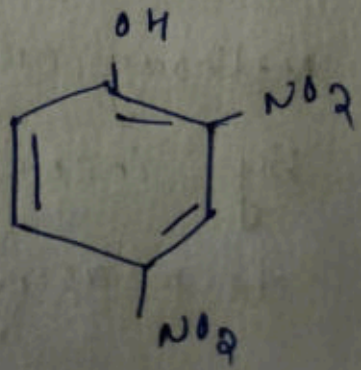
(5.) Halogen:-

→ Halogens are electron withdrawing by inductive effect but electron donating by resonance.

Ex:-







(F) Discuss the various methods of preparation

Ans:

1. Reduction of nitro Compound.

- It is the most common Methods.

Reaction:-

$$Ar - NO_2 \xrightarrow[Sn/Hcl/Fe/Zn]{Reduction} Ar-NH_2.$$

2. Reduction of cyanides.

It gives primary amines which an extra $-CH_2$ group.

reaction:-

$$Ar-CN \xrightarrow[H_2/Ni \text{ or } LiAlH_4]{Reduction} Ar-CH_2-NH_2$$

3. Reduction of Amides.

Reaction:-

$$Ar-CONH_2 \xrightarrow[LiAlH_4]{Reduction} Ar-CH_2-NH_2$$

→ It is used for Aromatic Primary amines.

4. from Haloarenes:

reaction:-

$$Ar-X + 2NH_3 \xrightarrow[Cu_2O]{\Delta} Ar-NH_2 + HX$$

5. from phenol:

Phenol can be converted into Aniline using ammonia under high temp. & pressure.

reaction:-

$$C_6H_5OH + NH_3 \xrightarrow[ZnCl_2]{\Delta} C_6H_5NH_2 + H_2O$$

6. Hoffmann Bromamide degradation.

Reaction:-

$$Ar-CONH_2 \xrightarrow{Br_2/NaOH} Ar-NH_2$$

7. Sandmayer reaction:-

→ Aromatic diazonium Salts can be converted into amino derivatives.

$$C_6H_5-N_2^+Cl \xrightarrow[H_3PO_2/SnCl_2]{} C_6H_5-NH_2$$

9. Write short Note on Kekule Structure of Benzene.

ANS→

The German chemist August Kekule (1865) proposed the first satisfactory structure of Benzene According to his history.

1. Hexagonal Ring:- Benzene Consists of a ring of six Carbon atoms arranged in a regular hexagon.

2. Alternating double bond:- The six Carbons are linked by alternating Single & double bond.

3. Valency Satisfication:- Each carbon atom is bonded to one Hydrogen atom.

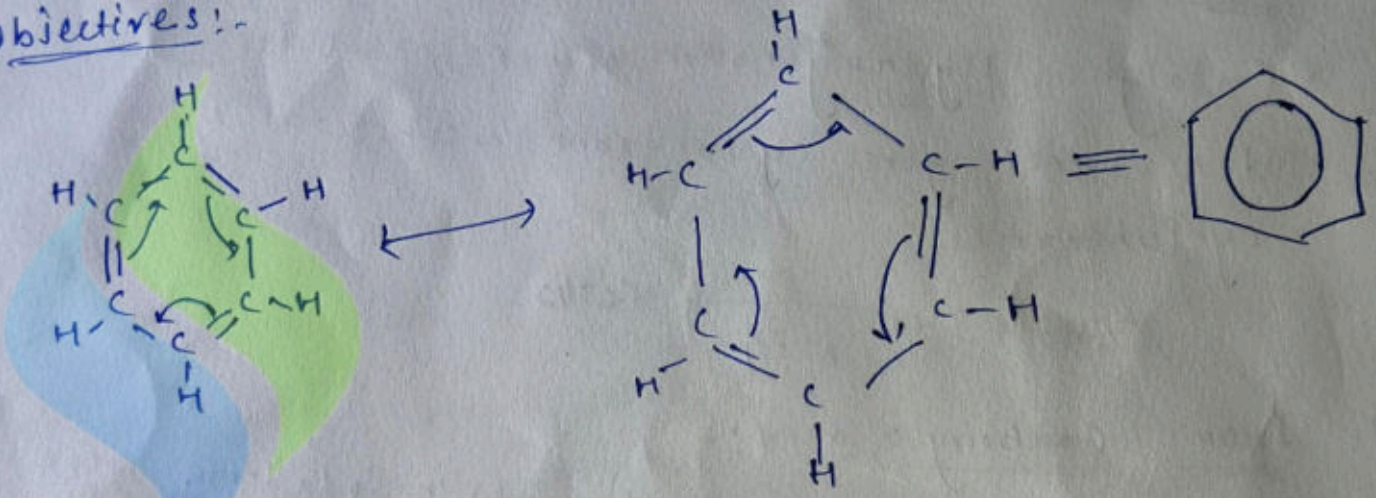
4. Resonance Idea:- Kekule suggested that the double bonds are Not Fixed.

Limitation :-

→ Kekule structure predicts the presence of three double bonds. So benzene should behave like an alkene.

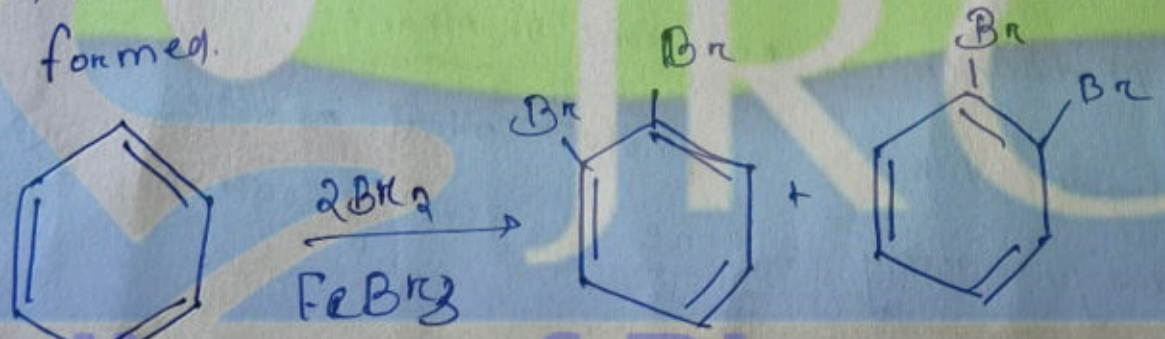
→ All Six-carbon - carbon bonds on benzene are of equal length, intermediate between a single & double bond.

Objectives :-



Example

Two isomers of dibromobenzene should be formed.



(A) (B)

(h) Mention the general method of prep^n of cycloAlkanes

ANS → cycloalkane are Saturated cyclic Hydrocarbons (C_nH_{2n}).

1. from Dihalogen Derivatives :-

Dihaloalkanes react with Sodium metal in dry ether to form cycloalkanes.

$X-(CH_2)_n-X + 2Na \xrightarrow{\text{ether}} (CH_2)_n + 2NaX$.

2. By Dieckmann's Condensation:-
Diesters with suitable chain length undergoes intramolecular claisen condensation to form cyclic β-keto esters.

3. By reduction of Aromatic Compounds:-
→ Catalytic Hydrogenation of benzene & its derivatives gives cyclohexane & substituted cyclohexanes.

$C_6H_6 + 3H_2 \xrightarrow[Ni/Pt]{} C_6H_{12}$.

4. From Carboxylic acid:-
Dicarboxylic acids on heating with Soda lime give cycloalkanes.

5. By photochemical reactions of Alkanes:-
Higher Alkanes on photochemical reactions may undergo ring closure to give cycloalkanes.

Example

$RCH=CHR + H_2 \xrightarrow{\text{Catalyst}} RCH_2CH_2R$

$RX \xrightarrow{\text{reducing agent}} RH$

(i) Explain the effect of substituents on electrophilic substitution of benzene.

ANS →

PART - C

8.3. Discuss the Mechanism of Nitration reaction & friedal crafts reaction of benzene.

ANS → Nitration of benzene.

Benzene undergoes electrophilic substitution reaction with the Nitronium ion (NO_2^+) Generated From the mixture of conc. Nitric acid & H_2SO_4.

→ H_2SO_4 protonates HNO_3 to form Nitroniumion.

→ The NO_2^+ ion attacks the π electron cloud of benzene to form a sigma complex.

→ Deprotonation of the sigma complex restores Aromaticity, yielding nitrobenzene.

Mechanism

1. formation of electrophile:-

$$HNO_3 + H_2SO_4 \rightarrow NO_2^+ + HSO_4^- + H_2O$$

2. Attack on Benzene ring:-

THE π electron of benzene attack NO_2^+.

3. Deprotonation:-

$$C_6H_6 + HNO_3 \xrightarrow{H_2SO_4} C_6H_5NO_2 + H_2O$$

Friedal Craft reaction:

Friedal-Crafts Alkylation:-

1. Generation of Electrophile - A Lewis acid catalyst reacts with an alkyl halide to form a carbocation.

$$R\text{-}Cl + AlCl_3 \longrightarrow R^+ + AlC$$

2. Attack on Benzene - Benzene attacks the carbocation, forming an arenium ion.

3. Rearrangement - carbocation rearrangement can occur before it attacks the benzene. Sometimes leading to different alkylated products.

4. Restoration of aromaticity - Loss of proton regenerates the aromatic ring.

Friedal Craft Acylation:-

1. Generation of electrophile - An acyl chloride reacts with $AlCl_3$, generating a resonance-stabilized acylium ion (RCO^+).

2. No rearrangement - Due to resonance stabilisation, carbocation rearrangement does not occur in acylation.

3. Regeneration - The $AlCl_3$ catalyst is regenerated at the end of the reaction.

4. Restoration - The Acylium ion attacks benzene yielding an acylarenium ion, giving the acyl ketone as the product.

Q.5. Explain Bayer's strain theory. Mention its limitation.

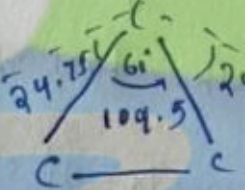
Ans → Bayer's strain theory, proposed by Adolf Von Baeyer in 1885, explains the stability of cyclic compounds based on the deviation of bond angles from the ideal tetrahedral angle of 109°28 found in sp^3 hybridised Carbon atoms.

→ planner rings are All Available. Tetrahedral angles that deviate from the Norm produce cycloalkanes.

→ The large ring systems donot exists due to Negative strain.

Cyclopropane:-

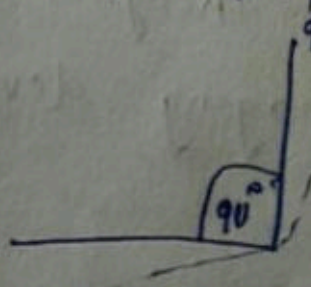
An equilateral triangle is formed by three carbon atoms found in cyclopropane. C-C-C bonds in cyclopropane have a 60° Angle.



$$\frac{109.5^\circ - 60^\circ}{2} = 24.75$$

Cyclobutane:-

4 carbon Atoms are arranged in a square: they occupy the corners. This means C-C-C bonds have an angle of 90°. The angle strain on each bond is $\frac{1}{2}(109^\circ.28 - 90^\circ) = 9^\circ 44'$.



Derivation:-

Sl No.	Name	Angle strain
1	cyclo-propane	24°44'
2	" butane	9°44'
3	" pentane	0°44'
4	" Hexane	5°16'
5	" heptane	9°33'
6	" octane	12°46

Limitation

1. planner Assumption:- Bayer Assumed that all cyclic molecules are planner, ~~Actually~~ small rings like cyclopropane or Larger rings like cyclohexane.
2. It doesnot account for the fact that many people who experience similar levels of strain do not turn to crime.
3. It mainly emphasizes crimes connected to Material Success, failing to adequetly explain White collar crimes.
4. It gives valuable insights into societal pressures & their role in encouraging deviance.

Q6. Write any five methods of preparation & reactions of phenol.

Ans: Five Methods of Preparation:-

1. Cumene Process (Hock process):-

Cumene (Isopropylbenzene) is oxidised by air to form cumene hydroperoxide, which on acid treatment decomposes to yield phenol & acetone as a byproduct. This is the main industrial method due to its efficiency & valuable byproduct form.

2. Benzene sulfonic acid:-

Benzene is first Converted into benzene sulfonic acid, which upon fusion with Molten sodium Hydroxide produces sodium phenoxide.

3. from Chlorobenzene:-

Chlorobenzene is fused with NaOH at high temp. & high pressure forming Sodium phenoxide.

4. from Diazonium Salts:-

Aniline is converted into benzene diazonium chloride by treatment with sodium Nitrite & HCl at low temp.

from Aniline:-

Aniline undergoes diazotization to form diazonium salts which upon hydrolysis yield phenol.

Five chemical reactions of phe...

1. Reaction of sodium!-

Phenol reacts with Sodium Metal to form sodium phenomide & Hydrogen gas.

$2C_6H_5OH + 2Na \rightarrow 2C_6H_5ONa$

2. Reaction with Bromine!-

Phenol reacts ~~with~~ readily with bromine water to give 2,4,6 tribromophenol, a white precipitate.

$C_6H_5OH + 3Br_2 \rightarrow C_6H_2Br_3OH.$

3. Reaction with Nitric acid!-

Phenol reacts with dil. HNO_3 to give a mixture of ortho- & para position.

$C_6H_5OH + HNO_3 \rightarrow$ o- & p-N.

4. Esterification!-

Phenol reacts with Acyl chloride or acid Anhydrides to form Ester.

$C_6H_5OH + CH_3COCl \rightarrow C_6H_5O$

5. React^n with NaOH!-

Phenol reacts with NaOH to form phenolate ion.

$C_6H_5OH + NaOH \rightarrow C_6H_5ONa.$