KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)

COIMBATORE-21

DEPARTMENT OF CHEMISTRY

B.Sc Chemistry

Semester-III

16CHU303 ORGANIC CHEMISTRY III 4H 4C

(Nitrogen Containing Functional Groups, Heterocyclic chemistry and natural products)

Instruction Hours/week:L: 4 T:0 P:0 Marks: Internal: 40 External: 60 Total:100

Scope

The course deals with the preparation and properties of nitrogen containing functional groups, alkaloids, heterocyclic compounds and terpenes.

Programme Outcome

1. To provide the preparation and properties of amines, diazonium salts and polynuclear hydrocarbons.
2. To provide knowledge about the preparation and reactions of alkaloids along with the mechanism
3. To provide the preparation and reactions of nitrogen containing hetrocyclic compounds.
4. To provide a knowledge about the terpenes.

Programme Learning outcome

1. The student has a firm foundations in the fundamentals and application of Nitrogen containing functional groups, heterocyclic compounds and natural products in particular about alkaloids and terpenes.
2. They are able to identify and solve chemical problems in the hetecocyclic chemistry and obtained the skill to further learning of organic chemistry.
3. They are able to develop the ability to effectively communicate scientific information

UNIT I

Nitrogen Containing Functional Groups

Preparation and important reactions of nitro compounds, nitriles and isonitriles.

Amines: Preparation and properties: Effect of substituent and solvent on basicity; Gabriel phthalimide synthesis, Carbylamine reaction, Mannich reaction, Hoffmann's exhaustive methylation, Hofmann-elimination reaction; Distinction between 1°, 2° and 3° amines with Hinsberg reagent and nitrous acid.

UNIT II

Diazonium Salts: Preparation and their synthetic applications.

Polynuclear Hydrocarbons

Aromaticity of polynuclear hydrocarbons, structure elucidation of naphthalene; Preparation and properties of naphthalene, phenanthrene and anthracene.

UNIT III

Heterocyclic Compounds

Classification and nomenclature, Structure, aromaticity in 5-numbered and 6-membered rings containing one heteroatom; Synthesis, reactions and mechanism of substitution reactions of: Furan, Pyrrole (Paal-Knorr synthesis, Knorr pyrrole synthesis, Hantzsch synthesis), Thiophene, Pyridine (Hantzsch synthesis),

UNIT IV

Indole(Fischer indole synthesis and Madelung synthesis), Quinoline and isoquinoline, (Skraup synthesis, Friedlander's synthesis, Knorr quinoline synthesis, Doebner- Miller synthesis, Bischler-Napieralski reaction, Pictet-Spengler reaction, Pomeranz-Fritsch reaction)

UNIT V

Alkaloids

Natural occurrence, General structural features, Isolation and their physiological action, Hoffmann's exhaustive methylation, Emde's modification; Structure elucidation and synthesis of Nicotine. Medicinal importance of Nicotine, Hygrine, Quinine, Morphine, Cocaine, and Reserpine.

Terpenes

Occurrence, classification, isoprene rule; Elucidation of stucture and synthesis of Citral.

Suggested Readings

Text Books:

1. Morrison, R. T. & Boyd, R. N.(1992). *Organic Chemistry*. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).
2. Finar, I. L. (2013). *Organic Chemistry*. Volume 1. Edition V, Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).

Reference Books

1. Finar, I. L.(2002). *Organic Chemistry*: *Stereochemistry and the Chemistry of Natural Products*. Volume 2. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).
2. Acheson, R.M. (1976). *Introduction to the Chemistry of Heterocyclic compounds*. John Welly& Sons.
3. Graham Solomons, T.W.(2012). *Organic Chemistry*. John Wiley & Sons, Inc.

4. Kalsi, P. S.(2009). *Textbook of Organic Chemistry*. 1st Ed. New Age International (P) Ltd. Pub.
5. Clayden, J., Greeves, N., Warren, S. & Wothers, P.(2012). *Organic Chemistry*. Oxford University Press.
6. Singh, J.; Ali, S.M. & Singh, J. (2010). *Natural Product Chemistry*. PrajatiParakashan.

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COIMBATORE-21

DEPARTMENT OF CHEMISTRY

LECTURE PLAN

Name of the Staff	:	**Dr. S.RAVI**
Department	:	Chemistry
Title of the Paper	:	**ORGANIC CHEMISTRY-III (Nitrogen Containing Functional Groups, Heterocyclic chemistry and natural products)**
Paper Code	:	**16CHU303**
Class	:	II-B. Sc-Chemistry
Year and Semester	:	II-Year (2017) and III-Semester
Total Hours	:	61 Hours

UNIT-I **HOURS REQUIRED-12**

S.No.	Lecture Hour	Topics to be Covered	Support Materials
1.	1	Introduction to Nitrogen containing functional groups	T2: 711, 719; T1: 702;
2	1	Preparation and important reactions of nitro compounds, nitriles and isonitriles	T2: 711, 719; T1: 702; T3:355,357
3	1	Preparation and important reactions of nitriles and isonitriles	T1: 702; T3:355,357
4	1	*Amines:* Preparation	T2: 678, T3:367
5	1	*Amines:* properties	T2: 678, T3:367
6	1	Effect of substituent and solvent on basicity	T2:679
7	1	Gabriel phthalimide synthesis, Carbylamine reaction	T1:1012, T3:193, 370
8	1	Mannich reaction, Hoffmann's exhaustive methylation	T1:724,T3:375
9	1	Hofmann-elimination reaction	T3:379-381, T1:704
10	1	Distinction between 1°, 2° and 3° amines	T1:746, 734
11	1	Distinction between 1°, 2° and 3° amines with Hinsberg reagent and nitrous acid	T1:746, 734
12	1	Recapitulation and discussion of important questions	

Text books:

T1. Morrison, R. N. & Boyd, R. N. (1992). *Organic Chemistry*. New Delhi: Dorling Kindersley Pvt. Ltd. (Pearson Education).

T2. Arun Bahl (2005). Advanced Organic Chemistry., S.Chand & Company Ltd., Ram Nagar New Delhi.

T3. Finar, I. L. (2013). *Organic Chemistry*. Volume 1. Edition V, Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).

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UNIT-II

HOURS REQUIRED -11

S.No.	Lecture Hour	Topics to be Covered	Support Materials
1.	1	Diazonium Salts: Preparation	T1: 736-737, T3: 826
2.	1	Diazonium Salts: synthetic applications	T3: 781-783
3.	1	Diazonium Salts: synthetic applications	T3: 781-783
4	1	Polynuclear hydrocarbons	T3: 781-783
5.	1	Aromaticity of polynuclear hydrocarbons	T3: 781-783
6.	1	structure elucidation of naphthalene	T3: 793
7.	1	structure elucidation of naphthalene	T3: 793
8.	1	Preparation and properties of naphthalene	T3: 793
9	1	Preparation and properties of Phenanthrene	T3: 817
10	1	Preparation and properties of Anthracene	T3: 811, 817
11	1	Recapitulation and discussion of important questions	

Text books:

T1. Morrison, R. N. & Boyd, R. N. (1992). *Organic Chemistry*. New Delhi: Dorling Kindersley Pvt. Ltd. (Pearson Education).

T3. Finar, I. L. (2013). *Organic Chemistry*. Volume 1. Edition V, Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).

UNIT-III

HOURS REQUIRED -12

S.No.	Lecture Hour	Topics to be Covered	Support Materials
1.	1	Heterocyclic Compounds Introduction	T3:826
2	1	Heterocyclic Compounds: Classification	T3:826
3	1	Heterocyclic Compounds: nomenclature	T3:826
4	1	Structure, aromaticity in 5-numbered and 6-membered rings containing one heteroatom	T3:828, 848
5	1	Synthesis, reactions and mechanism of substitution reactions of: Furan	T3:828, 837
6	1	Synthesis, reactions and mechanism of substitution reactions of:Pyrrole	T3:828, 837
7	1	Paal-Knorr synthesis,	T3:837
8	1	Knorr pyrrole synthesis	T3:837
9	1	Hantzsch synthesis	T3:838
10	1	Synthesis of Thiophene	T3:834
11	1	Synthesis of Pyridine- Hantzsch synthesis	T3:838
12	1	Recapitulation and discussion of important questions.	

Text books:

T3. Finar, I. L. (2013). Organic Chemistry. Volume 1. Edition V, Dorling Kindersley (India) Ltd. (Pearson Education).

UNIT-IV

HOURS REQUIRED -11

S.No.	Lecture Hour	Topics to be Covered	Support Materials
1.	1	Indole - Fischer indole synthesis	T2:791
2.		Indole- Madelung synthesis	T2:791
3.	1	Quinoline – synthesis, Skraup synthesis	T2:785, 788
4.	-	Isoquinoline synthesis	T2:785, 788
5.	1	Friedlander's synthesis	T4: 738, 877
6.	1	Knorr quinoline synthesis	T2:786-788, T4:900
7.	1	Doebner- Miller synthesis	T4:900-901; 761,780
8.	1	Bischler-Napieralski reaction,	T4:900-901; 761,780
9	1	Pictet-Spengler reaction	T2: 789-792
10	1	Pomeranz-Fritsch reaction	789-791
11	1	Recapitulation and discussion of important questions	

Text books:

T2. Arun Bahl (2005). Advanced Organic Chemistry., S.Chand & Company Ltd., Ram Nagar New Delhi.

T4: Finar, I. L.(2002). *Organic Chemistry*: *Stereochemistry and the Chemistry of Natural Products*. Volume 2. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).

UNIT-V

HOURS REQUIRED -15

S.No.	Lecture Hour	Topics to be Covered	Support Materials
1.	1	General Introduction to Natural products	T4:370, 710
2.	1	Alkaloids: Natural occurrence, General structural features	T4:710
3.	1	Alkaloids: Isolation and their physiological action	T4:710
4.	1	Hoffmann's exhaustive methylation	T4:711-712
5	1	Emde's modification	T4:713
6	1	Structure elucidation of Nicotine.	T4:731
7	1	synthesis of Nicotine	T4: 731-733
8	1	Medicinal importance of Nicotine, Hygrine, Quinine,	T4: 722, 752, 762
9	1	Medicinal importance of Morphine, Cocaine, and Reserpine.	
10	1	**Terpenes** Occurrence, classification, isoprene rule;	T4: 368-369, 370
11	1	Elucidation of stucture and synthesis of Citral.	T4: 368-369, 370
12	1	Recapitulation and discussion of important questions.	
13	1	Discussion of previous ESE question papers.	
14	1	Discussion of previous ESE question papers.	
15	1	Discussion of previous ESE question papers.	

Text books:

T4: Finar, I. L.(2013). *Organic Chemistry*: *Stereochemistry and the Chemistry of Natural Products*. Volume 2. Edition V, Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).

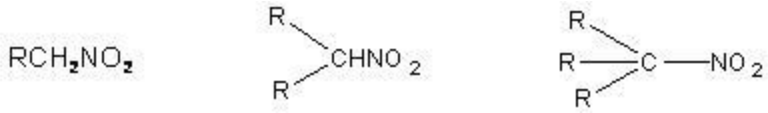
UNIT I
Nitrogen Containing Functional Groups

Preparation and important reactions of nitro compounds, nitriles and isonitriles. *Amines:* Preparation and properties: Effect of substituent and solvent on basicity; Gabriel phthalimide synthesis, Carbylamine reaction, Mannich reaction, Hoffmann's exhaustive methylation, Hofmann-elimination reaction; Distinction between 1°, 2° and 3° amines with Hinsberg reagent and nitrous acid.

UNIT I

Nitro compounds

Nitro alkanes are derivatives of alkanes. They are isomeric to nitrites (esters) classified as primary, secondary and tertiary depending on the nature of carbon atom to which nitro group is linked.



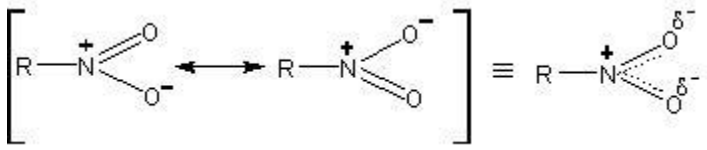
Primary nitro alkane Secondary Nitro alkane Tertiary nitro alkane

—NO_2 group is an ambident group. If it attacks through nitrogen. It is called nitro and if it attacks through oxygen atom, it is called nitrite. Hence nitrites and nitro compounds are isomers.

What are ambident nucleophiles?

Nucleophiles which can attack from two sites such as CN^-, NO_2^- are called ambident nucleophiles

Evidences show that nitrogen is attached to one of the oxygen atoms by a double bond and to the other by a dative bond. The resonance hybrid is shown as under which confirms the spectroscopic evidence that both nitrogen – oxygen bonds have same bond length.



Resonating forms Hyrbid structure

Out of three hybrid orbitals of nitrogen one overlaps with alkyl group and two with oxygens while the unhybridized p orbital of N – atom containing a pair of electrons and lying perpendicular to the plane of hybrid orbitals overlaps sideway with half filled 2 p – orbitals of two oxygen atoms. This forms π-bond above and below the plane of molecule.

Preparation of Nitro Compounds

(i) From alkyl halides:

Alkyl halides react with silver nitrite in ethanolic solution to give nitro compounds. Alkyl nitrite is formed in minor quantity. This reaction is used to prepare 1^o nitro compounds primarily while $2^o$and 3^o halides give major proportion of alkenes due to β – elimination. Contrary to this alkali nitrites give alkyl nitrites as major product. This is due to ionic nature of alkali nitrite.

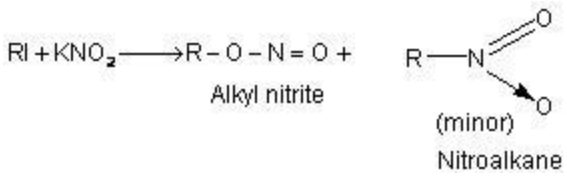
But if the reaction is carried out in solvents like DMF or DMSO, then even $NaNO_2$ or KNO_2 give good yield (about 60%) of nitro compound.

Reactions:

$$R—I + AgNO_2 \longrightarrow RNO_2 + AgI$$

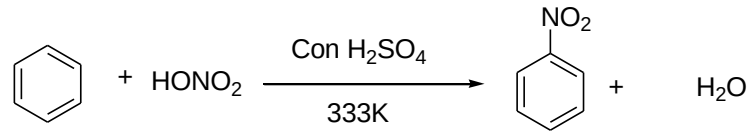
$$C_2H_5I + AgNO_2 \longrightarrow C_2H_5NO_2 + AgI$$

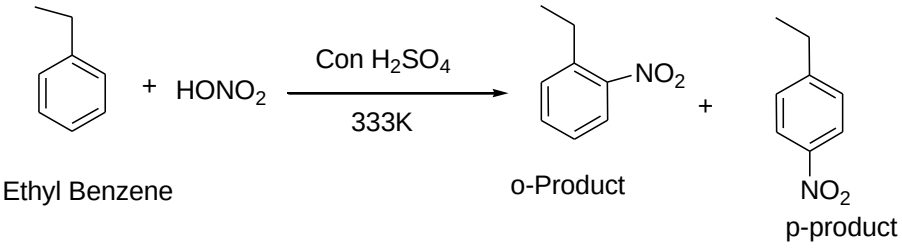
Nitroethane



(ii) Nitration:

Nitro derivatives of aromatic compounds like nitrobenzene are produced when benzene is allowed to react with nitrating mixture.(conc. HNO_3/conc.H_2SO_4).

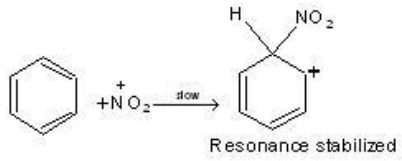


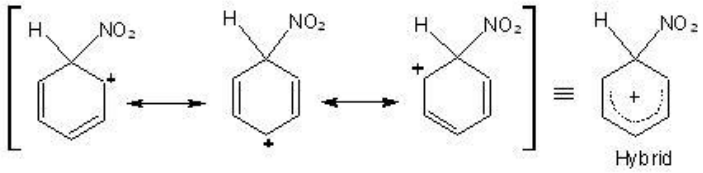


Mechanism:

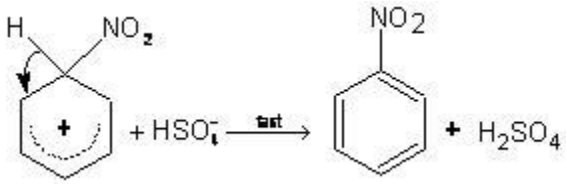
Generation of nitronium ion

Attack of the nitronium ion NO_2^+ on benzene molecule





Loss of proton:



Nitrobenzene

Direct nitration of alkane involves vapour phase nitration at high temperature.

$$R — H + HONO_2 \xrightarrow[675\ K]{} R — NO_2 + H_2O$$

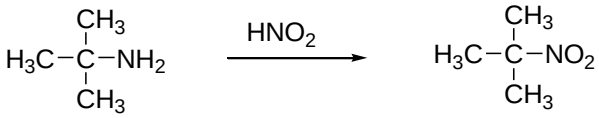
low yield

Problem faced in the method is that at such high temperature, a mixture of nitro alkanes is formed due to C – C cleavage.

e.g. $CH_3CH_2CH_3 + HNO_3 \longrightarrow CH_3CH_2CH_2NO_2 + CH_3CH_2NO_2 + CH_3NH_2$ + other products

(iii) From amines:

3° nitroalkanes can be produced as follows:



Distinguish test between nitroalkanes and alkyl nitrites

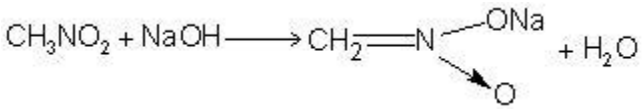
1. Nitroalkane on reduction with H_2/Ni produce 1° amines while alkyl nitrites produce alcohols and NH_3

$CH_3CH_2NO_2 \xrightarrow{[6H]} CH_3CH_2NH_2 + H_2O$

$CH_3CH_2 — O — N = O \xrightarrow{[6H]} CH_3CH_2OH_2 + NH_3 + H_2O$

Ethyl nitrite

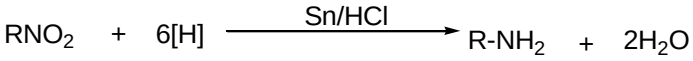
2.Nitroalkanes do not get hydrolysed in basic conditions while nitrites produce alcohols



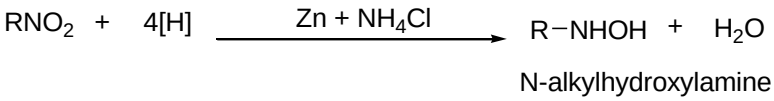
$CH_3\ O – N = O + NaOH \longrightarrow CH_3OH + NaNO_2$

Reduction

With Sn/HCl or catalytic hydrogenation, nitroalkanes are reduced to amines.

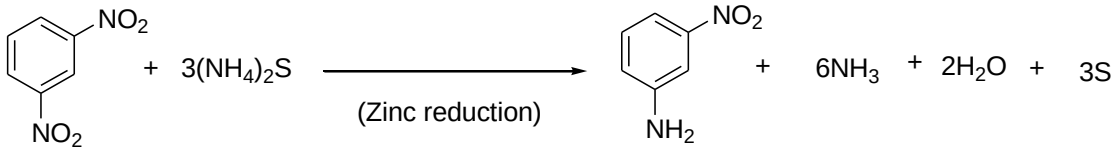


If neutral reducing agent like Zn dust + NH_4Cl is used, hydroxylamines are obtained as major product.



N-alkylhydroxylamine

In the presence of $(NH_4)_2S$ or Na_2S, selective reduction takes place.



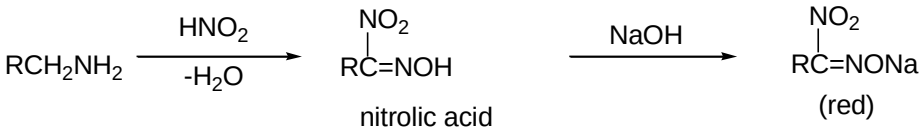
Nitrobenzene gives different products with different reagents and in different mediums.

Medium	**Reagent**	**Product**
Acid	Sn/HCl	Aniline
Neutral	Zn/NH_4Cl	N-phenyl hydroxylamine
	$Na_3AsO_3/NaOH$	Azoxybenzene

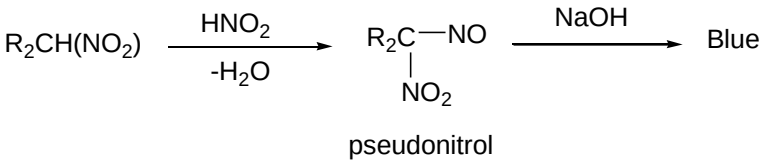
		O ↑ ($C_6H_5N{=}NC_6H_5$)
Alkaline	Zn/NaOH, CH_3OH	Azobenzene
	Zn/NaOH, C_2H_5OH	Hydrazobenzene
Metallic hydride	$LiAlH_4$	aniline
Electrolytic	Dil. H_2SO_4	p-aminophenol

(ii) Action of HNO_2

1° nitroalkane gives nitrolic acid which gives red colour with NaOH.

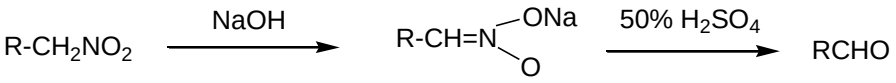


2°nitroalkanes give pseudonitrol with HNO_2.

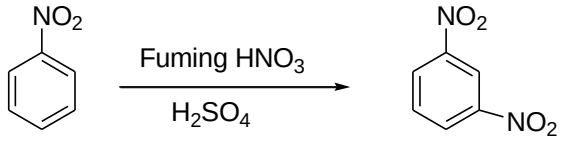


3° nitroalkanes does not react with HNO_2

(iii) Nef carbonyl synthesis Na or K salt of 1° or 2° nitroalkanes give carbonyl compounds onacidification with 50% H2SO4 at room temperature. This reaction is called Nef carbonyl synthesis.

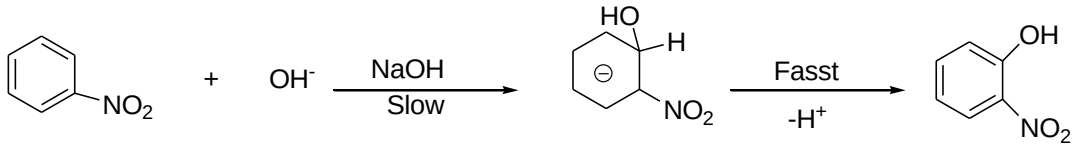


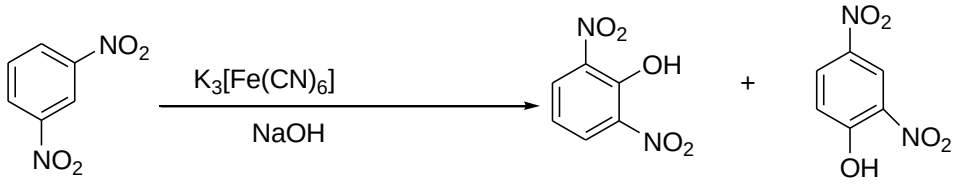
(iv) Electrophifiesubstitution On nitration, nitrobenzene gives m-dinitrobenzene (as $-NO_2$ is a m-directing group and strongly deactivating).



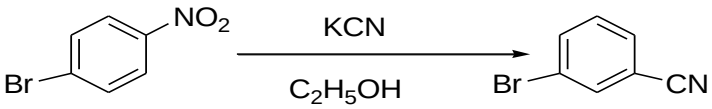
It does not give Friedel-Craft's alkylation.

(v) Nucleophilicsubstitution reaction -NO_2 group activates the ring towards nucleophilic substitution.





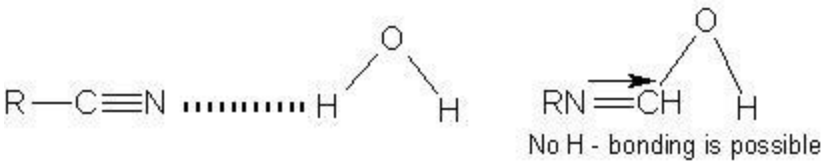
(Von Richter reaction)



Cyanides and Isocyanides

Both alkyl cyanides (RCN) and alkyl isocyanides (RNC) are organic derivatives of hydrocyanic acid HCN. Alkali cyanides are ionic $\left(:C\equiv\bar{N}:\right)$ and cyanide ion is ambident in nature (can form covalent bond either from carbon or nitrogen).AgC = N is covalent, hence lone pair on nitrogen is mainly available for covalent bond formation, resulting in predominant formation of isocyanides.

Illustration . How would you account for the fact that alkyl cyanides are soluble in water but alkyl isocyanides are insoluble in water?
Solution: Alkyl cyanides possess the tendency to form H – bonding with water which is absent with isocyanides



Alkyl Cyanides'

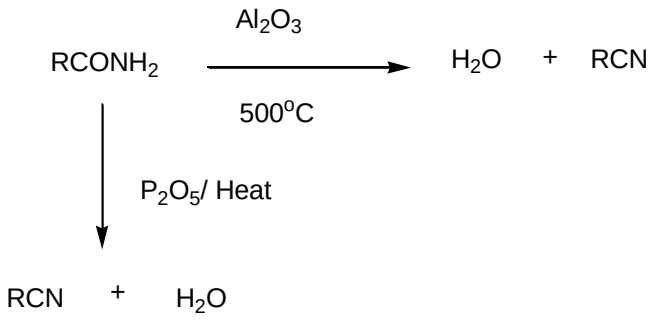
These compound have formula RCN. These are the derivatives of RCN.

According to IUPAC system, cyanides are named as 'alkane nitrile', e.g.,

C_3H_7CN	C_6H_5CN
Butanenitrile	benzenenitrile

Methods of preparation of Cyanides

1.Dehydration of Amides:



High molecular weight acid amides are dehydrated to the corresponding cyanide by heat alone.

$$CH_3(CH_3)_6\ OCNH_2 \xrightarrow{Heat} CH_3(CH_2)_6\ CN$$

2. From RX:

$$RX + KCN \longrightarrow RCN + KX$$

This method is satisfactory only if R is 1^o or 2^o group. If it is 3^o group, then it is converted into alkene.

$$CH_3CH_2Cl + KCN \rightarrow CH_3CH_2CN + KCl$$

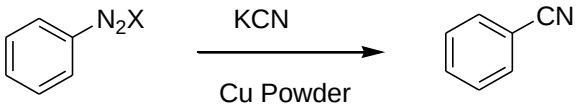
3. By Grignard's reagent and Cyanogen chloride reaction:

$$RMgCl + CICIN \rightarrow RCN + MgCl_2$$

This is best method for preparing 3^o alkyl cyanides.

$$(CH_3)_3CMgCl + CICN \rightarrow (CH_3)_3\ CCN + MgCl_2$$

4. From Diazonium salt

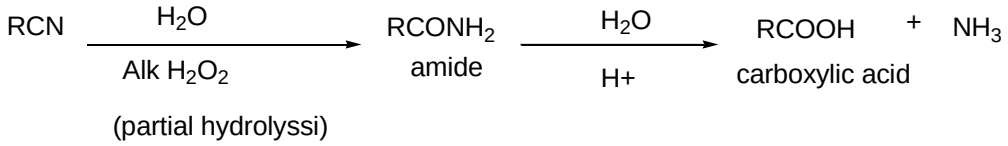


Physical properties

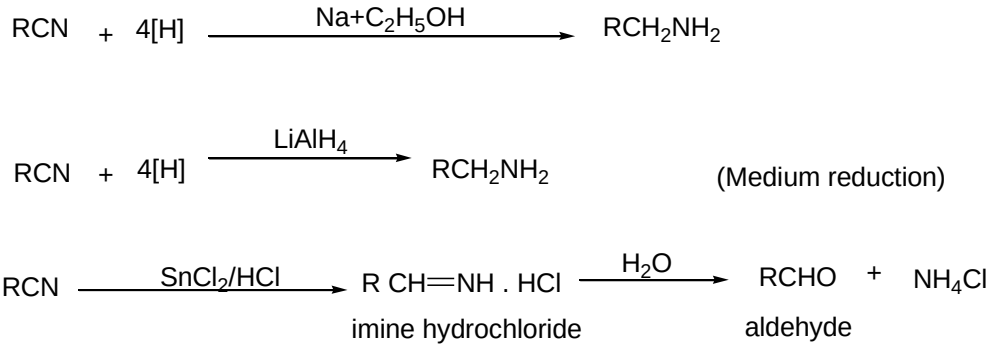
1. These are neutral compound with pleasentodour, similar to bitter almonds.
2. These are soluble in water as well as organic solvents.
3. These are poisonous but less than HCN.

Chemical Properties

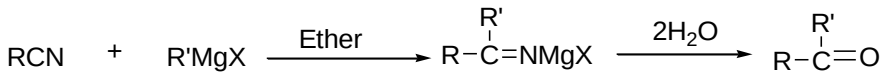
i) Hydrolysis



ii) Reduction



iii) Reaction with Grignard reagent



Alkyl iscoyanides (RNC)

Accordinlg to IUPAC system, these are named as 'alkane isonitrile'

e.g., CH_3NC methyl isonitrile

C_6H_5NC benzene isonitrile

Methods of Preparation of Isocyanides

1. By heating an alkyl iodide with AgCN in aqueous ethanolic solution

$$Rl + AgCN \rightarrow RNC + Agl$$

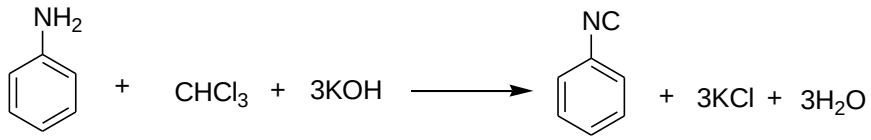
$$C_2H_5l + AgCN \rightarrow C_2H_5NC + Agl$$

Ethylisocyanide

2. By carbylamine reaction

Heating a mixture of 1° amine and chloroform with ethanolic potassium hydroxide

$$RNH_2 + CHCl_2 + 4KOH \longrightarrow RNC + 3KCl + 3H_2O$$



Mechanism proceeds via intermediate formation of dichloromethylene or, dichlorocarbene produced from chloroform in alkaline solution. (Via a-elimination)

$$CHCl_3 + KOH \longrightarrow KCl + H_2O + :CCl_2$$

Properties of Isocyanides

1. Alkyl isocyanides are poisonous, unpleasant smelling, with lower boiling points than isomeric cyanides.

2. RNC are not very soluble in water, nitrogen atom not having a lone pair of electrons available for hydrogen bonding.

Reactions:

1. Hydrolysis:

$$RNC + 2H_2O \xrightarrow{Acid} RNH_2 + HCO_2H$$

$$CH_3NC + 2H_2O \xrightarrow{Acid} CH_3NH_2 + HCO_2H$$

RNC are not hydrolysed by alkalis.

2. Reduction:

$$RNC \xrightarrow{H_2/Pt} R\ NHCH_3$$

2^o amine

$$CH_3NC \xrightarrow{H_2/Pt} CH_3NHCH_3$$

Methyl isocyanide Dimethyl amine

3. When alkyl isocyanides are heated for a long time, they arrange to form cyanide

$$RNC \rightarrow R\ CN$$

$$CH_3CH_2NC \rightarrow CH_3CH_2CN$$

4. With non metals:

(i) $RNC + X_2 \longrightarrow RNCX_2$

$CH_3NC + Cl_2 \longrightarrow CH_3NCCl_2$

(ii) $RNC + S \longrightarrow RNCS$

Alkyl isothiocyanates

$CH_3NC + S \longrightarrow CH_3NCS$

5. Oxidation with HgO:

$$RNC + HgO \rightarrow RNCO + Hg$$

Akylisocyanates

$$CH_3NC + HgO \rightarrow CH_3NCO + Hg$$

Amines

Amines constitute an important class of organic compounds derived by replacing one or more hydrogen atoms ofNH_3 molecule by alkyl/aryl group(s).

$R-NH_2$	$R-NH-R$	$R-\underset{\underset{R}{\vert}}{N}-R$	$C_6H_5-NH_2$
Primary (1°)	secondary(2°)	tertiary(3°)	aromatic amine

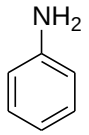
In the IUPAC system, the amines are regarded as alkanamines, e.g.,

$CH_3-CH_2-NH_2$	$CH_3CH_2-NH-CH_3$	$CH_3-CH_2-N(C_2H_5)_2$
Ethanamine	N-methyl ethanamine	N,N-diethylethanamine

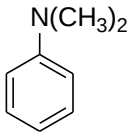
Structure

The nitrogen atom in amine is spa-hybridised. The three hybrid orbitals are involved in bond formation and one hybrid atomic orbital contains the lone pair of electrons, giving the pyramidal geometry of amines.

Aryl amines - NH_2 group is directly attached to the benzene ring



aniline



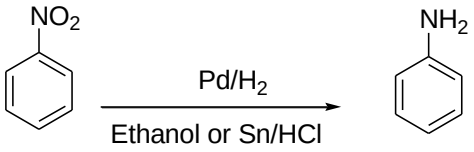
N,N-dimethylaniline

Methods of Preparation of Amines

(i) Reduction of nitro compounds

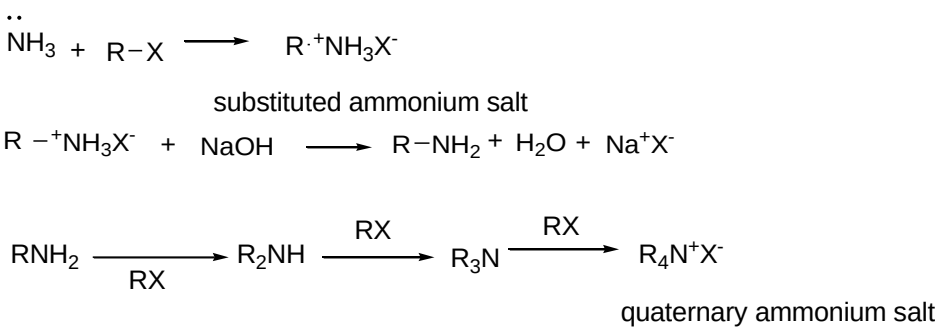
$$R-NO_2 \xrightarrow[\text{Reduction}]{} R-NH_2 + 2H_2O$$

Reduction can takes place by Sn/HCl, Ni/H_2, Zn/NaOH, Pd/H_2



The reduction of nitroalkane or nitrobenzene in neutral medium gives hydroxyl amines.

(ii) Ammonolysis of alkyl halides

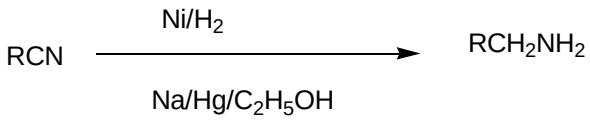


Ammonolysis has the disadvantage of yielding a mixture of primary, secondary and tertiary amines and also a quaternary ammonium salt.However, primary amine is obtained as a major product by taking large excess of NH_3.

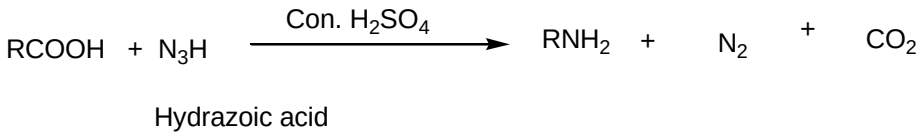
Order of reactivity of halides 'with amines is RI >RBr> RCI.

Aromatic amines could not be prepared since aryl halides are much less reactive towards nucleophilic substitution reactions.

(iii) Reduction of nitriles or cyanides

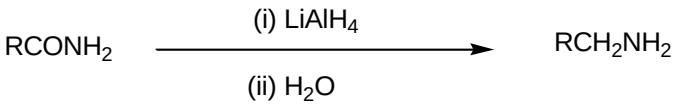


Schmidt Reaction

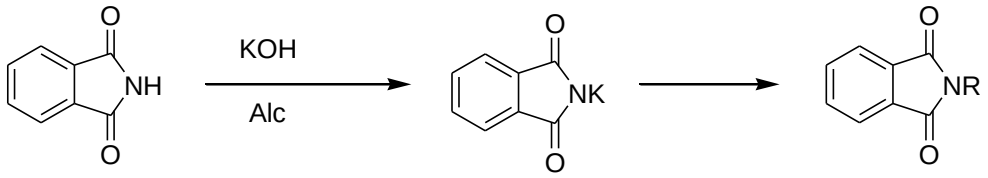


It is a modification of Curtius degradation

(v) Reduction of amides



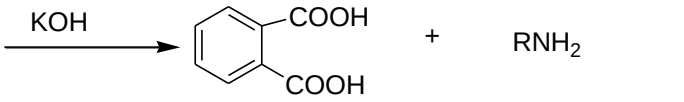
Gabriel Phthalimide reaction



Phthalimide

Potassium phthalimide

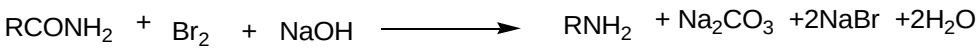
N-alkylphthlimide



primary amines

It only produces 1 0 amines. This method is not suitable for 1° arylamine because aryl halide does not give nucleophilic substitution reaction.

(viii) Hofmann bromamide degradation reaction



In Hofmann degradation reaction, the amine formed has one carbon less than the parent amide.To obtain primary amine with same number of carbon atoms from primary amide, reduction isdone with LiAlH4/ether.

Physical Properties of Amines

1. The lower aliphatic amines are gases with fishy smell.

2. Primary amines witb three or more carbon atoms are liquid and higher members are all solids.

3. Lower aliphatic amines are water suluble because they can form hydrogen bonds with water molecules, however the solubility decreases with increase in hydrophobic alkyl group.

4. Boiling points order primary > secondary > tertiary

5. Tertiary amines does not have intermolecular association due to the absence of hydrogen atom available for hydrogen bond formation.

Basic Strength of Amines

Amines act as Lewis bases due to the presence of lone pair of electrons on the nitrogen atom.More the Kb (dissociation constant of base), higher is the basicity of amines.Lesser the pKb‘ higher is the basicity of amines.

Aliphatic amines (CH3NH2) are stronger bases than NH_3 due to the electron releasing +/ effectof the alkyl group.

Among aliphatic methyl amines, the order of basic strength in aqueous solution is as follows

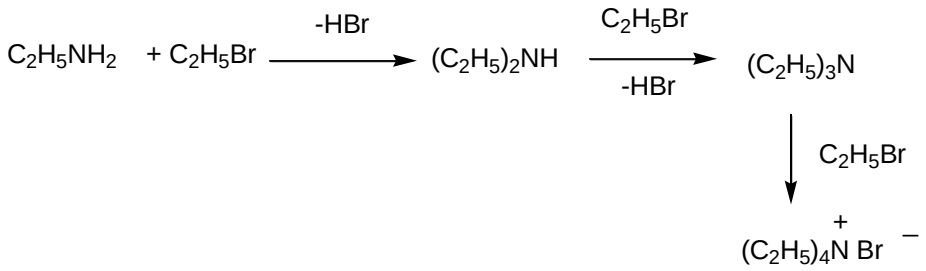
$(C_2H_5NH > (C_2H_5)_3N > C_2H_5NH_2 > NH_3$
$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$

Aromatic amines are weaker basesthan aliphatic amlnes and NH3,due to the fact that the electron pair on the nitrogen atom is involved in resonance with the π-electron pairs of the ring.Electron releasing groups (e.g.,-CH_3,-OCH_3,-NH_2 etc.) increase the basic strength of aromaticamines while electron withdrawing groups (like – NO2, -X,-CN etc.) tend to decrease the same.o-substitutedaromaticamines are usually weaker basesthan aniline irrespective of the nature ofsubstituent whether electron releasing or electron withdrawing. This is called ortho effect and isprobably due to sterk and electronic factors.

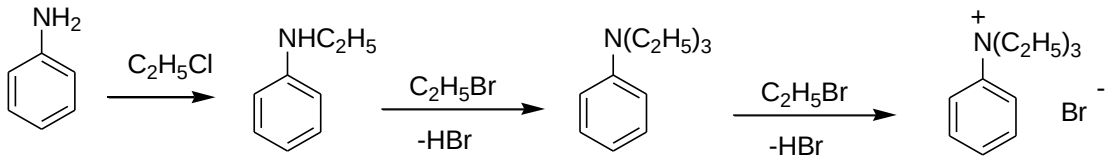
Chemical Properties of Amines

(i) Alkylation

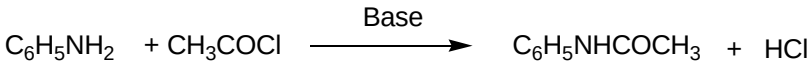
All the three types of amines react with alkyl halides to form quaternary ammonium salt as the final product provided alkyl halide is present in excess.

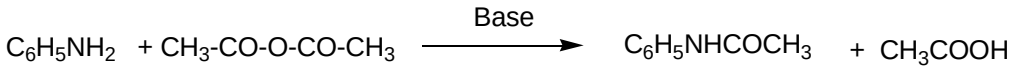


Aromatic amines also undergo alkylation as given below.

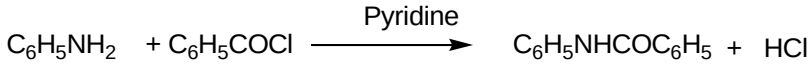


(ii) Acylation



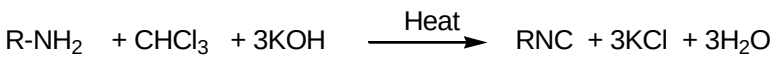


(iii) Benzoylation



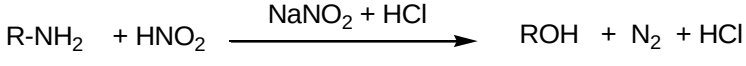
Benzoylation of aniline is known as Schotten-Baumann reaction

(iv) Carbylamine reaction



RNC(Isocyanide) is having a bad smell

(v) Reaction with nitrous acid

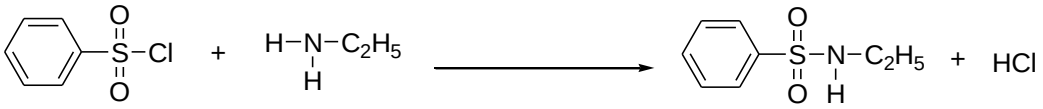


But secondary and _tertiary amines react with nitrous acid in different manner.

Methyl amine give dimethyl ether with HNO_2.

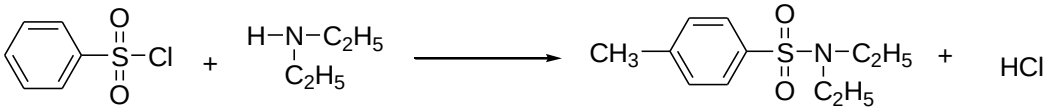
(vi) Reaction with aryl sulphonyl chloride [Hinsberg reagent]

The reaction of benzenesulphonyl chloride with primary amine yield N-ethyl benzene sulphonyl amide.



(soluble in alkali)

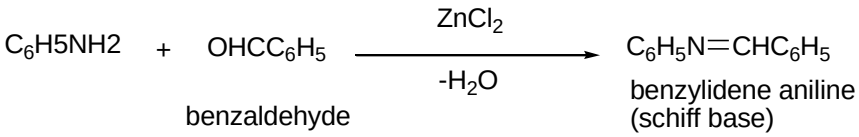
The reaction of benzenesulphonyl chloride with secondary amine yields N,N-diethyl benzene sulphonamide.



(insoluble in alkali)

Tertiary amines does not react with benzenesulphonyl chloride.

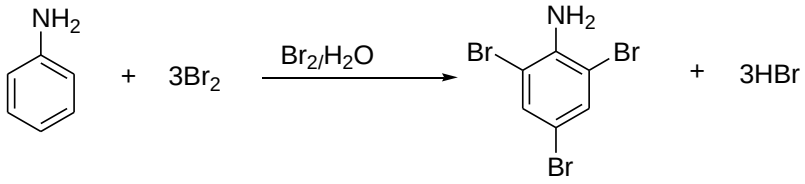
(vii) Reaction with aldehydes Schiff base is obtained.



benzaldehyde

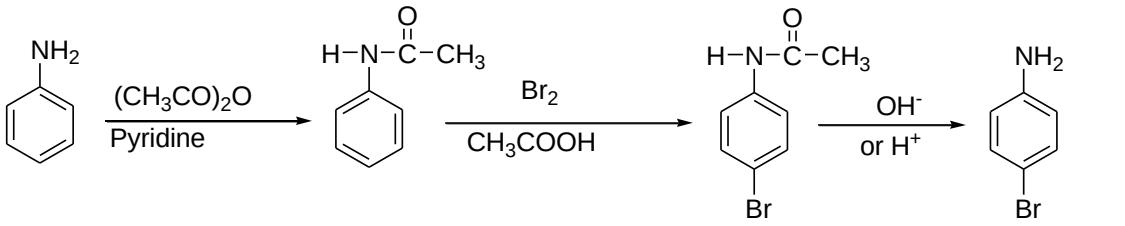
benzylidene aniline
(schiff base)

(viii) Electrophihc substitution reactions Aniline is ortho and para directing towards electrophilic substitution reaction due to high electron density at ortho and para-positions.



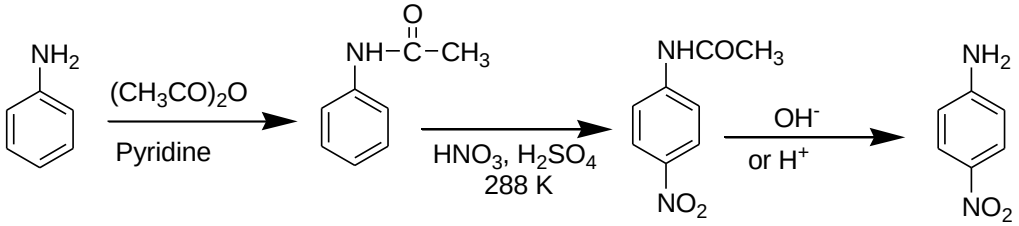
2,4,6-tribromoaniline
(light yellow ppt)

To prepare monosubstituted derivative, activating effect of -NH2 group must be controlled. It can be done by protecting the -NH2 group by acetylation with acetic anhydride.



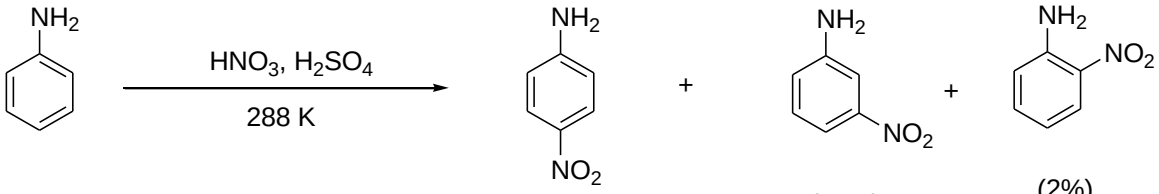
p-bromoaniline

(b) Nitration Direct nitration of aniline is not possible as it is susceptible to oxidation, thus amino group is first protected by acetylation.



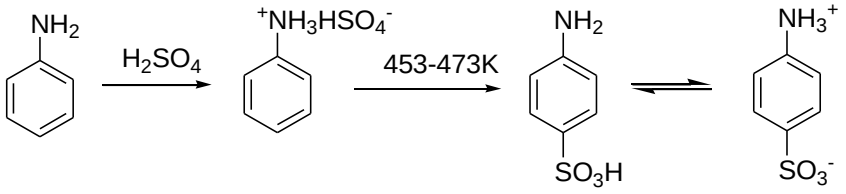
p-nitroaniline

In strongly acidic medium, aniline is protonated as anilinium ion which is meta directing so it gives meta product also.



(51%) (47%) (2%)

c) Sulphonation on sulphonation aniline gives sulphanilic acid, as the major product.



Sulphanilic acid zwitter ion

Aniline does not undergo Friedel-Crafts reaction due to salt formation with aluminium chloride, the Lewis acid, which is used as a catalyst. Due to this, nitrogen of aniline acquires positive charge and hence. behave like a strong deactivating group for further chemical reaction.

(ix) Oxidation Use of diffrent oxidising agents gives different products.

e.g.,

Oxidizing agent	Product
Acidified $KMnO_4$ (or $Na_2Cr_2O_7$ + $CuSO_4$ + dil. Acid)	Aniline black (a dye)
Chromic acid ($Na_2Cr_2O_7$ + Conc. H_2SO_4)	p-benzoquinone
Caro'ss acid (H_2SO_5)	Nitrobenzene and nitrossobenzene
Conc. Nitric acid	decomposes

Separation of Mixture of Amines (1°, 2° and 3°)

(a) Fractional distillation:

This method Is based on the boiling points of amines and is used satisfactorily in Industry.

(b) **Hofmann's method:**

Diethyloxalate is called Hofmann's reagent with which mixture of amines is treated.

- 1° amine forms solid dialkyl oxamide (CONHR)2
- 2° amine forms liquid dialkyl oxamlc ester(CONR2-COOC2H5)
- 3° amlnes do not react

(c) Hlnsberg's method: see the .chemical reactions.

POSSIBLE QUESTIONS

UNIT I

1. Nitroalkanes on reaction with Sn/HCl give
   a. Alcohol b. **Primary amine** c. secondary amine d. tertiary amine

2. Catalytic reduction of nitrocompounds in presence of Hydrogen and nickel gives
   a. **Primary amine** b. Hydroxyl amine c. Nitrosoamine d. N-alkyl hydroxylamine

3. Nitration of phenol with dil nitric acid gives
   a. **A mixture of o- and p-nitro phenol** b. m-nitrophenol c. A mixture of m- and o- nitrophenol d. A mixture of m- and p- nitro phenol

4. Reduction of nitrobenzene in neutral medium gives

a. **Phenyl hydroxylamine** b. Hydrazo benzene c. Azo benzene d. aniline

5. Nitroethane on reaction with Sn/HCl give
   a. Ethanol b. **ethylamine** c. Diethyl amine d. triethylamine

6. Nitro alkanes can be obtained by
   a. **Oxidation of oximes** b. Oxidation of aldehydes c. Nitration of ketones d. Nitration of oximes

7. Which is soluble in water
   a. **Alkyl cyanides** b. Alkyl isocyanides c. aldehydes d. amines

8. Choose a tertiary amine
   a. Methyl amine b. aniline c. **Trimethyl amine** d. Diphenyl amine

9. Nitration of propane gives
   a. Propyl nitrite b. **Nitro propane** c. Propyl amine d. Iso Propyl amine

10. Nitrolic acid dissolves in sodium hydroxide to give
    a. Blue colour solution b. **Red colour solution** c. Colour less precipitate d. Pink colour turbid solution

11. Reduction of nitrobenzene in neutral medium gives
    a. **Phenyl hydroxylamine** b. Hydrazo benzene c. Azo benzene d. aniline

12. When the reduction is carried out using sodium and alcohol, it is called
    a. Clemmensen reduction b. **Mendius reduction** c. Stephen's reduction d. Wolf-kishner reduction
    b. Nitration of propane gives
    a. Propyl nitrite b. **Nitro propane** c. Propyl amine d. Iso Propyl amine

13. Nitrolic acid dissolves in sodium hydroxide to give
    a. Blue colour solution b. **Red colour solution** c. Colour less precipitate d. Pink colour turbid solution

14. Reduction of nitrobenzene in neutral medium gives
    a. Phenyl hydroxylamine b. Hydrazo benzene c. Azo benzene d. aniline

15. When the reduction is carried out using sodium and alcohol, it is called
    a.Clemmensen reduction b. **Mendius reduction** c. Stephen's reduction d. Wolf-kishner reduction

16. Nitroalkanes on reaction with Sn/HCl give
    a.Alcohol b. **Primary amine** c. secondary amine d. tertiary amine

17. Catalytic reduction of nitrocompounds in presence of Hydrogen and nickel gives
    a.Primary amine b. Hydroxyl amine c. Nitrosoamine d. N-alkyl hydroxylamine

18. Nitration of phenol with dil nitric acid gives
    a.A mixture of o- and p-nitro phenol b. m-nitrophenol c. A mixture of m- and o- nitrophenol d. A mixture of m- and p- nitro phenol

19. Reduction of nitrobenzene in neutral medium gives
    a.Phenyl hydroxylamine b. Hydrazo benzene c. Azo benzene d. aniline

PART B

1. How nitrobenzene is prepared
2. Explain the Tautomerism present in aliphatic nitro compounds
3. Show that aliphatic compounds are acidic in nature
4. What is meant by carbylamines reaction
5. Why ammonia is a stronger base than aniline

PART C

1. a.Distinguish primary, secondary and tertiary amines using p-toluene sulphonyl chloride Reagent.
2. Write notes on
   a. Hofmann exhaustive methylation b. Gabriel Phthalamide synthesis
   a.Discuss the action nitrous acid on primary, secondary and tertiary amines
3. Write any three methods how nitro compounds are prepared
4. Explain the relative bascities of amines
5. Write any three methods how amines are prepared
6. Explain the reduction of an aromatic nitro compound in different conditions
7. Write notes on the preparation and properties of nitriles and isonitriles
8. Explain the reduction of aliphatic nitrocompounds in different conditions
9. Distinguish primary, secondary and tertiary amines using p-toluene sulphonyl chloride reagent

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)
II B.Sc. Chemistry
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

UNIT I

Multiple choice questions (Each carries one mark: for online examination)

S.No	Questions	Option A	Option B	Option C	Option D	Answer
1.	Nitroalkanes on reaction with Sn/HCl give	alcohol	Primary amine	Secondary amine	Tertiary amine	Primary amine
2.	Nitroethane on reaction with Sn/HCl give	ethanol	ethylamine	Diethyl amine	triethylamine	ethylamine
3.	Nitration of alkanes gives	Nitro compounds	Alkyl nitrites	Primary amines	Secondary amines	Nitro compounds
4.	Nitration of propane gives	Propyl nitrite	Nitro propane	Propyl amine	Isopropyl amine	Nitro propane
5.	On boiling an aqueous solution of sodium nitrite with an alpha halogen carboxylic acid, it gives	Nitro compound	Alkyl nitrites	alkyl amines	Chloro methyl amines	Nitro compound
6.	On boiling an aqueous solution of sodium nitrite with an alpha chloro acetic acid, it gives	Nitromethane	Methyl nitrites	Methyl amines	Chloro methyl amines	Nitro methane
7.	Catalytic reduction of nitrocompounds in	Primary amine	Hydroxyl amines	Nitroso amines	N-alkyl hydroxylamine	Primary amine

	presence of Hydrogen and nickel gives					
8.	Catalytic reduction of nitro methane in presence of Hydrogen and nickel gives	Methyl amine	Methyl hydroxyl amine	nitrosoamine	N-alkyl hydroxylamine	Methyl amine
9.	In neutral reducing medium nitro compounds are reduced to	Primary amine	Hydroxyl amines	Nitroso amines	N-alkyl hydroxylamine	N-alkyl hydroxylamine
10.	Primary nitro alkanes react with nitrous acid to form	Carboxylin acid	Nitrolic acid	Seudo nitrole	Hydroxyl amine	Nitrolic acid
11.	Nitro methane react with nitrous acid to form	Acetic acid	Nitrolic acid	pseudo nitrole	Hydroxyl amine	Nitrolic acid
12.	Nitro alkanes can be obtained by	Oxidation of oximes	Oxidation of aldehydes	Nitration of ketones	Nitration of oximes	Oxidation of oximes
13.	Nitro alkanes can be obtained by	Reduction of oximes	Hydrolysis of alpha nitro alkenes	Action of potassium nitrate on alkyl halides	Oxidation of aldehydes	Hydrolysis of alpha nitro alkenes
14.	Nitro alkanes can be obtained by	Reduction of oximes	Hydrogenation of alpha nitro alkenes	Action of Silver nitrite on alkyl halides	Oxidation of aldehydes	Action of Silver nitrite on alkyl halides
15.	Nitro methane can be obtained by	Reduction of oximes	Hydrogenation of alpha nitro alkenes	Action of Silver nitrite on methyl bromide	Oxidation of aldehydes	Action of Silver nitrite on methyl bromide
16.	Nitrolic acid dissolves in sodium hydroxide to give	Blue colour solution	Red colour solution	Colour less precipitate	Pink colour turbid solution	Red colour solution
17.	Nitration of phenol with dil nitric acid gives	o-nitro phenol	m-nitrophenol	A mixture of m- and o-nitrophenol	A mixture of m- and p- nitro phenol	o-nitro phenol

18.	Nitration of phenol with dil nitric acid gives	A mixture of o- and p-nitro phenol	m-nitrophenol	A mixture of m- and o-nitrophenol	A mixture of m- and p- nitro phenol	A mixture of o- and p-nitro phenol
19.	The –OH group in phenol is a	Ortho directing group	Meta directing group	Para directing group	Ortho and para directing group	Ortho and para directing group
20.	Organic derivatives of hydrocyanic acid are called	Alkyl cyanides	Formates	Acetates	Alkanoic acids	Alkyl cyanides
21.	Organic derivatives of hydrocyanic acid are called	Alkyl iso cyanides	Formates	Acetates	Alkanoic acids	Alkyl cyanides
22.	Which is soluble in water	Alkyl cyanides	Alkyl isocyanides	aldehydes	amines	Alkyl cyanides
23.	Which is insoluble in water	Alkyl cyanides	Alkyl isocyanides	alcohol	acetone	Alkyl isocyanides
24.	Dehydration of amides gives	Alkyl cyanides	Alkyl isocyanides	alcohol	acetone	Alkyl cyanides
25.	Dehydration of acetamide gives	methyl cyanides	Methyl isocyanides	methanol	acetone	methyl cyanides
26.	Reduction of nitrobenzene in acid medium gives	Phenyl hydroxylamine	Hydrazo benzene	Azo benzene	aniline	aniline
27.	Reduction of nitrobenzene in neutral medium gives	Phenyl hydroxylamine	Hydrazo benzene	Azo benzene	aniline	Phenyl hydroxylamine
28.	Electrolytic reduction of nitro benzene gives	Phenyl hydroxylamine	Hydrazo benzene	Azo benzene	para amino phenol	para amino phenol
29.	Reduction of nitrobenzene in alkali medium(Zn/NaOH) gives	Phenyl hydroxylamine	Hydrazo benzene	Azo benzene	para amino phenol	Azo benzene
30.	Reduction of nitrobenzene in alkali medium(Zn/NaOH, in methanol) gives	Phenyl hydroxylamine	Hydrazo benzene	Azo benzene	para amino phenol	Hydrazo benzene

31.	Example for a primary amine	Methyl amine	Ethyl methyl amine	Trimethyl amine	Dimethyl amine	Methyl amine
32.	One of the following is a secondary amine	Methyl amine	aniline	Trimethyl amine	Dimethyl amine	Dimethyl amine
33.	Choose a tertiary amine	Methyl amine	aniline	Trimethyl amine	Dimethyl amine	Trimethyl amine
34.	Example for an alkyl amine	Methyl amine	aniline	toludine	Diphenyl amine	Methyl amine
35.	Choose an aromatic amine	Methyl amine	aniline	Trimethyl amine	Dimethyl amine	aniline
36.	Suitable example for a mixed amine	Methyl amine	Ethyl methyl amine	Trimethyl amine	Dimethyl amine	Ethyl methyl amine
37.	Amines have the	Pyramidal shape	Square planar shape	Trigonal shape	Octahedral shape	Pyramidal shape
38.	Which is having a pyramidal shape	Amine	acetylene	alkenes	Boron trifluoride	Amine
39.	When the reduction is carried out using sodium and alcohol, it is called	Clemmensen reduction	Mendius reduction	Stephen's reduction	Wolf-kishner reduction	Mendius reduction
40.	Gabriel synthesis is carried out for the preparation of	Aldehydes and ketones	alcohols	Primary amines	Carboxylic acids	Primary amines
41.	Hinsberg method is used for the separation of a mixture of	Primary, secondary and tertiary alcohols	Primary, secondary and tertiary amines	Ortho, meta and para nitrophenols	Ortho, meta and para aminophenols	Primary, secondary and tertiary amines
42.	On treatment with bromine and potassium hydroxide amides are converted into	Aldehydes and ketones	alcohols	Primary amines	Carboxylic acids	Primary amines
43.	The reagents used in Hofmann's degradation of amides are	Sodium and alcohol	Ammonium hydrogen sulphide	Hydrogen in presence of nickel	bromine and potassium hydroxide	bromine and potassium hydroxide
44.	Phthalimide is	Hofmann's	Gabriel	Carbylamine	Hofmann's	Gabriel

	converted into primary amine in	degradation	synthesis	reaction	elimination	synthesis
45.	Hinsberg's reagent is	p-toluenesulphonyl chloride and NaOH	bromine and potassium hydroxide	Sodium and alcohol	Hydrogen in presence of nickel	p-toluenesulphonyl chloride and NaOH
46.	In Hinsberg's test for the separation of amines , primary amines form	Sodium salt of alkyl sulphonamide soluble in alkali	Dialkyl sulphonamide which is incoluble in alkali	Gets converted into secondary amine	Hydroxylamine hydrochloride	Sodium salt of alkyl sulphonamide soluble in alkali
47.	In Hinsberg's test for the separation of amines , secondary amines form	Sodium salt of alkyl sulphonamide soluble in alkali	Dialkyl sulphonamide which is incoluble in alkali	Gets converted into secondary amine	Hydroxylamine hydrochloride	Dialkyl sulphonamide which is incoluble in alkali
48.	In Hinsberg's test for the separation of amines , tertiary amines form	Sodium salt of alkyl sulphonamide soluble in alkali	Dialkyl sulphonamide which is incoluble in alkali	Gets converted into secondary amine	Does not react	Does not react
49.	Aromatic primary amines react with nitrous acid to form	N-nitroso amines	Benzene diazonium chloride	Trialkyl ammonium nitrite	Nitrogen and alcohol	Benzene diazonium chloride
50.	Aliphatic primary amines react with nitrous acid to form	N-nitroso amines	Benzene diazonium chloride	Trialkyl ammonium nitrite	Nitrogen and alcohol	Nitrogen and alcohol
51.	Aliphatic secondary amines react with nitrous acid to form	Yellow colour N-nitroso amines	Benzene diazonium chloride	Trialkyl ammonium nitrite	Nitrogen and alcohol	Yellow colour N-nitroso amines
52.	Tertiary amines react with nitrous acid to form	Yellow colour N-nitroso amines	Benzene diazonium chloride	Trialkyl ammonium nitrite	Green colour p-nitroso-N-dimethyl amine	Green colour p-nitroso-N-dimethyl amine
53.	Carbylamine test is answered by	Primary amine	Secondary amine	Tertiary amine	Quarternary salt	Primary amine
54.	A compound when	Primary amine	Secondary	Tertiary	Quarternary	Primary amine

	heated with chloroform and alcoholic potassium hydroxide gives a strong offensive smell		amine	amine	salt	
55.	A compound when heated with chloroform and alcoholic potassium hydroxide gives a strong offensive smell	Methyl amine	Dimethyl amine	Trimethyl amine	Quarternary salt	Methyl amine
56.	A primary amine when heated with chloroform and alcoholic potassium hydroxide gives	An offensive smell	Pleasant smell	A red precipitate	flourscence	An offensive smell
57.	A primary amine when heated with chloroform and alcoholic potassium hydroxide gives	Isocyanides	Alkyl cyanides	Amino aldehydes	Amino ketones	Isocyanides
58.	Which is more basic	Trimethyl amine	Dimethyl amine	methylamine	ammonia	Dimethyl amine
59.	Which is more basic	P-toludine	m-toludine	o-toludine	aniline	P-toludine
60.	Which is more basic	p-nitroaniline	m-nitroaniline	aniline	ammonia	ammonia

UNIT II
Diazonium Salts & Polynuclear Hydrocarbons

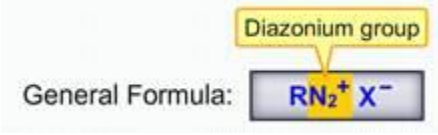
Diazonium Salts: Preparation and their synthetic applications.

Polynuclear Hydrocarbons

Aromaticity of polynuclear hydrocarbons, structure elucidation of naphthalene; Preparation and properties of naphthalene, phenanthrene and anthracene.

Benzene Diazonium Chloride ($C_6H_5N_2^+;Cl^-$)

Diazonium salts have the general formula

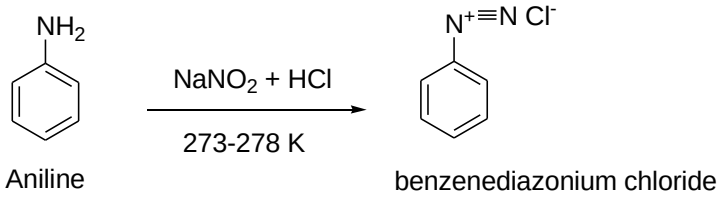


Where X = Cl^-, Br^-, HSO^{4-}, BF^{4-}...etc

Preparation

Diazotisation reaction:

$$C_6H_5NH_2 + NaNO_2 + 2HCl \xrightarrow{273\text{-}278\ k} C_6H_5N{=}N{-}Cl + NaCl + 2H_2O$$



The excess acid in diazotisation reaction is necessary to maintain proper acidic medium for the reaction and to prevent combination of diazonium salt formed with the undiazotised amine. Diazonium salts are prepared and used in aqueous solutions because in solid state, they explode.

Properties

It is a colourless crystalline solid, soluble in water. It has tendency to explode when dry.

Reactions Benzene diazonium chloride undergoes two main types of reaction

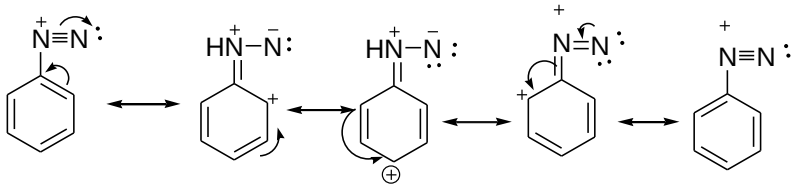
• **Substitution of the diazonium group** *nitrogen expelled*

• **Coupling reactions** *the nitrogen atoms are retained*

Aryl diazonium salts are used as intermediates to synthesise a wide variety of organic compounds. Primary alkyl diazonium ions are not very stable. They decompose easily and tend to be explosive when dry. Aryl diazonium salts are stable only for short times at low temperatures. Resonance structures help to stabilise the ion by delocalising the positive charge around the aromatic ring.

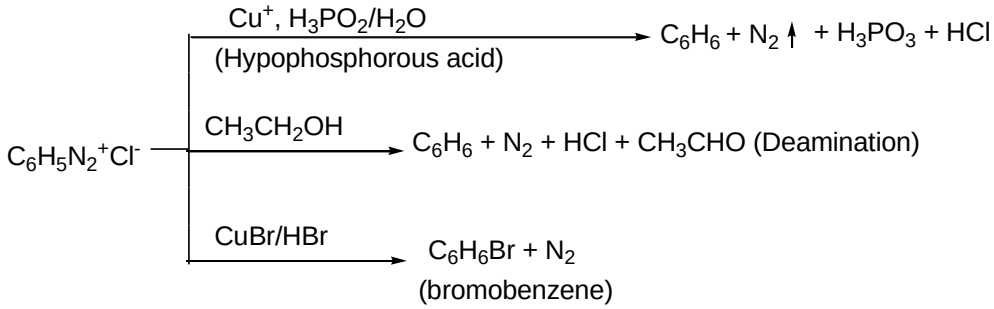
Stability of Arenediazonium salts

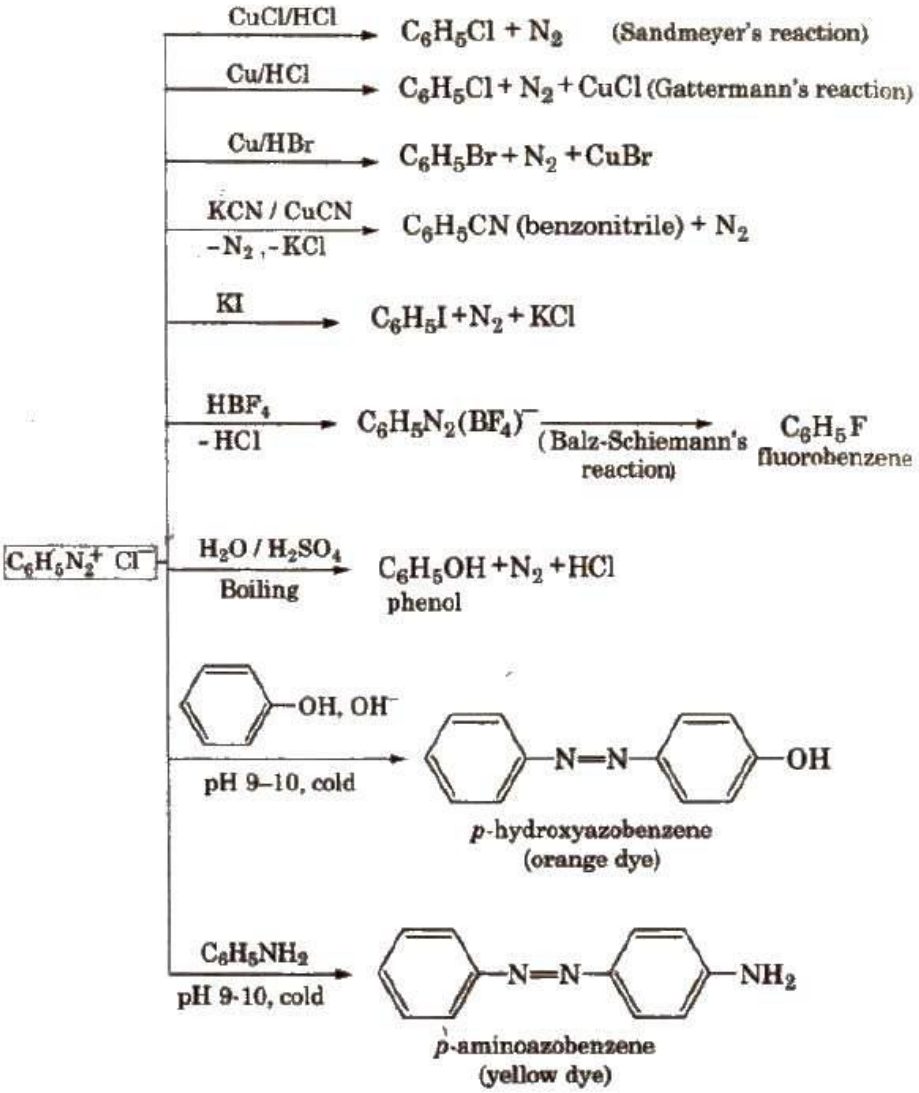
It is relatively more stable than the alkyldiazonium salt. The arene diazonium ion is resonance stabilised as is indicated by the following resonating structures:



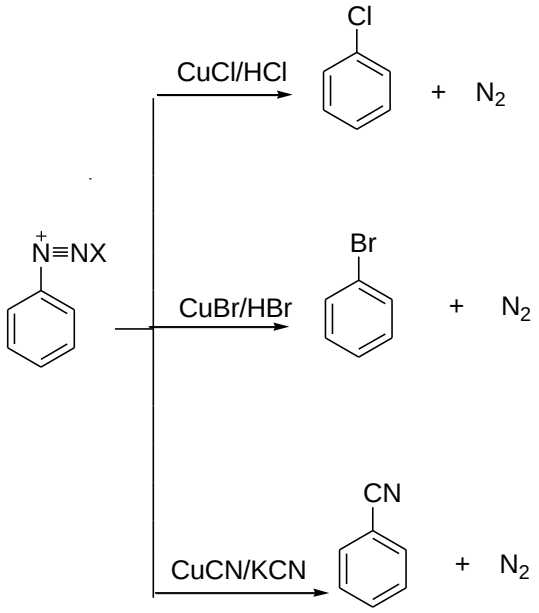
Various resonating structures of arenediazonium ion

Chemical reactions

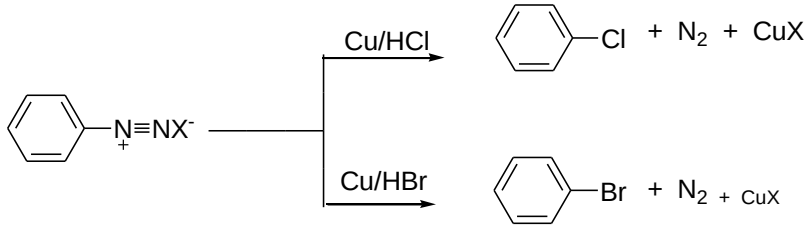




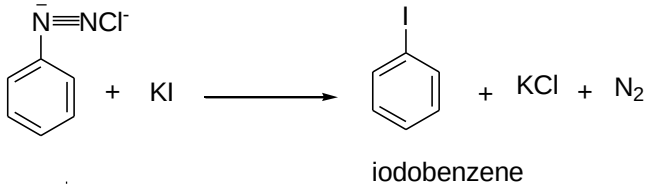
In the **Sandmeyer reactions**, diazonium groups are replaced by chloride, bromide or cyanide in the presence of copper (I) ions.



In the **Gatterman reactions**, diazonium groups are replaced with Chlorine (or) Bromine by treating the diazonium salt solution with haloacid in the presence of copper powder.

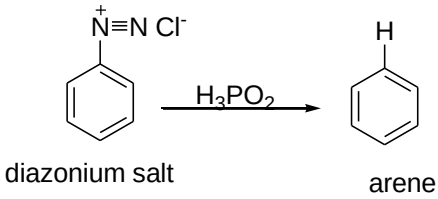


Diazonium group may be replaced by iodine by treatment with potassium iodide.

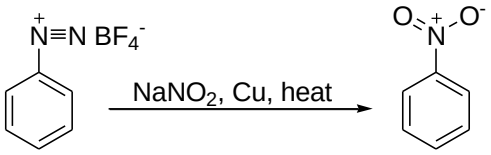


The **Schiemann reaction** is a method for the production of aryl fluorides.

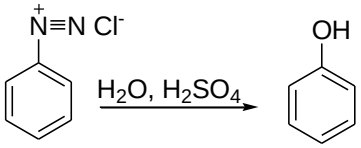
In reductive deamination, the diazonium group is replaced by hydrogen after treatment with mild reducing agents such as hypophosphorous acid (or) ethanol.



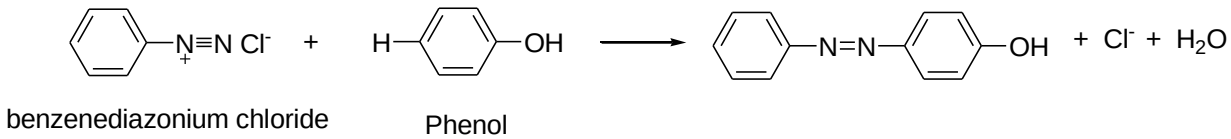
In nitration reactions, the diazonium group is replaced by an $-NO_2$ group.



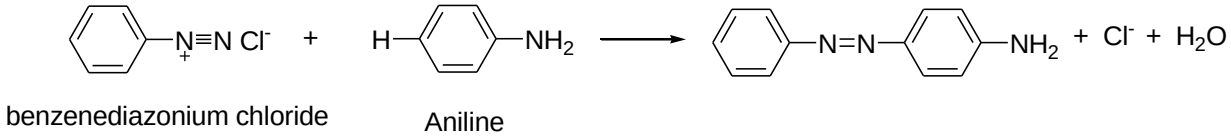
Phenols can be prepared from diazonium salts by hydrolysing with dilute sulphuric acid and heating.



Azo coupling reactions occur when diazonium salts react with phenol (or) aniline.



benzenediazonium chloride Phenol

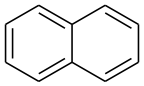


benzenediazonium chloride Aniline

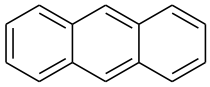
Polynuclear Hydrocarbons

Classification of Polynuclear Hydrocarbons
compounds with benzene nuclei linked through one or more carbon

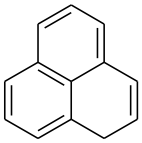
2. condensed polynuclear hydrocarbons: the compounds in which two or more rings are fused due to the sharing of two or more carbon atoms by two or more rings. They are known as fused or condensed polynuclear hydrocarbons. E.g.,



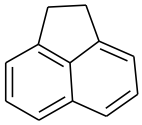
Naphthalene



Anthracene



phenanthrene



Acenaphthene

The chemistry of isolated polynuclear compounds is similar to that of simple aromatic hydrocarbons. However, the condensed polynuclear hydrocarbons like naphthalene, anthracene.

Polynuclear Hydrocarbons may be divided into two groups,

Compounds classified as heterocyclic probably constitute the largest and most varied family of organic compounds. After all, every carbocyclic compound, regardless of structure and functionality, may in principle be converted into a collection of heterocyclic analogs by replacing one or more of the ring carbon atoms with a different element. Even if we restrict our consideration to oxygen, nitrogen and sulfur (the most common heterocyclic elements), the permutations and combinations of such a replacement are numerous.

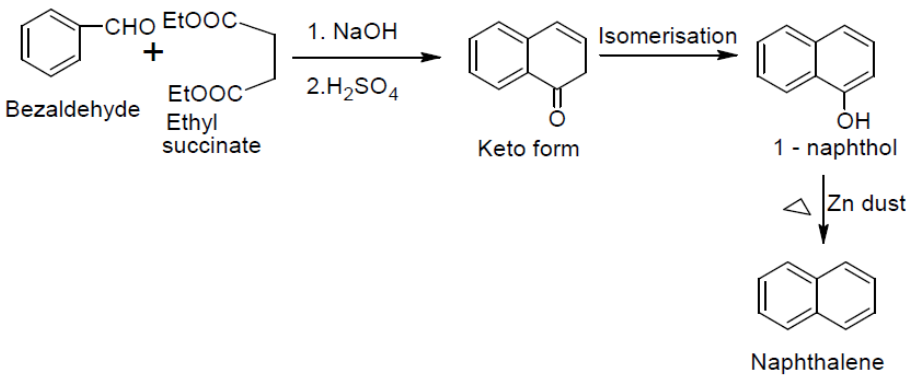
Naphthalene ($C_{10}H_8$)

Naphthalene is the simplest example of a polycyclic aromatic hydrocarbon containing the benzene rings fused in ortho positions.

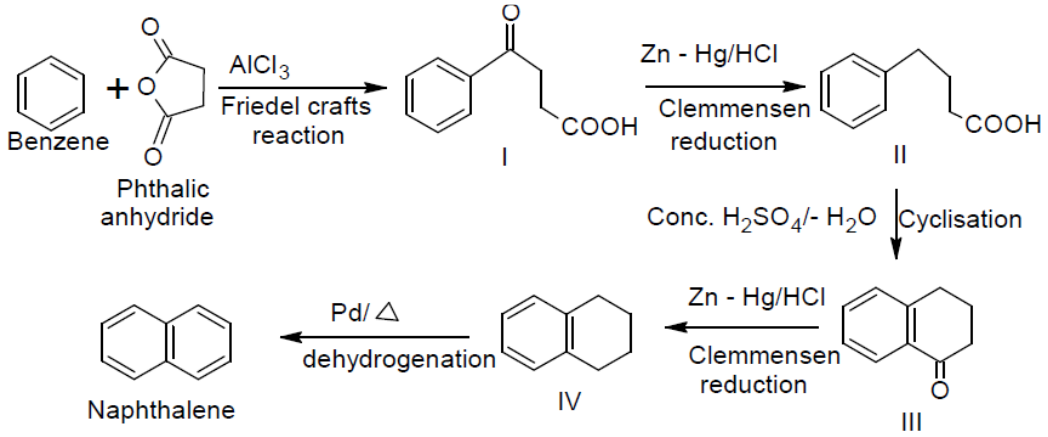
Source and its isolation: It is largest single compound present in coal-tar. It is obtained from 'middle or heavy oil' by chilling these fractions when naphthalene crystallizes out. The crude naphthalene is separated by pressing or centrifuging. The resultant solid mass is washed with hot water and aqueous alkali to remove traces of oils and phenols. It is then washed with dilute sulphuric acid to remove basic impurities. Finally it is purified by sublimation.

Method of preparation : It can be prepared by using following methods-

1. From benzaldehyde and ethyl succinate (Fitting and Erdmann Synthesis): The reaction of benzaldehyde and ethyl succinate in the presence of basic catalyst like sodium hydroxide or potassium tertiary butoxide followed by cyclisation and isomerisation gives α- naphthol which further on reduction with Zn dust afforded naphthalene.



Haworth synthesis (1932) : Friedel crafts reaction of succinic anhydride with benzene in presence of $AlCl_3$ gives a ketonic acid I which is reduced to II. This on cyclisation gives ketone III which on reduction yields tetralin IV. Dehydrogenation of tetralin gives naphthalene.



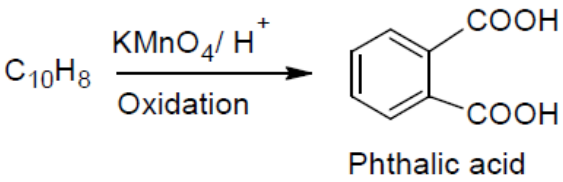
Constitution or Structure of Naphthalene:

Analytical evidence: The structure of naphthalene was arrived at by following analytical evidence.

1. On the basis of analytical data its molecular formula is found to be $C_{10}H_8$.

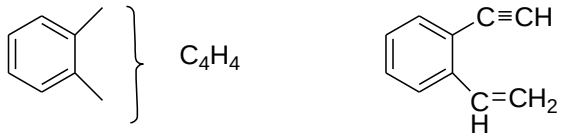
2. Like benzene it is resistsnt to addition reactions though less than benzene. It resembles benzene in other chemical properties also and undergoes electrophilic substitution reactions like halogenation, nitration etc., more readily than benzene.

3. Its nuclear substituted hydroxy derivative are phenolic in nature and amino derivatives undergo diazotization and coupling reactions. This again shows it to be similar to benzene the structure**.** Graebe in 1869 obtained phthalic acid (o-benzene dicarboxylic acid) on oxidation of naphthalene with acid permanganate . This showed that at least one benzene ring is present in naphthalene and there may be two side chains in ortho positions to each other.



Phthalic acid

Hence the formula of the naphthalene may be written as (I).The two side chains on the basis of valency requirements must be highly unsaturated and formula (II) may be suggested for it.

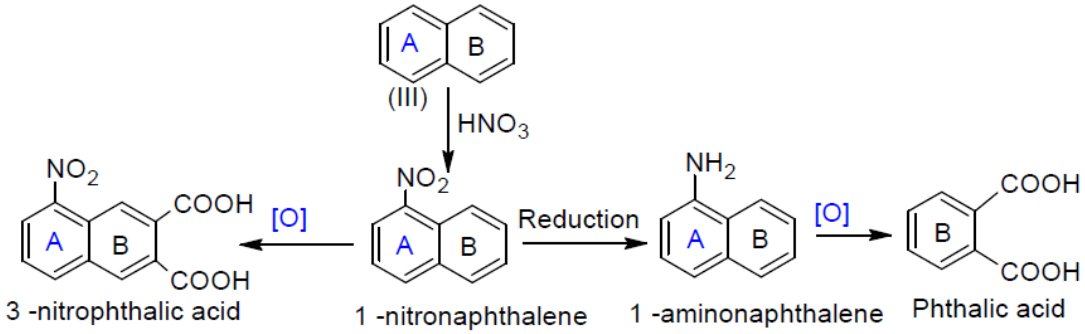


However ,such structure would be in contrast to known aromatic character of naphthalene. Therefore, structure (II) and related structures for naphthalene are ruled out.

5. Graebe further proved that naphthalene consists of two benzene rings fused in o-positions. This was based on following experimental proof:

Naphthalene gave phthalic acid on oxidation**.** When naphthalene was nitrated it yielded nitrophthalene which oxidation gave 3-nitro phthalic acid. This showed that nitro group was present in the benzene ring and side chains were oxidized. But when nitro group of nitro naphthalene was reduced to amino group and the resulting aminonaphthalene oxidized, phthalic acid and not amino phthalic acid was obtained. An amino group attached to benzene ring is known to render the ring highly susceptible to oxidative degradation. The logical conclusion therefore could be that during the oxidation of aminonaphthalene – it was the benzene ring containing an amino group which was destroyed and the benzene ring present in oxidation product phthalic acid is other than that which had the nitro group. It was therefore concluded that two benzene rings were fused in ortho-position i.e. naphthalene contained two

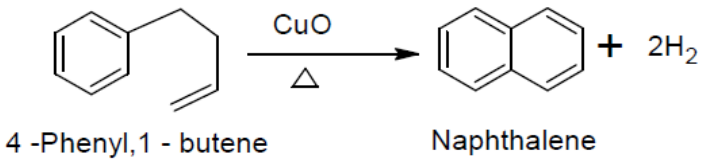
benzene rings. In oxidation of nitronaphthalene, nitro phthalic acid was obtained because nitro group attached to benzene ring made the ring resistant to oxidation.



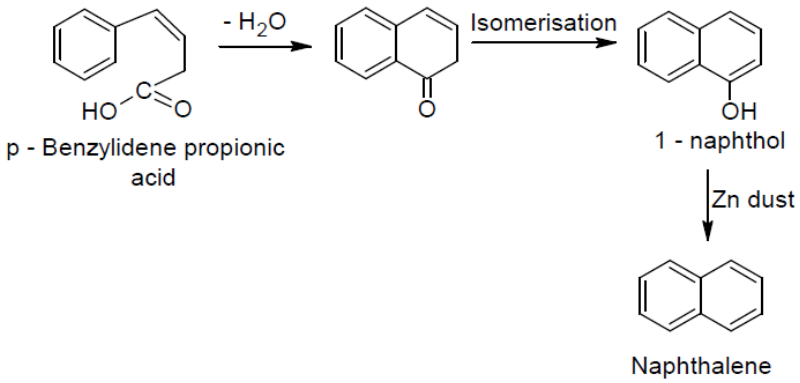
The above scheme clearly demonstrates the presence of two benzene rings fused in o-positions. The structure (III) was intuitively suggested by Erlenmeyer in 1866 and is known as Erlemeyer's structure of naphthalene.

Synthetic evidence: Synthetic evidence which support the Erlenmeyer's formula for naphthalene, some are given below:

a) If 4-phenylbutene-1 is passed over red hot calcium oxide, naphthalene is obtained.

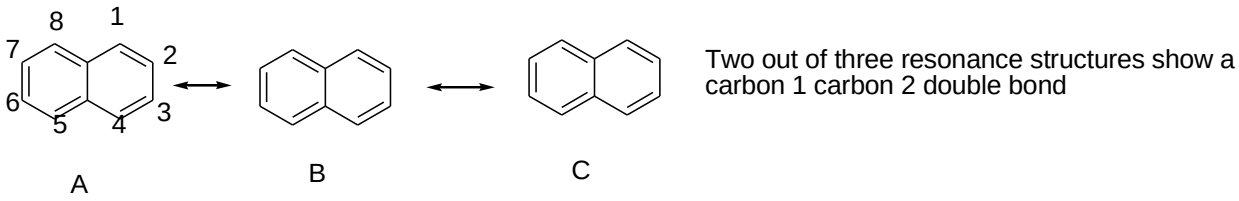


Fittig's synthesis: Cyclisation of p-benzylidene propionic acid gives α- naphthol which on distillation with zinc dust yields naphthalene.

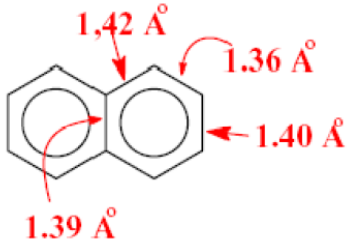


Modern views about structure of Naphthalene: Like benzene, the structure of naphthalene can be explained on the basis of following concepts.

i) Resonance concept: Naphthalene is considered to be the resonance hybrid of various contributing structures of which following three are important.



Naphthalene is planar molecule. X-ray studies have indicated that all carbon-carbon bonds in naphthalene are not equivalent. The C_1-C_2 bond is having relatively greater double bond character and is 1.36A_o as compare to C_2-C_3 bond having greater single bond character length 1.40A_o. This is obvious, if we see the contributing structures in which C_1-C_2 bond are double bond in structures B and C and single bond character in the structure A. Thus it has a two-third double bond character. On the other hand C_2-C_3 bond is a single bond in structures B and C and double bond in structure A. Thus it has two-third single bond character.



The resonance energy of naphthalene is 61 Kcals. Since the resonance energy of benzene is 36 Kcals, the additional energy due to second benzene ring is only 25 Kcals. This decreased

resonance energy is in accordance with relatively greater reactivity of naphthalene.

II) Molecular orbital concept: All carbon atoms in naphthalene are in sp^2 hybridization state and lie at the corners of two fused hexagons. Each one of the carbon atom is attached to two other carbon atoms and one hydrogen by σ-bonds formed by the overlapping of trigonal sp^2 hybrid orbitals. The unhybridized *p* orbital at each carbon overlaps with the *p* orbitals on its side forming a л electron cloud above and below the plane of the ring containing all the carbon and hydrogen atoms. The л electron cloud has a shape of 8 and consists of two partially overlapping sextets-thus imparting aromatic character to naphthalene. However, since a pair of л electros is common to both the rings, it has less aromatic character than benzene.It must be noted that it contains 10л electrons, a number for exhibiting aromatic character according to Huckel's rule.

The M.O,picture of naphthalene also explains the nature of substitution reactions. Since it has a л electron cloud on either side of the plane of the ring, it acts as a source of electrons and its important reactions are electrophilic substitution reactions.

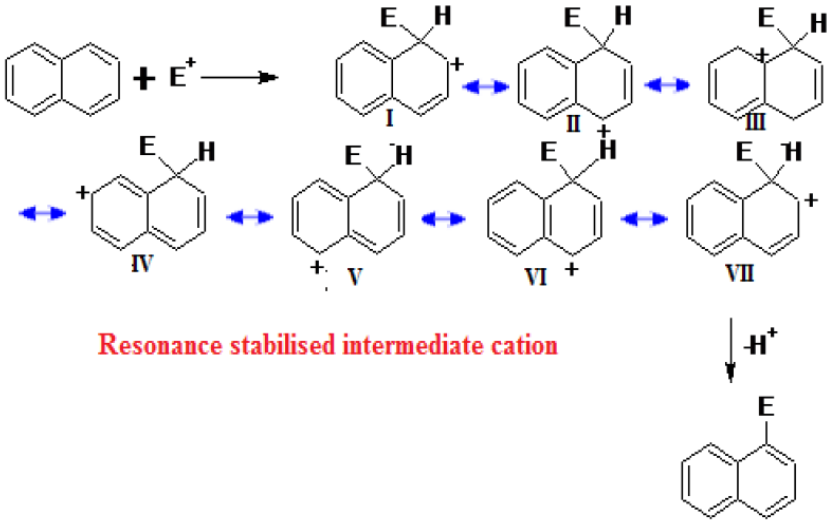
Physical properties: Naphthalene exist as a colourless lustrous plates, m.p. 353K, insoluble in water but soluble in alcohol, ether and benzene. It has strong characterstic odour. It is volatile and sublimes on heating.

Chemical properties : It resembles benzene in its reactions. However, it is more reactive than benzene and forms the addition and substitution products much more readily. It is also more susceptible to oxidation and reduction**.** Like benzene, it undergoes electrophilic substitution reactions and normally occurs more readily at α-position than β-position. Because, the carbonium ion intermediate formed by attack on β-position is less stabilized by resonance as the benzenoid structure of both rings is distributed in contributory structures.

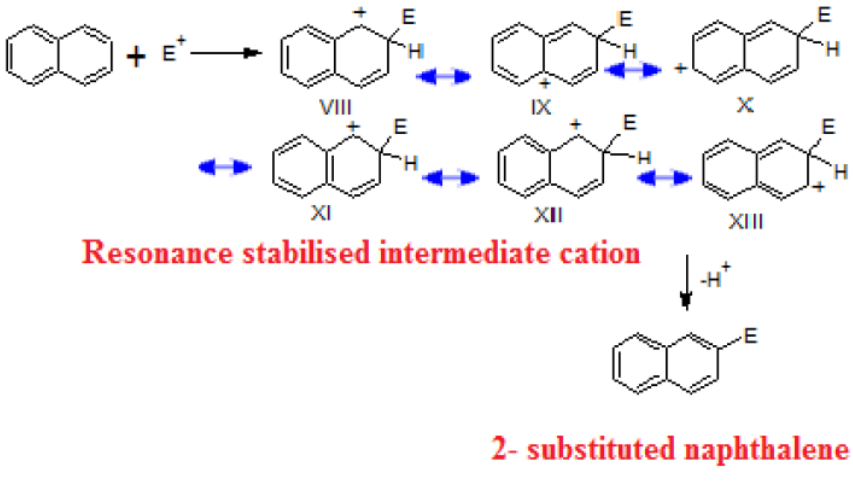
Electrophilic substitution reaction: When electrophilic attack takes place at 1- or α-

position and 2- or β-position.

For substitution at α- or 1- position:



For substitution at β- or 2-position:

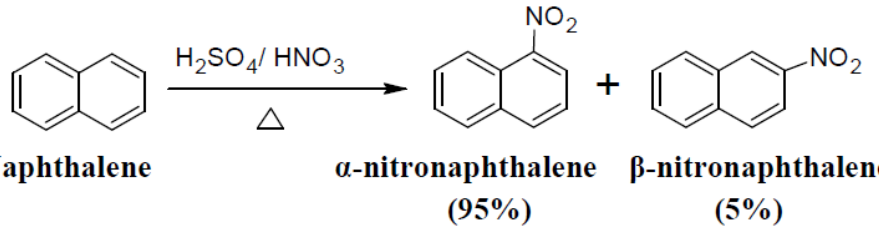


E^+ represents an electrophile and may be Cl - , Br - . I – in halogenation , NO2 + in nitration SO3 in sulphonation, R+ or RCO+ in friedel –crafts reaction. From a comparative study of resonance stabilized intermediate carbocation of 1- and 2- substitution, it is obvious that

structures I,II,VI,VII, VIII and XII are more stable because they contain at least one benzene ring intact (because benzene has a large resonance energy).

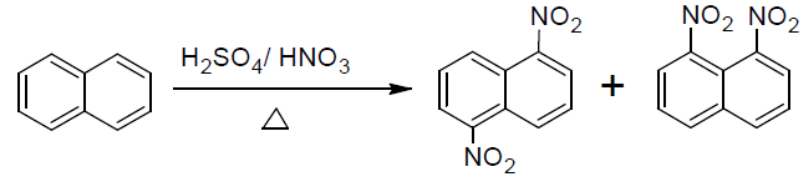
Out of these four i.e. I,II,VI and VII are involved during α-substitution while only two i.e. VIII and XII are involved during β-substitution. Consequently, the carbocation formed during the α-substitution and transition state leading to that ion is much more stable than the carbocation and the corresponding transition state formed during the β-substitution. Hence the α-substitution is the preferred orientation of substitution in naphthalene.

Nitration: Nitration of naphthalene with mixture of concentrated nitric acid and sulphuric acid yields predominantly the α-nitro naphthalene (95%) with minor amounts (5%) of β-Nitro naphthalene.



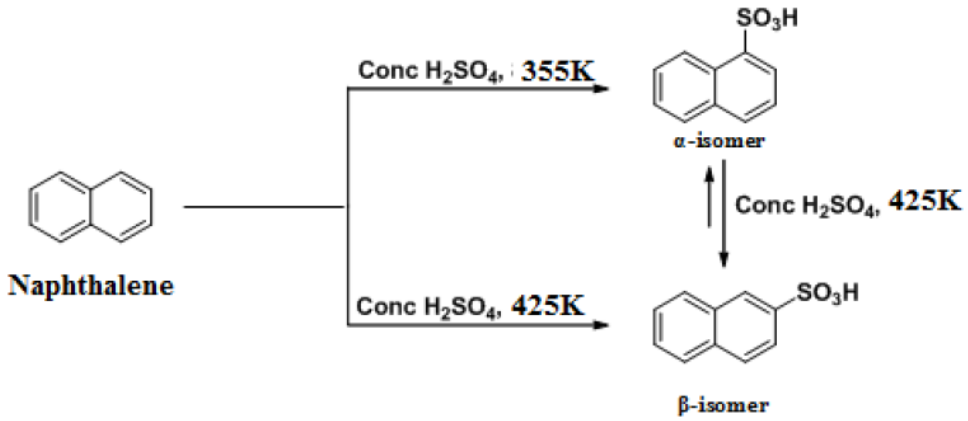
Naphthalene **α-nitronaphthalene (95%)** **β-nitronaphthalene (5%)**

However at higher temperature a mixture of 1,5-and 1,8-dinitro naphthalene are formed.



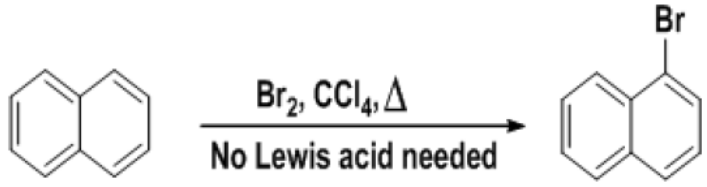
Naphthalene 1,5-dinitro naphthalene 1,8-dinitro naphthalene

Sulphonation : Naphthalene can be sulphonated at 355K to yield mainly i-naphthalene sulphonic acid whereas if the reaction is carried out at 425K, 2-naphthalene sulphonic acid is the main product. This is reversible. It has been shown that when 1-naphthalene sulphonic acid is heated, it is highly converted in to the 2-isomer.

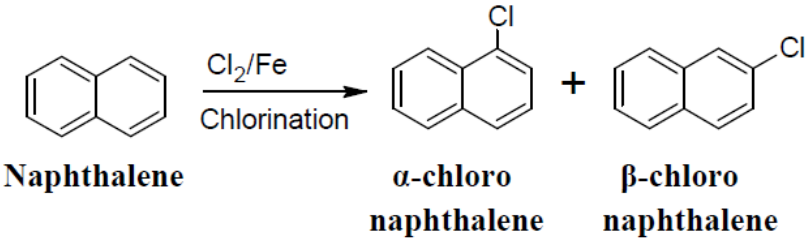


Halogenation:

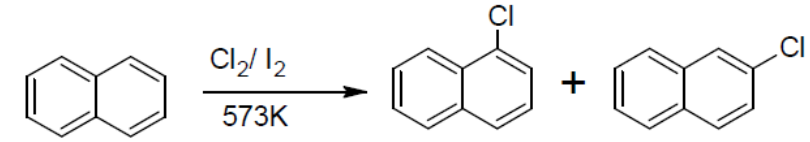
Halogenation of naphthalene takes place very readily and no catalyst is needed for the purpose. The reaction takes place almost exclusively at 1- positions. When brominated in boiling carbon tetrachloride solution, naphthalene gives 1-bromo derivative in good yield. 1-Chloronaphthalene can be obtained either by reacting naphthalene with sulphuryl chloride (SO2Cl2) in presence of aluminium chloride at 298K or by chlorination in the presence of ferric chloride.



Naphthalene **α-bromo naphthalene**



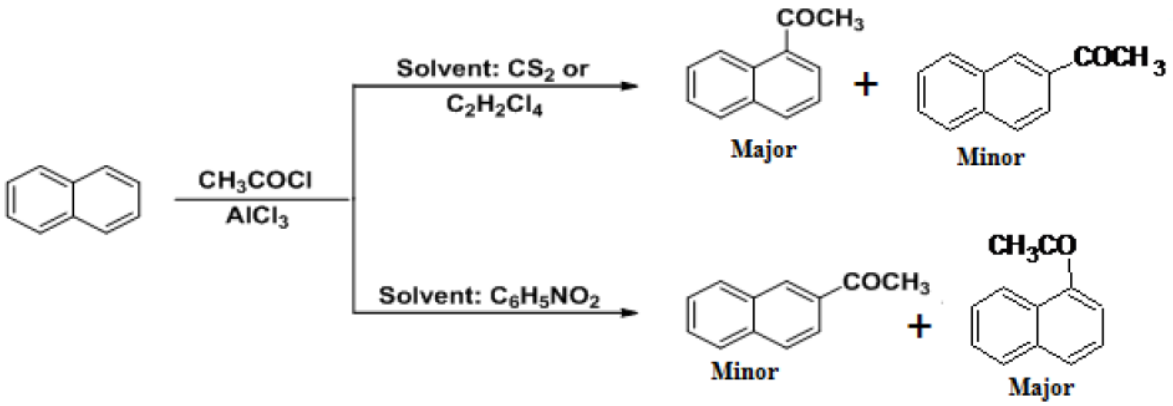
Naphthalene **α-chloro naphthalene** **β-chloro naphthalene**



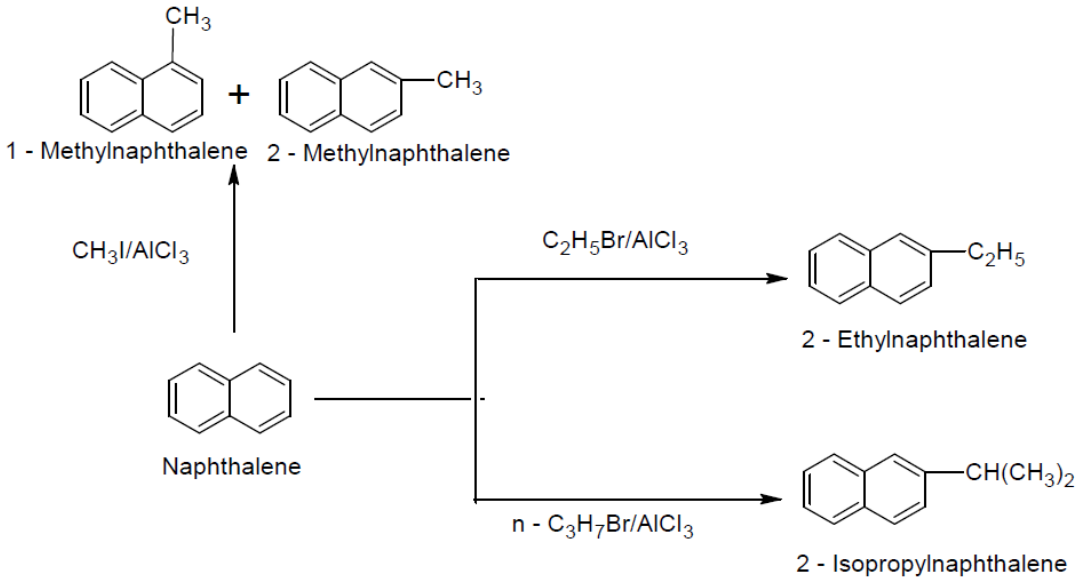
Naphthalene **α-isomer** **β-isomer**

Friedel crafts Reaction: Naphthalene undergoes friedel crafts acylation and alkylation gives acylated and alkylated product.

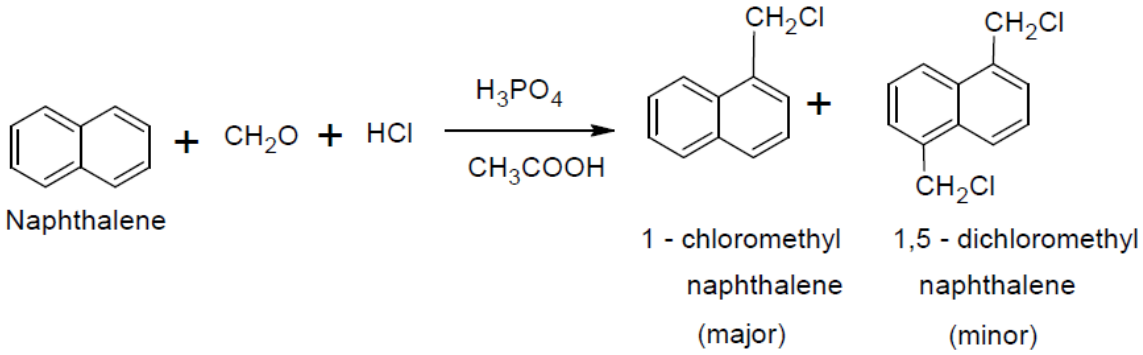
a) Friedel crafts acylation: Acylation of naphthalene gives 1- and 2- acyl naphthalene as a product but their proportion depends on the solvent used. For instant, acyl chloride in the presence of anhydrous aluminium chloride in carbon disulphide gives 1- and 2-acyl naphthalene in the ratio 3:1 wheras in nitrobenzene as the solvent the ratio is 1:9.



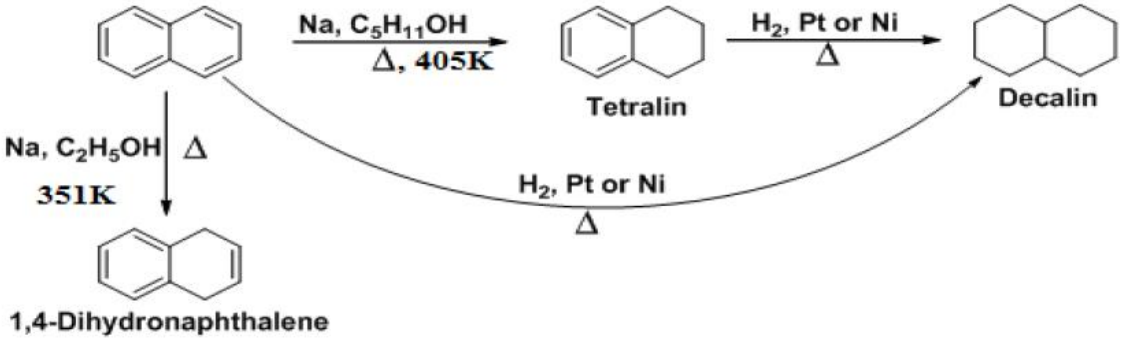
Friedel craft alkylation: Alkylation of naphthalene gives a mixture of α-and β-isomers is obtained, their relative proportions depending on the reaction conditions and the size of alkyl group to be introduced. Thus with CH3I a mixture α-and β-methyl naphthalenes is formed, while C2H5Br gives mainly β-ethylnaphthalene and n-C3H7Br forms only β-isopropyl naphthalene, with alcohols usually polyalkylated products are formed.



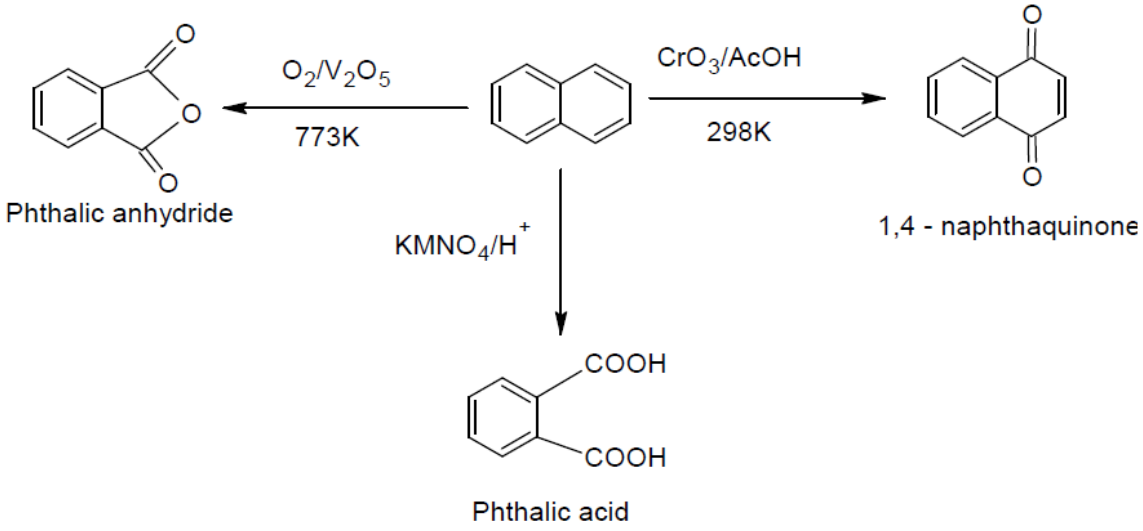
Chloromethylation: Naphthalene on reaction with paraformaldehyde , hydrochloric acid,glacial acidic acid and phosphoric acid gives α- chloromethyl naphthalene as the main product (56%) together with 1,5-bichloromethylnaphthalene.



Reduction: Unlike benzene, naphthalene on reduction forms number of products which depends on reducing agents used .Naphthalene on reduction with Na in C2H5OH (Birch reduction) gives 1,4-dihydronaphthalene, with sodium in amyl alcohol at 405K gives tetralin and with Pt/Ni gives decalin. Tetralin and decalin are widely used as solvents for vernishes, lacquers etc.

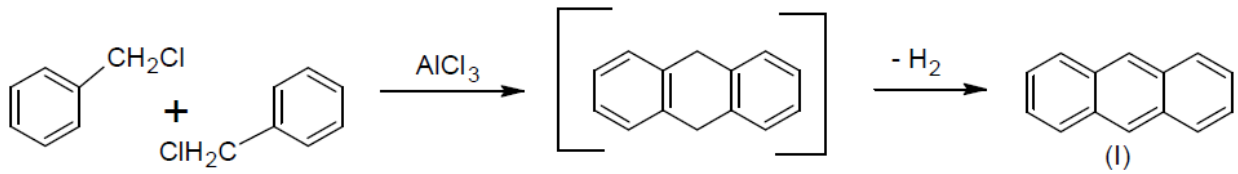


Oxidation: Naphthalene on oxidation with oxygen or air in the presence of vanadium pentoxide catalyst forms phthalic anhydride .In place of vanadium pentoxide,Conc. Sulphuric acid with mercuric sulphate can be used and in presence of potassium permanganate in acid it gives phthalic acid while with chromic acid in acetic acid gives 1,4-naphthaquinone

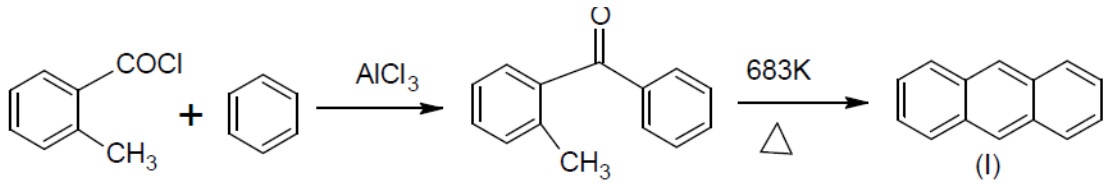


Anthracene , C14H10

Friedel crafts alkylation between two molecules of benzyl chloride gives 9.10-dihydroanthracene which is oxidized readily under the reaction conditions yielding anthracene.

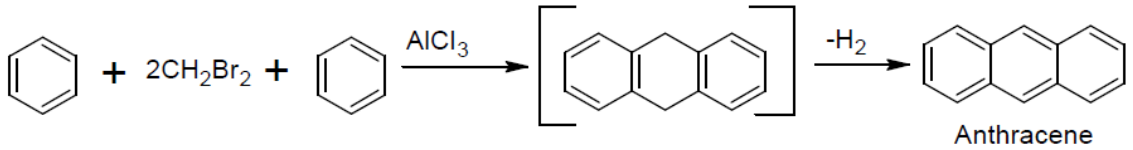


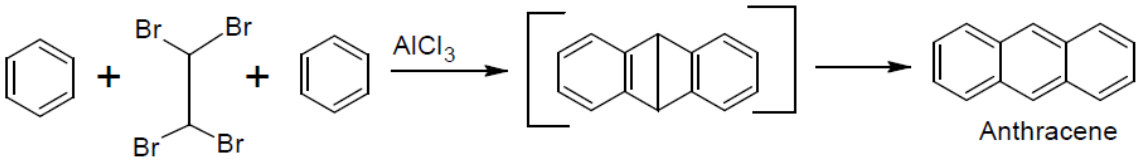
2.This method is based on Elbs reaction in which a polynuclear aromatic hydrocarbon having an anthracene moiety is formed by pyrolysis of a diaryl ketone containing a methyl or methylene group ortho to the carbonyl group.



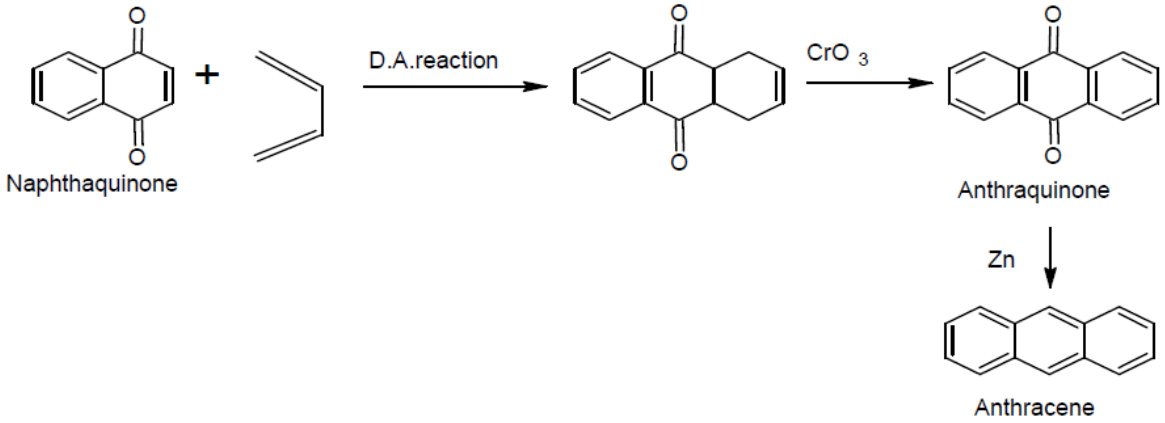
From benzene and methylene dibromide and acetylene tetrabromide:

This method involving Friedel crafts alkylation of benzene with either methylene dibromide or with acetylene tetrabromide.





This synthesis consists in Diels-Alder reaction between naphthaquinone and butadiene followed by oxidation of the intermediate with chromic acid in glacial acetic acid to give anthraquinone which on distillation with zinc dust yields anthracene.

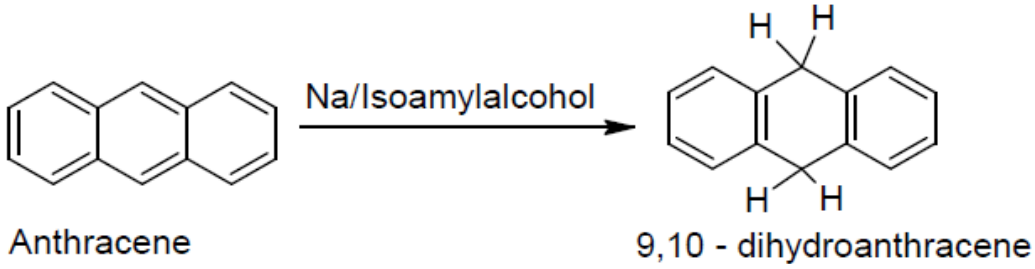


It is a colourless solid, m.p.489K, with a green-yellow or blue fluorescence. It is insoluble in water and sparingly soluble in organic solvents.

Chemical reaction: It resembles benzene and naphthalene in many of its chemical reactions. It is very reactive at positions 9- and 10.Electrophilic substitution,such as halogenations or nitration, preferably gives 9- or 9-,10-disustituted products. The greater reactivity of the 9,10-positions is readily understandable if we consider the relative stabilities of the σ-complexes formed as a result of electrophile attack 1-,2- and 9-positions. The attack at 1- or 2- position forms a carbocation having a naphthalene moiety whereas the σ-complex formed by attack at 9-position has two benzene rings. The resonance stabilization in the latter will be more since

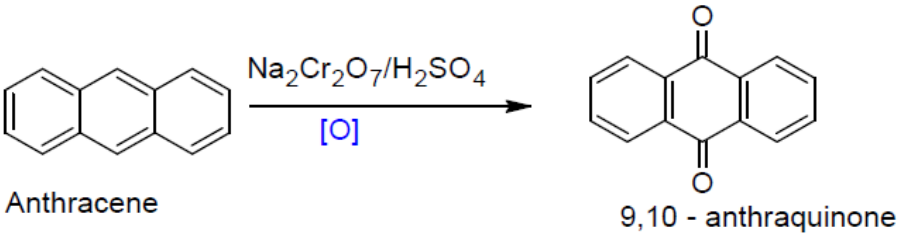
the total resonance energy of two benzene rings is greater than that of a naphthalene ring.

1. Reduction: When reduced with sodium and isoamyl alcohol it forms 9,10-dihydroanthracene which on heating or on reaction with conc. H2SO4 reforms anthracene.

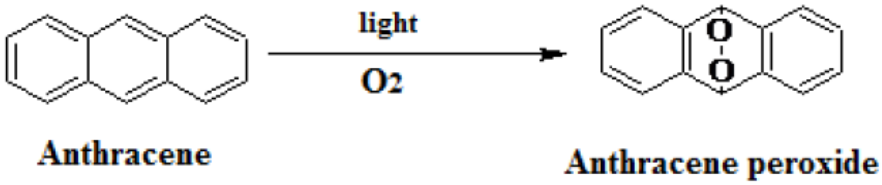


Catalytic reduction (H_2/Ni at 473-523K) gives tetra-, octa- and finally perhydroanthracene ($C_{14}H_{24}$).

2. Oxidation: It is readily oxidized with chromic acid to 9,10-anthraquinone**.**

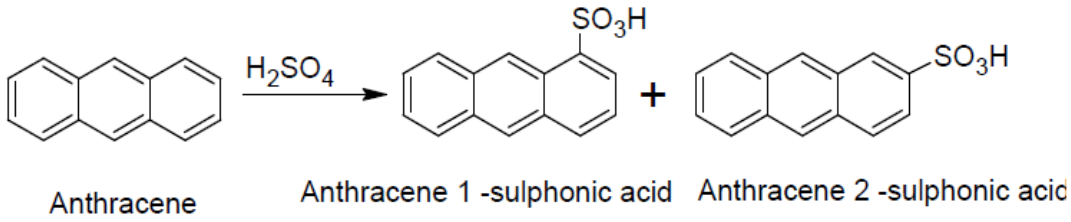


It adds one molecule of oxygen in the presence of light to form a colourless peroxide.



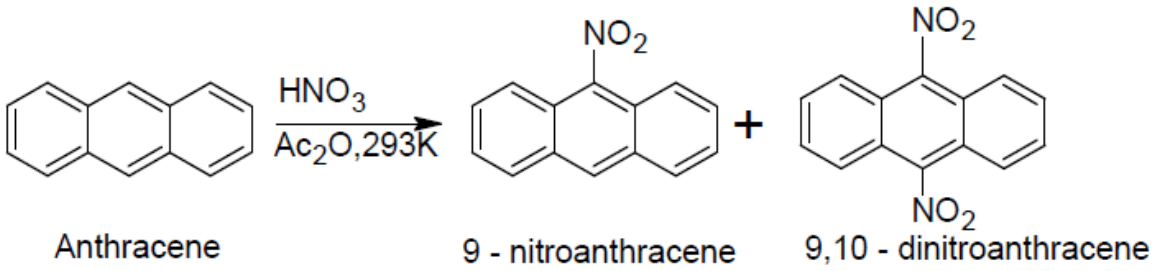
Electrophilic substitution reactions: It undergoes electrophilic substitution reactions like sulphonation,nitration, halogenations etc.

I] Sulphonation: It reacts with H2SO4 to form a mixture of 1-and 2- sulphonic acids.

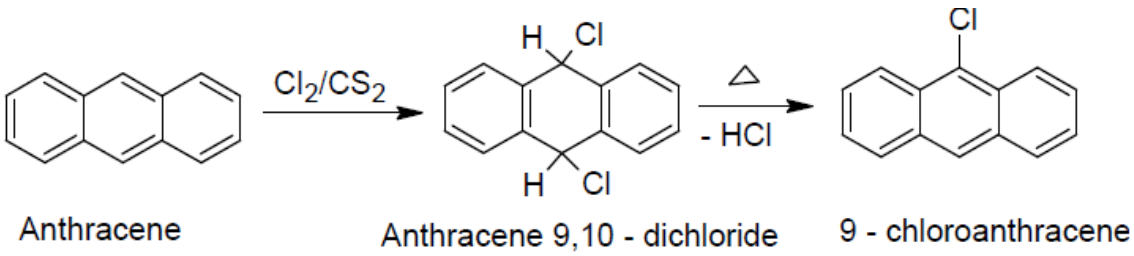


At higher temperatures the 2- sulphonic acid is the main product. However, unlike naphthalene, the 1-sulphonic acid of antharcene does not rearrange to 2- sulphonic acid. Sulphonation with conc.H2SO4 gives 1,5-and 1,8-anthracene disulphonic acids.

Nitration: Anthracene on nitration with concentrated nitric acid in the presence of acetic anhydride gives a mixture of 9-nitro anthracene and 9,10-dinitro anthracene.



Halogenation: Chlorination with chlorine in carbon disulphide solvent in cold gives anthracene dichloride which on heating or treatment with alkali yields 9-chloroanthracene.

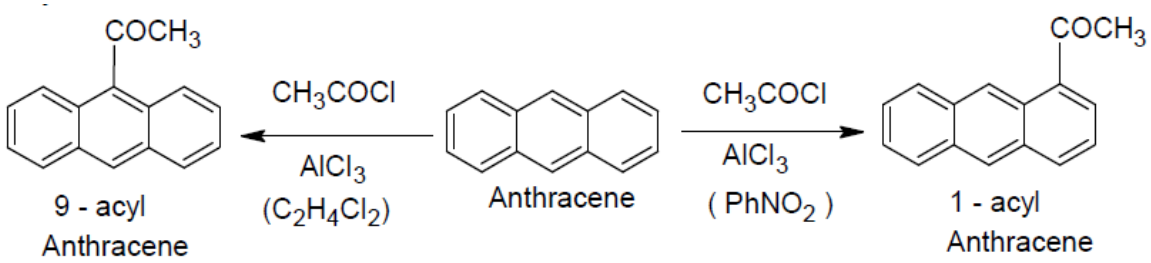


9-chloroanthracene may also be obtained by heating anthracene with cuprous chloride in carbon tetrachloride solution. Reaction of sulphuryl chloride with anthracene gives 9,10-dichloro,9,10-dihydro-anthracene. Both 9-chloroanthracene and anthracene dichloride on

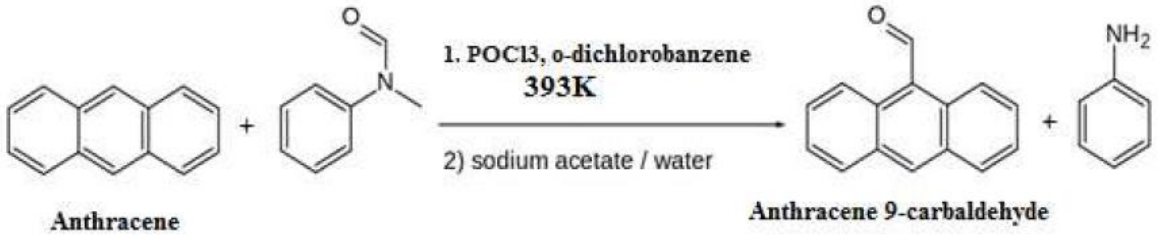
oxidation form anthraquinone.

Bromination in carbon tetrachloride follows the same course first forming anthracene dibromide (9,10-dibromo-9,10- dihydro anthracene which on heating yields 9-bromo anthracene.

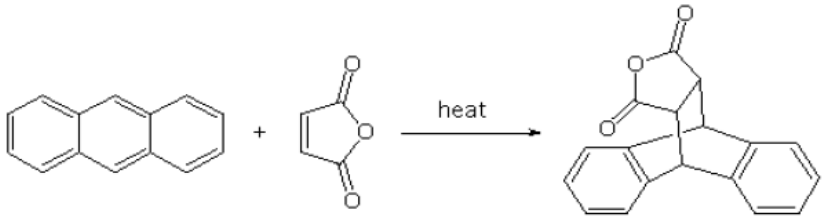
IV] Friedel craft acylation: Friedel crafts acylation of anthracene with acetyl chloride in benzene or nitrobenzene gives a complex mixture. However, the main product in nitro benzene as solvent is the 1-acetyl derivative whereas in ethylene dichloride it is the 9-acetyl derivative.



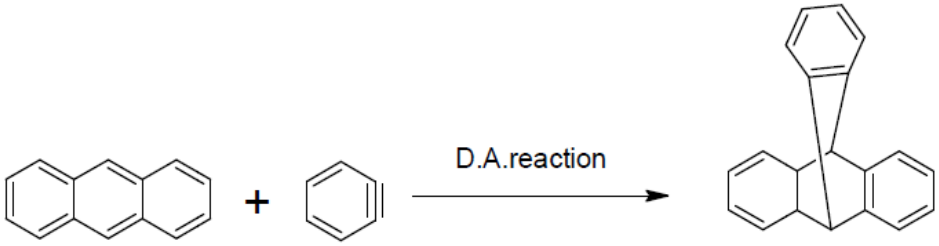
Formylation by Vilsmeier – Haack method: Anthracene can be formylated exclusively at the 9-position. The reaction of anthracene with *N*-methylformanilide, also using phosphorus oxychloride gives Anthracene 9-carbaldehyde.



5. Diels-Alder Reaction: Anthracene undergoes facile Diels-Alder reaction with maleic anhydride and benzyne to give 1,4- addition products.

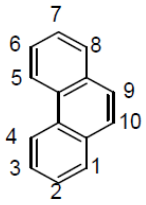


anthracene | maleic anhydride | 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic anhydride



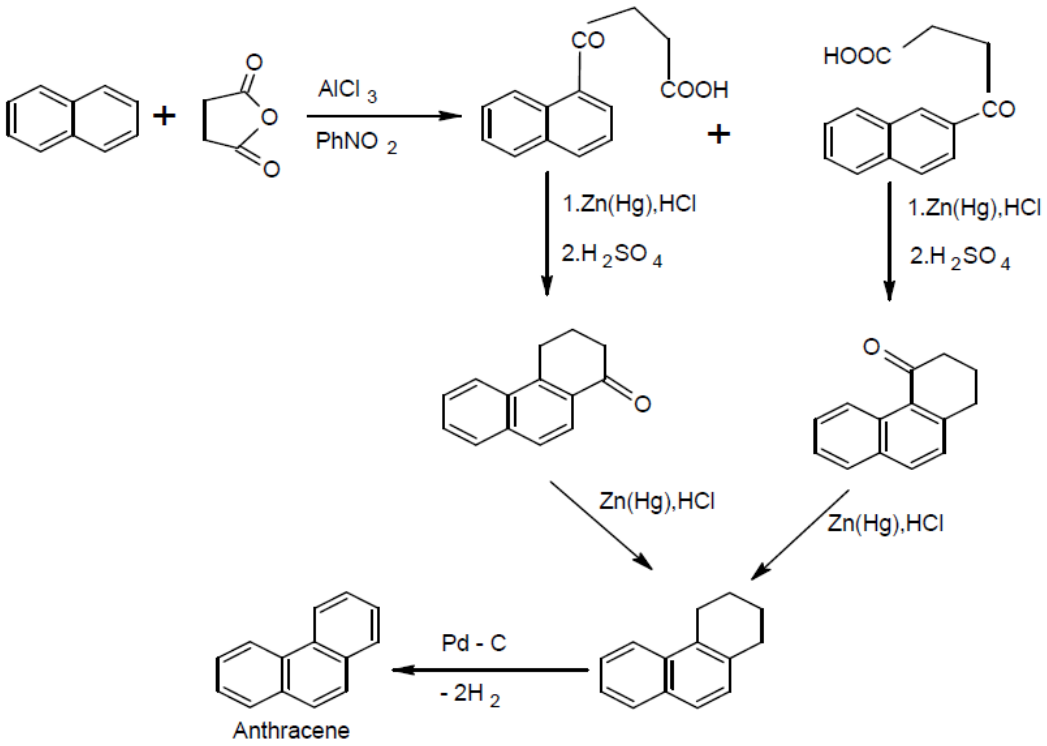
Anthracene | Benzyne | Triptycene

Phenanthrene –



Phenanthrene

Haworth synthesis: Succinoylation of naphthalene produces two isomeric keto acids: β-(1-naphthoyl) propionic acid and β-(2-naphthoyl) propionic acid. These two isomers can be readily separated. Clemmensen reduction affords γ-(1-naphthyl) butyric acid and γ-(2-naphthyl)-butyric acid respectively. Acid catalysed cyclisation gives 1-keto-1,2,3,4-tetrahydro- and 4-keto-1,2,3,4-tetrahydrophenanthrene. Clemmensen reduction of either isomer followed by aromatization.



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1.What are polynuclear compounds ? How they are classified ? Give examples of each group.
2. Discuss the constitution of naphthalene.
3. What is modern view regarding the structure of naphthalene ?
4. How will you show that naphthalene has two benzene rings fused in o-position ?
5. Write note on:
i) Orientation in naphthalene ring system.
ii) Electrophilic substitution reactions of naphthalene.
iii) Bucherer reaction
iv) Aromatic nature of naphthalene
v) Sulphonation of naphthalene
vi) Electrophilic substitution reactions of anthracene
6. How can α- and β- naphthols and naphthylamines be obtained ?
7. In what respect anthracene and phenanthrene resemble benzene? Explain why position 9,10 are reactive in them.
8. Give one synthesis for each one of the following:
i) Anthracene ii) Naphthalene c) Phenanthrene
9. Explain why α- position of naphthalene is more reactive than β-position ?
10.What product(s) are formed when naphthalene is reacted with :
a) Cl2/Fe b) CrO3/AcOH at298K c) Conc.H2SO4 at 355K d) HNO3/ Conc.H2SO4
11. Describe the isolation of anthracene from coal tar.
12 . How will be establish the structure of anthracene on the basis of analytical evidence ?
13. Write the resonating structures of anthracene and naphthalene
14. How will you synthesize α- and β-naphthols?

15. Explain in Haworth synthesis, the clemmensen reduction of the keto acid is essential before cyclisation.
16. What are the methods used for synthesis of phenanthrene?
17.Explain anthracene is more reactive than naphthalene.
18. Why the 9,10-position of anthracene are very reactive ?
19. Illustrate the following:
i) Elbs reaction for the synthesis of anthracene
ii) Bardhan-Sengupta synthesis of phenanthrene
20. Comment on the modern views about the naphthalene structure.
21. What are naphthyl amines? How are they prepared ? Give their chemical reactions.
22. Why naphthalene is less aromatic than benzene
23. Give the oxidation and reduction reactions of naphthalene.
24. How will you prepared naphthalene from benzaldehyde and benzene ?
25. How will you synthesize naphthalene ? Give its chemical reactions with respect to sulphonation, chloromethylation and friedel crafts alkylation.

POSSIBLE QUESTIONS

UNIT II

PART A

Multiple Choice Questions

1. The correct structure of benzene diazonium chloride which explain all the properties of the compound was given by
   a. Greiss b. Kekule c. **Bloomstrand** d. Huckel

2. Benzene diazonium chloride is prepared from
   a. An aromatic primary amine with sodium nitrite b. **An aromatic primary amine and nitrous acid** c. Aromatic primary amine with hydrochloric acid d. Secondary amine with sodium nitrite

3. On warming the solution diazonium salt with water it gives
   a. Bromo benzene b. aniline c. Copper d. **phenol**

4. Electrophilic substitution of naphthalene takes place at
   a. 1^{st} position b. 2^{nd} position 3. **1^{st} or 2^{nd} position** 4. 8^{th} position

5. $-N_2Cl$ group can be replaced by –H by means of
   a. **Hypophosphorous acid** b. Phosphoric acid c. Phosphorous acid d. Metaphosphoric acid

6. Benzene diazonium chloride reacts with cuprous chloride to give
   a. **Chlorobenzene** b. aniline c. Copper diazonium chloride d. diazomethane

7. Phthalic acid is obtained when oxidized with acid permanganate
   a. **Naphthalene** b. anthracene c. phenanthrene d. benzaldehyde

8. Nitration of naphthalene with con.nitric acid and sulphuric acid at higher temperature gives
   a. 1,5-di nitro naphthalene b. 1,8-di nitro naphthalene c. **A mixture of 1,5-di nitro naphthalene and 1,8-di nitro naphthalene** d. 3- nitro naphthalene
9. Coupling reaction involves the reaction between benzene diazonium chloride and
   a. Ether b. Carboxylic acid c. Carboxylic acid derivatives d. **aniline**

10. Benzene diazonium chloride reacts with cuprous bromide to give bromobenzene, This reaction is
    a. **Sandmeyer reaction** b. Gattermann reaction c. Gattermannkoch reaction d. Clemenson reduction

11. An Example for polynuclear hydrocarbons
a. **Napthalene** b. aniline c. phenol d. benzaldehyde

12. When compared to benzene naphthalene is more susceptible to
a. Hydrolysis b. Oxidation c. reduction d. **Oxidation and reduction**
13. Coupling reaction involves the reaction between benzene diazonium chloride and
a. Ether b. Carboxylic acid c. Carboxylic acid derivatives d. **aniline**

14. Benzene diazonium chloride reacts with cuprous bromide to give bromobenzene, This reaction is
a. **Sandmeyer reaction** b. Gattermann reaction c. Gattermannkoch reaction d. Clemenson reduction

15. Phthalic acid is obtained when oxidized with acid permanganate
a. Naphthalene b. anthracene c. phenanthrene d. benzaldehyde

16. Nitration of naphthalsene with con.nitric acid and sulphuric acid at higher temperature gives
a. 1,5-di nitro naphthalene b. 1,8-di nitro naphthalene c. **A mixture of 1,5-di nitro naphthalene and 1,8-di nitro naphthalene** d. 3- nitro naphthalene

17. The correct structure of benzene diazonium chloride which explain all the properties of the compound was given by
a.Greiss b. Kekule c. **Bloomstrand** d. Huckel

18. Benzene diazonium chloride is prepared from
a. An aromatic primary amine with sodium nitrite b. **An aromatic primary amine and nitrous acid** c. Aromatic primary amine with hydrochloric acid d. Secondary amine with sodium nitrite

19. On warming the solution diazonium salt with water it gives
a. Bromo benzene b. aniline c. Copper d. **phenol**
20. Electrophilic substitution of naphthalene takes place at
a. 1^{st} position b. 2^{nd} position 3. **1^{st} or 2^{nd} position** 4. 8^{th} position

PART B

1. How benzene diazonium chloride is prepared
2. Write short notes on Sandmeyer reaction
3. How phenanthrene is prepared
4. Differentiate phenanthrene and anthracene
5. Explain what is meant by coupling reaction

PART C

1. What are the synthetic applications of benzene diazonium chloride
2. Explain the preparation and properties of naphthalene
3. Starting from benzene diazonium chloride how to prepare
   (i) iodobenzene (ii) Phenol (iii) aminoazobenzene (iv) Benzene
4. What is diazotization? How toluene diazonium chloride is prepared in the laboratory.
5. How phenol react with diazonium salts
6. Describe five reactions of diazonium salts in which nitrogen is evolved.
7. Explain the preparation and properties of Phenanthrene
8. Elucidate the structure of naphthalene
9. How to prepare anthracene. What are its properties.

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)
II B.Sc. Chemistry
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

UNIT II

Multiple choice questions (Each carries one mark: for online examination)

S.No	Questions	Answer A	Answer B	Answer C	Answer D	Answer
1.	The correct structure of benzene diazonium chloride which explain all the properties of the compound was given by	Greiss	Kekule	Bloomstrand	Huckel	Bloomstrand
2.	Diazotisation of aniline can be carriedout at the temperature range	73-78K	173-178K	373-378K	273-278K	273-278K
3.	$-N_2Cl$ group can be replaced by –H by means of	Hypophosphorous acid	Phosphoric acid	Phosphorous acid	Metaphosphoric acid	Hypophosphorous acid
4.	Coupling reaction involves the reaction between benzene diazonium chloride and	ether	Carboxylic acid	Carboxylic acid derivatives	phenol	phenol
5.	Coupling reaction involves the reaction between benzene diazonium chloride and	ether	Carboxylic acid	Carboxylic acid derivatives	aniline	aniline
6.	Benzene diazonium chloride can be converted into fluorobenzene using	CuF	Cu/HF	HBF_4	F_2	HBF_4
7.	The coupling reaction between benzene diazonium	Strongly alkaline medium	Weakly alkaline medium	Strongly acidic medium	Weakly acidic medium	Weakly alkaline medium

	chloride and animine takes place in					
8.	Sodium nitrite and dil hydrochloric acid gives	Nitric acid	Sulphuric acid	Sulphurous acid	Nitrous acid	Nitrous acid
9.	An aromatic primary amine reacts with Sodium nitrite and dil hydrochloric acid gives	Benzene diazonium chloride	nitrosoamine	Yellow colour nitroso compound	Diazo methane	Benzene diazonium chloride
10.	An aromatic primary amine reacts with nitrous acid to give	Benzene diazonium chloride	nitrosoamine	Yellow colour nitroso compound	Diazo methane	Benzene diazonium chloride
11.	Benzene diazonium chloride is prepared from	An aromatic primary amine with sodium nitrite	An aromatic primary amine and nitrous acid	Aromatic primary amine with hydrochloric acid	Secondary amine with sodium nitrite	An aromatic primary amine and nitrous acid
12.	Benzene diazonium chloride reacts with cuprous chloride to give	Chlorobenzene	aniline	Copper diazonium chloride	diazomethane	Chlorobenzene
13.	Benzene diazonium chloride reacts with cuprous bromide to give	Bromo benzene	aniline	Copper diazonium chloride	diazomethane	Bromo benzene
14.	Benzene diazonium chloride reacts with cuprous cyanide to give	cyano benzene	aniline	Copper diazonium chloride	diazomethane	cyano benzene
15.	Benzene diazonium chloride reacts with copper and hydrogen chloride to give	Chlorobenzene	aniline	Copper diazonium chloride	diazomethane	Chlorobenzene
16.	Benzene diazonium chloride reacts with cuprous bromide to give bromobenzene	Sandmeyer reaction	Gattermann reaction	Gattermann koch reaction	Clemenson reduction	Sandmeyer reaction
17.	Benzene diazonium chloride reacts with copper and potassium cyanide to give	cyano benzene	aniline	Copper diazonium chloride	diazomethane	cyano benzene
18.	Benzene diazonium chloride reacts with copper and	Bromo benzene	aniline	Copper diazonium chloride	diazomethane	Bromo benzene

	hydrogen bromide to give					
19.	Benzene diazonium chloride reacts with copper and hydrogen bromide to give	Sandmeyer reaction	Gattermann reaction	Gattermann koch reaction	Clemenson reduction	Gattermann reaction
20.	On warming the solution diazonium salt with potassium iodide solution to give	Bromo benzene	aniline	Copper diazonium chloride	Iodo benzene	Iodo benzene
21.	On warming the solution diazonium salt with water it gives	Bromo benzene	aniline	Copper diazonium chloride	phenol	phenol
22.	Decomposing diazonium fluoborate with sodium nitrite solution in the presence of copper powder it gives	Bromo benzene	aniline	Copper diazonium chloride	nitrobenzene	nitrobenzene
23.	P-amino azobenzene is obtained by reacting benzene diazonium chloride with	aniline	phenol	benzaldehyde	benzophenone	aniline
24.	P-hydroxy azobenzene is obtained by reacting benzene diazonium chloride with	aniline	phenol	benzaldehyde	benzophenone	phenol
25.	Compounds in which two or more rings are fused due to the sharing of two or more carbon atoms by two or more rings are called	Condensed polynuclear hydrocarbons	Aromatic compounds	Aliphatic compounds	Mixed amines	Condensed polynuclear hydrocarbons
26.	An Example for polynuclear hydrocarbons	Napthalene	aniline	phenol	benzaldehyde	Napthalene
27.	Phenanthrene is a	Condensed polynuclear hydrocarbons	Aromatic aldehyde	Aromatic ketone	Aromatic alcohol	Condensed polynuclear hydrocarbons
28.	An Example for polynuclear hydrocarbons	Anthracene	aniline	phenol	benzaldehyde	Anthracene
29.	In naphthalene benzene rings are fused in	Para positions	Meta positions	Ortho positions	Ortho and meta positions	Ortho positions

30.	Resistant to addition reaction	Naphthalene	ethylene	propylene	butylene	Naphthalene
31.	Undergoes electrophilic substitution reactions	Anthracene	ethylene	propylene	butylene	Naphthalene
32.	Naphthalene on oxidation with acid permanganate gives	Benzoic acid	Furoic acid	Phthalic acid	Phthalic anhydride	Phthalic acid
33.	Phthalic acid is obtained when oxidized with acid permangnate	Naphthalene	anthracene	phenanthrene	benzaldehyde	Naphthalene
34.	4-phenylbutene is passed over red hot calcium oxide to give	Naphthalene	anthracene	phenanthrene	benzaldehyde	Naphthalene
35.	Nitronaphthalene on oxidation gives	Benzoic acid	Furoic acid	Nitro Phthalic acid	Phthalic anhydride	Nitro Phthalic acid
36.	Aminonapthalene on oxidation gives	Benzoic acid	Furoic acid	Phthalic acid	Phthalic anhydride	Phthalic acid
37.	Alpha naphthol on distillation with Zinc gives	Naphthalene	anthracene	phenanthrene	benzaldehyde	Naphthalene
38.	Shape of naphthalene molecule is	tetrahedral	planar	trigonal	bipyramidal	planar
39.	The length of C1-C2 bond is	1.36A	1.40A	1.54A	1.22A	1.36A
40.	The length of C2-C3 bond is	1.36A	1.40A	1.54A	1.22A	1.40A
41.	The resonance enthalpy of naphthalene is	80 K cal	61 K cal	180 K cal	30 K cal	61 K cal
42.	All the carbon atoms in naphthalene are in	SP hybridisation	SP^2 hybridisation	SP^3 hybridisation	D^2 SP hybridisation	SP^2 hybridisation
43.	When compared to benzene naphthalene is more susceptible to	Hydrolysis	Oxidation	reduction	Oxidation and reduction	Oxidation and reduction
44.	Electrophilic substitution of naphthalene takes place at	1^{st} position	2^{nd} position	1^{st} or 2^{nd} position	8^{th} position	1^{st} or 2^{nd} position
45.	Nitration of naphthalene with con.nitric acid and sulphuric acid at higher temperature gives	1,5-di nitro naphthalene	1,8-di nitro naphthalene	A mixture of 1,5-di nitro naphthalene and 1,8-di nitro	3- nitro naphthalene	A mixture of 1,5-di nitro naphthalene and 1,8-di nitro naphthalene

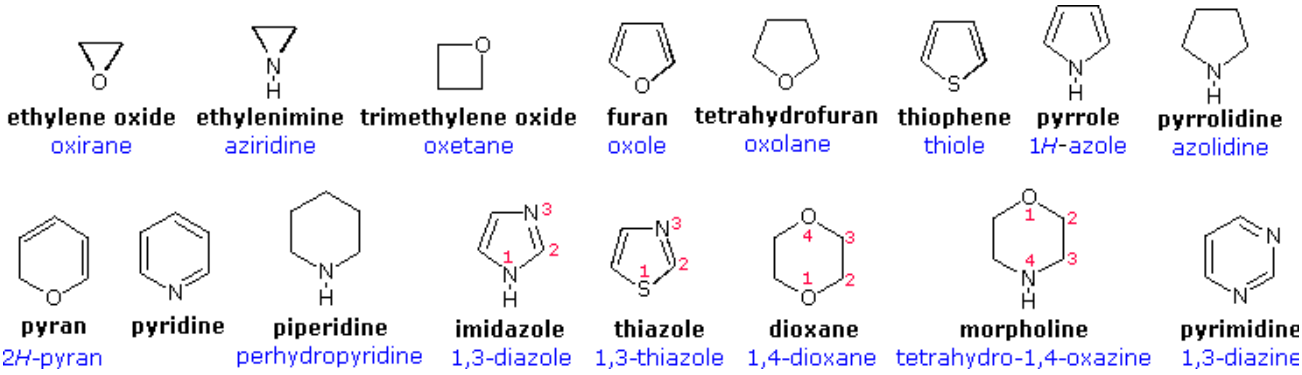
				naphthalene		
46.	Nitration of naphthalene with con.nitric acid and sulphuric acid gives predominantly	1-nitro naphthalene	2- nitro naphthalene	3- nitro naphthalene	4- nitro naphthalene	1-nitro naphthalene
47.	Sulphonation of naphthalene at 355K yields	1-naphthalene sulphonic acid	2- naphthalene sulphonic acid	A mixture of 1- and 2- naphthalene sulphonic acid	Cannot be sulphonated	1-naphthalene sulphonic acid
48.	Sulphonation of naphthalene at 425K yields	1-naphthalene sulphonic acid	2- naphthalene sulphonic acid	A mixture of 1- and 2- naphthalene sulphonic acid	Cannot be sulphonated	2-naphthalene sulphonic acid
49.	The reaction of naphthalene with sulphuryl chloride in presence of aluminium chloride gives	1-chloronaphthalene	2-chloronaphthalene	5-chloro naphthalene	1-, 2-, and 5-chloronaphthalene	1-chloronaphthalene
50.	Chlorination of naphthalene with ferric chloride gives	1-chloronaphthalene	2-chloronaphthalene	5-chloro naphthalene	1-, 2-, and 5-chloronaphthalene	1-chloronaphthalene
51.	Acylation of naphthalene gives	1-acyl naphthalene	2-acyl naphthalene	1- and 2- acyl naphthalene	A mixture of 1-acyl and 2-acyl naphthalene	A mixture of 1-acyl and 2-acyl naphthalene
52.	The ratio between 1- and 2-acyl naphthalene when the reaction takes place in presence of anhydrous $AlCl_3$	03:01	01:09	2;4	3;6	03:01
53.	The ratio between 1- and 2-acyl naphthalene when the reaction takes place in presence of nitrobenzene	03:01	01:09	2;4	3;6	01:09
54.	Naphthalene on reaction with paraformaldehyde, HCl, acetic acid and phosphoric acid gives	1-chloromethyl naphthalene	2-chloromethyl naphthalene	1- and 2-chloromethyl naphthalene	Polymer of naphthalene	1-chloromethyl naphthalene
55.	Naphthalene on Birch reduction gives	1,4-dihydro	1,2-dihydro Naphthalene	1,3-dihydro Naphthalene	2,4-dihydro Naphthalene	1,4-dihydro Naphthalene

56.	Naphthalene on reduction with Na and ethyl alcohol gives	1,4-dihydro Naphthalene	1,2-dihydro Naphthalene	1,3-dihydro Naphthalene	2,4-dihydro Naphthalene	1,4-dihydro Naphthalene
57.	Naphthalene on reduction with Na and amyl alcohol gives	1,4-dihydro Naphthalene	1,2-dihydro Naphthalene	1,3-dihydro Naphthalene	tetralin	tetralin
58.	Naphthalene on reduction with Pt and Nickel gives	1,4-dihydro Naphthalene	1,2-dihydro Naphthalene	5-decalin	tetralin	decalin
59.	Naphthalene on oxidation with oxygen in presence of Vanadium Pentoxide forms	Benzoic acid	Furoic acid	Phthalic acid	Phthalic anhydride	Phthalic anhydride

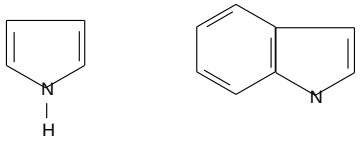
UNIT III
Heterocyclic Compounds

Classification and nomenclature, Structure, aromaticity in 5-numbered and 6-membered rings containing one heteroatom; Synthesis, reactions and mechanism of substitution reactions of: Furan, Pyrrole (Paal-Knorr synthesis, Knorr pyrrole synthesis, Hantzsch synthesis), Thiophene, Pyridine (Hantzsch synthesis),

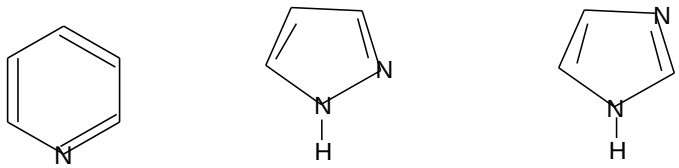
Heterocyclic compounds



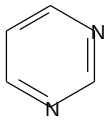
Some important heterocyclic compounds with N-heteroatom



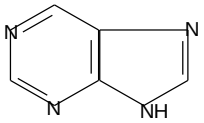
Pyrrole **Indole**



Pyridine **Pyrazole** **Imidazole**



Pyramidine



Purine

Nomenclature

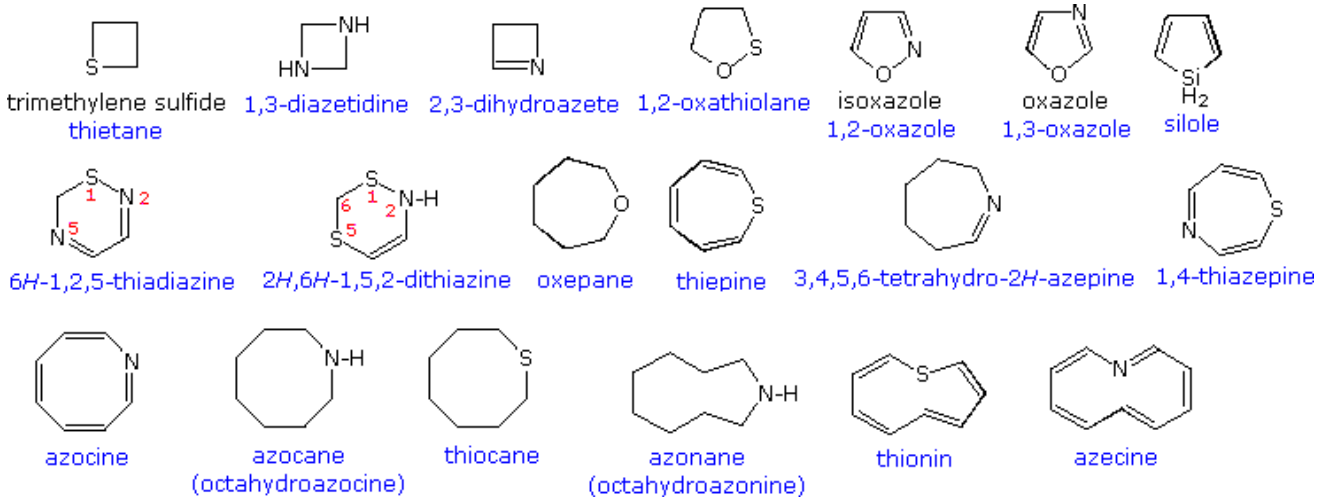
Devising a systematic nomenclature system for heterocyclic compounds presented a formidable challenge, which has not been uniformly concluded. Many heterocycles, especially amines, were identified early on, and received trivial names which are still preferred.

An easy to remember, but limited, nomenclature system makes use of an elemental prefix for the heteroatom followed by the appropriate carbocyclic name. A short list of some common prefixes is given in the following table.

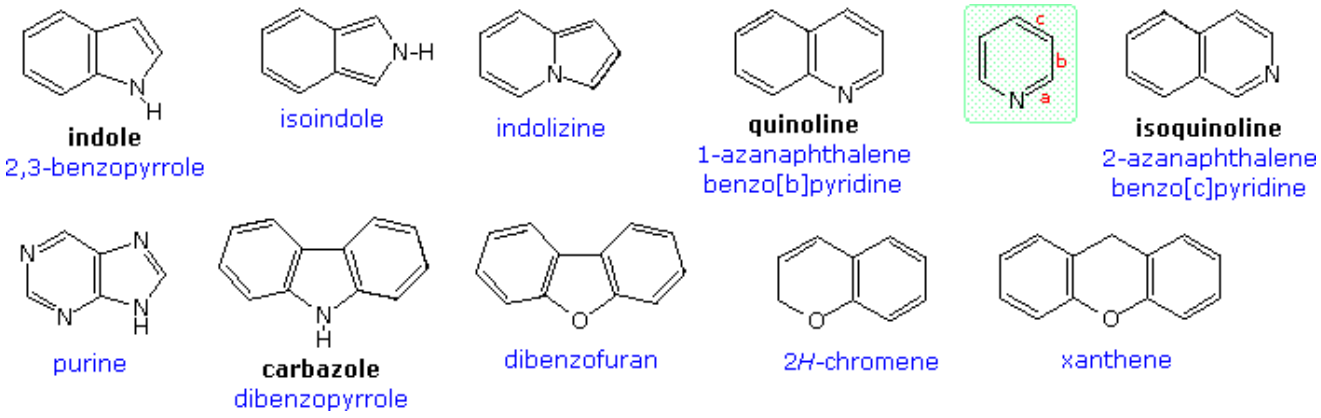
Examples of this nomenclature are:

- ethylene oxide = oxacyclopropane
- furan = oxacyclopenta-2,4-diene
- pyridine = azabenzene
- morpholine = 1-oxa-4-azacyclohexane.

Element	oxygen	sulfur	selenium	nitrogen	phosphorous	silicon	boron
Valence	II	II	II	III	III	IV	III
Prefix	Oxa	Thia	Selena	Aza	Phospha	Sila	Bora



All the previous examples have been monocyclic compounds. Polycyclic compounds incorporating one or more heterocyclic rings are well known. A few of these are shown in the following diagram. Thus, the location of a fused ring may be indicated by a lowercase letter which designates the edge of the heterocyclic ring involved in the fusion, as shown by the pyridine ring in the green shaded box.



Heterocyclic rings are found in many naturally occuring compounds. Most notably, they compose the core structures of mono and polysaccharides, and the four DNA bases that establish the genetic code

Classification

Heterocyclic compounds are:

- Heterocyclic compounds with three - membered rings
- Heterocyclic compounds with four - membered rings
- Heterocyclic compounds with five - membered rings
- Heterocyclic compounds with six - membered rings

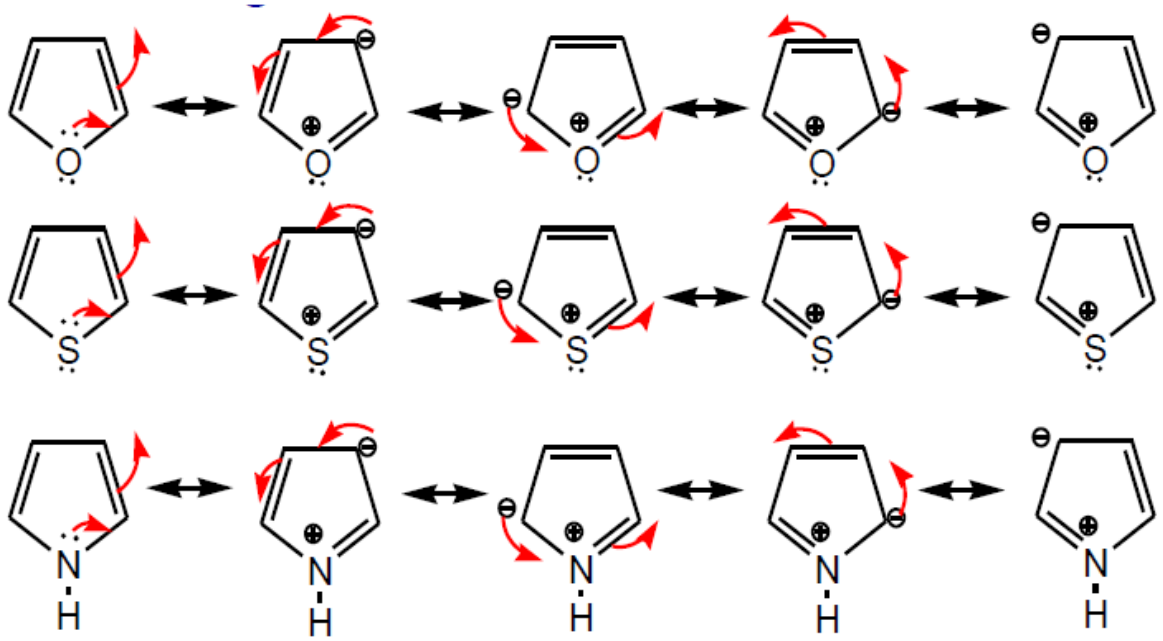
Aromaticity

Pyrrole furan and thiophene are aromatic because they fulfill the criteria for aromaticity, the extent of delocalization of the nonbonding electron pair is decisive for the aromaticity.
The grading of aromaticity is in the order of:

furan< pyrrole < thiophene< benzene

this order is consistent with the order of electronegativity values for oxygen (3.44), nitrogen (3.04) and thiophene.

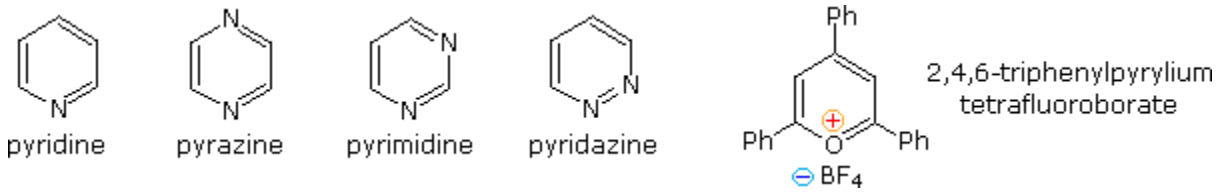
They tend to react by electrophilic substitution due appearance of –ve charge on carbon atoms due to delocalization of electron as shown in the resonance structures.



Evidences of aromatic character in pyrrole

1) All ring bonds are intermediates between single and double bonds.
2) It tends to react by electrophilic substitution
3) Its exceptional lack of basicity and acidity as a secondary amine compared to the aliphatic analog (pyrrolidine). This can be explained on the basis of participation of N lone pair in aromatic sextet thus the dipole moment of pyrrole compared with pyrolidine is reverted and thus protonation occurs at carbons not at N.

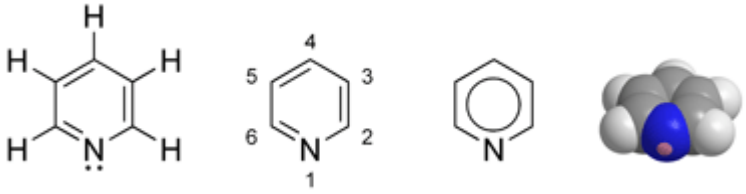
Fully unsaturated six-membered nitrogen heterocycles, such as pyridine, pyrazine, pyrimidine and pyridazine, have stable aromatic rings. Oxygen and sulfur analogs are necessarily positively charged, as in the case of 2,4,6-triphenylpyrylium tetrafluoroborate.



Heterocyclic compound with six membered rings

Pyridine

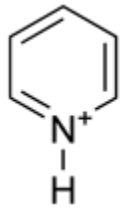
Pyridine is a simple aromatic heterocyclic organic compound with the chemical formula C_5H_5N used as a precursor to agrochemicals and pharmaceuticals, and is also an important solvent and reagent. It is structurally related to benzene, wherein one CH group in the aromatic six-membered ring is replaced by a nitrogen atom. It exists as a colorless liquid with a distinctive, unpleasant fish-like odor. The pyridine ring occurs in many important compounds, including nicotinamides.



Reactions

As a base

In organic reactions pyridine behaves both as a tertiary amine, undergoing protonation, alkylation, acylation, and N-oxidation at nitrogen, and as an aromatic compound, undergoing Nucleophilic substitutions.



Pyridinium cation

The nitrogen atom on pyridine features a basic lone pair of electrons. Because this lone pair is not delocalized into the aromatic pi-system, pyridine is basic with chemical properties similar to tertiary amines. The pKa of the conjugate acid is 5.21. Pyridine is protonated by reaction with acids and forms a positively charged aromatic polyatomic ion called pyridinium. The bond lengths and bond angles in pyridine and the pyridinium ion are almost identical. In addition, the pyridinium cation is isoelectronic with benzene. Pyidine is widely used as a ligand in coordination chemistry. Also important are its chelating derivatives 2,2'-bipyridine, consisting of two pyridine molecules joined by a single bond, and terpyridine, a molecule of three pyridine rings linked together.

Nucleophilic reactions at the ring

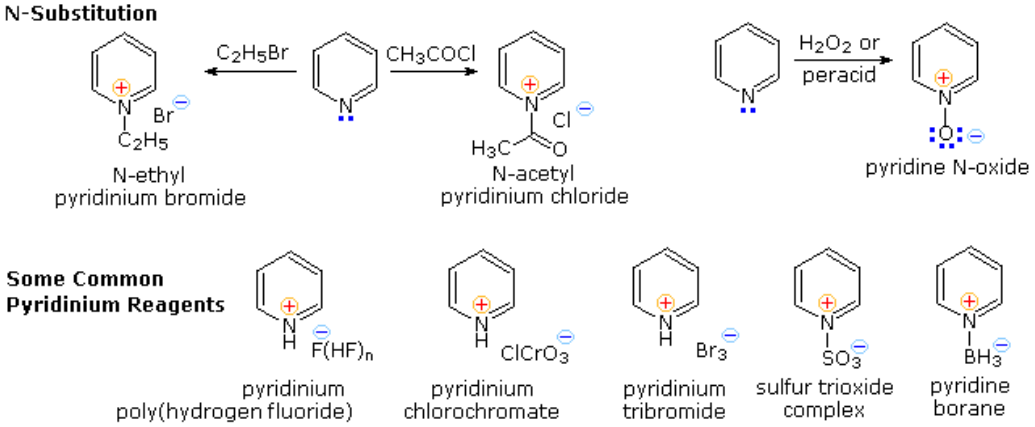
Nucleophilic aromatic substitution occurs at C-2 and at C-4. For example in the Chichibabin reaction, pyridine reacts with sodium amide to give 2-aminopyridine. In the Emmert reaction, named for Bruno Emmert), pyridine reacts with a ketone in presence of aluminium or magnesium and mercuric chloride to give the carbinol also at C_2. Pyridine is also used as a denaturant for antifreeze mixtures, for ethyl alcohol, for fungicides, and as a dyeing aid for textiles.

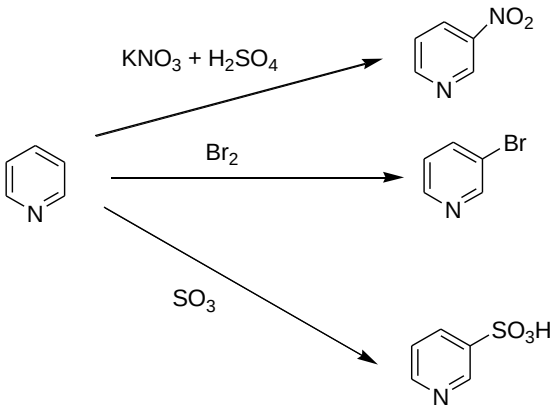
Electrophilic Substitution of Pyridine

Pyridine is a modest base (pKa=5.2). Since the basic unshared electron pair is not part of the aromatic sextet, as in pyrrole, pyridinium species produced by N-substitution retain the

aromaticity of pyridine. As shown below, N-alkylation and N-acylation products may be prepared as stable crystalline solids in the absence of water or other reactive nucleophiles. The N-acyl salts may serve as acyl transfer agents for the preparation of esters and amides. Because of the stability of the pyridinium cation, it has been used as a moderating component in complexes with a number of reactive inorganic compounds. Several examples of these stable and easily handled reagents are shown at the bottom of the diagram. The poly(hydrogen fluoride) salt is a convenient source of HF for addition to alkenes and conversion of alcohols to alkyl fluorides, pyridinium chlorochromate (PCC) and its related dichromate analog are versatile oxidation agents and the tribromide salt is a convenient source of bromine. Similarly, the reactive compounds sulfur trioxide and diborane are conveniently and safely handled as pyridine complexes.

Amine oxide derivatives of 3º-amines and pyridine are readily prepared by oxidation with peracids or peroxides, as shown by the upper right equation. Reduction back to the amine can usually be achieved by treatment with zinc (or other reactive metals) in dilute acid.

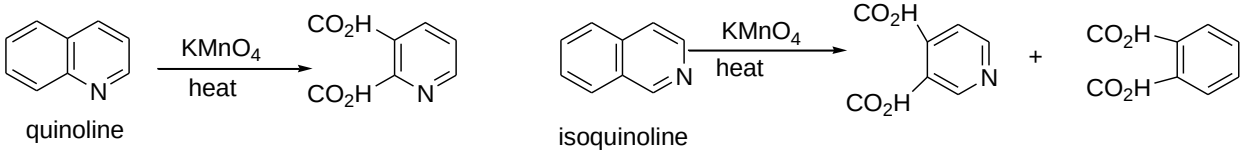




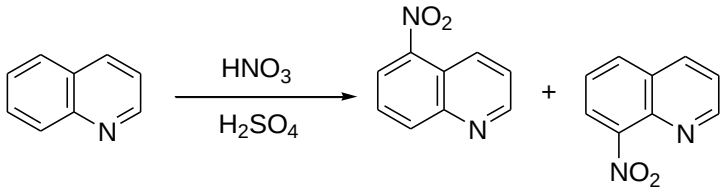
Subtitution

Properties of fused ring systems

Oxidation



Substitution



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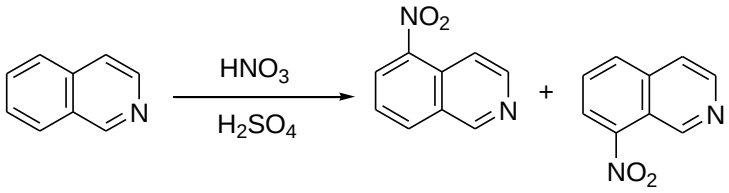

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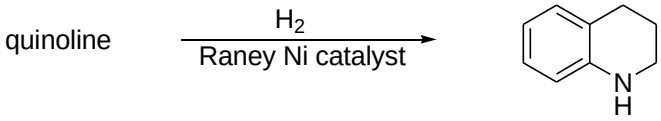
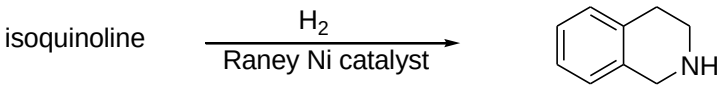
Reduction

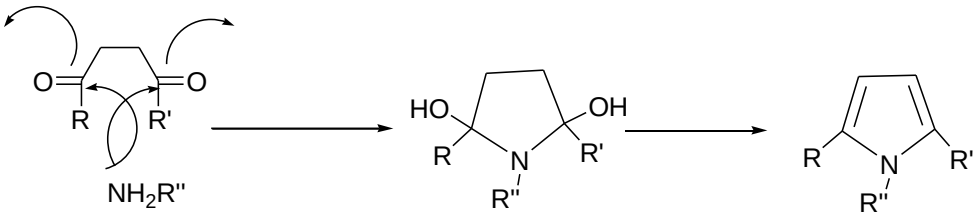




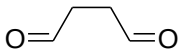
Heterocyclic compound with five-membered rings

Synthesis

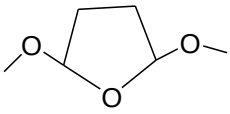
Strategy a: Paal – Knorr Synthesis

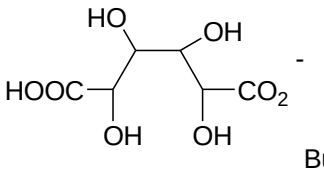


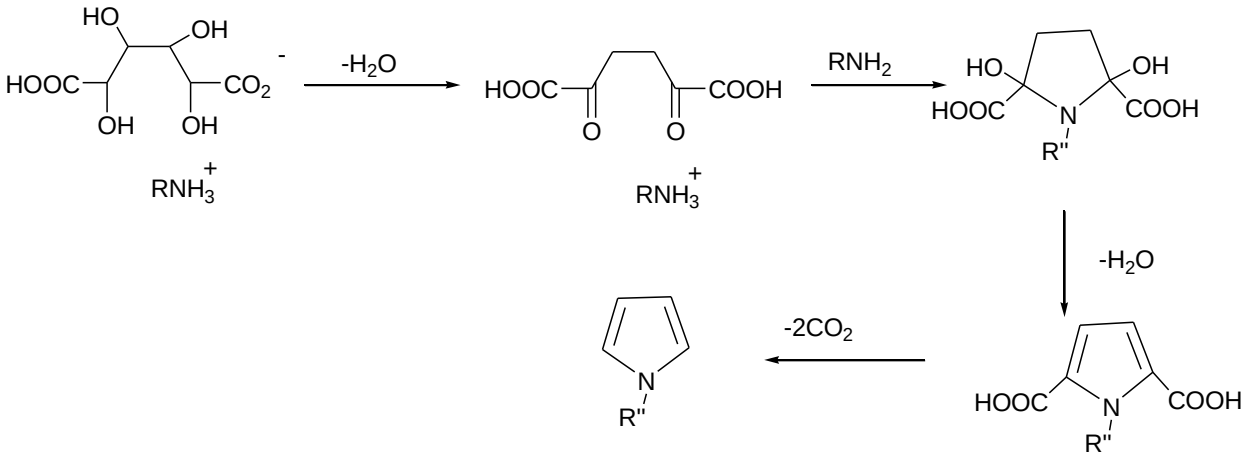
R'' = H, alkyl, aryl

R, R' = H  Unstable

Synthons



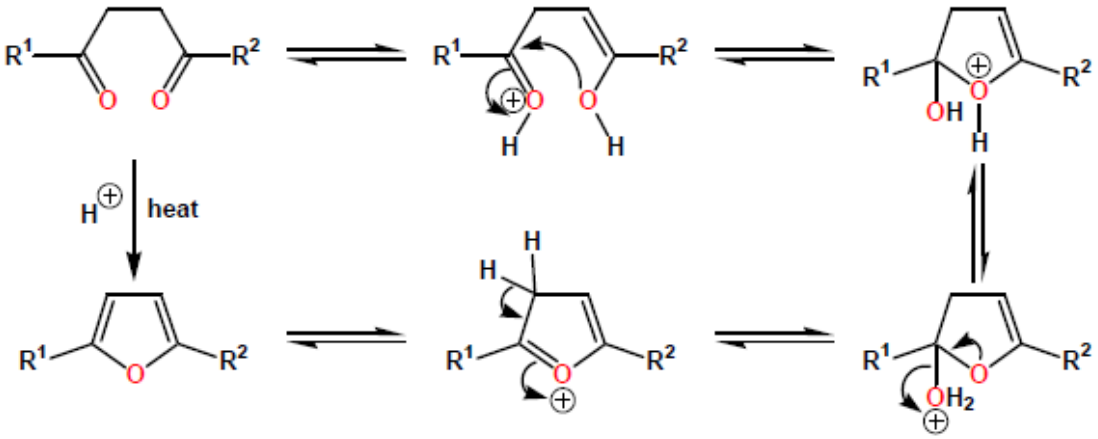




The **Paal–Knorr Synthesis** in is a reaction that generates either furans, pyrroles or thiophenes from 1,4-diketones . It is a synthetically valuable method for obtaining substituted furans and pyrroles, common structural components of many natural products.

The furan synthesis requires an acid catalyst.
In the pyrrole synthesis a primary amine participates and in that of
Thiophene for instance the compound phosphorous pentasulphide participates

Paal Knorr synthesis of furan
When 1,4-diketones are heated in presence of an acid it yields furans.



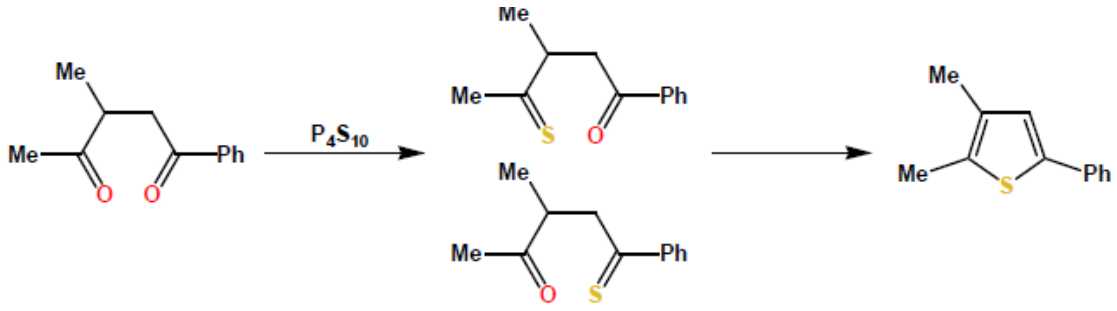
The reaction is usually reversible and can be used to convert furans into 1,4-diketones
• A trace of acid is required – usually TsOH (p-$MeC_6H_4SO_3H$)

The mechanism was proposed to occur via attack of the protonated carbonyl with the forming enol. In the commonly accepted mechanism, these diones would go through a common enol intermediate, meaning that the meso and *d*,*l*-racemic isomers would cyclize at the same rate as they form from a common intermediate.

The protonated carbonyl is attacked by the amine to form the hemiaminal. The amine attacks the other carbonyl to form a 2,5-dihydroxytetrahydropyrrole derivative which undergoes dehydration to give the corresponding substituted pyrrole. The reaction is typically run under protic or Lewis acidic conditions, with a primary amine. Use of ammonium hydroxide or ammonium acetate (as reported by Paal) gives the N-unsubstituted pyrrole.

Synthesis of Thiophenes by Paal Knorr type reaction ("4+1")

Reaction might occur *via* the 1,4-*bis*-thioketone

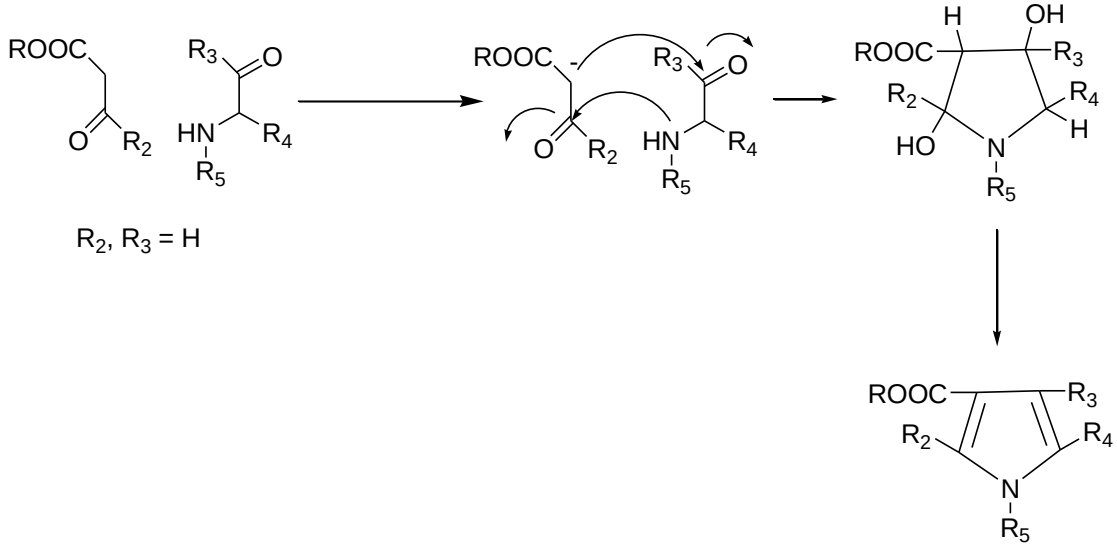


Thiophene synthesis is achieved via a mechanism very similar to the furan synthesis. The initial diketone is converted to thioketonea with a sulfurizing agent, which then undergoes the same mechanism as the furan synthesis. Most sulfurization agents are strong dehydrators and drive completion of the reaction. Early postulates toward the mechanism of the Paal-Knorr furan synthesis suggested that the thiophene was achieved by sulfurization of the furan product. Campaigne and Foye showed that treatment of isolated furans from the Paal-Knorr furan synthesis with phosphorous pentasulfide gave inconsistent results with the treatment of 1,4-dicarbonyls with phosphorus pentasulfide, which ruled out the sulfurization of a furan mechanism and suggests that the reaction proceeds via sulfurization of a dicarbonyl, producing a thioketone.

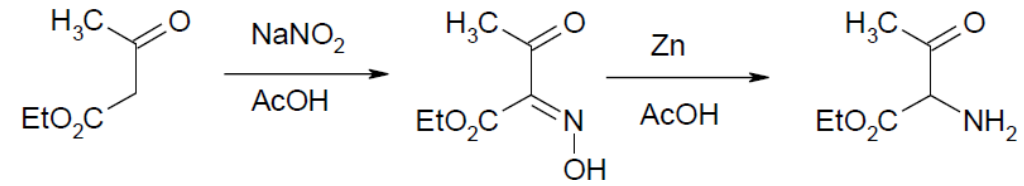
Strategy b; Knorr synth

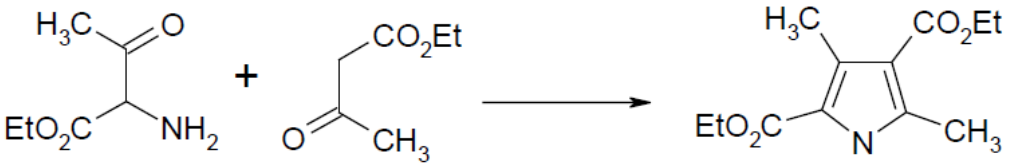
The Knorr pyrrole synthesis is a widely used chemical reaction that synthesizes substituted pyrroles. The method involves the reaction of an α-aminoketone and a compound containing a methylene group α- to a carbonyl group. The original Knorr synthesis employed two equivalents of ethyl acetoacetate, one of which was converted to ethyl 2- oximinoacetoacetate by dissolving it in glacial acetic acid, and slowly adding one equivalent of saturated aqueous sodium nitrite, under external cooling. Zinc dust was then stirred in, reducing the oxime group to the amine. This reduction consumes two equivalents of zinc and four equivalents of acetic acid. By this method we can prepare different pyrrole derivatives as: 2,4 substituted pyrrole or 2,3,4,5 substituted pyrrole.

General reaction is



Example



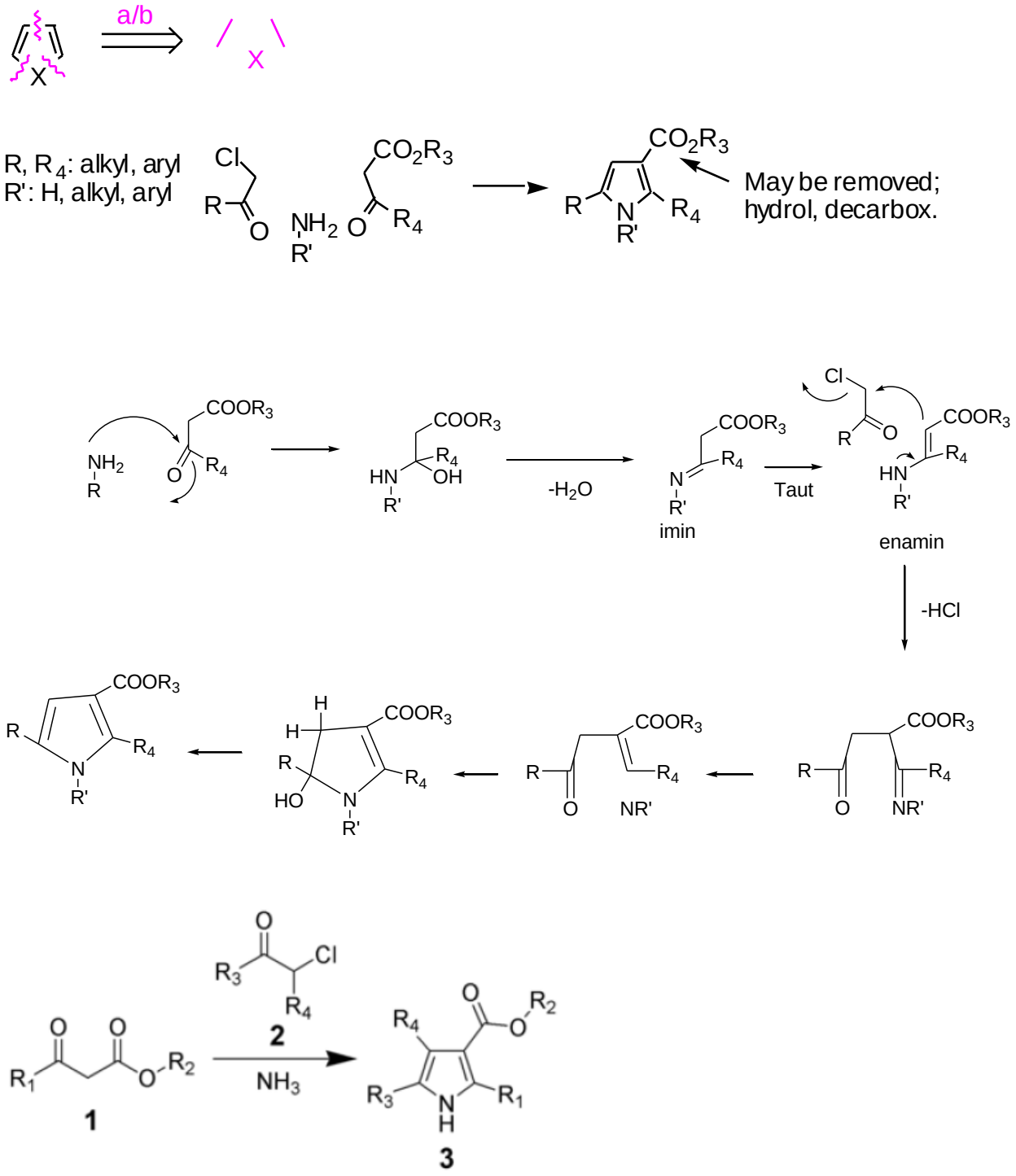


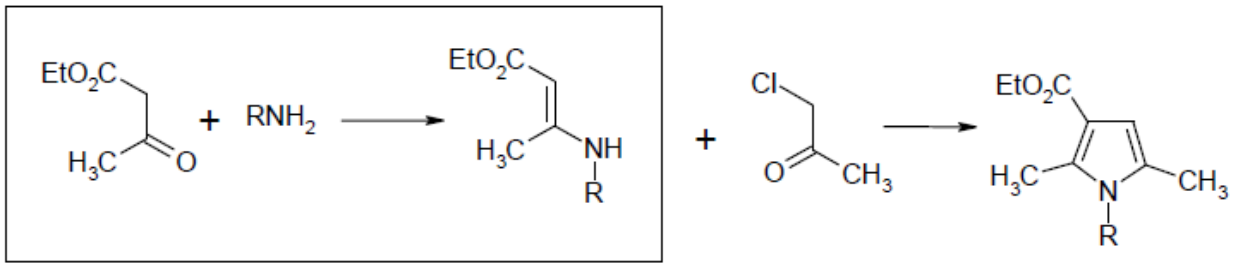
Hantzsch Synthesis

The Hantzsch pyrrole synthesis Is the chemical reaction of β-ketoesters with ammonia (or primary amines) and α-haloketones to give substituted pyrroles. Note: direct reaction of β-ketoesters with α- haloketones gives furan [Fiest-Benary furan synthesis], and this can be a troublesome side reaction. By this method we can prepare different pyrrole derivatives as:1,2,5

substituted pyrrole or 2,5 substituted pyrrole or 1,2,3,5 substituted pyrrole or 2,3,5 substituted pyrrole

Strategy a and b combined;





Electrophilic Substitution

The order of the aromatic character is

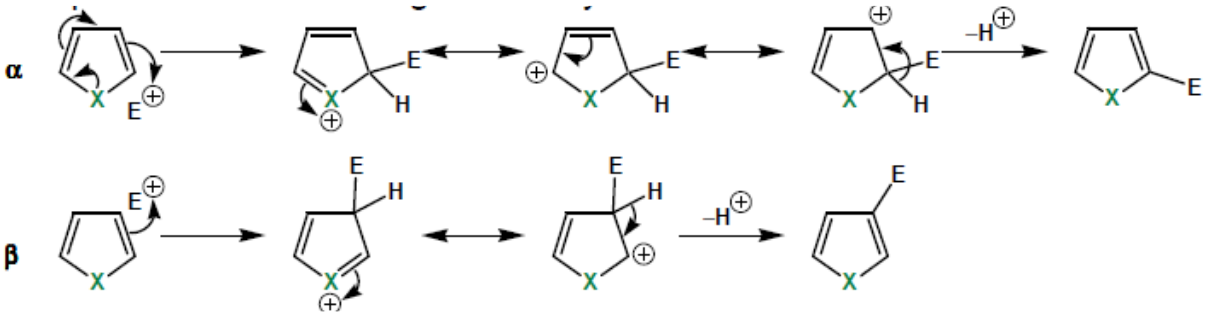
Pyrrole > furan > thiophene > benzene

• Thiophene is the most aromatic in character and undergoes the slowest reaction

• Pyrrole and furan react under very mild conditions

• a-Substitution favoured over b-substitution more resonance forms for intermediate and so the charge is less localised (also applies to the transition state)

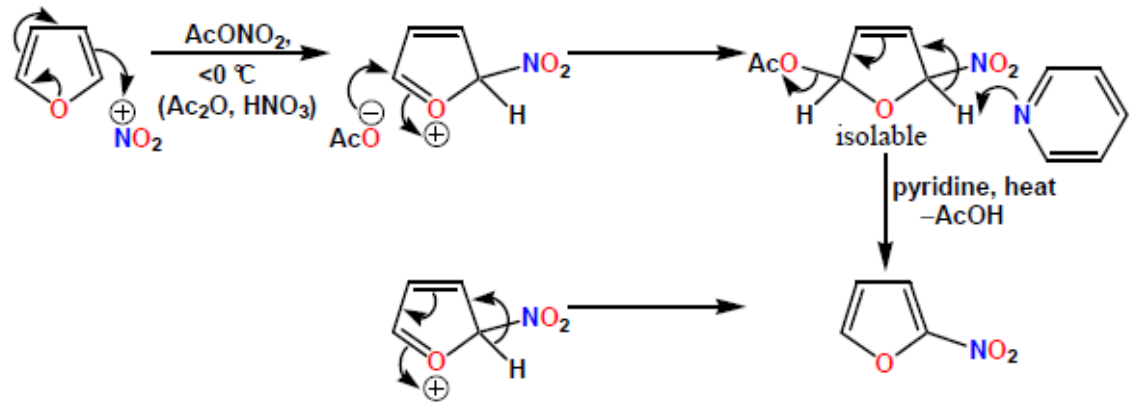
• Some b-substitution usually observed – depends on X and substituents



Nitration of furans

Nitration can occur by an addition-elimination process

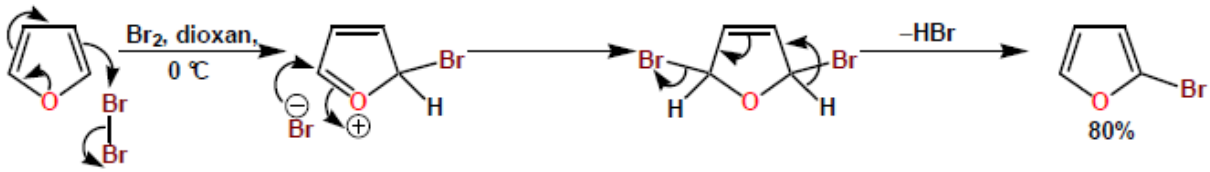
• When NO_2BF_4 is used as a nitrating agent, the reaction follows usual mechanism



Bromination of Furans

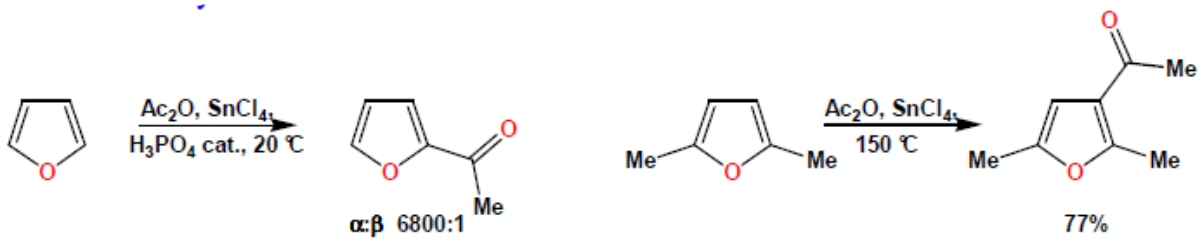
Furan reacts vigorously with Br2 or Cl2 at room temp. to give polyhalogenated products

• It is possible to obtain 2-bromofuran by careful control of temperature

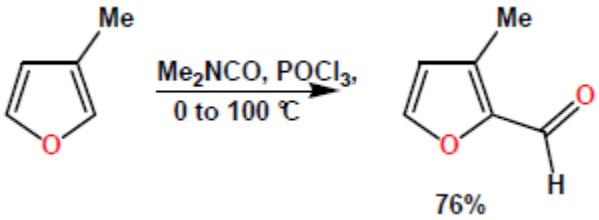


Friedel-Crafts Acylation of Furan

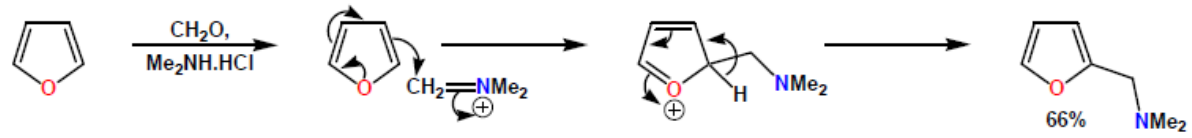
Blocking groups at the a positions and high temperatures required to give acylation



Vilsmeier Formylation of Furan



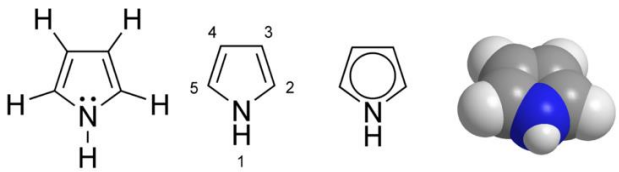
Mannich Reaction



Pyrrole

Pyrrole, is a heterocyclic aromatic organic compound, a five-membered ring with the formula C_4H_4NH. Substituted derivatives are also called ***pyrroles***. For example, $C_4H_4NCH_3$ is N-methylpyrrole. Porphobilinogen is a trisubstituted pyrrole, which is the biosynthetic precursor to many natural products.

Pyrroles are components of more complex macrocycles, including the porphyrins of heme, the chlorins and bacteriochlorins of chlorophyll, and porphyrinogens.



Pyrrole

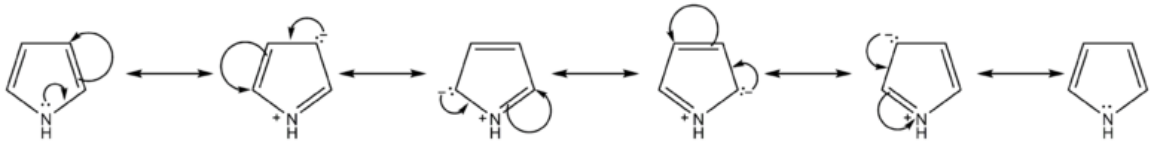
Properties

Pyrrole has very low basicity compared to amines and other aromatic compounds like pyridine, wherin the ring nitrogen is not bonded to a hydrogen atom. This decreased basicity is attributed to the delocalization of the lone pair of electrons of the nitrogen atom in the aromatic ring. Pyrrole is a very weak base with a pKaH of about −4. Protonation results in loss of aromaticity, and is, therefore, unfavorable.

Reactivity

Both NH and CH protons in pyrroles are moderately acidic and can be deprotonated with strong bases such as butyllithium and the metal hydrides. The resulting "pyrrolides" are nucleophilic. Trapping of the conjugate base with an electrophile (e.g., an alkyl or acyl halide) reveals which sites were deprotonated based on which ring positions actually react as nucleophiles. The product distribution of such a reaction can often be complex and depends on the base used (especially the counterion, such as lithium from butyllithium or sodium from sodium hydride), existing substitution of the pyrrole, and the electrophile.

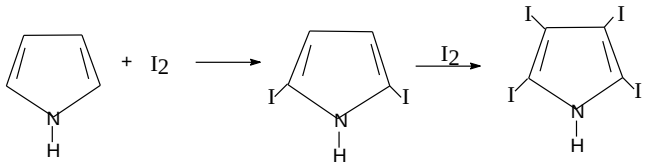
The resonance contributors of pyrrole provide insight to the reactivity of the compound. Like furan and thiophene, pyrrole is more reactive than benzene towards nucleophilic aromatic substitution because it is able to stabilize the positive charge of the intermediate carbanion. This is because the nitrogen can donate a lone pair into the ring by resonance.



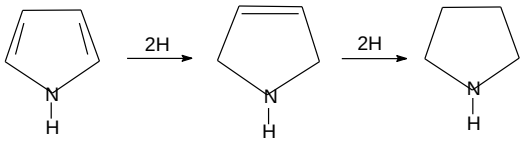
Pyrrole undergoes electrophilic aromatic substitution at the 2 and 5 positions, though the substitution product at positions 3 and 4 is obtained in low yields.

Chemical properties

- With iodine



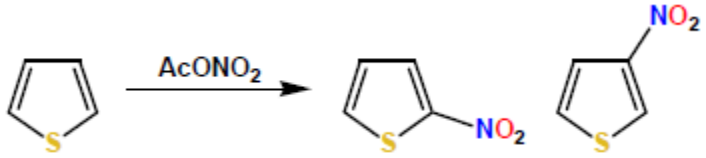
- Hydrogenaration



Reactions of thiophene

Nitration of Thiophenes

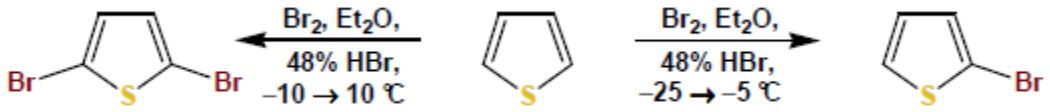
Reagent AcONO2 generated *in situ* from c-HNO3 and Ac2O



Halogenation of Thiophenes

Occurs readily at room temperature and even at -30 °C

• Careful control or reaction conditions is required to ensure mono-bromination



Paal-Knorr Pyrrole Synthesis Generally Substituted pyrrole may be synthesized through the cyclization of 1,4-diketones in combination with ammonia (NH3) or amines, The ring-closure is proceeded by dehydration (condensation), which then yields the two double bonds and thus the aromatic π system. The formation of the energetically favored aromatic system is one of the driving forces of the reaction.

UNIT III

PART A

Multiple Choice Questions

1. Pyridine has a delocalized pi molecular orbital containing
   a. 8 electrons b. **6 electrons** c. 4 electrons d. 12 electrons

2. Most stable heterocyclic compounds are
   a. **5 or 6 membered compounds** b. 4 membered compounds c. 7 membered compounds d. 12 membered compounds

3. One among the following is a condensed heterocyclic compound
   a. **Isoquinoline** b. Thiopyran c. Thiophene d. Pyrimidine

4. The IUPAC name of Furan is
   a. Azole b. **oxole** c. thiole d. azine
5. Pyrrole has a delocalized pi molecular orbital containing
   a. 4 electrons b. **6 electrons** c. 8 electrons d. 12 electrons

6. Five membered heterocyclic compound are derived from benzene by replacement of
   a. a C=C by a hetero atom b. **A carbon of benzene by an hetero atom** c. Reaction with ammonia d. Reaction of benzene with sulphur trioxide

7. One among the following is a condensed heterocyclic compound
   a. **Isoquinoline** b. Thiopyran c. Thiophene d. Pyrimidine

8. Acetonyl acetone on dehydration with phosphorous pentoxide gives
   a. **Furan** b. pyrrole c. Thiophene d. pyran
9. One among the following is called an hetero atom

   a. Hydrogen b. Carbon c. **Sulphur** d. silicon

10. In naming the compound the first priority is given to the hetero atom
    a. Oxygen b. Nitrogen c. Sulphur d. Phosphorous

11. The IUPAC name of thiophene is
    a. azole b. oxole c**. thiole** d. azine

12. Ammonium mucate is distilled in the presence of glycerol gives
    a. Furan b. **pyrrole** c. thiophene d. pyridine

13. Pyrrole has a delocalized pi molecular orbital containing
    a. 4 electrons b. **6 electrons** c. 8 electrons d. 12 electrons

14. Five membered heterocyclic compound are derived from benzene by replacement of
    a. C=C by a hetero atom b. **A carbon of benzene by an hetero atom** c. Reaction with ammonia d. Reaction of benzene with sulphur trioxide

15. One among the following is a condensed heterocyclic compound
    a. Isoquinoline b. Thiopyran c. Thiophene d. Pyrimidine

16. Acetonyl acetone on dehydration with phosphorous pentoxide gives
    a. Furan b. pyrrole c. Thiophene d. pyran

17. One among the following is called an hetero atom
    a. Hydrogen b. Carbon c. **Sulphur** d. silicon

18. In naming the compound the first priority is given to the hetero atom
    a. Oxygen b. Nitrogen c. Sulphur d. Phosphorous

19. The IUPAC name of thiophene is
    a. azole b. oxole c**. thiole** d. azine

20. Ammonium mucate is distilled in the presence of glycerol gives
    a. Furan b. **pyrrole** c. thiophene d. pyridine

PART B

1. Write any one synthesis of pyrrole
2. Write any one synthesis of furan
3. Write any synthesis of thiophene
4. Why pyrrole is more aromatic than furan
5. Why pyridine is more basic than pyrrole.

PART C

1. Discuss the electrophilic aromatic substitution reactions of furan
2. Discuss the aromaticity present in furan, thiophene and pyrrole.
3. Explain Paal-Knorr synthesis to prepare furan and pyrrole.
4. How pyridine is prepared by Hantzsch synthesis
5. Discuss the electrophilic reactions of furan
6. Explain how pyrrole is prepared by (i) Paal-Knorr synthesis, (ii) Knorr pyrrole synthesis, (iii) Hantzsch synthesis
7. Explain the following reactions in detail (i) Gattermann Koch Synthesis (ii) Friedelcrafts acylation of furan (iii) pyrrole is acidic in nature
8. Discuss the aromaticity present in furan thiophene and pyrrole.

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)
II B.Sc. Chemistry
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

UNIT III

Multiple choice questions (Each carries one mark: for online examination)

S.No	Questions	Answer A	Answer B	Answer C	Answer D	Answer
1.	Naphthalene on oxidation chromic acid in acetic acid forms	1,4 napthoquinone	Furoic acid	Phthalic acid	Phthalic anhydride	1,4 napthoquinone
2.	Pyridine has a delocalized pi molecular orbital containing	8 electrons	6 electrons	4 electrons	12 electrons	6 electrons
3.	Pyrrole has a delocalized pi molecular orbital containing	4 electrons	6 electrons	8 electrons	12 electrons	6 electrons
4.	Furan has a delocalized pi molecular orbital containing	6 electrons	4 electrons	8 electrons	12 electrons	6 electrons
5.	Thiophene has a delocalized pi molecular orbital containing	4 electrons	6 electrons	8 electrons	12 electrons	6 electrons
6.	Furan reacts with ammonia in the presence of alumina at 400 C to give	Pyridine	Furfural	Pyrrole	Furoic acid	Pyrrole
7.	When aniline is heated with glycerol in the presence of sulphuric acid and nitrobenzene, it gives quinoline. The reaction is called	Fischer synthesis	Skraup synthesis	Diazotisation	Corey-House synthesis	Skraup synthesis
8.	Cyclic compounds having atleast one atom other than carbon in the ring are termed as	Heterocyclic compounds	Carbocyclic compounds	Alicyclic compounds	Polycyclic compounds	Heterocyclic compounds
9.	Example for an hetero atom	Hydrogen	Carbon	Oxygen	silicon	Oxygen

10.	Pickup an hetero atom from the following	Hydrogen	Carbon	Nitrogen	silicon	Nitrogen
11.	One among the following is called an hetero atom	Hydrogen	Carbon	Sulphur	silicon	Sulphur
12.	Most stable heterocyclic compounds are	5 or 6 membered compounds	4 membered compounds	7 membered compounds	12 membered compounds	5 or 6 membered compounds
13.	Five membered heterocyclic compound are derived from benzene by replacement of	a C=C by a hetero atom	A carbon of benzene by an hetero atom	Reaction with ammonia	Reaction of benzene with sulphur trioxide	A carbon of benzene by an hetero atom
14.	Five membered heterocyclic compound are derived from benzene by replacement of	a C=C by a hetero atom	A carbon of benzene by an hetero atom	Reaction with ammonia	Reaction of benzene with sulphur trioxide	A C=C by a hetero atom
15.	Example for an five membered heterocyclic compound	Indole	Pyridine	Furan	Pyrimidine	Furan
16.	Choose an five membered heterocyclic compound	Indole	Pyridine	Pyrrole	Pyrimidine	Pyrrole
17.	One among the following is an 5-membered heterocyclic compound	Indole	Pyridine	Thiophene	Pyrimidine	Thiophene
18.	Example for an six membered heterocyclic compound	Indole	Pyridine	Furan	Pyrimidine	Pyridine
19.	Choose an six membered heterocyclic compound	Indole	Pyran	Pyrrole	Pyrimidine	Pyran
20.	One among the following is an 6-membered heterocyclic compound	Indole	Thiopyran	Thiophene	Pyrimidine	Thiopyran
21.	Example for an condensed heterocyclic compound	Indole	Pyridine	Furan	Pyrimidine	Indole
22.	Choose a condensed heterocyclic compound	Quinoline	Pyran	Pyrrole	Pyrimidine	Quinoline
23.	One among the following is a condensed heterocyclic compound	Isoquinoline	Thiopyran	Thiophene	Pyrimidine	Isoquinoline
24.	The first priority is given to the hetero atom	Oxygen	Nitrogen	Sulphur	Phosphorous	Oxygen
25.	Least priority is given to	Oxygen	Nitrogen	Sulphur	Phosphorous	Phosphorous

26.	The prefix used to IUPAC name a 5-membered oxygen containing heterocyclic compound is	oxa	thia	aza	Phospha	oxa
27.	The prefix used to IUPAC name a sulphur containing heterocyclic compound is	oxa	thia	aza	Phospha	thia
28.	The prefix used to IUPAC name a nitrogen containing heterocyclic compound is	oxa	thia	aza	Phospha	aza
29.	The suffix used to IUPAC name a 5-membered oxygen containing heterocyclic compound is	-ole	-ine	-epine	-aza	-ole
30.	The suffix used to IUPAC name a 6-membered oxygen containing heterocyclic compound is	-ole	-ine	-epine	-aza	-ine
31.	The suffix used to IUPAC name a 7-membered oxygen containing heterocyclic compound is	-ole	-ine	-epine	-aza	-epine
32.	The IUPAC name of Pyrrole is	azole	oxole	thiole	azine	azole
33.	The IUPAC name of Furan is	azole	oxole	thiole	azine	oxole
34.	The IUPAC name of thiophene is	azole	oxole	thiole	azine	thiole
35.	The IUPAC name of pyridine is	azole	oxole	thiole	azine	azine
36.	Dry distillation of mucic acid gives	Furan	pyrrole	thiophene	pyridine	Furan
37.	Furfural and steam passed over a catalyst consisting of Zn and Mn chromites at 673 K, it gives	Furan	pyrrole	thiophene	pyridine	Furan
38.	Acetonyl acetone on dehydration with phosphorous pentoxide gives	Furan	pyrrole	thiophene	pyridine	Furan
39.	Furan treated with acetyl nitrate to form	2-nitrofuran	3-nitrofuran	4-nitrofuran	3 and 4-nitro furan	2-nitrofuran
40.	Electrophilic substitution in furan takes place at	1,2 position	2, 5 position	3,4 position	2 and 3 position	2, 5 position
41.	Furan treated with pyridine-Sulphur	Furan-2-	Furan-pyridine	Pyridine 2-	3-furan	Furan-2-

	trioxide gives	sulphonic acid	adduct	sulphonic acid	sulphonic acid	sulphonic acid
42.	Furan treated with HCN and HCl in presence of aluminium chloride to form	Furoic acid	furfural	Aryl furan	2-acetyl furan	furfural
43.	Nitrogen analog of furan is called	Pyrrole	Pyridine	pyrimidine	dihydropyrrole	Pyrrole
44.	Distillation of succinimide with zinc dust gives	Furan	pyrrole	thiophene	pyridine	Pyrrole
45.	Ammonium mucate is distilled in the presence of glycerol gives	Furan	pyrrole	thiophene	pyridine	Pyrrole
46.	Acetonyl acetone on heating with ammonia gives	Furan	pyrrole	thiophene	pyridine	Pyrrole
47.	Which is more aromatic	Furan	pyrrole	thiophene	Allyl chloride	Thiophene
48.	Hantsch synthesis is to prepare	Furan	pyrrole	thiophene	pyridine	pyridine
49.	Process of heating 2 moles of ethylacetoacetate, acetaldehyde and ammonia to form pyridine is called	Hantsch synthesis	Clemenson reduction	Hoffmann degradation	Hoffmann elimination	Hantsch synthesis
50.	Heating of sodium succinate with phosphorous sulphide gives	Furan	pyrrole	thiophene	pyridine	thiophene
51.	Acetonyl acetone reacts with phosphorous pentasulphide to form	Furan	pyrrole	Dimethyl thiophene	pyridine	Dimethyl thiophene
52.	Which of the following reagents will re react with pyrrole to form 2-formylpyrrole	Formic acid	Chloroform/KOH	Hydrogen peroxide	Acetic anhydride	Chloroform/KOH
53.	Which of the following reagents will react with furan to form 2-furansulphonic acid	SO_3 in pyridine 100 C	Dil sulphuric acid at 200 C	Sulphur dioxide at 100 c	Dil sulphuric acid at 100 C	SO_3 in pyridine 100 C
54.	Pyridine reacts with a mixture of KNO_3 and H_2SO_4 at 300 C to give	1-nitropyridine	2-nitropyridine	3-nitropyridine	4-nitropyridine	3-nitropyridine
55.	Pyridine reacts with HCl to form	Pyridinium chloride	2-chloropyridine	3-chloropyridine	5-chloropyridine	Pyridinium chloride
56.	Pyrrole is less basic than pyridine because the lone pair of electrons on N-atom in pyrrole	Is part of the delocalized pi molecular orbital	Is not part of the delocalized pi molecular orbital	Resides in SP hybrid orbital	Resides in SP^2 hybrid orbital	Is part of the delocalized pi molecular orbital

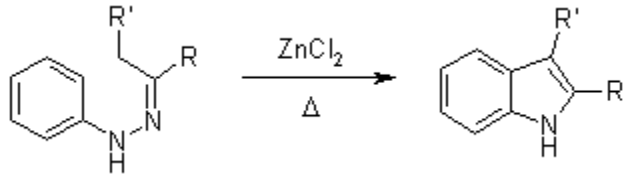
57.	Furan is less aromatic than pyrrole because	Oxygen is more electronegative than Nitrogen	Oxygen is less electronegative than Nitrogen	Nitrogen is more electronegative than oxygen	Nothing to do with electronegativity	Oxygen is more electronegative than Nitrogen
58.	Furan is less aromatic than thiophene because	Oxygen is more electronegative than sulphur	Oxygen is less electronegative than Sulphur	Sulphur is more electronegative than oxygen	Nothing to do with electronegativity	Oxygen is more electronegative than Sulphur
59.	Diels Alder adduct is formed when furan react with	Succinic anhydride	Maleic anhydride	Maleic acid	Succinic acid	Maleic anhydride
60.	Furan when reduced with Nickel in presence of hydrogen to form	Dihydrofuran	Tetrahydrofuran	1,6 diamino hexane	Adipic acid	Tetrahydrofuran
61.	Furan undergoes cycloaddition reaction with carbenes to form	Cyclopropane derivative	Cyclobutane derivative	Diels alder adduct	tetrahydofuran	Cyclopropane derivative

UNIT IV
SYNTHESIS OF HETEROCYCLIC COMPOUNDS

Indole(Fischer indole synthesis and Madelung synthesis), Quinoline and isoquinoline, (Skraup synthesis, Friedlander's synthesis, Knorr quinoline synthesis, Doebner- Miller synthesis, Bischler-Napieralski reaction, Pictet-Spengler reaction, Pomeranz-Fritsch reaction)

Fischer Indole Synthesis

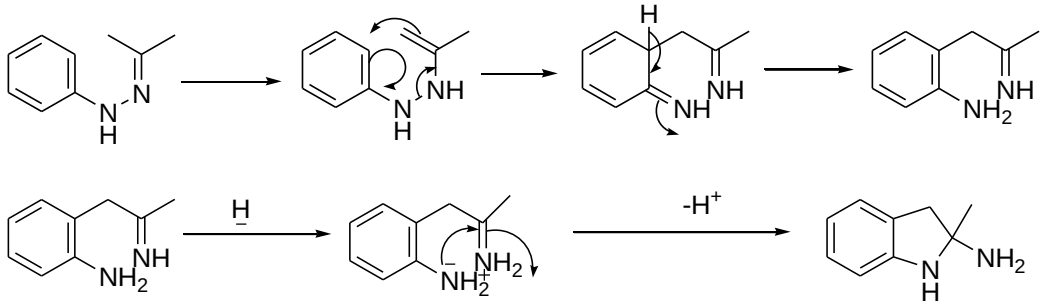
Fischer indole synthesis – this is the oldest way known to make indoles. The reaction is catalyzed by acid. The starting material is phenylhydrazone, and it is formed from the condensation of phenyl hydrazine and a ketone:

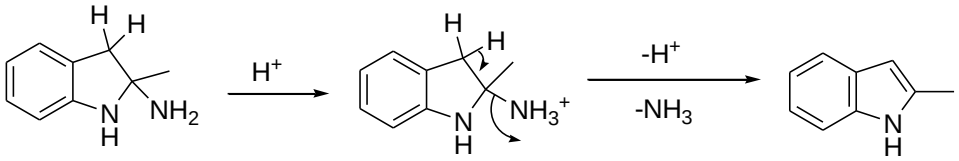


The conversion of aryl hydrazones to indoles; requires elevated temperatures and the addition of Brønsted or Lewis acids. Some interesting enhancements have been published recently; for example a milder conversion when *N*-trifluoroacetyl enehydrazines are used as substrates.

To convert this compound into an indole, the reaction follows the mechanism shown below:

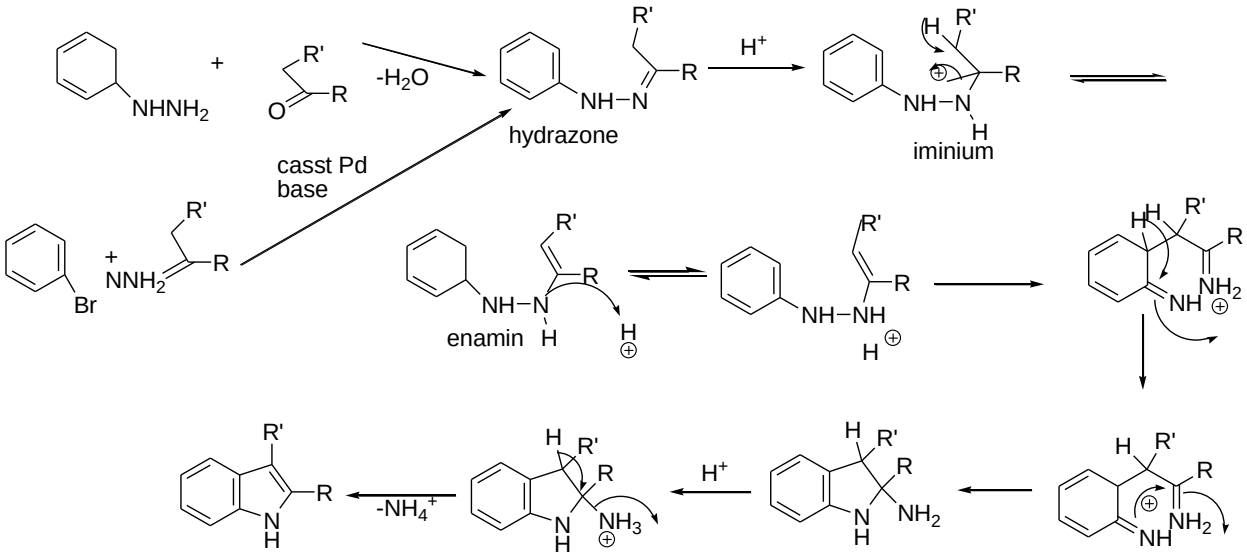
Mechanism of the Fischer Indole Synthesis





The key step is this reaction is the [3,3] sigmatropic rearrangement, and the driving force for that rearrangement is that you are forming new carbon-carbon bonds (strong) at the expense of breaking NN bonds (weak).

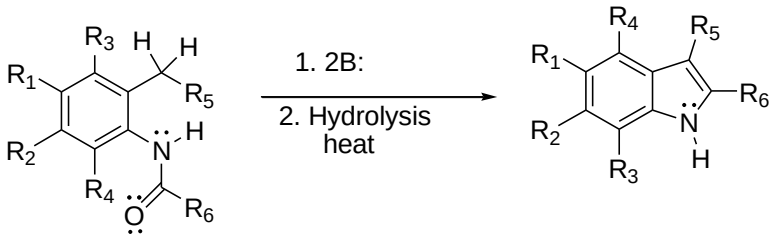
In general, a "sigmatropic rearrangement" refers to something where the only reaction involves moving sigma bonds. The product and the starting material have the same number and same types of atoms; the only difference is where the sigma bonds are located. Also, the rearrangement occurs via a concerted moving of electrons- all the bonds move at once. This particular rearrangement is called a 3,3 rearrangement. This reaction was discovered in 1883. Since then there have been a few advances in indole synthesis.



May be catalysed by lewis acid

The **Madelung synthesis** is a chemical reaction that produces (substituted or unsubstituted) indoles by the intramolecular cyclization of N-phenylamides using strong base at high temperature.The Madelung synthesis was reported in 1912 by Walter Madelung, when he observed that 2-phenylindole was synthesized using N-benzoyl-o-toluidine and two equivalents of sodium ethoxide in a heated, airless, reaction. Common reaction conditions include use

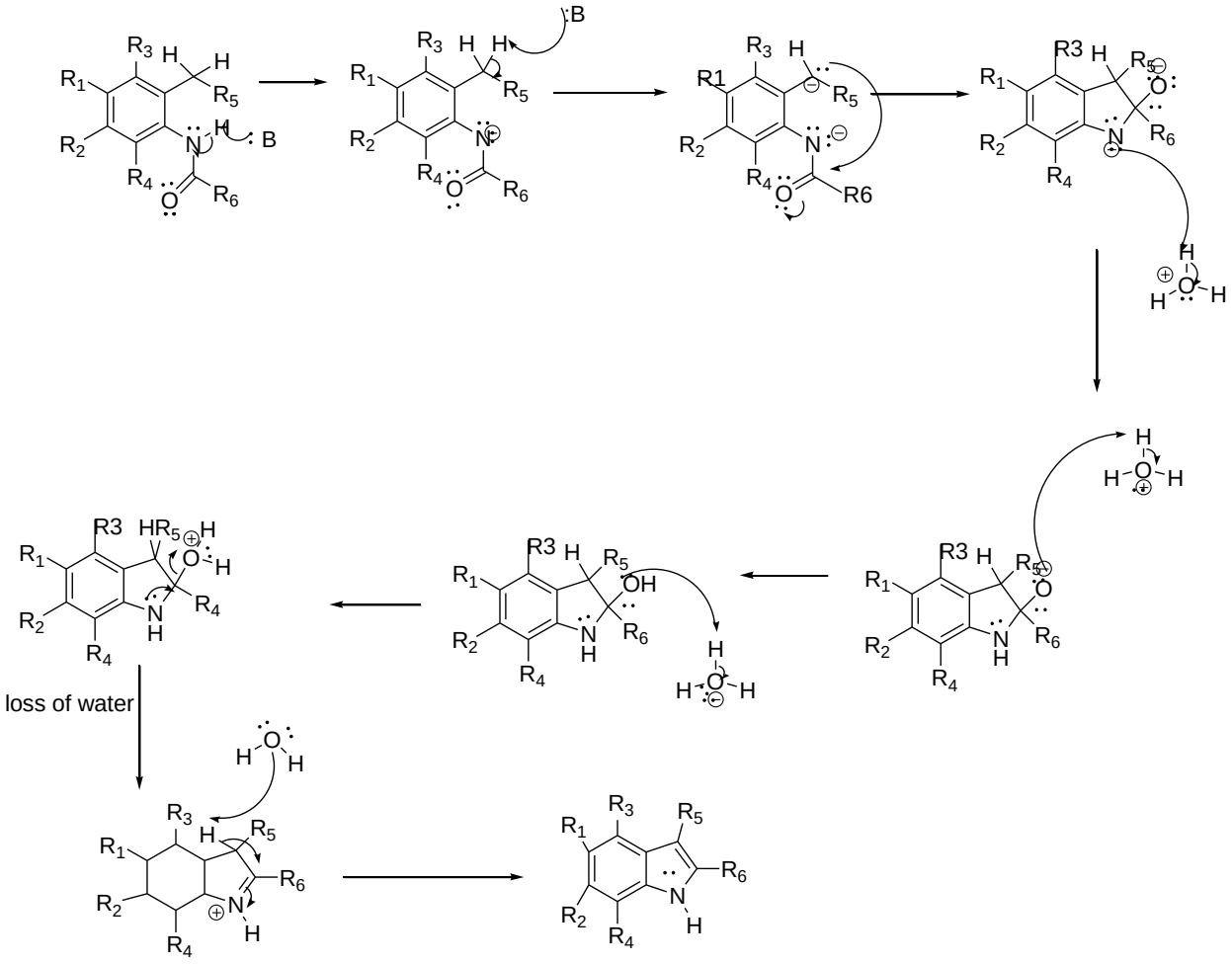
of sodium or potassium alkoxide as base in hexane or tetrahydrofuran solvents, at temperatures ranging between 200-400 °C. A hydrolysis step is also required in the synthesis. The Madelung synthesis is important because it is one of few known reactions that produce indoles from a base-catalyzed thermal cyclization of N-acyl-o-toluidines. The overall reaction for the Madelung synthesis follows.

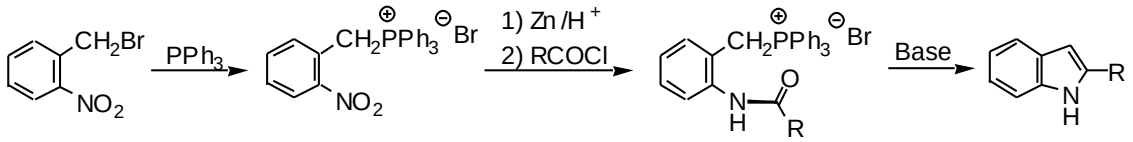


This method is essentially confined to the preparation of 2-alkinylindoles (not easily accessible through electrophilic aromatic substitution) because of the vigorous reaction conditions. A detailed reaction mechanism for the Madelung synthesis follows.

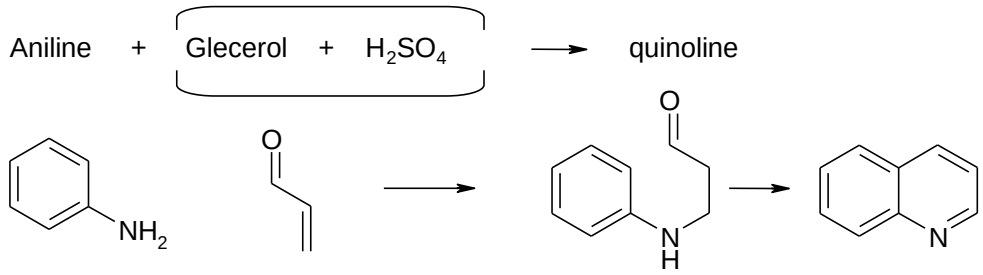
Mechanism of the reaction

The reaction begins with the extraction of a hydrogen from the nitrogen of the amide substituent and the extraction of a benzylic hydrogen from the substituent ortho to the amide substituent by a strong base. Next, the carbanion resulting from the benzylic hydrogen extraction performs a nucleophilic attack on the electrophilic carbonyl carbon of the amide group. When this occurs, the pi-bond of the amide is converted into a lone pair, creating a negatively charged oxygen. After these initial steps, strong base is no longer required and hydrolysis must occur. The negatively charged nitrogen is protonated to regain its neutral charge, and the oxygen is protonated twice to harbor a positive charge in order to become a good leaving group. A lone pair from the nitrogen forms a pi-bond to expel the positively charged leaving group, and also causes the nitrogen to harbor a positive charge. The final step of the reaction is an elimination reaction (specifically an E2 reaction), which involves the extraction of the other hydrogen that was once benzylic, before the bicyclic compound was formed, whose electrons are converted into a new pi-bond in the ring system. This allows the pi-bond formed by nitrogen in the preceding step to be converted back into a lone pair on nitrogen to restore nitrogen's neutral charge.

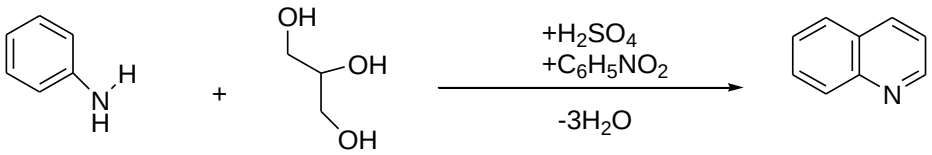




Quinoline Skraup Synthesis

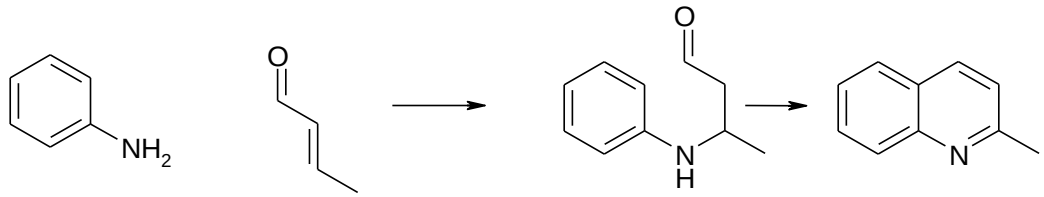


In the archetypal Skraup reaction, aniline is heated with sulfuric acid, glycerol, and an oxidizing agent such as nitrobenzene to yield quinoline.

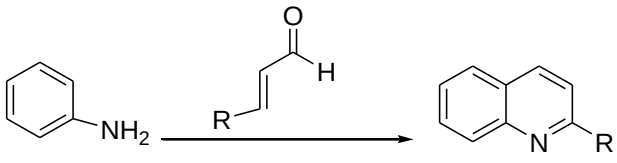


In this example, nitrobenzene serves as both the solvent and the oxidizing agent. The reaction, which otherwise has a reputation for being violent, is typically conducted in the presence of ferrous sulfate. Arsenic acid may be used instead of nitrobenzene and the former is better since the reaction is less violent

Doebner-von Millar



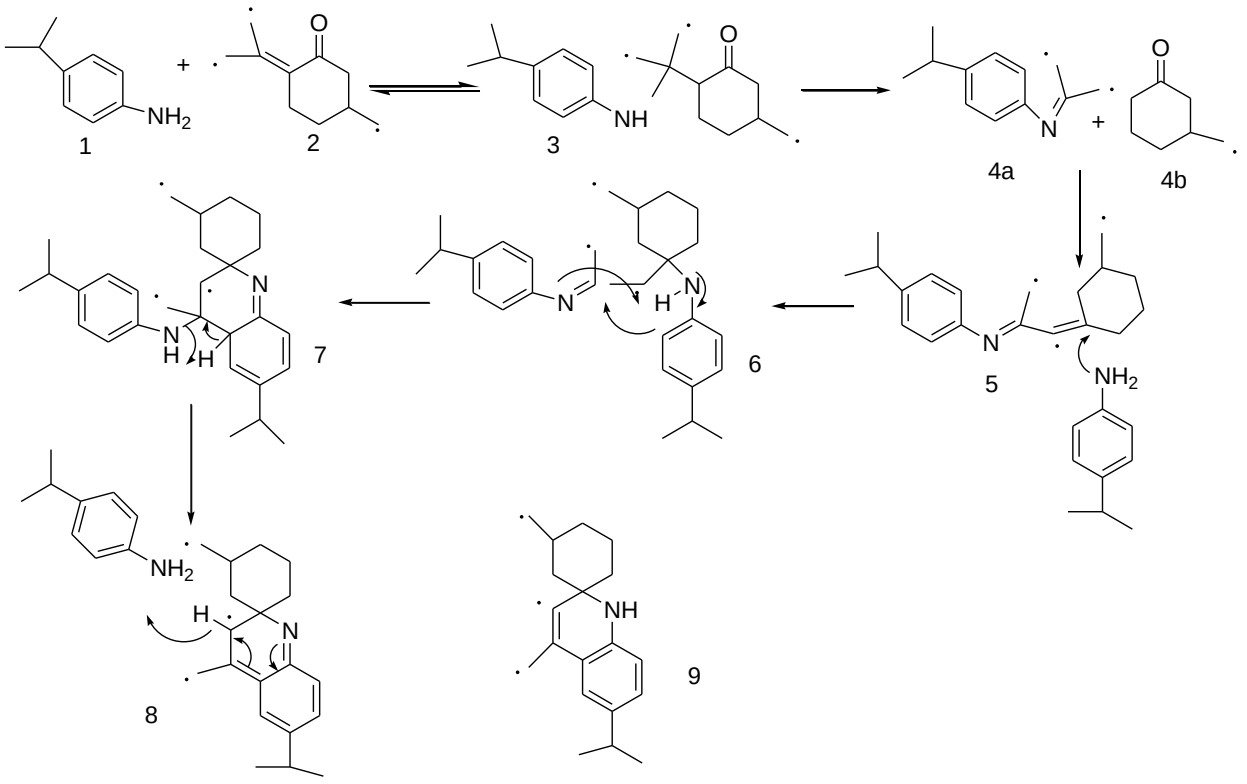
The **Doebner–Miller reaction** is the organic reaction of an aniline with α,β-unsaturated carbonyl compounds to form quinolines.



This reaction is also known as the **Skraup-Doebner-Von Miller quinoline synthesis**, and is named after the Czech chemist Zdenko Hans Skraup (1850–1910), and the Germans Oscar

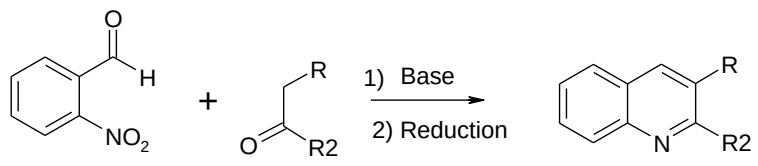
Döbner (Doebner) (1850–1907) and Wilhelm von Miller (1848–1899). When the α,β-unsaturated carbonyl compound is prepared in situ from two carbonyl compounds (via an Aldol condensation), the reaction is known as the **Beyer method for quinolines**. The reaction is catalyzed by Lewis acids such as tin tetrachloride and scandium(III) triflate and Brønsted acids such as *p*-toluenesulfonic acid, perchloric acid, amberlite and iodine.

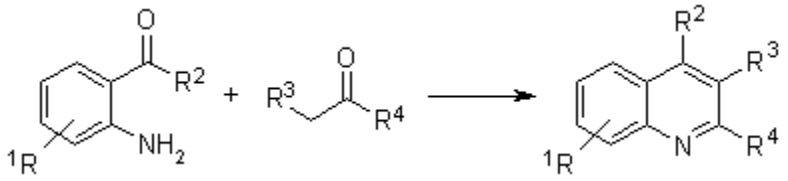
The reaction mechanism for this reaction and the related Skraup synthesis is a matter of debate. A 2006 study proposes a fragmentation-recombination mechanism based on carbon isotope scrambling experiments. In this study 4-isopropylaniline **1** is reacted with a mixture (50:50)of ordinary pulegone and the ^{13}C-enriched isomer **2** and the reaction mechanism is outlined in *scheme 2* with the labeled carbon identified with a red dot. The first step is a nucleophilic conjugate addition of the amine with the enol to the amine ketone **3** in a reversible reaction. This intermediate then fragmentates to the imine **4a** and the saturated cyclohexanone **4b** in a non-reversible reaction and both fragments recombine in a condensation reaction to the conjugated imine **5**. In the next step **5** reacts with a second aniline molecule in a nucleophilic conjugate addition to imine **6** and subsequent electrophilic addition and proton transfer to leads to **7**. elimination of one aniline molecule through **8** and rearomatization leads to final product **9**. Because α-amino protons are not available in this model compound the reaction is not taken to the fully fledged quinoline.



The fragmentation to **4a** and **4b** is key to this mechanism because it explains the isotope scrambling results. In the reaction only half the pulegone reactant (**2**) is labeled and on recombining a labeled imine fragment can react with another labeled ketone fragment or an unlabeled fragment and likewise a labeled ketone fragment can react with a labeled or unlabeled imine fragment. The resulting product distribution is confirmed by mass spectrometry of the final product

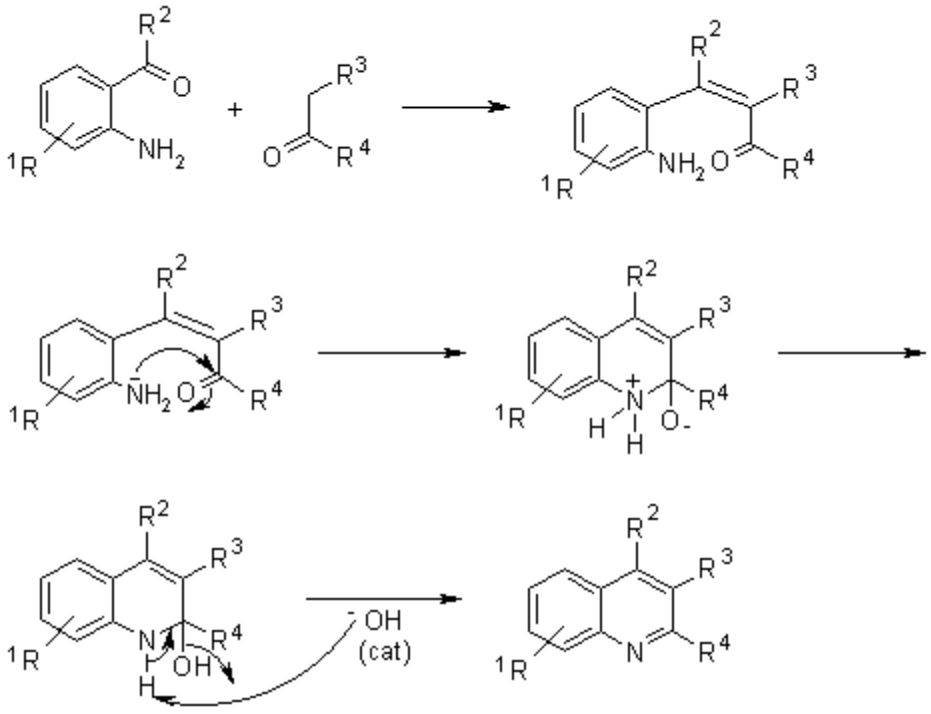
Friedlaender Synthesis



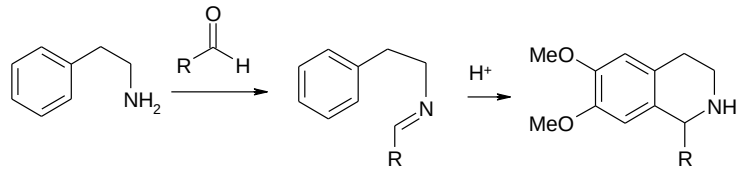


The starting materials for this quinoline synthesis are *o*-aminoaryl aldehydes or ketones and a ketone possessing an α-methylene group. After an initial amino-ketone condensation, the intermediate undergoes base- or acid-catalyzed cyclocondensation to produce a quinoline derivative.

Mechanism of the Friedlaender Synthesis



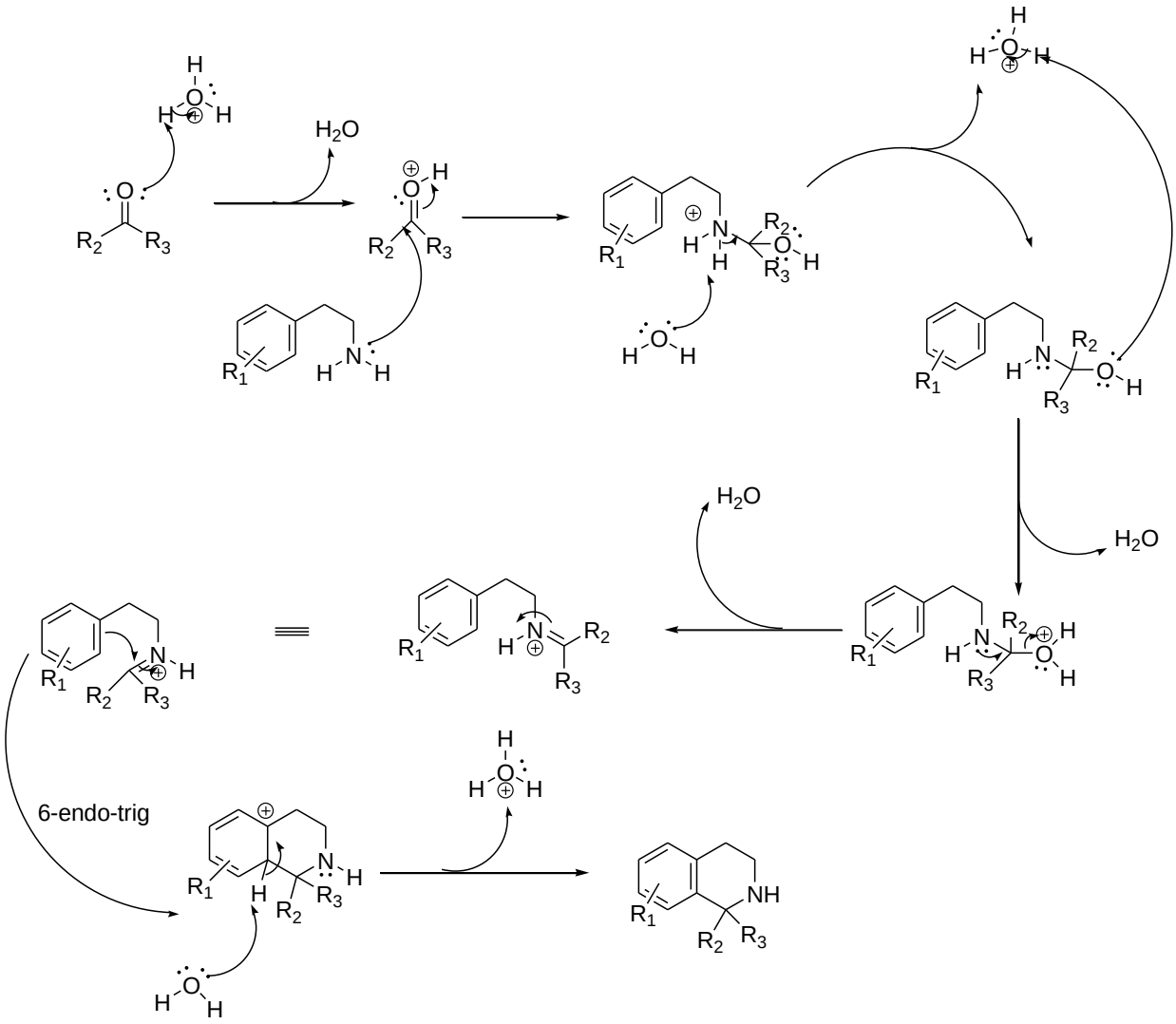
Pictet-Spengler Synthesis



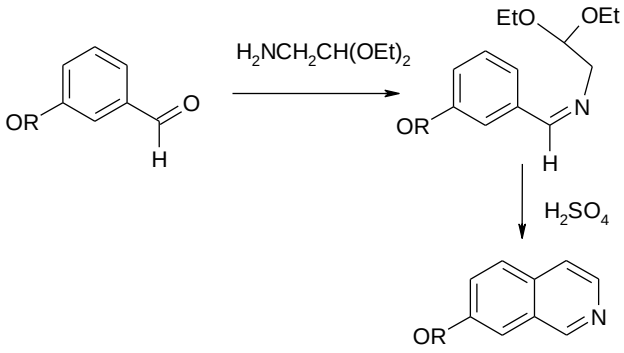
Pictet-Spengler reaction

The Pictet-Spengler reaction is an organic reaction used to convert a β-arylenylamine and an aldehyde or ketone to a tetrahydroisoquinoline using an acid catalyst. The mechanism begins with protonation of the carbonyl oxygen by the acid which is subsequently attacked by the amine reagent. Proton transfer steps and the release of a water molecule results in a protonated imine intermediate, which then undergoes a 6-endo-trig cyclization reaction with loss of aromaticity of the aryl ring. A final deprotonation step restores the aromaticity and results in the tetrahydroisoquinoline product.

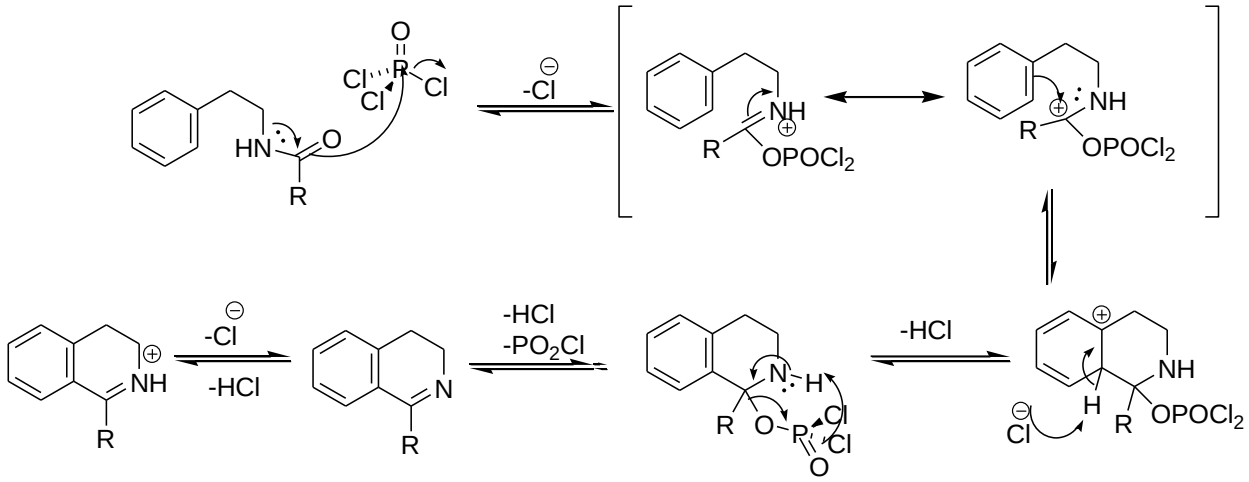
Mechanism



Pomeranz-Fritsch Synthysis



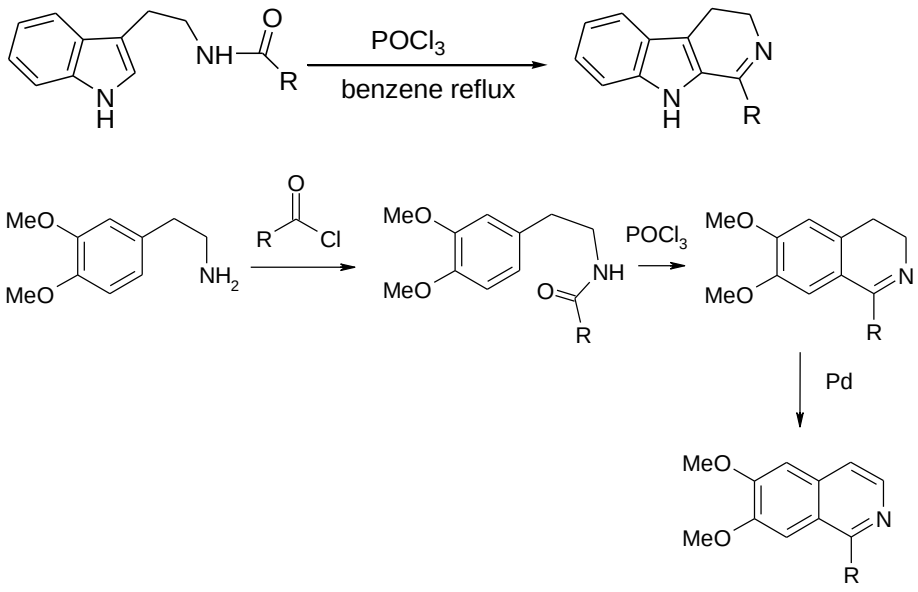
Mechanism



Isoquinoline Synthesis

Bischler-Napierlaski

The **Bischler–Napieralski reaction** is an intramolecular electrophilic aromatic substitution reaction that allows for the cyclization of β-arylethylamides or β-arylethylcarbamates. It was first discovered in 1893 by August Bischler and Bernard Napieralski, in affiliation with Basle Chemical Works and the University of Zurich. The reaction is most notably used in the synthesis of dihydroisoquinolines, which can be subsequently oxidized to isoquinolines.



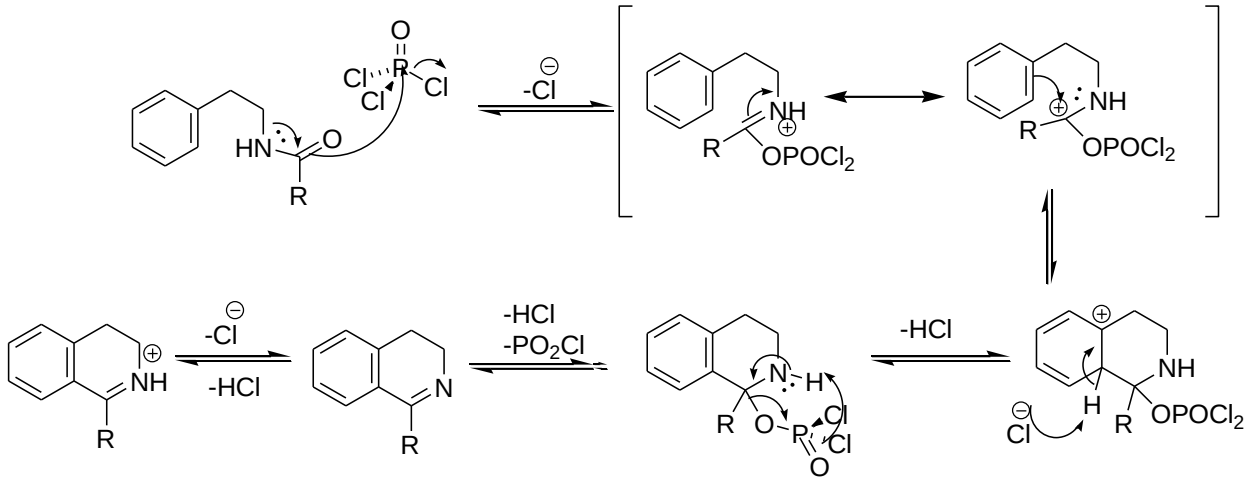
Two types of mechanisms have appeared in the literature for the Bischler–Napieralski reaction. Mechanism I involves a dichlorophosphoryl imine-ester intermediate, while Mechanism II involves a nitrilium ion intermediate (both shown in brackets). This mechanistic variance stems from the ambiguity over the timing for the elimination of the carbonyl oxygen in the starting amide. In Mechanism I, the elimination occurs with imine formation *after* cyclization; while in Mechanism II, the elimination yields the nitrilium intermediate *prior* to cyclization. Currently, it is believed that different reaction conditions affect the prevalence of one mechanism over the other (see reaction conditions).

In certain literature, Mechanism II is augmented with the formation of an imidoyl chloride intermediate produced by the substitution of chloride for the Lewis acid group just prior to the nitrilium ion. Because the dihydroisoquinoline nitrogen is basic, neutralization is necessary to obtain the deprotonated product.

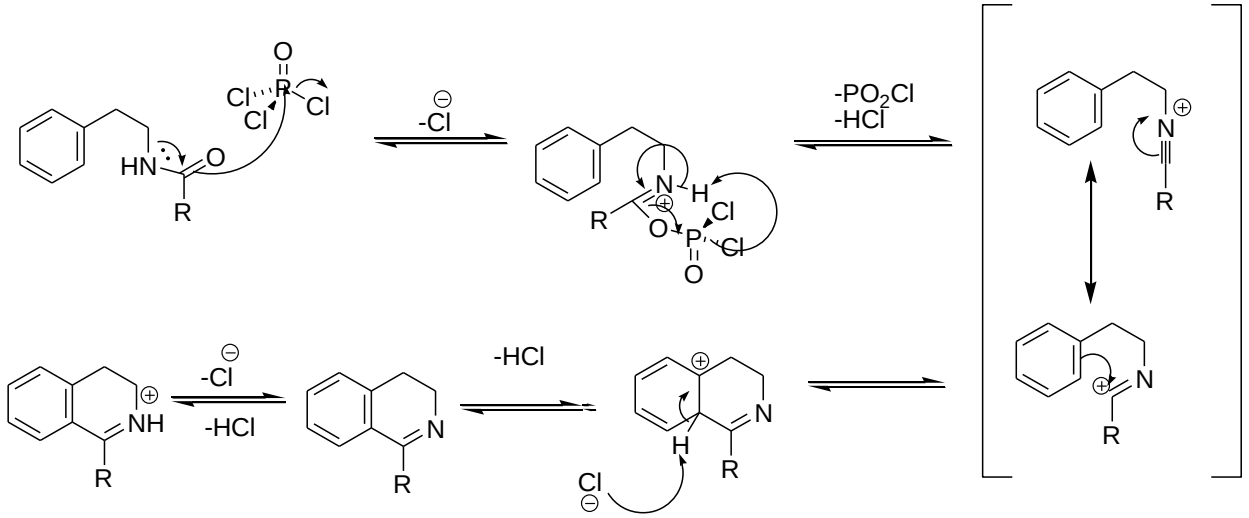
General reagents and reaction conditions

The Bischler–Napieralski reaction is carried out in refluxing acidic conditions and requires a dehydrating agent. Phosphoryl chloride ($POCl_3$) is widely used and cited for this purpose. Additionally, $SnCl_4$ and BF_3 etherate have been used with phenethylamides, while Tf_2O and polyphosphoric acid (PPA) have been used with phenethylcarbamates. For reactants lacking electron-donating groups on the benzene ring, phosphorus pentoxide (P_2O_5) in refluxing $POCl_3$ is most effective. Depending on the dehydrating reagent used, the reaction temperature varies from room temperature to 100 °C.

MECHANISM I



MECHANISM II



UNIT IV

PART A

Multiple Choice questions

1. Numbering of ring atoms starts at the hetero atom except
   a. Quinoline b**. Isoquinoline** c. benzofuran d. indole

2. To prepare indole, zinc chloride has to be heated with
   a. Benzaldehyde b. benzophenone c. Phenyl acetate d. **Phenyl hydrazone of acetone**

3. To prepare 2-alkyl indole by the cyclodehydration of o-acyl amidotoluene is carried out with
   a. Sodium ethoxide b. Zinc chloride c. **Potassium tertiary butoxide**
   d. Tin and HCl

4. Fischer,s synthesis is used to prepare
   a. Quinoline b. Isoquinoline c. **Indole** d. Pyran
5. The alternate name of indole is
   a. Quinoline b. Isoquinoline c. **benzopyrrole** d. indole

6. In Lipps synthesis of indole the starting material is
   a. o-amino chlorostyrene b. o-hydroxychlorostyrene c. o-nitro chlorostyrened. o-chlorochlorostyrene

7. In the synthesis of quinoline o-amino benzaldehydereacs with
   a. **Acetaldehyde** b. o-amino chlorostyrene c. o-hydroxychlorostyrene d. Maleic anhydride

8. Alkaloids are
   a. **Weakly basic** b. Strongly basic c. Weakly acidic d. Strongly acidic
9. The catalyst used in the Fischer indole synthesis is
   a. **Zinc chloride** b. Vanadium pentoxide c. Chromium oxide d. Sulphuric acid

10. Friedlander synthesis is used to synthesis
    a.**Quinoline** b. Isoquinoline c. indole d. pyrans

11. The process where Aniline and glycerol reacts in presence of sulphuric acid and nitrobenzene to give quinoline is
    a. Fischer indole synthesis b. Madelung synthesis c. **Skraup synthesis** d. Friedlander's synthesis
12. The alternate name of indole is
    a. Quinoline b. Isoquinoline c. **benzopyrrole** d. indole

13. In Lipps synthesis of indole the starting material is
    a. o-amino chlorostyrene b. o-hydroxychlorostyrene c. o-nitro chlorostyrene d. o-chlorochlorostyrene

14. To prepare 2-alkyl indole by the cyclodehydration of o-acyl amidotoluene is carried out with
    a. Sodium ethoxide b. Zinc chloride c. **Potassium tertiary butoxide** d. Tin and HCl

15. Fischer,s synthesis is used to prepare
    a. Quinoline b. Isoquinoline c. **Indole** d. Pyran

16. The catalyst used in the Fischer indole synthesis is
    a. **Zinc chloride** b. Vanadium pentoxide c. Chromium oxide d. Sulphuric acid

17. In Lipps synthesis indole is from from o-amino chlorostyrene and
    a. Sodium ethoxide b. Zinc chloride c. sodamide d. Tin and HCl

18. In the synthesis of quinoline o-amino benzaldehydereacs with
    a.Acetaldehyde b. o-amino chlorostyrene c. o-hydroxychlorostyrene d. Maleic anhydride

19. Alkaloids are
    a.Weakly basic b. Strongly basic c. Weakly acidic d. Strongly acidic

PART B

1. How indole is prepared by Lipps synthesis
2. Explain with suitable examples what are five and six membered heterocycles
3. How quinoline is prepared from Friedlander's synthesis
4. How isoquinoline is prepared from cinnamaldehyde
5. What is Pomeranz-Fritsch reaction

PART C

1. How quinoline is prepared by (i) Skraup synthesis (ii) The Dobner-Miller synthesis

2. Write note on Pictet-Spengler reaction and Pomeranz-Fritsch reaction.
3. How indole is prepared by Fischer indole synthesis. Explain the mechanism
4. How isoquinoline is prepared by BischlerNapieralski synthesis. Explain its mechanism
5. What is meant by BischlerNapieralski synthesis. Explain its mechanism
6. Discuss in detail about the Fischer indole synthesis. How heterocyclic compounds are prepared from that.
7. Explain the mechanisms of Pictet-Spengler reaction, Pomeranz-Fritsch reaction
8. How indole is prepared by (i) Madelung synthesis (ii) Bischler synthesis

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)
II B.Sc. Chemistry
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

UNIT IV

Multiple choice questions (Each carries one mark: for online examination)

S.No	Questions	Answer A	Answer B	Answer C	Answer D	Answer
1.	Numbering of ring atoms starts at the hetero atom except	Quinoline	Isoquinoline	benzofuran	indole	isoquinoline
2.	The alternate name of indole is	Quinoline	Isoquinoline	benzopyrrole	indole	benzopyrrole
3.	The alternate name of benzopyrrole is	Quinoline	Isoquinoline	indole	indole	indole
4.	In the Fischer indole synthesis the starting material is	benzaldehyde	benzophenone	Phenyl acetate	Phenyl hydrazone of acetaldehyde	Phenyl hydrazone of acetaldehyde
5.	The catalyst used in the Fischer indole synthesis is	Zinc chloride	Vanadium pentoxide	Chromium oxide	Sulphuric acid	Zinc chloride
6.	In the Fischer indole synthesis the starting material to prepare 2-methyl indole is	benzaldehyde	benzophenone	Phenyl acetate	Phenyl hydrazone of acetone	Phenyl hydrazone of acetone
7.	Heating phenyl hydrazone of acetaldehyde with zinc chloride gives	Quinoline	Isoquinoline	indole	indole	indole
8.	Heating phenyl hydrazone	Quinoline	Isoquinoline	2-methyl indole	indole	2-methylindole

	of acetone with zinc chloride gives					
9.	To prepare indole, phenyl hydrazone of acetone has to be heated with	Zinc chloride	Vanadium pentoxide	Chromium oxide	Sulphuric acid	Zinc chloride
10.	Preparation of indole from Heating phenyl hydrazone of acetaldehyde with zinc chloride is called	Fischer indole synthesis	Madelung synthesis	Lipps synthesis	Wolf kishner reduction	Fischer indole synthesis
11.	To prepare indole, zinc chloride has to be heated with	benzaldehyde	benzophenone	Phenyl acetate	Phenyl hydrazone of acetone	Phenyl hydrazone of acetone
12.	In Lipps synthesis of indole the starting material is	o-amino chlorostyrene	o-hydroxy chlorostyrene	o-nitro chlorostyrene	o-chloro chlorostyrene	o-amino chlorostyrene
13.	In Lipps synthesis of indole the catalyst used is	Sodium ethoxide	Zinc chloride	sodamide	Tin and HCl	Sodium ethoxide
14.	Preperation of indole from o-amino chlorostyrene and Sodium ethoxide is called	Fischer indole synthesis	Madelung synthesis	Lipps synthesis	Wolf kishner reduction	Lipps synthesis
15.	In Lipps synthesis of indole o-amino chlorostyrene is heated with	Sodium ethoxide	Zinc chloride	sodamide	Tin and HCl	Sodium ethoxide
16.	In Lipps synthesis of indole sodium ethoxide is heated with	o-amino chlorostyrene	o-hydroxy chlorostyrene	o-nitro chlorostyrene	o-chloro chlorostyrene	o-amino chlorostyrene
17.	In Lipps synthesis indole is from from o-amino chlorostyrene and	Sodium ethoxide	Zinc chloride	sodamide	Tin and HCl	Sodium ethoxide
18.	In Lipps synthesis indole is from from sodium ethoxide and	o-amino chlorostyrene	o-hydroxy chlorostyrene	o-nitro chlorostyrene	o-chloro chlorostyrene	o-amino chlorostyrene
19.	The method used to prepare 2-alkyl indole by the cyclodehydration of 0-acyl	Fischer indole synthesis	Madelung synthesis	Lipps synthesis	Wolf kishner reduction	Madelung synthesis

	amidotoluene is					
20.	To prepare 2-alkyl indole by the cyclodehydration of 0-acyl amidotoluene is carried out with	Sodium ethoxide	Zinc chloride	sodamide	Tin and HCl	sodamide
21.	To prepare 2-alkyl indole by the cyclodehydration of 0-acyl amidotoluene is carried out with	Sodium ethoxide	Zinc chloride	Potassium tertiary butoxide	Tin and HCl	Potassium tertiary butoxide
22.	The reaction involved in the conversion of 0-acyl amidotoluene into indole is	cyclodehydration	dehydration	hydrolysis	condensation	cyclodehydration
23.	cyclodehydration of 0-acyl amidotoluene with sodamide gives	Quinoline	Isoquinoline	pyrans	indole	indole
24.	cyclodehydration of 0-acyl amidotoluene with Potassium tertiary butoxide gives	Quinoline	Isoquinoline	pyrans	indole	indole
25.	Reaction of o-amino benzaldehyde with acetaldehyde in NaOH is	Fischer indole synthesis	Madelung synthesis	Lipps synthesis	Friedlander's synthesis	Friedlander's synthesis
26.	In the synthesis of quinoline o-amino benzaldehyde reacs with	Acetaldehyde	o-amino chlorostyrene	o-hydroxy chlorostyrene	o-nitro chlorostyrene	Acetaldehyde
27.	In the synthesis of quinoline acealdehyde reacs with	o-amino benzaldehyde	o-amino chlorostyrene	o-hydroxy chlorostyrene	o-nitro chlorostyrene	o-amino benzaldehyde
28.	o-amino benzaldehyde reacts with acetaldehyde in presence of ---------- to give quinoline	Sodium ethoxide	Zinc chloride	Potassium tertiary butoxide	Sodium hydroxide	Sodium hydroxide
29.	Friedlander synthesis is used to synthesis	Quinoline	Isoquinoline	indole	pyrans	Quinoline
30.	Madelung synthesis is used	Quinoline	Isoquinoline	indole	pyrans	indole

	to prepare					
31.	Fischer,s synthesis is used to prepare	Quinoline	Isoquinoline	indole	pyrans	indole
32.	Lipps synthesis is concerned with	Quinoline	Isoquinoline	indole	pyrans	indole
33.	In Friedlander synthesis the chief material used to synthesis quinoline is	o-amino benzaldehyde	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	o-amino benzaldehyde
34.	In Madelung synthesis the chief raw material is	o-amino benzaldehyde	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	o-acylamidotoluene
35.	In Fischer,s synthesis the chief raw material is	o-amino benzaldehyde	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	Phenyl hydrazone
36.	In Lipps synthesis the chief raw material is	o-amino benzaldehyde	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	o-amino chlorostyrene
37.	In Skraup synthesis nitrobenzene is used as a	Oxidising agent	Condensing agent	Dehydrating agent	Drying agent	Oxidising agent
38.	Aniline and glycerol reacts in presence of sulphuric acid and nitrobenzene to give	Quinoline	Isoquinoline	indole	pyrans	quinoline
39.	The process where Aniline and glycerol reacts in presence of sulphuric acid and nitrobenzene to give quinoline is	Fischer indole synthesis	Madelung synthesis	Skraup synthesis	Friedlander's synthesis	Skraup synthesis
40.	The catalyst used to prepare quinoline in Skraup synthesis is	Sodium ethoxide	Zinc chloride	Potassium tertiary butoxide	Sulphuric acid	Sulphuric acid
41.	For the synthesis of quinoline, in presence of sulphuric acid and nitrobenzene glycerol reacts with	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	aniline	aniline
42.	For the synthesis of quinoline, in presence of	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	glycerol	glycerol

	sulphuric acid and nitrobenzene aniline reacts with					
43.	α, β-unsaturated carbonyl compounds are prepared from	aldehydes	nitrocompounds	alcohols	phenols	aldehydes
44.	Modified form of Skraup synthesis is called	Fischer indole synthesis	Madelung synthesis	Dobner-Miller synthesis	Friedlander's synthesis	Dobner Miller synthesis
45.	The reaction to prepare α, β-unsaturated carbonyl compounds from aldehydes is	Aldol condensation	Knorr synthesis	Claisen condensation	Reimer-Tieman	Aldol condensation
46.	Dobner-Miller synthesis is the modified form of	Fischer indole synthesis	Madelung synthesis	Skraup synthesis	Friedlander's synthesis	Skraup synthesis
47.	In Dobner- Miller synthesis aniline reacts with	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	α, β-unsaturated carbonyl compounds	α, β-unsaturated carbonyl compounds
48.	In Dobner- Miller synthesis α, β-unsaturated carbonyl compounds reacts with	o-amino chlorostyrene	Phenyl hydrazone	o-acylamidotoluene	aniline	aniline
49.	Isoquinoline can be prepared from	Bischler Napieralski synthesis	Fischer indole synthesis	Madelung synthesis	Skraup synthesis	Bischler Napieralski synthesis
50.	Isoquinoline can be prepared from	Pomeranz Fritsch synthesis	Fischer indole synthesis	Madelung synthesis	Skraup synthesis	Pomeranz Fritsch synthesis
51.	Isoquinoline can be prepared from	Pictet-Spengaler synthesis	Fischer indole synthesis	Madelung synthesis	Skraup synthesis	Pictet-Spengaler synthesis
52.	The starting material in Pictet-Spengaler synthesis is	Phenyl ethyl amine	aminoacetal	Aryl ethylamine and an aldehyde	aniline	Aryl ethylamine and an aldehyde
53.	The starting material in Pomeranz Fritsch synthesis is	Phenyl ethyl amine	aminoacetal	Aryl ethylamine and an aldehyde	aniline	Aryl ethylamine and an aldehyde
54.	The starting material in Bischler Napieralski	Phenyl ethyl amine	aminoacetal	Aryl ethylamine and an aldehyde	aniline	Phenyl ethyl amine

	synthesis is					
55.	Bischler Napieralski synthesis is	Phenylethylamine reacts with formyl chloride, followed by reaction with P_2O_5 and Se	Benzaldehyde reacts with aminoacetal followed by reaction with sulphuric acid	Reaction of phenyl ethylamine with acetaldehyde followed with reduction	Cinnamaldehyde reacts with hydroxylamine	Phenylethylamine reacts with formyl chloride, followed by reaction with P_2O_5 and Se
56.	Pomeranz Fritsch synthesis is	Phenylethylamine reacts with formyl chloride, followed by reaction with P_2O_5 and Se	Benzaldehyde reacts with aminoacetal followed by reaction with sulphuric acid	Reaction of phenyl ethylamine with acetaldehyde followed with reduction	Cinnamaldehyde reacts with hydroxylamine	Reaction of phenyl ethylamine with acetaldehyde followed with reduction
57.	Pomeranz Fritsch synthesis involves	Phenylethylamine reacts with formyl chloride, followed by reaction with P_2O_5 and Se	Benzaldehyde reacts with aminoacetal followed by reaction with sulphuric acid	Reaction of phenyl ethylamine with acetaldehyde followed with reduction	Cinnamaldehyde reacts with hydroxylamine	Benzaldehyde reacts with aminoacetal followed by reaction with sulphuric acid
58.	Phenylethylamine reacts with formyl chloride, followed by reaction with P_2O_5 and Se to give	Quinoline	Isoquinoline	indole	pyrans	isoquinoline
59.	Benzaldehyde reacts with aminoacetal followed by reaction with sulphuric acid to give	Quinoline	Isoquinoline	indole	pyrans	isoquinoline
60.	Reaction of phenyl ethylamine with acetaldehyde followed with reduction gives	Quinoline	Isoquinoline	indole	pyrans	isoquinoline

UNIT V
Alkaloids and Terpenes

Alkaloids

Natural occurrence, General structural features, Isolation and their physiological action, Hoffmann's exhaustive methylation, Emde's modification; Structure elucidation and synthesis of Nicotine. Medicinal importance of Nicotine, Hygrine, Quinine, Morphine, Cocaine, and Reserpine.

Terpenes

Occurrence, classification, isoprene rule; Elucidation of stucture and synthesis of Citral.

Alkaloids

Alkaloids are naturally-occurring organic compounds containing nitrogen moiety, and are usually heterocyclic in nature. They are nitrogen based organic compounds, with nitrogen enclosed in an heterocyclic ring. The alkyl amines are referred to as proalkaloids.

Classification of alkaloids

(*i*) Pyrrolidine alkaloids *e.g.*, **Hygrine;**

(*ii*) Piperidine alkaloids *e.g.*, **Lobeline;**

(*iii*) Pyrrolizidine alkaloids *e.g.*, **Senecionine;**

(*iv*) Tropane alkaloids *e.g.*, **Atropine;**

(*v*) Quinoline alkaloids *e.g.*, **Quinine;**

(*vi*) Isoquinoline alkaloids *e.g.*, **Morphine;**

(*vii*) Aporphine alkaloids *e.g.*, **Boldine;**

(*viii*) Indole alkaloids *e.g.*, **Ergometrine;**

(*ix*) Imidazole alkaloids *e.g.*, **Pilocarpine;**

(*x*) Diazocin alkaloids *e.g.*, **Lupanine;**

(*xi*) Purine alkaloids *e.g.*, **Caffeine;**

(*xii*) Steroidal alkaloids *e.g.*, **Solanidine;**

(*xiii*) Amino alkaloids *e.g.*, **Ephedrine;**

(*xiv*) Diterpene alkaloids *e.g.*, **Aconitine.**

Characteristics of alkaloids

(1)They are basic in nature due to the presence of nitrogen in their ring.

(2) They have complex structures.

(3) They have bitter principles.

(4) They are mostly obtained from plant materials.

(5) They have high pharmacological and physiological activities.

Examples of alkaloids are:

(1) Quinine — an antimalarial drug isolated from a plant called Cinchonia officialis. Quinine is an antipyretic alkaloid. Its molecular formular is C20H24N2O2.. Functional groups present in quinine are: methoxyl –OCH3, hydroxyl –OH, tertiary amine group, etc.

(2) Morphine is highly narcotic Morphine is analgesicν Morphine is isolated from the plant Papavera omniferousν Morphine is an opium alkaloid.ν Nicotine is another example of alkaloid

(3) Cocaine is an alkaloid. - Cocaine is obtained from coca leaves, - Cocaine is the first local unaesthetic ever discovered by man, - Cocaine is highly narcotic, - Cocaine stimulates the central nervous system i.e. CNS depressant, - Cocaine can lead to psychiatric problem when taken in high dose or when addicted to it.

(4) Reserpine is the main constituent of Rauwolfia species,perticularly R.serpentina & R.vomitoria. • It is mainly used for the treatment of hypertension, headache, tension, asthma & dermatological disorders.

General Methods of Extraction and Isolation of Alkaloids

The general methods of extraction and isolation of the alkaloids from the plant sources one has to take into consideration the following steps in a sequential manner, namely:

(*i*) Separation of the alkaloid(s) from the main bulk of the non-alkaloidal substances,

(*ii*) Most of the alkaloid-containing plants, several alkaloids having closely related chemical structures are normally present, such as: the cinchona alkaloids consist of more than twentyfive alkaloids. There is hardly any known plant source that contains only one alkaloid exclusively,

(*iii*) Separation of each individual alkaloid from the mixture of alkaloids obtained from a particular plant source (*e.g.*, **cinchona bark**) using latest separation techniques, for instance, preparative **high-performances liquid chromatography, (HPLC)** column chromatography, by the help of chromatotron, and **high-performance thin-layer chromatography (HPTLC).**

Nevertheless, the general methods of isolation of alkaloids largely depend upon several vital factors, for instance: (*a*) the alkaline nature of most alkaloids, (*b*) the ability and ease of formation of alkaloidal salts with acids, and (*c*) the relative solubilities of the resulting alkaloidal salts either in polar organic solvents *e.g.*, ethanol, chloroform, isopropanol etc., or in aqueous medium.

The general methods of **extraction of alkaloids** from the plant sources solely depend upon the purpose and scale of the operation (*e.g.*, pilot scale or commercial scale). It is also based on the quantum and bulk of the raw material to be employed in the operation. Of course, for research purposes column chromatography using ion-exchange resins have been used successfully and effectively to strip the plant materials of their alkaloidal contents. However, in the commercial scale large volumes of aqueous extracts of plant materials are normally pumped through huge metallic columns packed with cationic resins, which in turn pick up all basic components (cations). Subsequently, the alkaloids (*i.e.*, the basic components are conveniently washed off by flushing the column with a moderately strong acid. The column having the cationic resins can be reused once again for the next drug substances.

By the advent of the latest separation techniques and the copious volume of informations accumulated through the intensive and extensive research carried out with regard to the conventional processes essentially associated with the separation as well as isolation of the hundreds of **alkaloids** from the natural plant sources, the following *five* steps are most important and vital, namely:

(*i*) Sample preparation

(*ii*) Liberation of free alkaloidal base

(*iii*) Extraction of alkaloidal base with organic solvent

(*iv*) Purification of crude alkaloidal extract

(*v*) Fractionation of crude alkaloids

All these *five* steps shall be discussed individually as under:

Sample Preparation

The first and foremost step is the sample preparation. The plant material is reduced to a moderately coarse powder by appropriate means using grinders and sieves, to facilitate maximum effective contact of the solvent with the ruptured alkaloid bearing tissues and cells. In the case of plant substances that are rich in oils and fats, such as: seeds, kernels, these non-alkaloidal chemical components need to be eliminated completely by extraction with a suitable non-polarsolvent like nhexane, light petroleum ether, in a soxhlet apparatus, which would not extract the alkaloids in question.

However, it is always advisable to shake the light-petroleum ether or n-hexane fraction with a dilute mineral acid and subsequently test the acidic solution for the presence of alkaloids.

Liberation of Free Alkaloidal Base

It has been observed that the **alkaloids** invariably occur in the plant sources as the salt of acids, such as: oxalates, tannates etc. Therefore, when the plant substance is exposed to an alkaline medium, the alkaloidal salts are readily converted to the corresponding alkaloid bases.

Choice of Alkali Indeed, the choice of a suitable *mineral base* (alkali) for the ease of liberation of the alkaloid from the salts is not only very vital but also equally significant and largely depend on the following factors, namely:

(*a*) **Natural state of the alkaloids:** It has been observed that the salt of a *strongly basic alkaloid* with a mineral acid usually tends to undergo cleavage under the influences of a stronger base. Likewise, the corresponding salt of a *weakly basic alkaloid* and a relatively weak organic acid shall require a rather weaker base for its cleavage.

(*b*) **Chemical characteristics of the alkaloidal base:** The usage of strong alkali *e.g.*, NaOH or KOH should be avoided as far as possible by virtue of the fact that certain alkaloids undergo hydrolysis on prolonged contact with a strong base.

Example

(*i*) **Hydrolysis of ester-alkaloids,** *e.g.*, **cocaine, hyoscyamine;**

(*ii*) **Phenolic alkaloids** *e.g.*, **cephaeline, morphine.** These **alkaloids** normally get solubilized while in contact with a strong alkali and, therefore milder alkaline reagents *e.g.*, dilute ammonia solution are necessary for their liberation.

(a) **Presence of fatty substances:** The usage of strong alkali is strictly prohibited in the case of fat containing plant materials because of the formation of saponified products causing troublesome emulsions. In such cases, it is always preferred to defat the plant substance before proceeding for the liberation of free alkaloids.

Ammonium Hydroxide Solution Dilute aqueous ammonium hydroxide solution is one of the choicest alkali most frequently used for the liberation of alkaloids from the plant sources. It enjoys a two-fold advantage. First, being its adequate alkalinity to liberate most of the common alkaloids, and second by, its volatile nature so that it may be removed by evaporation of the solvent. As it has a tendency to be extracted by solvent ether from the aqueous solution, therefore, it is almost necessary to get rid of it by evaporation and subsequent washing repeatedly. In normal practice, usually even the last traces of ammonia are removed when the combined ethereal extract is reduced to half of its original volume under vacuum.

NaOH or KOH Solution The **alkaloids** that occur naturally as their tannate salts specially require either NaOH or KOH solution for their subsequent liberation. In certain typical instance even the use of KOH or NaOH fails to cleave the tannate salts because of their intimately strong bondage with the alkaloid and extremely insoluble nature.

Example

(*i*) **Cinchona Bark:** It has got to be treated first by heating with dilute HCl so as to decompose the salts and liberate the alkaloids in the form of water soluble hydrochlorides, and

(*ii*) **Pomegranate Bark:** It does not have the tannin so tenaciously bound to the alkaloids as in the case of cinchona bark. Hence, NaOH solution is strong enough to cause on effective split of the alkaloidal salts. It also acts to control the solubility of the water-soluble pomegranate alkaloids by preventing their dissociation.

Extraction of Alkaloidal Base

The extraction of alkaloidal base may be accomplished by *three* different types of solvents that are discussed below, namely:

[A] Extraction with Water-Miscible Solvents A plethora of **alkaloids** and their respective salts are soluble in alcohols, such as: methanol, ethanol, isopropanol; therefore, these very solvents may also be employed for the extraction of the plant substances. The usual pretreatment of the crude drug with alkali may be avoided completely, because alcohol appears to affect dissolution of not only the *alkaloidal salts* but also the *free bases* found in the plant substances. It is, however, believed that alcohol predominantly exerts a *hydrolyzing effect* upon the alkaloidal tannates and other salts. In actual practice, neither pretreatment of the crude drug with an alkali nor acidification of the alcohol with a small amount of a mineral acid or an organic acid is required.

Note

1. The penetration and hence the subsequent extraction of the crude drug is almost complete with the help of four successive extractions with an alcohol. Further, the loss of solvent is comparatively less than the chlorinated solvents e.g., chloroform.

2. The extraction of total alkaloids with alcohol is highly recommended because of its maximum efficiency and economical viability.

[B] Extraction with Water-Immiscible Solvents In reality, the most widely used water-immiscible solvents for the extraction of alkaloids are: chloroform, diethyl ether (solvent ether) and isopropyl ether. However, a few other specific organic solvents, namely: ethylene chloride, carbon tetrachloride and **benzene*** may be employed with an evident advantage for certain specific alkaloids. Interestingly, *chloroform* is regarded as the choicest water-immiscible solvent for a broad-spectrum of alkaloids present in the plant kingdom and extracts them with varying degrees of ease.

Note: Chloroform is not suitable for the extraction of quaternary alkaloids e.g., tubocurarine.

[C] Extraction with Water The crude drug is subjected to extraction with water previously acidified with dilute solution of HCl, H_2SO_4 or CH_3COOH, which is subsequently rendered alkaline, preferably with dilute NH_4OH solution and finally extracted with a water-immiscible solvent as stated in [B] above.

Undoubtedly, water being an excellent and absolutely inexpensive polar solvent for the extraction of alkaloids, but if offers an enormous volume of disadvantages because it carries along with it a large number of other plant components, for instance: sugar, pigments

(*e.g.*, **chlorophylls**), starches, tannins, proteins etc., which ultimately puts across a collosal waste of time, energy and chemicals. Hence, its usage has been resulting to a bear minimum level.

In general, the alkaloids may be extracted by any of the following *three* well-defined and widely accepted processes, namely:

(*a*) Soxhlet Extraction Process

(*b*) Stas-Otto Process, and

(*c*) Kippenberger's Process.

All these three processes shall now be discussed briefly in the sections that follows:

(*a*) Soxhlet Extraction Process: The soxhlet assembly is a continuous extractor which is generally suitable for the extraction of alkaloids from powdered plant materials with the help of organic solvents. In this instance, the powdered drug is usually moistened with dilute ammonia solution and then packed loosely in the thimble of the Soxhlet apparatus; and the organic solvent affords a deep penetration of the moist drug thereby allowing the greatest possible extraction of the alkaloids from the exposed surfaces of the cells and tissues of the crude drug. Once, the extraction is ascertained to have completed, the solvent is filtered and evaporated in a **Rotary Thin-Film Evaporator** and the residue is treated further for the isolation of individual alkaloids.

(*b*) Stas-Otto Process: The **Stas-Otto process** essentially consists of treating the powdered and sieved drug substance with 90–95% (v/v) ethanol, previously acidified with tartaric acid. The proportion of crude drug to solvent should be maintained as 1 Kg to 1 L. The alcohol is distilled off under vacuum and the resulting aqueous residue is treated with petroleum-ether (60-80°C) to remove the fatty components completely. If any alkaloid is removed by the petroleum ether, it must be recovered by treating it with dilute mineral acid. Thus, the resulting aqueous extract is mixed with the main bulk of aqueous extract. The combined aqueous extract is filtered and evaporated to dryness preferably in a **Rotary *Thin*-Film Evaporator** under vacuum. The residue is extracted with absolute ethanol thereby dissolving the total alkaloids.

(*c*) Kippenberger's Process: In Kippenberger's process the powdered and sieved plant substance is first and foremost digested with solution of tannin (100 g) in glycerol (500 g) at a constant temperature of 40°C for a duration of 48 hours. The resulting mixture is further heated to 50°C so as to help in the complete coagnlation of proteinous substances, cooled to ambient temperature and finally filtered. The resulting filtrate is thoroughly shaken with petroleum ether to get rid of faulty materials (oils, fats and waxes), and the last traces of petroleum ether is

removed from the extract by heating either on a water-bath (electric) or exposure to Infra-Red Lamp. The fat-free crude plant extract is subsequently acidified and shaken with chloroform, successively to remove the bulk of the alkaloids, namely, atropine, codeine, colchicine, narcotine, nicotine, papaverine, spartenine and thebaine.

The resulting residual extract may still contain narceine, curarine and morphine. However, narceine and morphine may be isolated by passing freshly generated CO2 directly into extract so as to convert the alkali hydroxide into their corresponding carbonate, which is then ultimately subjected to solvent extraction using a mixture of alcohol and chloroform. Finally, the third alkaloid, curarine, may be extracted by agitation with a mixture of equal volumes of ether and chloroform.

However, a combination of **Kippenberger's process** and **Stas-Otto process** by its application to the final alcoholic extract obtained by the latter process is found to give better separation of alkaloids.

Purification of Alkaloidal Extract

The main bulk of the **crude alkaloidal extract** is invariably subjected to further purification by means of either anyone or combination of the following methods:

(*a*) Extraction with Acid Solution The extraction of the **alkaloid** from the bulk of the crude alkaloid solution in immiscible organic solvent is invariably carried out by shaking with an acid solution. In usual practice, the use of HCl is restricted when chloroform remains as the solvent because of the fact that quite a few alkaloidal hydrochlorides are distinctly soluble in the latter. However, dilute H_2SO_4 is always preferred over HCl for general use in the extraction of alkaloids. Subsequently, the acid solution is rendered alkaline with dilute NH4OH solution to liberate the alkaloids which is then extracted with an organic solvent. The solvent is removed under reduced pressure and the traces of moisture is removed with anhydrous sodium sulphate.

Note: The following two precautions may be observed, namely

(*i*) To avoid the formation of stubborn and troublesome emulsions a solution of gumtragacanth is often added to the aqueous-phase. In case, it still persists the two phases may be got separated by centrifugation, and

(*ii*) To discard the presence of foreign interfering extractive components present in plant substances, such as: pigments, resins, waxes, oils and fats, the use of a 2.5-5% (w/v) solution of lead acetate is made to the alkaloidal extract which precipitates them effectively. The excess of

lead present in the filtrate is removed by either passing H_2S gas through the Kipp's Apparatus or by adding sodium phosphate.

(*b*) Precipitation of Alkaloid with Precipitating Reagent The usual precipitation of the **alkaloid** as a complex compound is accomplished by the addition of a suitable precipitating reagent. The resulting alkaloidal complex is further purified by filtration, recrystallization and ultimately decomposed to obtain the desired free alkaloid(s).

Example

(*i*) **Tannic-acid Complex:** It is normally decomposed by treatment with freshly prepared $Pb(OH)_2$ or $Pb(CO_3)_2$.

(*ii*) **Precipitates obtained with $HgCl_2$, $AuCl_3$, $PtCl_4$, Mayer's Reagent:** These precipitates are decomposed by passing a stream of H_2S gas through its suspension.

(*iii*) **Precipitates with Double Salts:** The double salt obtained with Dragendorff's Regent is quickly boiled with 5% (w/v) $BaCO_3$ solution.

(*iv*) **Precipitates with Nitrogenous Acids:** The precipitates obtained with nitrogenous acids like picric acid and picrolonic acid are normally decomposed by treatment with either NH_4OH or NaOH.

(*v*) **Reineckate Complex:** The complex obtained from alkaloid with *Reinecke Salt*, NH_4 $[Cr(NH3)_2(SCN)_4]$, is normally decomposed by treating its solution in a mixture of acetone and water (1:1) with a silver sulphate solution. It is pertinent to mention here that the **free liberated alkaloid** from the complexes stated above, (*i*) through (*v*), may be further extracted for its final recovery with an appropriate organic solvent, such as: chloroform.

(*c*) The purification of **alkaloids** may also be accomplished by the formation of its crystallised alkaloidal salt by the addition of an appropriate mineral or organic acid, such as: hydrochloric, hydrobromic, perchloric, sulphuric, oxalic and tartaric acids.

(*d*) Various known **separation techniques,** namely: **partition, ion-exchange** and **column chromatography** are invariably used for the purification of a host of alkaloids.

Besides, various physical parameters like: specific rotation, melting point, solubility are frequently used as a definite criteria of ascertaining the purity of alkaloids.

Fractionation of Crude Alkaloids

It has been observed largely that most of the alkaloid-bearing plant materials usually contain a mixture of closely-related alkaloids. Therefore, it has become almost necessary to carry out an effective fractionation of crude alkaloids from the extract or solution of total crude alkaloids.

However, the traditional and orthodox methods of separation are not only difficult but also tedious and cumbersome. The commonly employed techniques of separation that were found to the reliable and dependable may be short-listed as follows:

(*i*) Fractional crystallization,

(*ii*) Fractional distillation, and

(*iii*) Derivatization with low solubility products.

The latest methods employed for the separation of **alkaloids** are the preparative **high performance liquid chromatography (HPLC), high performance thin-layer chromatography (HPTLC),** chromatotron, counter-current distribution and other chromatographic techniques including columnchromatography, ion-exchange chromatography.

Following are some of the typical situations whereby the mixture of **alkaloids** may be separated effectively, such as:

(*a*) A larger section of the **alkaloids** are easily soluble in chloroform and relatively less soluble in other organic solvents. In general, the order of solubility is as stated below chloroform > acetone > ethanol > methanol > ethyl acetate > ether > n-hexane. Keeping in view the above solubility profile of alkaloids in organic solvents, if one of the alkaloids is much less soluble in ethanol than chloroform, the fractional crystallization of this alkaloid is possible. In this particular instance the chloroform-fraction is concentrated to an appropriate level, and hot ethanol added in small proportions at intervals. Thus, upon cooling the alkaloid, which is less soluble in ethanol, separates out conveniently.

(*b*) In case, the fractional crystallization of the mixture of closely related alkaloids become tedious and ineffective, one may try to form their respective salts,** and then carry out the separation indicated above.

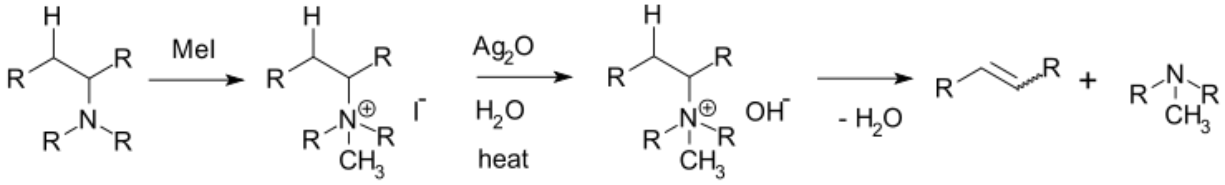
(*c*) The various acids, namely: HCl, HBr, HI, $HClO_4$, HNO_3, $C_2H_2O_4$, and $C_6H_3N_3O_7$, may either be employed in aqueous or methanolic solution. Thus, from the resulting methanolic solution, the salts of the respective alkaloids may be precipitated by the addition of ether. The precipitated crude alkaloidal salts may be further recrystallized from hot acetone containing a small proportion of methanol.

(*d*) In certain other specific instances, the salts of the respective oxalates, picrates and perchlorates may be precipitated from their solutions in acetone, by the addition of ethyl acetate.

Hofmann's Exhaustive Methylation Method:

The principle of this method is that compounds, which contain the structural unit =CH=C–N+R_3OH , eliminate a trialkylamine on pyrolysis at 200 °C or above to yield an olefin.

Hofmann elimination, also known as exhaustive methylation, is a process where a quaternary amine is reacted to create a Tertiary amine and an alkene by treatment with excess methyl iodide followed by treatment with silver oxide, water, and heat.

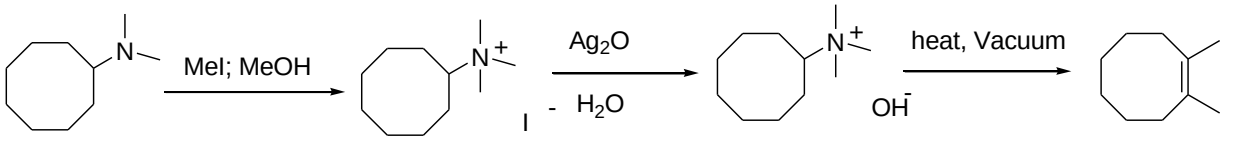


After the first step, a quaternary ammonium iodide salt is created. After replacement of iodine by an hydroxyl anion, an elimination reaction takes place to the alkene.

With asymmetrical amines, the major alkene product is the least substituted and generally the least stable, an observation known as the **Hofmann rule**. This is in direct contrast to normal elimination reactions where the more substituted, stable product is dominant (Zaitsev's rule).

The reaction is named after its discoverer, August Wilhelm von Hofmann.[1]

An example is the synthesis of trans-cyclooctene:



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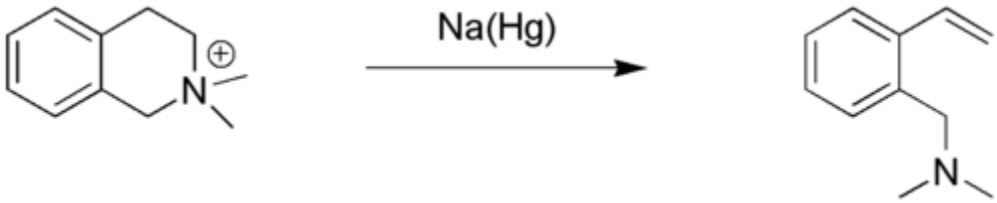
In a related chemical test called **Herzig–Meyer alkimide group determination** a tertiary amine with at least one methyl group and lacking a beta-proton is allowed to react with hydrogen iodide to the quaternary ammonium salt which when heated degrades to iodomethane and the secondary amine

The **Emde degradation** (also called **Emde-reaction** or **Emde-reduction**) is a method for the reduction of a quaternary ammonium cation to a tertiary amine with sodium amalgam.



This organic reaction was first described in 1909 by the German chemist Hermann Emde and was for a long time of great importance in structure elucidation of many alkaloids, for example that of ephedrine. Alternative reducing agents exist for this reaction; for instance, lithium aluminium hydride.

Alkaloids are naturally-occurring organic compounds containing nitrogen moiety, and are usually heterocyclic in nature. They are nitrogen based organic compounds, with nitrogen enclosed in an heterocyclic ring. The alkyl amines are referred to as proalkaloids. Characteristics of alkaloids (1)They are basic in nature due to the presence of nitrogen in their ring. (2) They have complex structures. (3) They have bitter principles. (4) They are mostly obtained from plant materials. (5) They have high pharmacological and physiological activities. Examples of alkaloids are: (1) Quinine — an antimalarial drug isolated from a plant called Cinchonia officialis

Nicotine

i. The molecular formula of nicotine is C_{10} H_{14} N_2.
ii. With HCI it forms the crystalline salt, nicotine dihydrochloride. This proves that nicotine is a diacid base.
iii. On treatment with CH3I, it forms dimethiodide. This suggests that nicotine is a ditertiary base
iv. Herzig - Meyer determination proves that nicotine contains one (-NCH3) group.
v. Nicotine on oxidation with KNnO4 or chromic acid gives nicotinic acid (Pyridine – 3-carboxylic acid).

The reaction shows that the side chain is saturated

The structure of nicotine is also proved by the following reaction. Nicotine when treated with bromine, forms dibromo nicotine. This on heating with barium hedroxide, breaks down to give nicotinic acid, malonic acid and methyl amine.

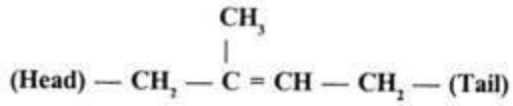
Introduction to Terpenes:

These substances constitute the largest group of secondary plant products and show some of the properties of lipids. They are insoluble in water and are derived from the union of a common 5-carbon unit called as isoprene which has a branched carbon skeleton. Isoprene in turn is derived from basic 5-C unit called as isopentane.

isoprene rule. Definition: the classical, outmoded statement that naturally occurring terpenes are built up by condensation of **isoprene** units by either a 1-4 linkage ("head to tail") or a 4-4 linkage ("tail to tail").

Introduction There are many different classes of naturally occurring compounds. Terpenoids also form a group of naturally occurring compounds majority of which occur in plants, a few of them have also been obtained from other sources. Terpenoids are volatile substances which give plants and flowers their fragrance. They occur widely in the leaves and fruits of higher plants, conifers, citrus and eucalyptus. The term 'terpene' was given to the compounds isolated from terpentine, a volatile liquid isolated from pine trees. The simpler mono and sesqui terpenes are chief constituent of the essential oils obtained from sap and tissues of certain plant and trees. The di and tri terpenoids are not steam volatile. They are obtained from plant and tree gums and resins. Tertraterpenoids form a separate group of compounds called 'Carotenoids' The term 'terpene' was originally employed to describe a mixture of isomeric hydrocarbons of the molecular formula C10H16 occurring in the essential oils obtained from sap and tissue of plants, and trees. But there is a tendency to use more general term 'terpenoids' which include hydrocarbons and their oxygenated derivatives. However the term terpene is being used these days by some authors to represent terpenoids. By the modern definition: "Terpenoids are the hydrocarbons of plant origin of the general formula $(C_5H_8)_n$ as well as their oxygenated, hydrogenated and dehydrogenated derivatives." Isoprene rule: Thermal decomposition of terpenoids give isoprene as one of the product. Otto Wallach pointed out that terpenoids can be built up of isoprene unit.

Except for isoprene itself, the isoprenoids or terpenoids are dimers, trimers, tetramers or polymers in which isoprene units are usually joined in a head to tail manner:



However, sometimes due to extensive metabolic modifications it is not easily possible to mark out the original 5-C units in isoprenoids.

Classification of Terpenes:

Terpenes are classified into many categories based on the no. of carbon atoms and isoprene residues present in their structure:

(i) Monoterpenes. They consist of 10-C atoms or two isoprene residues.

(ii) Sesquiterpenes. These contain 15-C atoms or three isoprene residues.

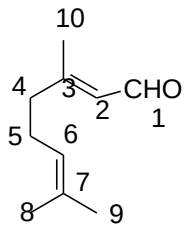
(iii) Diterpenes. These contain 20-C atoms or four isoprene residues.

(iv) Triterpenes. These consist of 30-C atoms or six isoprene units.

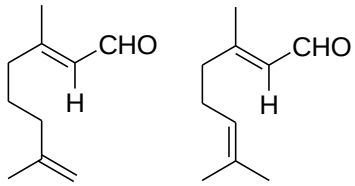
(v) Tetraterpenes. These consist of 40-C atoms or eight isoprene residues.

(vi) Polyterpenes. These consist of large number of isoprene residues

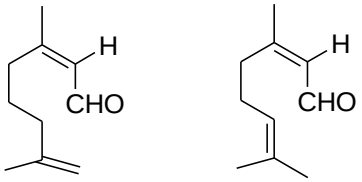
Citral



Mixture of at least 4 geometrical isomers of di-olefinic aldehydes

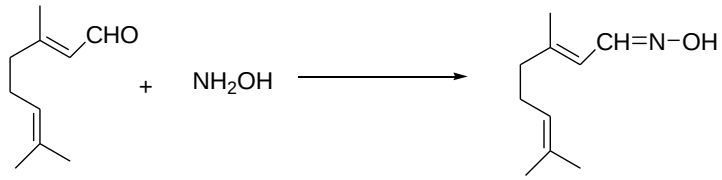


Geranial (citral a)

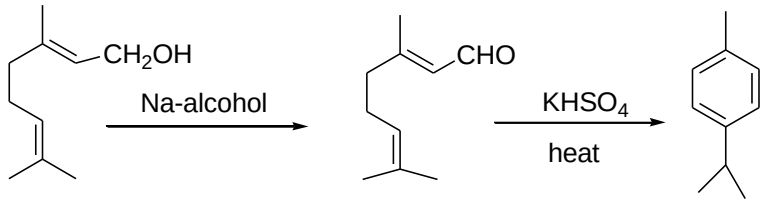


Neral (citral b)

Formation of an oxime of citral indicated the presence of an oxo group in citral.

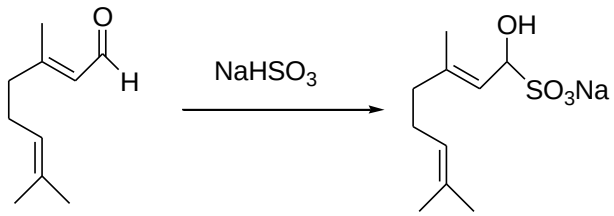


Citral when heated with potassium hydrogen sulphate afforded the known aromatic hydrocarbon, p-cymene, which fixed the position of methyl and isopropyl groups in citral.

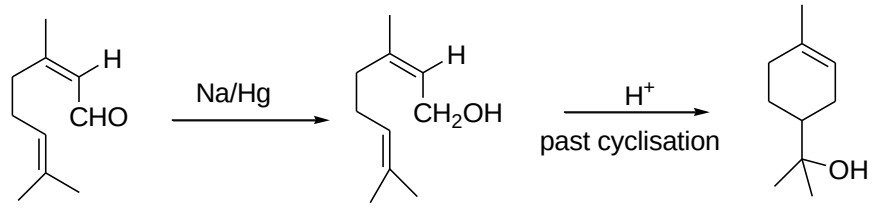


geraniol citral p-cymene

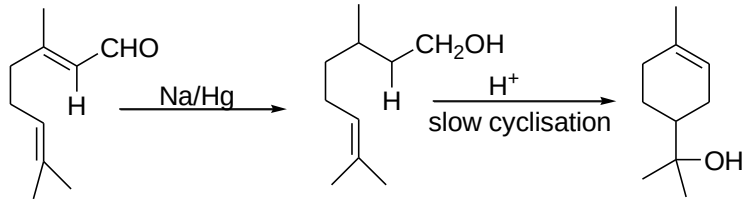
Citral formed both mono- and di- bisulphites by the addition of sodium bisulfite to reveal the presence of a **conjugated aldehyde** group. Its UV spectrum displayed a band at 238 nm to confirm this.



Citral on reduction with **sodium-amalgam** citral gave an alcohol, **geraniol,** $C_{10}H_{18}O$

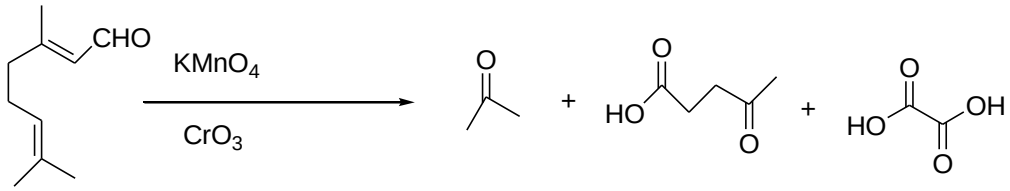


Neral or citral-b nerol α-terpineol

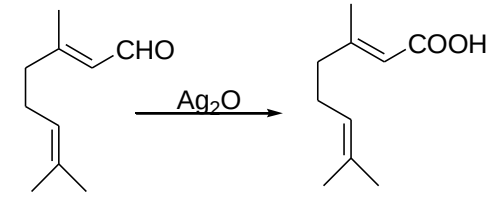


Geranial or citral-a geraniol

Citral on oxidation with alkaline permanganate, yielded **acetone**, **oxalic** and **levulenic acid**.



Citral oxidation with silver oxide afforded an acid **geranic acid**, $C_{10}H_{16}O_2$ containing the same number of carbon atoms suggesting that citral had an aldehyde group.



citral geranic acid

Based on the above data and coupled with the biogenetic considerations that **citral** is formed by the joining of **two isoprene** units in the head to tail fashion, structure of **citral** was assigned tentatively.

This structure was further supported by the degradation of **citral** on treatment with aqueous **potassium carbonate** when **6-methyl-hept-5-en-2-one** and **acetaldehyde** were obtained. The structure of **citral** was finally confirmed by its synthesis.

POSSIBLE QUESTIONS

UNIT V

PART A

Multiple Choice Questions

1. Occur in the plant sources as the salt of acids, such as: oxalates, tannates
   a. **Alkaloids** b. terpenes c. steroids d. carbohydrates

2. In Hoffmann exhaustive methylation, the Second step is
   a. Formation of quarternary salt b. **Conversion of quarternary salt in to hydroxide**
   c. Heating the quarternary hydroxide d. Elimination of alkene

3. Morphine is a
   a. Pyrrolidine type alkaloids b. Quinoline alkaloid c. Tropane alkaloids d. **Isoquinoline alkaloid**

4. The chief constituents of essential oils are
   a. **Monoterpenes and sesquiterpenes** b. Diterpenes c. triterpenes d. tetraterpenes
5. The starting material in Pomeranz Fritsch synthesis is
   a. Phenyl ethyl amine b. aminoacetal c. **Aryl ethylamine and an aldehydes** d. aniline

6. If a terpene consists of 10 carbon atoms then it is called
   a. **Monoterpenes** b. Sesquiterpenes c. Diterpenes d. Triterpenes

7. The reagent used in the Emde degradation is
   a. **sodium amalgam** b. Sodium/ethanol c. Sodium nitrate d. Fe/HCl

8. Heroin is a
   a. CNS drug- stimulants b. **CNS drug- Depressant** c. CNS drug- Hallucinogens d. Psycho-active drug

9. Triterpenes consists of
   a. 10 carbon atoms b. 20 carbon atoms c. **30 carbon atoms** d. 15 carbon atoms

10. Terpenes are built up by condensation of isoprene units by either a 1-4 linkage (head to

tail) is called
a. Hofmann rule b. **Isoprene rule** c. Zaysteff rule d. Flemings rule

11. Example for Tropane alkaloid
a. Hygrine b. Quinine c. **Atropine** d. Caffeine

12. Example for CNS drug- stimulants
a.**Nicotine** b. Benzodiazepines c. Psilocybin d. Cannabis

13. Occur in the plant sources as the salt of acids, such as: oxalates, tannates
a. Alkaloids b. terpenes c. steroids d. carbohydrates

14. In Hoffmann exhaustive methylation, the Second step is
a. Formation of quarternary salt b. **Conversion of quarternary salt in to hydroxide**
c. Heating the quarternary hydroxide d. Elimination of alkene

15. Morphine is a
a. Pyrrolidine type alkaloids b. Quinoline alkaloid c. Tropane alkaloids d. **Isoquinoline alkaloid**

16. The chief constituents of essential oils are
a. Monoterpenes and sesquiterpenes b. Diterpenes c. triterpenes d. tetraterpenes

17. The starting material in Pomeranz Fritsch synthesis is
a. Phenyl ethyl amine b. aminoacetal c. **Aryl ethylamine and an aldehydes**
d. aniline

18. If a terpene consists of 10 carbon atoms then it is called
a.Monoterpenes b. Sesquiterpenes c. Diterpenes d. Triterpenes

19. The reagent used in the Emde degradation is
a.**sodium amalgam** b. Sodium/ethanol c. Sodium nitrate d. Fe/HCl

20. Heroin is a
a. CNS drug- stimulants b. **CNS drug- Depressant** c. CNS drug- Hallucinogens d. Psycho-active drug

PART B

1. What is an alkaloid? Give examples
2. What is a terpene. Give an example
3. What is meant by isoprene rule?

4. What is meant by Emdes degradation
5. What is meant by Hoffmann exhaustive methylation

PART C

1. Explain the Occurrence, classification, isoprene rule in terpenes.

2. Explain with suitable examples (i) Hoffmann's exhaustive methylation, (ii) Emde'smodification.
3. Explain how alkaloids are extracted from plant materials
4. Explain the structure elucidation and synthesis of nicotine
5. Elucidate the structure of citral
6. Explain the natural occurrence, general structural features, isolation and their physiological action of alkaloids.
7. Explain the structure elucidation and synthesis of nicotine
8. Explain the medicinal importance of Medicinal importance of Nicotine, Hygrine, Quinine, Morphine, Cocaine, and Reserpine.

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II B.Sc. Chemistry
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

UNIT IV

Multiple choice questions (Each carries one mark: for online examination)

S.No	Questions	Answer A	Answer B	Answer C	Answer D	Answer
1.	Monoterpenes consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	30 carbon atoms	10 carbon atoms
2.	Sesquiterpenes consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	30 carbon atoms	15 carbon atoms
3.	Diterpenes consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	30 carbon atoms	20 carbon atoms
4.	Triterpenes consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	30 carbon atoms	30 carbon atoms
5.	If a terpene consists of 10 carbon atoms then it is called	Monoterpenes	Sesquiterpenes	Diterpenes	Triterpenes	Monoterpenes
6.	If a terpene consists of 20 carbon atoms then it is called	Monoterpenes	Sesquiterpenes	Diterpenes	Triterpenes	Diterpenes
7.	If a terpene consists of 15 carbon atoms then it is called	Monoterpenes	Sesquiterpenes	Diterpenes	Triterpenes	sesquiterpenes
8.	If a terpene consists of 30 carbon atoms then it is called	Monoterpenes	Sesquiterpenes	Diterpenes	Triterpenes	Triterpenes

9.	Polyterpenes consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	Many isoprene units	Many isoprene units
10.	Isoprene consists of	10 carbon atoms	15 carbon atoms	20 carbon atoms	5 carbon atoms	5 carbon atoms
11.	In terpenes the isoprene units are joined together by	Head-tail fashion	Tail-head fashion	By amide linkages	By ether linkages	Head-tail fashion
12.	Carotinoids are otherwise called as	Monoterpenes	Sesquiterpenes	Diterpenes	tetraterpenes	tetraterpenes
13.	The chief constituents of essential oils are	Monoterpenes and sesquiterpenes	Diterpenes	triterpenes	tetraterpenes	Monoterpenes and sesquiterpenes
14.	Monoterpenes and sesquiterpenes are usually	Volatile liquids	Low melting solids	High melting solids	Crystalline substances at room temperature	Volatile liquids
15.	Terpenes are built up by condensation of isoprene units by either a 1-4 linkage(head to tail) is called	Hofmann rule	Isoprene rule	Zaysteff rule	Flemings rule	Isoprene rule
16.	Example for an antimalarial drug	Quinine	Morphine	Terpineol	cymene	Quinine
17.	Quinine is used as an	Antimalarial drug	antibiotic	Diabetes inhibitor	Anticancer drug	Antimalarial drug
18.	Emde degradation is	reduction of a quaternary ammonium cation to a tertiary amine	reduction of a tertiary amine to a quaternary ammonium cation	reduction of a quaternary ammonium cation to a alkene	reduction of a quaternary ammonium cation to a tertiary alcohol	reduction of a quaternary ammonium cation to a tertiary amine
19.	The reagent used in the Emde degradation is	sodium amalgam	Sodium/ethanol	Sodium nitrate	Fe/HCl	sodium amalgam
20.	Emde degradation is used in the structure elucidation of	Alkaloids	terpenes	steroids	flavanoids	Alkaloids
21.	In Emde degradation instead of sodium amalgam what can be used	Lithium aluminium hydride	Sodium boro hydride	Sn/HCl	Zinc amalgam	Lithium aluminium hydride

22.	reduction of a quaternary ammonium cation to a tertiary amine in presence of sodium amalgam is	Emde degradation	Hoffmann exhaustive methylation	Hoffmann degradation	Clemensen reduction	Emde degradation
23.	Example for Pyrrolidine type alkaloids	Hygrine	Quinine	Atropine	Caffeine	Hygrine
24.	Example for Quinoline alkaloids	Hygrine	Quinine	Atropine	Caffeine	Quinine
25.	Example for Tropane alkaloids	Hygrine	Quinine	Atropine	Caffeine	Atropine
26.	Example for Purine alkaloids	Hygrine	Quinine	Atropine	Caffeine	Caffeine
27.	Hygrine alkaloid is an example for	Pyrrolidine type alkaloids	Quinoline alkaloid	Tropane alkaloids	Purine alkaloids	Pyrrolidine type alkaloids
28.	Quinine alkaloid is an example for	Pyrrolidine type alkaloids	Quinoline alkaloid	Tropane alkaloids	Purine alkaloids	Quinoline alkaloid
29.	Atropine is an example for	Pyrrolidine type alkaloids	Quinoline alkaloid	Tropane alkaloids	Purine alkaloids	Tropane alkaloids
30.	Caffeine is an example for	Pyrrolidine type alkaloids	Quinoline alkaloid	Tropane alkaloids	Purine alkaloids	Purine alkaloids
31.	Morphine is a	Pyrrolidine type alkaloids	Quinoline alkaloid	Tropane alkaloids	Isoquinoline alkaloid	Isoquinoline alkaloid
32.	Nicotine is used as a	parasympathomimetic stimulant	Metabolic enhancer	depressant	halucinogen	parasympathomimetic stimulant
33.	Hygrine is found in	Coca leaves	Chincona bark	Opium	plectranthus	Coca leaves
34.	Quinine is found in	Coca leaves	Chincona bark	Opium	plectranthus	Chincona bark
35.	Morphine is found in	Coca leaves	Chincona bark	Opium	plectranthus	Opium
36.	Cocaine is a	CNS drug- stimulants	CNS drug- Depressants	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- stimulants
37.	Pseudoephidrine is a	CNS drug- stimulants	CNS drug- Depressants	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- stimulants
38.	Nicotine is a	CNS drug- stimulants	CNS drug- Depressants	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- stimulants

39.	Caffeine is a	CNS drug- stimulants	CNS drug- Depressants	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- stimulants
40.	Tranquillisers are	CNS drug- stimulants	CNS drug- Depressant	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- Depressant
41.	Heroin is a	CNS drug- stimulants	CNS drug- Depressant	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- Depressant
42.	Morphine is a	CNS drug- stimulants	CNS drug- Depressant	CNS drug- Hallucinogens	Psycho-active drug	CNS drug- Depressant
43.	Example for CNS drug- stimulants	Cocaine	Benzodiazepines	Psilocybin	Cannabis	Cocaine
44.	Example for CNS drug- stimulants	Pseudoephidrine	Benzodiazepines	Psilocybin	Cannabis	Pseudoephidrine
45.	Example for CNS drug- stimulants	Nicotine	Benzodiazepines	Psilocybin	Cannabis	Nicotine
46.	Example for CNS drug- stimulants	Caffeine	Benzodiazepines	Psilocybin	Cannabis	Caffeine
47.	Example for CNS drug- Depressants	Caffeine	tranquillisers	Psilocybin	Cannabis	tranquillisers
48.	Example for CNS drug- Depressants	Caffeine	Benzodiazepines	Psilocybin	Cannabis	Benzodiazepines
49.	Occur in the plant sources as the salt of acids, such as: oxalates, tannates	alkaloids	terpenes	steroids	carbohydrates	alkaloids
50.	Alkaloids are	Weakly basic	Strongly basic	Weakly acidic	Strongly acidic	Weakly basic
51.	Alkaloids on prolonged contact with strong bases results in	condensation	dehydration	hydrolysis	Cyclic dehydration	hydrolysis
52.	Example for ester alkaloid	cocaine,	cephaeline	morphine	Nicotine	cocaine,
53.	Example for ester alkaloid	hyoscyamine	cephaeline	morphine	Nicotine	hyoscyamine
54.	Example for phenolic alkaloid	cocaine,	cephaeline	Nicotine	hyoscyamine	cephaeline
55.	Example for phenolic alkaloid	morphine	cocaine	Nicotine	hyoscyamine	morphine

56.	Alkaloids are converted into quarternary salt using	Methyl iodide	Sodium iodide	Sodium chlride	Petroleum ether	Methyl iodide
57.	A quaternary amine is reacted to create a Tertiary amine and an alkene in	Hoffmann exhaustive methylation	Fischer synthesis	Synthesis of quinoline	In the synthesis of morphine	Hoffmann exhaustive methylation
58.	In Hoffmann exhaustive methylation, the first step is	Formation of quarternary salt	Conversion of quarternary salt in to hydroxide	Heating the quarternary hydroxide	Elimination of alkene	Formation of quarternary salt
59.	In Hoffmann exhaustive methylation, the Second step is	Formation of quarternary salt	Conversion of quarternary salt in to hydroxide	Heating the quarternary hydroxide	Elimination of alkene	Conversion of quarternary salt in to hydroxide
60.	In Hoffmann exhaustive methylation, the Third step is	Formation of quarternary salt	Conversion of quarternary salt in to hydroxide	Heating the quarternary hydroxide	Elimination of alkene	Heating the quarternary hydroxide

Reg. No.....

[16CHU303]

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II B.Sc. Chemistry
INTERNAL EXAM I
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

Time: 2 hours Maximum: 50 Marks
Date:

PART A (20 x 1 = 20 Marks)
Answer all the questions

1. Nitroalkanes on reaction with Sn/HCl give
   a. Alcohol b. Primary amine c. Secondary amine d. Tertiary amine
2. Nitroso compounds show ---------- boiling point than hydrocarbons of comparable molecular weight
   a. Lower b. Higher c. Equal d. Irregular
3. Nitro alkanes can be obtained by
   a. Oxidation of oximes b. hydrolysis of α – nitroalkanes c. action of silver nitrate on alkyl cyanide d. hydrolysis of Nitriles
4. Aci-form of nitroalkane react with methyl magnesium iodide to form
   a. Methane b. Ethane c. Nitric acid d. sulphuric acid
5. O-nitrophenol involves
   a. Intermolecular hydrogen bonding b. Intramolecular hydrogen bonding c. intermolecular coordination bondingd. Intramolecular coordination bonding
6. Amines have the
   a. Pyramidal shape b. Square planar shape c. Trigonal shape d. Octahedral shape
7. When the reduction is carried out using sodium and alcohol, it is called
   a. Clemmensen reduction b. Mendius reduction c. Stephen reduction d. Gabriel reduction
8. Gabriel synthesis is carried out for the preparation of
   a. Aldehydes and ketones b. alcohol c. Primary amines d. carboxylic acids
9. Secondary amines can be obtained by the reduction of
   a. Nitriles b. N-iso amides c. Isonitriles and N-alkylamides d. aldehydes
10. Hisenberg method is used for the separation of a mixture of
    a. Primary, secondary and tertiary amines b. Primary, secondary and tertiary amides
    b. Primary, secondary and tertiary alcohols d. Primary, secondary and tertiary carboxylic acids

85 copies

11. The correct structure of benzene diazonium chloride which explain all the properties of the compound was given by
    a. Greiss b. Kekule c. Bloomstrand d. Huckel
12. Diazotisation of aniline can be carried out at the temperature range
    a. 73-78K b. 173-178K c. 500K d. 273K
13. The reaction of benzene diazonium chloride with copper and HCl to form chlorobenzene is called
    a. Sandmeyer reaction b. Gattermann reaction c. Gomberg Bachmann reaction d. Balz Schotten reaction
14. $-N_2Cl$ group can be replaced by –H by means of
    a. Hypophosphoric acid b. Phosphoric acid c. Phosphorous acid d. Metaphosphoric acid
15. Coupling reaction involves the reaction between benzene diazonium chloride and
    a. Ether b. carboxylic acid c. Carboxylic acid derivatives d. Phenol
16. Benzene diazonium chloride can be converted into flurobenzene using
    a. CuF b. Cu/HF c. HBF_4 d. F_2
17. The coupling reaction between benzene diazonium chloride and animine takes place in
    a. Strongly alkaline medium b. Weakly alkaline medium c. Strongly acidic medium d. Weakly acidic medium
18. Example for primary amine
    a. Methyl amine b. Dimethyl amine c. Triethyl amine d. diethyl amine
19. IUPAC name of ethyl amine is
    a. Amino ethane b. Ethane aminec. N-methyl amine d. N- ethanol amine
20. Picric acid is
    a. Trinitro phenol b. Tribromo phenol c. trinitro benzoic acid d. P-methyl benzoic acid

PART- B (3 x 2 = 6 Marks)

21. Why methyl amine is more basic than ammonia?
22. Draw the resonance structure of aniline.
23. How naphthalene is prepared?

PART- C (3 x 8 = 24 Marks)

24. Explain three methods for the preparation of nitrocompounds

    OR

    Explain the reduction property of nitro compounds in various mediums
25. Write notes on 1. Hofmann exhaustive methylation 2. Hofmann elimination

    OR

    How amines are separated by Hisenberg method
26. Explain the structure elucidation of Napthalene

    OR

    How benzene diazonium chloride is prepared. What are its synthetic applications.

Reg. No……..

[16CHU303]

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II B.Sc. Chemistry
INTERNAL EXAM I
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

ANSWER KEY

PART A

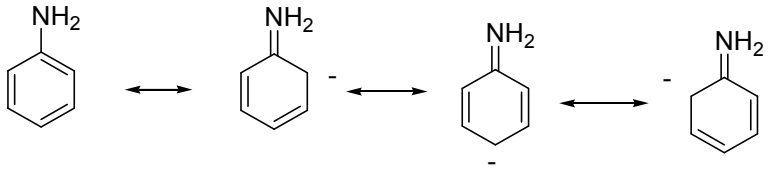
1. b. Primary amine
2. b. Higher
3. b. Oxidation of oximes
4. a. Methane
5. b. Intermolecular hydrogen bonding
6. a. Pyramidal shape
7. b. Gabriel reduction
8. c. Primary amines
9. c. Nitriles
10. a. Primary, secondary and tertiary amines
11. c. Bloomstrand
12. d. 273K
13. b. Gattermann reaction
14. a. Hypophosphoric acid
15. d. Phenol
16. c. HBF_4
17. c. Strongly alkaline medium
18. a. Methyl amine
19. a. Amino ethane
20. a. Trinitro phenol

PART B

21. Why methyl amine is more basic than ammonia?

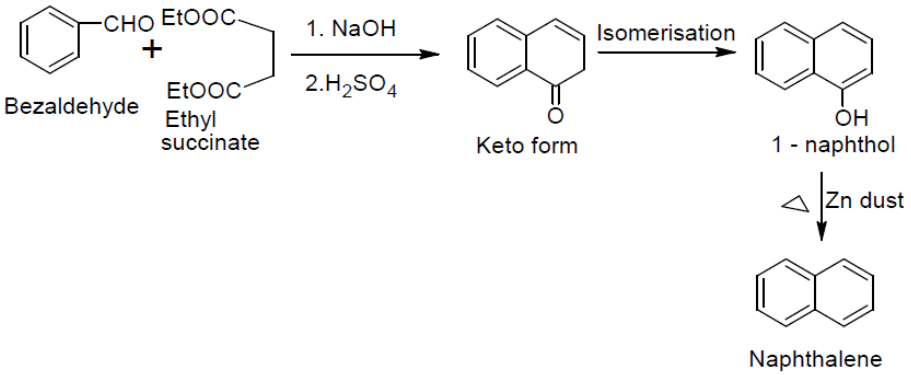
Methyl group has higher inductive effect than the H-atom. Due to more inductive effect in methylamine the availability of lone pair of electrons with nitrogen atoms is higher than in ammonia. So methyl amine is more basic than ammonia.

22. Draw the resonance structure of aniline



23. How naphthalene is prepared

From benzaldehyde and ethyl succinate (Fitting and Erdmann Synthesis): The reaction of benzaldehyde and ethyl succinate in the presence of basic catalyst like sodium hydroxide or potassium tertiary butoxide followed by cyclisation and isomerisation gives α- naphthol which further on reduction with Zn dust afforded naphthalene.



PART C

24.a. Explain three methods for the preparation of nitro compounds

Preparation of Nitro Compounds

(i) From alkyl halides:

Alkyl halides react with silver nitrite in ethanolic solution to give nitro compounds. Alkyl nitrite is formed in minor quantity. This reaction is used to prepare 1^o nitro compounds primarily while $2^o$and 3^o halides give major proportion of alkenes due to β – elimination. Contrary to this alkali nitrites give alkyl nitrites as major product. This is due to ionic nature of alkali nitrite.

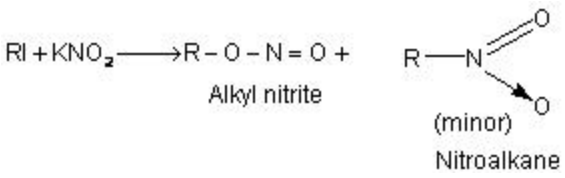
But if the reaction is carried out in solvents like DMF or DMSO, then even $NaNO_2$ or KNO_2 give good yield (about 60%) of nitro compound.

Reactions:

$$R—I + AgNO_2 \longrightarrow RNO_2 + AgI$$

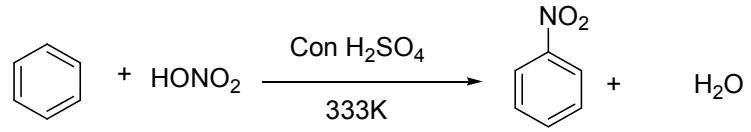
$$C_2H_5I + AgNO_2 \longrightarrow C_2H_5NO_2 + AgI$$

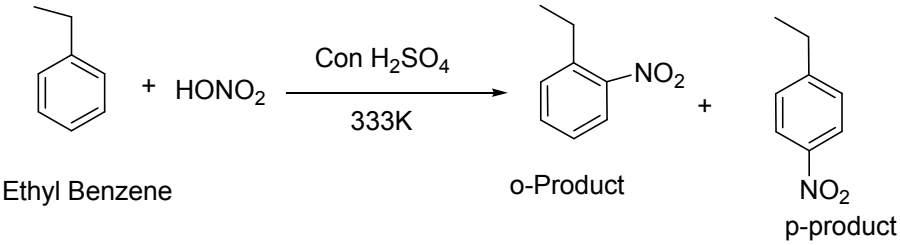
Nitroethane



(ii) Nitration:

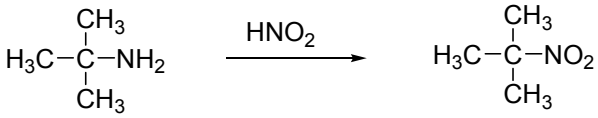
Nitro derivatives of aromatic compounds like nitrobenzene are produced when benzene is allowed to react with nitrating mixture.(conc. HNO_3/conc.H_2SO_4).





(iii) From amines:

3^o nitroalkanes can be produced as follows:



24.b. Explain the reduction property of nitro compounds in various mediums

Reduction

With Sn/HCl or catalytic hydrogenation, nitroalkanes are reduced to amines.

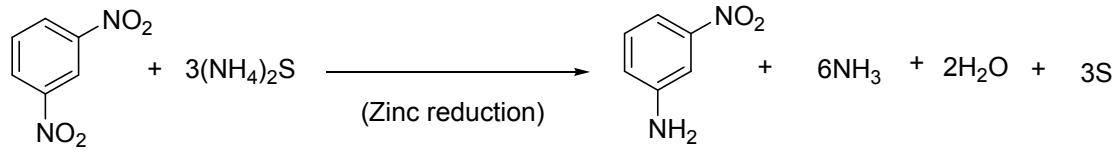
$$RNO_2 + 6[H] \xrightarrow{Sn/HCl} R\text{-}NH_2 + 2H_2O$$

If neutral reducing agent like Zn dust + NH_4Cl is used, hydroxylamines are obtained as major product.

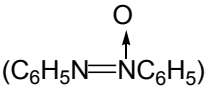
$$RNO_2 + 4[H] \xrightarrow{Zn + NH_4Cl} R{-}NHOH + H_2O$$

N-alkylhydroxylamine

In the presence of $(NH_4)_2S$ or Na_2S, selective reduction takes place.



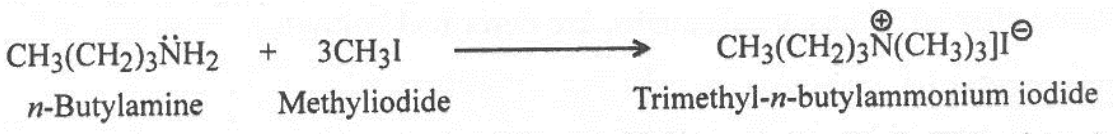
Nitrobenzene gives different products with different reagents and in different mediums.

Medium	**Reagent**	**Product**
Acid	Sn/HCl	Aniline
Neutral	Zn/NH_4Cl	N-phenyl hydroxylamine
	$Na_3AsO_3/NaOH$	Azoxybenzene 
Alkaline	$Zn/NaOH, CH_3OH$	Azobenzene
	$Zn/NaOH, C_2H_5OH$	Hydrazobenzene
Metallic hydride	$LiAlH_4$	aniline
Electrolytic	Dil. H_2SO_4	p-aminophenol

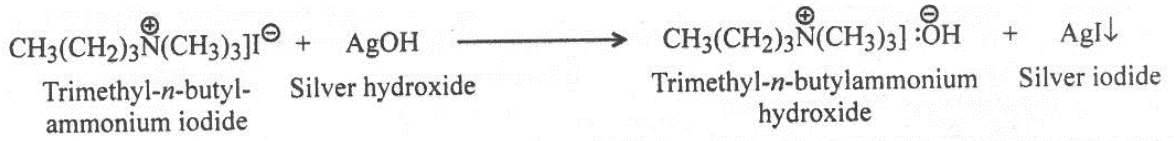
25.a. Write notes on 1. Hofmann exhaustive methylation 2. Hofmann elimination

Hofmann's Exhaustive Methylation can be applied to this amine in the following steps:

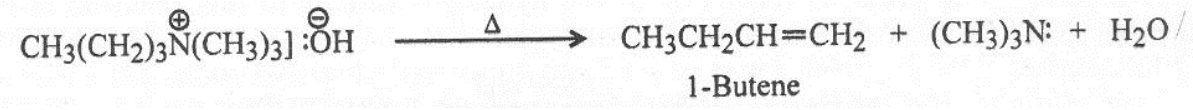
(i) n-Butylamine is methylated exhaustively by the interaction with methyl iodide to get the quaternary ammonium salt trimethyl n-butylammonium iodide).



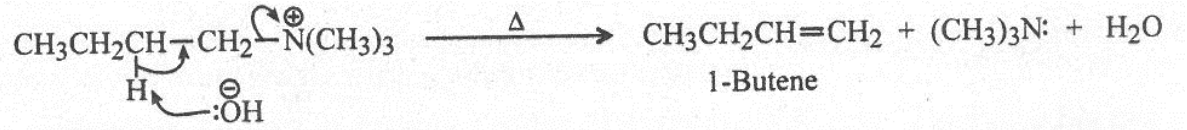
(ii) The quaternary ammonium salt obtained is step (i) is treated with AgOH when AgI precipitates out and a halogen free solid quaternary ammonium hydroxide forms.



(iii) The quaternary ammonium hydroxide obtained in step (ii) is heated strongly, it decomposes to form tertiary amine $(CH_3)_3$ N:, an alkene (1-butene) and water.



The step (iii) is a typical nucleophilic–β–elimination, as shown below:

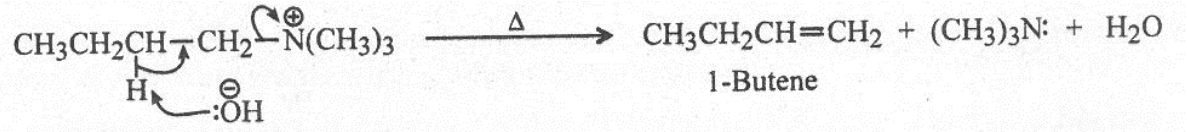


This elimination reaction is a general reaction applicable to all type of amines of varied structures. If the parent amine is an unknown nitrogenous base, we can identify the alkene formed in step (iii) and work backward to deduce the structure of the parent amine.

Hofmann elimination

This reaction is specially important in being an important tool for ascertaining the structure of unknown bases containing nitrogen (say, alkaloids occurring in nature). Let us illustrate this important reaction by taking a simple base, n-butylamine.

Nucleophilic–β–elimination, as shown below:



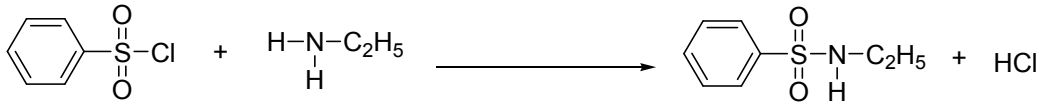
This elimination reaction is a general reaction applicable to all type of amines of varied structures. If the parent amine is an unknown nitrogenous base, we can identify the alkene formed in step (iii) and work backward to deduce the structure of the parent amine.

25.b. How amines are separated by Hisenberg method

Reaction with aryl sulphonyl chloride [Hinsberg reagent]

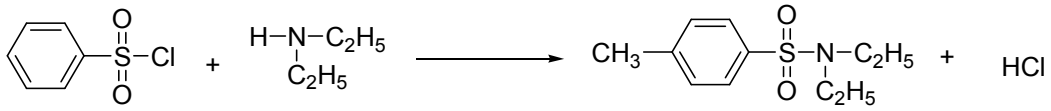
The reaction of benzenesulphonyl chloride with primary amine yield N-ethyl benzene sulphonyl amide.

The reaction of benzenesulphonyl chloride with primary amine yield N-ethyl benzene sulphonyl amide.



(soluble in alkali)

The reaction of benzenesulphonyl chloride with secondary amine yields N,N-diethyl benzene sulphonamide.



(insoluble in alkali)

Tertiary amines does not react with benzenesulphonyl chloride.

26.a. Explain the structure elucidation of Napthalene

Constitution or Structure of Naphthalene:

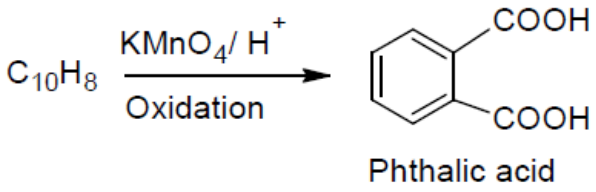
Analytical evidence: The structure of naphthalene was arrived at by following analytical evidence.

1. On the basis of analytical data its molecular formula is found to be $C_{10}H_8$.

2. Like benzene it is resistsnt to addition reactions though less than benzene. It resembles benzene in other chemical properties also and undergoes electrophilic substitution reactions like halogenation, nitration etc., more readily than benzene.

3. Its nuclear substituted hydroxy derivative are phenolic in nature and amino derivatives undergo diazotization and coupling reactions. This again shows it to be similar to benzene the structure**.**

Graebe in 1869 obtained phthalic acid (o-benzene dicarboxylic acid) on oxidation of naphthalene with acid permanganate . This showed that at least one benzene ring is present in naphthalene and there may be two side chains in ortho positions to each other.



Phthalic acid

Hence the formula of the naphthalene may be written as (I).The two side chains on the basis of valency requirements must be highly unsaturated and formula (II) may be suggested for it.

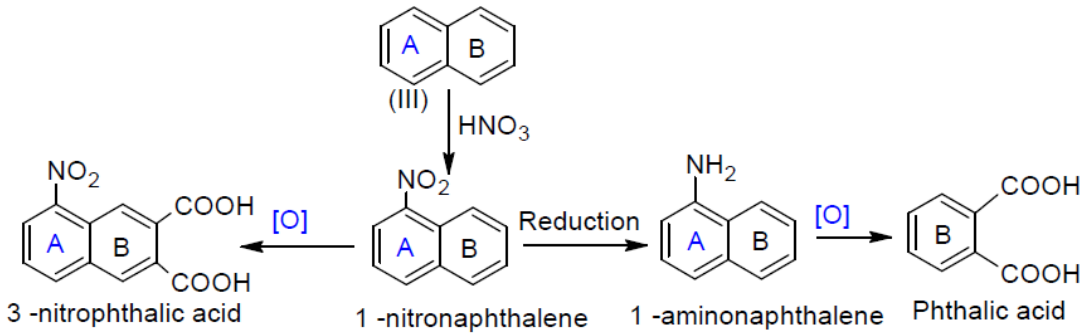
(I) (II)

However ,such structure would be in contrast to known aromatic character of naphthalene. Therefore, structure (II) and related structures for naphthalene are ruled out.

Graebe further proved that naphthalene consists of two benzene rings fused in o-positions. This was based on following experimental proof:

Naphthalene gave phthalic acid on oxidation**.** When naphthalene was nitrated it yielded nitrophthalene which oxidation gave 3-nitro phthalic acid. This showed that nitro group was present in the benzene ring and side chains were oxidized. But when nitro group of nitro naphthalene was reduced to amino group and the resulting aminonaphthalene oxidized, phthalic acid and not amino phthalic acid was obtained. An amino group attached to benzene ring is known to render the ring highly susceptible to oxidative degradation. The logical conclusion therefore could be that during the oxidation of aminonaphthalene – it was the benzene ring containing an amino group which was destroyed and the benzene ring present in oxidation product phthalic acid is other than that which had the nitro group. It was therefore

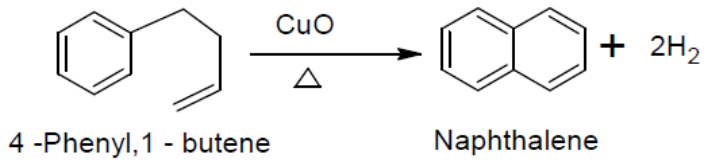
concluded that two benzene rings were fused in ortho-position i.e. naphthalene contained two benzene rings. In oxidation of nitronaphthalene, nitro phthalic acid was obtained because nitro group attached to benzene ring made the ring resistant to oxidation.



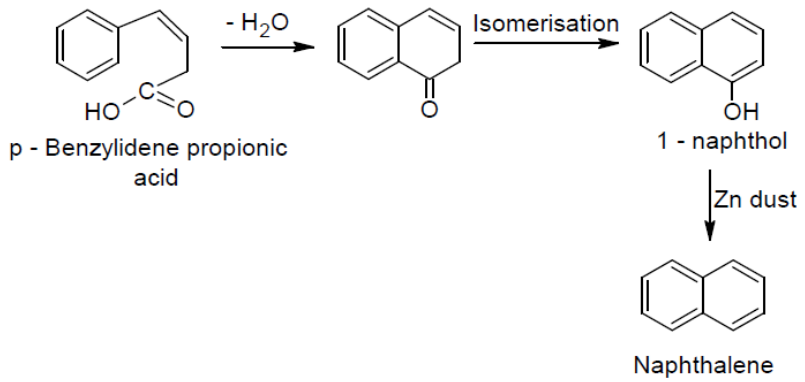
The above scheme clearly demonstrates the presence of two benzene rings fused in o-positions. The structure (III) was intuitively suggested by Erlenmeyer in 1866 and is known as Erlemeyer's structure of naphthalene.

Synthetic evidence: Synthetic evidence which support the Erlenmeyer's formula for naphthalene, some are given below:

a) If 4-phenylbutene-1 is passed over red hot calcium oxide, naphthalene is obtained.

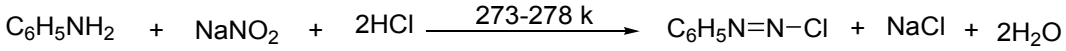


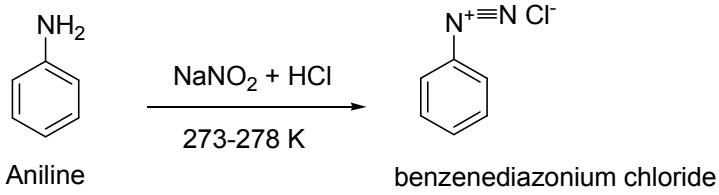
Fittig's synthesis: Cyclisation of p-benzylidene propionic acid gives α - naphthol which on distillation with zinc dust yields naphthalene.



26.b. How benzene diazonium chloride is prepared. What are its synthetic applications

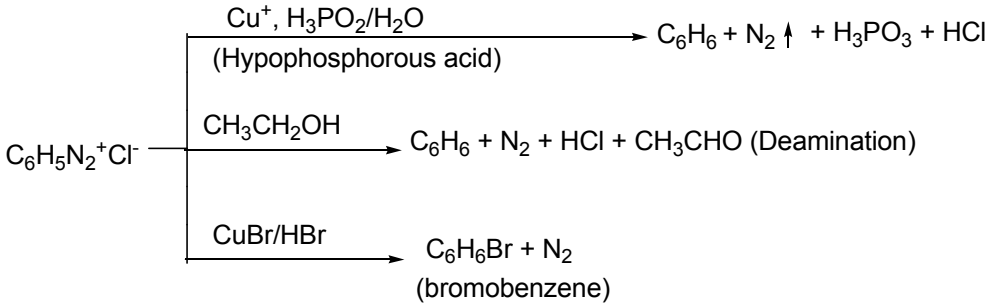
Preparation: Diazotisation reaction:

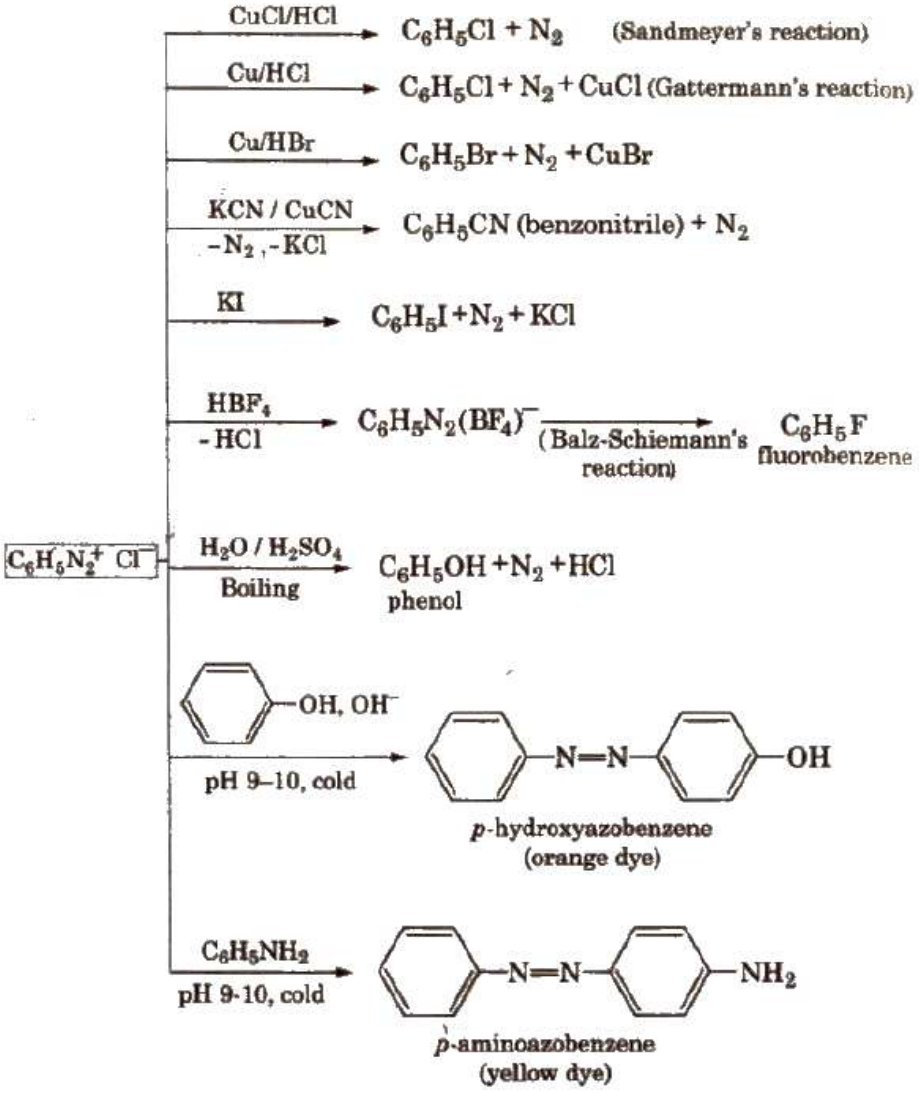




The excess acid in diazotisation reaction is necessary to maintain proper acidic medium for the reaction and to prevent combination of diazonium salt formed with the undiazotised amine.

Chemical reactions




CuCl/HCl
C6H5Cl + N2
(Sandmeyer's reaction)
Cu/HCl
C6H5Cl + N2 + CuCl (Gattermann's reaction)
Cu/HBr
C6H5Br + N2 + CuBr
KCN / CuCN
-N2 , -KCl
C6H5CN (benzonitrile) + N2
KI
C6H5I + N2 + KCl
HBF4
- HCl
C6H5N2(BF4)⁻
(Balz-Schiemann's reaction)
C6H5F
fluorobenzene
C6H5N2+ Cl⁻
H2O / H2SO4
Boiling
C6H5OH + N2 + HCl
phenol
OH, OH⁻
pH 9–10, cold
N=N
OH
p-hydroxyazobenzene
(orange dye)
C6H5NH2
pH 9-10, cold
N=N
NH2
p-aminoazobenzene
(yellow dye)

Reg. No……..

[16CHU303]

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)

II B.Sc. Chemistry
INTERNAL EXAM II
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

ANSWER KEY

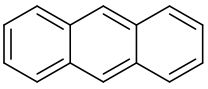
PART A

1.a. Condensed polynuclear hydrocarbons
2. a. Anthracene
3. c. ortho position
4. a. Napthalene
5. b. Planar
6. a. 1.36 A
7. a. a carbon atom of benzene ring by another hetero atom
8. c. Furan
9. b. 6 electrons
10. c. Pyrrole
11. b. 6 electrons
12.c. aza
13. a ole
14. a azole
15. a. 2-nitrofuran
16. b.Furan
17.b. 2,5-position
18. a. furan
19.a. furan
20.a. 2-nitrofuran

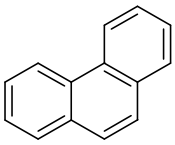
PART B

21. Differentiate phenanthrene and anthracene

Phenanthrene is a trinuclear angular aromatic hydrocarbon, whereas anthracene is a trinuclear linear aromatic hydrocarbon



Anthracene

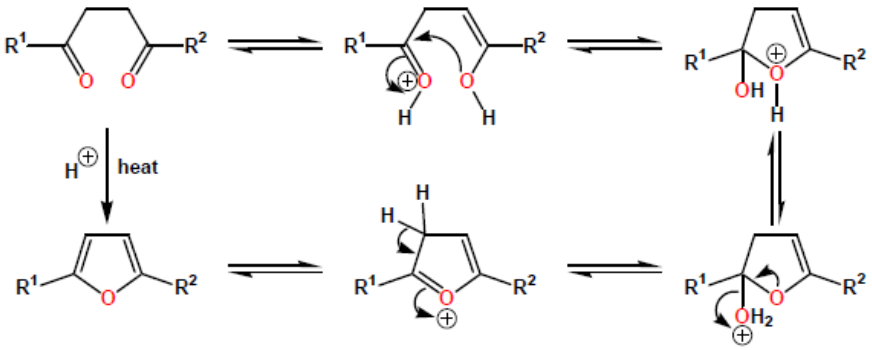


phenanthrene

22. Write any one synthesis of furan

Paal Knorr synthesis of furan

When 1,4-diketones are heated in presence of an acid it yields furans.



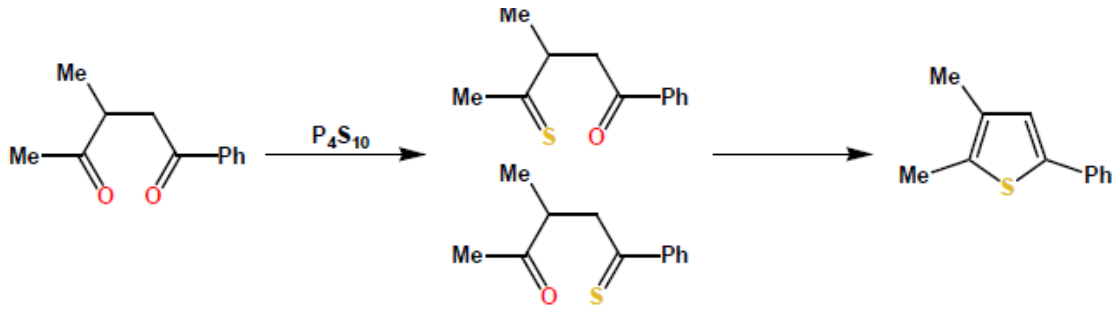
The reaction is usually reversible and can be used to convert furans into 1,4-diketones

• A trace of acid is required – usually TsOH (*p*-$MeC_6H_4SO_3H$)

23. How thiophene is prepared.

Synthesis of Thiophenes by Paal Knorr type reaction ("4+1")

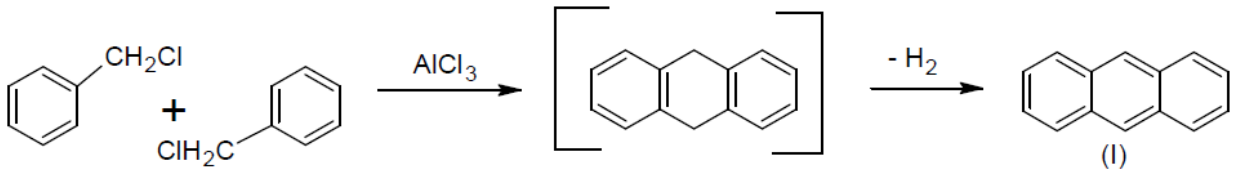
1,4 diketones when heated with phosphorous pentasulphide gives thiophene. Reaction might occur *via* the 1,4-*bis*-thioketone



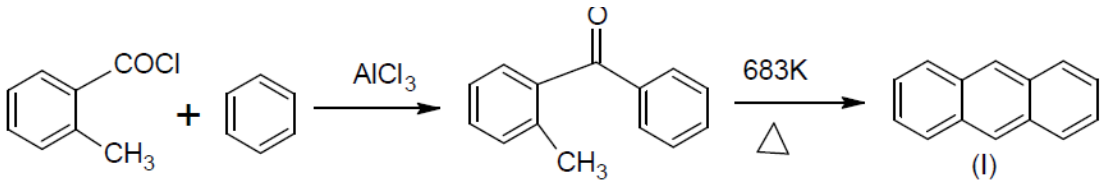
PART C

24.a. Explain the preparation and properties of anthracene

Friedel crafts alkylation between two molecules of benzyl chloride gives 9.10-dihydroanthracene which is oxidized readily under the reaction conditions yielding anthracene.

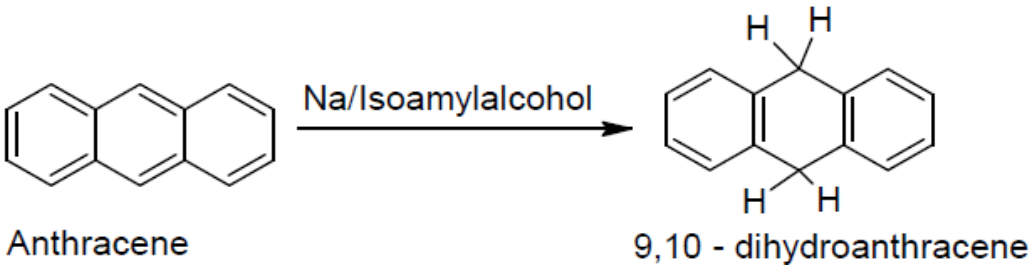


2.This method is based on Elbs reaction in which a polynuclear aromatic hydrocarbon having an anthracene moiety is formed by pyrolysis of a diaryl ketone containing a methyl or methylene group ortho to the carbonyl group.



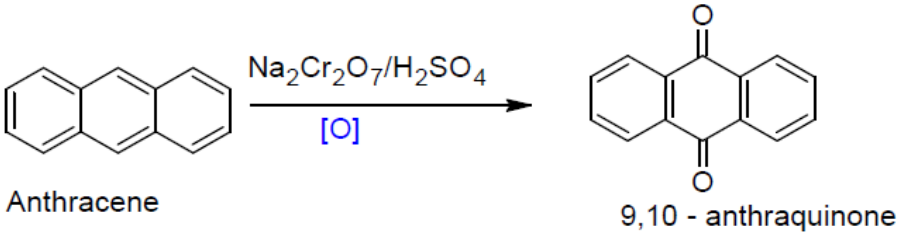
Properties

1. Reduction: When reduced with sodium and isoamyl alcohol it forms 9,10-dihydroanthracene which on heating or on reaction with conc. H2SO4 reforms anthracene.

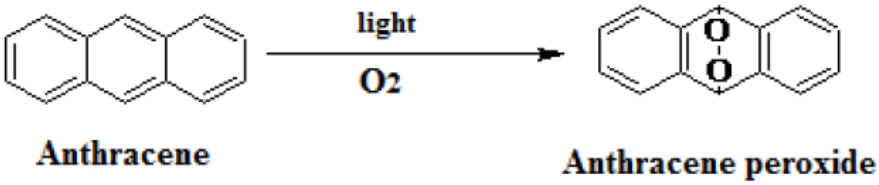


Catalytic reduction (H_2/Ni at 473-523K) gives tetra-, octa- and finally perhydroanthracene ($C_{14}H_{24}$).

2. Oxidation: It is readily oxidized with chromic acid to 9,10-anthraquinone**.**

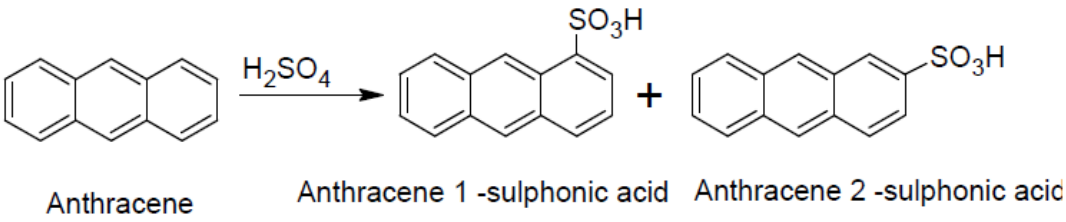


It adds one molecule of oxygen in the presence of light to form a colourless peroxide.



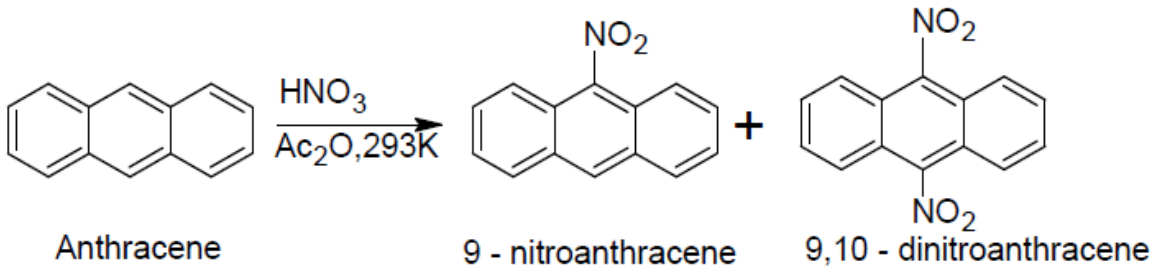
Electrophilic substitution reactions: It undergoes electrophilic substitution reactions like sulphonation,nitration, halogenations etc.

I] Sulphonation: It reacts with H2SO4 to form a mixture of 1-and 2- sulphonic acids.

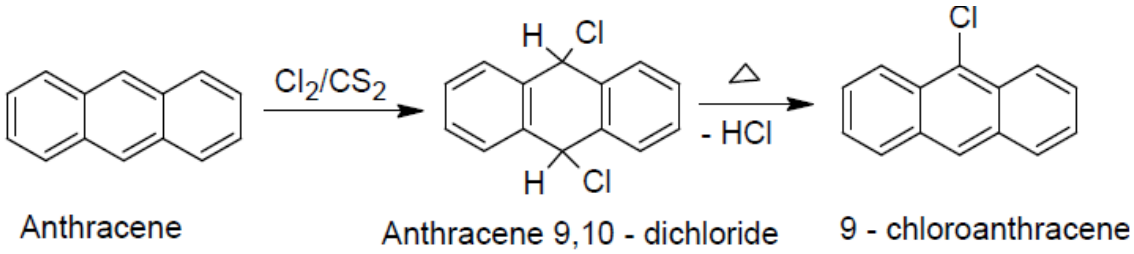


At higher temperatures the 2- sulphonic acid is the main product. However, unlike naphthalene, the 1-sulphonic acid of antharcene does not rearrange to 2- sulphonic acid. Sulphonation with conc.H2SO4 gives 1,5-and 1,8-anthracene disulphonic acids.

Nitration: Anthracene on nitration with concentrated nitric acid in the presence of acetic anhydride gives a mixture of 9-nitro anthracene and 9,10-dinitro anthracene.



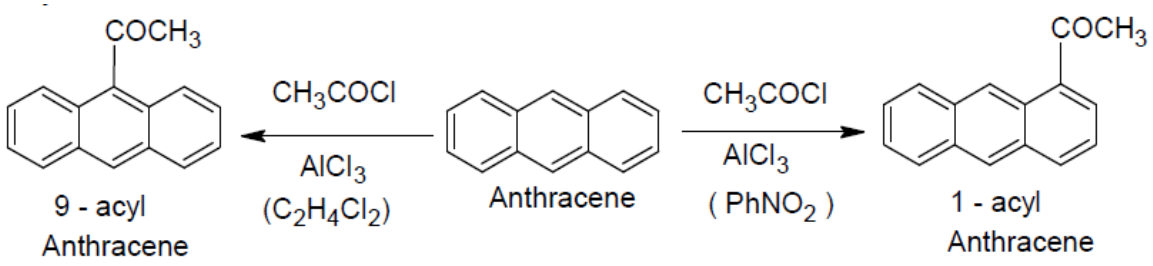
Halogenation: Chlorination with chlorine in carbon disulphide solvent in cold gives anthracene dichloride which on heating or treatment with alkali yields 9-chloroanthracene.



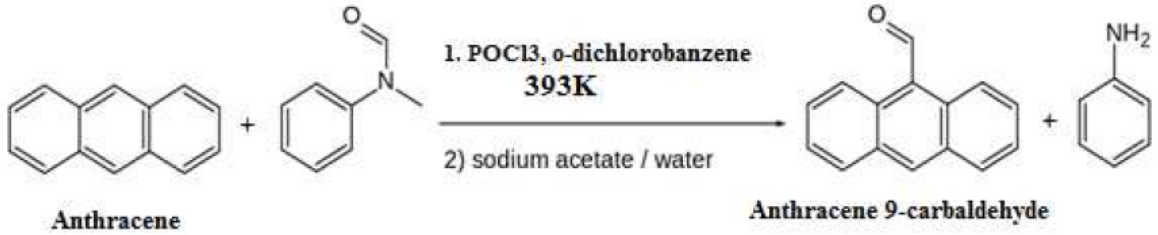
9-chloroanthracene may also be obtained by heating anthracene with cuprous chloride in carbon tetrachloride solution. Reaction of sulphuryl chloride with anthracene gives 9,10-dichloro,9,10-dihydro-anthracene. Both 9-chloroanthracene and anthracene dichloride on oxidation form anthraquinone.

Bromination in carbon tetrachloride follows the same course first forming anthracene dibromide (9,10-dibromo-9,10- dihydro anthracene which on heating yields 9-bromo anthracene.

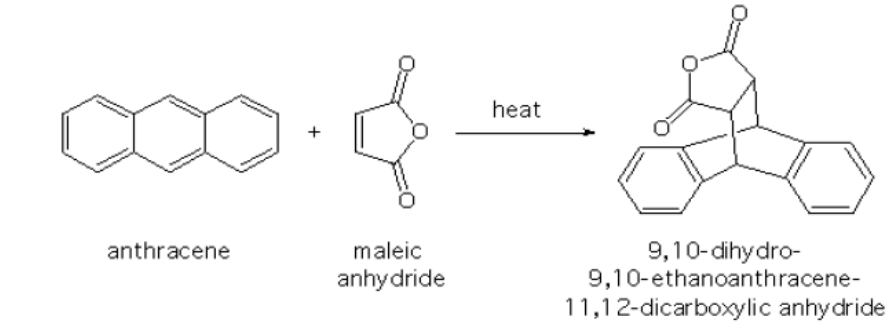
IV] Friedel craft acylation: Friedel crafts acylation of anthracene with acetyl chloride in benzene or nitrobenzene gives a complex mixture. However, the main product in nitro benzene as solvent is the 1-acetyl derivative whereas in ethylene dichloride it is the 9-acetyl derivative.

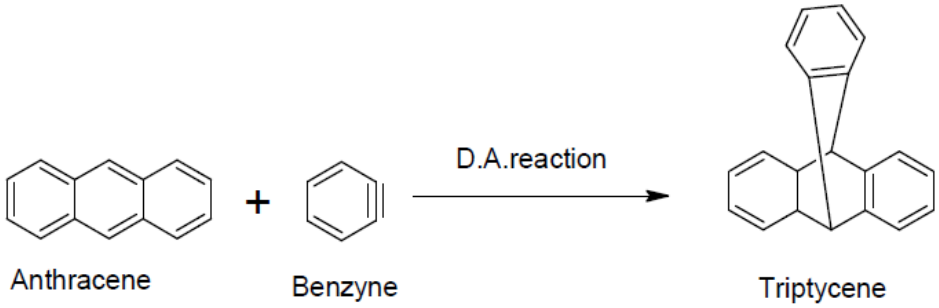


Formylation by Vilsmeier – Haack method: Anthracene can be formylated exclusively at the 9-position. The reaction of anthracene with *N*-methylformanilide, also using phosphorus oxychloride gives Anthracene 9-carbaldehyde.



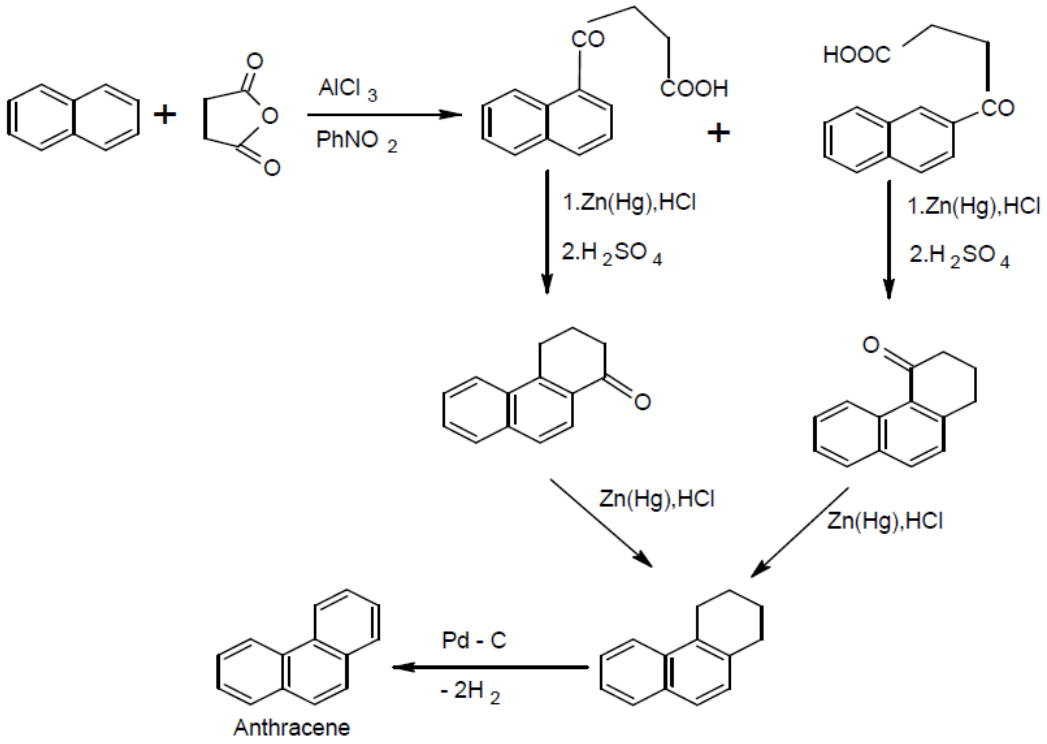
5. Diels-Alder Reaction: Anthracene undergoes facile Diels-Alder reaction with maleic anhydride and benzyne to give 1,4- addition products.





24.b. Explain any two methods of preparation of phenanthrene

Haworth synthesis: Succinoylation of naphthalene produces two isomeric keto acids: β-(1-naphthoyl) propionic acid and β-(2-naphthoyl) propionic acid. These two isomers can be readily separated. Clemmensen reduction affords γ-(1-naphthyl) butyric acid and γ-(2-naphthyl)-butyric acid respectively. Acid catalysed cyclisation gives 1-keto-1,2,3,4-tetrahydro- and 4-keto-1,2,3,4-tetrahydrophenanthrene. Clemmensen reduction of either isomer followed by aromatization.



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25.a. Explain the following reactions in detail

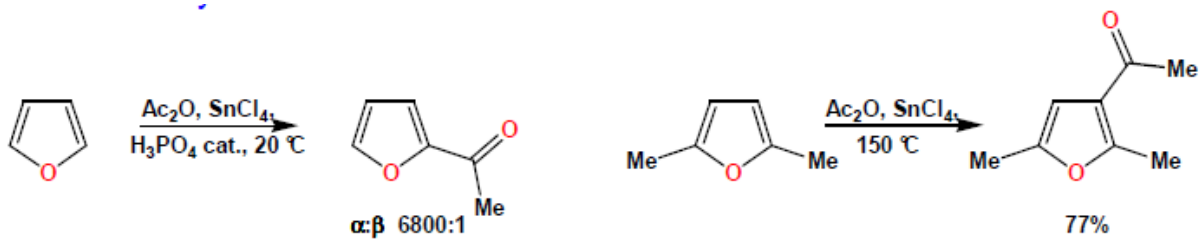
(i) Gattermann Koch reaction
(ii) Friedel Crafts acylation of Furan
(iii) Pyrrole is acidic in nature

Gattermann Koch Reaction

The **Gattermann reaction** is a chemical reaction in which aromatic compounds are formylated by hydrogen cyanide in the presence of a Friedel Crafts catalyst. The reaction can be simplified by replacing the $HCN/AlCl_3$ combination with Zinc cyanide. Although it is also highly toxic, $Zn(CN)_2$ is a solid, making it safer to work with than gaseous HCN; additionally, because the reaction uses HCl, $Zn(CN)_2$ also supplies the reaction with zinc chloride *in-situ*, where it acts as a Lewis acid catalyst.

(ii) **Friedel-Crafts Acylation of Furan**

Blocking groups at the a positions and high temperatures required to give b acylation



(iii) **Pyrrole is acidic in nature**

Both NH and CH protons in pyrroles are moderately acidic and can be deprotonated with strong bases such as butyllithium and the metal hydrides. The resulting "pyrrolides" are nucleophilic. Trapping of the conjugate base with an electrophile (e.g., an alkyl or acyl halide) reveals which sites were deprotonated based on which ring positions actually react as nucleophiles. The product distribution of such a reaction can often be complex and depends on the base used (especially the counterion, such as lithium from butyllithium or sodium from sodium hydride), existing substitution of the pyrrole, and the electrophile.

25.b. Discuss the aromaticity present in furan, thiophene and pyrrole

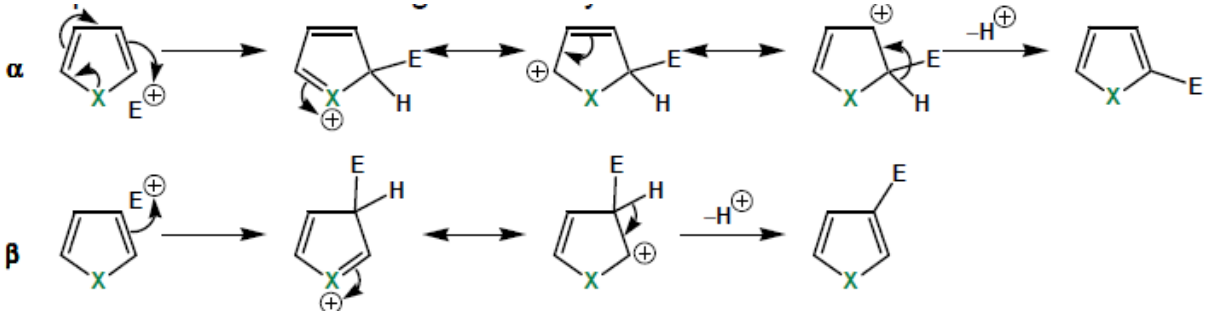
Pyrrole furan and thiophene are aromatic because: 1) they fulfill the criteria for aromaticity, the extent of delocalization of the nonbonding electron pair is decisive for the aromaticity, thus the grading of aromaticity is in the order of: furan< pyrrole < thiophene< benzene this order is consistent with the order of electronegativity values for oxygen (3.44), nitrogen (3.04) and thiophene.

They tend to react by electrophilic substitution due appearance of –ve charge on carbon atoms due to delocalization of electron as shown in the resonance structures.

Evidences of aromatic character in pyrrole
1) All ring bonds are intermediates between single and double bonds.
2) It tends to react by electrophilic substitution
3) Its exceptional lack of basicity and acidity as a secondary amine compared to the aliphatic analog (pyrrolidine). This can be explained on the basis of participation of N lone pair in aromatic sextet thus the dipole moment of pyrrole compared with pyrolidine is reverted and thus protonation occurs at carbons not at N

26.a. Discuss the electrophilic aromatic substitution reaction of furan

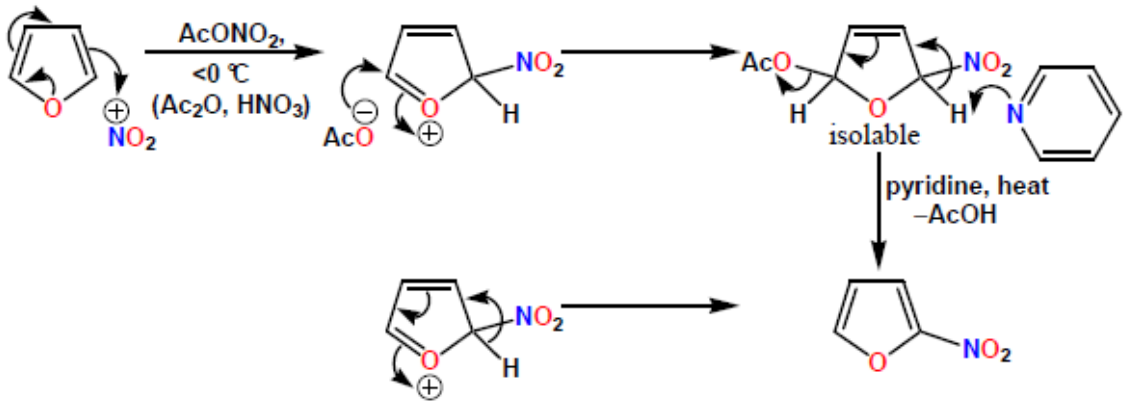
Some b-substitution usually observed – depends on X and substituents



Nitration of furans

Nitration can occur by an addition-elimination process

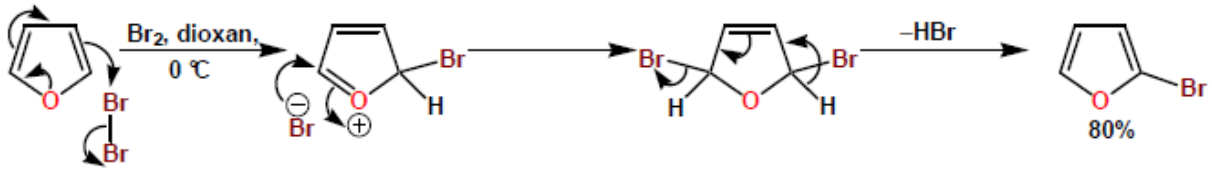
• When NO_2BF_4 is used as a nitrating agent, the reaction follows usual mechanism



Bromination of Furans

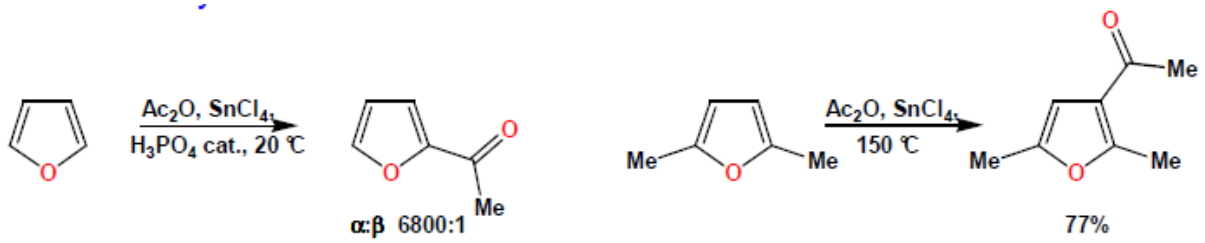
Furan reacts vigorously with Br2 or Cl2 at room temp. to give polyhalogenated products

• It is possible to obtain 2-bromofuran by careful control of temperature

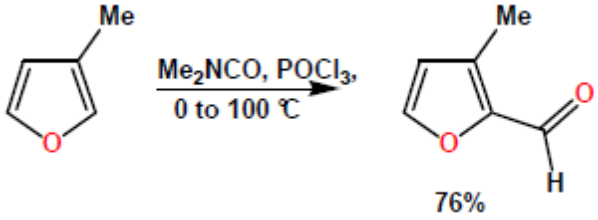


Friedel-Crafts Acylation of Furan

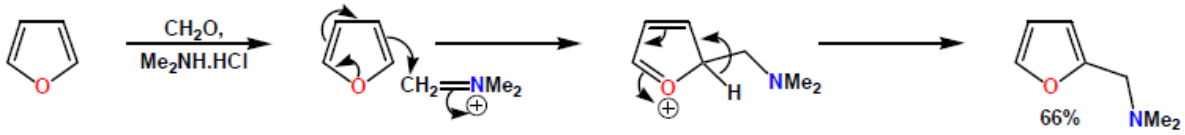
Blocking groups at the a positions and high temperatures required to give b acylation



Vilsmeier Formylation of Furan



Mannich Reaction

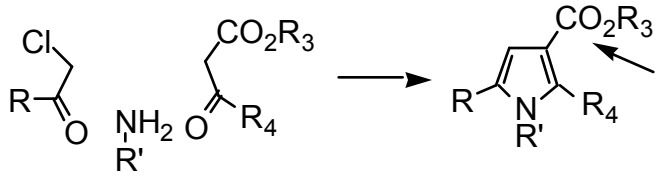


26. b. How pyridine is prepared by Hantzsch synthesis

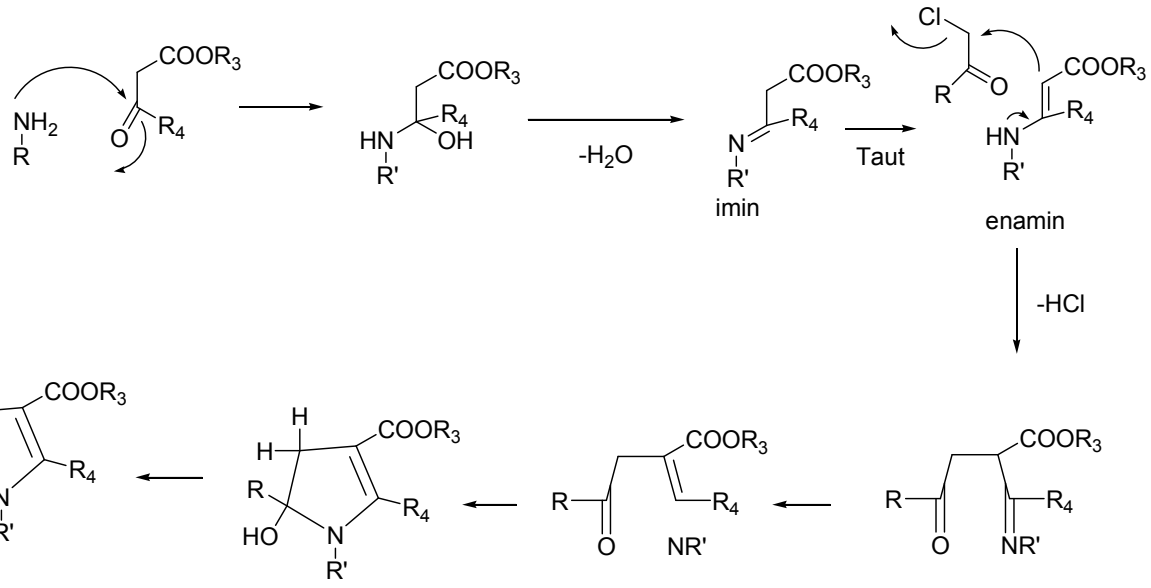
The Hantzsch pyrrole synthesis Is the chemical reaction of β-ketoesters (1) with ammonia (or primary amines) and α-haloketones (2) to give substituted pyrroles (3). Note: direct reaction of β-ketoesters (1) with α- haloketones (2) gives furan [Fiest-Benary furan synthesis], and this can be a troublesome side reaction.

by this method we can prepare different pyrrole derivatives as:1,2,5 substituted pyrrole or 2,5 substituted pyrrole or 1,2,3,5 substituted pyrrole or 2,3,5 substituted pyrrole

R, R_4: alkyl, aryl
R': H, alkyl, aryl



May be removed; hydrol, decarbox.



[16CHU303] **Reg. No……..**

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)

II B.Sc. Chemistry
INTERNAL EXAM II
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

ANSWER KEY

PART A

1. b. Isoquinoline
2. d. Phenyl hydrazone of acetone
3. c. Potassium tertiary butoxide
4. c. Indole
5. a. Isoquinoline
6. a. Furan
7. c. benzopyrrole
8. a. o-amino chlorostyrene
9. b. Acetaldehyde
10. a. Acetaldehyde
11. a. Weakly basic
12. a. Aryl ethylamine and aldehydes
13. a. Monoterpenes
14. b. Sodium amalgam
15. a. CNS drug- Depression
16. a. Alkaloids
17. b. Conversion of quarternary salt in to hydroxide .
18. b. Quinoline alkaloid
19. a. moterpenes and sesquiterpenes
20. b. Isoprene rule

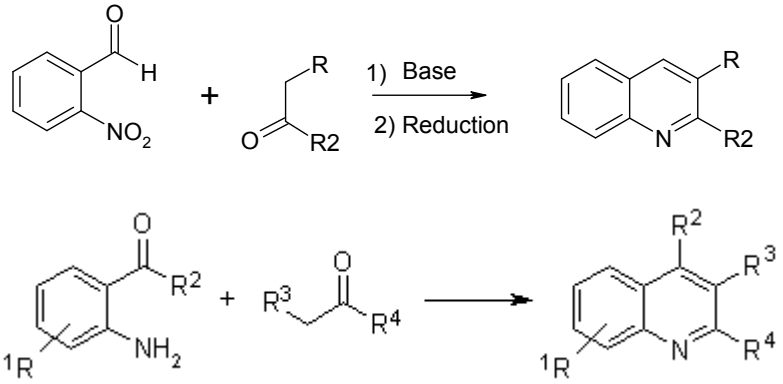
PART B

21. What is a terpene? Give an example

They are insoluble in water and are derived from the union of a common 5-carbon unit called as isoprene which has a branched carbon skeleton. Isoprene in turn is derived from basic 5-C unit called as isopentane.
Eg.Zingeberene

22. How quinoline is prepared from Friedlander's synthesis

Friedlaender Synthesis



The starting materials for this quinoline synthesis are *o*-aminoaryl aldehydes or ketones and a ketone possessing an α-methylene group. After an initial amino-ketone condensation, the intermediate undergoes base- or acid-catalyzedcyclocondensation to produce a quinoline derivative.

23. What is meant by isoprene rule?

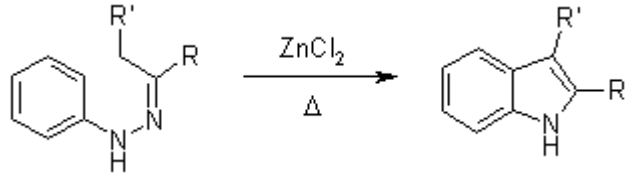
It states that naturally occurring terpenes are built up by condensation of **isoprene** units by either a 1-4 linkage ("head to tail") or a 4-4 linkage ("tail to tail").

PART C

24. a. How indole is prepared by Fischer indole synthesis. Explain the mechanism

Fischer Indole Synthesis

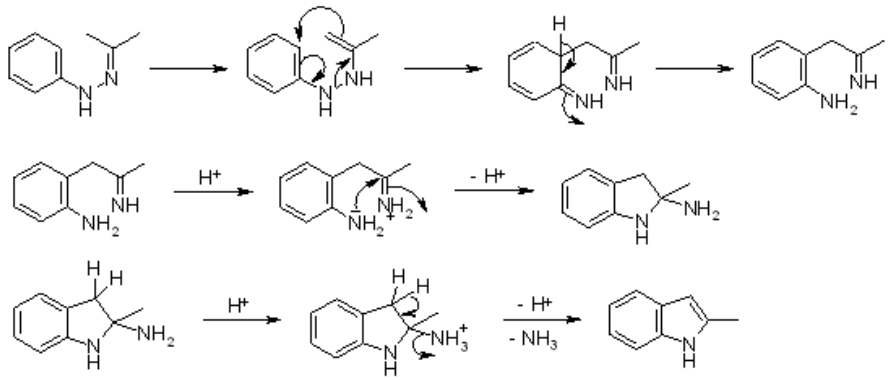
Fischer indole synthesis – this is the oldest way known to make indoles. The reaction is catalyzed by acid. The starting material is phenylhydrazone, and it is formed from the condensation of phenyl hydrazine and a ketone:



The conversion of aryl hydrazones to indoles; requires elevated temperatures and the addition of Brønsted or Lewis acids. Some interesting enhancements have been published recently; for example a milder conversion when *N*-trifluoroacetylenehydrazines are used as substrates.

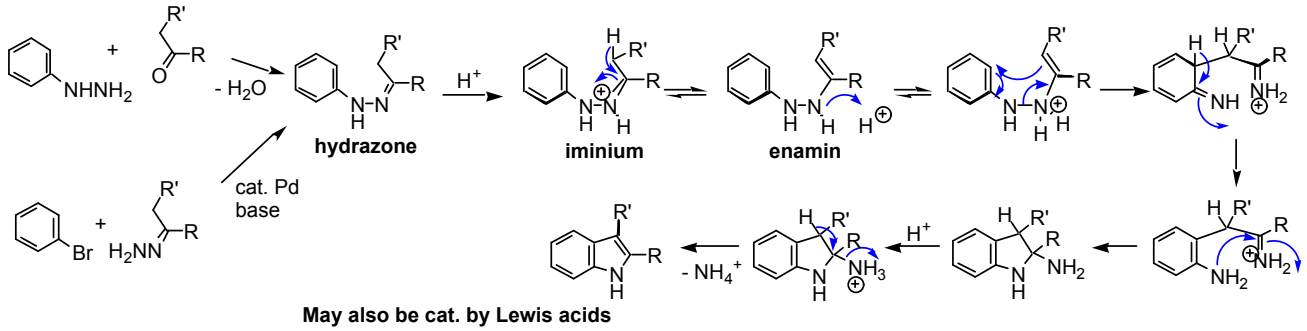
To convert this compound into an indole, the reaction follows the mechanism shown below:

Mechanism of the Fischer Indole Synthesis



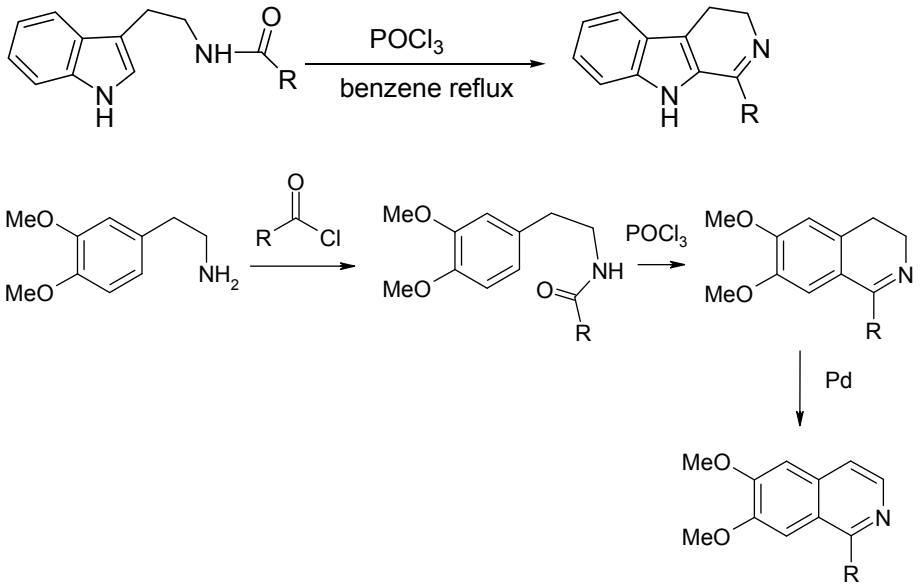
The key step is this reaction is the [3,3] sigmatropic rearrangement, and the driving force for that rearrangement is that you are forming new carbon-carbon bonds (strong) at the expense of breaking NN bonds (weak).

In general, a "sigmatropic rearrangement" refers to something where the only reaction involves moving sigma bonds. The product and the starting material have the same number and same types of atoms; the only difference is where the sigma bonds are located. Also, the rearrangement occurs via a concerted moving of electrons- all the bonds move at once. This particular rearrangement is called a 3,3 rearrangement. This reaction was discovered in 1883. Since then there have been a few advances in indole synthesis.



24.b. How isoquinoline is prepared by BischlerNapieralski synthesis. Explain its mechanism

The **Bischler–Napieralski reaction** is an intramolecular electrophilic aromatic substitution reaction that allows for the cyclisation of β-arylethylamides or β-arylethylcarbamates. It was first discovered in 1893 by Sugust Bischler and Bernard Napieralski , in affiliation with Basle Chemical Works and the University of Zurich. The reaction is most notably used in the synthesis of dihydroisoquinolines, which can be subsequently oxidized to isoquinolines.



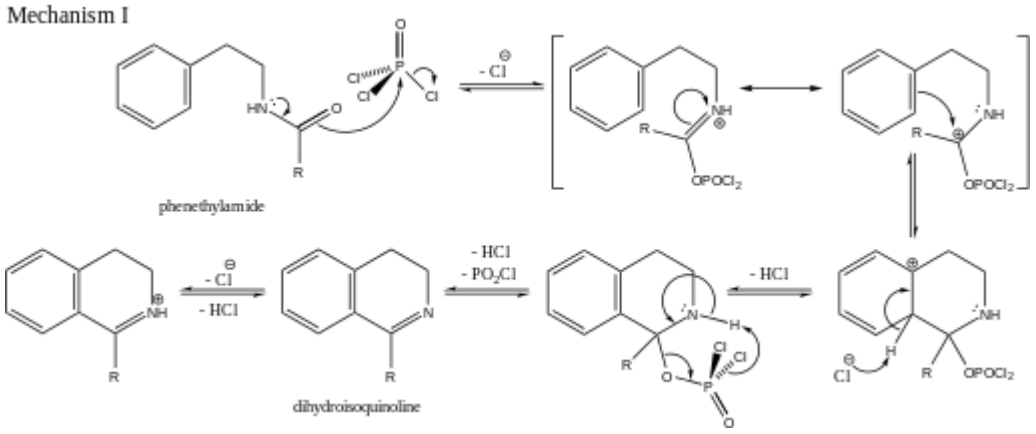
Two types of mechanisms have appeared in the literature for the Bischler–Napieralski reaction. Mechanism I involves a dichlorophosphoryl imine-ester intermediate, while Mechanism II involves a nitrilium ion intermediate (both shown in brackets). This mechanistic variance stems from the ambiguity over the timing for the elimination of the carbonyl oxygen in the starting amide. In Mechanism I, the elimination occurs

with imine formation *after* cyclization; while in Mechanism II, the elimination yields the nitrilium intermediate *prior* to cyclization. Currently, it is believed that different reaction conditions affect the prevalence of one mechanism over the other.

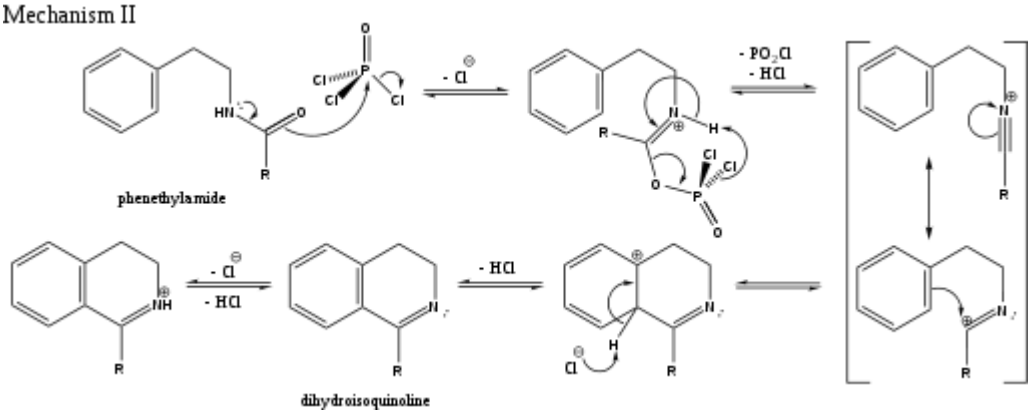
In certain literature, Mechanism II is augmented with the formation of an imidoyl chloride intermediate produced by the substitution of chloride for the Lewis acid group just prior to the nitrilium ion. Because the dihydroisoquinoline nitrogen is basic, neutralization is necessary to obtain the deprotonated product.

General reagents and reaction conditions

The Bischler–Napieralski reaction is carried out in refluxing acidic conditions and requires a dehydrating agent. Phosphoryl chloride ($POCl_3$) is widely used and cited for this purpose. Additionally, $SnCl_4$ and BF_3 etherate have been used with phenethylamides, while Tf_2O and polyphosphoric acid (PPA) have been used with phenethylcarbamates. For reactants lacking electron-donating groups on the benzene ring, phosphorus pentoxide (P_2O_5) in refluxing $POCl_3$ is most effective. Depending on the dehydrating reagent used, the reaction temperature varies from room temperature to 100 °C.

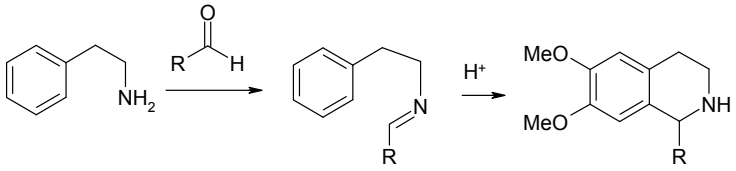


Mechanism II



25.a. Write note on Pictet-Spengler reaction, Pomeranz-Fritsch reaction

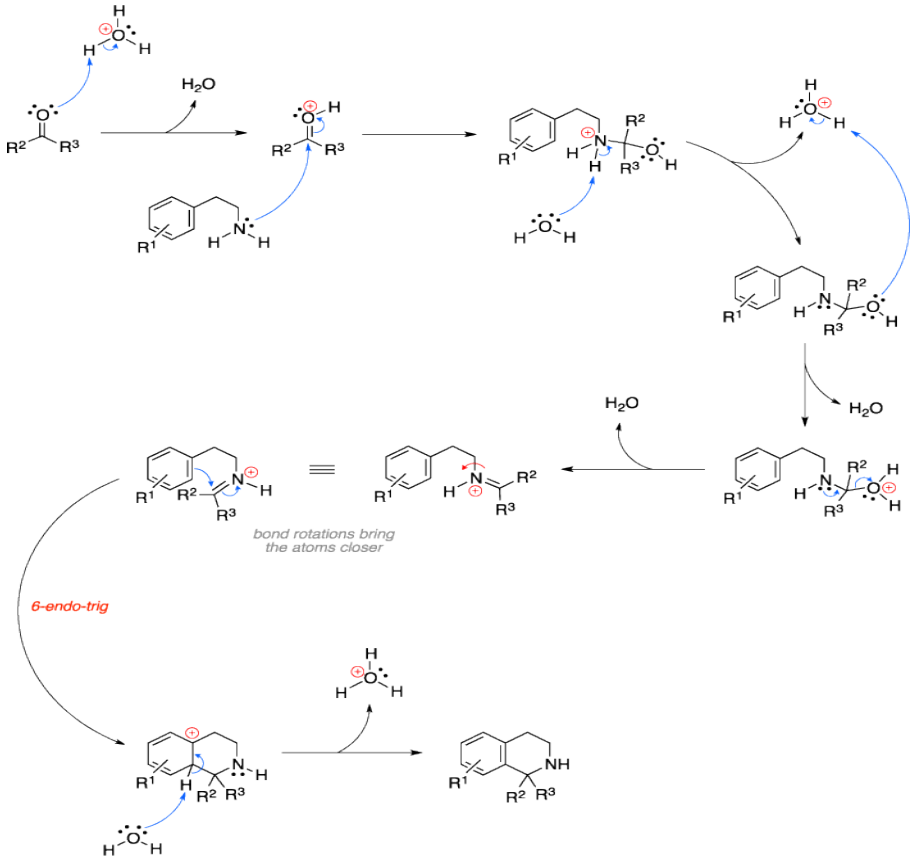
Pictet-Spengler Synthesis



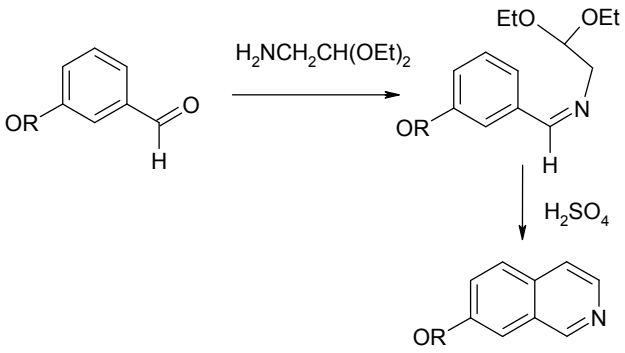
Pictet-Spengler reaction

The Pictet-Spengler reaction is an organic reaction used to convert a β-arylenylamine and an aldehyde or ketone to a tetrahydroisoquinoline using an acid catalyst. The mechanism begins with protonation of the carbonyl oxygen by the acid which is subsequently attacked by the amine reagent. Proton transfer steps and the release of a water molecule results in a protonated imine intermediate, which then undergoes a 6-endo-trig cyclization reaction with loss of aromaticity of the aryl ring. A final deprotonation step restores the aromaticity and results in the tetrahydroisoquinoline product.

Mechanism

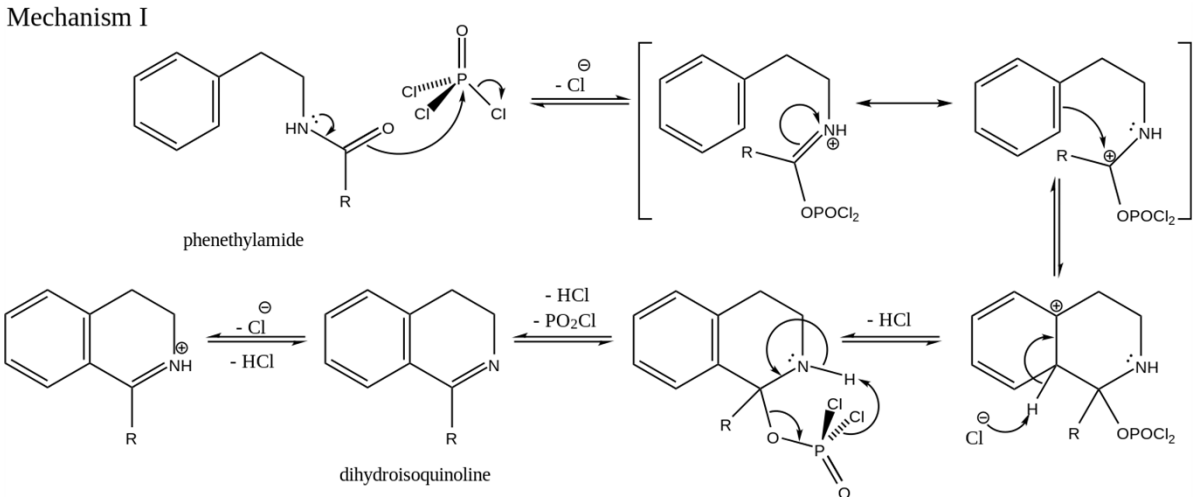


Pomeranz-Fritsch Synthysis



Mechanism

Mechanism I



25.b. Explain the medicinal importance of Nicotine, Quinine, Morphine and Cocaine

(1) Quinine — an antimalarial drug isolated from a plant called Cinchonia officialis. Quinine is an antipyretic alkaloid. Its molecular formular is C20H24N2O2.. Functional groups present in quinine are: methoxyl –OCH3, hydroxyl –OH, tertiary amine group, etc.

(2) Morphine is highly narcotic Morphine is analgesicν Morphine is isolated from the plant Papavera omniferousν Morphine is an opium alkaloid.ν Nicotine is another example of alkaloid

(3) Cocaine is an alkaloid. - Cocaine is obtained from coca leaves, - Cocaine is the first local unaesthetic ever discovered by man, - Cocaine is highly narcotic, - Cocaine stimulates the central nervous system i.e. CNS depressant, - Cocaine can lead to psychiatric problem when taken in high dose or when addicted to it.

(4) Nicotine is the main constituent of Rauwolfia species,perticularly R.serpentina & R.vomitoria. • It is mainly used for the treatment of hypertension, headache, tension, asthma & dermatological disorders.

26. a. Explain the Occurrence and classification in terpenes with examples

Terpenes are classified into many categories based on the no. of carbon atoms and iso-prene residues present in their structure:

(i) Monoterpenes. They consist of 10-C atoms or two isoprene residues.

(ii) Sesquiterpenes. These contain 15-C atoms or three isoprene residues.

(iii) Diterpenes. These contain 20-C atoms or four isoprene residues.

(iv) Triterpenes. These consist of 30-C atoms or six isoprene units.

(v) Tetraterpenes. These consist of 40-C atoms or eight isoprene residues.

(vi) Polyterpenes. These consist of large number of isoprene residues

26.b. Explain the structure elucidation and synthesis of nicotine

Nicotine

i. The molecular formula of nicotine is C_{10} H_{14} N_2.
ii. With HCI it forms the crystalline salt, nicotine dihydrochloride. This proves that nicotine is a diacid base.
iii. On treatment with CH_3I, it forms dimethiodide. This suggests that nicotine is a ditertiary base
iv. Herzig - Meyer determination proves that nicotine contains one ($-NCH_3$) group.
v. Nicotine on oxidation with $KMnO_4$ or chromic acid gives nicotinic acid (Pyridine – 3-carboxylic acid).

The reaction shows that the side chain is saturated

The structure of nicotine is also proved by the following reaction. Nicotine when treated with bromine, forms dibromo nicotine. This on heating with barium hedroxide, breaks down to give nicotinic acid, malonic acid and methyl amine.

Reg. No.....

[16CHU303]

KARPAGAM UNIVERSITY
KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)

II B.Sc. Chemistry
INTERNAL EXAM III
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

Time: 2 hours **Maximum: 50 Marks**
Date:

PART A (20 x 1 = 20 Marks)
Answer all the questions

1. Numbering of ring atoms starts at the hetero atom except
   a. Quinoline b. Isoquinoline c. benzofuran d. indole

2. To prepare indole, zinc chloride has to be heated with
   a. Benzaldehyde b. benzophenone c. Phenyl acetate d. Phenyl hydrazone of acetone

3. To prepare 2-alkyl indole by the cyclodehydration of o-acyl amidotoluene is carried out with
   a. Sodium ethoxide b. Zinc chloride c. Potassium tertiary butoxide d. Tin and HCl

4. Fischer,s synthesis is used to prepare
   a. Quinoline b. Isoquinoline c. Indole d. Pyran

5. One among the following is a condensed heterocyclic compound
   a. Isoquinoline b. Thiopyran c. Thiophene d. Pyrimidine

6. Acetonyl acetone on dehydration with phosphorous pentoxide gives
   a. Furan b. pyrrole c. Thiophene d. pyran

7. The alternate name of indole is
   a. Quinoline b. Isoquinoline c. benzopyrrole d. indole

8. In Lipps synthesis of indole the starting material is
   a. o-amino chlorostyrene b. o-hydroxy chlorostyrene c. o-nitro chlorostyrene
   d. o-chloro chlorostyrene

9. In the synthesis of quinoline o-amino benzaldehyde reacs with
   a. Acetaldehyde b. o-amino chlorostyrene c. o-hydroxy chlorostyrene
   d. Maleic anhydride

NO. of copies (90)

10. In the synthesis of quinoline o-amino benzaldehyde reacs with
    a. Acetaldehyde b. o-amino chlorostyrene c. o-hydroxy chlorostyrene
    d. Maleic anhydride

11. Alkaloids are
    a. Weakly basic b. Strongly basic c. Weakly acidic d. Strongly acidic

12. The starting material in Pomeranz Fritsch synthesis is

    a. Phenyl ethyl amine b. aminoacetal c. Aryl ethylamine and aldehydes
    d. aniline

13. If a terpene consists of 10 carbon atoms then it is called

    a. Monoterpenes b. Sesquiterpenes c. Diterpenes d. Triterpenes

14. The reagent used in the Emde degradation is

    a. Sodium amalgam b. Sodium/ethanol c. Sodium nitrate d. Fe/HCl

15. Heroin is a

    a. CNS drug- stimulants b. CNS drug- Depressant c. CNS drug-
    Hallucinogens d. Psycho-active drug

16. Occur in the plant sources as the salt of acids, such as: oxalates, tannates
    a. Alkaloids b. terpenes c. steroids d. carbohydrates

17. In Hoffmann exhaustive methylation, the Second step is
    a. Formation of quarternary salt b. Conversion of quarternary salt in to hydroxidec.
    Heating the quarternary hydroxide d. Elimination of alkene

18. Morphine is a
    a. Pyrrolidine type alkaloids b. Quinoline alkaloid c. Tropane alkaloids d. Isoquinoline
    alkaloid

19. The chief constituents of essential oils are
    a. Monoterpenes and sesquiterpenes b. Diterpenes c. triterpenes d. tetraterpenes

20. Terpenes are built up by condensation of isoprene units by a 1-4 linkage (head to tail) is called
    a. Hofmann rule b. Isoprene rule c. Zaysteff rule d. Flemings rule

PART-B (3 x 2= 6 Marks)
Answer ALL the Questions

21. What is a terpene? Give an example

22. How quinoline is prepared from Friedlander's synthesis

23. What is meant by isoprene rule?

PART- C (3 x 8= 24 Marks)

24. a. How indole is prepared by Fischer indole synthesis. Explain the mechanism

OR

b. How isoquinoline is prepared by Bischler Napieralski synthesis. Explain its mechanism

25. a. Write note on Pictet-Spengler reaction, Pomeranz-Fritsch reaction

OR

b. Explain the medicinal importance of Nicotine, Quinine, Morphine and Cocaine

26. a. Explain the Occurrence and classification in terpenes with examples

OR

b. Explain the structure elucidation and synthesis of nicotine

Reg. No……..

[16CHU303]

KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2016 & onwards)

II B.Sc. Chemistry
INTERNAL EXAM II
ORGANIC CHEMISTRY
(Nitrogen containing Functional group)

ANSWER KEY

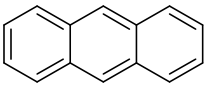
PART A

1.a. Condensed polynuclear hydrocarbons
2. a. Anthracene
3. c. ortho position
4. a. Napthalene
5. b. Planar
6. a. 1.36 A
7. a. a carbon atom of benzene ring by another hetero atom
8. c. Furan
9. b. 6 electrons
10. c. Pyrrole
11. b. 6 electrons
12.c. aza
13. a ole
14. a azole
15. a. 2-nitrofuran
16. b.Furan
17.b. 2,5-position
18. a. furan
19.a. furan
20.a. 2-nitrofuran

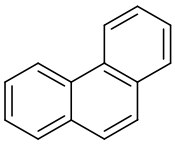
PART B

21. Differentiate phenanthrene and anthracene

Phenanthrene is a trinuclear angular aromatic hydrocarbon, whereas anthracene is a trinuclear linear aromatic hydrocarbon



Anthracene

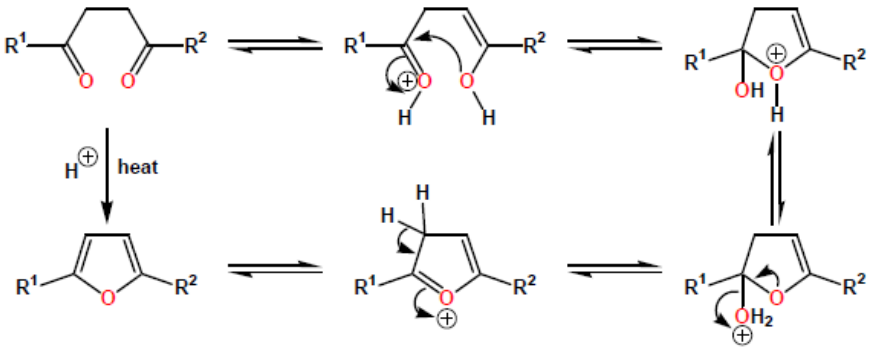


phenanthrene

22. Write any one synthesis of furan

Paal Knorr synthesis of furan

When 1,4-diketones are heated in presence of an acid it yields furans.



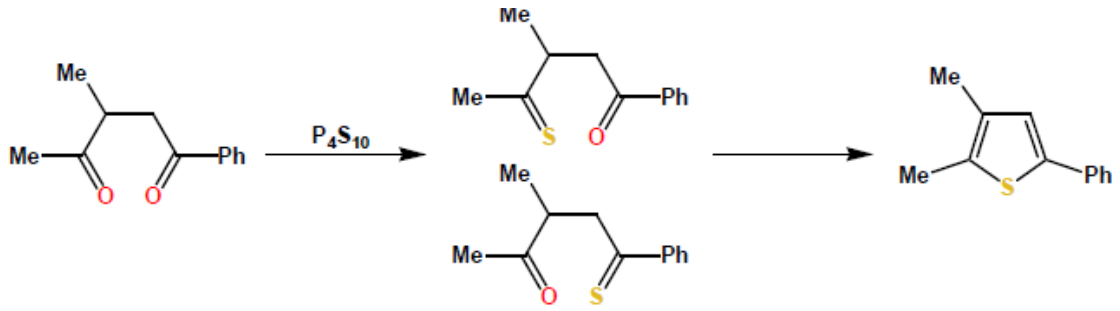
The reaction is usually reversible and can be used to convert furans into 1,4-diketones

• A trace of acid is required – usually TsOH (*p*-$MeC_6H_4SO_3H$)

23. How thiophene is prepared.

Synthesis of Thiophenes by Paal Knorr type reaction ("4+1")

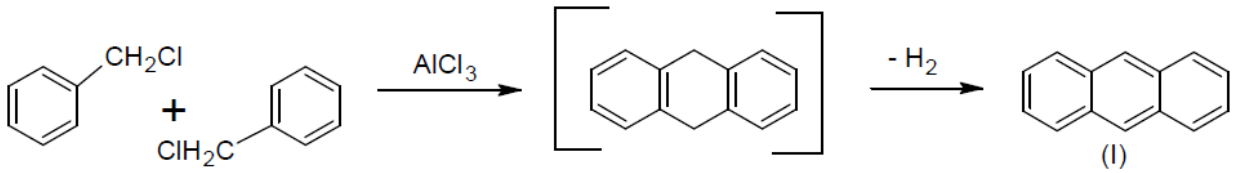
1,4 diketones when heated with phosphorous pentasulphide gives thiophene. Reaction might occur *via* the 1,4-*bis*-thioketone



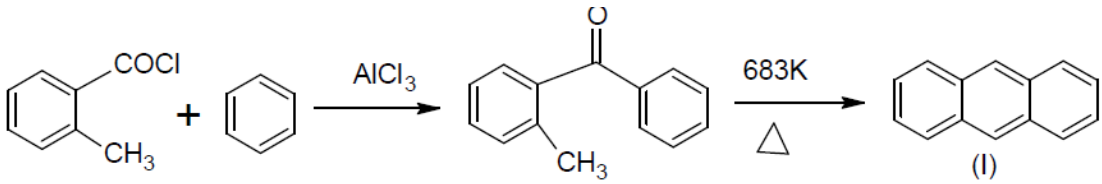
PART C

24.a. Explain the preparation and properties of anthracene

Friedel crafts alkylation between two molecules of benzyl chloride gives 9.10-dihydroanthracene which is oxidized readily under the reaction conditions yielding anthracene.

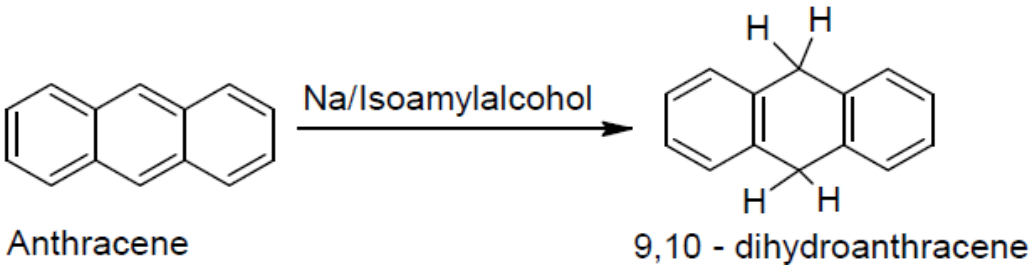


2.This method is based on Elbs reaction in which a polynuclear aromatic hydrocarbon having an anthracene moiety is formed by pyrolysis of a diaryl ketone containing a methyl or methylene group ortho to the carbonyl group.



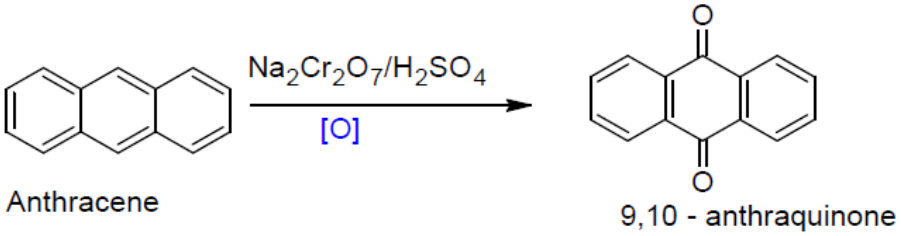
Properties

1. Reduction: When reduced with sodium and isoamyl alcohol it forms 9,10-dihydroanthracene which on heating or on reaction with conc. H2SO4 reforms anthracene.

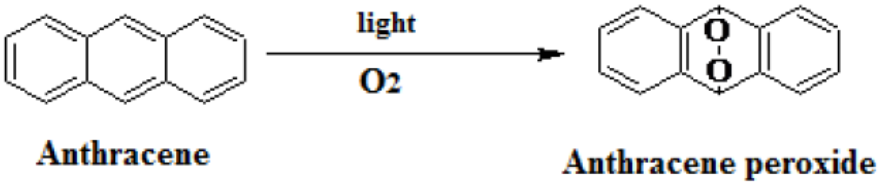


Catalytic reduction (H_2/Ni at 473-523K) gives tetra-, octa- and finally perhydroanthracene ($C_{14}H_{24}$).

2. Oxidation: It is readily oxidized with chromic acid to 9,10-anthraquinone**.**

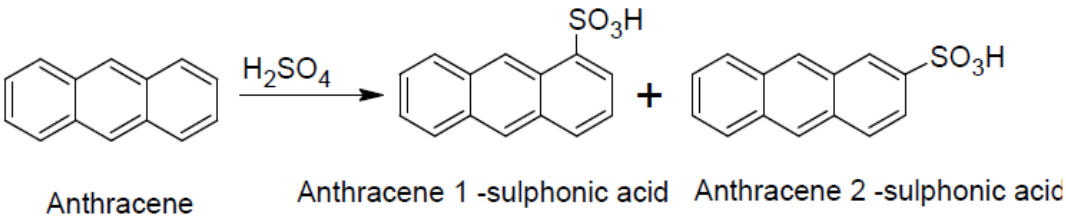


It adds one molecule of oxygen in the presence of light to form a colourless peroxide.



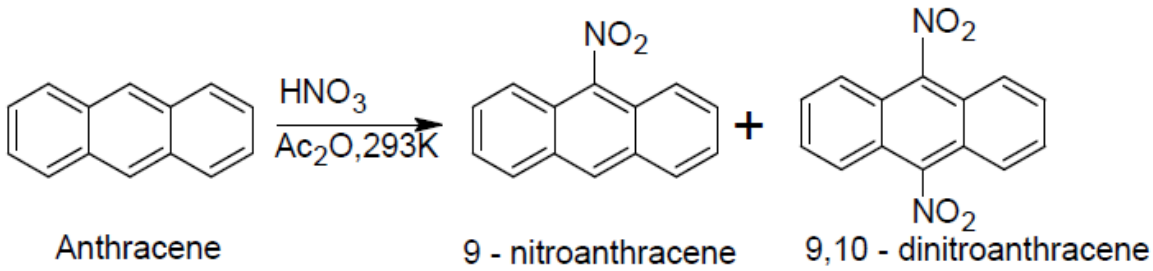
Electrophilic substitution reactions: It undergoes electrophilic substitution reactions like sulphonation,nitration, halogenations etc.

I] Sulphonation: It reacts with H2SO4 to form a mixture of 1-and 2- sulphonic acids.

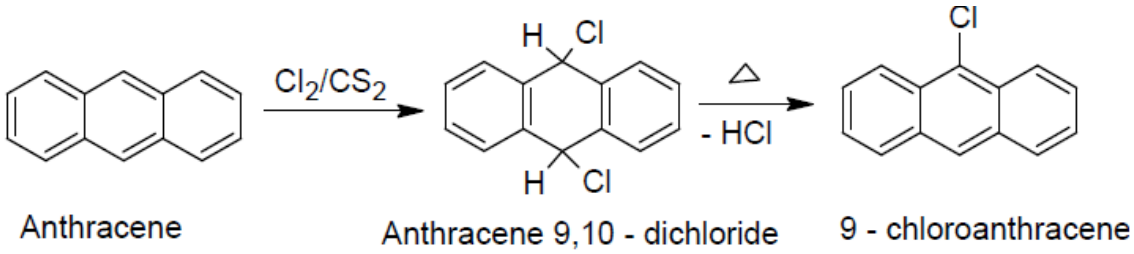


At higher temperatures the 2- sulphonic acid is the main product. However, unlike naphthalene, the 1-sulphonic acid of antharcene does not rearrange to 2- sulphonic acid. Sulphonation with conc.H2SO4 gives 1,5-and 1,8-anthracene disulphonic acids.

Nitration: Anthracene on nitration with concentrated nitric acid in the presence of acetic anhydride gives a mixture of 9-nitro anthracene and 9,10-dinitro anthracene.



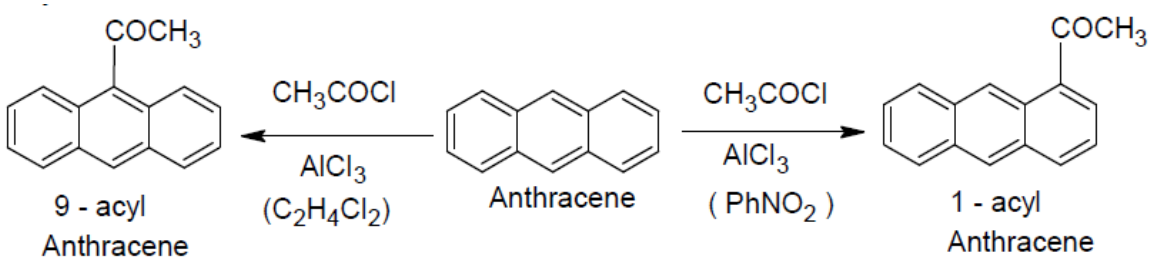
Halogenation: Chlorination with chlorine in carbon disulphide solvent in cold gives anthracene dichloride which on heating or treatment with alkali yields 9-chloroanthracene.



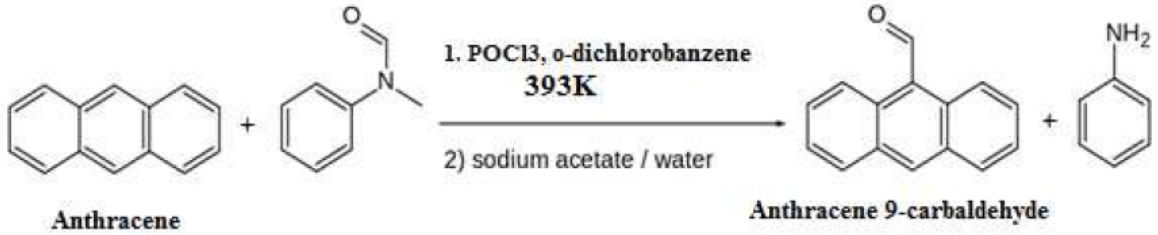
9-chloroanthracene may also be obtained by heating anthracene with cuprous chloride in carbon tetrachloride solution. Reaction of sulphuryl chloride with anthracene gives 9,10-dichloro,9,10-dihydro-anthracene. Both 9-chloroanthracene and anthracene dichloride on oxidation form anthraquinone.

Bromination in carbon tetrachloride follows the same course first forming anthracene dibromide (9,10-dibromo-9,10- dihydro anthracene which on heating yields 9-bromo anthracene.

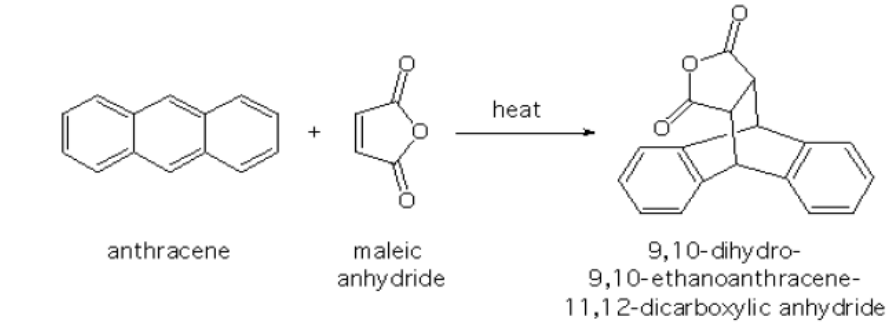
IV] Friedel craft acylation: Friedel crafts acylation of anthracene with acetyl chloride in benzene or nitrobenzene gives a complex mixture. However, the main product in nitro benzene as solvent is the 1-acetyl derivative whereas in ethylene dichloride it is the 9-acetyl derivative.

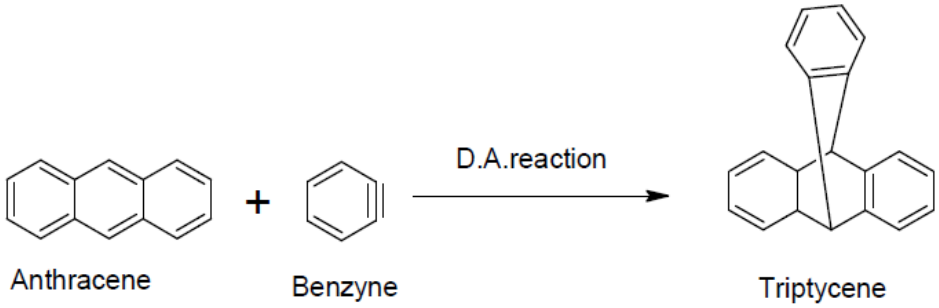


Formylation by Vilsmeier – Haack method: Anthracene can be formylated exclusively at the 9-position. The reaction of anthracene with *N*-methylformanilide, also using phosphorus oxychloride gives Anthracene 9-carbaldehyde.



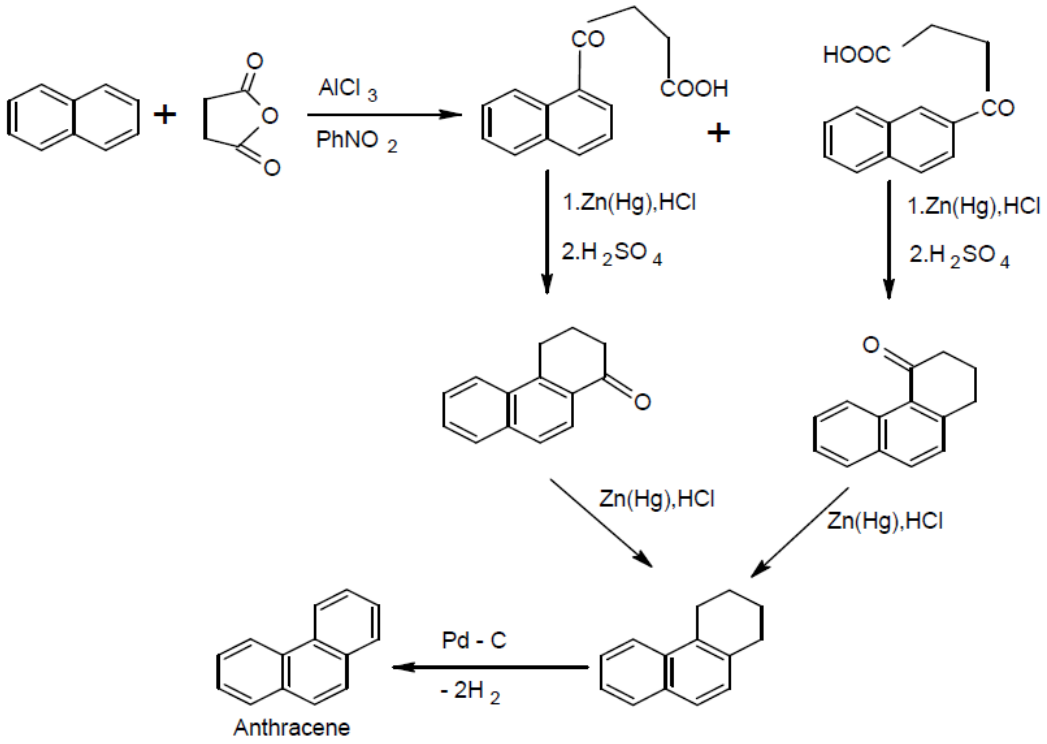
5. Diels-Alder Reaction: Anthracene undergoes facile Diels-Alder reaction with maleic anhydride and benzyne to give 1,4- addition products.





24.b. Explain any two methods of preparation of phenanthrene

Haworth synthesis: Succinoylation of naphthalene produces two isomeric keto acids: β-(1-naphthoyl) propionic acid and β-(2-naphthoyl) propionic acid. These two isomers can be readily separated. Clemmensen reduction affords γ-(1-naphthyl) butyric acid and γ-(2-naphthyl)-butyric acid respectively. Acid catalysed cyclisation gives 1-keto-1,2,3,4-tetrahydro- and 4-keto-1,2,3,4-tetrahydrophenanthrene. Clemmensen reduction of either isomer followed by aromatization.



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25.a. Explain the following reactions in detail

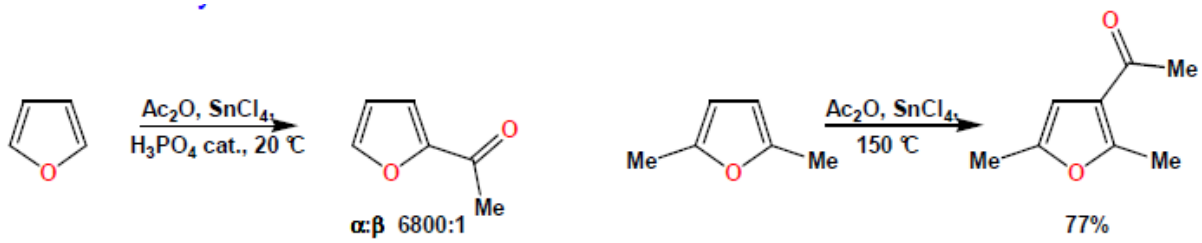
(i) Gattermann Koch reaction
(ii) Friedel Crafts acylation of Furan
(iii) Pyrrole is acidic in nature

Gattermann Koch Reaction

The **Gattermann reaction** is a chemical reaction in which aromatic compounds are formylated by hydrogen cyanide in the presence of a Friedel Crafts catalyst. The reaction can be simplified by replacing the $HCN/AlCl_3$ combination with Zinc cyanide. Although it is also highly toxic, $Zn(CN)_2$ is a solid, making it safer to work with than gaseous HCN; additionally, because the reaction uses HCl, $Zn(CN)_2$ also supplies the reaction with zinc chloride *in-situ*, where it acts as a Lewis acid catalyst.

(ii) **Friedel-Crafts Acylation of Furan**

Blocking groups at the a positions and high temperatures required to give b acylation



(iii) **Pyrrole is acidic in nature**

Both NH and CH protons in pyrroles are moderately acidic and can be deprotonated with strong bases such as butyllithium and the metal hydrides. The resulting "pyrrolides" are nucleophilic. Trapping of the conjugate base with an electrophile (e.g., an alkyl or acyl halide) reveals which sites were deprotonated based on which ring positions actually react as nucleophiles. The product distribution of such a reaction can often be complex and depends on the base used (especially the counterion, such as lithium from butyllithium or sodium from sodium hydride), existing substitution of the pyrrole, and the electrophile.

25.b. Discuss the aromaticity present in furan, thiophene and pyrrole

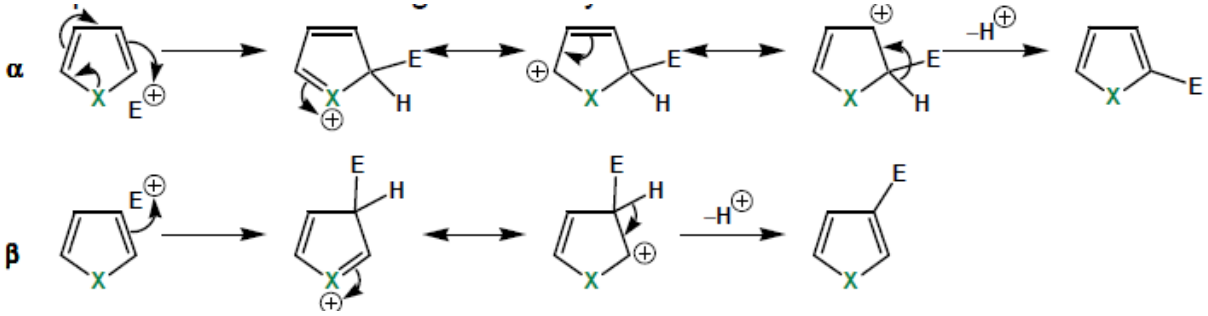
Pyrrole furan and thiophene are aromatic because: 1) they fulfill the criteria for aromaticity, the extent of delocalization of the nonbonding electron pair is decisive for the aromaticity, thus the grading of aromaticity is in the order of: furan< pyrrole < thiophene< benzene this order is consistent with the order of electronegativity values for oxygen (3.44), nitrogen (3.04) and thiophene.

They tend to react by electrophilic substitution due appearance of –ve charge on carbon atoms due to delocalization of electron as shown in the resonance structures.

Evidences of aromatic character in pyrrole
1) All ring bonds are intermediates between single and double bonds.
2) It tends to react by electrophilic substitution
3) Its exceptional lack of basicity and acidity as a secondary amine compared to the aliphatic analog (pyrrolidine). This can be explained on the basis of participation of N lone pair in aromatic sextet thus the dipole moment of pyrrole compared with pyrolidine is reverted and thus protonation occurs at carbons not at N

26.a. Discuss the electrophilic aromatic substitution reaction of furan

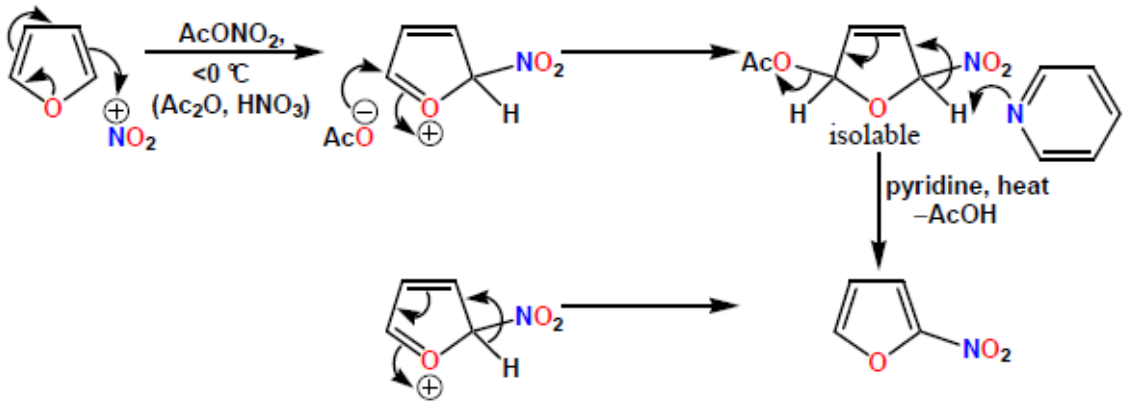
Some b-substitution usually observed – depends on X and substituents



Nitration of furans

Nitration can occur by an addition-elimination process

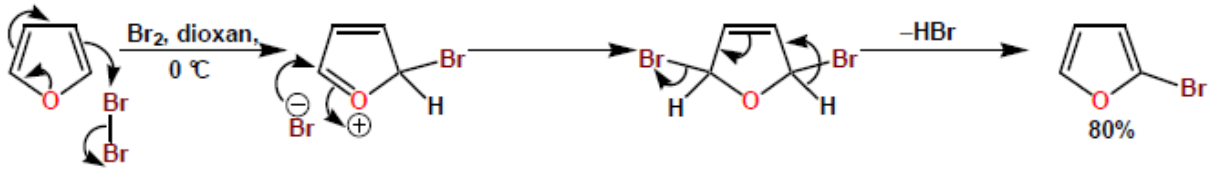
• When NO_2BF_4 is used as a nitrating agent, the reaction follows usual mechanism



Bromination of Furans

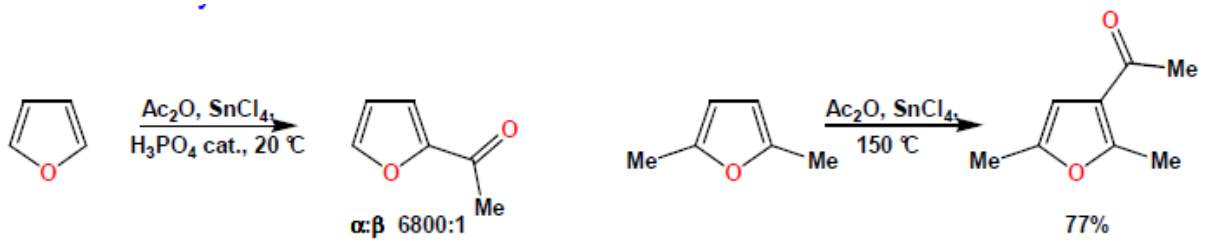
Furan reacts vigorously with Br2 or Cl2 at room temp. to give polyhalogenated products

• It is possible to obtain 2-bromofuran by careful control of temperature

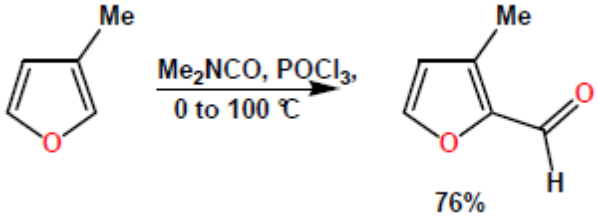


Friedel-Crafts Acylation of Furan

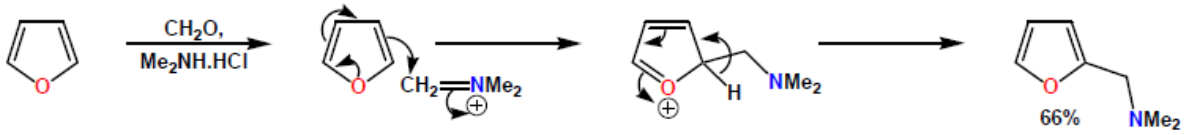
Blocking groups at the a positions and high temperatures required to give b acylation



Vilsmeier Formylation of Furan



Mannich Reaction

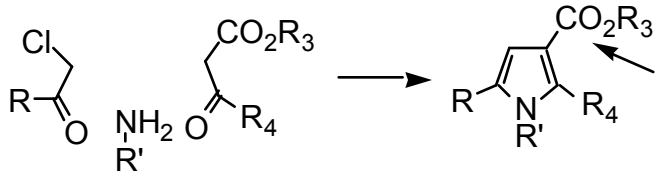


26. b. How pyridine is prepared by Hantzsch synthesis

The Hantzsch pyrrole synthesis Is the chemical reaction of β-ketoesters (1) with ammonia (or primary amines) and α-haloketones (2) to give substituted pyrroles (3). Note: direct reaction of β-ketoesters (1) with α- haloketones (2) gives furan [Fiest-Benary furan synthesis], and this can be a troublesome side reaction.

by this method we can prepare different pyrrole derivatives as:1,2,5 substituted pyrrole or 2,5 substituted pyrrole or 1,2,3,5 substituted pyrrole or 2,3,5 substituted pyrrole

R, R_4: alkyl, aryl
R': H, alkyl, aryl



May be removed; hydrol, decarbox.