Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

M.Sc. chemistry

Semester 3 Material

CHAPTER -1

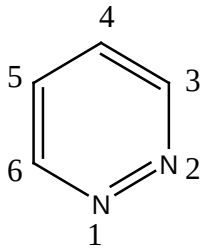
INTRODUCTION OF HETEROCYCLIC COMPOUNDS

PAPER CODE C-303

ORGANIC CHEMISTRY

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

PYRIDAZINE



Pyridazine 'or'
1,2 diazine

--> It was first identify by Fischer in 1886 and synthesized by Tauber in 1895.

Physical Properties:-

--> Colourless liquid,

--> B.P. = 207 ^{O}C and M.P. = -8 ^{O}C,

-->Soluble in benzene as well as water ,

-->Insoluble in cyclohexane,

-->Dipole moment is 4D,

-->It's spectra is aromatic,

-->Resonating energy is 12.3 Kcal/mole,

-->It is weak base and it make crystaline salt.

Spectral Data:-

UV, λ_{max} nm pH=7 : 247(3.04); 300(2.51).

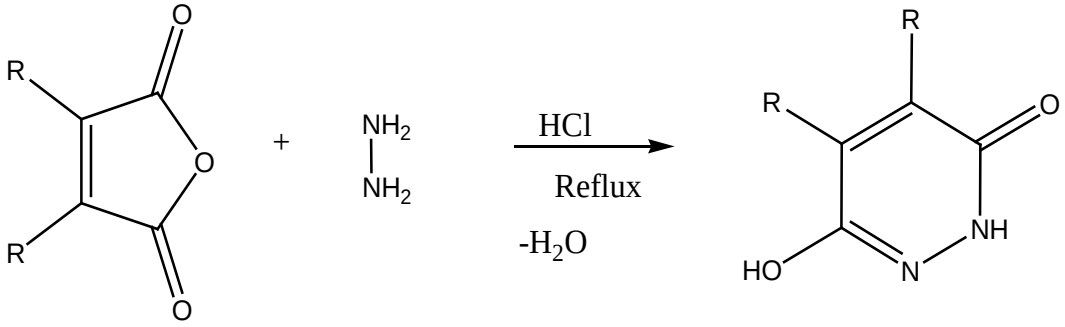
^{1}H NMR δ_{ppm} ($CDCl_3$) : C_3-H, 7.17; C_4-H, 7.68; C_5-H,7.68; C_6-H,9.17.

^{13}C NMR δ_{ppm} ($CDCl_3$) : C_3, 152.8; C_4, 127.6; C_5, 127.6; C_6, 152.

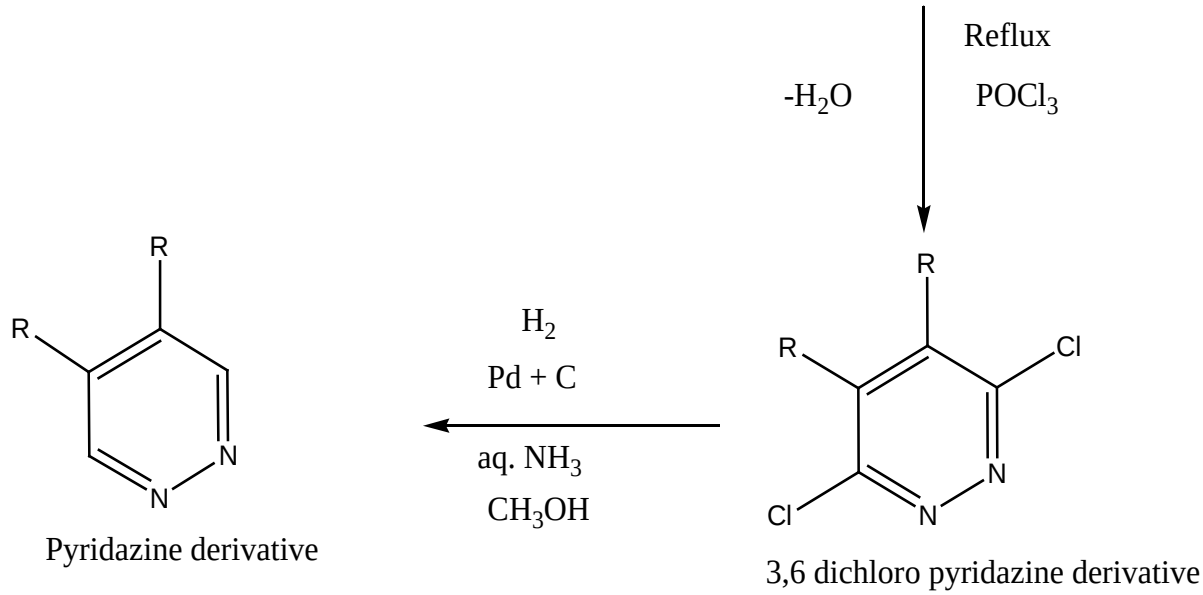
^{15}N NMR δ_{ppm} NH_3 =0 : 400.

Synthesis:-

(1)From Maleic Anhydride:-



Maleic anhydride deri. Hydrazine Maleic Hydrazide derivative

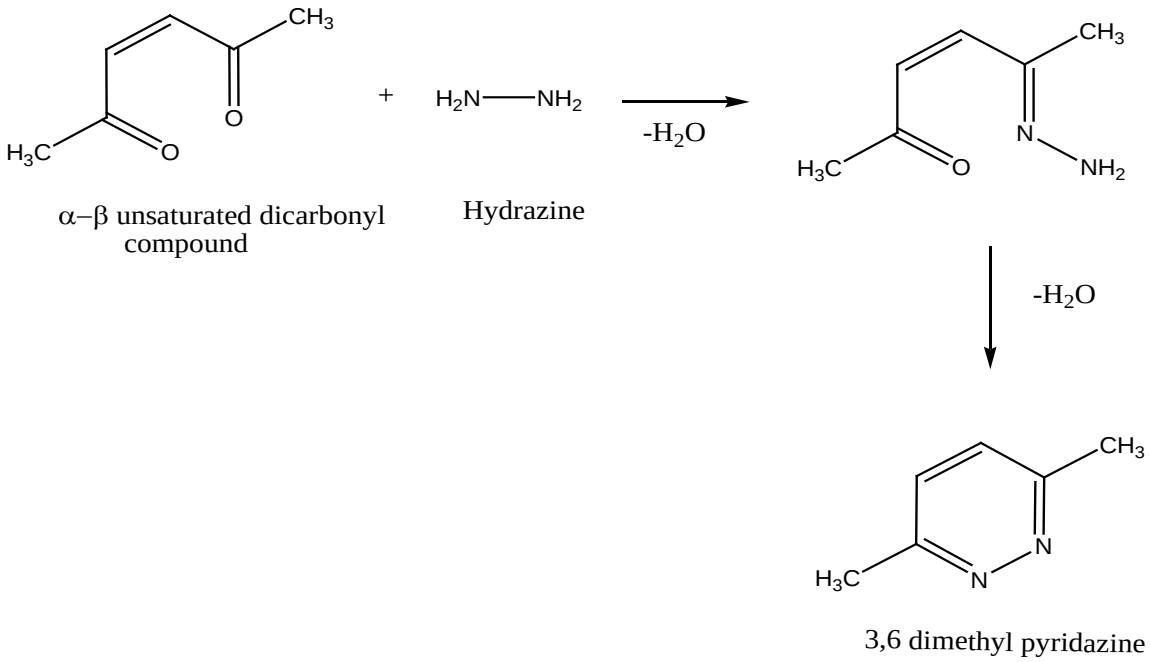


3,6 dichloro pyridazine derivative

Pyridazine derivative

(2) (4+2) condensation:-

From α-β unsaturated dicarbonyl compound:

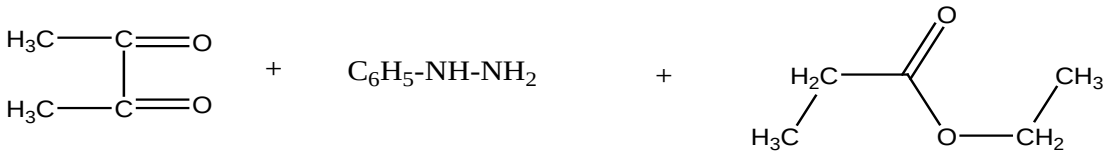


α–β unsaturated dicarbonyl compound

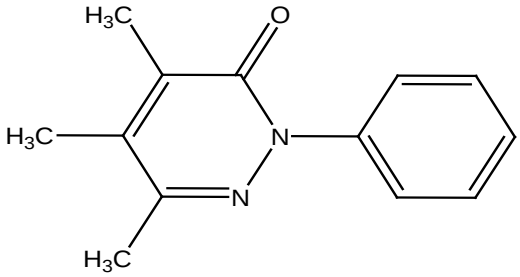
Hydrazine

3,6 dimethyl pyridazine

(3) Schmidt - Druey Method :-

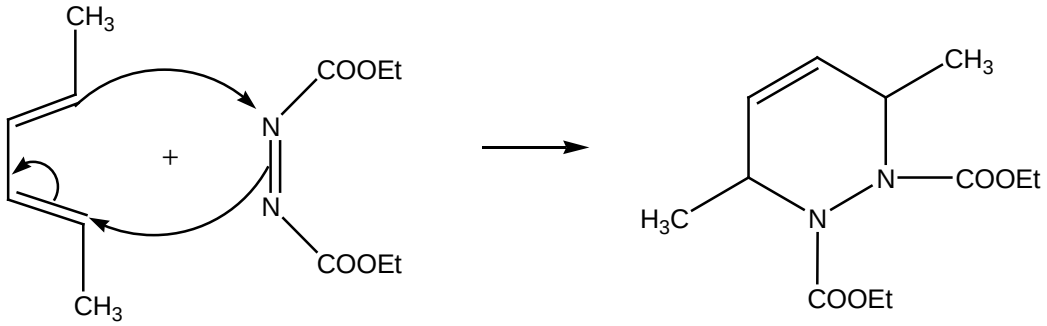


Butane 2,3 dion Phenyl Hydrazine ethyl propionate



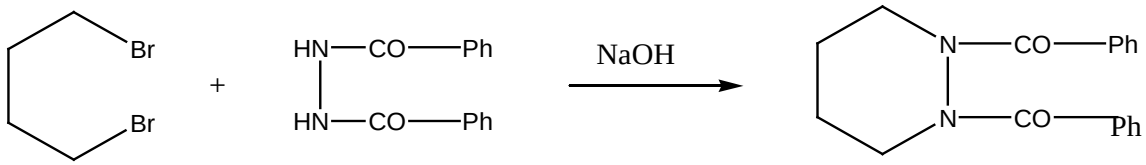
4,5,6 trimethyl 2 phenyl pyridazine 3-on

(4) Diels - Alder Reaction :-



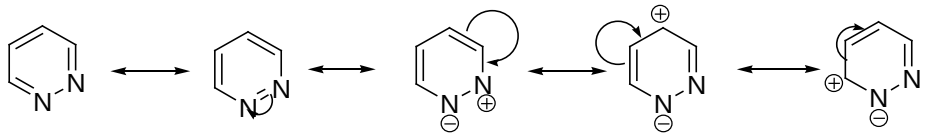
Hexane 2,4 Diene Azido carboxylic ester Tetra hydro pyridazine derivative

(5) From 1,4 Dihalide :-



1,4 Dibromo butane | Hydrazine derivative | Hexa hydro pyridazine derivative

RESONATING STRUCTURE:-



@Resonating Energy: 12.3 Kcal/mole

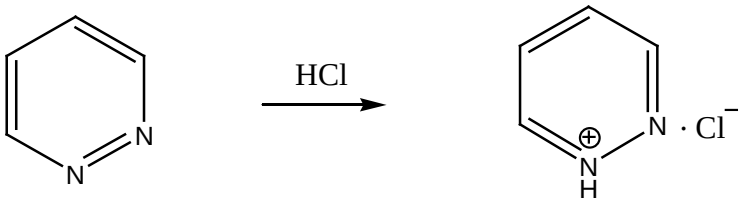
CHEMICAL PROPERTIES:-

(1)Electrophilic Reaction at Nitrogen:-

→ Electrophilic attack at ring nitrogen like protonation,alkylation and N-oxidation are described as under.

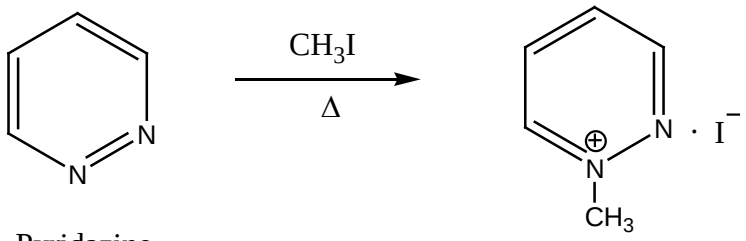
(i)Protonation:-

→ Pyridazine is a weak base and form a salts with mineral acid.



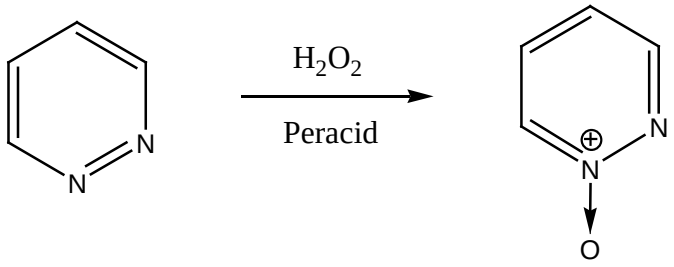
Pyridazine — Pyridazine salt

(ii)Alkylation:-



Pyridazine — Pyridazine salt

(iii) Oxidation:-



Pyridazine — 1- N- Oxide

(2) Electrophilic substitution at carbon atom:-

→ No sulphonation and nitration of pyridazine have been reported.

→ 3,4,5 & 6 position in pyridazine ring are electron deficient.

→ Pyridazine ring is resistant to electrophilic substituion even in presence of activating substituents.

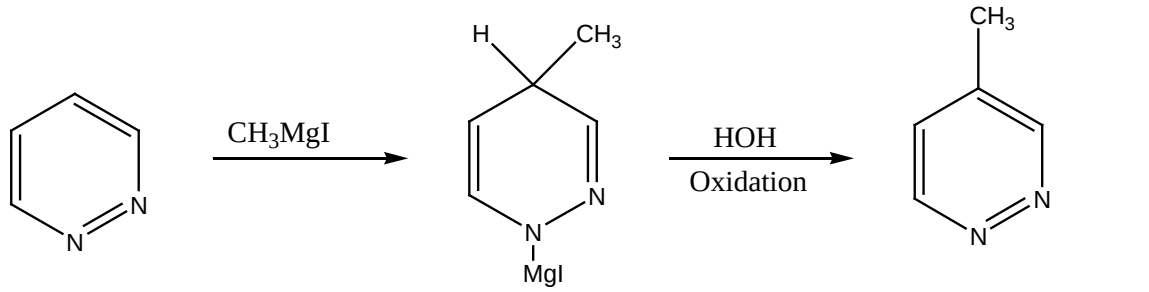
(3) Nucleophilic Reactions:-

The effect of the presence of second nitrogen makes carbon atoms of the ring more electron deficient. Therefore nucleophilic reactions occur at position C-3 & C-4.

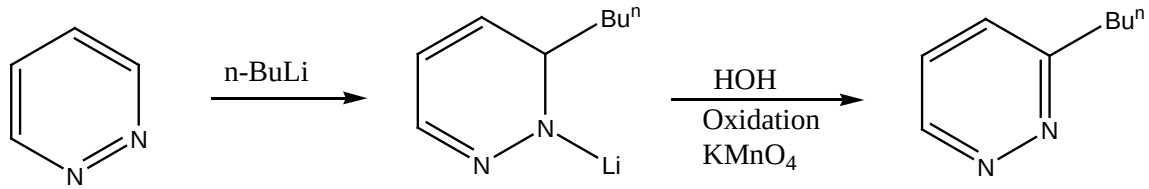
(iv) Action of Grignard reagent and Organolithium compounds:-

--> Grignard reaction occur at C-4 positon.

--> While organolithium occur at C-3 position.

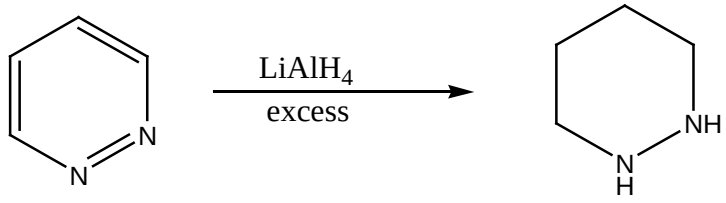


Pyridazine 4-methyl pyridazine

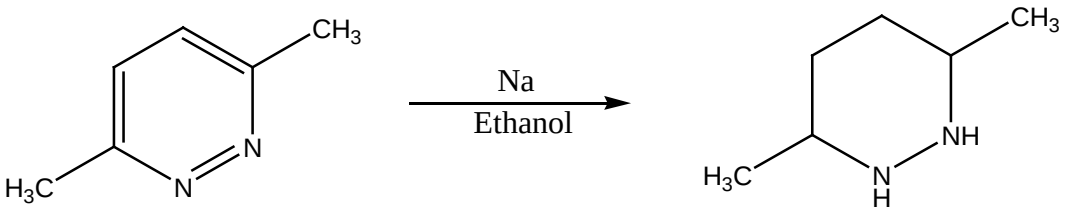


Pyridazine 3 Butyl Pyridazine

(4) Reduction:-



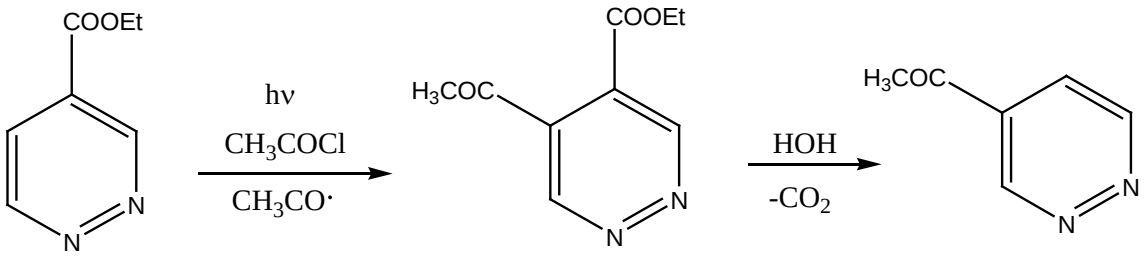
Pyridazine Hexahydro pyridazine



3,6 Dimethyl Pyridazine

3,6 Dimethyl
Hexahydro pyridazine

(v) Free radical reaction:-



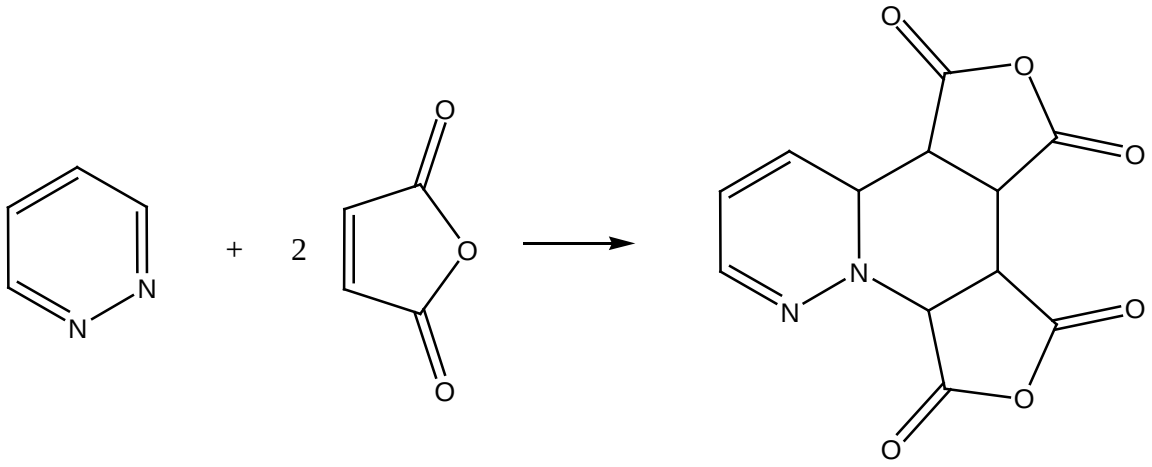
Pyridazine
4 carboxylic
ester

5-acyl
4-carboxylic
ester

4-acyl
pyridazine

(5) Cycloaddition reaction:-

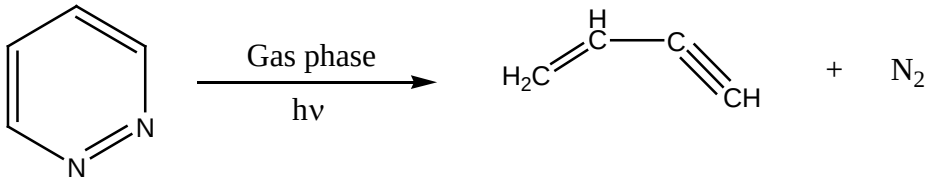
Pyridazine reacts with maleic anhydride to furnish 1:2 adduct at room temperature.



Pyridazine Maleic anhydride 1:2 Adduct

(6) Photochemical Reaction:-

The gas photolysis of pyridazine affords nitrogen and vinyl acetylene.



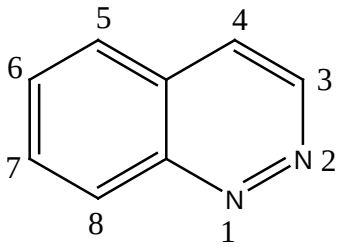
Pyridazine Vinyl acetylene

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

-::CINNOLINE::-

¤ Structrul Information and Introduction:-

--> It was first discovered by Von Richter in 1883. They generate do not occur in nature.



→ It is also known as **1,2-diazanaphthaline, Benzo[c]Pyridazine , 1,2- diazine.**

→ It is a benzo fused analogue of pyridaine.

¤ Physical Property:-

→ It is a pale yellow solid compound.

→ M.P. = 39 ^{O}C and B.P. = 114 ^{O}C

→ It possess aromatic character.

→ It is a weakly basic compound , P^{ka} = 2.70

→ It is toxic and it possess antibacterial activity.

¤ Spectal Data:-

UV λ_{max} nm : 276(3.45); 308(3.30); 322(3.34); 390(2.40)

^{1}H NMR δ_{ppm} ($CDCl_3$) : C_3-H=9.22; C_4-H,C_5-H,C_6-H,C_7-H=7.76; C_8-H=8.48

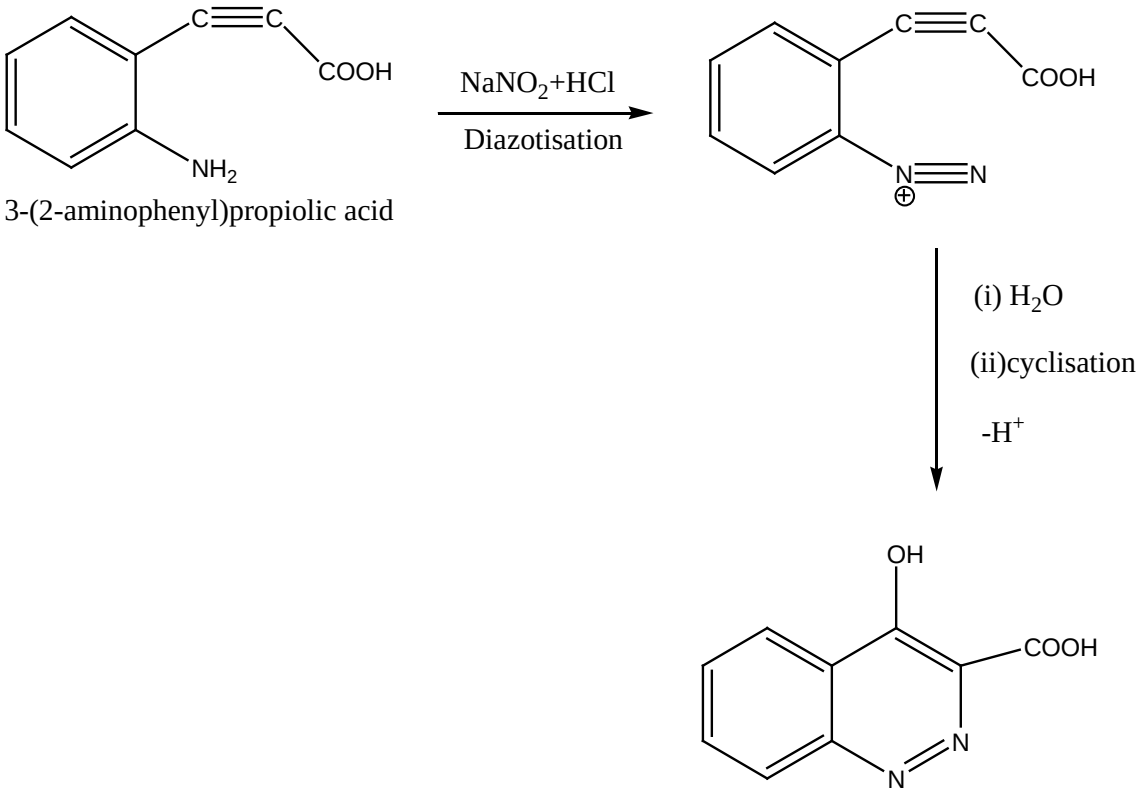
^{13}C NMR δ_{ppm} ($CDCl_3$) : C_3=146.1 ; C_4=124.6 ; C_5=127.9 ; C_6=132.3

C_7=132.1 ; C_8=129.5 ; C_9=151.0 ; C_{10}=126.8 .

¤ Synthesis:-

(1) Von Richter Synthesis:-

2-amino phenyl propiolic acid first rects with $NaNO_2$ and HCl and forms diazonium salts, following by intermolecular cyclization gives the 4-hydroxy 3-cinnolinic acid. The cyclisation take place with the addition of water molecule.

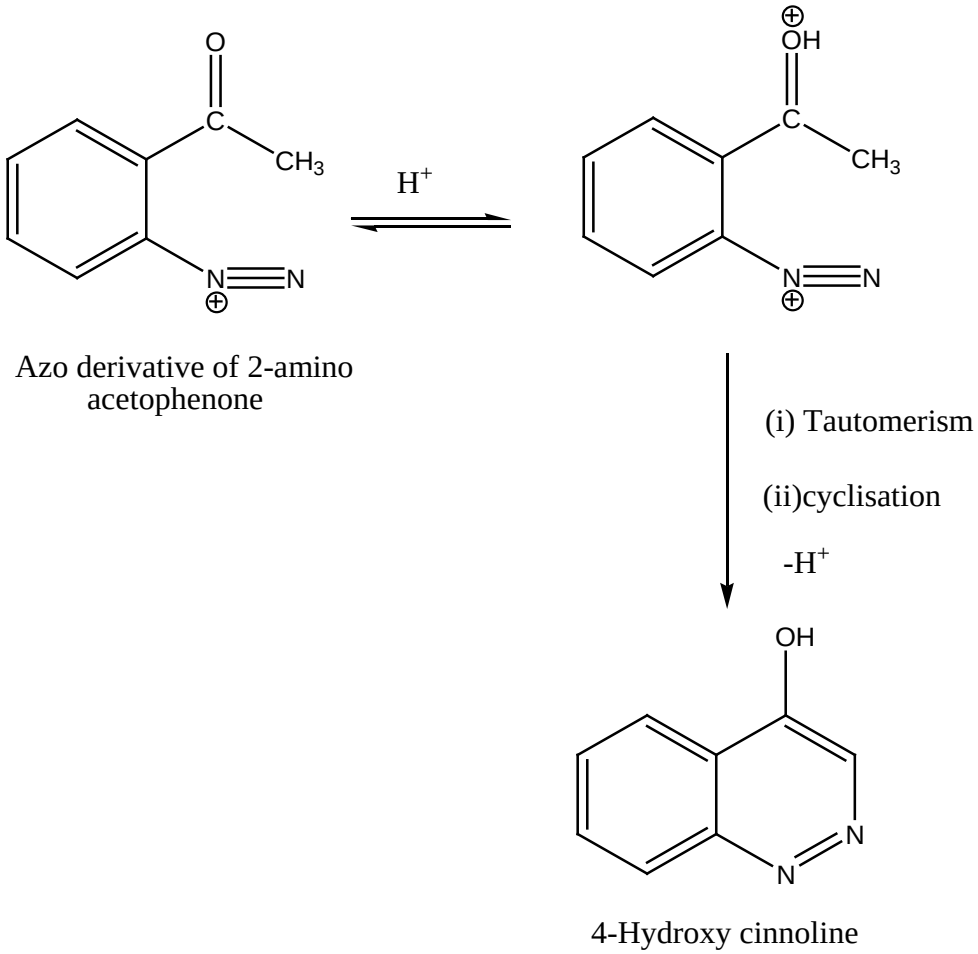


3-(2-aminophenyl)propiolic acid

4-hydroxycinnoline-3-carboxylic acid

(2) Borsche Synthesis:-

Borsche used the azoderivative of 2-amino acetophenone to synthesis cinnoline. If also take place via intramolecular cyclisation on action of acid.

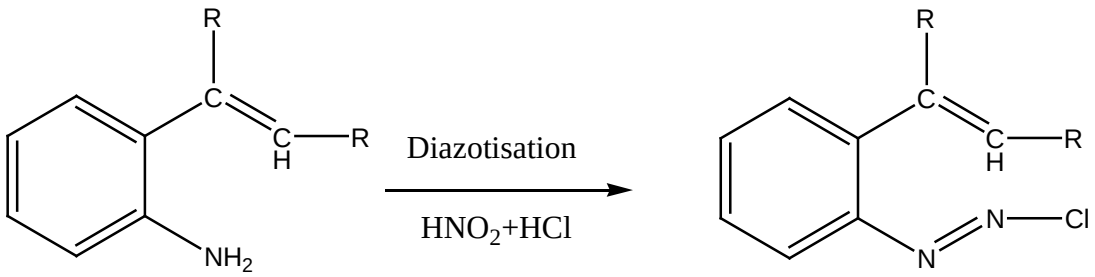


Azo derivative of 2-amino acetophenone

4-Hydroxy cinnoline

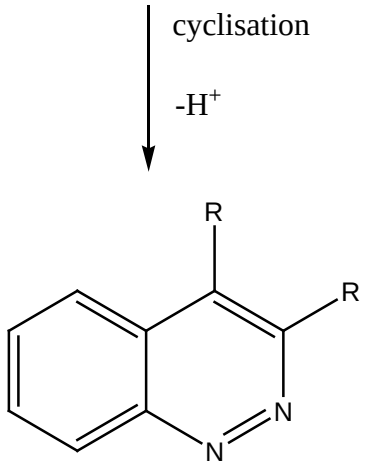
(3) Widman - Stoermer Synthesis:-

o-aminostyrine derivative on diazotisation and subsequent cyclisation in acid media on heating afford substituted cinnoline. The presence of electron withdrawing groups in the unsaturated side chain inhibits ring closure reaction.



o-amino styrine derivative

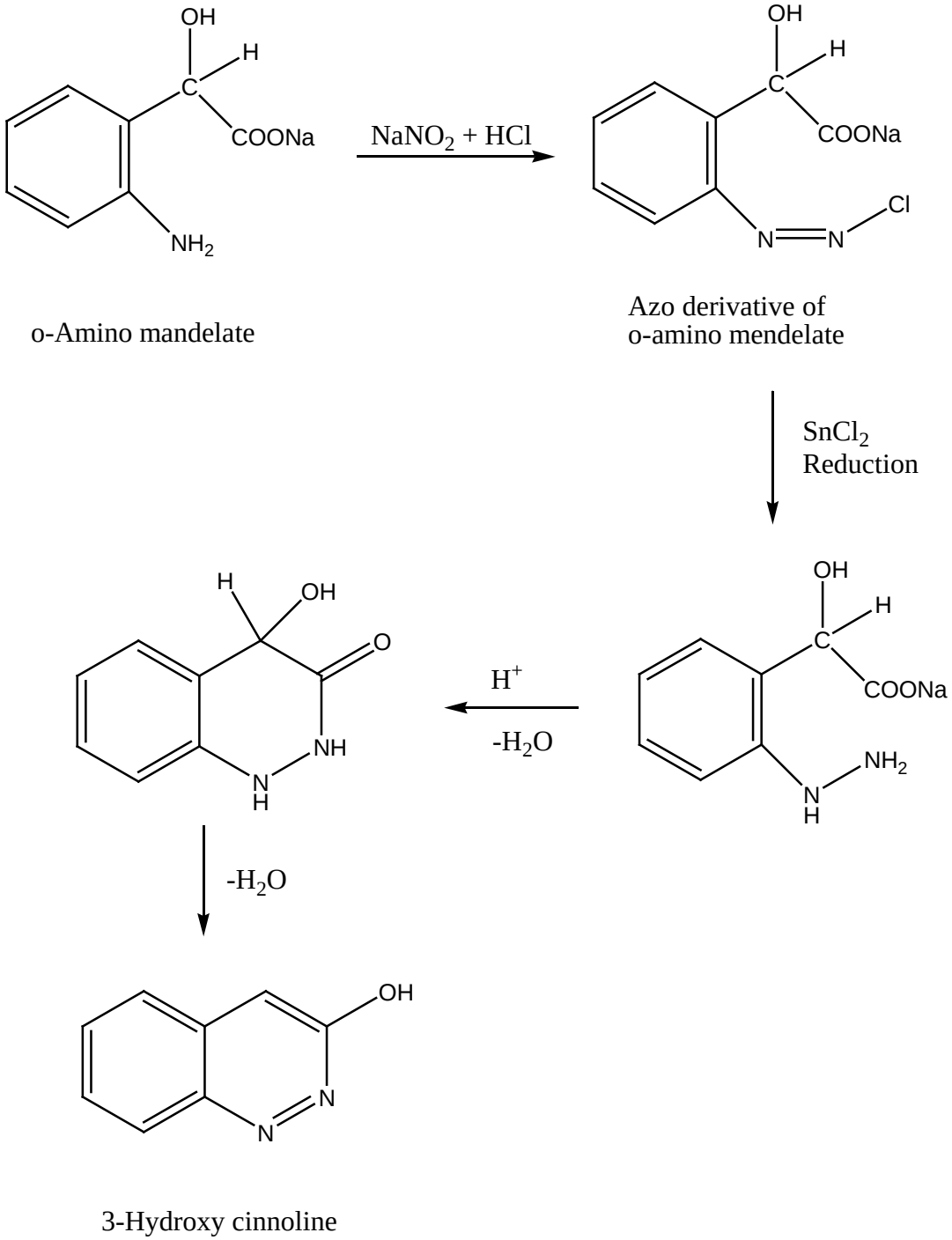
Diazonium salt of styrine deri.



4-Hydroxy cinnoline

(4) Neber - Bossel Synthesis:-

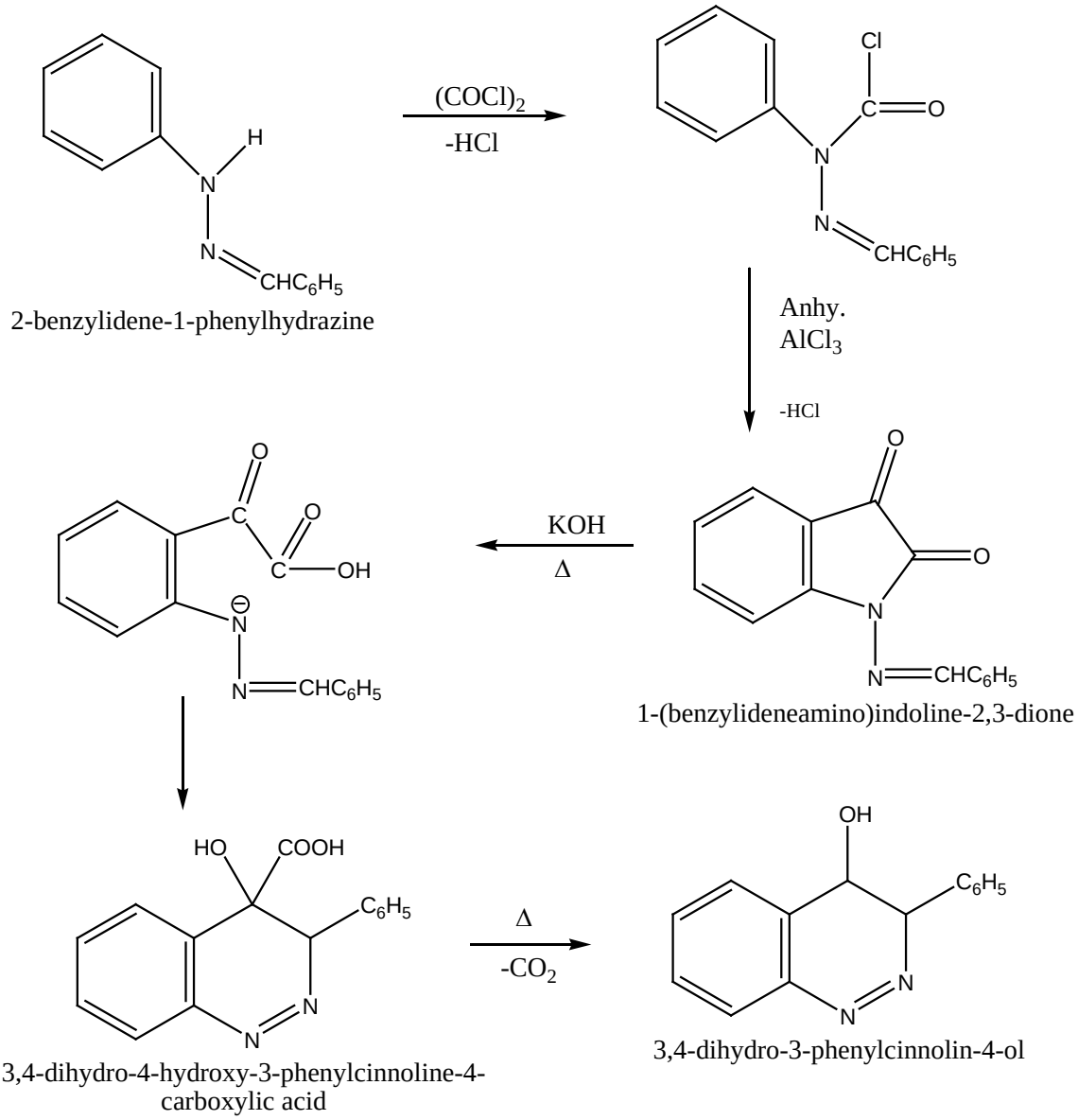
The procedure involve the diazotization of sodium o-aminomandelate with sodium nitrite and conc.HCl followed by reduction ($SnCl_2$). Cyclisation and dehydration to provide 3-hydroxy cinnoline.



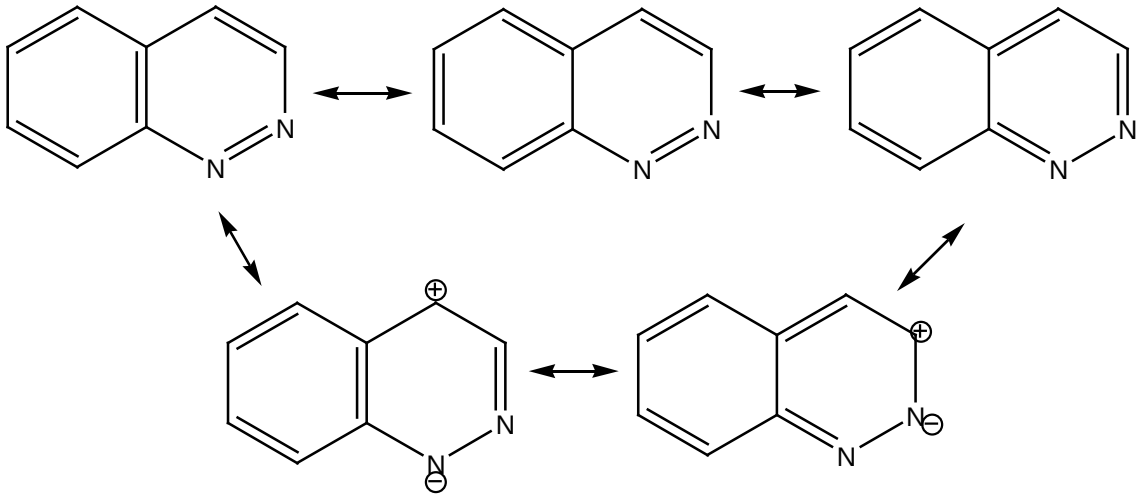
3-Hydroxy cinnoline

(5) From Benzaldehyde Phenylhydrazone:-

Benzaldehyde Phenylhydrazone teratment with Oxalyl chloride ($COCl_2$) followed by friedel craft cyclisation of the N-benzylideneamino N-phenyl oxamoyl cholride to N-benzylidene aminoisatin. This on reaction with hot potassium hydroxide solution yield 4-Hydroxy-3-phenylcinnoline.



Resonating Structure:-



From the above canonical forms we can say that the electrophilic substitution occurs either on nitrogen atom or on benzene ring.

Here, due to delocalized electron in benzene ring. Electrophilic substitution is more prefable on it at 5 and 8 position.

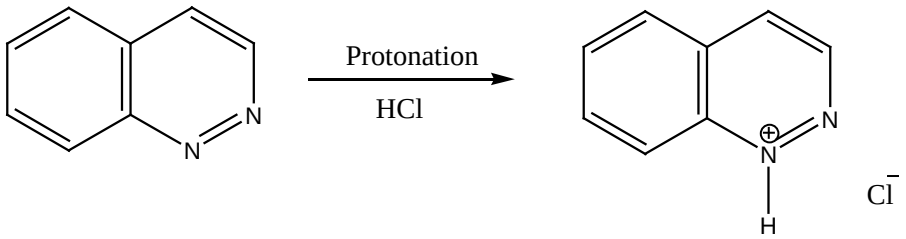
Above polar canonical form are observed and dipole moment is Zero, So nucliophilic substitution is easily take place at position 3 & 4 but more prefable is 4- position.

¤ Chemical Properties of Cinnoline:-

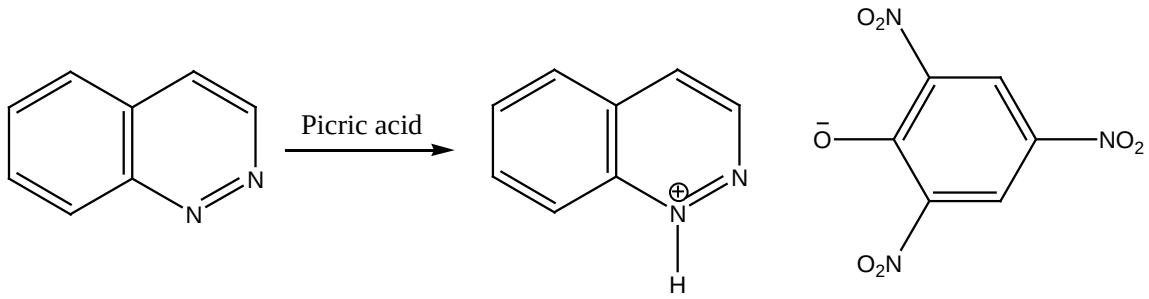
Electrophilic substitution at Nitrogen atom:-

➔ *(1) Protonation:-*

Cinnoline is a weak base react with HCl and picric acid and form salt with HCl and picric acid.



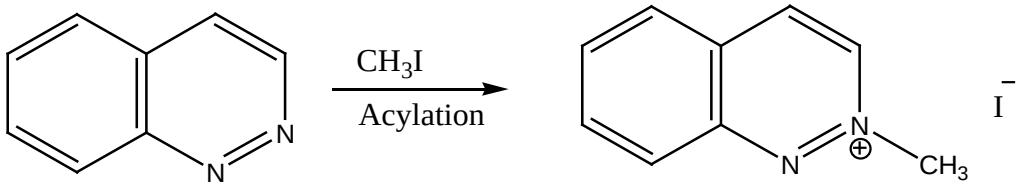
cinnoline — Hydrochloride salt of Cinnoline



cinnoline — Picric acid salt of Cinnoline

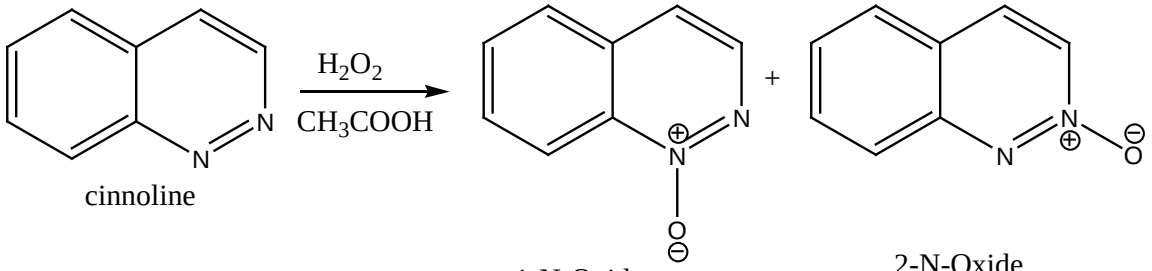
➔ *(2) Alkylation:-*

Cinnoline react with methyl ioded gives 2-methyl cinnoline.



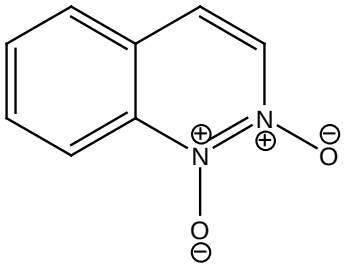
➔ *(3)Oxide Formation:-*

Cinnoline is oxidized with hydrogen peroxide in acetic acid to yield mixture of N-oxide i.e. 1-N-Oxide(26%), 2-N-Oxide(50%), 1,2-di-N-Oxide(3%).



cinnoline

1-N-Oxide + 2-N-Oxide +

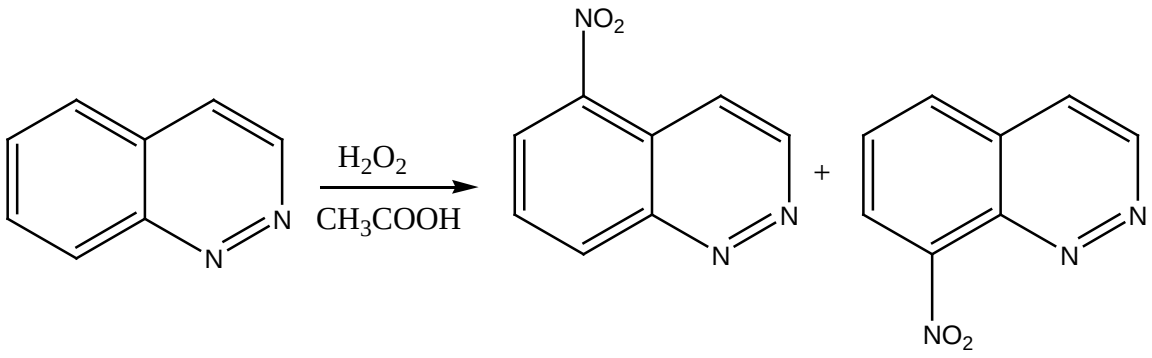


1,2-N-Oxide

 # Electrophilic Substitution Reaction at Carbon atom:-

➔ *(1) Nitration:-*

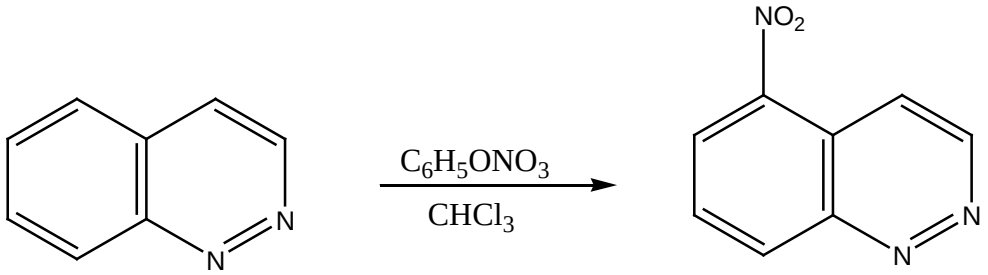
(i)Reaction with conc. HNO_3+H_2SO_4 , it gives the mixture of two product 5 and 8 nitro cinnoline.



cinnoline 5-nitrocinnoline 8-nitrocinnoline

(ii) Nitration of cinnoline with benzoyl nitrite and chloroform gives

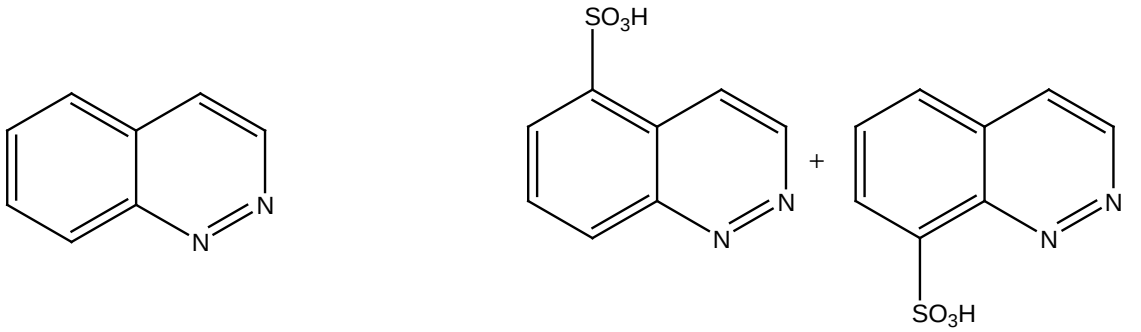
5-Nitro cinnoline.



cinnoline 5-nitrocinnoline

➔ *(2) Sulphonation:-*

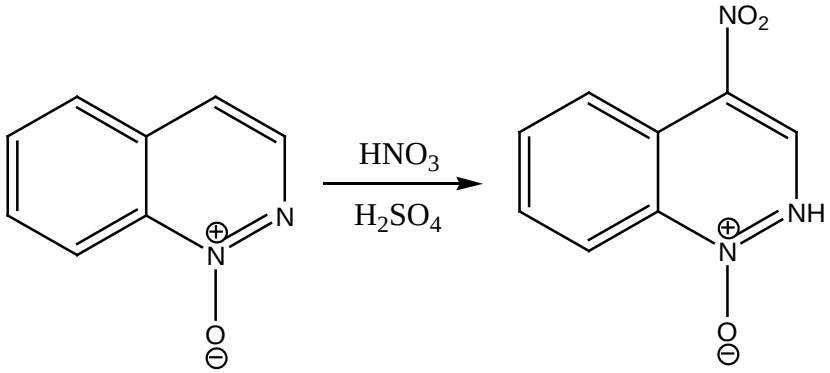
Reaction with conc. H_2SO_4 , it gives 5 and 8 substituted derivative.



cinnoline cinnoline-5-sulfonic acid cinnoline-8-sulfonic acid

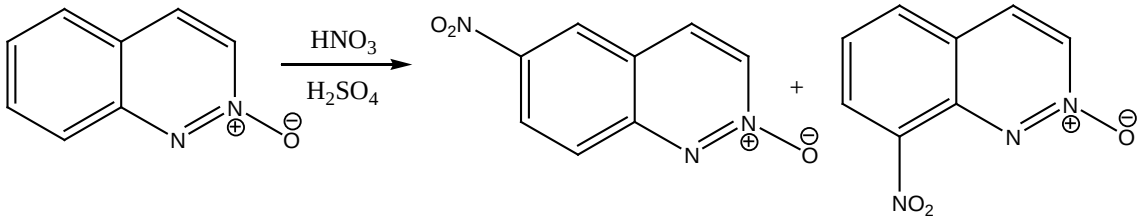
➔ *(3) Nitration of N-Oxide:-*

→ Nitration of cinnoline 1-N-oxide gives 4-nitro derivative.



1-N-Oxide cinnoline 4-nitrocinnoline 1-N-Oxide

→ Nitration of cinnoline 2-N-Oxide gives mixture of 5 and 8 nitro cinnoline 2-N-Oxide.



2-N-Oxide cinnoline

5-nitrocinnoline 2-N-Oxide

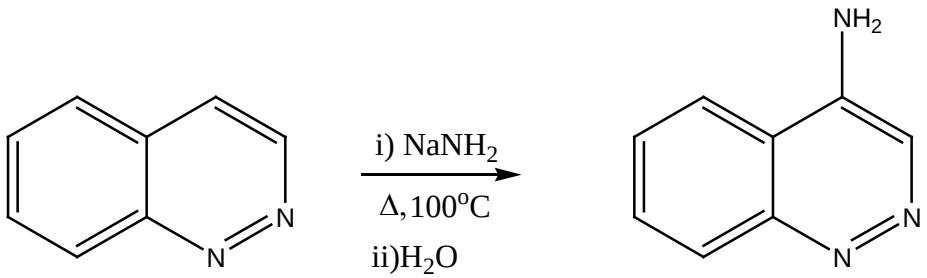
8-nitrocinnoline 2-N-Oxide

 # Nucliophilic Substitution Reaction:-

It is readily occurs at the 4-position of the cinnoline ring.

➔ *(i) Tchichibabin Reaction:-*

On heating with $NaNH_2$, Cinnoline gives 4-amino cinnoline.

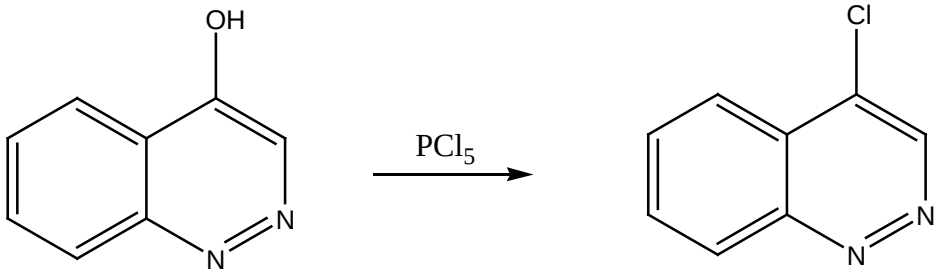


cinnoline

cinnolin-4-amine

➔ *(ii) Reaction with PCl_5 :-*

In 4-hydroxy cinnoline , hydroxy group can be easily replaced by chlorine with PCl_5 yielding 4-chloro cinnoline.

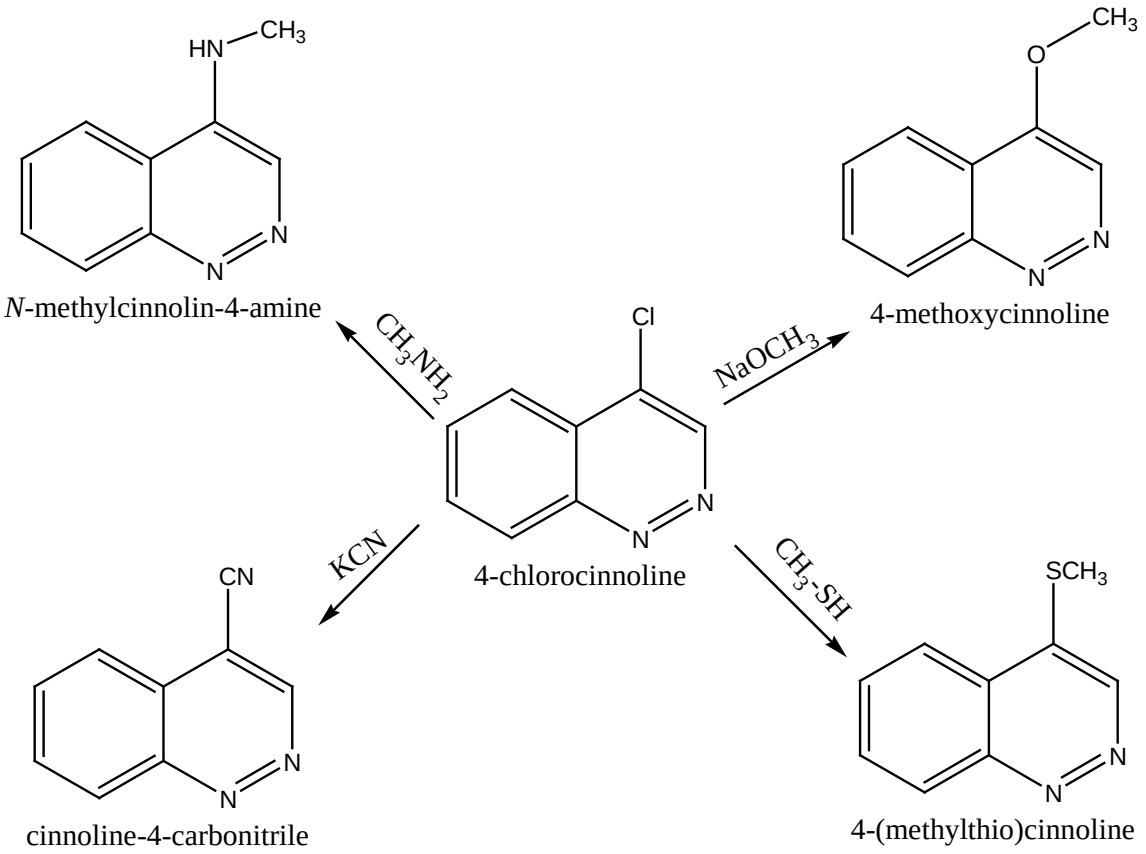


cinnolin-4-ol

4-chlorocinnoline

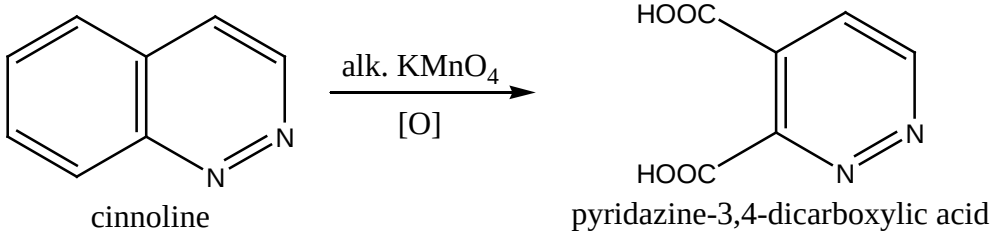
➔ 4-chloro cinnoline are very chemicaly reactive , so it reacts with methyl amine, sodium methoxide, KCN, and methyl mercaptan(CH_3-SH) and gives amino,

methoxy, cyno, and mercapto cinnoline.

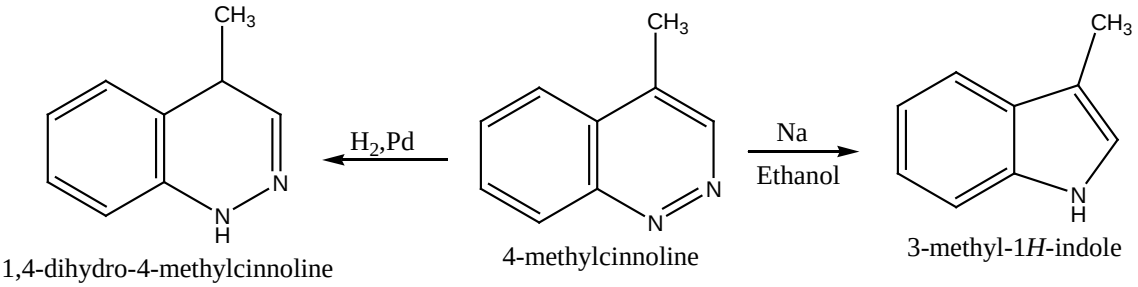


 # Oxidation Reaction:-

Cinnoline is oxidised using suitable agent to give pyridazine 3,4 di carboxylic acid.



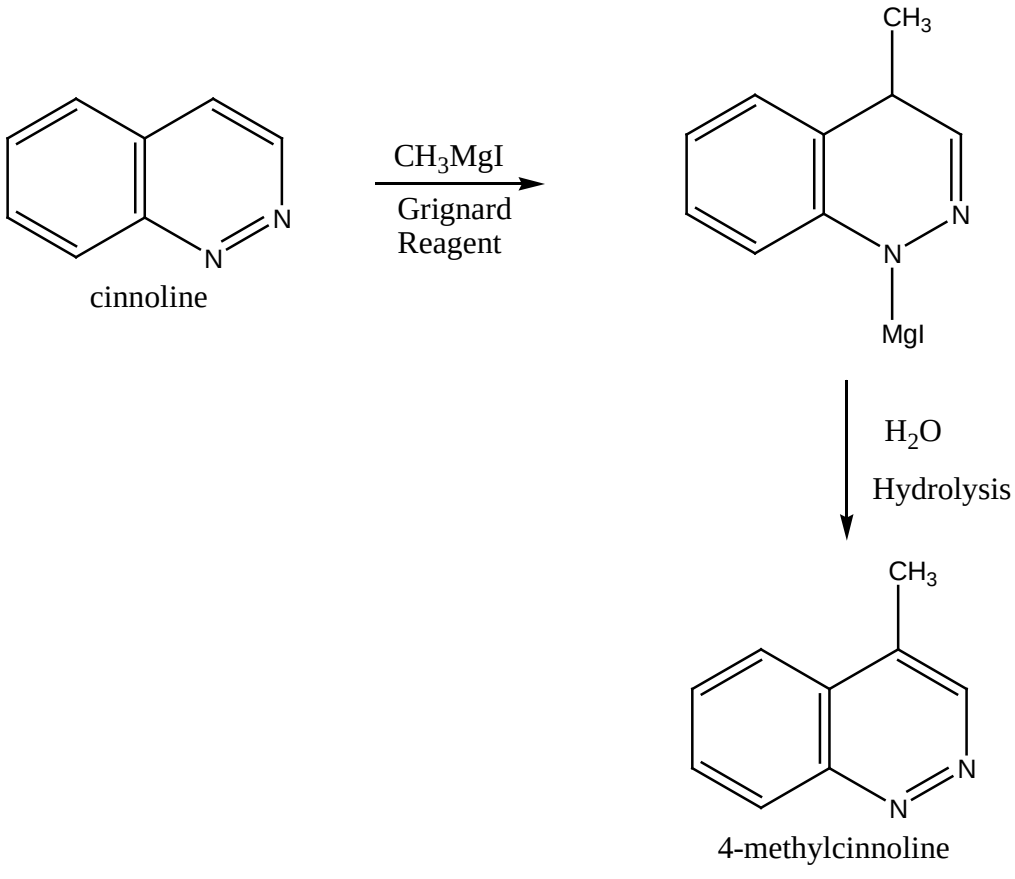
 # Reduction:-



1,4-dihydro-4-methylcinnoline — 4-methylcinnoline — 3-methyl-1*H*-indole

 # Action of Grignard Reagent:-

Action of Grignard reagent occurs at C-4 position and give 1,4 dihydro cinnoline derivative which on hydrolysis and dehydrogenation provides substituted cinnoline.



cinnoline — 4-methylcinnoline

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Assignment of Heterocyclic compound

(Six membered compound)

PYRIMIDINE

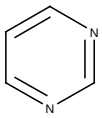
Name : Channa mejbin s.

Roll no. : 03 (Organic)

Submited to : Dr. V. H. Shah

Pyrimidine

structure :



Other name :

- **1, 3, diazine**

Intoduction :

- occurance from living organism.
- first synthesized by fankland and Kolbe in 1848.
- Biologically and pharmacologically it is very important diazine.
- pyrimidines uracil i.e thymine & cytosine are nucleotide based constitute the genetic code in RNA & DNA.
- Important pyrimidine derivative: Trimethoprim-antibacterial and Pyrimethamine-antimalarial.

physical properties:

- colourless compound
- soluble in water.
- melting point = 22.5°c
- boiling point = 124°c
- virtually flat ring.
- weak base as compared to pyridine.

Synthesis:

There are six synthesis of pyrimidine.

1. Pinner synthesis

2. Remfry-Hull synthesis

3. From malonic ester and malic acid.

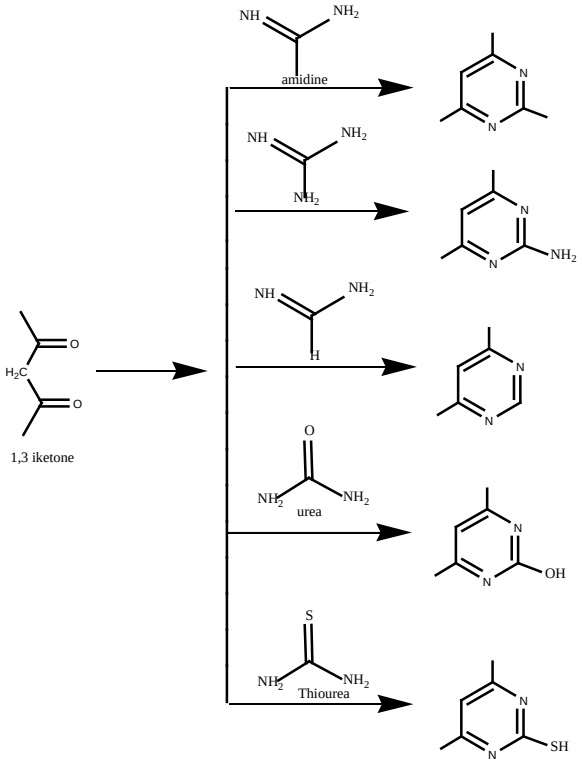
4. Biginelli reaction

5. (3+1+1+1) condensation

6. Aza-Wittig reaction.

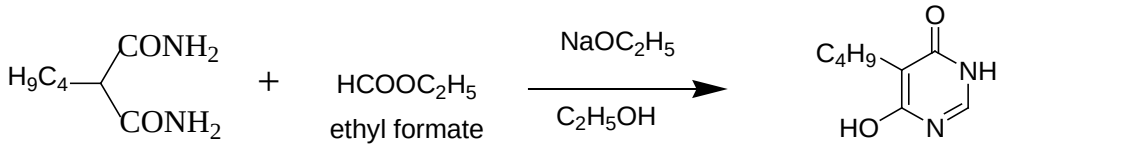
1. Pinner synthesis：

This is a most common route to synthesise pyrimidine derivative. Here 1,3 diketone under go reaction with amidines, guanidines urea and thioureas resulting in pyrimidines, 2-aminopyrimidines, 2-aminopyrimidones and 2-thiopyrimidones respectively.



2. Remfry-Hull synthesis:

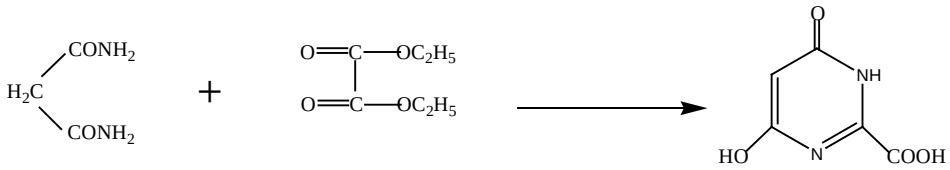
It is the condentation of α-butylmalondiamide with ethyl formate in ethanolic sodium ethoxide to provide 5-butyl- 6-hydroxypyrimidin-4(3H)one.



α-butylmalondiamide

5-butyl-6-hydroxypyrimidin-4(3*H*)-one

- Another reaction is diethyl oxalate reacts with malondiamide to gives 2-carboxy-6-hydroxypyrimidin-4-one.



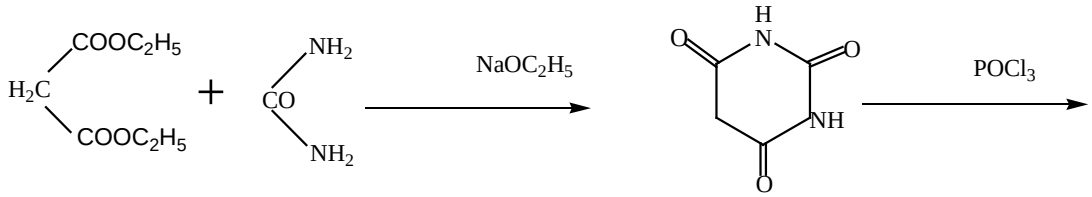
Malondiamide

Diethyl oxalate

2-carboxy,6-hydroxy
pyrimidine 4-one

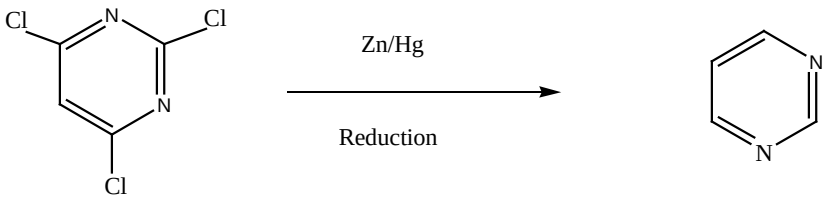
3. From malonic ester and malic acid

- Malonic ester with urea in presence of base to provide barbituric acid.It followed by the treatment of phosphorus oxycloride and reduction with zinc amalgam which results the formation of pyrimidine.



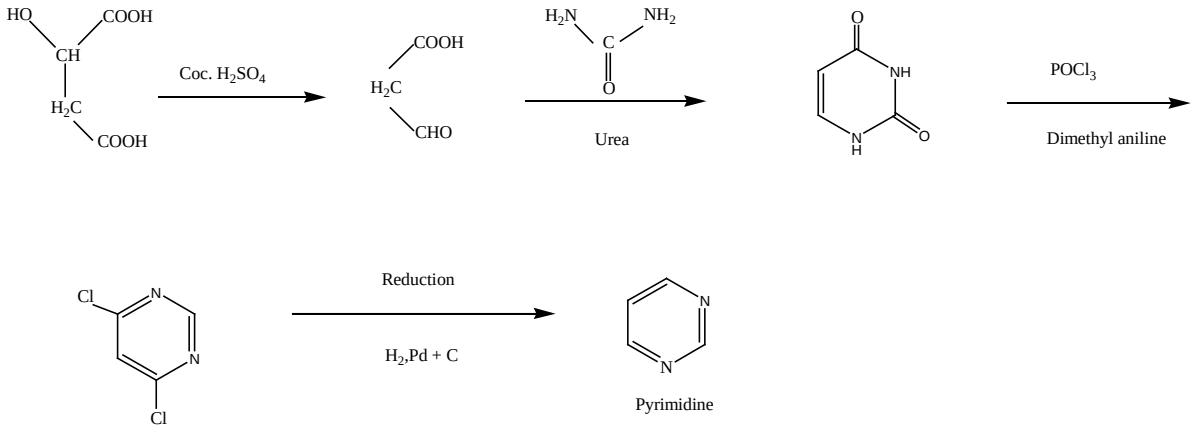
Malonicester

urea



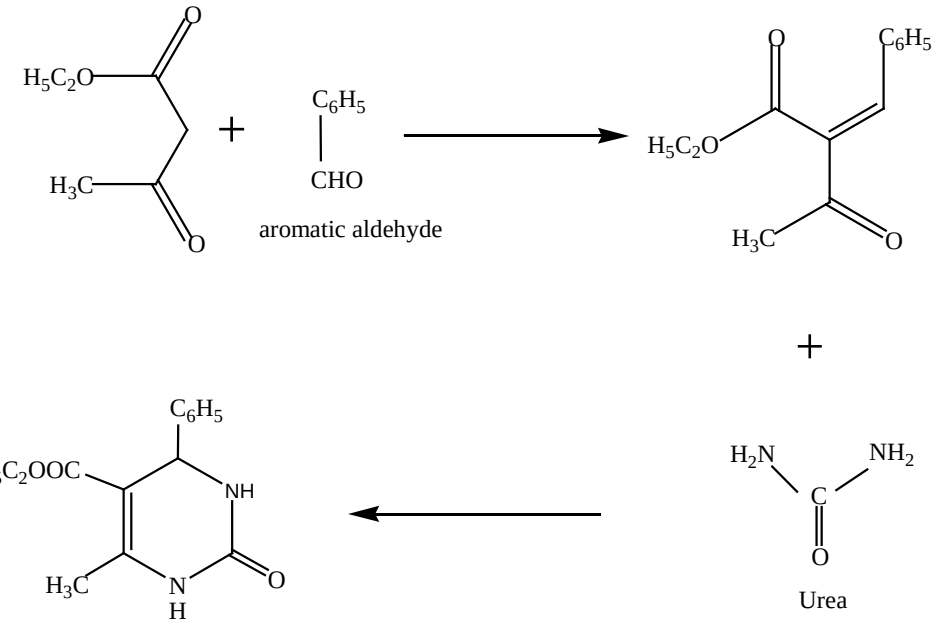
Pyrimidine

➢ In the other reaction malic acid with concentrated sulphuric acid gives formylacetic acid which on condensation with urea gives pyrimidin 2,4-dione which reacts with phosphorus oxycloride to form dicloropyrimidine which reduce to pyrimidine by halogen and palladium over a carban.



4. Biginelli reaction:

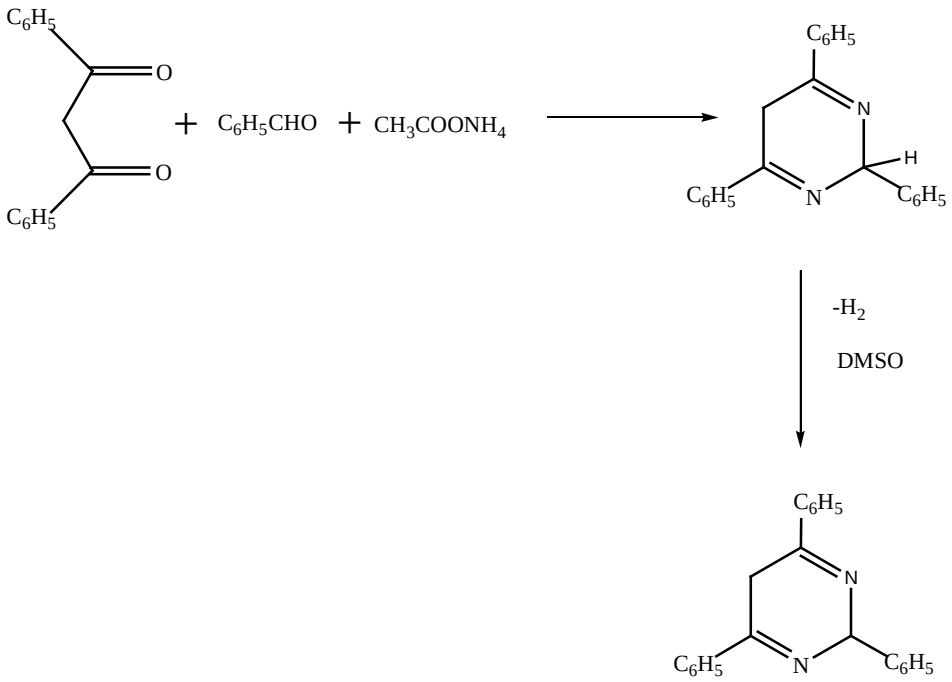
This reaction was pioneered in 1893. This reaction can be viewed as a multicomponent reaction.Here three component i.e. aromatic aldehyde, β-keto ester and urea or thiourea combines to yield dihydropyrimidines.



3,4-dihydropyrimidine-2(1H)-one

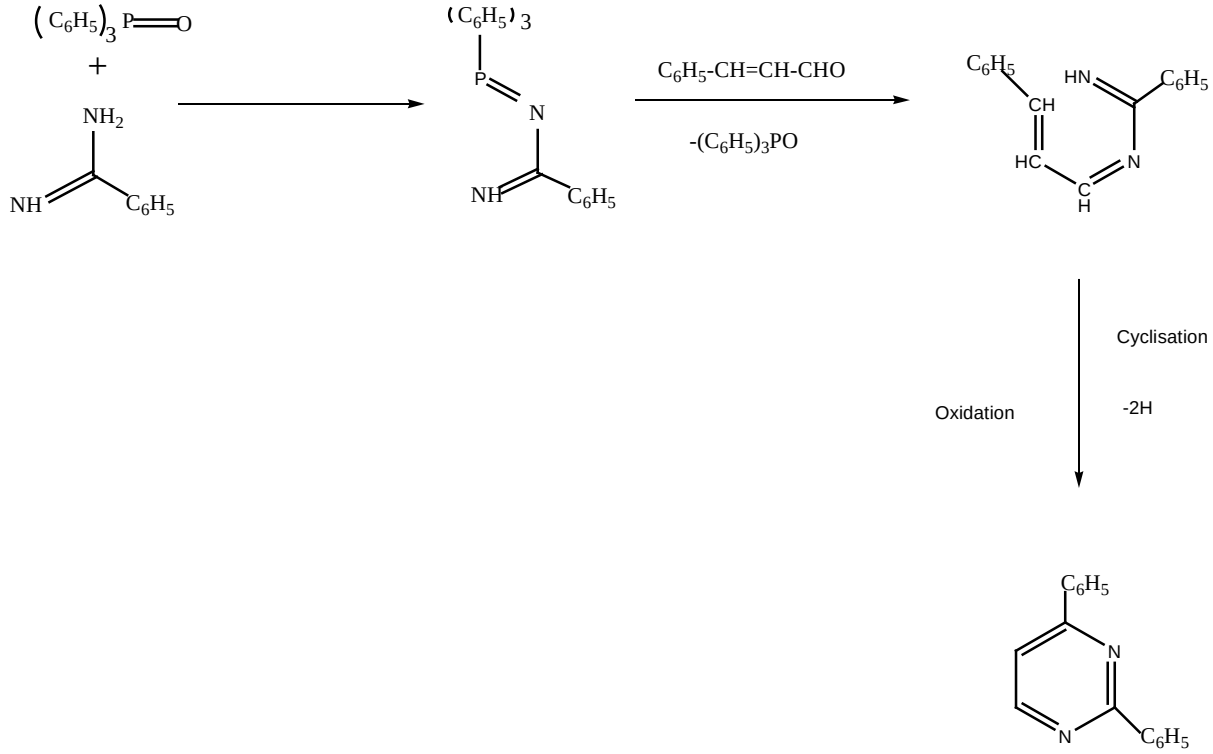
5.(3+1+1+1) condensation:

This is a new method to designed directly isolate substituted pyrimidines. Dibenzoylmethane reacts with benzaldehyde and anhydrous ammonium acetate in dry dimethaylsulphoxide to provide 2,4,6,-triphenylprimidine.

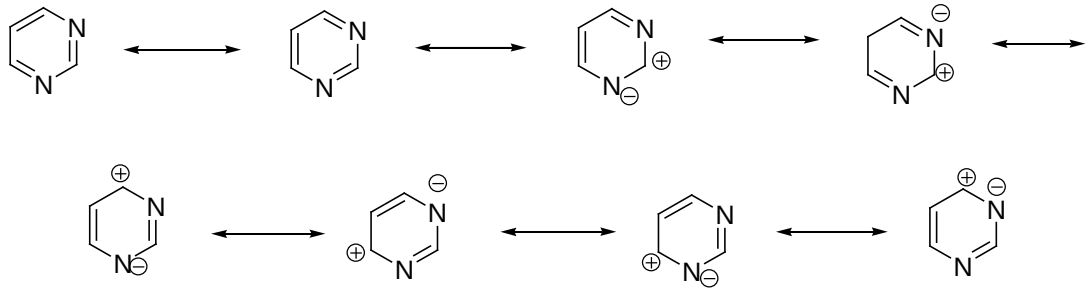


6. aza-Wittig reaction:

Benzamidine and wittig reagent undergoes aza-wittig reaction with α,β-unsaturater aldehyde like cinnamic aldehyde to form a product which on cyclisation and oxidation afords pyrimidine derivative.



Resonating structure :



Chemical reactivity:

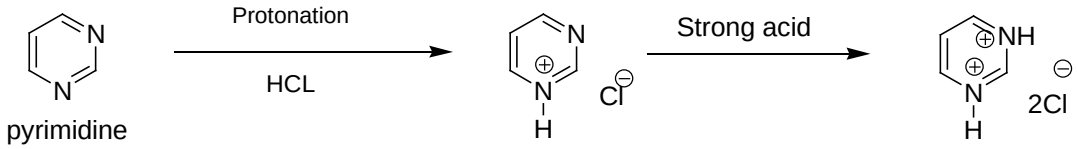
Due to effect of Ring Nitogen atom (electron withdrawing) electron deficiency arises at positinf C-2,C-4,and C-6 atom.

- Electrophilic substitution reaction occurs at C_5 position only.

- Nucleophilic substitution reaction occurs at C_2, C_4, C_6 position.

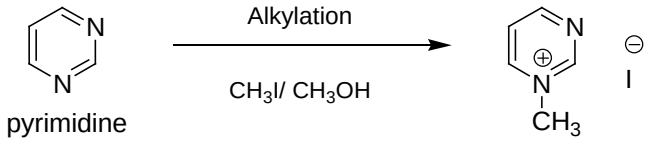
(A) Elecrophilic addition at Nitrogen atom:

1. Protonation :



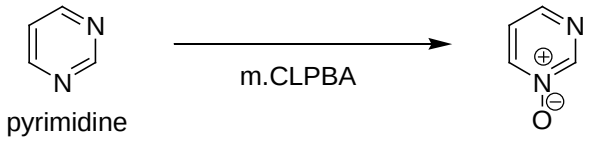
pyrimidine

2. Alkylation:



pyrimidine

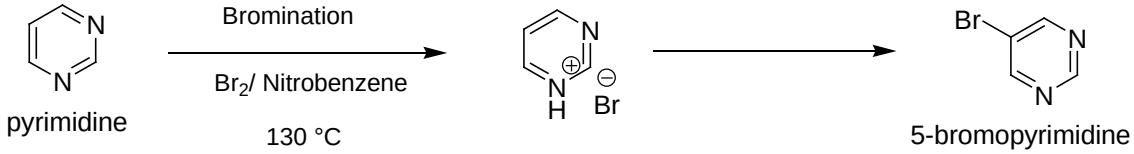
3.N-Oxide formation:



pyrimidine

(B) Electrophilic substitution at Carban:

4. Bromination:

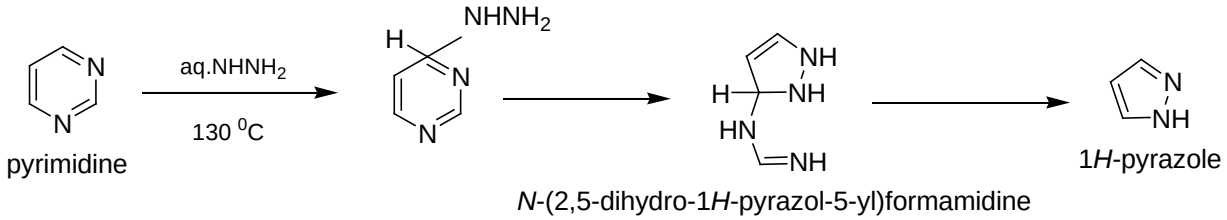


pyrimidine

5-bromopyrimidine

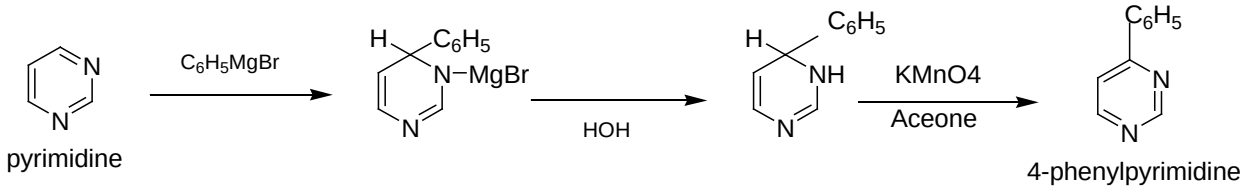
(C) Nucleophilic reaction:

5.Reaction with hydrazine:

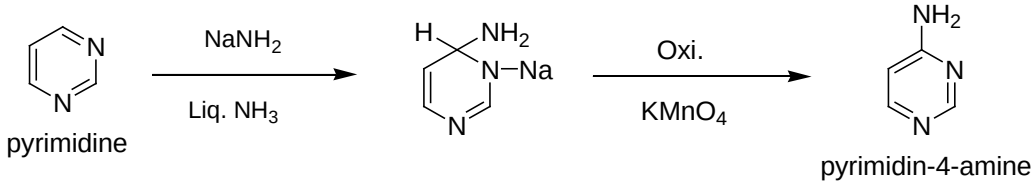


N-(2,5-dihydro-1*H*-pyrazol-5-yl)formamidine

6. Reaction with girgnard reagent :



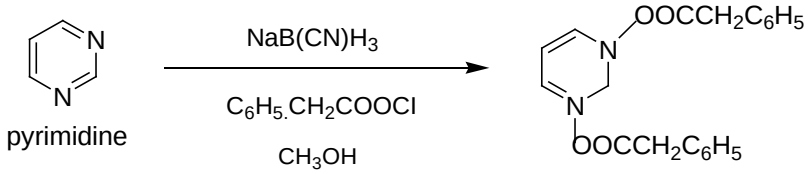
7. Chi-chi babin reaction :



(D) Reduction :

Pyrimidine ring is not affected by common reducing agents like sodium borohydride.

Primidine on reduction with sodium cyanoborohydride gives dihydro derivatives.



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Assignment of Heterocyclic compound

(Bi-cyclic ring system of Six membered compound)

QUINAZOLINE

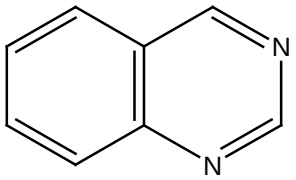
Name : Chuahan Rajul N.

Roll No. : 04 (Organic)

Submited to : Dr. V. H. Shah

Quinazoline

- **Structure:**



- **Other names:**

1. Phenmiazine

2. Benzo Pyrimidine

3. Benzo-1-3-diazine

4. 1,3-diazonaphthalene

5. 5,6-benzo pyrimidine

Introduction:

Pyimidine ring when fused with benzene ring at the 5,6-position results in quinazoline ring.

It was first synthesized by Gabriel in 1903.

Some quinazoline derivative exibit are:

A. hypnotic (methaqualone)

B. diuretic – increased out put of urine (quinethozone)

C. anti hypertensive

- **Physical Properties:**
  - Aromatic compound.
  - Colourless solid
  - Sweet odour
  - Weak base
  - Melting point = 48^0C
  - Boiling point = 253^0C
  - Soluble in water and most of organic solvent

- **Synthesis:**

There are six synthesis of Quinazoline are as under.

1. From O-acetamido acetophenone

2. Niemantowski reaction (4+2) condensation

3. From O-amino benzophenone and urea

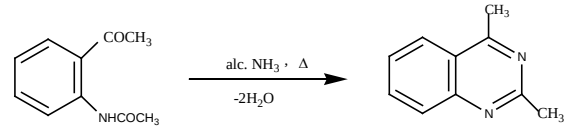
4. From O-Nitrobenzaldehyde and formamide

5. Bischer Synthesis (5+1) condensation

6. Reidel Synthesis (5+1) condensation

1. From O-acetamido acetophenone:

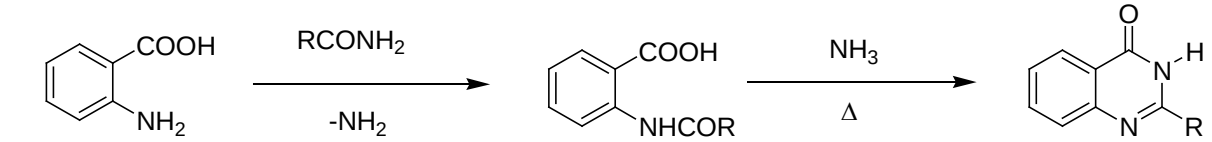
2,4-dimethylquinazoline can be obtained from O-acetamido acetophenone.



O-acetamido acetophenone 2,4-dimethylnquinazoline

2. Niemantowski reaction:

Anthranilic acid on fusion with aliphatic amide yields the 4-quinazolone derivative.

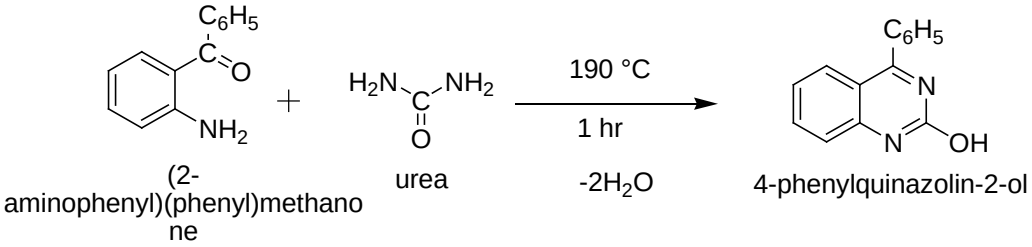


2-aminobenzoic acid

2-substituted 4-quinazolone

3. From O-amino benzophenone and Urea :

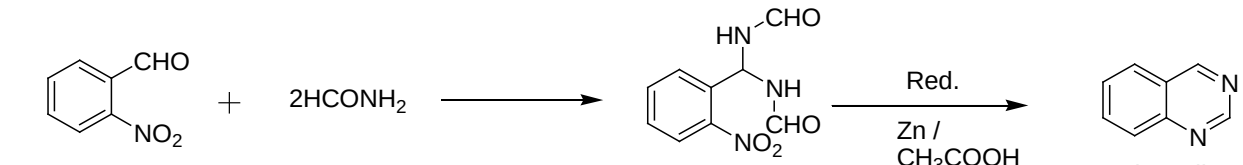
O-amino benzophenone condenses with urea on heating to afford 2-hydroxy-4-phenylquinazoline.



(2-aminophenyl)(phenyl)methanone | urea | 4-phenylquinazolin-2-ol

4. From O-nitro benzaldehyde and Formamide :

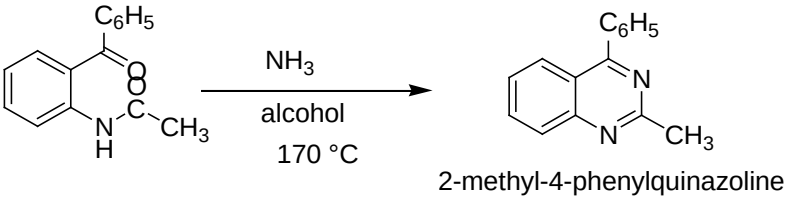
O- nitrobenzaldehde with formamide to yield bisfarmamide derivative which on reductive cyclisation with zinc and aectic acid furnisher the quinazoline.



2-nitrobenzaldehyde | quinazoline

5. Bichler Sythesis (5+1) condensations :

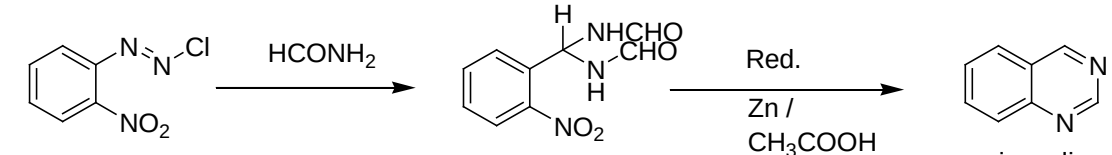
N-acyl derivative of O-aminobenzophenone or benzaldehyde reacts with alcoholic ammonia at elevated temperature to afford 2- methyl – 4- phenylquinazoline.



2-methyl-4-phenylquinazoline

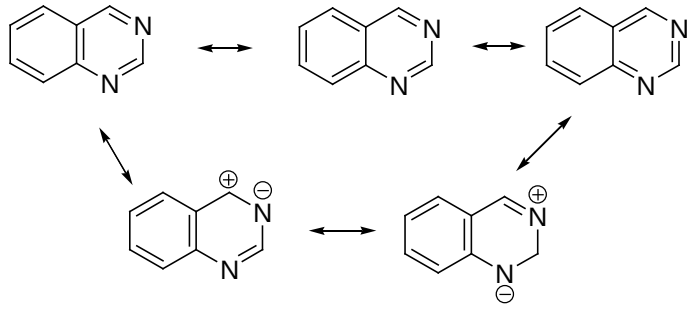
6. Reidel synthesis (5+1) condensations :

Bisformamide is obtained by the condensation of O-nitrobenzenediazonium chloride with formamide, as reidel synthesis.



(*E*)-2-chloro-1-(2-nitrophenyl)diazene | quinazoline

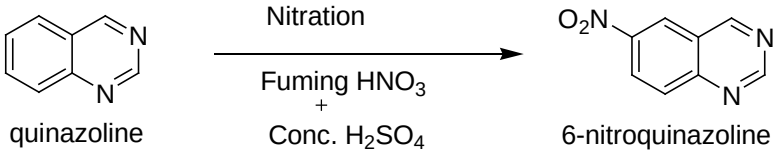
- **Resonating Structure :**



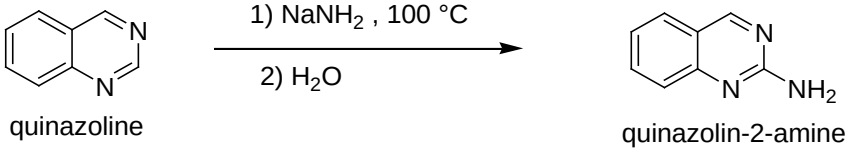
- Nucleophilic (nucleous loving , electron donor species – NH_2) reactin takes place at 2nd and 4th position by preferably place at 2nd position .
- Electrophilic (electron loving , electron deficient species , $-NO_2$) reaction takes place preferably at 6th positin.

• Chemical Properties :

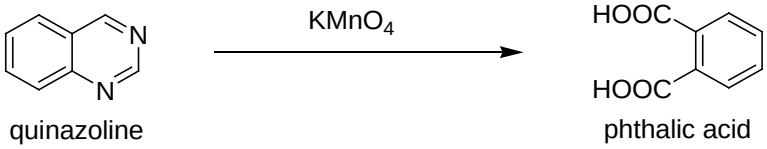
1. Electrophilic substitution reaction :



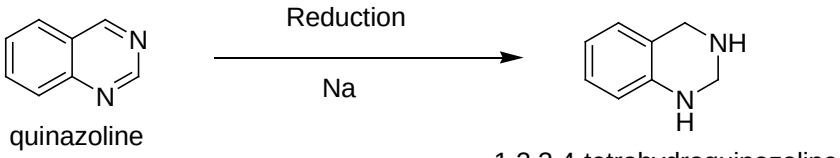
2. Nucleophilic substitution reaction :



3. Reaction with Oxidising agents :

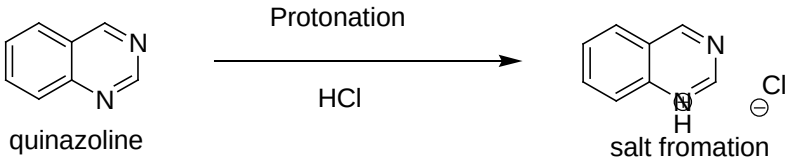


4. Reaction with Reducing agent :



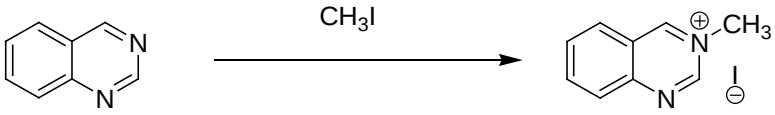
quinazoline — 1,2,3,4-tetrahydroquinazoline

5. Protonation :



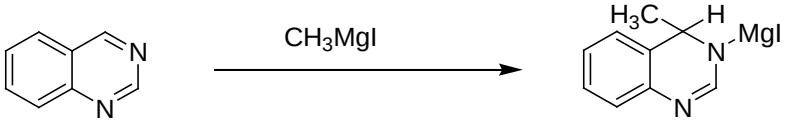
quinazoline — salt fromation

6. Alkylation :



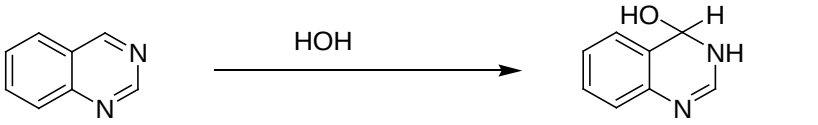
quinazoline — salt fromation

7. Grignard Reagent :



quinazoline

8. Hydrolysis :



quinazoline — 3,4-dihydroquinazolin-4-ol

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Chudasama Sangeetaba A.

M.Sc. – sem. - III Organic chemistry.

Roll No. - 5

Pyrazine

[1] Structure:-

[2] Name: - Pyrazine or 1, 4 diazine

[3] Introduction:-

- Pyrazine is derivatived from benzene by replacement of two ring carbon atoms by nitrogen at 1 & 4 positions.
- Pyrazine occurs in very small amount but some derivatives of Pyrazine such as pteridine & phenazine occurs in nature.
- Alkylpyrazines are used as flavoring agents & pyrizinamide is a drug used for tuberculosis. Thionazin, the soil insecticide is also very useful.
- It is also used as antibiotics, antitumor & diuretic agents.

[4] Physical properties:-

- Colorless, solid compound.
- Melting point- 54^0 C & boiling point – 121^0C
- Planner structure.
- Weaker base than either pyridazine or pyrimidine.
- Dipole moment zero because of the symmetric nature.
- The resonance energy is 24.3 k.cal/mol.

[5] Spectral data:-

- UV λmax nm pH=7 : 261 (3.77); 300 (2.93)
- ^{1}H NMR δ ppm ($CDCl_3$) : C_2-H, C_3-H, C_2H, C_6H;
- ^{13}C NMR δ ppm ($CDCl_3$); C_2, C_3, C_4, C_5, C_6: 145.6
- ^{15}N NMR NH_3 = 0, δ ppm, MSQ: 338

[5] Synthesis:-

There are 8 types of synthesis methods:-

- From α- diketones.
- From α- aminocarbonyl compounds.
- Aza- witting reaction.
- (2+1+2+1) Condensation.
- From Phenylazirine.
- From ethylene diamine with ethylene oxide or dibromoethane.
- Self condensation of glycin.
- Buchi method.

[1] From α- diketones:-

Condensation of diethyl dibutenone with 1,2 diamino ethane in presence of ether at o^0 C temp gives 2,3 di methyl 5,6 dihydropyrazine, which in different conditions gives Pyrazine.

[2] From α- aminocarbonyl compounds:-

α- Aminoketone on self condensation gives 2, 5 dihydro 2, 3, 5, 6 tetramethyl pyrazinewhich readily oxidized by air to 2,3,5,6 tetra hydro Pyrazine.

[3] From Phenylazirine:-

Dimerization of 2- Phenylazirine in the presence of molybdenum hexacarbonyl in THF gives 2, 5 biphenyl Pyrazine, 2, 5 biphenyl, 3, 6 dihydro Pyrazine, 2, 5 biphenyl dihydro Pyrazine.

[**3] Reaction of ethylene diamine with ethylene oxide or dibromo ethane.**

The reaction of ethylene diamine with ethylene oxide or dibromoethane gives hexahydropyrazine which on oxidation gives Pyrazine.

[5] Self condensation of glycin.

Self condensation of glycin results in the formation of 2, 5 diketo piperazine, which on oxidation gives 2, 5 dihydroxypyrazine.

[7] Resonance structure

There are two nitrogen atoms in Pyrazine, so carbon is electron deficient in Pyrazine.

Because of this electrophilicity restitution reaction are not done easily but nucleophilicity reaction occurs easily in Pyrazine.

[8] Chemical properties

- Protonation:-

Protonation of Pyrazine with sulfuric acid gives pyrazinium sulphate salt.

- N-oxidation reaction:-

N-oxidation reaction of Pyrazine with acetic anhydride & hydrogen peroxide gives Pyrazine N –oxide.

N- Oxidation reaction of Pyrazine with m- chlorobenzoic acid, trifloroacetic acid gives Pyrazine N, N dioxide.

- Electrophilicity substitution at 'C'.

Chlorination:-

The presence of two nitro atoms deactivates the ring towards electrophilic attack. Presence of electron donating group facilitates electrophilic attack.

This is proved by the chlorination of 2-methyl Pyrazine with Cl_2 in presence of CCl_4 at 40^0 C gives 2 methyl 3- chloro Pyrazine.

- Nucleophilic substitution:-

Pyrazine reacts with sodamide ($NaNH_2$) in liq. NH_3 to give 2- amino Pyrazine, this reaction is also known as chichibabin reaction.

Pyrazine when reacts with Cl_2, it gives 2- chloro Pyrazine, which reacts with $NaNH_2$ in liq. NH_3, it gives 2-amino Pyrazine, 2-cyno imidazole & imidazole.

- Reduction reaction:-

Reduction of Pyrazine with ethanol & sodium gives hexahydropyrazine.

Reduction of Pyrazine in presence of lithium with trimethylsilylchloride gives N, N trimethylsilyl hydropyrazine.

- Free radical reaction:-

Amidation:-

Pyrazine reacts with formamide & H_2O_2 with $FeSO_4$, H_2SO_4 at 60^0C, which gives free radical reaction & the product is 2-aminopyrazine.

Bromination:-

Free radical reaction of Pyrazine with HBr gives 2- Bromo Pyrazine.

Chlorination:-

Free radical reaction of Pyrazine with Cl_2 at 400^0 C gives 2- chloro Pyrazine.

Free radical reaction of Pyrazine with monoethyl oxalate & $Na_2S_2O_8$ with $AgNO_3$ in DCM & H_2SO_4 gives 2- carbethoxy Pyrazine.

- Photochemical reaction:-

It is known that Pyrazine ring is ion merized to other diazine under photolytic conditions. As an example 2, 6 dimethyl Pyrazine is isomerized to 2, 5 dimethyl pyrimidine.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Piperazine

[1] Structure:-

[2] Name: - Piperazine or Hexahydro Pyrazine.

[3] Introduction:-

Piperazine is fully reduced form of Pyrazine which is stable compound.

Piperazine is mostly useful in pharmaceuticals industries.

[4] Physical properties:-

[5] Spectral data:-

^{1}H NMR δ ppm ($CDCl_3$): C_2-H, C_3H, C_4H, C_5H, C_6H; 47.9

^{13}C NMR δ ppm ($CDCl_3$): C_2, C_3, C_4, C_5, C_6; 47.9

The preferred conformation is the chair conformation with N-H at the equatorial position.

Melting point – 106^0 C

Boiling point – 146^0 C

[6] Synthesis:-

There are three types of methods

- Self condensation of ethanol amine.
- From ethylene oxide with ethylene diamine.
- From ethylene with dibromoethane.

[1] Self condensation of ethanolamine:-

Self condensation of ethanolamine in presence of NH_3 at 150-22^0 C at 100-200 bar pressure gives piperazine.

[2] From ethylene oxide with ethylendiamine.

Reaction of ethylene oxide with ethylene diamine gives piperazine.

[3] From ethylene diamine with dibromoethane.

The condensation of ethylene diamine with diamine with dibromoethane gives piperazine.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Name: Dekivadiya Riddhi H.

M.Sc. Sem-3

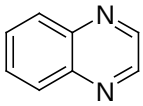
Topic: Quinoxaline

Roll No.: 6

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

QUINOXALINE

- **Structure :-**



- **Other name :-**
  (1) Benzo pyrazine
  (2) 1,4 diazanaphthalene

Quinoxaline is considerd to be derived from quinolene by the replacement of -CH= group by nitrogen atom at the 4th position. it is also regard as 1-4 diazanaphthalene.

- **Uses:-**

1) Quinoxaline used as a reactive dyes and pigments azo dyes, fluorecein dyes and pigments and it is also forms a part of certain antibiotics.
2) Some derivatives are posses antibecterial derivatives.

- **Physical properties:**

1) It's melting point is -27°C
2) It's boiling point is 112-115°C
3) It is weak base p^{ka} - 0.8

- **Spectral data:-**

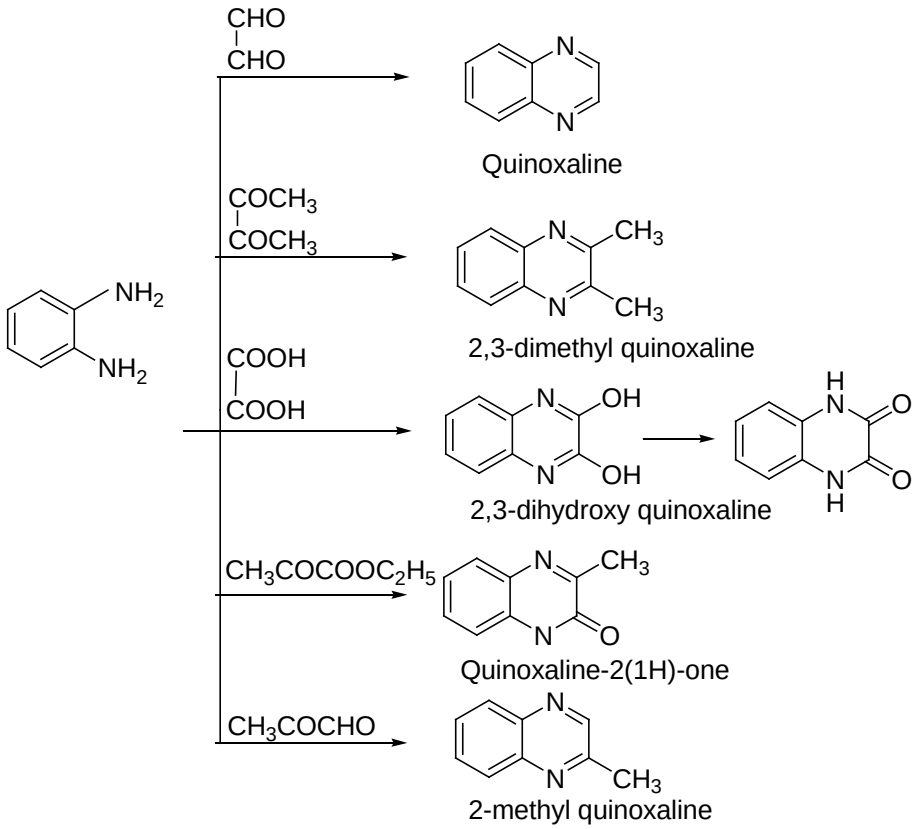
uv λ_{max} (Cyclohexane) : 304 (3.71), 316 (3.78), 339 (2.0), 375 (2.0)
^{1}H NMR δ_{ppm} : C_2- H, C_3-H, C_5-H, C_6-H, C_8-H, C_7-H (7.67)
^{13}C NMR δ_{ppm} : C_2,C_3 (145.5) C_5,C_8 (129.8)
C_6,C_7 (129.9) C_9,C_{10} (143.2)
^{15}N NM_3 = 0 δ_{ppm} : 398

- **Synthesis of Quinoxaline:**

➔ Quinoxaline is prepared by many processes.
1) Hins-berg reaction (4+2) condensation.
2) Preparation of substituted quinoxaline.
3) Reaction of 1-p tosylsulphonyl-2-phynyloxirane with o-phenylene diamine.
4) Reaction of catechol with ethylene diamine.

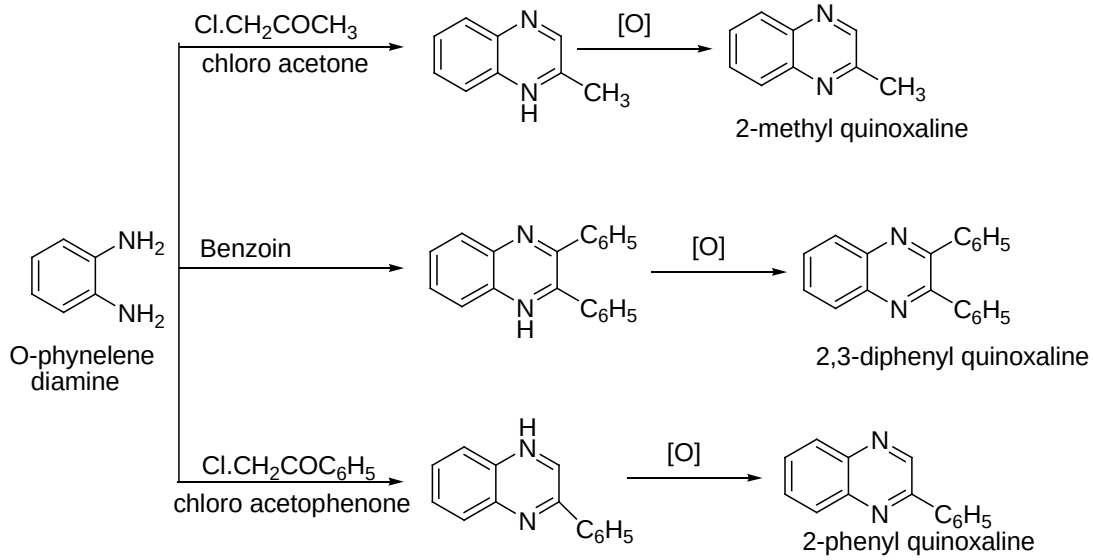
(1) Hins berg reaction (4+2) condensation.

A classical method of synthesis of involves the reaction of o-phynelene diamine with glyoxal to yield part of quinoxaline. other reagent are inclouddiacyl , oxalic acid, pyruvic ester and pyruvic aldehydel.



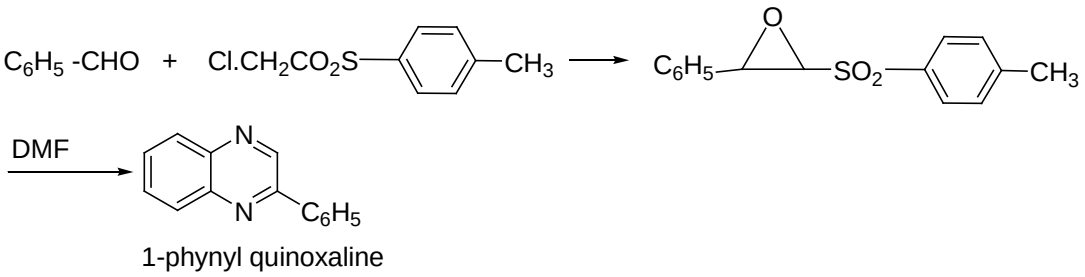
2) Preparation of substituted quinoxaline:-

The reaction of o-phynelene diamine with chloroacetone, ω-chloroacetophenone or benzoin to yield dihydro derivative which on spontaneous oxidation yields 2-substituted quinoxaline.



3) The reaction of 1-P-tosylsulphonlyl-2-phenyloxine with o-phenylene diamine.

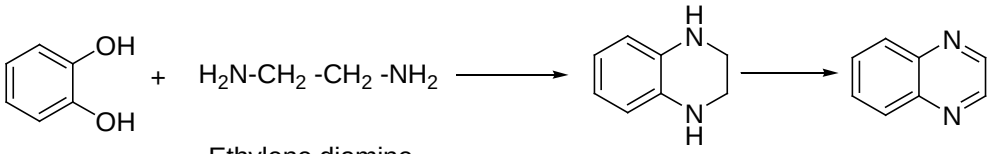
The reaction of 1-P-tosylsulphonlyl-2-phenyloxine with o-phenylene diamine 90°C in dimethyl formamide for 3 Hrs.



1-phynyl quinoxaline

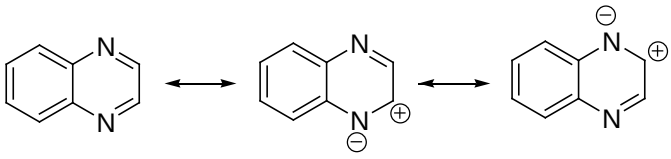
4) Reaction of catechol with ethylene diamine:-

The synthesis is based upon the reaction of catechol with ethylene diamine to product tetrahydroquinoxaline which on dehydrogenation affords quinoxaline.



Cetechol Ethylene diamine 1,2,3,4-tetrahydro quinoxaline quinoxaline

- **<u>Resonating stracture of quinoxaline:-</u>**

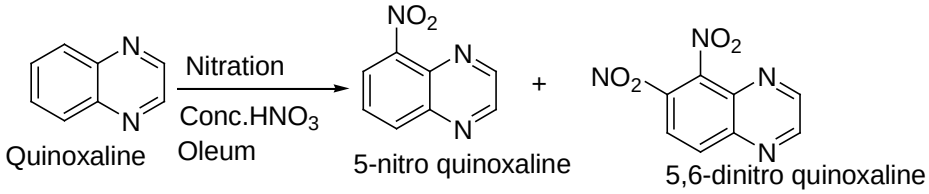


I II III

- **<u>Chemical properties of quinoxaline:-</u>**

➔ Electrophilic substitutions at carbon atom:-

- Electrophonic substitution in unsubstituted quinoxaline is unusual. The electron density is high at C5 and C8 position.
- Nitration carried out under vigorous condition. So we get 5 nitro and 5,6 dinitro quinoxaline (Mixture)

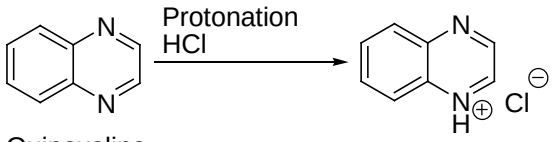


Quinoxaline 5-nitro quinoxaline 5,6-dinitro quinoxaline

➔ Electrophilic substitution reaction at Nitrogen atom.

❖ **Protonation:-**

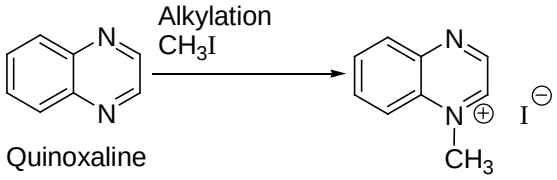
When quinoxaline react with the HCL (hydrochloric acid) to get quinoxaline salt.



Quinoxaline Quinoxalinium salt

❖ **Alkylation:-**

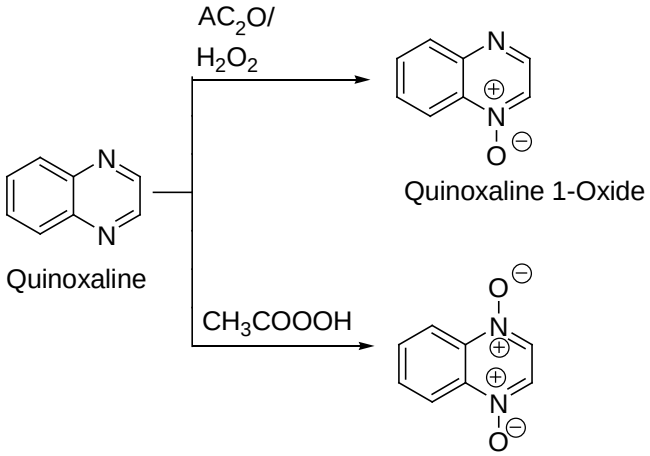
Quinoxaline react with the methyl iodide by alkylation process we get monoquaternary salt.



Quinoxaline Monoquaternary salt

❖ **N-oxide:-**

When quinoxaline react with the acetic anhydride or hydrogen peroxide to give the quinoxaline 1-oxide. while it react with per acetic acid it gives the dioxide.

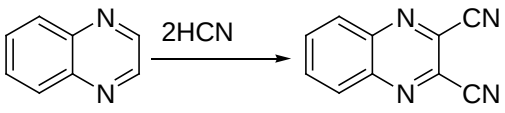


Quinoxaline Quinoxaline 1-Oxide

Quinoxaline 1,4-dioxide

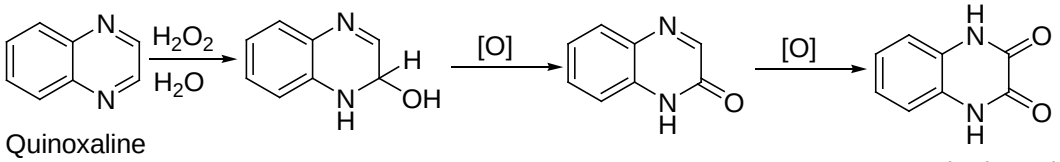
➢ **<u>Nucleophilic reactions of quinoxaline:-</u>**

When quinoxaline react with the hydrogen cyanide to get the Tetrahydro 2,3-dicyano quinoxaline.



Quinoxaline 2,3-4 dicyano quinoxaline

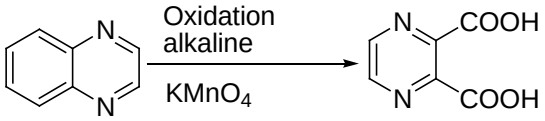
- Now, quinoxaline react with the H_2o_2 / H_2o to get 1,2-dihydro-2-hydroxy quinoxaline when it is oxidized to get the Tetrahydroquinoxalin 2,3-dione.



Quinoxaline — Tetrahydro quinoxaline 2,3-dione

- **Oxidation of quinoxaline:-**

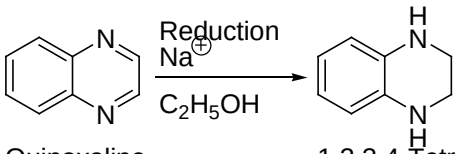
Quinoxaline react with alkaline potassium permanganate (alkaline $KMnO_4$) to we get the pyrazine 2,3-dicarboxylic acid.



Quinoxaline — Pyrazine 2,3-dicarboxylic acid

- **Reduction of quinoxaline:-**

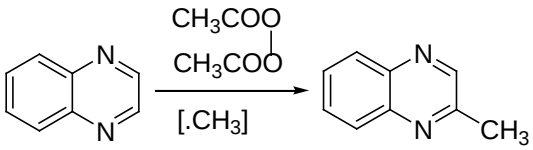
When quinoxaline is react with the sodium in ethanol it is reduced to get the 1,2,3,4-Tetrahydro quinoxaline.



Quinoxaline — 1,2,3,4-Tetrahydro quinoxaline

- **Alkylation**

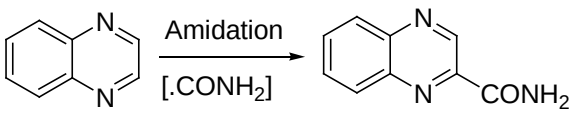
Quinoxaline react with the Acyl peroxide to produced the 2-methyl quinoxaline.



Quinoxaline — 2-methyl quinoxaline

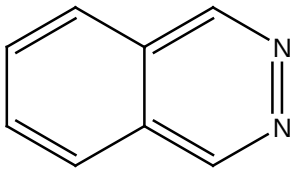
- **Amidation**

Quinoxaline react with the [·$CONH_2$] to produced 2-carbamoyl quinoxaline.



Quinoxaline — 2-Carbamoyl quinoxaline

PHTHALAZINE



Phthalazine is consired to be derived by fusion of pyridazine ring with benzene ring with benzene ring at 4-,5 position . It is also known as 2,3 diazanaphthalene or benzo [d]pyridazine . It was first prepared by Gabriel and Pinkus in 1893.

Physical properties

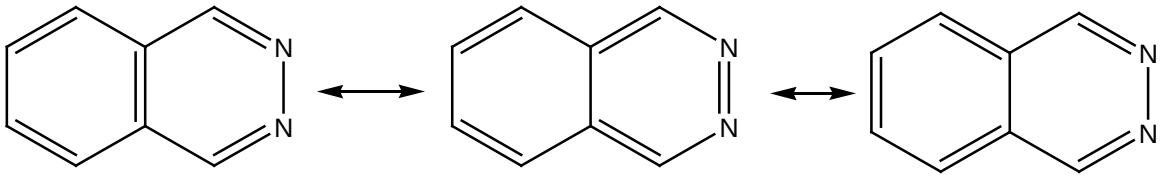
1)It is pale yellow solid substances

2)It's melting point is 90-91 c

3)It is soluble in water

4)It is monobasic acid

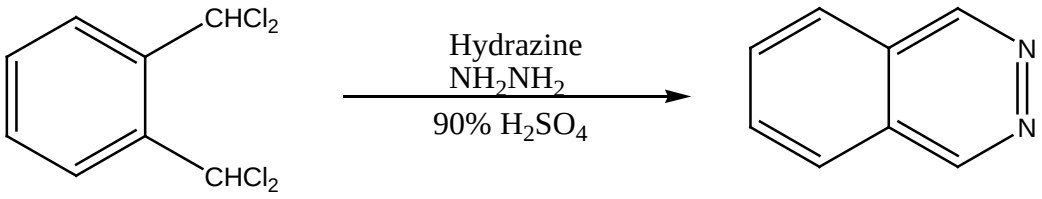
Resonance Structures:



Synthesis

1.(4+2) condenations

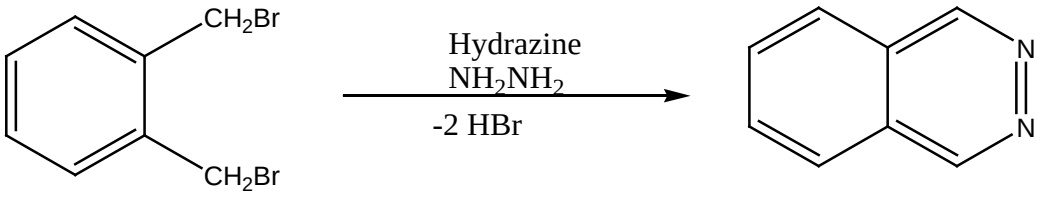
(a)phthalazine was first synthesis by the condensation of tetrachloro –o-xylene with hydrazine. The yieid can be increased by executing the reaction in 90% sulphuric acid



Tetrachloro o-xylene phthalazine

(b)Reaction of dibromo-o- xylene with hydrazine

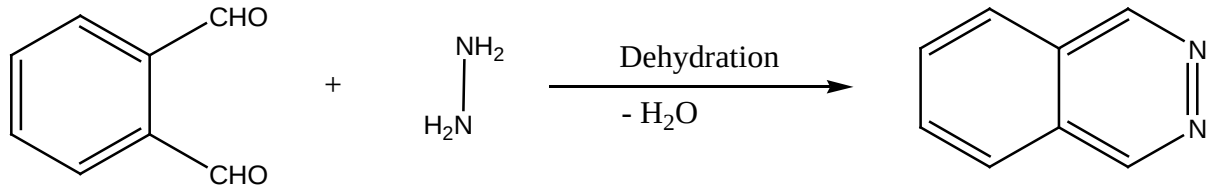
This procedure involve the reaction of dibromo –o-xylene with hydrazine dicarboxylic ester to produce tetrahydrophthalazine dicarboxylic ester which on hydrolysis and subsequent decarboxyation affords tetrahydrophthalazine.The intermediate on dehydrogenation provides phthalazine



1,2-bis(bromomethyl)benzene phthalazine

2)From o-phthaladehyde

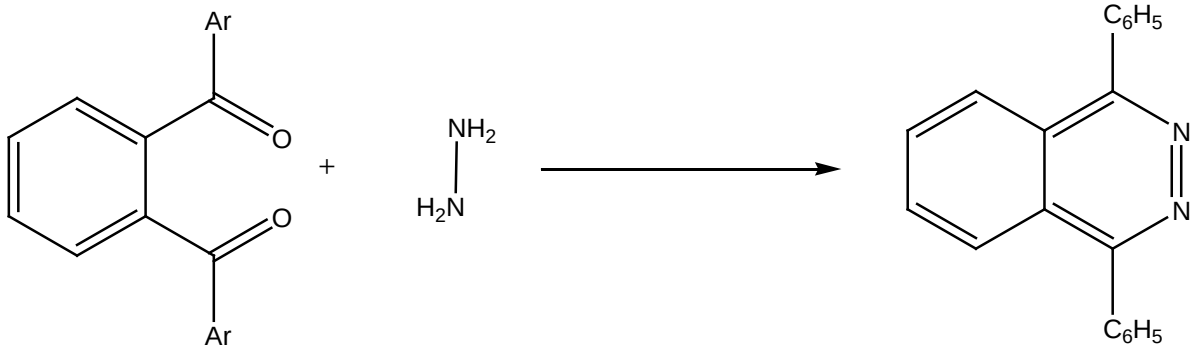
It is also prepared by the o-phthalaldehyde reaction with hydrazine under dehydration



1,2-bis(bromomethyl)benzene hydrazine phthalazine

3)From dibenzoyl ketone

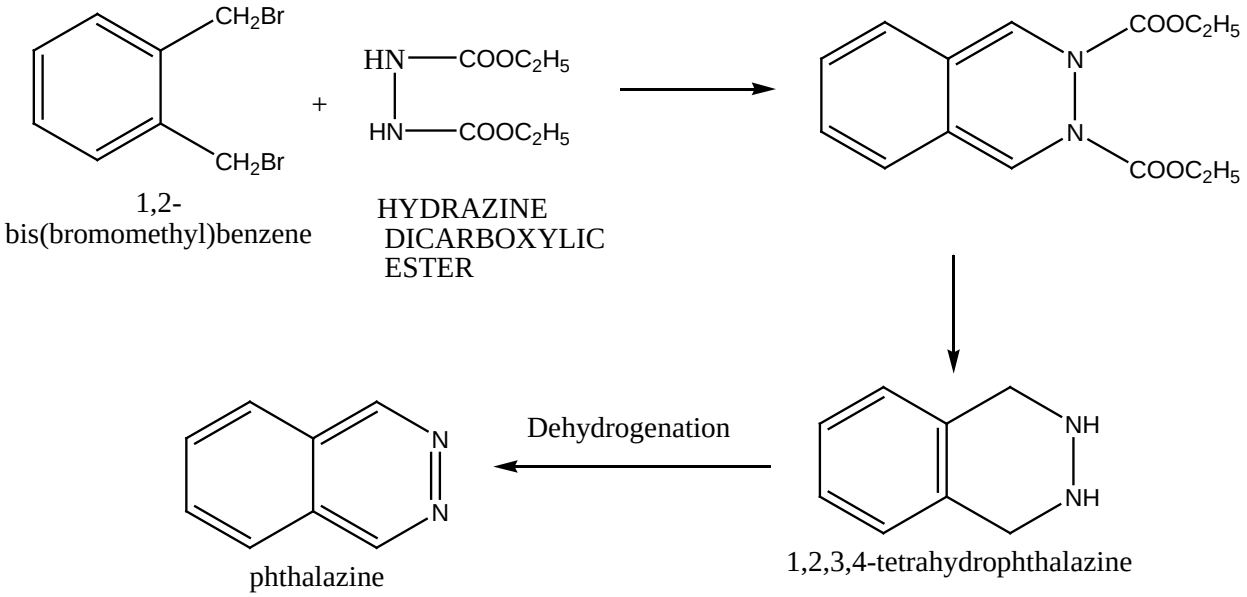
In this method phthalazine is synthesized by the condensation of o-dibenzoylbenzene with hydrazine



1,2-bis(bromomethyl)benzene hydrazine 1,4-diphenylphthalazine

4)From dibromo o-xylene

Phthalazine can be also synthesized by the reaction of dibromo-o-xylene with hydrazine dicarboxylic ester



1,2-bis(bromomethyl)benzene

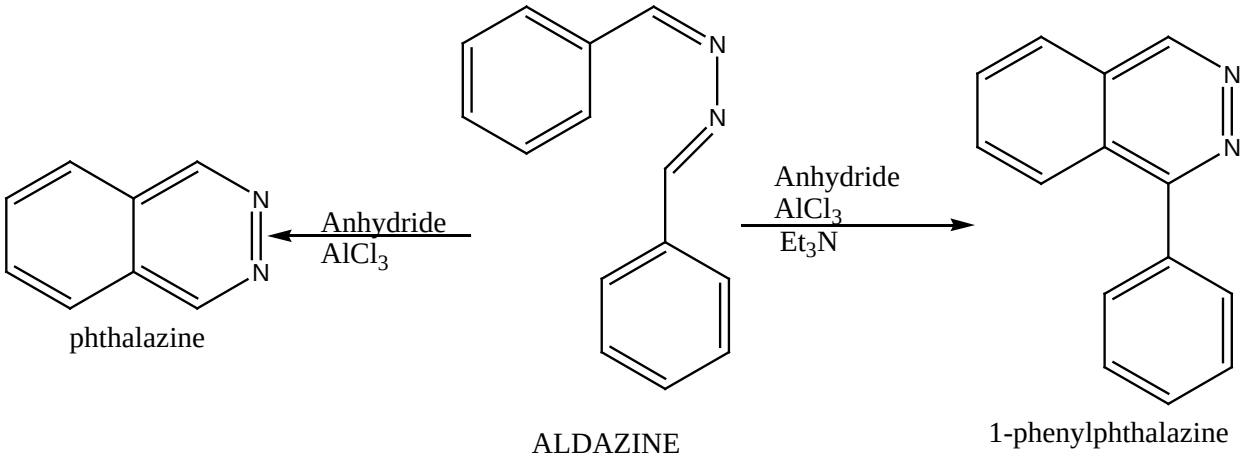
HYDRAZINE DICARBOXYLIC ESTER

1,2,3,4-tetrahydrophthalazine

phthalazine

5)From aldazine

Phthalazine can be also prepared by aldazine on treatment with aluminium chloride or mixture of aluminium chloride and triethylamine (2:1)at 200c yield corresponding phalazine or yieLDS corresponding phthalazine or phenylthalazine



phthalazine

ALDAZINE

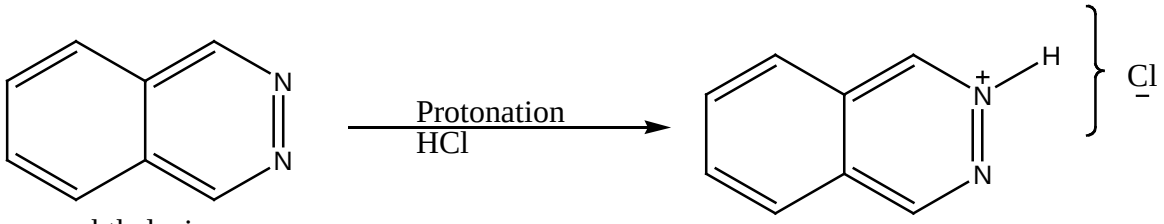
1-phenylphthalazine

Chemical properties

1)Electrophilic Reaction

(1) Protonation :

Protonation takes place in presence of HCl and protonated product is formed.



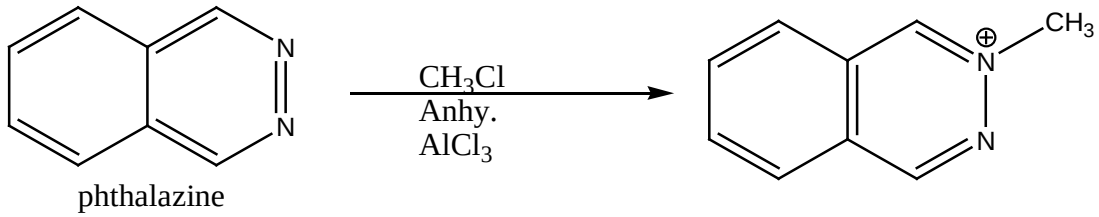
phthalazine

phthalazine

2)Alkylation:

In the alkylation the phalazine is react with methyl chloride in presence of the anhydride aluminium

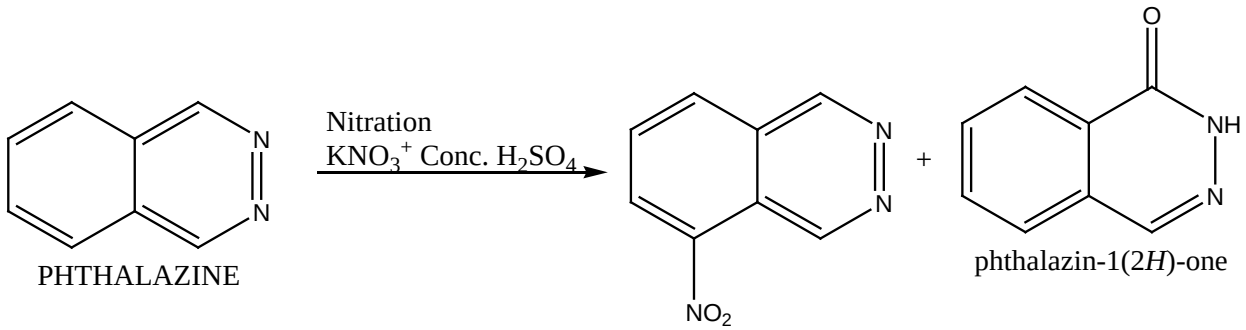
chloride.



phthalazine

3)Nitration

Phthalazine undergoes nitration process in presence of reagent KNO_3 and H_2SO_4 thaen product is form 5-nitrophathalazine and 1phathalazinone



PHTHALAZINE

5-nitrophthalazine

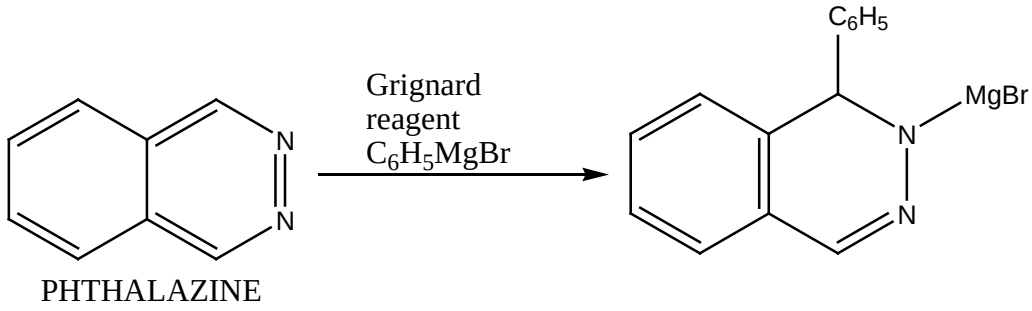
phthalazin-1(2*H*)-one

B] NUECLEOPHILIC REACTION

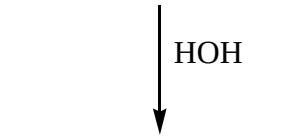
1) GRIGNARD REACTON

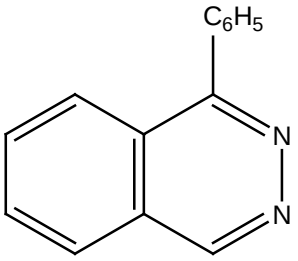
In the Grignard reaction phathalazine react with Grignard reagent C_6H_5MgBr fom the 1-

phephathalazine.



PHTHALAZINE



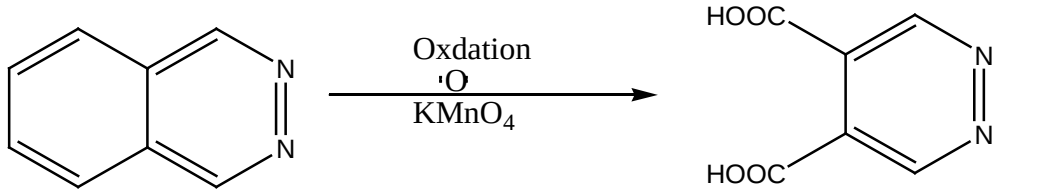


1-phenylphthalazine

2] OXIDATION

When the phthalazine is undergoes oxidation process

And the presence of potesium permanganent and it form pyridazine 4,5 dihydro acid

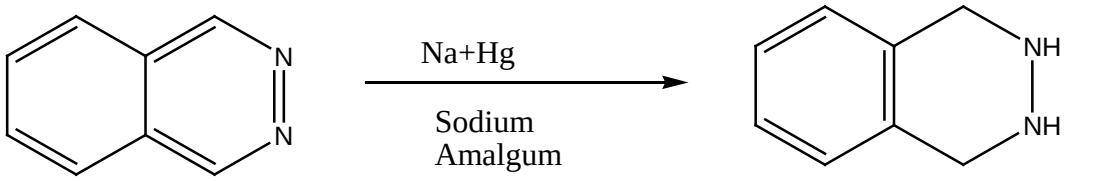


PHTHALAZINE

pyridazine-4,5-dicarboxylic acid

3]REDUCTION

When the phthalazine undergoes reduction process in the presence of reagent sodium amalgam form tetrahydrothalazine.



PHTHALAZINE

1,2,3,4-tetrahydrophthalazine

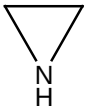
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Pratik B. Dholakia

Roll No. : 8

Heterocyclic Seminar

AZIRIDINE



Other Name : **Ethyleneimine** and **1 - Aza Cyclo Propane**

Structural Data : **C-N-C 59.6°** and **C-C-N 60.2°**

Bond Leangth : **C-C 1.480 A°** and **C-N 1.488 A°**

- **Physical Property :**

1. It is Colorless liquid.
2. It is Flammable and oily liquid.
3. It is easily miscible with water.
4. It has Ammoniacal odour.
5. It's boiling point is 56°C
6. It is weakly basic in nature and it's P^{Ka} value is 7.98.
7. Aziridine is a planner structure and rigid in nature.

8. It is toxic in nature and its polymerization is causes cancer.
9. It is harmful to body parts like skin and eye.

- **<u>Synthesis</u> :**

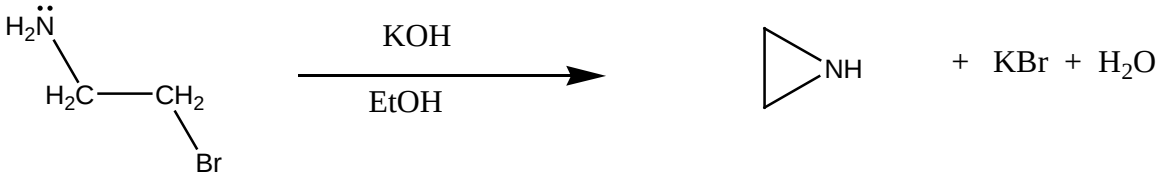
Two types of synthesis can be done.

- **Intra Molecular Cyclization**
- **Cyclo Addition Reaction.**

- **Intra Molecular Cyclization :**

(A) Grabrial Method…

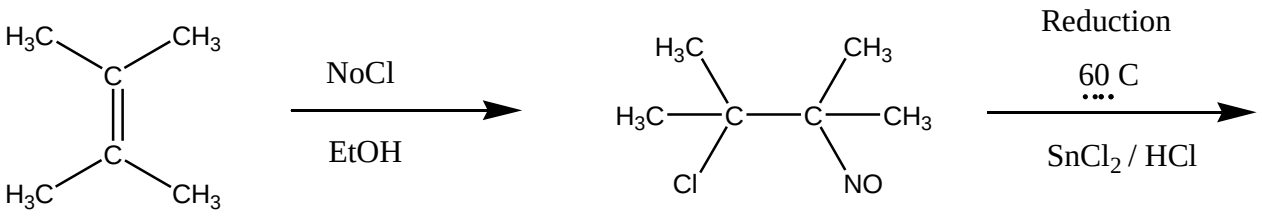
In 1888 aziridine was first time obtained by heating β-bromo ethyl amine in presence of KOH.



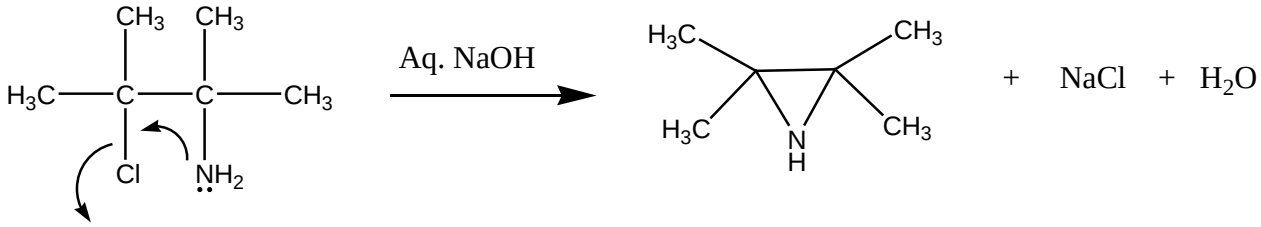
B- Bromo ethyl amine **Aziridine**

(B) <u>Aziridine Derivative Formation</u>…

With the help of Tetra alkyl alkene and Nitroso chloride we get the derivative of aziridine 2,2'3,3' tetra methyl aziridine.



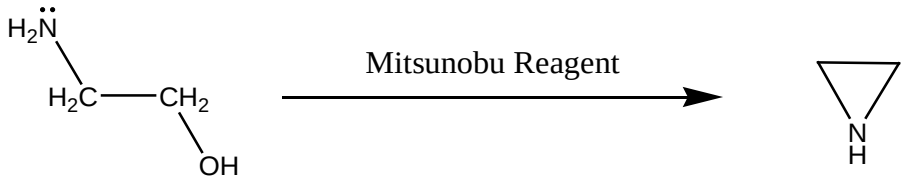
Tetra Alkyl Alkene



2,2',3,3' Tetra
Methyl Aziridine

(C) <u>Wenkert Method</u> …

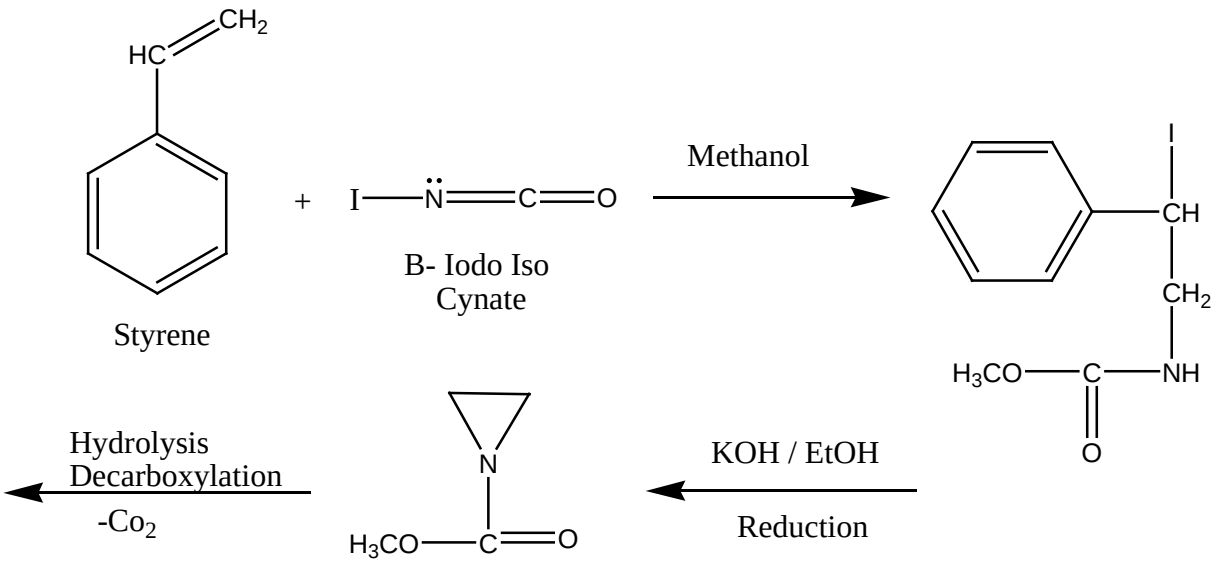
Ethanol Amine is directly formed a rind in the presence of **Mitsunobu Reagent.**
(Tri Phenyl Phosphane / Di Ethyl Azo Di Carboxylate.)



Ethonal Amine

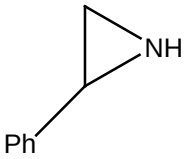
Aziridine

(D)Hassner's Method: (StereoSpecific Method)



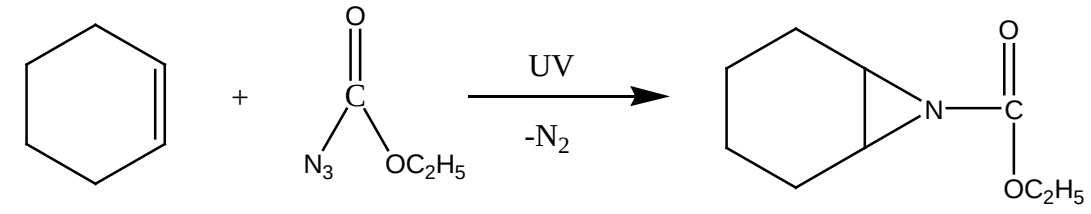
Styrene

B- Iodo Iso Cynate



2 Phenyl Aziridine

➢ Cyclo Addition Reaction :

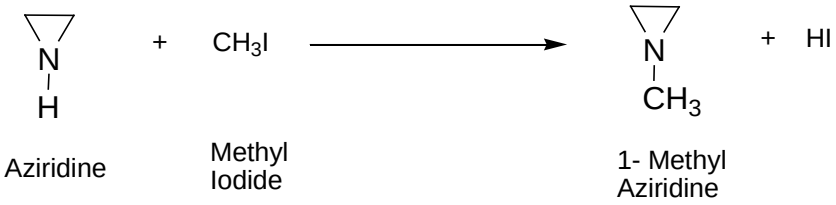


Cyclo hexene

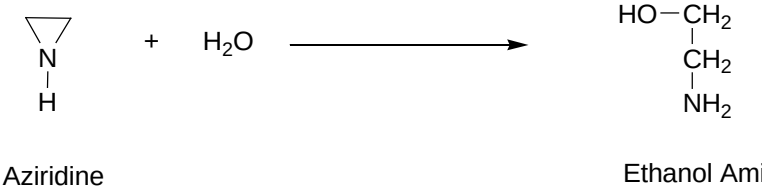
Ethyl Azido Formate

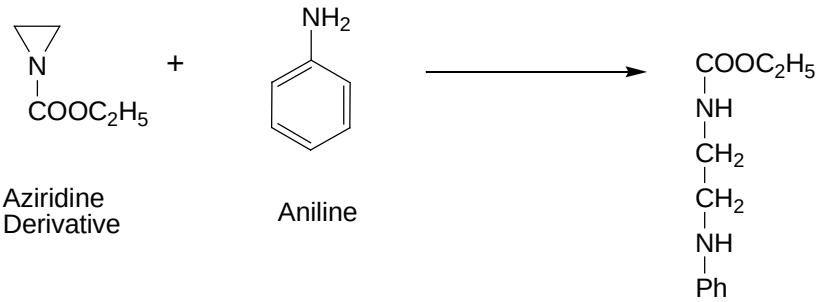
➢ Chemical Properties :

(1) Substitution Reaction…

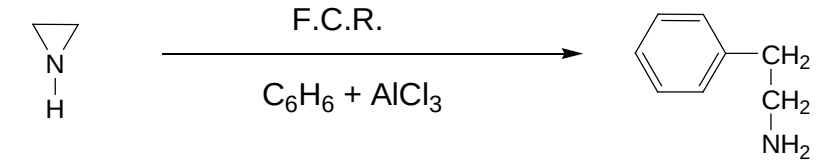


(2) Ring Opening Reaction :





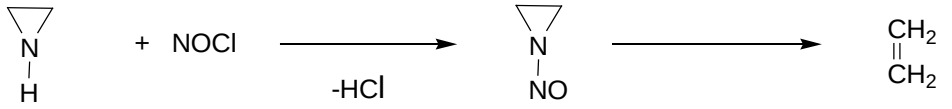
(3) Ring Expansion :



Aziridine

1- Phenyl
Ethyl Amine

(4) Nirtogen Extrusion :



Aziridine

Ethene

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

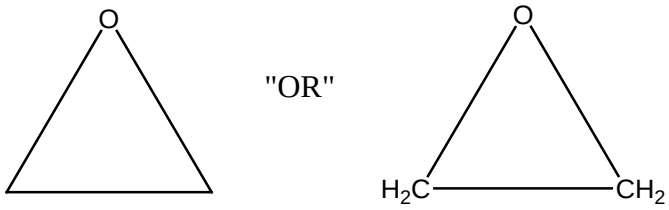
OXIRANE

❖ *Introduction:-*

⟹ Oxirane was first isolated by WARTZ in 1859.

⟹ It is higly saturated, three membered hetro cyclic compound, having oxygen as a hetro atom.

❖ *Structure:-*



⟹ Other Names:-

(1) Ethylene Oxidde,

(2) Oxa Cyclo Propane,

(3) α ,β- epoxy ethane,

(4) β - Oxido ethane.

❖ *Physical Properties:-*

⟹ Colourless liquid,

⟹ Inflamable liquid,

⟹ Boiling Point=10.7^{o}C,

⟹ Dipole moment = 1.88 D,

⟹ Faintly sweet odour.

❖ *Structural Information:-*

⟹ Bond length:- C-H --> 1.082 A^o

O-C --> 1.436 A^o

C-C --> 1.472 A^o

❖ *Spectral Data:-*

UV λ_{max} nm ⟹ 171 nm

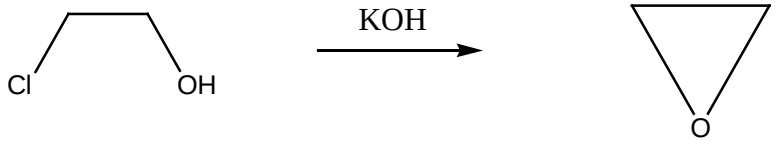
IR cm^{-1} ⟹ 1250 cm^{-1}

^1H NMR δ_{ppm} ⟹ 2.54(5,4H)

^{13}C NMR δ_{ppm} ⟹ 39.7(t,-CH_2)

❖ *Synthetic Method:-*

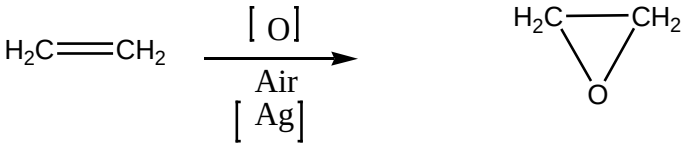
(1)Reaction of KOH on ethylene chlorohydrin gives Oxirane.



ethylene chlorohydrin oxirane

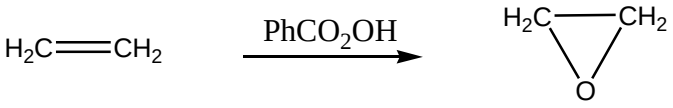
(2) Oxidation of alkenes:-

(i) Oxidation of ethylene in air, presence of silver catalyst gives oxirane.



ethene oxirane

(ii) Oxidation of ethylene with per acid (per benzoic acid) gives oxirane.

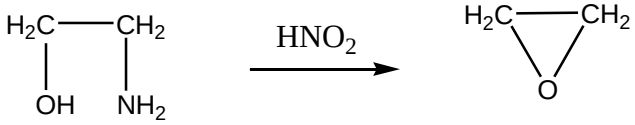


ethene oxirane

(3) Degradation Reaction:-

→ Hoffmann method:-

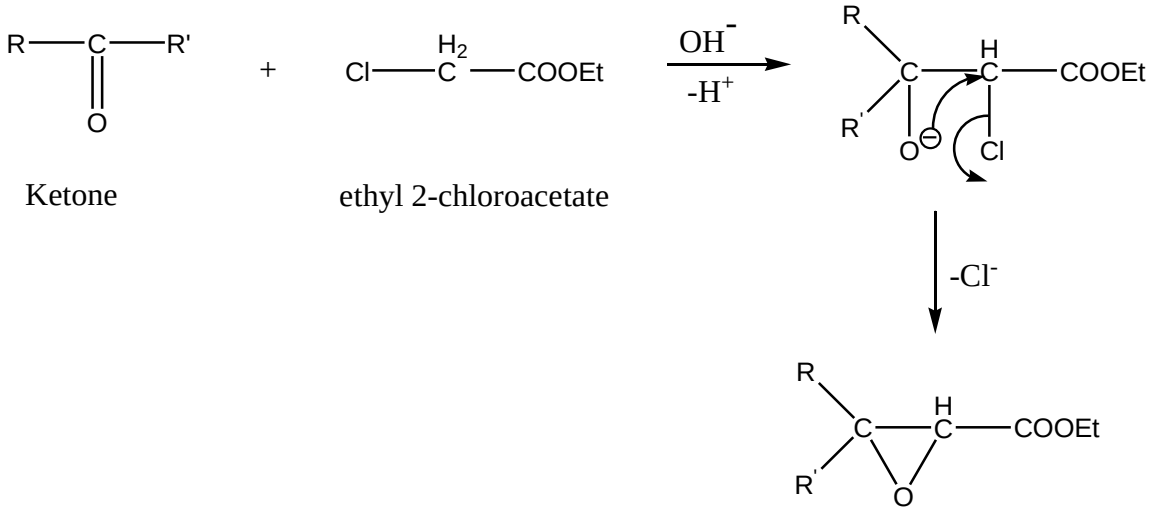
Reaction with α-amino alcohol with nitrous acid gives Oxirane.



α-aminoethanol oxirane

(4) Darzen reaction:-

Reaction occurs ketone and chloro ehtyl acetate in presence of base and gives oxirane derivatives.

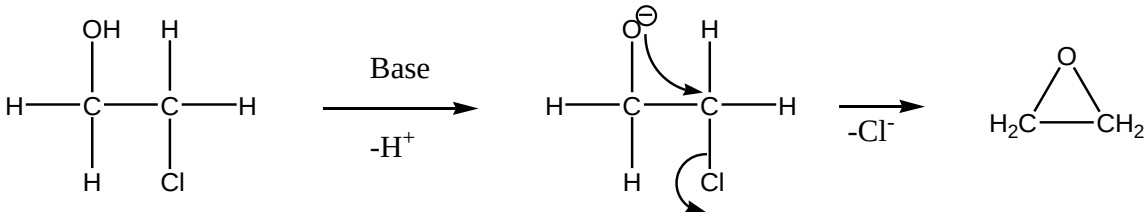


Ketone ethyl 2-chloroacetate

Oxirane derivative

(5) Ring closuer Method:-

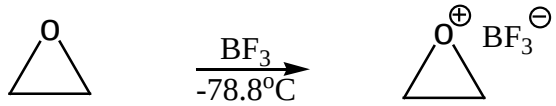
reaction of trans-ethylene halohydrie (trans-chlorohydrin) in presence of base and gives cyclisation to Oxirane ring.



trans-chloro hydrin oxirane

❖ *Chemical Properties:-*

(1) It forms addition compound with boron tri flouride (BF_3-Lewis acid) at like ether at -78.8°C .



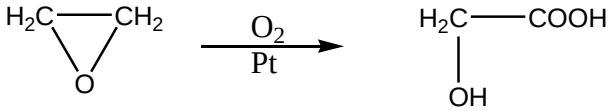
oxirane

→ Addition Reaction:-

On heating reversible dissociation occurs.

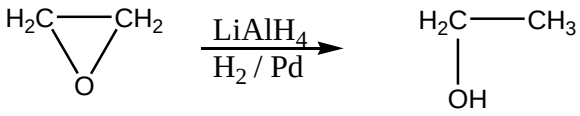
(2) Oxirane is weak electron donor as compare to other cyclic ether.

(3) On oxidation with oxygen in presence of platinum, it gives glycolic acid.



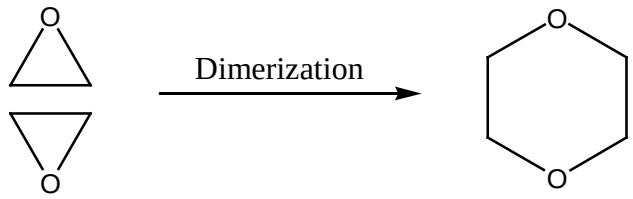
oxirane 2-hydroxyacetic acid

(4) On reduction with reducing agent, gives ethanol.



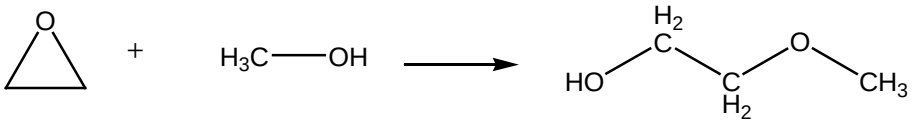
oxirane ethanol

(5) In suitable condition, dioxane is formed (Dimerization).



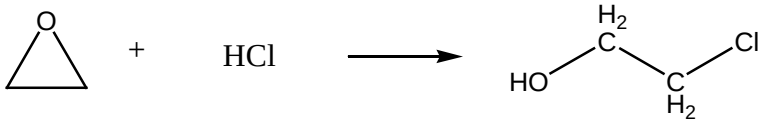
oxirane 1,4-dioxane

(6) In we used alcohol instead of water, glycol mono ether is obtain.



oxirane methanol glycol mono methyl ether

(7) Oxirane react with halogen acid, halohydrin is obtained.

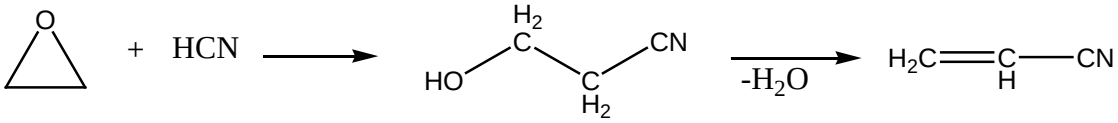


oxirane Ethylene chlorohydrin

→ <u>Electrophilic Reaction:-</u>

(8) Oxirane reacts with hydrocynic acid, acrylo nitrile is obtained.

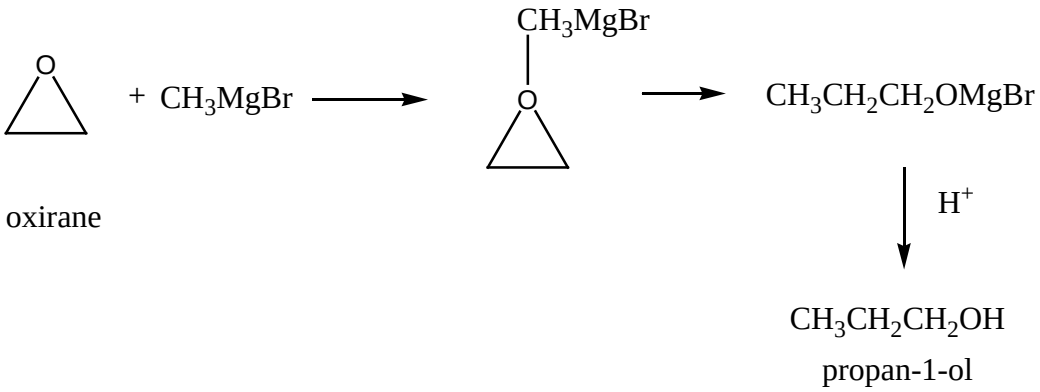
→ CH_3COCl , $NaHSO_3$, H_2S , R-COOH react in same manner.



oxirane Ethylene cynohydrin acrylonitrile

→ <u>Nucliophilic Reaction:-</u>

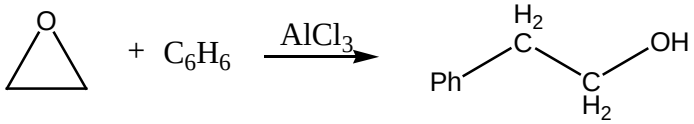
(9) Oxirane react with Grignard reagent, primary alcohol is obtain.



oxirane

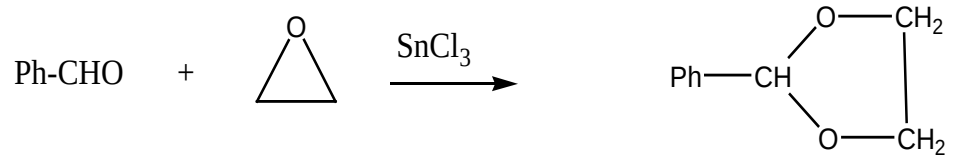
propan-1-ol

(10) Oxirane reacts with benzene in presence of $AlCl_3$ gives 2-phenyl ethanol.



oxirane 2-phenylethanol

(11) Reaction of oxirane with aldehyde <u>or</u> ketone in presence of stannic chloride ($SnCl_3$) it gives dioxolane, also some part is polymerise.

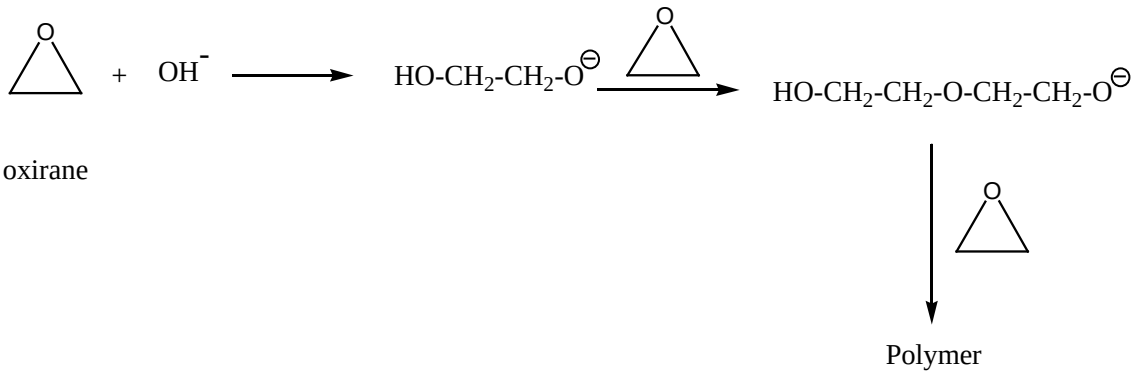


benzaldehyde oxirane 2-phenyl-1,3-dioxolane

(12) Polymerization:-

Reaction of oxirane in presence of base catalyst and gives polymer.

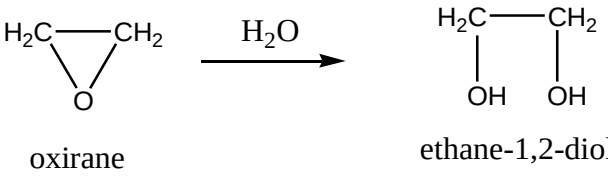
Initial step is addition of OH^- .



oxirane

❖ *<u>Application:-</u>*

(1) Formation of ethylene glycol. Oxirane is hydrolysed by H_2O and gives ethylene glycol.

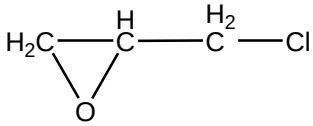


oxirane ethane-1,2-diol

(2) Industrial used of preparation of resins, Plasticizer, Synthetic rubber.

❖ *Derivative:-*

→ Epichlorohydrin



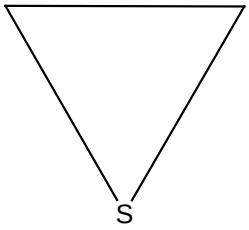
Que.:- Which is more stable ? Oxirane OR Aziridine , Why ?

Ans:- Oxygen is more electronegative than Nitrogen so the bond O-C is more polar than N-C bond.

So attraction is more and hence Oxirane is more stable than Aziridine.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Thiirane



IUPAC Name:thiirane

- Dihydrothiirane
- Ethylene sulphide
- Thiacyclopropane

➢ Physical properties:

- Thiranes are not found in nature.
- It is colourlessliqid,and it is b.p.55-56^{0}C.
- It is partially soluble in water and more soluble in organic solvents.
- It polymerises even in absence of light.
- It posses a dipole moment of 1.66D.
- The strain energy has been calculated to be 9K cal/mol.

Among the three membered hetrocyclic rings thiirane has the lowest strain energy and also shows the lowest electon density at the hetro atom.

Spectral data:

UV λmax (nm) : 260(40) n to σ* ; 205(4000)

IR Cm^{-1} : C-H Str. Is 1475 Cm^{-1}

^{1}H NMR δppm : 2.27(CH_2)

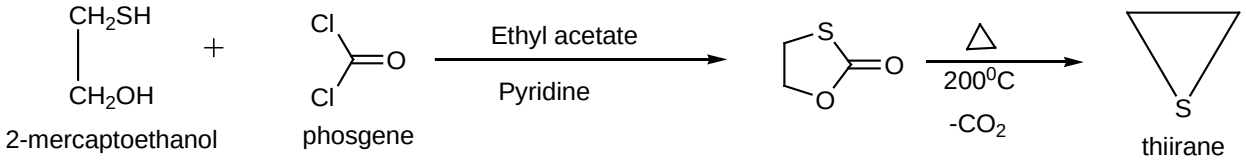
^{13}C NMR δppm : 18.1

- Synthetic methods :
  - From 2-mercaptoethanol
  - Ring closure reaction
  - From epoxide
  - From cyclic ethelene carbonates
  - From aldehyde and ketons
  - From diazoalkenes
  - From thio cyanogen

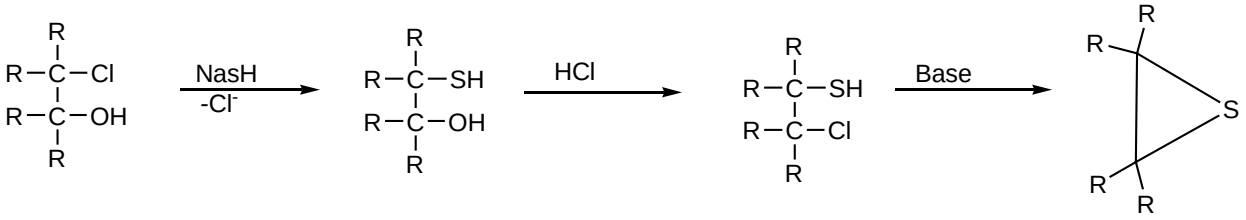
Synthesis:

(1) Ring closure reactions:

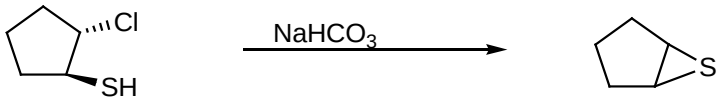
(A)



(B)

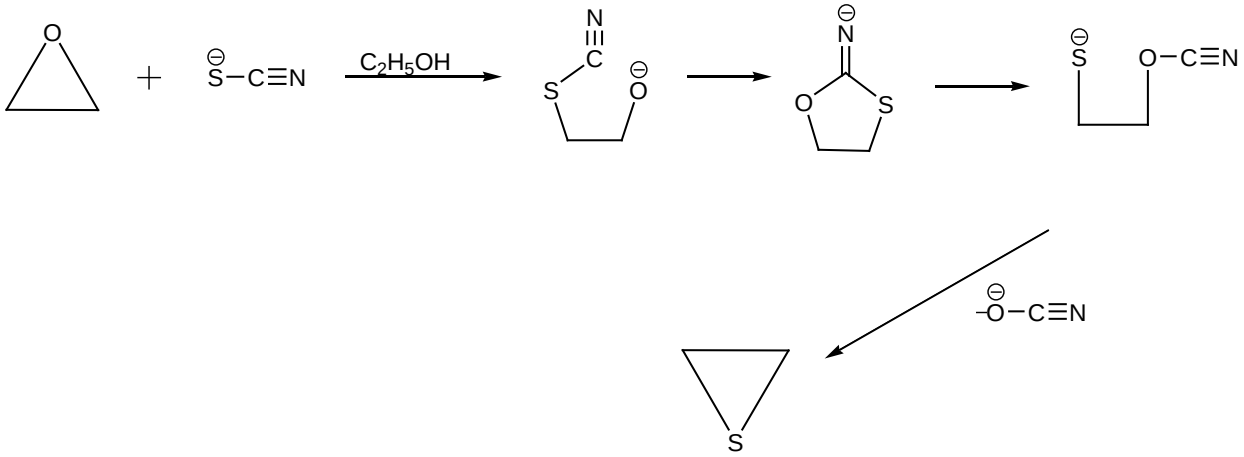


(C)

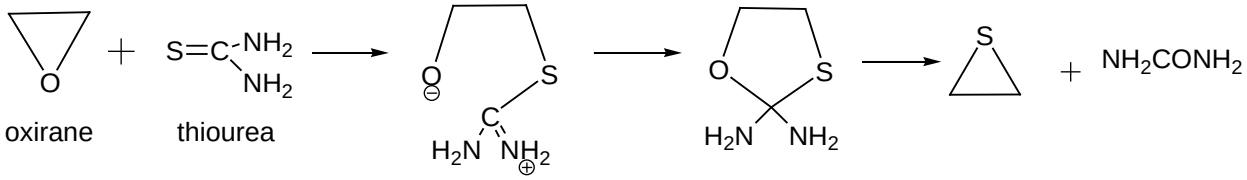


(2) From epoxide :

(A)

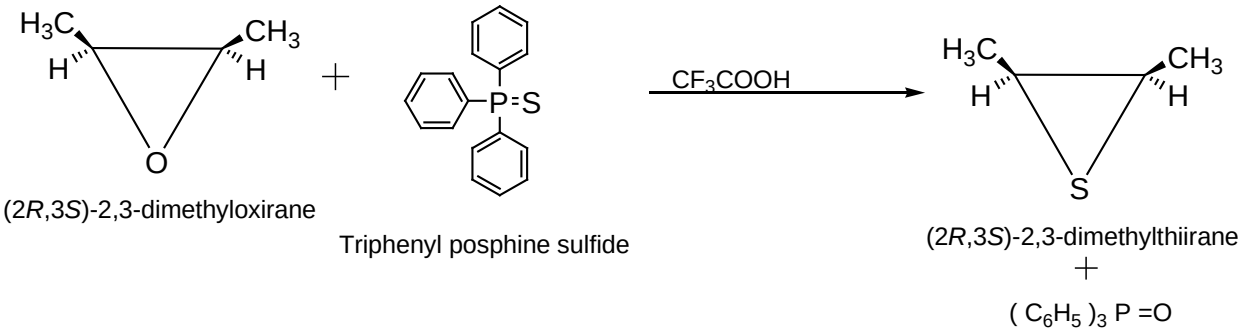


(B)



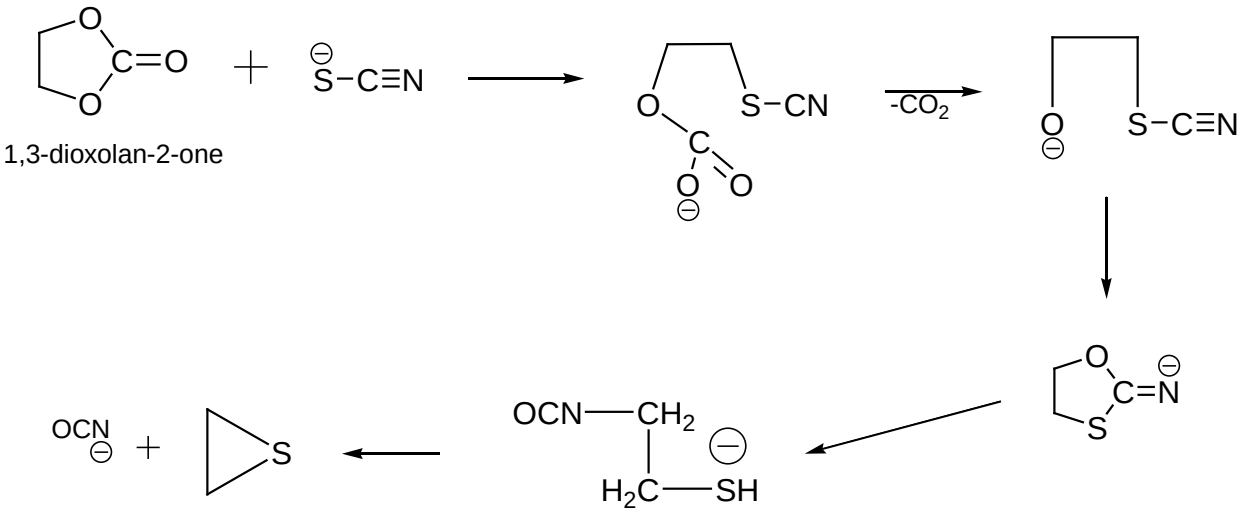
(C)

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



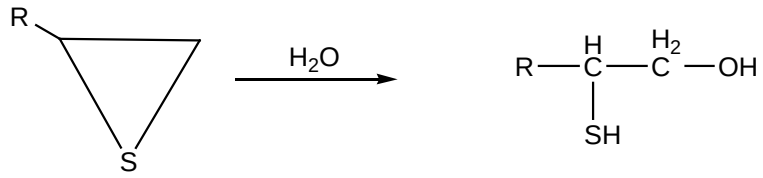
(2*R*,3*S*)-2,3-dimethyloxirane + Triphenyl posphine sulfide → (2*R*,3*S*)-2,3-dimethylthiirane + $(C_6H_5)_3P=O$

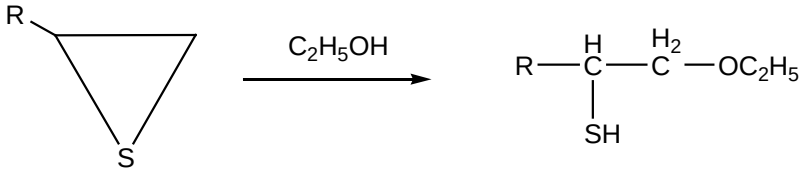
(3) From cyclic ethylene carbonates :

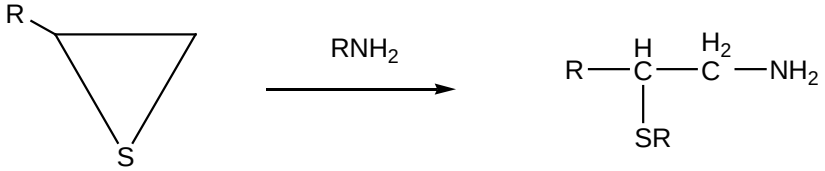


➢ Chemical properties :

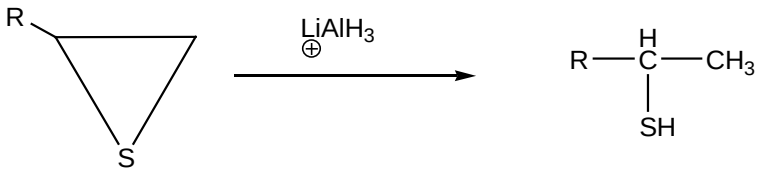
(1) Ring opening reaction.

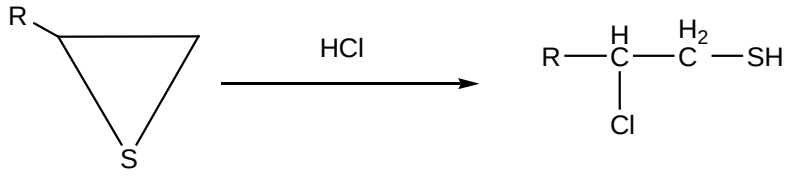


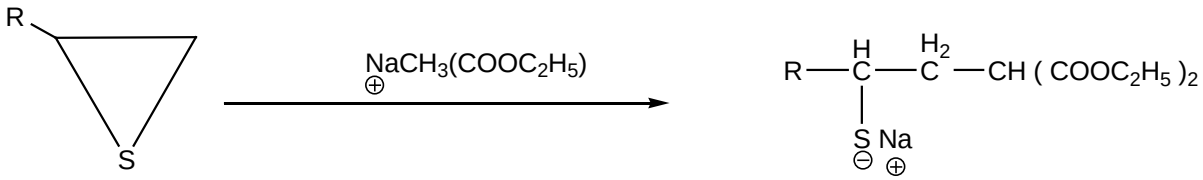


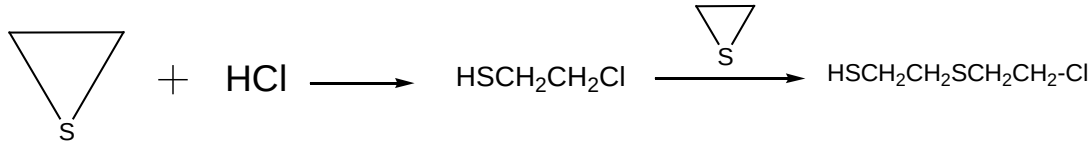


Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

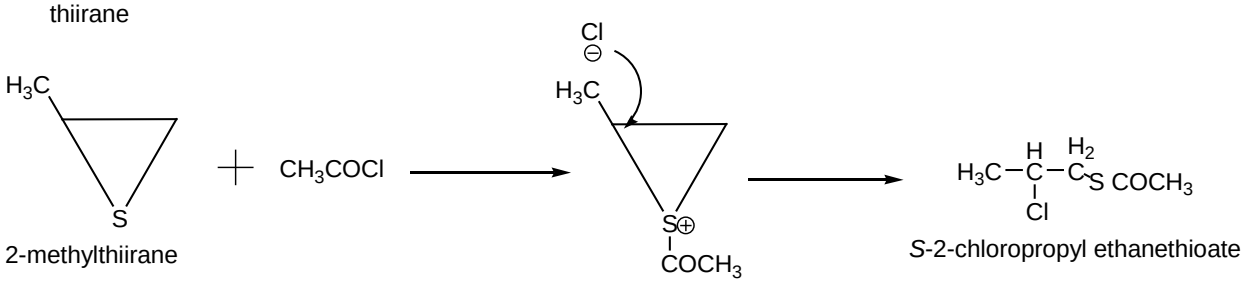








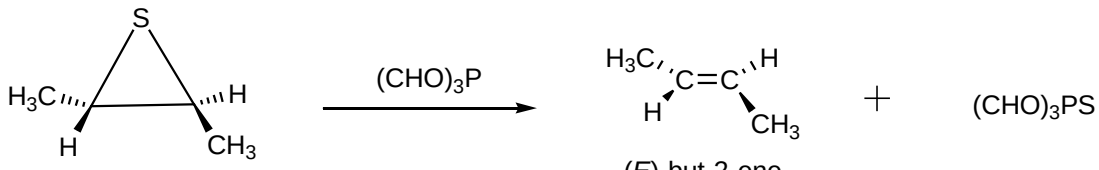
thiirane



2-methylthiirane

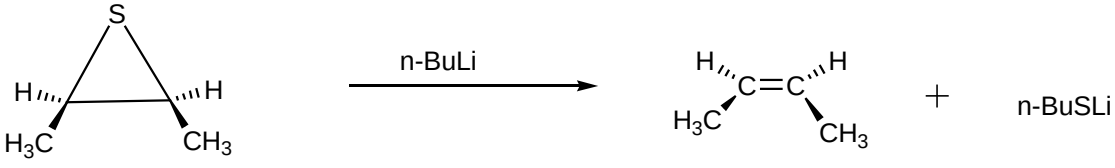
S-2-chloropropyl ethanethioate

(2) De sulphurisation.



(2*S*,3*S*)-2,3-dimethylthiirane

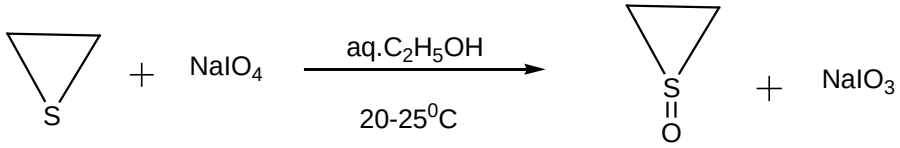
(*E*)-but-2-ene

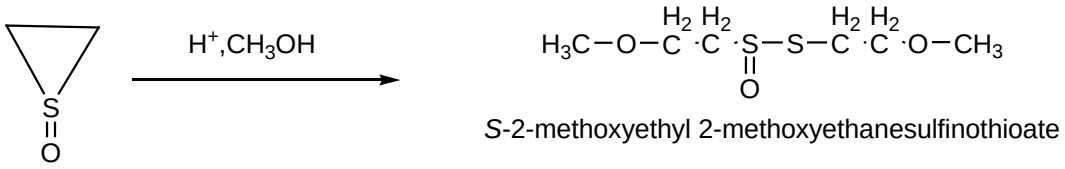


(2*R*,3*S*)-2,3-dimethylthiirane

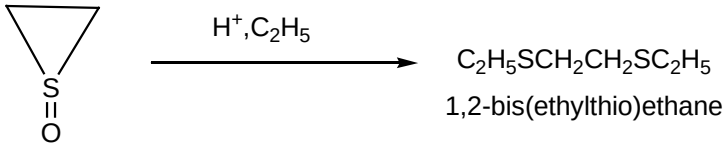
(*Z*)-but-2-ene

(3)Oxidation:



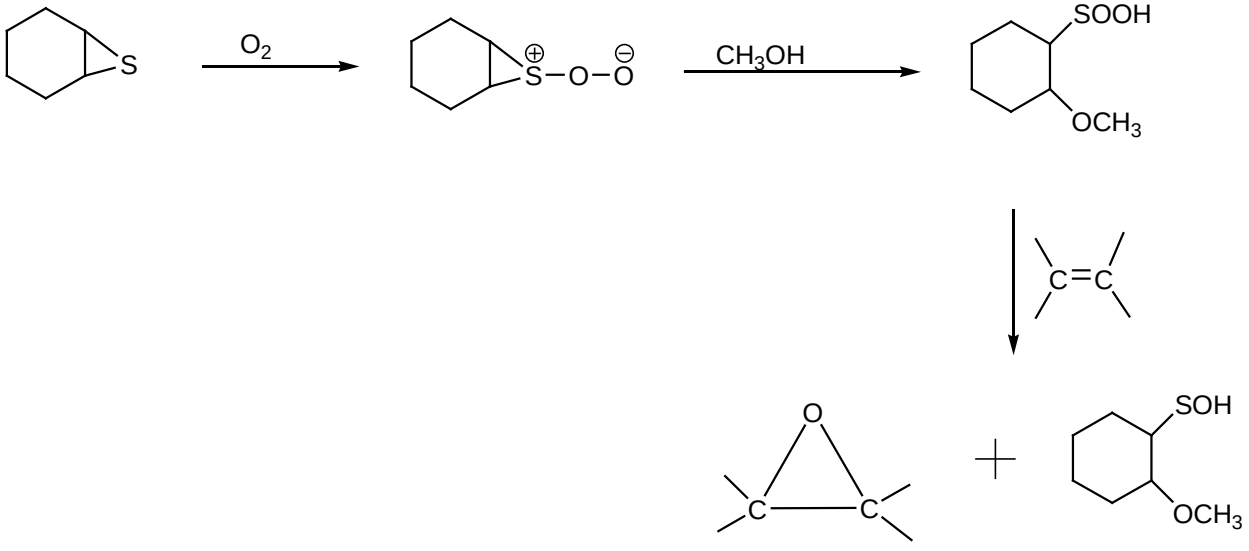


S-2-methoxyethyl 2-methoxyethanesulfinothioate

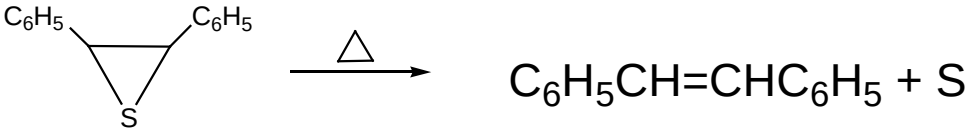


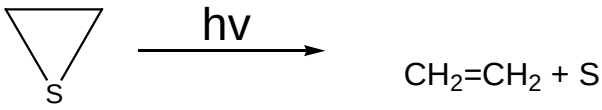
1,2-bis(ethylthio)ethane

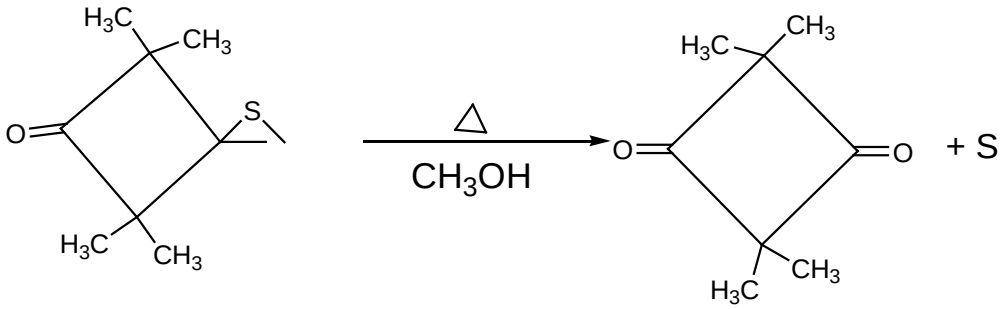
(4) Formation of peroxysulfenic acid:



(5) Thermal & photochemical reactions:



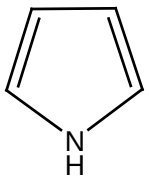




Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

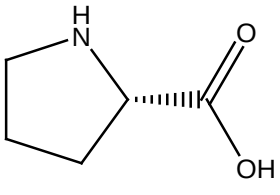
Pyrrole

- A 5-membered hetrocyclic compound
- Structure of pyrrole:  1-azole

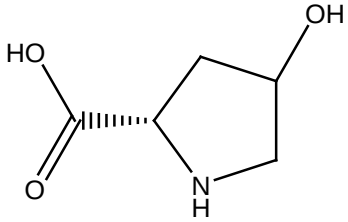
1-azocyclobutane

Introduction :

- Pyrrole belongs to a group of heterocyclic compounds containing a doubly unsaturated five membered ring composed of 4 C-atoms & 1 N-atom.
- Pyrrole ring system is found in the green leaf pigment, chlorophyll, in the red blood pigment, heamoglobin & in the blue dye indigo.
- Tetrahydropyrrrole or pyrrolidine is a part of the structure of protein as amino acids namely pyroline & hydroxyproline.



proline



hydroxyproline

- The presence of pyrrole was observed by Runge (1834) in the vapours obtained form the distillation of coaltar, bone oil & proteineous

substances which imported red colour to pine chips moistened with mineral acid.

- It was 1st isolated in pure form in 1857 bone oil while the structural formula was established in 1870.

Physical properties :

- Pyrrole is a colourless liquid with odour resembling to that of chloroform.
- Melting point : 24^0 C & Boiling point : 131^0 C
- It has planar pentagonal structure.
- It is slightly soluble in water but miscible in most of the organic solvents.

Spectral data :

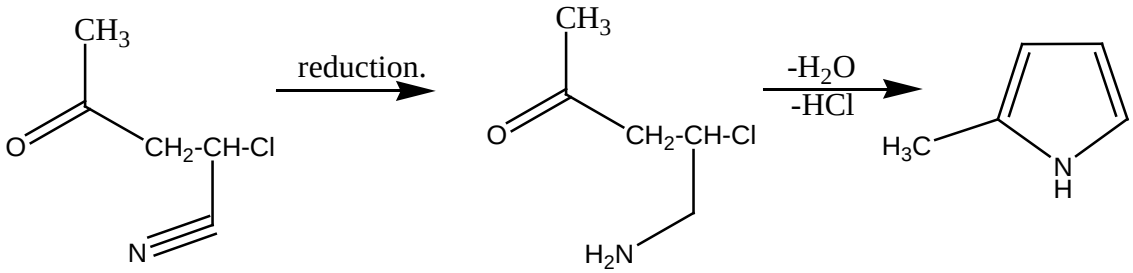
- UV λ_{max} nm : 210 (4.2)
- IR , KBr cm-1 : 3133 (C-H str) , 3108 (C-H str)

  3496 (N-H str)
- ^{1}H NMR ($CDCl_3$) δppm : C_2-H, C_5-H, 6.68 ;
  C_3-H, C_4-H, 6.62 ;
- ^{13}C NMR (CD_3COCD_3) δppm : C_1, C_4, 118.2 ;
  C_2, C_3, 107.2 ;

Syntesis :

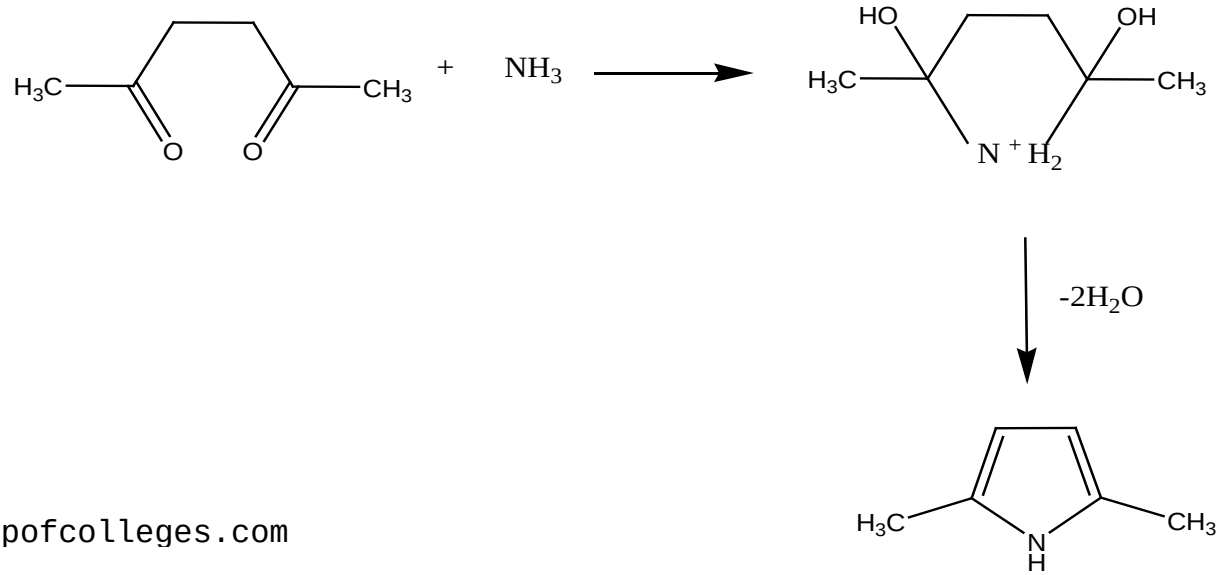
- The synthesis of pyrrole nucleus has been achieved by different routes.
- Cyclisation reactions
- Ring expansion reactions

- Ring contraction reactions
- Cyclisation reactions
- Intra molecular cyclisation of β-cyanoaldehyde or ketone leads to the formation of pyrrole ring.



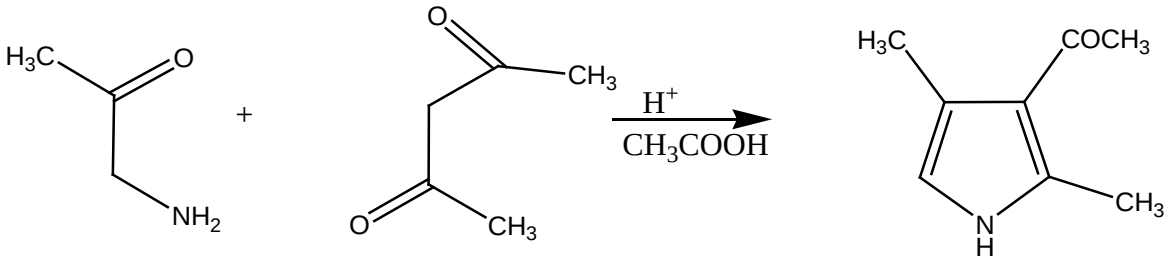
- Paal-knorr synthesis (4+1):

- The classiccal method of constructing 2,5-disubstituted pyrrole ring system involving (4+2) cyclisation reaction of 1,4 diketones with ammonia or it's ammonium salt, primary amine, hydroxylamine or hydrazines is known as paal-knorr synthesis.
- The reaction is acheived by heating appropriate diketone in benzene or toluene with ammonia in the presence of catalytic amount of acid.

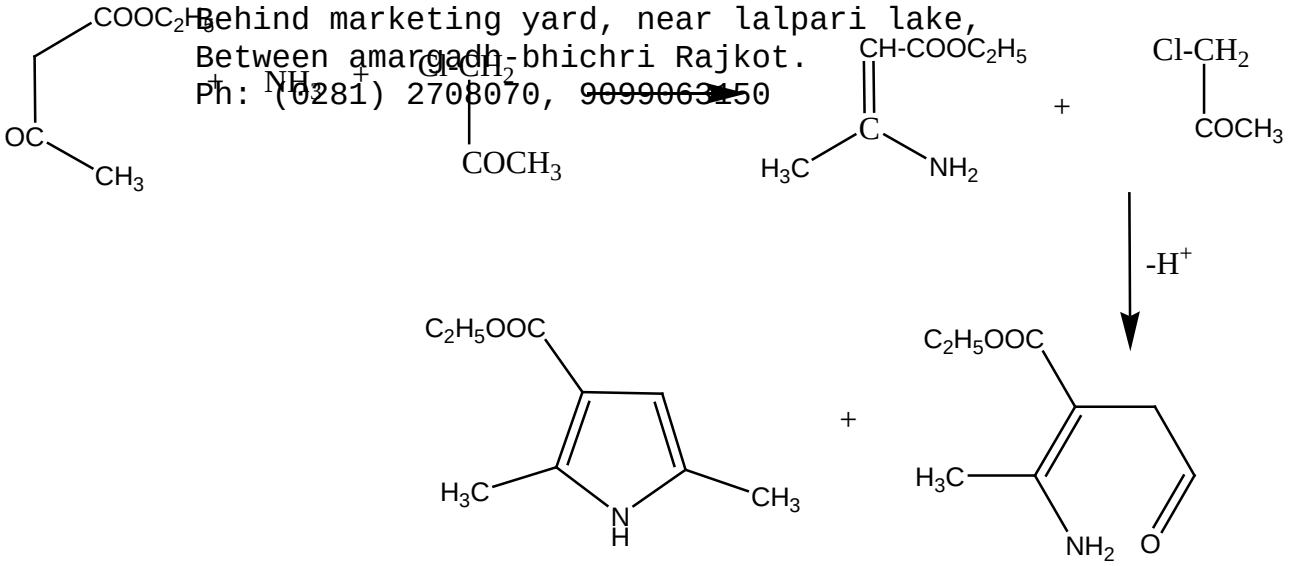


- Knorr pyrrol synthesis :

- It is the most extensively used route for pyrrole synthesis.
- It involves the cyclisation reaction (3+2) of α–amino ketones or α–amino β-keto esters in the presence of acetic acid.
- The reaction involves nucleophilic attack of amino group on electrophilic carbonyl carbon of β-diketone or β-ketoester with the formation of enamine intermediate.

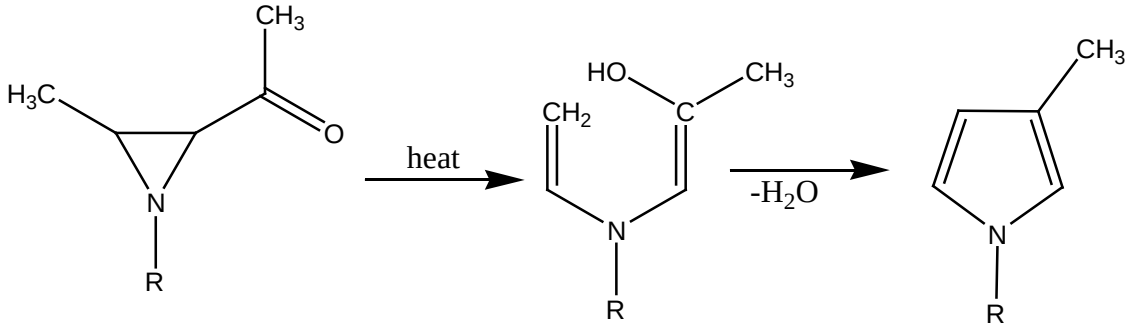


- Hantzsch synthesis :
- It is a (2+2+1) cyclisation, which generates pyrrole by the condensation of β-diketone or □-ketoester with □-halo ketone in the or aldehyde in the presence of either amonia or primary amine.
- The reaction proceeds via enamine intermediate which displace the Cl of α-halo ketone followed by cyclisation to yield corresponding pyrrole.



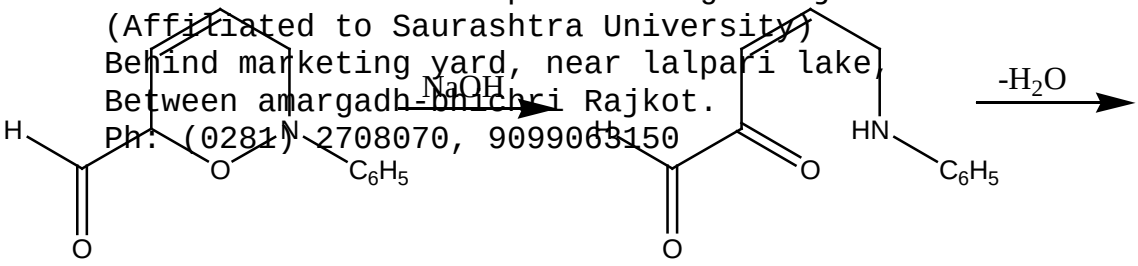
Ring expansion reactions

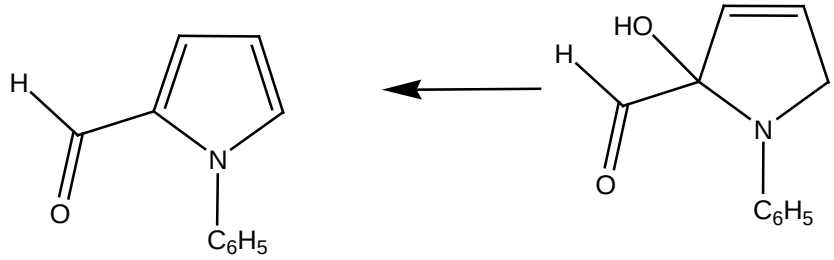
- 2-acetyl aziridine on rearrangement affords pyrrole derivative.



Ring contraction reaction

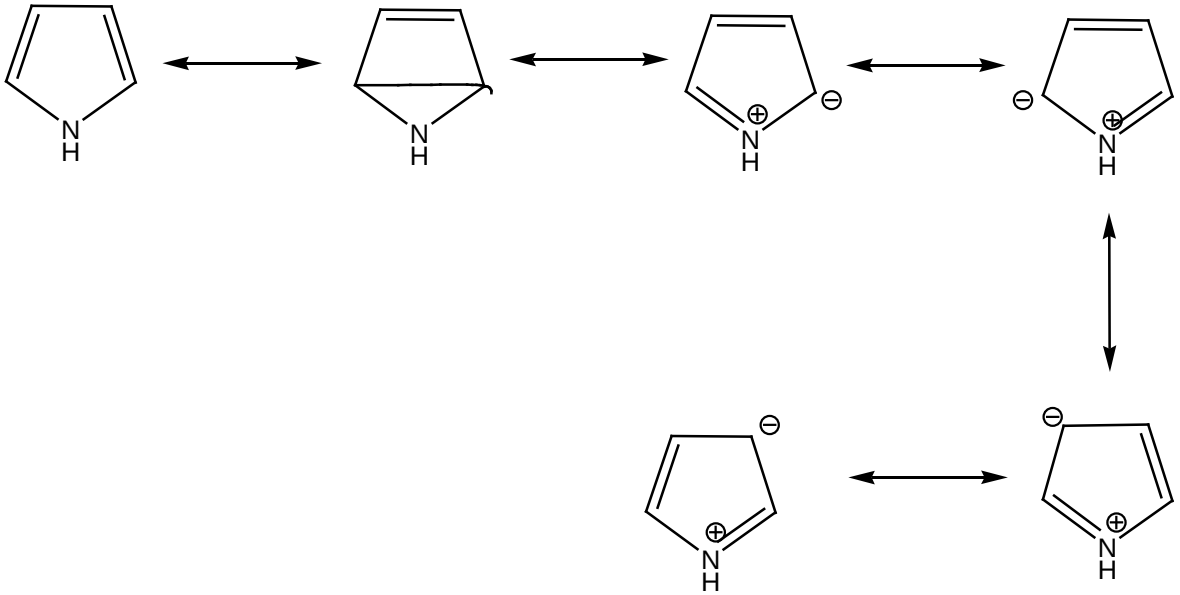
- Dihydro oxazine on ring contraction in the presence of a base affords pyrrole derivative.
- Ring closure is due to carbonyl-amine condensation to form a product which on dehydration provides pyrrole derivative.





Resonating structure

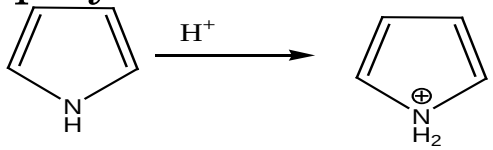
- The presence of lone pair of electrons on N-atom in pyrrole ring system causes hetero aromaticity.
- It is a weak base with pka -3.8.
- The resonating structure of pyrrole can be represented as under.

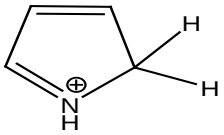


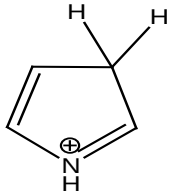
Chemical properties

- Electrophilic reaction:
- The Π-electrone excessive character of pyrrole nucleus renders the system extremely susceptible to attack by electrophilic reagents & reacts all most exclusively by substitution preferably at C_2. the electrophilic attacks on pyrrole nucleus are of two types.
  - ✓ Attack on hetero atom
  - ✓ Attack on carbon atom
- Attack on hetero atom:
  - Protonation :

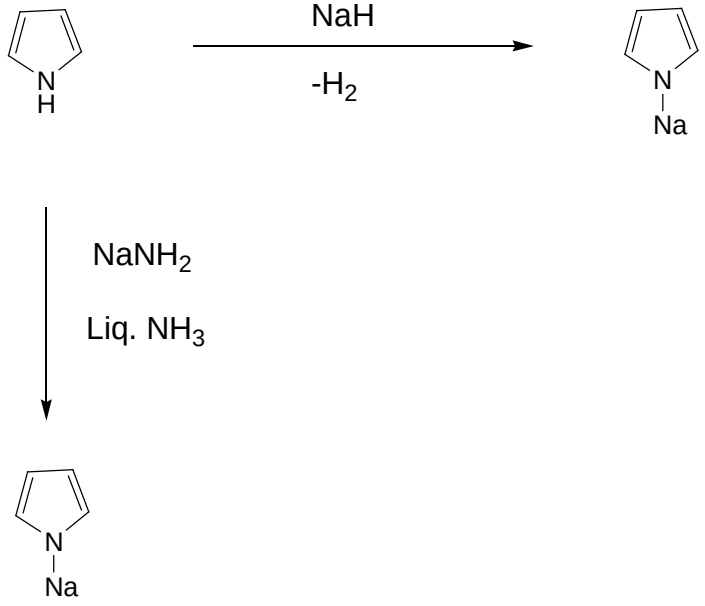
- The proton attached to the N-atom of pyrrole undergoes very rapid proton exchange in neutral, acidic or basic media while exchange of proton attached to the C-atom is much slower & occurs only under drastic condition.
  - This result in thermodynamically more stable 2H-pyrrolium cation as compare to 1H-pyrrolium cation.
  - When pyrrole is allowed to remain in contact with aqueous mineral acid. It also leads to rapid polymerization.



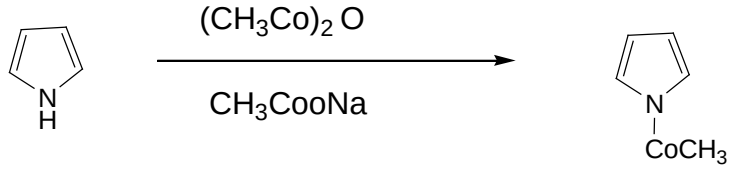




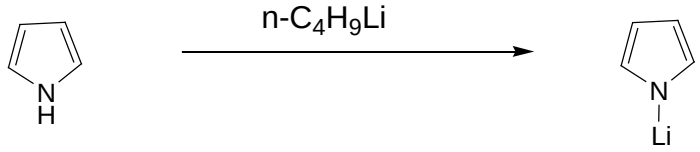
- Action of sodium hydride & sodamide in liquid ammonia :



- Acetylation with acetic anhydride and sodium acetate :



- n-butyl lithium :

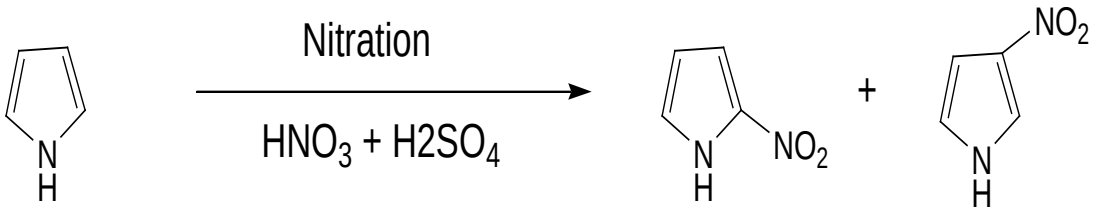


- Electrophilic attack on C-atom :
  - Nitration:

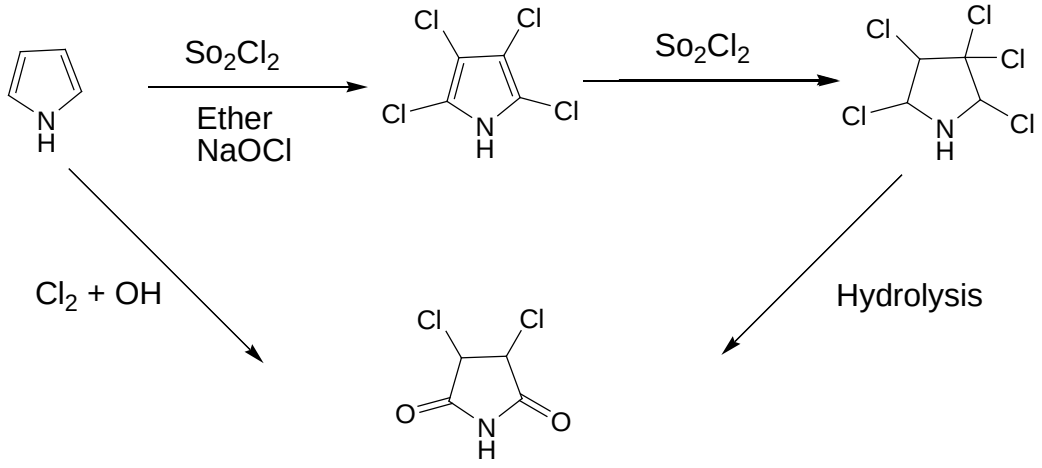
- Pyrrole is nitrated at lower temperature (at -10^0 C) using nitric acid in acetic anhydride to

afforded 2-nitro pyrrole & 3-nitro pyrrole in the ratio of 4:1.

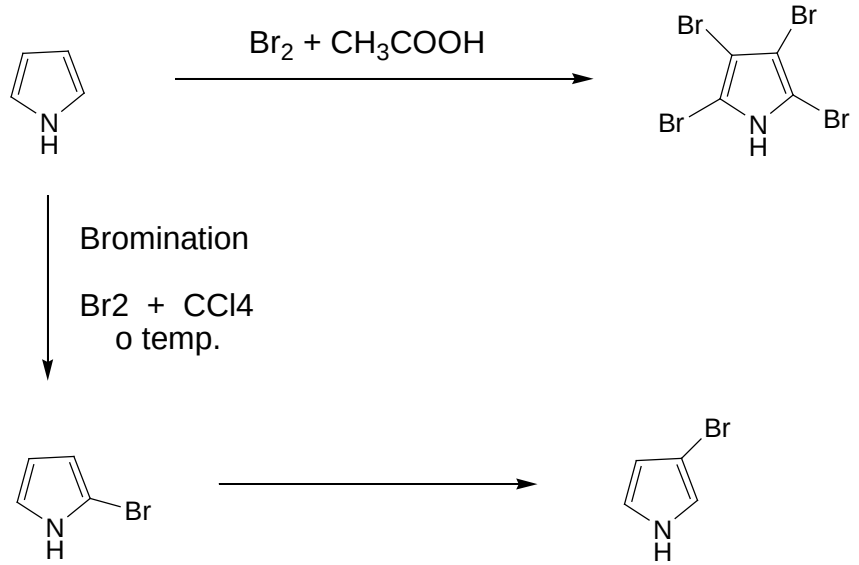
- Nitration of pyrrole under strong acidic condition or with common nitrating mixture result in decomposition of the ring.



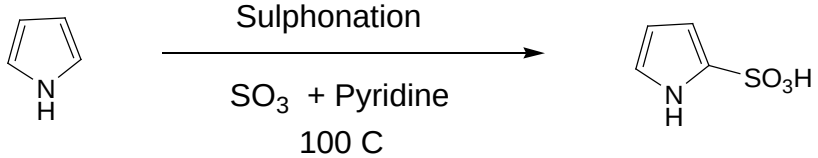
- Halogination :
- Chlorination :
- Pyrrole reacts with sulfuryl chloride (SO_2Cl_2) in ether or sodium hypo chlorite to give monochloro, tetracholro & pentachloro -2H-pyrrole.
- Pyrrole reacts with chlorine in alkaline medium it gives dichloromalemide of which is also obtained by hydrolysis of penta chloro pyrrole.



- Bromination :
- Pyrrole reacts with bromine in acetic acid as well as bromine in carbon tetrachloride to provide 2,3,4,5-tetra bromo pyrrole & 3-bromo pyrrole respectively.

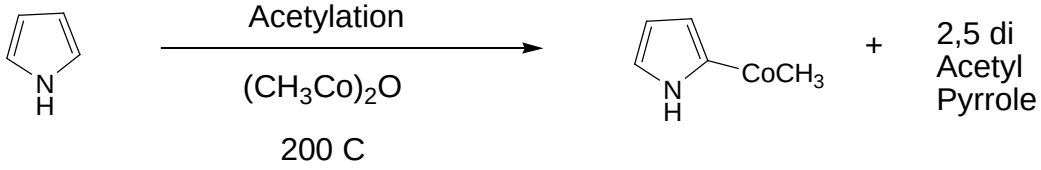


- Sulphonation :
- Sulphonation can be achieved using mild sulphonating agent like pyridine-sulphur tri oxide complex at 100^0 C which affords pyrrole-2-sulhonic acid. If both the α-positions are blocked the sulphonation proceeds at the α-position.



Acylation :

- Direct acylation of pyrrole using acetic anhydride at 200^0 C produces 2-aetyl pyrrole as major product along with 2,5 diacetyl pyrrole.
- The reaction of alkali metal salt of pyrrole with acyl halide results in N-acylpyrrole.

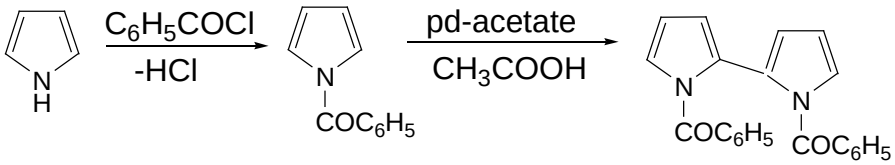


Nucleophilic reaction:

- Pyrrole is inert to nucleophilic substitution or addition reactions because of Π-electron excessive character.
- The nucleophilic reaction are promoted when electron withdrawing group are present in the pyrrole ring.

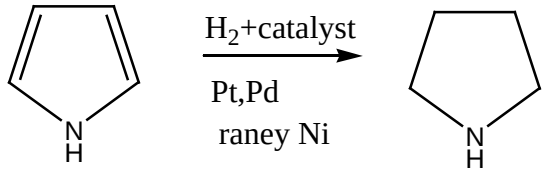
Oxidation :

- Oxidation of 1-benzoylpyrrole with palladium acetate in acetic acid yields 2,2'-bispyrrole as a major product.

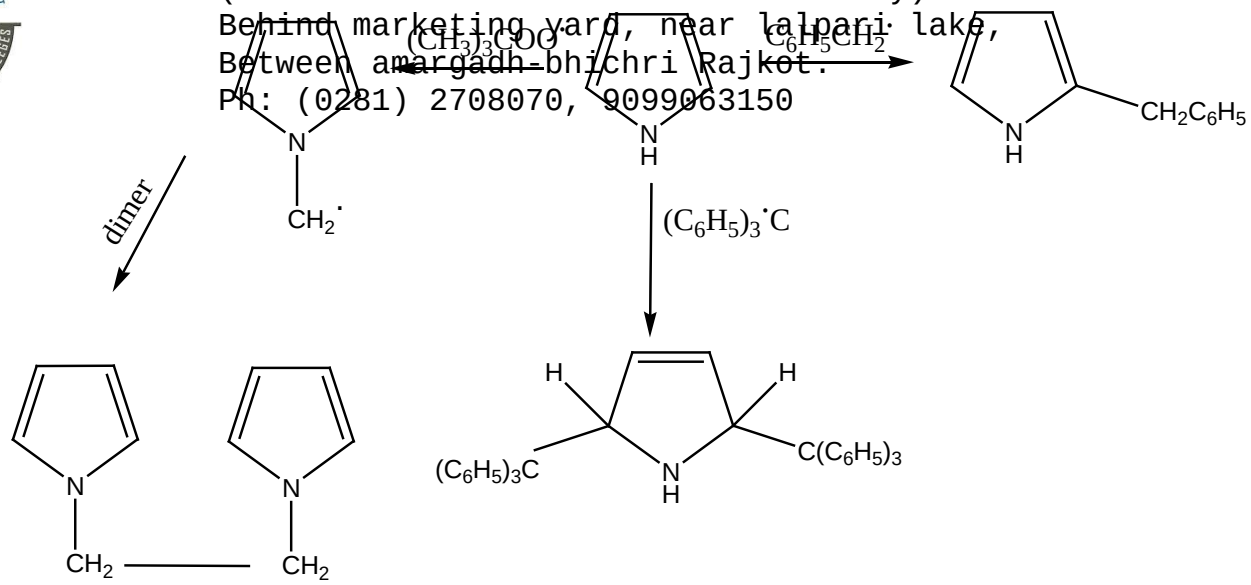


- Reduction :

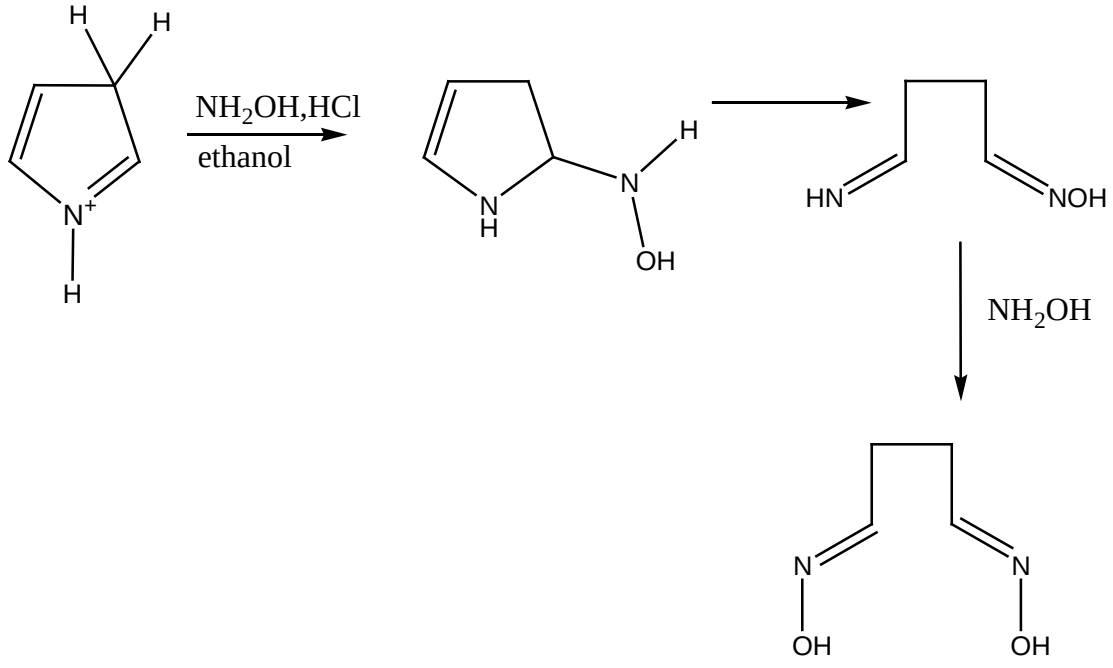
- Pyrrole is not reduced easily being an electron rich heterocycle.
- Catalytic reduction of pyrrole to pyrrolidine is accomplished with catalyst like palladium, platinum or raney Ni at moderate temprature & pressure.



- Reaction with free radicals:
- Generally free radical reactions proceed preferably at α-position of pyrrole ring system.
- Pyrrole reacts with benzyl radical, triphenyl methyl radical and t-butyl peroxy radical to provide corresponding 2-benzylpyrrole, 2,5-di (triphenyl methyl) pyrrole and 1,2-bis-N-pyrrole ethane.



- Ring opening reactions :
- Pyrrole reacts with hydroxylamine hydrochloride and sodium carbonate in ethanol to cause ring opening which leads to the formation of butandial dioxime and ammonia.



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Name :- Gohel Niraj Hiteshbhai

Roll no. :- 12 (Twelve)

M.Sc. Chemistry Sem-3

Branch :- Organic Chemistry

Assignment of

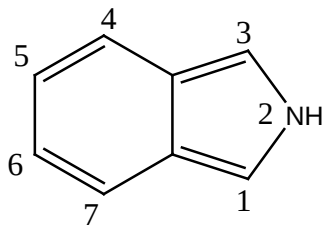
Heterocyclic compound

ISOINDOLE

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

-: ISOINDOLE :-

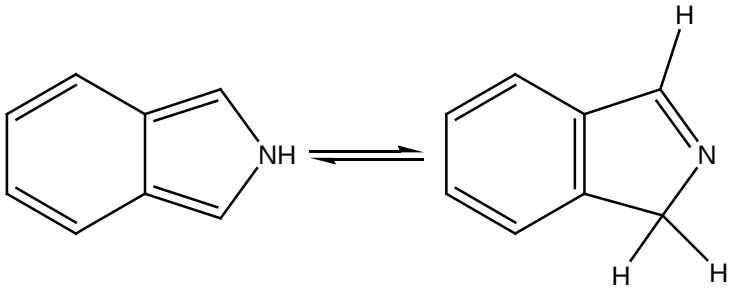
- Sructure:-



isoindole

- IUPAC Name :- Benzo [C] Pyrrole
- Other Name :- 2H – isoindole

- Isomer :-



2 H-isoindole 1 H-isoindole

Physical properties :-

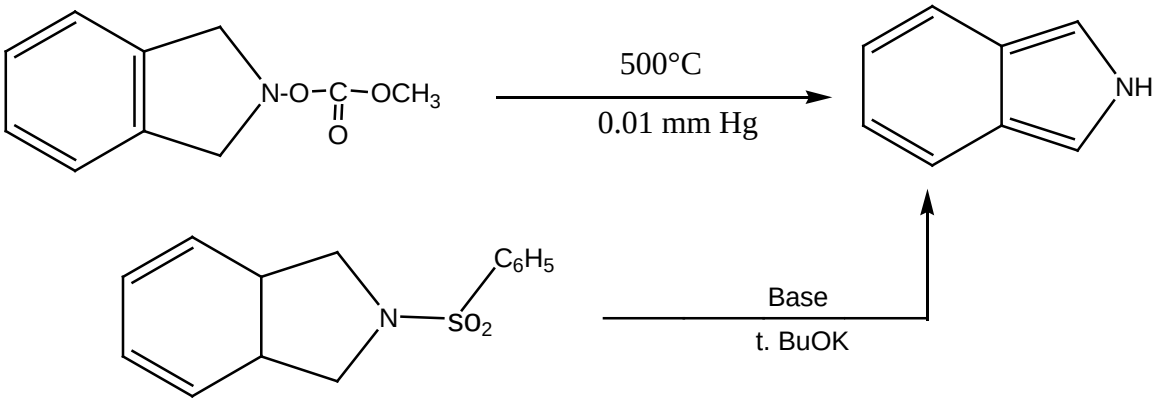
1. Isoindole is white solid compound.
2. It can be isolated at low temperature but decompose at room temperature.
3. It is stable only as its Diels-Alder adduct.
4. 2-Methyl isoindole is colourless compound
5. Melting point is 90-91°C.
6. Isoindole behalves as a typical secondary amine. The pKa is not known.

Synthesis :-

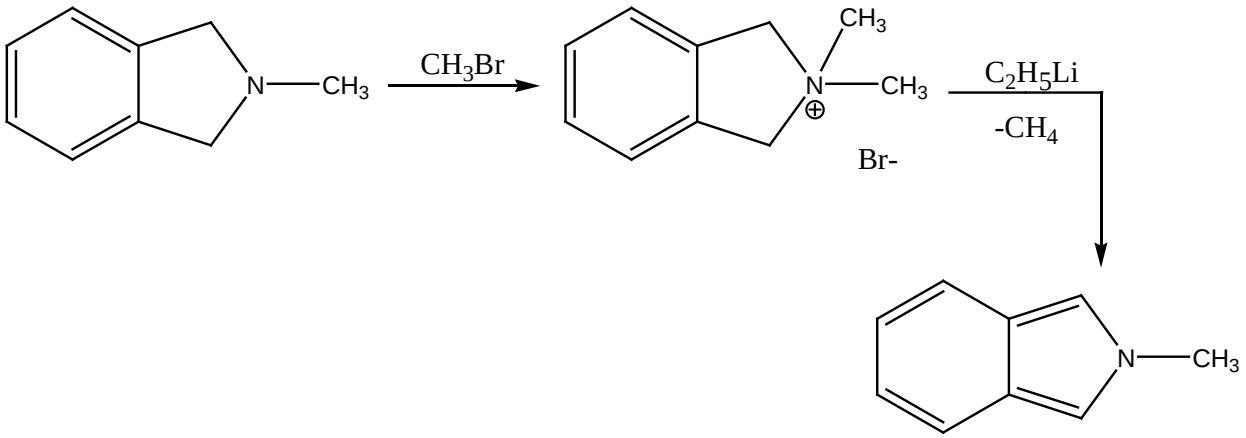
1. From isoindolines
2. From o-chloro benzyl amine
3. Cycloaddition of benzene and pyrrole
4. By reductive amination of o-dibenzoyl benzene

1) From isoindolines :-

a) The first synthesis of isoindole itself includes the vapour phase phase pyrolysis (500°C) of N-methoxy carbonyloxy isoindoline. The product was isolated at low temperature N-sulphonyl isoindole on base catalyst elimination leads to the formation of isoindole.

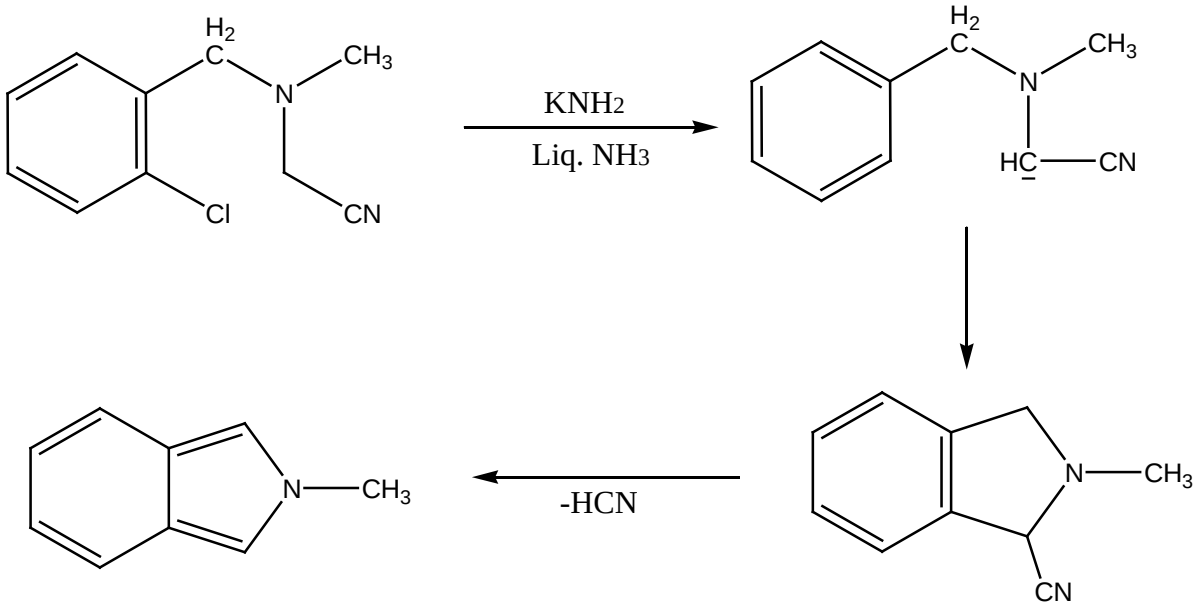


b) N-methyl isoindoline on methylation and treatone with phenyl lithium provide N-methyl isoindole.



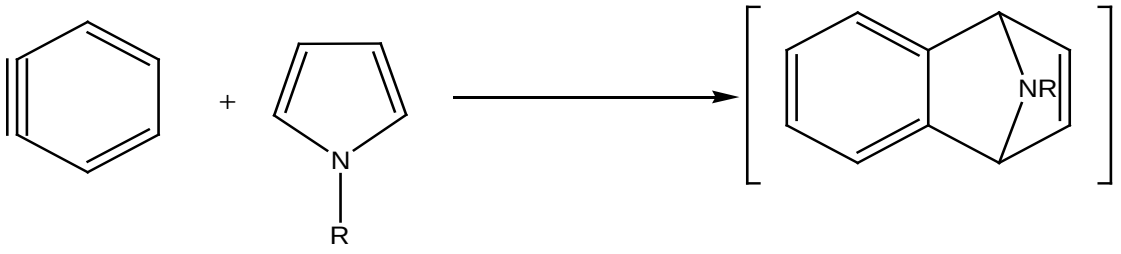
2) From o-chorobenzyl amine :-

o-chloro benzyl amine derivative with potassium amie in liquid ammonia undergoes cyclization to provide N-methyl isoindole. It involves intramolecular nucleophilic addition with loss of HCN.

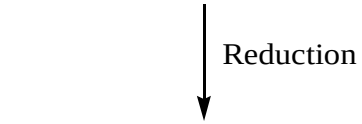


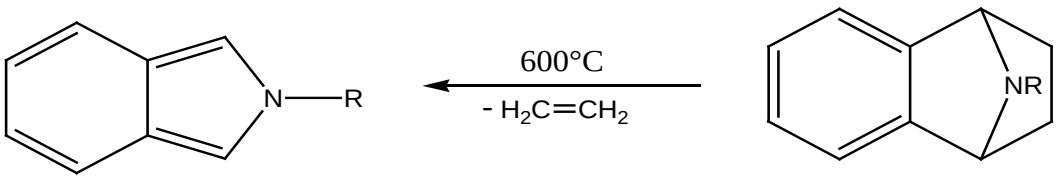
3) Cycloaddition of benzene and pyrrole :-

An alternative route involves cycloaddition of benzene and pyrrole to yield benzo-7-azobicyclo(2,2,1) heptanes followed by reduction and heating at 600°C to give retro-Diels-Alder reaction with loss of ethylene.



Benzyne Pyrole deri. Benzo 7-azabicyclo(2,2,1,) Heptane

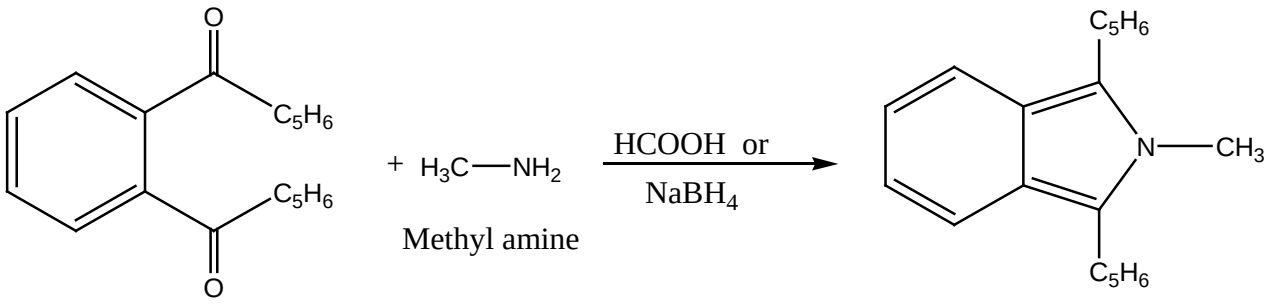




Isoinole dari.
2-Metyl Isoindole

4) Reductive amination of o-dibenzoyl benzene :-

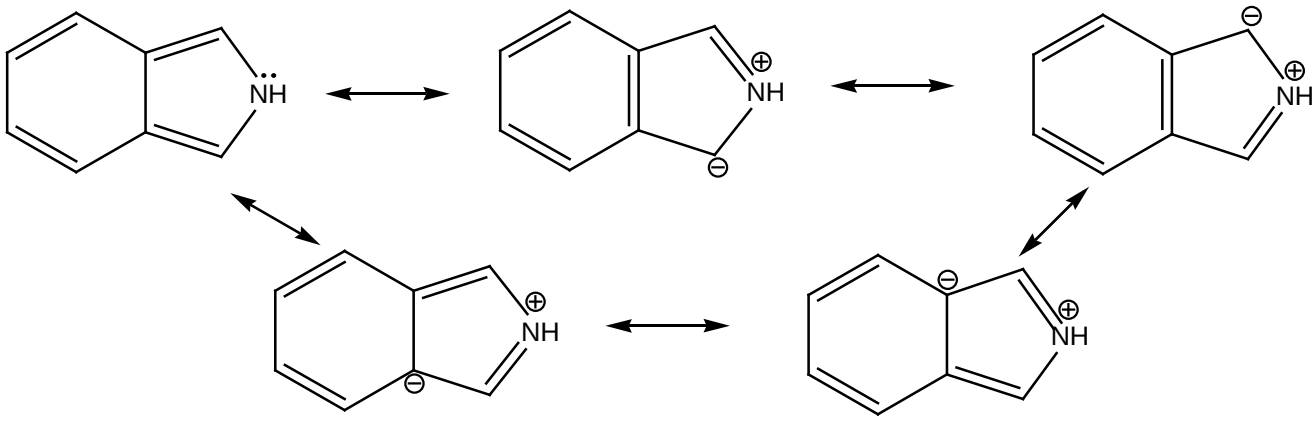
Reductive amination of o-dibenzoyl benzene with methyl amine in the presence of formic acid or sodium borohydrate provide substituted isoindole.



Dibenoyl Benzene Methyl amine l2-Methyl 1,3, dipheny Isoindole

Chemical properties :-

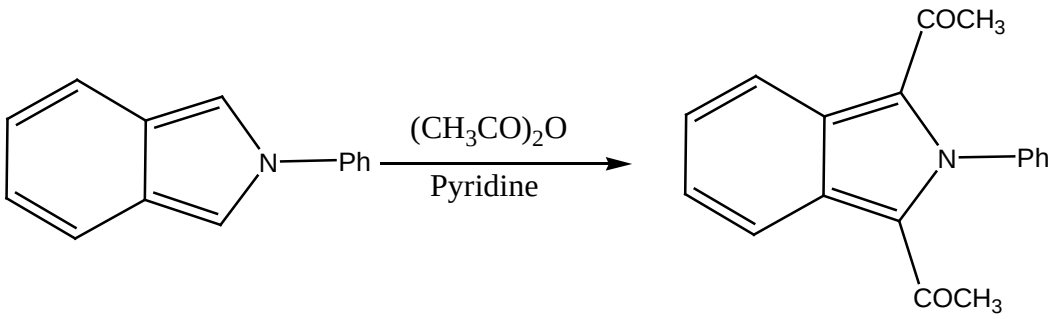
Resonating structure :-



Chemical reactivity :-

As the π-elctron density is high in isoindole ring at C-1 it undergoes elctrophilic substitution at C-1 and di-substitution at C-1 and C-3 position.

- Electrophilic reaction of 2-phenyl isoindole :-
  1. Acetylation :-

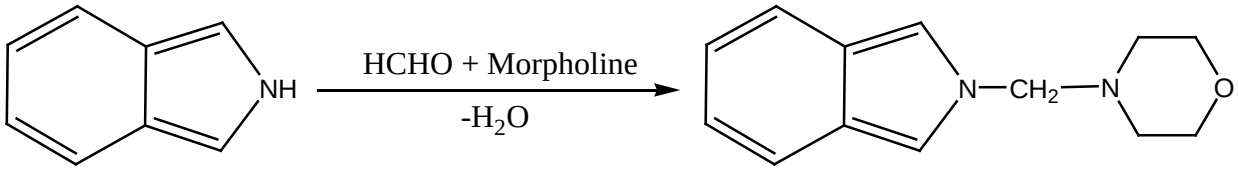


2-Phenyl Isoindole

1,3,-Diacetyl 2-Phenyl Isoindole

2-phenyl isoindole react with acetic anhydride in presence of pyridine to obtain 1,3 diacetyl 2-phenyl isoindole.

2. Mannich reaction :-

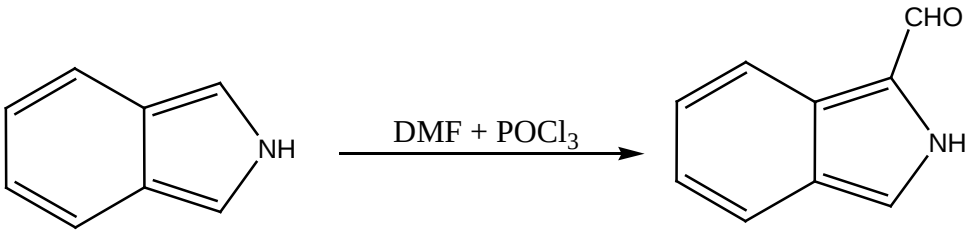


Isoindole

N-Morpholino Methyl Isoindole

Isoindole react with formaldehyde and morpholine to produced N-morpholino methyl isoindole . This reaction is known as Mannich reaction.

3. Vilsmeier-Haack reaction :-

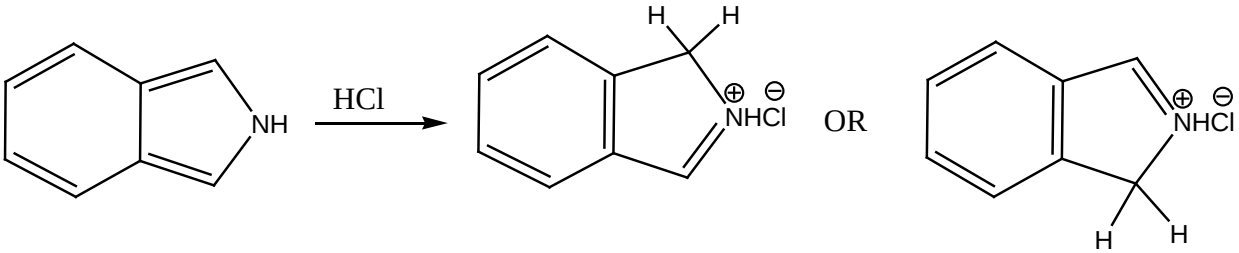


Isoindole

3-Formyl Isoindole

Isoindole react with dimethyl formanion with $POCl_3$ to produce 3-formyl isoindole.

4. Protonation :-



Isoindole

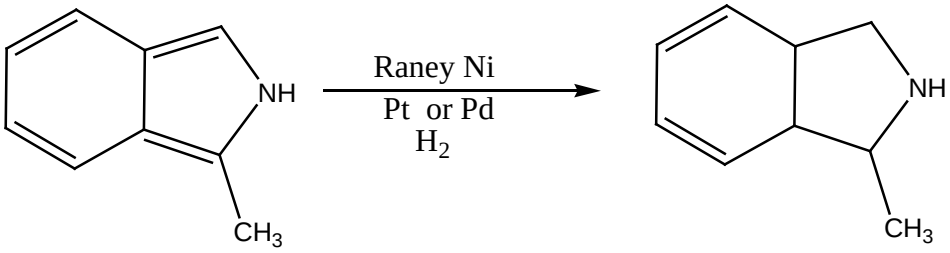
3-Hydro Isoindol deri.

1-Hydro Isoindol deri.

Isoindole react with hydrochloric acid to produce 1 or 3 position hydro isoindole derivative.

- Reduction :-

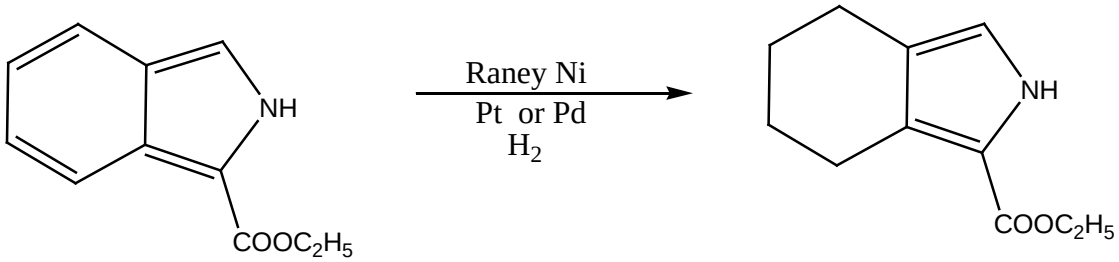
1.



1-Methyl Isoindole 1-metyl isoindoline

1-methyl isoindole reduce with Raney-Nickel and Pt with hydrogen gas to obtain 1-methyl isoiindoline.

2.

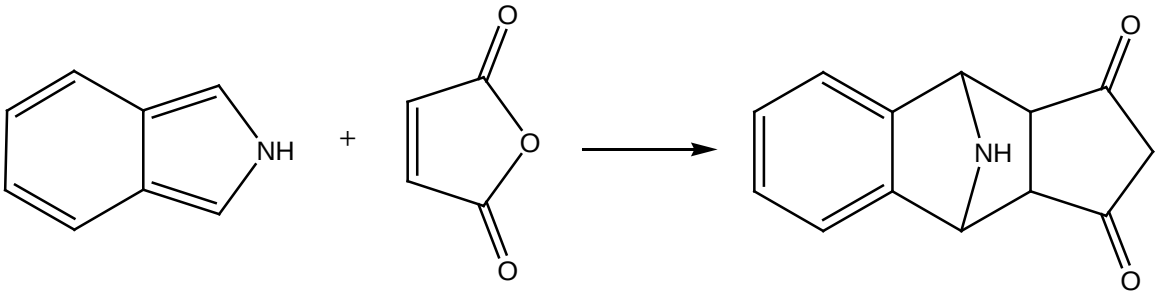


1-Carbethoxy Isoindole 4,5,6,7-tetrahydro Isoindole deri.

1-carbethoxy isoindole reduce with Raney-Nickel and Pt or Pd with H_2 gas to produce 4,5,6,7 tetra hydro isoindole derivative.

- Cycloaddition reaction (Diels-Alder reaction) :-

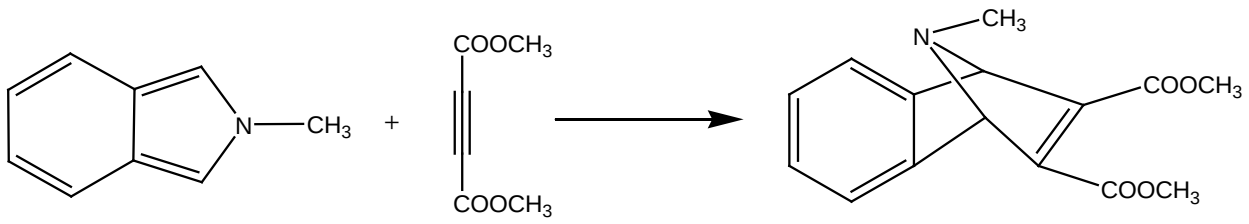
1.



Isoindole Maleic anhydride (4+2) Cyclo adduct

Isoindole treat with maleic anhydride to produce (4+2) cyclo adduct of isoindole.

2.



Isoindole | Dimethyl acetylene dicarboxylate | Diels-Alder Adduct

Isoindole treat with dimethyl acetylene dicarboxylate to obtain Diels-Alder adduct.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Name :- Gohil Ankita Jitendrabhai

Sub :- Heterocylic Chemistry

Roll No :- 13th

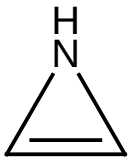
Std :- M.Sc. Sem-3rd

Topic :- Azirines

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

AZIRINES

Structure:-



1H-Azirine
2-Azirine
Enamines

2H-Azirine
1-Azirine
Imines

Azirines exist in 2 isomeric forms:-

1-azirine is stable as compared to 2-azirine,the instability of 2-azirine is attributed to the combined effects of nitrogen lone pair of electrons with the olifinic pi-electrons.

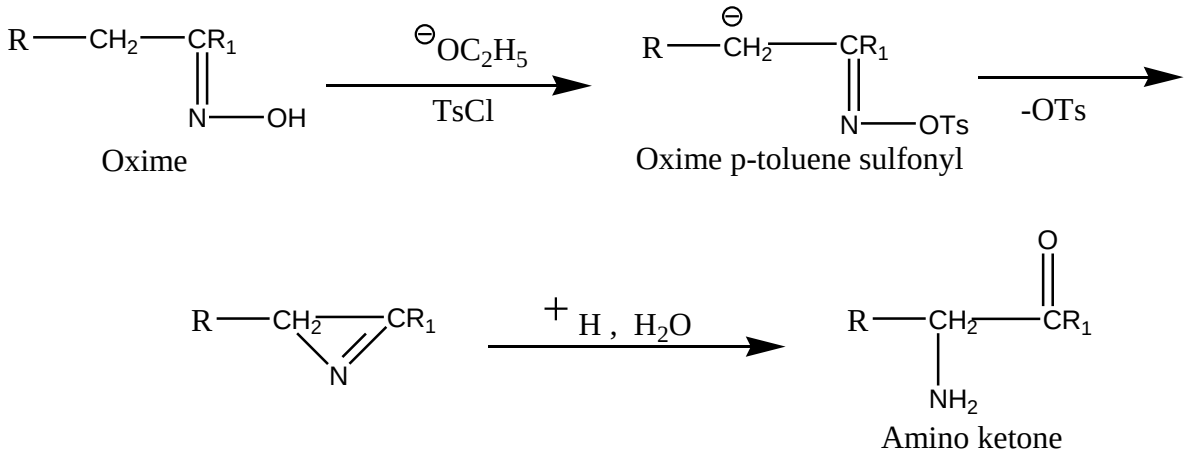
Physical properties:-

- Vile-smelling compound.
- Readily polymerize unless stored under cold and in an inert atmosphere.
- Highly irritant to skine.

Synthetic methods:-

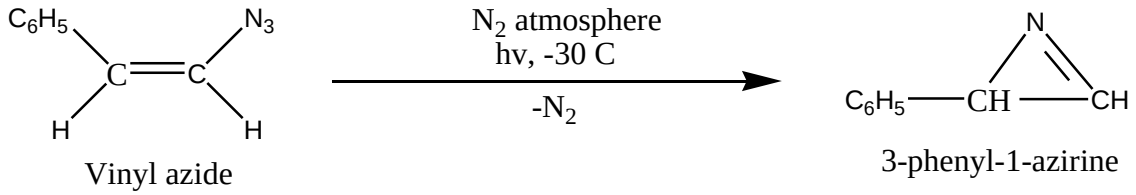
1. Neber rearrangement:-

Nember proposed 1-azirine as an intermediate in the base-catalyed rearrangement of oxime p-toluene sulfonyl derivative to alfa-amino ketone.

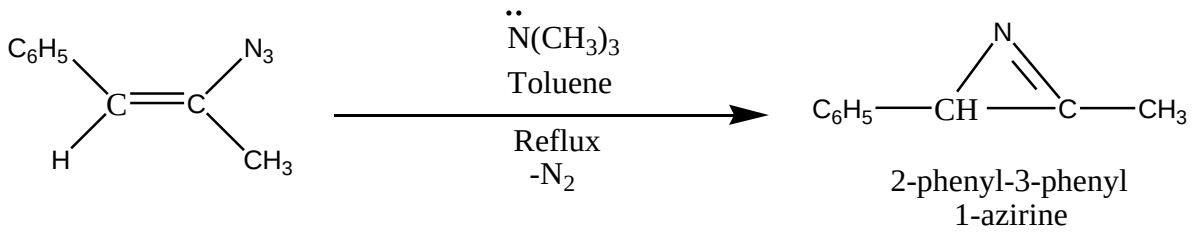


2. From vinyl azides:-

Photolysis of vinyl azides under nitrogen atmosphere at -30 C permits isolation of 1-azirine.



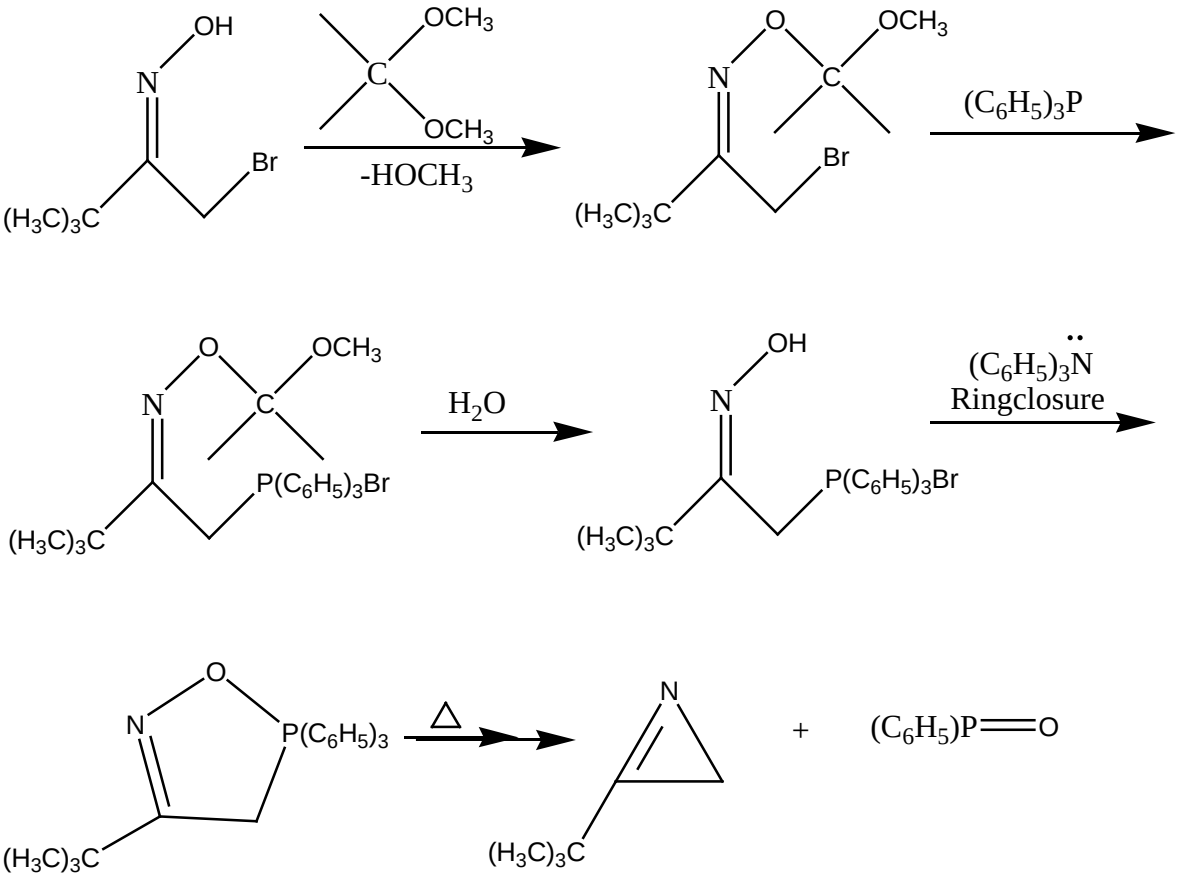
Refluxing a toluene solution of an azide in the presence of catalytic amount of a tertiary amine, as shown for styryl azide.



3. From alfa-bromo ketoxime:-

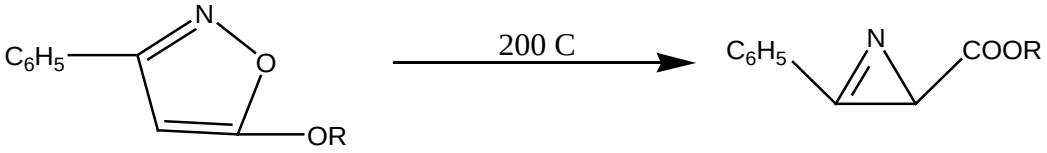
Hassnes reported the preparation of 1-azirine using alfa-bromo ketoxime.

The hydroxyl group of alfa-bromo ketoxime is first protected with triphenyl phosphine, then deprotected to regenerate the phosphonium salt. This salt is converted to oxazo phospholine which is thermolyzed to 2-t-butyl azirine.

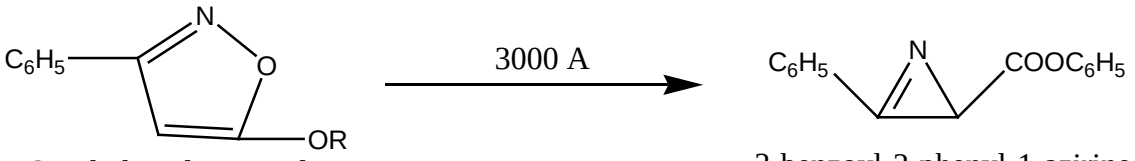


4. From pyrolysis or photolysis of isoxazoles:-

Nishiwaki, observed that pyrolysis of 5-alkoxy substituted isoxazoles resulted in the formation of isolable 1-azirines.



The photolysis of 3,5-diphenyl isoxazole produce 2-phenyl-3-benzol azirine, this reaction has been found to be wavelength at 3000 A.



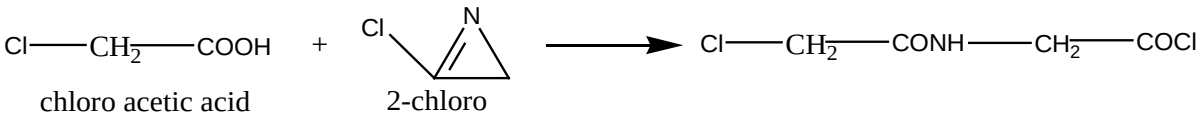
3,5-diphenyl isoxazol

3-benzoyl-2-phenyl-1-azirine

Chemical properties:-

1.Reaction with acid:-

Protonation of 1-azirine, followed dy ring opening, takes place in strong acid solution. The reaction with chioro acetic acid or benzoic acid, opens the ring and subsequently undergoes rearrangement.

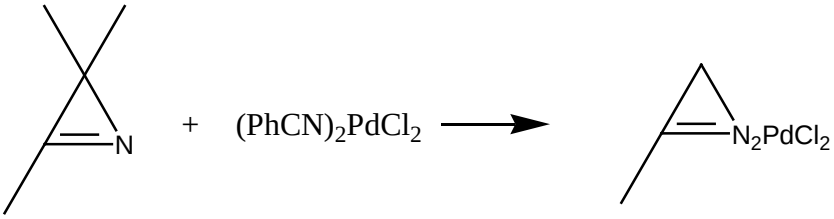


chloro acetic acid

2-chloro azirine

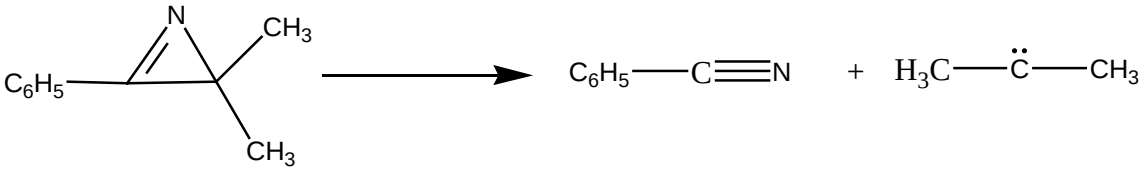
2.Formation of complexes:-

1-azirine from stable complexes with dichloro bis (benzo nitrile) palladium(2).



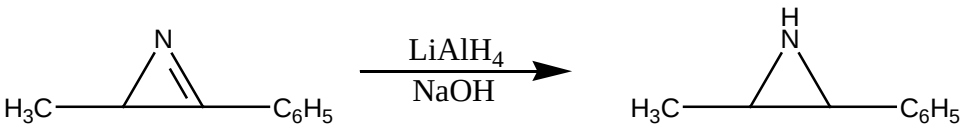
3.Ring opening reaction:-

2-phenyl-3,3 dimethyl-1-azirine yield phenyl cyanide and dimethyl carbine, the ultimate products formed are due to fragmentation via a carbine and a nitrile molecule.



4.Reduction:-

Azirines have been reduced by lithium aluminium hydride to produce aziridines.

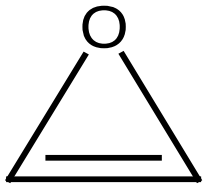


2-methyl-3-phenyl 1-azirine

2-methyl-3-phenyl aziridine

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

:: ***OXIRENE*** ::



¤ *Other Name:-*

(1)Acetylene Oxide

(2)1,2-Epoxythene

(3)Oxa cyclopropene

¤ *Physical Property:-*

→Molecular formula = C_2H_2O

→Molar mass = 42.04 gm/mole

→Oxirene are compound with three membered ring system characterised by the presence of oxygen as a hetero atom and a double bond belonging to the 4n-π electron ring system.

→Molecular orbital suggest that it is less stable by 50 KJ/mole ascompared to acyclic isomer.

→It can not be isolated but exists as an unstable intermidiate in numerous reaction.

¤ Synthesis:-

There are four method

1) From 1,2,3-Oxadiazole

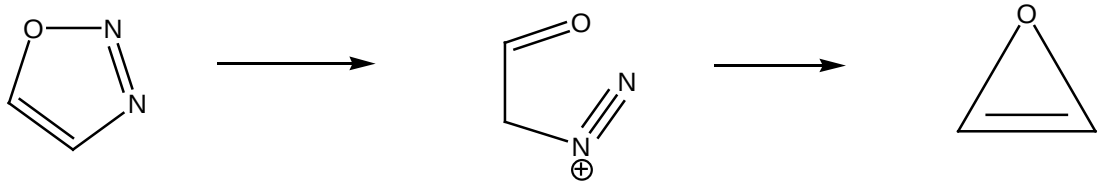
2) Peracid oxidation of acetylene

3) Wolff rearrangement

4)From the Diazo ketone

→ (1) From 1,2,3-Oxadiazole:-

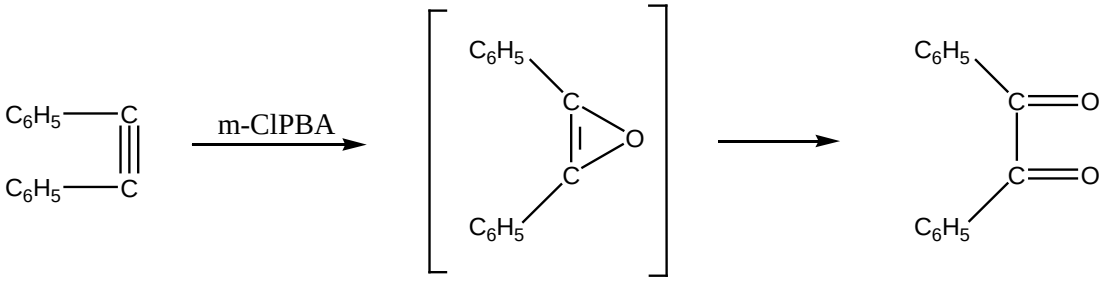
1,2,3-Oxadiazole is unknown but it's isomeric diazoketone on loss of Nitrogen gives Oxirene.



1,2,3-Oxadiazole Diazo ketone oxirene

→ (2) Peracid oxidation of acetylene:-

1,2-Diphenyl acetylene on oxidation with m-chloro per benzoic acid provide 1,2-diphenyl oxirene which is converted into benzil.

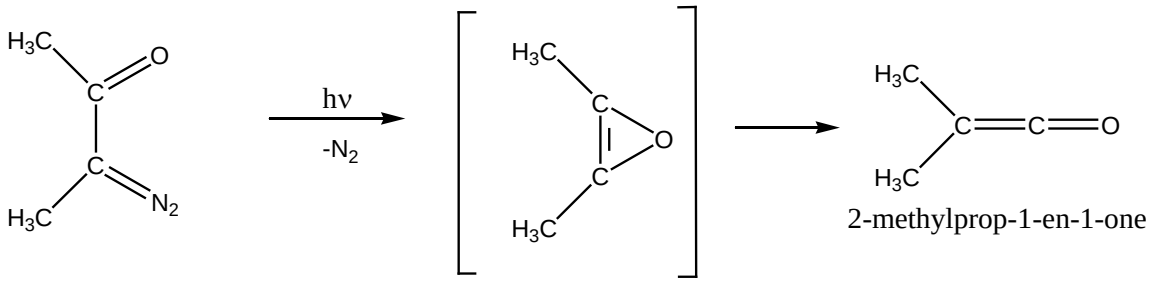


1,2-diphenylethyne 2,3-diphenyloxirene benzil

--> Oxirene is probably a true intermidiate but is separeted from ketene by low energy barrier.

→(3) wolff rearrangement:-

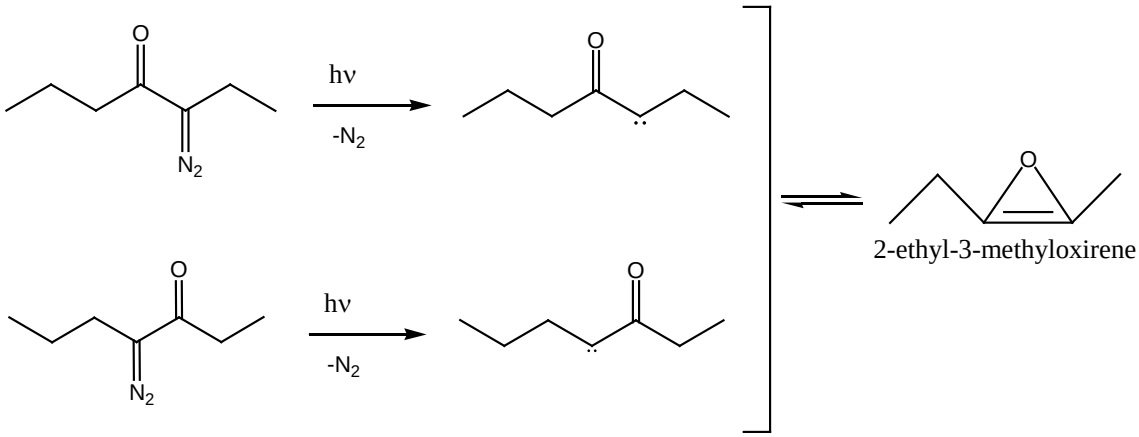
Oxirene has been observed as on intermediate in a photo chemical rearrangement of diazo ketone.



2-methylprop-1-en-1-one

→(4) From diazo ketone:-

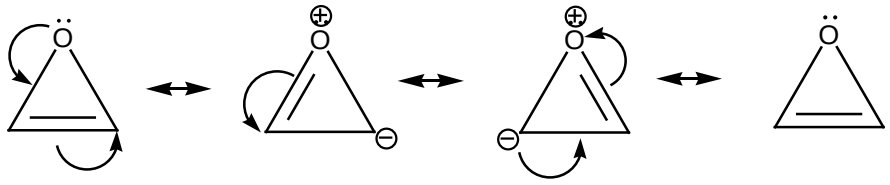
Cormier has shown that the oxirene could be generate from the diazo ketone via intermediate carbene.



2-ethyl-3-methyloxirene

→ Oxirene derivative hasalso been involved by various other workersin elimination, photlytic and retro cyclo addition reaction butalternative explanation are always available.

¤ Resonance in Oxirene:-



DIHYDROTHIIRENE

ETHYLENE SULPHIDE

THIACYCLO PROPANE

- **Formula:** C_2H_4S
- **Molecular weight:** 60.118

Introduction

It was first prepared by delepine in 1920

It is 3-member sulpher containing saturated hetrocyclic compound

Used

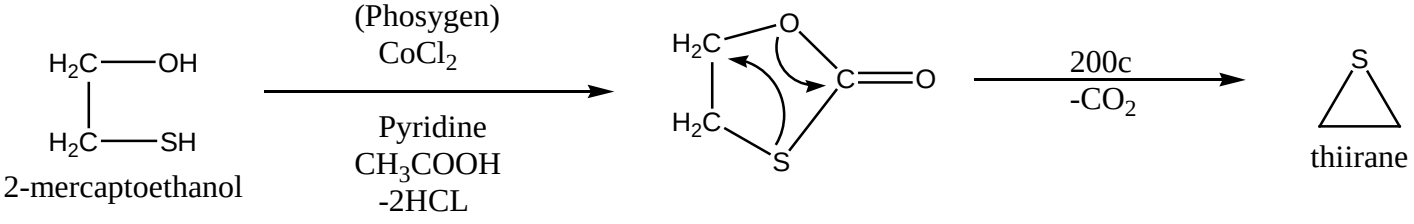
Certain thiirene are used in cosmetic and fluorinated thiirene may be employed as refregants and fire extenguishers

Physical Property

- Pale yellow liquid
- Sparingly soluble in water and easily soluble in organic solvent
- B.P. =55-56 C
- Dp = 1.66 which is higher thanethat of dimethyl sulphide (1.40D) but lower thane that of oxirane(1.88D)
- The difference in D.P. indicate that C – S bond is less polar than C – O bond
- Its ring strain is 9 K cal /Mole
- Bond length C-C 1.429 A Which is intermediate between ethane (1.54A) and ethylene (1.33A)C-C bond distance
- This suggests partial double bond character of C-C in thiirane
- C-S = 1.819A , H-C-H = 116A C-S –C = 48.4A

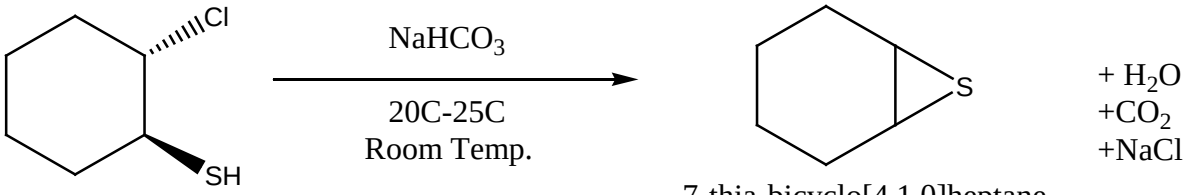
Synthesis

It can be prepared by the reaction of 2- mercapto ethanol and Phosgen in ethyl acetate and pyridine give mono thio ethylene carbonate which on decarboxylation at 200 C yieldThiirane



2) From trans – 2 chlorocyclo hexane thiol

Cyclo hexane sulphide can be obtained by the reaction of base(NaHCo3)at 20-25 room temp with trans -2 –chloro cyclohexane thiole

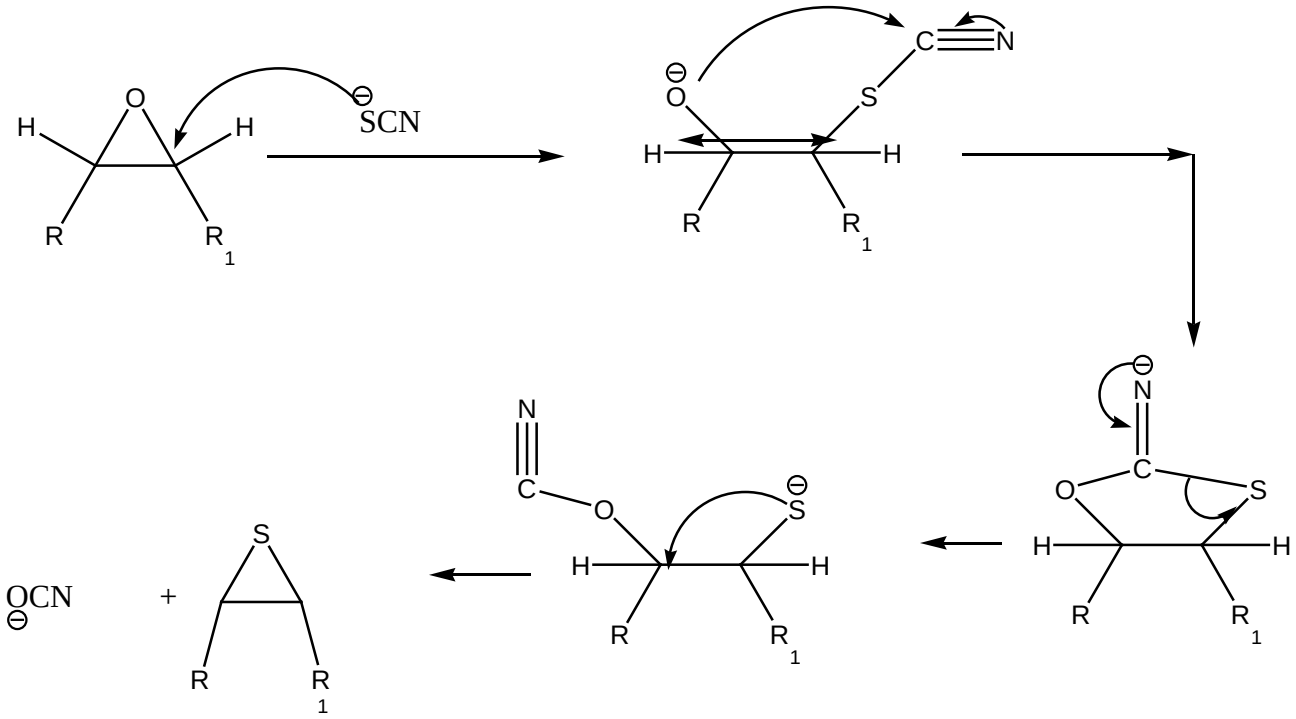


(1*S*,2*S*)-2-chlorocyclohexanethiol

7-thia-bicyclo[4.1.0]heptane

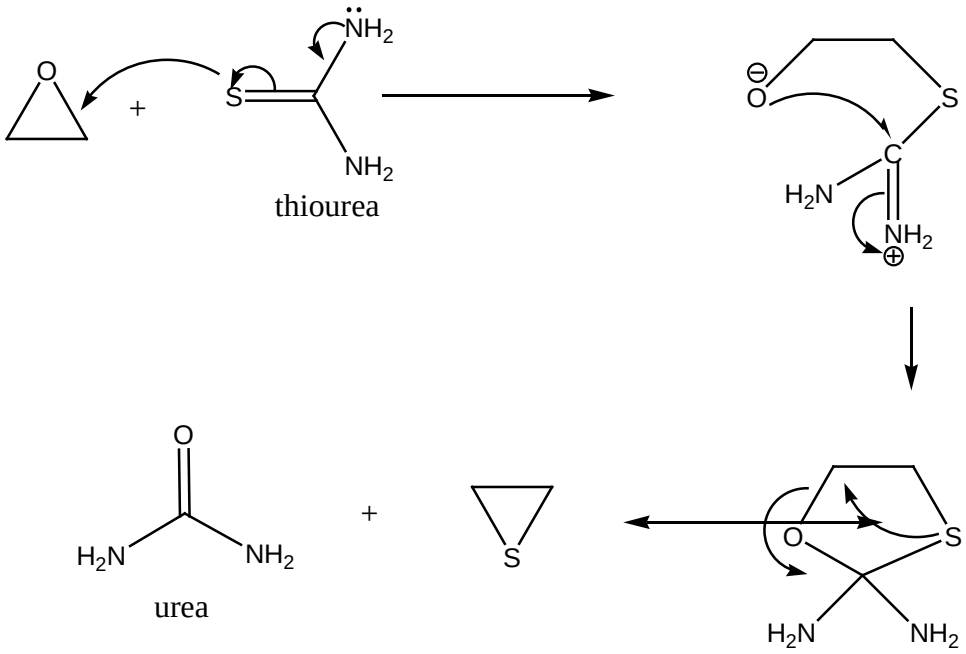
3) From Epoxide (Oxiranes) &Thioisocynate ion

Oxirane ring derivative is in attack on thiocynate ion to generate negative charge of oxygen. Now oxygen attack on thiocynate carbon to five member cyclic forn And nitrogen is donate lone pair an Sulpher is attack on positive charge of Carbon to give a Thiirane derivative

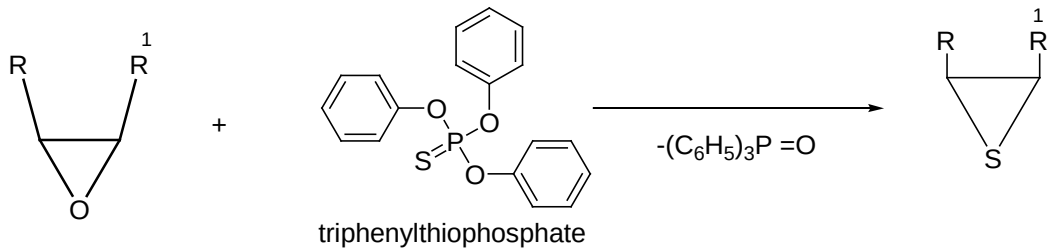


From Epoxide (Oxirane) &thio Urea

Thiourea nitrogen have lone pair is resonance an sulpher have negative change and it's behave a neuclophila in attack to epoxide ring and ring is opening andsecond step tu heating and urea is remove to give a thiirane



5) From epoxide &triphenyl phosphine sulfide

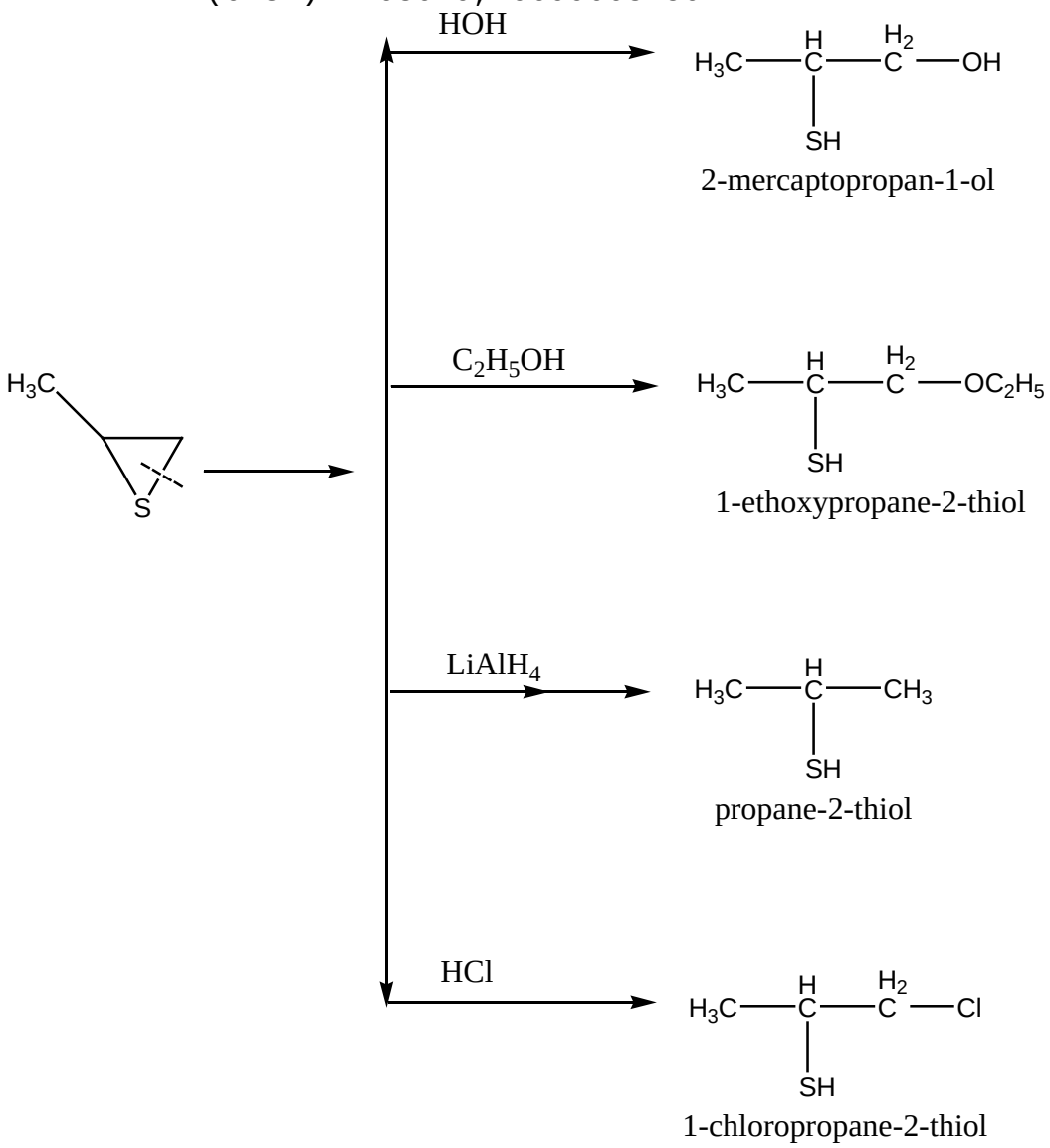


Chemical Property

Ring opening reaction

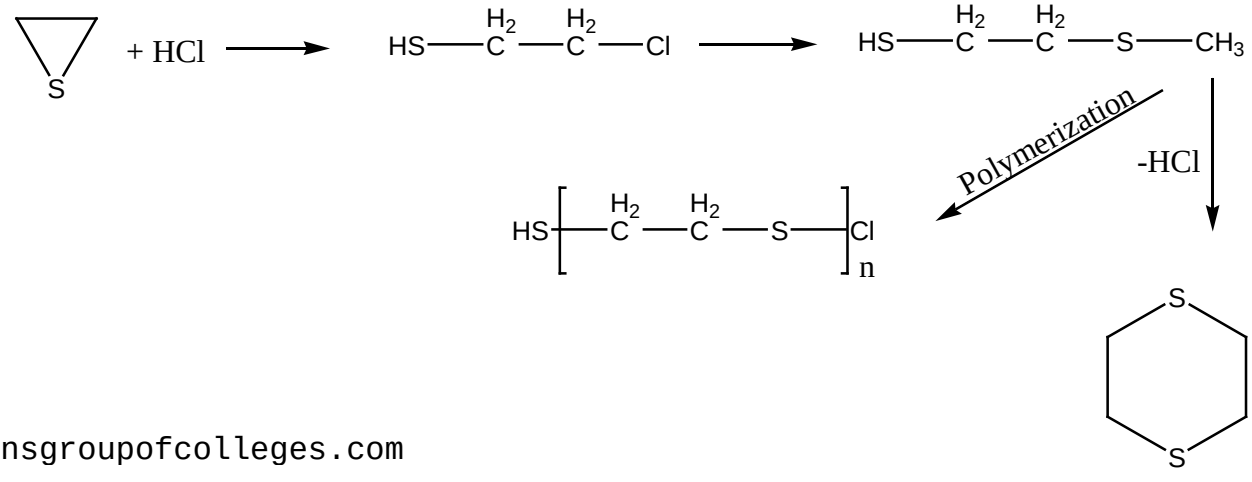
Electron density at sulpher is lower than that of oxygen. So it is less reactive towords electrophilic reagent but little gretertowardsnucleophilic reagent as compare to oxiranes

ile first attack at an unsubstituted carbon atom to open the ring in an unsymmetrical episulphide

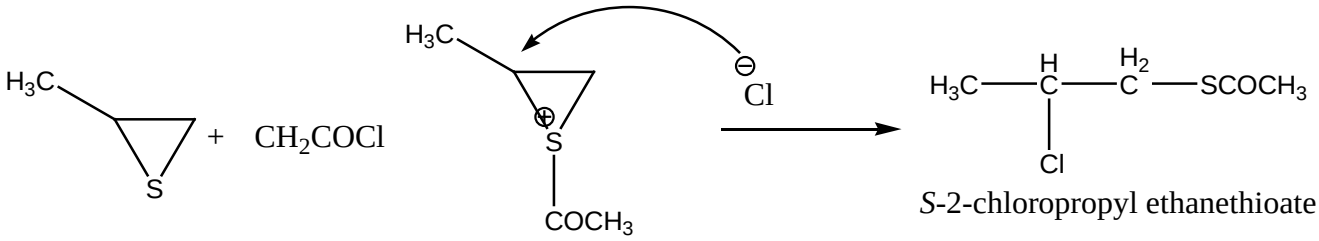


Polymerisation

If excess Conc. HCl is added to ethylene sulphide then monomer & Dimer of thiirane may be isolated and further reaction it is Polymerisation

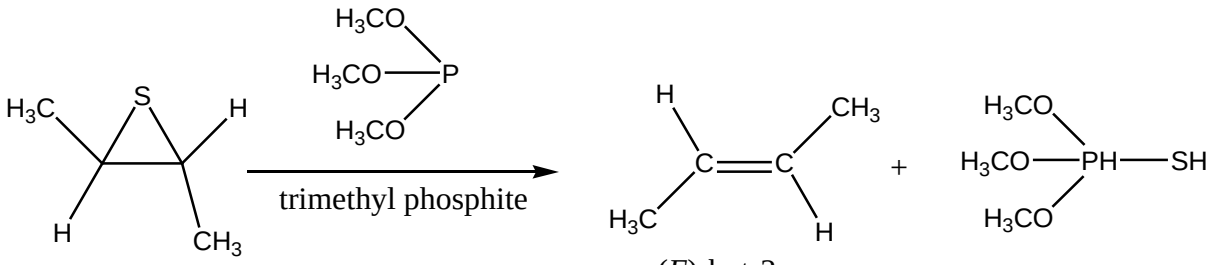


Electrophilic Ring opening reaction



S-2-chloropropyl ethanethioate

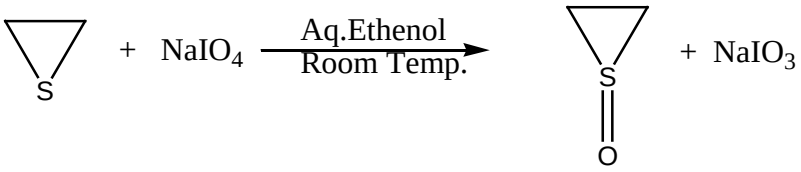
Desulferization



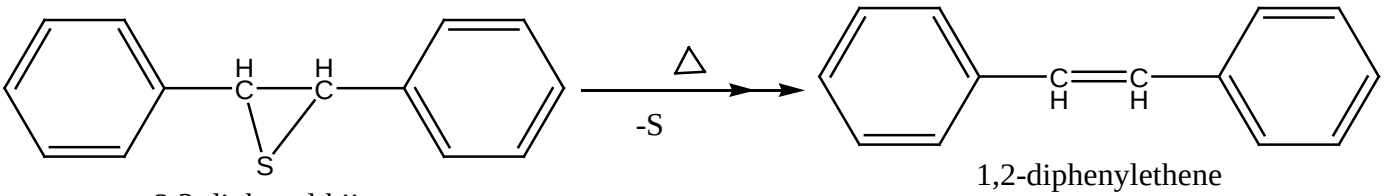
(*E*)-but-2-ene

Oxidation

Thiirane is oxidize sodium periodate NaIO4 in aquous ethanol forming ethylene sulphide



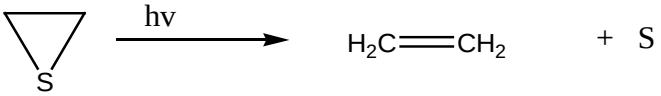
Thermal Reaction



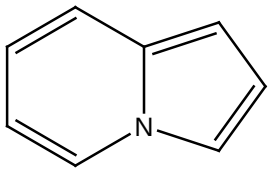
2,3-diphenylthiirane

1,2-diphenylethene

Photochemical reaction



Indolizine



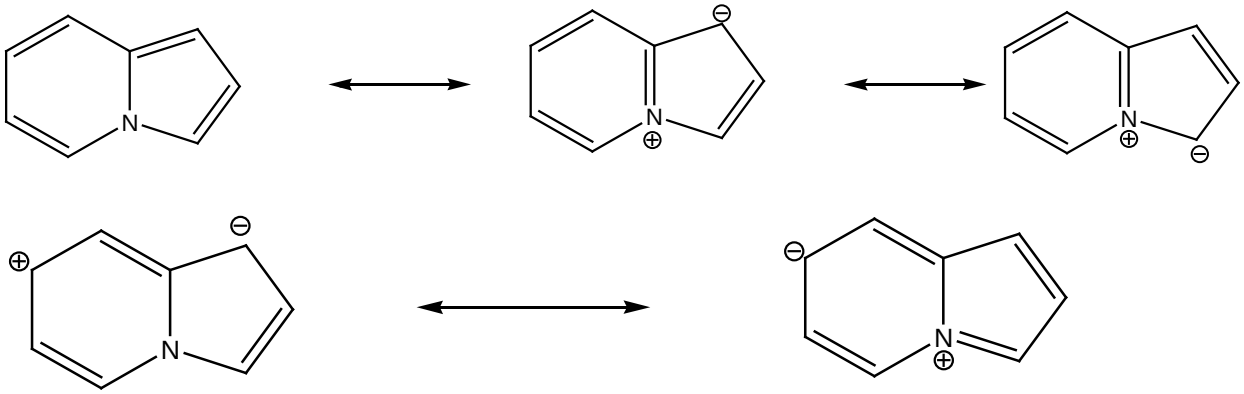
Other name :-

- Pyrrozoline
- Pyrrolo[1, 2, -a]
- Pyrrocoline

Physical Property :-

- Odour like naphthalene
- Aromatic character
- It has a ring junction nitrogen with fully conjugated 10 pie electron system.
- it is iso electronic with indole.
- and isoindole possesses several mesomeric structure.
- melting point is 74°C

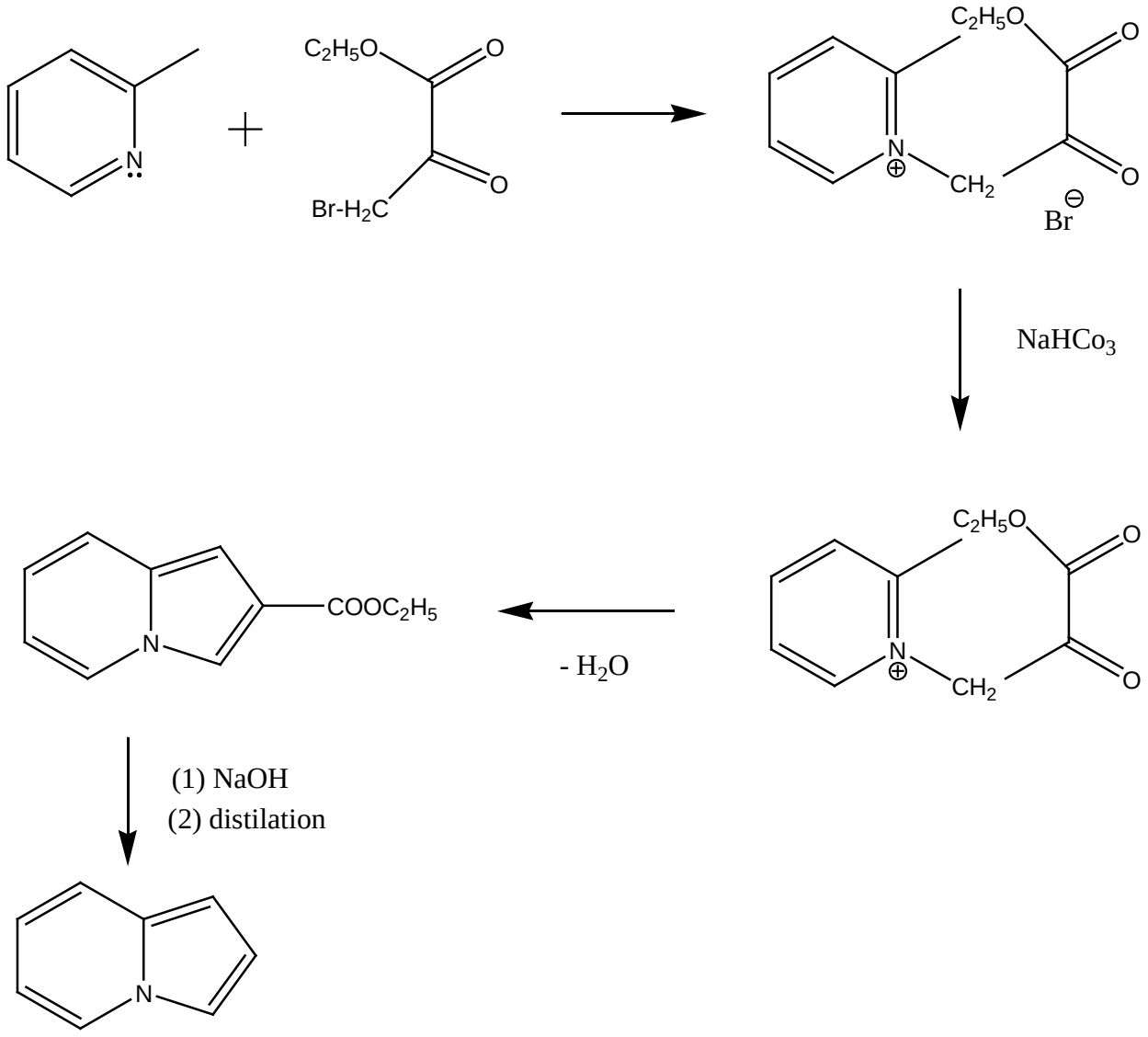
Resonating structure :-



synthesis :-

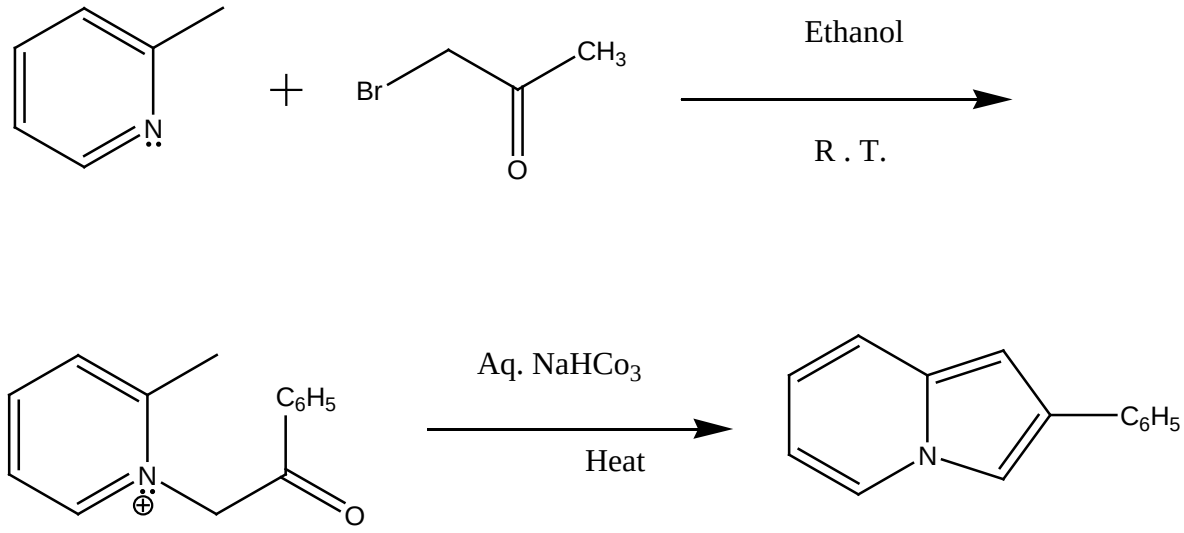
1. From α – Picoline :-

This is one of the elegert method involving reaction of substituted pyridine with an active methylene carbonyl compound a base .

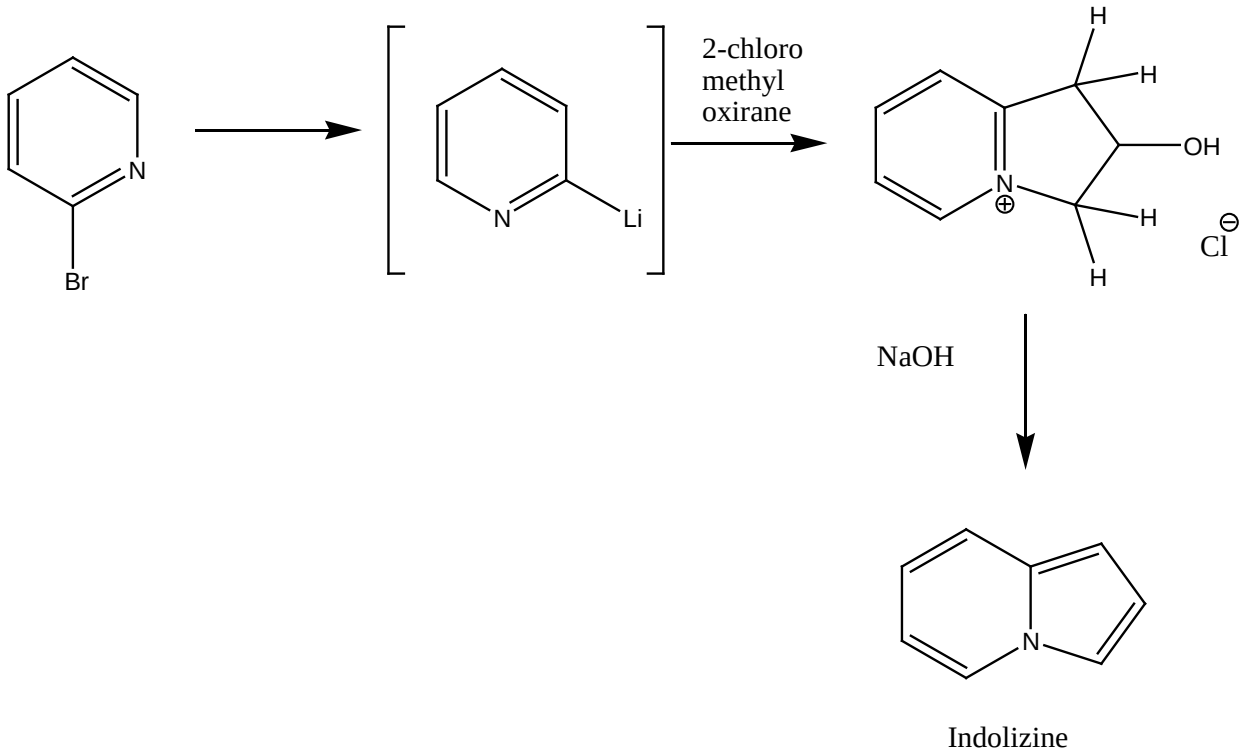


Indolizine

2. It involves the reaction of α – bromoacetophenone in ethanol with α- picoline to yield which on subsequert cyclisation in the presence of a base , furnishes 2 – phenylindolizine.



3. one of the most useful preparation of indolizine consists of a reaction between 2- pyrillithium and 2-chloromethyloxirane. A salt is produced which on treatment with NaOH yields the parent compound indolizine.

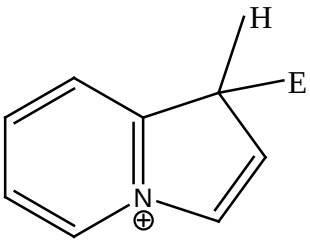


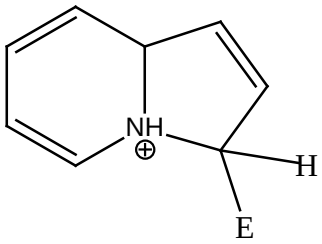
Indolizine

Chemical property :-

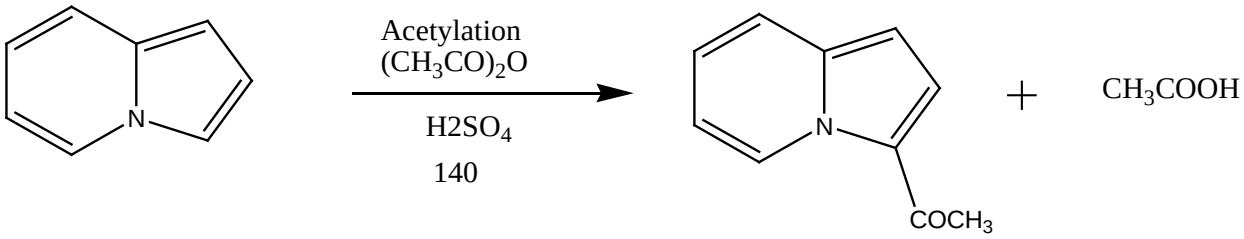
Indolizine is a weak base and protonates mainly at position – 3. the electrophilic attack takes place at C – 1 and C – 3 as the cations as under

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

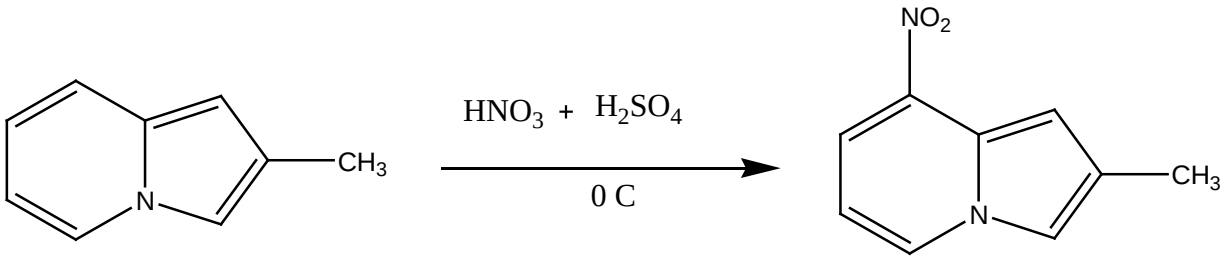




1. Acetylation :

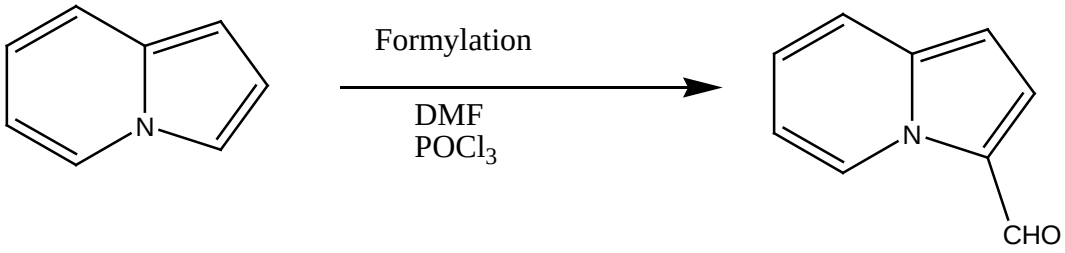


2. Nitration :

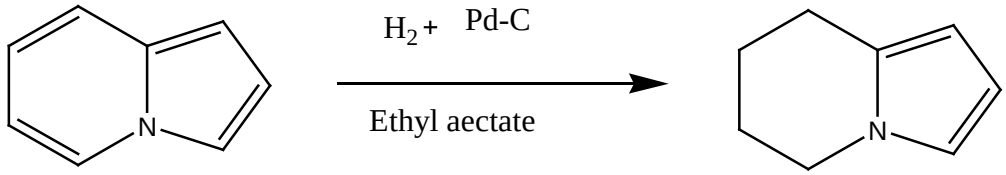


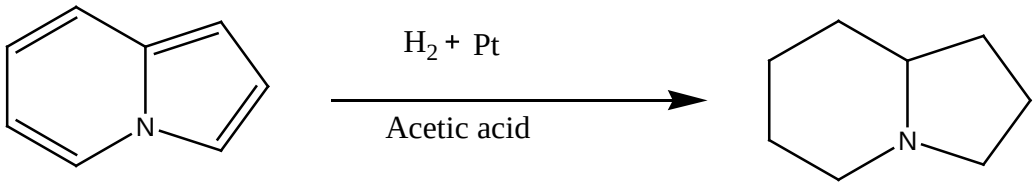
60%

3. Formylation :


Formylation
DMF
POCl3
N
N
CHO

4. Reduction :


H2 + Pd-C
Ethyl aectate
N
N


H2 + Pt
Acetic acid
N
N

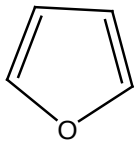
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

FURAN

INTRODUCTION

- In 1860 oxidation of furan with silver oxide to formed 2-furoic acid
- In 1870 barium furate heated with sodalime to formed furan

structure



IUPAC NAME :-1-oxo-cyclo butane

PHYSICAL PROPERTIES

1) furan is colourless liquid
2) odour like chloroform
3) It is soluble in most of organic solvent
4) boiling point is 31.5

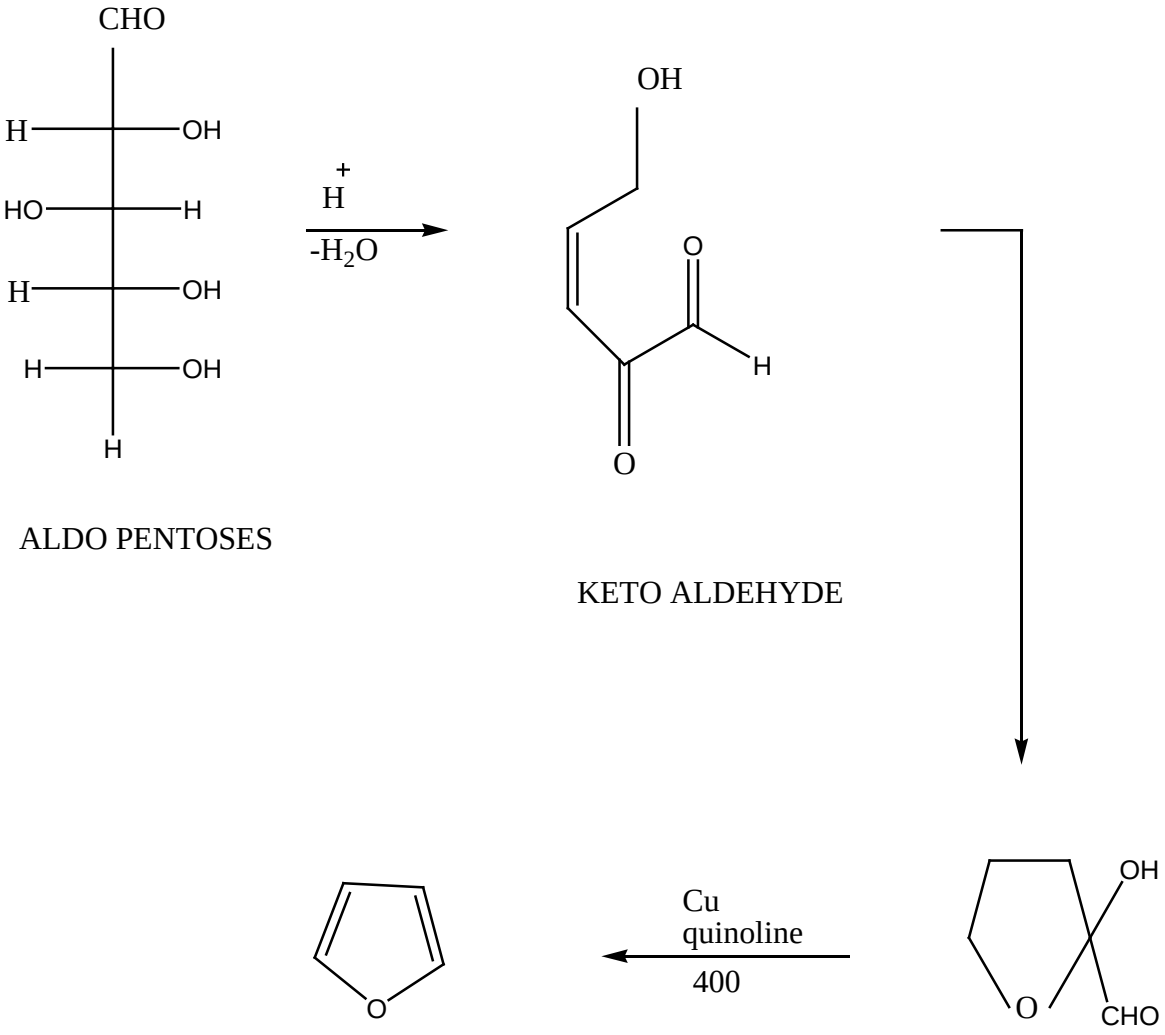
SPECTRAL DATA

UV spectral(nm)	:- 208(3.90)
H_1 NMR	:- C_2-H,C_5-H;(d) 7.29
	C_3-H,C_4-H;(d) 6.24
C^{13} NMR	:- C_2,C_5; 143.6
	C_3,C_4; 110.4

SYNTHESIS

1) FROM CARBOHYDRATES :-

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



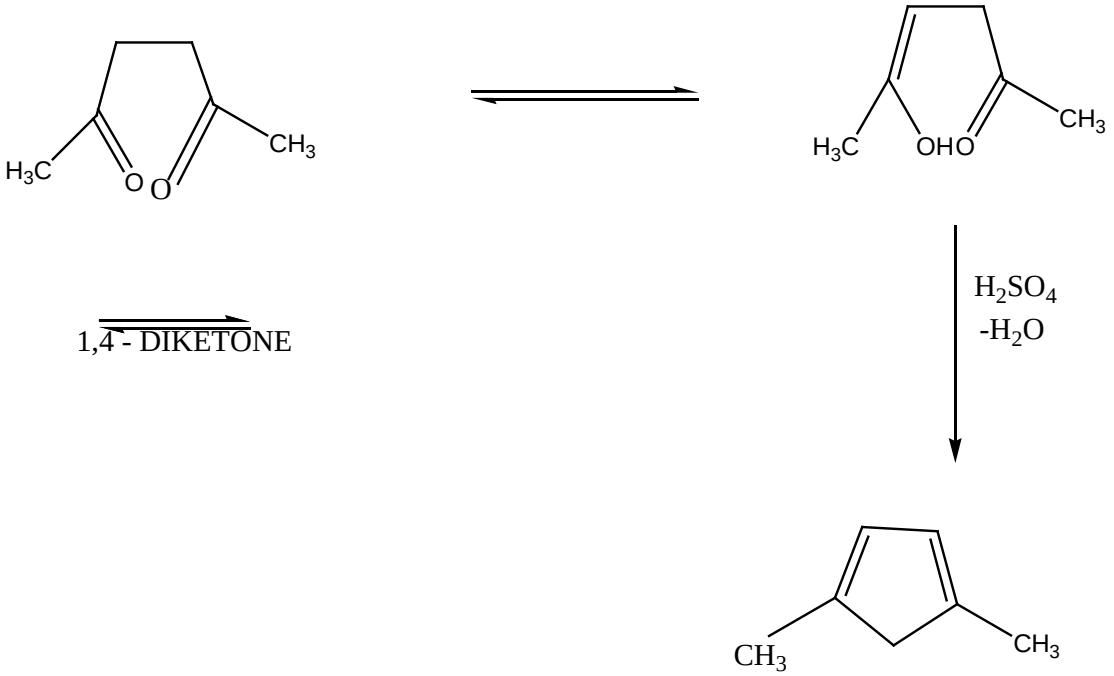
ALDO PENTOSES

KETO ALDEHYDE

FURAN

- Carbohydrates involving the acid catalysed dehydrate to aldopentoses or keto pentoses
- to formation of keto aldehyde
- It is steam distillation in the presence of copper and quinoline at 400 c furance to furan

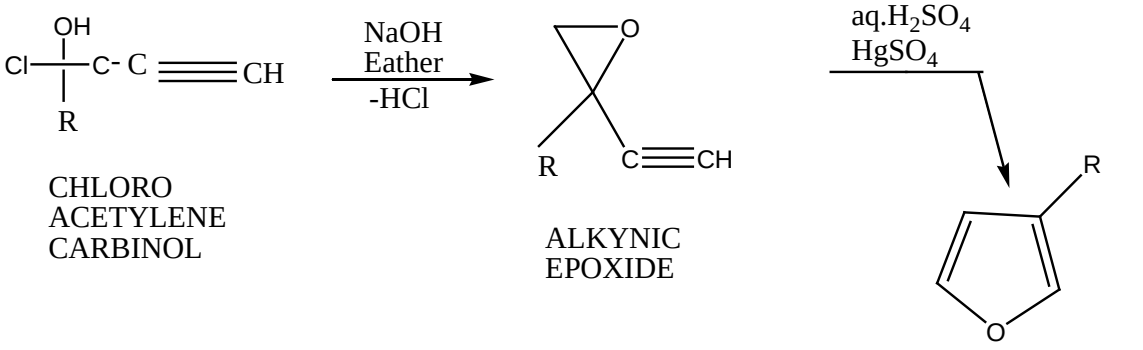
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



1,4 - DIKETONE

FURAN

3)



CHLORO
ACETYLENE
CARBINOL

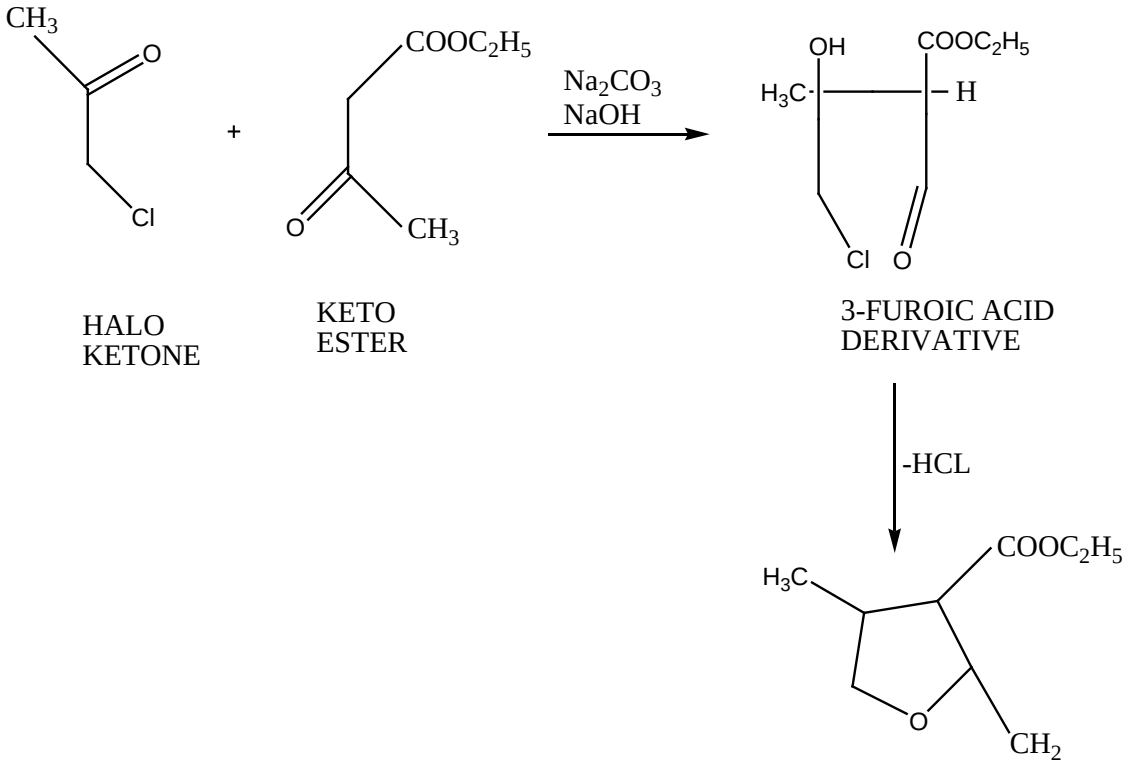
ALKYNIC
EPOXIDE

3-SUB.FURAN

⇨ Chloro acetylenic carbinol lead to formation to alkynic epoxide.

⇨ Alkynic epoxide react with aq.H_2SO_4 and mercuric sulphate to furan.

4) FEIST - BENARY CYCLISATION :-



HALO KETONE

KETO ESTER

3-FUROIC ACID DERIVATIVE

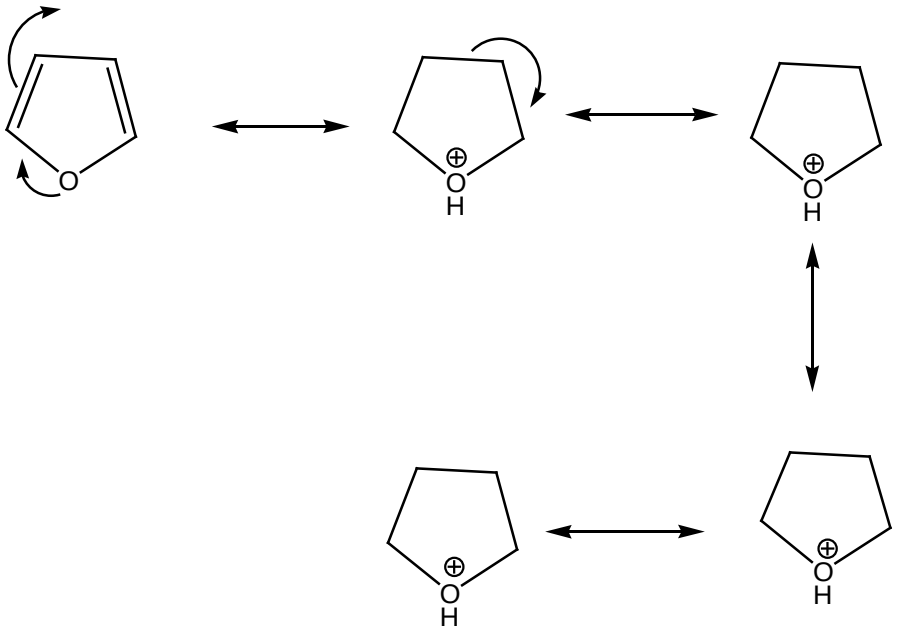
2,5 - DISUBSTITUTED FURAN

⇨ Halo ketone and keto ester react with sodium carbonate and sodium hydroxide to 3-furoic acid derivative

⇨ To remove HCl to 2,5 - disubstituted furan

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

RESONATING STRUCTURE :-



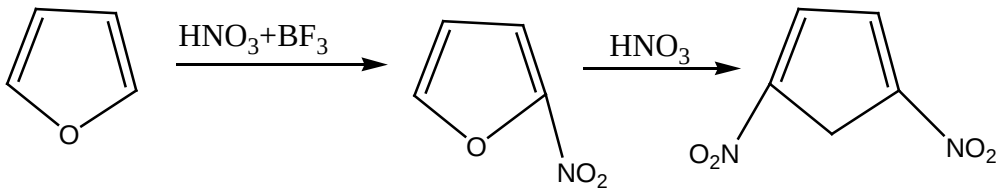
⇨ Lone pair of oxygen atom is donated by the ring carbon atoms.
Resonating energy :- 15.8 k.cal/mole.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Chemical properties

Electrophillic Reaction:-

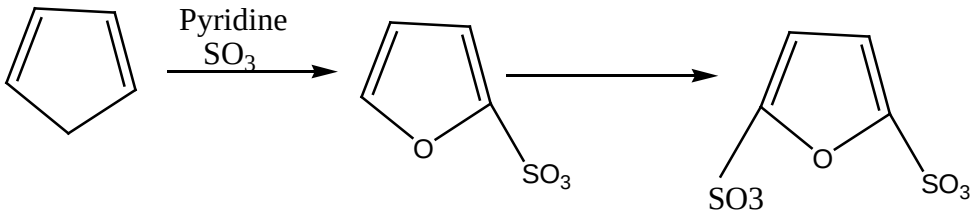
1) Nitration:-



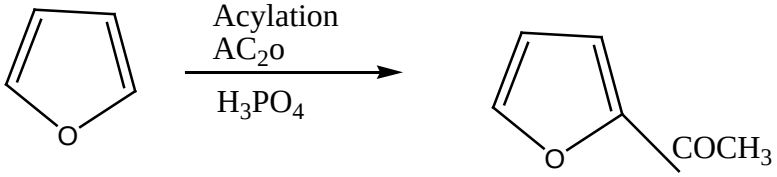
2-NITRO FURAN

2,5-DINITRO FURAN

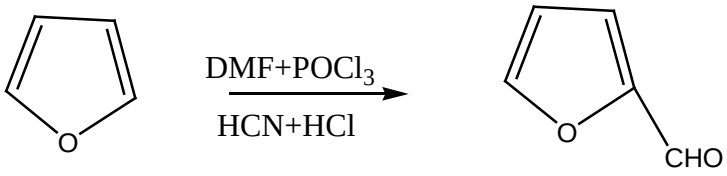
2) Sulphonation:-



3) Acylation :-

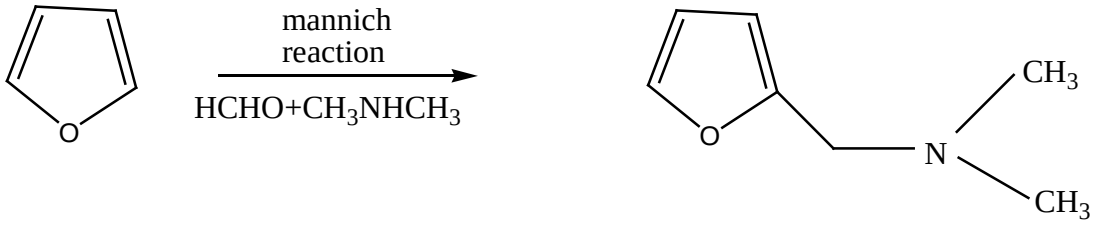


4) Vilsmeir - Haack Formylation :-



FUR FURAL

5) Mannich Reaction :-

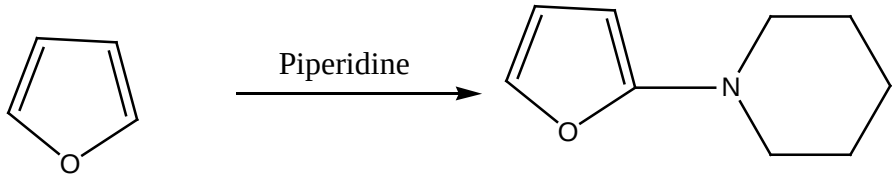


DIMETHYL AMINO
METHYL FURAN

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

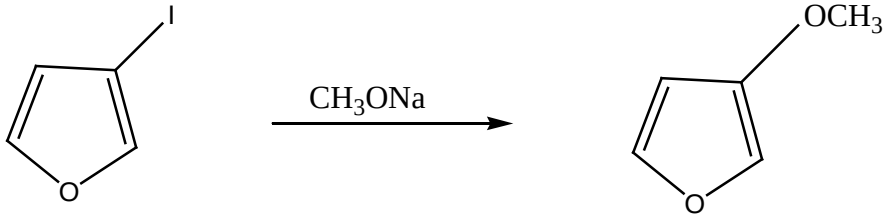
Nucleophilic Reaction :-

1)



2- Piperidine furan

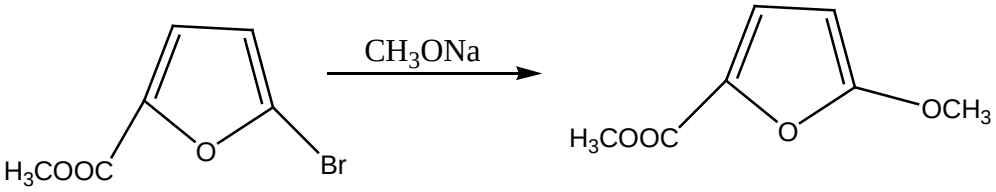
2)



3-Iodo furan

3- methoxy furan

3)



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Name: Kadvani Roshani N.

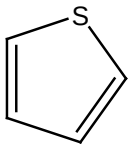
M.Sc. sem 3

C-303: Hetrocyclic compound

Roll No: 18

Topic : Thiophene

THIOPHENE



1-THIOL

THIOPHERE WAS DISCOVERED BY VICTOR MEYER IN 1882 AS A CONTAMINANT IN COAL TAR DISTILLATES OF BENZENE.

Thiophene and its derivatives occur in petroleum to the extent of 1 to 3% the xcontent of oil and coal is removed via hydrodesulphurization process

Thiophene ring system is incorporated in many natural products.

e.g = biotin (vitamin H) and pharmaceuticals.

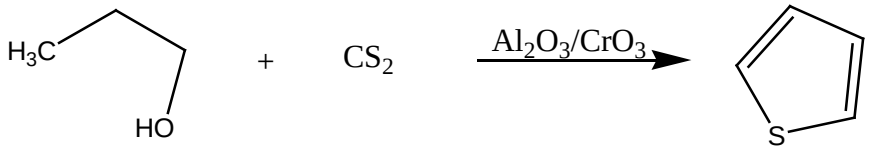
Physical properties

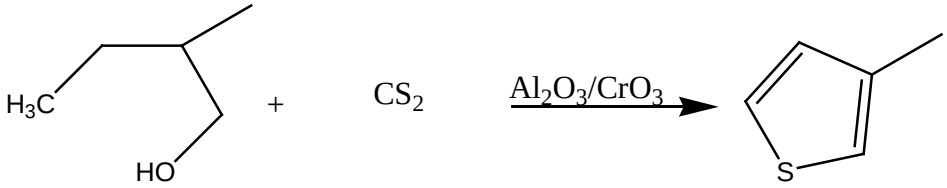
- Colourless liquid
- B.P. 84^0c M.P. -38.3^0c
- Planner molecule with sp^2 hybridisation
- The six π electrons in thiophene ring forms a sextet form 4π electrons of the 4 carbon atoms and two electrons of sulpur atom.

Synthesis

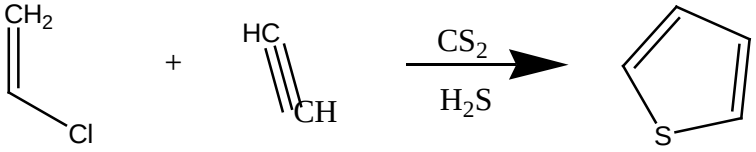
1. Croda synthesis:

The reation of CS_2 with butenol,2-methyl butenol,mixture of vinyl chloride and acetylene results



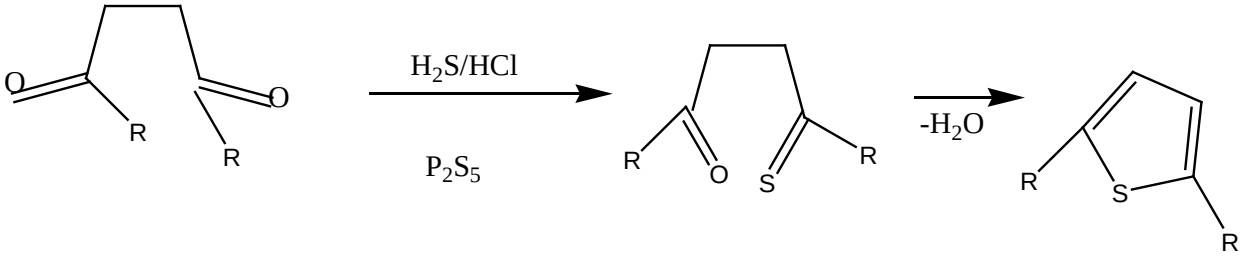


information of thiophene.



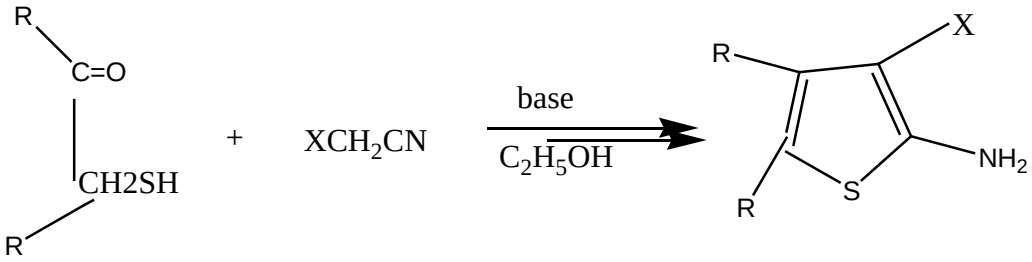
2.Paal synthesis:

1,4 dicarbonyl compound in presence of P_2S_5 to give thiophene derivative.



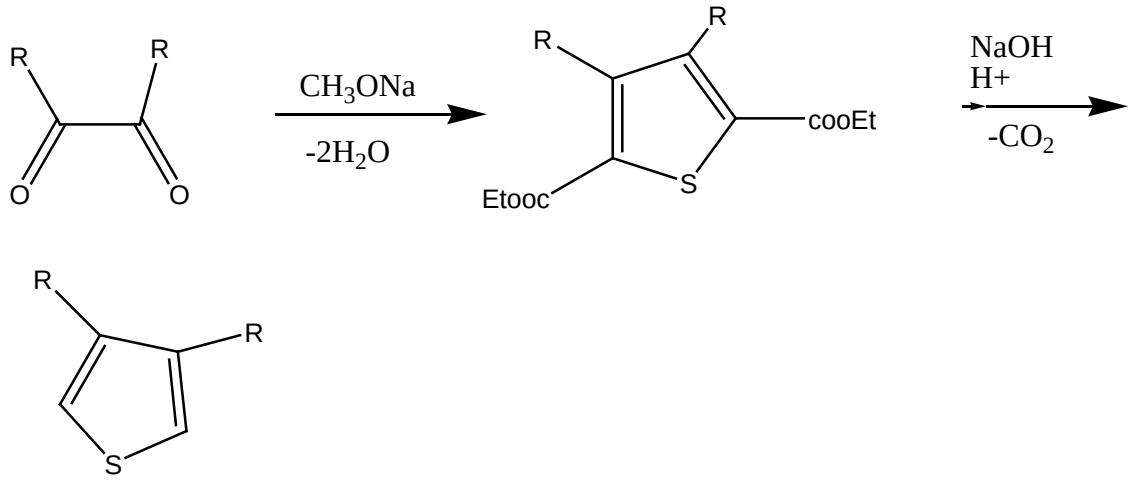
3.Gewald synthesis:

The reaction of α-mercapto ketone with activated methylene nitrilein presence of base togive 2-amino thiphene.



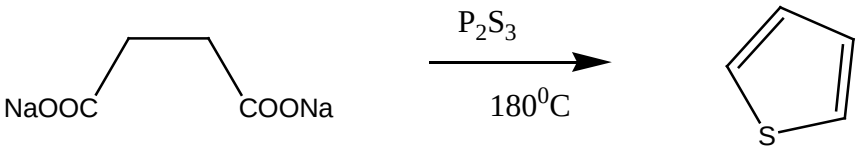
4.Hinsberg synthesis:

1,2-dicarbonyl com. On condensation with 3-thia penanedioic acid ester in presence of basic catalyst provide thiphene carboxylic ester. It involves a double aldol condensation. Hydrolysis and decarboxylation furnishes 3,4-disubstituted thiphene.

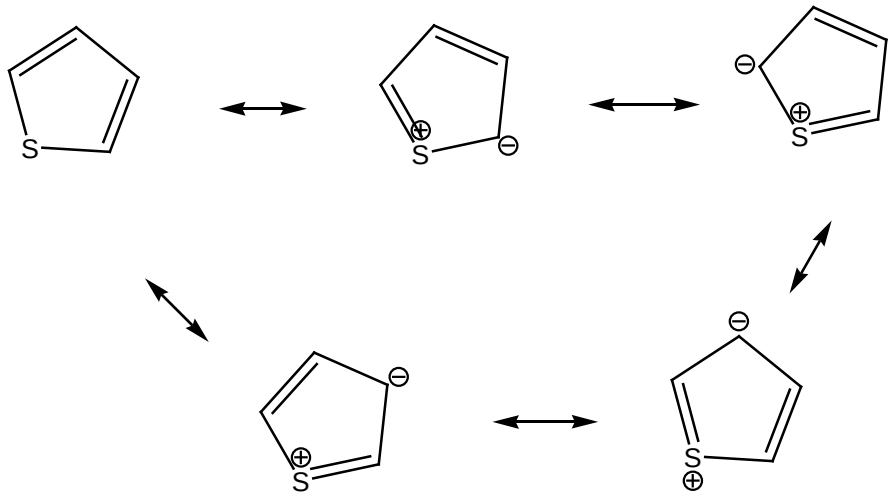


5.From sodium succinate:

Heating a mixture of sodium succinate and phosphorous trisulphide gives thiophene.



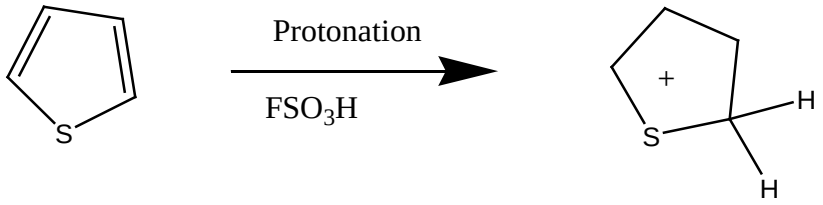
- Resonating structure:



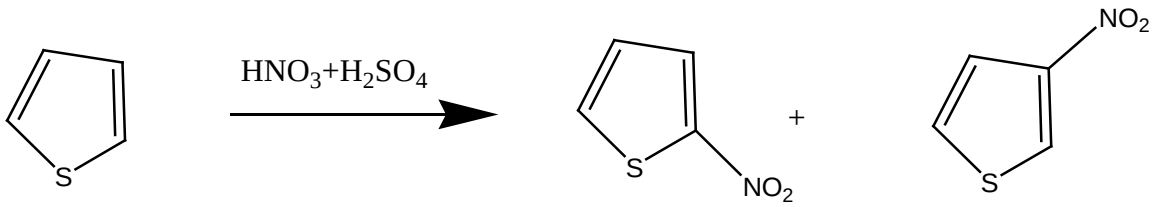
- Chemical properties:
  1. Electropilic substitution:

     Electropilic substitution takes places at 2 & 5 position.

- Protonation



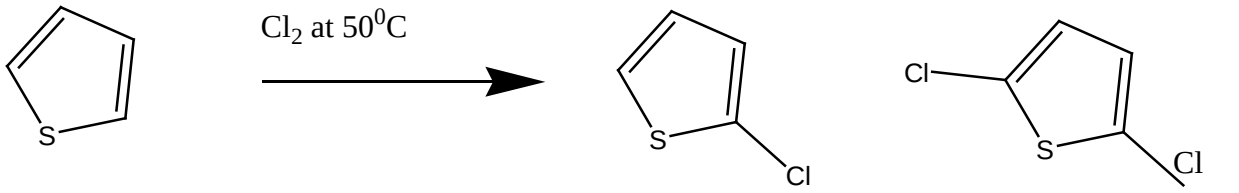
- Nitration:



95% 5%

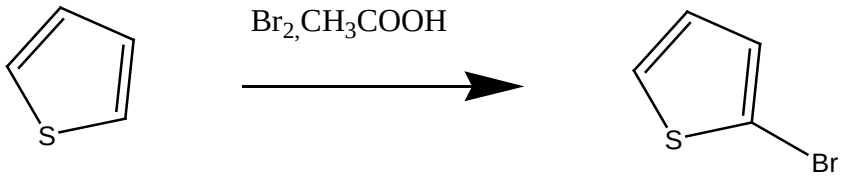
- Halogenation:

Chlorination:



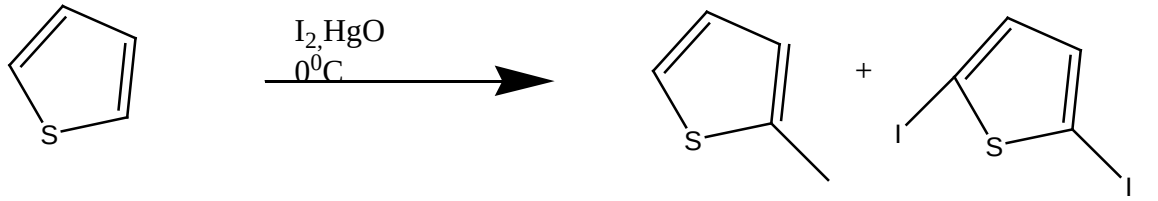
2-Chlorothiophene 2,4-Dichlorothiophene

Bromination:



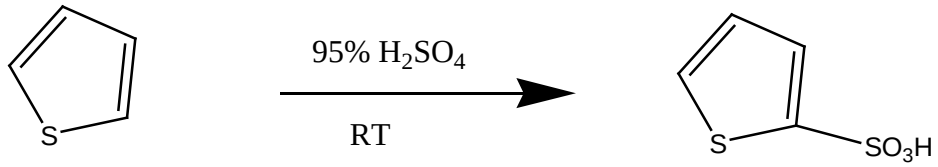
2-Bromothiphene

Iodination:



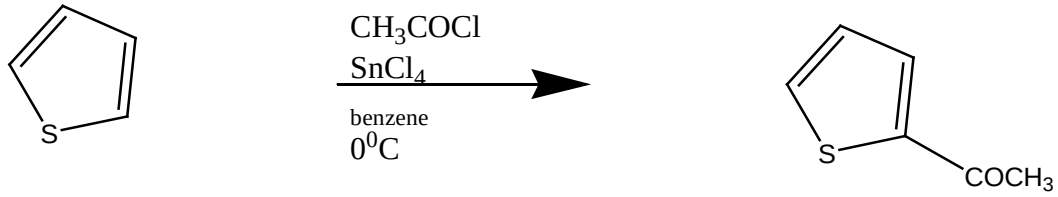
2-iodothiphene 2,4-diiodothiophene

- Sulphonation:



Thiophene-2-sulphonic acid

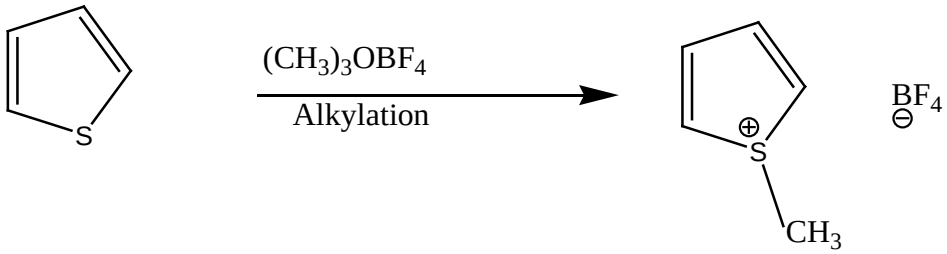
- Acylation:



2-Acetyl thiphene

- Electrophilic attack at S atom:

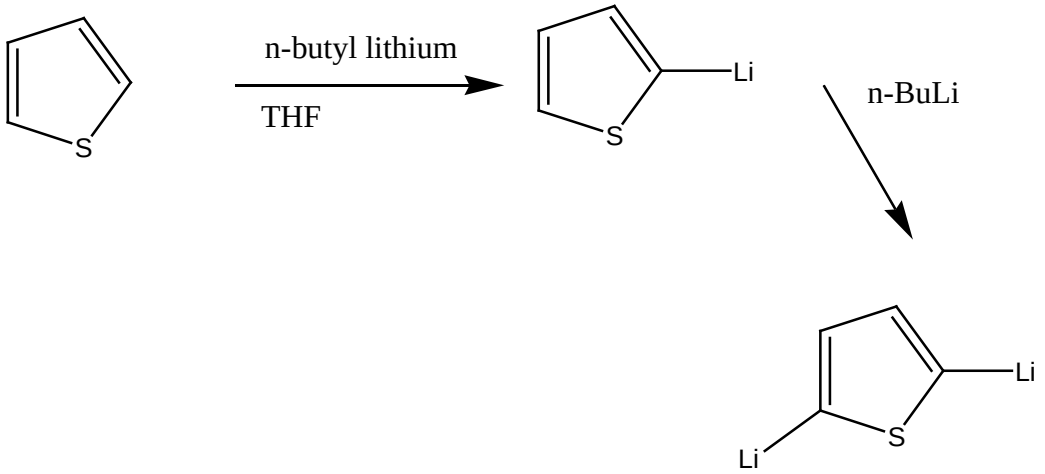
Alkylation:



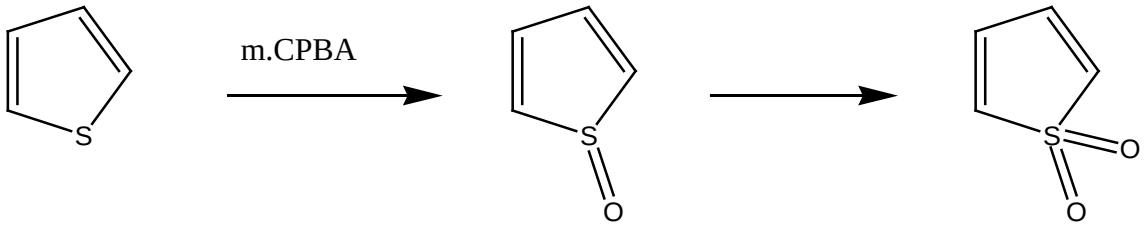
- Nucleophilic Reactions:

Nucleophilic reaction should be less effective in thiophene.

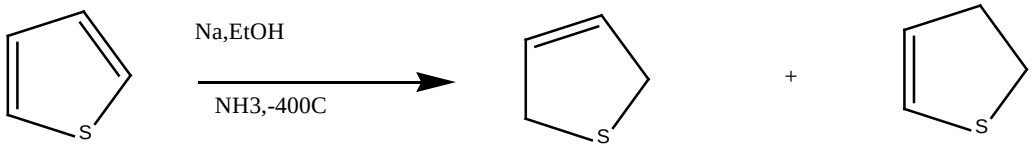
thiophene react with n-butyl lithium.



- Oxidation Reaction:

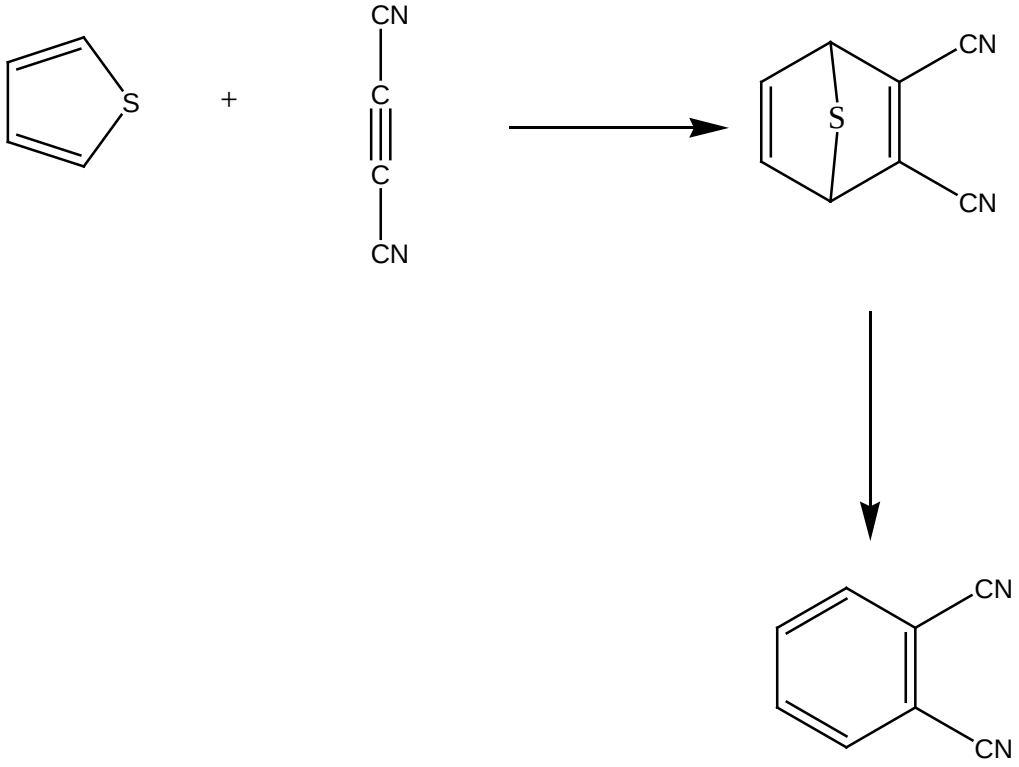


- Reduction reaction:



- Cyclo addition reaction (Diels alder reaction):

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

NAME: KALVAT MAHAMADATIK N.

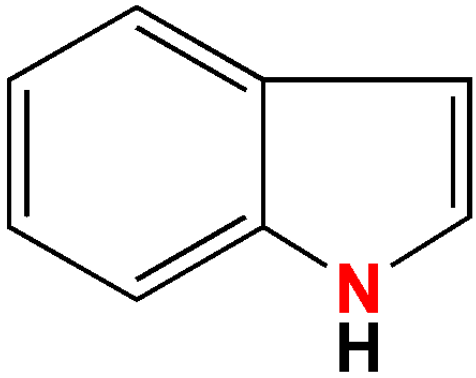
ROLL NO : 19

SUBJECT: HETEROCYCLIC SEMINAR

TOPIC: BENZOPYRROLE OR INDOLE

SUBMITTED TO : PROF. V.H.SHAH- SUDOC

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



benzopyyrole/Indole

Other name: (1)ketole

(2)2,3 benzopyyrole

(3) 1-benzopyyrole

Introduction:

The name of indole was derived from word india.in 16th century a blue dye is imported from india known as indole and further indigo.which treated with indigo dye and oleum.

Indigo are most occurring heterocyclic compound in nature

Exa: tryptophane is essential amino acid is indole derivative.

It is aromatic hetero cyclic compound consisting a 6 member planner benzene ring with fused with 5 member pyrole ring.

It is a common fragrance & precursuor to many pharmaceutical .it is a major constituent of coal tar and essential oil(jasmine oil)

Physical properties:

➡ It is a colourless solid,crystalline compound

m.p: 52 c & 254 c

soluble in organic solvent

pure indole is very pleasant smelling compound while impure indole is unpleasant smelling compound

molecular formula yet not clear

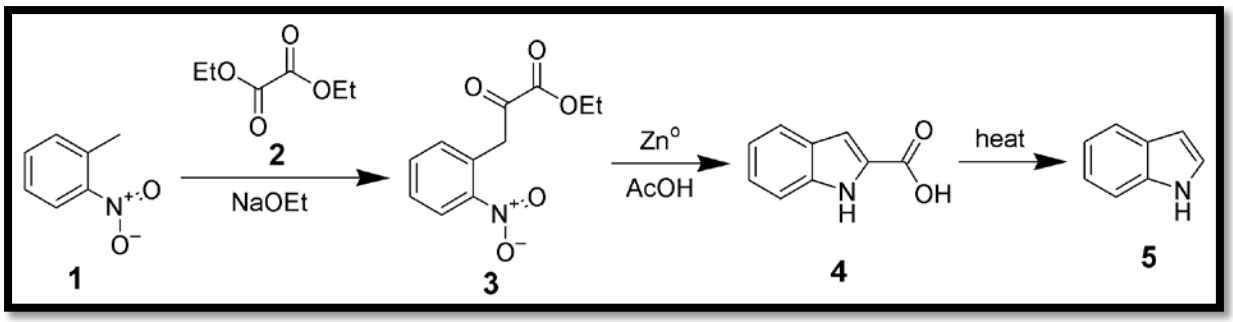
planner 10pie ster

reso ene : 47-49 k/cal mole

synthesis:

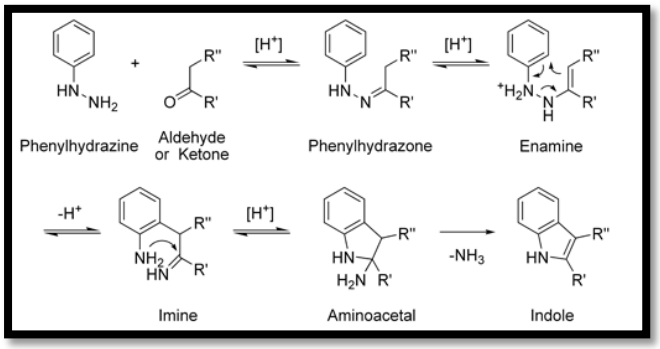
1: reissert indole synthesis:

The indole is synthesized by o-nitro toluene with diethyl oxalate in presence of sodium ethoxide to give o-nitrophenyl pyruvic acid foowed by reduction cyclisation to give indole



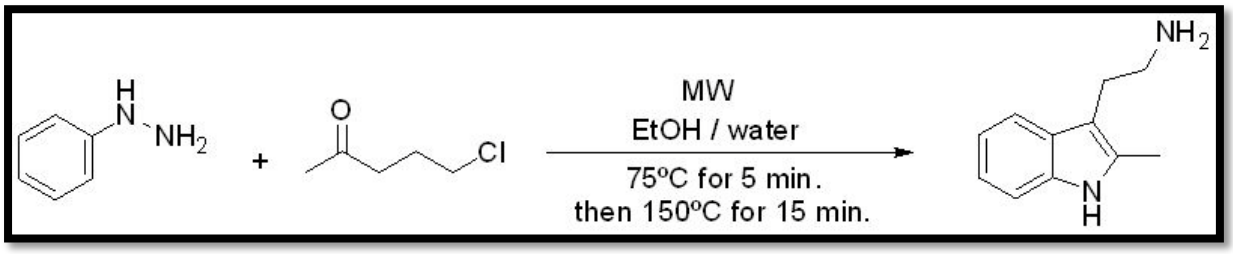
(2) Fischer indole synthesis

First discover by emil fischer in 1883.it is oldest & most reliable route for synthesis of indole.it involve reaareangement of arylhydrazone derived from aldehyde or ketone by an catalyst or heating.



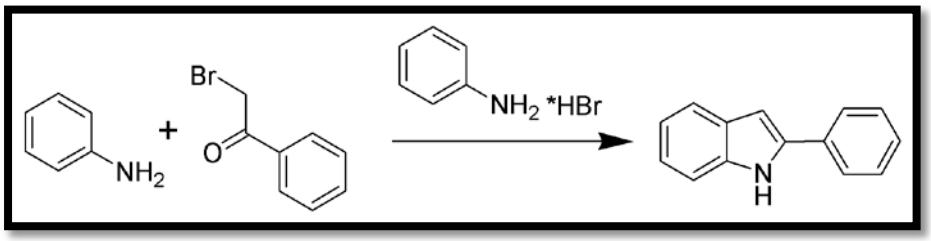
(3) grandberg synthesis:

Tryptamine is synthesized by interaction of 4- halobutane or its acetate with phenyk hydrazine in ethanol as reflux at room temp.



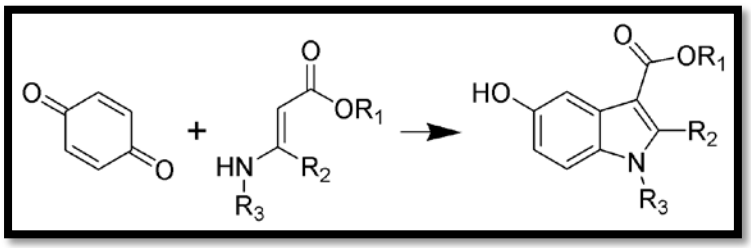
(4) Bischler mohlau synthesis:

This reaction is so lar least attention due to harsh reaction condition.the condensation of aryl amine with n-halogenated ketone in poresence of acid formation of indole.



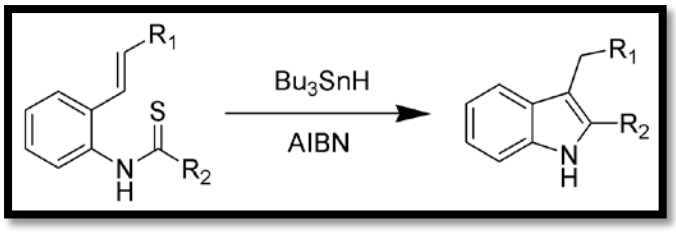
(5) Nenitzescu synthesis:

It involve the preparation of 5- hydroxyl indole by condensation of p-benzoquinone with beta amino crotonic ester (enamine) .

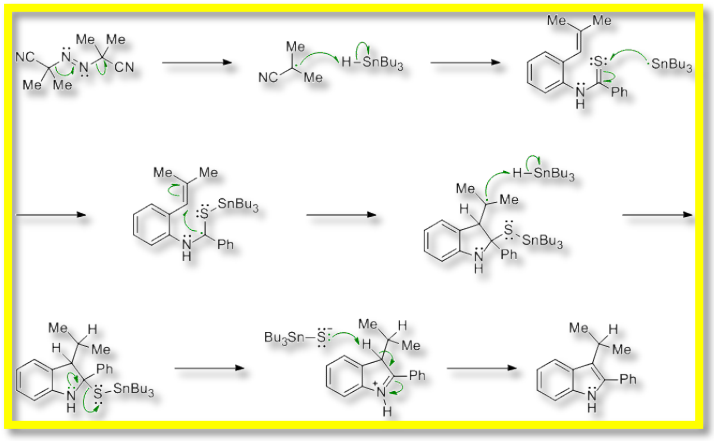


(6) Fukuyama synthesis:

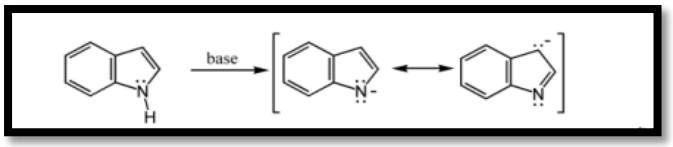
It is a free radical cyclisation of o isocyano cinnamic ester(styrene deri) with tri N- butylin hydride in acetone nitrile at 100 c to give 2-staanylindole derivative which hydrolysed to 3 acetic acid indole .



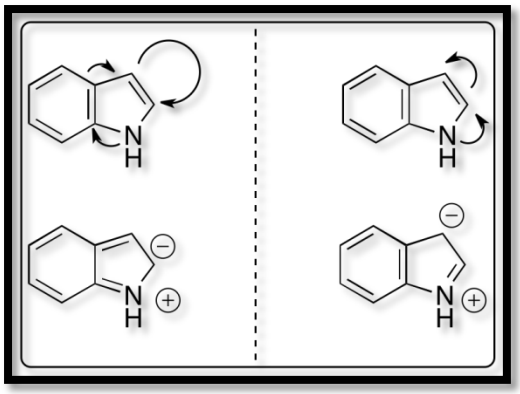
Mechanism:



Resonating structure of indole:



Resonating structure:



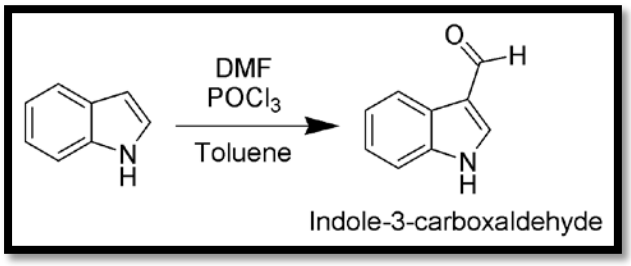
Chemical properties:

(1) Electrophilic reaction:

Indole is very less reactive compare to pyrrole.it is compaitible to electrophilic substitution reaction due ti its 14 ppie electrone at c2 and c3 position.but c3 is more dominant site.

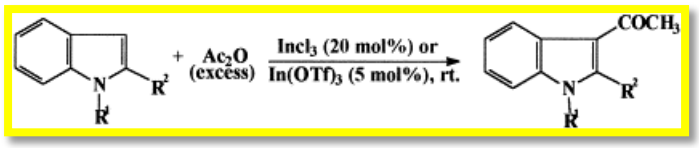
Formylation :

By reaction of vilsmeier hack formylation its takes place at c3 postion



Acylation

Acylation take place at c3 position also.

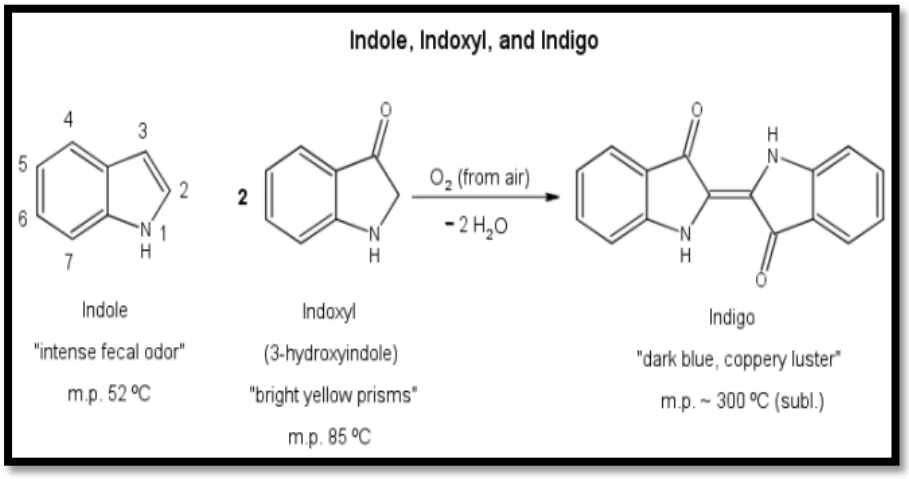


Nucleophilic substitution reaction:

Indole resistance to nucleophilic substitution reaction due to its 10 pie electrone.but it also obtain in small amount with presence of electrone withdrawing group. At c2, c4, and ,c7 position.

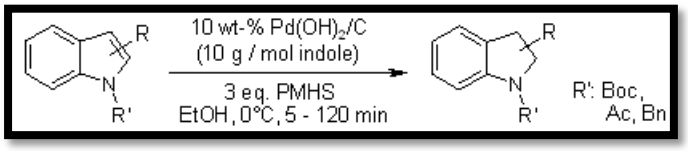
Oxidation:

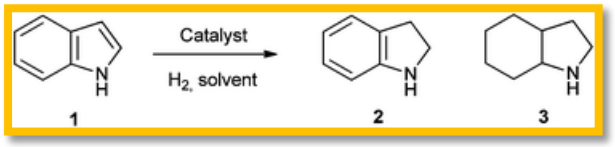
Indole undergoes oxidation with h2o2 to produce at indoxyl 3-hydroperoxy indole.indoxyl on deprotonates at 2nd position provides stabilised free radical which on dimerization give indigo.



Reduction:

On reduction with sn metal it gives indoline and octahydroindole

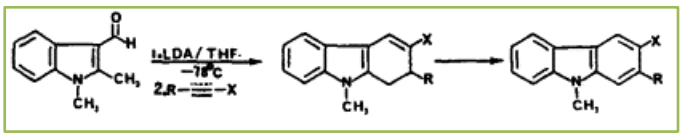




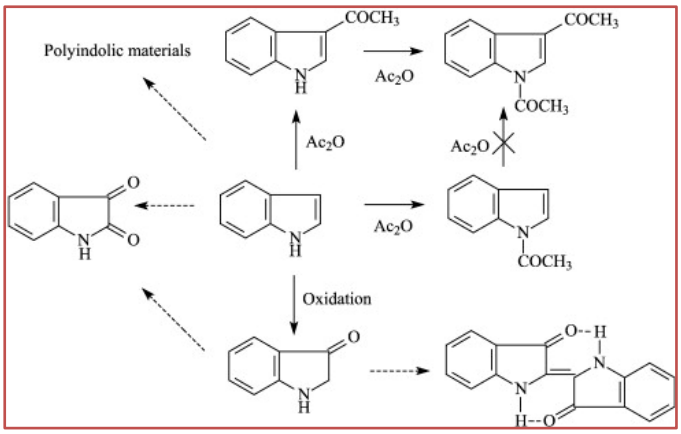
Octahydroindole

Cycloaddion reaction:

Indole on cycloaddition reaction with indole to give dihydroxy carbazole derivative.(alkyne as a reactant).



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

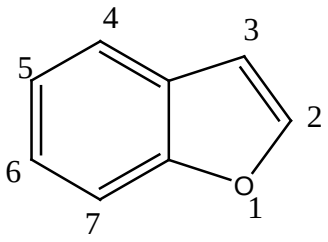


Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

-::BENZOFURAN::-

¤ Structrul Information and Introduction:-

--> It was first prepared by peskin in from coumarin,is known as coumasone.

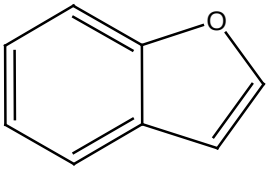


BENZOFURAN

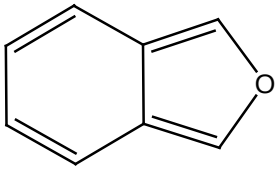
→ The compound was isolated by distillation of bituminous coal as picrate**.**

→ It is used for the preparation of synthetic resin,which is known as "COUMARONE RESIN".

→Two isomeric forms of benzofuran are known i.e. benzo[b]furan and benzo[c]furan. Benzofuran ring system is present in many natural products of pharmaceutical importance.



BENZO[b]FURAN



BENZO[c]FURAN

¤ Physical Property:-

→ Benzofuran is a colourless oil.

→ B.P. = 173 ^{O}C

→ it is water insoluble.

¤ Spectal Data:-

UV,λ_{max}(heptane)nm: 239.5(4.03), 240.5(4.03), 244.5(4.04), 250.5(3.91), 271.0(3.25), 269.0(3.23).

^{1}H NMR δ_{ppm}: C_2-H=7.78; C_3-H=6.76; C_4-H=7.63; C_5-H=7.23; C_6-H=7.30; C_7-H=7.50

^{13}C NMR δ_{ppm}: C_2=145.1; C_3=106.9; C_4=121.6; C_5=123.2; C_6=124.6

C_7=118.8; C_{39}=127.9; C_{79}=156.5.

¤ Synthesis:-

(1) From coumarins,

(2) From salicylaldehyde,

(3) Claisen rearrangement,

(4) Hansch reaction,

(5) From o-Iodophenol,

(6) From o-Acylmethoxysalicyl aldehydes,

(7) From o-Aryl ketoximes,

(8) From Aryloxyacetaldehydes,

(9) From o-hydroxyphenyl acetylene,

(10) From o-iodoanisole.

(1) from coumarins:-

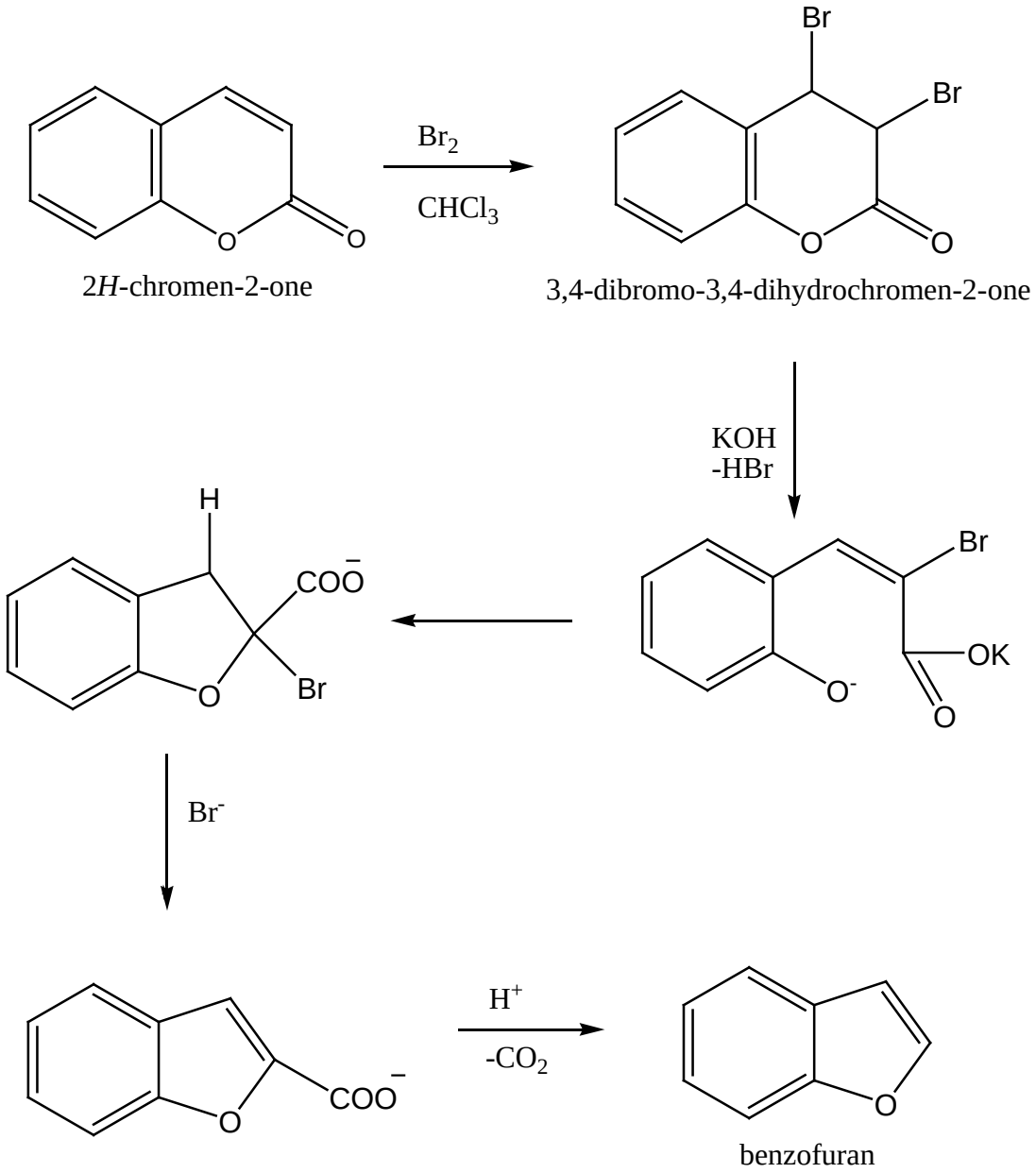
It was first prepared from coumarin by ring contraction involving following sequence of reaction

a)bromination of coumarin in chloroform to 3,4-dibromocoumarin,

b)Action of KOH causing ring opening,

C)cyclisation to form coumalic acid followed by subsequent decarboxylation to yield benzo[b]furan,

d)debromination and de-carboxylation.



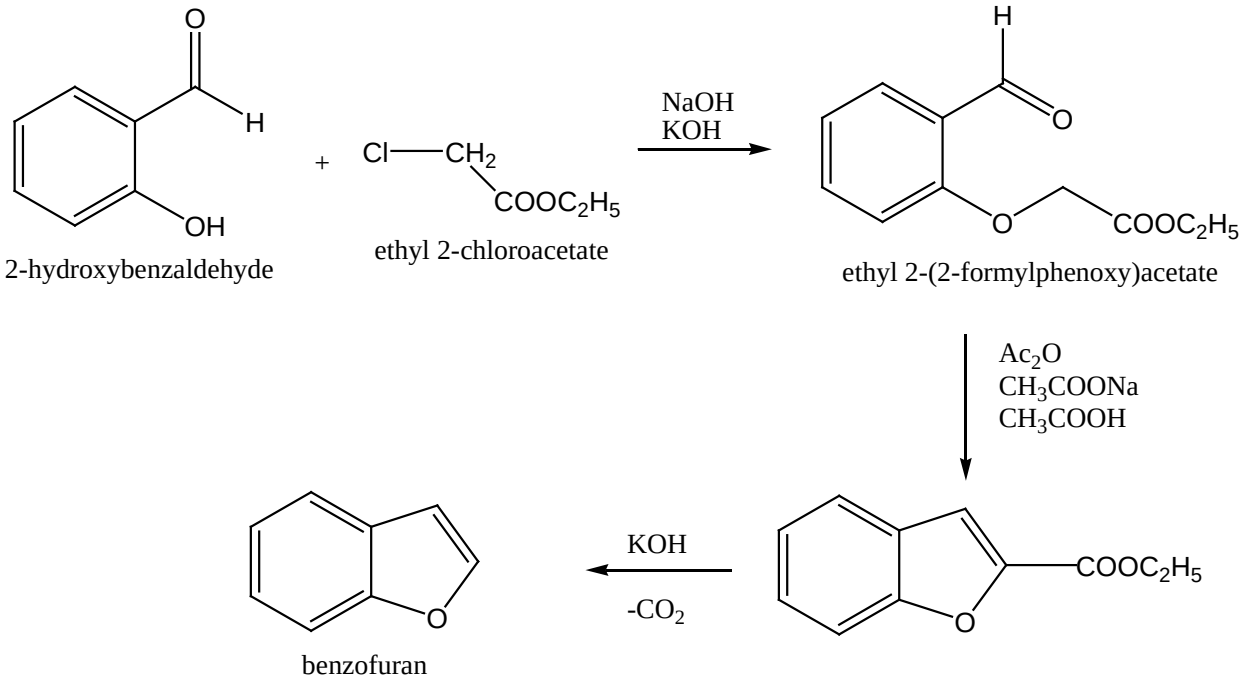
2*H*-chromen-2-one

3,4-dibromo-3,4-dihydrochromen-2-one

benzofuran

(2) From salicylaldehyde:-

→ The synthesis involves reacyion of salicylaldehyde with α-haloketones or esters followed by cyclisation and dehydration wich results in the formation of benzo[b]furan. intramolecules aldol condensation of o-formylasyloxyacetic acid lead to the formation of benzofuran.



2-hydroxybenzaldehyde

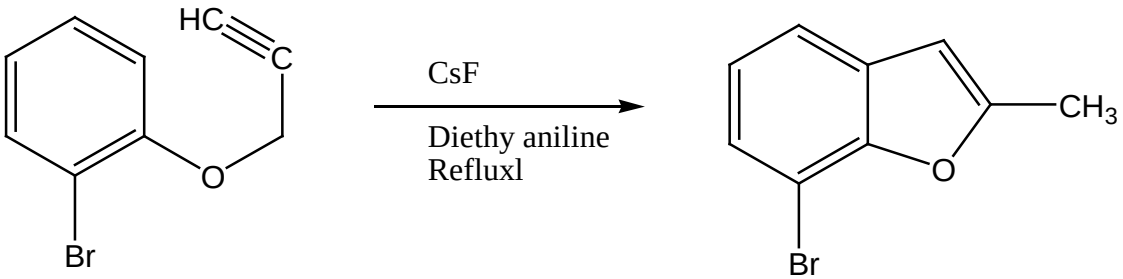
ethyl 2-chloroacetate

ethyl 2-(2-formylphenoxy)acetate

benzofuran

(3)Claisen Rearrangement:-

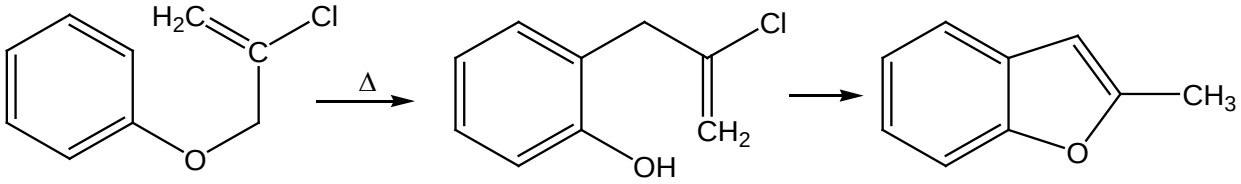
a) Propargyl aryl ether undergoes claisen rearrangement followed by cyclisation to yield 7-bromo-2- methyl benzofuran in the presence of CsF and dimethylaniline.



1-bromo-2-(prop-2-ynyloxy)benzene

7-bromo-2-methylbenzofuran

b) Claisen rearrangement of phenyl-2-chloro propenyl ether also provides 2-methyl benzofuran.



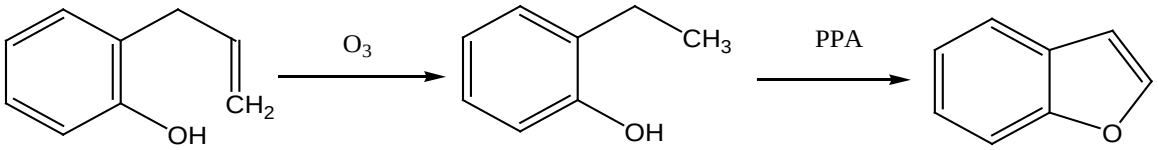
1-(2-chloroallyloxy)benzene → 2-(2-chloroallyl)phenol → 2-methylbenzofuran

(4) Hansch Reaction:-

→ Thering closure followed by cyclodehydrogenation of o-substituted phenols is known as Hansch reaction.

→ The ozonolysis of o-allylphenol results in the aldehyde formation via a claisen rearrangement of the aldehyde compound followed by acid catalyzed cyclisation in the presence of polyphosphoric acid provides benzofuran.

→

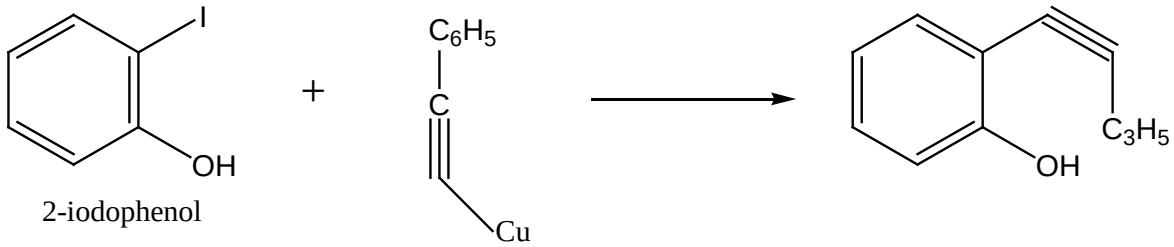


2-allylphenol → 2-ethylphenol → benzofuran

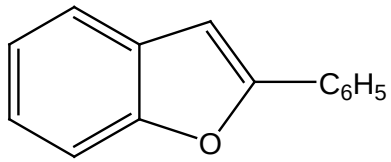
→

5) From o-iodophenol:-

The simple and single step synthesis involves reaction of o-iodophenol with aryl copperacwtylide in DMF at 125^0 c to provide o-hydroxyarylacetylene followed by subsequent cyclisation to 2-phenylbenzo[b]furan.

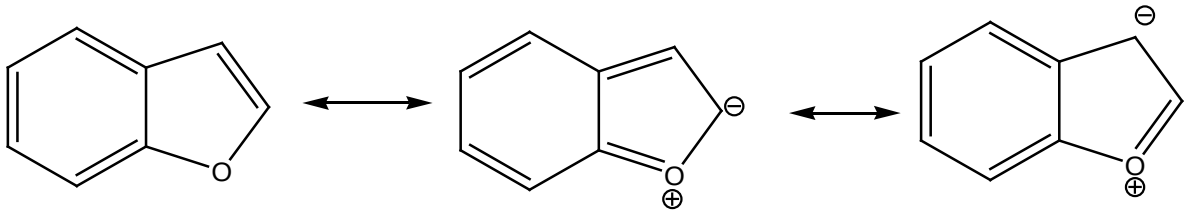


2-iodophenol



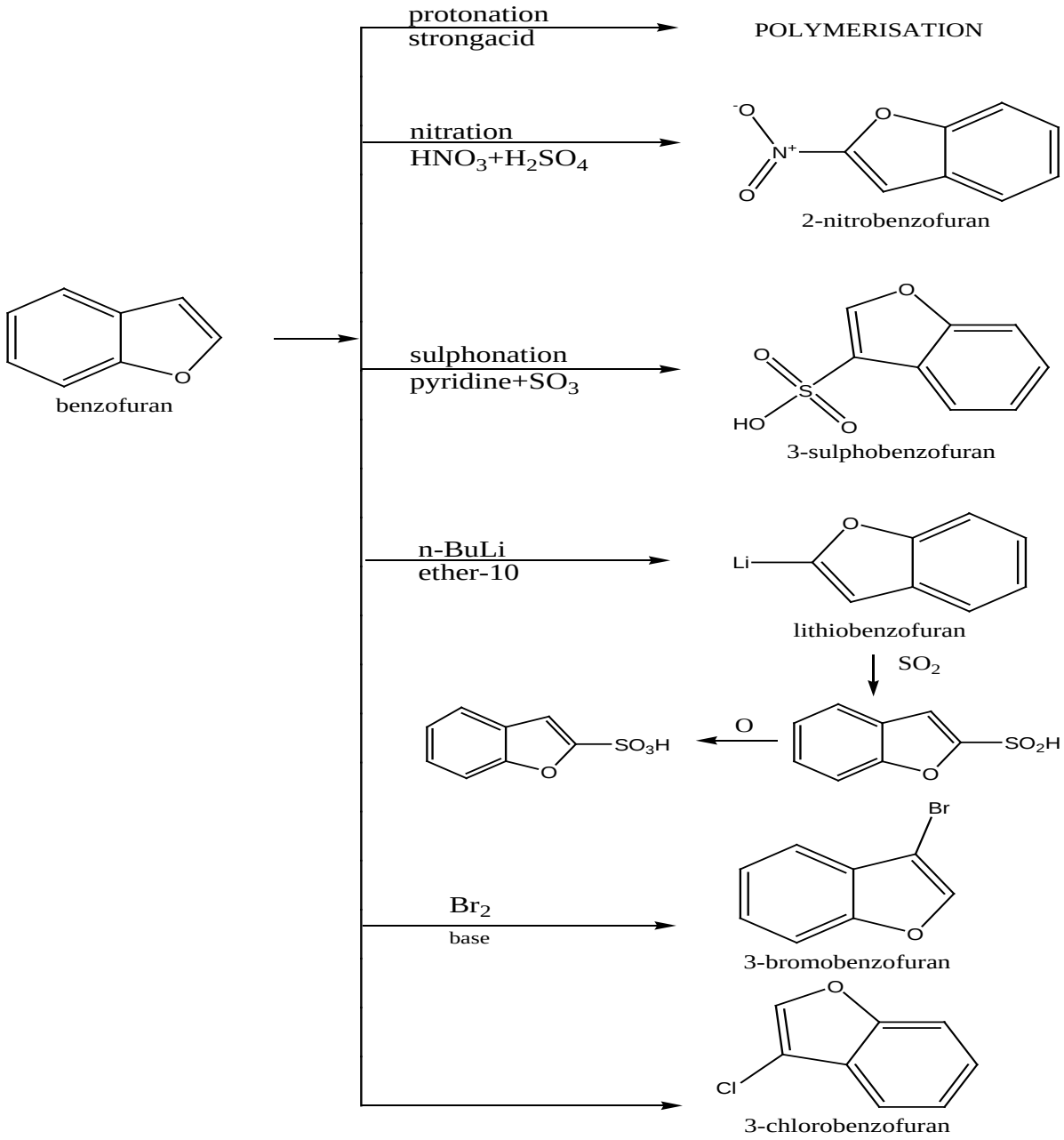
2-phenylbenzofuran

Resonating Structure:-

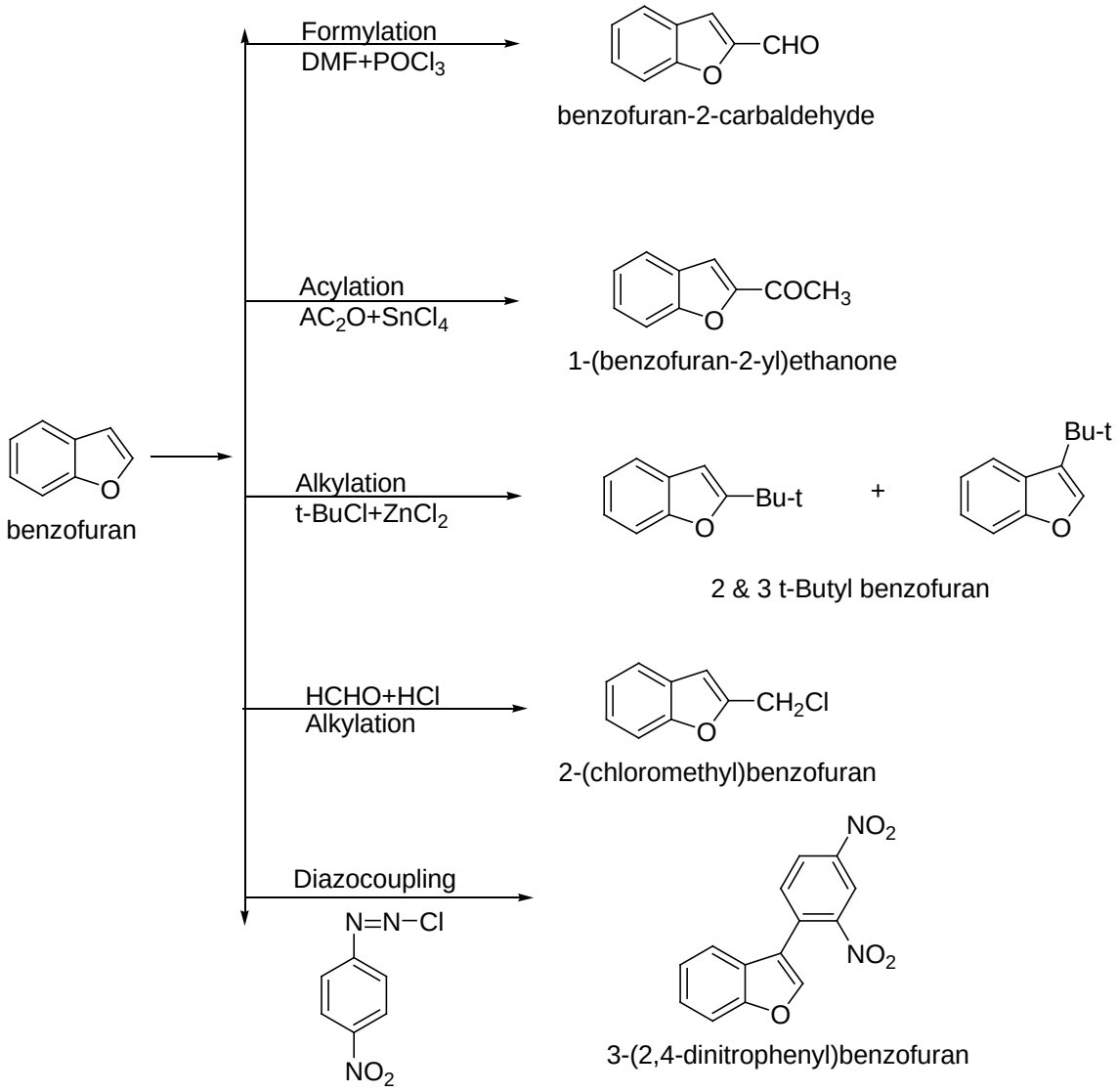


¤ Electrophilic reaction:-

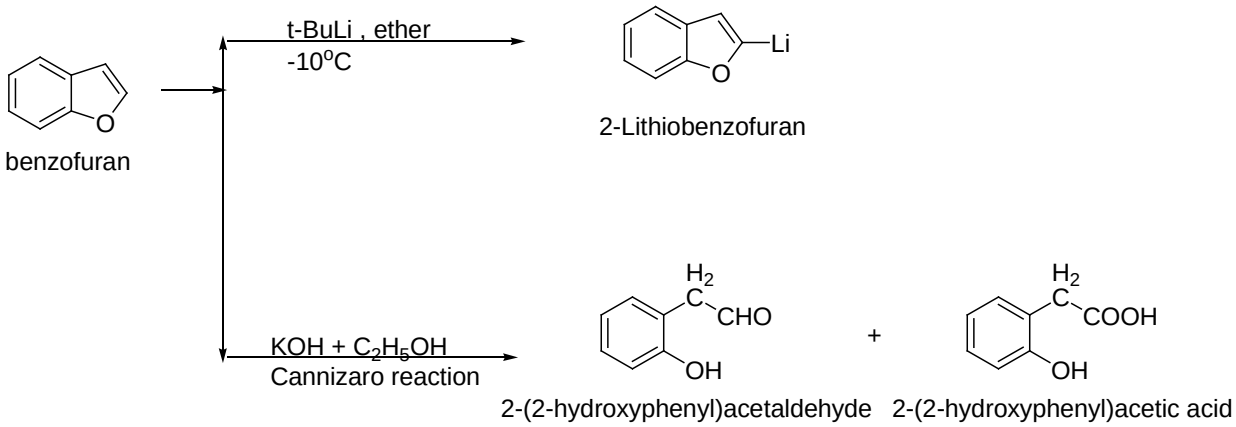
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



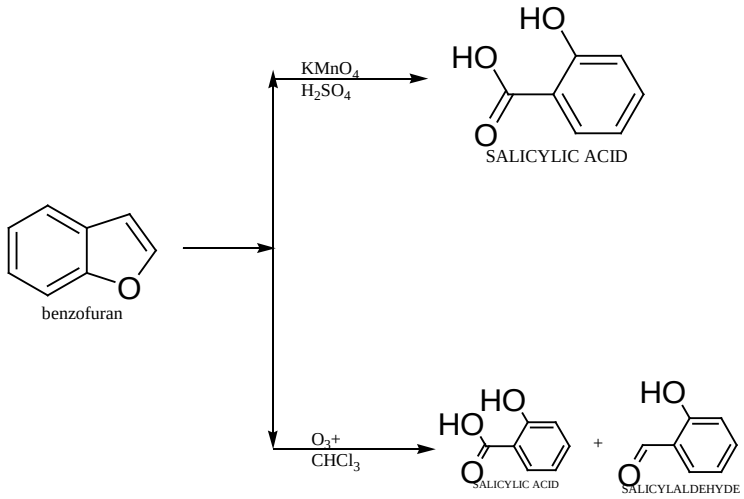
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



 # Nucliophilic reaction:-

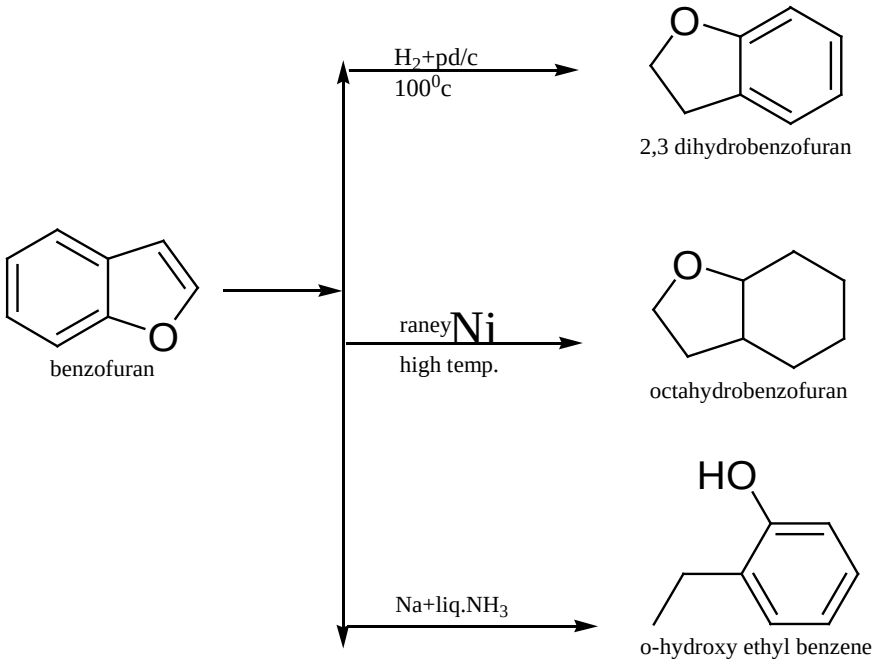


#oxidation reaction:-

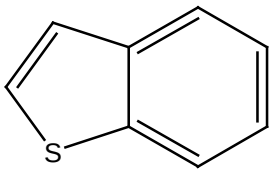


#reduction:-

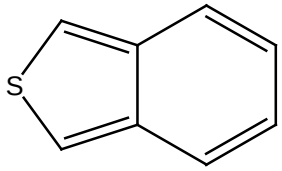
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



❖ BENZOTHIOPHENE



Benzo[b]thiophene
thionapthalene
Benzotiofuran



Benzo[c]thiophene
2-benzothiophene

➢ Introduction

- Benzothiphene was first obtained in 1893
- Benzothiphene being heterocyclic analogue of naphthalene is known as thionaphthalene
- It is available in coal tar, shark oil , crude petroleum and mineral oil

➢ Physical properties

- It is a colorless solid
- It's melting point-32℃ and boiling point - 220℃-221℃
- It possesses a diploe moment of 0.62D which is similar to thiophene
- It is stored in amber colour bottle
- It gives naphthalene like smell

➢ Spectral Data

- UV λmax (heptune)nm: 228(4.45) ; 2.58(3.74);
  263(3.71); 2.81(3.19); 288.5
  290.5(3.33); 297(3.52);
- ' H NMR δppm(CCl_4) : C_2-H , 7.33 , C_3-H , 7.23 ;
  C_4-H, C_5-H, 7.25 C_6-H, 7.23;
  C_7-H
- ^{13}CNMRδppm ($CDCl_3$) : C_2,126.21; C_3,123.79; C_4,123.50 C_5,124.10;
  C_6, 124.17;C_7,122; C_{3a},139.6; C_{7a},139.7

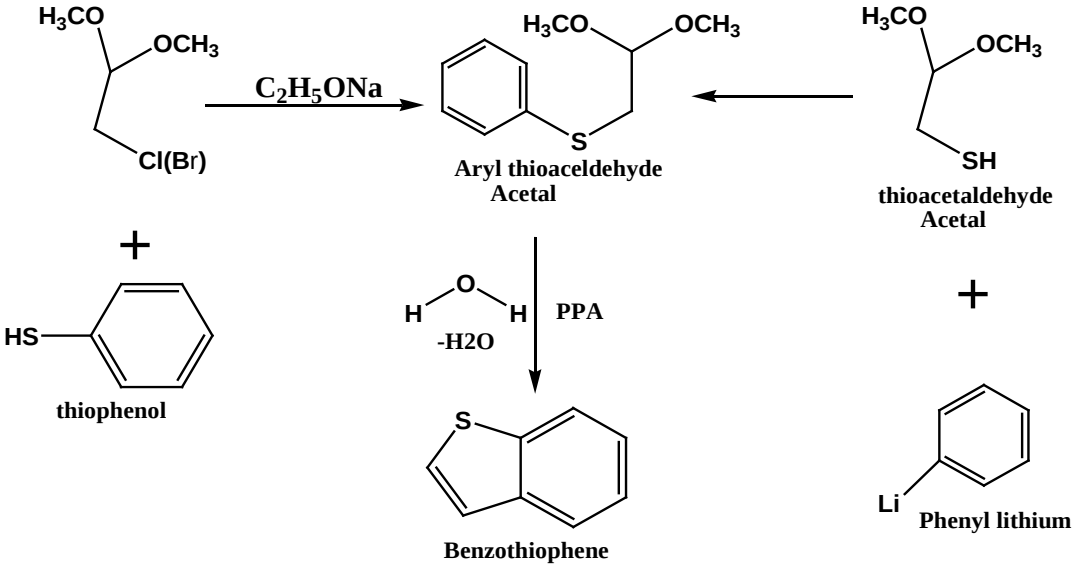
❖ NAME OF SYTHESIS:-

1. Cyclization of Arylthioacetaldehydeacetal
2. From cyclization of thiophenols
3. From O-MercaptoBenzaldehyde with α-halo acid
4. From O-MercaptoBenzoic acid with α-halo ketone
5. From diel's alder reaction
6. From oxidation cyclization of Mercaptocinnamic acid
7. Reaction of cinnamic acid with thionylchloride
8. O-MercaptoethylBenzene with $Cr_2 O_3$ /$Al_2 O_3$.
9. FromO-Mercapto β-chlorostyrene
10. From Arylketo sulfides.

➢ Synthesis

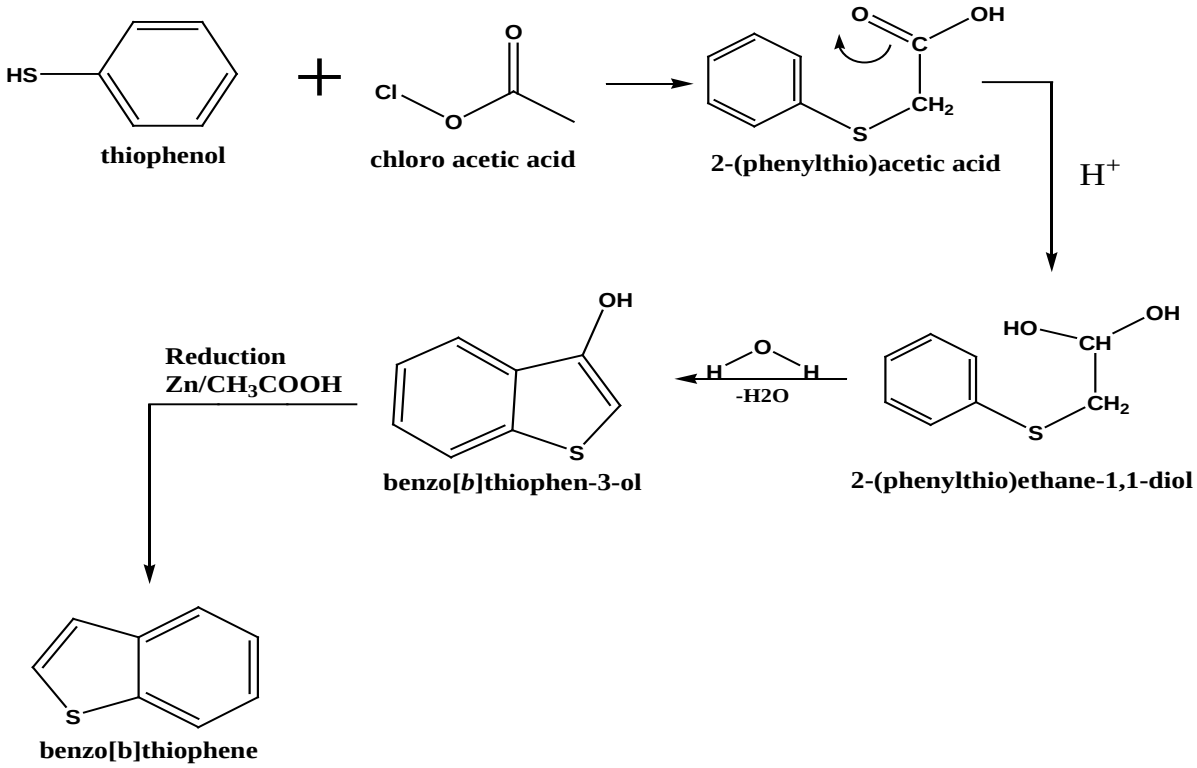
(1) Arylthioacetaldehydeacetal undergoes cyclization in the presence of payphosphoric acid (PPA) as a catalyst to give Benzothiophene

- The starting compound is prepared by the condensation of thiophenol with bromoor chloro acetaldehyde dialkylacetal
- Alternatively it is prepared by the reaction of phenyl lithium with thioacetaldehydeacetal

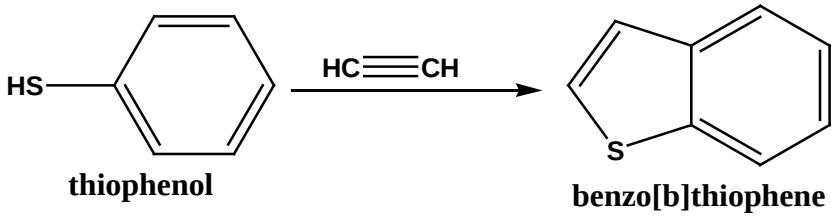


➢ (B) from thiophenol with chloro acetic acid

Arylthioacetic acid on cyclization provides 3-hydroxy Benzothiophene which on treatment with Zn/CH_3COOH affords Benzothiophene



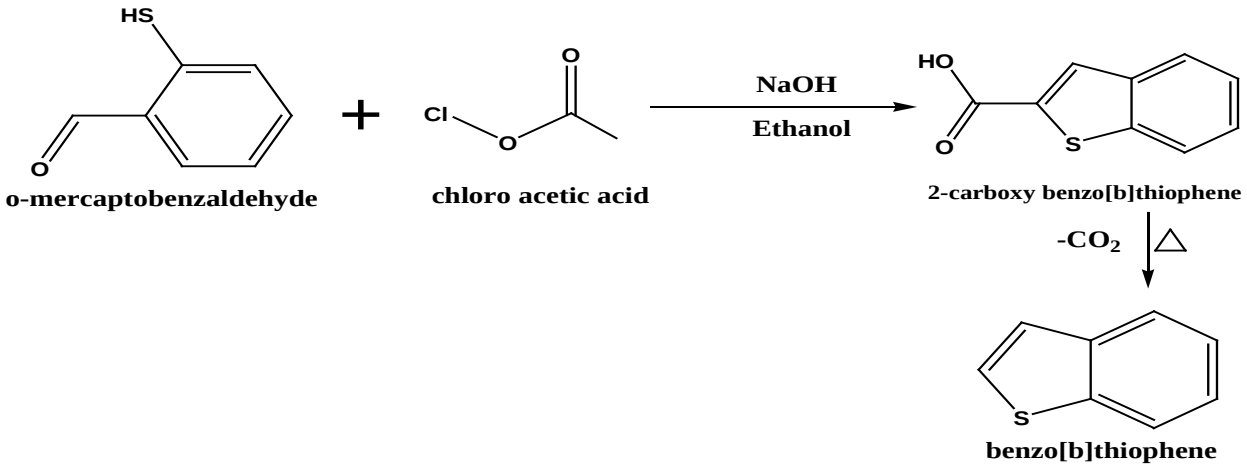
(c) thiophenol when heated with acetylene at 600℃-650℃ temp. ProvidesBenzo[b]thiophene



thiophenol benzo[b]thiophene

➢ (2)(a) From O-MercaptoBenzaldehyde with α-halo acid

The reaction of O-MercaptoBenzaldehyde with chloro acetic acid in the presence of alkali in ethanol provides Benzo[b]thiophene derivative

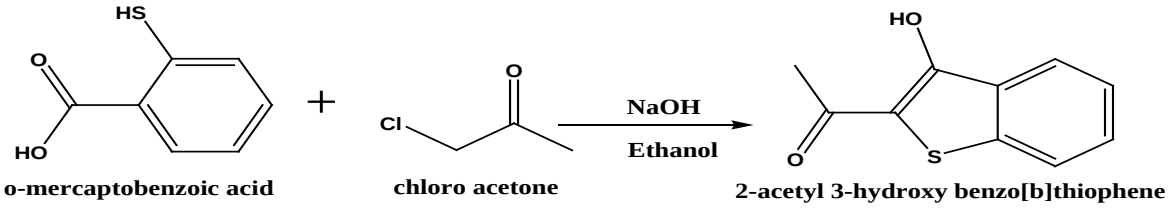


o-mercaptobenzaldehyde chloro acetic acid 2-carboxy benzo[b]thiophene

benzo[b]thiophene

➢ (2)[b] O-MercaptoBenzoic acid with α-halo acid

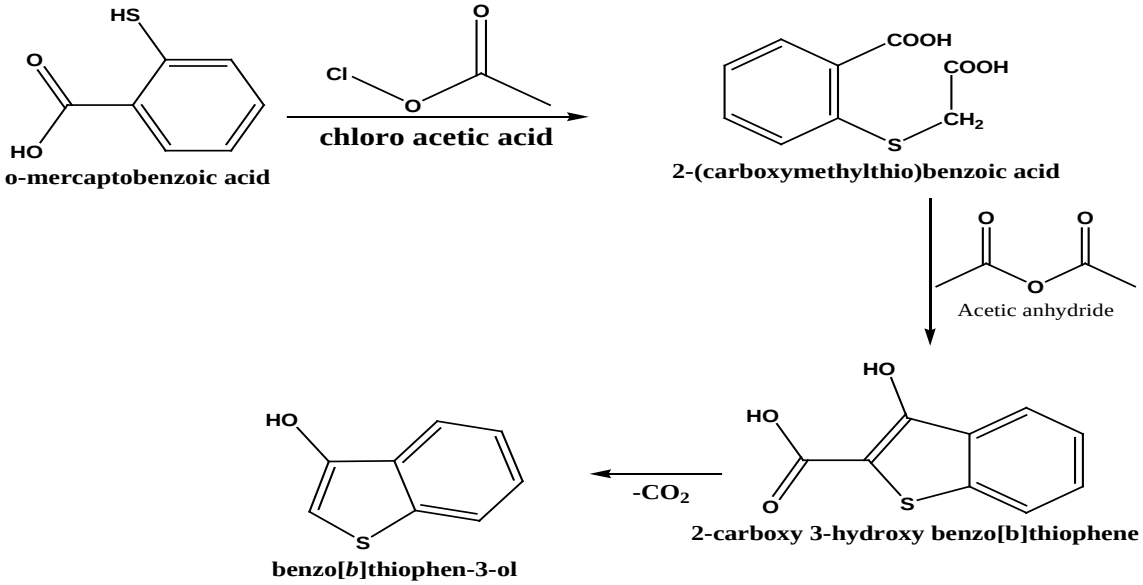
O-MercaptoBenzoic acid with chloro acetone in the presence of alkali in ethanol provides Benzo[b]thiophene derivative



o-mercaptobenzoic acid chloro acetone 2-acetyl 3-hydroxy benzo[b]thiophene

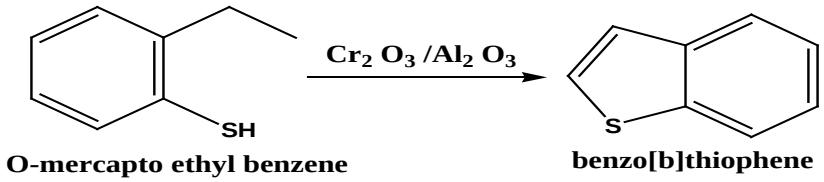
➢ (2)[c]O-carboxyphenylthio acetic acid with acetic anhydride

O-carboxyphenylthio acetic acid when cyclized with acetic anhydride affords 2-carboxy 3-hydroxy Benzothiophene which on de-carboxylation and Zinc dust treatment leads to the formation of 3-hydroxy Benzo[b]thiophene



(3) From cyclization of O-Mercapto ethyl Benzene

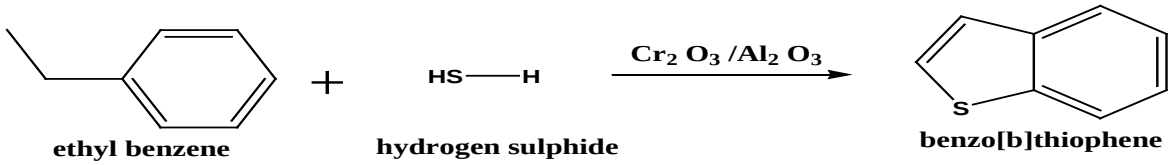
O-Mercapto ethyl Benzenecyclises using Cr_2O_3/Al_2O_3 at 475°C,to yieldBenzo[b]thiophene



O-mercapto ethyl benzene benzo[b]thiophene

(4) From ethyl Benzene with hydrogen sulphide

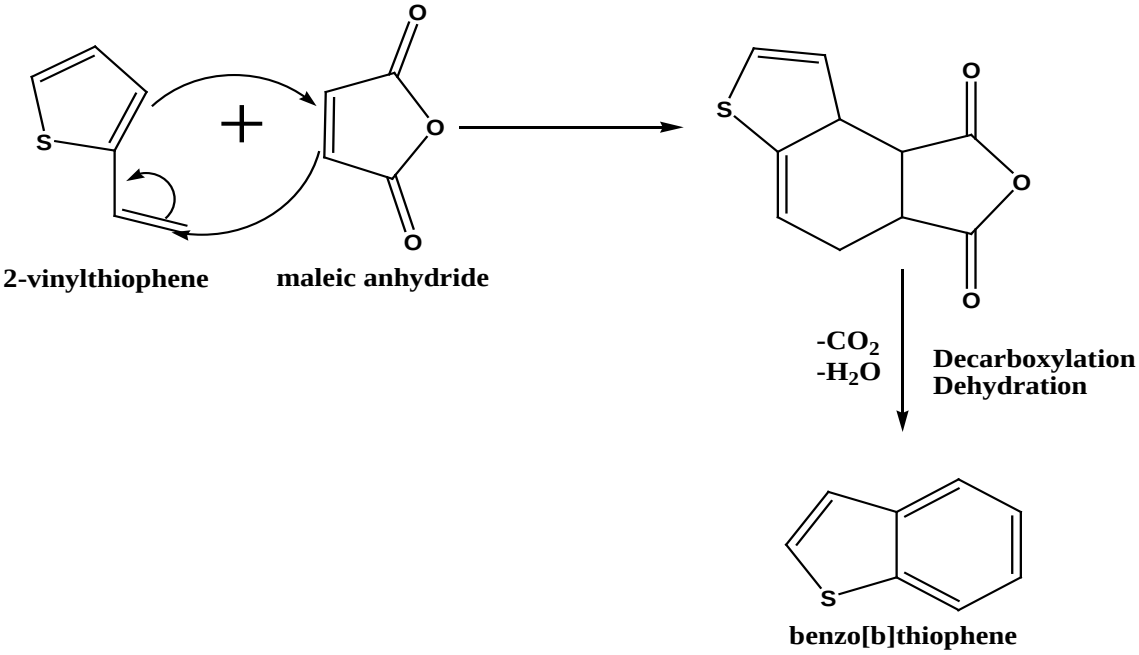
When vapor of ethyl Benzene and hydrogen sulphide is passedover Cr_2O_3/Al_2O_3 at 475°C reacts to produced Benzo[b]thiophene



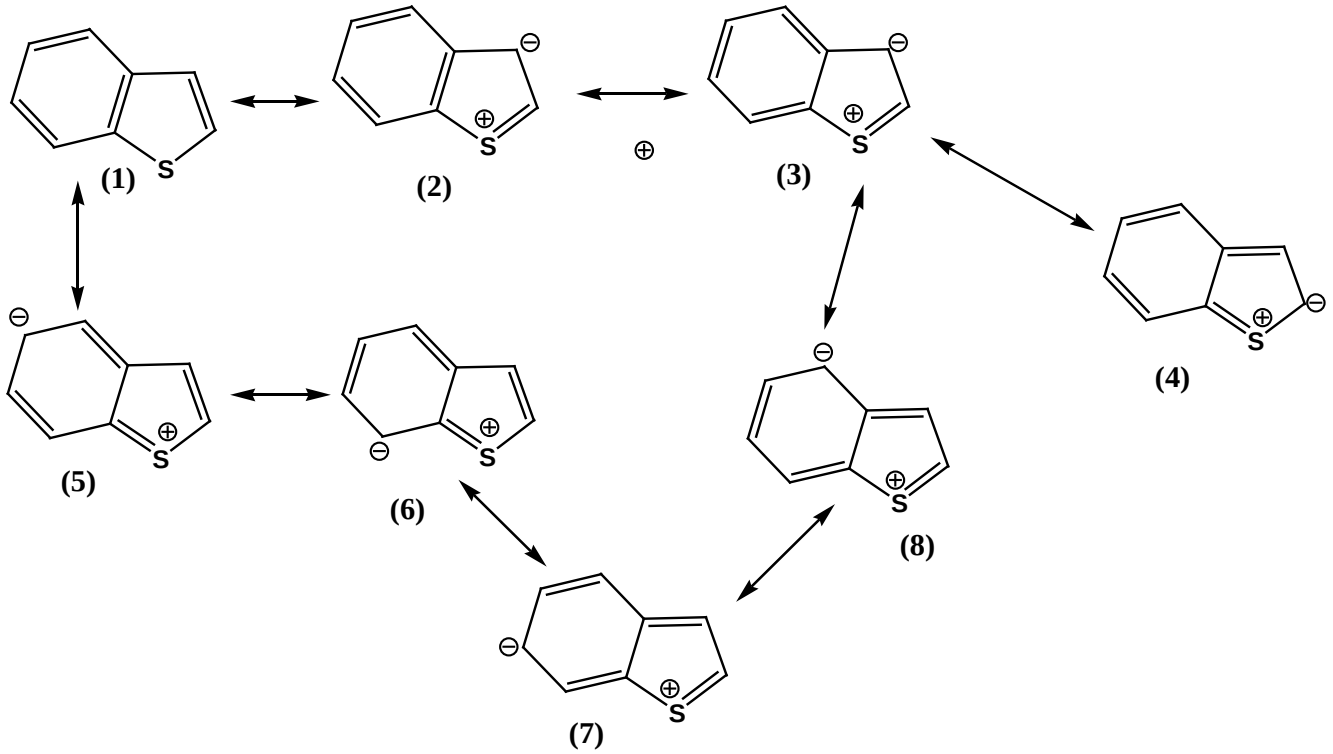
ethyl benzene hydrogen sulphide benzo[b]thiophene

(5) From [4+2] cycloaddition or Diel's Alder reaction

Benzo[b]thiophene can be prepared by Diel's Alder reactionof α-vinyl thiophene with maleic anhydride



➢ Resonating structure



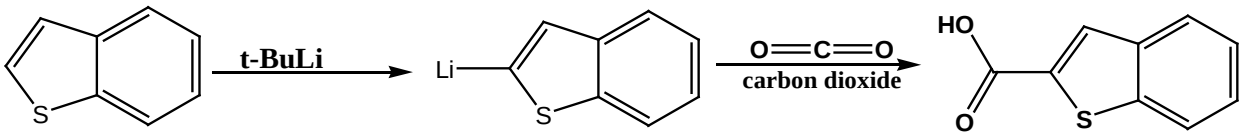
- In Benzo[b]thiophenenucleophilic substitution reaction is very difficult but reraly takes place at position 2nd and 3rd
- In Benzo[b]thiophene electrophilic substitution reaction takes place in the thiophene ring although at both the position α and β but preferentially at the β-position

➢ Nucleophilic substitution Reactions

In Benzo[b]thiophenenucleophilic substitution reaction is very difficult but reraly takes place at position 2nd and 3rd

1) Mettalation

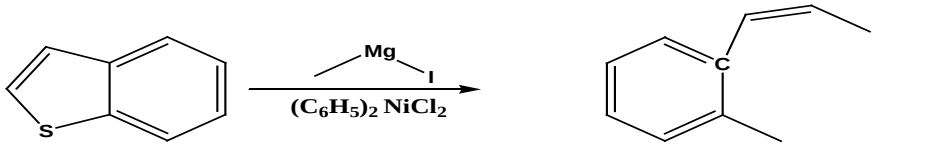
Benzo[b]thiophene is mettalised with t-BuLi to produced 2-LithioBenzo[b]thiophene which on carboxylation to produced 2-carboxyBenzo[b]thiophene



benzo[b]thiophene — 2-lithio benzo[b]thiophene — 2-carboxy benzo[b]thiophene

2) Grignard Reagent

Benzo[b]thiophene reacts with Grignard reagent to produce O-methyl β-methylstyrene.



Benzo[b]thiophene — **1-methyl-2-((*Z*)-prop-1-enyl)benzene**

➢ Electrophilic Substitution Reaction at "C"

The fusion of Benzene ring to the face 'b' of the Thiophene ring decreases the reactivity and thus causes Benzo[b]thiophene to exhibit lower reactivity than thiophene in Electrophilic substitution reaction.

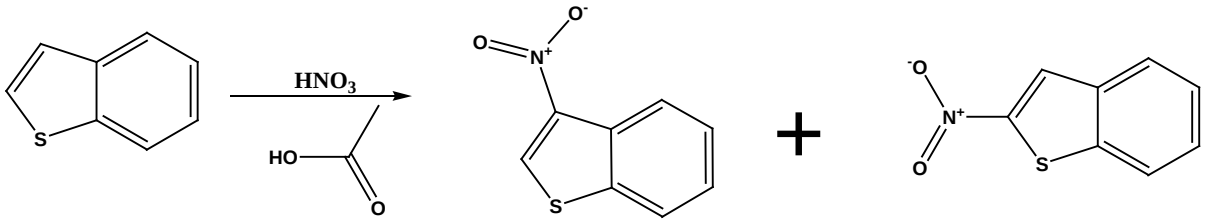
Benzo[b]thiophene undergoes electrophilic substitution reaction in the thiophene ring although at both the positions α and β but preferentially at the β-position.

(1)Nitration

Nitration of Benzo[b]thiophene with concentrated nitric acid in the presence of acetic acid results in a mixture of 3-nitro and 2-nitro Benzo[b]thiophenes in 5:1 ratio.

If acetyl group is present at the position 3, the thiophene ring is deactivated

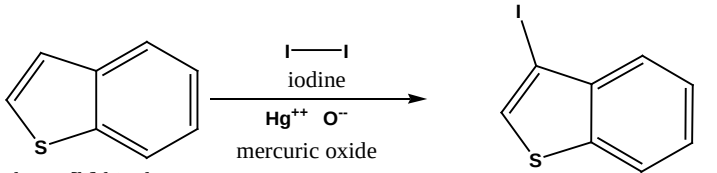
And the substitution occurs in the Benzene ring with the formation of a mixture of 4, 5, 6 and 7-nitroBenzo[b]thiophene



benzo[b]thiophene — 3-nitrobenzo[*b*]thiophene — 2-nitro benzo[b]thiophene

(2)Iodination

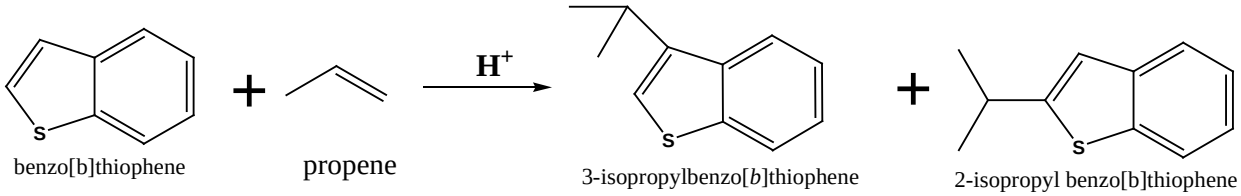
Iodination of Benzo[b]thiophene with iodine in the presence of mercuric oxide produces 3-iodo Benzo[b]thiophene



benzo[b]thiophene — 3-iodobenzo[*b*]thiophene

(3)Alkylation

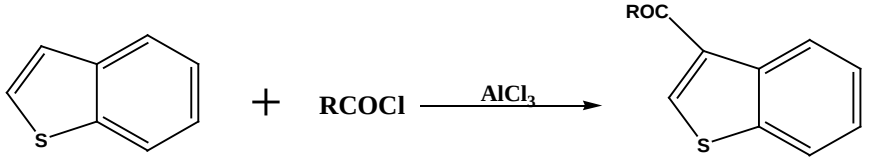
Alkylation of Benzo[b]thiophene with alkenes or alkanols in the presence of an acid provides a mixture of 2-and 3-alkylBenzo[b]thiophene



benzo[b]thiophene + propene → 3-isopropylbenzo[*b*]thiophene + 2-isopropyl benzo[b]thiophene

(4)Acylation

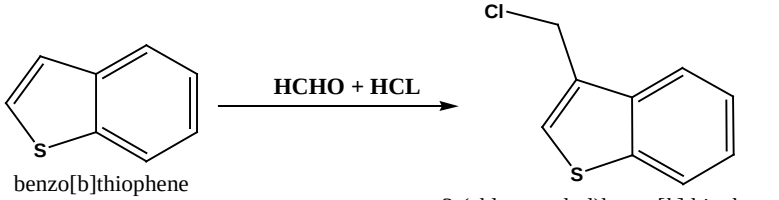
Acylation of Benzo[b]thiophene undergoes Frledel Crafts Acylation in the presence of lewis acid catalyst ($AlCl_3$, BF_3, $SnCl_4$,H_2SO_4) to provide 3-AcylBenzo[b]thiophene



benzo[b]thiophene → 3-acyl benzo[b]thiophene

(5)Chloromethylation

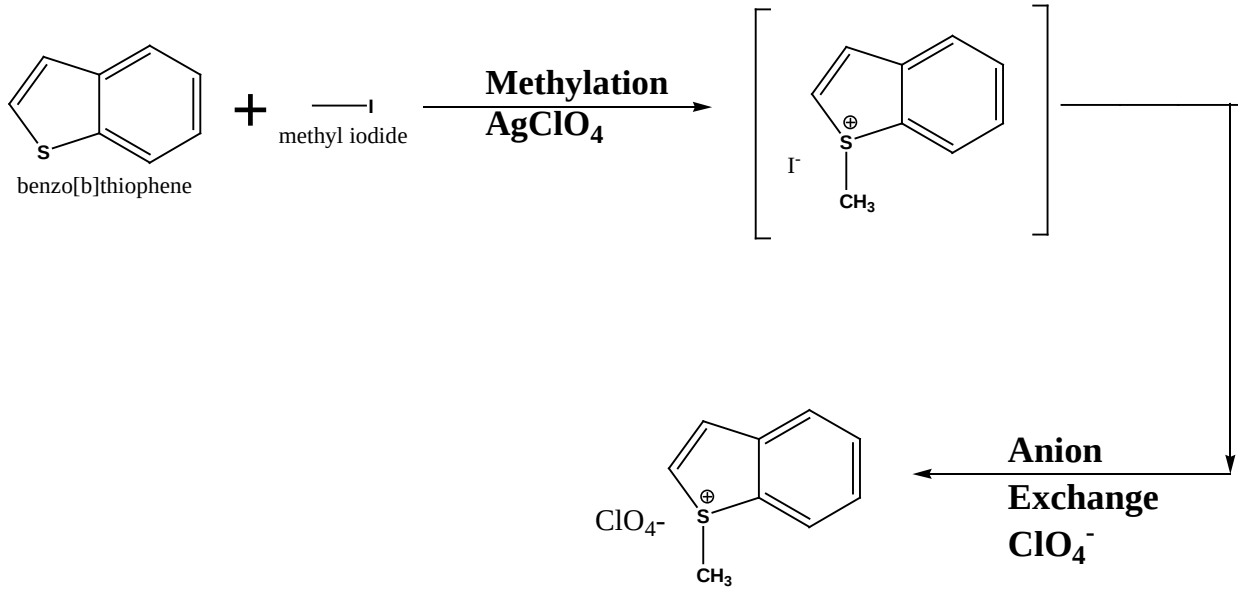
Benzo[b]thiophene undergoes Chloromethylation in the presence of HCHO and HCL to provide 3-chloromethylBenzo[b]thiophene



benzo[b]thiophene → 3-(chloromethyl)benzo[*b*]thiophene

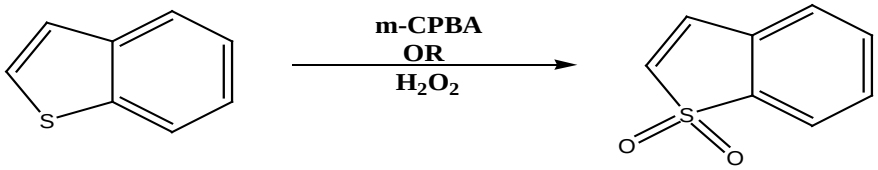
➢ Electrophilic Substitution Reaction at "S"

Benzo[b]thiophene undergoes S-Alkylation with strong alkylating reagent containing non-nucleophilic counter ions (ClO_4^-,PF_6^- and BF_4^-)



➢ Oxidation

Oxidation of Benzo[b]thiophene in the presence of m-chloroperBenzoicacid or hydrogen peroxide to form Benzo[b]thiophene 1,1dioxane

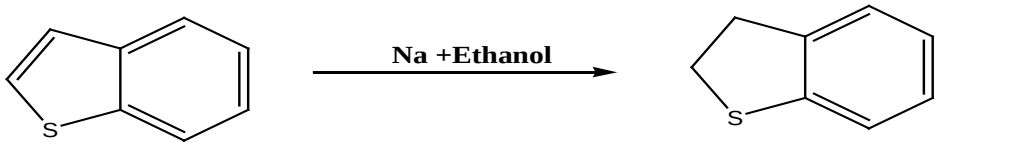


benzo[b]thiophene

benzo[b]thiophene 1,1 dioxane

➢ Reduction

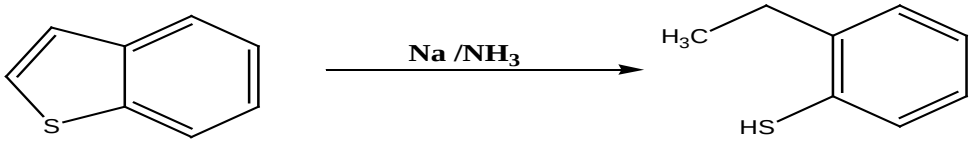
(1) Reduction of Benzo[b]thiophene in the presence of alkali in ethanol to form 2,3-dihydro Benzo[b]thiophene



benzo[b]thiophene

2,3 dihydrobenzo[b]thiophene

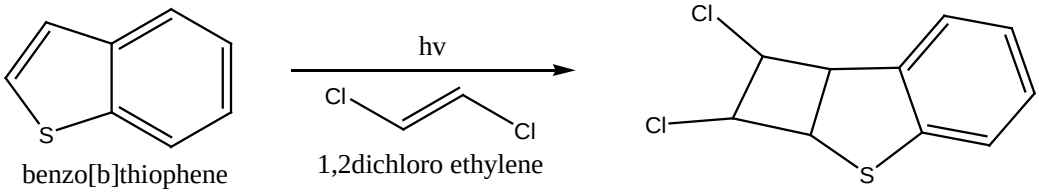
(2) The reduction with Na/NH_3 results in the cleavage of hetrocyclic ring with the formation of O-MercaptoethylBenzene



benzo[b]thiophene 2-ethylbenzenethiol

➢ Photochemical Reaction

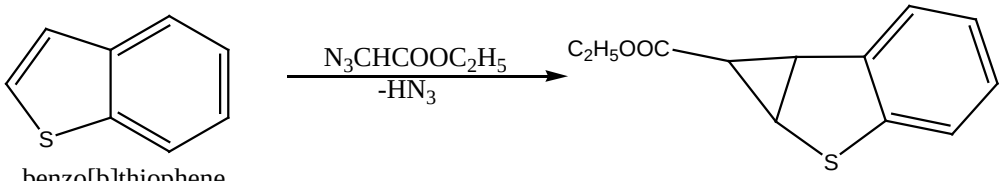
Benzo[b]thiopheneundergoes Photochemical Reaction with dichloro ethylene to form cycloadduct



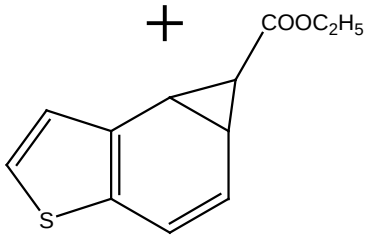
benzo[b]thiophene 1,2dichloro ethylene cycloadduct

➢ Reaction with Carbene

Benzo[b]thiophene undergoes reaction with diazoacetic ester to produced 2,3 and 4,5 cyclopropaneBenzo[b]thiophene carboxylic ester

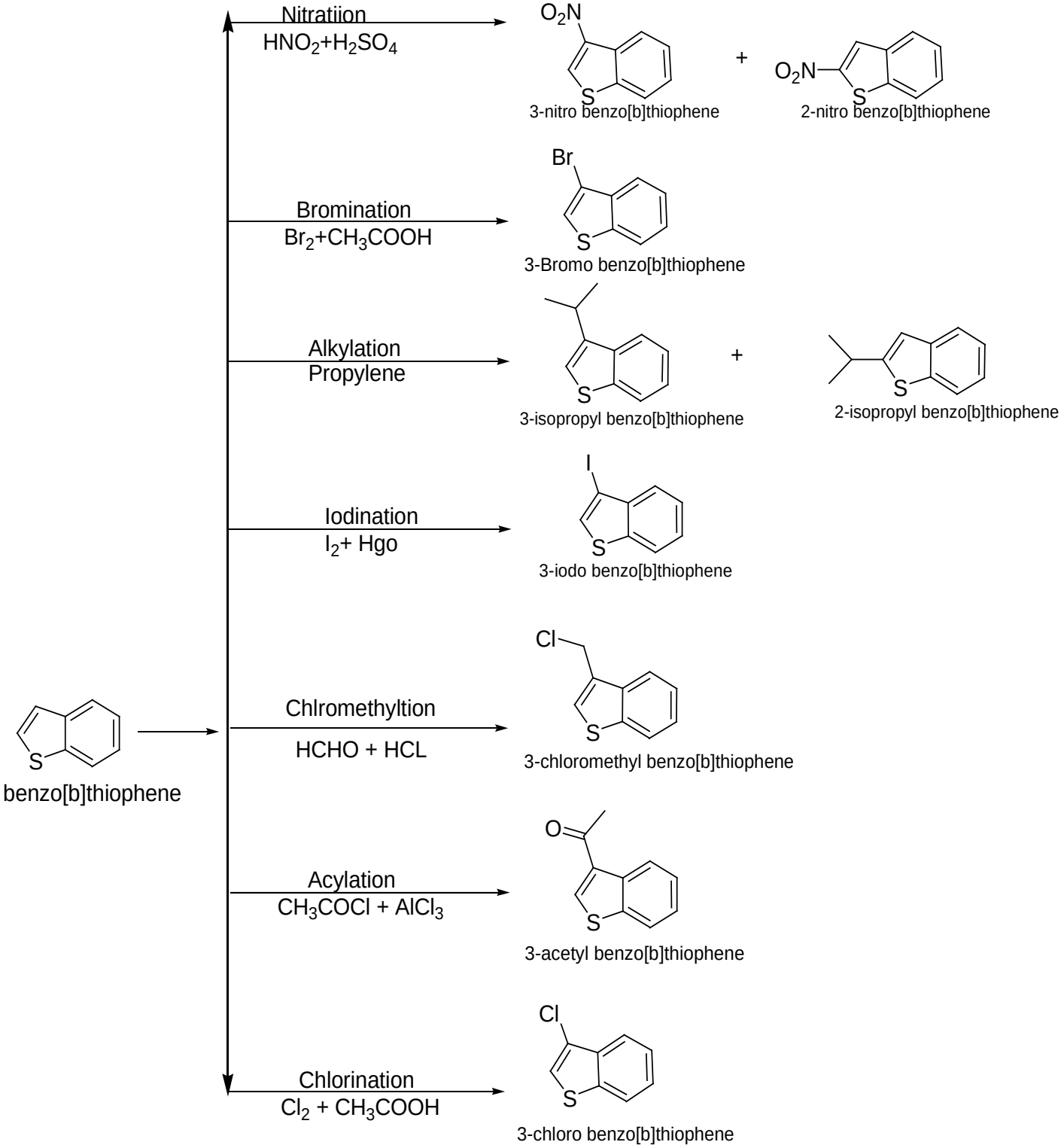


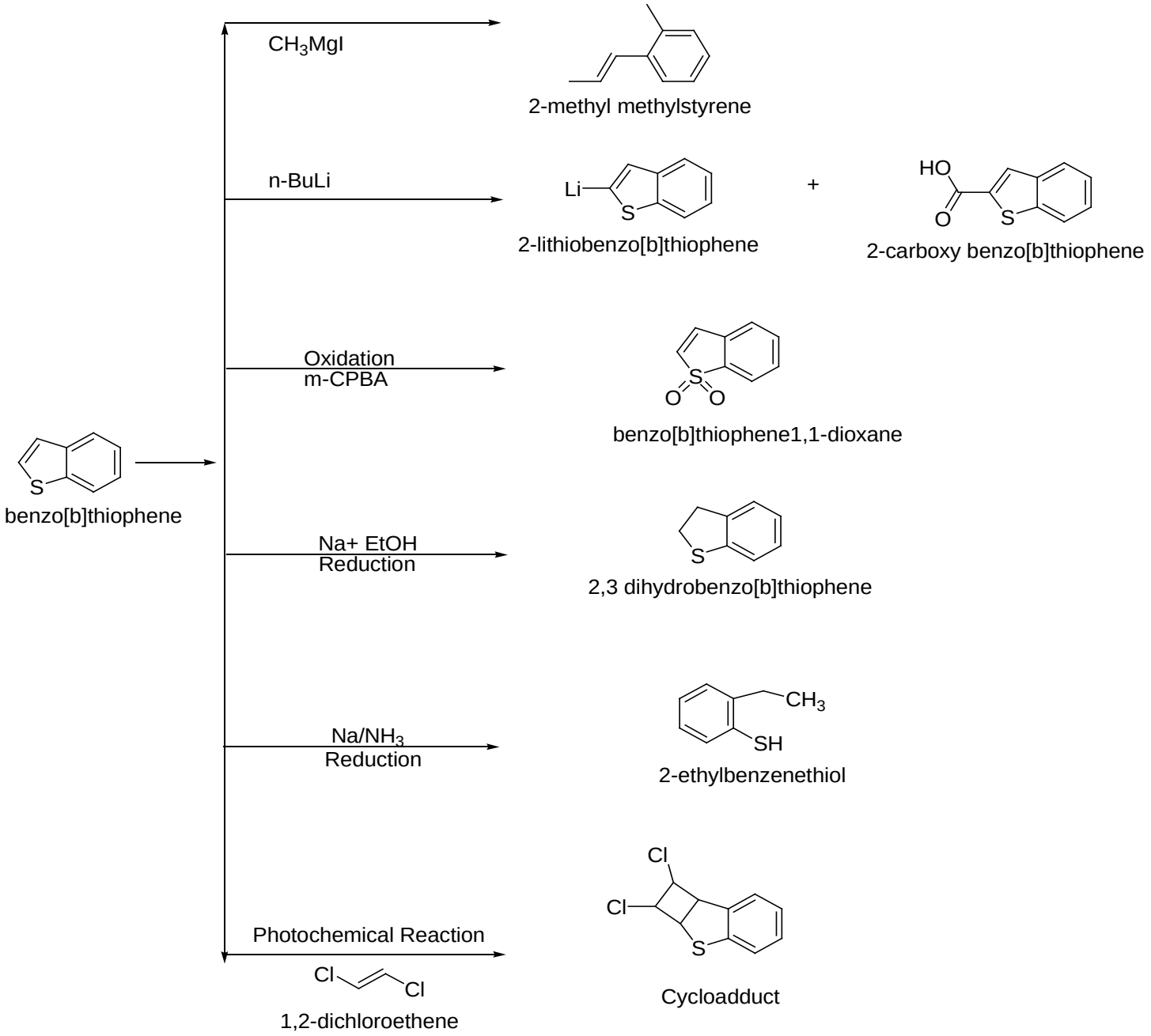
benzo[b]thiophene 2,3 cyclopropane benzo[b]thiophene carboxylic ester



4,5 cyclopropane benzo[b]thiophene carboxylic ester

➢ Chemical Properties




CH3MgI
2-methyl methylstyrene
n-BuLi
Li
S
2-lithiobenzo[b]thiophene
+
HO
O
S
2-carboxy benzo[b]thiophene
Oxidation
m-CPBA
S
O
O
benzo[b]thiophene1,1-dioxane
S
benzo[b]thiophene
Na+ EtOH
Reduction
S
2,3 dihydrobenzo[b]thiophene
CH3
SH
Na/NH3
Reduction
2-ethylbenzenethiol
Cl
Cl
S
Photochemical Reaction
Cl
Cl
1,2-dichloroethene
Cycloadduct

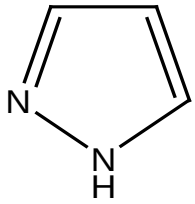
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

HETERCYCLIC CHEMISTRY ASSIGNMENT

NAME: KAPUPARA VIMAL H

ROLL NO - 22

-: PYRAZOLE :-



1*H*-pyrazole

→ **IUPAC NAME** :- 1,2-Diazole

→**INTRODUCTION** :-

→Pyrazole was first prepared by Buchner in 1889 by the decarboxylation of pyrazole 3,4,5-tricarboxylic acid.

→ The antipyretic activity of pyrazole derivetives was discoveerd in 1884 by KNORR

→ Many pyrazole systems have been explored for pharmaceutical , agrochemicals and dyes

→PHYSICAL PROPERTIES :-

→It is colorless solid,

→It's M.P= 70 C B.P=188 C

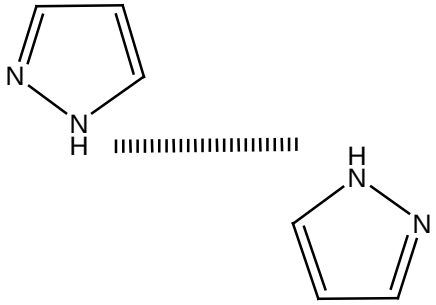
→It's soluble in water,

→It's insoluble in petrolium ether,

→It is weak base pKa=2.53

→It has a planar structure.

→It exists as dimar in concentrated solution due to hydrogen bonding.



→It is dipole moment =2.64D

→Resonating Energy = 29.3 K cal/mole.

→SPECTRAL DATA :-

→UV Λ MAX (ETHANOL) nm :-210 (3.53)

→^{1}H NMR δ ppm ($CDCl_3$) :-C_3-H- 7.55
:-C_4-H- 6.25
:-C_5-H- 7.55

→^{13}C NMR δ ppm ($CH Cl_3$) :-C_3- 134.3
:-C_4- 105.2
:-C_5- 135.3

→^{15}N NMR δ ppm ($CH Cl_3$) :-247.3

→SYNTHESIS :-

1) From Dicarbonyl compounds.

2) From Unsaturated ketones.

3) a)From acetylene with diazomethane.

b) From n-tributylstannylacetylene with diazoaceticester.

4) From Propargly aldehyde with hydrazine

5) From vinyl diazomethane.

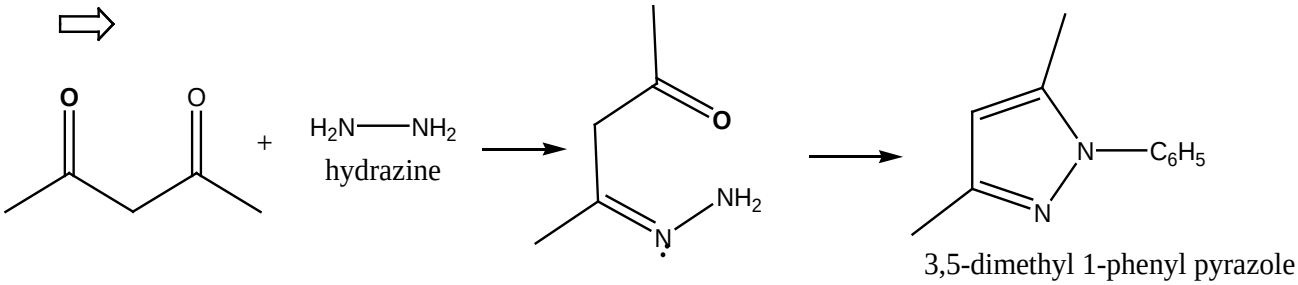
6) From 2-hydrazinochromone with hydrazine.

7) a) Dipolar addition to carbon-carbon bond.

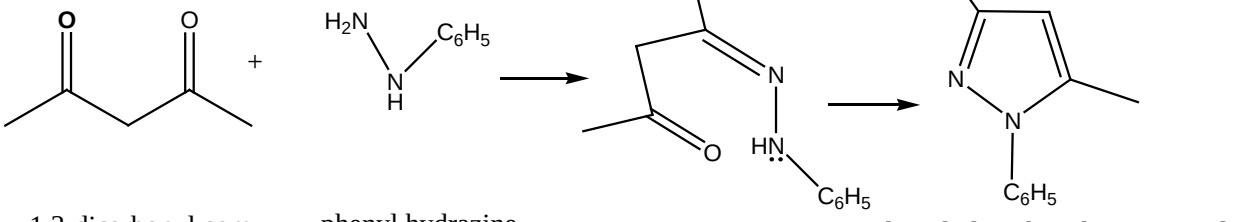
b) From acrylic ester with dimethylazomethane.

(1) From Dicarbonyl Compound.

→Pyrazole ring based on the condensation of 1,3-dicarbonyl compound or phenylhydrazine

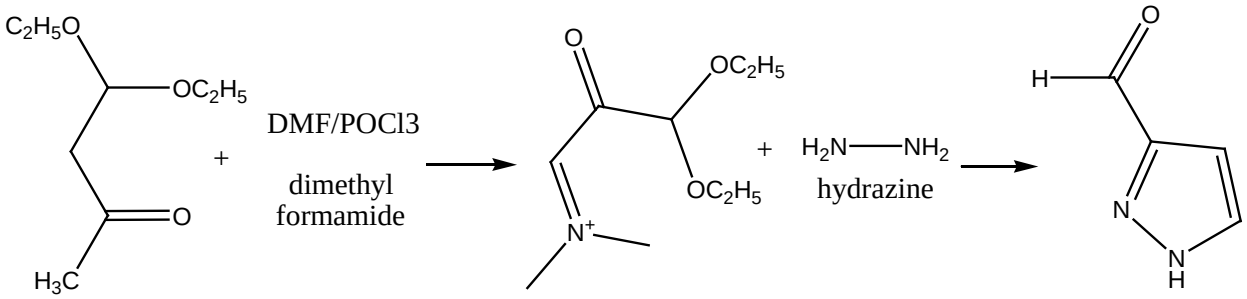


3,5-dimethyl 1-phenyl pyrazole



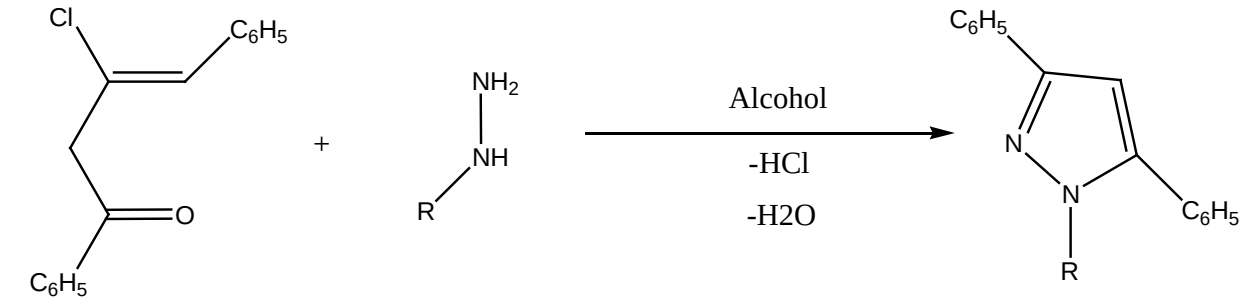
1,3-dicarbonyl com. phenyl hydrazine 3,5-dimethyl-1-phenyl-1*H*-pyrazole

→From 1,3-ketoaldehyde



(2) From Unsaturated ketones.

→(a) An alternative route to Pyrazole synthesis involves reaction of α,β-ethylenic carbonyl derivative with hydrazine.

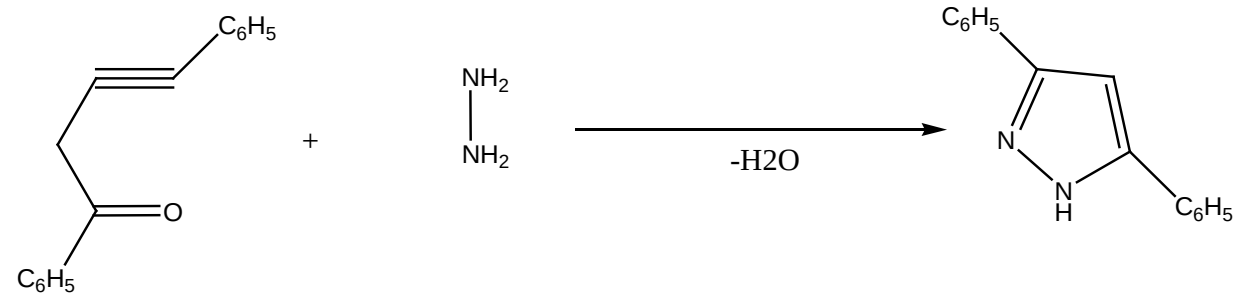


(*Z*)-3-chloro-1,4-diphenylbut-3-en-1-one

hydrazine

3,5-diphenyl pyrazol

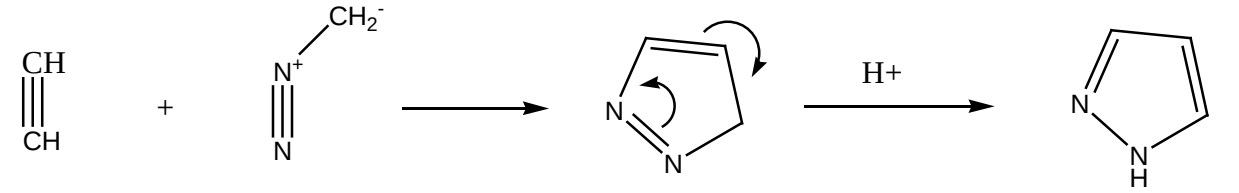
→(b) α,β-acetylenic carbonyl compound with hydrazine.



1,4-diphenylbut-3-yn-1-one hydrazine 3,5-diphenyl pyrazol

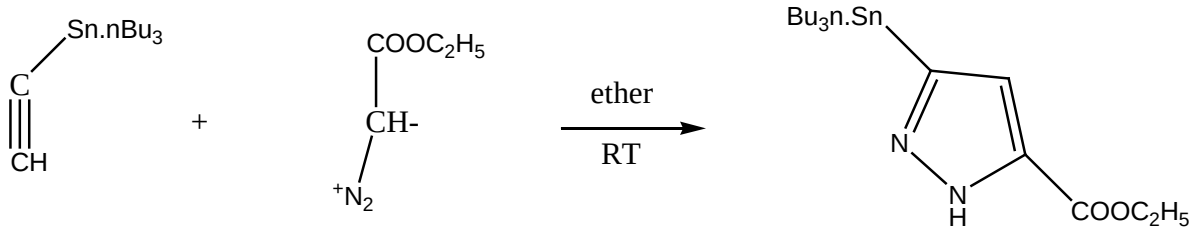
(3) [3+2] Cycloaddition Reaction.

→Acetylene reactes with diazomethane to give pyrazole.



ethyne Diazomathane 3*H*-pyrazole 1*H*-pyrazole

→Reaction of n-tributylstannyacetylene with diazoaceticester to give pyrazole.

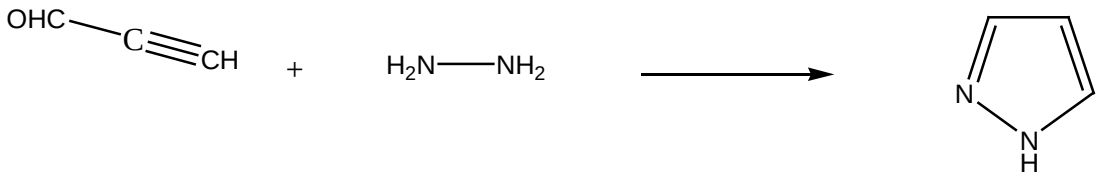


n-tributyl stannylacetylene

diazoacetic ester

3-tributyl stannyl 5-ethaylester pyrazole

(4)Propargyl aldehyde with Hydrazine.



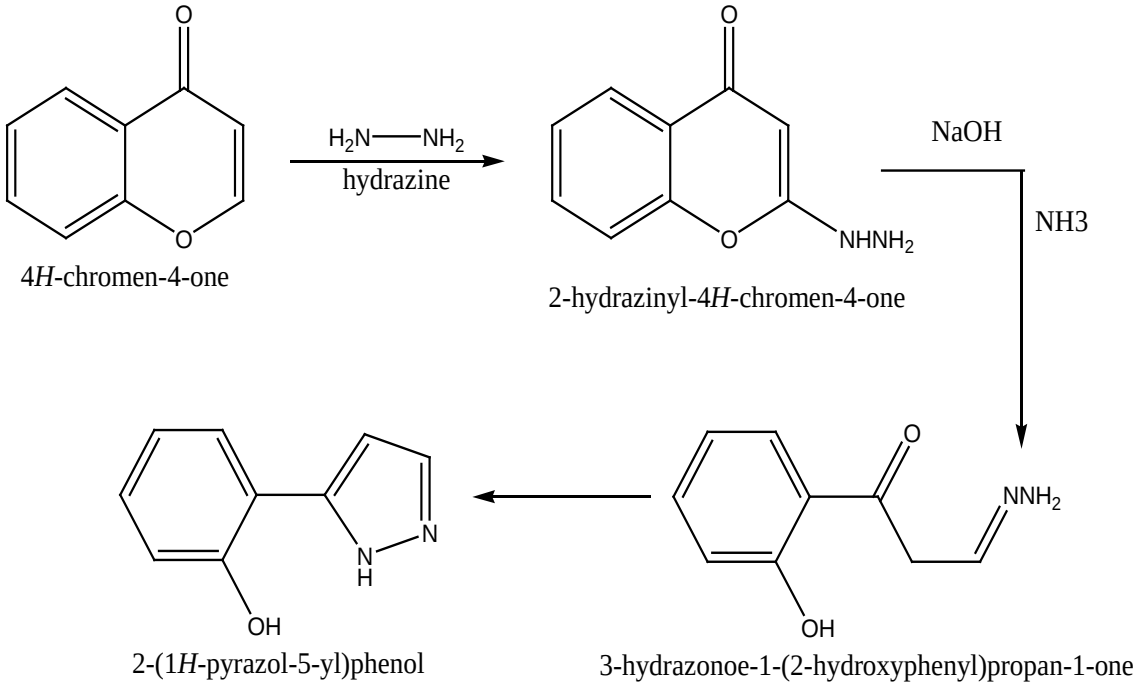
propiolaldehyde

hydrazine

1*H*-pyrazole

(5) Ring Opening Reaction.

→The reaction of 2-hydrazinocchromone which on ring opening and cyclisation yields 5-o-hydroxyphenylpyrazole.



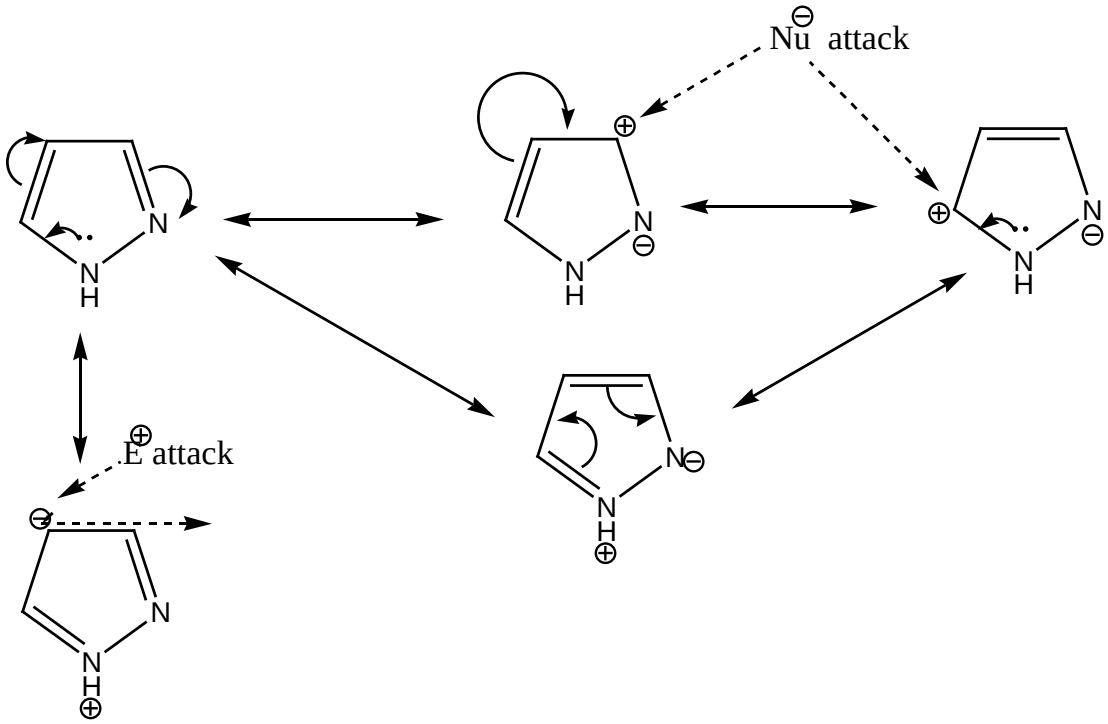
4*H*-chromen-4-one

2-hydrazinyl-4*H*-chromen-4-one

2-(1*H*-pyrazol-5-yl)phenol

3-hydrazonoe-1-(2-hydroxyphenyl)propan-1-one

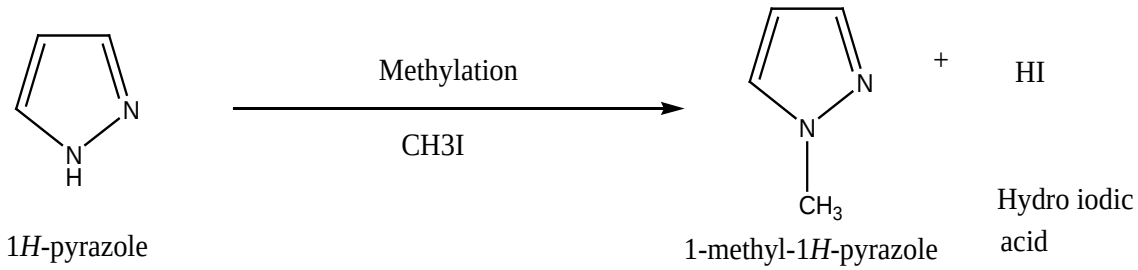
→ Resonating Structure:-



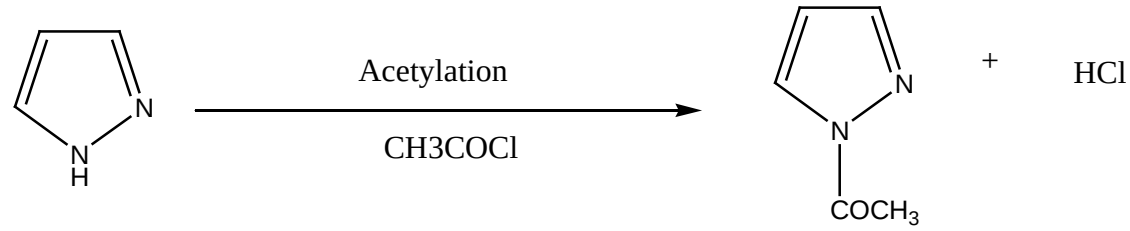
→CHEMICAL PROPERTIES :-

(a) Electrophilic substitution at "N" atom :-

(1) Methylation :-



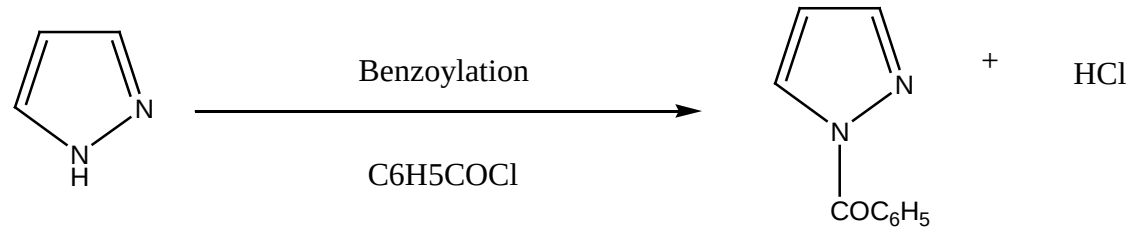
(2) Acetylation :-



1*H*-pyrazole

1-(1*H*-pyrazol-1-yl)ethanone

(3) Benzoylation :-



1*H*-pyrazole

phenyl(1*H*-pyrazol-1-yl)methanone

(4) Trimethylsilylation :-

1*H*-pyrazole

1-(trimethylsilyl)-1*H*-pyrazole

(b) Electrophilic Substitution at “C” atom :-

→ Pyrazole is less reactive then pyrrole due to the presence of pyridine type nitrogen atom.

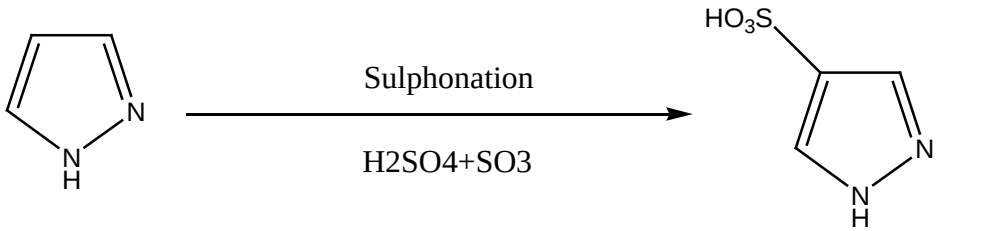
→Hence pyrazolium cation is deactivated towards electophilic.

→The electron density is maximum at C-4 position hence electophilic attacks at C-4.

(1) Nitration :-

1*H*-pyrazole 4-nitro-1*H*-pyrazole

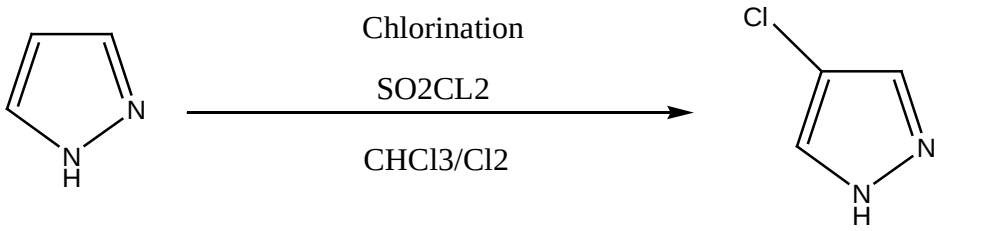
(2) Sulphonation :-



1*H*-pyrazole 1*H*-pyrazole-4-sulfonic acid

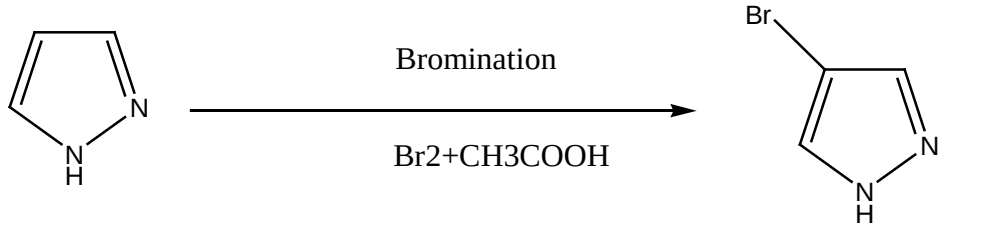
(3) Halogenation :-

→ Chlorination :-

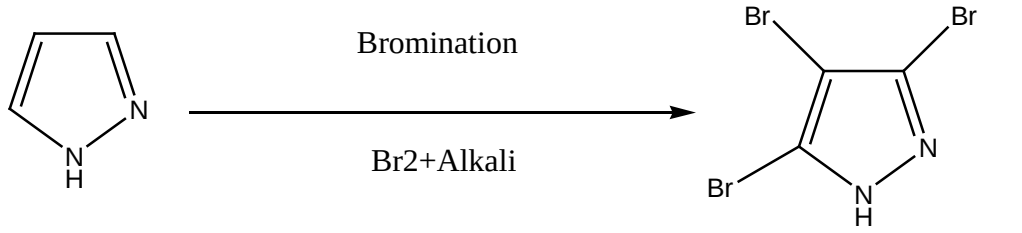


1*H*-pyrazole 4-chloro-1*H*-pyrazole

→ Bromination :-



1*H*-pyrazole — 4-bromo-1*H*-pyrazole

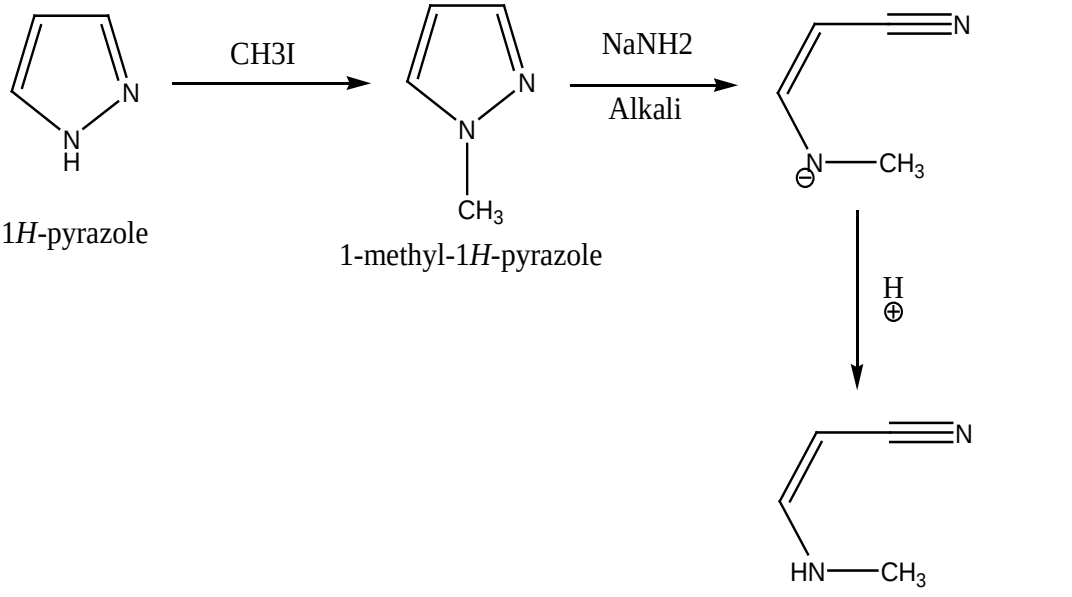


1*H*-pyrazole — 3,4,5-tribromo-1*H*-pyrazole

(c) Nucleophilic Substitution :-

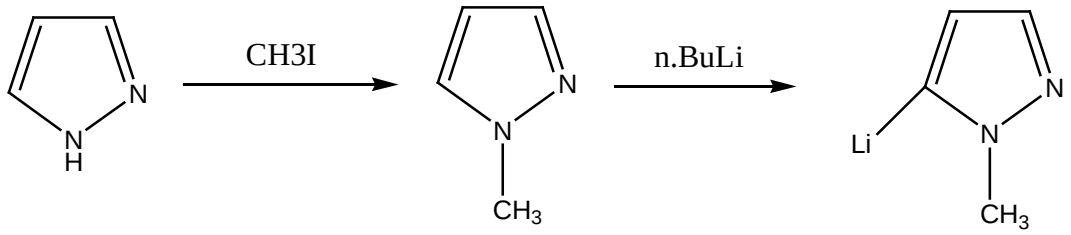
→ Pyrazole ring is resistant to reaction with Nucleophies.

→Pyrazole unsubstituted at 3-position undergoes ring opening with alkali (or)sodamide.



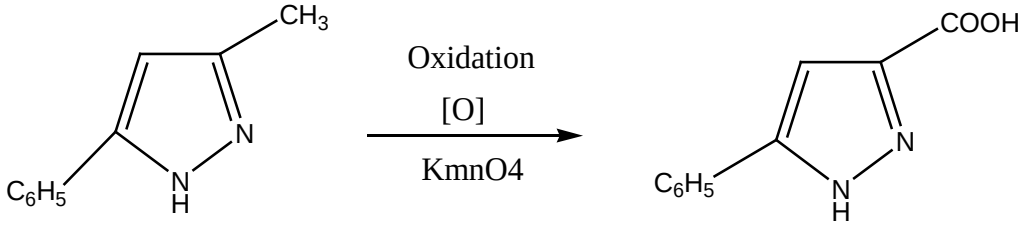
1*H*-pyrazole — 1-methyl-1*H*-pyrazole — (Z)-3-(methylamino)acrylonitrile

→ N-methylpyrazole is lithated at 5-postion.



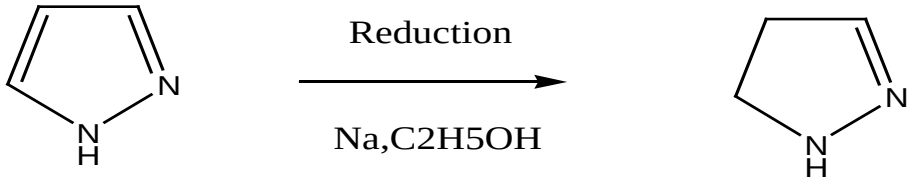
1*H*-pyrazole 1-methyl-1*H*-pyrazole N-methyl 5-lithiyam pyrazole

→Oxidation :-



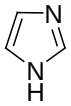
3-methyl-5-phenyl-1*H*-pyrazole 5-phenyl-1*H*-pyrazole-3-carboxylic acid

→Reduction :-



1*H*-pyrazole 4,5-dihydro-1*H*-pyrazole

Imidazol

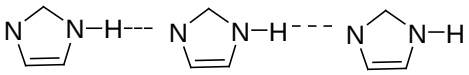


- ## Introduction

Imidazol is a hetero cyclic compound having two N-atoms in the ring. In the Imidazol ring there are two type of N-atom are present, one is pyrimidine and another is

- ## Physical Property

1. It is colorless compound.
2. m.p. is 90^{o} c and b.p. is 256^{o}c. Resion of higher b.p. is H-bonding is present in Imidazol.
3. H-bonding in Imidazol.

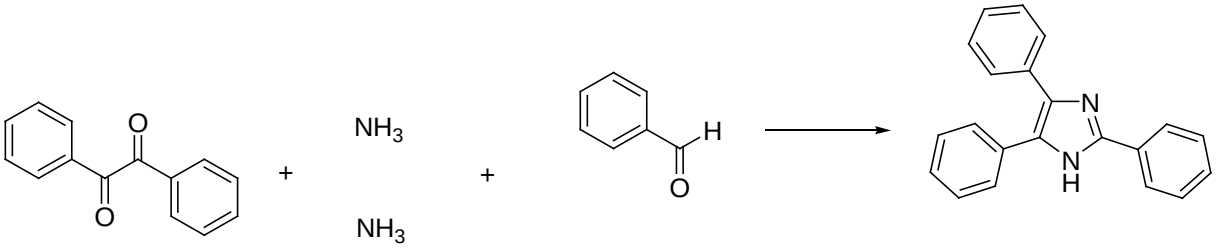


- ## Synthesis

1. The radiszeweski is synthesis :

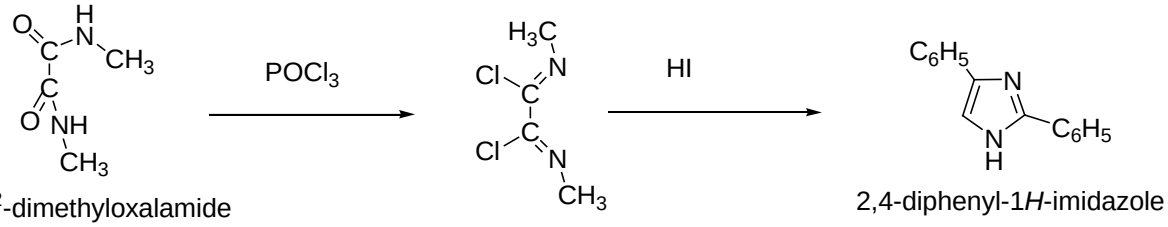
This is probably the most important synthesis of imidazoles

It consist of condensing a dicarbonyl comp. such as glyoxal, α-keto aldehyde or α-diketones with an aldehyde in the presence of ammonia.



2. Wollach synthesis

N' N'-disubstituted oxamide on reaction with phosphorous oxychloride forms intermediate which on reaction with hydroiodic acid furnishes N-substituted imidazole.

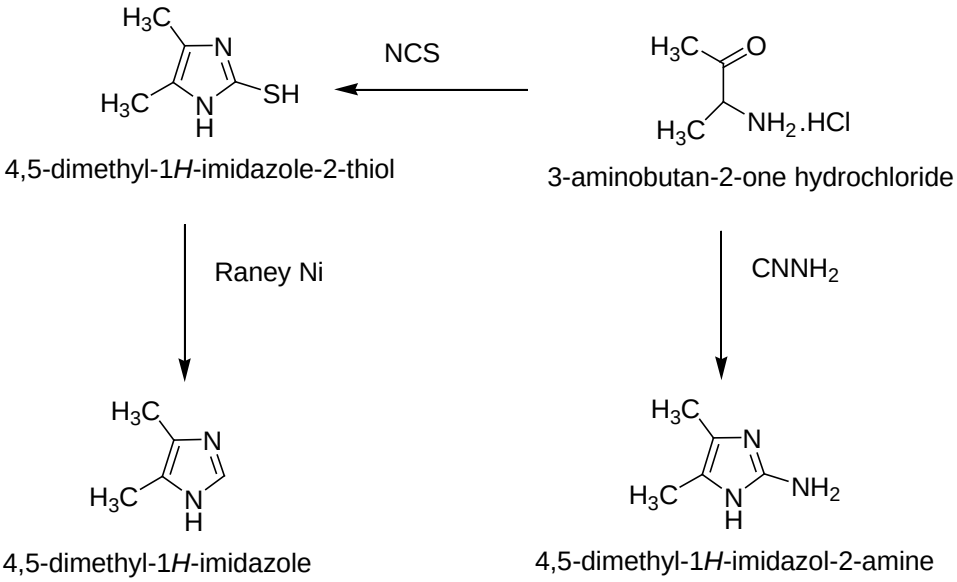


N[1],*N*[2]-dimethyloxalamide — 2,4-diphenyl-1*H*-imidazole

3. Markwaid synthesis :

The synthesis route involves the reaction of α-amino ketone hydrochloride with cynnates, thiocynnates or isothiocynnates to yield corresponding imidazoline-2-one or 3H imidazoline-2-thione(2-mercaptoimidazole) which can be easily converted to corresponding imidazole.

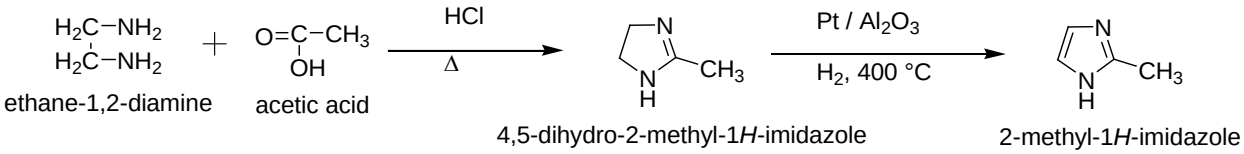
Amino ketone also can be reduced with cynnamide to yield 2-aminoimidazole.



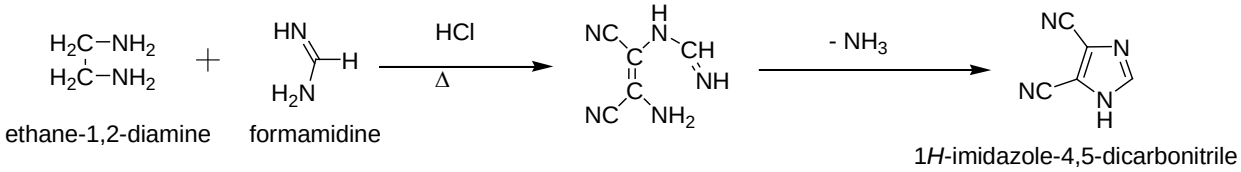
4,5-dimethyl-1*H*-imidazole-2-thiol — 3-aminobutan-2-one hydrochloride

4,5-dimethyl-1*H*-imidazole — 4,5-dimethyl-1*H*-imidazol-2-amine

(a) This simple and widely applicable route for synthesis of 2-alkylimidazole utilizes reaction of ethylene diamine with carboxylic acid,aldehydeor alcohol at high temp. and in the presence of dehydrogenating agent to provide imidazole in high yield.

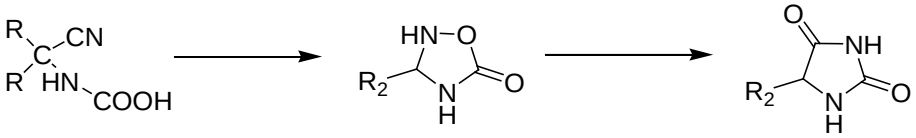


(b) The interaction of diaminomalinonitrite with formamidne forms a product which on cyclisation with loss ammonia afford 4, 5-dicynoimidazole.



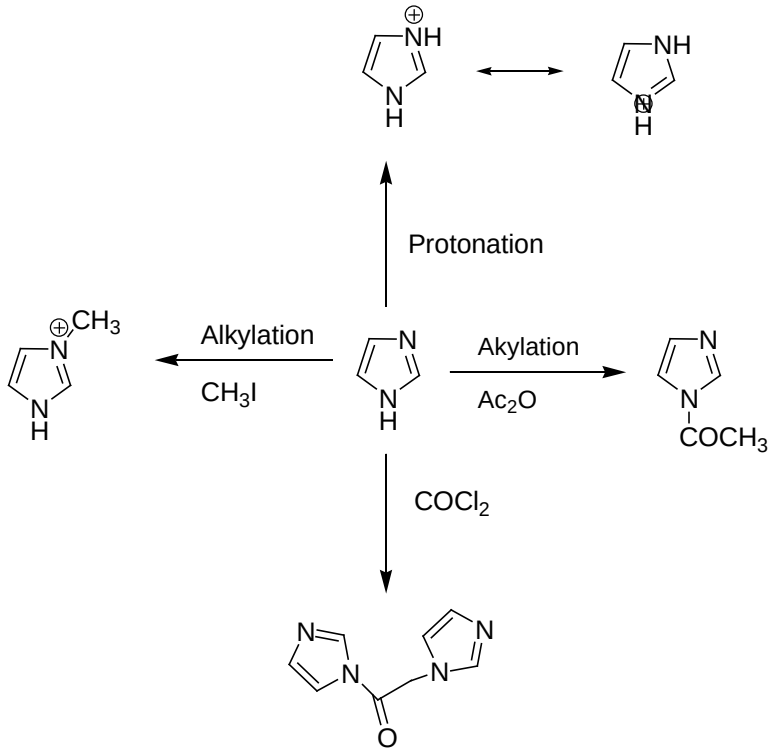
4. Bucherer Bergs :

This is widly uses for synthesis of imidazole derivative .In this, aldehyde and KCN or ketone and KCN and ammoniam carbonate is condensed.



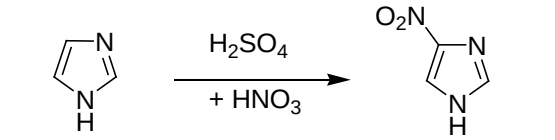
Chemical property :-

(a) Nucleophilic attack on N – atom :



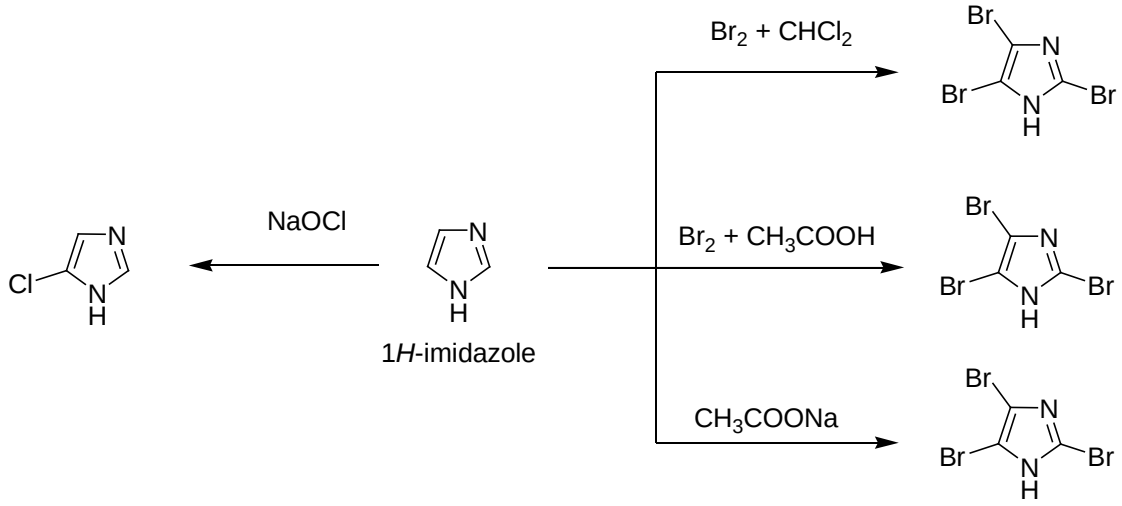
(b) Electrophilic attack at C- atom :-

(1)



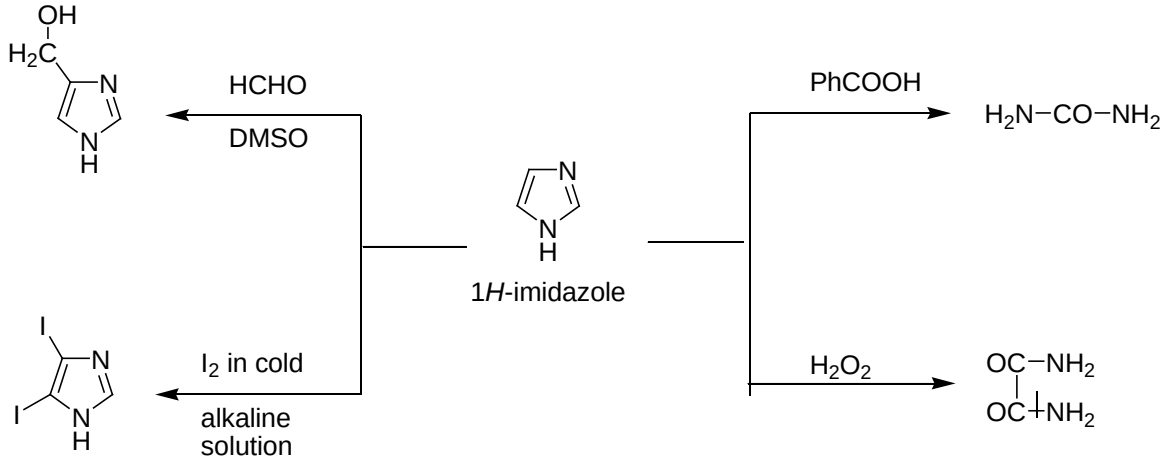
1*H*-imidazole 4-nitro-1*H*-imidazole

(2)

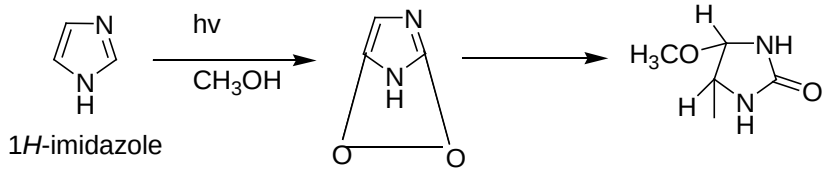


1*H*-imidazole

(c) Reaction with aldehyde :-



(d) Photochemical reaction :



oxazole

- It is derived from furan by the replacement of the =CH group by the azomethine N_2.
- It was first reported by hantzsch in 1887 but parent oxazole was synthesized in 1947 by a lengthy method.
- It is not natural peoduct.

Physical property :

- Colourless liquid
- pyridine like smell
- B.p is -69 to 70 °C
- Miscible in water and many organic solvent
- Weakly basic and pka = 0.8
- Aromatic in nature
- Dipole moment = 1.5 D

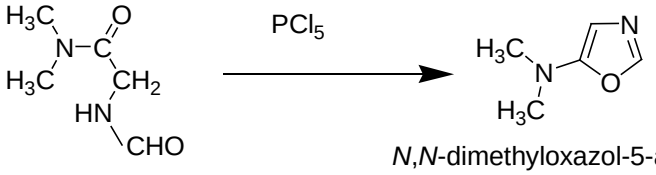
Sythesis :-

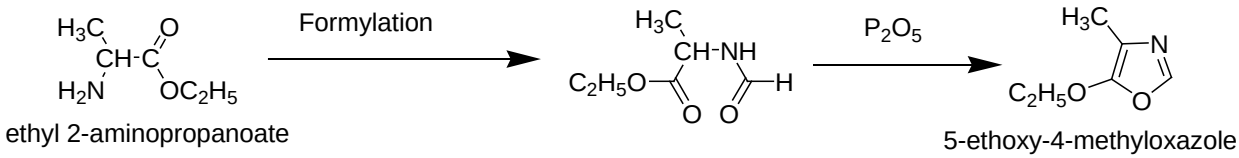
1. Robinson Gabriel synthesis.
2. Fischer synthesis
3. [4+1] condensations
4. Van leusen scollkopf method [3+2] condensations,
5. [3+2] condensations
6. Reduction of oxazole N- oxide
7. Ring expansion

1. Robinson Gabriel synthesis.

The classical general method for constructing oxazole ring system is based on the cyclodehydration of α= acylamino ketone in the presence of dehydracting agents like sulphuric acid, PCl_5, PPA, and anhydrous hydrofluoric acid.

The synthesis is modified to Prepare 5- alkoxyoxazole from esters of amino acid.

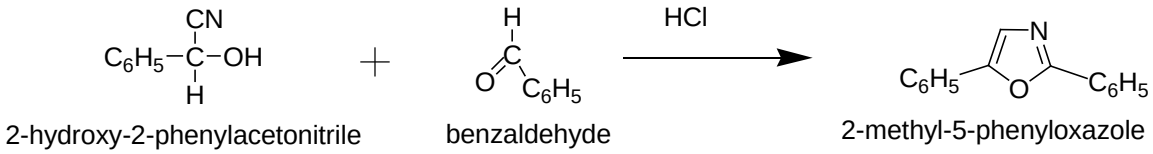




2. Fischer synthesis :-

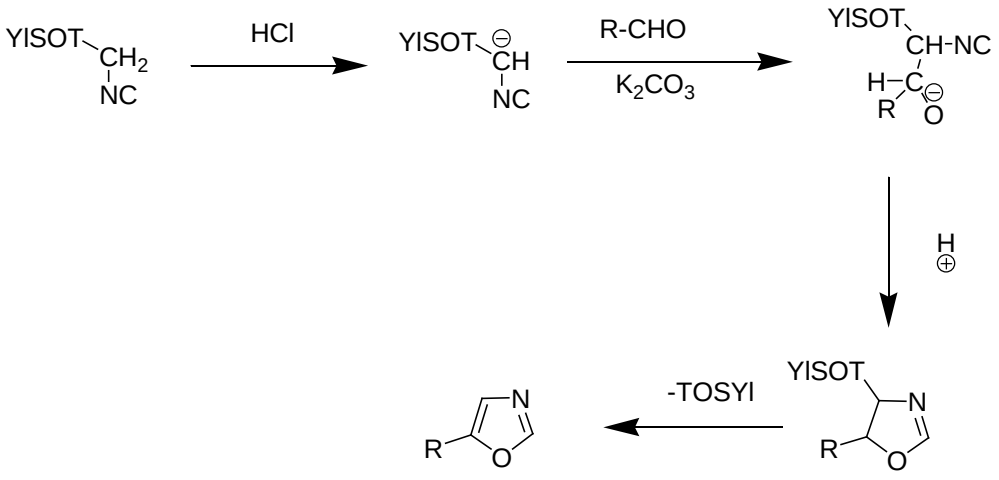
It involves reaction of an aldehyde cyanohydrin with aldehyde in the presence of HCl gas to accomplish 2,5-diaryoxazole.

This method is suitable for the synthesis of diaryloxazoles.



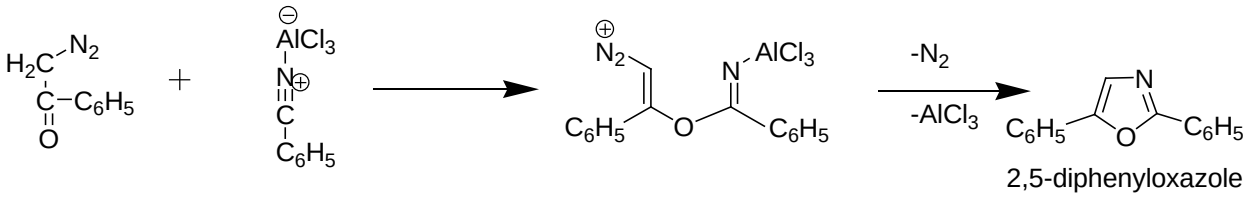
3. Van-leusen schollkopf method :-

This method is based on the reaction of tosylmethyl isocynide with aldehyde in the presence of potassium carbonate to afford 5- alkyl or 5- aryloxazole .

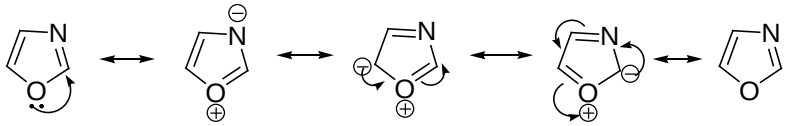


4. [3+2] condensations :

The synthesis is achieved by the interaction of α- diazoacetophenone with nitrile employing lewis acid as a condensing agent to provide 2,5 – disubstituted oxadizole.



Resonance structure :

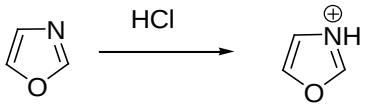


Chemical properties :

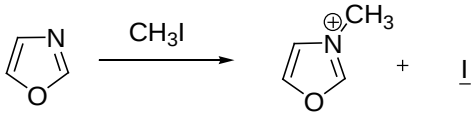
(a) Electrophilic attact at nitrogen :

- It regarded as a hybrid of pyridine and furan exbiting the characteristics of both compound.
- It undergoes protonation and N-alkylation due to pyridine type nitrogen and type properties due to furan type oxygen.

1. Protonation :



2. Alkylation :



(b) Electrophilic attack at carbon :

- Electrophilic attack occurs at the C-4 or C-5 position.
- Electrophilic substituted reactions of oxazole has not been investigated.

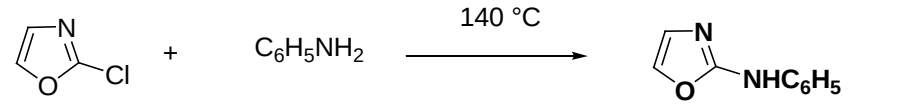
- Nitrtion , sulphonation , and chlorosulphonatuion reaction it self difficult because of the pyridine type nitrogen

(c) Nucliophilic Reaction:-

Nucliophilic reaction occurs at the position – 2 .

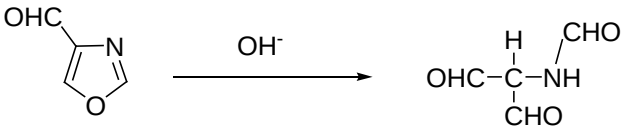
2-chloro oxazole derivative reacts with aniline at 140 °C and the reactivity of halogen atom attached at 2nd position.

1.

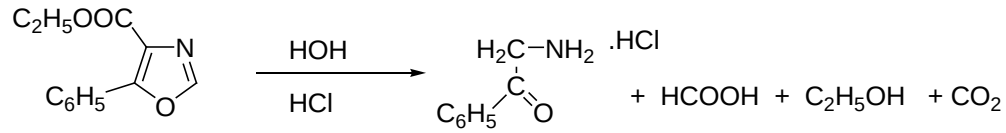


2-chlorooxazole aniline ***N*-phenyloxazol-2-amine**

2.



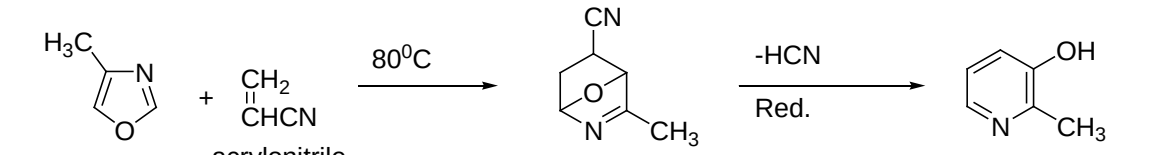
3.



ethyl 5-phenyloxazole-4-carboxylate

(2) Retro- Diels alder reaction:-

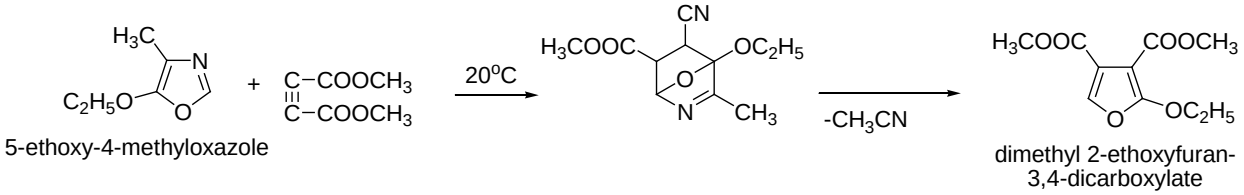
(I)



4-methyloxazole acrylonitrile 2-methylpyridin-3-ol

(ii)

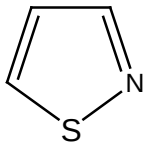
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



5-ethoxy-4-methyloxazole

dimethyl 2-ethoxyfuran-3,4-dicarboxylate

Isothiazole



other name : 1, 2, Thiazole

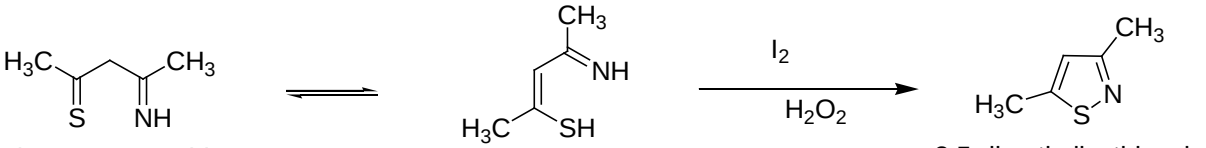
- Isothiazole is a five – membered heterocycle with sulphur and nitrogen located at the position 1 and 2 respectively.
- It was first synthesized in 1956.
- However its widely used derivative , saccharin , a sweetening agent, was prepared in 1879.

Physical properties :-

- Isothiazole is a pale yellow liquid.
- B.p is 112 °C
- It is miscible with most organic solvent .
- It is water soluble.
- Isothiazole is weakly basic because the lonepair on the azomethine nitrogen is not part of the aromatic sextet.
- Isothiazole is aromatic in character.

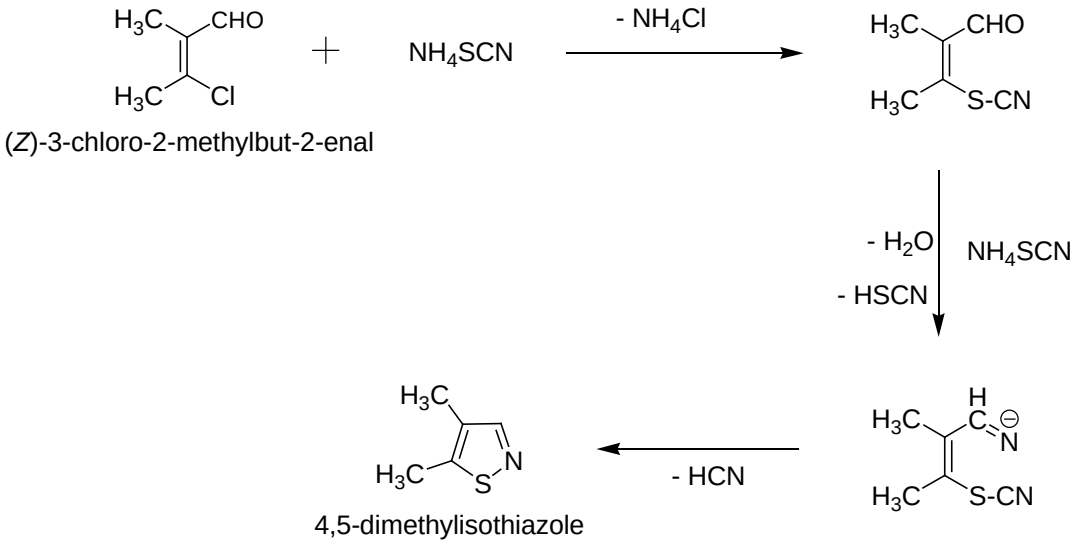
Synthesis:

1. Synthesis of isothiazole consist of oxaadative cyclisation of γ – iminothiol or its toutomer with iodine or hydrogen peroxide to accomplish 3, 5, - disubstituted isothiazole.



4-iminopentane-2-thione (*Z*)-4-iminopent-2-ene-2-thiol 3,5-dimethylisothiazole

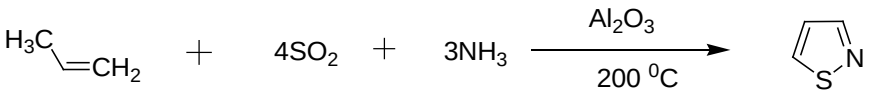
2. Anthor synthesis β – chlorovinyal aldehyde which undergoes cyclisation with two moles of ammonium thiocyanate to furnish 4, 5, disubstituted isothiazole.



(*Z*)-3-chloro-2-methylbut-2-enal

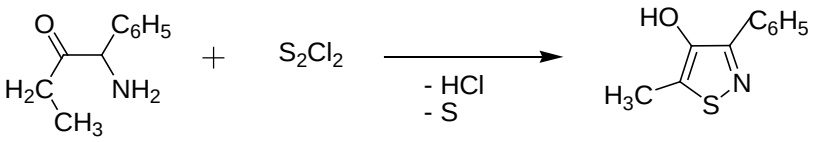
4,5-dimethylisothiazole

3. When a mixture of propylene, sulpher dioxide, and ammonia is passed over alumina at 200 °C isothiazole is obtained.

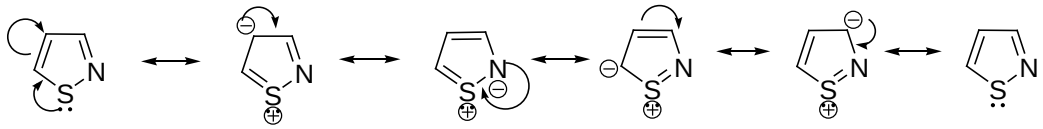


isothiazole

4. The reaction of α – propionylbenzyl amine with sulpher monochloride results in the formation of isothiazole derivative.

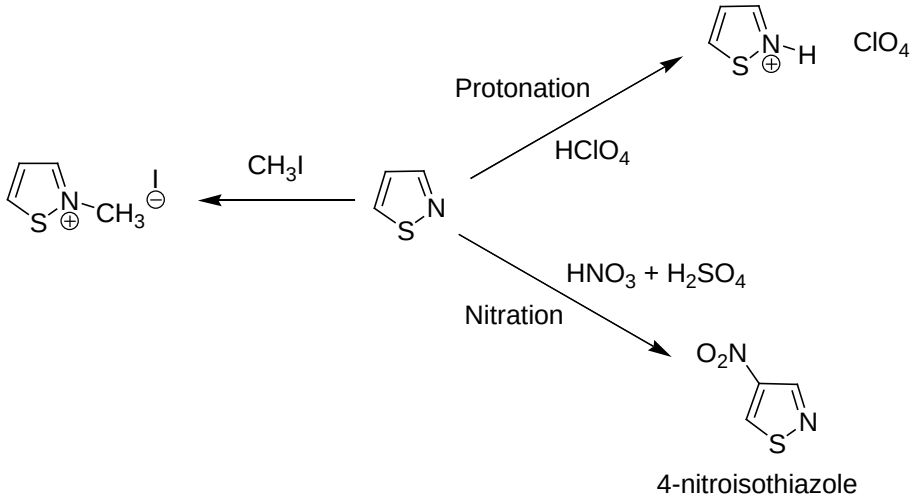


❖ Resonance structure :-

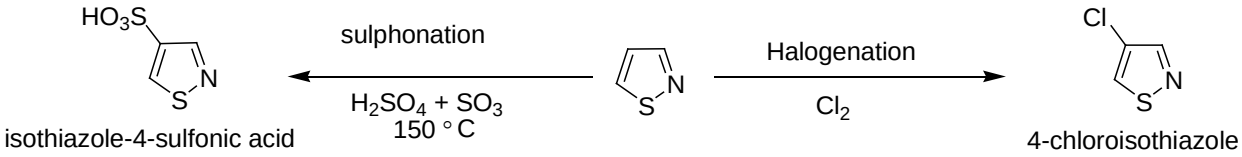


❖ Chemical Properties :-

(a) Electrophilic substitutions at nitrogen.

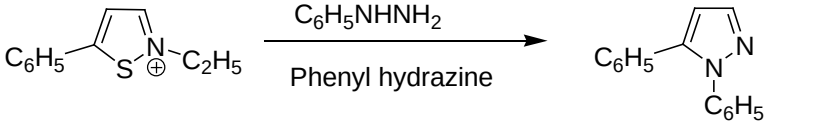


(b) Electrophilic substitution at carbon :



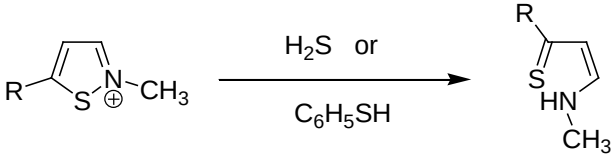
(c) Nucleophilic substitution :-

1. Isothiazolium salt reacts with phenyl hydrazine to yiled pyrazole.

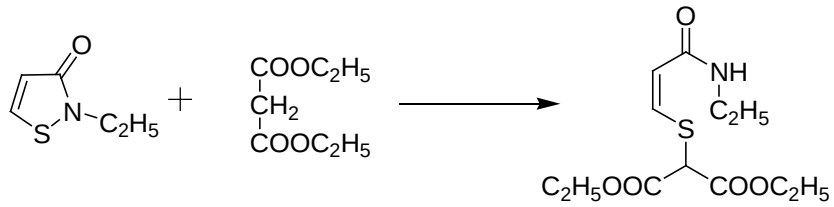


1,5-diphenyl-1*H*-pyrazole

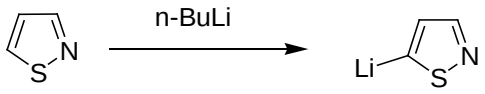
2. The reaction of 2-alkyisothiazolium salt with hydrogen sulphide or thiophenol result in the formation of acyclic product.



3. The reaction of 2-ethylisothiazole 1,3-one with malonic ester and sodium ethoxide cause ring opening.

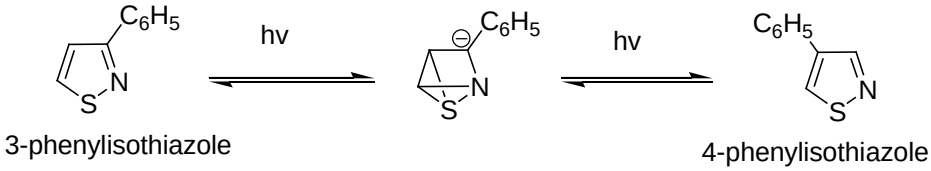


4. Isothiazole is lithiated at 5-position with n-BuLi.



(d) Photochemical Reaction :

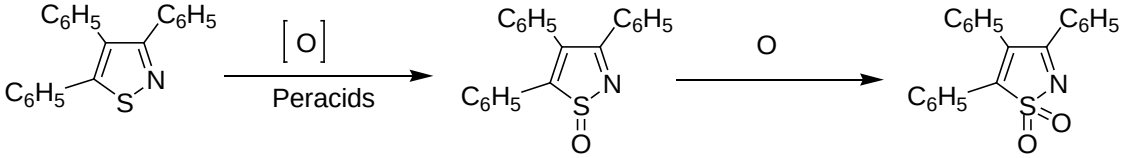
Isothiazole on photochemical reaction is transformed into thiazole via intermidate formation of zwitter ion type product.

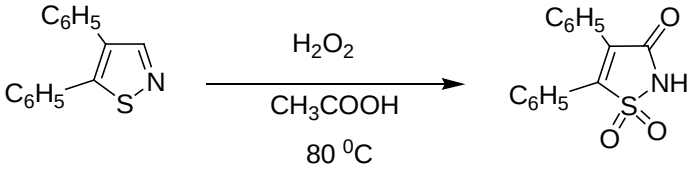


3-phenylisothiazole 4-phenylisothiazole

(e) Oxidation :

Trisubstituted isothiazole is oxidized in the presence of peracids to its sulphoxide and sulphone while 3-unsubstituted isothiazole on oxidation with hydrogen peroxide at 80 °C gives 1,1-dioxide of 3-isothiazolone derivative.

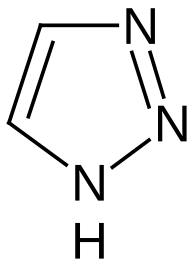




Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

1, 2, 3 – TRI AZOLE

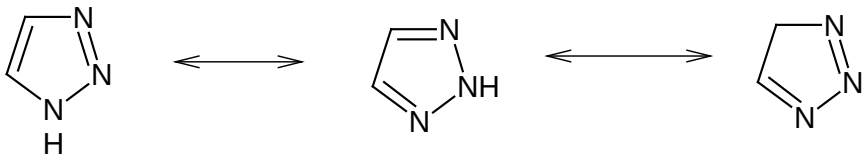


INTRODUCTION:-

1,2,3 - Tri Azole is referred to as a five member hetro cycle derived from pyrrole by replacing two carbon atoms by two nitrogen atoms at the 2 & 3 position in the ring. It is also named as V- tri Azole (vicinal).

Two isomeric tri azoles are known 1, 2, 3 - tri Azole and 1, 2, 4 - tri Azole.

1,2,3 - tri Azole exists in three tautomeric forms as under,



1H - 1,2,3 - Tri azole 2H - 1,2,3 - Tri azole 4H - 1,2,3 - Tri azole

2H – Tautomer predominates in solution of most orgnic solvents

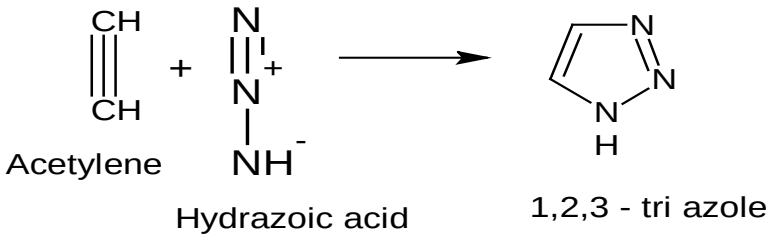
First Tri azole derivative, 1 – Phenyl – 4,5 – Dimethyl – 1,2,3 tri azole was prepared by Pechmann in 1988

Tri azoles are of systhetic importants and have been explored extensively for biological activities. A host of other application of 1,2,3 – tri azoles with functions as widely divergent as fluorescent brightening agents, stabilizer, agrochemicals, corrosion inhibitor, dye stuffs etc..

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

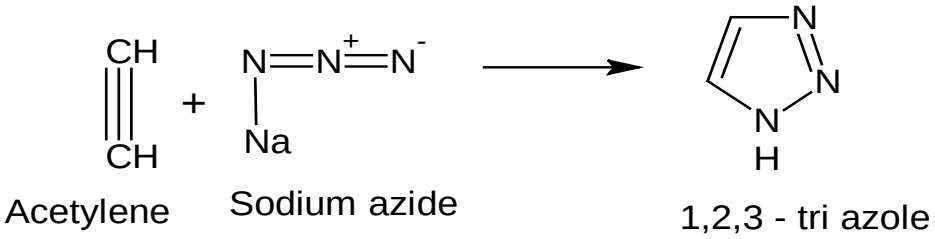
SYNTHESIS:-

1.



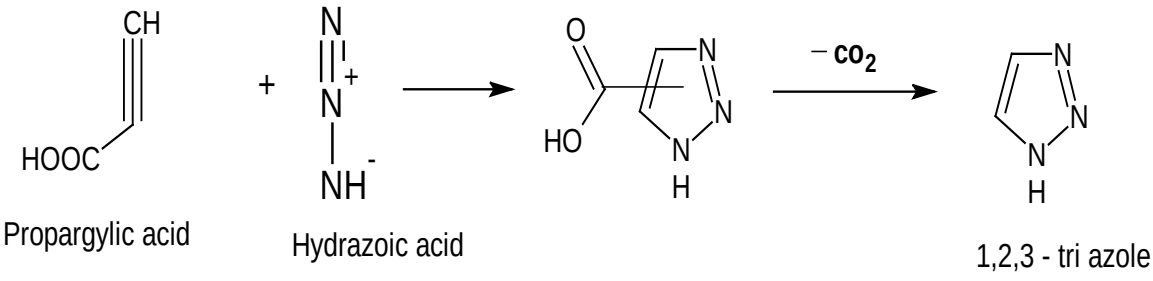
Acetylene heated with Hydrazoic acid to form 1,2,3 – tri azole.which is shown in above reaction.

2.



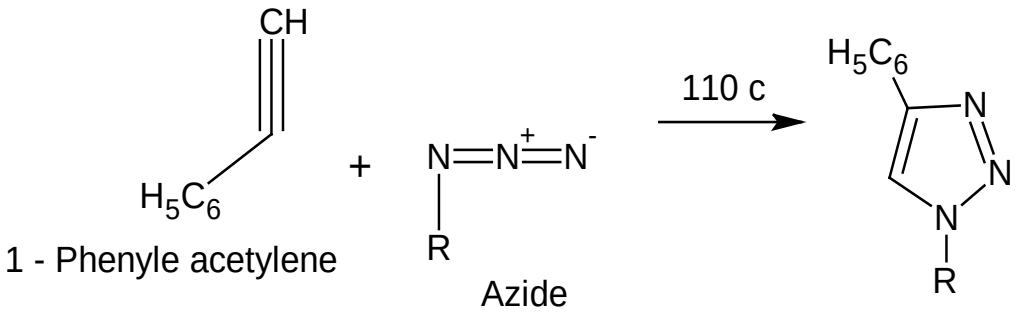
Acetylene reacts with Sodium azide in acidic media to form 1,2,3 – tri azole which is shown in above reaction.

3.



Propargylic acid heated with Hydrazoic acid at 110 C to form 1,2,3 – tri azole.

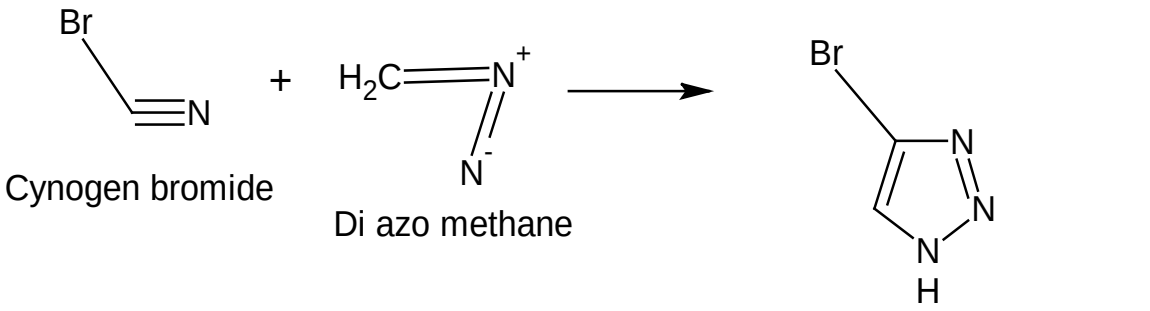
4.



1 - Phenyle acetylene Azide

1 – Phenyle acetylene heated with azide at 110 C to form 1,2,3 – tri azole derivative.

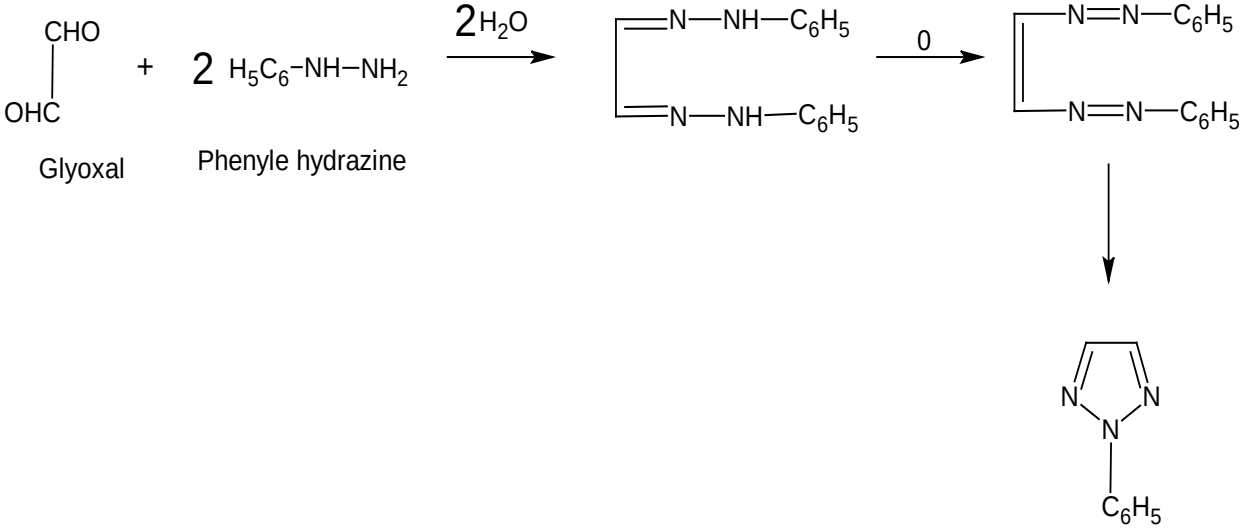
5.



Cynogen bromide Di azo methane 4 - bromo 1,2,3 - tri azole

This process consists of the reaction of cynogen bromide with diazomethane gives rise to 4-bromo-1,2,3-triazole.

6.



An aleternative route employs reaction of a,B – dicarbonyl compound with phenyl hydrazine to furnish hydrazone which on oxidation and on cyclisation with ferric chloride provides 2-phenyle-1,2,3-tiazole.The reaction of glyoxal and benzyl with phenyl htdrazine result in the formation of 2,4,5-triphenyl-1,2,3-triazole.

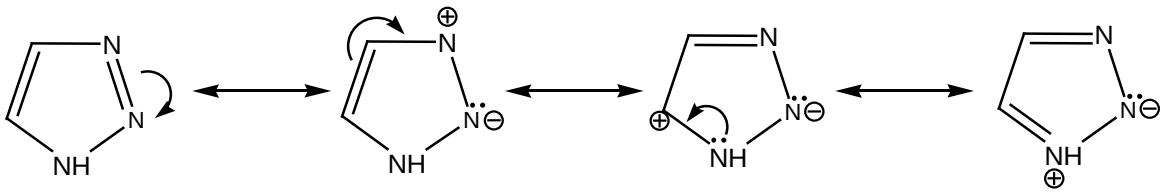
PHYSICAL PROPERTIES:-

It is weak base as well as weak acid so it is called Amphoteric in nature.

It is liquid.

It's boiling point is 204 C

RESONATING STRUCTURES:-



SPECTRAL DATA:-

UV(λ_{max}) nm:210 (3.6)

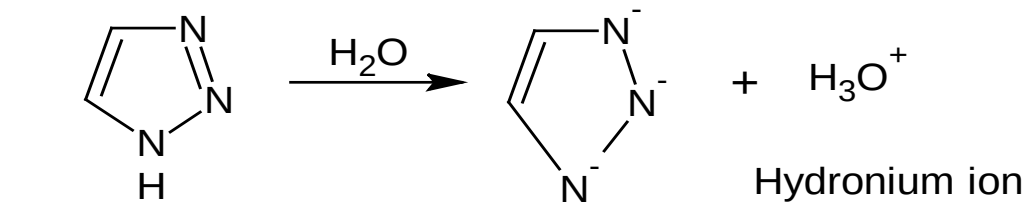
^{1}H NMR δppm ($CDCl_3$):C_4 –H, 7.75; C_5 –H, 7.78; N-H, 12.

C NMR δppm (Dioxane): C_4, 131.6 ; C_5, 131.6

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

CHEMICAL PROPERTIES:-

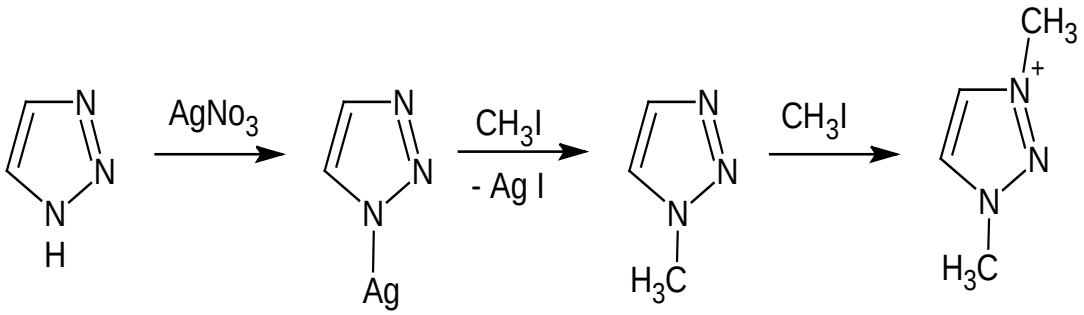
1. Protonation :-



1,2,3 - tri azole Trianion

1,2,3 – tri azole react with water leads to the formation of hydronium ion and trianion.

2. Methylation:-

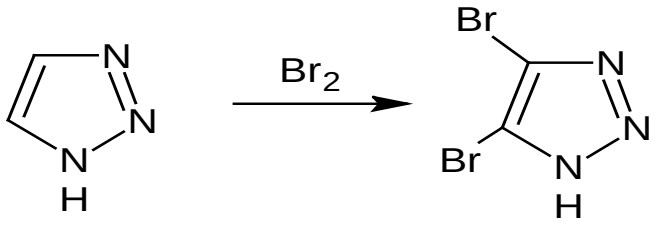


1,2,3 - tri azole

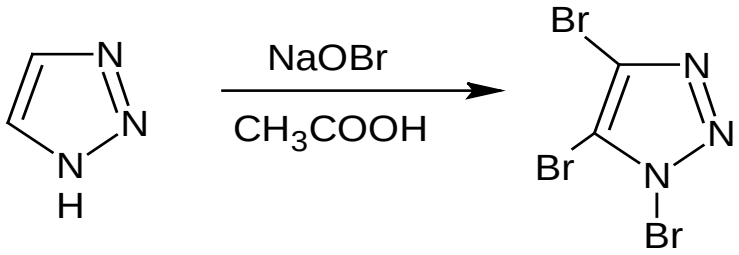
N-Alkylation can be readily carried out with alkyl halide,jimethyl sulphate, diazomethane or methyl –p-toluenesulphonate by Mannich reaction. Alkylation with diazomethane proceeds pregerentially at N-2 position with the formation of 2-methyl 2H 1,2,3-triazole.Use of methyl iodide with silver salt os 1,2,3-triazole resules in attack at N-1 position.

3. Electrophilic substitutions at Carbon :-

(1)

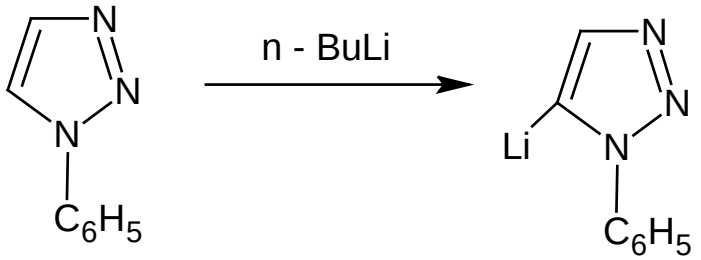


(2)



Bromination of 1,2,3-triazole occurs with bromine at 4,5-position to afford 4,5-dibromo-1,2,3-triazole but with excess of sojium hypobromite in acetic acid 1,4,5-tribromo derivative is obtained.

4. Nucleophilic Reaction :-

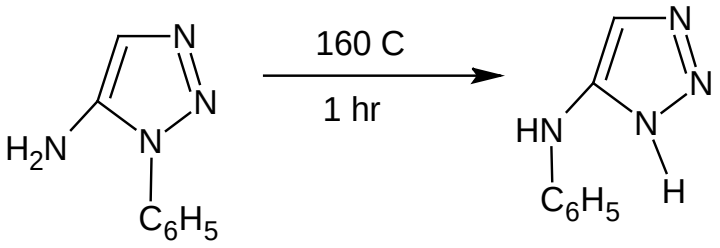


N-Substituted 1,2,3-triazole

5-lithio derivative

N-Substituted 1,2,3-triazole reacts with n-butyllithium at low temperature to give 5-lithio derivative.

5. Dimroth Rearrangement :-



1-phenyl-5-amino-1,2,3-triazole

5-phenylamino-1,2,3-triazole

It is an isomerisation where by ring nitrogen and its attached group gets rearranged with an imino group at the position to it.

1-phenyl-5-amino-1,2,3-triazole rearranges to 5-phenylamino-1,2,3-triazole when heated at 160 C temp. For 1 hr.

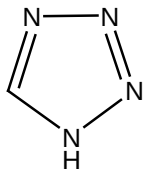
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Tetrazole

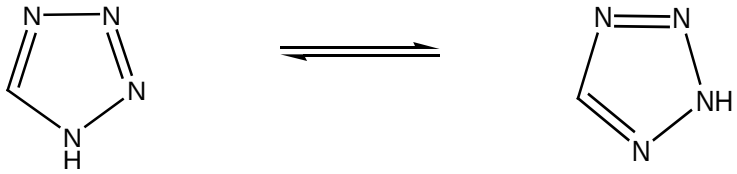
A 5-membered heterocyclic compound

Introduction :

- ✓ It has 4 hetero atom.
- ✓ It contains one pyrrole type and three pyridine type nitrogen.



- ✓ It has two tautomeric form. [1H-form & 2H-form]



1H-form 2H-form

- ✓ Tetrazole nucleus has been explored for biological activity because of two properties.
  - Comparable acidity of tetrazole group [-CN_4H] o and –COOH group.
  - Metabolically more stable than acid resistant to biological degradation. This makes it possible to use tetrazole as a isoteric substituent of various functional groups in the development of biologically acitve compounds.

Physical properties :

- ✓ It is colourless solid crystals.
- ✓ it's melting point is 156°C.
- ✓ It is aromatic in character.
- ✓ N- unsubstituted tetrazoles exhibit intermolecular H-bond.

Spectral data :

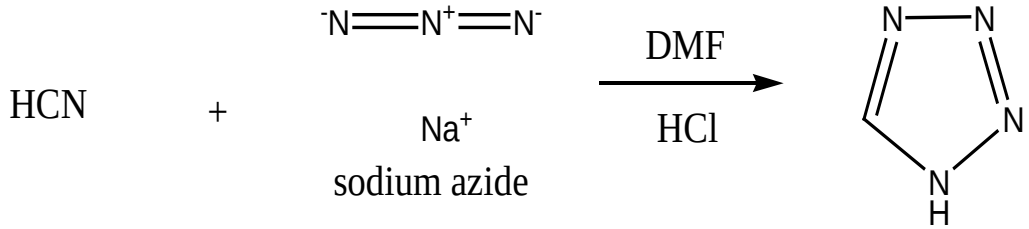
i. UV : λ_{max} : 200-220 nm
ii. ^{1}H NMR (D_2O) : C_5-H , 9.5
iii. ^{13}C NMR (DMF) : C_5-143.9

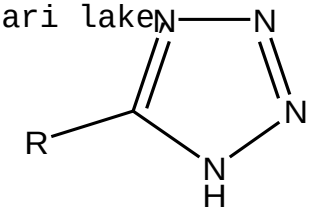
Synthesis :

- From imidoyl azide
- From nitriles
- From nitrilium salts
- From isoniriles
- From formazans
- By diazotization of amidrazone
- From acid hydrazides

From nitriles :

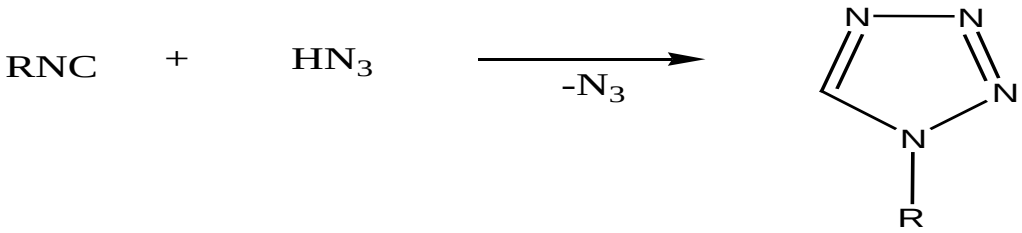
- ✓ 5-substituted tetrazole can be prepared by addition of HCN & nitrile (RCN) with NaN_3 (sodium azide) in DMF & HCL.



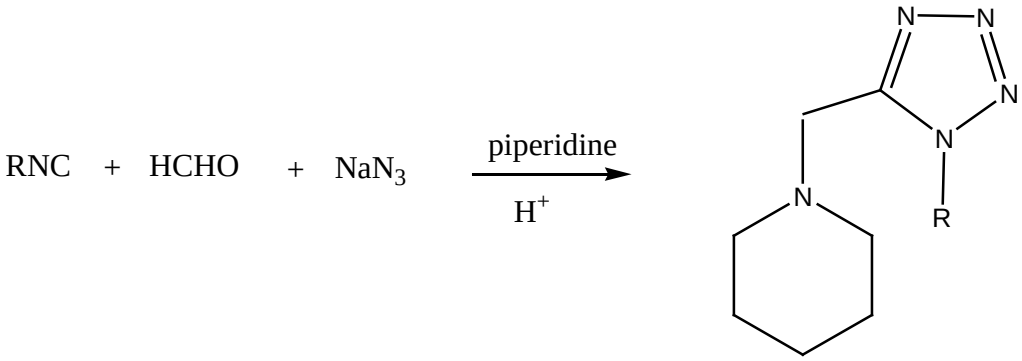


From isoniriles :

- ✓ The reaction of isocyanide with hydrazoic acid is a convenient method for preparation of 1-substituted tetrazole.



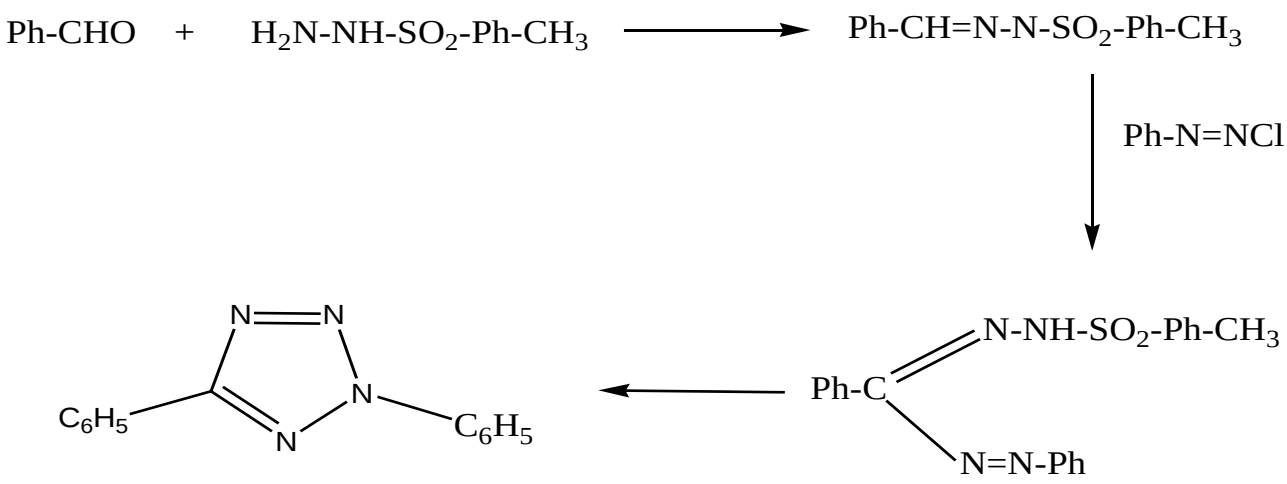
- ✓ The reaction of isonitrile with NaN3 in presence of mannich type reagent (HCHO + piperidine) give 1,5-disubstituted tetrazole.



From formazans :

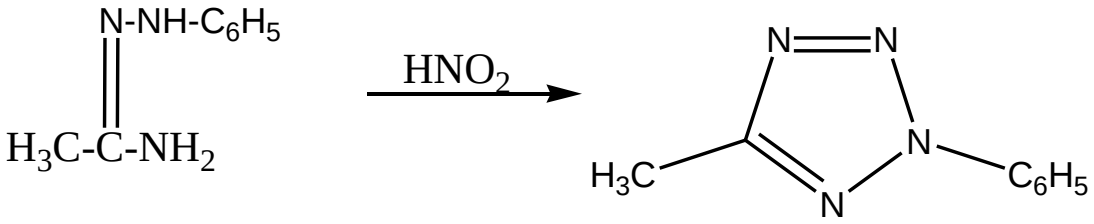
- ✓ 2,5 disubstituted tetrazole is prepared by the treatment of benzaldehyde and toluene P-sulphonyl

hydrazone with aromatic diazonium salt in sodium hydroxide – ethanol or pyridine.



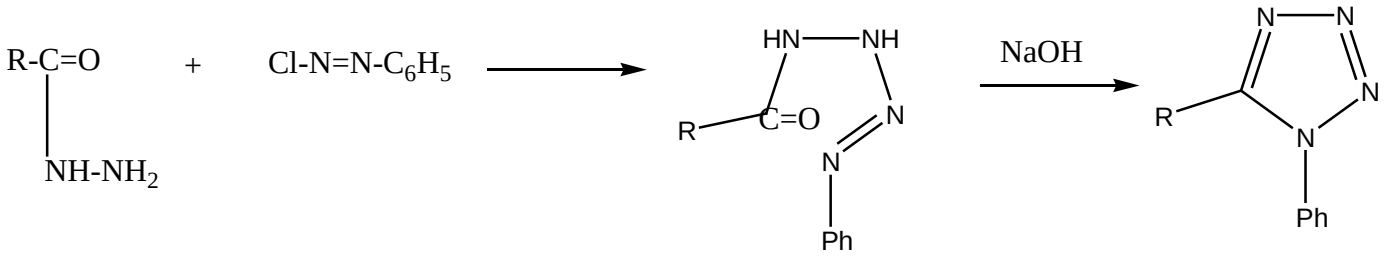
By diazotization of amidrazone :

- ✓ Diazotozation of substituted amidrazone with HNO2 gives imidoyl azide which undergoes cyclization to provide 2,5-disubstituted tetrazole.



From acid hydrazides :

- ✓ The reaction of acid hydrazide with diazonium chloride to afford tetrazene which on dehydration with base provides 1,5-disubstituted tetrazole.

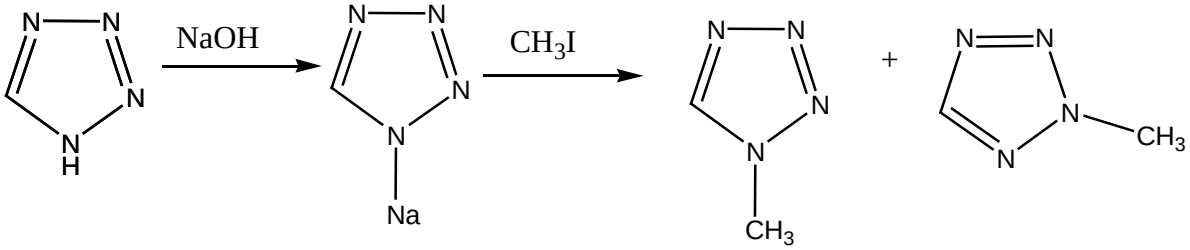


Chemical properties :

- ✓ Pyrrole type N : electron donating effect
- ✓ Pyridine type N : electron withdrawing effect
- ✓ Hence, ring becomes π-electron deficient.
- ✓ So, nucleophilic attack on N-atom take place.

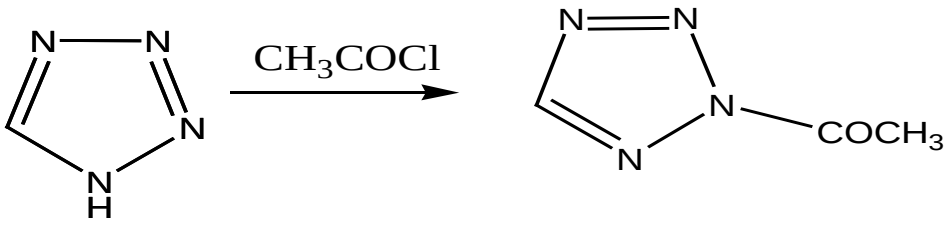
Electrophilic reaction at N-atom :

- Alkylation :



1-methyl tetrazole 2-methyl tetrazole

- Acylation :

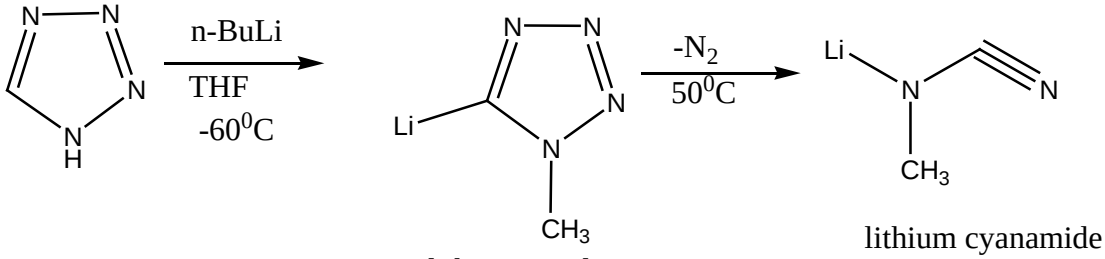


2-acetyl tetrazole

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Electrophilic substitution at C-atom :

- Bromination & mercuration :

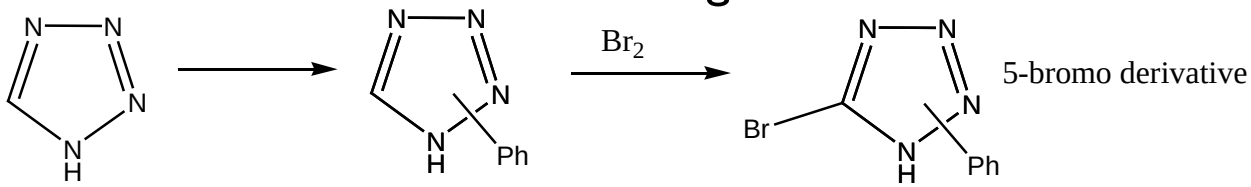


lithiotetrazole

lithium cyanamide

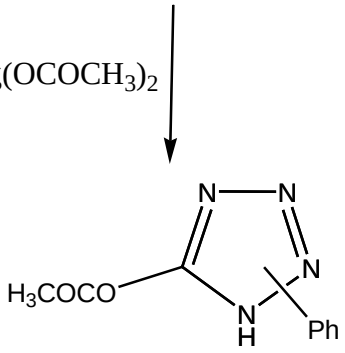
- **Nucleophilic reaction** :

substitution at ring c-atom....



1-phynyl tetrzole

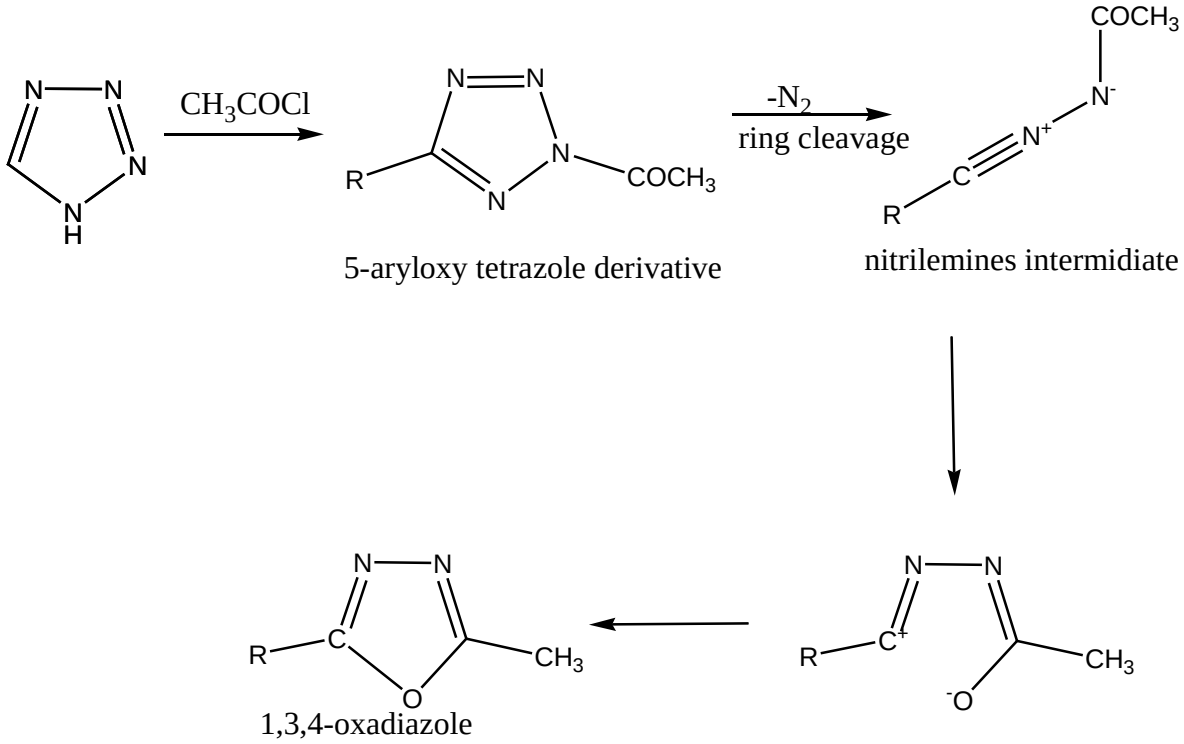
5-bromo derivative



5-acetoxy marcury derivative

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Thermal & photochemical reaction :



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Name :- Lunagariya Kaushik

Roll no. :- 28 (Twenty Eight)

M.Sc. Chemistry Sem-3

Branch :- Organic Chemistry

Assignment of

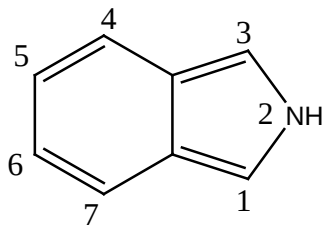
Heterocyclic compound

ISOINDOLE

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

-: ISOINDOLE :-

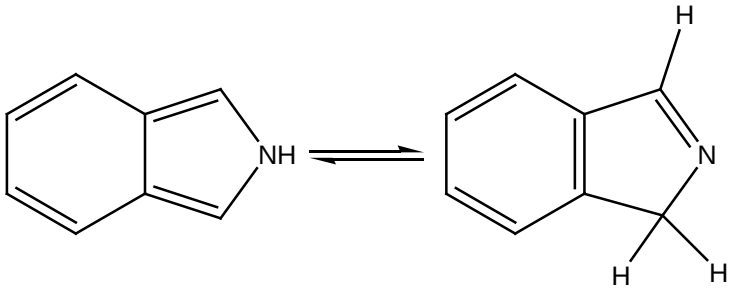
- Sructure :-



isoindole

- IUPAC Name :- Benzo [C] Pyrrole
- Other Name :- 2H – isoindole

- Isomer :-



2 H-isoindole 1 H-isoindole

Physical properties :-

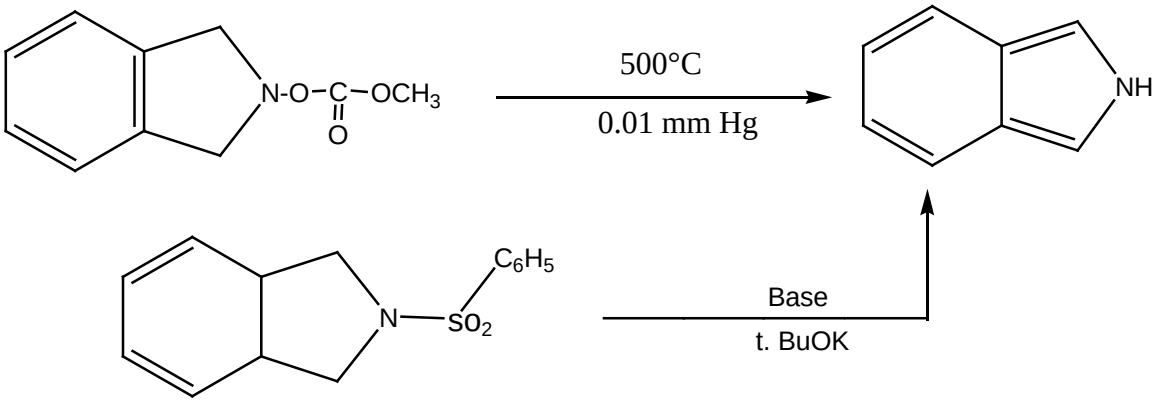
1. Isoindole is white solid compound.
2. It can be isolated at low temperature but decompose at room temperature.
3. It is stable only as its Diels-Alder adduct.
4. 2-Methyl isoindole is colourless compound
5. Melting point is 90-91°C.
6. Isoindole behalves as a typical secondary amine. The pKa is not known.

Synthesis :-

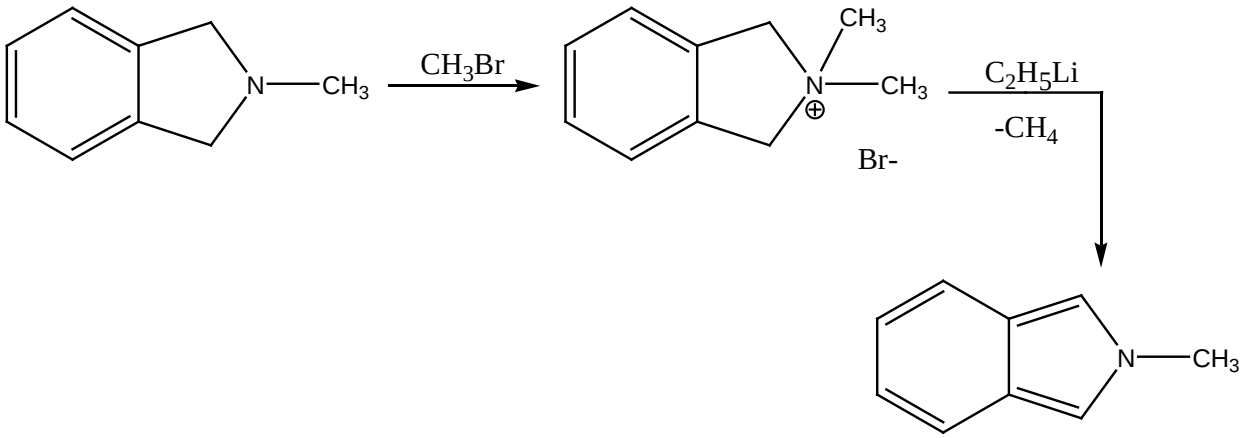
1. From isoindolines
2. From o-chloro benzyl amine
3. Cycloaddition of benzene and pyrrole
4. By reductive amination of o-dibenzoyl benzene

1) From isoindolines :-

a) The first synthesis of isoindole itself includes the vapour phase phase pyrolysis (500°C) of N-methoxy carbonyloxy isoindoline. The product was isolated at low temperature N-sulphonyl isoindole on base catalyst elimination leads to the formation of isoindole.

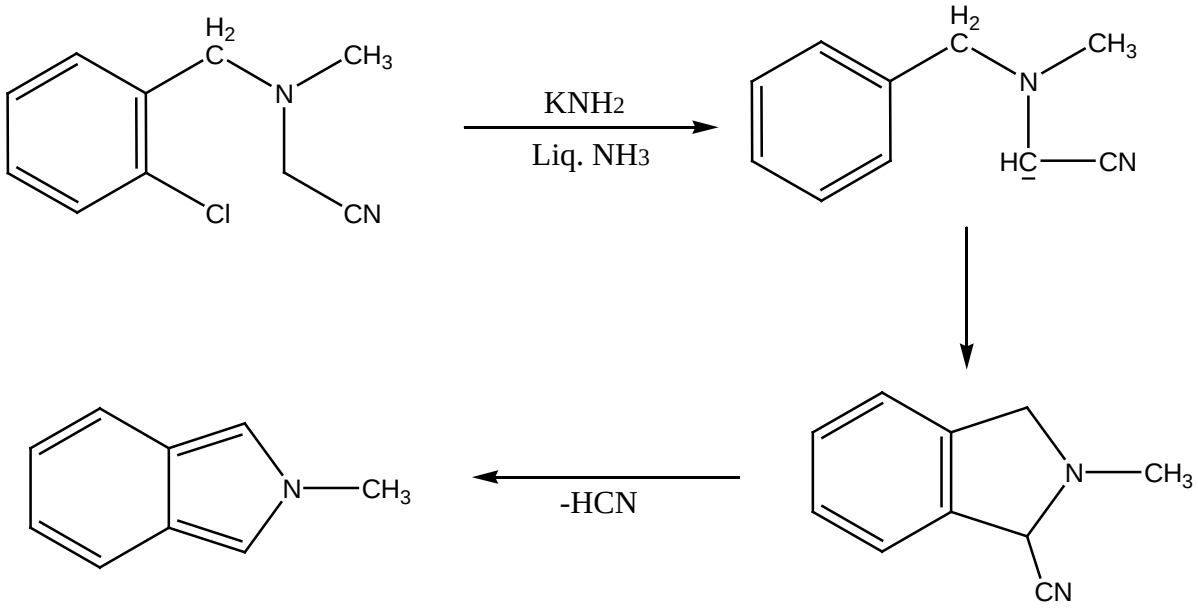


b) N-methyl isoindoline on methylation and treatone with phenyl lithium provide N-methyl isoindole.



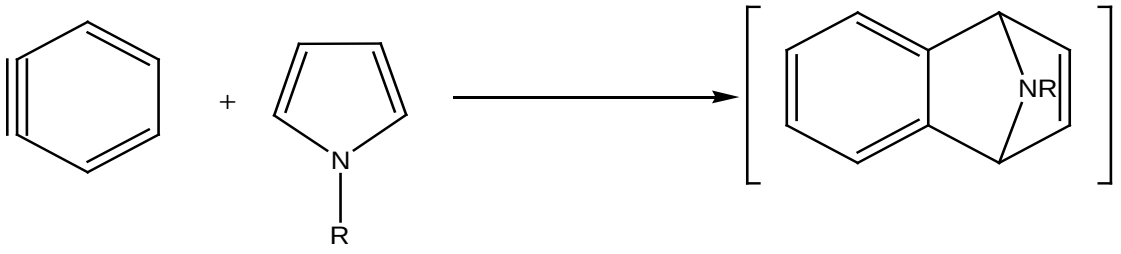
2) From o-chorobenzyl amine :-

o-chloro benzyl amine derivative with potassium amie in liquid ammonia undergoes cyclization to provide N-methyl isoindole. It involves intramolecular nucleophilic addition with loss of HCN.

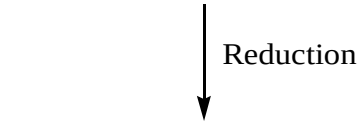


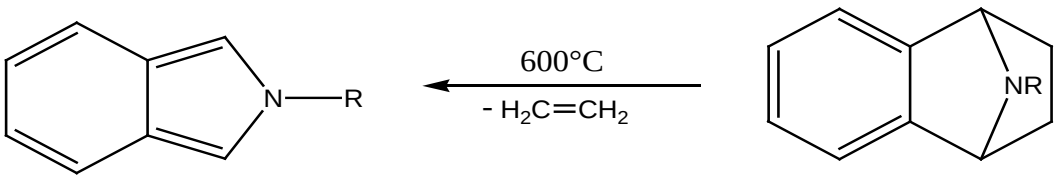
3) Cycloaddition of benzene and pyrrole :-

An alternative route involves cycloaddition of benzene and pyrrole to yield benzo-7-azobicyclo(2,2,1) heptanes followed by reduction and heating at 600°C to give retro-Diels-Alder reaction with loss of ethylene.



Benzyne Pyrole deri. Benzo 7-azabicyclo(2,2,1,) Heptane

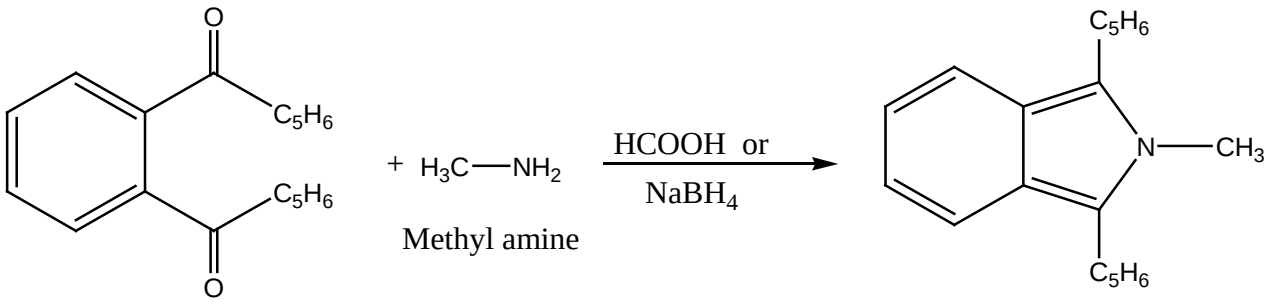




Isoinole dari.
2-Metyl Isoindole

4) Reductive amination of o-dibenzoyl benzene :-

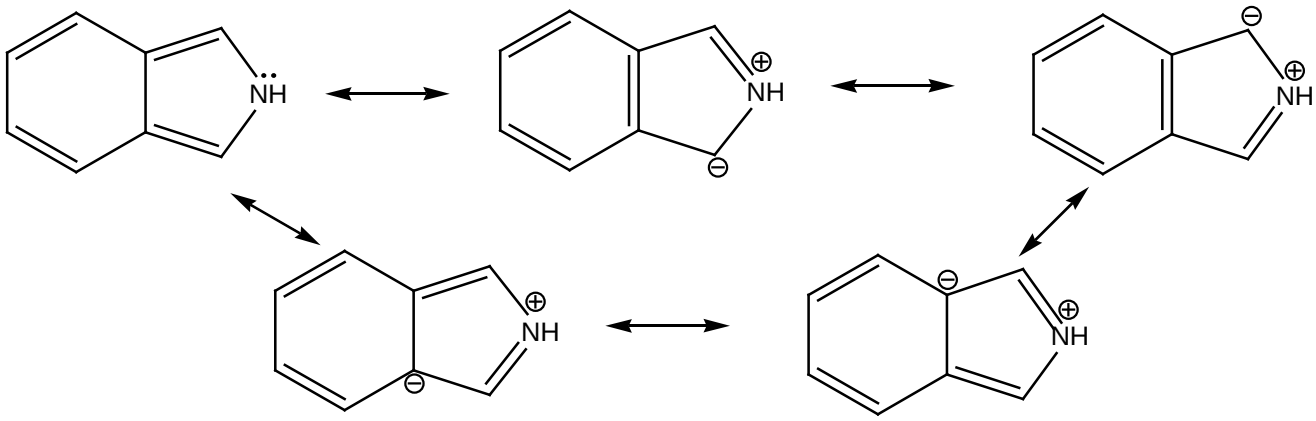
Reductive amination of o-dibenzoyl benzene with methyl amine in the presence of formic acid or sodium borohydrate provide substituted isoindole.



Dibenoyl Benzene Methyl amine l2-Methyl 1,3, dipheny Isoindole

Chemical properties :-

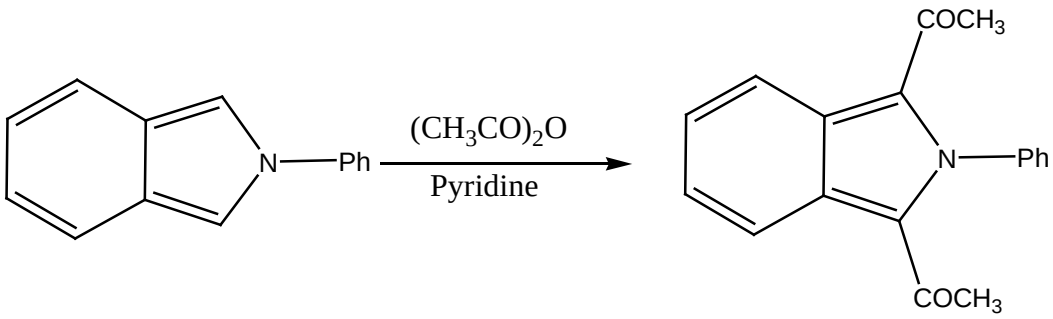
Resonating structure :-



Chemical reactivity :-

As the π-elctron density is high in isoindole ring at C-1 it undergoes elctrophilic substitution at C-1 and di-substitution at C-1 and C-3 position.

- Electrophilic reaction of 2-phenyl isoindole :-
  1. Acetylation :-

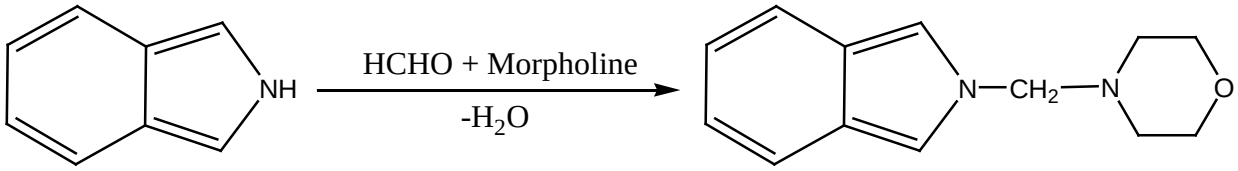


2-Phenyl Isoindole

1,3,-Diacetyl 2-Phenyl Isoindole

2-phenyl isoindole react with acetic anhydride in presence of pyridine to obtain 1,3 diacetyl 2-phenyl isoindole.

2. Mannich reaction :-

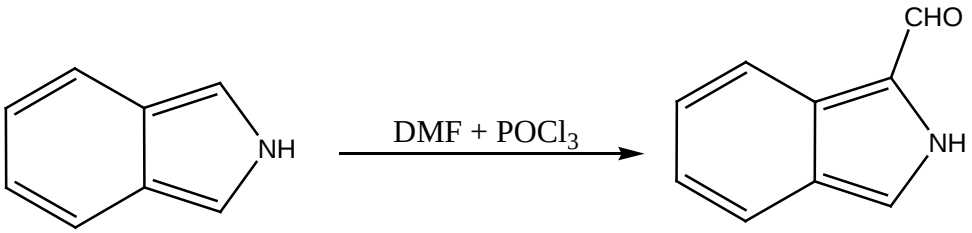


Isoindole

N-Morpholino Methyl Isoindole

Isoindole react with formaldehyde and morpholine to produced N-morpholino methyl isoindole . This reaction is known as Mannich reaction.

3. Vilsmeier-Haack reaction :-

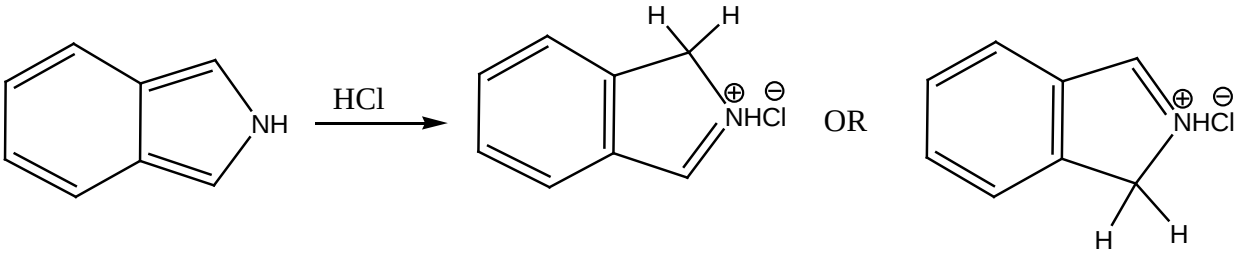


Isoindole

3-Formyl Isoindole

Isoindole react with dimethyl formanion with $POCl_3$ to produce 3-formyl isoindole.

4. Protonation :-



Isoindole

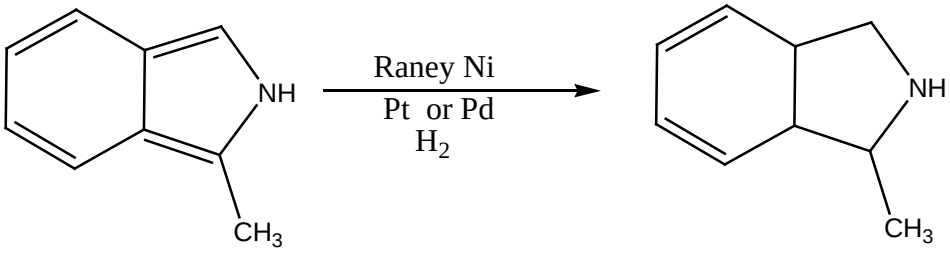
3-Hydro Isoindol deri.

1-Hydro Isoindol deri.

Isoindole react with hydrochloric acid to produce 1 or 3 position hydro isoindole derivative.

- Reduction :-

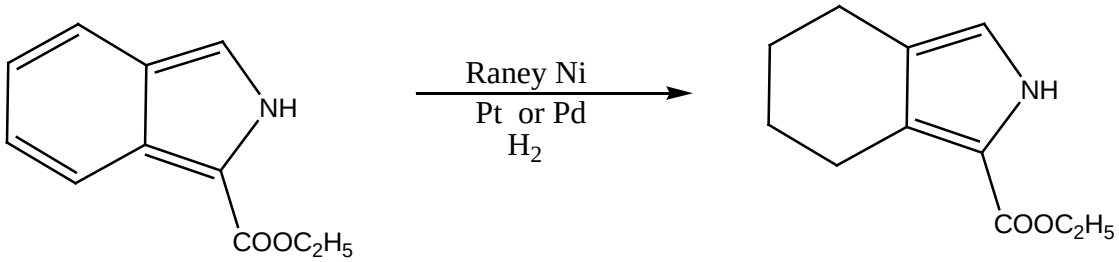
1.



1-Methyl Isoindole 1-metyl isoindoline

1-methyl isoindole reduce with Raney-Nickel and Pt with hydrogen gas to obtain 1-methyl isoiindoline.

2.

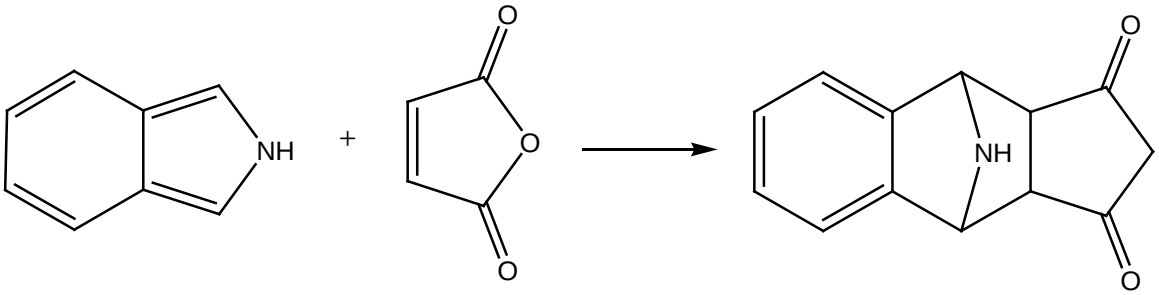


1-Carbethoxy Isoindole 4,5,6,7-tetrahydro Isoindole deri.

1-carbethoxy isoindole reduce with Raney-Nickel and Pt or Pd with H_2 gas to produce 4,5,6,7 tetra hydro isoindole derivative.

- Cycloaddition reaction (Diels-Alder reaction) :-

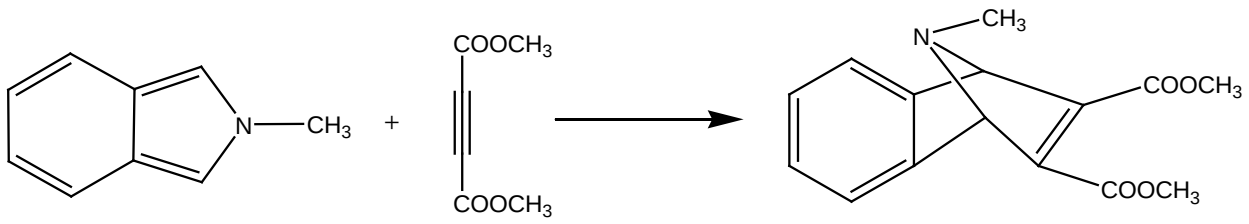
1.



Isoindole Maleic anhydride (4+2) Cyclo adduct

Isoindole treat with maleic anhydride to produce (4+2) cyclo adduct of isoindole.

2.

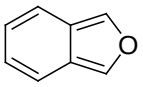


Isoindole | Dimethyl acetylene dicarboxylate | Diels-Alder Adduct

Isoindole treat with dimethyl acetylene dicarboxylate to obtain Diels-Alder adduct.

Isobenzo Furan

Structure:



Benzo [c] Furan

1,3DiphenylIsobenzo Furan

→It is unstable and very reactive so has not isolated in pure form.

Physical Property:

→It is yellow color solid.

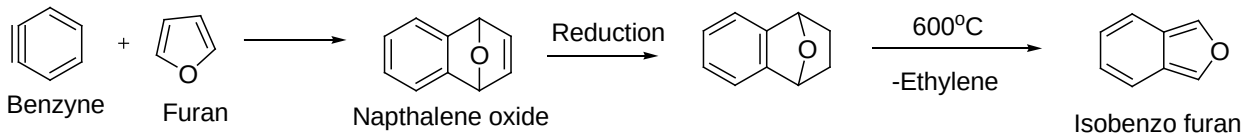
→Its melting point is 127°c

→Its solution has blue-green fluorescene

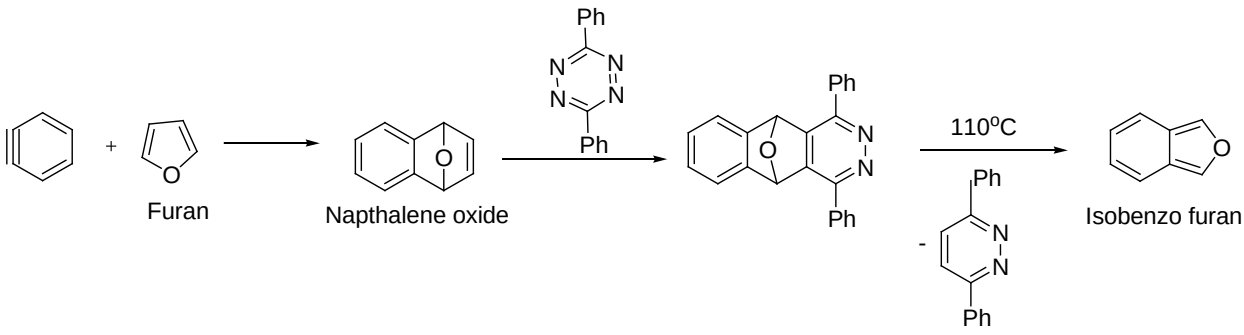
Synthesis:

1) From Napthalene oxide :

A. Naphthalene oxide obtained by (4+2) cycloaddition of furan with benzyne undergoes reduction followed by retro diels Alder reaction to give Isobenzo Furan.

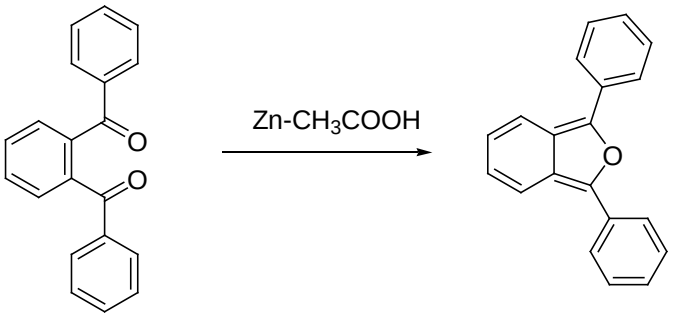


B .The cycloaddition reaction of Naphthalene oxide with 3,6Dipyridyl 1,2,4,5 tetra azine at 120°c in vaccume afford adduct which thermally fragments into Benzo [c] Furan via Retro Diels Alder reaction.



2) From o-Dibenzyol Benzene

The reductive cyclization of o-Dibenzyol Benzene with Zn dust in Acetic Acid.

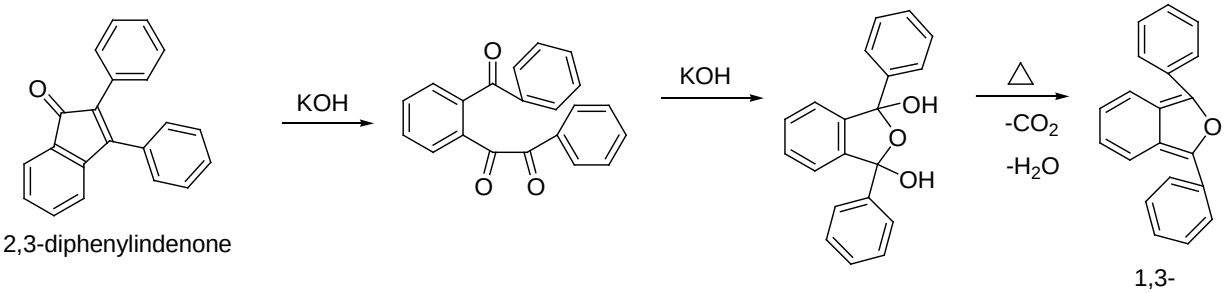


O-Dibenzyol benzene

1,3-Diphenyl Isobenzo furan

3)From 2,3 Diphenylindenane

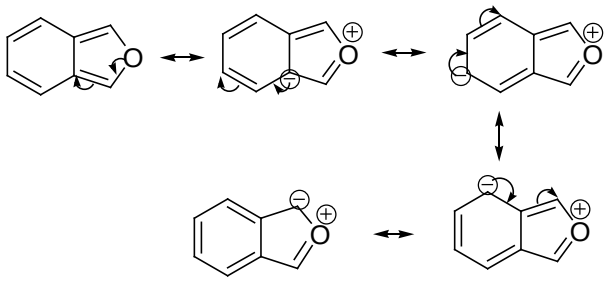
Benzilic acid rearrange to o-benzoyl benzill which is obtained by the reaction of alkali on 2,2Diphenylindenane



2,3-diphenylindenone

1,3-Diphenyl Isobenzo furan

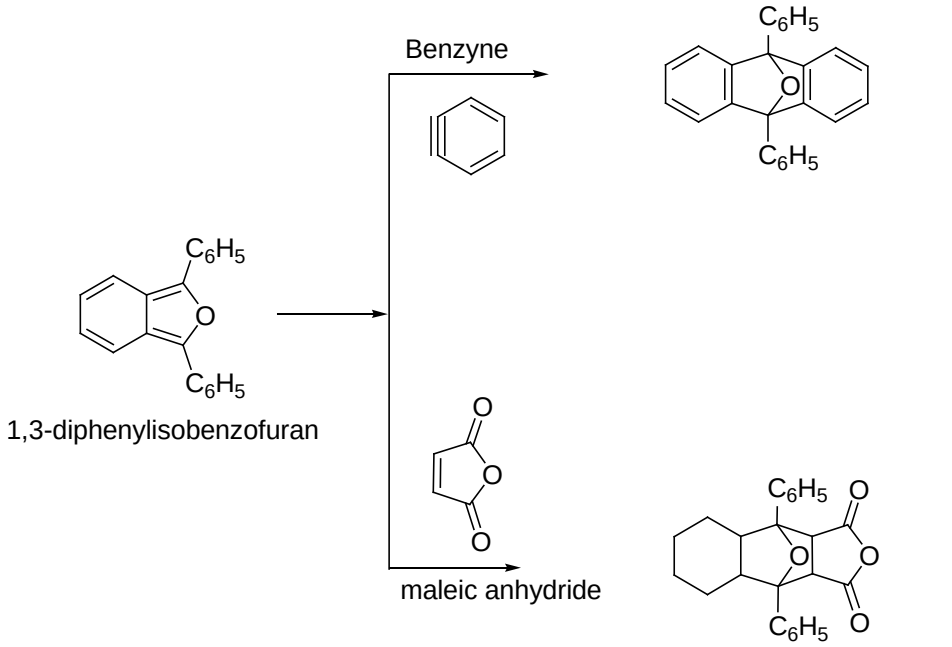
Resonating Structure:-



As the benzene ring in isobenzo furan does not possessπ-electron sextet, the resonance energy is quite less than benzofuran.

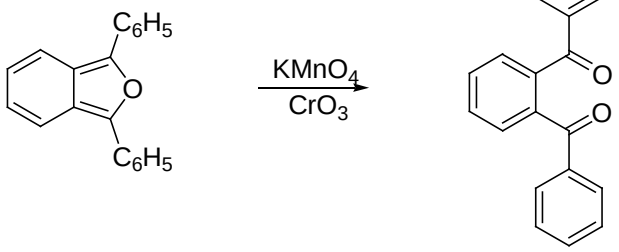
Chemical Properties:-

(1)Cyclo addition reaction :-



Cyclo addotion product

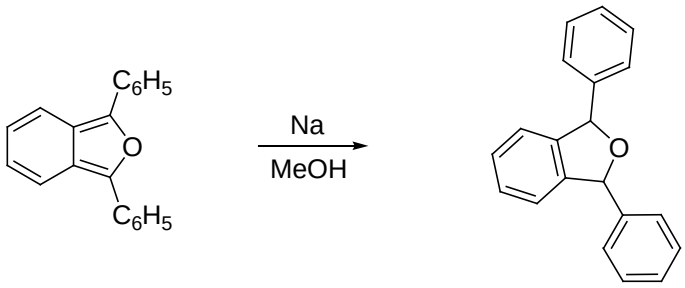
(2) Oxidation:-



1,3-diphenylisobenzofuran

1,2 dibenzoyl benzene

(3) Reduction:-



1,3-diphenylisobenzofuran

1,3 diphenyl -1,3 dihydro iso benzo furan

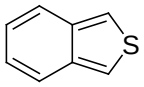
(4) Photo chemical Reaction:-

1,3diphenylisobenzo furan on UV irradiation in the presence of acetophenone as sensitizer gives dimer.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Isobenzothiophene

Structure:



Benzo [C] thiophene

Isothionapthalene

Introduction:

It is five membered heterocyclic compound containing 1 hetero atom and 1 fused aromatic ring.

Physical Property:

It is unstable moity.

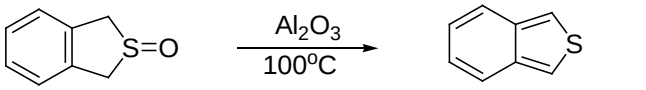
Its boiling point is -30^{0}c. and stable only at this boiling point. However, by substitution at c_1 and c_3 position it can be stabilized.

It is aromatic in nature.

It's smell is like the Naphthalene.

Chemical Synthesis:

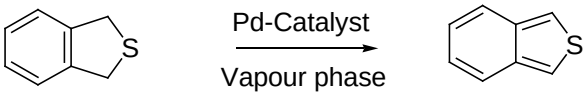
1) It can be prepared by reaction of 1,3,Dihydrobenzo[c]Thiophene 2 oxide trated with alluminium oxide at 1:2 proposion at 100^0 c temperature gives Isobenzothiophene.



1,3-Dihydro benzo
[c] thiophene 2-oxide

Isobenzothiophene

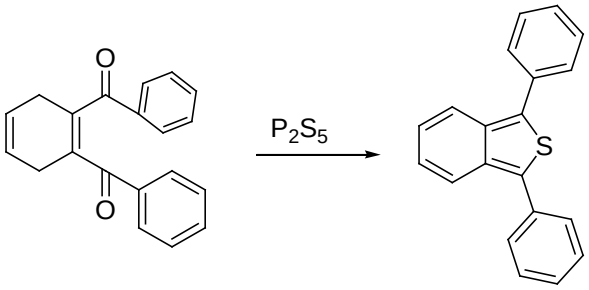
2) It also can be prepared by dehydrogenation of hydrobenzo[c]thiophene in vapour phase in the presence of Pd catalyst at 300^0 c temperature.



1,3-Dihydro benzo
[c] thiophene

Isobenzothiophene

3) The reaction of 1,2,Dibenzyol 1,4,Dihidrobenzene with phosphorus penta sulphide provide 1,3,diphenyl isobenzothiophene.



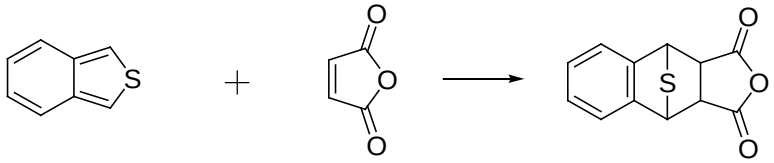
1,2-Dibenzyl 1,4-dihydrobenzene

1,3-Diphenyl isobenzothiophene

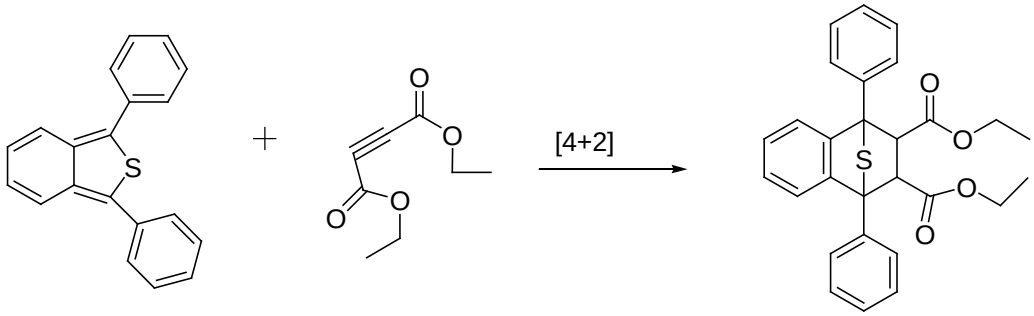
Chemical Properties:

It is very reactive and shows diene type characteristics.

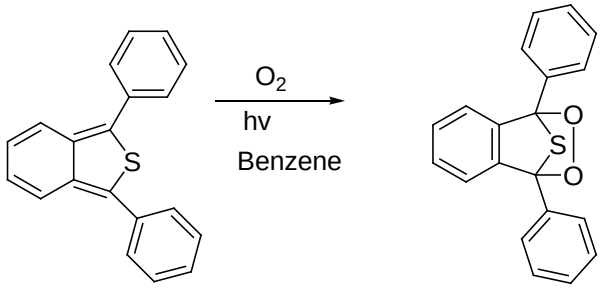
1) It undergoes (4+2) cyclo addition reaction with maleic anhydride and their derevatives.



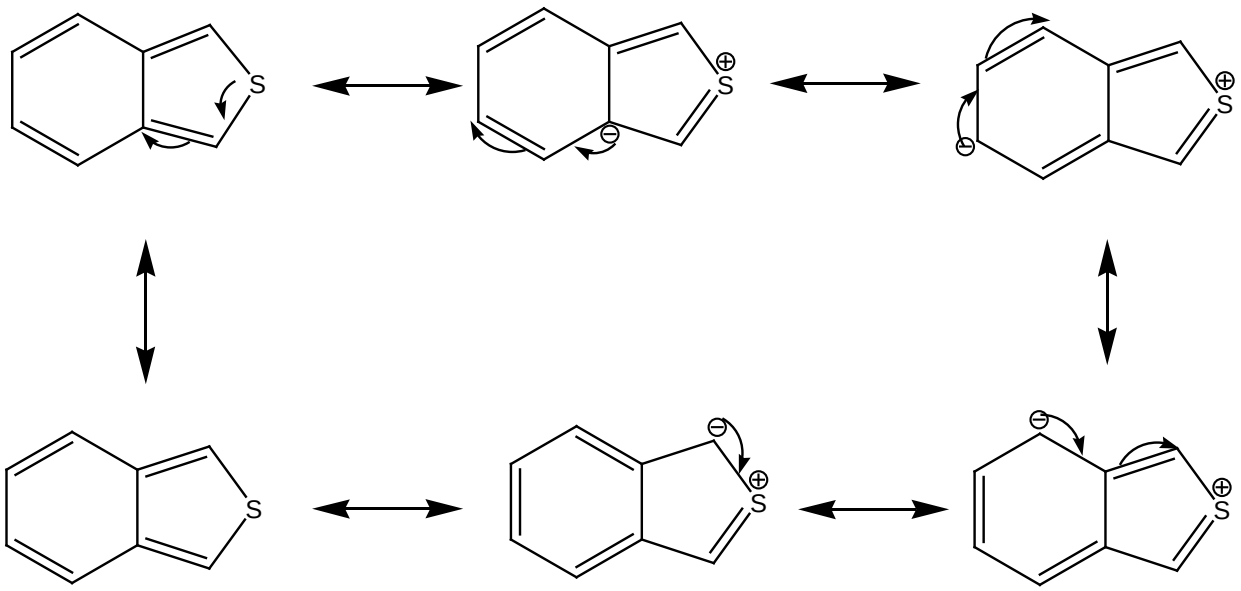
2) 1,3,Diphenyl isobenzothiophene gives (4+2) cyclo addition reaction with acetylene dicarboxylic ester.



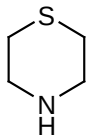
3) It gives photo chemical oxidation with singlet oxygen in presence of benzene to give 1,3, Dioxide.



Resonating Structure:



Thiazine:



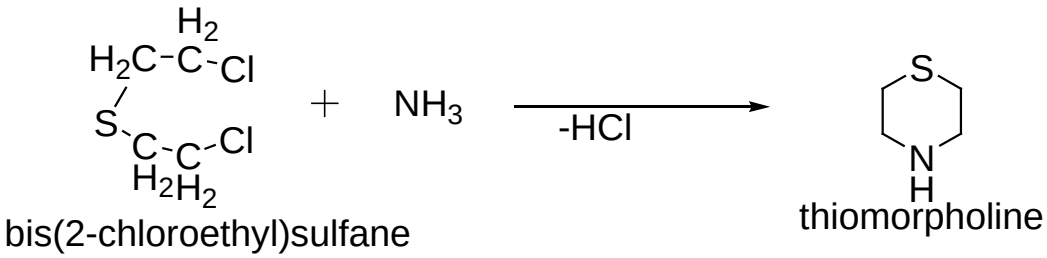
(1) Thiazine
(2) Tetra hydro 1,4 thiazine
(3) Thiomorpholine

Physical Properties:

(1)It is a colourless solution having a pyridine like smell
(2)Boiling Point is 169^0c
(3)It is asoluble in water
(4)It is act as strong base

Synthasis:

(1) In industrial process it can prepaid by reaction of ammoniya with dichorothio ethyl ether. It form Thiomorpholine



bis(2-chloroethyl)sulfane

thiomorpholine

Chemical properties:

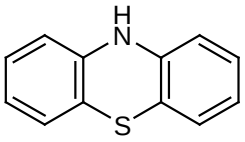
(1) It is a fully saturated molecule

(2) Does not contain double bond.so resonating structure is absent.

(3) It does not give electrophilic and neucliophilic reaction.

Phenothiazine:

Structure



phenothiazine

(1) Phenothiazine
(2) 2,3,5,6-dibenzo-1,4 thiazine

Physical properties:

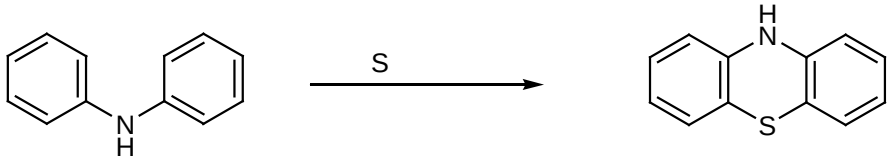
(1) It is first synthesis in 1885 by Bernthsen scientist
(2) It is simple yellow colouredcrystline substance.
(3) Melting Point is 180-181^0
(4) Boiling Point 371^0

(5) IT is insoluble in water but soluble In other organic solvent.

(6) It give a easily electrophilic reaction like Acylation, Alkylation, Nitration Etc.. But direct halogenation is not possible. Beacouse it give mixture of 1,9,3,7 derivative of halogen.eletrophilic reaction is carried out at 1,7 position

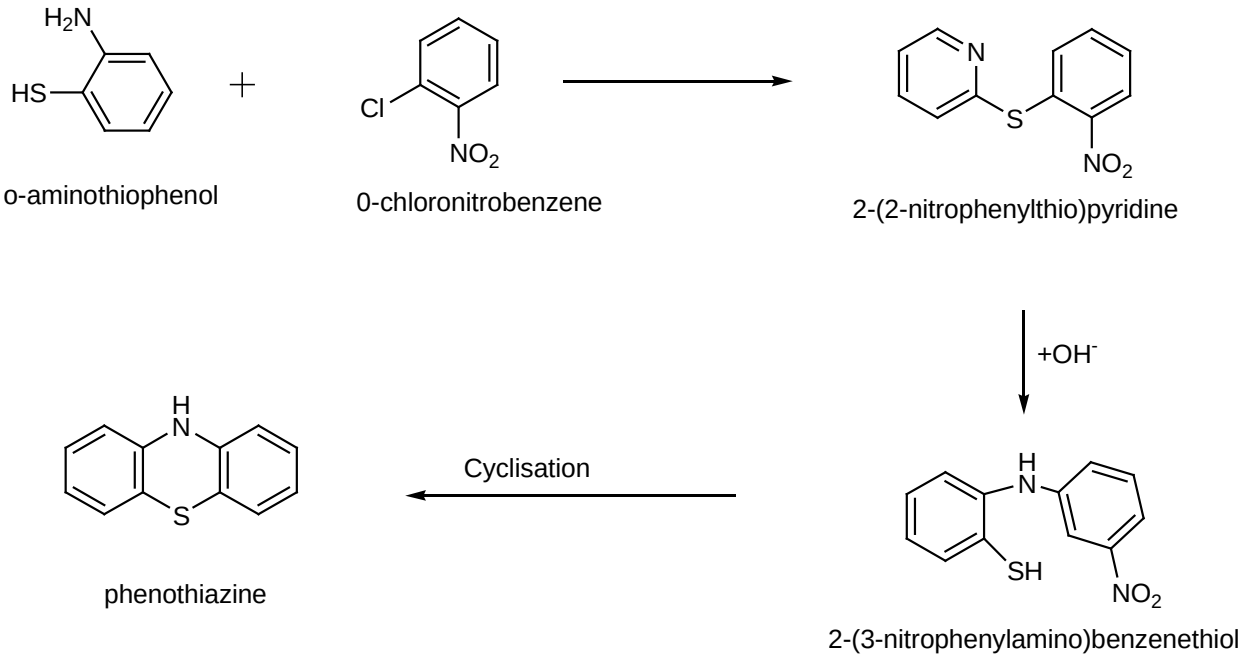
Synthasis:

(1) Heating of diphenylamine with sulpher powder it give phenothiazine

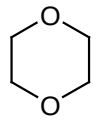


diphenylamine phenothiazine

(2) Reaction between o-chloro nitrobenzene and o-amino thiophenol. it give a diphenylesulphide derivative. meceptodiphenylamine.Itundergoss cyclisation reaction and form a phenothiazine.


H2N
HS
o-aminothiophenol
Cl
NO2
0-chloronitrobenzene
N
S
NO2
2-(2-nitrophenylthio)pyridine
+OH-
H
N
SH
NO2
2-(3-nitrophenylamino)benzenethiol
Cyclisation
H
N
S
phenothiazine

Dioxane:

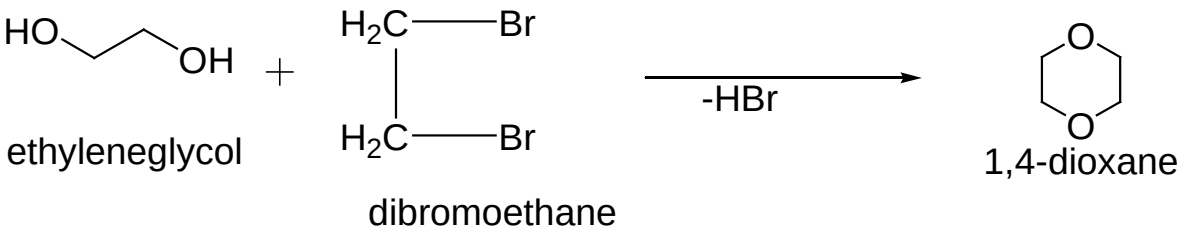


1,4-dioxane

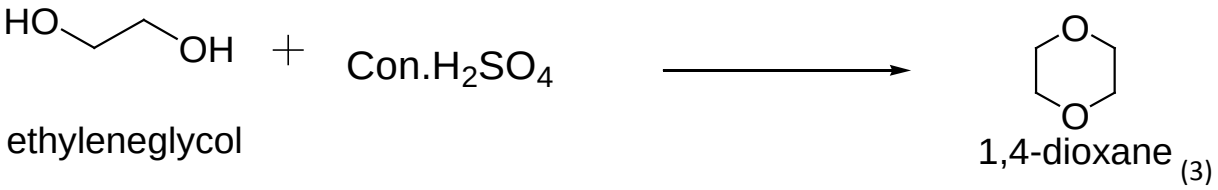
(1) It is coloueless liquid.
(2) B.P is 101^0
(3) It is soluble in water and other organic solvent.
(4) It form a peroxide in presence of sunlight and oxygen.
(5) At high tem. Upto 210^0 reaction between reany nickel and hydrogen it become explosive.

Synthasis

(1) Reaction between ethylene glycol and dibromoethane it form dioxane



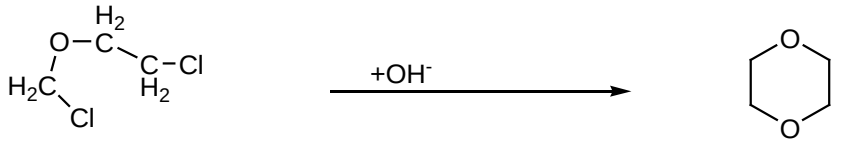
(2)Ethylene glycol react with strong con.H_2so_4 form a dioxal



ethyleneglycol

1,4-dioxane (3)

Reaction of dichloro ethyl ether in presence of alkali and form dioxane

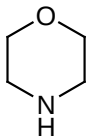


1-chloro-2-(chloromethoxy)ethane

1,4-dioxane

Oxazine:

Structure



morpholine

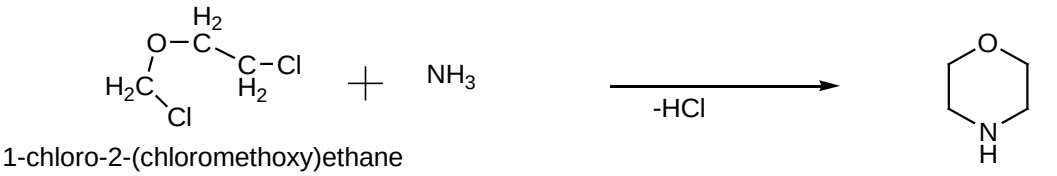
(1)Oxazine
(2)Tetra hydro 1,4oxazine
(3)Morpholine

Physical properties:

(1) It is a colourless liquid.
(2) It is hydrophilic in nature.
(3) It is water soluble.
(4) M.P is $228.3^{0}C$
(5) Pk^{a} value 8.7
(6) When it react with hydrogen peroxide it give a 4-agent.
(7) It is weak base as compare to piperidine.

Synthesis:

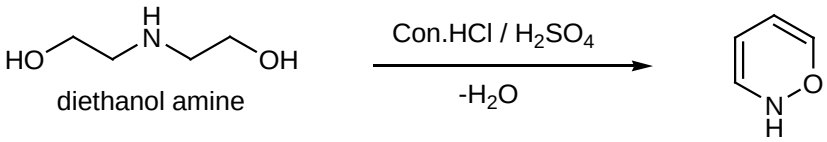
(1) Reaction between dichloro ethyl ether and ammonia at 50^0 c Tamp. And 150 Kg/cm^2



1-chloro-2-(chloromethoxy)ethane

morpholine

(2)Reaction between diethanol amine with 70% of Hcl or h_2so^4 at 160 Kg/cm^2 pressure.heating for 12 hours. So it givemoroholine.



diethanol amine

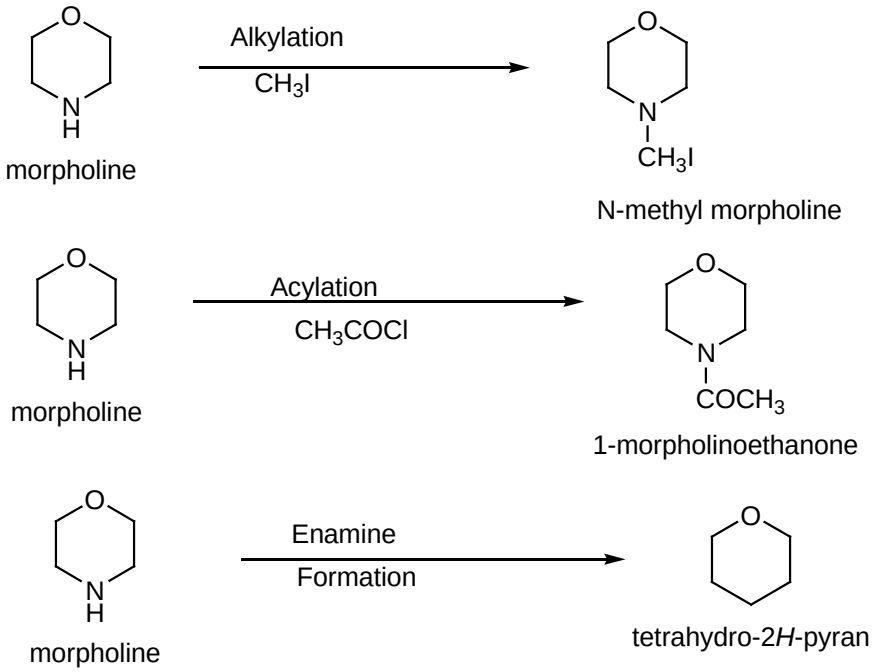
Oxazine

Chemical Properties:

Morpholineundergoss most of the reactions typical for secouundary amines. Because presence of ether oxygen.Itwithdrown electron from nitrogen.

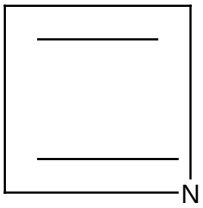
So it is less nucliophilic than piperidine.

Electrophilic attack on at nitrogen like Acylation, Enamine formation.



Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Azatine



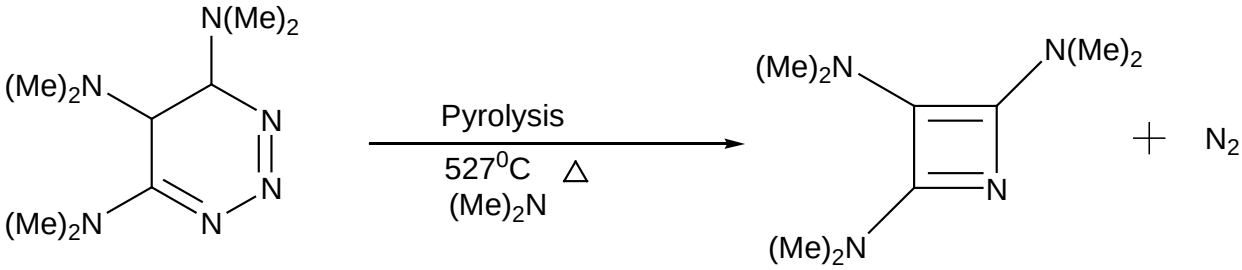
azete

➢ Physical properties :-

It is a reddish coloured crystalline compound. It's melting point is 37^0C.

➢ Synthesis:-

1. Synthesis of tries (dimethylamine) azatine.

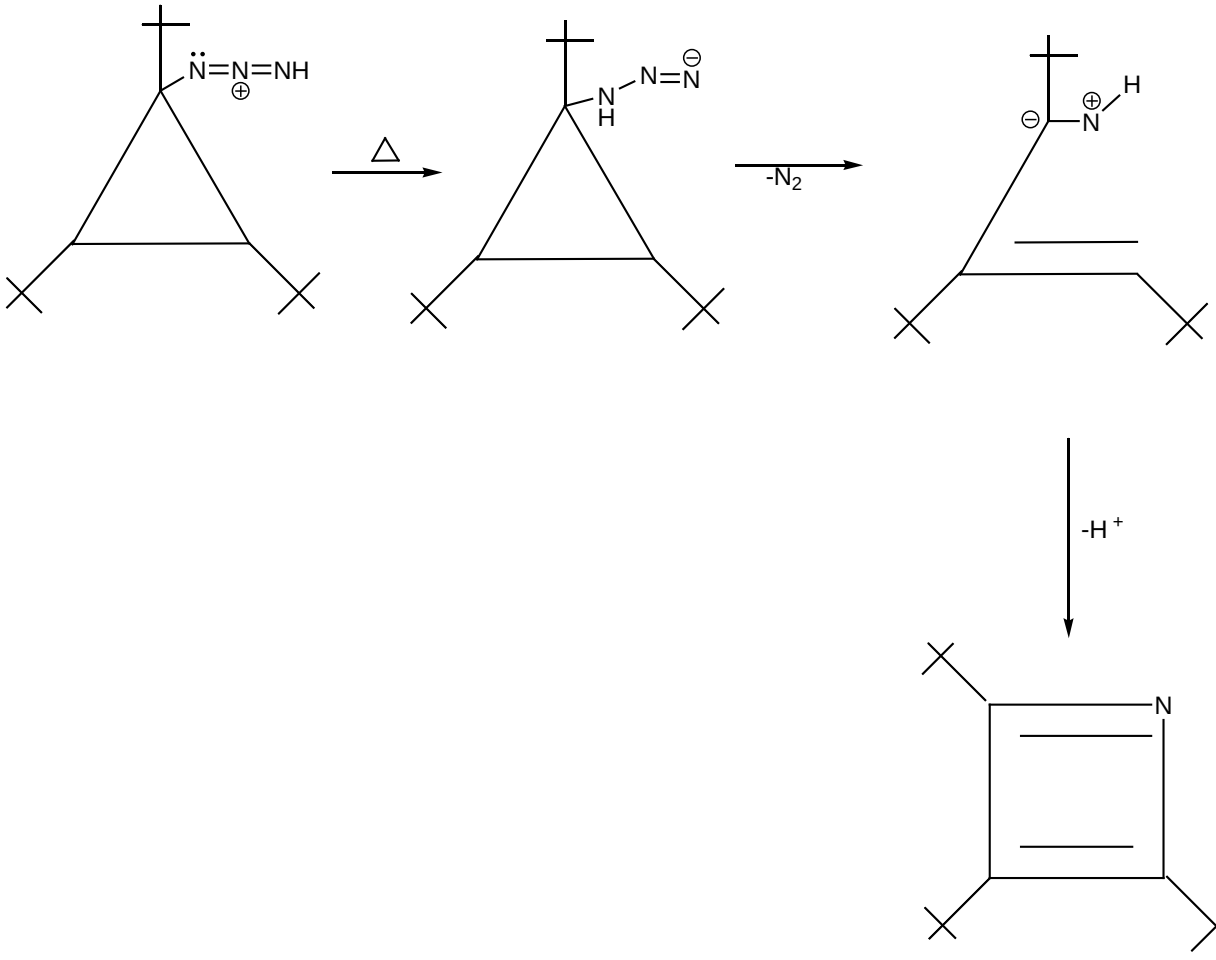


4,5,6 tris (dimethylamino) triazine

Tris (dimethyl amine)azate

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

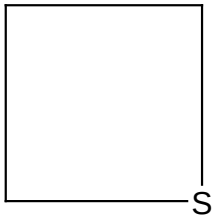
2.Synthesis of tri-tert,butylazate.



Tri tert,butyl azate

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Thitane



Thiacyclobutane

Trimethylenesulphide

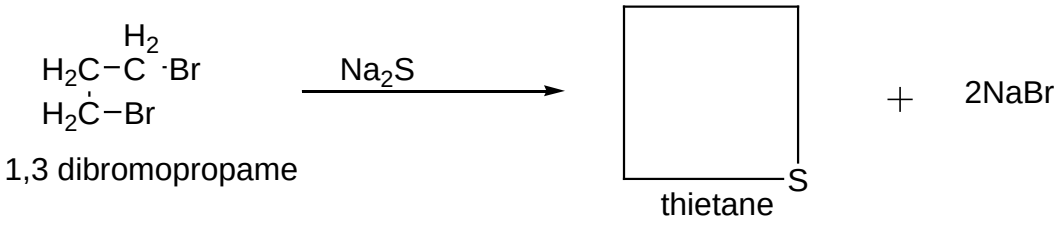
➢ Physical properties :

Thitane is a colourlessliqid.it's melting point is -73^{0}c &b.p is 95^{0}c. it has a plannar structure.

➢ Synthesis :

(1)Intramolecular ring closing reaction or cyclisation :

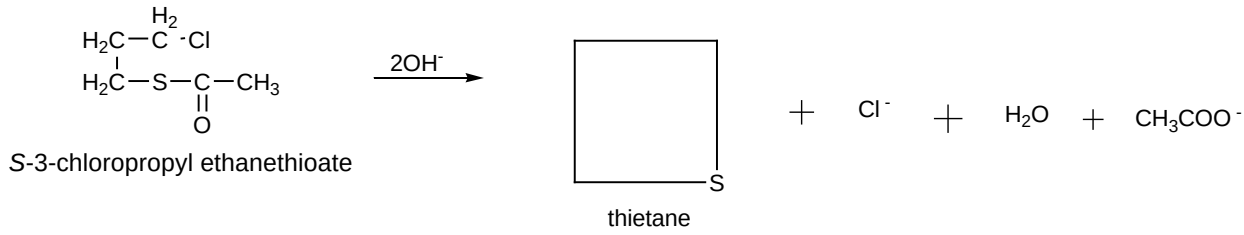
(1)



1,3 dibromopropame

thietane

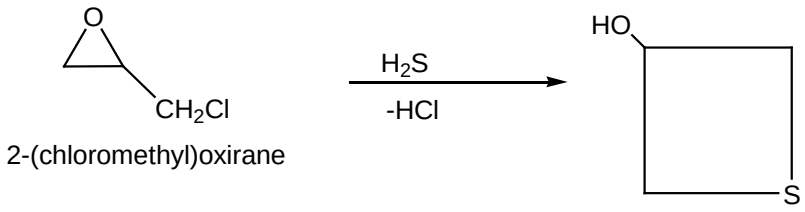
(2)



S-3-chloropropyl ethanethioate

thietane

(2) Ring expansion reaction :

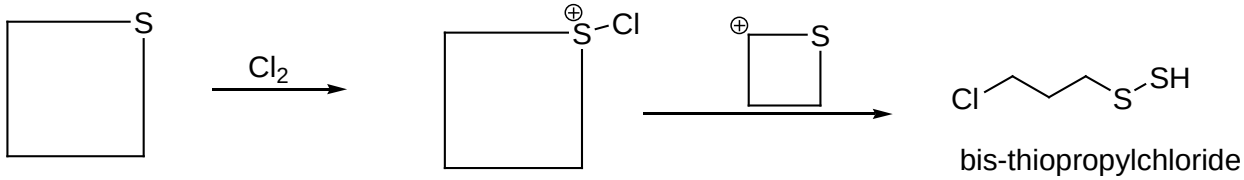


2-(chloromethyl)oxirane

thietan-3-ol

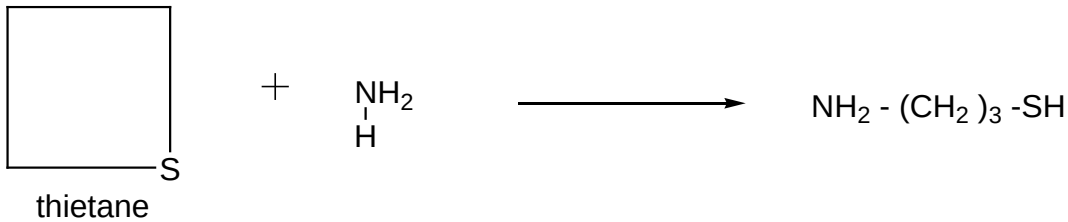
➢ Chemical properties :

(1) Ring opening reaction :



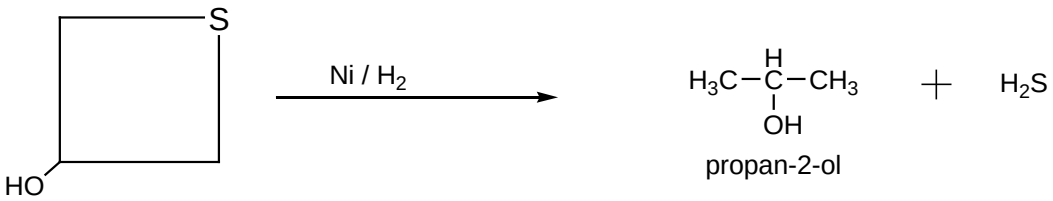
bis-thiopropylchloride

(2) Reaction with NH_3 :



thietane

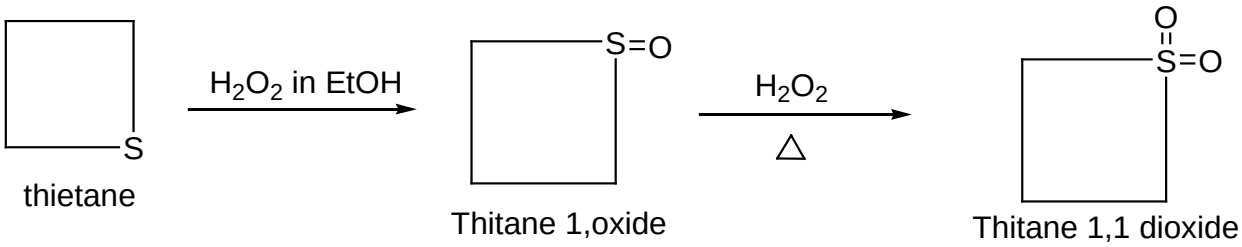
(3) Reduction with reney nickel :



thietan-3-ol

propan-2-ol

(4) **Oxidation** :



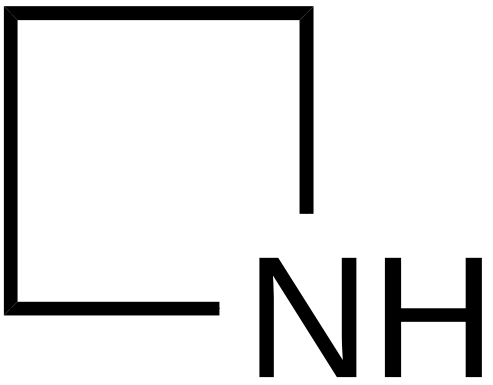
thietane

Thitane 1,oxide

Thitane 1,1 dioxide

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

Azetidine



Trimthylineamaine,azacyclo-butane

- Completely saturated four-membered ring azaheterocycles represents an understudied class of heterocycles. They are also referred to as trimethylneimine or azacyclobutane. Azetidrines are less strained molecules as compared to three-membered ring heterocycles, hence behave like normal secondary amine. Naturally occurring azetidine derivatives have been isolated from the family Liliaceae.

Synthesis

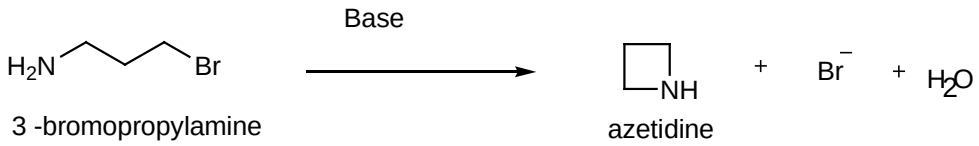
The synthesis of azetidines have been achieved in two ways.

1. Intramolecularcyclisations
2. Cycloaddition reactions

1.Intramolecularcyclisations

γ –Haloalkylamines have been used to prepare substituted azetidines by base-catalysedintramolecularcyclisations.

Azetidine was first synthesized by the intramolecular cyclisation of 3-bromopropylamine in the presence of alkali with poor yield.

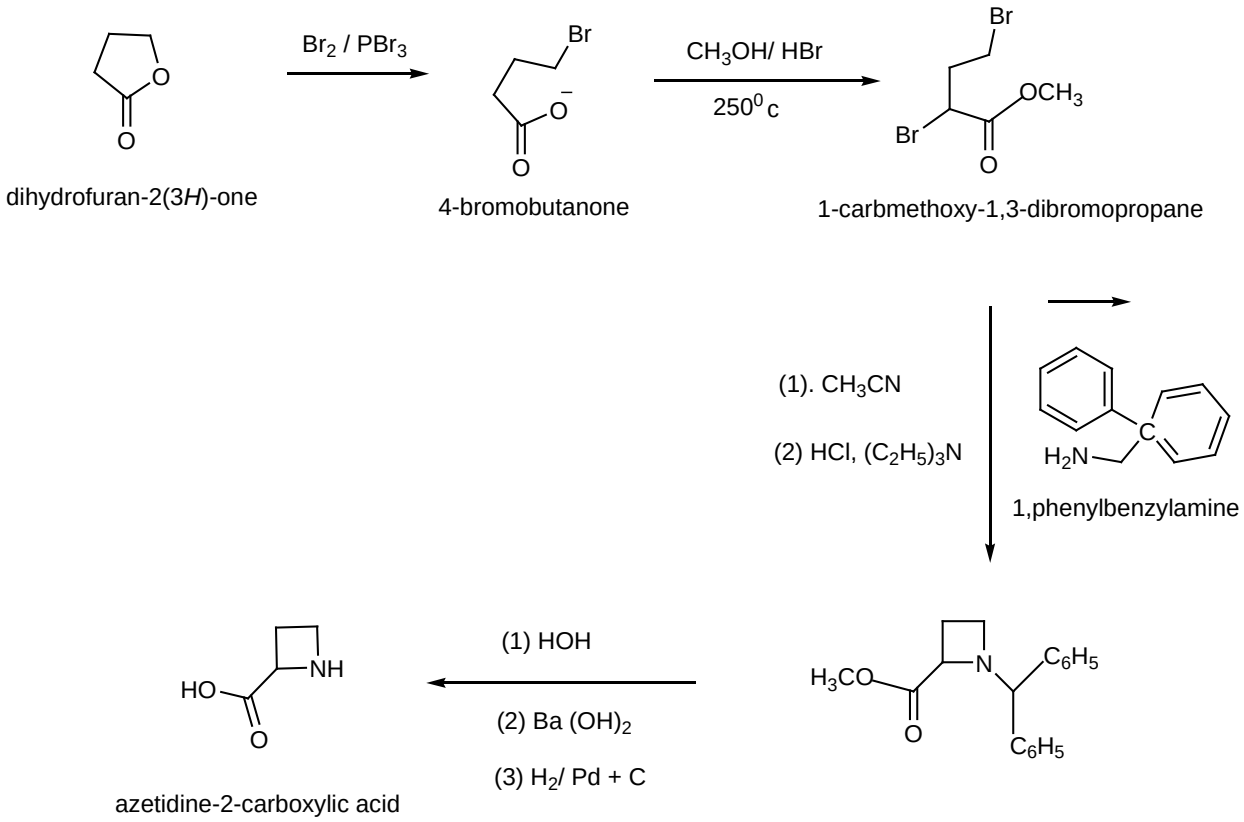


2.Cycloaddition reactions

(**a**) Analternative method involves cycloaddition of 1,3-dibromopropane with p-toluenesulphonamide in the presence of alkali. This results in the formation of N-p-toluenesulphonylazetidine which on reduction with sodium metal in alcohol yields azetidene.

(**b**) From**γ**- Lactone

The reaction of bromine and phosphorus tribromide on γ-lactone furnishes 4-bromobutanoate which on α-bromination and esterification gives 1-carbmethoxy-1,3-dibromopropene.the later on cyclisation with α-phenylbenzyl amine followed by hydrolysis and reduction affords azetidine-2-carboxylic acid.



dihydrofuran-2(3*H*)-one

4-bromobutanone

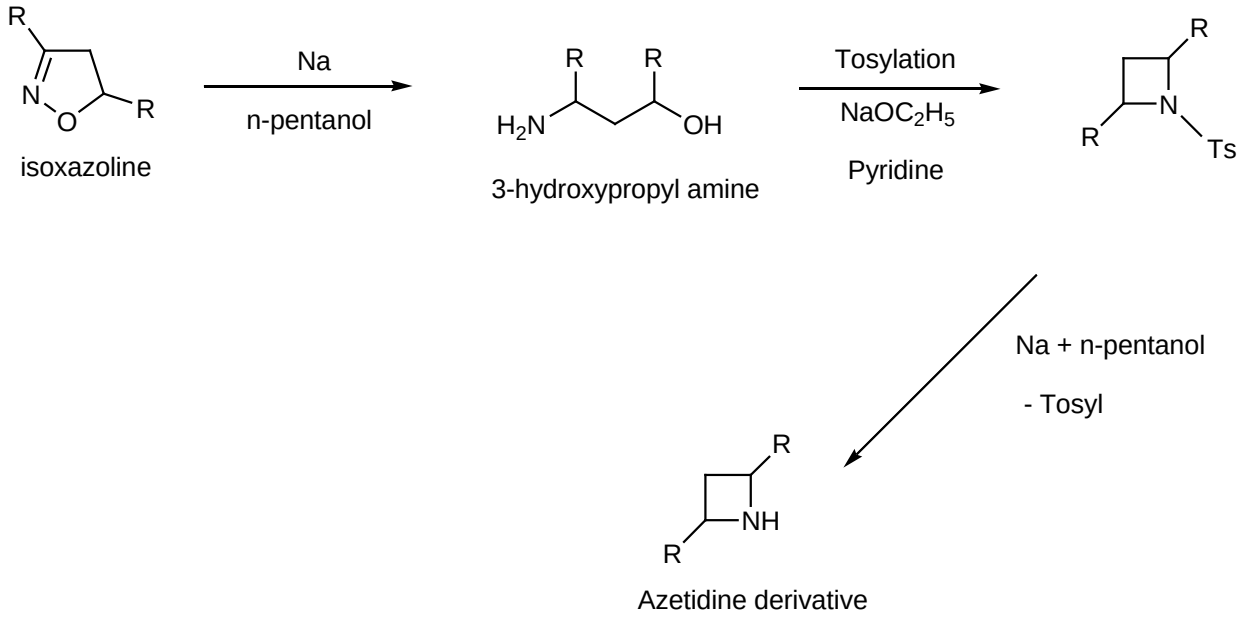
1-carbmethoxy-1,3-dibromopropane

1,phenylbenzylamine

azetidine-2-carboxylic acid

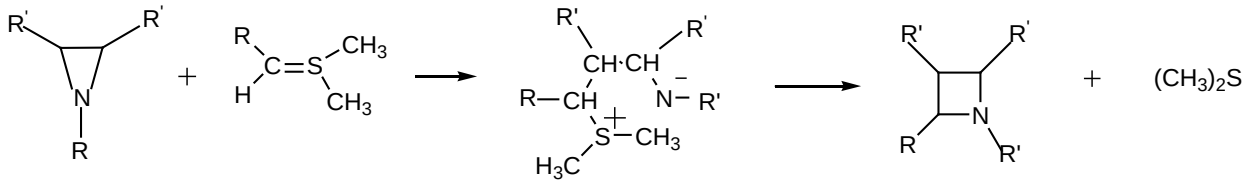
(C) From Isoxazolines

Conversion of 3-hydroxypropyl amine derivative obtained by ring opening reaction with the cleavage of N-O bond of substituted isoxazoline in to azetidine derivative *via*tosylation and detosylation with the help of sodium and alcohol is shown as under.



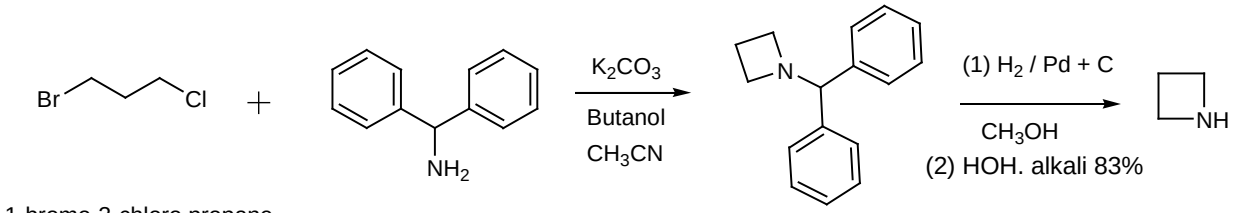
(d) From aziridines

Azitidine is obtained by the ring expansion of substituted aziridines with sulpherylides.



(e) From 1,3- dielectrophiles

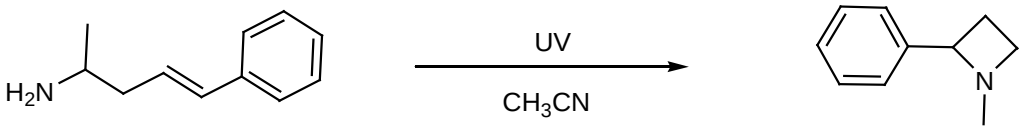
Another route to azetidines is the reaction of 1-bromo-3-chloropropane with benzhydryamine in the presence of potassium carbonate leading to the formation of 1-benzhydrylazetidine which on hydrogenolysis affords azetidine.



1-bromo-3-chloro propane | benzhydrylamine | 1-benzhydrylazetidine | azetidine

(f) Photochemical synthesis

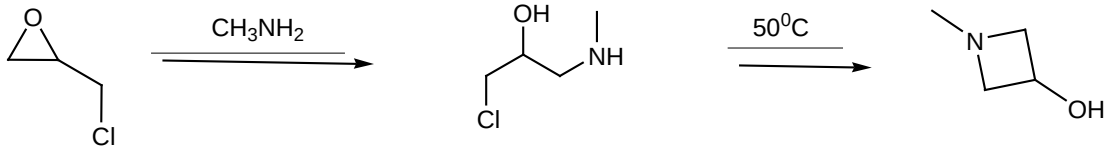
The exposure of UV-radiation to N-methylcinnamylmethyl amine in acetonitrile at 20*C furnishes 1-methyl-2-phenylazetidine with low yield.



N-methylcinnamylmethyl amine | 1-methyl-2-phenylazetidine

(g) From chloromethyloxirane

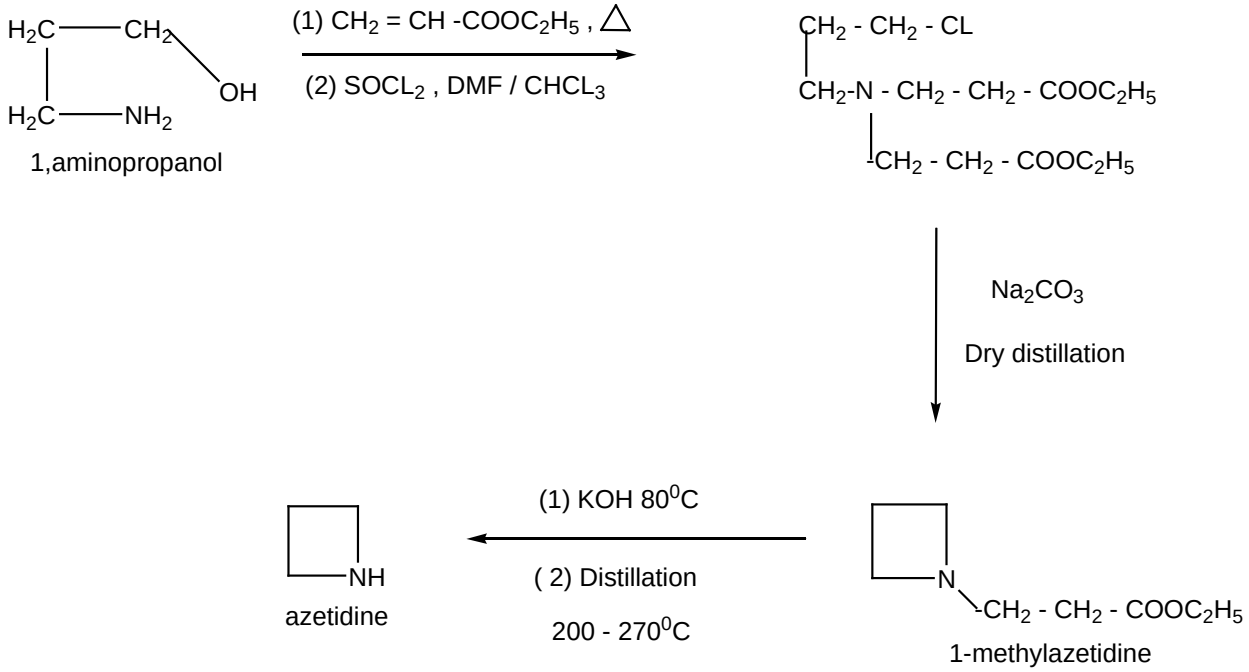
The reaction of chloromethyloxirane with methyl amine gives 1-methylamino-3-chloro-2-propanol which on ring closure provides 3-hydroxy-Nmethylazetidine.



chloromethyl oxirane | 1-methylamino-3-chloro-2-propanol | 3-hydroxy-N-methylazetidine

(H) From γ-aminopropanol

The most efficacious of synthesis of azetidine involves reaction of γ-amino propanol with acrylic ether which on subsequent treatment with thionyl chloride followed by dry distillation in the presence of sodium bicarbonate ylidsazetidine derivative. The resulting product on hydrolysis with potassium hydroxide and on dry distillation furnishes azetidine.



➢ Physical Properties

- Azetidine molecule is non-polar with puckered angle of 37^0c.
- Azetidine is a colourless liquid having ammoniacal smell.
- Fumes in air.
- Boiling point is 61^0c.
- Soluble in alcohol and water.

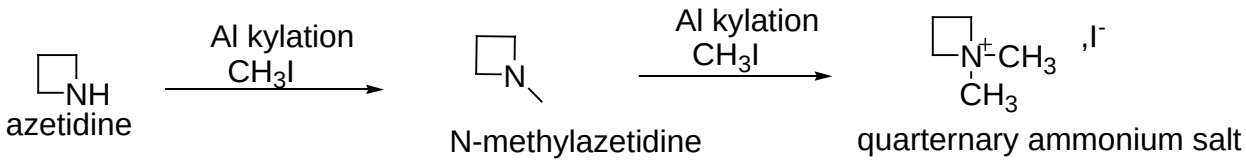
➢ Chemical Reactivity.

The strain in the azetidine ring system is reduced as compared to three-membered azeridinesysteam which reduces chemical reactivity.It behaves like secondry aliphatic amine. It undergoes following types of reactions.

1. The reactions at the hetroatom
2. Ring opening reactions
3. Rearrangement reactions
4. Radical reactions

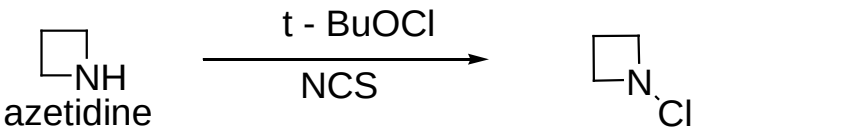
1.The reactions at the hetroatom

(a) Alkylation



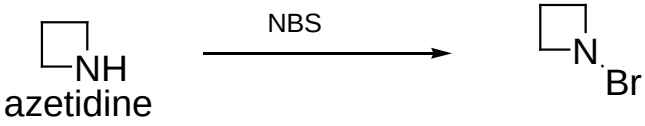
(b) Action of HNO_2

(c) NCS



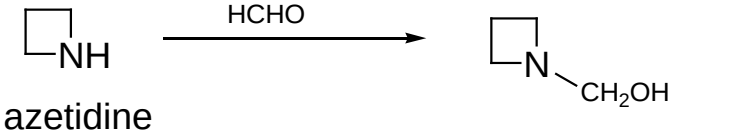
N - chloroazetidine

(d) NBS



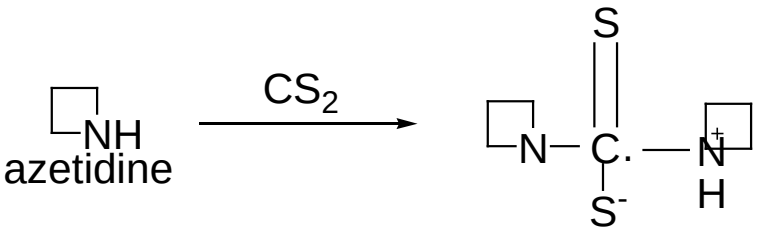
1-bromoazetidine

(e) Action of HCHO



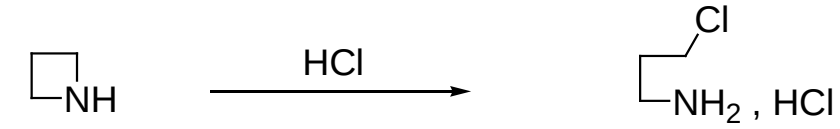
N-Hydroxy methylazetidine

(f) Action of CS_2



2.Ring opening reactions

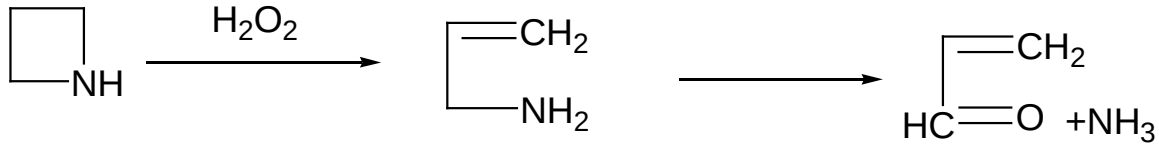
(a)Azetidine on heating with conc. Hydrochloric acid , azetidineyildes 3-chloropropyl amine hydrochloride.



azetidine

3-chloro propyl amine hydrochloride

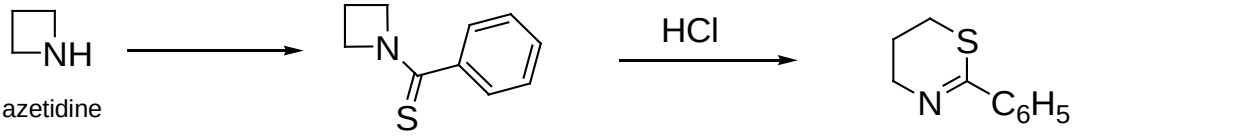
(b)Azetidine occurs with hydrogen peroxide to yield allyl amine which finally gives acraldehyde and ammonia.



azetidine

3.Rearrangement.

The reaction of azetidine proceeds with ring expansion. 1-thiobenzoylazetidine reacts with hydrochloric acid to provide 1,3-thiazine derivative.



azetidine

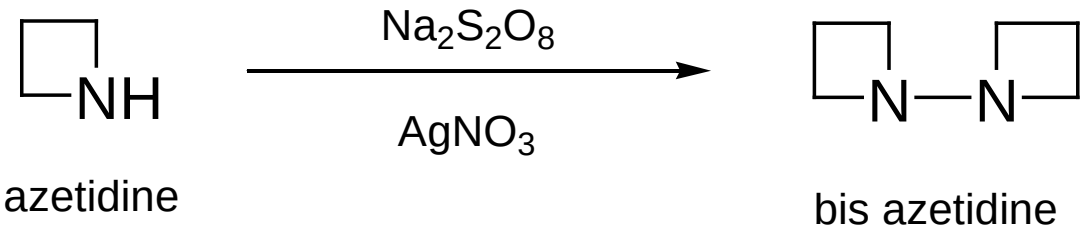
1-thiobenzoylazetidine

5,6-dihydro-2-phenyl-4*H*-1,3-thiazine

4.Radical reactions (1992)

Azetidine reacts with sodium persulphate in alkaline medium using silver nitrate as catalyst to provide bisazetidine.

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

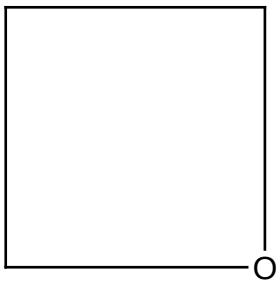


azetidine

bis azetidine

Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150

OXETANE



oxetane

Oxetanesare compounds with a four – membered saturated ring containing oxygen as a hetroatom , also named as a oxacyclobutanes. The parent compound was first described in 1858.

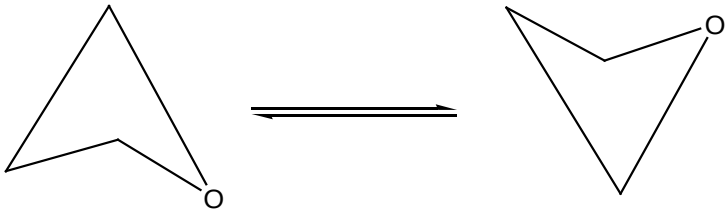
The four membered ring is not common in nature but it occurs in some physiologically active compound. An interesting compound is the bicyclic oxetane thromboxane Az, TXAZ. It is naturally occurring prostaglandin platelets in human blood as well as constriction of vascular and bronchial smooth muschels.

➢ Physical properties

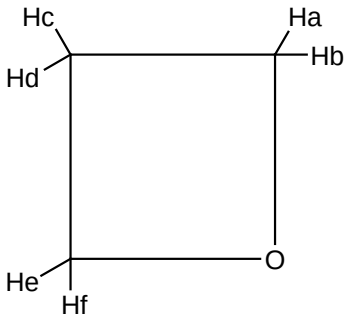
Oxetanes is colourlessliquid , boiling point is 47-80^0 C. and miscible with watrer& most organic solvents.

It can donate electrons much more easily than the three- membered hetrocycliccompound,oxirane.

Oxetane ring is slightly distorted square as the bond angle at the oxygen atom is 92 ^{0}C. The strain is reduced due to ring puckering between two non-planar structure.



The structure of oxetane has been deduced from microwave and raman spectroscopy.



➢ Spectral Data :

IR cm^{-1} : A charactristics absorption band at 980cm^{-1} due to ring streaching.

^{1}H NMR ($CDCl_3$) δ_{ppm} : H_a ,H_b; 4.73
H_c ,H_d; 2.72
H_e ,H_f ; 4.73

^{13}C NMR δ_{ppm} ; C_2 :72.1 , C_3 :23.1 , C_4 : 72.8

^{17}O NMR δ_{ppm} (H_2O) : -12 ,-20.5

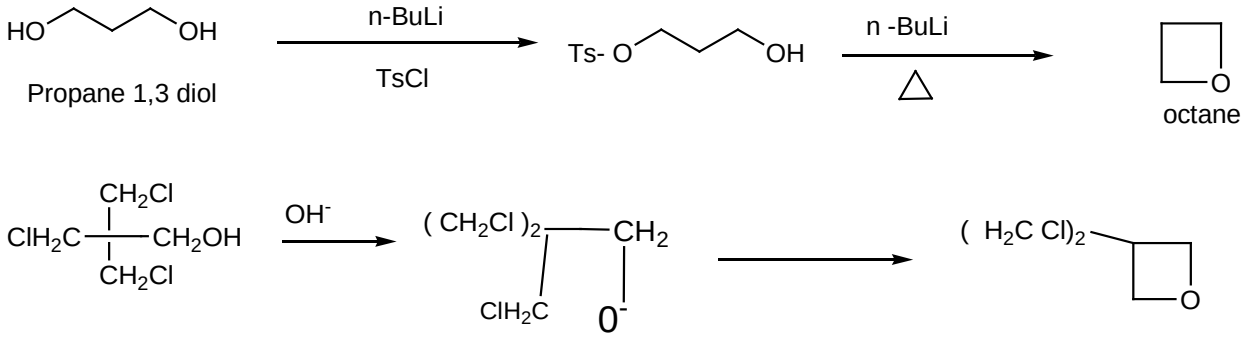
➢ Synthesis

1.Intramolecularcyclisations.

Acetyl 1,3-halohydrin undergoes cyclisation in the presence of a base to afford oxetane.

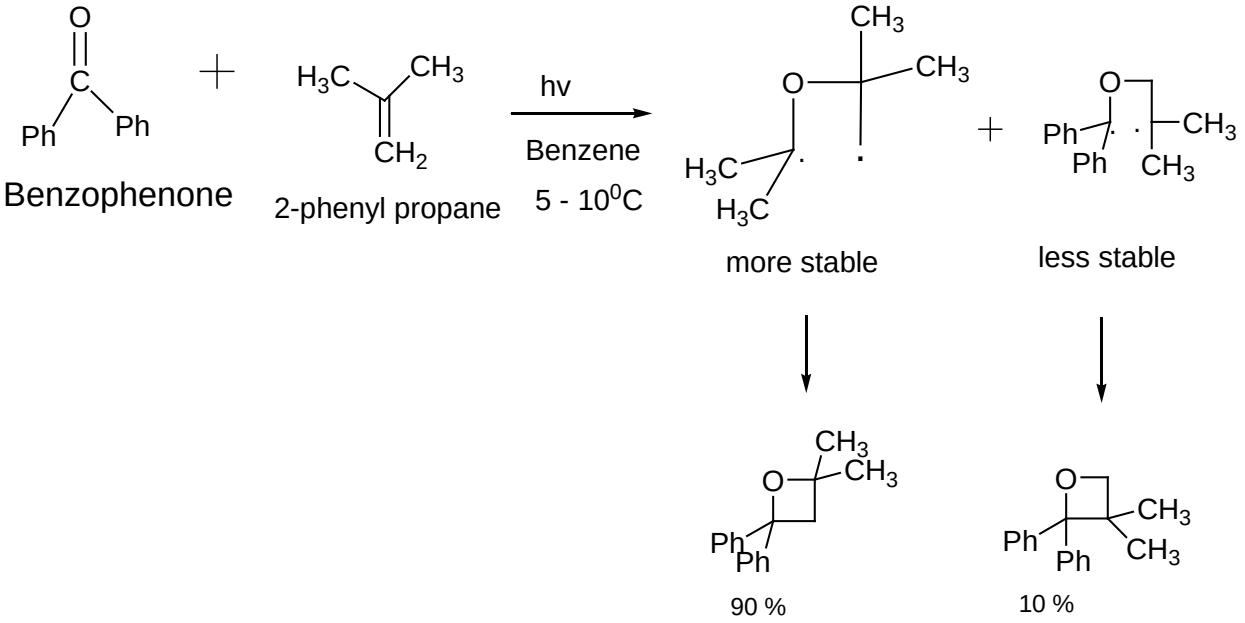
2.Intramolecular Williamson reaction.

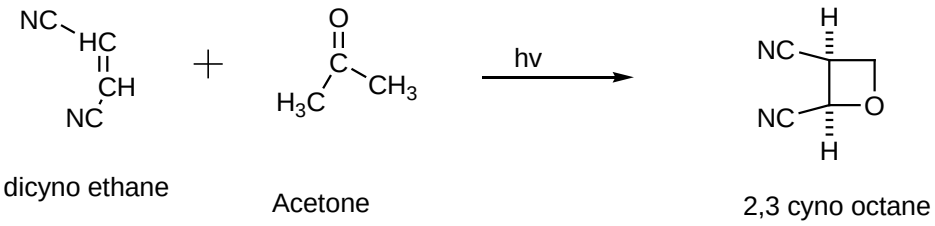
The synthesis involves intramolecular cyclisation of 1,3-propane diol with p-toluene sulphonyl chloride & n-butyl lithium.
1,3-propane diol is treated with n-butyl lithium(1m) in cold THF to provide monolithium salt which on treatment with p-toluenesulphonyl-chloride ylidesmonotosylate. The resulting product further cyclized by another cyclized by another mole of n-butyl lithium to provide high ylides of oxetane.



3.Paterno-Buchi reaction.

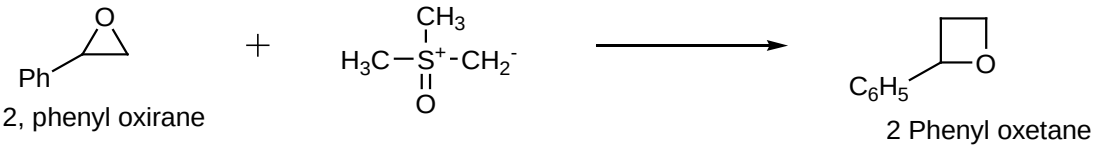
A more general and viable method for preparing oxetanes by photocycloaddition of ketones to alkenes has beed describe. It was demonstated at the turn of the century that oxetanes are available by photoaddition of ketone to alkene and was known as the paterno-buchi reaction.





4.Ring opening reaction.

The interation of dimethyloxosulphoniummethylide with 2-phenyl oxirane furnishes 2-phenyl oxetane due to insertion of methylene group.

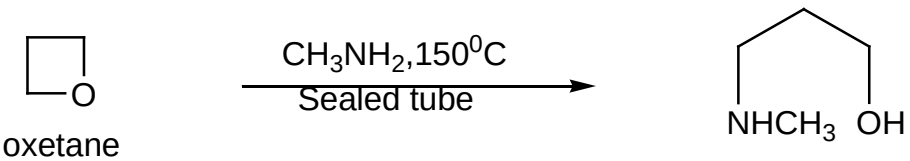


2, phenyl oxirane

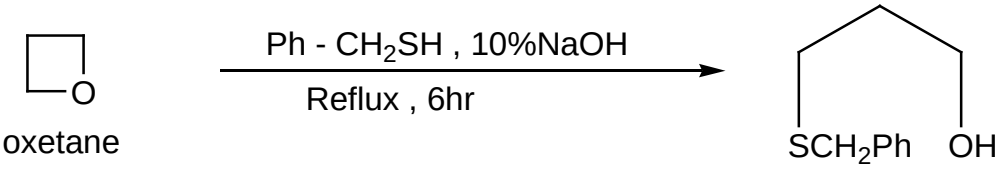
2 Phenyl oxetane

- **Chemical properties**.

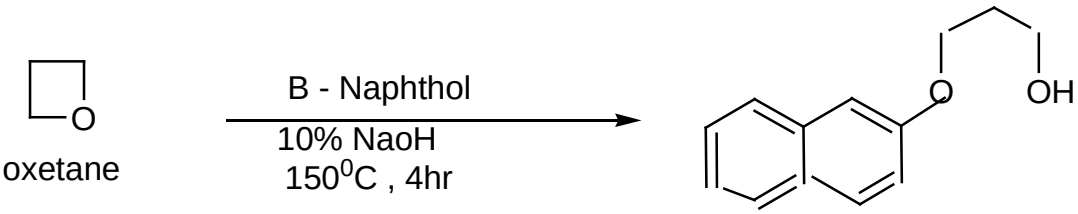
It undergo ring opening and photochemical reaction with nucliophiles at slower rate Hence vigaurous reaction condition are reqired for the cleavage of oxetane ring.



oxetane

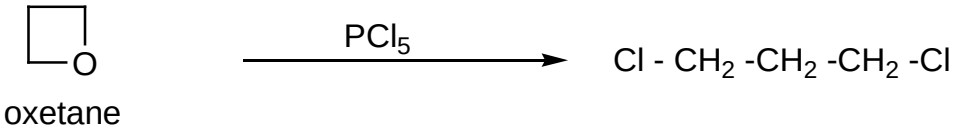


oxetane

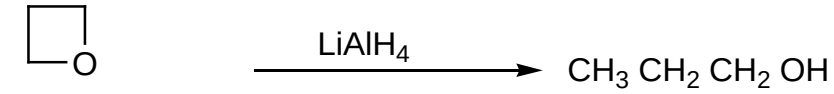


oxetane

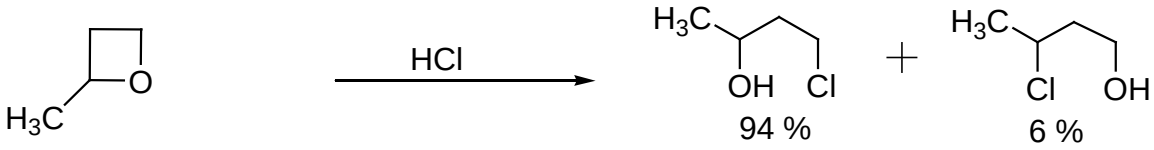
Shree H N Shukla Group of Colleges Rajkot
(Affiliated to Saurashtra University)
Behind marketing yard, near lalpari lake,
Between amargadh-bhichri Rajkot.
Ph: (0281) 2708070, 9099063150



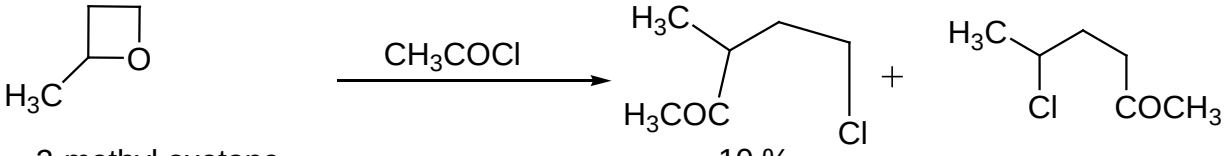
oxetane



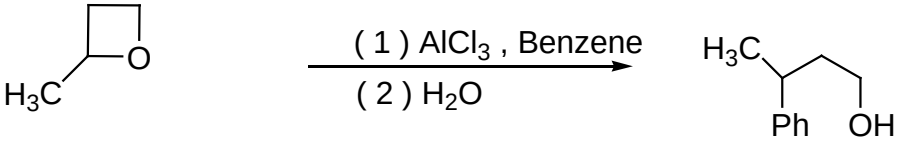
oxetane



2-methyl oxetane



2-methyl oxetane



2-methyl oxetane

2.Photochemical reactions.

Oxetanes , bearing chromophoric substituents tend to undergo interesting photochemical transformation.