Alkaloids

1. MORPHINE

* Morphine is the most imp. among the Opium alkaloids.
* It was 1st alkaloid to be isolated from by Scrturner plant. The other 2 closely related alkaloids are Codeine, and Thebaine. These alkaloids are commonly known as Morphine alkaloids. These constitute a sub group of the Opium alkaloids.

Biological activity:

* Reduces pain & cause hallucination
* Additive & central nervous system active compounds.
* Used as analgesic & sedative.
* Derivatives of Morphine are used to relief pain in terminal disease like cancer.

Constitution:

* M.F of Morphine – $C_{17}H_{19}NO_3$
* Morphine take up one mole of CH_3I gives Quaternary ammonium salt indicating the presence of Nitrogen as 3°.
* Morphine on acetylation (or) benzylation gives diacetyl (Heroin) (or) dibenzoyl derivative indicating the presence of 2 Hydroxyl groups.
* Morphine gives characteristic colour reac^n with $FeCl_3$ & soluble in aq. NaOH sol^n to form monosodium salt which is reconverted into Morphine by passing CO_2 Hence one of the hydroxyl group must be Phenolic.
* Morphine form monohalogeno product with halogen

acids indicates that alcoholic hydroxyl group is present in morphine.

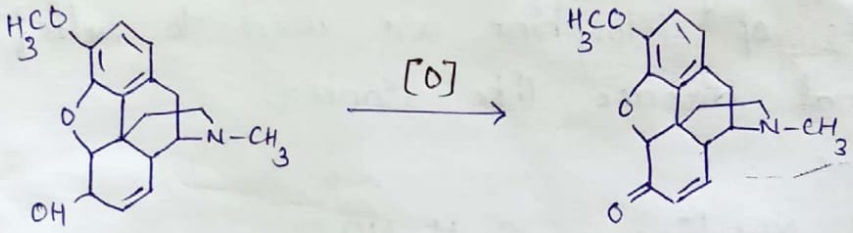
* Zn-dust distillation of the alkaloid gives Phenanthrene suggesting the skeleton

* Codeine ($C_{18}H_{21}NO_3$) is treated with CH_3I to form Codeine methiodide, which on heating with alkali gives α- codeimethine.

$$C_{18}H_{21}NO_3 \xrightarrow{CH_3I} C_{19}H_{24}NO_3I \xrightarrow[HI]{\Delta,\ Alkali} C_{19}H_{23}NO_3$$

(Codeine methiodide) (α-codeimethine).

* Codeine on oxidn gives codeinone indicating the other hydroxyl group is 2°.



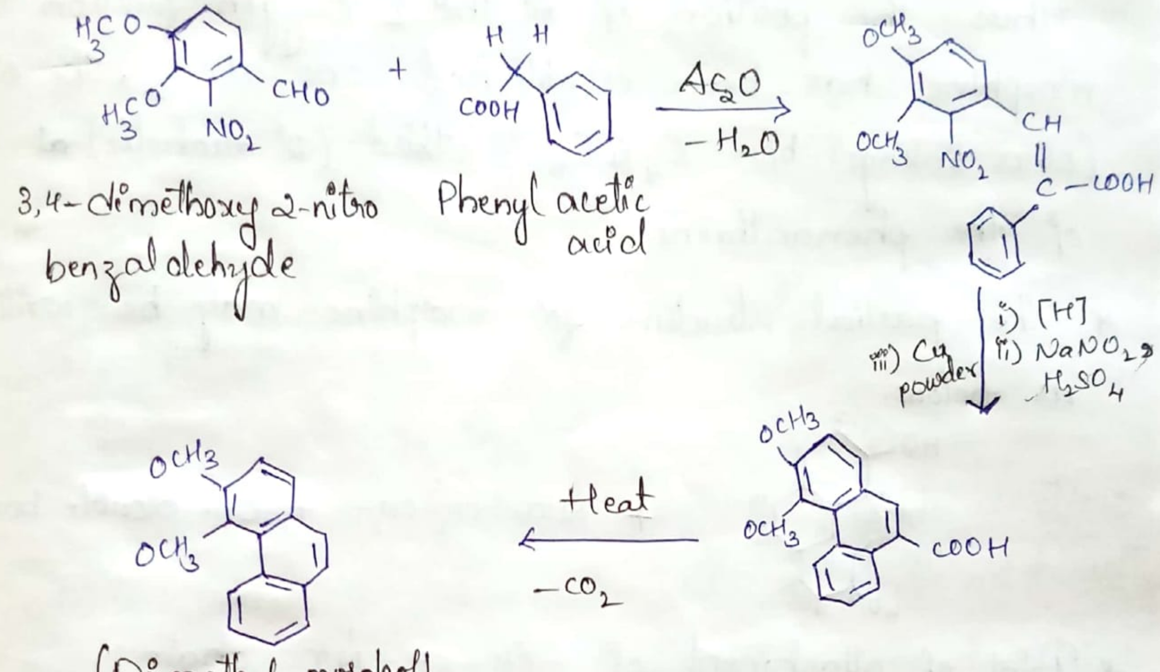
* α- codeimethine on heating with alkali, the double bond is shifted to give isomeric β- codeimethine. When either of these isomers are treated with CH_3I followed by alkali, Methyl morphenol is formed as main product along with trimethylamine & Ethylene. The methyl morphenol when heated with HBr gives Morphenol which on redn with Na & alcohol gives Morphol.

α- Codeimethine $\xrightarrow[Alkali]{\Delta}$ β- codeimethine

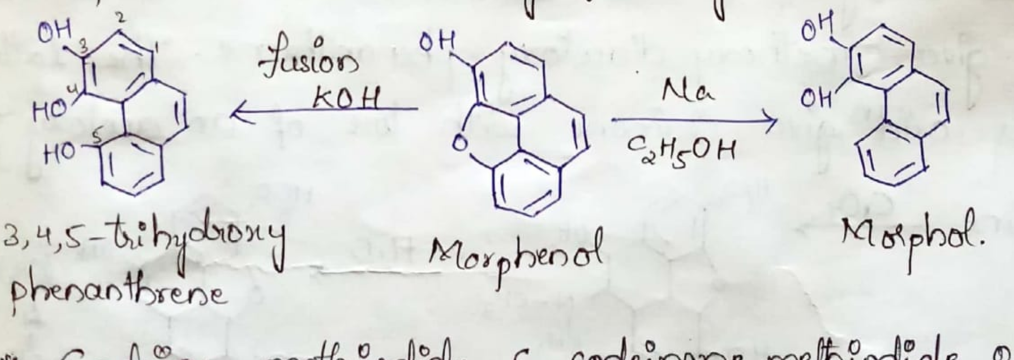
↓ i) CH_3I
ii) OH^-

Methylmorphenol $\xrightarrow[HBr]{\Delta}$ Morphenol $\xrightarrow{Na/C_2H_5OH}$ Morphol.

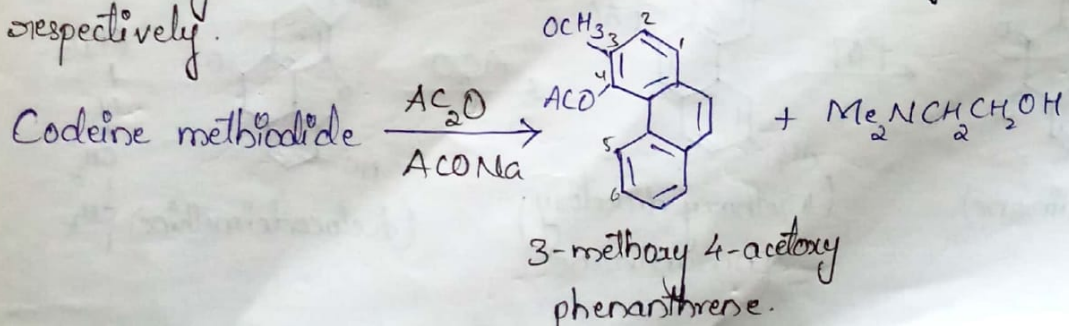
* Morphol is shown to be 3,4-dihydroxy phenanthrene by synthesis of its corresponding dimethyl derivative.

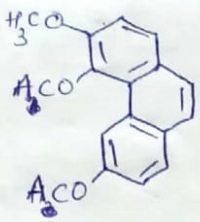


* Morphol is obtained by redc^n of morphenol which on fusion with KOH gives 3,4,5 - trihydroxy phenanthrene. The morphenol will be having following structure.



* Codeine methiodide & codeinone methiodide on heating separately with mixture of Ac_2O - ACONa gives 3-methoxy 4-acetoxy phenanthrane & 3-methoxy 4,6 diacetoxy phenanthrene, respectively.

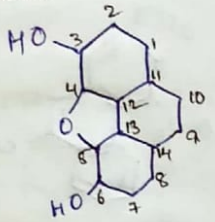


Codeinone methiodide $\xrightarrow[ACONa]{Ac_2O}$  + $Me_2NCH_2CH_2OH$ (Dimethyl amine Ethanol)

(3-methoxy 4,6-di acetoxy phenanthrene)

Thus the position of all the 3 Oxygen function in morphine has been established one at C_3, the other (ether linkage) blw C_4 & C_5 & third (2° alcoholic) at C_6 of the phenanthrene.

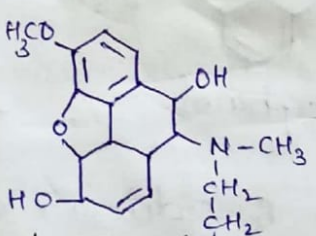
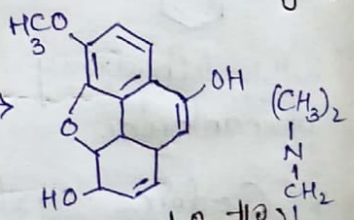
* The partial structure for morphine may be written as below.

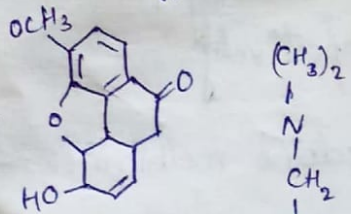
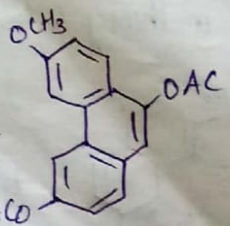
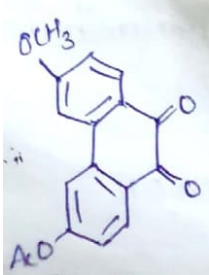


+ $\overset{|}{N}Me-CH_2-CH_2-$ + One double bond.

* Point of attachment of $-CH_2-CH_2-\overset{|}{N}Me$ chain:

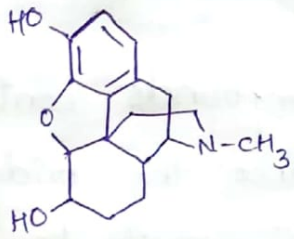
Codeine on oxid^n with CrO_3 gives hydroxy codeine along with codeinone. The hydroxy codeine on Hoffmann degradation gives a keto codeimethine. It is heated with Ac_2O gives methoxy diacetoxy phenanthrene. The latter on further oxid^n gives Quinone with loss of an acetoxy grp.

Codeine $\xrightarrow{CrO_3}$  (Hydroxy codeine) $\xrightarrow{H.D}$  (Hydroxy codeimethine)

 (Ketocodeimethine) $\xrightarrow[\Delta]{Ac_2O}$  (methoxy diacetoxy phenanthrene) $\xrightarrow{[O]}$  (Quinone)

* Gulland and Robinson in 1923 stated that "the formation of the phenanthrene derivative can take place for structural reasons unless the ethamine chain is displaced.

Partial structure of morphine may be written as

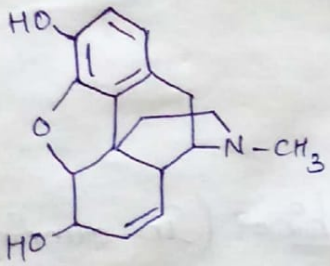


Now the only problem is to assign the position of double bond.

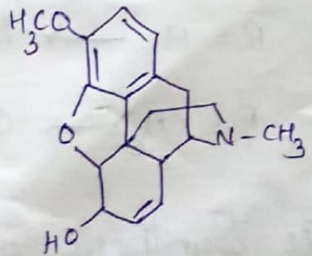
* Position of Double bond:

Codeine on treatment with PCl_5 yields α-chloro codeine which on treatment with aq. acetic acid sol^n gives mixture of codeine, isocodeine, pseudocodeine and allopseudo codeine. The 1st two give same ketone on oxid^n indicating that they differ only in the position of hydroxyl group at C_6. Other 2 give same ketone on oxid^n indicating that they differ only in the position of $-OH$ grp at C_8. These changes can be explained if the double bond is in blw C_7 & C_8

Morphine & Codeine may be drawn as below.

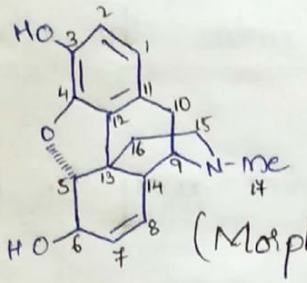


(Morphine)

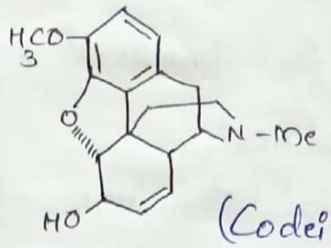


(Codeine)

* Stereochemistry of Codeine & Morphine:



(Morphine)

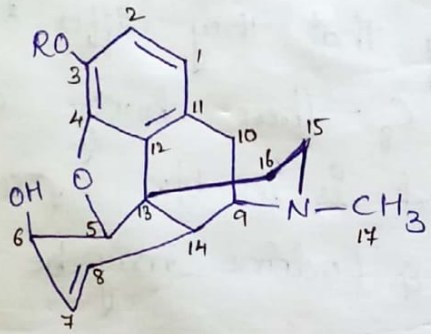


(Codeine)

Each of these compounds contains 5 chiral centres (5, 6, 9, 13, 14) But the since the bridged ring system across positions C_9 & C_{13} must be cis, 8 pairs of Enantiomers are position for each compound. The hydro-gen atoms at C_5, C_6 & C_{14} are all cis and the bridge at C_9 and C_{13} is also cis.

This stereo chemistry has been confirmed by x-ray analysis but it was not possible however to determine the absolute configuration by this method.

The confirmational formulate of morphine and Codeine may be written as below.



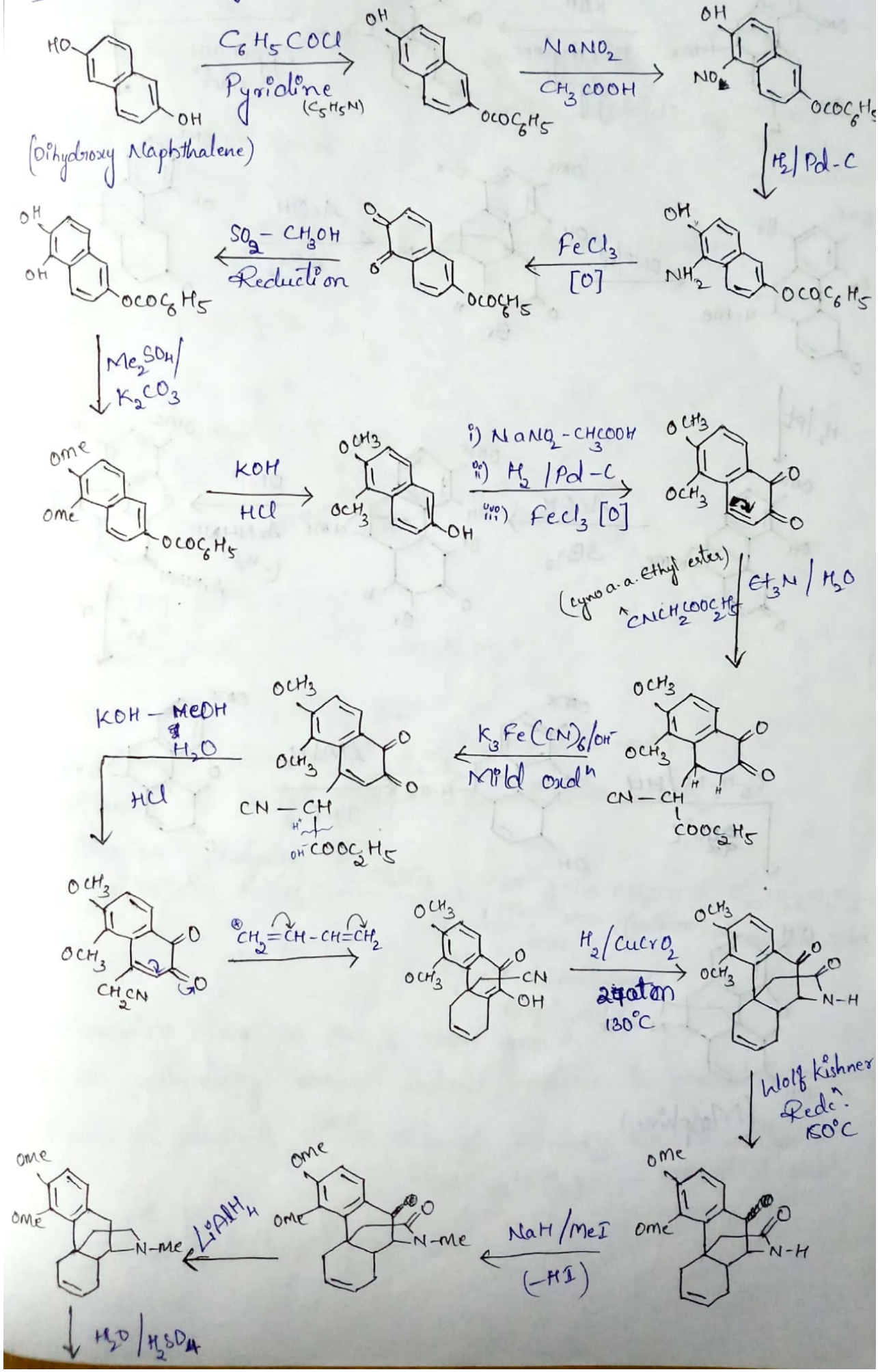
If R = H ⟶ Morphine.

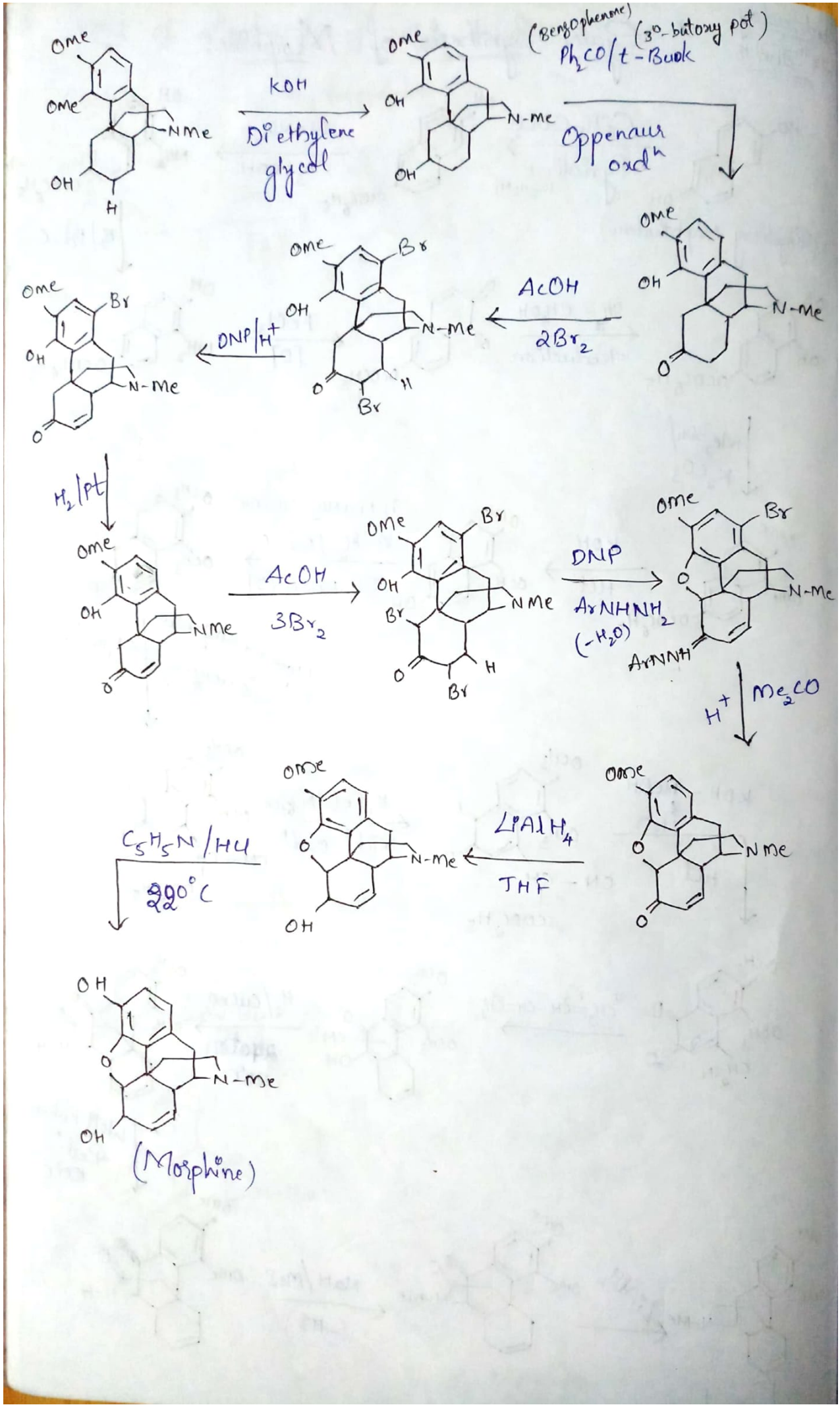
If $R = CH_3$ ⟶ Codeine.

Gates Synthesis of Morphine: (In running notes)

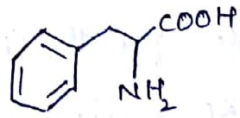
Wednesday
24th Jun' 18

* Gates Synthesis of Morphine:



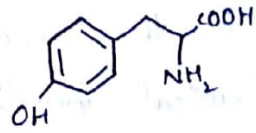


Biosynthesis of Morphine:



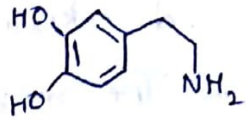
(Phenyl alanine)

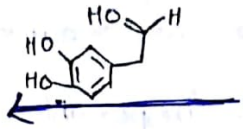
NADPH – NADP
O_2 – Hydratase Enzyme



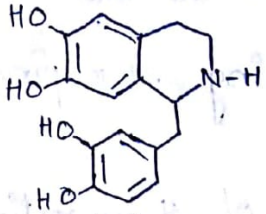
(L-Tyrosine)

1) Hydroxylation
2) Decarboxylation ($-CO_2$)

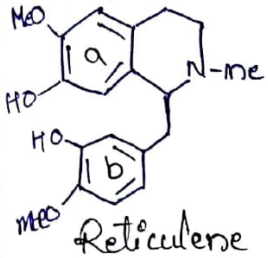




Selective Methylation

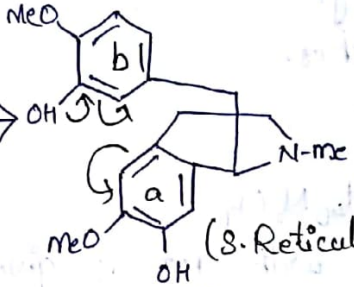


Norlaudanosoline



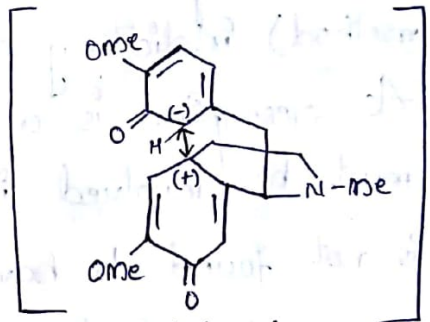
Reticulene

Bond rotⁿ



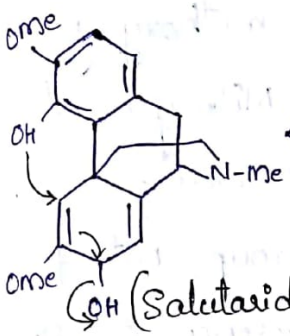
(S. Reticulene)

Oxidase
$-H_2$



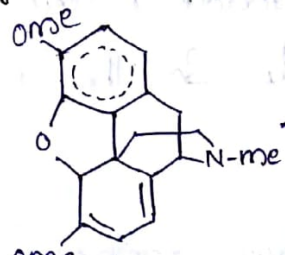
Salutaridinone

Inter condensation
1. Tautomerisation
2. Ketone redⁿ



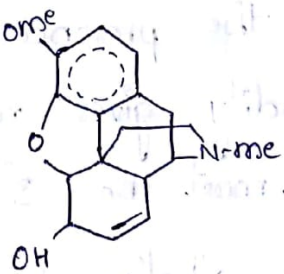
(Salutaridinol)

Dehydration gives Ether linkage



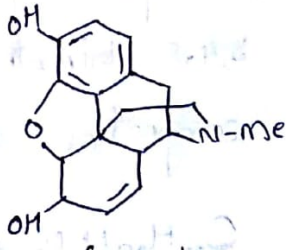
(Thiobiene)

1. Reductase
2. Isomerase



(Codeine)

① Dimethylation



(Morphine)

2. Reserpine

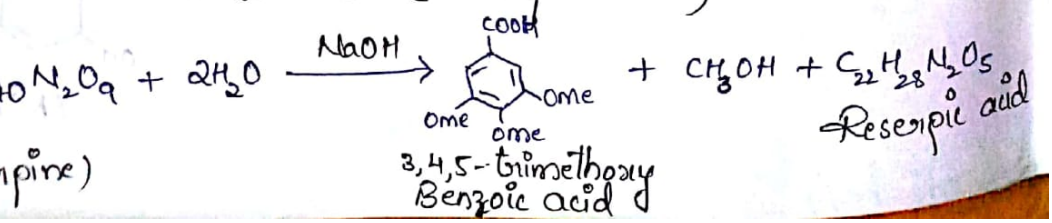
⇒ Reserpine is the main active principle for the Rauwolfia species. Chemical investigation over 60 various Rauwolfia species lead to the isolation of nearly 50 to 70 alkaloi-ds known as Rauwolfia alkaloids.

⇒ The most important being reserpine, Yohimbine, Ajamali-cine and Ajamaline

⇒ The snake like roots of Rauwolfia has been used for controlling hypertension, insomnia fevers, cholera, dizziness and headaches.

Constitution:

* M.F : $C_{33}H_{40}N_2O_9$
* On heating with HI it gives 5 moles of CH_3I (Zeisel method) indicating the presence of 5 methoxy groups.
* As reserpine is a weak base, both Nitrogen atoms must be involved in ring. Further as reserpine itself is not found to have any hydroxyl group but forms an acetyl derivative indicating the presence of an -NH group. It is further confirmed by the I.R spectra which reveals the presence of an Indole nucleus.
* Reserpine readily gives methyl iodide. So the second nitrogen atom must be 3°.
* Reserpine upon alkaline hydrolysis gives methanol, 3,4,5-trimethoxy benzoic acid and another acid of the composition $C_{22}H_{28}N_2O_5$ (Reserpic acid)



(Reserpine)

3,4,5-trimethoxy Benzoic acid

Reserpic acid

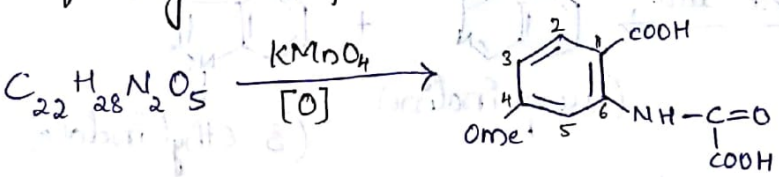
* Since Reserpine has no $-COOH$ (or) $-OH$ groups the introduction of 2 carboxylic acid groups (one in 3,4,5-trimethoxy benzoic acid & another in reserpic acid) & 2 alcoholic groups (one in CH_3OH & the other in reserpic acid) in the hydrolysis product suggest that Reserpine is diester. This is confirmed by the redn of reserpine with $LiAlH_4$ to give reserpic alcohol ($C_{22}H_{30}N_2O_4$) & 3,4,5-trimethoxy benzyl alcohol.

Structure of Reserpic acid:

* M.F : $C_{22}H_{28}N_2O_5$.

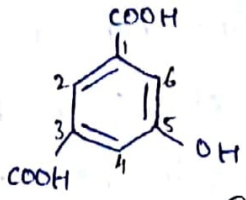
*i) By usual tests, Reserpic acid is found to possess 2 methoxy, one carboxylic, one 2° alcoholic, one $-NH$ & one 3° amino groups.

*ii) Reserpic acid on oxidn with $KMnO_4$ gives 4-methoxy-N-oxalyl anthranilic acid as one of the products confirming the presence of Indole nucleus.

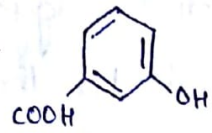


(4-Methoxy-N-Oxalyl anthranilic acid)

iii) * Reserpic acid on fusion with Potash gives 5-hydroxy isophthalic acid. Now since one of the acidic group is isophthalic acid must be an acidic group of reserpic acid itself. The hydroxyl group & carboxyl group in reserpic acid are meta to each other. This is also confirmed by Reserpic acid on heating with Ac_2O yields γ-Lactone.

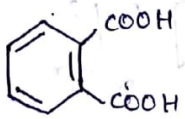
* $C_{22}H_{28}N_2O_5$ $\xrightarrow[\text{fusion}]{KOH}$ 

5-hydroxy Isophthalic acid

*  $\xrightarrow[Ac_2O]{\Delta}$ 

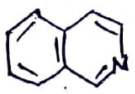
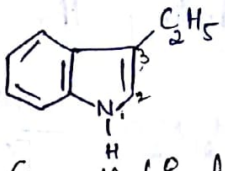
γ-Lactone

iv) * The compound $C_{19}H_{16}N_2$ (Yobyrine) condenses with aldehydes suggesting the presence of a pyridine ring with a $-CH_2-$ substituent adjacent to nitrogen. It gives 3 ethylindole and isoquinoline on zinc dust distillation, Phthalic acid on $KMnO_4$ oxidn, o-toulic acid on CrO_3 oxidn

i) $C_{19}H_{16}N_2$ $\xrightarrow[[O]]{KMnO_4}$ 

Yobyrine

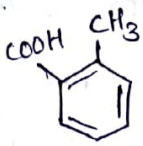
Phthalic acid

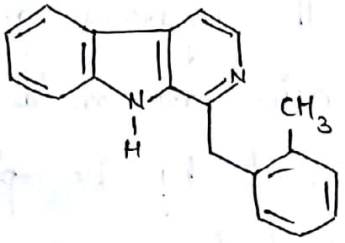
ii) $C_{19}H_{16}N_2$ $\xrightarrow{Zn\ dust}$  + 

(Isoquinoline)

(3-Ethyl indole)

All these reactions suggest the following structure to Yobyrine

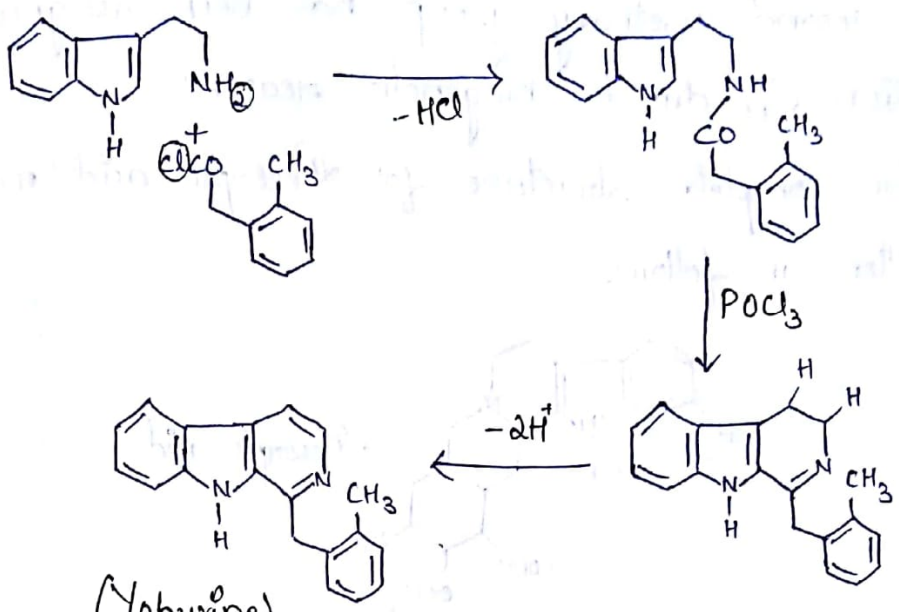
iii) $C_{19}H_{16}N_2$ $\xrightarrow[[O]]{CrO_3}$ 



(str of Yobyrine)

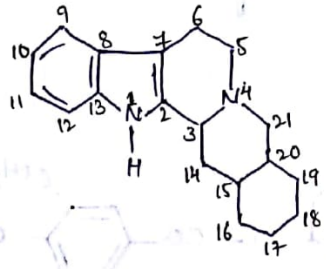
The above proposed structure for Yobyrine is confirmed by its synthesis.

Synthesis of Yobyrine:

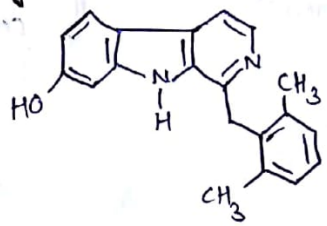


(Yobyrine)

* The formation of Yobyrine from reserpic acid indicates that the latter has the following type of carbon skeleton.

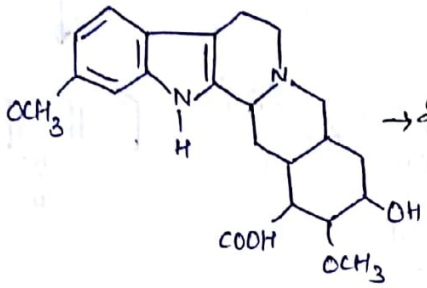


v)* From the point (ii) w.k.t one of the methoxy group is in the m-position to the -NH group of indole i.e., C_{11}. Presence of the carboxyl group at C_{16} is indicated by the dehydrogenation of reserpic acid with Selenium to give 11-hydroxy-16-methyl yobyrine (dehydrogenation of -COOH group is converted into CH_3)



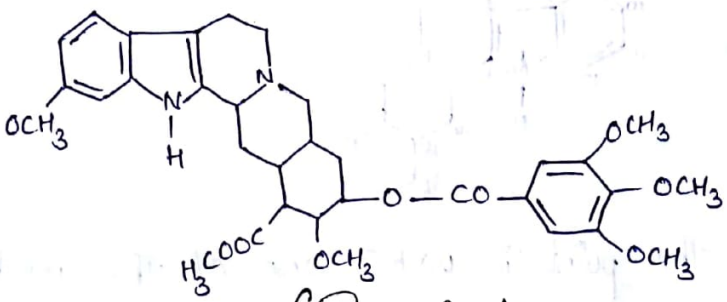
* Now since from point (iii) w.k.T acidic (-COOH) and hydroxyl groups are meta to each other. The hydroxyl group in Reserpic acid must be present on C_{18}. The second methoxy group has been assigned in position C_{17} due to biogenetic reasons.

* The complete structure for Reserpic acid may be written as follows.



→ Reserpic acid

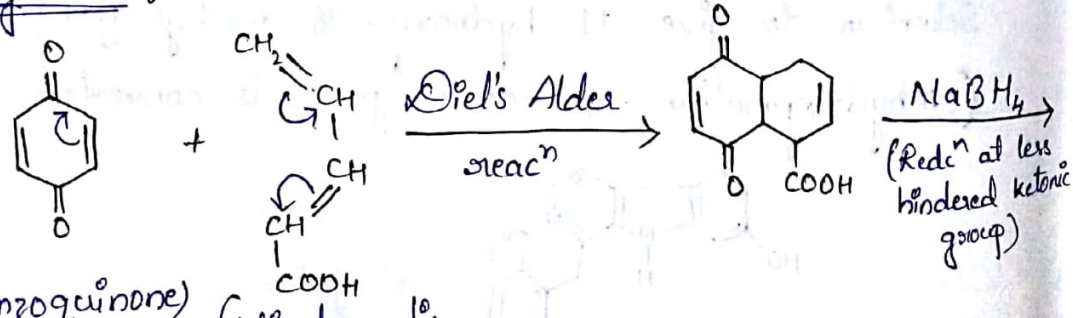
* On the basis of the above structure of Reserpic acid, Reserpine (a diester of Reserpic acid) has been assigned by the following structure.



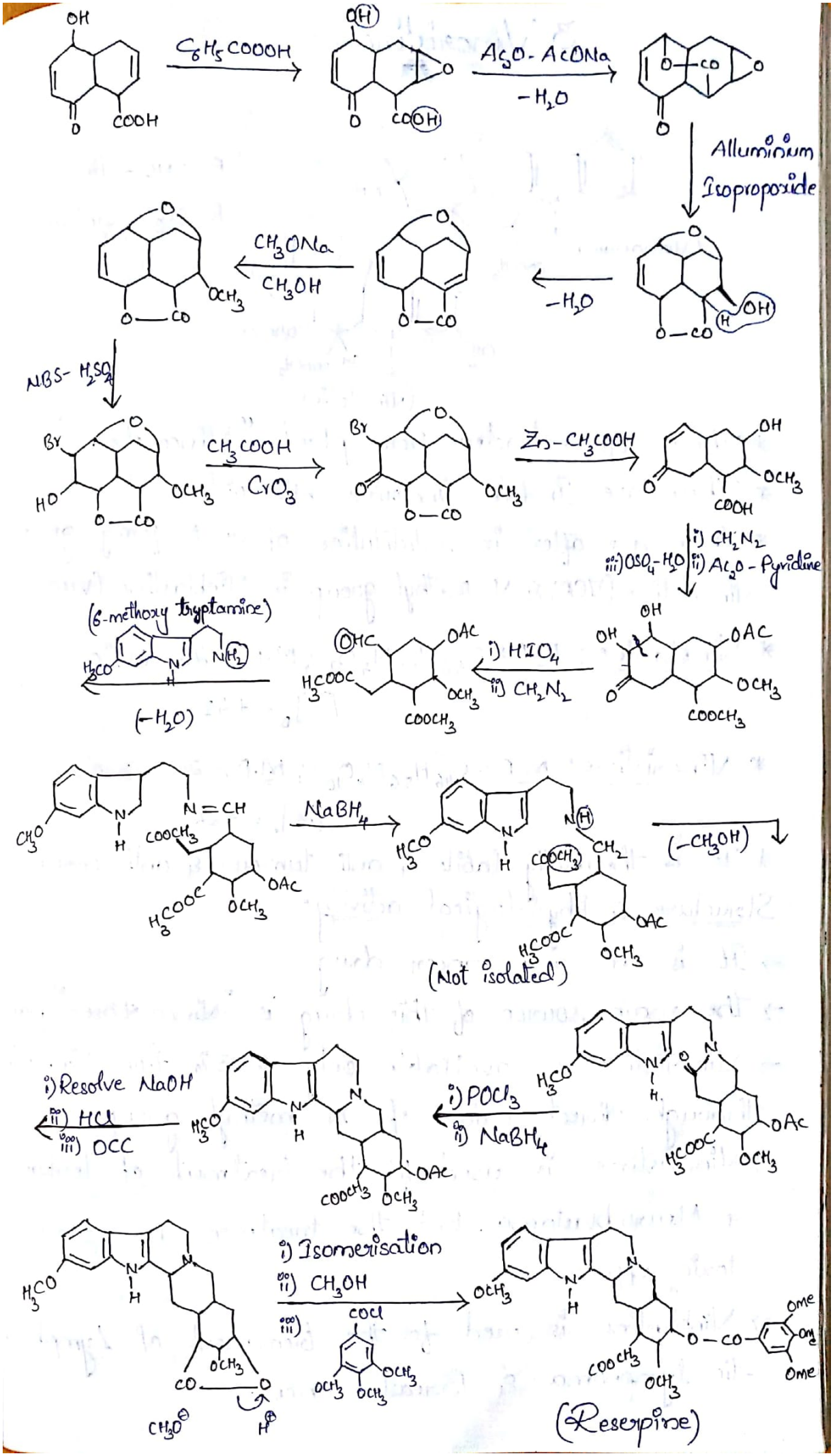
(Reserpine)

The above structure of Reserpine has been proved by its synthesis.

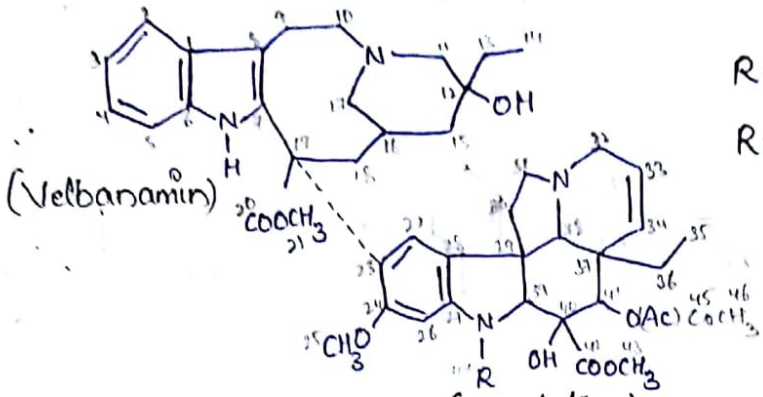
Synthesis:



(p-Benzoquinone) (Vinyl acrylic acid)



3. Vincristine



R = CHO – Vincristine
R = CH_3 – Vinblastine

$C_{46}H_{56}N_4O_{10}$

* These are extracted from plant "Vinca Rosea".
* These are Indole - Indoline Alkaloids.
* These are after in substitution of an N-formyl group in Vincristine (VCR) & N-methyl group in Vinblastine (VIB).

* Vinblastine : M.F :- $C_{46}H_{58}N_4O_9$; M.P :- 211 – 216°C

$[\alpha]_D = +42$

* Vincristine : M.F :- $C_{46}H_{56}N_4O_{10}$; M.P :- 218 – 220°C

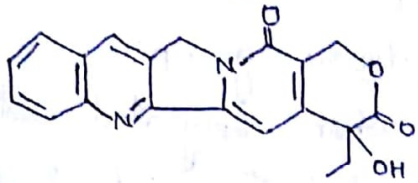
$[\alpha]_D = +26$

* It is thermally labile & anti-tumour & anti-carcinogenic

Structure & Physiological activity:

⇒ It is an anti-cancer drug.
⇒ The main source of this drug is "Vinca Rosea" plant.
⇒ Vincristine is available only 0.03% from Vinblastine through direct oxidⁿ of N-methyl group.
⇒ Vincristine is used for the treatment of leukemia & Neuroblastoma. But the treatment has some toxic effects.
⇒ Vinblastine is used for the treatment of Lymphocy-tic lymphoma & Breast cancer.

4. Camptothecin



Occurrence:

It was first isolated from the stem, roots of "Camptotheca acuminala" (Happy tree)

Isolation:

The dried plant material is extracted with hot hexane heptane followed by extraction with 95% Ethanol. The concentrated solution from the ethanol extract is partitioned b/w water and chloroform. The methanol insoluble material from the chloroform extract is subjected to chromatography followed by crystallisation from methanol acetanilide yield the Camptothecin as pale yellow needles.

Physiological activity:

⇒ It is an anti-Leukemic drug.

⇒ It exhibits a broad spectrum of anti-tumour in animals.

⇒ It inhibits the replication of DNA viruses, Adeno virus, Herpes virus. It has no effect on RNA viruses.

⇒ It was found effective in treatment of gastro-intestinal cancer & Brain cancer & Lung cancer & some other tumors.

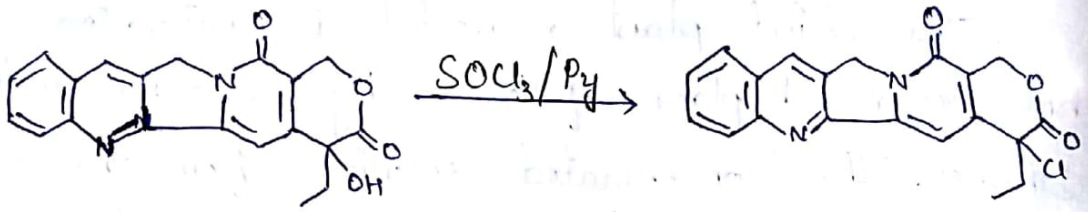
⇒ It is used in the treatment of skin diseases in China.

Structural Elucidation:

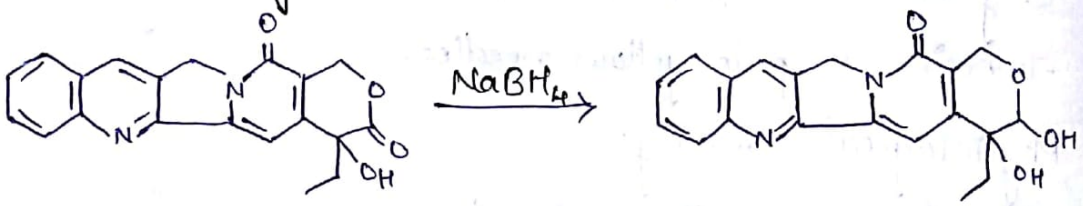
1. M.F : $C_{20}H_{16}N_2O_4$
2. Presence of 1 hydroxyl group:

Camptothecin when acetylated with Ac_2O / Pyridine gives mono acetyl derivative. It indicates that Camptothecin contains one hydroxyl group.

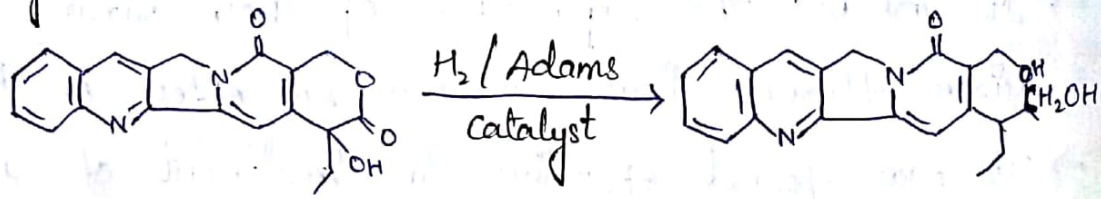
3. Camptothecin reacts with thionyl chloride & pyridine gives Chloro camptothecin.



4. Camptothecin on redⁿ with $NaBH_4$ gives Lactol derivative. It indicates that the Camptothecin contains Lactone moiety.

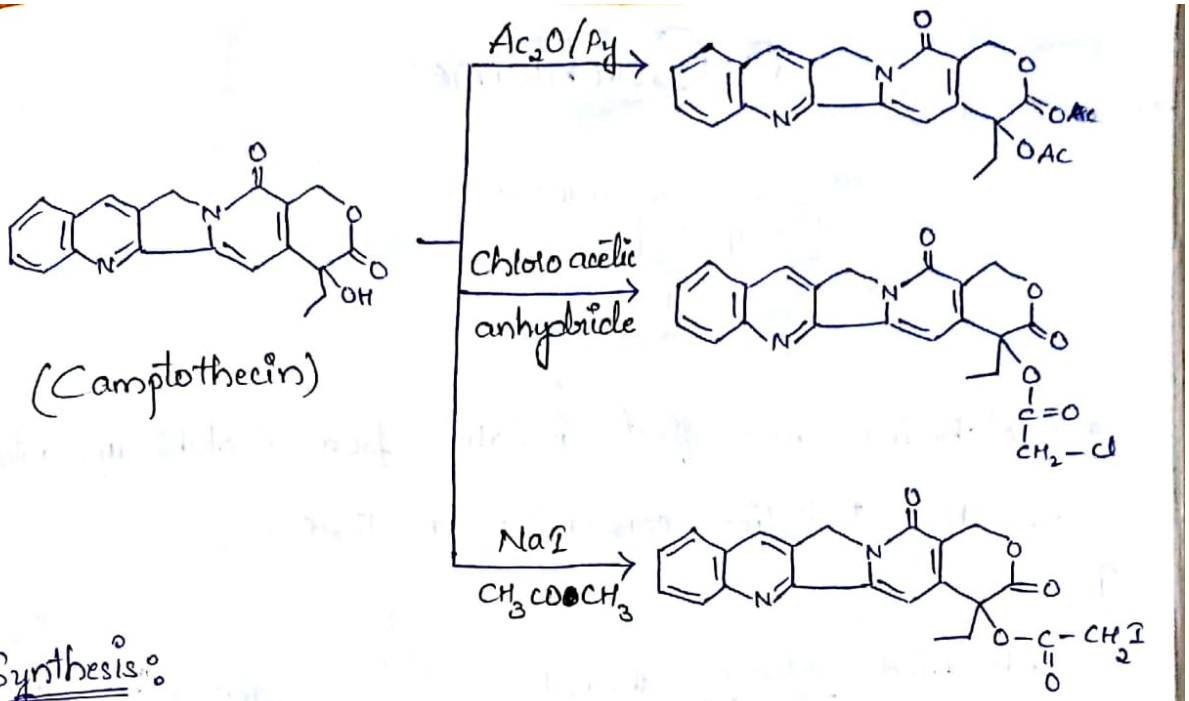


5. On exhaustive hydrogenation in presence of CH_3COOH & Adams catalyst (PtO_2), Camptothecin gives De-deca hydro derivative.

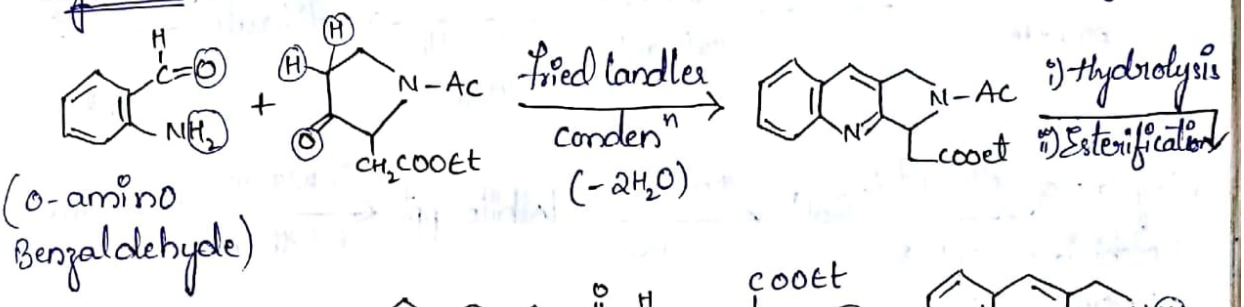


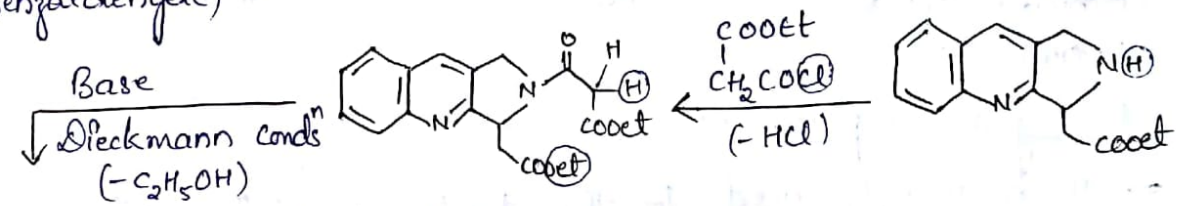
6. X-ray crystalographic studies of camptothecin showed that Camptothecin has [3,4-b] Quinoline system.

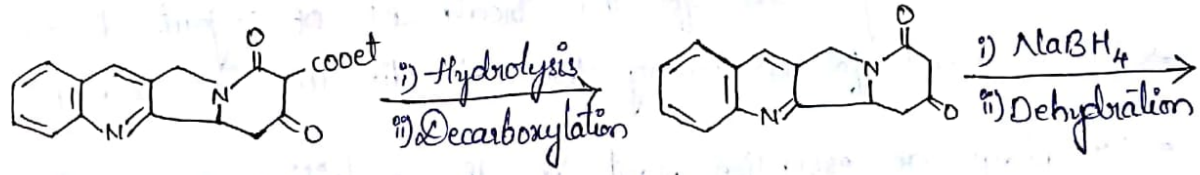
Actions of Camptothecin:

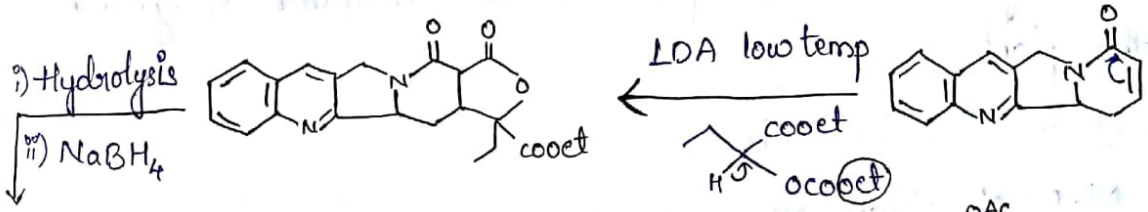


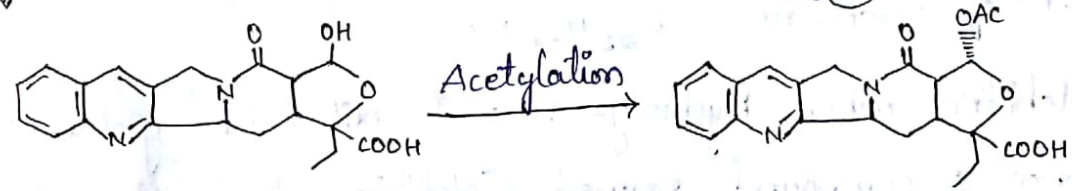
Synthesis :-



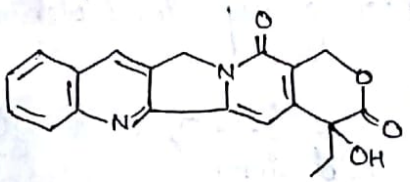






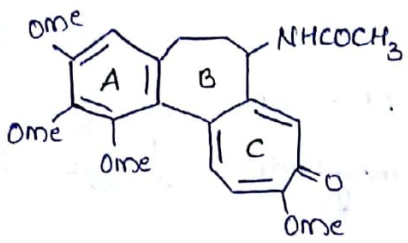


i) Acetate hydrolysis
ii) Hemi acetal redn
iii) Acidification
iv) Dehydrogenation



(Camptothecin)
[DL-form]

5. Colchicine



* Colchicine was first isolated from Colchicum autumnale -L by Pelletier caventou in 1820.

Isolation:

Seeds dried powder $\xrightarrow{\text{Ethanol}}$ Ethanol extract $\xrightarrow[\text{ii) filter}]{\text{Residue i) dil. with } H_2O}$ Filtrate $\xrightarrow[\text{ii) } CHCl_3 \text{ evaporation}]{CHCl_3 \text{ i) Org. layer}}$ Residue $\xleftarrow[\text{ii) Ethanol}]{\text{i) warm}}$ White ppt $\xleftarrow{\text{Residue with } CHCl_3}$ Sol^n $\xleftarrow{\text{Allowed to cool } 3^\circ C}$ Crystals of Colchicine (Yellow)

Biological importance:

⇒ It is mainly used for the treatment of "Gout" diseases.

⇒ It is used for arresting the cell division in both plant

⇒ It plays an essential part in the nutrition & growth of the plant.

Structural Elucidation:

* M.F of Colchicine - $C_{22}H_{25}NO_6$.

* Colchicine when hydrolysed with dil. acids yields methyl alcohol & compound named Colchicine indicating the presence of Enol methyl ether group in Colchicine.

$$C_{22}H_{25}NO_6 + H_2O \xrightarrow{\text{dil. acids}} \underset{\text{(Colchicine)}}{C_{21}H_{23}NO_6} + CH_3OH$$

* Presence of Acetamide group:

Colchicine when hydrolysed with strong acids gives

acetic acid & trimethyl colchicinic acid having 1°-amino group with loss of acetic acid. It indicates the presence of acetamide group ($-NHCOCH_3$).

Colchicine ($-NHCOCH_3$) $\xrightarrow{\text{Strong acids}}$ Trimethyl colchicinic acid ($-NH_2$) + CH_3COOH.

* Presence of 3-OMe groups:

When trimethyl colchicinic acid hydrolysis under vigorous conditions gives one mole of colchicinic acid & 3 moles of methyl halides indicating the presence of 3 methoxy groups.

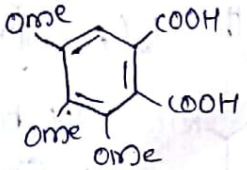
$C_{16}H_{12}NO_2\{-OCH_3, -OCH_3, -OCH_3$ (Trimethyl colchicinic acid) $\xrightarrow{HCl}$ $C_{16}H_{12}NO_2\{-OH, -OH, -OH + 3MeCl$.

* Colchicine on catalytic hydrogenation gives hexa hydro colchicine which forms mono epoxy derivative on treatment with perbenzoic acid indicating that hexahydro colchicine contains an isolated double bond. Therefore Colchicine contains 3 double bonds.

Colchicine $\xrightarrow{[H]}$ Hexahydro colchicine $\xrightarrow{\text{per acid } (C_6H_5COOH)}$ Mono epoxy derivative.

* Colchicine on oxidation gives 3,4,5-trimethoxy phthalic acid indicating the presence of benzanoid nucleus in Colchicine.

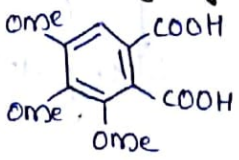
Colchicine $\xrightarrow{[O]}$



* Nature (or) Size of the rings:

Ring-A: Colchicine on oxidn with Potassium permanganate gives 3,4,5-trimethoxy phthalic acid. This

degradation products establishes the structure of ring A and also position of the 3-methoxy groups.

Colchicine $\xrightarrow[[O]]{KMnO_4}$ 

Thus ring-A is 6-membered.

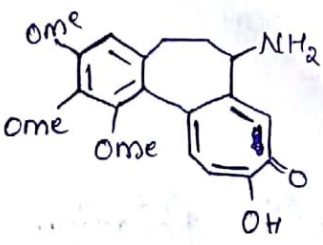
Ring-B:

Colchicine on treatment with KI gives N-acetyl iodocolchinol which on O-methylation followed by redⁿ gives N-acetyl colchinol methyl ether. Latter on heating with P_2O_5 forms two compounds namely de amino colchinol methyl ether & Iso de amino colchinol methyl ether.

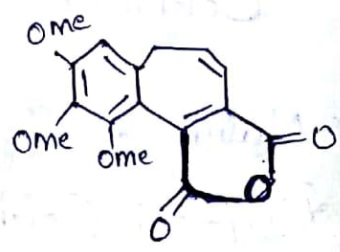
Colchicine $\xrightarrow{KI}$ N-acetyl Iodo colchi-nol $\xrightarrow[[H]]{O\text{-methylation}}$ N-acetyl colchinol methyl ether

N-acetyl colchinol methyl ether $\xrightarrow{P_2O_5, \Delta}$ De amino colchinol methyl Ether + Iso deamino colchinol methyl Ether

* Trimethyl colchinic acid on N-benzoylation form N-benzoyl trimethyl colchicinic acid & on oxidation gives N-benzoyl colchicinic anhydride which on heating with P_2O_5 gives Nitrogen free anhydride.

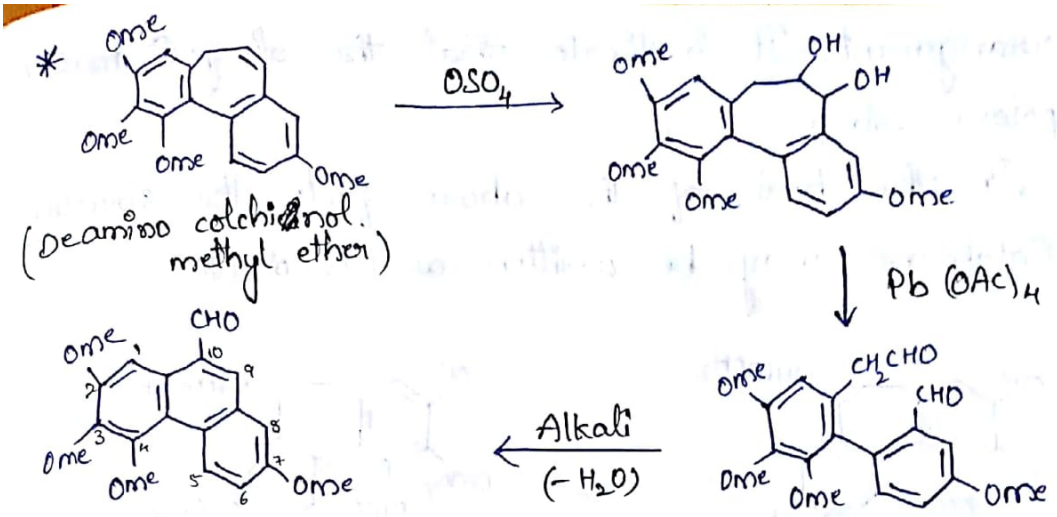


i) N-benzoylation
ii) Oxidation
iii) P_2O_5, Δ



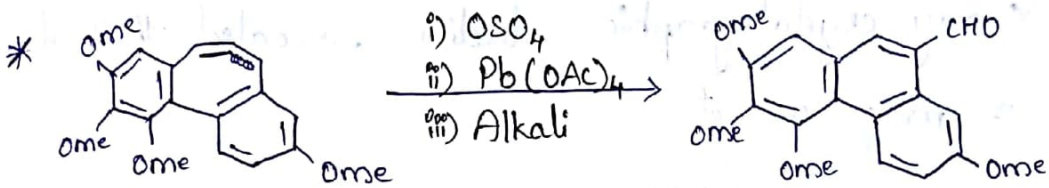
Trimethyl colchicinic acid

Anhydride.



(Deamino colchicinol methyl ether)

(2,3,4,7 - tetramethoxy 10- Phenanthraldehyde)



(Isodeamino colchinol methyl ether)

(2,3,4,7 - tetra methoxy 9- phenanthraldehyde)

These reac^{n}'s suggest that ring-B of Colchicine is 7-membered.

Ring-C: Although in the above reac^{n}'s, ring-C is drawn as 6-membered. Dewar in 1945 proposed that in Colchicine ring-C has a 7-membered Tropolone like structure.

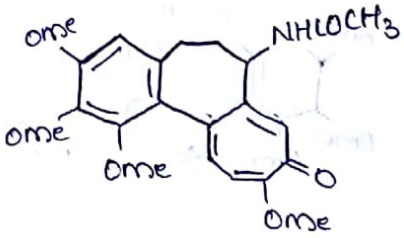
It is confirmed by the following evidences:

i) Colchicine on hydrogenation gives hexa hydro colchicine having Ethylenic double bond proved by formation of Epoxide. Thus, the 3 double bonds & keto group are in the same ring indicate that it is a 7-membered ring but not 6-membered.

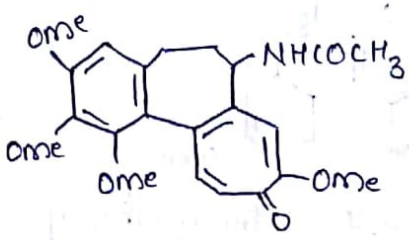
ii) Colchicine is treated with cold alkaline hypo iodide to give N-acetyl iodo colchinol through benzylic acid

rearrangement. It indicates that the ring-C must be Tropolone ring.

On the basis of the above facts, the structure of Colchicine may be written as (I) or (II).



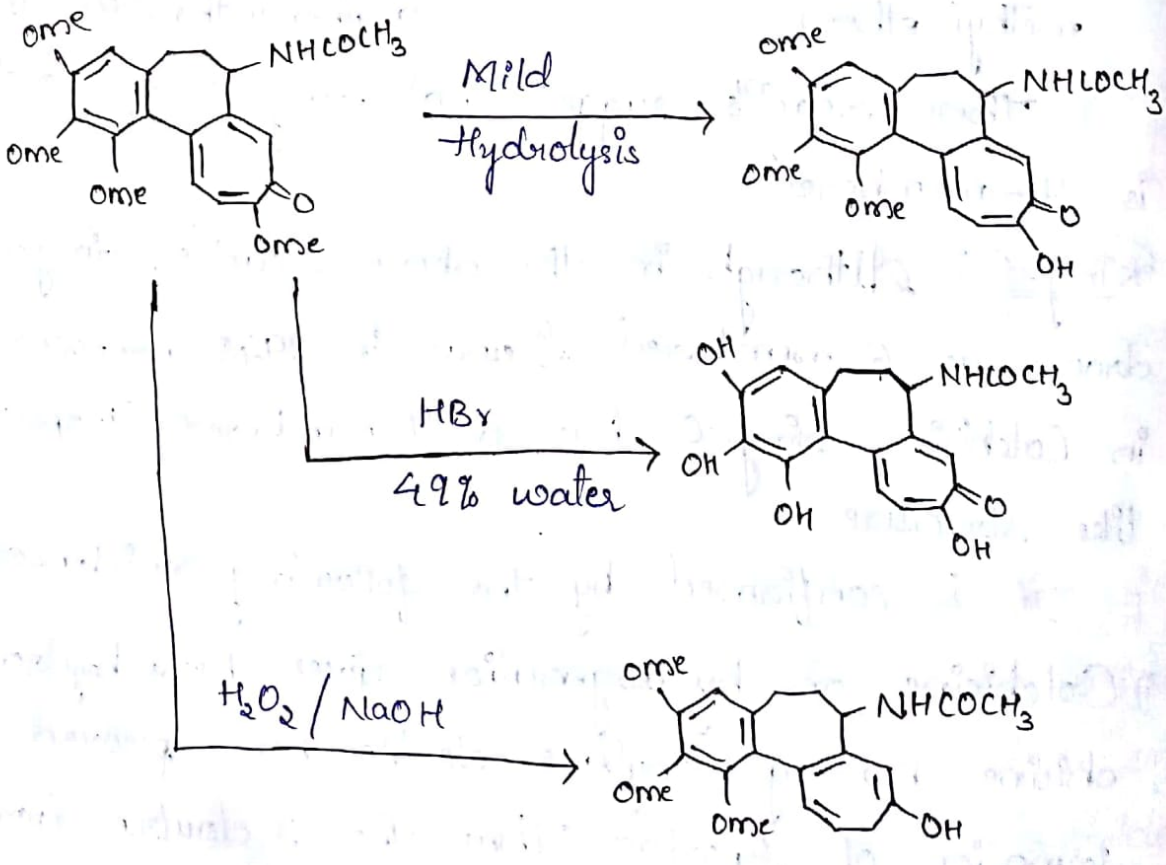
(I)



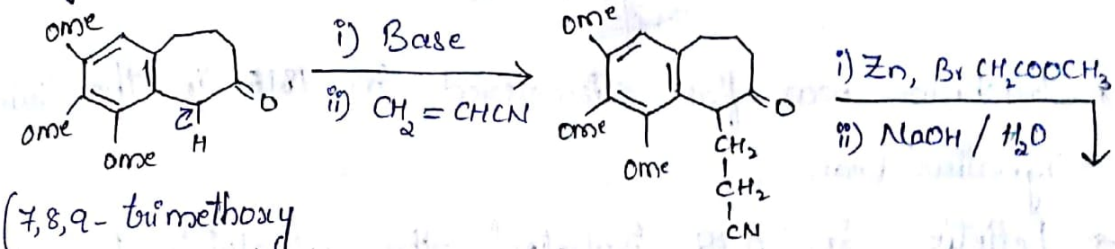
(II)

→ X-ray crystalographic studies revealed that structure (I) is more correct.

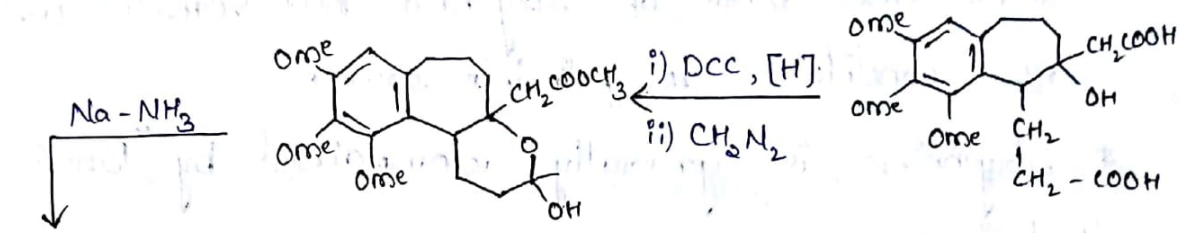
Conversions of Colchicine:

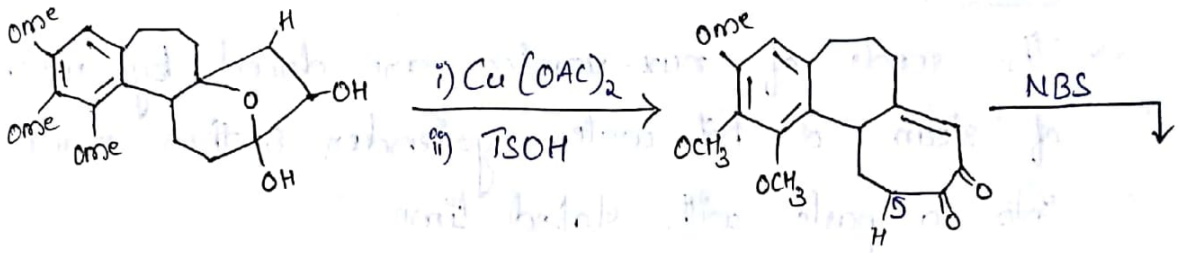


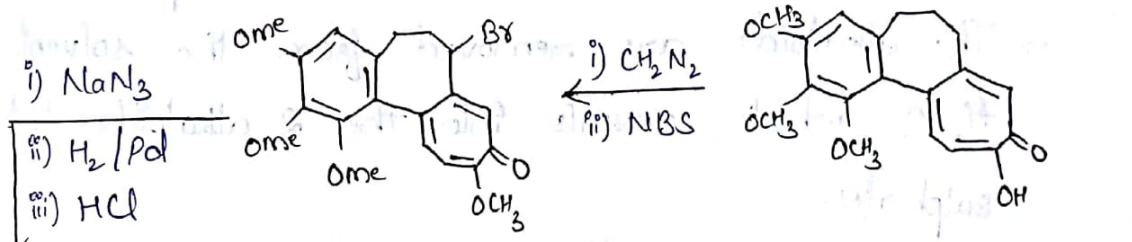
Synthesis:

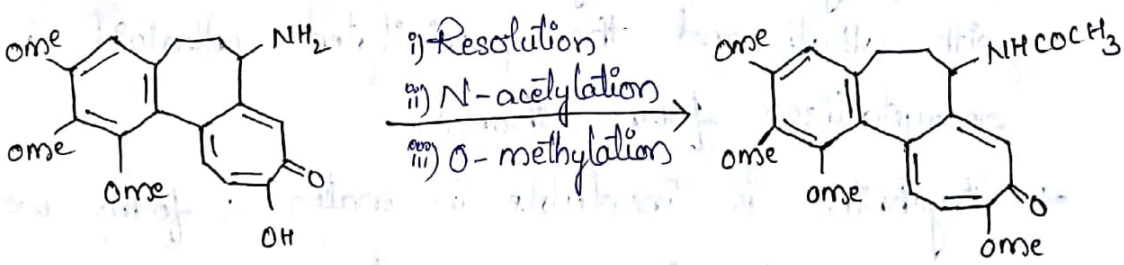


(7,8,9- trimethoxy benzo suberane)









(±) Trimethyl colchicinic acid)

(Colchicine)

6. Strychnine

* Strychnine was first discovered in 1818 in the Saint Ignatius' bean.
* Pelletier in 1818 isolated the alkaloid from the seeds and bark of Strychnos nux-vomica which now constitutes as principle source.
* Strychnine is generally accompained by "Brucine".

Isolation:

⇒ The seeds of nux-vomica are dried by means of steam or hot water griender & then made into a paste with slaked lime.

⇒ The mass is extracted with hot naptha or Chloroform

⇒ The alkaloids are removed from the solvent dil. H_2SO_4 which converts into the 2 alkaloids into their sulphates.

⇒ The crystallised strychine sulphate is decomposed with alkali and the precipitated alkaloid is recrystallized from ethanol.

⇒ Strychnine is insoluble in water & forms water soluble salt with HNO_3 and H_2SO_4.

⇒ In small doses Strychnine is power full stimulant and stimulates the respiratory & vascomotor nervous centres (Inter neurons).

Constitution:

⇒ M.F : $C_{21}H_{22}N_2O_2$.

⇒ Strychnine is not found to contain any -NMe group &

it is a strong mono acid tertiary base indicating that one of the Nitrogen is present as $-\overset{|}{N}-$.

⇒ The second nitrogen is found to be non-basic & present as an amide system. Strychnine on warming with KOH soln gives Strychnine acid having a 2° amine & carboxyl group.

⇒ The second oxygen atom does not respond to the usual reagent & hence probably it is present as an Ether linkage.

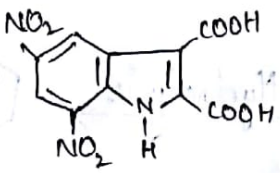
⇒ Dihydro Strychnidine ($C_{21}H_{26}N_2O$) ← Strychnidine ($C_{21}H_{24}N_2O$) ← E·R Strychnine ($C_{21}H_{22}N_2O_2$)

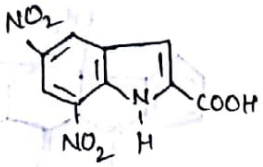
Strychnine ($C_{21}H_{22}N_2O_2$) $\xrightarrow{H_2\text{-}Pd}$ Dihydrostrychnine ($C_{21}H_{24}N_2O_2$)

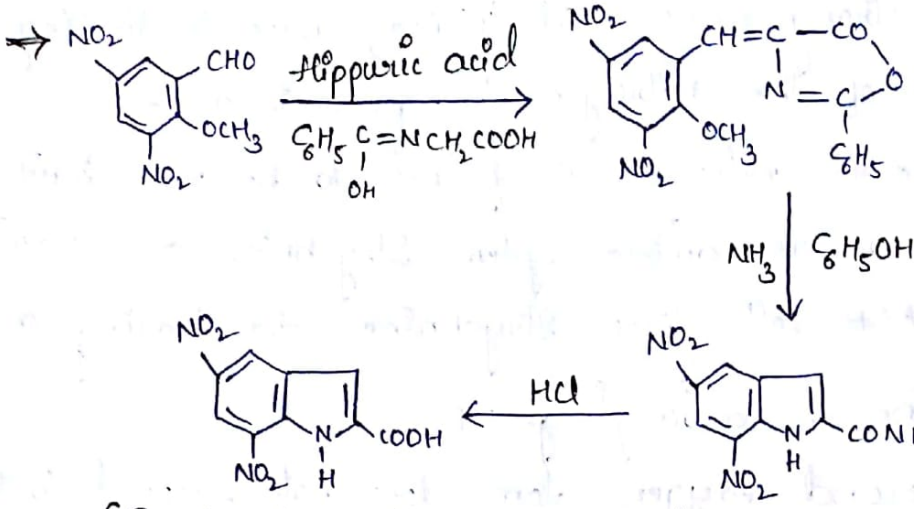
⇒ Strychnine & its simple derivatives but not strychnide condense with benzaldehyde to form Benzylidene derivative indicating that the Strychnine has a reactivity methylene group & hence the Strychnine must possess the following type of grouping.

$$-N-CO-CH_2$$

⇒ Strychnine $\xrightarrow{Conc.\ HNO_3}$ Dinitro strychol acid $\xrightarrow{(-CO_2)}$ Dinitrostrychol



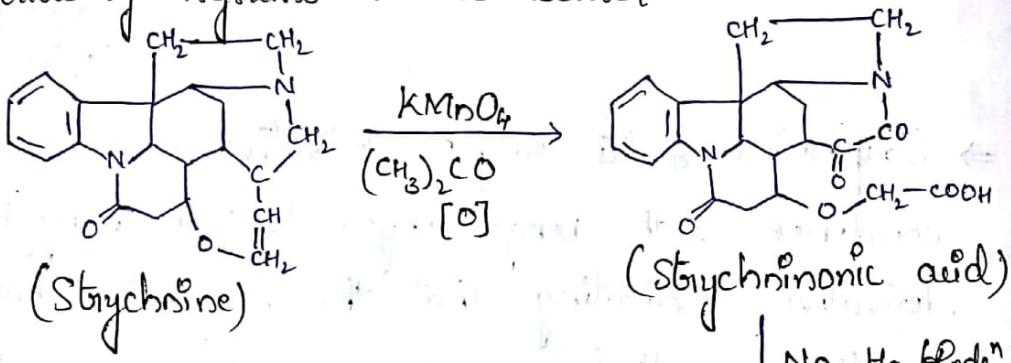




(Dinitrostrychol)

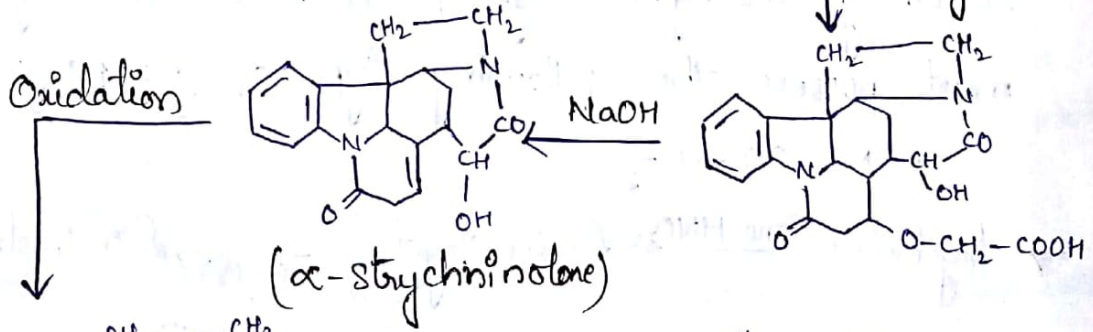
⇒ Strychninonic acid $\xrightarrow{Na/Hg}$ Strychninolic acid $\xrightarrow{NaOH}$ Strychninolone + $CH_2OH.COOH$

⇒ Strychninolone α, β yield malonic and oxalic acid respectively on oxidⁿ, indicating the ~~presence~~ following systems in 2 isomers.

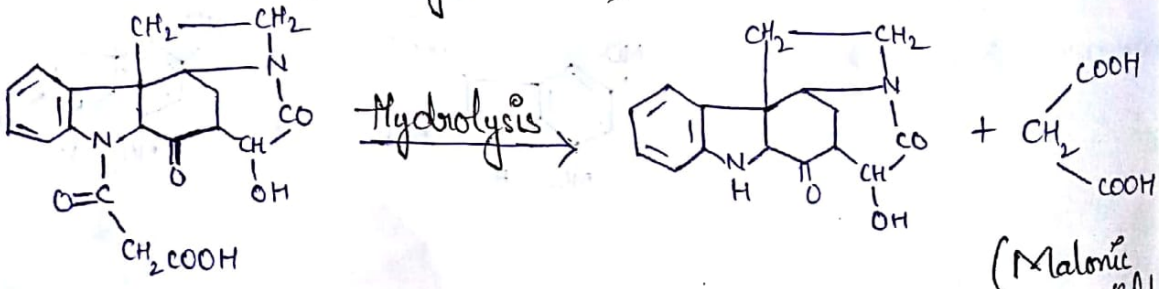


(Strychnine) (Strychninonic acid)

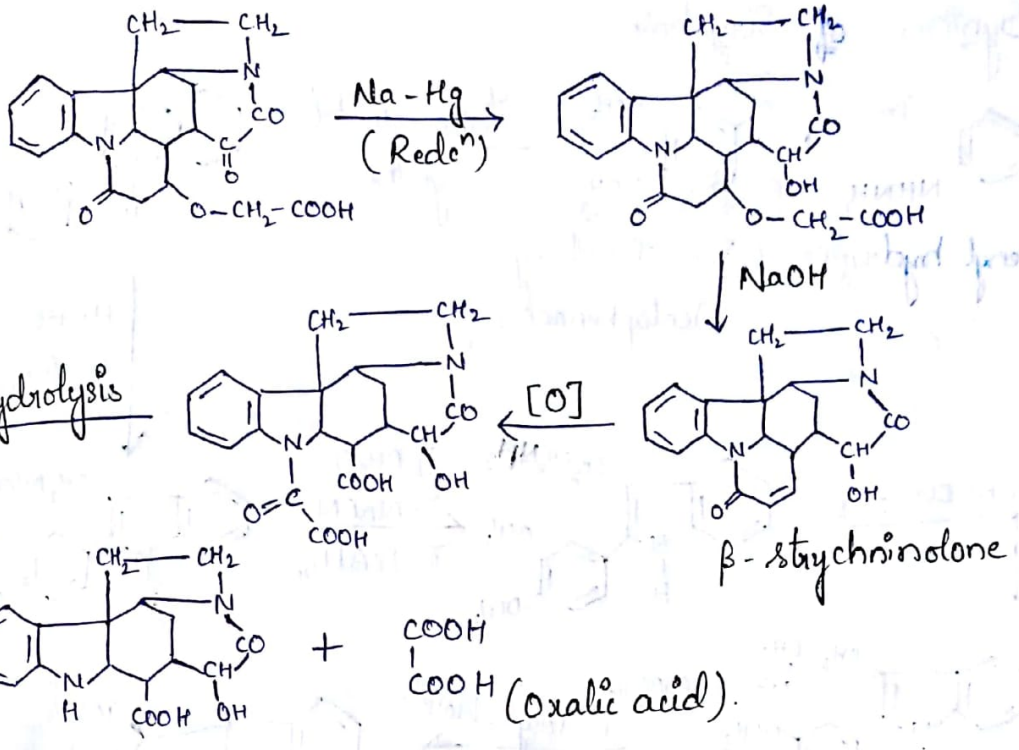
Na-Hg (Reducⁿ)



(α-strychninolone)

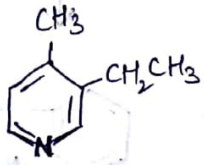


(Malonic acid)

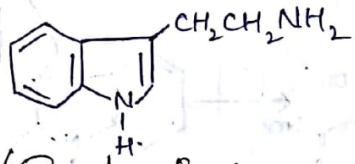


+ COOH
COOH (Oxalic acid).

⇒ Strychnine on distillation with lime gives in addition to Carbazole & Indole β-collidine & Tryptamine.



(β-collidine)

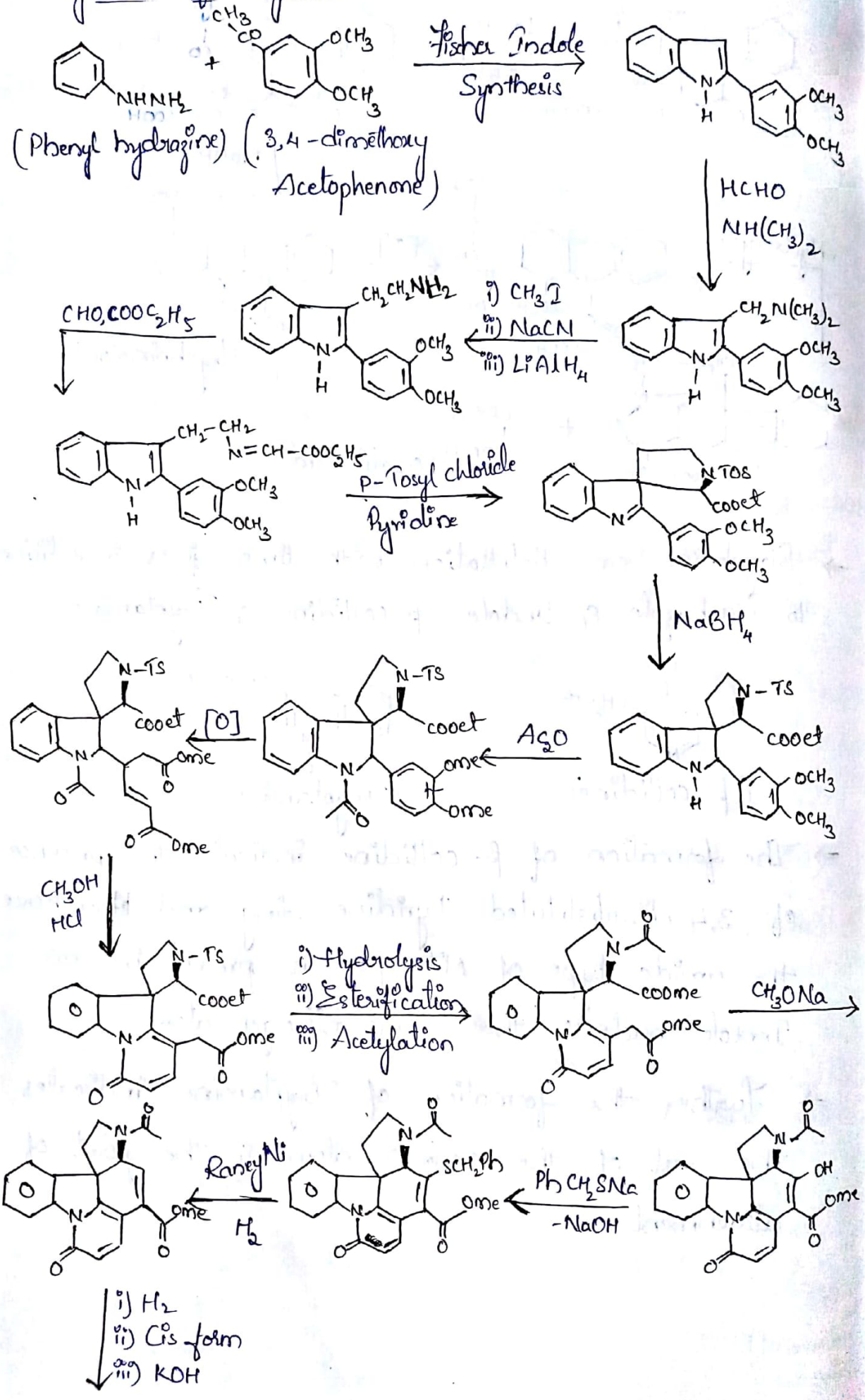


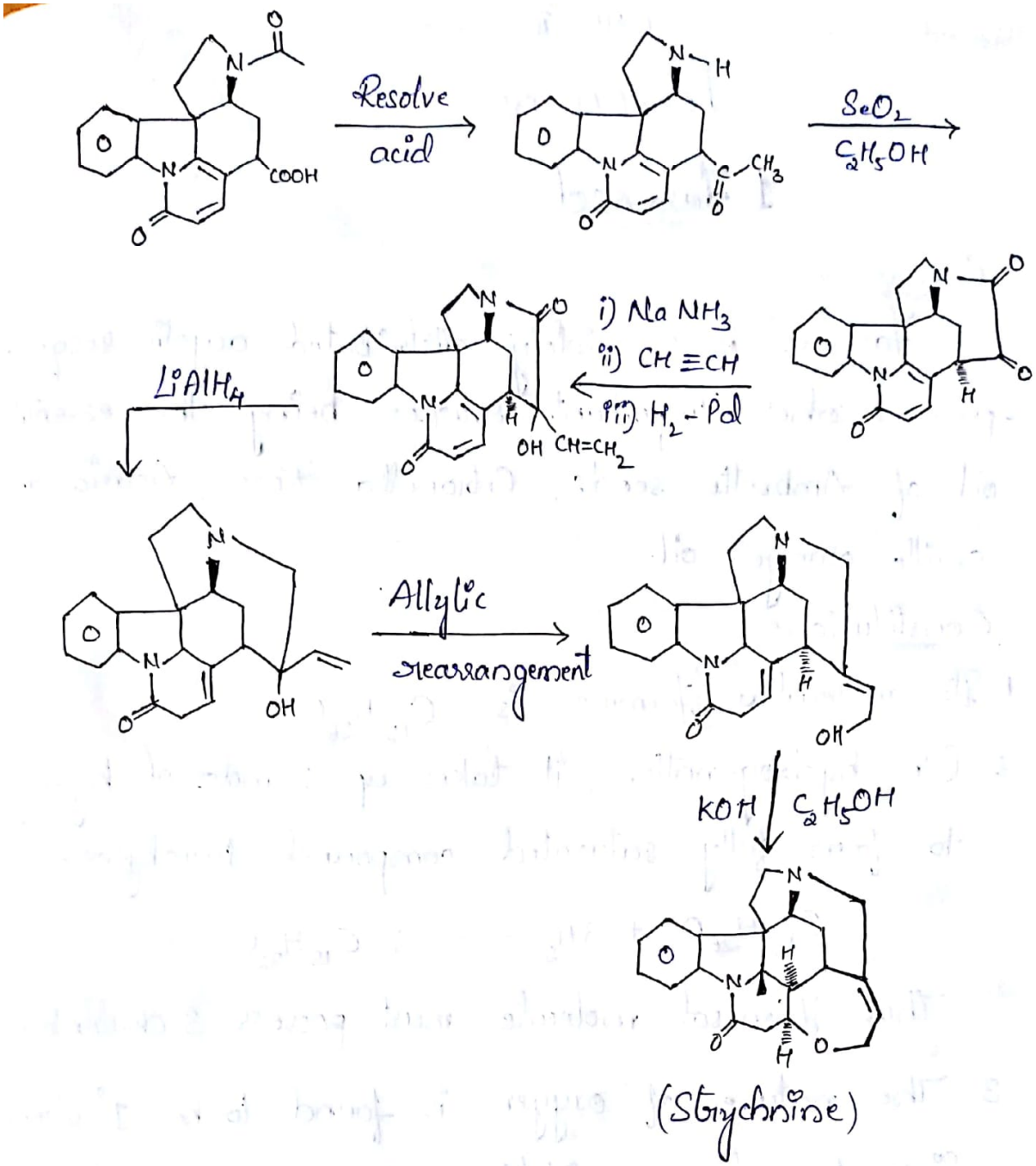
(Tryptamine)

⇒ The formation of β-collidine indicates the presence of 3,4 disubstituted Pyridine ring and ~~since~~ hence the amide type of Nitrogen is present in an Indole nucleus 'the 3° basic nitrogen atom'.

⇒ Further the formation of Tryptamine indicates the rest of the carbon atom & the point of attachment.

Synthesis of Strychnine:





(Strychnine)