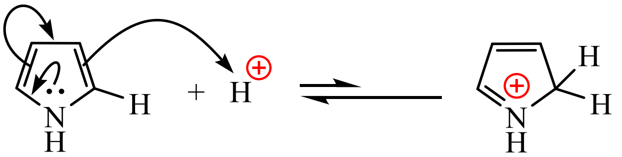
5) Pyrrole:

Pyrrole have been discovered for the first time by Anderson in (1857). It is a colorless liquid, b.p.= 129°C and its odor like chloroform.

Pyrrole is nonbasic compared to ordinary amines, since the lone pair of electrons on nitrogen is tied up by conjugation.

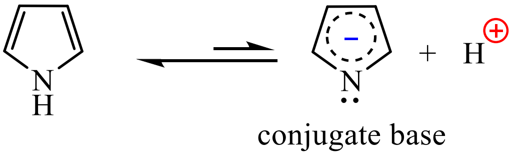


pKa= - 4.4

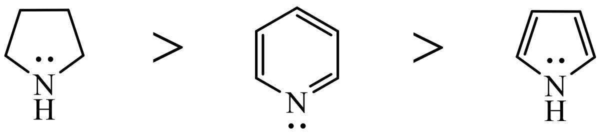
<u>Note</u>: very strong acid is required to affect protonation.

On the other hand, pyrroles are not only very nonbasic, they are in fact relatively acidic.

Clearly we can see that pKa for pyrrolidine = 35 as in amines while in pyrrole = 16.5, this increasing in acidity is due to the change from *sp*^{3} to *sp*^{2} hybridization and the delocalization of the negative (-ve) charge.



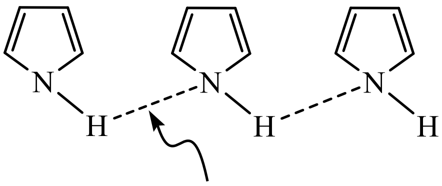
Thus pyrrole is very weak base compared with pyrrolidine and even pyridine as shown below:



(1) (2) (3)

1) The lone pair of electrons is free i.e. like aliphatic amines.
2) The lone pair doesn’t involve in resonance.
3) The lone pair is tied up by conjugation.

Pyrrole can form intermolecular hydrogen bonding, thus it possess boiling point higher than thiophene 84°C and furan 32°C which cannot form these bonds:



(an intermolecular hydrogen bonding)

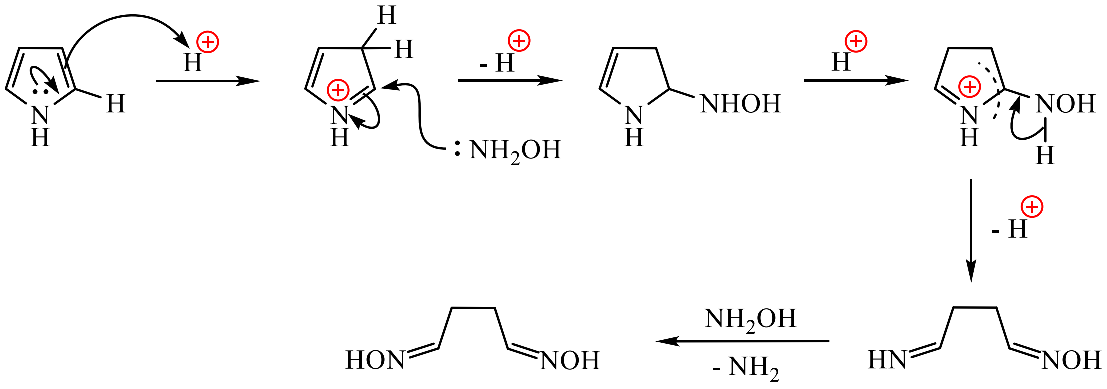
5.1) Chemical properties and reactions of pyrrole:

Pyrrole resist nucleophilic substitution or addition reactions, but it react with electrophilic reagents (electrophilic substitution reactions), furthermore it shows some acidic and basic properties (amphoteric) as mentioned previously.

5.1.1) Ring opening of pyrrole:

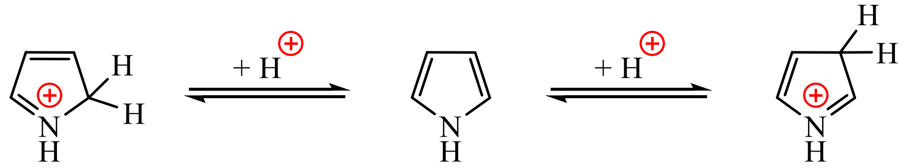
Pyrrole ring doesn't open easily by its treatment with acids or bases at room temperature.

But reaction of pyrrole at its boiling point with alcoholic hydroxylamine will give the dioxime of succinaldehyde.



5.1.2) Addition reactions:

Pyrrole has aromatic properties due to the presence of the lone pair of electrons that complete the aromatic sextet, on the other hand this lone pair made pyrrole act as very weak base pKa= - 4.4

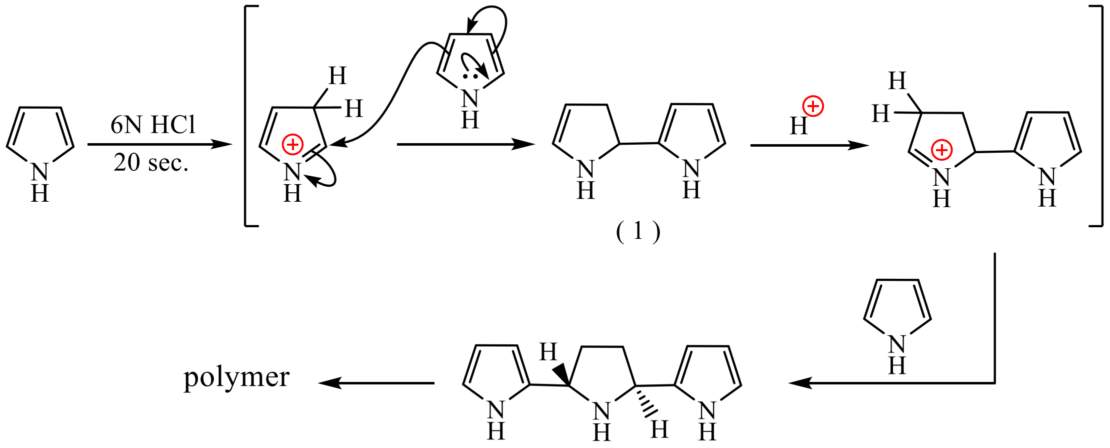


H2- pyrrolium cation

H3- pyrrolium cation

Protonation doesn’t occur on the nitrogen atom but 80% on C-2 and 20% on C-3.

Treatment of pyrrole with (6 N HCl) at 0°C for 20 sec. produce crystalline material (2) that formed from electrophilic addition of H3-pyrrolium cation to pyrrole molecule to give (1) which protonated at 4 position followed by addition to another pyrrole molecule to give the final product:

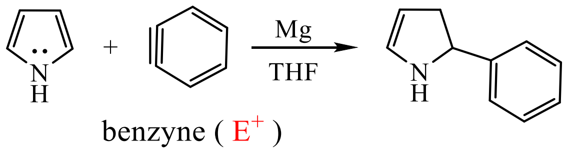


(2)

Note: strong acidic conditions will lead to polymerization.

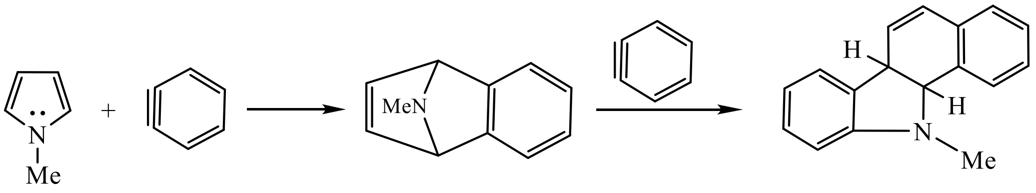
A few examples shows that pyrrole can react as a diene especially when the nitrogen atom substituted by alkyl group.

1)



substitution

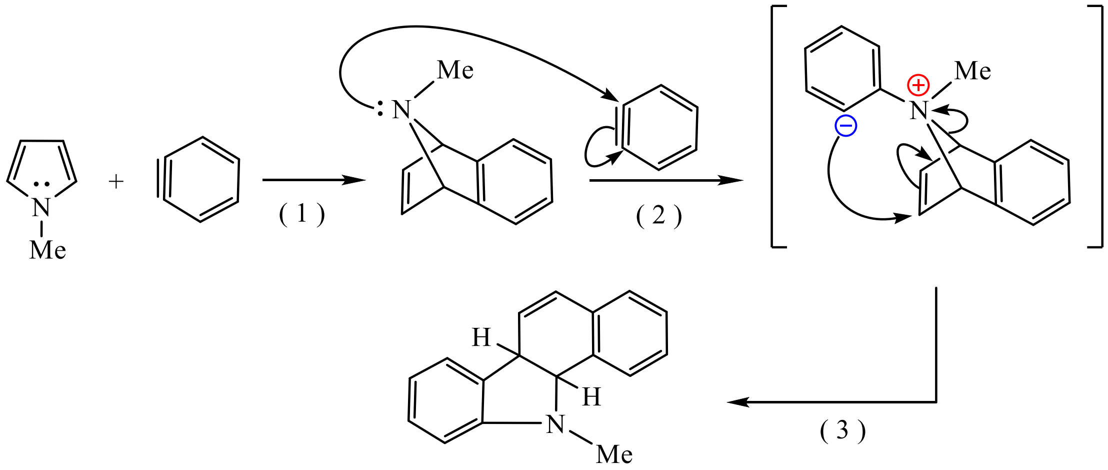
2)



Diels - Alder

The first reaction is an ordinary electrophilic substitution reaction, while the second reaction is combined of three steps as the following:

1) The first step is Diels – Alder reaction.
2) The second step is nucleophilic addition to benzyne.
3) The final step involve aza – Claisen rearrangement.



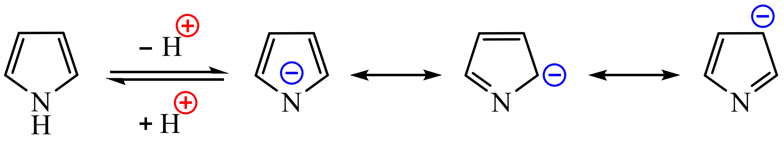
5.1.3) Substitution reactions:

Pyrrole undergoes two types of substitution reactions, the first one at the nitrogen atom while the second at one or more carbon atoms of pyrrole ring.

5.1.3.1) Substitution at nitrogen atom:

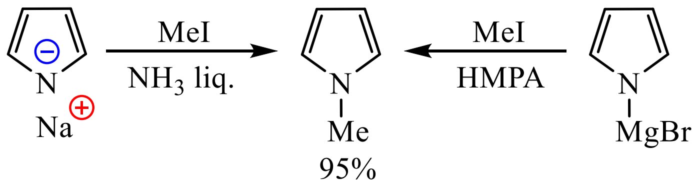
As a consequence of its weakly acidic properties, pyrrole react readily with strong bases to generate a reactive pyrrolyl anion. The aromatic properties for this anion more than pyrrole itself.

<u>Note</u>: Reaction of pyrrole with metals like potassium will produse the anion (pyrrolyl anion), and the hydrogen abstraction rate increase in the case of presence of (EWGs) on pyrrole ring which weaken the (N – H) bond i.e. increasing the acidity of pyrrole.



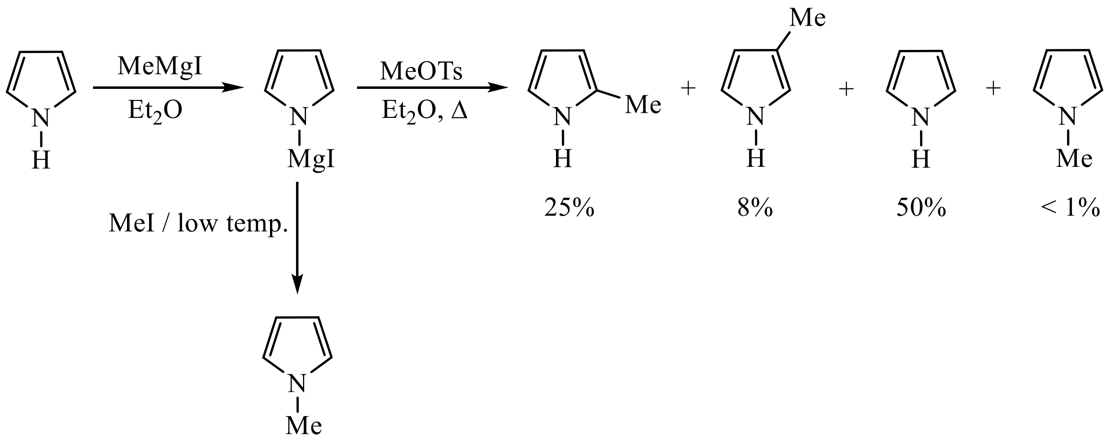
(pyrrolyl anion)

The salt used in the synthesis of substituted pyrrole (at nitrogen atom). e.g. Reaction of pyrrolyl anion with alkyl halide produce N–alkyl pyrrole in high yield.

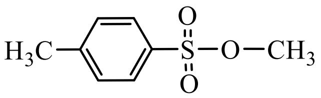


(HMPA): Hexamethylphosphoramide $[(CH_3)_2N]_3PO$, solvent for polymers, gases and organometalic compounds.

Another method that pyrrole undergoes substitution reaction at nitrogen by the reaction of pyrrole with Grignard reagent (RMgX) to produce pyrrolyl magnesium halide which react itself with alkyl halide at room temperature to produce 1-alkyl pyrrole (substitution at position 1). Increasing the temperature will cause addition at carbon atoms of pyrrole ring.

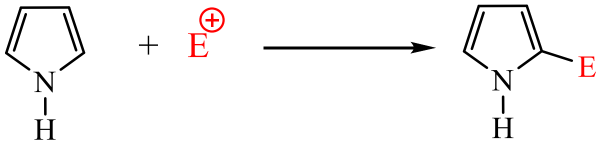


(MeOTs): Methyl p- toluene sulfonate or Methyl tosylate =



5.1.3.2) Substitution at carbon (electrophilic aromatic substitution):

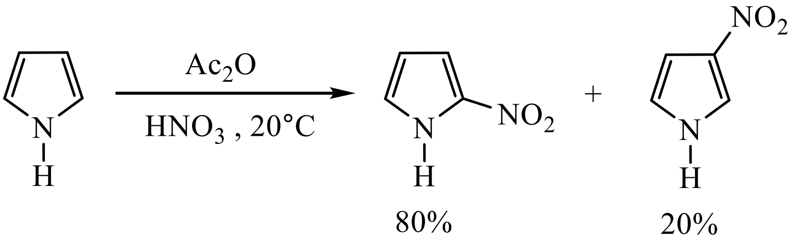
In general, pyrrole undergoes electrophilic substitution reaction at α–position as we mentioned previously. Pyrrole is much more reactive than benzene, the high reactivity of pyrrole (even furan and thiophene) makes it possible to use milder reagents comparing with those used in benzene or its derivatives, since drastic conditions will cause ring opening or polymerization, thus it is necessary to modify the usual reagents.



α C or (2&5)

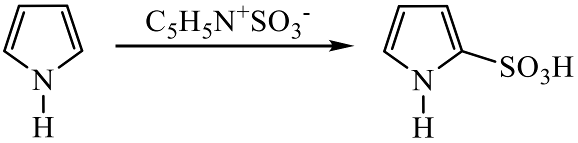
Reaction	**Electrophilic reagent**	**% yield**
Nitration	$AcNO_3$; Ac_2O (-10°C)	51
Sulfonation	$C_5H_5N^+SO^-_3$	90
Halogenation	SO_2Cl_2 / Et_2O , (0°C)	80
Acylation	Ac_2O / (150 - 200°C)	54

e.g.



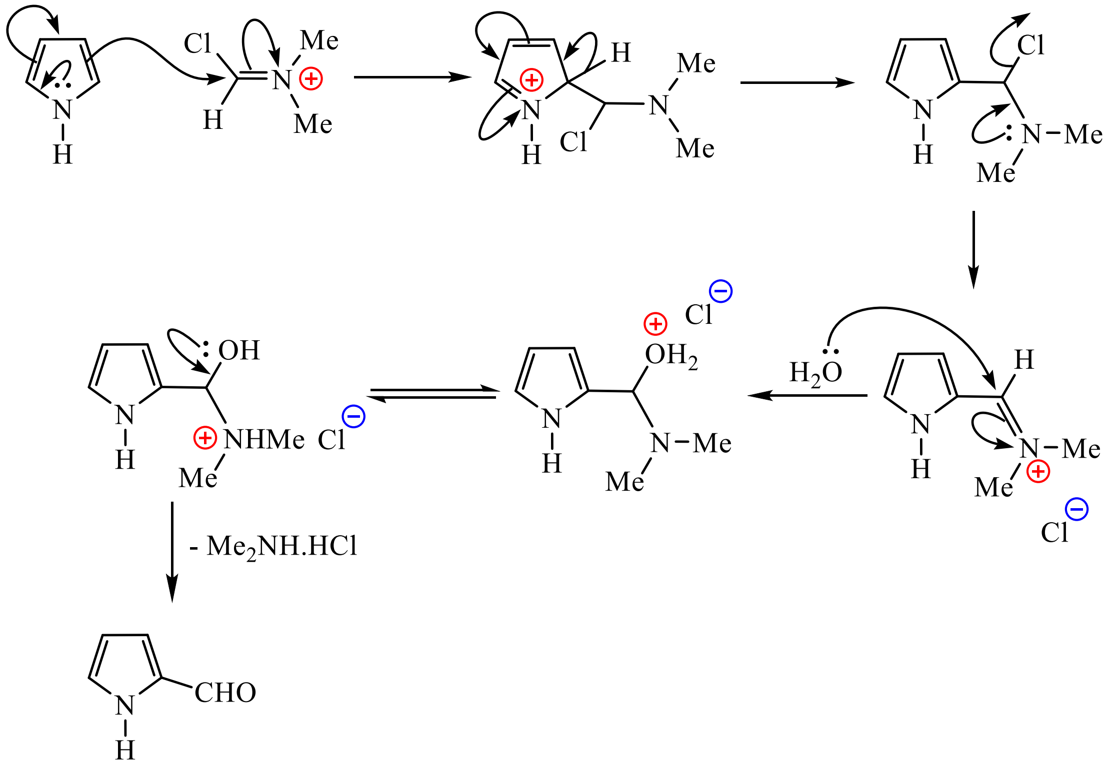
Notes:

1) A mixture of acetic anhydride and nitric acid will produce acetyl nitrate as a nitrating agent.
2) A mixture of concentrated nitric acid and sulfuric acid is not used in nitration since it will lead to pyrrole polymerization.



In addition to these regular electrophilic substitution reactions, pyrrole undergoes other reactions like the following:

1) Vilsmeier reaction:



Note: The electrophilic reagent that used in Vilsmeier reaction have been synthesized by the reaction of dimethylformamide (DMF) and phosphorus oxychloride (POCl$_3$) as the following: