Organic chemistry III

Heterocyclic Chemistry (5)

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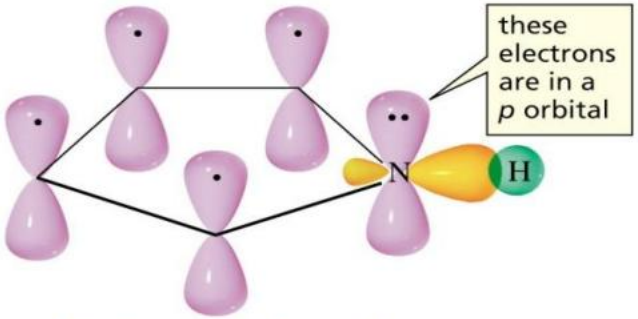
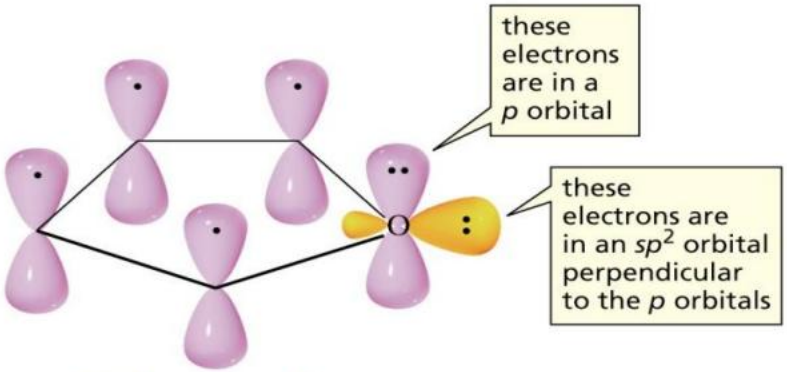
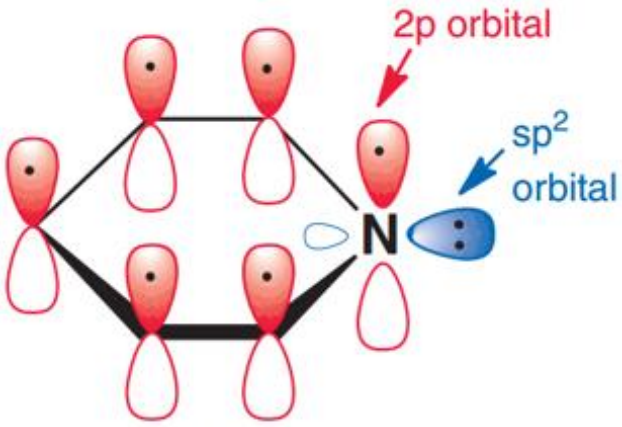


orbital structure of pyrrole



orbital structure of furan



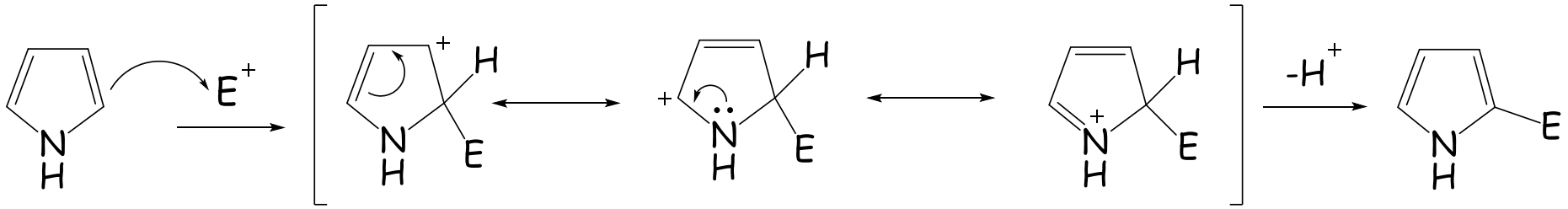
pyridine

- pyridine is a stronger base than pyrrole. The lone pair of the nitrogen atom is localized and does not participate in the aromaticity.
- While in pyrrole, the lone pair of the nitrogen atom participates in aromaticity and is therefore significantly less basic and less nucleophilic than pyridine.

Electrophilic substitution (S_E) at the carbon atoms:

- Pyrrole, furan, and thiophene are highly reactive for electrophilic substitution due to:

a) +M effect of the heteroatom.
b) Distribution of π electrons over 5 atoms only.
c) Stability of the intermediate σ-complex (see below).

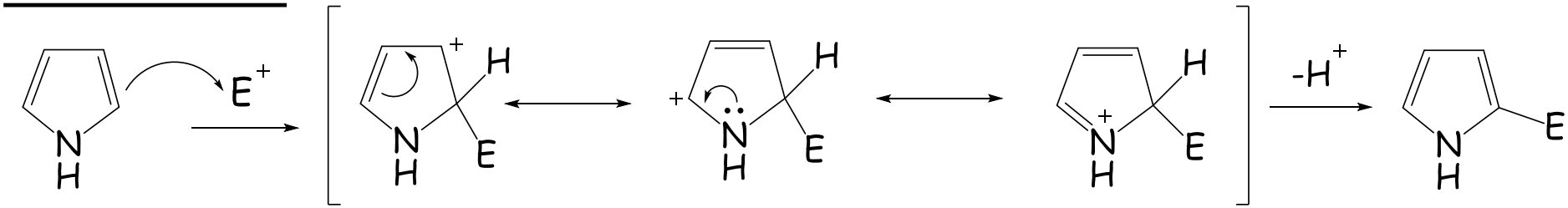


- Relative reactivities to electrophilic substitution :

Pyrrole > furan > thiophene

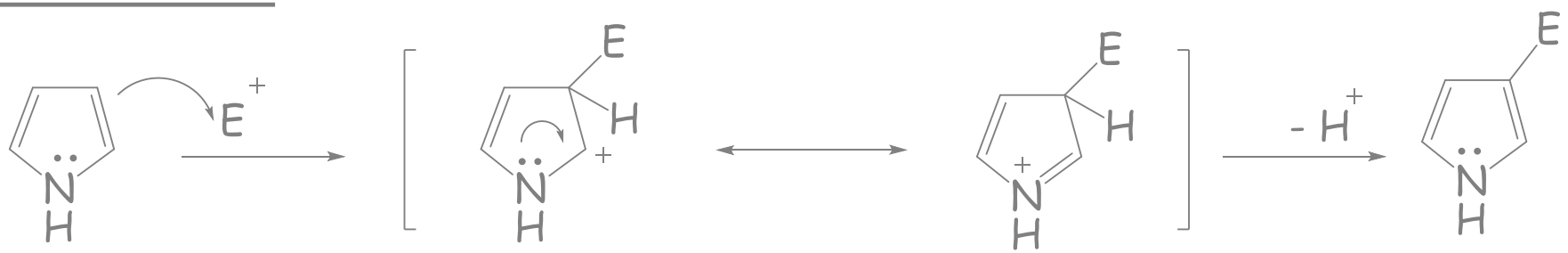
- Orientation of substitution :
  - S_E is more favorable at 2-(α-) position rather than 3-(β-) position due to greater delocalization of the +ve charge in the intermediate σ-complex.

C-2 attack:



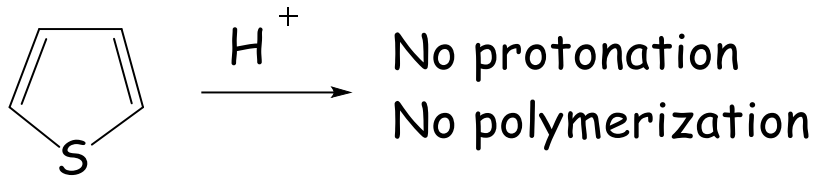
3-Resonance structures

C-3 attack:



Like other aromatic compounds, these five-membered heterocycles undergo nitration, halogenation, sulfonation, and Friedel–Crafts acylation. They are much more reactive than benzene, and resemble the most reactive benzene derivatives (amines and phenols) in undergoing such reactions as the Reimer–Tiemann reaction, nitrosation, and coupling with diazonium salts

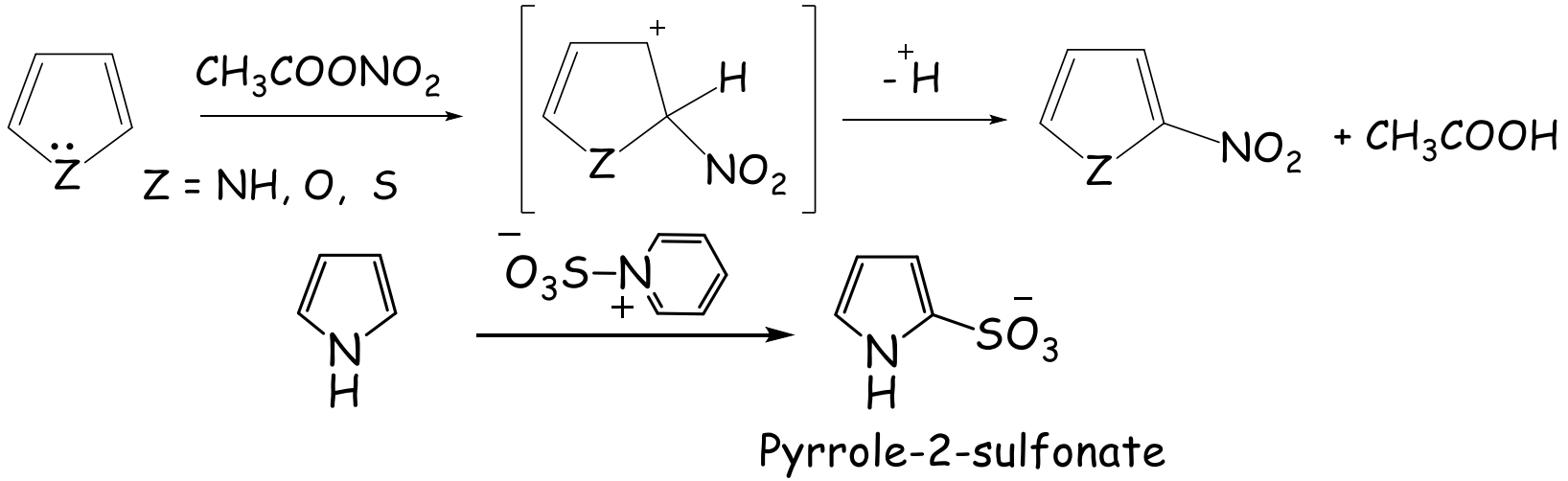
- Furan is unstable to strong acids and the C-protonated cations undergo hydrolytic ring opening.
- Thiophene is stable to mineral acids.



- Therefore, reactions of pyrrole and furan should be carried out in non-acidic solutions to avoid polymerization.
- Thiophene, being non-basic and not polymerized in acid solution, can react in acid solution.

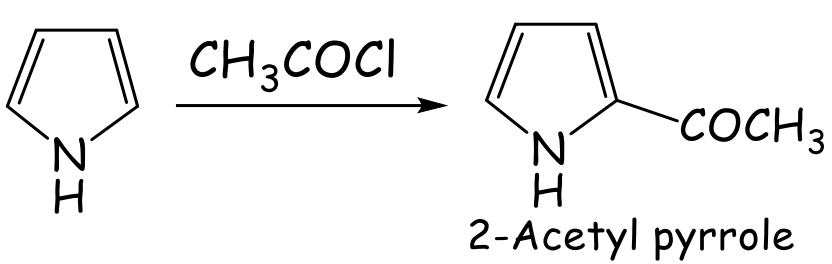
- Recall that strong acidic reagents cause polymerization of pyrrole and furan. Therefore, special reagents like non-acidic nitrating and sulfonating agents should be used, e.g., CH_3COONO_2 (acetyl nitrate) and pyridine-SO_3 complex (SO_3 dissolved in pyridine).

a) Nitration and sulfonation

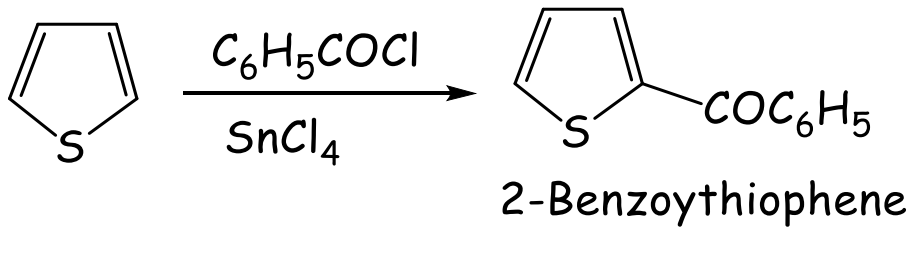


b) Acylation (Friedel-Craft's acylation):

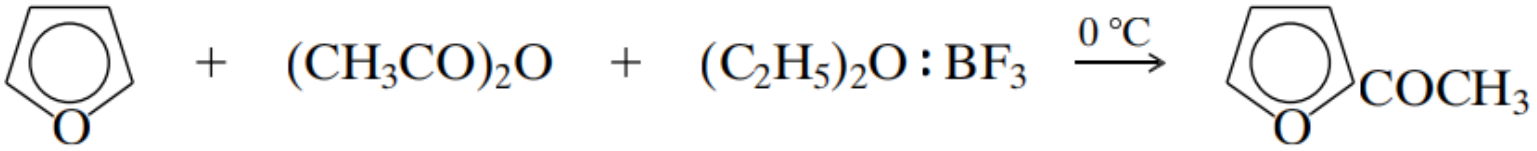
Pyrrole is highly reactive and needs no catalyst; while thiophene need Lewis acids.



2-Acetyl pyrrole



2-Benzoythiophene



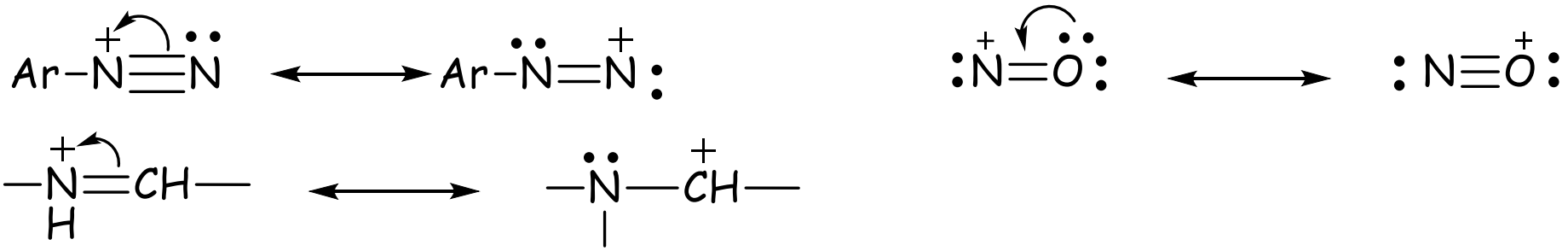
Furan

Boron trifluoride etherate

2-Acetylfuran

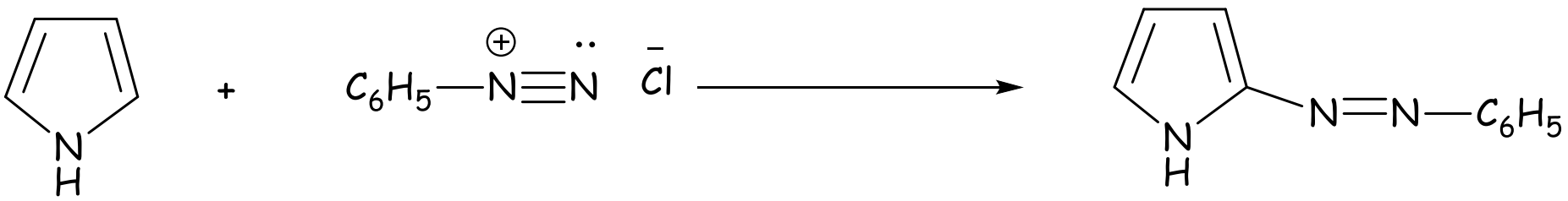
Reactions with weak electrophiles:

- Diazonium, nitrosonium, and iminium cations are weak electrophiles, since their positive charge is distributed over 2 atoms.



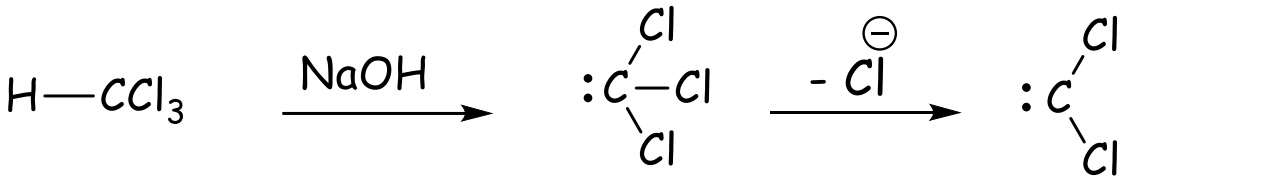
- Pyrrole and furan can react easily with these weak electophiles (benzenes and other deactivated aromatic rings cannot react).

1. Coupling with diazonium salts.

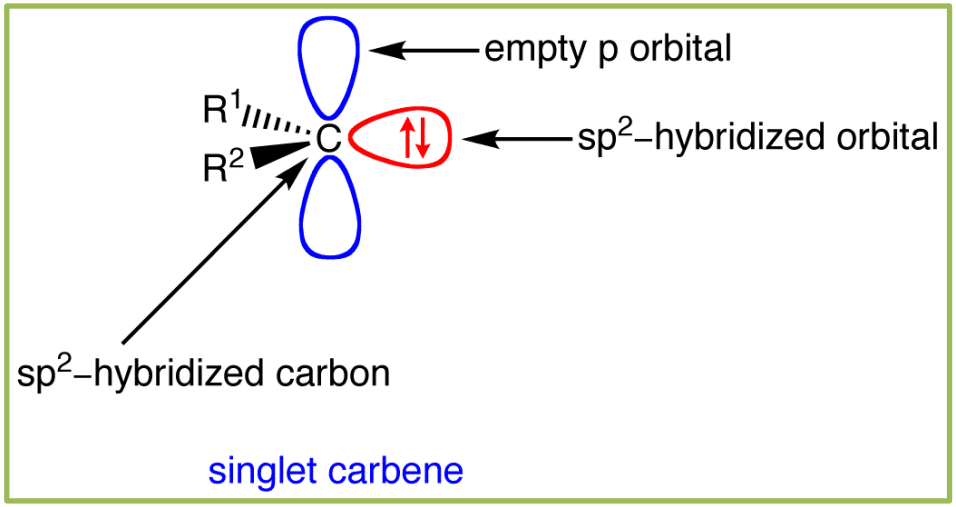


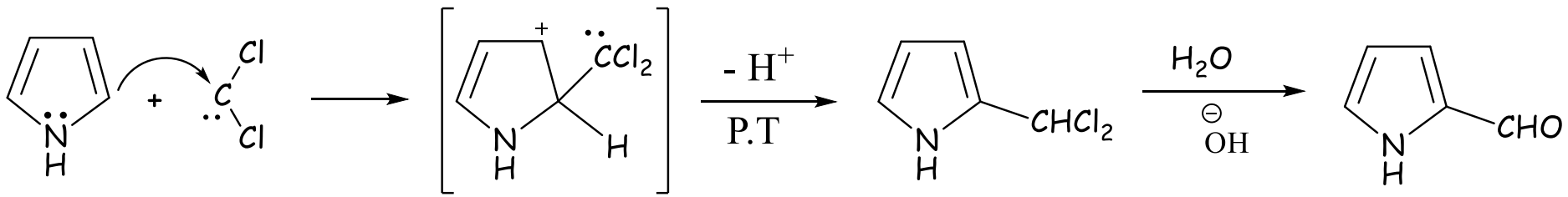
2-(phenylazo)pyrrole

II) Reimer-Tiemann's reaction (reaction with carbenes):



Dichlorocarbene

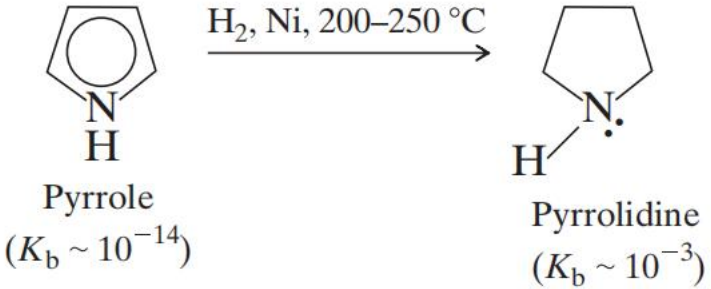


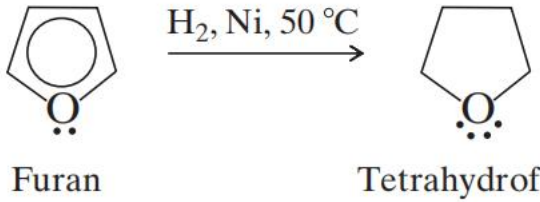


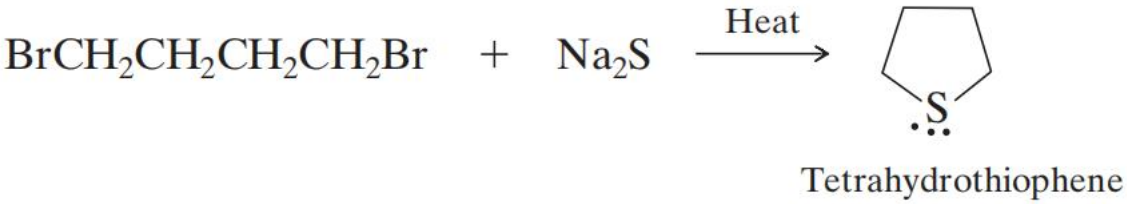
2-Pyrrolecarbacaldehy

Saturated five-membered heterocycles

Catalytic hydrogenation converts pyrrole and furan into the corresponding saturated heterocycles, pyrrolidine and tetrahydrofuran. Since thiophene poisons most catalysts, tetrahydrothiophene is made instead from open-chain compounds.







Saturation of these rings destroys the aromatic structure and, with it, the aromatic properties. Each of the saturated heterocycles has the properties we would expect of it: the properties of a secondary aliphatic amine, an aliphatic ether, or an aliphatic sulfide. With nitrogen's extra pair of electrons now available for sharing with acids, pyrrolidine (K_b' 10^{-3}) has the normal basicity of an aliphatic amine.
Hydrogenation of pyrrole increases the base strength by a factor of 10^{11} (100 billion); clearly a fundamental change in structure has taken place.

pyrrole has the characteristic aromatic shape: flat, like benzene—or, closer yet, like the cyclopentadienyl anion, with which it is isoelectronic. Pyrrolidine, on the other hand, is clearly aliphatic, and closely resembles cyclopentane, with an unshared pair of electrons taking the place of one hydrogen atom.

Predict the products of the treatment of pyrrolidine with:

a) aqueous HCl
(b) aqueous NaOH
(c) methyl iodide
(d) acetic anhydride