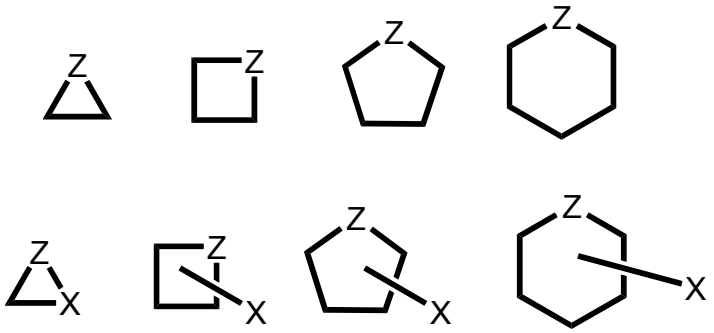
Composti eterociclici



Saturi, insaturi, aromatici , ……

Monocicli, bicicli, ecc…..

Nomenclatura degli eterocicli secondo Hantzsch-Widmann

Eteroatomo	Prefisso	Prefisso in inglese
O	ossa	oxa
S	tia	thia
N	aza	aza
P	fosfa	phospha
Si	sila	sila

Anello	Azotati insaturi	Azotati saturi	non azotati insaturi	non azotati saturi
3	-irina	-iridina	-irene	-irano

azirina

aziridina

ossirene

ossirano

4	-ete	-etidina	-ete	-etano

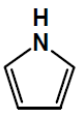
azete

azetidina

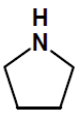
tiete

ossetano

Anello	Azotati insaturi	Azotati saturi	non azotati insaturi	non azotati saturi
5	-olo	-olidina	-olo	-olano



azolo
PIRROLO

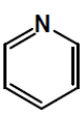


azolidina
PIRROLIDINA

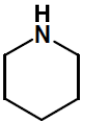
tiolo
TIOFENE

ossolano
TETRAIDROFURANO

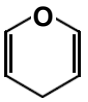
6	-ina (*)	-inano	-ina (*)	-ano



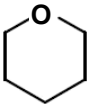
azina
PIRIDINA



azinano
PIPERIDINA

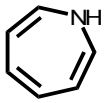


4*H*-ossina
4H-PIRANO

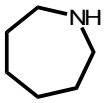


ossano
TETRAIDROPIRANO

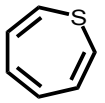
Anello	*Azotati insaturi*	*Azotati saturi*	*non azotati insaturi*	*non azotati saturi*
7	-epina	peridro…-epina	-epina	-epano



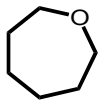
1*H*-azepina



peridroazepina
AZEPANO



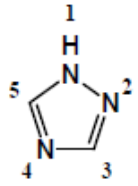
tiepina



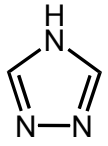
ossepano

Numerazione degli anelli con più eteroatomi

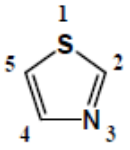
Sequenza di priorità: ***O*** **precede** ***S*** **precede** ***N***



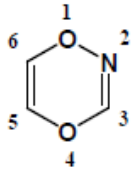
1*H*-1,2,4-triazolo
(*non* 1,3,5-triazolo)



4*H*-1,2,4-triazolo



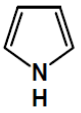
1,3-tiazolo
(*non* 1,3-azatiolo)



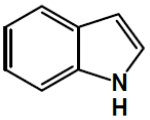
1,4,2-diossazina

furano

tiofene

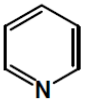


pirrolo

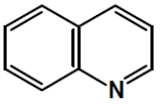


indolo

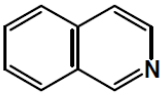
Tetraidrofurano
THF



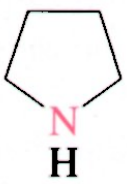
piridina



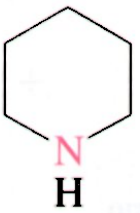
chinolina



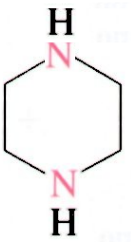
isochinolina



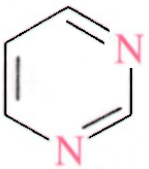
Pirrolidina



Piperidina



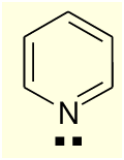
Piperazina

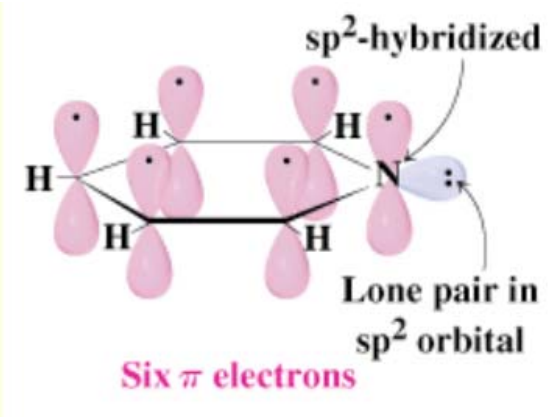


Pirimidina

Pyridine

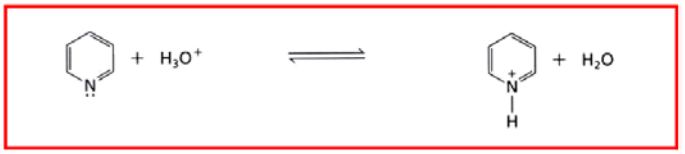
- The nitrogen lone pair electrons are <u>not part of the aromatic system</u> (perpendicular orbital)

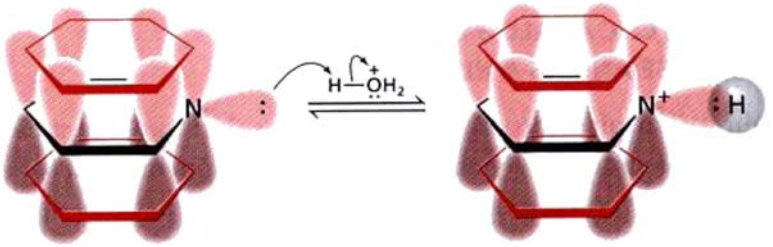




Pyridine

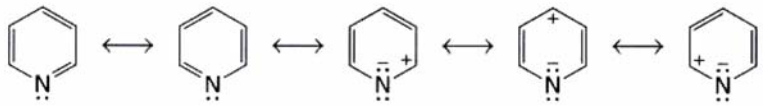
- Pyridine is a relatively weak base compared to normal amines but protonation does not affect aromaticity.





La reattività della piridina è diversa rispetto al benzene.

Infatti la piridina non subisce sostituzione aromatica elettrofila facilmente, ma solo in condizioni drastiche perché



1. L'anello è elettron deficiente a causa dell'effetto elettron attrattore dell'azoto (–I)

2. Il centro più nucleofilo della piridina, ovvero l'atomo di azoto, non reagisce facilmente per non rendere ancora più elettron-povero, e quindi ancor meno reattivo l'anello.

Dunque,

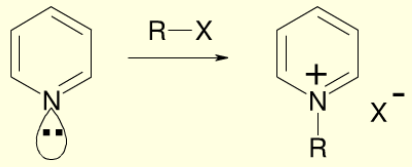
la piridina è un eterociclo elettron-povero

Pyridine

- Bond formation with electrophiles is easy.

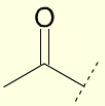
Eg Pyridine + acid → pyridinium salt

pKa 5.25

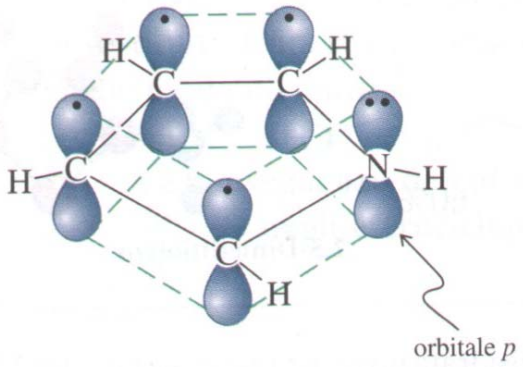


R = H
CH_3
NO_2
Br
OH

Alkylation / quaternisation

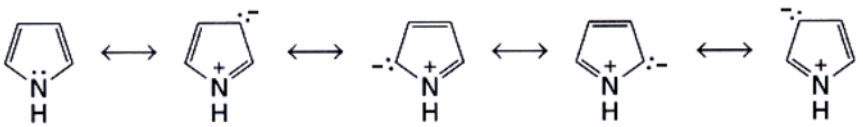


Pirrolo

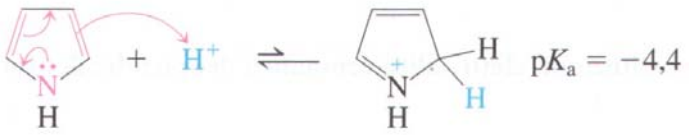


Pirrolo

Pirrolo: un eterociclo elettron-ricco

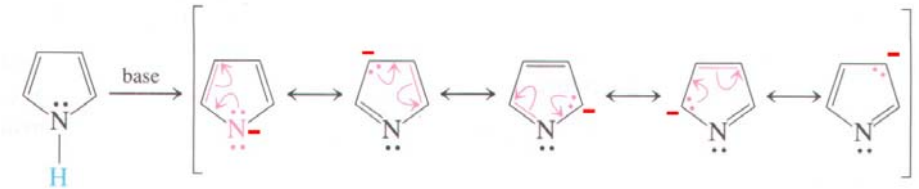


La protonazione del pirrolo

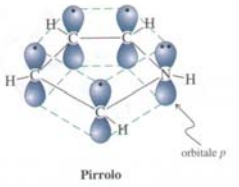


pK_b = 18.4

Il pirrolo è relativamente acido

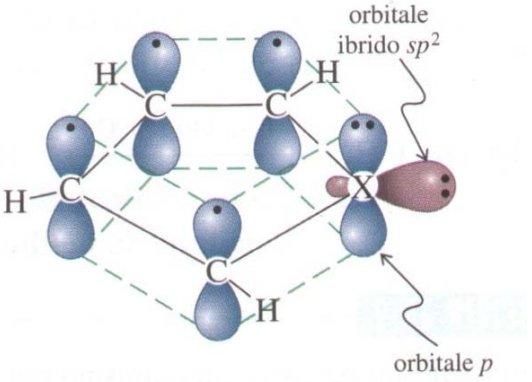


$pK_a = 16,5$



Pirrolo

N	O	
3.04	3.44	
	S	
	2.58	



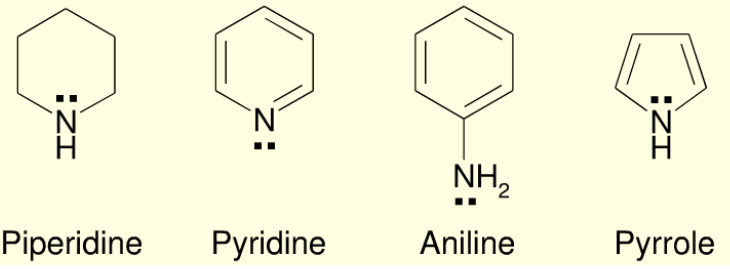
Furano (X = O)
Tiofene (X = S)

Confronti di aromaticità tra Furano, Tiofene, Pirrolo

	Furano	Tiofene	Pirrolo	Benzene
Energia di risonanza (Kcal/mole)	16	34	25	36

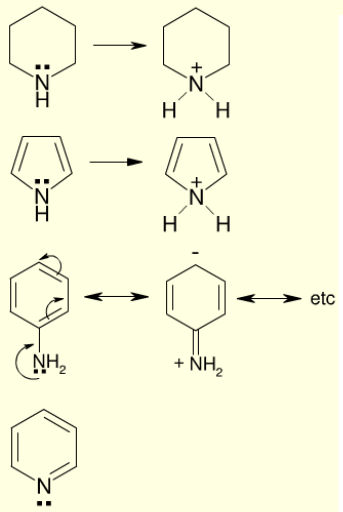
Tiofene > Pirrolo > Furano

Basicity: Relative Order of Basicity



Basicity

Decreasing basicity



Lone pair fixed at N.

Inductive stabilisation of cation.

Lone pair is part of aromatic system.

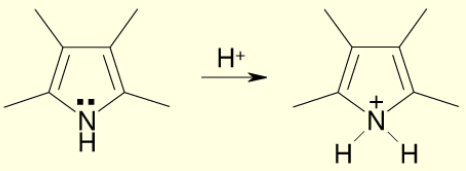
Protonation at N requires disruption of aromatic system ⇒ destabilisation

Lone pair on N contributes to the canonical forms representing the aromatic ring.

N is Sp^2 hybridised.

The lone pair is more tightly held than in Sp^3.

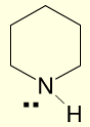
Basicity: Inductive Stabilisation of Cations by Alkyl Substituents



Electron donation from the methyl groups increases the basicity of 2,3,4,5-tetramethylpyrrole relative to pyrrole.

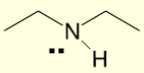
Basicity: Steric Hindrance

Piperidine is more basic than diethylamine.



pKa 11.29

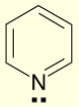
- No free rotation
- Lone pair not obscured



pKa 10.98

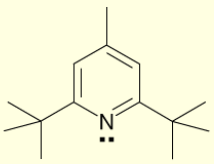
- Free rotation around N-C bond
- CH_3 groups can obscure the lone pair

Basicity: Steric Hindrance



Pyridine can act as a

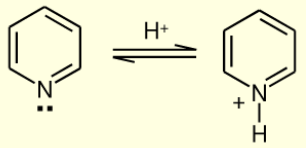
- nucleophile
- Base



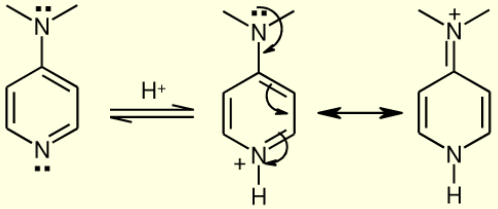
2,6-Di-tert-butyl-4-methylpyridine is

- basic
- but NOT nucleophilic.

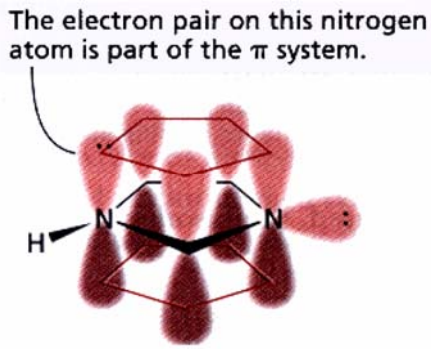
Basicity: Resonance Stabilisation



4-N,N-Dimethylaminopyridine (DMAP) is more basic than pyridine because the positive charge is stabilised by resonance.

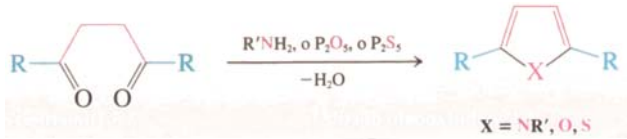


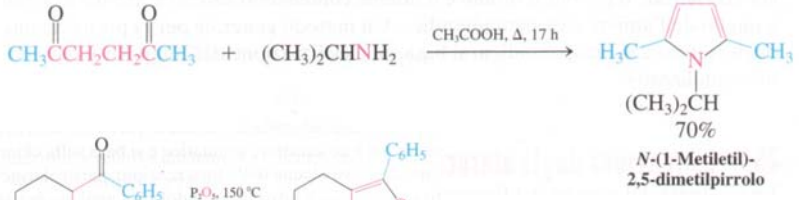
Imidazolo

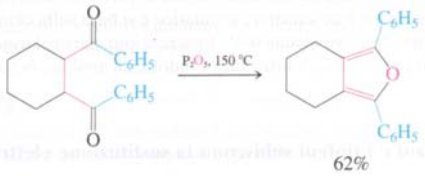


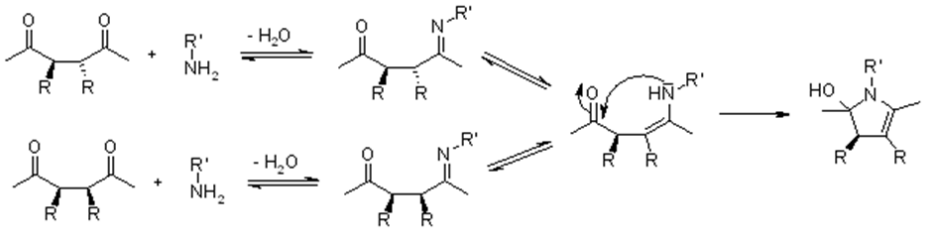
Preparazioni

sintesi di Paal-Knorr





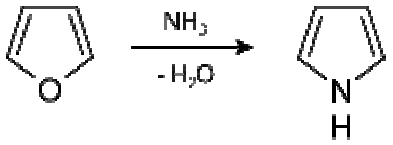


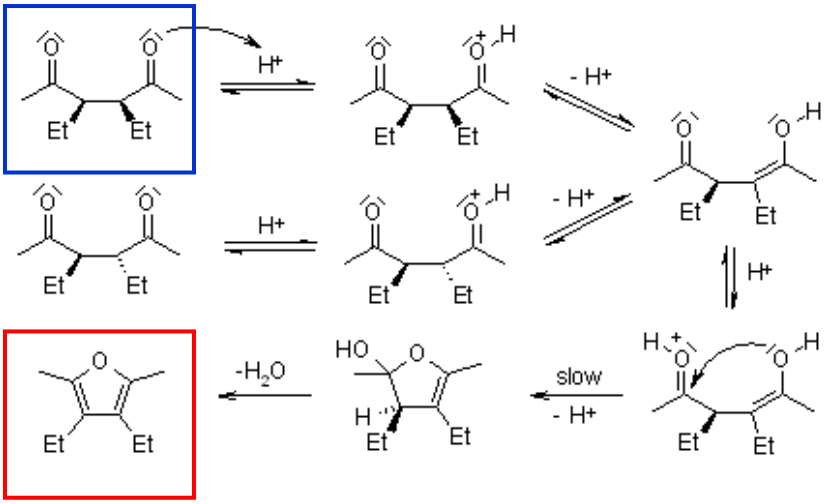


the stereochemical configuration of the unchanged dione is preserved during the reaction

J. Org. Chem., **1991**, *56*, 6924

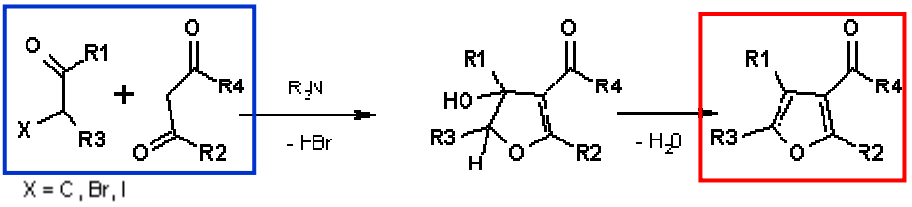
Preparazione industriale del pirrolo





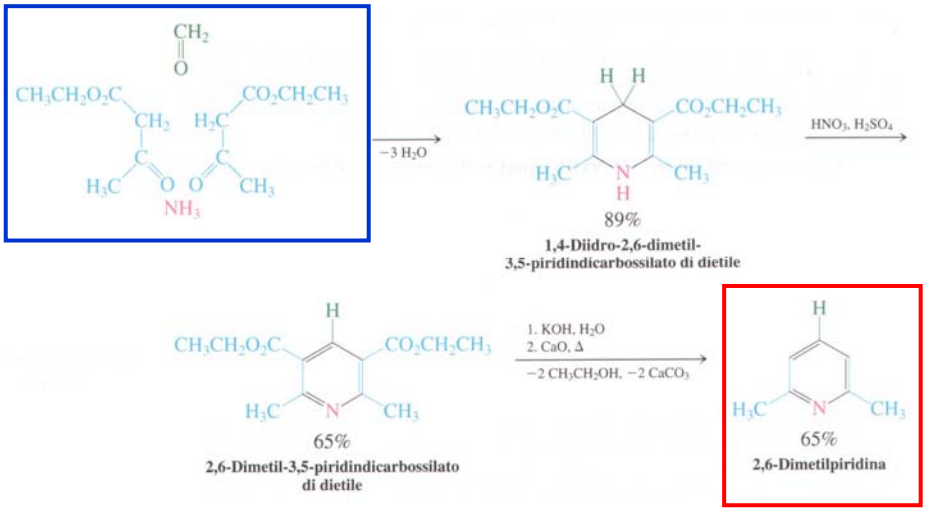
J. Org. Chem., **1995**, *60*, 301

Sintesi di Feist-Benary



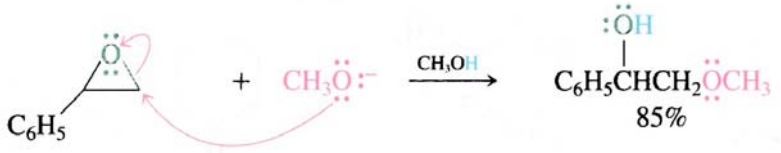
X = C , Br , I

sintesi della piridina di Hantzsch

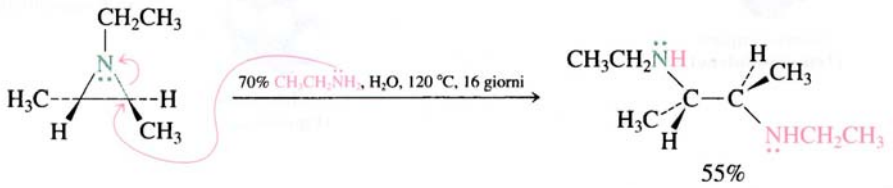


Reazioni

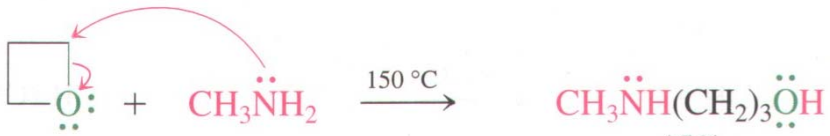
La tensione d'anello rende reattivi gli eterociclopropani e gli eterociclobutani



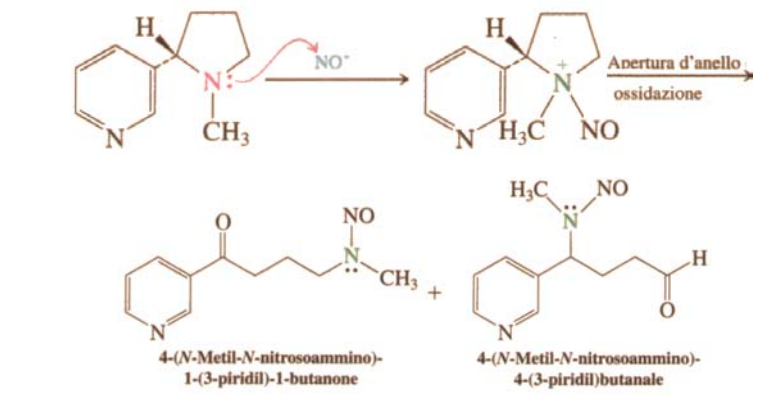
2-Fenilossaciclopropano — **2-Metossi-1-feniletanolo**

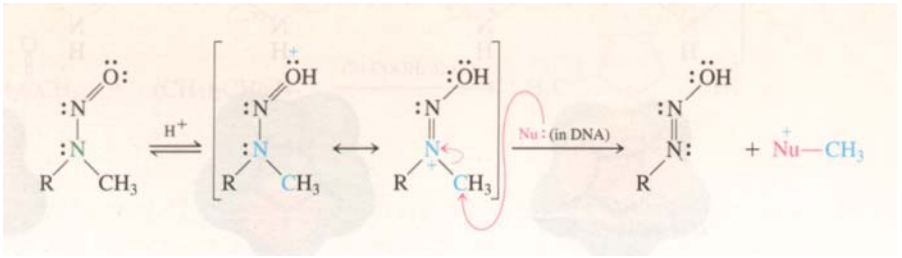


***N*-Etil-(2*S*,3*S*)-*trans*-2,3-dimetilazaciclopropano** — ***meso*-*N*,*N*′-Dietil-2,3-butandiammina**



***N*-Metil-3-ammino-1-propanolo**





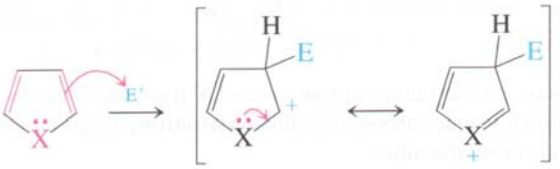
Eterocicli aromatici

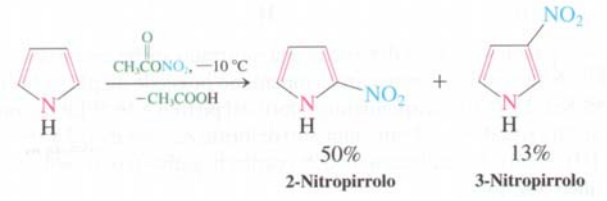
Reazioni

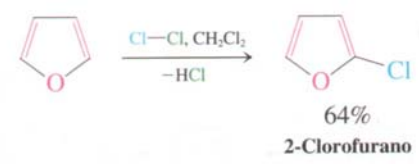
Sostituzione elettrofila aromatica

Attacco in C2

Attacco in C3

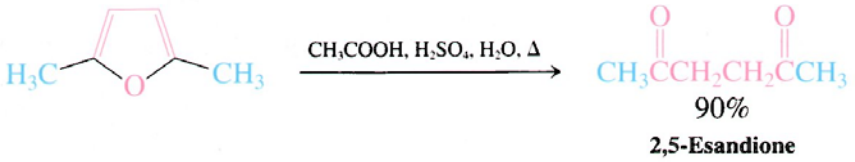






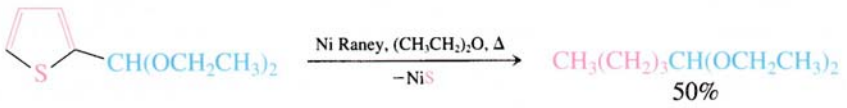
La reattività nucleofilica relativa del benzene e dei tre eterocicli aumenta nell'ordine benzene ≪ tiofene < furano < pirrolo.

L'idrolisi di un furano in un composto γ-dicarbonilico

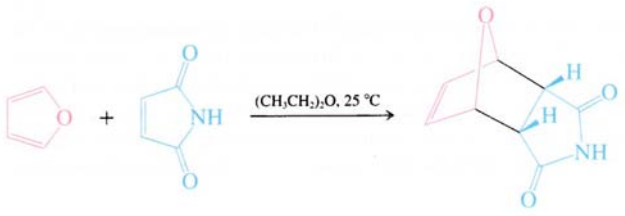


90%

2,5-Esandione

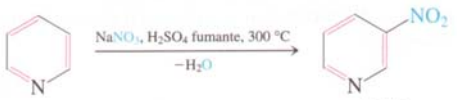


50%



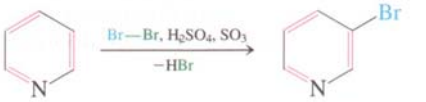
95%

La piridina subisce la sostituzione elettrofilica aromatica solo in condizioni estreme



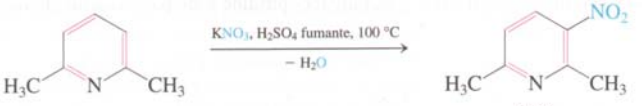
4,5%

3-Nitropiridina



86%

3-Bromopiridina



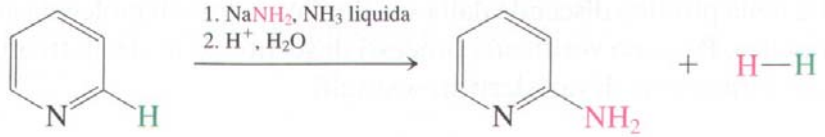
2,6-Dimetilpiridina

81%

2,6-Dimetil-3-nitropiridina

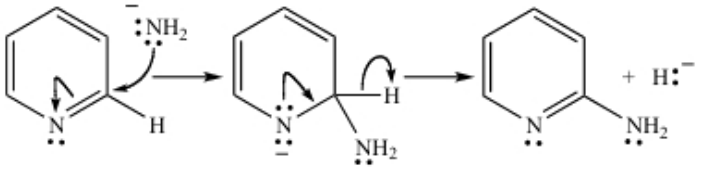
La piridina subisce la sostituzione nucleofilica con relativa facilità

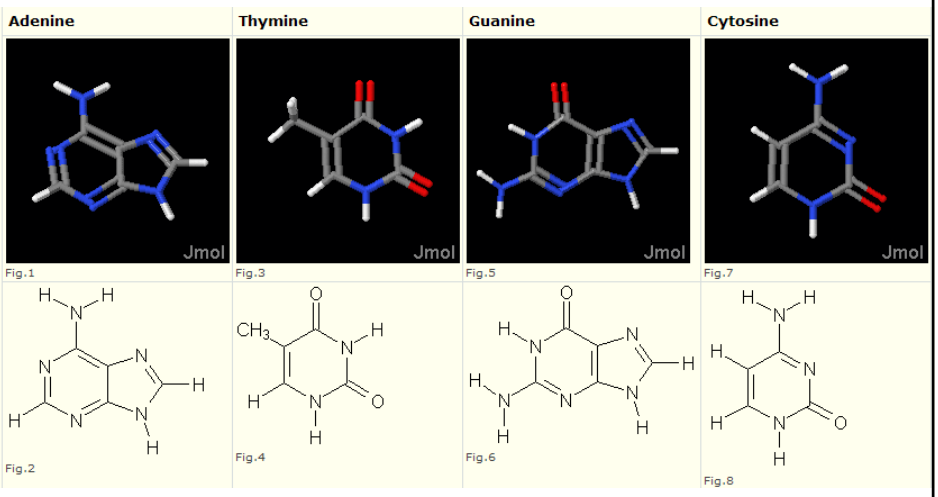
reazione di Chichibabin



70%

2-Amminopiridina





Hydrogen bridge bonds in the AT base pair

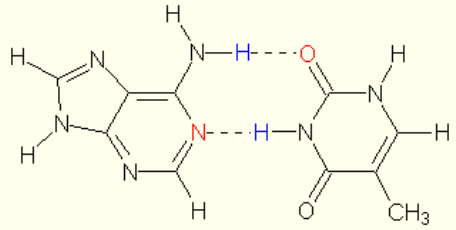


Fig.9

Hydrogen bridge bonds in the GC base pair

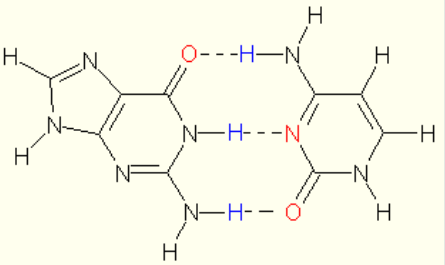


Fig.10