

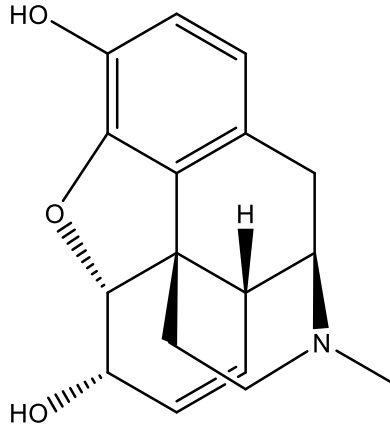
**ORGÁNICA III (QM2423)**

# **Compuestos Heterocíclicos**

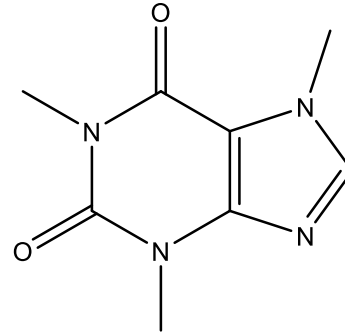


**UNIVERSIDAD SIMÓN BOLÍVAR  
DEPARTAMENTO DE QUÍMICA.**

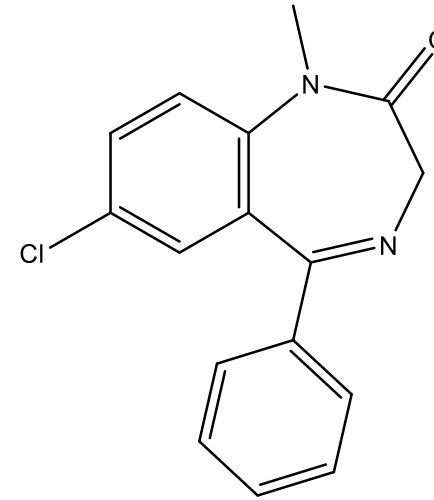
**Heterocíclicos:** Compuestos cíclicos en los que además de carbono, hay al menos un heteroátomo formando parte del anillo.



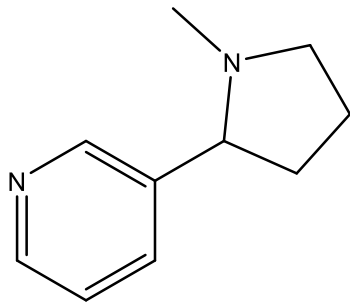
Morfina



Cafeína



Valium



Nicotina

Forman parte de los ácidos nucleicos, multitud de fármacos y de sustancias de interés biológico.

# Nomenclatura de Compuestos Heterocíclicos Saturados

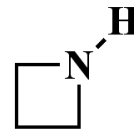
No contienen dobles enlaces.

Se nombran como un cicloalcano, añadiendo el prefijo para referirse al heteroátomo o utilizar el nombre genérico.

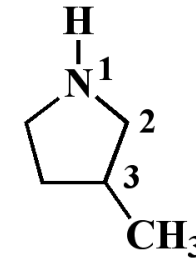
Aminas Cíclicas:



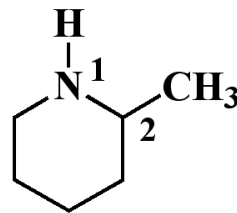
Azacyclopropane  
"aziridine"



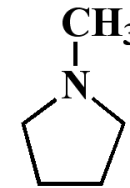
Azacyclobutane  
"azetidine"



3-Methylazacyclopentane  
"3-methylpyrrolidine"



2-Methylazacyclohexane  
"2-methylpiperidine"



N-ethylazacyclopentane  
"N-ethylpyrrolidine"

Nitrogeno es #1 cuando forma parte del anillo

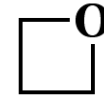
# Compuestos heterocíclicos con heteroátomos oxígeno y azufre



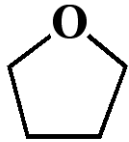
**Oxacyclopropane**  
"oxirane or ethylene oxide"



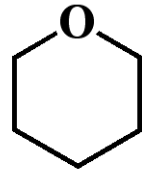
**Thiacyclopropane**  
"thiirane"



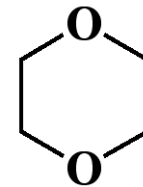
**Oxacyclobutane**  
"oxetane"



**Oxacyclopentane**  
"tetrahydrofuran"

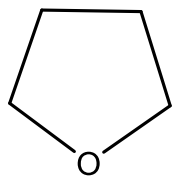


**Oxacyclohexane**  
"tetrahydropyran"

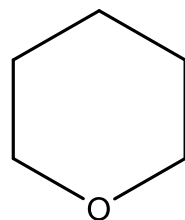


**1,4-Dioxacyclohexane**  
"1,4-dioxane"

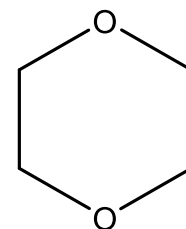
Los heterociclicos saturados que contienen cinco o más átomos tienen propiedades físicas y químicas típicas de los compuestos acíclicos con el mismo heteroátomo:



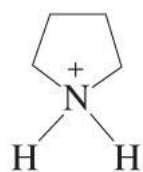
THF



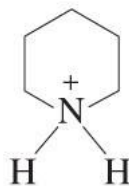
Tetrahidropirano



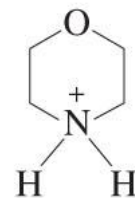
Dioxano



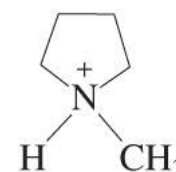
pyrrolidinium  
 $pK_a = 11.27$



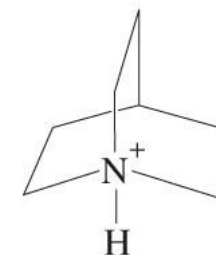
piperidinium  
 $pK_a = 11.12$



morpholinium  
 $pK_a = 9.28$



*N*-methylpyrrolidinium  
 $pK_a = 10.32$



quinuclidinium  
 $pK_a = 11.38$

the ammonium ions of:

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# Propiedades Ácido–Base de las Aminas

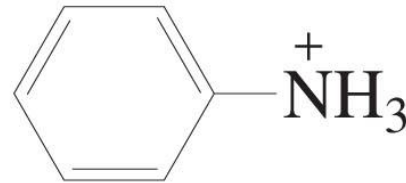
Las aminas son las bases orgánicas más comunes:



an ammonium ion

$$pK_a = 10.8$$

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an anilinium ion

$$pK_a = 4.58$$



an amine

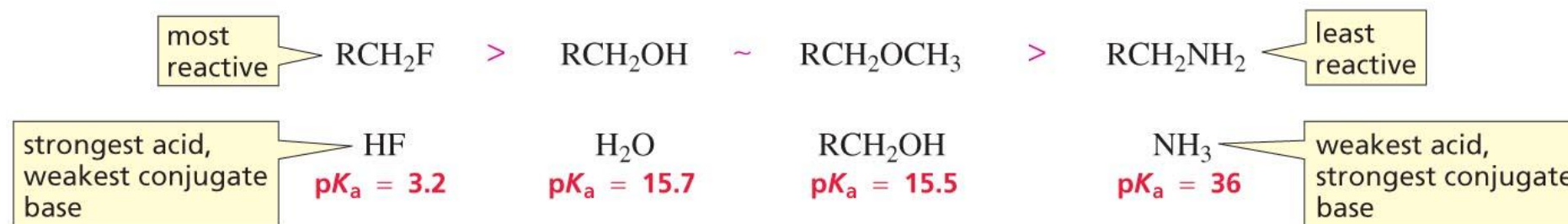
$$pK_a = 40$$

Los heterociclos saturados de cinco y seis miembros experimentan las mismas reacciones que sus análogos de cadena abierta.

Las aminas reaccionan como base y como nucleófilo

El par de electrones libres sobre el nitrógeno de la amina le da un carácter nucleofílico y de base:

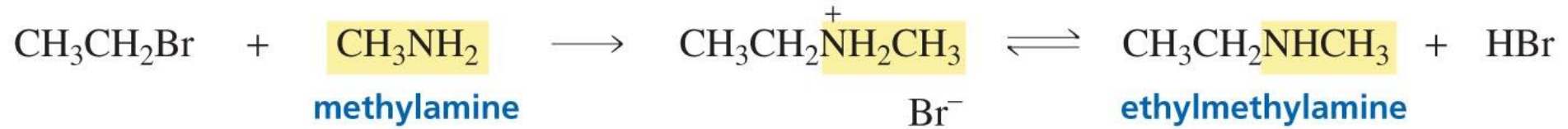
relative reactivities



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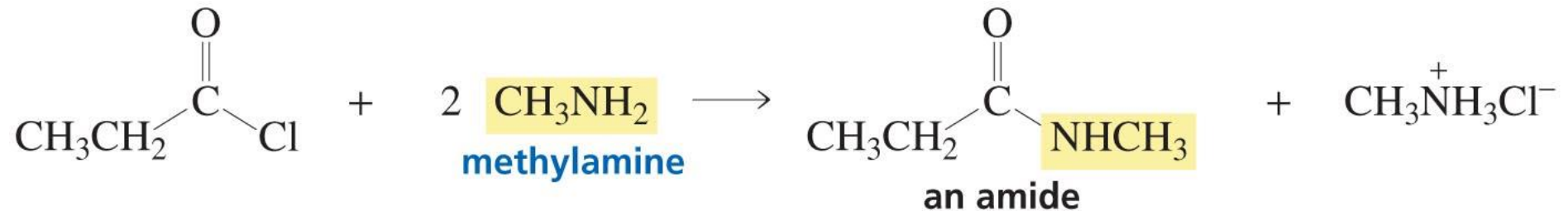
# Reacción de las Aminas

## Reacciones de sustitución nucleofílica:



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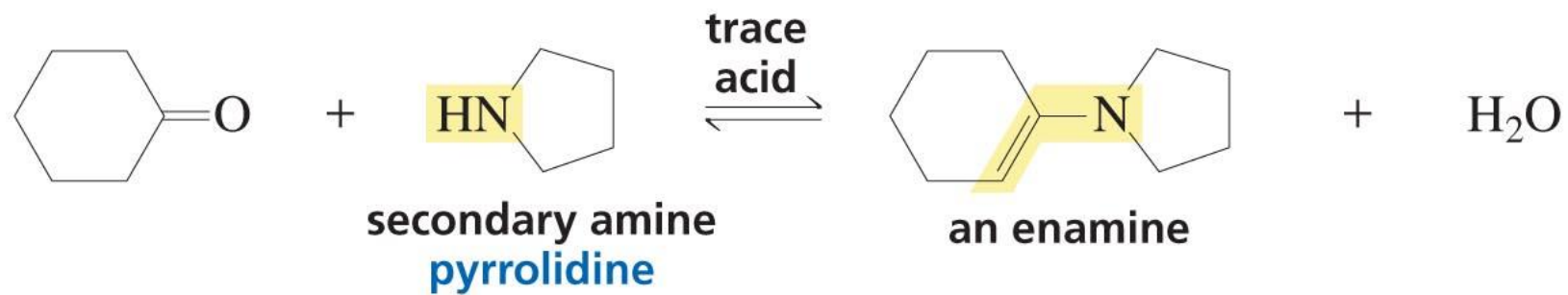
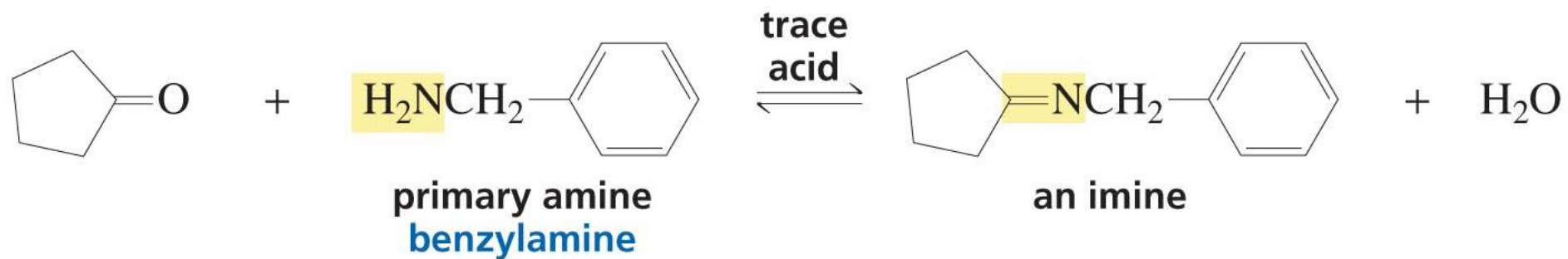
## Reacción de sustitución nucleofílica sobre un acilo:



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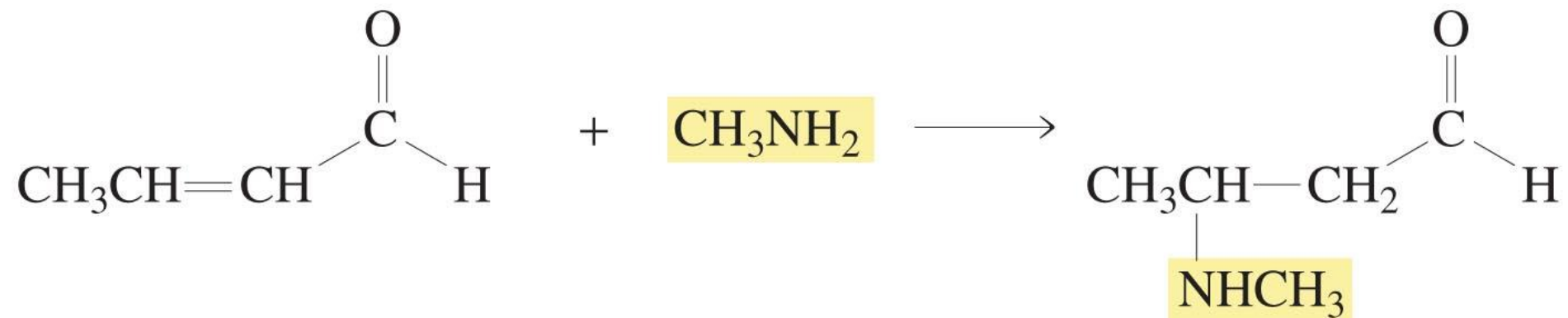


## Reacciones nucleofílicas de adición-eliminación:



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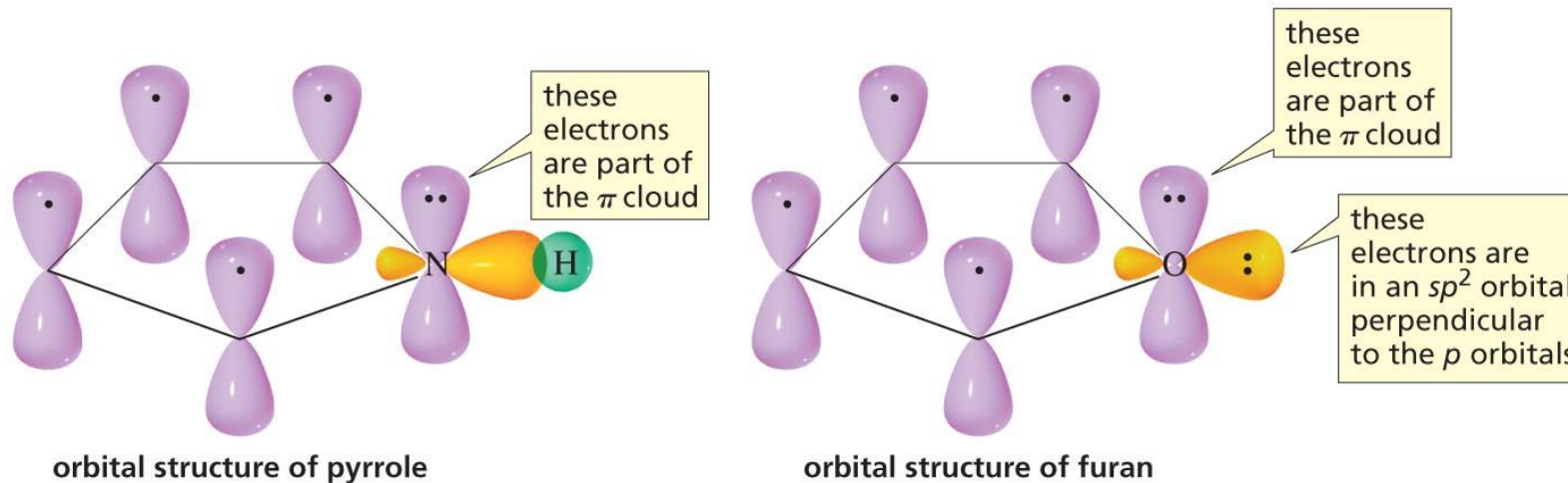
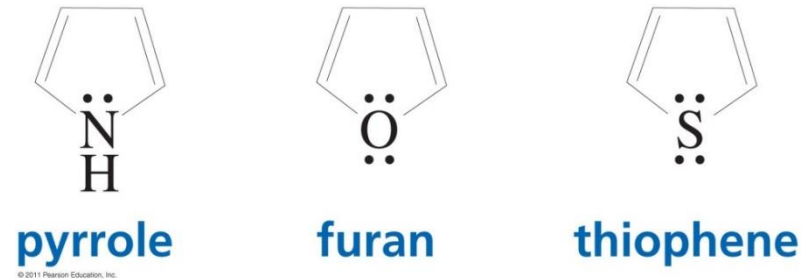
## Reacciones de adición conjugada:



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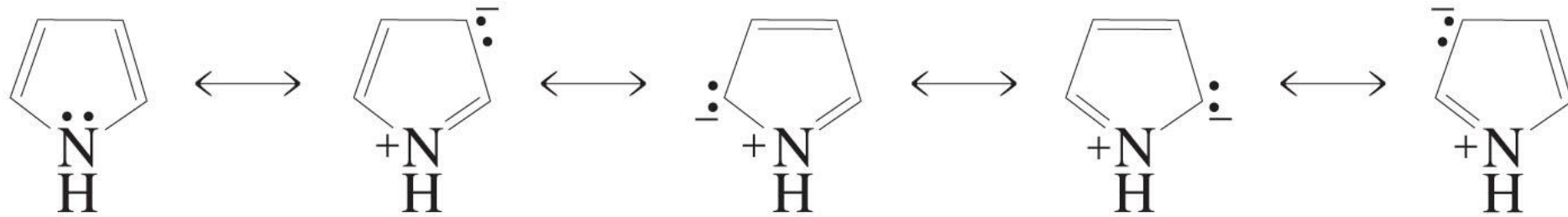
# Heterocíclicos Aromáticos de cinco miembros

Tienen tres pares de electrones  $\pi$  deslocalizados:  
Dos pares doble enlace y un par electrones libres

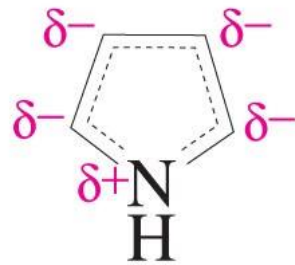


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# El pirrol es una base débil:

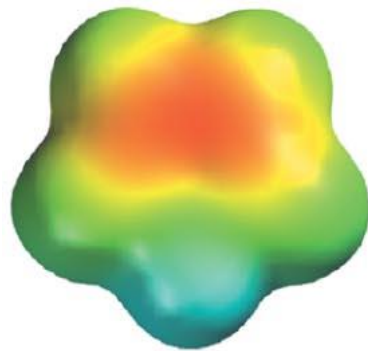


resonance contributors of pyrrole



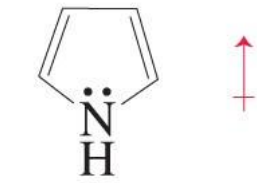
resonance hybrid

El momento dipolar en pirrolidina (derecha) se atribuye a la propiedad atractora de electrones del átomo de nitrógeno:

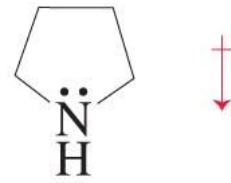


pyrrole

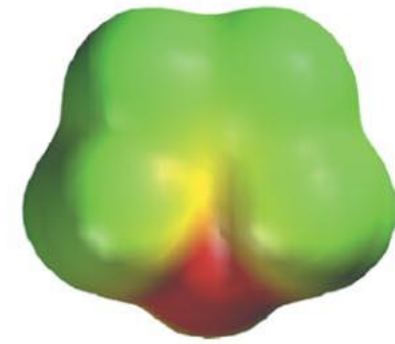
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$$\mu = 1.80 \text{ D}$$

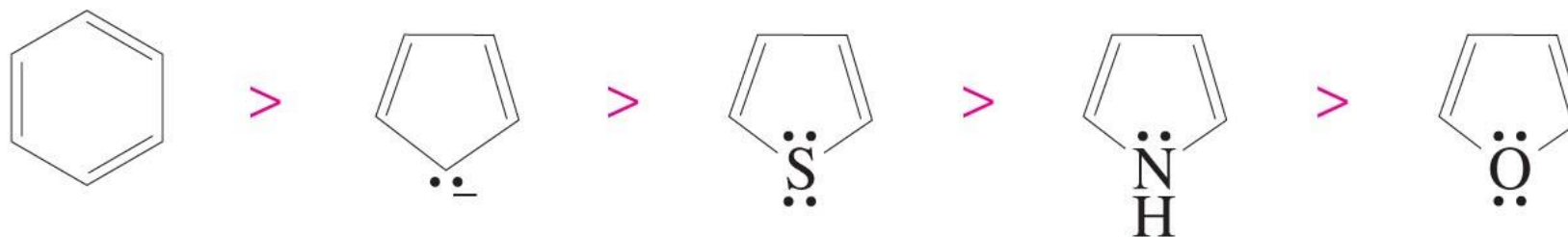


$$\mu = 1.57 \text{ D}$$



pyrrolidine

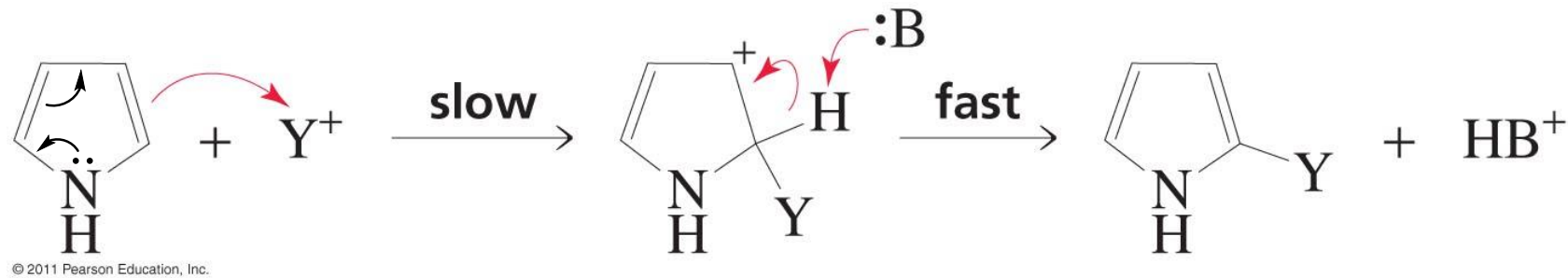
## relative delocalization energies of some aromatic compounds



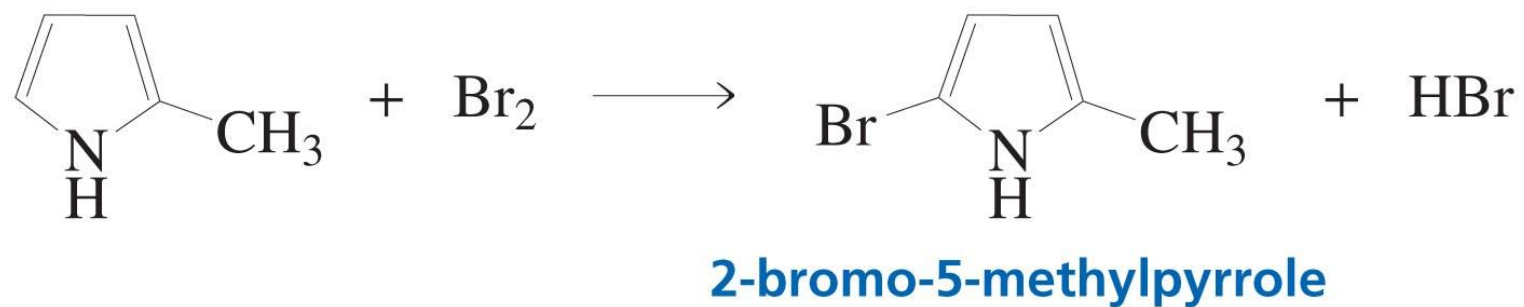
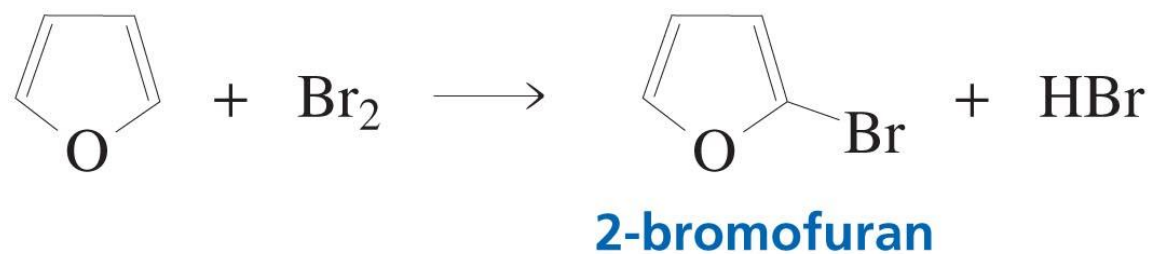
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# Reacciones

Pirrol, furano, y tiofeno experimentan sustitución electrofílica, preferiblemente sobre C-2:



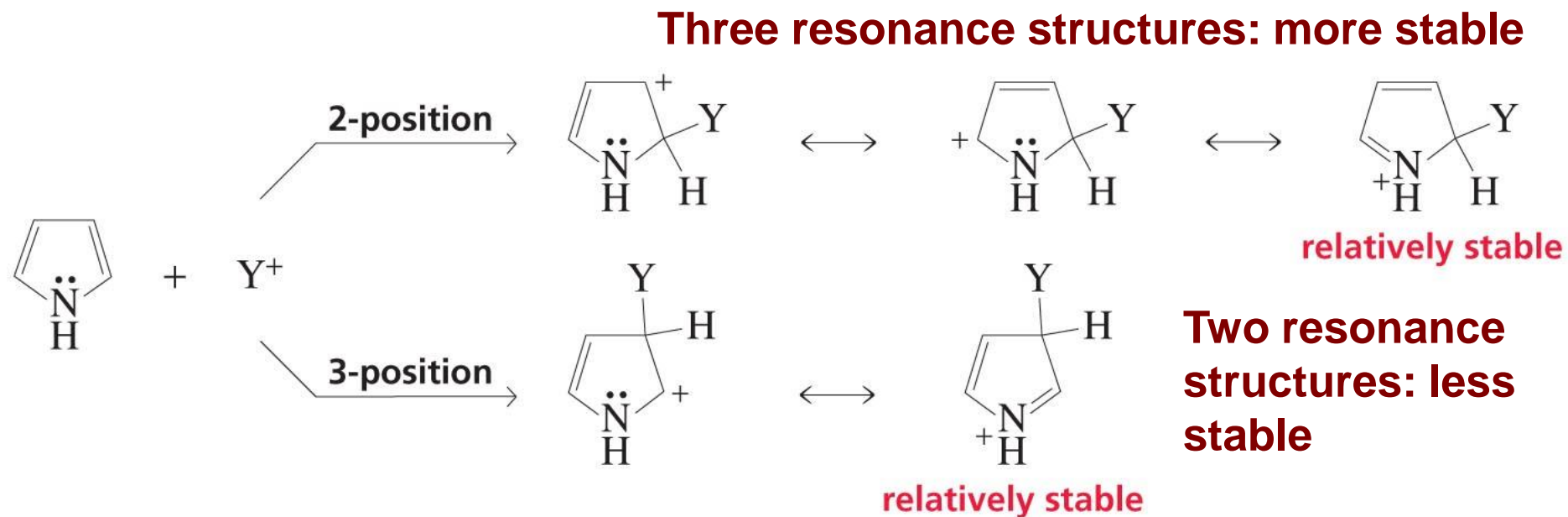
## Reacciones de sustitución electrofílica aromática:



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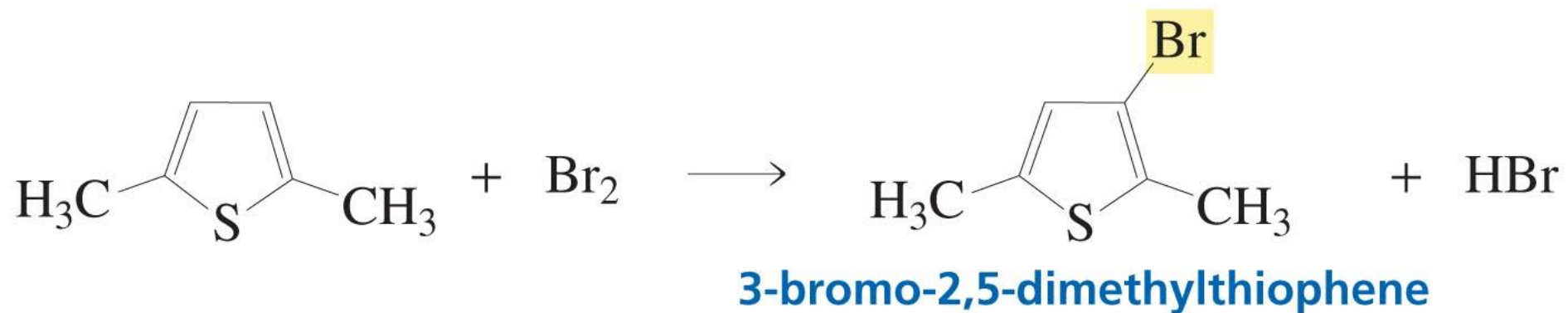


# Estructuras de los intermedios que pueden ser formados a partir de la reacción de un electrófilo sobre el C-2 y C-3 del pirrol



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Si ambas posiciones adyacentes al heteroátomo están ocupadas, la sustitución electrófilica ocurre sobre el C-3:



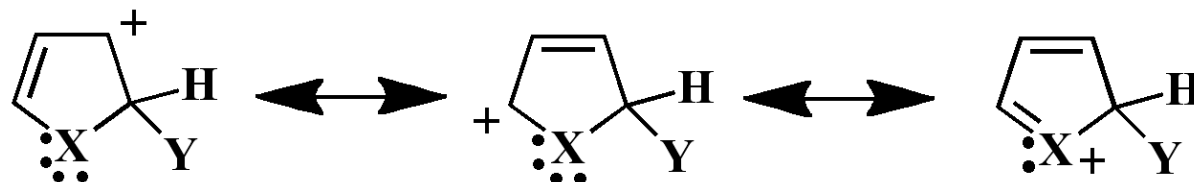
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## relative reactivity toward electrophilic aromatic substitution

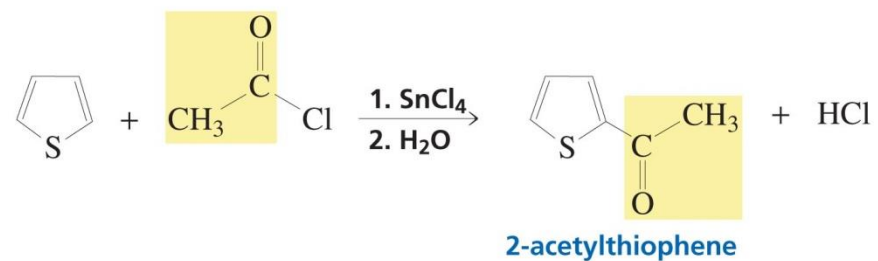


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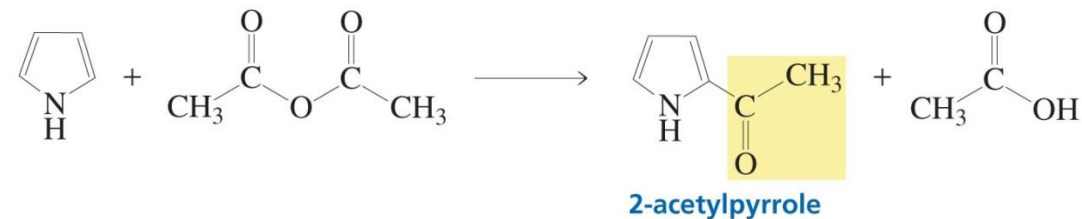
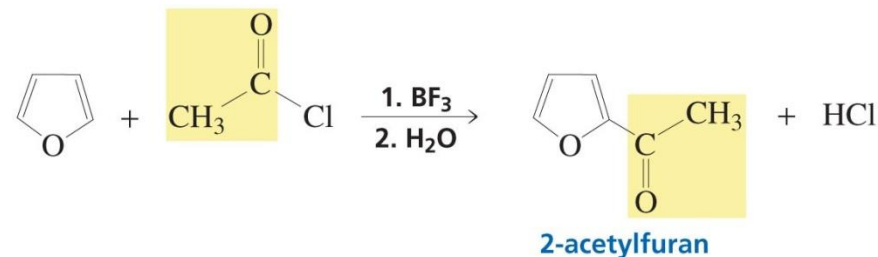
Estabilización del catión por el par de electrones libres:



# La reactividad de los heterocíclicos de cinco miembros en la reacción de Friedel–Crafts:

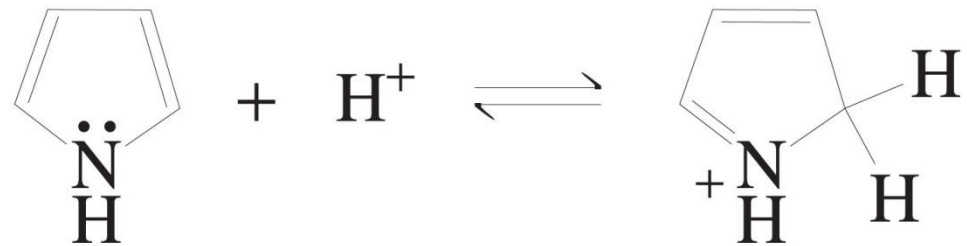


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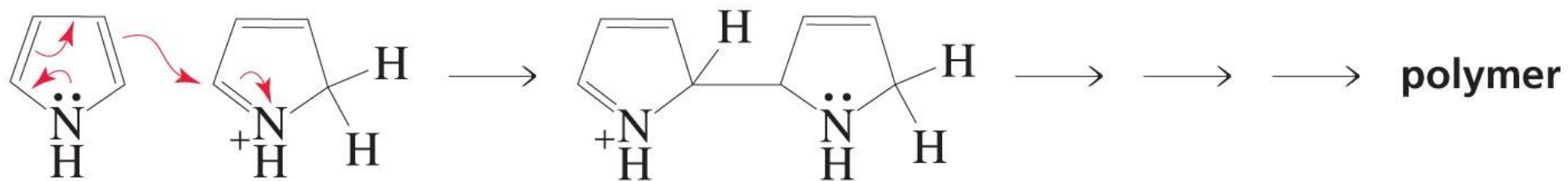
El híbrido de resonancia de pirrol indica que hay una carga positiva parcial sobre el nitrógeno:



**pK<sub>a</sub> = -3.8**

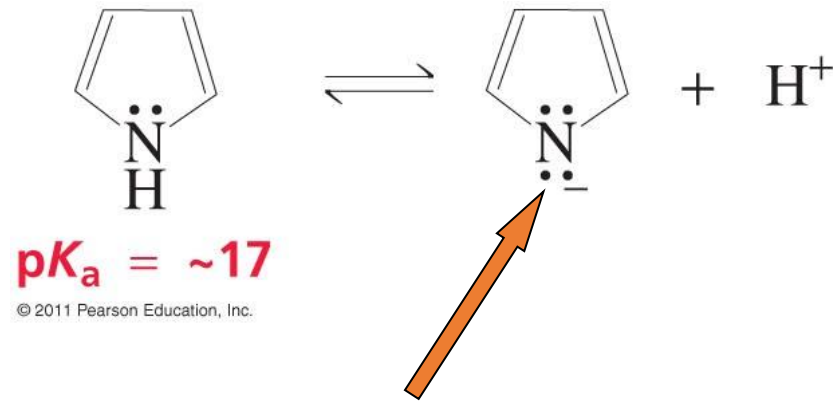
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El pirrol es inestable en una solución de ácido fuerte, ya que polimeriza

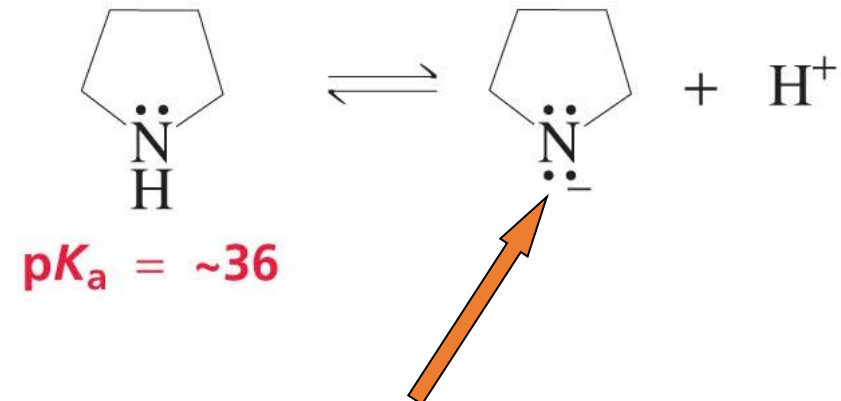


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El pirrol es más ácido que la pirrolidina debido a la estabilización de su base conjugada por resonancia

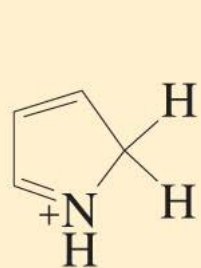


**Five resonance structures for the anion**

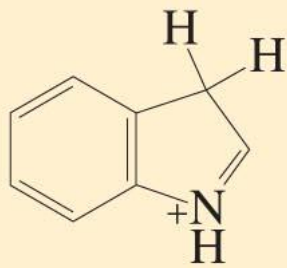


**Localized anion**

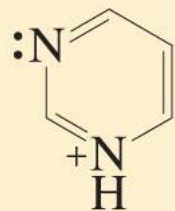
**Table 21.1 The  $pK_a$  Values of Several Nitrogen Heterocycles**



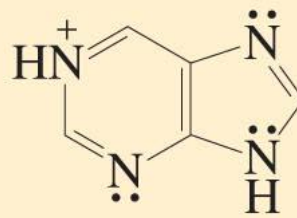
$pK_a = -3.8$



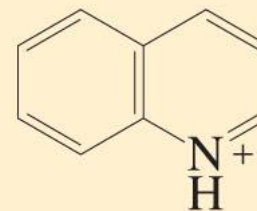
$pK_a = -2.4$



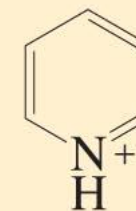
$pK_a = 1.0$



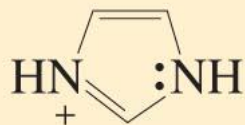
$pK_a = 2.5$



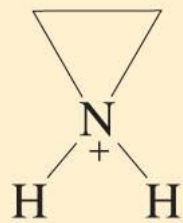
$pK_a = 4.85$



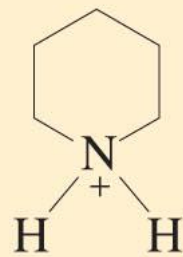
$pK_a = 5.16$



$pK_a = 6.8$



$pK_a = 8.0$



$pK_a = 11.1$



$pK_a = 14.4$

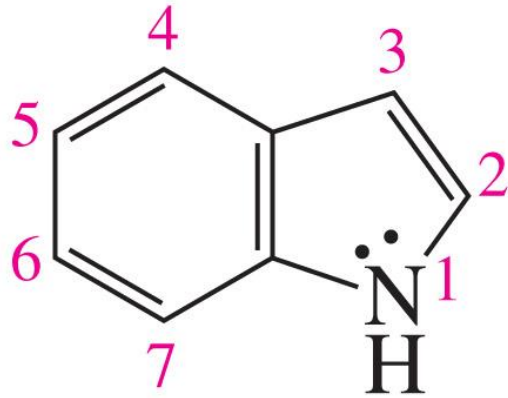


$pK_a = \sim 17$

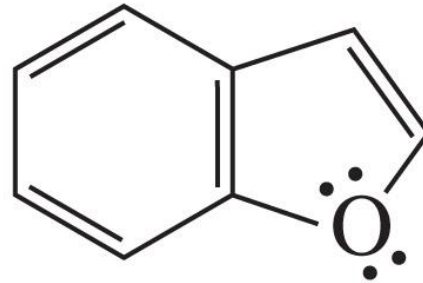


$pK_a = \sim 36$

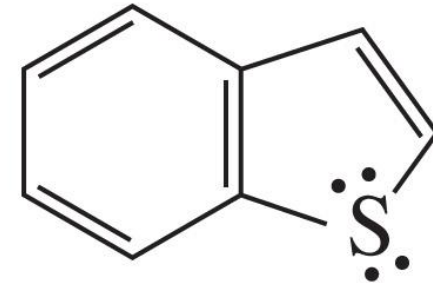
El Indol, benzofurano y benzotiofeno contienen todos un anillo aromático de cinco miembros fusionado a un anillo de benceno:



**indole**



**benzofuran**



**benzothiophene**