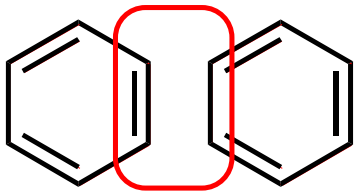
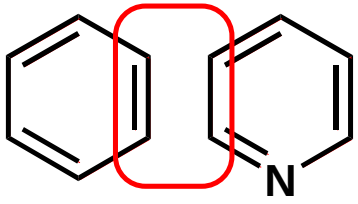
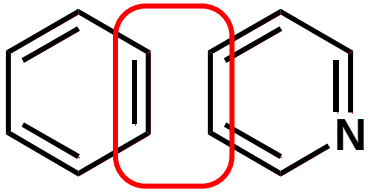
Características generales



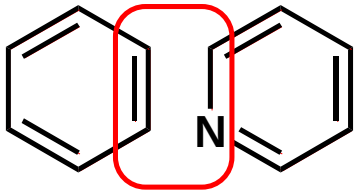
NAFTALENO



QUINOLINA

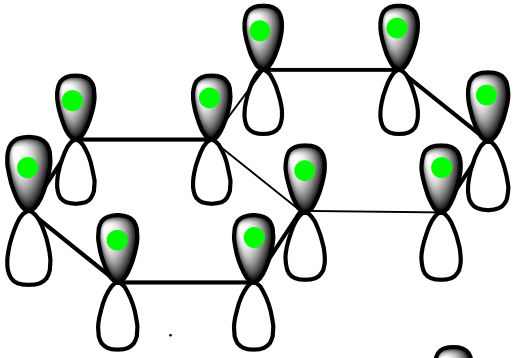


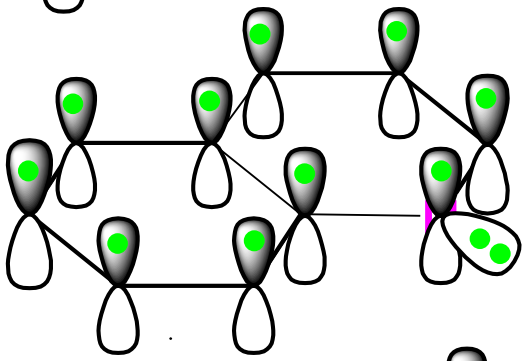
ISOQINOLINA

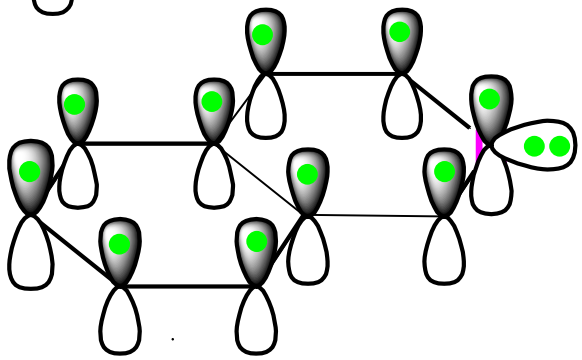


QUINOLIZINIO

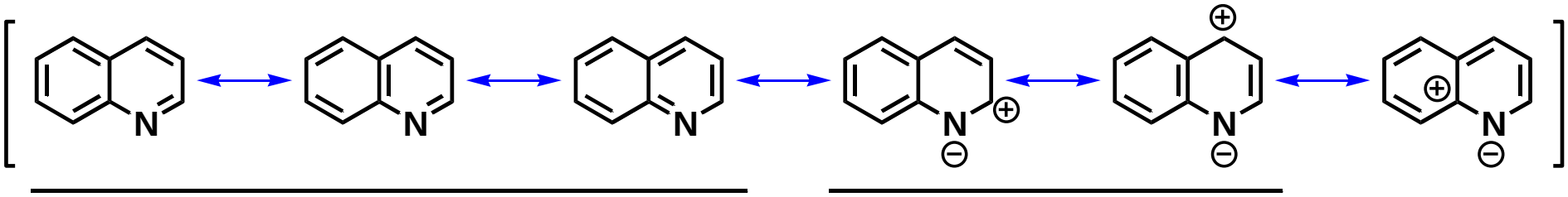
Estructura aromática con un sistema de 4n+2 electrones "pi"

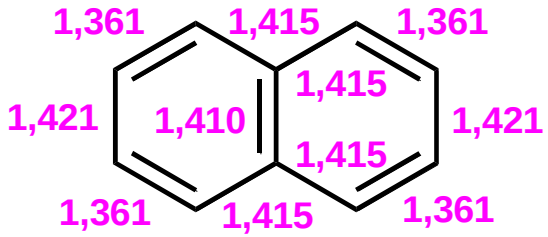


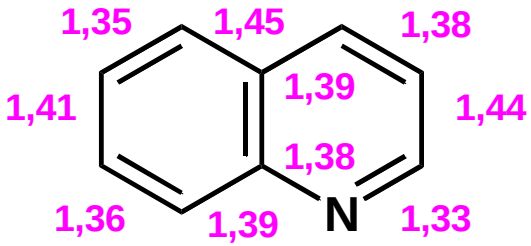


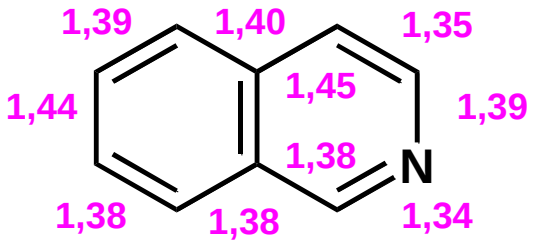


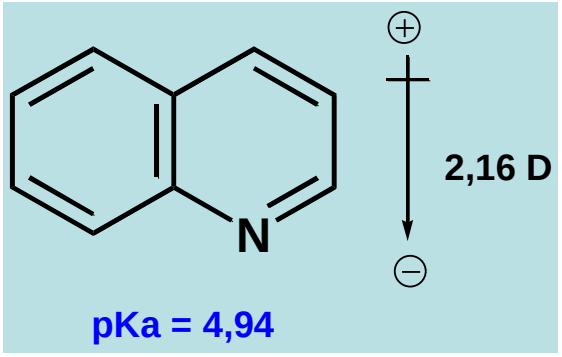
Características generales.

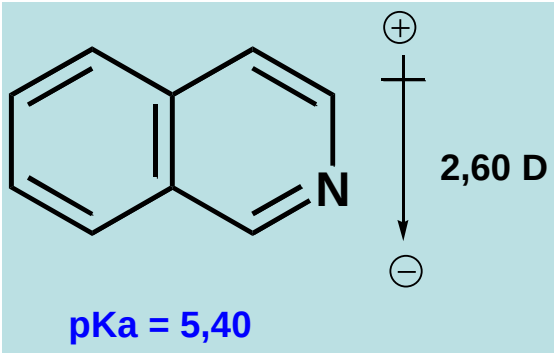


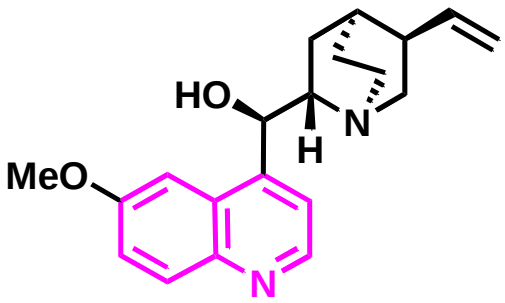




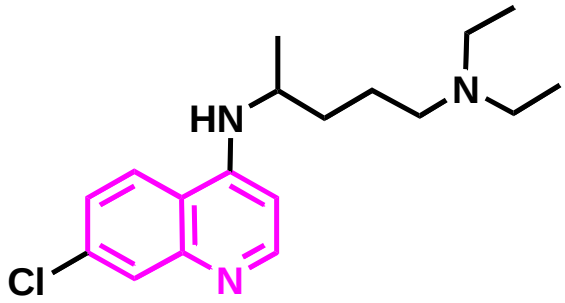




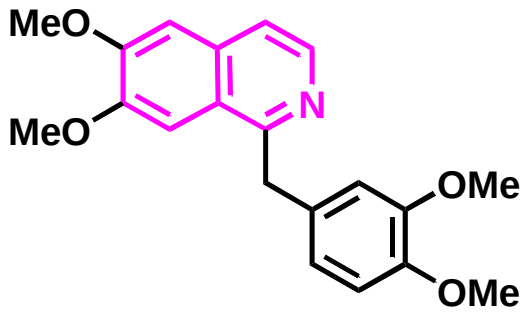




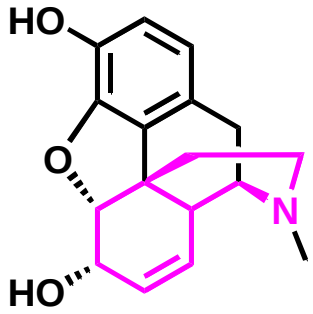
Quinina



Cloroquina

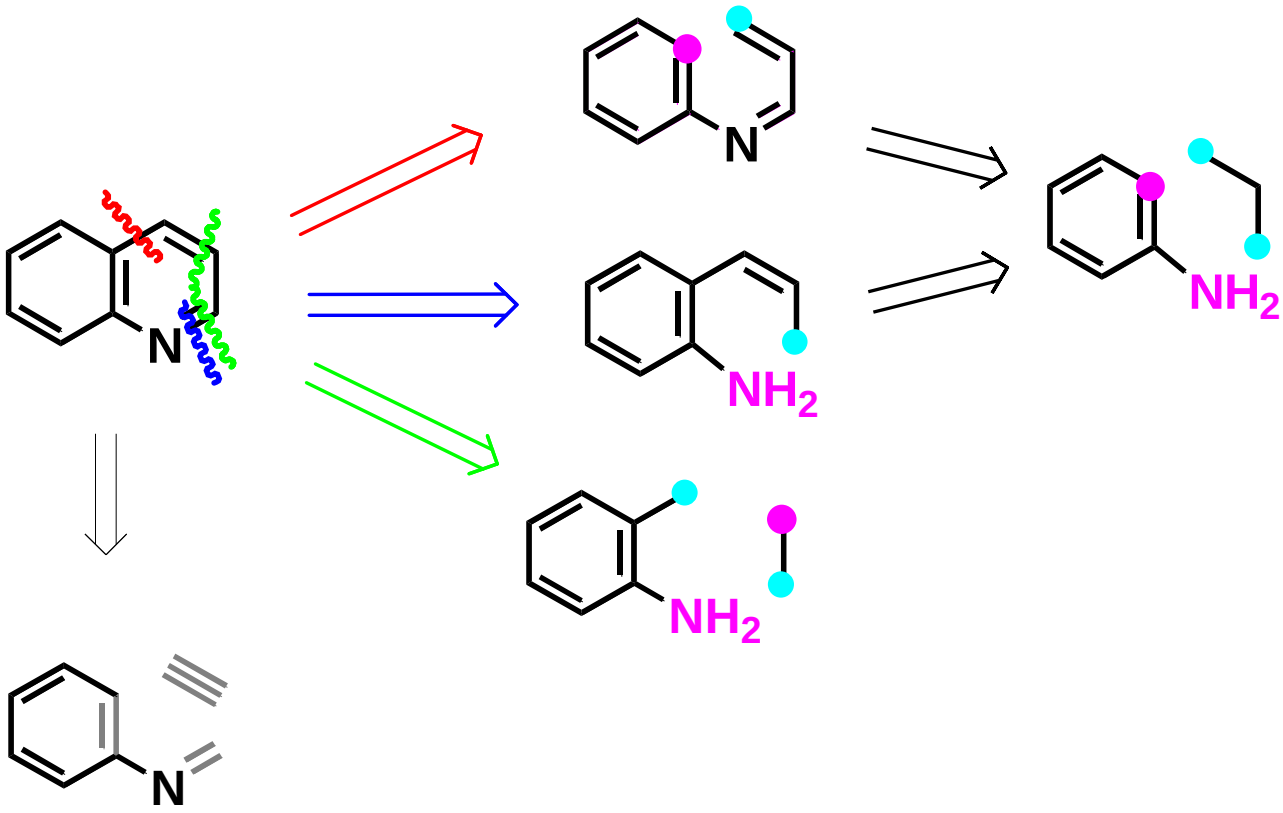


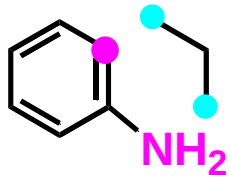
Papaverina



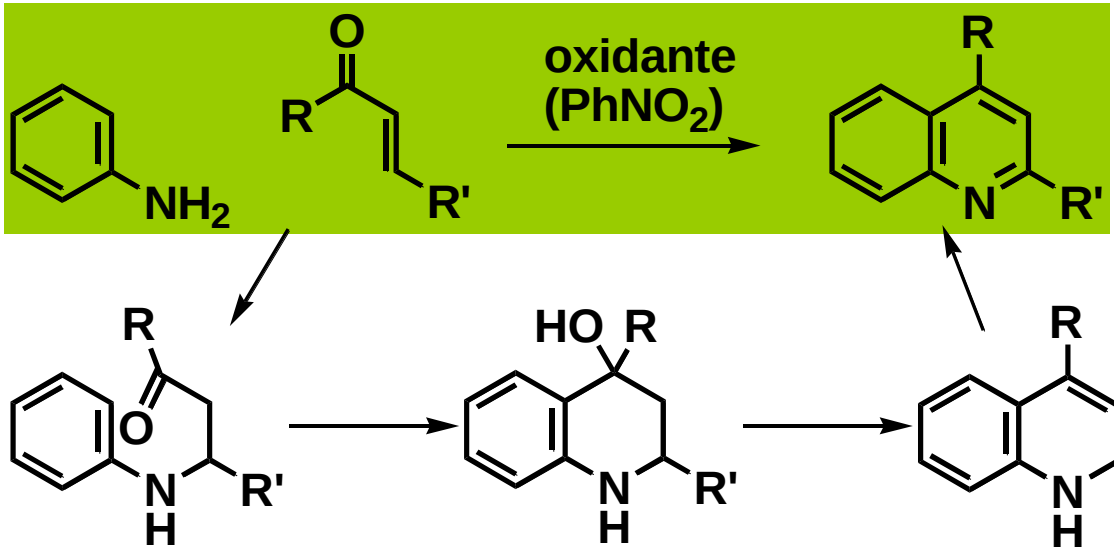
Morfina

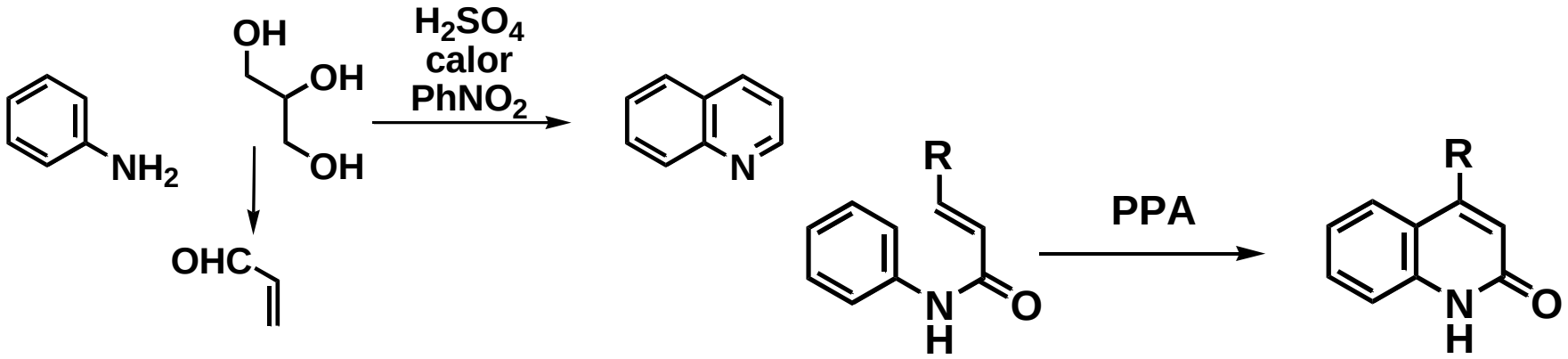
Síntesis.

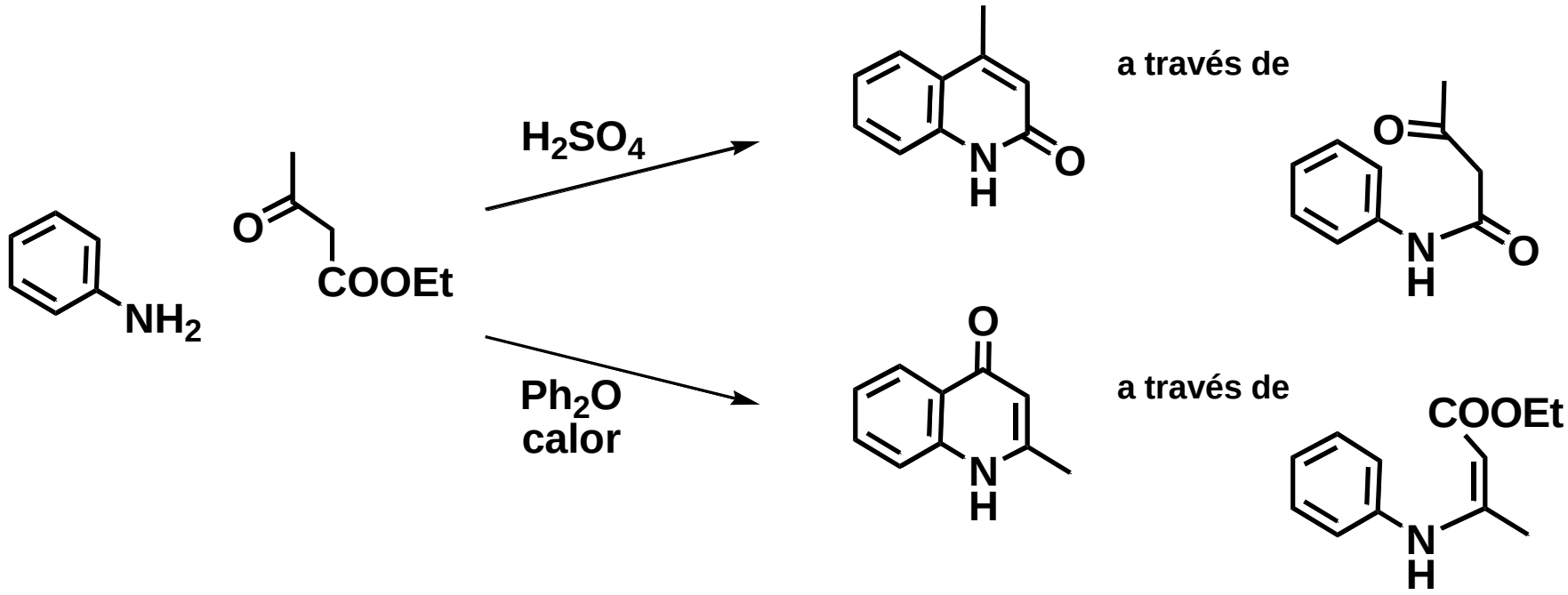




SÍNTESIS DE SKRAUP y relacionadas: Doebner-von Miller, Baeyer, Riehm







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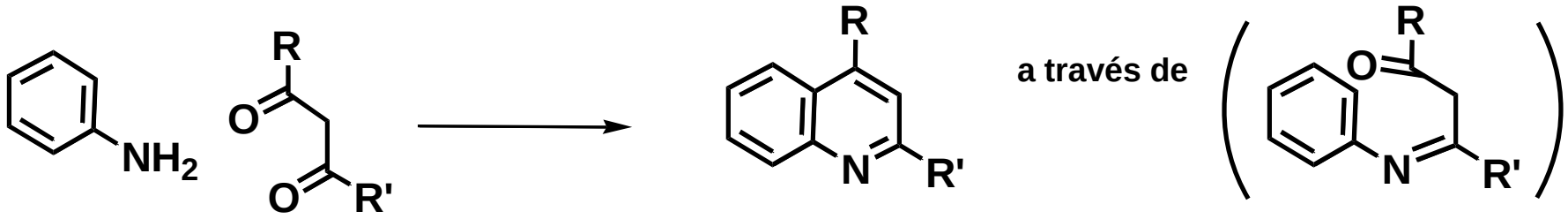

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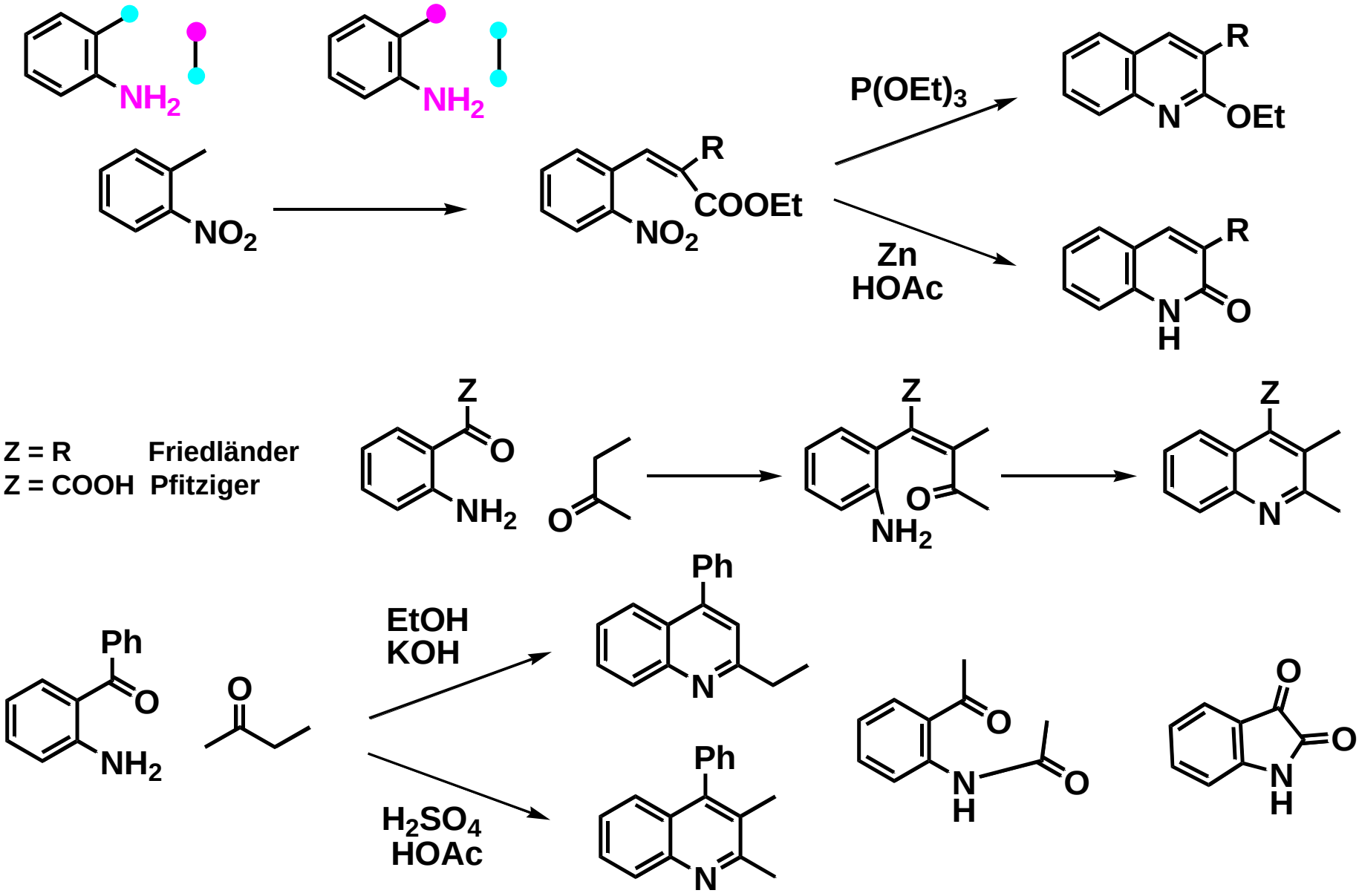
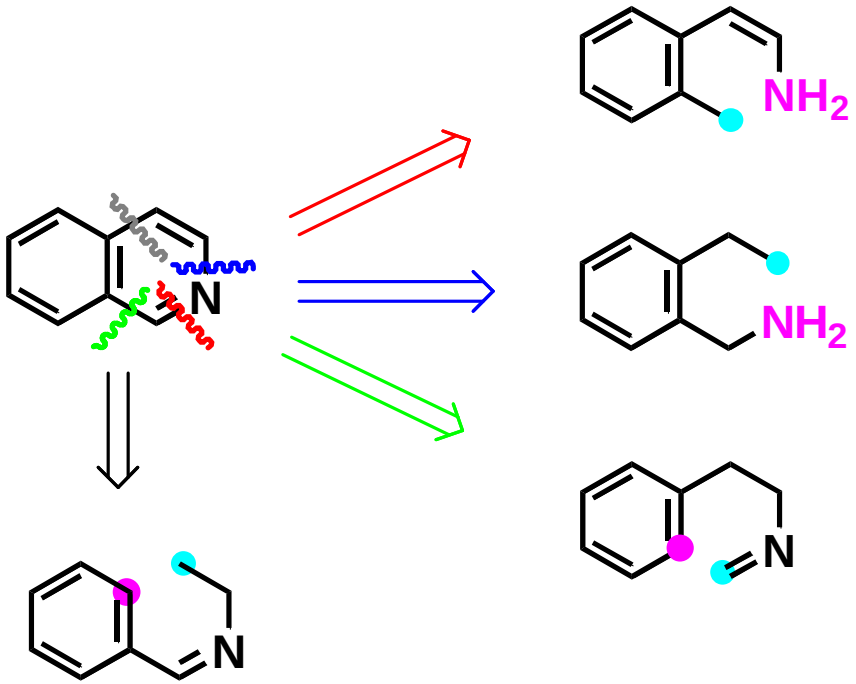

NH2
NH2
NO2
R
COOEt
NO2
P(OEt)3
R
N
OEt
Zn
HOAc
R
N
H
O
Z = R Friedländer
Z = COOH Pfitziger
Z
O
NH2
O
Z
O
NH2
Z
N
Ph
O
NH2
O
EtOH
KOH
Ph
N
H2SO4
HOAc
Ph
N
O
N
H
O
O
N
H

Síntesis.



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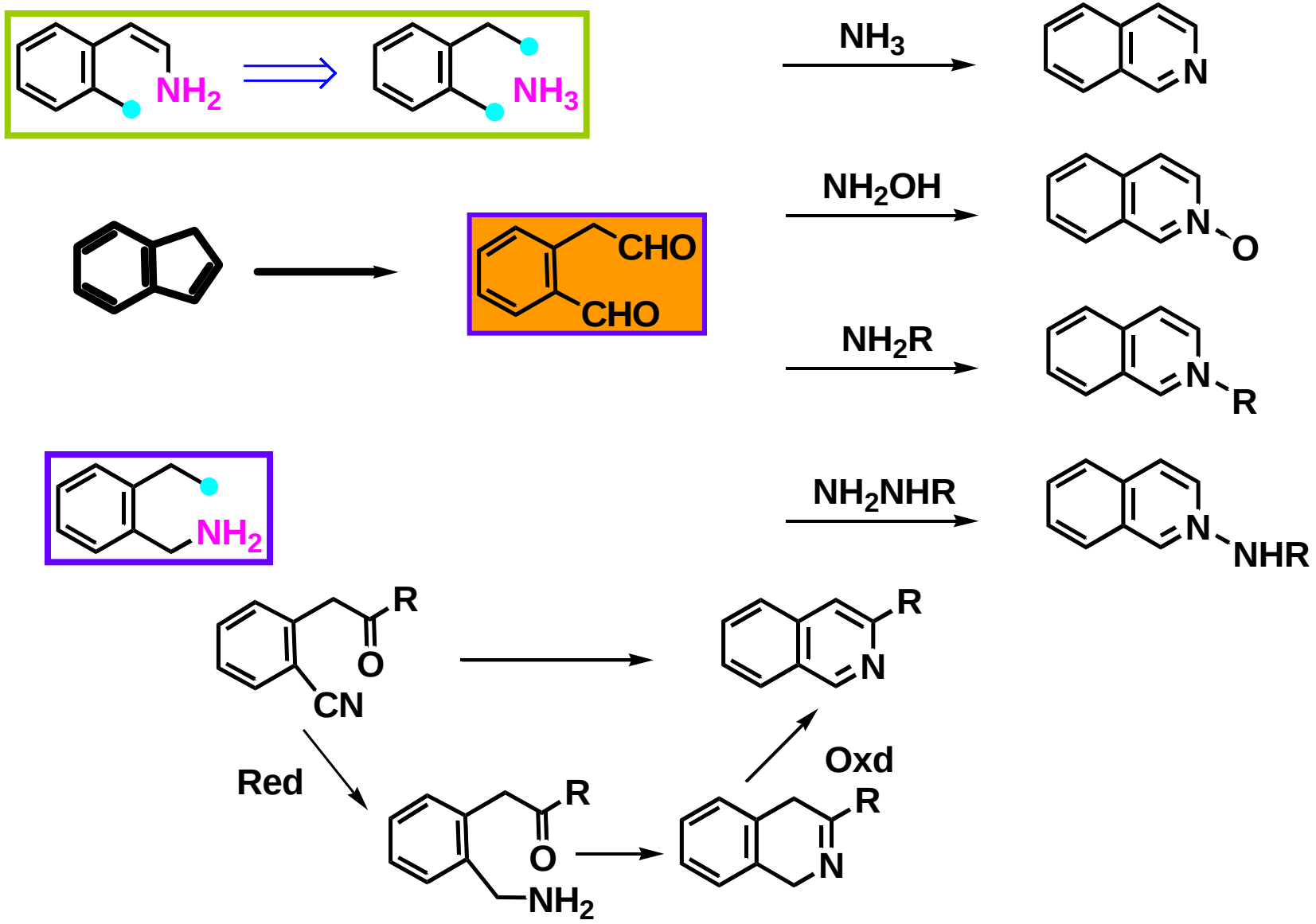
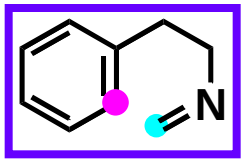
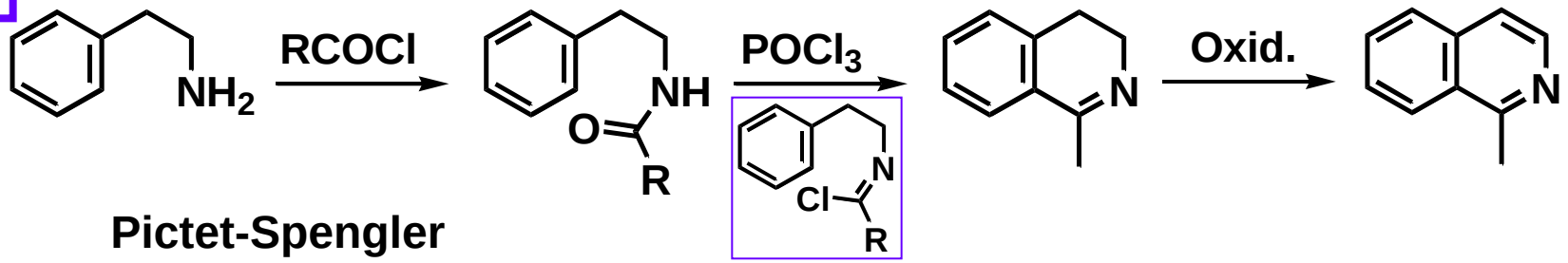
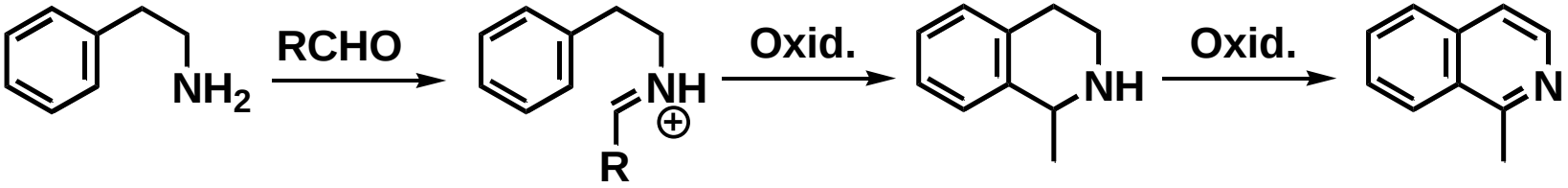

NH2
NH3
NH3
N
NH2OH
CHO
CHO
N
O
NH2R
N
R
NH2
NH2NHR
N
NHR
R
O
CN
R
N
Red
R
O
NH2
Oxd
R
N

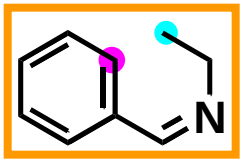


Bischler-Napieralski

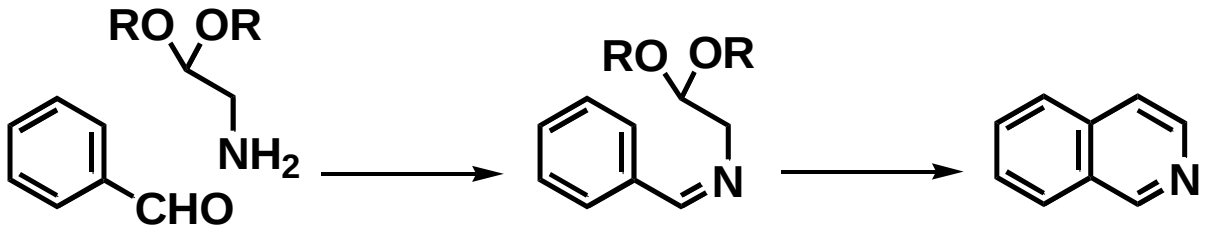


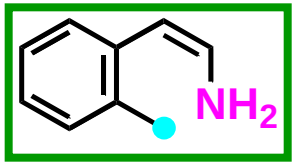
Pictet-Spengler

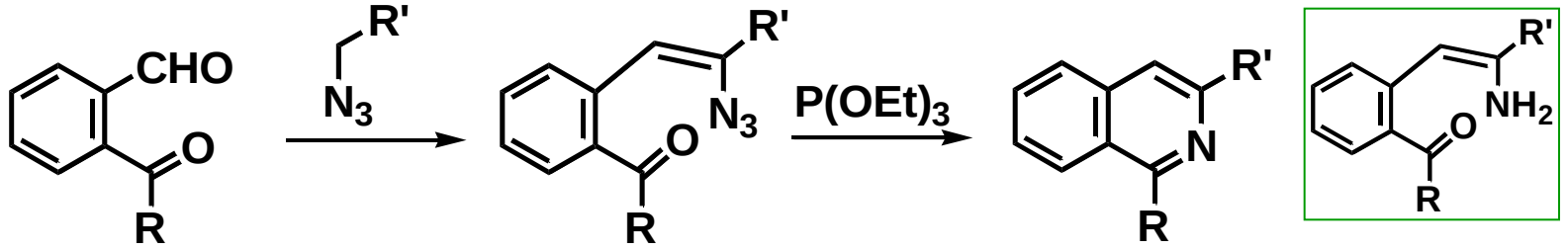


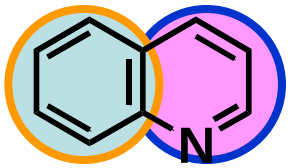


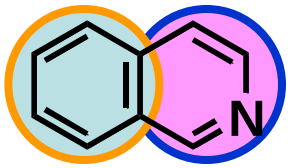
Pomeranz-Fritsch











- En el heteroátomo
- Como base
- Sustitución nucleofílica
- Sustituyentes

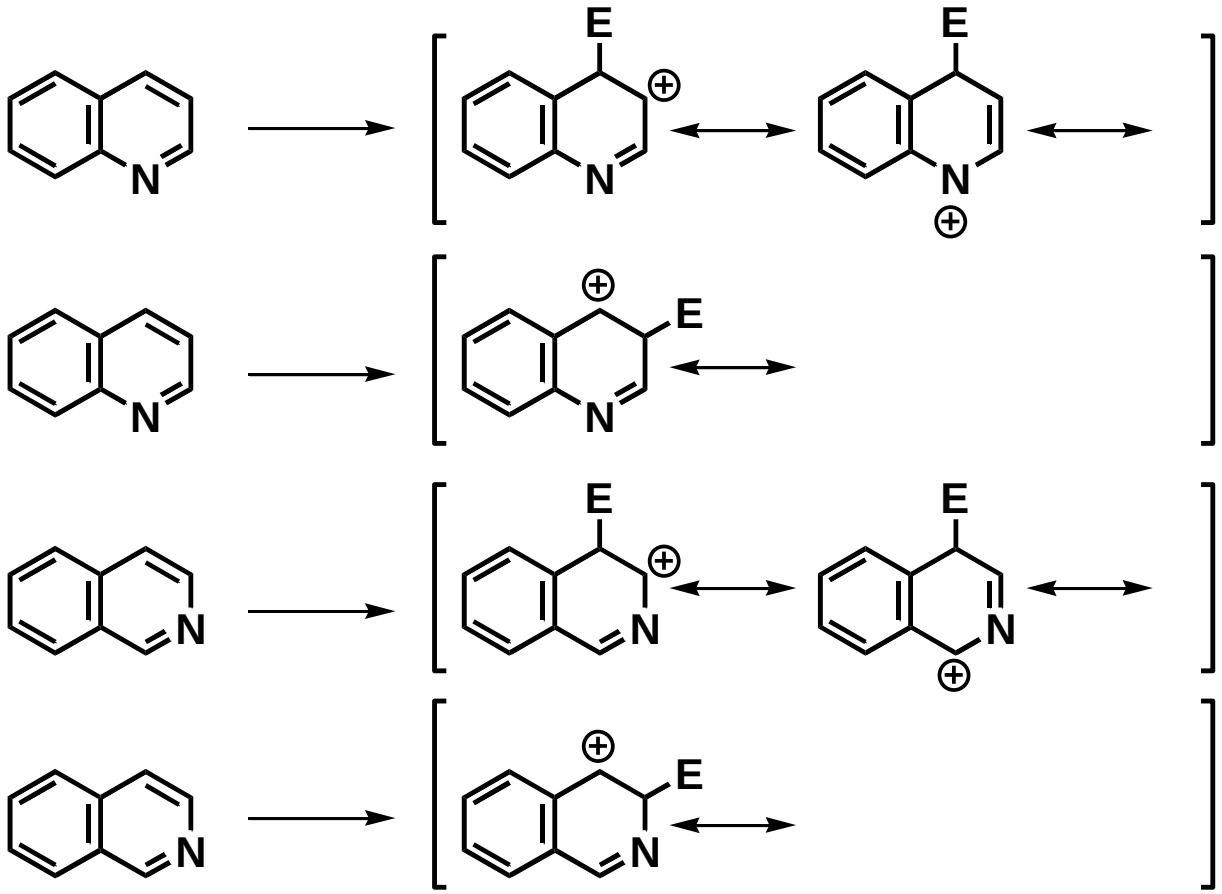
- Sustitución electrofílica
- Oxidación

SUSTITUCIÓN ELECTROFÍLICA

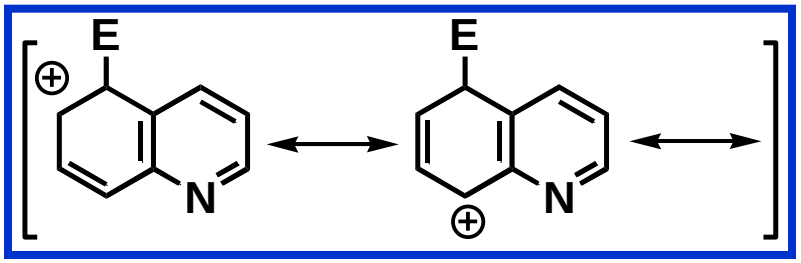
El anillo de piridina está desactivado para la sustitución electrofílica aromática (SEAr) en comparación con el anillo de benceno, por lo que se produce fundamentalmente en el anillo de de benceno.

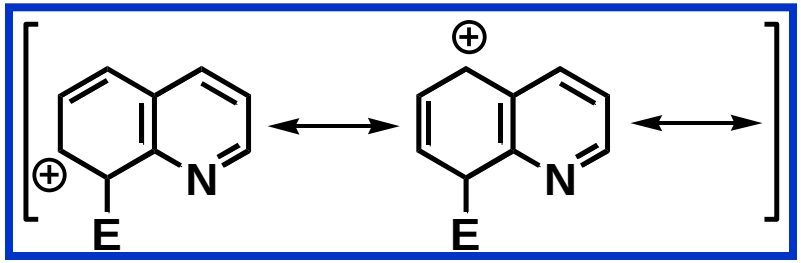
La sustitución tiene lugar en las posiciones contiguas a la unión de los anillos (5 y 8). La proporción depende de la reacción en concreto y de si se trata de quinolinas o de isoquinolinas.

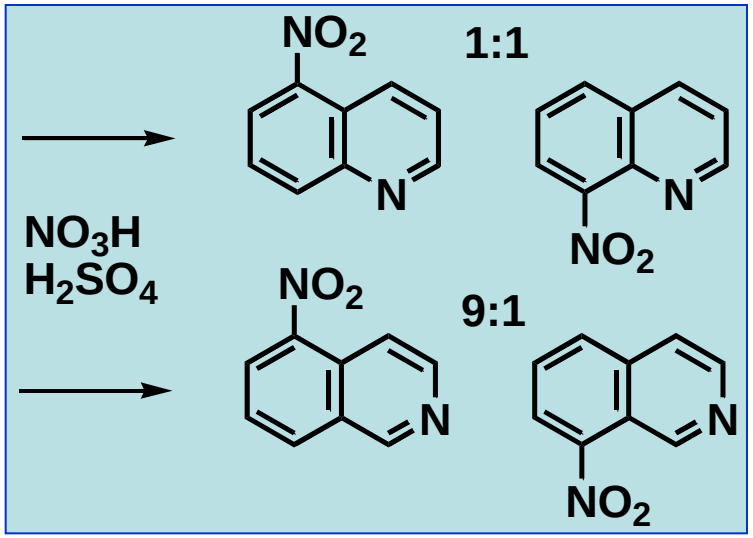
Puede producirse en el anillo de piridina en medios ácidos, debido a que se encuentra protonada, pero se trata de mecanismos diferentes (SNAr+Adic)

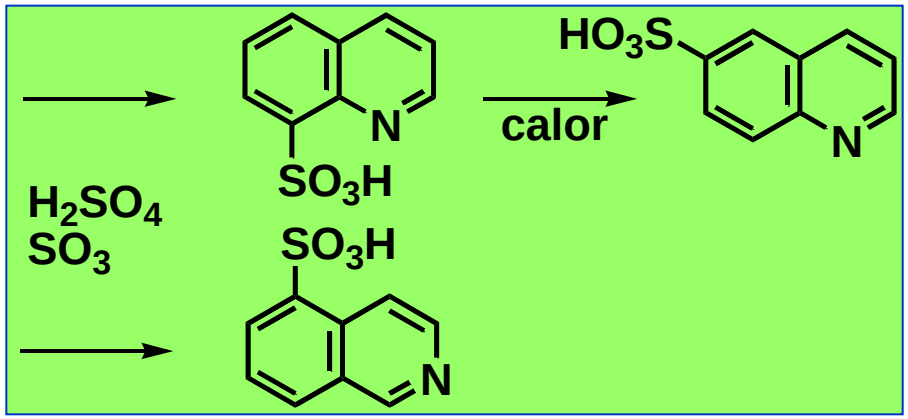


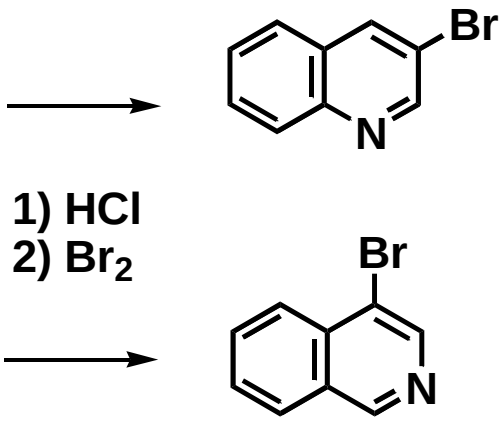
Menos favorable que la posibilidad por ataque al anillo de benceno, en el que la deficiencia electrónica no se encuentra en al anillo que posee el heteroátomo electronegativo.

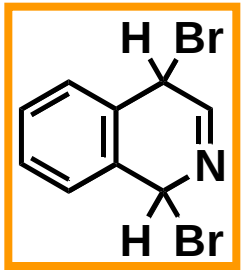


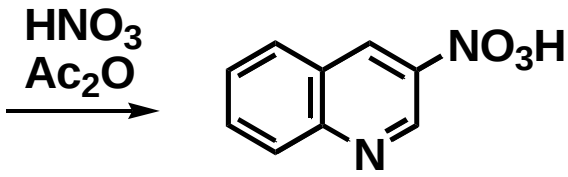



NO2
1:1
NO3H
H2SO4
NO2
NO2
9:1
NO2


HO3S
calor
H2SO4
SO3
SO3H
SO3H

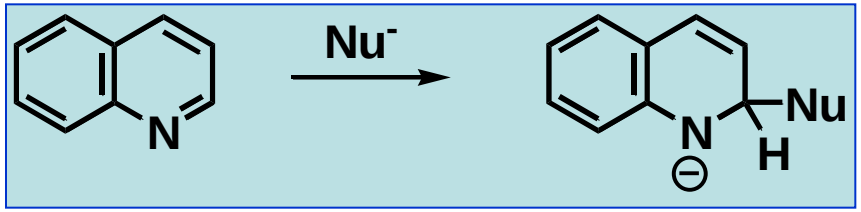

Br
1) HCl
2) Br2
Br

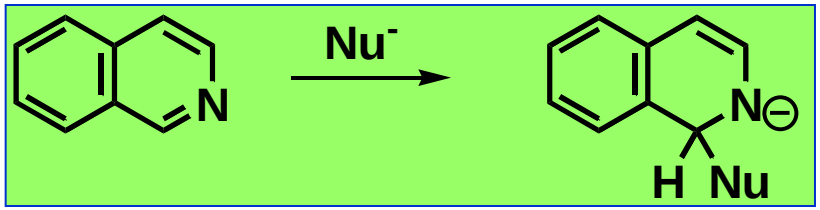

H Br
H Br


HNO3
Ac2O
NO3H

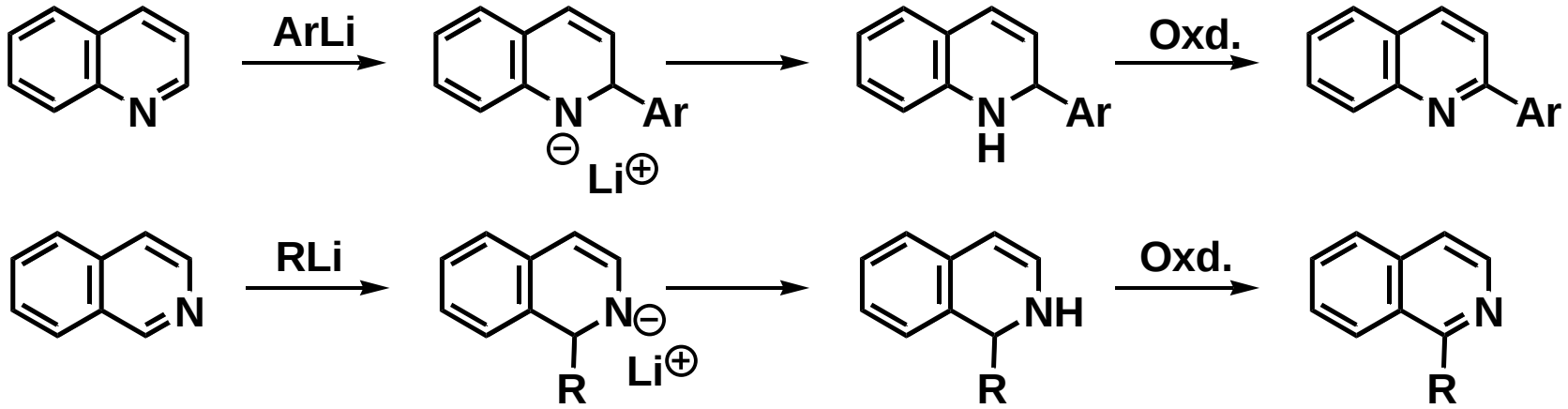
SUSTITUCIÓN NUCLEOFÍLICA

Como en el caso de la piridina, la existencia del heteroátomo electronegativo favorece el ataque de los nucleófilos sobre dicho anillo

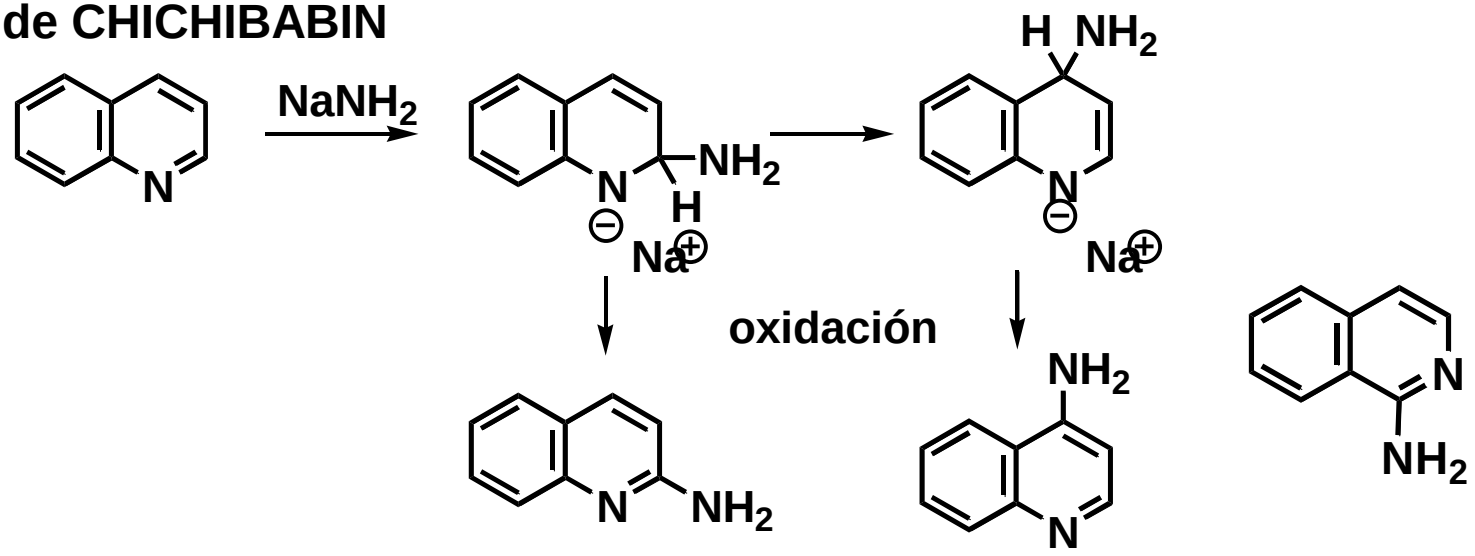




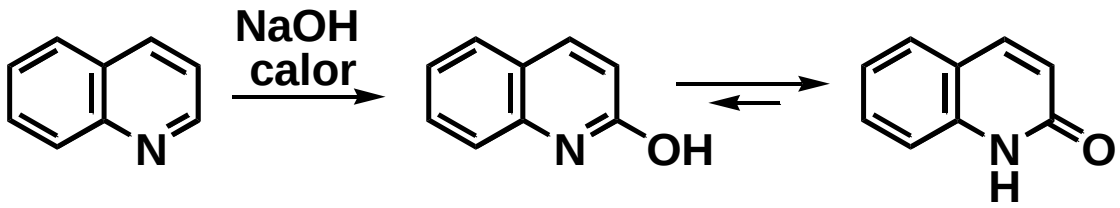
Reacción de ZIEGLER

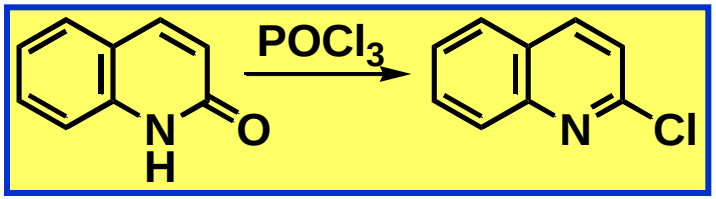


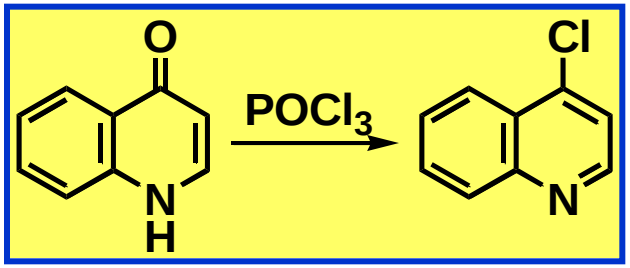
Reacción de CHICHIBABIN

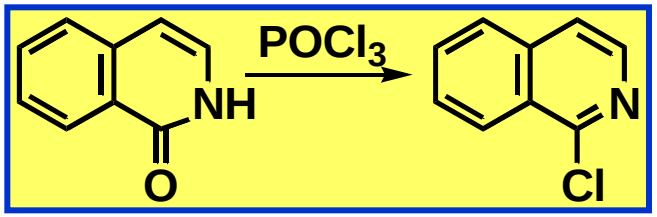


Otras

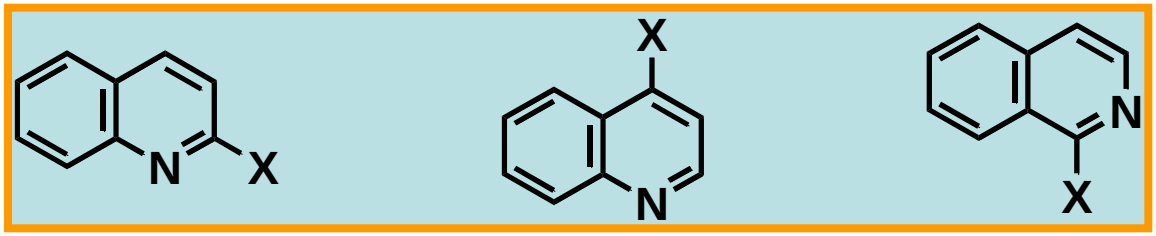


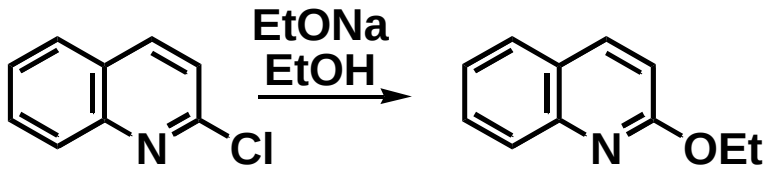


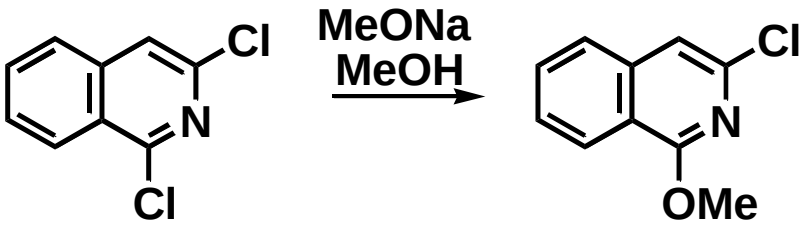




Sustitución de los halógenos mediante SNAr en posición 2 y 4 de quinolinas y en posición 1 en isoquinolinas. De forma semejante a lo que ocurre en las piridinas.

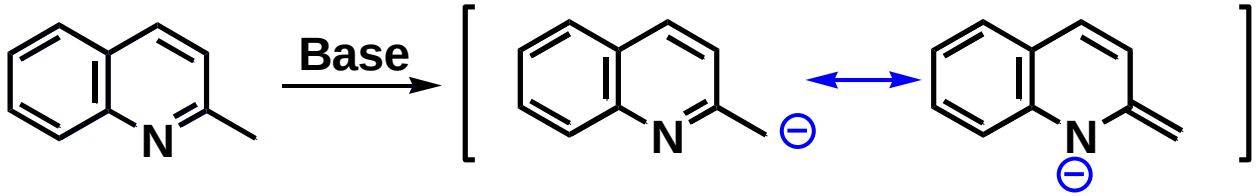


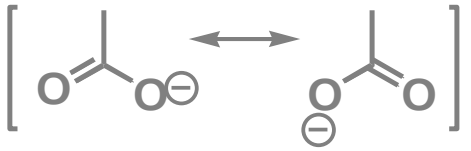


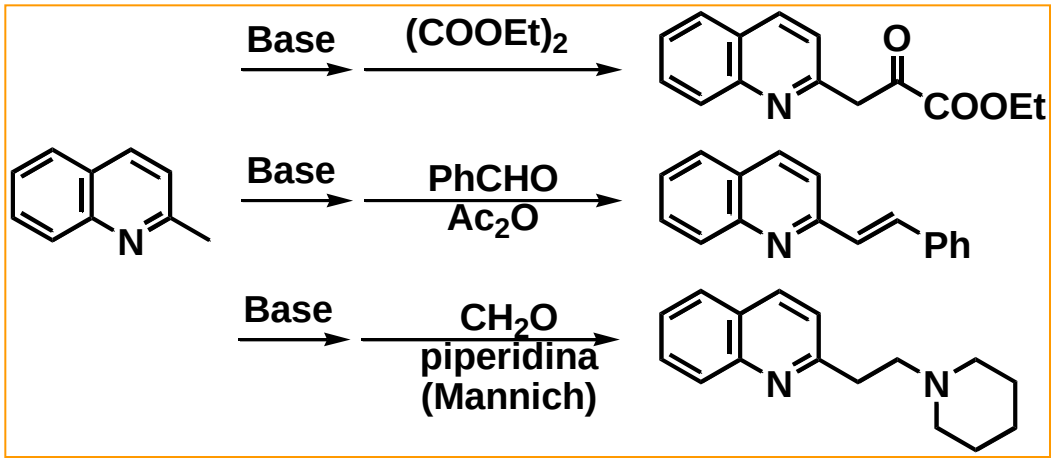


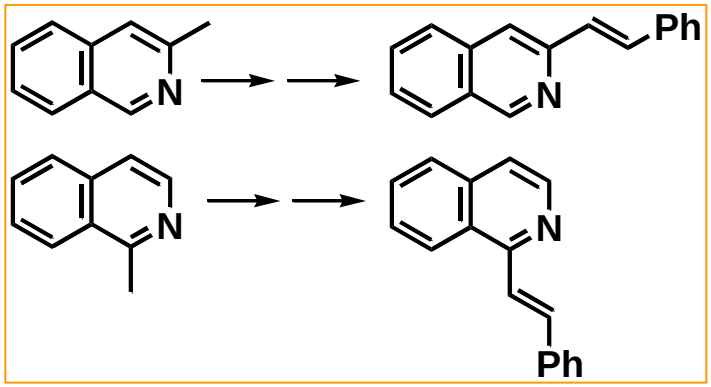
De igual manera, el mecanismo es un ataque del nucleófilo para dar un intermedio estabilizado por soportar el N los electrones, seguida de marcha del grupo saliente para recuperar el sistema aromático.

De igual forma que en la piridina, los hidrógenos de los grupos metilo en posiciones 2 y 4 de la quinolina y en 1 de la isoquinolina, son ligeramente ácidos y pueden ser sustraidos por bases suficientemente fuertes.
Se debe al efecto estabilizante del nitrógeno, que hace a las bases conjugadas comparables a los enolatos y carboxilatos

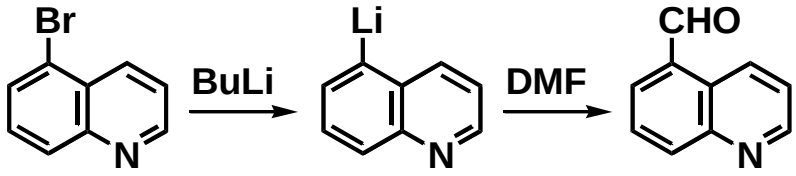








También se pueden metalar otras posiciones si están halogenadas, p.ej. en el anillo bencénico.



Como cabría esperar, se oxida más fácilmente en el anillo más rico en electrones (el de benceno) y se reduce más fácilmente en el anillo menos rico en electrones (el de piridina, que tiene el N atractor). Como en otros casos depende de las condiciones.