UNIVERSIDAD DE MÁLAGA

BLOQUE TEMÁTICO 5.- Inhibidores enzimáticos

Síntesis química de Inhibidores enzimáticos

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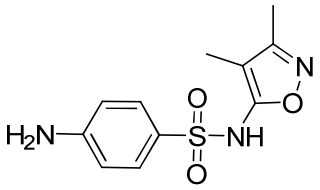
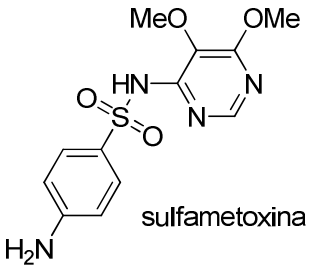
Facultad de Ciencias

Sulfonamidas

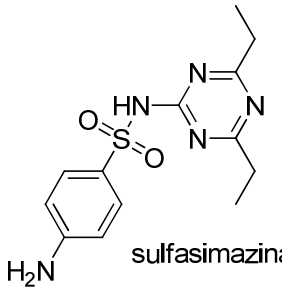
Un gran número de fármacos con actividad antibacteriana son amidas derivadas del ácido sulfanílico (ácido *p*-aminobencenosulfónico). Normalmente la amina implicada en el grupo sulfonamida es una amina primaria unida a un resto heterocíclico.



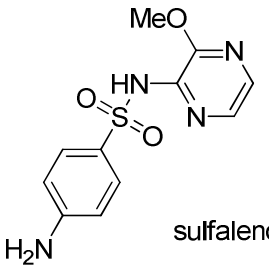
sulfisoxazol



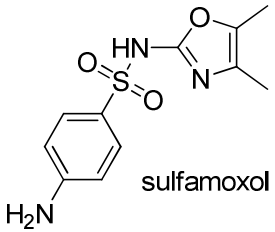
sulfametoxina



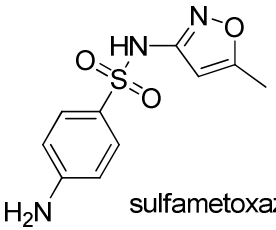
sulfasimazina



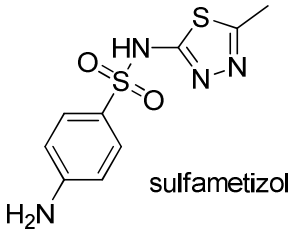
sulfaleno



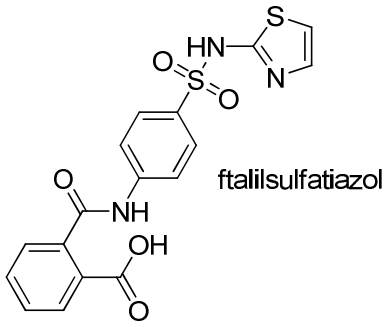
sulfamoxol



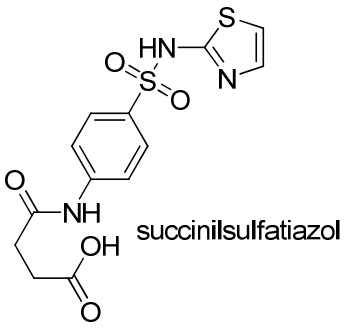
sulfametoxazol



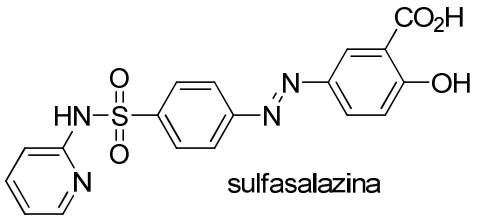
sulfametizol



ftalilsulfatiazol

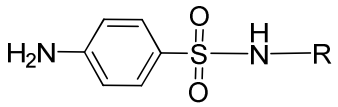


succinilsulfatiazol

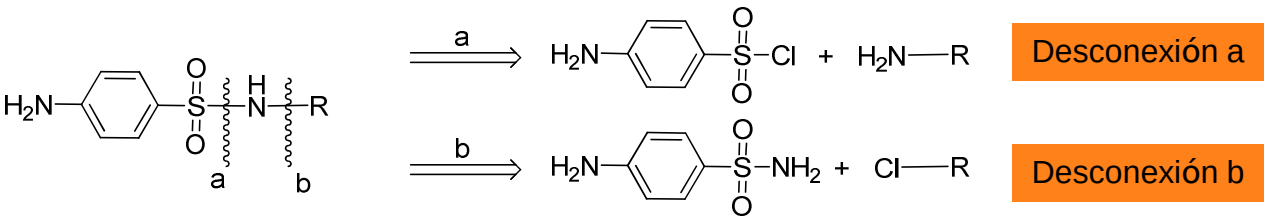


sulfasalazina

Sulfonamidas

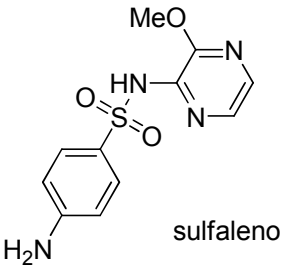


Posibles desconexiones para la formación de la sulfonamida

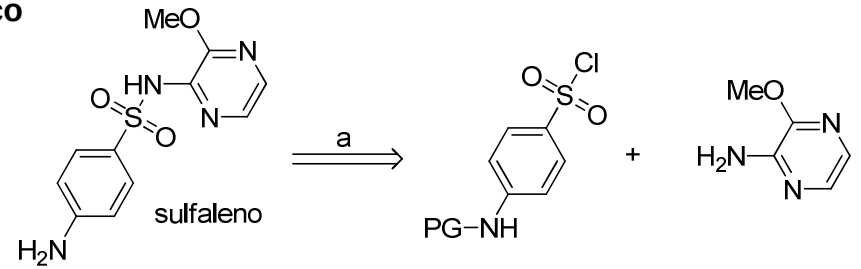


Sulfonamidas

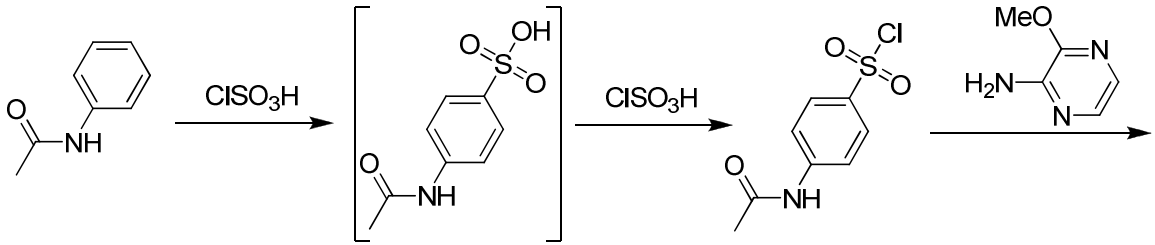
Desconexión a

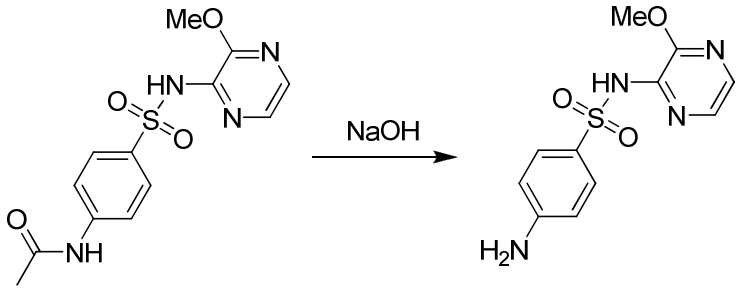


Análisis retrosintético



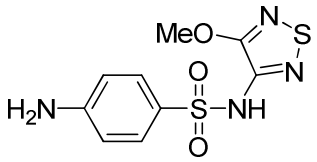
Síntesis





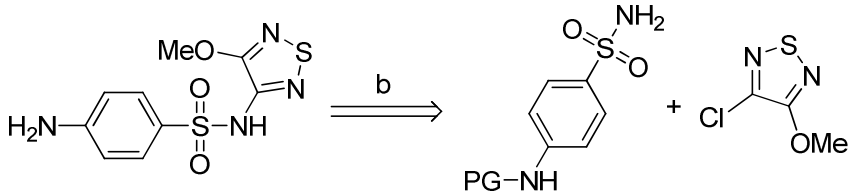
Sulfonamidas

Desconexión b



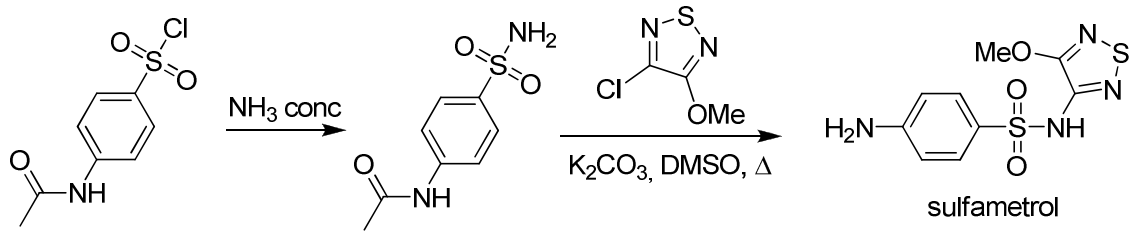
sulfametrol

Análisis retrosintético



sulfametrol

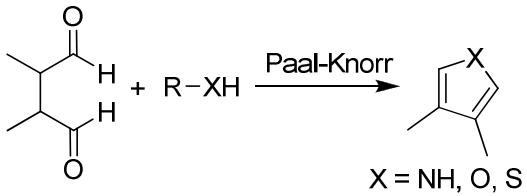
Síntesis



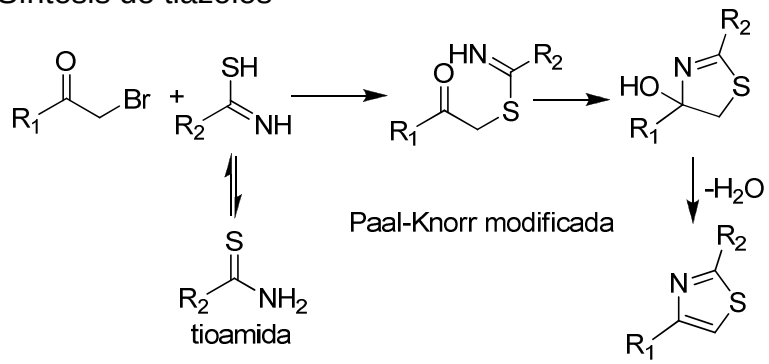
sulfametrol

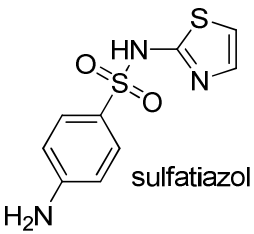
Sulfonamidas

Síntesis de Pirroles, furanos y tiofenos



Síntesis de tiazoles





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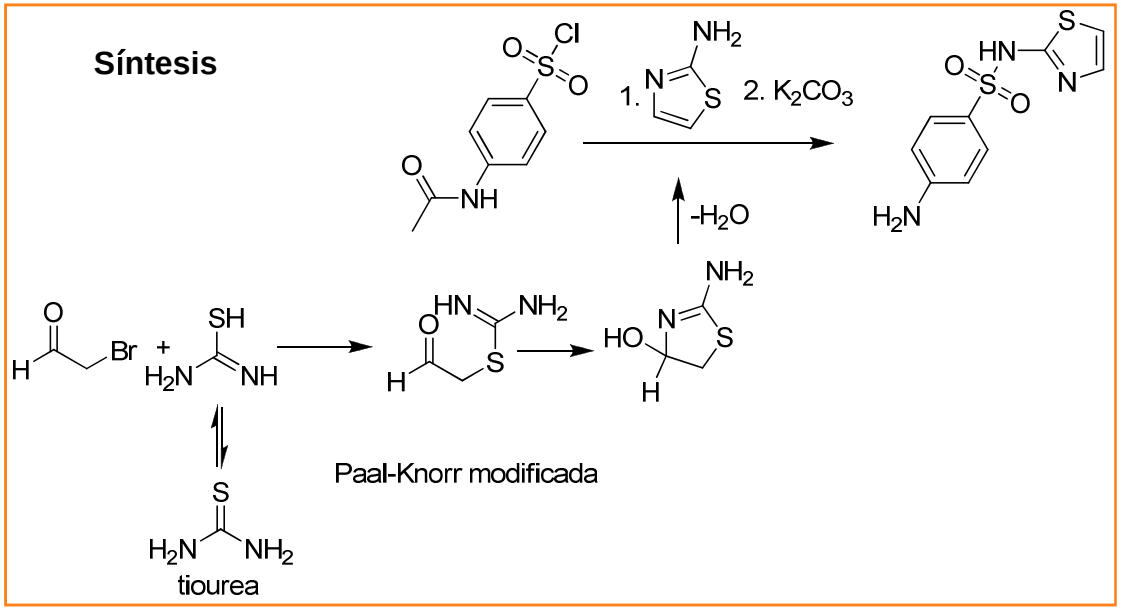
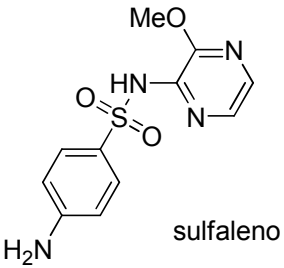
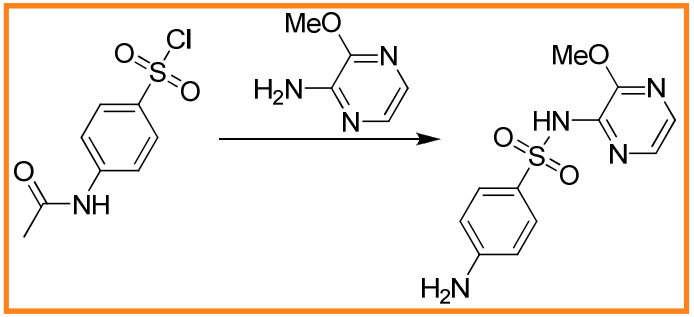


Sulfonamidas

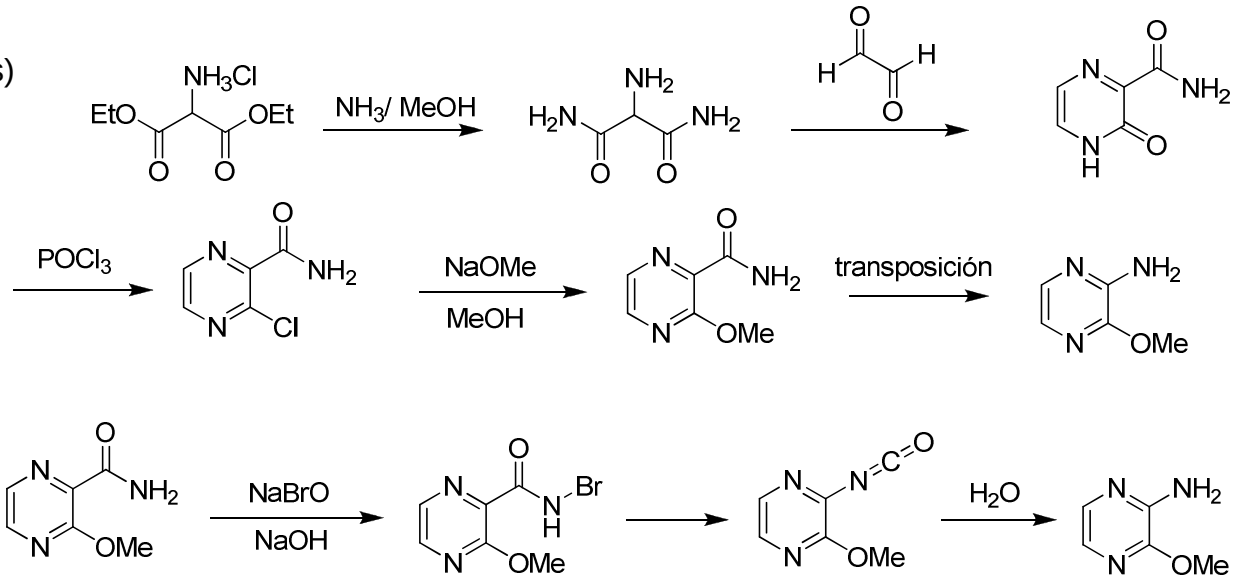


sulfaleno

Síntesis



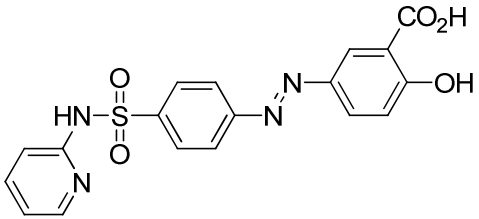
Síntesis de 1,4-diazinas (pirazinas)



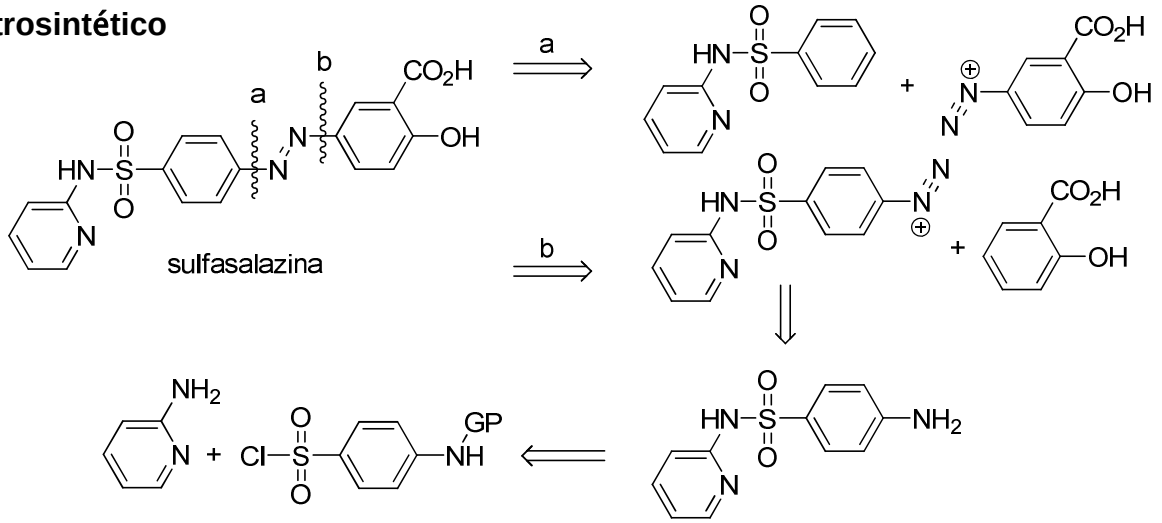
transposición de Hoffman

Sulfonamidas

Sulfasalazina



Análisis retrosintético



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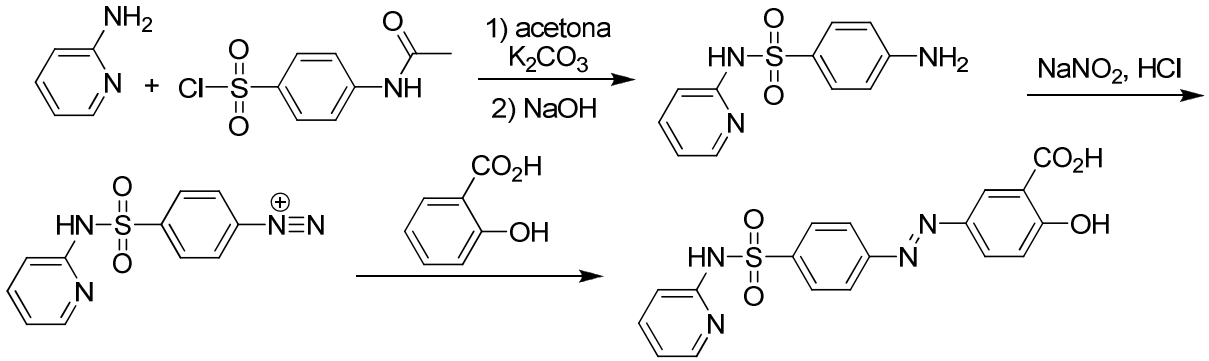
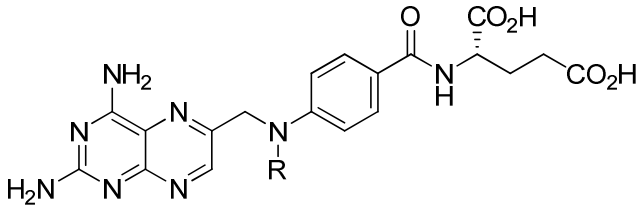
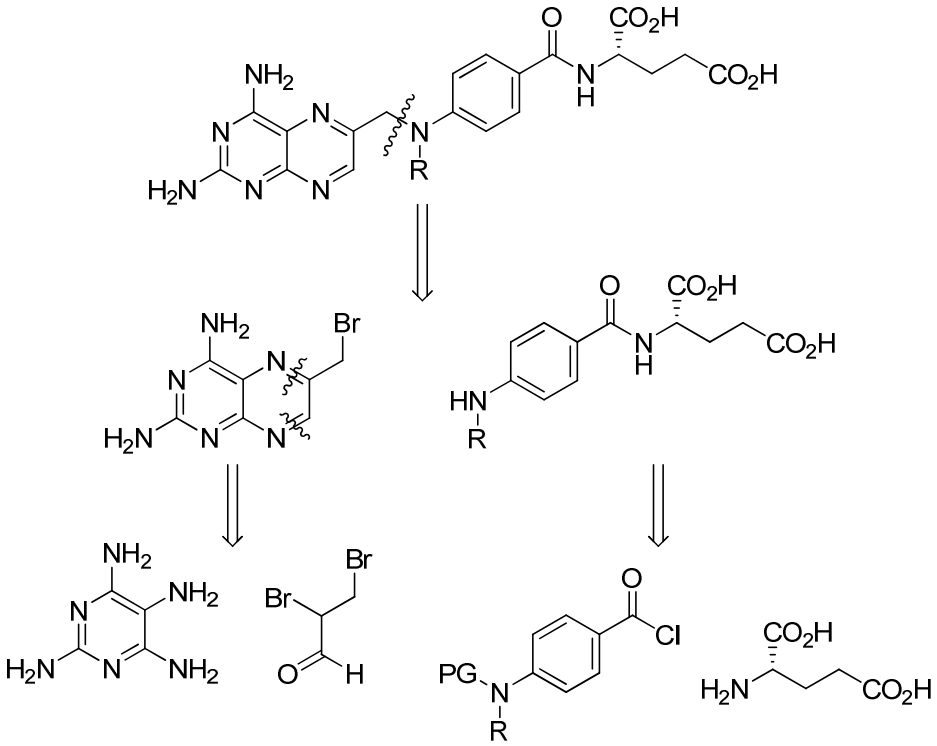


Inhbidores de la hidrofolato reductasa

Metotrexato

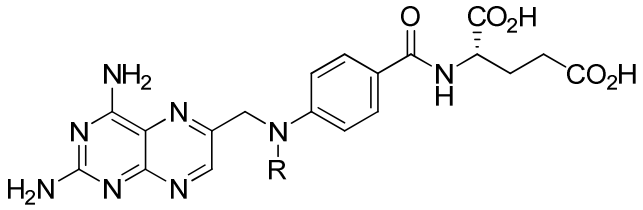


Análisis retrosintético



Inhbidores de la hidrofolato reductasa

Metotrexato



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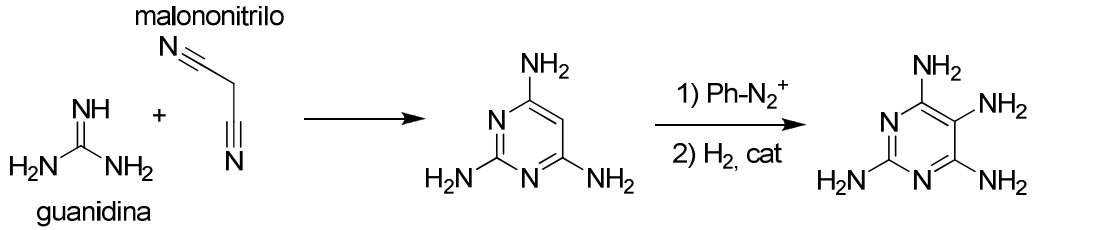
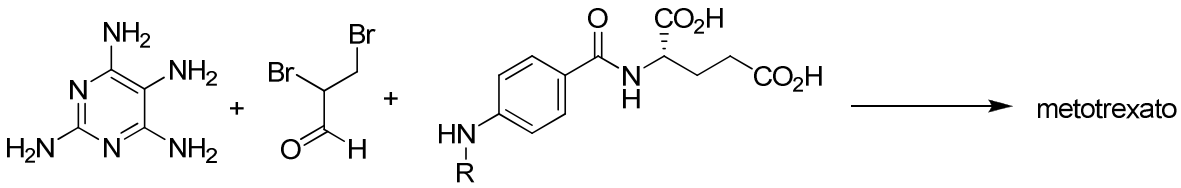
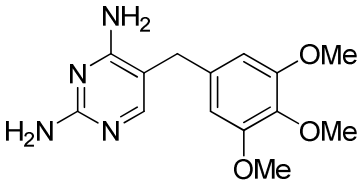


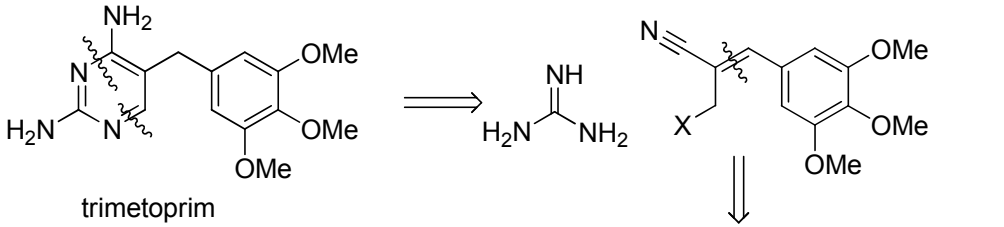


Inhbidores de la hidrofolato reductasa

Trimetoprim



Análisis retrosintético



trimetoprim

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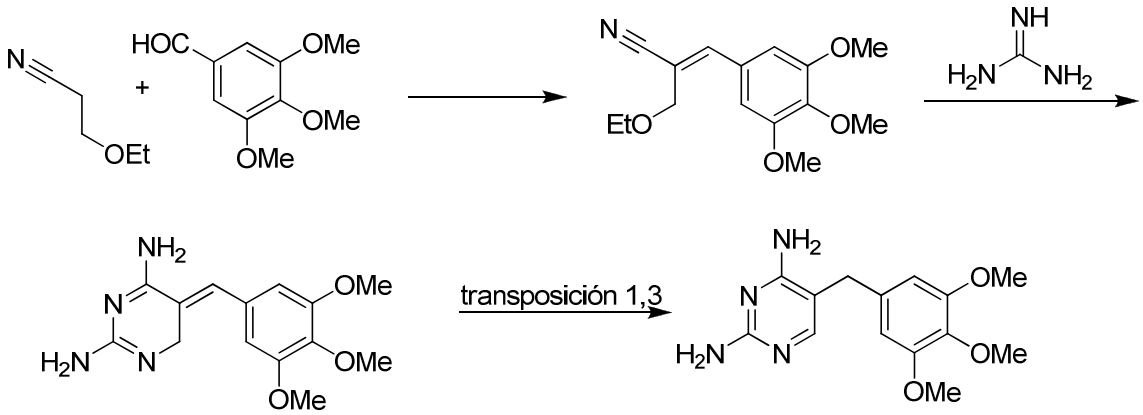
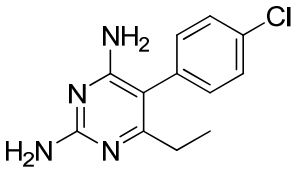


Inhbidores de la hidrofolato reductasa

Pirimetamina



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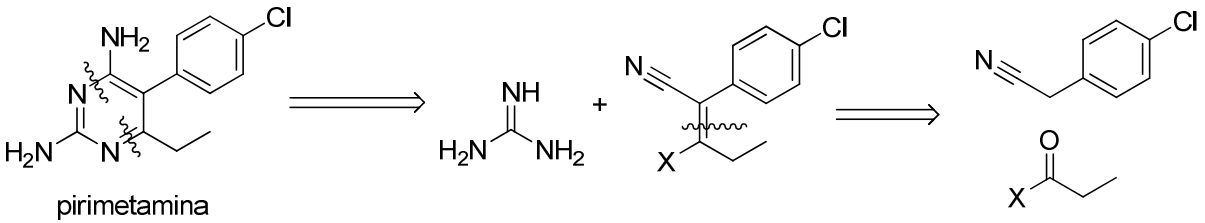
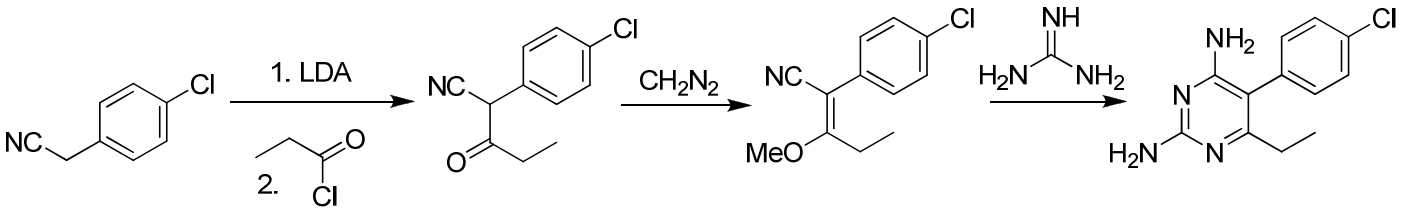


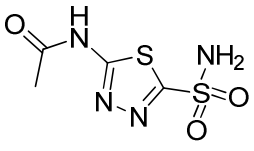
pirimetamina

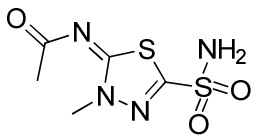
Síntesis

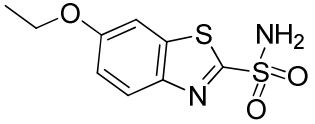


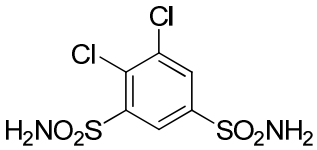
Inhbidores de la anhidrasa carbónica

Derivados de las sulfanamidas que actúan como inhibidores de la anhidrasa carbónica se utilizan en medicina como diuréticos así como en el tratamiento del glaucoma. Todas ellas relacionadas con el paso de CO_2 a H_2CO_3. Entre los fármacos más comunes tenemos la acetazolamida que está disponible en forma genérica.

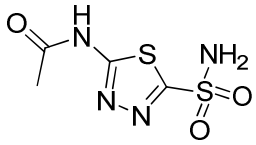

acetazolamida


metazolamida

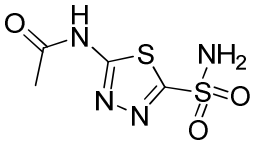

etoxizolamida

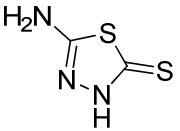

diclorfenamida

Acetazolamida

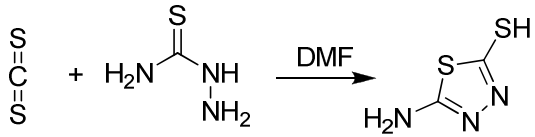


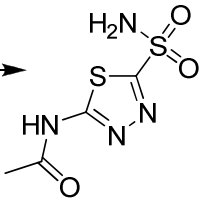
Análisis retrosintético


acetazolamida


5-amino-1,3,4-tiadiazol-2(3*H*)-tiona

Síntesis

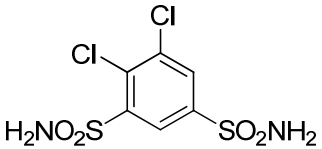

hidrazinacarbotioamida



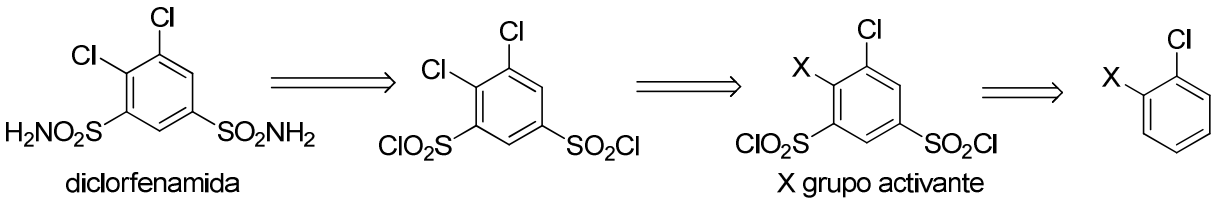
1 HCl, H_2O_2, H_2O, 10-15°C
2 10-15°C
3 NH_4OH, H_2O, < 20°C; 2 h, 50°C; 10 min, reflujo
4 HCl, H_2O, 0ºC, pH 1

Inhbidores de la anhidrasa carbónica

Diclorfenamida



Análisis retrosintético



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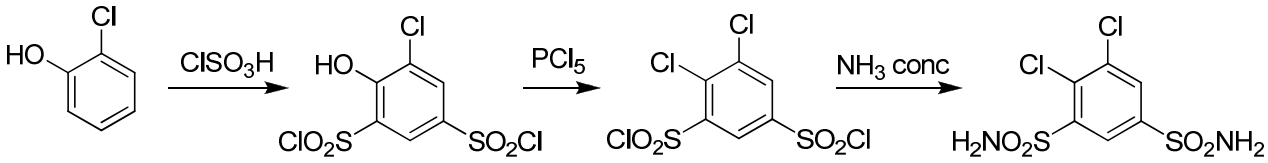
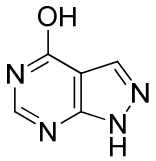
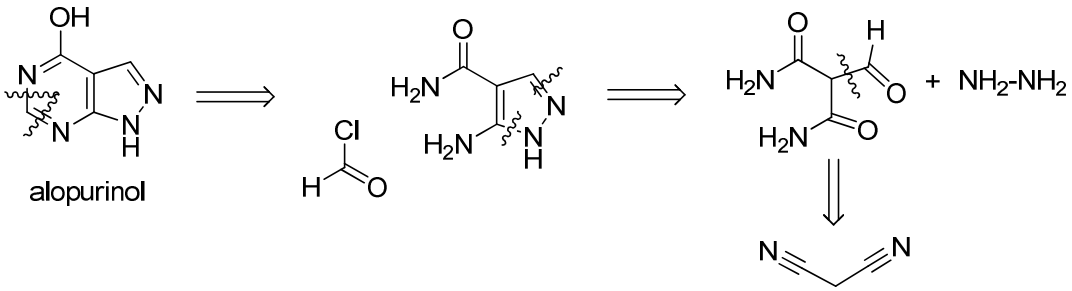


Inhibidores del metabolismo del ácido úrico

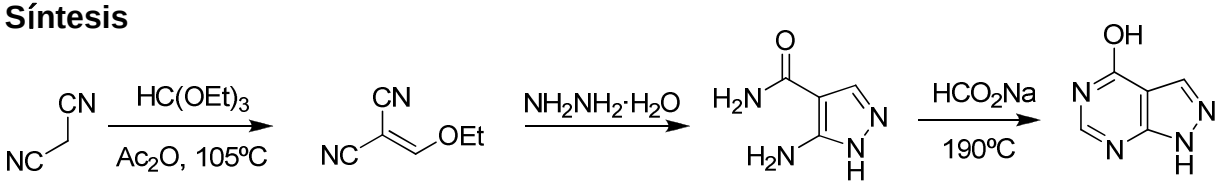
Alopurinol



Análisis retrosintético

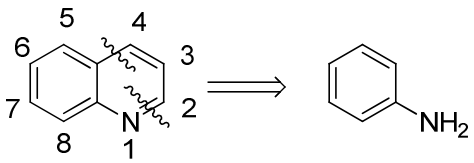


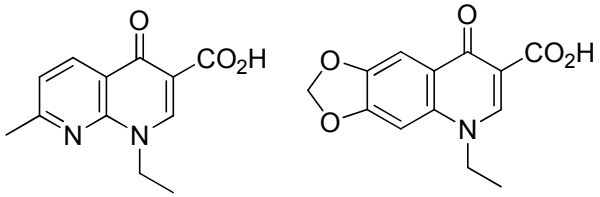
Síntesis

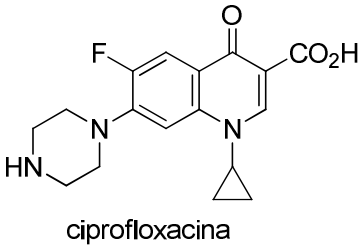


Inhibidores de la ADN-girasa

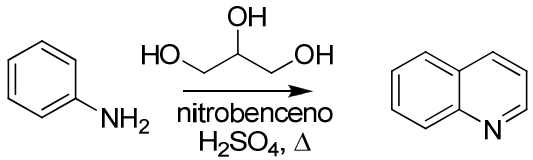
Un número importante de antibacterianos que inhiben la ADN-girasa y la topoisomerasa de bacterias tienen estructura de quinolona. Éstas se obtienen de la síntesis de la quinolina. El análisis retrosintético de las quinoleínas muestra que los enlaces más fáciles de formar son N-C2 y C4-C4a.





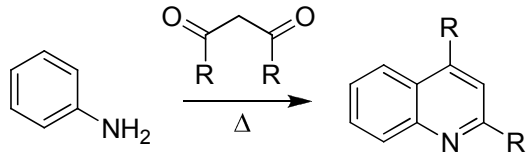


La **síntesis de Skraup** implica la reacción de anilina, glicerina y ácido sulfúrico en presencia de un oxidante (nitrobenceno, *m*-nitrobencenosulfonato, óxido de arsénico). En estas condiciones se forma acroleína por deshidratación de la glicerina que tras condensación, deshidratación y oxidación da a lugar a quinolina.

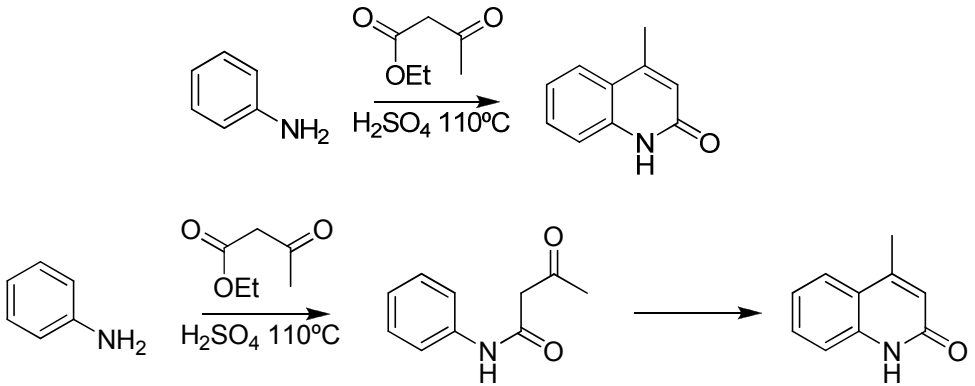


Inhibidores de la ADN-girasa

La **síntesis de Combes** hace reaccionar la anilina con un compuesto 1,3-dicarbonílico en medio ácido. La reacción implica la formación de una imina que tautomeriza a la correspondiente enamina, la cual cicla y deshidrata para dar quinolinas 2,4-disustituidas.



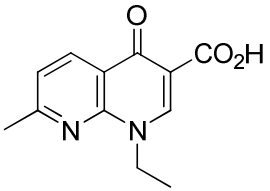
La **síntesis de Conrad-Limpach-Knorr** procede de la reacción de la anilina con un β-cetoéster en medio ácido. En este caso puede obtenerse una 2-quinolona o una 4-quinolona dependiendo de las condiciones de la reacción. Si la reacción se inicia a elevadas temperaturas se obtiene el producto termodinámico, una 2-quinolona, como consecuencia del ataque de la anilina al éster.



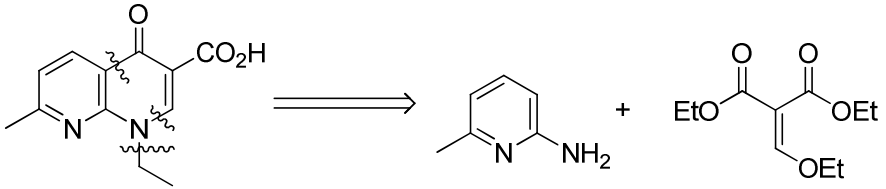
2-quinolonas

Inhibidores de la ADN-girasa

Ácido Nalidíxico

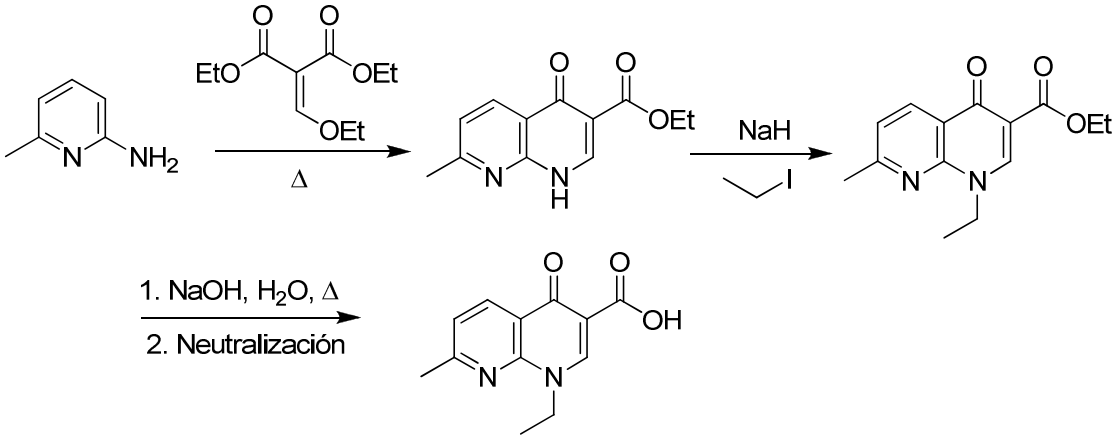


Análisis retrosintético



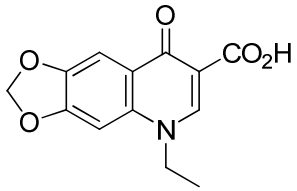
ácido nalidíxico

Síntesis

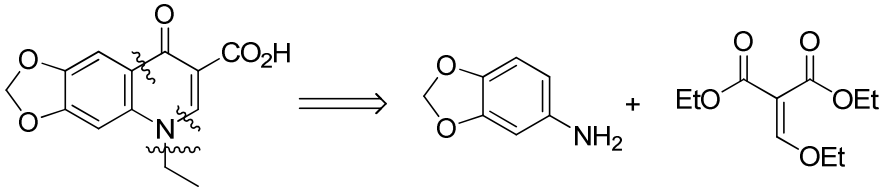


Inhibidores de la ADN-girasa

Ácido Oxolínico

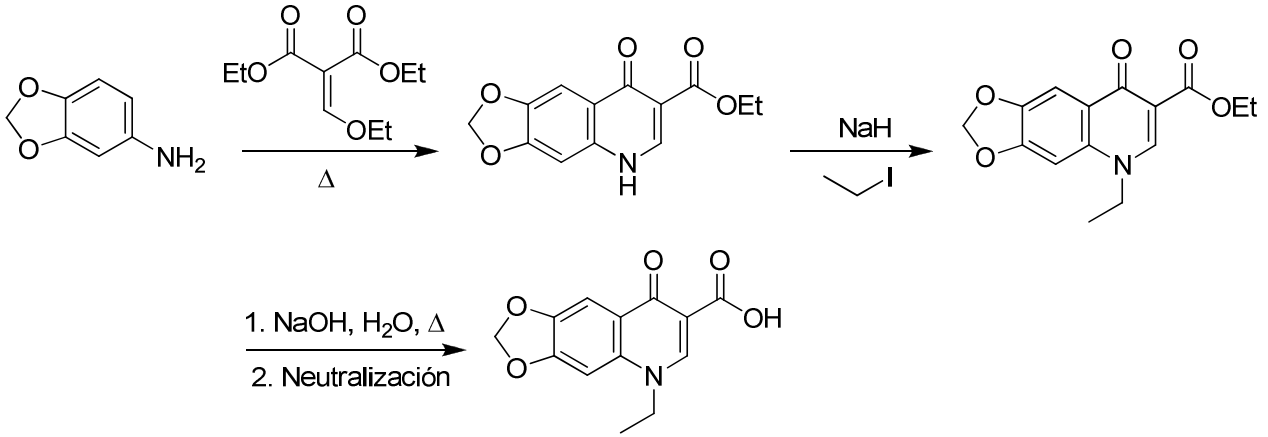


Análisis retrosintético



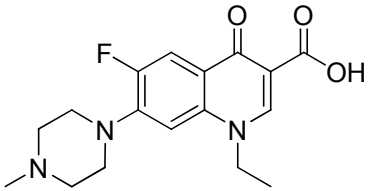
ácido oxolínico

Síntesis

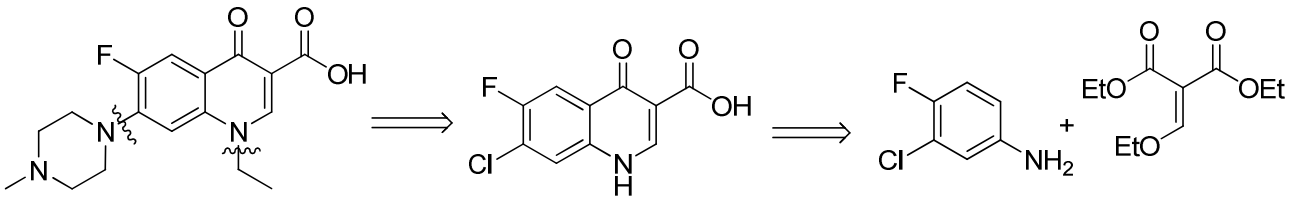


Inhibidores de la ADN-girasa

Pefloxazina

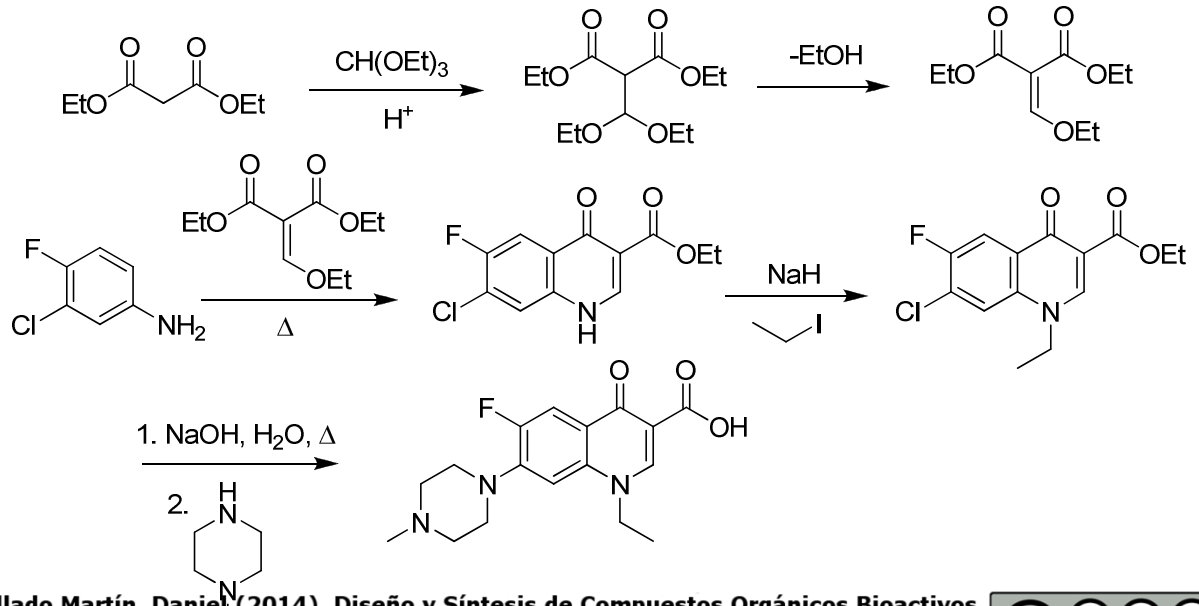


Análisis retrosintético



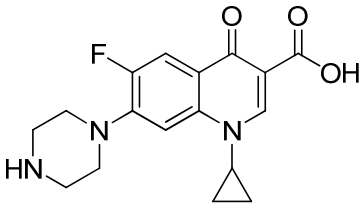
pefloxazina

Síntesis

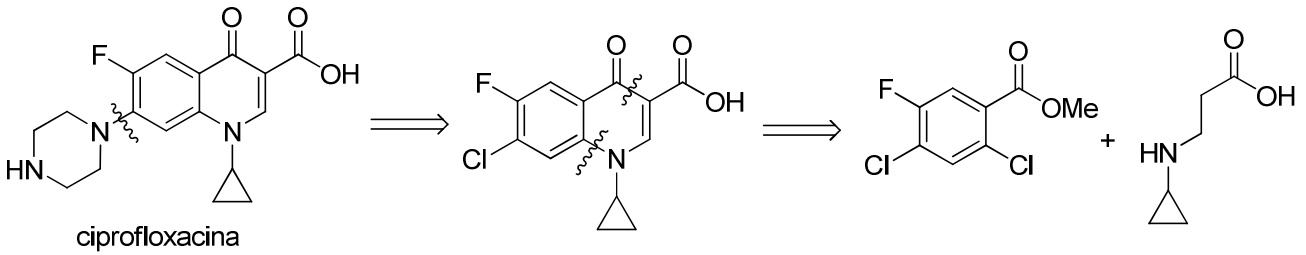


Inhibidores de la ADN-girasa

Ciprofloxacina



Análisis retrosintético



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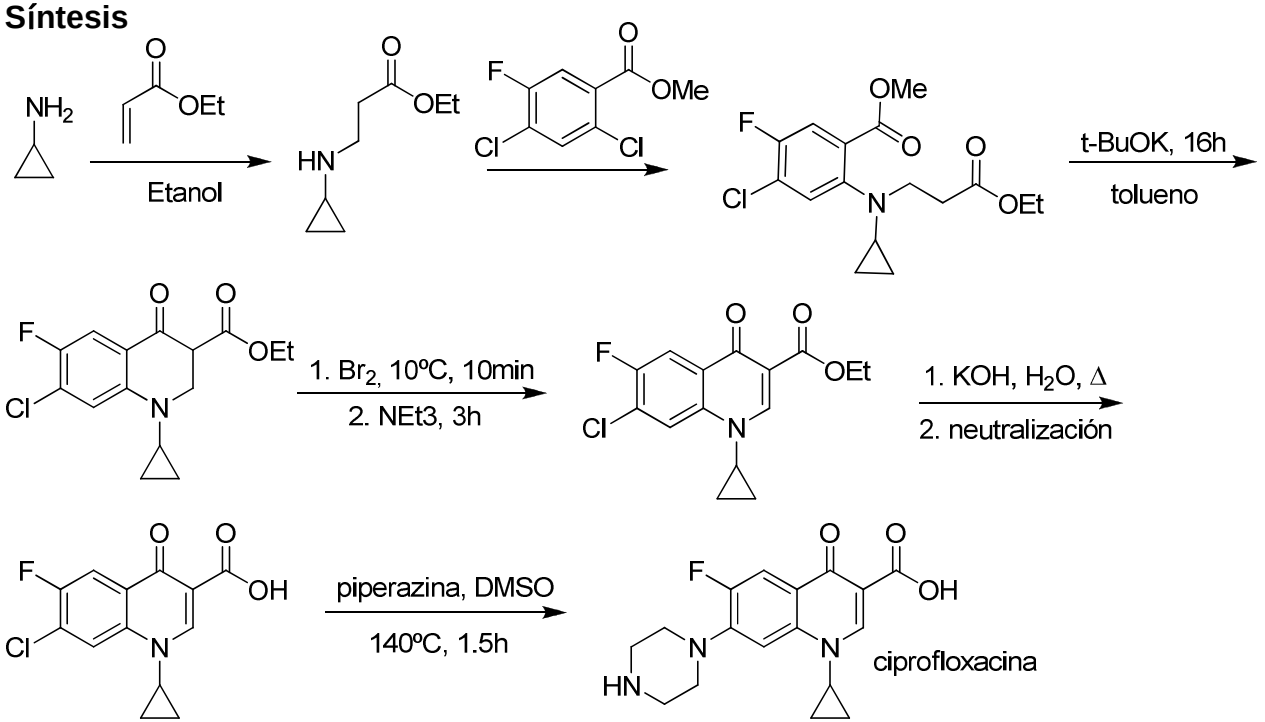
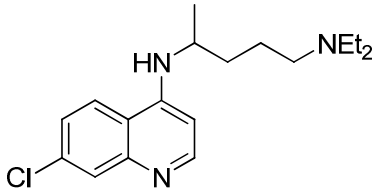


Antimaláricos

Ciprofloxacina



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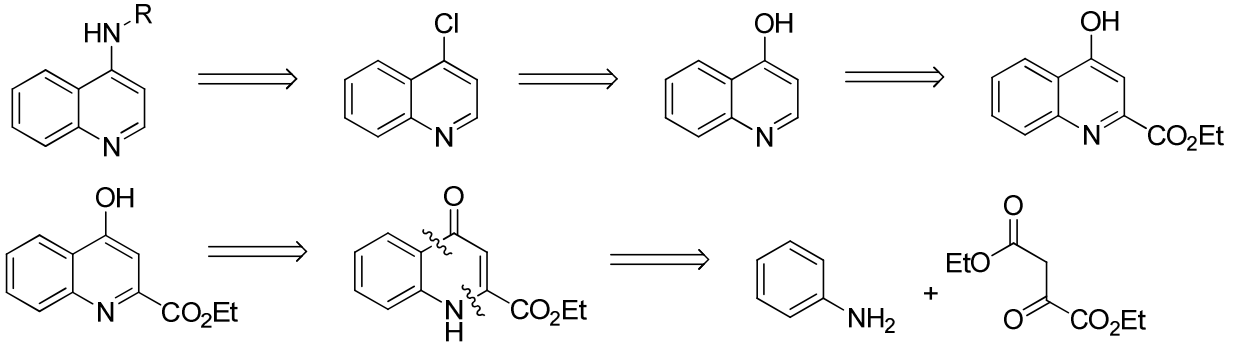

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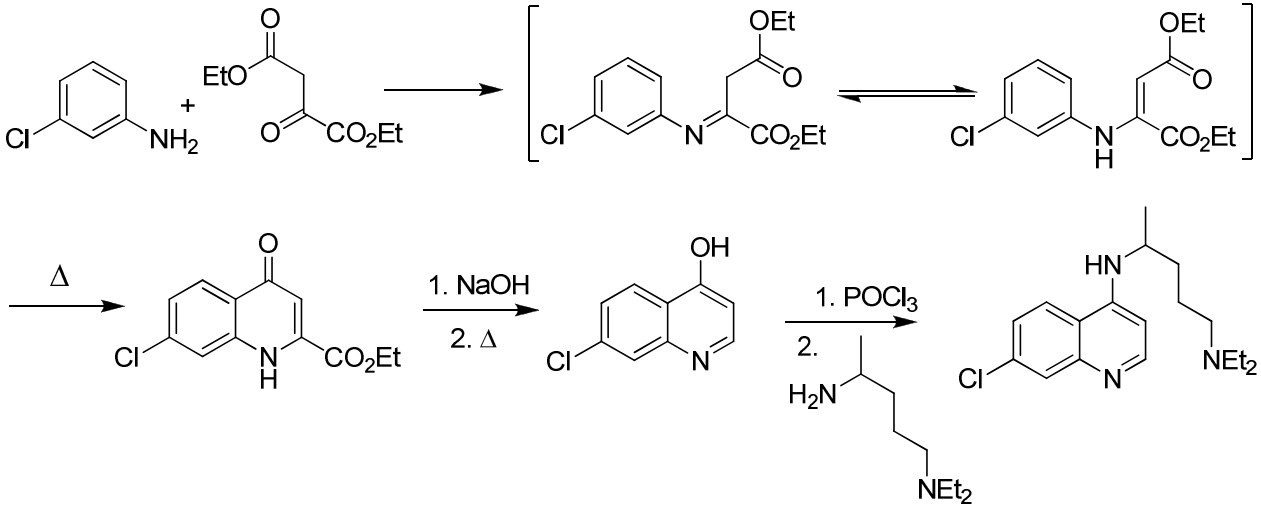
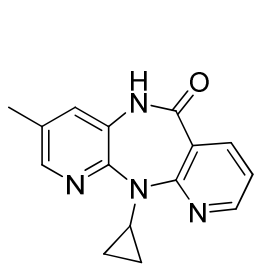


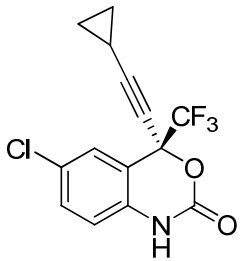
Inhibidores de la transcriptasa reversa

Inhibidores no análogos a nucleósidos

La enzima transcriptasa reveresa es la enzima primaria responsable de la conversión de la cadena simple de ARN vírico a la doble cadena de ADN. Los inhibidores no nucleósidos de la transcriptasa reversa más usados actualmente contra el sida son la nevirapina, delavirdina y efavirenz.



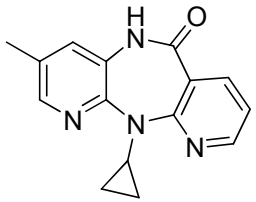
nevirapina



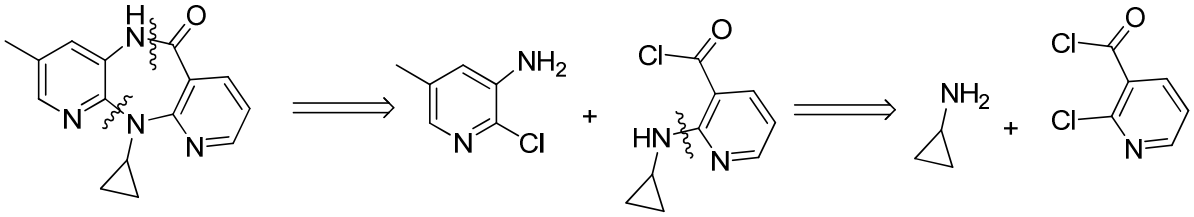
efavirenz

Inhibidores de la transcriptasa reversa

Nevirapina

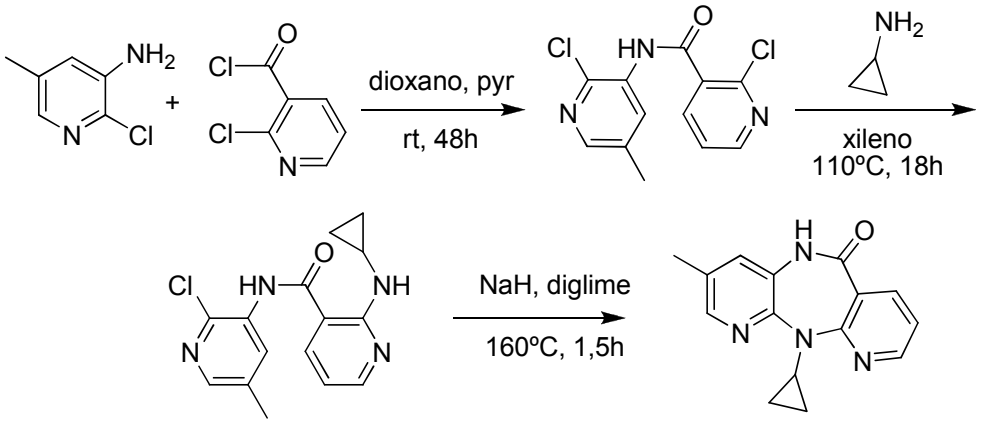


Análisis retrosintético



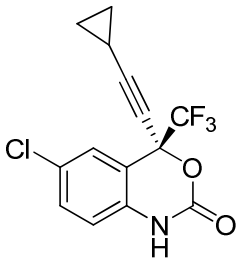
nevirapina

Síntesis

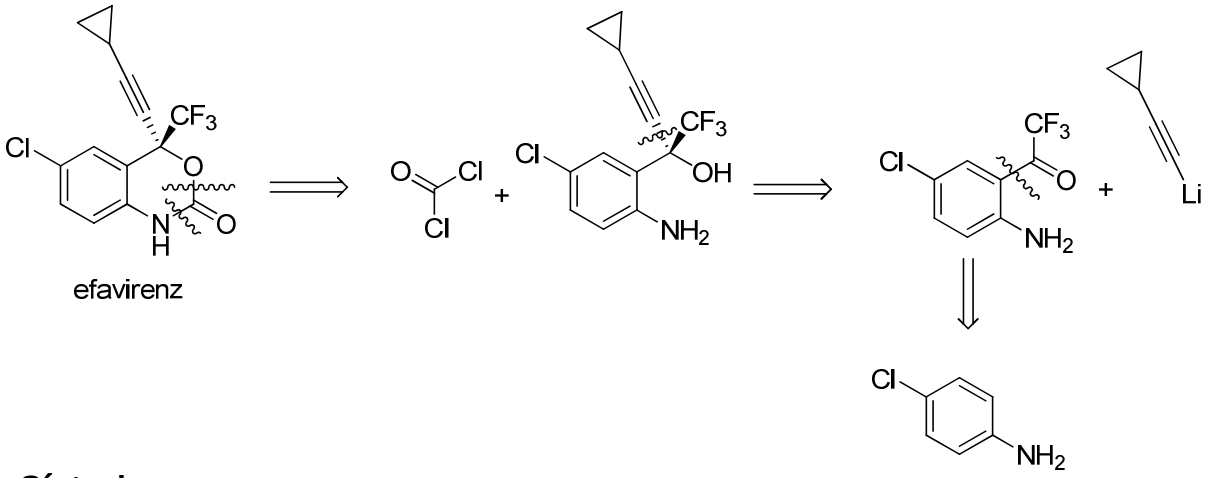


Inhibidores de la transcriptasa reversa

Efavirenz



Análisis retrosintético



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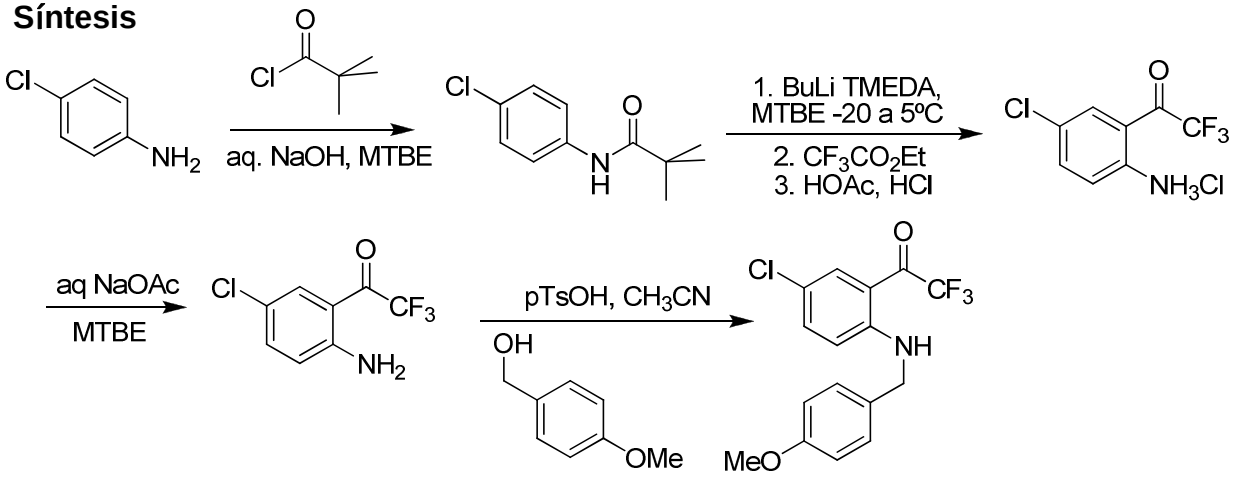
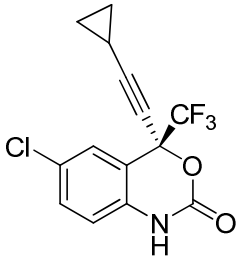


Inhibidores de la transcriptasa reversa

Efavirenz



Síntesis