



Aula 8 – 15/07

Tópicos Especiais em Química Medicinal

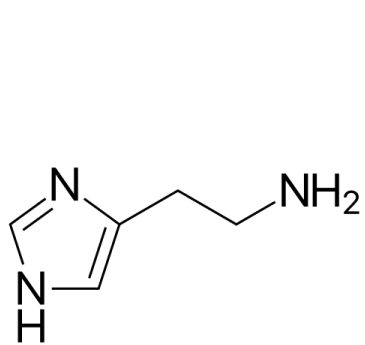
**Tópicos Especiais
em Química Medicinal**
Código: **BMF-777**
Carga Horária: 45 horas
Créditos: 3 créditos



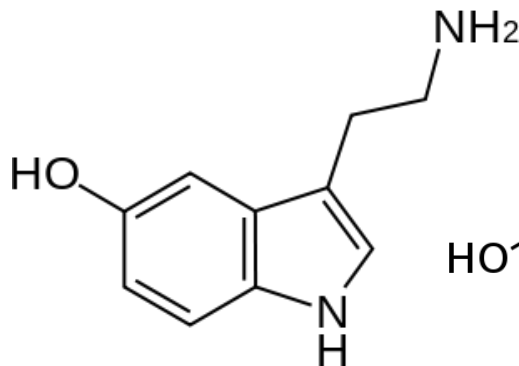
A fábula hindu dos sete cegos e o elefante...



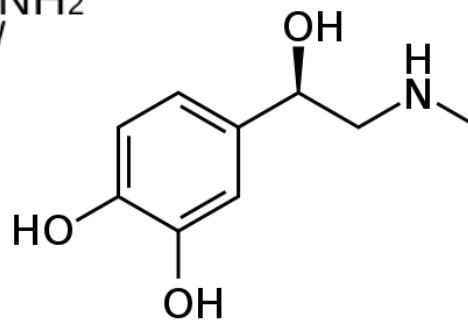
Efeitos conformacionais



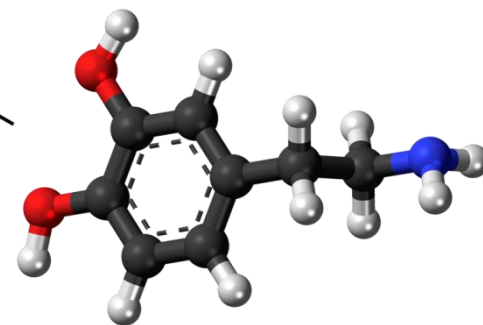
histamina



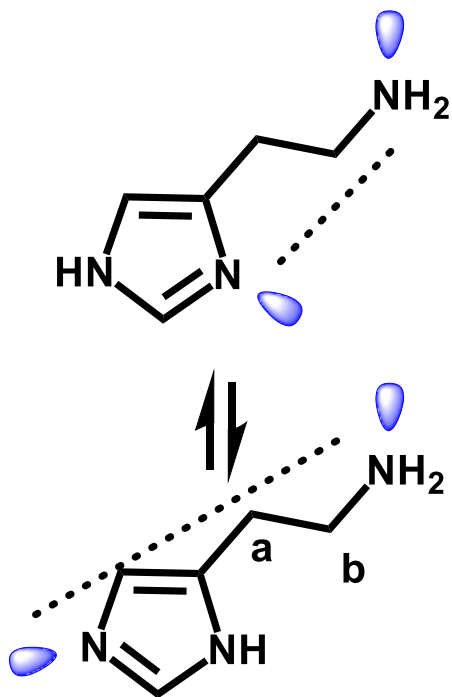
serotonina



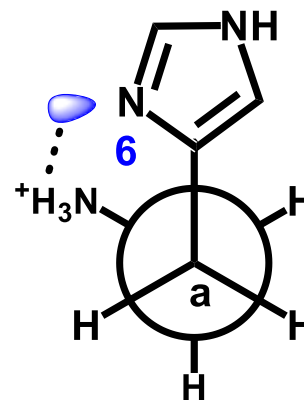
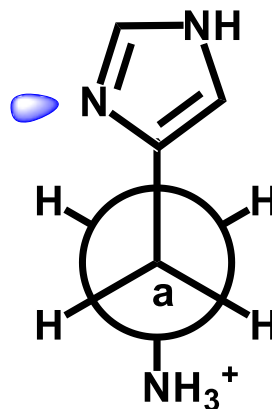
adrenalina



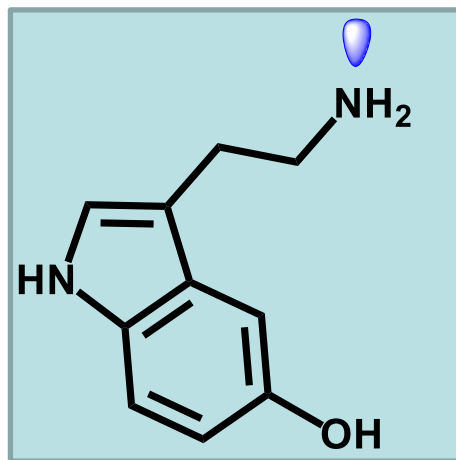
dopamina



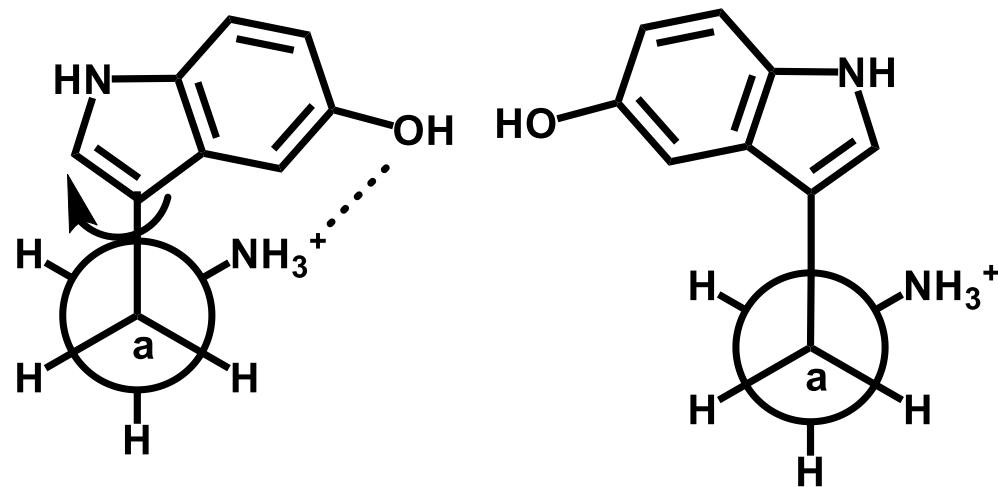
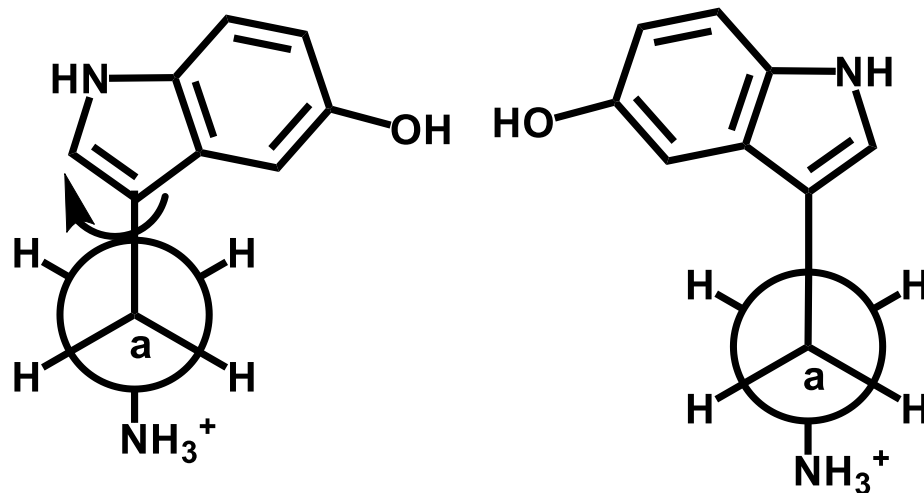
histamina



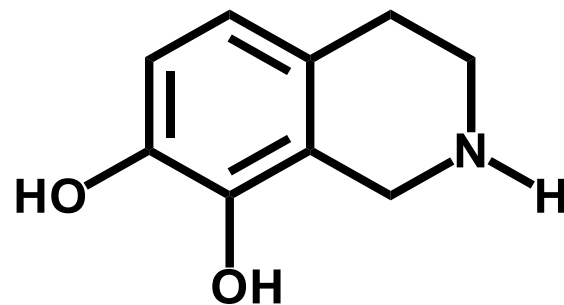
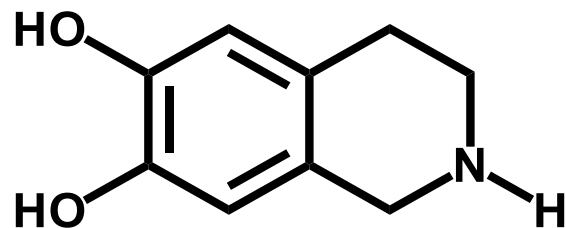
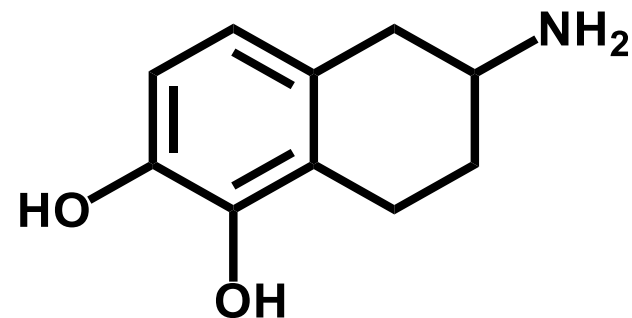
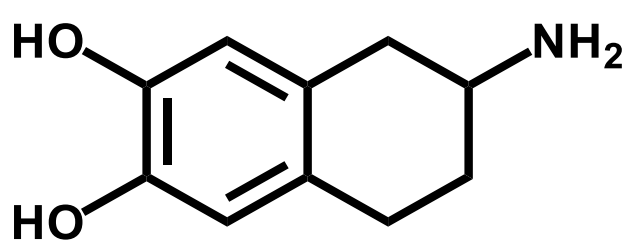
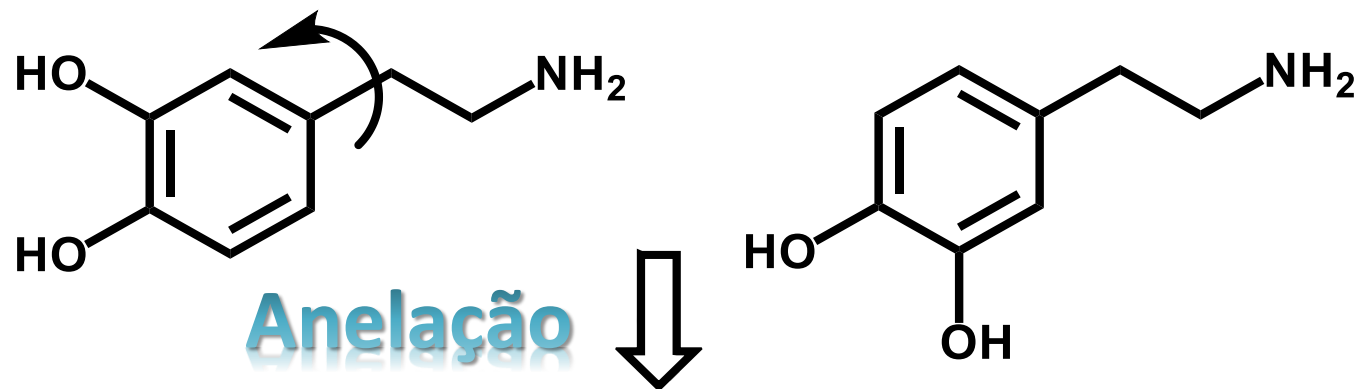
Efeitos conformacionais



serotonina

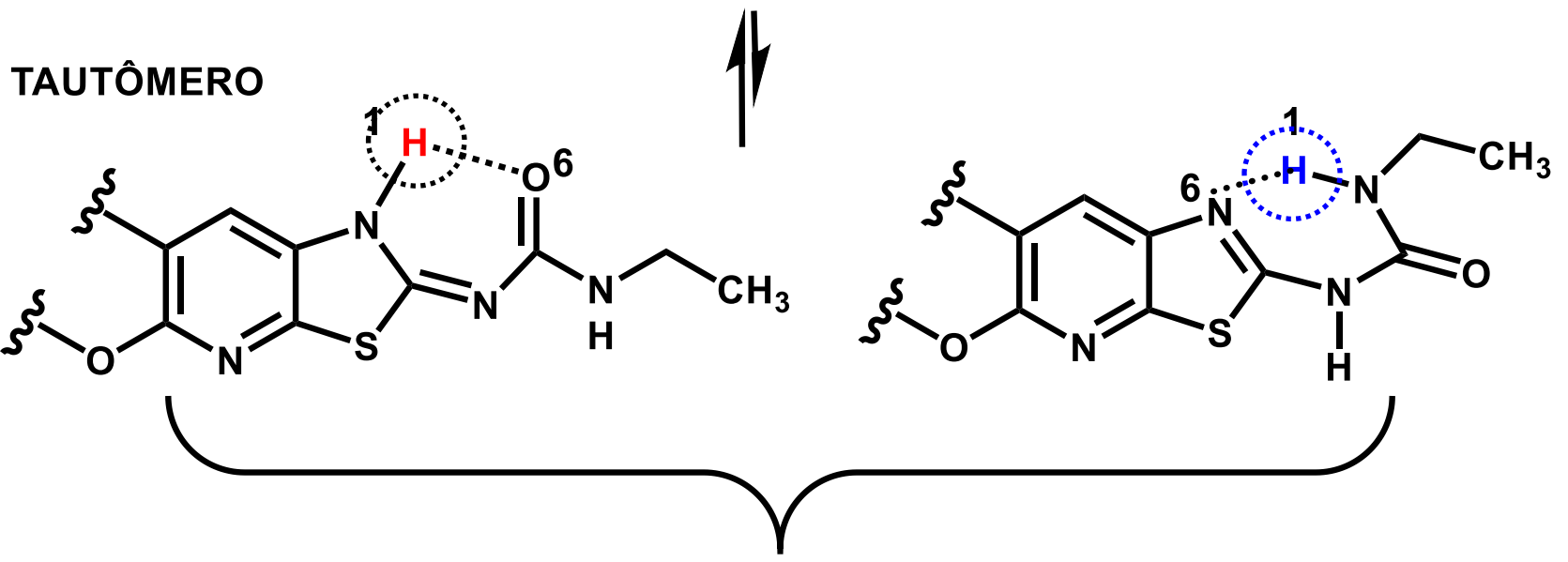
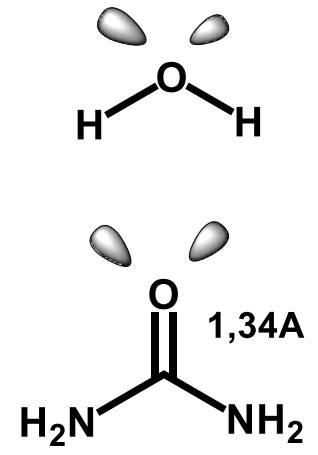
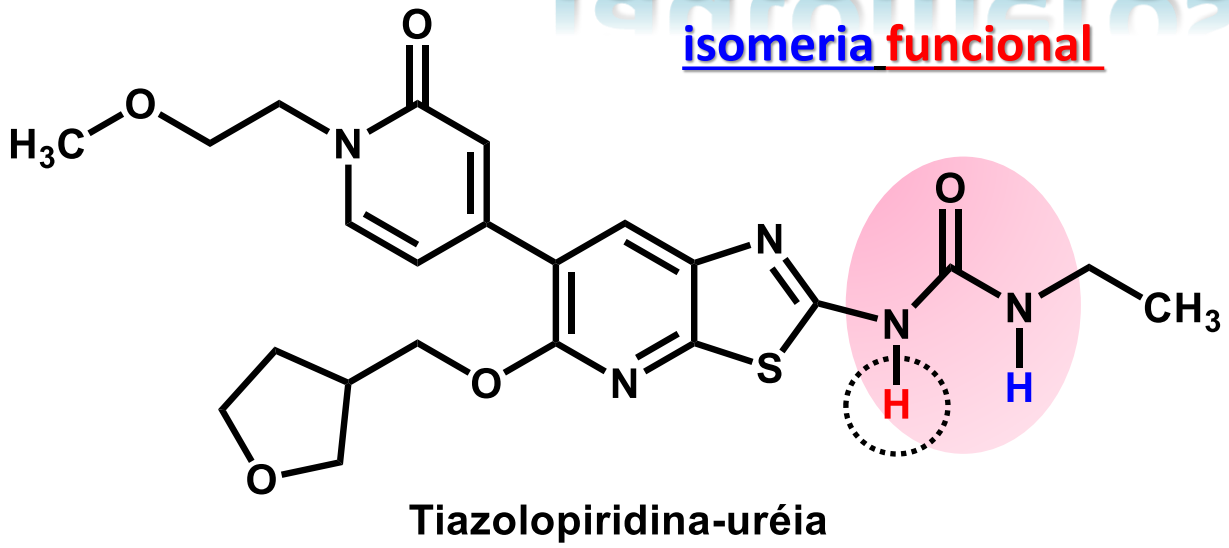


Determinação da conformação bioativa



Tautômeros

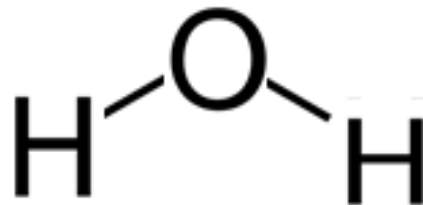
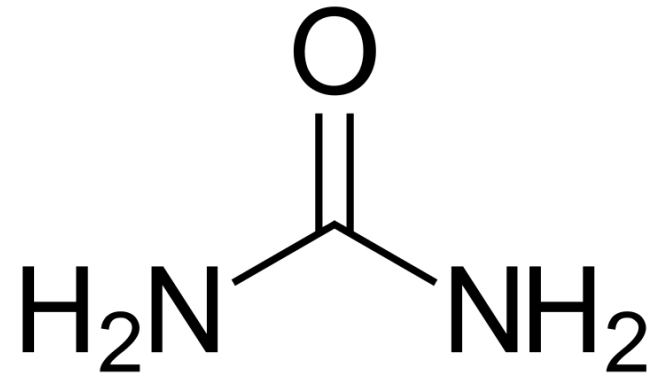
isomeria funcional



Interação-H intramolecular



A uréia e a água....

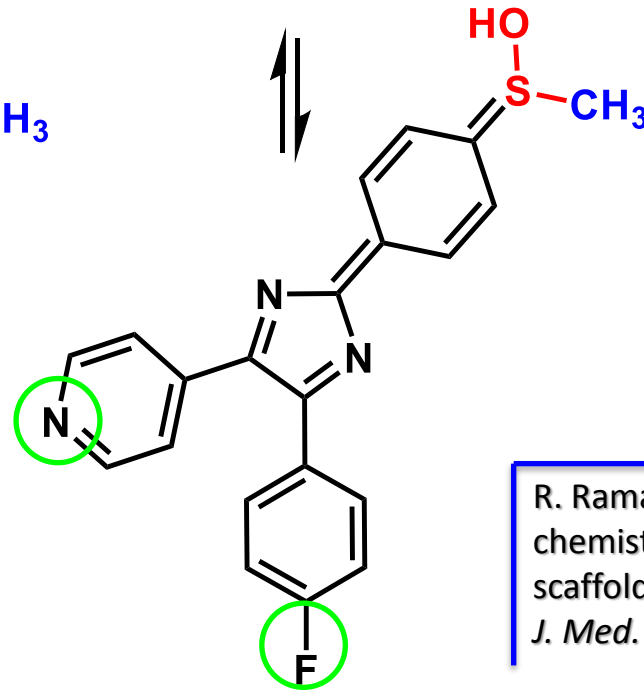
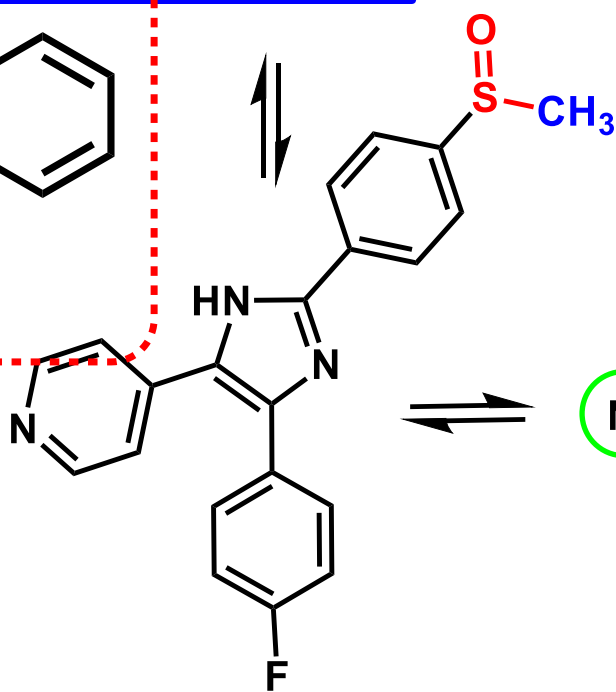
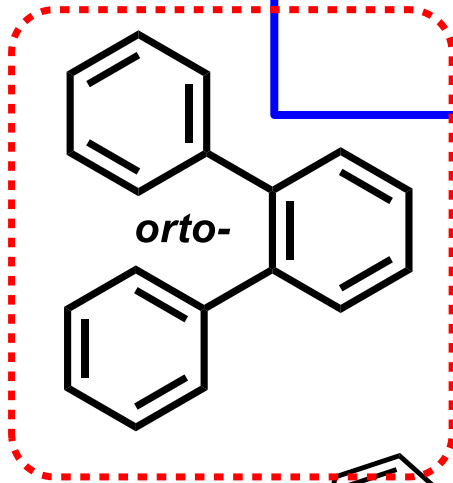
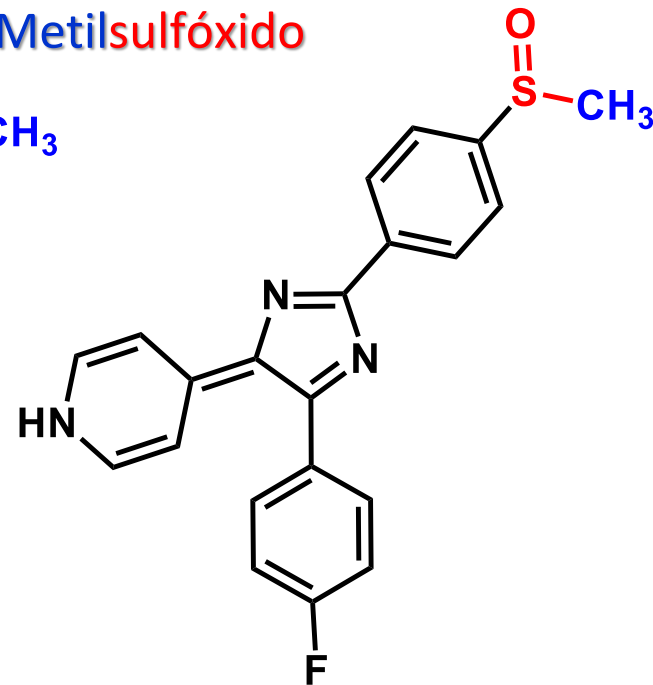
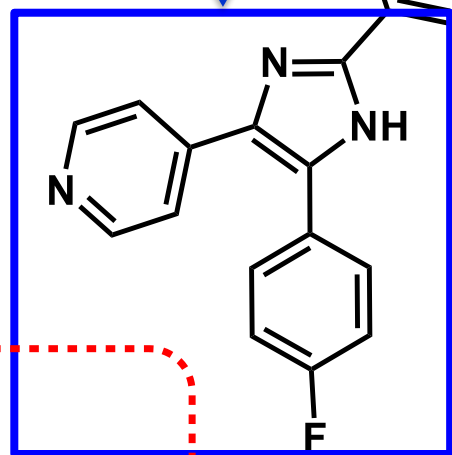


Similaridade molecular

Sistema terfenila

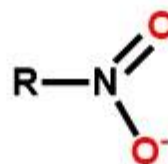
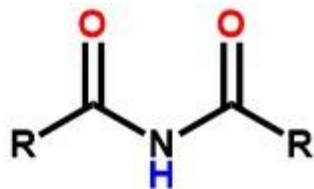
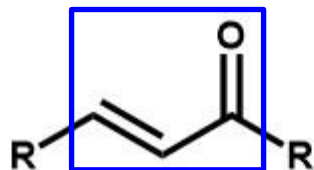
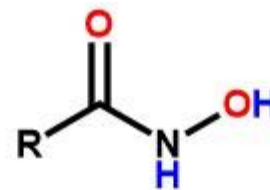
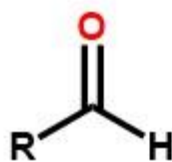
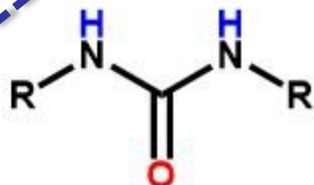
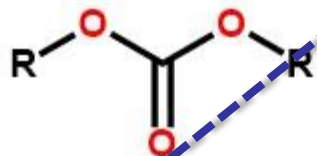
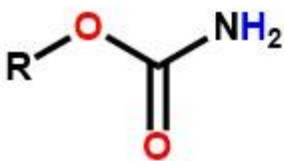
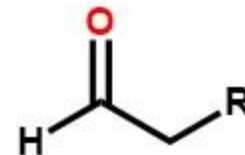
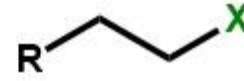
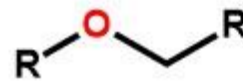
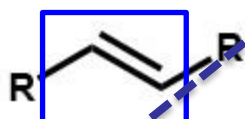
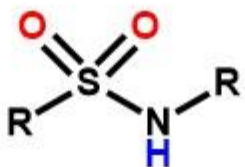
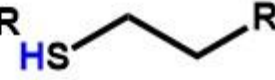
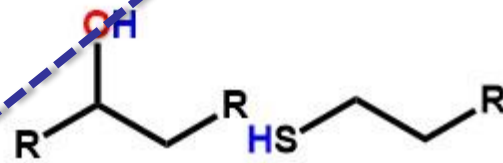
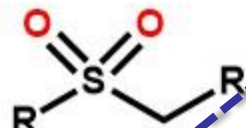
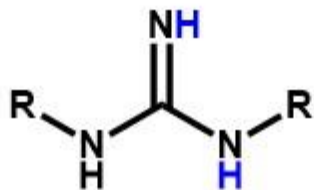
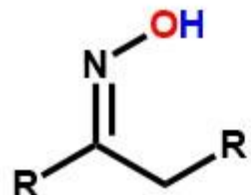
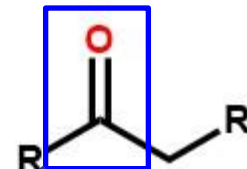
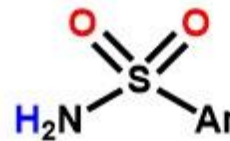
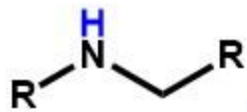
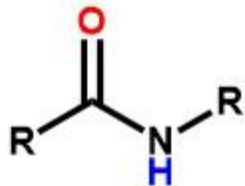
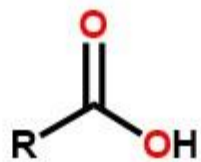
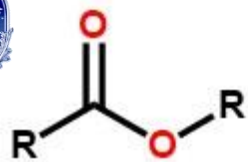
Metilsulfóxido

SB-203580



Tautômeros
isomeria funcional

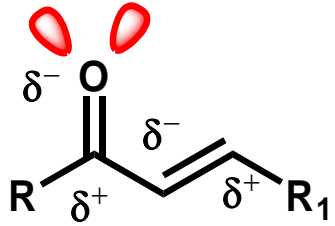
R. Ramajayam, Medicinal chemistry of vicinal diaryl scaffold: A mini review, *Eur. J. Med. Chem.* **2019**, 162, 1.





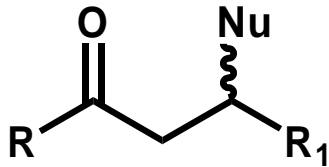
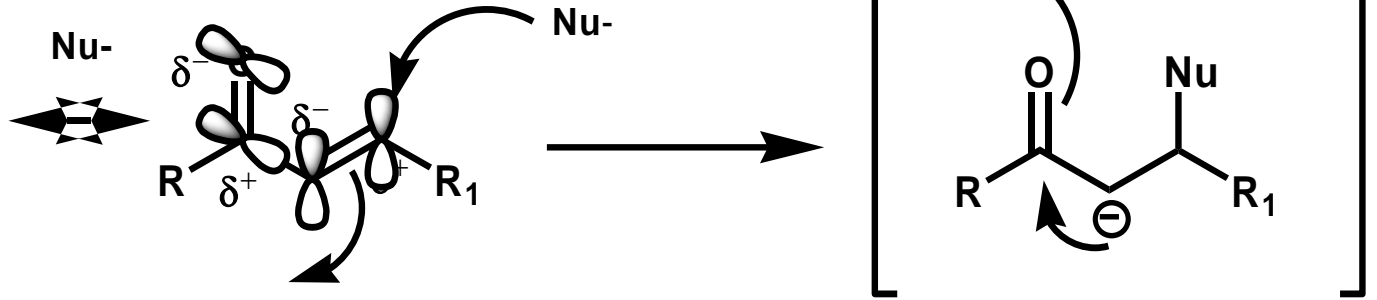
Formação de aducto de Michael

Enona (C=O α,β -ins)



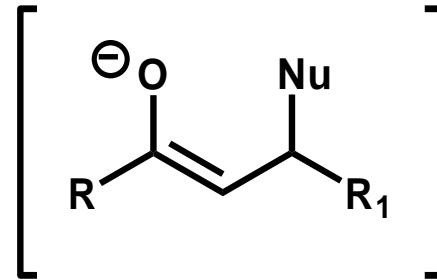
Função mixta

Nu- = nucleófilo biológico



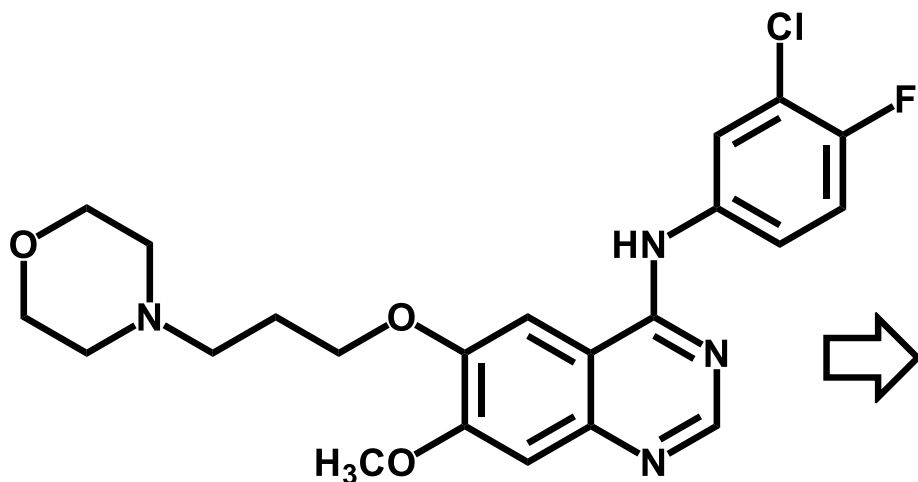
aduto

(irreversível)



Acrilamidas

Inibidores covalentes irreversíveis



Gefitinibe

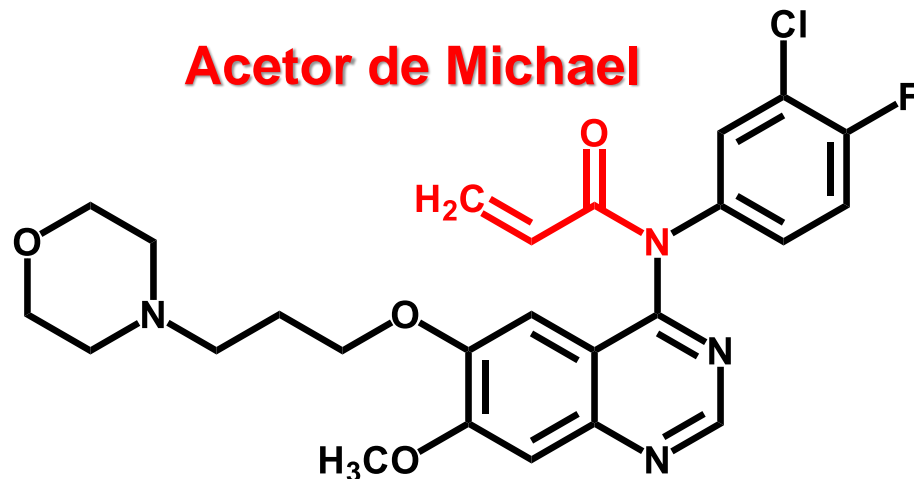
EGFR IC₅₀ < 0,5 nM

A549 IC₅₀ = 5,74 μM

Log D_{7,4} = 2,41



Acetor de Michael



Análogo N-acrilamida

EGFR IC₅₀ = 65,2 nM

A549 IC₅₀ = 0,15 μM

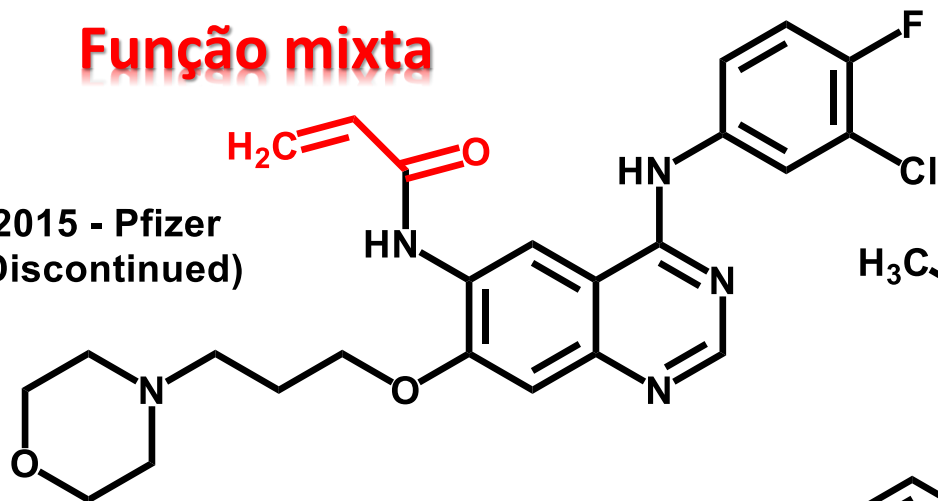
Log D_{7,4} = 2,01



Grupos funcionais reativos

Função mixta

2015 - Pfizer
(Discontinued)

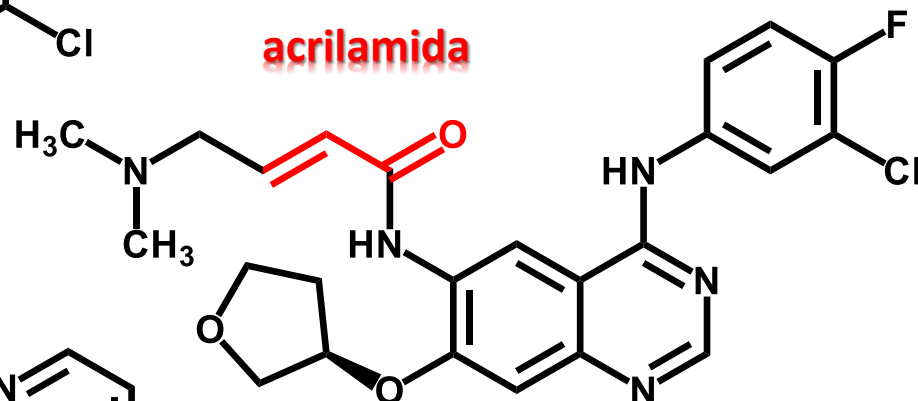


Canertinibe

$C_{24}H_{25}ClFN_5O_3$

EGFR / HER-2 / ErbB-4

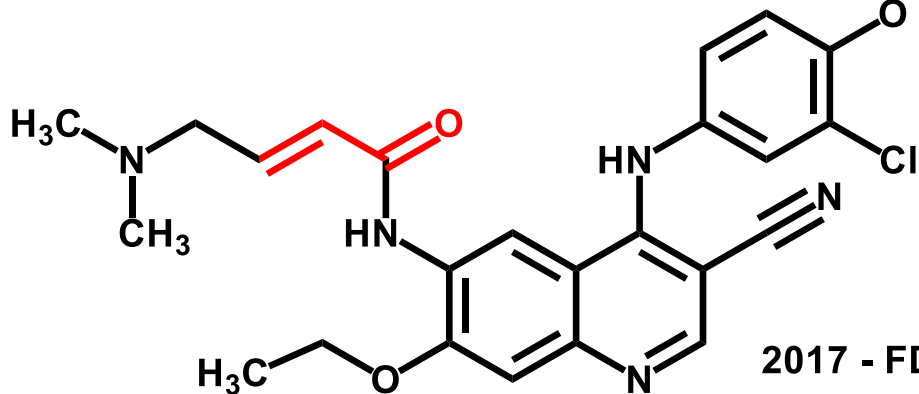
acrilamida



Afatinibe

$C_{24}H_{25}ClFN_5O_3$

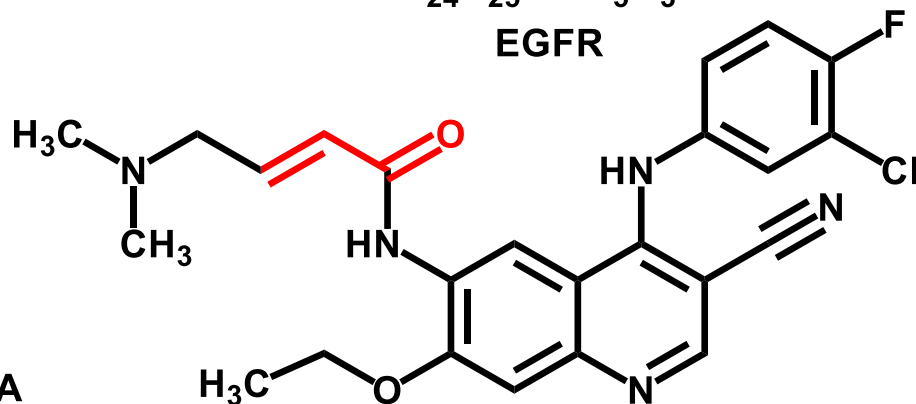
EGFR



Neratinibe

$C_{30}H_{29}ClN_6O_3$

2017 - FDA
HER-2



Pelitinibe

EGFR

$C_{24}H_{23}ClFN_5O_2$