Additions to imines

Reductive amination

Mannich reaction

$$CH_3$$
 H H_2N CH_3 $Mannich Reaction$ N CH_3 N CH_3 CH_2 CH_3 N CH_3 CH_3 CH_3 CH_4 CH_5 CH_5 CH_6 CH_7 CH_8 CH_8

Strecker reaction

Alkylation reactions

Simple alkylation with alkyl halides

Gabriel synthesis

H-N:
$$\frac{[1] \text{ KOH}}{[2] \text{ RX}} \xrightarrow{\text{OH}} \frac{\text{OH}}{\text{H}_2\text{O}} + \frac{\text{CO}_2^-}{\text{CO}_2^-}$$

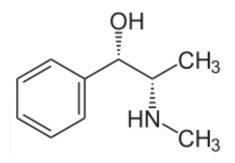
$$1^{\circ} \text{ amine}$$

Preparation of amines: By reduction

Nitro compounds
$$R-NO_2$$
 $rac{Or}{Fe, HCl}$ $rac{Or}{Fe, HCl}$ $rac{1° amine}{1° amine}$ Nitriles $R-C\equiv N$ $rac{[1] LiAlH_4}{[2] H_2O}$ $rac{R-NH_2}{1° amine}$ $rac{Old}{II}$ $rac{III}{II}$ $rac{II}{II}$ $rac{III}{II}$ $rac{III}$ $rac{III}{II}$ $rac{III}{II}$

Amines: Key components of bioactive compounds

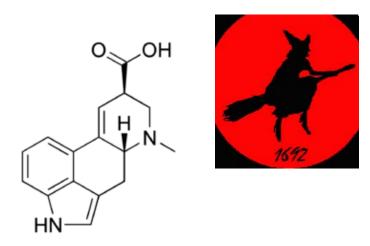
Synthetic medicinal agents





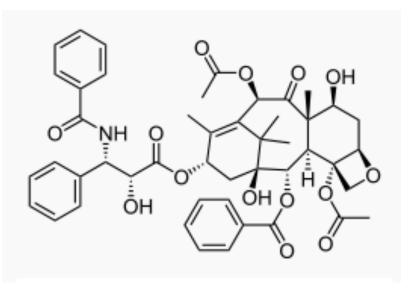
psuedoephedrin

Infamous natural products



Lysergic acid

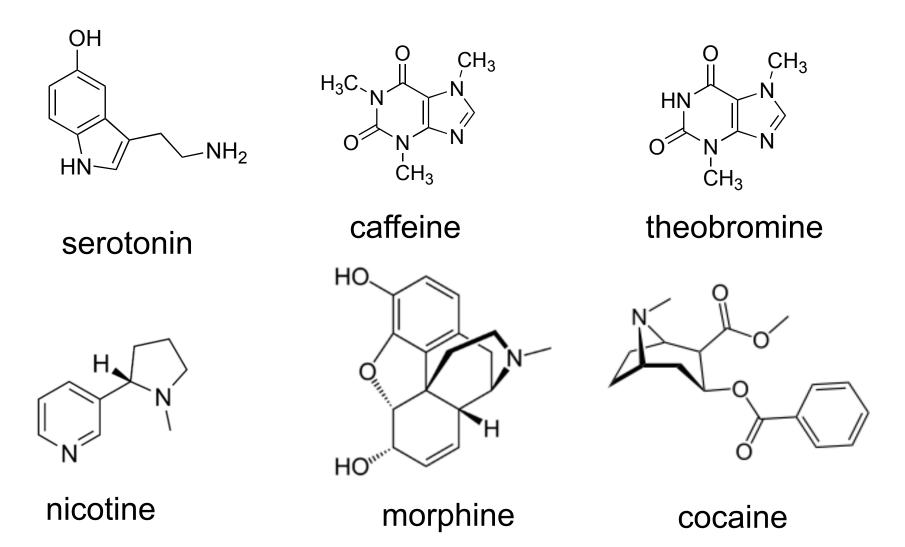
Beneficial natural products



Taxol® From Yew tree



Alkaloids: Nitrogen-containing Natural Products



Often target our receptors... and have a bitter taste

Natural Product: Quinine

chemical defense systems

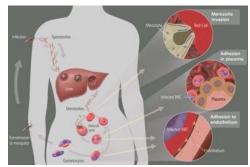
Isolated from cinchona tree (South America):



"Quina-Quina"
Muscle relaxant used by
Quechuas

1st used to treat malaria In Rome, 1631:





Quinine: the active ingredient

Isolated in early 1800's

Tonic Water: Contains Quinine





Tonic Water: Contains Quinine



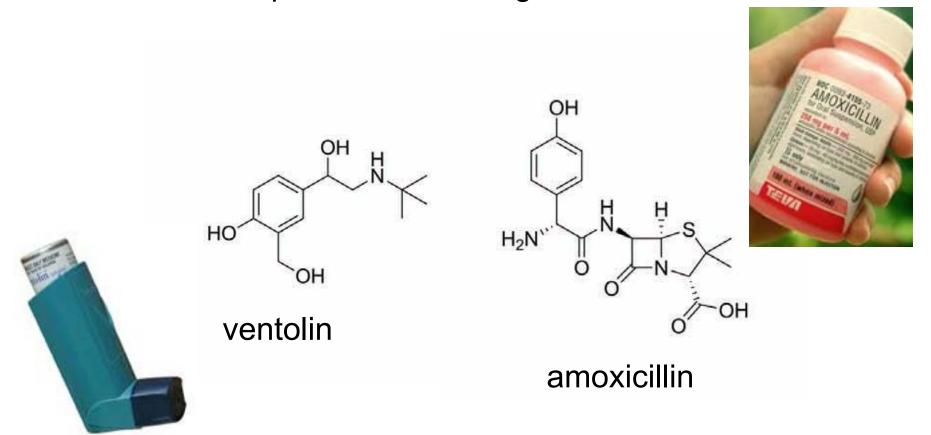




Pharmaceutical agents containing amines

Amines provide great properties: bind enzymes and exhibit good pharmacokinetics

Most pharmaceutical agents contain N



Top 5 name-brand drugs 2012 (by US sales)

http://cbc.arizona.edu/njardarson/group/ top-pharmaceuticals-poster NexIUM

(Esomeprazole)

AstraZeneca \$5,989 Million
ANTIULCERANTS

ANTIULCERANTS

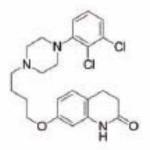
4 Advair Diskus

(Fluticasone Propionate)



2 Abilify

(Aripiprazole)





5 Cymbalta

(Duloxetine)

\$4,720 Million ANTIDEPRESS.& MOOD STAB.

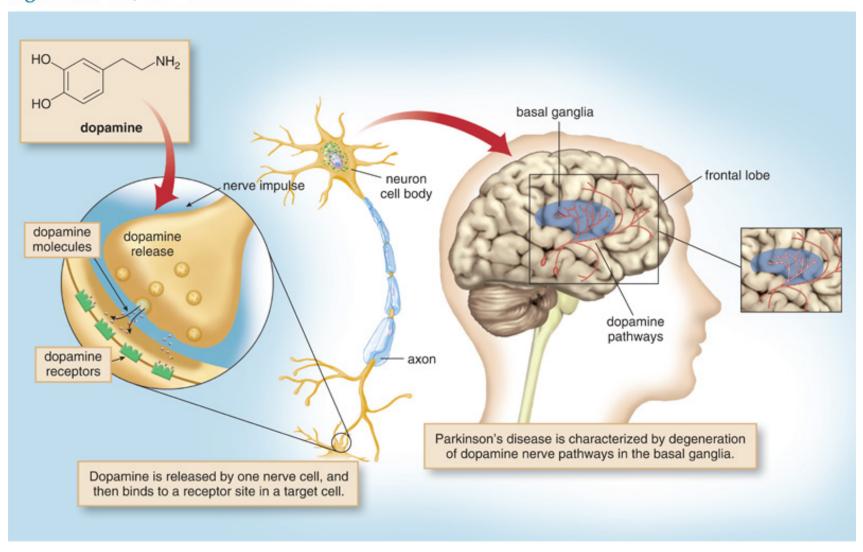
3 Crestor

(Rosuvastatin)



Dopamine: for Parkinson's

Figure 25.6 Dopamine—A neurotransmitter



See the movie: Awakenings (starring Robin Williams and Robert DeNiro)