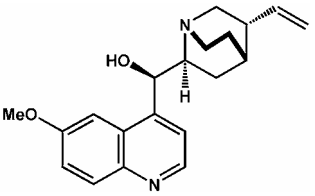
Quinine

Powdered dried bark of the cinchona tree, a native of South America, was made into a drink and used by the Quechua Indians of Peru to treat fevers.

"Discovered" by Jesuit priests in the 1620s, Barnabé de Cobo takes cinchona bark to Europe in 1632 to treat malaria.

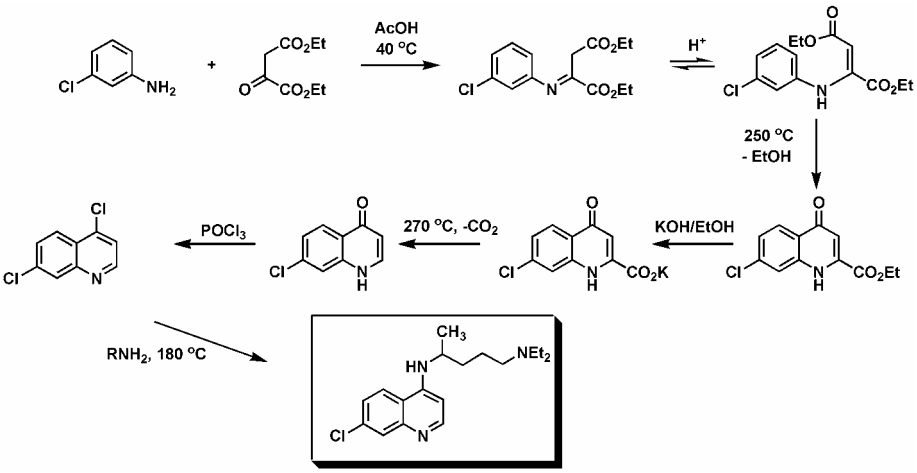
Quinine isolated in 1820 by Pierre Joseph Pelletier and Joseph Caventou



First Total Synthesis (1943) RB Woodward and WE von Doering

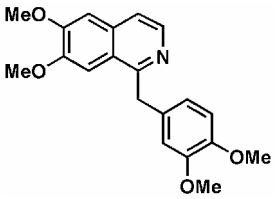
Synthesis of Chloroquine

using the Conrad-Limpach quinolone method



Papaverine

Papaverine is an opium alkaloid found in the opium poppy, but papaverine differs in both structure and pharmacological action from the other opium alkaloids.

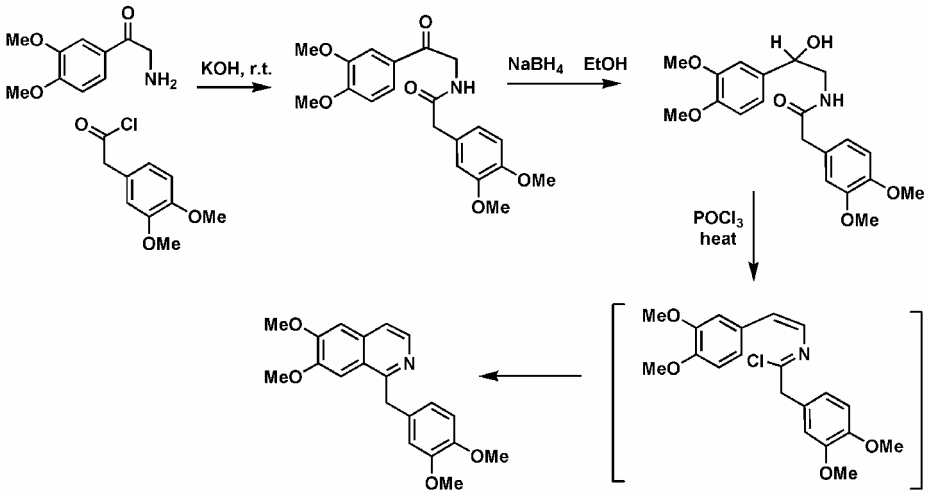


Paperverine is a smooth muscle relaxant. It belongs to the group of medicines called vasodilators.

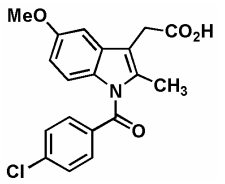
Vasodilators cause blood vessels to expand, thereby increasing blood flow, and are used to treat problems resulting from poor blood circulation.

Synthesis of Papaverine

using the Pictet Gams modification of the Bischler-Naperialski method

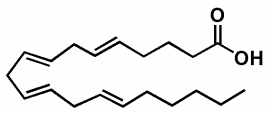


Indomethacin

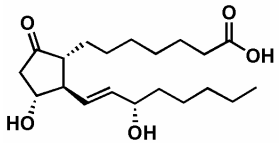


Indomethacin is a non-steroidal anti-inflammatory drug (NSAID) discovered in 1963

Indomethacin is a non-selective inhibitor of cyclooxygenase 1 and 2 (COX1 and COX2), enzymes that participate in biosynthesis of prostaglandins from arachidonic acid.



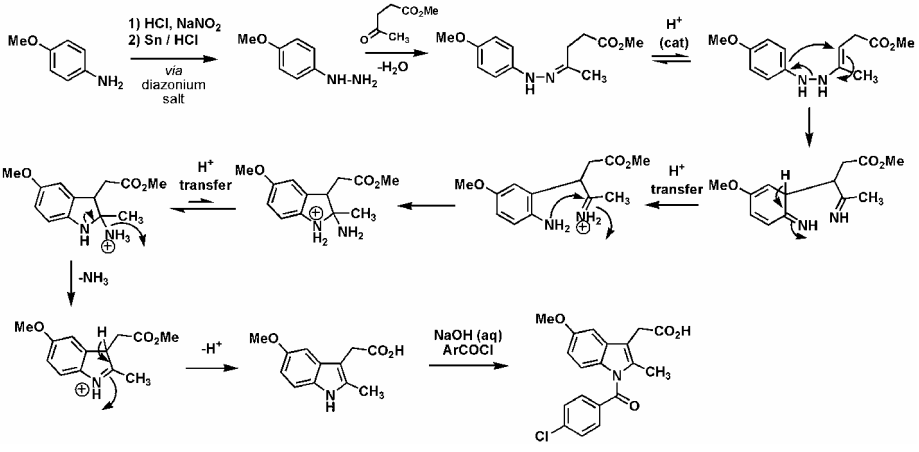
Prostaglandins are hormone-like molecules which have a wide variety of effects, some of which lead to pain, fever, and inflammation.



Prostaglandin E_1 (PGE_1)

Synthesis of Indomethacin

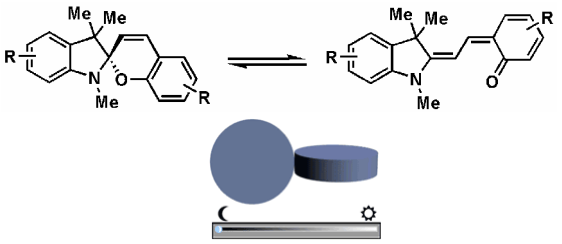
using the Fischer indole synthesis



Spirooxazines

Photochromic materials change colour upon the action of UV light or direct sunlight. A structural change alters the conjugation in the molecule and thus the absorption of the molecule in the visible part of the electromagnetic spectrum.

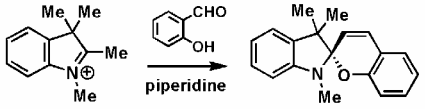
In this example the spiro system twists from a perpendicular (closed) form to a flat, planar (opened) structure *via* an electrocyclic ring opening reaction.

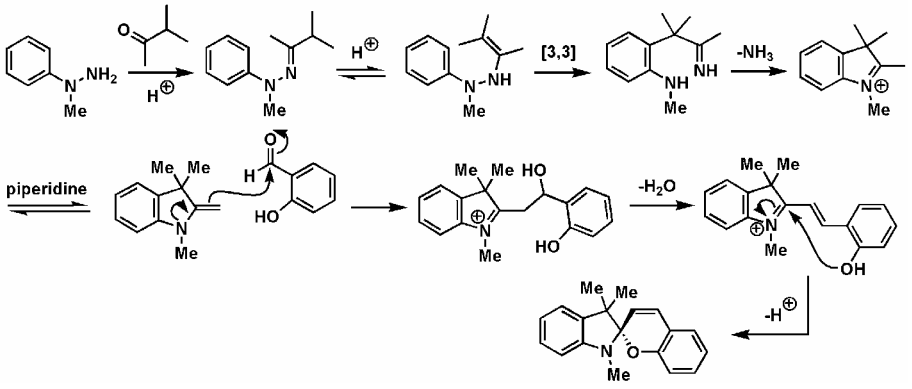


This allows the two halves to become conjugated, resulting in the absorption of visible light and a change from colourless to coloured

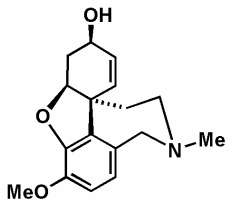
Synthesis of spirooxazines

Fischer indole followed by an aldol-like condensation and cyclization



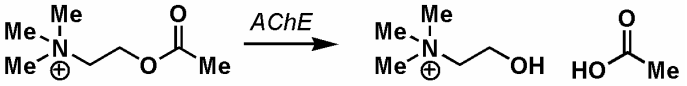


Galanthamine



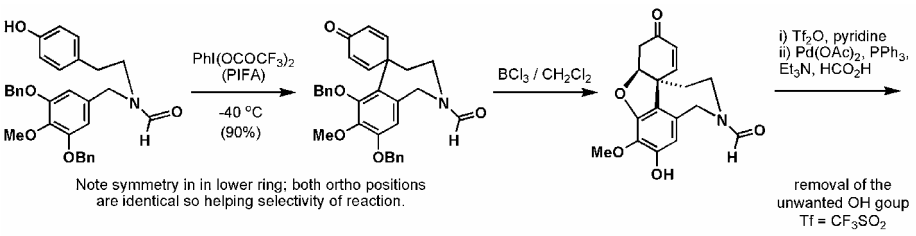
Galanthamine is isolated from the common snowdrop (*Galanthus nivalis*).

Galanthamine inhibits acetylcholine esterase (AChE) which is a key enzyme involved in the transmission of nerve impulses.



It has been approved for use as a treatment for Alzheimer's disease.

Synthesis of Galanthamine

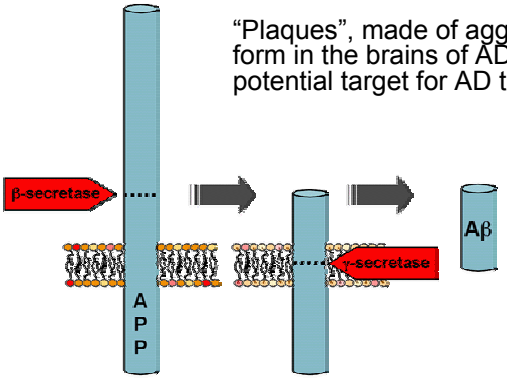


Note symmetry in in lower ring; both ortho positions are identical so helping selectivity of reaction.

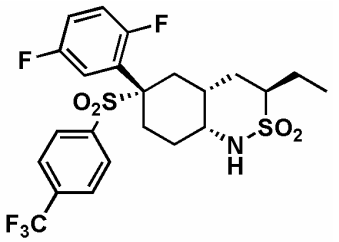
γ Secretase Inhibitors

Alzheimer's disease (AD) is a progressive and chronic neurodegenerative disease that leads to loss of intellect and memory.

A pathological characteristic of this disease the production of the 40-42 residue peptide amyloid-β (Aβ). The protease enzyme γ-secretase plays a critical role through cleavage of the β-amyloid precursor protein (βAPP).

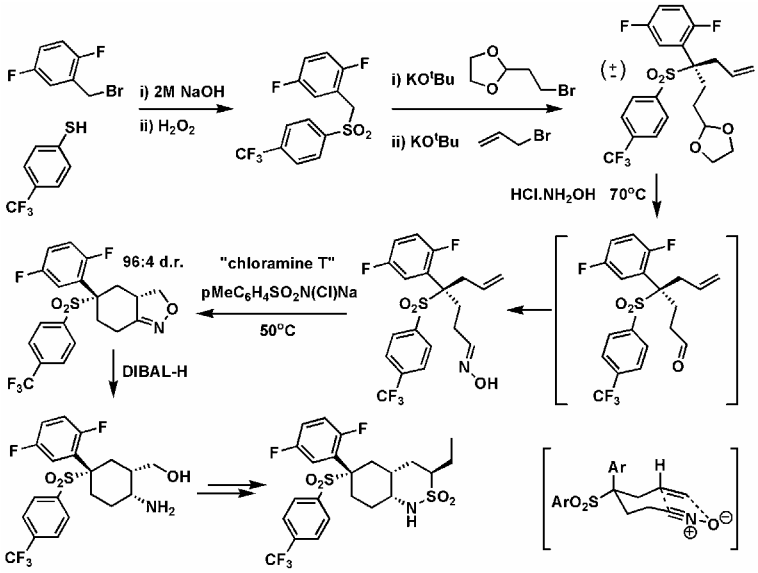


"Plaques", made of aggregates of the Aβ peptide, can form in the brains of AD patients. γ-Secretase is a potential target for AD therapeutic intervention.

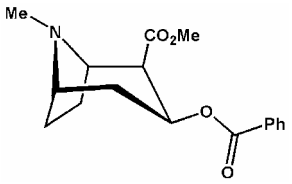


Merck lead compound

Inhibitor Synthesis



Cocaine



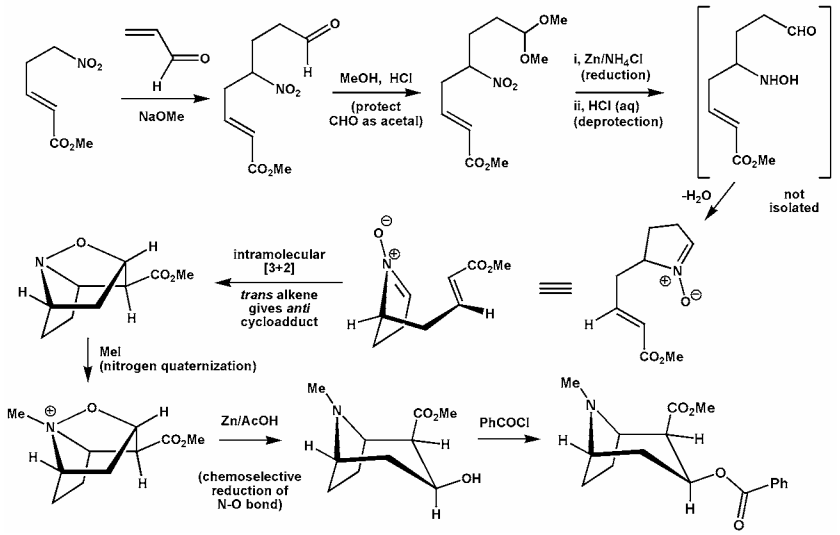
Cocaine is a crystalline tropane alkaloid that is obtained from the leaves of the coca plant.

It is a stimulant of the central nervous system and an appetite suppressant, creating what has been described as a euphoric sense of happiness and increased energy.

Cocaine is also a topical anaesthetic used in eye, throat, and nose surgery

The pharmacodynamics of cocaine are complex.

Synthesis of Cocaine



Further Information

The references below relate to the synthetic methods presented only. General information about the compounds and their applications can be found on the web and in the library.

- **Chloroquine:** *J. Am. Chem Soc.*, 1946, **68**, 113-116.
- **Papaverine:** *J. Org. Chem.*, 1981, **46**, 3742-3745 and *Chem. Ber.*, 1909, **42** 2951.
- **Indomethacin:** *J. Am. Chem Soc.*, 1955, **77**, 4319-4324 and *J. Am. Chem Soc.*, 1963, **85**, 488-489.
- **Photochromics:** see, for one example of many, *J. Heterocycl. Chem.*, 2004, **41**, 103-108 (synthesis of indolium salt) and *J. Heterocycl. Chem.*, 2002, **39**, 179-184 (synthesis of spirooxazine).
- **Galanthamine:** *Angew. Chem., Int. Ed. Engl.*, 2001, **40**, 3060.
- **γ-Secretase inhibitor:** *J. Org. Chem.* 2006, **71**, 3086-3092.
- **Cocaine:** *Tetrahedron Lett.*, 1978,1733-1736.