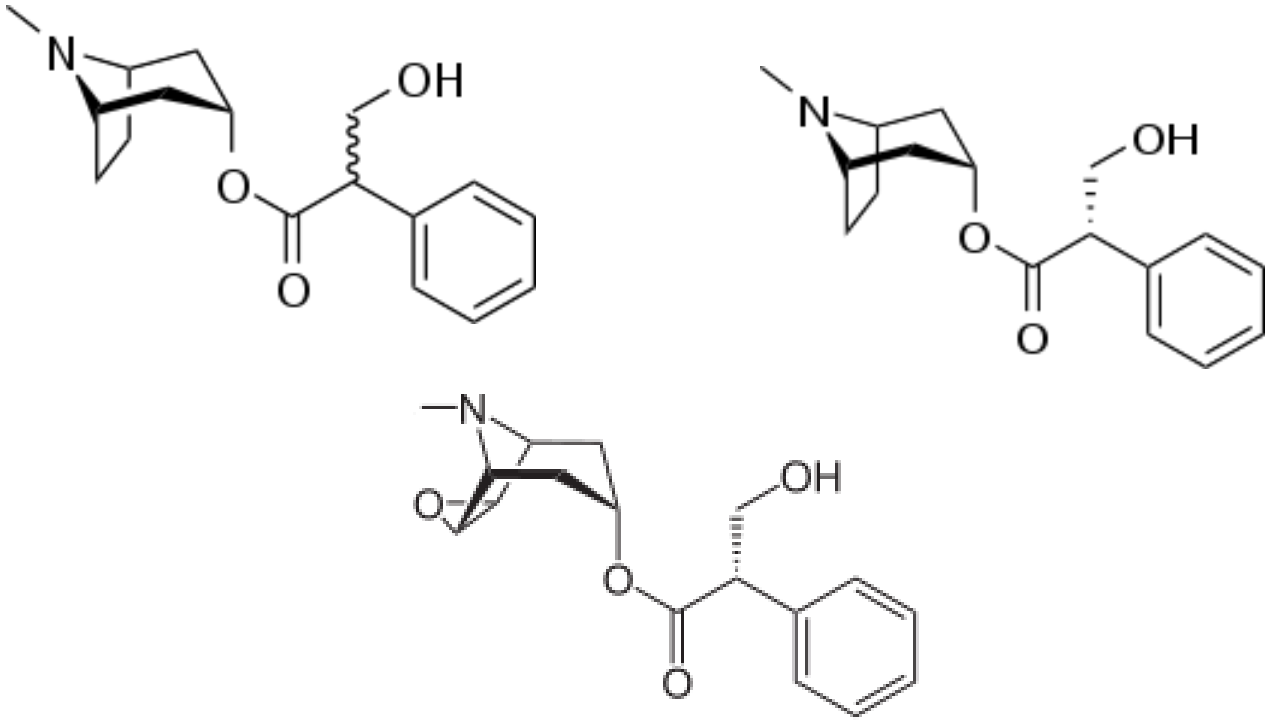
Pharmacognosy
Alkaloids

Lec 7

Tropane alkaloids

Atropine, hyoscyamine and hyosine (scopalamine)



Atropine (racemic alkaloid), hyosyamine L-form, scopalamine is epoxy-hyosyamine

Belladonna, Henbane and Thornapple

(-)-Hyoscyamine: from *Atropa belladonna* and *Hyoscyamus niger*.

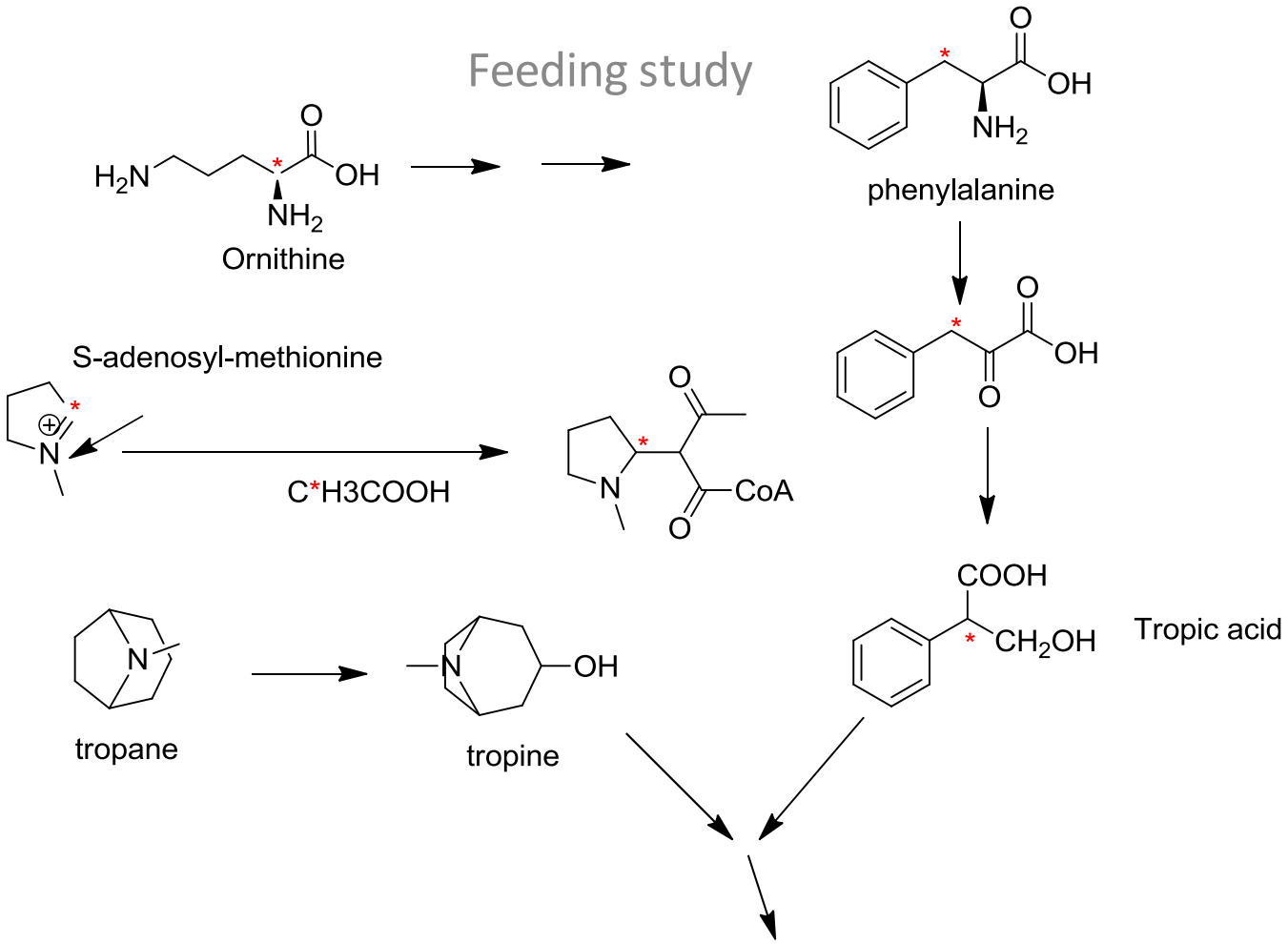
Atropine: the racemic mixture (±) of hyoscyamine, found in *A. belladonna*

Formerly used as a smooth muscle relaxant – now used in eye examinations to open the pupil (=mydriatic) and in acute arrythmias

Hyoscine (scopolamine): from *Datura stramonium* etc. used to prevent travel sickness and to dry up nasal secretions before anaesthesia

All are anti-cholinergic (anti-muscarinic)

Follow the label



(-) Hyosyamine from feeding of labeled ornithine to datura

Datura stramonium

Thornapple

Deadly nightshade

Atropa belladonna

me *Atropa* comes from the Greek Fate, who in mythology cut the thread of life.

onna' comes from the Italian utiful lady, and refers to the use of the juice of the berries of this is plant by ladies in the 16th century to dilate the pupils of the eye, considered an attractive feature

Atropine

Dilation of the pupil

Atropine is used as to dilate the pupil of the eye. It degrades slowly, typically wearing off in 2 to 3 days, so tropicamide (a synthetic shorter-acting cholinergic antagonist) is generally preferred as a mydriatic. The effects of atropine can last up to two weeks.

Atropine induces mydriasis by blocking contraction of the circular pupillary sphincter muscle, which is normally stimulated by acetylcholine release, thereby allowing the radial pupillary dilator muscle to contract and dilate the pupil. Atropine is contraindicated in patients predisposed to narrow angle glaucoma.

Henbane

Hyoscyamus niger

The name henbane came from the Anglo-Saxon *hennbana* = "killer of hens".

It was traditionally used in German pilsner beers as a flavouring, until the Bavarian Purity Law was passed in 1516 and outlawed the use of Henbane and allowed only the use of hops

Henbane was also known to have been used as an anaesthetic in the first Arab hospitals

Tropane alkaloids 2: Cocaine

From Coca leaves - a shrub, *Erythroxylum coca*, found only at high altitudes, in the Andes (Peru, Bolivia, and Columbia)

Coca (still) used by locals to ease altitude sickness and reduce hunger and fatigue

Cocaine is a CNS stimulant widely used illicitly, as the salt, the ‘free base’ and now as ‘crack’ (made with sodium bicarbonate)

cocaine rarely used medicinally now, and only as a local anaesthetic in eye surgery

Coca: *Erythroxylum coca*

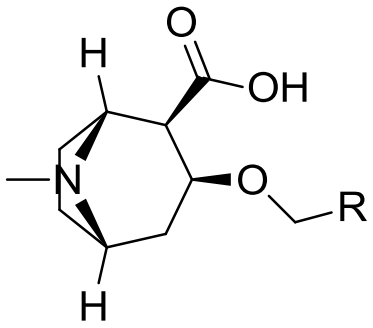
Cocaine occurs in the leaf as the free base – but this is not very stable so it is extracted using a dilute acid, to form the salt – and this is the form used pharmaceutically (e.g. cocaine hydrochloride)

It may later be converted back into the free base form because absorption is much faster for non-ionic (i.e. lipophilic) substances

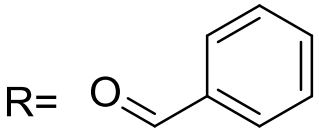
Cocaine

Prepared semisynthetically from of ecgonine

Adrenergic stimulant, local ansthetic cause addiction

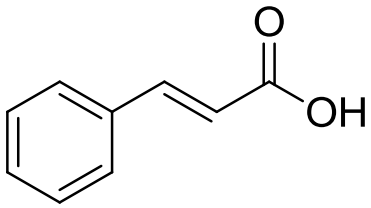


ecgonine

R= 

benzoic acid

or



cinnamic acid

cocaine is derivative of ecgonine

Alkaloid chemistry: crack cocaine

Base (alkaloid) + acid $\rightarrow$ alkaloid salt + water

e.g. Morphine + sulphuric acid $\rightarrow$ morphine sulphate + water

Cocaine base + HCl $\rightarrow$ cocaine HCl + water

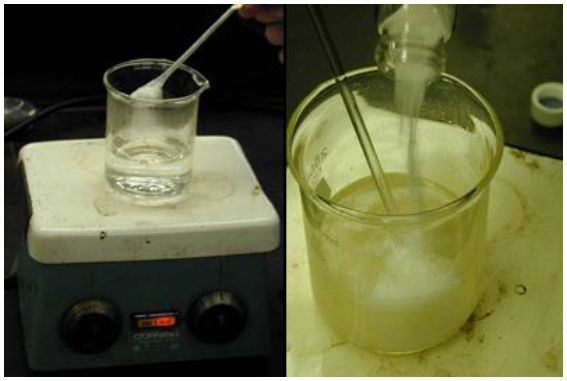
But a weak acid or base is displaced by a stronger one….. so

Cocaine HCl + stronger alkali (e.g. $NaHCO_3$) $\rightarrow$ cocaine base (crack) + salts + water

To make crack, 'powder' cocaine (i.e. the salt) is dissolved in a mixture of water and either ammonia or sodium bicarbonate (baking soda) added. The mixture is boiled to separate out the solid, and then it's cooled. The solid is then dried and cut up into small nuggets, or "rocks."

Although crack cocaine is a form of non-ionic cocaine, because production doesn't require the use of flammable solvents, it is safer to make than 'freebase'

Alkaloid chemistry: making crack (base) cocaine from the salt



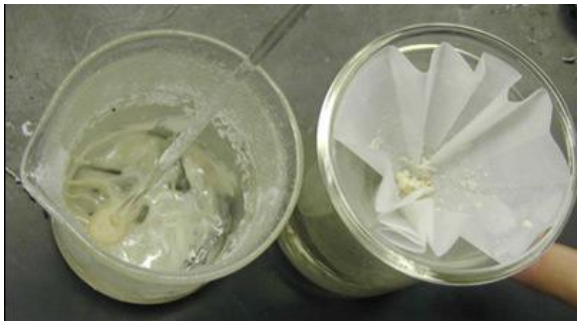
Step 1 (left): Dissolving powder cocaine in hot water

Step 2 (right): Adding sodium bicarbonate to the mixture

Step 3 (left): Boiling the solution to separate out the solids

Step 4 (right): Cooling the separated mixture

Step 5: Filtering the cooled mixture–



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Than you for listining

THE END