Aminoalcohol Esters

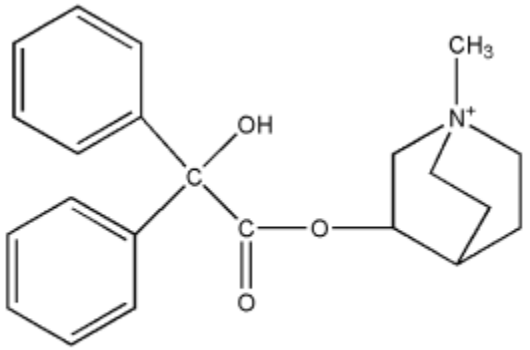
The solanaceous alkaloids are generally agreed to be potent parasympatholytics, but they have the undesirable property of producing a wide range of effects through their nonspecific blockade of autonomic functions.

Efforts to use the antispasmodic effect of the alkaloids most often result in side effects such as dryness of the mouth and fluctuations in pulse rate. Therefore, synthesis of compounds possessing specific cholinolytic actions has been a very desirable field of study.

Clidinium Bromide, USP.

Clidinium bromide, 3-hydroxy-1-methylquinuclidinium bromide benzilate (Quarzan), is a white or nearly white, almost odorless, crystalline powder that is optically inactive. It is soluble in water and alcohol but only very slightly soluble in ether and benzene.

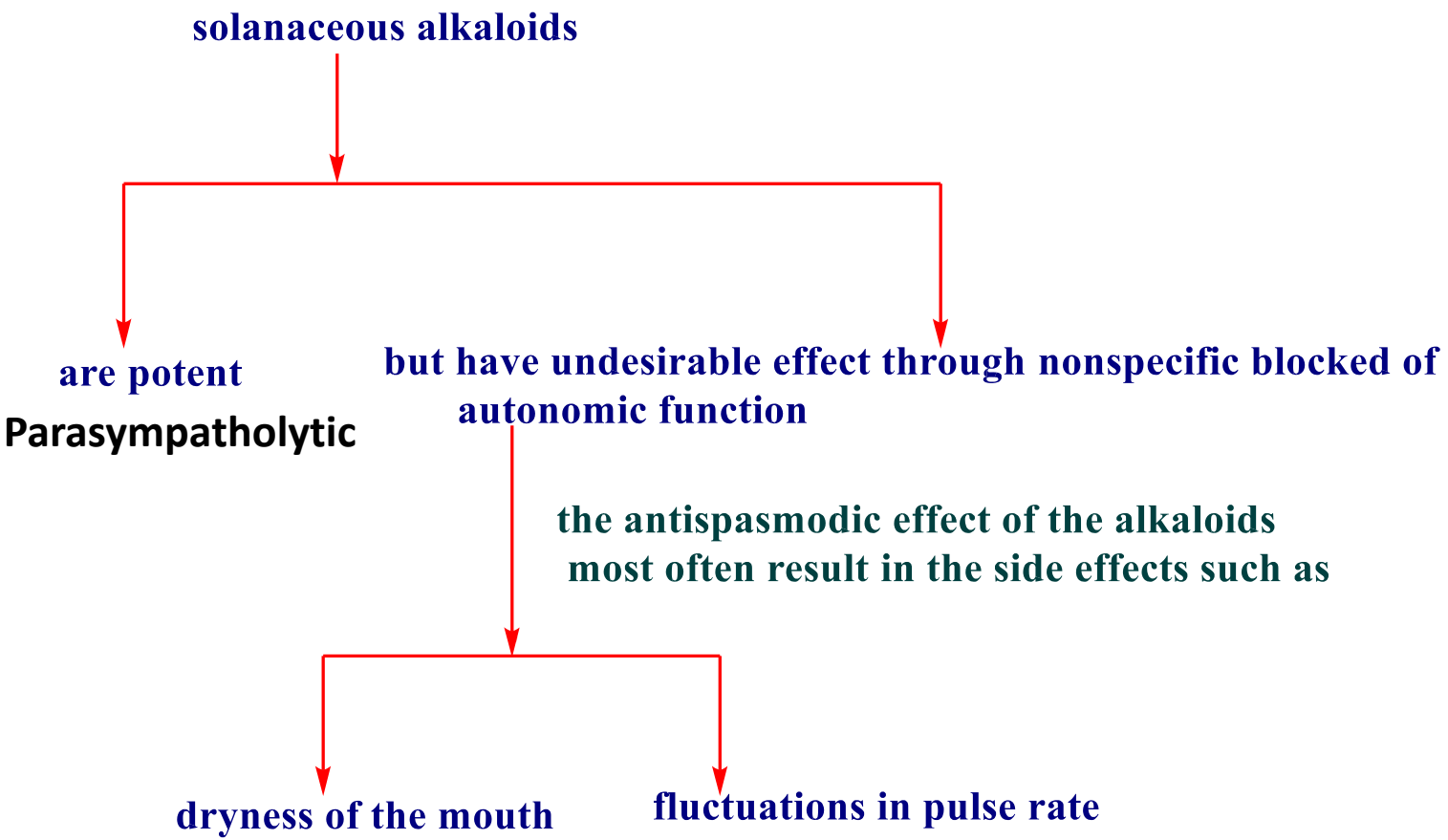
The rationale of the combination for the treatment of GI complaints is the use of an anxiety- reducing agent together with an anticholinergic agent, based on the recognized contribution of anxiety to the development of the diseased condition. It is suggested for peptic ulcer, hyperchlorhydria, ulcerative or spastic colon, anxiety states with GI manifestations, nervous stomach, irritable or spastic colon, and others.



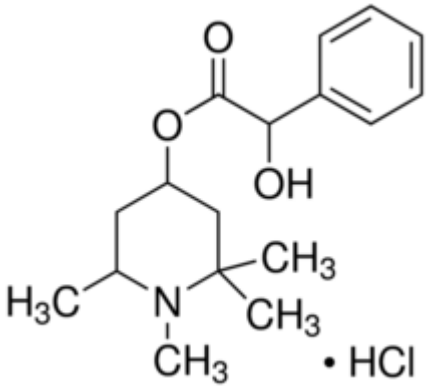
Clidinium Bromide

SYNTHETIC CHOLINERGIC BLOCKING AGENTS

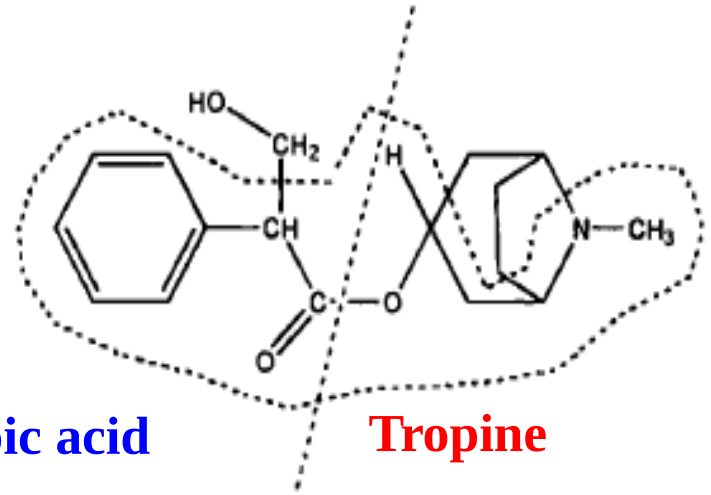
•Aminoalcohol Esters



Synthesis started with rather minor deviations from the atropine molecule, and this structural modification includes-:



Eucatropine



Tropic acid

Tropine

aminoalcohol portion of eucatropine → **monocyclic aminoalcohol**

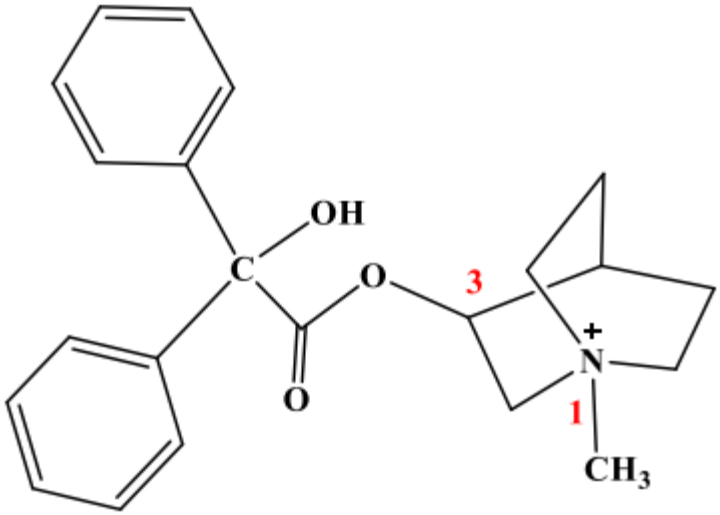
The aminoalcohol portion of eucatropine may be considered a simplification of the atropine molecule. In eucatropine, the bicyclic tropine has been replaced by a monocyclic aminoalcohol and mandelic acid replaces tropic acid → **mandelic acid**

The aminoalcohol ester anticholinergics → **antispasmodics or mydriatics**

aminoalcohol or aminoalcohol ether analogues of atropine → **antiparkinsonian drugs**

Products

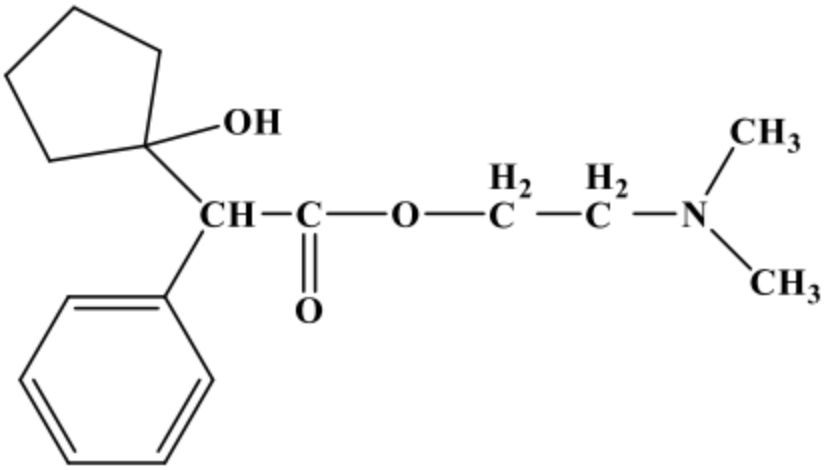
-1Clidinium Bromide.



3-hydroxy-I -methylquinuclidinium bromide benzilate

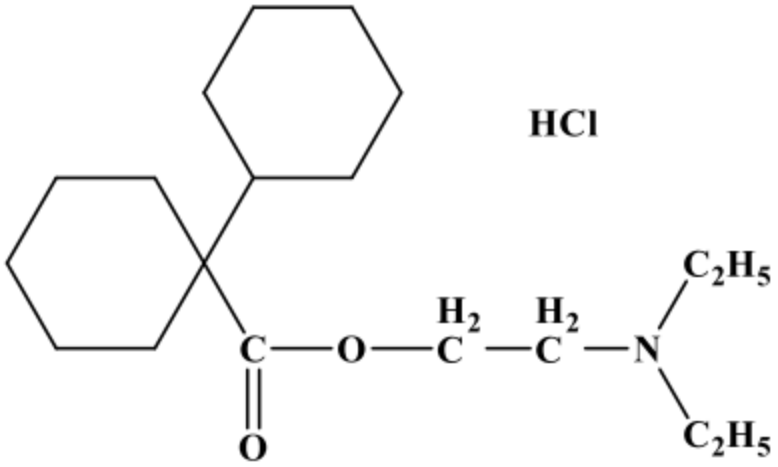
(1-methyl-1-azoniabicyclo{2,2,2}octan-3-yl) 2-hydroxy-2,2-diphenylacetate bromide

-2Cyclopentolate Hydrochloride



2-(dimethylamino)ethyl 2-(1-hydroxycyclopentyl)-2-phenylacetate Hydrochloride

-3Dicyclomine hydrochloride



2-(diethylamino)ethyl -1-cyclohexylcyclohexane- 1 -carboxylate hydrochloride
2-(diethylamino)ethyl bicyclohexyl- 1 -carboxylate hydrochloride

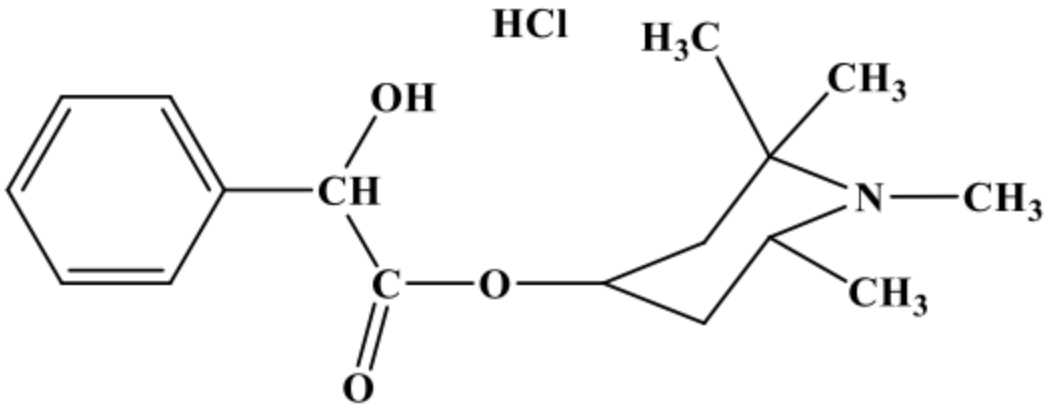
Dicyclomine hydrochloride has some muscarinic receptor subtype selectivity. It binds more firmly to M1 and M3 than to M2 and M4 receptors. Dicyclominc hydrochloride has one eighth of the neurotropic activity of atropine and approximately twice the musculotropic activity of papaverine. This preparation,has minimized the adverse effects associated with the atropine-type compounds.

Uses-:

It is used for its spasmolytic effect on various smooth muscle spasms. particularly those associated with the GI tract.

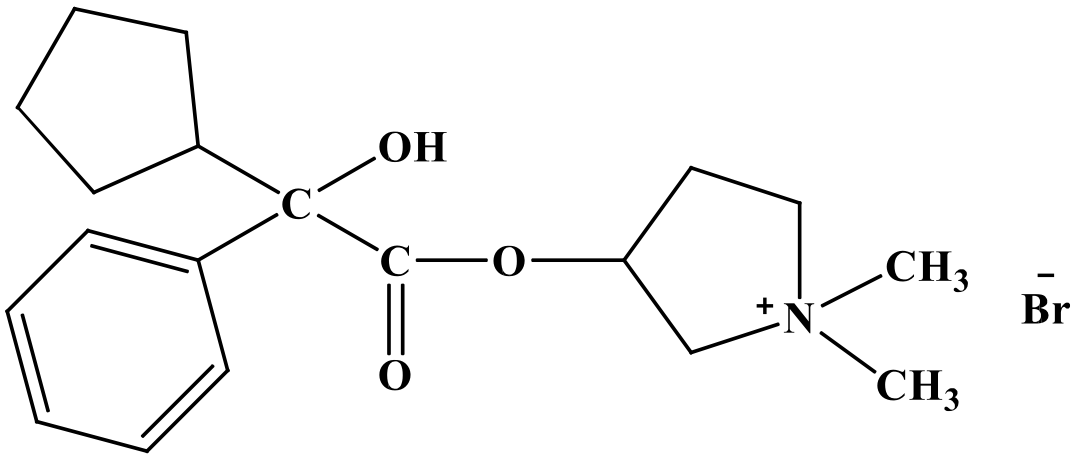
It is also useful in dysmenorrhea. Pylorospasm, and biliary dysfunction.

4- Eucatropine Hydrochloride



I ,2,2,6-tetramethyl-4-piperidyl mandelate hydrochloride

5- Glycopyrrolate



3-hydroxy- 1,1-dimethylpyrrolidinium bromide- α-cyclopentylmandelate

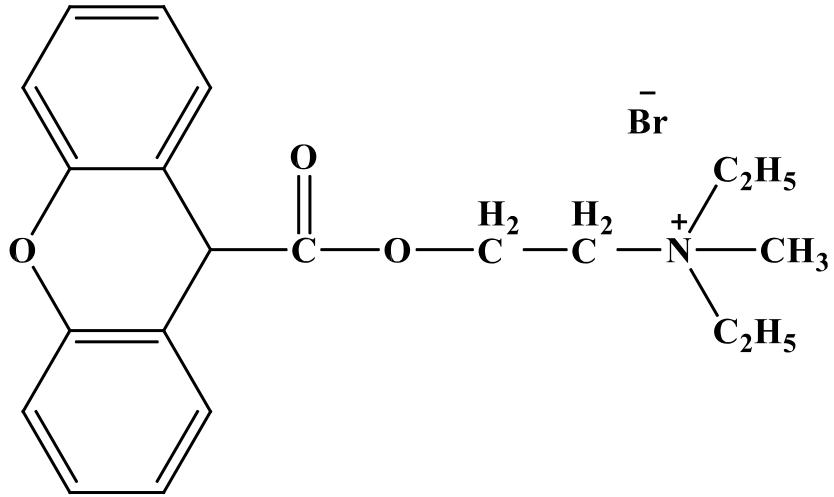
Uses:-

- **It has a spasmolytic effect on the musculature of the GI tract as well as the genitounnary tract.**

- **It diminishes gastric and pancreatic secretions and the quantity of perspiration and saliva.**
- **Glycopyrrolate is a more potent antagonist on M1 than on M2 and M3 receptors, The low affinity of M2 receptors may, in part, explain the low incidence of tachycardia during use of this drug as an antispasmodic.**
- **Because of its quaternary ammonium character glycopyrrolate rarely causes CNS disturbances, though in sufficiently high dosage it can bring about ganglionic and myoneural junction block.**

S/E:- it is has like atropine S/E(dryness of the mouth, urinary retention, blurred vision and Constipation)

6- Methantheline Bromide.



diethyl(2-hydroxyethyl)methylammonium bromide xanthene-9-carboxylat

It is a potent anticholinergic agent and acts at the nicotinic cholinergic receptors of the sympathetic and parasympathetic systems, as well as at the myoneural junction of the postganglionic cholinergic fibers.
Like other quaternary ammonium drugs. methantheline bromide is absorbed incompletely from the GI tract.

Uses:-

•Gastritis, intestinal hypermotility. **2- Pancreatitis.**

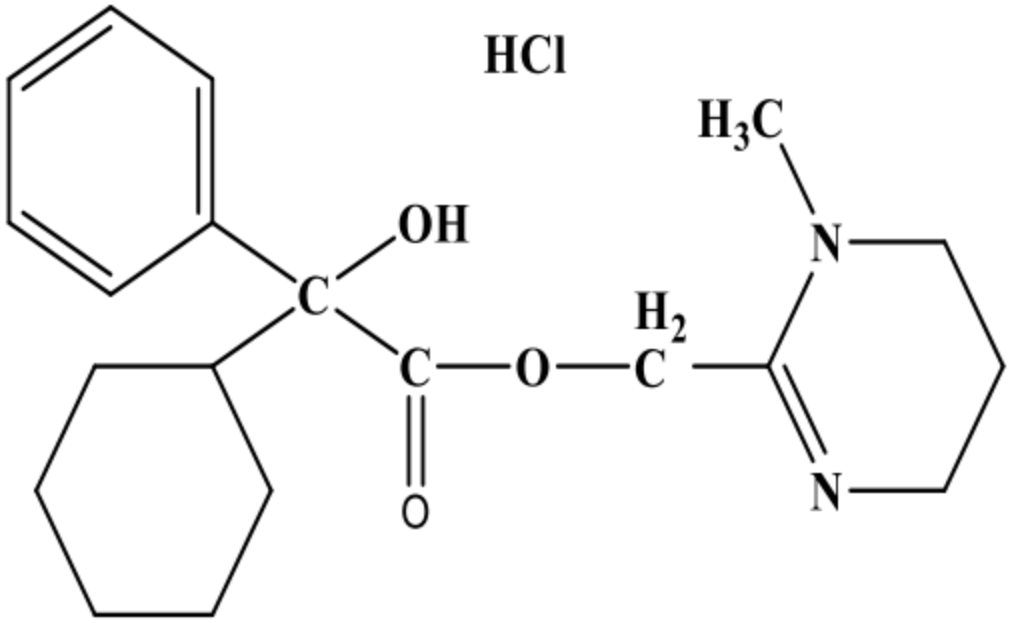
• hyperhidrosis. **4- Bladder irritability.**

• Cholinergic spasm. **6- Peptic ulcer.**

S/E :- like atropine (mydriasis. cycloplegia. dryness of mouth)

C/I:- glaucoma

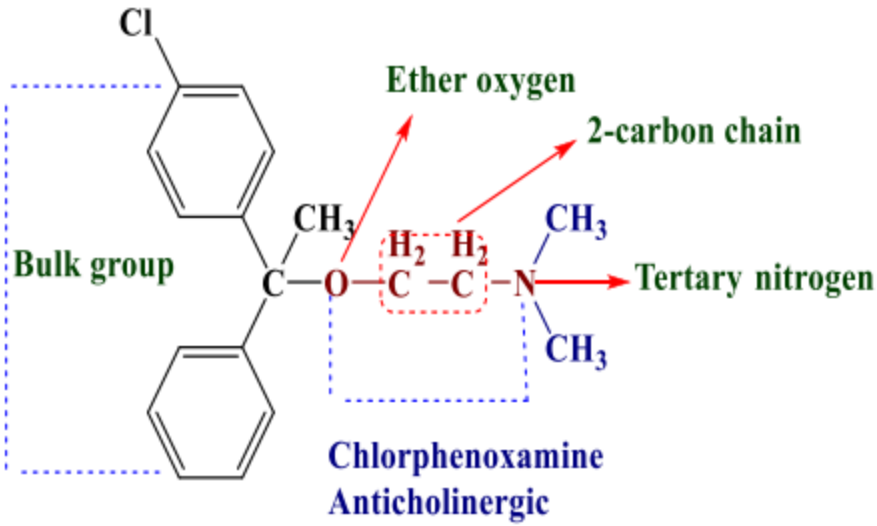
7- Oxyphencyclimine Hydrochloride

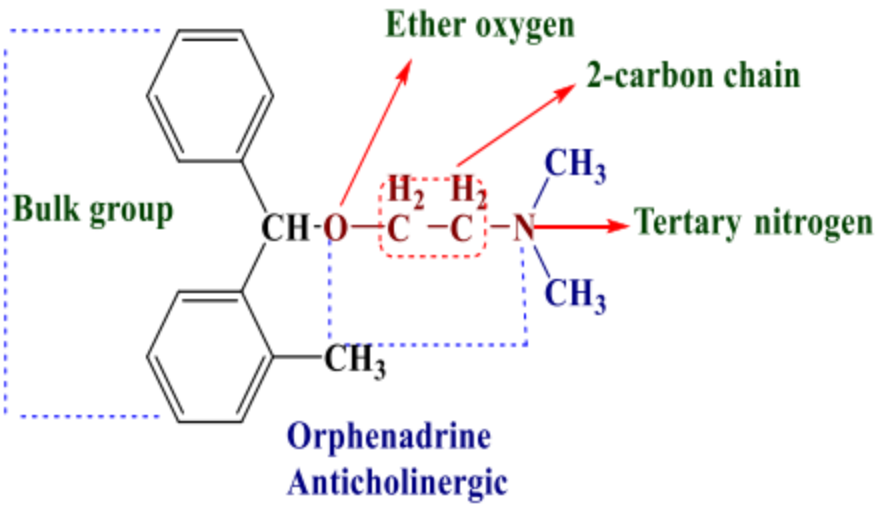


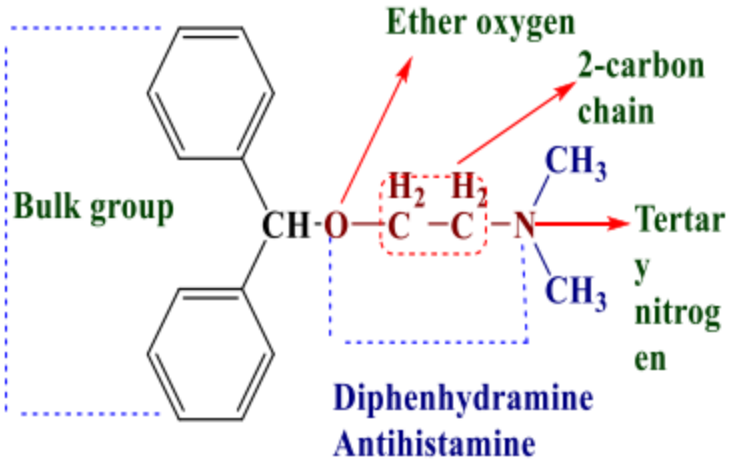
(1-methyl-1,4,5,6-tetrahydropyrimidin-2-yl)methyl 2-cyclohexyl-2-hydroxy-2-phenylacetate hydrochloride

I ,4,5,6-tetrahydro-(I -methyl-2-pyrimidinyl) methyl –α-phenyl cyclohexane glycolate monohydrochloride

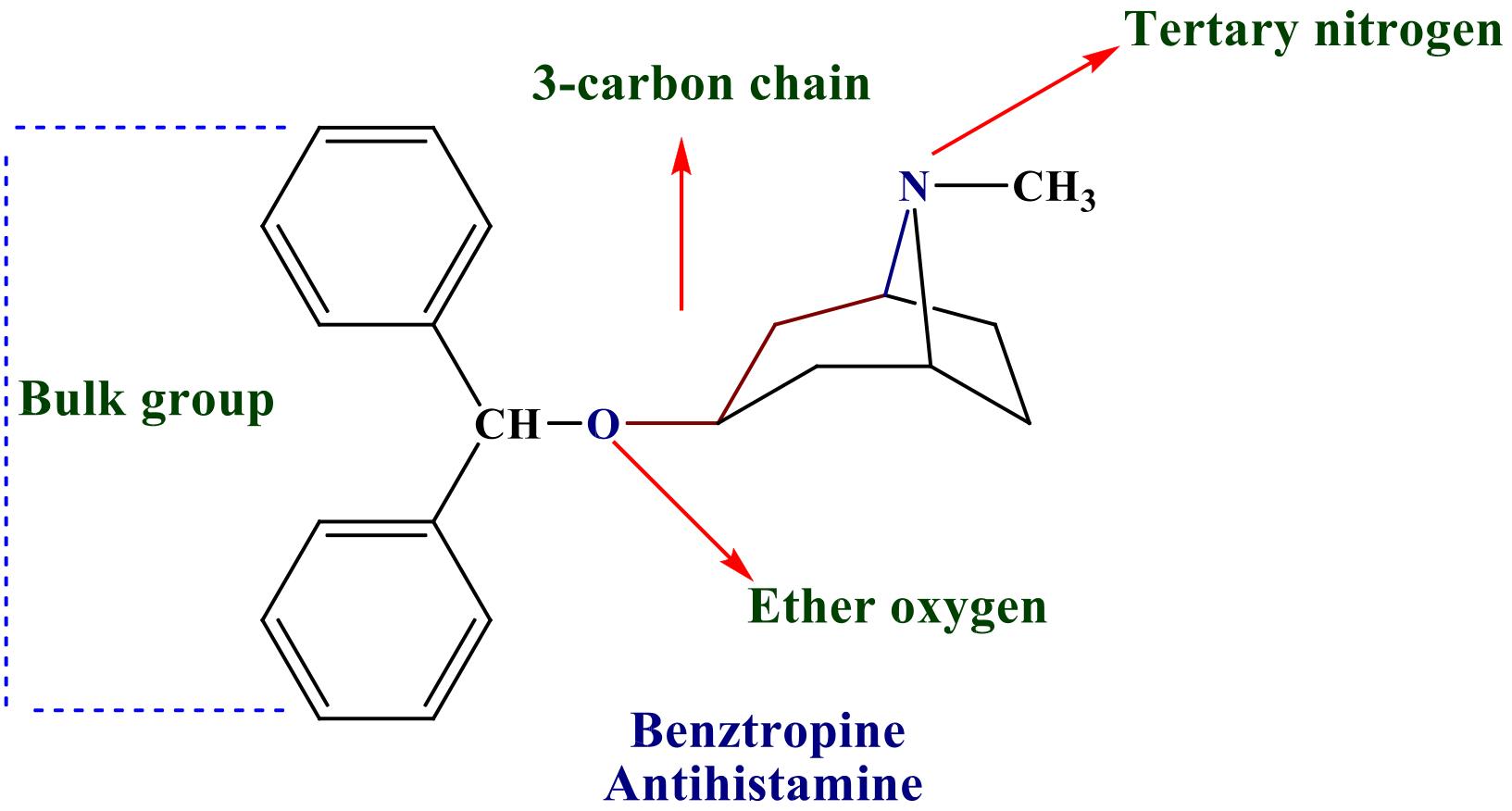
Aminoalcohol Ethers



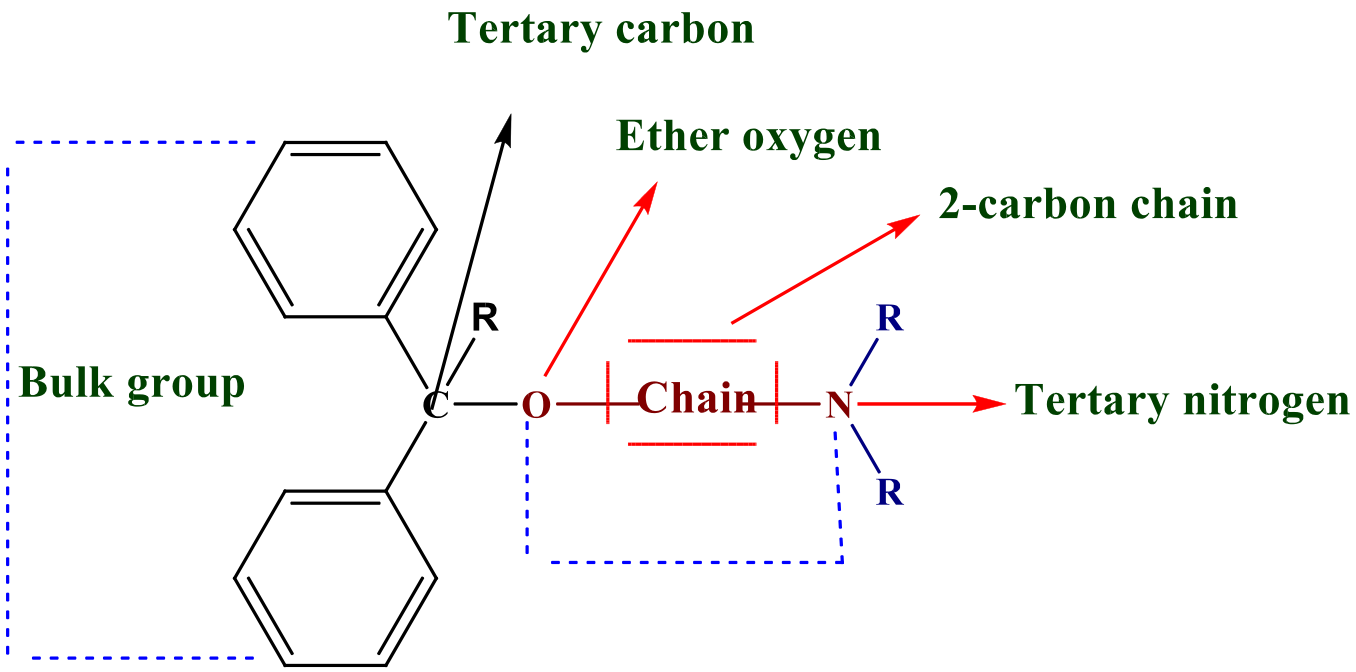




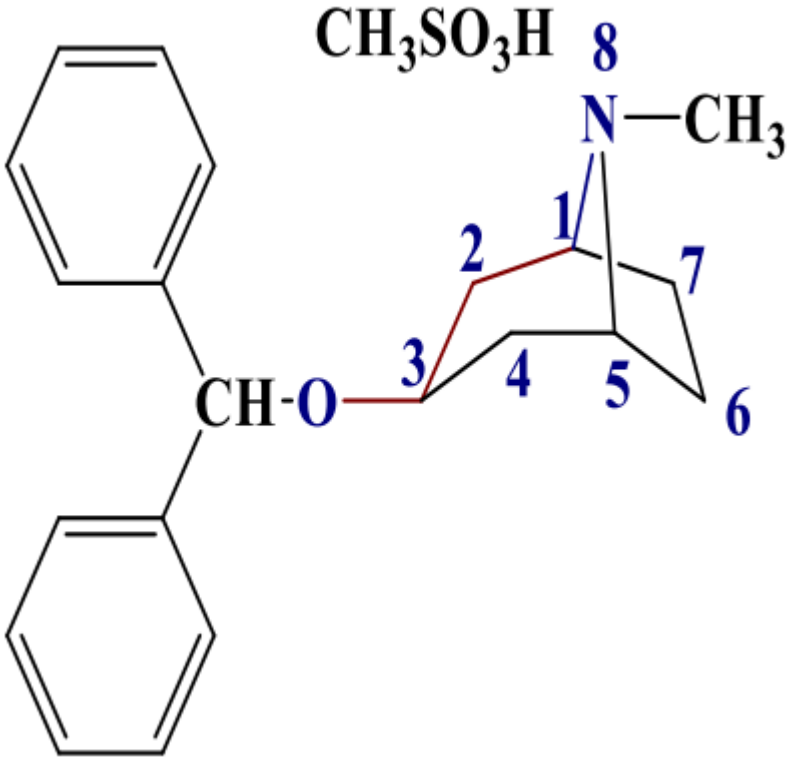
The aminoalcohol ethers thus far introduced have been used as antiparkinsonian drugs rather than as conventional anticholinergics (i.e., as spasmolytics or mydriatics). In general, they may be considered closely related to the antihistaminics and, indeed, do possess substantial antihistaminic properties.



Aminoalcohol ether (SAR)

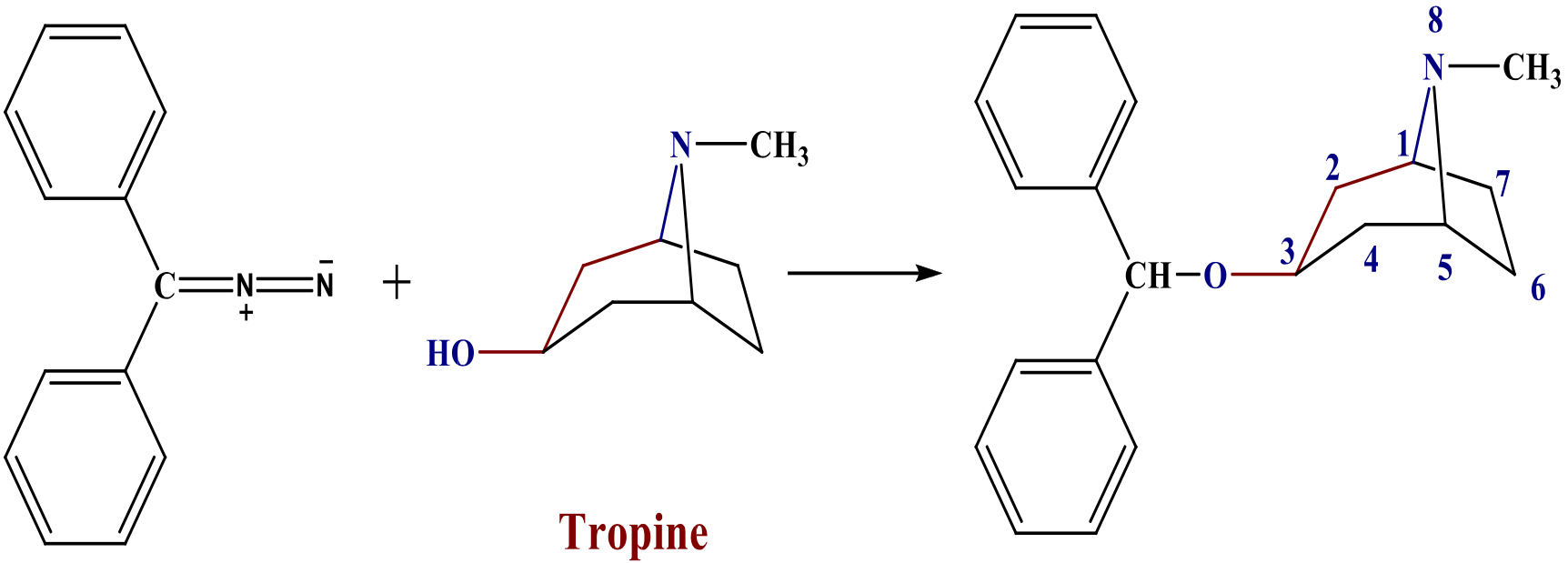


•Benztropine Mesylate



3α-(diphenylmethoxy)-8-methyl-8-azabicyclo[3.2.1]octane methansulfonate

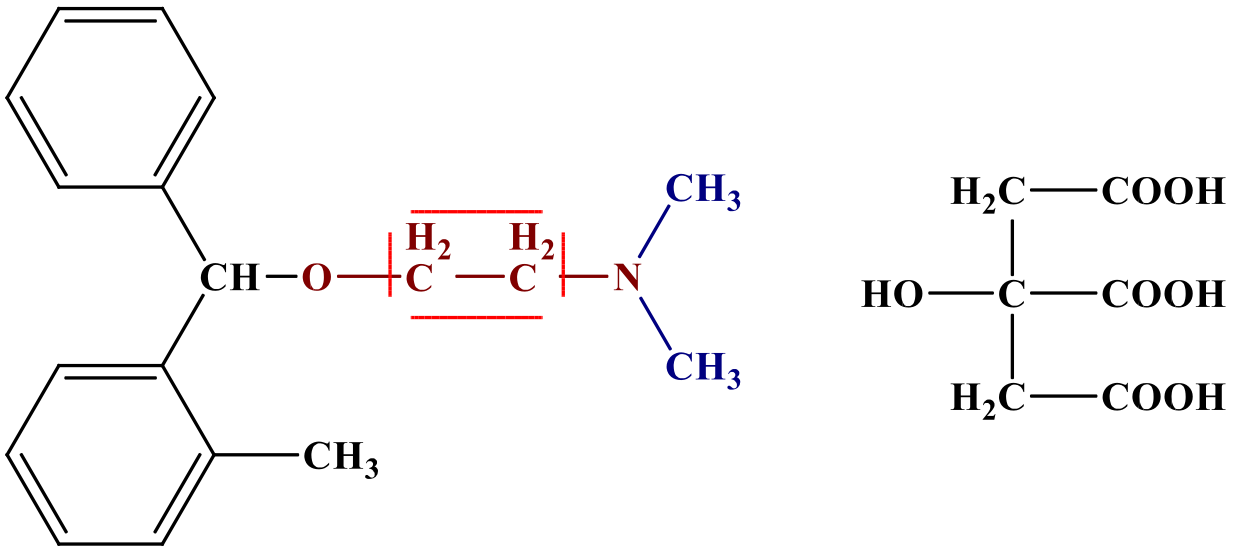
3α-(diphenylmethoxy)-1αH-5αH-tropane methansulfonate



Tropine

Diphenyldiazomethane

Orphenadrine Citrate



N,N-dimethyl-2-(o-methyl-α-phenylbenzyloxy) ethylamine citrate

Give the mechanism of Regeneration of phosphorylated AChE by 2-PAM (2-pyridinealdoximemethyl iodide(. (support your answer with chemical structure and example(