II. Drug suppressing the cholinergic activity
(Anticholinergics = Parasympatholytics)

A. Muscarinic antagonists
B. Nicotinic antagonists

II. Anticholinergics (Parasympatholytics)

They block muscarinic (cholinergic) receptors of effector cells, such as smooth muscle, outer gland and heart cells. They do not block the nicotinic type of cholinergic receptors (receptors in sympathetic and parasympathetic ganglion cells).

These drugs are also called **Anti-Muscarinic drugs**. They compete for the muscarinic receptor with acetylcholine released from vesicles and prevent only the muscarinic effects of exogenous acetylcholine and anticholinesterases.

They are also called **Spasmolytics,** because they remove spasms on smooth muscles

II. PARASYMPATOLITIC DRUGS (ANTICHOLINERGICS)

These compounds have selective effects. The reason for their selective effects is their ability to reach the site of influence.

The anticholinergic action by drugs apparently depends on their ability to reduce the number of free receptors that can interact with ACh.

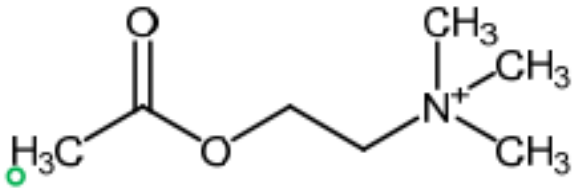
According to suggested hypotheses; that blocking compounds with high affinity to the receptors act by reducing the number of free receptors or the efficacy of the endogenous neurotransmitter.

These compounds are defined as cholinergic blocking drugs, parasympatholytics or cholinolytics. This group of compounds will be studied in two subclasses.

Muscarinic Antagonists
Nicotinic Antagonists

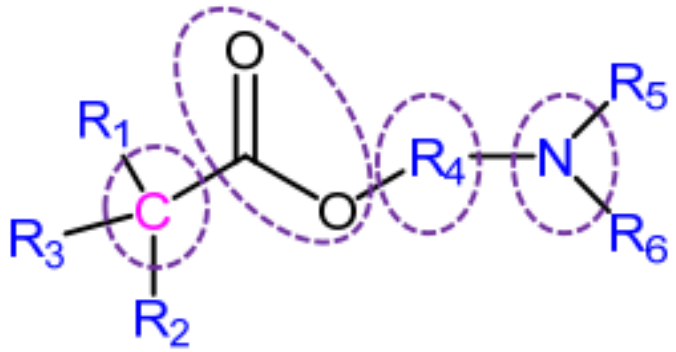
Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, page:572

Structure Activity Relationship (SAR) Studies



Acetylcholine (ACH)

Acetyl CH3 group is substituted with at least one phenyl ring for antimuscarinic activity



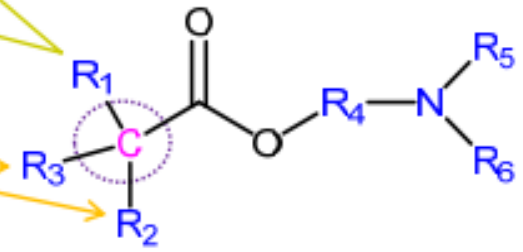
Acetylcholine analogue antimuscarinics

https://www.slideshare.net/kaami16/cholinergic-antagonists-medicinal-chemistry

Substitutions at α-carbon with respect to ester group

1. May be a hydrogen atom, a hydroxyl group, a hydroxymethyl group, or a carboxamide
2. Hydroxyl group or a hydroxymethyl group, the antagonist usually is more potent

R_2 and R_3 should be carbocyclic or heterocyclic rings (phenyl, cyclohexyl, cyclopentyl) for maximal antagonist potency



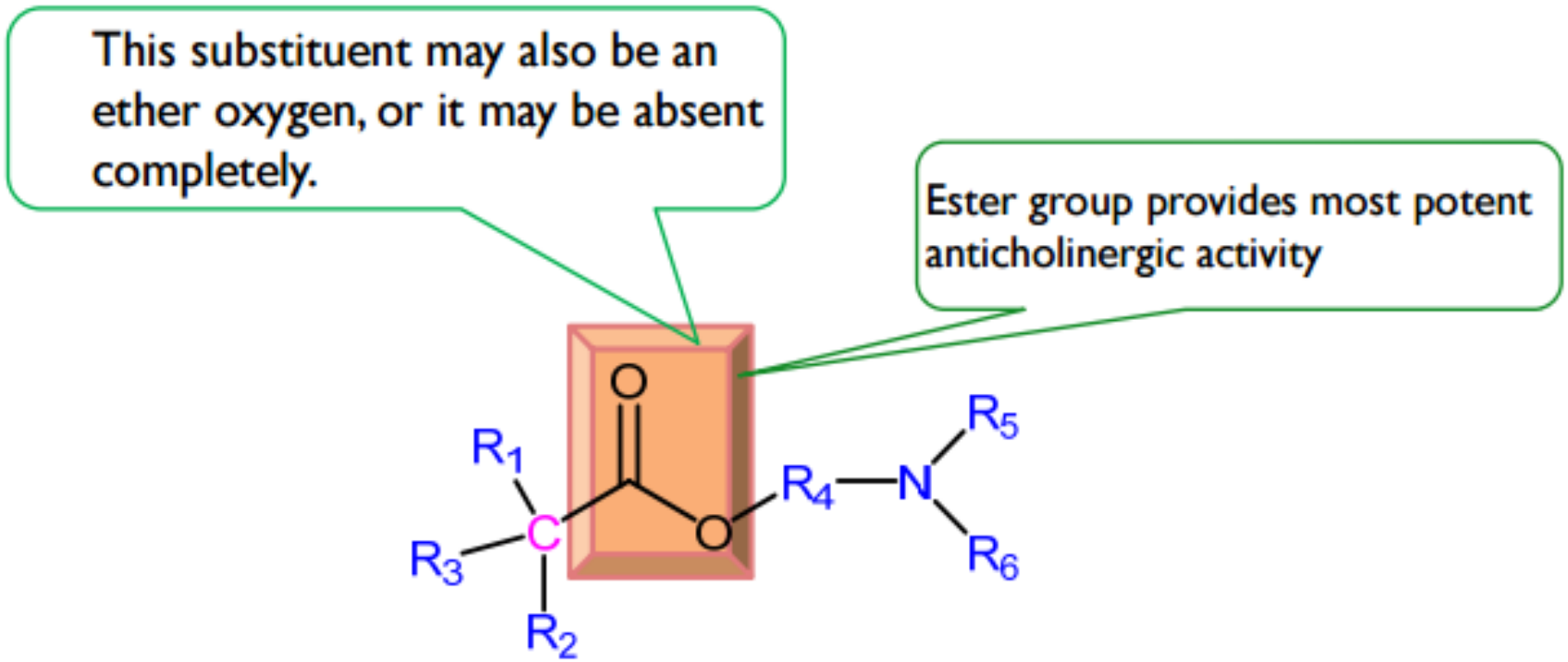
Substitution of naphthalene rings at R_2 and R_3 affords inactive compounds, because of steric hindrance at the muscarinic receptor.

Bigger R_2 and R_3 groups bind to the hydrophobic region outside the Ach receptor site

The hydroxyl group at R_1 presumably increases binding strength by participating in a hydrogen bond interaction at the receptor.

https://www.slideshare.net/kaami16/cholinergic-antagonists-medicinal-chemistry

Changes at ester group



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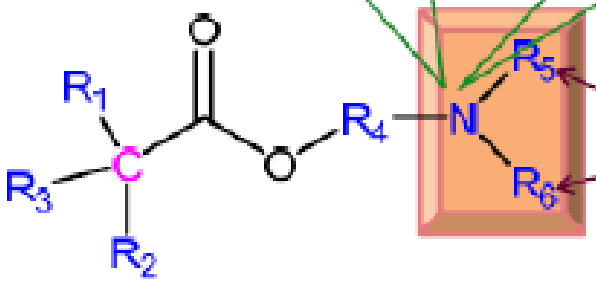
Substitution at the amine group

Compounds possessing the quaternary ammonium group exhibit nicotinic antagonist activity at high doses.

Quaternary ammonium compounds possess most potent anticholinergic activity



Methyl, ethyl, propyl, or isopropyl groups are tolerated

Tertiary amines also possess antagonist activity, presumably by binding to the receptor in the protonated form.

Quaternary ammonium drugs are primarily used in the treatment of ulcers or other conditions for which a reduction in gastric secretions and reduced motility of the gastrointestinal tract are desired

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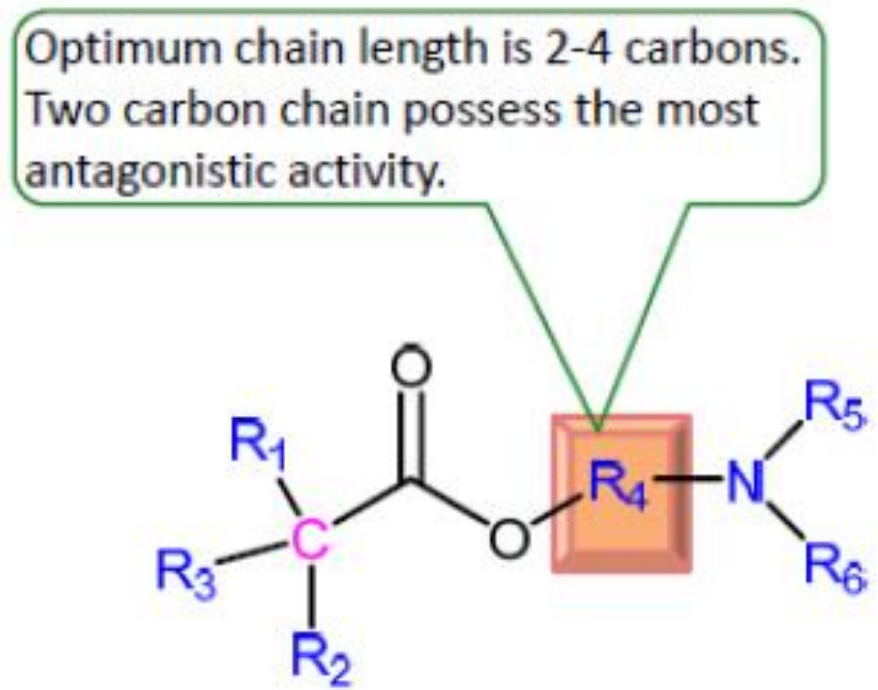
Changes at R_4 position



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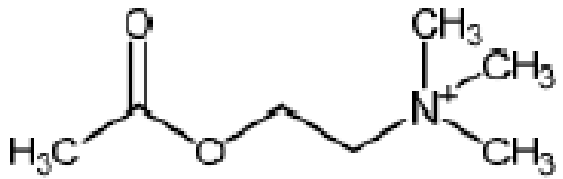
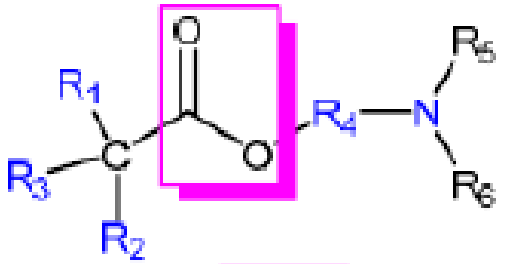
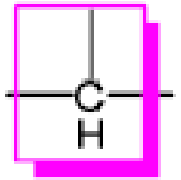
The Pharmacophore for all classes of antimuscarinics



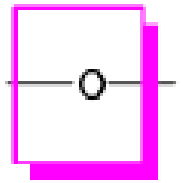
Acetylcholine (ACH)



R_1 = OH : Aminoalcohol ester
R_1 = $CONH_2$: Aminoamide ester



R_1 = OH : Aminoalcohol
R_1 = $CONH_2$: Aminoamides



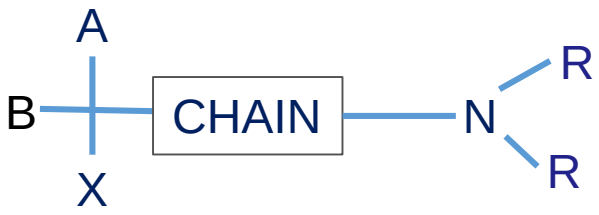
R_1 = OH : Aminoalcohol ether
R_1 = $CONH_2$: Aminoamide ether

Acetylcholine analogue antimuscarinics

https://www.slideshare.net/kaami16/cholinergic-antagonists-medicinal-chemistry

A. Muscarinic Antagonists

Structure-Activity Relationships



A, B: Bulky groups, Cycloalkyl, aromatic

X: H, OH, $CONH_2$ (carboxamide)

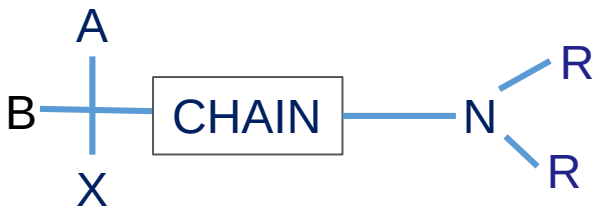
Anticholinergic compounds may be considered chemicals that have some similarity to ACh but contain additionally substituents that enhance their binding to the cholinergic receptor. .

• **The Cationic Head**: It is generally considered that the anticholinergic molecules have a primary point of attachment to cholinergic site through the cationic head (i.e. the positively charged nitrogen).

For quaternary ammonium compounds, there is no question of what is implied, but for tertiary amines, one assumes, with good reason, that the cationic head is achieved by protonation of the amine at physiological pH.

A. Muscarinic Antagonists

Structure-Activity Relationships



A, B: Bulky groups, Cycloalkyl, aromatic

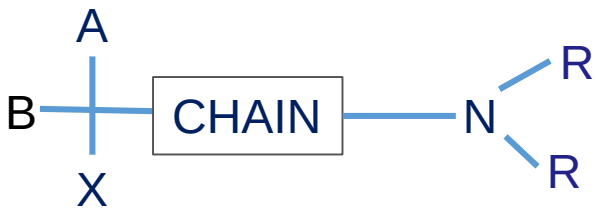
X: H, OH, $CONH_2$ (carboxamide)

-Steric factor that cause diffusion of the onium charge or produce a less-than-optimal drug-receptor interaction result in a decrease of parasympathomimetic properties and allow the drug to act as antagonist because of other bonding interactions.

Ariens has shown that carbocholines engage in a typical competitive action with ACh, though they are less effective than the corresponding compounds possessing a cationic head, suggesting that hydrophobic bonding may play an important role in these drug-receptor interactions.

A. Muscarinic Antagonists

Structure-Activity Relationships



A, B: Bulky groups, Cycloalkyl, aromatic

X: H, OH, $CONH_2$ (carboxamide)

- The nitrogen-linked alkyl groups (R) may be greater than methyl (as opposed to agonists). When N1 groups are ethyl or isopropyl, the effect is maximized but toxicity is increased.

- Quaternary N can be in the ring {eg; pyridine, piperidine, pyrrolidine). While agonists have to carry quarternary nitrogen, the antagonist's nitrogen may be tertiary or quaternary. However, it should be noted that the tertiary nitrogen atom is charged when it interacts with the receptor.

•

A. Muskarinik Antagonistler

Yapı-Aktivite İlişkileri

A, B: Bulky groups, Cycloalkyl, aromatic
X: H, OH, $CONH_2$ (carboxamide)

- **The Hydroxyl Group** :

Not requisite for activity, a suitably placed alcoholic hydroxyl group increases antimuscarinic activity over that of a similar compound without the hydroxyl group.

The position of the hydroxyl group relative to the nitrogen appears to be fairly critical, with the diameter of the receptive area estimated to be about 2 to 3 **Aº**.

It is assumed that the hydroxyl group contributes to the strength of binding, probably by hydrogen bonding to an electron-rich portion of the receptore surface.

Yapı-Aktivite İlişkileri

A, B: Bulky groups, Cycloalkyl, aromatic
X: H, OH, $CONH_2$ (carboxamide)

- **The Esteratic group**

Many of the highly potent antimuscarinic compounds possess an ester grouping, and this may be a contributing feature for effective binding.

This is reasonable because the agonist possess a similar function or binding to the same site.

An esteratic function is not necessary for activity, because several types of compounds do not possess such a group (e.g., ethers, aminoalcohols).

Yapı-Aktivite İlişkileri

A, B: Bulky groups,
Cycloalkyl, aromatic
X: H, OH, $CONH_2$ (carboxamide)

Cyclic substitution :

The active compounds have at least one cyclic substituent (phenyl thienyl, or other) is a common feature in almost all anticholinergic molecules.

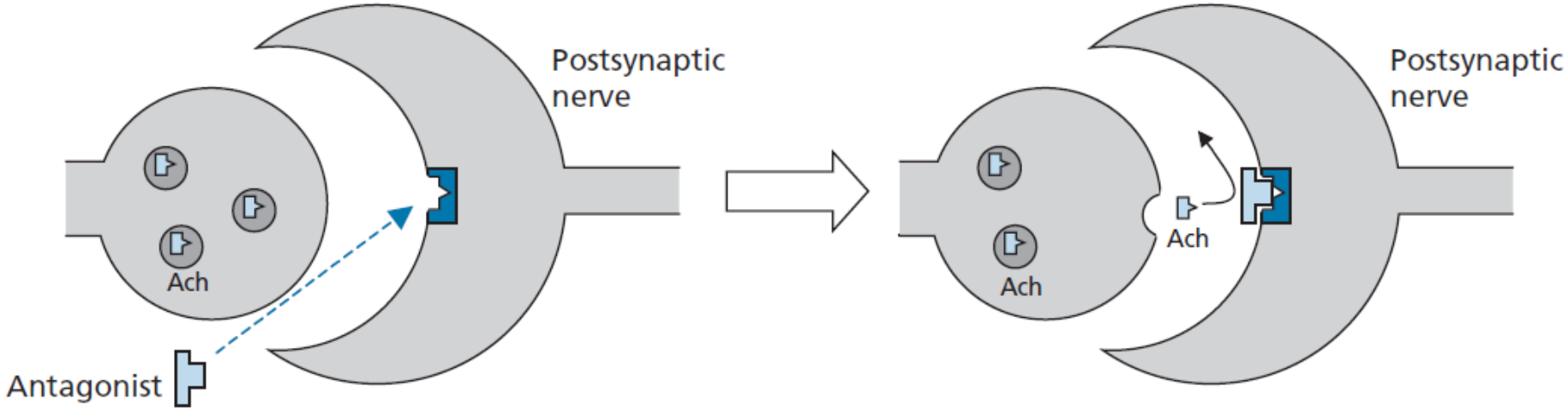
Aromatic substitution is often used in connection with the acidic moiety of the ester function.

Bulky acids {Mandelic, Tropical, Benzilik, etc.} are required for activity. (Very large acyl groups may be present (A and B = aromatic or heteroaromatic ring), This is in contrast to agonists that only acetyl groups are acceptable.

Antagonism of muscarinic cholinergic receptor

Effects and uses of muscarinic antagonists

Cholinergic receptor antagonists bind to the receptor but do not activate receptors.



Action of an antagonist to block a receptor.

Clinical effects of muscarinic antagonists:

- **Antisecretory effect: reduced salivation (antisialagogue), reduced perspiration (anhidrotic), and reduced acid and gastric secretion**
- **Antispasmodic effect: lowered tone and motility of the GI tract and the genitourinary tract**
- **Mydriatic effect: Dilation of the pupil of the eye**

Clinical uses:

- **Shutting down digestion for surgery**
- **Ophthalmic examinations**
- **Treatment of Parkinson's disease**
- **Treatment of anticholinesterase poisoning**
- **Motion sickness**

A. Muscarinic Antagonists

Classifications

1. Solanaceous alkaloids and analogues

2. Synthetic cholinergic blocking agents
   - Aminoalcohol esters
   - Aminoalcohol ethers
   - Aminoalcohols
   - Aminoamides
   - Quaternary amin derivatives
   - Miscellaneous
   - Papaverine alkaloids and analogues

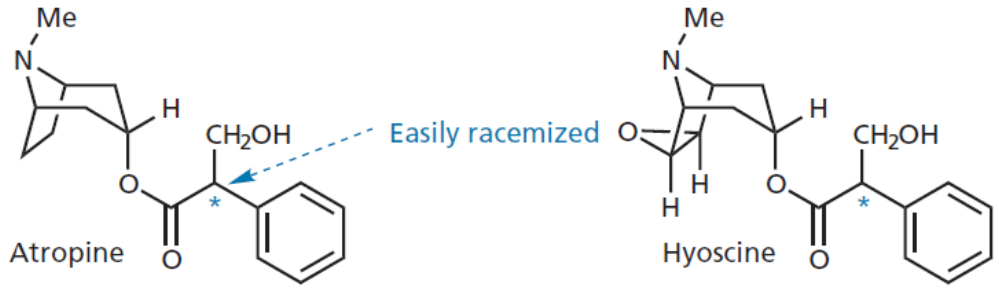
1. Solanaceous alkaloids analogues and its synthetic derivatives

The solanaceous alkaloids, represented by (-)-hyoscyamine, atropine, and scopolamine (hyoscine) are the forerunners of the class of antimuscarinic drugs. These alkaloids are found principally in henbane (*Hyoscyomus niger*), deadly nightshade (*Atropa belladonna*).

All of the solanaceous alkaloids are esters of the bicyclic aminoalcohol.

Solanaceous alkaloids are racemate because of the asymmetric carbon atom on tropic acid.

Atropine ve hyoscine (Scopolamine)



Atropine and hyoscine.

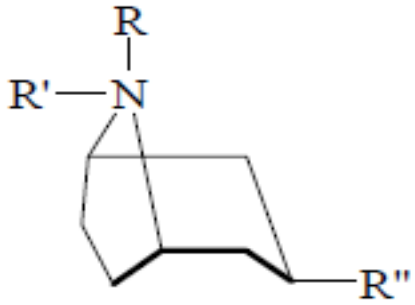
The proper enantiomorph is necessary for high antimuscarinic acitivity, as illustrated by the potent (-) hyoscyamine in comparison with the weakly active (+)-hyoscyamine. .

Solanaceae alkaloids are antimuscarinic. They were used in hemorrhoides because of their weak local anesthetic effects. They stimulate the respiratory center.
They lead to mydriasis. They commonly use as antispasmodic.

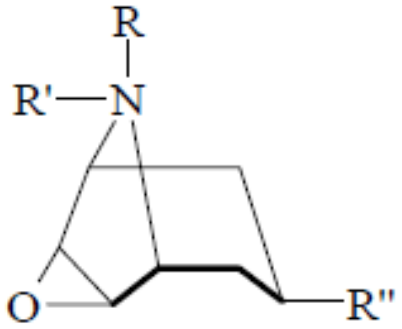
Solanaceous alkaloids (the Tropin structures) and their synthetic derivatives

- **Atropine**
- **Hyoscyamine**
- **Scopolamine HBr**
- **Homatropine HBr**
- **Ipratropium Br**
- **Tiotropium Br**
- **N-Buthylscopolamine**
- **Oxytropium bromide**

Solanaceous alkaloids (the Tropin structures) and their synthetic derivatives

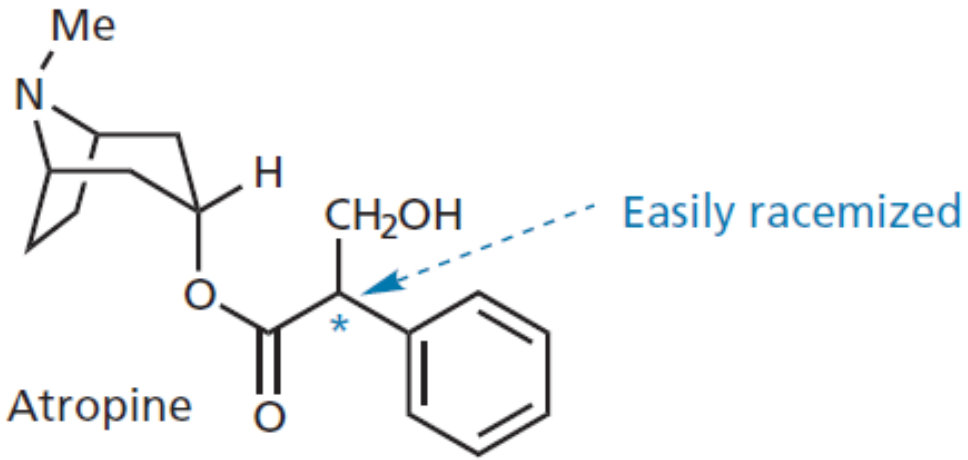


Compound	R	R'	R''
Atropine **(+/-)-α-(Hydroxymethyl)benzen acetic acid 8-methyl-8-aza-bicyclo[3.2.1]oct-3-yl ester**	$-CH_3$	-	$-OCOCHCH_2OH$ C_6H_5
Hyoscyamine **(-)-α-(Hydroxymethyl)benzen acetic acid 8-methyl-8-aza-bicyclo[3.2.1]oct-3-yl ester**	$-CH_3$	-	$-OCOCHCH_2OH$ C_6H_5
Homatropine **α-Hydroxybenzen acetic acid 8-methyl-8-aza-bicyclo[3.2.1]oct-3-yl ester**	$-CH_3$	-	$-OCOCHOH$ C_6H_5
Ipratropium bromide **3-(3-Hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-isopropyl-8-azonazbicyclo[3.2.1]octan bromide**	$-CH(CH_3)_2$	$-CH_3$	$-OCOCHCH_2OH$ C_6H_5

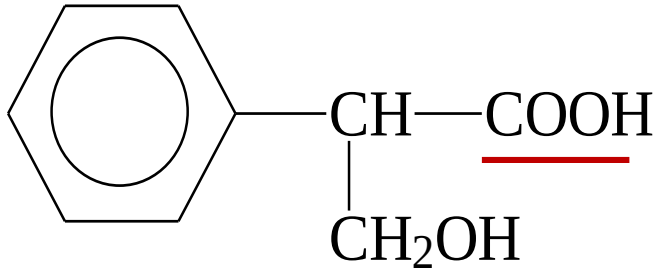


Compound	R	R'	R''
Scopolamine	$-CH_3$	-	$-OCOCHCH_2OH$ C_6H_5
N-Buthylscopolamine	$-CH_3$	$-C_4H_9$	$-OCOCHCH_2OH$ C_6H_5
Oxytropium bromide	$-CH_3$	$-C_2H_5$	$-OCOCHCH_2OH$ C_6H_5

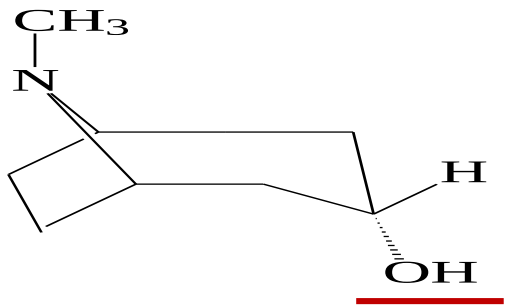
ATROPINE = TROPINTROPAT



- ✓ It is anticholinergic that blocks muscarinic receptors.
- ✓ It competitively binds to muscarinic receptor and antagonizes it thus blocking all cholinergic effects
- ✓ It is an alkaloid extracted from Solanaceae plant and was the first anticholinergic
- ✓ It is an ester of tropine and tropic acid and used as a sulphate salt in racemic form.
- ✓ At therapeutic does it can penetrate the brain and stimulate the CNS



Tropic Acid (α-(hydroxymethyl)-benzenacetic acid



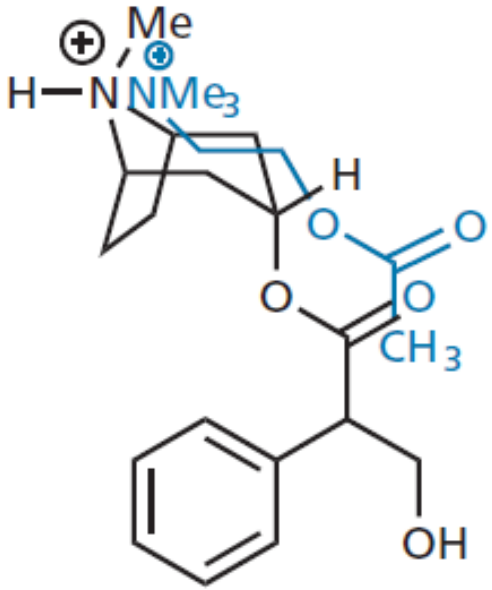
Tropine (8-methyl-8-azabicyclo-[3.2.1]octan-3-ol)

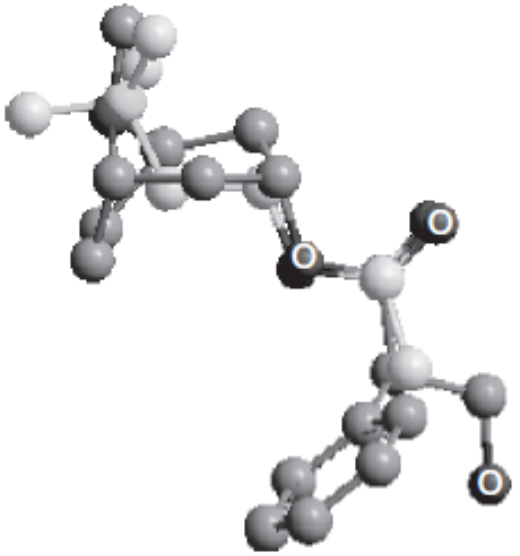
Uses:

- ✓ Decrease GIT motility
- ✓ Treat bradycardia
- ✓ Reduce secretion before surgery
- ✓ Traet iritis (painful inflammation of eye) Dilation of eye pupils.
- ✓ Organophosphate poisoning (only to decrease muscarinic action, not an antidote like PAM) (Antidote for Anticholinesterase poisoning).

Atropine with ACh

- Relative positions of ester and nitrogen similar in both molecules
- Nitrogen in atropine is ionised
- Amine and ester are important binding groups (ionic + H-bonds)
- Aromatic ring of atropine is an extra binding group (vdW)
- Atropine binds with a different induced fit - no activation
- Atropine binds more strongly than acetylcholine

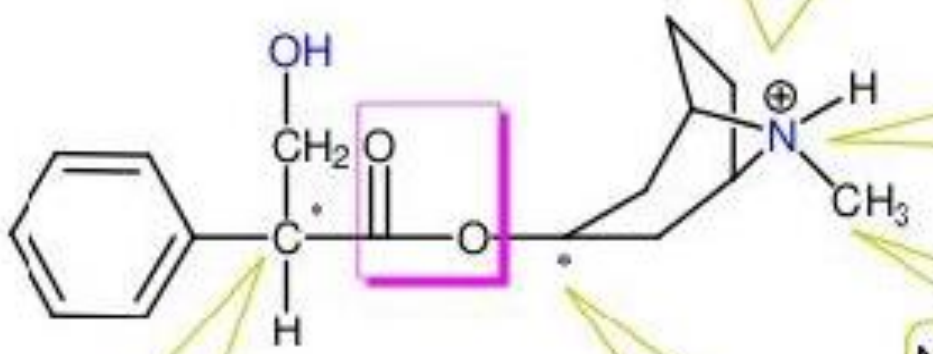




Acetylcholine skeleton superimposed on to the atropine skeleton.

Atropine: Classic Prototype for Antimuscarinics

Amino alcohol ester pharmacophore



Quaternary Nitrogen binds to the anionic Asp residue in the muscarinic receptor

When the Nitrogen made is quaternary, molecule looses oral availability, but effective by inhalation

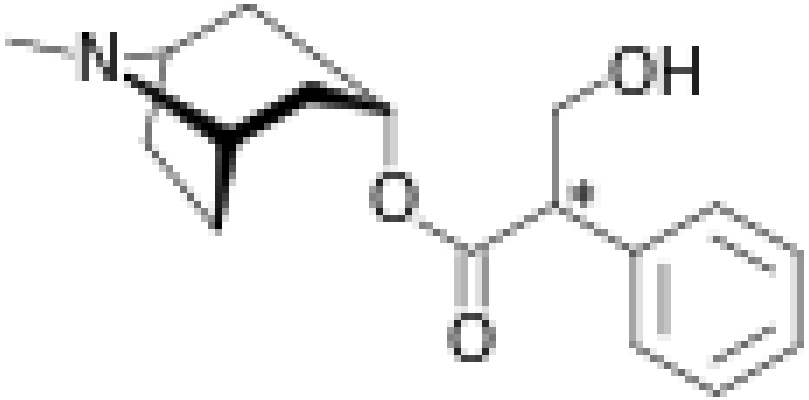
Methyl is optimal substitution on Quaternary Nitrogen

R-isomer is 100 fold more active than and *S*- isomer

There is little difference between *R*- and *S*- configurations

- The naturally occurring alkaloid, (–)-hyoscyamine, upon base-catalyzed racemization gives (±)-hyoscyamine or atropine.
- **Uses:** antidote for anticholine esterase poisoning, Decrease GIT motility, Dilation of pupils

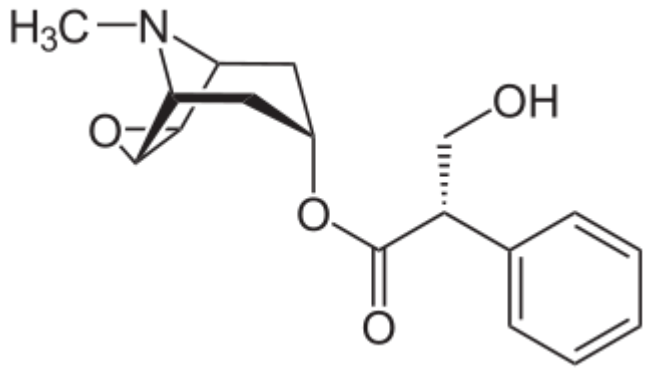
Atropine metabolism;



- Aromatic hydroxylation,
- Ester hydrolysis and then formation of glucuronate through the alcohol function,
- N-demethylation

SCOPOLAMINE ANTIMAREN / ANTINOZAN

It has a stronger effect than atropine. It is used in painful spasms and motion sickness. In overdose [1 mg], speech disorder, movement and mental activities decrease.



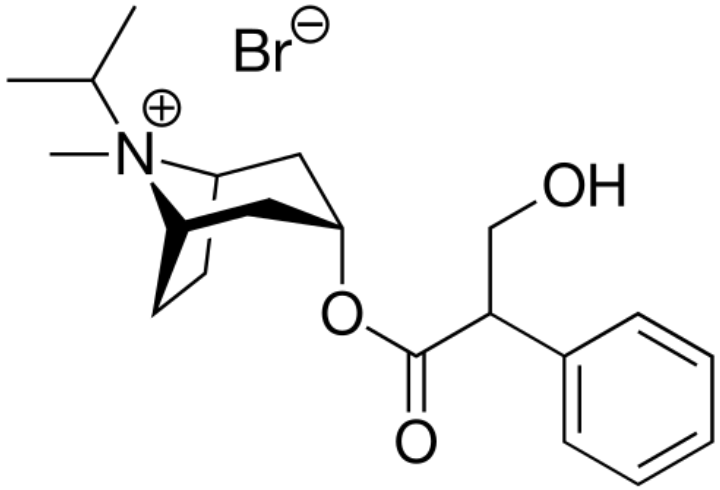
N-BUTHYLSCOPOLAMINE (Hyoscine-N-buthyl Br); (Buscopan, Buskas, Buskalgin,Buscotek, Buskoplan, Pankopan, Spazmol, Tranco-Buscopan)

It is a potent anti-spasmodic and semi-synthetic compounds.

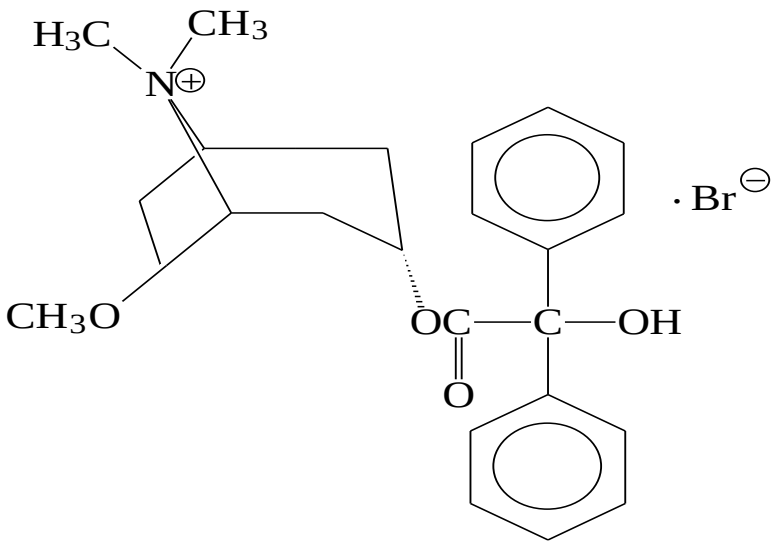
Parenteral use is preferred because it is absorbed in a low rate when taken orally. It is used in GI spasms and especially bile and renal colic.

IPRATROPIUM: **3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8_(1-methylethyl)-8-azoniabicyclo[3.2.1]octane bromide**

Ipratropium is a quaternary ammonium derivative of atropine. It is used to treat the symptoms of chronic obstructive pulmonary disease (COPD) and asthma. It is used by inhaler or nebulizer. It can not enter the CNS due to the positive charge in its structure.



TROPENZILINE Br PALEROL



6-methoxytropine benzylate methyl bromide

Reduces the motility and tone of the GIT, it has both antispasmodic and analgesic effect and hence;

-Gastrododuonal ulcer, gastritis, colitis, kidney stone, cystitis, cystopyelitis etc. Used in gastrointestinal and urogenital spasms,

-Contraindicated: In glaucoma and prostatic hypertrophy patients. for alcohol and sedatives,

-It makes sedation. Therefore, person who work in high places and driving should be warned.

2. Synthetic cholinergic blocking agents

- **Aminoalcohol Esters**

They are used as an **antispasmodic, mydriatic ve antiparkinson.**

Another important feature in many of the synthetic anticholinergic used as antispasmodics is that they contain a quaternary nitrogen, presumably to enhance activity.

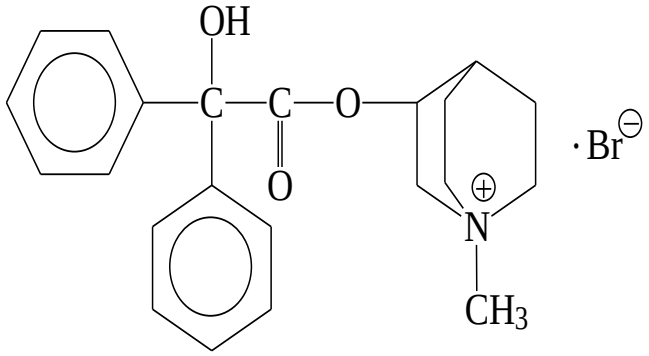
These compounds combine anticholinergic activity of the antimuscarinic type with some ganglionic blockade.

2. Synthetic cholinergic blocking agents

- **Aminoalcohol Esters**

- Clidinium Bromide
- Cyclopentolate Hydrochloride
- Dicyclomine Hydrochloride
- Eucatropine Hydrochloride
- Mepenzolate Bromide
- Oxyphencyclimine Hydrochloride
- Glycopyrrolate
- Methantellin
- Propantheline Bromide

Clidinium Bromide LIBRAX PRODARTAL



N-methyl-3-quinuclidinyl-benzilate bromide

- The anticholinergic agent is marketed alone and in combination with the minor tranquilizer chlordiazepoxide (Librium) in a product known as Librax. 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.

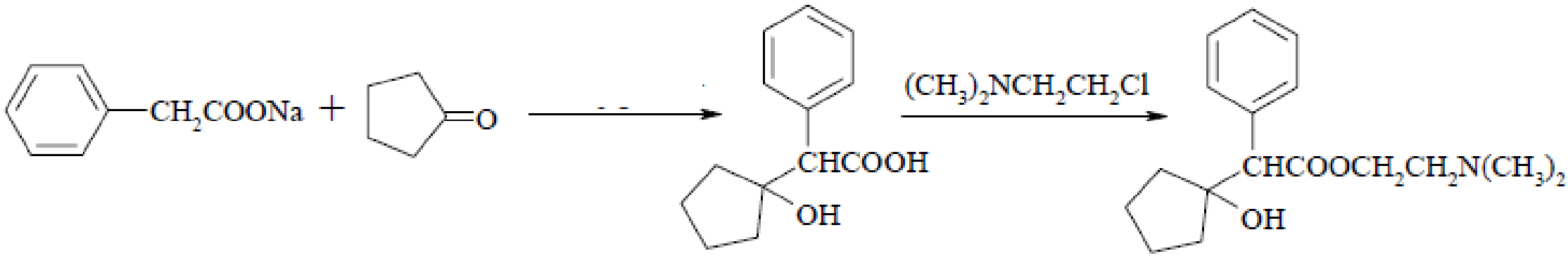
- It is suggested for peptic ulcer, ulcerative or spastic colon, anxiety states with GI manifestations, nervous stomach, irritable or spastic colon and others.

- Clidinium bromide is contraindicated in glaucome and other conditions that may be aggravated by the parasympatholytic action, such as prostatic hypertrophy in elderly men, which could lead to urinary retention.

Cyclopentolate SİKLOMİD, SİKLOPLEJİN

It is used only for its effects on the eye, where it acts as a parasympatholytic. When it drops in the eye, it quickly produces cycloplegia and mydriasis. The effect ends in a short time, does not irritate the eyes.

Synthesis



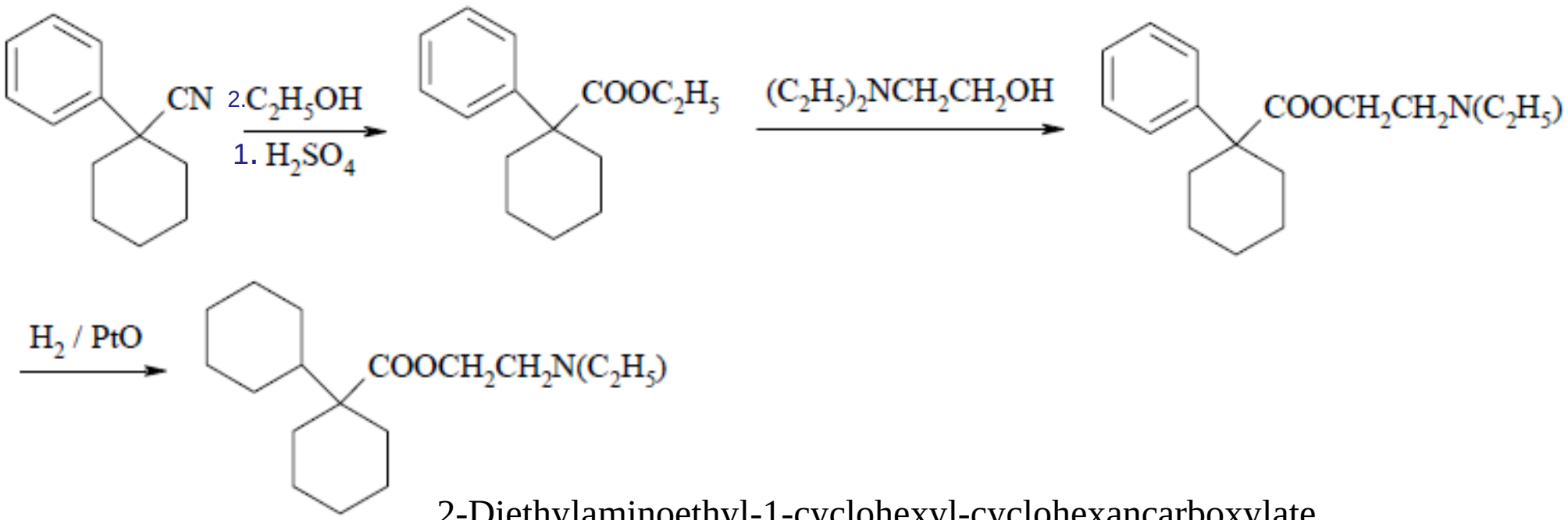
(*RS*)-2-Dimethylaminoethyl-1-hydroxy-α-phenylcyclopentaneacetate

Dicyclomine Hydrochloride

It is used to treat the symptoms of irritable bowel syndrome (a disorder in large intestine that causes cramping, abdominal pain, bloating, gas), specifically hypermotility, in adults.

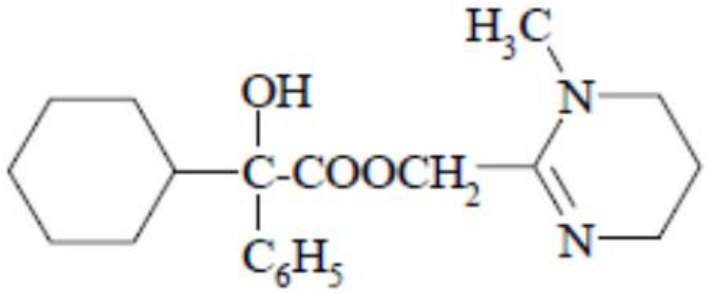
It is used for its spasmolytic effect on various smooth muscle spasm, particularly those associated with the GI tract as an oral or parenteral.

Synthesis



2-Diethylaminoethyl-1-cyclohexyl-cyclohexancarboxylate

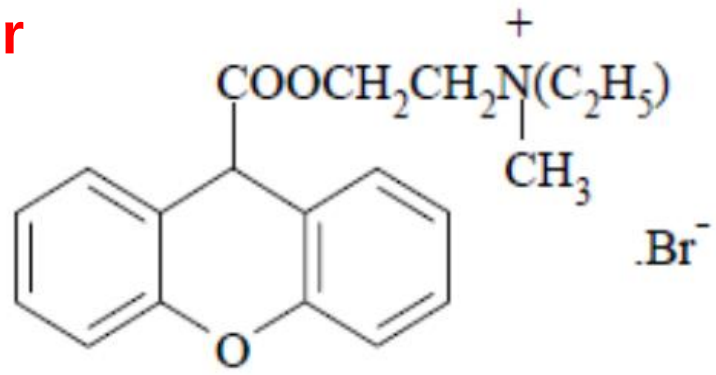
Oxyphencyclimine DARİCON, AN-KOL



1,4,5,6-Tetrahydro-1-methyl-2-pyrimidinyl)methyl α-phenylcyclohexaneglycolate

It is used as antispasmodic. It is absorbed from the GI tract and has a duration of action of up to 12 hours.

Methantheline Br

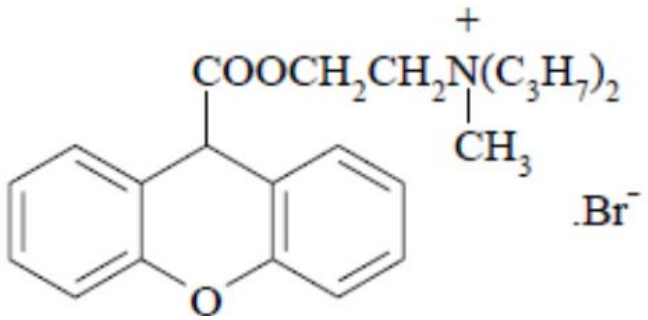


Diethyl(2-hydroxyethyl)methylammonium bromide xanthene-9-carboxylate

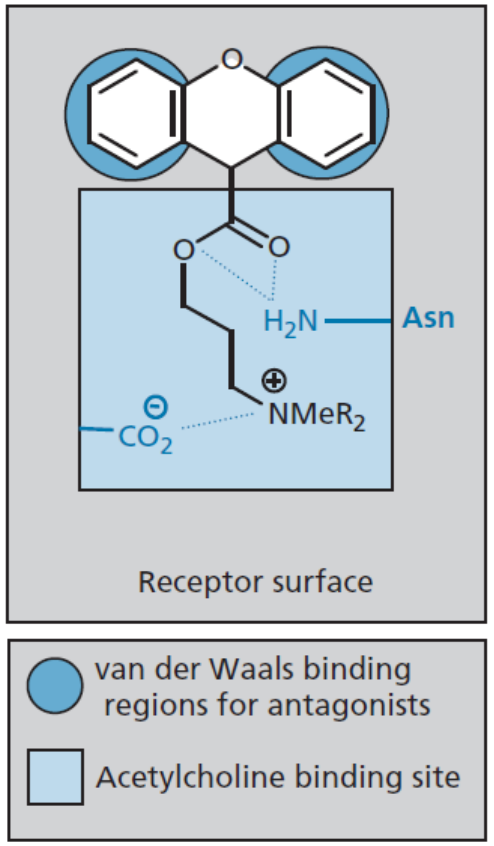
It has a xanthene ring in its structure. It has an more potent antispasmodic effect than atropine. It has a ganglio blocker effect.

Side reactions are atropine-like (mydriasis, cycloplegia, dryness of mouth). The drug is contraindicated in glaucoma. Toxic doses may bring about a curar-like action, a not too suprising fact when it is considered that ACh is the mediating factor for neural transmission at the somatic myoneural junction. This side effect can be counteracted with neostigmine methylsulfate. Propantheline can be preferred.

Propantheline Bromide BANTİNOVA



(2-Hydroxy-ethyl)diisopropylmethylammonium bromide xanthene-9-carboxylate



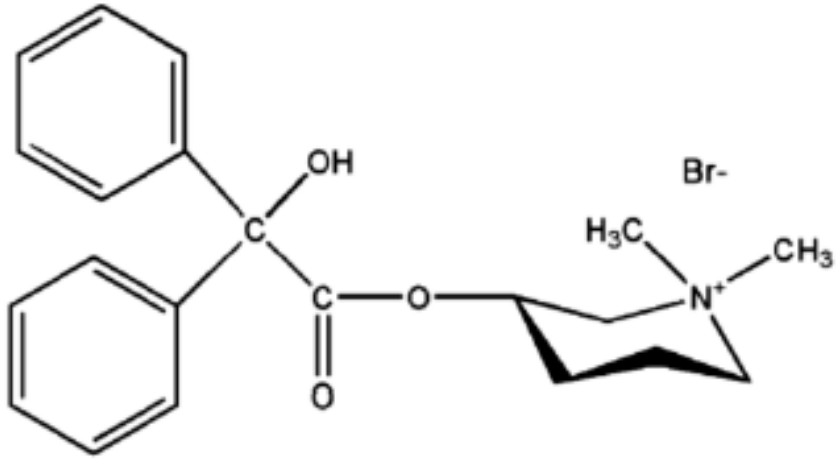
The binding of propantheline to the muscarinic receptor.

Its chief difference from methantheline bromide is in its potency, which has been estimated variously to be 2 to 5 times as great.. Strongly inhibits tonus and motility in the gastrointestinal tract. So, it is used in peptic ulcer and gastritis (reduces gastric acid secretion)

The inhibitory effect of the stomach on acid secretion is also very strong. In addition, a single dose of [15-20 mg] is used against enuresis nocturia.

Mepenzolate Bromide

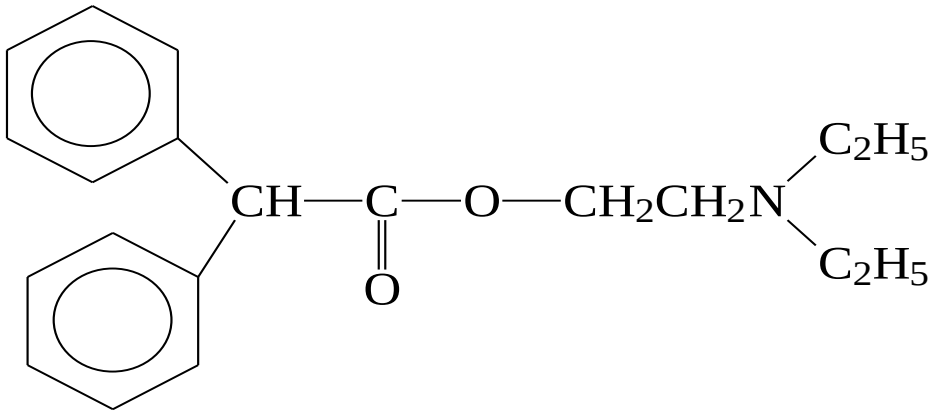
- ✓ It has an activity about one half that of atropine in reducing ACh induced spasms of the ileum.
- ✓ The selective action on colonic hypermotility is said to relieve pain, cramps, and bloating and to help curb diarrhea.



Mepenzolate Bromide

N-Methyl-3-piperidyl-benzilate methyl bromide

Adiphenine SPAZMO-PANALGINE

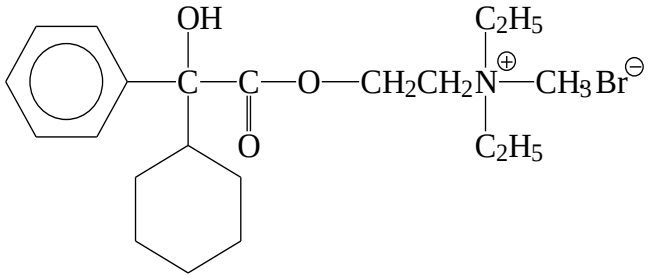


Diphenylacetic acide-2-diethylamino-ethylester ;HCl

It is used to treat spasm and peptic ulcer. While its spasmolytic effect is 25 times stronger than atropine, it has the same level of spasmodic effect as papaverine

Quaternary amine derivatives;

Oxyphenonium Br ANTRENYL



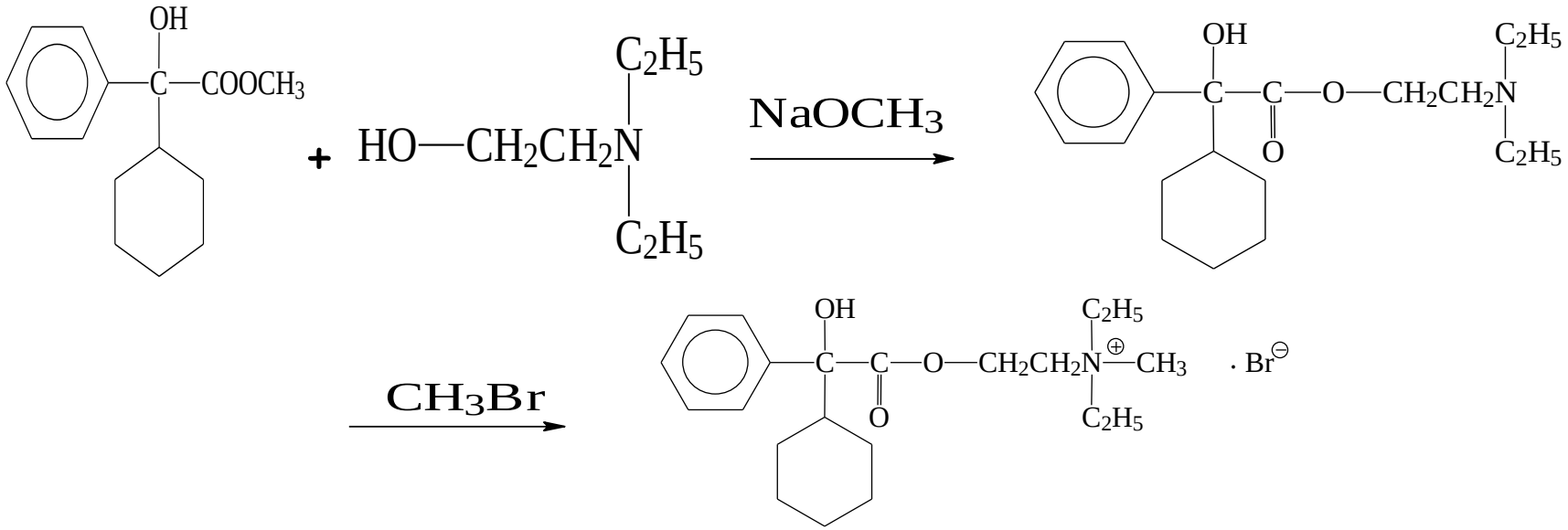
2-(2-Cyclohexyl-2-hydroxy-2-phenylacetoxy)-*N,N*-diethyl-*N*-methyl ethanammonium bromide

It is an antimuscarinic drug. It is used to treat peptic ulcer and gastric hypermotility

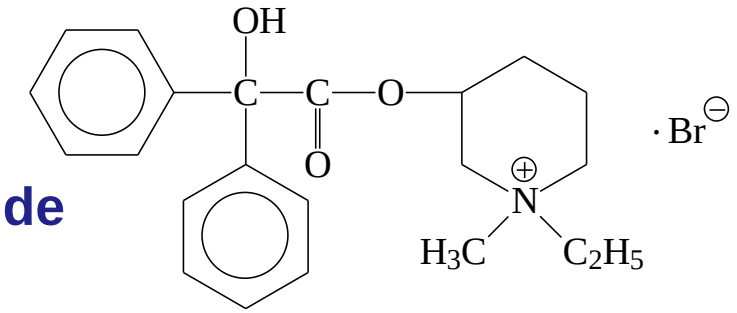
Contraindicated: In Glaucome, prostat hypertrophy.

Side effect: Dry mouth, visual impairment, dizziness

Synthesis ;



Pipenzolate methyl bromide PIPTAL

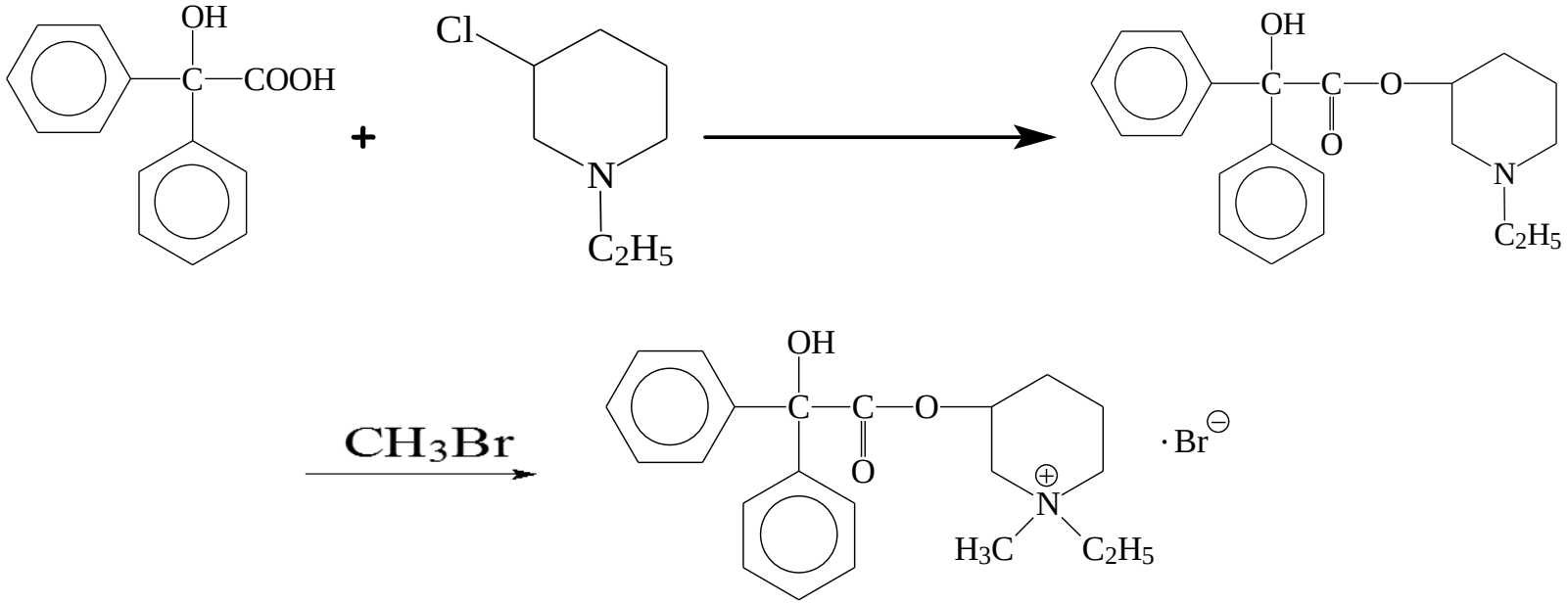


N-Ethyl-3-piperydinyl benzilate methyl bromide

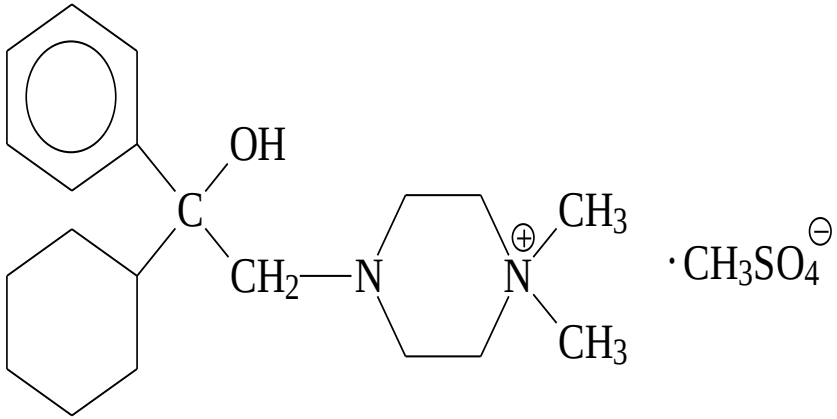
Pipenzolate bromide is an antimuscarinic. It binds to muscarinic acetylcholine receptors as an antagonist therefore preventing ACh from binding to the receptors. It is used flatulent dyspepsia, infantile colics.

-Side effects: Urinary stiffness, constipation and blurred vision

Synthesis ;



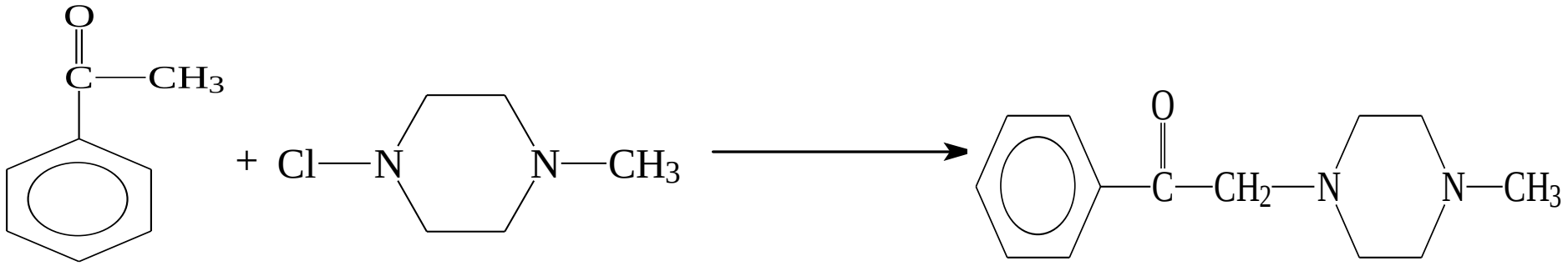
Hexocyclium Methylsulfate TRAL TRALIN

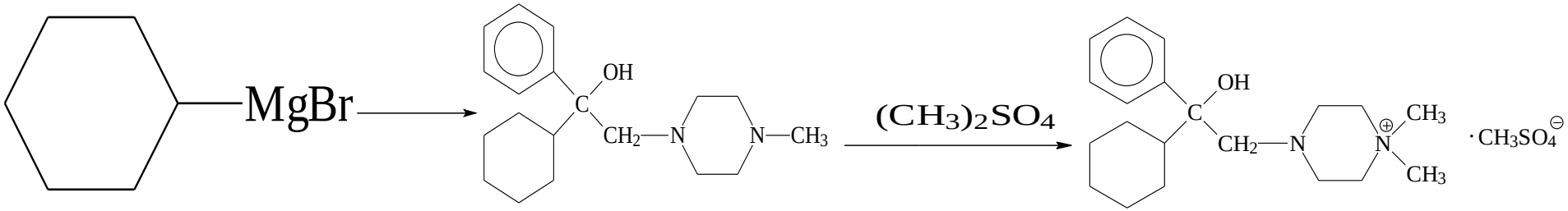


4-(2-cyclohexyl-2-phenyl-2-hydroxyethyl)-1,1-dimethyl piperazinium methyl sulfate

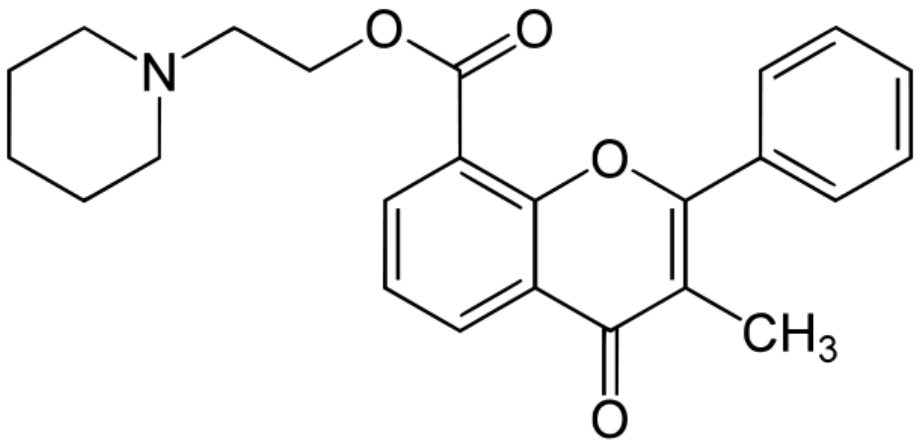
Anticholinergic

Synthesis:





Flavoxate-HCl URISPAS



3-Methyl-4-oxo-2-phenyl-4*H*-1-benzopiron-8-carboxylic acide-2-piperidino-ethyl ester

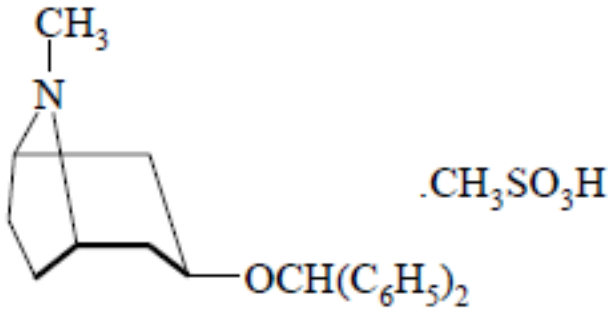
8-(2-piperidino-ethyl)-3-methyl-4-oxo-2-phenyl-4H-1-benzopiron-8-carboxylate

Urinary system antispasmodic

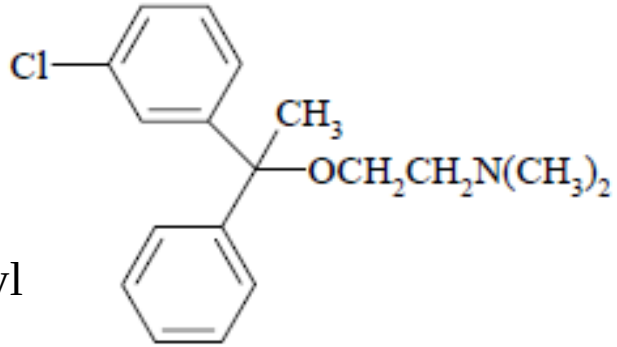
• Aminoalcohol ethers

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

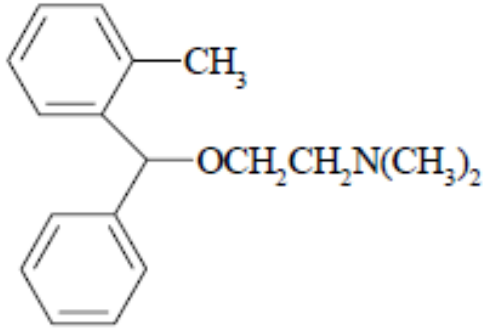
Benzotropine mesylate
8-Methyl-8-azabicyclo[3.2.1]oct-3-yl benzhydryl ether methanesulfonate



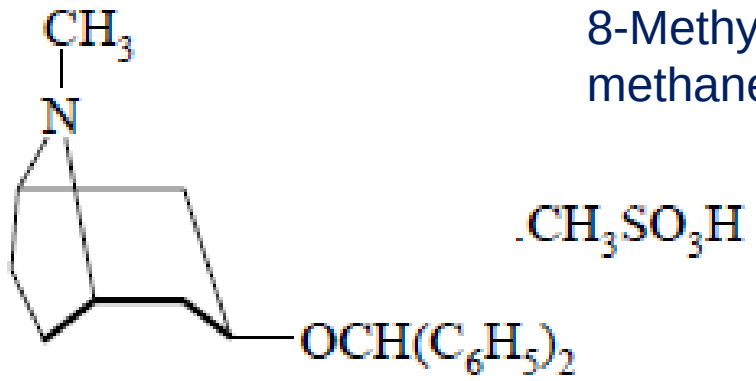
Chlorphenoxamine
[1-(p-chlorophenyl)-1-phenyl]ethyl (2-dimethylaminoethyl)ether



Orphenadrine citrate
N,N-dimethylaminoethyl-2-methylbenzhydryl ether



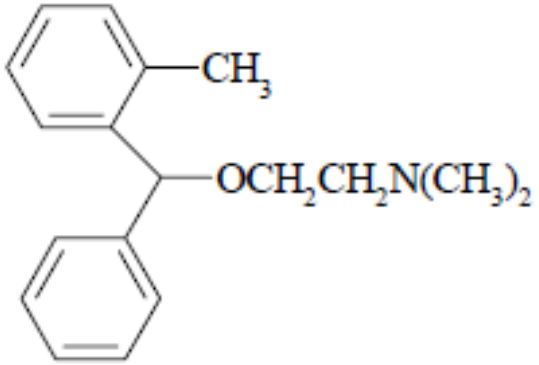
Benzotropine mesylate



8-Methyl-8-azabicyclo[3.2.1]oct-3-yl benzhydryl ether methanesulfonate

- ✓ **Benzotropine mesylate has anticholinergic, antihistaminic, and local anesthetic properties.**
- ✓ **Its anticholinergic effect makes it applicable as an antiparkinsonian agent.**
- ✓ **It is about potent an anticholinergic as atropine and shares some of the side effects of this drug, such as mydriasis and dryness of mouth.**

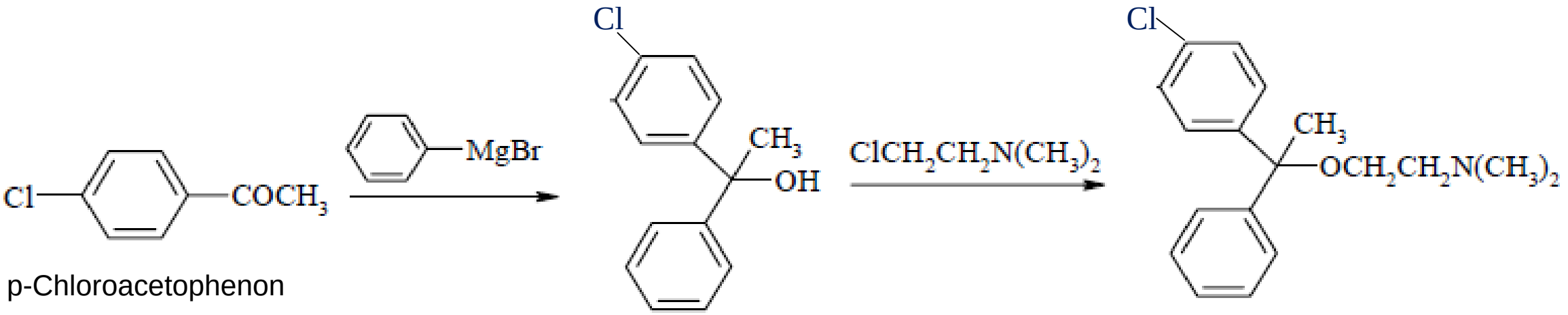
Orphenadrine citrate



N,N-dimethylaminoethyl-2-methylbenzhydryl ether

- Orphenadrine citrate, is closely related to diphenhydramine structurally but has much lower antihistaminic activity and much higher anticholinergic action.
- Likewise, it lacks the sedative effects characteristic of diphenhydramine.
- Pharmacological testing indicates that it is not primarily a peripherally acting anticholinergic because it has only weak effects on smooth muscle, on the eye, and on secretory glands.
- It does reduce voluntary muscle spasm, however, by a central inhibitory action on cerebral motor areas, a central effect similar to that of atropine.

Synthesis of chlorphenoxamine:



p-Chloroacetophenon

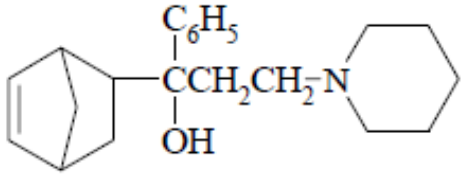
[1-(p-chlorophenyl)-1-phenyl]ethyl (2-dimethylaminoethyl)ether

2. Synthetic cholinergic antogonists

- **Aminoalcohols**

Formula

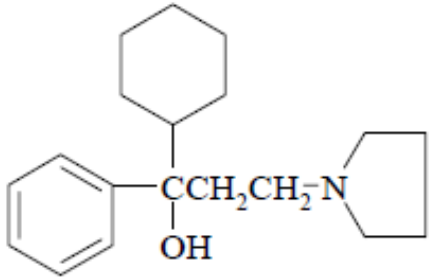
Biperiden
α-Bicyclo[2.2.1]hept-5-en-2-yl-α-phenyl-1-piperidinylpropanol



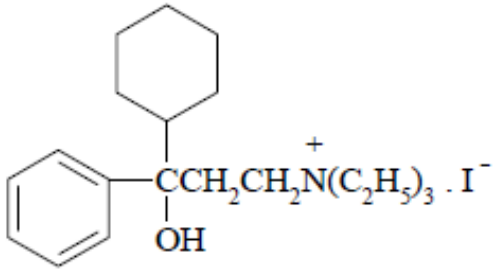
Antispasmodic.

Its used in Parkinson's disease for eliminating akinesia, rigidity, and tremor.

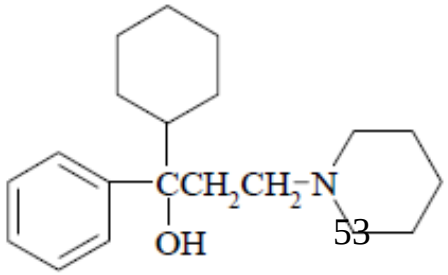
Procyclidine
1-Cyclohexyl-1-phenyl-3-pyrrolidinepropanol



Tridihexetyl iodide
(3-Cyclohexyl-3-hydroxy-3-phenylpropyl)triethylammonium iodide



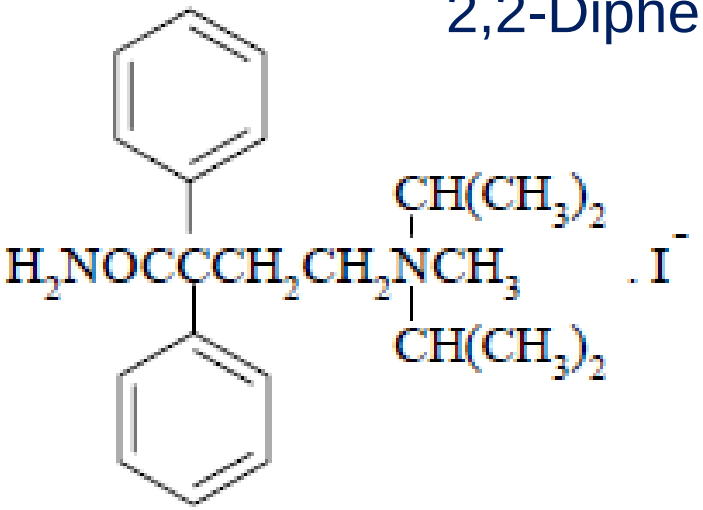
Trihexyphenidyl
1-Cyclohexyl-1-phenyl-3-piperidinylpropanol



- **Aminoamides**

Isopropamide iodide

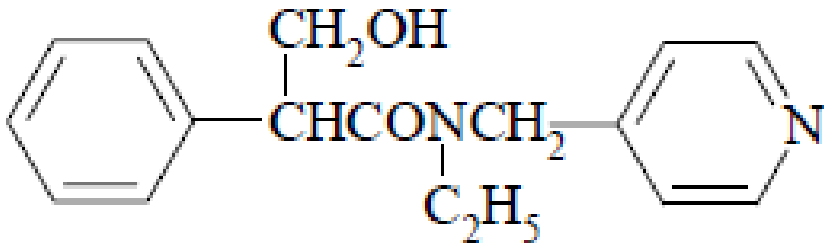
2,2-Diphenyl-4-diisopropylaminobutyramide methyl iodide



- **This drug is a potent anticholinergic, producing atropine-like effects peripherally.**
- **It is used as adjunctive therapy in the treatment of peptic ulcer and other conditions of the GI tract associated with hypermotility and hyperacidity.**

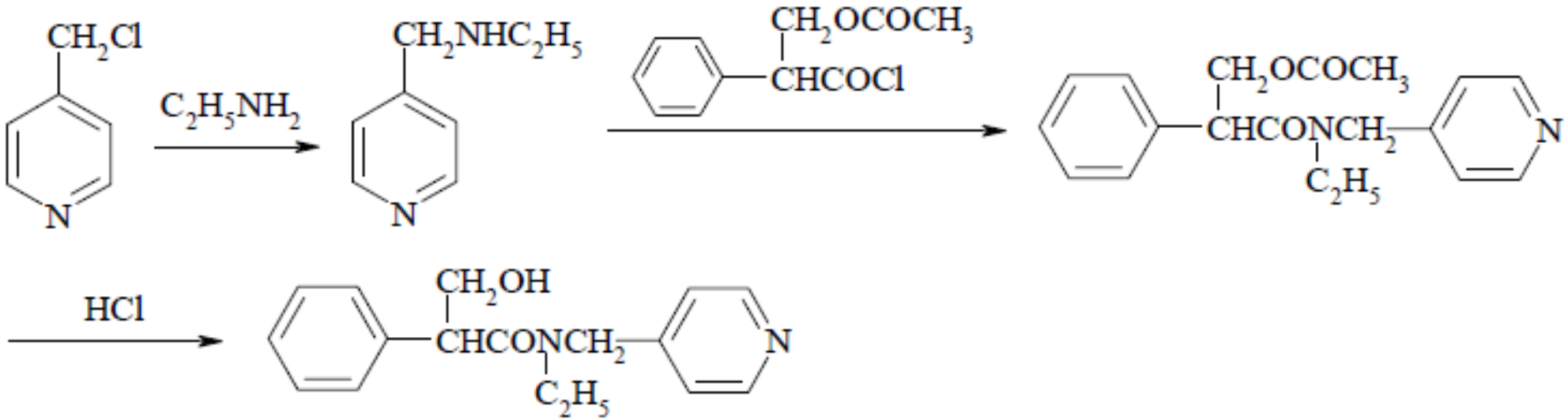
Tropicamide

MIDRIACYL

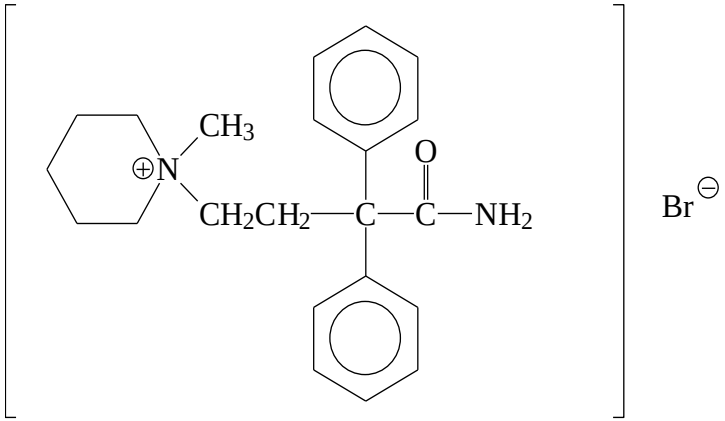


N-Ethyl-α-(hydroxymethyl)-N-(4-pyridylmethyl)benzeneacetamide

It is an effective anticholinergic for ophthalmic use when mydriasis is produced by relaxation of the sphincter muscle of the iris. Its maximum effect is achieved in about 20 to 25 minutes and lasts for about 20 minutes, with complete recovery in about 6 hours.



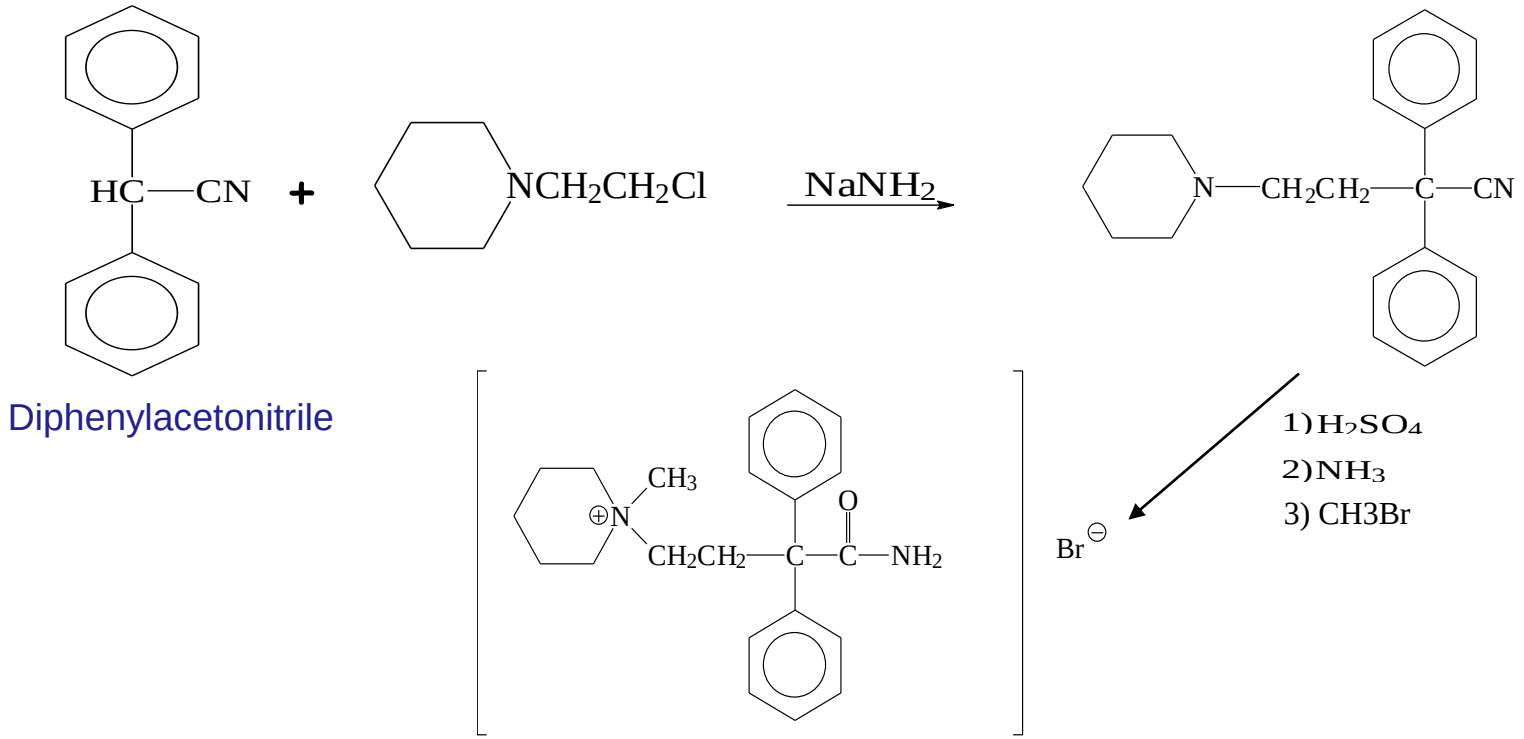
Fenprevinium Br BARALGINE



It is an anticholinergic and antispasmodic. It is marketed as a combination drug with pitofenone_HCl and either nimesulide or metamizole to treat smooth muscle spasms and pain.

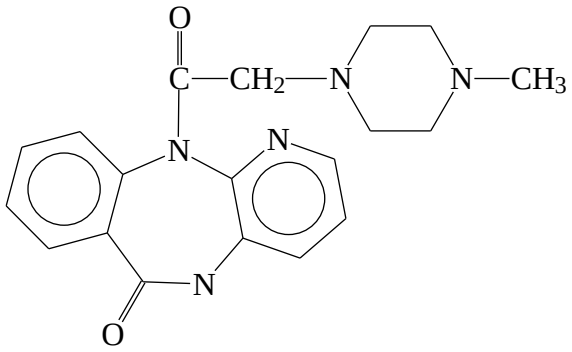
2,2-Diphenyl-4-(1-methyl-piperidinium)butyramide-bromide

Sentezi:



Diphenylacetonitrile

Pirenzepine GASTROZEPIN



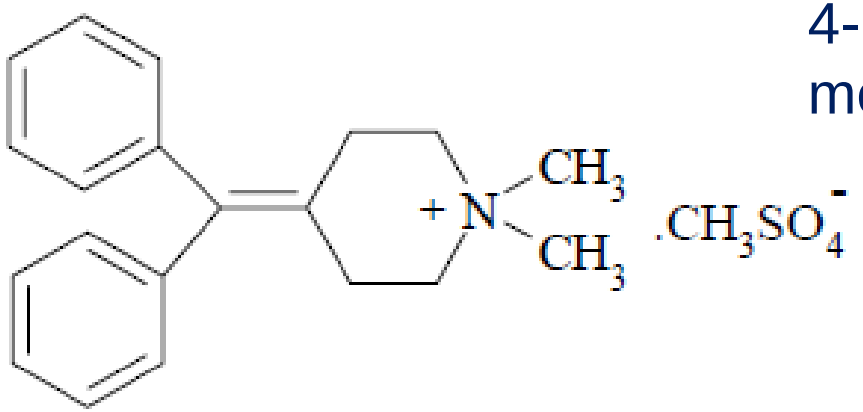
5,11-Dihydro-11-[(4′-methyl-1′-piperazinyl)acetyl]-6H-pyrido-[2,3-b] [1,4] benzodiazepine-6-one

Pirenzepine, which includes tricyclic structure, is gastro-selective. It was found to be close to Histamine H2 receptore blockers in the treatment of peptic ulcer. Selective M1 antagonist.

Decreases gastric acid secretion – promotes ulcer healing

- Miscellaneous

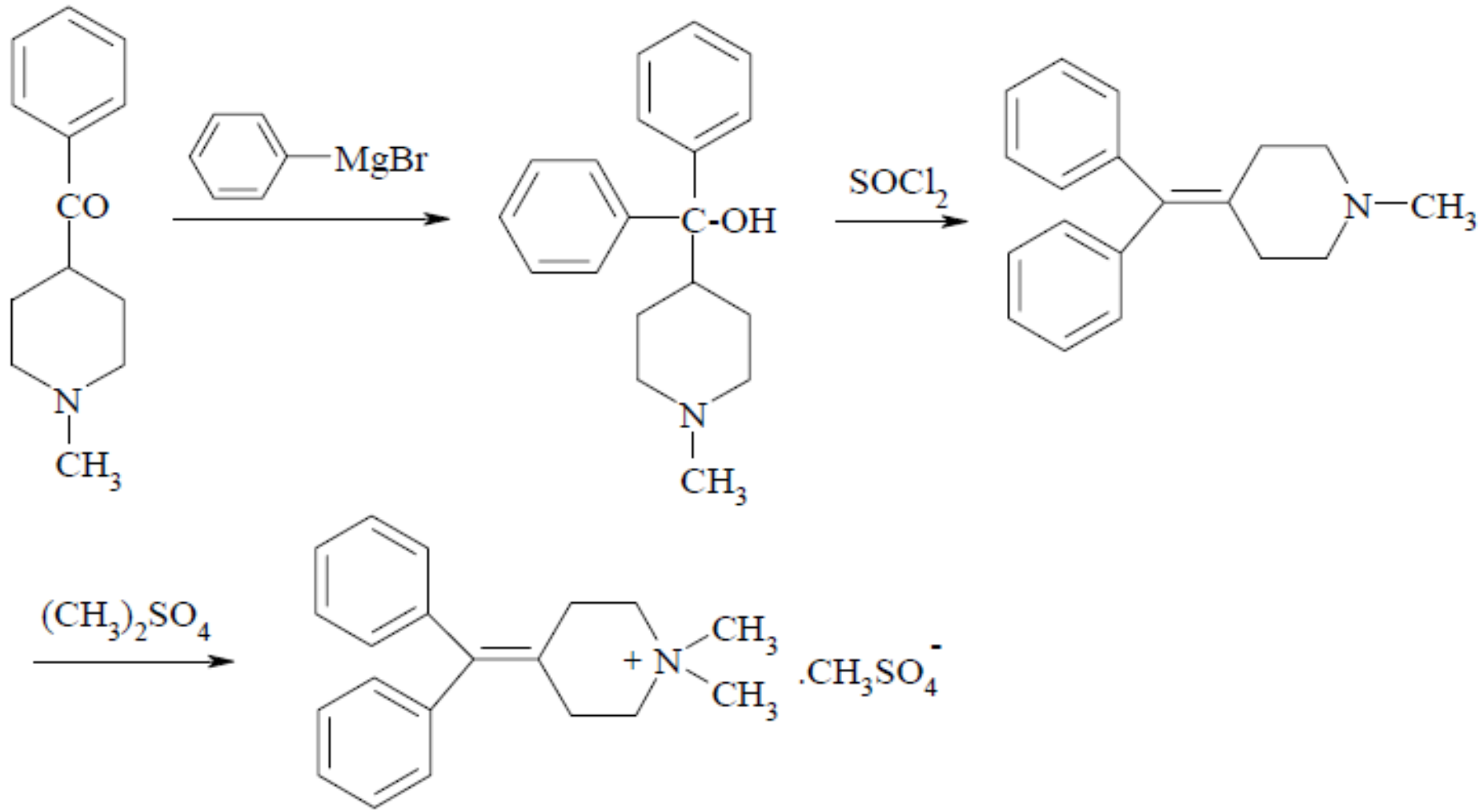
Diphemanil methylsulfate



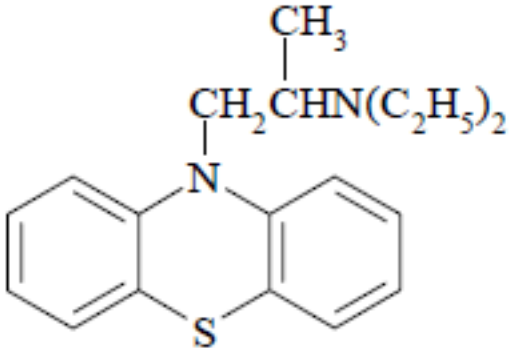
4-(Diphenylmethylene)-1,1-dimethylpiperidinium methylsulfate

It is a potent anticholinergic compound. It is useful in the treatment of peptic ulcer, hypermotility and acidity

Synthesis of Diphemanil methylsulfate

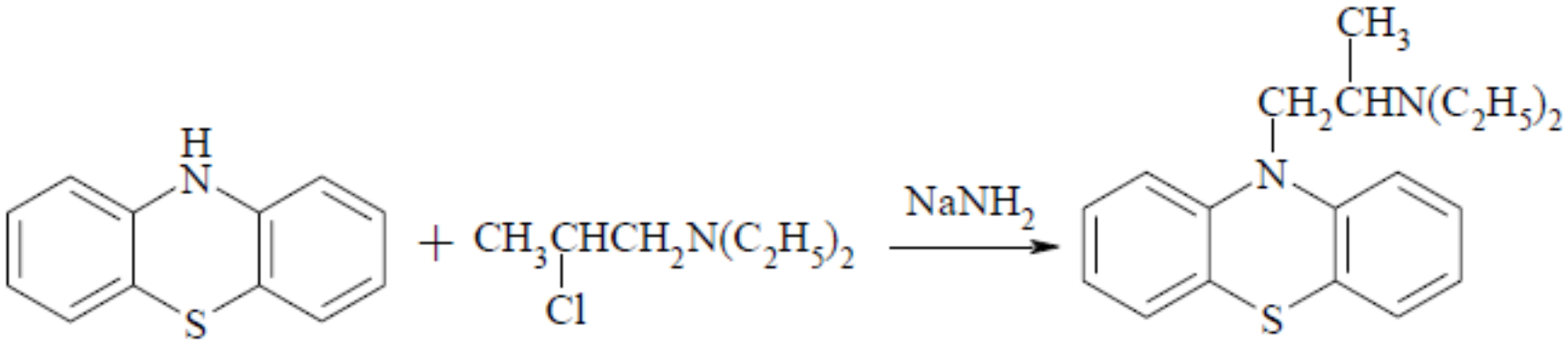


Ethopropazine



10-[2-(diethylaminopropyl)]phenothiazine

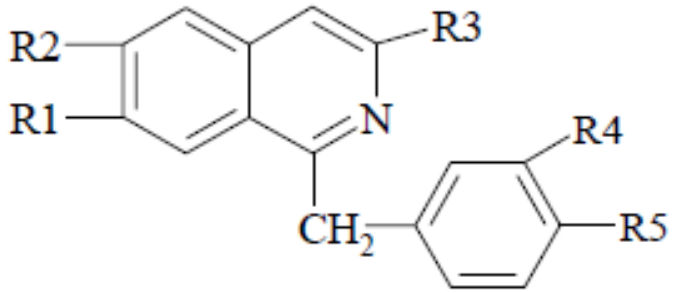
Especially useful in the symptomatic treatment of parkinsonism.



Fenotiyazinin sodyum amidür varlığında 2-Kloro-N,N-dietilpropilamin ile reaksiyonu sonucu elde edilir.

• Papaverine alkaloids and synthetic derivatives

Papaverine is an **isoquinoline** derivative. Its main effect is as a spasmolytic on smooth muscle, acting as a direct, nonspecific relaxant on vascular, cardiac, and other smooth muscle.



Compound	R1	R2	R3	R4	R5
Papaverine 6,7-Dimethoxy-1-veratrylisoquinoline	$-OCH_3$	$-OCH_3$	-H	$-OCH_3$	$-OCH_3$
Etaverine **1**-(3,4-Dimethoxybenzyl)-6,7-diethoxyisoquinoline	$-OC_2H_5$	$-OC_2H_5$	-H	$-OC_2H_5$	$-OC_2H_5$
Dimoksilin$^+$	$-OCH_3$	$-OCH_3$	$-CH_3$	$-OCH_3$	$-OC_2H_5$