Antiparasitics

= compounds used for treatment of parasitary infestations

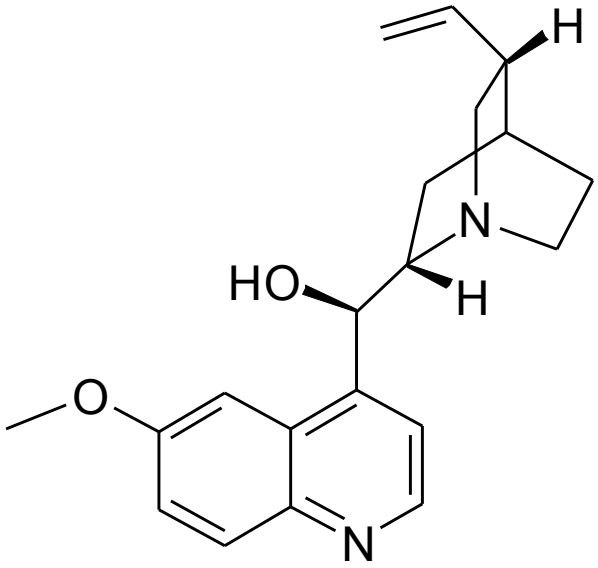
1. Antoprotozal drugs
2. Anthelmintics
3. Insecticides, ixodecides and repellents

1. Antiprotozoal drugs

= compounds killing pathogenic protozoa

1.1. Antimalarial drugs

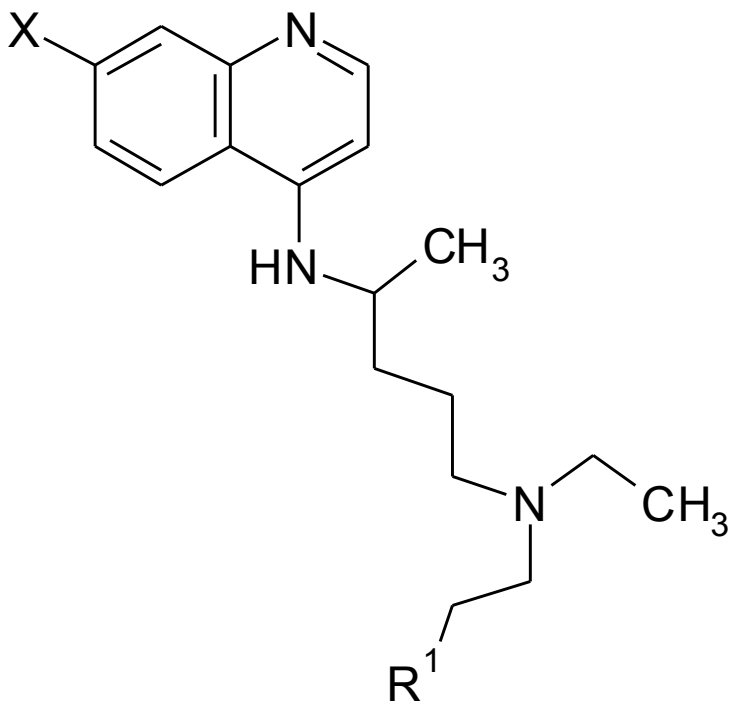
- infectious agents – protozoa of the genus *Plasmodium: P. vivax, P. falciparum, P. malariae, P. ovale*



quinine

- isolation from cinchona bark *Cortex chinae* (+ its stereoisomers quinidine, cinchonine, cinchonidine)
- except antimalarial effects has also antirheumatic and antipyretic ones
- „lead compound“ for design of newer antimalarials with quinoline skeleton

Antimalarial drugs
Quinoline derivatives



X = Cl R^1= H **chloroquine**

Delagil® tbl.

X = F R^1= H **fluoroquine**

X = Cl R^1= OH **hydroxychloroquine**

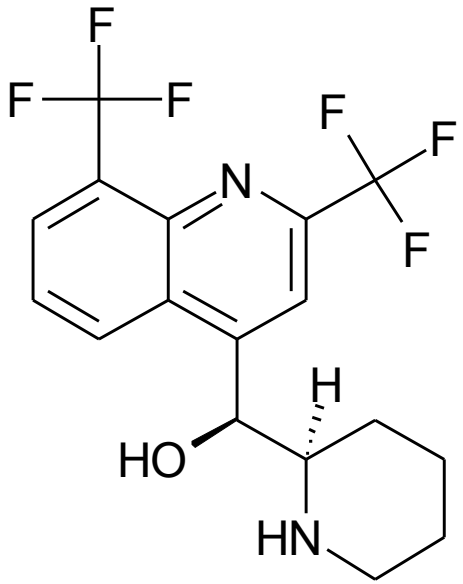
Plaquenil® drg.

·also treatment of rheumatoid arthritis

·mech. of action: inhibition of transformation of heme, which is toxic for the parasite, into hemozoine, which is not (= „malarial pigment“ - non-toxic for *Plasmodium*)

Antimalarial drugs

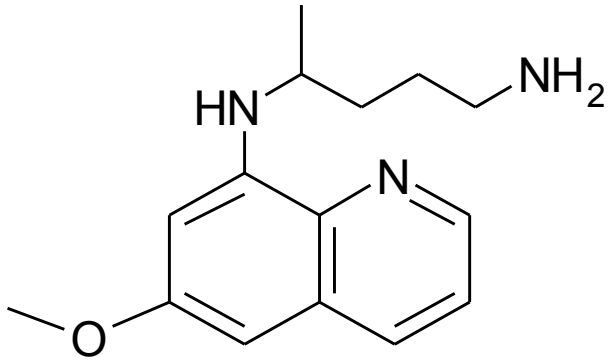
Quinoline derivatives



mefloquine

Lariam® tbl.

- also prophylactic before a travel to a tropic region

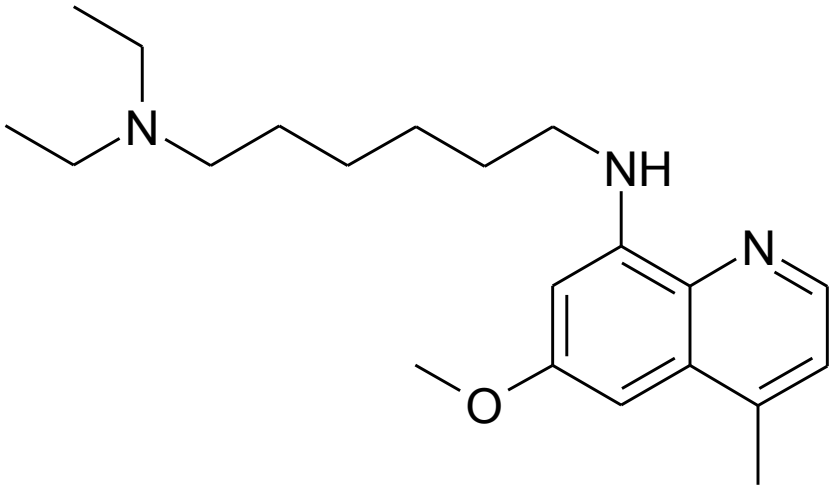


primaquine

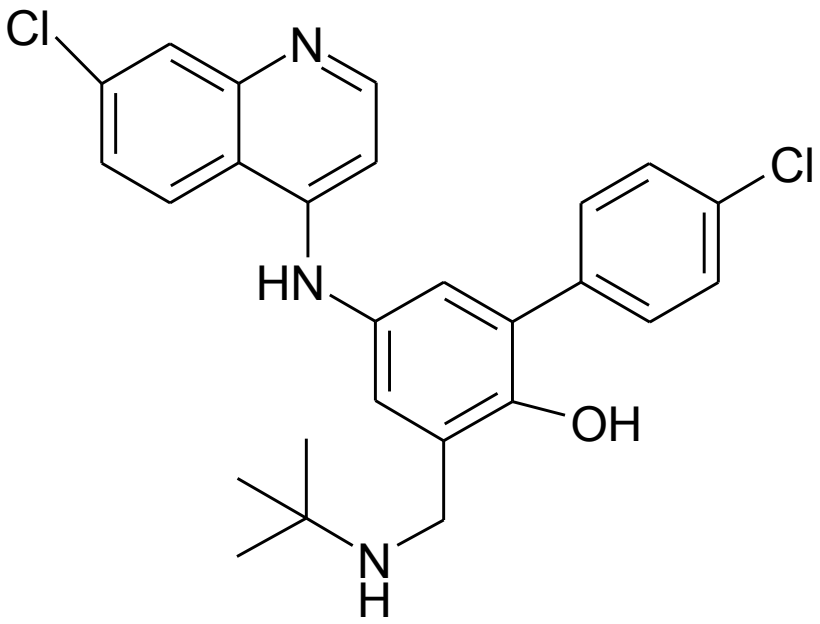
Primaquine® tbl. obd.

Antimalarial drugs

Quinoline derivatives



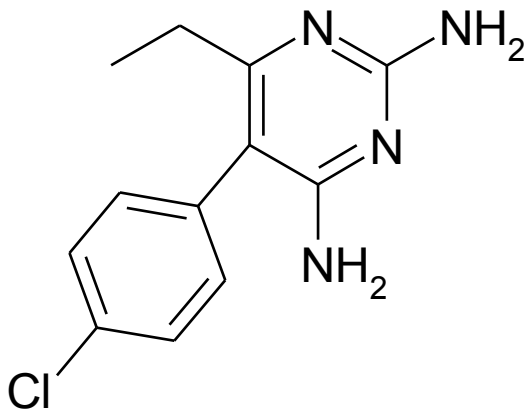
sitamaquine

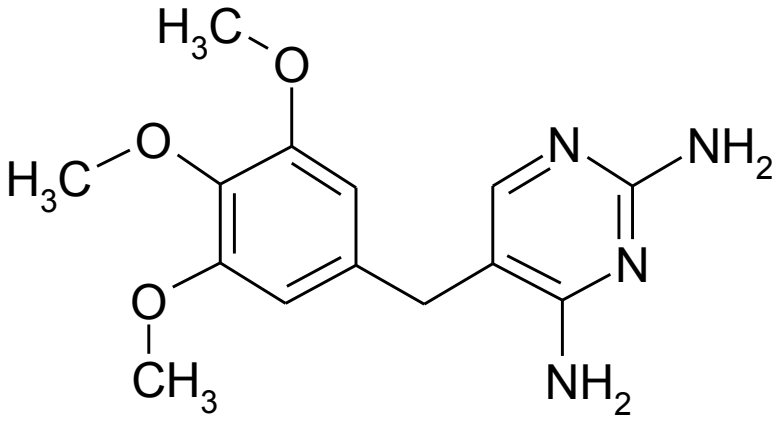


tebuquine

Antimalarial drugs

Pyrimidine derivatives





pyrimethamine

Daraprim®

- also treatment of toxoplasmosis in combination with sulfadiazine

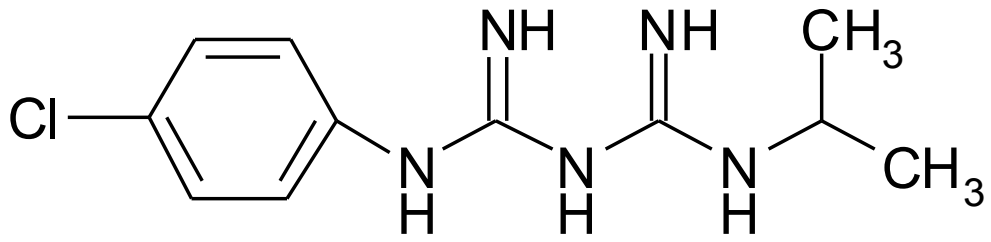
trimethoprim

Triprim ® tbl.

- now more frequently used in antibacterial combinations with sulfonamides

Antimalarial drugs

Biguanide derivatives



proguanil

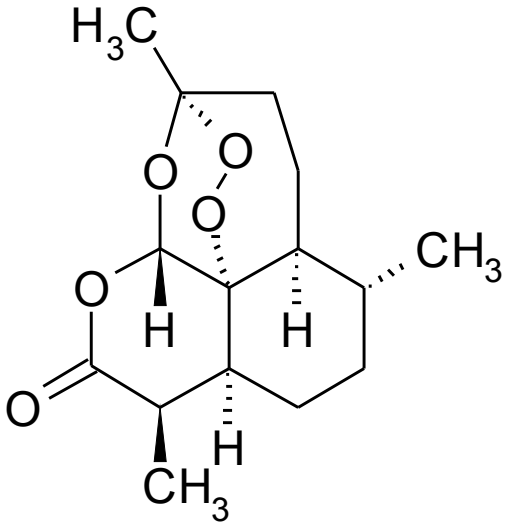
Malarone® por. tbl. flm.

- spectrum: *P. falciparum*
- mech. of action: inhibition of dihydrofolate reductase
- avoids formation of tissue schizonts (hypnozoites)

Antimalarial drugs

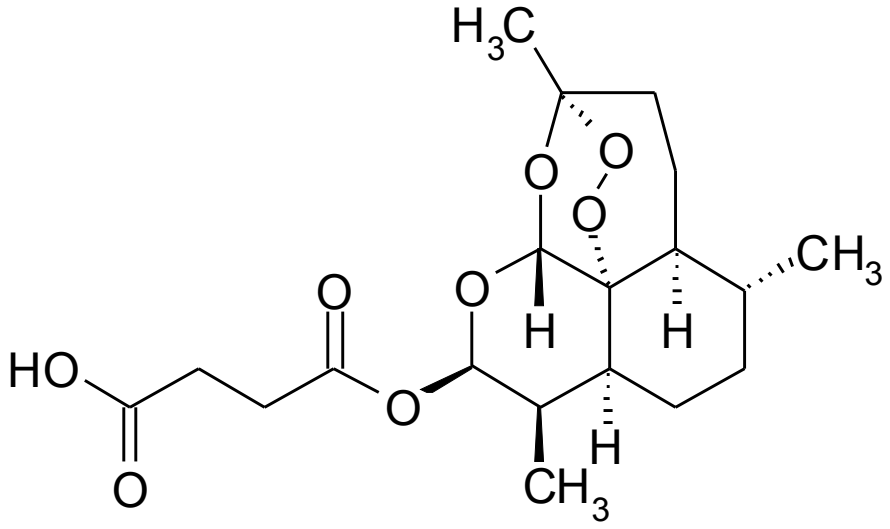
Artemisinin and its analogues

- cyclic endoperoxides
- mech. of action: forming of free radicals, toxic for *Plasmodium*, catalyzed by Fe of heme



artemisinin

- sesquiterpene lactone isolated from wormwood *Artemisia annua*
- poor biological availability

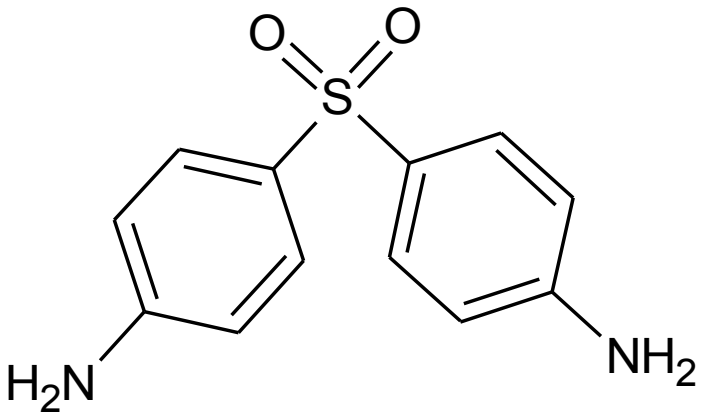


artesunate

- used as sodium salt for i.m. administration

Antimalarial drugs

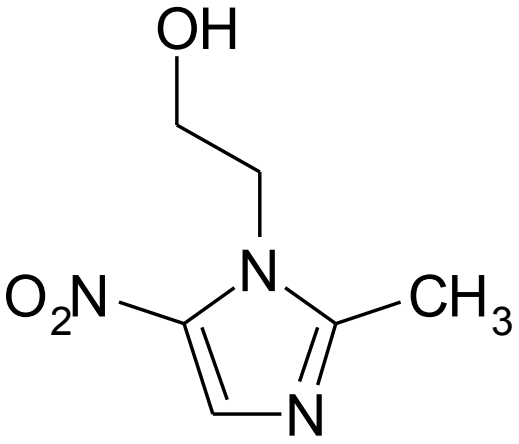
Sulfones



dapson
1,1´-bis(4-aminophenyl)sulfone

- mode of action: inhibition of folic acid synthesis, inhibition of dihydropteroate synthase (like sulfonamides) in particular
- also drug for leprosy

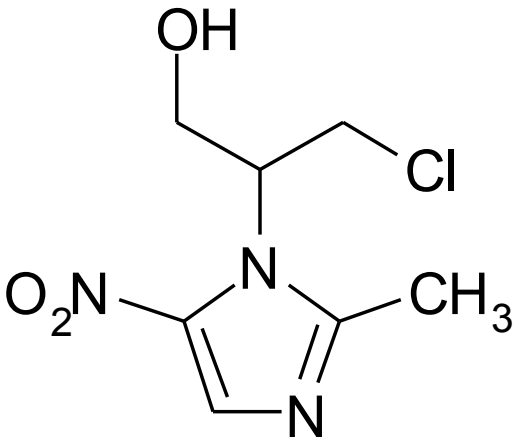
1.2 Antiprotozoal drugs other than antimalarials
5-nitroimidazole derivatives



metronidazole

Entizol® tbl., tbl. vag.

- spectrum: *Trichomonas vaginalis, Entamoeba histolytica*, *Treponema,* anaerobic bacteria
- mechanism of action: interference with metabolism

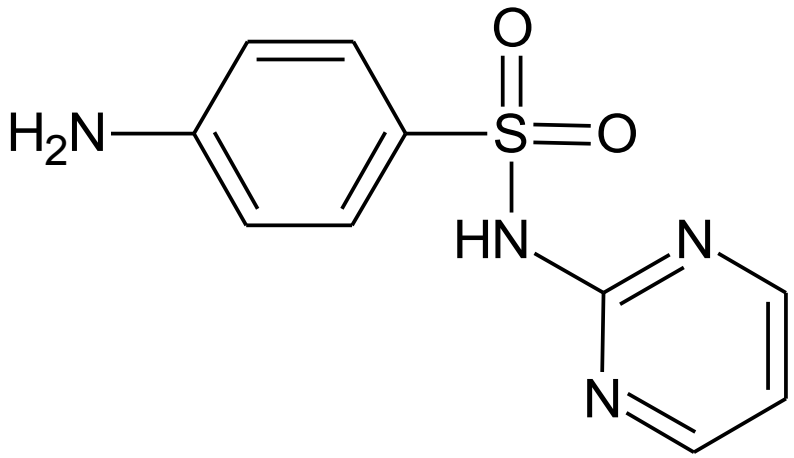


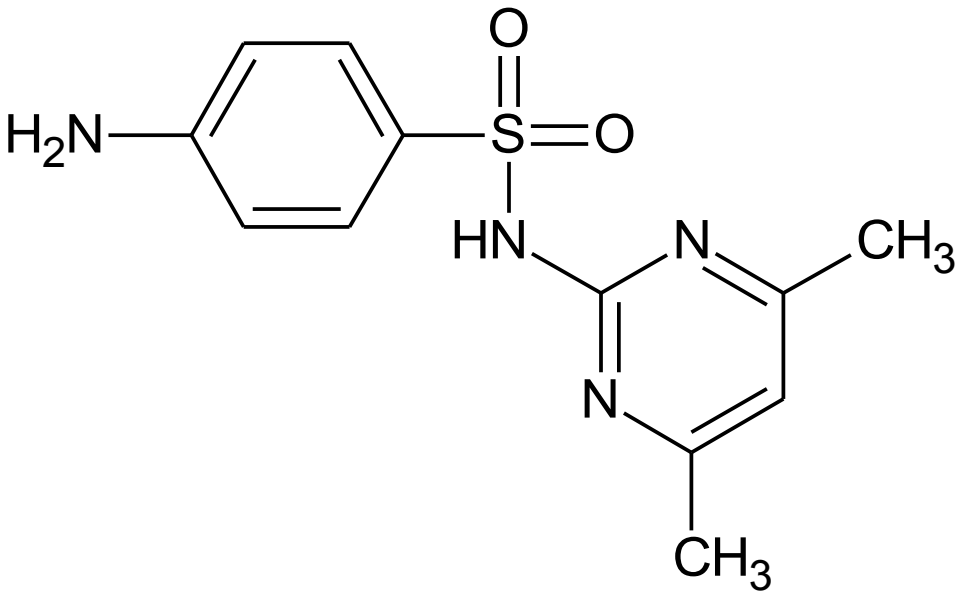
ornidazole

Avrazor® inj.

- spectrum: *Trichomonas vaginalis, Entamoeba histolytica, Giardia intestinalis, Bacteroides,* anaerobic bacteria
- mechanism of action: interference with metabolism

1.2 Antiprotozoal drugs other than antimalarials
Sulfonamides





sulfadiazine

- One of the short-acting sulfonamides used in combination with pyrimethamine to treat toxoplasmosis in patients with acquired immunodeficiency syndrome and in newborns with congenital infections.

sulfadimidine

syn. sulfamethazine [USP]

- sodium salt against coccidiosis (caused namely by *Eimeria sp.*) in poultry and rabbits

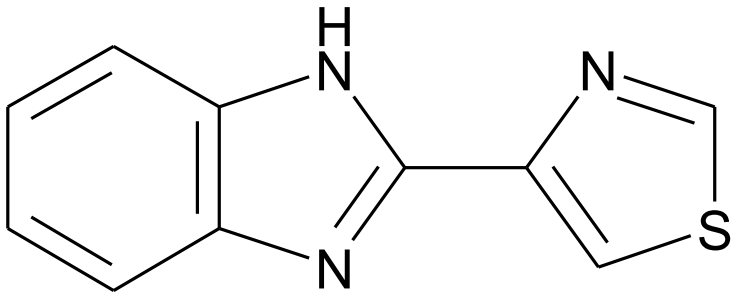
SULFADIMIDIN BIOVETA ® plv. sol. ad us. vet.

- mode of action: inhibition of dihydropteroate synthase

2. Anthelmintics

= compounds against parasitic worms

Benzimidazole derivatives



tiabendazole

syn. thiabendazole [USAN, BAN]

~~Mintezol® tbl.~~

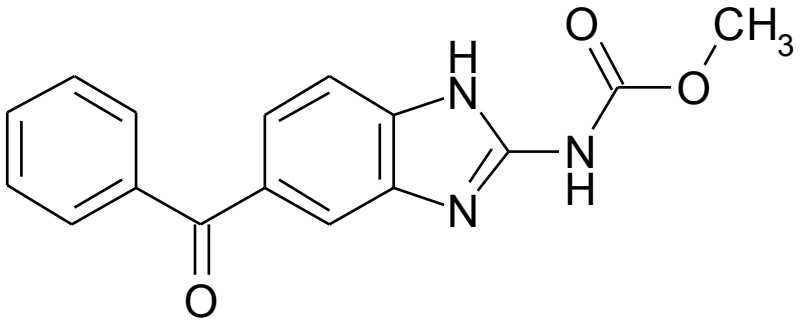
·also fungicidal effect

2. Anthelmintics

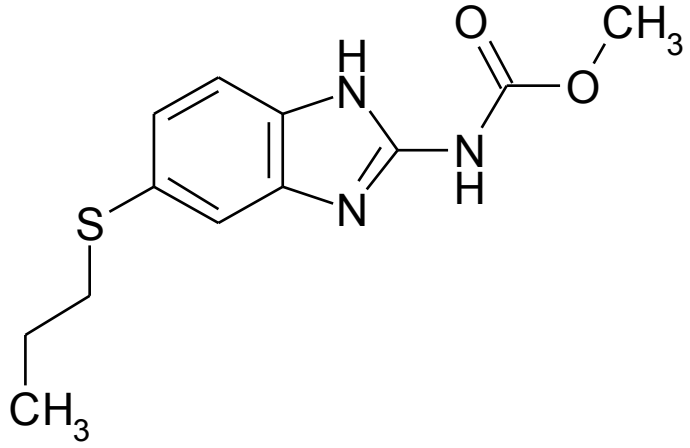
Benzimidazole derivatives

Methyl 1*H*-benzimidazole-2-carbamates

- mech. of action: selective inhibition of mitosis of both worms and protozoa (binding to tubuline)



mebendazole
Vermox® tbl., por. sus.

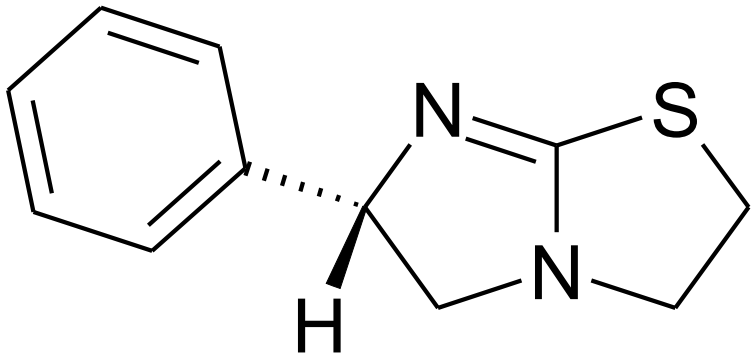


albendazol
~~Zentel® por. sus.~~

- spectrum: human pinworm *Enterobius vermicularis,* whipworm *Trichuris trichiura,* human large roundworm *Ascaris lumbricoides,* hookworm *Ancylostoma duodenale,* threadworm *Strongyloides strercoralis,* tapeworms *Taenia spp.* etc., also protozoa *Girardia lamblia, Trichomonas vaginalis*

Anthelmintics

Imidazothiazole derivatives



levamisole

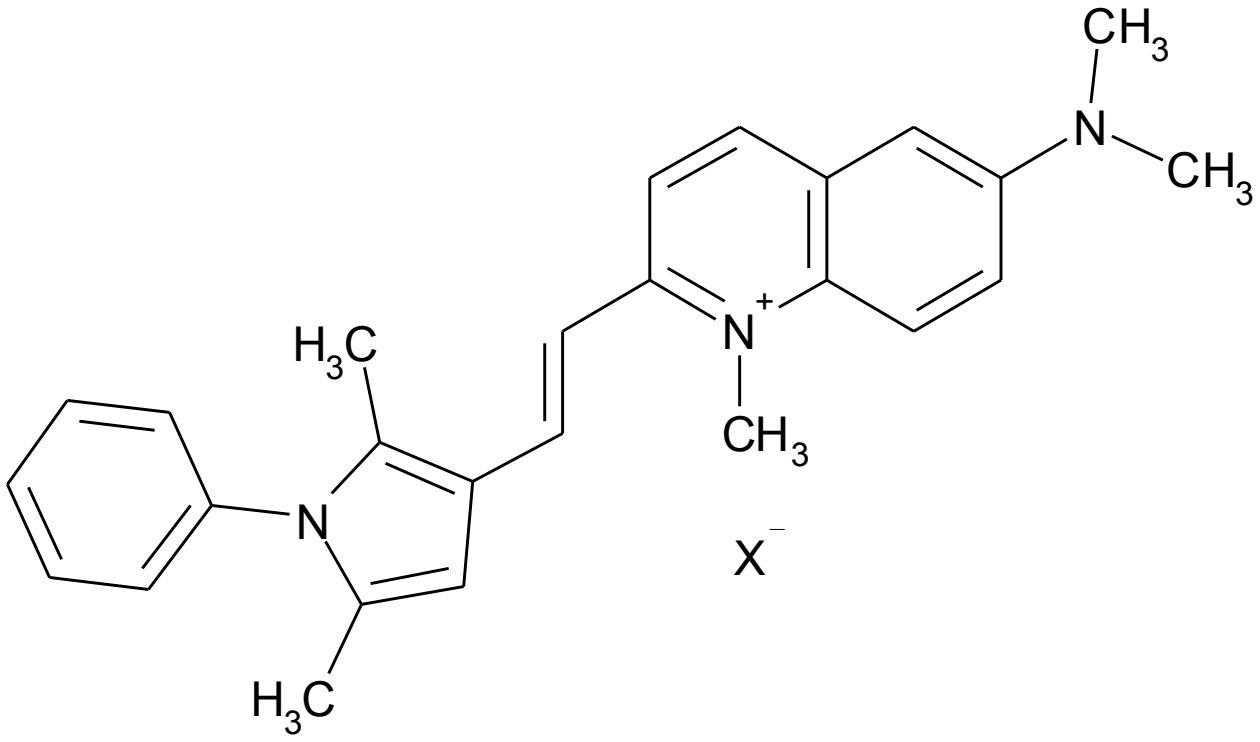
S-(-)-2,3,5,6-tetrahyro-6-phenylimidazo[2,1-b]thiazole

~~Decaris® tbl.~~

- ascaridosis, ancylostomosis, strongyloidosis, trichuriosis
- also immunomodulation effect – useful in rheumatoid arthritis, *lupus erythematodes*

Anthelmintics

Quinoline derivatives

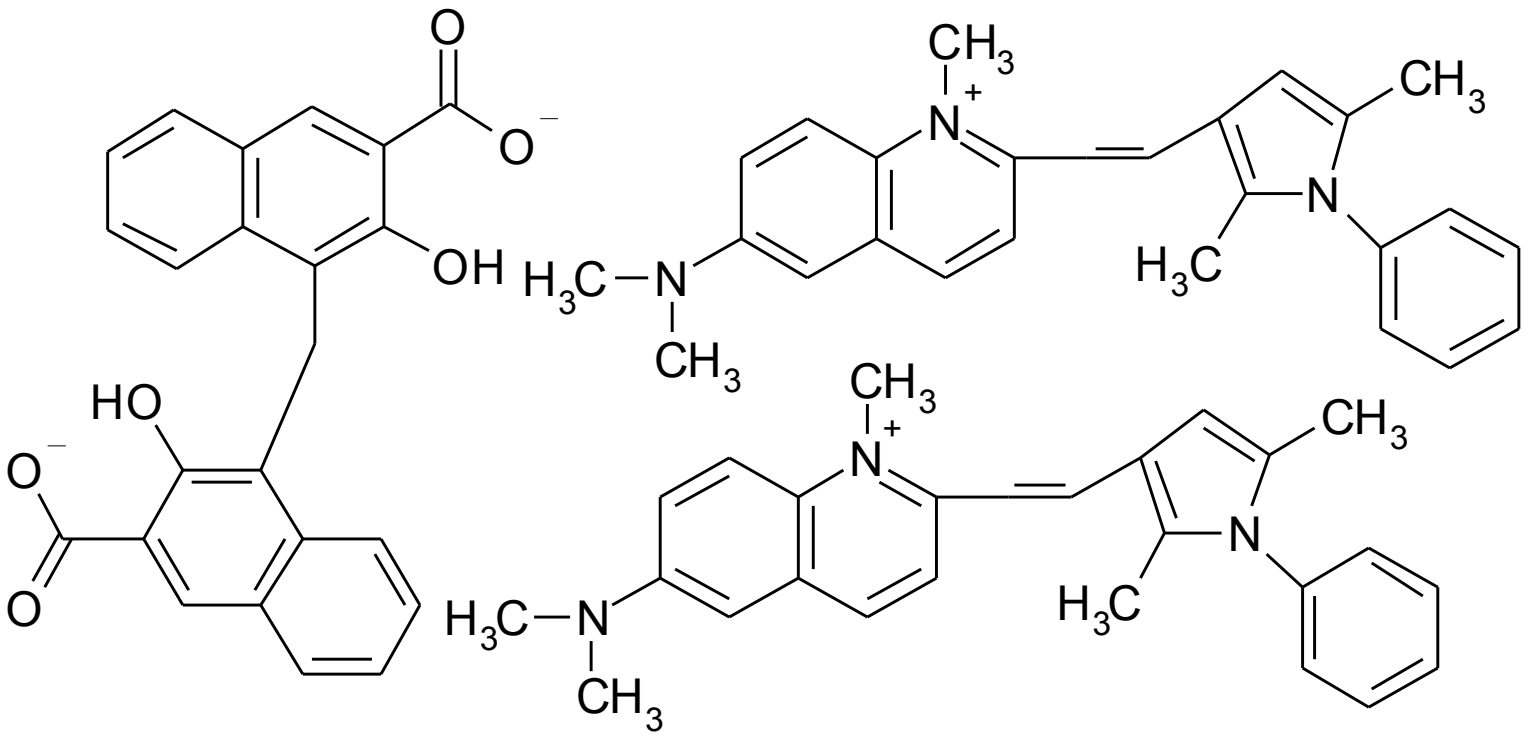


pyrvinium

~~Pyrvinium® susp.~~ as embonate, i.e. salt with 4,4-methylenebis(3-hydroxynaphtalene-2-carboxylic)acid

- human pinworm *Enterobius vermicularis*

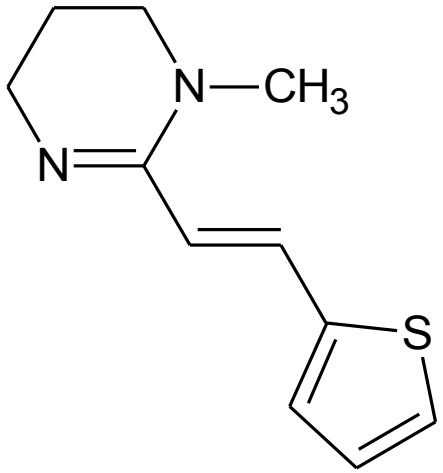
Pyrvinium embonate



·pyrvinium embonate (syn. pamoate)

Anthelmintics

Tetrahydropyrimidine derivatives



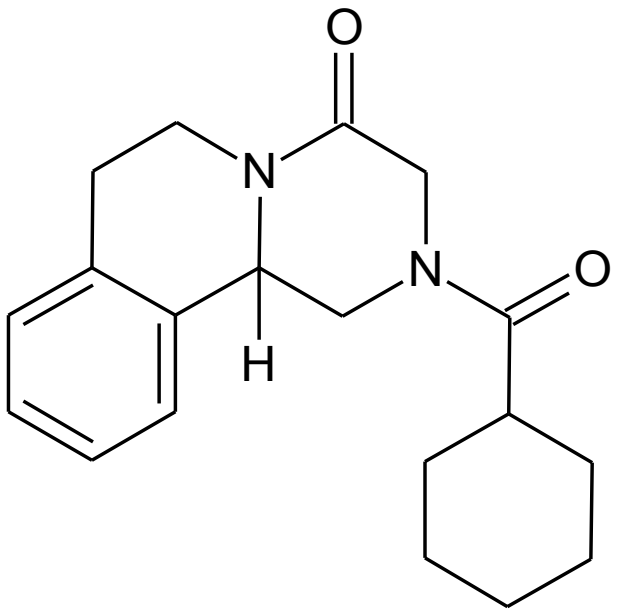
1-methyl-2-[(*E*)-2-(thiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine

pyrantel

- mechanism of action: depolarizing neuromuscular-blocking agent, that causes persistent nicotinic activation resulting in spastic paralysis of susceptible nematodes
- drug of second-choice after benzimidazoles for treatment of ascariasis, hookworm, and pinworm infections
- effective after a single dose

Anthelmintics

Pyrazinoisoquinoline derivatives



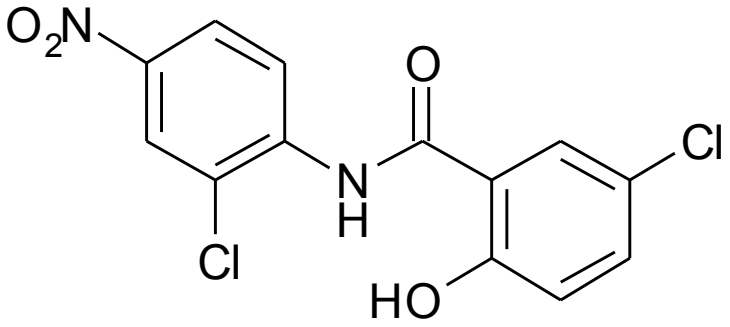
2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino[2,1-*a*]isoquinolin-4-one

praziquantel

- treatment of schistosomiasis (blood-flukes or bilharzia or *Schistosoma* infection)

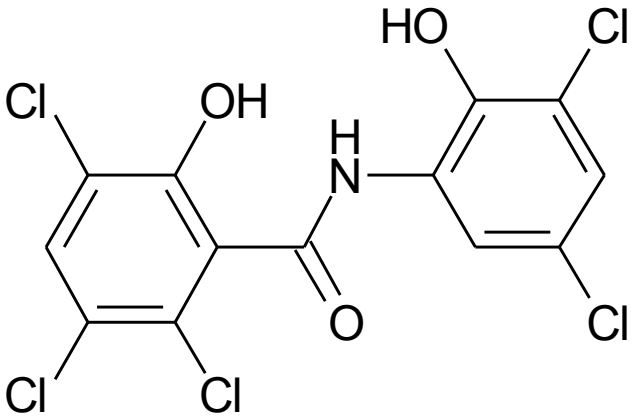
Anthelmintics

Halogenated salicylanilides



niclosamide

- tapeworms

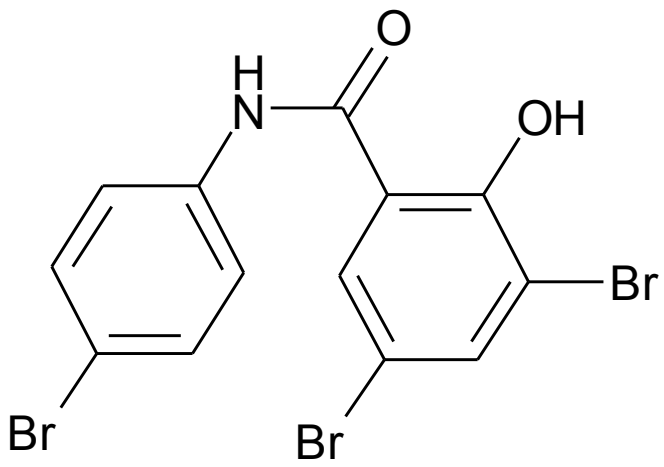


oxyclozanide

- veterinary medicine: for fasciola (liver fluke) and tapeworms infestations in grazing animals (cattle)

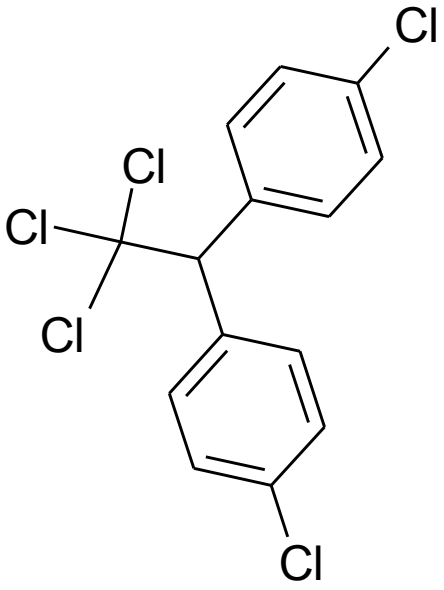
Anthelmintics

Halogenated salicylanilides



tribromsalan

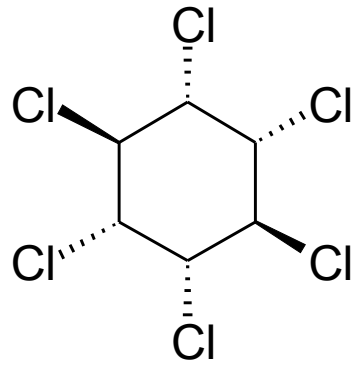
3. Insecticides
Chlorinated compounds



DDT

·fundamental importance for eradication of stings which spreaded malaria and yellow fever

·accumulated in organism and in the environment ⇒ not used any more



γ-hexachlorocyclohexane

lindan

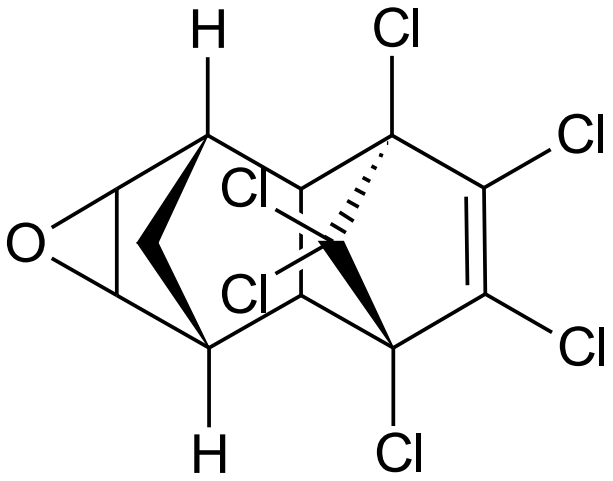
Skabicid® drm. eml.

·spectrum: *Sarcoptex scabiei, Phtirius pubis,* louse *Pediculus capitis*

·topical treatment of scabies

·contact, alimentary and inhalation neural poisons for insects

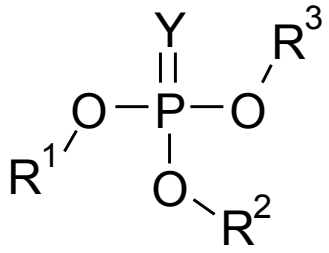
Insecticides
Chlorinated compounds

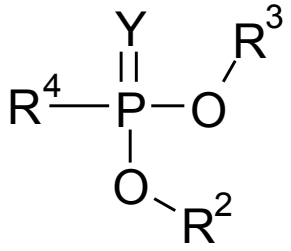


dieldrine

- mechanism of action: inhibition of GABA-receptors
- obsolete: resistance, residues in environment

Insecticides
Organic compounds of phosphorus
Esters of (thio)phosphoric acid & (thio)phosphonic acids





Y= O, S

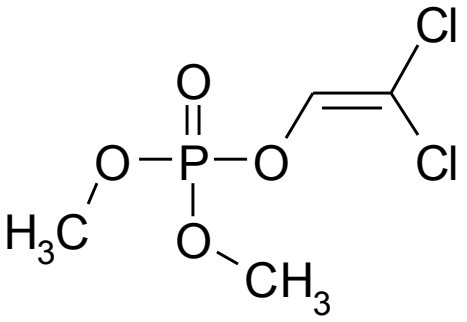
R^1- R^4 = alkyl, aryl

organophosphates,
organophophothioates

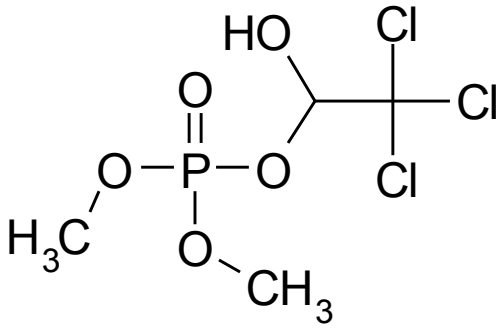
organophosphonates,
organophosphothionates

- irreversible cholinesterases inhibitors ⇒ strong parasympathomimetics

Insecticides
Organic compounds of phosphorus
Esters of phosphoric acid & phosphonic acids



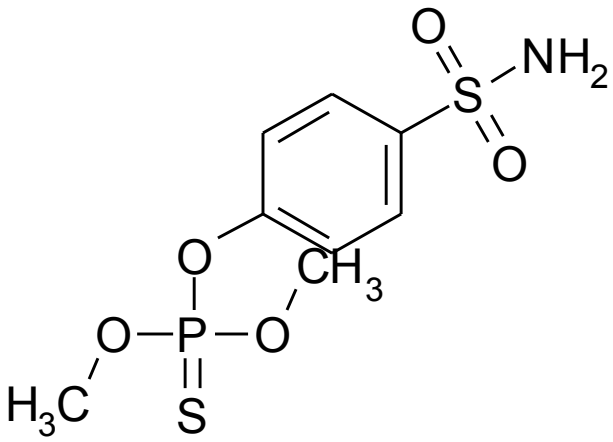
dichlorvos
Nuvan Top® spray a.u.v.



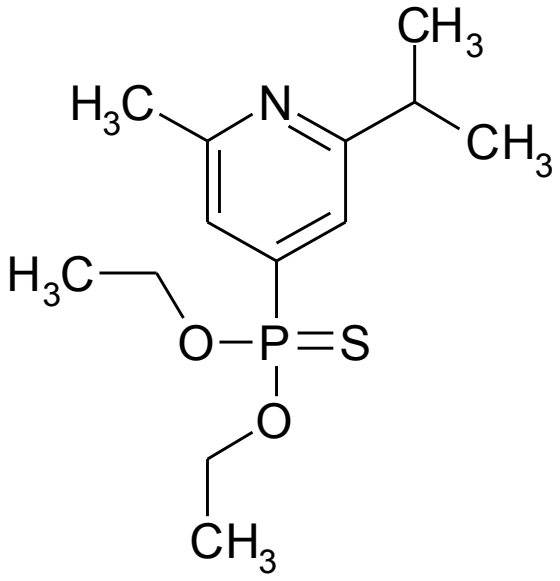
metriphonate
syn. trichlorfon [USAN]
Arpalit® spray a.u.v.

▪against fleas in furs (hair) of dogs and cats

Insecticides
Organic compounds of phosphorus
Esters of thiophosphoric acid & thiophosphonic acids

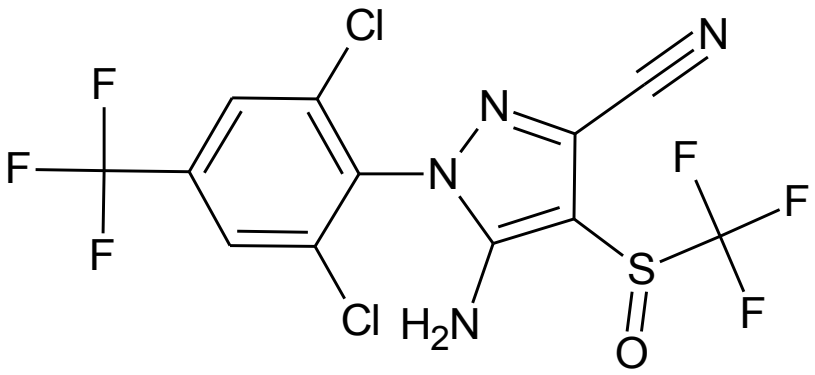


cythioate
Cyflee® sol. a.u.v.



dimpylate
syn. diazinon
Droplix® a.u.v.
·transcutaneously absorbed, kills parasites on whole body surface

Insecticides
Selective inhibitors of GABA-receptors



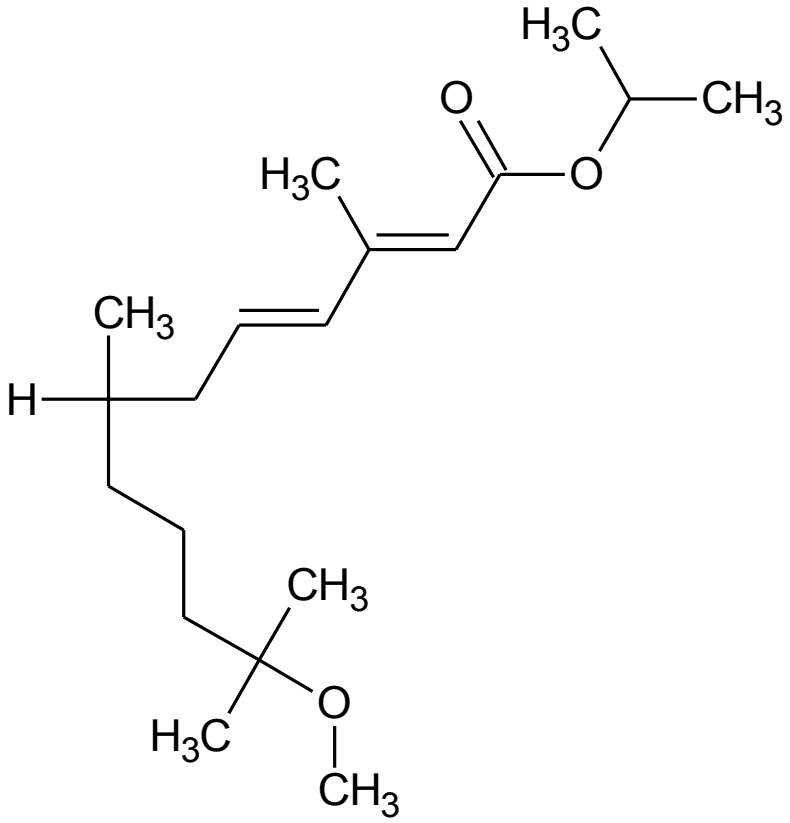
fipronil

•blocks GABA-receptors of insects which basically differs from mammalian ones in both structure and function

•highly selective toxicity for insects

Certifect ® „spot-on“ pipettes (+ (S)-methoprene and amitraz) against ticks, fleas and chewing lice in dogs

Insecticides
Insect hormone analogues



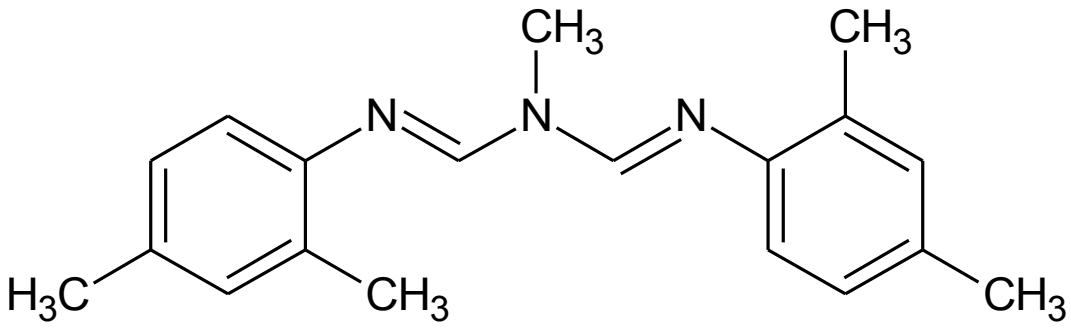
methoprene

- juvenile hormone analogue and insect growth regulator used to control insects by disrupting metamorphosis
- absorbed into flea eggs or larvae, where it stops their development
- effective also in controlling mosquito larvae

Certifect ®

Ixodecides

- kill ticks (arthropods)



N'-(2,4-dimethylphenyl)-*N*-{(*E*)-[(2,4-dimethylphenyl)imino]methyl}-*N*-methylimidoformamide

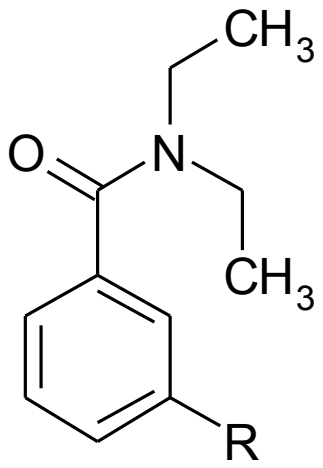
1,5-bis(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene

amitraz

- mode of action: stimulates the nervous systems of ticks, leading to hyperactivity and death of them.

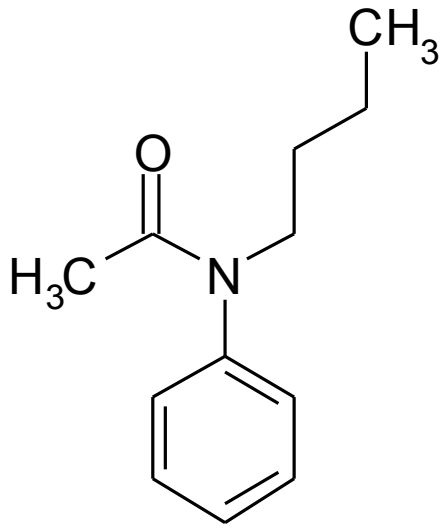
Certifect ®

Repellents



R = H
N,N-diethylbenzamide

R = CH_3
N,N-diethyl-*m*-toluamide
(= 3-methylbenzoic acid diethylamide)



N-butylacetanilide
(= N-butyl-N-phenylacetamide)

- only repel, do not kill insects and ticks
- used in repellent gels, creams and lotiones in concentrations 10 – 20 %