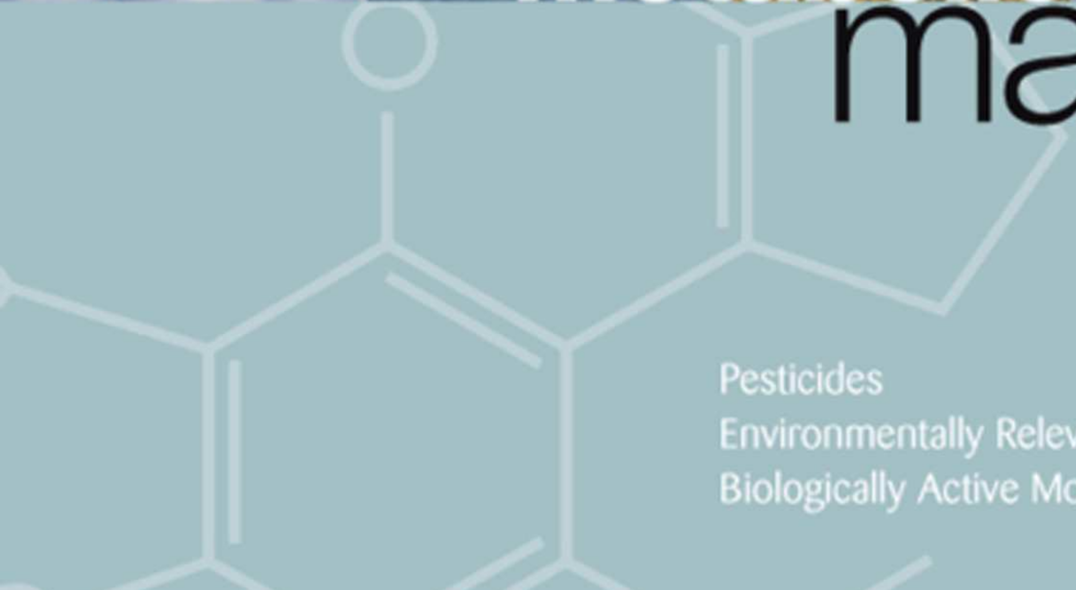
metabolic maps



Pesticides
Environmentally Relevant Molecules
Biologically Active Molecules

Hiroyasu Aizawa

Metabolic Maps

Metabolic Maps

Pesticides, Environmentally Relevant Molecules and Biologically Active Molecules

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Preface

Eighteen years have passed since the publication of *Metabolic Maps of Pesticides* Volume 1 and ten years have passed since the publication of Volume 2.

This new edition, *Metabolic Maps: Pesticides, Environmentally Relevant Molecules and Biologically Active Molecules*, covers the references that have been published since approximately 1985 concerning the metabolic fate of pesticides, pharmaceuticals, natural products, and chemicals of environmental concern. For visual comprehension of the labile sites of the parent compounds being attacked by the environmental systems through such reactions as degradation, hydrolysis, photolysis, metabolism, and so on, three-dimensional graphics of the chemical structures, produced by CS Chem3D, a trademark of CambridgeSoft Corporation, are shown. The labile sites of the molecules against degradation reactions in the environmental systems are indicated by arrows for the individual parent compounds. The SMILES chemical notation of each compound is shown together with the three-dimensional graphics so that the reader may predict the degradability or physicochemical parameters such as pKa, log *P*, degradation patterns, and so on, for the compounds with the aid of the appropriate commercial computer software using SMILES notations. The predicted physicochemical parameters of log *P* for the compounds that appear in this volume have been calculated with SciLogP Ultra software, a trademark of Academic Press, Inc., and are summarized in a table as an example of the parameters predicted by the computer.

Tremendous progress of computer technology in chemistry as well as in other scientific areas has been achieved in these decades, and there is no doubt that this technology will make great strides in the 21st century in various scientific fields. The prediction of new chemical structures for biologically active compounds and the safety assessment of the chemicals will be greatly aided by advanced computer chemistry systems and will help scientists design chemicals much more efficiently and effectively than in the past.

Many people believe that the 21st century will be one in which environmental protection will result in human beings enjoying better health than they did in the 20th century. Scientists will continue to conduct research and development of more useful and safer chemicals on a global basis. I am confident that the three books of this series, *Metabolic Maps of Pesticides Volume 1* and *Volume 2* and this new edition, will be a valuable resource, especially when the data in these books are combined, for the scientist engaged in R&D to find useful chemical tools.

I would like to dedicate these three volumes to Yukie, my wife, for her invaluable support of my work over a long period of time.

Hiroyasu AIZAWA

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1

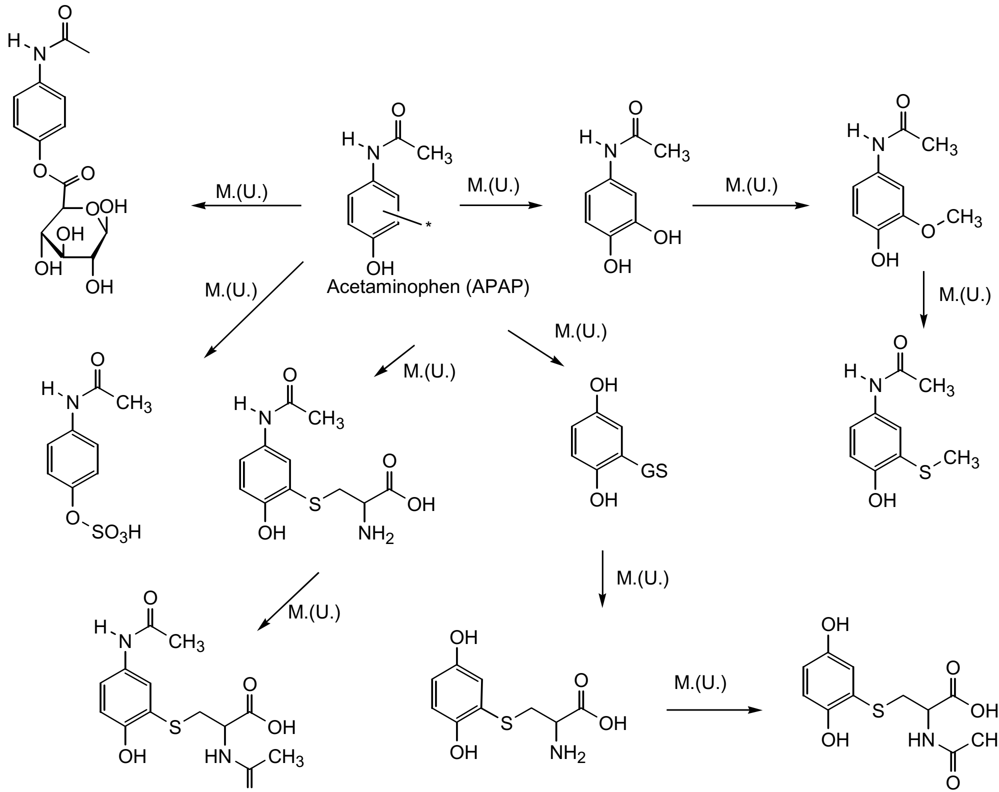
Acid Amides

Acetaminophen (APAP)

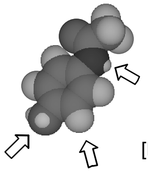
Not a pesticide

Mammal
Adult male BALC/c mice (18–23 g)[1]

Acetaminophen (APAP) is metabolized by mice, and nine metabolites are identified in the urine. The main metabolites are APAP-glucuronide and 3-cysteinyl-APAP. Hydroquinone metabolites of *S*-(2,5-dihydroxyphenyl)cysteine and *S*-(2,5-dihydroxyphenyl)-*N*-acetylcysteine result from the benzoquinone metabolite of APAP.



GS: Glutathione residue



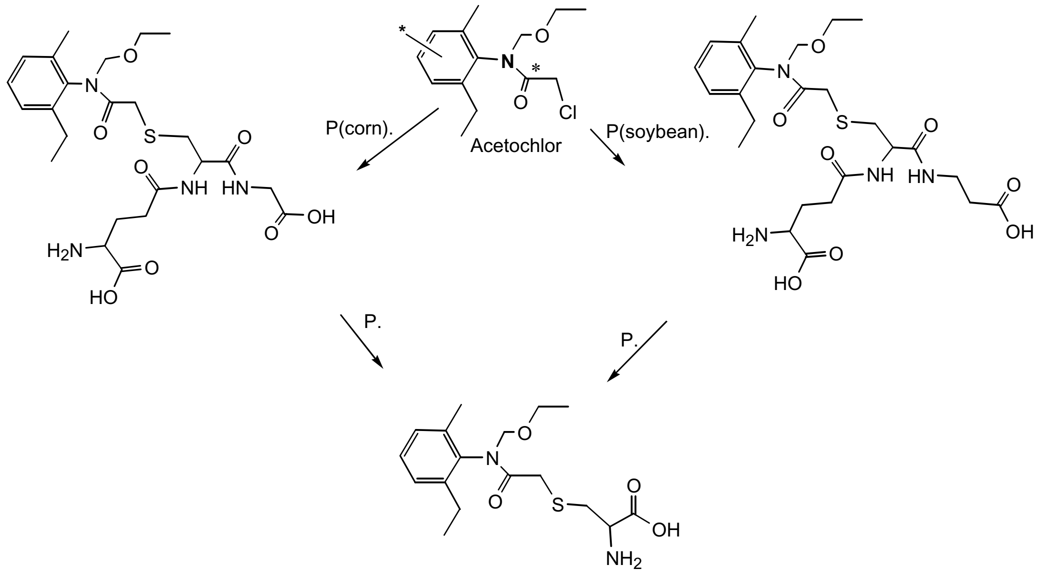
[H]N(C(C)=O)C1=CC=C(O)C=C1

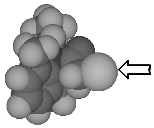
Acetochlor

A pre-emergent herbicide: control of grass weeds and some broadleaf weeds in corn and soybeans

Plant
Corn and soybean seedlings[2]

The initial metabolism of acetochlor is investigated to delineate the detoxification pathway using tolerant corn and soybean seedlings. Acetochlor is rapidly absorbed and metabolized by etiolated corn seedlings to the glutathione conjugate and is also rapidly metabolized by etiolated soybean seedlings. However, the initial metabolite by soybean seedlings is the homoglutathione conjugate, not the glutathione conjugate.





CCOCN(C(CCl)=O)C1=C(CC)C=CC=C1C

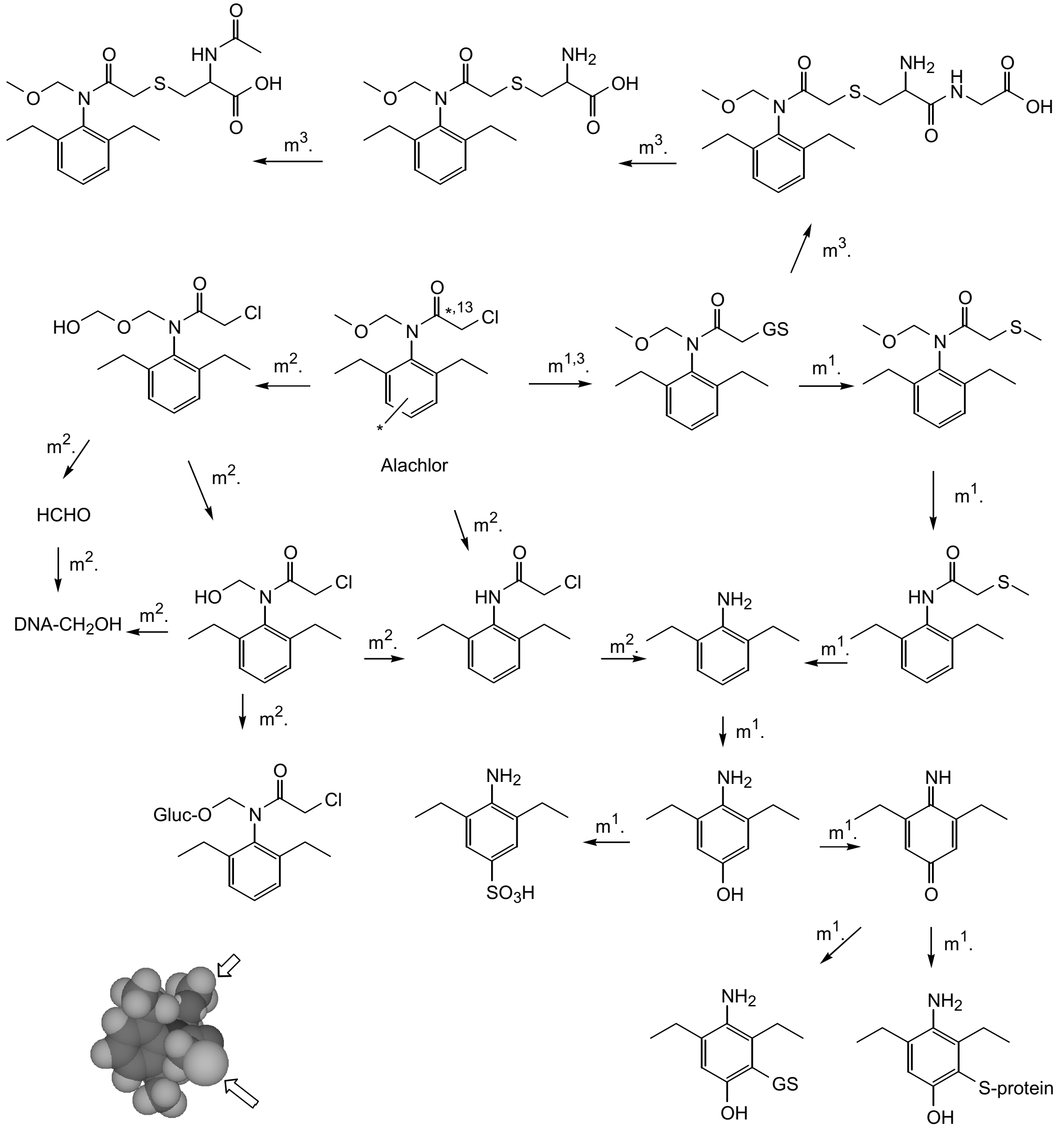
Alachlor

A pre-emergent herbicide: control of weeds in corn and soybeans

Fungus
Soil fungus: *Cunninghamella elegans*[3]

Microsome[1]
Long–Evans rats, CD-1 mice[4]

The metabolism of alachlor using *in vitro* incubations with microsomal fractions prepared from liver and nasal turbinate tissues of rat and mouse (m^1) results in conversion to 3,5-diethylbenzoquinone-4-imine via the key intermediate of 2,6-diethylaniline, the formation



CCC1=CC=CC(CC)=C1N(C(CCl)=O)COC

GS: glutathione residue
Gluc: glucuronic acid residue

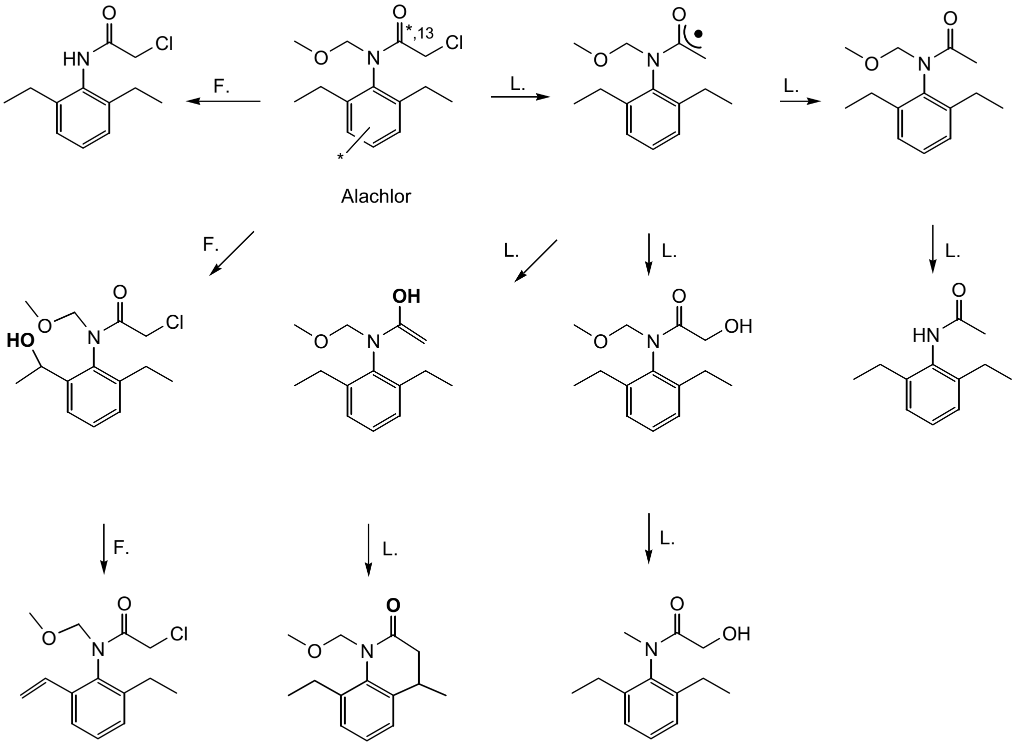
Microsome[2]
Calf thymus DNA alone; calf thymus DNA with horseradish peroxisome (HRP) and with mouse liver microsomes alone and with NADPH *in vitro*; DNA and protein in mice *in vivo* (see the text for details)[5]

Microsome[3]
Liver and kidney homogenates of Long–Evans rats; CD-1 albino mice; male and female Rhesus monkeys (*Macaca multatta*)[6]

Light
A Hanovia–Cornad medium-pressure mercury vapor lamp[7]

of which requires catalysis by microsomal arylamidases. 2,6-Diethylaniline is oxidized to 4-amino-3,5-diethylphenol resulting in quinone imine by further oxidation. Rat nasal tissue possesses high enzymatic activity which can promote the formation of the reactive quinone imine. A methylsulfide metabolite of alachlor is shown to be a precursor to 2,6-diethylaniline. The deposition of radioactivity in the rat nasal tissue is more pronounced following oral administration of the methylsulfide metabolite of alachlor.

The extent of DNA adduct formation by alachlor and its metabolites is used as a guide to deduce the causal agent(s) in the carcinogenicity of this herbicide. Metabolic studies (m^2) indicate that 2-chloro-*N*-hydroxymethoxymethyl-*N*-(2,6-diethylphenyl)-acetamide is an intermediate in forming 2-chloro-*N*-(2,6-diethylphenyl)acetamide and presumably formaldehyde in the mouse liver microsomal mixed-function oxidase system and in yielding *O*-glucuronide



of 2-chloro-*N*-hydroxymethyl-*N*-(2,6-diethylphenyl)acetamide in the urine of alachlor-treated mice.

Incubation of alachlor in the presence of glutathione (GSH) with the cytosolic fraction from rat, mouse, and monkey (m^3) produces the GSH conjugate of alachlor as the initial metabolite. The conjugation occurs through thiol displacement of the chlorine atom of alachlor and is catalyzed by glutathione *S*-transferase (GST). Kidney cell-free preparations of rats and monkeys readily degrade the alachlor GSH conjugate through the mercapturic acid pathway to the corresponding cysteinylglycine, cysteine, and *N*-acetylcysteine conjugates of alachlor.

Upon UV irradiation, $^{14/13}C$-alachlor is dechlorinated and forms a number of intermediates that retain the aromatic ring and carbonyl carbons. These compounds include hydroxyalachlor, norchloralachlor, 2′,6′-diethylacetanilide, 2-hydroxy-2′,6′-diethyl-*N*-methylacetanilide, and a lactam. The fungus transforms 98.6% of ^{14}C-alachlor added to the fermentation broth, and metabolism occurs predominantly by benzylic hydroxylation of one of the arylethyl side chains. Two major metabolites are isomers of 2-chloro-*N*-(methoxymethyl)-*N*-[2-ethyl-6-(1-hydroxyethyl)-phenyl]acetamide and 2-chloro-*N*-(2,6-diethylphenyl)acetamide. The minor metabolite is 2-chloro-*N*-(methoxymethyl)-*N*-(2-vinyl-6-ethlyphenyl)acetamide. *N*-Dealkylation by fungal biotransformation is also observed.

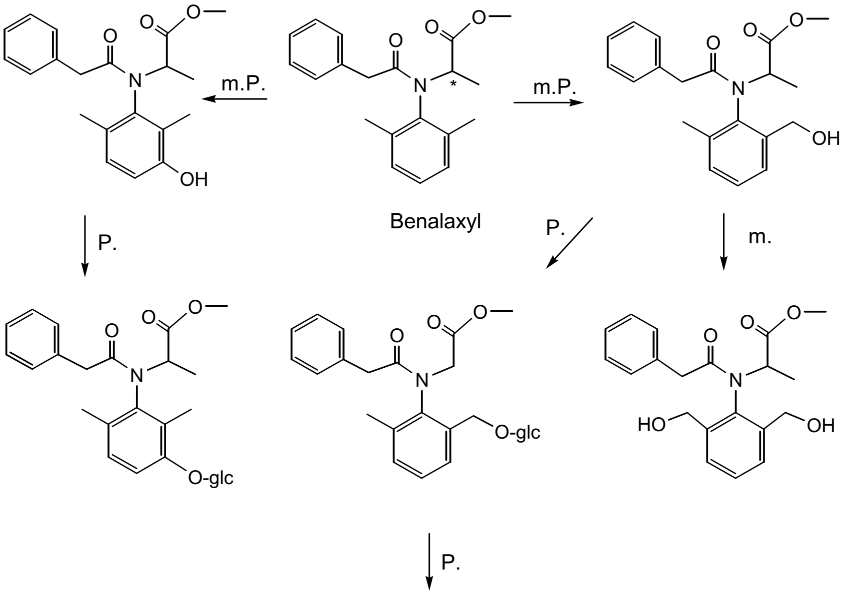
Benalaxyl

A fungicide: control of oomycetes, *Plasmopara viticola* on grapes, *Pseudoperonospora humuli* on hops, *Phytophthora infestants* on potatoes, *Plasmopara tabacia* on tobacco, and *Pythium* spp. on turf

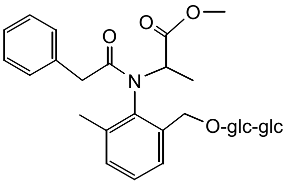
Microsomes
Male rat liver microsomes[8]

Plant
Grape leaves of 90 day-old grape plant[8]

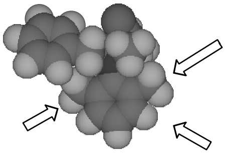
The fate of ^{14}C-benalaxyl as affected by mancozeb is determined on the surface and in the tissues of grape leaves 7 days after the single foliar application of a mixture with mancozeb. The main oxidative scheme with rat liver microsomes is quite similar to that observed in plants. The only differences are represented by a further hydroxylation on the second *ortho* methyl group, and only traces of the *meta* hydroxylation take place on the xylene ring.



Benalaxyl



glc: glucoside residue



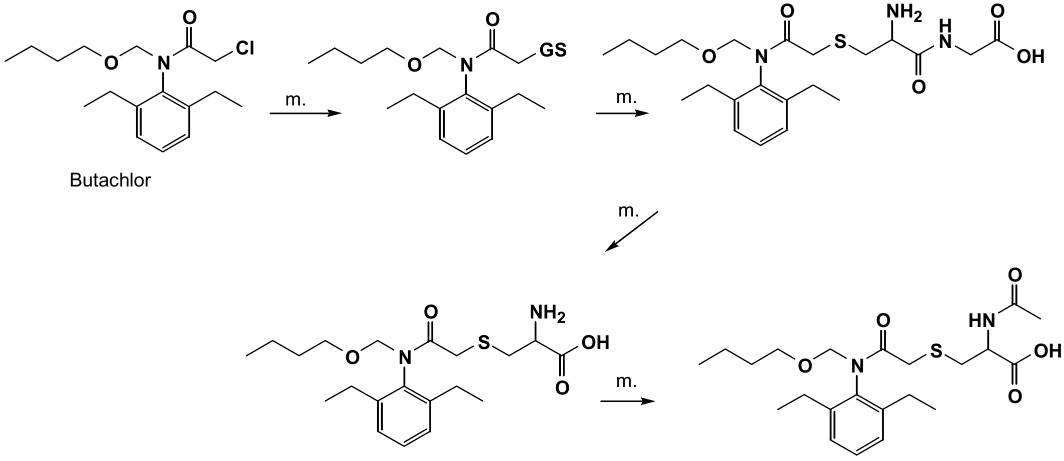
CC(C(OC)=O)N(C(CC2=CC=C
C=C2)=O)C1=C(C)C=CC=C1C

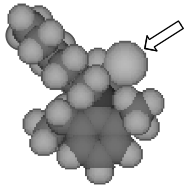
Butachlor

A pre-emergent herbicide

Microsome
Liver and kidney tissue fractions of Long–Evans 10–12 week-old rats (250–300 g)^{9}

In vitro incubation of butachlor with rat liver fractions forms a considerable amount of glutathione conjugate, while the conjugating activity is not efficient for the kidney S9 fraction. Further biotransformation of the glutathione conjugate to mercapturate is not observed in the liver S9 fraction. Butachlor is initially conjugated with glutathione in the liver and is apparently transported to the kidneys where it is transformed to mercapturic acid.





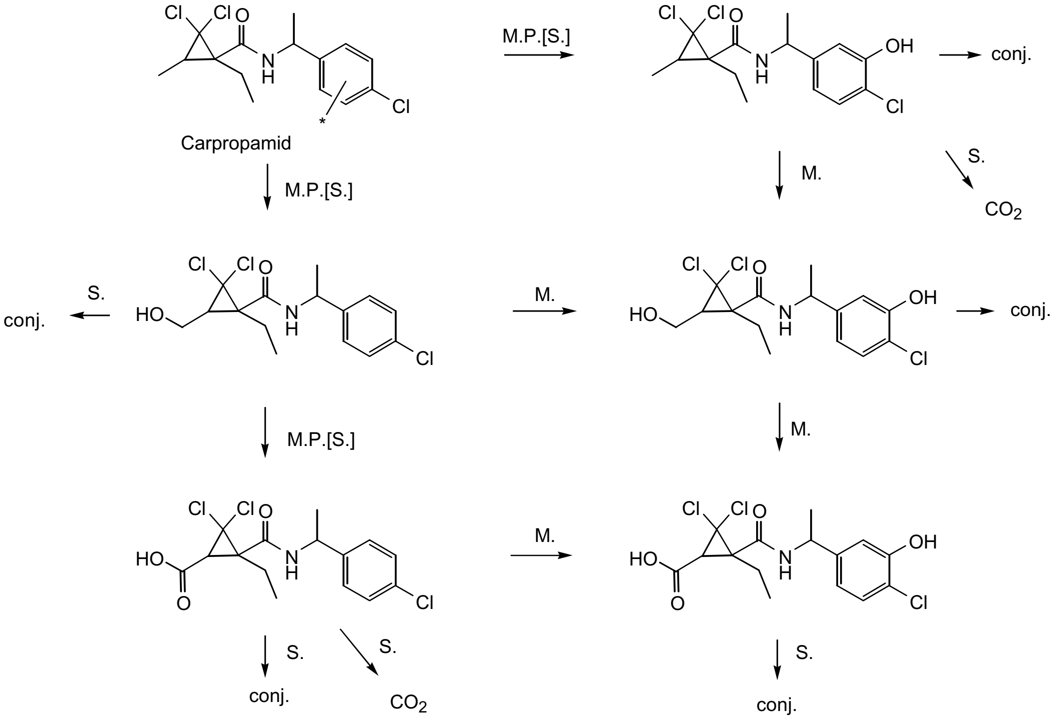
CCC1=CC=CC(CC)=C1
N(C(CCl)=O)COCCCC

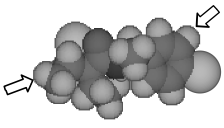
Carpropamid

A systemic fungicide: control of rice blast disease

Mammal/Plant/Soil
Sprague–Dawley Stamm rats; rice plant: *Oryza sativa* cv. Fujiminori; paddy soils: JAPR Furukawa, Ishikawa AES, JAPR Inst., Miyazaki AES[10]

Carpropamid is degraded gradually and in a similar way in rice plants (including rice cell cultures), mammals, typical paddy soils, and water. The degradation process includes oxidation of the methyl group of the cyclopropane ring or in the 4-chlorophenyl ring. In mammals and plants, various water-soluble conjugates are formed. In soils, carpropamid is completely degraded to carbon dioxide.





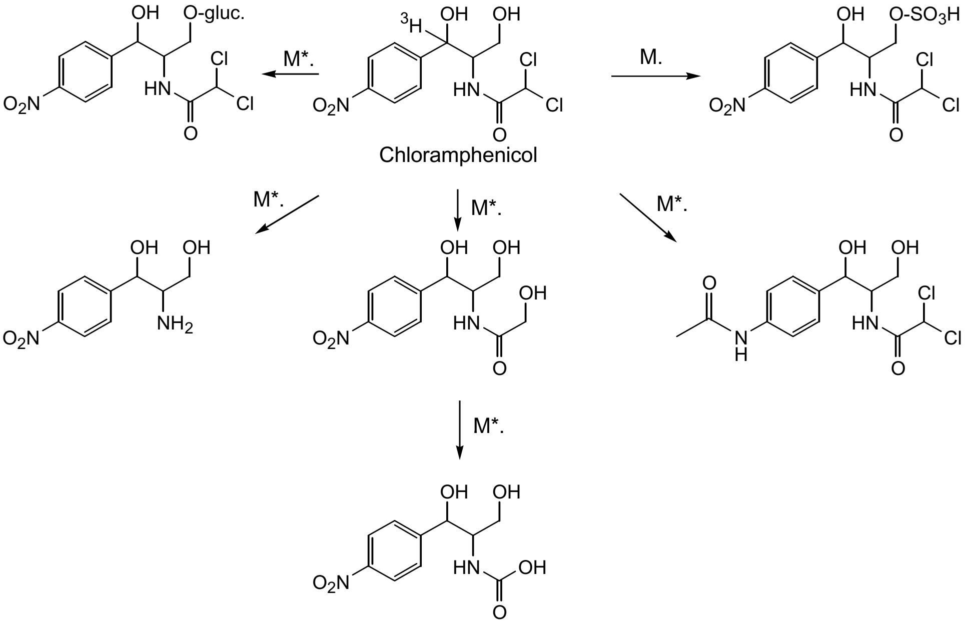
ClC1(Cl)C(C)C1(C(NC(C)C
2=CC=C(Cl)C=C2)=O)CC

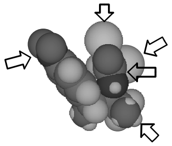
Chloramphenicol

Not a pesticide: for pharmaceutical use

Mammal
Goats[11]

Six metabolites of chloramphenicol are identified, among which the sulfate conjugate is characterized in goat urine.





OC(C(NC(C(Cl)Cl)=O)CO)([H])
C1=CC=C([N+]([O-])=O)C=C1

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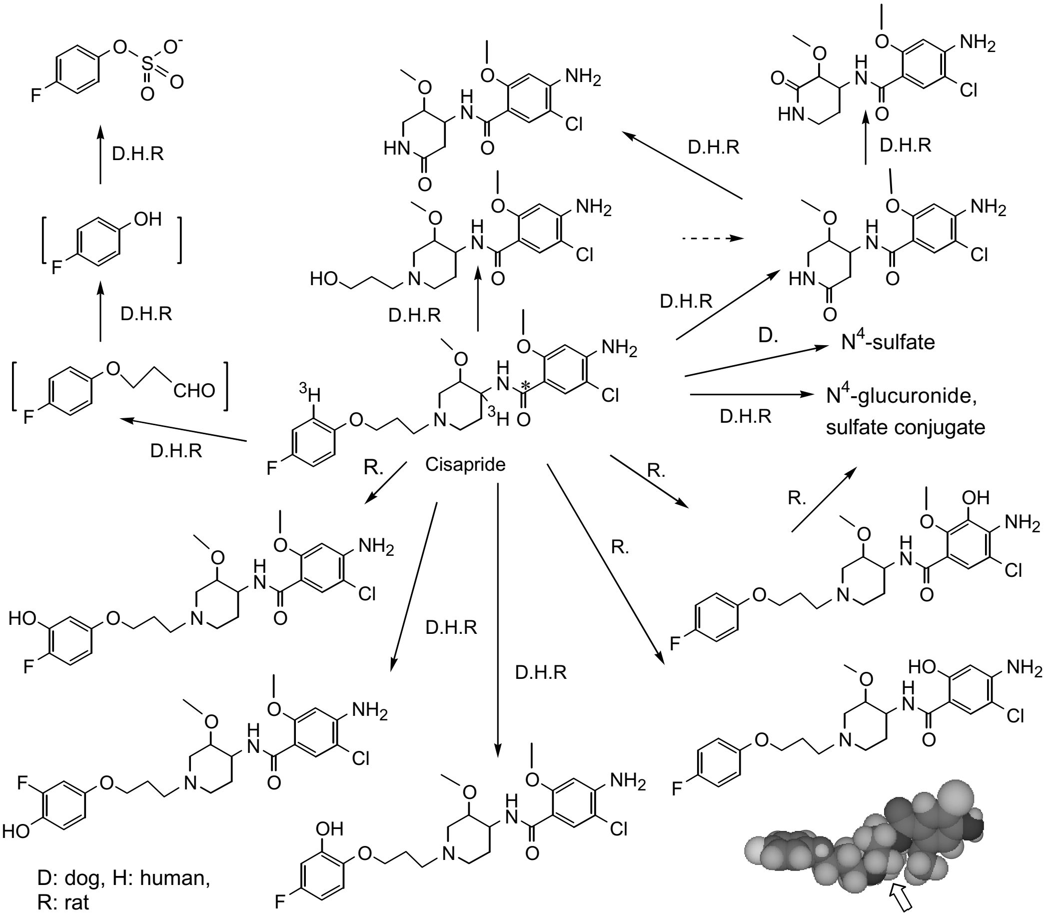
* Ref. 12

Cisapride

Not a pesticide

Mammal
Male beagle dogs, healthy male volunteers[13]
Female rats[14]
Rats, rabbits, and dogs[15]

Cisapride ^{14}C labeled at the carbonyl carbon and ^{3}H labeled at the fluorophenyl moiety or at the piperidine ring is investigated using some animals. *N*-Dealkylation at the nitrogen of the piperidine ring, resulting in the main urinary metabolite norcisapride, and aromatic hydroxylation of the fluorinated phenyl ring are the major metabolic pathways in dogs and humans. Norcisapride excretion accounts for 14% of the dose in dogs and 41–45% in humans. Minor metabolic pathways are *O*-dearylation of the 4-fluorophenyl group and oxidation on the piperidine ring (rat, rabbits and dogs: Lavrijsen *et al.* (1986)[15]).



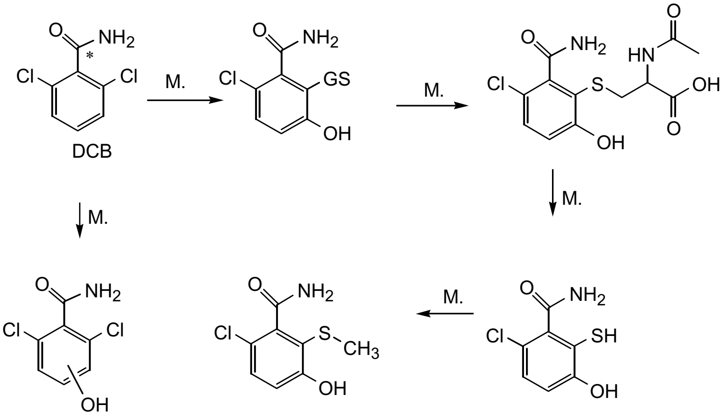
FC1=CC([H])=C(OCCCN2CCC(NC(C3=CC(Cl)=C(N)C=C3OC)=O)([H])C(OC)C2)C=C1

2,6-Dichlorobenzamide (DCB)

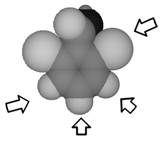
Not a pesticide

Mammal
Male Sprague–Dawley rats (200–240 g)[16]

Oral doses of DCB are excreted by rats as DCB, two monohydroxy-DCBs, 2-chloro-5-hydroxy-6-(methylthio)benzamide, and 2-chloro-5-hydroxy-6-[*S*-(*N*-acetyl)-cysteinyl]benzamide. Biliary excretion (33% of the dose), enterohepatic circulation, and intestinal microfloral metabolism are involved in the formation of 2-chloro-5-hydroxy-6-(methylthio)benzamide. The major route for the metabolism of DCB is the conjugation with glutathione in a process involving phenyl ring hydroxylation at the *ortho* position to the *S*-glutathionyl moiety. Two mechanisms can be processed for the formation of hydroxylated metabolites resulting from the epoxidation at the 2- and 3-positions of the phenyl ring (for the proposed mechanisms: see the text).



GS: glutathione residue



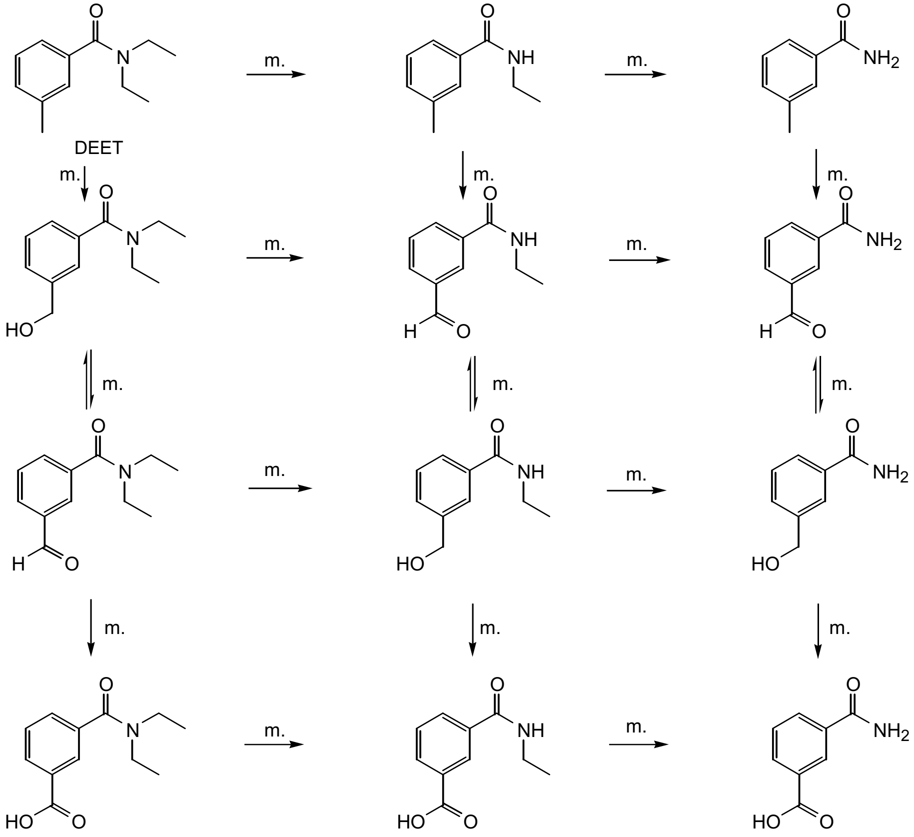
ClC1=CC=CC(Cl)=
C1C(N([H])[H])=O

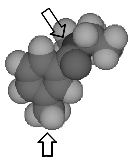
N,*N*-Diethyl-*meta*-toluamide (DEET)

An important insect repellent used for protection of man from mosquitoes and other biting insects

Microsome
Liver microsomes of 10 week-old male Wistar rats[17]

The phenobarbital-treated rat liver microsomal incubation with *N*,*N*-diethyl-*m*-toluamide (DEET) yields the three major metabolites, *N*-ethyl-*m*-toluamide, *N*,*N*-diethyl-*m*-(hydroxymethyl)benzamide, and *N*-ethyl-*m*-(hydroxymethyl)benzamide and the two minor metabolites, toluamide and *N*,*N*-diethyl-*m*-formylbenzamide. The metabolic transformation involves





O=C(N(CC)CC)C
1=CC=CC(C)=C1

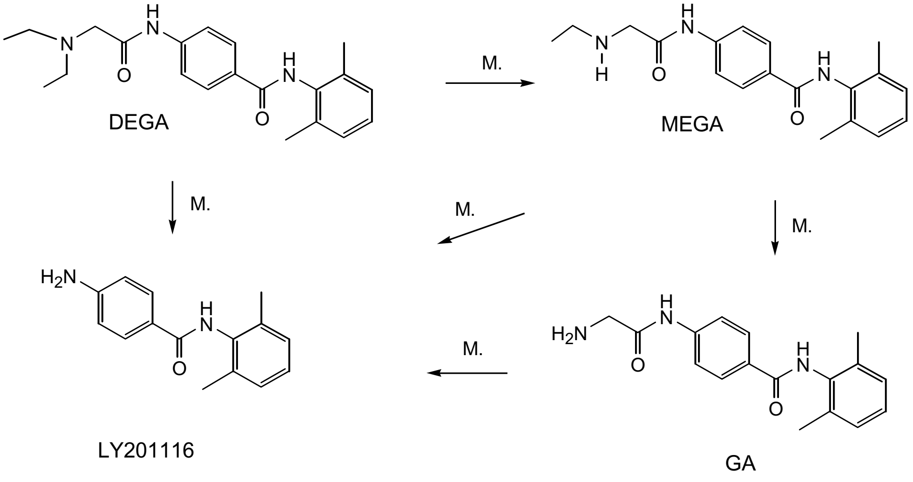
N-dealkylation which is competitive with the oxidation of the methyl group on the phenyl ring. The aldehydes that are derived from the hydroxymethyl analogs are reduced back to the corresponding alcohols.

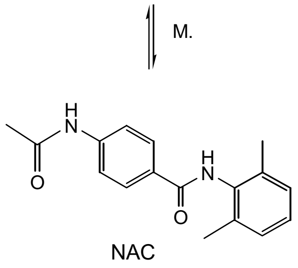
N-(2,6-Dimethylphenyl)-4-[[(diethylamino)acetyl]amino]benzamide (DEGA)

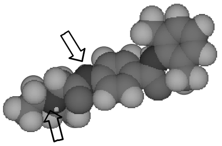
Not a pesticide: prodrug of anticonvulsant LY201116

Mammal
Male Crl:CF1^R Charles River mice (20–25 g)[19]

In mice, DEGA is metabolized by consecutive *N*-deethylation to form MEGA and GA and then to *N*-acetylated NAC via LY201116 which reforms LY201116.







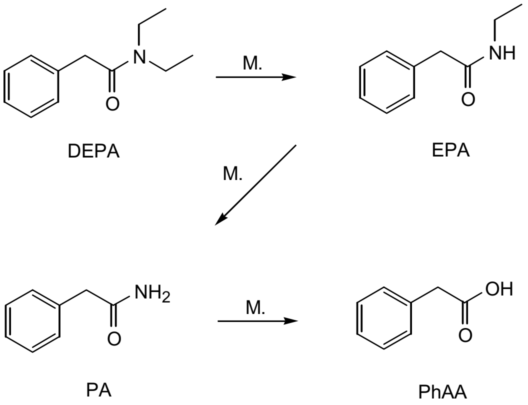
CCN(CC)CC(NC1=CC=C(C(NC2
=C(C)C=CC=C2C)=O)C=C1)=O

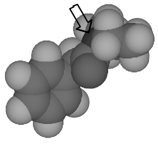
N,N-Diethylphenylacetamide (DEPA)

An insect repellent

Mammal
Young male albino rats (Wistar strain, 71 ± 8.5 g)[18]

When rats are exposed to whole-body attack by diethylphenylacetamide (DEPA), DEPA enters the systemic circulation when it is inhaled, and crosses air−lung and lung−blood barriers to be biodegraded and excreted. DEPA is converted by dealkylation and hydrolysis to the two acetamides, ethylphenylacetamide (EPA) and phenylacetamide (PA), and to phenylacetic acid (PhAA) which are excreted and identified as urinary metabolites.





O=C(N(CC)CC)CC1=CC=CC=C1

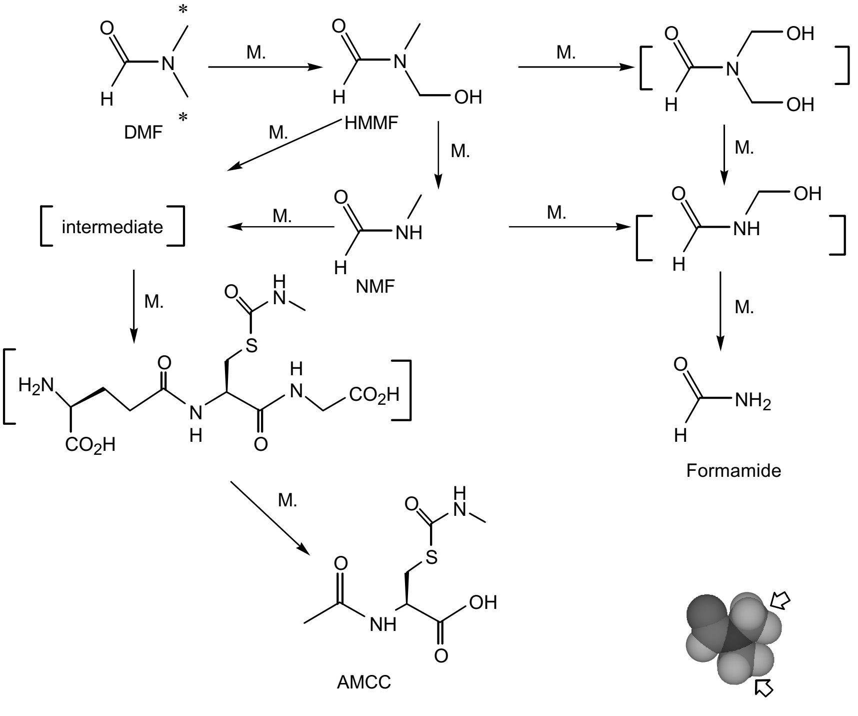
N,N-Dimethylformamide (DMF)

Not a pesticide

Mammal

Male BALB/c mice (19–26 g); male Sprague–Dawley rats (235–270 g); male Syrian hamsters (100–114 g); ten healthy volunteers (5 males and 5 females aged between 26 and 56 years and of 52–94 kg body weight)[20]

Three urinary metabolites are identified in humans and rodents, and the metabolites quantified are *N*-(hydroxymethyl)-*N*-methylformamide (HMMF), resulting in *N*-methylformamide (NMF) and *N*-acetyl-*S*-(*N*-methylcarbamoyl)cysteine (AMCC). Ten volunteers who absorb between 28 and 60 μmol/kg DMF during an 8 h exposure to DMF in air at 6 mg/m^3 excrete in the urine within 72 h between 16.1 and 48.7% of the dose as HMMF, between 8.3 and 23.9% as formamide, and between 9.7 and 22.8% as AMCC. AMCC together with HMMF is also detected in the urine of workers after occupational exposure to DMF. There is a quantitative difference between the metabolic pathway of DMF to AMCC in humans and rodents.



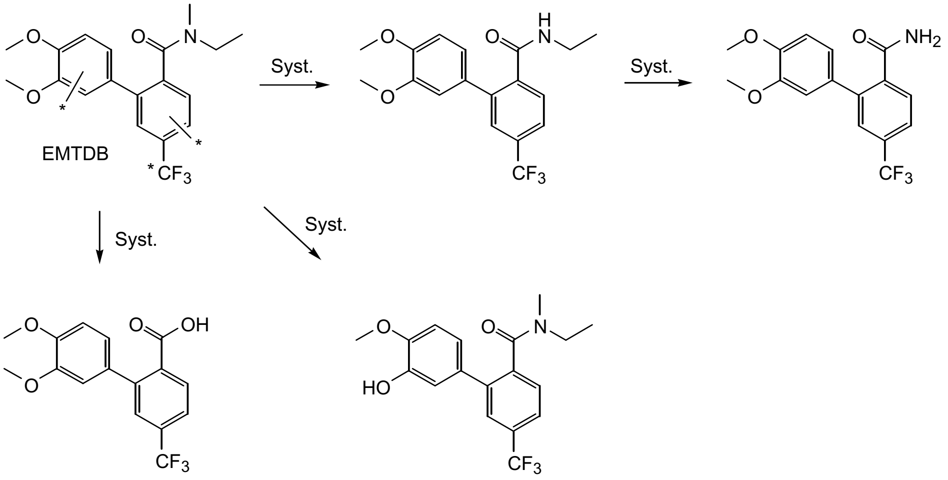
[H]C(N(C)C)=O

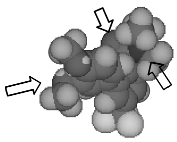
N-Ethyl-*N*-methyl-4-(trifluoromethyl)-2-(3,4-dimethoxyphenyl) benzamide (EMTDB)

A fungicide

System
Cell suspension cultures of *Acer pseudoplatanus*[21]

A fluorinated fungicide [*N*-ethyl-*N*-methyl-4-(trifluoromethyl)-2-(3,4-dimethoxyphenyl)benzamide (EMTDB) is metabolized by plant cell cultures of *Acer pseudoplatanus*, yielding approximately 10 fluorinated metabolites observed in the cultures, five of which are identified. The metabolism of EMTDB mostly occurs through ring demethoxylation or mono *O*-demethylation and *N*-dealkylation. The more lipophilic derivatives diffuse into the culture medium; in contrast, the more hydrophylic ones remain inside the cells.





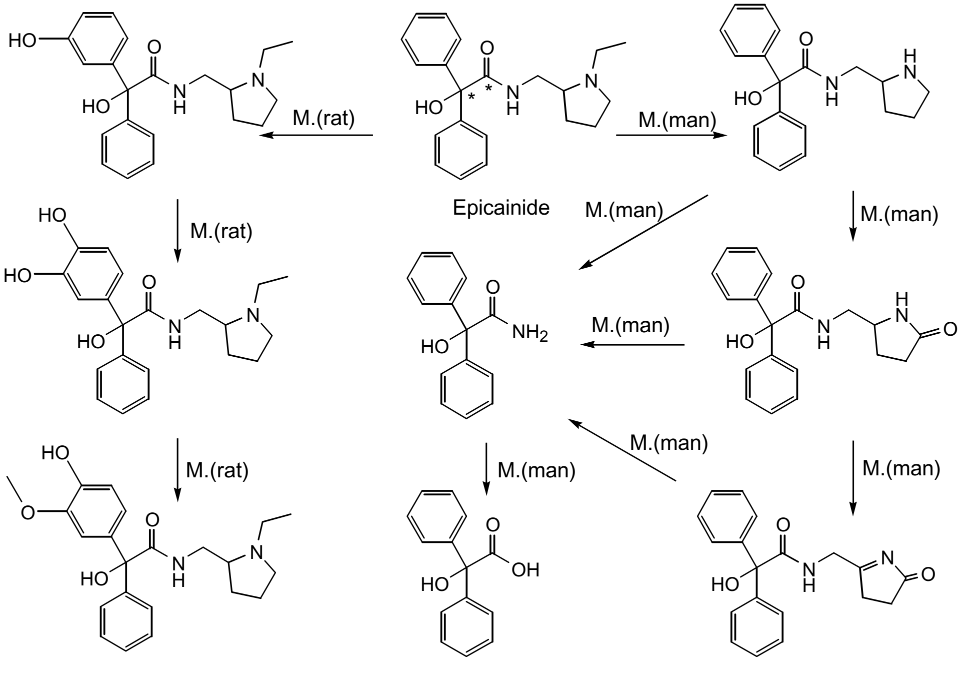
COC(C(OC)=C2)=CC=C2C1=CC
(C(F)(F)F)=CC=C1C(N(C)CC)=O

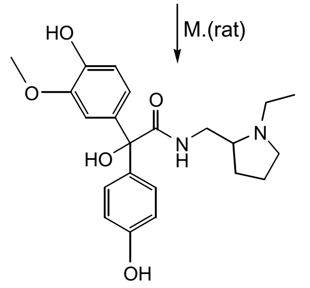
Epicainide

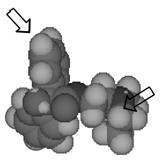
Not a pesticide

Mammal
Male Sprague–Dawley rats (200 g, Iffa, Credo, Lyon, France); human volunteers: six healthy males aged between 24 and 46 years old[22]

In rats, two phenyl rings linked to the quaternary carbon atom of epicainide undergo metabolic attack by the mono-oxygenases. The hydroxylation and subsequent methylation of one of the hydroxy groups in the phenyl rings are predominant degradation reactions of epicainide. In contrast, the phenyl rings of epicainide remain unchanged in man. The degradation reaction mainly occurs in the ethylpyrrolidine ring, resulting in *N*-deethylation, subsequent oxidation of the pyrrolidine moiety, and reduction or hydrolysis of the amide function of epicainide.







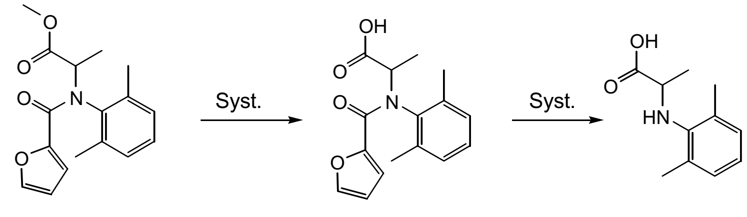
OC(C2=CC=CC=C2)(C(NCC3C
CCN3CC)=O)C1=CC=CC=C1

Furalaxyl

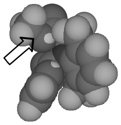
A fungicide: widely used for soil-less tomato culture

System
In Cooper nutrient solution (pH 5.8, at between 19 and 23 °C) of tomato crops: cv. Concerto under a controlled system[23]

Incorporation of furalaxyl into the refreshed nutrient solution is made several times at different plant growth stages, and fulalaxyl is decomposed in the nutrient solution into *N*-(2,6-dimethylphenyl-*N*-(2-furanylcarbonyl)-DL-alanine and *N*-(2,6-dimethylphenyl)-DL-alanine by an enzymatic process.



Furalaxyl



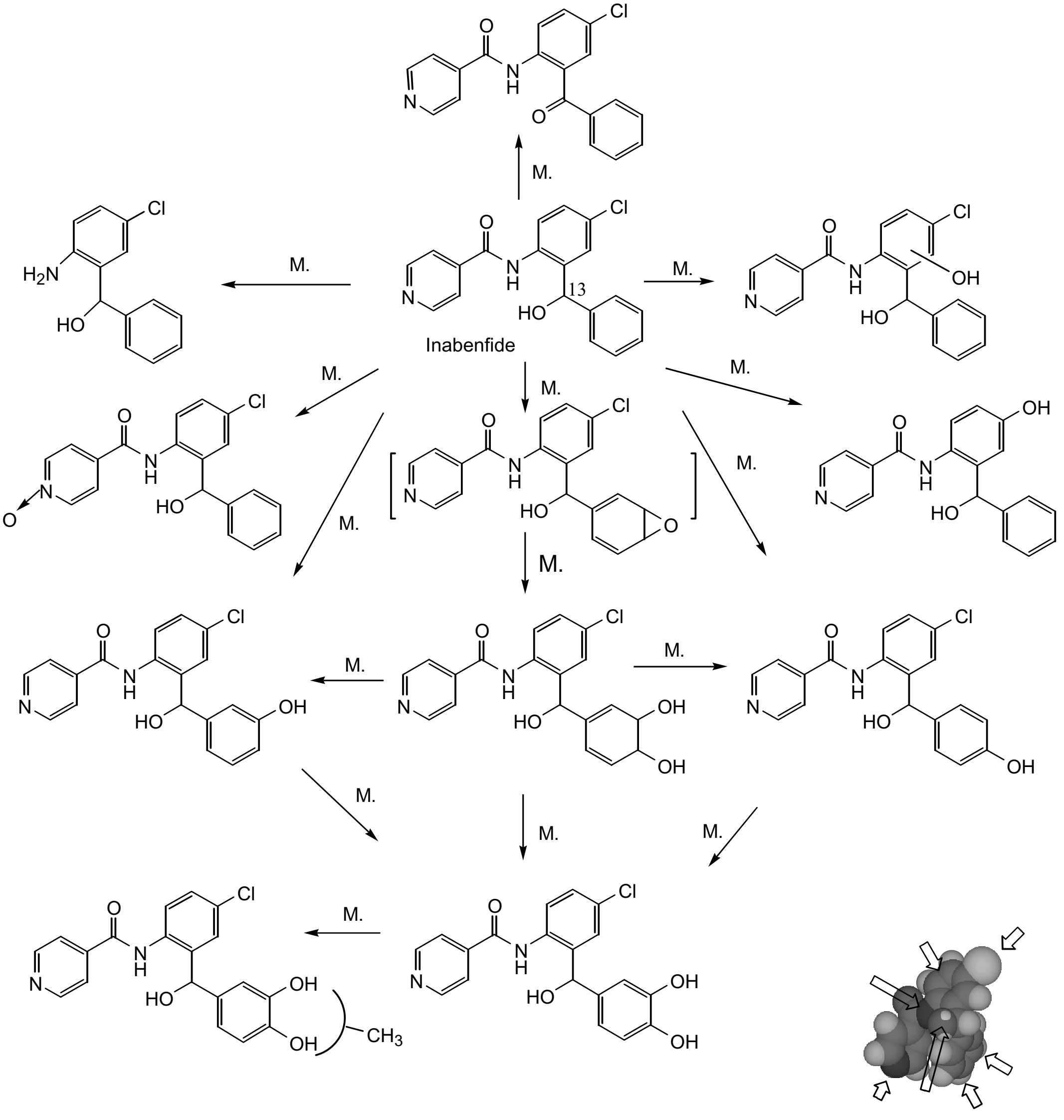
O=C(N(C2=C(C=CC=C2C)C)
C(C(OC)=O)C)C1=CC=CO1

Inabenfide

A plant growth regulator

Mammal
Rat[24]

In rats, inabenfide is mainly hydroxylated on the phenyl ring which is not substituted by a chlorine atom through epoxidation. Oxidation of the benzyl alcohol gives benzophenone. The other hydroxylation is the substitution of the chlorine with hydroxyl of the other



O=C(NC2=C(C(O)C3=CC=CC=C3)
C=C(Cl)C=C2)C1=CC=NC=C1

phenyl ring possessing a chlorine atom. Also, hydrolysis of the amide bond resulting in the corresponding aniline and *N*-oxidation of the pyridine nitrogen can be observed.

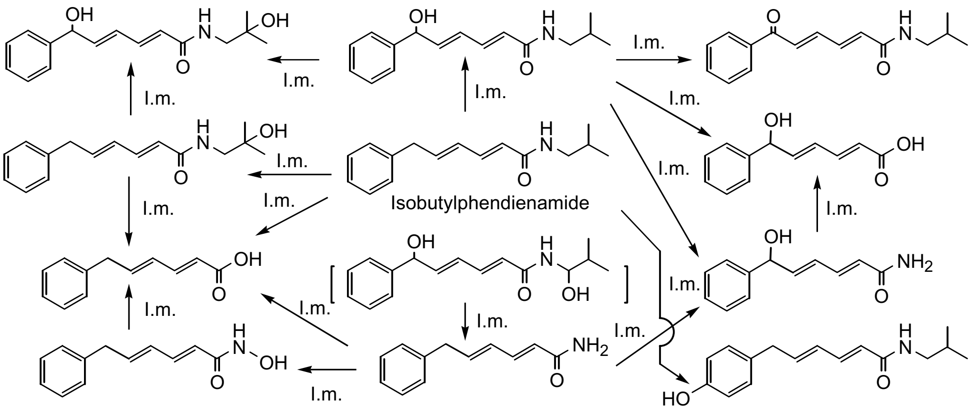
Isobutylphendienamide [(2*E*,4*E*)-*N*-isobutyl-6-phenylhexa-2,4-dienamide]

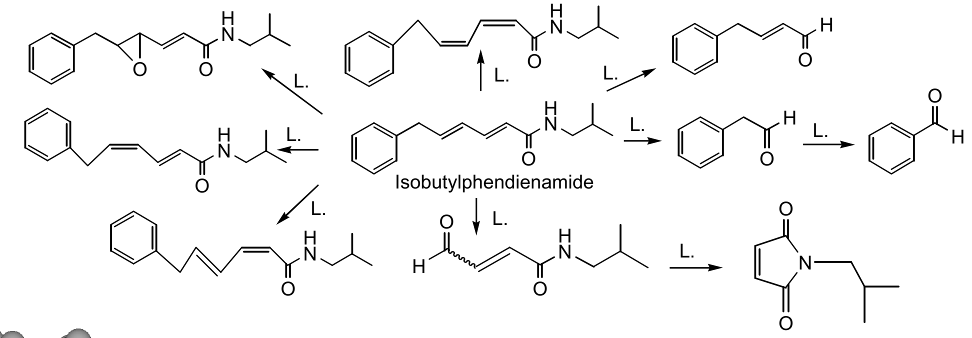
A prototype insecticide

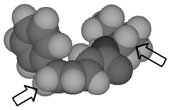
Light
A Rayonet photoreactor (The Southern New England UV Co., Middletown, CT) equipped with 16 3500 or 3000 RPR lamps[25]

Insect
Three hundred adult houseflies (*Musca domestica* L., SCR strain)[26]

Nine metabolites of isobutylphendienamide are identified in the mouse and rat liver microsomal oxygenase system, rat hepatocytes, and/or houseflies. Isobutylphendienamide yields the corresponding unsubstituted amide via *N*-methylene hydroxylation in the microsomal oxygenase system. Both of these amides are readily hydrolyzed by rat but not by mouse amidases. The unsubstituted amide in mouse







O=C(NCC(C)C)C=CC
=CCC$_1$=CC=CC=C$_1$

Isobutylphendienamide [(2*E*,4*E*)-*N*-isobutyl-6-phenylhexa-2,4-dienamide]

(continued)

Microsomes

Liver microsomes from male albino Swiss−Webster mice and male albino rats (Simonsen Lab. Gilroy, CA)[26]

microsomes appears to undergo sequential enzymatic oxidation and hydrolysis to the corresponding carboxylic acids. Additional metabolites are the β-hydroxylisobutyl, 6-hydroxy, 6-keto, and *p*-hydroxy derivatives of the isobutylphendienamide and the 6-hydroxy derivatives of the *N*-(β-hydroxyisobutyl) compound and of the unsubstituted amide and carboxylic acid.

On irradiation of the isobutylphendienamide at 310 and 360 nm in ethanol with benzophenone, the allylic radicals derived from the isobutylphendienamide retain their *trans* geometry during coupling with ethanol-derived radicals. Other photoproducts retaining the isobutyl moiety are the 4,5-epoxide of the isobutylphendienamide, the aldehyde from cleavage of the 4,5 double bond, and *N*-isobutylmaleimide. Photooxidation also yields phenylacetaldehyde in major amounts and trace levels of (2*E*)-4-phenylbut-2-enal and benzaldehyde.

Metalaxyl (Ridomil)

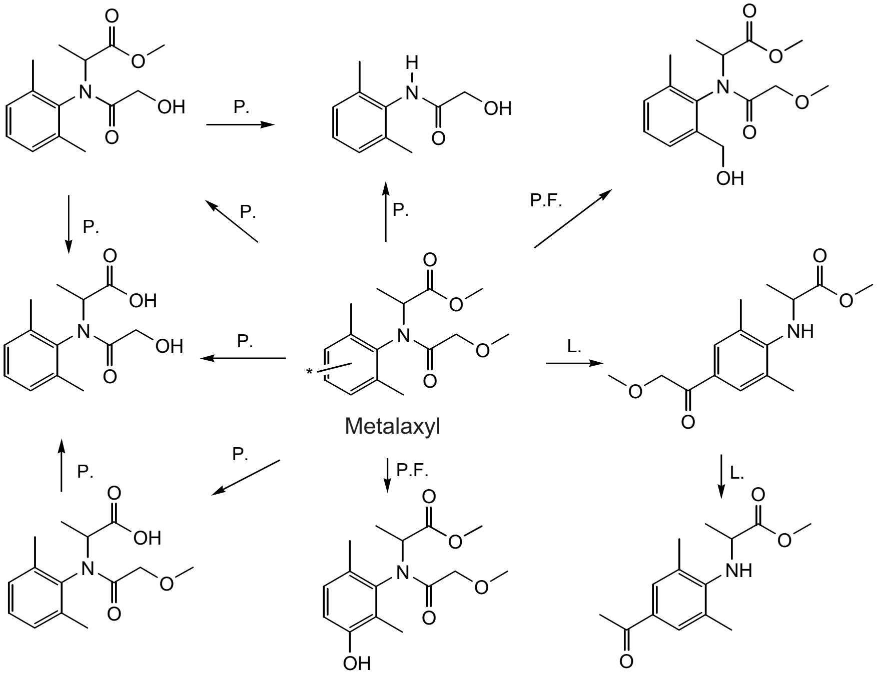
A fungicide: control of plant diseases caused by oomycetous fungi

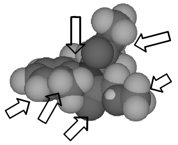
Fungus
Syncephalastrum racemosum (Cohn) Schroeter[27]

Light
UV irradiation with a 30 W germicidal lamp (Angstrom 2537, GE)[28]

Plant
Cell suspension culture of lettuce: *Latuca sativa* L. cv. ‘Suzan’ and grapevine: *Vitis vinifera* L. cv. Cabernet Sauvignon[29]

O-Demethylation is one of the major routes of metalaxyl degradation in the plant cell suspension culture. Although hydroxylation of methyl groups in the phenyl ring predominates in both lettuce and grapes, species differences are evident in grapes, whereas *N*-dealkylation and aryl hydroxylation are less important in lettuce. Two isomeric metabolites of methyl hydroxylation and the hydroxylated metabolite of the phenyl ring are identified as fungus metabolites. By UV irradiation of metalaxyl in aqueous solution, two rearrangement products of the *N*-acyl group to the 4-position on the phenyl ring are identified.





CC$_1$=C(N(C(C(OC)=O)C)
C(COC)=O)C(C)=CC=C$_1$

Metazachlor

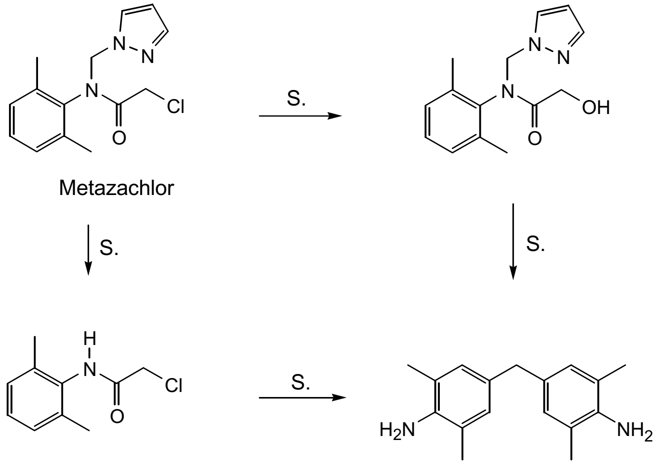
A herbicide: use for winter rape *(Brassica napus* L.), turnip, cabbages, and leek crops

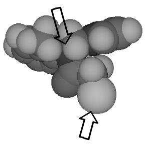
Soil

Soil in the field at Melle, Belgium (loam type soil, pH 6.0)[30]

Soil in the fields at Elverdinge, Belgium (a loam soil, pH 6.1) and Gembloux, Belgium (a silt loam, pH 5.8)[31]

Metazachlor is transformed in soil into 2-hydroxy-*N*-(2,6-dimethylphenyl)-*N*-(1H-pyrazol-1-ylmethyl)acetamide, 2-chloro-*N*-(2,6-dimethylphenyl)acetamide, and 4,4′-methylenebis-(2,6-dimethylbenzenamine), and the soil concentration of the benzenamine is lower than 0.1 ppm.





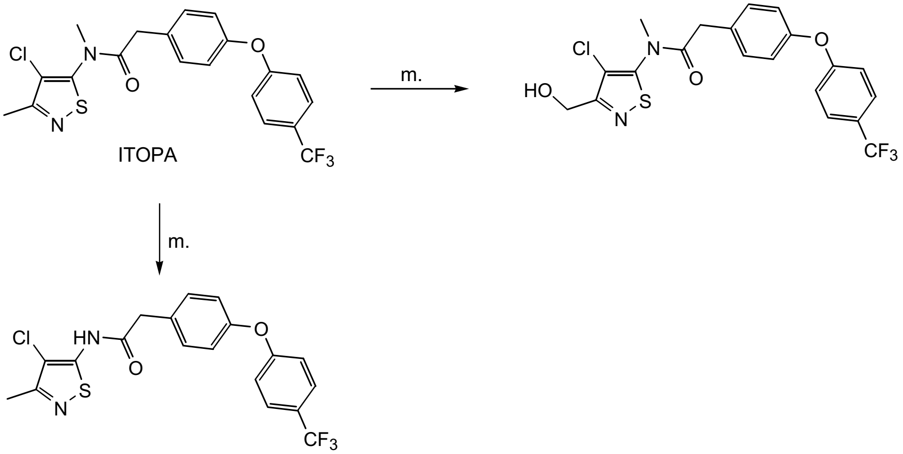
CC$_1$=C(N(CN$_2$N=CC=C$_2$)
C(CCl)=O)C(C)=CC=C$_1$

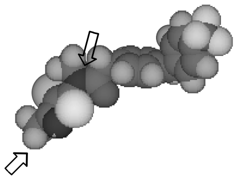
N-(Methylisothiazolin-5-ylidene)phenylacetamide (ITOPA)

A proinsecticide: inhibition of mitochondrial electron transport activity

Microsomes
Microsomal preparations from mid-guts of −100 last instar tobacco budworm (*Heliothis virescens*) larvae (400−500 mg each), from rainbow trout (*Oncorhynchus mykiss*) livers, and from livers of male adult Sprague−Dawley rats[32]

In the microsomes of rat liver, mid-guts of tobacco budworm larvae, and trout liver, *N*-(chloro-3-methyl-5-isothiazolyl)-*N*-methyl-2-[*p*-[α,α,α-trifluoro-*p*-toly)oxy]phenyl]acetamide (ITOPA) undergoes NADPH-dependent metabolism, which is catalyzed by mono-oxygenase enzymes. The primary metabolite in rats is found to arise from ring methyl hydroxylation, while *N*-demethylation to *N*-(4-chloro-3-methyl-5-isothiazoyl)-2-[*p*-(α,α,α-trifluoro-*p*-tolyl)oxy]phenyl]acetamide is observed.





ClC1=C(N(C)C(CC2=CC=C(OC3=CC=C(C(F)(F)F)C=C3)C=C2)=O)SN=C1CO

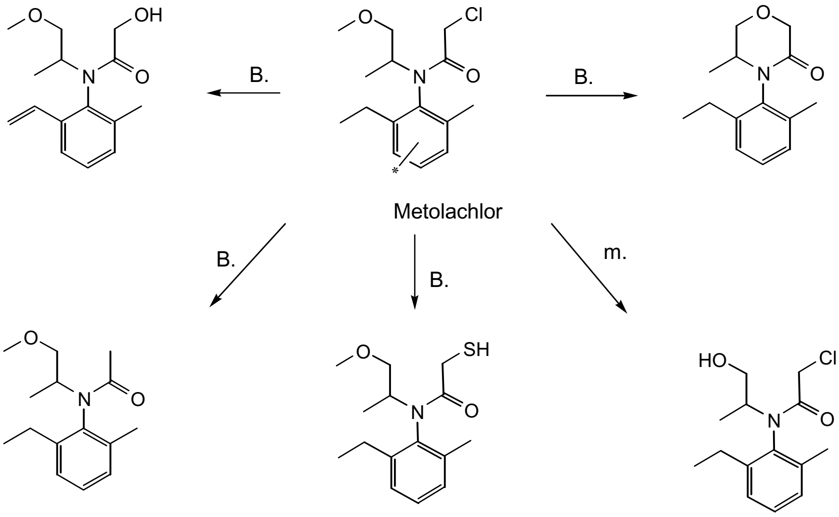
Metolachlor

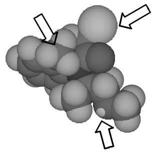
A germination inhibitor

Bacterium
A stable bacterial community, J4-A, isolated from a 9 week-old metolachlor-enriched chemostat consisted of three different types of bacterium: (1) short straight rods with rounded ends, motile with a single polar flagellum, gram positive; (2) straight rods, non-motile, gram positive; (3) curved rods, motile with two polar flagella, gram negative[33]

Microsome
Microsomal fraction isolated from grain sorghum (*Sorghum bicolor* cv. Funk G522DR)[34]

A stable bacterial community absorbs and transforms metolachlor from a liquid medium. From the medium of the 7 day-old culture of the bacterial community, 2-hydroxy-*N*-(2-methyl-6-vinylphenyl)-*N*-(2-methoxy-methylethyl)acetamide and 4-(2-ethyl-6-methylphenyl)-5-methyl-3-morpholinone are identified. The products recovered from cells of J4-A include dechlorinated metolachlor, a thiol compound, a more complicated conjugate, and a non-sulfur-containing conjugate. By sorghum microsomes, *O*-demethylation occurs in the metolachlor degradation process.





CC1=CC=CC(CC)=C1
N(C(CCl)=O)C(COC)C

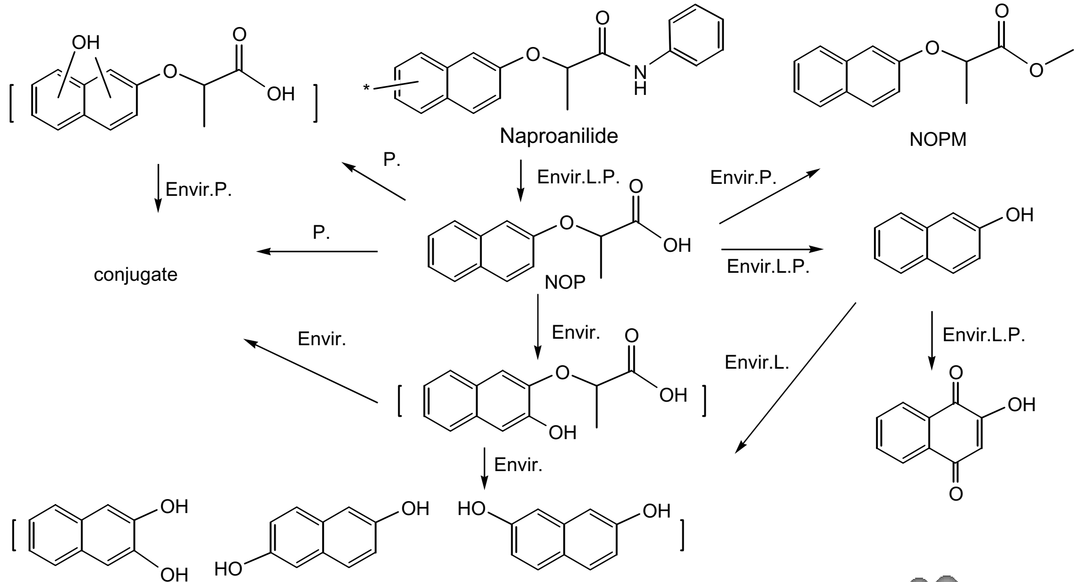
Naproanilide

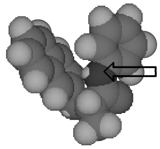
A herbicide: control of annual and perennial weeds in rice paddy fields

Environment
Rice plants: Indica type: *Oryza sativa* cv. Tainon No. 65; rice brown planthopper: *Nalaparvata lugens*; wolf spider: *Lycosa pseudoannulata*; grasshopper: *Oxya intricata*; alga: *Oedogonium cardiacum*; giant duckweed: *Spirodela polyrhiza*; water flea: *Daphnia pule*; mosquito larva: *Culex pipiens quinquefasciatus*; paddy snail: *Cipangopaludina chinesis*; mosquito fish: *Gambusia affinia*; water; sand[35]

Plant
Rice plants: *Oryza sativa* L. cv. Nihonbare; Weed: *Sagittaria pygmaea* M_{IQ}[36]

In the rice paddy ecosystem, naproanilide is biodegraded by the rice plant and organisms in the paddy field and by soil organisms and is mainly hydrolyzed to 2-(2-naphthoxy)propionic acid (NOP) and its methyl ester (NOPM). In rice plants (*Oryza sativa* L.) and *Sagittaria pygmaea* M_{IQ}, naproanilide is metabolized to phytotoxic NOP. In rice plants, NOP subsequently undergoes hydroxylation and rapid conjugation with glucose. Phytotoxic NOP is produced only in a small amount. In *S. pygmaea*, the amounts of NOP and NOPM are significantly greater than those in rice plants. The difference in metabolites of naproanilide shows a possible mechanism of their herbicidal selectivity. Naproanilide and NOP in aqueous solution are rapidly degraded under sunlight





CC(C(NC3=CC=CC=C3)=O)O
C2=CC1=CC=CC=C1C=C2

Light

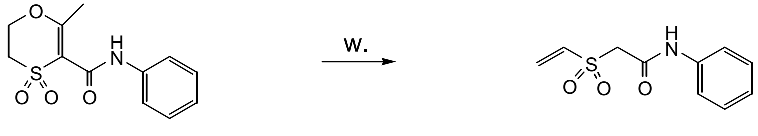
Sunlight (45 000 to 125 000 lux in summer, 19 000 to 58 000 lux in winter) and UV light (Nikko Sekiei Model NY, 100 W) in aqueous solution and sunlight in surface water[37] and UV light. The disappearance of naproanilide in the paddy field is largely attributed to photochemical degradation in the surface water.

Oxycarboxin

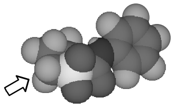
A fungicide

Aqueous solution
H_2O, CH_3OH, CH_3CN, CH_2Cl_2 at 22.2 or 5.0 °C for 96 h[38]

The oxathiin ring of the oxycarboxin undergoes a glass-catalyzed ring-opening reaction resulting in a simple step for hydrolytic removal of an acetyl group to give 2-(vinylsulfonyl)acetanilide in aqueous solution. The decomposition of oxycarboxin involves the container and is surface-type dependent.



Oxycarboxin



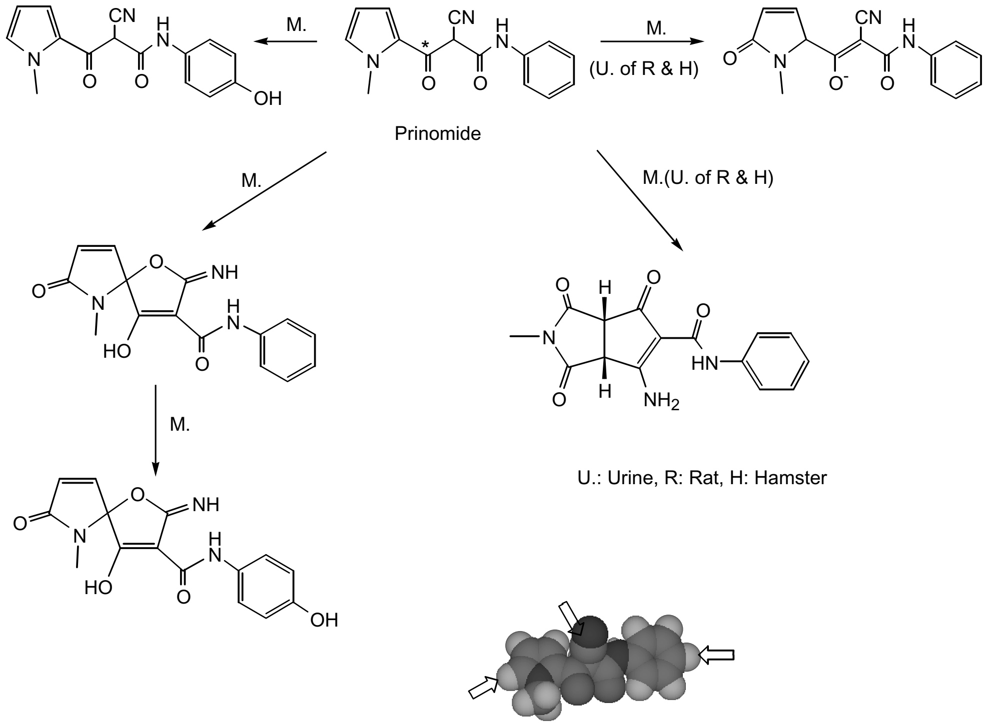
O=S1(CCOC(C)=C1C(N
C2=CC=CC=C2)=O)=O

Prinomide (CGS 10787B)

Not a pesticide: investigational anti-inflammatory compound

Mammal
Male mice (Crl: CD-1), male Sprague–Dawley rats (Crl: CDRB), male beagle dogs; male Syrian hamsters; male baboons (*Papio papio*); male cynomolgus monkeys (*Macaca fascicularis*)[39]

The metabolism of prinomide is qualitatively similar in all species of animals investigated. Major metabolites identified are the *p*-hydroxyphenyl and spiro derivatives. Another metabolite is a complete rearrangement product in the form of a bicyclic succinimide derivative. The lactam is identified in fresh rat and hamster urine.



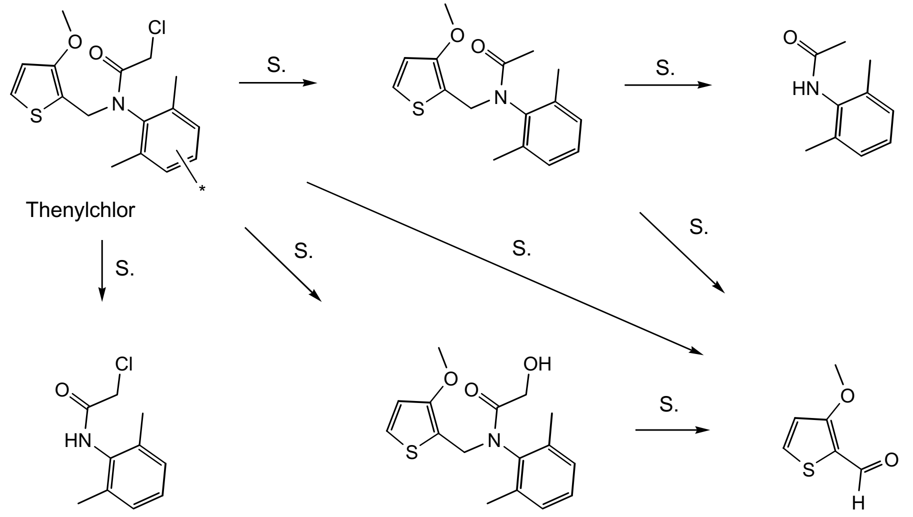
O=C(C(C#N)C(NC2=CC=C
C=C2)=O)C1=CC=CN1C

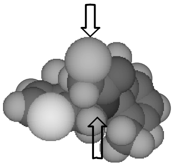
Thenylchlor (NSK-850)

A herbicide: control of grass in paddy fields

Soil
Paddy soils (mineral soils and volcanic ash soils)[40]

^{14}C-Thenylchlor (NSK-850) is degraded in three kinds of paddy soil with a half-life of 1–3 weeks after application. Two major metabolites are identified as *N*-acetyl and *N*-hydroxylmethylcarbonyl derivatives which are derived from the replacement of the chlorine atom of thenylchlor by hydrogen and hydroxyl groups, respectively.





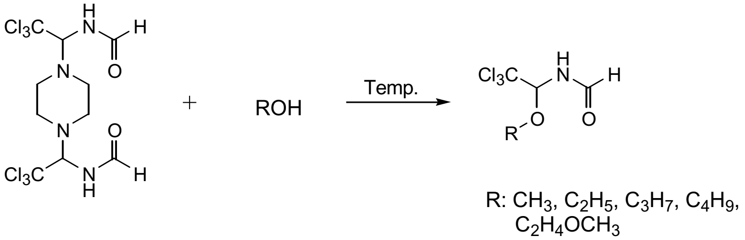
CC1=CC=CC(C)=C1N(C(C
Cl)=O)CC2=C(OC)C=CS2

Trifoline (Saprol)

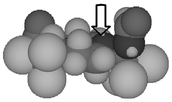
A systemic fungicide: control of powdery mildew, scab, rust, monilia, and leaf spot diseases on a wide range of crops

Temperature
Alcohol solution in a closed tube at 160 °C for 30 min[41]

Thermal reaction of trifoline with several alcohols in a closed glass tube gives *N*-(1-alkoxy-2,2,2-trichloroethyl) formamides.



Trifoline



[CCl3]C(NC([H])=O)N1CCN(C(NC([H])=O)[CCl3])CC1

2

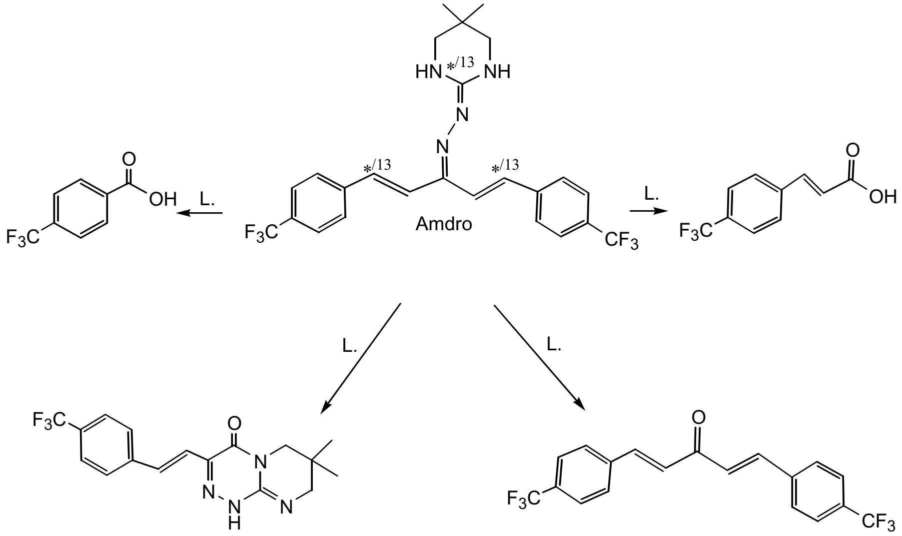
Amidines, Guanidines, and Hydrazines

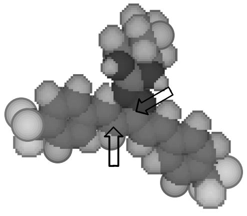
Amdro (AC 217,300)

An insecticide: control of the red imported fire ant (*Solenopsis invicta*)

Light
Distilled water in a Mallory environmental chamber (Mallory Engineering Inc.) equipped with an Atlas xenon light system (Atlas Electric Devices Co.) using borosilicate inner and outer filters to simulate natural sunlight at 6000 W and 27 °C[42]

Amdro (AC 217,300) is rapidly photodegraded under borosilicate-filtered xenon arc lamps at 27 °C as a suspension in distilled water. The half-life of amdro is calculated as 42 min and four degradation products are identified as 1,5-bis(α,α,α-trifluoro-*p*-tolyl)-1,4-pentadien-3-one, α,α,α-trifluoro-*p*-toluic acid, *p*-(trifluoromethyl)cinnamic acid, 6,7,8,9-tetrahydro-7,7-dimethyl-3-[*p*-(trifluoromethyl)styryl]-4*H*-pyrimido[2,1-*c*]-*as*-triazin-4-one. These degradation products are identical to those of the metabolites by insect.





CC2(C)CNC(NC2)=NN=C(C=CC3=CC=C(C(F)(F)F)C=C3)C=CC1=CC=C(C(F)(F)F)C=C1

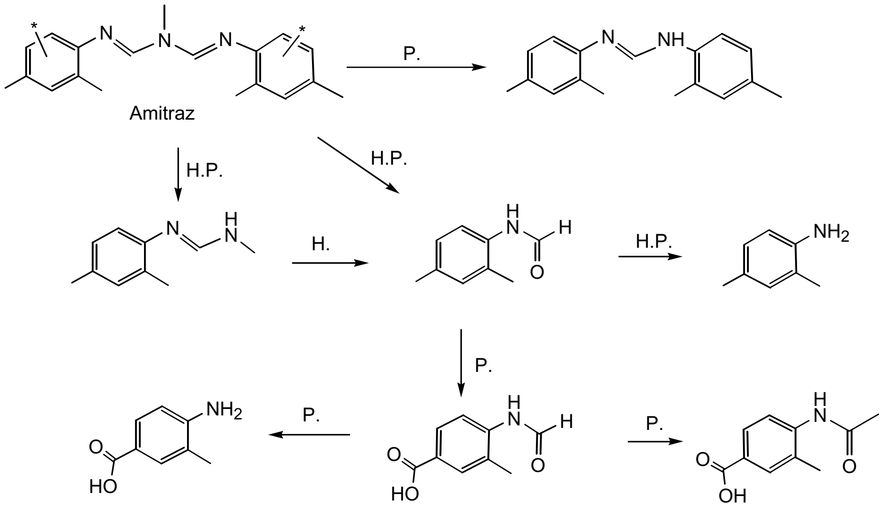
Amitraz (Mitac/Tactic)

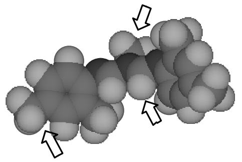
An acaricide: control of mites on fruit and ectoparasites on livestock

Hydrolysis
Methanol or acetonitrile in buffer water[43]

Plant
Lemons (var. Eureka on Poncirus rootstock)[44]

^{14}C-Amitraz is applied on lemons grown under glasshouse conditions at final harvest and the applied radioactivity is quantitatively recovered, predominantly in the peel (86%). The total residue at harvest contains amitraz, *N*-methyl-*N*′-(2,4-xylyl)formamidine, and formyl-2′,4′-xylydine and conjugates of 4-amino-*m*-toluic acid and the conjugated metabolites which are convertible to 2,4-xylidine. Amitraz is readily hydrolyzed at low pH values, forming acid-stable formyl-2,4-xylydine which can be further hydrolyzed to 2,4-xylidine.





CC1=CC=C(N=CN(C)C=NC2
=C(C)C=C(C)C=C2)C(C)=C1

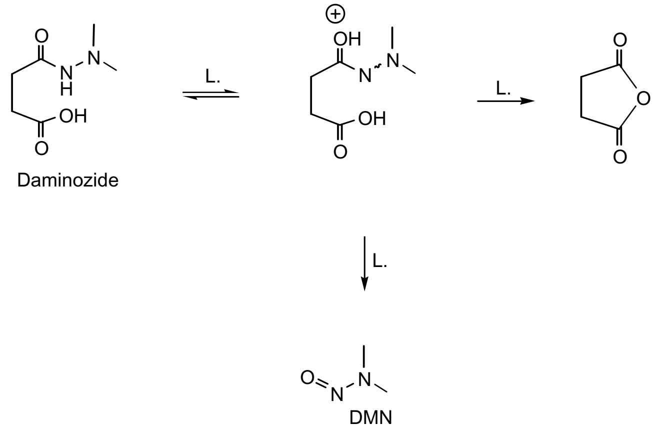
Daminozide (Alar)

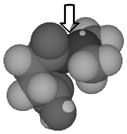
A plant growth regulator: use on apples

Light

In 5 mm Pyrex NMR tubes, irradiating with an incandescent lamp (60 W)[45]

Daminozide is oxidized by photochemically generated singlet oxygen, with rose bengal as a sensitizing agent in methanol-d_4 to yield equimolar amounts of *N*,*N*-dimethylnitrosamine (DMN) and succinic anhydride as the only products detected by ^1H and ^{13}C NMR. The reaction is efficiently inhibited by 2,5-dimethylfuran as a competitor for, or sodium azide as a quencher of, singlet oxygen. Humic acid, similar to that found in natural and waste waters, and a red pigment isolated from apple peel also sensitize the photodegradation of daminozide to produce DMN and succinic anhydride.





O=C(NN(C)C)CCC(O)=O

Guazatine triacetate (Befran)

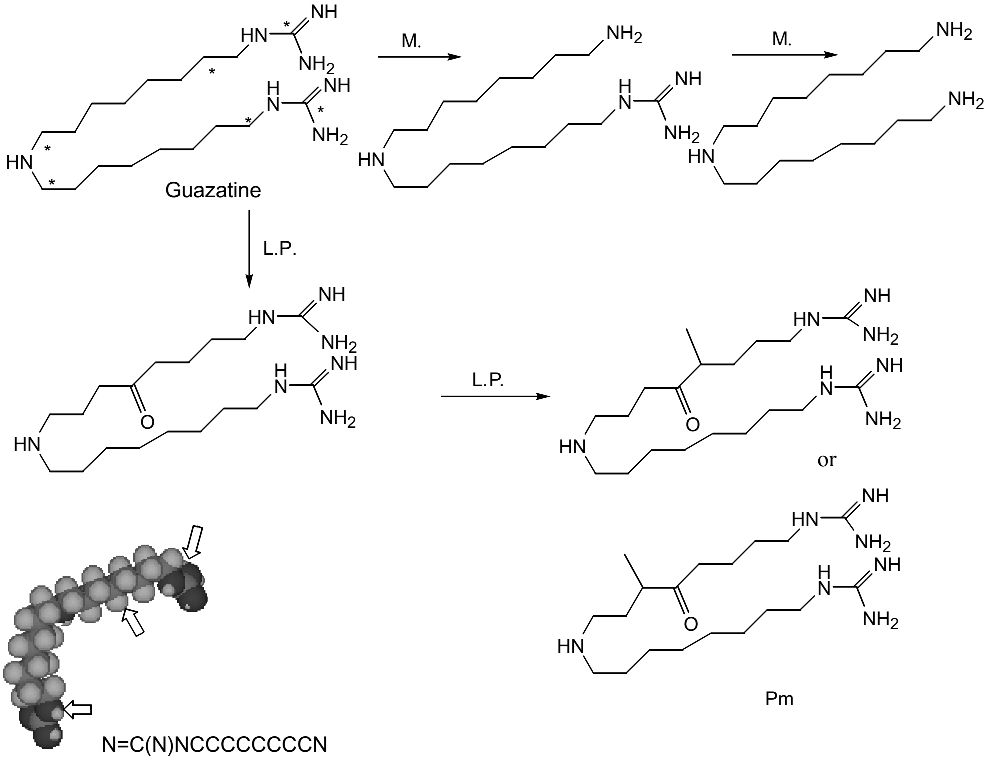
A fungicide: control of Japanese apple canker and snow mold in wheats

Mammal
Adult male rats (Wistar–Imamichi strain, 7 week-old)[46]

Light
Artificial sunlight lamps (Toshiba DR400T/L, Toshiba Electric Co.)[47]

Plant (light)
Dwarf apple trees (*Malus pumila* sp. cv. 'Inu-apple'), with a dwarf aronia tree (*Malus micromalus*) in a controlled growth chamber with a light intensity of approximately 30 klux by artificial sunlight lamp 9 Toshiba DR400T/L[48]

The deamidation of guazatine (GZ) is a primary mode of GZ-biotransformation in rats but is not significantly mediated by either hydrolysis or transamidation to glycine or ornithine. In photolysis, Pm is formed by photooxidation of the methylene group (probably at the 3 or 5 position). One of the minor photoproducts identified is considered to be an intermediate of Pm formation. In apple plants, the same degradation products are identified on the surface of the leaves as photodegradation products.



N=C(N)NCCCCCCCCN
CCCCCCCCNC(N)=N

3

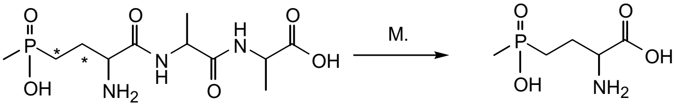
Amino Acid–Phosphinic Acids

Bialaphos

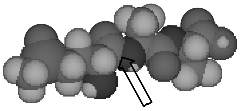
A non-selective herbicide

Mammal
Male 5 week-old ICR-strain mice (17.5 g)[49]

When ^{14}C-bialaphos [L-2-amino-4-[(hydroxy)(methyl)phosphinoyl]butyryl-L-alanyl-L-alanine] is administered in an aqueous solution to mice, the metabolite of bialaphos which is identified as 2-amino-4-[(hydroxy)(methyl)phosphinoyl]butyric acid is excreted in the feces and urine.



Bialaphos



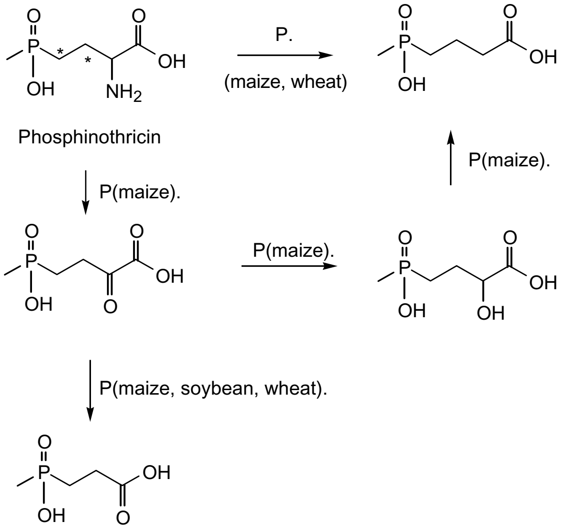
CP(CCC(N)C(NC(C)C(NC
(C)C(O)=O)=O)=O)(O)=O

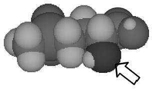
Phosphinothricin

A non-selective herbicide

Plant
Cell suspension cultures of soybean: *Glycine max* L.; wheat: *Triticum aestivum* L.; maize: *Zea mays* L.[50]

When ^{14}C-phosphinothricin [homoalanin-4-yl-(methyl)phosphinic acid] is incubated in the cell suspension cultures of soybean, wheat, and maize, in maize cells which take up to 50% of the applied radioactivity, four different metabolites are detected which are identified as 4-methylphosphinico-2-oxo-butyric acid, 4-methylphosphinico-2-hydroxybutyric acid, 4-methylphosphinicobutyric acid, and 3-methylphosphinicopropionic acid. In soybean and wheat cultures, 10 and 6% of the applied radioactivity is taken up, respectively. In soybean, only one metabolite, 3-methylphosphinicopropionic acid, is detected, whereas in wheat, 4-methyl-phosphinicobutyric acid is additionally present.





CP(CCC(N)C(O)=O)(O)=O

4

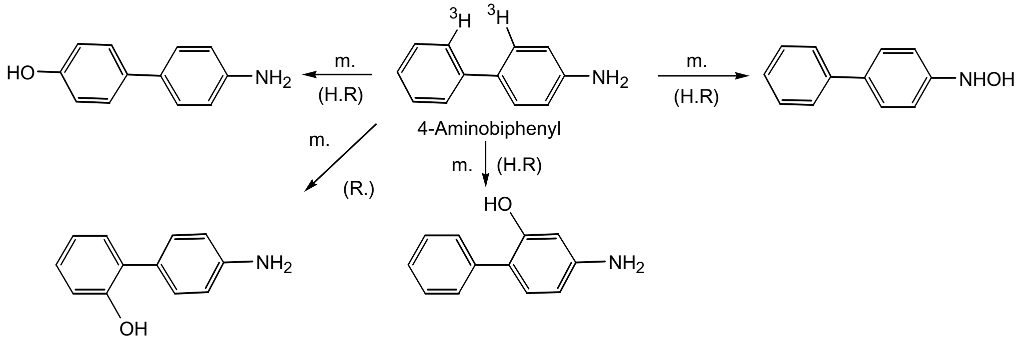
Anilines and Nitrobenzenes

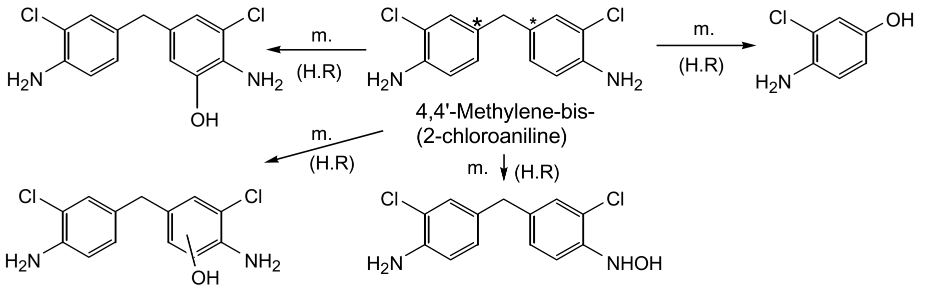
4-Aminobiphenyl and 4,4′-methylene-bis-(2-chloroaniline)

Not pesticides: carcinogens

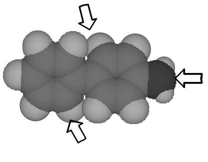
Microsome
Human liver microsomes; ten purified rat hepatic cytochromes P-450[51]

Ring oxidation of 4-aminobiphenyl occurred only to a minor extent in microsomes. In contrast, *N*-oxidation of 4,4′-methylene-bis-(2-chloroaniline) is preferentially catalyzed by the phenobarbital-induced enzymes P-$450_{PB\text{-}B}$ and P-$450_{PB\text{-}D}$ to cause ring oxidation and methylene carbon oxidation. 4,4′-Methylene-bis-(2-chloroaniline) ring oxidation and methylene carbon oxidation show varied cytochrome P-450 selectivity and accounted for 14–79% of total oxidation products.



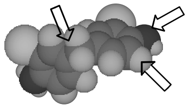


H: human, R: rat



4-Aminobiphenyl

NC(C=C2[3H][3H]3)=C
C=C2C1=C3C=CC=C1



4,4'-Methylene-bis-
(2-chloroaniline)

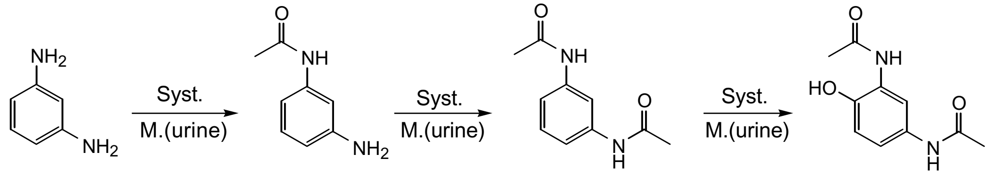
ClC1=C(N)C=CC(CC2=
CC=C(N)C(Cl)=C2)=C1

1,3-Diaminobenzene (*m*-Phenylenediamine)

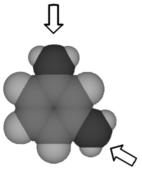
Not a pesticide

System/mammal
Rat liver perfusion of male Wistar rats (SPF) weighing approximately 250 g from Mollegaard Breeding Center and urine[52]

By the perfused rat liver, 1,3-diaminobenzene (MPD) is metabolized to three identified *N*-acetylated derivatives *N*-acetyl-1,3-diaminobenzene, *N*,*N*′-diacetyl-1,3-diaminobenzene, and *N*,*N*′-diacetyl-2,4-diaminophenol which are identical to the metabolites excreted in rat urine.



MPD



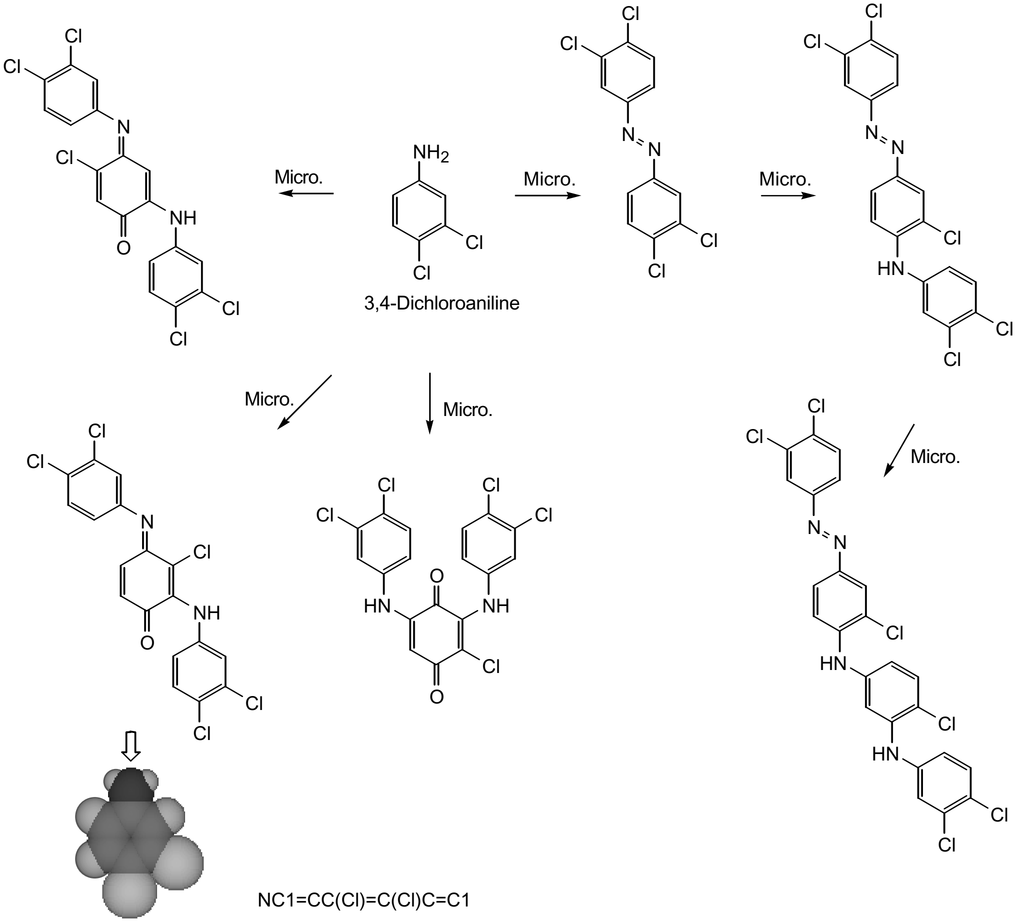
NC1=CC(N)=CC=C1

3,4-Dichloroaniline

Not a pesticide

Microorganism
Agar cultures of the basidiomycete *Filoboletus* sp. TA9054[53]

The basidiomycete *Filoboletus* sp. TA9054 metabolizes 3,4-dichloroaniline and forms several condensation products on solid media and in liquid culture, and no oligomers are produced. Six metabolites are identified as 3,3′-4,4′-tetrachloroazobenzene, 4-(3,4-dichloroanilino)-3,3′,4′-trichloroazobenzene, 4-[(3,4-dichloroanilino)-4-(3,4-dichloroanilino)]-3,3′4′-trichloroazobenzene, 2-(3,4-dichloroanilino)-*N*-(3,4-dichlorophenyl)-4-(chlorophenylene), 6-(3,4-dichloroanilino)-*N*-(3,4-dichlorophenyl)-4-(chlorophenylene), and 3,5-bis(3,4-dichloroanilino)-1,4-chlorobenzoquinone.



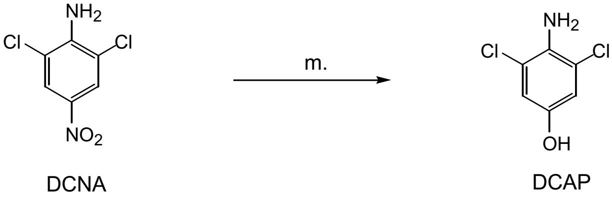
NC1=CC(Cl)=C(Cl)C=C1

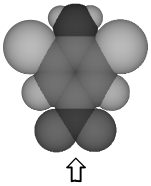
2,6-Dichloro-4-nitroaniline (DCNA)

A fungicide and herbicide

Microsome
Liver microsomes of Sprague–Dawley rats[54]

The metabolism of 2,6-dichloro-4-nitroaniline (DCNA) in rat hepatic microsomes gives rise to the unique metabolite 3,5-dichloro-4-aminophenol (DCAP).





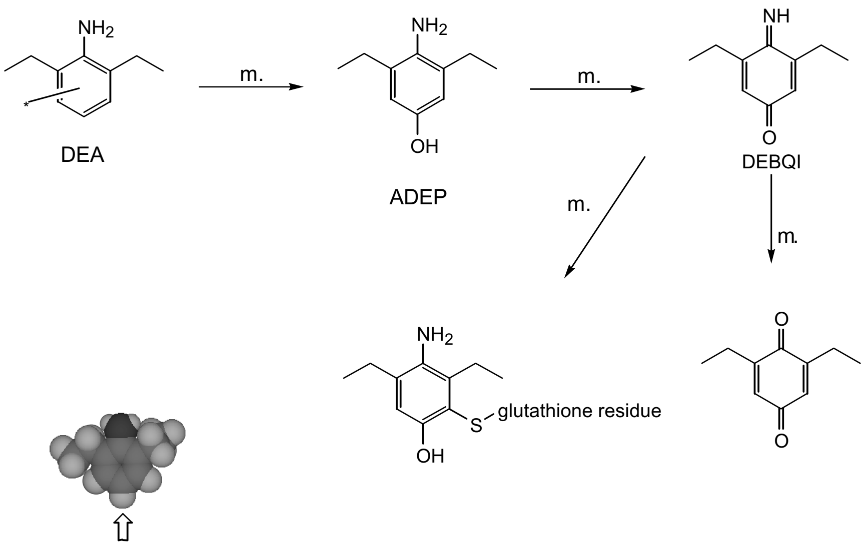
ClC1=CC([N+]([O-])
=O)=CC(Cl)=C1N

2,6-Diethylaniline (DEA)

Not a pesticide

Microsomes
Liver homogenate from male Long−Evans rats (average body weight 250 g)[55]

Incubation of 2,6-diethylaniline (DEA) with NADPH-fortified rat liver microsomal enzymes produces 4-amino-3,5-diethylphenol (ADEP) as the major oxidation product. ADEP is shown to undergo further oxidation to 3,5-diethylbenzoquinone-4-imine (DEBQI), which is isolated as a minor metabolite during DEA oxidation.



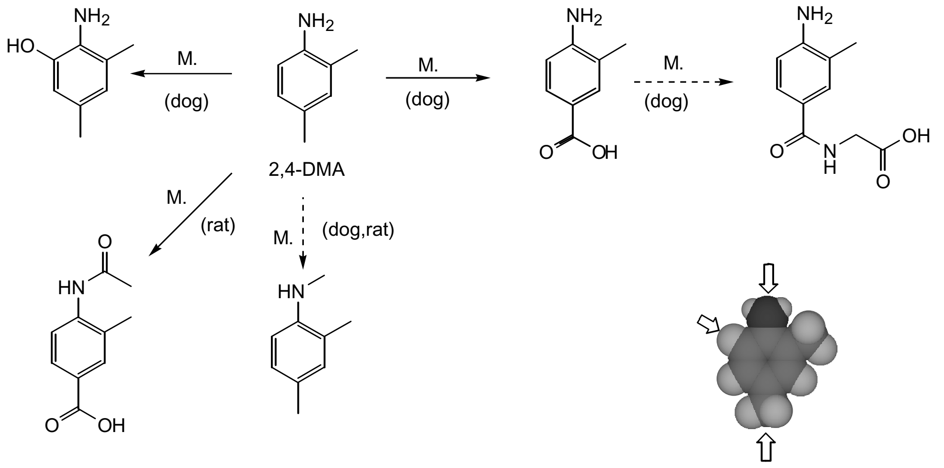
NC1=C(CC)C=CC=C1CC

2,4- and 2,6-Dimethylanilines

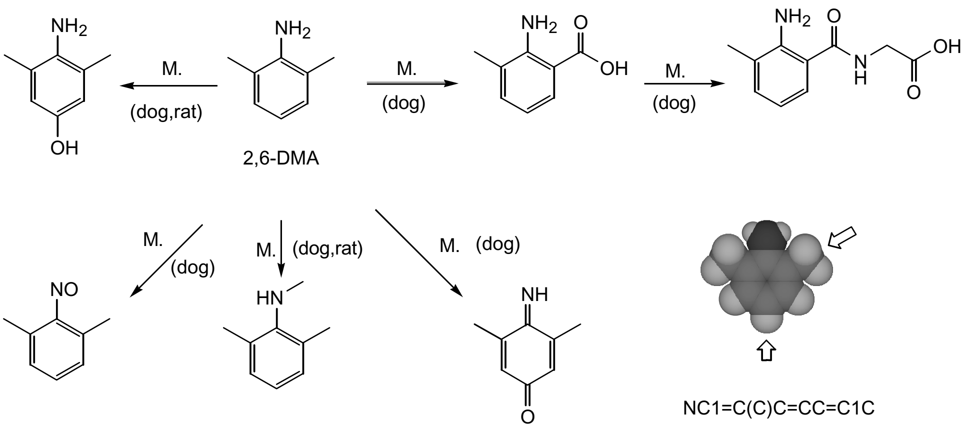
Not pesticides

Mammal
Male Fischer 344 rats, (12 week-old) (Hilltop Lab Animals Inc., Scottsdale, PA), male prebred beagles, (2 year-old) (LSU School of Veterinary Medicine breeding program)[56]

The major urinary metabolite of 2,4-dimethylaniline (2,4-DMA) in rats is *N*-acetyl-4-amino-3-methylbenzoic acid, while in dogs, it is 6-hydroxy-2,4-dimethylaniline. Dogs also produce a smaller amount of unacetylated 4-amino-3-methylbenzoic acid and its glycine conjugate. 2,6-Dimethylaniline (2,6-DMA) is metabolized principally to 4-hydroxy-2,6-dimethylaniline in both species, but dogs also produce a significant quantity of 2-amino-3-methylbenzoic acid



NC1=C(C)C=C(C)C=C1



NC1=C(C)C=CC=C1C

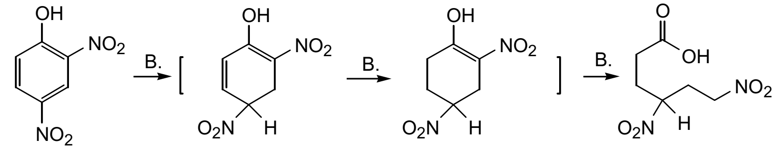
along with a trace amount of the glycine conjugate of the latter metabolite and 2,6-dimethylnitrosobenzene. Trace levels of an unknown postulated to be 3,5-dimethyl-4-iminoquinone are found in dog urine.

2,4-Dinitrophenol

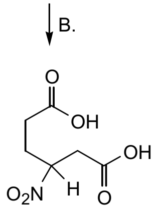
Not a pesticide

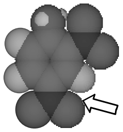
Bacterium
Rhodococcus sp. strain RB1 isolated by aerobic enrichment cultivation of an activated sludge from a waste water plant in Alicante, Spain[57]

The bacterial strain RB1, which is isolated by enrichment cultivation with 2,4-dinitrophenol, degrades this phenol into two aliphatic acids. One metabolite results from the release of the 2-nitro group as nitrile, with the production of aliphatic nitro compound, 3-nitroadipate. Then, the 3-nitro group is released from this metabolite as nitrile. The other metabolite is 4,6-dinitrohexanoic acid possessing two nitro groups from 2,4-dinitrophenol.



2,4-Dinitrophenol





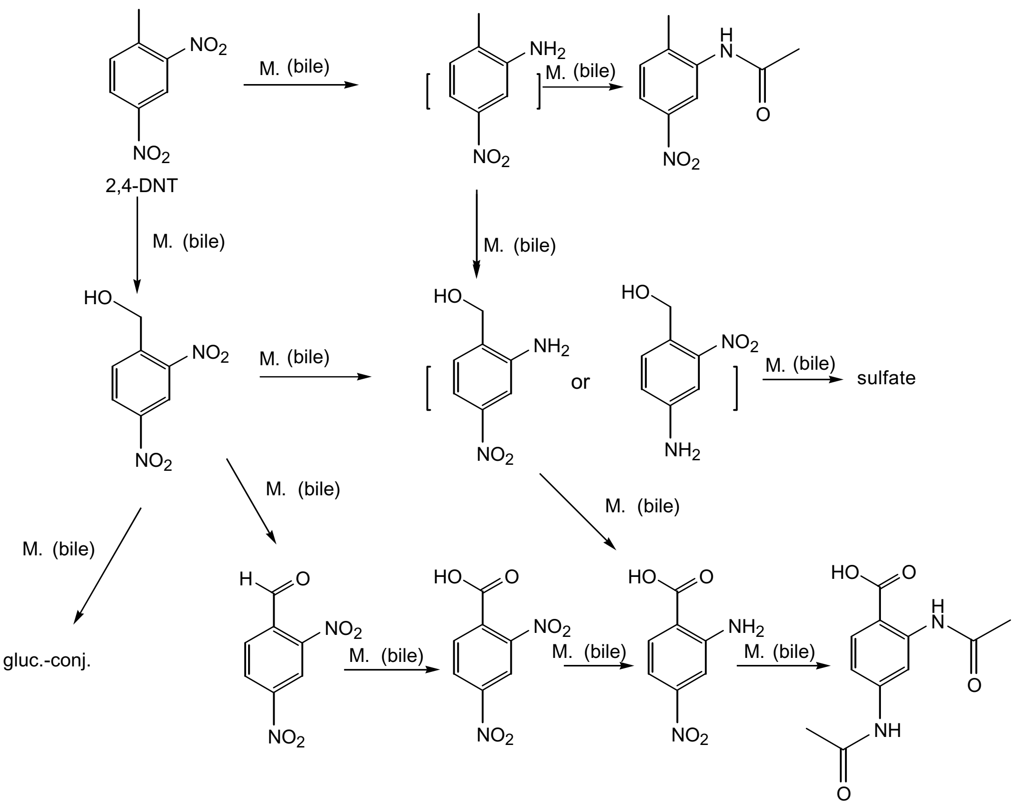
OC1=C([N+]([O-])=O)C
=C([N+]([O-])=O)C=C1

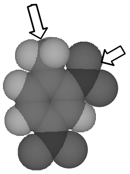
2,4-Dinitrotoluene (2,4-DNT)

Not a pesticide

Mammal
Male Wistar rats (weighing 180–200 g)[58]

The major biliary metabolite of 2,4-dinitrotoluene (2,4-DNT) in the rat is the glucuronide conjugate of 2,4-dinitrobenzyl alcohol and the minor metabolites are 2,4-dinitrobenzyl alcohol, 2,4-dinitrobenzaldehyde, 2-acetylamino-4-nitrotoluene, 4-amino-2-nitro or 2-amino-4-nitrobenzyl alcohol sulfate, 2,4-dinitrobenzoic acid, 2,4-diacetylaminobenzoic acid, and 2-amino-4-nitrobenzoic acid.





CC1=C([N+]([O-])=O)C=C
([N+]([O-])=O)C=C1

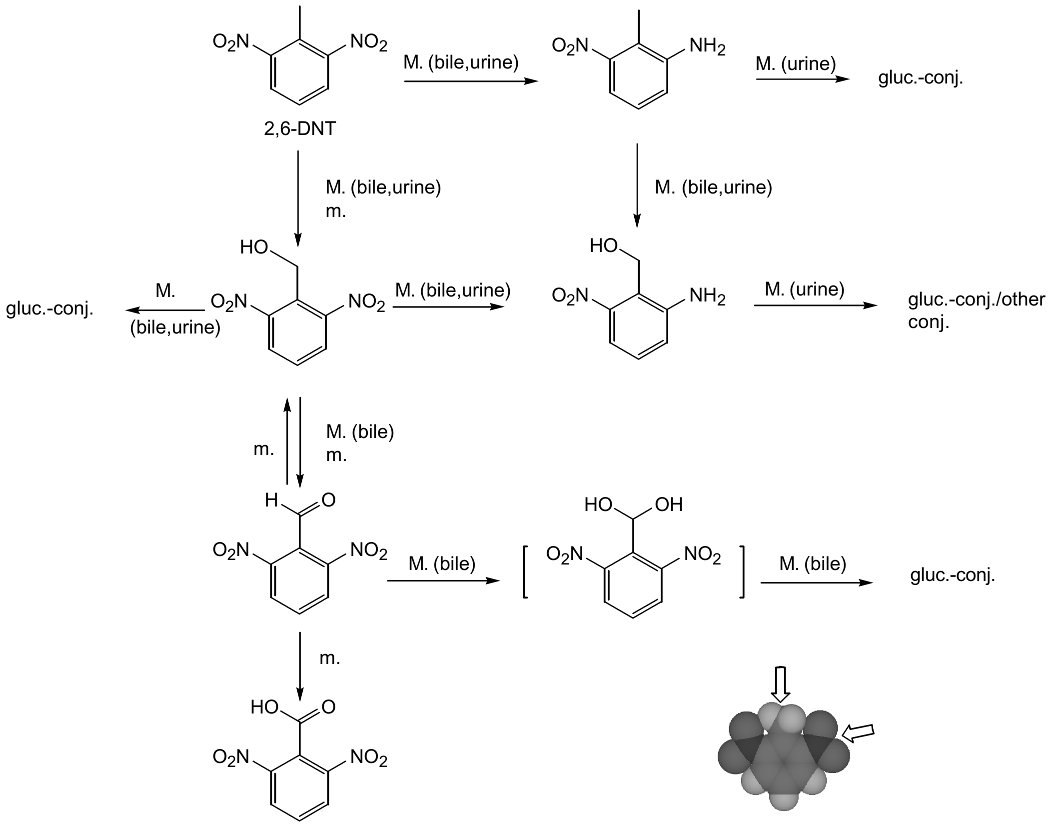
2,6-Dinitrotoluene (2,6-DNT)

Not a pesticide

Mammal
Male Wistar rats (weighing 180–200 g, Sankyo Laboratories)[59]

Microsomes
Microsomal and cytosolic preparations from rat livers from male Wistar rats (weighing 180–200 g)[59]

2-Amino-6-nitrotoluene, 2,6-dinitrobenzyl alcohol, 2-amino-6-nitrobenzyl alcohol, and the conjugates of the latter two alcohols are detected in the urine of male Wistar rats as metabolites of 2,6-dinitrotoluene (2,6-DNT). In addition to the metabolites identified in the urine, 2,6-dinitrobenzaldehyde is detected in the rat bile. Incubation of 2,6-DNT with a hepatic microsomal preparation gives 2,6-dinitrobenzyl alcohol. Incubation of benzyl alcohol with a microsomal plus cytosol preparation gives 2,6-dinitrobenzaldehyde, and incubation of 2,6-dinitrobenzaldehyde with cytosol preparations gives 2,6-dinitrobenzyl alcohol and 2,6-dinitrobenzoic acid.



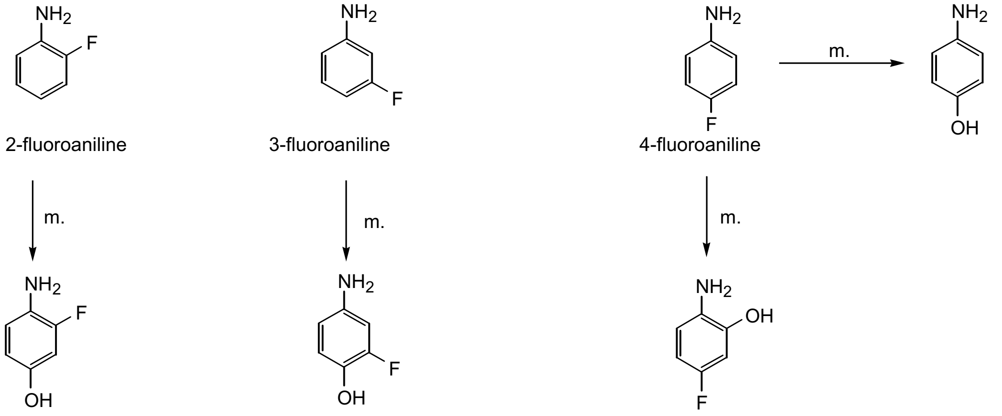
CC1=C([N+]([O-])=O)C=C
C=C1[N+]([O-])=O

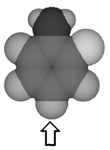
2-, 3- and 4-Fluoroanilines

Not pesticides

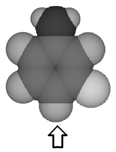
Microsome
Microsomal preparation from the perfused livers of male Wistar rats (ca 300 g), untreated (control) or treated with inducers of cytochrome P-450 isozymes[60]

2-Fluoro and 3-fluoroanilines are preferentially hydroxylated at the *para*-position, and 4-fluoroaniline is both *p*- and *o*-hydroxylated to a significant extent by rat liver microsomes and is not accompanied with an NIH shift to give 4-hydroxyl-3-fluoroaniline.

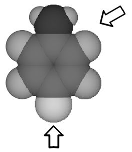




NC1=C(F)C=CC=C1



NC1=CC(F)=CC=C1



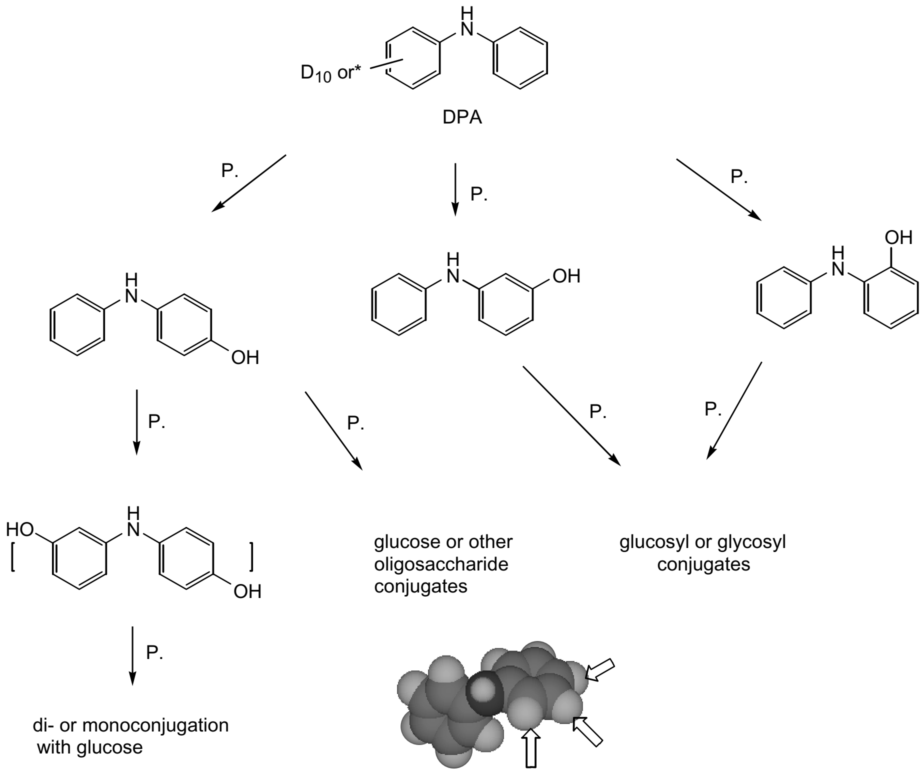
NC1=CC=C(F)C=C1

Diphenylamine

A fungicide: control of superficial scald (a respiratory breakdown of fruit cells)

Plant
Red Delicious apples (*Malus punila*) averaging 200 g in size[61]

The major metabolite of diphenylamine (DPA) identified in stored apples is a glucose conjugate of 4-hydroxydiphenylamine, and additional metabolites, characterized as glycosyl conjugates of 2-hydroxy-DPA, 3-hydroxy-DPA, 4-hydroxy-DPA, or dihydroxy-DPA, are also detected along with their intact (i.e. non-conjugated) forms in apple pulp.



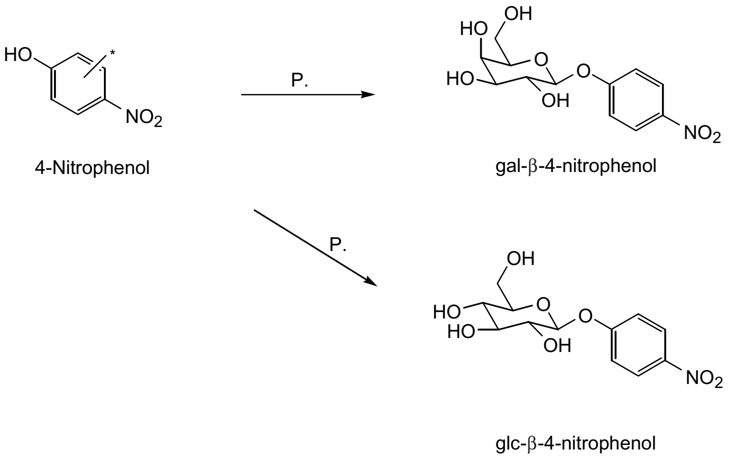
C1(NC2=CC=CC=C2)=CC=CC=C1

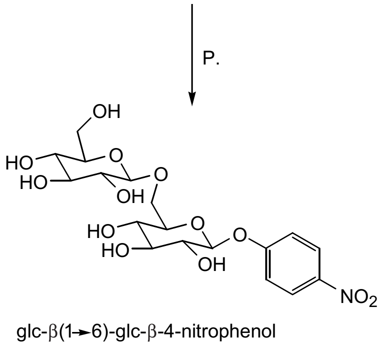
4-Nitrophenol

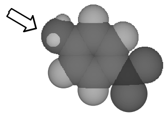
A pesticide metabolite

Plant
Cell suspension cultures of *Datura stramonium* L. (jimsonweed)[62]

4-[U-^{14}C]Nitrophenol is conjugated as its β-glucoside (ca 22% of applied ^{14}C) and gentiobioside, glc-β(1 → 6)-glc-β-4-nitrophenol (ca 64%), while about 7% of the parent remains unchanged in cell suspension cultures of *Datura stramonium* (L.). Gal-β-4-nitrophenol is found to be a minor metabolite.







OC1=CC=C([N+]([O-])=O)C=C1

gal: galactose residue
glc: glucose residue

Pendimethalin

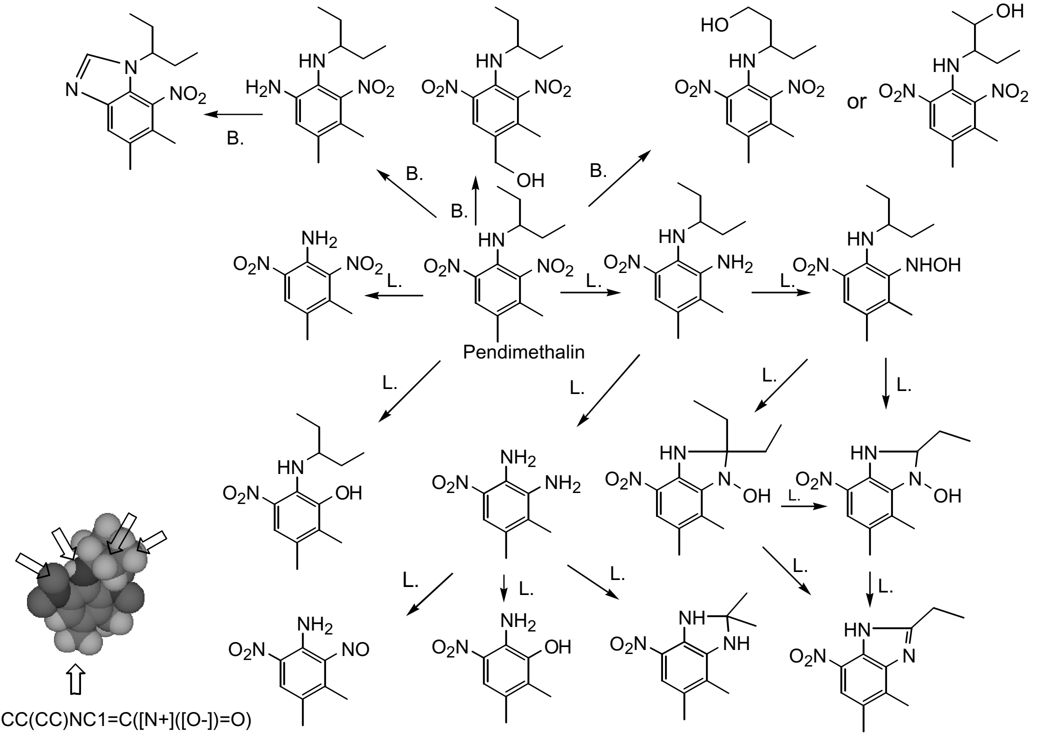
A selective herbicide: effective against most annual grasses and certain broadleaf weeds in cotton, soybean, and other crops
An insecticide: control of suckers in tobacco

Light
A GEF 40/BL bulb (emitting at 300–450 nm); natural sunlight for 2 months (8 h per day from May to June in New Delhi; a solar simulator (Applied Photophysics 9500 solar simulator); irradiated by UV and natural sunlight on a soil surface of sandy loam (pH 6.1)[63]

Bacterium
Soil bacteria of *Bacillus* sp. and *Alcaligenes* sp. isolated from the soils (volcanic ash, alluvial soil) in Kannondai Ibaraki, Japan[64]

Mammal
Royal Hart Wistar-strain male rats[65]

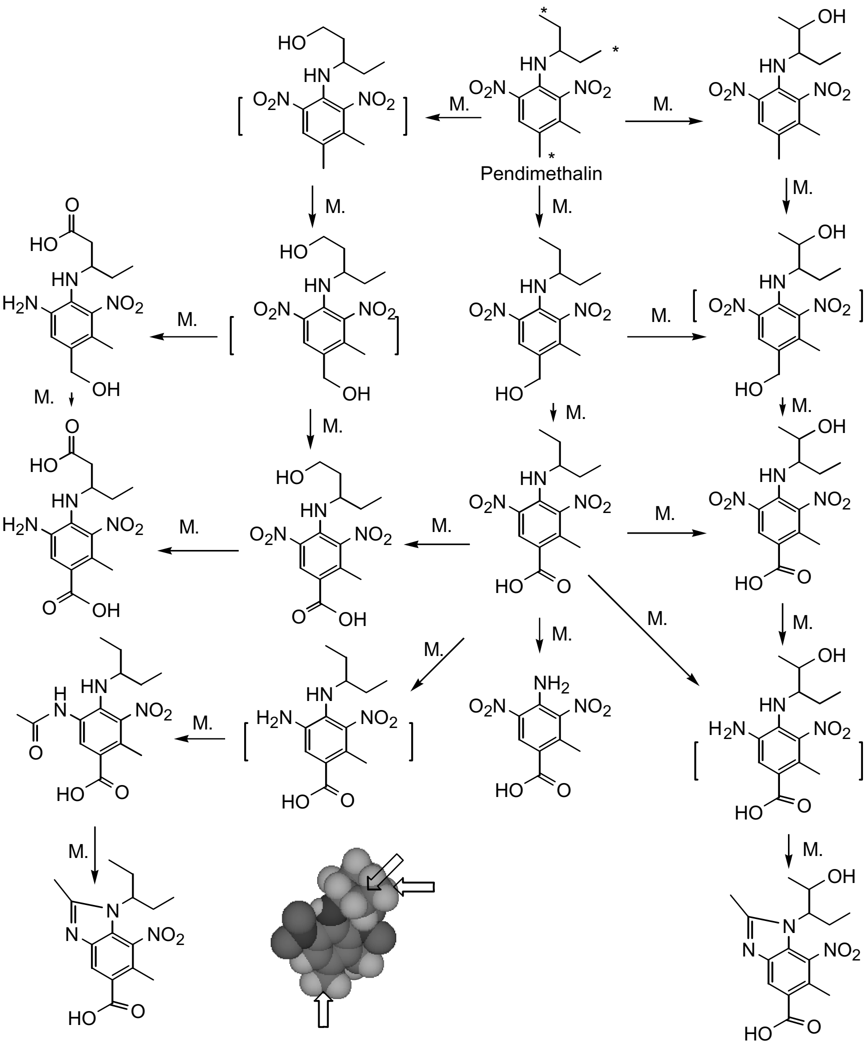
Irradiation of pendimethalin in methanol yields, in addition to the minor dealkylated product, the major products 2-amino-6-nitro-*N*-(1-ethylpropyl)-3,4-xylidine and 2-nitroso-6-nitro-3,4-xylidine. Pendimethalin degrades rapidly through reductive cyclization of the amino group and adjacent *N*-ethylpropyl to give a cyclized benzimidazole product. The photodecomposition of pendimethalin involves oxidative dealkylation, nitro reduction, and cyclization. By soil bacteria, pendimethalin degrades through different pathways from the photodegradation reaction, resulting in benzimidazole and hydroxylated products of the *N*-alkyl and xylyl methyl groups. The major metabolic routes of pendimethalin by rats involves hydroxylation of the 4-methyl and the *N*-ethyl group, oxidation of these alkyl groups to carboxylic acids,



CCC(CC)NC1=C([N+]([O-])=O)
C(C)=C(C)C=C1[N+]([O-])=O

Pendimethalin **(continued)**

nitro reduction, cyclization, and conjugation in the urine and the tissues. Products of cyclization reactions giving methylbenzimidazole-carboxylic acids are unique metabolites to the liver and kidney.



5

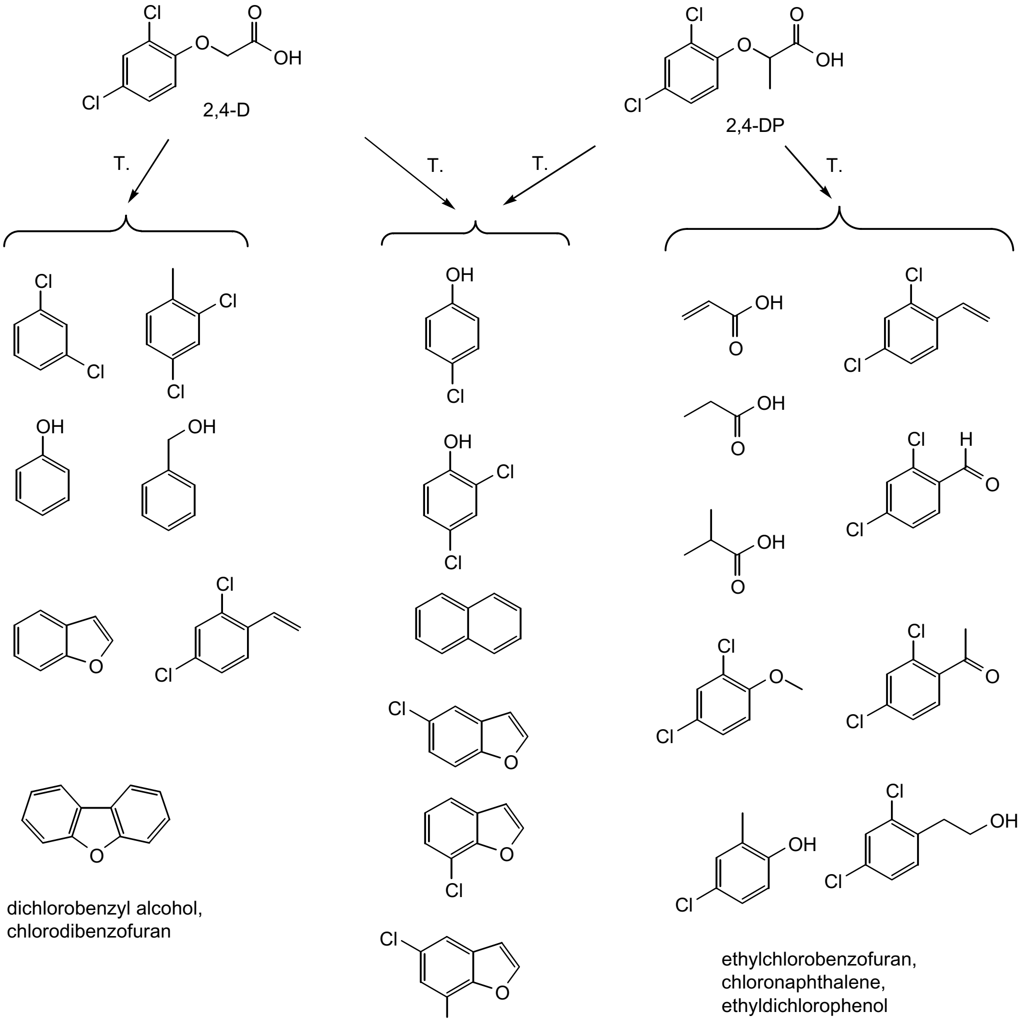
Aryloxy Acids

2,4-D and 2,4-DP

Herbicides

Temperature
Pyrolysis in a helium atmosphere in the range 200−1000 °C[66]

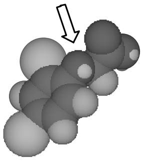
Vapor-phase pyrolysis and combustion of 2,4-D [(2,4-dichlorophenoxy)acetic acid] and 2,4-DP [(2,4-dichlorophenoxy)propionic acid] in the range 200−1000 °C is performed in laboratory reactors.



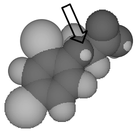
dichlorobenzyl alcohol,
chlorodibenzofuran

methylchlorobenzofuran,
chloronaphthalene,
chloronaphthol,
dichloronaphthalene

ethylchlorobenzofuran,
chloronaphthalene,
ethyldichlorophenol



ClC1=C(OCC(O)=O)C=CC(Cl)=C1



ClC1=C(OC(C)C(O)=O)C=CC(Cl)=C1

The degradation products by pyrolysis are identified and, from both of these, free acid herbicides 4-chlorophenol, 2,4-dichlorophenol, naphthalene, 5-chlorobenzofuran, 7-chlorobenzofuran, and 5,7-dichlorobenzufuran are the common thermal degradation products.

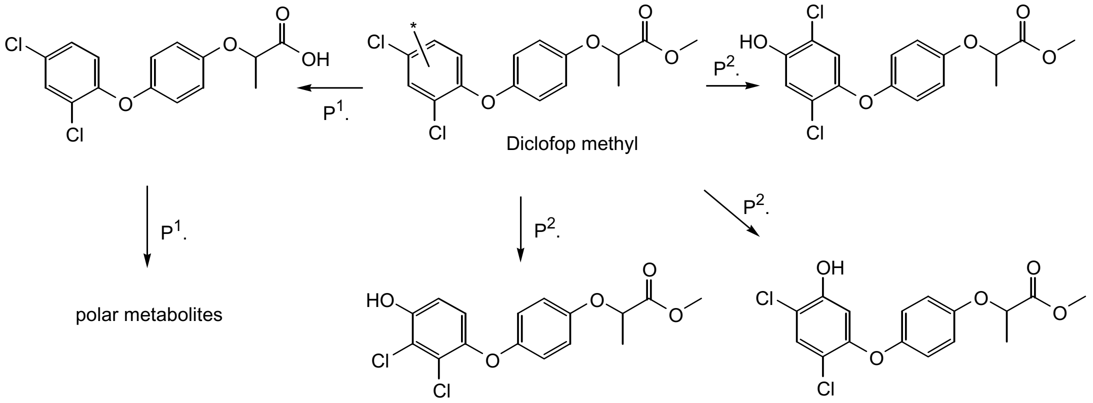
Diclofop methyl

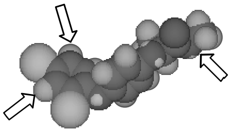
A selective herbicide: control of *Alopecurus myosuroides* (black-grass, slender foxtail), a major annual grass weed in winter cereal crops in Western Europe

Plant[1]
Black-grass (slender foxtail): *Alopecurus myosuroides* designated Peldon A1 and Lincs. E1[67]

Plant[2]
Wheat: *Triticum aestivum* L.[68]

Two resistant biotypes of black-grass (Peldon A1 and Lincs. E1 of *Alopecurus myosuroides*) exhibit moderately enhanced metabolism of ^{14}C-diclofop methyl. Diclofop methyl is hydrolyzed to the corresponding propionic acid which undergoes further degradation to give polar metabolites. The amounts of the metabolites depend on the metabolism activity of the individual biotypes. In wheat, three isomeric hydroxylated metabolites are identified in a major metabolic pathway after acid hydrolysis of the glucoside conjugates.





CC(OC1=CC=C(C=C1)OC2=C
C=C(C=C2Cl)Cl)C(OC)=O

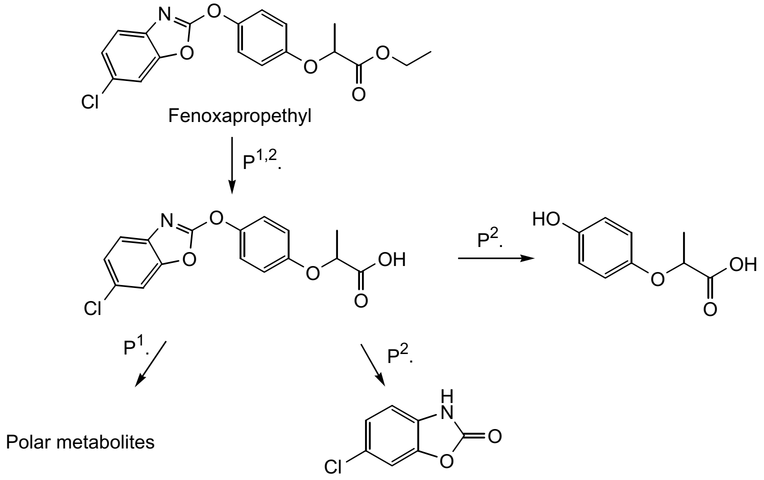
Fenoxaprop ethyl

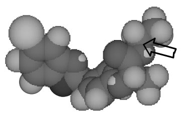
A selective herbicide: control of *Alopecurus myosuroides* (black-grass, slender foxtail), a major annual grass weed in winter cereal crops in Western Europe

Plant^{1}
Black-grass (slender foxtail): *Alopecurus myosuroides* designated Peldon A1 and Lincs. E1[67]

Plant^{2}
Wheat: *Triticum aestivum* L.; barley: *Hordeum vulgar* L.; crabgrass: *Digitaria ischaemum* (Schreb, Muhl.)[69]

A resistant biotype of Peldon A1 of *Alopecurus myosuroides* shows moderately enhanced metabolism of ^{14}C-fenoxaprop ethyl. However, in the more resistant Lincs. E1, the metabolism rates of fenoxaprop ethyl are intermediate between Peldon A1 and the susceptible Rothamsted biotype. Fenoxaprop ethyl is hydrolyzed to the corresponding propionic acid which undergoes further degradation to give polar metabolites. The amounts of the metabolites depend on the metabolism activity of the individual biotypes. By wheat, barley, and crabgrass plants, fenoxaprop ethyl is de-esterified to fenoxaprop, resulting in a phytotoxic-free acid, 6-chloro-2,3-dihydrobenzoxazol-2-one, and 4-hydroxyphenoxypropionic acid.





ClC1=CC=C2C(OC(OC3=CC=C
(OC(C)C(OCC)=O)C=C3)=N2)=C1

Fluazifop butyl

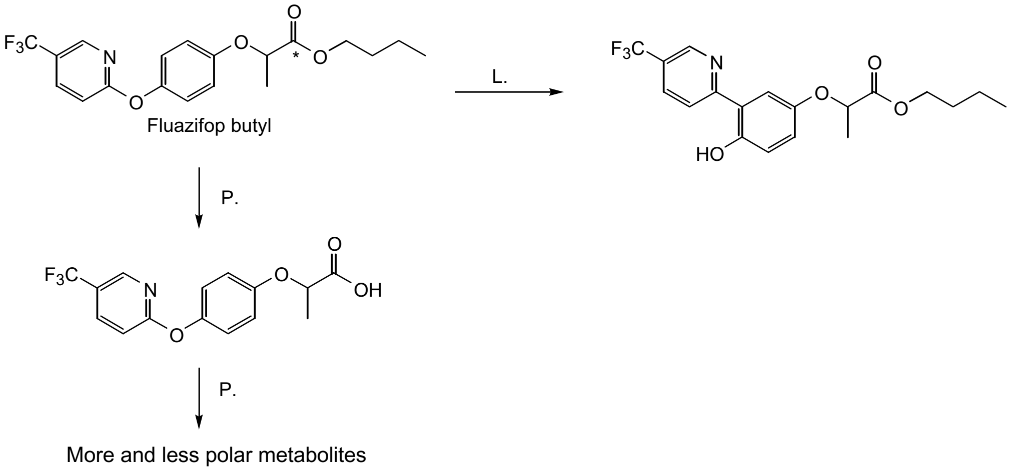
A herbicide: a potent inhibitor of plasticidic enzyme acetyl-coenzyme A carboxylase

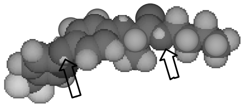
---

Light
A Camag low-pressure mercury lamp emitting at 354 nm on to borosilicate glass petri dishes[70]

Plant
Soybean: cv. S-1346[71, 72]

Fluazifop butyl as a thin film on glass is photorearranged by UV irradiation to the isomer butyl-(*RS*)-2-[4-hydroxy-3-(5-trifluoromethyl-2-pyridyl)phenoxy]propionate. Plants of both resistant and susceptible populations of *Digitaria sanguinalis* rapidly hydrolyze ^{14}C-fluazifop butyl to corresponding acid in leaves, but fluazifop acid is metabolized to other compounds at a more rapid rate in the resistant plants. An enhanced metabolism of toxophore, fluazifop acid is a likely mechanism of resistance in this population. The plants of putative resistant and susceptible population of *Digitaria sanguinalis* (L.) Scop had survived the application of 212 g/ha fluazifop-P-butyl in the year of collection.[72]





CC(C(OCCCC)=O)OC1=CC=C
(OC2=NC=C(C(F)(F)F)C=C2)C=C1

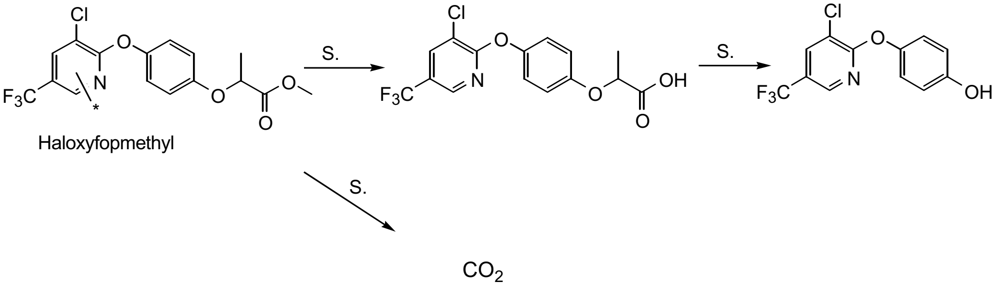
Haloxyfop methyl

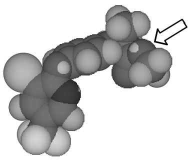
An experimental post-emergent herbicide: control of annual and perennial grasses in a variety of broad-leaved crops

---

Soil
Clay loam (pH 6.0); sandy loam (pH 7.6); heavy clay (pH 7.7)[73]

In all soils tested, ^{14}C-haloxyprop methyl is rapidly hydrolyzed to the corresponding haloxyprop acid, providing there is moisture in excess of the wilting point. In air-dried soils, little hydrolysis of haloxypropm ethyl to acid occurs. In moist sterile soils, there is a loss of solvent extractable radioactivity with time. These losses follow first-order kinetics, with half-lives of 27, 38, and 92 days respectively in the sandy loam, heavy clay, and clay loam soil types.





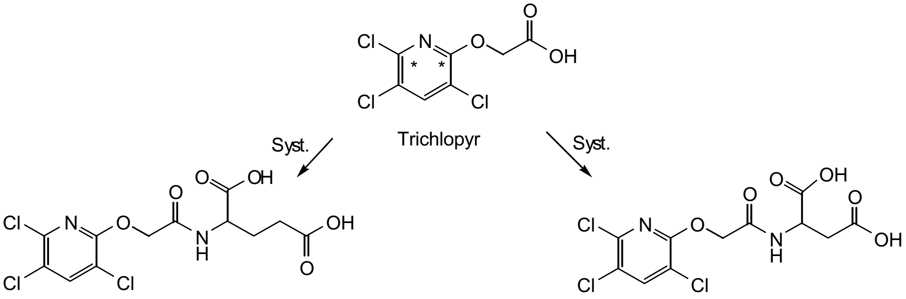
ClC1=C(OC2=CC=C(OC(C)C(OC)=O)
C=C2)N=CC(C(F)(F)F)=C1

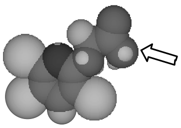
Trichlopyr

A post-emergent herbicide: control of a wide range of broad-leaved and woody weeds, use for forestry and right-of-way clearance

System
Cell culture of soybean: *Glycine max*. var. Harcor[74]

After 7 days in a soybean cell suspension culture, the major metabolites of trichlopyr are formed and identified as the aspartate (major) and glutamate (minor) amide conjugates.





OC(COC1=NC(Cl)=C(Cl)C=C1Cl)=O

6

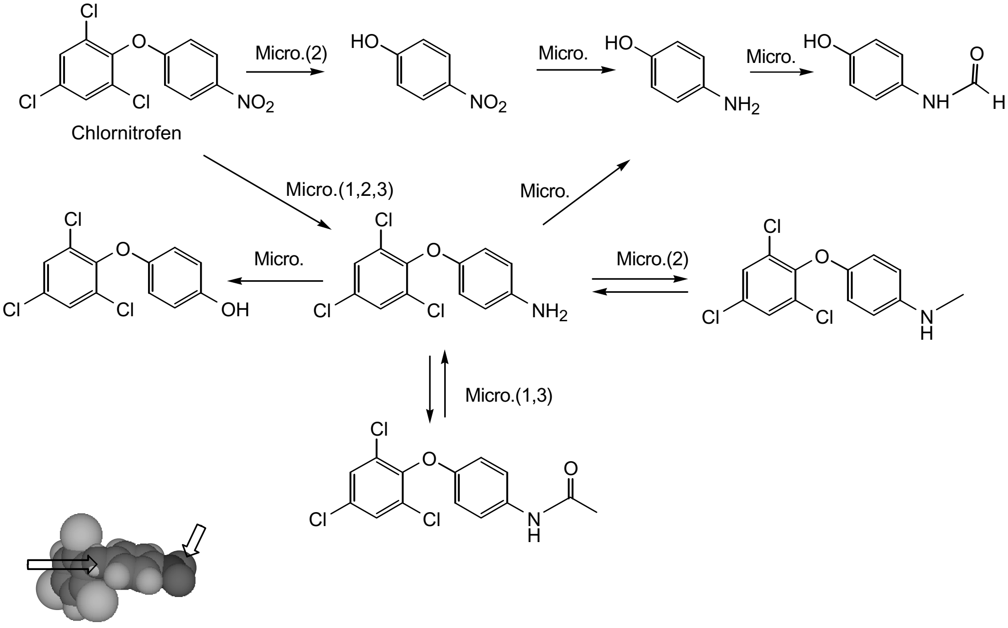
Biphenyl Ethers

Chlornitrofen (MC-338)

A herbicide

Microorganism
Corynebacterium sp. (1); *Streptomyces* sp. (2); *Penicillium* sp. (3)[75]

Degradation of chlornitrofen by microorganisms isolated from soils gives rise to the reduction of the nitro group of chlornitrofen to the amino analog, and the successive *N*-acetylation or *N*-methylation and the cleavage of the ether linkage are dominant metabolic pathways. The metabolic pathways, however, differ depending on microorganisms and the media. The replacement of the amino group by hydroxyl group, the reduction and successive formylation of *p*-nitrophenol, and the cleavage of the phenyl ring ultimately to produce CO_2 are also observed.



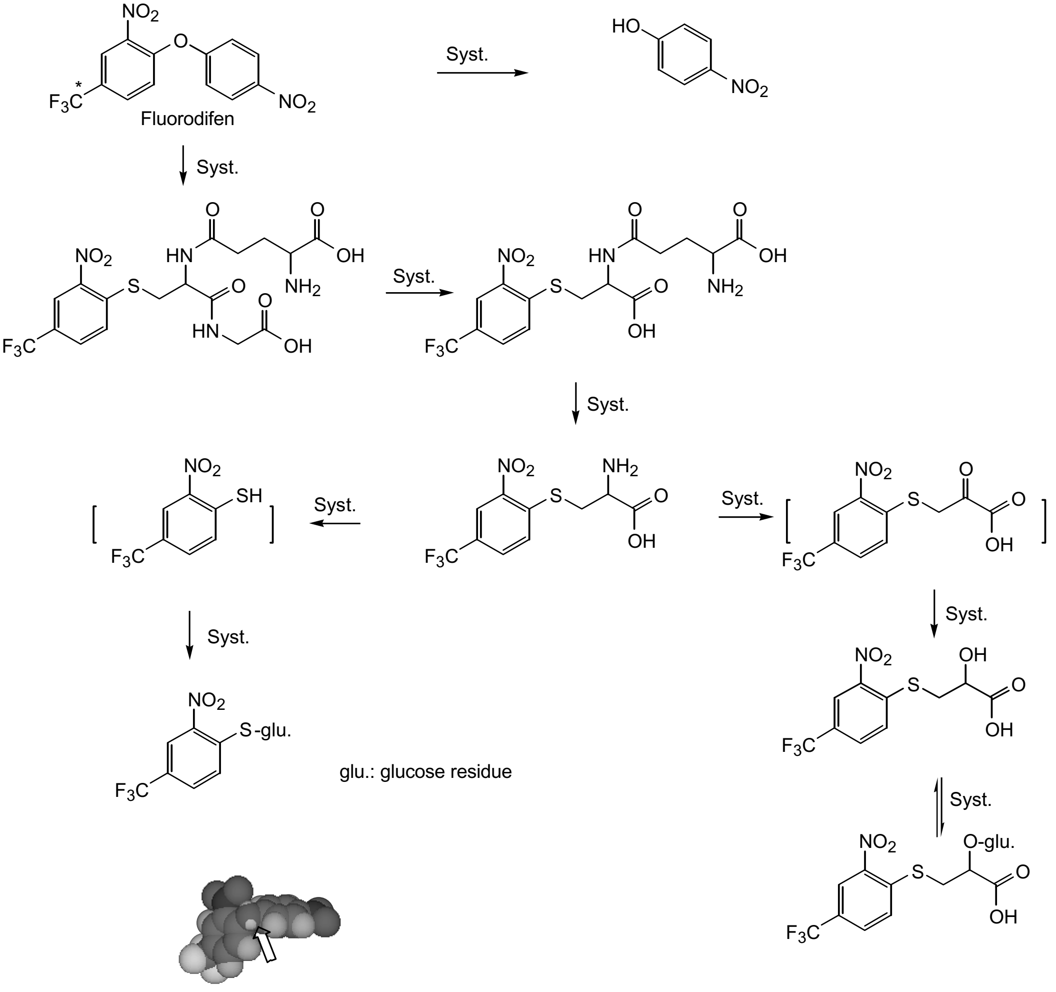
ClC1=C(OC2=CC=C([N+]([O-])=O)C=C2)C(Cl)=CC(Cl)=C1

Fluorodifen

A herbicide

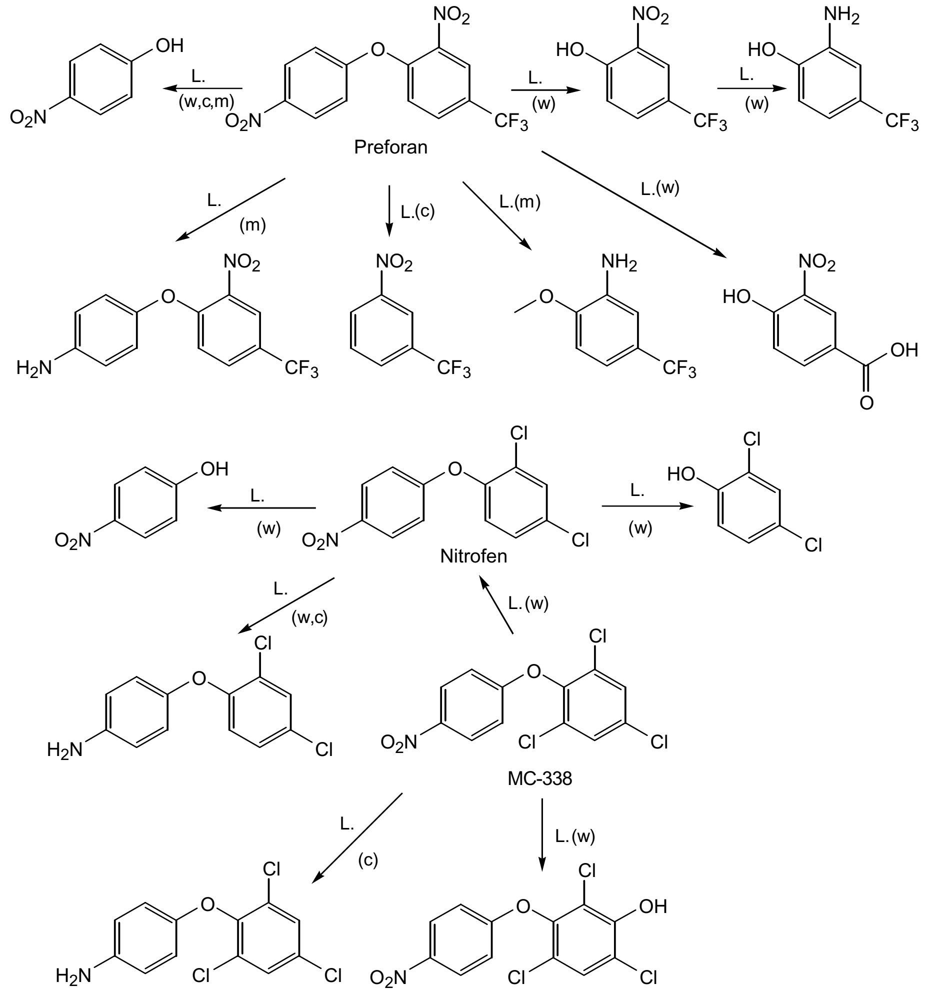
System
A spruce cell suspension culture: *Picea abies* L. Karst[76]

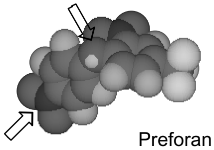
$^{14}CF_3$-Fluorodifen is rapidly metabolized by a spruce cell suspension culture, and the primary route of metabolism involves the cleavage of the diphenyl ether bond by glutathione which is further metabolized sequentially to the corresponding γ-glutamylcysteine conjugate, cysteine conjugate and two novel metabolites of *S*-glucoside, and *S*-(3-thio-2-*O*-glucosyl)lactic acid conjugates of 4-trifluoromethyl-2-nitrobenzene.



O=[N+]([O-])C1=C(OC2=CC=C([N+]
([O-])=O)C=C2)C=CC(C(F)(F)F)=C1

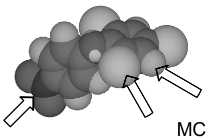
Preforan, Nitrofen, MC-338, MC-4379, MC-3761, MC-5127, MC-6063, and MC-7181





Preforan

O=[N+]([O-])C1=CC=C(OC2=CC=C(C(F)(F)F)C=C2[N+]([O-])=O)C=C1



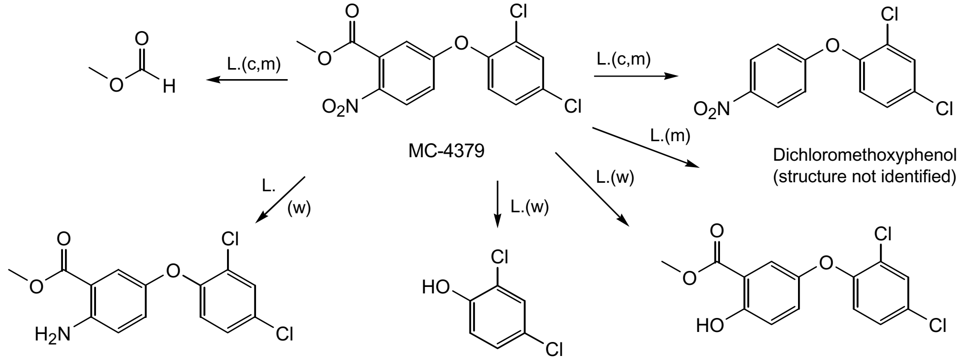
MC-338

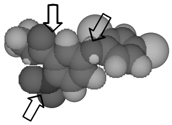
ClC1=CC(Cl)=CC(Cl)=C1OC2=CC=C([N+]([O-])=O)C=C2

Preforan, Nitrofen, MC-338, MC-4379, MC-3761, MC-5127, MC-6063, and MC-7181

Light
A Rayonette reactor (The Southern N. E. Ultraviolet Co., Middletown, CT)[77]

Photopysis products of eight substituted diphenyl ethers (preforan, nitrofen, MC-338, MC-4379, MC-3761, MC-5127, MC-6063, and MC-7181) irradiated by a Raryonette reactor in solutions of water, cyclohexane, and methanol indicates that the major reaction pathways of these biphenyl ethers include reductive dehalogenation, decarboxyalkylation, reduction of nitro substituents to amines, and cleavage of the ether linkage to yield phenols.



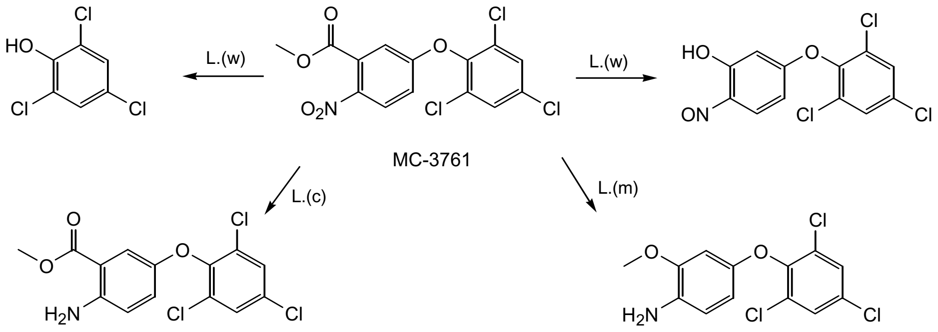


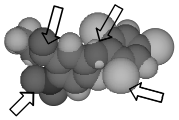
ClC1=CC(Cl)=CC=C1OC2=CC(C(OC)=O)=C([N+]([O-])=O)C=C2

(w: water suspension,
c: cyclohexane,
m: methanol)

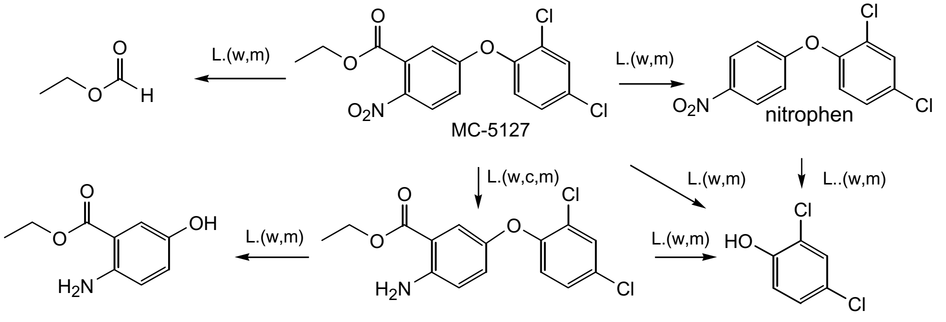
Preforan, Nitrofen, MC-338, MC-4379, MC-3761, MC-5127, MC-6063, and MC-7181

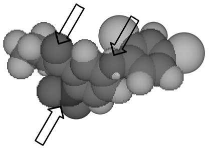
(continued)





ClC1=CC(Cl)=CC(Cl)=C1OC2=CC
(C(OC)=O)=C([N+]([O-])=O)C=C2





ClC1=CC(Cl)=CC=C1OC2=CC(C
(OCC)=O)=C([N+]([O-])=O)C=C2

(w: water suspension,
c: cyclohexane,
m: methanol)

Preforan, Nitrofen, MC-338, MC-4379, MC-3761, MC-5127, MC-6063, and MC-7181

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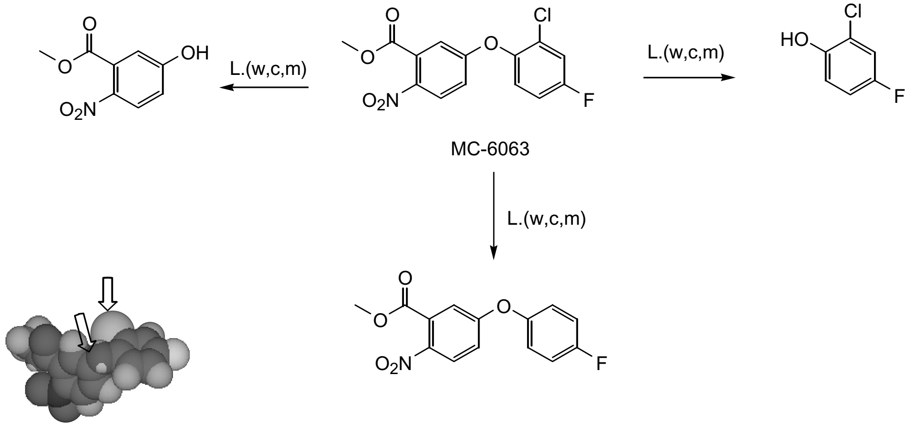
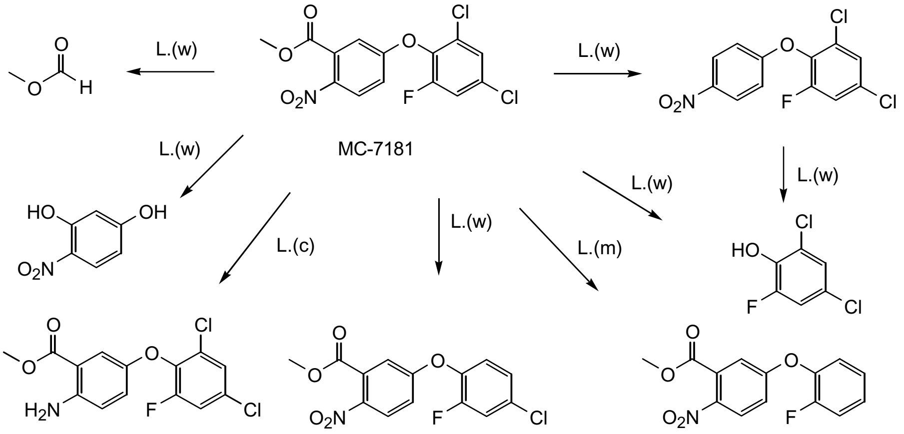
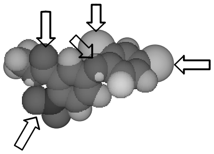


MC-6063

ClC1=CC(F)=CC=C1OC2=CC(C(OC)=O)=C([N+]([O-])=O)C=C2



MC-7181



ClC1=CC(Cl)=CC(F)=C1OC2=CC(C(OC)=O)=C([N+]([O-])=O)C=C2

(w: water suspension,
c: cyclohexane,
m: methanol)

7

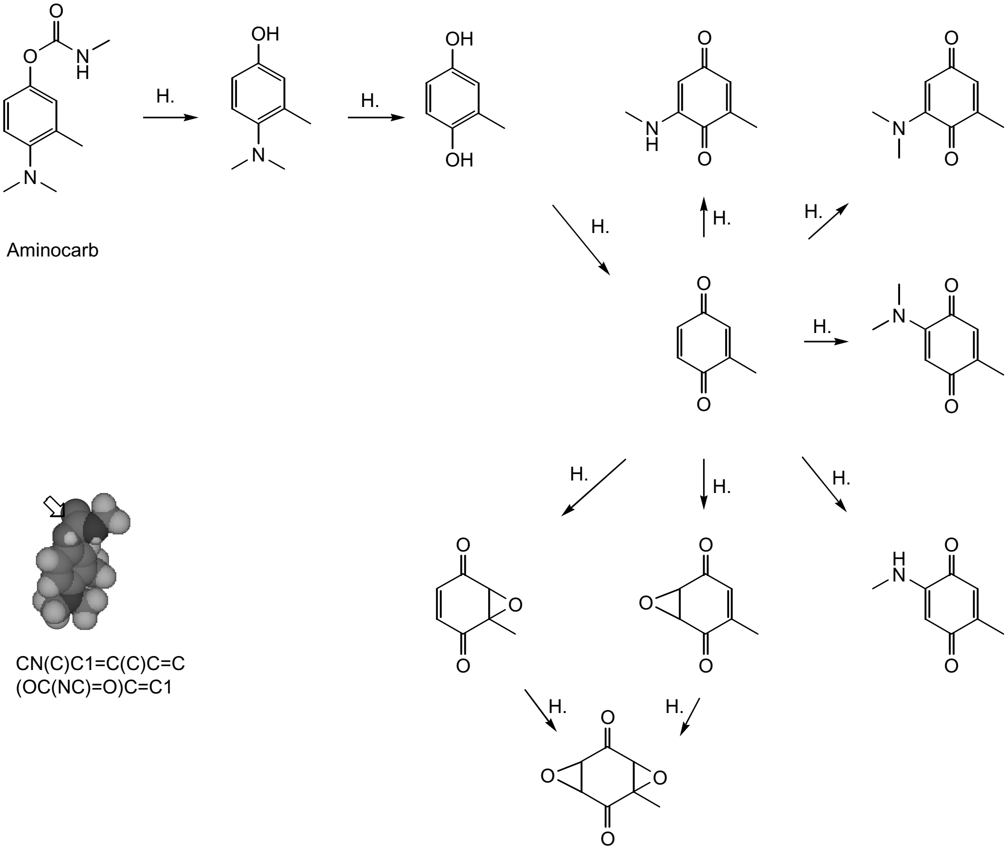
Carbamates

Aminocarb (Matacil)

A broad-spectrum insecticide

Hydrolysis
Purified water (pH 6.4) at 25 °C[78]

Aminocarb in purified water is hydrolyzed to 4-(dimethylamino)-3-methylphenol which is in turn converted to 2-methyl-1,4-benzoquinone either by direct means or via 2-methyl-1,4-dihydroquinone. The benzoquinone reacts readily with methylamine and diethylamine present in solution to give four red chemicals. In addition, mono- and diepoxides of 2-methyl-1,4-benzoquinone are formed.



Aminocarb

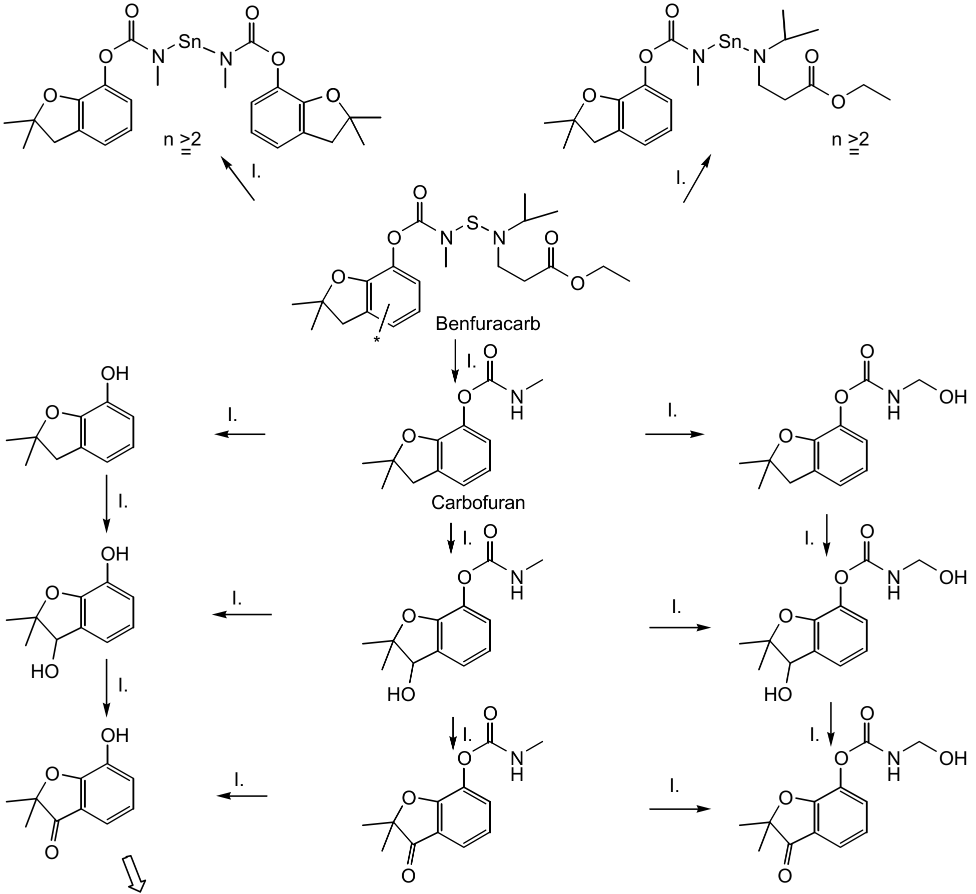
CN(C)C1=C(C)C=C
(OC(NC)=O)C=C1

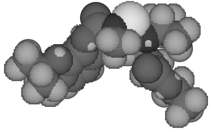
Benfuracarb

An insecticide

Insect
Four day-old female houseflies: Takatsuki strain[79]

When ^{14}C-benfuracarb is applied topically to houseflies, the houseflies metabolize benfuracarb easily to form carbofuran which in turn is oxidized at the 3-position of the ring and *N*-methyl group, resulting in further conjugates of the metabolites. Major metabolites are carbofuran, 3-hydroxycarbofuran, *N*-hydroxymethylcarbofuran, 3-ketocarbofuran, 2,3-dihydro-2,2-dimethyl-3-hydroxybenzofuran-6-ol, 3-hydroxy-*N*-hydroxymethylcarbofuran, and 3-keto-*N*-hydroxymethylcarbofuran.





CC(C2)(C)OC1=C2C=CC=C1OC
(N(C)SN(CCC(OCC)=O)C(C)C)=O

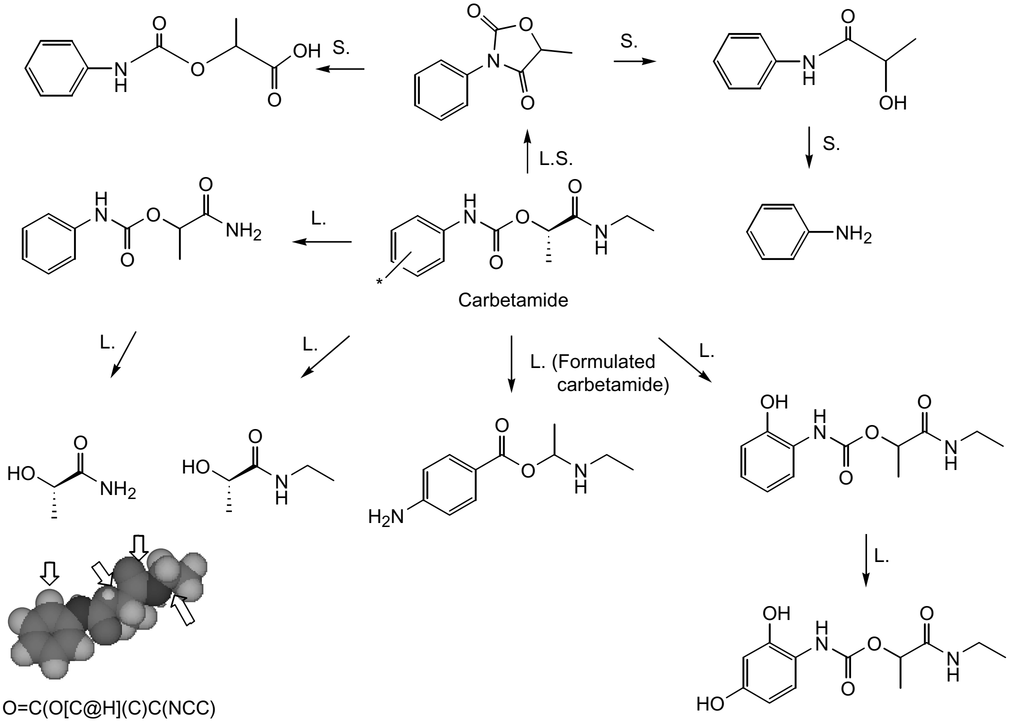
Carbetamide

A selective pre- and post-emergent herbicide: control of grass and some broadleaf weeds in lucerne, sugarbeet, and rape, by inhibiting cell division in young tissues of root and shoot

Light
Irradiation of UV with a Philips HPK 125 W high-pressure mercury vapor lamp in aqueous solutions with H_2O_2 or TiO_2[80]

Soil
Roussilon Plain sandy loam soil in France (pH 8.3)[81]

Photodegradation of carbetamide in solution with UV irradiation in the presence of UV$-H_2O_2$ and $-TiO_2$ primarily occurs at the *o*- and *p*-positions, but not at the *m*-position of the phenyl ring, and the preferential photoproduct isolated is *ortho*-hydroxylated carbetamide. 5-Methyl-3-phenyl-oxazolidine dione is isolated only in the presence of TiO_2. The cyclization may result from radical coupling with the dissolved oxygen. *N*-De-ethylation of the ethylcarbamoyl group and hydroxylation on the carbamoyloxy linkage occur to yield free amine of carbetamide and lactamide analogs. It is interesting to note that formulated carbetamide is phototransformed to *N*-ethyllactamide-4-aminobenzoate as a major product via the rearrangement reaction similar to the Photo-Fries reaction.



O=C(O[C@H](C)C(NCC)
=O)NC1=CC=CC=C1

The degradation kinetics of carbetamide and its potential metabolites are measured at different temperatures in both unsterilized and sterilized alkaline soil. The chemical degradation of carbetamide importantly gives *N*-phenyl-3-methyloxazolidine-2,5-dione which results in 2-(phenylcarbamoyloxy)-propionic acid and *N*-phenyl-2-hydroxypropionamide and the aniline in the soil. The purely biological degradation of this compound cannot clearly yield degradation products that are different from those by chemical degradation in non-sterilized soils.

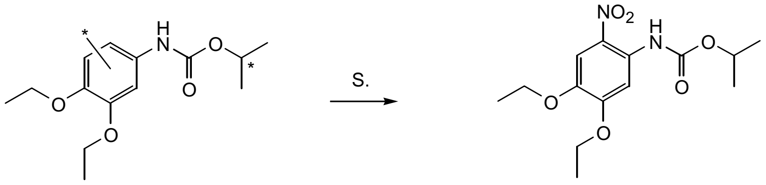
Diethofencarb

A fungicide: control of benzimidazole-resistant strains of various fungi including *Botrytis* spp., *Cercospora* spp., and *Venturia* spp., but almost ineffective against benzimidazole-susceptible strains

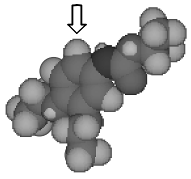
Soil

Ushiku loam (pH 6.9/H_2O); Sapporo clay loam (pH 5.3/H_2O); Azuchi sandy loam (pH 5.1/H_2O); Muko sand (pH 6.6/H_2O)[82]

In aerobic upland soils under laboratory conditions, the half-life of ^{14}C-diethofencarb is 0.3–6.2 days and the major metabolite is a nitrated derivative at the 6-position of the phenyl ring. Diethofencarb slowly degrades under anaerobic upland conditions and hardly degrades in sterilized soils.



Diethofencarb



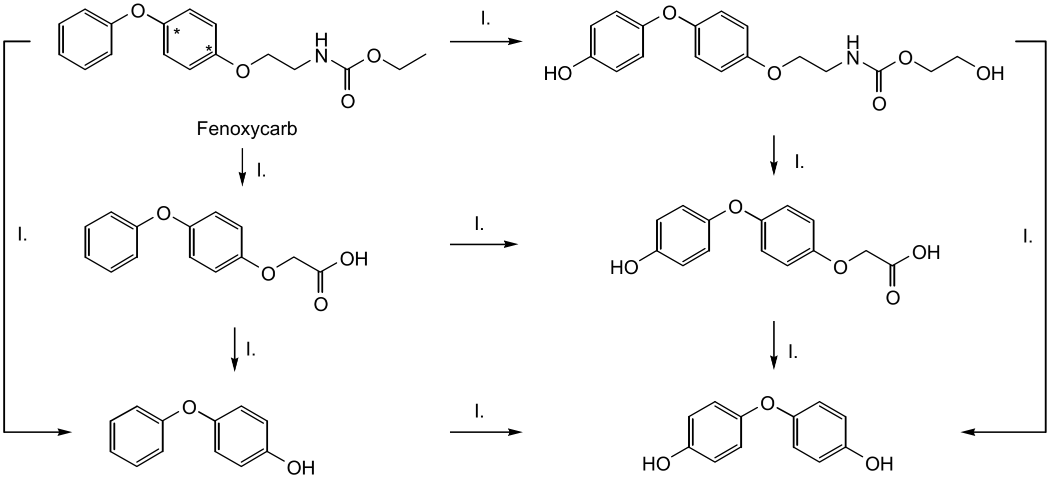
CCOC1=CC=C(NC(O
C(C)C)=O)C=C1OCC

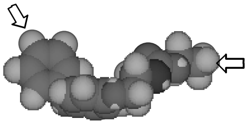
Fenoxycarb

An insecticide: non-neurotoxic carbamate with insect juvenile hormone activity

Insect
Fourth and fifth instars of tobacco budworm: *Heliothis virescens* F.[83]

When the insect larvae of tobacco budworm are fed with ^{14}C-fenoxycarb, at the time of gut purge, the whole of the radio-labeled material is excreted. The main metabolites of fenoxycarb are identified and show hydroxylation of the aromatic rings which makes the excretion easier. Cleavage of the molecule to give carboxylic acid metabolites confirms the hypothesis that the fenoxycarb is not cleaved by esterase.





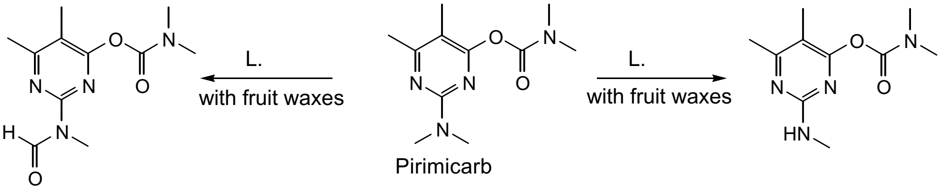
O=C(OCC)NCCOC(C=C2)
=CC=C2OC1=CC=CC=C1

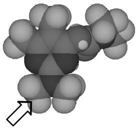
Pirimicarb

An insecticide

Light
A high-pressure mercury lamp (125 W; Helios Italquartz, Milan; $I_\lambda = 3.9 \times 10^{-7}\,EL^{-1}\,s^{-1}$) with waxes from nectarines, oranges [*Citrus sinensis* L. (O_R)], and mandarin oranges [*Citrus reticulata* L. (M)][84]

The influence on the qualitative photochemical behavior of pirimicarb which leads to the photoproducts *N*-formylpirimicarb and demethylpirimicarb is modified by the waxes that are extracted from nectarines, oranges, and mandarin oranges. The formation of the photoproducts is hindered by the waxes.





CC1=NC(N(C)C)=NC
(OC(N(C)C)=O)=C1C

8

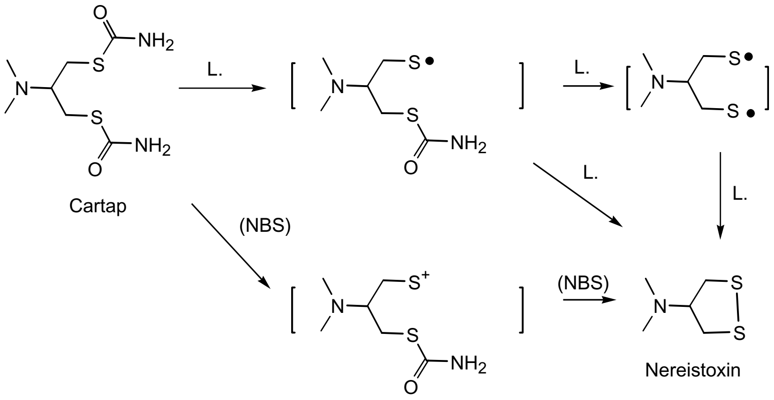
Dithio- and Thiolcarbamates

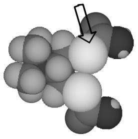
Cartap hydrochloride

An insecticide

Light
A germicidal lamp (Toshiba, $\lambda = 245$ nm); a UV lamp (Toshiba, $\lambda = 373$ nm); a photoreactor equipped with a high-pressure lamp (Riko Chemical Ind. Ltd, $\lambda > 300$ nm)[85]

Nereistoxin, 4-*N*,*N*-dimethylamino-1,2-dithiolane, is produced from cartap hydrochloride as a main product through photoreaction under UV irradiation in aqueous and methanolic solutions, and on glass and silica gel surfaces. Cartap hydrochloride is also oxidized with *N*-bromosuccinimide (NBS) to give nereistoxin.





CN(C)C(CSC(N)=
O)CSC(N)=O

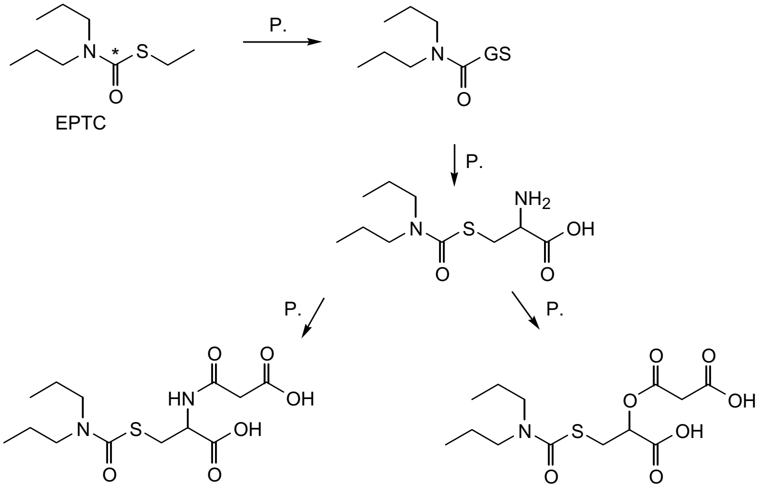
EPTC

A selective herbicide: control of weeds in a wide variety of crops including corn, cotton, and beans

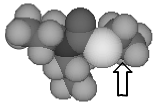
---

Plant
Corn: *Zea mays* L.; Cotton: *Gossypium hirsutum* L. Stoneville 519; soybean: *Glycin max* L. Wilkin; peanut: *Arachis hypogaea* L.[86]

A new class of xenobiotic metabolite derived from the glutathione conjugate is produced by corn, cotton, and corn cell suspension cultures treated with ^{14}C-EPTC (*S*-ethyl dipropylthiocarbamate). This metabolite is characterized as *S*-(*N*,*N*-dipropylcarbamoyl)-*O*-malonyl-3-thiolactic acid and is not detected in soybean plants or peanut cell suspension cultures. A second major metabolite of EPTC, *S*-(*N*,*N*-dipropylcarbamoyl)-*N*-malonylcysteine, is present in all tissues.



GS: glutathione residue



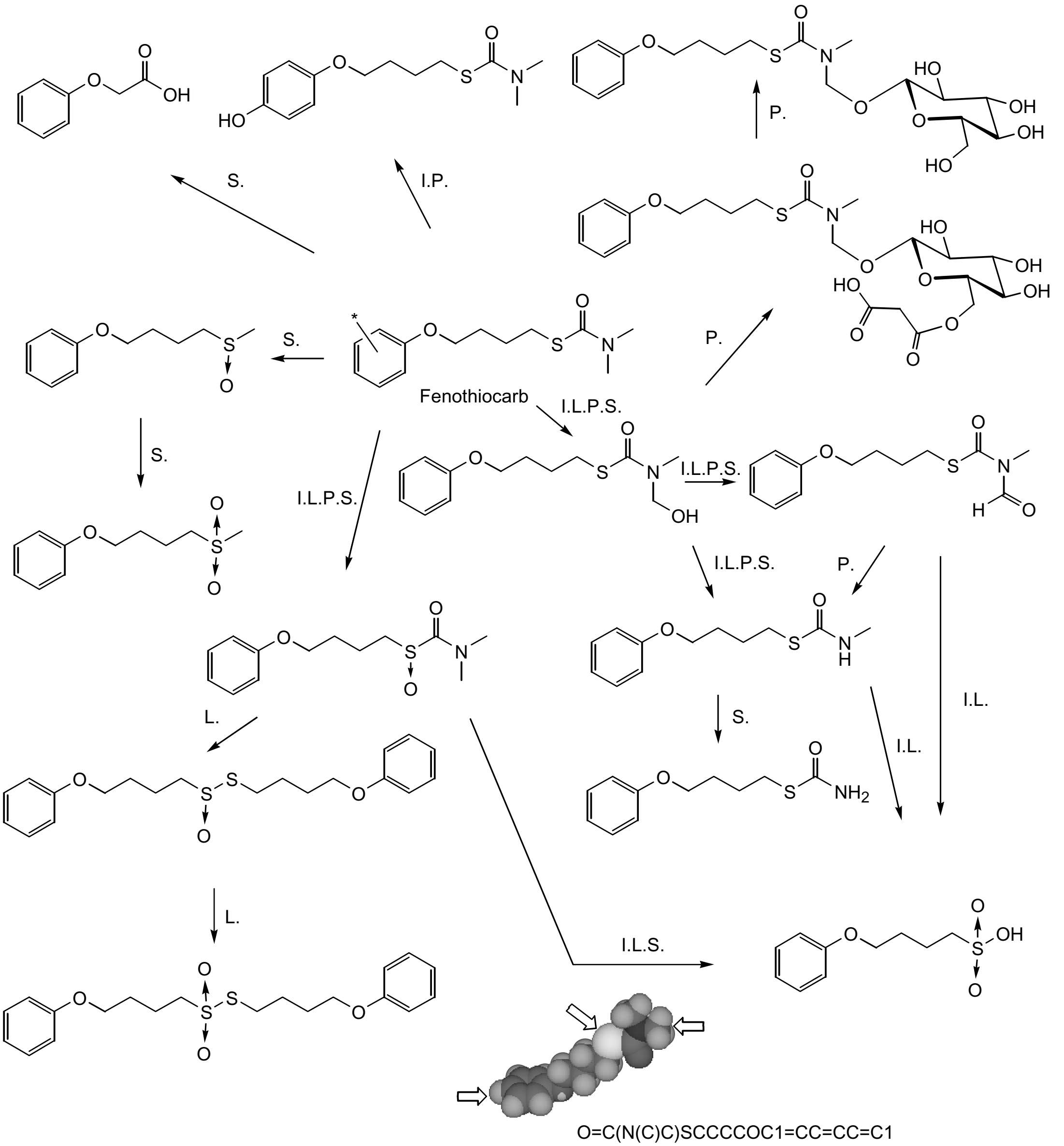
CCCN(CCC)C(SCC)=O

Fenothiocarb

An acaricide: control of citrus red mite, *Panonycus citri* (McGregor)

Insect
Citrus red mite: *Panonychus citri* McGregor[87]

When the red mite, applied with ^{14}C-fenothiocarb by the contact method, metabolizes fenothiocarb, resulting in several metabolites via the primary oxidation of the *N*-methyl moiety. The photodegradation of fenothiocarb on silica gel plate exposed to sunlight gives rise to several degradation



O=C(N(C)C)SCCCCOC1=CC=CC=C1

Light
Sunlight from the middle of September to the end of October on silica gel plates[88]

Plant
Three year-old summer orange seedlings; mandarin orange trees[89]

Soil
Okitsu sandy clay loam (pH 6.37/H_2O); Ibaraki sandy loam (pH 5.22/H_2O)[90]

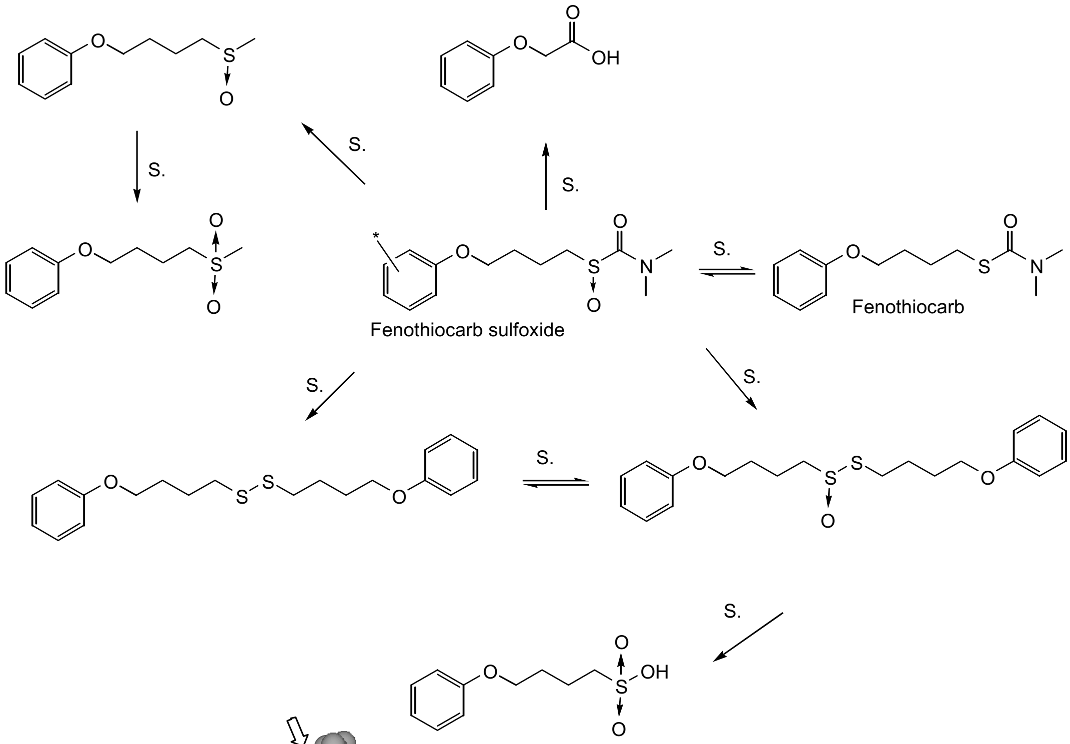
products. A primary photochemical reaction seems to be the oxidation of the sulfur atom to form its sulfoxide. Under greenhouse conditions, when fenothiocarb is applied to the citrus trees, the major metabolites identified in the leaves, rinds, and edible fruit are 6-*O*-malonyl-β-D-glucosode of *N*-hydroxymethyl fenothiocarb, *N*-formylfenothiocarb, and glucoside conjugate of phenol (not shown in the map), respectively. In soils, fenothiocarb is more rapidly degraded under upland conditions than under flooded conditions. Main degradation pathways include oxidation of the sulfur atom which results in the formation of methyl-4-phenoxybutylsulfoxide, its sulfone, and 4-phenoxybutylsulfonic acid.

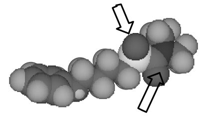
Fenothiocarb sulfoxide

A metabolite of fenothiocarb

Soil
Okitsu alluvial, sandy clay loam
(pH 6.37/H_2O); Ibaraki volcanic ash, sandy loam (pH 5.22/H_2O)[91]

Fenothiocarb sulfoxide, which is the major metabolite in soils, disappears rapidly in soils. Methyl-4-phenoxybutylsulfone, bis(4-phenoxybutyl)thiolsulfinate, methyl 4-phenoxybutylsulfoxide, and 4-phenoxybutylsulfonic acid are identified as major degradation products. Fenothiocarb, bis(4-phenoxybutyl)disulfide, and phenoxyacetic acid are identified as relatively minor products. Fenothiocarb sulfoxide disappears much faster than fenothiocarb and the fenothiocarb sulfoxide-treated soils form more bound residues.





O=C(N(C)C)[S+]([O-])C
CCCOC1=CC=CC=C1

Molinate (Ordram)

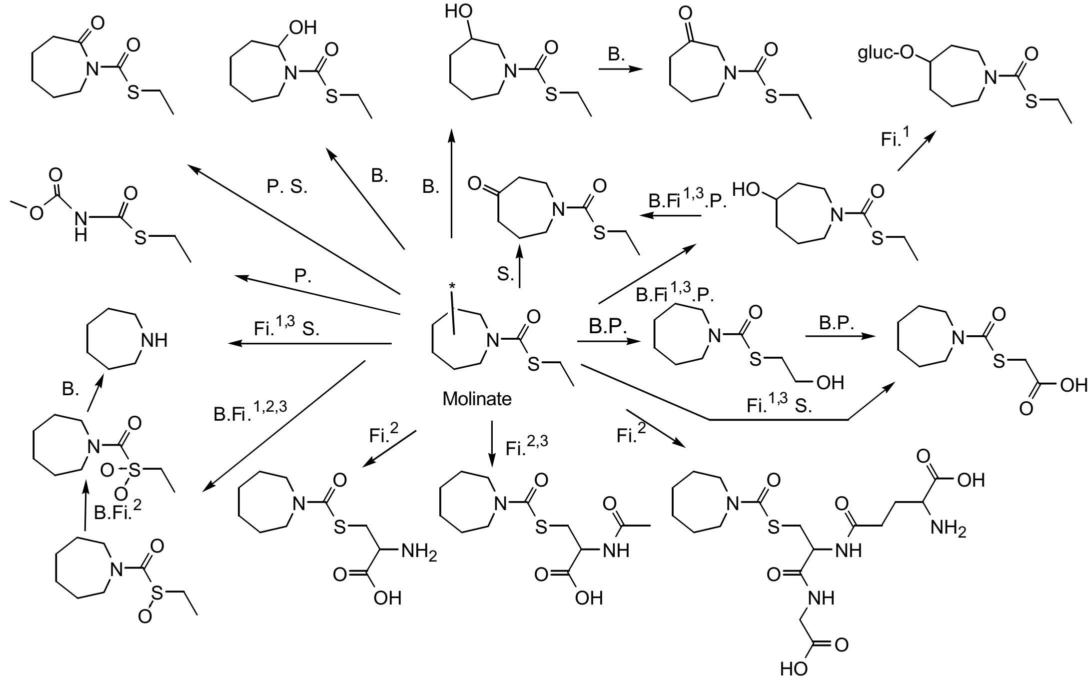
A herbicide: control of barnyard grass (*Echinochloa* spp.)

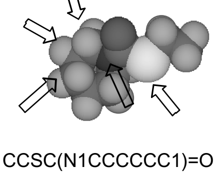
Bacterium
Soil microorganisms: *Mycobacterium* sp.; *Flavobacterium* sp.; *Streptomyces* sp.; *Fuzarium* sp.[92]

Fish¹
Juvenile white sturgeon (*Acipenser transmontanus*); common carp (*Cyprinus carpio*)[93]

Fish²
Whole blood of the juvenile white sturgeon (*Acipenser transmontanus*); common carp (*Cyprinus carpio*)[94]

Juvenile white sturgeon and common carp are exposed to ^{14}C-molinate in a flow-through metabolism system and oxidize molinate to form several products and hydrolyze or conjugate with glutathione (GSH), the sulfoxide, or sulfone. Both fish form a D-glucuronic acid conjugate. The higher toxicity of molinate in common carp may be due to greater bioconcentration, slower depuration, and less efficient metabolic deactivation. In the blood of common carp, molinate is oxidized by erythrocytes to the sulfoxide and possibly the sulfone, then conjugated with GSH or cysteine and cleaved to form mercapturic acid in both erythrocytes and plasma. Conjugation and possible hemoglobin carbamylation occur only after sulfoxidation of molinate. Molinate is distributed uniformly throughout the soil layers, and its degradation products are





CCSC(N1CCCCCC1)=O

Molinate (Ordram) (continued)

Fish[3]
Spider bass (14 month-old)[95]

Plant
Rice plant (*Oryza sativa* L. cv. Mutsunishiki)[96]

Soil
A paddy mineral soil at Nagoya Univ. Farm (OC 1.12%, pH (H_2O) 5.48, (KCl) 4.35)[97]

identified as 2-oxomolinate, 4-oxomolinate, molinate acid, and hexamethyleneimine. In rice plants, 4-hydroxymolinate, 2-oxomolinate, 4-oxomolinate, *S*-ethyl-*N*-carboxymethylthiocarbamate, molinate acid, and molinate alcohol are detected. By the soil microorganisms, oxidation of the *S*-ethyl moiety is considered to be the main pathway, and hydroxy and oxoderivatives on the azepine ring are identified.

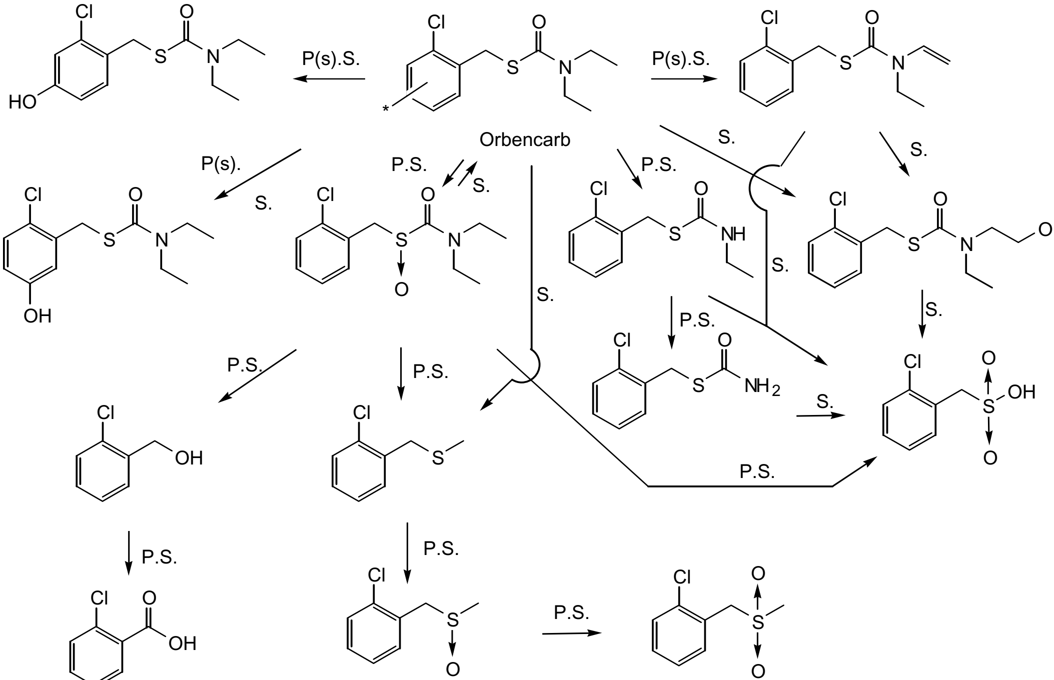
Orbencarb

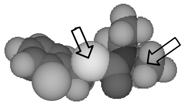
A pre-emergent herbicide: alone or together with linuron for control of weeds in upland fields

Plant
Soybean: *Glycin max* var. Enray[98] Cotton: *Gossypium* spp.[99]

Soil
Tsukuba light clay (pH 4.55/H_2O); Nagano light clay (pH 5.05/H_2O); Saga light clay (pH 6.67/H_2O)[100]

When ^{14}C-orbencarb is applied to the soil surface, plants absorb the radioactivity and orbencarb is rapidly transformed to water-soluble metabolites in the plants. The major metabolites identified are 2-chlorobenzyl alcohol and 2-chlorobenzoic acid both in free and conjugated forms, 2-chlorobenzyl sulfonic acid and methyl 2-chlorobenzylsulfone. Hydroxylated metabolites at the phenyl ring and *N*-vinyl metabolite are found in soybean plants. Orbencarb degrades more rapidly in soils under upland conditions than in soils under flooded conditions. The major degradation products in the soils are orbencarb sulfoxide, monodesmethylorbencarb, methyl-2-chlorobenzylsulfoxide, methyl-2-chlorobenzylsulfone, and 2-chlorobenzylsulfonic acid.





O=C(N(CC)CC)SC
C1=C(Cl)C=CC=C1

P(s) : soybean only

9

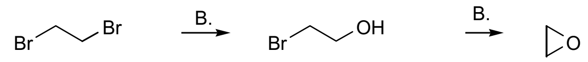
Halogenated Aliphatics

1,2-Dibromoethane

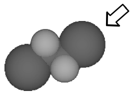
Not a pesticide

Bacterium
Mycobacterium sp. strain GP1[101]

The bacterial strain GP1 can utilize 1,2-dibromoethane as a sole carbon and energy source. The first step in 1,2-dibromoethane is catalyzed by a hydrolytic haloalkane dehalogenase and the resulting 2-bromoethanol is rapidly converted to ethylene oxide, preventing the accumulation of 2-bromoethanol and 2-bromoacetaldehyde. However, the further metabolic pathway(s) is unclear.



1,2-Dibromoethane



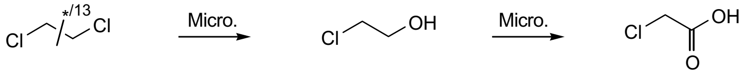
BrCCBr

1,2-Dichloroethane

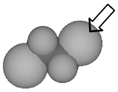
Not a pesticide

Microorganism
Soil microorganisms: *Methylosinus trichosporium* OB-3b[102]

Resting cell suspensions of the soil methylotroph *Methylosinus trichosporium* OB-3b rapidly dehalogenate 1,2-dichloroethane, resulting in the formation of chloroethanol via direct hydroxylation of one of the C–Cl bonds, and this ethanol is rapidly oxidized to yield chloroacetic acid.



1,2-Dichloroethane



ClCCCl

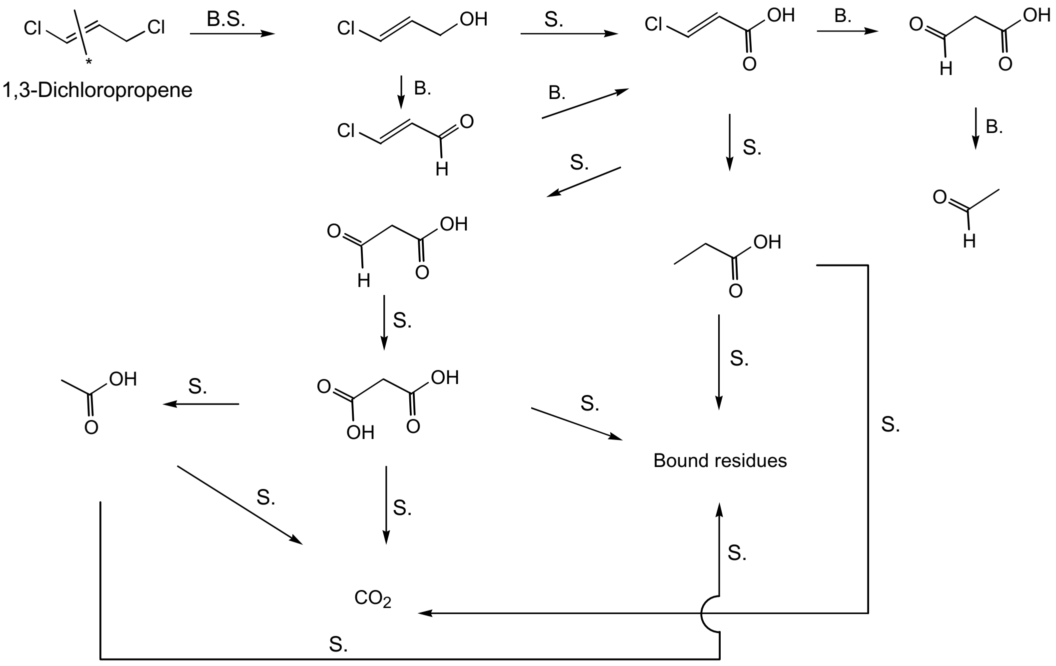
1,3-Dichloropropene

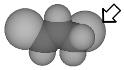
A soil fumigant

Bacterium
The gram-negative bacterium isolated from soil: *Pseudomonas cichorii 170*[103]

Soil
Fuquay loamy sand (pH 4.7), Catlin silt loam (pH 6.6), and Wahiawa silty clay[104] Horizon A (pH 4.7) and Horizon B (pH 4.1) in the dark at 25 °C.

Degradation of ^{14}C-1,3-dichloropropene in aerobic soils in the dark at 25 °C at concentration of approximately 100 μg g^{-1} results in the formation of 3-chloroallyl alchohol, 3-chloroacrylic acid, numerous minor carboxylic acid metabolites, and carbon dioxide. In addition, there is extensive incorporation of ^{14}C labeled material into the soil organic matter in the soils. By a specific bacterium (*Pseudomonas cichorii 170*) which is isolated from soil, 1,3-dichloropropene is degraded in different pathways from those of soil degradation. The terminal degradate by this bacterium is acetoaldehye which undergoes mineralization.





ClCC=CCl

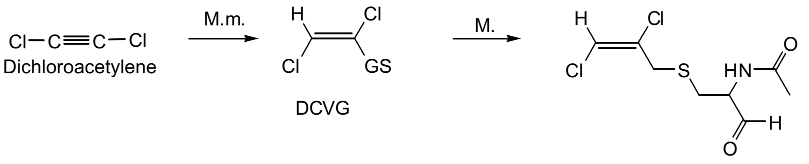
Dichloroacetylene

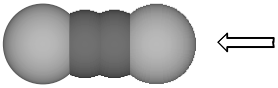
Not a pesticide: a potent nephrotoxin and nephrocarcinogen in rodents

Mammal
Male Wistar rats (200–250 g) exposed to dichloroacetylene in an exposure chamber[105]

Microsome
Liver and kidney microsomes for male Wistar rats (200–250 g)[105]

By the incubation of dichloroacetylene with rat liver and kidney subcellular fractions, the formation of *S*-(1,2-dichlorovinyl)glutathione (DCVG) is observed, and *N*-acetyl-*S*-(1,2-dichlorovinyl)-L-cysteine is identified as a urinary metabolite in rats.





ClC#CCl

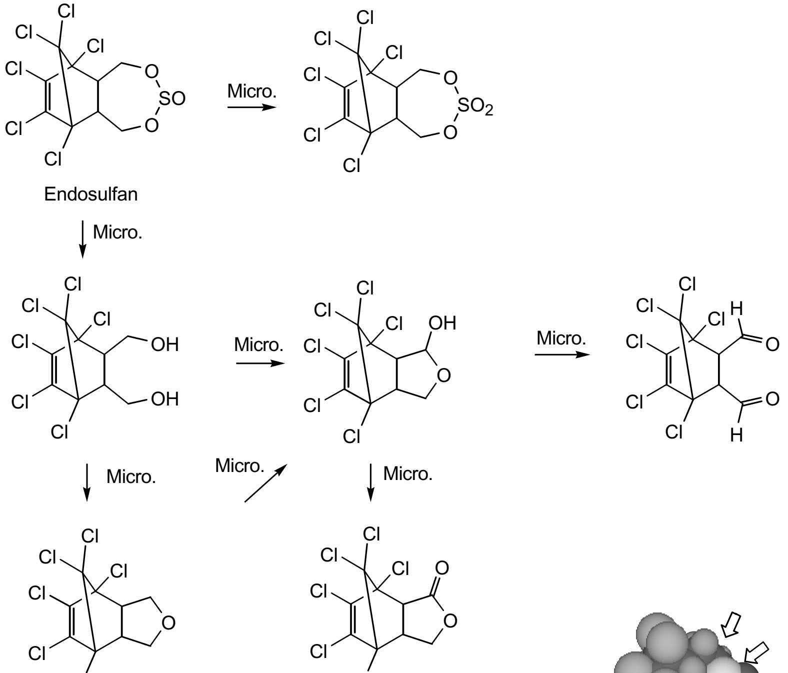
GS: glutathione residue

Endosulfan

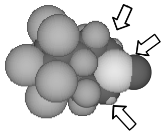
An insecticide

Microorganism
Phanerochaete chrysosporium BU-1[106]

When endosulfan is incubated with microorganisms, endosulfan is extensively degraded in nitrogen-deficient, carbon-deficient, and nitrogen-rich cultures of *Phanerochaete chrysosporium* and is primarily oxidized to endosulfan sulfate, which is a terminal end product, or hydrolyzed to the non-sulfur-containing metabolites. An initial hydrolysis of endosulfan results in the formation of the intermediate metabolite or endosulfan diol, which further undergoes oxidation to yield endosulfan hydroxyether followed by the formation of endosulfan lactone or tentatively identified endosulfan dialdehyde.



Endosulfan



ClC1(Cl)C2(Cl)C3C(COS
(OC3)=O)C1(Cl)C(Cl)=C2Cl

Hexachloro-1,3-butadiene

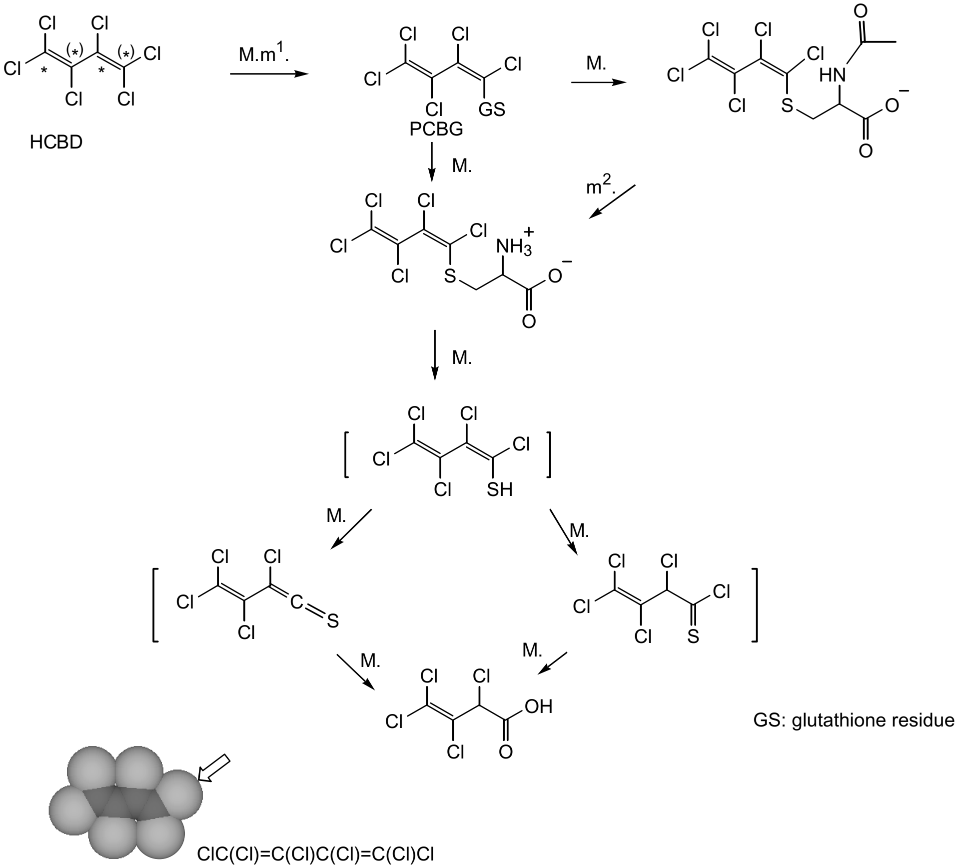
Not a pesticide: a strong and specific nephrotoxin in rats and mice

Mammal
Female and male NMRI mice (21–24 g)[107]

Microsome[1]
Microsomal, cytosolic, and mitochondrial fractions of liver and kidneys of female and male NMRI mice (25–30 g)[108]

Microsome[2]
Renal cytosol of male and female Alderley Park (Wistar-derived) rats[109]

In the presence of glutathione (GSH), mouse liver microsomes and cytosol transform ^{14}C-hexachloro-1,3-butadiene (HCBD) to *S*-(pentachlorobutadienyl)glutathione (PCBG). PCBG formation in subcellular fractions from a mouse kidney is very limited. After an oral dose of HCBD to mice, PCBG in feces, and *S*-(pentachlorobutadienyl)-*L*-cysteine, *N*-acetyl-*S*-(pentachlorobutadienyl)-*L*-cysteine, and 1,1,2,3-tetrachlorobutenoic acid in the urine are identified as the metabolites.



GS: glutathione residue

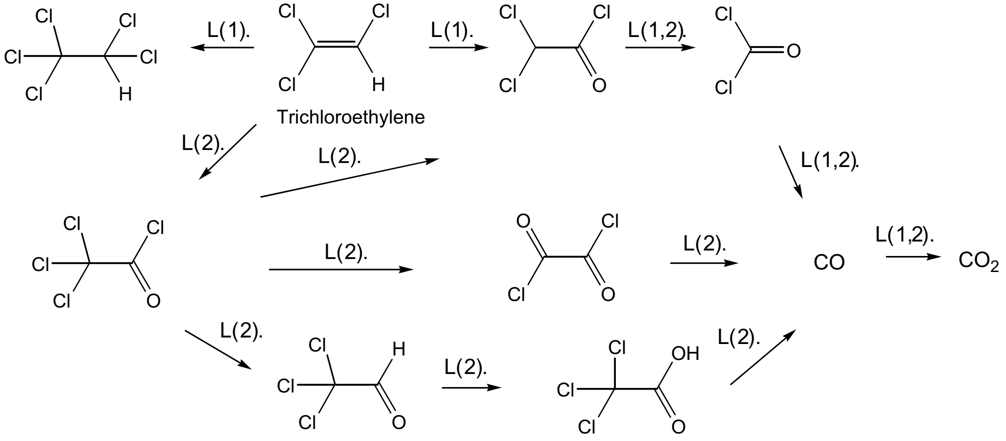
ClC(Cl)=C(Cl)C(Cl)=C(Cl)Cl

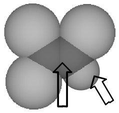
Trichloroethylene

Not a pesticide

Light
Photoirradiation: 5 mW of near UV light (350−450 nm) (1) in the presence of O_2 and Degussa P-25 powder; (2) in the presence of TiO_2 photocatalyst consisting of highly dispersed TiO_2 (roughly 25% of monolayer) on the surface of transparent porous Vycor glass (PVG)[110]

From the photooxidation reaction medium (1) of trichloroethylene, the formation of dichloroacetyl chloride, CO, phosgene, and pentachloroethane and their conversion to the final product, CO_2, are identified. By the second TiO_2 photocatalyst reaction (2), trichloroacetaldehyde, dichloroacetyl chloride, CO, and phosgene with the new identified intermediates oxalyl chloride, trichloroacetyl chloride, and trichloroacetic acid are observed.





ClC(Cl)=C([H])Cl

10

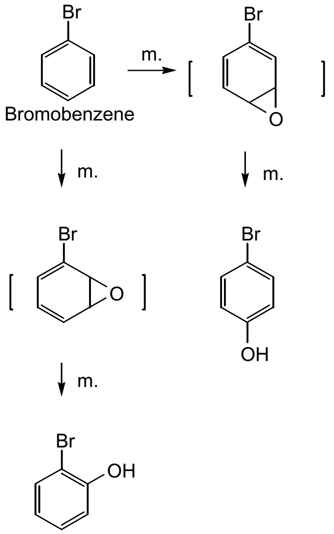
Halogenated Aromatics

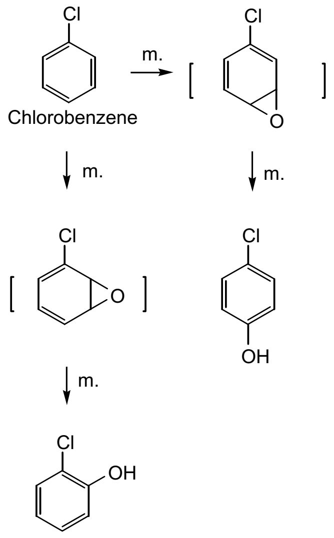
Bromobenzene and Chlorobenzene

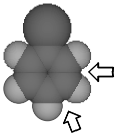
Not pesticides

Microsome
Liver microsomes: male B6C3F1 mice (20–30 g); 15 year-old female and 26 year-old male humans[111]

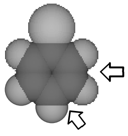
Bromobenzene and chlorobenzene are metabolized by human and mouse hepatic microsomes to two different epoxide intermediates, which rearrange to form either *o*- or *p*-bromo- and *o*- or *p*-chlorophenols, respectively. Humans preferentially metabolize halobenzenes through the hepatotoxic 3,4-epoxide pathway, suggesting that humans may be more susceptible than mice to halobenzene-induced hepatotoxicity.







BrC1=CC=CC=C1



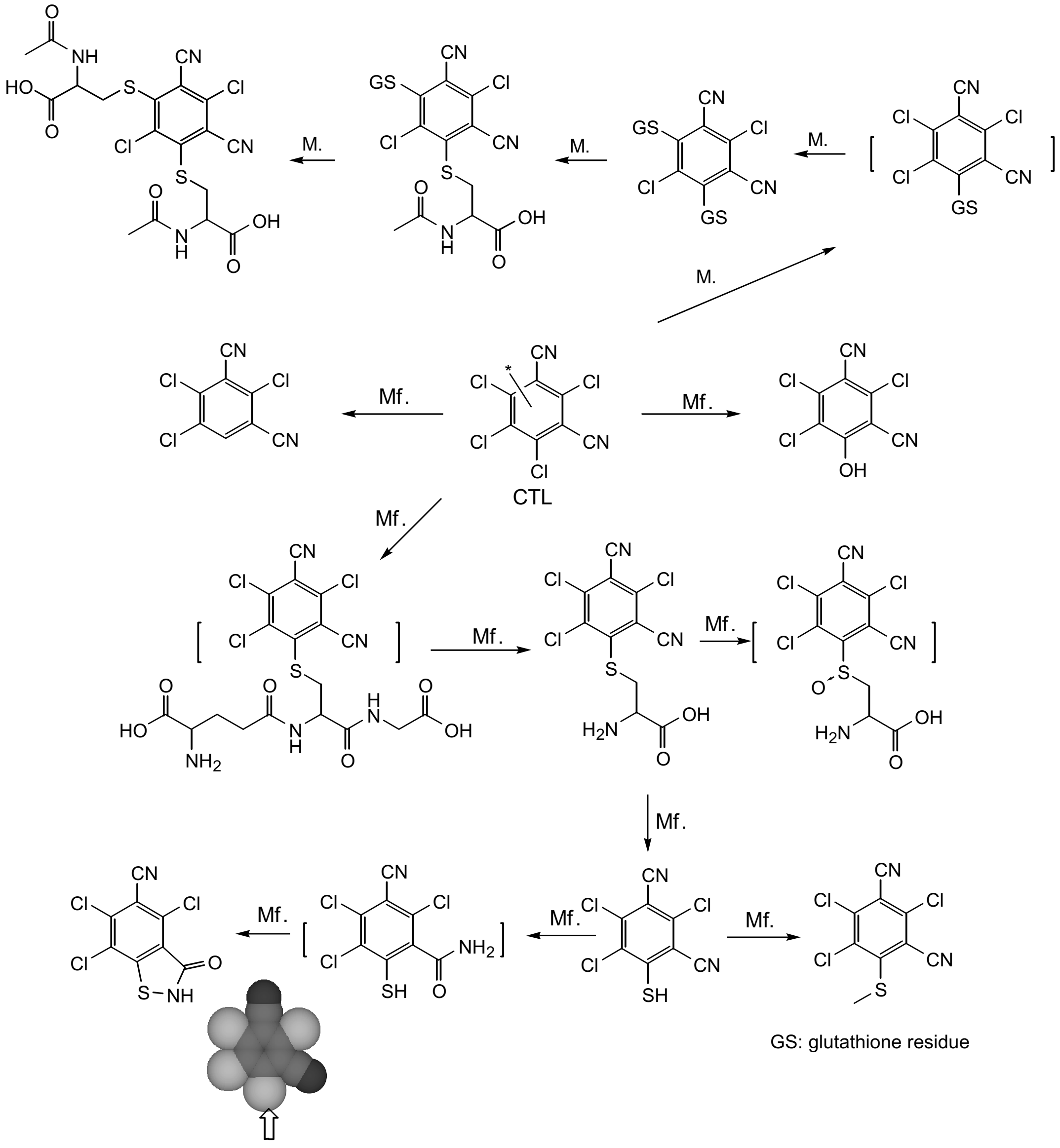
ClC1=CC=CC=C1

Chlorothalonil (Daconil)

A fungicide with broad spectra and contact activity

Mammal
Male and female Sprague–Dawley rats (200–300 g)[112]

By *in vitro* incubation of ^{14}C-chlorothalonil (CTL) with rat stomach, duodenum, and cecum contents, with dog stomach, duodenum, and colon contents, and with human feces and stomach contents, transformation of CTL mostly occurs in rat cecum contents, dog colon



ClC1=C(C(Cl)=C(C(Cl)=C1C#N)Cl)C#N

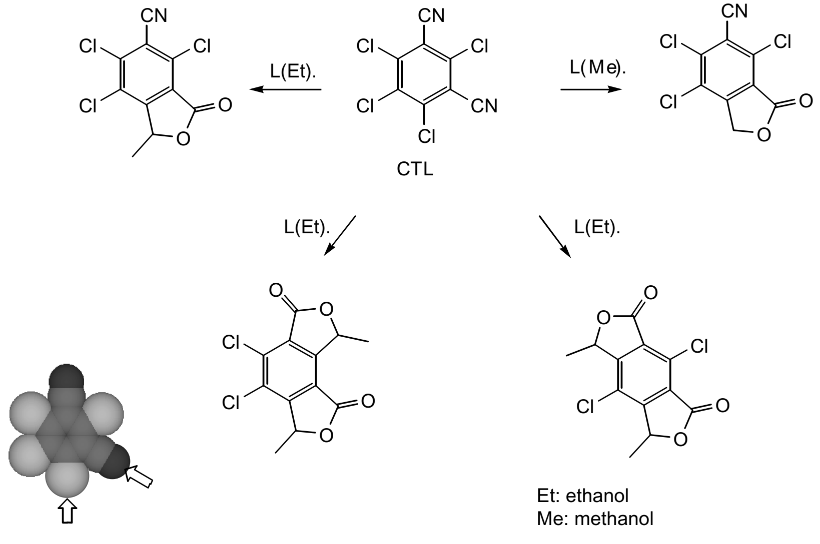
Chlorothalonil (Daconil) (continued)

Microflora
Obtained from the cecum of 7 week-old male Sprague–Dawley rats; digestive contents (stomach and duodenum) of three male 6 month-old beagle dogs; stomach content and feces of an informed consenting male adult human[113]

Light
Irradiation with a 16 W UV lamp (Applied Photophysics, London) in ethanol and methanol[114]

contents, and human feces, in which unchanged CTL accounts for 46.7, 29.7, and 22.6% of applied radioactivity, respectively. In those incubations, the identified metabolites are 2,5,6-trichloro-4-methylthioisophthalonitrile, 2,5,6-trichloro-4-thioisophthalonitrile, 3-thia-1-cyano-2,5,6-trichloroisoindolinone, 2,5,6-trichloro-4-hydroxyisophthalonitrile, and 2,5,6-trichloroisophthalonitrile. In rats, CTL is transformed to 4,6-bis(*N*-acetylcystein-*S*-yl)-2,5-dichloroisophthalonitrile.

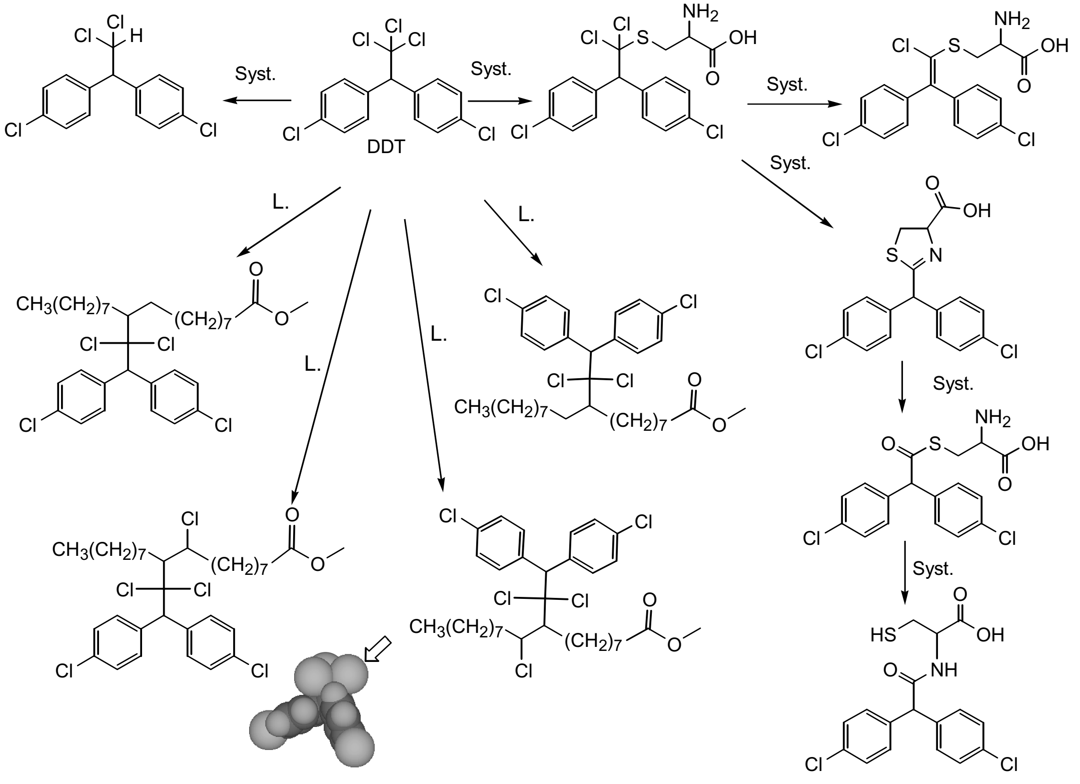
The photolysis of CTL solutions in alcohols (ethanol and methanol separately) with exposure to UV irradiation yields 4,5,7-trichloro-6-cyano-3-methylbenzo-γ-lactone and dichlorobenzo-bis-γ-lactone derivatives as major degradation products in ethanol. In methanol, 4,5,7-trichloro-6-cyanobenzo-γ-lactone is the only photoproduct detected.



Light
A mixture of DDT and methyl oleate irradiated in a quartz tube using a 150 W high-pressure mercury lamp (TQ 150 Hanau Quarzlampen GmbH)[115]

System
An homogeneous solution of the solvent (0.05M NH_4HCO_3, pH 7.7/ethanol, 5 : 6) contained 0.12 mM DDT, 0.034 mM hemin, and 12 mM cysteine; protein concentrations: 1 μM, 10 μM, 100 μM[116]

Upon UV irradiation with methyl oleate, DDT is extensively added to the carbon–carbon double bond of methyloleate via radical mechanisms. Besides chlorinated stearic acids, several addition products are formed, offering new possibilities to produce bound residues in plants. A mixture of hemin and excess cysteine (the hemin–cysteine model system) is able to degrade DDT partially and the major degradation products are three water-soluble, non-toxic conjugates of DDT metabolites with cysteine which lose two or three of the five chlorine atoms of DDT. In the presence of a designed 24-residue polypeptide or β-casein, two DDT-binding proteins, an additional fourfold increase in the rate of DDT degradation is observed. Although the concentrations of DDT and cysteine occurring in an organism would be expected



ClC(C=C1)=CC=C1C(C2=CC=C
(C=C2)Cl)C(SCC(N)C(O)=O)(Cl)Cl

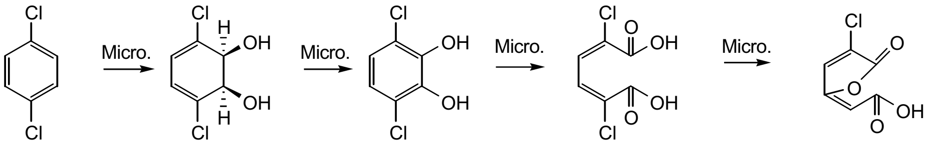
to be lower than those in the experiments described, the formation of water-soluble conjugates of DDT with cysteine (and other amino acids) could also play a role in metabolism and excretion of DDT *in vivo*.

1,4-Dichlorobenzene

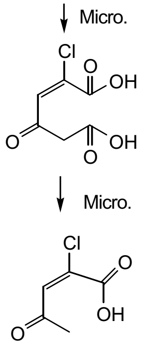
Not a pesticide

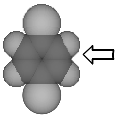
Microorganism
Xanthobacter flavus 14p1 isolated from sludge of the river Mulde in Germany[117]

1,4-Dichlorobenzene undergoes degradation by the *Xanthobacter flavus* 14p1 isolated from river sludge by selective enrichment with 1,4-dichlorobenzene, resulting in the degradation products 3,6-dichloro-*cis*-1,2-dihydroxycyclohexa-3,5-diene and 3,6-dichlorocatechol. 2,5-Dichloromuconic acid and 2-chloromaleylacetic acid, as well as the decarboxylation product 2-chloroacetoacrylic acid, are identified after enzymatic conversion of 3,6-dichlorocatechol.



1,4-Dichlorobenzene





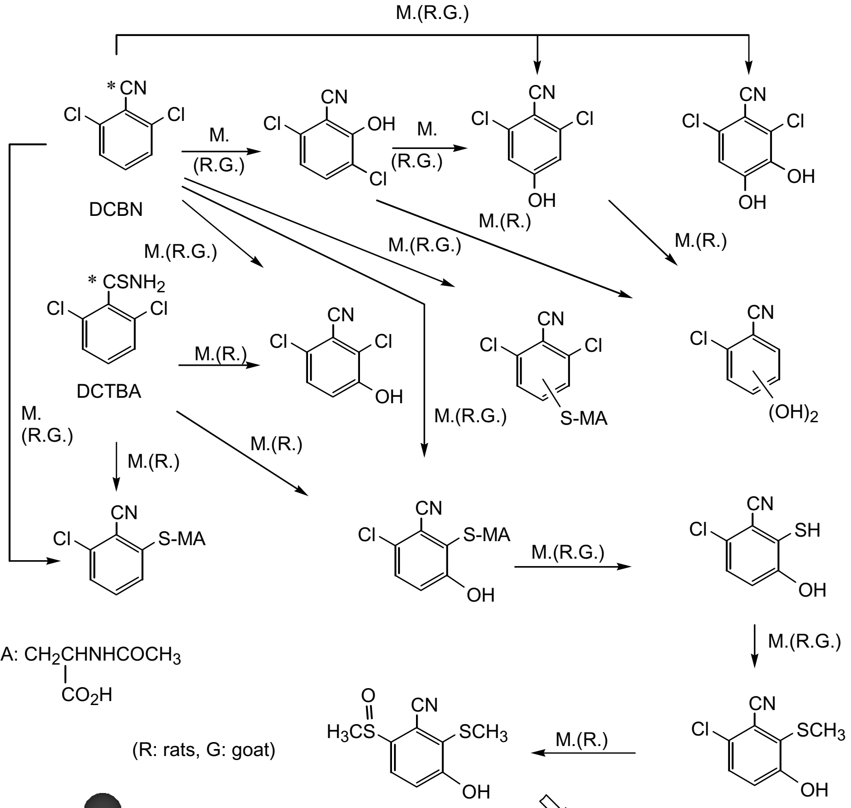
ClC1=CC=C(Cl)C=C1

2,6-Dichlorobenzonitrile (DCBN) and 2,6-Dichlorothiobenzamide (DCTBA)

Not pesticides

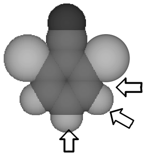
Mammal
Male Sprague–Dawley rats (280–300 g); goats (a lactating goat, 69 kg; a female goat, 48.8 kg)[118]

Twelve metabolites are isolated from either urine or bile from either rats (11 metabolites) or goats (seven metabolites) given single oral doses of ^{14}C-labeled 2,6-dichlorobenzonitrile (DCBN). Five of these metabolites are also excreted in urine from rats dosed orally with 2,6-dichlorothiobenzamide (DCTBA) which is an acid amide analog. All metabolites from either

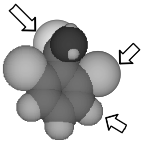


MA: $CH_2CHNHCOCH_3$ with CO_2H on the CH

(R: rats, G: goat)



ClC1=CC=CC(Cl)=C1C#N



ClC1=CC=CC(Cl)=C1C(N)=S

2,6-Dichlorobenzonitrile (DCBN) and 2,6-Dichlorothiobenzamide (DCTBA)

(continued)

DCBN or DCTBA are benzonitriles with the following ring substituents: Cl_2, OH (three isomers); Cl_2, $(OH)_2$; Cl, $(OH)_2$; Cl, OH, SH; Cl, OH, SCH_3; $SOCH_3$, OH; Cl_2, *S*-(*N*-acetyl)cysteine; Cl, *S*-(*N*-acetyl)cysteine; Cl, OH, *S*-(*N*-acetyl)cysteine.

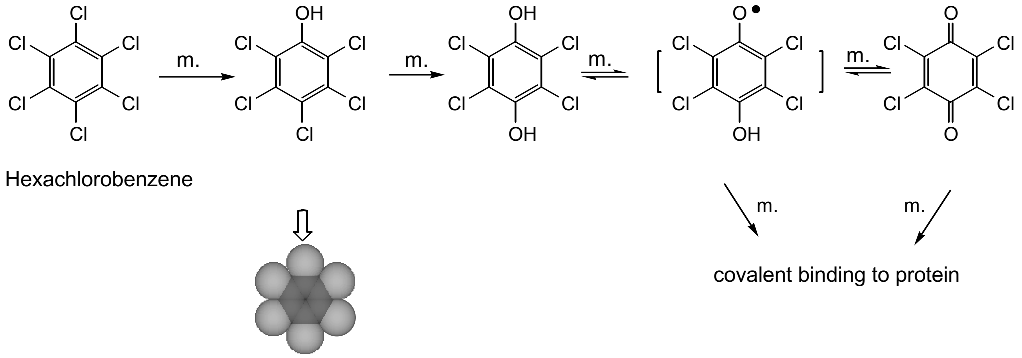
The thiobenzamide moiety of DCTBA is converted to the nitrile in all extracted urinary metabolites. No hydrolysis of the nitrile in DCBN to either amide or an acid is detected. Urine is the major route for excretion; however, enterohepatic circulation occurs.

Hexachlorobenzene

A fungicide

Microsome
Liver microsomes from 12 week-old male Wistar rats[119]

With the incubation of rat liver microsomes, hexachlorobenzene is metabolized to give pentachlorophenol and tetrachlorohydroquinone, and, in addition, a considerable amount of covalent binding to protein is detected (250 pM pentachlorophenol, 17 pM tetrachlorohydroquinone, and 11 pM tetrachlorobenzoquinone covalent binding in an incubation containing 50 μM hexachlorobenzene).



ClC1=C(Cl)C(Cl)=
C(Cl)C(Cl)=C1Cl

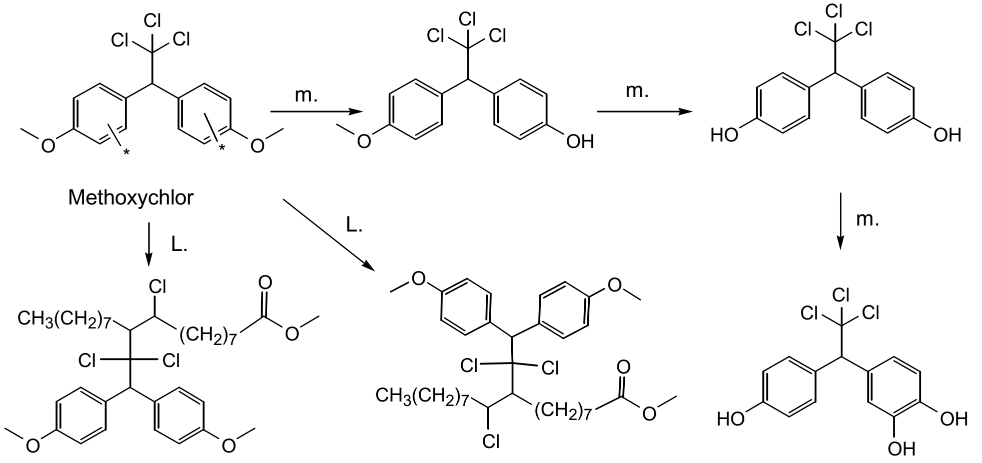
Methoxychlor

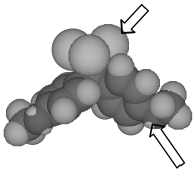
An insecticide

Light
A mixture of methoxychlor and methyl oleate irradiated in a quartz tube using a 150 W high-pressure mercury lamp (TQ 150 Hanau Quarzlampen GmbH)[120]

Microsome
Microsomal preparation of liver of male Sprague–Dawley CD rats (90–100 g) from Charles River Breeding Laboratory; human liver from eight kidney transplant donors[121]

Upon UV irradiation with methyl oleate, methoxychlor is extensively added to the carbon–carbon double bond of methyl oleate via radical mechanisms. Besides chlorinated stearic acids, several addition products are formed, offering new possibilities to produce bound residues in plants. The incubation of methoxychlor with liver microsomes from untreated and phenobarbital-treated rats and donors, in the presence of NADPH, yields three phenolic metabolites: monodemethylated and didemethylated methoxychlor and its hydroxylated (trihydroxy) methoxychlor. The metabolic route of methoxychlor by monooxygenases involves sequential demethylations to the dihydroxy derivative and a subsequent ring hydroxylation.





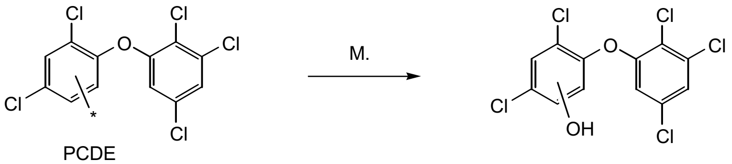
COC1=CC=C(C(C(Cl)(Cl)Cl)
C2=CC=C(OC)C=C2)C=C1

2,2′,4,4′,5-Pentachlorodiphenyl ether (PCDE)

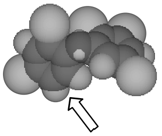
Not a pesticide

Mammal
Male Sprague−Dawley rats from Charles River Laboratory (300−350 g)[122]

When rats are given ^{14}C-2,2′,4,4′,5-pentachlorodiphenyl ether (PCDE) orally, a total of 55% and 1.3% of administered dose is excreted in feces and urine, respectively, in 7 days. More than 64% of the fecal radioactivity is due to unchanged PCDE, while hydroxylated PCDE accounts for 23%. Hydroxylation may occur on the phenyl ring bearing two chlorine substituents.



PCDE



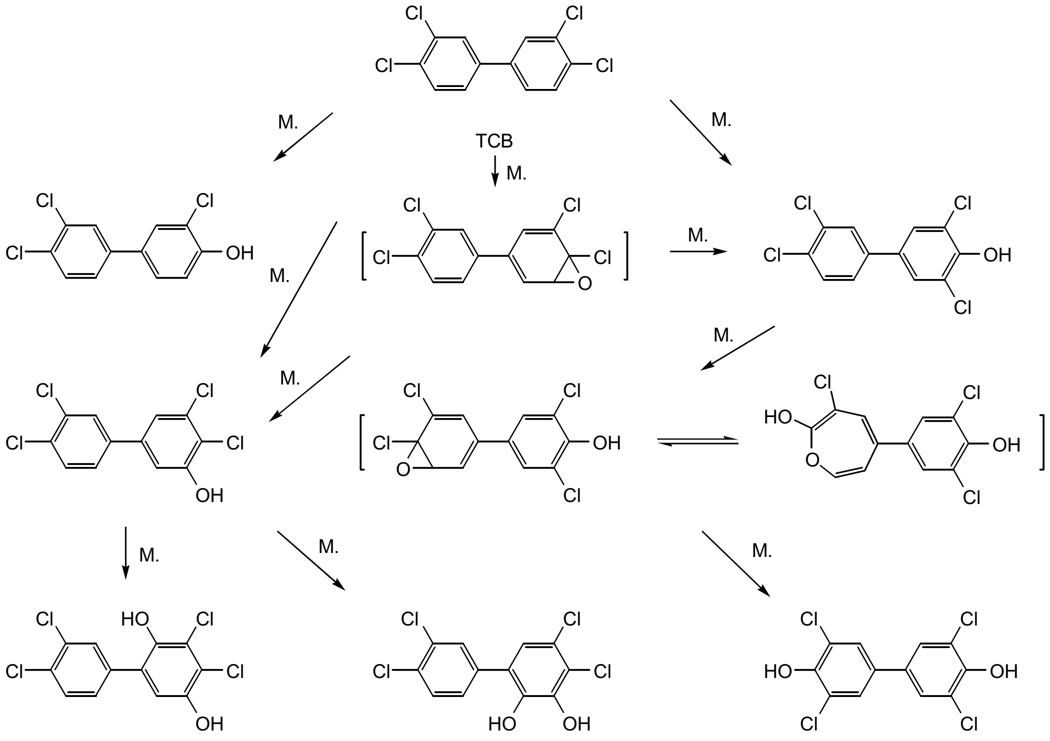
ClC1=C(OC2=CC(Cl)=CC(Cl)=C2Cl)C=CC(Cl)=C1

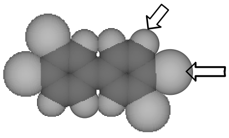
3,4,3′,4′-Tetrachlorobiphenyl

Not a pesticide

Mammal
Ten male Wistar rats (ca 150 g)[123]

When 3,4,3′,4′-tetrachlorobiphenyl (TCB) is orally administered to rats, seven hydroxylated metabolites are identified in the rat feces. The major metabolites are 5-hydroxy-3,4,3′,4′-TCB and 4-hydroxy-3,5,3′,4′-TCB. One further metabolite isolated is an oxepin, existing in a state of equilibration with the 4′,5′-epoxide of the major metabolite, 4-hydroxy-3,5,3′,4′-TCB.





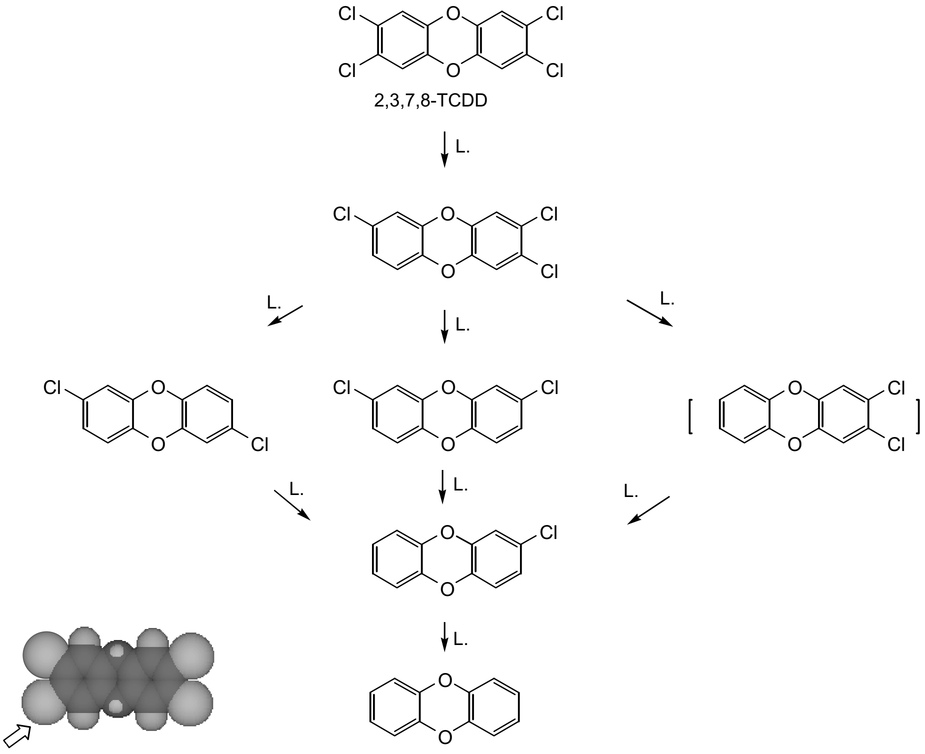
ClC1=C(Cl)C=CC(C2=CC
=C(Cl)C(Cl)=C2)=C1

2,3,7,8-, 1,3,6,8- and 1,2,3,4-Tetrachlorodibenzo-*p*-dioxins (TCDDS)

Not pesticides

Light
A JASCO CRM-FA xenon lamp irradiator at 252.6 nm[124]

The photodegradation of 2,3,7,8-, 1,3,6,8-, and 1,2,3,4-tetrachlorodibenzo-*p*-dioxins (TCDDs) under xenon lamp irradiation results in only reductive dechlorination. From 2,3,7,8-TCDD, 2,3,7-trichlorodibenzo-*p*-dioxin (2,3,7-TrDCC), 2,7- and 2,8-dichlorodibenzo-*p*-dioxins (2,7- and 2,8-DCDD), 2-monochlorodibenzo-*p*-dioxin (2-MCDD), and dibenzo-*p*-dioxin (DD) are identified. From 1,3,6,8-TCDD, the six degradation products 1,3,6-TrCDD, 1,3-DCDD, 1,6-DCDD, 1-MCDD, 2-MCDD, and DD are identified, while the nine degradation products 1,2,3-TrCDD,

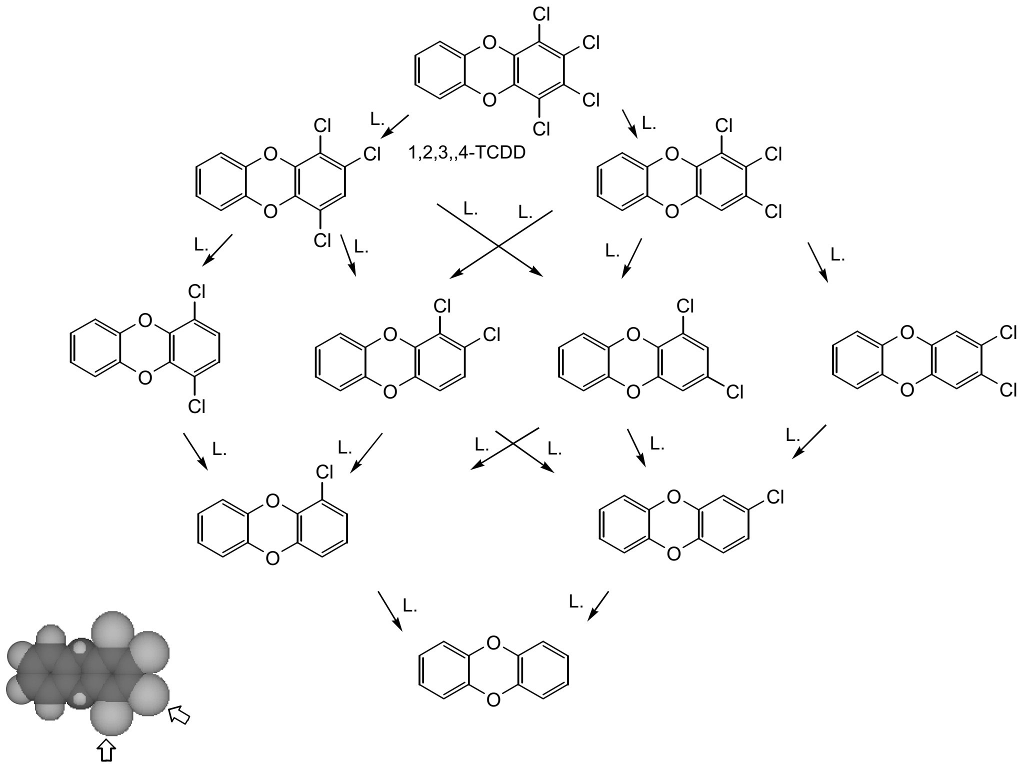


ClC1=C(Cl)C=C(OC(C=C(Cl)C(Cl)=C3)=C3O2)C2=C1

2,3,7,8-, 1,3,6,8- and 1,2,3,4-Tetrachlorodibenzo-*p*-dioxins (TCDDS)

(continued)

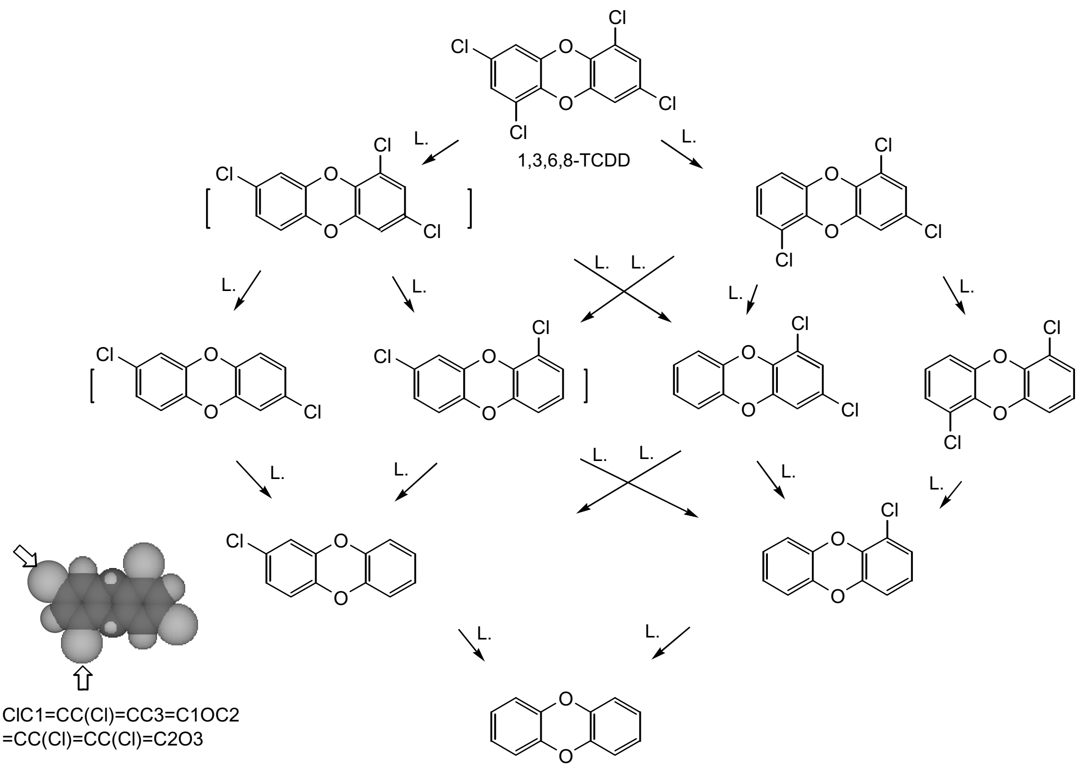
1,2,4-TrCDD, 1,2-DCDD, 1,3-DCDD, 1,4-DCDD, 2,3-DCDD, 1-MCDD, 2-MCDD, and DD are detected from 1,2,3,4-TCDD. In the photodegradation reaction, chlorine atoms in the 2-, 3-, 7- and/or 8-positions are dechlorinated more rapidly than those in the other positions.



ClC3=C(Cl)C2=C(C(Cl)=
C3Cl)OC1=CC=CC=C1O2

2,3,7,8-, 1,3,6,8- and 1,2,3,4- Tetrachlorodibenzo-*p*-dioxins (TCDDS)

(continued)



ClC1=CC(Cl)=CC3=C1OC2
=CC(Cl)=CC(Cl)=C2O3

11

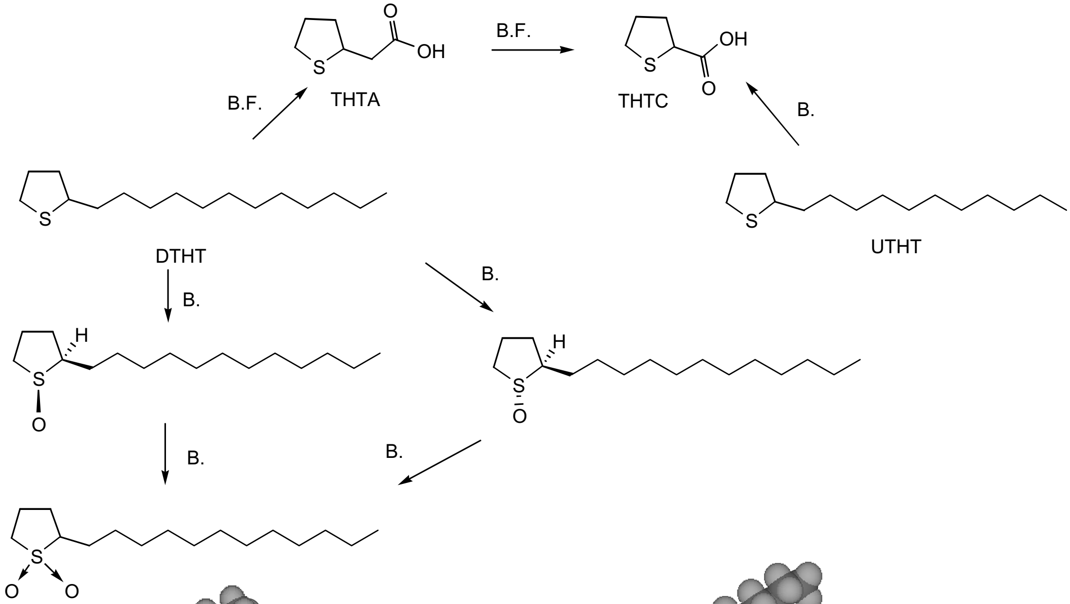
Five-membered Heterocycles

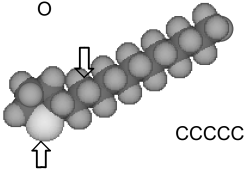
2-*N*-Dodecyltetrahydrothiophene (DTHT) and 2-*N*-Undecyltetrahydrothiophene (UTHT)

Not pesticides

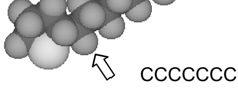
Bacteria/Fungi
Bacterial isolates/fungal isolates:
Paecilomyces sp.; *Beauverai* sp.; *Penicilium* sp.; *Verticillium* sp.[125]

Although *n*-alkyl-substituted tetrahydrothiophenes are found in non-biodegraded petroleum, they are not found in petroleums that have undergone biodegradation in their reservoirs. These observations suggest that this group of compounds with an alkyl chain length from approximately C_{10} to at least C_{30} is biodegradable. By five gram-positive, *n*-alkane-degrading bacterial isolates, the alkyl side chains of 2-*n*-undecyltetrahydrothiophene (UTHT) and 2-*n*-dodecyltetrahydrothiophene (DTHT) are oxidized, and the major intermediates found in the cultures are 2-*n*-tetrahydrothiophenecarboxylic acid (THTC) and





CCCCCCCCCCCCC1SCCC1



CCCCCCCCCCCC1CCCS1

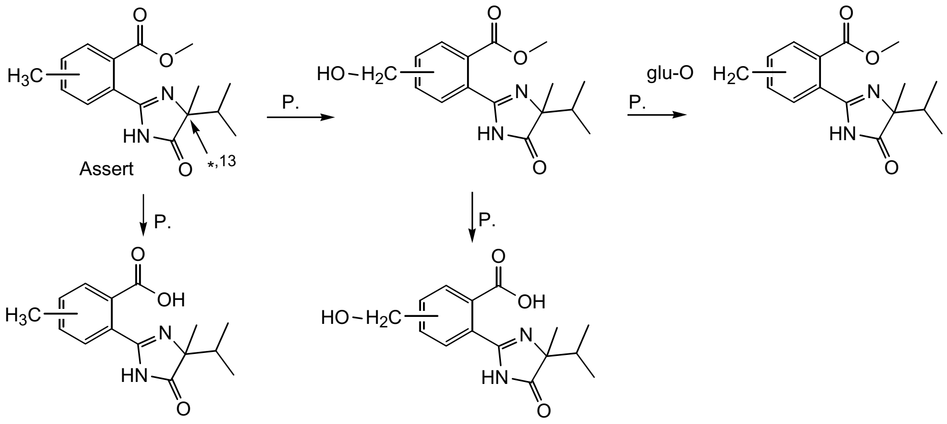
2-tetrahydrothiopheneacetic acid (THTA), respectively. By four fungi, DTHT is degraded to yield both THTA and THTC. By 28 day-old bacterial and fungal cultural incubation, THTC and THTA are metabolized further to unidentified products.

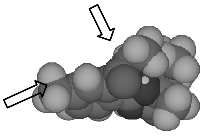
Assert (isomeric mixture of methyl 6-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-*meta*-toluate and methyl 2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-*para*-toluate)

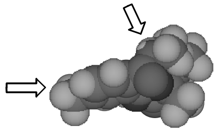
A herbicide: control of wild oat (*Avena fatua*), slender foxtail (*Alopecurus myosuroides*), and other weedy grasses in wheat, barley, and maize

Plant
Wheat; corn; wild oat[126]

The hydrolytic activation of the individual esters in the mixture of assert herbicide to yield the free acids occurs only in wild oat, with the more herbicidal *meta* isomer producing a two- to threefold greater concentration of the free acid than the *para* isomer. Detoxification in corn and wheat occurs by rapid oxidation of the aryl methyl group to the corresponding alcohol, followed by the glucose conjugation.




meta-Toluate


para-Toluate

O=C(C1=CC(C)=CC=C1C
(NC2=O)=NC2(C(C)C)C)OC

O=C(C1=CC=C(C)C=C1C
(NC2=O)=NC2(C(C)C)C)OC

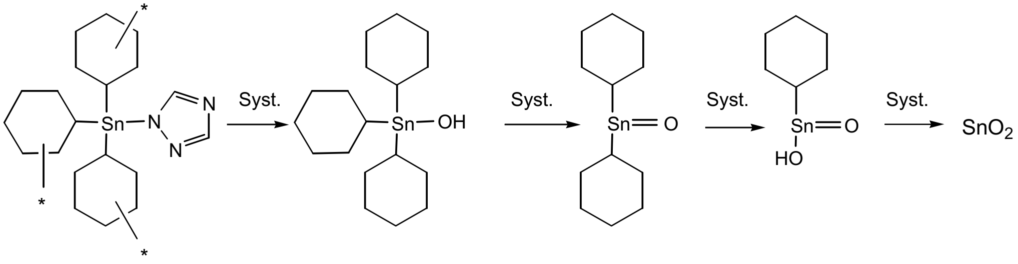
Azocyclotin

An acaricide with contact effects

System

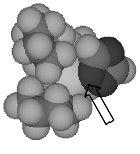
The microcosms consisted of a cubic water column of approximately 700 L and a sediment layer of 15–20 cm with an additional undisturbed sediment core of 60 cm diameter and 60 cm depth (sediment particle size: sand = 98%, silt = 1%, clay = 1%, pH 8.8, organic carbon 0.6%, water pH 7.5, organic carbon 16.4 mg L^{-1}) (see the text for more details)[127]

The sedimentation of particles coated with the pesticide is relatively fast. Shortly after application of ^{14}C-azocyclotin, distribution, solubilizing, and metabolism in fresh water microcosms begin, and azocyclotin is quickly hydrolyzed to cyhexatin (tricyclohexyltin hydroxide) by splitting of the triazole residue, and, according to the solubility of cyhexatin, cyhexatin is mainly absorbed to sediment and the layer of biota in direct contact with the sediment and further undergoes successive metabolism to result in dicyclohexyltin oxide and cyclohexyltin acid.



Azocyclotin

Cyhexatin



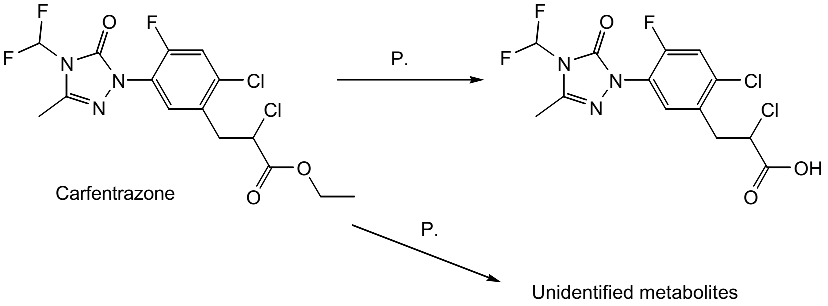
O[Sn](C2CCCCC2)(C3CC
CCC3)C1CCCCC1

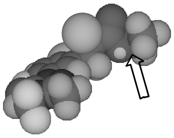
Carfentrazone

A peroxidizing herbicide

Plant
Fourteen day-old greenhouse-grown soybean: *Glycine max* (L.) Merr. cv. Hutcheson; the weeds of ivyleaf morning glory: *Ipomea hederacea* (L.) Jacq.; velvetleaf (*Abutilon theophrasti* Medic.)[128]

^{14}C-Carfentrazone is more readily absorbed by the foliage of soybean than by weeds, with 56, 7, and 10% of the applied radioactivity recovered from the foliage of soybean, ivyleaf morning glory, and velvetleaf, respectively. Soybean metabolizes carfentrazone more rapidly than weeds, with 28% of the parent compound remaining in the treated tissue of soybean and 48 and 67% in ivyleaf morning glory and velvetleaf, respectively. All species accumulate similar amounts of the free acid derivative of carfentrazone which is the only identified metabolite. Since both carfentrazone and the free acid are potent inhibitors of protoporphyrinogen oxidase, the result indicates that the tolerance of soybean to carfentrazone may be attributed to its better ability to metabolize carfentrazone to unidentified metabolites, relative to weeds.





FC(F)N1C(C)=NN(C2=CC(CC(Cl)C(O
CC)=O)=C(Cl)C=C2F)C1=O

Clomazone (FMC57020)

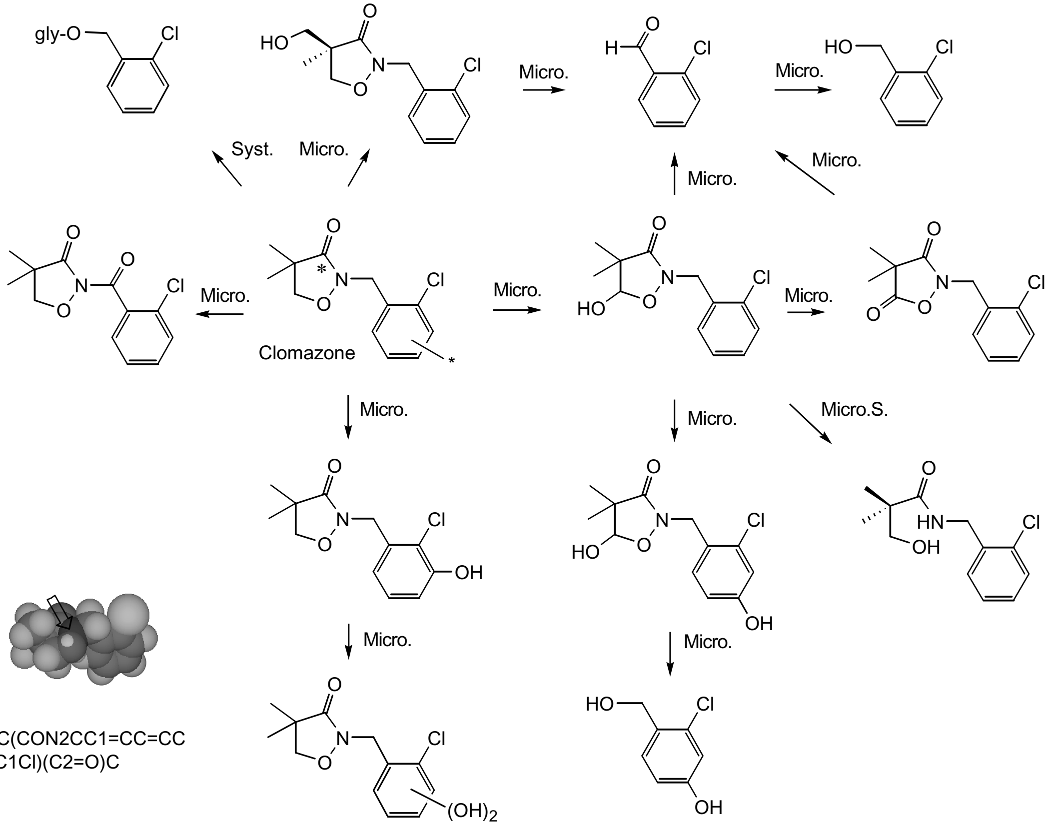
A soil-applied herbicide: control of many grass and broadleaf weeds in soybeans, cotton, and some vegetable crops

Microorganism
Aspergillus niger (UI-X172);
Cunninghamella echinulata (NRRL-3655)[129]

Soil
Sandy loam and silt loam soils[130]

System
Tolerant soybean: *Glycin max* (L.) Merr. cv. Crosby; susceptible cotton: *Gossypium hirsutum* (L.) cv. Stoneville 825[131]

By the preparative incubation of clomazone with microorganisms that have the ability to metabolize clomazone, the metabolites are identified via major biotransformation reactions which involve hydroxylation at the 5-methylene carbon and one of the 3-methyl groups of the isoxazolidone ring and at the 3′-position of the phenyl ring. Minor metabolic routes include dihydroxylation on the phenyl ring, cleavage of the isoxazolinone ring, or complete removal of the isoxazolinone ring to form 2-chlorobenzyl alcohol. Under aerobic conditions of soils, degradation of clomazone proceeds primarily by CO_2 evolution and the formation of bound soil residues. In flooded soils, clomazone is found rapidly to degrade via the formation of the reductive product



CC(CON2CC1=CC=CC=C1Cl)(C2=O)C

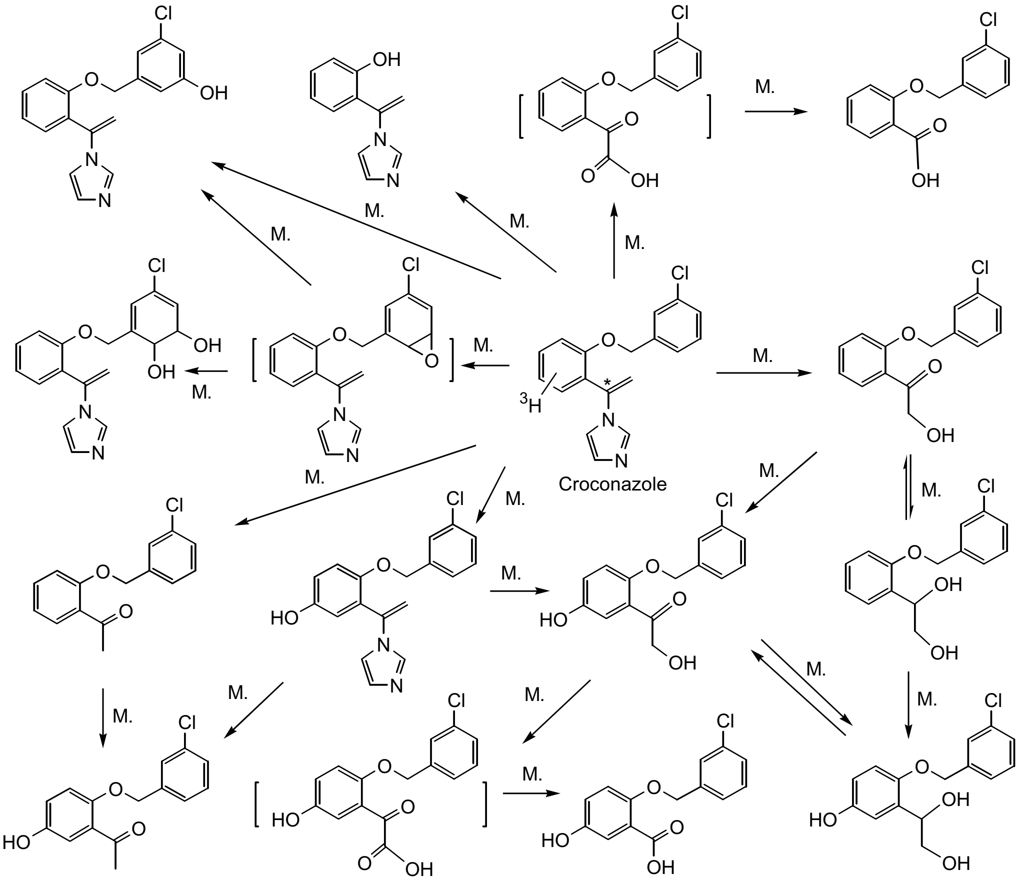
N-[(2-chlorophenyl)methyl]-3-hydroxy-2,2-dimethylpropionamide. In tolerant soybean cell suspension cultures, the only metabolite identified is β-glycosyl-2-chlorobenzyl alcohol.

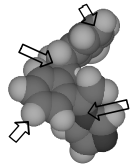
Croconazole

Not a pesticide: a potent antimycotic agent

Mammal
Male rabbits: JW-NIBS strain
(2.2–3.0 kg)[132]

When male rabbits are administered croconazole by intravenous injection, as many as 16 metabolites are excreted in the urine and 13 metabolites are identified. The biotransformation reaction of croconazole includes ring hydroxylation, *O*-dechlorobenzylation, and the loss of the imidazole ring.





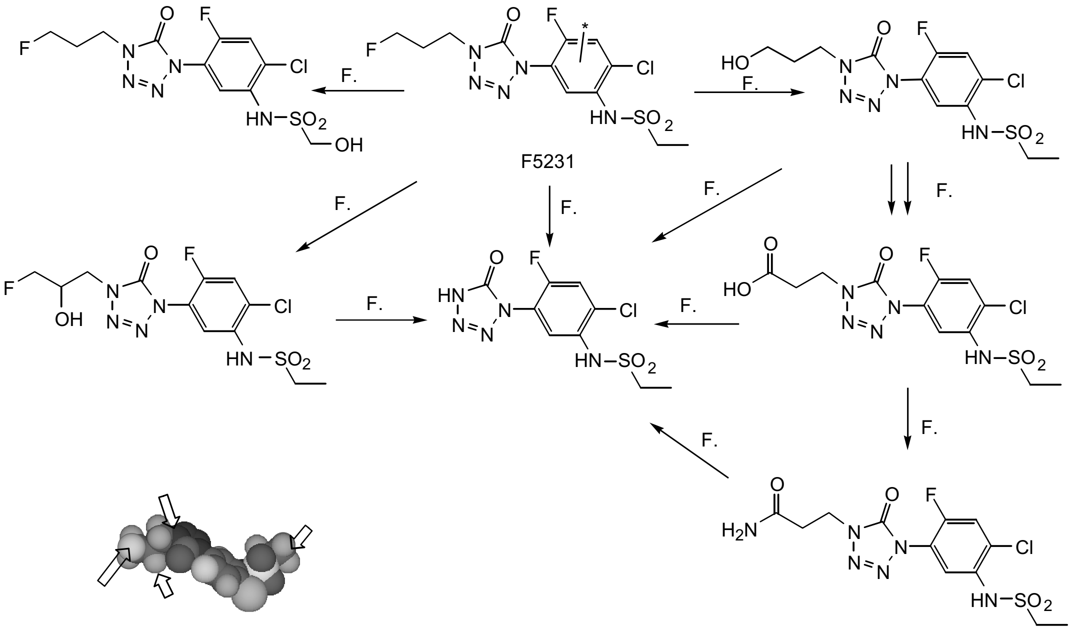
ClC1=CC(COC2=CC=CC=C2C
(N3C=CN=C3)=C)=CC=C1

F5231

A peroxidizing herbicide

Fungus
The filamentous fungus: *Absidia pseudocylindrospora* Hesseltine et Ellis (ATCC24169)[133]

The majority (88–99%) of the initially added radioactivity from ^{14}C-F5231 is ethyl acetate extractable in the culture filtrates of the biotransformation cultures of the fungus. Six degradation products as a result of the microbial transformation of F-5231 are identified which do not include the compounds where aromatic or tetrazolinone rings are modified. Instead, attack occurs only at the ethylsulfonylamino and fluoropropyl portions, resulting in hydroxylethylsulfonamide and two hydroxylated propyl derivatives that finally lead to *N*-dealkylated 1,4-dihydro-5*H*-tetrazol-5-one.



FCCCN1N=NN(C2=CC(NS(CC)
(=O)=O)=C(Cl)C=C2F)C1=O

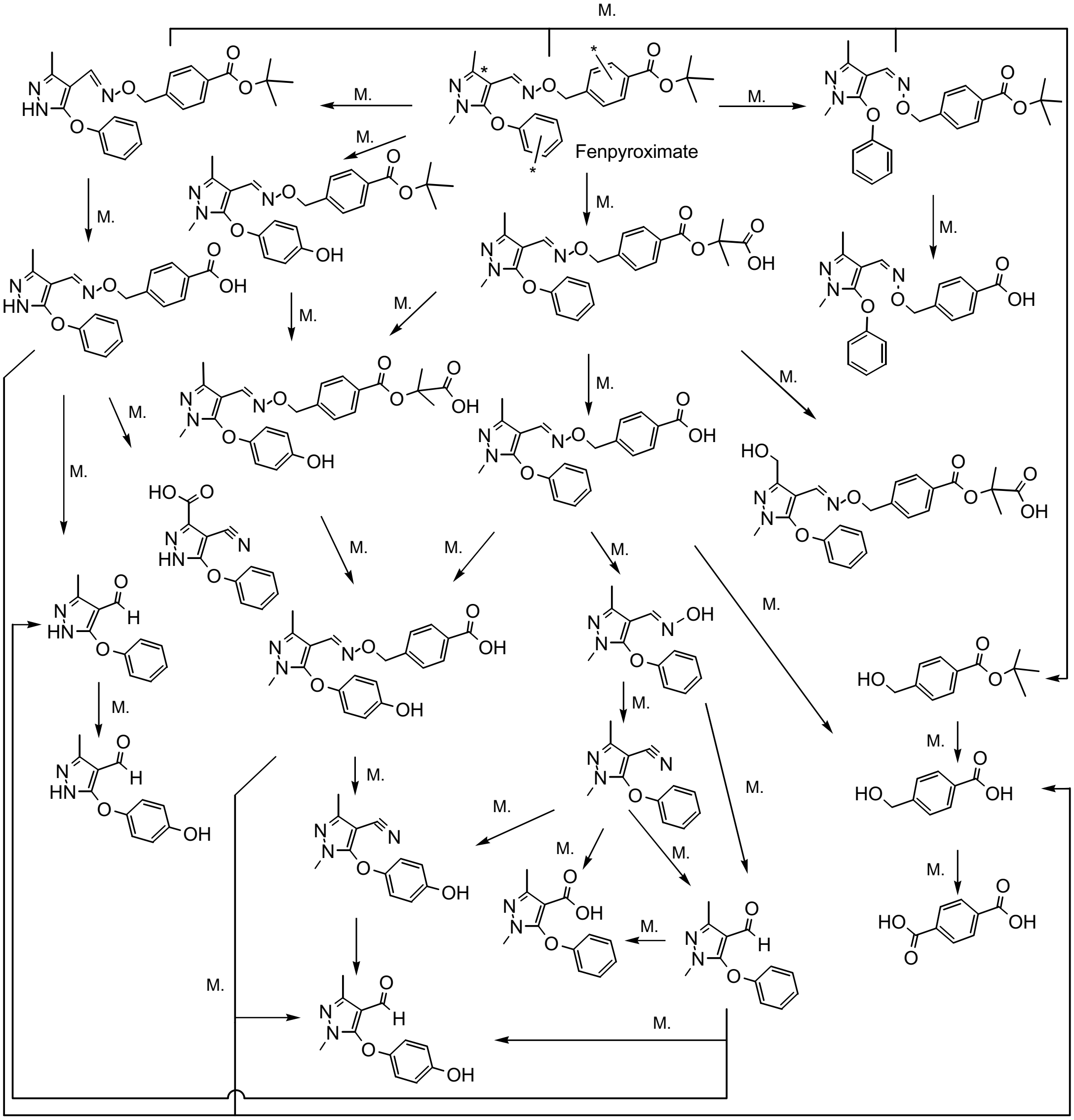
Fenpyroximate

An acaricide: control of phytophagous mites, *Tetranychidae*, *Eriophyidae*, and *Tarsonemidae*

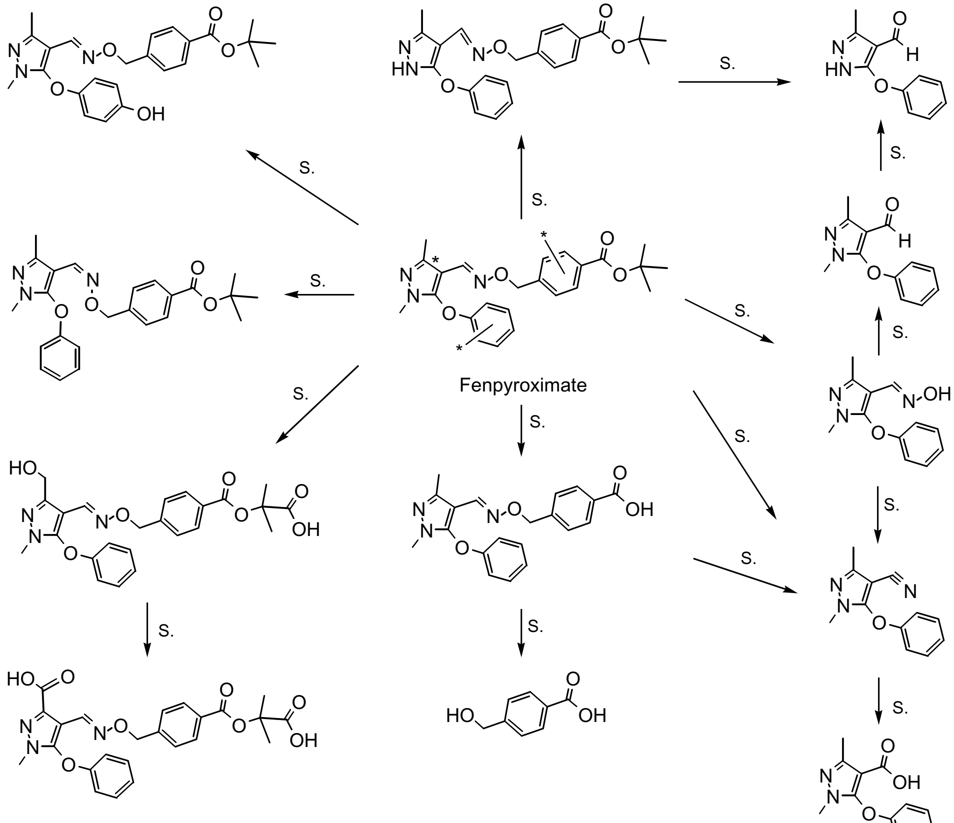
Mammal
Male Sprague–Dawley rats (six week-old, 200 ± 10 g)[134]

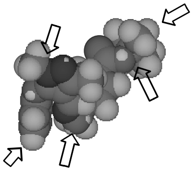
Soil
Ehime diluvial sand soil (pH 5.8);
Kanagawa volcanic ash loam (pH 5.5)[135]

When fenpyroximate is administered orally to rats, radiocarbons from ^{14}C-fenpyroximate are rapidly and almost completely excreted in the urine and feces within 72 h, and fenyproximate seems to be metabolized via oxidation of the *tert*-butyl group and methyl group at the 3-position in the pyrazole ring, *p*-hydroxylation in the phenoxy moiety, *N*-demethylation, hydrolysis of the *tert*-butyl ester, cleavage of the oxime



ether bond, and/or *E*/*Z* isomerization. In soils, 12 degradation products are identified, and in sterilized soils the degradation of fenpyroximate and CO_2, evolution are negligible. Fenpyroximate degrades through hydrolysis of *tert*-butyl ester, isomerization or cleavage of the oxime ether, *N*-demethylation, oxidation of the methyl group at the 3-position on the pyrazole ring, and hydroxylation of the phenoxy ring, and is finally mineralized to CO_2 and/or bound to soil organic matter.





CN1N=C(C)C(C=NOCC3=CC=C(C(OC
(C)(C)C)=O)C=C3)=C1OC2=CC=CC=C2

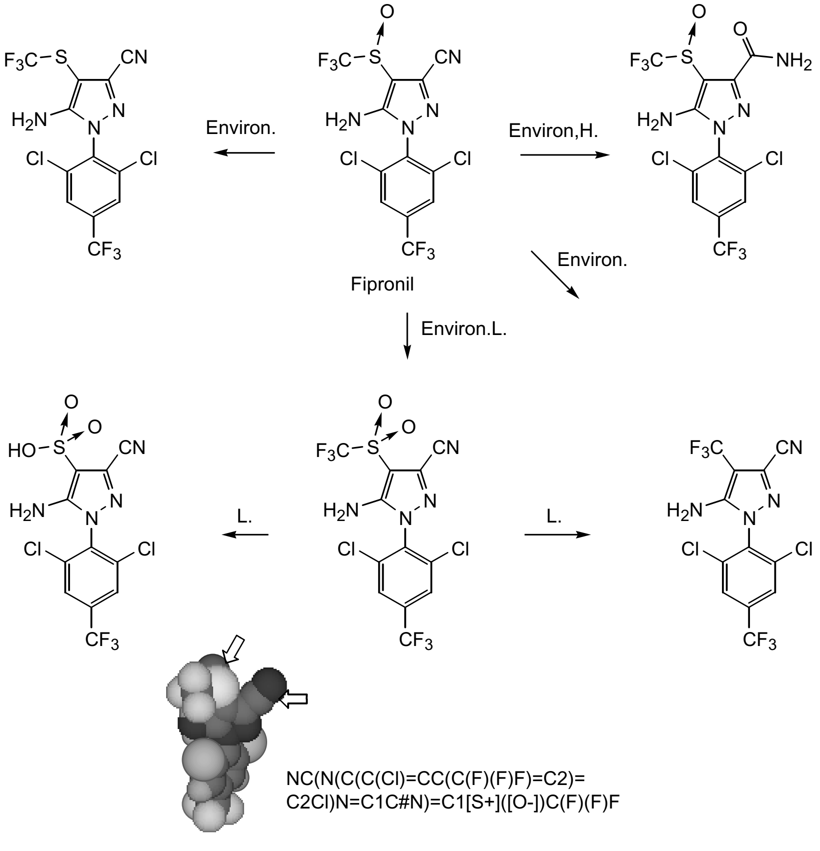
Fipronil

An insecticide: control of rice insects, thrips, termites, and click beetles

Environment
Two plots of 1600 m^2 and 1215 m^2 at Banizoumbou and Saguia of the Niamey region of Niger[136]

Hydrolysis/Light
In 2.5% methanol in water in the dark; irradiation with a xenon lamp (1.8 kW, 14.6 A)[137]

Through the abiotic degradation of fipronil in aqueous solution and on the soil surface, 5-amino-3-carbamoyl-1-[2,6-dichloro-4-(trifluoromethyl)-phenyl]-4-[(trifluoromethyl)sulfinyl]pyrazole is the only hydrolysis product detected. Fipronil in acidic aqueous solution exposed under a xenon lamp degrades with the concomitant appearance of 5-amino-3-cyano-1-[2,6-dichloro-4-(trifluoromethyl)-phenyl]-4-(trifluoromethyl)pyrazole and 5-amino-3-cyano-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]pyrazole-4-sulfonic acid. Under field conditions, when fipronil is applied in formulation, four metabolites which include one product resulting from reduction on the sulfur atom of fipronil are detected.



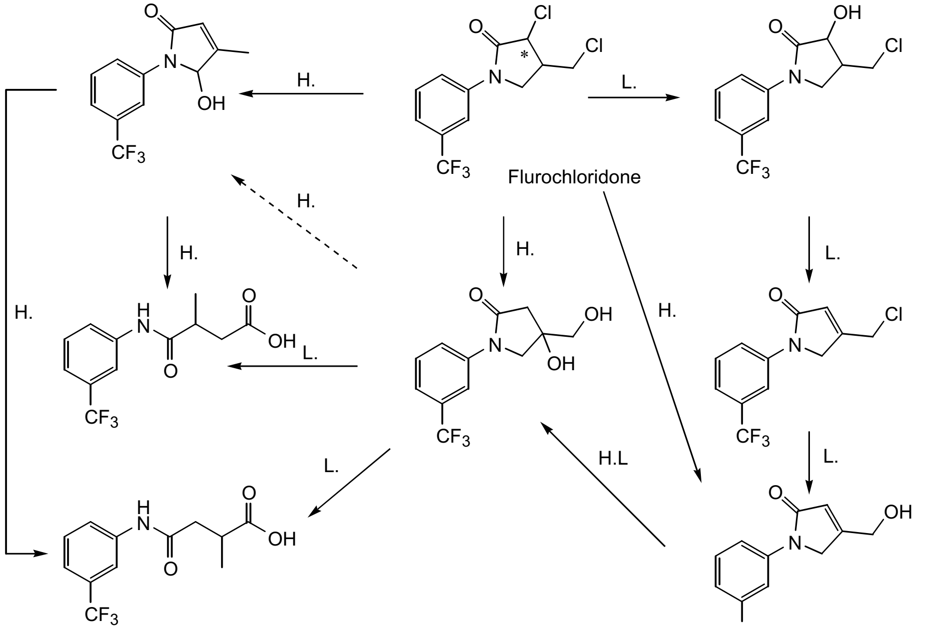
NC(N(C(C(Cl)=CC(C(F)(F)F)=C2)=
C2Cl)N=C1C#N)=C1[S+]([O-])C(F)(F)F

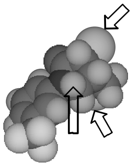
Flurochloridone

A selective herbicide: reduction of chlorophyll and carotenoid production in wheat (*Triticum aestivum* var. L. Mericopa) and corn (*Zea mays* var. L. Merit)

Hydrolysis/Photolysis
Clark and Lubs' buffer aqueous solutions at pH 5, 7, and 9 at 25 °C and 40 °C in the photoreactor chamber with a UV black light lamp (GE No. F40 BL)[138]

From hydrolytic and photolytic studies of flurochloridone in buffer solution, no hydrolysis of flurochloridone occurs at pH 5, 7, or 9 at 25 °C or at pH 5 at 40 °C. Appreciable hydrolysis occurs at 40 °C at pH 7 and 9 with half-lives of 190 and 140 days, respectively. Five hydrolytic degradation products and six photolytic degradation products are identified. The major photolytic degradation product which contains 39% of the radioactivity is 4-(chloromethyl)-3-hydroxy-1-[3-(trifluoromethyl)phenyl]-2-pyrrolidinone with a mixture of *cis* and *trans* isomers. The formation of this major degradation product suggests that the major photolytic pathway involves homolytic cleavage of the carbon−chlorine bond at the 3-position of the pyrrolidinone ring and the free radical intermediate





O=C1C(Cl)C(CCl)CN1C2
=CC=CC(C(F)(F)F)=C2

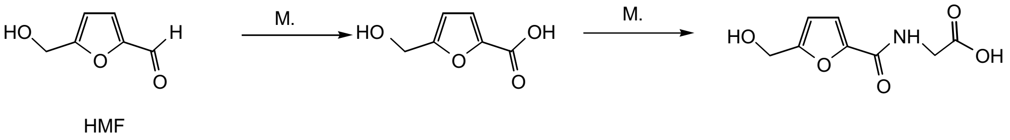
can react with water to give the major product or eliminate the hydrogen radical to form 4-(chloromethyl)-1,5-dihydro-1-[3-(trifluoromethyl)phenyl]pyrrol-2*H*-one.

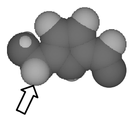
5-Hydroxymethyl-2-furaldehyde

Not a pesticide: a major product of sugar degradation

Mammal
Male Sprague-Dawley rats[139]

When 5-hydroxymethyl-2-furaldehyde (HMF) is administered orally or intravenously to rats, HMF or its metabolites are rapidly eliminated in the urine with the recovery of 95–100% after 24 h. HMF is completely converted to two metabolites which are identified as 5-hydroxymethyl-2-furoic acid and *N*-(5-hydroxymethyl-2-furoyl)glycine.





OC(C1=CC=C(CO)O1)=O

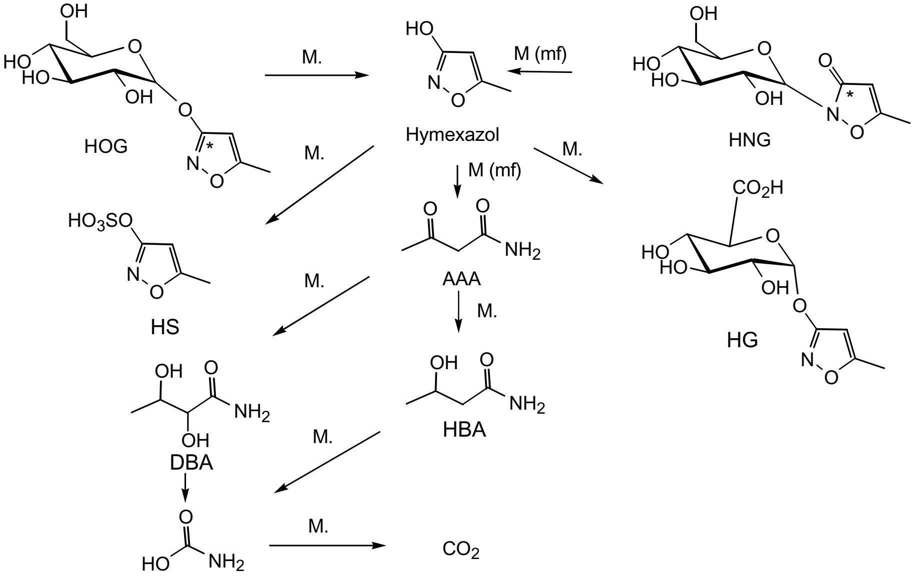
Hymexazol *O*- and *N*-glucosides

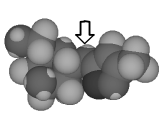
Plant metabolites of hymexazol (a plant growth stimulant as well as a fungicide for control of soil-borne diseases)

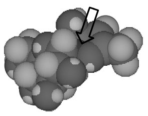
Mammal
Wistar-strain male rats (130–150 g)[140]

Mammal/Microflora
Wistar-strain male rats (150–200 g)[141]

Hymexazol *O*-glucoside (HOG) and hymexazol *N*-glucoside (HNG) show a remarkable difference in absorption, excretion, and metabolism by rats. When orally administered to rats, 90% of administered HOG is excreted in the urine, 45% of which is unchanged HOG, whereas 47 and 46% of HNG are excreted in the urine and feces, respectively most of which in the urine and 26% of which in the feces consist of unchanged HNG. Urinary metabolites of HOG are hymexazol, 5-methyl-3-isoxazolyl sulfate (HS), and 3-β-D-glucopyranuronosyloxy-5-methylisoxazole (HG), while those of HNG are hymexazol, HS, HG, (−)-*erythro*-(2*R*,3*R*)-dihydroxybutylamide (DBA), and acetoacetamide (AAA). In *in vitro* metabolism by rat cecal microflora (mf) under anaerobic conditions, HNG




HOG


HNG

CC1=CC(O[C@]([H])([C@@]2(O)[H])O
C([H])(CO)[C@@]([H])(O)[C@@]2(O)
[H])=NO1

OC1N([C@]([H])([C@@]2(O)[H])OC([H])
(CO)[C@@]([H])(O)[C@@]2(O)[H])OC
(C)=C1

Hymexazol *O*- and *N*-glucosides

(continued)

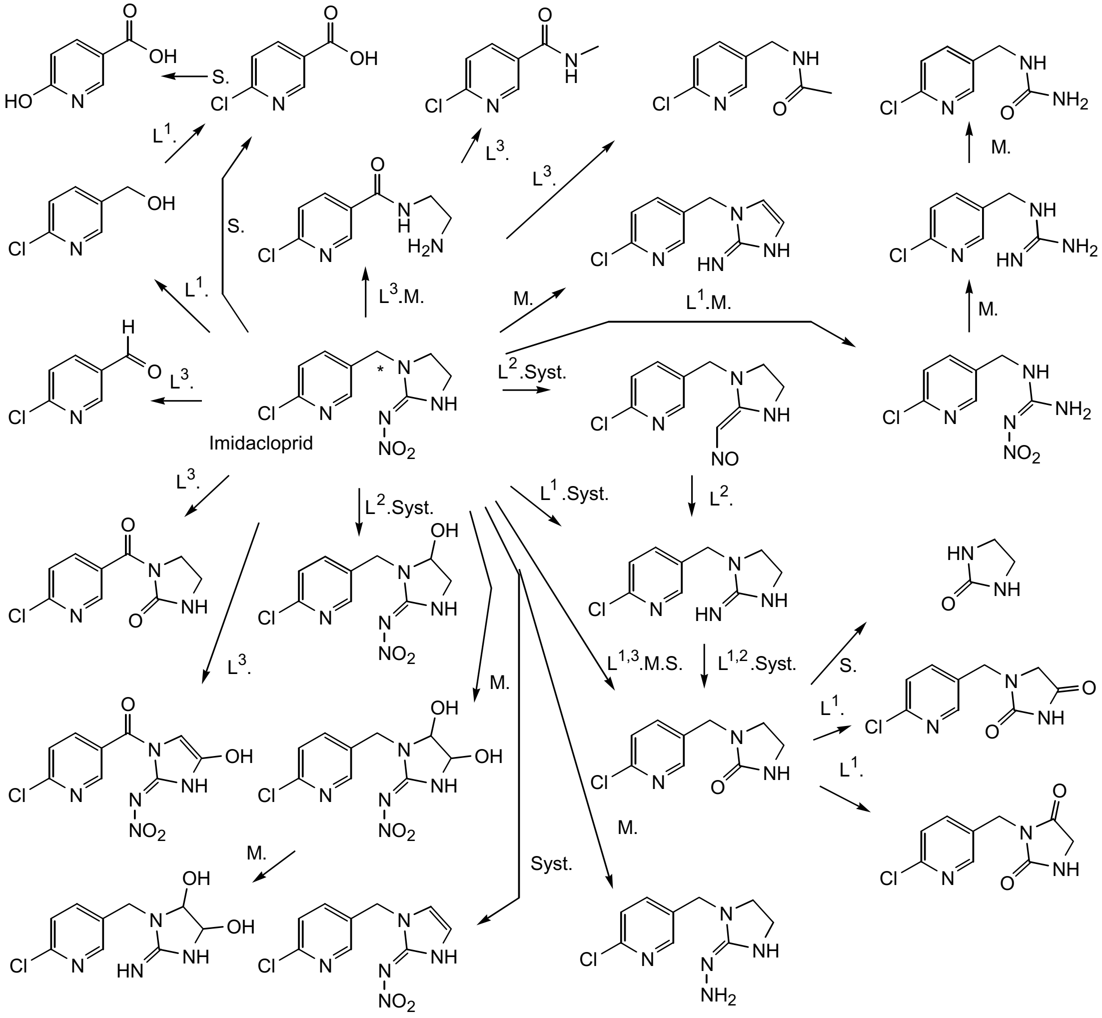
is biotransformed to hymexazol which is further converted to AAA. Orally administered HNG is biotransformed in the gastrointestinal tract to hymexazol and AAA, which are rapidly absorbed, and metabolized mainly to HS, HG, and DBA, and then these metabolites are excreted in the urine.

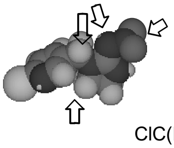
Imidacloprid

A systemic insecticide: control of sucking insects, soil insects, termites, and some species of chewing insects

Light[1]
Irradiation in HPLC grade and tap water with a high-pressure mercury lamp: HPK 125 W, Philips[142]

The photolytic degradation of imidacloprid in different conditions yields diversified degradation products as indicated in the pathways. Photolysis in water gives 6-chloronicotinaldehyde, *N*-methylnicotinic acid amide, 1-(6-chloro-3-pyridinyl)methyl-2-imidazolinone and





ClC(N=C1)=CC=C1CN(C
CN2)C2=N[N+]([O-])=O

Light[2]
Surface of the tomato plant outdoors[143]

Light[3]
Irradiation in deionized water with a high-pressure mercury lamp: HPK 125 W, Philips[144]

Mammal
145

Soil
Soils from sugarbeet field (pH 6.81/H_2O) at Lubbeek, Belgium[146]

System
Tobacco smoke of cigarettes made from imidacloprid-treated tobacco[147]

6-chloro-3-pyridylmethylethylenediamine which are identified as main degradates together with a complex mixture of degradation products. On the surface of the tomato plant, four of the 14 metabolites are identified. In tobacco smoke, five degradates are detected, and in field soils, four metabolites are identified from the treated sugarbeet. As for the mammalian metabolites, the pathways are drawn tentatively by the author (see Klein[145]).

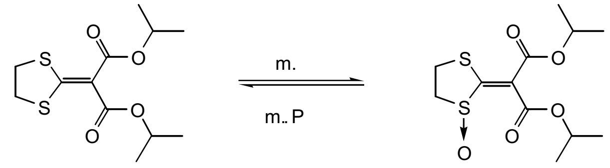
Isoprothiolane/ Isoprothiolane sulfoxide

A fungicide/an insecticide

Microsome
Rat liver preparation of male Sprague–Dawley rats (6 week-old, ca 200 g)[148]

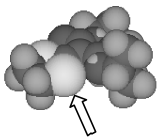
Plant
Rice: *Oryza sativa* L. cv. Kinmaze[148]

Isoprothiolane is easily oxidized by rat liver 9000 g supernatant to produce its racemic sulfoxide in this process, NADPH is an effective cofactor but NADH is not. The liver microsomes, however, preferentially form its (+)-isomer in an enantiomeric excess of 38–43%. The sulfoxidation of isoprothiolane by rice plants proceeds too slowly to determine the metabolites. Both isoprothiolane (+)- and (−)-sulfoxides undergo rapid racemization by rat cytosol (105 000 g supernatant) or rice plants, accompanied with reduction to isoprothiolane.

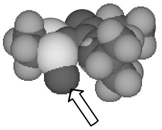


Isoprothiolane

Isoprothiolane sulfoxide



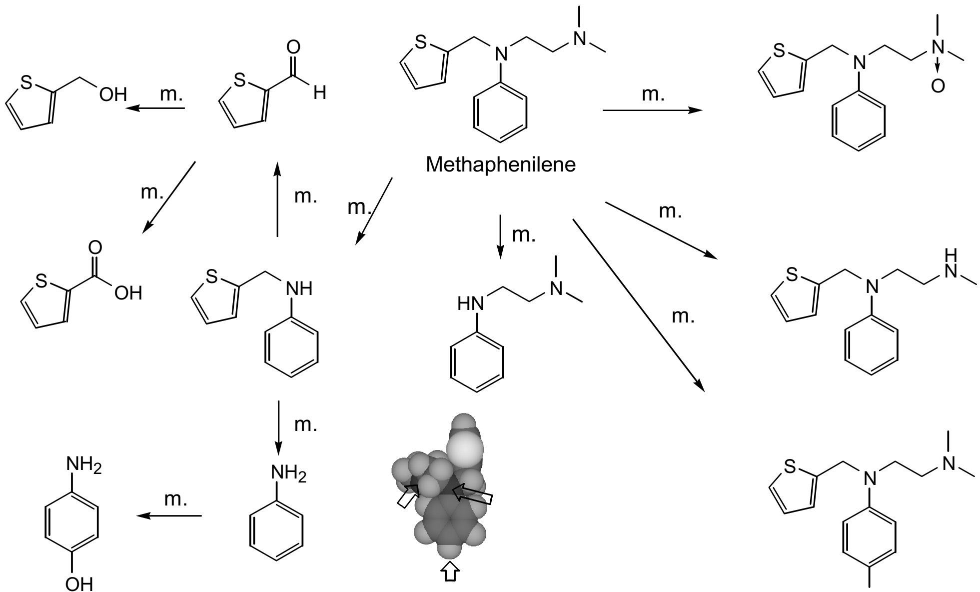
O=C(OC(C)C)C(C(OC
(C)C)=O)=C1SCCS1



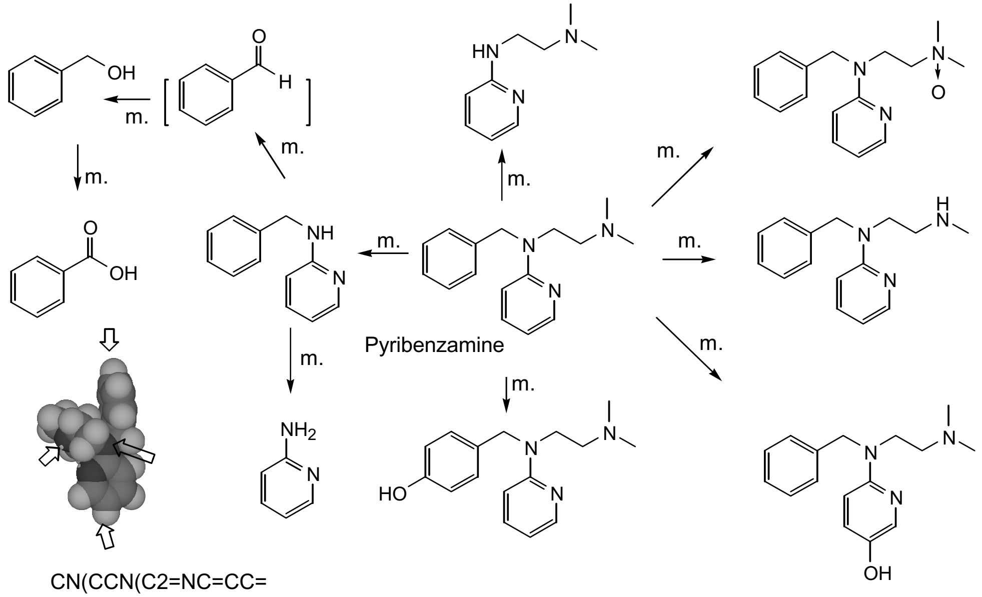
O=C(C(C(OC(C)C)=O)=C
1SCC[S+]1[O-])OC(C)C

Methaphenilene and Pyribenzamine

Not pesticides: antihistamic agents



CN(C)CCN(CC2=CC=
CS2)C1=CC=CC=C1



CN(CCN(C2=NC=CC=
C2)CC1=CC=CC=C1)C

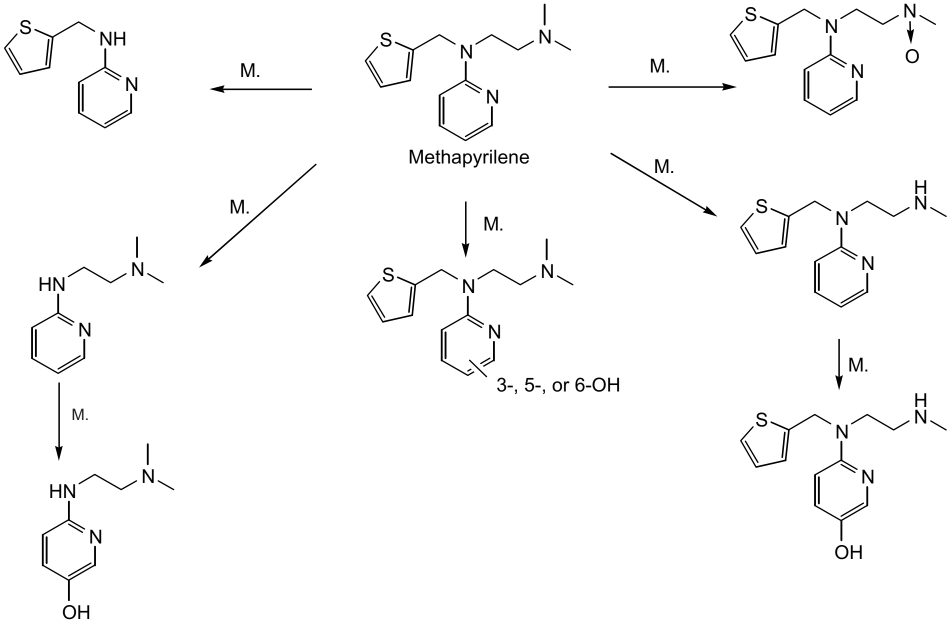
Microsome Liver microsomes of male Sprague–Dawley rats (200–250 g) from Bantin-Kingman (Fremont, CA)[149]	When methaphenilene and pyribenzamine are incubated with rat liver microsomes, both compounds are metabolized via *N*-oxide formation and *N*-dealkylation which includes removal of the dimethylamino moiety, the thiophenylmethyl moiety of methaphenilene, and the benzyl moiety of pyribenzamine.

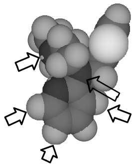
Methapyrilene

Not a pesticide: antihistamic agent

Mammal
Albino male Sprague–Dawley rats
(150–250 g) from Simonsen Laboratory[150]

Methapyrilene is excreted in the urine when orally administered to rats and undergoes ring hydroxylation, direct dealkylation, side chain oxidation, and subsequent removal and *N*-oxidation. The metabolic removal of the 2-thiophenylmethyl moiety is a significant metabolic pathway. Several other metabolites are identified, including (3-, (5-, and (6-hydroxypyridyl)methapyrilene, *N*′-(2-pyridyl)-*N*,*N*-dimethyl-ethylenediamine, and *N*′-[2-(5-hydroxylpyridyl)]-*N*,*N*-dimethylethylenediamine.





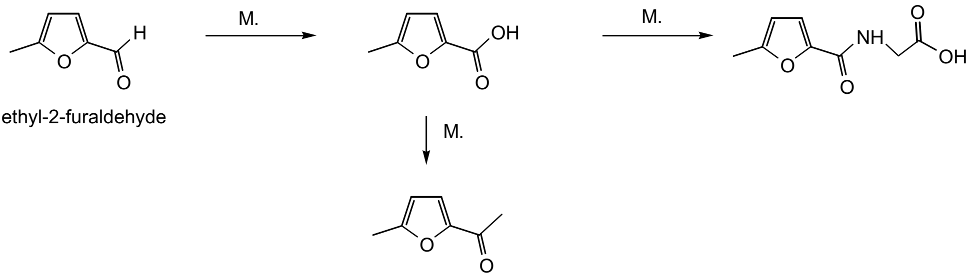
CN(C)CCN(CC2=CC=C
S2)C1=NC=CC=C1

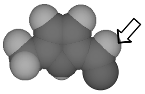
5-Methyl-2-furaldehyde

Not a pesticide: a naturally occurring substance

Mammal
Male Wistar-strain rats (230–250 g)[151]

The biotransformation of 5-methyl-2-furaldehyde is the conversion to 5-methylfuroylgycine and 5-methyl-2-furylmethylketone by rats.





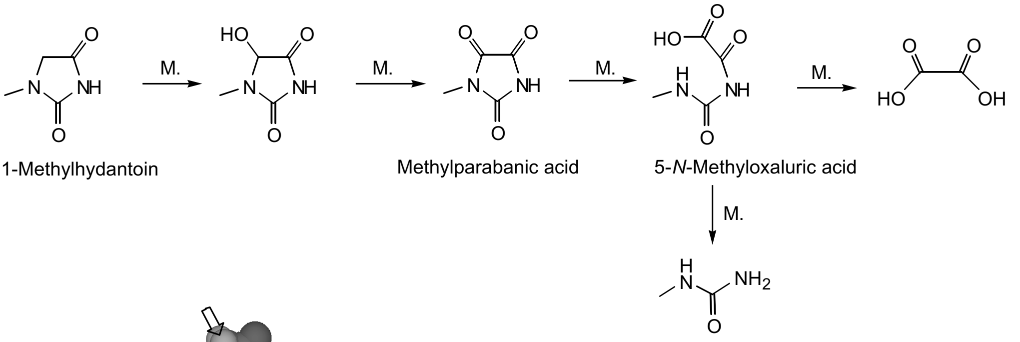
CC1=CC=C(C([H])=O)O1

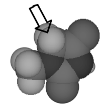
1-Methylhydantoin

A plant growth regulator

Mammal
Rabbits[152]

The metabolic pathway of 1-methylhydantoin via 5-hydroxy-1-methylhydantoin, methylparabanic acid, and 5-*N*-methyloxaluric acid proves to be a major and general metabolic pathway in rabbits.





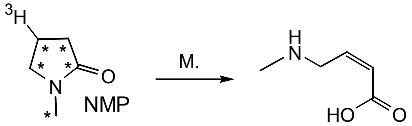
O=C(CN1C)NC1=O

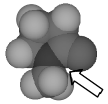
N-Methyl-2-pyrrolidinone (NMP)

Not a pesticide: a versatile industrial solvent

Mammal
Male Sprague–Dawley rats (250–350 g) from SASCO, Inc.[153]

Rats are administered radio-labeled *N*-methyl-2-pyrrolidinone (NMP), and the major route of excretion by rats is via the urine. The major metabolite, representing 70–75% of the administered dose, is 4-(methylamino)butenoic acid. This unsaturated intact product may be formed from the elimination of water, and a hydroxyl group may be present on the metabolite prior to acid hydrolysis.





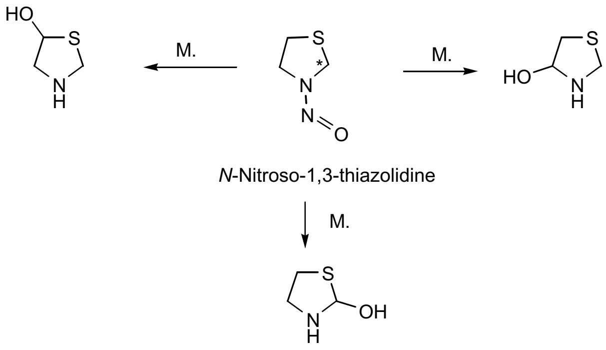
CN1CCCC1=O

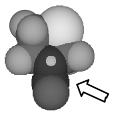
N-Nitroso-1,3-thiazolidine

Not a pesticide

Mammal
Male Sprague–Dawley rats (200–250 g)[154]

N-Nitroso-1,3-thiazolidine administered by gavage to rats is excreted mostly in the urine with a small amount in respired air. The major metabolite in the urine is 2-hydroxy-1,3-thiazolidine, and minor quantities of the isomers 4- and 5-hydroxy-1,3-thiazolidines are detected. The presence of hydroxy-1,3-thiazolidine indicates that α-hydroxylation and denitrosation are major metabolic pathways of *N*-nitroso-1,3-thiazolidine.





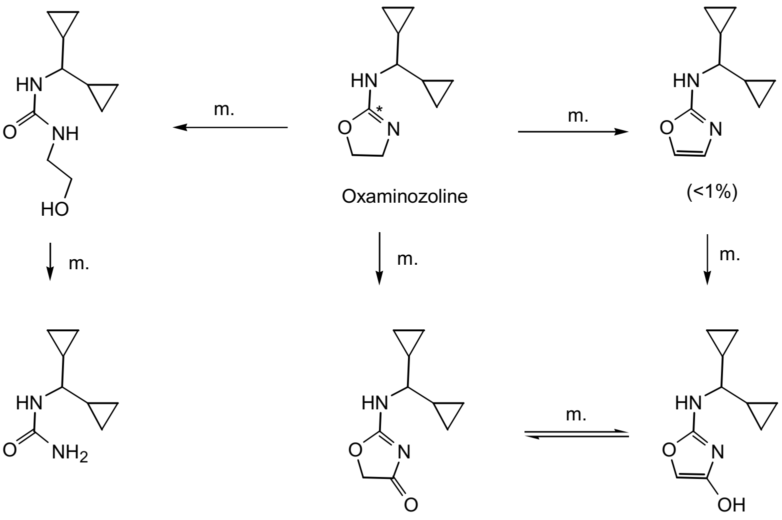
O=NN1CCSC1

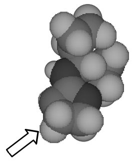
Oxaminozoline

Not a pesticide: an α_2-adrenergic receptor

Microsome
Hepatocytes obtained from the liver of Sprague–Dawley rats (180–200 g) by perfusion with collagenase[155]

In short-term rat hepatocyte cultures, oxaminozoline is metabolized and its four metabolites resulting from oxidation or hydrolysis are identified, three of which are identical to those reported *in vivo*. The presence of an additional minor metabolite in culture may be due to the higher metabolic rate of oxaminozoline in this model system.

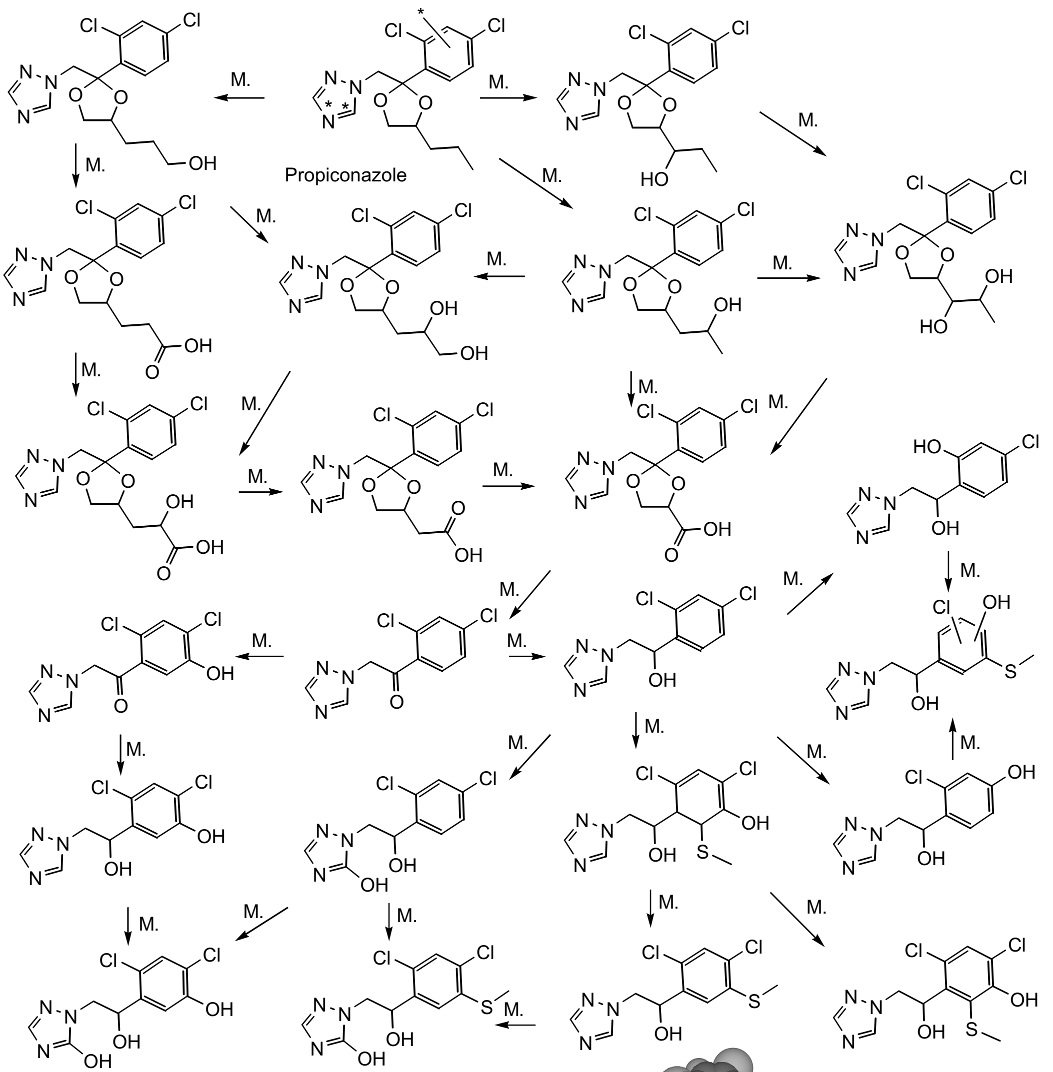


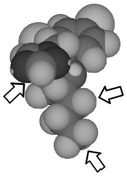


C1(NC(C3CC3)C2CC2)=NCCO1

Light
Irradiation in methanol and hexane with a medium-pressure mercury vapor lamp in a quartz apparatus; natural sunlight with sieved sandy loam soil[156]

The numerous metabolites of propiconazole are identified from rat urine and feces. Major sites for enzymatic attack are the propyl side chain and the cleavage of the dioxane ring. The 2,4-dichlorophenyl ring is attacked in various ways including the formation

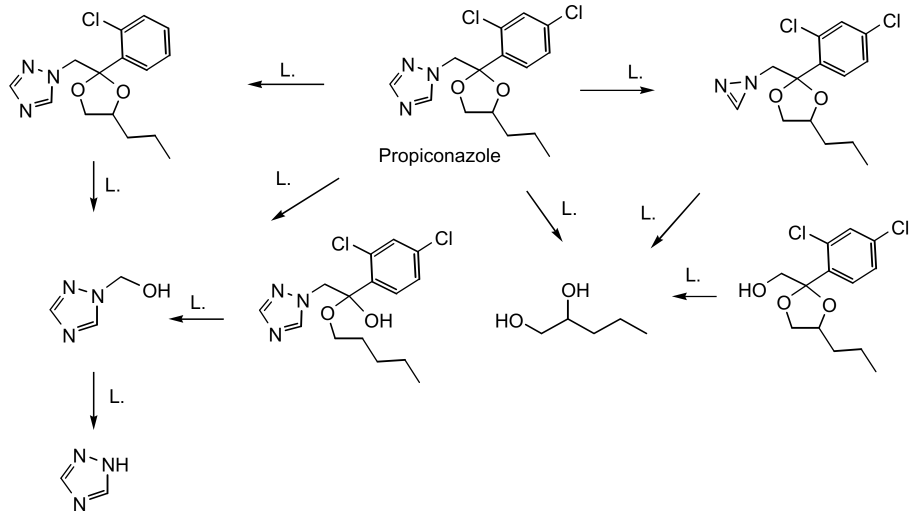


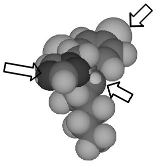


CCCC(O3)COC3(C2=CC=C(Cl)
C=C2Cl)CN1C=NC=N1

Mammal
Young male adult Tif: RAI f-strain rats (SPF); male and female CD-1 mice[157]

of a cyclohexadiene ring system, hydroxylation, replacement of the chlorine substituent by a hydroxy group, and introduction of a methylthio group. The 1,2,4-triazole ring is oxidatively attacked, leading to hydroxy derivatives. The vast majority of the alcoholic and phenolic metabolites are excreted as sulfuric acid and glucuronic acid conjugates. The major metabolic pathway in mice is via cleavage of the dioxane ring. Photolysis causes cleavage of the C_1-triazole bond of propiconazole, liberating 1,2,4-triazole as the major product. Six more degradation products are identified which are not included in the mammalian metabolites.





CCCC(O3)COC3(C2=CC=C(Cl)
C=C2Cl)CN1C=NC=N1

Pyrazolate

A herbicide: control of both annual and perennial weeds in paddy fields

Fish/Light/Mammal/Plant/Soil/Soil microorganism[158]

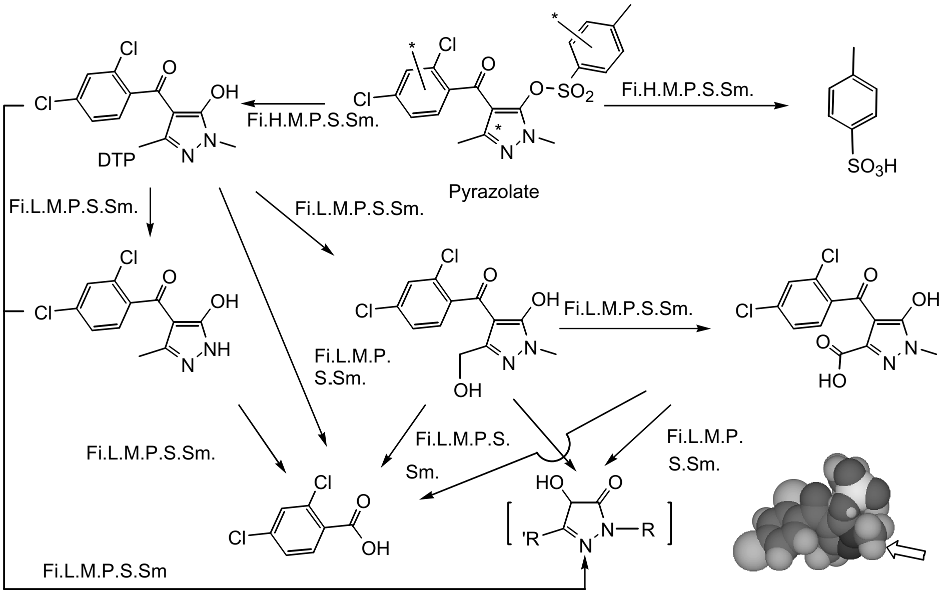
Hydrolysis
Buffer solutions prepared by dissolving component salts of KCl, HCl, KH_2PO_4, glycine, and/or NaOH in distilled water; artificial gastric (pH 1.5) and intestinal (pH 7,5) fluids[159]

Mammal
Male Wistar-strain rats from the Imamichi Institute For Animal Production (130–150 g)[160]

Plant
Rice: *Oryza sativa* L., cv. Nihonbare[161]

Soil
Soils from rice paddy fields in Shiga alluvial light clay (pH 5.8); Iwate volcanic ash sandy loam (pH 5.6)[162]

Hydrolysis of pyrazolate (DTP) in buffer solutions and in artificial gastric and intestinal fluids proceeds predominantly through base- and acid-catalyzed processes in the regions above pH 7 and below pH 3, respectively, whereas both processes occur between pH 3 and pH 7. The hydrolysis products are *p*-toluenesulfonic acid and 4-(2,4-dichlorobenzoyl)-1,3-dimethyl-5-hydroxypyrazole. The metabolism study of DTP in fish, rats, plant, soils, and soil microorganisms shows that the metabolites in these systems are mostly derived from the herbicidal entity of pyrazolate resulting from *N*-demethylation and hydroxylation followed by further oxidation of the methyl group of the pyrazole ring and the cleavage of the carbonyl linkage (see Nakagawa *et al.*)[158].



O=C(C2=C(Cl)C=C(Cl)C=C2)C1=C(OS
(C3=CC=C(C)C=C3)(=O)=O)N(C)N=C1C

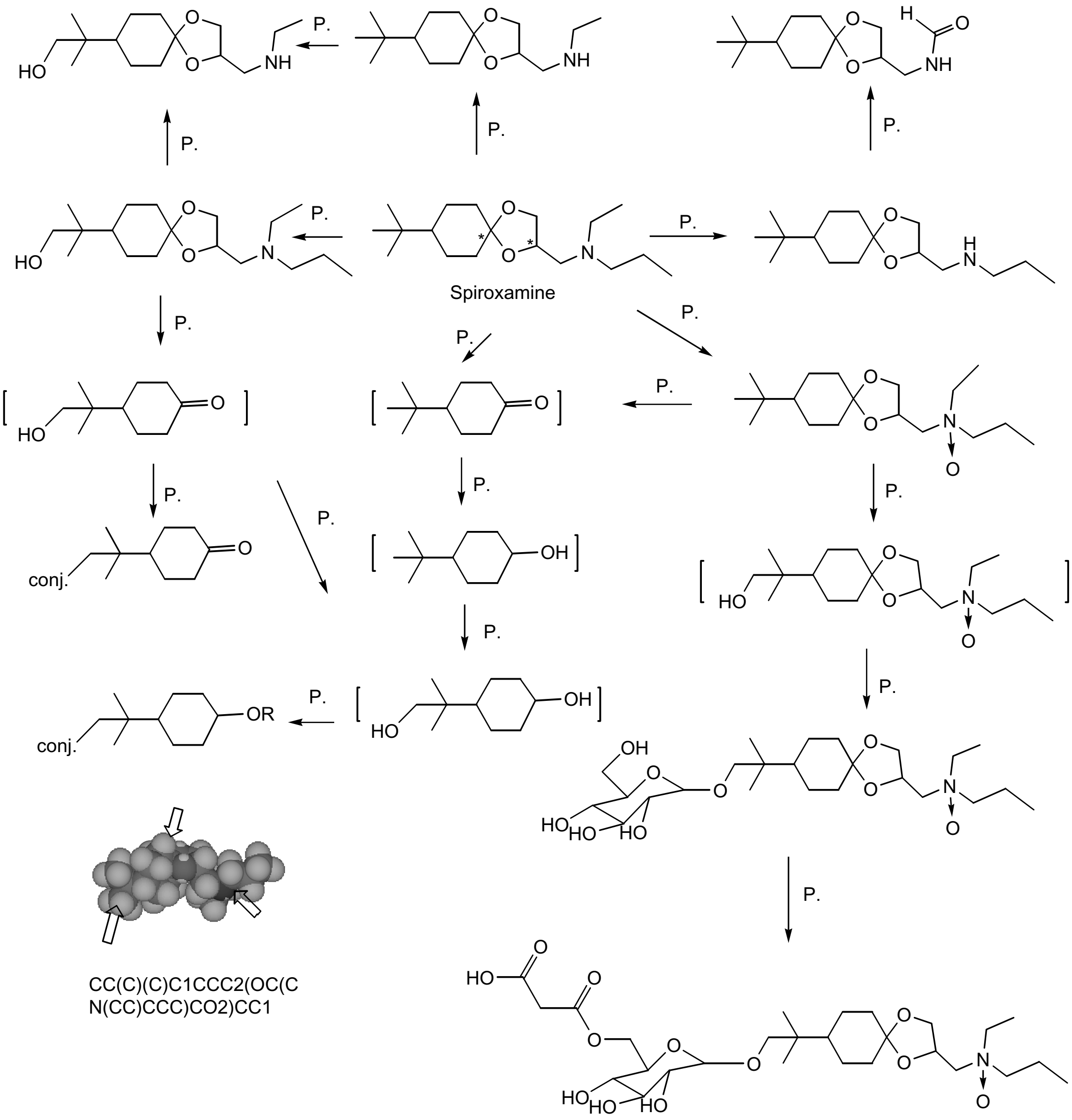
Spiroxamine (KWG4168)

A fungicide: use in cereal and grape cultivation either as a single-agent product or in combination with other fungicidal substances

Plant
Summer wheat[163]

Mammal
Rats; lactating goats; laying hens[163]

Spiroxamine is metabolized rapidly in plants, soils, water, and animals via similar degradation pathways. The metabolic pathways include hydrolysis and oxidation at several places in the molecule. Side chains are also degraded to various water-soluble conjugates in animals and in plants, and at the end of

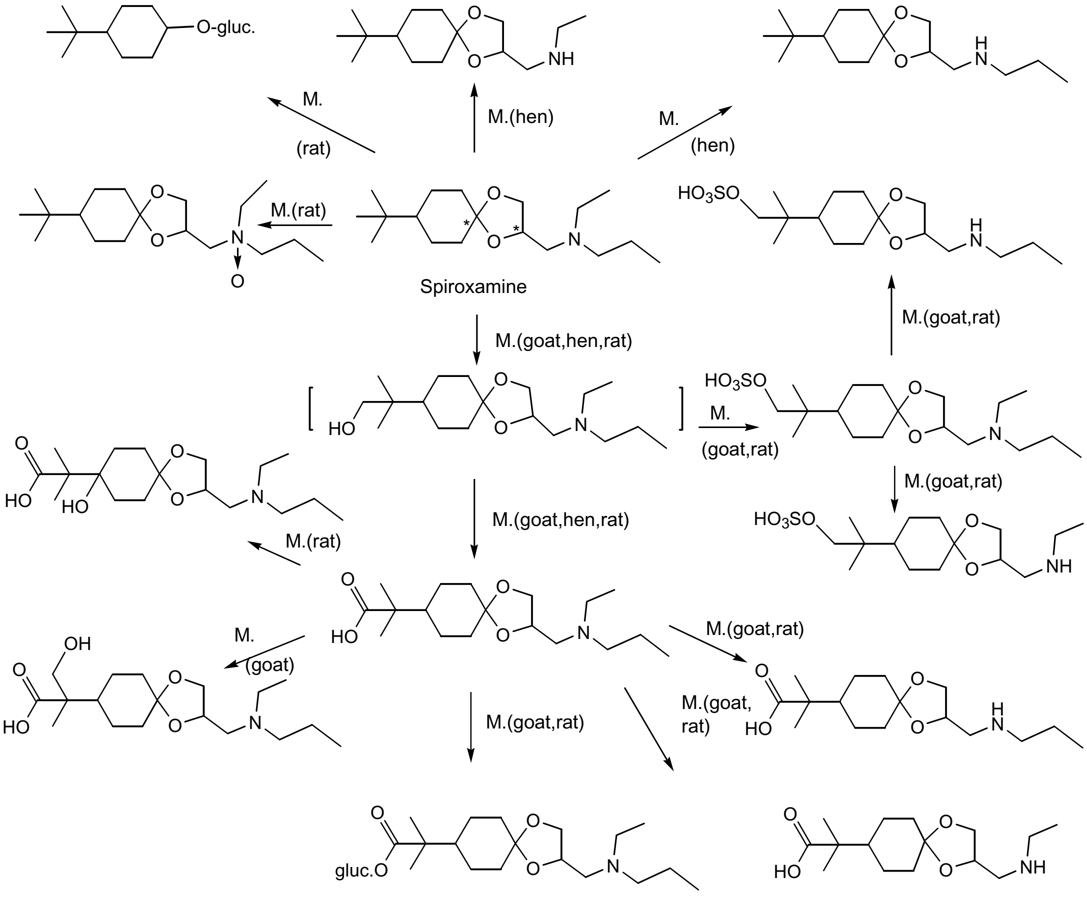


CC(C)(C)C1CCC2(OC(C
N(CC)CCC)CO2)CC1

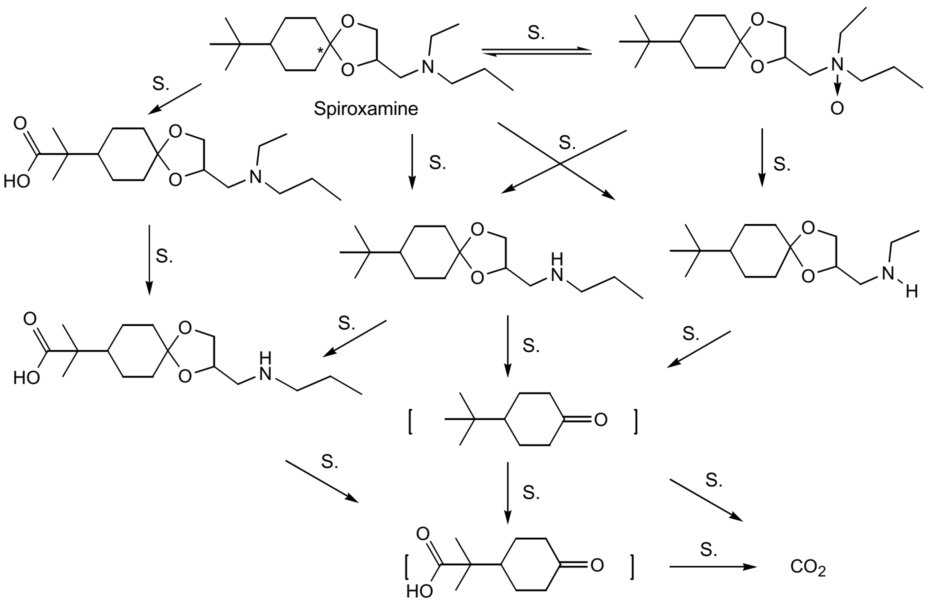
Spiroxamine (KWG4168) (continued)

Soil
Four soils[163]

complete degradation to natural constituents, carbon dioxide is formed in soils as the principal metabolite. The favorable sorption characteristics rule out any possibility of appreciable translocation in soil. In wheat, the total residue is determined in forage, grain, and harvest-ready straw. In the field studies, the residues in the grain are mostly below 0.05 mg kg^{-1}, and only in a few cases up to 0.3 mg kg^{-1}. In the milk of cows ingesting spiroxamine residues with the feed, no residues are found in the least favorable case. In eggs of laying hens, the residue concentrations are below the limit of quantification. There are no residue concentrations detected in the hen fat, meat, and liver.



gluc.: glucuronic acid residue



gluc.: glucuronic acid residue

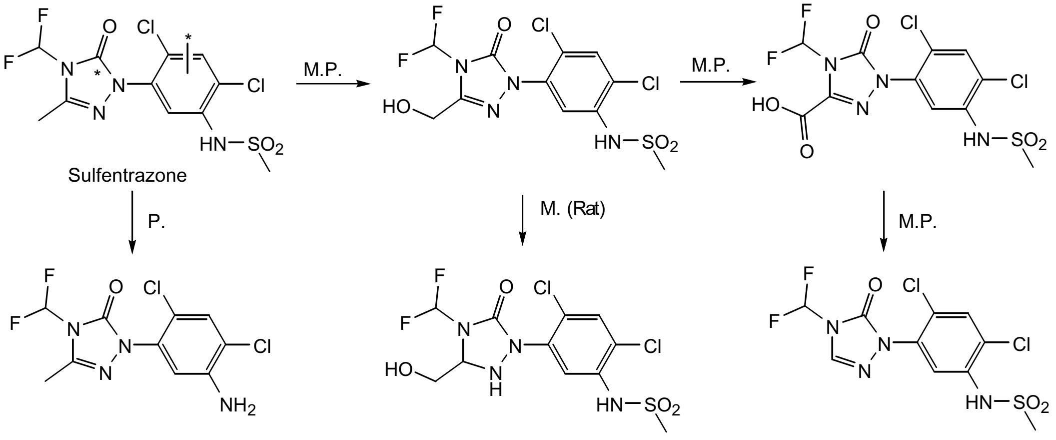
Sulfentrazone (F6285)

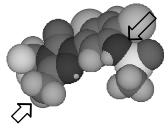
A pre-emergent herbicide: control of broad-spectrum grass and broadleaf weeds

Plant
Sicklepod (*Senna obtusifolia*); coffee senna (*Cassia occidentalis*)[164]

Mammal
Lactating dairy goats; white leghorn hens; Sprague–Dawley rats (BR/Charles River Laboratory, Inc.)[165]

When ^{14}C-sulfentrazone is applied to coffee senna and sicklepod through the roots, 83% of the parent compound remains in coffee senna leaf tissue after 9 h exposure and in contrast, sicklepod takes up relatively less sulfentrazone through the root and metabolizes sulfentrazone in the foliage more rapidly than coffee senna. The primary detoxification reaction appears to be oxidation of the methyl group on the triazolinone ring, resulting in the formation of the more polar hydroxymethyl derivative. The aniline analog is identified as a plant-specific metabolite. The tolerance of sicklepod to sulfentrazone is primarily due to a relatively high rate of metabolism of sulfentrazone compared with coffee senna. When ^{14}C-sulfentrazone is administered orally to rats, goats, and hens in a daily diet, administered radioactivity is quantitatively excreted in the urine, feces, or hen excreta. In all of the species, unchanged sulfentrazone and two non-conjugated metabolites are found, which are 3-hydroxymethyl and carboxylic acid derivatives, the latter of which decomposes at high temperature or acidic pH to give the corresponding desmethyl analog of sulfentrazone. In rats, a minor reduction metabolite is detected which is tentatively characterized as the 2,3-dihydro-3-hydroxymethyl derivative.





FC(F)N1C(C)=NN(C2=CC(NS(C)(=O)=O)=C(Cl)C=C2Cl)C1=O

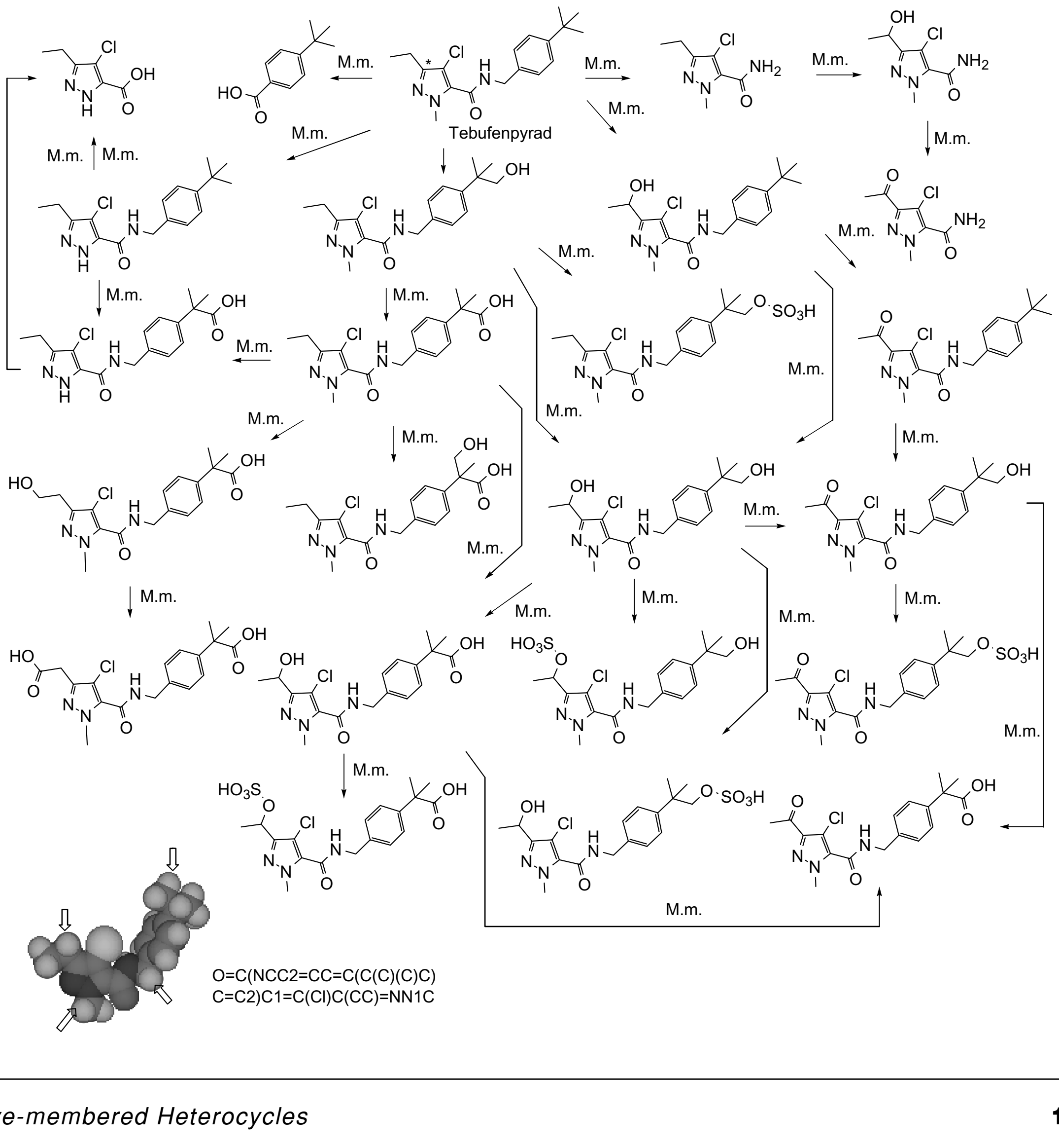
Tebufenpyrad

An acaricide: control of two-spotted spider mites, *Tetranichus ultae*; citrus red mite, *Panonychus citri*, etc.

Mammal
Male 6 week-old Fischer rats[166]

Microsome
Liver homogenate of male Sprague–Dawley rats (7 week-old)[166]

By incubation of tebufenpyrad with rat liver homogenate, tebufenpyrad undergoes biotransformation to yield the major metabolites *N*-(4-*tert*-butylbenzyl)-4-chloro-3-(1-hydroxyethyl)-1-methylpyrazole-5-carboxamide via hydroxylation of the ω-1-carbon of the ethyl group and *N*-[4-(1-carboxy-1-methylethyl)benzyl]-4-chloro-3-ethyl-1-methylpyrazole-5-carboxamide via oxidation of the methyl group in the *tert*-butyl moiety to the carboxylic acid derivatives.



O=C(NCC2=CC=C(C(C)(C)C)
C=C2)C1=C(Cl)C(CC)=NN1C

Tebufenpyrad

(continued)

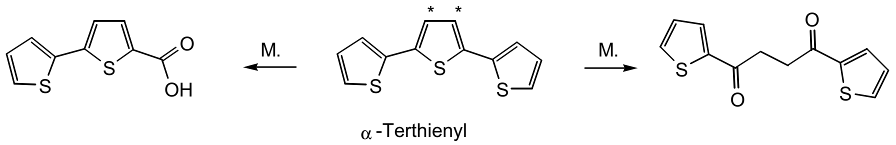
When the rat is orally dosed tebufenpyrad, the major metabolism pathway is via both hydroxylation and oxidation reactions to yield *N*-[4-(1-carboxy-1-methylethyl)benzyl]-4-chloro-3-(1-hydroxyethyl)-1-methylpyrazole-5-carboxamide which is mainly excreted in the urine.

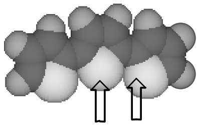
α-Terthienyl

A botanical insecticide: natural product, control of malathion-resistant and sensitive mosquito *Culex tarsalis* larvae

Mammal
Male Sprague–Dawley rats (av. 238 g)
from Charles River Canada, Inc.[167]

When ^{14}C-α-terthienyl is administered orally to rats in a single dose, two metabolites [1,4-di(2′-thienyl)]-1,4-butadione and 2-2′-bithiophene-5-carboxylic acid are identified in the urine.





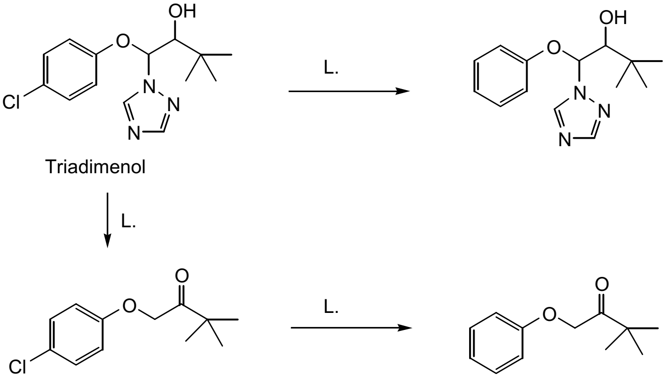
C1(C2=CC=C(C3=CC=CS3)S2)=CC=CS1

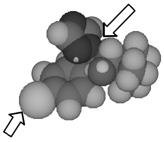
Triadimenol

A systemic fungicide: the major metabolite of triadimefon

Light
A medium-pressure mercury vapor lamp (400 W) in a borosilicate glass system[168]

When triadimenol is irradiated by UV light in methanol solution, two major degradation products are identified as 1-(4-chlorophenoxy)-3,3-dimethylbutan-2-one and 1-phenoxy-3,3-dimethyl-1-(1*H*-1,2,4-triazol-1-yl)butan-2-ol. When a spray deposit on apple leaves is exposed outdoors to natural sunlight, the only product detected is the butanone metabolite. The butanone metabolite has very low fungicidal activity against apple powdery mildew, whereas the butanol metabolite gives some control of infection.

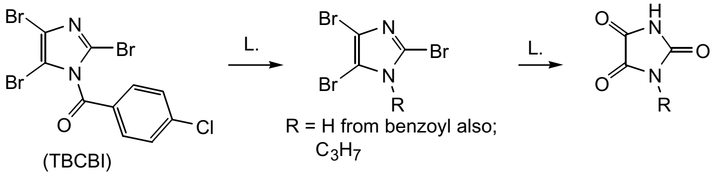




ClC(C=C2)=CC=C2OC(C
(O)C(C)(C)C)N1C=NC=N1

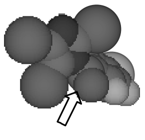
Light
Solutions of the chemicals in dry methanol containing methylene blue irradiated in a Pyrex photoreactor equipped with a mercury high-pressure lamp (Philips HPK 125)[169]

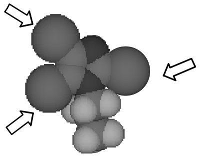
Sensitized photooxidation of 2,4,5-tribromoimidazole results in rapid degradation to the parabanic acid derivatives. Similarly, 2,4,5-tribromo-1-(4-chlorobenzoyl)imidazole (TBCBI) affords parabanic acid. However, the photolysis of 2,4,5-trichloro-1-(4-



(TBCBI)

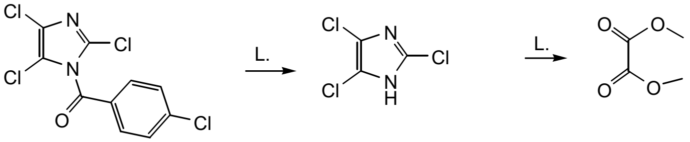
R = H from benzoyl also; C_3H_7



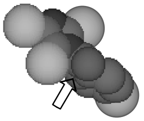


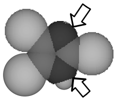
BrC1=C(N(C(Br)=N1)C(C2
=CC=C(C=C2)Cl)=O)Br

R :C_3H_7 ; BrC1=C(Br)N(CCC)C(Br)=N1



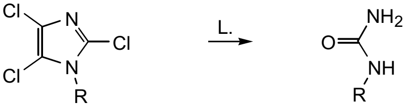
(TCCBI)





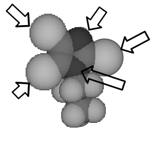
ClC1=C(Cl)N(C(C2=CC=
C(Cl)C=C2)=O)C(Cl)=N1

ClC1=C(Cl)NC(Cl)=N1



(TCI)

R : CH_3, C_3H_7



R :C_3H_7; ClC1=C(Cl)N(C(Cl)=N1)CCC

chlorobenzoyl)imidazole (TCCBI) and 2,4,5-trichloroimidazole (TCI) results in a ring cleavage to give dimethyl oxalate, ammonium chloride, and alkyl ureas.

Vinclozolin

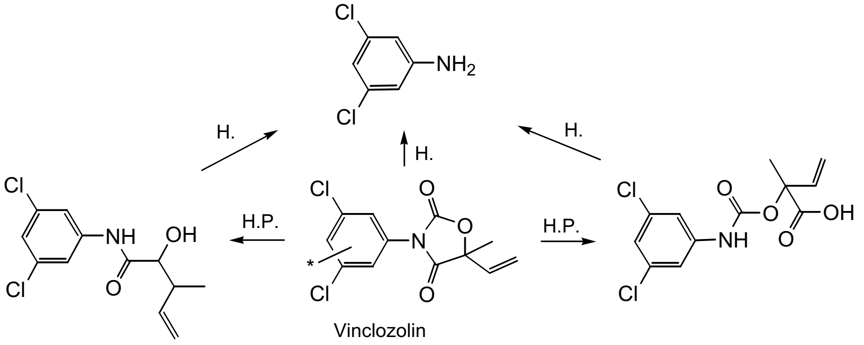
A protectant fungicide: control of fungal diseases caused by *Botrytis* spp., *Sclerotinia* spp., and *Monilia* spp. in grapes, fruits, vegetables, ornamentals, hops, rapeseed, and turfgrass

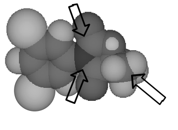
Hydrolysis
Buffer solutions of 0.01M prepared with sterilized deionized water by adjusting pH 4.5–8.3 at 13–35 °C[170]

Plant
Garden pea: *Pisum sativum* cv. Improved Laxton's Progress; red kidney bean: *Phaseolus vulgaris* cv. Red Kidney[171]

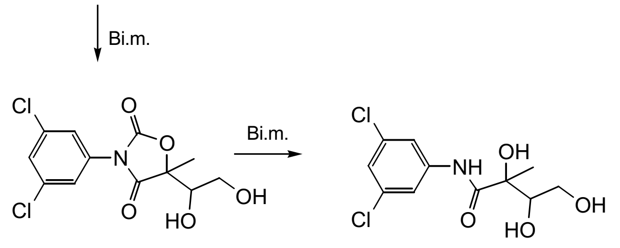
Bird/Microsome
Laying hens: brown hybrid strain/hen liver 9000 g supernatant[172]

On hydrolysis of vinclozolin in several aqueous buffers, the 2,4-oxazolidinedione ring opens to yield 2-[[(3,5-dichlorophenyl)carbamoyl]oxy]-2-methyl-3-butenoic acid and 3′,5′-dichloro-2-hydroxy-2-methylbut-3-enanilide independently. The conversion to the 3-butenoic acid is reversible, which leads to the formation of vinclozolin by cyclization. 3,5-Dichloroaniline is detected as a minor degradation product. None of the hydrolytic degradation products is detected in the directly treated plants. However, vinclozolin and two hydrolytic degradation products, but not 3,5-dichloroaniline, are detected in the leaves of pea and bean plants grown in nutrient solutions containing either vinclozolin or its degradation product, the 3-butenoic acid. The primary biotransformation products of vinclozolin in hen tissues *in vivo* and *in vitro* are derived from the parent compound by epoxidation of the vinyl group, followed by hydration of the epoxide intermediate, and hydrolytic cleavage of the heterocyclic ring.





O=C1N(C2=CC(Cl)=CC(Cl)
=C2)C(C(C=C)(C)O1)=O



12

Five-membered Heterocycles (fused)

Azafenidin

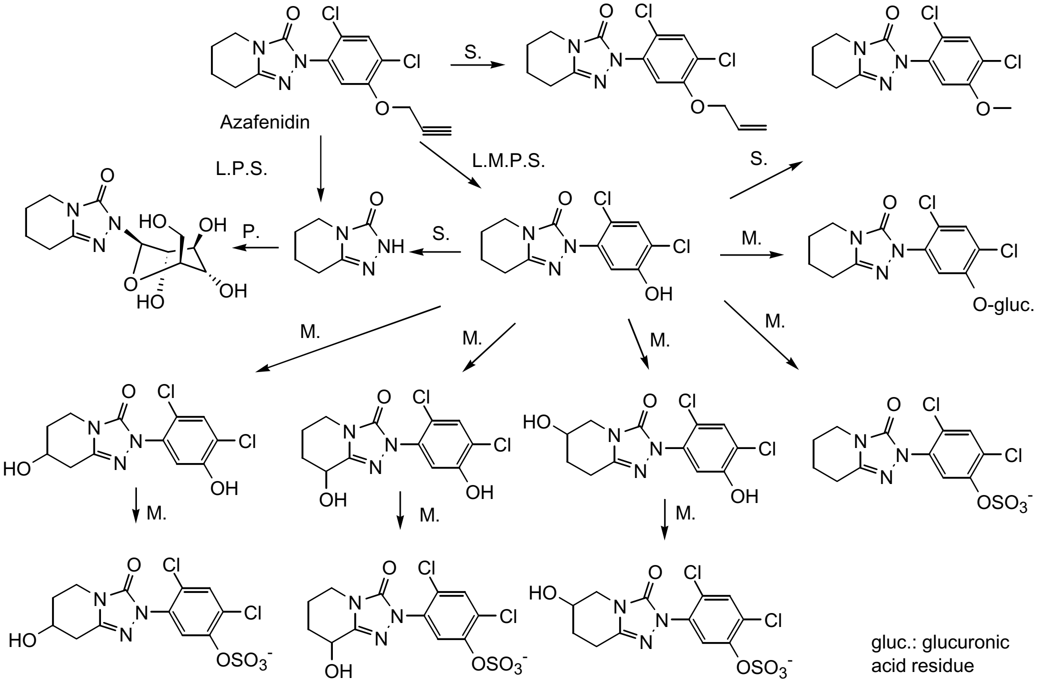
A herbicidal peroxidizer: control of broad-spectrum grass and broadleaf in citrus, grapes, and olive orchards

Light/Soil
Soil under simulated sunlight[173]

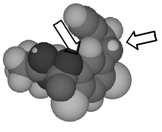
Plant
Citrus[174]
Grapes[175]

Mammal
Rats; lactating goats[176]

A common degradation reaction of azafenidin in light, plants and soil is *O*-dealkylation, and interesting minor reactions in soil are the subsequent methylation of the *O*-dealkylated degradation product and the reduction of the propynyl group under anaerobic conditions. In soil and light, azafenidin is also readily split to form the triazolinone heterocycle. Azafenidin is readily metabolized in rats and lactating goats through *O*-dealkylation, hydroxylation of the triazolinone ring in several positions, and glucuronide and sulfate conjugation.



gluc.: glucuronic acid residue



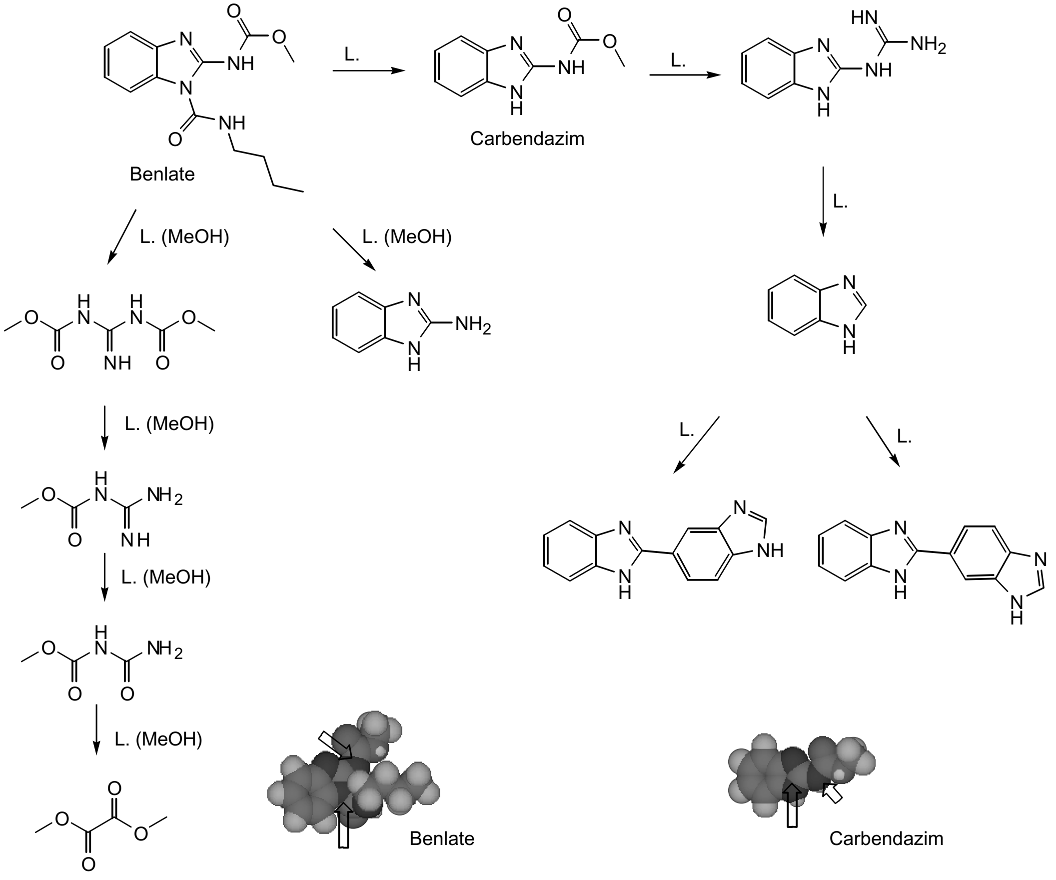
O=C2N(C3=CC(OCC#C)=C(Cl)
C=C3Cl)N=C1CCCCN12

Benlate (Benomyl) and Carbendazim

Fungicides

Light
UV irradiation in aqueous hydrochloric solution and in methanol solution containing methylene blue[177]

When benlate is degraded by the singlet oxygen photoreaction either in methanol or in aqueous hydrochloric solutions, carbendazim is identified as a major degradation product with the other nine degradation products from both reactions, including 2-guanidinobenzimidazole, benzimidazole, and 2,4′- and 2,5′-bibenzimidazoles which are identical to the photodegradation products of carbendazim by the singlet oxygen photoreaction in aqueous hydrochloric acid solution.



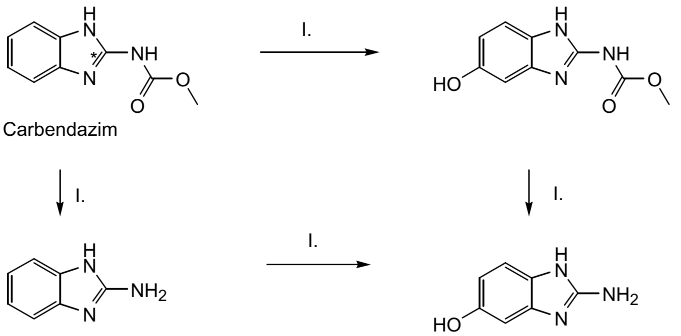
O=C(NCCCC)N2C1=CC=
CC=C1N=C2NC(OC)=O

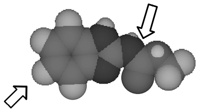
O=C(NC2=NC1=CC
=CC=C1N2)OC

Carbendazim

A systemic fungicide

Insect (mites) Bulb mites[178]	When the mites are exposed to ^{14}C-carbendazim, the major carbendazim metabolite identified in the bulb mites is 5-hydroxy-2-aminobenzimidazole. Low levels of 2-aminobenzimidazole and 5-hydroxy-2-benzimidazole carbamate are also identified.





O=C(OC)NC2=NC1
=CC=CC=C1N2

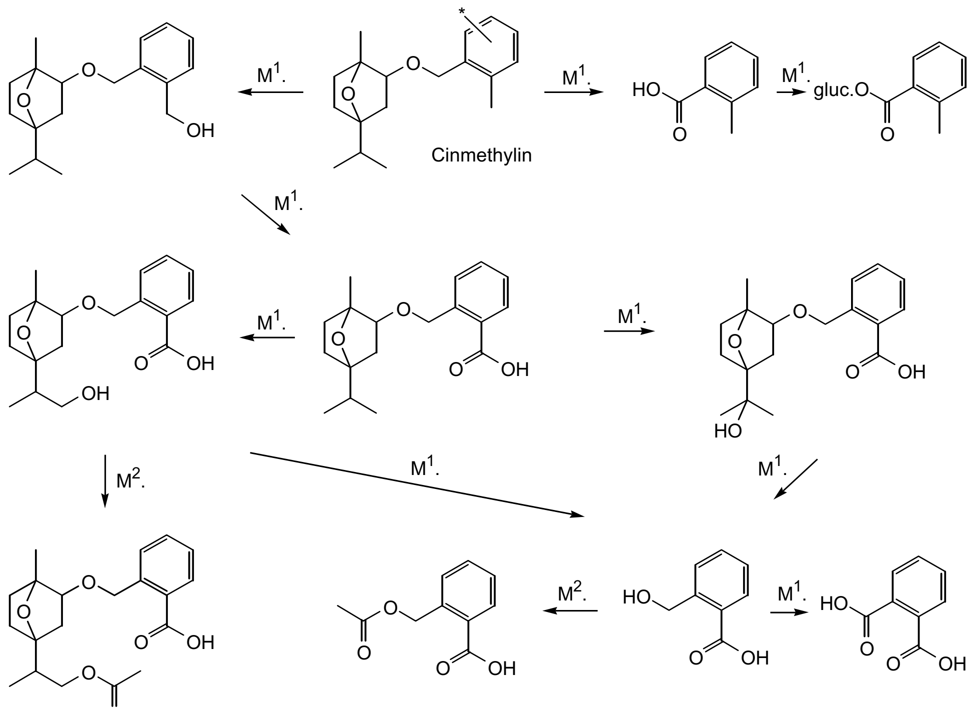
Cinmethylin

A broad-spectrum pre-emergent herbicide: control of various weeds in soybeans, peanuts, and cotton

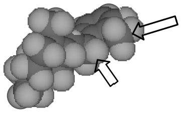
Mammal[1]
Male and female rats (Fischer 344, 10–16 week-old, 150–200 g)[179]

Mammal[2]
Male and female Fischer-344 albino rats (7 week-old, 175–200 g)[180]

When rats are administered ^{14}C-cinmethylin orally, the major route of its elimination is via urinary excretion. A complex degradation pattern of cinmethylin is observed and the metabolic pathways involve hydroxylation, oxidation at the benzyl and cineol portions, conjugation with glucuronic acid and glycine, and cleavage of the ether linkage. When rats are administered ^{14}C-cinmethylin by stomach incubation, two minor metabolites are identified as *o*-(acetoxymethyl)benzoic acid and 9-(acetoxymethyl)-α-carboxycinmethylin.



gluc.: glucuronic acid residue



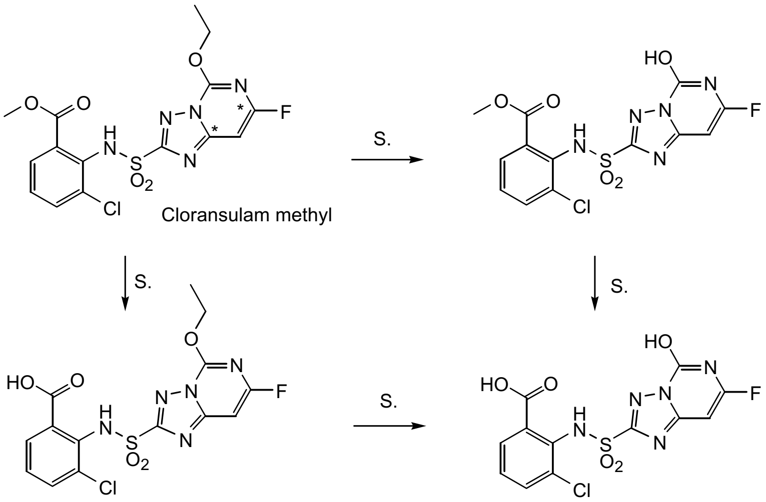
CC1(O2)C(OCC3=C(C)C
=CC=C3)CC2(C(C)C)CC1

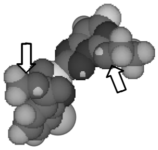
Cloransulam methyl

A herbicide: control of broadleaf weeds in soybean

Soil
Hanford loam: coarse-loamy (pH 7.0);
Cecil loamy sand (pH 6.3)[181]

When ^{14}C-cloransulam methyl is incubated with soils, the degradation proceeds via the hydrolysis of the ester group and *O*-de-ethylation on the triazolopyrimidine ring to yield the three identified metabolites, cloransulam, 5-hydroxycloransulam methyl, and 5-hydroxycloransulam. These metabolites are significantly less phytotoxic than the parent herbicide.





O=C(OC)C1=C(NS(C2=NN3C(C=C(F)
N=C3OCC)=N2)(=O)=O)C(Cl)=CC=C1

Fluthiacet methyl (KIH-9281)

A herbicide: promotion of the leakage of electrolytes from cotyledons of velvetleaf (*Abtilon theophtasti* Medic) and cotton (*Gossypium hirsutum* L.) and inhibition of chlorophyll biosynthesis in cotyledons of velvetleaf and cotton

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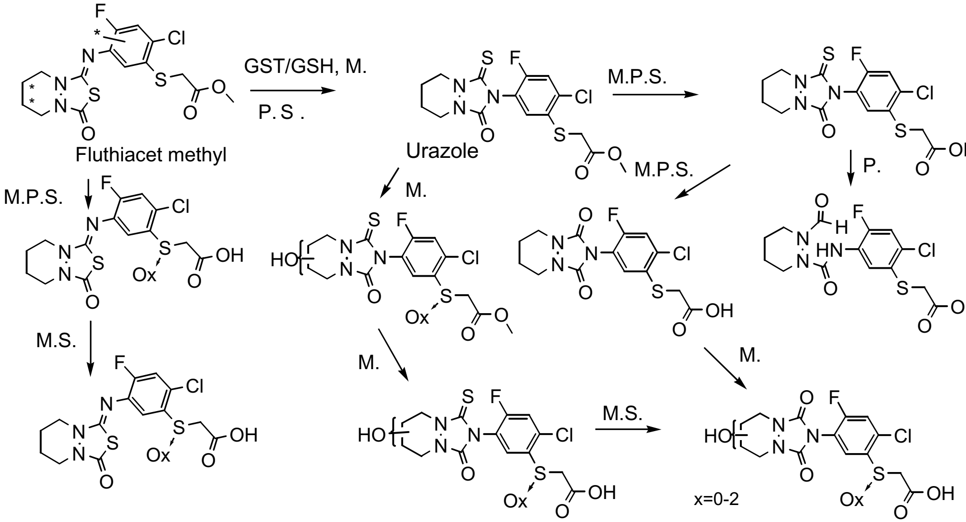
GST/GSH
Soybean; corn; rat liver microsomes; china jute[182]

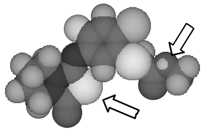
Plant
Soybean; onamomi[183]
Seeds of cotton (*Gossypium hirsutum* L. var. Cocher); corn (*Zea mays* L. var. Pioneer 3352); soybean [*Glycin max* (L.) Merr. var. Deltapine 506]; velvetleaf (*Abtilon theophrasti* Medic); cocklebur (*Xanthium strumarium* L.)[184]

Mammal/Soil
Female and male rats; upland and alluvial volcanic ash soil[185]

Fluthiacet methyl is converted to its isomer, urazole, by glutathione S-transferase (GST) and glutathione (GSH) from some plants and rat liver microsomes. Fluthiacet methyl inhibits Protox (protoporphyrinogen oxidase) activity after conversion to the corresponding urazole by GST and GSH. Fluthiacet methyl is chemically converted to urazole with a thiol anion in media by the nucleophilic reaction. It is also suggested that a free acid of urazole, desulfated urazole, and the oxidative ring-cleaved formyl degradation products result from hydrolysis with esterase from soybean seedlings.

When fluthiacet methyl is administered orally to rats in a single dose, 63–85% of the dose is excreted in the feces and 10–23% in the urine, respectively, after 48 h. The main metabolite is the isomer of fluthiacet methyl (urazole) which is also identified in the soil degradation products. Monohydroxylated products on the pyridazine ring are identified as metabolites by rats only.





FC1=CC(Cl)=C(SCC(OC)=O)C
=C1N=C3SC(N2CCCCN23)=O

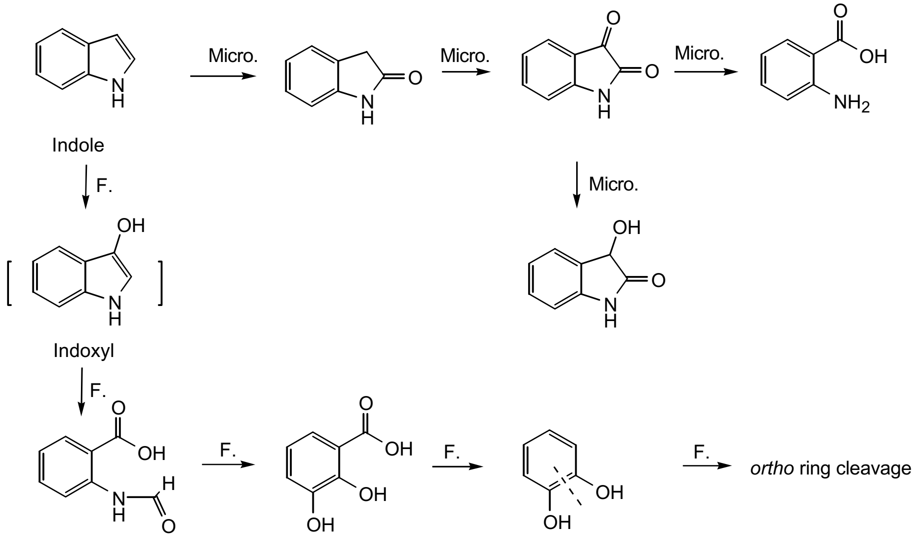
Indole

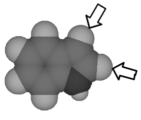
Not a pesticide

Fungus
Aspergillus niger[186]

Microorganism
Municipal sewage sludge (State College, PA) with a mineral salt medium[187]

The indole is metabolized in a mineral salt medium inoculated with 9% anaerobically digested nitrate-reducing sewage sludge, resulting in the sequential occurrence of four structurally related compounds: oxindole, isatine, dioxindole, and anthranilic acid. Indole is metabolized by fungus via indoxyl (3-hydroxyindole), *N*-formylanthranilic acid, anthranilic acid, 2,3-dihydroxybenzoic acid, and catecol, which is further degraded by an *ortho* cleavage.





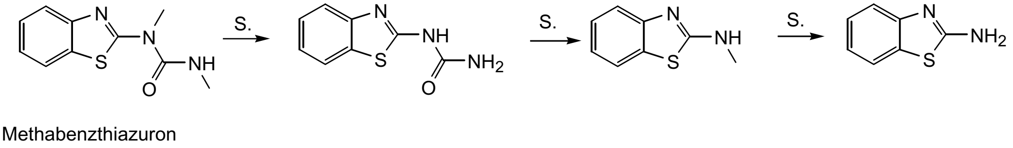
C12=CC=CC=C1C=CN2

Methabenzthiazuron

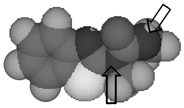
A herbicide: for grain and vegetables including peas

Soil
Melle loam (pH 6.1); Ingooigem sandy loam (pH 5.9); two kinds of Gembloux silt loam (pH 5.5 and 5.9)[188]

When methabenzthiazuron is presowing applied to the soil of pea fields, three degradation products are detected as (2-benzothiazoyl)urea, 2-(methylamino)benzothiazole and 2-aminobenzothiazole. The latter two amines represent a majority of the soil bound residues.



Methabenzthiazuron



CNC(N(C)C2=NC1
=CC=CC=C1S2)=O

3,4-(Methylenedioxy) methamphetamine

Not a pesticide: amphetamine-like subjective effects, empathy-enhancing properties

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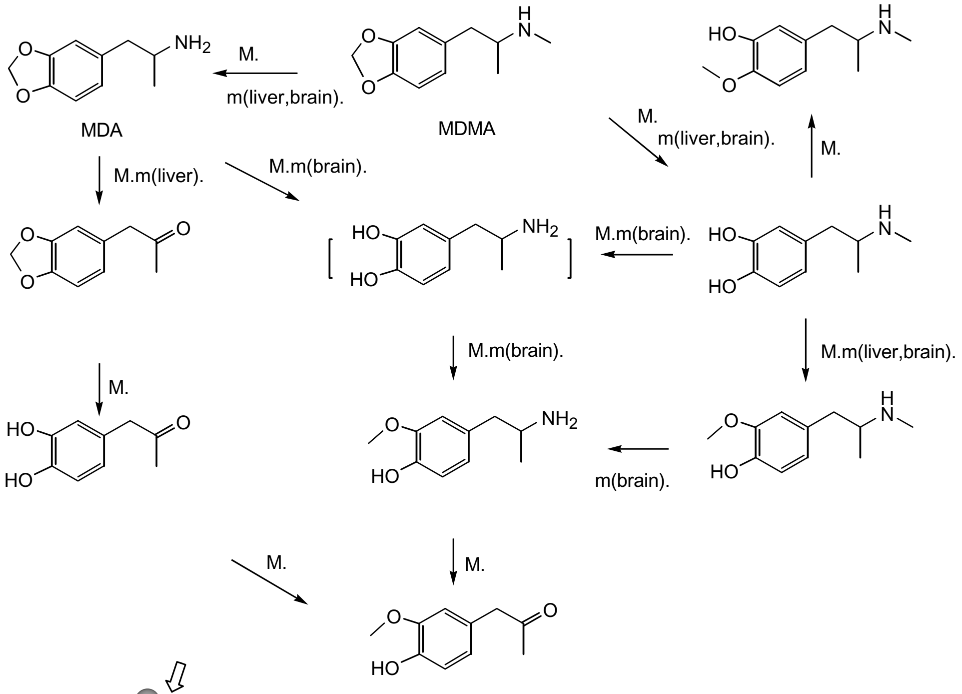
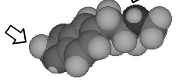
Mammal
Male Sprague–Dawley rats[189]

Microsome
The 10 000 g liver and brain supernatant of male Sprague–Dawley rats[189]

Four biotransformation pathways of 3,4-(methylenedioxy)methamphetamine (MDMA) in rats are identified as *N*-demethylation, *O*-dealkylation, deamination, and conjugation (*O*-methylation, *O*-glucuronidation, and/or sulfation). Specific MDMA metabolites identified are 3-hydroxy-4-methoxymethamphetamine, 4-hydroxy-3-methoxymethamphetamine, 3,4-dihydroxymethamphetamine, 4-hydroxy-3-methoxyamphetamine, 3,4-(methylenedioxy)amphetamine (MDA), (4-hydroxy-3-methoxyphenyl)acetone, [3,4-(methylenedioxy)phenyl]acetone, and (3,4-dihydroxyphenyl)acetone. MDMA is metabolized by





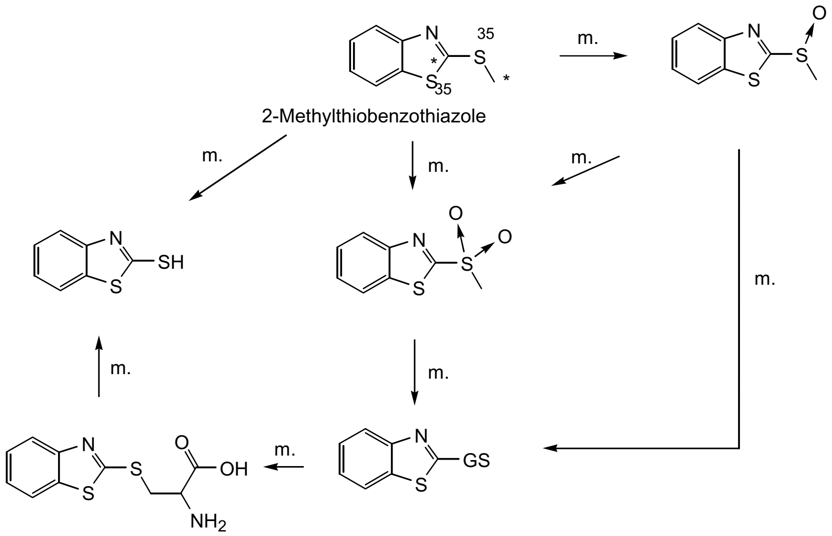
CC(NC)CC1=CC(OCO2)=C2C=C1

10 000 g rat liver supernatant to 4-hydroxy-3-methoxymethamphetamine, 3,4-dihydroxymethamphetamine, MDA, and [3,4-(methylenedioxy)phenyl]acetone. Also, the 10 000 g rat brain supernatant metabolizes MDMA to 4-hydroxy-3-methoxymethamphetamine, 3,4-dihydroxymethamphetamine, 4-hydroxy-3-methoxyamphetamine, and MDA.

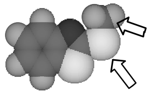
2-Methylthiobenzothiazole **Not a pesticide**

Microsome
Enzyme preparation of liver homogenates from male Sprague–Dawley rats (250–320 g)[190]

When 2-methylthiobenzothiazole and ^{35}S-labeled glutathione (GSH) are incubated with rat liver microsomes, both ^{35}S-labeled *S*-(2-benzothiazolyl)glutathione and 2-mercaptobenzothiazole are isolated from the reaction mixtures. Glutathione-*S*-transferase appears to be involved in the *S*-(2- benzothiazolyl)glutathione formation. Although sulfur is exchanged in this pathway, the net result of this pathway which involves oxidation of the methylthio group and GSH conjugation is an apparent *S*-demethylation of the methylthio group. Another *S*-demethylation pathway that does not involve GSH conjugation also functions *in vitro*.



GS: glutathione residue



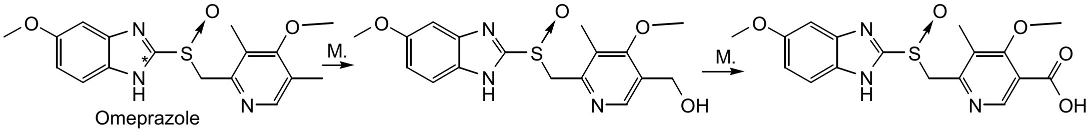
CSC2=NC1=CC=CC=C1S2

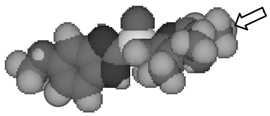
Omeprazole

Not a pesticide: use for antisecretory agent

Mammal
Ten healthy male humans (27–39 years old, 65–84 kg)[191]

When male humans are given ^{14}C-omeprazole orally, an average of 79% of the dose is recovered in the urine in 96 h. Omeprazole is completely metabolized and at least six metabolites are identified. Two major metabolites are hydroxyomeprazole and omeprazole acid.





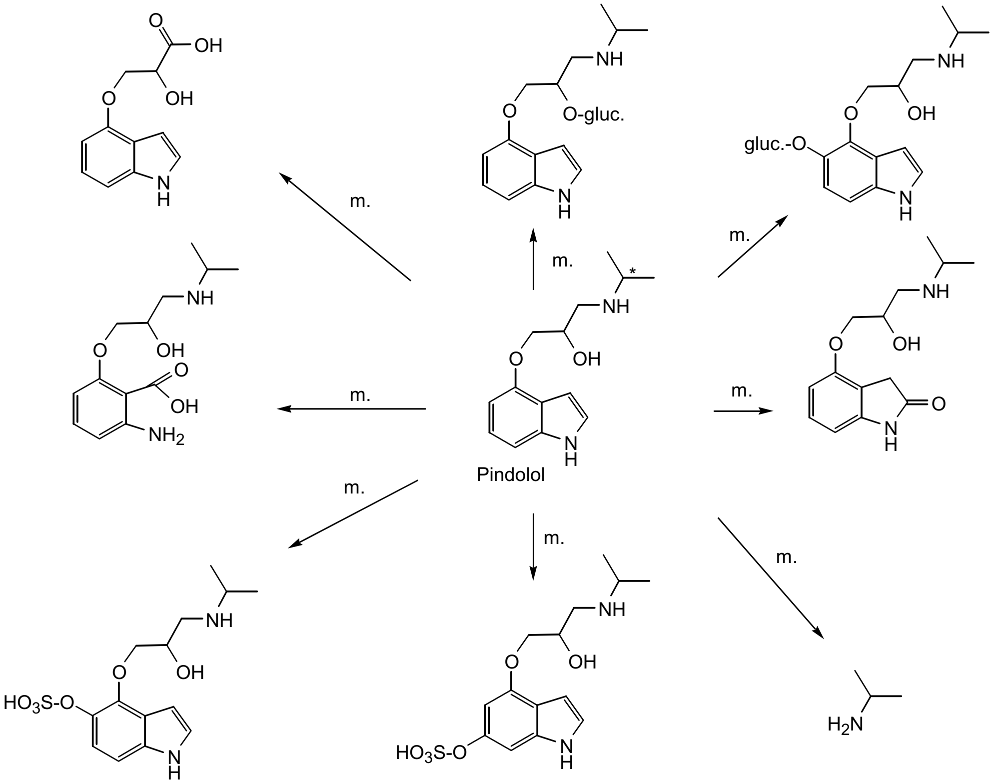
CC(C(OC)=C3C)=CN=C3C[S+]
([O-])C2=NC1=CC(OC)=CC=C1N2

Pindolol

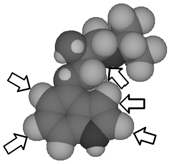
Not a pesticide: a β-adrenergic blocking drug

Microsome
Adult human hepatocytes from the liver of kidney transplantation donors[192]

Several metabolites of pindolol formed *in vitro* are detected after a 24 h incubation of human hepatocytes in both pure culture and co-culture by adding rat liver epithelial cells. The hepatocytes are able to oxidize the isopropyl amine moiety and the pyrrole ring of the indole moiety and conjugate pindolol as sulfates and glucuronides.



gluc.: glucuronic acid residue



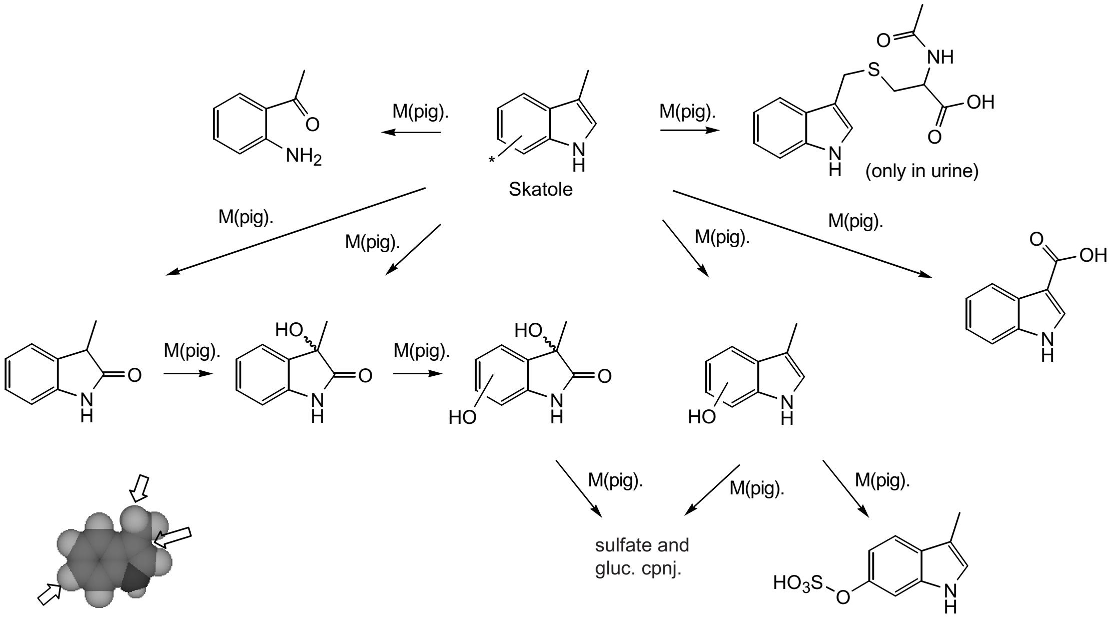
CC(C)NCC(COC1=C2
C(NC=C2)=CC=C1)O

Skatole

Not a pesticide: a contributor to boar taint

Mammal
A 5 month-old normal pig (84 kg)[193]

Three major metabolites of ^{14}C-skatole are found in the plasma/urine of pigs given skatole and are identified as 6-sulfatoxyskatole, 3-hydroxy-3-methyloxindole, and the mercapturate adduct of skatole, 3-[(*N*-acetylcysteine-*S*-yl)methyl]indole. For other pathways, see the references in the text.



CC2=CNC1=CC=CC=C12

13

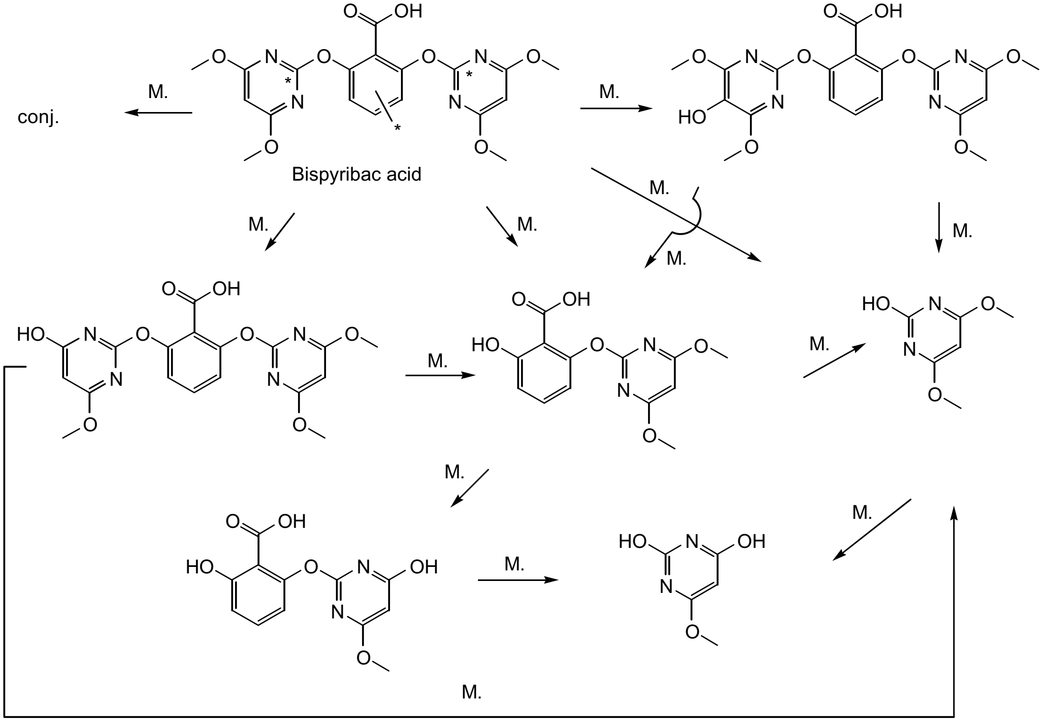
Six-/more membered Heterocycles

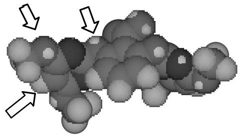
Bispyribac sodium

A herbicide: control of wide species of weeds, especially for barnyard grass, broadleaf signal grass, smart weed, cocklebur, and day flower

Mammal
Male and female Fischer F344/NSlc 7 week-old rats[194]

More than 90% of the radioactivity is excreted in rat urine 96 h after the rats are orally administered ^{14}C-bispyribac sodium. Most of the radioactivity detected in the urine, feces, liver, and plasma consists of unchanged bispyribac sodium. The metabolites identified are derived from hydroxylation on the pyrimidine ring, *O*-demethylation, cleavage of the ether linkage between pyrimidine and phenyl rings yielding 5-hydroxylated and mono-*O*-desmethylbispyribac acids, and salicylic acid and 2-pyrimidinole derivatives.





O=C(O)C1=C(OC3=NC(OC)=CC(OC)=N3)C=CC=C1OC2=NC(OC)=CC(OC)=N2

Bromacil

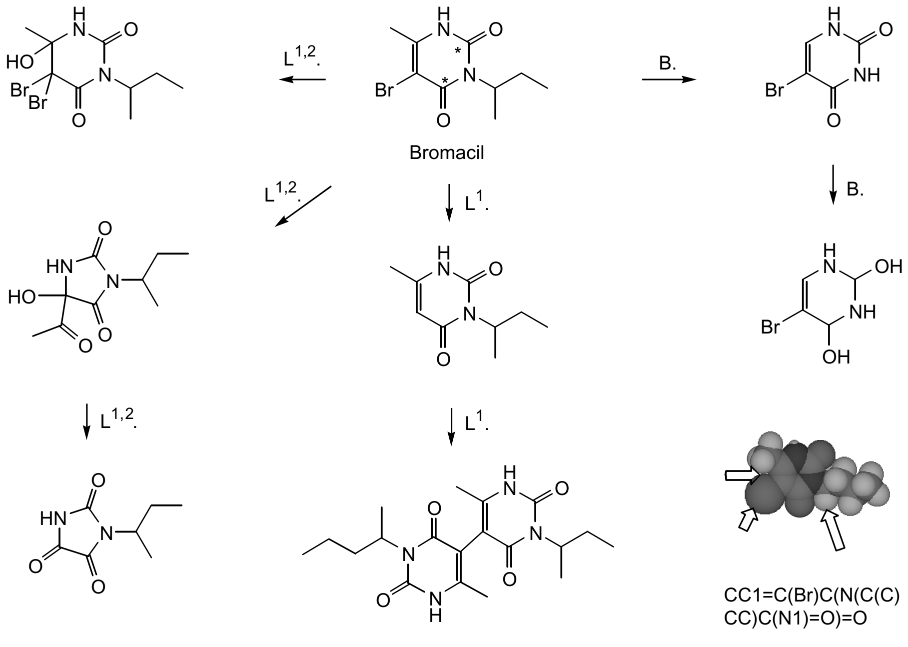
A herbicide: control of a wide range of annual and perennial grass, broadleaf weeds, and certain woody species on non-cropland areas

Bacteria
Pseudomonas sp. strain 50 235 isolated from soil[195]

Light[1]
Ozonization: a PCI model GL-1B ozone generator; UV irradiation: a Conrad-Hanovia (L5 464 000) low-pressure mercury lamp; sunlight with methylene blue[196]

Light[2]
A PCI model GL-1B ozone generator[197]

The microorganism, a *Pseudomonas* sp. isolated from soil by using bromacil as a sole source of carbon and energy, shows a potential to decontaminate soil samples fortified with bromacil under laboratory conditions. The degradation pathways of bromacil by the *Pseudomonas* sp. may include 5-bromouracil as an intermediate which leads to 5-bromodihydroxyluracil. Ozonization, UV photolysis, and sensitized sunlight photodegradation of aqueous bromacil solution lead to photodegradation products. The ozonization yields three main products which are identified as 3-*sec*-butyl-5-acetyl-5-hydroxyhydantoin, 3-*sec*-butylparabanic acid, and 3-*sec*-butyl-5,5-dibromo-6-hydroxyuracil. The main products of photoirradiation are 3-*sec*-butyl-6-methyluracil, its dimeric compound, and 3-*sec*-butyl-5-acetyl-5-hydroxyhydantoin.



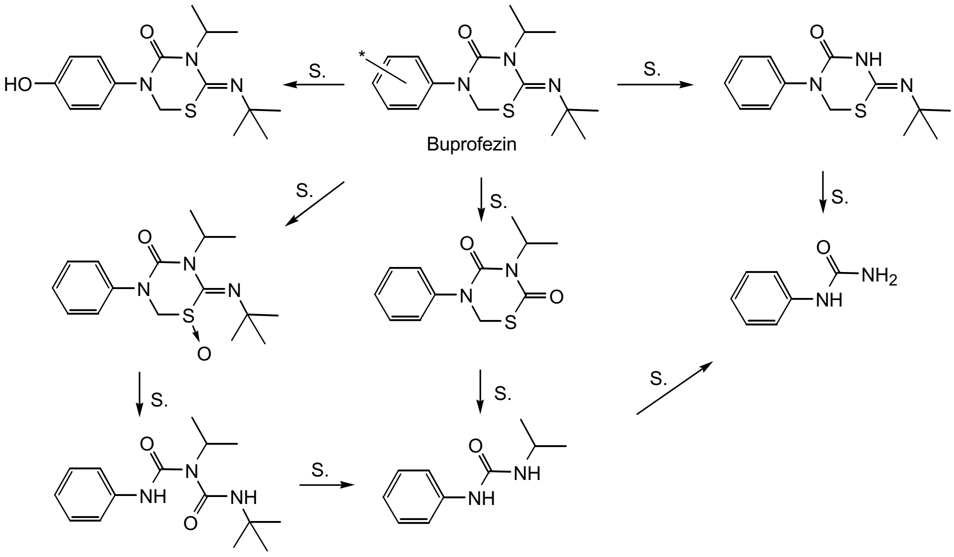
CC1=C(Br)C(N(C(C)CC)C(N1)=O)=O

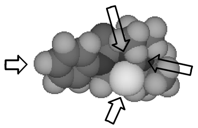
Buprofezin (Applaud)

An insect growth regulator: control of harmful insect pests including the brown planthopper, *Nilaparvata lugens* STAL, and the greenhouse whitefly, *Trialeurodes vaporariorum* WESTWOOD

Soil
Ehime paddy alluvial silty clay loam (pH 6.4/H_2O, 4.7/KCl); Ehime upland dilluvial sandy loam (pH 7.0/H_2O, 6.3/KCl)[198]

Buprofezin gradually decomposes in soils under flooded and upland conditions, with half-lives of 104 and 80 days, respectively. After 150 days, five degradation products are identified as 2-*tert*-butylimino-5-(4-hydroxyphenyl)-3-isopropylperhydro-1,3,5-thiadiazin-4-one, 3-isopropyl-5-phenylperhydro-1,3,5-thiadiazin-2,4-dione, 1-*tert*-butyl-3-ispropyl-5-phenylbiuret, 1-isopropyl-3-phenylurea, and phenylurea. As minor products, 2-*tert*-butylimino-5-phenylperhydro-1,3,5-thiadiazin-4-one or buprofezin sulfoxide are found in the flooded or in the upland soils. Since neither formation of $^{14}CO_2$ nor hydroxylation is observed in the sterile soils, buprofezin seems to have undergone complete mineralization in soils under both conditions through biological transformation by soil microorganisms.





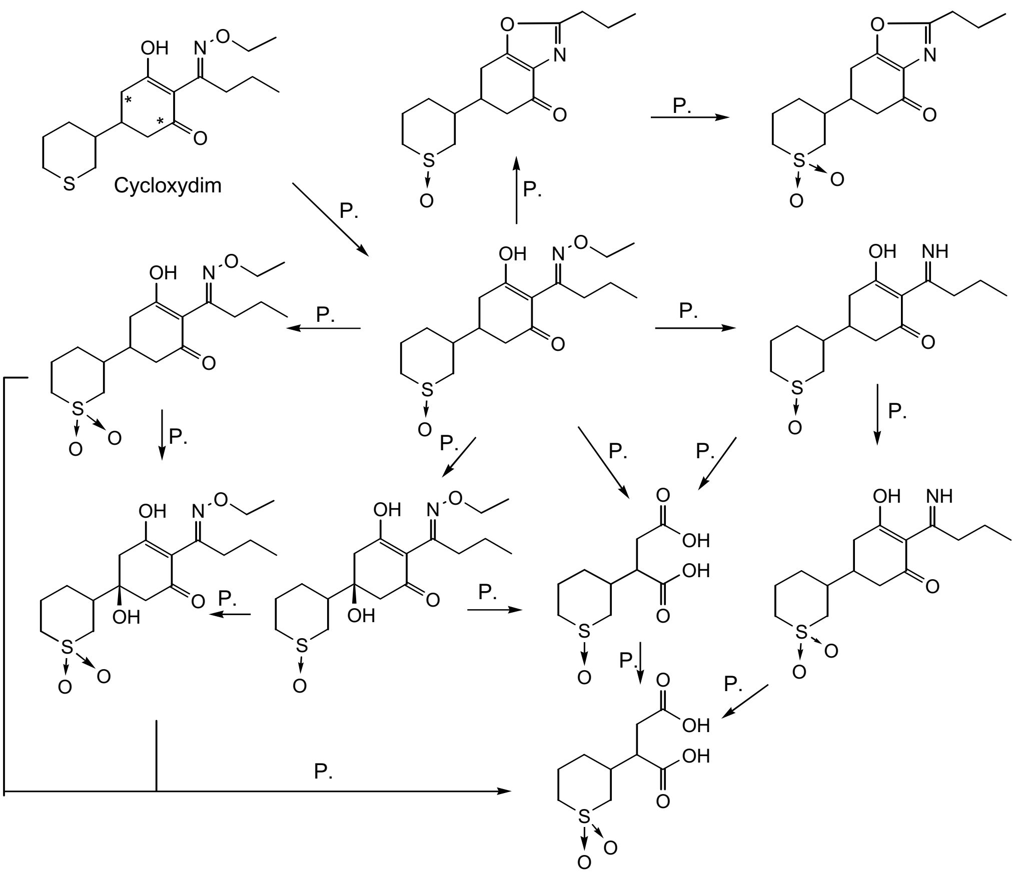
O=C1N(C2=CC=CC=C2)C
SC(N1C(C)C)=NC(C)(C)C

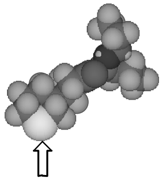
Cycloxydim

A post-emergent selective herbicide: control of both annual and perennial grasses in broadleaf plants

Plant
Soybean plants var. SRF 450[199]

Cycloxydim is rapidly metabolized in soybean plants, and four series of different types of metabolite in either free or conjugated form are identified. Transformation products are formed by chemical and/or enzymatic reactions involving a range of oxidation, a rearrangement, and cleavage of the cyclohexanone ring or ethoxyimino side chain.





OC(C2)=C(C(CCC)=NOC
C)C(CC2C1CSCCC1)=O

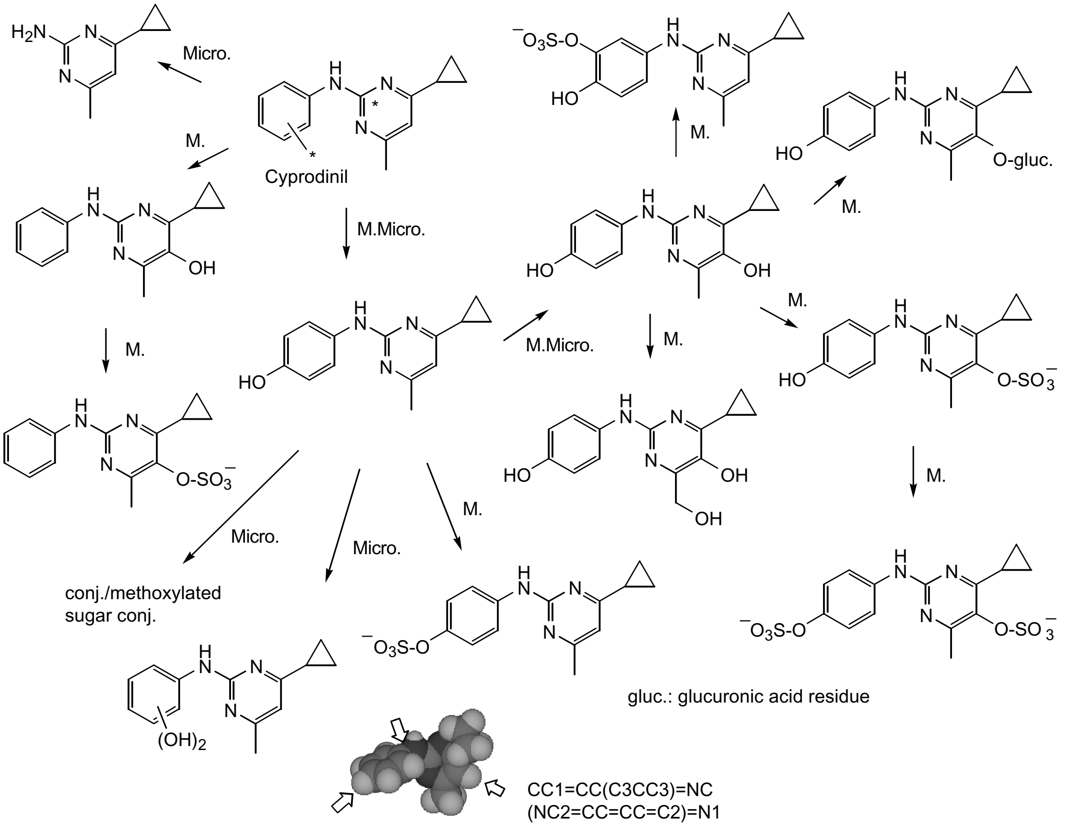
Cyprodinil

A fungicide: control of a variety of phytopathogenic fungi

Mammal
Male and female young rats (Tif: RAI SPF, 195–215 g)[200]

Microorganism
The microbial cultures from the American Type Culture Collection: *Cunninghamella echinulata* sp.; *Absidia pseudocylindraspora* sp.; *Streprotmyces griseus* sp.; etc.[201]

After single oral administration of ^{14}C-cyprodinil to rats, cyprodinil is rapidly eliminated principally in the urine. The pattern of the metabolic profile in the urine exhibits a significant sex-related difference with respect to the major metabolite. Males and females both produce *N*-4-(hydroxyphenyl)-4-cyclopropyl-5-hydroxy-6-methylpyrimidin-2-yl-amine. Female rats conjugate this dihydroxy metabolite with sulfate exclusively at the 5-hydroxypyrimidinyl moiety, while males form equal amounts of the monosulfate and disulfate conjugates. Ten cultures of 12 collected microorganisms produce a monohydroxylated metabolite and the filamentous fungus, *Beauveria bassiana* ATCC 7159, produces a methoxylated glycoside of the monohydroxylated metabolite. Dihydroxylated metabolites and a molecular cleavage product, 4-cyclopropyl-6-methyl-2-pyrimidinylamine, are detected in certain cultures.



gluc.: glucuronic acid residue

CC1=CC(C3CC3)=NC
(NC2=CC=CC=C2)=N1

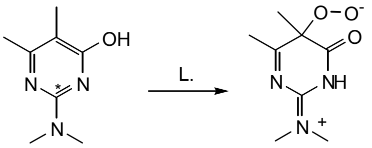
2-Dimethylamino-5,6-dimethylpyrimidin-4-ol

Not a pesticide: hydrolysis product of pirimicarb fungicide

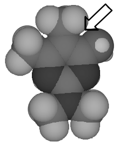
Photolysis

Solutions of methylene blue and 2-dimethylamino-5,6-dimethylpyrimidin-4-ol in $CDCl_3$ and d_6-acetone in an NMR sample tube with irradiation from a 600 W tungsten−halogen lamp while dry oxygen is bubbled through the solution[202]

Photolysis of solutions of methylene blue and 2-dimethylamino-5,6-dimethylpyrimidin-4-ol gives the photolysis product of the zwitterion which is stable in solution at ambient temperature. It is suggested that, when the zwitterion is in contact with the silica gel of the TLC plate, it gives some degradation products, and if the zwitterion were to be formed in the environment on photooxidation of the pyrimidinol, and in contact with plant and soil surfaces, then it would react or break down to give further products.



2-Dimethylamino-5,6-dimethylpyrimidin-4-ol



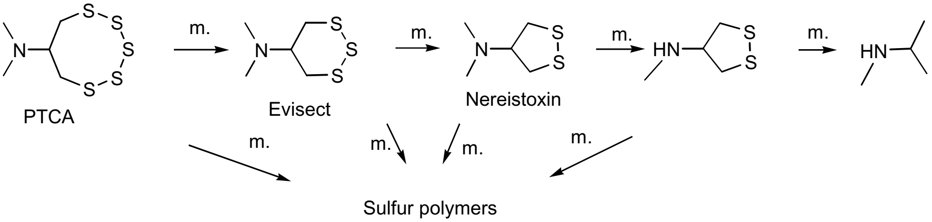
CN(C)C1=NC(O)=C(C)C(C)=N1

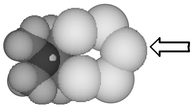
7-*N*,*N*-Dimethylamino-1,2,3,4,5-pentathiocyclooctane (PTCA)

An insecticide: control of rice striped borer (*Chilosuppressalis*) and yellow borer (*Tryporyza incertulas*) and cotton insects

Microsome
Liver microsomes of male Wistar rats (200–250 g) from Shanghai Center for Laboratory Animals[203]

By rat liver microsomal incubation, polythioalkane, 7-*N*,*N*-dimethylamino-1,2,3,4,5-pentathiocyclooctane (PTCA) is metabolized to yield six major metabolites which are identified as evisect, nereistoxin, monomethyl nereistoxin, 2-methylaminopropane, and sulfur polymers. The process is catalyzed mainly by enzymatic reactions, such as desulfuration and demethylation (see cartap, page 83).





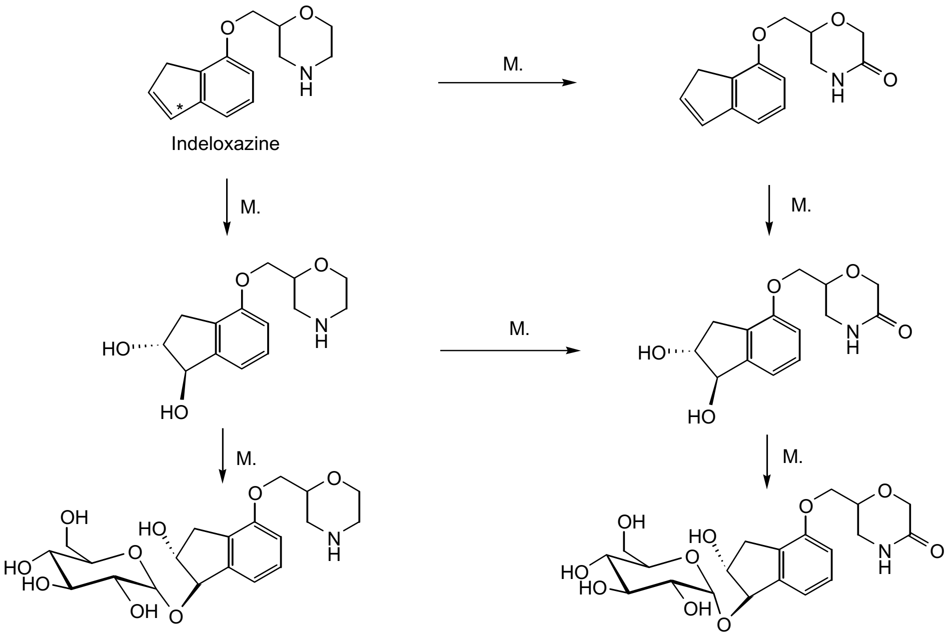
CN(C)C1CSSSSSC1

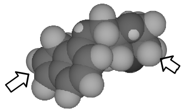
Indeloxazine hydrochloride

Not a pesticide: a pharmaceutical

Mammal
Male Sprague–Dawley rats (200–235 g)[204]

After oral administration of indeloxazine hydrochloride to rats, two conjugates, which are labile to α-glucosidase hydrolysis but refractory to β-glucosidase, are isolated from the urine and identified as α-D-glucopyranosides of *trans*-4-(2-morpholinylmethoxy)-1,2-indandiol and *trans*-6-[[(1,2-dihydroxy-4-indanyl)oxy]-methyl]-3-morpholinone.





C1(CC=C3)=C3C=CC
=C1OCC2CNCCO2

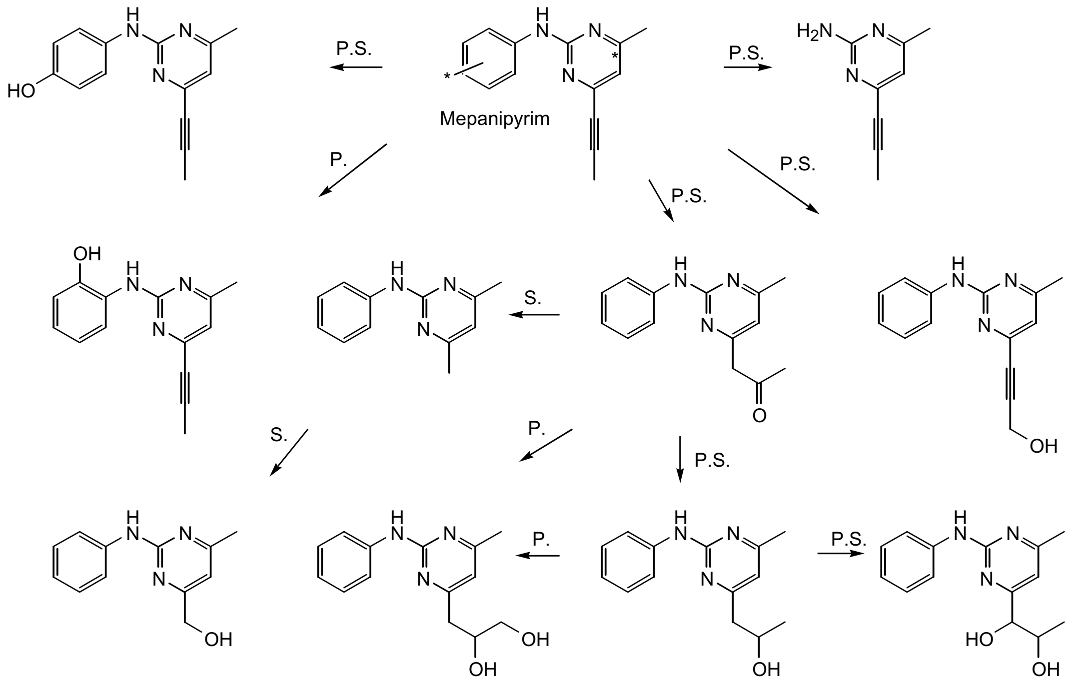
Mepanipyrim

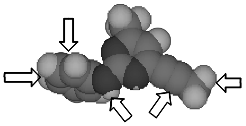
A fungicide: control of gray mold, scab, and brown rot caused by *Botrytis cinerea*, *Venturia inaequaris* and *Monilinia fructicola*, respectively

Plant
Tomato seedlings: *Lycopersicum esculentum* MIIL[205]

Soil
Kikugawa alluvial (pH 5.72/H_2O); Ushiku volcanic ash (pH 4.69/H_2O)[206]

By tomato seedlings, ^{14}C-mepanipyrim is biotransformed via the pathways including elimination of the phenyl group, hydroxylation of the propynyl moiety, and hydroxylation at the phenyl ring to yield several kinds of metabolite, and 2- and 4-[4-methyl-6-(1-propynyl)pyrimidin-2-ylamino]phenols, 1-(2-anilino-6-methylpyrimidin-4-yl)-2-propanol, and 4-methyl-6-(1-propynyl)pyrimidin-2-ylamine are tentatively identified as major metabolites. In soils under laboratory conditions, ^{14}C-mepanipyrim undergoes degradation to give the degradation products and the main pathway is elimination of the phenyl group.





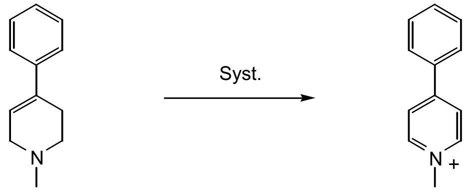
CC1=NC(NC2=CC=CC=C2)=NC(C#CC)=C1

N-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine

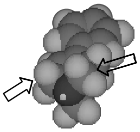
Not a pesticide: a neurotoxin

System
Cell culture of rat pheochromocytoma PC12h cells[207]

N-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in a rat pheochromocytoma cell line is oxidized to give the *N*-methyl-4-phenylpyridinium ion.



MPTP



CN1CC=C(C2=CC=CC=C2)CC1

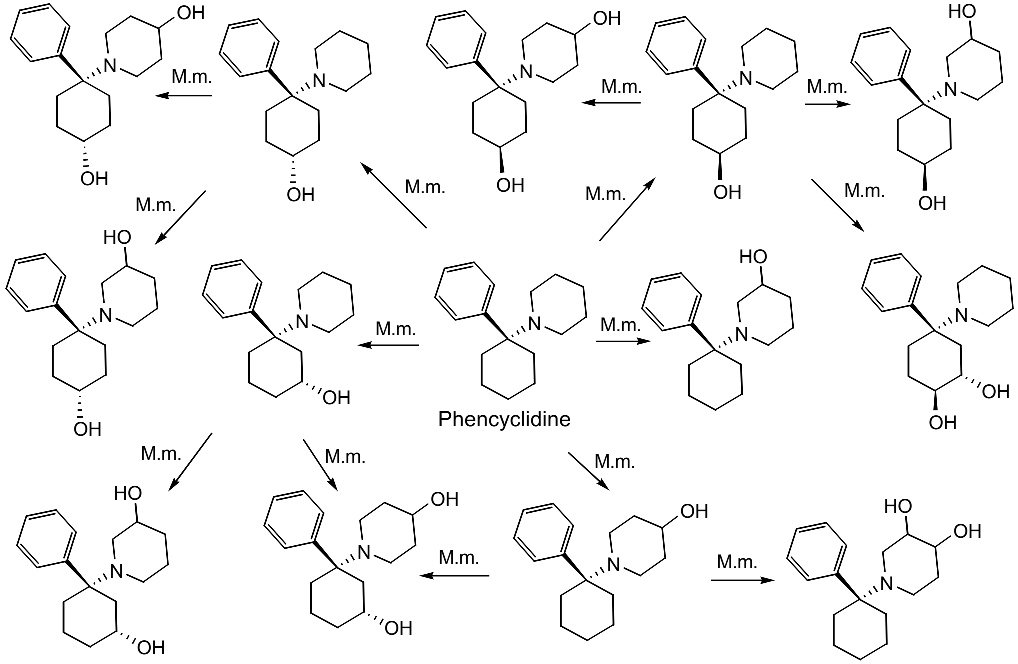
Phencyclidine

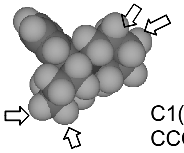
Not a pesticide: a non-competitive *N*-methyl-D-aspartate antagonist

---

Mammal/Microsome
Six male mice (albino HAD:ICR-BR, 30–35 g); two male Sprague–Dawley rats (200–220 g)/liver microsome preparations[208]

When mice and rats are administered phencyclidine intraperitoneally, several hydroxylated metabolites are identified in the urine. A new metabolite, 1-phenyl-1-(1-piperidinyl-3-ol)cyclohexane, is identified in the urine and liver microsomal preparations.





C1([C@]2(N3CCCCC3)
CCCCC2)=CC=CC=C1

---

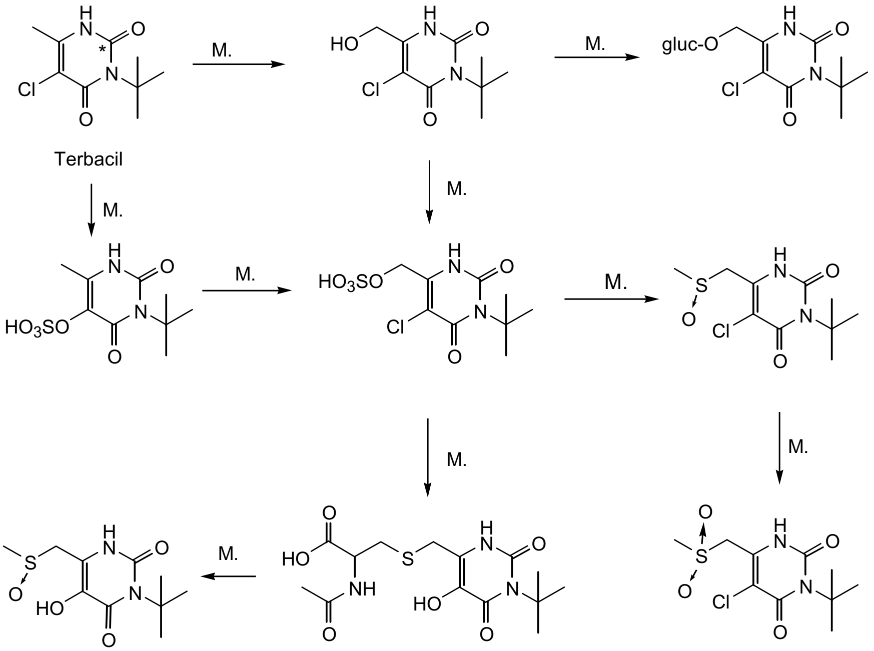
* Note: Three different hydroxylated metabolites are assayed by microsomal preparations of human liver and placenta[209]

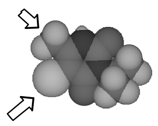
Terbacil

A selective herbicide: control of many annual and some perennial weeds on crops

Mammal
Male and female adult CD rats
(ca 200 g)[210]

When rats are administered terbacil orally, the primary biotransformation products of terbacil in the urine are derived from hydroxylation of the 6-methyl group and are identified as the aglycone, glucuronide, and sulfate. The other conjugated metabolite is the mercapturic acid conjugate of the 6-methyl substituent. Minor metabolites are identified as sulfoxides and sulfone at the 6-methyl substituent of terbacil.





CC1=C(Cl)C(N(C(C)(C)C)C(N1)=O)=O

14

Six-/more membered Heterocycles (fused)

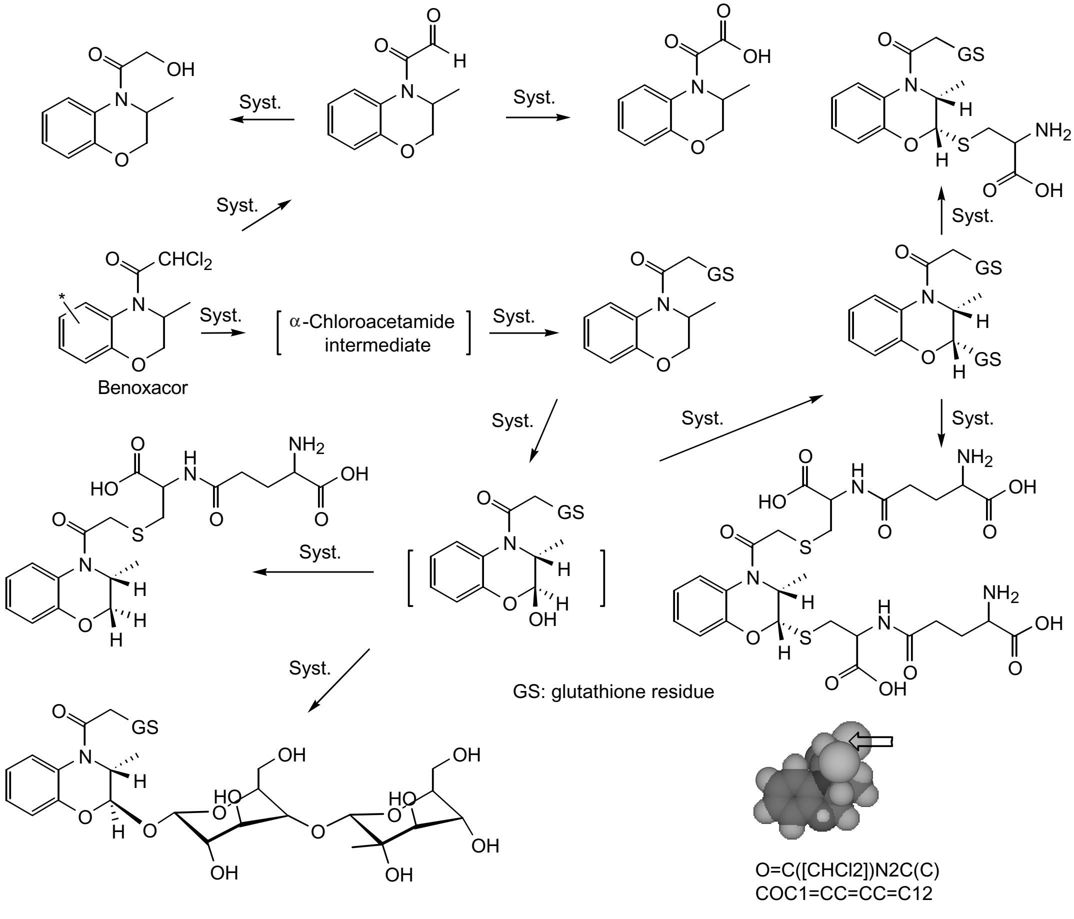
Benoxacor

A herbicide safener: protection of seedlings against toxic effects of the α-chloroacetanilide herbicide, metolachlor, use in maize

---

System
Cell cultures of corn: *Zea Mays* cv. Black Mexican Sweet[211, 212]

In cell suspension cultures of corn (*Zea mays*) with ^{14}C-benoxacor, benoxacor is rapidly metabolized to six detectable metabolites within 0.5 h. Twelve metabolites are detected in extracts from the treated cells for 24 h. Of the three predominant metabolites present, two metabolites are the catabolic formylcarboxamide and carboxycarboxamide derivatives of benoxacor. The third one is the mono glutathione conjugate of benoxacor. This metabolite consists of a single glutathione molecule linked via the cysteinyl sulfhydryl group to the *N*-dichloroacetyl α-carbon of benoxacor. A catabolic α-hydroxyacetamide derivative is detected as well as its amino acid



GS: glutathione residue

O=C([CHCl2])N2C(C)
COC1=CC=CC=C12

conjugates either containing glutathione residue or presumably derived from the glutathione residue. A disaccharide conjugate is identified as *S*-(*O*-diglycoside)glutathione conjugate.

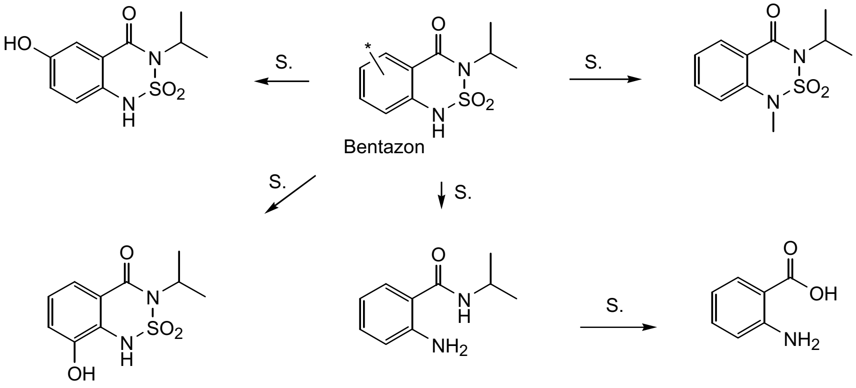
Bentazon

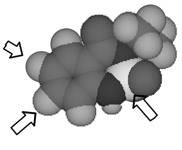
A post-emergent herbicide: control of broadleaf weeds and sedges in soybeans

Soil

Dundee silt loam (history of bentazon application, pH 5.67, 5.41); Drummer silty clay loam (pH 4.52, 6.25); Miami silt loam (pH 6.45, 6.58); Saybrook silt loam (pH 5.01, 6.31); Dundee silt loam (no history of bentazon application, pH 5.79, 5.60)[213]

^{14}C-Bentazon degrades in soils under conventional tillage and no-tillage (3–18 years) with varying histories of bentazon application. The half-life for bentazon degradation ranges from 4.6 to 49.5 days; half-lives for some no-tillage soils with the longest histories of application are lower than those of conventional tillage soils. Half-lives for soils with no bentazon history are 3–11 times higher than the half-lives of those previously exposed to bentazon. *N*-Methylbentazon is the most consistently observed metabolite. The other metabolites identified in soils result from hydroxylation on the phenyl ring and the cleavage of the benzothiadiazine ring, yielding 6- and 8-hydroxybentazons and anthranilic acid via 2-amino-*N*-isopropylbenzamide.





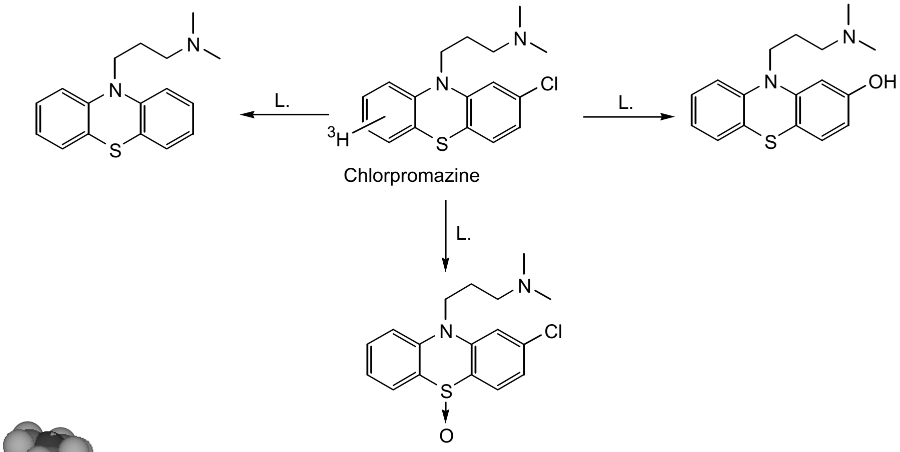
O=C(C1=CC=CC=C1N
2)N(C(C)C)S2(=O)=O

Chlorpromazine

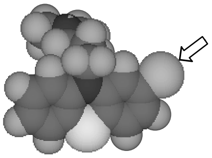
Not a pesticide: neuroleptic drug

Photolysis
Irradiation with UV-A on the shaven skin of female albino Wistar rats[214]

The *in vivo* photodegradation of chlorpromazine in rat skin exposed to UV-A results in the formation of promazine and 2-hydroxypromazine in irradiated rats, but not in the skin of rats kept in the dark. Chlorpromazine sulfoxide is a major metabolite of chlorpromazine, found in smaller quantity in the skin of irradiated rats compared with those kept in the dark. Chlorpromazine sulfoxide is not a photoproduct of chlorpromazine under the experimental conditions.



Chlorpromazine sulfoxide
(not a photoproduct)



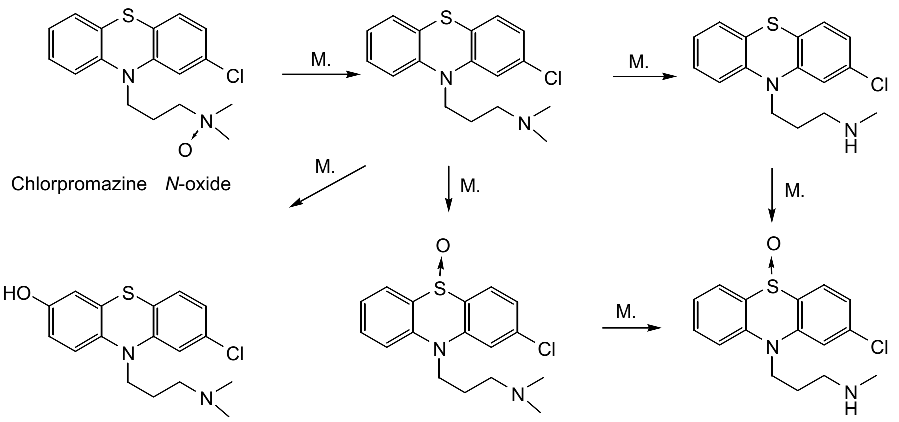
CN(C)CCCN2C3=C(C=CC
(Cl)=C3)SC1=CC=CC=C12

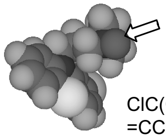
Chlorpromazine *N*-oxide

Not a pesticide: a metabolite in patients under chronic treatment with chlorpromazine (a pharmaceutical)

Mammal
Female Lewis rats (200–250 g)[215]

When female rats are administered chlorpromazine *N*-oxide orally, the metabolites identified in both urine and feces are chlorpromazine, 7-hydroxychlorpromazine, chlorpromazine sulfoxide, *N*-desmethylchlorpromazine and *N*-desmethylchlorpromazine sulfoxide. Chlorpromazine *N*-oxide and any metabolite that retains the intact *N*-oxide function, such as chlorpromazine *N*,*S*-dioxide, cannot be identified in any of the extracts.





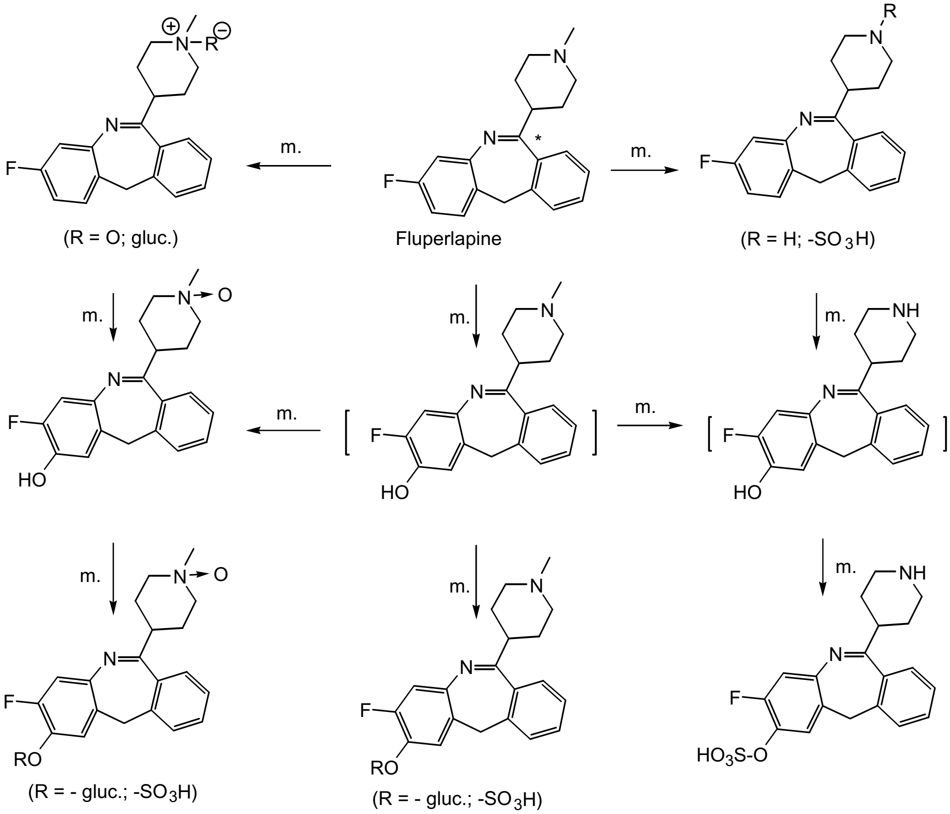
ClC(C=C3)=CC2=C3SC1=CC
=CC=C1N2CCC[N+](C)([O-])C

Fluperlapine

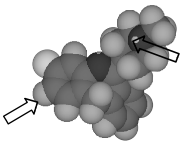
Not a pesticide: a drug showing neuroleptic properties

Microsome
Adult human hepatocytes from the liver of kidney transplantation donors[216]

Seven metabolites of fluperlapine are detected by culturing with incubation of human hepatocytes. The major metabolite is the *N*-oxide and the formation of sulfates remains high although decreases with time in the culture. Two glucuronides found *in vivo* are not detected in any of the cultures.



gluc.: glucuronic acid residue



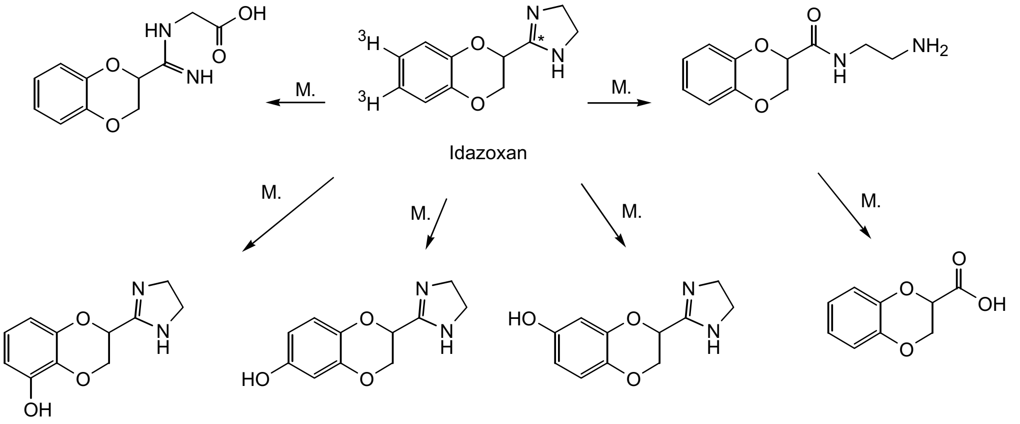
CN(CC4)CCC4C2=NC1=CC
(F)=CC=C1CC3=C2C=CC=C3

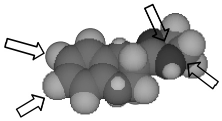
Idazoxan

Not a pesticide: a selective antagonism at α_2-adrenoreceptors

Mammal
Male and female Sprague–Dawley rats; male Lister hooded rats[217]

When rats are administered radio-labeled idazoxan orally, the biotransformation of idazoxan is by hydroxylation at the 6- and 7-positions to form phenolic metabolites, which are excreted as glucuronide and sulfate metabolites in the urine, but unconjugated in the feces. Other minor metabolic pathways are 5-hydroxylation or oxidative degradation of the imidazoline ring, but these pathways are of quantitatively minor importance in rats.





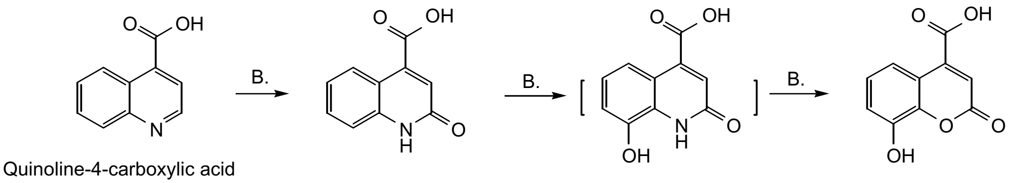
C1(OC3)=CC=CC=C1OC3C2=NCCN2

Quinoline-4-carboxylic acid

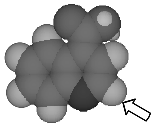
Not a pesticide

Bacterium
Microbacterium sp.[218]

The bacterium which is isolated from soil enrichment culture degrades quinoline-4-carboxylic acid to give the two identified metabolites 2-oxo-1,2-dihydroquinoline-4-carboxylic acid and 8-hydroxy-2-oxo-2*H*-benzopyran-4-carboxylic acid.



Quinoline-4-carboxylic acid



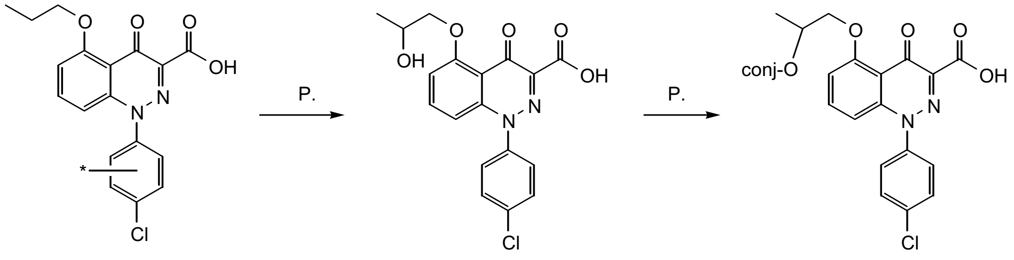
O=C(O)C2=CC=NC1=CC=CC=C12

SC-1271

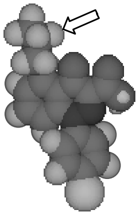
A pollen suppressant: chemical hybridizing agent for wheat and other small grains

Plant
Wheat: *Triticum aestivum* L. var. *Yecora rojo*[219]

When SC-1271 is applied to the penultimate or flag leaf at the stage when the floral spike of wheat is about 2 cm in length, wheat metabolizes SC-1271 by ω-1 hydroxylation of the propoxy group. The hydroxylated metabolite is more slowly converted to one or more β-glucosides, which eventually become the major metabolites.



SC-1271



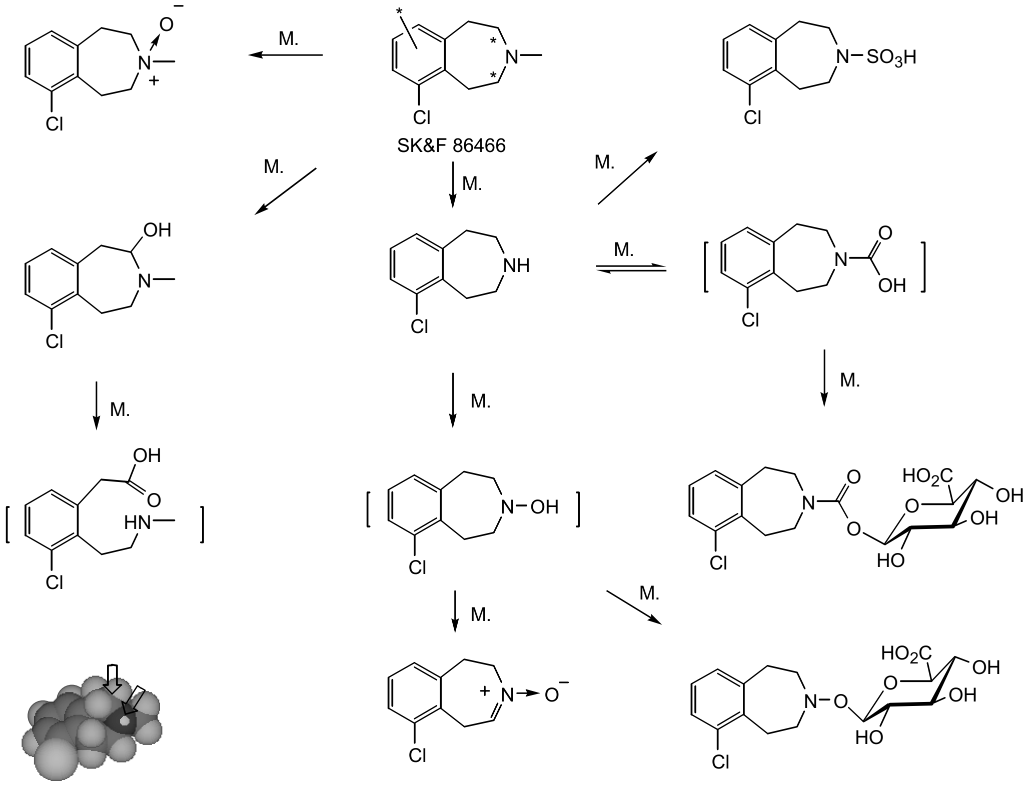
CC(O)COC(C=CC=C1N(N=C2C(O)
=O)C3=CC=C(C=C3)Cl)=C1C2=O

SK&F 86466

A pharmaceutical: a potent α_2-adrenoceptor antagonist

Mammal
Female beagle dogs from Marshall Res. Animals[220]

When ^{14}C-SK&F 86466 is administered to dogs, the metabolites excreted in the urine are identified. The parent compound undergoes oxidation to yield *N*-oxide or *N*-demethylation resulting in the primary metabolite, 6-chloro-2,3,4,5-tetrahydro-1*H*-3-benzazepine, which further undergoes *N*-sulfoconjugation to yield the corresponding sulfonate. Two glucuronide conjugates derived from the desmethyl metabolites are identified. The pathways leading to either ring opening or formation of a nitroene do not occur to any major extent in this species.



CN2CCC1=C(Cl)C=CC=C1CC2

15

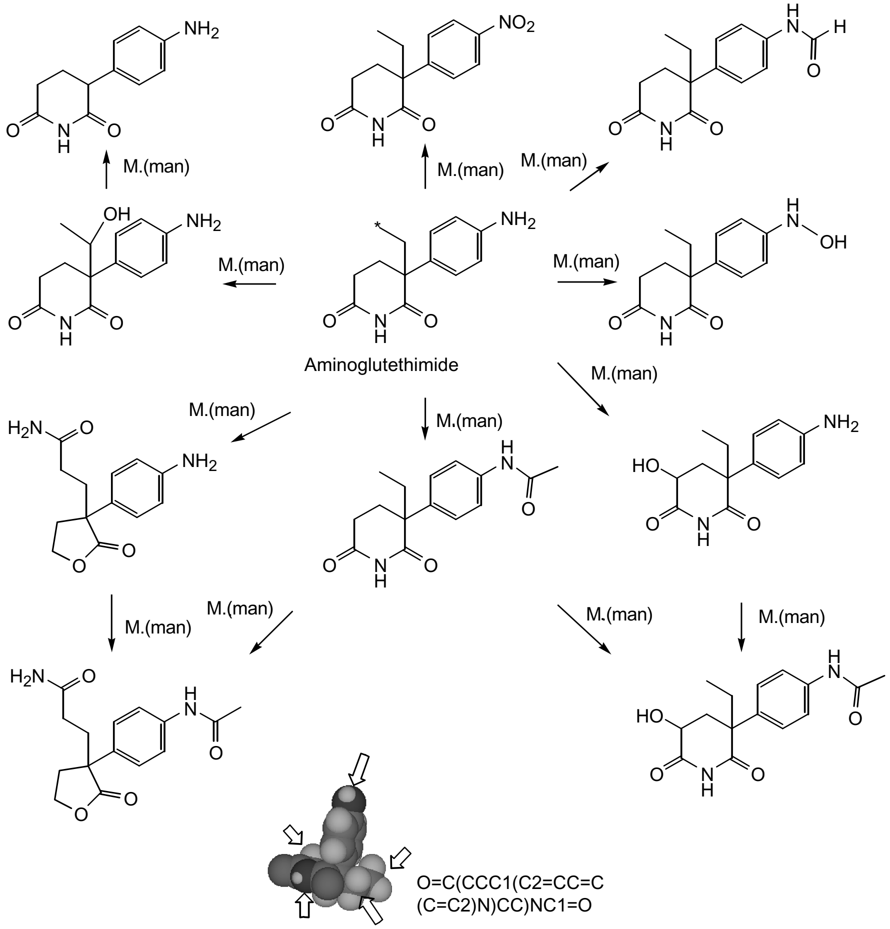
Imides

Aminoglutethimide

Not a pesticide: for pharmaceutical use

Mammal
Male and female albino Wistar rats; male Dunkin–Hartley guinea pigs; male New Zealand white rabbits; male beagle dogs; human volunteers[221]

Following administration of a single oral dose of ^{14}C-aminoglutethimide to rats, guinea pigs, rabbits, and man, more than 89% of the dose is excreted in urine and feces within 72 h, and dogs eliminate only 51% in this time. Extensive metabolism occurs in all species, with *N*-acetylaminoglutethimide being the major metabolite except for dogs and man. In the latter two species, the unchanged drug is the main product excreted. As shown in the pathways, it appears that aminoglutethimide is metabolized by several pathways in man and, of the ten metabolites, only two are present in any quantity, namely *N*-acetylaminoglutethimide and *N*-hydroxyaminoglutethimide, the latter increasing during the course of treatment.



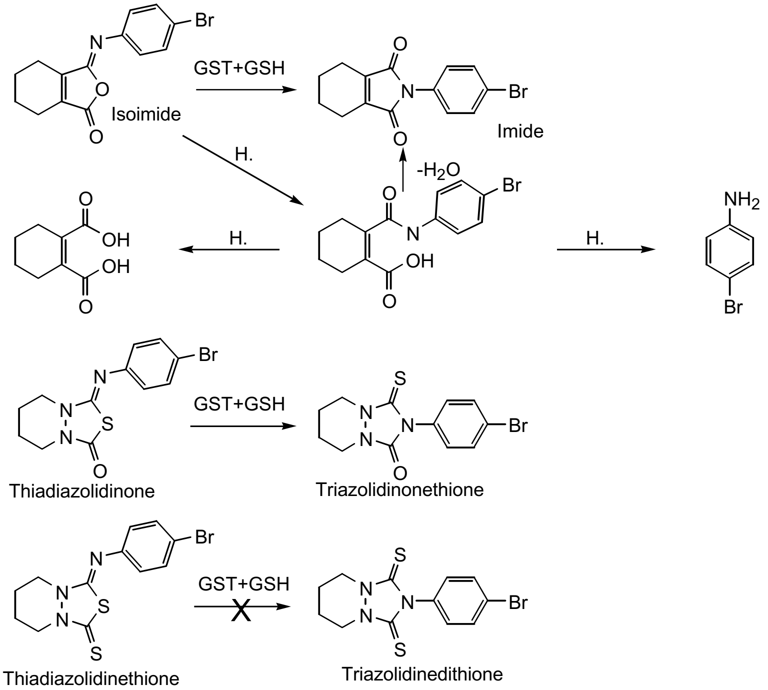
O=C(CCC1(C2=CC=C
(C=C2)N)CC)NC1=O

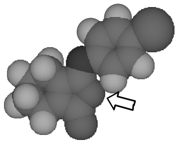
N-(Bromophenyl)-3,4,5,6-tetrahydroisophthalimide and 5-(4-Bromophenylimino)-3,4-tetramethylene-1,3,4-thiadiazolidin-2-one

A herbicidal peroxidizer

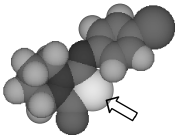
Hydrolysis/GST/GSH
Glutathione *S*-transferase; reduced glutathione[222]

A herbicidal peroxidizer, *N*-(bromophenyl)-3,4,5,6-tetrahydroisophthalimide (isoimide) is isomerized to *N*-(4-bromophenyl)-3,4,5,6-tetrahydrophthalimide (imide) directly and rapidly in the presence of equine

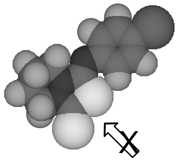




O=C(OC2=NC3=CC=C
(Br)C=C3)C1=C2CCCC1



O=C(N2N1CCCC2)SC1
=NC3=CC=C(C=C3)Br



S=C(S3)N1CCCCN1C3
=NC2=CC=C(Br)C=C2

N-(Bromophenyl)-3,4,5,6-tetrahydroisophthalimide and 5-(4-bromophenylimino)-3,4-tetramethylene-1,3,4-thiadiazolidin-2-one

(continued)

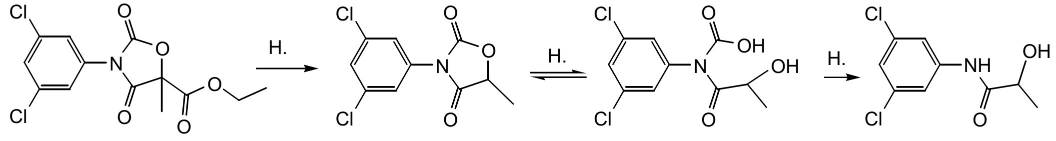
glutathione *S*-transferase (GST) with reduced glutathione (GSH), and is also converted into the imide via 4-bromophenyl-3,4,5,6-tetrahydrophthalamic acid by hydrolysis. GST converts 5-(4-bromophenylimino)-3,4-tetramethylene-1,3,4-thiadiazolidin-2-one (thiadiazolidinone) into its isomer 4-bromophenyl-1,2-tetramethylene-1,2,4-triazolidin-3-one-5-thione (triazolidinonethione) but hardly converts 5-(4-bromophenylimino)-3,4-tetramethylene-1,3,4-thiadiazolidine-2-thione (thiadiazolidinethione) into 4-bromophenyl-1,2-tetramethylene-1,2,4-triazolidine-3,5-dithione (triazolidinedithione). Isoimide and thiadiazolidinone strongly inhibit protoprophyrinogen oxidase activity after isomerization. GST catalyzes a quick activation of *N*-aryl-3,4,5,6-tetrahydroisophthalimides and 5-arylimino-3,4-tetramethylene-1,3,4-thiadiazolidin-2-ones in the presence of GSH by isomerization. Although GST has generally been described as a detoxifying enzyme in pesticide toxicology, herbicidal activation by the metabolic isomerization is a new function of GST and GSH.

Chlozolinate, Vinclozolin, and Procymidone

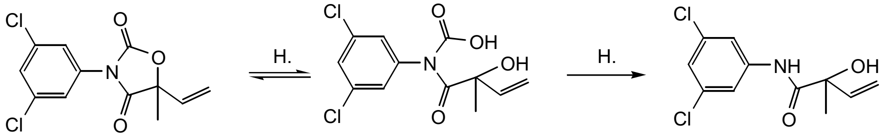
Fungicides: control of *Botrytis cineria* on various crops, particularly grapes

Hydrolysis
In wine with the pH adjusted to 4.0 at 30.0 ± 0.5 °C[223]

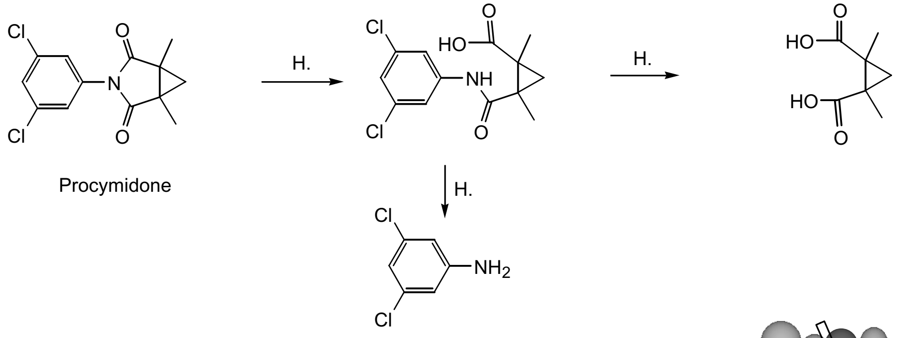
The fungicides, chlozolinate, vinclozolin, and procymidone, are added to wine after fermentation and the degradation products are isolated and identified. Chlozolinate undergoes a rapid hydrolytic loss of the ethoxycarbonyl substituent to give an oxazolidine that further undergoes hydrolytic cleavage to give 3′,5′-dichloro-2-hydroxypropanilide. The oxazolidine ring of vinclozolin undergoes a similar hydrolysis reaction to give the corresponding anilide,



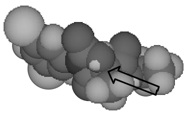
Chlozolinate



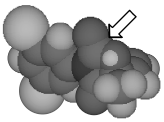
Vinclozolin



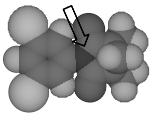
Procymidone



ClC1=CC(Cl)=CC(N(C(O2)=O)C(C2(C(OCC)=O)C)=O)=C1



ClC1=CC(Cl)=CC(N(C(C(C=C)(C)O2)=O)C2=O)=C1



ClC1=CC(Cl)=CC(N(C(C3(C)C2(C)C3)=O)C2=O)=C1

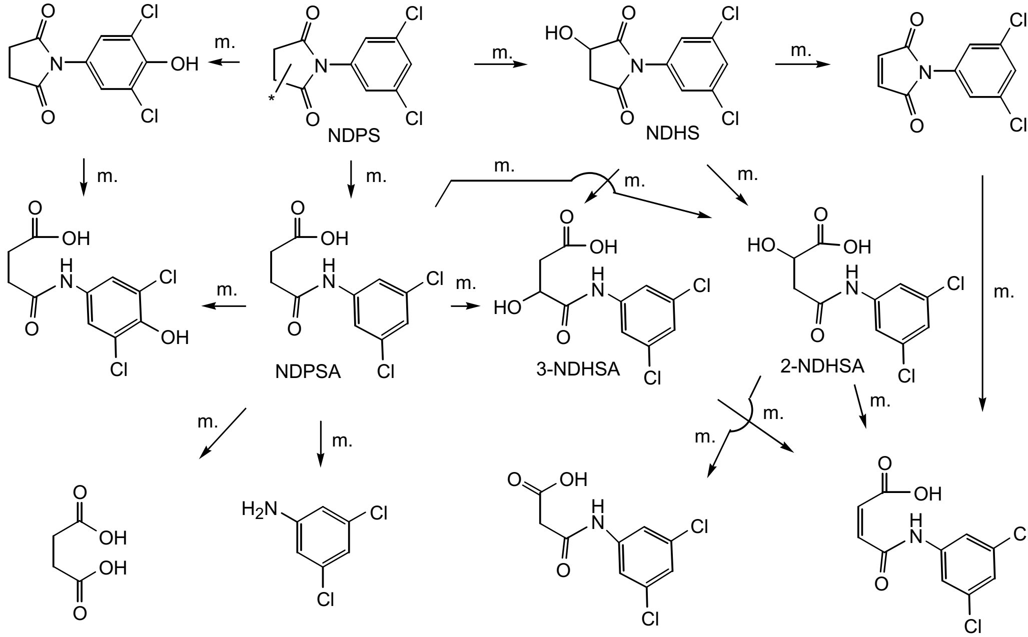
3′,5′-dichloro-2-hydroxy-2-methylbut-3-eneanilide. Both of these anilides are stable in wine for 150 days. A different degradation behavior is observed with procymidone and leads to the formation of 3,5-dichloroaniline, which, in turn, breaks down in wine.

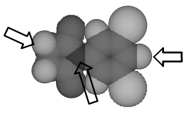
N-(3,5-Dichlorophenyl) succinimide (NDPS)

A nephrotoxicant

Microsome
Liver and kidney homogenates of male Fischer 344 rats (150–175 g) from Charles River Breeding Labs; liver homogenates of male New Zealand white rabbits (1.5–2.9 kg) from Myrtle's Rabbitry[224]

The nephrotoxicant, *N*-(3,5-dichlorophenyl)succinimide (NDPS), undergoes non-enzymatic hydrolysis to *N*-(3,5-dichlorophenyl)succinamic acid (NDPSA) in buffer, rat liver and kidney homogenates, and rabbit liver homogenates. In the presence of NADPH, rat liver homogenates convert NDPS to NDPSA and *N*-(3,5-dichlorophenyl)-2-hydroxysuccinamic acid (2-NDHSA). Using liver homogenates from phenobarbital-treated rats, *N*-(3,5-dichlorophenyl)-3-hydroxysuccinimide (NDHS) and *N*-(3,5-dichlorophenyl)-3-hydroxysuccinamic acid (3-NDHSA) are also detected.





O=C(CC1)N(C2=CC
(Cl)=CC(Cl)=C2)C1=O

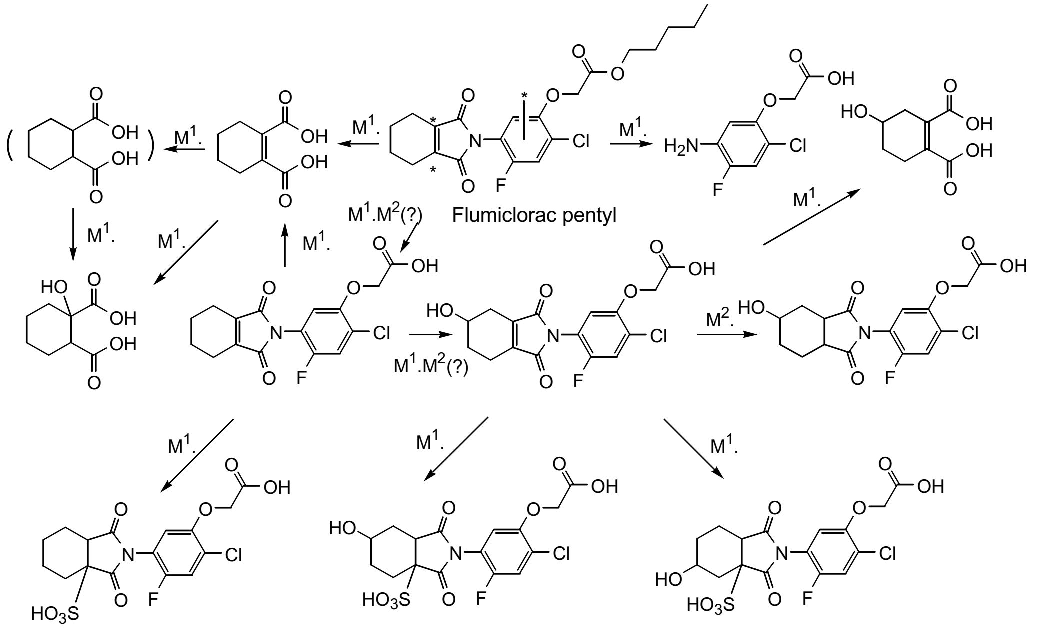
Flumiclorac pentyl (S-23031)

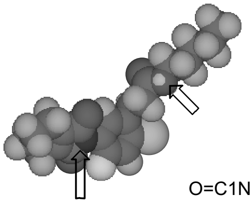
A selective, post-emergent herbicide for control of broadleaf weeds in soybean fields

Mammal[1]
Male and female Sprague–Dawley rats
(6 week-old, Charles River Japan)[225]

Mammal[2]
Male Sprague–Dawley rats (Charles River Japan)[226]

In the feces and urine of rats, more than 90% of administered ^{14}C-flumiclorac pentyl is excreted within 48 h of treatment. Flumiclorac pentyl is rapidly and extensively metabolized. The major fecal metabolites are identified as the sulfonic acid conjugates, and the major urinary metabolite is identified as 5-amino-2-chloro-4-fluorophenoxyacetic acid. The metabolic reactions include cleavage of the ester linkage, cleavage of the imide linkage, hydroxylation and following reduction at the cyclohexene ring of the cyclohexene-1,2-dicarboxylic acid moiety, and incorporation of a sulfonic acid group into the carbon–carbon double bond of the 3,4,5,6-tetrahydrophthalimide moiety.





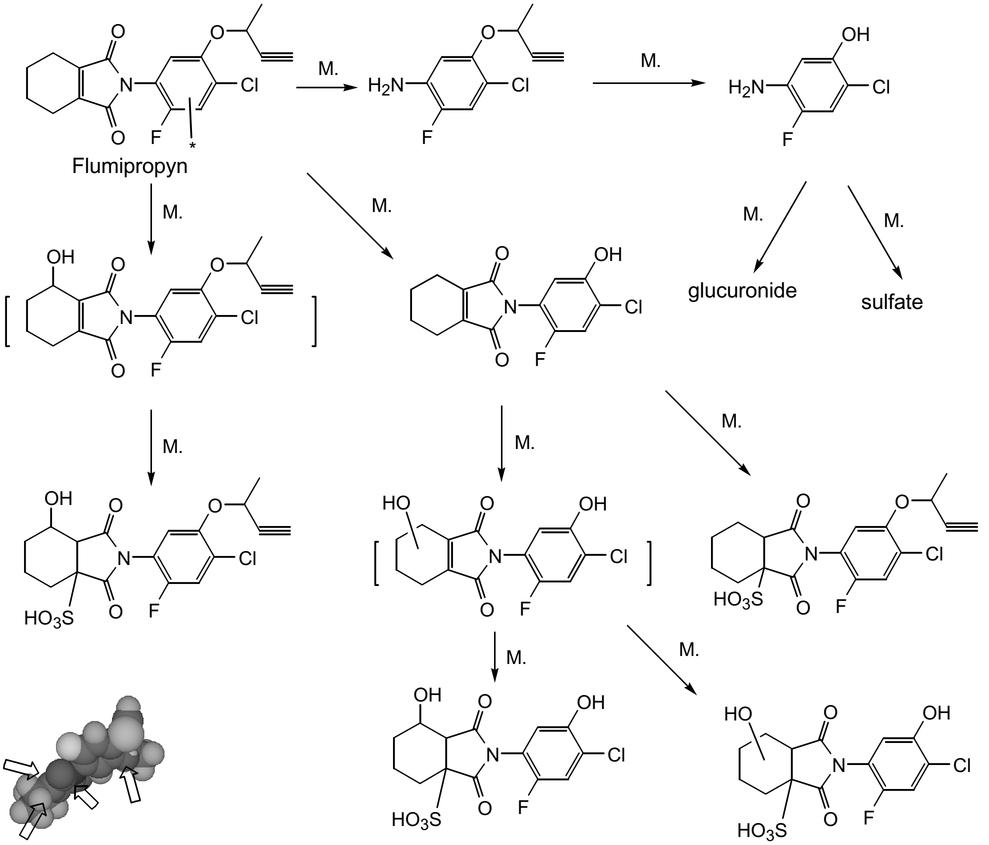
O=C1N(C3=C(F)C=C(Cl)C(OCC(OC
CCCC)=O)=C3)C(C2=C1CCCC2)=O

Flumipropyn (S-23121)

A pre- and post-emergent herbicide: control of broadleaf weed in cereal agriculture

Mammal
Male and female Sprague–Dawley rats (6 week-old) from Charles River Japan Inc.[227]
Hepatic cytosol preparation: male Sprague–Dawley rats (7 week-old) from Charles River Japan Inc.; male Syrian golden hamsters from SLC Japan; male New Zealand white rabbits from Kitayama LABES Co., Ltd; 7 month-old beagle dogs from Kasho Co., Ltd[228]

The major urinary metabolites of flumipropyn by rats are found to be 4-chloro-2-fluoro-5-hydroxyaniline, its sulfate, and glucuronide, and the major fecal metabolites in addition to the parent compound are six sulfonic acid conjugates with a sulfonic acid group incorporated into the double bond of the 3,4,5,6-tetrahydrophthalimide moiety. No acetylated derivative of 4-chloro-2-fluoro-5-[(1-methyl-2-propynyl)oxy]aniline is identified in mammalian cytosol preparations *in vitro*[228].



O=C1N(C3=C(F)C=C(Cl)C(OC(C#C)C)=C3)C(C2=C1CCCC2)=O

Mixture of three hydroxylated isomers

MK-129

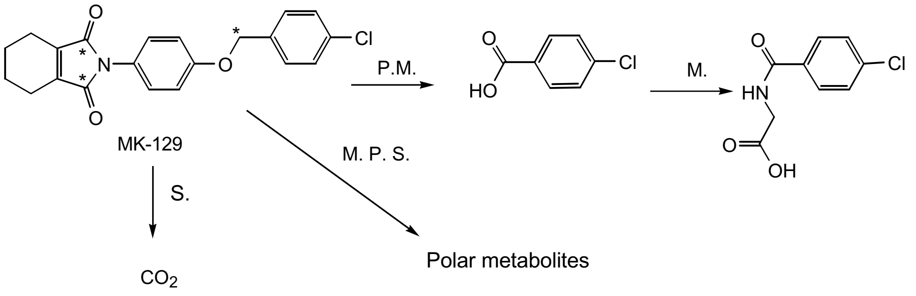
A herbicidal peroxidizer: control of broadleaf weeds and sedge in rice paddy fields

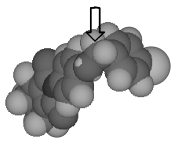
Mammal
Male Wistar rats[229]

Plant
Rice plants; barnyard grass[230]

Soil
Tochigi soils (pH 5.5); Saitama soils (pH 5.6); Kanagawa soils (pH 6.2)[231]

Both rice plants and barnyard grass produce 12 metabolites of MK-129 and, of these, 4-chlorobenzoic acid is the main metabolite. Infant seedlings of barnyard grass metabolize MK-129 more slowly than the fourth leaf stage, although the metabolic activity of infant rice seedlings is almost at the same level as that of the fourth leaf stage of the rice plants.
When ^{14}C-MK-129 is administered to rats orally, about 85% and 2–4% of radioactivity are excreted in the feces and urine, respectively, after 1 day of administration (94% and 3–5% after 7 days). Eighty percent of radioactivity excreted in the feces results from unchanged MK-129, and the main metabolites identified in the urine are 4-chlorobenzoic acid and 4-chlorohippuric acid. The other metabolites derived from both benzyl and carbonyl ^{14}C-MK-129 are polar metabolites and are not identified. The main metabolite of ^{14}C-MK-129 in three different kinds of soil is $^{14}CO_2$ under both oxidative flood and upland conditions.





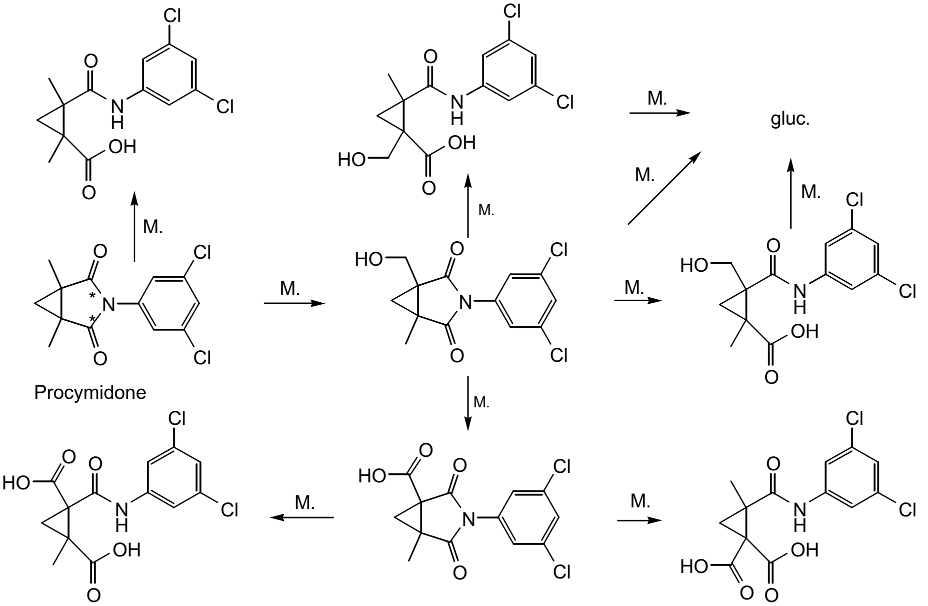
O=C1N(C3=CC=C(OCC4=CC=C(Cl)
C=C4)C=C3)C(C2=C1CCCC2)=O

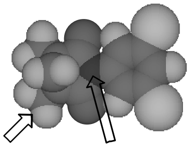
Procymidone (Sumilex, S-7131)

A fungicide: control of plant diseases such as gray mold and sclerotinia rot

Mammal
Three female New Zealand white (NZW) rabbits (about 3 kg, Kitayama LABES Co., Ltd, Nagano, Japan)[232]

Ninety five percent of the administered radiocarbon is rapidly excreted in the urine and feces from the body of female rabbits within 3 days of administration. The main metabolites in female rabbits are glucuronide conjugates of three hydroxylated procymidone metabolites which are not found in rats and mice. These metabolites are generated by the following metabolic reactions of oxidation of one of the methyl groups to carboxylic acid via hydroxymethyl, cleavage of the imide linkage, and glucuronide formation of the three hydroxylated procymidone metabolites. There appears to be such activity towards hydroxylated procymidone metabolites only in female rabbits and no





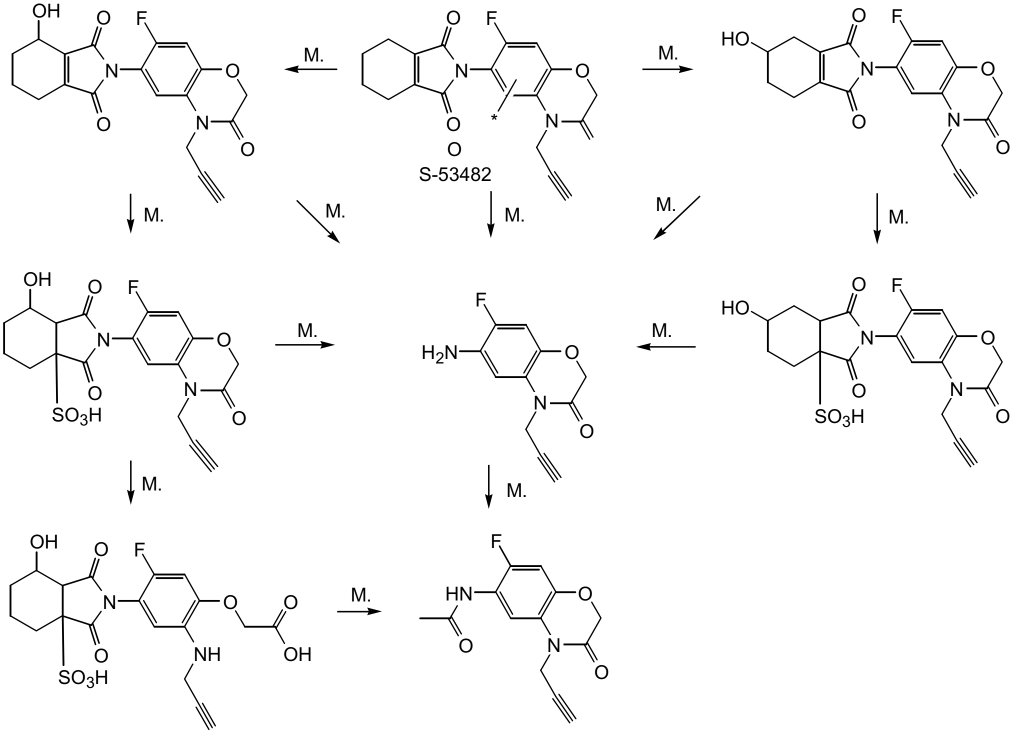
CC1(C2)C2(C)C(N(C3=CC(Cl)=CC(Cl)=C3)C1=O)=O activity in female rats, suggesting that the difference in the conjugation activity causes the species difference of procymidone metabolism between female rabbits and rats.

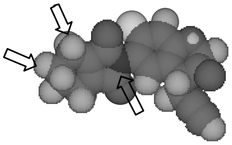
S-53482

A selective post-emergent herbicide: control of annual broadleaf weeds

Mammal
Charles River derived CD (Sprague–Dawley) 6 week-old male and female rats[233]

When the rats are given a single oral dose of ^{14}C-S-53482, seven metabolites are identified in the urine and the feces. Alcohol derivatives and the acetoanilide derivative are isolated from the urine, and three sulfonic acid conjugates with a sulfonic acid group incorporated into the double bond of the 3,4,5,6-tetrahydrophthalimide moiety are isolated from the feces.





O=C1N(C3=CC(C(CC#C)C(CO4)=O)=C4C=C3F)C(C2=C1CCCC2)=O

16

Natural Products

(+)- and (−)-Abscisic acids

Plant growth regulators: promotion of maturation of the somatic embryo of white spruce

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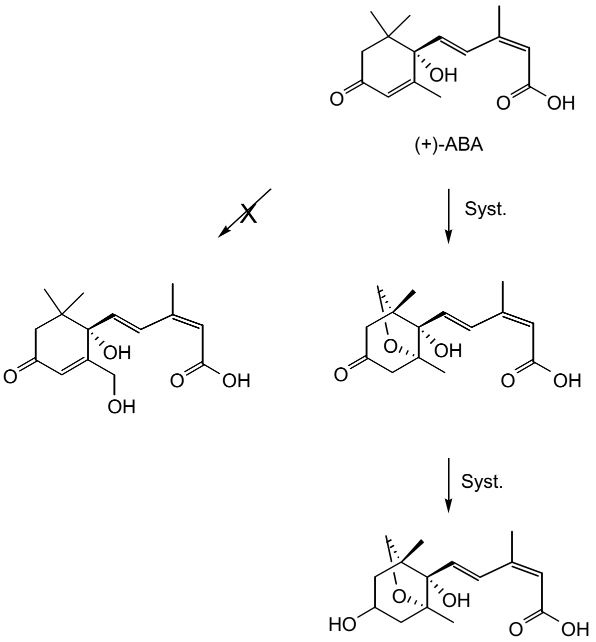
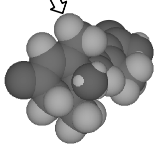
System
Somatic embryo suspension cultures of white spruce: *Picea glauca* (Moench) Voss[234]

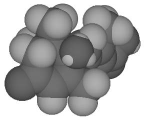
Somatic embryo suspension cultures of white spruce containing (+)-abscisic acid (ABA) metabolize (+)-ABA almost completely to yield quantitatively phaseic acid with slight further transformation into dihydrophaseic acid within 7 days. (−)-ABA remains essentially unchanged under the same culture conditions, and when the cells are supplied with racemic (±)-ABA, only the (+) enantiomer is metabolized.





(+)-ABA

CC1(C)[C@](C=CC(C)=CC(O)=O)(O)C(C)=CC(C1)=O



(-)-ABA

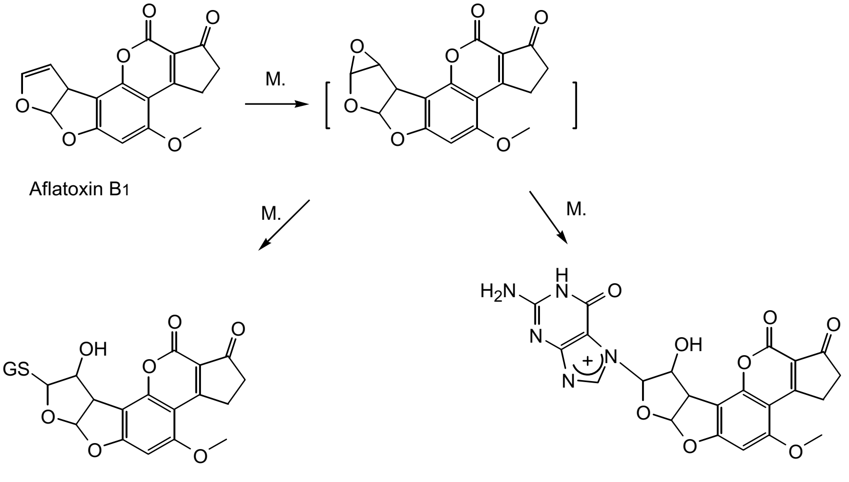
CC1(C)[C@@](C=CC(C)=CC(O)=O)(O)C(C)=CC(C1)=O

Aflatoxin B_1

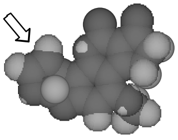
Not a pesticide: a natural toxin, a potent hepatocarcinogen

Mammal
235

Aflatoxin B_1 can be activated via the monooxygenase reaction which then reacts with the N7 atom of B-DNA guanine. Conjugation of aflatoxin B_1 8,9-epoxide is an important detoxification route. Although aflatoxin B_1 8,9-epoxide can be hydrolyzed to the diol by epoxide hydrolase, the diol product is toxic, since it reacts readily with proteins by Schiff base formation or binds to DNA. Glutathione conjugation prevents toxicity of both the epoxide and its hydrolysis product. The aflatoxin glutathione conjugate is subsequently excreted from the hepatocyte into bile as a major biliary metabolite.



GS: glutathione residue



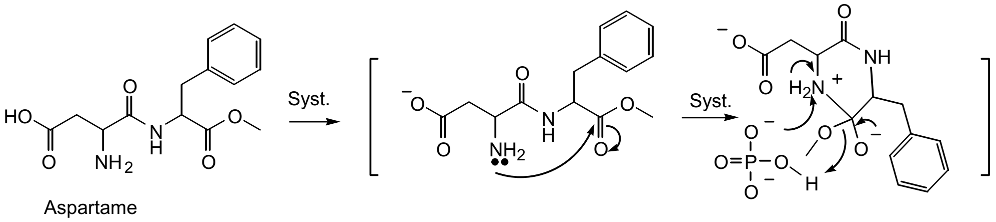
O=C(O4)C5=C(CCC5=O)C3=C4
C2=C(C=C3OC)OC1OC=CC12

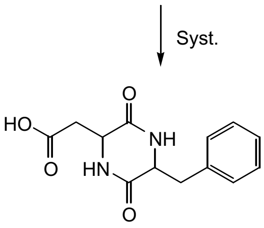
Aspartame

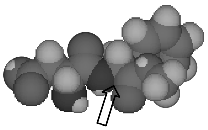
Not a pesticide: high-intensity sweetener

System
Phosphate and citrate buffer solutions (pH 3 and 7) at 25 °C[236]

The rate of aspartame degradation is faster in a phosphate buffer solution than in a citrate buffer solution at the same pH and buffer concentration. The primary mechanism by which aspartame degrades, the formation of diketo piperazine, involves the nucleophilic attack of carbonyl by the free amine, which requires proton transfer.







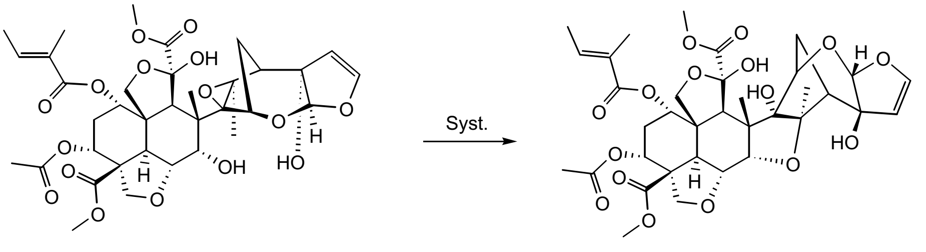
OC(CC(N)C(NC(CC1=CC=CC=C1)C(OC)=O)=O)=O

Azadirachtin

A natural insecticide

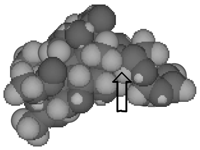
System
Methanol solution at 90 °C[237]

The natural insecticide azadirachtin is most stable in mildly acidic solutions between pH 4 and 6 at room temperature and unstable in alkaline and strong acidic conditions. While azadirachtin is relatively stable to heating in the seeds or as a pure solid, it is rapidly destroyed or altered by heating in aqueous solution and methanol. In methanol at 90 °C, it is quantitatively converted to 3-acetyl-1-tigloylazadirachtinin.



Azadirachtin

3-Acetyl-1-tigloylazadilachtinin



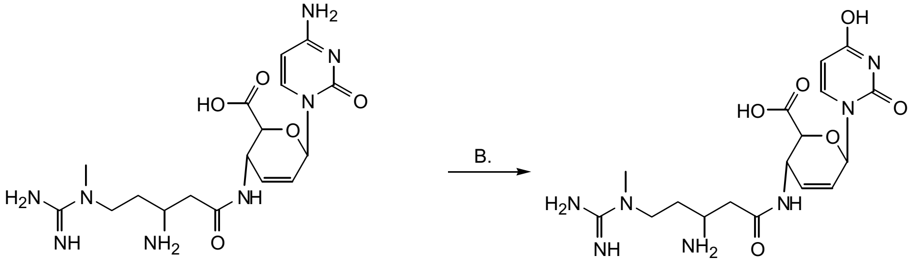
C[C@@]2([C@@]5([C@@H](O7)C6)O[C@@]5(C)C6[C
@]8(O)[C@]7(OC=C8)[H])[C@H](O)[C@H]4[C@@]1([H])
[C@@](CO4)(C(OC)=O)[C@H](OC(C)=O)C[C@H](OC
(C(C)=CC)=O)[C@]13[C@H]2[C@@](O)(C(OC)=O)OC3

Blasticidin S

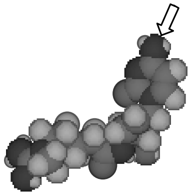
A microbial fungicide: control of rice blast disease, *Pyricularia oryzae*

Bacterium
Bacillus cereus K55-S1[238]

Several blasticidin S-resistant microorganisms are found to produce blasticidin S deaminase which catalyzes the hydrolytic deamination of the cytosine moiety in blasticidin S to give a non-toxic deaminohydroxy derivative.



Blasticidin S



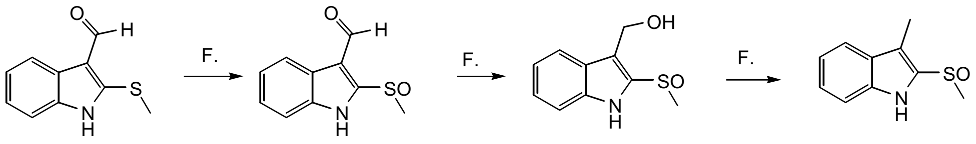
NC(N(C)CCC(N)CC(NC1C(C(O)=O)O
C(N2C(N=C(N)C=C2)=O)C=C1)=O)=N

Brassicanal A

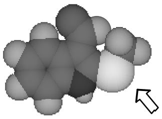
A natural product: a brassica phytoalexin

Fungus
Leptosphaeria maculans (Desm.) Ces. et de Not., asexual stage *Phoma lingnam* (Tode ex Fr.) Desm: BJ-125; ENG 53; Unity[239]

Three main biotransformation products are identified by fungal cultures of the blackleg fungus with brassicanal A. The final transformation product from brassicanal A is via oxidation of the sulfur atom of the methylmercapto group and then hydrogenation of the formyl group to a methyl group to give 3-methylindole-2-methylsulfoxide which undergoes no further metabolism to afford transformed products.



Brassicanal A



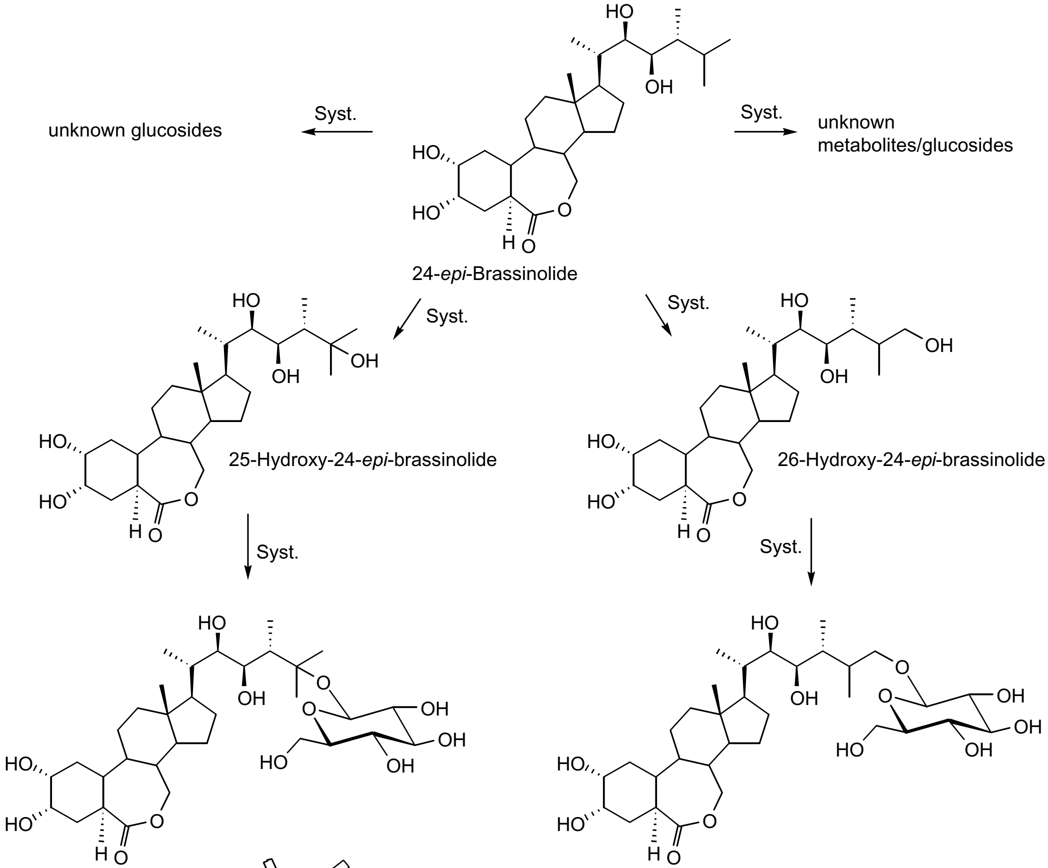
O=C([H])C2=C(SC)
NC1=CC=CC=C12

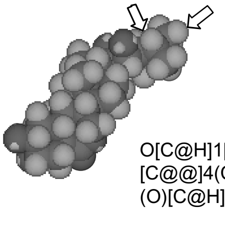
24-*epi*-Brassinolide

A natural product: a plant hormone

System
Tomato cell suspension cultures:
Lycopresicon esculentum[240]

Two isomeric metabolites, 25-β- and 26-β-D-glucopyranosyloxy-24-*epi*-brassinolides, are formed in tomato cell suspension cultures with endogenously applied 24-*epi*-brassinolide. The two-step metabolic process involves hydroxylation of the side chain at C25 and C26, respectively, followed by glucosidation of the newly formed hydroxyl groups. The ratio between both metabolites is altered by *in vivo* treatment of the cell cultures with various cytochrome P-450-specific inhibitors, indicating the involvement of





O[C@H]1[C@@H](O)C[C@@](C(OCC3C2CC
[C@@]4(C)C3CC[C@@H]4[C@H](C)[C@@H]
(O)[C@H](O)[C@H](C)C(C)C)=O)([H])C2C1

two different enzyme systems. Biosynthetically prepared 25-hydroxy-24-*epi*-brassinolide, reapplied to the cell cultures, is exclusively glucosylated at the 25-hydroxyl group, strongly suggesting regiospecificity of the corresponding glucosyltransferase.

Ecdysone

Not a pesticide: insect molting hormone, control of insect pupation

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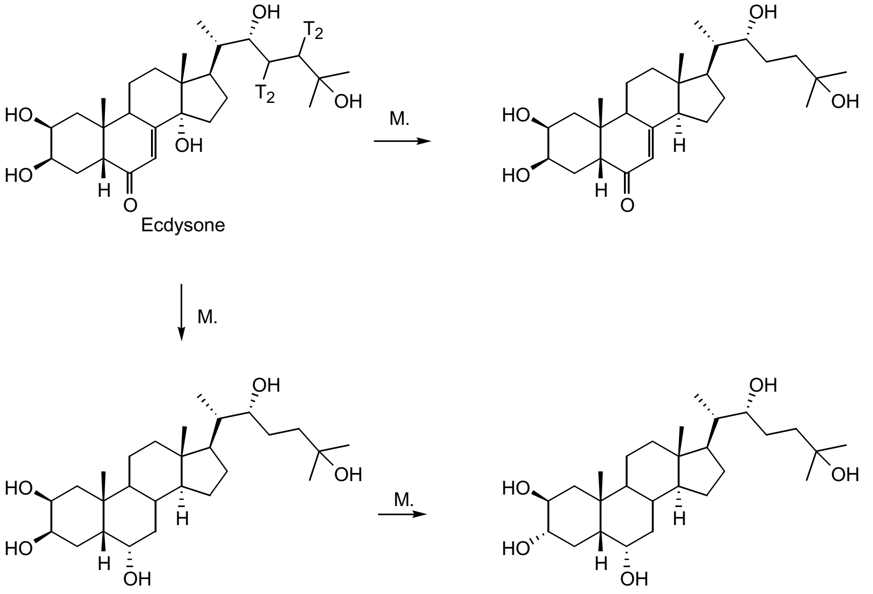
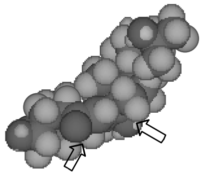
Mammal
Male white mice: *Mus musculus*
(approximately 30 g)[241]

When white mice are administered ^{3}H-ecdyson, (2β,3β,14α,22(R),25-pentahydroxy-5β-cholest-7-ene-6-one) by injection intraperitoneally, ecdysone is metabolized via hydroxylation at C14, followed by reduction of ring B into the 6α-hydroxy derivative and epimerization at C3.



T: ^{3}H



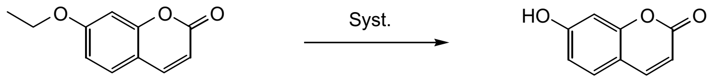
O[C@H]([C@@H](C[C@]1(C(C=C2[C@@]3
(CC[C@@H]4[C@H](C)[C@@H](CCC(C)(C)O)
O)O)=O)[H])O)C[C@@]1(C2CC[C@@]34C)C

7-Ethoxycoumarin and Androstenedione

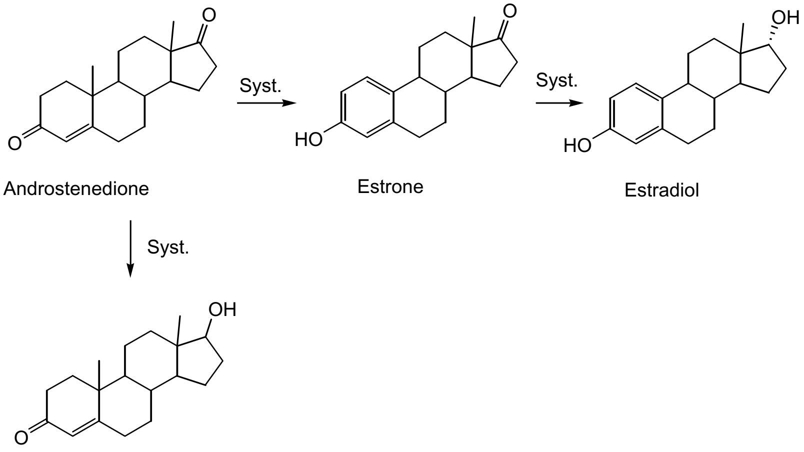
Not pesticides

System
In vitro perfusion of the human placental lobule[242]

The *in vitro* perfusion of the human placental lobule with 7-ethoxycoumarin gives 7-hydroxycoumarin, and perfusion with androstenedione gives the conversion products, estrone, estradiol, and testosterone. The human placenta has only a limited capacity for the metabolism of xenobiotics.



7-Ethoxycoumarin

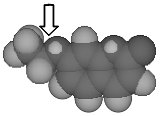


Androstenedione

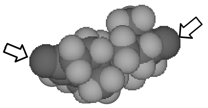
Estrone

Estradiol

Testosterone



O=C2C=CC1=CC
=C(OCC)C=C1O2



CC12C(CCC3C2CCC4(C)
C3CCC4=O)=CC(CC1)=O

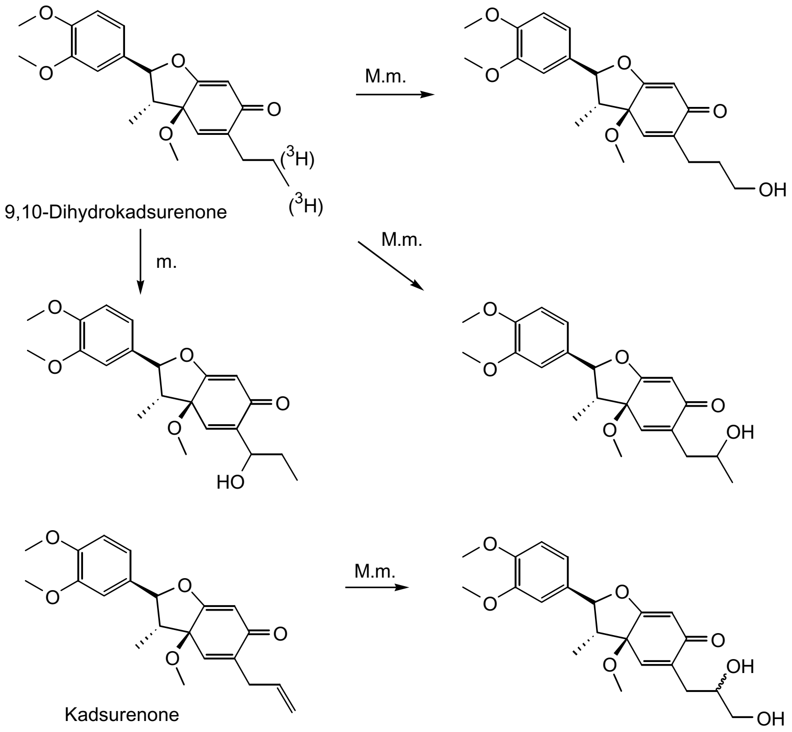
Kadsurenone and 9,10-Dihydrokadsurenone

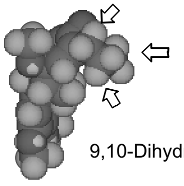
Not pesticides: natural products for the treatment of asthma and arthritic conditions

Mammal
Adult male rhesus monkeys (2.7–2.8 kg)[243]

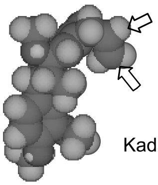
Microsome
Rat liver microsomes[243]

When rhesus monkeys are administered 9,10-dihydrokadsurenone by intravenous dosing, the metabolites are identified as glucuronide conjugates from the urine. The principal pathway of biotransformation of 9,10-dihydrokadsurenone in monkeys is hydroxylation of the C5 propyl side chain to give two metabolites, 10-hydroxy- and 9-hydroxy-9,10-dihydrokadsurenones which are excreted as glucuronides. Rat liver microsomal incubation with





9,10-Dihydrokadsurenone



Kadsurenone

COC1=C(OC)C=C([C@H]2[C@@H](C)[C
@](C=C3CCC)(OC)C(O2)=CC3=O)C=C1

COC1=C(C=C(C=C1)[C@@H]([C@H]2C)
OC([C@@]2(C=C3CC=C)OC)=CC3=O)OC

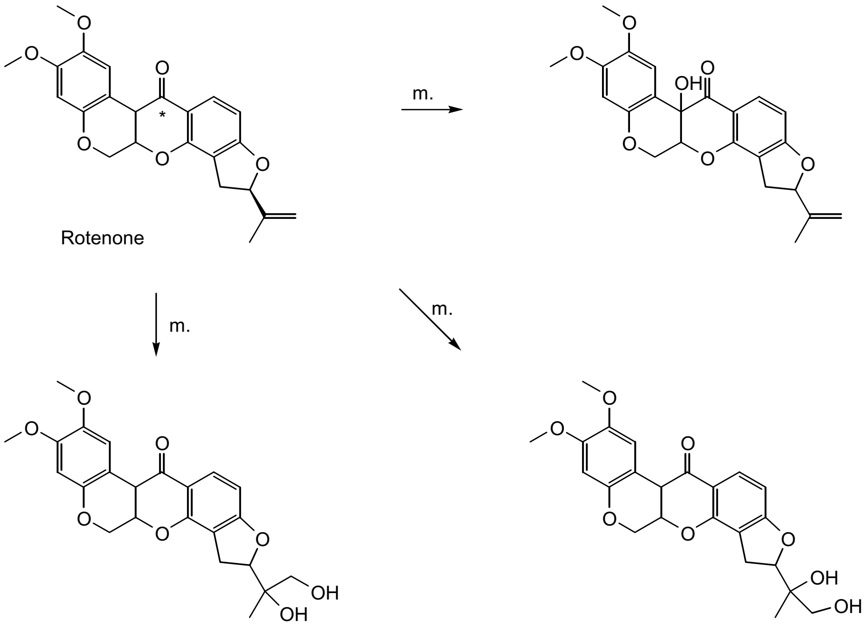
9,10-dihydrokadsurenone yields 10-, 9-, and 8-hydroxy-9,10-dihydrokadsurenones as major metabolites. Kadsurenone is metabolized at the C5 allyl side chain by monkeys. A major metabolite of rat liver microsomal incubation of kadsurenone is 9,10-dihydroxykadsurenone.

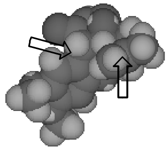
Rotenone

A naturally occurring pesticide

Microsome
Hepatic microsomes of rainbow trout:
Oncorhynchus mykiss[244]

By hepatic microsomal incubations from rainbow trout with ^{14}C-rotenone, three major and several minor metabolites of rotenone are observed, the major ones being identified as rotenolone and two epimeric forms of 6′,7′-dihydroxyrotenone.





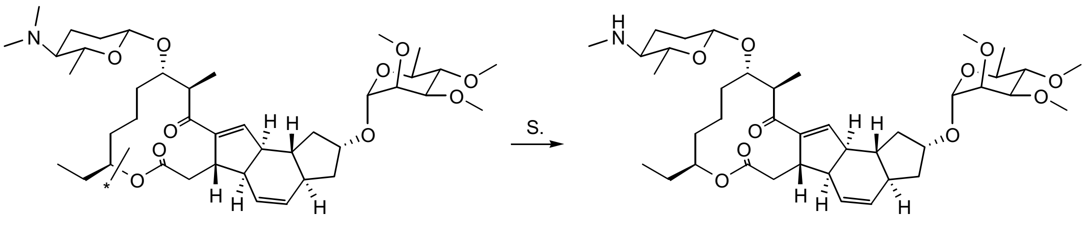
COC1=CC2=C(OCC(OC4=
C3C=CC5=C4C[C@H](C(C)
=C)O5)C2C3=O)C=C1OC

Spinosad

An insecticide: a natural product for control of insect pests including lepidoptera in cotton, brassica, leafy vegetables, tomatoes, and other crops

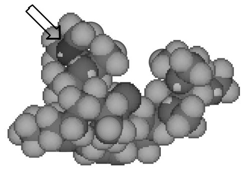
Soil
Commerce silt loam (Georgia, USA);
Hanford sandy loam (California, USA)[245]

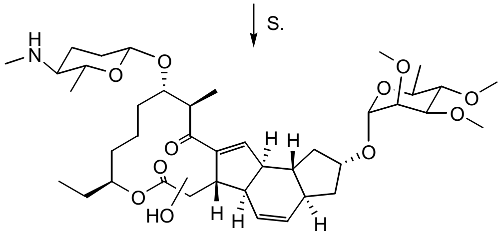
Spinosad consists of two major components, namely psinosyns A (ca 85%) and D (ca 15%). When either ^{14}C-spinosyn A or -spinosyn D is applied in the soil under aerobic conditions, the major degradation product of spinosyn A is spinosyn B, resulting from



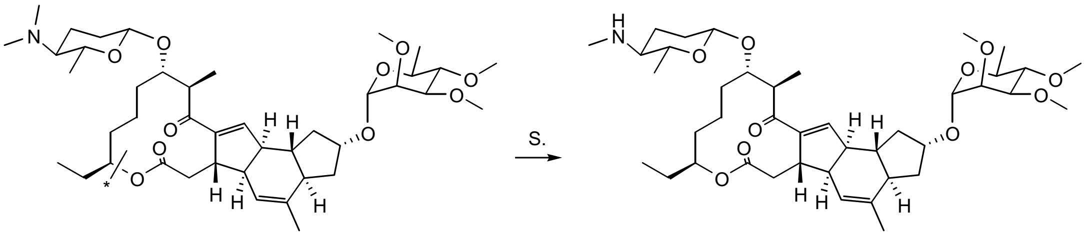
Spinosyn A

Spinosyn B

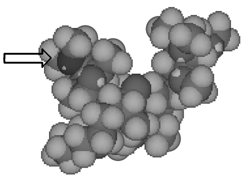




CC1C(N(C)C)CCC(O[C@@H]3[C@@H](C)C(C2=C[C@]4([H])[C@](C=C[C@@]5([H])[C@@]4([H])C[C@H](OC6OC(C)C(OC)C(OC)C6OC)C5)([H])[C@]2([H])CC(O[C@@H](CC)CCC3)=O)=O)O1



Spinosyn D



CC(C(CC2)N(C)C)OC2O[C@H]([C@H]1C)CCC[C@@H](OC(C[C@@]3(C(C1=O)=C[C@]([C@@]3([H])C=C(C)[C@@]4(C[C@H]5OC(OC(C6OC)C)C(C6OC)OC)[H])([C@@]4(C5)[H])[H])[H])=O)CC demethylation on the forosamine sugar. Other degradation products are hydroxylation products of psinosyns A and B, probably on the aglycone portion of the molecule.

Zearalenone

Not a pesticide: a second metabolite of the *Fuzairum* species possessing estrogenic and growth-promoting activity in animals

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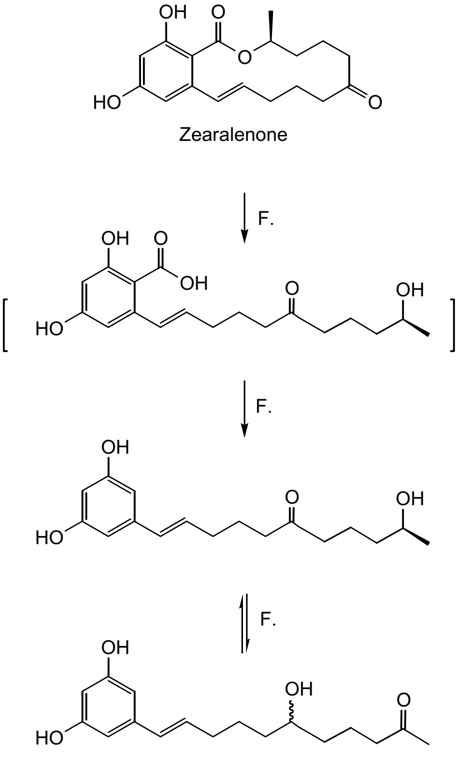
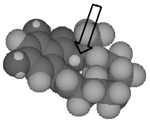
Fungus
Gliocladium roseum[246]

When zearalenone is subjected to microbial transformation by a fungus, *Gliocladium roseum*, it is converted to a 1 : 1 mixture of 1-(3,5-dihydroxyphenyl)-10′-hydroxy-1-undecen-6′-one and 1-(3,5-dihydroxyphenyl)-6′-hydroxy-1-undecen-10′-one.





OC1=C(C(O[C@@H](C)CCC2)
=O)C(C=CCCCC2=O)=CC(O)=C1

17

Organophosphorous Compounds

Azinphos methyl

A broad-spectrum insecticide and acaricide: use in a wide variety of fruits, vegetables, and field crops, as well as ornamentals and forest and shade trees

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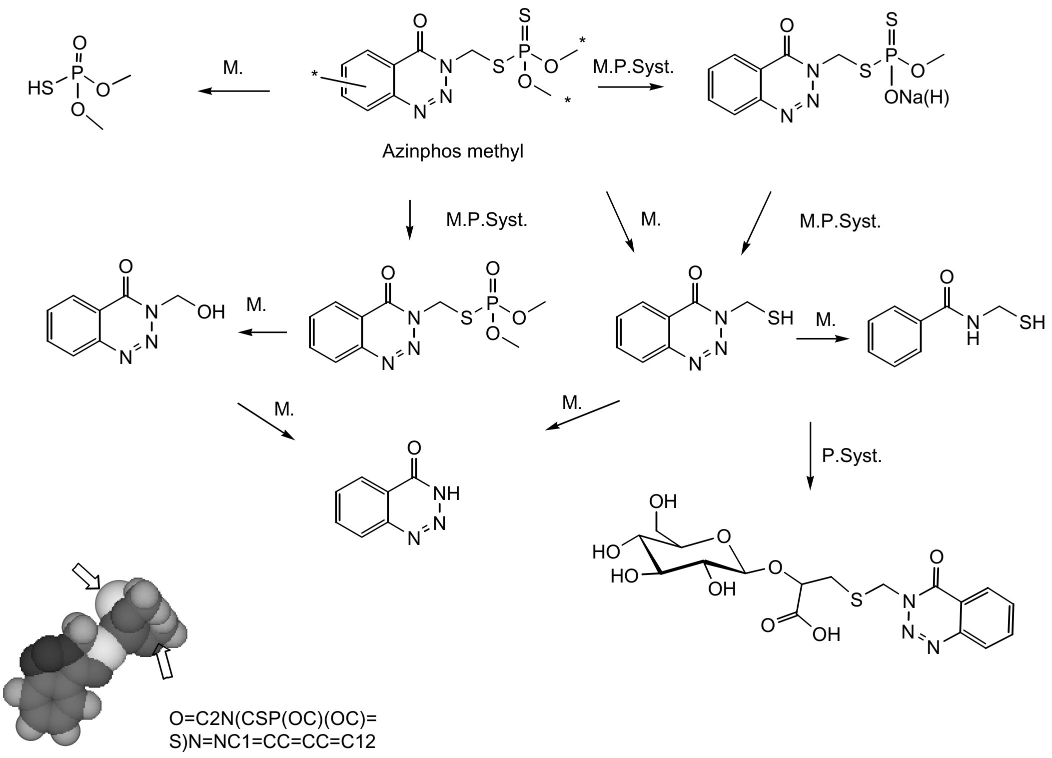
Mammal
Male *rhatus* rats (200 g)[247]

Plant/System
Apple tree: var. James Grieve; heterotrophic apple cell suspension cultures: var. Boskop[248]

In the apple tree, ^{14}C-azinphos methyl is metabolized to a small degree and, by the cell culture, 71% of the applied activity consists of unchanged azinphos methyl and its oxon is identified as a metabolite in a small amount. Two major metabolites are identified in the aqueous phase of the peel extract and in the cell extracts of the cell cultures. The major one is a conjugate of mercaptomethylbenzazimide with 2-(1-glucopyranosyl)propionic acid, and the minor one is monodesmethylazinphos methyl. In rats, following the administration of a single dose of azinphos methyl, the major radioactivity is eliminated in the expired air within 48 h. The metabolites in the urine result from the cleavage of P–S–C and P–O–CH_3 bonds yielding *O,O*-dimethyl phosphorothioic acid together with mercaptomethylbenzamide and mono-*O*-demethylated azinphos methyl, respectively.



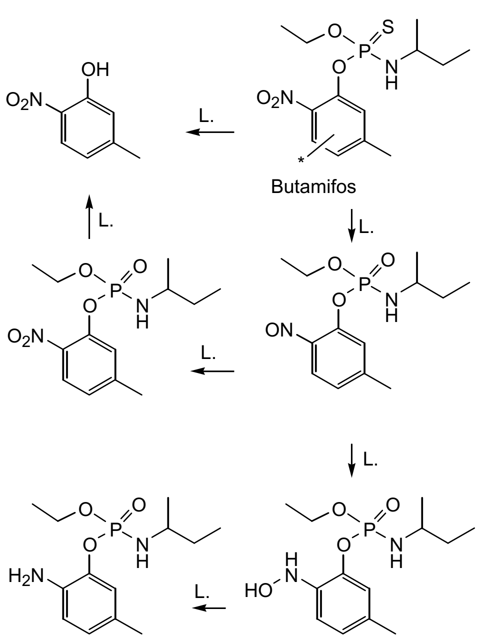
O=C2N(CSP(OC)(OC)=
S)N=NC1=CC=CC=C12

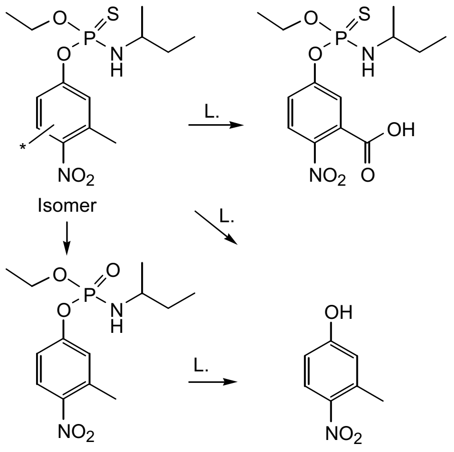
Butamifos (Cremart) and its isomer

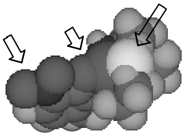
A pre-emergent herbicide: control of a broad spectrum of weeds

Light
Irradiation in an aqueous acetonitrile solution with a 500 W xenon arc lamp (UXL-500D, Ushio)[249]

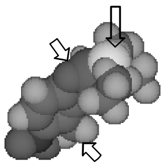
In water, butamifos undergoes photoinduced intramolecular oxygen transfer from the nitro group to the P=S moiety, resulting in the formation of the nitrosooxon derivative. Through the successive reduction of the nitroso group to hydroxyamino and amino groups, as well as oxidation to the nitro group, the nitrosooxon derivative is finally photodegraded to various polar compounds. The isomer of butamifos is photodegraded more slowly than butamifos in air, and its main photodegradation pathway in water is oxidation of the arylmethyl group to form a corresponding carboxylic acid derivative.







S=P(NC(C)CC)(OCC)OC1=CC(C)=CC=C1[N+]([O-])=O



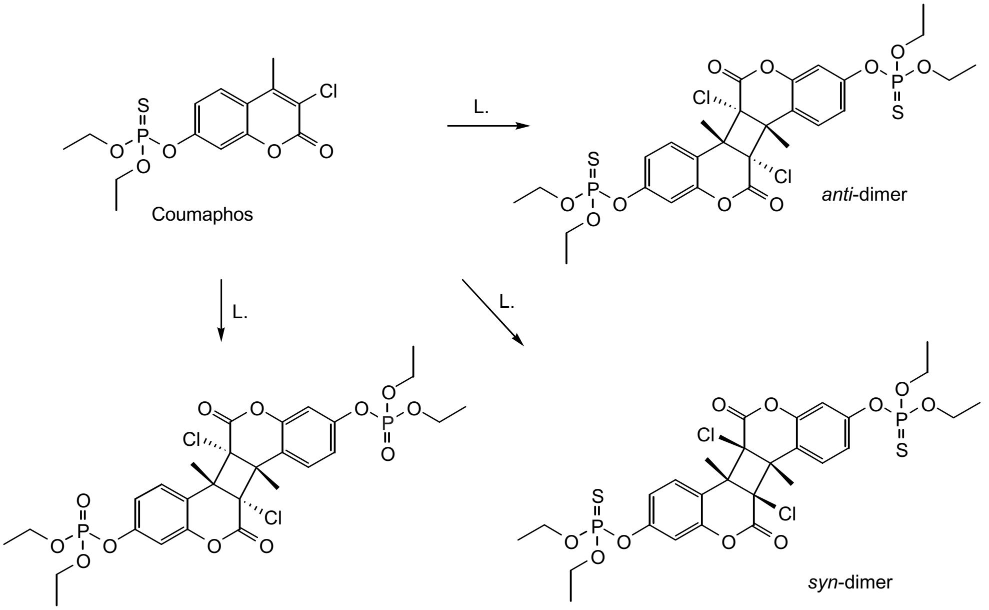
S=P(OC1=CC(C)=C([N+]([O-])=O)C=C1)(NC(CC)C)OCC

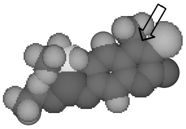
Coumaphos

An insecticide

Light
UV irradiation with a mercury high-pressure lamp in a Pyrex reactor[250]

By UV irradiation of coumaphos in solutions, three dimeric products are isolated and identified as the head-to-tail *anti*-dimer, its oxidation product, and the head-to-tail *syn*-dimer.





CC(C1=CC=C(OP(OCC)(OCC)(C)=S)C=C1O2)=C(Cl)C2=O

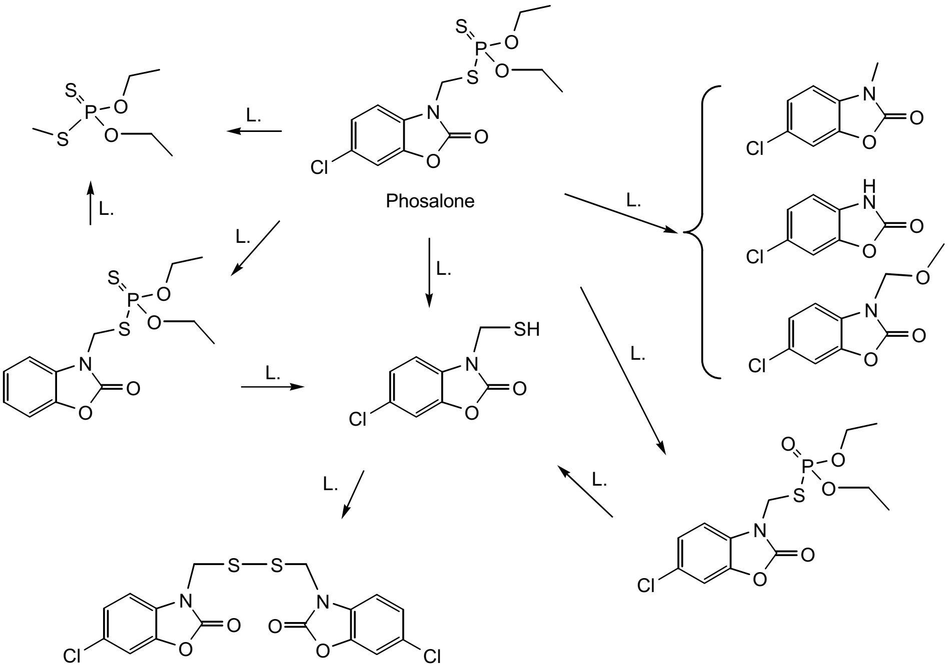
Phosalone

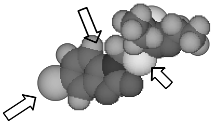
An insecticide: control of variety of insect pests which may attack crops such as grapes, apples, peas, potatoes, rice, and cotton

---

Light
UV light from a high-pressure mercury lamp (125 W); simulated sunlight with an Applied Photophysics 9500 solar simulator[251]

Photodegradation of phosalone in solvent yields dechlorinated phosalone. Irradiation in methanol affords *O*,*O*-diethyl-*S*-methylphosphorothioate and 6-chloro-3-methoxymethyl-2-oxobenzoxazoline with other common products. Photolysis of phosalone in the solid state as a thin film on a glass surface produces a number of photoproducts including 6-chloro-3-mercaptomethyl-2-oxobenzoxazoline and its dimeric disulfide.





O=C2OC1=CC(Cl)=CC=C1
N2CSP(OCC)(OCC)=S

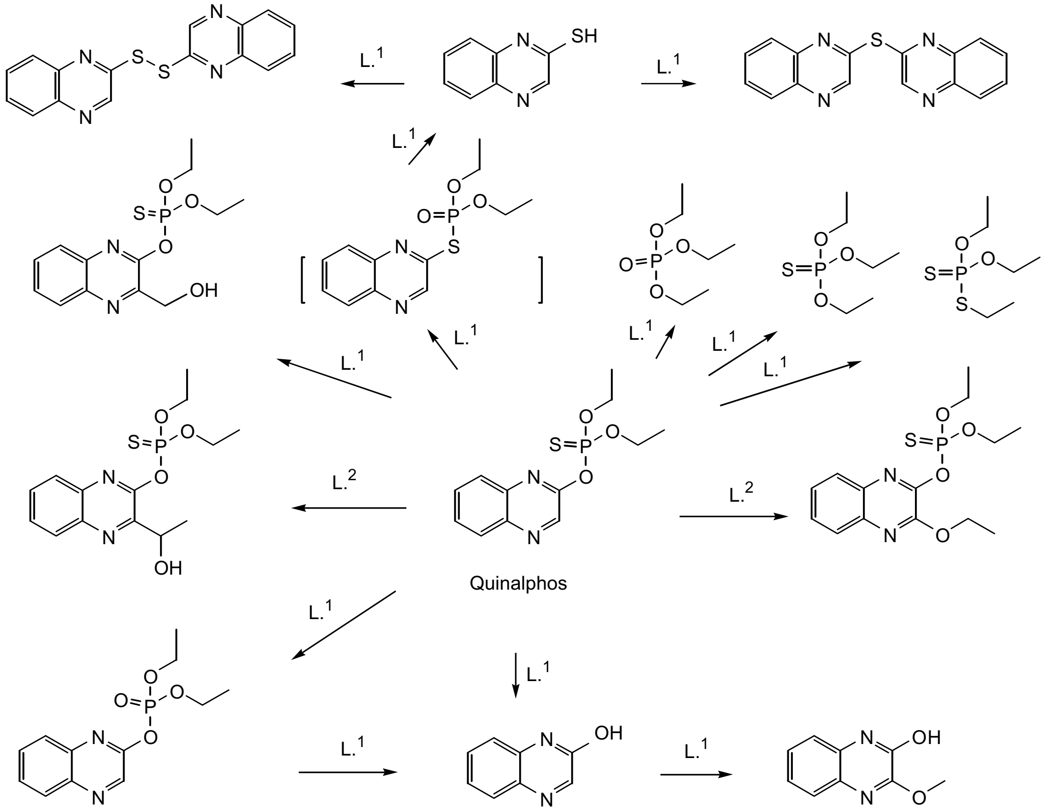
Quinalphos

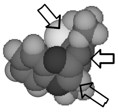
An insecticide: use for the treatment of important crops in tropical and subtropical zones

Light[1]
Irradiation in methanol with light from a high-pressure 120 W mercury vapor lamp (Philips)[252]

Light[2]
Irradiation in ethanol with a 100 W medium-pressure mercury lamp for 7 h[253]

In methanol solution, quinalphos undergoes photodegradation reactions of isomerization, oxidation, and deesterification, together with other degradation reactions, resulting in several degradation products. However, the photolysis of quinalphos in ethanol solution yields the two products, *O*,*O*-diethyl-*O*-(3-ethoxyquinoxalin-2-yl)phosphorothioate and *O*,*O*-diethyl-*O*-[3(1-hydroxyethyl)-quinoxalin-2yl]phosphorothioate, both of which are derived from the reaction of the photoexcited quinalphos molecule with the solvent.





S=P(OCC)(OCC)OC2=
NC1=CC=CC=C1N=C2

18

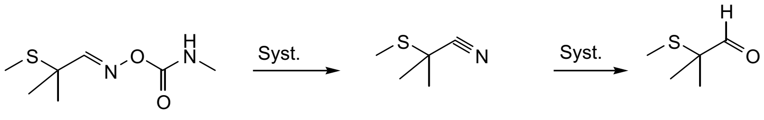
Oximes

Aldicarb

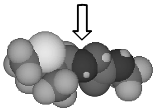
A systemic insecticide

System
In a deuterated citrate phosphate buffer solution with $Cu(NO_3)_2.3H_2O$[254]

In an aqueous buffer solution in the pH range 2.91–5.51, the Cu(II) ion promotes the decomposition of aldicarb, forming the degradation products 2-methyl-2-(methylthio)propionitrile and 2-methyl-2-(methylthio)propanal.



Aldicarb



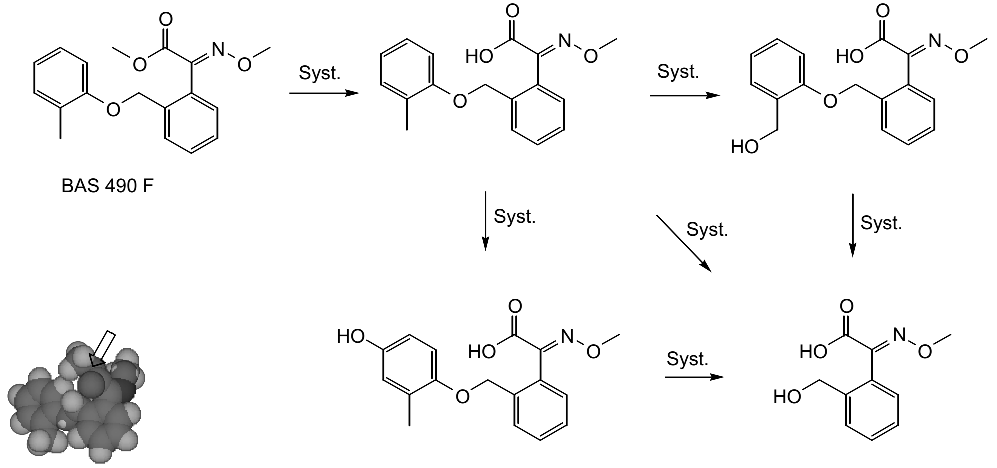
CSC(C)(C)C=NOC(NC)=O

BAS 490 F (Kresoxim methyl)

A fungicide

System
Cryopreserved hepatocyte suspensions: male Wistar rats (150–250 g, Chbb-Thom strain); male 6 month-old pigs (100–120 kg, conventional strains), 10 week-old young female goats (18–20 kg, Bunte Deutsche Edelziege); 8 week-old hens (1.6–1.8 kg, Lohmann)[255]
[256]

By hepatocyte suspensions prepared from goats, pigs, hens, and rats that have been cryopreserved and thawed, BAS 490 F is metabolized via the same pathways as observed using fresh rat hepatocytes. The rate of hydrolysis of ^{14}C-BAS 490 F leading to a carboxylic acid derivative seems to be constant between the cryopreserved and fresh hepatocytes except for goats. The oxidation reaction at the methyl group of the phenoxy ring, leading to the hydroxymethyl analog of the carboxylic acid of BAS 490 F, significantly decreases after cryopreservation, whereas the formation of (*E*)-2-methoxyimino-2[2-(4-hydroxy-2-methylphenyloxymethyl)phenyl] acetic acid by hydroxylation at the 4-position of the phenoxy ring remains at a constant rate. In pig hepatocytes, the two hydroxylated metabolites of the phenoxy ring, carboxy BAS 409 F and (*E*)-2-methoxyimino-2-*o*-hydroxymethylphenyl acetic acid, are formed to a lesser extent after cryopreservation.



BAS 490 F

CON=C(C(OC)=O)C1=CC=C
C=C1COC2=CC=CC=C2C

19

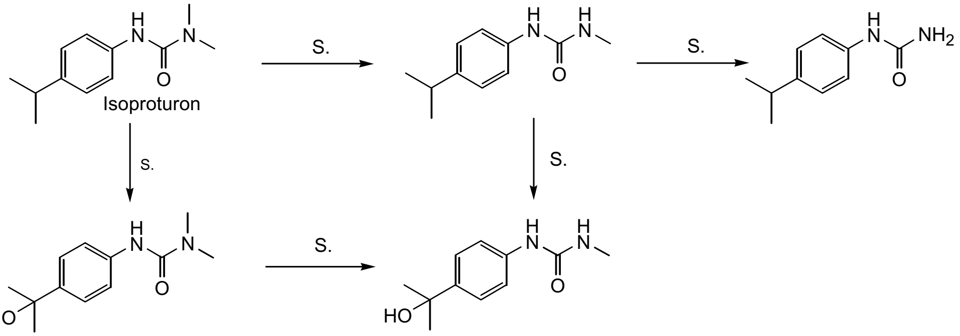
Phenylureas and Related Compounds

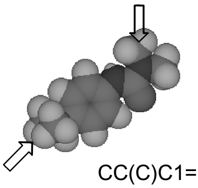
Isoproturon

A herbicide: pre- and post-emergent control of weeds in wheat

Soil
Soil samples collected from the agricultural area of FMA (Forschungsverbund Agraroekosysteme Munhen) in Scheyern[257]

The major degradation product of isoproturon in most soil samples is identified as 2-hydroxyisoproturon, and the polar metabolites characterized are monodesmethylisoproturon and 2-hydroxymonodesmethylisoproturon. The detection of isoproturon in soil solution down to 170 cm depth and in creek water in concentrations exceeding 4 μg l^{-1} and also of the polar metabolites in concentrations up to 0.9 μg l^{-1} indicates the mobility of this phenylurea herbicide and its degradation products.





CC(C)C1=CC=C(N
C(N(C)C)=O)C=C1

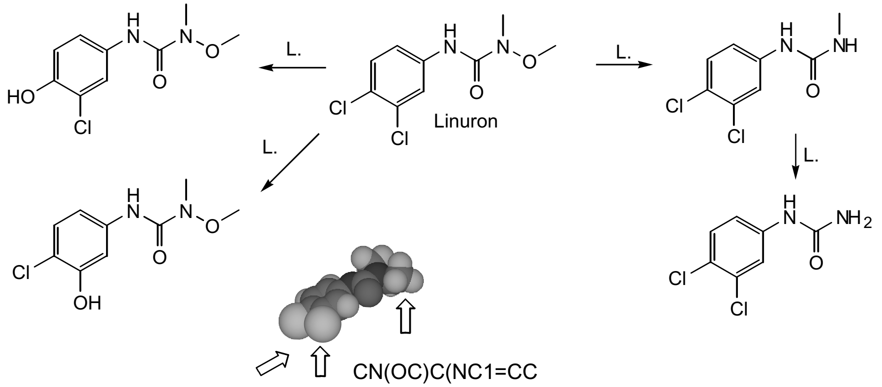
Linuron and Chlorbromuron

Herbicides

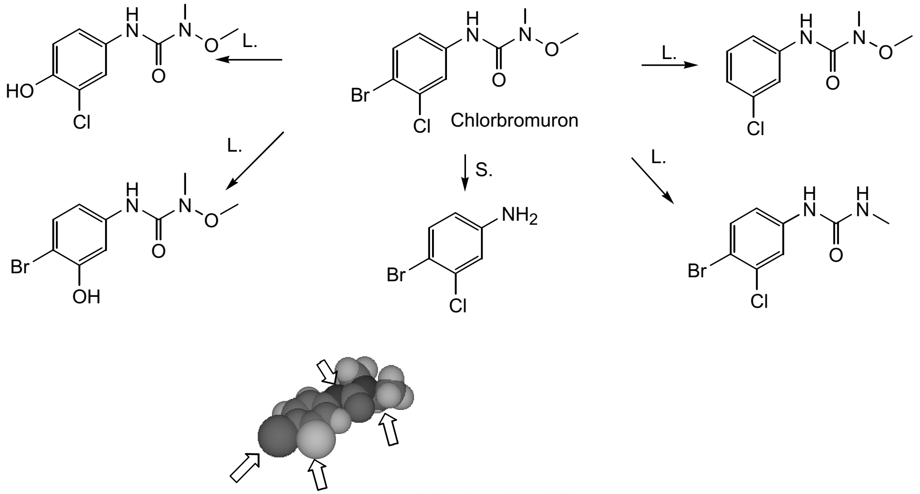
Light
Irradiation by fluorescent lamps of the Duke GL 20E type with black light lamps[258]

Soil
pH 5.97; pH 5.5[259]

The main photoproducts initially formed in the phototransformation of linuron and chlorbromuron in aqueous solution result from photolysis, i.e. hydroxylation with release of the halide ion, and from elimination of a methoxy group. The orientation of the reaction depends on the wavelength: short wavelengths (254 nm) favor demethoxylation and photolysis in the *meta* position,



CN(OC)C(NC1=CC
=C(Cl)C(Cl)=C1)=O



CN(C(NC1=CC=C(C
(Cl)=C1)Br)=O)OC

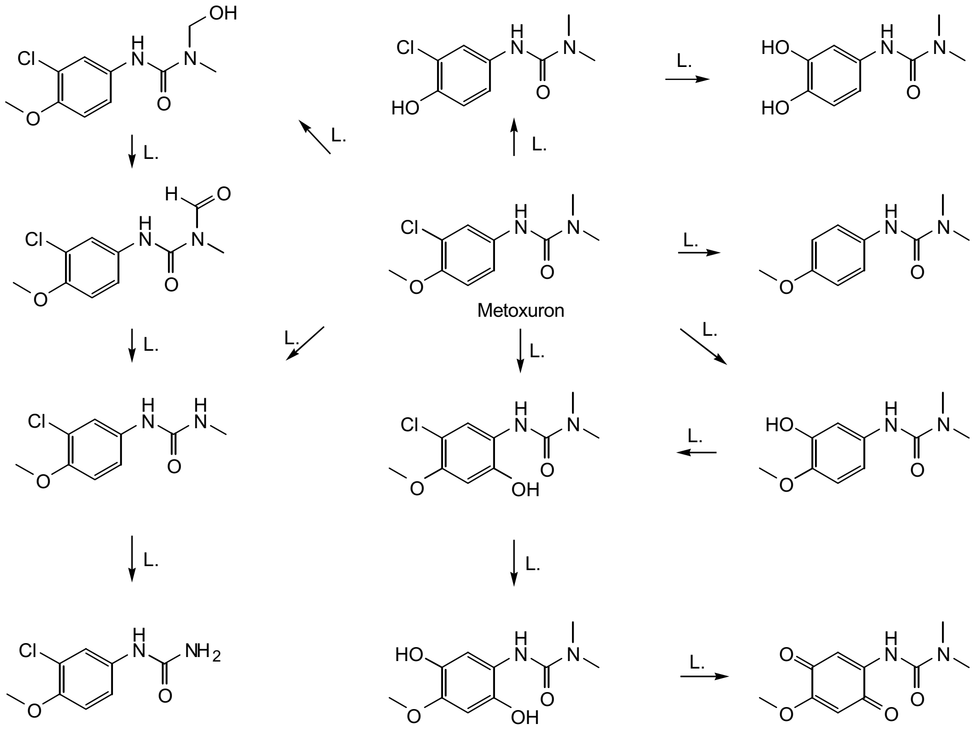
whereas, with black light longer than 330 nm, photolysis in the *para* position is the main reaction observed. In soils, 4-bromo-3-chloroaniline is identified as a soil degradation product of chlorbromuron.

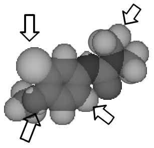
Metoxuron

A herbicide

Light
UV irradiation with a Philips HPK 125 W high-pressure mercury vapor lamp in aqueous solutions with H_2O_2 or TiO_2[260]

Photodegradation of metoxuron with UV irradiation in the presence of UV-H_2O_2 and -TiO_2 primarily proceeds with the replacement of the chlorine atom with the hydroxy group and the attack of OH radicals at the 6-position on the phenyl ring. The principal photoproducts identified are 3-(4-methoxy-2,5-paraquinone)-1,1-dimethylurea, hydroxymetoxuron, 3-(3-hydroxy-4-methoxyphenyl)-1,1-dimethylurea, 3-(3-chloro-4-hydroxyphenyl)-1,1-dimethylurea, and 3-(3-chloro-4-methoxyphenyl)-1,1dimethylurea.





CN(C)C(NC1=CC
(Cl)=C(OC)C=C1)=O

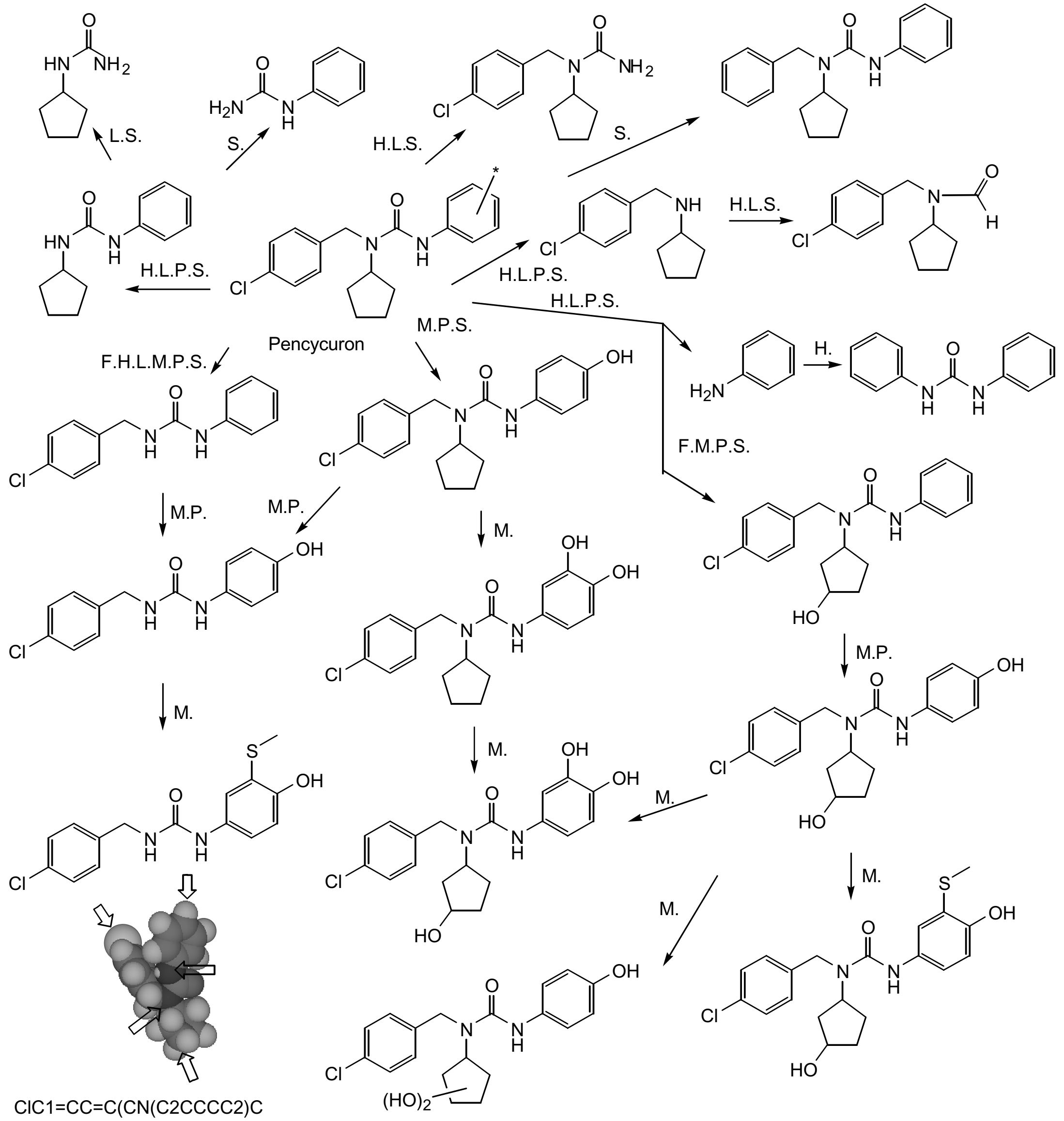
Pencycuron

A fungicide: control of *Rhizoctonia solani* Kuhn [telemorph *Thanatephorus cucumeris* (Frank) Donk]

Fungus
Rhizoctonia solani strains[261]

Hydrolysis, Light, Mammal, Plant, Soil
[262]

The metabolic profiles of pencycuron in fungus, hydrolysis, mammals, photodecomposition, plants, and soils are illustrated. Both tolerant and sensitive fungal species *Rhizoctonia solani* metabolize pencycuron to give *cis*- and *trans*-3-hydroxycyclopentyl pencycurons which are less active than pencycuron.



ClC1=CC=C(CN(C2CCCC2)C
(NC3=CC=CC=C3)=O)C=C1

20

Phosphono Amino Acids and Related Compounds

Glyphosate (Roundup)

A non-selective, broad-spectrum, post-emergent herbicide

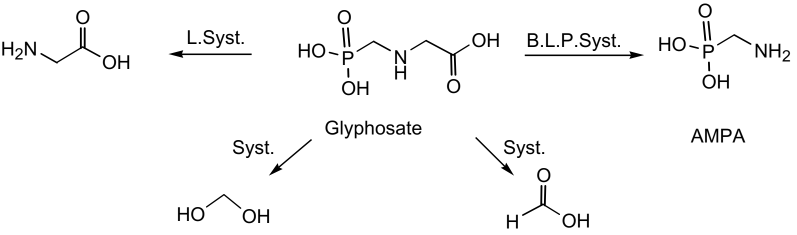
Bacterium
Arthrobacter atrocyaneus (DSM 20217)[263]
Pseudomonas sp. strain LBr[264]

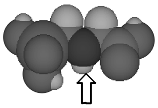
Light
UV light in deionized water; sunlight in artificial water[265]

Plant
Cell cultures of soybean: *Glycine max* L. Merrill cv. Mandarin; wheat: *Triticum aestivum* L. Heines Koga II; maize: *Zea mays* L. cv. Black Mexican Sweet
Seedlings of wheat: *Triticum aestivum* L. (10 day-old); spruce: *Picea abies* L. Karst, (4 week-old); tobacco: *Nicotiana tabacum* cv. Bel B, (4 week-old); soybean: *Glycine max* L. (7 week-old)[266]

System
Chemical oxidation in D_2O with *m*-chloroperoxybenzoic acid[267]
Metal complexes with Cu, Ni, Fe, Ca, and Mg in water[268]

The photolytic degradation of glyphosate results in the formation of glycine, (aminomethyl)phosphonic acid (AMPA), and NH3. Glyphosate undergoes nitrogen−carbon cleavage on reaction with *m*-chloroperoxybenzoic acid, leading ultimately to many of the same products formed on their metabolism and environmental degradation. It is suggested that insoluble complexes of glyphosate with iron(III), copper(II), calcium, and magnesium ions are formed at near-neutral pH, a mechanism of which is the inactivation of glyphosate in contaminated groundwater.[268] The bacterium degrades high levels of glyphosate, primarily by converting to AMPA. Appreciable uptake of glyphosate is observed with seedlings and leaves and to a lesser extent with culture cells in the form of non-metabolized glyphosate, with AMPA as the only detectable metabolite.





OP(CNCC(O)=O)(O)=O

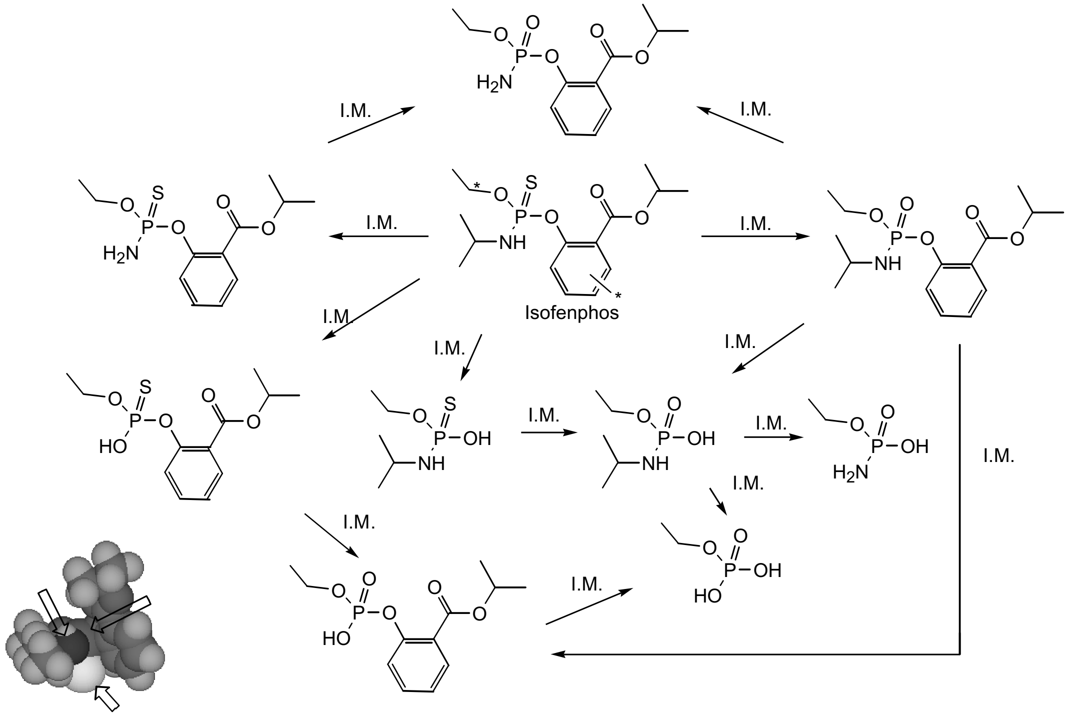
Isofenphos

A proinsecticide

Insect
Two day-old insecticide-susceptible housefly: *Musca domestica* L., CSMA strain; third instar lavae of cuperous chafer: *Anomala cupera* Hope[269]

Mammal
Wistar rats (7 week-old, 180−200 g)[270]
[271]

^{14}C-Isofenphos is bioactivated by mixed-function oxidases that ultimately give *N*-desisopropylisofenphos oxon, a product with 2300-fold greater inhibitory potency than isofenphos oxon towards housefly head acetylcholinesterase.[271] By housefly and the cuperous chafer, isofenphos is metabolized to give detoxified metabolites without the bioactivated *N*-desisopropylisofenphos oxon. No difference in kinds of metabolite is found between the two insects. When rats are administered ^{14}C-isofenphos, most of the radioactivity is recovered from the water fraction of the urine and feces. Aminoisofenphos and isofenphos oxon are detected in the benzene fraction, and the other six metabolites are identified as water-soluble metabolites which include *O*-ethylhydrogen phosphoramidate and *O*-ethylhydrogen isopropylphosphoramidothioate. Water-soluble metabolites are predominantly formed through cleavage of the P−O−aryl linkage.



S=P(OCC)(NC(C)C)OC1=C
(C(OC(C)C)=O)C=CC=C1

21

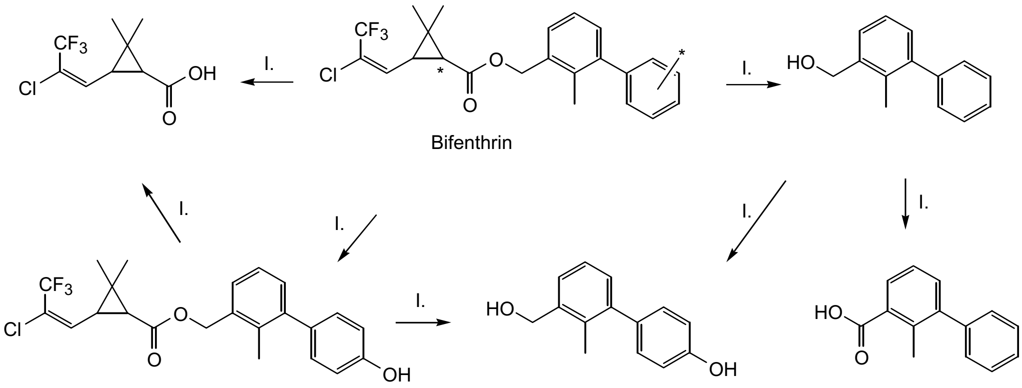
Pyrethroids

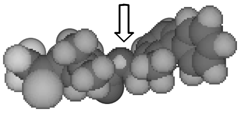
Bifenthrin

An insecticide

Insect (mites)
The bulb mites: *Rhizoglyphus robini* Clamparede[272]

When mites are administered ^{14}C-bifenthrin either by injection or by contact, bifenthrin is efficiently metabolized by the mites and the metabolites identified arise from the combination of ester cleavage, oxidation, and conjugation reactions and are the 4′-hydroxy derivative of the ester, the primary ester cleavage products, the acid, and its 4′-hydroxy derivative from the alcohol moiety, as well as several unidentified metabolites.





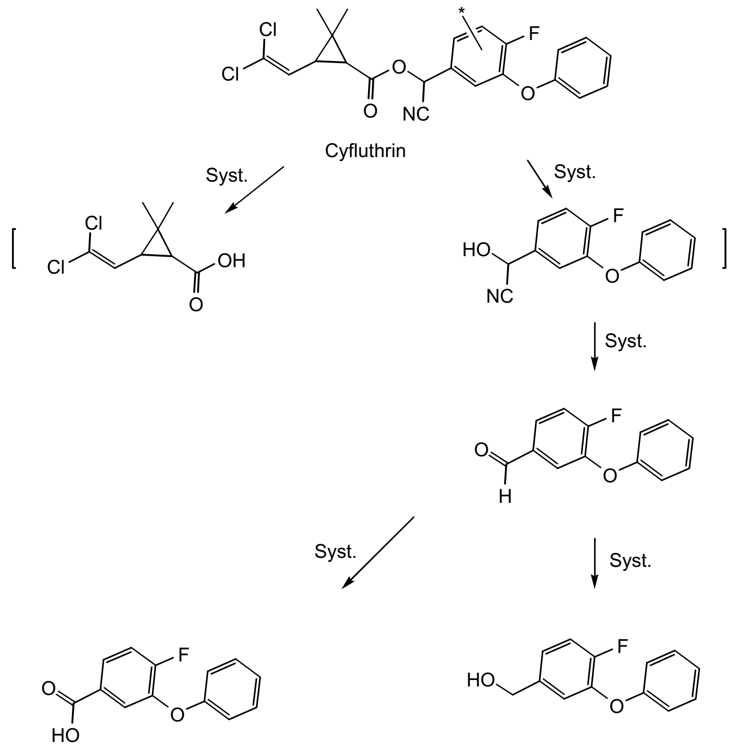
CC1(C)C(C=C(C(F)(F)F)Cl)C1C(OCC2
=C(C)C(C3=CC=CC=C3)=CC=C2)=O

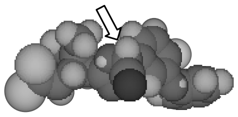
Cyfluthrin

An insecticide

System
Incubation with a reaction mixture of 0.05M phosphate buffer, pH 7.0[273]

The non-enzymatic hydrolyzed products of ^{14}C-cyfluthrin are isolated and identified by the incubation reaction mixture of a buffer solution. The products are derived from the hydrolysis of the ester linkage of cyfluthrin via cyanhydrin. This results in the corresponding aldehyde which undergoes both oxidation and reduction to give rise to carboxylic acid and benzyl alcohol, respectively.





CC1(C)C(C=C(Cl)Cl)C1C(OC(C#N)C2=CC(OC3=CC=CC=C3)=C(F)C=C2)=O

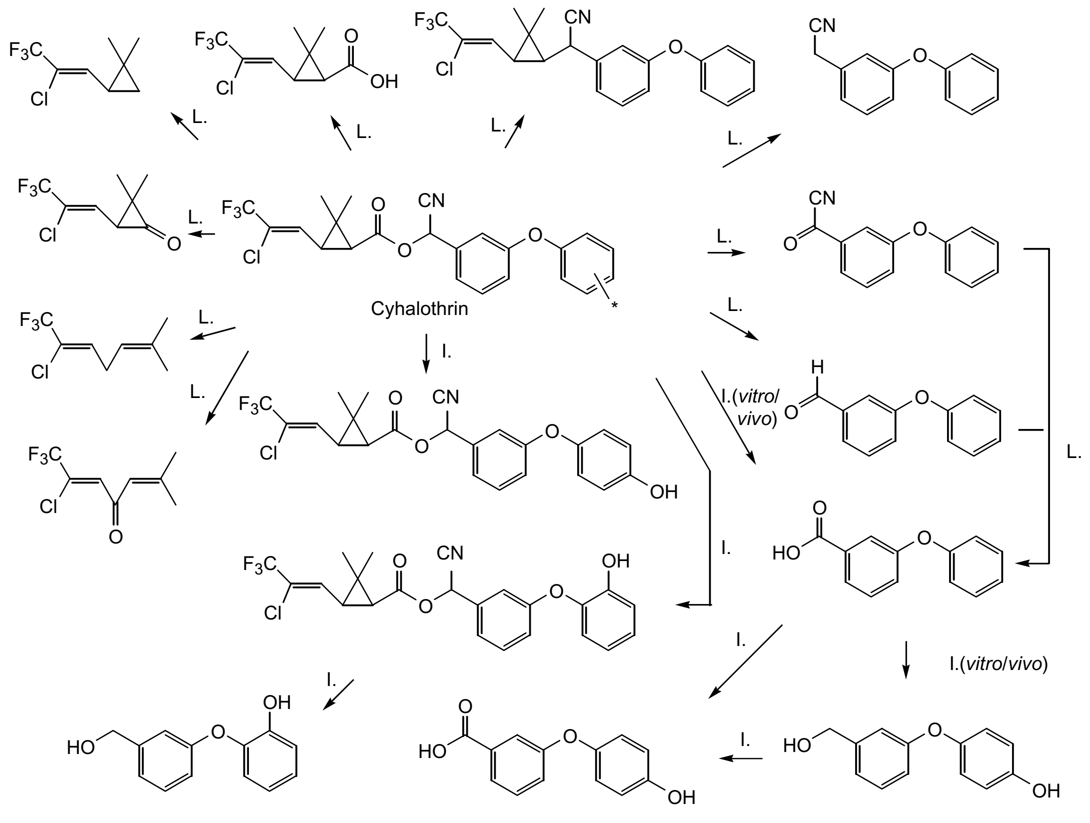
Cyhalothrin

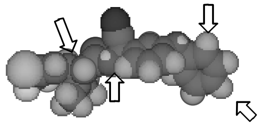
An insecticide

Insect
Worker honey bees: *Apis mellifera* L.8 (*in vivo*); the mid-guts of the honey bees (*in vitro*)[274]

Light
UV irradiation: at 300 nm with eight RPR3000 lamps in a Rayonette photoreactor[275]

The solution and solid-phase photodecomposition of cyhalothrin involves *E*/*Z* and *cis*/*trans* isomerization reactions and frees radical processes leading to decarboxylation, ester cleavage, proton abstraction, oxygen scavenging, and reactions with solvent-generated radicals. The major degradation products are decarboxylated analogs which are also isomerized at the cyclopropyl and vinyl groups. *In vitro* incubation of ^{14}C-cyhalothrin with honey bee mid-guts yields the principal metabolite identified as 4-hydroxy-3-phenoxybenzyl alcohol with a small amount of 3-phenoxybenzoic acid. *In vivo* metabolism with honey bees shows the major metabolites





CC1(C)C(C=C(Cl)C(F)(F)F)C1C(OC(C#
N)C2=CC=CC(OC3=CC=CC=C3)=C2)=O

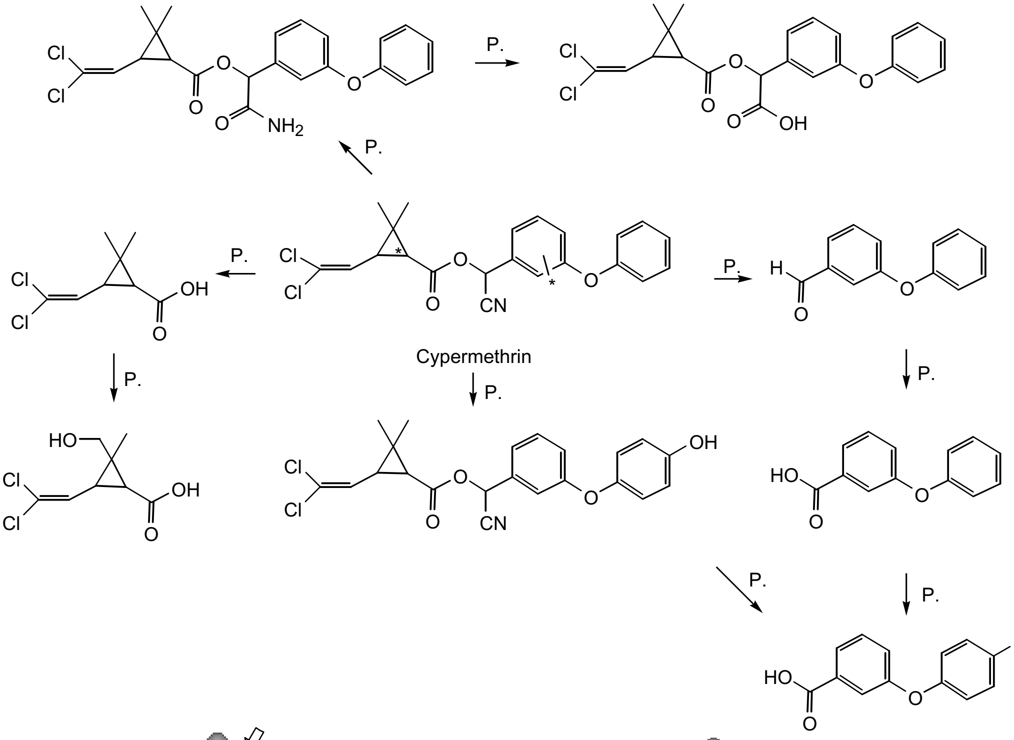
4′-hydroxy- and 2′-hydroxy-3-phenoxybenzyl alcohols and 4′-hydroxy-3-phenoxybenzoic acid. Prochloraz delays the metabolism, detoxication, and excretion of cyhalothrin by inhibition of microsomal oxidation, effectively enhancing the toxicity to the honey bee.

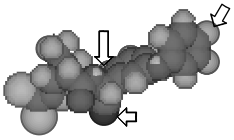
Cypermethrin

An insecticide

Plant
Cabbage: cv. Shikidori[276]

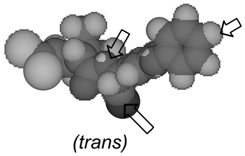
In cabbage plants, (1*R)-cis*- and (1*R)-trans*-isomers of cypermethrin undergo epimerization to (1*S*)-isomers, *cis*/*trans* isomerization, ester bond cleavage, hydroxylation of the phenoxy group in the alcohol moiety or the geminal methyl group in the acid moiety, hydration of the cyano group to an amido group with subsequent hydrolysis to the carboxylic acid, and the conjugation of the carboxylic acid, and alcohols with sugars.





(cis)

CC([C@H]1C=C(Cl)Cl)([C@@H]1C(OC(C2=CC(OC3=CC=CC=C3)=CC=C2)C#N)=O)C



(trans)

CC([C@@H]1C=C(Cl)Cl)([C@@H]1C(OC(C2=CC(OC3=CC=CC=C3)=CC=C2)C#N)=O)C

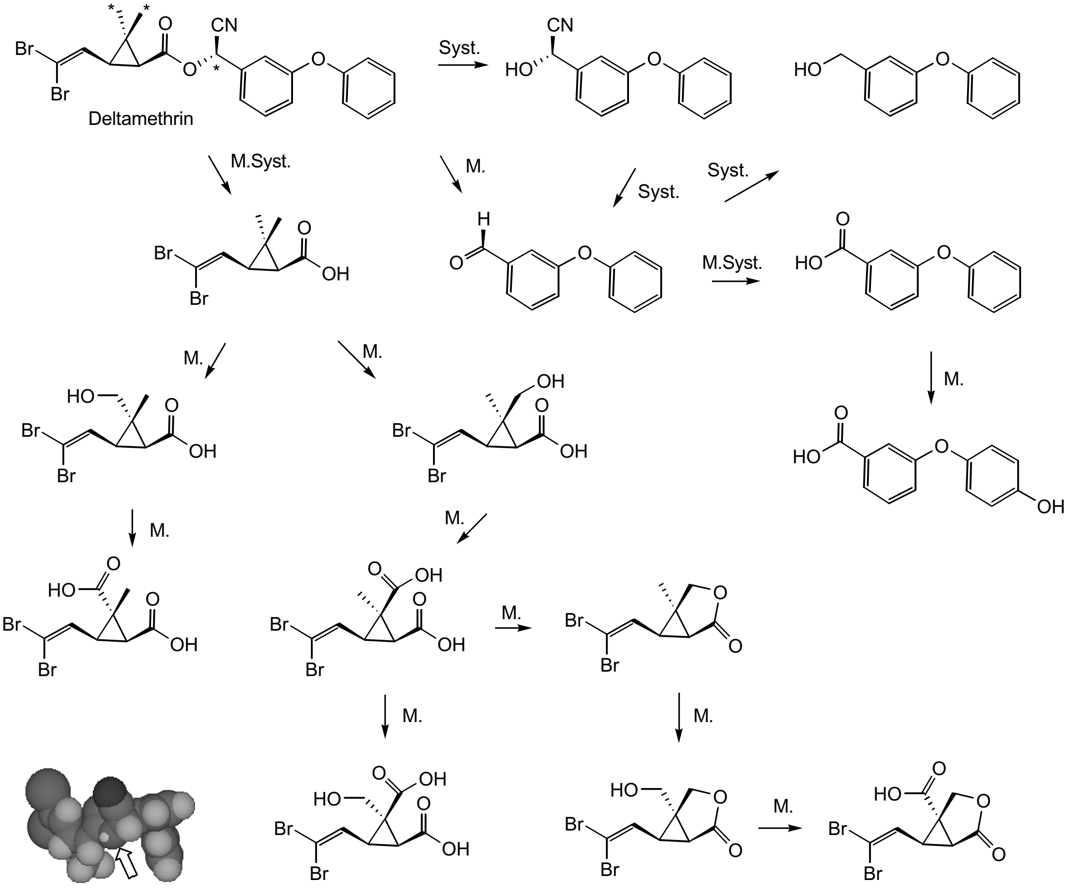
Deltamethrin

An insecticide

Mammal
Dairy lactating cows: Holstein (557 kg); Ayrshire (504 kg)[277]

System
Cell culture of plant cells of unicellular algae: *Dunaliella bioculata* (marine phytoplancton, Cambridge collection); mouse fibroblast cell line (NCTC clone L 929)[278]

After oral administration of ^{14}C-deltamethrin to lactating dairy cows, deltamethrin is metabolized and excreted in the bile and urine with very little accumulation in major edible tissues. The major portion (78–82%) of the radioactivity in feces is deltamethrin. Only 4–6% is eliminated in the urine and 0.42–1.62% is secreted in the milk. The primary biotransformation is via the hydrolysis of the ester linkage followed by oxidation of the geminal methyl groups of cyclopropane carboxylic acids and phenoxy benzaldehyde, resulting in dicarboxylic acid, lactonecarboxylic acid, or phenoxybenzoic acid



C[C@@]1(C)[C@H](C=C(Br)Br)[C@@H]1C(O[C
@H](C2=CC=CC(OC3=CC=CC=C3)=C2)C#N)=O

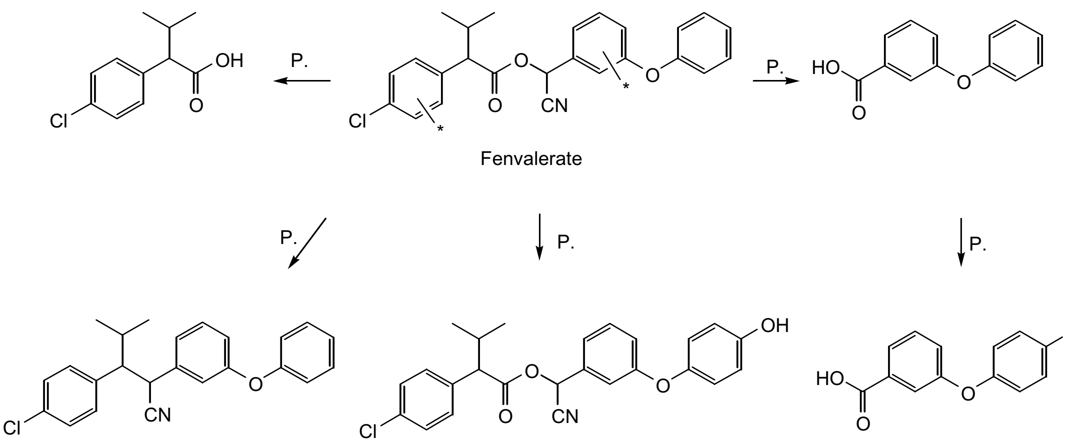
derivatives. Deltamethrin is not metabolized within algae cells and mouse fibroblasts, but is partially transformed into less or not active isomers. In algae and fibroblast culture media, many metabolites of deltamethrin resulting mostly from hydrolysis of the molecule are found. This metabolism seems to be linked with the release of enzymes by cells into the culture medium.

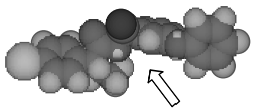
Fenvalerate

An insecticide

Plant
Spring wheat: cv. Bonanza[279]

After foliar treatment of ^{14}C-fenvalerate on wheat plants, the amount of residual radioactivity in the grain and hull is below the limit of reliable measurement. Individual degradation products accounting for more than 1% of the applied radioactivity are not present in the foliage or straw. Important degradation pathways include decarboxylation and ester cleavage.





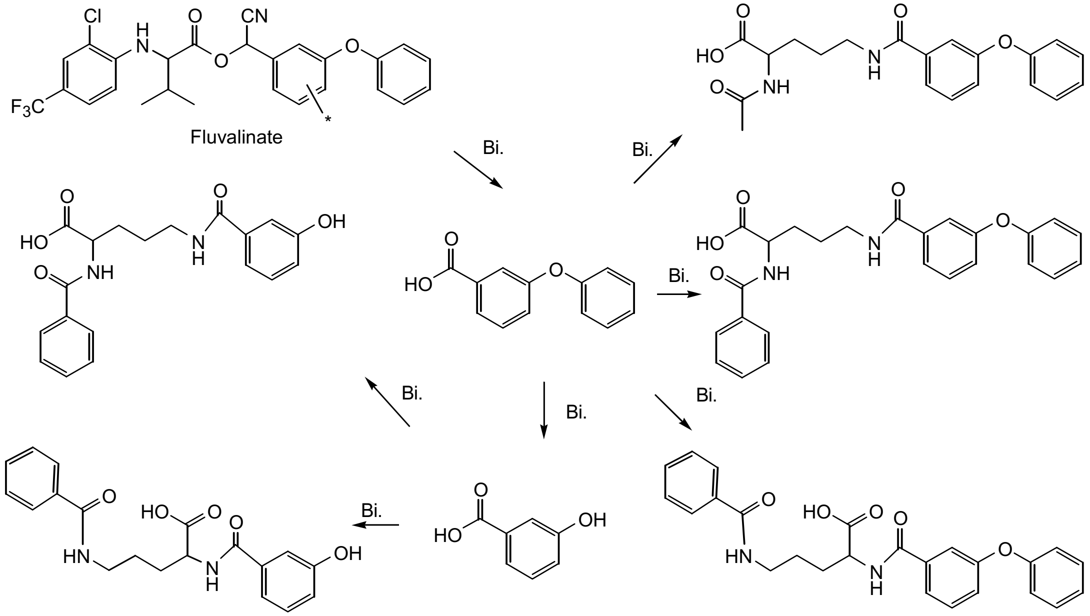
ClC1=CC=C(C(C(C)C)C(OC(C#N)C2=C
C(OC3=CC=CC=C3)=CC=C2)=O)C=C1

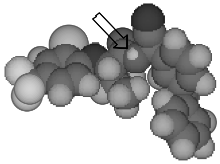
Fluvalinate

An insecticide

Bird
Healthy leghorn hens from Jensen Farms, Tracy, CA (1.4–2.4 kg)[280]

Metabolism of ^{14}C-fluvalinate by chickens produces 3-phenoxybenzoic acid, which is further degraded by two pathways. The first pathway involves *O*-dephenylation and is the major metabolic route. The second pathway converts the carboxylic metabolites into four conjugates of benzoylornithine together with the conjugate of acetylornithine. The predominant conjugate is 2*N*-(3-hydroxybenzoyl)-5*N*-benzoylornithine.



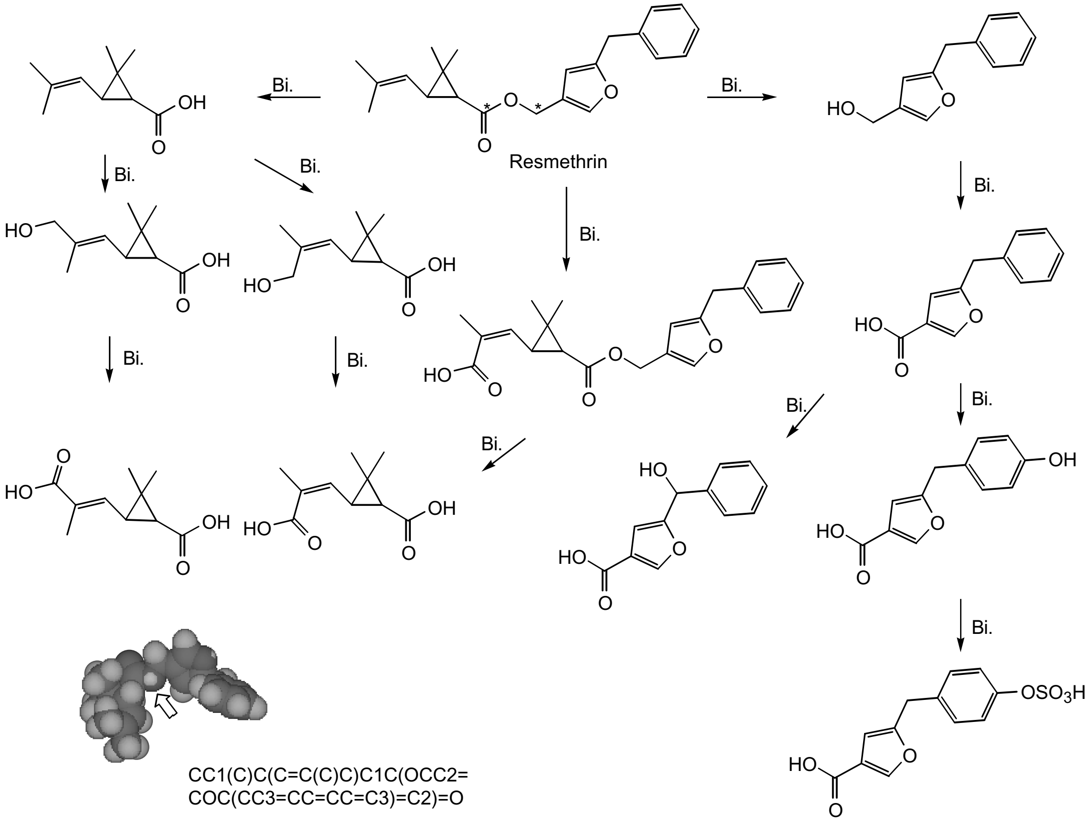


ClC1=C(NC(C(C)C)C(OC(C#N)C2=CC=CC(O
C3=CC=CC=C3)=C2)=O)C=CC(C(F)(F)F)=C1

cis-and *trans*-Resmethrins

Bird
Twenty four white leghorn hens (1.8 kg average)[281]

Cis-1*RS* and *trans*-1*RS* isomers of ^{14}C-resmethrin are individually administered orally to white leghorn hens, and more than 90% of the radioactivity is eliminated in the excreta within 24 h of treatment. The metabolic routes for both resmethrin isomers arise from ester hydrolysis and oxidation of the hydrolytic products. Some of these metabolites are further conjugated with glucuronic acid, sulfate, or other unidentified compounds before excretion.



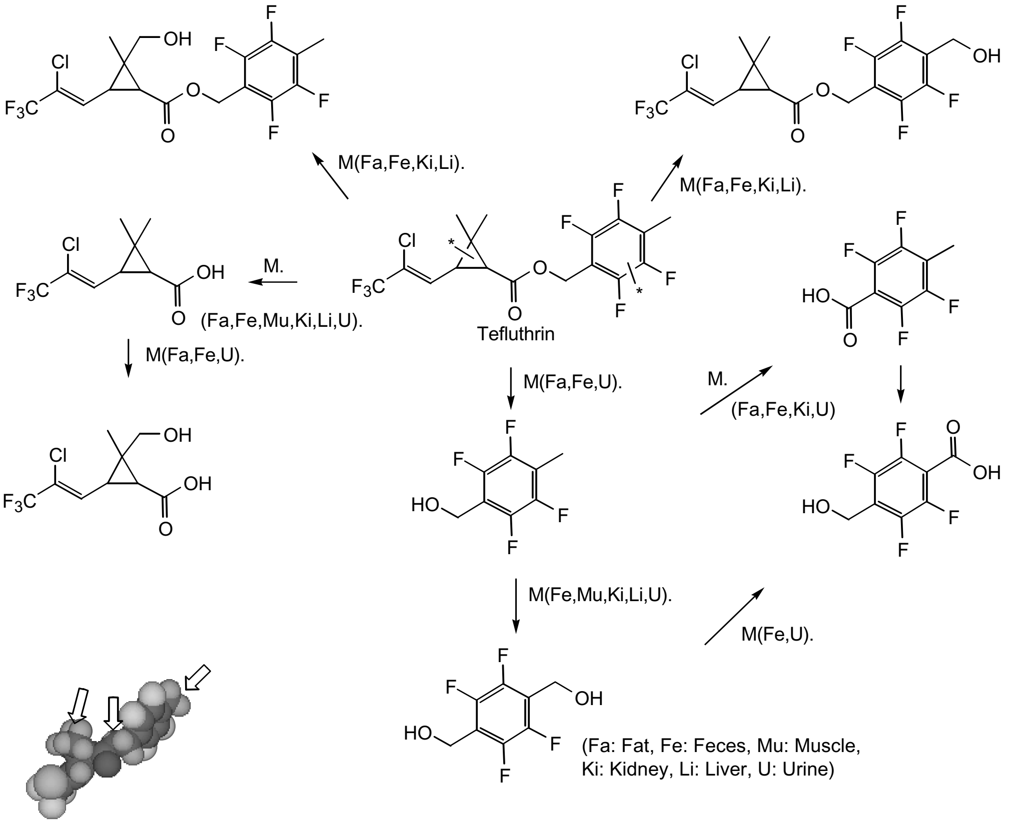
CC1(C)C(C=C(C)C)C1C(OCC2=COC(CC3=CC=CC=C3)=C2)=O

Tefluthrin

An insecticide

Mammal
A goat (2.32 kg)[282]

When a goat is dosed with ^{14}C-tefluthrin orally, extensive metabolism occurs in the goat by ester cleavage and oxidation at a variety of positions on the molecules. Low radioactive residues are detected in the milk, fat, and muscle, with tefluthrin as the largest individual component of the residue. Higher residues are present in the kidney and liver, and only a small percentage of this residue is due to tefluthrin. The remainder in the kidney and liver is a complex mixture of metabolites. In total, eight metabolites are identified in the feces and urine as well as other tissues such as fat, muscle, kidney, and liver.



(Fa: Fat, Fe: Feces, Mu: Muscle, Ki: Kidney, Li: Liver, U: Urine)

ClC(C(F)(F)F)=CC1C(C)(C)C1C(O
CC2=C(F)C(F)=C(C)C(F)=C2F)=O

22

Sulfonylureas

Amidosulfuron

A post-emergent herbicide: control of broadleaf weeds in cereal and other crops

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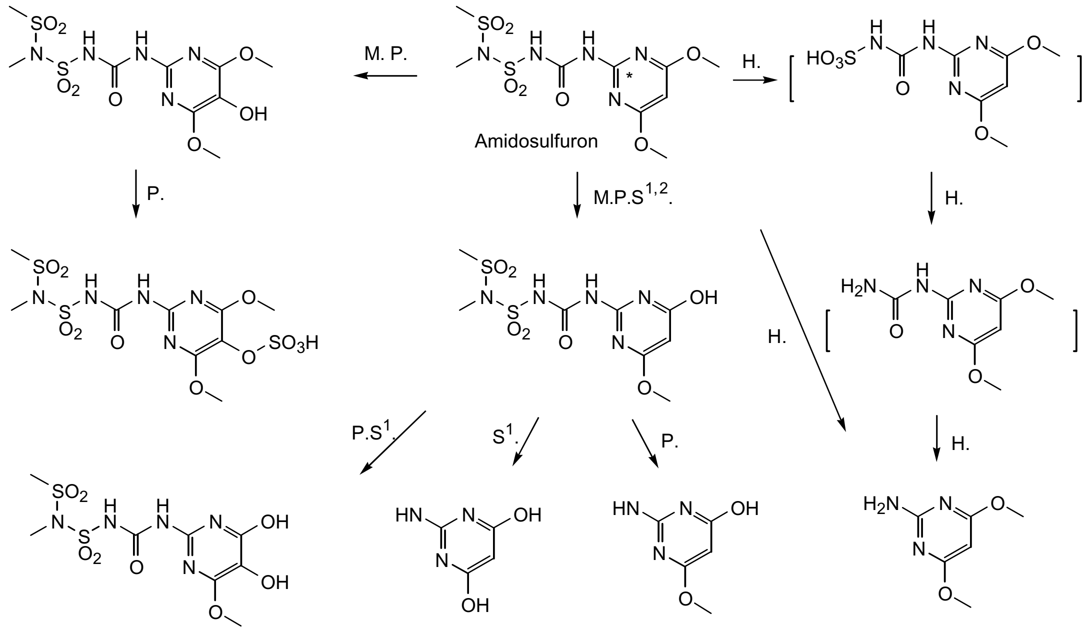
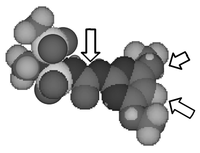
Hydrolysis/Mammal/Plant/Soil[1]
283

Soil[2]
Prairie soils: coarse loamy soil (pH 6.4–7.1/H_2O); fine loamy soil (pH 7.9–8.2/H_2O); fine silty soil (pH 6.2–7.5/H_2O)[284]

The hydrolysis of ^{14}C-amidosulfuron in buffer aqueous solutions under various conditions results in 2-amino-4,6-dimethoxypyrimidine as the major hydrolyzed product. In soils, *O*-demethylated amidosulfuron is the major degradation product. In mammals and plants, primary hydroxylation at the pyrimidine ring is a characteristic degradation reaction yielding 5-hydroxyamidosulfuron.





CN(S(C)(=O)=O)S(NC(NC1=NC(OC)=CC(OC)=N1)=O)(=O)=O

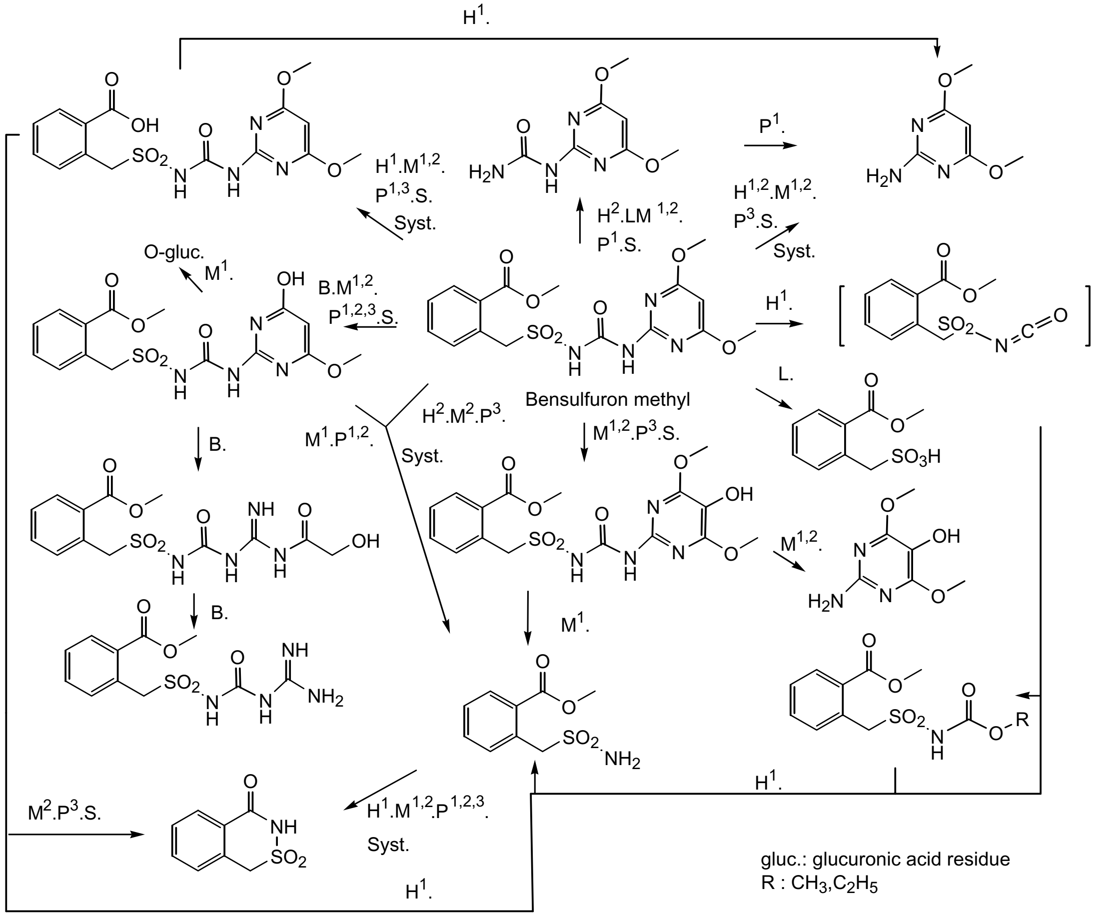
Bensulfuron methyl

A selective herbicide: control of most annual and perennial broadleaf weeds for use in transplanted and direct-seeded rice fields

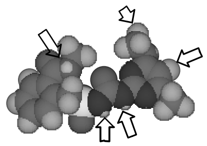
Hydrolysis[1]
Aqueous solution at pH 5–11 and 30 or 50 °C[285]

Mammal
Rat; goat[286]

Bensulfuron methyl is metabolized by mammals and birds and the major metabolites identified include mono-*O*-demethylated and 5-hydroxylated bensulfuron methyl and 5-hydroxy-2-amino-3,5-dimethoxypyrimidine. As bird metabolites, cleavage of the pyrimidine ring of bensulfuron methyl is observed



gluc.: glucuronic acid residue
R : CH_3,C_2H_5



O=C(OC)C1=CC=CC=C1CS(ONC
(NC2=NC(OC)=CC(OC)=N2)=O)=O

Plant[1]
Rice plant[287]

Plant[2]
Rice seedlings: *Oryza sativa* L., cv. Tsukinohikari, *japonica*; cv. Lemont, *indica x japonica*[288]

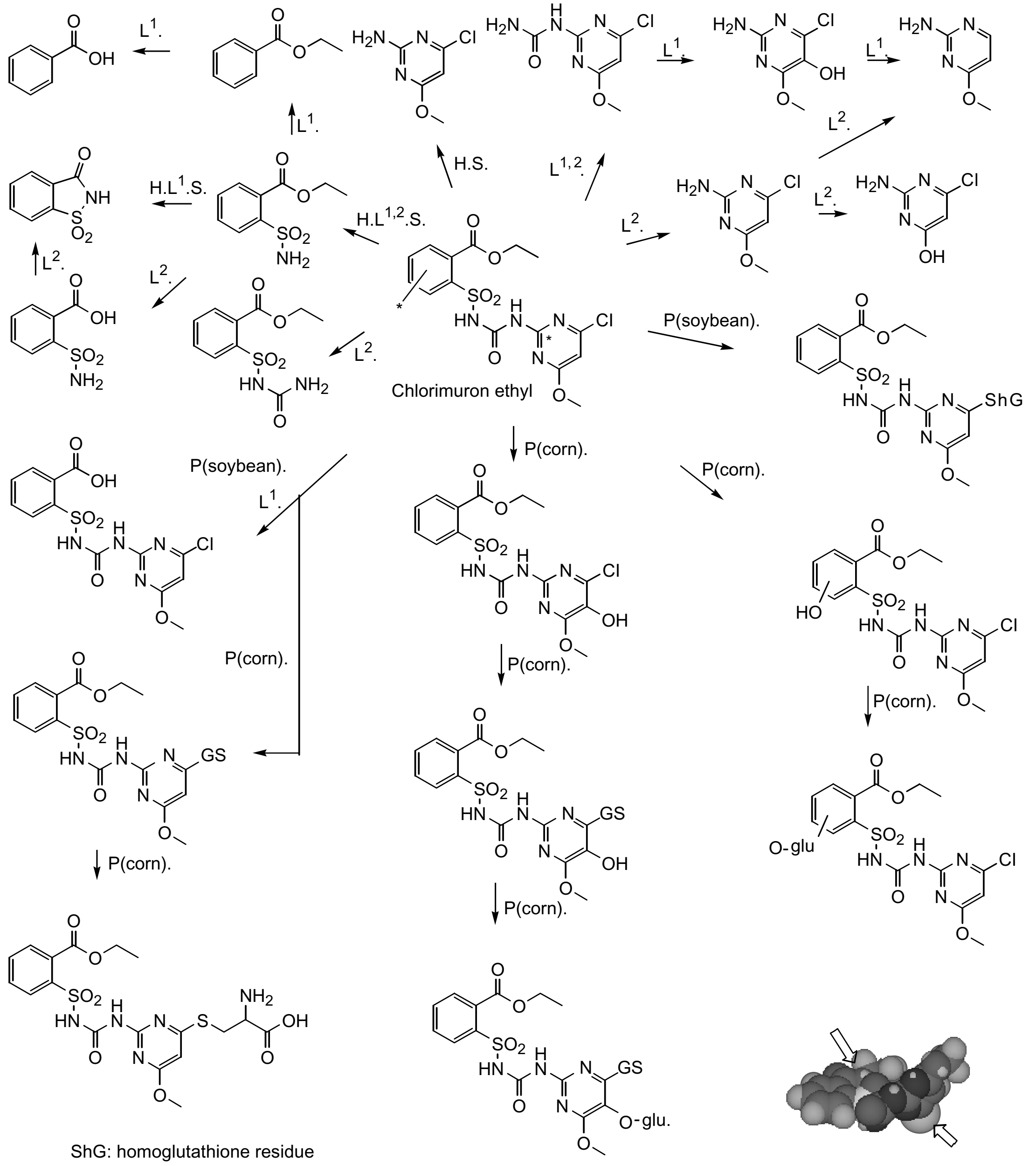
Bird/Hydrolysis[2]*/Light/Mammal*[2]*/Plant*[3]*/Soil*
289

System
Minerals: kaolinite (Prolab), silica gel (Kiesegel 60, Merck), montmorillonite K 10 (Fluka), alumina (Aluminium oxyd 90 aktiv neutral, Merck)[290]

which results in two pyrimidine ring-opening metabolites. In rice plants, bensulfuron methyl undergoes rapid *O*-demethylation at one of the methoxy groups on the pyrimidine ring which will proceed through hydroxylation at the methyl group. Alcoholysis and hydrolysis of bensulfuron methyl (H^1) involve mainly the breakdown of the urea moiety which leads to several degradation products, some of which are also identified as metabolites in mammals and plants.

Chlorimuron ethyl

A broad-spectrum herbicide: for pre-emergent, preplant-incorporated, and post-emergent use in soybean



ShG: homoglutathione residue
GS: glutathione residue
O-glu.: glucose residue

O=C(OCC)C1=CC=CC=C1S(NC(N
C2=NC(OC)=CC(Cl)=N2)=O)(=O)=O

Hydrolysis¹
Water (pH 7.45) collected from a representative area in Ontario (Iona station)[291]

Hydrolysis²
On alluvial soil (pH 8.1) under UV light and sunlight by a 15 E UV lamp; sunlight[292]

Plant
Soybean: *Glycine max*. cv. Williams; common cocklebur: *Xanthium pensylvancium* Wallr.; redroot pigweed: *Amaranthus retroflexus*[293]
Corn: *Zea mays* L., Northrup King hybrid PX 9144[294]

Light
A medium-pressure mercury lamp (125 W, Philips)[295]

Soil
Soils collected from the Harrow Research Centre (pH 5.05)[296]

Excised soybean seedlings rapidly metabolize ^{14}C-chlorimuron ethyl, but common cocklebur and redroot pigweed, which are sensitive to chlorimuron ethyl, metabolize much more slowly. Two metabolites are primarily identified. By intact corn seedlings, chlorimuron ethyl undergoes biotransformation to give more metabolites and under UV light is photodegraded into smaller fragments.

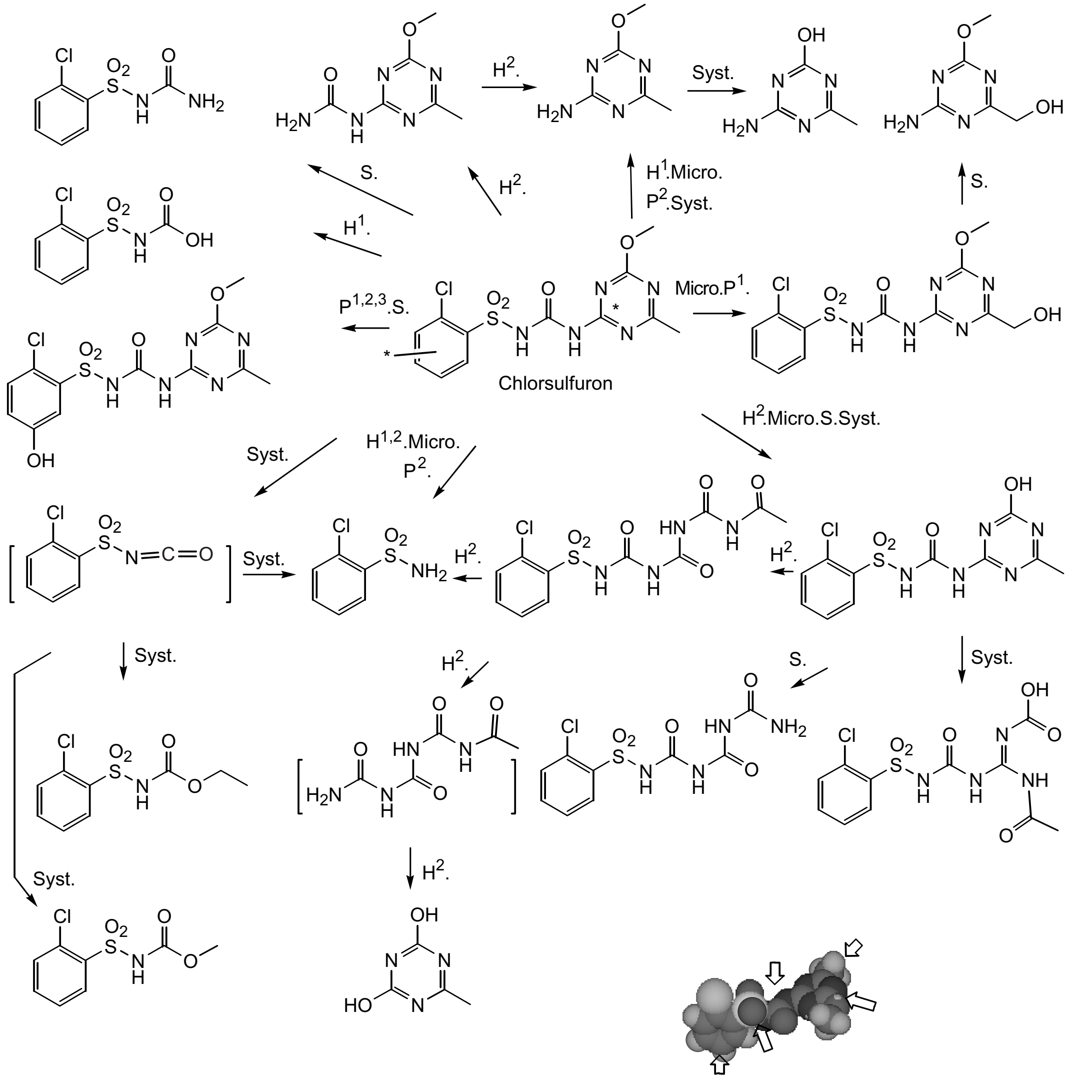
Chlorsulfuron

A post-emergent herbicide: control of a wide range of broadleaf weeds and some grasses, use for some cereals

Hydrolysis[1]
Deionized water distilled from alkaline potassium permanganate[297]

Hydrolysis[2]
pH 5[298]

Chlorsulfuron is metabolized in wheat and in tolerant broadleaves via different pathways where hydroxylation occurs on the methyl group of the triazine ring and at the phenyl ring of the chlorsulfuron in respective plants. With chemical degradation of chlorsulfuron on dry minerals (Syst.), two pathways of degradation are observed, one of which is direct



ClC1=C(S(NC(NC2=NC(C)=NC(OC)=N2)=O)(=O)=O)C=CC=C1

Mammal
Rat; goat[299]

Plant[1]
Wheat; flax; black nightshade[300]

Plant[2]
Wheat[301]

Plant[3]
Diclofop methyl-resistant (SR4/84) rigid ryegrass: *Lolium rigidum* Gaudin[302]

Microorganism
Isolates from soil[303]

Soil
Soils under aerobic and anaerobic conditions[304]

System
Kaolinite; silica; bentonite H^+; monmorillonite K10 with/without solvents[305]

hydrolysis of the urea function and the other is *O*-demethylation of the methoxy substituent. By hydrolysis and in soils, chlorsulfuron undergoes degradation reactions involving *O*-demethylation, hydroxylation, and cleavage of the triazine ring, resulting in diverse degradation products.

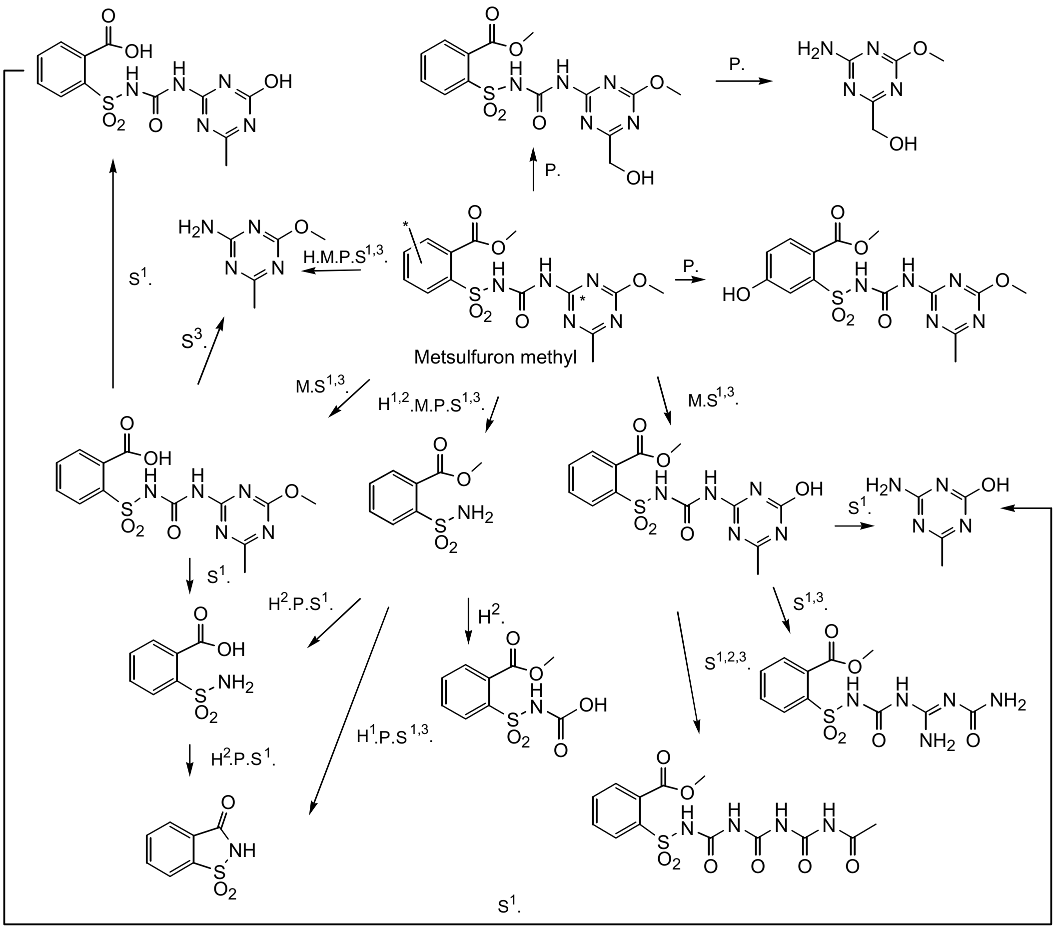
Metsulfuron methyl

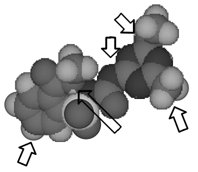
A herbicide: control of broadleaf weeds, use for wheat, oat, barley, and some other crops

Hydrolysis[1]/*Mammal*/*Plant*/*Soil*[1]
306

Hydrolysis[2]
Deionized water distilled from alkaline potassium permanganate[307]

In soils, under aerobic conditions, metsulfuron methyl is degraded by the cleavage of the sulfonylurea linkage, resulting in the formation of methyl 2-(aminosulfonyl)benzoate, 4-methoxy-6-methyl-2-amino-1,3,5-triazine, and saccharin as major products. Under anaerobic conditons, free acid of metsulfuron methyl and the resulting *O*-demethylation product are identified. The formation of two ring-opening products





O=C(OC)C1=CC=CC=C1S(NC(NC2
=NC(C)=NC(OC)=N2)=O)(=O)=O

Soil^{2}
Soils from the plane of Roussilon at St-Nazaire (pH 6.3/H_2O)[308]

Soil^{3}
Matapeake silt loam (pH 5.2)[309]

at the triazine moiety is observed. Under acidic conditions, hydrolytic degradation products identified are involved in the soil degradation products. In plants, the specific metabolites are identified as the hydroxylation product of the phenyl ring of metsulfuron methyl and 4-methoxy-6-hydroxymethyl-2-amino-1,3,5-triazine. Mammalian metabolites are also included in the soil metabolites.

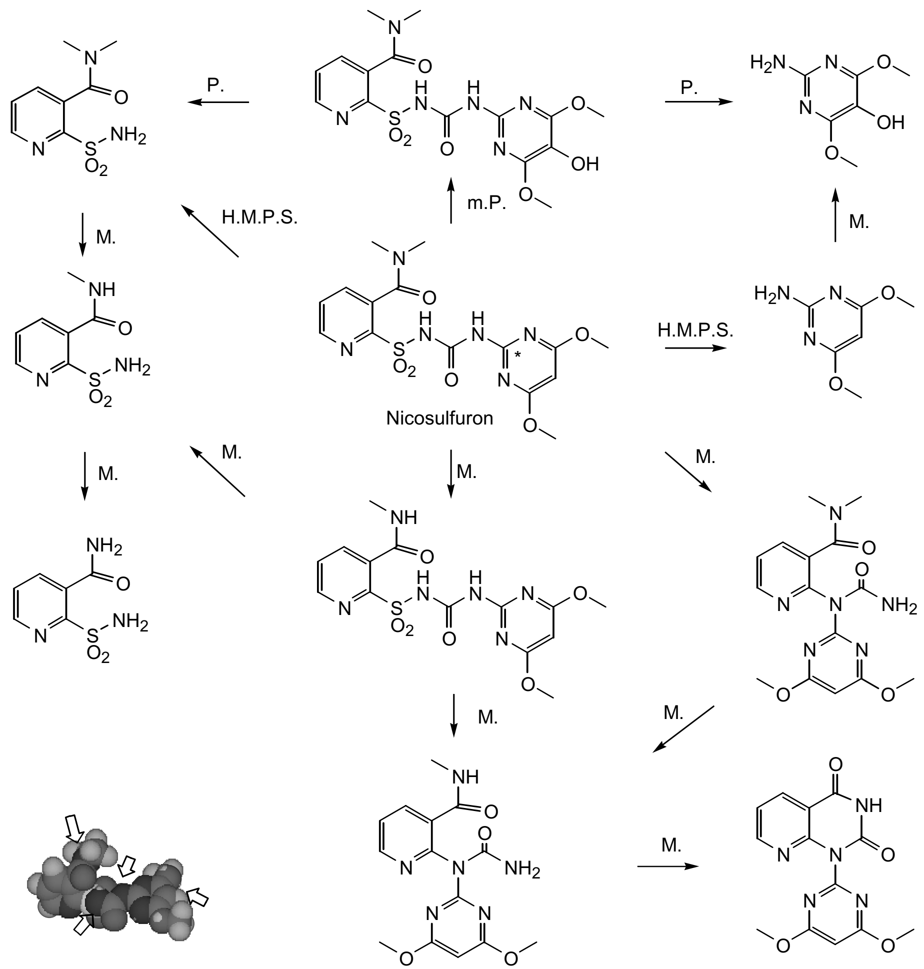
Nicosulfuron

A selective systemic herbicide: control of broadleaf weeds and annual and perennial grass in maize

Hydrolysis/Mammal/Plant/Soil
310

Microsome
Microsomes isolated from 3.5 day-old etiolated maize seedlings: Pioneer 3180[311]

In the four systems investigated, the primary degradation pathway is to yield pyridine sulfonamide and 4,6-dimethoxy-2-aminopyrimidine. The plant and its microsomal system include the hydroxylation pathway at the 4-position of the pyrimidine ring, resulting in hydrolysis products by the cleavage of the sulfonylurea linkage. In mammals, contraction or rearrangement of the sulfonylurea linkage for nicosulfuron and *N*-demethylated nicosulfuron yields two unique products which have the *N*-pyridyl-*N*-pyrimidyl urea moiety and result in the uracil metabolite.



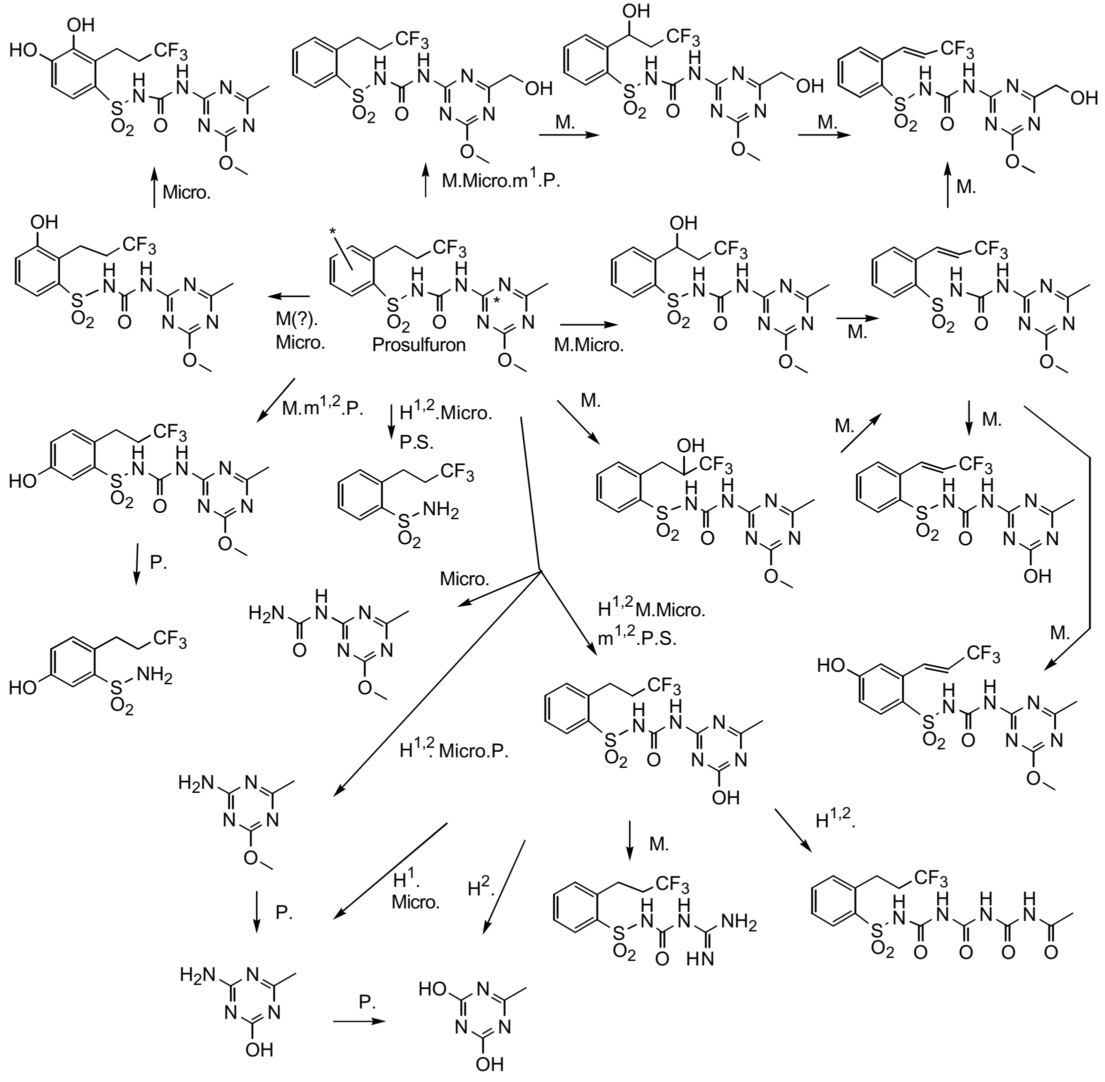
O=C(C1=CC=CN=C1[A]NC(NC2
=NC(OC)=CC(OC)=N2)=O)NC

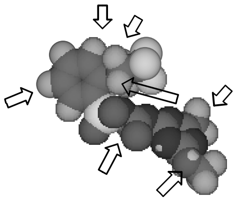
Prosulfuron

A selective post-emergent herbicide: control of broadleaf weeds in corn and other cereals

Hydrolysis[1]/Mammal/Microorganism/Plant/Soil
312

As shown below, the degradation profiles of prosulfuron by hydrolysis, mammal, soil microorganism, plant, plant microsome, and soil are





O=C(NC2=NC(OC)=NC(C)=N2)NS
(C1=CC=CC=C1CCC(F)(F)F)(=O)=O

Microsome[1]
Microsomes from wheat: *Triticum aestivum* L. var. Olaf[313]

Microsome[2]
Microsomes from grain sorghum: *Sorghum bicolor* L. Moench, Funk G522DR and DK 41K; corn: *Zea mays* L. Pioneer 3254[314]

Hydrolysis[2]
Buffer solution at pH 5 (0.01M HOAc/NaOAc)[315]

well investigated. In addition to the degradation products derived by the common cleavage reaction of the sulfonylurea linkage, the predominant hydroxylation reaction occurs on the phenyl ring and the trifluoropropyl side chain by mammal and soil microorganisms, resulting in the formation of the hydroxylated metabolites which mostly retain the sulfonylurea moiety in the structures.

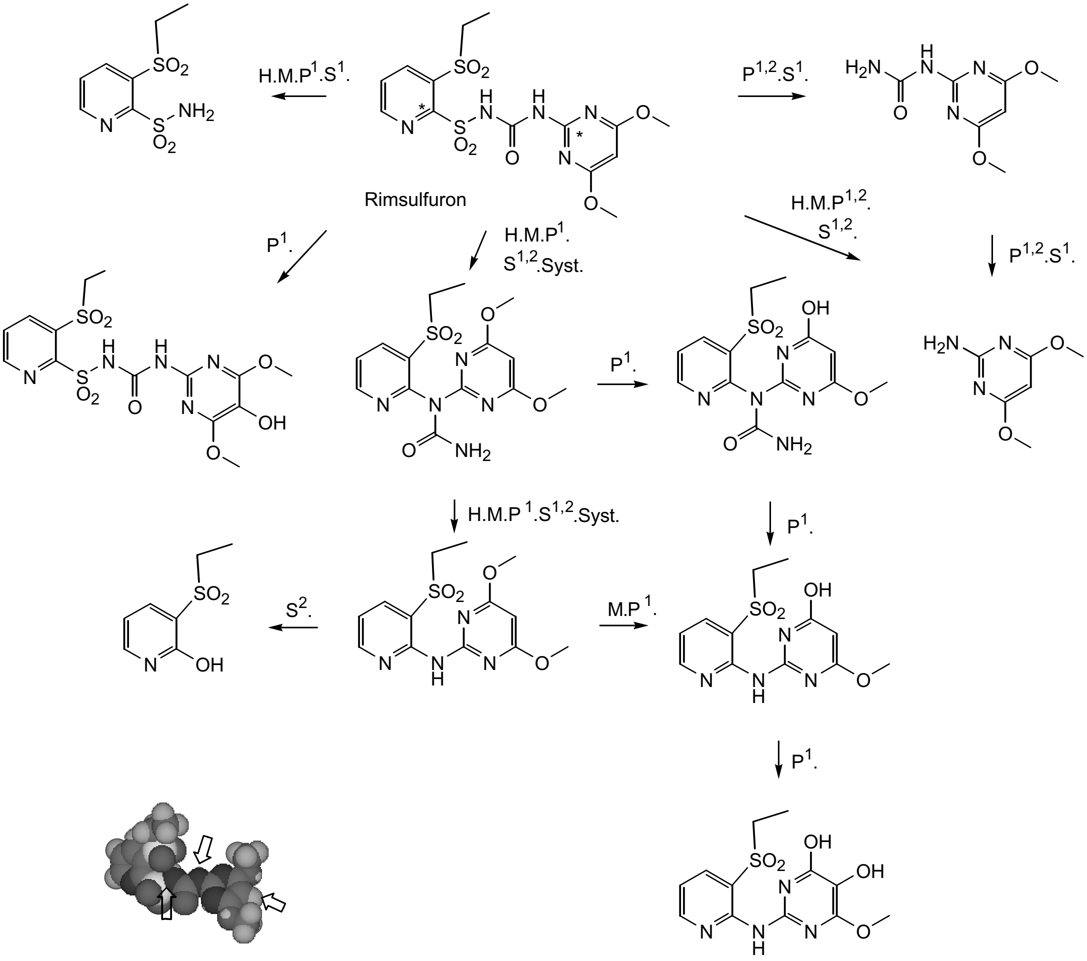
Rimsulfuron

A post-emergent, selective herbicide: control of broadleaf weeds and annual and perennial grasses in maize, potatoes, and tomatoes

Hydrolysis/Mammal/Plant[1]/Soil[1]
[316]

Plant[2]
Black nightshade (*Solanum nigrum*); eastern black nightshade (*Solanum ptycanthum*); hairy nightshade (*Solanum sarrachoides*)[317]

The primary degradation pathway in most of the systems examined is the contraction or rearrangement and hydrolysis of the sulfonylurea linkage to yield two products that have *N*-pyridyl-*N*-pyrimidyl urea and *N*-pyridyl-*N*-pyrimidylamine moieties, and fragments of pyridine sulfonamide, 4,6-dimethoxy-2-pyrimidylurea, and 4,6-dimethoxy-2-amino-pyrimidine, respectively. In plants, demethylation and hydroxylation reactions follow the



CCS(C1=CC=CN=C1S(NC(NC2=NC
(OC)=CC(OC)=N2)=O)(=O)=O)(=O)=O

Soil[2]
Field soils at Melle, Belgium (pH 6.2 under laboratory conditions and pH 6.7 under field conditions)[318]

System
On the clay of a smectite (hectorite) with Al^{3+} (San Bernardino County, CA)[319]

contraction or rearrangement to give *N*-3,4-dihydroxy-5-methoxy-2-pyrimidyl-*N*(3-ethylsulfonyl-2-pyridyl)amine.

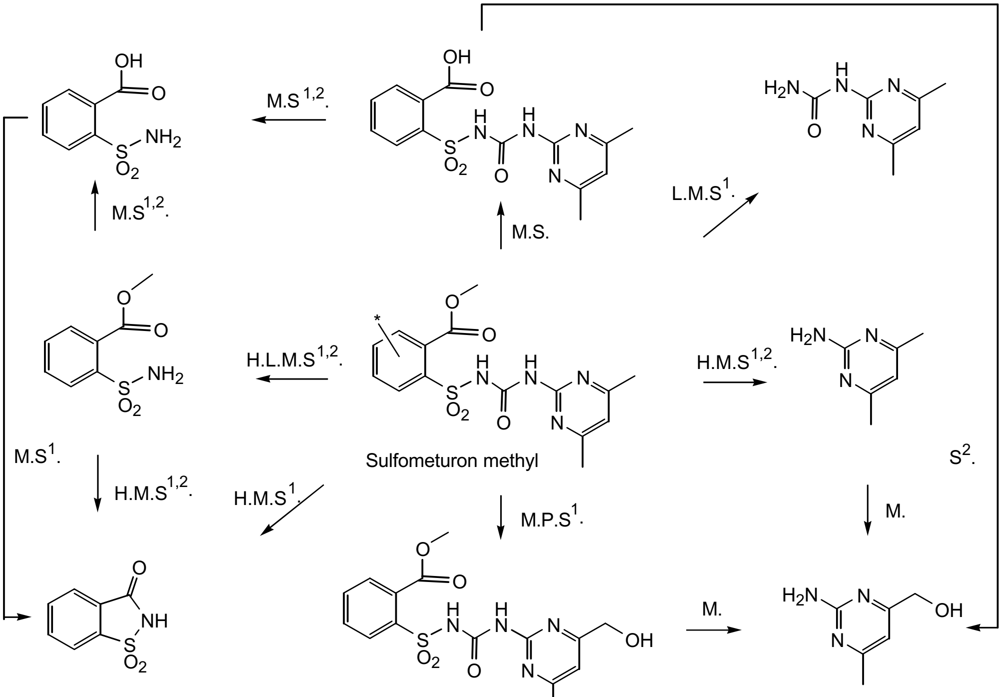
Sulfometuron methyl

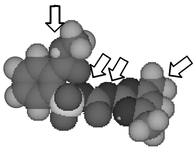
A broad-spectrum herbicide: control of annual and perennial grasses and broadleaf weeds in non-crop sites, bermuda grass, turf, and forestry

Hydrolysis/Light/Mammal/Plant/Soil[1]
[320]

Soil[2]
Field soils at Newark, DE; Raleigh, NC; Rosetown, SK; Pendelton, OR; Fort Collins, CO; Gainesville, FL; Wahalak, MS[321]

Sulfometuron methyl is relatively stable at neutral and basic pH and undergoes cleavage of the sulfonylurea linkage to yield methyl-2-(aminosulfonyl)benzoate and 4,6-dimethyl-2-aminopyrimidine as major hydrolysis products, and saccharin as the terminal product. These products are also observed as major degradation products in soils. In plants, monohydroxymethylsulfometuron methyl is the primary metabolite which is also identified as a mammalian and soil metabolite and undergoes further degradation by mammals to give 2-amino-4-hydroxymethyl-6-methylpyrimidine.





O=C(OC)C1=CC=CC=C1S(NC(N
C2=NC(C)=CC(C)=N2)=O)(=O)=O

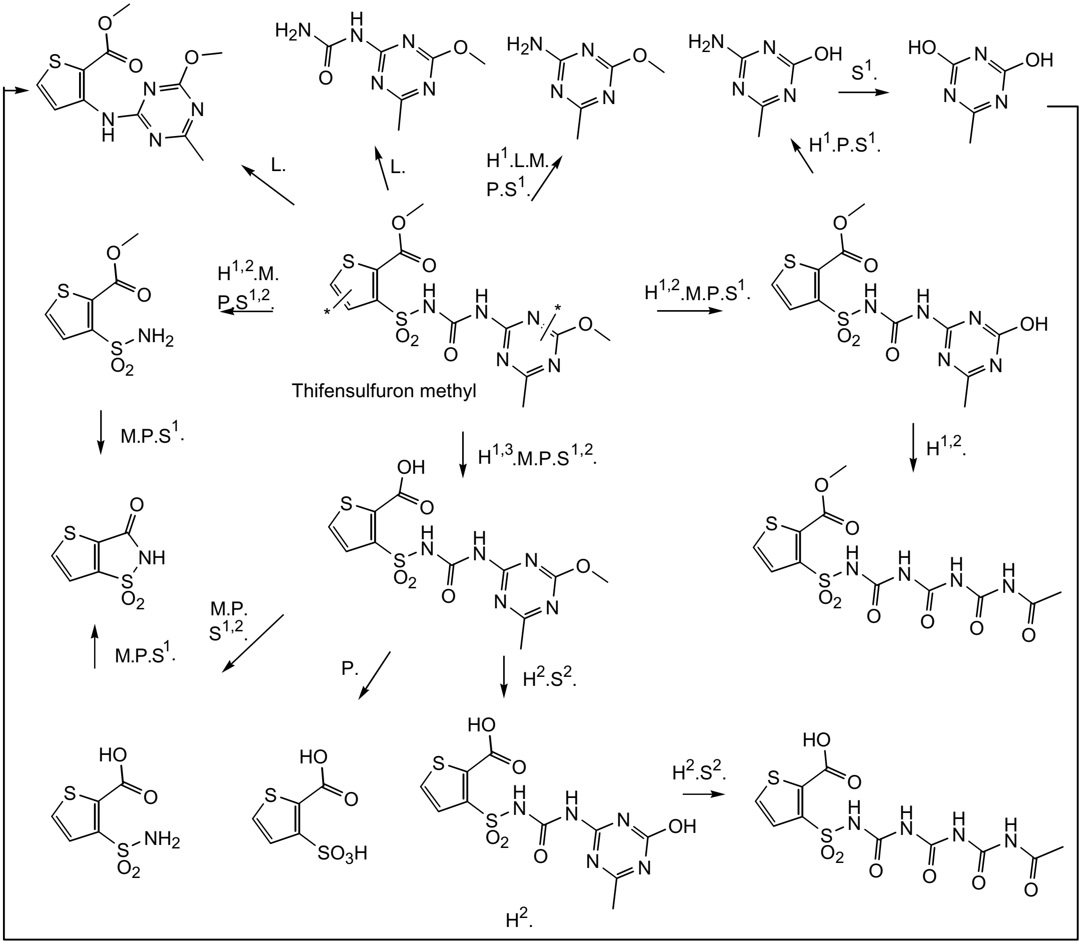
Thifensulfuron methyl

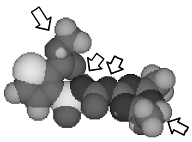
A selective post-emergent herbicide: control of broadleaf weeds in wheat, barley, maize, and soybeans

Hydrolysis[1]/*Light*/*Mammal*/*Plant*/*Soil*[1]
[322]

Hydrolysis[2]
Aqueous buffer solutions (pH 4 and 5) at 28 °C[323]

The hydrolytic degradation of thifensulfuron methyl is pH dependent and, in alkaline condition, specifically yields the corresponding free acid. Primary degradation cleaves the sulfonylurea moiety to give two typical hydrolyzed products, sulfonamide and aminotriazine analogs, derived from thifensulfuron methyl in acidic and neutral conditions. Hydrolysis of the ester linkage proceeds in mammals, plants, soils,





O=C(OC)C1=C(S(NC(NC2=NC(C)=NC(OC)=N2)=O)(=O)=O)C=CS1

Hydrolysis[3]
Aqueous buffer solutions (pH 9 and 10) at 28 °C[323]

Soil[2]
Field soils at St-Nazaire (pH 6.3); Salanque (pH 7.8) in the south of France[324]

and also chemical hydrolysis, and opening of the triazine ring occurs to yield the acetyltriuret analog identified. On the other hand, by hydrolysis, *O*-demethylated thifensulfuron methyl undergoes opening of the triazine ring to give the corresponding acetyltriuret analog. Under photolytic conditions, methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminothiophene-2-carboxylate is identified.

Triasulfuron

A selective pre- and post-emergent herbicide: control of broadleaf weeds in cereals

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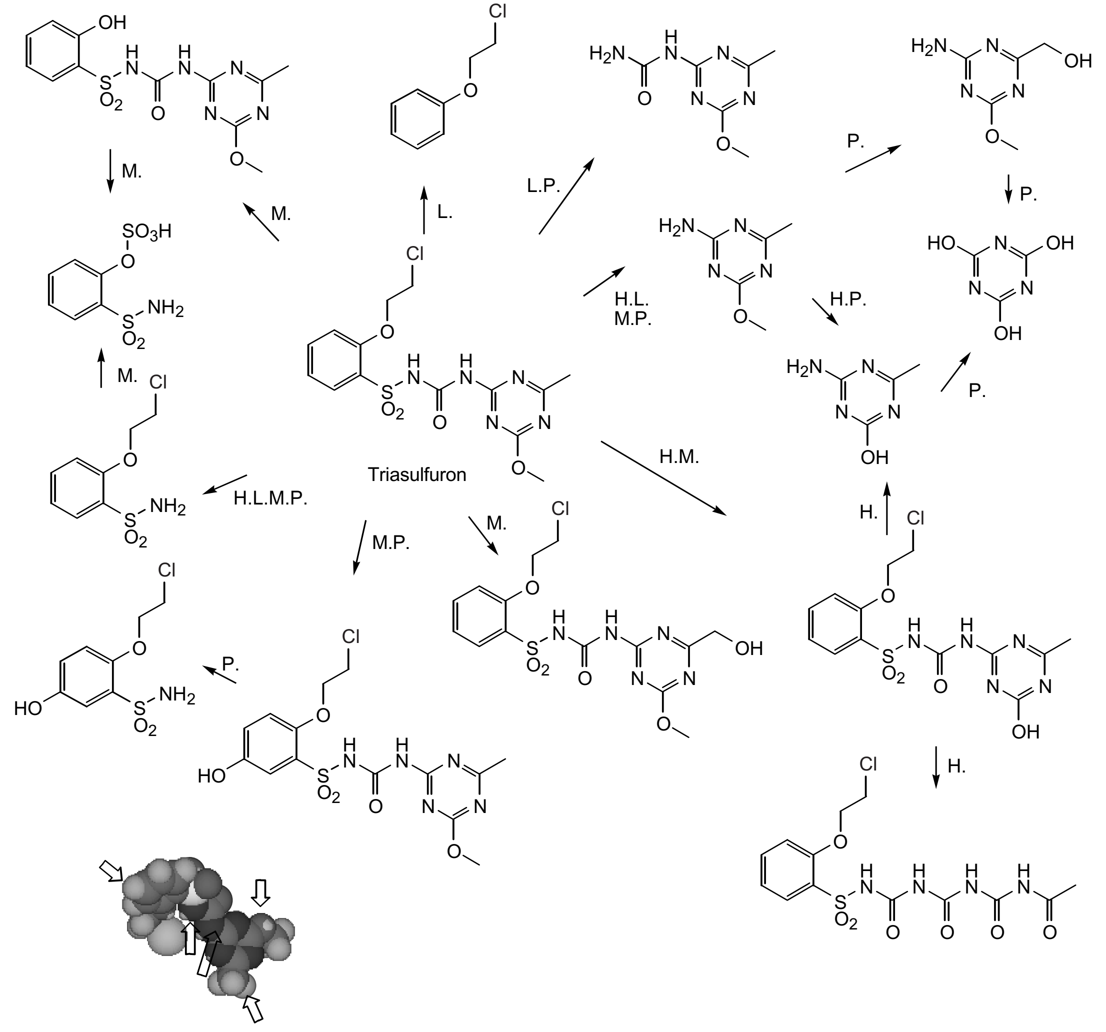
Hydrolysis/Mammal/Plant
325

Light
UV irradiation at 254 nm in a merry-go-round Rayonet photoreactor with low-pressure mercury lamps; sunlight[326]

Triasulfuron undergoes hydrolytic degradation, especially under acidic conditions, giving rise to cleavage of the sulfonylurea linkage, producing the major products 2-(2-chloroethoxy)benzenesulfonamide and 4-methyl-6-methoxy-2-amino-1,3,5-triazine and the minor product acetyltriuret. In plants, hydroxylation occurs at the 5-position of the phenyl ring to yield 5-hydroxytriasulfuron as a primary metabolite which is a major metabolite from the plant microsomal system.



O=C(NC2=NC(OC)=NC(C)=N2)N
S(C1=CC=CC=C1OCCCl)(=O)=O

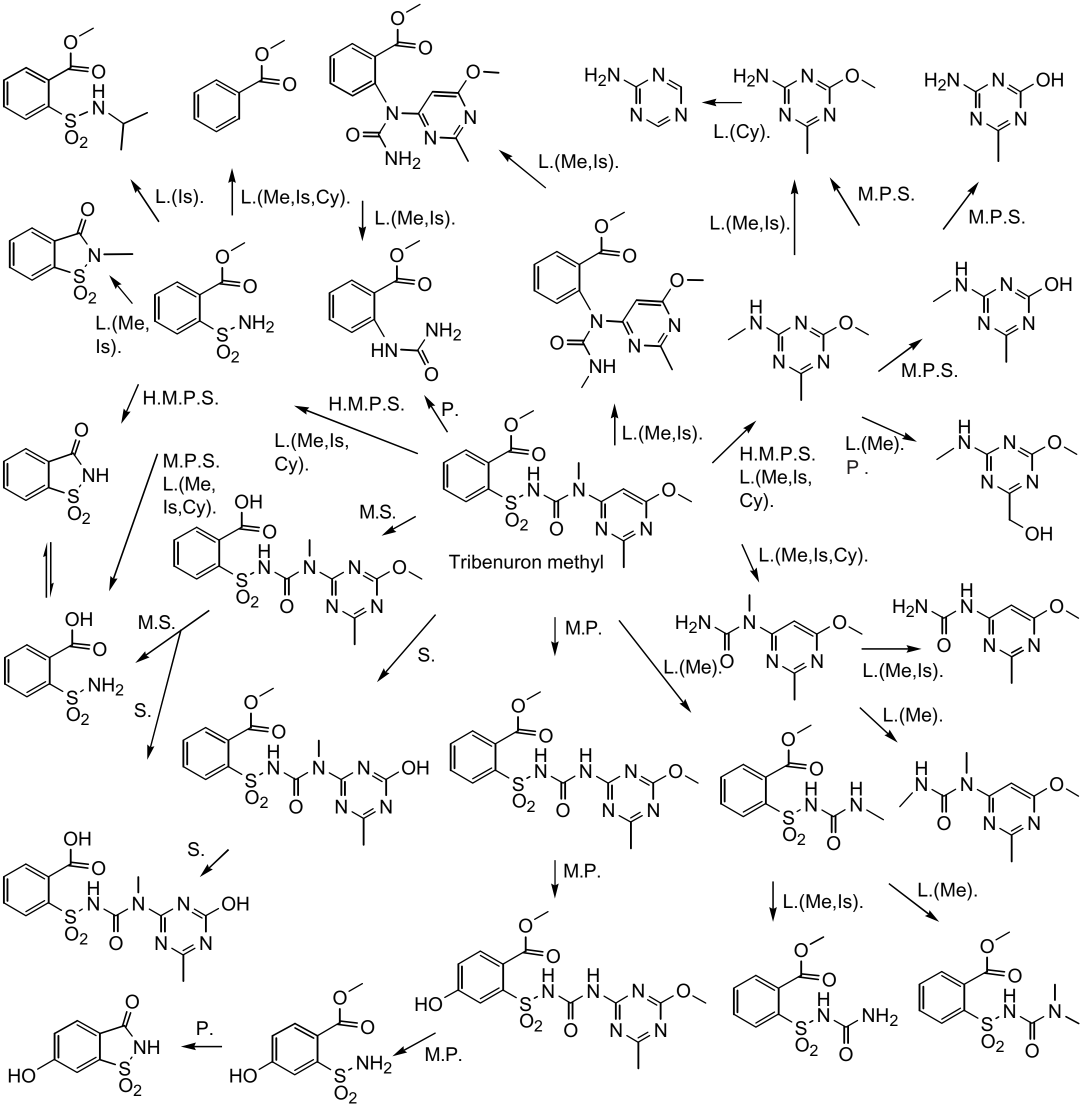
By mammals, orally administered triasulfuron is mainly excreted in the urine, and *O*-dealkylation of 2-chloroethoxy and 6-methoxy groups, and hydroxylation at the 5-position of the phenyl ring and at the 4-methyl group of the triazine ring are observed. By UV irradiation, 2-chloroethoxybenzene is interestingly identified with (4-methoxyl-6-methyl-1,3,5-triazine)urea, and, in sunlight, with these two products, 2-amino-4-methoxyl-6-methyltriazine and 2-(2-chloroethoxy)benzenesulfonamide are identified.

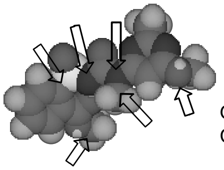
Tribenuron methyl

A systemic and selective post-emergent herbicide: control of broadleaf weeds in cereals

Hydrolysis/Mammal/Plant/Soil
327

The chemical structure of tribenuron methyl possesses a mono-*N*-methyl group in the sulfonylurea linkage which is a unique sulfonylurea herbicide and





O=C(OC)C1=CC=CC=C1S(NC(N(C)
C2=NC(C)=NC(OC)=C2)=O)(=O)=O

Me: methanol; Is: isopropanol;
Cy: cyclohexane

Light

UV irradiation with a medium-pressure mercury vapor lamp (125 W, Philips) in methanol, isopropanol, and cyclohexane[328]

undergoes complex degradation reactions in the environment. Tribenuron methyl degrades into many degradation products, as indicated in the pathways by photolytic and hydrolytic chemical reactions and by biological degradations by mammal, plant, and soil. It is interesting to note that photolysis in different solvents yields diverse products depending on the individual solvents.

23

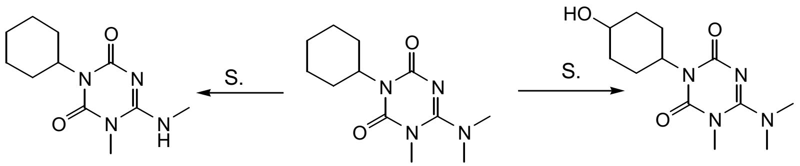
Triazines and Related Compounds

Hexazinone

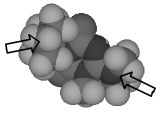
A herbicide

Soil
Clay of the Ryland series orthic humic gelysol type; sand of the Abitibi series orthic humoferric podzol type in Lamplug, Cochrane, Ontario, Canada[329]

In clay and sand soils, hexazinone is metabolized by hydroxylation at the 4-position of the cyclohexane ring and mono-*N*-demethylation to give [3-(4-hydroxycyclohexyl)-6-(dimethylamino)-1-methyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione], and [3-cyclohexyl-6-(methylamino)-1-methyl-1,3,5-triazine-2,4-(1*H*,3*H*)-dione, respectively. *N*-Demethylated metabolite is found in a comparatively higher percentage than the hydroxylated metabolite in both clay and sand soils.



Hexazinone



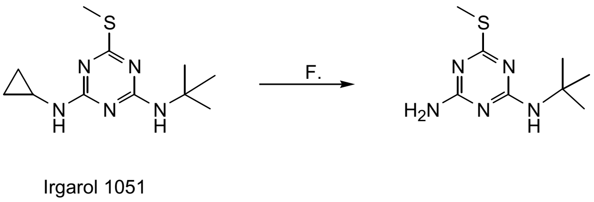
O=C2N(C(N(C(N(C)C)=
N2)C)=O)C1CCCCC1

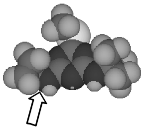
Irgarol 1051

Plant growth regulator: algae growth inhibitor (antifouling), for use in copper-based antifouling paints

Fungus
White rot fungus: *Phanerochaete chrysosporium*[330]

Metabolism of irgarol 1051 by the fungus *Phanerochaete chrysosporium* proceeds mainly via partial *N*-dealkylation at the cyclopropylamino group, resulting in a tentatively identified 2-methylthio-4-*tert*-butylamino-6-amino-1,3,5-triazine.





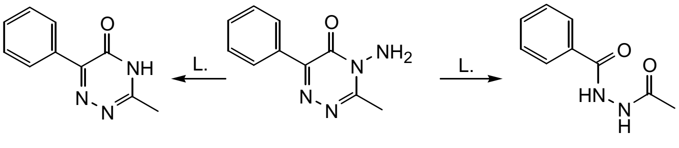
CSC1=NC(NC(C)(C)C)
=NC(NC2CC2)=N1

Metamitron

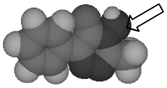
A herbicide

Light
Xenon lamp XOP7 (500 W, Philips, Germany); true daylight outside[331]

Degradation of metamitron by photolysis is strongly dependent on solvents and oxygen, and no photoreaction is found in methanol, acetonitrile, and hexane, nor in oxygen-free water. In water solution, photolytic degradation occurs and results in the formation of desaminometamitron and a ring-opening polar benzoylacetyl hydrazine (tentatively assigned).



Metamitron



O=C1N(N)C(C)=NN=C1
C2=CC=CC=C2

24

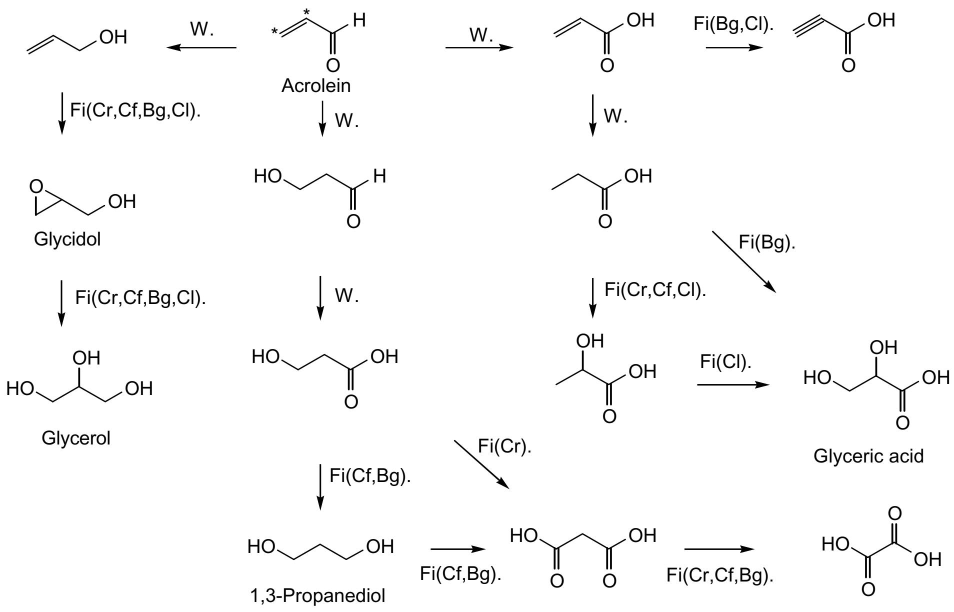
Miscellaneous

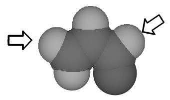
Acrolein (Magnacide H)

An aquatic herbicide: use for agricultural irrigation canals

Fish/Water
Juvenile channel catfish: *Ictalurus punctatus*; crayfish: *Orconectes virilis*; bluegill sunfish: *Lepomis macrochirus*; mature freshwater unionacean clams: *Elliptio complanata*; a statistic exposure system in culture water drawn from a 125 m deep bedrock well[332]

When fish are exposed to ^{14}C-acrolein, the metabolites are identified from the edible tissues and there is very little similarity in the metabolism of acrolein among the test species. The most notable observation is that acrolein is never detected in any tissues sampled, and glycidol, glycerol, 1,3-propanediol, and glyceric acid are the major metabolites found in catfish, crayfish, bluegill, and clams, respectively.





C=CC([H])=O

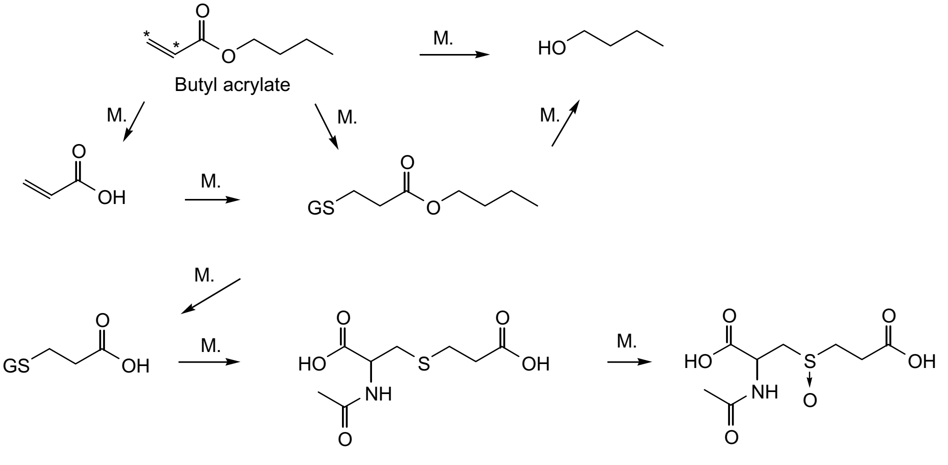
Cr: crayfish; Cf: catfish;
Bg: bluegill; Cl: clams

Butyl acrylate

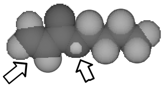
Not a pesticide

Mammal
Male 8−10 week-old Fischer 344 rats (180−220 g) from Charles River Breeding Laboratory[333]

After oral administration to rats, ^{14}C-butyl acrylate is metabolized primarily to CO_2, accounting for elimination of up to 75% of the radioactivity administered. Elimination in urine and feces accounts for approximately 10 and 2% of the dose, respectively. The major portion of butyl acrylate is hydrolyzed to acrylic acid, which is further metabolized to compounds available for oxidation. Two major metabolites identified in the urine are *N*-acetyl-*S*-(2-carboxyethyl)cysteine and its *S*-oxide. A smaller portion of butyl acrylate is conjugated with glutathione, and these conjugates result in the formation of the mercapturic acid excreted in the urine.



GS: glutathione residue



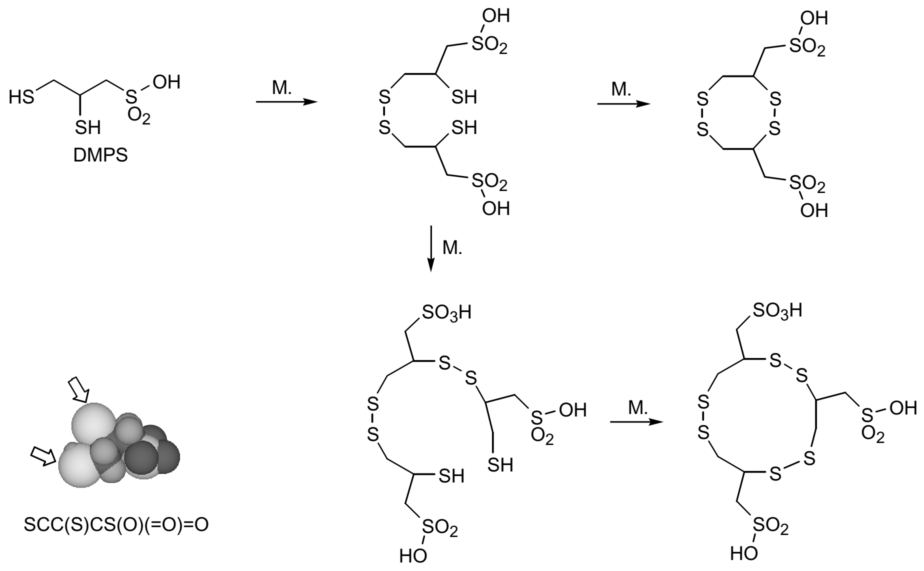
C=CC(OCCCC)=O

2,3-Dimercaptopropane-1-sulfonic acid (DMPS)

Not a pesticide: a heavy metal chelating agent

Mammal
Male New Zealand white rabbits (1.5–2.0 kg) from Blue Ribbon Ranch, Tucson, AZ[334]

After ^{14}C-2,3-dimercaptopropane-1-sulfonic acid (DMPS) is administered orally to rabbits, disulfide metabolites of DMPS are identified in the urine, which are cyclic polymeric disulfides of dimeric and trimeric forms and acyclic polymeric disulfides of DMPS. One of the acyclic disulfides is a DMPS dimer. The cyclic disulfides increase with time, suggesting that the acyclic forms are intermediates and oxidized to the cyclic forms. The rapid formation of stable 8-membered cyclic dimeric and 12-membered cyclic trimeric disulfides of DMPS strongly suggests that oxidation–reductions are occurring. Both spontaneous and enzymatic oxidation mechanisms appear to be involved.



SCC(S)CS(O)(=O)=O

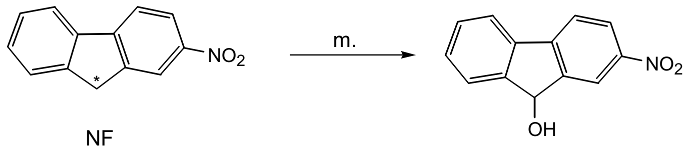
2-Nitrofluorene (NF)

A carcinogen

Microsome

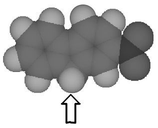
Microsome preparations from the lung of Sprague–Dawley rats (1–13 week-old)[335]

Lung microsomal metabolism of 2-nitrofluorene (NF) increases in parallel with the accumulation of P-450_b homologous mRNA and microsomal cytochrome P-450_b protein concentration. The formation of the major metabolite, and potent mutagen, 9-hydroxy-2-nitrofluorene (9-OHNF) is significantly inhibited by the addition of polyclonal *anti*-P-450_b-IgG, and by the addition of the inhibitor, proadifen, to incubations with lung microsomal protein.



NF

9-OHNF



O=[N+]([O-])C(C=C3)=CC2
=C3C1=CC=CC=C1C2

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Log *P* values of the compounds, calculated by SciLog P Ultra

1. Acid Amides	Log *P* values	Structure (SMILES)
Acetaminophen (APAP)	0.67	CC(= O)Nc1ccc(cc1)O
Acetochlor	2.87	CCOCN(c1c(cccc1CC)C)C(=O)CCl
Alachlor	2.93	CCc1cccc(c1N(COC)C(=O)CCl)CC
Benalaxyl	3.30	CC(N(c1c(cccc1C)C)C(=O)Cc1ccccc1)C(=O)OC
Butachlor	4.33	CCc1cccc(c1N(COCCCC)C(=O)CCl)CC
Carpropamid	5.52	ClC1(C(C1(CC)C(=O)NC(c1ccc(cc1)Cl)C)C)Cl
Chloramphenicol	0.29	ClC(C(=O)NC(C(c1ccc(cc1)N(=O)O)O)CO)Cl
Cisapride	2.70	Fc1ccc(cc1)OCCCN1CCC(C(C1)OC)NC(=O)c1cc(c(cc1OC)N)Cl
2,6-Dichlorobenzamide (DCB)	1.78	Clc1cccc(c1C(=O)N)Cl
N,*N*-Diethyl-*meta*-toluamide (DEET)	2.49	O=C(c1cccc(c1)C)N(CC)CC
N-(2,6-Dimethylphenyl)-4-[[(diethylamino)acetyl]amino]benzamide (DEGA)	2.83	Cc1cccc(c1NC(=O)c1ccc(cc1)NC(=O)CN(CC)CC)C
N,*N*-Diethylphenylacetamide (DEPA)	2.39	O=C(Cc1ccccc1)N(CC)CC
N,*N*-Dimethylformamide (DMF)	−0.36	O=CN(C)C
N-Ethyl-*N*-methyl-4-(trifluoromethyl)-2-(3,4-dimethoxyphenyl)benzamide (EMTDB)	3.92	COc1ccc(cc1OC)c1cc(ccc1C(=O)N(CC)C)C(F)(F)F
Epicainide	2.75	OC(c1ccccc1)(c1ccccc1)C(=O)NCC1CCCN1CC
Furalaxyl	2.56	O=C(c1occc1)N(c1c(cccc1C)C)C(C(=O)OC)C
Inabenfide	3.32	O=C(c1ccncc1)Nc1c(cc(cc1)Cl)C(c1ccccc1)O
Isobutylphendienamide	3.58	O=C(C=CC=CCc1ccccc1)NCC(C)C
Metalaxyl	2.34	Cc1c(c(ccc1)C)N(C(=O)COC)C(C)C(=O)OC
Metazachlor	1.79	Cc1c(c(ccc1)C)N(C(=O)CCl)Cn1nccc1
N-(Methylisothiazolin-5-ylidene)phenylacetamide (ITOPA)	4.85	Cc1nsc(c1Cl)N(C(=O)Cc1ccc(cc1)Oc1ccc(cc1)C(F)(F)F)C
Metolachlor	3.18	Cc1c(c(ccc1)CC)N(C(=O)CCl)C(C)COC
Naproanilide	3.86	CC(Oc1cc2c(cccc2)cc1)C(=O)Nc1ccccc1
Oxycarboxin	1.32	O=S1(=O)CCOC(=C1C(=O)Nc1ccccc1)C
Prinomide	2.08	O=C(c1cccn1C)C(C(=O)Nc1ccccc1)C#N
Thenylchlor	3.08	Cc1cccc(c1N(Cc1c(ccs1)OC)C(=O)CCl)C
Trifoline	0.96	O=CNC(N1CCN(CC1)C(C(Cl)(Cl)Cl)NC = O)C(Cl)(Cl)Cl

2. Amidines Guanidines, and Hydrazines	Log *P* values	Structure (SMILES)
Amdro	4.42	CC1(CNC(=NN=C(C=Cc2ccc(cc2)C(F)(F)F)C=Cc2ccc(cc2)C(F)(F)F)NC1)C
Amitraz	5.37	Cc1ccc(c(c1)C)N=CN(C=Nc1c(cc(cc1)C)C)C
Daminozide	−1.32	O=C(CCC(=O)O)NN(C)C
Guazatine triacetate	0.97	N=C(NCCCCCCCCNCCCCCCCCNC(=N)N)N

3. Amino Acid-Phosphonic Acids	Log *P* values	Structure (SMILES)
Bialaphos	−3.44	CP(=O)(CCC(C(=O)NC(C(=O)NC(C(=O)O)C)C)N)O
Phosphinothricin	−3.35	CP(=O)(CCC(C(=O)O)N)O

4. Anilines and Nitrobenzenes	Log *P* values	Structure (SMILES)
4-Aminobiphenyl	2.86	Nc1ccc(c2ccccc2)cc1
4,4′-Methylene-bis-(2-chloroaniline)	3.58	Clc1c(ccc(c1)Cc1ccc(c(c1)Cl)N)N
1,3-Diaminobenzene (MPD)	0.11	Nc1cc(ccc1)N
3,4-Dichloroaniline	2.82	Nc1cc(c(cc1)Cl)Cl
2,6-Dichloro-4-nitroaniline (DCNA)	1.38	ON(c1cc(c(c(c1)Cl)N)Cl)O
2,6-Diethylaniline (DEA)	2.55	Nc1c(cccc1CC)CC
2,4-Dimethylaniline (2,4-DMA)	1.93	Nc1c(cc(cc1)C)C
2,6-Dimethylaniline (2,6-DMA)	1.84	Nc1c(cccc1C)C
2,4-Dinitrophenol	0.59	Oc1ccc(cc1N(O)O)N(O)O
2,4-Dinitrotoluene (2,4-DNT)	1.22	ON(c1ccc(c(c1)N(O)O)C)O
2,6-Dinitrotoluene (2,6-DNT)	0.91	ON(c1c(c(ccc1)N(O)O)C)O
2-Fluoroaniline	1.18	Nc1c(cccc1)F
3-Fluoroaniline	1.29	Nc1cc(ccc1)F
4-Fluoroaniline	1.12	Nc1ccc(cc1)F
Diphenylamine (DPA)	3.2	c1cccc(c1)Nc1ccccc1
4-Nitrophenol	1.05	Oc1cccc(c1)N(O)O
Pendimethalin	0.77	CCC(Nc1c(c(c(cc1N(O)O)C)C)N(O)O)CC

5. Aryloxy Acids	Log *P* values	Structure (SMILES)
2,4-D	2.76	Clc1c(ccc(c1)Cl)OCC(=O)O
2,4-DP	3	Clc1c(ccc(c1)Cl)OC(C(=O)O)C
Diclofop methyl	4.7	CC(Oc1ccc(cc1)Oc1ccc(cc1Cl)Cl)C(=O)OC
Fenoxaprop ethyl	4.31	Clc1cc2c(cc1)N=C(O2)Oc1ccc(cc1)OC(C(=O)OCC)C
Fluazifop butyl	4.89	CC(Oc1ccc(cc1)Oc1ncc(cc1)C(F)(F)F)C(=O)OCCCC
Haloxyfop methyl	4.35	Clc1c(ncc(c1)C(F)(F)F)Oc1ccc(cc1)OC(C(=O)OC)C
Trichlopyr	2.31	OC(=O)COc1nc(c(cc1Cl)Cl)Cl

6. Biphenyl Ethers	Log *P* values	Structure (SMILES)
Chlornitrofen (MC-338)	5.12	Clc1c(c(cc(c1)Cl)Cl)Oc1ccc(cc1)N(=O)O
Fluorodifen (preforan)	3.79	ON(c1c(ccc(c1)C(F)(F)F)Oc1ccc(cc1)N(O)O)O
Nitrofen	4.6	Clc1ccc(c(c1)Cl)Oc1ccc(cc1)N(=O)O
MC-3761	3.77	Clc1c(c(cc(c1)Cl)Cl)Oc1cc(c(cc1)N(=O)O)C(=O)OC
MC-4379	3.37	COC(=O)c1c(ccc(c1)Oc1ccc(cc1Cl)Cl)N(=O)O
MC-5127	3.46	CCOC(=O)c1c(ccc(c1)Oc1ccc(cc1Cl)Cl)N(=O)O
MC-6063	2.87	COC(=O)c1c(ccc(c1)Oc1ccc(cc1Cl)F)N(=O)O
MC-7181	3.02	COC(=O)c1c(ccc(c1)Oc1c(cc(cc1Cl)Cl)F)N(=O)O

7. Carbamates	Log *P* values	Structure (SMILES)
Aminocarb (matacil)	1.51	CN(c1c(cc(cc1)OC(=O)NC)C)C
Benfuracarb	3.01	CC1(Oc2c(cccc2OC(=O)N(SN(C(C)C)CCC(=O)OCC)C)C1)C
Carbetamide	1.22	O=C(Nc1ccccc1)OC(C(=O)NCC)C
Diethofencarb	2.68	CCOc1ccc(cc1OCC)NC(=O)OC(C)C
Fenoxycarb	3.51	O=C(NCCOc1ccc(cc1)Oc1ccccc1)OCC
Pirimicarb	1.76	Cc1nc(nc(c1C)OC(=O)N(C)C)N(C)C

8. Dithio- and Thiolcarbamates	Log *P* values	Structure (SMILES)
Cartap hydrochloride	−0.23	CN(C(CSC(=O)N)CSC(=O)N)C
EPTC	3.01	CCCN(C(=O)SCC)CCC
Fenothiocarb	2.97	O=C(SCCCCOc1ccccc1)N(C)C
Fenothiocarb sulfoxide	1.64	O=C(S(=O)CCCCOc1ccccc1)N(C)C
Molinate	2.47	CCSC(=O)N1CCCCCC1
Orbencarb	3.31	O=C(SCc1c(cccc1)Cl)N(CC)CC

9. Halogenated Aliphatics	Log *P* values	Structure (SMILES)
1,2-Dibromoethane	2.26	BrCCBr
1,2-Dichloroethane	1.64	ClCCCl
1,3-Dichloropropene	2.13	ClCC=CCl
Dichloroacetylene	2.32	ClC#CCl
Endosulfan	3.86	ClC1(C2(C(=C(C1(C1C2COS(=O)OC1)Cl)Cl)Cl)Cl)Cl
Hexachloro-1,3-butadiene (HCBD)	5.11	ClC(=C(C(=C(Cl)Cl)Cl)Cl)Cl
Trichlorethylene	2.29	ClC(=CCl)Cl

10. Halogenated Aromatics	Log *P* values	Structure (SMILES)
Bromobenzene	2.90	Brc1ccccc1
Chlorobenzene	2.63	Clc1ccccc1
Chlorothalonil (daconil)	4.79	Clc1c(c(c(c(c1Cl)Cl)C#N)Cl)C#N
DDT	6.67	Clc1ccc(cc1)C(c1ccc(cc1)Cl)C(Cl)(Cl)Cl
1,4-Dichlorobenzene	3.58	Clc1ccc(cc1)Cl
2,6-Dichlorobenzonitrile (DCBN)	3.12	Clc1c(c(ccc1)Cl)C#N
2,6-Dichlorothiobenzamide (DCTBA)	2.98	Clc1c(c(ccc1)Cl)C(=S)N
Hexachlorobenzene	5.73	Clc1c(c(c(c(c1Cl)Cl)Cl)Cl)Cl
Methoxychlor	5.56	COc1ccc(cc1)C(c1ccc(cc1)OC)C(Cl)(Cl)Cl

3,4,3′,4′-Tetrachlorobiphenyl	6.57	ClC1=C(Cl)C=CC(C2=CC=C(Cl)C(Cl)=C2)=C1
2,2′,4,4′,5-Pentachlorodiphenyl ether (PCDE)	6.56	Clc1c(ccc(c1)Cl)Oc1cc(cc(c1Cl)Cl)Cl
1,2,3,4-Tetrachlorodibenzo-*p*-dioxin	6.26	Clc1c(c2c(c(c1Cl)Cl)Oc1ccccc1O2)Cl
1,3,6,8-Tetrachlorodibenzo-*p*-dioxin	6.42	Clc1cc(cc2c1Oc1cc(cc(c1O2)Cl)Cl)Cl
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin	6.68	Clc1c(cc2c(c1)Oc1c(cc(c(c1)Cl)Cl)O2)Cl

11. Five-membered Heterocycles	Log *P* values	Structure (SMILES)
2-*N*-Dodecyltetrahydrothiophene (DTHT)	5.46	CCCCCCCCCCCCC1SCCC1
2-*N*-Undecyltetrahydrothiophene (UTHT)	5.49	CCCCCCCCCCCC1SCCC1
Assert *meta* isomer	2.48	O=C(c1cc(ccc1C1=NC(C(=O)N1)(C(C)C)C)C)OC
Assert *para* isomer	2.48	O=C(c1ccc(cc1C1=NC(C(=O)N1)(C(C)C)C)C)OC
Azocyclotin	3.19	C1CC(CCC1)[Sn](C1CCCCC1)(n1ncnc1)C1CCCCC1
Carfentrazone	5.02	FC(N1C(=NN(C1=O)c1cc(c(cc1F)Cl)CC(C(=O)OCC)Cl)C)F
Clomazone	2.49	CC1(CON(C1=O)Cc1ccccc1Cl)C
Croconazole	4.99	Clc1cc(ccc1)COc1ccccc1C(=C)n1ccnc1
F5231	1.03	FCCCN1N=NN(C1=O)c1cc(c(cc1F)Cl)NS(=O)C1C
Fenpyroximate	5.12	Cn1nc(c(c1Oc1ccccc1)C=NOCc1ccc(cc1)C(=O)OC(C)(C)C)C
Fipronil	1.63	Nc1c(c(nn1c1c(cc(cc1Cl)C(F)(F)F)Cl)C#N)[S+]([O−])C(F)(F)F
Flurochloridone	3.3	O=C1N(c2cccc(c2)C(F)(F)F)CC(C1Cl)CCl
5-Hydroxymethyl-2-furaldehyde	0.38	O=Cc1ccc(o1)CO
Hymexazol-*N*-glucoside (HNG)	−1.87	O=C1N(C2OC(C(O)C(C2O)O)CO)OC(=C1)C
Hymexazol-*O*-glucoside (HOG)	−1.73	Cc1cc(no1)OC1OC(C(O)C(C1O)O)CO
Imidacloprid	1.02	Clc1ccc(cn1)CN1C(=NN(=O)O)NCC1
Isoprothiolane	3	O=C(C(=C1SCCS1)C(=O)OC(C)C)OC(C)C
Isoprothiolane sulfoxide	1.67	O=C(C(=C1[S+](CCS1)[O−])C(=O)OC(C)C)OC(C)C
Methaphenilene	3.04	CN(CCN(c1ccccc1)Ccsccc1)C
Pyribenzamine	2.48	CN(CCN(c1ncccc1)Cc1ccccc1)C
Methapyrilene	2.49	CN(CCN(c1ncccc1)Cc1sccc1)C
5-Methyl-2-furaldehyde	1.08	Cc1ccc(o1)C=O
1-Methylhydantoin	−0.81	O=C1NC(=O)N(C1)C
N-Methyl-2-pyrrolidinone (NMP)	−0.36	CN1CCCC1=O
N-Nitroso-1,3-thiazolidine	−0.03	O=NN1CCSC1

(*continued*)

11. Five-membered Heterocycles (continued)	Log *P* values	Structure (SMILES)
Oxaminozoline	0.83	O1CCN=C1NC(C1CC1)C1CC1
Propiconazole	3.53	CCCC1COC(c2ccc(cc2Cl)Cl)(O1)Cn1cncn1
Pyrazolate	4.19	O=c(c1c(nn(c1OS(=O)(=O)c1ccc(cc1)C)C)C)c1ccc(cc1Cl)Cl
Spiroxamine	4.83	CC(C1CCC2(CC1)OC(CO2)CN(CCC)CC)(C)C
Sulfentrazone	2.72	FC(N1C(=NN(C1=O)c1cc(c(cc1Cl)Cl)NS1(=O)(=O)C)C)F
Tebufenpyrad	4.63	O=C(c1c(c(nn1C)CC)Cl)NCc1ccc(cc1)C(C)(C)C
α-Terthienyl	5.14	c1csc(c1)c1sc(cc1)c1sccc1
Triadimenol	2.98	Clc1ccc(cc1)OC(n1cncn1)C(C(C)(C)C)O
2,4,5-Tribromo-1-(4-chlorobenzolyl)imidazole (TBCBI)	3.54	Brc1c(n(c(n1)Br)C(=O)c1ccc(cc1)Cl)Br
2,4,5-Trichloroimidazole (TCI)	2.73	Clc1c(n(c(n1)Cl)Cl)Cl
2,4,5-Trichloro-1-(4-chlorobenzoyl)imidazole (TCCBI)	3.5	Clc1c(n(c(n1)Cl)C(=O)c1ccc(cc1)Cl)Cl
Vinclozolin	3.12	O=C1N(c2cc(cc(c2)Cl)Cl)C(=O)C(O1)(C=C)C

12. Five-membered Heterocycles (fused)	Log *P* values	Structure (SMILES)
Azafenidin	1.96	O=C1N(c2cc(c(cc2Cl)Cl)OCC#C)N=C2N1CCCC2
Benlate	1.91	O=C(N1c2ccccc2N=C1NC(=O)OC)NCCCC
Carbendazim	1.32	O=C(NC1=Nc2ccccc2N1)OC
Cinmethylin	5.3	CC12C(CC(O2)(CC1)C(C)C)OCc1c(cccc1)C
Cloransulammethyl	1.19	O=C(c1c(c(ccc1)Cl)NS(=O)(=O)c11nc1cc(nc(n1n1)OCC)F)OC
Fluthiacetmethyl	2.32	Fc1cc(c(cc1N=C1SC(=O)N2N1CCCC2)SCC(=O)OC)Cl
Indol	2.28	c1ccc2c(c1)C=CN2
Methabenzthiazuron	1.56	CNC(=O)N(C1=Nc2ccccc2S1)C
3,4-(Methylenedioxy)methamphetamine	2.13	CC(Cc1cc2c(cc1)OCO2)NC
2-Methylthiobenzothiazole	3.07	CSC1=Nc2ccccc2S1
Omeprazole	1.54	Cc1cnc(c(c1OC)C)C[S+](C1=Nc2cc(ccc2N1)OC)[O−]
Pindolol	1.45	CC(NCC(COc1c2c(ccc1)NC=C2)O)C
Skatole	2.25	CC1=CNc2ccccc12

13. Six-/more membered heterocycles	Log *P* values	Structure (SMILES)
Bispyribac acid	2.53	O=C(c1c(cccc1Oc1nc(cc(n1)OC)OC)Oc1nc(cc(n1)OC)OC)O
Bromacil	1.34	CC1=C(C(=O)N(C(=O)N1)C(CC)C)Br
Buprofezin	3.05	O=C1N(c2ccccc2)CSC(=NC(C)(C)C)N1C(C)C
Cycloxydim	3.65	OC1=C(C(=O)CC(C2CSCCC2)C1)C(=NOCC)CCC
Cyprodinil	2.67	Cc1cc(nc(n1)Nc1ccccc1)C1CC1
2-Dimethylamino-5,6-dimethylpyrimidin-4-ol	1.27	CN(c1nc(c(c(n1)C)C)O)C
Dimethylaminopentathiocyclooctane (PTCA)	1.24	CN(C1CSSSSSC1)C
Indeloxazine hydrochloride	2.19	c1ccc(c2c1C=CC2)OCC1CNCCO1
Mepanipyrim	3.43	Cc1nc(nc(c1)C#CC)Nc1ccccc1
N-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine	2.48	CN1CC=C(c2ccccc2)CC1
Phencyclidine	4.5	C1C(c2ccccc2)(N2CCCCC2)CCCC1
Terbacil	1.27	CC1=C(C(=O)N(C(=O)N1)C(C)(C)C)Cl

14. Six-/more membered heterocycles (fused)	Log *P* values	Structure (SMILES)
Benoxacor	2.13	O=C(N1c2ccccc2OCC1C)C(Cl)Cl
Bentazon	1.15	CC(N1C(=O)c2ccccc2NS1(=O)=O)C
Chlorpromazine	5.24	CN(CCCN1c2c(ccc(c2)Cl)S2ccccc12)C
Chlorpromazine *N*-oxide	5.24	Clc1cc2c(cc1)Sc1ccccc1N2CCC[N+](C)(C)[O−]
Fluperlapine	4.7	CN1CCC(C2=Nc3c(ccc(c3)F)Cc3c2cccc3)CC1
Idazoxan	1.26	c1ccc2c(c1)OC(C1=NCCN1)CO2
Quinoline-4-carboxylic acid	1.83	O=C(c1ccnc2ccccc12)O
SC 1271	3.83	CCCOc1c2c(ccc1)N(c1ccc(cc1)Cl)N=C(C2=O)C(=O)O
SK&F 86466	2.82	CN1CCc2c(cccc2CC1)Cl

15. Imides	Log *P* values	Structure (SMILES)
Aminoglutethimide	0.97	O=C1CCC(c2ccc(cc2)N)(C(=O)N1)CC
Isoimide	3.56	O=C1C2=C(CCCC2)C(=Nc2ccc(cc2)Br)O1
Thiadiazolidinone	2.5	O=C1N2CCCCN2C(=Nc2ccc(cc2)Br)S1
Thiadiazolidinethione	3.47	S=C(S3)N1CCCCN1C3=NC2=CC=C(Br)C=C2
Chlozolinate	2.95	Clc1cc(cc(c1)N1C(=O)OC(C1=O)(C(=O)OCC)C)Cl
Procymidone	3.15	Clc1cc(cc(c1)N1C(=O)C2(C(C1=O)(C2)C)C)Cl
Vinclozolin	3.12	Clc1cc(cc(c1)N1C(=O)OC(C1=O)(C=C)C)Cl
N-(3,5-Dichlorophenyl)succinimide (NDPS)	1.86	O=C1N(c2cc(cc(c2)Cl)Cl)C(=O)CC1
Flumiclorac pentyl	4.7	O=C1N(c2c(cc(c(c2)OCC(=O)OCCCCC)Cl)F)C(=O)C2=C1CCCC2
Flumipropyn	2.74	O=C1N(c2c(cc(c(c2)OC(C)C#C)Cl)F)C(=O)C2=C1CCCC2
MK-129	4.26	O=C1N(c2ccc(cc2)OCc2ccc(cc2)Cl)C(=O)C2=C1CCCC2
Procymidone	3.15	C1c1cc(cc(c1)N1C)=O)C2(C1=O)(C2)C)C)C1
S-53482	1.95	O=C1N(c2cc3c(cc2F)OCC(=O)C3CC#C)C(=O)C2=C1CCCC2

16. Natural products	Log *P* values	Structure (SMILES)
(+)- and (−)-Abscisic acids	1.7	CC1(C(C(=CC(=O)C1)C)(C=CC(=CC(=O)O)C)O)C
Aflatoxin B_1	2.08	O=C1C2=C(c3c(c4c(cc3OC)OC3C4C=CO3)O1)CCC2=O
Androstenedione	3.15	CC12C(=CC(=O)CC1)CCC1C2CCC2(C1CCC2=O)C
Aspartame	−1.21	OC(=O)CC(C(=O)NC(C(=O)OC)Cc1ccccc1)N
Azadirachtin	0.04	CC1(C23C4OC5C(C(C2(O3)C)C4)(C=CO5)O)C(C2C3C(C(CC(C33C1C(OC3)(O)C(=O)OC)OC(=O)C(=CC)C)OC(=O)C)(CO2)C(=O)OC)O
Blasticidin S	−2.54	NC(=N)N(CCC(CC(=O)NC1C(OC(N2C(=O)N=C(C=C2)N)C=C1)C(=O)O)N)C
Brassicanal A	2.09	O=CC1=C(Nc2ccccc12)SC
2,4-*epi*-Brassinolide	2.97	OC1C(CC2C(C1)C1C(C3C(CC1)(C(CC3)C(C(C(C(C(C)C)C)O)O)C)C)COC2=O)O
Ecdysone	1.96	OC1C(CC2C(C1)(C1C(=CC2=O)C2(C(CC1)(C(CC2)C(C)C(CCC(C)(C)O)O)C)O)C)O
7-Ethoxycoumarin	2.46	O=C1C=Cc2ccc(cc2O1)OCC
Kadsurenone	3.47	COc1c(cc(cc1)C1C(C2(C(=CC(=O)C(=C2)CC=C)O1)OC)C)OC
9,10-Dihydrokadsurenone	4.25	COc1c(cc(cc1)C1C(C2(C(=CC(=O)C(=C2)CCC)O1)OC)C)OC
Rotenone	3.88	COc1cc2c(cc1OC)OCC1C2C(=O)c2c(c3c(cc2)OC(C3)C(=C)C)O1

Spinosyn A	5.34	CC1C(CCC(O1)OC1C(C(=O)C2=CC3C(C2CC(=O)OC(CCC1)CC)C=CC1C3CC(C1)OC1OC(C(C(C1OC)OC)OC)C)C)N(C)C
Spinosyn D	4.75	CC1C(CCC(O1)OC1C(C(=O)C2=CC3C(C2CC(=O)OC(CCC1)CC)C=C(C1C3CC(C1)OC1OC(C(C(C1OC)OC)OC)C)C)C)N(C)C
Zearalenone	1.98	Oc1c2c(cc(c1)O)C=CCCCC(=O)CCCC(OC2=O)C

17. Organophosphorous Compounds	Log *P* values	Structure (SMILES)
Azinphos methyl	3.13	O=C1c2ccccc2N=NN1CSP(=S)(OC)OC.C
Butamifos	2.84	S=P(Oc1cc(ccc1N(=O)O)C)(NC(CC)C)OCC
Butamifos isomer	3.56	S=P(Oc1cc(c(cc1)N(=O)O)C)(NC(CC)C)OCC
Coumaphos	4.66	CC1=C(C(=O)Oc2cc(ccc12)OP(=S)(OCC)(OCC)C)Cl
Phosalone	4.28	O=C1Oc2cc(ccc2N1CSP(=S)(OCC)OCC)Cl
Quinalphos	3.75	S=P(Oc1nc2ccccc2nc1)(OCC)OCC

18. Oximes	Log *P* values	Structure (SMILES)
Aldicarb	1.69	CSC(C=NOC(=O)NC)(C)C
BAS 490 F (Kresoxim methyl)	3.76	CON=C(c1ccccc1COc1ccccc1C)C(=O)OC

19. Phenylureas and Related Compounds	Log *P* values	Structure (SMILES)
Isoproturon	2.27	CC(c1ccc(cc1)NC(=O)N(C)C)C
Linuron	2.96	CN(C(=O)Nc1ccc(c(c1)Cl)Cl)OC
Chlorbromuron	3.16	CON(C(=O)Nc1ccc(c(c1)Cl)Br)C
Metoxuron	2.24	CN(C(=O)Nc1cc(c(cc1)OC)Cl)C
Pencycuron	4.15	Clc1ccc(cc1)CN(C1CCCC1)C(=O)Nc1ccccc1

20. Phosphono Amino Acids and Related Compounds	Log *P* values	Structure (SMILES)
Glyphosate	−3.32	OP(=O)(CNCC(=O)O)O
Isofenphos	4.05	S=P(Oc1c(cccc1)C(=O)OC(C)C)(OCC)NC(C)C

21. Pyrethroids	Log *P* values	Structure (SMILES)
Bifenthrin	5.78	FC1(C(C1C(=O)OCc1c(c(ccc1)c1ccccc1)C)C=C(Cl)C(F)(F)F)C
Cyfluthrin	5.91	CC1(C(C1C(=O)OC(c1cc(c(cc1)F)Oc1ccccc1)C#N)C=C(Cl)Cl)C
Cyhalothrin	5.55	CC1(C(C1C(=O)OC(c1cccc(c1)Oc1ccccc1)C#N)C=C(Cl)C(F)(F)F)C
Cypermethrin	5.99	CC1(C(C1C(=O)OC(c1cc(ccc1)Oc1ccccc1)C#N)C=C(Cl)Cl)C
Deltamethrin	6.12	CC1(C(C1C(=O)OC(c1cccc(c1)Oc1ccccc1)C#N)C=C(Br)Br)C
Fenvalerate	5.75	Clc1ccc(cc1)C(C(=O)OC(c1cc(ccc1)Oc1ccccc1)C#N)C(C)C
Fluvalinate	5.3	Clc1c(ccc(c1)C(F)(F)F)NC(C(=O)OC(c1cccc(c1)Oc1ccccc1)C#N)C(C)C
Resmethrin	6.04	CC1(C(C1C(=O)OCc1coc(c1)Cc1ccccc1)C=C(C)C)C
Tefluthrin	4.81	Cc1c(c(c(c(c1F)F)COC(=O)C1C(C1C=C(Cl)C(F)(F)F)(C)C)F)F

22. Sulfonylureas	Log *P* values	Structure (SMILES)
Amidosulfuron	0.13	CN(S(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)S(=O)(=O)C
Bensulfuron methyl	1.68	O=C(c1ccccc1CS(=O)(=O)N1C(=O)Nc2nc(cc(n2)OC)OC)OC
Chlorimuron ethyl	2.55	O=C(c1ccccc1S(=O)(=O)N2C(=O)Nc2nc(cc(n2)Cl)OC)(OCC)C
Chlorsulfuron	1.76	Clc(cccc1)S(=O)(=O)N1C(=O)Nc2nc(nc(n2)OC)C
Metsulfuron methyl	1.35	O=C(c1ccccc1S(=O)(=O)N1C(=O)Nc2nc(nc(n2)OC)C)OC
Nicosulfuron	1.42	O=C(c1cccnc1S(=O)(=O)N1C(=O)Nc2nc(cc(n2)OC)OC)N(C)C
Prosulfuron	0.93	COc1nc(nc(n1)NC(=O)N1S(=O)(=O)c2ccccc2CCC(F)(F)F)C
Rimsulfuron	0.09	COc1cc(nc(n1)NC(=O)N1S(=O)(=O)c2ncccc2S(=O)(=O)C2C)OC
Sulfometuron methyl	2.18	O=C(c1ccccc1S(=O)(=O)N1C(=O)Nc2nc(cc(n2)C)C)OC
Thifensulfuron methyl	1.29	O=C(c1sccc1S(=O)(=O)N1C(=O)Nc2nc(nc(n2)OC)C)OC
Triasulfuron	1.53	COc1nc(nc(n1)NC(=O)N1S(=O)(=O)c2ccccc2OCCCl)C
Tribenuron methyl	0.92	COc1nc(nc(n1)N(C(=O)N1S(=O)(=O)c2ccccc2C(=O)OC)C)C

23. Triazines and Related Compounds	Log *P* values	Structure (SMILES)
Hexazinone	1.24	O=C1N=C(N(C(=O)N1C1CCCCC1)C)N(C)C
Irgarol 105	2.86	CSc1nc(nc(n1)NC1CC1)NC(C)(C)C
Metamitron	1.83	O=C1N(C(=NN=C1c1ccccc1)C)N

24. Miscellaneous	Log *P* values	Structure (SMILES)
Acrolein	0.12	C=CC=O
Butyl acrylate	2.56	C=CC(=O)OCCCC
Dimercaptopropane sulfonic acid (DMPS)	0.05	SCC(CS(=O)(=O)O)S
2-Nitrofluorene (NF)	4	O=N(c1cc2c(c3c(c2)cccc3)cc1)O

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