

The Agrochemical Industry

A. M. Malte* and A. T. Lilani*

INTRODUCTION

Scope of the Chapter

This chapter deals with the chemicals used in agriculture mainly to protect, preserve, and improve crop yields. The term “agrochemical” is used broadly. Much agrochemical research and some advanced development is directed toward the introduction of genes that may provide disease, insect, or viral resistance into plants or other organisms. Further progress is being made in improving the protein, fat, or carbohydrate composition of the plant itself. Microorganisms are being propagated and currently marketed that are insecticidal (e.g., *Bacillus thuringiensis*) fungi that are herbicidal, bacteria that are fungicidal, nematodes that are widely biocidal, and so on, are all products or candidate products for use in agriculture.

Arbitrarily excluded from discussion in this chapter are those substances that serve as fundamental nutrients, which are treated in Chapters 24 and 22 on fertilizers and nitrogen

technology, respectively. Nevertheless, it is the current practice of the farmer, particularly in advanced agriculture, to integrate nutritional and plant-protection application schedules, and even provide single formulations that include both fertilizers and pesticides. Further, plant nutrition at this stage of scientific sophistication is far more complex than the older classical “N-P-K” applications alone.

Many chemicals that accelerate plant growth act as hormonal agents, modifying plant metabolic processes at some stage of development. Because these substances are manufactured and marketed by the agrochemical industry, they are included as subject matter here. Also included in this chapter are chemicals that are significant to public health. Many organisms are vectors in the dissemination of human and animal disease. Because products of the pesticide industry control the insect, the rodent, the mollusk, and so forth (the vectors), they often are the most effective and sometimes the only practical means for controlling some of the most serious health problems of humankind, especially, but not exclusively, in the underdeveloped countries. An historical analog would be the use of rodenticides in the control of plague.

*Gharda Chemicals, Ltd., Dist. Thane, Maharashtra, India.

History

It is probable that farmers' treatment of crops with foreign substances dates back into pre-history. The Bible abounds with references to insect depredations, plant diseases, and some basic agricultural principles such as periodic withholding of land in the fallow state. Homer speaks of "pest-averting sulfur." More recently, in the nineteenth century, there was a great increase in the application of foreign chemicals to agriculture. Discovered or, more precisely, rediscovered was the usefulness of sulfur, lime sulfur (calcium polysulfides), and Bordeaux mixture (basic copper sulfates). With the exception of the organic compound formaldehyde, inorganic chemicals provided farmers with their major weapons.

The earliest of the organic compounds generally were chemicals derived from natural products or crude mixtures of chemicals in states of very elementary refinement. Extracts of ground-up plant tissue were useful in the control of insects. Such extracts were employed in agriculture quite often before the chemist had elucidated the structure or synthesized the molecule responsible for biological activity. These extracts included the pyrethroids, rotenoids, and nicotinoids, which continue to be derived in large part from plant extracts. Crude petroleum fractions were recognized for their effectiveness in the control of mites, scale, and various fungi, as well as for their phytopathological properties.

Although a few synthetic organics were already known, the great revolution in the use of organic chemicals in agriculture roughly coincides with the period of the onset of World War II. The more important of these discoveries were DDT (invented by Othmar Zeidler in late 1800s, insecticidal properties discovered by Mueller in 1939), 2,4-D (Jones patent—1945), benzenehexachloride (ICI and French development—ca. 1940), and the organic phosphate esters (Schrader—begun in the late 1930s, revealed in the 1940s).

These new chemicals were so enormously more potent than their predecessors in their biological activity (frequently by orders of magnitude) that they very rapidly

displaced almost all of the chemicals previously employed. The classical chemicals of today, some discovered in the 1950s and 1960s, are predominantly extensions of this almost revolutionary transition from inorganics to synthetic organics that dates from the period of World War II (Table 17.1). It is fair to say that within the United States the agrochemical industry since the late 1950s has been dominated by synthetic organic chemicals.

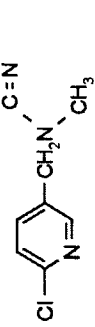
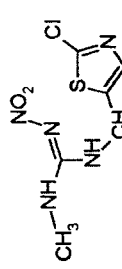
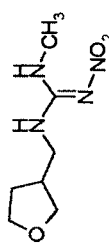
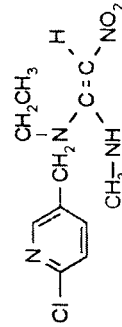
ROLE OF THE AGROCHEMICAL INDUSTRY

The world's population, which stands as 6 billion today and will continue to grow over the years, needs food. This food needs to be grown on the arable land available today, without further destruction of forest resources, wetlands, or mangroves. Thus, improving farm productivity by reducing losses experienced during crop cycles and post harvest is a major challenge. Agrochemicals, which are selective toxicants, provide an important tool. Available agrochemicals need to be deployed judiciously and newer ones must be developed to minimize impacts on water supplies and food quality. Presently, it is believed that more than a third of global farm output is lost due to ineffective pest control.

The agrochemical industry has the responsibility of using the power of science and technology for providing the world population with not only sufficient food but with food of increased nutritional value. On another, less obvious front, it needs to be noted that some 75 percent of the global population use medicinal plants for primary health care, and these plants also require crop protection. In yet another related area, public health, vector control is more dependable than are curative drugs in combating diseases such as malaria, yellow and dengue fevers.

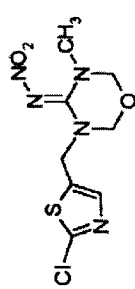
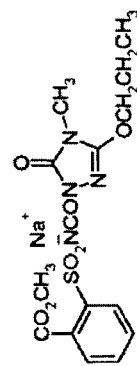
The agrochemical industry is large, complex, and involves many facets and many players. Listing several of these, from multinational manufacturer to individuals who apply the product in the field, will help in visualizing the breadth of the industry.

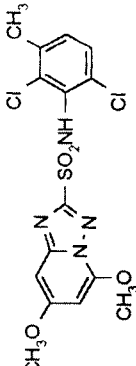
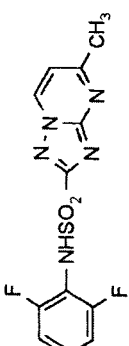
TABLE 17.1 New Chemistry

<i>Chemical (Chemical Class) (Year of Reporting)</i>	<i>Company's Name</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Known Profile of Use</i>	<i>Environmental Fate</i>
Acetamiprid (Neonicotinoid) (1992)	Nippon soda		Nicotinic acetyl-choline receptor agonist	Systemic insecticide with translaminar activity and with contact and stomach action	Control of Hemiptera, Thysanoptera and Lepidoptera by soil and foliar application on a wide range of crops especially vegetables, fruit, and tea	<i>Plants.</i> Slowly degraded on or in plants, forming five identified metabolites <i>Soil.</i> DT ₅₀ in clay loam 1 day, in light clay 1–2 days. DT ₅₀ for total residues 15–30 days
Clothianidin* (Nitromethylene neonicotinoid)	Takeda		Nicotinic acetyl-choline receptor agonist	Insecticide affecting the synapses in insects' central nervous system	Control of sucking and chewing insects by soil, foliar and seed application on rice, fruit, and vegetables	—
Dinotefuran* (Nitromethylene neonicotinoid) (1998)	Mitsui		Nicotinic acetyl-choline receptor agonist	Insecticide active by ingestion and contact; also exhibits root systemic activity	For control of a range of Hemipterous and other pests	—
Nitfenpyram (Nitromethylene neonicotinoid) (1993)	Takeda		Nicotinic acetyl-choline receptor agonist	Systemic insecticide with translaminar activity with contact and stomach action	Control of aphids, thrips, leafhoppers, whitefly and other sucking pests on rice and glass house crops	<i>Soil.</i> DT ₅₀ in soil 1–15 days, depending on soil type

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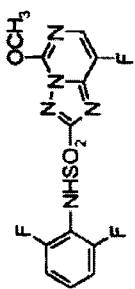
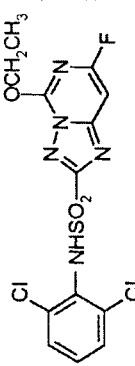
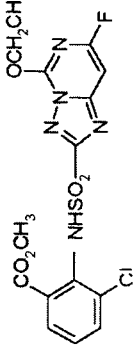
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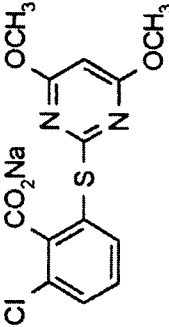
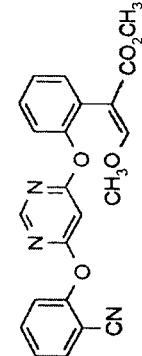
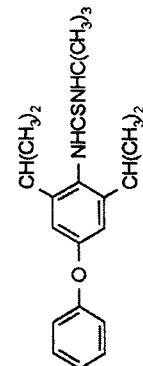
Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Thiamethoxam (Neonicotinoid) (1998)	Novartis		Nicotinic acetyl-choline receptor agonist	Insecticide with contact stomach and systemic activity	For the control of aphids, whitefly, thrips, ricehoppers, ricebugs, ealybugs, whitegrubs, olorado potato beetle, flea beetles, wireworms, ground beetles, leaf miners and some lepidopterous species. Foliar and soil applications: cole crops, leafy and fruity vegetables, potatoes, rice, cotton, deciduous fruits, citrus, tobacco, soybeans. For seed treatment: maize, sorghum, cereals, sugarbeet, oil seed rape, cotton, peas, beans, sunflower, rice, potatoes	<i>Animals.</i> Quickly and completely absorbed, rapidly distributed in the body and rapidly eliminated <i>Plants.</i> Degradation/metabolism has been studied in six different crops with soil, foliar and seed treatment application. The qualitative metabolic pattern was similar for all types of applications and for all studied crops <i>Soil.</i> Soil DT ₅₀ (median) 51 days
Propronycarbazonone* (Sulfonylamino- carbonyltriazo- none) (1999)	Bayer		Amino-acid synthesis inhibitor	Herbicide translocated both acro- petally and basipetally within both xylem and phloems	Post-emergence control of annual and some perennial grasses and some broadleaf weeds in wheat, rye, triticale	<i>Animals.</i> Rapid and nearly complete (>88%) within 48 hr, primarily via feces; 75–89% unchanged parent compound in urine and feces <i>Plants.</i> The unchanged parent compound and its 2-hydroxypropoxy metabolite are regarded as the relevant residues for plants <i>Soil.</i> Soil DT ₅₀ c. 36 days. Field dissipation DT ₅₀ c. 9 days

<p>Flucarbazone—sodium (Sulfonylamino-carbonyl-triazolinone) (1999)</p>	<p>Bayer</p>	<p>Amino-acid synthesis inhibitor</p> <p>Herbicide absorbed through foliage and roots and translocated acropetally and basipetally</p>	<p>Wheat for post-emergence control of grass weeds especially <i>Avena fatua</i> and <i>Setaria viridis</i> and some broad-leaved weeds</p> <p><i>Animals.</i> Almost completely excreted via feces and urine within 48 hr</p> <p><i>Plants.</i> Extensively metabolized. The relevant residues are the parent compound and the N-desmethyl metabolite</p> <p><i>Soil.</i> Average soil DT₅₀ 17 days. Not mobile in soil</p>
<p>Metosulam (Triazolopyridine) (1993)</p>	<p>Dow Agro-Sciences</p>	<p>Amino-acid synthesis inhibitor</p> <p>Herbicide readily taken up by roots and foliage</p> 	<p>Post-emergence control of many important broadleaf weeds including <i>Galium aparine</i>, <i>Stellaria media</i>, (<i>O</i>-demethylation) in urine (DT₅₀ 54–60 hr in rodents, 73 hr in dogs)</p> <p><i>Plants.</i> Poorly absorbed metabolized by hydroxylation of the ring methyl, to give a 3-hydroxymethyl- metabolite and its glycoside</p> <p><i>Soil.</i> Field DT₅₀ in the 0–10 cm horizon has a mean value of 25 days degradation via the 5- and 7-hydroxy analogue to 5-amino-N-(2,6-dichloro-3-methylphenyl)-1H-1,2,4-triazole-3-sulfonamide and CO₂. Does not have leaching potential</p>
<p>Flumetsulam (Triazolopyrimidine)</p>	<p>Dow Agencies</p>	<p>Amino-acid synthesis inhibitor (ALS or AHAS)</p> <p>Systemic Herbicide absorbed by roots and leaves of plants and translocated to growth points</p> 	<p>Used alone and in combination with trifluralin or metolachlor for control of broad-leaved weeds and grasses in Soyabeans, field peas, maize</p> <p><i>Animals.</i> Rapidly cleared via urine and feces with no metabolites. 5-Hydroxy metabolite found in the hen</p> <p><i>Plants.</i> DT₅₀ in maize 2 hr soya beans 18 hr, <i>Chenopodium</i> 131 hr. Metabolites depend on the species; 5-hydroxy or 5-methoxy derivatives are common</p> <p><i>Soil.</i> DT₅₀ in soil (25°C, pH 6–7, o.m. content 2–4%, 1–2 mos DT₅₀ in soil (pH 6–7, o.m. content 2–4%) 1–2 months</p>

(continued)

TABLE 17.1 Continued

Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Florasulam (Triazolo- pyridine)	Dow Agencies (1999)		Aminoacid synthesis (ALS or AHAS)	Herbicide taken up by inhibitor and shoots, and translocated in both xylem and phloem	Post-emergence control of broad-leaved weeds both roots <i>aparine</i> , <i>Stellaria media</i> , <i>Polygonum convolvulus</i> , <i>Matricaria</i> spp., and various cruciferae in cereals and maize	<i>Soil.</i> DT ₅₀ 2–18 days; neither florasulam nor its degradates should leach especially <i>Galium</i>
Diclosulam (Triazolopyri- midine)	Dow Agencies		Acetolactate synthase inhibitor	Herbicide taken up by roots and foliage and translocated to new growing points. Lethal amounts in meristems halting cell division and resulting in plant death	Soil applied control of broad-leaved weeds in Peanuts, soyabeans	<i>Animals.</i> Metabolized primarily by dealkylation of the ethoxy group and hydrolysis of the sulfonamide linkage <i>Soil.</i> Dissipation occurs primarily through microbial degradations of DT ₅₀ (in a wide variety of soils) c. 33–65 days
Cloransulam- methyl (Triazolo- pyrimidine) (1997)	Dow Agencies		Acetolactate synthase inhibitor	Herbicide having plant meristems as the primary site of activity	Control of broad- leaved weeds in Soyabeans. Applied to the soil surface or incorporated pre- or post-emergence	<i>Animals.</i> In female rats, excreted mainly via the urine; in male rats, excreted in both urine and feces. After 72 hr, <0.1% of the dose was found in any tissue <i>Soil.</i> Photolysis on soil surface, DT ₅₀ 30–70 days (corrected for metabolism) The apparent transformation DT ₅₀ in aerobic soils 9–13 days (est.). May be mobile

<p>Pyrithiobac-sodium (Pyrimidinyl oxybenzoic analogue) (1991)</p>	<p>Ihara/ Kumao</p>		<p>Amino-acid synthesis inhibitor (ALS or AHAS)</p>	<p>—</p>	<p><i>Animals.</i> More than 90% excreted in urine and feces within 48 hr; the major excreted metabolite was the <i>O</i>-desmethyl derivative. <i>Plants.</i> At 62 dat, no residues were found; major metabolites were the phenol formed by mono-demethylation, and its glucose conjugate <i>Soil.</i> Microbial and photochemical degradation play a major role in degradation t; DT₅₀ in silty soil 60 days</p>
<p>Azoxystrobin (Strobilurin) (1992)</p>	<p>Zeneca</p>		<p>Inhibitor of mitochondrial respiration</p>	<p>Fungicide with protectant, curative, radcitant, translaminar and systemic properties</p>	<p><i>Animals.</i> Majority of radiolabel is excreted in the faeces. Of a large number of metabolites, only the glucuronide of azoxystrobin acid is present at > 10% of the administered dose <i>Plants.</i> Metabolism was extensive, but parent azoxystrobin was the only major (> 10%) residue <i>Soil.</i> In soil, in the dark, six identified metabolites were formed; over 1 year, 45% of applied radiolabel is evolved as CO₂; DT₅₀ 1-8 weeks. Low to moderate mobility in soil; typical K_{oc} for azoxystrobin c. 500</p>
<p>Diafenthiuron (Strobilurin) (1988)</p>	<p>Novartis</p>		<p>Converted by light into the corresponding carbodiimide, which is an inhibitor of mitochondrial respiration</p>	<p>Insecticide, Acaricide having contact stomach action. Also shows some ovicidal action</p>	<p><i>Animals.</i> Major portion excreted with the feces. Degraded to yield its corresponding carbodimide, which, in turn forms urea and fatty acid derivatives <i>Plants.</i> Shows a complex metabolism pattern <i>Soil.</i> Diafenthiuron and its main metabolites show a strong sorptivity to soil particles. Degradation in soils proceeds rapidly: DT₅₀ < 1 hr to 1.4 days</p>

(continued)

TABLE 17.1 Continued

Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Fenamidon* (strobilurin) (1992)	Aventis		Inhibitor of mitochondrial respiration by blocking electron transport at ubiquinone; cytochrome oxidoreductase	Protectant and aerative fungicide	Under development for control of a range of Oomycete diseases	—
Kresoxim-methyl Strobilurin type: (Strobilurin) (1992)	BASF		Inhibitor of mitochondrial respiration by blocking electron transfer between cytochrome b and cytochrome C ₁ control	Fungicide with protective, curative, and long residual disease control	Control of scab, powdery mildew, mildew, scald, net blotch, glume blotch on apples, pears, vines, cucurbits, Sugarbeet, cereals, vegetables	<i>Animals.</i> Widely distributed and quickly eliminated; no bioaccumulation. The major routes of excretion were feces and urine. Thirty two different metabolites were identified <i>Plants.</i> Residues in cereals and pome fruit at harvest are <0.05 mg/kg, in grapes and vegetables <1 mg/kg <i>Soil.</i> Rapidly degraded. In soil, DT ₉₀ (lab.) <3 days, the main metabolite is the corresponding acid. Very mobile in soil. However, in lysimeter studies, only low levels of kresoxim-methyl and its metabolite were found in leachates
Tebufenpyrad (Pyrazole) (1993)	Mitsubishi chemical		Mitochondrial respiration inhibitor. Acts as an inhibitor	Nonsystemic Acaricide active by contact and ingestion.	Control of all stages of <i>Tetranychus</i> , <i>Panonychus</i> , <i>Oligonychus</i> , <i>Eotetranychus</i> spp.,	<i>Animals.</i> Metabolite is N-[4-(1-hydroxymethyl-1-methyl-ethylbenzyl)-4-chloro-3-(1-hydroxyethyl)-1-methyl-pyrazole-5-carboxamide] <i>Plants.</i> As for animals

of electron transport chain at site I

Exhibits translaminar movement following application to leaves

on fruit, vines, citrus, vegetables, hops, ornamentals, melons, cotton

Soil. Aerobic degradation occurs in soil, DT₅₀ 20-30 days

Trifloxys-trobin
Strobilurin type:
(Strobilurin)
(1998)

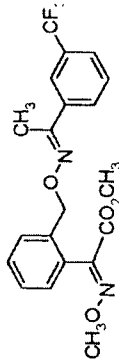
Novartis

Inhibits mitochondrial respiration by blocking electron transfer at the Q₀ centre of Cytochrome bc1

Mesostemic broadspectrum fungicide with preventive and curative activity and displaying rain-fastness. Redistributed by superficial vapor movement and also have translaminar activity

For control of powdery mildew, leaf spots, rusts, bunch and fruit rots of cereals, Pome fruit, grapes, Peanuts, bananas, vegetables

Animals. Absorbed from the gastrointestinal tract, rapidly metabolized and quickly and completely eliminated from the body
Plants. Rapidly degraded
Soil. Dissipates rapidly. DT₅₀ 4.2-9.5 days. No leaching potential



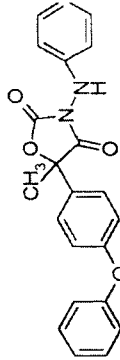
Famoxadone*
Strobilurin type:
(Oxazolimedione)
(1996)

DuPont

Inhibits mitochondrial electron transport, by blocking ubiquinolcytochrome C oxidoreductase at complex III

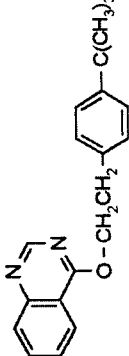
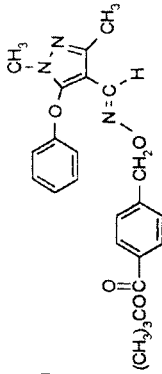
Control of mildew, potato and tomato late and early blights, wheat leaf and glume blotch and barley net blotch in grape, potato, tomato, wheat, barley

Animals. Elimination is rapid. Unmetabolised famoxadone was the major component in the feces; mono- (at 4'-phenoxyphenyl) and di- (also at 4-phenylamino) hydroxylated famoxadone were the primary fecal metabolites. In urine, products arising from cleavage of the heterocyclic ring were found. Metabolism was complex, involving hydroxylation, cleavage of the oxazolimedione-aminophenyl linkage, cleavage of the phenoxyphenyl ether linkage and opening of the oxazolimedione ring



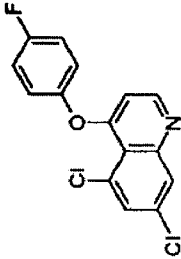
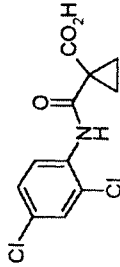
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TABLE 17.1 Continued

Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Fenazaquin Strobilurin type: (Oxazolinedione) (1992)	Dow Agro- sciences		Inhibitor of mitochondrial electron transport chain by binding with complex I at co-enzyme site Q	Contact Acaricide with good knockdown activity on motile forms as well as true ovicidal activity. Preventing eclosion of mite eggs	Control of <i>Euteranychus</i> , <i>Panonychus</i> , <i>Tetranychus</i> , <i>Brevipalpus phoenici</i> in almonds, apples, citrus, cotton, grapes, ornamentals	—
Fenpyroximate Pyrazole (acaricide) (1990)	Nihon Nohyaki		Inhibitor of mito- chondrial electron transport at complex I	Acaricide having quick knockdown activity against	Effective against some phytophagous mites. Control of Tetranychidae, Tarsonemidae, Penurpalpidae and	Soil. DT ₅₀ 26.3–49.7 days

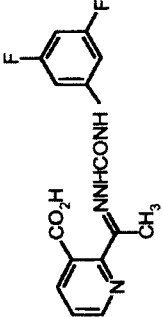
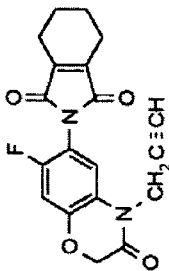
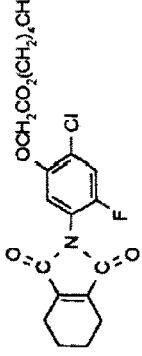
Plants. In grapes and potatoes, famoxadone was the main residue; no residues were found in potato tubers. In wheat, famoxadone was extensively metabolised, primarily by hydroxylation, followed by conjugation

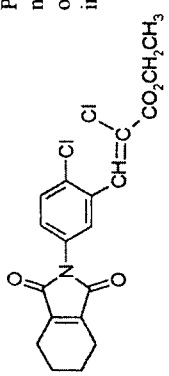
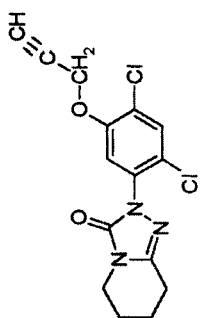
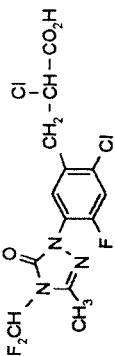
Soil. In laboratory soil, DT₅₀ 6 days (aerobic), 28 days (anaerobic). Degradation routes include hydroxylation (at the 4'-phenoxyphenyl position), ring opening (with formation of a glycolic acid derivative), and is primarily microbial

<p>Quinoxifen (Quinoline) (1996)</p>	<p>Dow Agro- sciences</p>		<p>Growth signal disruptor</p>	<p>larvae, nymphs and adults mainly by contact and ingestion</p>	<p>Eriophyidae. In citrus, apple, pear, peach, grapes</p>	<p>Control of powdery mildew in cereals</p>	<p><i>Plants.</i> Only slightly metabolized in wheat, with low residues found in the crop. Extensively photodegraded on the wheat leaf surface, giving multiple polar degradation products. On grapes and cucumbers, the main residue was unchanged quinoxifen <i>Soil.</i> DT₅₀ (field) 123–494 days (biphasic); nonleaching. The main metabolite in the soil (also classed as nonleaching) was formed by hydroxylation at the 3-position of the quinoline ring; a minor metabolite (DCHQ), formed by cleavage of the ether bridge, was observed, especially in acidic soil</p>
<p>Cyclanilide Strobilurin type: (Oxazolimedione) (1994)</p>	<p>Aventis</p>		<p>Inhibits Polar auxin transport</p>	<p>Plant growth regulator</p>	<p>Cotton and other crops</p>	<p><i>Animals.</i> Rapidly excreted, primarily as unchanged cyclanilide <i>Plants.</i> Little degradation occurs in plants; cyclanilide is the major residue <i>Soil.</i> Low to moderate persistence, DT₅₀ c. 16 days under aerobic conditions.</p>	
<p>Degrades</p>	<p>Primarily by microbial activity. Medium to low mobility</p>						

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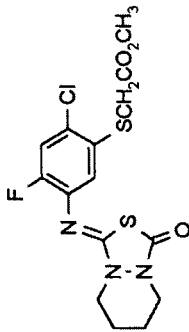
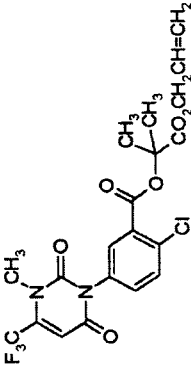
TABLE 17.1 Continued

Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Diflufenzopyr (Semi-carbazone) (1999)	BASF		Inhibits auxin transport, apparently by binding with a carrier protein on the plasmalemma	Systemic, post-emergence herbicide	Control of annual broad leaved and perennial weeds in maize	<i>Animals.</i> Partially absorbed and rapidly eliminated; 20–44% of the dose was eliminated in urine and 49–79% in feces. Total radioactive residues in tissues <3% of the administered dose. Eliminated primarily as unchanged parent compound <i>Soil.</i> Average DT ₅₀ in field soil 4.5 days. Very mobile. Metabolites also very mobile. However, based upon proposed use, US EPA does not expect diflufenzopyr to reach drinking water
Flumioxazin (N-phenyl-phthalimide)	Sumitomo		Protoporphyrinogen oxidase inhibitor	Herbicide absorbed by foliage and germinating seedlings tissue	Control of many annual grasses, pre- and post-emergence in soyabeans, peanuts, orchards and other crops	—
Flumiclorac-pentyl N-phenyl phthalimide (1998)	Sumitomo valent		Protoporphyrinogen oxidase inhibitor	Fast acting, contact herbicide. When applied to foliage of susceptible plants. It is readily absorbed into plant	Control of problem broad leaved weeds including <i>Xanthium strumarium</i> , <i>Chenopodium album</i> , <i>Ambrosia artemisiifolia</i> , <i>Datura stramonium</i> , <i>Amaranthus</i> sp., <i>Sida spinosa</i> , <i>Euphorbia maculata</i> , <i>Abutilon theophrasti</i> , pre- and post-emergence in soyabeans and maize	In soya beans and maize, the major metabolite is 2-chloro-4-fluoro-5-(4-hydroxy-1, 2-cyclohexane-dicarboximido) phenoxyacetic acid formed by reduction of the tetrahydrophthaloyl double bond and hydroxylation; other metabolic pathways include cleavage of the ester, and cleavage of the imide linkage <i>Soil.</i> Rapidly degraded in soil: DT ₅₀ 0.48–4.4 days in loamy-sand soil (pH 7); degrades have DT ₅₀ c. 2–30 days. The a.i. is immobile in soil; degrades have low to medium mobility

<p>Cimidon-ethyl N-phenyl- phthalimide (1998)</p>	<p>BASF</p>		<p>Protoporphyrinogen IX oxidase inhibitor</p>	<p>Post-emergence control of annual broad-leaved weeds especially <i>Galium aparine</i>, <i>Lamium</i> sp. and <i>Veronica</i> sp. in winter and spring small grain cereals</p>	<p><i>Animals.</i> Following limited, but rapid, absorption, and widespread distribution in organs and tissues, the a.i. is extensively metabolised and rapidly excreted <i>Plants.</i> The a.i. is extensively metabolised <i>Soil.</i> Readily biodegradable. Soil DT₅₀ 0.6–2 days (lab., aerobic conditions, 20°C); rapidly mineralized</p>
<p>Azafenidin (Triazolinone) (1998)</p>	<p>Dupont</p>		<p>Protoporphyrinogen oxidase inhibitor through roots and shoots. Herbicide absorbed through roots citrus, grapes, olives, Improves the efficacy of other post-emergence herbicides and increases the speed of action of contact herbicides</p>	<p>Pre-emergence control of annual and perennial weeds in sugarcane and other perennial crops</p>	<p><i>Soil.</i> Degrades in soil by microbial and photolytic process. In the field, in a range of 4 soils, mean DT₅₀ c. 25 days mean DT₉₀ c. 169 days. There was minimal movement in soil column leaching studies</p>
<p>Carfentrazone-ethyl (Triazolinone) (1993)</p>	<p>FMC</p>		<p>Protoporphyrinogen oxidase inhibitor limited translocation</p>	<p>Post-emergence control of a wide range of broad leaved weeds especially <i>Galium aparine</i>, <i>Abutilon theophrasti</i>, <i>Ipomoea hederacea</i>, <i>Chenopodium album</i> and several mustard species in cereals</p>	<p><i>Animals.</i> c. 80% is rapidly absorbed and excreted in the urine within 24 hrs. The major metabolite was the corresponding acid. Further metabolism appears to involve oxidative hydroxylation of the methyl group or dehydrochlorination to form the corresponding cinnamic acid <i>Plants.</i> Rapidly converted to the free acid, which is hydroxylated and then oxidised at the triazolinone methyl to form the dibasic acid; DT₅₀ (carfentrazone-ethyl) <7 days, DT₅₀ (carfentrazone) <28 days</p>

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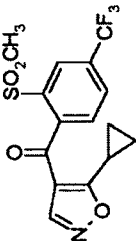
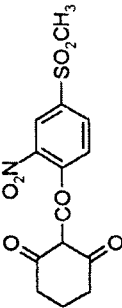
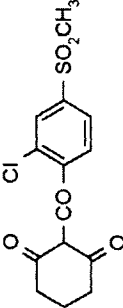
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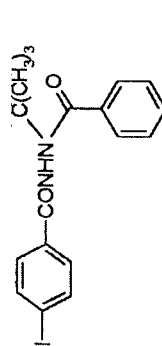
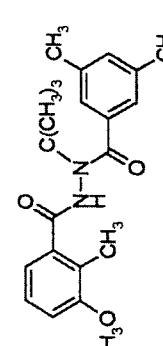
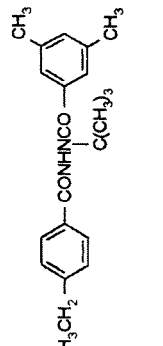
Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Fluthiacet-methyl (Thiadiazole) (1993)	Ihara/ Kumai (Also reported by Ciba- Geigy AG)		Protoporphyrinogen oxidase inhibitor	Selective, herbicide requiring light for activity	Post-emergence control of broad-leaved weeds e.g., <i>Abutilon theophrasti</i> , <i>Chenopodium album</i> , <i>Amaranthus retroflexus</i> , <i>Xanthium strumarium</i> in maize and soybeans	<i>Soil.</i> Broken down in the soil by microbial action. Strongly adsorbed to sterile soils in nonsterile soils, rapidly converted to the free acid, which has low soil. In the laboratory, soil DT ₅₀ is a few hours, degrading to the free acid, which in turn has DT ₅₀ 2.5–4.0 days <i>Animals.</i> Within 48 hr 80% is eliminated via the feces, 14% via urine. Metabolism proceeds via hydrolysis of the methyl ester, isomerisation at the thiazole ring and hydroxylation of the tetrahydropyridazine moiety <i>Plants.</i> Organosoluble metabolites are similar to those in animals <i>Soil.</i> DT ₅₀ (hydrolysis, pH 7) 18 days (photolysis on soil) 21 days (UV light) 2 hr. In loam soil, DT ₅₀ 1.2 days (25°C, 75% of max. water capacity)
Butafenacil (Pyrimidindione) (1998)	Novartis		Protoporphyrinogen oxidase inhibitor	Non-selective contact herbicide, rapidly absorbed by the foliage. Translocation occurs only within leaves	Control of a wide range of annual and perennial broadleaved weeds in fruits, orchards, vineyards, citrus, non-crop land	<i>Soil.</i> Rapidly degraded in soil: DT ₅₀ 1–2 days

<p>Carpopamid (MBI: dehydrase) (1994)</p>	<p>Bayer</p>	<p>Inhibitor of melanin biosynthesis, by inhibiting the dehydration reactions from Scytalone to 1,3,8-trihydroxy naphthalene and from vermelone to 1,8-dihydroxy naphthalene</p>	<p>Systemic, protective fungicide</p>	<p>Control of <i>Pyricularia oryzae</i> as protective treatment or seed treatment</p>	<p><i>Animals.</i> Readily excreted via feces and urine. Metabolized oxidatively, mainly in the liver <i>Plants.</i> Absorbed by the roots and translocated to the shoots. The major residue in rice was carpropamid <i>Soil.</i> Metabolized oxidatively under paddy soil conditions; CO₂ was the major metabolite. The calculated half-lives ranged from several weeks to several months, resp. Low mobility</p>
<p>Fenoxamil* (MBI: dehydrase)</p>	<p>BASE, Nihon Nohyaku</p>	<p>Melanin biosynthesis inhibitor Inhibits dehydratase enzymes, which dehydrate scytalone to trihydroxy naphthalene and vermelone to dihydroxy naphthalene</p>	<p>Systemic, protective fungicide with residual effects</p>	<p>Under development for control of rice blast by foliar or into-water application in rice</p>	<p>—</p>
<p>Benzofenap (Pyrazole)</p>	<p>Mitsubishi/ Acentis</p>	<p><i>p</i>-Hydroxy-phenyl pyruvate dioxygenase inhibitor</p>	<p>Systemic Herbicide, absorbed principally through root and bases of target weeds</p>	<p>Used in combination with pyributicarb and bromo-butide, controls annual and perennial broadleaved weeds in rice</p>	<p><i>Plants.</i> No detectable residues in rice crops (detection limit 0.005 ppm). <i>Soil.</i> DT₅₀ 38 days. Nonmobile</p>

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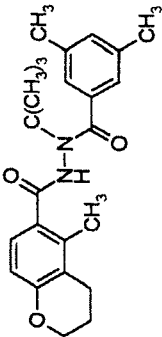
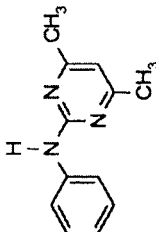
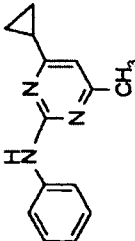
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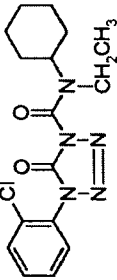
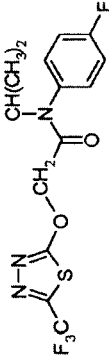
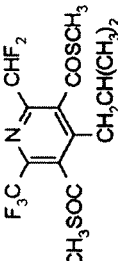
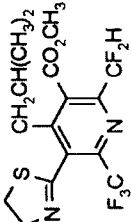
Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Isoxaflutole (Isoxaaxole) (1995)	Aventis		<i>p</i> -Hydroxy-phenyl pyruvate dioxygenase inhibitor	Herbicide, Systemic by either root or foliar uptake.	For pre-emergence or pre-plant broad spectrum grass and broad-leaved weeds control in maize	<i>Animals.</i> Rapidly excreted <i>Plants.</i> Residue levels at harvest are very low, and comprise mainly a nontoxic metabolite <i>Soil.</i> Degradation proceeds via hydrolysis and microbial degradation, with final mineralization to CO ₂ . Isoxaflutole and its major metabolites are nonmobile under field conditions
Mesotrione (Triketone) (1999)	Zeneca		<i>p</i> -Hydroxy-phenyl pyruvate dioxygenase inhibitor	Herbicide, Uptake is foliar and via the root, with both acropetal and basipetal translocation	Pre- and post-emergence control of broad leaved weeds such as <i>Xanthium strumarium</i> , <i>Ambrosia trifida</i> , <i>Abutilon theophrasti</i> , <i>chenopodium</i> , <i>Amaranthus</i> and <i>polygonum</i> spp. and some grass weeds in maize	<i>Soil.</i> Stable to hydrolysis under sterile conditions at pH 5–9, with <10% degradation after 30 days (25°C). Degradation is influenced by soil pH; DT ₅₀ 31.5 days (pH 5.0% o.c. 2.0) to 4.0 d (pH 7.7% o.c. 0.9).
Sulcotrione (Triketone) (1991)	Zeneca		<i>p</i> -Hydroxy-phenyl pyruvate dioxygenase inhibitor	Herbicide Absorbed predominantly by leaves but also by roots	Post-emergence control of broad-leaved weeds and grasses in maize and sugarcane	<i>Animals.</i> Rapidly excreted in the urine, the major metabolite being 4-hydroxysulcotrione <i>Plants.</i> Deactivated by the formation of 2-chloro-4-methylsulfonylbenzoic acid <i>Soil.</i> DT ₅₀ 1–11 days. The major metabolite is 2-chloro-4-methylsulfonylbenzoic acid

<p>Halo fenozide (Diacylhydrazine) (1997)</p>	<p>Rohm & Hass</p>		<p>Ecdysone agonist</p>	<p>Systemic, ingested insecticide active by root application. Interferes with moulting affecting larval stages of insects. Also reduces fecundity in treated adults and have some ovicidal properties</p>	<p>Control of Coleoptera and Lepidoptera in turf and ornamentals</p>	<p>Soil. Soil dissipation DT₅₀ (field) 42–267 days (five sites); turf DT₅₀ 3–77 days</p>
<p>Methoxyfenozide (Diacylhydrazine) (1997)</p>	<p>Rohm & Hass</p>		<p>Ecdysone agonist</p>	<p>Insecticide active primarily by ingestion, also with contact, ovicidal and root systemic activity</p>	<p>Control of lepidopterous larvae in vines tree fruits, vegetables, row crops</p>	<p>Animals. Rapidly absorbed, metabolized via phase II conjugation and eliminated Soil. Aerobic soil metabolism DT₅₀ 336–1100 days; field DT₅₀ 23–268 days</p>
<p>Tebufenozide (Diacylhydrazine) (1996)</p>	<p>Rohm & Hass</p>		<p>Ecdysone agonist</p>	<p>Insecticide Lethal accelerates moulting process</p>	<p>Control of lepidopterous larvae in rice, fruit, row crops, nut-crops, vegetables, vines and forestry</p>	<p>Animals. 16 whole-molecule metabolites are formed as a result of oxidation of the alkyl substituents of the aromatic rings, primarily at the benzylic positions Plants. In apples, grapes, rice, and sugar beet, the major component is unchanged tebufenozide. Small amounts of metabolites result from oxidation of the alkyl substituents of the aromatic ring, primarily at the benzylic positions Soil. Metabolic DT₅₀ in soil 7–66 days; DT₅₀ for field dissipation 4–53 days. No mobility below 30 cm</p>

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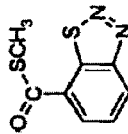
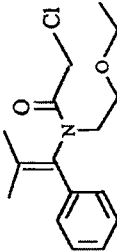
TABLE 17.1 Continued

Chemical (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Chromafenozide (Diacylhydrazine) (1996)	Nippon Kayaku; Sankyo		Ecdysone agonist	Insecticide Initiating a precocious incomplete lethal moult	Control of lepidopteran larvae in rice, fruit, vegetables, tea, cotton, beans, and forestry	<i>Animals.</i> Rapidly excreted with 48 hr and is not persistent in tissues and organs. The major component excreted is unchanged chromafenozide. <i>Plants.</i> Many minor metabolites are detected in small amounts, but the major component is unchanged chromafenozide. <i>Soil.</i> DT ₅₀ for field dissipation 44–113 days (unpland soil), 22–136 days (paddy soil)
Pyrimethanil (Aminopyrimidine) (1992)	Aventis		Inhibitor of methionine biosynthesis leading to inhibition of the secretion of enzymes for fungal infection	Fungicide Protectant in <i>Botrytis</i> and both protective and curative action in <i>Venturia</i>	For control of grey mould on vines, fruits, vegetables and ornamentals and of leaf scab on pome fruit	<i>Animals.</i> Rapidly absorbed, extensively metabolised and rapidly excreted. No evidence of accumulation, even on repeated dosing. Metabolism proceeds by oxidation to phenolic derivatives which are excreted as glucuronide or sulfate conjugates <i>Plants.</i> Little metabolism occurs in fruit <i>Soil.</i> Rapid degradation, DT ₅₀ 7–54 days. Low potential for leaching
Cyprodinil (Anilino pyrimidine) (1994)	Novartis		Inhibitor of methionine biosynthesis and secretion of fungal hydrolytic enzymes	Systemic Fungicide into plants after foliar application and transport throughout the tissue and acropetally in the xylem. Inhibits penetration	Control wide range of pathogens like <i>Tapestia yellundae</i> , <i>T. acyiformis</i> , <i>Erysiphe</i> spp., <i>Pyrenophora teres</i> , <i>Rhynchosporium secalis</i> , <i>Botrytis</i> spp., in cereals, grapes, pome fruit, stone fruit, strawberries, vegetables, field crops and ornamentals, barley <i>Alternaria</i> spp., <i>Venturia</i> spp. and	<i>Animals.</i> Rapidly absorbed and almost completely eliminated with urine and faeces. Metabolism proceeds by 4-hydroxylation of the phenyl and 5-hydroxylation of the pyrimidine rings, followed by mono- or di-sulfation. No evidence for accumulation or retention of cyprodinil or its metabolites <i>Plants.</i> Metabolism mainly via hydroxylation of the 6-methyl group of the pyrimidine ring, as well as hydroxylation of the phenyl and pyrimidine rings <i>Soil.</i> DT ₅₀ 20–60 Days Formation of bound residues the major route for dissipation. Immobile in soil

Fentrazamide (Tetrazolinone) (1997)	Bayer		Cell division inhibitor. Primary target site may be fatty acid metabolism	and mycelial growth both inside and on the leaf surface	monilinia spp.	Control of barnyard grass <i>Echinochloa</i> spp. and annual sedges in rice for pre-emergence	<p><i>Animals.</i> The main pathway of biotransformation proceeded via hydrolytic cleavage of the parent compound</p> <p><i>Plants.</i> No parent compound was detected in any plant fraction</p> <p><i>Soil.</i> Thoroughly degraded and mineralized. Calculated half-lives were in the range of a few days and several weeks, respectively. Immobile</p>
Flufenacet (Oxyacetamide) (1995)	Bayer		Cell division inhibitor. Primary target site may be fatty acid metabolism	Pre- and early Post-emergence herbicide	Selective herbicide with broad spectrum grass control and control of some broad leaved weeds in maize, soybeans, sunflower, wheat, rice	<p><i>Animals.</i> Rapidly excreted. Metabolism takes place via cleavage of the molecule, followed by conjugation of the fluorophenyl moiety with cysteine and formation of a thiadazolone and its various conjugates</p> <p><i>Plants.</i> Rapidly and extensively metabolized; no parent compound was detected, even at early sampling dates</p> <p><i>Soil.</i> Rapidly degraded, immobile</p>	
Dithiopyr (Pyridine) (1994)	Rohm & Hass		Inhibits cell division by disrupting spindle microtubule formation	—	Pre-emergence and early post-emergence control of annual grass and broad-leaf weeds in turf	<p><i>Animals.</i> Rapidly absorbed, extensively metabolized and rapidly excreted</p> <p><i>Soil.</i> DT₅₀ in soil 17–61 days, depending on the formulation type. The major soil metabolites are the di-acid, the normal mono-acid and the reverse mono-acid; these metabolites, themselves, dissipate almost completely within 1 year</p>	
Thiazopyr (Pyridine) (1994)	Rohm & Hass		Inhibits cell division by disrupting spindle	Herbicide causing root growth inhibition and	Pre-emergence control of annual grass and some broad-leaved weeds in tree fruit,	<p><i>Animals.</i> Rapidly and extensively metabolized and eliminated. Oxidized by rat liver microsomes via sulfur and carbon oxidations and via oxidative de-esterification</p>	

(continued)

TABLE 17.1 Continued

Chemical (Chemical Class) (Year of Reporting)	Company's Name	Structure	Biochemistry	Mode of Action	Known Profile of Use	Environmental Fate
Acibenzolar-S- methyl Plant activator/ Plant host defense induces (1995)	Novartis		Acts as a functional analogue of the natural signal molecule for systemic activated resistance, salicylic acid	Activates plants' natural defense mechanism (systemic activated resistance [SAR]). Has no intrinsic fungicidal activity	For control of fungal infections in wheat under development against a range of diseases in rice, bananas, vegetables, and tobacco	<i>Plants.</i> Initially metabolized in the dithiothiazole ring by plant oxygenases to the sulfoxide, sulfone, hydroxy derivative and thiazole, and is also de-esterified to the carboxylic acid <i>Soil.</i> Degraded by both soil microorganisms and hydrolysis. Average DT ₅₀ 64 days (8–150 days). Minimal mobility. The monoacid metabolite also has limited mobility <i>Animals.</i> Rapidly absorbed and also rapidly almost completely eliminated with urine and feces. No evidence of accumulation or retention of acibenzolar-S-methyl or its metabolites <i>Plants.</i> The metabolism proceeds via hydrolysis with subsequent conjugation with sugars, or by oxidation of the phenyl ring followed by sugar conjugation <i>Soil.</i> Dissipates via hydrolysis; DT ₅₀ 0.3 day. The product further degrades, DT ₅₀ 20 days; metabolites become completely degraded and mineralized. Strong adsorption to soil, low mobility
Pethoxamid Acetamide (2001)	Tokuyama		Presumed to be acting by inhibiting fatty acid biosynthesis	Precise mode of action not yet been clarified. Absorbed by roots and young shoots after application to soil surface	Controls grass weeds including <i>Echinochloa crus-galli</i> , <i>Digitaria sanguinalis</i> and <i>Setaria geniculata</i> and broad leaf weeds such as <i>Amaranthus retroflexus</i> , <i>Chenopodium album</i> , <i>Convolvulus arvensis</i> and <i>Polygonum pericaria</i>	—

The “players” include:

1. Large, multinational companies engaged in discovery, manufacture, and distribution of agrochemicals, seeds, and other products of biotechnology.
2. Large corporate entities engaged in the manufacturer and distribution of off-patent agrochemicals.
3. Companies engaged in the formulation and distribution of agrochemicals purchased from (1) or (2) above.
4. Retailers who make end-use products available to growers.
5. Extension workers from governmental or nongovernmental sources who provide guidance on the proper use of agrochemicals in the field.
6. Professional consultants who perform activities in (5) to individual growers.
7. Pest control operators who are professionally trained to properly apply restricted use of agrochemicals as well as other agrochemicals deployed in disease vector control and termite control.

For the year 2000, it was estimated that the global sales revenue of the agrochemical industry amounted to US\$30 billion. This breaks down as follows.

Herbicides	US\$14 billion	73% for cereals, maize, soybeans, fruits, vegetables
Insecticides	US\$8 billion	71% for fruits, vegetables, cotton, rice
Fungicides	US\$6 billion	70% for cereals, fruits, vegetables
Others	US\$1 billion	

The revenues were distributed globally approximately as follows: North America—27.2 percent; Far East—26 percent; Europe—25.5 percent; Latin America—14.8 percent; and the rest of the world—6.5 percent.

CHARACTERISTICS OF THE AGROCHEMICAL INDUSTRY

Among the distinguishing characteristics of the agrochemical industry are: (1) the multitude of chemical agents employed, (2) a limited price range (which derives from the

limited chemical complexity, in turn driven by the economics of agricultural production), (3) a fairly rapid obsolescence of the chemicals used, and (4) a high degree of government regulation for the production, application, shipment, and use of agrochemicals.

Government Regulation

In the United States, the first state laws on insecticides were enacted in 1900 to establish standards of purity for the arsenical Paris green (copper acetoarsenite) which is no longer used in agriculture in the United States. Gradually these laws were extended to cover a wide list of inorganic compounds and plant extracts, many of them, like Paris green, extremely toxic to humans. Included in this group are such compounds as arsenic combined with copper, lead, and calcium; phosphorus pastes for ants and roaches; strychnine in rodent baits; thallium in ant and rodent baits; and selenium for plant-feeding mites. Mercury, both as a corrosive sublimate and as calomel, was used as an insect repellent and later as a seed disinfectant. Sodium fluoride was a common ant poison, and sodium cyanide, calcium cyanide, and HCN itself were general fumigants (Table 17.2). Nicotine sulfate was used generally in the garden and on the farm. These compounds, among the most toxic of any known at that time, were widely marketed without supervision under any of the early state laws. There was no provision for public health, either in regulating the amounts applied or regarding the possible danger of minute amounts (residues) remaining on the marketed produce. The need to protect the applicator, farmer, laborer, and the general public against the dangerous qualities of the insecticides, or their residues on crops, provided the motives for all the legislation that followed.

Governmental concern was first related to standardization of the manufactured chemical and protection of the farmer in relation to the product that he or she purchased. This was then extended to the handling of the chemical in interstate commerce, to the protection of the consumer of raw agricultural products

TABLE 17.2 Fumigants

<i>Chemical</i> (<i>Chemical Class</i>)	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Chloropicrin	Cl_3CNO_2	—	Fumigant	—
Dazomet (Methyl isothiocyanate precursor)		Nonselective inhibition of enzymes by degradation products	A pre-planting soil fumigant, acting by decomposition to methyl Eothocyanate	<i>Plants.</i> Following application to strawberries, no residues of dazomet or of its degradation products methyl isothiocyanate, dimethyl- or monomethylthiourea were detected at >0.01 ppm in the fruit <i>Soil.</i> In the presence of moisture, undergoes degradation to methyl-(methylaminomethyl) dithiocarbamic acid, which then undergoes further degradation to methyl isothiocyanate, formaldehyde, hydrogen sulfide and methylamine
1,3-dichloropropene (Chloroalkene)	—	—	Soil fumigant nematicide	—
Methyl Bromide	CH_3Br	—	Fumigant insecticide and nematicide	<i>Animals/Plants.</i> Metabolism not totally elucidated; inorganic bromide ion is formed

(e.g., apples, corn, and lettuce), and, in other legislation, to the protection of the consumer of finished goods (e.g., canned juice, margarine, cereal food, meat, and milk). Included in this legislation were provisions that protect the shipper of the chemical, the applicator of the chemical, and all personnel proximal to the application of the chemical. Legislation now regulates chemicals applied to crops or foods as protective agents—pesticides, emulsifiers, solvents, packaging materials (wax, container materials, plasticizers, antioxidants, etc.).

Toward the end of the 1960s, a new area of concern arose: the effect of the manufacture and application of pesticide chemicals *on the environment* was recognized. Concern for the environment was the subject matter of Rachel Carson's book, *Silent Spring*, which was published in 1962. In 1970, this new focus led to the establishment of the Environmental Protection Agency (EPA; aka US-EPA), which was given authority to regulate virtually all aspects of agrochemical manufacture and use in the United States. Since its inception, the principal objectives of the EPA's agrochemical activities have been to: (1) establish procedures that ensure that new pesticides will

not pose unreasonable risks to human health and the environment, and (2) terminate the use of those previously registered pesticides that exceed certain risk criteria. Among the requirements called for are studies on mammalian toxicology (including lifetime animal feeding studies), environmental chemistry (persistence, mobility, etc.), and effects on fish and other wildlife. New product registrations are granted only after EPA scientists and administrators are satisfied that use of the product does not pose unreasonable risk to humans or hazard to the environment. All aspects of the environment are considered. Soil, air, and water (streams, lakes, oceans, rivers, marshes, and underground aquifers) are matters of environmental concern, as are the living organisms that reside therein. The protocols employed to ensure safety are complex and not infrequently are at the boundaries of scientific capability. The registration of any new product is a highly complicated and expensive procedure. As to the second objective, much the same criteria are used in judging whether or not to allow continued use of previously registered pesticides.

Although comprehensive regulatory legislation was developed first and most extensively in the United States, all the technically developed nations of the World now regulate the manufacture, sale, and use of agricultural chemicals. The criteria used are not unlike those which were developed over the past several years in the United States. In Europe, the European Economic Community (EEC) in 1991 adopted Directive 91/414/EEC which, included the following goals.*

1. Coordinate the overall arrangements for authorization of plant protection products within the European Union. Whereas it is intended to coordinate the process for considering the safety of particular substances at the Community level, individual Member States have responsibility for product authorization.
2. Establish a list of active substances which have been shown to be without unacceptable risk to humans or the environment.
3. Maintain an up-to-date listing (Annex I of the Directive) of active substances which have been authorized.
4. Member States can authorize the sale and use of plant protection products only if they are listed in Annex I.

Under provisions of directive 91/414/EEC, all existing agrochemicals are being reviewed and new ones approved using common database criteria. The review process started in 1993 and is expected to be completed by 2008. Many agrochemicals will cease to be used in the European Union because of the failure of participating companies to submit full dossiers on them. Additionally, water quality directive 98/83/EC demands detectability for a given agrochemical in water below 1 ppb.

The 29 country member Organization for Economic Cooperation and Development Working Group offers a common platform to the national pesticide regulators for discussion

of activities on conventional, biological, and microbial pesticides.

On a broader scale, several years ago the Food and Agriculture Organization of the United Nations adopted the International Code of Conduct on the Distribution and Use of Pesticides.[†] A few of the many provisions of that Code are listed below to give a general idea of its thrust.

1. Governments have the overall responsibility and should take the specific powers to regulate the distribution and use of pesticides in their countries.
2. The pesticide industry should adhere to the provisions of this Code as a standard for the manufacture, distribution, and advertising of pesticides, particularly in countries lacking appropriate legislation and advisory services.
3. Manufacturers and traders should supply only pesticides of adequate quality, packaged, and labeled as appropriate for each specific market.

Manufacture of Agrochemicals

The manufacturing route to an agrochemical can have multiple options. The route chosen may depend on commercial availability of desired reagents, engineering capabilities, byproduct formation, separation techniques, and so on. This is on par with the manufacture of drugs, dyestuffs, or speciality chemicals. One feature unique to agrochemicals is a detailed and precise label preapproved by a regulatory body on the product safety, usage instructions, compatibility statements, and other statements as deemed necessary for the needs of medical professionals and general public information.

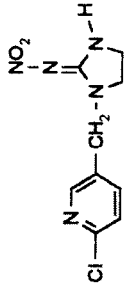
Classes of Agrochemicals

Agrochemicals that control insects by growth regulation, or by mortality through contact or stomach action are called *insecticides* (Table 17.3a,b). Those that control competing weeds (grasses, broad leaved plants, or sedges) through preplant incorporation, pre-emergence, early post- or post-emergence application with respect to the main crop are called *herbicides* (Table 17.4a–d). These

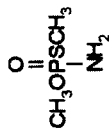
*<http://www.pesticides.gov.uk/>

[†]<http://www.fao.org/ag/agp/agpp/pesticide/Code/References.htm>

TABLE 17.3a Insecticides for Sucking Pests

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Acephate (Organophosphorous)	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{S-P-NHCOCH}_3 \\ \\ \text{OCH}_4 \end{array}$	Cholinesterase inhibitor	Systemic insecticide	<p><i>Animals.</i> Metabolized to methamidophos (q.v.). Plant Residual activity lasts for c. 10–15 days. The major metabolite is methamidophos (q.v.).</p> <p><i>Soil.</i> Readily biodegraded and non-persistent; soil DT₅₀ 2 days (aerobic) to 7 days (anaerobic). Methamidophos (q.v.) has been identified as a soil metabolite</p>
Imidacloprid (Neonicotinoid)		Acts as an antagonist by binding to post-synaptic nicotinic receptors in the insects' central nervous system	Systemic insecticide with translaminar activity and with contact and stomach action. Readily taken up by plant and further distributed acropetally, with good root-systemic action	<p><i>Animals.</i> The radioactivity was quickly and almost completely absorbed from the gastrointestinal tract and quickly eliminated (96% within 48 hr, mainly via the urine). Only c. 15% was eliminated as unchanged parent compound; the most important metabolic steps were hydroxylation at the imidazolidine ring, hydrolysis to 6-chloronicotinic acid, loss of the nitro group with formation of the guanidine and conjugation of the 6-chloronicotinic acid with glycine. All metabolites found in the edible organs and tissues of farm animals contained the 6-chloronicotinic acid moiety</p> <p><i>Plants.</i> Metabolized by loss of the nitro group hydroxylation at the imidazolidine ring, hydrolysis to 6-chloronicotinic acid and formation of conjugates; all metabolites contained the 6-chloropyridinylmethylene moiety</p> <p><i>Soil.</i> The most important metabolic steps were oxidation at the imidazolidine ring, reduction or loss of the nitro group, hydrolysis to 6-chloronicotinic acid and mineralisation. Medium adsorption to soil, imidacloprid and soil metabolites are to be classified as immobile</p>

Methamidophos
(Organophosphorous)



Cholinesterase
inhibitor

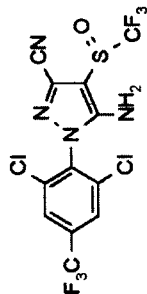
Systemic insecticide with
contact and stomach
action

Animals. Absorbed rapidly and distributed uniformly among all organs and tissues. More than half of the radioactivity was rapidly eliminated from the body, mainly via urine and respiratory air. Radioactivity remaining in the animal was incorporated into endogenous compounds (carbon-1 pool) and eliminated with the natural turnover of these compounds. Metabolism in the rat was by deamination and demethylation.

Plants. Taken up rapidly and translocated into the leaves

Soil. Rapidly degraded in soil; field DT₅₀ c. <2 days

Fipronil
(Phenyl pyrazole)



Acts as a potent
blocker of the
GABA-regulated
chloride channel

Broad spectrum
insecticide, toxic by
contact and ingestion.
Moderately systemic.
Good to excellent
residual control following
foliar application

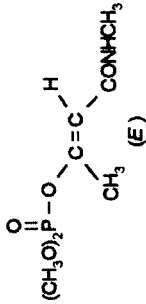
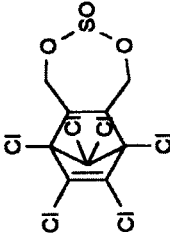
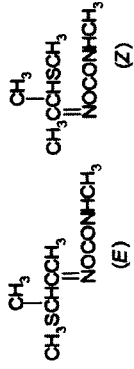

In plants, animals and the environment, fipronil is metabolized via reduction to the sulfide, oxidation to the sulfone, and hydrolysis to the amide
Animals. Distribution is rapid. Elimination is mainly via the feces as fipronil and its sulfone. The two major urinary metabolites were identified as conjugates of ring-opened pyrazole products. The distribution of radioactive residues in tissues was extensive after 7 days

Plants. Uptake of fipronil into plants was low (c. 5%). At crop maturity, the major residue components were fipronil, the sulfone, and the amide. Following foliar application to cotton, cabbage, rice and potatoes, at crop maturity, fipronil and the photodegradate were the major residue components

Soil. Readily degraded: major degradates in soil (aerobic) are sulfone and amide, (anaerobic) are sulfide and amide. Present a low risk of downward movement in soil

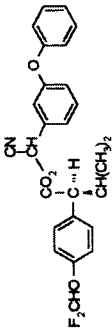
(continued)

TABLE 17.3a Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Monocrotophos (Organophosphorous)		Cholinesterase inhibitor	Systemic insecticide with contact and stomach action	<i>Animals.</i> In mammals, following oral administration, 60–65% is excreted within 24 hr, predominantly in the urine <i>Soil.</i> Rapidly degraded in soil; DT ₅₀ (lab.) 1–5 days
Endosulfan (Cyclodiene organochlorine)		Antagonist of the GABA receptor-chloride channel complex	Nonsystemic insecticide with contact and stomach action	<i>Animals.</i> The principal route of elimination is feces; most of the radioactivity is excreted within the first 48 hr. Metabolized rapidly to less-toxic metabolites and to polar conjugates. <i>Plants.</i> The plant metabolites (mainly endosulfan sulfate) were also found in animals 50% of residues are lost in 3–7 days (depending on plant species) <i>Soil.</i> DT ₅₀ 30–70 days. The main metabolite was endosulfan sulfate, which is degraded more slowly. DT ₅₀ for total endosulfan (alpha- and beta-endosulfan and endosulfan sulfate) in the field is 5–8 months. No leaching tendency
Butocarbexim (Oxime carbamate)		Cholinesterase inhibitor	Systemic insecticide with contact and stomach action	<i>Animals.</i> Metabolized to butoxycarbexim, and excreted in the urine as butoxycarbexim and its degradation products <i>Plants/Soil.</i> The methylamine moiety is split off, and the sulfur atom is oxidized to sulfoxide and sulfone. DT ₅₀ in soil 1–8 days DT ₅₀ for metabolites 16–44 days
Disulfoton (Organophosphorous)		Cholinesterase inhibitor	Systemic insecticide, absorbed by roots, with translocation to all parts of the plant	<i>Animals.</i> ¹⁴ C-disulfoton is rapidly absorbed, metabolized, and the radioactivity excreted in the urine. The main metabolites are disulfoton sulfoxide and sulfone, their corresponding oxygen analogues and diethylthiophosphate

Plants. Very rapidly metabolized. The metabolism is the same as in animals
Soil. Very rapidly degraded. The metabolism is similar to that in animals and plants. It exhibits medium to low mobility in soil

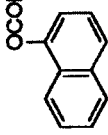
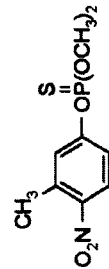
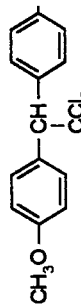
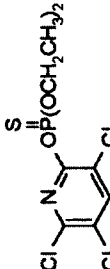
Flucythrinate
(Pyrethroid)



Nonsystemic insecticide with contact and stomach action

Animals. 60–70% is eliminated within 24 hr, and >95% within 8 days, in the feces and urine. In the facets, the parent compound makes up most of the material excreted, but in the urine and in tissue, several metabolites are present. The major route of degradation is through hydrolysis, with subsequent hydroxylation of the hydrolysis products
Soil. Immobile DT₅₀ c. 2 months

TABLE 17.3b Insecticides for Chewing Pests

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Carbaryl (Carbamate)		Weak cholinesterase inhibitor	Insecticide with contact and stomach action and slight systemic properties	<i>Animals.</i> Does not accumulate in body tissues, but is rapidly metabolized to nontoxic substances, particularly 1-naphthol. This, together with the glucuronic acid conjugate, is eliminated predominantly in the urine and feces <i>Plants.</i> Metabolites are 4-hydroxycarbaryl, 5-hydroxycarbaryl and methylol-carbaryl <i>Soil.</i> DT ₅₀ (aerobic) 7–14 days in a sandy loam and 14–28 days in a clay loam
Fenitrothion (organophosphorous)		Cholinesterase inhibitor	Nonsystemic insecticide with contact and stomach action	<i>Animals.</i> Rapidly excreted in the urine and feces. After 3 days c. 90% has been excreted by rats, mice and rabbits. The most important metabolites are dimethylfenitrooxon and 3-methyl-4-nitrophenol <i>Plants.</i> DT ₅₀ 4 days; 70–85% is degraded within 2 weeks. Major metabolites are 3-methyl-4-nitrophenol, the oxygen analogue and their decomposition products desmethylfenitrothion, dimethylphosphorothionic acid and phosphorothionic acid <i>Soil.</i> DT ₅₀ 12–28 days under upland conditions, 4–20 days under submerged conditions. The major metabolites under upland conditions are 3-methyl-4-nitrophenol and CO ₂ , whereas, under submerged conditions, the major decomposition product is aminofenitrothion
Methoxychlor (Organochlorine)			Insecticide with contact and stomach action	<i>Animals.</i> Degradation in animals is principally by O-dealkylation to the corresponding phenol and diphenol, and by dehydrochlorination to 4,4'-dihydroxybenzophenone
Chlorpyrifos (Organophosphorous)		Cholinesterase inhibitor	Nonsystemic insecticide with contact, stomach and respiratory action	<i>Animals.</i> Rapid metabolism occurs, the principal metabolite being 3,5,6-trichloropyridin-2-ol. Excretion is principally in the urine <i>Plants.</i> Residues are metabolized to 3,5,6-trichloropyridin-2-ol which is conjugated and sequestered <i>Soil.</i> Field DT ₅₀ for soil-incorporated applications 33–56 days for soil-surface applications 7–15 days. Primary route of degradation is transformation to 3,5,6-trichloropyridin-2-ol, which is subsequently degraded to organochlorine compounds and CO ₂

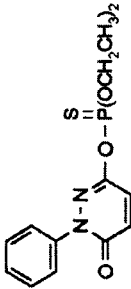
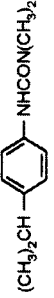
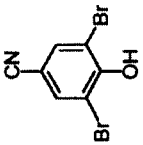
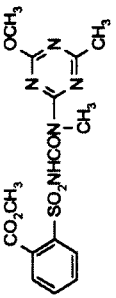
Oxamyl (Oxime carbamate)	$(\text{CH}_3)_2\text{NCO} \overset{\text{S}}{\underset{\text{SCH}_3}{\text{C}}} = \text{NCO} \text{NHCH}_3$	Cholinesterase inhibitor	Contact and systemic insecticide, absorbed by foliage and roots	<p><i>Animals.</i> Hydrolyzed to an oximino metabolite (methyl <i>N</i>-hydroxy-<i>N',N'</i>-dimethyl-1-thiooxamimidate) or converted enzymically via <i>N,N</i>-dimethyl-1-cyanoformamide to <i>N,N</i>-dimethylloxamic acid. Conjugates of the oximino compound, the acid, and their monomethyl derivatives constituted over 70% of the metabolites excreted in the urine and feces</p> <p><i>Plants.</i> Hydrolyzes to the corresponding oximino compound which, in turn, conjugates with glucose. Total breakdown into natural products has been demonstrated</p> <p><i>Soil.</i> Degraded rapidly in soil, DT₅₀ c. 7 days</p>
Pyridaphenthion (Organophosphorous)		Cholinesterase inhibitor	Insecticide with contact and stomach action	<p><i>Animals.</i> In mice and rats, the parent compound, <i>O</i>-ethyl-<i>O</i>-(3-oxo-2-phenyl-2<i>H</i>-pyridazine-6-yl) phosphorothioate and the corresponding phosphate are found</p> <p><i>Plants.</i> In rice, phenyl maleich ydrazide, <i>O,O</i>-diethyl thiophosphoric acid, and PMH glycoside are formed</p> <p><i>Soil.</i> DT₅₀ 11-24 days</p>

TABLE 17.4a Cerebral Herbicides

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Activity</i>	<i>Environmental Fate</i>
Isoproturon (Urea)	$(CH_3)_2CH-\text{C}_6\text{H}_4-\text{NHCON}(CH_3)_2$ 	Photosynthetic electron transport inhibitor at the photosystem II receptor site	Selective systemic herbicide, absorbed by roots and leaves, with translocation	Graminicide and broadleaf weeds controller	<i>Animals.</i> 50% is eliminated within 8 hr, predominantly in urine <i>Plants.</i> Degradation mainly via hydroxylation of the isopropyl group to 1,1-dimethyl-3-[4(2'-hydroxy-2'-propyl)phenyl] urea; <i>N</i> -dealkylation also occurs <i>Soil.</i> Undergoes enzymic and microbial demethylation at the nitrogen, and hydrolysis of the phenylurea to 4-isopropylamine DT ₅₀ 6–28 days
Bromoxynil (Hydroxybenzoni- trile)		Photosynthetic electron transport inhibitor at the photosystem II receptor site, also uncouples oxidative phosphorylation	Selective contact herbicide with some systemic activity. Absorbed by foliage with limited translocation	Broadleaf weed controller	<i>Animals/plants.</i> Metabolism by hydrolysis of the ester and nitrile groups with some debromination occurring <i>Soil.</i> DT ₅₀ c. 10 days. Degraded by hydrolysis and debromination to less toxic substances such as hydrobenzoic acid
Tribenuronmethyl (Sulfonyl urea)		Branched chain amino acid synthesis (ALS and AHAS) inhibitor. Acts by inhibiting biosynthesis of the essential amino acids valine and isoleucine, hence stopping cell division and plant growth	Rapidly absorbed by foliage and roots and translocated throughout the plant	Broad leaf weed controller	<i>Soil.</i> Degrades by hydrolysis and direct microbial degradation. Hydrolysis is faster in acidic than alkaline soils. DT ₅₀ 1–7 days

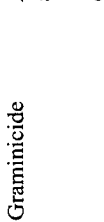


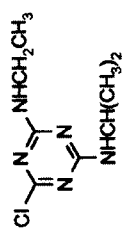
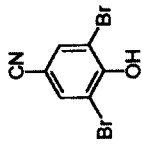
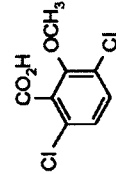
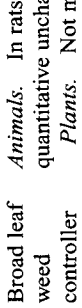
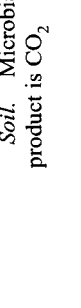

<p>Clodinafopropargyl [(2-(4-aryloxyphenoxy)propionic acid)]</p>		<p>Fatty acid synthesis inhibitor, by inhibition of acetyl CoA carboxylase (Assase)</p>	<p>Post-emergence, systemic herbicide</p>	<p>Graminicide</p>	<p><i>Animals.</i> Hydrolyzed to the corresponding acid <i>Plants.</i> Rapidly degraded to the acid derivative as major metabolite <i>Soil.</i> Undergoes rapid degradation to the free acid (DT₅₀ < 2 hr) and then further to phenyl and pyridine moieties which are bound to the soil and mineralized. The free acid is mobile in soil, but is further degraded with DT₅₀ 5–20 days; negligible leaching potential</p>
<p>Carfentrazoneethyl (Triazolinone)</p>		<p>Protoporphyrinogen oxidase inhibitor leading to membrane disruption</p>	<p>Absorbed by foliage with limited translocation</p>	<p>Broad leaf weed controller</p>	<p><i>Animals.</i> About 80% excreted in urine within 24 hr. Major metabolite is corresponding acid. Further metabolism appears to involve oxidative hydroxylation of the methyl group or dehydrochlorination to form corresponding Cinnamic acid <i>Plants.</i> Converted to free acid, which is hydroxylated and oxidized at triazolinone methyl to form the dibasic acid. DT₅₀ < 7 days <i>Soil.</i> Degradation by microbial action. Strongly adsorbed to sterile soils. In nonsterile soils, rapidly converted to free acid, which has low soil binding. In laboratory soil DT₅₀ is a few hours</p>
<p>Flufenacet (Oxyacetamide)</p>		<p>Inhibits cell division and growth. Primary target site may be fatty acid metabolism</p>	<p>Pre and early post-emergence herbicide</p>	<p>Broad spectrum herbicide controlling grasses and broad leaved weeds</p>	<p><i>Animals.</i> Rapidly excreted by rat, goat, and hen. Metabolism via cleavage of the molecule followed by conjugation of fluorephenyl moiety with cysteine and formation of a thiazolone and its various conjugates <i>Plants.</i> Rapidly metabolized, residues accounted based on total amount of <i>N</i>-fluorephenyl-<i>N</i>-isopropyl derived residues <i>Soil.</i> Rapidly degraded in soil. No threat of leaching</p>

Table 17.4b Maize Herbicides

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Atrazine (1,3,5-triazine)		Photosynthetic electron transport inhibitor at the photosystem II receptor site	Selective systemic herbicide, absorbed principally through roots, but also through foliage, with translocation acropetally in the xylem and accumulation in the apical meristems and leaves	Cross spectrum weed controller	<i>Animals.</i> Rapidly and completely metabolized, primarily by oxidative dealkylation of the amino groups and by reaction of chlorine atom with endogenous thiols. Diaminochlorotriazine is the main primary metabolite, which readily conjugates with glutathione. More than 50% of the dose is eliminated in the urine and around 33% in feces within 24 hr <i>Plants.</i> In tolerant plants, readily metabolized to hydroxyatrazine and amino acid conjugates, with further decomposition of hydroxyatrazine by degradation of side-chains and hydrolysis of resulting amino acids on the ring together with evolution of CO ₂ <i>Soil.</i> Major metabolites are desethylatrazine and hydroxyatrazine; DT ₅₀ 16–77 days
Bromoxynil (Hydroxybenzotriazole)		Photosynthetic electron transport inhibitor at the photosystem II receptor site, also uncouples oxidative phosphorylation	Selective contact herbicide with some systemic activity. Absorbed by foliage with limited translocation	Broadleaf weed controller	<i>Animals/plants.</i> Metabolism by hydrolysis of the ester and nitrile groups with some debromination occurring <i>Soil.</i> DT ₅₀ c. 10 days: Degraded by hydrolysis and debromination to less toxic substance such as hydrobenzoic acid
Dicamba (Benzoic acid)		Synthetic auxin (acting like indolylacetic acid)	Selective systemic herbicide, absorbed by the leaves and roots, with ready translocation throughout the plant via both symplastic and apoplastic systems	Broadleaf weed controller	<i>Animals.</i> Rapidly eliminated in the urine, partly as a glycine conjugate <i>Plants.</i> Degradation rate varies greatly with species. In wheat, the major metabolite is 5-hydroxy-2-methoxy-3,6-dichlorobenzoic acid, while 3,6-dichlorosalicylic acid is also a metabolite <i>Soil.</i> Microbial degradation occurs, the principal metabolite being 3,6-dichlorosalicylic acid. DT ₅₀ <14 days

<p>Clopyralid (Pyridinecarboxylic acid)</p>		<p>Synthetic auxin (acting like indanyl acetic acid)</p>	<p>Selective systemic herbicide, absorbed by roots and leaves with translocation both acropetally and basipetally and accumulation in meristematic tissue</p>	<p>Broad leaf weed controller</p>	<p><i>Animals.</i> In rats, there is rapid and almost quantitative unchanged elimination in urine <i>Plants.</i> Not metabolized in plants <i>Soil.</i> Microbial degradation occurs. Major product is CO₂</p>
<p>Metolachlor (Chloroacetamide)</p>		<p>Cell division inhibitor</p>	<p>Selective herbicide, absorbed predominantly by the hypocotyls and shoots. Inhibits germination</p>	<p>Grass weed controller</p>	<p><i>Animals.</i> Rapidly oxidized by rat liver microsomal oxygenases via dechlorination, O-demethylation and side-chain oxidation <i>Plants.</i> Metabolism involves natural product conjugation of the chloroacetyl group and hydrolysis and sugar conjugation at the ether group. Final metabolites are polar, water-soluble, and nonvolatile <i>Soil.</i> Major aerobic metabolites are derivatives of oxamic and sulfonic acids. DT₅₀ = 20 days</p>
<p>Nicosulfuron (Sulfonylurea)</p>		<p>Branched chain amino-acid (ALS) and (AHAS) synthesis inhibitor. Acts by inhibiting biosynthesis of essential amino acids valine and isoleucine, hence stopping cell division and plant growth</p>	<p>Selective systemic herbicide, absorbed by roots and leaves with rapid translocation in xylem and phloem to the meristematic tissues</p>	<p>Graminicide and broadleaf weed controller</p>	<p><i>Animals.</i> Nicosulfuron and its metabolites do not bioaccumulate. Hydrolysis of the sulfonylurea bridge and hydroxylation were the main metabolic pathways <i>Plants.</i> Degraded rapidly. DT₅₀ 1.5-4.5 days main metabolic pathways were hydrolysis of the sulfonyl urea bridge to form the pyridine sulfonamide and pyrimidine amine, and hydroxylation on the pyrimidine ring <i>Soil.</i> DT₅₀ 24-43 days</p>

(continued)

Table 17.4b Continued

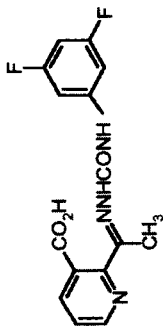
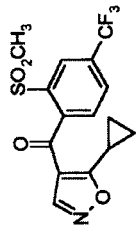
Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Diflufenzopyr (Semi-carbazone)		Inhibits auxin transport, apparently by binding with a carrier protein on the plasmalemma	Systemic, post-emergence herbicide	Graminicide and broad leaf weed controller	<i>Animals.</i> 20–44% of oral dose eliminated in urine and 49–79% in feces. Intravenous administration showed excretion of 61–89% in urine. Elimination DT ₅₀ in urine and feces was about 6 hr. Eliminated mainly as the parent compound <i>Soil.</i> Average DT ₅₀ in field: 4.5 days very mobile
Isoxaflutole (Isoxazale)		<i>p</i> -hydroxyphenyl pyruvate dioxygenase inhibitor	Systemic by either root or foliar uptake	Graminicide and broadleaf weed controller	<i>Animals.</i> Rapidly excreted <i>Plants.</i> Residues at harvest comprise mainly of a nontoxic metabolite <i>Soil.</i> Degradation via hydrolysis and microbial degradation with final mineralization to CO ₂ . Mobile under simulated conditions. However, under field conditions, residues remain in the surface horizons

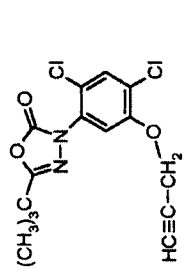
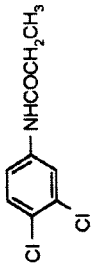
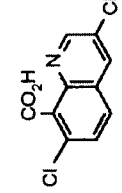
TABLE 17.4c Rice Herbicide

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Imazosulfuron (Sulfonylurea)		Branched chain amino acid synthesis (ALS and AHAS) inhibitor. Acts by inhibiting biosynthesis of the essential amino acids valine and isoleucine, hence stopping cell division and plant growth.	Absorbed by plants mainly through roots and translocated throughout the plant. Inhibits shoot growth and restarts root development	Broad leaf weed and sedge controller	Unknown
Anilofos (Organophosphorous)		Inhibits cell division	Selective herbicide, absorbed through roots and to some extent, through leaves	Grass weed and sedge controller	<i>Soil.</i> Metabolizes into Chloroaniline and CO ₂ DT ₅₀ :30-45 days
Azimsulfuron (Sulfonylurea)		Branched chain amino acid synthesis (ALC or AHAS) inhibitor. Acts by inhibiting biosynthesis of essential amino acids valine and isoleucine, hence stopping cell division and plant growth	Post-emergence herbicide with mainly foliar uptake, translocated in xylem and phloem	Broad leaf weed and sedge controller and control of <i>Echinochloa</i> spp.	<i>Animals.</i> >95% was extracted within 2 days 6-73% in unmetabolized form. The major metabolic pathway was O-demethylation followed by pyrimidine ring hydroxylation and subsequent O-conjugation, a pyrimidine ring-cleaved guanidine was also identified <i>Plants.</i> Metabolism was rapid; little parent compound was found in any plant tissue at maturity <i>Soil.</i> The most significant mechanisms are indirect photolysis and soil metabolism, together with chemical hydrolysis

(continued)

TABLE 17.4c Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Mefenacet (Oxyacetamide)		Inhibits cell division and growth	Selective herbicide	Graminicide	<i>Animals.</i> Degrades to <i>N</i> -methylaniline which is subsequently demethylated, acetylated and hydroxylated to 4-aminophenol and its sulfate and glucuronide conjugates <i>Plants.</i> Besides 4-aminophenol, benzothiazolone and benzothiazoylacetic acid are found, both of which are formed by hydroxylation <i>Soil.</i> Metabolites formed are benzothiazole and benzothiazolyl-acetic acid
Cyhalofop-butyl (Aryloxyphenoxy propionate)		Fatty acid synthesis inhibitor, by inhibition of acetyl CoA Carboxylase (ACCase)	—	Graminicide	<i>Animals.</i> Metabolized by hydrolysis to acid which may further break down to other metabolites which in turn are rapidly excreted <i>Soil.</i> Rapidly metabolized to acid. DT ₅₀ 2–10 hr in field
Oxadiazon (Oxadiazole)		Protoporphyrinogen oxidase inhibitor	Selective contact herbicide	Graminicide and broadleaf weed controller	<i>Animals.</i> 93% is eliminated within 72 hr, predominantly in the urine <i>Plants.</i> Rapidly metabolized. Metabolites do not accumulate <i>Soil.</i> Strongly adsorbed by soil colloids and humus with very little migration or leaching. DT ₅₀ c. 3–6 months

<p>Oxadiargyl (Oxadiazole)</p>		<p>Protoporphyrinogen oxidase inhibitor</p>	<p>Selective herbicide active mainly pre- emergence; effects being at germination. It is not absorbed by plants</p>	<p>Broad leaf weed and grass and annual sedge controller</p>	<p><i>Animals.</i> Rapidly excreted with no accumulation <i>Plants.</i> Very low levels of residues at harvest in lemons, sunflowers and rice <i>Soil.</i> DT₅₀ (lab, aerobic) 18-72 days</p>
<p>Propanil (Anilide)</p>		<p>Photosynthetic electron transport inhibitor at the photosystem II receptor site</p>	<p>Selective contact herbicide with a short duration of activity</p>	<p>Broadleaf weed and grass controller</p>	<p><i>Animals.</i> The major metabolic pathway in microsomal incubations was acylamidase hydrolysis to 3,4- dichloroaniline <i>Plants.</i> Hydrolyzed by an aryl acylamidase to 3,4-dichloroaniline and propionic acid as metabolic intermediates <i>Soil.</i> Rapid microbial degradation to aniline derivative occurs. Degradation products are proportionate which is rapidly metabolized to CO₂ and 3,4- dichloroaniline which is bound to soil</p>
<p>Quinclorac (quinoline- carboxylic acid)</p>		<p>Synthetic auxin (acting like indolyacetic acid), also inhibitor of cell wall (cellulose) biosynthesis</p>	<p>Rapidly absorbed through the foliage</p>	<p>Graminicide</p>	<p><i>Animals.</i> More than 90% excreted in the urine within 5 days <i>Plants.</i> Systematically translocated to the roots and to the leaves <i>Soil.</i> Only slightly adsorbed by the soil. Depending on soil type and organic matter content, the chemical is relatively mobile. Degraded by micro- organisms, 3-chloro-8-quinolinecarboxylic acid being the major metabolite</p>

(continued)

TABLE 17.4c Continued

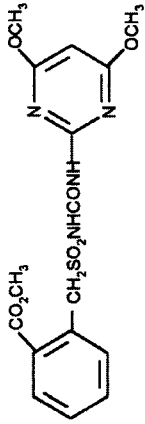
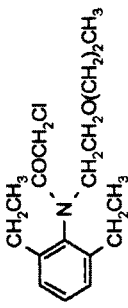

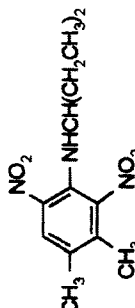
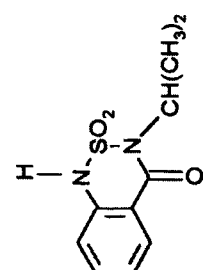
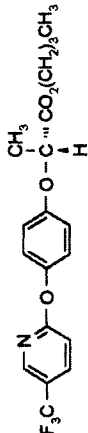
Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Bensulfuron- methyl (Sulfonylurea)		Branched chain amino acid synthesis (ALS and AHAS) inhibitor. Acts by inhibiting biosynthesis of the essential amino acids valine and isoleucine, hence stopping cell division and plant growth	Selective systemic herbicide, rapidly absorbed by root and foliage with rapid translocation to meristematic tissue	Broad leaf weed and sedge controller	<i>Animals.</i> Almost completely biotransformed and rapidly excreted in urine and feces <i>Plants.</i> After uptake by rice, converted to a nonherbicidal metabolite <i>Soil.</i> DT ₅₀ 4–20 weeks on Planagan and Keyport silt loam soils. In rice fields, DT ₅₀ in water averages 4–6 days
Pretlachlor (Chloroacetamide)		Cell division inhibitor	Selective herbicide, readily taken up by hypocotyls, mesocotyls, and coleoptiles, and to a lesser extent by roots of germinating weeds	Broad leaf weed, grass, and sedge controller	<i>Animals.</i> Substitution of the chlorine atom for glutathione to form a conjugate. Cleavage of the ether bond to yield an ethyl alcohol derivative. Both metabolites are susceptible to further degradation <i>Plants.</i> Substitution of chlorine atom to form a conjugate. Cleavage of the ether bond to yield an ethyl alcohol derivative. Hydrolytic and reductive removal of the chlorine atom <i>Soil.</i> Applied to paddy water, disappeared from the water by adsorption to the soil, where it is rapidly degraded under practical conditions, median DT ₅₀ (lab) 30 days. Due to strong soil adsorption, unlikely to leach

TABLE 17.4d Soyabean Herbicides

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Glyphosate (Glycine derivative)	$\text{HO}_2\text{CCH}_2\text{NHCH}_2\text{P}(\text{OH})_2$ 	Inhibits 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS), an enzyme of the aromatic acid and biosynthesis pathway. This prevents synthesis of essential aromatic amino acids needed for protein biosynthesis	Systemic herbicide, absorbed by rapid translocation throughout the plant	Non-selective herbicide	<p><i>Animals.</i> In mammals, following oral administration, glyphosate is very rapidly excreted unchanged and does not bioaccumulate</p> <p><i>Plants.</i> Slowly metabolized to aminomethylphosphonic acid (1/066-51-9)], which is the major plant metabolite</p> <p><i>Soil/environment.</i> In soil (field), DT₅₀ 3-174 days, depending on edaphic and climatic conditions. In water, DT₅₀ varies from a few to 91 days. Photodegradation in water occurs under natural conditions, DT₅₀ ca 28 days; no substantial photodegradation in soil was recorded over 31 days. In a lab. whole system with water and sediment, DT₅₀ ca 14 days (aerobic), 14-22 days (anaerobic). The major metabolite in soil and water is aminomethylphosphonic acid</p>
Pendimethalin (Dinitro-aniline)		Microtubule assembly inhibitor	Selective herbicide absorbed by roots and leaves	Graminicide and broad-leaf weed controller	—
Bentazone (Benzothiadiazinone)		Photosynthetic electron transport inhibitor at photosystem II receptor site	Selective, contact herbicide, absorbed by leaves with very little translocation, but also absorbed by roots, with translocation acropetally in the xylem	Broad leaf weed controller	<p><i>Animals.</i> In rats, the major metabolic routes for pendimethalin involve hydroxylation of the 4-methyl and N-1-ethyl groups, oxidation of these alkyl groups to carboxylic acids, nitro-reduction, cyclisation and conjugation (J. Zulian, <i>J. Agric. Food Chem.</i>, 1990, 38, 1743)</p>

(continued)

TABLE 17.4d Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Activity	Environmental Fate
Fluazifop- <i>P</i> -butyl (Aryloxypropenoxypropionate)		Fatty acid synthesis inhibitor, by inhibition of acetyl CoA carboxylase (ACCase)	Quickly absorbed through the leaf surface, hydrolyzed to fluazifop- <i>P</i> - and located through the phloem and xylem, accumulating in the rhizomes and stolons of perennial grasses and meristems of annual and perennial grasses	Graminicide	<p><i>Plants.</i> In plants, the 4-methyl group on the benzene ring is oxidized to the carboxylic acid via the alcohol. The amino nitrogen is also oxidized. At harvest time, residues in crops are below the validated sensitivity of the analytical method (0.05 ppm)</p> <p><i>Soil/environment.</i> In soil, the 4-methyl group on the benzene ring is oxidized to the carboxylic acid via the alcohol; the amino nitrogen is also oxidized. DT₅₀ in soil is 3–4 months (A. Walker & W. Bond, <i>Pestic. Sci.</i>, 1977, 8, 359). Kd ranges from 2.23 (0.01% o.m., pH 6.6) to 1638 (16.9% o.m., pH 6.8) (H. J. Pedersen et al., <i>Pestic. Sci.</i>, 1995, 44, 131)</p> <p><i>Animals.</i> In mammals, fluazifop-<i>P</i>-butyl is metabolized to fluazifop-<i>P</i>, which is rapidly excreted</p> <p><i>Plants.</i> In plants, fluazifop-<i>P</i>-butyl is rapidly hydrolyzed to fluazifop-<i>P</i>, which is then partly conjugated. Ether cleavage gives the pyridone and propionic acid metabolites, which may both be further metabolized or conjugated</p> <p><i>Soil/Environment.</i> c. 5800. In moist soils, rapid degradation of fluazifop-<i>P</i>-butyl occurs, DT₅₀ <24 hr. The major degradation product is fluazifop-<i>P</i>, which is hydrolyzed to 5-trifluoromethylpyrid-2-one, and 2-(4-hydroxyphenoxy)propionic acid, both of which are further degraded, ultimately to CO₂</p>

Soil/environment. In laboratory soil (40% MHC, pH 5.3-7.7), DT₅₀ 2-9 days (20°C). Field DT₅₀ <4 week. Koc 39-84. For degradation route, see fluzafifop-*P*-butyl

Animals. In rats, following oral administration, 92% was excreted in the urine and 5% in the feces within 24 hours. Residue levels in blood, liver, kidney, muscle, and fat tissues were <0.01 ppm after 48 hr

Plants. Rapidly metabolized in non susceptible plants; half-life in soya beans 1.6 days. The primary metabolic route in maize is oxidative hydroxylation at the carbon atom of the ethyl substituent on the pyridine ring

Soil/environment. Half-life in soil 1-3 months

Animals. In rats, nearly all of administered sulfentrazone is excreted in the urine within 72 hr

Plants. In soya beans, over 95% of the parent sulfentrazone is metabolized to the nonpolar, ring-hydroxymethyl analogue within 12 hr. This analogue is also rapidly converted, over the same time period, to three polar metabolites, two of which are glycosidic derivatives and one a nonglycoside metabolite

Soil/environment. Stable in soil (DT₅₀ 18 months). In water, stable to hydrolysis (pH 5-9), but readily undergoes photolysis (DT₅₀ <0.5 days). Low affinity for organic matter (Koc 43), but is mobile only in soils with high sand content. Low potential to bioaccumulate

Branched chain amino acid synthesis (ALS and AHAS) inhibitor reducing levels of valine, leucine, isoleucine leading to disruption of protein and DNA synthesis

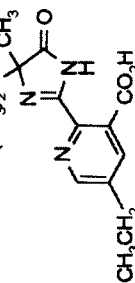
Systemic herbicide absorbed by roots and foliage with translocation in xylem and phloem and accumulation in meristematic regions

Germicide and broad leaved weed controller

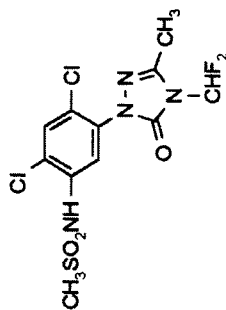
Protoporphyrinogen oxidase inhibitor (Chlorophyll biosynthesis pathway)

Herbicide absorbed by roots and foliage, with translocation primarily in the apoplasm and limited movement in phloem

Graminicide and broadleaf weed controller



Imazethapyr (Imidazo-linone)



Sulfentrazone (Triazol-inone)

interfere with chlorophyll formation and/or activity, and various other metabolic processes in the weeds at much higher efficiency than the main crop. Agrochemicals that control fungal diseases are called *fungicides* (Table 17.5a,b), and those with plant hormonelike action are called *plant growth regulators* (Table 17.6). Agencies such as WHO (World Health Organization) and the US EPA separate agrochemicals into different classes as per agreed upon toxicity levels, as a useful guide to consumers. In many countries, field usage of more toxic agrochemicals is restricted to trained personnel only.

DELIVERY SYSTEMS OF AGROCHEMICALS

Agrochemicals are generally formulated with surface-active agents in dry forms (WP, WDG) or wet forms (EC, SC) for efficient delivery at the site of action. This might include sticking to the foliage, translaminar action in the leaves or through uptake by the root system. An efficient delivery system plays an important role in optimizing dosages per hectare of a given agrochemical in order to achieve maximum efficiency of pest control while reducing risk to personnel and livestock. Selective uses of appropriate sprayers, nozzles are other aids for the same purpose. Good farm practices during spray application and clean-up controls wasteful nontarget dissipation.

Obsolescence of Agrochemicals

Resistance to agrochemicals occurs through the natural selection. Fungi with short life cycles exhibit the most pronounced resistance development. Insects are in an intermediate category with respect to life cycle, while weeds (plants) take much longer. Resistance management is brought through rotational or combination uses of agrochemicals with differing modes of action. Sublethal dosages are strictly to be avoided, as are extreme over-applications. These measures improve the functional lifetime of a product. These practices are very pertinent since major breakthroughs with a new class of agrochemicals

usually occur only once in 25 years or so. Availability of safer, more efficacious, cost effective agrochemicals tends to render prevailing agrochemicals obsolete.

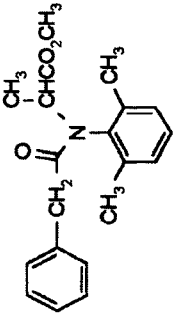
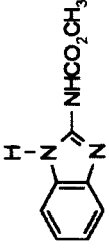
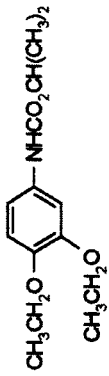
Even with all of the advances to date, it would be wrong to state that all issues of plant protection are adequately addressed. There are still issues defying solutions, and these will continue to attract R&D efforts. As higher and higher farm productivities are achieved, coupled with more judicious distribution of food, the growing global population should enjoy higher levels of nutrition. Agrochemicals will continue to play an important role in health care, protection of farm produce, production of medicinal plants of value, and offer recyclable feedstock to produce chemicals currently derived solely from diminishing petroleum feed stocks. Hence, the value of the agrochemical industry should be judged more on its multiple impacts on the improved human condition rather than its modest size.

PRODUCTS OF THE AGROCHEMICAL INDUSTRY

Many of the chemical structures of agrochemicals demonstrating similar target-(enzyme) specific biological activity can be rationalized under the term *BIOISOSTERISM*. Bioisosterism is a phenomenon where molecules possessing related structure have similar or antagonistic properties. Bioisosterism is the biological analogue of isosterism, which is the close physical similarity of molecules or ions having the same number of atoms and valence electrons, such as CO and N₂. This similarity is thought to explain certain analogies among the physical constants of molecules.

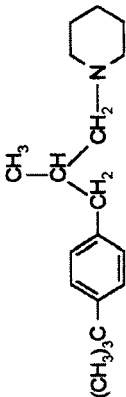
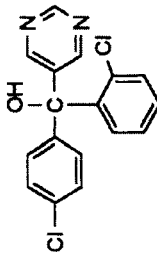
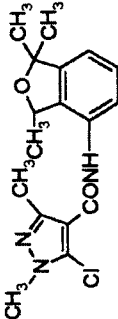
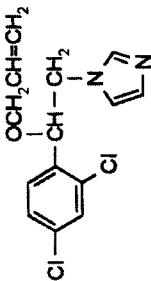
No two substituents are exactly alike. Any substitution impacts size, shape, electronic distribution, lipophilicity, pKa, chemical reactivity, susceptibility to metabolism, and the like. The bioisosteric approach is the total change induced by substituent replacement on the potency, selectivity, duration of action, bioavailability and toxicity, of an agrochemical. The following groups are examples of

TABLE 17.5a Systemic Fungicides

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Benalaxyl (Acylalanine)		Nucleic RNA-polymerase inhibitor	Systemic fungicide absorbed by roots, stems, leaves with translocation acropetally to all parts of the plant including subsequent growth	<i>Animals.</i> Rapidly metabolized, and eliminated in the urine (23%) and feces (75%) within 2 days <i>Plants.</i> Slowly metabolized to glycosides in soil <i>Soil.</i> Slowly degraded by soil microorganisms to various acidic metabolites. DT ₅₀ in silt loam soil 77 days
Carbendazim (Benzimidazole)		Inhibits beta-tubulin synthesis	Systemic fungicide, absorbed through roots and green tissues, with translocation acropetally. Acts by inhibiting development of the germ tubes, the formation of appressoria and the growth of mycelia	<i>Animals.</i> 66% was eliminated in the urine within 6 hr <i>Plants.</i> Readily absorbed by plants. One degradation product is 2-aminobenzimidazole <i>Soil.</i> 2-Aminobenzimidazole has been found as a minor metabolite. DT ₅₀ in soil 8-32 days under outdoor conditions. Mainly decomposed by microorganisms
Diethofencarb (N-phenyl carbamate)			Systemic fungicide, readily absorbed through leaves and roots and translocated throughout the plant	<i>Animals.</i> 98.5-100% of ¹⁴ C was excreted within 7 days. The major metabolic routes were deethylation of the 4-ethoxy group, cleavage of the carbamate linkage, acetylation, and finally formation of the glucuronide and sulfate conjugates <i>Plants.</i> Readily degraded in plants <i>Soil.</i> Readily degraded in soil; DT ₅₀ <1-6 days under aerobic conditions; only very slightly degraded under anaerobic sterilized conditions

(continued)

TABLE 17.5a Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Fenpropidin (Piperidine)		Ergosterol biosynthesis inhibitor, by inhibition of steroid reduction (sterol— Δ^{14} —reductase) and isomerisation (Δ^8 to Δ^7 —isomerase)	Systemic foliar fungicide with translocation acropetally in the xylem	<i>Animals.</i> Rapidly absorbed, distributed, metabolised and excreted in the urine and feces. No bioretention potential. <i>Plants.</i> Relatively rapid and extensive degradation. Principal metabolic pathway involves hydroxylation of the piperidine ring and oxidation of the tertiary butyl group. DT ₅₀ in wheat and barley plants c. 4–11 days <i>Soil.</i> Strongly adsorbed and extensively degraded, DT ₅₀ 58 (loam)—95 (sandy loam). Fenpropidin and its metabolites have little or no tendency to leach
Fenarimol (Pyrimidine)		Ergosterol biosynthesis inhibitor	Systemic fungicide, translocated acropetally within the plant	<i>Animals.</i> Rapidly excreted <i>Plants.</i> Forms numerous photodegradation products. <i>Soil.</i> DT ₅₀ 14–130 (average 79) days
Furametpyr (Oxathiin)		Inhibitor of mitochondrial succinate oxidation	Fungicide with systemic and translaminar action	—
Imazailil (Imidazole)		Steroid demethylation inhibitor	Systemic fungicide	<i>Animals.</i> 90% is eliminated in the metabolized form within 4 days <i>Plants.</i> Transformed into (-2,4-dichlorophenyl)-1 <i>H</i> -imidazole-1-ethanol <i>Soil.</i> DT ₅₀ (field) 4–5 d; DT ₉₀ (field) 54–68 days

Metaxyl-M
(Phenylamide:
acylaniline)

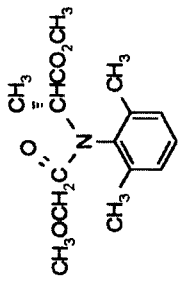
Inhibits protein
synthesis in fungi, by
interference with the
synthesis of ribosomal
RNA

Systemic fungicide,
absorbed through leaves,
stems and roots

Animals. Rapidly absorbed and also rapidly and almost completely eliminated in urine and feces. Metabolism proceeds via hydrolysis of the ester bond, oxidation of the 2-(6)-methyl group and of the phenyl ring and *N*-dealkylation. Residues in tissues were generally low and there was no evidence for accumulation or retention of metalaxyl-M or its metabolites

Plants. Metabolized by more than four types of phase I reaction (oxidation of the phenyl ring, oxidation of the methyl group, cleavage of the methyl ester and *N*-dealkylation) to form eight metabolites; at phase II, most of the metabolites are sugar conjugated

Soil. DT₅₀ in soil 21 days (realistic range 5–30 days).



Propiconazole
(Triazole)

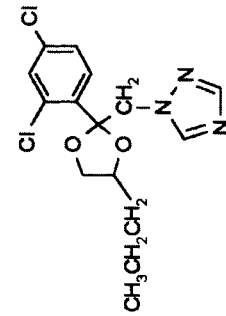
Steroid demethylation
inhibitor

Systemic foliar fungicide,
translocated
acropetally in the xylem

Animals. Rapidly absorbed and also rapidly and almost completely eliminated with urine and feces. Residues in tissues were generally low and there was no evidence for accumulation or retention of propiconazole or its metabolites. The major sites of enzymic attack are the propyl side-chain and the cleavage of the dioxolane ring, together with some attack at the 2,4-dichlorophenyl and 1,2,4-triazole rings

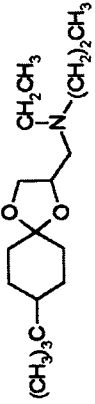
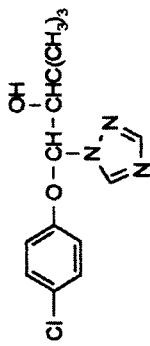
Plants. Degradation through hydroxylation of the *n*-propyl side-chain and deketalisation of the dioxolane ring. After cleavage of triazole, triazolealanine is formed as the main metabolite. Metabolites are conjugated mostly as glucosides

Soil. DT₅₀ in aerobic soils (25°C) 40–70 days. The main degradation pathways are hydroxylation of the propyl side-chain and the dioxolane ring, and finally formation of 1,2,4-triazole. Immobile in soil



(continued)

TABLE 17.5a Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Spiroxamine (Spiroketalamine)		Sterol biosynthesis inhibitor acting mainly by inhibition of Δ^{14} -reductase	Systemic fungicide, which readily penetrates into the leaf tissue followed by acropetal translocation to the leaf tip	<i>Animals.</i> Highly absorbed followed by fast elimination from the body (>97% within 48 hr). The radioactivity was readily distributed from the plasma into peripheral compartments. The main metabolite was the compound oxidized to the carboxylic acid in the <i>t</i> -butyl moiety. Metabolism proceeds either via oxidation of the <i>t</i> -butyl moiety to yield the carboxylic acid compound or via des-alkylation of the amino group resulting in the des-ethyl and des-propyl derivatives of spiroxamine <i>Plants.</i> Extensively metabolized by oxidation, desalkylation and cleavage of the ketal structure; the resulting metabolites bearing a hydroxylated <i>t</i> -butyl group or an aminodiol were further conjugated <i>Soil.</i> Readily degraded, ultimately to CO ₂ ; oxidation on the <i>t</i> -butyl moiety and des-alkylation of the amine are the primary reaction steps. The des-alkylated compounds were either further oxidised to the corresponding acids or further degraded to a ketone metabolite. Soil DT ₅₀ (lab. and field) in the range 35–64 days. Bound rapidly to the sediment
Triadimenol (Triazole)		Inhibits gibberellin and ergosterol biosynthesis and hence the rate of cell division	Systemic fungicide absorbed through roots and leaves with ready translocation in young growing tissues but less ready translocation in older, woody tissues	<i>Animals.</i> Metabolized mainly by oxidation of the <i>tert</i> -butyl moiety to the corresponding alcohol and then to carboxylic acid. A small fraction of these compounds was conjugated <i>Plants.</i> The most important breakdown reactions are conjugation with various sugar compounds (especially hexose) and oxidation at the <i>tert</i> -butyl moiety. The resulting primary alcohol is likewise partly conjugated

Soil. Triadimenol is a degradation product of triadimefon (*q.v.*). Degradation involving hydrolytic cleavage leads to the formation of 4-chlorophenol. DT₅₀ (sandy loam) 110–375 days; (loam) 240–270 days

Animals. 83–96% is excreted unchanged in the urine and feces within 2–3 days. However, metabolism occurs in the liver, mostly to triadimenol (*q.v.*) and its glucuronic acid conjugates. Half-life in blood plasma is c. 2.5 hr

Plants. In plants, the carbonyl group is reduced to a hydroxyl group, with the formation of triadimenol (*q.v.*)

Soil. In soil, the carbonyl group is reduced to a hydroxyl group, with the formation of triadimenol (*q.v.*). DT₅₀ of triadimefon in sandy loam c. 18 days, in loam c. 6 days

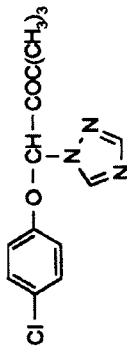
Soil. A range of nonfungitoxic metabolic end-products are formed, presumably including piperazine. DT₅₀ in soil c. 3 weeks. Does not accumulate in the environment

Systemic fungicide, absorbed by roots and leaves with ready translocation in young growing tissues but less ready translocation in older, woody tissues

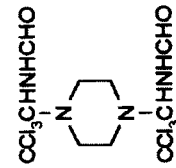
Steroid demethylation (ergosterol biosynthesis) inhibitor

Systemic fungicide, absorbed by leaves and roots with translocation acropetally

Ergosterol biosynthesis inhibitor


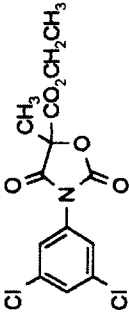
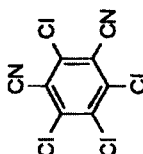


Triadimefon
(Triazole)



Triforine
(Piperazine)

TABLE 17.5b Contact Fungicides

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Bordeaux mixture (inorganic)	—	Cu ⁺⁺ is taken up by the spores during germination and accumulates until a sufficiently high concentration is achieved to kill the spore cell	Foliar fungicide	<i>Animals.</i> Copper is an essential element and is under homeostatic control in mammals
Chinomethionat (Quinoxaline)		—	Selective, non-systemic contact fungicide	<i>Animals.</i> Rapidly metabolized, and c. 90% is eliminated within 3 days in the feces and urine. The main metabolite is chinomethionat acid (dimethylmercaptoquinoxaline-6-carboxylic acid), which also occurs in the conjugated form <i>Plants.</i> No penetration of the a.i. or metabolites in the fruit pulp was observed. The only metabolite detected was dihydromethylquinoxalinedithiol <i>Soil.</i> DT ₅₀ in standard soil land 2: 1–3 days
Chlozolinate (Dicarboximide)		Inhibitor of Lipid Peroxidation in mitochondrial membranes	Contact fungicide	<i>Animals.</i> Readily absorbed, metabolized and excreted. Metabolites identified in urine are: 3-(3,5-dichlorophenyl)-5-methylloxazolidin-2,4-dione, N-(3,5-dichlorophenyl)-2-hydroxypropionamide, O-1-carboxyethyl-N-3,5-dichloro-phenyl carbamate, and N-(3,5-dichloro-2(or 4)-hydroxyphenyl)-2-hydroxypropionamide and its sulfate and glucuronide conjugates <i>Plants.</i> Undergoes hydrolysis and decarboxylation processes, giving the same metabolites as those identified in animals. <i>Soil.</i> In silt-loam, sandy loam and clay loam soils, hydrolysis and decarboxylation occur; aerobic DT ₅₀ < 7 hr
Chlorothalonil (Chloronitrile)		Conjugation with, and depletion of thiols (particularly glutathione) from germinating fungal cells, leading to disruption of glycolysis and energy production, fungistasis and fungicidal action	Nonsystemic foliar fungicide	<i>Animals.</i> Not well absorbed following oral dosing. It reacts with glutathione in the gut lumen, or immediately on absorption into the body, to give mono-, di- or tri- glutathione conjugates. These may be excreted through urine or feces, or subject to further metabolism resulting in thiol or mercapturic acid derivatives. In ruminants, the 4-hydroxy metabolite may also be present <i>Plants.</i> The majority of the residue remains as parent compound. The most abundant metabolite, 4-hydroxy-2,5,6-trichloroisophthalonitrile, is generally <10% of applied parent

Soil. Low mobility to immobile. In aerobic and anaerobic soil studies, DT₅₀ is 5–36 days. Degradation is faster in biotic aquatic systems, typical DT₅₀ (aerobic) <8 hr, (anaerobic) <10 days

Animals. Readily excreted via feces. No major metabolites, but a high number of minor metabolites were identified. The important metabolic reactions were cleavage of the oxirane ring, hydroxylation of the phenyl rings and conjugation

Plants. There is extensive degradation

Soil. Degradation is by microbial activity, DT₅₀ c. 2–3 months

Animals. Rapidly metabolized initially by cleavage of the imidazole ring and quantitatively eliminated from the body. Although absorption following dermal exposure is low, residues in plasma and tissues are rapidly eliminated from the body

Plants. The primary metabolite, *N*-formyl-*N'*-1-propyl-*N*-(2-(2,4,6-trichlorophenoxy)ethyl)urea, is formed from cleavage of the imidazole ring. This is degraded to *N*-propyl-*N*-(2-(2,4,6-trichlorophenoxy)ethyl)urea, which occurs in both free and conjugated forms. Other metabolites include 2-(2,4,6-trichlorophenoxy)ethanol, 2-(2,4,6-trichlorophenoxy)acetic acid, traces of 2,4,6-trichlorophenol and conjugates of the above. Little unchanged prochloraz is present

Soil. Degrades in the soil to a range of mainly volatile metabolites. Well adsorbed onto soil particles, and is not readily leached DT₅₀ 5–37 days

Plants. Extensively metabolized, forming ethylenethiourea, ethylenethiourea monosulfide, ethylenethiourea disulfide, and sulfur as transitory intermediates. Terminal metabolites are natural products, especially those derived from glycine

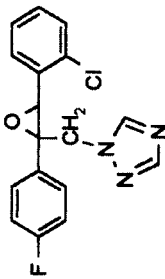
Soil. Rapidly degraded by hydrolysis, oxidation, photolysis, and metabolism. DT₅₀ in soil c. 6–15 days

Plants. Degradation proceeds primarily by microbial reduction

Soil. Slight oxidation to the volatile oxides

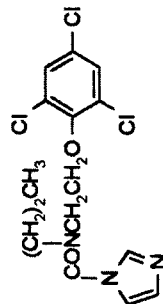
Preventive and curative fungicide

Inhibitor of C-14-demethylase in sterol biosynthesis



Epoxiconazole (Triazole)

Steroid demethylation (ergosterol biosynthesis) inhibitor



Prochloraz (Imidazole)

Fungicide with protective action

Non-specific thiol reactant, inhibiting respiration



Nonsystemic fungicide

Nonspecific thiol reactant, inhibiting respiration

Sulfur (inorganic)

TABLE 17.5b Continued

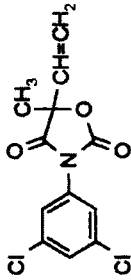
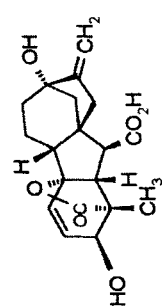
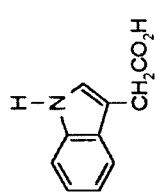
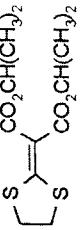
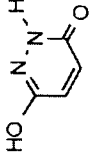
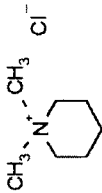
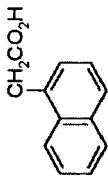
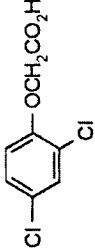
Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Vinclozolin (Dicarboximide)		—	Nonsystemic fungicide	<p><i>Animals.</i> The major metabolic routes are epoxidation of the vinyl group, followed by hydration of the intermediate epoxide, and by hydrolytic cleavage of the heterocyclic ring. Eliminated in approximately equal proportions in the urine and feces, with the principal metabolite being <i>N</i>-(3,5-dichlorophenyl)-2-methyl-2,3,4-trihydroxybutanamide</p> <p><i>Plants.</i> The primary metabolites are (1-carboxy-1-methyl)allyl 3,5-dichlorophenylcarbamate and <i>N</i>-(3,5-dichlorophenyl)-2-hydroxy-2-methyl-3-butenamide. Alkaline hydrolysis leads to loss of 3,5-dichloroaniline from vinclozolin and its metabolites. The metabolites exist as conjugates</p> <p><i>Soil.</i> Metabolism occurs by loss of the vinyl group, cleavage of the 5-membered ring and eventual formation of 3,5-dichloroaniline. Soil degradation takes place with half-lives of several weeks, and mainly leads to the formation of bound residues</p> <p><i>Animals.</i> Mostly eliminated within 1–2 days leaving 1–2% of the dose in the tissue and carcass after 7 days</p> <p><i>Plants.</i> The major metabolite is dimethylamine salt of dimethyldithiocarbamic acid; tetramethylthiourea, carbon disulfide and sulfur can also be formed. Dimethyldithiocarbamic acid can be present as the free acid or as the metabolic conversion products DDC-β-glucoside, DDC-α-aminobutyric acid and DDC-α-alanine</p> <p><i>Soil.</i> A. aerobic DT₅₀ 42 hr. Unlikely to leach</p>
Ziram (Dimethyldithio- carbamate)	$[(\text{CH}_3)_2\text{NCS}_2]_2\text{Zn}$	Inhibitor of enzymes containing copper ions or sulfonyl groups	Basic contact, foliar fungicide	

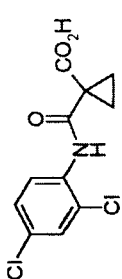
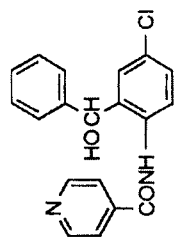

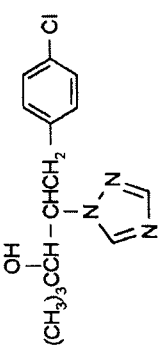
TABLE 17.6 Plant Growth Regulators

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Chloromequat chloride (Quaternary ammonium)	$\text{ClCH}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3 \text{Cl}^-$	Gibberellin biosynthesis inhibitor	Inhibits cell elongation. Also influences developmental cycle, leading to increased flowering and harvest. May also increase chlorophyll formation and root development	<i>Animals.</i> 97% is eliminated within 24 hr, principally unchanged <i>Plants.</i> Converted to choline chloride <i>Soil.</i> Rapidly degraded by microbial activity. DT ₅₀ in 4 soils averaged 32 days at 10°C; 1–28 days at 22°C. Low to medium mobility
Ethephon (Ethylene generator)	$\text{ClCH}_2\text{CH}_2\text{P}(\text{OH})_2$	—	Plant growth regulator with systemic properties. Penetrates into the plant tissue and is decomposed to ethylene, which affects growth processes	<i>Animals.</i> Rapidly excreted intact via the urine, and as ethylene via the expired air <i>Plants.</i> Rapidly undergoes degradation to ethylene <i>Soil.</i> Rapidly degraded and strongly adsorbed; unlikely to leach
Gibberellic acid (Gibberellins)		—	Shows physiological and morphological effects on the plant parts above soil surface at extremely low concentrations. Translocated Plant Growth Regulator	—
Indol-3-ylacetic acid (Auxin)		—	Affects cell division and cell elongation	<i>Soil.</i> Rapidly degraded in soil

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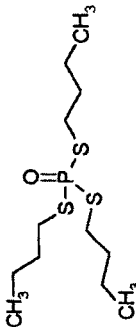
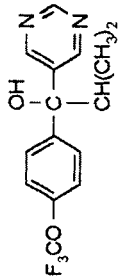

TABLE 17.6 Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Isoprothiolane (Phosphorothiolate)		Inhibits penetration and elongation of infection hyphae, by inhibiting formation of infection peg or cellulose secretion	Absorbed by leaves and roots with translocation acropetally and basipetally	—
Maleic hydrazide		Inhibits cell division in the meristematic regions.	Absorbed by leaves and roots with translocation in xylem and phloem	<i>Animals.</i> 43–62% of the dose excreted unchanged within 48 hr <i>Plants.</i> Various acids, e.g., succinic, fumaric, and maleic, are found as metabolites <i>Soil.</i> DT ₅₀ c. 11 hr
Mepiquat chloride (Quaternary ammonium)		Inhibits biosynthesis of gibberellic acid	Plant Growth regulator, absorbed and translocated throughout the plant	<i>Animals.</i> c. 48% is excreted in the urine c. 38% in the feces, with <1% remaining in the tissues. The unmetabolized material constitutes c. 90% in each case <i>Soil.</i> DT ₅₀ 10–97 days at 20 ± 2°C and 40% of maximum water-holding capacity
1-naphthyl acetic acid (Synthetic auxin)		—	Plant Growth Regulator with auxin like activity	—
2,4-Dichlorophenoxy acetic acid (aryloxyalkanoic acid)		Synthetic auxin, acting like indolylacetic acid	Salts are readily absorbed by the roots while esters are readily absorbed by foliage. Translocation occurs, with accumulation principally at the meristematic regions of shoots and roots. Acts as a growth inhibitor	<i>Animals.</i> Elimination is rapid, and mainly as the unchanged substance. Following single doses of up to 10 mg/kg, excretion is almost complete after 24 hr, although, with higher doses, complete elimination takes longer. The maximum concentration in organs is reached after c. 12 hr <i>Plants.</i> Metabolism involves hydroxylation, decarboxylation, cleavage of the acid side-chain, and ring opening <i>Soil.</i> Microbial degradation involves hydroxylation, decarboxylation, cleavage of the acid side-chain, and ring opening. Half-life in soil <7 days. Rapid degradation in the soil prevents significant downward movement

Cyclanilide (Anilide)		Inhibits polar auxin transport	—	<p><i>Animals.</i> Rapidly excreted, primarily as unchanged cyclanilide</p> <p><i>Plants.</i> Little degradation occurs in plants; cyclanilide is the major residue</p> <p><i>Soil.</i> Low to moderate persistence, DT₅₀ c. 16 days under aerobic conditions. Degrades primarily by microbial activity. Medium to low mobility</p>
Inabenfide (Pyridine)		Inhibits gibberellin biosynthesis	Plant Growth Regulator which shortens lower internodes and upper leaf blades	<p><i>Animals.</i> The major urinary metabolite is 4-hydroxyinabenfide</p> <p><i>Plants.</i> Metabolized to inabenfide ketone</p> <p><i>Soil.</i> Half-life under Japanese paddy field conditions, c. 4 months</p>
Thidiazuron (Phenylurea)		Cytokinin activity	Plant Growth Regulator absorbed by the leaves which stimulates formation of an abscission layer between the plant stem and leaf petioles, causing drooping of the entire green leaves	<p><i>Animals.</i> Metabolism involves hydroxylation of the phenyl group, followed by formation of water-soluble conjugates. Following oral administration, the compound is excreted in the urine and feces within 96 hr</p> <p><i>Plants.</i> Only small amounts of residue (normally <0.1 mg/kg) are likely in cottonseed</p> <p><i>Soil.</i> Strongly absorbed by soil. DT₅₀ in soil c. 26–144 days (aerobic), 28 days (anaerobic)</p>
Paclobutrazol (triazole)		Inhibits gibberellin and sterol biosynthesis and hence the rate of cell division	Plant Growth Regulator taken up into xylem through the leaves, stems or roots and translocated to the growing sub-apical meristems. Produces more compact plants and enhances flowering and fruiting	<p><i>Soil.</i> Soil DT₅₀ 0.5–1.0 years in general; in calcareous clay loam (pH 8.8, 14% o.m.), DT₅₀ <42 days; in coarse sandy loam (pH 6.8, 4% o.m.), DT₅₀ > 140 days</p>

(continued)

TABLE 17.6 Continued

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Tribufos (Phosphorothioate)		—	Plant Growth Regulator absorbed by leaves. Stimulates formation of an abscission layer between the plant stem and the leaf petioles, causing the dropping of entire green leaves	<i>Animals.</i> Rapidly absorbed and metabolized; 96% of the administered radioactivity was excreted within 72 hr. Metabolism proceeds by hydrolysis followed by methylation and successive oxidation of butylmercaptan, yielding the main metabolite (3-hydroxy)-butylmethylsulfone <i>Plants.</i> Unmetabolized tribufos is the primary residue in treated cotton <i>Soil.</i> Very strongly adsorbed, leaching is extremely unlikely. The half-life under field conditions is 2–7 weeks. The main metabolite is 1-butane sulfonic acid
Flurprimidol (Pyrimidinyl carbanoI)		Gibberellin synthesis inhibitor	Plant Growth Regulator absorbed by the leaves and roots with translocation in the xylem and ploem. Reduces internode elongation	<i>Animals.</i> In mammals, the skin forms a significant barrier to absorption. Following oral administration, excretion follows in the urine and feces within 48 hr, and more than 30 metabolites have been identified. No accumulation potential <i>Soil.</i> Degradation in soil under aerobic conditions leads to more than 30 metabolites
Chlorpropham (Carbamate (mi))		Mitosis inhibitor (Micronubule organization)	Absorbed by roots and coleoptile and readily translocated acropetally	<i>Animals.</i> The principal metabolic route is by hydroxylation at the para position and conjugation of the resultant 4-hydroxychlorpropham with sulfate. There is also some hydroxylation of the isopropyl residue

Plants. Three major metabolites have been identified, isopropyl N-4-hydroxy-3-chlorophenylcarbamate, isopropyl N-5-chloro-2-hydroxyphenylcarbamate and 1-hydroxy-2-propyl-3'-chlorocarbanilate. These aglycones are found in plants as water-soluble conjugates of glucose or other plant components

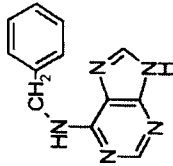
Soil. Microbial degradation leads to the production of 3-chloroaniline by an enzymic hydrolysis reaction, with liberation of CO₂. DT₅₀ in soil c. 65 days (15°C), 30 days (29°C)

Animals. Almost all of administered ¹⁴C was excreted in urine and faeces. Three metabolites were identified

Plants. More than nine metabolites were identified. Urea is an end product

Soil. 16 Days after application to soil at 22°C, 6-benzylaminopurine had degraded to 5.3% (sandy loam) and 7.85% (clay loam soil) of applied dose. Other studies indicate DT₅₀ 7-9 weeks

6-Benzylaminopurine
(Cytokinin)



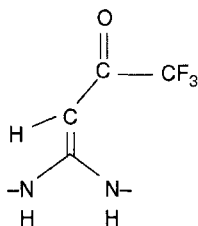
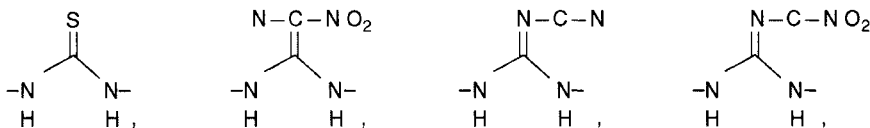
Synthetic cytokinin,
little translocated

Stimulates RNA,
RuDP-
carboxylase,
NADP-
glyceraldehyde-3-
phosphate-
dehydrogenase,
protein synthesis

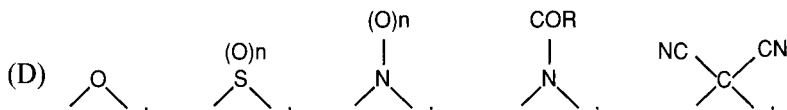
bioisosterism:

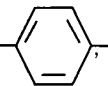


(A) $-\text{CO}_2\text{H}$, $-\text{SO}_2\text{NHR}$, $-\text{SO}_3\text{H}$, $-\text{PO}(\text{OH})_2$, $-\text{PO}(\text{OH})\text{NH}_2$, $-\text{CONHCN}$

(B) $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{CF}_3$, $-\text{CN}$, $-\text{SCN}$, $-\text{N}(\text{CN})_2$, $-\text{C}(\text{CN})_3$



(C) $-\text{OH}$, $-\text{NHCOR}$, $-\text{NHSO}_2\text{R}$, $-\text{CH}_2\text{OH}$, $-\text{NHCONH}_2$, $-\text{NHCN}$, $-\text{CH}(\text{CN})_2$



(E) $-(\text{CH}=\text{CH})_n$, , , , and so on

(F) $-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$, $-\text{C}\equiv\text{N}$

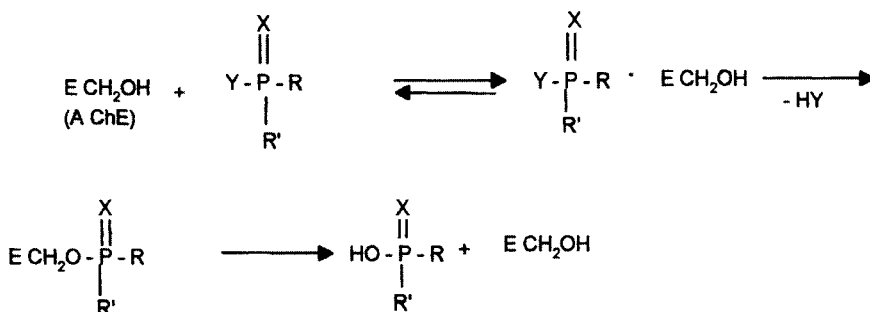
(G) $-\overset{|}{\underset{|}{\text{C}}}-$, $-\overset{|}{\underset{|}{\text{Si}}}-$

STRUCTURAL BASIS OF AGROCHEMICALS

Organophosphorous Agrochemicals

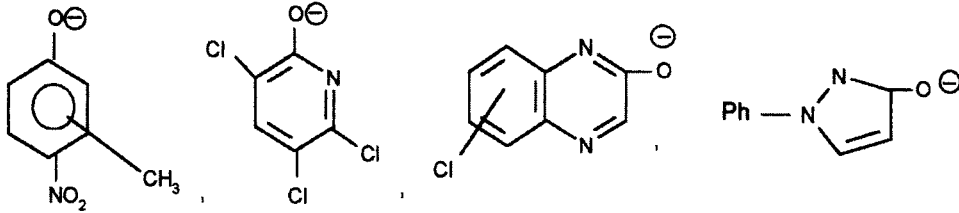
The concept of bioisosterism has been used to theoretically evaluate structural variation within the lead structures of synthetic or natural origin prior to and during the preparation of molecules of specified efficacy, safety, stability, and so on.

Insecticides (Tables 17.3a,b). Organophorous insecticides bind to Acetylcholinesterase (AChE), that is,

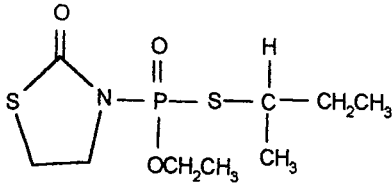


where R and R' are lower alkyl alkoxy, alkylthio, or substituted amino groups; X is oxygen or sulfur; and Y is a good leaving group, for example aryloxy groups substituted with electron withdrawing substituents.

Others are: fosamine (herbicide used on noncrop areas, in meadows and pastures), piperofos (used in rice), and anilofos (used on rice).

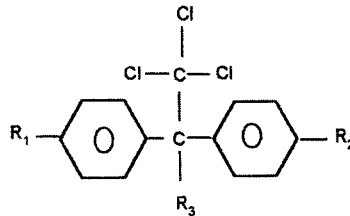


Y can also be a mixed (C, N, S) heterocycle as in the case of the nematicide Fosthiazate.



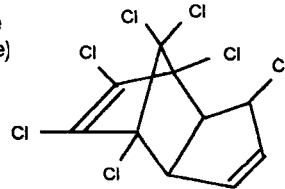
Nematicide (Fosthiazate)

Organochlorine

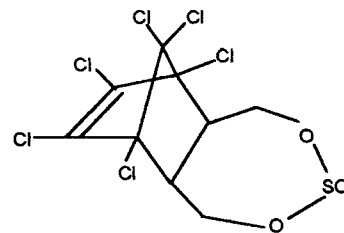


R₁ = R₂ = Cl, R₃ = H-DDT
 R₁ = R₂ = Cl, R₃ = OH-Dicofol.

Organochlorine—Cyclodiene

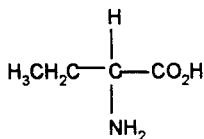
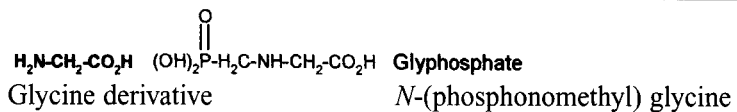


Heptachlor

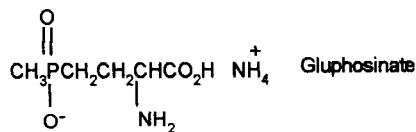


Endosulfan

Herbicides (not numerous) (Tables 30.4a-d).
 Organophosphorous herbicides are derived from amino acids, for example,

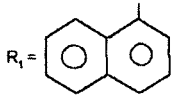
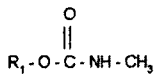


Homoalanine derivate

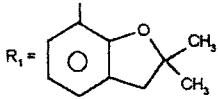


Ammonium 4[Hydroxy(methyl)phosphonoyl]homoalalinate

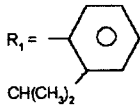
Carbamates



Carbaryl

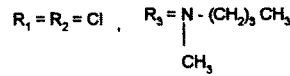
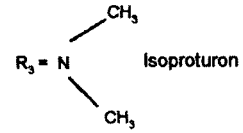
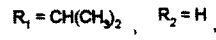
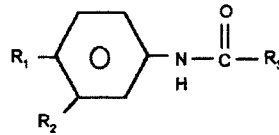


Carbofuran

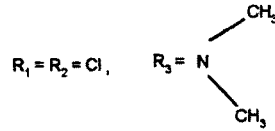


Isoprocarb

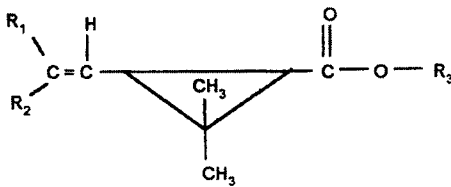
Ureas



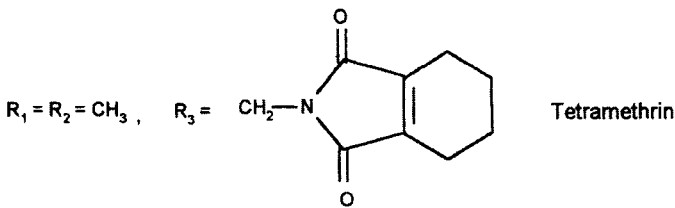
Neburon



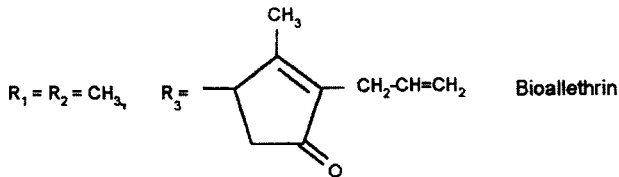
Pyrethroids



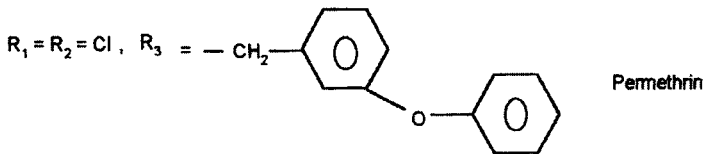
(a)



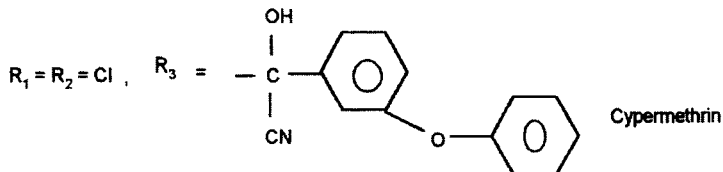
(b)

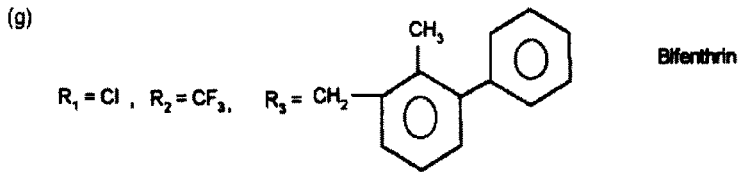
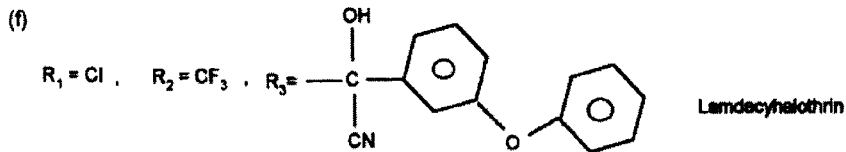
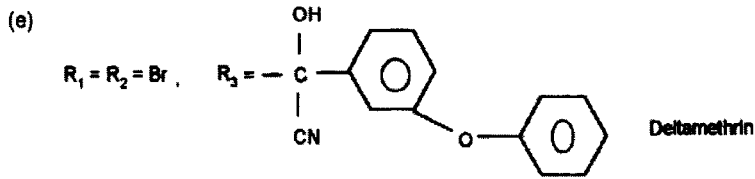


(c)

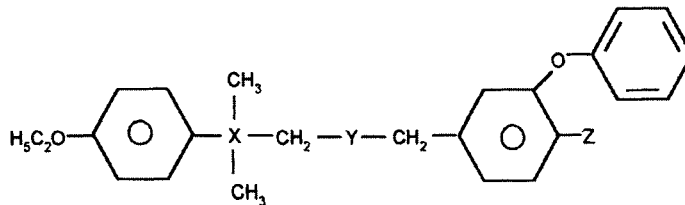


(d)



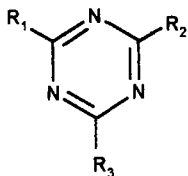


Nonester pyrethroids/“Si” in lieu of “C”



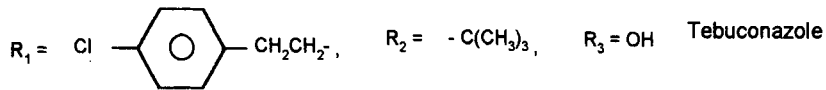
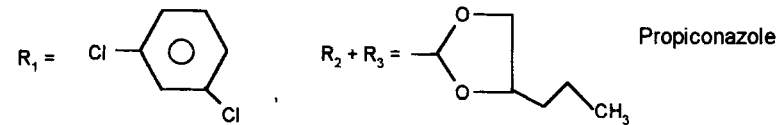
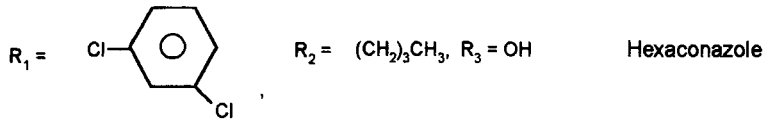
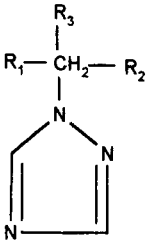
$X = \text{C}$, $Y = \text{O}$, $Z = \text{H}$ Ethofenprox
 $X = \text{Si}$, $Y = \text{CH}_2$, $Z = \text{F}$ Silafluofen

Triazines

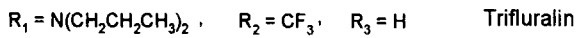
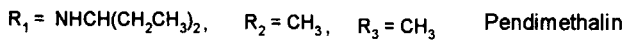
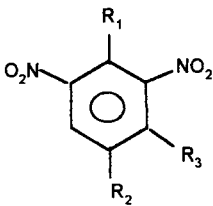


$R_1 = \text{Cl}$, $R_2 = \text{NHCH}_2\text{CH}_3$, $R_3 = \text{NHCH}_2\text{CH}_3$ Simazine
 $R_1 = \text{Cl}$, $R_2 = \text{NHCH}_2\text{CH}_3$, $R_3 = \text{NHCH}(\text{CH}_3)_2$ Atrazine
 $R_1 = \text{Cl}$, $R_2 = \text{NHCH}_2\text{CH}_3$, $R_3 = \text{NH}-\text{C}(\text{CH}_3)_2$ Cyanazine
|
CN

Azoles

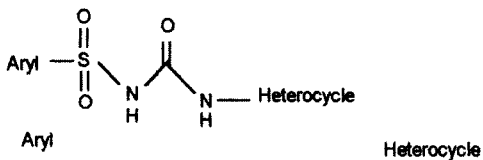


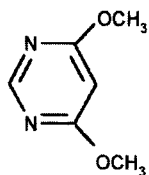
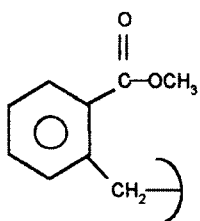
Dinitroanilines



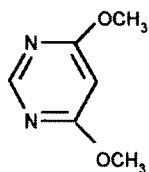
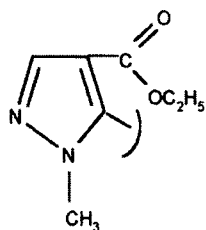
Chloracetanilides

Sulfonyl Ureas

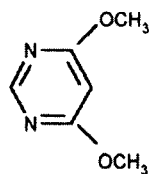
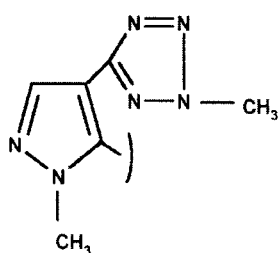




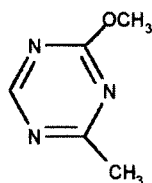
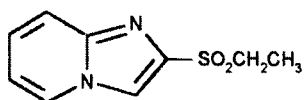
Rice Herbicide
Bensulfuron



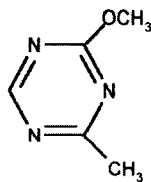
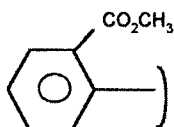
Rice Herbicide
Pyrazosulfuron



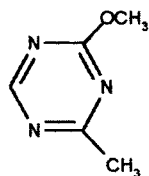
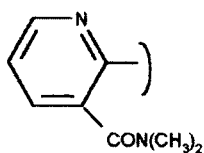
Rice Herbicide
Azimsulfuron



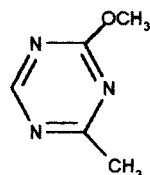
Wheat Herbicide
Sulfosulfuron



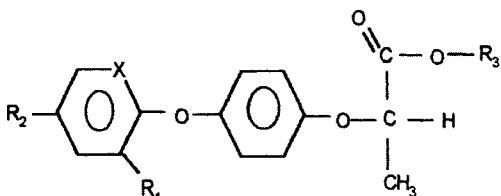
Wheat Herbicide
Metsulfuron



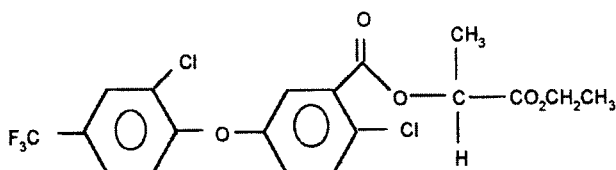
Corn Herbicide
Nicosulfuron



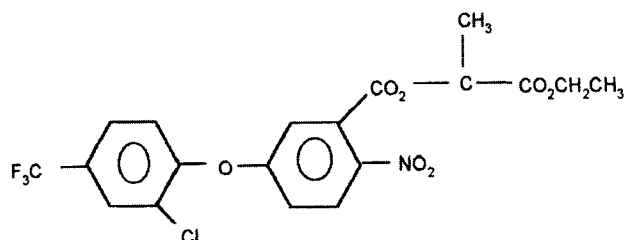
Corn Herbicide
Rimsulfuron

**Aryloxyphenoxypropionic Acids
(Cereal Herbicides)**Clodino/cyhalo/diclo/fenoxa/fluazi/
haloxypropaquizafop

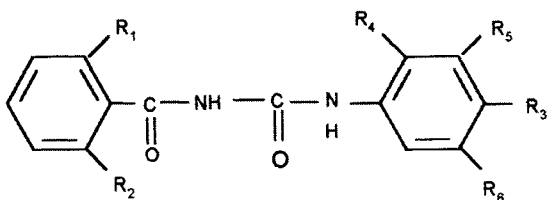
1. X = H, R = H, R₂ = H, R₃ = Methyl-Diclofop
2. X = H, R₁ = F, R₂ = CN, R₃ = *n*-Butyl-Cyhalofop
3. X = N, R₂ = Cl, R₁ = F, R₃ = CH₂-C≡CH-Clodinofof
4. X = N, R₁ = H, R₂ = CF₃, R₃ = *n*-Butyl = -Fluazifop 4.5

Diarylether Carboxylic Acids (Cereal Herbicides)

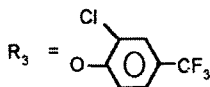
HC-252



Fluoroglycofen

*Benzoyl Ureas (Insect Growth Regulators)
(Table 17.7)*R₁ = R₂ = F,R₃ = Cl,R₄ = R₅ = R₆ = H

Diflubenzuron

R₁ = R₂ = F,R₄ = F, R₅ = R₆ = H

Flufenoxuron

R₁ = R₂ = F,R₃ = OCF₂CHF₂,R₄ = H,R₅ = R₆ = Cl

Hexaflumuron

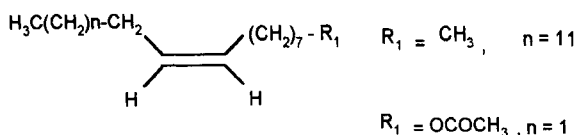
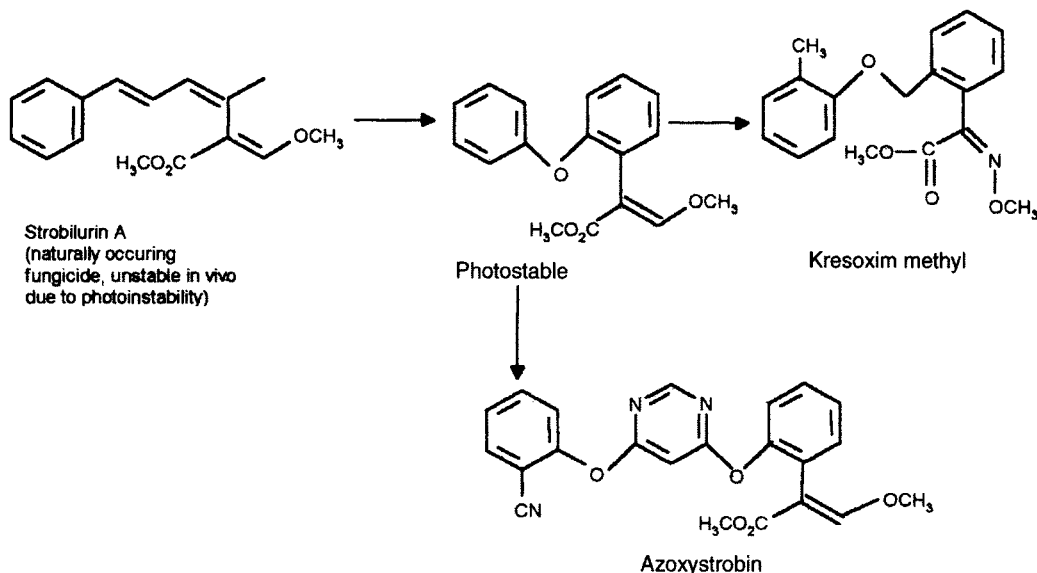
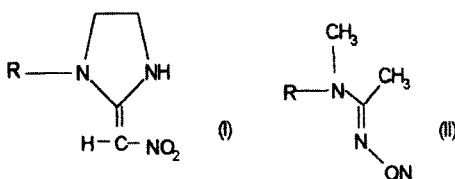
PheromonesR₁ = CH₃, n = 11Mating hormone of
houseflySex pheromone of
oriental fruitmoth

TABLE 17.7 Insect Growth Regulators

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Diflubenzuron (Benzoylurea)		Chitin synthesis inhibitor and so interferes with the formation of insect cuticle	Nonsystemic insect growth regulator with contact and stomach action. Acts at the time of insect moulting or at hatching of eggs	<p><i>Animals.</i> Elimination is partly as the unchanged parent compound in the feces, partly as hydroxylated metabolites (for c. 80%) and as 4-chlorophenylurea plus 2,6-difluorobenzoic acid (for c. 20%). The intestinal absorption is strongly related to the dosage administered—the higher the dosage, the more (relatively) is excreted unchanged in the feces.</p> <p><i>Plants.</i> Nonsystemic. Nonmetabolized on plants</p> <p><i>Soil.</i> Strongly absorbed by soil/humic acid complex and is virtually immobile in soil. Rapidly degraded in soil, with a half-life of <7 days. The principal degradation products are 4-chlorophenylurea and 2,6-difluorobenzoic acid</p>
Cyromazine (Triazine)		Interfere with moulting and pupation	Insect Growth Regulator with contact action. When used on plants action is systemic. If applied to leaves, it exhibits a strong translaminar effect, applied to soil it is translocated acropetally after absorption by roots	<p><i>Animals.</i> Efficiently excreted, mainly as the parent compound</p> <p><i>Plants.</i> Rapidly metabolized. The principal metabolite is melamine</p> <p><i>Soil.</i> Cyromazine and its main metabolite melamine are moderately mobile. Efficiently degraded by biological mechanisms</p>
Fenoxycarb (Carbamate)		—	Nonneurotoxic insect growth regulator with contact and stomach action. Exhibits a strong juvenile hormone activity, inhibiting metamorphosis to the adult stage and interfere with the moulting of early instar larvae	<p><i>Animals.</i> The major metabolic path is ring hydroxylation to form ethyl [2-[p-(p-hydroxyphenoxy)phenoxy]ethyl]carbamate</p> <p><i>Plants.</i> Rapidly degraded in plants</p> <p><i>Soil.</i> Low mobility in soil, no bioaccumulation. Relatively fast degradation.: DT₅₀ 1.7–2.5 months (lab.), few to 31 days (field)</p>

TABLE 17.7 Continued

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Hydroprene (Juvenile hormone mimetic)	$ \begin{array}{c} \text{CH}_3 \\ \\ (\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}_2 \\ \\ \text{C}=\text{C} \\ / \quad \backslash \\ \text{H} \quad \quad \text{H} \\ \quad \quad \\ \text{CH}_3 \quad \quad \text{C}=\text{C} \\ \quad \quad \quad / \quad \backslash \\ \quad \quad \quad \text{H} \quad \quad \text{CO}_2\text{CH}_2\text{CH}_3 \end{array} $	—	Prevents metamorphosis to viable adults when applied to larval stage	<p><i>Plants.</i> Degradation principally involves ester hydrolysis, <i>O</i>-demethylation, and oxidative splitting of the double bond</p> <p><i>Soil.</i> Rapidly decomposed, DT₅₀ is only a few days</p>
Buprofezin (Cyclic urea)		Probable chitin synthesis and prostaglandin inhibitor. Hormone disturbing effect, leading to suppression of ecdysis	Contact and stomach action, not translocated in the plant. Inhibits moulting of nymphs and larvae, leading to death. Also suppresses oviposition by adults, treated insects lay sterile eggs	<p><i>Animals.</i> Low residues were found in nearly all ruminant and poultry tissues. Extensive metabolism was observed, with a large number of minor metabolites being produced</p> <p><i>Plants.</i> Limited metabolism in most plant species; minor metabolites indicate a pathway involving hydroxylation or oxidative loss of the <i>tert</i>-butyl group, followed by opening of the heterocyclic ring</p> <p><i>Soil.</i> DT₅₀ (25°C) 104 days (flooded conditions, silty clay loam, o.c. 3.8%, pH > 6.4), 80 days (upland conditions, sandy loam, o.c. 2.4%, pH 7.0)</p>

Strobilurins (Fungicide)*Neonicotinoids (Sucking pest control insecticides)*

LC₉₀ (Against Rice Plant hopper)

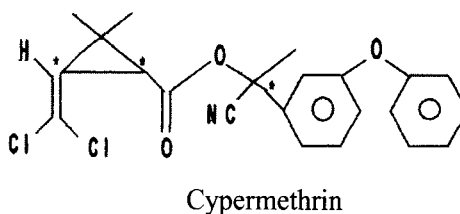
- R = (a) 4-chlobenzyl—40 ppm
 (b) 3-pyridinobenzyl—08 ppm—improved spectrum of activity
 (c) 6-chloropyridino-3-benzyl—0.32 ppm
 (I)—Imidacloprid
 (d) 6-chloropyridino-3-benzyl-(II)—Acetamiprid

a.....d having isosteric relationships. Distance between "N" in pyridine to acidic proton in (I) crucial to activity.

ROLE OF CHIRALITY

Whenever a chemical structure has one or more asymmetric centers or double bonds, either diastereoisomerism or geometric isomerism is possible. Usually only one of the specific stereoisomers is responsible for all or most of the biological activity. An example is

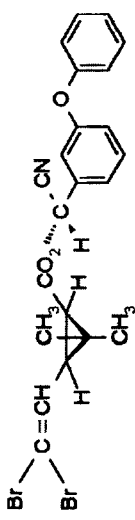
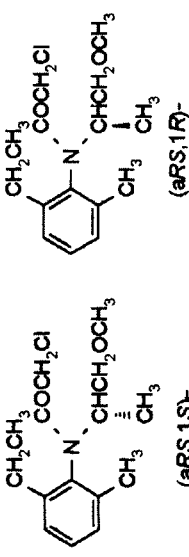
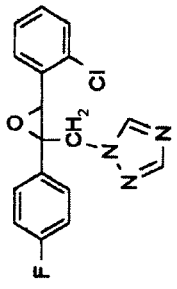
cypermethrin,



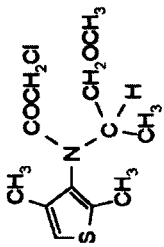
which possesses three asymmetric centers and hence eight possible isomers. Of eight possible isomers, the 1*R*-*cis*-*S* isomer is the most biologically active isomer, and the bromo analogue is deltamethrin, commercialized in 1984. In the search for low-dose agrochemicals, chiral synthesis plays an important role. For example, one methodology, as used for deltamethrin, is the separation of *cis* and *trans* acids, resolution of the *cis* acid using a chiral amine to prepare the 1*R*-*cis*-acid. Condensation of the 1*R*-*cis*-acid chloride with in situ generated cyanohydrin, derived from metaphenoxybenzaldehyde, offers a mixture of "1*R* *cis* ∝ *S*" and "1*R* *cis* ∝ *R*" deltamethrin. The crystallization of the mixture under conditions of epimerization allows isolation of high purity 1*R* *cis* ∝ *S* deltamethrin. Today, stereoisomer separations are also relatively facile using chiral phases in preparing HPLC.

Table 17.8 lists examples of chiral agrochemicals.

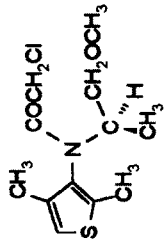
TABLE 17.8 Chiral Chemistry

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Deltamethrin (Pyrethroid)		Prevents sodium channels from functioning so that no transmission of nerve impulses can take place	Nonsystemic insecticide with contact and stomach action	<i>Animals.</i> Eliminates within 2–4 days. The phenyl ring is hydroxylated, the ester bond hydrolyzed, and the acid moiety is eliminated as the glucoside and glycine conjugates <i>Soil.</i> Undergoes microbial degradation within 1–2 weeks DT ₅₀ in field <23 days. Soil photolysis DT ₅₀ 9 days. No risk of leaching
S-Metolachlor (Chloroacetamide)		Cell division inhibitor	Selective herbicide, absorbed predominantly by the hypocotyls and shoots; inhibits germination	<i>Animals.</i> Rapidly oxidized by rat liver. Oxygenases via dechlorination, O-demethylation and side-chain oxidation, conjugation by glutathione S-transferases <i>Plants.</i> Metabolism involves dechlorination and conjugation to glutathione-S-transferases, followed by further degradation to polar, water soluble, nonvolatile metabolites <i>Soil.</i> Major aerobic metabolites are derivatives of oxalic and sulfonic acids; DT ₅₀ (field): 11–30 days. DT ₉₀ (field): 36–90 days
Epoxiconazole (Azole)		Inhibits C ¹⁴ demethylase in sterol biosynthesis	Preventive and curative fungicide	<i>Animals.</i> Readily excreted via feces. Metabolic reactions are cleavage of the oxirane ring, hydroxylation of the phenyl rings and conjugation. No major metabolites; high number of minor metabolites <i>Soil.</i> Degradation by microbial activity. DT ₅₀ a. 2–3 months

Dimethenamid
(Chloroacetamide)

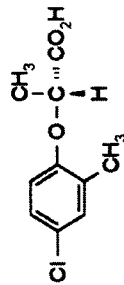


dimethenamid



dimethenamid-P

Mecoprop-P
(Aryloxyalkanoic acid)



Cell division inhibitor

Herbicide absorbed by coleoptile

Animals. Metabolites in rat, goat, and hen include glutathione, cysteine, and thioglycolic acid
Plants. Metabolism in maize leads to thiolactic acid besides above
Soil. Rapidly degraded in soil, probably through microbial action, with DT₅₀: 8–43 days, depending upon soil type and weather conditions. Photolysis DT₅₀ on soil a. 7.8 days

Systemic auxin, acting like indoly/acetic acid

Selective herbicide, absorbed by leaves, with translocation to the roots

Animals. In mammals predominantly eliminated as conjugates in urine
Plants. Hydroxylated at the methyl group with formation of 2-hydroxy methyl-4-chlorophenoxy propionic acid
Soil. Degraded predominantly by microorganisms to 4-chloro-2-methyl phenol, followed by ring hydroxylation at the 6-position and ring opening. DT₅₀ (aerobic) : 3–13 days

Basis of Chemistry Used in Synthesis of Agrochemicals

Agrochemicals belong to a variety of chemical classes. Each chemical class demands certain key building blocks. Some examples are: cyanuric chloride (triazines), iminodiacetic acid (glyphosate), 2,6-disubstituted anilines (chloracetanilides), dialkoxythiophosphoryl chlorides (organophosphorous group), metaphe-noxybenzaldehyde/alcohol (pyrethroid), isocyanates—alkyl/aryl (carbamates / ureas), sulfonyliso-cyanates (sulphonyl ureas), dialkyl/dihalovinyl-dimethyl-cyclopropane carboxylic acid chloride (pyrethyroids), dihalophenols (phenoxyherbicides), chlorocresols (dichlorophen, etc.), ethylenediamine (dithiocarbamates).

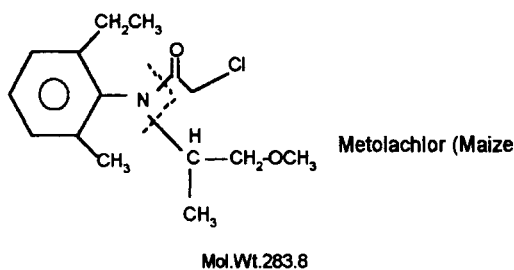
During the synthesis of specific building blocks (key intermediates, penultimate intermediates, or target-active ingredients) a whole range of chemical reactions are deployed. Examples obviously include aromatic electrophilic and nucleophilic substitution, Diels Alder cycloadditions, telemerizations, "N," or "O" alkylations, and so on. New and safer reagents are often employed, for example diphosgene/triphosgene/diarylcarbamates, in lieu of phosphene in the manufacture of carbamates and sulfonyl ureas. Toxic reagents are

generated for immediate chemical reaction (consumption) avoiding hazards of storage through leakage. As an example, the standard production of alkyl isocyanates for production of carbonates—from alkalimetal cyanates and alkyl halides or sulfates—can be replaced with the in situ generation of arylisocyanates from arylamines and urea to produce target aryl alkyl ureas.

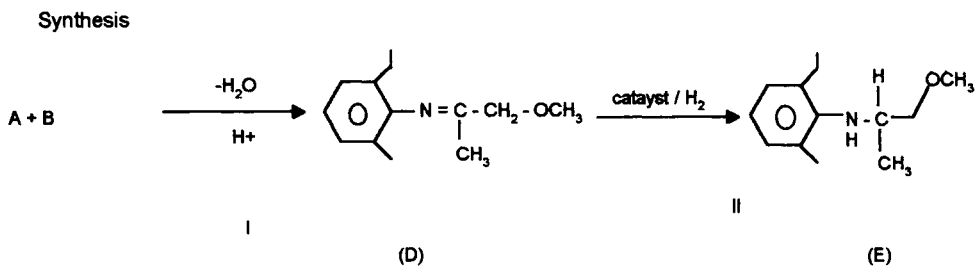
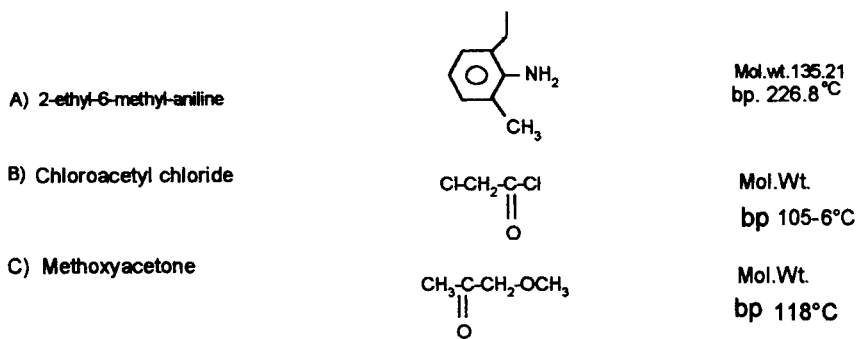
Case Study—Chemistry and Manufacture of Metolachlor

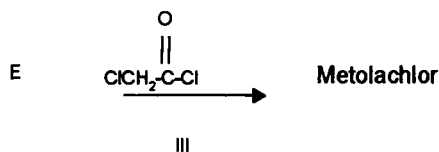
A typical example of agrochemical manufacture is provided by the maize herbicide (Table 17.2b), *metolachlor*.

The chemistry of metolochlor synthesis is shown below, followed by a description of the manufacturing process.



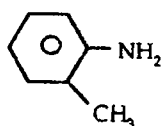
Building blocks for synthesis of metolachlor are:



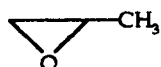


The nature of the catalyst employed during the hydrogenation of (D) offers (E) as a racemate of 1S and 1R isomers, or enriched in 1S isomer which leads into *racemic (R/S) metolachlor* or *S-metolachlor*. A chiral catalyst allows the 1S isomer enrichment to be favored.

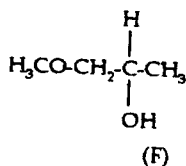
The raw materials used in the commercial synthesis of metolachlor include 2-ethyl 6-methyl-aniline, which can be built up from



ortho-toluidine and ethylene (ex ethanol if required) at high temperature and pressure over metallic aluminum. Methoxyacetone is built up from



propylene oxide and its reaction with sodium methoxide in methanol, which favors opening from the least hindered side and results in



the methylether of 2,3-propanediol. Due operational care is necessary in handling propylene oxide as it is extremely flammable and poisonous.

The methyl ether of 2,3-propanediol can be oxidized to methoxyacetone in the vapor or liquid phase using a suitable catalyst or oxidant, respectively. To achieve production of high purity metolachlor, which is a liquid (mp. 62.1°), it is necessary to control the quality of all input materials, monitor reaction progress, terminate each reaction step effectively, and

use solvents that can be effectively eliminated to very low levels without volatilization losses of metolachlor (100°C/0.001 mmHg).

Reaction step I is conveniently carried out in a stainless steel reactor using a hydrocarbon solvent to expel water of the reaction as an azeotrope. Completion of the reaction can be determined by measuring the water of reaction or through disappearance of both the 2-ethyl-6-methyl aniline and methoxyacetone by gas chromatography (GC) or high performance liquid chromatography (HPLC).

In the reaction step II, the energetics of saturation of an olefinic Schiff base linkage are favorable and quantitative over most hydrogenation catalysts. 1S isomer enrichment can be achieved through use of a chiral catalyst and the enrichment may be monitored through chiral HPLC. A stainless steel reactor is considered adequate for this operation.

Reaction step III is "N-acylation." It is conveniently carried out in a refluxing chlorinated aliphatic hydrocarbon; the hydrogen chloride gas which is evolved should be scrubbed in aqueous caustic soda. Precautions are necessary when handling the highly corrosive chloroacetyl chloride. This step should be carried out in a glass lined reactor.

Effluents from the reaction are the water of reaction in step I, and hydrogen chloride gas in step III.

Usage of Agrochemicals

Agroclimatic conditions, soil type, irrigation, as opposed to rain as the source of water, and other factors all govern the nature of crop cultivation and also the nature of pest attack. Soil preparation, seed dressing, pre-sowing, pre-plant incorporation, pre-emergence, early-post-, or late post-emergence, right through harvest are all various stages during which agrochemicals find use. Protection of farm produce or seeds from pest attack is dependant

on the use of agrochemicals. Ectoparasite control of livestock and poultry is another area of agrochemical usage. Disease vector control from flies, mosquitoes, and cockroaches on one hand and protection of dwellings from termites and other wood borers on the other are both significant consumers of agrochemicals. Different insecticides are used to control insects during the different stages of insect life cycle. The habitat of the insects, whether dwelling above or below the soil surface, and the different feeding habits of individual groups of insects dictate the use of specific insecticides. Use of herbicides depends upon the weed spectrum as per crop and climatic conditions. The competing growth stages of the weeds, as compared to the crop, as well as nature of weeds (e.g., grasses, broadleaf weeds, or sedges) and the efficacy characteristics of individual herbicides need to be synchronized for effective control. Biannual versus annual, or perennial weeds need be treated with different specific herbicides.

The various fungicides have either specific or broad spectrum efficacy. These can be deployed for either prophylactic or curative action. Beyond the farm crops and horticulture, maintenance of turf and lawns free of insects and weeds, and the preservation of natural and agricultural forestry are significant markets for insecticides and herbicides.

All agrochemicals must be used at well-researched recommended dosages. Sublethal dosages as well as single agrochemicals used repeatedly leads to resistance development. It is therefore important to use agrochemicals with an independent mode of action in rotation or in well-conceived mixtures to decrease resistance development. Different formulations of a given agrochemical are deployed when the intention is for soil application for absorption by root system or by foliar uptake. Different sprayers with specific nozzles allow better efficacy. Aerial spraying demands yet different formulations.

Differential selective or broad spectrum agents include nematocides (Table 17.9), acaricides, ovicides, molluscicides (Table 17.10), algicides (Table 17.11), bactericides

(Table 17.12), and rodenticides (Table 17.13), which control damage from nematodes, mites, eggs, snails/slugs, algae, bacteria, and rodents, respectively.

Insecticides control insects with differential feeding habits, which have a reasonably predictable pattern per crop and agroclimatic condition. Systemic insecticides (Table 17.3a) find use to control insects that feed by sucking plant juices. Insecticides with contact and stomach action control insects feeding (Table 17.3b) on foliage, stems, and fruits. Insect growth regulators (Table 17.7) find a complementary role to make insects more prone to control. Plant growth regulators (Table 17.6) direct nutrition to fruit formation by controlling vegetative growth. Herbicides (Tables 17.4a–d) are used for farm preparation, pre-plant incorporation, pre-early post, and post-emergence application to control competing weeds. Fungicides (Tables 17.5a,b) are used for seed dressing (control from soil fungi), and for the prophylactic and curative protection from fungal attack. Economic threshold levels, use of pheromone traps (Table 17.14) to measure insect population and the like are tools to use agrochemicals judiciously. Agrochemicals, when used rotationally or in mixtures of two with differential modes of action (e.g., mixture of an insecticide with insect growth regulator, mixture of herbicides or fungicides with different modes of action) help tackle the problem of resistance development.

BIOTECHNOLOGY FOR FARM PRODUCTIVITY

Biotechnology using recombinant DNA has affected farm productivity in some areas and may become more significant over time. A full discussion of this interesting subject is beyond the present scope of this chapter, but mention of some aspects may be appropriate.

The determination of DNA sequences of genes for resistance to pests and pathogens, cloned from a number of crop species, suggests the existence of certain domains in the protein products. These are shared among

TABLE 17.9 Nematicides

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Aldicarb (Oxime Carbamate)	$ \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{S}-\text{C}-\text{CH}=\text{NOCONHCH}_3 \\ \\ \text{CH}_3 \end{array} $	Cholinesterase inhibitor. Metabolically activated to Aldicarb sulfoxide	Systemic nematicide with contact and stomach action	<p><i>Animals.</i> Absorbed rapidly and completely; >80% is excreted in the urine within 24 hr, >96% within 3–4 days. Aldicarb is oxidized to the sulfoxide and sulfone, which undergo further metabolism.</p> <p><i>Plants.</i> The sulfur atom is oxidized to sulfoxide and sulfone groups. Further degradation leads to the formation of oximes, nitriles, amides, acids, and alcohols which are present in the plant only in conjugated form.</p> <p><i>Soil.</i> Sulfur atom is oxidized to sulfoxide and sulfone groups. Further degradation leads to the formation of oximes, nitriles, amides, acids, and alcohols</p>
Fenamiphos (Organophosphorous)		Cholinesterase inhibitor	Systemic nematicide with contact action. Absorbed by roots with translocation to the leaves	<p><i>Animals.</i> In mammals, following oral administration, there is rapid metabolism involving oxidation to the sulfoxide and sulfone analogues, followed by subsequent hydrolysis, conjugation and excretion via the urine, some <i>N</i>-dealkylation also occurs.</p> <p><i>Plants.</i> Degradation is by thiooxidation and hydrolysis. The major metabolites are fenamiphos sulphoxide and fenamiphos sulfone.</p> <p><i>Soil.</i> Degradable on soil surfaces. Duration of activity in soil is c. 4 months. Compound with low mobility. Soil DT₅₀ (aerobic and anaerobic) several weeks. The major degradation products are fenamiphos sulfoxide and fenamiphos sulfone and their phenols</p>
1,3-dichloropropene (Chloroalkenes)	—	—	Soil fumigant nematicide.	—

TABLE 17.10 Molluscicides

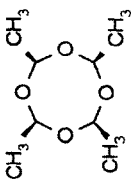
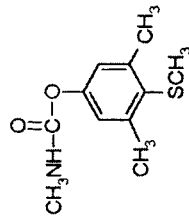
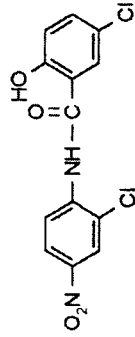
Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Metaldehyde		---	Molluscicide with contact and stomach action. Poisoned slugs secrete large quantities of slime, desiccate and die. Their mucus cells are irreversibly destroyed	Soil. Aerobic and anaerobic microorganisms in soil decompose metaldehyde to CO ₂ and water
Methiocarb (Carbamate)		Cholinesterase inhibitor	Molluscicide with neurotoxic toxic effect	<i>Animals.</i> Rapidly absorbed and excreted, principally in the urine, with only a small proportion in the feces. Metabolism involves hydrolysis, oxidation, and hydroxylation, followed by excretion in free or conjugated form. There is a continuous decrease of activity in all organs. <i>Plants.</i> Methylthio group is oxidized to sulfoxide and sulfone, with hydrolysis to the corresponding thiophenol, methylsulfoxide-phenol, and methylsulfonyl-phenol <i>Soil.</i> Degradation is rapid. The importance metabolites are methylsulfinylphenol and methylsulfonylphenol
Niclosamide (Amilide)		---	Molluscicide with respiratory and stomach action	<i>Animals.</i> The major metabolite in the urine was the reduced compound 2',5-dichloro-4'-aminosalicylamide. Several labile conjugates were also detected. The major constituent in the faeces was unchanged niclosamide, although considerable amounts of 2',5-dichloro-4'-aminosalicylamide were also present <i>Soil.</i> Degradation followed pseudo-first order kinetics, DT ₅₀ 0.3 days

TABLE 17.11 Algicides

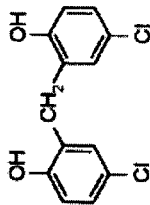
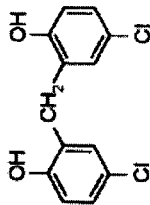
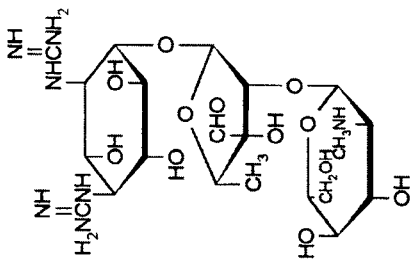
<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Nabam (Multi-site alkylenebis (dithiocarbamate))	$\text{NaSCSNHCH}_2\text{CH}_2\text{NHCSSNa}$ 	Non-specific thiol reactant, inhibiting respiration	—	<i>Plants.</i> The principal metabolite is ethylenethiourea. Other metabolites include ethylenethiuram monosulfide, ethylenethiuram disulfide, and sulfur
Dichlorophen (Chlorophenol)		—	Contact action	—

TABLE 17.12 Bactericides

Chemical (Chemical Class)	Structure	Biochemistry	Mode of Action	Environmental Fate
Bronopol (Chemical Class)		Oxidation of mercapto group of bacterial enzymes. Inhibition of dehydrogenase activity leads to irreversible membrane damage	—	<i>Animals.</i> Rapidly absorbed and rapidly excreted, mainly in the urine. The major metabolite is 2-nitropropane-1,3-diol <i>Plants.</i> Biochemical degradation leads to the metabolite 2-nitropropan-1,3-diol
Kasugamycin (Antibiotic)		Protein synthesis inhibitor, inhibits binding of Met-RNA to the mRNA-30S complex thereby preventing amino acid incorporation	Systemic bactericide	<i>Animals.</i> Mostly excreted in the urine within 24 hr. After oral administration to rats at 200 mg/kg, 96% of administered dose remained in the digestive tract 1 hr after administration <i>Plants/soil.</i> Degraded to kasugamycinic acid and kasuganobiosamine; finally degraded to ammonia, oxalic acid, CO ₂ and water
Oxolinic acid (Pyridone)		—	Systemic bactericide	—
Probenazole		—	Systemic bactericide, absorbed by roots and translocated acropetally	<i>Soil.</i> Half-life in soil <24 hr (alluvial or volcanic soil)
Tecloftalam (Benzoic acid)		—	Bacteriostat	<i>Soil/Environment.</i> DT ₅₀ 4–10 days undergoing loss of chlorine from the benzoic acid ring

Streptomycin
(antibiotic)

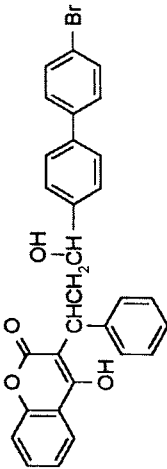
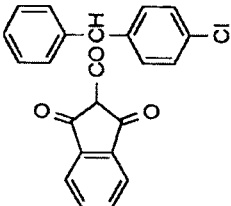


Inhibits protein synthesis by binding to the 30S ribosomal subunit, causing a misreading of the genetic code

Bactericide with systemic action

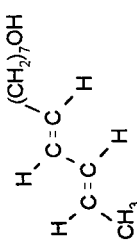
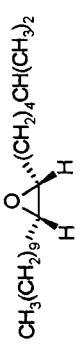
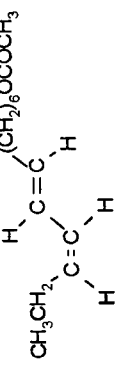
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TABLE 17.13 Rodenticides

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Bromadiolone (Coumarin anticoagulant)		Second generation anticoagulant rodenticide which also blocks prothrombin formation	—	<i>Soil.</i> Leaching behavior is inversely related to clay and organic matter content of soils. In soil column and soil layer studies, 97% was remaining in the top soil, with 0.1% in leachate
Phosphine ^a	PH_3	—	Respiratory, metabolic and nerve poison. Evolves nonflammable mixture of phosphine, ammonia and carbon dioxide	<i>Animals.</i> Phosphine is probably metabolised to nontoxic phosphates <i>Plants.</i> In stored products, phosphine undergoes oxidation to phosphoric acid
Chlorophacinone (Indandione anticoagulant)		Blocks prothrombin formation and uncouples oxidative phosphorylation	—	<i>Animals.</i> 90% is eliminated in the feces within 48 hr in the form of metabolites

^aIncludes aluminium phosphide, zinc phosphide, magnesium phosphide.

TABLE 17.14 Insect Pheromones

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Codlemone (Pheromone)		—	Acts by disruption of mating, either in trapping or in disorientation mode	<i>Plants.</i> Rapidly oxidized on the surface of leaves <i>Soil.</i> Rapidly degraded in soil to CO ₂
Disparlure (Pheromone)		—	Acts both as an attractant and as a mating disruptant	—
Dodeca-7,9-dienyl Acetate (Pheromone)	 <p>(7E,9Z)- isomer</p>	—	Acts as an attractant and by disruption of mating in the disorientation mode	—

(continued)

TABLE 17.14 Continued

<i>Chemical (Chemical Class)</i>	<i>Structure</i>	<i>Biochemistry</i>	<i>Mode of Action</i>	<i>Environmental Fate</i>
Gossypure (Pheromone)	<p style="text-align: center;">(Z,Z) -</p>	—	Acts as an attractant and by disruption of mating	—
Methyl eugenol (Synthetic pheromone)	<p style="text-align: center;">(Z,E) -</p>	—	Synthetic attractant	—

plant species and are shared among genes, which can provide resistance to viruses, fungi, bacteria, nematodes, and insects. It may be possible to design durable resistance genes that have a broad spectrum of activity. Modification of genes controlling key steps in signal-transduction pathways and resulting in the generation of defense responses may influence the speed and type of plant response. This may then lead to pest and disease resistance. Herbicide tolerance is already widely used in the United States. Genetic modification of secondary plant metabolism through the synthesis of novel toxins or increased levels of existing toxins and through synthesis of molecules which regulate pest or pathogens colonization, development or morphogenesis may enhance crop resistance to pests and pathogens. Knowledge of plant signaling processes and the role of secondary plant metabolites in regulating insect behavior offer opportunities to manipulate relevant biosynthetic pathways. This, in turn, may increase the ability of plants to deter pest colonization, inhibit pest development and reproduction, and attract natural enemies of its pests through semiochemical production.

Genes of microbial, animal or plant origin, coding for toxins, inhibitors of pathogenicity factors, such as the lecithins, or degradative enzymes, such as chitinases and proteases, may enhance resistance to pests or pathogens when expressed in transgenic plants (e.g., genetically modified (GM) crops expressing *B. thuringiensis* (Bt) toxins) (Table 17.15). However, the effect of GM crops on predator and parasites, as well as on pollinators, need to be monitored. Also, development of resistance to GM plants by target insects requires careful monitoring. Genetically modified predators and parasites for enhanced adaptability or baculoviruses with modified genes for toxin production for enhanced efficacy of viruses as biological control agents are currently being investigated. Virus resistant squash and papaya are already available in U.S. markets. Good levels of antibody expression in plants have not yet been

achieved due to technical problems. Discovery of new essential processes of pests and pathogens and their genetic make-up/gene function could lead to novel chemistries having such processes as target systems. Combination of genomics and biochemical screening procedures may lead to a range of new chemical control methods for agrochemical industry while increasing the screening rates of the molecules. Genetic processes are also used to understand pesticide resistance within pest populations, leading to high-resolution diagnostics for resistant alleles, especially for pests with multiple resistance mechanisms. Molecular techniques, used in ecological research to elucidate the structure of populations and to estimate gene flow between populations occupying discrete habitat patches, help in the formation of ecological modification strategies for maintaining biodiversity as farmland promoting sustainable pest management. The risk assessment of the release of GM organisms in the environment may be aided by assessing the gene flow among populations in agricultural systems.

Regulatory Scene Regarding Products of Biotechnology

The health effects of eating genetically modified foodstuffs, especially the allergenicity, are being investigated by the FAO/WHO Codex Alimentarius Commission, and its relevant subsidiary bodies have reflected the result of these studies. An Intergovernmental Task Force of Foods Derived from Biotechnology is being established to develop standards, guidelines, and recommendations as deemed to be appropriate for foods developed through biotechnology.

In the United States, the U.S. Department of Agriculture (USDA), EPA, and FDA are involved in the regulation of products of biotechnology. State and federal statutes and standards must be satisfied prior to registration. At present, no requirements are in place for the varietal registration of new crops. The

TABLE 17.15 Biological Agents

<i>Biological Agents</i>	<i>Usage</i>
<i>Amblyseius</i> spp. (a number of predatory mite species)	Control of thrips
<i>Anagrus otomus</i>	A wasp, parasite of leafhoppers
<i>Aphelinus abdominalis</i>	A wasp, parasite of aphids used in protected crops
<i>Aphidius colemani</i>	A wasp, parasite of aphids used in protected crops
<i>Aphidoletes aphidimyza</i>	Predatory midge, consumer of aphids in protected crops
<i>Chrysoperla carnea</i>	Entomophagus lacewing larva
<i>Cryptolaemus montrouzieri</i>	Beetle, consumer of mealybugs used in orchards, vines, and protected crops
<i>Dacnusa sibirica</i>	A wasp, parasite of leaf miners used in protected crops
<i>Diglyphus isaea</i>	A wasp, parasite of leaf miners
<i>Encarsia formosa</i>	A wasp, parasite of glasshouse whitefly—most widely used
<i>Hippodamia convergens</i>	Ladybird—consumer of aphids and other pests
<i>Leptomastix dactylopii</i>	A wasp, parasite of mealybugs used in horticultural and fruit crops
<i>Metaphycus holvodus</i>	A wasp, parasite of soft scales used in orchards and in protected crops
<i>Orius</i> spp.	Predatory bug. A number of species are used for control of thrips
<i>Phytoseiulus persimillus</i>	Spider mite consuming mite, used in protected crops
<i>Trichogramma</i> spp.	A number of species of wasp, parasitic of Lepidoptera in protected crops
<i>Bacillus sphaericus</i>	Used against mosquito larvae
<i>Beauveria bassiana</i>	Entomopathogenic fungus under development for use on control of a wide range of coleopteran, homopteran, and heteropteran pests
<i>Helicoverpa zea NPV</i>	Nuclear polyhedrosis virus used for control of heliothis and <i>Helicoverpa</i> in cotton and tobacco
<i>Heterorhabditis bacteriophora</i> and <i>H. megidis</i>	Insect parasitic nematodes used for control of Japanese beetles, black vine weevils, etc.
<i>Mamestra brassicae NPV</i>	NPV used for control of lepidoptera
<i>Metarhizium anisopliae</i>	Entomopathogenic fungus under development for control of locusts
<i>Spodoptera exigua NPV</i>	For control of beef armyworm in various crops
<i>Steinernema</i> spp.	Parasitic nematode that searches for enters and kills target pests
<i>Ampelomyces quisqualis</i>	Hyperparasite of the Erysiphaceae genus, which causes powdery mildew diseases
<i>Bacillus subtilis</i>	Seed treatment for control of <i>Rizoctonia solani</i> , <i>Fusarium</i> spp., <i>Alternaria</i> spp., <i>Aspergillus</i> spp., etc. in cotton, legumes of other crops
<i>Candida oleophila</i>	Selective fungal antagonist for control of post harvest disease in citrus and pome fruit
<i>Eilicocladium</i> spp.	Used for the control of foliar pathogens in seedlings and as a post-harvest treatment. <i>G. vorens</i> is used for the control of soil diseases
<i>Streptomyces griseoviridis</i>	Bacterium used for control of <i>Fasaurium</i> and other pathogens
<i>Trichoderma</i> spp.	Mitosporic fungi used for control of range of soil/foliar pathogens
<i>Microlarinus lareynii</i>	Attacks seedheads of puncture vine
<i>Urophora sirunasova</i>	Gallfly attacks seedhead of yellow star thistle
<i>Bangastemus orientalis</i>	Weevil—attacks seedhead of yellow star thistle
<i>Coleophora parthenica</i>	Attacks stem of Russian thistle

following table gives a picture of the present regulatory review process. the structural features of such secondary metabolites will act as important leads in the

<i>New Trait/Organism</i>	<i>Regulatory Review Conducted by</i>	<i>Reviewed for</i>
Viral resistance in food crop	USDA EPA FDA	Safe to grow Safe for the environment Safe to eat
Herbicide tolerance in food crop	USDA EPA FDA	Safe to grow New use of companion herbicide Safe to eat
Herbicide tolerance in ornamental crop	USDA EPA	Safe to grow New use of companion herbicide
Modified oil content in food crop	USDA FDA	Safe to grow Safe to eat
Modified flower color ornamental crop	USDA	Safe to grow
Modified soil bacteria Degrades pollutants	EPA	Safe for environment

FUTURE DIRECTIONS

Allelopathy

Herbicides comprise 60–70 percent of total usage of pesticides in developed countries. Plants develop resistance to herbicides which in turn demands altered management strategies through improved herbicides and/or herbicide mixtures. This may involve different modes of action, for short-term efficacy and long-term control to be effective.

Allelopathy is the action of secondary metabolites in plants, algae, bacteria or fungi, which influences the growth and development of other species. This may help in overcoming such problems of resistance through development of crop varieties having greater ability to smother weeds, use of natural phytotoxins from plants or microbes as herbicides, and use of synthetic derivatives of natural products as herbicides. Another way allelopathy may be used in agriculture is through isolation, identification, and synthesis of the active compounds from an allelopathic plant or a microorganisms species. Knowledge of

development of future herbicides to tackle resistance phenomena.

Biorational Approach to Chemical Synthesis

Knowledge of pest biochemistry will open multiple target sites to which agrochemicals of appropriate structure could be directed. This is to say that new modes of action will emerge and may overcome some of the presently unmet needs. These include such items as:

- Need for insecticides with *multiple modes of action*
- Need for *higher selectivity* herbicides to control weeds that resemble the main crop
- Fungicides and insecticides of *high safety* to preserve agricultural produce
- Control agents for plant intake to *minimize damage* from soil fungi, soil insects, and nematodes
- *Safer and more effective* rodenticides and bird repellants
- Antivirals and antibacterials

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