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PYRIMIDINE CHEMISTRY IN CROP PROTECTION¹

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Abstract - This review aims to give an overview of the significance of pyrimidine derivatives in crop protection. The main herbicidally, fungicidally and insecticidally active pyrimidine classes are presented, together with their synthetic routes, their modes of action and their biological efficacies. Quinazolines and other bicyclic pyrimidine derivatives are also covered.

CONTENTS

1 INTRODUCTION

2 HERBICIDES

- 2.1 Sulfonylureas
- 2.2 Triazolopyrimidine Sulfonanilides
- 2.3 Uracils
- 2.4 Miscellaneous Herbicidally Active Pyrimidines

3 FUNGICIDES

- 3.1 Strobilurins
- 3.2 Anilinopyrimidines
- 3.3 Miscellaneous Fungicidally Active Pyrimidines

4 INSECTICIDES

- 4.1 Complex I Inhibitors
- 4.2 Miscellaneous Insecticidally Active Pyrimidines

5 PYRIMIDINE AS AN ISOSTERIC REPLACEMENT FOR OTHER HETEROCYCLES

- 5.1 Herbicidally Active Pyrimidines
- 5.2 Fungicidally Active Pyrimidines
- 5.3 Insecticidally Active Pyrimidines

6 CONCLUSION

1 INTRODUCTION

Pyrimidine is probably the most important diazine. Pyrimidine is essential for any form of life due to its presence in all naturally occurring nucleobases. Since the discovery of the first pyrimidine derivative in 1818,² there has been a great interest in this heterocycle as a component of agrochemicals or pharmaceuticals. The progress in the extensive preparative and theoretical investigations on pyrimidines³ and quinazolines⁴ has been summarized periodically in exhaustive reviews. In addition, specific facets of the chemistry of pyrimidines and quinoxalines, such as their metallation,⁵ their *N*-oxides,⁶ their oxo derivatives⁷ or their name reactions, such as the Biginelli reaction⁸ and the Pinner reaction,⁹ have been reviewed recently. This review deals with the agrochemical aspects of pyrimidines and their bicyclic derivatives. All pesticidally active nucleosides with a pyrimidine or purine nucleobase have already been covered already in the preceding issue of this series of reviews on chemistry in crop protection.¹

2 HERBICIDES

2.1 Sulfonylureas

Sulfonylurea herbicides¹⁰⁻¹² inhibit *acetolactate synthase* (ALS), an enzyme involved in the early stage of the biosynthesis of branched-chain amino acids, resulting in a rapid cessation of plant cell division and growth.¹³ The three branched-chain amino acids valine, leucine and isoleucine are called “essential” because mammals lack biosynthetic pathways to produce them and therefore must obtain them from their diet. This selectivity towards plants undoubtedly contributes to the favorable environmental and toxicology profile of sulfonylureas. Other features such as high efficacy and thus extremely low use rates (5 – 30 g/ha) as well as excellent crop selectivity meant that the discovery of sulfonylureas in 1975 by G. Levitt at DuPont¹⁴ was the beginning of a completely new era in chemical weed control. The subsequent tremendous worldwide research and development effort has led to the commercialisation of, so far, 22 different pyrimidine sulfonylureas for selective weed control in over a dozen major crops.

Sulfometuron-methyl (**5**),¹⁵ one of the first pyrimidine sulfonylureas on the market, clearly demonstrates the structure-activity requirements: two rings are linked *via* a sulfonylurea bridge. The sulfonyl moiety is usually connected to a phenyl ring with an electron-withdrawing *ortho*-substituent. Linked to the amine end of the sulfonylurea bridge is most often a 2-pyrimidine bearing two alkyl and / or alkoxy substituents in the 4- and 6-positions. Even small alterations from this basic structure lead to distinct differences in the selectivity between crop and weed plants. Nevertheless, many variations of this general structure are known. The phenyl ring can be replaced by a five-membered¹⁶ or six-membered¹⁷ heterocycle, as in pyrazosulfuron-ethyl (**1**) and nicosulfuron (**2**), a bicyclic system,¹⁸ as in **3** or even by an acyclic chain,¹⁹

connected to the phenyl ring *via* a methylene group, as in bensulfuron-methyl (**9**),²⁰ a nitrogen atom, as in orthosulfamuron (**8**)²¹ or an oxygen atom, as in ethoxysulfuron (**7**).²²

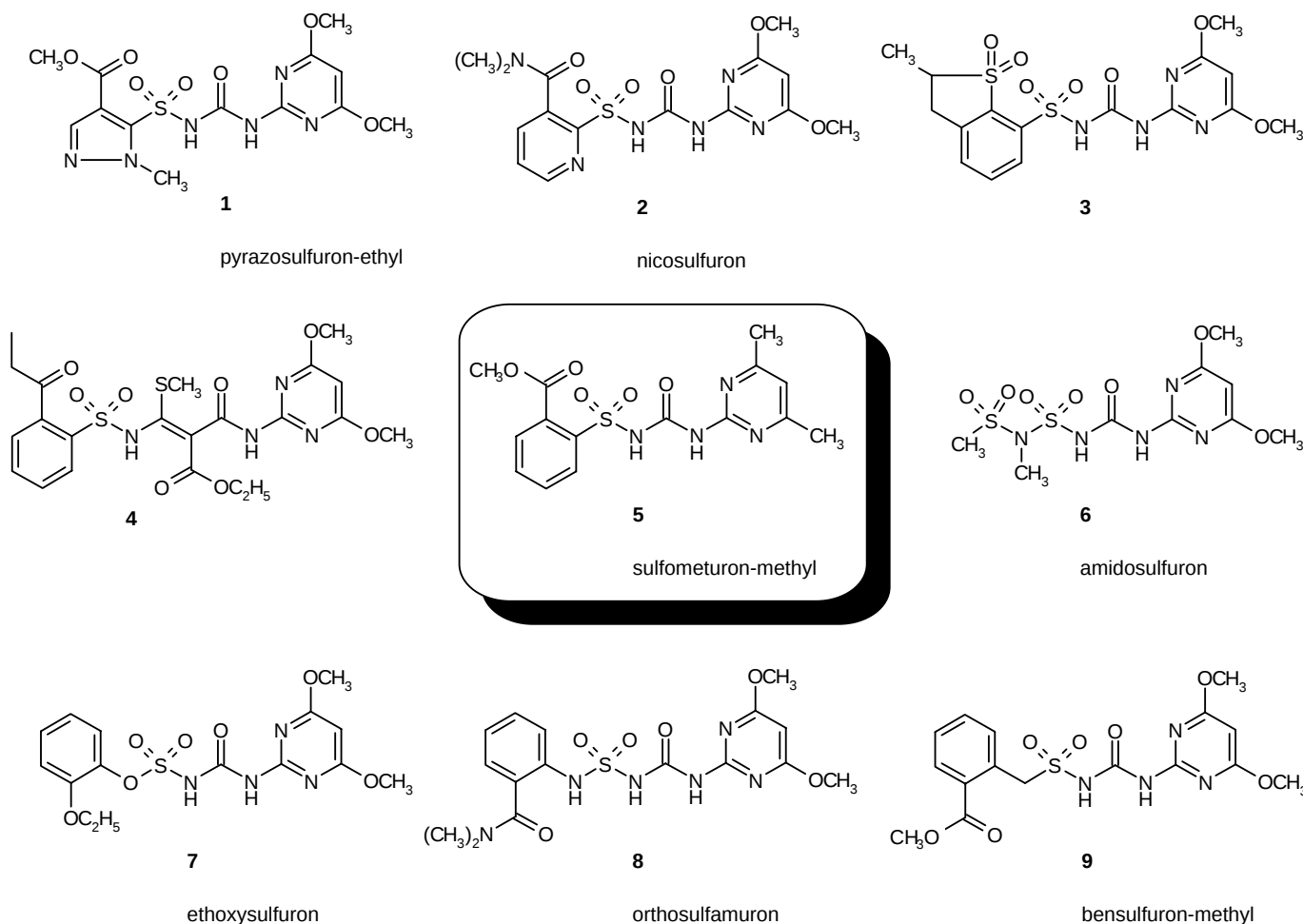


Figure 1

Furthermore, the elongation of the sulfonyl urea bridge to a vinylogous sulfonyl urea,²³ as in **4**, or the shortening to a sulfonylamide,²⁴ as in **10**, a sulfide,²⁵ as in pyriftalid (**11**), or to an ether,²⁶ as in pyriminobac-methyl (**12**), while the other typical structural elements, leads to very active ALS inhibitors (Figure 2). The methyl or methoxy substituents in the pyrimidine ring can be replaced by halogen or haloalkoxy groups, as in chlorimuron-ethyl (**14**)²⁷ and primisulfuron-methyl (**17**).²⁸ Last, but not least, a very important variation of pyrimidine sulfonylurea herbicides is the replacement of the pyrimidine ring by a similar substituted triazine, as demonstrated by metsulfuron-methyl (**16**).²⁹ Also the application of pyridine, as in **13**, and pyrazine rings, as in **15**, as pyrimidine replacements have been described.³⁰

The substitution pattern of the pyrimidine ring usually exerts a strong influence on the selectivity of the sulfonylurea herbicides, which means the tolerance against crop plants. Therefore a thorough exploration of 4,6-disubstituted 2-aminopyrimidines was undertaken. The pyrimidine sulfonylurea (**22**) is a selective post-emergence cotton herbicide with excellent activity against *Sinapis alba* (white mustard) and *Stellaria*

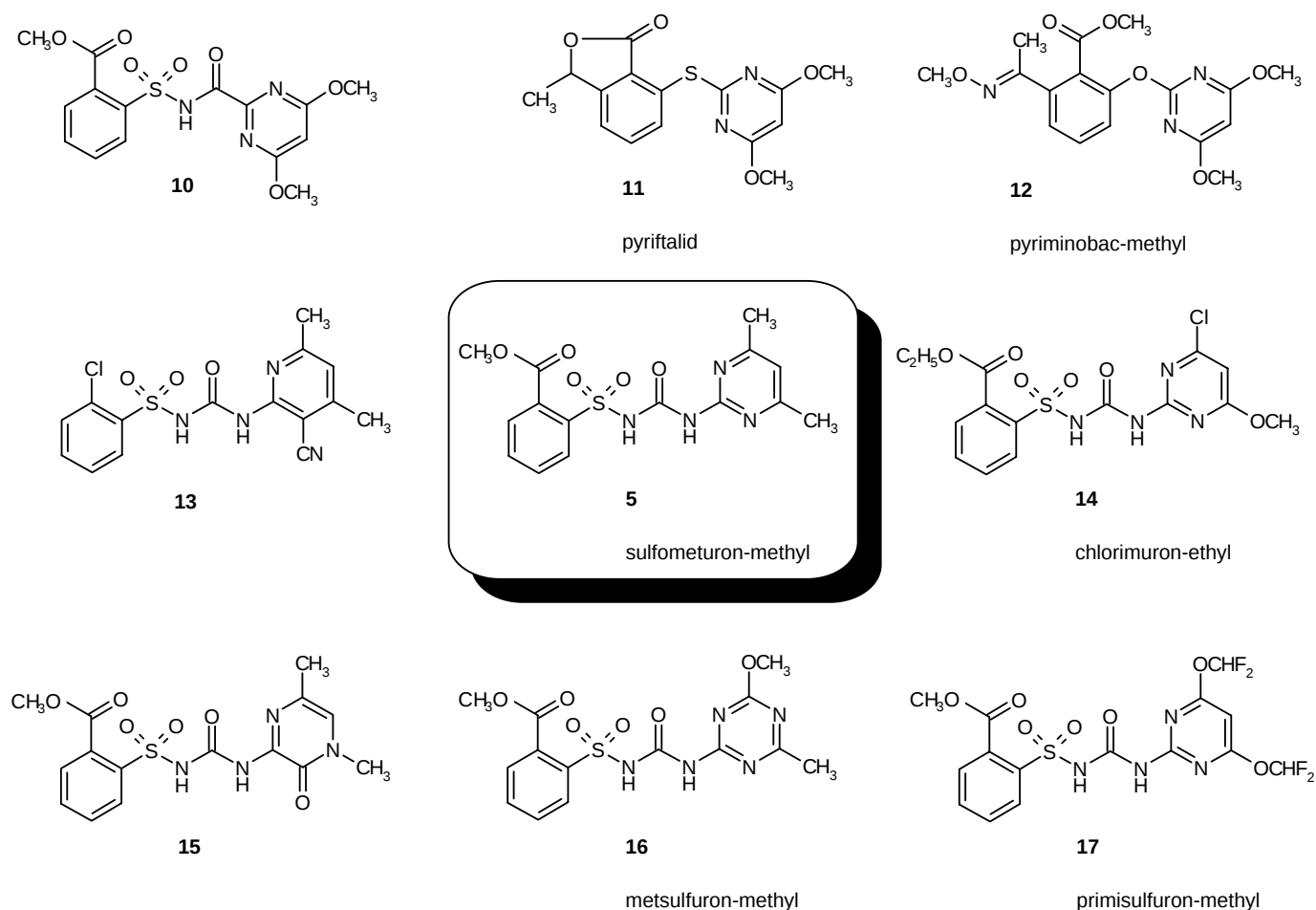
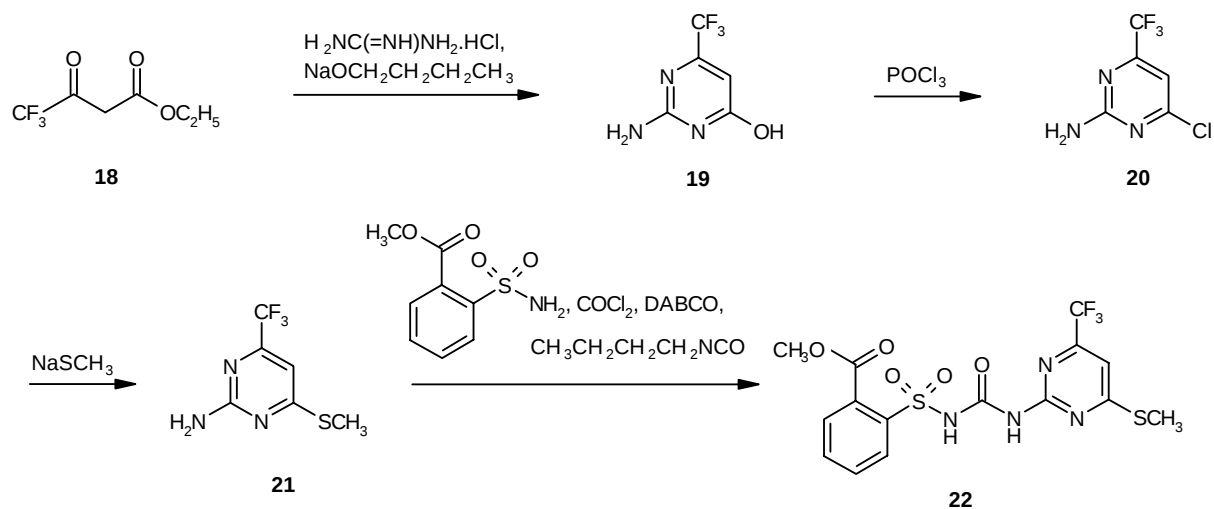


Figure 2

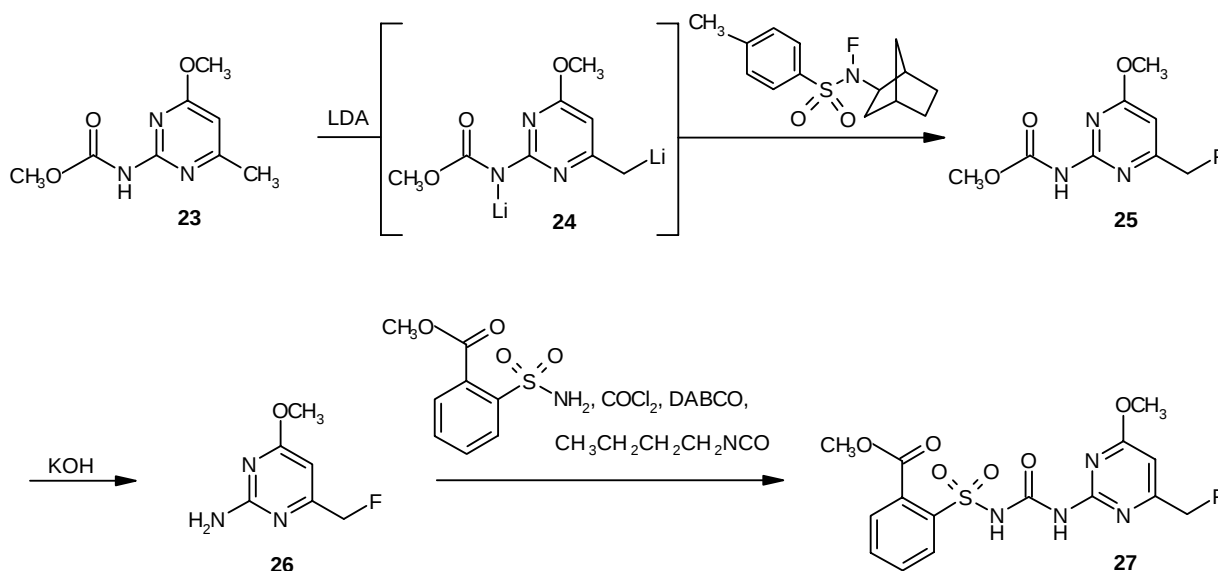
media (chickweed).³¹ It is synthesized by coupling of 2-amino-4-methylthio-6-trifluoromethylpyrimidine (21) with an appropriate sulfonyl isocyanate, which is usually prepared *in situ* from the corresponding sulfonamide (Scheme 1). The pyrimidine building block (21) is obtained in three steps by condensation of ethyl 4,4,4-trifluoroacetoacetate (18) with guanidine hydrochloride,³² subsequent chlorination with



Scheme 1

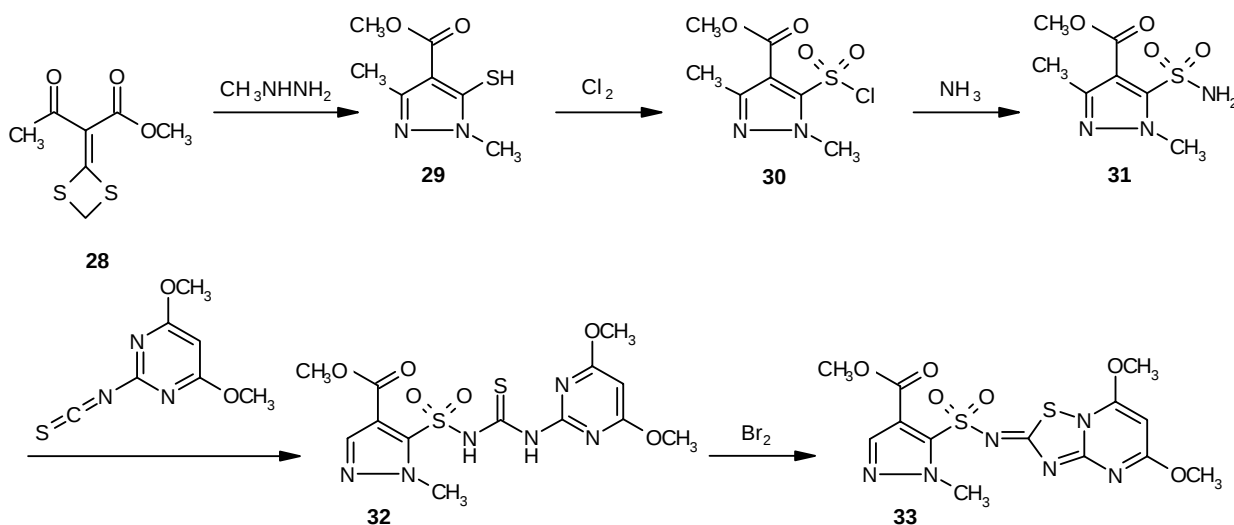
phosphorus oxychloride and finally nucleophilic substitution with sodium methylthiolate.³¹

The methyl carbamate (**23**) can be cleanly converted with two equivalents of lithium diisopropylamide into the soluble dianion (**24**), which undergoes electrophilic fluorination with *N*-(*exo*-2-norbornyl)-*N*-fluoro-*p*-toluenesulfonamide (Scheme 2).³³ The resulting carbamate (**25**) is then hydrolyzed with aqueous



Scheme 2

base to afford the 6-fluoromethylpyrimidine (**26**), which can be further transformed into sulfonylurea herbicides such as **27**.^{12,30}



Scheme 3

Sulfonylthioureas such as **32**, which can be prepared by condensation of a sulfonamide (**31**) with a pyrimidin-2-ylisothiocyanate, may be converted under oxidative conditions into herbicidally active 1,2,4-

thiadiazolo[2,3-*a*]pyrimidine derivatives such as **33** (Scheme 3).^{11,34} **33** exhibits especially good activity against *Cyperus difformis* (smallflower umbrellaplant) and *Lindernia procumbens*, an annual paddy rice weed. **33** can also be regarded as a sulfonylthiourea, with the thiourea sulfur atom linked to the pyrimidine ring, which suggests the possibility that 1,2,4-thiadiazolo[2,3-*a*]pyrimidines might act as pro-herbicides because metabolic hydrolysis could result in the active ring-opened form. Similar oxadiazolopyrimidines have also been described.³⁰

2.2 Triazolopyrimidine Sulfonanilides

Triazolopyrimidine sulfonanilide herbicides^{35,36} also inhibit acetolactate synthase (ALS).³⁷ This class of compounds, which was discovered in the mid-1980's at Dow, closely related in structure to the sulfonylureas, having some parts of the sulfonylurea bridge inverted and other parts of it incorporated into a five-membered ring, which is annelated to the sulfonylurea pyrimidine. They are very effective for controlling various broadleaf and grass weed species at low doses while maintaining high levels of selectivity to agronomically important crop species such as corn, soybean and wheat. The seven

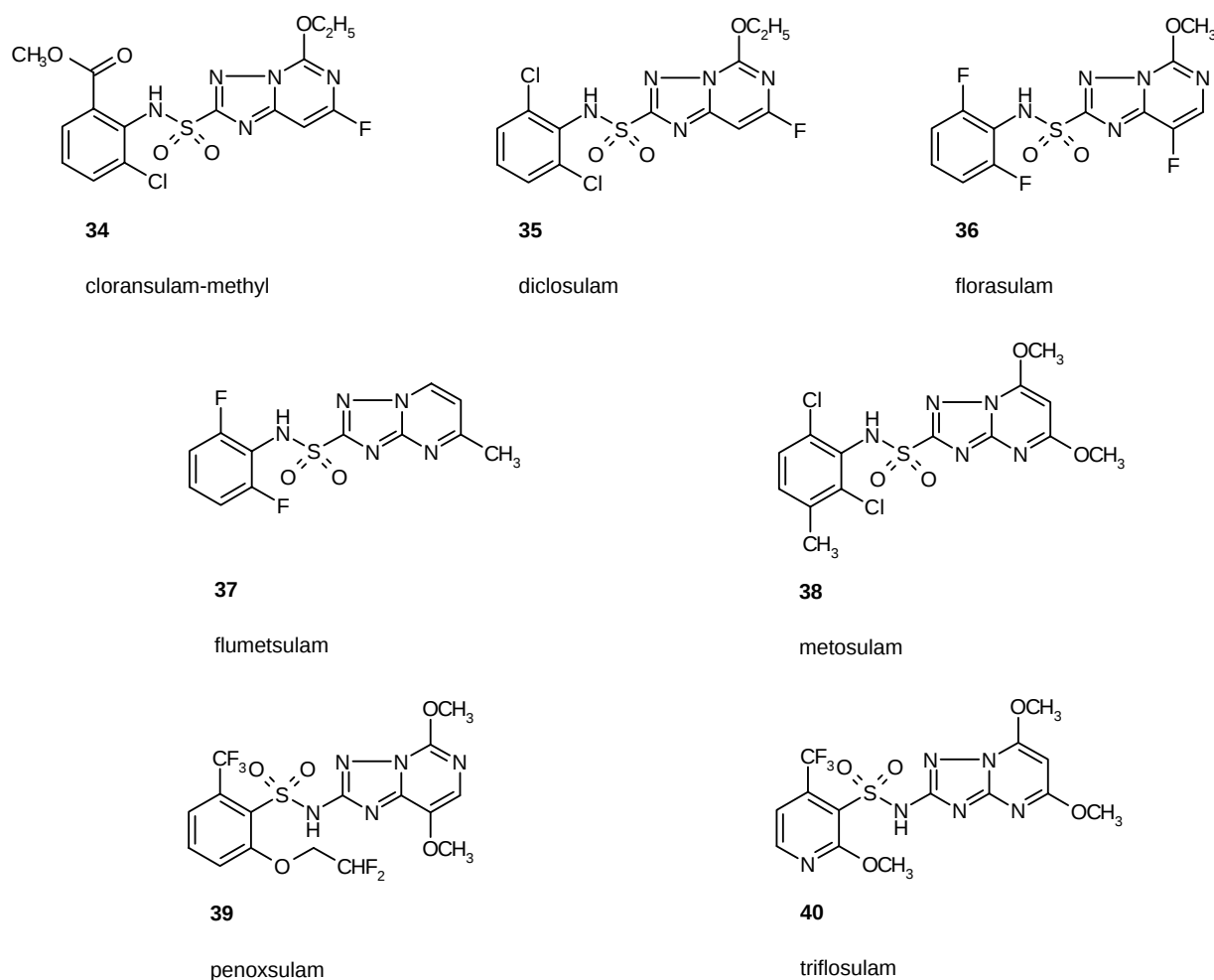
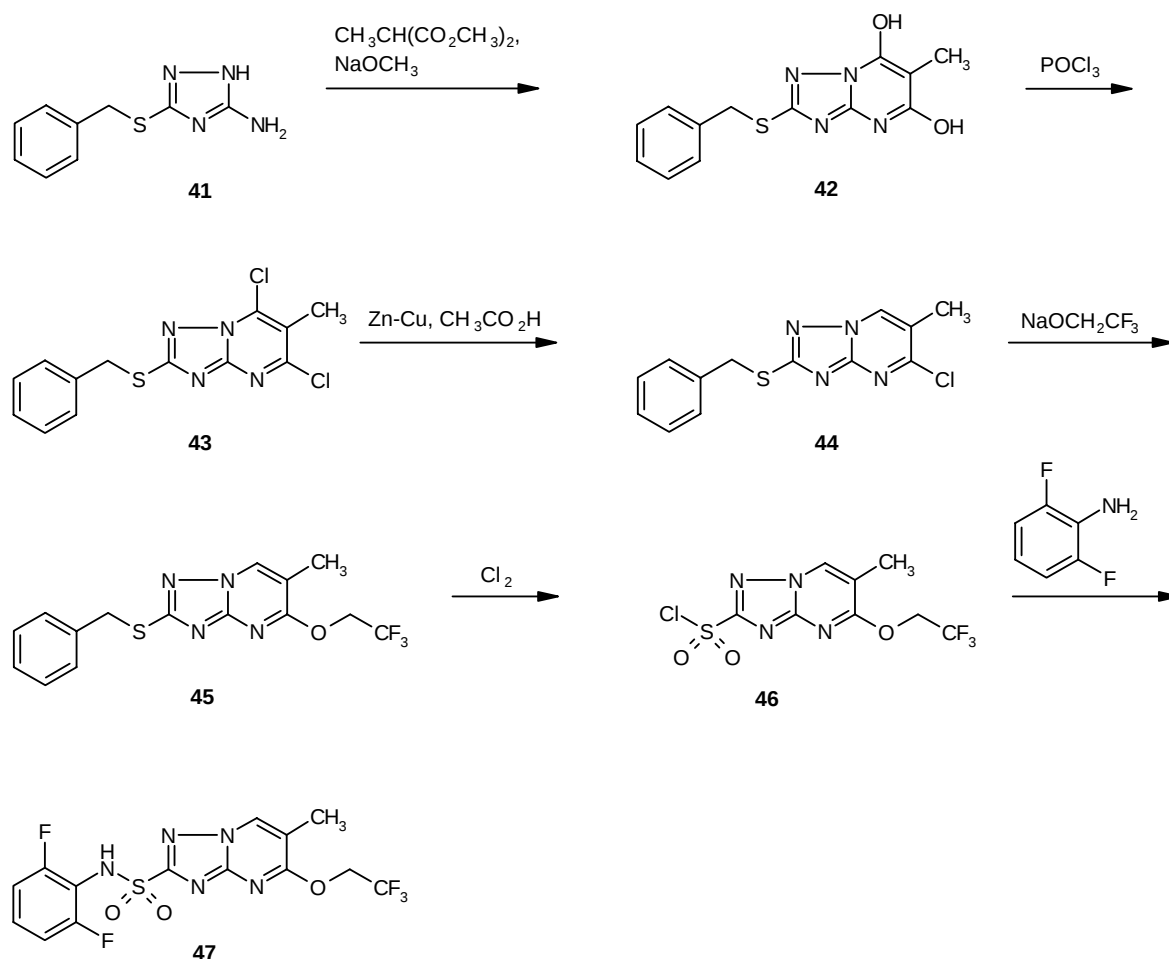


Figure 3

triazolopyrimidine sulfonanilide herbicides commercialised so far are displayed in Figure 3.

The influence of halogen,³⁸ alkyl,³⁸ haloalkyl³⁸ and alkoxy³⁹ substituents in the heterocyclic portion of triazolopyrimidine sulfonanilides on their herbicidal activity was investigated thoroughly. During such structure-activity relationship studies, the synthesis of 5,6-disubstituted 1,2,4-triazolo[1,5-*a*]pyrimidine derivatives was envisaged. In the standard triazolopyrimidine synthesis from a 3-aminotriazole and a β -dicarbonyl compound, the 7-position is always occupied by a substituent.⁴⁰ The selective removal of chlorine from this 7-position in **43** with zinc-copper in the presence of acetic acid allows the straightforward synthesis of the interesting herbicide (**47**) (Scheme 4).^{35,41}



Scheme 4

Further examples of herbicidally active, fused bicyclic pyrimidine derivatives include furo[3,2-*d*]pyrimidines,⁴² thieno[2,3-*d*]pyrimidines,⁴³ pyrazolo[1,5-*a*]pyrimidines,⁴⁴ and imidazolo[1,2-*a*]pyrimidines.⁴⁵

2.3 Uracils

An important step in the biosynthesis of chlorophyll is the transformation of protoporphyrinogen-IX into protoporphyrin-IX. This dehydrogenation is catalyzed by the enzyme *protoporphyrinogen-IX-oxidase* (PPO). The inhibition of this enzyme results in the accumulation of the substrate protoporphyrinogen-IX, which acts as a kind of photosensitizer and induces the formation of radicals. These radicals attack in an uncontrolled autoxidation essential elements of the plant cell, e.g. lipids in the cell membrane, resulting in a rapid burning of parts of the plant.⁴⁶ Examples for such PPO-inhibitors are uracils, of which the commercialized ones are shown in Figure 4.

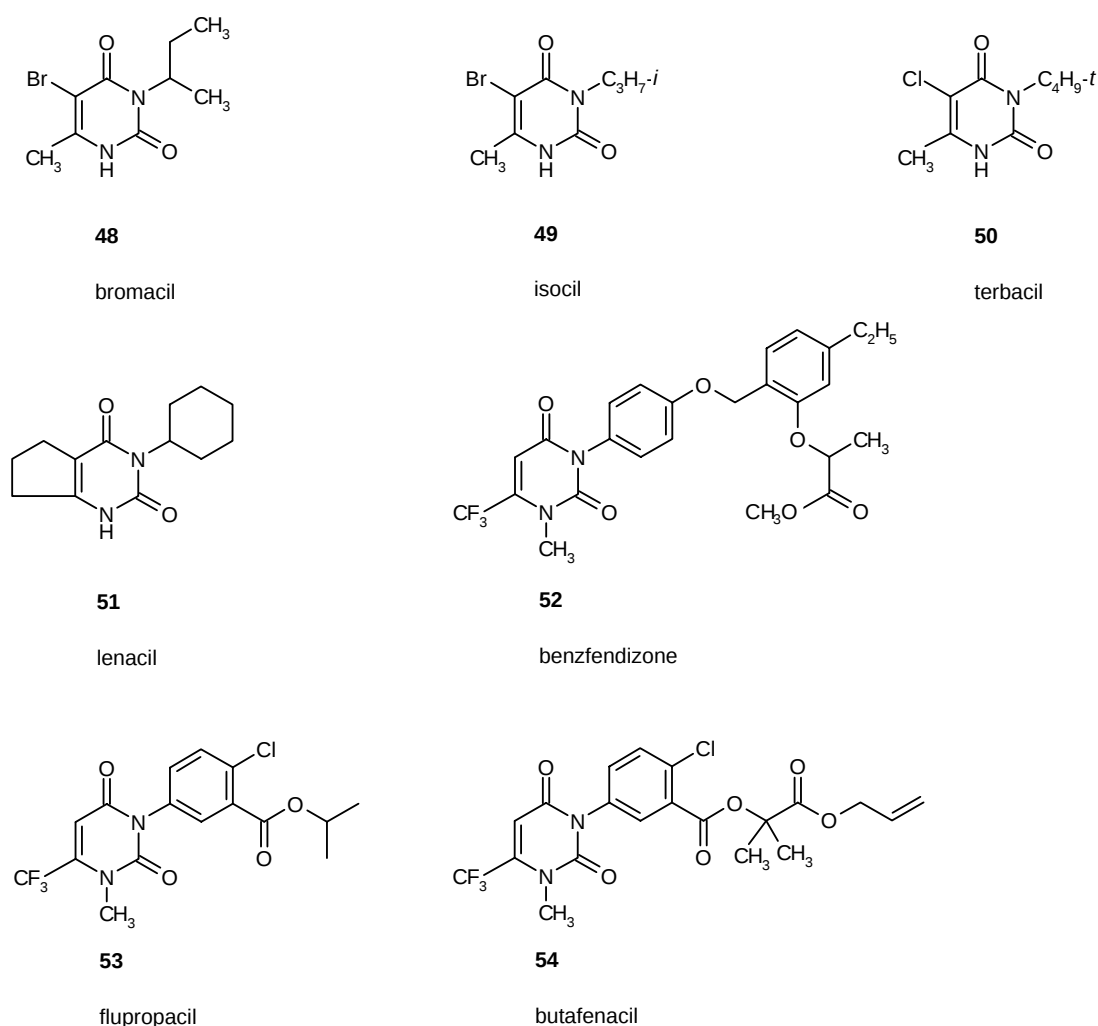
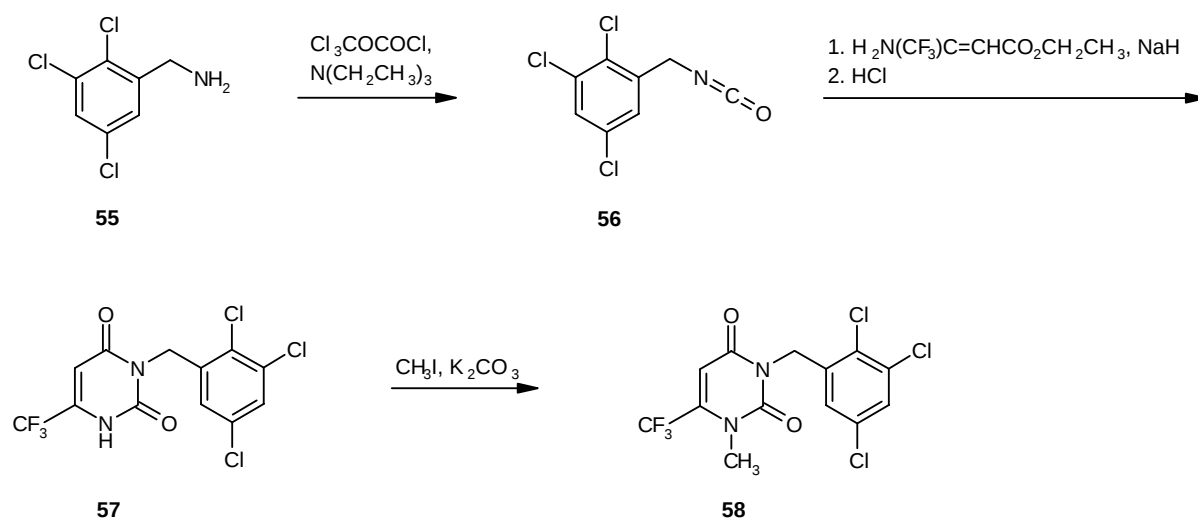


Figure 4

The 3-benzyluracil (**58**) displays good pre-emergent control of broadleaf weeds like *Abutilon theophrasti* (velvetleaf), *Amaranthus albus* (pigweed), *Convolvulus arvensis* (field bindweed), *Pharbitis purpurea* (tall morningglory), *Polygonum lapathifolium* (pale smartweed), *Solanum nigrum* (black nightshade), *Stellaria media* (chickweed), and grasses such as *Digitaria adscendens* (crabgrass), *Setaria faberii* (giant foxtail) and *Sorghum halepense* (Johnsongrass) at use rates of 10 – 30 g / ha.⁴⁷ It can be

prepared by condensation of the trichlorobenzyl isocyanate (**56**) with ethyl 3-amino-4,4,4-trifluorocrotonate and subsequent *N*-methylation (Scheme 5).⁴⁷



Scheme 5

The uracil (**59**) with a special dimethylbenzofuranone moiety possesses excellent pre-emergent efficacy against *Abutilon theophrasti* (velvetleaf) and *Pharbitis purpurea* (tall morningglory) (Figure 5).⁴⁸ The 3-alkoxyuracil (**60**) shows good activity against *Sinapis arvensis* (wild mustard) and *Lolium multiflorum*

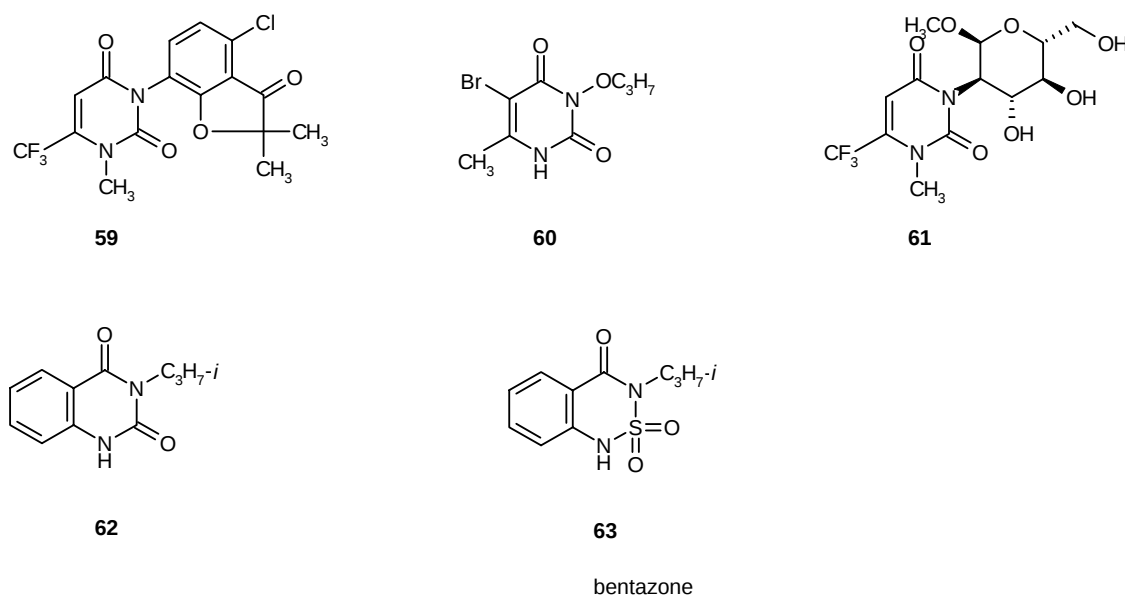


Figure 5

(Italian ryegrass).⁴⁹ Further examples of herbicidally active uracils are the glucosamine derivative (**61**)⁵⁰ and the quinazolinone (**62**).⁵¹ Analogues of the latter were prepared because of its surprising broad-

spectrum herbicidal activity against *Artemisia vulgaris* (mugwort), *Chenopodium album* (lambsquarters), *Lamium amplexicaule* (henbit), *Polygonum persicaria* (ladythumb), *Sinapis arvensis* (wild mustard), *Stellaria media* (chickweed) and *Urtica urens* (burning nettle), leading to the discovery of bentazone (**63**).⁵²

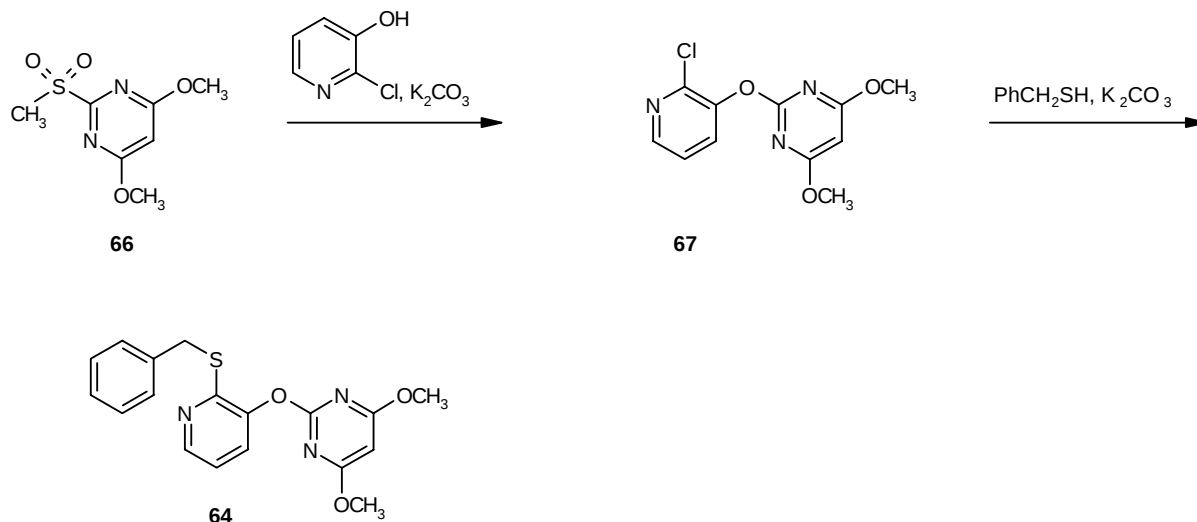
2.4 Miscellaneous Herbicidally Active Pyrimidines

We have already seen in the first two chapters that the dimethoxy substitution in a pyrimidine ring plays an important role in herbicide chemistry. In contrast to the structurally related ALS inhibitor (**65**), the pyridine derivative (**64**) acts as a bleaching herbicide and is especially active against *Echinochloa crus-galli* (barnyardgrass), *Digitaria sanguinalis* (large crabgrass), *Polygonum lapathifolium* (pale smartweed), *Scirpus mucronatus* (roughseed bulrush) and *Setaria faberii* (giant foxtail) (Figure 6).⁵³



Figure 6

The straightforward synthesis of **64** is demonstrated in Scheme 6. The nucleophilic *ipso*-substitution of the 2-pyrimidinyl sulfone⁵⁴ leads in the conversion of 4,6-dimethoxy-2-methanesulfonylpyrimidine (**66**) with 2-chloro-3-pyridinol to the 2-(pyridin-3-yloxy)pyrimidine (**67**), which is then converted with benzylmercaptan into the final product (**64**).⁵³



Scheme 6

The diarylpyrimidine (**68**)⁵⁵ and the phenoxybenzylpyrimidine (**69**)⁵⁶ are further examples of *phytoene desaturase* inhibiting bleaching herbicides (Figure 7).

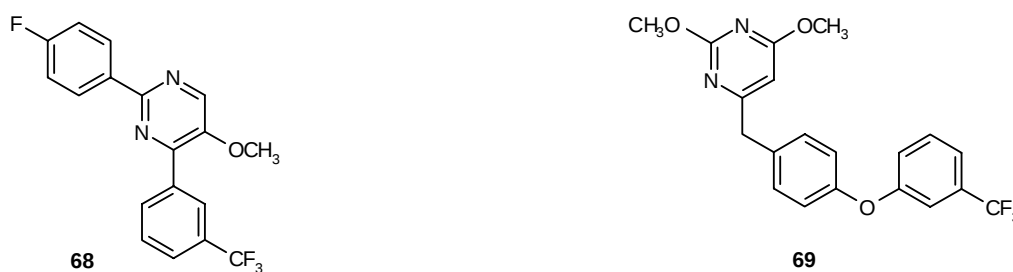
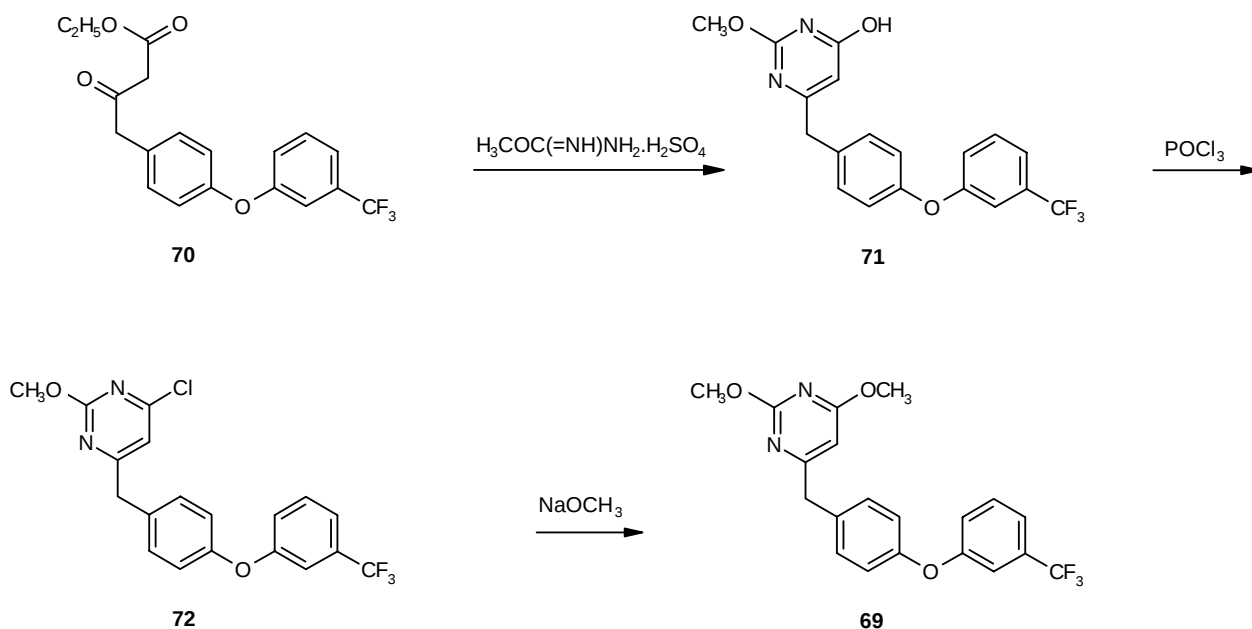


Figure 7

The simple dimethoxypyrimidine derivative (**69**) is highly active against *Echinochloa crus-galli* (barnyardgrass), *Digitaria adscendens* (crabgrass), *Polygonum lapathifolium* (pale smartweed), *Amaranthus albus* (pigweed), *Chenopodium album* (lambsquarters) and *Cyperus iria* (rice flatsedge).⁵⁶ It is prepared by condensation of *O*-methylisourea⁵⁷ with the 3-trifluoromethylphenoxyphenylacetoacetate (**70**) to give the hydroxypyrimidine (**71**), which is then converted into the desired dimethoxypyrimidine (**69**) via chlorination and methoxylation (Scheme 7).⁵⁶



Scheme 7

Pyrimisulfan (**73**)⁵⁸ and the *acetohydroxy-acid synthase*-inhibiting bis-pyrimidylpyrazolinone (**74**)⁵⁹ are further examples of the broad variety of dimethoxypyrimidine herbicides (Figure 8).

The 2-(pyrazolyl-1-yl)-4-phenoxyypyrimidine (**75**)⁶⁰ and its benzyl analog (**76**)⁶¹ displayed strong

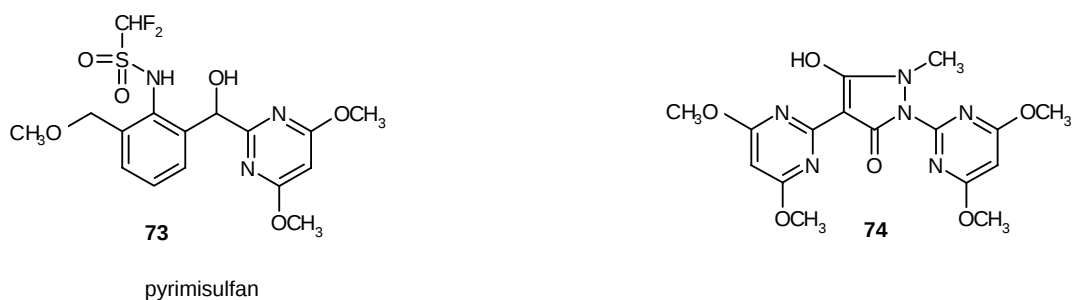


Figure 8

broadleaf weed control at use rates of 5 – 10 g / ha in cereal field trials (Figure 9). Their herbicidal activity results from the inhibition of carotenoid biosynthesis.^{60,61} The thienopyrimidine (**77**) is especially active against *Setaria faberii* (giant foxtail).⁶²

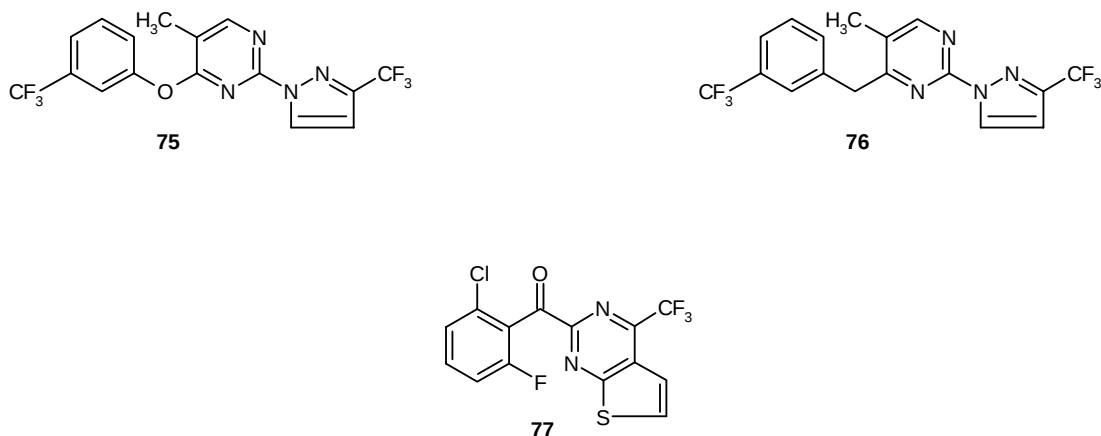


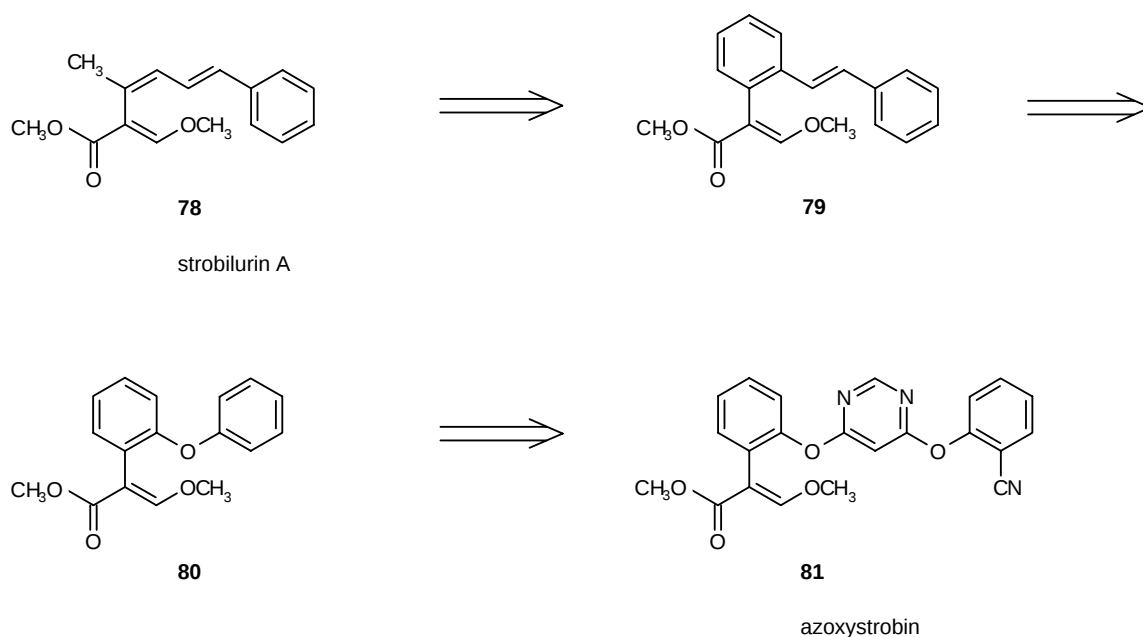
Figure 9

3 FUNGICIDES

3.1 Strobilurins

The strobilurin fungicides are inhibitors of mitochondrial respiration, by binding at the QoI site of cytochrome *bc*₁ (complex III).⁶³ Strobilurin A (**78**) was isolated from the mushroom *Strobilurus tenacellus*. Although its fungicidal properties were soon discovered, its agrobiological testing was difficult because of its photostability. The incorporation of the *Z*-olefinic bond of strobilurin A (**78**) in a phenyl ring was a first breakthrough in attempts to prepare photostable strobilurin analogues. The replacement of the stilbene double bond of **79** by an ether bridge and the exchange of the phenyl ring by a pyrimidine are further steps in the invention pathway to the broad-spectrum fungicide azoxystrobin (**81**) (Scheme 8).⁶⁴

The pyrimidine system seems to play a distinguished role in the sidechain of strobilurin fungicides, because it often results in low log P values and therefore enables the systemic movement of the



Scheme 8

compound through the plant. Figure 10 displays three commercialised strobilurins bearing a pyrimidine ring. Azoxystrobin (**81**) and fluoxastrobin (**82**) are fungicides, while fluacrypyrim (**83**) is an insecticide.

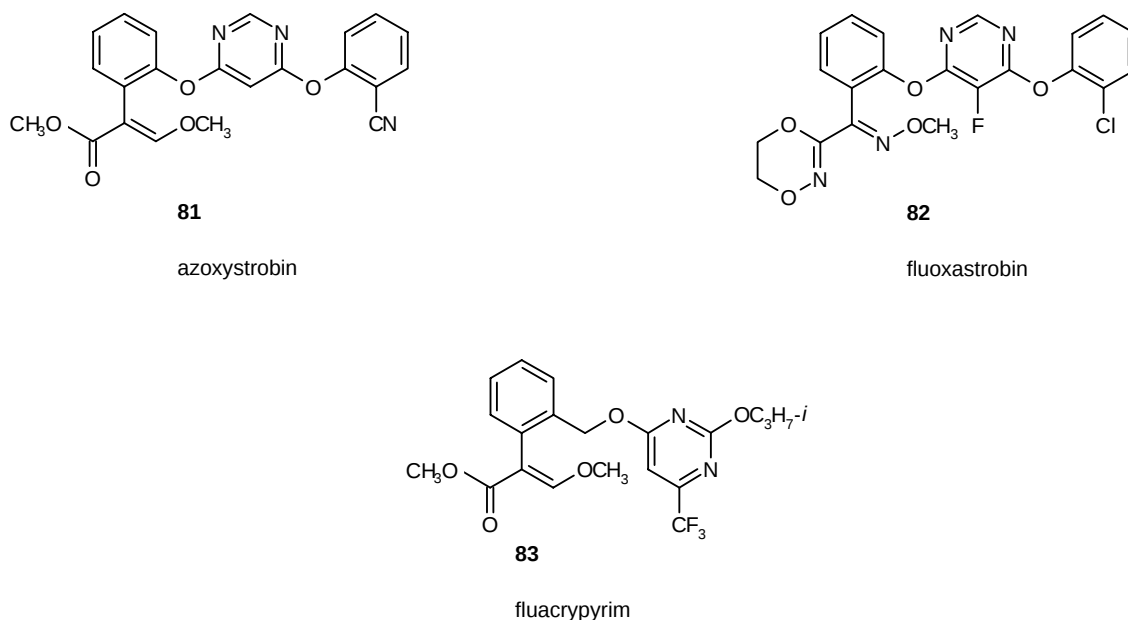
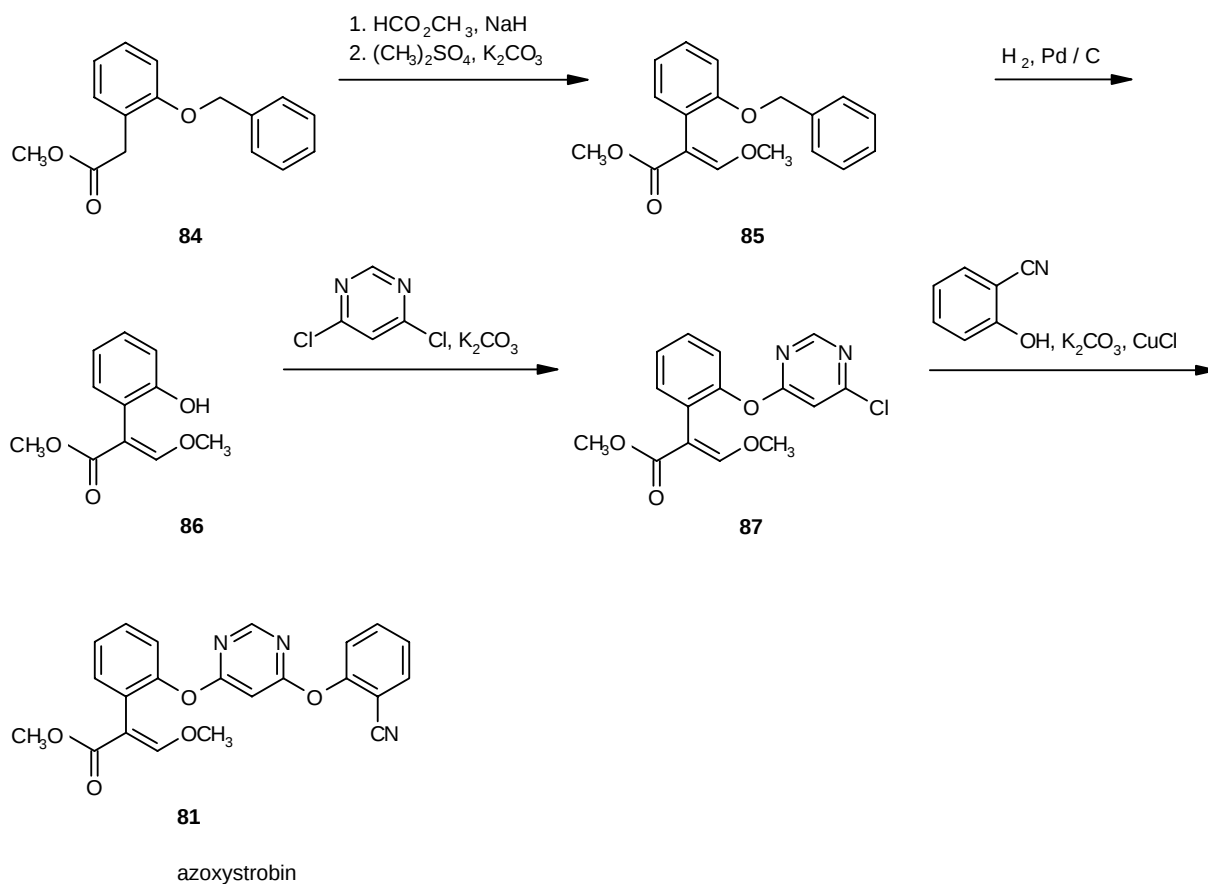


Figure 10

Key steps in the laboratory synthesis of azoxystrobin (**81**) are the consecutive aryloxylation of 4,6-dichloropyrimidine with two different phenol components. (Scheme 9).⁶⁵



Scheme 9

Because of the positive influence of the pyrimidine heterocycle on the physical properties as well as the biological activity of azoxystrobin (**81**), other derivatives, such as **88** and **89**,⁶⁶ have also been prepared, wherein the positions of the pyrimidine and phenyl rings have been switched (Figure 11).

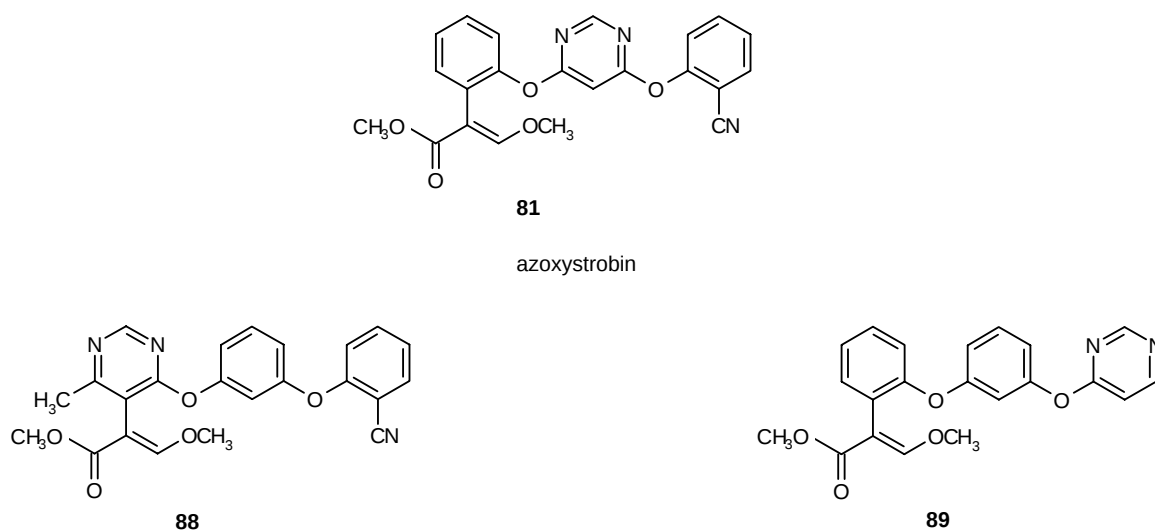
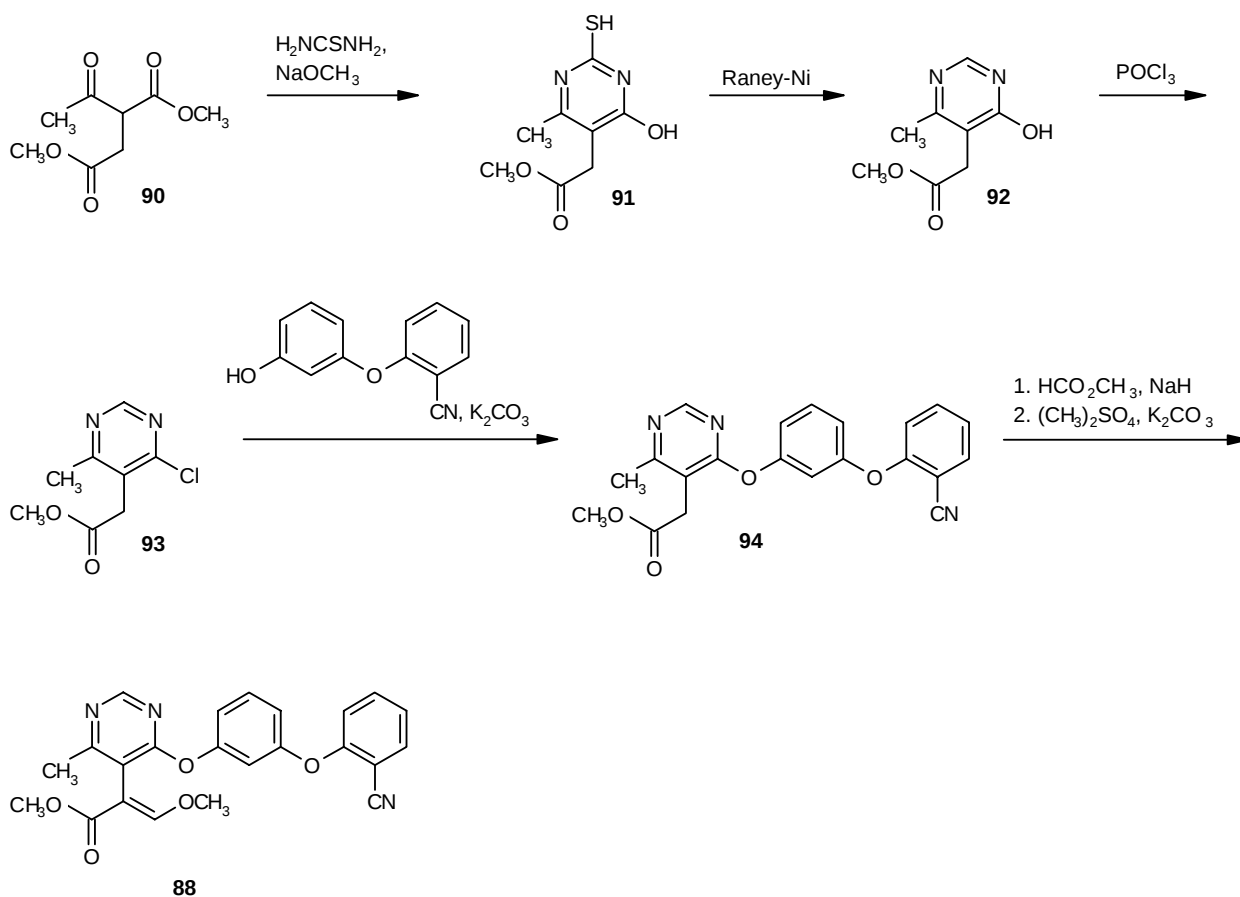


Figure 11

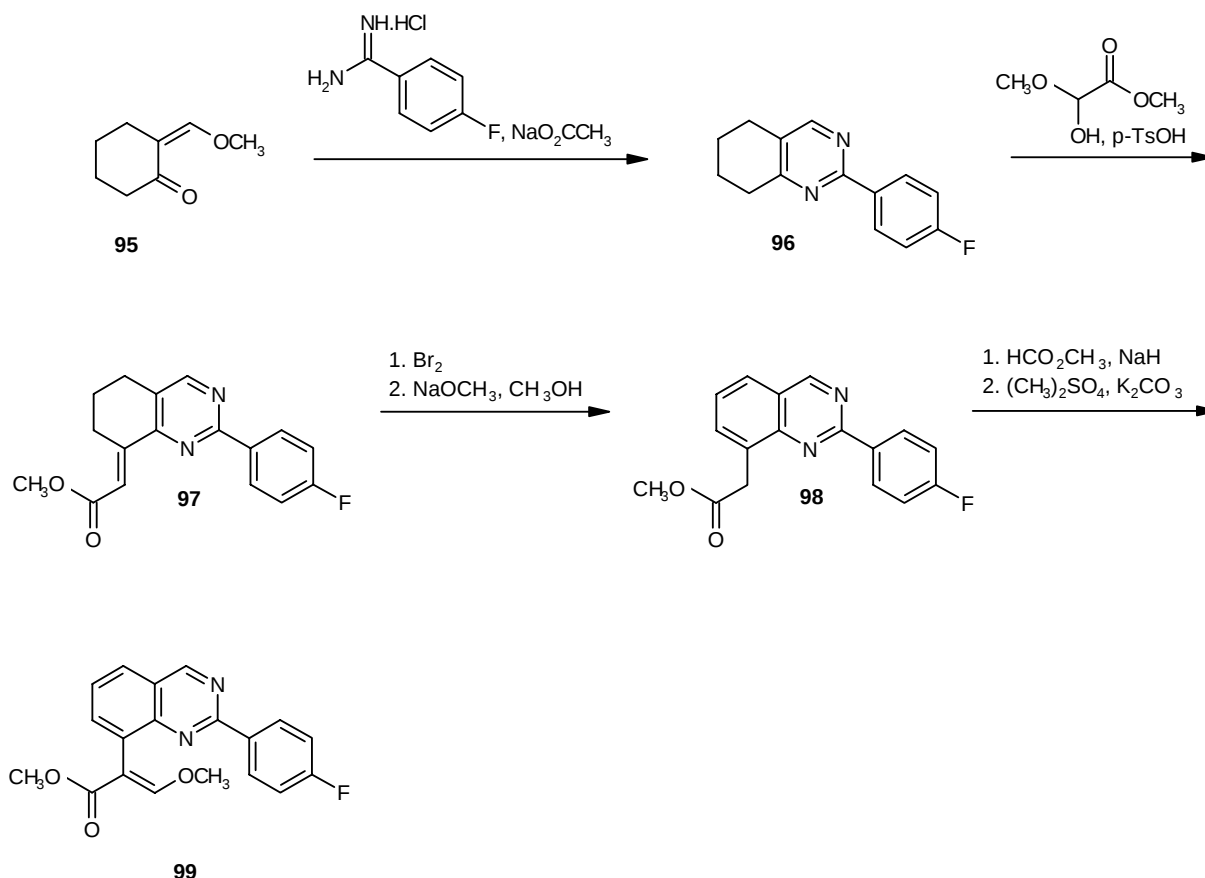
The strobilurin fungicide (**88**), having the pyrimidine ring bearing the β -methoxyacrylate pharmacophore, could be obtained by the reaction sequence shown in Scheme 10. Pinner-type condensation of dimethyl acetylsuccinate (**90**) with thiourea led to the pyrimidine (**91**), which was transformed into **93** via desulfurization and chlorination.⁶⁷ Ullmann coupling of this versatile intermediate to the phenoxyphenol sidechain and subsequent formylation and *O*-methylation resulted in the azoxystrobin analog (**88**), in which the phenyl ring bearing the β -methoxyacrylate pharmacophore and the pyrimidine ring have been exchanged. Compound (**88**) is very active against *Botrytis cinerea* (grey mould), *Puccinia recondita* (brown rust) and *Septoria nodorum* (glume blotch).



Scheme 10

The installation of the β -methoxyacrylate function in the 8-position of a 2-substituted quinazoline also led to highly active strobilurin derivatives. Their preparation starts from the condensation of 2-methoxymethylenecyclohexanone (**95**) with an appropriate amidine salt (Scheme 11). This reaction generates in good yield the 2-substituted 5,6,7,8-tetrahydroquinazoline (**96**), which can be further transformed in a regioselective aldol-type condensation with methyl glyoxylate methyl hemiacetal as carbonyl component to the acrylate (**97**).⁶⁸ The aromatization of the tetrahydroquinazoline (**97**) to the

quinazoline (**98**) is achieved by benzylic bromination with bromine followed by elimination of hydrogen bromide under basic conditions.⁶⁸ A similar aromatization of tetrahydroquinazolines has been described using *N*-bromosuccinimide as bromination agent.⁶⁹ Finally, formylation and *O*-methylation delivered the target molecule (**99**), which showed especially good activity against the cereal diseases *Erysiphe graminis* (powdery mildew) and *Puccinia recondita* (brown rust).



3.2 Anilinopyrimidines

Andoprim (**100**),⁷⁰ pyrimethanil (**101**),⁷¹ cyprodinil (**102**)⁷² and mepanipyrim (**103**)⁷³ constitute the class of anilinopyrimidines, which is very effective against phytopathogens such as *Botrytis cinerea* (grey mould), *Venturia inaequalis* (apple scab) and *Pseudocercospora herpotrichoides* (eyespot) (Figure 12). Different hypotheses have been put forward for their mode of action. These anilinopyrimidines inhibit the fungal secretion of hydrolytic enzymes such as protease, cellulase, lipase or cutinase which play an important role in the infection process.⁷⁴ On the other hand, several amino acids, particularly methionine, reverse the fungitoxicity of anilinopyrimidines.⁷⁵ Biochemical studies conducted with *Botrytis cinerea* indicated that these compounds inhibit the biosynthesis of methionine, the primary target site being cystathionine- β -lyase.⁷⁵ The anilinopyrimidines are readily accessible either by cyclocondensation of a

phenylguanidine with the appropriate β -diketone or by reacting an aniline with a suitable pyrimidine bearing a leaving group in the 2-position.

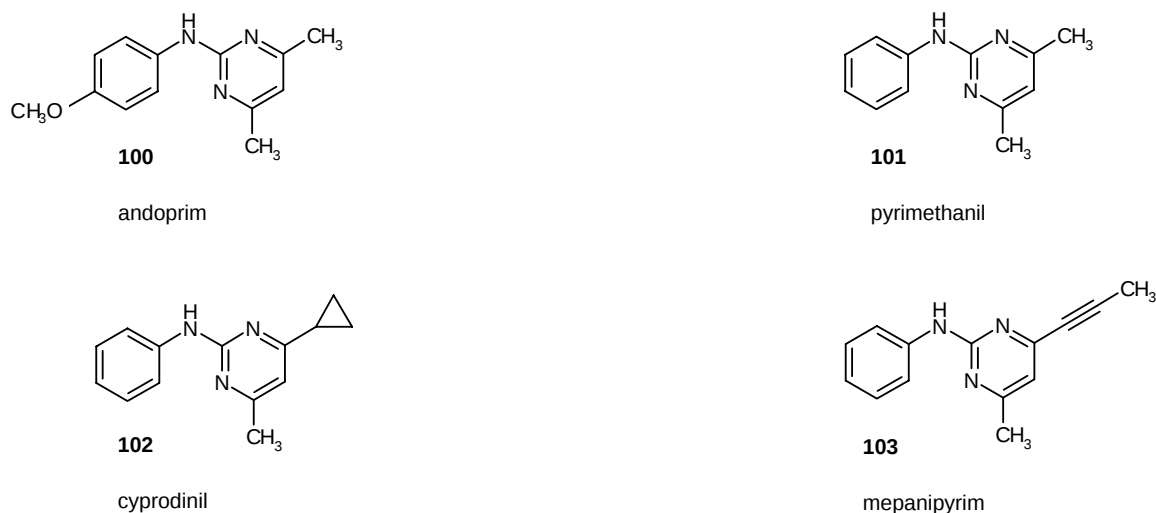
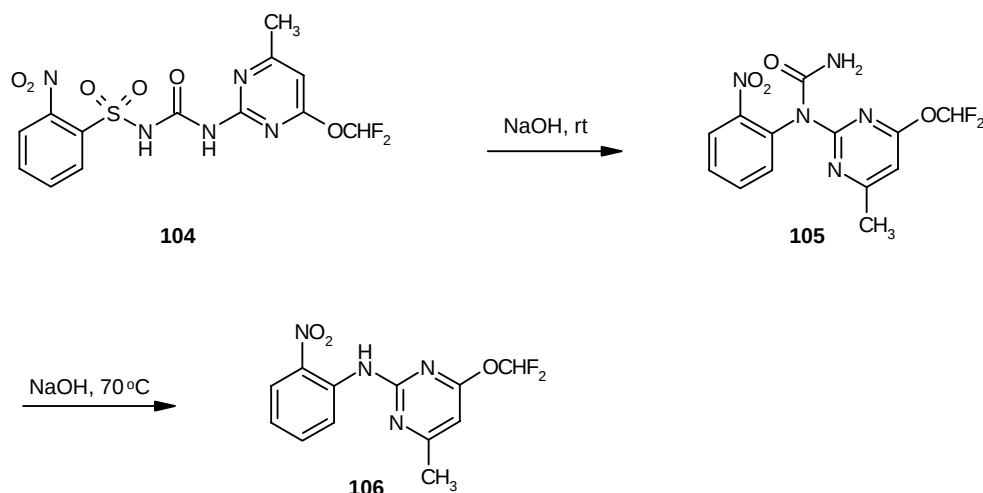


Figure 12

The fungicidally active anilinopyrimidine (**106**), which was later optimized to the commercial product cyprodinil (**102**), was coincidentally discovered during a study of the hydrolytic behaviour of the sulfonylurea herbicide (**104**) (Scheme 12).⁷² Under basic conditions, the asymmetric disubstituted urea derivative (**105**) was formed, which in turn was further hydrolyzed to the anilinopyrimidine (**106**). Similar metabolic transformations of sulfonylureas to anilinopyrimidines have also been observed in soil.⁷⁶



Scheme 12

The pyrimidinylhydrazone ferimzone (**107**)⁷⁷ and its cyclic analog (**108**)⁷⁸ are a kind of vinylogous anilinopyrimidines (Figure 13). Both compounds are very active against *Erysiphe graminis* (powdery

mildew), *Septoria nodorum* (glume blotch) and *Magnaporthe grisea* (rice blast).



Figure 13

Also the class of pyrimidinol fungicides possesses striking similarities to the anilinopyrimidines (Figure 14).⁷⁹

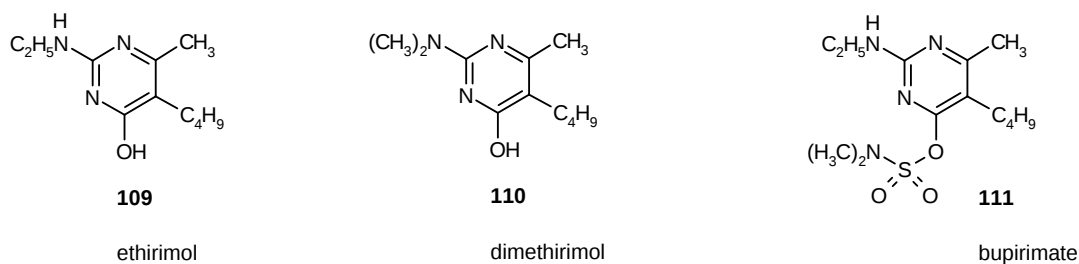


Figure 14

3.3 Miscellaneous Fungicidally Active Pyrimidines

The pyrimidin-5-ylmethanol fungicides fenarimol (**112**), nuarimol (**113**) and triarimol (**114**) exhibit protective and curative action against a variety of fungal diseases, including *Erysiphe graminis* (cereal powdery mildew), *Uncinula necator* (grape powdery mildew), *Venturia inaequalis* (apple scab) and *Sclerotinia fruticola* (peach brown rot) (Figure 15).⁸⁰ They are, like the large and commercially important family of triazole fungicides, inhibitors of sterol biosynthesis in fungi by preventing C-14 demethylation

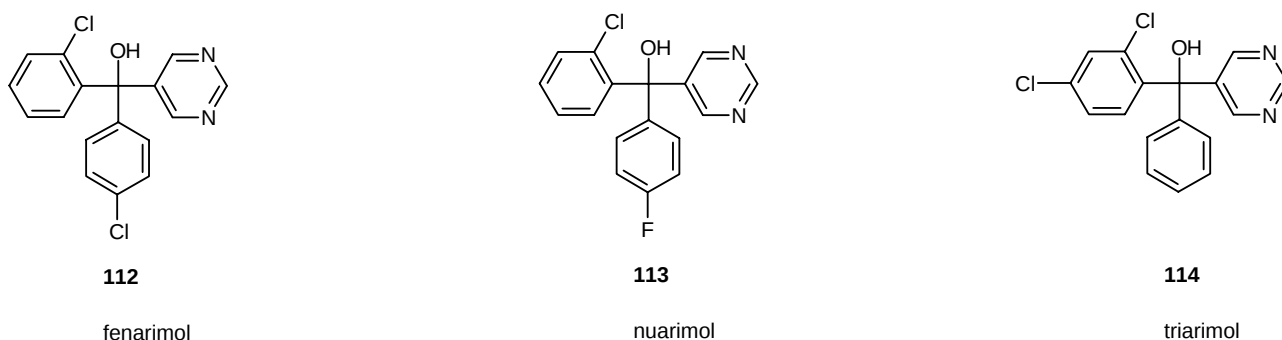


Figure 15

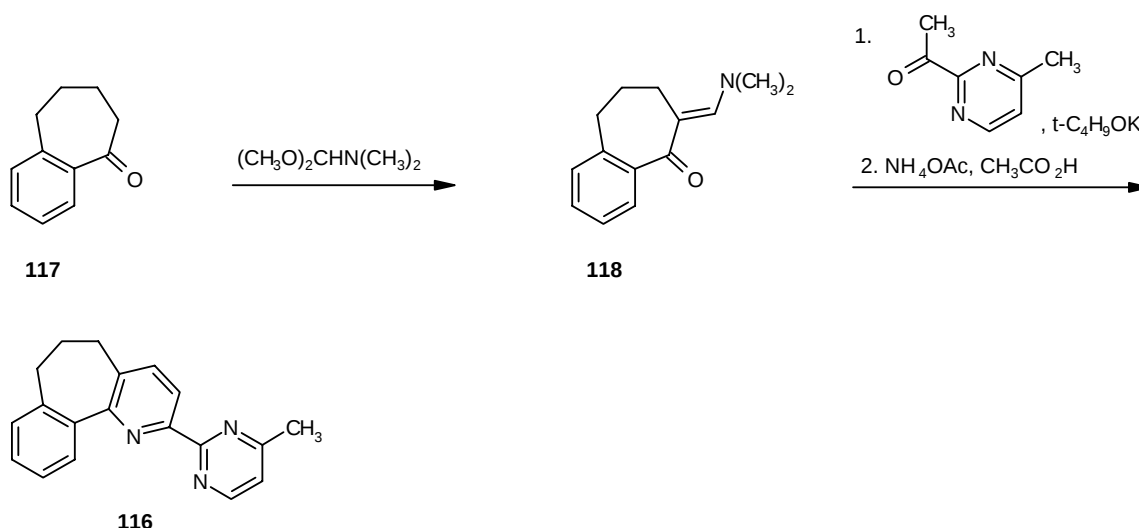
and C-22 dehydrogenation of sterols.⁸⁰

Furthermore, pyridylpyrimidines such as **115** are fungicidally active against a broad range of phytopathogens (Figure 16).⁸¹ Their efficacy is due to their ability to complex copper and to cycle this metal through fungal cell membranes, where it accumulates internally to toxic levels.⁸² Molecular modelling suggested that the phenyl ring of **115** should be twisted out of plane relative to the pyridine for optimum copper chelation to occur. Therefore conformationally restricted analogs of **115** with a carbon bridge between the phenyl and pyridine rings have also been prepared to control the dihedral angle between these two rings.⁸³ **116**, one of these bridged analogs, exhibits excellent activity against *Septoria nodorum* (wheat leaf blotch), *Pseudocercospora herpotrichoides* (wheat eyespot) and *Magnaporthe grisea* (rice blast).⁸³



Figure 16

The synthesis of **116** starts from 1-benzosuberone (**117**), which is converted into the enaminone (**118**) by condensation with *N,N*-dimethylformamide dimethyl acetal (Scheme 13). Subsequent pyridoannulation is effected by reaction of the potassium enolate of 2-acetyl-4-methylpyrimidine with the enaminone (**118**). Ring closure of the resulting non-isolable 1,5-enedione leads directly to the



Scheme 13

desired pyrimidine-substituted tricyclic ring system (**116**).^{83,84}

Several pyrazolo[3,4-*d*]pyrimidines have been reported to possess fungicidal activity. The pyrimidine-4-thione (**119**) is very active against *Pythium ultimum* (damping-off),⁸⁵ *Corticium solani* (black scurf)⁸⁵ and *Magnaporthe grisea* (rice blast)⁸⁶, whereas the pyrimidin-4-ones (**120**)⁸⁷ and (**121**)⁸⁸ are able to control

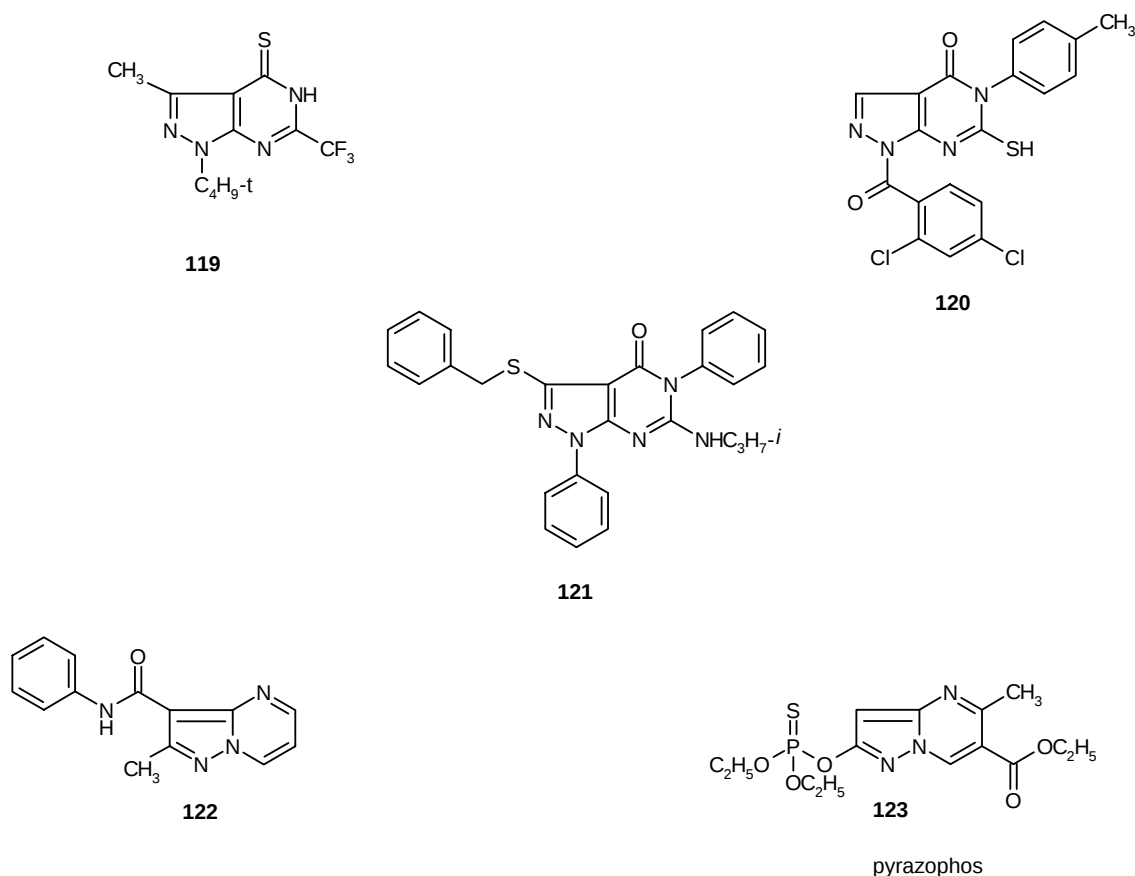


Figure 17

Helminthosporium oryzae (brown spot of paddy)⁸⁷ or *Botrytis cinerea* (grey mould)⁸⁸ respectively (Figure 17). Pyrazolo[1,5-*a*]pyrimidines also display fungicidal activity. **122** is a potent inhibitor of mycelial growth of *Rhizoctonia solani* (black scurf).⁸⁹ The phosphorothionate pyrazophos (**123**) was developed as

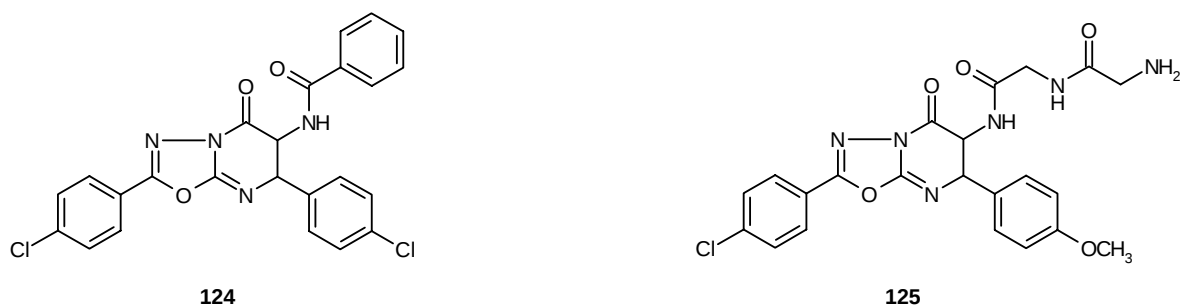


Figure 18

a fungicide because of its excellent activity against the barley diseases *Erysiphe graminis* (powdery mildew) and *Pyrenophora teres* (net blotch).⁹⁰

The 1,3,4-oxadiazolo[3,2-*a*]pyrimidine scaffold also seems to be linked to fungicidal activity. For example, the benzamide (**124**) is a potent inhibitor of *Helminthosporium oryzae* (brown spot of paddy),⁹¹ whereas the glycine dipeptide (**125**) is active against *Fusarium oxysporum* (root rot) (Figure 18).⁹²

Further examples for fungicidally active fused bicyclic pyrimidines are the thiazolo[3,2-*a*]pyrimidin-7-one (**126**), which is active against *Helminthosporium oryzae* (brown spot of paddy) and *Fusarium oxysporum* (root rot),⁹³ and the triazolo[1,5-*a*]pyrimidine (**127**), which is a powerful inhibitor of *Rhizoctonia solani* (black scurf) (Figure 19).⁹⁴

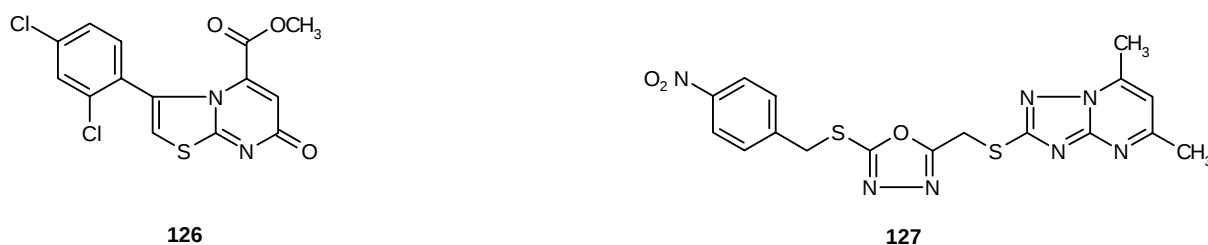


Figure 19

Several quinazolin-4-ones are also known to possess fungicidal efficacy. The aminothiazole (**128**), for example, displays high levels of activity against *Helminthosporium sativum* (root rot) (Figure 20).⁹⁵ Fluquinconazole (**129**) belongs to the triazole class of fungal sterol biosynthesis inhibitors, which block the C-14 demethylation of lanosterol. Fluquinconazole is particularly active against diseases of apple, giving excellent control of *Venturia inaequalis* (apple scab) and *Podosphaera leucotricha* (powdery

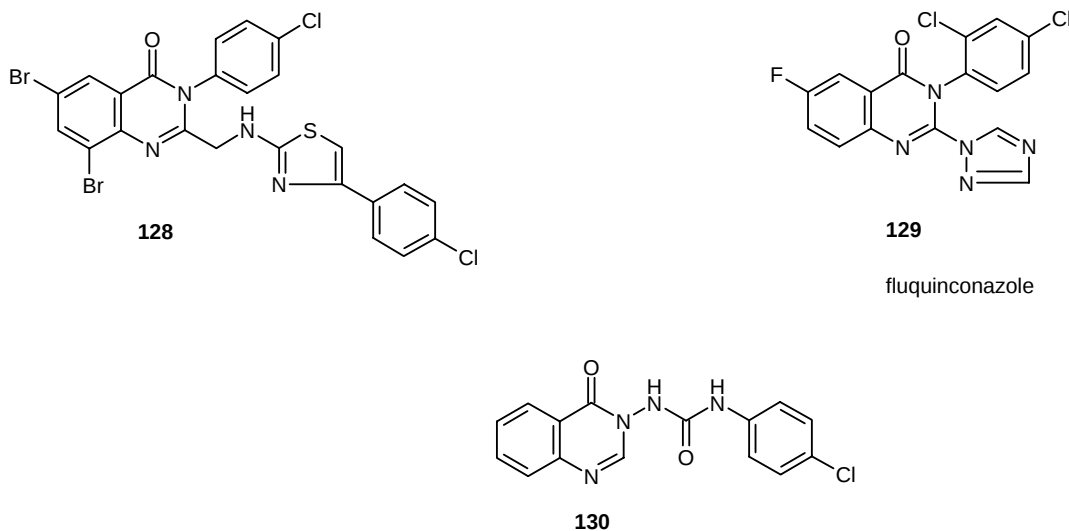
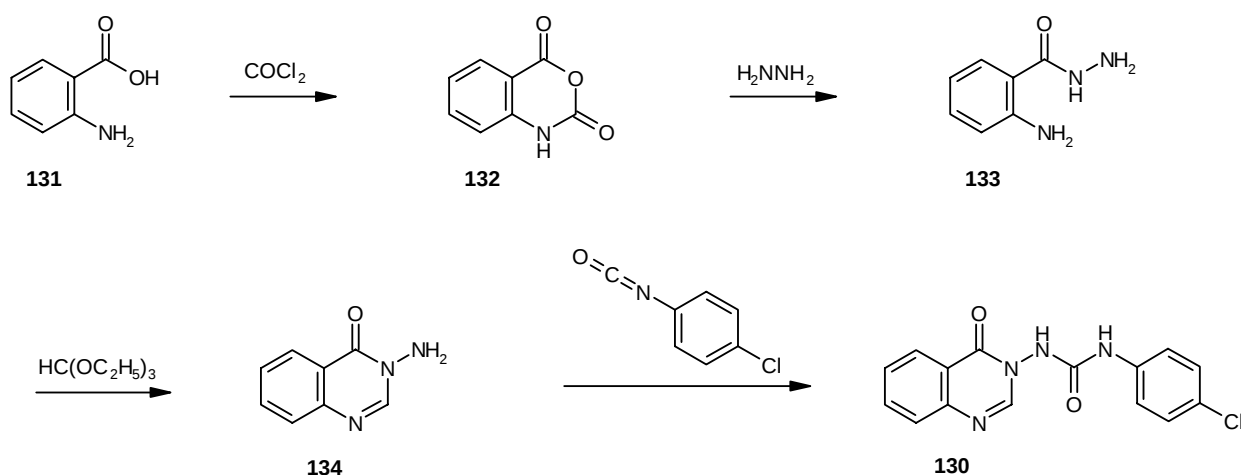


Figure 20

mildew).⁹⁶ The *N*-quinazolinone-*N'*-phenylurea (**130**) is quite active against *Cercospora beticola* (sugarbeet cercospora) and *Mycosphaerella fijiensis* (banana black sigatoka).⁹⁷

The large-scale synthesis of the urea derivative (**130**) starts from anthranilic acid (**131**), which is cyclized with phosgene to give isotoic anhydride (**132**) and then ring-opened again with hydrazine to obtain 2-aminobenzohydrazide (**133**) (Scheme 14). A second ring-closure leads to 3-aminoquinazolin-4-one (**134**), which is directly converted with 4-chlorophenyl isocyanate into the desired phenylurea (**130**).⁹⁷



Scheme 14

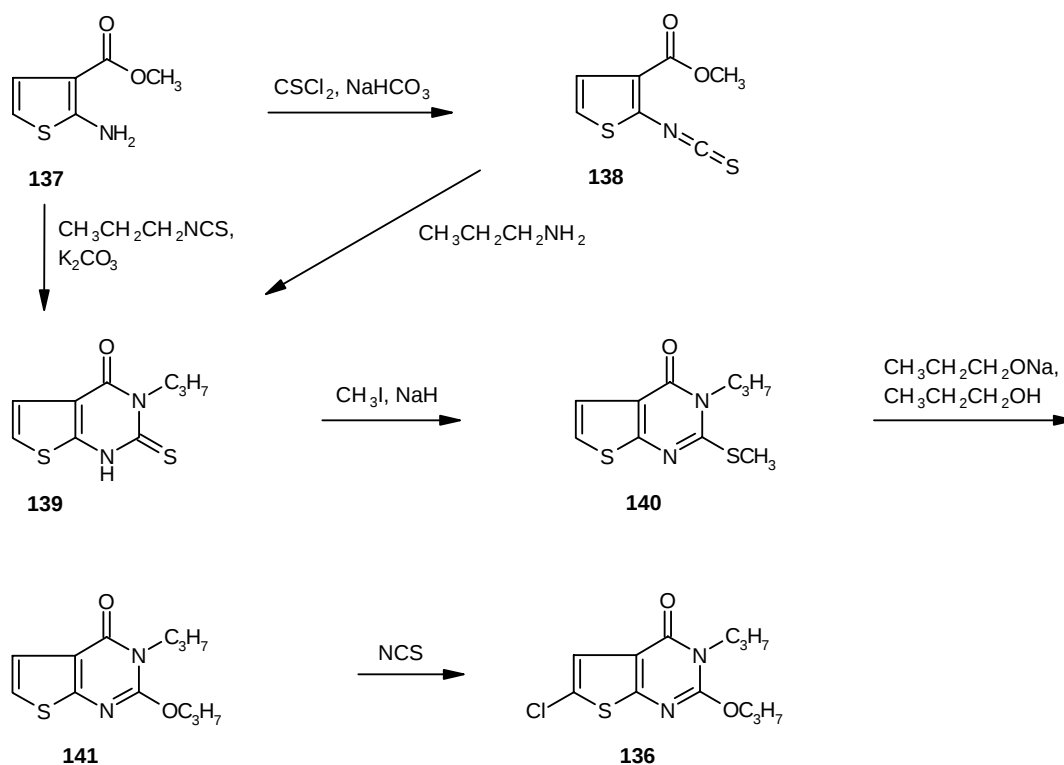
The quinazolin-4-one proquinazid (**135**) and the thienopyrimidin-4-one (**136**) exhibit extraordinarily high curative activity against powdery mildew diseases of cereals (*Erysiphe graminis*), grape (*Uncinula necator*) and apple (*Podosphaera leucotricha*) (Figure 21).⁹⁸



Figure 21

The synthesis of **136** is outlined in Scheme 15. The key intermediate (**139**) is usually prepared by ring-closure of an isothiocyanate with an amine, but the isothiocyanate can be linked either to the thiophene starting material, as in **138**, or to the acyclic coupling partner. After methylation of the thione function of **139**, the resulting methylthio group is substituted with a propoxyl group. Finally, regioselective

introduction of a chlorine atom in the *ortho*-position of the sulfur atom of **141** is achieved by reaction with *N*-chlorosuccinimide in pyridine.⁹⁸



Scheme 15

Diflumetorim (**142**) has been commercialized because of its high activity against *Erysiphe graminis* (powdery mildew) and *Puccinia recondita* (brown rust) in cereals and ornamentals (Figure 22).⁹⁹ The quinazoline (**143**) efficiently controls *Erysiphe graminis* (cereal powdery mildew).¹⁰⁰ Both compounds are respiration inhibitors, acting on the mitochondrial complex I. This mode of action will be discussed in detail in the next chapter.



Figure 22

4.1 Complex I Inhibitors

The excellent activity of the acaricide fenazaquin (**144**)¹⁰¹ against several different spider mite species, e.g. *Tetranychus urticae* (two-spotted spider mite) and *Panonychus ulmi* (European red mite), results from its ability to interrupt the mitochondrial electron transport by inhibition of NADH:ubiquinone oxidoreductase (complex I) (Figure 23).¹⁰² This prevents the respiration of the target organisms. The quinazoline (**145**), in which the *tert*-butyl group of fenazaquin is mimicked by a cyclic ketal, also offers excellent control of both *T. urticae* and *P. ulmi*, and it was once evaluated for development as a commercial acaricide.¹⁰³ The introduction of a fluorine atom on the quinazoline scaffold of fenazaquin and the addition of a further phenyl ring in the phenethyl side chain, to give the analog (**146**), leads to a dramatic change in biological efficacy. Fenazaquin is predominantly active against mites, whereas **146** has a much broader insecticidal spectrum with good activity against e.g. *Aphis gossypii* (cotton aphid), *Diabrotica undecimpunctata* (Southern corn rootworm) and *Trichoplusia ni* (cabbage looper).¹⁰⁴

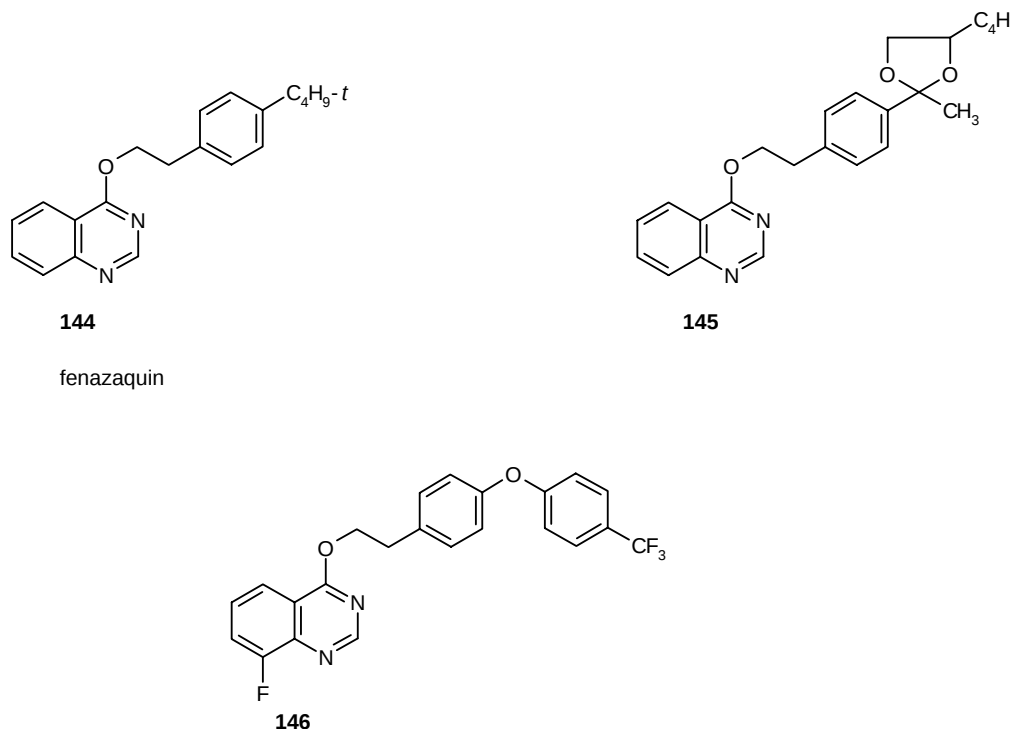
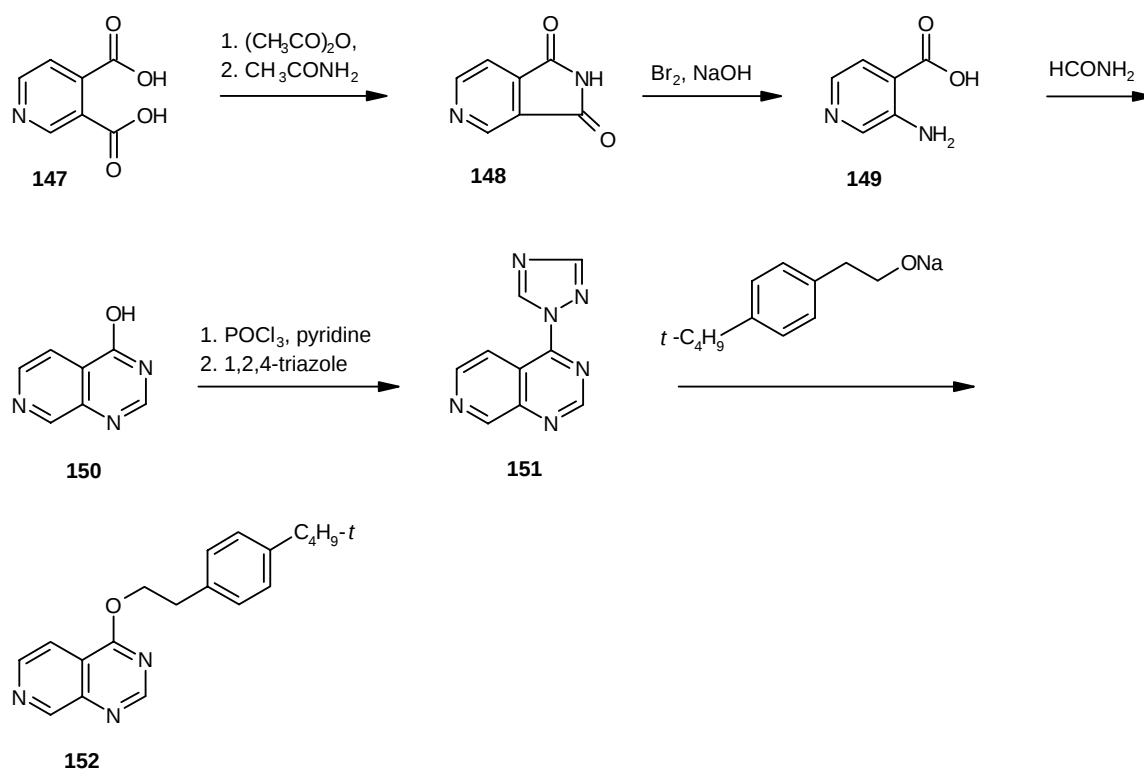


Figure 23

Several different fenazaquin analogs have been prepared in which the phenyl moiety of the quinazoline scaffold is replaced by a heterocyclic ring, such as purine, pteridine, furopyrimidine, thienopyrimidine, pyrazolopyrimidine, isoxazolopyrimidine, isothiazolopyrimidine, pyridopyrazine or pyrimidinopyrimidine. The pyrido[3,4-*d*]pyrimidine fenazaquin analog (**152**) could be prepared starting from pyridine-3,4-dicarboxylic acid (chinchomeric acid, **147**), which is converted into chinchomeronimide (**148**) (Scheme 16).¹⁰⁵ This imide can be regioselectively ring-opened under Hofmann rearrangement

conditions to give 3-aminoisonicotinic acid (**149**),¹⁰⁴ which is cyclized to 4-hydroxy-pyrido[3,4-d]pyrimidine (**150**) with formamide. Compound (**150**) is then converted *via* the chloride into the triazole (**151**), which is activated for nucleophilic substitution in this position, but much more stable than the usually used chloride. The triazolyl group is finally replaced by the required sodium alkoxide.¹⁰¹



Scheme 16

Pyrimidifen (**153**) and flufenimer (**154**) are two modern complex I inhibitors, developed especially for the control of mites in fruits and vegetables (Figure 24).¹⁰⁶

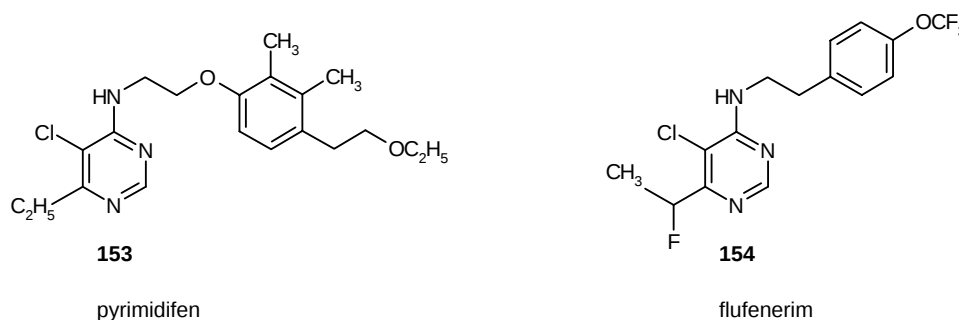


Figure 24

The cyclopropyl derivative (**155**), which bears the pyrimidine moiety of pyrimidifen (**153**), possesses

excellent activity against *Plutella xylostella* (diamondback moth), *Nilaparvata lugens* (brown rice planthopper) and *Tetranychus urticae* (two-spotted spider mite) (Figure 25).¹⁰⁷ The control of *Tetranychus urticae* (two-spotted spider mite) is also the strength of the oxime derivative (**156**).¹⁰³ Finally, the arylacetamide (**157**) shows good activity against *Heliothis virescens* (tobacco budworm) and *Aphis gossypii* (cotton aphid).¹⁰⁸

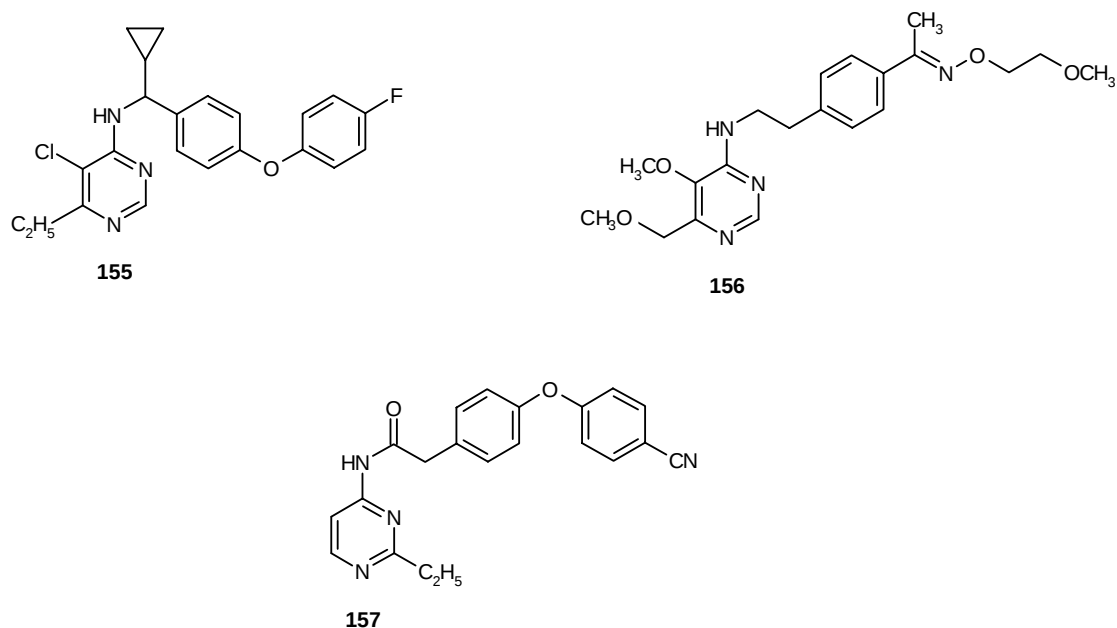


Figure 25

4.2 Miscellaneous Insecticidally Active Pyrimidines

Several 2-aminopyrimidines display strong insecticidal activities. The 2,4-diaminopyrimidine (**158**) inhibits dihydrofolate reductase and is quite efficient against *Helicoverpa zea* (corn earworm), *Heliothis virescens* (tobacco budworm) and *Trichoplusia ni* (cabbage looper) (Figure 26).¹⁰⁹ The 2-isopropylaminopyrimidine (**159**) was found to possess good activity, especially against rice pests.¹¹⁰



Figure 26

The substitution of the pyrimidine ring with a *tert*-butyl group seems to be favorable for insecticidal activity. The GABA-gated chloride channel blocker (**160**) is very active against *Musca domestica* (house

fly) (Figure 27).¹¹¹ The pyrethroid analog (**161**) exhibits selective activity against spider mites.¹¹² The 3,4-dihydroquinazolin-2-one (**162**), which is a bicyclic analog of pymetrozine, is quite active against pyrethroid or carbamate resistant aphids.¹¹³

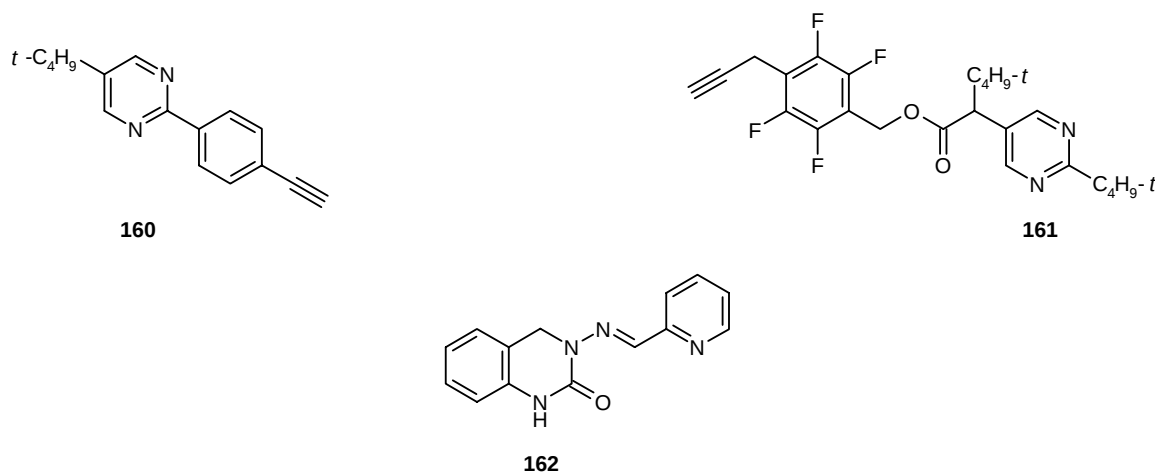


Figure 27

Due to its unique physicochemical properties, the pyrimidine ring is a common structural feature in the older insecticide classes of phosphorothionates and carbamates, which inhibiting *acetylcholinesterase*. This enzyme plays a central role in the transport of nerve impulses, and its inhibition results in a steady excitement with lethal results. Most phosphorothionate insecticides are relatively poor intrinsic inhibitors of this target, but are converted by cytochrome P-450-containing monooxygenase systems into the corresponding phosphates, which are potent inhibitors.¹¹⁴ Figure 28 shows four examples from these

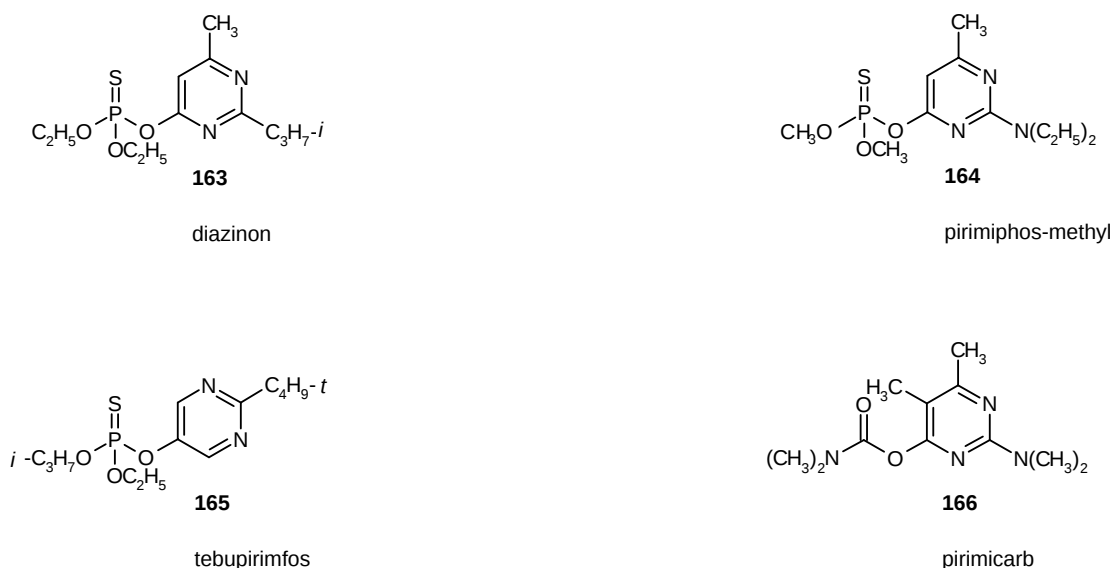


Figure 28

insecticide classes which are still in use today.

5 PYRIMIDINE AS AN ISOSTERIC REPLACEMENT FOR OTHER HETEROCYCLES

5.1 Herbicidally Active Pyrimidines

The quaternary pyridinium salt (**168**) was prepared as an analog of the total herbicide paraquat (**167**), but the herbicidal activity is clearly weaker (Figure 29).¹¹⁵ The pyrimidinone (**170**) was found to have good

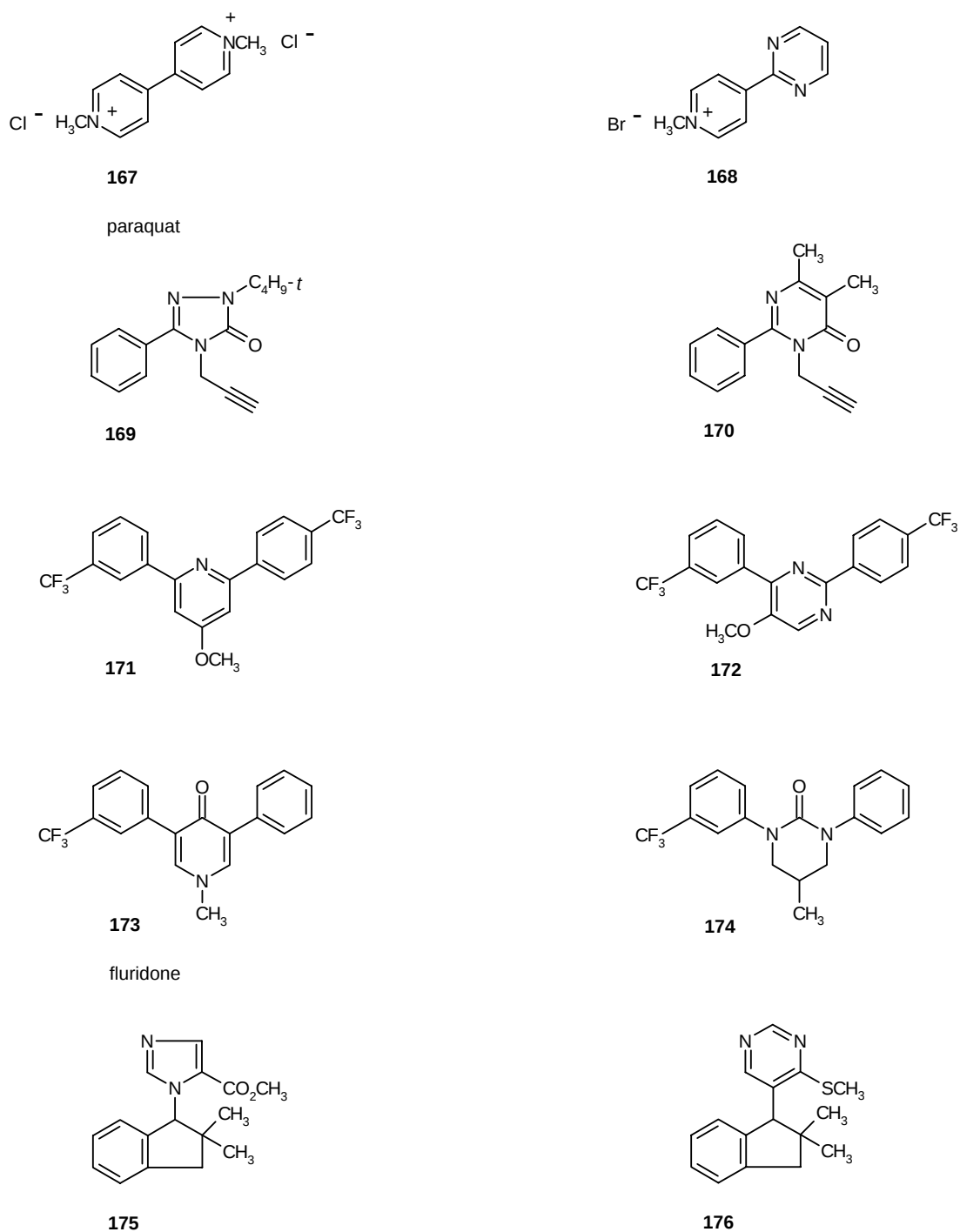
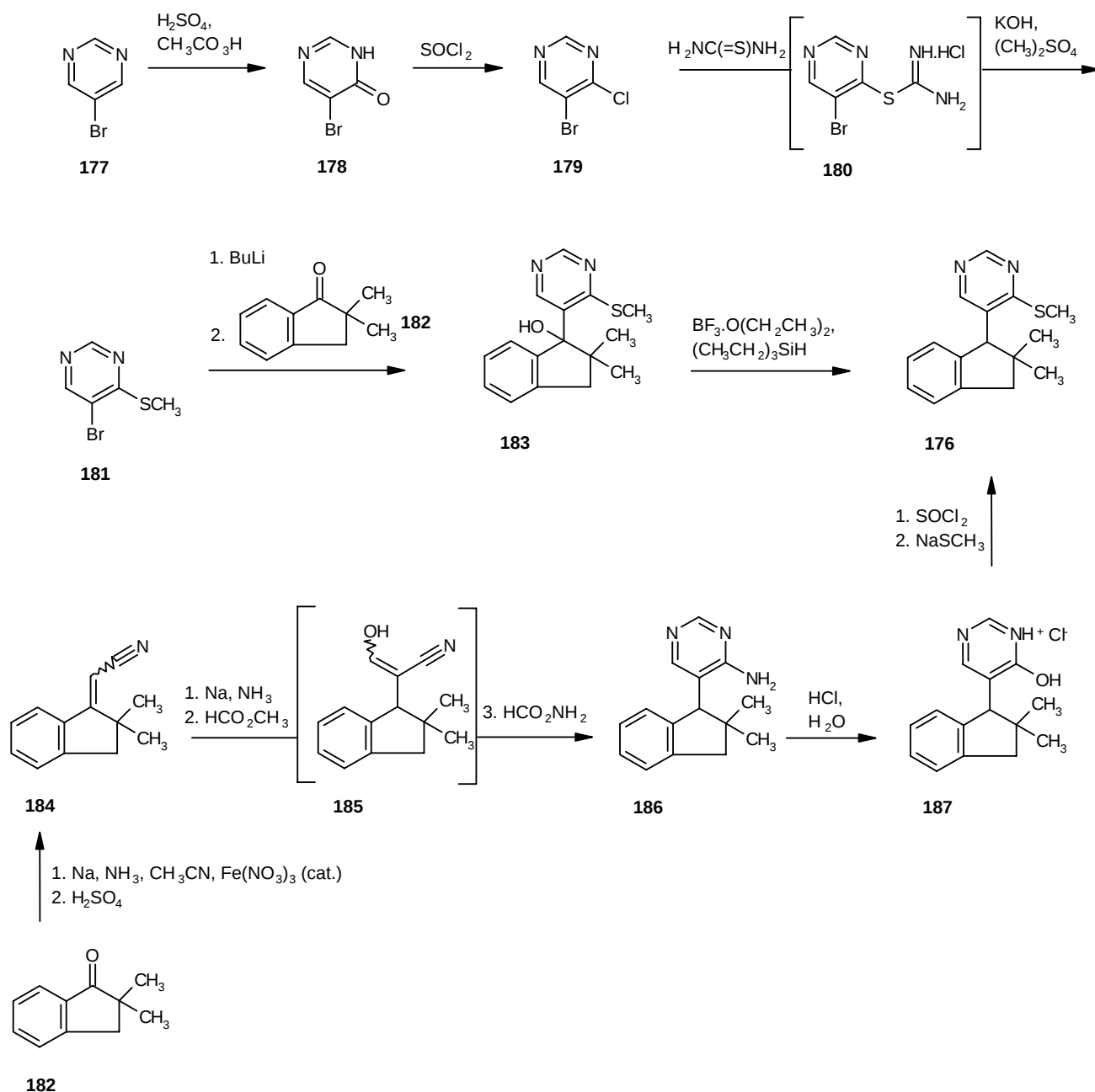


Figure 29

pre-emergence broad spectrum herbicidal activity, equivalent to that of the triazolone lead compound **(169)**.¹¹⁶ Both compounds are bleaching herbicides and inhibit carotenoid biosynthesis by accumulation of phytoene, phytofluene and *zeta*-carotene. The same mode of action applies also to the diphenylpyrimidine **(172)**,¹¹⁷ which is an analog of the herbicidal diarylpyridine **(171)**.¹¹⁸ **172** possesses pre- and post-emergent activity against *Abutilon theophrasti* (velvetleaf) and *Echinochloa frumentacea* (Japanese millet).¹¹⁷ Also fluridone **(173)** and its tetrahydropyrimidinone analog **(174)** are bleachers.¹¹⁹ The cyclic urea **(174)** is very active against monocotyledonous weeds, such as *Setaria virides* (green foxtail) and *Sorghum halepense* (Johnsongrass) as well as dicotyledonous weeds, such as *Chenopodium*



Scheme 17

album (lambsquarter) and *Portulaca oleracea* (purslane).¹¹⁹ The imidazole derivative (**175**), which was prepared in a program towards fungicidal activity, showed surprisingly high herbicidal activity against *Digitaria sanguinalis* (large crabgrass).¹²⁰ This compound inhibits sterol biosynthesis in plants by blocking *obtusifoliol 14 α -methyl demethylase*. Its pyrimidine analog (**176**) is also an efficient herbicide, especially against rice weeds.¹²¹

Two completely different synthesis routes to **176** have been worked out, both of which use 2,2-dimethylindan-1-one (**182**) as source for the indanyl scaffold of **176** (Scheme 17).¹²¹ The first approach starts from 5-bromopyrimidine (**177**), which can be hydroxylated with peracetic acid to give 5-bromopyrimidin-4-one (**178**).¹²² The hydroxypyrimidine (**178**) is transformed into the methylthio-pyrimidine (**181**) via the chloride (**179**) and the thiuronium salt (**180**). Metal-halogen exchange of **181** with butyl lithium and subsequent addition of the lithiated pyrimidine intermediate to 2,2-dimethylindan-1-one (**182**) led to the tertiary alcohol (**183**), which could be converted into the desired herbicide (**176**) by Lewis acid-mediated silane reduction.¹²¹ The second synthesis of **176** employs the transformation of 2,2-dimethylindan-1-one (**182**) into the 4-aminopyrimidine (**186**) via the two nitrile intermediates (**184**) and (**185**), which takes place in liquid ammonia (Scheme 17). The 4-amino substituent can then be transformed into the methylthio group of the final product (**176**) via hydroxy and chloro intermediates.¹²¹

5.2 Fungicidally Active Pyrimidines

Quinoxifen (**188**) possesses significantly better activity against *Erysiphe graminis* (cereal powdery mildew) than its quinazoline analog (**189**) (Figure 30).¹²³ The strobilurin derivative (**190**), in which the

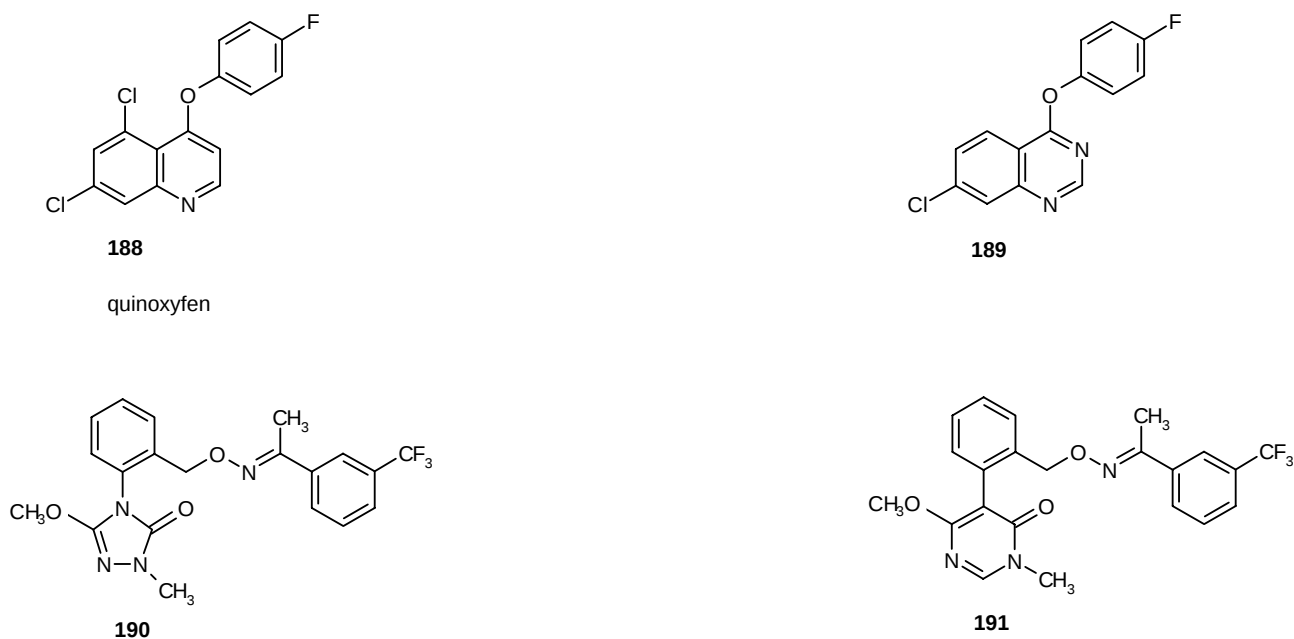
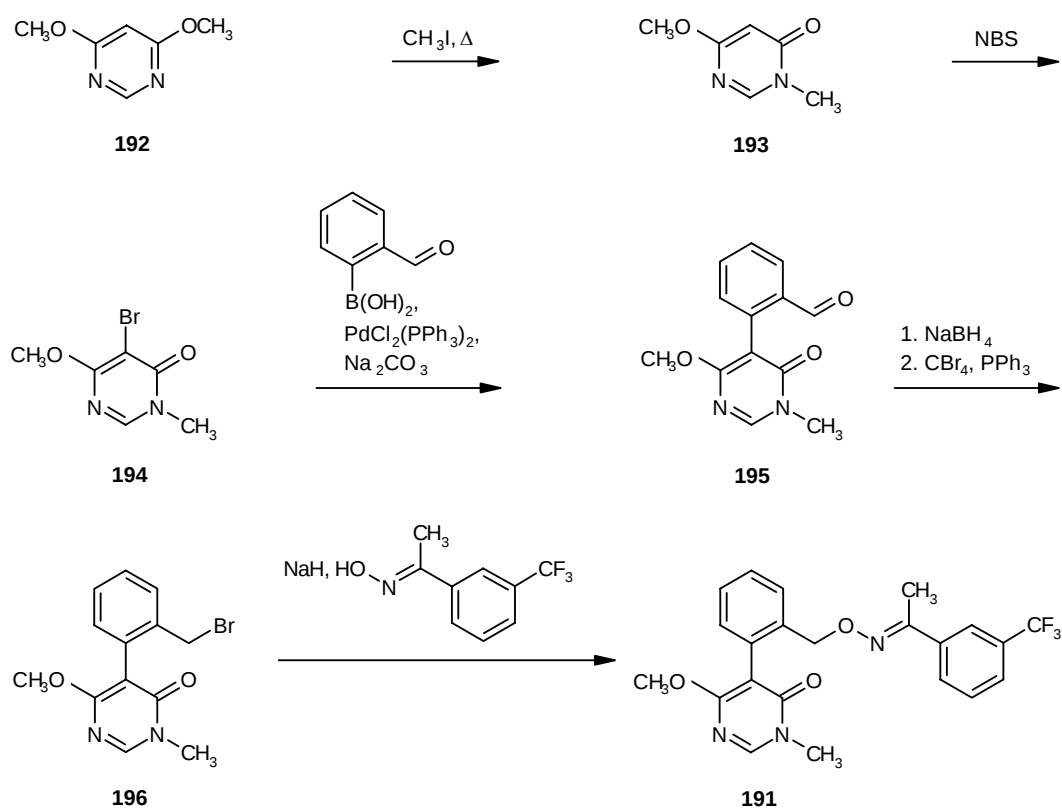


Figure 30

common β -methoxyacrylate pharmacophore is replaced by a triazolinone, displays astonishing good efficacy against a broad range of plant diseases,¹²⁴ and its pyrimidinone analog (**191**) is fungicidally active as well.¹²⁵

The critical step enabling a concise synthesis of **191** is the Suzuki coupling of 2-formylphenylboronic acid with the key intermediate (**194**) (Scheme 18). This tetrasubstituted pyrimidine (**194**) can, in turn, be obtained in two steps from 4,6-dimethoxypyrimidine (**192**) by *N*-methylation and subsequent regioselective bromination of the resulting pyrimidinone (**193**). Reduction of **195** with sodium borohydride followed by bromination of an intermediate alcohol gave the benzyl bromide (**196**), which was linked to 3-trifluoromethylacetophenone oxime to afford the desired product (**191**).¹²⁵

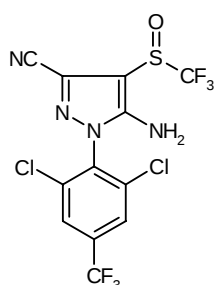


Scheme 18

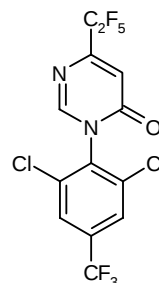
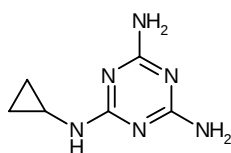
5.3 Insecticidally Active Pyrimidines

Fipronil (**197**) is a highly efficient insecticide which acts by blocking the GABA-regulated chloride channel (Figure 31).¹²⁶ The pyrimidinone analog (**198**) also displays high insecticidal activity especially against public health pests like mosquitoes and cockroaches.¹²⁷ The triaminopyrimidine dicyclanil (**200**) is at least as active against blowfly strike on sheep and screwworm infestation on cattle as its triazine role model cyromazine (**199**).¹²⁸ Both compounds are insect growth regulators, inhibiting the biosynthesis of chitin. The same mode of action applies to the oxazoline (**201**), which is a broad-acting insecticide and

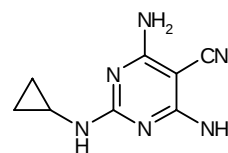
acaricide.¹²⁹ Its tetrahydropyrimidine analog (**202**) is highly active against *Spodoptora littoralis* (cotton leafworm).¹³⁰

**197**

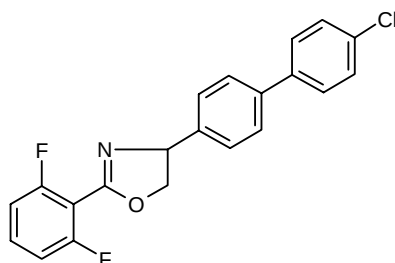
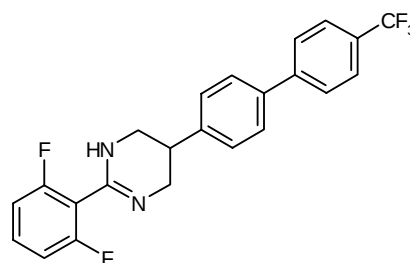
fipronil

**198****199**

cyromazine

**200**

dicyclanil

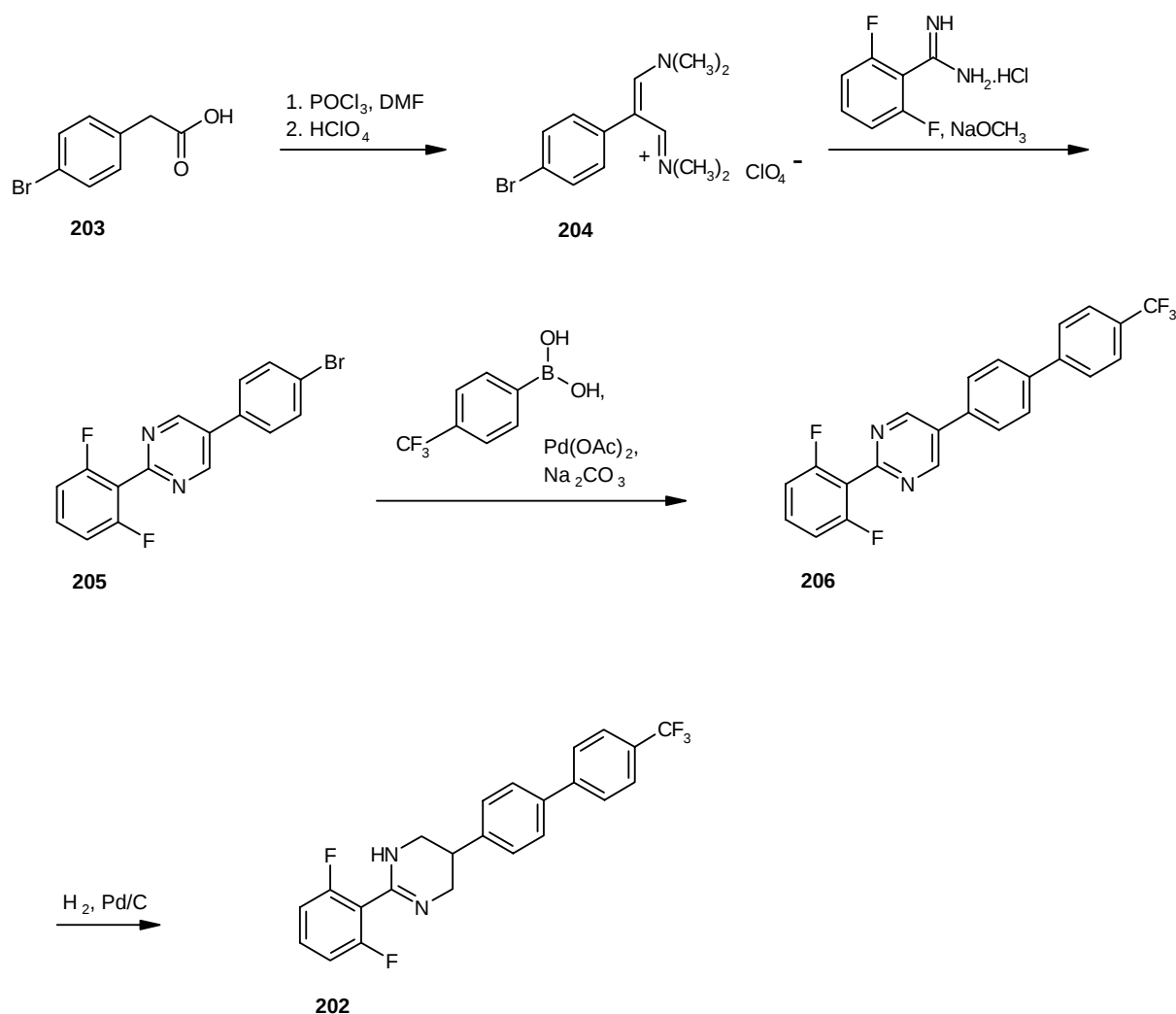
**201****202****Figure 31**

The synthesis of the tetrahydropyrimidine (**202**) is depicted in Scheme 19. The key step is the coupling of the vinamidinium salt (**204**) with 2,6-difluorobenzamidine to give the diaryl-substituted pyrimidine (**205**),¹³¹ which is subsequently reacted with 4-trifluoromethylphenylboronic acid under Suzuki coupling conditions. The resulting pyrimidine (**206**) is reduced to the desired tetrahydropyrimidine (**202**) via catalytic hydrogenation.¹³⁰

6 CONCLUSION

Many pyrimidine derivatives display significant biological activities in the control of weeds, insects and fungi. Their structural diversity is impressive as well as the wide range of different modes of action

involved. It seems that, in pesticidally active compounds, several different five and six membered heterocycles can be replaced by pyrimidine without loss of biological efficacy.



Scheme 19

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

1. Part three of a series of reviews about "Chemistry in Crop Protection". For part two see: C. Lamberth, *Heterocycles*, 2005, **65**, 667.
2. G. Brugnatelli, *Ann. Chim. Phys.*, 1818, **8**, 201.
3. For excellent reviews on pyrimidine chemistry see: S. von Angerer, in "Science of Synthesis", Cat. 2: Hetarenes and Related Ring Systems, Vol. 16: Six-Membered Hetarenes with Two Identical

- Heteroatoms, ed. by Y. Yamamoto, Thieme, Stuttgart, 2004, pp. 379 - 572; M. G. Hoffmann, A. Nowak, and M. Müller, in "Methods of Organic Chemistry (Houben-Weyl)", Vol. E9b / Part 1: Hetarenes IV, ed. by E. Schaumann, Thieme, Stuttgart, 1998, pp. 1 – 249; K. Undheim and T. Benneche, in "Comprehensive Heterocyclic Chemistry II", ed. by A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Pergamon, Oxford, 1996, pp. 93 – 231; D. J. Brown, "The Pyrimidines", Wiley-Interscience, New York, 1994; D. J. Brown, in "Comprehensive Heterocyclic Chemistry", ed. by A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, pp. 57 – 155.
4. For excellent reviews on quinazoline chemistry see: D. J. Brown, "Quinazolines", Wiley-Interscience, New York, 1996; M. A. E. Shaban, M. A. M. Taha, and E. M. Sharshira, in "Advances in Heterocyclic Chemistry", Vol. 52, ed. by A. R. Katritzky, Academic Press, San Diego, 1992, pp. 1 – 153; W. L. F. Armarego, in "Advances in Heterocyclic Chemistry", Vol. 24, ed. by A. R. Katritzky and A. J. Boulton, Academic Press, New York, 1979, pp. 1 – 62.
 5. A. Turck, N. Ple, F. Mongin, and G. Queguiner, *Tetrahedron*, 2001, **57**, 4489; G. A. El-Hilti, *Heterocycles*, 2000, **53**, 1839.
 6. Y. Kurasawa, A. Takada, and H. S. Kim, *J. Heterocycl. Chem.*, 1995, **32**, 1085; H. Yamanaka, T. Sakamoto, and S. Niitsuma, *Heterocycles*, 1990, **31**, 923.
 7. P. S. Reddy, P. P. Reddy, and T. Vasantha, *Heterocycles*, 2003, **60**, 183; A. Katoh, T. Nishio, and C. Kashima, *Heterocycles*, 1987, **26**, 2223.
 8. C. O. Kappe and A. Stadler, *Org. React.*, 2004, **63**, 1; C. O. Kappe, *Acc. Chem. Res.*, 2000, **33**, 879; C. O. Kappe, *Tetrahedron*, 1993, **49**, 6937.
 9. J. Li and J. M. Cook, in "Name Reactions in Heterocyclic Chemistry", ed. by J.-J. Li, Wiley-Interscience, Hoboken, 2005, pp. 536 – 539.
 10. H. M. Brown and J. C. Cotterman, in 'Chemistry of Plant Protection Vol. 10: Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis – Recent Developments', ed. by J. Stetter, Springer, Berlin, 1994, pp. 47 – 81.
 11. S. K. Gee and J. V. Hay, in 'Chemistry of Plant Protection Vol. 10: Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis – Recent Developments', ed. by J. Stetter, Springer, Berlin, 1994, pp. 15 – 46.
 12. J. V. Hay, *Pestic. Sci.*, 1990, **29**, 247.
 13. J. V. Schloss, in 'Chemistry of Plant Protection Vol. 10: Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis – Recent Developments', ed. by J. Stetter, Springer, Berlin, 1994, pp. 3 – 14; H. M. Brown and P. C. Kearney, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 32 – 49; H. M. Brown, *Pestic. Sci.*, 1990, **29**, 263.

14. G. Levitt, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 16 – 31.
15. R. A. LaRossa and J. V. Schloss, *J. Biol. Chem.*, 1984, **259**, 8753.
16. S. Yamamoto, T. Sato, K. Morimoto, and T. Nawamaki, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 34 – 42; J. Cuomo, S. K. Gee, and S. L. Hartzell, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 62 – 73.
17. S. Murai, Y. Nakamura, T. Akagi, N. Sakashita, and T. Haga, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 43 – 55; S. Murai, T. Haga, K. Fujikawa, N. Sakashita, and F. Kimura, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 98 – 106.
18. S. P. Artz, B. L. Finkelstein, M. A. Hanagan, M. P. Moon, R. J. Pasteris, and M. P. Rorer, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 50 – 61.
19. D. S. M. D'Souza, I. A. Black, and R. T. Hewson, *Proc. Br. Crop Prot. Conf. – Weeds*, 1993, 567.
20. S. Takeda, T. Yuyama, R. C. Ackerson, R. C. Weigel, R. F. Sauers, W. Neal, D. G. Gibian, and P. K. Tseng, *Zasso Kenkyu*, 1985, **30**, 284.
21. M. E. Condon, T. E. Brady, D. Feist, P. M. Harrington, T. Malefy, P. A. Marc. L. Quakenbush, D. Shaner, J. M. Lavanish, and B. Tecle, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998, pp. 79 – 94.
22. E. Hacker, K. Bauer, H. Bieringer, H. Kehne, and L. Willms, *Proc. Br. Crop Prot. Conf. – Weeds*, 1995, 73.
23. H. G. McFadden, J. L. Huppatz, and C. H. L. Kennard, *Z. Naturforsch.*, 1993, **48c**, 356.
24. P. Babczinski and T. Zelinski, *Pestic. Sci.*, 1991, **31**, 305.
25. C. Lüthy, H. Zondler, T. Rapold, G. Seifert, B. Urwyler, T. Heinis, H. C. Steinrücken, and J. Allen, *Pest Manag. Sci.*, 2001, **57**, 205.

26. M. Tamaru, N. Masuyama, M. Sato, F. Takabe, J. Inoue, and R. Hanai, *Pestic. Sci.*, 1997, **49**, 76; M. Tamaru, T. Takehi, N. Masuyama, and R. Hanai, *Pestic. Sci.*, 1996, **47**, 327; M. Tamaru and Y. Saito, *Pestic. Sci.*, 1996, **47**, 125; Y. Nezu, M. Miyazaki, K. Sugiyama, N. Wada, I. Kajiwarra, and T. Miyazawa, *Pestic. Sci.*, 1996, **47**, 115; M. W. Drewes, in 'Chemistry of Plant Protection Vol. 10: Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis – Recent Developments', ed. by J. Stetter, Springer, Berlin, 1994, pp. 161 – 187.
27. J. S. Claus, *Weed Techn.*, 1987, **1**, 114.
28. W. Maurer, H. R. Gerber, and J. Rufener, *Proc. Brighton Crop Prot. Conf. – Weeds*, 1987, 41.
29. A. P. Selley, P. J. Haney, and J. R. Austin, *Proc. Brighton Crop Prot. Conf. – Weeds*, 1985, 931.
30. W. T. Zimmerman, C. L. Hillemann, T. P. Selby, R. Shapiro, C. P. Tseng, and B. A. Wexler, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 74 – 86.
31. G. Hamprecht, H. Mayer, K.-O. Westphalen, and H. Walter, *Pestic. Sci.*, 1999, **55**, 566.
32. H. Gershon, A. T. Grefig, and A. A. Scala, *J. Heterocycl. Chem.*, 1983, **20**, 219; A. Giner-Sorolla and A. Bendich, *J. Am. Chem. Soc.*, 1958, **80**, 5744.
33. W. E. Barnette, *J. Am. Chem. Soc.*, 1984, **106**, 452.
34. N. Okajima, I. Aoki, T. Kuragano, and Y. Okada, *Pestic. Sci.*, 1991, **32**, 91.
35. W. A. Kleschick, in 'Chemistry of Plant Protection Vol. 10: Herbicides Inhibiting Branched-Chain Amino Acid Biosynthesis – Recent Developments', ed. by J. Stetter, Springer, Berlin, 1994, pp. 119 – 143;
36. M. J. Costales, W. A. Kleschick, and B. C. Gerwick, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 26 – 33; W. A. Kleschick, M. J. Costales, J. E. Dunbar, R. W. Meikle, W. T. Monte, N. R. Pearson, S. W. Snider, and A. P. Vinogradoff, *Pestic. Sci.*, 1990, **29**, 341.
37. B. C. Gerwick, M. V. Subramanian, V. I. Loney-Gallant, and D. P. Chandler, *Pestic. Sci.*, 1990, **29**, 357.
38. W. A. Kleschick, M. J. Costales, B. C. Gerwick, J. B. Holtwick, R. W. Meikle, W. T. Monte, N. R. Pearson, S. W. Snider, M. V. Subramanian, J. C. VanHeertum, and A. P. Vinogradoff, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 10 – 16.

39. W. A. Kleschick, C. M. Carson, M. J. Costales, J. J. Doney, B. C. Gerwick, J. B. Holtwick, R. W. Meikle, W. T. Monte, J. C. Little, N. R. Pearson, S. W. Snider, M. V. Subramanian, J. C. VanHeertum, and A. P. Vinogradoff, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 17 – 25.
40. W. A. Kleschick and J. Bordner, *J. Heterocycl. Chem.*, 1989, **26**, 1489.
41. W. T. Monte, W. A. Kleschick, and J. Bordner, *J. Heterocycl. Chem.*, 1999, **36**, 183.
42. S. Kawamura, J. Sato, T. Hamada, M. Sakaki, and Y. Sanemitsu, *Biosci. Biotech. Biochem.*, 1992, **56**, 1897.
43. V. J. Ram, H. K. Pandey, and A. J. Vlietinck, *J. Heterocycl. Chem.*, 1981, **18**, 1277; V. J. Ram, *Arch. Pharm.*, 1979, **312**, 19.
44. T. P. Selby, T. A. Andrea, L. R. Denes, B. L. Finkelstein, T. P. Fuesler, and B. K. Smith, in 'Synthesis and Chemistry of Agrochemicals, Vol. 3', ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 91 – 102.
45. C. A. Maggiali, M. R. Minigiardi, G. Morini, and F. Ronchini, *Acta Nat. de l'Ateneo Parmense*, 1983, **19**, 105; C. A. Maggiali, M. R. Minigiardi, G. Morini, F. Ronchini, and F. Mossini, *Acta Nat. de l'Ateneo Parmense*, 1982, **18**, 93.
46. S. O. Duke and C. A. Rebeiz (Eds.), 'Porphyrin Pesticides', ACS Symposium Series 559, American Chemical Society, Washington DC, 1994.
47. M. J. Konz, H. R. Wendt, T. G. Cullen, K. L. Tenhuisen, and O. M. Fryszman, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 67 – 78.
48. G. Theodoridis, J. T. Bahr, S. Crawford, B. Dugan, F. W. Hotzman, L. L. Maravetz, S. Sehgel, and D. P. Suarez, in 'Synthesis and Chemistry of Agrochemicals, Vol. 6', ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 96 – 107.
49. A. L. Cossey and J. N. Phillips, *J. Agric. Food Chem.*, 1981, **29**, 716; B. T. Brown, J. N. Phillips, and B. M. Rattigan, *J. Agric. Food Chem.*, 1981, **29**, 719.
50. B. Kamireddy and W. M. Murray, *Pure Appl. Chem.*, 1996, **68**, 743.
51. A. Zeidler, A. Fischer, and G. Scheuerer, *Z. Naturforsch.*, 1969, **24B**, 740.
52. G. Hamprecht, A. Zeidler, K. H. König, and D. Mangold, *Kemia – Kemi*, 1974, **1**, 590.
53. A. Goh, S. Kudo, and K. Endo, in 'Synthesis and Chemistry of Agrochemicals, Vol. 4', ACS

- Symposium Series 584, ed. by D. R. Baker, J. G. Fenyes, and G. S. Basarab, American Chemical Society, Washington DC, 1995, pp. 186 – 196.
54. D. Font, M. Heras, and J. M. Villalgordo, *Synthesis*, 2002, 1833; T. Sawayama, R. Yamamoto, H. Kinugasa, and H. Nishimura, *Heterocycles*, 1977, **8**, 299.
55. G. Sandmann, *Pestic. Biochem. Physiol.*, 2001, **70**, 86.
56. Y. Nezu, M. Miyasaki, K. Sugiyama, and I. Kajiwara, *Pestic. Sci.*, 1996, **47**, 103.
57. M. Botta, M. Cavalieri, D. Ceci, F. De Angelis, G. Finizia, and R. Nicoletti, *Tetrahedron*, 1984, **40**, 3313.
58. Agrow, No. 463, January 7th 2005, p. 18.
59. S. Scheiblich, M. Geringer, and B. Kind, *Pestic. Sci.*, 1999, **55**, 636.
60. T. P. Selby, J. E. Drumm, R. A. Coats, F. T. Coppo, S. K. Gee, J. V. Hay, R. J. Pasteris, and T. M. Stevenson, in ‘Synthesis and Chemistry of Agrochemicals, Vol. 6’, ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 74 – 84;
61. T. M. Stevenson, T. P. Selby, G. M. Koether, J. E. Drumm, X. J. Meng, M. P. Moon, R. A. Coats, T. V. Thieu, A. E. Csalnuovo, and R. Shapiro, in ‘Synthesis and Chemistry of Agrochemicals, Vol. 6’, ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 85 – 95.
62. K. Tanaka, A. Takahashi, N. Umeda, H. Yamada, H. Adachi, and T. Kawana, *Pestic. Sci.*, 1999, **55**, 370.
63. D. W. Bartlett, J. M. Clough, J. R. Godwin, A. A. Hall, M. Hamer, and B. Parr-Dobrzanski, *Pest Manag. Sci.*, 2002, **58**, 649; H. Sauter, W. Steglich, and T. Anke, *Angew. Chem.*, 1999, **111**, 1416, *Angew. Chem., Int. Ed.*, 1999, **38**, 1328; J. M. Clough, P. J. de Fraine, T. E. M. Fraser, and C. R. A. Godfrey, in ‘Synthesis and Chemistry of Agrochemicals, Vol. 3’, ACS Symposium Series 504, ed. by D. R. Baker, J. G. Fenyes, and J. J. Steffens, American Chemical Society, Washington DC, 1992, pp. 372 – 383; K. Beutement, J. M. Clough, P. J. De Fraine, and C. R. A. Godfrey, *Pestic. Sci.*, 1991, **31**, 499.
64. J. M. Clough, *Nat. Prod. Rep.*, 1993, **10**, 565.
65. J. M. Clough and C. R. A. Godfrey, *Chemistry in Britain*, 1995, 466; J. M. Clough, V. M. Anthony, P. J. de Fraine, T. E. M. Fraser, C. R. A. Godfrey, J. R. Godwin, and D. Youle, ‘ACS Conference Proceedings Series: Eighth International Congress of Pesticide Chemistry, Options 2000’ ed. by N. N. Ragsdale, P. C. Kearney, and J. R. Plimmer, American Chemical Society, Washington DC, 1995, pp. 59 – 73.
66. J. M. Clough, D. A. Evans, P. J. de Fraine, T. E. M. Fraser, C. R. A. Godfrey, and D. Youle,

- 'Natural and Engineered Pest Management Agents', ACS Symposium Series 551, ed. by P. A. Hedin, J. J. Menn, and R. M. Hollingworth, American Chemical Society, Washington DC, 1994, pp. 37 – 53.
67. G. W. Craig, M. Eberle, C. Lamberth, and T. Vettiger, *J. Prakt. Chem.*, 2000, **342**, 504.
68. A. Zumbunn, C. Lamberth, and F. Schaub, *Synth. Commun.*, 1998, **28**, 475.
69. K. Burger, F. Hein, U. Wassmuth, and H. Krist, *Synthesis*, 1981, 904.
70. G. Grunwaldt, H. Lyr, R. Wollgiehn, and M. Klepel, *Pestic. Sci.*, 1990, **30**, 323.
71. A. Daniels and J. A. Lucas, *Pestic. Sci.*, 1995, **45**, 33.
72. U. Müller, A. Hubele, H. Zondler, and J. Herzog, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 237 – 245.
73. T. Nagata, K. Masuda, S. Maeno, and I. Miura, *Pest Manag. Sci.*, 2003, **60**, 399.
74. R. J. Milling and C. J. Richardson, *Pestic. Sci.*, 1995, **45**, 43; I. Miura, T. Kamakura, S. Maeno, S. Hayashi, and I. Yamaguchi, *Pestic. Biochem. Physiol.*, 1994, **48**, 222.
75. R. Fritz, C. Lanen, V. Colas, and P. Leroux, *Pestic. Sci.*, 1997, **49**, 40; P. Masner, P. Muster, and J. Schmid, *Pestic. Sci.*, 1994, **42**, 163.
76. J. Rouchaud, O. Neus, and C. Moulard, *Pest Manag. Sci.*, 2003, **59**, 940; S. Koch Singles, G. M. Dean, D. M. Kirkpatrick, B. C. Mayo, A. D. Langford-Pollard, A. C. Barefoot, and F. Q. Bramble, *Pestic. Sci.*, 1999, **55**, 288; J. Rouchaud, O. Neus, D. Callens, and R. Bulcke, *J. Agric. Food Chem.*, 1997, **45**, 3283; G. E. Schneiders, M. K. Koeppe, M. V. Naidu, P. Horne, A. M. Brown, and C. F. Mucha, *J. Agric. Food. Chem.*, 1993, **41**, 2404.
77. K. Konishi, T. Kuragano, and K. Matsuura, *Agric. Biol. Chem.*, 1986, **50**, 2427.
78. Z.-Y. Chang, P. J. Delaney, J. O'Donoghue, and R. Wang, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 228 – 236.
79. J. R. Finney, G. M. Farrell, and K. J. Bent, *Proc. Brit. Insect. Fung. Conf.*, 1975, 667; R. M. Bebbington, D. H. Brooks, M. J. Geoghegan, and B. K. Snell, *Chem. & Ind.*, 1969, 1512.
80. H. D. Sisler, N. N. Ragsdale, and W. F. Waterfield, *Pestic. Sci.*, 1984, **15**, 167.
81. S. L. Hargreaves, B. L. Pilkington, S. E. Russell, and P. A. Worthington, *Tetrahedron Lett.*, 2000, **41**, 1653.
82. B. C. Baldwin, A. J. Corran, and M. J. Robson, *Pestic. Sci.*, 1995, **44**, 81.
83. J. P. Daub and D. L. Piotrowski, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 246 - 257.

84. D. L. Jameson and L. E. Guise, *Tetrahedron Lett.*, 1991, **32**, 1999.
85. C. B. Vicentini, T. Poli, A. C. Veronese, V. Brandolini, M. Manfrini, M. Guarneri, and P. Giori, *Pestic. Sci.*, 1989, **27**, 77; T. Poli, C. B. Vicentini, V. Brandolini, A. C. Veronese, M. Manfrini, M. Guarneri, and P. Giori, *Pestic. Sci.*, 1989, **25**, 161.
86. C. B. Vicentini, G. Forlani, M. Manfrini, C. Romagnoli, and D. Mares, *J. Agric. Food Chem.*, 2002, **50**, 4839.
87. S. Giri, A. K. Shukla, and Nizamuddin, *J. Indian Chem. Soc.*, 1990, **67**, 153.
88. H.-Q. Wang, Z.-J. Liu, L.-M. Yang, and M.-W. Ding, *J. Heterocycl. Chem.*, 2004, **41**, 393.
89. J. L. Huppatz, *Aust. J. Chem.*, 1985, **38**, 221.
90. T. Kohts and H. Buchenauer, *Proc. Br. Crop Prot. Conf. – Pests Dis.*, 1984, 917.
91. L. D. S. Yadav, R. K. Tripathi, R. Dwivedi, S. N. Shukla, and H. Singh, *Ind. J. Chem.*, 1994, **33B**, 565.
92. L. D. S. Yadav, D. S. Yadav, and R. Yadav, *J. Agric. Food Chem.*, 1996, **44**, 1565.
93. R. H. Khan and R. C. Rastogi, *J. Agric. Food Chem.*, 1991, **39**, 2300.
94. G. F. Yang, Z. M. Liu, and X. H. Qing, *Chin. Chem. Lett.*, 2001, **12**, 877.
95. J. M. Pattanaik, M. Pattanaik, and D. Bhatta, *Ind. J. Chem.*, 1998, **37B**, 1304.
96. P. E. Russell, A. Percival, P. M. Coltman, and D. E. Green, *Proc. Br. Crop Prot. Conf. – Pests Dis.*, 1992, 411.
97. J. J. Takasugi, L. A. Witucki, D. J. France, L. S. Evans, C. L. Kohls, and M. V. Neypes, in 'Synthesis and Chemistry of Agrochemicals, Vol. 4', ACS Symposium Series 584, ed. by D. R. Baker, J. G. Fenyes, and G. S. Basarab, American Chemical Society, Washington DC, 1995, pp. 384 – 395.
98. H. Walter and R. Zeun, *Chimia*, 2003, **57**, 692.
99. Y. Yamanaka, M. Morimoto, K. Fujii, T. Tanaka, Y. Fukuda, and K. Nishimura, *Pestic. Sci.*, 1999, **55**, 896; Y. Yamanaka, M. Moritomo, K. Fujii, T. Tanaka, Y. Fukuda, and K. Nishimura, *Pestic. Sci.*, 1998, **54**, 223.
100. B. A. Dreikorn, P. R. Graupner, J. W. Liebeschuetz, and M. Yap, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 273 – 283; M. C. H. Yap, B. A. Dreikorn, L. N. Davis, R. G. Suhr, S. V. Kaster, N. V. Kirby, G. Paterson, P. R. Graupner, and W. R. Erickson, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 258 - 272.
101. R. E. Hackler, R. G. Suhr, J. J. Sheets, C. J. Hatton, P. L. Johnson, L. N. Davis, R. G. Edie, S. V.

- Kaster, G. P. Jourdan, J. L. Jackson, and E. V. Krumkalns, in 'Advances in the Chemistry of Insect Control III', ed. by G. G. Briggs, Special Publication - Royal Society of Chemistry, Vol. 147, Royal Society of Chemistry, Cambridge, 1994, pp. 70 – 84.
102. E. Wood, B. Latli, and J. E. Casida, *Pestic. Biochem. Physiol.*, 1996, **54**, 135; R. M. Hollingworth and K. I. Ahammadsahib, *Rev. Pestic. Toxicol.*, 1995, **3**, 277; T. Friedrich, P. van Heek, H. Leif, T. Ohnishi, E. Forche, B. Kunze, R. Jansen, W. Trowitzsch-Kienast, G. Hoefle, H. Reichenbach, and H. Weiss, *Eur. J. Biochem.*, 1994, **219**, 691; R. M. Hollingworth, K. I. Ahammadsahib, G. Gadelhak, and J. L. McLaughlin, *Biochem. Soc. Trans.*, 1994, **22**, 230.
103. C. Lamberth, E. Hillesheim, D. Bassand, and F. Schaub, *Pest Manag. Sci.*, 2000, **56**, 94.
104. R. E. Hackler, C. J. Hatton, M. B. Hertlein, P. L. Johnson, J. M. Owen, J. M. Renga, J. J. Sheets, T. C. Sparks, and R. G. Suhr, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998 pp. 147 - 156.
105. J. D. Crum and C. H. Fuchsman, *J. Heterocycl. Chem.*, 1966, **3**, 252; H. H. Fox and J. T. Gibas, *J. Org. Chem.*, 1958, **23**, 64.
106. J. G. Okun, P. Lummen, and U. Brandt, *J. Biol. Chem.*, 1999, **274**, 2625; K. Goka, Y. Yoshida, and A. Takafuji, *Appl. Entomol. Zool.*, 1998, **33**, 171.
107. T. Obata, K. Fujii, H. Yoshiya, K. Tsutsumiuchi, and H. Yoshioka, *Pestic. Sci.*, 1992, **34**, 133.
108. P. L. Johnson, R. E. Hackler, J. J. Sheets, T. Worden, and J. Gifford, in 'Synthesis and Chemistry of Agrochemicals, Vol. 5', ACS Symposium Series 686, ed. by D. R. Baker, J. G. Fenyes, G. S. Basarab, and D. A. Hunt, American Chemical Society, Washington DC, 1998, pp. 136 - 146.
109. J. M. Wierenga, T. G. Cullen, J. A. Dybas, R. N. Henrie, C. J. Peake, and M. J. Plummer, *Pest Manag. Sci.*, 2000, **56**, 233.
110. W. A. Kleschick, L. N. Davis, M. R. Dick, J. R. Garlich, E. J. Martin, N. Orr, S. C. Ng, D. J. Pernich, S. H. Unger, G. B. Watson, and R. N. Zuckermann, 'Agrochemical Discovery', ACS Symposium Series 774, ed. by D. R. Baker and N. K. Umetsu, American Chemical Society, Washington DC, 2001, pp. 205 – 213.
111. D. A. Pulman, I. H. Smith, J. P. Larkin, and J. E. Casida, *Pestic. Sci.*, 1996, **46**, 237.
112. M. J. Bushell and R. Salmon, in 'Advances in the Chemistry of Insect Control III', ed. by G. G. Briggs, Special Publication - Royal Society of Chemistry, Vol. 147, Royal Society of Chemistry, Cambridge, 1994, pp. 103 – 116.
113. A. F. Grapov, *Russ. Chem. Rev.*, 1999, **68**, 697.
114. C. Lamberth, *J. Sulfur Chem.*, 2004, **25**, 39.
115. H. Fischer and L. A. Summers, *J. Heterocycl. Chem.*, 1980, **17**, 333.

116. C. M. Tice, L. M. Bryman, R. C. Roemmele, E. C. Taylor, P. Zhou, J. Jurczak, and A. Jezewski, in 'Synthesis and Chemistry of Agrochemicals, Vol. 6', ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 51 – 60; C. M. Tice and A. C.-T. Hsu, in 'Synthesis and Chemistry of Agrochemicals, Vol. 6', ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 41 – 50.
117. S. Kawamura, J. Sato, T. Hamada, M. Sakaki, and Y. Sanemitsu, *J. Agric. Food Chem.*, 1993, **41**, 288.
118. P. Babczinski, U. Heinemann, G. Sandmann, S. Kawamura, T. Hamada, R. Sato, and Y. Sanemitsu, *J. Agric. Food Chem.*, 1992, **40**, 2497; S. Kawamura, T. Hamada, R. Sato, Y. Sanemitsu, G. Sandmann, and P. Babczinski, *J. Agric. Food Chem.*, 1991, **39**, 2279.
119. P. Babczinski, M. Blunck, G. Sandmann, K. Shiokawa, and K. Yasui, *Pestic. Biochem. Physiol.*, 1995, **52**, 45; P. Babczinski, G. Sandmann, R. R. Schmidt, K. Shiokawa, and K. Yasui, *Pestic. Biochem. Physiol.*, 1995, **52**, 33; P. Babczinski, M. Blunck, G. Sandmann, R. R. Schmidt, K. Shiokawa, and K. Yasui, *Pestic. Sci.*, 1990, **30**, 339.
120. G. M. Ramos Tombo and D. Bellus, *Angew. Chem.*, 1991, **103**, 1219; *Angew. Chem., Int. Ed.*, 1991, **30**, 1193; L. Streit, M. Moreau, J. Gaudin, E. Ebert, and H. Vanden Bossche, *Pestic. Biochem. Physiol.*, 1991, **40**, 162.
121. W. R. Shiang and R. L. Swafford, in 'Chemistry of Crop Protection', ed. by G. Voss and G. Ramos, Wiley-VCH, Weinheim, 2003, pp. 30 – 39; T. J. Dietsche, D. B. Gorman, J. A. Orvik, G. A. Roth, and W. R. Shiang, *Org. Proc. Res. Dev.*, 2000, **4**, 275.
122. T. J. Kress, *J. Org. Chem.*, 1985, **50**, 3073.
123. M. J. Coghlan, E. V. Krumkalns, B. A. Caley, H. R. Hall, and W. R. Arnold, in 'Synthesis and Chemistry of Agrochemicals, Vol. 2', ACS Symposium Series 443, ed. by D. R. Baker, J. G. Fenyes, and W. K. Moberg, American Chemical Society, Washington DC, 1991, pp. 538 – 552.
124. R. J. Brown, B. Ashworth, J. E. Drumm, D. A. Frazier, M. A. Hanagan, C. Happersett, G. E. Koether, D. J. Robinson, K.-M. Sun, and P. Wojtkowski, in 'Synthesis and Chemistry of Agrochemicals, Vol. 6', ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 327 – 339.
125. T. M. Stevenson, B. A. Crouse, T. V. Thieu, C. Gebreysus, B. L. Finkelstein, M. R. Sethuraman, C. M. Dubas-Cordery, and D. L. Piotrowski, *J. Heterocycl. Chem.*, 2005, **42**, 427.
126. L. M. Cole, R. A. Nicholson, and J. E. Casida, *Pestic. Biochem. Physiol.*, 1993, **46**, 47; F. Colliot,

- K. A. Kukorowski, D. W. Hawkins, and D. A. Roberts, *Proc. Br. Crop Prot. Conf. – Pests Dis.*, 1992, 29.
127. A. J. Whittle, in 'Advances in the Chemistry of Insect Control III', ed. by G. G. Briggs, Special Publication - Royal Society of Chemistry, Vol. 147, Royal Society of Chemistry, Cambridge, 1994, pp. 156 – 170.
128. F. L. Bowen, P. Fisara, P. Junquera, D. T. Keevers, R. H. Mahoney, and H. R. Schmid, *Aust. Vet. J.*, 1999, **77**, 454; O. S. Anziani, A. A. Guglielmone, and H. Schmid, *Vet. Parasitol.*, 1998, **76**, 229.
129. T. M. Stevenson, V. E. Amoo, G. C. Chiang, E. Keskeny, J. K. Long, B. A. Crouse, P. Sharpe, K. Hillegass, L. Jones, and C. Yatsko, in 'Synthesis and Chemistry of Agrochemicals, Vol. 6', ACS Symposium Series 800, ed. by D. R. Baker, J. G. Fenyes, G. P. Lahm, T. P. Selby, and T. M. Stevenson, American Chemical Society, Washington DC, 2002, pp. 188 – 198.
130. M. Eberle, S. Farooq, A. Jeanguenat, D. Mousset, A. Steiger, S. Trah, W. Zambach, and A. Rindlisbacher, *Chimia*, 2003, **57**, 705.
131. H. Zschke, *Z. Chem.*, 1977, **17**, 63.