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A Review on Synthetic Hetrocyclic Compounds in Agricultural and other Applications

Suvarna Arunkumar S

Medigraph Pharmaceuticals Pvt. Ltd in New Panvel, Maharastra, India

Abstract: Heterocyclic chemistry offers an example for the lack of distinct demarcations; in fact, it pervades the plurality of the other chemical disciplines. Heterocyclic are inextricably woven into the life processes. The vital interest of the agrochemical industries in heterocyclic is often connected with their natural occurrence. Synthetic chemistry provides cornucopia of heterocyclic systems. Heterocyclic compounds play the same major role in crop and animal treatment as they do in medicine. We will consider here only the use of synthetic compounds on crops in the field; many agents have been developed that function as insecticides, fungicides, herbicides, and plant growth regulators (PGRs), and these agents are generally called pesticides. Main aim of this paper is to present the information regarding the heterocyclic compounds that constitute the largest family or organic compounds. These are extremely important with wide array of synthetic, agricultural and industrial applications.
Keywords: Synthesized compounds, heterocyclic substances, agricultural.

Introduction:

This will attempt to bring out some of the highlights of heterocyclic compounds particularly of pesticidal importance in the area of organic chemistry. This reviews the history, importance and classification of pesticides and discusses briefly about their economic importance in the farming sector. The crop protection chemicals widely used in agriculture to control various pests are classified as insecticides, fungicides, rodenticides, herbicides and fumigants depending upon their mode of activity. Among pesticides, insecticides are widely used chemicals to control various diseases caused by different insects.

Nitrogen, oxygen and sulfur containing heterocyclic compounds are key building blocks used to develop compounds of biological or medicinal interest to chemists. A vast number of nitrogen containing heterocyclic building blocks have applications in pharmaceuticals and agrochemical research and drug discovery. Heterocyclic compounds also have a practical use as components in dyes, antioxidants, copolymers, bases, and ligands.

As in pharmaceutical research, the industry synthesizes many thousands of compounds for testing in the previously mentioned areas; many are found to have some level of activity, but often not with enough to justify commercial development. The cost of production also may prevent the introduction of new agents to the market, as will mammalian toxicity considerations. Nevertheless, the field is large and of great importance in the vast area of agriculture. The real value of synthetic agrochemicals only became apparent by the discovery in the 1940s of the powerful insecticides Dichlorodiphenyltrichloroethane [DDT; more properly 1,1-bis(p-chlorophenyl)-2,2,2-trichloroethane], and esters of organophosphorus acids such as parathion ($(EtO)_2P(S)OC_6H_4NO_2$-p), among other compounds. Research on pesticides and PGRs became a major activity of many industrial

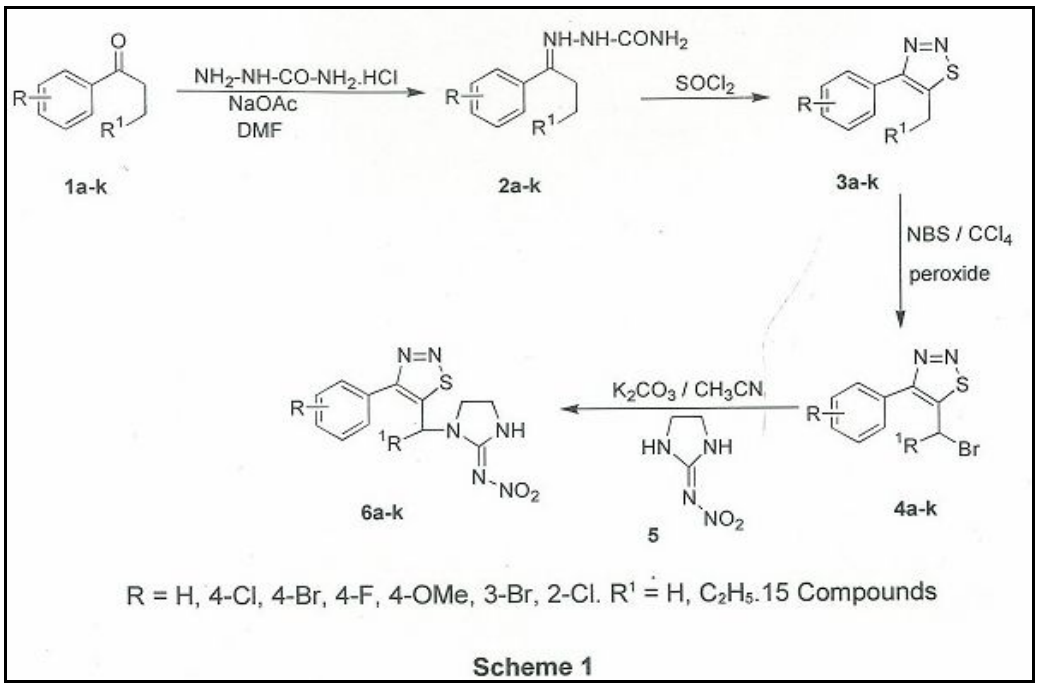
firms, and a great variety of structures were found to have commercial value, heterocycles being prominent among them. This will summarize some of the heterocyclic compounds that were commercialized during the early years of pesticide and PGR research. Viewing these compounds provides an excellent introduction to the wide range of heterocyclic ring systems found in the more active agents.

The present work explains synthesis of thiadiazole, isoxazole, benzimidazole, dihydropyrimidinones, and benzodiazepine derivatives, and their biological importance such as insecticidal and fungicidal properties.

Material and Methods

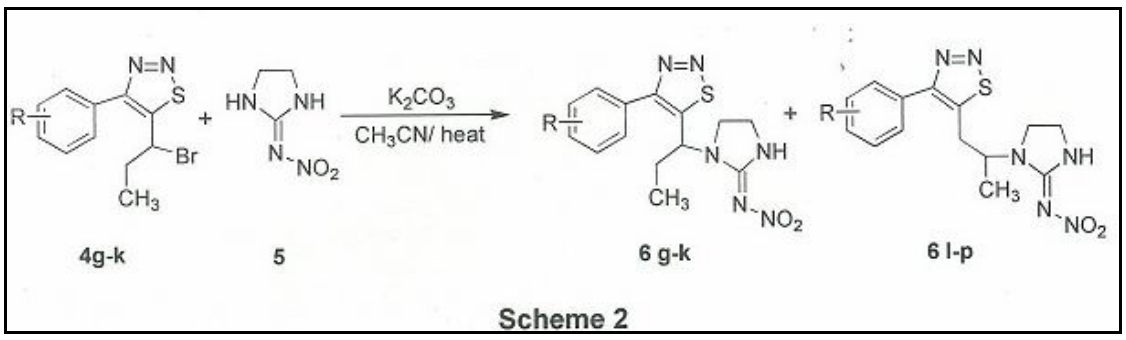
Synthesis of new thiadiazolyl derivatives containing imida- zolidin taxophore akin to imidacloprid

This deals with the synthesis of 1,2,3-thiadazolyl imidazole derivatives as neo nicotinoid insecticides. This study relates in essence to N-(4- aryl-5-1,2,3-thiadiazolylmethyl)-2-nitroiminoimidazoline derivatives. Retro synthetic analysis of target molecules requires appropriately substituted propio and valerophenones as starting materials for 1,2,3-thiadiazole derivatives and 2-nitroimino imidazole as an intermediate. The semicabzones of propio and valero-phenone (**2a-k**) are cyclised with thionyl chloride to obtain 5-alkyl-4-aryl-1,2,3-thiadiazole (**3a-k**), which is further transformed into 1-oxo-2-1-[1-(4-aryl-1,2,3-thiadiazol-5-yl)methyl/propyl]-tetrahydro-1*H*-2-imidazolyliden-1-hydraziniumolate (**6a-p**). The sequence of synthetic methodology is depicted in Scheme **1**.



Scheme 1

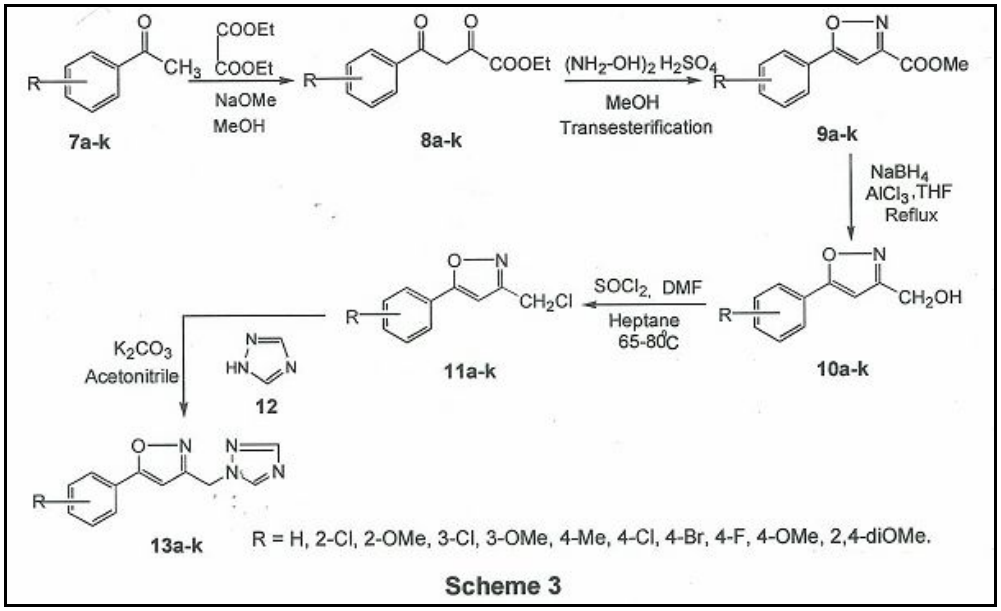
The formation and characterization of unusual compound (**6 l-p**) obtained in the condensation of 4-aryl-5-(1-bromopropyl)-1,2,3-thiadiazole with 2-nitroimine imidazole is described (Scheme **2**).



Scheme 2

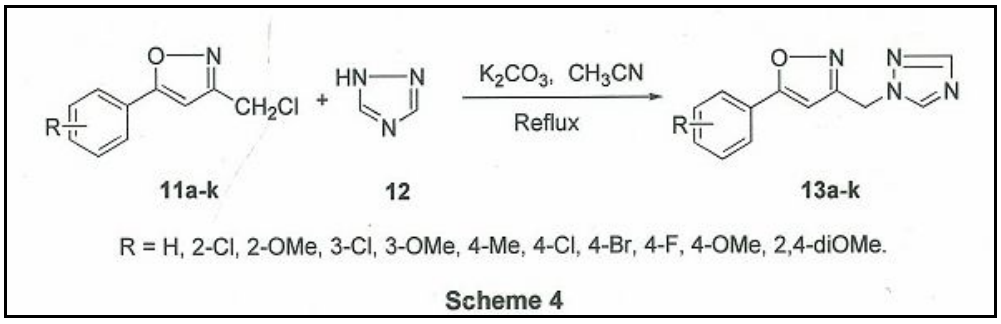
Synthesis of isoxazolyltriazole derivatives as fungicides

With a view to obtaining biologically active isoxazole derivatives containing triazole moiety, synthesis of a series of compounds have been conceived and the synthetic strategy is described in the Scheme 3. The triazole moiety has been found to be an important taxophore to exhibit fungitoxic properties inhibiting the cell wall synthesis and also known as C-14 demethylation inhibitor (to act as fungicide). Most of the exploited azole fungicides contain an aromatic ring system, and to the best of the author's knowledge no compound with isoxazole heterocyclic moiety has so for been synthesized and studied for their fungitoxic properties.



Scheme 3

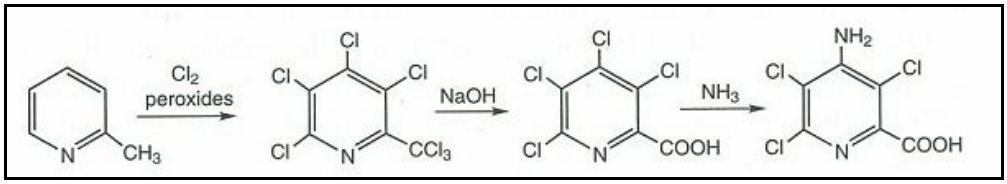
The target molecule 5-aryl-3-(4H-1,2,4-triazol-4-yl methyl) isoxazole (13a-k) is prepared by N-alkylation of 1H-1,2,4-triazole (12) with 5-aryl-3-chloromethyl- isoxazole under mild basic conditions using different bases in polar solvent (Scheme 5). The yields obtained are in the range of 80-90 %. The possibility of formation of C-4 alkylated product is ruled out based on the unequivocal characterization of the product using spectral data.



Scheme 4

Synthesis of Picloram

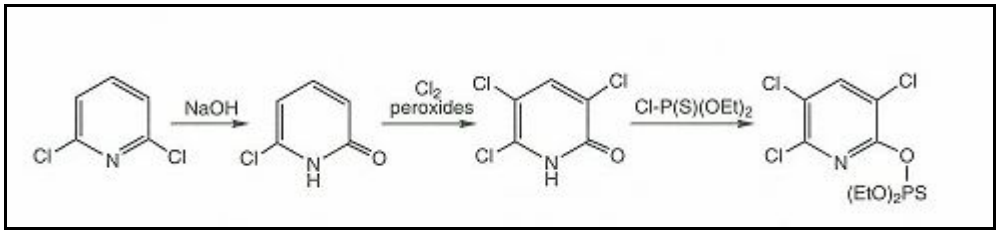
Picloram is a herbicide that selectively kills broadleaf weeds. Its synthesis is shown in scheme 5. Picloram has auxin-like (growth-promoting) properties; it acts by increasing plant growth so rapidly as to use up the normal nutrients and kill the plant.



Scheme 5

Synthesis of Chlorpyrifos

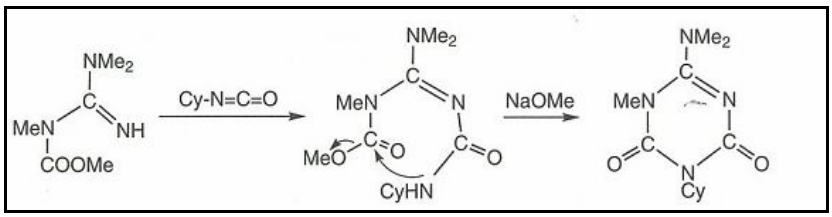
Chlorpyrifos belongs to the family of organophosphorus insecticides, all of which function by inhibition of the enzyme cholinesterase. It is synthesized by the reactions of Scheme 6.



Scheme 6

Synthesis of Hexazinone

It may be synthesized as in Scheme 7 by condensing guanidine derivative and cyclohexyl isocyanate to form intermediate which is then cyclized by the NH-to-ester condensation found frequently in pyrimidine synthesis to give hexazinone



Scheme 7

Applications of Heterocyclic Compounds in Agricultural

1) Triazine Derivatives

Various 1,3,5-triazines have extremely valuable properties as herbicides. It was stated in 1984[1a] that they constitute the most important class of heterocyclic compounds in all of agrochemistry. The most prominent is atrazine, which at high concentration is a total herbicide, but at lower concentrations is useful for preemergence control of weeds. Many triazines have been investigated, and several have appeared on the market. Some of these are shown in Figure 1.All are based on the sequential displacement of .chlorine from cyanuric chloride (2,4,6-trichloro-1,3,5-triazine,) with nucleophiles.

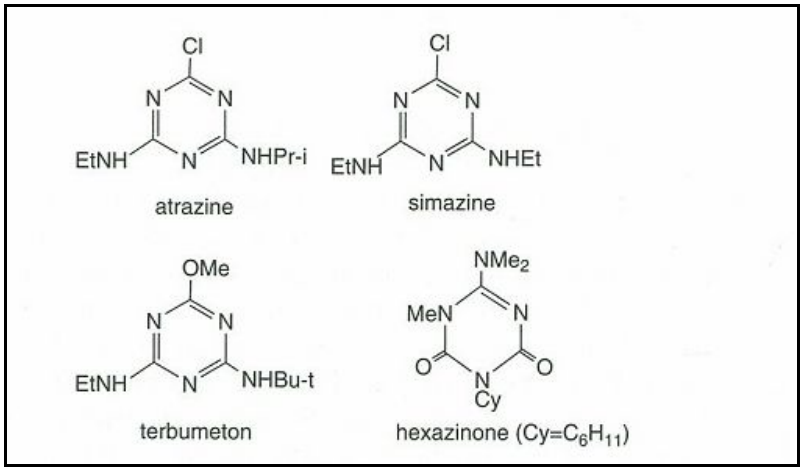


Figure 1

2) Pyridine Derivatives.

Some useful pyridine derivatives are shown in Figure 2. It will be shown that these derivatives exhibit a variety of types of biochemical activity. Paraquat and diquat are both quaternary salts based on bipyridyls. Pyridine is the starting material for both compounds. They are non-selective, rapid action herbicides that act on all green plants through interference with the photosynthetic electron-transport system. Fluridone is a herbicide that is a gamma-pyridone derivative. It is a carotenoid inhibitor; this is a well-known type of activity that interferes with the photosynthesis process in such a way as to lead to production of the plant-lethal singlet oxygen.

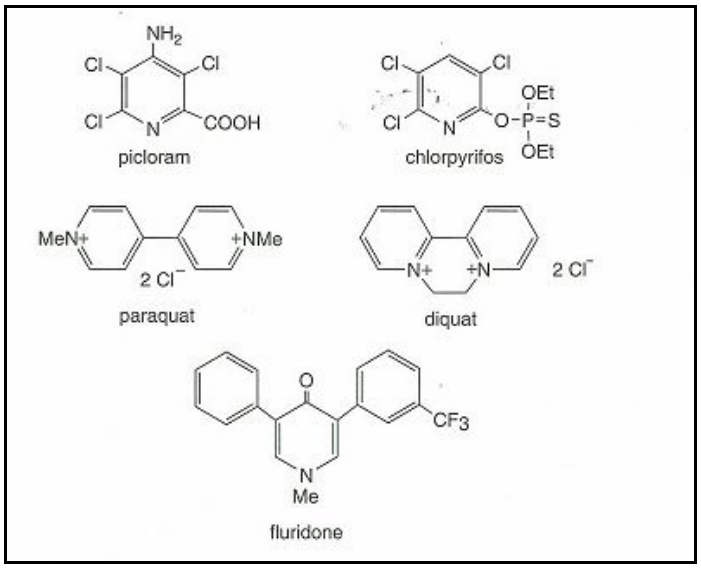
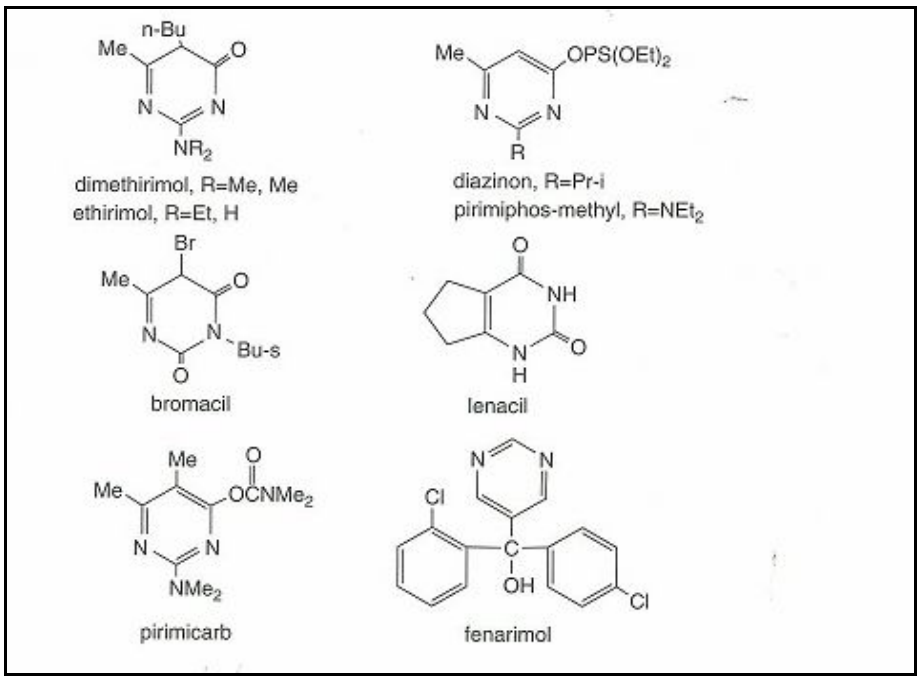


Figure 2. Some pyridine agrochemicals

3) Pyrimidine Derivatives.

Some prominent pyrimidine-based agrochemicals are shown in Figure 3.



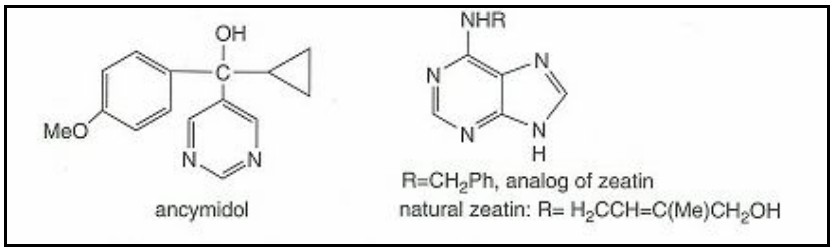
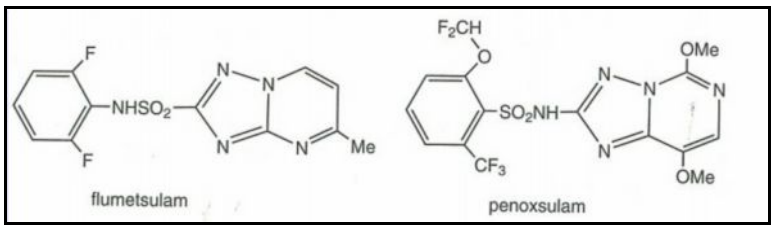


Figure 3

The synthesis of these compounds employs the conventional cycliza-tion methods of pyrimidine chemistry For example dimethirimol is prepared by reaction of the n-butyl derivative of ethyl acetoacetate with N, N-dimethylguanidine. This agent and ethirimol are fungicides, which seem to act through interference with the metabolism of adenine in the plant. Bromacil and lenacil are analogs of uracil and are made from cyclizations around urea; both are used as total herbicides. Diazinon, pirimiphos, and pirimicarb are insecticides that react with the enzyme cholinesterase that is involved in the nervous system. Their immediate precursors are 4-carbonyl derivatives of the pyrimidines, which are dominant forms in keto-enol tautomerism; the acyl groups are added by attack on oxygen of the enolic form. Fenarimol is prepared by condensation of dichlorobenzophenone and 5-lithiopyrimidine. It is a useful fungicide that acts to block ergosterol biosynthesis in the fungi. Several heterocyclic compounds are effective blockers of sterol biosynthesis. Plant -growth regulating power is found in ancymidol, which acts by inhibiting gibberellin biosynthesis. Gibberellins are cyclic diterpenes of 19-20 carbons that are growth-promoting agents in plants; their inhibition retards the growth of plants without killing the plant. An analog of the naturally occurring purine derivative zeatin (which controls cell division) has value in improving the storage of plants.

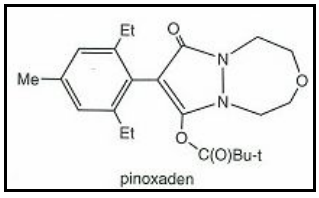
4) Triazolopyrimidines.

Flumetsulam was the first of a new family of herbicides containing the triazolo[5,1-a]pyrimidine ring system[2]. Important in this compound also was the presence of a sulfonamido group. Here, the ring system has [1,5-c] fusion and the reversed structure of the sulfonamide group. It is active against grass and broadleaf weeds. Triazolopyrimidines exhibit their herbicidal activity by inhibiting the enzyme acetolactate synthase[3].



5) Pinoxaden.

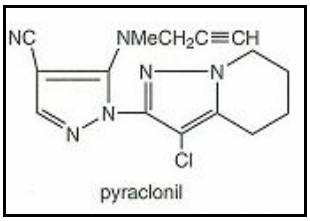
This herbicide is active against grass weed species in the growing of grain cereal crops, especially rice. It is an inhibitor of acetylcoenzyme A carboxylase. Its structure evolved from considerations of the pyrazolidine-3,5-diones (and their enol derivatives), many of which have valuable herbicidal activity[4].



6) Alkyne-Containing Heterocycles.

Many heterocycles with alkyne groups have potent pesticidal activity and constitute another broad family receiving attention. As herbicides, they serve as inhibitors of the enzyme protoporphyrinogen-IX

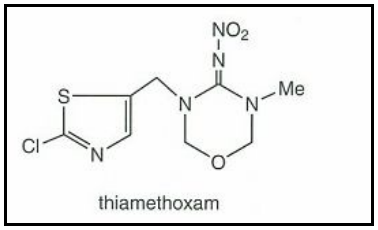
oxidase, which catalyzes the last step in the biosynthesis of chlorophyll. A typical herbicidal heterocycle under development is pyraclonil, which is shown along with several other useful alkynyl-heterocycles[5].



pyraclonil

7) Thiamethoxam.

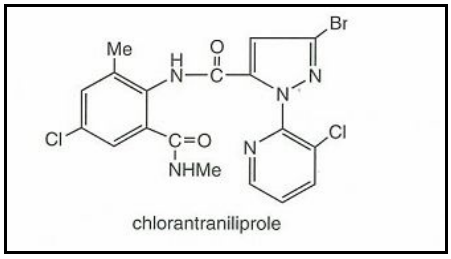
This new insecticide is classed as a member of the important neonicotinoid family, which act as agonists of the nicotinic acetylcholine receptor. Thiamethoxam has systemic activity, meaning that a level of it or active metabolic products[6] is maintained in the plant and ingested by the attacking insects. It is especially used in the protection of tomato crops.



thiamethoxam

8) Chlorantraniliprole.

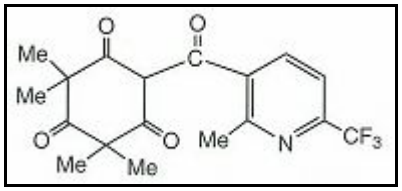
Diamide insecticides are another class of recently introduced crop protection agents, which behave as activators of ryanodine receptors in the insect. This leads to uncontrolled calcium release in muscles. Chlorantraniliprole is a member of this family and is in commercial use for protection from various pests[7].



chlorantraniliprole

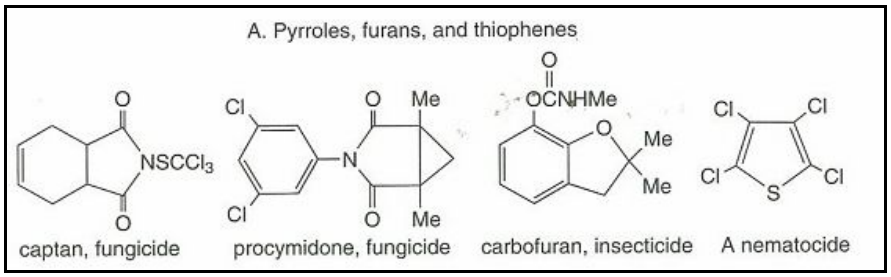
9) Triketones with Heterocyclic Substituents.

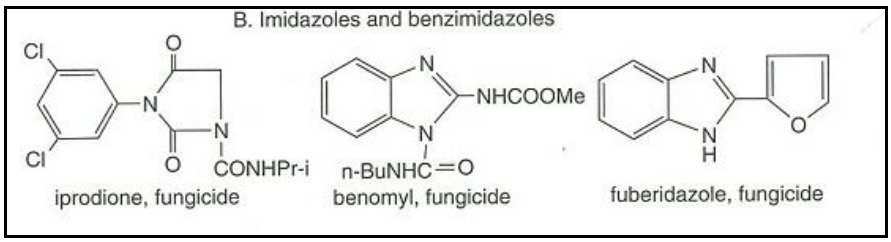
Triketones represent a well-studied, but still developing, family of herbicides. Some with pyridyl substituents are among the most active. The triketones are inhibitors of the plant enzyme 4-hydroxyphenylpyruvate dioxygenase (HPPD), which plays a key role in the biosynthesis of plastoquinone and tocopherol[8]. Nicotinoyl syncarpic acid is shown as a typical structure of this type. Its potent herbicidal activity led to synthetic work that has yielded many related structures in an effort to improve selectivity in the herbicidal action.

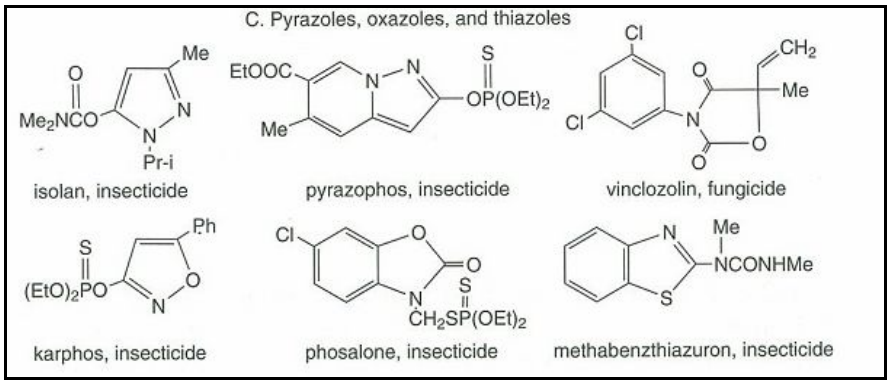


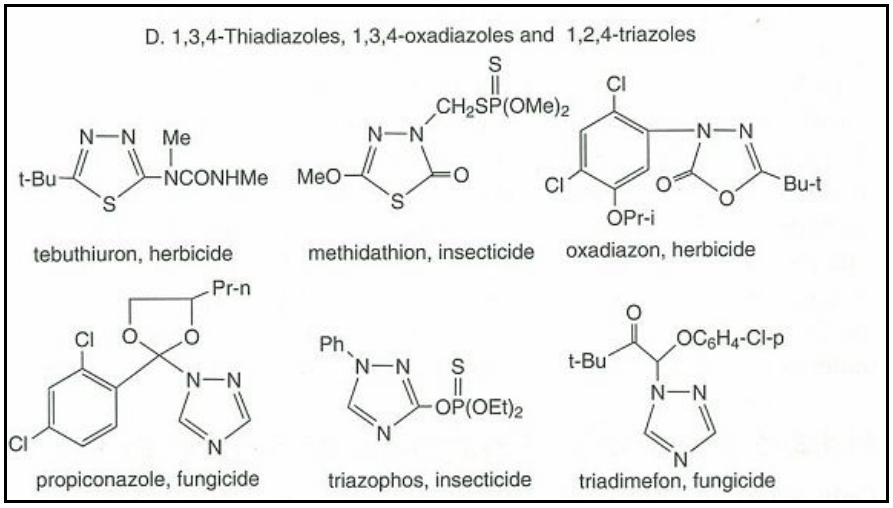
nicotinoyl syncarpic acid

Examples of the Results from More Recent Research Only a few illustrative structures will be shown here, defining some trends in research of the 2000s.





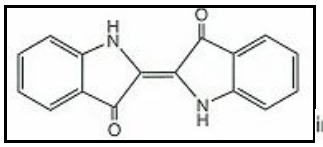




Applications of Heterocyclic Compounds in Commercial Fields

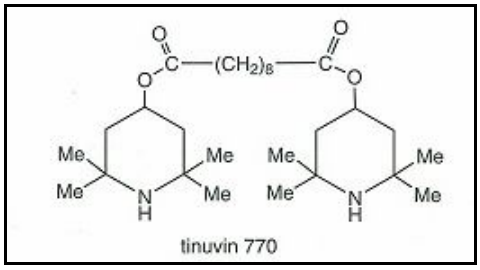
Heterocyclic compounds are of great importance in many different fields of commerce. They represent specialized, well-developed areas of technology. An extremely important application of heterocyclic compounds is in the field of dyes and pigments. Extended conjugation is an important ingredient for a compound to be colored, and heterocyclic systems, usually multicyclic, in great numbers have been constructed around this principle[9]. Industrial organic chemistry can trace its beginnings back to the (accidental) discovery of mauveine in 1856 by W. H. Perkin; it was the first organic compound to be prepared synthetically at the

industrial scale. Another heterocyclic compound, indigo was derived from natural sources and was used for centuries before it was synthesized in 1883 and later made commercially. These two early compounds display the extended conjugation so important in the development of new dye and pigment chemicals[1b]. Technology in the area of photography is highly developed, making use of heterocyclic compounds in various ways in the several steps of the process[1c,d].



indigo

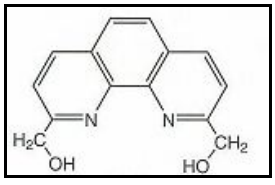
Heterocyclic compounds can participate in polymer technology in several ways. They can be pendants on a polymer chain, as might be formed from the polymerization of vinyl monomers with heterocyclic substituents. There are processes where the polymer is formed by closing heterocyclic rings. Finally, heterocyclic groups can be added to previously formed polymers[1e]. Hindered heterocyclic amines are used as light stabilizers in plastic and coating formulations, protecting against degradation by ultraviolet radiation. These agents are known as hindered amine light stabilizers (HALSs) and are commonly derivatives of 2,2,6,6-tetramethylpiperidine[10]. An example of a HALS agent is Tinuvin 770 (BASF), which is a diester of sebacic acid and 4-hydroxy-2,2,6,6-tetramethylpiperidine. It is thought to act through the formation of a piperidinoxyl radical[11].



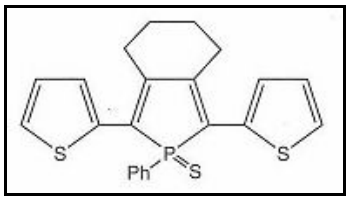
tinuvin 770

A thriving and highly important field is the construction of coordination complexes from metallic species and heterocycles. These com-plexes can be useful as reaction catalysts and have other uses as well. To illustrate the catalyst area (which is large), the zirconium complex formed from the anion of indenylindoyl anion and $ZrC1_4$ is offered as an example. The complex has the formula Zr_2C1_2 and is an excellent catalyst for the polymerization of olefins.

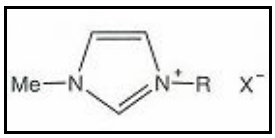
Another valuable property is the selective binding of certain metallic species[13]. An example of this type of ligand is the 1,10- phenanthroline derivative (PDALC), which selectively binds to larger metallic cations such as Ca++ and Pb++. The crystallized coordination complex formed from calcium perchlorate has the formula $[Ca(PDALC)_2](ClO_4)_2 \cdot H_2O$. Certain heterocyclic ligands have special value in selective complexation because, as in the case of PDALC, the backbone containing the ligating nitrogen atoms can be rigid and offer a cavity of fixed geometry to receive the metal.



A relatively new and still developing field is the use of hetero-cyclic compounds in electro-optical applications, which includes light-emitting diodes (LEDs), thin-film transistors, and photovoltaic cells. One type of useful structure has several heterocyclic rings such as pyrrole or thiophene joined in a linear fashion. The phosphole ring system is a new participant in this type of array. This is illustrated by compound in which two thiophene rings are attached to a central phosphole ring (as the sulfide). This compound has LED properties; when deposited as a thin film between a bilayer cathode and anode, yellow light was emitted by application of a low voltage[14]. Other related structures are being examined for similar electro-optical activity.



Another new application of heterocyclic compounds is in the field of ionic liquids. These compounds generally are quaternary salts of certain heterocyclic bases, and they are finding use as high-boiling polar solvents for extractions or as reaction media[15]. Common, among the ionic liquids known so far are salts of imidazole, which are shown as follows.



Conclusion:

The Review described in this, demonstrates the synthesis of new chemical entities adopting various strategies and the compounds are screened for pesticidal activity in order to find a lead molecule for a specified biological activity and explains synthesis of thiadiazole, isoxazole, picloram, and benzodiazepine derivatives, and their biological importance such as insecticidal and fungicidal properties.

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