

**ORGANOSULFUR AND RELATED COMPOUNDS: SYNTHESIS,
BIOLOGICAL ACTIVITIES AND APPLICATIONS AS
AGRICULTURAL PESTICIDES**

INAUGURAL LECTURE SERIES 29

By

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OGBOMOSO**

**ORGANOSULFUR AND RELATED COMPOUNDS: SYNTHESIS,
BIOLOGICAL ACTIVITIES AND APPLICATIONS AS
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Protocols

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Chairman, Committee of Provost and Deans.

All Deans here present, especially Dean, Pure and Applied Sciences.

Professors and members of the academic community.

Respected members of the Non-teaching community.

Royal fathers and religious leaders here present.

My family and relations.

Greatest Ladokites.

Gentlemen of the press.

Distinguished guests.

Ladies and gentleman.

PREAMBLES

To God be the glory. Great things He have done in my life. He gave me the gift of life and counted me worthy to stand before this body of scholars and this distinguished audience to deliver my inaugural lecture today 13th of June 2019.

Vice Chancellor sir, please permit me to recount two major events that brought me into the field of Chemistry.

Event 1

Late Dr. Akintobi who was the staff adviser for incoming students at the Department of Chemistry University of Ife (now Obafemi Awolowo University) is the man that brought me to study Chemistry in the first place because originally I was offered admission to read Physics. It was during the freshers registration programme that he convinced me about the enormous benefits of being a chemist. I agreed with him then and now looking back I never have any regret for doing so.

Event 2

After my mandatory National Youth Service Scheme at Ekamarun Anglican Grammar School, Ifon, Ondo State, I joined the Ondo State Teaching Service at Adeyeri Grammar School Iyere, Owo as a class teacher. At that time, I never dreamt of pursuing an academic career despite being the best graduating student in my department because I couldn't afford the cost of a higher degree. However, the story changed in the period of my encounter with Professor Jide Ige of the Department of Chemistry. He mentored me and opened my eyes to the possibility of pursuing a master's degree and at the same time be employed as a Graduate Assistant. He did not stop at that, he recommended me to Professor J. F. Ojo who was the Head of Chemistry Department then. Eventually, I was offered appointment as a Graduate Assistant.

Mr. Vice Chancellor Sir, need I say that an inaugural lecture is a *once in a lifetime opportunity* given to a Professor to showcase his/her works to the university community and the general public. Still, some say it is payment of some form of debt the Inaugural Lecturer owes the community. Nonetheless, it is patent from both views that it is a gain-gain situation where both parties have a romance of knowledge with each other. Sotonye, E. (2018).

Vice Chancellor Sir

Please kindly permit me to proceed straight to my lecture

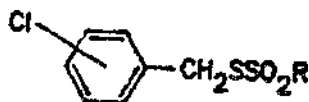
INTRODUCTION

Sulfur-based Agricultural Chemicals

The use of elemental sulfur and its compounds as pesticides was known to the ancient Greeks as early as 1000 B.C.; however, the first ever record to suggest the application of sulfur for the control of pest diseases was not made until 1803 by Forsyth (1983). He recommended a concoction of tobacco, sulfur, quicklime and elder bud for the control of powdery mildew on fruits of trees. The use of sulfur as an effective remedy for the control of peach mildew was also reported to the London Horticultural Society in 1824. It was suggested that sulfur be painted on heat pipes in green-houses for the control of greenhouse diseases and that the oxidation products of sulfur had fungicidal properties. By the middle of the nineteenth century, sulfur had gained a lot of popularity for its fungicidal properties, and its use as a fungicide gradually increased until the fungicidal properties of Bordeaux mixture in the control of mildew of grapes were discovered.

The introduction of dithiocarbamates for plant disease control during the 1930's marks the beginning of the use of organic chemicals on an important scale for the control of plant diseases. Tisdale *etal.*(1934) patented compounds of the general molecular formula $X(Y)NCSSZ$, where X is hydrogen or alkyl, Y is hydrogen, alkyl or aryl, and Z is metallic in nature, and thiuram disulfide derivatives, as fungicides, bactericides, and microbiocides. The use of ethylenebisdithiocarbamate as a bactericide, or fungicide was also discovered. It was reported that disodium ethylenebisdithiocarbamate was highly active against fungi. This compound, however, appeared to have little future as a practical fungicide because of its

instability and water solubility until Henberger et al. demonstrated that it could be stabilized and made to adhere to foliage. This was accomplished by the addition of zinc sulfate and lime in aqueous solution to this compound, forming zineb (zinc ethylenebis(dithiocarbamate)) on exposure to air. Thiocyanates and isothiocyanates were found to show some promise as insecticides as well as fungicides, the most active being ethylene and trimethylenedithiocyanates; other workers confirmed this finding. The lower aliphatic isothiocyanates were found to exhibit only very low activity possibly because of their high volatility. The xanthates and xanthyl sulfides ROCSSM , $(\text{ROCSS-})_2$, $(\text{ROCS})_2\text{S}$ were screened for their fungistatic properties and it was observed that the most active compound was potassium methyl xanthate; against *Botrytis cinerea* and *Fusarium caeruleum* it was fungistatic up to a rating of 7 on a scale of 1-10. The tuberculostatic, bacteriostatic and fungistatic activities of *S*-alkylisothiosemicarbazonium iodides and their N^4 -(*p*-chlorophenyl) derivatives have been studied *in vitro* and the N^4 -(*p*-chlorophenyl) derivatives were found to be five times more active than the non-substituted *S*-alkylisothiosemicarbazonium iodides which were only 2% as active as the parent thiosemicarbazone. The inhibitory effects of some organic sulfur compounds on *Histoplasma capsulatum* have been investigated; eight classes of organic sulfur compounds comprising 42 substances were tested *in vitro* for activity against the yeast phase of *H. capsulatum*. Activity was found in classes of thiols, thioacids, disulfides, thiosulfonates, sulfinates, and sulfenamides, but the reaction products of thiols with aldehydes or ketones were found unpromising. The thiosulfonates (1)

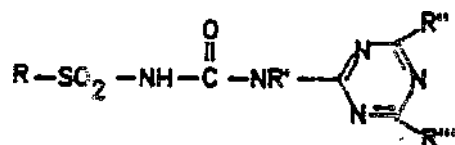


(1)

were patented as antiviral drugs by Shimabara *et al* (1971) Also, *N*-phenylsulfenamide and its substituted derivatives have been prepared and patented as fungicides by Fenyes, (1970)

Only a few studies have been made of the fungicidal activities of alkyl sulfides and mercaptans but none of these compounds showed a high order of activity and they are primarily of academic interest.

Sulfur and its compounds continue to be important agrochemicals, as shown by the large variety of new sulfur-based crop protection chemicals in current development around the world. The sulfonylurea herbicides (Schloss, 1971) are about one to two orders of magnitude more active than the standard herbicides used for weed control in agriculture. These sulfonylureas have the general structure (2) shown below.



(2)

The variations on the right-hand side of the molecule possessing activity are relatively few: triazine and pyrimidine rings are allowed and the substituents can be methyl, methoxyl or other small radicals. On the left-hand side, many variations are possible with a wide variety of aromatic, heterocyclic and even aliphatic groups. Selectivity against various plant species is obtained with these structural variations.

Sodium tetrathiocarbonate, a new soil fumigant, recently under field development by Union Oil Co. of California, is made from carbon disulfide, sulfur and caustic soda. Tetrathiocarbonate gives a broad spectrum control of nematodes, nitrifying bacteria, grape *phylloera* and a wide range of soil fungi. It is water

soluble and can be added with irrigation water and, being low in phytotoxicity, it can be used even on some established plants such as citrus trees and grape vines.

The familiar, sulfur-containing types of agrochemicals continue to have new variations, mostly in the direction of increased activity towards target organisms and improved selectivity so that non-target organisms are not affected. Thus, new benzylthiocarbamate herbicides and new *S*-alkyl thiophosphate anticholinesterase insecticides have been developed and introduced.

Organosulfur compounds can be derived from both plant and animal sources; sulfur is essential for life, and these compounds are abundant in nature. The most common source of sulfur for humans is through a diet composed of broccoli, cauliflower, cabbage, garlic, onion, meat, eggs, and fish (Sener *et al.*, 2007; Vazquez-Prieto and Miatello, 2010). Organosulfur compounds can be classified based on the functional groups to which sulfur is attached. The allium genus of flowering plants, which includes garlic and onions, contains important compounds such as cysteine sulfoxides and γ -glutamylcysteines. The hydrolysis of cysteine sulfoxides accounts for the flavor and pungency of garlic and onions (Vazquez-Prieto and Miatello, 2010). The cysteine sulfoxides are of four types: alliin, methiin, propiin, and isoalliin. Onions are especially rich in isoalliin, whereas garlic is rich in alliin. Alliin is converted into allicin by a hydrolyzing enzyme when garlic cells are crushed during chewing or cooking. Allicin is a very unstable compound that can be readily converted to more stable compounds depending on the conditions; for example, it is converted to dithiin when extracted with oil, ajoene when extracted with ethanol, and diallyl disulfide/diallyl trisulfide or *S*-allylcystine/*S*-allylmercaptocysteine when extracted with aqueous solutions (Sener *et al.*, 2007; Vazquez-Prieto and Miatello, 2010). Experimental evidence demonstrates that all allicin-derived compounds have similar antibiotic, antioxidant, antithrombic, and lipid-lowering properties. Indeed, these properties are thought to render protection against various chronic disease conditions such as hypertension, atherosclerosis,

obesity, and related diseases (Sener et al., 2007; Vazquez-Prieto and Miatello, 2010).

Clinical studies suggest that supplementing diets with garlic to elevate blood allicin levels can significantly reduce systolic blood pressure in hypertensive patients (Kris-Etherton *et al.*, 2002; Sener *et al.*, 2007). Although the mechanism(s) of protection remains unknown, data strongly indicate that the main beneficial effect stems from its antioxidant property. Organosulfur compounds decrease Reactive Oxygen Species (ROS) levels by inhibiting ROS generating systems, such as nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, or preventing the degradation of antioxidant enzymes, such as glutathione *S*-transferase. Additionally, organosulfur compounds can increase the bioavailability of NO by increasing eNOS expression or preventing the formation of NO/peroxynitrite (ONOO⁻; Kris-Etherton *et al.*, 2002; Vazquez-Prieto and Miatello, 2010). Other evidence indicates that organosulfur compounds can inhibit ACE, which will increase vasodilation and decrease peripheral resistance, leading to decrease in blood pressure, and limit endothelial injury, demonstrating their antihypertensive properties. Organosulfur compounds have also been shown to reduce the risk of acute vascular inflammation and atherosclerosis. Although the mechanism is not fully elucidated, *in vitro* models suggest that organosulfur compounds work to inhibit cyclooxygenase, HMG-CoA, and platelet aggregation (Vazquez-Prieto and Miatello, 2010).

Organosulfur Compounds as Nutraceuticals

Nutraceuticals, the “drugs for healthy people” will forestall and in some cases cure some pathological conditions, e.g., those associated with the metabolic syndrome. The bioactive constituents extracted and targeted from several foods principally of vegetal origin (phytochemicals) are known and data regarding

their use in nutrition is increasing. They represent a frontier to be explored at the interface between nutrition and pharmacy and a brand new vital tool to forestall the onset of health condition and to limit the utilization of prescribed drugs in an exceedingly preventive professional active approach.

Organosulfur compounds (OSC) are widely present in our bodies and the natural environment. There are two principal groups of vegetables that contain OSC with special properties. Garlic, onion, shallot, leek, and chives are well-known representatives of the *Allium* genus (family *Amaryllidaceae*) that contain *S*-alk(en)yl-l-cysteine sulfoxides. Cabbage, cauliflower, Brussels sprouts, and kale are representatives of the *Brassica* genus, and rucola (rocket salad) is representative of the *Eruca* genus of the mustard or cruciferous family (*Brassicaceae*), which contain *S*-methyl cysteine-l-sulfoxide. OSC as nutraceutical agents not only can serve as direct antioxidants trapping electrons but also can have nonantioxidant effects, such as antiplatelet, fibrinolytic, anti-inflammatory, immunomodulatory, and antiaging actions. These properties of OSC are useful in the prophylaxis and treatment of various pathological states, such as cardiovascular diseases, cancer, neurodegenerative disorders, and diabetes; they have antibacterial, antiviral, and some other activities. Theories have emerged that explain these properties of OSC by their correction of redox-sensing and redox-signaling property

Organosulfur Compounds from Medicinal Plants

The organosulfur compounds are a special type of phytochemical found in various *Allium* species. The organosulfur compounds in garlic are known to differ slightly from those in onion varieties and consequently may have different health benefits. Two major kinds of organosulfur compounds are present in

onion varieties, especially in garlic- γ -glutamyl-*S*-cysteines and cysteine sulfoxides (ca., alliin). When raw garlic cloves are crushed, chopped or chewed, an enzyme known as alliinase is released. Alliinase catalyses the formation of sulfenic acids from cysteine sulfoxides (Fig. 1). Sulfenic acids can spontaneously react with each other to form unstable thiosulfinates compounds. In the case of alliin, the resulting sulfenic acids react with each other to form a thiosulfinate (half-life in crushed garlic at 23 °C is 2.5 days) (Lawson *et al.*, 1998). Thiosulfinate formation is very rapid and can be completed within 10–60 s after crushing a garlic clove. Allicin breaks down and forms a variety of fat-soluble organosulfur compounds, including diallyl trisulfide (DATS), diallyl disulfide (DADS) and diallyl sulfide (DAS), or in the presence of oil or organic solvents, as ajoene and vinylthiols (Block, 1985). Water-soluble organosulfur compounds, such as *S*-allylcysteine (SAC), are formed from γ -glutamylcysteines during long-term incubation of crushed garlic in aqueous solutions, as in the manufacture of mature garlic extracts (Fig. 1).

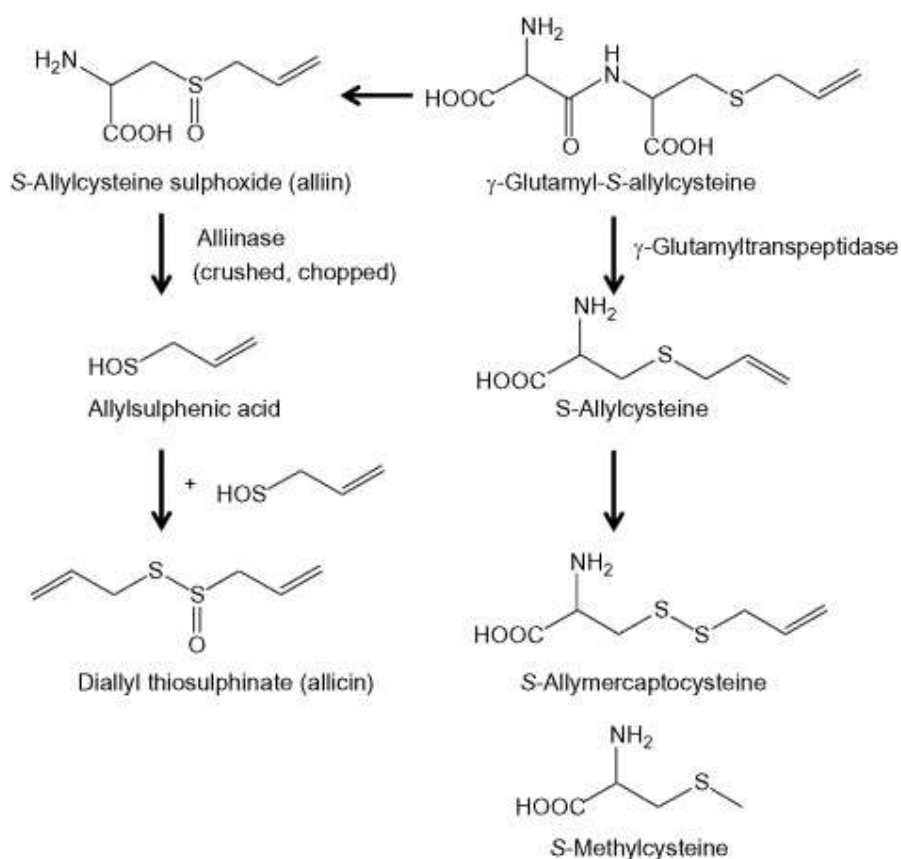


Fig. 1 Biosynthesis and transformation of various organosulfur-containing compounds.

The oil-soluble organosulfur compound, allicin, is easily transformed into oil-soluble polysulfides, mostly DADS, DAS, DATS and also diallyl tetrasulfide. Chemical compositions of the various preparations obtained by extraction of oil-soluble garlic fractions also depend on the specific extraction conditions such as temperature, treatment time interval and solvent polarity. Analysis of allicin solution that has been allowed to stand at room temperature for 20 h showed the following bioorganic composition: 66.7% DADS, 14.6% DATS, 13.3% DAS and 5.4% diallyl tetrasulfide (Lee *et al.*, 2003). Various

findings suggest that higher polysulfides, such as diallyl penta-, hexa- or hepta sulfides, can be formed but their concentrations are often low (O'Gara *et al.*, 2000). When extraction conditions are optimized, allicin can be transformed into vinylthiins and structures of the *Z*- or *E*-ajoene type. The vinylthiin compound was first identified by gas chromatographic analysis as a product of thermal degradation of allicin (Brodnitz *et al.*, 1971; Lee *et al.*, 2003). These structures are formed by dimerization of thioacrolein created via allicin β -elimination. Ajoene (4,5,9-trithiadodeca-1,6,11-triene-9-oxide) was generated via allicin S-thiolation and 2-propenesulphenic acid addition. Originally, ajoene was isolated from an ether fraction of garlic extract as a potential antithrombotic agent (Block *et al.*, 1984). (Fig. 2)

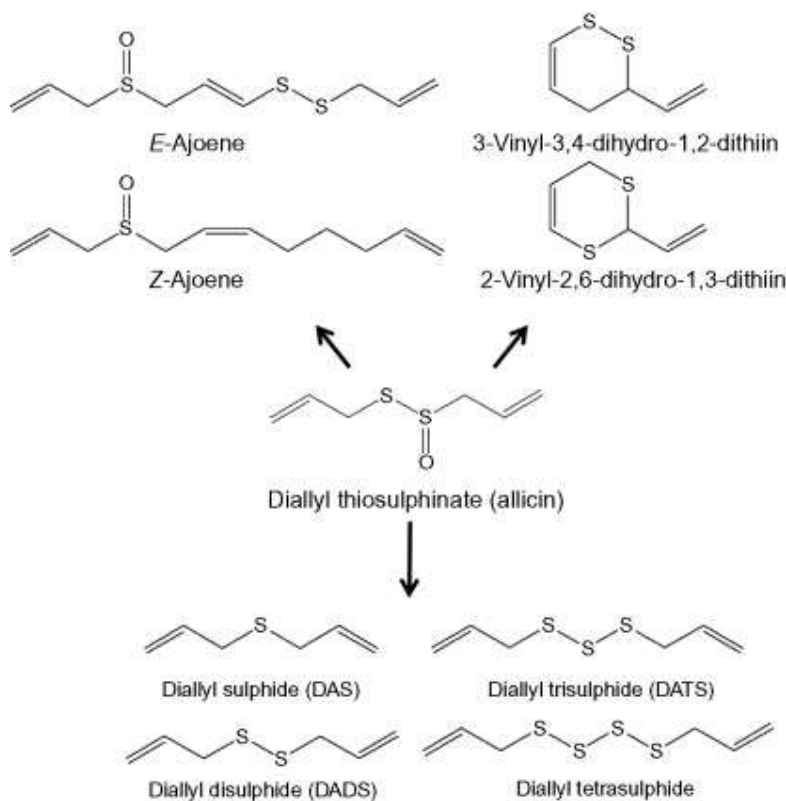


Fig. 2 Biotransformation of various oil-soluble compounds from allicin.

The reactions of allicin with -SH group can yield SAC or *S*-allylmercaptocysteine (SAMC), both of which are water-soluble organosulfur compounds (Rabinkov *et al.*, 2000). Unlike oily sulfur compounds, water-soluble

compounds are odourless and have a more delicate and less characteristic flavour (Kodera *et al.*, 2002). These phytochemicals are formed during aqueous garlic extraction, when the initial compound γ -glutamyl-*S*-allylcysteine (GSAC) is transformed into SAC. This reaction is catalysed by γ -glutamyltranspeptidase (γ -GT). SAC along with its derivatives, *S*-methylcysteine (SMC) and SAMC, are components of aqueous extracts of garlic and possess various biological activities, under both *in vitro* and *in vivo* conditions.

Garlic- and onion-derived organosulfur compounds have been shown to suppress the *in vitro* activities of inflammatory enzymes such as cyclooxygenase and lipoxygenase (Ali *et al.*, 2000) and to inhibit the expression of iNOS in inflammatory white blood cells (macrophages) (Dirschet *et al.*, 1998). Some organosulfur compounds have been shown to inhibit expression of the inflammation signalling molecules in cultured macrophages and human peripheral blood mononuclear cells (Chang *et al.*, 2005). Various findings have demonstrated that garlic extracts and their derived compounds can exhibit anti-inflammatory effects through inhibition of the NF- κ B activity induced by various receptor agonists, including TNF- α and LPS (Keiss *et al.*, 2003). Expression of iNOS was also shown to be inhibited by garlic extract in activated macrophages (Dirschet *et al.*, 1998; Liu *et al.*, 2006a). In addition, Youn *et al.* (2008) demonstrated that garlic extracts can modulate inflammatory responses through suppression of TLR activation.

Table wines: sensory characteristics and sensory analysis

Most reduced organosulfur compounds are considered undesirable. They typically induce foul odors at even trace amounts. Well-known examples are ethyl and methyl mercaptans and dimethyl sulfide. Their formation in wine depends on the development of strongly reducing conditions. Recently, though,

a number of thiol compounds have been identified as critical constituents of several grape varietal aromas. Examples are 4-mercapto-4-methylpentan-2-ol and 3-mercaptohexan-1-ol. They produce odors reminiscent of citrus zest/cat urine and grapefruit, respectively. Both compounds are important in the varietal character of Sauvignon Blanc (Tominaga *et al.*, 1998), whereas the former is an important odorant in Scheurebe (Guth, 1997). In addition, 4-mercapto-4-methylpentan-2-one and 3-mercaptohexyl acetate (Tominaga *et al.*, 1996), and especially benzenemethanethiol (benzyl mercaptan) (Tominaga *et al.*, 2003) contribute to the varietal box-tree (smoky) aroma of some Sauvignon Blanc wines. Although seemingly not a varietally distinctive thiol, 3-mercaptohexanol is an important aromatic constituent of several rosé wines (Murat, 2005).

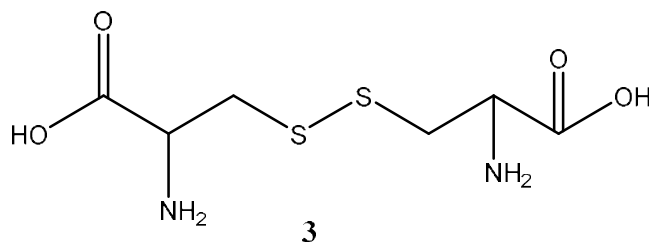
Thiourea

Thiourea is an organo-sulfur compound with formula $\text{SC}(\text{NH}_2)_2$. It is structurally similar to urea except that oxygen atom is replaced by a sulfur atom. The properties of urea and thiourea differ significantly. Thiourea has a wide range of applications. In plants, low concentration of thiourea was used as a dormancy breaking agent. The effect was correlated with catalase inhibition which facilitates H_2O_2 mediated oxidation of NADPH that acts as oxidant in pentose pathway to produce glucose. Later, it was adopted as a plant growth regulator. During recent years, thiourea has been widely used for enhancing plant growth, stress tolerance and crop yield. At the physiological level, these effects are due to coordinated regulation of plant source-to-sink relationship and enhanced translocation of metabolites from source (leaves) to sink (pods). At molecular level, thiourea effects are related with its ability to scavenge broad range of reactive oxygen species, such as H_2O_2 and superoxide radical, produced under biological system. Since, ROS mediated signaling, also termed as “Redox signaling” is well established as one of the central regulators of stress signaling in plants. Thiourea application was utilized as a strategy to delineate redox

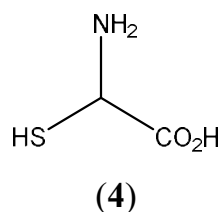
regulated components associated with calcium and ABA signaling in germinating seeds of *Brassica juncea*. The molecular level changes induced by thiourea were also positively reflected in terms of improved energetics, antioxidant defense plant-water homeostasis and sulfur metabolism in plants against different environmental stresses. Apart from indirect effects of thiourea which are associated with its ROS scavenging action, the direct effects have also been demonstrated at higher thiourea concentration (in mM range; for indirect effects thiourea was provided in μM). These include irreversible inhibition of catalase, antinitrification), and antiweeding properties of thiourea.

REVIEW OF NATURALLY OCCURRING DI-, TRI-, AND POLY-SULFIDES AND RELATED COMPOUNDS

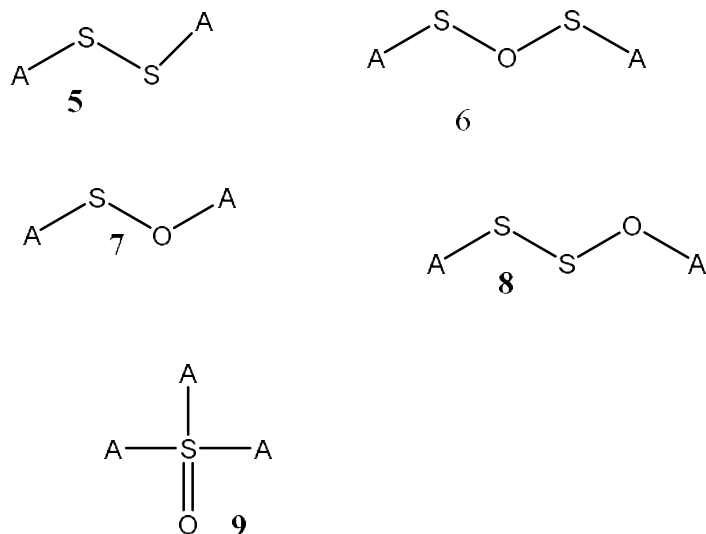
While investigating plant extracts for antibacterial activity, it was observed that a freshly prepared infusion of ground garlic cloves possessed high anti-bacterial activity, when tested by the cylinder-plate method used for the assay of penicilline. It is also known that *Allium sativum*, the common garlic, is endowed with various therapeutic virtues both in legend and in the scientific literature. The antibacterial activity had been attributed to the presence of diallyl disulfide, unstable sulfur in alkyl polysulfides, a bacteriophage, acrolein or similar unsaturated aldehydes, in the garlic extracts. As far back as 1922, the disulfide cystine (**3**) was found in the protein keratin which occurs in hair, skin, and nails, and its biological importance was recognized.



Glutathione, an oxidation-reduction catalyst, was discovered in yeast, red blood cells and animal tissues, and was shown to be the tripeptide, glutamyl-cysteinyl-glycine. Its oxidized form was shown to be a derivative of cysteine (4) while its reduced form contained a cystine residue.



The anti-bacterial agent allicin has been isolated from onion in the pure state as a colourless liquid. The compound was found to contain approximately 40% sulfur by weight, and no nitrogen or halogens. The oil cannot be distilled without decomposition, it is irritating to the skin, and the odour is much more characteristic of garlic than the various allyl disulfides. Its action was found to be more bacteriostatic than bactericidal and it is about equally effective against *Gram* positive and *Gram* negative organisms. The molecular weight of allicin was found to be approximately 167 and this, together with other analytical data, indicated an empirical and molecular formula of $\text{C}_8\text{H}_{10}\text{OS}_2$ (molecular weight of 162). Alkaline hydrolysis yielded sulfur dioxide and some allyl disulfide. Five possible structures (5-9), where A represents the allyl group, were proposed.



The most remarkable occurrence of organic disulfides reported so far is that of methyl disulfide in the cavities of quartz of the palaeozoic period. Methyl disulfide and isopropyl disulfide are present in the odours from *eucalyptus*. Allyl disulfide and allyl propyl disulfide are found in the oil of garlic and allyl s-butyl disulfide in *asafetida*. The essential oil of *Agathosmaapiculata Meyer* contains 30% of n-butyl 1-pentenyl disulfide. Methyl disulfide is also present in the gases from sulfite pulp digesters.

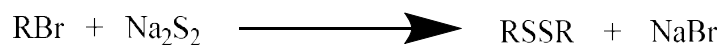
Methods of preparation of symmetrical organic disulfides

The first synthetic organic disulfide was made by Zeise who distilled ethyl disulfide from a mixture of potassium ethyl sulphate and barium disulfide.

Because of the importance of the methods of synthesis for this class of compounds, some specific examples already reported in the literature will now be given.

Reaction of alkyl halides with disodium disulfide

Earlier attempts at making symmetrical disulfides used the reaction of an alkyl halide and sodium disulfide as depicted by the equation in Scheme 1.



Scheme 1

Although alkyl disulfides are obtained in fairly good yields by this method, a problem arises from the fact that sodium "disulfide" is a random mixture of compounds including Na_2S , Na_2S_2 , Na_2S_3 and possibly Na_2S_4 , Na_2S_5 and Na_2S_8 . Therefore, in addition to the alkyl disulfide, other products such as the trisulfides and polysulfides are formed. For the lower members of the series, this may not be a serious problem because fractionation can be used to separate the disulfides from the polysulfides because of the wide differences in their boiling points.

Reaction of sulfur with organic compounds

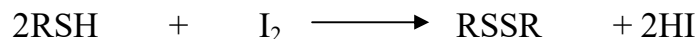
The reactions of various organic compounds when heated with sulfur are also known to give disulfides, although products obtained from this kind of reaction are not pure and may contain mono-, di-, and polysulfides depending on the nature of the starting materials and the conditions of heating. However, disulfides have been obtained from phenols, naphthols, aniline, and saturated and unsaturated hydrocarbons. An unsaturated disulfide was reportedly formed from amylene and sulfur under certain conditions. Dibenzyl disulfide has been obtained from benzophenone in several ways. Certain aldehydes and ketones give good yields of disulfides when heated with hydrogen sulfide under controlled conditions.

Reaction of sulfur chlorides with organic compound

Several organic compounds, such as thiophene, acetoacetanilide, and aromatic hydrocarbons, give disulfides when they are treated with sulfur monochloride. Sulfur monochloride acts as a chlorinating, as well as a sulfurising agent, when it is allowed to react with trithioformaldehyde, producing $(\text{C}_1\text{CH}_2)_2\text{S}_2$. Some monosulfides and polysulfides are formed in addition to the desired disulfide when sulfur monochloride reacts with ethylene and amylene. When *o*-nitrophenylthiosulphenyl chloride, (*o*- $\text{O}_2\text{NC}_6\text{H}_4\text{SSCl}$), is added to an unsaturated hydrocarbon a disulfide is formed.

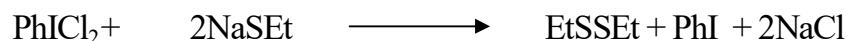
Oxidation of mercaptans

This is the simplest method for the preparation of disulfides, and is depicted in Scheme 2.



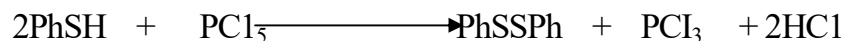
Scheme 2

The hydriodic acid formed is a strong reducing agent and the reaction does not go to completion unless this acid is removed, either by solution in water or by combination with a base. This method also is the neatest way of preparing alkyl disulfides. The thiol is dissolved in benzene, over a layer of water, and iodine is added until it is no longer decolourized. The hydriodic acid that is formed dissolves in the water layer and the benzene solution of the disulfide is separated and fractionated. Chlorine can also convert a mercaptan to the disulfide. However, care must be taken to conduct the reaction in such a way that it will not be violent. Any other compound that gives up chlorine readily may also be used instead of chlorine, thus phenyliodosochloride reacts with sodium mercaptide as shown in Scheme 3.



Scheme 3

Phosphorus pentachloride gives up two chlorine atoms when it reacts with phenyl mercaptan, to give the disulfide (Scheme 4).

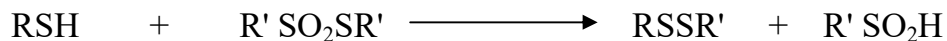


Scheme 4

Unsymmetrical disulfides and cyclic polymeric disulfides

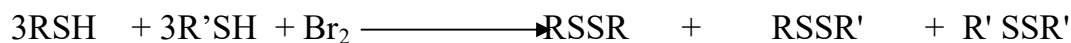
Unsymmetrical disulfides are sulfides of the general formula RSSR' , where R and R' are different groups. Nucleophilic displacement of a sulfinic acid from thiosulfonates by thiols has been exploited to produce a wide variety of unsymmetrical disulfides. While the reactions proceed readily and completely in most cases, even at -86°C , subsequent,

disproportionation of both products is a complication whose importance varies greatly with structure. The reaction proceeds according to Scheme 5.



Scheme 5

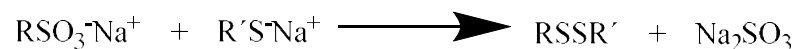
The relative stabilities of some disulfides toward disproportionation have been studied in detail. The treatment of two mercaptans with bromine has been reported to give a mixture of three disulfides, one of which is unsymmetrical (Scheme 6).



Scheme 6

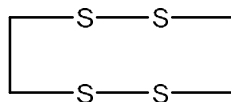
These disulfides may be separated by fractional distillation. Other oxidizing agents have been reportedly used for this reaction.

The reaction of a mercaptide with Bunte salt has been reported to give an unsymmetrical disulfide as shown in Scheme 7.

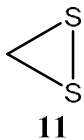


Scheme 7

A neat way of preparing a pure unsymmetrical disulfide is by the reaction a sulphenyl halide with a mercaptide. The reaction of S-alkylthioisothiuronium chloride with a mercaptan, in the presence of a base, also gives pure unsymmetrical disulfide. The treatment of ethylene and trimethylenedimercaptans with bromine yields solids to which structures (10) and (11), respectively, have been assigned.

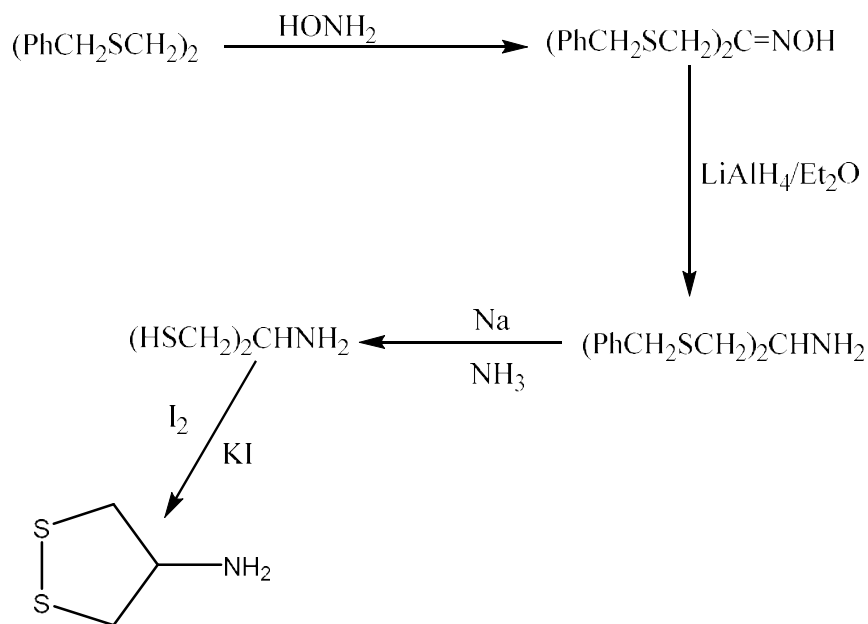


20



Compounds of the same composition as (10) were reportedly made in two other ways, one by oxidation of ethylene dimercaptan and the other by the reaction of ethylene bromide with sodium disulfide.

A number of aliphatic disulfides, not previously reported, have been prepared by adaptations of more or less well known methods as mentioned earlier. α,α' -Diethyl-, α,α' -di-n-propyl-, α,α' -di-n-butyl- and α,α' -diphenyl-D, L-cystine have been prepared via hydantoin intermediates. 9,10-Diphenyl 2-anthranyl disulfide and 2-anthraquinonyl disulfide have been prepared by the reduction of the corresponding sulphonyl chlorides with zinc and acetic acid. The preparation of a number of 5- and 6-membered cyclic disulfides has been reported, all of which with one exception were new. The method of Price *et al.* for the synthesis of naphthalene-1, 8-disulfide was simplified and improved upon by these workers. 4-Amino-1, 2-dithiolane has been prepared by the following reaction (Scheme 8)



Scheme 8

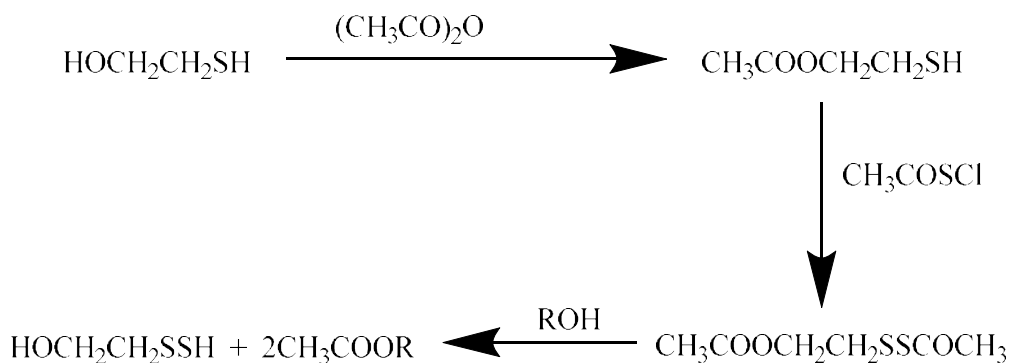
Eight variously substituted benzoyl disulfides were prepared by the reaction of the corresponding benzoyl chlorides with aqueous sodium disulfide. Leek-type flavorings have been prepared by the reaction of aliphatic thiosulfonates with an alkali metal sulfide and were identified as a mixture of aliphatic disulfides (30%) and trisulfides.

This review on these classes of compounds would be incomplete if alkyldisulfides and the chemistry of disulfides were not included since these explain certain peculiar properties of these compounds.

Alkyl hydrodisulfides synthesised so far are methyl, ethyl, benzyl, benzhydryl, and trityl hydrodisulfides, the latter three of which have been reported to be stable for a few weeks. The lower members are only stable for a few minutes after being isolated in a pure state.

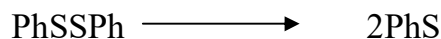
Compounds containing the hydrodisulfide, -SSH, group have been postulated by biochemists as intermediates in various enzymatic reactions. However, α -amino hydrodisulfide, $\text{H}_2\text{NCH}(\text{R})\text{CH}_2\text{SSH}$, which has been named thiocystine and proposed as an intermediate of the enzymatic cleavage of cystine, has never been isolated. Only circumstantial evidence is available to support the intermediate formation of thiocystine and similar polysulphonic species containing labile sulfur.

The preparation of 2-hydroxyethyl hydrodisulfide has been reported, as shown in Scheme 9. This compound was said to be unstable and the workers were unable to obtain accurate analytical results; however, they claimed that the NMR spectrum showed proton signals due to the -SSH, -OH, and -CH₂CH₂- groups only. It was suggested that a trace amount of the corresponding trisulfide was present as impurity.



Scheme 9

Disulfides are susceptible to decomposition, due to the lability of the sulfur-sulfur bond. It is known that diphenyl disulfide dissociates into free radicals (Scheme 10).



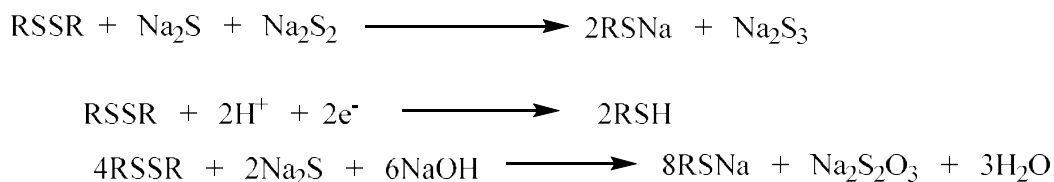
Scheme 10

Aryl disulfides are also decomposed by ultraviolet light but the quantum yield is small. Diphenyl disulfide is decomposed by aluminum chloride to give the mono-sulfide and other products. The primary decomposition products of benzyl disulfide were reported to be stilbene, hydrogen sulfide, and sulfur (Scheme 11).



Scheme 11

Aliphatic disulfides are not very stable to heat, di-n-propyl disulfide being the highest member of the series that can be distilled at atmospheric pressure. The pyrolysis of an aliphatic disulfide gives a mixture which was reported to contain mercaptan, mono-sulfide and hydrogen sulfide. An interesting important fact about disulfides is the ease and completeness with which they are reduced to mercaptans. With sodium sulfide or the disulfide, they are reduced to mercaptans (Scheme 12).



Scheme 12

In the presence of water, triphenylphosphine reduces diphenyl sulfide to the mercaptan. Disulfides undergo oxidation with hydrogen peroxide to give sulphenic acids or oxidation may stop at RSO_2SR . Perbenzoic acid was reported to give a lower oxidation product, RSOSR , or RSO_2SR . Whether the oxidation product of an unsymmetrical aryl disulfide by a peracid is $\text{ArSO}_2\text{Sar}'$ or $\text{ArSSO}_2\text{Ar}'$ depends on the substituents in the aryl groups.

Review of biological activity of the plant *Petiveria alliacea*

Petiveria alliacea is a plant which can be found mainly in the tropical regions of Venezuela, Colombia, Puerto Rico and several parts of Africa. It was found that the young and active part of the plant was resistant to 2, 4-D when treated with a solution spray (0.075%). It has also been reported that this plant shows resistance to diuron.

Alcohol, acetone, and petroleum ether extracts, and powders from *P. alliacea*, have been tested for toxicity on adult houseflies, mosquito larvae, and thirteen other insect species and leaf feeders, and found to show low activity. When an alcohol extract of the dried ground bark and leaves of the plant was tested for the presence of alkaloids, a negative result was obtained, thus showing that any medicinal or biological activity possessed by this plant must be due to substances other than alkaloids.

A systematic and quantitative study has been reported on the volatile isothiocyanates obtained from the seeds of *Petiveria alliacea*. Isothiocyanates of the general molecular formula RNCS, where R = Me, allyl, isopropyl s-butyl, 3-butenyl, benzyl and phenylethyl were said to be present.

Thin-layer chromatographic analysis for coumarins in the ether extracts of the root of this plant has shown the presence of nineteen coumarins. Also, preliminary tests for other active substances in the root of this plant have shown that tannins, essential oils, anthracene derivatives, saponins, alkaloids, triterpenoids or flavinoids are absent.

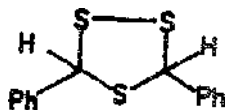
The isolation, structural elucidation and synthesis of an antimicrobial substance from *P. alliacea* has been reported, the active component being obtained from the chloroform-soluble fraction of the total water-alcohol extract of the stems and roots of the plant. The authors identified the compound (12) by nuclear magnetic resonance (nmr) and mass spectroscopy.



(12)

They also prepared the active compound (12) by the reaction of sulfur dichloride with benzyl mercaptan and mercaptoethanol.

Trithiolaniacin (13), a novel trithiolane, has also been isolated from the chloroform extract of the wet root of *P. alliacea* collected at the end of the rainy season.



(13)

The structure of this compound (13) was determined by spectroscopic methods. Other products including benzaldehyde, benzoic acid, trans-stilbene, and sulfur were also claimed to be present in the chloroform extract.

A phytochemical study of *P. alliacea* has been reported. The plant was found to show higher nitrate values at the end of summer than at the onset of winter. When the vegetal

materials from this plant were digested in *vitro*, nitrates were obtained 1.5-2.5 h from the start of digestion and the maximum accumulation of nitrites (from nitrate reduction) occurred at 4 h.

The alcoholic extracts of various parts of *P.alliacea* and of other plants, particularly the non-saponifiable portions of these extracts, have been tested for their ability to protect mice against a lethal injection of *Escherichia coli*. When injected at 50 mg kg⁻¹ the extracts, and/or the non-saponifiable portions of this plant, have protective activity. This activity was associated with the lipophilic constituents of the non-saponifiable fraction and occurred especially with plant extracts known for their skin-healing properties.

A highly polar compound isolated from *P. alliacea*, was shown to be *trans-N*-methyl-4-methoxyproline, on the basis of its microanalytical and spectral data. Dibenzyl trisulfide, previously unknown as a natural product, was also claimed to be isolated from the root of the plant.

Compounds PhCH₂XCH₂Y where X = S₂(**14**), S₃(**15**); Y = Ph, CH₂OH, when X = S₂; then Y = Ph (**16**), have been found useful for prophylactic and therapeutic treatment of liver disorders. When the roots of *Petiveriaalliacea* were extracted with methanol, and the extract treated with water and ethyl acetate, the organic layer of which was chromatographed on silica gel, the following compounds were obtained:

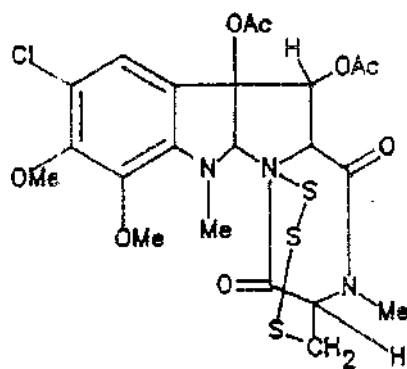


It was also found that a mixture of PhCH₂SSCH₂Ph and PhCH₂SSSCH₂Ph at 200 mg kg⁻¹ showed 69% and 78% improvement of abnormal blood coagulation time and glutamate-pyruvate transaminase in D-galactosome-induced liver disorder in rats.

Synthetic analogues and derivatives of the active component (**12**) of *P. alliacea* have also attracted interest. Some polysulfide mixtures containing PhCH₂SSCH₂CH₂Cl (26%), PhCH₂SSSCH₂CH₂Cl (56%) and PhCH₂SSSSCH₂CH₂Cl (18%) were found to inhibit the growth of *Staphylococcus aureus* and *Mycobacterium tuberculosis* at 12.5 g cm³ and *Candida albicans* and *Trichopytca mentagrophytes* at 5.3 g cm³.

Trisulfide from the fungus *Pithomyceschartarum*

Sporidesmin (17) has been isolated from the fungus *Pithomyceschartarum*.

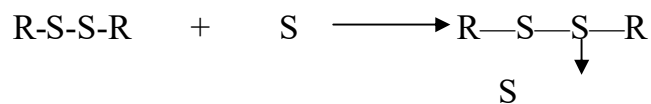


(17)

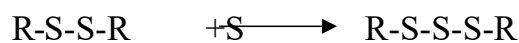
It is one of the metabolites responsible for liver damage and facial eczema in sheep. The author's assigned structure (17) that corresponds to the cysteine analogue of sporidesmin with three sulfur atoms linked together in an unusual nine membered ring.

Structure of organic trisulfides

The question that has arisen over the years is the disposition of the third sulfur atom in an organic trisulfide, since there is no doubt that there is a sulfur atom attached to each of the alkyl carbon atoms by a fixed bond. Also, much had been made of the fact that sulfur can be added to a disulfide, or removed from a trisulfide or higher polysulfide. It had been suggested that the extra sulfur is added to one of the sulfur atoms of the disulfide instead of being inserted between them (Scheme 13).

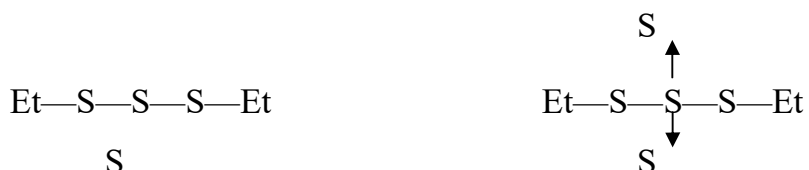


Or



Scheme 13

Various structures have been proposed and these have been reviewed. It had also been claimed that in the oxidation of ethyl trisulfide, tetrasulfide, and pentasulfide, all are converted to the trisulphoxide EtSOSOSOEt , which was taken as establishing the basic structure EtSSSEt in all cases, and inferring that the structures of the tetrasulfide and pentasulfide are, respectively, as follows:



The known liability of the S—S bond does not support the above argument. This liability is manifested in chemical reactions and may have little or nothing to do with the validity of conclusions deduced from physical measurements. It was claimed that electron and X-ray diffraction data, and Raman, ultraviolet, and X-ray emission spectra, indicate the presence of zig-zag sulfur chains as opposed to conclusions obtained from measurements of dipole moment, parachor, and viscosity which are considered less reliable. A two-fold axis of symmetry, shown by X-rays, appeared to exclude the possibility that sulfur atoms are attached to the chain. From a study of the crystal structure of β,β' -diiododiethyl trisulfide, it was concluded that the zig-zag chain in the sulfur atoms is the correct one.

Synthetic Pesticides

It is only in the present century, however, that synthetic chemicals have been introduced for pest control and the large expansion in their use since World War II has led to serious concern about the dangers of environmental pollution. The dangers were highlighted by Rachel Carson in her book "Silent Spring", first published in the USA in 1962 and the UK in 1963, and then republished and reprinted on various occasions from 1966 to 1977. The dangers were especially clear in the case of organochlorine insecticides such as DDT, for which the combination of stability and lipoidal solubility led to accumulation in food

chains, the death of fish, and alarming reductions in certain bird populations. It was predicted that the ever increasing application of toxic chemicals in the environment would lead to the extinction of much wild-life and the development of illness and nervous disorders in animals and in man.

One direct consequence of Rachel Carson's book was the establishment in 1972 of the Environmental Protection Agency (EPA) in the USA and of similar agencies for the control of pesticides in other countries. In the UK, for example, the use of pesticides is regulated by the Food and Environment Act, Part III (1935) and the Control of Pesticides Act (1986) which give the government power to control all aspects of pesticide use. Approved pesticides are listed by the Ministry of Agriculture, Fisheries and Food (MAFF). The regulatory requirements for new pesticides are stringent. The EPA requires detailed information on product chemistry, residue chemistry, environmental fate, wildlife effects, and toxicology, before a compound can be registered. The toxicological studies alone require data to be provided on acute toxicity (by three routes of exposure), eye and dermal irritancy, dermal sensitization, delayed neurotoxicity, repeat dose 90-day studies in a rodent and non-rodent species, chronic feeding studies (usually one year), oncogenicity studies in two species, teratogenicity studies in two species, two generation reproduction studies, gene mutation studies, structural chromosome effects, and general metabolism. Together with the necessary field trials over a number of years and the development of manufacture and marketing etc., the cost for the introduction of one new pesticide is of the order of tens of millions of pound sterling and can only be met by large organizations.

The desirable properties of a new pesticide for it to be environmentally acceptable are that it should have low mammalian toxicity, be selective in its action and not toxic to non-target species, and that it should degrade to harmless residues.

Some of the major types of well-known pesticide are shown in Table 1.

Table 1: Some major Types of Well-established Pesticide

Insecticides	Fungicides	Herbicides
Organochlorine	Sulfur	Chlorophenoxyalkanoic acids
Organophosphorus	Copper compounds	Chlorobenzoic acids
Carbamate	Organomercurials	Chloroalkanoic acids
Benzylurea	Phenols, quinines heterocyclics*	Bipyridinium compound glyphosate

* e.g. Carboximides, benzimidazoles, oxathins, piperazines, morpholines, pyrimidines, imidazoles, triazoles, etc.

Among the insecticides, the organochlorine types are now banned in many countries, except for special applications, because of their persistence and slow rate of degradation in the environment. The organophosphorus types are generally good from this point of view, as they undergo complete degradation to phosphoric acid and simple organic fragments within a reasonable time and leave no harmful residues if used in accordance with the manufacturer's instructions. They are not generally selective, however, and may kill useful species as well as unwanted pests. The more toxic types, such as parathion (LD_{50} 3mg/kg)**, are now superseded but care is still necessary in the handling of these cholinesterase inhibitors and the possible effects of impurities should be recognized. Malathion, which is widely used as a contact insecticide both in

agriculture and for the control of mosquitoes and ectoparasites, has very low mammalian toxicity (LD_{50} ca. 1300mg/kg) but sometimes ago there were a number of cases of poisoning including five fatalities amongst field workers in Pakistan which were attributed in part to the presence of an unusually high level of isomalathion (i.e. the *O, S*- dimethyl isomer) which had been formed in the water-dispersible powder formulation during shipment and storage and which potentiated the activity of malathion itself. In addition, a number of organophosphorus pesticides are under investigation as possible mutagens and dichlorvos has been identified as a possible carcinogen.

The carbamates are an important group of insecticides but some have high mammalian toxicities; aldicarb, which is one of the most effective nematocides in use, is extremely toxic (LD_{50} ca. 1mg/kg) and suitable replacements are highly desirable.

The pyrethroids and benzoylureas, discussed below, are typical of the more modern, environmentally-friendly insecticides that are now becoming established. They are generally of low mammalian toxicity, high insecticidal activity (application rates are therefore low), and undergo degradation to harmless residues. Selective action is also shown in a number of cases.

Fungicides in general do not cause serious environmental harm if properly used, although a number of possible dangers should be recognized. Copper is, of course, a general poison and the excessive use of either copper or sulfur based fungicides may lead to accumulation in the soil with deleterious effects on earth worms and soil fauna. Drainage of copper into rivers can also kill fish and algae. The organomercury compounds, so important for many years as seed-dressings for cereal crops and for the treatment of rice blast, are relatively toxic and present a particular hazard to seed-eating birds. In many countries these compounds are now either banned or restricted and the development of suitable replacements is important.

The dithiocarbamates are the oldest of the purely organic fungicides,

having been introduced in 1934 by Du Pont and they are still very widely used. They are of very low mammalian toxicity (LD_{50} 400-8000mg/kg) and there is little evidence of environmental damage being caused by their use. There have, however, been some ill effects observed in chronic toxicity feeding studies involving high doses of zineb, maneb, and mancozeb, which may be due to the presence of ethylene thiourea, residues of which should therefore be kept at a low level.

Some other well established fungicides, viz captan and benomyl, although of very low mammalian toxicity and previously considered to be extremely safe, have more recently been identified as possible carcinogens.

Among the herbicides, the most widely used are probably the aryloxyacetic acids. There does not appear to be any significant evidence for harmful environmental effects if these are used correctly. The most serious problems have arisen with 2, 4, 5 – T (now withdrawn), because of the possible formation of 2, 3, 7, 8 – tetrachlorodibenzo-p-dioxin as a by-product during manufacture. This dioxin is one of the most toxic compounds known (LD_{50} ca. 0.03mg/kg) and is also a dangerous teratogen.

The bipyridinium herbicides (paraquat and diquat) are very effective as total herbicides and are completely inactivated on contact with soil. They are, however, highly toxic compounds and can be dangerous if handled carelessly. Paraquat, if swallowed, generally has fatal consequences and there is no antidote. Its use is therefore either controlled or even banned in certain countries.

Glyphosate, which is mentioned again below, is currently one of the most widely used systemic herbicides, of very low mammalian toxicity and without any obviously harmful effects in the environment.

Examples of some of the newer types of pesticide are given below. Some are modeled on natural products, some are derived from microorganisms, and

others are new synthetic types having novel modes of action.

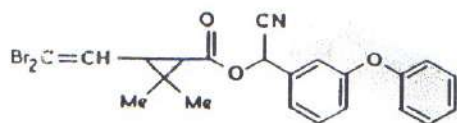
Insecticides

The introduction of synthetic pyrethroids during the last fifty year period represented a great advance. Whereas the natural pyrethrins (**18**), extracted in the form of pyrethrum from *Chrysanthemum cinerariaefolium*, have been in use on a considerable scale since the middle of the last century, they are very susceptible to photolytic oxidation and for many purposes are not sufficiently persistent.

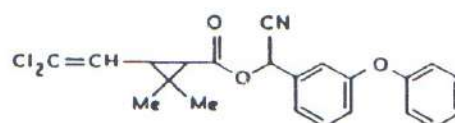


(**18**) (*1R*)-*trans* isomers

Considerable improvements both in stability and in insecticidal activity were obtained in various synthetic analogues developed by Elliott *et al.* at Rothamsted Experimental Station. Deltamethrin (**19**) and cypermethrin (**20**), are important examples of these types, which combine outstanding activity with very low toxicity towards mammals and birds. Deltamethrin (LD_{50} 135-5000mg/kg) is effective at an application rate of 2.5-12.5g per hectare and cypermethrin (LD_{50} 250 – 4150mg/kg) at 20 – 75g per hectare. Lambda-cyhalothrin (**21**), introduced by ICI in 1980, is rather more toxic to mammals (LD_{50} 56 – 79mg/kg), but has the advantage of low contact toxicity to bees.



(*1R*)-*cis* (*S*)- α isomer



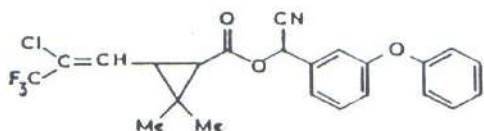
mixed (*1RS*)-*cis*, *trans*

(*RS*)- α - isomer

(19)

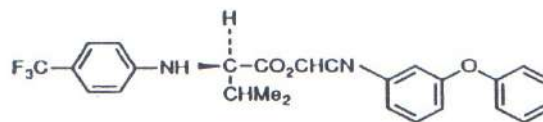
(20)

An example which combines very low mammalian toxicity ($LD_{50} > 3000 \text{ mg/kg}$) with lack of danger to bees is tau-fluvalinate (**22**), first reported in 1980 and introduced by the Zeocon Corporation (now Sandoz). This compound, although classed as a synthetic pyrethroid, does not contain the cyclopropane ring which is characteristic of the natural products. These, and other synthetic pyrethroids, are finding increasing application as safe and highly active insecticides which degrade to leave no harmful residues. At the present time the synthetic pyrethroids account for about 15% of the total insecticide market.



mixed (Z)-(1R)-cis (S)- α and
(Z)-(1S)-cis (R)- α isomers

(21)



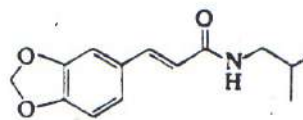
(RS)- α isomer

(22)

Other naturally occurring insecticides which have attracted attention are the isobutylamides, typified by pellitorine (**23**) and fagaramide (**24**) which occur in a number of *Compositae* and *Rutaceae* spp. Numerous related derivatives that occur in *Piperaceae* spp and their synthetic analogues were studied by workers at Rothamsted. Of the aryl substituted types (**25**), the most active synthetic analogues were those containing 4-bromo- or 3,4-dibromo-substituents. Other related derivatives (**26**) were four times more active than DDT and the pyrethroids against house flies that had developed resistance to these insecticides.



(23)

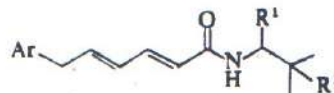


(24)



R = H (natural product)
 R = 4-bromo- or 3,4-dibromo

(25)



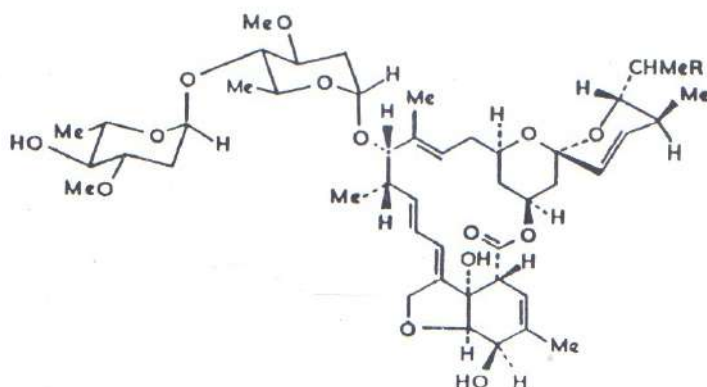
Ar = Ph, 3, 5 - F₂C₆H₅, or
 dibenzofuranyl
 R¹ and R² = H or Me

(26)

The complex natural products known as avermectins (27) were discovered in the Japanese soil microorganism *Streptomyce avermitillis* and introduced by Merck Sharp and Dohme under the name abamectin, which is a mixture of the B₁a (R = Et) and B₁b (R = Me) derivatives. Anthelmintic and acaricidal activity was reported by Putter *et al.* (1981). The avermectins are highly active against nematodes and are amongst the most active insecticides known. Their mammalian toxicity is, however, high (LD₅₀ 10mg/kg) and they are toxic to bees. They bind strongly to soil, however, and degrade rapidly under the influence of soil microorganisms with no bioaccumulation. A number of chemical modifications with increased activity have been reported but there are no synthetic analogues.

Among the more important insecticides are the benzoyl phenylureas which were introduced by Philips-Duphar in the early 1970's. these insect growth regulators are typified by diflubenzuron(28), reported by J. J. van Daalen (1972). Diflubenzuron interferes with chitin synthesis and moulting, leading to the death

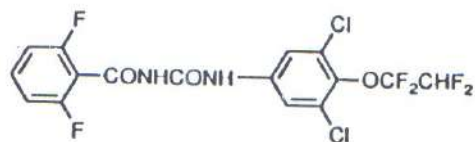
of larvae, pupae, and non-viable adults. It has very low toxicity towards mammals ($LD_{50} > 464 \text{ mg/kg}$), and towards fish and birds, is not harmful to bees and predatory insects, and is effective at a rate of 30-120g per hectare. Degradation in soil occurs with a half-life of < 7 days giving mainly 4-chlorophenylurea and 2, 6-difluorobenzoic acid. Other examples with similarly favourable environmental characteristics include hexaflumuron, introduced by Dow in Latin America for control of the larvae of Lepidoptera, coleopteran, homoptera and dipteran on top fruit, cotton, and potatoes (Sbraiga *et al.*, 1983), flufenoxuron (**29**), introduced by Shell (Anderson *et al.*, 1986) for the control of the immature stages of many phytophagous mite and insect pests, and the Duphar product flucyclohexuron (**30**) (Grosscurt *et al.*, 1988), which is active against the eggs and young active stages of mites and insect larvae at a spray concentration of 0.001-0.002g/l and a dosage rate of 20-40g per hectare. There is still much active research in this area.



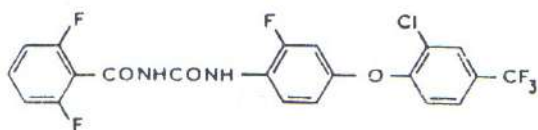
(27)



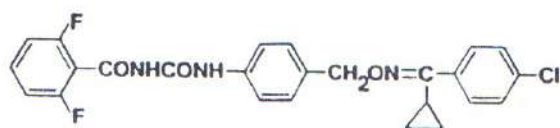
(28)



(29)



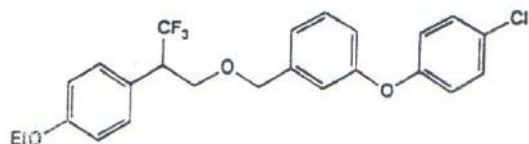
(30)



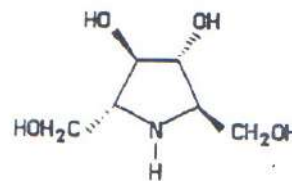
(31)

New types of safe insecticide are continually being sought. At the Brighton Crop Protection Conference (November 1992), papers were presented on eight new insecticidal compounds. Two examples are given here in illustration. Flufenprox (**32**), developed by workers at ICI, is a new type of bis-alkyl ether which provides broad-spectrum insect control but which is relatively harmless to spiders and predatory mites. It has very low mammalian toxicity ($LD_{50} > 5000 \text{ mg/kg}$) and presents little hazard to fish or earthworms. The compound is applicable either alone or mixed with other insecticides or fungicides, especially in rice. Dosage rates are typically 150-200g per hectare.

Another example, (2R, 3R, 4R, 5R)-2, 5-bis (hydroxymethyl) pyrrolidine-3, 4-diol (**33**), is a natural product obtained from tropical legumes and has been shown to have a range of activities against plant parasitic nematodes. Reported jointly by workers at the Scottish Crop Research Institute and the Royal Botanic Gardens, Kew, it is considered to have low mammalian toxicity and to have considerable potential in integrated pest control strategies.



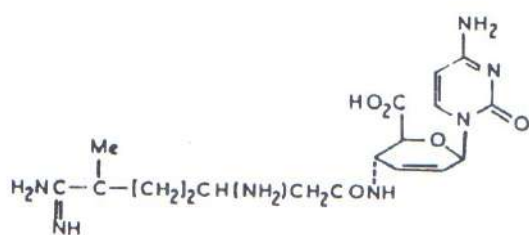
(32)



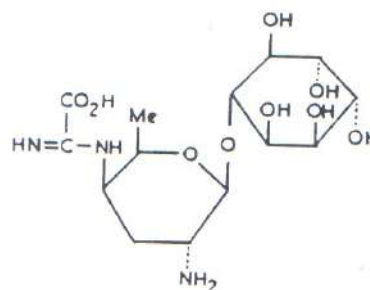
(33)

Fungicides

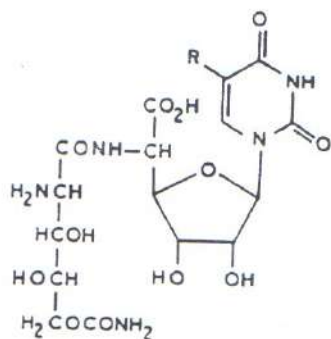
Discovery of the antifungal antibiotic blasticidins (34) in 1958 was followed by the development of other, less toxic antifungals derived from microorganisms, including kasugamycin (35), the polyoxins (36), and validamycin (37). Blasticidin (LD_{50} ca. 56mg/kg) and kasugamycin are effective against rice blast at dosage rates of 10-20g per hectare, whilst validamycin controls rice sheath blight at 45-90g per hectare. Validamycin is not directly fungicidal but acts by interfering with normal mycelial growth of the pathogen on the plant. The zinc salt of polyoxin D is also used for the control of sheath blight of rice and polyoxin B controls *Alternaria* and other species at an application rate of 100-200g per hectare. Kasugamycin, the polyoxins and validamycin have extremely low mammalian toxicities ($LD_{50} > 15,000$ mg/kg). All are very safe environmentally and it is likely that new pesticides from microbial sources will be developed in the future.



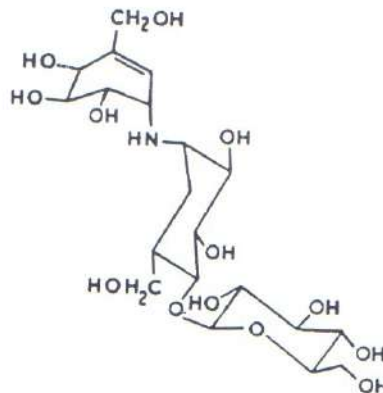
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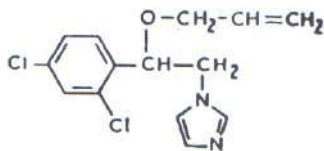
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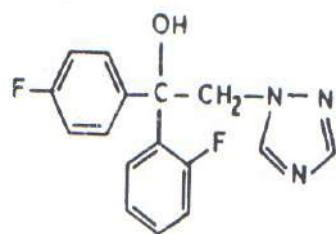
One of the more pressing needs for some years has been the development of replacements for organomercury compounds for use as cereal seed dressings. The toxic nature of mercury, and its biological conversion to methylmercury which can accumulate in food chains, have led to the use of organomercurials being restricted or banned in many countries. Some of the approved replacements include benzimidazoles, imazalil, triazoles, carboxamides guazatine, ethirimol, iprodione, dithiocarbamates, copper oxyquinolate, and ampropylfos. Of these, I shall refer specifically to the triazoles, of which new examples are continually being introduced, and to guazatine and ampropylfos with which our own department in London has been associated.

Imazalil (38) was introduced by Janssen Pharmaceutica in 1969 as the first imidazole fungicide (LD_{50} 320mg/kg) and it is still widely used as a seed dressing for cereal crops for the control of *Fusarium* and *Helminthosporium* spp and as a spray against powdery mildews.

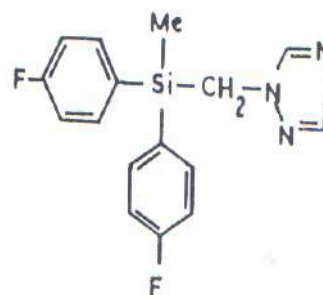


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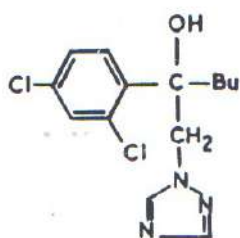
The 1, 2, 4-triazoles are, however, superior to the corresponding imidazoles for the control of phytopathogenic fungi. Examples developed during the last decade include flutriafol (39) (ICI, 1983), flusilazole (40) (Du Pont, 1984), hexaconazole (41) (ICI, 1986), and myclobutanil (42) (Rohm and Hass, 1986). Mammalian toxicities are very low (LD_{50} typically $> 1000 - 2000\text{mg/kg}$) and rates of application as seed dressings are 7.5g per 100kg of seed (for flutriafol) and 10 – 20g per 100kg of seed (for myclobutanil). Their mode of action is similar to that of imazalil (i.e. they are inhibitors of ergosterol biosynthesis).



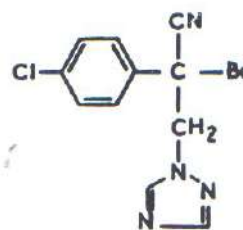
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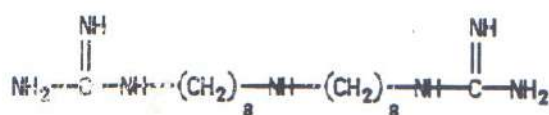
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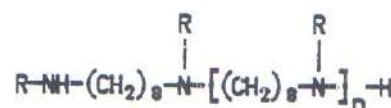
(42)

The fungicide formerly known as guazatine (43), and originally patented together with a range of similar guanidine derivatives for pharmaceutical use,

was developed at Murphy Chemical Ltd in the UK as an alternative to organomercury compounds for the control of seed-borne diseases of cereal crops. Further development by KemaNord AB in Sweden then led to the manufacture of a mixture of related guanidine derivatives (44) in which 77-83% of the amino groups in a mixture of 1, 8-diamino-octane, 1, 17-diamino-9-azaheptadecane, and other higher polyamine oligomers derived from 1, 8-diamino-octane, are converted to guanidine groups. This mixture (to which the name guazatine is now applied) is used at a rate of 0.6-0.8g per kg of seed for the control of *Septoria nodorum*, *Tilletia caries*, *Fusarium* spp. and *Helminthosporium* spp. in cereal crops, and it is also active against rice blast. It has relatively low mammalian toxicity (227-300mg/kg), is repellent to birds, and is non-toxic to bees when used as directed.



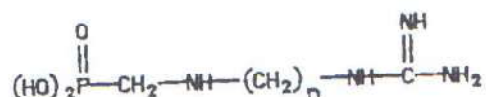
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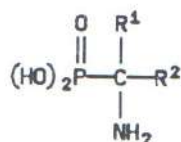
(44)

Collaboration between the Department of Chemistry, University of North London and KenoGard AB has involved analytical and mass spectrometric studies of guazatine and the preparation of radiolabelled material for environmental studies. Hudson *et al.* (1983) have also carried out wide ranging investigation of the synthesis and fungicidal activity of further compounds as potential replacements for organomercurials. In the first instance, they prepared a new series of compounds (45), based also on α, ω -diamines, in which both guanidine and phosphonic acid groupings were present. These compounds

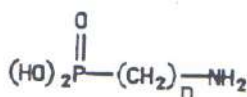
showed good activity against *Pyricularia oryzae*, *Botrytis cinerea*, *Septoria nodorum*, *Drechslera sativa*, and *Fusarium avenaceum* and led us to investigate the fungicidal activity of α - and ω -aminophosphonic acids (**46**, **47**) and α - and ω -guanidinophosphonic acids (**48**, **49**) more generally. Of these compounds, the aminophosphonic acids showed the best activity and were patented for use as agricultural fungicides, especially as seed-dressing agents.



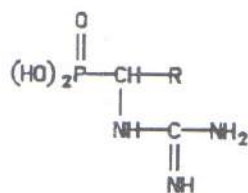
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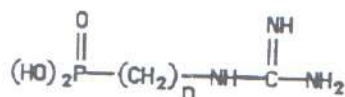
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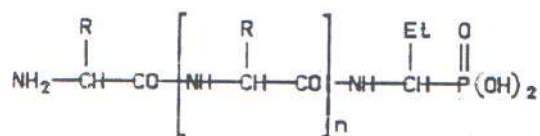
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They also prepared a number of phosphonopeptides (**50**) derived from PNL62 (29, $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Et}$) by combination with various α -amino acid residues. The activities against *Drechslera* spp. Of dipeptides ($n = 0$) containing an L-, D-, or DL-alanine residue are shown in Table 2 and it is clear that the L-alanine residue must be present for significant activity to be observed. There is also an indication of slightly higher activity in the peptides that contain the aminophosphonic acid residue in the R- rather than the S-configuration. The

tripeptide α -(L-alanyl-L-alanyl)-aminoprophanephosphonic acid also showed very good activity and in all cases the active compounds were superior to imazalil in their control of *Drechslera teres*.



(50)

Table 2: Fungicidal Activity of Phosphonopeptides (33, R = Me)*

N	Configuration at			Activity (%) against		
	P	Ala I	Ala II	<i>D. teres</i>	<i>D. gramineae</i>	<i>D. avenae</i>
0	RS	-	-	98	72	84
0	RS	L	-	98	61	93
0	R	L	-	100	84	91
0	S	L	-	88	28	84
0	RS	D	-	7	0	0
0	RS	DL	-	92	75	82
1	RS	L	L	100	-	98 ^a
	(Imazalil)			47	-	87

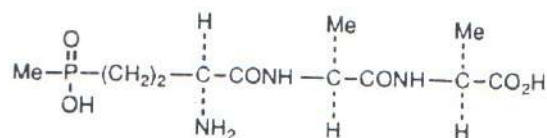
* (Tested as seed dressing agent at 0.4g/kg of seed); ^alower concentration.

It is of interest to note that fungicidal activity against *Botrytis cinerea*, and against *Piricularia oryzae* and *Rhizoctonia solanion* rice, was observed for the tripeptide phosphinothricyl-L-alanine (51), which was isolated from *Streptomyces viridochromogenes* and *S. hygroscopicus*, although the main interest in this natural product has been on account of its herbicidal activity.

Herbicides

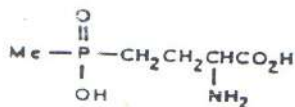
The herbicidal activity of phosphinothricyl-L-alanyl-L-alanine (51)

referred to above led to the development of this compound by the Meiji Seika company as an approved herbicide under the name bilanafos. In the form of the sodium salt it has an acute oral toxicity to rats of LD₅₀ 264-404mg/kg. similarly, the ammonium salt of the free aminophosphinic acid, phosphinothricin (**52**) (a methylphosphinic analogue of glutamine), was introduced by Hoechst



(51)

AG under the name glufosinate (LD₅₀ 1620-2000mg/kg). application rates for both of these compounds are in the range of 1 – 3kg per hectare. Considerable effort has been made, and is still being made, to find synthetic analogues and derivatives of phosphinothricin that have improved herbicidal activity. It is interesting to note that one of the most successful and widely



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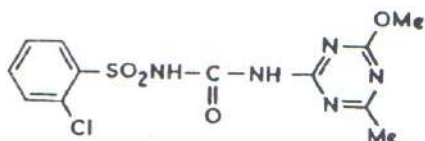


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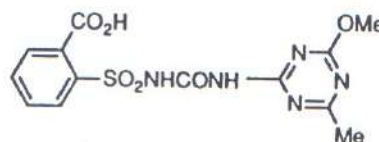
used non-selective systemic herbicides at the present time is the synthetic aminophosphonic derivative glyphosate (phosphonomethylglycine). A known compound at the time, its herbicidal activity was reported by Baird *et al.* in 1971 and it is widely used either as the isopropylamine salt (Monsanto product) or the trimethylsulfonium salt (marketed by ICI). It has very low mammalian toxicity (LD₅₀ 5600mg/kg), low toxicity to bees, and is applied at a rate of 0.34-2.24kg per hectare. It is strongly adsorbed to soil in which it undergoes microbial

degradation with the liberation of carbon dioxide to give aminomethylphosphonic acid as the principal metabolite.

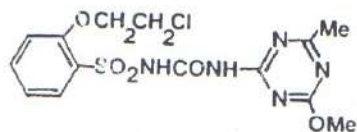
Some of the most interesting herbicides introduced recently are the highly active, yet selective, sulfonylureas which appear to act by inhibition of cell division. These systemic herbicides, which are useful e.g. for the control of broad-leaved weeds in cereal crops, are typified by the Du Pont products chlorsulfuron (**54**) and metsulfuron (**55**), and by triasulfuron (**56**), introduced by Ciba-Geigy. In all cases these compounds have very low mammalian toxicity.



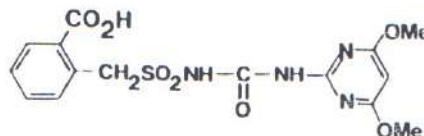
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Contribution to knowledge

Vice Chancellor Sir, I wish to highlight my research activities over the years.

The contributions can be classified into two sections. The first section is in the area of environmental chemistry which are presented in 1 – 8. The next section deals mainly on synthesis, characterization and evaluation of the various oligosulfides for their pesticidal activities.

1. Fatoki and Ayodele (1999) investigated zinc and copper contents of road-side tree barks which were monitored as possible indicators of the level of pollution resulting from motor vehicles. A positive correlation was obtained between the zinc level and traffic density; but none for copper.
2. Olajire and Ayodele (1997) analysed road-side soil samples for their heavy metal contents as possible indicators of the level of contamination from passing motor vehicles. The results show that there were probably other factors responsible for the low levels of these metals in the samples, besides motor vehicles pollution.
3. Olajire and Ayodele (2003) determined Pb, Cu, Zn, Ni, Fe, and Mn content of leaf and tree bark samples as possible indicators of environmental pollution resulting from automobile exhaust in motor parks. The authors found high pollution automobile parks showed higher level of these elements. They also demonstrates the suitability of tree barks and leaves as bio indicators of environmental, metal pollution and also provides greater awareness to the people in Ogbomoso and its environs about the atmospheric pollution levels in automobile parks.
4. Olajire (2005) and co-workers determined the heavy metal contents of solid waste sample from a number of sites in a number of cities in Nigeria. They highlighted the fact that levels of some highly toxic metals were quite higher than the internationally acceptable levels thereby sending a note of warning to the Nigerian public.
5. Olajire and coworkers (1999) determined the aliphatic and aromatic contents of compost-amended soil samples from a number of sites in Lagos. The results showed the presence of high carbon number aliphatic hydrocarbon and some probable aromatic ones. The authors highlighted the danger these compounds could pose to the environment.

6. Amuda *et al.*(2005) used concentrations of Cd, Pb, and Zn in surface sediments of Ibadan lakes to study modern atmospheric depositions of the metals. They found that Cd concentration was in the range stipulated for natural levels. Pb and Zn concentrations were higher than the range stipulated for natural levels. When compared with pre-industrial values, they found that the concentrations have increased by factors of 5-10 for Pb, 3-5 for Cd and 2 for Zn. The relative abundance of the metals in the sediments was found as $Pb > Zn > Cd$.
7. Olajire *et al.*(2005) reported the potential risk of soil, surface and ground water contamination by trace metals leached from highway construction solid wastes. From the toxicity test results, they found that leachates were in concentrations that did not exceed toxic concentrations for aquatic test. The results indicate low risk of surface and ground water contamination resulting from construction and wastes.
8. Olajire *et al.*(2003) determine metal species (Cd, Pb, Cu, Ni and Zn) in solution of soil extracts. They found that lead was significantly associated with the non-residual fractions in soils studies, indicating that this metal was potentially more bio-available than other metals analysed. Cadmium and Nickel were found mainly in the residual or the exchangeable fraction in most of the soils, while Cu and Zn were mainly associated with the organic fractions. The overall order of contamination was found to be $Pb > Zn > Cu > Ni > Cd$. Also, the mobility indexes of copper and nickel correlated strongly and positively with their total content, indicating that the anthropogenically added metals remained in relatively weakly bond forms
9. Ayodele *et al* (2001) reported the kinetics and mechanism of periodate oxidation of the complex *tris* (4, 4¹ - dimethyl-2, 2¹bypyridine) Iron (II). We found that the complex undergoes extensive protonation in acid medium and that both protonated and the unprotonated species such as IO_3 and $H_6IO_6^+$ undergoes electron transfer reaction with the complex. A

- reaction order of 0.2 with respect to $[\text{IO}_4^-]$ suggests that the reaction proceeds via a complex mechanism. The authors discussed the mechanism of the reaction and conclude that the formation of ion pair suggests that the reaction proceeds through an outer-sphere mechanism.
10. K. Mani Bushan and coworkers (1998) prepared a number of diarylethylenes and studied their photoisomerisations process in various solvents. The results showed that 4-methoxynaphthyl-4-nitrostyrene undergoes a one-way *cis to trans* isomerisation in polar solvents and a two-way isomerisation in non-polar solvents. A theoretical explanation was put forward for such behavior.
 11. Ayodele *et al* (1999) synthesized a number of benzyl phthalimido disulfides. The authors highlighted problems associated with the preparation of unsymmetrical disulfides. They were however able to prepare benzyl phthalimido disulfides using a method that consisted of two steps. The various compounds synthesized were fully characterized by elemental analysis, ^1H NMR, ^{13}C NMR and mass spectrometric techniques. All the synthesized compounds are new and they have potential for application as fungicides.
 12. Ayodele *et al* (1999) synthesized a number of novel Alkane- α - ω -bis (2-hydroxyethyl disulfides) and screened the compounds for their fungicidal activity. We were able to demonstrate that all the synthesized compounds showed very good activity against the test organism and that the activity of these compounds were comparable with those of quazatine/imazalil and phenyl mercury acetate which are two well established fungicides. The compounds have potential application as fungicide. Also, the mass spectrometry of these novel compounds were discussed.
 13. Ayodele *et al* (2000) synthesized novel organosulfur compounds of the general type $\text{ArCH}_2\text{S}_n\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ ($n = 1 - 4$, $\text{Ar} = \text{Ph}; 2\text{-MeC}_6\text{H}_4$:

4- MeOC₆H₄; n = 1 - 3. Ar = 2 - ClC₆H₄; n = 3 4-FC₆H₄; n = 3 or 4, Ar = Furyl) as analogues of the trisulfide PhCH₂SSSCH₂CH₂OH (an antimicrobial compound which occurs in the plant *Petivariaalliacea*. They also examine the potential application of these compounds as agricultural fungicides. They found that *in vitro* test against *Fusarium culmorum*, *Fusarium oxysporum* and *Gauenomycesgraminis* showed that all compounds gave >80% control of these organisms at 1000ppm. Tests at 100 and 100ppm showed varying levels of control but the activity did not depend significantly on the number of sulfur atoms present. They also found that selected compounds were active *in vivo* against *Erysiphe graminis* on barley seedlings, *Botrytis fabae* and *Uromycesviciae fabae* on bean seedlings, *Podosphaeria leucotricha* on apple seedlings, and *phylophthorainfestans* on potato leaf all of which are pathogenic fungi of economic significance in agriculture.

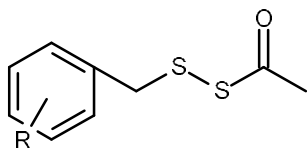
14. Ayodele and co-workers (2001) reported the synthesis of novel trisulfides of the general type R₃SSSR where R = benzyl or substituted benzyl group as part of their efforts in the search for suitable compounds as agrochemicals (fungicides). We found out that these novel compounds showed good activity and were able to control the three fungi investigated even at low compound concentration. They also demonstrated that the synthesized compounds showed activity comparable with those of guanzatine / imazalil and phenyl mercury acetate which are two well established fungicides hence establishing their potential usefulness as good fungicides.

15. Amuda and co-workers (2001) quantified different parts of crayfish for naphthalene uptake. They found that cephalothorax containing hepatopancreas (a food absorption organ) have greater uptake than the tail flesh or tail skeleton. They also found that some crustaceans in the

freshwater serving as food for man are capable of accumulating naphthalene on exposure to ^{14}C -naphthalene + 5% AF of crude oil and also capable of discharging when placed in an oil-free environment.

16. Ayodele and co-workers (2002) reported and discussed the electron impact mass spectral data for a range of benzyl 2-hydroxyethyl mono-, di-, tri- and tetrasulfides, dibenzyl di- and tri-sulfides, benzyl phthalimido disulfides, and a number of related compounds including benzyl acetyl disulfide, 2-hydroxyethyl phthalimido disulfide and trichloromethyl phthalimido disulfide. The authors noted that there are few mass spectrometric data for benzyl oligosulfides in the literature. They found that molecular ions were generally weak for these oligosulfides under the condition of their measurement; although certain exceptions include those derived from dibenzyl disulfides and benzyl acetyl disulfide were recorded. They also found that the most abundant ions are in all cases formed by simple carbon-sulfur cleavage which gives the stable benzyl (or tropylium) and 2-hydroxyethyl (or protonated ethylene oxide) cations. The most abundant ions result in certain cases from carbon-sulfur cleavage with the elimination of a neutral benzyl radical from sulfur-sulfur cleavage, possibly with hydrogen transfer, and from elimination of sulfur. They found that additional characteristic ions are exhibited by the phthalimido derivatives.

17. Ayodele *et al* (2003) synthesized novel organosulfur compound of the general type:



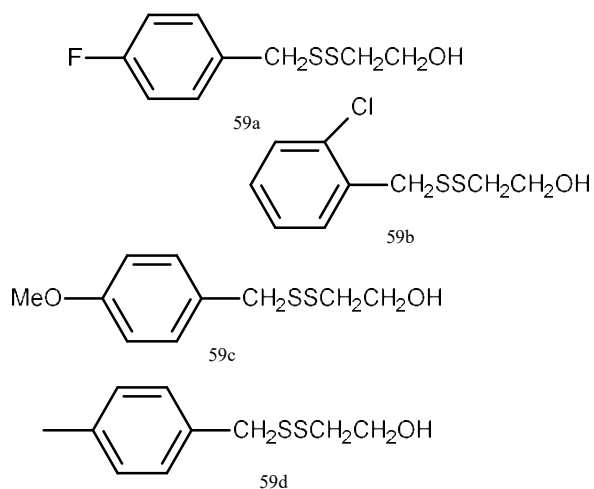
Where R = o-CH₃(58a); p-CH₃(58b); o-Cl(58c); p-Cl(58d); p-OCH₃(58e);H(58f) and p-F(58g)

The compounds were characterized by elemental analysis, nuclear magnetic resonance (¹H NMR and ¹³C NMR) and mass spectrometric techniques. We found that the biological screening showed that the synthesized compounds possess very high fungicidal activity.

18. Odunola *et al.* (2005) reported the synthesis of multidonor alcohol compounds of the type: (OMeC₆H₄)₂ (CH₂)_n OR OH [R = Me, N = 2 (I), R = Me, N = 3 (II) R = Me. n = 4 (III), and R = Et, n = 3 (IV) were synthesized. The synthesized compounds which are all new were well characterized by elemental analysis, infrared, ¹H and ¹³C NMR. These compounds possess donor functionalised groups, which would be useful as ligand moieties in constructing new molecular precursors.

19. Amuda *et al.* (2003) studies the effect of adding NaCl to molten alkali metal nitrites. They found that this addition increases their specific heats which in turn increases their energy storage capacity. The electrochemical studies showed higher corrosion rate, a lower polarization resistance and a decrease of activation energy of the mild steel in the presence of NaCl.

20. Ayodele (2005) synthesized oligosulfides compounds:



(**59a – 59d**) and screen them *in vivo* for their bioactivity. All the compounds were tested against five fungi that included *Erysiphe graminis* on barley seedlings. *Botrytis fabae* on bean seedlings, *Podosphaera leucotricha* on apple seedlings. *Uromyces viciae-fabae* on bean seedlings and *Phytophthora infestans* on potato leaf. All the compounds tested were found to be fungicidal against these organisms. The *para*-fluorosubstituted unsymmetrical disulfide gave the greatest spectrum of disease control, reducing infection in all host-pathogen systems examined.

21. Ayodele and co-workers (2005) investigated the polymerization of 1,3-butadiene using a new neodymium based catalyst system: $\text{Nd}(\text{Carboxylate})_3/\text{diisobutylaluminum hydride/crotyl chloride}$ (carboxylate = versatate or naphthenate). The percentage *cis* (% *cis*) content obtained from the polymers varies from 96.8 - 98.2 while the percent vinyl is less than 1. The Gel Permeation Chromatographic (GPC) analyses of the results obtained on the polymers are presented and discussed. The result suggests a great potential for polymers produced using the catalyst systems particularly with respect to processing.

22. Ayodele (2005) reported and discussed the ^{13}C nuclear magnetic resonance spectra data for a range of benzyl 2-hydroxyethyl mono-, di-, tri-, and tetra-sulfides. He found that the methylene carbon of the benzylic group (ArCH_2S) in unsymmetrical di-, tri-, and tetra-sulfides respectively resonates at a fairly constant chemical shift value 6), while that of the unsymmetrical monosulfides absorbs upfield at 5.35. I also found that the absorption of the methylene carbon of the benzylic group in unsymmetrical mono-, di-, tri-, and tetra-sulfides does not show any significant dependence on the substituents in the benzene ring because the chemical shift values obtained for this carbon atom in the various compounds are fairly constant.
23. Ayodele and co-workers (2005) synthesized a number of novel benzothiazol-2-yl 2-hydroxyethyl disulfides and screened them for their fungicidal activity. The authors were able to demonstrate that all the synthesized compounds showed very good activity against the test organism and that the activity of these compounds were comparable with those of guazatine /imazalil and phenyl mercury acetate which are two well established fungicides. The compounds have potential application as fungicide. Also, the mass spectrometry of these novel compounds were discussed.
24. Ayodele *et al.* (2005) synthesized a number of substituted benzylhydrodisulfides and screened the compounds for their fungicidal activity. The authors were able to demonstrate that all the synthesized compounds showed very good activity against the test organism and that the activity of these compounds were comparable with those of quazatine/imazalil and phenyl mercury acetate which are two well established fungicides. The compounds have potential application as fungicide. Also, the mass spectrometry of these novel compounds were discussed.

25. Ayodele and co-workers (2011) reported the synthesis of novel organic sulfides as part of their efforts in the search for suitable compounds as agrochemicals (fungicides). They found out that these novel compounds showed good activity and were able to control the three fungi investigated even at low compound concentration. They also demonstrated that the synthesized compounds showed activity comparable with those of guanzatine / imazalil and phenyl mercury acetate which are two well established fungicides hence establishing their potential usefulness as good fungicides.
26. Ayodele *et al.* (2005) synthesized novel organosulfur compounds of the general type:
$$\text{H}_2\text{C}=\text{CH}(\text{CH}_2)_n\text{S}_n\text{CH}_2\text{CH}_2\text{OH}, n = 1, n = 2, n = 3 \text{ and } n = 4.$$
The compounds were characterized by elemental analysis, nuclear magnetic resonance (^1H NMR and ^{13}C NMR) and mass spectrometric techniques. They found that the biological screening showed that the synthesized compounds possess very high fungicidal activity.
27. K. Mani Bushan *et al.* (1998) highlight the importance of light-induced *cis-trans* isomerization indicating that it is a most important fundamental process in photochemical, photobiological and technological chemistry. They prepared several ethylene derivatives, dienes, trienes and pentanes and studied their photoisomerization. They found that steady state composition, ϕ_{iso} , ϕ_{fluor} , fluorescence lifetimes and product characterization data supported that the singlet excited olefin has a highly polarized or charge transfer or zwitterionic nature. They also identified "quantum chain" isomerization originating from singlet excited state thereby making the synthesized olefins potential candidates for molecular opto-electric and opto-mechanical switching and storage devices.

Conclusion

In conclusion, therefore, many of the long established pesticides may be considered to be environmentally safe if used in accordance with the manufacturer's instructions, although some may be dangerous if used carelessly and a number are under investigation for possible harmful effects such as mutagenicity or carcinogenicity. There is a clear need for the continual introduction of compounds which are more environmentally acceptable than the more traditional pesticides compounds that are more selective and do not harm useful forms of life, are free of long term chronic toxicity effects, and are sufficiently active to be applied at low dosage rates (typically of the order of tens of grams per hectare, rather than kilograms per hectare which is more usual for traditional pesticides). This latter characteristic, and the ability to undergo total degradation and leave no harmful residues, are particular features of many modern pesticides.

In addition, we were able to demonstrate that several of the synthesized compounds showed very good fungicidal activity against the test organism and that the activity of these compounds were comparable with those of quazatine/imazalil and phenyl mercury acetate which are two well established fungicides. The compounds have potential application as fungicide. Also, the ^1H , ^{13}C nuclear magnetic resonance spectral data and mass spectrometry of these novel compounds were discussed.

RECOMMENDATIONS

The good efforts of the Federal Government of Nigeria through the Education Trust Fund (TETFUND) in the provision of (i) Scholarship to academic staff of Nigerian public Universities for the pursuance of higher degrees (ii) sponsorships at both local and international conferences, (iii) provision of

laboratory equipment and other physical infrastructures etc are highly commendable.

However, I hereby wish to recommend as follows:

- (i) That the end users and in this case academic researchers should be taken along in the provision of these facilities. The supply of specialized equipment should be handled by competent contractors that understand these equipment and the use for which they are meant for.
- (ii) That Government in addition to the above should adequately fund education by providing all other essential infrastructures particularly electricity.
- (iii) That the industry and academia should collaborate such that Industry should sponsor research projects and researchers in turn should avail the other party their research findings, patents and innovations for the overall development of the country and humanity as a whole.

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LADOKE AKINTOLA UNIVERSITY OF TECHNOLOGY

CITATION OF PROFESSOR EZEKIEL TEMIDAYO AYODELE

Professor Ezekiel Temidayo Ayodele, a Professor of Organic Chemistry, was born about six decades ago to Mr. Enoch Ayodele and Mrs. Felicia Ayodele of Isokun Street, Ilesa. He attended Ilesa Grammer School from 1971 to 1975 and 1976 to 1978 where, he completed his School Certificate and Higher School Certificate respectively. He also attended University of Ife (now Obafemi Awolowo University), Ile-Ife from 1978 to 1981 and 1984 to 1986, respectively where He bagged B.Sc. (Hons) Chemistry and M.Sc. Chemistry respectively. Professor Ayodele proceeded to the University of North London, United Kingdom in the year 1991 to pursue his Ph.D. degree and he obtained the degree (Ph.D. Chemistry) in 1994.

In terms of Distinction and Awards, Prof. Ayodele won several Scholarships and Fellowship awards among them are Federal Government Award in 1980; University of Ife Award in 1980; Overseas Development Administration Shared Scholarship, between 1991 and 1994 to pursue his Ph. D. in the University of North London; Third World Academy of Sciences postdoctoral fellowship between 1997 and 1998 at Indian Institute of Chemical Technology, Hyderabad, India; DAAD short Visit Fellowship in 2002 at University of Duisburg, Germany; DAAD Short Visit Fellowships in 2006, 2009 and 2018 at the University of Regensburg, Germany.

Prof. Ayodele was appointed as a Graduate Assistant at the University of Ife (now Obafemi Awolowo University), Ile-Ife in 1983. He was a Visiting Lecturer at the University of North London in 1994. Prof. Ayodele joined the services of Oyo State University of Technology (OSUTECH) now (Ladoke Akintola University of Technology), Ogbomoso as an Assistant Lecturer in 1990 and rose

to the position of a Professor of Organic Chemistry in the year 2005. He was a visiting Professor to Bells University of Technology, Otta, Ogun State between 2008 and 2009 and Osun State University between 2016 and 2018. He is an external Examiner to Obafemi Awolowo University, Ile-Ife.

Prof. Ayodele is a member of senate of Ladoke Akintola University of Technology, Ogbomoso. He was a Departmental Examination Officer between 1999 and 2002. He was a Coordinator of Science Laboratory Technology Scheme in 2001. He was the Head of the Department of Pure and Applied Chemistry, LAUTECH between 2005 and 2008. He was elected as the Dean of the Faculty of Pure and Applied Sciences, the position he held for two consecutive terms between 2012 and 2016. Prof. Ayodele was a member of the Governing Council of Osun State College of Technology, Esa-Oke in 2005 to 2006.

Professor Ayodele has published 30 articles in reputable local and international journal outlets. He co-published a book titled Introduction to University General and Physical Chemistry, the book is indispensable to students. Prof. Ayodele's current research is in the studies of Chemistry of Organosulphur compounds that may have applications in Agriculture. He is a member of Chemical Society of Nigeria.

Professor Ayodele is happily married with children and grandchildren.

Ladies and Gentlemen, please join me to congratulate an erudite scholar of international repute as he present 29th Inaugural Lecture Series of the Ladoke Akintola University of Technology, Ogbomoso, Nigeria.