Research Article **Bio Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

X-RAY CRYSTALLOGRAPHIC AND I-R STUDIES OF SYSTEMIC FUNGICIDE THIOPHANATE METHYL

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ABSTRACT

The activity of fungicides is intimately related to its chemical structure. Knowledge of the chemical structure is useful for the synthesis of new compounds with more specific actions and fewer adverse reactions, to increase/decrease the duration of action of the original drug or fungicide to get a more potent compound, to restrict the action to a specific system of the body or plant and to reduce the adverse reactions, toxicity and other disadvantages associated. The interactions of fungicides with the macromolecule of the parasite are dependent on the stereochemistry of these compounds. In order to design more effective fungicides, it is necessary to analysis the three dimensional structure of these compounds and if possible the receptor molecule. Recently it has been observed that some of the fungicides are losing their effects. So we can design analogous compounds as a substitute, if their structures are known. A rational approach to test these fungicides is to know the three dimensional structure of these compounds and macromolecular receptor sites.The structures of these compounds can be obtained by X-ray diffraction method in crystalline form and they will invariably be similar to their structure in solutions. The single crystals of Thiophanate Methyl was grown.The Crystal system is Triclinic with space group P-1 and the unit cell parameters obtained are a = 10.191(5) A^0, b = 11.203(5)A^0, c = 17.151(5) $A^{0,}$ α = 76.909(5) deg., β = 86.051(5) deg., γ = 72.426(5) deg. The composition of crystal Thiophanate methyl is confirmed by infra-red spectra. It has been found that Thiophanate methyl has both the preventive and curative actions and is most active in the thioallophanic acid group. Substitution on benzene ring decreases the fungitoxicity, A CH_2 group introduced between the benzimidazole ring and the amino group reduces the antifungal action of the active substance, thus modified. The fungicidal effect decreases with increasing length of alkyl chain.

KEYWORDS: **X-ray crystallography, Systemic fungicides, , Thioallophanic acid**

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INTRODUCTION

Thiophanates, without a heterocyclic ring, may be regarded as derivative of o-phenylenediamine with one hydrogen on each amino group substituted by a thioallophanic acid ($H_2NCSNHCOOH$).The various members of these groups are: thiophanate [1,2-bis(3-ethoxycarbonyl-2-thioureido)benzene], thiophanate methyl [1,2-bis(3-methoxycarbonyl-2-thioureido)benzene], NF 48[1(3- methoxycarbonyl-2-thioureido)-2-aminobenzene].The conversion products of thiophanates in aqueous solution are similar to benzimidazoles; thiophanate is converted to ethyl benzimidazole carbamate (EBC) and thiophanate-methyl to methyl benzimidazole cabamate. A correlation was found between the formation of MBC and the fungi toxicity of the latter form that are responsible for its fungicidal activity. These fungicides were developed and marketed by Nippon Soda Co. Ltd., Ohtemach, Tokyo, Japan and the United Kingdom by May & Baker Ltd., Onger, Sussex, London. Thiophanate is marketed in Japan under the trade name Topsin.Thiophanates are absorbed by various plant parts, such as the leaves and fruits after spray or dust application, or the roots after soil drench, or by the stem or trunk injection. Generally they are taken up by the roots at the plants; and the active substances are then acropetally translocated through the xylem to the leaves. In the leaves they travel peripherically accumulates at the edges and tips .Uptake of Thiophanate methyl (TPM) has been reported by germinating soybean seed (Kirkpatrick and Sinclair, 1973), in soybean plant (Kirkpatrick and Sinclair, 1976), cucumber and barley (Mercer, 1971), cucumber, pea and aster (Fuchs, et al., 1972), cotton (Buchenauer, et al, 1973b) Demonstrate and marrow (Doma, et al.,1971).Buchenauer, et al. (1973b) demonstrated uptake of TPM through roots after soil application and absorption through cotton foliage. Translaminar and transcuticular movements of thiophanate-methyl have been reported. Translocation of thiophanate methyl predominantly occurs in the apoplast although some uptake and transport of MBC (its breakdown product) in symplast has been reported (Solel, et al., 1973). In several cases studied, no movement from the leaves into the fruit was observed (Brown and Albrigo, 1972).Leroux and Gredt (1977) reported the absorption of thiophanates by excised maize roots.

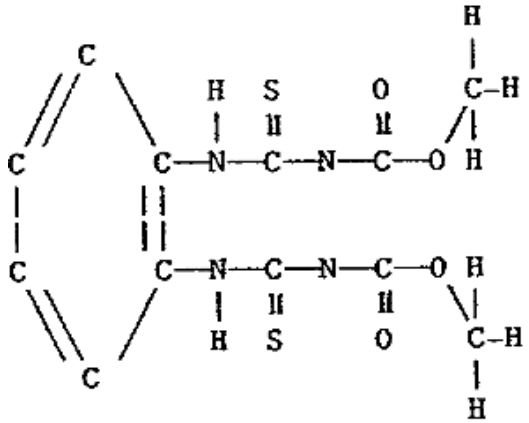

Figure I
Chemical structure of Thiophanate Methyl

Experimental

First the crystals of existing fungicides are grown in lab. Colorless well formed crystals of Thiophanate Methyl of size 0.30 x 0.20 x 0.20 mm were obtained by slow evaporation from a solution of Acetone at 290^{o} K temp. The crystals obtained were rectangular in shape. The crystal density is calculated by floatation method in the mixture of benzene and carbon-tetrachloride. For that the crystal was placed in RD bottle filled with carbon tetrachloride then benzene is added to the solution until the crystal floats in the middle of mixture. Thus the crystal and solution are of same density and density of solution is measured with pyknometer. The determination of structural perturbation in fungicide derivatives and comparison of the result of their molecular association with other receptor sites by X-Ray crystallography techniques will be done then. In parallel with these structural studies, spectroscopic studies are carried out on them. For IR spectroscopy pellet method was used, firstly pellet of pure KBr and KBr with 2% of Thiophanate methyl was made. Then the pellets are placed on the sample holder of the IR spectrometer to study the composition by means of the graph obtained, between Wavelength and Absorbance as shown in figure II. The goal is then to tie together the structural and spectroscopic studies to have more comprehensive account of the precise shape of these molecules, the non-covalent interaction which are likely to be involved in and the changes introduced in molecular geometry and electronic structure of these compounds as a result of their molecular association with other compounds.

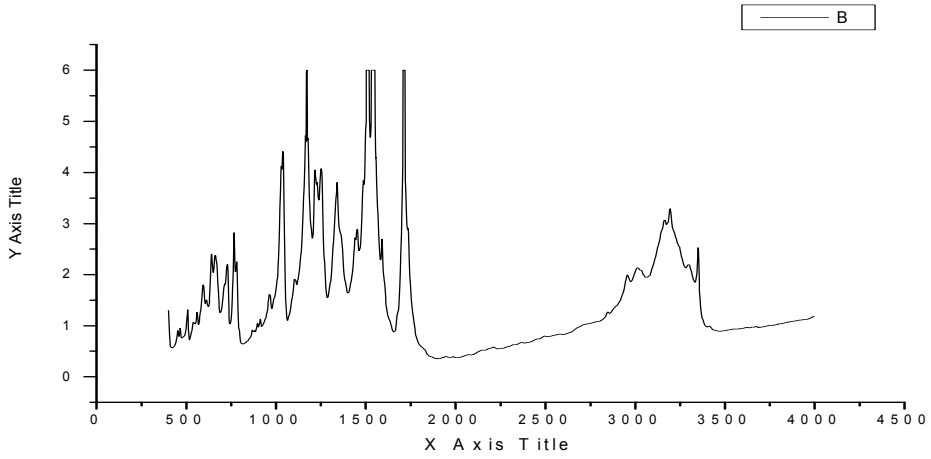

Figure II
IR data of Thiophanate Methyl

MATERIALS AND METHODS

The three dimensional intensity data are collected on a computerized automatic 4-circle CAD-4 Enraf-Nonious Diffractometer at SAIF Madras. The preliminary information about the crystal is listed in TableI. The unit cell parameters are determined by directly on CAD-4 Enraf Nonius 4-circle automatic Diffractometer The structure determination is carried out on VAX machine using SHELXS-97. All the non-hydrogen atoms are located in the beginning itself.

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5.1 Refinement

The positional co-ordinates, which were obtained from SHELXS 97 and isotropic temperature factors, are subjected to refinement by SHELXL refinement program. After so many cycles of refinement the R factors dropped to .0541 .Further refinement of the structure is carried out with individuals an isotropic temperature factors of the exponential form.- $2P_1\ ^2[h^2a^{*2}U_{11}+----------+2hKa^*bxU_{12}]$ The hydrogen atoms are fixed at this stage by geometrical considerations and are not refined. Refinement of the structure is terminated after two more cycles when the derivations in the parameters become much smaller than the corresponding estimated standard deviation.

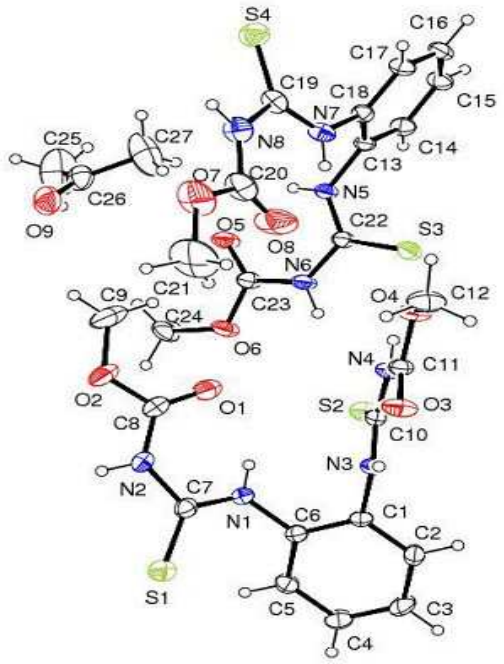

Figure III
ORTEP of Thiophanate methyl

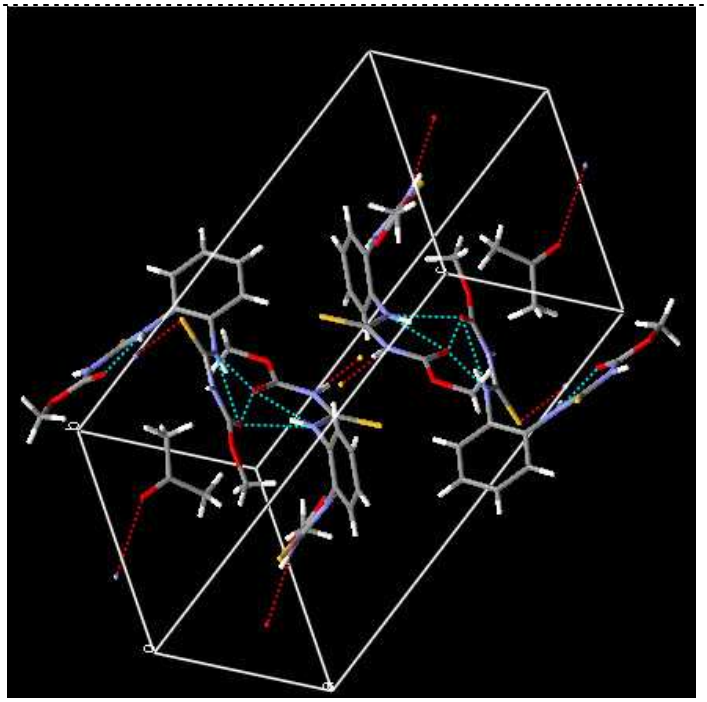

Figure IV
Packing diagram of Thiophanate methyl

RESULTS AND DISCUSSION

Atomic coordinates (x 10^4) and equivalent Isotropic displacement parameters for (A^2 x 10^3) Thiophanate methyl is shown in TableII. Bond lengths [A] Bond angles [deg] for Thiophanate methyl is shown in TableI III.Anisotropic The anisotropic displacement factor exponent takes the form:
$2P_1\ ^2[h^2a^{*2}U_{11}+----------+2hKa^*bxU_{12}]$ Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for Thiophanate methyl is shown in Table V. Torsion angles [deg] are shown in Table IV. The ORTEP diagram and the packing diagrams of Thiophanate Methyl crystal is shown in figure III and IV respectively.The average bond distance of C-H is 0.9600Å. In Benzene ring distance between C(1)-C(2) is 1.374(2), C(2)-C(3) is 1.381(3) C(3)-C(4) is 1.382(3) , C(4)-C(5) is 1.368, C(5)-C(6) is 1.385(2) and C(1)-C(6) is 1.385(2) . These distances are short and this may be due to delocalization of electrons from the benzene rings This shows the regular behavior of benzene ring. C(7)-S(1) is 1.654(2), C(10)-S(2) is 1.661,C(1)-N(3) is 1.427(2)and C(6)-N(1) is

1.421(2)are equivalent to standard values. Bond distance C(7)-N(1) is 1.321(2), C(7)-N(2) is 1.395(2) ,C(10)-N(3) is 1.329(2) and C(10)-N(4) is 1.377(2) (standard value 1.47) are shorts due to twists in the molecules. The whole molecules appeared to be twisted and folded and reason may be stacking – constraint. The equations of the Least squares planes, calculated using Blow method. The torsion angles of C(6)-C(1)-C(2)-C(3) is 1.2(3), N(3)-C(1)-C(2)-C(3) is 176.52(18), C(1)-C(2)-C(3)-C(4) is 0.9(3) , C(2)-C(3)-C(4)-C(5) is -0.9(3), C(3)-C(4)-C(5)-C(6) is -1.2(3), C(2)-C(1)-C(6)-C(5) is -3.3(3) show that this ring is almost symmetric. The crystal structure consists of parallel sheets stacked along a-axis. The molecules overlap while running along the a-axis. The groups are stacked in such a way that they generate significant Vander-Walls interaction between them.

Sample Table I

Preliminary Crystal structure data for Thiophanate methyl

Parameters	Values
Empirical formula	C27 H34 N8 O9 S4
Formula weight	742.86
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system,	Triclinic
Space group	P-1
Volume	1818.2(13) A^3
Z	2
Calculated density	1.357 Mg/m^3
Absorption coefficient	0.320 mm^{-1}
F (000)	776
Crystal size	0.30 x 0.20 x 0.20 mm
Unit cell dimensions	a = 10.191(5) A^0, b = 11.203(5) A^0, c = 17.151(5) A^0
	α = 76.909(5)deg., β = 86.051(5) deg., γ = 72.426(5)deg.
θ range for data collection	1.22 - 25.00 deg.
Limiting indices	-12<=h<=12, - 13<=k<=13, -20<=l<=20
Reflections collected / unique	32179 / 32179 [R (int) = 0.0000]
Completeness to theta = 25.00	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9398 and 0.9100
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	32179 / 8 / 472
Goodness-of-fit on F^2	1.087
Final R indices [I>2sigma (I)]	R1 = 0.0541, wR2 = 0.1587
R indices (all data)	R1 = 0.0657, wR2 = 0.1790
Extinction coefficient	0.0195(9)
Largest diff. peak and hole	0.361 and - 0.352e.A^{-3}

Sample Table II

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for new. U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	U (eq.)	x	y	z
C (1)	-4667(2)	-6283(2)	3752(1)	31(1)
C (2)	-5447(2)	-6687(2)	4384(1)	43(1)
C (3)	-5494(2)	-7939(2)	4559(1)	54(1)
C (4)	-4745(2)	-8788(2)	4105(1)	47(1)
C (5)	-3968(2)	-8387(2)	3475(1)	41(1)
C (6)	-3951(2)	-7123(2)	3281(1)	33(1)
C (7)	-3351(2)	-6717(2)	1866(1)	39(1)
C (8)	-1835(2)	-5331(2)	1433(1)	52(1)
C (9)	-386(3)	-4133(3)	806(2)	96(1)
C (10)	-3658(2)	-4564(2)	3713(1)	30(1)
C (11)	-4983(2)	-2341(2)	3136(1)	34(1)
C (12)	-5905(2)	-133(2)	2640(2)	59(1)
C (13)	987(2)	-1066(2)	3681(1)	31(1)
C (14)	1642(2)	-1102(2)	4366(1)	41(1)
C (15)	1611(2)	32(2)	4569(1)	44(1)
C (16)	910(2)	1186(2)	4092(1)	43(1)
C (17)	270(2)	1219(2)	3408(1)	41(1)
C (18)	323(2)	87(2)	3192(1)	34(1)
C (19)	-179(2)	736(2)	1755(1)	43(1)
C (20)	-1768(2)	-189(3)	1240(2)	64(1)
C (21)	-3236(4)	-794(4)	514(2)	132(1)
C (22)	20(2)	-2778(2)	3626(1)	34(1)
C (23)	1394(2)	-4669(2)	3132(1)	39(1)
C (24)	2328(2)	-6560(2)	2657(2)	59(1)
C (25)	4170(4)	-3667(4)	877(2)	13(2)
C (26)	2740(3)	-2876(2)	707(1)	57(1)
C (27)	2145(4)	-1955(3)	1223(2)	123(1)
N (1)	-3193(2)	-6665(2)	2615(1)	38(1)
N (2)	-2598(2)	-6081(2)	1303(1)	45(1)
N (3)	-4684(2)	-4971(1)	3549(1)	32(1)
N (4)	-3855(2)	-3262(1)	3492(1)	35(1)
N (5)	1040(2)	-2257(1)	3482(1)	34(1)
N (6)	246(2)	-3966(1)	3456(1)	41(1)
N (7)	-355(2)	101(2)	2495(1)	41(1)
N (8)	-961(2)	597(2)	1167(1)	55(1)
O (1)	-1674(2)	-5113(2)	2063(1)	83(1)
O (2)	-1314(2)	-4857(2)	750(1)	70(1)
O (3)	-5998(1)	-2528(1)	2934(1)	50(1)
O (4)	-4797(1)	-1193(1)	3037(1)	47(1)
O (5)	2413(1)	-4343(1)	2940(1)	52(1)
O (6)	1222(1)	-5752(1)	3049(1)	51(1)
O (7)	-2330(2)	-38(2)	534(1)	92(1)
O (8)	-1941(2)	-921(2)	1830(1)	93(1)
O (9)	2079(2)	-2956(2)	188(1)	76(1)
S (1)	-4360(1)	-7413(1)	1542(1)	57(1)
S (2)	-2197(1)	-5526(1)	4150(1)	44(1)
S (3)	-1510(1)	-2047(1)	3972(1)	51(1)
S (4)	862(1)	1638(1)	1479(1)	59(1)

Sample Table III

Bond lengths [A^0] and angles [degree] for Thiophanate Methyl

Atoms	Bond Length[A^0]	Atoms	Bond Length[A^0]
C (1)-C (2)	1.374(2)	C (8)-O (1)	1.192(2)
C (1)-C (6)	1.385(2)	C (8)-O (2)	1.319(2)
C (1)-N (3)	1.427(2)	C (8)-N (2)	1.366(3)
C (2)-C (3)	1.381(3)	C (9)-O (2)	1.440(3)
C (2)-H (2)	0.9300	C (9)-H (9A)	0.9600
C (3)-C (4)	1.382(3)	C (9)-H (9B)	0.9600
C (3)-H (3)	0.9300	C (9)-H (9C)	0.9600
C (4)-C (5)	1.368(3)	C (10)-N (3)	1.329(2)
C (4)-H (4)	0.9300	C (13)-C (18)	1.375(2)
C (5)-C (6)	1.385(2)	C (13)-C (14)	1.378(2)
C (5)-H (5)	0.9300	C (13)-N (5)	1.435(2)
C (6)-N (1)	1.421(2)	C (14)-C (15)	1.382(2)
C (7)-N (1)	1.321(2)	C (12)-H (12B)	0.9600
C (7)-N (2)	1.395(2)	C (12)-H (12C)	0.9600
C (7)-S (1)	1.654(2)	C (14)-H (14)	0.9300
C (15)-C (16)	1.377(3)	C (16)-C (17)	1.369(3)
C (15)-H (15)	0.9300	C (16)-H (16)	0.9300
C (10)-N (4)	1.377(2)	C (22)-N (5)	1.322(2)
C (10)-S (2)	1.6613(18)	C (22)-N (6)	1.375(2)
C (11)-O (3)	1.203(2)	C (25)-H (25A)	0.9600
C (11)-O (4)	1.3273(19)	C (25)-H (25B)	0.9600
C (11)-N (4)	1.362(2)	C (25)-H (25C)	0.9600
C (12)-O (4)	1.442(2)	C (26)-O (9)	1.187(3)
C (12)-H (12A)	0.9600	C (26)-C (27)	1.476(3)
C (12)-H (12B)	0.9600	C (27)-H (27A)	0.9600
C (12)-H (12C)	0.9600	C (27)-H (27B)	0.9600
C (14)-H (14)	0.9300	C (27)-H (27C)	0.9600
C (15)-C (16)	1.377(3)	N (1)-H (1A)	0.784(13)
C (15)-H (15)	0.9300	N (2)-H (2A)	0.866(15)
C (16)-C (17)	1.369(3)	N (3)-H (3A)	0.803(14)
C (16)-H (16)	0.9300	N (4)-H (4A)	0.855(14)
C (17)-C (18)	1.385(2)	C (23)-N (6)	1.360(2)
C (17)-H (17)	0.9300	C (24)-O (6)	1.448(2)
C (18)-N (7)	1.416(2)	N (5)-H (5A)	0.836(13)
C (19)-N (7)	1.336(2)	N (6)-H (6A)	0.849(13)
C (19)-N (8)	1.390(2)	N (7)-H (7A)	0.820(14)
C (19)-S (4)	1.653(2)	N (8)-H (8A)	0.868(15)
C (20)-O (8)	1.190(3)	C (23)-O (5)	1.203(2)
C (20)-O (7)	1.331(3)	C (23)-O (6)	1.318(2)
C (20)-N (8)	1.356(3)	C (22)-S (3)	1.6657(19)
C (21)-O (7)	1.435(3)	C (25)-C (26)	1.468(4)
C (21)-H (21A)	0.9600	C (24)-H (24B)	0.9600
C (21)-H (21B)	0.9600	C (24)-H (24A)	0.9600
C (21)-H (21C)	0.9600		

Table IV

Torsion Angles [deg.] for the between the atoms in Thiophanate Methyl

Atoms	Torsion Angles [deg.]	Atoms	Torsion Angles[deg.]
C (2)-C (1)-C (6)	120.08(15)	C (4)-C (5)-C (6)	120.15(17)
C (2)-C (1)-N (3)	119.48(15)	C (4)-C (5)-H (5)	119.9
C (6)-C (1)-N (3)	120.27(15)	C (6)-C (5)-H (5)	119.9
C (1)-C (2)-C (3)	119.86(17)	C (1)-C (6)-C (5)	119.66(16)
C (1)-C (2)-H (2)	120.1	C (1)-C (6)-N (1)	118.78(14)
C (3)-C (2)-H (2)	120.1	C (5)-C (6)-N (1)	121.55(15)
C (2)-C (3)-C (4)	120.10(18)	N (1)-C (7)-N (2)	114.94(16)
C (2)-C (3)-H (3)	119.9	N (1)-C (7)-S (1)	126.85(14)
C (4)-C (3)-H (3)	119.9	N (2)-C (7)-S(1)	118.19(15)
C (5)-C (4)-C (3)	120.05(17)	O (1)-C (8)-O (2)	124.62(19)
C (5)-C (4)-H (4)	120.0	O (1)-C (8)-N (2)	125.79(19)
C (3)-C (4)-H (4)	120.0	O (2)-C (8)-N (2)	109.58(1)

Sample Table V

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for Thiophanate methyl.

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1A)...O(1)	0.784(13)	2.000(15)	2.644(2)	139.3(16)
N(1)-H(1A)...S(2)	0.784(13)	2.938(15)	3.5015(18)	130.9(15)
N(8)-H(8A)...O(9)#1	0.868(15)	2.338(18)	3.073(3)	142.6(18)
N(7)-H(7A)...O(8)	0.820(14)	2.031(17)	2.680(2)	135.8(17)
N(7)-H(7A)...S(3)	0.820(14)	2.889(17)	3.484(2)	131.2(16)
N(5)-H(5A)...O(5)	0.836(13)	2.028(14)	2.667(2)	132.7(13)
N(5)-H(5A)...O(3)#2	0.836(13)	2.339(14)	3.045(2)	142.5(13)
N(4)-H(4A)...S(3)	0.855(14)	2.461(14)	3.3136(18)	174.6(16)
N(6)-H(6A)...S(2)	0.849(13)	2.612(14)	3.4549(19)	172.7(16)
N(3)-H(3A)...O(3)	0.803(14)	2.007(15)	2.659(2)	138.1(16)
N(3)-H(3A)...O(5)#3	0.803(14)	2.386(16)	3.028(2)	137.7(15)
N(2)-H(2A)...O(9)#4	0.866(15)	2.105(16)	2.950(2)	165(2)

Symmetry transformations used to generate equivalent atoms

#1 -x,-y,-z #2 x+1,y, z #3 x-1,y, z #4 -x,-y-1,-z

CONCLUSIONS

Thioallophanic acid derivatives i.e. Thiophanate Methyl effects -

- Further substitution on benzene ring decreases the fungitoxicity of the compounds.
- Thiophanate methyl has both the preventive and curative actions
- The hydrogen of the amino group results in biological inactivity
- A CH_2 group introduced between the benzimidazole ring and the amino group weakens hydrogen bounding tendency at the amino group and accordingly reduces the antifungal action of the active substance, thus modified.
- The ester group does not substantially affect activity, however the fungicidal effect decreases with increasing length of alkyl chain Working chemically

R1----------NH--------CO----------R2

It is assumed that in plant cells the active substances are bound to the site of action by a hydrogen bond or by a charge transfer complex formed through the amino group. The R1 group promotes the penetration of the molecule into the cells while R2 group provides for optimal electron density at the carbonyl group.

Particularly good results are attained against apple and pear scab and on various crops against powdery mildew, Botrytis and Sclertinia spp.

The Thiophanates are also effective against diseases that occur in the period after harvest. When used systematically, thiophanate methyl substantially decreases acarus populations because the compound is an effective ovicide against Tetranychus urticae (Cole et.al., 1971). Thus we study the structure of variety of such compounds and correlate their structure with biological activity, so that more safer and effective fungicides at reasonable price can be developed.

ACKNOWLEDGEMENTS

My sincere thanks to Sophisticated Analytical Instrument Facility (SAIF), IIT MADRAS, for providing the facility of CAD-4 Diffractometer and valuable help in Data collection. I am thankful to Consortium of Scientific Research (UGC-DAE-CSR), Indore, for Infra-red spectroscopic measurement of the sample

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REFERENCES

1. Brown M C, Waller C D, Charlet C, The use of Flutriafol based fungicides for the control of sugarbeet diseases in France, Proc. Br. Crop. Prot. Conf.-Pests and Diseases, 3:1055-1061, (1986)
2. Matolcsy Gy, Nadasy M, Andriska V, Pesticide Chemistry , Volume 32 ,Elsevier Science Publishing Co.:396-399,
3. Leroux P, Gerdt M, Fritz R, Similarities and differences between the mode of action of imazalil, triadimenfon triarimol and triforine, Phytiat-Phytopharm, 25(4):317, (1976).
4. Frederick M, Ladd C, Palmer R, Structure determination by X-ray crystallography, 4 thEdition, Kluwer Academic/Plenum Publishers, New York,pp: 681-695, (2003)
5. Mercer E I, The biosynthesis of Ergosterol, Pesticide Science 15(2): 133–155, (1984)
6. Vyas S C, Handbook of Systemic Fungicides Compounds, Tata McGraw-Hill, (1993) Vol.-2 .
7. Sheldrick G M, SHELXS-97, Program for the solution of crystal structure, (1997).
8. Sheldrick G M, SHELXL-97, Program for crystal structure determination,(1997).

9. Jolmson C K, ORTEP, Report ORNL-3794, Oak Ridge National laboratory, Temessee, U.S.A. (1965).
10. Blow D M, Acta Crystallographica 13(2):168, (1960)
11. Hayes W J, Laws Jr. E R (eds.), Handbook of Pesticide Toxicology- Volume 3, Classes of Pesticides. New York, NY: Academic Press, Inc., 1458, (1991)
12. Brouwer DH et al, Bull Environ Contam Toxicol 58: 976-984, (1997)
13. Hemmen Van JJ et al, Landbouww Med Fac, Univ Gent 57/3b: 1271-1283, (1992)
14. Willoughby O H, Meister Pub Co. p. C 383, Farm Chemicals Handbook (2000).