Comparative X-Ray Structure analysis of systemic fungicides (N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide) AND cis N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide)

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Abstract: There are large numbers of chemicals compounds for the protection of crops, available commercially in the market but their effects dependent on the climate, type of soil, and other physical parameters. The interactions of proposed fungicides with the macromolecule of the parasite are dependent on the stereochemistry of these compounds. In order to design more effective synthetic fungicides, it is necessary to analyze the three dimensional structure of these compounds and if possible the receptor molecule. The structures of these compounds can be obtained by X-ray diffraction method in crystalline form and they will invariably be similar to their structures in solution. The composition of the crystal **(N-(2,6 dim ethyl phenyl)-N-(2-keto-1-methyl butyl) 3- hydroxypropanamide)** is confirmed by comparing the infra-red spectra of the two components. The unit cell parameters are a =7.865(1)Å, b =13.122(2)Å, c =15.130(1)Å, α =90(1)^o, β=101.75(2)^o, γ=90(1)^o. The space group is determined to be $P2_1/c$. The calculated density of the crystal is 1.1919g/cm^3 and measured density is 1.192g/cm^3.All the lengths in the Benzene ring vary from 1.3705(2)Å to 1.4176(1)Å, show a good agreement with their standard value of 1.395Å. The Unit cell parameters of **cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide)** are a=10.5665(7)Å, b=6.6413(3)Å, c=19.3973(12)Å and Z=4. Thus the space group is determined to be $P2_1/c$ and crystal of monoclinic system. We can see that there are some differences in unit cell parameters in both the crystals. We will see how these differences affect the systemic fungicides biological activity. We compare the structures of both the systemic fungicides. [Nature and Science. 2007;5(3):37-43]. (ISSN: 1545-0740).

Keywords: X-ray crystallography, Triagonal Hybridization, systemic fungicides

I. Introduction

FUNGICIDES: Important class of chemicals/ drugs used widely for the protection of crops.

Structure-Activity Relationship

The activity of a drug is intimately related to its chemical structure. Knowledge about the chemical structure of a chemical is useful for:-

1. Synthesis of new compounds with more specific actions and fewer adverse reactions.
   (a) To increase/decrease the duration of action of the original drug or to get a more potent compound.
   (b) To restrict the action to a specific system of the body.
   (c) To reduce the adverse reactions, toxicity and other disadvantages associated.
2. Synthesis of competitive antagonists.
3. Understanding the basic chemical groups responsible for drug action.

Action of Systemic Fungicides

Very little is known about the mechanism of these fungicides. The following are the possibilities:-

1. Inactivation of the enzymes and toxins of the pathogens.
2. Selective accumulation of the fungicide due to greater permeability of the fungus cell wall.
3. Damage to the membranes of the fungal hyphens and inhibition of structures, such as aspersoria, cushion formation emergence of germ tubes and formation of haustoria's.

4. Inhibition of fungal enzymes or their destruction, Systemic fungicides are more specific in their action than non-Systemic fungicides.

II. Experiments

Crystals of **(N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide)** are grown at 4^o-5^o from its solution in Toluene by slow evaporation method Crystallization of **cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide)** is done by slow evaporation from a solution of methyl alcohol at 40°C temp. The crystals found were pale yellow in color and rectangular in shape.. The unit cell parameters are determined directly by automatic computerized 4 - circled Enraf Nonious CAD-4 diffractometer in ω-2θ scan mode.

DATA COLLECTION AND STRUCTURE SOLUTION: The three dimensional intensity data are collected on a computerized automatic 4-circled CAD-4 Enraf-Nonious diffractometer and the crystal structure is solved using the SHELXS-97.

Refinement: The structure determination is carried out on VAX machine using SHELXS-97 program. All the non hydrogen atoms are located in the beginning itself. The co-ordinates thus obtained are fed to SHELXL-97 for refinement. The final R index is 0.045 for all the observed reflection 3849 (including all the unique reflections) for **(N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide).** For **cis N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide)** the R factor dropped to 0.0516 after several cycles of refinement. To reduce R factor to 0.0437, further refinement of the structure was carried out with individuals' anisotropic temperature factors exponent of the form.

$-2Pi\ ^\ 2[h^2a^{*2}U_{11}+----------+2hKa^*b^*U_{12}]$

The hydrogen atoms are fixed by geometrical consideration at this stage, but not included in refinement. Refinement of the structure is terminated after two more cycles when all the shifts in Parameter's become much smaller than the corresponding estimated standard deviations. The final R value is 0.0437 for all the 8018 reflections for **cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide).**

III. Result And Discussion

The ORTEP diagram of **(N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide)** is shown in **fig 1** and the ORTEP diagram of **cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide)** is shown in **fig 2**. Bond length for **(N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide)** is given in **Table 1** and Bond Angles in **Table 2.** Bond length for **cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide)** is given in **Table 3** and Bond Angles in **Table 4. In N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3-hydroxypropanamide)** the geometry around N(1), C(13) and C(10) appears to be normal as all the lengths are close to single bond normal valuesand the angles are according to the configuration. The C-N distances are similar to that observed in structures having triagonal hybridization.The equations for the mean planes were calculated by the method suggested by Blow (1960). All the lengths in the Benzene ring vary from 1.3705(2)Å to 1.4176(1)Å, show a good agreement with their standard value of 1.395Å. The deviations of the inner bond angles in the Benzene ring from 120º are slightly greater than 2σ (=0.7º).The geometry around N(1), C(13) and C(10) appears to be normal as all the lengths are close to single bond normal values and the angles are according to the configuration. The C-N distances are similar to that observed in structures having triagonal hybridization.It is of interest to see in **cis N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide)** the geometry of Phthalimide group. The C (1)-C (2) bond length is much shorter 1.309(4) Å compared to standard values, whereas the largest bond distance is C (5)-C (6) of 1.543(3)Å But as far as bond angles are concerned, they vary from 110.7 (2) ° to 120.2(3) °, thus suggest that the ring is compressed as expected. The five-member ring shows usual behavior. The geometry around S (1), C (10) and C(12) appears to be normal as all the lengths are close to single normal bond values and angles are according to the configuration. The N (8)-S(1)-C(1O) angle of 102.2(9)° shows that the chain is almost right angle to phthalimide group. The angle of twist between phthalimide group and remaining chain N (8)-S (1)-C (10)-C (11) is of -74.9(2) °. The phthalimide

group appears to be planner, as we calculated mean planes using Blow's method. If we look to the angles between different planes, it appears that the molecule is highly twisted and folded.

Table 1. Bond distances in {A} involving non -hydrogen atoms with estimate standard deviations in parentheses

O(1)	- C(10)	1.2191(1)
O(2)	- C(14)	1.1953(2)
O(3)	- C(11)	1.2382(2)
N(1)	- C(1)	1.4429(2)
N(1)	- C(10)	1.3618(1)
N(1)	- C(13)	1.4680(1)
C(1)	- C(2)	1.4056(2)
C(1)	- C(6)	1.4176(1)
C(2)	- C(3)	1.3972(1)
C(2)	- C(8)	1.4987(1)
C(3)	- C(4)	1.3811(2)
C(4)	- C(5)	1.3705(2)
C(5)	- C(6)	1.3900(1)
C(6)	- C(7)	1.4859(2)
C(10)	- C(20)	1.5530(2)
C(11)	- C(20)	1.3919(1)
C(13)	- C(14)	1.5112(2)
C(13)	- C(17)	1.5321(1)
C(14)	- C(15)	1.3435(1)
C(15)	- C(16)	1.4389(2)

Table 2. Bond angles {A} of non-hydrogen atoms with estimated standard deviations in parentheses

C(1)	- N(1)	- C(10)	121.43(1)
C(1)	- N(1)	- C(13)	120.97(1)
C(10)	- N(1)	- C(13)	116.33(2)
N(1)	- C(1)	- C(2)	118.39(1)
C(2)	- C(1)	- C(6)	121.87(1)
N(1)	- C(1)	- C(6)	119.73(2)
C(1)	- C(2)	- C(3)	117.40(2)
C(1)	- C(2)	- C(8)	121.63(2)
C(3)	- C(2)	- C(8)	120.93(2)
C(2)	- C(3)	- C(4)	121.54(2)
C(3)	- C(4)	- C(5)	119.86(1)
C(4)	- C(5)	- C(6)	122.12(2)
C(1)	- C(6)	- C(5)	117.15(1)
C(5)	- C(6)	- C(7)	121.05(1)
C(1)	- C(6)	- C(7)	121.80(1)
O(1)	- C(10)	- N(1)	122.35(1)
O(1)	- C(10)	- C(20)	121.96(2)
C(10)	- N(1)	- C(13)	116.33(1)
O(3)	- C(11)	- C(20)	113.99(2)
N(1)	- C(13)	- C(14)	111.32(1)
C(14)	- C(13)	- C(17)	108.37(1)
N(1)	- C(13)	- C(17)	112.44(2)
N(1)	- C(13)	- C(17)	112.44(1)
O(2)	- C(14)	- C(13)	126.87(1)
C(13)	- C(14)	- C(15)	109.26(1)
C(14)	- C(15)	- C(16)	116.79(2)

C(10) - C(20) - C(11) 112.98(2)

Table 3. bond length [A] with estimated standard deviation in parenthesis for cis N-(1, 1 ,2,2-tetrachloroethylthio)-4-cyclohexene-1 ,2-dicarboximide

S (1) - N (8)	1.6854 (17)
S (1) - C (10)	1.820 (2)
C1 (1) -C (10)	1.773 (2)
C1 (2) - C (10)	1.767 (2)
C1 (3) - C (11)	1.764 (2)
C1 (4) - C (11)	1.768 (2)
C (1) - C (2)	1.309 (4)
C (1) - C (6)	1.491 (4)
C (3) - C (4)	1.534 (3)
C (4) - C (9)	1.502 (3)
C (4) - C (5)	1.533 (3)
C (5) -C (7)	1.517 (3)
C (5) -C (6)	1.543 (3)
C (7) - O (13)	1.196 (3)
C (7) - N (8)	1.414 (3)
N (8) -C (9)	1.400 (3)
C (9) -C (12)	1.203 (3)
C (10) - C (11)	1.537 (3)

Table 4. Bond Angle [Degree] with estimated standard deviation in parenthesis

N (8) -S (1) - C (10)	102.23 (9)
C (2) -C (1) -C (6)	120.2 (2)
C (2) -C (1) -H (1)`	119.9
C (6) - C (1) - H (1)	119.9
C (6) -C (1) - C (3)	120.1 (2)
C (1) - C (2) - H (2)	120.0
C (1) - C (2) - H (2)	120.0
C (2) - C (3) -C (4)	110.7 (2)
C (2) - C (3) - H (3A)	109.5
C (4) - C (3) -H (3A)	109.5
C (2) - C (3) -H (3B)	109.5
C (4) - C (3) -H (3B)	109.5
H (3A) -C (3) - H (3B)	108.1
C (9) - C (4) - C (5)	105.33 (16)
C (9) - C (4) - C (3)	109.33 (18)
C (5) -C (4) - C (3)	114.73 (18)
C (9) - C (4) -H (4)	109.0
C (5) - C (4) -H (4)	109.0
C (3) -C (4) - H (4)	109.0
C (7) -C (5) - C (4)	105.50 (16)
C (7) -C (5) -C (6)	110.37 (19)
C (4) -C (5) -C (6)	114.00 (19)
C (7) -C (5) -H (5)	108.9
C (4) -C (5) -H (5)	108.9
C (6) -C (5) -H (5)	108.9
C (1) -C (6) -C (5)	111.56 (19)
C (1) -C (6) -H (6A)	109.3
C (5) -C (6) -H (6A)	109.3

C (1) -C (6) -H (6B)	109.3
C (5) -C (6) -H (6B)	109.3
H (6A) -C(6) -H (6B)	108.0
O (13) -C (7) -N (8)	124.32 (19)
O (13) -C (7) -C (5)	127.97 (19)
N (8) -C (7) -C (5)	107.71 (17)
C (9) -N (8) -C (7)	112.26 (17)
C (9) -N (8) -S (1)	123.74 (14)
C (7) -N (8) -S (1)	122.99 (14)
O (12) -C (9) -N (8)	123.40 (19)
O (12) -C (9) -C (4)	127.6 (2)
N (8) -C (9) -C (4)	108.95 (17)
C (11) -C (10) - C1(2)	109.07 (15)
C (11) -C (10) - C1(1)	110.81 (15)
C1 (2) -C (10) - C1 (1)	109.99 (12)
C (11) -C (10) -S (1)	113.91 (15)
C1 (2) - C (10) -S (1)	110.64 (11)
C (1) -C (10) -S (1)	102.26 (11)
C (10) -C (11) -C1 (3)	111.09 (16)
C (10) -C (11) -C1 (4)	111.84 (16)
C1 (3) -C (11) -C1 (4)	109.11 (13)

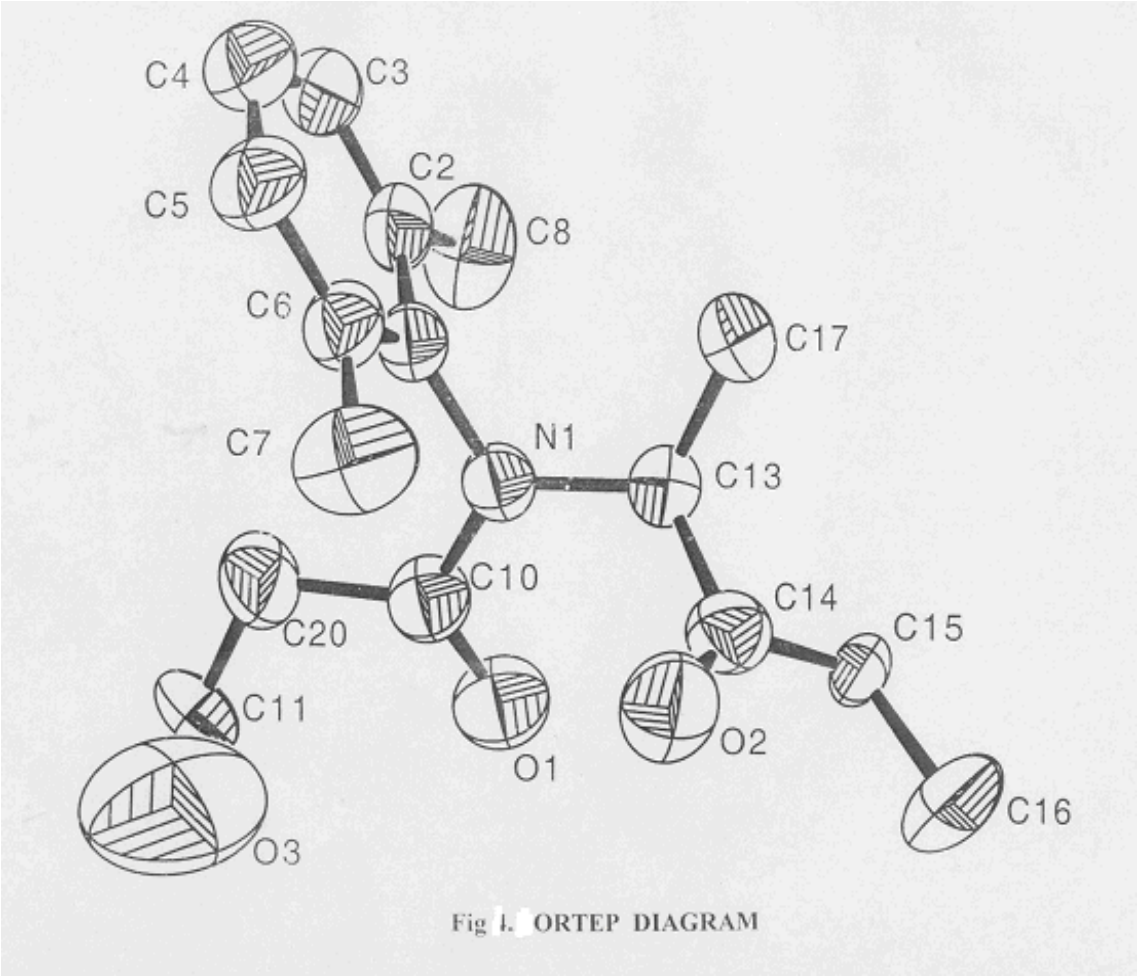

Fig 1. ORTEP DIAGRAM

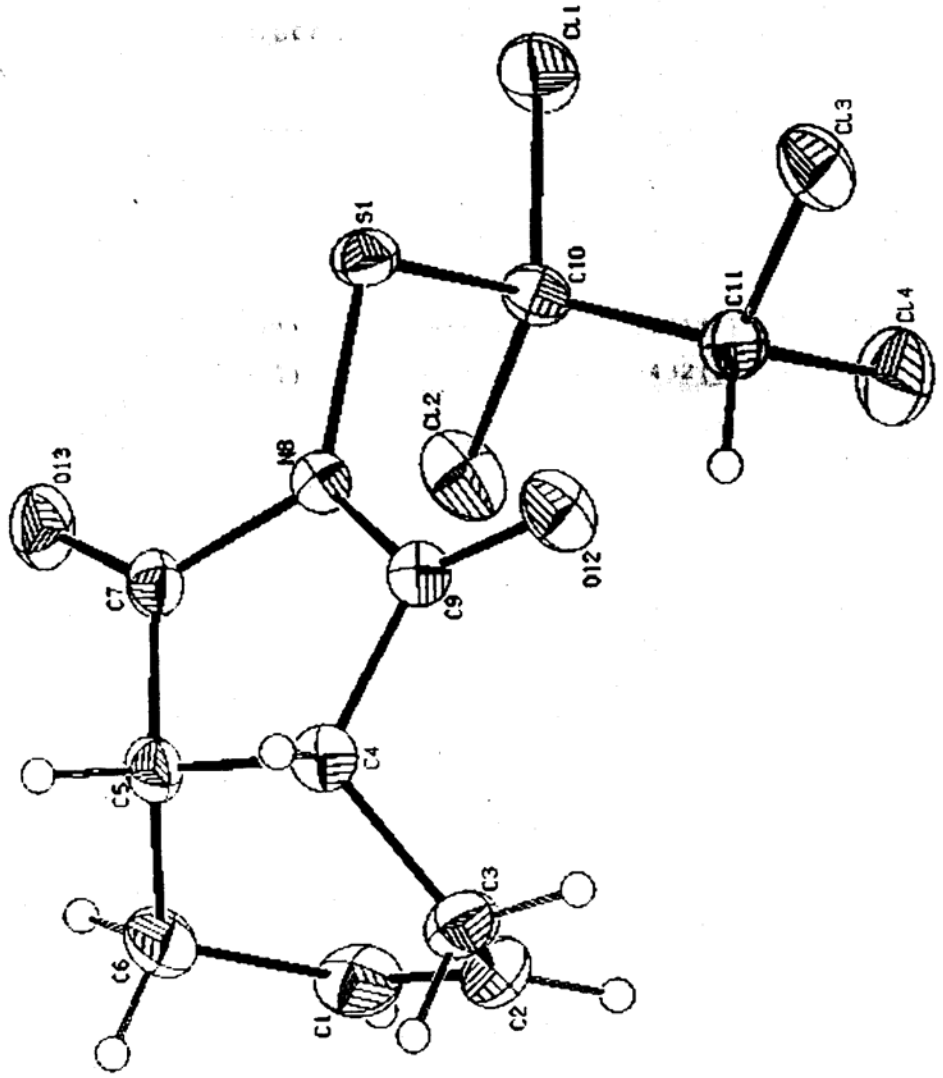

Fig. 2: ORTEP for cis-N-(1,1,2,2-tetrachloroethylthio)-4-cyclohexene-1,2-dicarboximide

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