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X-Ray Crystallographic Studies On Systemic Fungicide (N-(2,6 Dimethyl Phenyl)-N-(2-Keto-1-Methyl Butyl) 3-Droxypropanamide)

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ABSTRACT

In recent part it has been observed that some of these fungicides are loosing their effects and becoming resistant to them. Analogous compounds can be designed as 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 as well as their molecular complex 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. Crystal and molecular structure of (N-(2,6 dimethyl phenyl)-N-(2-keto-1-methyl butyl) 3- hydroxypropanamide). The composition of these crystals are confirmed by comparing the infra-red spectra of the two components. The unit cell parameters were determined by directly automatic computerised 4-circled Enraf Nonious CAD-4 Diffractometer in the ω-2θ scan mode using graphite filtered Mok α radiation.These data showed 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 was determined to be P21/c. The density of the crystal was measured by floatation method in the mixture of benzene and carbontetrachloride at room temp.Its calculated density is 1.1919g/cm3 and measured density is 1.192g/cm3.All the lengths in the Benzene ring vary from 1.3705(2)Å to 1.4176(1)Å, show a good greement with their standard value of 1.395Å. The deviations of the inner bond angles in the Benzene ring from 120^0 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.

KEYWORDS X-ray crystallography; Systemic fungicides; Triazole structure.

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INTRODUCTION

The word fungicide has originated from two Latin words: namely, fungus and Caedo. The word Caedo means 'to kill'. Thus literally speaking a fungicide would be any agency which has the ability to kill a fungus. Some chemicals do not kill fungi but they inhibit fungus growth temporarily. If the fungus is freed from such substances, it would revive. Such a chemical is called a 'fungistat' and the phenomenon of temporarily inhibiting the growth is called 'fungistasis'. Even though fungistats do not 'kill' fungi, they are broadly termed as fungicide. Normally the word fungicide is defined as a chemical substance which can prevent damage caused to plants and their product by a fungi. There are large numbers of chemicals compounds for theprotection 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. (N-(2,6 dimethylphenyl)-N-(2-keto-1-methyl butyl)-3-hydroxypropanamide) is the systemic fungicide having molecular weight 274.33. It is a colorless crystalline compound melting at 78^0 to 80^0C, it is 37ppm soluble in water. it is readily soluble in most organic solvents except saturated hydrocarbons such as hexane. It is stable in acid and neutral media. It may be stored at below 30ºC and away from fire and spark. In sealed containing at low temp., it is stable for at least two years.

EXPERIMENTAL

$C_{16}H_{20}NO_3$ sample obtained from CIBA-geigy limited agro division research and development CH4002 basle Switzerland. After several failures to grow the crystal at room temp(>300^0K), it could be grown at 4^0-5^0 from its solution in toluene by slow evaporation method. The unit cell parameters were determined by directly automatic computerized 4-circled Enraf Nonious CAD-4 diffractometer in the ω-2θ scan mode using graphite filtered Moka radiation these data showed a=7.865(1)Å, b=13.122(2)Å, C=15.130(1)Å, α=90(1)^0, β=101.75(2)^0, γ=90(1)^0. The space group was determined to be P21/c. The density of the crystal was measured by floatation

TABLE 1: Preliminary crystal data

Chemical name	[N-(2,6dimethylphenyl)-N-(2-keto-1- methylbutyl)-3-hydroxypropanamide]
Chemical formula	C_{16} H_{20} NO_3
System	Monoclinic
Space group	$P2_1/c$
A	7.865(1)Å
B	13.122(2)Å
C	15.130(1)Å
α	90 (1)^0
β	101.75(2)^0
γ	90(1)^0
V	1528.8 cubic Å
Dm	1.1929g/cm^3
Dc	1.1919g/cm^3
Mw	274.33
Mode of data collection	CAD-4 Enraf-Nonius 4-circled automatic
Structure refinement	SHELXL-97
Intensity reflection	459 532 0110
Mode of data collection	ω-2θ
λ(MoKα)	71073Å
No. of reflections measured	3849
No. of Unique reflections	2478
Temp. of crystal during data collection	293^{0}K
Theta range	1-73^0
Absorption coefficient	0.082 mm^{-1}
Symmetry element	X, Y, Z
	-X, 1/2+Y, 1/2-Z
	-X, -Y, -Z
	X, -1/2-Y, -1/2+Z
Lp correction	Applied
Absorption correction	Nor applied

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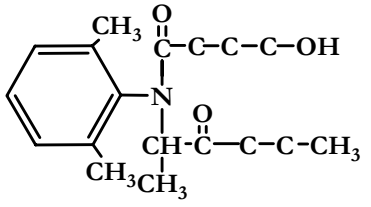

N-(2,6dimethylphenyl)-N-(2-keto-1-methylbutyl)-3-hydroxypropanamide

Figure 4.1

method in the mixture of benzene and carbon tetrachloride at room temp. its calculated density is 1.1919g/cm^3 and measured density is 1.192g/cm^3. The preliminary information about the crystal is given in TABLE 1. Chemical structure of N-(2,6-dimethylphenyl)-N-(2-keto-1-methylbutyl)3-hydroxypropanamide is given in figure 4.1

Data collection and structure solution

The three dimensional intensity data were collected on a computerized automatic 4 circled CAD-4 Enraf Nonious diffractometer using graphite filtered Mokα(0.71073Å) radiation at deptt. of biophysics, AIIMS New Delhi. The present data were corrected for Lorentz and polarisation effects but no absorption correction is applied. The total number of reflections were 3849. The observed reflections corresponding to the intensity limit I.2σ were 2478.Three reflections (4,5,9),(5,3,2),(0,1,10) were selected for intensity reflections.In the present case the values of hkl were varied from -10 to 10 ,-16 to17 and-17 to19 respectively. The structure was solved using the SHELXS-97 Program.

Refinement

The structure determination was carried out on VAX machine using SHELXS-97 program. All the non hydrogen atoms are located in the beginning itself. The coordinates thus obtained are fed to SHELXL-97 for refinement. The final R index was 0.045 for all the observed reflection 3849(including all the unique reflections). The final positional and isotropic thermal parameters are given in TABLE 2

RESULT AND DISCUSSION

The perspective view of the molecule and numbering scheme are shown in figure 4.2. The ORTEP diagram is shown in figure 4.3. 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 120^0 are slightly greater than 2σ(=0.7^0). Bond length of non-hydrogen atoms is shown in TABLE 4. Bond angles{A} of non-hydrogen atoms is shown in TABLE 5.

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 interesting to note that the torsion angles C(1)-N(1)-C(13)-C(14), C(20)-C(10)-N(1)-C(13) and N(1)-C(13)-C(14)- C(15) are 130.21(1)^0,-171.91(2)^0 and 151.74(1)^0, respectively. The appear-

TABLE 2: Atomic coordinates of non hydrogen atoms and the equivalent isotropic thermal parameters with estimated standard deviationin parentheses

Atoms	x	y	z	Ueq.(A)^2
O(1)	0.47814(2)	0.22713(1)	0.23053(2)	0.07621(1)
O(2)	0.35378(1)	0.23229(2)	0.41337(1)	0.07944(2)
O(3)	0.20904(2)	0.06656(1)	0.11325(2)	0.22132(2)
N(1)	0.27484(1)	0.34325(1)	0.24784(1)	0.04660(1)
C(1)	0.11722(2)	0.39680(2)	0.20874(2)	0.04694(2)
C(2)	0.12763(2)	0.47877(1)	0.15027(2)	0.05672(1)
C(3)	-0.02609(1)	0.53069(2)	0.11451(2)	0.07352(1)
C(4)	-0.18340(2)	0.50088(2)	0.13327(2)	0.07949(2)
C(5)	-0.19077(2)	0.41863(1)	0.18819(2)	0.06976(1)
C(6)	-0.04306(1)	0.36488(2)	0.22863(1)	0.05552(1)
C(7)	-0.05419(2)	0.27726(2)	0.28940(1)	0.08381(2)
C(8)	0.29751(2)	0.51231(1)	0.12965(2)	0.08441(2)
C(10)	0.33650(1)	0.26606(1)	0.20304(1)	0.05710(2)
C(11)	0.26650(2)	0.14178(1)	0.07950(2)	0.05521(1)
C(13)	0.39416(2)	0.38337(1)	0.32767(2)	0.05230(2)
C(14)	0.44163(1)	0.30252(2)	0.39960(2)	0.05462(1)
C(15)	0.60014(2)	0.32255(1)	0.44918(2)	0.04048(2)
C(16)	0.65889(2)	0.25916(1)	0.52701(1)	0.08381(1)
C(17)	0.31834(1)	0.47496(2)	0.36919(2)	0.01202(1)
C(20)	0.21896(1)	0.23465(2)	0.23465(2)	0.01465(2)

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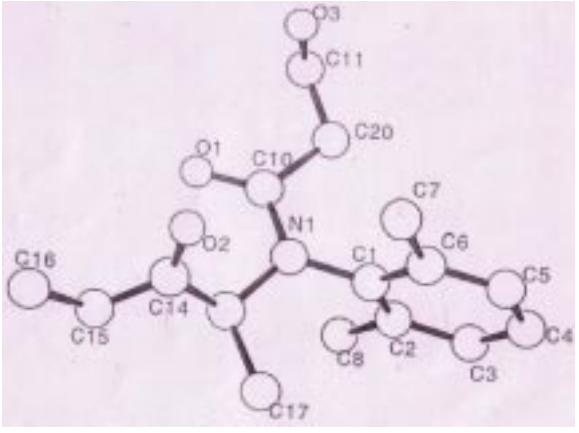

Figure 4.2: The perspective view and numbering scheme of N-(2,6 dimethylphenyl)-N-(2-keto-1-methylbutyl)-3-hydroxypropanamide

TABLE 4: 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)

ance of C(7)-C(6)-C(1)-N(1) and C(8)-C(2)-C(1)-N(1), torsional angles, the dispositions of two methyl group is symmetrical. The benzene ring, the planes O(2)-C(14)-C(15)-C(16) and C(11)-C(20)-C(10)-N(1) are essentially planar within the errors of estimation. The molecule appears to be highly twisted and folded with respect to the angles between different planes.

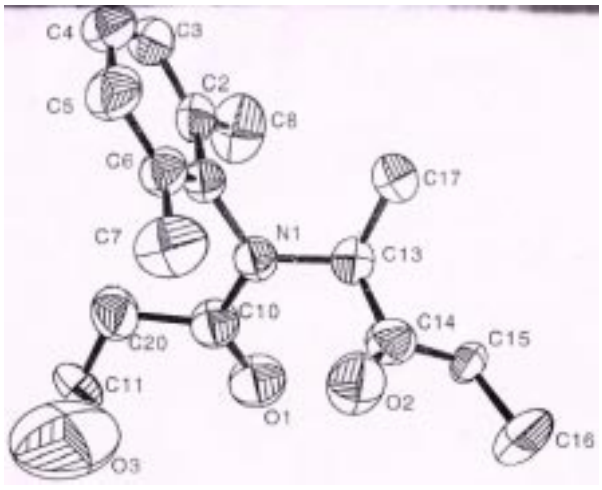

Figure 4.3: ORTEP diagram

TABLE 5: 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)
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)

Hydrogen bonding and molecular packing

Some non-bonded contacts are listed in TABLE 3. The packing diagram is shown in figure 4.4. The

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TABLE 3: Non bonded contacts

C(4)	-H(4A).O(2b)	0.960(1)	2.617(2)	3.336(1)	131.95(2)
C(11)	H(11A).O(2a)	0.960(2)	2.531(2)	3.196(1)	126.39(1)
C(20)	H(20A).O(2b)	0.960(1)	2.752(2)	3.409(1)	126.27(2)

Symmetry codes: [a]=x,1/2-y,-1/2+z, [b]=-x,1/2+y,1/2-z

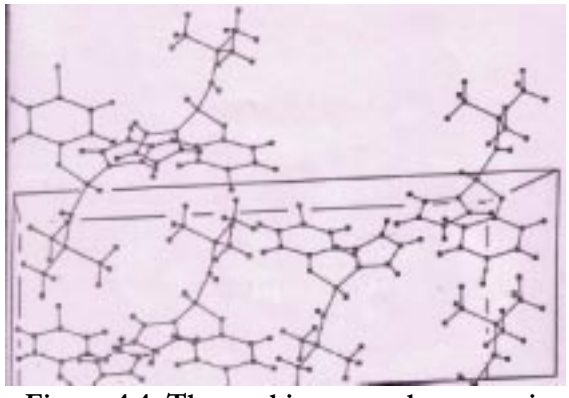

Figure 4.4: The packing seen down a-axis

molecules are stacked along a-axis and held firmly through some non-bonded contacts. No hydrogen bond is found to exist. The non-polar groups are stacked in such a way that they also generate significant van der wall's interaction between them.

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