

# Comparative X-ray crystallographic study on Triazoles systemic fungicides

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**Abstract:** Triazoles compounds contain a ring composed of two carbon atoms and three nitrogen atoms. A systemic fungicide, RH-124(4-n-butyl-1, 2, 4-triazole, BT), has been introduced as an experimental fungicide, possessing high selective activity against brown rust of wheat. However, substitution on nitrogen atom in position 1 in the triazoles producing an amazing variety of compounds such as triadimefon, triadimenol, and biloxazol, have been discovered, which are known inhibitors of fungal sterol biosynthesis. These compounds possess a trityl carbon that can act as a carbonium ion, an organic ion carrying a positive at a carbon location. Tridimefon is volatile and reduced within plants to form tridimenol. While both forms are fungitoxic, the fungitoxicity of triadimefon depends on the rate at which fungi formed triadimenol which is active principle of fungitoxicity. Tricyclazole has excellent systemic properties in rice and is highly effective in field, but requires high concentration of fungicide to inhibit growth in **vitro of Pyricularia oryzae**. The activity of fungicides is intimately related to its chemical structure. Knowledge about the chemical structure of a chemical 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 to get a more potent compound, to restrict the action to a specific system of the body and to reduce the adverse reactions, toxicity and other disadvantages associated. We can understand the basic chemical groups responsible for drug action<sup>1</sup>.

Recently it has been observed that some of the fungicides are losing their effects. So 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.

**Keywords**-X-ray crystallography, Systemic fungicides, Triazole structure X-Ray diffraction

## Introduction:

A systemic fungicide is defined as systemic fungi toxic compound that controls a fungus pathogen remote from the point of application and that can be detected or identified<sup>2</sup>. These compounds are absorbed by the plant and get translocated within it, thus providing protection as well as eradicating already established infection. Tricyclazole (TCE), a new systemic fungicide for the control of blast of rice (*Pyricularia oryzae*) is being developed under Code number EL-291(BEAM) by research and development division of Eli-Lilly & Co., Greenfield, Indiana, USA. Result from greenhouse and field studies show that TCE is readily absorbed by roots and translocated to leaves and provides residual disease control after a single soil or foliar application.

The antifungal compounds belonging to the N- substituted triazole. Here we will compare three Triazole Tridimenol, Tridimefon and Tricyclazole.

## Experimental:

First grow the crystals of existing fungicides available and synthesize their derivatives in lab. 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. In parallel with these structural studies, spectroscopic studies carried out on them. 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. 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.. The density of crystal is measured by floatation method with the mixture of benzene and Bromoform. . The unit cell parameters are determined by directly on CAD-4 Enraf Nonius 4-circle automatic Diffractometer

**Data collection and Structure Solution:** The intensity data are collected on a computerized automatic CAD-4 Enraf Nonius 4-circled Diffractometer . The data collection is

done on  $\omega$ -2 $\theta$  scan mode. The structure determination is carried out on VAX machine using SHELXS-97<sup>3</sup>. All the non-hydrogen atoms are located in the beginning itself.

**Refinement:** The positional co-ordinates, which were obtained from SHELXS 97 and isotropic temperature factors, were subjected to refinement by SHELXL<sup>4</sup> refinement program. Further refinement of the structure was carried out with individuals an isotropic temperature factor of the exponential form.

$$-2P_1^{\frac{1}{2}}[h^2a^*^2U_{11} + \dots + 2hKa^*bxU_{12}]$$

reduced R factor. The hydrogen atoms are fixed at this stage by geometrical considerations and are not refined. Refinement of the structure was terminated after two more cycles when all the deviations in parameters became much smaller than the corresponding estimated standard derivations.

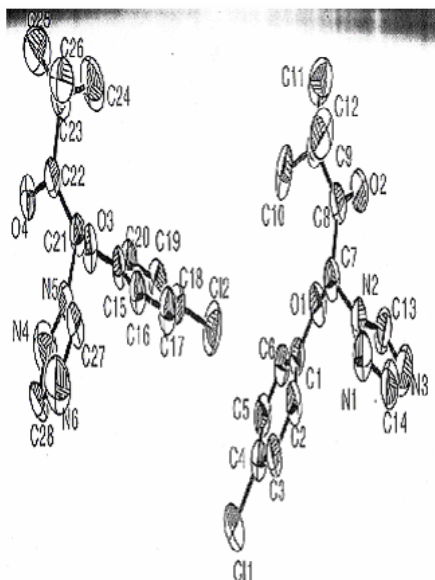


Figure 1. ORTEP Diagram of Tridimenol

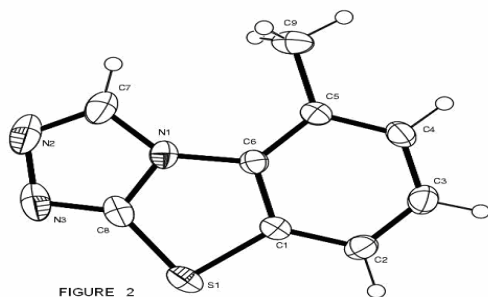


FIGURE 2  
ORTEP Diagram of Tricyclazole

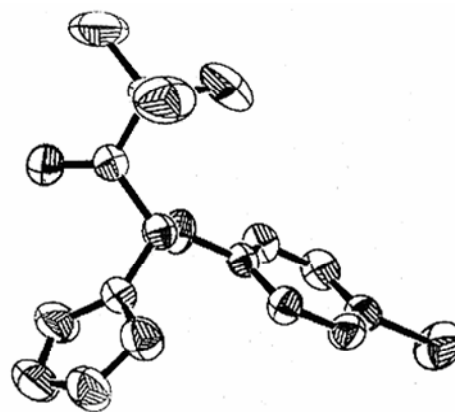


Fig 3 ORTEP diagram of tridimefon

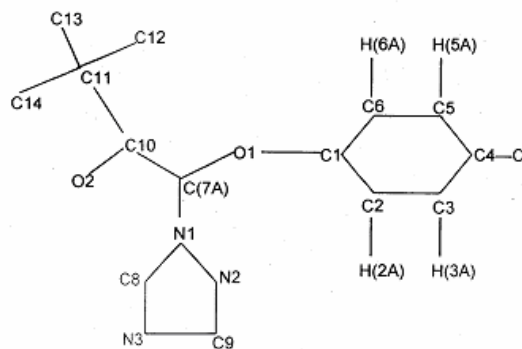


fig.4 : Molecular Numbering Scheme of Triadimefon

## Results and Discussion:

The ORTEP<sup>5</sup> diagrams of Tridimenol, Tricyclazole and Tridimefon is shown in fig.1 fig2 , fig 3 and 4. When we

compare the structure of Tridimenol, Tricyclazole and Tridimefon. We can see that in **TRIDIMENOL** the average bond distances of C-H and N-H types are 0.96(2)Å and 0.90(1)Å respectively. The bond lengths and angles in the benzene rings show regular features in all the molecules. The C(4)-Cl(1) and Cl(2)-C(18) distances are 1.748(1)Å and 1.747(2)Å. The whole molecules appeared to be twisted and folded and reason may be due to stacking constraints. The bond distances around C(7) and C(21) are as usual shorter than single bond values<sup>10</sup>. They may also appear to bear a partial double bond character. The C(7)-O(1) and C(21)-O(3) distances are 1.4028(1)Å and 1.4114(2)Å respectively. These distances do not change significantly in similar structures, despite variable intermolecular interactions through them. The bond distances in the five member rings are comparable to corresponding distances in heterocyclic rings 1.339(Å)<sup>11</sup>. In **TRIDIMEFON** The average bond distance of C-H is 0.96(2)Å. The bond lengths and angles in the benzene ring show regular features in both the molecules. The Cl(1A)-C(4A) and Cl(1B)-C(4B) distances are 1.733Å and 1.738Å comparable to other structure. These distances are short and this may be due to delocalization of electrons from the benzene rings. The whole molecules appeared to be twisted and folded and reason may be stacking - constraint. The bond distances around C(7A) and C(7B) are usual shorter than single bond values. They may also appear to bear a partial double bond character. The O(1A)-C(7A) and O(2B)-C(7B) distances are 1.423(2) Å and 1.411(2) Å respectively. These distances do not change significantly in similar structures, despite variable intermolecular interactions through them. The bond distances in the triazolyl rings are comparable to corresponding distances in heterocyclic rings 1.339 (Å).

The molecule is found to adopt a conformation such that the triazolyl ring is inclined angle of 72.9(9)° to the aromatic ring and at an angle of 61.5(9)° to O(1A), C(7A) grouping. The resulting arrangement lead approach of the ortho-H, H(2A) to the triazolyl, atoms N(1A) and N(2A) such that both N-H distances lie within the Sum of the Vander Walls radii of N and H. There is an accompanying distortion of the exocyclic angles at C(1A) with the C(2A)-C(1A)-O(1A) angle of 124.65(17)° being considerably larger than the value found for O(1A)-C(1A)-C(6A) is 114.97(17)°.

The triazolyl ring is planar with C(7A) lying only 0.063(7)Å from the mean plane. Although the C(8A) and C(9A)-N(3A) distance is somewhat larger than C(8A)-N(3A) and C(9A)-N(2A), in keeping with the uncharged canonical valence form. All four C-N distances are shorter than a normal single bond (1.47Å). The N(1A)-N(2A) bond is also shorter than a normal single bond (1.45Å). The three atoms bonded to N(1) are almost coplanar with it. Taken together these data indicate extensive delocalization within the heterocyclic ring. The most noteworthy feature of the heterocyclic ring is the asymmetry of the exocyclic angles at N(1A) [130.80°]. We have observed a similar pattern in related triazole systems and it appears to be a function of a

triazolyl ring itself rather than the influence of any inter or intramolecular interactions.

The C(11A), C(10A), C(7A), O(1A), C(1A) backbone is rather compressed resulting in the main from the orientation of the tert-butyl group, the C(1A)-C(10A)-C(7A)-O(1A) torsion being only 99.17(19)°.

From the least square plane equation by Blow's method, the benzene and triazolyl rings are partially planar since the atomic displacements are much less than their e.s.d.s. The triazolyl ring is inclined to the aromatic ring at an angle of 72.9(9)°.

In **TRICYCLAZOLE** the average bond distances of C-H is 0.96(2)Å. The bond distances of C(7)-N(1) is 1.368Å, C(8)-N(1) is 1.360 Å. The bond distances of N(2)-N(3) is 1.396Å, C(8)-S(1) is 1.7316Å. The triazol ring is distorted in shape<sup>7</sup>. The average bond distances for C-N and N-N bonds are 1.354Å and 1.396Å. The bond lengths and angles in the benzene ring show regular features in the molecule. C-C distances are short and shortening may be due to delocalization of electrons from the benzene rings<sup>8</sup>. The whole molecules appeared to be twisted and folded and reason may be due to stacking constraints<sup>9</sup>. The average value of bond lengths and angles in the rings derived from most reliable set of data by Spencer<sup>10</sup> are 1.377Å and 119°, respectively. The variations observed are within the limit of estimation errors. The dimensions of the methyl groups are normal and comparable with those in 0-methyl obtusaquinone and moscaline hydrobromide<sup>11</sup>. The average bond angle around C(9) is 109.5°. The molecule is found to adopt a conformation such that the triazol ring is inclined angle of 72.9(9)° to the aromatic ring<sup>12</sup>. The resulting arrangement lead approach of the ortho-H, H(2A) to the triazol, atoms N(1) and N(2) such that both N-H distances lie within the Sum of the Vander Walls radii of N and H<sup>13</sup>. The equations of the Least squares planes, calculated using Blow method and the displacements of the relevant atoms from the mean planes for different planar groups together with the respective<sup>14</sup>

The triazol ring is planar with C(7) lying only 0.063(7)Å from the mean plane. All four C-N distances are shorter than a normal single bond (1.47Å). The N(1)-N(2) bond is also shorter than a normal single bond (1.45Å). The three atoms bonded to N(1) are almost coplanar with it. Taken together these data indicate extensive delocalization within the heterocyclic ring. The most noteworthy feature of the heterocyclic ring is the asymmetry of the exocyclic angles at N(1A) [130.80°]. We have observed a similar pattern in related triazole systems and it appears to be a function of a triazolyl ring itself rather than the influence of any inter or intramolecular interactions. The torsion angles of C(6)-C(1)-C(2)-C(3) is -0.9(3)°. The torsion angles of S(1)-C(1)-C(2)-C(3) is 179.43(15)° and C(3)-C(4)-C(5)-C(9) is 179.49(19)° show that this ring is almost symmetric. It is interesting to note that when there are minor differences in the cell parameters and growth conditions in the two independent studies, the molecular geometry, overall dimensions, crystal packing are almost same under the error limits whatever

small differences are there, they are not really significant, which suggest that the molecular parameters remain unchanged even there is a change in growth condition the crystal forces, therefore, they don't alter the molecular geometry. 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.

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