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# SYNTHESIS, SPECTROSCOPIC STUDIES, AND CRYSTAL STRUCTURE OF 3-(1-HYDROXYIMINOETHYL)-1-PHENYL-4-HYDRO-1,2,4-TRIAZINE-5,6-DIONE METHANOL SOLVATE

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Abstract- 3-(1-Hydroxyiminoethyl)-1-phenyl-4-hydro-1,2,4-triazin-5,6-dione, has been prepared from the chiral 1-phenyl-3-acetyloxime-5-benzyl-4,5-dihydro-1,2,4-triazin-6-one in the presence of organotin(IV) compounds in methanol solution. It crystallizes as a 1:1 methanol solvate in the monoclinic space group P $2_1/c$ with the lattice parameters: a = 1517.6(1), b = 563.64(3), c=1500.34(13) pm and β = 90.35(1)°. The molecules, in which the heterocyclic ring is planar, are dimer *via* strong oxime-methanol and methanol-dione hydrogen bonds and by additional N—H---O bridges linking the heterocyclic rings.

## INTRODUCTION

The chiral compound 1-phenyl-3-acetyloxime-5-benzyl-4,5-dihydro-1,2,4-triazin-6-one (**1**), which is the precursor of the title compound (**2**), was originally prepared as a potential bidentate Schiff-base ligand, by reacting available α-aminoacid esters with hydrazonoyl chlorides, followed by oximation of the C3 acetyl group.[1,2] Thus the nature of the substituent at C5 is dependent on the type of the α-aminoacid ester used.[2] The coordination chemistry of the ligand system exemplified by **1** with transition metals has been investigated and interesting results have been reported.[2-5] Because of the importance of organotin(IV) complexes with Schiff-bases as models in biological studies,[6,7] we decided to explore the behaviour of ligand **(1)** with organotin(IV) compounds. It was rather unexpected to find that ligand **(1)** did not coordinate to tin but instead organotin(IV) compounds appear to play a catalytic role in its oxidation to

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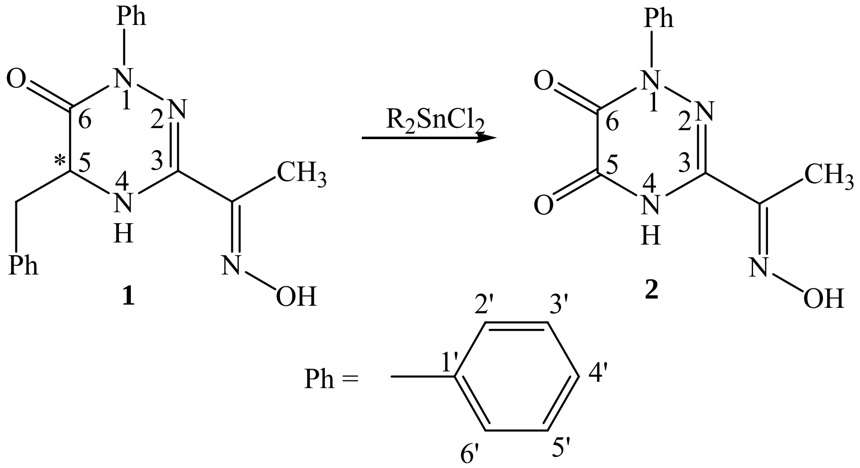
the analogous triazine-5,6-dione derivative **(2)** (Scheme I). We, therefore, report here the synthesis and structural characterization of the new dione **(2)**. It is worthnoting that some structurally similar triazine-5,6-diones possess biological activities e.g. as crop protection agents.[8]

**Scheme I**



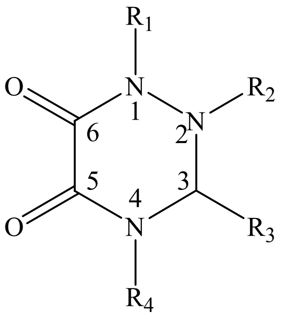
## RESULTS AND DISCUSSION

The aim of this work was to explore the behaviour of the oxime ligand system (exemplified by **1**, Scheme I) with organotin(IV) compounds such as $R_2SnCl_2$(R=Me, Et, Ph) in order to study the structural aspects of the resulting organotin(IV) complexes. The first attempts were based on the direct interaction between the reactants in methanol at various reaction conditions. No product could be isolated despite extensive variations of the reaction conditions such as mole ratios and reflux time. When the reaction mixture was refluxed for about four days, the dione **(2)** was obtained as yellowish needle-like crystals. Further experiments were performed to verify the effect of changing the substituent at C5 (in **1**) or the organotin(IV) compound and in all cases no effect was observed, always the dione **(2)** was obtained. Furthermore, refluxing the ligand **(1)** in methanol for four days or exposing it to the atmosphere does not change its identity, and so Scheme I represents a direct and simple route for obtaining the dione **(2)**.

Further attempts to make the ligand **(1)** react with organotin(IV) compounds were based on the use of a deprotonating agent (base) mixed with the ligand solution prior to the addition of the organotin(IV) compound. These attempts always resulted in the formation of unidentifiable and insoluble white materials.

Relatively few 1,2,4-triazin-5,6- dione derivatives are known in the literature and some of them possess biological activities. Therefore, we thought that it will be useful to review these derivatives structurally (as in Scheme II).[8-16] It is worth noting that the dione (**3.9**, Scheme II), which is closely related to our dione **(2)**, has been prepared from the parent 1-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6-one *via* aerial oxidation.[8] Since this dione (**3.9**) was found to function as a crop protection agent, an effort was made to prepare it *via* independent synthetic routes. This effort was not successful and the facile aerial oxidation of 1-methyl-3-phenyl-4,5-dihydro-1,2,4-triazin-6-one to the dione **(3.9)** was attributed to the lack of a blocking substituent at C5.[8] In fact one of the parent compounds of our dione **(2)** contains no substituents at C5 and no aerial oxidation was observed.[1,17]

**Scheme II**



**3**

| | **$R_1$** | **$R_2$** | **$R_3$** | **$R_4$** | **Ref.** |
|---|---|---|---|---|---|
| **3.1** | H | H | H | - | 9 |
| **3.2** | H | - | 2-Py | H | 10 |
| **3.3** | H | - | $CH_3$ | $NH_2$ | 11 |
| **3.4** | H | - | $SCH_3$ | $NH_2$ | 12 |
| **3.5** | H | H | Ph, 2-Py | - | 13 |
| **3.6** | H | $CH_3$ | 4-$CH_3$Ph | - | 14 |
| **3.7** | 4-$NO_2$Ph | H | Ph | - | 15 |
| **3.8** | 2-$NO_2$Ph | - | COOEt | H | 16 |
| **3.9** | $CH_3$ | - | Ph | H | 8 |
| **2** | Ph | - | $CCH_3$(NOH) | H | this work |

## X-RAY STRUCTURAL RESULTS

Figure 1 shows the molecule with its heterocyclic triazine-dione ring and the phenyl and acetyloxime substituents. A few compounds with analogous heterocyclic dione rings have been reported.[18-21] Most of them are planar as expected from a combination of sp$^2$ ring atoms, suggesting occupied $p_z$ orbitals at the nitrogen atoms N(1) and N(4); one[21] has a boat configuration with significantly higher sums of bond lengths and bond angles. A comparison of bond features in **2 (**Table.1**)** shows a consistent array of atomic distances: the short C-O bonds of equal length are very slightly longer than predicted for pure double bonds due to hydrogen bonding (see below). C(5)-C(6) corresponds with a single bond in a planar ring[22] whereas the adjacent C-N bonds, lying in the range of 135 to 136 pm, can be regarded as C(sp$^2$)-N(sp$^2$) bonds with low double bond character.[23] This is supported by the fact that reduction of the π-bond character of a C-O group[20] shortens the neighbouring C-N bond by increased overlap of the occupied $p_z$ orbital at the nitrogen atom. Most reports agree about a value of 138 pm to 139 pm for a N-N single bond in the plane of a heterocycle[24] – the value for a nonplanar case is 142 pm.[21] The only bond in the ring system, which has appreciable double bond character is C(3)-N(2). Being 129 pm of length it is significantly shorter than similar bonds in comparable compounds. This is found in an analogous way in a series of oximes where the acetyloxime group is connected to the carbon atom of a N=C-N moiety.[25,26] The values of 148 pm for C(3)-C(4), 128 pm for C(4)-N(5), and 139 pm for N(5)-O(3) match well with the data retrieved from literature.

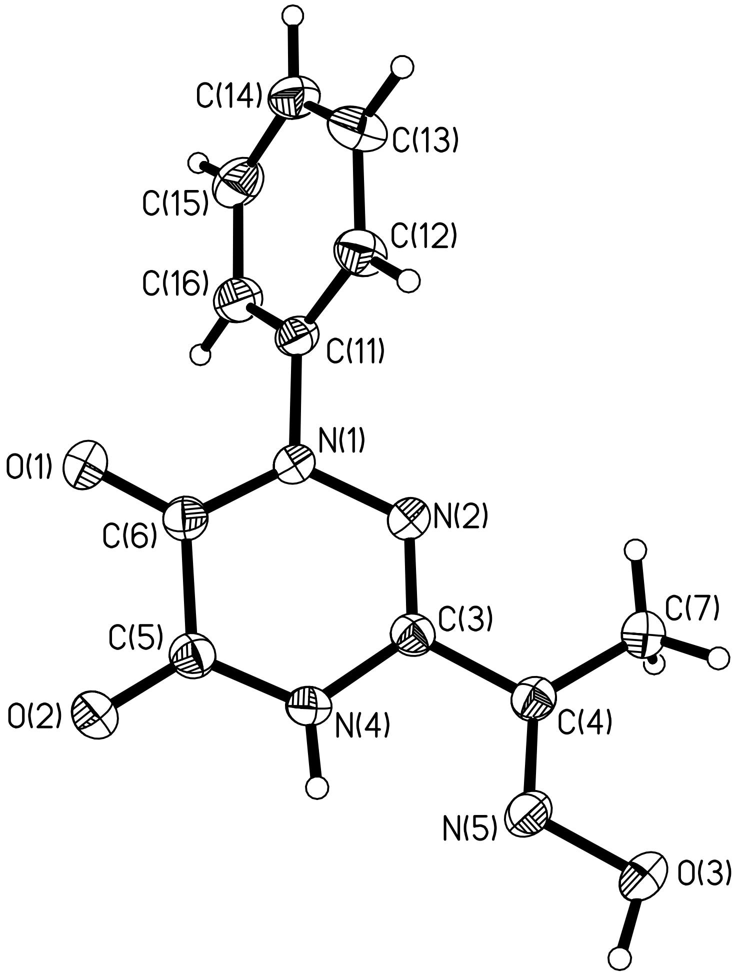


**Figure 1.** Perspective drawing of **2** without the solvate molecules. The numbering scheme is given. Atoms are represented as thermal ellipsoids on the 50% probability level.

Bond angles within the ring system are determined by the distribution of external π-bonds and lone σ electron pairs at ring atoms. Both factors, which are found at C(5), C(6), and N(2) sharpen the opposing angles below 120°, all other ring angles are wider than the regular $sp^2$ angle.

In the crystal **(2)** occurs as 1:1 methanol solvate. From Figure 2 it is to be seen that the molecules of **2** dimerize by strong hydrogen bonds oxime-methanol (O(4)---H(2) 180 pm) and a weaker bifurcating bridge methanol-dione (O(1)---H(3) 217 pm and O(2)---H(3) 236 pm). Additionally the triazine rings are linked by the hydrogen bonds O(2)---H(1) (206 pm). As a consequence of symmetry the almost coplanar heterocyclic rings are parallel. Maximal deviation of the ring atoms from their best plane is 2.9 pm. The triazine forms interplanar angles of 62.8° with the phenyl ring and 6.6° with the plane C7-C4-N5-O3 of the acetyloxime group.

**Table 1. Selected bond lengths [pm] and angles [deg] for (2)**

| | |
|---|---|
| O(1)-C(6) | 122.0(2) |
| O(2)-C(5) | 122.0(2) |
| O(3)-N(5) | 138.6(2) |
| O(3)-H(2) | 91(2) |
| N(1)-C(6) | 1361(2) |
| N(1)-N(2) | 138.8(2) |
| N(1)-C(11) | 144.8(2) |
| N(2)-C(3) | 129.1(2) |
| N(4)-C(5) | 135.1(2) |
| N(4)-C(3) | 138.1(2) |
| N(4)-H(1) | 87(2) |
| N(5)-C(4) | 128.0(2) |
| C(3)-C(4) | 147.5(2) |
| C(5)-C(6) | 150.8(2) |
| C(4)-C(7) | 149.3(2) |
| O(4)-C(8) | 141.1(2) |
| O(4)-H(3) | 88(3) |
| O(4)---H(2) | 180(2) |
| O(1)---H(3) | 217(2) |
| O(2)---H(1) | 206(2) |

| | |
|---|---|
| N(5)-O(3)-H(2) | 99.5(13) |
| C(8)-O(4)-H(3) | 108.1(13) |
| C(6)-N(1)-N(2) | 125.4(1) |
| C(6)-N(1)-C(11) | 119.8(1) |
| N(2)-N(1)-C(11) | 114.3(1) |
| C(12)-C(11)-N(1) | 118.5(1) |
| C(16)-C(11)-N(1) | 120.0(1) |
| C(3)-N(2)-N(1) | 116.5(1) |
| C(5)-N(4)-C(3) | 122.5(1) |
| C(5)-N(4)-H(1) | 118.2(12) |
| C(3)-N(4)-H(1) | 119.2(12) |
| C(4)-N(5)-O(3) | 113.0(1) |
| N(2)-C(3)-N(4) | 123.9(1) |
| N(2)-C(3)-C(4) | 118.9(1) |
| N(4)-C(3)-C(4) | 117.2(1) |
| O(2)-C(5)-N(4) | 124.8(1) |
| O(2)-C(5)-C(6) | 119.5(1) |
| N(4)-C(5)-C(6) | 115.7(1) |
| O(1)-C(6)-N(1) | 123.8(1) |
| O(1)-C(6)-C(5) | 120.5(1) |
| N(1)-C(6)-C(5) | 115.7(1) |
| N(5)-C(4)-C(3) | 112.4(1) |
| N(5)-C(4)-C(7) | 126.7(1) |
| C(3)-C(4)-C(7) | 120.9(1) |

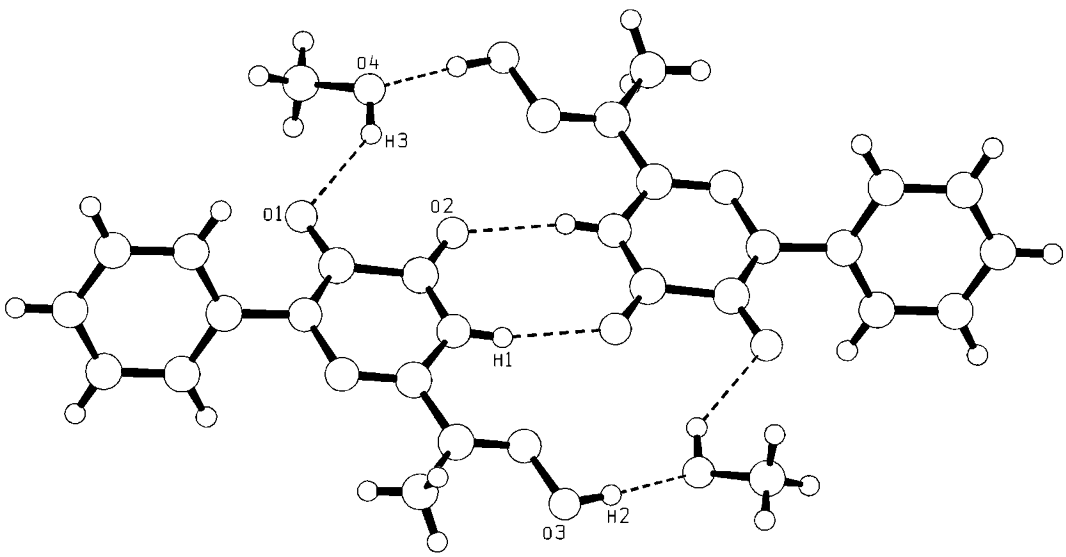


**Figure 2** SCHAKAL[31]-plot showing the hydrogen bonding system joining the dimers. For clarity only O- and H- bridging atoms of the asymmetric unit are numbered.

## EXPERIMENTAL

NMR spectra were recorded on a Bruker WM-400 MHz spectrometer for solutions in $CDCl_3$ +DMSO-$d_6$ with TMS as internal reference. MS spectra were recorded on a Varian MAT CH 7A Mass Spectrometer (EI 70 eV). The elemental analyses were performed by the analytical laboratory of Fachbereich Chemie der Universität Marburg, Germany.

### *L-1-Phenyl-3-acetyloxime-5-benzyl-4,5-dihydro-1,2,4-triazin-6-one (1)*

The preparation of this compound has been described previously.[2]

### *3-Hydroxyiminoethyl-1-phenyl-4-hydro-1,2,4-triazine-5,6-dione (2)*

A solution of $(CH_3)_2SnCl_2$ or $(C_2H_5)_2SnCl_2$ (0.22 g or 0.25 g, 1 mmol) and the oxime ligand **(1)** (0.64 g, 2 mmol) in methanol (100 mL) was refluxed (oil bath) at 80ºC with constant stirring for about 100 h. The solution was then cooled to rt and kept in the fume hood; slow evaporation over a period of few days afforded yellowish needle like crystals. These were filtered off, briefly air-dried, and recrystallized from methanol. Yield: (0.45 g, 80%), mp 267ºC. Anal. Calcd for $C_{11}H_{10}N_4O_3.CH_3OH$: C 51.80, H 5.07, N 20.14, Found C 51.57, H 5.11, N 18.89. MS (EI, 70eV) [m/z(%)] $C_{11}H_{10}N_4O_3^+$ 246(35) molecular ion, 218(25), 202(7), 175(2), 159(2), 119(8), 105(4), 91(100), 77(35), 65(9), 51(6),42(35). $^1$H-NMR(DMSO-$d_6$): δ 2.14(s, 3H, $CH_3$), 7.38(t ,1H, J=7.4 Hz, H-4′), 7.41, 7.49(dd, 2H, J=7.4, 7.8 Hz, H-3′/H-5′), 7.67(d, 2H, J=7.8 Hz, H-2′/ H-6′), 10.97(br s, 1H, C=N~OH), 11.81(s, 1H, $N_4$-H); $^{13}$C NMR(DMSO-$d_6$): δ 8.8($CH_3$), 122.4(C-2′/C-6′), 128.0 (C-4′), 128.7 (C-3′/C-5′), 138.0(C=NOH), 140.1 (C-3), 146.4(C-1′), 154.0($C_6$=0), 154.1($C_5$=0).

**Table 2. Crystal data, measurement and structure refinement details for 2.**

| | | |
|---|---|---|
| Habitus, colour | needle, yellow | |
| Crystal size | .4 x .05 x .03 $mm^3$ | |
| Crystal system | monoclinic | |
| Space group | $P2_1/c$ | Z = 4 |
| Unit cell dimensions | a = 1517.58(12) pm | |
| | b = 563.64(3) pm | $\beta$ = 90.35(1)°. |
| | c = 1500.34(13) pm | |
| Volume | 1283.3(2) $nm^3$ | |
| Cell determination | 5000 reflections | |
| Empirical formula | C12 H14 N4 O4 | |
| Formula weight | 278.23 | |
| Density (calculated) | 1.440 $Mg/m^3$ | |
| Absorption coefficient | 0.111 $mm^{-1}$ | |
| F(000) | 600 | |

| | |
|---|---|
| Diffractometer type | IPDS(Stoe) |
| Wavelength | 0.71073 Å |
| Temperature | 193(2) K |
| Theta range for data collection | 2.68 to 25.90°. |
| Index ranges | -18<=h<=18, -6<=k<=6, -18<=l<=18 |
| Scan method | phi scans |
| Data reduction software | INTEGRATE (Stoe) [27], XCAD4 [28] |

| | |
|---|---|
| Reflections collected | 9536 |
| Independent reflections | 2433 [R(int) = 0.0338] |
| Completeness to theta = 25.90° | 97.7 % |
| Observed reflections | 1747[I>2sigma(I)] |
| Reflections used for refinement | 2433 |
| Largest diff. peak and hole | 0.176 and -0.141 e $10^{-6}$ $pm^{-3}$ |
| Solution | direct/ difmap |
| Refinement | Full-matrix least-squares on $F^2$ |
| Treatment of hydrogen atoms | difmap, individual |
| Programs used | SHELXS-97 [29], SHELXL-97 [29], SHELXTL [30] |
| Data / restraints / parameters | 2433 / 0 / 237 |
| Goodness-of-fit on $F^2$ | 0.927 |
| R index (all data) | wR2 = 0.0799 |
| R index conventional [I>2sigma(I)] | R1 = 0.0314 |

### *Crystal Structure Determination of 2*

A small needle-like crystal was taken from an immersion of highly viscous paraffin oil, mounted on top of a glass capillary, cooled down to 193 K and irradiated in an IPDS diffractometer by a Mo-Kα X-ray beam of 0.5 mm diameter. After data reduction[27] the data set was used without absorption correction. Direct methods[28] were applied for structure solution. In the course of several cycles of least squares refinements and subsequent difference Fourier syntheses[29] the residuals converged to values of 0.0314 (R1) and 0.080 (wR2). All atoms were refined individually and, except for the hydrogen atoms, with anisotropic temperature factors. Details about the structure and structure solution and refinement can be found in Table 2.

CCDC–211831 contains the supplementary crystallographic data for this paper.

These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK;
Fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

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