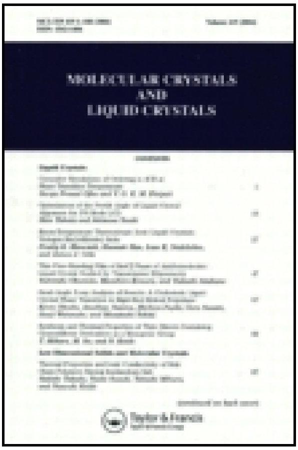

Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals

Synthesis and Characterisation of a Novel Zinc Pyrithione Hydrate

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Synthesis and Characterisation of a Novel Zinc Pyrithione Hydrate

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Cambridge, CB2 1EW, U.K.*

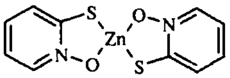
A novel hydrate of zinc pyrithione, a fungicidal material, has been synthesised and its structure determined by powder X-ray diffraction in conjunction with molecular-modelling techniques. The hydrate exhibits solubility in water greater than that of zinc pyrithione and dehydrates at elevated temperatures to reform the original material.

Keywords: zinc pyrithione; 1-hydroxy-2(1*H*)-pyridinethione; molecular modelling; Rietveld refinement; hydrates; solubility

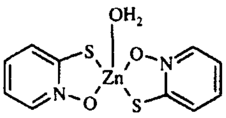
INTRODUCTION

Modification of the solid-state structures of materials can give rise to changes in their physicochemical properties.[1] The formation of crystalline hydrates is one such method of structure modification. The presence of additional water molecules in a crystal lattice will influence the intermolecular interactions (affecting the lattice energy) and the entropy of the solid, thus influencing the free energy, solubility, dissolution rate, and stability.[2] In addition, many solid-state properties such as tabletting and grinding characteristics are altered. For biologically-active materials, the formation of hydrates can have important consequences for bioavailability and product performance.

We are currently studying the solid-state chemistry of zinc pyrithione, denoted $Zn(PT)_2$, a fungicidal agent commonly used in antidandruff shampoos and for the in-can protection of aqueous functional fluids.[3,4] In the course of this work, a novel hydrate, $Zn(PT)_2(H_2O)$, has been synthesised and its solid-state structure determined by powder X-ray diffraction in conjunction with molecular-modelling techniques. A study of some relevant physicochemical properties has also been made.



Zinc Pyrithione, $Zn(PT)_2$



$Zn(PT)_2(H_2O)$, **I**

SYNTHESIS AND INITIAL CHARACTERISATION

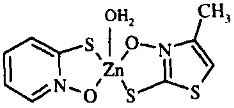
$Zn(PT)_2(H_2O)$, **I**, was synthesised by the combination of aqueous solutions of $Na(PT).xH_2O$ (0.002 mmol) and $ZnCl_2$ (0.001 mmol) at 2.5°C. The white precipitate was filtered, washed with cold water and dried in air. Elemental analysis gave: C: 35.6; H: 3.0; N: 8.3% compared with C: 35.8; H: 3.0; N: 8.3% calculated for **I**. The infra-red spectrum showed a broad peak at 3300 – 3600 cm^{-1} indicating the presence of coordinated water. Thermogravimetric analysis showed a single weight loss of 5.3% in the range 70 – 80°C. This compares with 5.2% calculated for the complete loss of water from **I**.

POWDER X-RAY DIFFRACTION (PXRD)

PXRD analyses were carried out using a Stoe STADI-P high-resolution diffractometer with Ge(111)-monochromated Cu Kα radiation (λ = 1.5406Å) and a position-sensitive detector (PSD) covering *ca.* 6° in 2θ. Patterns were measured in transmission geometry using an ω-2θ scan technique over the 2θ range 3-85° with a step size of 0.5° and a count time of 360 seconds per step (total measuring time *ca.* 16 hours). High-temperature PXRD was performed on the same instrument equipped with a furnace attachment. Samples were loaded in 0.5 mm glass capillaries and heated *in situ* with the capillary open to the atmosphere.

STRUCTURE MODELLING AND REFINEMENT

The starting model for structure refinement was derived from the single-crystal structure of Zn(PT)(MTT)(H_2O), **II**, where MTT represents the 3-hydroxy-4-methyl-2(*3H*)-thiazolethione ligand.[5]



Zn(PT)(MTT)(H_2O), **II**

The PXRD pattern (Figure 1) of **I** suggested it to be isomorphous with **II**, which crystallises in space group $P2_12_12_1$ with lattice parameters a = 7.198(2), b = 11.729(2), c = 15.970(6)Å. The PXRD pattern of **I** could be indexed completely on the basis of an orthorhombic lattice with similar unit-cell parameters: a = 7.119(3), b = 11.897(5), c = 15.588(10)Å.

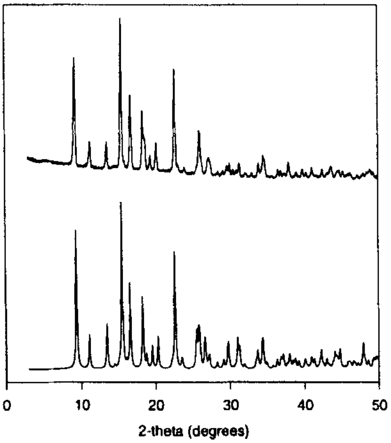


FIGURE 1 Observed PXRD pattern of **I** (top) and the pattern simulated from the single-crystal structure of **II** (bottom).

I was modelled by replacing the MTT ligand in **II** with a PT ligand and normalising the bond distances and angles of both PT ligands to those observed for 1-hydroxy-2(1*H*)-pyridinethione.[6] The entire molecule was then treated as a rigid body during subsequent Rietveld refinement. Isotropic displacement parameters were fixed at 0.07Å^2 for Zn and S, and 0.05Å^2 for O, N and C. In the final cycle of refinement, hydrogens were placed geometrically on the aromatic rings with C-H distances of 0.95Å. H1A and H1B, associated with the water molecule, were placed along the O3···O1^{i} and O3···O2^{ii} vectors in order to give the optimum hydrogen bond geometry, with O-H distances of 0.82Å (Figure 4). All hydrogens were assigned a fixed isotropic displacement parameter of 0.05Å^2 and no attempt was made to refine their coordinates. Refinement converged to give $R_p = 0.076$, $wR_p = 0.097$ and $\chi^2 = 4.23$. The molecular unit of **I** is shown in Figure 2 and the final difference curve is shown in Figure 3.

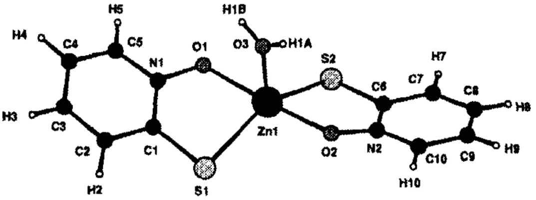


FIGURE 2 Molecular unit of **I**.[7]

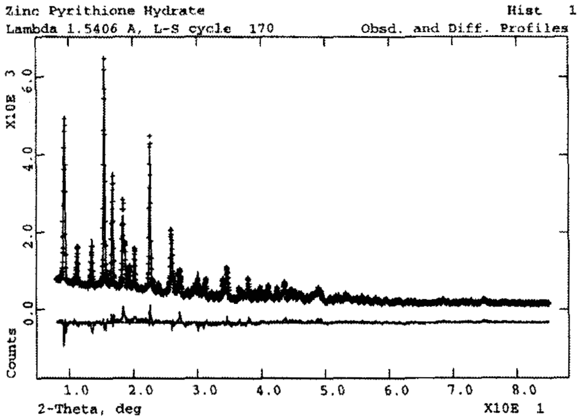


FIGURE 3 Final difference curve for Rietveld refinement of **I**.

SOLID-STATE STRUCTURE

Atomic coordinates for **I** are listed in Table 1. The structure consists of extended chains running parallel to the crystallographic *c* axis (Figure 4). Molecules are linked *via* hydrogen bonds, with each coordinated water forming two bonds, one to each molecule adjacent in the chain ($O3\cdots O1^{i}$ = 2.505(5), $O3\cdots O2^{ii}$ = 2.637(5)Å; symmetry codes (i): $-½+x$, $½-y$, $-z$; (ii): $½+x$, $½-y$, $-z$). Within the chains, the aromatic rings are coplanar and separated by 3.626(8) (Å), a suitable geometry for face-to-face aromatic interactions. The chains pack in a herringbone arrangement with the aromatic rings in a suitable geometry for edge-to-face aromatic interactions (Figure 5).

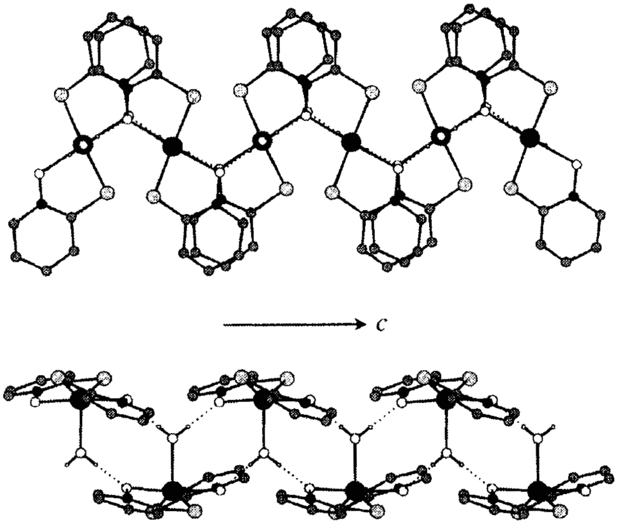


FIGURE 4 Perpendicular views of chains in **I** with hydrogen bonds shown by dotted lines. H atoms on aromatic rings omitted for clarity.

TABLE 1 Fractional atomic coordinates for **I**.

Atom	*x / a*	*y / b*	*z / c*	**Atom**	*x / a*	*y / b*	*z / c*
Zn1	0.152(2)	0.347(3)	0.087(2)	H1A	0.065	0.231	-0.048
S1	0.042(3)	0.279(4)	0.216(3)	H1B	0.222	0.187	-0.019
S2	0.277(3)	0.519(4)	0.048(3)				
O1	0.408(3)	0.276(4)	0.129(3)	H2	0.096	0.091	0.323
O2	-0.099(3)	0.418(4)	0.041(3)	H3	0.342	-0.032	0.344
O3	0.141(3)	0.234(4)	-0.009(3)	H4	0.619	-0.013	0.266
N1	0.388(3)	0.195(4)	0.186(3)	H5	0.644	0.129	0.165
N2	-0.079(3)	0.507(4)	-0.007(3)				
C1	0.225(3)	0.186(4)	0.231(3)	H7	0.216	0.699	-0.064
C2	0.209(4)	0.100(5)	0.290(4)	H8	-0.039	0.759	-0.143
C3	0.354(4)	0.027(5)	0.303(4)	H9	-0.321	0.660	0.137
C4	0.518(4)	0.038(5)	0.256(4)	H10	-0.343	0.501	-0.054
C5	0.532(4)	0.121(5)	0.197(4)				
C6	0.088(3)	0.564(4)	-0.010(3)				
C7	0.101(4)	0.658(5)	-0.061(4)				
C8	-0.049(4)	0.694(5)	-0.108(4)				
C9	-0.217(4)	0.635(5)	-0.105(3)				
C10	-0.228(4)	0.542(5)	-0.055(3)				

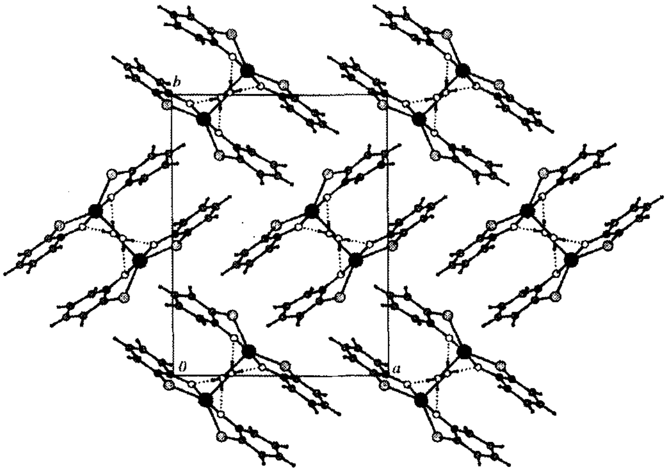


FIGURE 5 View of **I** along *c* axis showing the packing of the hydrogen-bonded chains in a herringbone manner.

PHYSICOCHEMICAL PROPERTIES

Formation of the hydrate of $Zn(PT)_2$ will modify its physicochemical properties and may lead to improved product performance. Properties relevant to its application as a fungicide include solubility and thermal stability. Solubilities were determined by suspending a known mass in water, sonicating for 5 mins and separating the undissolved solid by centrifugation. The solubility of **I** was found to be *ca.* 0.08 g dm^{-3} compared with 0.02 g dm^{-3} reported for the existing $Zn(PT)_2$ material.[4] Thus, formation of the hydrate leads to a significant improvement in the product solubility.

TGA analysis of **I** showed it to lose water above *ca.* 70°C. To examine the solid-state structure of the dehydrated product, PXRD measurements were made at 100°C. It was found that at this temperature, **I** reverts to $Zn(PT)_2$ and the material does not rehydrate on returning to room temperature. On standing in air, **I** was found to dehydrate slowly; PXRD of **I** after one month clearly showed lines corresponding to $Zn(PT)_2$. Thus, although **I** offers improved solubility over the existing product, $Zn(PT)_2$, its thermal stability is low and it reverts to $Zn(PT)_2$ on standing in air.

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