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Structural Studies of Diazine Oximes.
I. The Crystal and Molecular Structure of *syn*-4-Pyrimidinecarboxaldehyde Oxime

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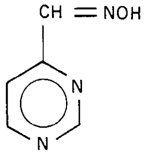
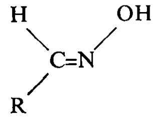
syn-4-Pyrimidinecarboxaldehyde oxime crystallizes in the space group *Pccn* with 8 molecules in a cell of dimensions $a=8{\cdot}500 \pm 0{\cdot}002$, $b=12{\cdot}101 \pm 0{\cdot}002$ and $c=11{\cdot}732 \pm 0{\cdot}010$ Å. The experimental and calculated densities are 1·34 and 1·35 g cm^{-3}, respectively. The crystal structure has been determined by direct methods. An *E* map based on 327 generated phases showed all the non-hydrogen atoms. The hydrogen atoms were located from a difference map. A full-matrix least-squares refinement based on 787 observed reflexions gave a final conventional *R* index of 0·048. The molecules are closely planar and are connected by single hydrogen bonds to form infinite chains parallel to the (110) plane.

Introduction

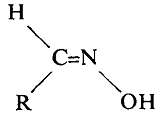
Quaternary salts of heterocyclic aldoximes (Pettelkau, 1972; Schoene, 1967) proved to be good reactivators of phosphorylated acetylcholine esterase if their pK_a values are between 7·6 and 8·1 (Hagedorn, Stark & Lorenz, 1972). Additionally the aldoxime group has to be *syn*-configurated as generally preferred in connexion with aromatics. Some derivates of 4-pyrimidinecarboxaldehyde oxime (hereafter abbreviated to 4PCO) were also included in these investigations.



4PCO has been synthesized by several procedures leading in all cases to the same compound (m.p. ≃150°C), to which Ashani, Edery, Zahavy, Künberg & Cohen (1965) assigned the *syn* configuration. However, Bredereck, Simchen & Speh (1970) described it recently as having an *anti* configuration.



syn



anti

In the course of our investigation we found two modifications of 4PCO, two isomers (m.p. 150·7 and 166·6–169·9°C), which clearly differ in their chemical and physical properties. A detailed study of the isomerization process, in connexion with the structures of both isomers, will be published later on. The present paper reports the structure determination of the compound whose properties are identical with those of the product described in previous works (Ashani, Edery, Zahavy, Künberg & Cohen, 1965; Bredereck, Simchen & Speh, 1970).

Experimental

Single crystals of *syn*-4PCO were obtained by slow evaporation in methanol of a purified specimen. The crystals were transparent and colourless. The symmetry, space group and approximate lattice parameters were determined from Weissenberg and precession photographs taken with Mo $K\alpha$ radiation. Precise lattice parameters were obtained by least-squares refinement of the θ values for several reflexions measured on a diffractometer. The crystallographic data are:

syn-4-Pyrimidinecarboxaldehyde oxime
$C_5H_5N_3O$; F.W. 123·115; m.p. 150°C.
Orthorhombic; $Z=8$; $\lambda(\text{Mo } K\alpha)=0{\cdot}7107$ Å;
$a=\ 8{\cdot}500 \pm 0{\cdot}002$ Å
$b=12{\cdot}101 \pm 0{\cdot}002$
$c=11{\cdot}732 \pm 0{\cdot}010$.
Volume of the unit-cell, $V=1206{\cdot}73$ Å^3.
$D_m=1{\cdot}34$; $D_x=1{\cdot}35$ g. cm^{-3}.
Absorption coefficient for Mo $K\alpha$ radiation, $\mu=1{\cdot}09$ cm^{-1}
Space group *Pccn*. $F(000)=512$.

The crystal chosen for the structure determination was ground to a nearly perfect sphere of radius $R=0{\cdot}025$ cm. With Mo $K\alpha$ radiation the absorption errors are quite small for a sphere of this size ($\mu R=0{\cdot}027$). Three-dimensional data were collected on a Nonius CAD-4 four-circle automatic diffractometer with graphite-monochromated Mo $K\alpha$ radiation, using a scintillation detector with pulse-height discrimination. Two suitable reflexions were chosen as standards and monitored periodically during the data-collection process. Subsequent analysis of these reflexions indicated that no crystal decomposition occurred during the time required to collect the intensities. Reflexions with measured intensities $I_o < 2\sigma(I)$ were considered statistically insignificant. Applying this criterion, 787 reflexions were 'observed' and used in the calculations. The data were corrected for Lorentz and polarization factors in the usual manner.

Determination of the structure

Structure factors were placed on an approximately absolute scale by means of a K curve (Karle & Hauptman, 1953), and normalized structure-factor magnitudes were derived. The statistical distribution of the $|E|$ values strongly indicate a centric unit cell, as may be seen from a comparison of the following values:

	Observed	Theoretical Centric	Theoretical Acentric
$\langle\|E\|\rangle$	0·804	0·798	0·886
$\langle\|E\|^2\rangle$	1·000	1·000	1·000
$\langle\|E^2-1\|\rangle$	0·992	0·968	0·736
$\|E\|>1{\cdot}0$	0·3209	0·3173	0·3679
$\|E\|>2{\cdot}0$	0·0439	0·0455	0·0183
$\|E\|>3{\cdot}0$	0·0021	0·0027	0·0001

The structure was solved by using the symbolic addition procedure (Karle & Karle, 1966). From a list of the $\sum_2$ interactions for 370 reflexions with $|E|>1{\cdot}3$, three linearly independent, origin-determining reflexions were chosen such that simultaneously the number of the $\sum_2$ interactions and magnitudes of the E factors were large. The reflexions 762, 661 and 4,15,14 were arbitrarily assigned positive phases. From these three starting reflexions a total of 80 reflexions could be assigned symbolic phases by using the $\sum_2$ interactions. As the analysis went further, a total of 327 phases could be determined within 75% probability of being correct.

An E map based on the 327 determined phases showed all the non-hydrogen atoms of the structure as the most prominent peaks. Structure factors based on these coordinates and assuming isotropic temperature factors of 1·66 Å^2 gave an R index of 0·346. The f-curves for neutral atoms (Hanson, Herman, Lea & Skillman, 1964) were used.

Two cycles of full-matrix least-squares refinement by means of the program *CRYLSQ* written by F. A. Kundell, assuming isotropic temperature factors and unit weights, decreased the R index to 0·147. The subsequent introduction of anisotropic temperature factors resulted in a further reduction to $R=0{\cdot}079$.

A difference map was calculated at this stage, and the positions of the five hydrogen atoms appeared in this map as dominant maxima, having peak densities ranging from 0·4 to 0·6 e Å^{-3}. Two more cycles of least-squares refinement assuming isotropic temperature factors for the hydrogen atoms led to a final R index of 0·048. The atomic coordinates and thermal vibration parameters are given in Table 1 together with their standard deviations.*

Table 1. *Final atomic parameters*

Standard deviations are given in parentheses.

(*a*) Fractional coordinates

	x/a	y/b	z/c
C(1)	0·6174 (4)	0·1164 (3)	0·5513 (3)
C(2)	0·5466 (4)	0·1870 (3)	0·6279 (3)
C(3)	0·4599 (5)	0·2937 (3)	0,4821 (3)
C(4)	0·6022 (4)	0·1413 (2)	0·4361 (2)
C(5)	0·6696 (4)	0·0728 (3)	0·3449 (3)
N(1)	0·4675 (4)	0·2773 (2)	0·5945 (2)
N(2)	0·5222 (4)	0·2309 (2)	0·4005 (2)
N(3)	0·7538 (4)	−0·0102 (2)	0·3718 (2)
O	0·8056 (3)	−0·0683 (2)	0·2765 (2)
H(1)	0·672 (4)	0·049 (3)	0·574 (2)
H(2)	0·548 (4)	0·179 (3)	0·708 (3)
H(3)	0·395 (5)	0·359 (3)	0·452 (3)
H(4)	0·637 (4)	0·097 (3)	0·260 (3)
H(5)	0·859 (6)	−0·125 (4)	0·294 (4)

(*b*) Thermal parameters in the form

$$\exp\,[-2\pi^2(U_{11}h^2a^{*2}+\ldots+2U_{12}hka^*b^*+\ldots)\times 10^{-3}].$$

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	54 (2)	39 (2)	38 (2)	3 (2)	−4 (2)	4 (1)
C(2)	63 (2)	50 (2)	34 (1)	1 (2)	−4 (2)	2 (2)
C(3)	67 (3)	52 (2)	54 (2)	17 (2)	2 (2)	7 (2)
C(4)	40 (2)	38 (2)	37 (1)	− 4 (2)	2 (1)	3 (1)
C(5)	51 (2)	45 (2)	39 (2)	5 (2)	4 (2)	5 (1)
N(1)	63 (2)	50 (2)	45 (1)	7 (2)	2 (1)	−1 (1)
N(2)	69 (2)	51 (2)	42 (1)	16 (2)	3 (1)	8 (1)
N(3)	52 (2)	47 (2)	41 (1)	2 (1)	6 (1)	1 (1)
O	79 (2)	59 (2)	46 (1)	24 (2)	12 (1)	3 (1)

	$10^3\,U$
H(1)	11 (8)
H(2)	19 (9)
H(3)	56 (14)
H(4)	28 (10)
H(5)	74 (19)

Description and discussion of the structure

Molecular structure

The shape of the molecule, as it exists in the crystal, is shown schematically in Fig. 1. The averaged values of the C–N and C–C bond lengths within the pyrimidine ring are 1·339 and 1·384 Å, respectively. The ring appears to depart from the *mm* symmetry, but only in the lengths of the two bonds C(1)–C(2) and C(1)–C(4). The angles at the nitrogen atoms are less than 120° by about 4°, in agreement with values found previously in similar heterocyclic systems. The angles at the carbon atoms are all greater than 120° [that at C(3) considerably so] with the exception of that at C(1), which is only 117·3°. These results compare well with those found in the structure of pyrimidine (Wheatley, 1960).

The bond lengths C(5)–N(3), 1·273 Å, and N(3)–O, 1·393 Å, of the oxime group indicate a structure predominantly $>$C=N–O– with small contribution from $\geq$C–N=O. Similar results were obtained in the structures of *syn*- and *anti*-*p*-chlorobenzaldoximes (Jerslev, 1957) and in that of *anti*-α-bromoacetophenone oxime (Smith, Heidema, Kaiser, Wetherington & Moncrief, 1972). The oxime bond lengths in Å for these three

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* The list of observed and calculated structure factors has been deposited with the National Lending Library, England, as Supplementary Publication No. SUP 30137. Copies may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

compounds, compared with the present ones, are as follows:

	C(4)–C(5)	C(5)–N(3)	N(3)–O
syn-p-chlorobenzaldoxime	1·45	1·26	1·38
anti-p-chlorobenzaldoxime	1·55	1·26	1·39
anti-α-bromoacetophenone oxime	1·474	1·291	1·409
syn-4PCO	1·469	1·273	1·393 .

The bond length C(4)–C(5) of 1·469 Å could indicate that the resonance between the oxime group and the pyrimidine ring bestows some double-bond character on this bond. It is furthermore likely that the observed spread in the values of the C–N and C–C bond lengths within the ring is related to this apparent resonance system. Thus, it may be seen from Fig. 1 that the C(4)–N(2) bond (1·346 Å) adjacent to the C(4)–C(5) bond is somewhat lengthened, whereas the next nearest bond N(2)–C(3) is shortened (1·332 Å). The same effect is present for the other branch, where the nearest bond C(4)–C(1) is slightly longer (1·391 Å) than the nearest C(1)–C(2) bond (1·377 Å).

The averaged values of the C–H (1·01 Å) and O–H (0·85 Å) bond lengths are of the usual order of magnitude.

The molecule of *syn*-4PCO is basically planar, as can be seen from the deviations of the atoms from the least-squares planes (Table 2), calculated by the method of Schomaker, Waser, Marsh & Bergman (1959). The oxime group is slightly twisted (5°) from the plane through the pyrimidine ring around the C(4)–C(5) bond.

Crystal structure

The crystal structure is shown in partial projection along the *a* axis in Fig. 2. The molecules lie closely parallel to the (110) plane, connected by single hydrogen bonds between the oxygen atom (oxime group) and the N(1) atom (pyrimidine ring) of a neighbouring molecule on the same plane, forming infinite chains (Fig. 3). The hydrogen bond in question, O–N(1), has a value of 2·711 Å implying bond lengths of 0·85 and 1·99 Å for O–H(5) and H(5)–N(1), respectively, and an angle O–H(5)–N(1) of 153°. This situation also implies an N(3)–H(5) distance of 1·88 Å, as shown in Fig. 1. All other intermolecular distances also have normal values and some of the shortest approaches are shown in Figs. 2 and 3.

All intramolecular distances and angles together with their standard deviations are given in Table 3.

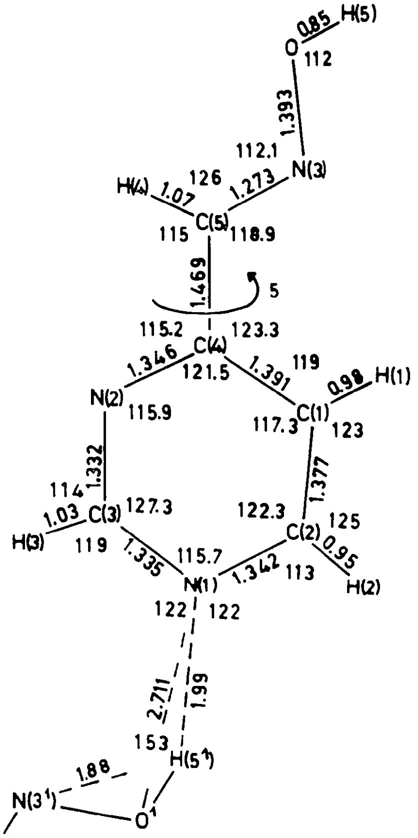

Fig. 1. Bond lengths (Å) and bond angles (°) in *syn*-4PCO. The hydrogen bond is also shown.

Table 2. *Deviations of atoms from least-squares planes*

The planes are expressed as $Ax+By+Cz=D$, where x, y and z are the fractional coordinates of the atoms.

Plane I	Atom	Deviation	Plane II	Atom	Deviation
$A=7{\cdot}116$	C(1)	−0·008 Å	$A=7{\cdot}147$	C(1)	0·003 Å
$B=6{\cdot}601$	C(2)	−0·011	$B=6{\cdot}531$	C(2)	−0·005
$C=0{\cdot}463$	N(1)	0·007	$C=0{\cdot}486$	N(1)	0·003
$D=5{\cdot}426$	C(3)	0·010	$D=5{\cdot}438$	C(3)	0·002
	N(2)	0·000		N(2)	−0·003
	C(4)	−0·005		C(4)	0·001
	C(5)	−0·020			
	N(3)	0·043			
	O	−0·015			

Plane III	Atom
$A=\ 6{\cdot}965$	C(5)
$B=\ 6{\cdot}922$	N(3)
$C=-0{\cdot}427$	O
$D=\ 5{\cdot}021$	

Angle between the normals to planes II and III = 5°

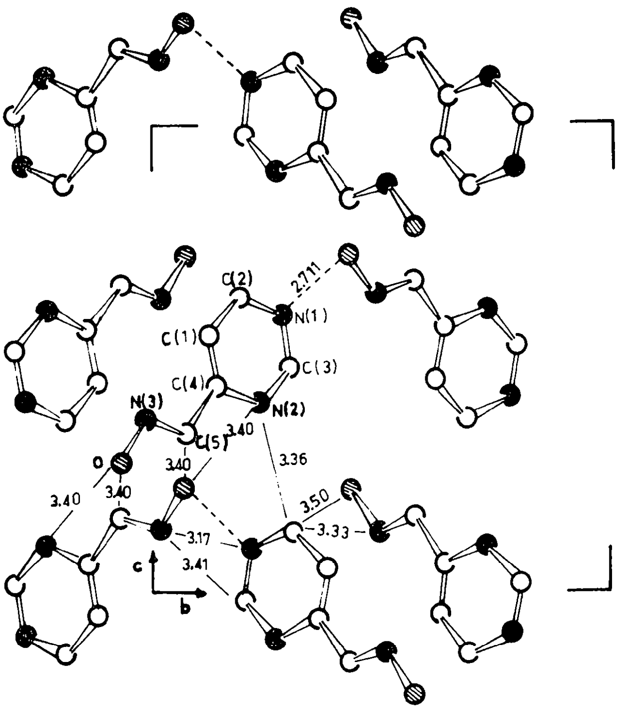

Fig. 2. Partial projection of the structure along the *a* axis. Some of the shortest intermolecular distances in Å are given. Dashed lines represent the hydrogen bonds.

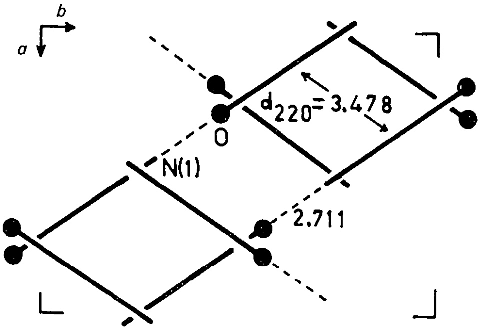

Fig. 3. Molecular packing diagram as viewed down the *c* axis, showing the averaged intermolecular spacing of 3·478 Å. The molecules are represented by segments and for clarity only the oxygen atoms are drawn as circles. Dashed lines represent hydrogen bonds.

Most of the computations required in the analysis were carried out using the X-RAY 70 system of crystallographic programs (Stewart, Kundell & Baldwin, 1970) on the 1108 UNIVAC computer of the University of Freiburg, Germany.

Table 3. *Bond lengths and bond angles in syn-4PCO*

Standard deviations are given in parentheses.

C(4)–C(1)	1·391 (4) Å	C(4)–C(1)–C(2)	117·3 (3)°
C(1)–C(2)	1·377 (5)	C(1)–C(2)–N(1)	122·3 (3)
C(2)–N(1)	1·342 (4)	C(2)–N(1)–C(3)	115·7 (3)
N(1)–C(3)	1·335 (5)	N(1)–C(3)–N(2)	127·3 (3)
C(3)–N(2)	1·332 (5)	C(3)–N(2)–C(4)	115·9 (3)
N(2)–C(4)	1·346 (4)	N(2)–C(4)–C(1)	121·5 (3)
C(4)–C(5)	1·469 (4)	N(2)–C(4)–C(5)	115·2 (3)
C(5)–N(3)	1·273 (4)	C(1)–C(4)–C(5)	123·3 (3)
N(3)–O	1·393 (4)	C(4)–C(5)–N(3)	118·9 (3)
C(1)–H(1)	0·98 (3)	C(5)–N(3)–O	112·1 (3)
C(2)–H(2)	0·95 (3)	C(4)–C(1)–H(1)	119 (2)
C(3)–H(3)	1·03 (4)	H(1)–C(1)–C(2)	123 (2)
C(5)–H(4)	1·07 (3)	C(1)–C(2)–H(2)	125 (2)
O ––H(5)	0·85 (5)	H(2)–C(2)–N(1)	113 (2)
		N(1)–C(3)–H(3)	119 (2)
		H(3)–C(3)–N(2)	114 (2)
		C(4)–C(5)–H(4)	115 (2)
		H(4)–C(5)–N(3)	126 (2)
		N(3)–O ––H(5)	112 (3)

Hydrogen bond

O^1 ––N(1)	2·711 (4) Å	O^1–H(5^1)–N(1)	153 (5)°
H(5^1)–N(1)	1·99 (5)		

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