Acta Cryst. (1974). **B30**, 793

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

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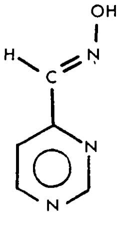
(*Received* 26 *October* 1973; *accepted* 22 *November* 1973)

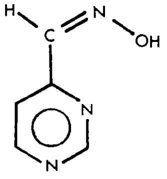
anti-4-Pyrimidinecarboxaldehyde oxime crystallizes in the monoclinic system, space group $P2_1/c$, with four molecules in a cell of dimensions $a = 3{\cdot}770 \pm 0{\cdot}003$, $b = 10{\cdot}509 \pm 0{\cdot}004$, $c = 14{\cdot}063 \pm 0{\cdot}006$ Å and $\beta = 96{\cdot}69 \pm 0{\cdot}02°$. The experimental and calculated densities are 1·47 and 1·48 g cm^{-3}, respectively. The structure was solved by the symbolic addition procedure. All the non-hydrogen atoms were located on an E map based on 268 developed phases. The difference map showed the hydrogen atoms. Full-matrix least-squares refinement based on 550 observed reflexions converged to an R index of 0·071. The molecules are planar and are connected by single hydrogen bonds to form infinite chains similar to those found in the *syn* configuration of this compound.

Introduction

Some derivatives of 4-pyrimidinecarboxaldehyde oxime (hereafter abbreviated to 4PCO) were included in several investigations in connexion with their ability to reactivate the phosphorylated acetylcholine esterase. Only one configurational isomer of 4PCO (m.p. 150·7 °C) was synthesized, to which Ashani, Edery, Zahavy, Künberg & Cohen (1965) assigned a *syn* configuration, while Bredereck, Simchen & Speh (1970) assumed an *anti* configuration.



syn



anti

Martinez-Ripoll & Lorenz (1973) recently reported the crystal and molecular structure of that compound (m.p. 150·7 °C), and showed that it exhibited a *syn* configuration. We describe here the crystalline and molecular structure of the *anti* configurational 4PCO. The first synthesis of this compound (m.p. 166·6–169·9 °C) was carried out by Lorenz (1973).

Experimental

anti-4PCO was crystallized from a methanolic solution as transparent yellow plates. The space group and approximate lattice parameters were obtained from Weissenberg and precession photographs taken with Mo $K\alpha$ radiation. Precise lattice parameters were obtained by a least-squares fit of the θ values for several reflexions. The crystal data are:

anti-4-Pyrimidinecarboxaldehyde oxime,
$C_5H_5N_3O$; F.W. 123·115; m.p. 166·6–169·9 °C.
Monoclinic; $Z = 4$; $\lambda(\text{Mo } K\alpha) = 0{\cdot}7107$ Å;

$a = 3{\cdot}770 \pm 0{\cdot}003$ Å
$b = 10{\cdot}509 \pm 0{\cdot}004$ $\beta = 96{\cdot}69 \pm 0{\cdot}02°$
$c = 14{\cdot}063 \pm 0{\cdot}006$.
Volume of the unit cell, $V = 553{\cdot}37$ Å^3.
$D_m = 1{\cdot}47$; $D_x = 1{\cdot}48$ g cm^{-3}.

Absorption coefficient for Mo $K\alpha$ radiation,
$\mu = 1{\cdot}09$ cm^{-1}.
Space group $P2_1/c$. $F(000) = 256$.

A single-crystal of dimensions $0{\cdot}3 \times 0{\cdot}4 \times 0{\cdot}5$ mm was selected for the X-ray investigation. A Nonius CAD-4 four-circle automatic diffractometer and graphite-monochromated Mo $K\alpha$ radiation were used in connexion with a scintillation detector and pulse-height discrimination. Two reflexions were monitored periodically during the data-collection process. Subsequent analysis of these reflexions indicated no crystal decomposition during the time required to collect the intensities. Reflexions were collected in the range of $6° < \theta < 37°$. Of this total, 550 reflexions were considered 'observed' by the criterion $I > 2\sigma(I)$, and were used in the calculations. The structure amplitudes were obtained after the usual Lorentz and polarization reduction. No correction for absorption was applied because of the small size of the crystal used.

Determination of the structure

Normalized structure magnitudes, $|E|$, were calculated and placed on an approximately absolute scale by means of a K curve (Karle, Hauptman & Christ, 1958). The statistical distribution of $|E|$'s obtained indicates a centric unit cell as may be seen from comparison of the following values:

	Observed	Theoretical	
		Centric	Acentric
$\langle\|E\|\rangle$	0·807	0·798	0·886
$\langle\|E\|^2\rangle$	1·000	1·000	1·000
$\langle\|E^2-1\|\rangle$	0·958	0·968	0·736
$\|E\|>1{\cdot}0$	0·3310	0·3173	0·3679
$\|E\|>2{\cdot}0$	0·0472	0·0455	0·0183
$\|E\|>3{\cdot}0$	0·0013	0·0027	0·0001 .

The phase problem was solved in a straightforward way by the symbolic addition procedure (Karle & Karle, 1966). The origin was fixed by assigning positive phases to the reflexions $11\bar{2}$, 069 and 0,5,12 chosen from a list of the $\sum_2$ interactions for 304 reflexions with $|E|>1{\cdot}3$. From these three starting reflexions and using the $\sum_2$ interactions, a total of 268 phases could be determined within 75% probability of being correct.

An E map based on the 268 developed phases showed all the non-hydrogen atoms of the structure as the highest peaks. A structure-factor calculation at this stage, assuming isotropic temperature factors of 1·50 Å^2, gave $R=\sum||F_o|-|F_c||/\sum|F_o|=0{\cdot}346$. Scattering factors used were those for neutral atoms (Hanson, Herman, Lea & Skillman, 1964).

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, lowered the R index to 0·191. Introduction of anisotropic temperature factors resulted in a further reduction to a value of $R=0{\cdot}091$.

A difference map, calculated at this stage, had the largest positive densities of *ca.* 0·2 e Å^{-3}, except at possible hydrogen-atom positions where the density varied from 0·4 to 0·6 e Å^{-3}. Two more cycles of least-squares refinement with isotropic thermal parameters for the hydrogen atoms reduced the discrepancy to $R=0{\cdot}071$. Table 1 lists the atomic coordinates and thermal vibration parameters together with their standard deviations.*

Description and discussion of the structure

Molecular structure

A schematic drawing of the molecule is shown in Fig. 1. The angles at the nitrogen atoms (pyrimidine ring) are less than 120°, in agreement with values found previously in similar heterocyclic systems (Wheatley, 1960). The angles at the carbon atoms are greater than 120° [that at C(3) considerably so] with the exception of that at C(1), which is only 117·2°. All these results agree well with those found in the structure of *syn*-4PCO (Martinez-Ripoll & Lorenz, 1973).

Table 1. *Final atomic parameters*

Standard deviations are given in parentheses.

(*a*) Fractional coordinates

	x/a	y/b	z/c
C(1)	0·3119 (19)	0·2661 (7)	0·2381 (4)
C(2)	0·1676 (20)	0·2598 (8)	0·1429 (5)
C(3)	−0·0214 (20)	0·4604 (7)	0·1498 (5)
C(4)	0·2754 (17)	0·3790 (6)	0·2853 (4)
C(5)	0·4050 (19)	0·4088 (7)	0·3855 (5)
N(1)	−0·0016 (15)	0·3568 (6)	0·0970 (3)
N(2)	0·1040 (15)	0·4780 (5)	0·2397 (4)
N(3)	0·5732 (16)	0·3407 (6)	0·4520 (4)
O	0·6458 (15)	0·2187 (5)	0·4239 (3)
H(1)	0·434 (20)	0·196 (8)	0·266 (5)
H(2)	0·196 (18)	0·194 (7)	0·113 (5)
H(3)	−0·151 (18)	0·526 (7)	0·117 (5)
H(4)	0·352 (20)	0·491 (8)	0·406 (5)
H(5)	0·752 (17)	0·194 (6)	0·473 (5)

(*b*) Thermal parameters in the form

$$\exp\,[-2\pi^2(U_{11}h^2a^{*2}+\ldots+2U_{12}hka^*b^*+\ldots)\times10^{-3}]$$

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	44 (4)	30 (4)	25 (3)	−3 (4)	−2 (3)	0 (3)
C(2)	53 (5)	40 (5)	34 (4)	−2 (4)	6 (3)	−13 (4)
C(3)	46 (5)	45 (5)	36 (4)	−2 (4)	−4 (3)	3 (4)
C(4)	33 (3)	19 (3)	24 (3)	−5 (3)	3 (2)	5 (3)
C(5)	46 (4)	34 (4)	27 (3)	−4 (4)	−8 (3)	−5 (3)
N(1)	39 (3)	40 (4)	26 (3)	−8 (3)	−9 (2)	0 (3)
N(2)	53 (4)	30 (3)	30 (3)	−4 (3)	−3 (3)	0 (2)
N(3)	56 (4)	34 (3)	29 (3)	1 (3)	−1 (3)	−12 (3)
O	69 (4)	49 (3)	27 (2)	13 (3)	−14 (2)	−4 (2)

	$10^3\ U$
H(1)	25 (28)
H(2)	14 (23)
H(3)	15 (18)
H(4)	24 (24)
H(5)	15 (19)

The bond lengths C(5)–N(3), 1·285 Å, and N(3)–O, 1·378 Å, of the oxime group suggest a structure predominantly $>$C=N–O– with a small contribution from $\geqslant$C–N=O. The bond length C(4)–C(5) of 1·470 Å indicates the presence of some double-bond character, probably due to the resonance between the oxime group and the pyrimidine ring. Similar results were obtained for the structure of *syn-p*-chlorobenzaldoxime (Jerslev, 1957). The bond lengths in the oxime group of this compound, compared with our results in *syn-* and *anti*-4PCO, are listed below:

	C(4)–C(5)	C(5)–N(3)	N(3)–O
syn-p-Chlorobenzaldoxime	1·45 Å	1·26 Å	1·38 Å
syn-4PCO	1·469	1·273	1·393
anti-4PCO	1·470	1·285	1·378

The molecule of *anti*-4PCO is 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 twisted only 1° from the plane through the pyrimidine ring around the C(4)–C(5) bond (5° in *syn*-4PCO).

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* A table of observed and calculated structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30304 (4 pp.). Copies of this table may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

An interesting feature of this structure is the close proximity of the OH group to the C(1) atom of the pyrimidine ring, which contrasts with the expected geometry considering the possible steric hindrance with the hydrogen atom bonded to C(1), and which would prevent planarity of the molecule. A very short intramolecular approach occurs between the oxygen atom and the C(1) atom of the pyrimidine ring (Fig. 1), with distances C(1)· · ·O = 2·810 Å and H(1)· · ·O = 2·28 Å both less than the sum of the van der Waals radii (3·22 and 2·72 Å, respectively), implying an opening of the C(4)–C(5)–N(3) angle (131·3°). Several examples of short intramolecular C· · ·O distances have appeared in the literature and have been summarized by Sutor (1963). They occur mainly in heterocyclic molecules and in compounds with a conjugated double-bond system or a series of double bonds. Sutor (1963) suggests an evaluation of the angles C–H· · ·O, H–C· · ·O and H· · ·O· · ·C (Fig. 1), implied by the short approach, as a possible criterion for hydrogen bonding. However, until the limits of the angles are known, it cannot be definitely stated whether these short C· · ·O distances are true hydrogen bonds or whether they should be considered as a polarization bonding (Dougill & Jeffrey, 1953; de Santis, Giglio & Liquori, 1960). Care should be taken in the consideration of these angles, and other factors, such as the need for the hydrogen atom to be directed towards the lone-pair orbital of the oxygen atom or, as suggested by Hamilton (1961), the tendency of the covalent bond angles to remain undistorted, should also be taken into account.

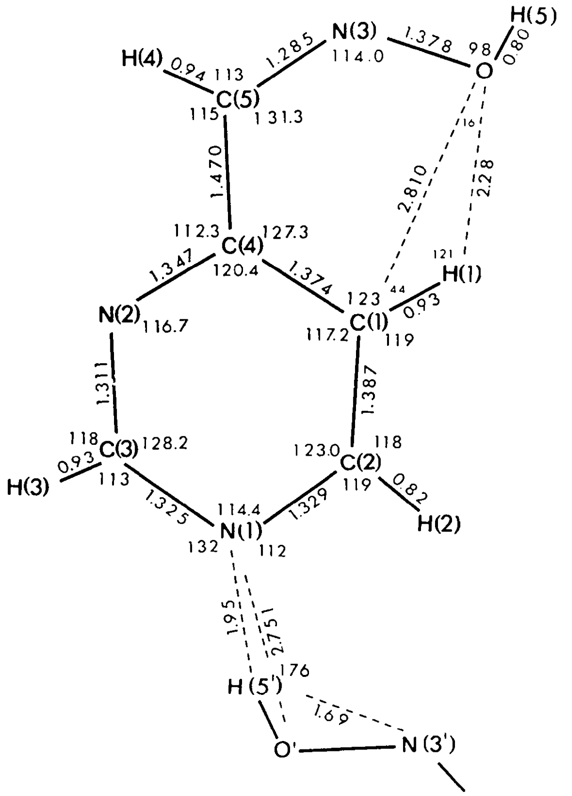

Fig. 1. Bond lengths (Å) and bond angles (°) in *anti*-4PCO. The hydrogen bond and the intramolecular approximation are also shown.

The averaged values of the C–H (0·91 Å) and O–H (0·80 Å) bond lengths are of the usual order of magnitude. All intramolecular distances and angles together with their standard deviations are given in Table 3.

Crystal structure

The crystal structure of *anti*-4PCO viewed along the *a* axis is shown in Fig. 2. The molecules lie nearly parallel to the (11$\bar{2}$) plane, and are connected by single hydrogen bonds between the N(1) atom (pyrimidine ring), being the best H-acceptor, and the oxygen atom (oxime group) of a neighbouring molecule on the same plane, to form infinite chains as in the case of *syn*-4PCO (Martinez-Ripoll & Lorenz, 1973). The hydrogen bond O· · ·N(1), 2·751 Å, implies bond lengths of 0·80 and 1·95 Å for O–H(5) and H(5)· · ·N(1), respectively, and an angle O–H(5)· · ·N(1) of 176° (Fig. 1). All other intermolecular distances have normal values and some of the shortest approaches are shown in Fig. 2.

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
$A=-3·416$	C(1)	−0·006 Å	$A=-3·407$	C(1)	0·001 Å
$B=-3·347$	C(2)	−0·004	$B=-3·389$	C(2)	0·000
$C=$ 5·375	C(3)	0·007	$C=$ 5·409	C(3)	0·001
$D=-0·670$	C(4)	−0·006	$D=-0·678$	C(4)	−0·001
	C(5)	−0·009		N(1)	−0·001
	N(1)	0·003		N(2)	0·000
	N(2)	0·003			
	N(3)	0·002			
	O	0·011			

Plane III	Atom
$A=-3·430$	C(5)
$B=-3·270$	N(3)
$C=$ 5·324	O
$D=-0·673$	

Angle between the normals to planes II and III = 1°

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

Standard deviations are given in parentheses.

C(4)–C(1)	1·374 (8) Å	C(4)–C(1)–C(2)	117·2 (6)°
C(1)–C(2)	1·387 (8)	C(1)–C(2)–N(1)	123·0 (7)
C(2)–N(1)	1·329 (9)	C(2)–N(1)–C(3)	114·4 (6)
N(1)–C(3)	1·325 (9)	N(1)–C(3)–N(2)	128·2 (7)
C(3)–N(2)	1·311 (8)	C(3)–N(2)–C(4)	116·7 (6)
N(2)–C(4)	1·347 (7)	N(2)–C(4)–C(1)	120·4 (5)
C(4)–C(5)	1·470 (7)	N(2)–C(4)–C(5)	112·3 (5)
C(5)–N(3)	1·285 (8)	C(1)–C(4)–C(5)	127·3 (6)
N(3)–O	1·378 (7)	C(4)–C(5)–N(3)	131·3 (7)
C(1)–H(1)	0·93 (7)	C(5)–N(3)–O	114·0 (5)
C(2)–H(2)	0·82 (6)	C(4)–C(1)–H(1)	123 (5)
C(3)–H(3)	0·93 (6)	H(1)–C(1)–C(2)	119 (5)
C(5)–H(4)	0·94 (7)	C(1)–C(2)–H(2)	118 (5)
O——H(5)	0·80 (5)	H(2)–C(2)–N(1)	119 (5)
		N(1)–C(3)–H(3)	113 (4)
Short intramolecular distances		H(3)–C(3)–N(2)	118 (4)
O–C(1)	2·810 (7)	C(4)–C(5)–H(4)	115 (4)
O–H(1)	2·28 (6)	H(4)–C(5)–N(3)	113 (4)
		N(3)–O——H(5)	98 (5)
Hydrogen bond			
O′——N(1)	2·751 (6) Å	O′–H(5′)–N(1)	176 (5)°
H(5′)–N(1)	1·95 (5)		

The general phenomenon that most of the aromatic *syn*-aldoximes have lower melting points than the *anti* configurations is also observed in the case of *syn*-4PCO (m.p. 150·7 °C) and *anti*-4PCO (m.p. 166·6–169·9 °C), but not as a consequence of the different types of molecular association (chains and dimers) as was assumed by Jerslev (1957). The explanation of this observation in 4PCO is probably to be found in the additional intramolecular short distances in *anti*-4PCO.

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

The authors are grateful to Dr W. Littke for the facilities made available to obtain the intensity data. Thanks are also due to the Deutsche Forschungs-Gemeinschaft for making available some laboratory equipment. We are indebted to Professor I. Hagedorn and Professor G. Brauer for their sponsorship of this work.

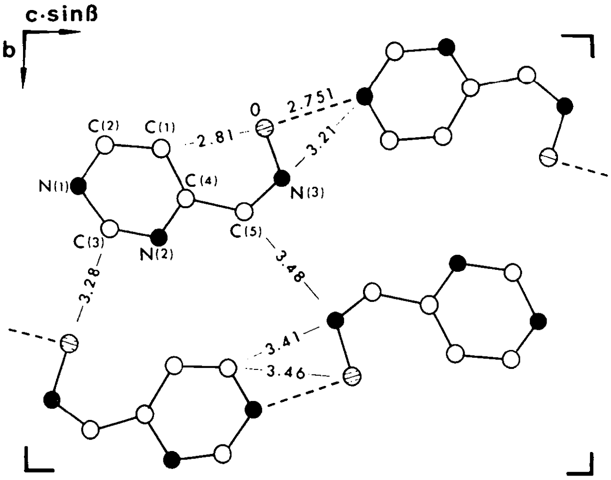

Fig. 2. The crystal structure of *anti*-4PCO as viewed along the *a* axis. Some of the shortest intermolecular distances (in Å) are given. Dashed lines represent the hydrogen bonds.

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