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THE MOLECULAR STRUCTURE OF 2-ACETAMIDO-8-METHYL-4,9-DIOXO-6,7-DIPHENYL-6,7,8,9-TETRAHYDRO-4H-PYRAZINO(1,2-a)-s-TRIAZINE DIHYDRATE

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Abstract—The molecular structure of an acetylated oxidation product of 5 - methyl - 6,7 - diphenyl - 5,6,7,8 - tetrahydropterin has been determined by X-ray analysis. The final R-index is 7·6% using 1740 non-zero reflexions. Seven hydrogen atoms, four of which belong to two moles of water of crystallization, could not be unequivocally located and were left out the refinement. The structure consists of a pyrazino-(1,2-a)-s-triazine ring system containing two carbonyl groups. There is no hydroxyl group bonded to the ring skeleton; the phenyl rings are in a *cis*-position.

The main product of the reaction of molecular oxygen with 5 - methyl - 6,7 - diphenyl - 5,6,7,8 - tetrahydropterin, a model compound in the study of some enzymatic reactions,[1] is assigned from spectroscopic measurements and chemical behaviour, structure **1**[2] whereas Jongejan, Mager and Berends[3] propose structure **2**.

To determine the actual configuration of the molecule this X-ray investigation was started. Because of great difficulties encountered in growing crystals of **2**, the acetylated compound **3** was used instead.

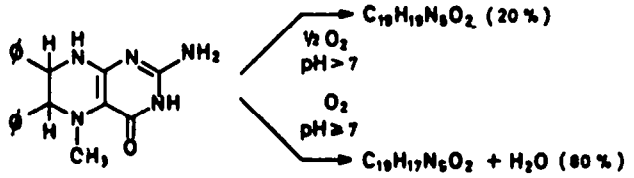
EXPERIMENTAL

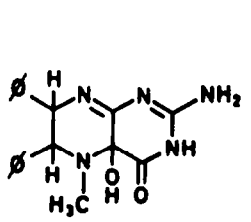
A sample of the compound, $C_{21}H_{19}N_5O_3$, was kindly provided by J. A. Jongejan from the Biochemical and Biophysical Laboratory of the University of Technology Delft. Crystals of rather poor quality were grown from a 1:1 ethanol/water solution.* The crystals are monoclinic, space group $P2_1/c$ with a = 9·171 (3), b = 10·164 (4), c = 23·219 (9) Å, β = 94·31 (2)° and Z = 4. Three dimensional intensity data were collected with the CAD3-Nonius diffractometer using CuK_α radiation and the $\theta/2\theta$-scan mode with a maximum θ-value of 60·00°. High intensities were reduced by nickel filters. No correction for absorption was made. The crystal had approximate dimensions of 0·1 × 0·5 × 0·1 mm in the a, b and c direction respectively and was mounted about the b-axis.

Structure determination

The structure was solved by the direct phase-determining method based on the symbolic addition method for centrosymmetrical structures[4]. The E-map did not reveal all heavy atoms. After five subsequent difference syntheses all heavy atoms and two atoms, which were assumed† to be oxygen atoms of water molecules, were found.

Blocked full-matrix anisotropic least-squares refinement, using 1746 observed (non-zero) reflections, converged to R(= $\Sigma||F_o|-$





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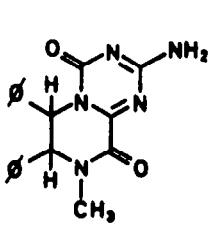

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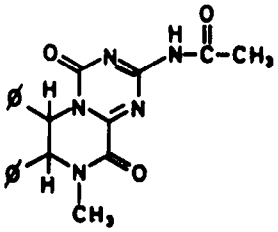

3

*Crystals grown from methanol decompose. The enclosed methanol vaporized very rapidly.

†This assumption was confirmed by an elementary analysis of the crystals by Mr. M. van Leeuwen of our laboratory.

Table 1. Final parameters with e.s.d.'s in parentheses. The fractional atomic coordinates are multiplied by 10^4 for the non-hydrogen atoms and by 10^3 for the hydrogen atoms. The expression for the anisotropic thermal parameters ($Å^2 \times 10^3$) is:

$$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + a^*b^*khU_{12} + b^2c^2klU_{23} + c^*a^*lhU_{31}]$$

The isotropic factors (U) are in $Å^2 \times 10^3$.

Atom	x/a	y/b	z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	4159(6)	484(8)	4383(3)	61(4)	108(6)	69(4)	−15(4)	7(3)	14(4)
N(3)	5202(6)	2618(6)	4307(2)	65(2)	86(4)	59(3)	−20(4)	10(3)	15(3)
N(5)	8663(6)	2513(5)	3702(2)	54(3)	62(4)	73(4)	−10(3)	8(3)	−2(3)
N(8)	6318(6)	834(6)	3896(2)	58(3)	65(4)	74(4)	−11(3)	7(3)	9(3)
N(23)	3132(6)	2358(7)	4769(2)	56(3)	143(6)	66(4)	−12(4)	23(3)	22(4)
C(2)	4184(8)	1740(9)	4475(3)	71(5)	96(6)	54(4)	−10(5)	−3(4)	14(4)
C(3a)	6247(7)	2113(7)	4027(3)	60(4)	79(5)	48(4)	−14(4)	7(3)	9(4)
C(4)	7444(7)	3045(8)	3889(3)	65(5)	68(5)	57(4)	−7(4)	8(4)	6(4)
C(5a)	9954(9)	3365(8)	3704(4)	61(5)	79(6)	109(7)	−12(5)	6(5)	−1(5)
C(6)	8886(7)	1076(7)	3676(3)	50(4)	68(5)	83(5)	−1(4)	5(3)	8(4)
C(6a)	10002(7)	730(7)	3252(3)	54(4)	67(5)	99(6)	−1(4)	−1(4)	−7(4)
C(7)	7438(8)	349(7)	352(3)	58(4)	60(5)	98(6)	−1(4)	−1(4)	13(4)
C(7a)	6849(6)	341(7)	290(3)	50(4)	57(4)	82(5)	−7(3)	8(3)	1(4)
C(9)	5236(9)	−45(9)	4078(3)	83(6)	72(6)	84(6)	−24(5)	−17(5)	26(5)
C(10)	7099(8)	−753(8)	2573(4)	71(5)	77(6)	110(8)	−10(8)	13(5)	−20(5)
C(11)	6600(11)	−800(12)	1999(5)	76(6)	126(9)	13210)	−21(6)	37(6)	−57(8)
C(12)	5851(10)	250(14)	1742(4)	77(6)	159(10)	82(6)	−37(7)	15(5)	−27(8)
C(13)	5586(8)	1355(10)	2068(4)	75(5)	108(7)	74(6)	−16(5)	1(4)	7(5)
C(14)	6080(8)	1375(8)	2645(3)	69(4)	69(5)	73(5)	−7(4)	−1(4)	3(4)
C(15)	9981(8)	1284(8)	2707(4)	66(5)	80(6)	89(6)	−3(4)	20(5)	−6(5)
C(16)	11010(11)	918(10)	2339(4)	95(6)	95(7)	113(7)	−28(6)	24(6)	−17(6)
C(17)	12079(11)	20(12)	2510(6)	75(7)	121(10)	161(11)	−15(7)	18(7)	−67(9)
C(18)	12086(11)	−523(12)	3055(7)	73(7)	114(10)	190(12)	24(6)	−28(8)	−47(10)
C(19)	11053(8)	−188(8)	3446(4)	53(4)	87(6)	146(8)	17(4)	−11(5)	−29(6)
C(20)	1170(11)	2742(15)	5379(5)	101(8)	231(14)	123(8)	6(9)	60(7)	18(10)
C(21)	2039(10)	1740(14)	5058(4)	84(7)	186(12)	85(7)	−16(8)	14(5)	29(8)
O(4a)	7276(5)	4218(5)	3960(2)	78(3)	66(3)	97(4)	−8(3)	28(3)	−4(3)
O(9a)	5363(6)	−1205(6)	3955(2)	84(4)	77(4)	125(4)	−27(3)	2(3)	20(4)
O(22)	1805(8)	556(9)	5061(3)	112(3)	200(8)	111(5)	−54(6)	27(4)	29(6)
O(W1)	6650(9)	102(7)	93(3)	251(8)	148(6)	122(5)	45(6)	59(6)	36(5)
O(W2)	7416(8)	2901(9)	424(4)	153(6)	216(9)	316(11)	86(6)	−110(7)	−173(8)
H(61)	938(7)	79(7)	407(3)	71					
H(71)	770(8)	−49(7)	361(3)	68					
H(101)	759(9)	−158(8)	277(3)	91					
H(111)	682(10)	−152(9)	177(4)	109					
H(121)	548(9)	23(10)	140(4)	105					
H(131)	510(8)	217(8)	188(3)	77					
H(141)	602(8)	215(7)	284(3)	70					
H(151)	933(8)	196(8)	259(3)	81					
H(161)	1112(9)	141(9)	201(4)	96					
H(171)	1276(9)	−37(9)	224(4)	105					
H(181)	1264(10)	−111(9)	317(4)	103					
H(201)	183(10)	290(10)	574(4)	111					
H(202)	15(9)	217(8)	552(3)	111					
H(221)	987(9)	400(8)	391(4)	79					
H(222)	1070(8)	285(8)	384(3)	79					
H(223)	1020(7)	360(7)	320(3)	79					

$|F_c|/\Sigma|F_o| \times 100) = 10{\cdot}9\%$. At this stage several hydrogen atom-positions were obtained from a difference Fourier synthesis. They were included in the refinement with fixed isotropic thermal parameters. Continued refinement, alternated with the search for more protons and with the omission of six very strong low-order reflections reduced R to 7·6%. The four water protons and three other protons could not be located unequivocally and were not included in the refinement. The final difference map showed a residual density of 0·35 $eÅ^{-3}$ at positions where protons might be located.

The final atomic coordinates, the temperature factors and their standard deviations as calculated from the least-squares refinement are given in Table 1. A list of F_o and final F_c values is available from the laboratory.

RESULTS

Figure 1 shows the bond distances and bond angles in the molecule. For the sake of clarity the bond angles involving hydrogen atoms are not included. The structure

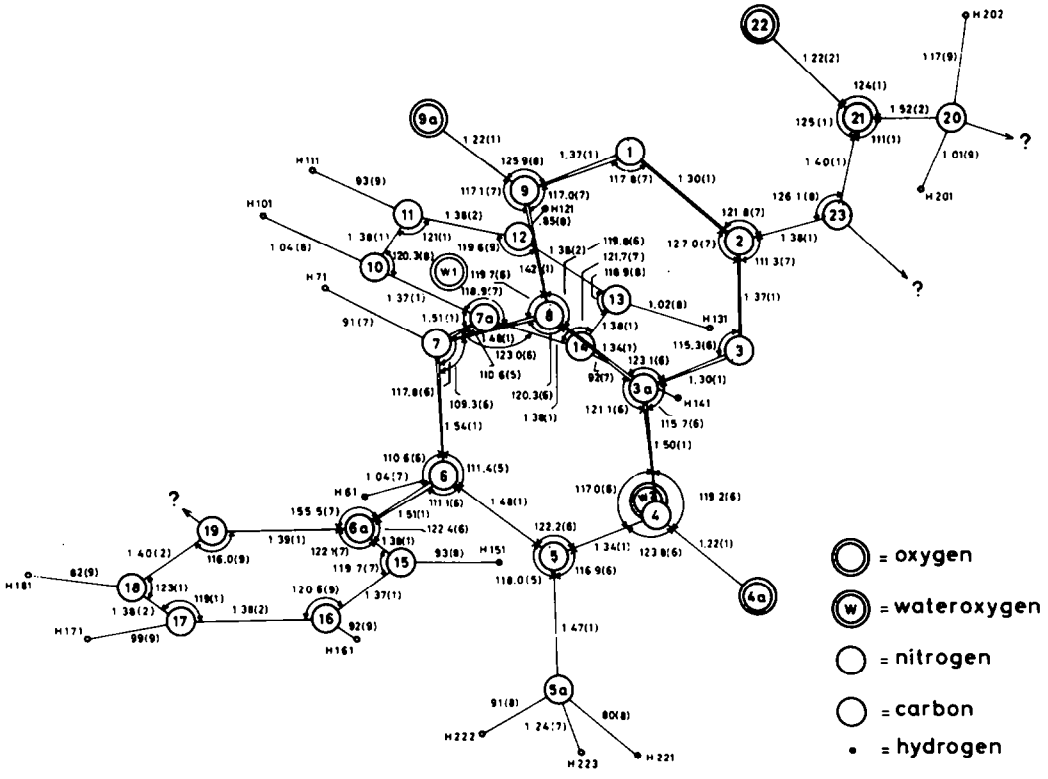

Fig. 1.

Table 2. Shortest intermolecular distances

Atom to Atom	in molecule at	distance in Å
O(W1)–N(3)	$(x, -y+\frac{1}{2}, z-\frac{1}{2})$	3·18
O(W1)–O(4a)	$(x, -y+\frac{1}{2}, z-\frac{1}{2})$	2·82
O(W1)–N(23)	$(-x+1, y-\frac{1}{2}, -z+\frac{1}{2})$	2·81
O(W1)–O(W1)	$(-x+1, -y, -z)$	3·03
O(W1)–O(W2)	(x, y, z)	3·02
O(W2)–N(3)	$(x, -y+\frac{1}{2}, z-\frac{1}{2})$	3·21
O(W2)–O(22)	$(-x+1, y+\frac{1}{2}, -z+\frac{1}{2})$	3·03
O(W2)–O(9a)	$(-x+1, y+\frac{1}{2}, -z+\frac{1}{2})$	3·16
O(W2)–N(1)	$(-x+1, y+\frac{1}{2}, -z+\frac{1}{2})$	3·05
O(W2)–O(W1)	$(-x+1, y+\frac{1}{2}, -z+\frac{1}{2})$	3·02
O(22)–O(W2)	$(-x+1, y-\frac{1}{2}, -z+\frac{1}{2})$	3·03
O(22)–N(8)	$(-x+1, -y, -z+1)$	3·19
O(22)–C(9)	$(-x+1, -y, -z+1)$	3·29

analysis clearly shows the fusion of the s-triazine and pyrazine rings: via the C(3a) N(8) bond. The CO distances indicate a double bond character of the CO bonds. Therefore, a single bonded hydroxyl group can be decisively excluded.

The phenylrings are *cis*.

Relevant intermolecular distances, smaller than 3·3 Å are given in Table 2. There is no evidence for hydrogen bonding to occur, although the O(W1)N(5) and the O(W1)O(2) distances indicate weak interactions. The weak packing in the crystal can explain the poor quality of the crystal and the high temperature movement observed.

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