

The Crystal and Molecular Structure of Tetracycline Hexahydrate

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The crystal structure of tetracycline hexahydrate, $C_{22}H_{24}N_2O_8 \cdot 6H_2O$, has been elucidated by direct methods and refined by least squares to a final R of 0.056 for 1724 independent counter reflexions. Four formula units are contained in a cell with $a = 12.084$ (5), $b = 21.58$ (1), $c = 9.561$ (5) Å, space group $P2_12_12_1$. The conformation is similar to that of 5-hydroxytetracycline and the structure is extensively hydrogen-bonded.

Introduction

The tetracyclines are broad-spectrum antibiotics and this investigation is part of a project involving the elucidation of the molecular conformation of neutral tetracycline, its hydrochloride and the mono-anionic form. We are concerned with the conformational effects of pH on these molecules and their Mg and Ca complexes. Metal complexation by the tetracyclines is of great significance in medicine because, for example, these ligands can deplete the body of Ca.

Experimental

The crystals were prepared by dissolving tetracycline hydrochloride in warm water. Hydrolysis and subsequent crystallization of the free base occurred overnight. Yellow lozenge-shaped crystals were obtained. Microanalysis yielded the following results:

	%C	%H	%N
found	47.80	6.70	4.90
calculated for $C_{22}H_{24}N_2O_8 \cdot 6H_2O$	47.82	6.57	5.07

Oscillation and Weissenberg photographs (Cu $K\alpha$ radiation, $\lambda = 1.542$ Å) showed that the crystal was orthorhombic, and the space group $P2_12_12_1$ was indicated by systematic absences. Accurate cell parameters (Table 1) were obtained by least-squares analysis of the settings of 25 high-order reflexions

Table 1. Crystal data

Molecular formula	$C_{22}H_{24}N_2O_8 \cdot 6H_2O$
Molecular weight	552.5
Space group	$P2_12_12_1$
$a = 12.084$ (5) Å	$D_m = 1.46$ g cm ⁻³
$b = 21.58$ (1)	$D_c = 1.47$ for $Z = 4$
$c = 9.561$ (5)	$\mu(\text{Mo } K\alpha) = 0.80$ cm ⁻¹
$V = 2493.25$ Å ³	$F(000) = 1176$

measured on a Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.7107$ Å). For data collection a single crystal $0.25 \times 0.25 \times 0.21$ mm was used. The density was determined by flotation in a mixture of *m*-xylene and carbon tetrachloride.

In the angular range $3^\circ \leq \theta \leq 23^\circ$, 2009 reflexions were recorded by the $\omega-2\theta$ scan technique (scan width $0.9^\circ\theta$, scan speed $0.03^\circ\theta$ s⁻¹). Of these reflexions, 1724 had $I_{rel} > 2\sigma(I_{rel})$ and were considered as observed. Three reference reflexions were measured every hour. The individual deviations from their mean values were ± 1.3 , ± 2.0 and $\pm 3.1\%$ which indicated crystal stability. Lorentz-polarization corrections were applied but the data were not treated for absorption.

Solution and refinement of the structure

The structure was solved by multisolution tangent refinement with the *SHELX* program system. The starting set of reflexions is shown in Table 2. The first three reflexions were used to define the origin and the fourth to fix the enantiomorph. 128 permutations were generated by means of the starting set and, after eight cycles of weighted tangent refinement for each phase permutation, eight *E* maps were calculated. The *E* maps were ranked by a reliability index R_A (Sheldrick, 1977), and the second *E* map ($R = 0.142$), yielded the

Table 2. Reflexions used in the starting set with allowed phases

h k l	ϕ (rad)
11, 0, 4	0
0 9 4	$\pi/2$
7 0 1	$\pi/2$
2 1 2	$\pi/4, 3\pi/4,$
9 8 2	$\pi/4, 3\pi/4, 5\pi/4, 7\pi/4$
7 9 5	$\pi/4, 3\pi/4, 5\pi/4, 7\pi/4$
5 8 6	$\pi/4, 3\pi/4, 5\pi/4, 7\pi/4$

positions of 29 of the 31 tetracycline atoms. Subsequent least-squares refinement and a difference map showed the positions of the remaining tetracycline atoms and the waters of crystallization. Two cycles of refinement with all the non-hydrogen atoms treated isotropically yielded $R = 0.111$.

At this stage a difference map was calculated with O(15), O(6), N(15) and C(16) omitted from the struc-

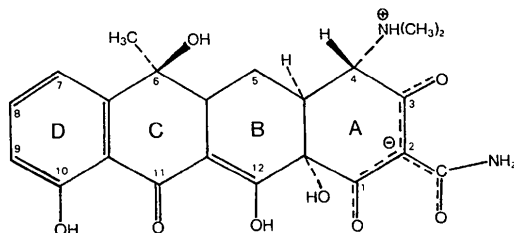


Fig. 1. Zwitterionic structure of tetracycline.

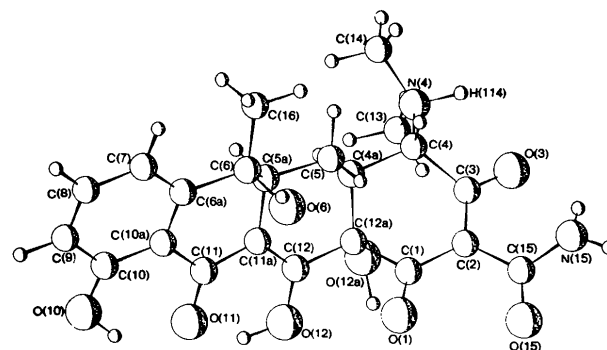


Fig. 2. Perspective view of the molecule with atomic nomenclature.

Table 3. Fractional atomic coordinates ($\times 10^4$) and anisotropic temperature factors of the heavy atoms ($\text{\AA}^2 \times 10^3$)

	x	y	z	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	3176 (5)	7503 (3)	6329 (6)	27 (4)	30 (4)	19 (3)	1 (3)	-2 (3)	1 (3)
C(2)	2700 (5)	6910 (3)	6113 (6)	31 (4)	26 (4)	27 (4)	-1 (3)	0 (3)	4 (3)
C(3)	3300 (5)	6470 (3)	5304 (6)	28 (4)	29 (3)	27 (3)	5 (3)	-6 (3)	0 (3)
C(4)	4563 (4)	6472 (2)	5428 (5)	26 (3)	28 (3)	19 (3)	-2 (3)	1 (3)	-3 (3)
C(4a)	5118 (4)	7105 (2)	5716 (5)	20 (3)	25 (3)	28 (3)	-1 (3)	-2 (3)	0 (2)
C(5)	5585 (4)	7111 (2)	7207 (5)	34 (3)	26 (3)	23 (3)	0 (3)	3 (3)	5 (3)
C(5a)	6263 (4)	7696 (2)	7492 (5)	25 (3)	30 (3)	23 (3)	0 (3)	1 (3)	-2 (3)
C(6)	6615 (5)	7753 (3)	9017 (6)	30 (4)	27 (3)	31 (4)	4 (3)	2 (3)	-2 (3)
C(6a)	7262 (5)	8359 (2)	9210 (6)	25 (4)	31 (4)	25 (4)	-4 (3)	6 (3)	-7 (3)
C(7)	8107 (4)	8405 (2)	10183 (6)	37 (4)	44 (4)	34 (3)	2 (3)	-5 (3)	-4 (3)
C(8)	8641 (4)	8967 (3)	10396 (6)	37 (4)	61 (4)	39 (4)	-6 (4)	-10 (3)	-14 (3)
C(9)	8356 (4)	9487 (3)	9651 (6)	42 (4)	40 (3)	47 (4)	-6 (3)	0 (4)	-14 (3)
C(10)	7492 (5)	9455 (3)	8682 (7)	32 (4)	38 (4)	31 (4)	-4 (4)	2 (4)	0 (3)
C(10a)	6948 (5)	8890 (3)	8451 (6)	25 (4)	26 (4)	35 (4)	-5 (3)	2 (3)	-4 (3)
C(11)	6043 (5)	8853 (3)	7442 (6)	26 (4)	33 (4)	26 (4)	3 (3)	1 (3)	-1 (3)
C(11a)	5637 (5)	8262 (2)	7007 (6)	23 (3)	23 (3)	22 (3)	-3 (3)	2 (3)	-4 (3)
C(12)	4782 (4)	8228 (3)	4088 (6)	20 (3)	26 (3)	20 (3)	4 (3)	-3 (3)	1 (3)
C(12a)	4293 (4)	7631 (3)	5539 (6)	26 (4)	30 (3)	21 (3)	3 (3)	0 (3)	-1 (3)
C(13)	4991 (5)	6450 (2)	2825 (5)	38 (3)	46 (4)	30 (3)	-7 (3)	5 (3)	4 (3)
C(14)	6217 (4)	5918 (3)	4482 (7)	28 (3)	52 (4)	52 (4)	-7 (4)	7 (3)	17 (3)
C(15)	1605 (5)	6754 (3)	6679 (6)	31 (4)	37 (4)	23 (4)	6 (3)	-3 (4)	3 (4)
C(16)	7272 (4)	7181 (2)	9461 (6)	60 (4)	34 (3)	33 (3)	2 (3)	-15 (3)	11 (3)
N(4)	5057 (3)	6125 (2)	4202 (4)	32 (3)	28 (2)	30 (3)	-5 (2)	2 (2)	0 (2)
N(15)	1295 (4)	6154 (2)	6616 (5)	38 (3)	27 (3)	76 (4)	-2 (3)	15 (3)	-9 (2)
O(1)	2779 (3)	7923 (2)	7066 (4)	39 (2)	35 (2)	45 (3)	-14 (2)	14 (2)	-3 (2)
O(3)	2907 (3)	6020 (2)	4658 (4)	31 (2)	40 (2)	49 (3)	-15 (2)	4 (2)	-5 (2)
O(6)	5621 (3)	7789 (1)	9872 (3)	40 (2)	43 (2)	21 (2)	2 (2)	1 (2)	-10 (2)
O(10)	7233 (3)	9973 (2)	7978 (4)	59 (3)	31 (2)	52 (3)	5 (2)	-11 (3)	-12 (2)
O(11)	5635 (3)	9358 (1)	6957 (4)	35 (2)	27 (2)	45 (2)	7 (2)	-9 (2)	-4 (2)
O(12)	4288 (3)	8735 (1)	5577 (4)	38 (2)	26 (2)	31 (2)	7 (2)	-7 (2)	7 (2)
O(12a)	3986 (3)	7701 (1)	4091 (3)	29 (2)	29 (2)	27 (2)	0 (2)	-10 (2)	3 (2)
O(15)	969 (3)	7148 (1)	7212 (4)	24 (2)	33 (2)	38 (2)	-5 (2)	7 (2)	11 (2)
OW(1)	10645 (3)	5060 (2)	8734 (5)	50 (3)	34 (2)	111 (4)	0 (3)	-16 (3)	-1 (2)
OW(2)	8321 (3)	5957 (2)	7152 (4)	70 (3)	79 (3)	43 (3)	6 (3)	9 (3)	-22 (3)
OW(3)	8102 (3)	5874 (2)	1744 (4)	52 (3)	56 (3)	53 (3)	12 (2)	1 (3)	-7 (2)
OW(4)	6308 (4)	5338 (2)	7903 (5)	91 (4)	70 (3)	70 (4)	-6 (3)	-9 (3)	21 (3)
OW(5)	6252 (4)	5257 (2)	813 (5)	75 (4)	89 (4)	64 (3)	-5 (3)	3 (3)	10 (3)
OW(6)	9507 (3)	6104 (2)	9584 (4)	53 (3)	46 (3)	49 (3)	5 (2)	-1 (3)	-3 (2)

Table 4. Fractional coordinates of the hydrogen atoms ($\times 10^3$)

	x	y	z
H(4)	475	622	638
H(4a)	578	716	497
H(51)	610	671	735
H(5a)	701	766	689
H(52)	490	709	793
H(6)	562	768	1091
H(7)	835	800	1077
H(8)	929	899	1116
H(9)	879	991	981
H(10)	654	997	749
H(114)	452	572	410
H(12)	466	911	601
H(121)	342	798	383
H(131)	415	658	258
H(132)	528	613	203
H(133)	552	685	284
H(141)	622	563	541
H(142)	676	630	461
H(143)	649	564	360
H(151)	58	599	704
H(152)	156	588	584
H(161)	804	720	890
H(162)	684	676	915
H(163)	742	717	1057
H \bar{W} (11)	1142	513	881
H \bar{W} (12)	1040	528	956
H \bar{W} (21)	853	605	620
H \bar{W} (22)	865	606	806
H \bar{W} (31)	747	571	128
H \bar{W} (32)	801	625	236
H \bar{W} (41)	650	491	775
H \bar{W} (42)	703	550	798
H \bar{W} (51)	616	485	119
H \bar{W} (52)	628	520	-19
H \bar{W} (61)	910	605	1041
H \bar{W} (62)	976	651	974

In the final refinement the H atoms bonded to N(4) and the ring C atoms were constrained at 1.08 Å, their positions being dictated by the geometry of the molecule. The methyl H atoms were refined as rigid groups. The hydroxyl, water and amino H atoms were

Table 5. Bond lengths (Å)

C(2)—C(1)	1.418 (8)	C(8)—C(9)	1.373 (8)
C(12a)—C(1)	1.572 (8)	C(10a)—C(10)	1.402 (8)
O(1)—C(1)	1.243 (7)	O(10)—C(10)	1.341 (7)
C(3)—C(2)	1.424 (8)	C(9)—C(10)	1.398 (8)
C(15)—C(2)	1.469 (8)	C(11)—C(10a)	1.461 (8)
O(3)—C(3)	1.245 (7)	C(11a)—C(11)	1.429 (8)
C(4)—C(3)	1.530 (7)	O(11)—C(11)	1.282 (7)
N(4)—C(4)	1.514 (6)	C(12)—C(11a)	1.358 (8)
C(4)—C(4a)	1.546 (6)	C(5a)—C(11a)	1.508 (7)
C(4a)—C(5)	1.533 (7)	C(12a)—C(12)	1.512 (8)
C(5a)—C(5)	1.530 (6)	O(12)—C(12)	1.338 (6)
C(6a)—C(6)	1.534 (8)	C(4a)—C(12a)	1.520 (7)
O(6)—C(6)	1.455 (7)	O(12a)—C(12a)	1.441 (6)
C(5a)—C(6)	1.524 (8)	N(15)—C(15)	1.349 (7)
C(16)—C(6)	1.529 (8)	O(15)—C(15)	1.254 (7)
C(10a)—C(6a)	1.409 (8)	C(14)—N(4)	1.496 (6)
C(7)—C(6a)	1.385 (8)	C(13)—N(4)	1.495 (6)
C(7)—C(8)	1.388 (7)		

constrained to ride on their corresponding O and N atoms with a bond length of 1.00 ± 0.05 Å. The isotropic temperature factors of the H atoms were refined as three single parameters, one each for the ring H and H(114), the methyl H, and the hydroxyl, amino and water H atoms. These refined to 0.036, 0.059 and 0.141 Å² respectively.

This technique of constrained least-squares refinement, with rigid groups, bond-length constraints and location and refinement of H atoms, is discussed by Sheldrick (1977). The refinement converged to $R_w = \Sigma w^{1/2} |F_o - F_c| / \Sigma w^{1/2} |F_o| = 0.042$ and $R = 0.056$ with $w = 1/\sigma^2$. As a check for the correctness of the structure a difference map was computed. This had no peaks $> 0.09e \text{ Å}^{-3}$. Tables 3 and 4 show the final atomic coordinates and temperature factors.*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32209 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 6. Bond angles (°)

C(12a)—C(1)—C(2)	115.9 (5)	C(5a)—C(6)—C(6a)	109.0 (4)	C(12)—C(11a)—C(11)	119.7 (5)
O(1)—C(1)—C(2)	125.7 (5)	C(5a)—C(6)—O(6)	108.2 (4)	C(5a)—C(11a)—C(11)	117.5 (5)
O(1)—C(1)—C(12a)	118.4 (5)	C(16)—C(6)—C(6a)	113.0 (5)	C(5a)—C(11a)—C(12)	122.5 (5)
C(3)—C(2)—C(1)	118.4 (5)	C(16)—C(6)—O(6)	108.4 (4)	C(12a)—C(12)—C(11a)	124.5 (5)
C(15)—C(2)—C(1)	121.2 (5)	C(16)—C(6)—C(5a)	110.2 (4)	O(12)—C(12)—C(11a)	122.2 (5)
C(15)—C(2)—C(3)	120.4 (5)	C(10a)—C(6a)—C(6)	119.6 (5)	O(12)—C(12)—C(12a)	113.3 (4)
O(3)—C(3)—C(2)	126.6 (5)	C(7)—C(6a)—C(6)	121.2 (5)	C(12)—C(12a)—C(1)	108.6 (4)
C(4)—C(3)—C(2)	117.6 (5)	C(7)—C(6a)—C(10a)	119.0 (5)	O(12a)—C(12a)—C(1)	104.9 (4)
C(4)—C(3)—O(3)	114.9 (5)	C(8)—C(7)—C(6a)	120.3 (5)	O(12a)—C(12a)—C(12)	110.1 (4)
N(4)—C(4)—C(4a)	113.8 (4)	C(7)—C(8)—C(9)	121.4 (5)	C(4a)—C(12a)—C(1)	112.2 (4)
N(4)—C(4)—C(3)	109.4 (4)	C(8)—C(9)—C(10)	119.4 (5)	C(4a)—C(12a)—C(12)	110.0 (4)
C(4a)—C(4)—C(3)	116.7 (4)	O(10)—C(10)—C(10a)	122.4 (5)	C(4a)—C(12a)—O(12a)	110.8 (4)
C(4)—C(4a)—C(5)	109.5 (4)	C(9)—C(10)—C(10a)	119.8 (5)	O(15)—C(15)—C(2)	123.1 (5)
C(4)—C(4a)—C(12a)	110.9 (4)	C(9)—C(10)—O(10)	117.7 (5)	N(15)—C(15)—O(15)	119.9 (5)
C(5)—C(4a)—C(12a)	109.7 (4)	C(10)—C(10a)—C(6a)	120.0 (5)	N(15)—C(15)—C(2)	117.0 (5)
C(4a)—C(5)—C(5a)	111.7 (4)	C(11)—C(10a)—C(6a)	119.8 (5)	C(14)—N(4)—C(13)	110.3 (4)
C(5)—C(5a)—C(11a)	110.2 (4)	C(11)—C(10a)—C(10)	120.2 (5)	C(14)—N(4)—C(4)	112.2 (4)
C(5)—C(5a)—C(6)	112.7 (4)	C(11a)—C(11)—C(10a)	119.8 (5)	C(13)—N(4)—C(4)	115.4 (4)
C(11a)—C(5a)—C(6)	111.6 (4)	O(11)—C(11)—C(10a)	118.7 (5)		
O(6)—C(6)—C(6a)	107.9 (4)	O(11)—C(11)—C(11a)	121.5 (5)		

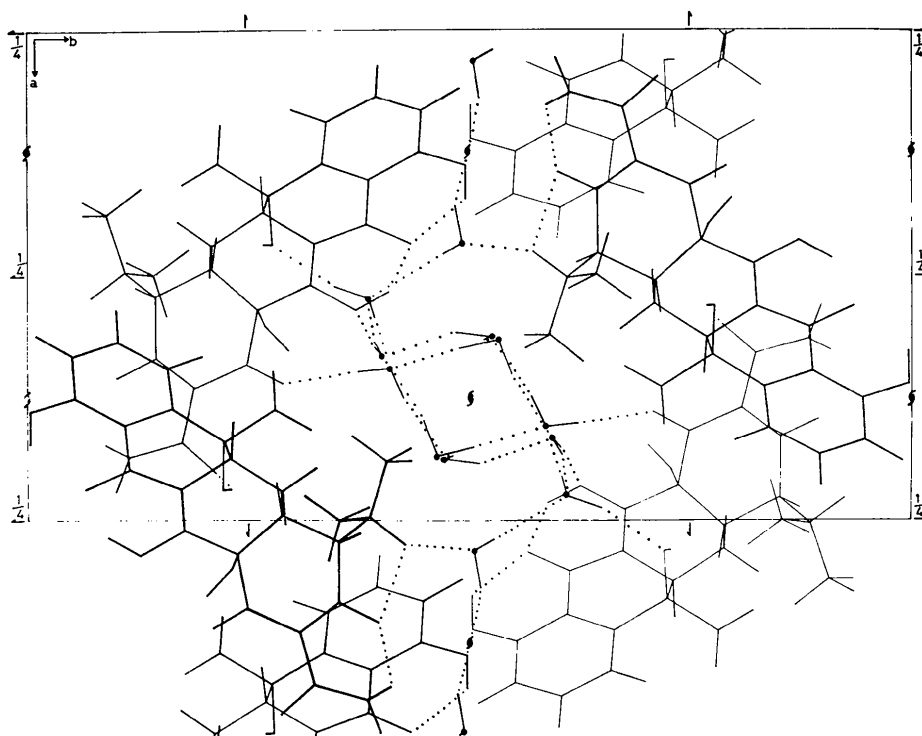


Fig. 3. [001] projection showing the hydrogen-bonding (dotted lines).

Table 7. Torsion angles ($^{\circ}$)

Ring A	
C(2)—C(1)—C(12a)—C(12)	-169.8
C(12a)—C(1)—C(2)—C(3)	4.7
C(1)—C(2)—C(3)—C(4)	35.0
C(2)—C(3)—C(4)—C(4a)	-31.7
C(3)—C(4)—C(4a)—C(5)	110.1
C(4)—C(4a)—C(12a)—C(1)	48.2
Ring B	
C(11)—C(11a)—C(12)—C(12a)	179.2
C(11a)—C(12)—C(12a)—C(1)	102.7
C(5)—C(4a)—C(12a)—C(12)	48.1
C(4)—C(4a)—C(5)—C(5a)	173.3
C(4a)—C(5)—C(5a)—C(6)	172.8
C(5)—C(5a)—C(11a)—C(12)	-18.4
Ring C	
C(10)—C(10a)—C(11)—C(11a)	167.8
C(10a)—C(11)—C(11a)—C(12)	178.8
C(6)—C(5a)—C(11a)—C(11)	41.7
C(5)—C(5a)—C(6)—C(6a)	-178.6
C(5a)—C(6)—C(6a)—C(7)	-148.0
C(6)—C(6a)—C(10a)—C(11)	-2.7
Ring D	
C(8)—C(9)—C(10)—C(10a)	-1.9
C(9)—C(10)—C(10a)—C(11)	180.0
C(7)—C(6a)—C(10a)—C(10)	0.0
C(6)—C(6a)—C(7)—C(8)	-176.4
C(6a)—C(7)—C(8)—C(9)	0.0
C(7)—C(8)—C(9)—C(10)	1.6

Description of the structure and discussion

The structural formula of the compound is shown in Fig. 1 while a perspective view of the molecule with atomic nomenclature is shown in Fig. 2. The principal bond lengths and angles are given in Tables 5 and 6. The bond lengths and angles at C(1)—C(2) (1.418 Å) and C(2)—C(3) (1.424 Å) are characteristic of an sp^2 -conjugated system. Neither these results nor those reported for the structures of 5,12a-diacetyloxytetracycline (Von Dreele & Hughes, 1971), 7-chlorotetracycline (Donohue, Dunitz, Trueblood & Webster, 1963) and 5-hydroxytetracycline (Cid-Dresner, 1965) are compatible with a formal double bond at C(2)—C(3). The molecule is zwitterionic, the protonated N(4) being positively charged whilst the sequence O(1)—C(1)—C(2)—C(3)—O(3) and the amide group, which is partially conjugated, carries the negative charge (Fig. 1). The conformation of the amide group in this structure is opposite to that of the three other tetracycline structures referred to above. The choice of position of N(15) and O(15) was based on the following considerations: (1) the peak height of O(15) was larger than N(15) in a difference map calculated with both these atoms omitted from the structure factor calculation; (2) N(15)—O(3), 2.717 Å, is a normal N—O hydrogen-bond distance; (3) two peaks assumed to be H atoms were found at 1.1 and

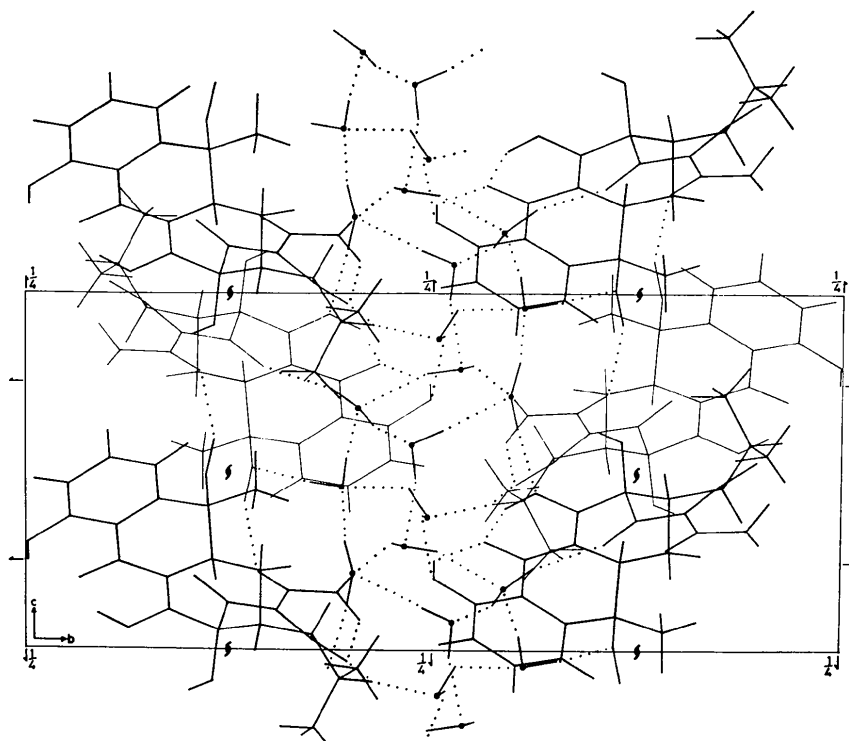


Fig. 4. [100] projection showing the hydrogen-bonding (dotted lines).

Table 8. *Hydrogen-bond lengths (Å) and angles (°)*

N(4) ^j ...OW(1)	2.731	OW(3)...O(1) ⁱⁱ	2.862
H(114) ^j ...OW(1)	1.742	HW(32)...O(1) ⁱⁱ	1.880
N(4) ^j -H(114) ^j ...OW(1)	150.0	OW(3)-HW(32)...O(1) ⁱⁱ	161.1
OW(4)...OW(2)	2.866	N(4)...O(3)	2.644
HW(42)...OW(2)	2.003	H(114)...O(3)	2.126
OW(4)-HW(42)...OW(2)	150.5	N(4)-H(114)...O(3)	106.5
OW(5) ^j ...OW(2)	2.960	N(15)...O(3)	2.717
HW(51) ^j ...OW(2)	2.077	H(152)...O(3)	2.001
OW(5)-HW(51) ^j ...OW(2)	155.9	N(15)-H(152)...O(3)	127.2
OW(4)...OW(3) ⁱ	2.930	OW(6)...O(6) ^{iv}	2.791
HW(41)...OW(3) ⁱ	2.021	HW(62)...O(6) ^{iv}	1.851
OW(4)-HW(41)...OW(3) ⁱ	160.1	OW(6)-HW(62)...O(6) ^{iv}	165.1
OW(6)...OW(3) ^v	2.718	OW(1)...O(10) ⁱⁱⁱ	3.048
HW(61)...OW(3) ^v	1.794	HW(11)...O(10) ⁱⁱⁱ	2.386
OW(6)-HW(61)...OW(3) ^v	166.7	OW(1)-HW(11)...O(10) ⁱⁱⁱ	125.9
OW(5) ^v ...OW(4)	2.789	O(10)...O(11)	2.538
HW(52) ^v ...OW(4)	1.832	H(10)...O(11)	1.794
OW(5) ^v -HW(52) ^v ...OW(4)	163.5	O(10)-H(10)...O(11)	132.4
OW(3)...OW(5)	2.750	O(12)...O(11)	2.489
HW(31)...OW(5)	1.833	H(12)...O(11)	1.572
OW(3)-HW(31)...OW(5)	163.8	O(12)-H(12)...O(11)	146.3
OW(2)...OW(6)	2.750	OW(2)...O(12) ⁱⁱ	2.935
HW(22)...OW(6)	1.782	HW(21)...O(12) ⁱⁱ	1.986
OW(2)-HW(22)...OW(6)	165.3	OW(2)-HW(21)...O(12) ⁱⁱ	168.3
OW(1)...OW(6)	2.761	O(6) ^{vi} ...O(15)	2.823
HW(12)...OW(6)	2.064	H(6) ^{vi} ...O(15)	1.873
OW(1)-HW(12)...OW(6)	126.4	O(6) ^{vi} -H(6) ^{vi} ...O(15)	153.6

Symmetry code

(i) $1\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$;(ii) $\frac{1}{2} + x, 1\frac{1}{2} - y, 1 - z$;(iii) $2 - x, -\frac{1}{2} + y, 1\frac{1}{2} - z$;(iv) $\frac{1}{2} + x, 1\frac{1}{2} - y, 2 - z$;(v) $x, y, 1 + z$ (vi) $-\frac{1}{2} + x, 1\frac{1}{2} - y, 2 - z$

1.0 Å from N(15) in the correct geometric positions. The length C(11a)—C(12) of 1.358 Å is typical for a localized double bond. In comparison with the other tetracycline structures both the C—N bonds are somewhat elongated, but the remaining C—C lengths are similar.

The conformation of the molecule is similar to that of 5-hydroxytetracycline (Cid-Dresner, 1965). Table 7 lists the torsion angles in the tetracycline ring system. The structure is extensively hydrogen-bonded. Table 8 lists both the intra- and inter-molecular hydrogen bonds. The water molecules form a network of hydrogen bonds which is concentrated in columns about alternate twofold screw axes running in the [001] direction. Figs. 3 and 4 show the [001] and [100] projections of one such column of the hydrogen-bonding network.

All calculations were carried out on a Univac 1106 computer at the University of Cape Town.

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The Structure of Aliphatic Amine Adducts of Uranyl Acetylacetonate. III. Dioxobis(2,4-pentanedionato)mono(2-*N*-isopropylaminopentan-4-one)uranium(VI)

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Crystals of the title compound are monoclinic with $a = 8.392(5)$, $b = 18.274(7)$, $c = 16.713(6)$ Å, $\beta = 114.4(2)^\circ$, $Z = 4$, space group $P2_1/c$. The structure was determined by Patterson and Fourier methods and refined by full-matrix least squares to a final R of 0.059 for 1891 reflexions. The U atom has pentagonal-bipyramidal coordination and the *N*-isopropylacetylacetoneamine is bonded to U *via* O. There is an intramolecular N—H...O hydrogen bond which governs the geometry of the molecule.

Introduction

In two earlier structural determinations of compounds of this type we have shown that the conformation of the adduct moiety is dependent on the formation of intramolecular N—H...O hydrogen bonds (part I: Haigh, Nassimbeni, Pauptit, Rodgers & Sheldrick, 1976; part II: Nassimbeni, Orpen, Pauptit, Rodgers & Haigh, 1977). We have carried out the present analysis

to study the conformational effects on the ligand brought about by the steric influence of an isopropyl substituent at N.

Experimental

The compound was prepared as previously described (Haigh & Thornton, 1971). A single crystal was ground