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The Crystal Structure of Novobiocin

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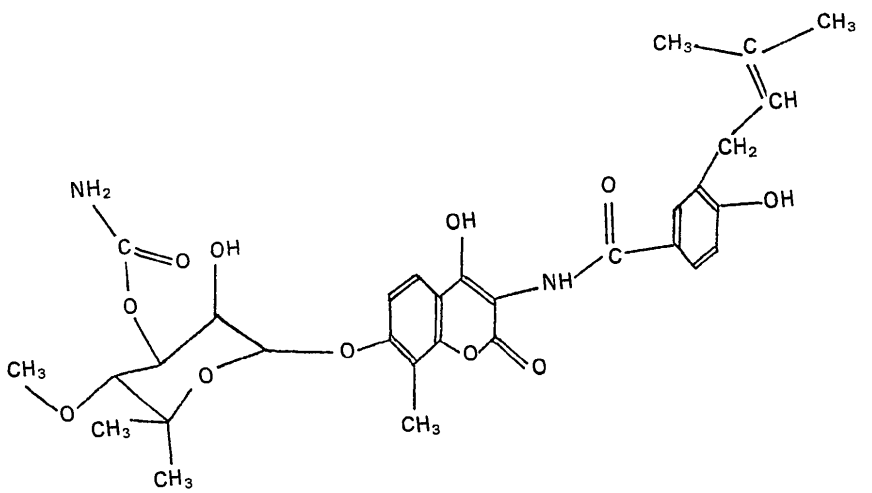
The structure of the antibiotic novobiocin with formula $C_{31}H_{36}N_2O_{11}.H_2O$ has been determined.



It crystallizes in the orthorhombic system with space group $P2_12_12_1$ and four molecules in a unit cell of dimensions $a=8{\cdot}577$, $b=13{\cdot}610$, $c=26{\cdot}357$ Å (standard deviation 0·20%). The structure was solved by the weighted tangent formula from intensity measurements obtained by visual comparison and the equi-inclination Weissenberg method. Full-matrix least-squares refinement yielded an R value of 0·14 for observed data using isotropic thermal parameters and excluding hydrogen atoms from the refinement. The coumarin and substituted benzene ring joined by the peptide bond all lie in one plane, with the isobutenyl and sugar groups on the same side of this plane. The structure contains one water molecule per asymmetric unit hydrogen-bonded to three novobiocin molecules; this plays a major role in stabilizing the structure. In addition there is likely to be some intermolecular interaction between the nitrogen of the carbamyl group and the –O– of an adjacent sugar ring, and intramolecular hydrogen bonding between the peptide oxygen and the –OH of the coumarin system. The structure viewed normally to the main plane of the molecule forms a series of almost overlapping rings (the coumarin with the substituted benzene). The crystal studied contained approximately one Ca^{2+} ion per 35 novobiocin molecules.

Introduction

Novobiocin, 7-[3-*O*-carbamyl-5,5-dimethyl-4-*O*-methyl-α-L-lyxosyl]-4-hydroxy-3-[4-hydroxy-3-(3-methylbut-2-enyl)benzamido]-8-methylcoumarin (Golding & Rickards, 1963), exhibits a fairly broad spectrum of antibacterial activity and is active mainly against Gram-positive bacteria, particularly *Staphylococcus aureus*. It is used clinically for treatment of penicillin-resistant staphylococcal infections.

Strong evidence exists to suggest that novobiocin inhibits growth by combining with Mg^{2+} ions (Brock, 1967), further evidence suggests however that this does not provide the complete explanation of the mode of action of the antibiotic (Morris & Russell, 1971). The presence and positioning of the carbamyl group are of major importance to the activity of novobiocin (Hoeksema & Smith, 1961). Brock (1967) suggests that this group may interact with the enolic group or some other electron-donating group of the molecule. The antibacterial activity of novobiocin cannot be attributed to any particular part of its unique chemical structure; the intact molecule appears to be necessary for full activity.

Novobiocin crystallizes in two forms (Hoeksema & Smith, 1961). Form 2 was used throughout this study. The three-dimensional crystal and molecular structure described in this paper has been determined in the anticipation that this will lead, with evidence already

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obtained, to a plausible explanation of the activity of the antibiotic. A recent review describes the discovery and characteristics of novobiocin and its antibacterial action (Morris & Russell, 1971).

Experimental

Novobiocin was obtained from the Boots Pure Drug Company as the calcium salt. This was converted to the free acid by hydrolysis in 0·1 *M* HCl, the free acid was then extracted from the aqueous solution using ethyl acetate and obtained as pale-yellow crystals by slow evaporation of the solvent. The crystals obtained were of form 2.

The crystal used for X-ray intensity measurements was an irregular flat plate approximately $0{\cdot}7 \times 0{\cdot}5 \times 0{\cdot}1$ mm. The unit-cell dimensions are $a = 8{\cdot}577$, $b = 13{\cdot}610$, $c = 26{\cdot}357$ Å with standard deviation 0·20%. The systematic absences $h00$, $h = 2n+1$, $0k0$, $k = 2n+1$, $00l$, $l = 2n+1$ indicated space group $P2_12_12_1$. The density measured by flotation in a mixture of dichloromethane and chloroform was 1330 kg m^{-3}. The cal-

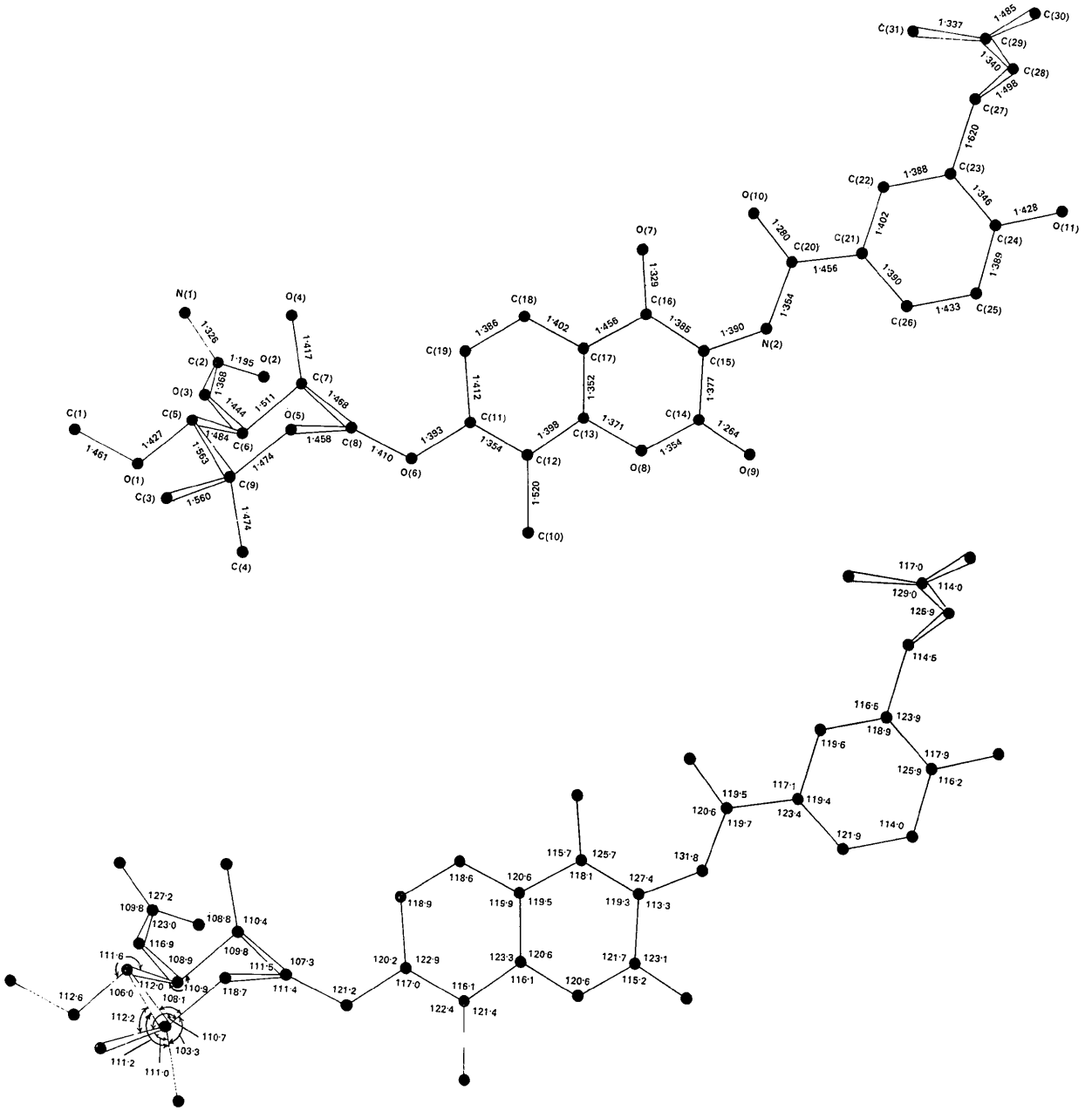

Fig. 1. Interatomic distances and interbond angles in the novobiocin molecule [the molecule is shown in perspective except for the sugar ring which has been rotated through approximately 80° about C(8)].

culated density was 1360 kg m^{-3} for four molecules per unit cell (including one water molecule per asymmetric unit).

Data for intensity measurement were obtained by the equi-inclination method on a Stoe–Weissenberg camera using Ni-filtered Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å) and the multiple-film technique. The crystal for these measurements was rotated about the b axis. The intensities of the X-ray reflexions were obtained by visual comparison with a precalibrated density scale obtained from the 205 reflexion. Constant exposure conditions were used and the interlayer scale factor set at unity. The intensities of 3030 unique reflexions were examined of a possible 3987 in the Cu $K\alpha$ sphere of reflexion. A total of 2487 reflexions were of measurable intensity. The absorption coefficient $\mu = 876$ m^{-1}; no absorption correction was applied to the intensity measurements.

Structure determination

Some initial calculations were carried out on an IBM 1130 computer with programs written by the authors. The major computations were carried out using the X-RAY 70 system on the ICL 1906 A at the Atlas Computer Laboratory, Chilton. In all the calculations the scattering factor tables given in *International Tables for Crystallography* (1962) were used.

The structure was solved using the weighted tangent formula (Germain, Main & Woolfson, 1971).

$$\tan \phi_{\mathbf{h}} = \frac{\sum_{\mathbf{h}'} \omega_{\mathbf{h}'} |E_{\mathbf{h}'} E_{\mathbf{h}-\mathbf{h}'}| \sin (\phi_{\mathbf{h}'} + \phi_{\mathbf{h}-\mathbf{h}'})}{\sum_{\mathbf{h}'} \omega_{\mathbf{h}'} |E_{\mathbf{h}'} E_{\mathbf{h}-\mathbf{h}'}| \cos (\phi_{\mathbf{h}'} + \phi_{\mathbf{h}-\mathbf{h}'})} = \frac{T_{\mathbf{h}}}{B_{\mathbf{h}}} ,$$

where

$$\omega_{\mathbf{h}'} = 0{\cdot}5 + 0{\cdot}5 \tanh [0{\cdot}5 \, . \, EC(\mathbf{h}) \, . \, EC(\mathbf{h}') \, . \, EC(\mathbf{h}-\mathbf{h}') \times \sigma_3/\sigma_2^{1{\cdot}5}] ,$$

where

$$EC(\mathbf{h}) = (T_{\mathbf{h}}^2 + B_{\mathbf{h}}^2)^{1/2},$$

$$\sigma_r = \sum_{j=1}^{N} Z_j^r ,$$

Z_j is the atomic number of the jth atom, N is the total number of atoms per unit cell.

The starting set consisted of five reflexions with high $|E_{\mathbf{h}}|$. Three origin-determining reflexions and one enantiomorph-defining reflexion were chosen to conform to procedures described by Hauptman & Karle (1956) and Karle & Hauptman (1956). One reflexion was phased from the $\sum_1$ relationship (Hauptman & Karle, 1953). The starting set was chosen from a preliminary list of reflexions with $E \geq 1{\cdot}80$ (112 reflexions); due regard was paid to their ability to interact to form $\sum_2$ relationships with other reflexions within the $E \geq 1{\cdot}80$ list. The starting set was expanded within this E list by the sum of angles formula

$$\langle \alpha(\mathbf{h}) \rangle = \alpha(\mathbf{h}') + \alpha(\mathbf{h}-\mathbf{h}')$$

to check on the rate of phase determination and to test for inconsistencies at an early stage in the refinement process. Details of the starting set are given in Table 1.

Tangent refinement was carried out in a series of seven cycles, the E limit being lowered after each cycle. Phase estimates for all $E \geq 1{\cdot}40$ (355 reflexions) were obtained. An E map using these reflexions showed

Table 1. *The starting set for phase determination*

	Reflexion h k l	E	Phase	Number of $\sum_2$ interactions within $E \geq 1{\cdot}80$ list
Origin-fixing reflexions	6 5 0	2·14	0	11
	6 0 11	2·05	$-\pi/2$	11
	1 0 29	2·19	$-\pi/2$	6
Enantiomorph-defining reflexion	0 3 6	3·61	$-\pi/2$	24
$\sum_1$ reflexion	0 6 10	2·21	π	15

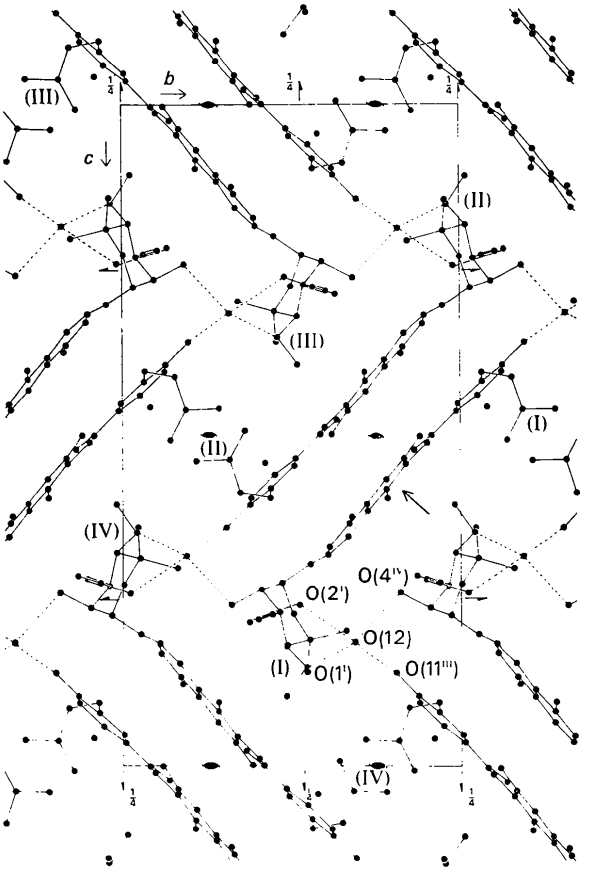

Fig. 2. The novobiocin crystal structure viewed along the x axis (hydrogen bonds to the water molecule are shown as dashed lines).

clearly the 24 atoms of the coumarin and benzene ring system joined by the peptide bond. Most of the remaining non-hydrogen atoms could have been located from this map but some atoms in the isobutenyl side chain and the sugar system were not clearly defined. The usual Fourier technique using the known atomic position to phase the observed F_o was used to determine the position of the remaining non-hydrogen atoms plus one additional atom assumed to be associated with a water molecule.

Refinement of the structure

The 45 atoms located on the electron-density map resulted in an R value of 0·26, where $R=\sum||F_o|-|F_c||/\sum|F_o|$. Five cycles of full-matrix least-squares refinement minimizing the function $\sum\omega[|F_o|-|F_c|]^2$ with individual isotropic temperature factors, unit weights and including refinement of interlayer scale factors resulted in $R=0{\cdot}15$. An F_o-F_c synthesis showed an excess of electron density in the region of the double bond C(28)–C(29) corresponding to approximately 2·0 e Å^{-3}. The possibility of this electron density being due to the presence of dihydronovobiocin was eliminated by a study of the n.m.r. spectrum of the crystalline material. Assumed disorder within the crystal structure with the isobutenyl chain in some other configuration could not account for the observed excess electron density. Atomic absorption spectrophotometric analysis showed that the crystalline free acid contained some calcium, and therefore it is assumed that Ca^{2+} ions are held in this region. The refinement process was continued with the inclusion of this further atomic position. The temperature factor was held constant at 5·0 Å^2. Site occupancy refinement for the assumed Ca^{2+} position indicated an occupancy of approximately 1 Ca^{2+} ion to 35 novobiocin molecules. A weighting function $\omega=1/[\Delta F]^2$ was used in the final refinement process, where $\Delta F=0{\cdot}055F_o+1{\cdot}17$ this equation obtained from a graph of $|\Delta F|$ *vs* $|F_o|$. The final R value was 0·14 using only the observed reflexions, individual isotropic temperature factors and omitting the 38 hydrogen atoms; the largest shift/error was 0·1009. An F_o-F_c Fourier synthesis indicated significant anisotropic thermal vibrations in some atoms. No further refinement was carried out pending the determination of an accurate data set.

Discussion of the structure

The final parameters are given in Table 2. A list of the observed and calculated structure factors and phase angles for all reflexions examined is given in Table 3. The bond distances and angles are listed with their standard deviations in Tables 4 and 5 and are shown in context in Fig. 1.

The coumarin and substituted benzene, with the peptide bond, all lie approximately in one plane, with the isobutenyl side chain on the same side of the main plane as the sugar ring. The temperature factors of the carbon atoms of the isobutenyl side chain are significantly higher than average, consistent with the lack of rigid bonding of this group and probable distortion due to the proximity of the assumed Ca^{2+} ions in some molecules. The bond distances C(23)–C(27) at 1·620 Å and C(29)–C(31) at 1·337 Å are respectively considerably higher and lower than the expected value of approximately 1·54 Å; this is assumed to result from the presence of the Ca^{2+} ions in this region. The distance of 2·446 Å between O(7) and O(10) suggests the presence of intramolecular hydrogen bonding between these atoms.

Table 2. *Final positional and temperature parameters*

Positional parameters are given as fractions of cell edges × 10^4. Temperature factors are of the form $\exp(-B\sin^2\theta/\lambda^2)$ and are given in Å^2. Standard deviations in parentheses are with respect to the last figures given.

	x	*y*	*z*	*B*
C(1)	6006 (17)	4830 (12)	8932 (5)	4·93 (27)
C(2)	7865 (14)	4397 (11)	7749 (4)	3·68 (20)
C(3)	3235 (16)	6578 (12)	7976 (5)	4·83 (26)
C(4)	1831 (16)	5467 (12)	8578 (5)	4·46 (25)
C(5)	4333 (13)	4858 (10)	8201 (4)	3·40 (19)
C(6)	5095 (12)	4615 (10)	7711 (4)	3·17 (18)
C(7)	3977 (12)	4085 (10)	7363 (4)	3·16 (18)
C(8)	2616 (13)	4709 (10)	7262 (4)	3·76 (21)
C(9)	2837 (13)	5497 (10)	8125 (4)	3·39 (19)
C(10)	4435 (13)	6765 (10)	6241 (4)	3·20 (18)
C(11)	2091 (13)	6110 (10)	6708 (4)	3·31 (18)
C(12)	2695 (12)	6707 (9)	6347 (3)	2·87 (17)
C(13)	1619 (11)	7237 (9)	6058 (3)	2·49 (15)
C(14)	1275 (12)	8328 (9)	5368 (4)	3·11 (18)
C(15)	9691 (12)	8374 (9)	5448 (3)	2·92 (17)
C(16)	9034 (12)	7813 (10)	5831 (4)	3·11 (18)
C(17)	68 (12)	7233 (9)	6150 (3)	2·87 (17)
C(18)	9470 (12)	6670 (9)	6551 (4)	3·08 (17)
C(19)	486 (13)	6083 (10)	6826 (4)	3·46 (20)
C(20)	7400 (12)	9156 (9)	5021 (4)	3·04 (18)
C(21)	6936 (13)	9876 (10)	4641 (4)	3·45 (20)
C(22)	5343 (12)	9941 (9)	4526 (3)	2·84 (17)
C(23)	4824 (14)	653 (11)	4190 (4)	4·01 (22)
C(24)	5879 (13)	1221 (10)	3951 (4)	3·45 (20)
C(25)	7474 (16)	1229 (12)	4042 (5)	4·68 (26)
C(26)	7977 (14)	509 (11)	4404 (4)	4·03 (22)
C(27)	2989 (18)	624 (12)	4045 (5)	5·01 (28)
C(28)	2122 (28)	1554 (19)	4157 (8)	8·68 (53)
C(29)	1610 (22)	1840 (15)	4614 (6)	6·58 (38)
C(30)	842 (23)	2818 (17)	4615 (7)	7·57 (45)
C(31)	1725 (30)	1377 (20)	5060 (9)	9·44 (60)
N(1)	8954 (14)	3736 (10)	7853 (4)	5·01 (23)
N(2)	8931 (11)	9013 (8)	5120 (3)	3·42 (17)
Ca	2192 (45)	867 (33)	4580 (13)	5·00*
O(1)	5338 (9)	5416 (7)	8522 (3)	3·55 (14)
O(2)	8059 (10)	5220 (8)	7603 (3)	4·57 (18)
O(3)	6420 (9)	3987 (7)	7807 (3)	4·00 (16)
O(4)	3511 (11)	3195 (8)	7597 (3)	4·66 (18)
O(5)	1871 (8)	5028 (6)	7731 (3)	3·36 (14)
O(6)	3136 (8)	5517 (6)	6973 (2)	3·16 (13)
O(7)	7548 (9)	7835 (7)	5973 (3)	3·91 (15)
O(8)	2226 (9)	7804 (6)	5676 (3)	3·34 (13)
O(9)	1956 (11)	8799 (7)	5019 (3)	4·37 (17)
O(10)	6360 (11)	8624 (8)	5234 (3)	5·01 (19)
O(11)	5320 (13)	1914 (9)	3587 (4)	5·68 (22)
O(12)	7468 (12)	6861 (8)	8154 (4)	5·67 (22)

* Held constant.

Table 3. *Observed and calculated structure factors*

Each entry lists in order, l, $10F_o$, $10F_c$ and $\varphi \times 10^3/2\pi$, where φ is the phase angle in radians. Unobserved reflexions were given $0{\cdot}5 \times$ threshold value and are denoted by *.

Table 4. *Bond distances and their standard deviations* (Å) *after weighted least-squares refinement*

C(19)–C(18)	1·386 (16)	C(23)–C(27)	1·620 (19)
C(18)–C(17)	1·402 (15)	C(27)–C(28)	1·498 (30)
C(17)–C(13)	1·352 (13)	C(28)–C(29)	1·340 (28)
C(13)–C(12)	1·398 (14)	C(29)–C(30)	1·485 (30)
C(12)–C(11)	1·354 (15)	C(29)–C(31)	1·337 (30)
C(11)–C(19)	1·412 (16)	C(11)–O(6)	1·393 (14)
C(17)–C(16)	1·456 (15)	O(6)—C(8)	1·410 (15)
C(16)–C(15)	1·385 (15)	C(8)—C(7)	1·468 (17)
C(15)–C(14)	1·377 (15)	C(7)—C(6)	1·511 (15)
C(14)–O(8)	1·354 (13)	C(6)—C(5)	1·484 (14)
O(8)—C(13)	1·371 (12)	C(5)—C(9)	1·563 (17)
C(16)–O(7)	1·329 (13)	C(9)—O(5)	1·474 (13)
C(12)–C(10)	1·520 (15)	O(5)—C(8)	1·458 (13)
C(14)–O(9)	1·264 (14)	C(7)—O(4)	1·417 (16)
C(15)–N(2)	1·390 (15)	C(6)—O(3)	1·444 (14)
N(2)—C(20)	1·345 (14)	O(3)—C(2)	1·368 (15)
C(20)–O(10)	1·280 (15)	C(2)—O(2)	1·195 (17)
C(20)–C(21)	1·456 (16)	C(2)—N(1)	1·326 (18)
C(21)–C(26)	1·390 (18)	C(5)—O(1)	1·427 (14)
C(26)–C(25)	1·433 (20)	O(1)—C(1)	1·461 (16)
C(25)–C(24)	1·389 (18)	C(9)—C(3)	1·560 (21)
C(24)–C(23)	1·346 (18)	C(9)—C(4)	1·474 (16)
C(23)–C(22)	1·388 (17)	Ca^{2+}–C(27)	1·602 (38)
C(22)–C(21)	1·402 (15)	Ca^{2+}–C(28)	1·455 (45)
C(24)–O(11)	1·428 (16)	Ca^{2+}–C(29)	1·417 (49)
		Ca^{2+}–C(31)	1·497 (44)

Fig. 2 shows the structure viewed along the *a* axis, showing the back-to-back arrangement of molecules related by the twofold screw axis along this direction. Fig. 3 shows part of the structure viewed normal to the plane containing the coumarin and substituted benzene system (in the direction of the arrow in Fig. 2). From this it can be seen that the molecule extends $2a$ in the x direction and the molecules related by the twofold screw axis (represented by full and dashed lines in Fig. 3) almost overlap in certain regions. In particular one half of the coumarin system of molecule (I) nearly overlaps with the substituted benzene ring of molecule (II) and the same half of the coumarin system of molecule (II) almost overlaps the substituted benzene ring of molecule (I) in the next unit cell. The separation of these rings is approximately 3·4 Å and hence they are attracted by van der Waals forces. Only molecules related by the twofold screw axis along the x direction are affected by this attraction of the overlapping rings.

There is one water molecule per asymmetric unit shown as O(12) in Fig. 3. The water molecule is in a position where hydrogen bonding can be assumed to

Table 5. *Bond angles and their standard deviations* (°)

C(19)–C(18)–C(17)	118·57 (0·95)	C(23)–C(24)–O(11)	117·85 (1·05)
C(18)–C(17)–C(13)	119·89 (0·96)	C(25)–C(24)–O(11)	116·21 (1·13)
C(17)–C(13)–C(12)	123·29 (0·93)	C(22)–C(23)–C(27)	116·45 (1·11)
C(13)–C(12)–C(11)	116·13 (0·92)	C(24)–C(23)–C(27)	123·87 (1·12)
C(12)–C(11)–C(19)	122·88 (1·06)	C(23)–C(27)–C(28)	114·50 (1·44)
C(11)–C(19)–C(18)	118·91 (1·03)	C(27)–C(28)–C(29)	125·90 (1·94)
C(18)–C(17)–C(16)	120·59 (0·90)	C(28)–C(29)–C(30)	114·00 (1·76)
C(12)–C(13)–O(8)	116·12 (0·82)	C(28)–C(29)–C(31)	128·97 (2·17)
C(17)–C(16)–C(15)	118·13 (0·91)	C(30)–C(29)–C(31)	117·01 (1·81)
C(16)–C(15)–C(14)	119·34 (1·00)	C(19)–C(11)–O(6)	120·17 (0·97)
C(15)–C(14)–O(8)	121·67 (0·95)	C(12)–C(11)–O(6)	116·95 (0·94)
C(14)–O(8)—C(13)	120·56 (0·80)	C(11)–O(6)—C(8)	121·23 (0·83)
O(8)—C(13)–C(17)	120·56 (0·90)	O(6)—C(8)—O(5)	111·43 (1·00)
C(13)–C(17)–C(16)	119·52 (0·93)	O(6)—C(8)—C(7)	107·29 (0·90)
C(17)–C(16)–O(7)	115·72 (0·90)	C(8)—C(7)—C(6)	109·80 (1·03)
O(7)—C(16)–C(15)	125·71 (1·02)	C(7)—C(6)—C(5)	110·86 (0·88)
C(11)–C(12)–C(10)	122·42 (0·97)	C(6)—C(5)—C(9)	112·00 (0·85)
C(13)–C(12)–C(10)	121·38 (0·91)	C(5)—C(9)—O(5)	108·07 (0·93)
C(15)–C(14)–O(9)	123·06 (1·04)	C(9)—O(5)—C(8)	118·68 (0·78)
O(8)—C(14)–O(9)	115·19 (0·94)	O(5)—C(8)—C(7)	111·54 (0·85)
C(16)–C(15)–N(2)	127·39 (0·94)	C(8)—C(7)—O(4)	110·43 (0·93)
C(14)–C(15)–N(2)	113·27 (0·94)	C(6)—C(7)—O(4)	108·82 (0·85)
C(15)–N(2)—C(20)	131·77 (0·98)	C(7)—C(6)—O(3)	108·90 (0·97)
N(2)—C(20)–O(10)	120·63 (1·05)	C(5)—C(6)—O(3)	109·06 (0·83)
N(2)—C(20)–C(21)	119·69 (0·98)	C(6)—O(3)—C(2)	116·91 (1·00)
O(10)–C(20)–C(21)	119·54 (0·99)	O(3)—C(2)—O(2)	112·98 (1·14)
C(20)–C(21)–C(26)	123·42 (1·03)	O(2)—C(2)—N(1)	127·19 (1·19)
C(20)–C(21)–C(22)	117·15 (1·01)	N(1)—C(2)—O(3)	109·76 (1·20)
C(21)–C(22)–C(23)	119·61 (1·04)	C(6)—C(5)—O(1)	111·63 (0·89)
C(22)–C(23)–C(24)	118·94 (1·09)	C(9)—C(5)—O(1)	105·99 (0·96)
C(23)–C(24)–C(25)	125·87 (1·20)	C(5)—O(1)—C(1)	112·64 (0·99)
C(24)–C(25)–C(26)	113·99 (1·23)	C(5)—C(9)—C(3)	112·18 (0·97)
C(25)–C(26)–C(21)	121·94 (1·12)	C(5)—C(9)—C(4)	111·19 (0·96)
C(26)–C(21)–C(22)	119·40 (1·07)	O(5)—C(9)—C(3)	110·72 (0·89)
		O(5)—C(9)—C(4)	103·26 (0·91)
		C(3)—C(9)—C(4)	111·04 (1·11)

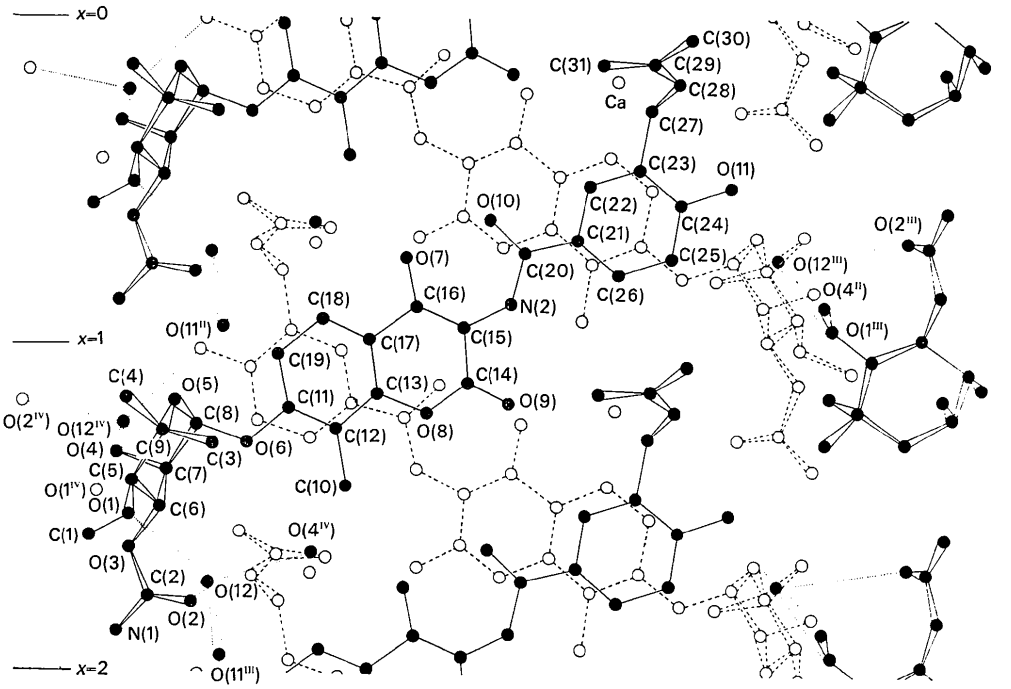

Fig. 3. Part of the novobiocin structure viewed normal to the main plane of the molecule (in the direction of the arrow in Fig. 2) showing the near overlapping of some rings in symmetry-related molecules and the hydrogen bonds to the water molecule (dotted lines).

take place between itself and three novobiocin molecules. Fig. 2 shows that two of these are related by the twofold screw axis along x (effectively holding opposite ends of the molecules together), the remaining hydrogen bonds are to O(1) and O(2) on a symmetry related sugar ring, resulting in a continuous linkage of the sugar rings in the y direction by hydrogen bonds.

There is possibly further intermolecular hydrogen bonding between O(5) and the carbamyl nitrogen N(1) on adjacent molecules (Fig. 3), the separation of these atoms being 3·083 Å. Thus the sugar rings of adjacent molecules are linked in the x direction. The hydrogen-bond distances involved between the donor and acceptor atoms are shown in Table 6. The distance of 4·481 Å between N(1) and the enolic oxygen O(7) on the coumarin system eliminates the possibility of interaction between these groups (Brock, 1967).

Table 6. *Distances and their standard deviations* (Å) *between donor and acceptor atoms involved in hydrogen bonding*

Donor	Acceptor	Type of bond	
O(4)	O(12)	OH ···H_2O	2·814 (14)
O(12)	O(2)	H_2O···C=O	2·712 (15)
O(12)	O(1)	H_2O···–O–	2·854 (14)
O(11)	O(12)	OH ···H_2O	2·771 (14)
O(7)	O(10)	OH ···C=O	2·446 (12)
N(1)	O(5)	NH ···–O–	3·075 (15)

At this stage it would seem highly desirable to recrystallize the novobiocin again in an attempt to produce crystals suitable for more accurate data collection and possibly to eliminate the presence of Ca^{2+} ions. This work is in progress and further discussion of the structure will be published later.

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The Crystal Structure of $Y_7O_6F_9$

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The compound $Y_7O_6F_9$ is an anion-excess, fluorite-related phase, which is a basic structural unit in a series of intergrowth phases in the Y_2O_3–YF_3 system. It crystallizes in the space group *Abm*2 with orthorhombic cell dimensions $a=5{\cdot}420\pm0{\cdot}001$, $b=38{\cdot}58\pm0{\cdot}01$, $c=5{\cdot}527\pm0{\cdot}001$ Å and four formula units per unit cell. Despite the presence of 'inverse overlap' the structure of $Y_7O_6F_9$ has been solved and the unit cell shown to contain two regions of almost undistorted structure types, fluorite and YF_3-type, between which a gradual and coherent change in structure type occurs. $Y_7O_6F_9$ is an important structure in the development of the 'vernier concept' for intergrowth phases in the Y_2O_3–YF_3 system.

Introduction

The composition region $YX_{2.13}$–$YX_{2.22}$ (X = O + F) of the Y_2O_3–YF_3 system contains an apparently infinite number of long-period fluorite-related superstructure phases which are based on one-dimensional ordered intergrowth of several simpler 'basic unit orthorhombic phases' (Mann & Bevan, 1972). These 'basic unit orthorhombic phases' are members $n=4,5,6,7,8$ of the homologous series $Y_nO_{n-1}F_{n+2}$, and have unit cells with dimensions a,nb,c, where a, b, and c are dimen-

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