

The Crystal Structure of Myxin

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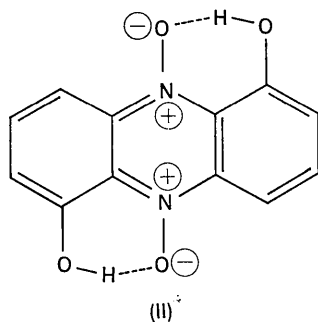
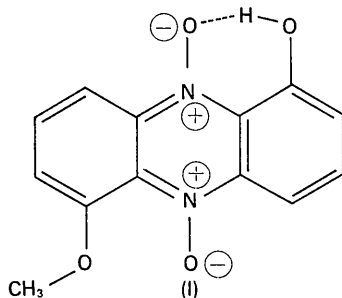
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A crystal-structure analysis of the antibiotic myxin has been carried out at -160°C . The crystal is monoclinic, $P2_1/a$, with $a=15.08$, $b=29.36$, $c=4.87$ Å, $\beta=99.9^{\circ}$, $Z=8$, formula $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_4$. The structure was determined entirely by the symbolic addition method. Ultimate refinement was by block-diagonal least-squares to an R index of 0.052. Myxin was found to be 1-hydroxy-6-methoxyphenazine 5,10-dioxide, a simple derivative of the antibiotic iodinin. The packing is unusual in that there is one apparently non-bonded intermolecular oxygen-oxygen distance of 2.577 Å.

Introduction

The X-ray analysis of this recently discovered antibiotic was undertaken in order to test the molecular structure proposed for it by Edwards & Gillespie (1966). Contrary to their expectations, the present analysis indicated the structure (I) for myxin, which is thus seen to be a simple derivative of the known antibiotic iodinin (II; Clemo & Daghish, 1950). This conclusion has been reached independently by Weigele & Leimgruber (1967), who achieved the synthesis of myxin by alternative procedures. The present work serves merely to confirm their finding, and to provide a reasonably quantitative description of the molecule.



Experimental

Crystal data at -160°C : monoclinic
 $a=15.08 \pm 0.01$, $b=29.36 \pm 0.02$, $c=4.870 \pm 0.003$ Å,
 $\beta=99.90 \pm 0.05^{\circ}$

[Assumed wavelengths: 1.54050 Å (Cu $K\alpha_1$); 1.54434 Å (Cu $K\alpha_2$)]

$V=2124.1$ Å³; formula $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_4$; F.W. 258.2

$D_x=1.614 \pm 0.004$ g.cm⁻³; $D_m=1.54 \pm 0.02$ g.cm⁻³ (at 20°C); $Z=8$

$\mu=11.9$ cm⁻¹ (Cu $K\alpha$).

Space group $P2_1/a$ (from precession and Weissenberg photographs. Systematic absences: $h0l$ for h odd; $0k0$ for k odd).

Molecular symmetry: none.

The material supplied was brick-red, acicular c . A needle of cross section 0.1×0.1 mm was cut to yield a specimen 0.2 mm long. The cell constants and relative intensities were measured with a General Electric XRD 5 spectrogoniometer and goniostat equipped with a scintillation counter. Copper $K\alpha$ radiation was used, and reasonable monochromatization was achieved by means of a $K\beta$ filter and a reverter (pulse-height analyser). In view of the large number of reciprocal-lattice points within the copper sphere, it was decided to use the rapid stationary-crystal, stationary-counter method, with the counter centred on $K\alpha_1$ (Furnas, 1957). The more intense reflexions in all ranges were also measured by the moving-crystal, moving-counter method, and a curve was prepared for the correction of the high-angle intensities for lost counts due to dispersion. Goniostat settings were precomputed, and applied by hand. The specimen was maintained at the working temperature of -160°C by immersion in a stream of cold gaseous nitrogen which was itself surrounded by an envelope of dry nitrogen at room temperature. Of the 4746 accessible reflexions (those for which $2\theta \leq 165^{\circ}$) significant counts were recorded for 3335. Absorption corrections were considered to be unnecessary. The range of the observed intensities was about 1 to 16,000.

Structure determination

The structure was determined entirely by symbolic addition procedures, using the Σ_2 relationship (Karle & Karle, 1966). Preliminary operations, such as derivation of the K curve, calculation of E values, and listing of triplets for $E \geq 1.500$ were carried out using

Table 1. Final parameters (and *e.s.d.*'s) of non-hydrogen atoms

Molecule <i>A</i>	<i>x</i> ($\times 10^5$)	<i>y</i> ($\times 10^5$)	<i>z</i> ($\times 10^5$)	$\pm(x, y, z; \frac{1}{2} + x, \frac{1}{2} - y, z)$			U_{11} ($\text{\AA}^2 \times 10^4$)	U_{12} ($\text{\AA}^2 \times 10^4$)	U_{13} ($\text{\AA}^2 \times 10^4$)	U_{22} ($\text{\AA}^2 \times 10^4$)	U_{23} ($\text{\AA}^2 \times 10^4$)	U_{33} ($\text{\AA}^2 \times 10^4$)	B_1 (\AA^2)	B_2 (\AA^2)	B_3 (\AA^2)
				$-2\pi^2(U_{11}a^*2l^2 + 2U_{12}a^*b^*hk + 2U_{13}a^*c^*hl + U_{22}b^*2k^2 + 2U_{23}b^*c^*kl + U_{33}c^*2l^2)$	B_1 are the principal radii of the vibration ellipsoids										
C(1)	34241 17	12730 8	68160 50	247 12	-73 10	32 9	192 13	5 11	192 13	5 9	181 11	1.10	1.43	2.36	
C(2)	28246 16	16331 9	60455 50	169 11	-65 10	74 9	279 13	-62 10	279 13	-62 10	199 12	1.02	1.31	2.64	
C(3)	29775 16	19503 8	41063 50	160 11	-11 9	44 9	210 13	-50 9	210 13	-50 9	190 11	1.14	1.25	1.98	
C(4)	37817 15	19131 8	29089 47	168 11	-29 9	45 9	170 9	-29 9	170 9	-29 9	183 11	1.10	1.25	1.72	
N(5)	39925 13	22288 6	10565 39	162 9	18 8	27 8	144 9	-4 7	144 9	-4 7	181 9	1.05	1.35	1.46	
C(6)	47660 15	21930 8	-463 46	150 10	-12 9	24 9	153 9	-38 9	153 9	-38 9	163 11	0.93	1.20	1.55	
C(7)	49518 16	25279 8	-19603 48	190 11	3 9	25 9	140 9	-6 9	140 9	-6 9	194 11	1.10	1.46	1.60	
C(8)	57232 17	24942 8	-30432 48	222 11	-28 9	40 9	179 13	-10 9	179 13	-10 9	187 11	1.30	1.46	1.86	
C(9)	63259 16	21302 8	-23751 49	168 11	-23 9	63 9	192 13	-4 9	192 13	-4 9	198 11	1.06	1.50	1.75	
C(10)	61639 15	17913 8	-5554 49	156 11	7 9	28 9	153 9	-15 9	153 9	-15 9	204 11	1.14	1.27	1.66	
C(11)	53627 15	18185 8	7033 48	162 11	-10 9	33 9	153 9	-15 9	153 9	-15 9	175 11	1.13	1.27	1.46	
N(12)	51566 13	14961 6	25587 40	167 9	12 8	37 8	153 9	11 7	153 9	11 7	197 10	1.16	1.32	1.58	
C(13)	43769 16	15449 8	36937 48	211 11	-32 9	29 9	162 9	-41 9	162 9	-41 9	168 11	0.95	1.52	1.80	
C(14)	41958 16	12214 8	56717 48	237 12	-49 9	46 9	157 9	-1 9	157 9	-1 9	175 11	1.05	1.36	2.04	
O(15)	23842 12	22866 6	33346 38	228 9	52 8	112 7	297 9	35 8	297 9	35 8	292 10	1.31	2.06	2.90	
O(16)	34534 11	25772 6	3163 37	200 8	56 7	68 7	175 9	34 7	175 9	34 7	300 9	1.02	1.74	2.49	
O(17)	56538 13	11520 6	33036 41	294 10	64 8	117 8	262 9	101 8	262 9	101 8	385 11	1.58	2.00	3.68	
O(18)	67152 11	14319 6	1281 37	200 8	60 7	106 7	227 9	49 7	227 9	49 7	298 9	1.11	1.64	2.80	
C(19)	74576 17	13869 9	-13775 56	197 11	34 10	105 10	236 13	-4 11	236 13	-4 11	333 14	1.17	1.96	2.73	

Table 1 (cont.)

Molecule B	x ($\times 10^5$)	y ($\times 10^5$)	z ($\times 10^5$)	U_{11} ($\text{\AA}^2 \times 10^4$)	U_{12} ($\text{\AA}^2 \times 10^4$)	U_{13} ($\text{\AA}^2 \times 10^4$)	U_{22} ($\text{\AA}^2 \times 10^4$)	U_{23} ($\text{\AA}^2 \times 10^4$)	U_{33} ($\text{\AA}^2 \times 10^4$)	B_1 (\AA^2)	B_2 (\AA^2)	B_3 (\AA^2)
C(20)	48274	34603	28744	255	17	-4	162	10	262	1.20	1.75	2.51
	17	8	53	12	10	10	13	10	13			
C(21)	43806	36896	47867	204	30	23	201	21	271	1.32	1.80	2.22
	16	8	53	12	10	10	13	10	13			
C(22)	47212	40865	60324	198	53	21	201	44	208	1.04	1.74	2.05
	16	8	51	11	10	10	13	10	12			
C(23)	55351	42691	52963	206	32	22	131	14	198	0.92	1.57	1.77
	16	8	49	11	9	9	9	11	11			
N(24)	58987	46656	64555	239	52	32	166	-24	199	1.02	1.59	2.16
	14	7	41	10	8	8	9	8	10			
C(25)	66737	48380	57815	205	35	-19	170	11	200	1.03	1.51	2.15
	16	8	49	11	9	9	13	9	12			
C(26)	70188	52464	70652	275	56	24	179	-11	245	1.21	1.87	2.48
	18	8	54	13	10	10	13	10	12			
C(27)	77808	54272	63843	304	17	-14	153	-13	262	1.15	1.79	2.88
	19	8	55	13	10	11	13	10	13			
C(28)	82325	52088	44437	232	-28	33	210	24	258	1.48	1.85	2.22
	17	9	54	12	10	10	13	10	13			
C(29)	79246	48060	31781	222	16	30	197	11	208	1.45	1.71	1.82
	17	8	50	12	10	10	13	10	12			
C(30)	71046	46103	37858	219	31	1	179	29	193	1.08	1.71	1.97
	17	8	50	12	9	9	13	9	12			
N(31)	67262	42192	25253	206	43	35	175	-5	199	1.12	1.56	1.87
	13	7	41	10	8	8	9	8	10			
C(32)	59595	40365	33396	200	41	2	162	29	187	0.94	1.62	1.85
	16	8	49	11	9	9	13	9	11			
C(33)	56072	36248	21398	249	33	13	148	-16	210	1.08	1.58	2.20
	17	8	50	12	10	10	9	9	12			
O(34)	42979	42956	79017	240	35	84	245	-24	276	1.37	2.18	2.33
	12	6	37	9	7	7	9	7	9			
O(35)	55082	48835	82779	290	35	100	245	-94	274	0.99	2.44	2.80
	13	6	37	9	8	8	9	7	9			
O(36)	70482	40155	5906	296	19	95	249	-63	251	1.25	2.33	2.56
	13	6	37	9	7	7	9	7	9			
O(37)	83584	45780	13905	242	0	81	266	-43	317	1.68	2.01	2.72
	12	6	38	9	8	8	9	8	10			
C(38)	92168	47444	10707	283	3	94	332	-48	397	2.04	2.48	3.35
	20	10	64	14	12	12	13	13	16			

the programs of Hall (Ahmed, Hall, Pippy & Huber, 1966). The signing of reflexions was carried out entirely by hand, using a stringent probability criterion and many checks for consistency. About ten symbols were assigned, but all of these were eventually eliminated. The signs of 555 reflexions were estimated, and only one of these ultimately proved to be incorrect. A Fourier synthesis of the E values indicated clearly the positions of all 38 non-hydrogen atoms in the asymmetric unit.

Refinement was begun by means of Fourier syntheses, and completed with eight cycles of block-diagonal least-squares analysis. The program used was that of Ahmed (Ahmed *et al.*, 1966), written in FORTRAN IV for the IBM system 360 computer. The quantity minimized is $\Sigma w(F_o - F_c)^2$. The matrices used are 3×3 for the position parameters and 6×6 (or 1×1 for isotropic thermal motion) for the thermal parameters of each atom. The scale of F_o and the overall isotropic temperature factor are refined with a 2×2 matrix (Cruickshank, 1961). Schomaker's correction is applied to the shifts of the thermal parameters (Hodgson & Rollett, 1963). The weighting scheme used was: $\sqrt{w} = 18/F_o$ for $F_o \geq 18$; $\sqrt{w} = F_o/18$ for $F_o < 18$. The nominal minimum observable value of F_o was 4.5. No convergence acceleration factors were used. Thermal motion was assumed to be isotropic for the hydrogen atoms (initially located in a difference map) and anisotropic for the others. The scattering factor curves of Hanson, Herman, Lea & Skillman (1964) were used throughout. A small correction for extinction was applied to the three most intense reflexions. It did not exceed 16% of the observed intensity for any reflexion and, considering the nature of the weighting scheme, was of negligible importance in the refinement. Unacceptable discrepancies between F_o and F_c were found for 6 weak reflexions. These reflexions (identified in Table 4) were omitted from the least-squares totals in the final cycles. In the last cycle no parameter shift for a non-hydrogen atom exceeded 0.3 e.s.d.'s. Final parameters for all atoms are given in Tables 1 and 2. It will be observed that the temperature factors for the hydrogen atoms are considerably smaller than the mean isotropic values for the atoms to which they are attached, and are sometimes negative. This is the typical result of using an inappropriate scattering-factor curve for bonded hydrogen.

Thermal motion and correction of bond lengths

Despite the working temperature of -160°C , thermal motion in the structure is appreciable, and it is necessary to consider the possible effects on the observed bond lengths. An analysis in terms of rigid-body modes has therefore been carried out in the manner described by Cruickshank (1956). The analysis is of course not entirely realistic, as it is impossible to specify a unique centre of libration. Such a centre has been assumed to lie at the centroid of the equally-weighted non-hydro-

Table 2. Final parameters (and e.s.d.'s) of hydrogen atoms

Molecule <i>A</i>	$\pm(x, y, z; \frac{1}{2} + x, \frac{1}{2} - y, z)$			<i>B</i>
	$\times 10^4$	$\times 10^4$	$\times 10^4$	
H(1)	3324	1060	7947	-0.35 Å ²
	19	10	58	0.52
H(2)	2337	1665	6870	-1.14
	17	8	50	0.44
H(7)	4563	2760	-2389	-0.77
	18	9	54	0.47
H(8)	5873	2732	-4233	-0.09
	20	10	60	0.55
H(9)	6833	2123	-3082	0.16
	20	10	62	0.58
H(14)	4696	950	6245	-1.10
	17	8	52	0.44
H(15)	2616	2454	2252	0.34
	21	11	64	0.61
H(19a)	7860	1643	-982	-0.59
	18	9	55	0.49
H(19b)	7776	1107	-683	0.51
	21	10	65	0.63
H(19c)	7249	1370	-3288	0.62
	21	11	64	0.64
Molecule <i>B</i>				
H(20)	4541	3166	2104	0.07
	20	10	61	0.56
H(21)	3802	3540	5297	-0.52
	18	9	56	0.51
H(26)	6675	5401	8418	0.15
	20	10	62	0.58
H(27)	7967	5712	7117	0.10
	20	10	61	0.57
H(28)	8726	5350	3983	-0.43
	19	9	56	0.52
H(33)	5960	3465	835	-1.03
	17	8	51	0.44
H(34)	4674	4558	8278	1.53
	24	11	71	0.74
H(38a)	9153	5052	114	0.83
	22	11	68	0.66
H(38b)	9452	4527	-217	0.60
	22	11	67	0.64
H(38c)	9656	4752	3076	0.69
	22	11	65	0.64

gen atoms of each molecule; however, only the 14-atom phenazine nuclei have been treated as rigid bodies. The results, summarized in Table 3, are reasonable: for each nucleus the r.m.s. deviation of observed from calculated U_{ij} 's is 0.0017 \AA^2 , compared with an average e.s.d. of 0.0009 \AA for the observed U_{ij} 's. The most important point is that the greatest amplitude of libration of either nucleus about any axis is only 1.8° , so that corrections to bond lengths in the phenazine nuclei are unnecessary. However, a further analysis which includes the four oxygen atoms of each molecule indicates increased librations, and worse agreement. It is thus reasonable to infer non-rigid behaviour (probably wagging) of the N-O and C-O bonds. These bonds have therefore been corrected for riding motion of the oxygen atoms (Busing & Levy, 1964). Because of the appreciable (though small) libration of the phenazine

nuclei these corrections have probably been somewhat overestimated. The situation for the methoxyl groups is more complicated. These groups undoubtedly behave non-rigidly, but the correlation between the motions of oxygen atom and methyl group is quite unknown. For the O-CH₃ distances, therefore, only upper and lower bounds can be given, and the range of possible values is quite large (Busing & Levy, 1964). Details of the bond lengths, and their corrections, are given in Table 5.

Assessment of results

The agreement between observed and calculated structure amplitudes is reasonable (Table 4), and there can be no doubt of the essential correctness of the proposed structure. The agreement residual ($R = \sum ||F_o| - |F_c|| / \sum |F_o|$) is 0.052, for observed reflexions only. A difference synthesis shows no detail inconsistent with the proposed structure, as the residual electron density does not exceed the limits $\pm 0.3 \text{ e.}\text{\AA}^{-3}$. The e.s.d. of position of the non-hydrogen atoms ranges from 0.0017 to 0.0031 Å, depending on type and thermal motion, and the average e.s.d. of bond lengths is 0.0035 Å. With the exception of the O-CH₃ distances (discussed in the previous section), differences between corresponding non-hydrogen bond lengths in the two mol-

ecules are not significant. This statement is true for both corrected and uncorrected values, and suggests that the nominal e.s.d.'s are realistic. For the O-CH₃ distances, however, the difference between the uncorrected values is 0.029 Å. As the nominal e.s.d.'s are 0.0031 Å and 0.0036 Å, the difference is certainly significant, and an explanation is necessary. Several hypotheses can be advanced:

- The true O-CH₃ distance differs significantly in the two otherwise identical molecules.
- Serious systematic errors in the intensity data affect the apparent O-CH₃ distance in one or both molecules. These errors either do not affect the other distances, or affect corresponding distances equally.
- The difference in the magnitude and character of the thermal motion of the two methoxy groups is sufficient to cause the observed difference in the apparent bond lengths.

Of these hypotheses, (c) seems by far the most plausible. The range of possible values for each O-CH₃ distance is given in Table 5. If it is assumed that the true distance is the same for each molecule, then it is reasonable to conclude that this distance lies somewhere in the region of overlap of the two ranges.

Table 3. *Rigid-body thermal parameters*
(Phenazine nucleus only)

Molecule A

Assumed centre of libration 6.982, 5.416, 0.790

$$\mathbf{T} = \begin{pmatrix} 156 & -1 & 0 \\ & 138 & -13 \\ & & 172 \end{pmatrix} \times 10^{-4} \text{ \AA}^2 \quad \mathbf{L} = \begin{pmatrix} 12 & & 5 \\ & 10 & 8 \\ & & 26 \end{pmatrix} \times 10^{-1} (\text{^\circ})^2$$

$$\sigma(\mathbf{T}) = \begin{pmatrix} 6 & & 6 \\ & 6 & 7 \\ & & 7 \\ & & & 8 \end{pmatrix} \times 10^{-4} \text{ \AA}^2 \quad \sigma(\mathbf{L}) = \begin{pmatrix} 12 & & 10 \\ & 6 & 6 \\ & & 5 & 9 \end{pmatrix} \times 10^{-1} (\text{^\circ})^2$$

Principal axes of T

Eigenvalue	Direction cosines ($\times 10^3$)		
0.0178	30	-312	950
0.0159	999	-29	-40
0.0135 Å ²	38	950	311

Principal axes of L

Eigenvalue	Direction cosines ($\times 10^3$)		
2.90	160	404	901
1.46	840	424	-339
0.43 (°) ²	519	-811	271

Molecule B

Assumed centre of libration 9.384, 13.088, 2.104

$$\mathbf{T} = \begin{pmatrix} 214 & & -16 \\ & 43 & 6 \\ & & 181 \end{pmatrix} \times 10^{-4} \text{ \AA}^2 \quad \mathbf{L} = \begin{pmatrix} 31 & & 5 \\ & 6 & -6 \\ & & 18 \end{pmatrix} \times 10^{-1} (\text{^\circ})^2$$

$$\sigma(\mathbf{T}) = \begin{pmatrix} 6 & & 6 \\ & 6 & 7 \\ & & 7 \\ & & & 9 \end{pmatrix} \times 10^{-4} \text{ \AA}^2 \quad \sigma(\mathbf{L}) = \begin{pmatrix} 12 & & 4 \\ & 10 & 12 \\ & & 4 \\ & & & 3 \end{pmatrix} \times 10^{-1} (\text{^\circ})^2$$

Principal axes of T

Eigenvalue	Direction cosines ($\times 10^3$)		
0.0240	884	417	-213
0.0183	89	297	951
0.0126 Å ²	460	-859	225

Principal axes of L

Eigenvalue	Direction cosines ($\times 10^3$)		
3.34	919	368	145
2.52	164	-688	707
0.98 (°) ²	359	-626	-692

The reference system is orthogonal, with $x||\mathbf{a}$, $y||\mathbf{b}$, $z||\mathbf{c}^*$

Table 4. Observed and calculated structure factors (x 10)

An asterisk following 10F0 indicates that the reflexion was too weak to observe; the estimated threshold value is given instead. A minus sign preceding 10F0 indicates that the reflexion has been omitted from the least-squares analysis.

Table with multiple columns for different reflections (L, FO, FC) and their corresponding observed and calculated values. The table is organized into several groups, each with a header row indicating the reflection type and a grid of numerical data below.

THE CRYSTAL STRUCTURE OF MYXIN

Table 4 (cont.)

A large grid of numerical data organized into columns and rows, representing crystal structure parameters for Myxin. Each row contains multiple columns of numbers, often grouped by a label like 'L FO FC' or 'H, K, L'. The data includes positive and negative integers, representing different structural coordinates or parameters.

Table 4 (cont.)

Table with multiple columns of numerical data, organized in a grid-like structure. Each column contains a series of numbers, some with signs, representing data points for various categories. The columns are labeled with letters and numbers (e.g., L FO FC, M FO FC, N FO FC, etc.), and the rows are labeled with letters and numbers (e.g., M FO FC, N FO FC, O FO FC, etc.).

Table 4 (cont.)

L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC	L	FD	FC
Mn 14, K= 4	-2 106	117 72	-4 114	-101	-2 246	262	-3 77	-72	0	110	105	-4 436	-27	0	74	50	Mn 16, K= 18	Mn 17, K= 7	Mn 17, K= 7	Mn 17, K= 17	Mn 18, K= 8	Mn 18, K= 8	Mn 18, K= 17	Mn 18, K= 17	Mn 18, K= 24	Mn 18, K= 24	Mn 18, K= 24	Mn 18, K= 31	Mn 18, K= 31						
0 52*	-6																																		
1 250	146																																		
2 194	-130																																		
3 270	255																																		
4 200	158																																		
5 143	14																																		
6 143	-140																																		
7 58	50																																		
8 50	-70																																		
Mn 14, K= 5	-1 453	463																																	
0 123	131																																		
1 250	350																																		
2 321	306																																		
3 311	-303																																		
4 92	71																																		
5 52	17																																		
6 46*	47																																		
7 127	117																																		
Mn 14, K= 6	-3 478	-13																																	
0 105	-101																																		
1 238	-241																																		
2 185	-183																																		
3 47	45																																		
4 200	-209																																		
5 42*	52																																		
6 98	105																																		
7 57	-35																																		
Mn 14, K= 7	-4 436	35																																	
0 235	-231																																		
1 548	-550																																		
2 140	138																																		
3 137	-126																																		
4 250	287																																		
5 157	-167																																		
6 227	-242																																		
7 81	-80																																		
Mn 14, K= 8	-4 73	73																																	
0 135	163																																		
1 47	61																																		
2 57	-56																																		
3 117	118																																		
4 61	46																																		
5 140	-12																																		
6 56	44																																		
Mn 14, K= 9	Mn 14, K= 16																																		
0 468	-38																																		
1 81	-80																																		
2 132	-126																																		
3 62*	37																																		
4 310	318																																		
5 132	-137																																		
6 112	-126																																		
7 45	-60																																		
Mn 14, K= 10	Mn 14, K= 17																																		
0 218	-220																																		
1 448	119																																		
2 37	64																																		
3 40*	36																																		
4 332	352																																		

The nominal e.s.d. of position of the hydrogen atoms is about 0.03 Å. However, the standard deviation of the lengths of the eighteen C-H distances in the structure is about 0.06 Å, and this value is probably a more realistic measure of the errors in the hydrogen positions.

Discussion

The molecular geometry is summarized in Figs. 1 and 2 and Tables 5 and 6. Both molecules are approximately planar, but each departs from planarity in a different way, doubtless because of differences in environment. Such differences may also be responsible for the marginally significant difference between the corresponding angles C(7)-C(8)-C(9) and C(26)-C(27)-C(28) ($\Delta = 1.1^\circ$; the difference is significant at the 0.1% level). For other pairs of corresponding angles, differences are not significant. Corresponding bond lengths (except, perhaps O-CH₃, previously discussed) are effectively equal, and it is appropriate to treat as definitive their mean values as in Fig. 1(b).

The N-O distances in the average molecule differ by 0.035 Å (a difference of only 0.016 Å would be significant at the 0.01% level). The reason for this difference may be the presence, on one side of the molecule, of the chelated hydrogen atom; the lone-pair electrons of the oxygen atom on this side of the molecule are presumably delocalized in forming the weak (OH)···O bond. On the other side of the molecule

Table 5. Comparison of intramolecular distances (Å) in the two independent molecules of myxin

	Uncorrected length	Corrected length	Mean	Mean e.s.d. × 1000
C(1)-C(2)	1.400	-	1.406	4
C(20)-C(21)	1.411	-		
C(2)-C(3)	1.374	-		
C(21)-C(22)	1.372	-		
C(3)-C(4)	1.438	-		
C(22)-C(23)	1.440	-	1.439	4
C(4)-N(5)	1.368	-		
C(23)-N(24)	1.367	-		
N(5)-C(6)	1.370	-		
N(24)-C(25)	1.365	-	1.368	3
C(6)-C(7)	1.416	-		
C(25)-C(26)	1.410	-		
C(7)-C(8)	1.361	-		
C(26)-C(27)	1.358	-	1.360	4
C(8)-C(9)	1.404	-		
C(27)-C(28)	1.411	-		
C(9)-C(10)	1.382	-		
C(28)-C(29)	1.377	-	1.380	4
C(10)-C(11)	1.448	-		
C(29)-C(30)	1.440	-		
C(11)-N(12)	1.380	-		
C(30)-N(31)	1.379	-	1.380	3
N(12)-C(13)	1.390	-		
N(31)-C(32)	1.393	-		
C(13)-C(14)	1.412	-		
C(32)-C(33)	1.406	-	1.409	4
C(14)-C(1)	1.383	-		
C(33)-C(20)	1.375	-		
C(4)-C(13)	1.415	-		
C(23)-C(32)	1.412	-	1.414	4

Table 5 (cont.)

	Uncorrected length	Corrected length	Mean	Mean e.s.d. $\times 1000$
C(6)—C(11)	1.428	—	1.426	4
C(25)—C(30)	1.425	—		
C(3)—O(15)	1.342	1.350	1.352	3
C(22)—O(34)	1.347	1.353		
C(10)—O(18)	1.349	1.356	1.358	3
C(29)—O(37)	1.353	1.359		
N(5)—O(16)	1.318	1.325	1.323	3
N(24)—O(35)	1.313	1.321		
N(12)—O(17)	1.273	1.287	1.288	3
N(31)—O(36)	1.280	1.288		
O(18)—C(19)	1.446	1.446	1.446 to 1.498	
		1.521		
		1.418		
O(37)—C(38)	1.417	1.498		
O(15)—O(16)	2.511	—	2.503	
O(34)—O(35)	2.496	—		
O(17)—O(18)	2.546	—	2.549	
O(36)—O(37)	2.553	—		
O(15)—H(15)	0.84	—	0.90	70
O(34)—H(34)	0.96	—		
O(16)—H(15)	1.74	—	1.66	70
O(35)—H(34)	1.58	—		
C(1)—H(1)	0.86	—	0.94	60
C(20)—H(20)	1.01	—		
C(2)—H(2)	0.90	—	0.97	60
C(21)—H(21)	1.04	—		
C(7)—H(7)	0.90	—	0.96	60
C(26)—H(26)	1.01	—		
C(8)—H(8)	0.96	—	0.95	60
C(27)—H(27)	0.93	—		
C(9)—H(9)	0.89	—	0.90	60
C(28)—H(28)	0.91	—		
C(14)—H(14)	1.10	—	1.06	60
C(33)—H(33)	1.01	—		
C(19)—H(19 <i>a</i>)	0.96	—		
C(19)—H(19 <i>b</i>)	0.98	—		
C(19)—H(19 <i>c</i>)	0.93	—	0.99	60
C(38)—H(38 <i>a</i>)	1.01	—		
C(38)—H(38 <i>b</i>)	1.00	—		
C(38)—H(38 <i>c</i>)	1.08	—		

absence of such a bond allows the lone-pair electrons to remain localized on the oxygen atom, and thus to contribute to the ionic character of the N—O bond. The result should be a shorter bond, as observed. It is therefore surprising to learn that this oxygen atom is the more easily removed by reduction (Edwards, 1967). One might naively predict the opposite, assuming bond length to be a criterion of bond strength.

The O—H---O distance in the average molecule is 0.046 Å less than the equivalent non-bonded distance O---OCH₃. This quantity is presumably the reduction which results from the presence of the chelated hydrogen atom.

It remains to describe some unusual intermolecular relationships in the structure. In Fig. 2(b) it can be seen that molecule *B* is very close to the one related to it by the centre of symmetry at $\frac{1}{2}, \frac{1}{2}, 1$. Moreover, this centre lies only 0.041 Å from the mean plane of the phenazine nucleus of either molecule, and it follows that the two molecules are practically coplanar. This circumstance, together with the unusual proximity, suggests some sort of bonding, as otherwise packing

considerations might be expected to favour a staggered arrangement. (Such bonding, however, is apparently not strong enough to override packing considerations elsewhere in the structure, as the intermolecular contacts of molecule *A* are quite normal.) The observed distance O(35)---O(35) (1) is 2.553 Å, with e.s.d. 0.004 Å. If the thermal motion of these atoms is reasonably assumed to be non-correlated, the corrected distance is 2.577 Å, but in any case the upper bound is only 2.602 Å (Busing & Levy, 1964). This is very much less than the sum of van der Waals radii (2.80 Å); it is in fact in the range of distances usually reported for O—H---O bonds, but there is no hydrogen atom,

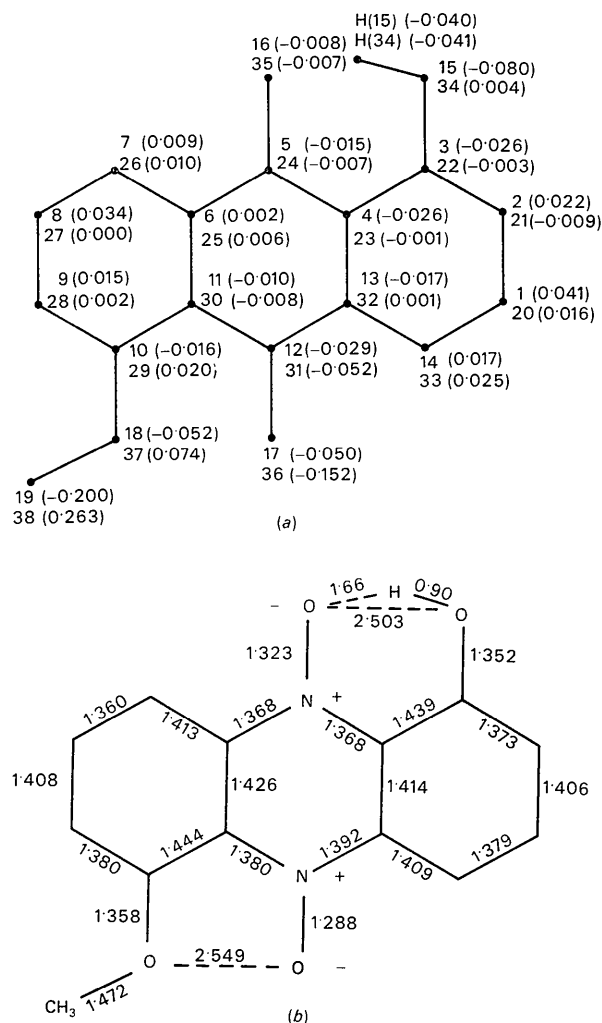


Fig. 1. Molecular geometry. (a) The numbering scheme for both molecules, and the distances (Å) of the non-hydrogen atoms, and of the chelated hydrogen atoms, from the mean plane of the appropriate phenazine nucleus. The equations of these mean planes are: Molecule *A*, $0.3743x + 0.5423y + 0.7522z - 6.1655 = 0$; Molecule *B*, $0.4223x - 0.5230y + 0.7404z + 1.3344 = 0$. (The reference system is orthogonal, with $x||a; y||b, z||c^*$.) (b) Intramolecular distances (Å). The formal charges also are indicated on this sketch (Edwards & Gillespie, 1966).

nor any significant residual electron density in the region between these atoms. The distance O(35)---H(34) (1) (2.39 Å with e.s.d. 0.06 Å) is also significantly less than the corresponding sum of van der Waals radii (2.60 Å).

No other intermolecular distance in the structure is significantly less than the sum of the appropriate van der Waals radii. Minimum values for non-hydrogen atoms [other than those given in Fig. 2(b)] are: O---O, 3.37 Å; N---O, 3.08 Å; N---N, 3.28 Å; C---O, 3.12 Å; C---N, 3.26 Å; C---C, 3.13 Å. The last

quantity is the distance between the methyl carbon atom C(38) and the one related to it by the centre of symmetry at $1, \frac{1}{2}, 0$, and is unusually small. However, the shortest H---H distance involved in this contact is 2.43 Å, and there is therefore no violation of packing principles. (Perhaps the most surprising aspect of this short methyl-methyl distance is that it has not been reported before. A possible reason is that most observations have been made for structures at room temperature, and presumably most of the methyl groups studied have been in a condition of hindered rotation.

Table 6. Comparison of bond angles in the two independent molecules of myxin

		Mean			Mean
C(2)—C(1)—C(14)	121.6°	} 121.8°	C(13)—N(12)—O(17)	117.8°	} 117.8°
C(21)—C(20)—C(33)	122.1		C(32)—N(31)—O(36)	117.9	
C(1)—C(2)—C(3)	121.3	} 121.0	C(4)—C(13)—C(14)	120.6	} 120.8
C(20)—C(21)—C(22)	120.8		C(23)—C(32)—C(33)	120.9	
C(2)—C(3)—C(4)	118.7	} 118.6	C(4)—C(13)—N(12)	120.8	} 120.4
C(21)—C(22)—C(23)	118.4		C(23)—C(32)—N(31)	120.1	
C(2)—C(3)—O(15)	120.6	} 120.4	N(12)—C(13)—C(14)	118.6	} 118.8
C(21)—C(22)—O(34)	120.1		N(31)—C(32)—C(33)	119.0	
C(4)—C(3)—O(15)	120.7	} 121.1	C(1)—C(14)—C(13)	118.4	} 118.3
C(23)—C(22)—O(34)	121.5		C(20)—C(33)—C(32)	118.2	
C(3)—C(4)—N(5)	121.6	} 121.2	C(10)—O(18)—C(19)	116.4	} 116.6
C(22)—C(23)—N(24)	120.9		C(29)—O(37)—C(38)	116.9	
C(3)—C(4)—C(13)	119.3	} 119.4	C(3)—O(15)—H(15)	106	} 102
C(22)—C(23)—C(32)	119.5		C(22)—O(34)—H(34)	99	
N(5)—C(4)—C(13)	119.1	} 119.4	N(5)—O(16)—H(15)	99	} 99
N(24)—C(23)—C(32)	119.6		N(24)—O(35)—H(34)	99	
C(4)—N(5)—C(6)	121.1	} 121.1	C(2)—C(1)—H(1)	123	} 119
C(23)—N(24)—C(25)	121.1		C(21)—C(20)—H(20)	116	
C(4)—N(5)—O(16)	120.2	} 120.1	C(14)—C(1)—H(1)	115	} 119
C(23)—N(24)—O(35)	120.0		C(33)—C(20)—H(20)	122	
C(6)—N(5)—O(16)	118.6	} 118.8	C(1)—C(2)—H(2)	120	} 119
C(25)—N(24)—O(35)	119.0		C(20)—C(21)—H(21)	118	
N(5)—C(6)—C(7)	118.9	} 118.6	C(3)—C(2)—H(2)	119	} 120
N(24)—C(25)—C(26)	118.4		C(22)—C(21)—H(21)	121	
C(5)—C(6)—C(11)	120.0	} 120.0	C(6)—C(7)—H(7)	119	} 119
C(24)—C(25)—C(30)	120.0		C(25)—C(26)—H(26)	119	
C(7)—C(6)—C(11)	121.0	} 121.3	C(8)—C(7)—H(7)	122	} 122
C(26)—C(25)—C(30)	121.6		C(27)—C(26)—H(26)	122	
C(6)—C(7)—C(8)	118.9	} 119.0	C(7)—C(8)—H(8)	119	} 119
C(25)—C(26)—C(27)	119.2		C(26)—C(27)—H(27)	118	
C(7)—C(8)—C(9)	121.9	} 121.4	C(9)—C(8)—H(8)	119	} 120
C(26)—C(27)—C(28)	120.8		C(28)—C(27)—H(27)	121	
C(8)—C(9)—C(10)	121.2	} 121.4	C(8)—C(9)—H(9)	119	} 119
C(27)—C(28)—C(29)	121.7		C(27)—C(28)—H(28)	118	
C(9)—C(10)—C(11)	119.0	} 119.0	C(10)—C(9)—H(9)	119	} 120
C(28)—C(29)—C(30)	119.1		C(29)—C(28)—H(28)	120	
C(9)—C(10)—O(18)	123.5	} 123.4	C(13)—C(14)—H(14)	117	} 117
C(28)—C(29)—O(37)	123.4		C(32)—C(33)—H(33)	117	
C(11)—C(10)—O(18)	117.6	} 117.6	C(1)—C(14)—H(14)	124	} 124
C(30)—C(29)—O(37)	117.6		C(20)—C(33)—H(33)	125	

Table 6 (cont.)

		Mean			Mean
C(6)—C(11)—C(10)	118.0	117.8	O(18)—C(19)—H(19a)	110	109
C(25)—C(30)—C(29)	117.5		O(18)—C(19)—H(19b)	106	
C(6)—C(11)—N(12)	119.5	O(18)—C(19)—H(19c)	111		
C(25)—C(30)—N(31)	119.5	O(37)—C(38)—H(38a)	110		
C(10)—C(11)—N(12)	122.5	O(37)—C(38)—H(38b)	106		
C(29)—C(30)—N(31)	123.0	O(37)—C(38)—H(38c)	110		
C(11)—N(12)—C(13)	119.4	119.5	H(19a)—C(19)—H(19b)	109	110
C(30)—N(31)—C(32)	119.6		H(19b)—C(19)—H(19c)	111	
C(11)—N(12)—O(17)	122.9	H(19c)—C(19)—H(19a)	110		
C(30)—N(31)—O(36)	122.4	H(38a)—C(38)—H(38b)	107		
		H(38b)—C(38)—H(38c)	111		
		H(38c)—C(38)—H(38a)	113		

E.s.d.'s of angles not involving hydrogen range from 0.19 to 0.24°.

E.s.d.'s of angles involving hydrogen are about 4°.

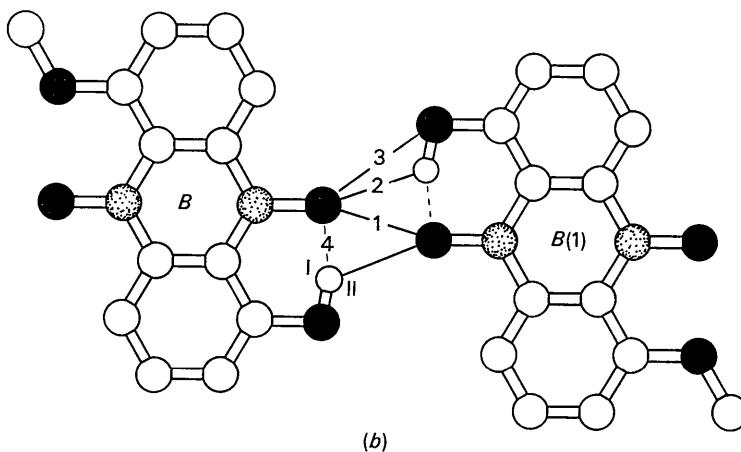
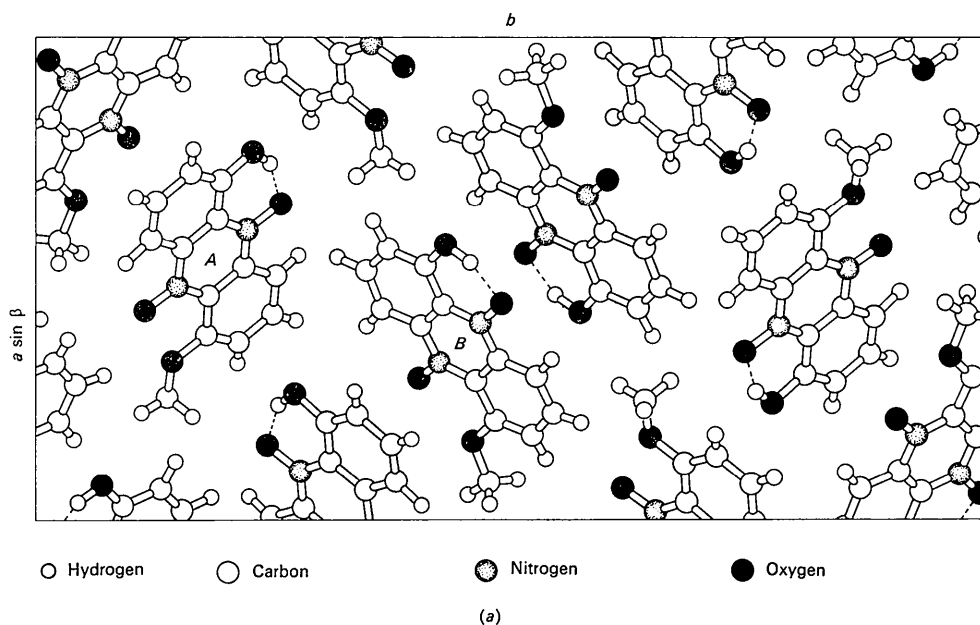


Fig. 2. Packing details. (a) The structure, viewed along c . (b) Molecules B and $B(1)$ (related by the centre at $\frac{1}{2}, \frac{1}{2}, 1$) viewed normal to the mean plane of the phenazine nucleus. The distances indicated are: 1, O(35)—O(35)(1) = 2.553 Å (2.577 Å if corrected for non-correlated thermal motion); 2, O(35)—H(34)(1) = 2.39 Å; 3, O(35)—O(34)(1) = 3.028 Å; 4, O(35)—H(34) = 1.58 Å. The angles indicated are: I, O(34)—H(34)—O(35) = 159°; II, O(34)—H(34)—O(35)(1) = 124°.

A rotator can be expected to require more space than a stationary group; perhaps the short distance in this case indicates that the group is really stationary.) This comparison of C---C and H---H distances emphasizes the necessity of considering the positions of any hydrogen atoms involved in intermolecular contacts. The shortest intermolecular distances involving hydrogen atoms [other than those given in Fig. 2(b)] are, with their e.s.d.'s: O---H, 2.49 (6) Å; N---H, 3.25 (6) Å; H---H, 2.30 (9) Å. None of these distances is significantly less than the sum of appropriate van der Waals radii. It therefore seems unlikely that the exceptional distances given in Fig. 2(b) represent a reduction in the van der Waals radii resulting from the low temperature.

A more plausible explanation of the unusual proximity is that the hydrogen atom H(34) participates in a bifurcated bond, joining O(34) not only to O(35) but also to O(35) (1). The combined pull of the two weak symmetry-related bonds O(34)–H(34)---O(35) (1) and O(34) (1)–H(34) (1)---O(35) is sufficient to balance the repulsion between O(35) and O(35) (1). However, there are some objections to this hypothesis. The distance O(34)---O(35) (1) is 3.028 Å, and thus is readily explicable as a normal van der Waals contact. Also, if H(34) were even weakly bonded to O(35) (1), it could be expected to move towards that atom, with a consequent increase in the angle C(22)–O(34)–H(34). In fact this angle is 99°, compared with the corresponding value of 106° in molecule *A*. The e.s.d. of these angles is about 4°, so that the difference is probably not significant; however such evidence as is available does not support the hypothesis. Finally, it can be seen in Fig. 2(b) that the opposing attractive and repulsive forces are not in equilibrium; O(34)---O(35) (1) could be reduced, and O(35)---O(35) (1) increased by a translation of the molecule parallel to the long axis of

the phenazine nucleus. In spite of these objections, the hypothesis of the bifurcated hydrogen bond is probably the best that can be advanced at this time. It is hoped that work now in progress in this laboratory on the crystal structure of iodinin (II) will throw additional light on the problem.

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The Crystal and Molecular Structure of L-Cysteine

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The structure of L-cysteine, HSCH₂.CH(NH₂).COOH, has been determined from three-dimensional X-ray diffraction data, and refined until $R=0.127$. The crystals are monoclinic, $P2_1$, with $a=11.51$, $b=5.240$, $c=9.517$ Å, $\beta=109.13^\circ$. The bond lengths and angles in the two cysteine molecules (zwitterions) in the asymmetric unit are not significantly different from each other or from expected values, but their conformations differ by twists of 118° around the C _{α} –C _{β} bond and 33° around C–C _{α} bond.

The crystal structure of L-cysteine,
HS.CH₂.CH(NH₂).COOH,
has been determined. The free amino acid was

obtained from L-cysteine hydrochloride by neutralization with sodium hydroxide and crystallization from hot water.