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The Crystal and Molecular Structure of the Alkaloid Jamine, $C_{21}H_{35}N_3$ from *Ormosia jamaicensis*

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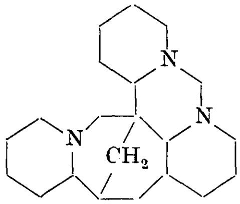
A number of related alkaloids of unknown structure have been isolated from the *Ormosia* species. The molecular structure and stereoconfiguration of one of the alkaloids, $C_{21}H_{35}N_3$, has been elucidated. The space group is $P\bar{1}$ with cell dimensions: $a = 6{\cdot}79$, $b = 10{\cdot}61$, $c = 13{\cdot}41$ Å; $\alpha = 95°$, $\beta = 97° \, 20'$, $\gamma = 103° \, 55'$. The molecule is composed of six six-membered rings, five of which have the chair configuration and one the boat configuration. The chemical formula is found to be



Since the alkaloid is in the form of a free base, there is no hydrogen bonding.

The structure was solved by obtaining phases directly from the structure factor magnitudes by the symbolic addition procedure. By hand computation, 286 phases were determined from which a well-resolved E-map was computed.

Introduction

The seeds of *Ormosia panamensis* Benth. and related species contain a number of related alkaloids (Lloyd & Horning, 1958, 1960, 1961; Konovalova, Diskina & Rabinovich, 1951; Hassall & Wilson, 1961; Hess & Merck, 1919; Eisner & Šorm, 1959; Clarke & Grundon, 1960, 1963). One of these alkaloids is ormosanine, $C_{20}H_{35}N_3$, which forms an adduct with formaldehyde to give $C_{21}H_{35}N_3$. This formaldehyde adduct is identical to the naturally occurring alkaloid jamine in *Ormosia jamaicensis* (Naegeli, Wildman & Lloyd, 1963). The molecular structures of these alkaloids have not been known. Recently a detailed chemical study has been published (Naegeli, Wildman & Lloyd, 1963; Naegeli, Naegeli, Wildman & Highet, 1963), along with a preliminary account of the molecular structure (Karle & Karle, 1963*a*).

Experimental

Crystals of jamine were kindly supplied by Drs H. A. Lloyd and P. Naegeli of the National Institutes of Health. The material is colorless and crystallizes in very thin laths with irregular edges. Jamine occurs naturally as a racemate, hence it may be expected that the material crystallizes in a centrosymmetric space group.

The long edge of the crystals was parallel to the a axis. A crystal was mounted on the a axis and equi-inclination Weissenberg photographs for layers 0 through 4 and precession photographs for $hk0$, $hk1$, $h0l$ and $h1l$ were taken. It was found that the unit cell is triclinic with the following dimensions:

$a = 6{\cdot}79 \mp 0{\cdot}02$ Å $\alpha = 95° \; 0' \mp 20'$
$b = 10{\cdot}61 \mp 0{\cdot}02$ Å $\beta = 97° \; 20' \mp 20'$
$c = 13{\cdot}41 \mp 0{\cdot}03$ Å $\gamma = 103° \; 55' \mp 20'$

For two molecules in the unit cell, the density was computed to be 1·184.

The intensities were estimated visually with a calibrated film strip. These data were punched on IBM cards directly from the primary data sheets and processed on the IBM 7090 computer (Norment, 1962). The computer corrected the data for spot size, Lorentz and polarization factors and adjusted the data to an absolute scale. In addition to the structure factor magnitudes, $|F|$, the normalized structure factor magnitudes, $|E|$, were computed. For a triclinic space group,

$$E_{\mathbf{h}}^2 = F_{\mathbf{h}}^2 \Big/ \sum_{j=1}^{N} f_{j\mathbf{h}}^2 \qquad (1)$$

where N is the number of atoms in the unit cell, and f_j is the atomic scattering factor for the jth atom. The total number of data read was 1831, including 307 reflections which were assigned zero intensity. Statistical averages for the normalized structure factors are listed in Table 1. The experimental values

Table 1. *Normalized structure factors*

	Experimental	Centrosym.	Non-centrosym.
$\langle \lvert E \rvert \rangle$	0·728	0·798	0·886
$\langle \lvert E^2-1 \rvert \rangle$	1·083	0·968	0·736
$\langle \lvert E \rvert^2 \rangle$	0·994	1·000	1·000

are compared with theoretical values computed for crystals with randomly distributed atoms. The statistical averages imply that the crystal is centrosymmetric and that its space group is therefore $P\bar{1}$.

Phase determination

The phases were determined by the symbolic addition procedure (Karle & Karle, 1963*b* and to be published). The origin was specified by assigning signs to three linearly independent reflections (Hauptman & Karle, 1953). In addition, the signs of five other reflections were specified with a letter. These eight assignments, which form the basic set for applying the Σ_2 formula, are shown in Table 2.

Table 2. *Assignment of three origin specifying reflections and five other reflections as a starting set for the application of* Σ_2

Sign	*hkl*	$\lvert E \rvert$
+	$1\bar{1}\bar{7}$	3·76
+	214	6·89
+	352	4·74
a	0,2,10	2·63
b	361	4·82
c	019	2·28
d	$1\bar{9}2$	3·15
g	$02\bar{2}$	2·30

The Σ_2 formula is (Hauptman & Karle, 1953)

$$sE_{\mathbf{h}} \sim s \sum_{\mathbf{k}} E_{\mathbf{k}} E_{\mathbf{h}-\mathbf{k}} \tag{2}$$

where *s* means 'sign of'. It is the counterpart, from the probability point of view, of the general inequality (34) of Karle & Hauptman (1950).

The reflections chosen to have signs *a*, *b*, *c*, *d* and *g* (where each letter represents + or −) were selected on the basis that they had many relationships applicable to the Σ_2 formula among themselves and with the origin specifying reflections. The letters were assigned one at a time as needed to proceed with (2). In addition, the assignments are all associated with large values for $|E|$, giving high probabilities that the indications from the Σ_2 formula are correct. The probability that the sign of $E_{\mathbf{h}}$ is plus is determined by the formula (Woolfson, 1954; Hauptman & Karle, 1953)

$$P_+(E_{\mathbf{h}}) = \tfrac{1}{2} + \tfrac{1}{2} \tanh \frac{\sigma_3 |E_{\mathbf{h}}| \sum_{\mathbf{k}} E_{\mathbf{k}} E_{\mathbf{h}-\mathbf{k}}}{\sigma_2^{3/2}} \tag{3}$$

where

$$\sigma_n = \sum_{j=1}^{N} Z_j^n ,$$

Z_j being the atomic number of the *j*th atom in a cell containing *N* atoms. In the course of application, as many combinations as possible were used to determine each phase. To facilitate the application of Σ_2, a computer program was prepared to list the sets of interacting pairs for each *hkl* arranged in order of decreasing $|E|$ values. In this manner, 203 phases for reflections with $|E| > 1{\cdot}5$ were determined as a function of *a*, *b*, *c*, *d* and *g*. It should be emphasized that it is feasible to perform the entire phase determination by hand without the aid of a high-speed computer.

In order to reduce the number of unknowns, other types of phase determining relations could be applied. In this determination, only the Σ_1 formula for space group $P\bar{1}$ was used (Hauptman & Karle, 1953),

$$sE_{2\mathbf{h}} \sim s(E_{\mathbf{h}}^2 - 1) \,. \tag{4}$$

The probability that $E_{2\mathbf{h}}$ be positive can be computed from the relationship

$$P_+(E_{2\mathbf{h}}) = \tfrac{1}{2} + \tfrac{1}{2} \tanh \frac{\sigma_3 |E_{2\mathbf{h}}| (E_{\mathbf{h}}^2 - 1)}{2\sigma_2^{3/2}} \tag{5}$$

where

$$\sigma_n = \sum_{j=1}^{N} Z_j^n \,.$$

The application of (4) and (5) to the reflection $04\bar{4}$ whose $|E| = 1{\cdot}52$ indicated that it had a positive sign with a probability of 0·88. Since the phase of the $04\bar{4}$ reflection was determined to be *c* from Σ_2 and probably + from Σ_1, *c* was tentatively assigned the + value (which proved to be correct).

The remaining four unknown symbols gave rise to the sixteen possibilities listed in Table 3. Some simple criteria were used for eliminating most of the possibilities. Those sets with a large number of

Table 3. *Sets of possible phases based on the four unknowns, a, b, d and g*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
a	−	+	+	−	+	−	+	−	−	+	+	−	−	+	+	−
b	−	−	−	−	+	+	+	+	−	−	−	−	+	+	+	+
d	−	−	−	−	+	+	+	+	+	+	+	+	−	−	−	−
g	+	+	−	−	+	+	−	−	+	−	+	−	+	−	+	−
No. positive	105		94		203			92	94	90					124	86
No. negative	98		93		0			94	98	101					68	106
No. indeterminate	0	37	16	40	0	35	40	17	11	12	40	34	40	34	11	11

indeterminate phases were considered unlikely possibilities. For example, if, for a particular reflection, the Σ_2 relation gave a nearly equal number of phase indications a and bg, then the phase would be indeterminate for some of the combinations listed in Table 3, *e.g.* set 2. Eight of the sets in Table 3 had 34 or more indeterminate phases, as compared with 17 or less for the other eight sets, and therefore were eliminated from initial consideration. Furthermore, set 5, having all positive signs, and set 15, having a large predominance of positive signs, were eliminated since an atom at the origin was not expected.

Set 1 did not have any Σ_2 inconsistencies, which was an unusual occurrence. The E-map, a three-dimensional Fourier map with E values rather than F values for the coefficients, computed for the combination of signs in set 1 was not at all meaningful. This is an illustration of a pitfall of sign determining procedures based solely on chains of positivity for the products of signs occurring in individual Σ_2 terms.

An additional criterion used to choose the more probably correct combinations among the remaining sets in Table 3 was based on space considerations. For two rather large molecules to be accommodated in the unit cell, the reflections 002 and 020, which had moderately large $|E|$ values, should probably both be negative. Each of these reflections had many Σ_2 contributors and the phase of each was determined to be abc. Since c is probably $+$, a and b should have opposite signs. Sets 3, 8, 10 and 16 satisfy these criteria. Three-dimensional E-maps were computed with the use of the $+$ and $-$ values for a, b, d and g, as indicated in sets 3, 8, 10 and 16. The map from set 16 was the correct one. Set 10 produced a map very similar to 16 except that the whole molecule was translated too close to a center of symmetry. Maps from sets 3 and 8 revealed only a portion of the molecules.

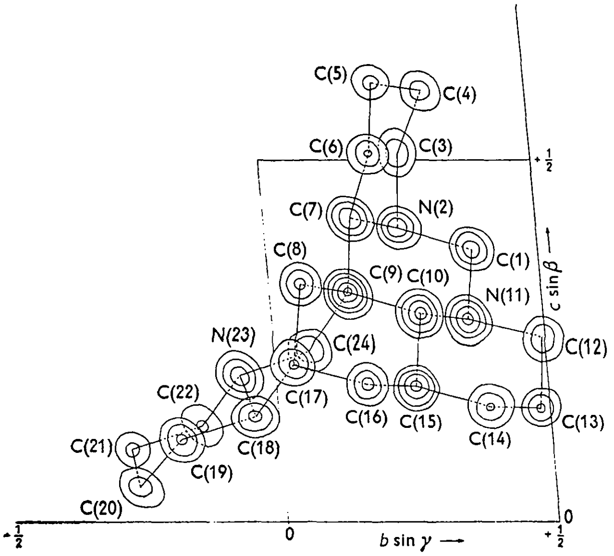


Fig. 1. Sections of a three-dimensional E-map projected on the (100) plane. 286 terms with $|E| > 1{\cdot}35$ and the phases determined from the symbolic addition procedure were used. The contours are at equally spaced, arbitrary levels.

The density map computed from set 16 contained 192 terms or eight terms per atom (excluding H atoms). It was not as well resolved as E-maps obtained in our previous structure determinations (mostly in space group $P2_1/c$). Hence phases were obtained for 94 additional reflections with $|E|$ values as low as 1·35 giving a total of 286 phases or nearly 12 terms per atom. The three-dimensional E-map computed with 286 terms is illustrated in Fig. 1. Sections through areas of maximum density are projected on the (100) plane. The 24 largest peaks corresponded to the 24 atoms in the molecule. At this point, the three nitrogen atoms were indistinguishable from the carbon atoms. It was shown later that all 286 phases were correctly determined.

Structure

The coordinates of the twenty-four atoms as read from the density map in Fig. 1 were subjected to a least-squares refinement with the ORFLS program (Busing, Martin & Levy, 1962) which was adapted in our laboratory to the IBM 7030 (STRETCH). Individual scale factors were used for each level ($h=0 \rightarrow 7$) since diffraction data could be obtained only about the a axis. Initially all atoms were weighted equally, as carbon atoms, and isotropic temperature factors were used. After the second cycle the R index was 22%. At this point, the isotropic temperature factors for atoms 2, 11 and 23 were considerably lower, about 2·0, than those for the remainder of the atoms, where B was greater than 3·3. It seemed reasonable that these three atoms were the nitrogen atoms. Another cycle of refinement with isotropic temperature factors and atoms 2, 11 and 23 weighted as nitrogen atoms reduced R to 20·7% and increased the B values for these atoms to greater than 3·3. Two cycles of refinement with anisotropic temperature factors brought R to 16·9%. No hydrogen atoms were included in the refinement. The value of R is not unreasonable considering the fact that the crystals were very thin and rather irregular. The data could be collected only along one axis. The fractional coordinates and anisotropic temperature factors are tabulated in Table 4.

An electron density map computed with all the data is illustrated in Fig. 2. Atoms 2, 11 and 23 designated as nitrogen atoms are appropriately heavier than the remainder of the atoms which are carbons. The molecule is composed of six six-membered rings, five of which have the chair configuration. The ring formed by atoms C(9)C(8)C(17)C(18)N(23)C(24) has the boat configuration, dictated, perhaps, by steric hindrance. There are six asymmetric carbon atoms in the molecule at C(7), C(9), C(10), C(15), C(17)

Table 4. *Fractional coordinates for jamine*

The thermal parameters are of the form $T = \exp\,[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)$.
Each thermal parameter is multiplied by 10^4

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0·1382	0·3760	0·3810	183	89	52	−13	38	−10
N(2)	0·0436	0·2501	0·4104	163	95	42	−7	34	−16
C(3)	0·9407	0·2645	0·4999	120	189	61	−32	35	−25
C(4)	0·1060	0·3114	0·6007	259	170	45	17	18	−21
C(5)	0·2397	0·2179	0·6134	210	135	42	−44	12	−4
C(6)	0·3522	0·2030	0·5180	180	135	43	−49	2	3
C(7)	0·1747	0·1605	0·4231	132	87	42	−11	21	−20
C(8)	0·4181	0·0593	0·3307	146	100	61	62	29	−8
C(9)	0·2622	0·1396	0·3210	156	70	38	−43	19	−13
C(10)	0·3588	0·2739	0·2888	181	79	47	−27	43	−5
N(11)	0·2141	0·3592	0·2825	220	80	48	4	35	−3
C(12)	0·3126	0·4906	0·2606	372	87	58	−7	63	11
C(13)	0·3955	0·4852	0·1572	296	122	71	33	68	8
C(14)	0·5445	0·3937	0·1591	234	107	71	−41	67	7
C(15)	0·4348	0·2581	0·1854	184	87	59	1	51	1
C(16)	0·5723	0·1628	0·1871	202	94	80	−4	58	8
C(17)	0·4761	0·0307	0·2219	105	116	63	−30	16	−9
C(18)	0·2726	0·9525	0·1517	59	92	61	−7	39	−9
C(19)	0·3038	0·8145	0·1156	156	102	82	13	−9	−27
C(20)	0·1005	0·7322	0·0461	114	117	74	21	16	−20
C(21)	0·9186	0·7254	0·0979	136	98	66	−19	39	−20
C(22)	0·9011	0·8656	0·1342	149	113	55	−18	3	−26
N(23)	0·0959	0·9365	0·2012	75	66	55	−18	18	−13
C(24)	0·0672	0·0648	0·2420	81	87	51	−12	−10	4
Standard error									
C	0·0020	0·0012	0·0009	25	15	8	19	14	8
N	0·0016	0·0009	0·0007	20	11	6	15	11	6

and C(18). The bonds to the three nitrogen atoms form pyramids with nearly tetrahedral angles. Another view of the stereoconfiguration is shown in Fig. 3. The individual bond lengths and bond angles are shown in Fig. 4. The average of twenty C–C bond lengths is 1·555 Å and the average of nine C–N bond lengths is 1·470 Å. The average of twenty-five C–C–C angles is 109·8°, ten N–C–C angles 110·7° and nine C–N–C angles 111·1°.

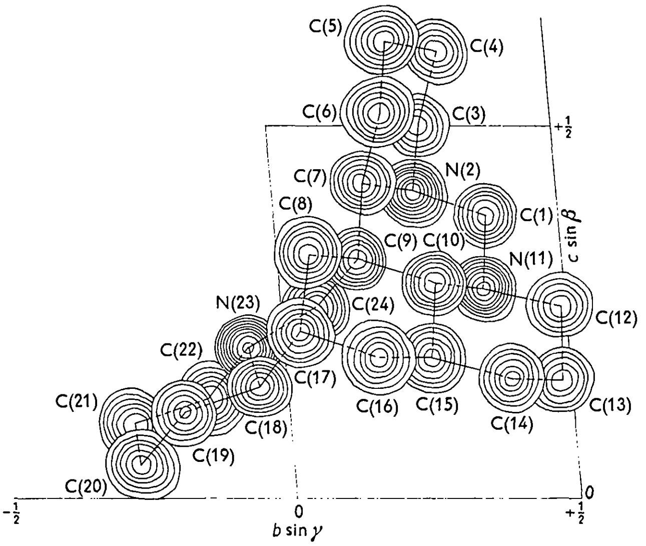


Fig. 2. Sections of a three-dimensional electron density map employing all the data. The contours are spaced at 1 e.Å^{-3}, starting with the 1 e.Å^{-3} contour.

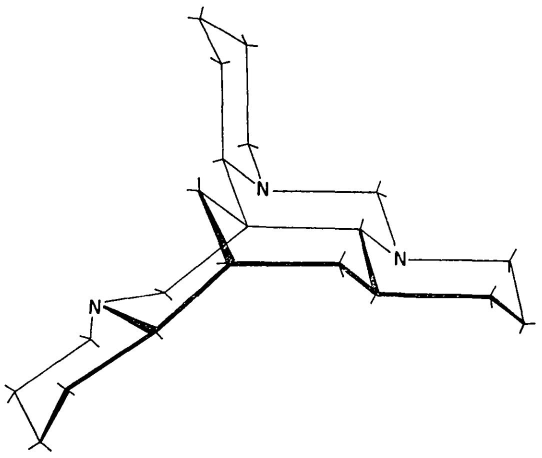


Fig. 3. A view of the stereoconfiguration of jamine.

The molecule is in the form of a free base, hence there is no hydrogen bonding. There are no close approaches between molecules. The shortest intermolecular distances are between C(13) and C(19′) at 3·77 Å and between C(13) and C(20″) at 3·72 Å. All other intermolecular distances are greater than 3·80 Å.

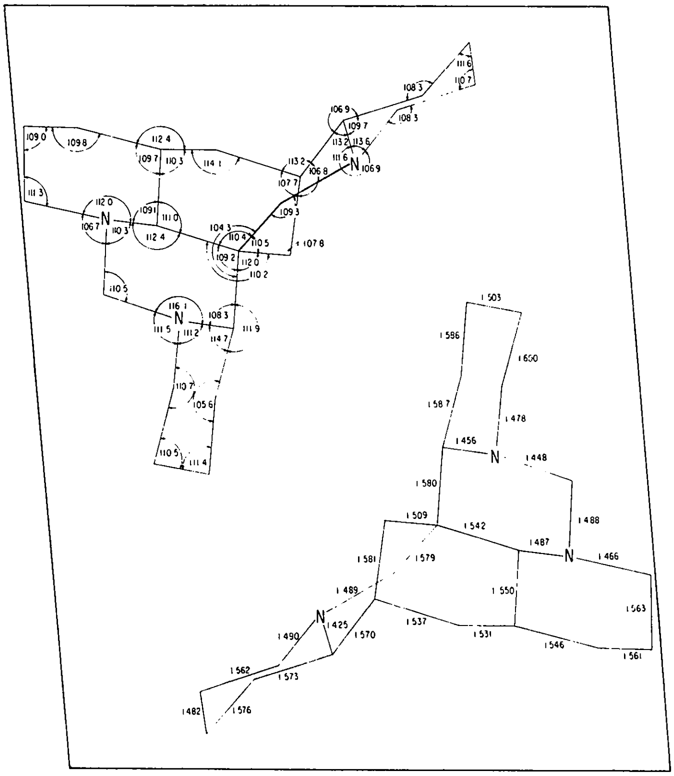


Fig. 4. Bond distances and angles in jamine. See Fig. 2 for the numbering of the atoms. The standard deviation for the bond lengths is 0·019 Å and for the angles 1·1°.

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