

## The Triplet Monoclinic and Co-Crystallizing Triclinic Polymorphs of the Quasi-Racemates of (–)-Podopetaline and (–)-Ormosanine

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### Abstract

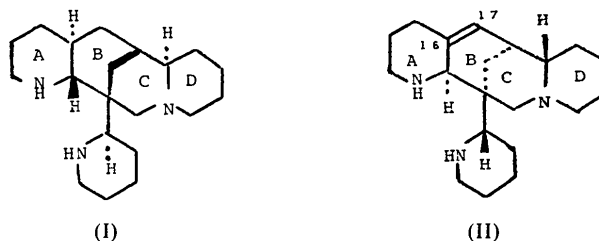
An extract of *Podopetalum ormondii* yields crystals containing two alkaloids, but repeated recrystallization fails to resolve the two components. The crystals are typically triplets consisting of a monoclinic phase *m* and two identical, but differently oriented, triclinic phases *t*1 and *t*2. Three data sets were collected, two from a virtual twin from which most of *t*2 had been cut away and one from a virtually single *m* crystal. Both *m* and *t* data sets were centric but proved to belong to  $P2_1$  and  $P1$  respectively. Both contain chirally opposite (and hence pseudo-symmetrically related) 1:1 ordered arrays of (–)-podopetaline and (–)-ormosanine. Many of the bond lengths of the molecules in the *t* phase lay outside acceptable ranges. This could be caused by the *t* phase containing small, but significant amounts of the corresponding (+) isomers or other closely related alkaloid molecules of this series. *m* phase:  $C_{20}H_{35}N_3 \cdot C_{20}H_{33}N_3$ , total  $M_r = 633.03$ ,  $P2_1$ ,  $a = 10.418$  (2),  $b = 19.634$  (3),  $c = 18.685$  (3) Å,  $\beta = 104.51$  (2)°,  $U = 3700.0$  (1.1) Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.145$  g cm<sup>-3</sup>,  $Cu K\alpha$ ,  $\lambda = 1.5418$  Å,  $\mu(Cu K\alpha) = 5.2$  cm<sup>-1</sup>,  $F(000) = 1400$ ,  $T = 298$  K.  $R = 0.085$  for 4319 significant reflections. *t* phase: as for *m* phase except,  $P1$ ,  $a = 10.426$  (8),  $b = 19.574$  (9),  $c = 11.202$  (9) Å,  $\alpha = 122.10$  (6),  $\beta = 105.25$  (6),  $\gamma = 89.50$  (5)°,  $U = 1844$  (2) Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.149$  g cm<sup>-3</sup>,  $\mu(Cu K\alpha) = 5.21$  cm<sup>-1</sup>,  $F(000) = 700$ .  $R = 0.093$  for 3386 significant reflections.

### Introduction

The ormosia alkaloids form a group closely related chemically to the  $C_{20}H_{35}N_3$  alkaloid ormosanine (I). The X-ray structure analysis of a derivative of (±)-ormosanine (I) (Karle & Karle, 1964) provided a key to the structures of the ormosanine alkaloids, many of which are simply diastereoisomers. In this group both optically active and racemic forms are known, sometimes being obtained from the same plant. Such phenomena are of considerable biosynthetic interest.

The crystal structure and absolute configuration of (–)-podopetaline (II), a member of this group isolated from *Podopetalum ormondii*, has been determined as the hydrobromide (Mackay, Satzke & Mathieson, 1975). This alkaloid, 16,17-dehydro-ormosanine, is unusual in this group in having a structural variation in the form of a 16,17 double bond. From the same plant extract another diastereoisomer has been isolated in these laboratories, 6-epipodopetaline, and its crystal structure determined (Cheng, McLean, Misra & Nyburg, 1976). This same extract affords (after repeated crystallization) another fraction, m.p. 433–434 K, which was recognized by liquid chromatography and mass spectrographic analysis to contain both  $C_{20}H_{35}N_3$  and  $C_{20}H_{33}N_3$  components. Separation could only be effected by chemical modification with formaldehyde giving products identified as having come from (–)-ormosanine and (–)-podopetaline.

The aim of the present study was not an accurate determination of the molecular structures of the components (–)-podopetaline and (–)-ormosanine since these can be inferred from the known structures of derivatives or of closely related alkaloids in this series. Indeed, the complex nature of the crystalline material which gave rise to overlapping X-ray reflections and the lack of reflections at high  $2\theta$  prevented accurate molecular structures from being determined. (Both monoclinic and triclinic forms prove to have 92 independent atoms per unit cell.) This unpromising material seemed to us, however, to present a crystallographic problem of some interest; namely, why did repeated crystallization fail to resolve the components, what were the structures of the monoclinic and two triclinic phases found to be present and how, if at all, were the structures of these phases related?



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In the event, we were able to produce a monoclinic specimen virtually free from triclinic contamination and obtain a moderately accurate structure analysis. The triclinic phase, however, seems to be partially disordered and only approximate atomic coordinates could be obtained.

A brief report on the results has been published elsewhere (Misra, Wong-Ng, Cheng, McLean & Nyburg, 1980).

### Experimental

Repeated recrystallization of the material from acetone failed to resolve it into single chemical components. Moreover all crystals examined by X-rays proved to be triplets consisting of a monoclinic ( $m$ ) and two triclinic ( $t1$ ,  $t2$ ) phases. From attempts made to cleave these triplets it seemed that the  $t$  phases are normally attached to opposite sides of the  $m$  phase.

The relation between the three reciprocal lattices, shown in Fig. 1, was determined from precession photographs. The concurrence of the three  $z^*$  axes should be noted. The only systematic absences observed were  $0k_m0$  for  $k_m$  odd although the  $h_m0l_m$  reflections were systematically weak for both  $h_m$  odd and  $l_m$  odd. The relative orientations of the unit cells can be inferred from the reciprocal lattices and are given in Fig. 2, illustrating our general impression that  $t$  phases flank the  $m$  phase.

Many reflections from the three phases overlap. Despite this, it is possible to choose enough non-overlapping reflections, center them on the diffractometer, and obtain the unit-cell dimensions. Crystal data are given in the *Abstract* and Table 1. Each set of centered reflections yields an orientation matrix  $\mathbf{p}$  whose successive rows give the  $X$ ,  $Y$  and  $Z$  components in orthogonal diffractometer space of the vectors  $\mathbf{a}^*$ ,  $\mathbf{b}^*$  and  $\mathbf{c}^*$ . Writing unit reciprocal vectors

along the diffractometer axes as  $\mathbf{u}^*$  we have therefore  $\mathbf{a}^* = \tilde{\mathbf{p}}\mathbf{u}^*$  where  $\tilde{\mathbf{p}}$  is the transpose of  $\mathbf{p}$ . Hence for two crystallographic axial systems obtained from the same crystal  $\mathbf{a}_1^* = \tilde{\mathbf{p}}_2\tilde{\mathbf{p}}_1^{-1}\mathbf{a}_1^*$  and from this can be obtained the relation between indices,  $\mathbf{h}_2 = \mathbf{p}_2^{-1}\mathbf{p}_1\mathbf{h}_1$ . If '1' represents  $t$  and '2' represents  $m$  the product  $\mathbf{p}_2^{-1}\mathbf{p}_1 = \mathbf{s}_1$  obtained from the diffractometer data was

$$\begin{pmatrix} -1.0023 & -0.0009 & -0.0089 \\ 0.0063 & -1.0061 & -0.0146 \\ 0.9934 & 0.5991 & 2.0004 \end{pmatrix}.$$

For purposes of the following discussion this can be approximated without serious error to

$$\begin{pmatrix} h_m \\ k_m \\ l_m \end{pmatrix} = \begin{pmatrix} -1 & 0 & 0 \\ 0 & -1 & 0 \\ 1 & \frac{3}{5} & 2 \end{pmatrix} \begin{pmatrix} h_{t1} \\ k_{t1} \\ l_{t1} \end{pmatrix}. \quad (1)$$

For  $t2$  similarly,

$$\begin{pmatrix} h_m \\ k_m \\ l_m \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & -1 & 0 \\ -1 & -\frac{3}{5} & -2 \end{pmatrix} \begin{pmatrix} h_{t2} \\ k_{t2} \\ l_{t2} \end{pmatrix}$$

i.e.  $\mathbf{h}_m = \mathbf{s}_2\mathbf{h}_{t2}$ .

The matrices relating unit-cell vectors are the same as those relating corresponding indices (see Fig. 2). The  $a$ ,  $b$  and  $\gamma$  parameters of the  $m$  and  $t$  phases are such as to make the  $C$  cell faces virtually congruent.

### Preliminary attempt at structure solution of the $m$ phase

Some triplet crystals could be cleaved to give what proved to be virtually ( $m+t$ ) twins, almost free from any second  $t$  phase. One such (for details, see Table 1) was aligned by its non-overlapping reflections on an automated Picker diffractometer using Ni-filtered  $\text{Cu K}\alpha$  radiation. Reflections were considered sig-

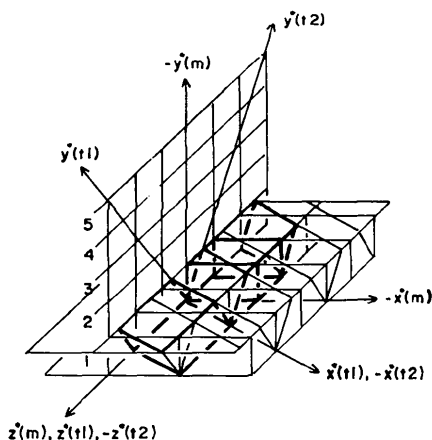


Fig. 1. Reciprocal lattices of the monoclinic,  $m$ , and two triclinic,  $t1$  and  $t2$ , phases. One reciprocal cell of each phase is drawn in heavy lines.

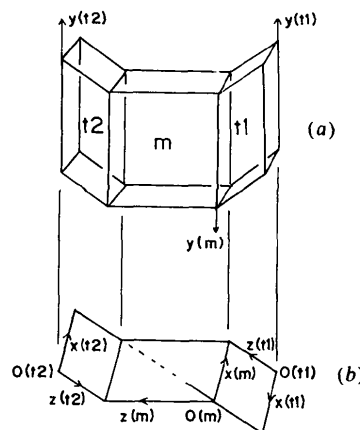


Fig. 2. Unit cells of the three phases, (a) in perspective, (b) in  $y$  projection.

Table 1. Additional crystal and refinement data

Both phases are colorless.

	Monoclinic (from <i>m</i> crystal)	Triclinic (from <i>m</i> + <i>t</i> crystal)
Crystal size (mm)	0.33 × 0.48 × 0.26	0.40 × 0.32 × 0.19
Axis mounting	<i>x</i>	<i>y</i>
$\theta$ (max.) (°)	64	64
Scan mode	$\theta$ -2 $\theta$	$\theta$ -2 $\theta$
Speed (° min <sup>-1</sup> )	2	2
Reflections, total	6128	5745
Reflections, significant [ $F > 2\sigma(F)$ ]	4319	3386
Weighting scheme	Unit weights	
Final (shift/e.s.d.) <sub>max</sub>	0.3	0.8

nificant on the criterion  $F_o > 2\sigma(F_o)$  where  $\sigma(F_o)$  was taken as  $\{[\sigma(I)Lp]^2 + 0.02F_o^4\}^{1/2}$ , *Lp* being the Lorentz-polarization factor.

As noted above,  $h_m 0 l_m$  reflections for both  $h_m$  and  $l_m$  odd were systematically weak and hence the space group was assumed to be pseudo- $P2_1/c$ . Reflections with  $|k_m| = 0$  or  $5n$  were not used for phasing by direct methods because they overlap with those for which  $|k_r| = 0$  or  $5n$  (see Fig. 1). From the remaining data, those 476 reflections having  $|E| > 1.4$  were used in *MULTAN* (Germain, Main & Woolfson, 1971) in an attempt to solve the structure. *E*-statistics favored a centric distribution. However, the most probable sets of phases yielded *E* maps which could not be interpreted.

#### Preliminary attempt to solve the *t* structure

The same crystal was used to collect the *t* data. Details are given in the *Abstract* and Table 1. Again reflections with  $|k_r| = 0$  or  $5n$  were eliminated. The *E* distribution was centric. Those 408 reflections having  $|E| > 1.4$  were used in *MULTAN* assuming the space group to be  $P\bar{1}$ . The best *E* map did reveal 46 atomic positions which could fairly reasonably be assigned to two molecules each of 23 non-hydrogen atoms. However, the structure would not refine below  $R = 0.35$ .

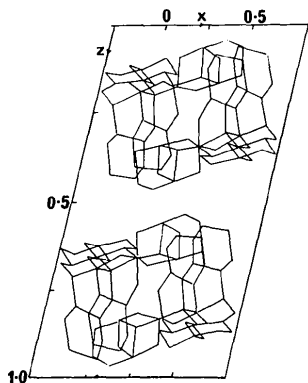


Fig. 3. *E* map for *m* phase based on incorrect space group,  $P2_1/c$ .

#### Solution of the *m*-phase structure

A second crop of crystals obtained from acetone yielded one crystal which proved to be free from any *t* phase. From this crystal we were able to establish with more certainty that although reflections  $h_m 0 l_m$  with  $h_m, l_m$  odd were weak they were generally present. Hence the only possible space groups appeared to be  $P2_1$  or  $P2_1/m$ . The 495 reflections having  $|E| > 1.71$  were used for direct phasing in both space groups but no fruitful results were obtained. It seemed clear that the structure was either pseudo- $P2_1/c$  or pseudo- $P2_1/a$  (or possibly even  $P2_1/n$ ) and hence it was assumed that phasing in  $P2_1/c$  might be worth re-attempting using this better data set. The most probable *E* map showed 16 overlapping possible molecular images spaced approximately one bond length apart (Fig. 3). Attempts were made to solve the structure by maintaining those atomic images which could possibly correspond to non-conflicting molecules and preserving only the screw axes of  $P2_1$ . No such attempts yielded refinable atomic coordinates. In a final attempt, we took instead the averaged atomic coordinates of eight closely related pair images. [In this it happens we rediscovered a procedure first reported by Duffin (1968).] The screw axes were preserved (which left them in non-standard positions for  $P2_1$ ). These averaged coordinates were successfully refined on *F* by block-diagonal least squares using *ORXFLS* (Busing, Martin & Levy, 1971) with atomic scattering factors from Cromer & Mann (1968). Hydrogen atoms were fixed in calculated positions with  $B = 6.0 \text{ \AA}^2$ , taking C-H and N-H equal to  $1.0 \text{ \AA}$ . The final conventional *R* factor was 0.085. Fractional atomic coordinates and equivalent isotropic temperature factors are given in Table 2.\*

#### Solution of the *t*-phase structure

The successful solution of the *m*-phase structure for which, despite a strongly centric *E* distribution, the true space group was not centric, led us to attempt a similar approach for the *t* phase. The tentative structure in  $P\bar{1}$ , which would not refine, was slightly distorted by small arbitrary shifts in some atomic positions and refinement attempted in  $P\bar{1}$ . (Details of refinement as for the *m* phase.) The final *R* was 0.093 but atom C(C18) had a non-positive-definite temperature factor and several bond lengths lay outside acceptable limits. However, despite the somewhat approximate nature of the coordinates they are given in Table 3 since they are needed to discuss the relation between the overall *t* structure and the *m* structure.\*

\* Lists of structure factors, anisotropic thermal parameters and calculated hydrogen positions have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38863 (47 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Fractional atomic coordinates ( $\times 10^4$ ) and  $B_{eq}$  values ( $\text{\AA}^2$ ) with their e.s.d.'s for non-hydrogen atoms of the  $m$  phase

$B_{eq} = \frac{4}{3} \sum_i \sum_j \beta_{ij} a_i a_j$ . The origin has been moved  $z = \frac{1}{4}$  from its standard setting for  $P2_1$ ; equivalent positions:  $x, y, z; \bar{x}, \frac{1}{2} + y, \frac{1}{2} - z$ .

(-)-Ormosanine molecules				(-)-Podopetaline molecules					
	$x$	$y$	$z$	$B_{eq}$		$x$	$y$	$z$	$B_{eq}$
N(A1)	967 (7)	-98 (4)	3126 (4)	4.5 (2)	N(C1)	4007 (6)	1813 (3)	6865 (4)	3.7 (2)
C(A2)	1542 (9)	4 (5)	3927 (5)	5.2 (3)	C(C2)	3546 (8)	1913 (5)	6079 (4)	4.3 (2)
C(A3)	1254 (12)	-603 (7)	4347 (7)	7.0 (4)	C(C3)	3844 (8)	1264 (5)	5669 (5)	4.7 (3)
C(A4)	-142 (11)	-766 (5)	4163 (6)	5.8 (3)	C(C4)	5358 (9)	1146 (5)	5917 (6)	5.9 (3)
C(A5)	-767 (12)	-815 (4)	3354 (5)	5.9 (3)	C(C5)	5856 (10)	1076 (5)	6743 (5)	5.0 (3)
C(A6)	-482 (8)	-188 (4)	2955 (5)	3.6 (2)	C(C6)	5498 (7)	1738 (4)	7108 (4)	3.4 (2)
C(A7)	-1040 (9)	-255 (5)	2109 (5)	4.4 (2)	C(C7)	6046 (8)	1705 (4)	7956 (5)	3.8 (2)
C(A8)	46 (8)	-303 (4)	1734 (4)	3.5 (2)	C(C8)	4837 (8)	1649 (4)	8297 (4)	3.6 (2)
C(A9)	912 (8)	371 (4)	1868 (4)	3.1 (2)	C(C9)	3987 (7)	2306 (4)	8110 (4)	2.7 (2)
C(A10)	1354 (7)	447 (4)	2722 (4)	2.9 (2)	C(C10)	3566 (7)	2367 (4)	7260 (4)	2.9 (2)
C(A11)	-24 (8)	959 (4)	1480 (4)	2.9 (2)	C(C11)	4896 (7)	2916 (4)	8473 (4)	2.8 (2)
N(A12)	671 (6)	1615 (3)	1541 (3)	2.7 (2)	N(C12)	4177 (6)	3572 (3)	8349 (3)	2.9 (2)
C(A13)	-108 (8)	2129 (4)	1102 (5)	4.3 (2)	C(C13)	4985 (8)	4131 (4)	8750 (5)	3.9 (2)
C(A14)	-1417 (9)	2251 (5)	1343 (7)	5.2 (3)	C(C14)	6282 (9)	4202 (5)	8566 (5)	4.3 (3)
C(A15)	-2173 (9)	1562 (5)	1373 (5)	4.5 (3)	C(C15)	7017 (8)	3538 (5)	8642 (5)	4.6 (3)
C(A16)	-1242 (8)	1005 (5)	1790 (5)	4.1 (2)	C(C16)	6170 (7)	2962 (4)	8215 (4)	3.3 (2)
C(A17)	-1954 (7)	329 (4)	1752 (4)	3.6 (2)	C(C17)	6890 (8)	2272 (4)	8292 (4)	4.0 (2)
C(A18)	2105 (8)	269 (4)	1558 (4)	3.4 (2)	C(C18)	2707 (7)	2219 (4)	8409 (4)	2.5 (2)
C(A19)	1795 (8)	147 (4)	706 (5)	4.1 (2)	C(C19)	3030 (7)	2124 (4)	9246 (4)	3.8 (2)
C(A20)	3029 (8)	-29 (5)	452 (4)	4.5 (3)	C(C20)	1723 (7)	2009 (4)	9509 (4)	3.2 (2)
C(A21)	4083 (8)	567 (5)	700 (4)	4.5 (3)	C(C21)	766 (9)	2558 (5)	9231 (5)	4.2 (2)
C(A22)	4300 (7)	689 (5)	1529 (5)	4.1 (2)	C(C22)	516 (7)	2633 (5)	8380 (5)	4.1 (2)
N(A23)	3066 (5)	848 (3)	1715 (4)	3.0 (2)	N(C23)	1792 (6)	2783 (3)	8198 (3)	3.2 (2)
N(B1)	736 (6)	5025 (4)	8056 (4)	3.8 (2)	N(D1)	4162 (6)	3168 (3)	1951 (3)	2.8 (2)
C(B2)	1265 (9)	4914 (5)	8850 (5)	5.5 (3)	C(D2)	3582 (9)	3105 (4)	1152 (5)	4.3 (2)
C(B3)	1160 (9)	5576 (6)	9277 (5)	5.1 (3)	C(D3)	3734 (11)	3722 (5)	732 (4)	5.2 (3)
C(B4)	-328 (10)	5775 (5)	9136 (6)	6.0 (3)	C(D4)	5262 (10)	3909 (5)	895 (4)	5.0 (3)
C(B5)	-858 (9)	5847 (5)	8273 (5)	5.4 (3)	C(D5)	5850 (8)	3925 (5)	1718 (5)	4.4 (2)
C(B6)	-698 (7)	5162 (4)	7885 (4)	3.2 (2)	C(D6)	5577 (8)	3294 (4)	2091 (4)	3.5 (2)
C(B7)	-1316 (7)	5168 (4)	7058 (4)	3.1 (2)	C(D7)	6136 (8)	3272 (4)	2946 (5)	4.2 (2)
C(B8)	-233 (7)	5267 (4)	6617 (4)	3.1 (2)	C(D8)	5077 (8)	3332 (4)	3361 (4)	3.6 (2)
C(B9)	660 (7)	4631 (4)	6761 (4)	2.5 (2)	C(D9)	4206 (7)	2694 (4)	3204 (4)	3.0 (2)
C(B10)	1008 (9)	4450 (4)	7587 (4)	3.8 (2)	C(D10)	3893 (7)	2539 (4)	2346 (4)	3.0 (2)
C(B11)	-198 (7)	4065 (4)	6288 (4)	3.4 (2)	C(D11)	5047 (8)	2106 (5)	3641 (4)	3.8 (2)
N(B12)	428 (6)	3386 (4)	6481 (4)	4.1 (2)	N(D12)	4423 (6)	1439 (3)	3418 (4)	3.3 (2)
C(B13)	-360 (9)	2820 (5)	6042 (6)	4.7 (3)	C(D13)	5159 (9)	867 (4)	3812 (5)	4.6 (3)
C(B14)	-1584 (10)	2747 (5)	6305 (6)	5.3 (3)	C(D14)	6474 (9)	803 (5)	3566 (6)	5.4 (3)
C(B15)	-2347 (8)	3390 (5)	6119 (5)	4.5 (3)	C(D15)	7268 (8)	1461 (5)	3779 (6)	5.5 (3)
C(B16)	-1562 (8)	4008 (5)	6467 (5)	3.8 (2)	C(D16)	6457 (7)	2081 (4)	3512 (5)	4.0 (2)
C(B17)	-2074 (7)	4504 (5)	6810 (5)	4.2 (2)	C(D17)	6953 (7)	2603 (4)	3187 (5)	4.1 (2)
C(B18)	1994 (8)	4790 (4)	6522 (4)	3.0 (2)	C(D18)	2959 (7)	2816 (4)	3450 (4)	3.3 (2)
C(B19)	1716 (8)	5054 (4)	5720 (5)	3.8 (2)	C(D19)	3140 (8)	3017 (4)	4274 (4)	3.9 (2)
C(B20)	3100 (10)	5218 (6)	5549 (5)	5.1 (3)	C(D20)	1857 (9)	3167 (5)	4447 (5)	5.0 (3)
C(B21)	3993 (9)	4606 (6)	5715 (5)	4.9 (3)	C(D21)	885 (9)	2546 (5)	4256 (5)	4.9 (3)
C(B22)	4135 (9)	4373 (5)	6488 (5)	4.6 (3)	C(D22)	720 (7)	2370 (5)	3447 (4)	4.1 (2)
N(B23)	2836 (6)	4211 (4)	6634 (4)	3.6 (2)	N(D23)	2019 (6)	2226 (4)	3308 (4)	3.6 (2)

## Discussion

The striking result to emerge from the successfully solved  $m$  structure is that it is ordered, containing (-)-ormosanine molecules *A* and *C*, and (-)-podopetaline molecules *B* and *D* in 1:1 ratio. These molecules differ only in the presence of a double bond at C(16), C(17) in (-)-podopetaline and this has relatively little effect on the overall geometry. Fig. 4 shows ORTEP plots (Johnson, 1965) of both molecules in the  $m$  phase so oriented that their close similarity in geometry can be seen and their opposite chirality evident. The geometry of the (-)-ormosanine molecules is exactly what has been generally inferred from the known structure of ( $\pm$ )-jamine [Karle & Karle (1964); this molecule is derived from ormosanine, having an extra methylene group bridging N(12), N(23)], namely, that all the six-membered rings save ring *C* (see I), which is a boat, have the chair conformation and that ring *C* is *trans*-fused to

ring *D*. The podopetaline molecules have similar geometry to the ormosanine molecules except that ring *B* containing the double bond has a 'sofa' conformation with only C(8) significantly out of plane.

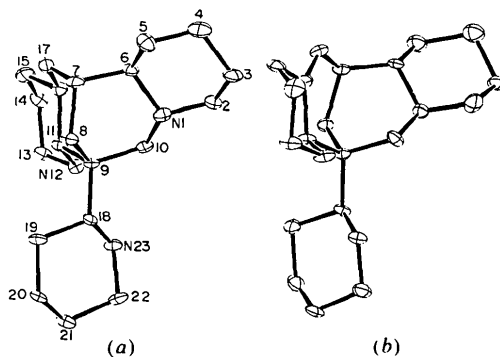


Fig. 4. ORTEP plots of molecules in  $m$  phase, (a) (-)-ormosanine showing atomic numbering, (b) (-)-podopetaline (same atomic numbering). The configurations shown are absolute.

Table 3. Approximate fractional atomic coordinates ( $\times 10^4$ ) and  $B_{eq}$  values for non-hydrogen atoms of the *t* phase

This phase is probably disordered. Thus the e.s.d.'s obtained from least-squares refinement are unrealistically low and are not given.

	x	y	z	$B_{eq}$		x	y	z	$B_{eq}$
(-)-Ormosanine molecules									
N(A1)	2211	6994	1116	2.8	N(C1)	2722	1267	-1119	7.6
C(A2)	2343	7394	2689	3.3	C(C2)	2510	624	-2886	9.3
C(A3)	3128	8266	3546	4.3	C(C3)	1789	1030	-3536	7.6
C(A4)	4440	8277	3176	8.7	C(C4)	511	1406	-3128	6.5
C(A5)	4071	7823	1500	3.8	C(C5)	1199	1886	-1664	12.6
C(A6)	3411	6961	753	3.5	C(C6)	1537	1520	-846	4.2
C(A7)	3119	6508	-863	2.6	C(C7)	1866	2063	854	5.1
C(A8)	1577	6300	-1665	3.3	C(C8)	3385	2307	1586	4.8
C(A9)	883	5748	-1328	3.8	C(C9)	4091	1565	1370	2.5
C(A10)	1343	6204	392	4.8	C(C10)	3601	899	378	6.4
C(A11)	1456	4929	-2091	2.9	C(C11)	3642	1141	1938	5.8
N(A12)	841	4313	-1897	4.6	N(C12)	4142	456	1768	4.6
C(A13)	1245	3560	-2690	3.8	C(C13)	3771	125	2589	4.1
C(A14)	2699	3553	-2305	5.7	C(C14)	2227	-78	2127	5.1
C(A15)	3384	4281	-2388	6.9	C(C15)	1536	672	2446	6.9
C(A16)	2990	5005	-1721	5.8	C(C16)	2094	976	1571	6.1
C(A17)	3678	5633	-1616	5.1	C(C17)	1356	1690	1570	5.1
C(A18)	-6.26	5682	-1969	2.7	C(C18)	5643	1829	1852	2.3
C(A19)	-1189	5330	-3555	6.6	C(C19)	6236	2578	3720	5.8
C(A20)	-2713	5393	-3976	5.5	C(C20)	7723	2747	4138	6.2
C(A21)	-3433	4912	-3525	4.4	C(C21)	8455	1994	3501	5.4
C(A22)	-2768	5290	-1871	4.9	C(C22)	7837	1451	1932	4.1
N(A23)	-1433	5187	-1649	4.4	N(C23)	6397	1146	1541	3.7
(-)-Podopetaline molecules									
N(B1)	-2852	-1180	1340	5.4	N(D1)	-2229	3029	-1288	9.2
C(B2)	-2487	-663	2784	4.9	C(D2)	-2600	2649	-2757	6.4
C(B3)	-1897	-1031	3678	8.3	C(D3)	-3010	1769	-3506	10.9
C(B4)	-639	-1287	3273	5.7	C(D4)	-4410	1704	-3076	4.6
C(B5)	-754	-1850	1635	4.1	C(D5)	-4211	2199	-1550	8.6
C(B6)	-1435	-1441	827	5.4	C(D6)	-3499	3151	-582	5.1
C(B7)	-1748	-2016	-900	4.0	C(D7)	-3336	3655	920	5.6
C(B8)	-3195	-2326	-1666	5.0	C(D8)	-1821	3748	1756	5.3
C(B9)	-3850	-1559	-1258	4.5	C(D9)	-1075	4298	1445	3.5
C(B10)	-3534	-980	304	4.4	C(D10)	-1529	3921	-156	5.0
C(B11)	-3490	-1277	-2270	1.8	C(D11)	-1409	5127	2357	4.9
N(B12)	-3961	-461	-1836	3.3	N(D12)	-936	5677	1876	3.4
C(B13)	-3665	-197	-2718	5.5	C(D13)	-1239	6603	2929	7.0
C(B14)	-2082	-23	-2318	4.6	C(D14)	-2866	6482	2325	5.6
C(B15)	-1538	-700	-2448	7.3	C(D15)	-3426	5968	2674	4.7
C(B16)	-1901	-1085	-1849	4.2	C(D16)	-2976	5045	1769	7.8
C(B17)	-1151	-1503	-1420	5.3	C(D17)	-3812	4390	1462	4.4
C(B18)	-5432	-1853	-1891	5.1	C(D18)	485	4305	1930	3.8
C(B19)	-6076	-2476	-3464	3.8	C(D19)	1022	4572	3526	4.2
C(B20)	-7575	-2775	-3937	4.7	C(D20)	2570	4474	3967	5.8
C(B21)	-8291	-2125	-3608	5.2	C(D21)	3358	4965	3530	6.2
C(B22)	-7676	-1397	-1846	4.9	C(D22)	2676	4657	1934	6.7
N(B23)	-6264	-1173	-1607	3.8	N(D23)	1226	4753	1549	4.3

However, the podopetaline cation in the crystal of the hydrobromide has a quite different conformation (Mackay, Satzke & Mathieson, 1975). Ring *C* has a chair conformation and is *cis*-fused to ring *D*. Hart, Johns, Lambertson, Mackay, Mathieson & Satzke (1972) assumed that the conformation of (-)-podopetaline would be the same as that found for the cation in the hydrobromide. They assigned the correct conformation to ormosanine and attributed the supposed difference to podopetaline to the latter's lack of a hydrogen atom at C(16), thus allowing ring *C* to take up a chair conformation. Clearly podopetaline is not prevented from taking up the same conformation as ormosanine and does so in the present structure. The conformational difference between podopetaline and its cation corresponds to an inversion at N(1). It is thus tempting to regard this as the site of quaternization. Hydrogen positions were not determined by Mackay, Satzke & Mathieson (1975) who favor N(23) as the site of quaternization on the grounds that the  $\text{Br}^-$  anion is closest to, and lies

mid-way between, two such N(23) atoms on adjacent molecules.

From the substantial number of accurate analyses of molecular structures of this type it is clear that C-C single bonds range from 1.51-1.59 Å and the non-quaternary N-C bonds from 1.46-1.48 Å. This is so in epiormosanine (Mackay, McCall & Poppleton, 1976), and in homodasycarpine (Wang, Duesler, Thayer, Heckendorn, Rinehart & Paul, 1978). In (-)-podopetaline hydrobromide some of the reported bond lengths lie outside these ranges, two C-C bonds being given as 1.60 Å and, quite exceptionally, N-C bonds ranging from 1.45 to 1.55 Å. In the *m* phase under study here, in the ormosanine molecules the ranges are C-C, 1.44-1.57 Å; C-N, 1.47-1.52 Å; in podopetaline, C-C (single), 1.47-1.59 Å; (double), 1.35 and 1.36 Å; C-N, 1.47-1.56 Å. On this basis the *m*-phase molecular structures are about as accurate as those given for (-)-podopetaline hydrobromide. There are no short intermolecular contacts in the *m* phase, the shortest H...H distance being 2.11 Å

between H(C8) and H(C19) (at  $x-1, y, z$ ) of a pair of adjacent (-)-ormosanine *C* molecules.

As noted above, some of the bond lengths in molecules of the *t*-phase structure lay outside the accepted ranges given above and thus the coordinates listed in Table 3 must be regarded as approximate. One possible cause for this is that the *t* phase contains minor amounts of contaminating molecules and is thus not strictly ordered. In this series of alkaloids it is possible for single plant species to produce both enantiomeric forms. This may well be the reason why specific optical rotations measured on certain 'purified' alkaloids in this series vary from plant to plant and laboratory to laboratory. It is conceivable that in the *t* phase each molecular site contains, as minor contaminant, a molecule closely related chemically and of the same chirality. (It is of some interest to note that small amounts of chemically related contaminants often induce polymorphism.) Working on the assumption that the *t* phase has a major and a minor component at each molecular site we attempted to find what these components were. Using program *BMFIT* (Yuen & Nyburg, 1979) the atomic coordinates obtained for (-)-ormosanine molecule *A* and for (-)-podopetaline molecule *B* in the *m* phase were used to match the coordinates given in Table 3. The results are set out in Table 4. These results clearly imply that the major components at the *t* sites *A* and *C* are (-)-ormosanine and at sites *B* and *D*, (-)-podopetaline. (Hence the assignments in Table 3. Had the structure been free from minor contaminants the smallest of the sums of squares of deviations would have been zero, the intermediate value 1.10 and the largest 87.77.) An attempt was made to see if the structure could be more satisfactorily refined on the assumption that the minor components were the (+) enantiomers of ormosanine and podopetaline. The best fitting coordinates from *BMFIT* were used as those of the major components and the next best fitting coordinates those of the minor components. These coordinates were kept fixed and the temperature factors associated with each atom were those obtained from the *t*-phase refinement. Full-matrix least squares was used to refine the major occupancies, the total occupancy of each atom being kept at unity. Refinement gave occupancies for molecules *A*, *B*, *C* and *D* respectively, 0.96 (2), 0.78 (2), 0.97 (2) and 0.90 (2). *R* at this stage was 0.15. Refinement of the anisotropic temperature factors for all 184 independent non-hydrogen atoms was clearly unwarranted. Accordingly the temperature factors of corresponding atoms in the major and minor molecules were constrained to be the same. Three cycles of full-matrix least-squares refinement did little to improve the residual which fell to 0.13. Four atoms C(B13), C(B19), C(B20) and C(D20) had non-positive-definite temperature factors. Expenditure of further effort and time on refinement was felt to be

Table 4. Sums of squares of atomic displacements  $\Delta^2$  ( $\text{\AA}^2$ ) obtained from *BMFIT* when molecules *A* and *B* of the *m* phase are matched with the coordinates of the corresponding atoms of the *t* phase

The major site occupant in each case is assumed to be, in each column, that for which  $\Delta^2$  is least.

<i>m</i> -phase molecule	<i>t</i> -phase molecule			
	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>
(-)-Ormosanine, <i>A</i>	0.112	87.63	0.256	86.70
(+)-Ormosanine*	86.87	0.669	90.07	0.872
(-)-Podopetaline, <i>B</i>	87.45	0.252	90.70	0.189
(+)-Podopetaline†	0.997	87.58	1.237	86.39

\* Mirror image of (-)-ormosanine molecule, *A*.  
† Mirror image of (-)-podopetaline molecule, *B*.

unjustified. Thus the exact nature of the minor components in the *t* phase (if indeed there are any) remains uncertain. [They may not be the (+) enantiomers of ormosanine and podopetaline.] However, there is little doubt about the major structure and therefore, although they are approximate, the coordinates given in Table 3 will be used to discuss the relation between the two phases.

#### Molecular packing; relation between the *m* and *t* phases

The *y* projection of the *m* structure is shown in Fig. 5. This is somewhat crowded and a key to it is given in Fig. 6 where only the piperidine rings of each

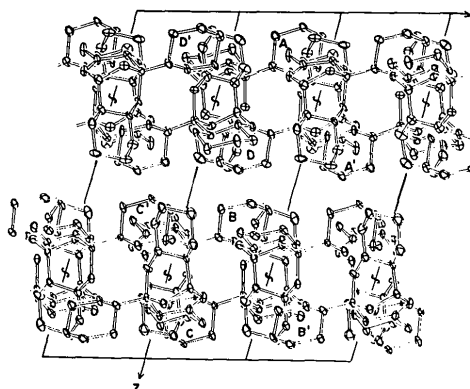


Fig. 5. Structure of *m* phase in *y* projection.

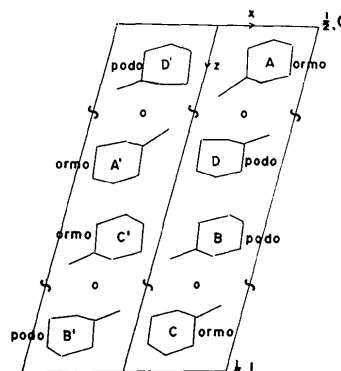


Fig. 6. Key to structure of *m* phase.

molecule are shown. There are two independent (-)-ormosanine molecules *A* and *C* and two independent (-)-podopetaline molecules *B* and *D* per cell. Screw axes generate the other four molecules per cell as shown. The structure shows strong pseudo-halving along *a* and *c* in the *y* projection. Hence the extreme weakness of the  $h_m 0 l_m$  reflections with  $h_m$  or  $l_m$  odd. This halving can be checked by reference to Table 2. For exact halving in the *x* direction, the *x* coordinates of (-)-ormosanine molecule *A* should differ from those of *C'* (screw related to those of *C*, see Fig. 6) by  $x = \frac{1}{2}$ . Choosing the screw axis at  $(0, y, \frac{3}{4})$  the coordinates of *C'* will be  $1 - x_C, 1\frac{1}{2} - z_C$ . Thus for *x*-halving,  $1 - x_C$  needs to equal  $x_A + \frac{1}{2}$ , i.e.  $x_A = \frac{1}{2} - x_C$ . This condition will be found to be well satisfied in Table 2. A similar argument leads to the requirement  $z_A = 1 - z_C$  also quite well satisfied. Similar relations apply to the (-)-podopetaline molecules *B* and *D*, namely,  $x_B = \frac{1}{2} - x_D$  and  $z_B = 1 - z_D$ .

As noted above, the (-)-ormosanine and (-)-podopetaline molecules are of opposite chirality. They are so disposed in the crystal as to subtend pseudo centers of symmetry: for molecules *A* and *D* at  $(0.2535, 0.1535, 0.2518)$  and for molecules *B* and *C* at  $(0.2370, 0.3476, 0.7454)$ . (Other pseudo centers in the unit cell are of course generated by the screw axes.) These pseudo centers are discussed below.

The structure of the *m* phase (and, as will be seen, of the *t* phase also) is that of a quasi-racemate. This designation is used by Fregda & Ekstedt (1965) who made a number of such materials in which the components differ slightly chemically and have opposite chiralities. The crystal structure of at least one such quasi-racemate has been determined, that of 1:1 (+)-*m*-methoxyphenoxypionic acid-(-)-*m*-bromophenoxypionic acid (Karle & Karle, 1966). The molecules in this crystal structure also subtend pseudo centers of symmetry.

The packing of two adjacent cells of the *t* structure is given in Fig. 7 together with an explanatory diagram in Fig. 8. The *m* and *t* structure *y* projections are, to within experimental limits, identical. In fact, as will

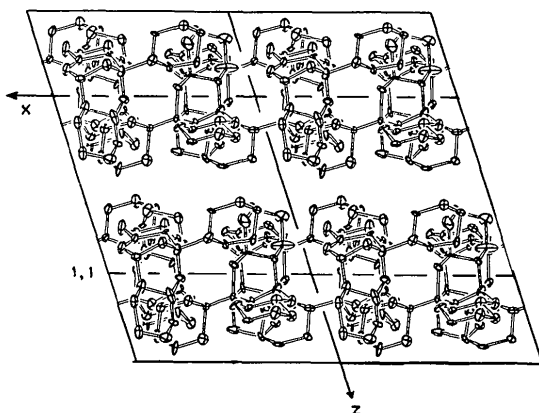


Fig. 7. Structure of *t* phase in *y* projection.

be seen below, repeats of the *t* structure bounded by planes  $z_t = -\frac{1}{2}$  and  $\frac{1}{2}$  are identical to *m* half repeats bounded by  $z_m = \frac{1}{2}z_t + \frac{1}{4}$  and  $\frac{1}{2}z_t + \frac{3}{4}$ . Accordingly there are again pseudo centers present in the *t* structure, those for molecules *A* and *D* being at  $(-0.0051, 0.5014, 0.0024)$  and for molecules *B* and *C* at  $(0.0060, -0.0001, 0.0005)$ . These pseudo centers can be taken to lie at  $(0, \frac{1}{2}, 0)$  and  $(0, 0, 0)$  which is only to be expected, since the *P1* structure was derived from the (false)  $P\bar{1}$  structure by the application of small perturbations to break the symmetry. The *t* structure shows local (not lattice) screw axes in the same relative positions as the screw axes in the *m* structure. Thus the screw axis at  $(-\frac{1}{4}, y, 0)$  gives relations  $x_B = -\frac{1}{2} - x_D$  and  $z_B = -z_D$ . (The *y* axis is not orthogonal to the *xz* plane so that the presence of pseudo screw axes cannot be fully demonstrated without recourse to an orthogonal axial system.) These local screw axes relate molecules lying between  $z_t = \pm\frac{1}{2}$ , they do not relate molecules lying outside this repeat.

#### Relation between atomic coordinates in the *m* and *t* phases

The transformation from *t* to *m* coordinates is  $x_m = \mathbf{t}x_t$ , where  $\mathbf{t}$  is the inverse of the transpose of  $\mathbf{s}_1$  in equation (1), namely

$$\mathbf{t} = \begin{pmatrix} -1 & 0 & \frac{1}{2} \\ 0 & -1 & \frac{3}{10} \\ 0 & 0 & \frac{1}{2} \end{pmatrix}.$$

This applies if the two systems have a common origin. If there are displacements  $\Delta x, \Delta y, \Delta z$  of the *t* origin with respect to the *m* origin, the relation between coordinates has to be modified to  $x_m = \mathbf{t}x_t + \Delta \mathbf{x}$ , i.e.

$$\left. \begin{aligned} x_m &= \frac{1}{2}z_t - x_t + \Delta x \\ y_m &= \frac{3}{10}z_t - y_t + \Delta y \\ z_m &= \frac{1}{2}z_t + \Delta z \end{aligned} \right\} \quad (2)$$

The elements of  $\Delta \mathbf{x}$  can be obtained from the displacement between corresponding pseudo centers. For molecules *A* and *D* in the two phases  $\Delta \mathbf{x}$  is  $(\frac{1}{4}, 0.6535, \frac{1}{4})$ . Substitution in equations (2) yields the relation between coordinates in the two phases. The same relation is found to relate *m* molecules *A', D'* to *t* molecules *C, B* and hence *m* molecules *A, D, A', D'* are packed identically to *t* molecules *A, D, C, B*. A similar analysis for *m* molecules *B, C, B', C'*

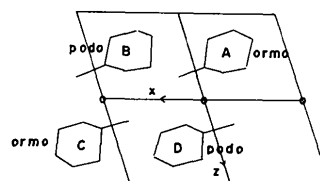


Fig. 8. Key to structure of *t* phase.

shows that  $\Delta \mathbf{x} = (\frac{3}{4}, 0.3476, \frac{3}{4})$ , the packing for these molecules being identical to that for  $t$  molecules  $B$ ,  $C$ ,  $D$ ,  $A$ . Hence the  $t$  structure bounded by  $z_t = \pm \frac{1}{2}$  is identical to the  $m$  structure bounded by either  $z_m = 0, \frac{1}{2}$  or  $z_m = \frac{1}{2}, 1$  but different origin shifts are required in the two cases.

The structural relation between  $m$  and  $t$  phases is shown in  $x$  projection in Figs. 9, 10 and 11. In these diagrams each molecule is represented by a vector joining atoms C(4) to C(13). Fig. 9 shows the  $t$  structure and Figs. 10 and 11 two ways in which the  $t$

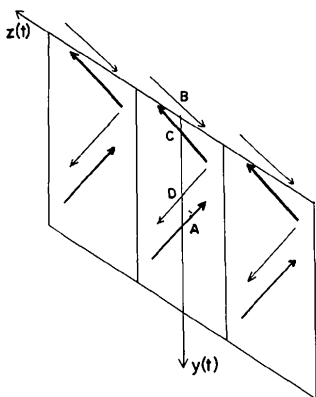


Fig. 9. Key to  $t$  phase in  $x$  projection. Vectors connect atoms C(4) and C(13) in each case. Heavy lines, (-)-ormosanine, light lines (-)-podopetaline.

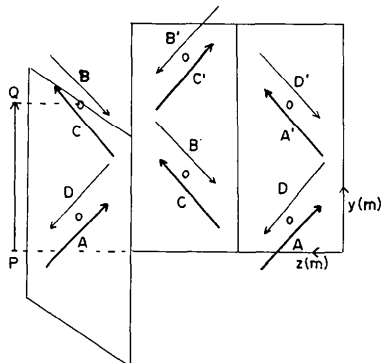


Fig. 10. Boundary between  $t$  (left) and  $m$  (right) phases showing one way in which a  $t$  cell can be considered to be a continuation of the  $m$  phase.  $PQ$  is the  $y$  displacement of the  $t$  origin with respect to the  $m$  origin.

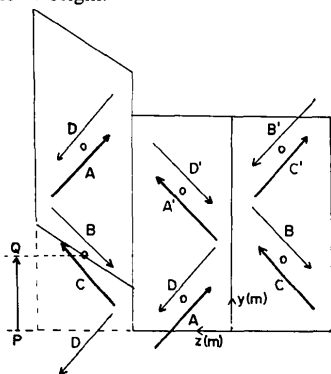


Fig. 11. As for Fig. 10 showing alternative way of satisfying continuity at the phase boundary.

structure could abut the  $m$  structure at the twin boundary so that it could be considered to belong equally to either phase. These two ways differ simply in which  $m$  repeat ( $z_m = 0$  to  $\frac{1}{2}$  or  $z_m = \frac{1}{2}$  to  $1$ ) is chosen to abut the  $t$  phase. Thus the  $m$ -phase structure can be considered to be made up of alternating layers, each layer having packing identical to that of the  $t$  structure between  $z_t = \pm \frac{1}{2}$  but requiring different shifts in origin.

In conclusion, X-ray structure analysis has clearly answered the questions raised in the *Introduction*. It has shown that both the  $m$  and the  $t$  phases are quasi-racemates whose components, like those of many genuine racemates, cannot be resolved by crystallization. It also shows how the two phases are closely related structurally. It is tempting to speculate beyond these conclusions. If this particular plant extract does contain relatively small amounts of say, the (+) enantiomers as contaminants, it is possible that the  $m$  phase crystallizes out first, virtually free from contaminants. As the concentration of contaminants in solution thereby increases so they induce transformation to, and become incorporated in, a new  $t$  phase.  $t$ -phase crystals then grow epitaxially on the  $m$ -phase crystals. Because of unit-cell parameter congruence the two obvious sites for epitaxial overgrowth are the two opposing  $C$  faces of the  $m$  crystals. Hence the formation of triplets.

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