X-Ray Determination of the Molecular Structure and Absolute Configuration of Vincamine and of its Hydrobromide Methanolate

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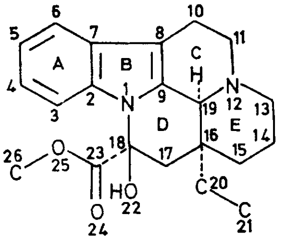
The structure and absolute configuration of the indole alkaloid vincamine (I) have been determined by *X*-ray analysis of the natural product and of its hydrobromide methanolate (II). A comparison of both molecular structures shows that protonation and different crystal packing have no measurable effect on bond lengths and bond angles, but noticeable differences in torsion angles and consequently in the finer details of the conformation are observed. Crystal data: (I), space group $P2_12_12_1$, $Z = 4$, $a = 7{\cdot}708(4)$, $b = 14{\cdot}527(7)$, $c = 16{\cdot}776(6)$ Å; (II), space group $P2_1$, $Z = 2$, $a = 7{\cdot}390(2)$, $b = 17{\cdot}843(3)$, $c = 9{\cdot}437(4)$ Å, $\beta = 115{\cdot}69(2)°$. The structures were solved from diffractometer data by the multi-solution (I) and heavy-atom methods (II), and refined by least-squares techniques to *R* 0·042 [(I), 1341 reflections] and 0·045 [(II), 2033 reflections].

THE indole alkaloid vincamine (I) was first isolated from *Vinca minor L.* and characterised.[1] The structure was elucidated[2] and the absolute configuration determined by interpretation of o.r.d. spectra.[3] Some doubts remained, however, about the relative and absolute configuration and it was thought worthwhile to do an *X*-ray analysis of vincamine hydrobromide. The crystal investigated, taken from the mother liquor, proved during the structural analysis to be the base, not the salt as expected, and this structure could therefore not be used to determine the absolute configuration because of the absence of bromine as anomalous scatterer. A second sample of the salt was prepared with an excess of HBr and the structure of the hydrobromide, as its methanolate (II) then solved.



(I)

Crystallographic numbering of vincamine (I)

The results of the structural investigation of (I) and (II) confirm the earlier suggested configuration[2,3] and the chirality has been determined to be 16*S*, 18*S*, 19*S*.

EXPERIMENTAL

Prismatic needles of both (I) and (II) were crystallised from methanol–acetone. Crystals of (I) were stable in the air, but those of (II) decayed to a powder within a few days, probably owing to loss of solvent of crystallisation. Crystals sealed in a thin-walled capillary however, stayed in good condition for a long time.

TABLE 1

Crystallographic and experimental data for alkaloids (I) and (II)

	(I)	(II)
(*a*) Crystal data:		
Empirical formula	$C_{21}H_{26}N_2O_3$	$C_{21}H_{26}N_2O_3$,HBr,CH_3OH
M	354·450	467·409
Space group	$P2_12_12_1$	$P2_1$
a/Å	7·708(4)	7·390(2)
b/Å	14·527(7)	17·843(3)
c/Å	16·776(6)	9·437(4)
β/deg.		115·69(2)
U/Å^3	1878·5(1·5)	1121·3(5)
D_c/g cm^{-3}	1·21	1·34
Z	4	2
μ/cm^{-1}	0·84	29·3
(*b*) Intensity measurements:		
Radiation	Mo-K_α	Cu-K_α
λ/Å	0·7107	1·5418
Range sin(θ/λ)/Å^{-1}	0·54	0·56
Scan	ω—2θ	ω—2θ
No. ind. reflxns.	1403	2206
Significant reflxns.*	1341	2033
$\langle\lvert E\rvert\rangle$ †	0·843	0·891(0·886)
$\langle\lvert E^2 - 1\rvert\rangle$	0·840	0·661(0·736)
$\langle E^2\rangle$	0·991	0·979(1·000)

* Having $I > 3\sigma(I)$. † Theoretical value in parentheses.

Preliminary cell dimensions and space group were determined from precession photographs. Intensities and accurate cell dimensions were measured on a four-circle diffractometer †) with graphite monochromatised radiation.

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† A Syntex P$\bar{1}$ diffractometer was used, courtesy of Scintag, Wetzikon.

[1] E. Schlittler and A. Furlenmeier, *Helv. Chim. Acta*, 1953, **36**, 2017.

[2] J. Trojánek, O. Strouf, J. Holubek, and Z. Čekan, *Tetrahedron Letters*, 1961, 702.

[3] J. Trojánek, Z. Koblicová, and K. Bláha, *Chem. and Ind.*, 1965, 1261.

Pertinent crystallographic and experimental data are summarised in Table 1 for both compounds. No absorption corrections were applied. Data were placed on an absolute scale by means of a Wilson plot.

Structural Analysis and Refinement. (*a*) *Vincamine* (I). The structure was solved by the application of the multi-solution method,[4] starting with two centric (two-dimensional) and two general reflexions as variable phases, one structure invariant, and four reflexions defining origin and enantiomorph as an initial set for phase expansion.

TABLE 2

Co-ordinates and vibrational parameters, with estimated standard deviations in parentheses as calculated in the least-squares refinement. The B_{ij} values of the vibrational ellipsoid refer to the expression: $T = \exp -(h^2B_{11} + k^2B_{22} + l^2B_{33} + 2hkB_{12} + 2hlB_{13} + 2klB_{23})$

(*a*) Vincamine (I)

(i) Co-ordinates of the heavier atoms

	x	*y*	*z*		*x*	*y*	*z*
N(1)	−0·0835(4)	0·4078(2)	0·3754(2)	C(14)	0·2801(6)	0·2908(3)	0·2101(3)
C(2)	−0·0384(6)	0·4427(3)	0·4498(2)	C(15)	0·1361(6)	0·3628(3)	0·2091(2)
C(3)	−0·0582(7)	0·5292(3)	0·4818(3)	C(16)	−0·0428(5)	0·3193(3)	0·2222(2)
C(4)	0·0008(8)	0·5448(3)	0·5585(3)	C(17)	−0·1855(6)	0·3928(3)	0·2381(2)
C(5)	0·0780(7)	0·4739(4)	0·6023(2)	C(18)	−0·1560(5)	0·4586(2)	0·3089(2)
C(6)	0·0983(6)	0·3866(3)	0·5712(2)	C(19)	−0·0368(5)	0·2584(2)	0·2979(2)
C(7)	0·0397(5)	0·3703(3)	0·4932(2)	C(20)	−0·1013(8)	0·2584(3)	0·1511(2)
C(8)	0·0454(5)	0·2918(3)	0·4418(2)	C(21)	−0·0839(10)	0·2996(5)	0·0693(3)
C(9)	−0·0297(5)	0·3162(2)	0·3721(2)	O(22)	−0·0399(4)	0·5300(1)	0·2907(1)
C(10)	0·1276(7)	0·2001(3)	0·4524(2)	C(23)	−0·3328(6)	0·5005(3)	0·3329(2)
C(11)	0·1038(6)	0·1406(3)	0·3765(2)	O(24)	−0·3711(6)	0·5771(2)	0·3187(3)
N(12)	0·1098(4)	0·1921(2)	0·2997(2)	O(25)	−0·4351(4)	0·4439(2)	0·3704(2)
C(13)	0·2787(6)	0·2390(3)	0·2887(2)	C(26)	−0·5990(7)	0·4817(4)	0·3982(3)

(ii) Vibrational parameters of the heavier atoms ($\times 10^5$)

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	1509(71)	375(17)	298(13)	13(32)	−14(28)	−7(13)
C(2)	1324(82)	460(23)	302(17)	−89(41)	42(34)	−31(17)
C(3)	2172(113)	488(25)	400(20)	−69(49)	12(42)	−39(20)
C(4)	2693(133)	620(30)	406(22)	−225(60)	54(46)	−110(22)
C(5)	1996(110)	897(38)	334(19)	−406(60)	−16(40)	−88(23)
C(6)	1416(87)	709(32)	334(19)	−197(50)	−42(36)	−40(21)
C(7)	1186(79)	520(24)	279(16)	−159(42)	−19(33)	38(17)
C(8)	1289(82)	456(23)	298(16)	−1(40)	−61(33)	56(17)
C(9)	1185(78)	377(20)	293(16)	−23(38)	−11(32)	28(15)
C(10)	2373(118)	507(26)	354(20)	191(52)	−25(43)	71(19)
C(11)	1797(99)	409(22)	408(20)	103(43)	−71(42)	74(19)
N(12)	1386(68)	383(17)	365(15)	27(33)	3(30)	1(14)
C(13)	1341(88)	492(24)	377(19)	−6(42)	114(36)	−2(20)
C(14)	1494(95)	580(28)	447(22)	30(46)	83(40)	30(22)
C(15)	1609(95)	488(24)	381(19)	−17(43)	115(39)	88(19)
C(16)	1460(87)	429(22)	287(17)	44(42)	−27(33)	9(16)
C(17)	1730(93)	425(23)	334(17)	75(44)	−34(36)	47(18)
C(18)	1326(80)	357(21)	310(17)	16(37)	−60(32)	61(16)
C(19)	1239(78)	355(20)	334(17)	3(37)	32(34)	5(16)
C(20)	2830(136)	601(29)	351(20)	383(62)	−224(46)	−84(21)
C(21)	3830(188)	1068(48)	431(25)	517(93)	−137(64)	−70(29)
O(22)	1412(59)	407(15)	456(14)	−17(28)	90(26)	93(12)
C(23)	1396(83)	420(22)	375(19)	9(40)	38(34)	65(18)
O(24)	2729(100)	590(21)	1297(35)	530(41)	988(53)	411(24)
O(25)	1550(68)	538(18)	763(21)	52(31)	378(33)	166(17)
C(26)	1674(108)	776(37)	699(31)	−32(58)	373(50)	42(29)

(iii) Co-ordinates and isotropic temperature factors for hydrogen

	x	*y*	*z*	*B*/Å²		*x*	*y*	*z*	*B*/Å²
H(3)	−0·106(7)	0·578(3)	0·455(2)	3·08(120)	H(152)	0·146(7)	0·408(3)	0·254(3)	3·65(123)
H(4)	−0·030(7)	0·611(3)	0·584(3)	3·65(125)	H(171)	−0·186(6)	0·436(3)	0·188(2)	2·13(108)
H(5)	0·120(7)	0·485(3)	0·654(3)	4·35(136)	H(172)	−0·297(6)	0·363(2)	0·245(2)	1·76(99)
H(6)	0·174(8)	0·333(4)	0·592(3)	5·10(159)	H(19)	−0·150(6)	0·213(2)	0·302(2)	1·63(97)
H(101)	0·057(8)	0·170(3)	0·496(3)	5·38(152)	H(201)	−0·038(7)	0·207(3)	0·150(3)	3·43(122)
H(102)	0·263(8)	0·217(3)	0·458(3)	6·02(165)	H(202)	−0·252(4)	0·218(2)	0·151(2)	0·22(77)
H(111)	−0·024(6)	0·110(3)	0·376(2)	2·21(99)	H(22)	−0·093(9)	0·577(4)	0·263(3)	5·98(170)
H(112)	0·191(6)	0·093(2)	0·378(2)	1·97(97)	H(261)	−0·660(7)	0·506(3)	0·350(3)	4·60(133)
H(131)	0·380(6)	0·186(3)	0·283(2)	2·64(114)	H(262)	−0·570(7)	0·541(3)	0·434(3)	4·73(131)
H(132)	0·303(5)	0·287(2)	0·335(2)	1·34(90)	H(263)	−0·667(8)	0·431(3)	0·423(3)	5·49(139)
H(141)	0·259(7)	0·259(3)	0·165(3)	4·46(139)	H(211)	0·059(7)	0·318(3)	0·061(3)	4·81(130)
H(142)	0·402(6)	0·318(3)	0·211(2)	2·52(107)	H(212)	−0·150(7)	0·366(3)	0·067(3)	5·16(135)
H(151)	0·131(6)	0·396(3)	0·156(2)	2·07(101)	H(213)	−0·130(8)	0·246(3)	0·029(2)	5·70(139)

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[4] G. Germain and M. M. Woolfson, *Acta Cryst.*, 1968, *B*, **24**, 91.

Table 2 (*Continued*)

(*b*) Vincamine hydrobromide methanolate (II)

(i) Co-ordinates of the heavier atoms

	x	*y*	*z*
N(1)	0·0892(7)	0·1768(2)	0·6040(5)
C(2)	0·2408(8)	0·2143(3)	0·5849(6)
C(3)	0·4114(9)	0·2497(3)	0·6971(7)
C(4)	0·5350(9)	0·2859(3)	0·6416(8)
C(5)	0·4948(11)	0·2864(3)	0·4873(8)
C(6)	0·3283(11)	0·2508(3)	0·3753(7)
C(7)	0·1979(8)	0·2142(3)	0·4246(6)
C(8)	0·0127(9)	0·1742(3)	0·3465(6)
C(9)	−0·0466(8)	0·1526(3)	0·4568(6)
C(10)	−0·1031(10)	0·1521(4)	0·1759(7)
C(11)	−0·3102(11)	0·1206(4)	0·1493(7)
N(12)	−0·2984(8)	0·0684(3)	0·2809(5)
C(13)	−0·1741(10)	0·001(5)	0·2942(7)
C(14)	−0·1636(12)	−0·0488(4)	0·4292(9)
C(15)	−0·0787(9)	−0·0064(3)	0·5829(7)
C(16)	−0·2065(9)	0·0632(3)	0·5758(7)
C(17)	−0·1087(9)	0·1145(3)	0·7206(6)
C(18)	0·0941(8)	0·1486(3)	0·7494(6)
C(19)	−0·2319(8)	0·1122(3)	0·4340(6)
C(20)	−0·4196(11)	0·0413(4)	0·5592(9)
C(21)	−0·4177(12)	−0·0088(5)	0·6920(9)
O(22)	0·2543(6)	0·0974(2)	0·8108(4)
C(23)	0·1411(9)	0·2132(3)	0·8716(6)
O(24)	0·2412(8)	0·2050(2)	1·0054(5)
O(25)	0·0453(6)	0·2757(2)	0·8052(5)
C(26)	0·0776(12)	0·3368(4)	0·9149(9)
Br	0·2540(1)	−0·0010(0)	0·1081(0)
C(Me)	0·2983(17)	−0·1561(5)	−0·1776(11)
O(Me)	0·3547(16)	−0·1626(4)	−0·0280(9)

(ii) Thermal vibrational parameters of the heavier atoms ($\times 10^5$)

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	1744(113)	298(16)	912(61)	14(36)	464(70)	4(26)
C(2)	1711(136)	248(19)	1236(84)	61(43)	649(90)	9(32)
C(3)	2288(165)	317(22)	1342(92)	19(49)	834(104)	−31(36)
C(4)	1848(156)	336(24)	1869(109)	−99(50)	750(109)	−115(42)
C(5)	2392(166)	354(24)	1965(112)	−110(56)	1257(115)	−6(43)
C(6)	2746(187)	364(24)	1391(98)	44(57)	995(114)	42(39)
C(7)	1949(142)	281(20)	1170(82)	31(45)	766(92)	41(33)
C(8)	2354(163)	295(20)	1054(78)	48(58)	693(95)	43(33)
C(9)	1813(140)	262(19)	1085(82)	92(43)	556(88)	−28(32)
C(10)	2629(179)	416(26)	1158(90)	−113(58)	746(107)	−73(39)
C(11)	2859(191)	470(29)	1113(87)	−90(64)	501(111)	−109(43)
N(12)	2078(131)	370(20)	1357(78)	−77(43)	567(85)	−166(33)
C(13)	3117(178)	334(20)	1900(104)	85(80)	1119(114)	−191(58)
C(14)	3292(222)	312(25)	2328(141)	7(62)	1219(149)	−226(47)
C(15)	2625(156)	233(18)	1771(95)	95(56)	967(102)	13(42)
C(16)	1953(150)	261(20)	1476(93)	6(45)	795(99)	−23(35)
C(17)	2407(163)	276(20)	1344(88)	60(47)	969(102)	19(35)
C(18)	1973(144)	283(20)	995(78)	90(44)	599(89)	1(31)
C(19)	1901(148)	262(20)	1308(84)	2(43)	534(93)	−109(34)
C(20)	2660(188)	354(25)	2228(127)	−221(58)	1468(130)	−77(46)
C(21)	4061(250)	473(34)	2878(157)	−372(86)	2294(172)	−79(66)
O(22)	2196(108)	302(14)	1197(59)	216(33)	529(67)	21(23)
C(23)	2009(148)	339(21)	975(75)	35(49)	693(87)	−8(33)
O(24)	4197(167)	369(17)	1201(64)	156(45)	939(87)	−74(27)
O(25)	2517(118)	278(14)	1666(70)	130(35)	992(76)	−14(26)
C(26)	3653(244)	290(23)	2554(152)	−54(62)	1768(165)	−170(47)
Br	2919(15)	368(1)	1856(9)	−250(6)	625(10)	121(4)
C(Me)	5840(384)	508(37)	2501(166)	290(99)	1905(215)	266(64)
O(Me)	9803(409)	692(36)	3138(149)	1142(105)	2895(213)	344(58)

(ii) Co-ordinates of hydrogens (calc. positions)

	x	*y*	*z*
H(3)	0·435	0·250	0·815
H(4)	0·668	0·313	0·714
H(5)	0·595	0·313	0·453
H(6)	0·299	0·254	0·257
H(101)	−0·028	0·107	0·151
H(102)	−0·115	0·197	0·105
H(111)	−0·372	0·090	0·045
H(112)	−0·403	0·164	0·148
H(12)	−0·440	0·054	0·263
H(131)	−0·024	0·014	0·316
H(132)	−0·240	−0·032	0·184
H(141)	−0·061	−0·098	0·441
H(142)	−0·301	−0·073	0·407
H(151)	−0·067	−0·044	0·677
H(152)	0·068	0·012	0·611
H(171)	−0·090	0·085	0·823
H(172)	−0·204	0·161	0·708
H(19)	−0·350	0·148	0·423
H(201)	−0·497	0·092	0·569
H(202)	−0·508	0·018	0·451
H(211)	−0·570	−0·025	0·674
H(212)	−0·341	0·009	0·804
H(213)	−0·353	−0·065	0·685
H(261)	−0·004	0·383	0·856
H(262)	0·234	0·349	0·968
H(263)	0·037	0·319	1·003
H(22)	0·344	0·098	0·902
HME(4)	0·153	−0·153	−0·215
HME(1)	0·307	−0·117	0·010
HME(2)	0·364	−0·109	−0·198
HME(3)	0·346	−0·204	−0·217

The E map, calculated with the most consistent set of phases, clearly indicated by our consistency factors,* showed the complete structure. Refinement proceeded *via* isotropic and anisotropic least-squares calculations, followed by a difference Fourier-map to locate the hydrogen atoms, and further least-squares refinement including a total of 338 atomic parameters, a scale factor and an isotropic extinction coefficient. The extinction coefficient reached a value of 1·4(3), assuming an overall isotropic F of 0·02 cm. A final R of 0·042 over all 1341 significant structure factors was reached at convergence of all parameters.

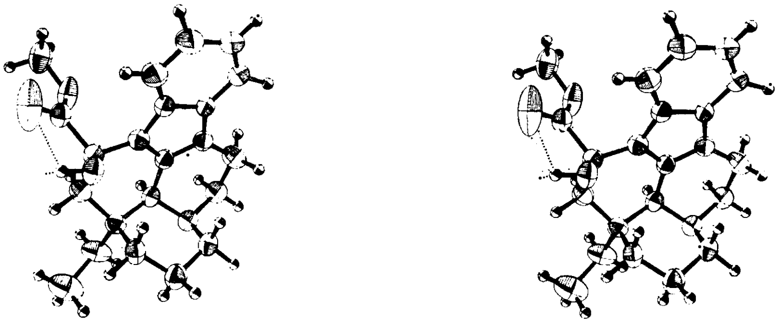

FIGURE 1 Stereoview of (I)

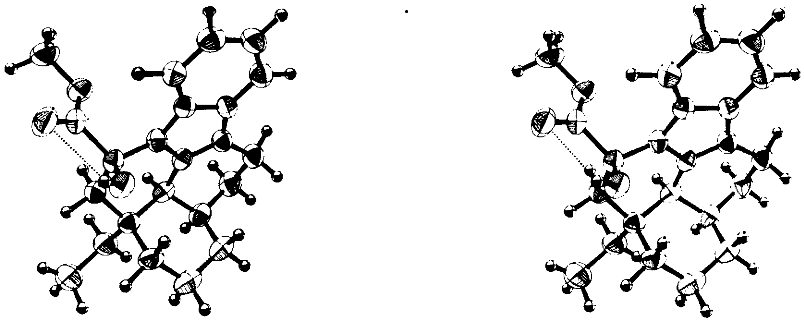

FIGURE 2 Stereoview of (II)

(*b*) *Vincamine hydrobromide monomethanolate*. The structure was solved by the heavy-atom technique. From the bromine-phased F_o-map a fragment of four atoms, forming a chemically reasonable chain [atoms N(1), C(18), C(23), O(25), as it later turned out] was located and in three subsequent Fourier syntheses, phased on improved fragments, the structure was solved. Anisotropic refinement of the structure by least-squares calculations, including hydrogen atoms in calculated theoretical positions, concluded at R 0·045 for all 2033 significant structure factors (261 atomic parameters, one scale factor).

Observed and calculated structure factors for both (I) and (II) are listed in Supplementary Publication No. SUP 20773 (23 pp., 1 microfiche).†

Determination of the Absolute Configuration.—At an intermediate stage of refinement of the vincamine hydrobromide structure an R-factor ratio test was made [5] which unequivocally indicated the chirality of the structure, so that no further measurements of Friedel pairs were considered necessary. The two R-factors were 0·0929 and 0·0867, which gave a ratio of 1·0715. With 1788 degrees of freedom (number of observations minus parameters) at a significance level of 0·005 the R-factor ratio has to be $>$1·0021, which it clearly is.

RESULTS AND DISCUSSION

Atomic co-ordinates and temperature factors for both molecules together with their standard deviations are listed in Table 2; stereoviews of the molecules are shown in Figures 1 and 2. Bond lengths and angles, and torsion angles are given in Tables 3—5. The agreement of corresponding bond lengths and bond angles in the two molecules is good; the mean value of t $[=|\Delta p|/\sqrt{\sigma_1^2 + \sigma_2^2}]$ for bond lengths is $\langle t_{\mathrm{BL}}\rangle$ 1·1, for bond angles $\langle t_{\mathrm{BA}}\rangle$ 1·3, with extreme values not $>$3·6. Equally good agreement does not hold, however, for the torsion angles (Table 5). Although there are no dramatic differences between equivalent torsion angles the deviation of corresponding atoms from each other as found by superposition of the two indole

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* Consistency factors are defined as:

$$R = (\sum_h |E_h . E_c|)/(\sum_h |E_h . E_{\mathrm{max.}}|)$$

$$Z = \sum_h |E_h . E_c|,$$

where $E_c = \{([\sum_k |E_k E_{h-k}| \cos(\phi_k + \phi_{h-k})]^2 + \sum_k |E_k E_{h-k}| \sin(\phi_k + \phi_{h-k})]^2\}^{1/2}$ and $E_{\mathrm{max.}} = \sum_k |E_k E_{h-k}|$.

† See Notice to Authors No. 7 in *J.C.S. Dalton*, 1972, Index issue.

[5] W. C. Hamilton, *Acta Cryst.*, 1965, **18**, 502.

TABLE 3

(*a*) Bond lengths (Å) involving heavier atoms

	(I)	(II)
N(1)–C(2)	1·391(6)	1·382(8)
N(1)–C(9)	1·394(6)	1·385(8)
N(1)–C(18)	1·450(6)	1·447(8)
C(2)–C(3)	1·376(7)	1·397(9)
C(2)–C(7)	1·413(6)	1·405(9)
C(3)–C(4)	1·384(8)	1·392(10)
C(4)–C(5)	1·398(8)	1·355(11)
C(5)–C(6)	1·380(8)	1·381(11)
C(6)–C(7)	1·404(7)	1·400(10)
C(7)–C(8)	1·430(6)	1·432(9)
C(8)–C(9)	1·352(6)	1·349(9)
C(8)–C(10)	1·487(7)	1·511(10)
C(9)–C(19)	1·504(6)	1·478(9)
C(10)–C(11)	1·549(7)	1·545(11)
C(11)–N(12)	1·491(6)	1·524(10)
N(12)–C(13)	1·481(6)	1·498(10)
N(12)–C(19)	1·485(6)	1·524(9)
C(13)–C(14)	1·518(7)	1·518(12)
C(14)–C(15)	1·525(7)	1·511(11)
C(15)–C(16)	1·533(7)	1·544(9)
C(16)–C(17)	1·556(7)	1·540(9)
C(16)–C(19)	1·547(6)	1·540(9)
C(16)–C(20)	1·553(7)	1·563(10)
C(17)–C(18)	1·540(6)	1·528(9)
C(18)–O(22)	1·404(5)	1·406(8)
C(18)–C(23)	1·546(6)	1·560(9)
C(20)–C(21)	1·503(9)	1·534(12)
C(23)–O(24)	1·176(7)	1·164(8)
C(23)–O(25)	1·301(6)	1·324(8)
O(25)–C(26)	1·454(7)	1·451(10)

(*b*) Bond lengths (Å) involving hydrogens [vincamine (I) only]

C(3)–H(3)	0·92(5)	C(15)–H(152)	1·01(5)
C(4)–H(4)	1·08(5)	C(17)–H(171)	1·05(5)
C(5)–H(5)	0·94(6)	C(17)–H(172)	0·97(5)
C(6)–H(6)	1·04(6)	C(19)–H(19)	1·09(4)
C(10)–H(101)	1·01(6)	C(20)–H(201)	0·89(5)
C(10)–H(102)	1·07(6)	C(20)–H(202)	1·03(7)
C(11)–H(111)	1·08(5)	C(21)–H(211)	1·14(6)
C(11)–H(112)	0·97(5)	C(21)–H(212)	1·10(6)
C(13)–H(131)	1·11(5)	C(21)–H(213)	1·09(6)
C(13)–H(132)	1·07(4)	O(22)–H(22)	0·92(6)
C(14)–H(141)	0·90(6)	C(26)–H(261)	0·99(6)
C(14)–H(142)	1·02(5)	C(26)–H(262)	1·08(5)
C(15)–H(151)	1·02(5)	C(26)–H(263)	0·99(6)

TABLE 4

Bond angles (deg.)

	(I)	(II)
N(1)–C(2)–C(3)	130·9(5)	129·5(6)
N(1)–C(2)–C(7)	107·3(4)	108·8(6)
N(1)–C(9)–C(8)	110·1(4)	110·4(6)
N(1)–C(9)–C(19)	123·7(4)	121·4(6)
N(1)–C(18)–C(17)	109·6(4)	110·5(6)
N(1)–C(18)–O(22)	107·3(4)	106·7(5)
N(1)–C(18)–C(23)	109·8(4)	110·4(5)
C(2)–N(1)–C(9)	108·0(4)	107·2(5)
C(2)–N(1)–C(18)	127·0(4)	127·1(6)
C(2)–C(3)–C(4)	118·4(5)	116·6(7)
C(2)–C(7)–C(6)	119·5(5)	119·4(6)
C(2)–C(7)–C(8)	107·2(4)	105·9(6)
C(3)–C(2)–C(7)	121·8(5)	121·6(6)
C(3)–C(4)–C(5)	120·6(6)	122·3(8)
C(4)–C(5)–C(6)	121·7(6)	121·8(8)
C(5)–C(6)–C(7)	118·1(5)	118·3(7)
C(6)–C(7)–C(8)	133·3(5)	134·7(7)
C(7)–C(8)–C(9)	107·4(4)	107·7(6)
C(7)–C(8)–C(10)	131·0(5)	130·7(7)
C(8)–C(9)–C(19)	125·8(4)	128·2(7)
C(8)–C(10)–N(11)	110·6(5)	109·4(6)
C(9)–N(1)–C(18)	124·7(4)	123·5(6)
C(9)–C(8)–C(10)	121·4(5)	121·5(7)
C(9)–C(19)–N(12)	108·5(4)	106·6(6)
C(9)–C(19)–C(16)	111·2(4)	113·2(6)
C(10)–C(11)–N(12)	115·2(4)	112·8(7)
C(11)–N(12)–C(13)	111·5(4)	112·5(6)
C(11)–N(12)–C(19)	108·7(4)	109·9(6)
N(12)–C(13)–C(14)	110·1(4)	110·2(7)
N(12)–C(19)–C(16)	114·2(4)	113·6(6)
C(13)–N(12)–C(19)	111·6(4)	113·8(6)
C(13)–C(14)–C(15)	110·1(4)	111·5(8)
C(14)–C(15)–C(16)	111·7(4)	111·7(6)
C(15)–C(16)–C(17)	112·1(4)	113·4(6)
C(15)–C(16)–C(19)	109·1(4)	109·6(6)
C(15)–C(16)–C(20)	112·7(4)	111·9(6)
C(16)–C(17)–C(18)	116·9(4)	116·2(6)
C(16)–C(20)–C(21)	116·7(5)	114·3(7)
C(17)–C(16)–C(19)	105·9(4)	105·5(6)
C(17)–C(16)–C(20)	108·5(4)	107·6(6)
C(17)–C(18)–O(22)	112·6(4)	113·6(5)
C(17)–C(18)–C(23)	108·4(4)	108·2(5)
C(18)–C(23)–O(24)	122·8(5)	122·8(6)
C(18)–C(23)–O(25)	114·3(4)	111·8(6)
C(19)–C(16)–C(20)	108·3(4)	108·5(6)
O(22)–C(18)–C(23)	109·1(4)	107·3(5)
C(23)–O(25)–C(26)	116·3(4)	114·0(6)
O(24)–C(23)–O(25)	122·9(5)	125·3(7)

TABLE 5

Torsion angles (deg.) standard deviations 0·8—1·0°)

	(I)	(II)
(i) Ring C		
C(8)–C(10)–C(11)–N(12)	−35	−42
C(10)–C(11)–N(12)–C(19)	63	65
C(11)–N(12)–C(19)–C(8)	−53	−52
N(12)–C(19)–C(9)–C(8)	25	25
C(19)–C(9)–C(8)–C(10)	2	−6
C(9)–C(8)–C(10)–C(11)	3	13
(ii) Ring D		
N(1)–C(9)–C(19)–C(16)	−21	−32
C(9)–C(19)–C(16)–C(17)	48	50
C(19)–C(16)–C(17)–C(18)	−62	−59
C(16)–C(17)–C(18)–N(1)	40	45
C(17)–C(18)–N(1)–C(9)	−7	−22
C(18)–N(1)–C(9)–C(19)	−1	18
(iii) Ring E		
N(12)–C(13)–C(14)–C(15)	−60	−58
C(13)–C(14)–C(15)–C(16)	58	59
C(14)–C(15)–C(16)–C(19)	−52	−54
C(15)–C(16)–C(19)–N(12)	51	49
C(16)–C(19)–N(12)–C(13)	−55	−50
C(19)–N(12)–C(13)–C(14)	58	53
(iv) Extra-annular		
C(19)–C(16)–C(20)–C(21)	169	179
C(2)–N(1)–C(18)–O(22)	−57	−59
C(2)–N(1)–C(18)–C(23)	61	57
O(22)–C(18)–C(23)–O(24)	−17	−27
C(18)–C(23)–O(25)–C(26)	−177	178
O(24)–C(23)–O(25)–C(26)	3	1
(v) Connecting rings C and D		
C(8)–C(9)–C(19)–C(16)	151	151
N(1)–C(9)–C(19)–N(12)	−148	−158
(vi) Connecting rings C and E		
C(9)–C(19)–N(12)–C(13)	70	75
C(16)–C(19)–N(12)–C(11)	−178	−177
(vii) Connecting rings D and E		
C(15)–C(16)–C(19)–C(9)	−73	−73
C(17)–C(16)–C(19)–N(12)	171	171

systems amounts to as much as 0·5—0·6 Å. It appears that protonation of N(12) and/or different packing of Vincamine does not affect bond lengths and bond angles to a measurable extent but small significant distortions of the molecular framework can be observed.

Table 6

Hydrogen bond geometry (distances/Å, angles/deg.)

	D · · · A*	D–H	H · · · A	D–H · · · A
(a) (I)				
O(22)–H · · · O(24)	2·68	0·92	2·32	103
O(22)–H · · · N(12)	2·89	0·92	1·98	178
(b) (II)				
O(22)–H · · · O(24)	2·65	0·81	2·37	101
MeO–H · · · Br^-	3·37	1·02	2·36	170
$\overset{+}{N}$(12)–H · · · Br^-	3·23	1·02	2·26	171

* D = Donor, A = acceptor; bond D–H · · · A.

The indole group in both molecules is planar, with mean deviations of 0·013 (I) and 0·011 Å (II). The three atoms C(10), C(19), and C(18) which are directly bonded to the indole deviate considerably out of the indole plane in various amounts and directions. The c and d rings would be expected to have an envelope conformation with N(12) and C(16) the flaps. In the structure of (I) the deviation from this conformation is relatively small, but for (II) the deviations are so big that the ring conformations are closer to a twist form with the two-fold axes bisecting C(8)–C(9) and N(12)–C(11) for ring c, and C(9)–N(1) and C(16)–C(17) for ring d (see torsion angles in Table 5). Ring e in both structures is in the chair conformation with only small deviations. The ethyl side-chain is antiplanar to C(16)–C(19) in both molecules [synclinal to C(16)–C(15) and C(16)–C(17)] which is sterically the best position. The two substituents on C(18), the hydroxy- and the methyl ester-groups, are in almost identical dispositions in both molecules. The torsion angles between the hydroxy- and the keto-oxygen of the carboxy-groups are —17 (I) and —27° (II) indicating an intramolecular hydrogen bond. For (I) the hydroxy-hydrogen has been located from the difference-Fourier map and has been refined. Interatomic distances and angles of the intramolecular hydrogen-bonds are given in Table 6. In both molecules the methyl in the ester group is coplanar with the carboxy-group and is in a *cis*-position.

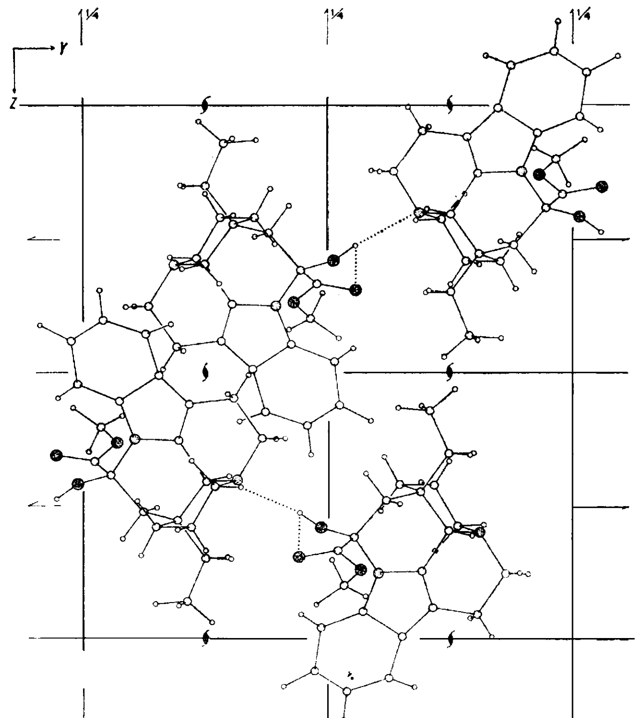

Figure 3 Packing diagram of (I). Dotted lines indicate hydrogen bonds

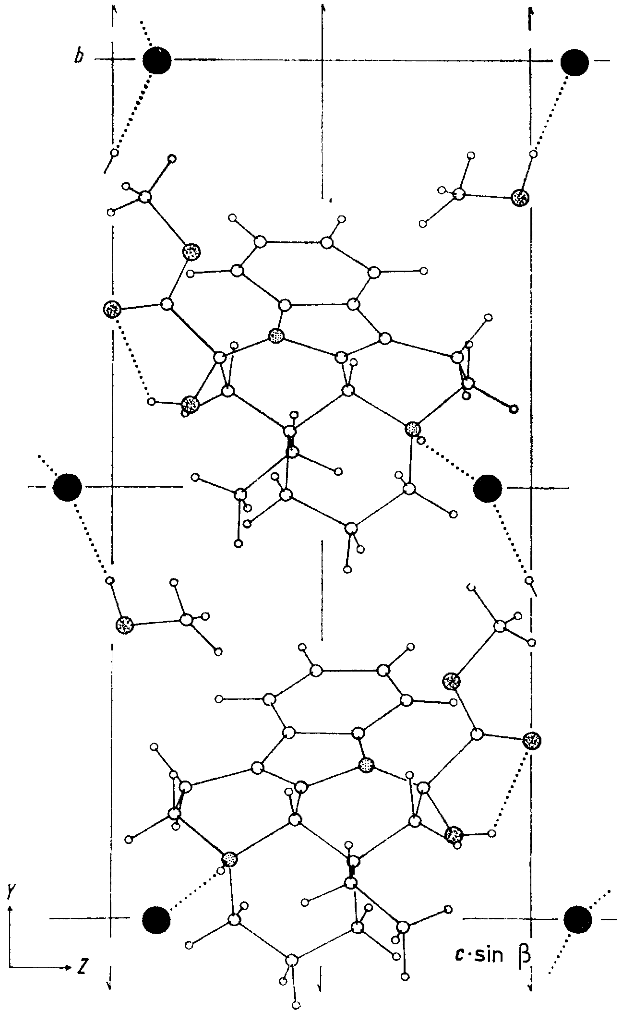

Figure 4 Packing diagram of (II). Dotted lines indicate hydrogen bonds

Apart from the intramolecular hydrogen bond already mentioned there are further intermolecular hydrogen bonds, listed in Table 6 and shown in the packing diagrams (Figures 3 and 4). The most interesting of these is the bifurcated hydrogen bond in (I) consisting of the intramolecular O(22)–H · · · O(24) and the intermolecular O(22)–H · · · N(12). There are no unusually short intermolecular contacts.

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