Table 9. Intermolecular distances less than 3.8 Å

$C(1) - O(1^{i})$	3·594 Å
$O(1) - C(14^{vi})$	3.736
$C(2) - O(2^{iv})$	3.321
$O(2) - O(2^{iv})$	3.597
$O(2) - C(2^{i})$	3.600
$O(2) - C(3^{i})$	3.289
$O(2) - C(4^{i})$	3.780
$O(2) - O(4^{i})$	3.592
$C(3) - O(2^{iv})$	3.397
$C(4) - O(4^{i})$	3.756
$O(5) - C(5^{i})$	3.696
$O(5) - C(12^{ii})$	3.534
$C(6) - C(12^{ii})$	3.728
$C(6) - C(10^{v})$	3.759
$O(6) - C(10^{v})$	3.582
$C(7) - C(8^{i})$	3.777
$C(7) - C(9^{i})$	3.793
$C(8) - C(11^{1})$	3.608
$C(14) - O(4^{111})$	3.772

used in the work, for valuable discussions and assistance with the collection of the data. The authors also wish to thank Dr Rolf Norrestam for helpful discussions and Dr Don Koenig for correcting the English of this paper.

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# Structure and Absolute Configuration of the Alkaloid Clivorine\*

# By Karin Bjåmer Birnbaum<sup>†</sup>

Biochemistry Laboratory, National Research Council of Canada, Ottawa, Canada, K1A 0R6

## (Received 17 March 1972)

Clivorine hydrate,  $C_{21}H_{27}NO_7$ .  $H_2O$ , m.p. 147–149 °C, crystallizes in the orthorhombic space group  $P2_12_12_1$  with four molecules in a unit cell of dimensions a=12.765 (1), b=14.772 (1), c=11.145 (1) Å (at -160 °C). The densities are:  $D_x=1.34$  g.cm<sup>-3</sup> (at -160 °C),  $D_m=1.28$  g.cm<sup>-3</sup> (at room temperature). The structure was determined by the symbolic-addition method from data collected at -160 °C on a four-circle diffractometer using the  $\theta/2\theta$  scan technique. It was refined by the block-diagonal least-squares method to R=0.0388 for 2506 observed reflexions. There is a trans-annular interaction between the nitrogen atom and the carbonyl carbon atom across the eight-membered ring: the N···C(8) distance is 1.993 (3) Å and the C(8)=-O(6) bond is 1.258 (3) Å. Molecules of clivorine are hydrogen bonded *via* the water molecules and form spirals extended in the direction of the c axis.

#### Introduction

The alkaloid clivorine was isolated from *Ligularia* clivorum Maxim. by Klásek, Vrublovský & Šantavý (1967). On the basis of chemical evidence and p.m.r. spectral data the structure (I), which has the empirical formula  $C_{21}H_{29}NO_8$ , was ascribed to it (Klásek, Sedmera & Šantavý, 1970). In order to determine the configuration at C(3), C(4) and C(5) it was decided to carry out an X-ray analysis. The result, reported in a preliminary communication (Birnbaum, Klásek, Sedmera, Snatzke, Johnson & Šantavý, 1971), showed the structure to be the hydrate of (II) with the empirical formula  $C_{21}H_{27}NO_7$ .  $H_2O$ .



<sup>\*</sup> Issued as N.R.C.C. No. 12763.

<sup>†</sup> Guest worker.

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## Crystal data

Clivorine hydrate,  $C_{21}H_{27}NO_7$ .  $H_2O$ , F. W. 423·47, m.p. 147–149 °C. Orthorhombic, a=12.765 (1), b=14·772 (1), c=11.145 (1) Å (at  $-160\pm5$  °C); V=2101·6 Å<sup>3</sup> [Cu  $K\alpha_1$  ( $\lambda=1.54051$  Å) and Cu  $K\alpha_2$  ( $\lambda=$ 1·54433 Å) radiations were used].  $D_m=1.28$  g.cm<sup>-3</sup> (by flotation in aqueous potassium iodide at room temperature),  $D_x=1.34$  g.cm<sup>-3</sup> (at -160 °C), Z=4, F(000)=904,  $\mu$ (Cu  $K\alpha$ ) = 8·7 cm<sup>-1</sup>. Systematic absences: h00 absent when h is odd, 0k0 absent when k is odd and 00/ absent when l is odd. Space group  $P2_12_12_1$ .

## Experimental

Clivorine, kindly supplied by Professor Santavý, was crystallized from acetone in the form of well developed colourless bipyramids. A crystal, cut to a size of  $0.50 \times$  $0.43 \times 0.40$  mm, was mounted along the b axis on a G. E. XRD-5 manual four-circle diffractometer equipped with a scintillation counter and a pulse-height analyser. Ni-filtered Cu Ka radiation was employed. The crystal was bathed in a stream of  $N_2$  gas kept at  $-160 \pm 5$  °C. The cell dimensions are weighted averages obtained from measurements of axial reflexions and their e.s.d.'s were derived from r.m.s. deviations. The intensity data were collected by the moving-crystal, moving-counter  $(\theta/2\theta)$  scan technique. The following scans were used:  $2.0^{\circ}$  for reflexions with  $2\theta \le 100^{\circ}$ ,  $3.0^{\circ}$ for  $100^\circ < 2\theta \le 130^\circ$ ,  $4^\circ$  for  $130^\circ < 2\theta \le 155^\circ$  and  $5^\circ$  for  $155^{\circ} < 2\theta \le 163^{\circ}$ . The scans were symmetrical and the background was measured for 15 sec on each side of the scan. Brass attenuation filters were used when the count rate exceeded 20,000 c.p.s. A standard reflexion, 0,0,10, was measured after about every 30 reflexions and used for scaling the data. When the intensity of the standard reflexion had decreased by 15% the crystal was discarded. A second crystal of approximately the same size was mounted in the same manner. It showed no evidence of deterioration during the collection of the remaining data. Of the 2628 independent reflexions with  $2\theta \le 163^\circ$ , 2515 (95%) were observed above threshold value. The threshold was taken as a net count of 200, or 10% of the background, whichever was higher. The intensities were corrected for Lorentz and polarization factors but no absorption correction was applied, the maximum and minimum transmission coefficients  $e^{-\mu t}$  being 0.71 and 0.65 respectively.

### Structure determination

The structure was solved by direct methods (Karle & Karle, 1966). The scale factor and overall isotropic temperature factor  $(B=1.37 \text{ Å}^2)$  were derived from a Wilson plot and used to calculate the normalized structure factors, |E|. Initial attempts to determine symbols by employing the  $\sum_2$  formula, followed by tangent refinement, did not lead to a solution of the structure although different origin-defining reflexions were tried. All *E* maps calculated from these phases had a common feature: one peak much larger than any other. Success was achieved by the method of Germain & Woolfson (1968) using the following reflexions as a starting set:

h	k	l	E	$\varphi$
0	11	7	4.04	$\pi/2$
11	3	0	3.20	$\pi/2$
4	5	0	2.39	0
0	2	5	2.03	0
6	2	8	3.12	$\pm \pi/4$
2	6	9	2.75	$\pm 3\pi/4$
4	7	8	2.70	



Fig. 1. Stereoscopic view. The thermal ellipsoids enclose 80 % probability.

The first three reflexions defined the origin and the fourth defined the enantiomorph. All 64 possible combinations of the phases  $\pm \pi/4$  and  $\pm 3\pi/4$  for the last three reflexions were tried and for each set the phases of 235 reflexions ( $|E| \ge 1.6$ ) were then determined by the tangent formula. Two sets resulted in much lower values of R (Karle) =  $\sum ||E_o| - |E_c||/\sum |E_o|$ , viz. 0.187 and 0.179, as compared to 0.265–0.352 for the others. The set with the lowest R (Karle) value was extended to include 360 reflexions ( $|E| \ge 1.45$ ) and these were used in the calculation of an E map. On this map all the non-hydrogen atoms were located on the 30 highest peaks. A structure factor calculation based on these coordinates gave a value of  $R = \sum ||F_o| - |F_c||/\sum |F_o| = 0.27$ .

### Structure refinement

Coordinates, thermal parameters and the scale factor were refined by the block-diagonal approximation of the least-squares method, minimizing the expression  $\sum w(|F_o| - |F_c|)^2$ . The matrices used were  $9 \times 9$  for coordinates and thermal parameters ( $4 \times 4$  for isotropic thermal motion) of each atom. The scale factor and the overall isotropic thermal parameter were refined by a  $2 \times 2$  matrix. A shift factor of 0.8 was used throughout the refinement.

After the sixth cycle (R=0.082), the hydrogen atoms of clivorine were located on peaks varying in heights from 0.28 to 0.58 e.Å<sup>-3</sup> on a low-angle ( $\sin \theta/\lambda \le$ 0.40 Å<sup>-1</sup>) difference Fourier map. They were subsequently refined with isotropic thermal parameters. The positions of the water hydrogen atoms were determined from peaks 0.25 e.Å<sup>-3</sup> high on difference Fourier maps calculated at later stages. H(O81) was

C(4) C(4) C(I) (I)). СН₃ ОĦ СН₃ H' H СН₃ ĊH₃ ÓAc (a) (b) C(1)н сн, (c)

Fig. 2. Newman projections down the C(2)-C(3) bond (the numbering scheme refers to that of clivorine): (a) clivorine, (b) jacobine, (c) retusamine.

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included in the refinement but not H(O82); the position of the latter was determined only from the final difference Fourier map.

The following weighting scheme, chosen so as to reflect the trends in  $|\Delta F|$ 's, was used:

 $w = w_1 w_2$ 

when  $|F_o| \leq p_1$ 

where

and

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$$w_1 = p_1/|r_0|$$
 when  $|r_0| > p_1$   
 $w_2 = \sin^2 \theta/p_2$  when  $\sin^2 \theta \le p_2$   
 $w_3 = 1$  when  $\sin^2 \theta > p_3$ 

11 1 1

The parameters were adjusted during the refinement in order to make  $w(\Delta F)^2$  as linear as possible with respect to  $|F_0|$  and  $\sin^2 \theta$ . The final values were  $p_1 = 22.0$ and  $p_2 = 0.293$ .

The scattering curve of the oxygen atoms was corrected for anomalous dispersion by  $\Delta f''=0.1$  (International Tables for X-ray Crystallography, 1962) and both absolute configurations were refined. Convergence was reached in the two cases at R=0.0399, R'= $[\sum w(\Delta F)^2/\sum wF_0^2]^{1/2}=0.0488$  and at R=0.0388, R'=0.0476 for 2506 observed reflexions. After the last cycle of refinement most parameter shifts were less than  $0.1\sigma$  and the largest one was  $0.5\sigma$ . The ratio of the two R' values is 1.025 and it is thus clear (Hamilton, 1965) that the absolute configuration giving the lower values of R and R' is the correct one. All drawings and diagrams are presented with respect to a right-handed set of crystal axes and show the correct absolute configuration.

The final difference map showed minima and maxima ranging from -0.32 to +0.28 e.Å<sup>-3</sup>, the e.s.d. of the map being 0.06 e.Å<sup>-3</sup> (Cruickshank, 1949). The water oxygen atom lies in the lowest negative region and this may indicate that its occupancy is slightly lower than 100%. The other significant features could be attributed either to H(O82) or to bonding and lone-pair electrons.

The scattering factors of Hanson, Herman, Lea & Skillman (1964) were used throughout the analysis for C, N and O atoms and those for bonded H atoms were taken from Stewart, Davidson & Simpson (1965).

The final coordinates and thermal parameters are listed in Table 1. The listed e.s.d. values were obtained from the inverse of the least-squares matrix. Table 2 shows the observed and calculated structure factors. The unobserved reflexions are marked with an asterisk. They were given the threshold value but were excluded from the least-squares refinement. In addition, the reflexions 222; 130; 6,4,10;0,10,10;3,16,7;0,18,1;

3,18,3 and 4,18,2 were excluded from the refinement because missetting of the diffractometer was suspected in some cases and double reflexion in others. Inspection of the structure-factor values of strong reflexions revealed that 114 was affected by extinction and this reflexion was also excluded.

•	The thermal	increase and isometic	All coordin	lates are $\times 10^5$ and $2-2411$ $t_{22}=3241$	d all $U_{ij}$ 's are $\times 1$	[04.	110 + ****017 - 110	[\*9*~77]	
	I ne unermai	-vioration expression	оп useu was: exp I —	$7\pi^{-1}$	22K+D + + U 331+C.	++7023KID.C.+	7013 ma.c. + 701	15mku v JJ.	
	×	ų	И	$U_{11}$	$U_{22}$	$U_{33}$	$2U_{23}$	$2U_{13}$	$2U_{12}$
	19692 (17)	63506 (14)	-15002 (21)	111 (9)	66 (6)	157 (10)	- 19 (17)	51 (17)	11 (15)
	30236 (17)	63841 (15)	- 8410 (20)	110 (9)	140 (10)	108 (9)	-7 (17)	6 (17)	40 (17)
	34715 (18)	73587 (15)	- 9476 (20)	140 (9)	103 (9)	120 (9)	-12 (17)	- 53 (17)	-43 (16)
	27776 (18)	80267 (15)	- 3030 (20)	159 (10)	122 (10)	113 (9)	-53 (17)	- 48 (17)	-47 (17)
	22675 (18)	87266 (15)	- 8019 (20)	121 (9)	132 (10)	135 (10)	- 20 (17)	- 39 (17)	- 50 (16)
	23511 (18)	89046 (15)	-21205 (21)	(6) 611	116 (10)	155 (10)	14 (18)	- 30 (17)	15 (16)
	15845 (18)	85502 (16)	-40175 (20)	151 (10)	140 (10)	103 (9)	32 (18)	17 (17)	-9 (17)
	9212 (17)	77516 (16)	-44945 (21)	136 (10)	147 (10)	135 (10)	-3 (18)	- 52 (17)	40 (17)
	5177 (17)	70577 (15)	-36161(20)	109 (9)	108 (9)	134 (9)	-38 (17)	- 84 (17)	-21 (16)
~	11768 (18)	62295 (15)	- 34089 (22)	135 (9)	114 (10)	175 (10)	-43 (18)	- 66 (19)	- 14 (16)
_	- 4439 (18)	71503 (15)	-31735 (21)	129 (10)	122 (10)	178 (11)	-12 (18)	-17 (18)	- 40 (17)
_	- 10759 (19)	79453 (17)	- 35792 (25)	115 (10)	191 (11)	258 (12)	-24 (21)	8 (19)	6 (18)
_	- 738 (20)	93532 (16)	- 40423 (24)	181 (11)	122 (10)	248 (12)	- 53 (20)	-40 (20)	73 (18)
_	10747 (19)	94374 (16)	-43902 (22)	(11) 161	153 (10)	178 (11)	42 (19)	- 33 (19)	-4 (18)
~	- 8242 (22)	84435 (20)	- 56570 (25)	248 (12)	307 (14)	217 (13)	-33 (23)	- 249 (22)	124 (23)
_	16223 (20)	93591 (17)	- 1086 (21)	179 (11)	160 (11)	153 (10)	-46 (18)	18 (18)	- 37 (19)
~	11350 (20)	100756 (17)	- 5591 (24)	208 (11)	168 (11)	225 (11)	-24 (20)	35 (21)	87 (19)
~	46017 (19)	74306 (17)	- 4846 (25)	144 (10)	202 (11)	275 (13)	-38 (22)	-136 (21)	- 7 (19)
_	29095 (21)	60607 (16)	4492 (22)	243 (12)	160 (11)	126 (10)	73 (18)	32 (20)	47 (18)
~	34779 (17)	49560 (16)	-17362 (20)	124 (9)	112 (10)	143 (10)	34 (17)	- 39 (17)	1 (16)
~	43372 (19)	44231 (17)	- 23033 (24)	153 (10)	177 (11)	228 (11)	- 58 (20)	19 (20)	(21) 69
	-4158 (16)	84469 (13)	- 44299 (19)	154 (8)	144 (9)	171 (9)	-41 (16)	- 81 (16)	53 (15)
	11340 (13)	63196 (11)	- 10050 (16)	121 (7)	138 (8)	216 (8)	- 18 (13)	102 (14)	2 (12)
	37824 (12)	58145 (11)	- 14610 (15)	(1) 16	136 (7)	157 (7)	-3 (13)	- 18 (13)	32 (11)
	26061 (13)	46765 (11)	-15333 (17)	148 (7)	133 (7)	268 (9)	- 30 (14)	40 (14)	- 19 (12)
	29974 (14)	93880 (13)	- 25764 (16)	170 (7)	285 (9)	205 (8)	121 (16)	- 52 (14)	- 182 (14)
	15898 (13)	84730 (11)	- 27142 (15)	142 (7)	147 (7)	117 (7)	4 (13)	-9 (12)	-64 (12)
	11118 (14)	75097 (12)	-55546 (15)	239 (8)	199 (8)	133 (8)	-71 (13)	22 (14)	36 (14)
	21083 (12)	64023 (11)	- 26921 (15)	61 (7)	139 (7)	153 (7)	13 (13)	- 32 (12)	22 (11)
	20538 (18)	85067 (16)	- 73553 (20)	379 (11)	417 (12)	269 (10)	91 (19)	138 (19)	87 (20)

Table 1. Final fractional coordinates and thermal parameters  $(\mbox{\AA}^2)$ 

(a) Non-hydrogen atoms

Table 1 (cont.)

	x	у	Ζ	$U_{\rm iso}$ (Å <sup>2</sup> )
H(31)	348 (2)	747 (2)	-183(2)	3 (6)
H(41)	271 (3)	798 (2)	52 (3)	18 (8)
H(71)	233 (3)	849 (2)	-432(3)	22 (8)
H(101)	76 (3)	581 (2)	-303(3)	19 (8)
H(102)	140 (2)	601 (2)	-415(3)	10 (7)
H(111)	-78(3)	673 (3)	-270(4)	31 (9)
H(121)	-127(3)	833 (2)	-290(3)	29 (9)
H(122)	-172(3)	771 (3)	- 395 (4)	38 (10)
H(131)	-50(3)	985 (2)	-439(3)	20 (8)
H(132)	-14(3)	938 (2)	-319(3)	22 (8)
H(141)	139 (3)	994 (3)	-405(3)	28 (9)
H(142)	118 (3)	947 (2)	-522(3)	24 (8)
H(151)	-154(3)	877 (3)	- 565 (4)	41 (11)
H(152)	-95(4)	779 (3)	- 597 (4)	55 (13)
H(153)	-33(2)	874 (2)	-614(3)	15 (7)
H(161)	162 (3)	920 (2)	71 (3)	18 (8)
H(171)	75 (3)	1045 (3)	-11(3)	28 (9)
H(172)	122 (3)	1021 (2)	-136 (3)	17 (7)
H(181)	459 (3)	732 (2)	37 (3)	19 (8)
H(182)	489 (3)	803 (2)	-66(3)	23 (8)
H(183)	506 (2)	707 (2)	-87(2)	-4(5)
H(191)	247 (3)	642 (2)	88 (3)	16 (7)
H(192)	364 (3)	599 (2)	77 (3)	17 (8)
H(193)	255 (2)	544 (2)	42 (3)	17 (7)
H(211)	500 (3)	472 (3)	-225 (3)	31 (9)
H(212)	416 (3)	444 (2)	- 322 (3)	23 (8)
H(213)	430 (3)	389 (3)	-193 (3)	28 (9)
H(O81)	161 (4)	821 (4)	-668(5)	59 (14)
H(O82)*	200	923	-716	

\* The position of this atom was derived from the final difference Fourier map and thus neither e.s.d.'s nor  $U_{\rm iso}$  are given.

#### Description and discussion of the structure

The structure and absolute configuration of clivorine has been determined to be (II). It is illustrated better by the stereoscopic diagram, Fig. 1. Clivorine is related to several pyrrolizidine alkaloids whose structures have been elucidated by X-ray analysis (Mathieson, 1967; Wodak, Sussman & Levinthal, 1971), and the absolute configurations of two of them, viz. jacobine (Fridrichsons, Mathieson & Sutor, 1963) and retusamine (Wunderlich, 1967), have also been determined. A comparison of the three alkaloids reveals that the configuration at C(7) (referring to the numbering scheme used for clivorine) is identical in all of them. There are, however, differences at C(2) and C(3) and they are shown in the three Newman projections (Fig. 2). As can be seen, the configuration at C(2) is the same in jacobine and retusamine but differs from that in clivorine. On the other hand, clivorine and jacobine have the same configuration at C(3), retusamine being different at that asymmetric centre.

The bond lengths and angles for non-hydrogen atoms are shown in Fig. 3. They are not corrected for thermal vibration; an analysis in terms of a rigid body (Schomaker & Trueblood, 1968) revealed that the largest libration component was only  $4 \cdot 1(^{\circ})^2$  and consequently the corrections to coordinates were negligible. The C–H bond lengths range from 0.89 to 1.05 Å, their e.s.d.'s The N···C(8) distance of 1.993 (3) Å is approximately 1 Å shorter than the sum of the van der Waals radii, indicating a transannular interaction between these atoms. Consequently, the C(8)==O(6) distance of 1.258 (3) Å is significantly longer than a normal C=O bond length of  $1.215 \pm 0.005$  Å (Sutton, 1965). This interaction implies a re-hybridization of C(8) to a state intermediate between  $sp^2$  and  $sp^3$  which is manifested by the fact that C(8) is displaced by



Fig. 3. (a) Bond lengths. Their e.s.d.'s are 0.003-0.004 Å. (b) Valency angles. Their e.s.d.'s are 0.2°.

0.213 (2) Å from the plane through the three atoms to which it is bonded. The C-C bond lengths involving C(8) are consistent with  $sp^3$  hybridization of that atom.

It should also be noted that all bond angles involving the partial bond are fairly close to tetrahedral. N is displaced by 0.366 (2) Å from the plane through the

# Table 2. Observed and calculated structure factors

All F values are  $\times 10$ . Reflexions marked with an asterisk are unobserved and  $F_{th}$  is given for them instead of  $F_o$ . The reflexions 114, 222, 130, 6,4,10, 0,10,10, 3,16,7, 0,18,1, 3,18,3 and 4,18,2 were excluded from the least-squares calculations (see text).

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Table 2 (cont.)

L [ro] [ro]	L 101 101 1 L 101 1001	L len len L len jec	I i fent fert i fent fe	-1 L [Fe] [Fe]	] e len leal e len lea	[ L KA KA] L KA	Fel L Fel Fel	1 1 m m
He 4, K+ 11 1 224 237 2 236 234 3 221 330 4 279 346 5 784 38	3         212         200         3         21+         3           4         73         71         4         210         215           1         53         68         5         180         184           6         63         68         6         101         101           7         240         231         7         91         9           8         12*         120         8         14*         151	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	p 1** 10* p 37* 1 c 70 45 1 30* 1 10 13* 137 2 10* 1 10 13* 137 2 10* 1 0 7. ** 13 4 5* 1 0 7. ** 13 4 5*	r         c         5+5         5+92           4         1         +2         4-1           7         2         34*         1f1           3         4         -7         -7           *         4         6         -77           *         7         221         272	7         241         275         2         40         40           8         137         13         3         32         31           14         5         7         14         100         93           14         5         7         14         100         93           10         42         33         14         17.         87         16           1         200         34         10         100         10         100         10	4 114 107 4 79 4 03 84 7 20 6 121 20 7 84 78 44 1. K 8 71 20 1 20 2 4 14 16 1 4 16 1 20 1 4 16 1 4 16 1 20 1 4 16 1 20 1 4 16 1 4 16 1 20 1 4 16 1 4 16 1 20 1 4 16 1 4 1	72 1 09 94 7 4 103 174 5 40 73 105 He 7, Xe 16 42 0 154 100	* 72 67 * 14 43 * 71 77 * * * * 17 0 175 141
6 15 87 7 106 103 8 302 104 9 158 144 10 89 86 11 100 99	0         60         64         0         278         14           10         11         10         15         51           H=         9, N=         11         12         30           0         67         68         11         24         30           0         67         68         11, N=         12         30           2         121         117         0         344         397	17 61 87 4 43 97 40 7, 40 12 8 47 40 0 45 40 12 8 47 40 0 45 40 12 8 47 40 1 131 142 2 184 123 Hot 16, 70 13	1         172         0         27         1           1         4         0         111         10           3         270         24         111         10           4         270         24         111         10           6         12         27         24         111         10           6         12         27         24         111         10           6         12         12         0         6         27         1	+         1+0         172           -         -         -         46         45           +         4         111         131         -           -         -         -         -         -         -           -         -         -         -         -         -         -           -          -         -	i         123         110           ?         116         121         **         0, **         15           4         208         205         1         194         194           5         215         205         1         194         194           5         215         205         1         194         194           6         415         205         205         24         10           7         15         205         24         14         44	H 5, F 17 7 152 C A1 47 7 160 1 175 146 4 167 3 244 15 5 16 126 4 234 74 6 126	1+3 1 23 10 1+0 2 46 41 107 2 30 34 121 4 1#4 181 120 4 1#4 181 120 4 1#4 181	1 47 48 2 96 107 3 88 97 4 211 222
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4 1** 1*0 5 170 1*4 * 117 107 7 214 236 8 62 63 0 49 57	7         125         134           H= 10, Y= 11         8         15-         171           0         170         125         9         87         60           1         2+0         755         10         40         40           2         177         174         11         90         91           3         78         71          9         71	0         107         103         6         *16         1*2           10         2**         759         H= 1**         1*         1*           H=         4.*         12         0         35         26           0         2**         795         1         100         80           1         700         2**         2         72         70	0         24         7         114         0           1         707         103         8         142         14           7         74         61         1         1         14         14         14         14         14         14         14         14         14         14         14         14         14         14         14         14         14         15         16         10	1     e     103     107       7     45     36       8     154     167       3     9     76     69       4     -     -     -       5     15     2     -       6     -     -     -	3         87         95         9         41         36           4         39         32         1         77#         18           5         81         93         2         721         317           6         127         143         3         30         34           7         117         66         4         137         104           6         161         177         7         1#7         1*0	2 174 176 4 57 2 174 176 4 67 3 142 147 4 239 4 200 11 7 49 5 200 73 6 48 71 He 3. K	53 1 114 200 #0 7 56 41 20 . 200 13 63 4 47 7# 5 37 #E 16 6 80 01	0 702 70° 1 40 47 1 50 70 76 1 75 70
10 114 114 Nº A, Kº 11 0 164 172 1 95 91 2 179 119	4 117 110 H+ 7, K+ 12 5 46 47 0 216 274 4 11 26 1 13 317 7 107 94 2 19 184 7 26 213 H+ 11, F= 11 4 57 46	?         1A6         17A         3         50         4.2           ?         83         92         4.21         4.1         4.4           4.2         217         ?         80         77           *         97         100         6         168         171           *         168         171         H= 12+         K= 12           7         16*         90         127         121	a 153 147 2 84 4 9 44 9 105 1 9 99 89 80 4 23 4 10 75 84 8 45 4	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	6         4*         64           14         7         3*         64           0         125         173         8         71         35           1         46         31         2         43         49         \mu_2, \$	He         T, F=         15         1         24-6           0         29         18         7         24           1         54         54         7         60           2         54         54         7         60           3         4-6         55         6         4.4	47 20 H= 1, K= 17 48 0 A0 127 110 1 120 140 70 2 35 30 c5 * 125 131	2 75+ 75 2 75+ 775 4 104 704 4+ 1, K+ 10 0 70+ 44
7 347 373 4 59 56 5 129 150 6 194 194 7 163 196 8 183 174	0 144 147 e 110 166 1 141 147 e 110 166 2 43 44 7 79 77 3 80 86 e 108 108 4 116 98 9 4 46 50 5 74 10 10 76 51	4 70 40 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	* 156 142 * 7 37 76 * 8 170 124 2 9 121 127 *	4 191 168 1 172 177 5 249 279 7 174 128 6 156 146 7 40 30 7 145 141 4 130 129 H= 8, K= 14 6 70 89	$\begin{bmatrix} 4 & 57 & 47 & 7 & 19 \\ e & 747 & 77 & 7 & 8 \\ 6 & 59 & e^7 & & & \\ & & & & & & & \\ e^{-4}s & 8, \ x = 14 & C & 130 \\ 0 & 17^* & 130 & 1 & 2C^7 \end{bmatrix}$	51 4 74 21 102 5 71 74 6 3t 63 103 He 2, 14 17 701 0 64 96	1 40 477 3 173 177 3 141 144 4 140 141 14 2, 8 18
4 96 03 10 00 08 He 7, 4+ 11 0 36 24 1 127 126	t 107 103 + 12, r 11 0 124 133 7 58 52 1 231 38 1 120 125 7 33 38 2 48 6 7 3 144 155	2         218         207         7         74.4         144           1         07         84         3         109         100           4         111         107         4         10         100           5         121         103         4         125         111           4         143         145         a         114         116           7         55         h7         7         7         7	5 7# 7% 4 08 0 4 194 107 4 194 0 7 119 134 4 194 9 8 40 40 0 04 04 H+ 10, K+ 1 0 20* 1	6 C 145 1*7 7 1 77* 40 7 2 182 187 7 2 182 187 7 2 76 206 7 6 727 290	0 1c1 178 7 14* 147 1 77 75 8 179 151 2 160 1*0 3 210 164 3* 3, K= 15 4 151 167 0 183 104 5 117 105 1 77 77	1         107         176         2         109           2         41         25         3         134           3         105         90         4         44           4         117         119         5         83           5         72         44         6         178	113 1 ** 45 155 2 191 183 273 3 27 79 78 4 5* 45 160 4 1*6 135 6 62 51	0 141 179 1 82 80 2 2% 28 3 34* 41 4 79 82
2 162 162 3 169 167 4 35 37 5 21* 207 6 76 80 7 97 67	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	9         130         131         8         234         12           9         40         45         0         6         0           9         10         10         11         76           10         70         27         14         76           10         70         27         44         17           10         69         44         0         73         61	4, 4, 4, 4, 13 1 107 4 0 147 444 7 111 10 1 44 90 7 84 1 2 41 76 4 4 3 131 172 1 16 11 4 214 71	4 6 94 89 4 7 209 213 7 8 136 134 2 9 10 43 1 He 4, K- 14	6 25 25 2 7 00 81 7 84 71 H= 0, K= 14 4 161 ?A7 C 93 64 = 310 1'7 1 99 01 A 91 70 7 80 63 7 113 111	He         Q, Y=         He         K, Y           0         334         1*1         0         70           1         143         1%4         1         118           2         42         47         2         144           1         126         104         1%         1%	14         84         He         3.         W=         17           121         0         44         49         159         159         1         147         155         24         2         217         214         107         1         171         171         171         171	0 146 176 1 143 144 7 144 143 3 63 105
8 134 127 9 134 120 He 8, Ke 11 7 71 69 1 177 178	i 107 108 10 141 143 2 142 146 44 44 12 44 0, 84 12 0 240 744 0 217 215 1 144 187 1 117 215 1 144 187	2         61         96         1         137         115           3         140         147         2         114         165           4         198         144         2         114         165           5         150         144         4         47         40           6         150         144         4         47         40           7         82         41         6         34         10	4         134         129         H=         11.         K=         1           4         704         212         0         23         1	2 0 200 201 9 1 20 29 1 2 27 15 A 7 111 109 1 6 9 59 5 74 48	3 8° 6° 6 127 131 4 42 37 5 70 75 10 4, K* 15 0 319 308 10, K* 14 1 34 139 0 111 114 7 107 192	He 0, K= 15 = 75 0 700 705 6 184 1 277 235 7 144 140 He 4, K 3 41 44 0 61 4 72° 1 1 141	74         4         71         43           170         4         171         178           16         He         4, Ke         17           50         0         22*         7           144         1         41         61	H- 4, K- 10 0 20- 41 1 155 141 2 51 159 H- 5, K- 10
2 203 205	2 141 141 3 147 145	0 49 76 7 121 124	H= 9' K= 13   H= 0' K= 1	-   - 174 173	1 7 744 726 1 5 269 293	1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		1.0.1.4.1.4

Table 3. Weighted least-squares planes

Plane 1	Pla	ane 2	Р	lane 3	P	lane 4	Pl	ane 5	P	lane 6
⊿		Δ		⊿		⊿		⊿		Δ
$\begin{array}{llllllllllllllllllllllllllllllllllll$	$C(8)  C(9)  C(11)  C(12)  N  H(111)  C(10)*  \chi^2$	$\begin{array}{c} -0.003 \text{ \AA} \\ 0.002 \\ 0.000 \\ -0.004 \\ 0.003 \\ 0.093 \\ 0.188 \\ = 13 \end{array}$	C(7) C(8) N C(13) C(14)* x	$ \begin{array}{c} -0.016 \text{ Å} \\ 0.020 \\ -0.017 \\ 0.022 \\ 0.649 \\ ^2 = 270 \end{array} $	C(1) C(2) O(1) O(7) C(10)* $\chi$	$\begin{array}{c} 0.016 \text{ \AA} \\ -0.004 \\ -0.003 \\ -0.002 \\ 0.232 \\ 2 = 72 \end{array}$	C(20) C(21) O(2) O(3) C(2)*	$\begin{array}{c} 0.000 \text{ \AA} \\ 0.000 \\ 0.000 \\ 0.000 \\ -0.074 \\ 2 = 0 \end{array}$	C(5) C(6) O(4) O(5) C(7)* H(O82) χ	$\begin{array}{c} -0.002 \text{ Å} \\ 0.010 \\ -0.002 \\ -0.001 \\ 0.058 \\ * -0.042 \\ 2^2 = 25 \end{array}$
$\chi^2 = 256$	Pl	ane 7	F	lane 8	Р	lane 9	Pl	ane 10	P	lane 11
	C(2) C(3) C(4)	⊿ 0.0 Å 0.0 0.0	C(1) C(2) C(4) C(5)	$\begin{array}{c} \Delta \\ -0.060 \text{ Å} \\ 0.103 \\ -0.152 \\ 0.108 \\ \epsilon = 9804 \end{array}$	O(7) C(1) C(5) C(6)	$\begin{array}{c} \Delta \\ -0.015 \text{ Å} \\ 0.030 \\ -0.028 \\ 0.028 \\ 2 = 615 \end{array}$	O(5) C(6) O(7) C(10) χ <sup>2</sup>	$ \begin{array}{c} \Delta \\ -0.008 \\ 0.014 \\ -0.005 \\ 0.013 \\ 2 = 106 \end{array} $	O(5) C(7) C(8) C(9) X	$\begin{array}{c} \Delta \\ -0.007 & \text{\AA} \\ 0.026 \\ -0.026 \\ 0.014 \\ 2 = 337 \end{array}$
* Atoms exclude	d from the	e calculation	s of the	plane.						

Equations of the planes (X, Y, Z are coordinates in Å):

1	0.800X + 0.580Y + 0.156Z = 9.663 Å
2	0.363X + 0.545Y + 0.756Z = 2.872
3	0.153X + 0.285Y - 0.946Z = 8.158
4	0.042X - 0.998Y - 0.038Z = -9.214
5	-0.298X + 0.310Y - 0.903Z = 2.690
6	0.603X - 0.791Y - 0.106Z = -8.346
7	-0.525X + 0.139Y - 0.839Z = 0.073
8	0.559X + 0.168Y - 0.812Z = 4.395
9	-0.990X + 0.111Y - 0.091Z = -1.329
10	0.528X + 0.106Y - 0.843Z = 4.960
11	0.845X - 0.531Y - 0.069Z = -4.710

Some dihedral angles between the planes:  $\angle 2,3$   $\angle 7,8$   $\angle 8,9$   $\angle 9,10$   $\angle 10,11$  $120\cdot3^{\circ}$   $114\cdot3^{\circ}$   $117\cdot4^{\circ}$   $115\cdot7^{\circ}$   $117\cdot6^{\circ}$ 

three atoms to which it is bonded. This transannular interaction may be compared to those found in protopine (Hall & Ahmed, 1968*a*) and in cryptopine (Hall & Ahmed, 1968*b*). The latter are across ten-membered rings and are weaker than the one in the present structure: the N···C(=O) distances are 2.555(3) and 2.581 (5) Å respectively, and the C=O bond lengths are 1.218 (3) and 1.208 (5) Å respectively. Consequently, the carbonyl carbon atom is much closer to  $sp^2$  hybridization, and in protopine it is displaced by only

0.11 Å from the plane through the three atoms to which it is bonded.

The C(20)–O(2) bond [1·361 (3) Å] is significantly longer than the equal C(1)–O(7) and C(6)–O(5) bonds, whose average length is 1·340 (2) Å. There are two bond lengths, C(2)–C(3) [1·554 (3) Å] and C(1)–C(2) [1·534 (3) Å], which are longer than normal, presumably owing to high substitution.

The conformation of the eight- and twelve-membered rings can be seen from the torsional angles (Fig. 4). The eight-membered ring can be described as follows: one half is flat, C(8), C(9), C(11), H(111), C(12) and N being coplanar (Plane 2); the other half is close to being envelope-shaped with the flap tilted away from Plane 2. C(14), which forms the flap, is displaced by 0.649 (2) Å from the mean plane through C(7), C(8), N and C(13) (Table 3). The dihedral angle between the two planes is 120.3°. The conformation of the twelve-membered ring can also be seen in Fig. 5. It can be described in terms of the mean planes 7 to 11 (Table 3) and the dihedral angles between these planes which range from 114.3 to 117.6°. The atoms of the transdiene system (Plane 1 are approximately coplanar. On the other hand, both the large displacement of O (4) from Plane 1 [0.988(2) Å] and the long C(5)–C(6) bond [1.497(3) Å] indicate decreased delocalization of electrons in the conjugated ester system, which is not surprising in view of the cross-conjugation. The position of the corresponding band in the infrared spectrum at 1725  $cm^{-1}$  (Klásek *et al.*, 1967) does not reveal the expected shift to a higher frequency, being in a region where carbonyl frequencies of saturated and unsaturated esters overlap (Felton & Orr, 1955).

## Hydrogen bonding and packing

The relevant bond lengths and angles are shown in Fig. 6. Both hydrogen atoms of the water molecules are donated to carbonyl groups. The  $H \cdots O$  distances are 0.6 and 0.3 Å shorter than 2.4 Å, the sum of the van der Waals radii. H(O81) lies in the plane defined by C(8), O(6) and O(8), and H(O82) lies in the ester plane through C(5), C(6), O(4) and O(5).

The hydrogen bonds are also marked on the stereoscopic packing diagram (Fig. 7). The molecules of clivorine are linked by hydrogen bonds *via* the water molecules and form spirals around the twofold screw axes parallel to c at x = 1/4, y = 0 and at x = 3/4, y = 1/2 in each unit cell.

Apart from the hydrogen bonds, there are no intermolecular distances shorter than van der Waals contacts.

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Fig. 4. Torsional angles (Klyne & Prelog, 1960). Their e.s.d.'s (Huber, 1961) are 0.3°.



Fig. 5. Partial structure viewed along the b axis.



Fig. 6. Bond lengths and angles for the hydrogen bonds. O(4) and O(6) are at  $(\frac{1}{2} - x, 2 - y, z - \frac{1}{2})$ .



Fig. 7. Stereoscopic packing diagram. Broken lines indicate hydrogen bonds. The origin is at the rear, lower-left corner. The directions of the axes are  $a \rightarrow , b\uparrow$ .

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