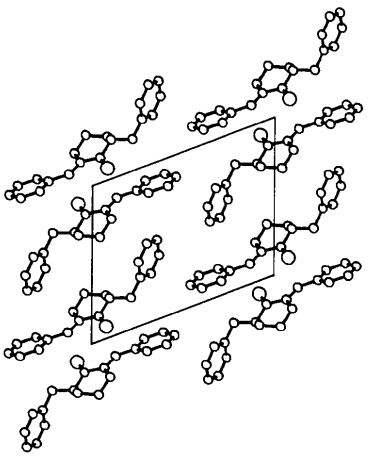

Fig. 2. The crystal structure viewed along *c*.

dimerization and may account for the loss of crystallinity upon dimerization (Forward & Whiting, 1969). This distance should be compared with the 4·174 (5) Å found for BBCP (Nakanishi, Jones, Thomas, Hursthouse & Motevalli, 1981), a structure shown to undergo a single-crystal → single-crystal photodimerization (Nakanishi, Jones & Thomas, 1980). An additional factor contributing to the loss of crystallinity upon reaction may be found in the relatively low melting point of the solid. Melting-point depression as a result of formation of product may well lead to the loss of topochemical control upon the reaction (Nakanishi, Ueno & Sasada, 1976).

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Vincamine 2-Oxoglutarate (Oxovinca). Two independent X-ray Structure Determinations

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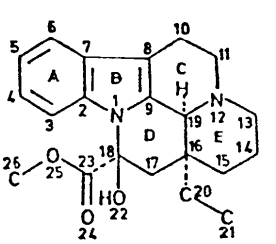
Abstract. $C_{21}H_{27}N_2O_3^+.C_5H_5O_5^-$, $M_r = 500{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 20{\cdot}058$ (4), $b = 7{\cdot}556$ (1), $c = 16{\cdot}249$ (4) Å, $Z = 4$, $D_c = 1{\cdot}35$ Mg m^{-3}, μ(Cu $K\alpha$) = 0·79 mm^{-1}. Final $R = 0{\cdot}098$ and $R_w = 0{\cdot}121$ for 1204 observed reflexions. The title compound is a more efficient brain vasodilator drug than pure vincamine. The two molecules are similar, except for the methyl ester radical which is rotated ~180° from one molecule to the other. Cations and anions are linked through NH···O and OH···O hydrogen bonds forming continuous chains parallel to **c**.

Introduction. Vincamine (I) is a well known brain vasodilator drug. To increase its action time, several derivatives were obtained in the ELMU Laboratory of Madrid. One of them, the title compound, hereafter oxovinca, has a half-life three times greater than that of vincamine, and shows less and shorter hypotensic secondary action. Gas-chromatography studies on the residual drugs in urine (Montoro, Vilar, Calatayud, de



(I)

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la Fuente & Vila Coro, 1978) showed that vincamine begins to hydrolyze after the first hour of administration forming vincaminic acid, which is not active. Oxovinca, on the contrary, does not hydrolyze at all and is present in urine after the sixth hour of administration.

The X-ray determination of the molecular structure and absolute configuration of vincamine and of its hydrobromide methanolate was reported by Weber & Petcher (1973). Mainly to discover any structural reason for the non-hydrolysis of oxovinca in the body, an X-ray analysis was performed.

Two independent analyses were made, with crystals obtained from water and dimethylformamide solutions. There were, however, some difficulties with the crystals obtained from water. These were pseudoprismatic with three zone axes forming angles of ~1°. These suspected twinned crystals were monoclinic, $P2_1$, with a = 19·973 (3), b = 7·591 (1), c = 15·999 (4) Å, β = 90·49 (3)°, $Z = 4$. Nevertheless, the reciprocal axes a^* and c^* showed extinctions when the corresponding indices were odd, and also the planes a^*b^*, b^*c^* were pseudomirrors. Thus, the crystals were pseudo-orthorhombic $P2_12_12_1$. On the other hand, analysis of the peak diffraction profiles indicates a single reciprocal lattice, so the crystal data were collected with Mo $K\alpha$ radiation. It was not possible to solve the structure in the $P2_1$ lattice. Nevertheless, averaged data for the $P2_12_12_1$ lattice gave the crystal structure of the unique independent vincamine molecule plus the α-oxoglutaric moiety. The vincamine molecule presented statistical disorder for the ethyl and methyl ester radicals, the latter being the overlap of two groups rotated by ~180°. This disorder was interpreted as the result of the overlapping of the two independent molecules in the $P2_1$ cell. The H atoms were placed by geometry, when possible; a difference synthesis showed no more H atoms. An anisotropic refinement, isotropic for C(21) and O(26), including fixed H atoms gave R = 0·11. Tables for and the description of this crystal structure are not given, because the values are similar and less accurate than those found for the crystals obtained from dimethylformamide solution.

Crystals from dimethylformamide solution have the lattice described in the *Abstract*, which is significantly different from that for crystals obtained from water solution. Moreover, they have a unique prismatic zone axis. Intensities were collected with Cu $K\alpha$ radiation; 2075 independent reflexions up to θ = 60° were measured in the $\omega/2\theta$ scan mode; of these, 1204 had $I > 2\sigma(I)$. No absorption correction was made. The structure was solved by *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1977) and a full-matrix anisotropic refinement [except C(20) and C(21) which were refined isotropically]. The H atoms were positioned, when possible, by geometrical considerations. A final difference map showed H atoms attached to O(22), O(33) and N(12). In the area around N(12) and O(34) a peak appeared for H(12) but no peak appeared near O(34), confirming the protonation of N(12). The absolute configuration assumed was that found by Weber & Petcher (1973) and the anomalous-dispersion factors were included in the calculations. In the last cycles a weighting scheme was applied to prevent trends in $\langle wA^2F\rangle$ *vs* $\langle F_o\rangle$ and $\langle \sin\theta/\lambda\rangle$. The refinement converged to R = 0·098 and R_w = 0·121. Atomic parameters are listed in Table 1.* Calculations were carried out with XRAY 70 (Stewart, Kundell & Baldwin, 1970).

* Lists of structure factors, anisotropic thermal parameters and H atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35781 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Positional parameters* (×10⁴) *and equivalent isotropic thermal parameters* (Å² ×10³)

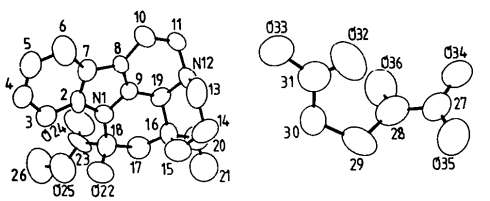
$$U_{eq} = \tfrac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
N(1)	4501 (5)	−192 (14)	727 (6)	56 (4)
C(2)	5124 (6)	345 (19)	983 (9)	60 (5)
C(3)	5748 (7)	134 (20)	618 (8)	68 (5)
C(4)	6293 (7)	817 (26)	1024 (10)	82 (7)
C(5)	6241 (8)	1736 (25)	1736 (13)	91 (7)
C(6)	5612 (9)	1997 (21)	2105 (14)	96 (8)
C(7)	5050 (6)	1254 (17)	1710 (9)	59 (5)
C(8)	4360 (6)	1327 (18)	1892 (8)	54 (5)
C(9)	4057 (6)	465 (19)	1290 (8)	55 (4)
C(10)	3983 (7)	2223 (25)	2545 (10)	87 (7)
C(11)	3247 (7)	1904 (24)	2503 (8)	79 (6)
N(12)	3000 (5)	1862 (17)	1603 (7)	70 (4)
C(13)	3106 (7)	3540 (20)	1145 (13)	86 (7)
C(14)	2885 (9)	3251 (29)	262 (11)	95 (7)
C(15)	3226 (9)	1871 (28)	−176 (10)	91 (7)
C(16)	3126 (6)	111 (22)	276 (9)	71 (5)
C(17)	3558 (8)	−1423 (24)	−40 (11)	89 (7)
C(18)	4325 (7)	−1039 (21)	−11 (10)	81 (6)
C(19)	3324 (6)	219 (18)	1191 (8)	61 (5)
C(20)	2373 (10)	−579 (27)	220 (13)	106 (6)
C(21)	2139 (13)	−979 (38)	−511 (17)	146 (8)
O(22)	4588 (5)	−110 (17)	−695 (6)	94 (4)
C(23)	4659 (9)	−3037 (33)	98 (4)	98 (9)
O(24)	4557 (10)	−3888 (24)	639 (12)	154 (9)
O(25)	4987 (8)	−3420 (21)	−552 (11)	138 (7)
C(26)	5271 (15)	−5335 (38)	−473 (21)	179 (15)
C(27)	3715 (9)	−1561 (26)	−2681 (12)	83 (7)
C(28)	3790 (9)	−3325 (31)	−3021 (15)	104 (9)
C(29)	4212 (9)	−4688 (28)	−2648 (12)	101 (8)
C(30)	3891 (8)	−6522 (24)	−2636 (14)	99 (8)
C(31)	3215 (10)	−6407 (32)	−2226 (13)	96 (8)
O(32)	2980 (7)	−5059 (23)	−1906 (10)	129 (6)
O(33)	2833 (6)	−7847 (20)	−2283 (10)	119 (6)
O(34)	3225 (6)	−671 (17)	−2925 (9)	111 (6)
O(35)	4124 (7)	−1000 (18)	−2180 (9)	113 (6)
O(36)	3474 (8)	−3742 (21)	−3675 (11)	138 (7)

Discussion. Fig. 1 shows the structure of oxovinca. The bond lengths, bond angles and some torsion angles are in Tables 2, 3 and 4 respectively. The geometry of the vincamine moiety is similar to that of vincamine and BrH–vincamine. So, for general comment on the bond lengths, bond angles and ring conformations we refer to Weber & Petcher (1973). There are, however, some specific comments for the oxovinca molecule. The protonated N(12) in oxovinca has a geometry more similar to that for the protonated N(12) in BrH–vincamine than for the neutral N(12) of pure vincamine. Thus, while N(12)–C(13) is identical (1·49 Å) for the three compounds, N(12)–C(11) and N(12)–C(19) are longer for N^+ (1·53 Å) than for N (1·49 Å). Moreover, the average bond angle CNC is greater for N^+ (111·9°) than for N (110·6°), indicating a smaller repulsion between H–N^+ and N^+–C bonds than between $\ddot{N}$ and N–C bonds. These facts, besides the location of H(12) for N(12), reinforce the actual protonation of N(12) in oxovinca. The negative charge of this salt should be distributed between O(34) and O(36), which are between singly and doubly bonded to C(27) and C(28), respectively. The methyl ester radical in oxovinca is rotated ~180° around C(18)–C(23) with respect to the molecules in both vincamine and BrH–vincamine. The torsion angle for O(22)–C(18)–C(23)–O(25) of −12° could support the presence of an O(22)H···O(25) H bond in oxovinca, in the same way as the torsions of O(22)–C(18)–C(23)–O(24) in vincamine (−17°) and BrH–vincamine (−27°) support the presence of a H bond between the hydroxy and the keto O atoms of the carboxy groups. Also, the O(22)···O(25) distance in oxovinca of 2·64 Å is similar to the O(22)···O(24) distances in vincamine and BrH–vincamine of 2·68 and 2·65 Å respectively. Although the position of H(22), located on a difference map, does not allow it to contribute to an O(22)H··· O(25) H bond, but only to O(22)H···O(35) (Table 5), there are some doubts about this position of H(22) which appears poorly at 1·3 Å from O(22). Thus, it could also be possible that another position of H(22)

Table 2. *Bond lengths* (Å) *involving heavy atoms* (*average e.s.d.* 0·02 Å)

N(1)–C(2)	1·38	C(16)–C(17)	1·54
N(1)–C(9)	1·37	C(16)–C(19)	1·54
N(1)–C(18)	1·40	C(16)–C(20)	1·60
C(2)–C(3)	1·39	C(17)–C(18)	1·57
C(2)–C(7)	1·37	C(18)–O(22)	1·42
C(3)–C(4)	1·38	C(18)–C(23)	1·66
C(4)–C(5)	1·35	C(20)–C(21)	1·31
C(5)–C(6)	1·41	C(23)–O(24)	1·11
C(6)–C(7)	1·41	C(23)–O(25)	1·28
C(7)–C(8)	1·42	O(25)–C(26)	1·56
C(8)–C(9)	1·32		
C(8)–C(10)	1·47	C(27)–C(28)	1·45
C(9)–C(19)	1·49	C(27)–O(34)	1·26
C(10)–C(11)	1·50	C(27)–O(35)	1·23
C(11)–N(12)	1·54	C(28)–C(29)	1·46
N(12)–C(13)	1·49	C(28)–O(36)	1·28
N(12)–C(19)	1·55	C(29)–C(30)	1·53
C(13)–C(14)	1·52	C(30)–C(31)	1·51
C(14)–C(15)	1·44	C(31)–O(32)	1·24
C(15)–C(16)	1·53	C(31)–O(33)	1·33



(*a*) (*b*)

Fig. 1. Molecular structure of oxovinca: (*a*) vincamine cation and (*b*) α-oxoglutaric anion.

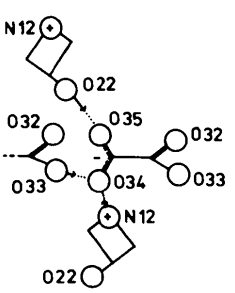


Fig. 2. Schematic packing through H bonds of oxovinca.

Table 3. *Bond angles* (°) *involving heavy atoms* (*average e.s.d.* 1°)

N(1)–C(2)–C(3)	131	C(13)–C(14)–C(15)	116
N(1)–C(2)–C(7)	108	C(14)–C(15)–C(16)	109
N(1)–C(9)–C(8)	112	C(15)–C(16)–C(17)	115
N(1)–C(9)–C(19)	122	C(15)–C(16)–C(19)	112
N(1)–C(18)–C(17)	111	C(15)–C(16)–C(20)	112
N(1)–C(18)–O(22)	111	C(16)–C(17)–C(18)	114
N(1)–C(18)–C(23)	103	C(16)–C(20)–C(21)	118
C(2)–N(1)–C(9)	106	C(17)–C(16)–C(19)	102
C(2)–N(1)–C(18)	128	C(17)–C(16)–C(20)	106
C(2)–C(3)–C(4)	118	C(17)–C(18)–O(22)	116
C(2)–C(7)–C(6)	120	C(17)–C(18)–C(23)	103
C(2)–C(7)–C(8)	108	C(18)–C(23)–O(24)	123
C(3)–C(2)–C(7)	121	C(18)–C(23)–O(25)	109
C(3)–C(4)–C(5)	123	C(19)–C(16)–C(20)	108
C(4)–C(5)–C(6)	120	O(22)–C(18)–C(23)	113
C(5)–C(6)–C(7)	118	C(23)–O(25)–C(26)	109
C(6)–C(7)–C(8)	132	O(24)–C(23)–O(25)	128
C(7)–C(8)–C(9)	106		
C(7)–C(8)–C(10)	132	C(27)–C(28)–C(29)	123
C(8)–C(9)–C(19)	126	C(27)–C(28)–O(36)	120
C(8)–C(10)–C(11)	114	C(28)–C(27)–O(34)	117
C(9)–N(1)–C(18)	125	C(28)–C(27)–O(35)	120
C(9)–C(8)–C(10)	122	C(28)–C(29)–C(30)	114
C(9)–C(19)–N(12)	105	C(29)–C(28)–O(36)	117
C(9)–C(19)–C(16)	111	C(29)–C(30)–C(31)	109
C(10)–C(11)–N(12)	111	C(30)–C(31)–O(32)	125
C(11)–N(12)–C(13)	114	C(30)–C(31)–O(33)	116
C(11)–N(12)–C(19)	107	O(32)–C(31)–O(33)	119
N(12)–C(13)–C(14)	108	O(34)–C(27)–O(35)	123
N(12)–C(19)–C(16)	111		
C(13)–N(12)–C(19)	114		

Table 4. *Torsion angles* (°) (*average e.s.d.* 2°)

(i) Ring *C*	
C(8)–C(10)–C(11)–N(12)	−38
C(10)–C(11)–N(12)–C(19)	66
C(11)–N(12)–C(19)–C(9)	−57
N(12)–C(19)–C(9)–C(8)	29
C(19)–C(9)–C(8)–C(10)	−2
C(9)–C(8)–C(10)–C(11)	6
(ii) Ring *D*	
N(1)–C(9)–C(19)–C(16)	−30
C(9)–C(19)–C(16)–C(17)	56
C(19)–C(16)–C(17)–C(18)	−65
C(16)–C(17)–C(18)–N(1)	42
C(17)–C(18)–N(1)–C(9)	−10
C(18)–N(1)–C(9)–C(19)	4
(iii) Ring *E*	
N(12)–C(13)–C(14)–C(15)	−59
C(13)–C(14)–C(15)–C(16)	59
C(14)–C(15)–C(16)–C(19)	−53
C(15)–C(16)–C(19)–N(12)	49
C(16)–C(19)–N(12)–C(13)	−51
C(19)–N(12)–C(13)–C(14)	53
(iv) Extra-annular	
C(19)–C(16)–C(20)–C(21)	−171
C(2)–N(1)–C(18)–O(22)	−51
C(2)–N(1)–C(18)–C(23)	70
O(22)–C(18)–C(23)–O(25)	−12
O(22)–C(18)–C(23)–O(24)	173
C(18)–C(23)–O(25)–C(26)	−177
O(24)–C(23)–O(25)–C(26)	−3
(v) Connecting rings *C* and *D*	
C(8)–C(9)–C(19)–C(16)	149
N(1)–C(9)–C(19)–N(12)	−150
(vi) Connecting rings *C* and *E*	
C(9)–C(19)–N(12)–C(13)	70
C(16)–C(19)–N(12)–C(11)	−178
(vii) Connecting rings *D* and *E*	
C(15)–C(16)–C(19)–C(9)	−68
C(17)–C(16)–C(19)–N(12)	173
(viii) α-Oxoglutaric anion	
O(34)–C(27)–C(28)–O(36)	17
O(34)–C(27)–C(28)–C(29)	−163
O(35)–C(27)–C(28)–C(29)	18
C(27)–C(28)–C(29)–C(30)	137
C(28)–C(29)–C(30)–C(31)	−54
C(29)–C(30)–C(31)–O(32)	−4
C(29)–C(30)–C(31)–O(33)	170

Table 5. *Hydrogen-bond geometry*

D = donor, *A* = acceptor.

D–H···*A*	*D*···*A*	*D*–H	H···*A*	∠*DHA*
O(22)H···O(35)	2·67 Å	1·3 Å	1·7 Å	129°
O(33)H···O(34)	2·50	1·0	1·6	143
N(12)H···O(34)	2·73	1·1	1·7	170

would permit a bifurcated H bond between O(22) and O(35), O(25). The other two H bonds present in the oxovinca structure, N(12)H···O(34) and O(33)H···O(34), are detailed in Table 5. The α-oxoglutaric anions link different vincamine cations through H bonds, forming continuous helical chains parallel to **c**. Different chains are also connected through the H bonds between the α-oxoglutaric anions. Fig. 2 shows the packing schematically.

Any structural difference between oxovinca and vincamine could influence the non-hydrolysis of the former. It seems, however, that the proximity of the ester O atom to the hydroxy group, with the possibility of linking by a H bond, could protect the ester O(25) from hydrolysis. Oxovinca from water solution, however, has the methyl ester radical in both positions: with O(25) near O(22) and O(24) near O(22). So the solvent could influence the hydrolysis of the drug.

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4-(α-Hydroxy-4-methoxybenzyl)-3,5-diiodobenzyl Alcohol

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Abstract. $C_{15}H_{14}I_2O_3$, triclinic, $P\bar{1}$, $a = 9{\cdot}507$ (3), $b = 9{\cdot}735$ (4), $c = 9{\cdot}383$ (2) Å, $\alpha = 99{\cdot}06$ (2), $\beta = 111{\cdot}56$ (3), $\gamma = 84{\cdot}28$ (2)°, $Z = 2$, $M_r = 482{\cdot}06$, $D_c = 2{\cdot}00$ Mg m^{-3}; for 4204 observed data $R = 8{\cdot}2\%$. The conformation of the two phenyl rings is twist-skewed, and the bridging C–C–C angle is 114°.

Introduction. An important feature of the thyroid hormone structure (Fig. 1*a*) is the O bridge linking the two iodophenyl rings. The thyroid hormones are characterized by a bridging angle of 120° and a diphenyl ether conformation which is either skewed (mutually perpendicular and bisecting) or twist-skewed

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