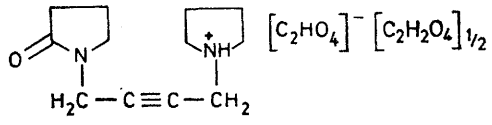
Crystal Structure of Oxotremorine Sesquioxalate, 1-[4-(2-oxopyrrolidin-1-yl)but-2-ynyl]pyrrolidinium Sesquioxalate

By **Peter J. Clarke,*† Peter J. Pauling, and Trevor J. Petcher,‡** William Ramsay, Ralph Forster and Christopher Ingold Laboratories, University College London, Gower Street, London WC1E 6BT

The crystal structure of the title compound (I) has been determined from *X*-ray diffraction data. Crystals are triclinic, $a = 8{\cdot}183(4)$, $b = 14{\cdot}449(6)$, $c = 8{\cdot}879(4)$ Å, $\alpha = 125{\cdot}00(3)$, $\beta = 89{\cdot}32(3)$, $\gamma = 98{\cdot}30(3)°$, $Z = 2$, space group $P\bar{1}$. The structure was solved by direct methods and refined by full-matrix least-squares to R 0·104 for 1895 three-dimensional diffractometer data. There is considerable disorder in the positions of the oxalic acid and oxalate anion. The pyrrolidine ring adopts the envelope conformation with the nitrogen 0·54 Å out of the plane of the carbon atoms, and the nitrogen substituent in the pseudo-equatorial position. The pyrrolidone ring is almost planar. The structure is linked by a series of hydrogen bonds between the oxotremorine cation and the oxalic acid and oxalate moieties.

TREMORINE, 1,1′-(but-2-ynylene)dipyrrolidine, is metabolised in the liver [1] to the pharmacologically active compound oxotremorine, 1-[4(pyrrolidin-1-yl)but-2-ynyl]pyrrolidin-2-one, which may also be prepared synthetically and is used to simulate experimentally the



(I)

effects of Parkinsonism.[2] The protonated form of oxotremorine, 1-[4-(2-oxopyrrolidin-1-yl)but-2-ynyl]pyrrolidinium], is a potent muscarinic agonist.[3] We report here the crystal structure of (I), the sesquioxalate of oxotremorine, as part of a continuing study of structure–activity relationships among cholinergic drugs.

EXPERIMENTAL

Crystals of (I) are poorly developed plates exhibiting the forms {100}, {010}, and {001}. The plane of the plate is (100), and the crystals give biaxial interference figures.

Crystal Data.—$[C_{12}H_{19}NO]^+[C_2HO_4]^-,\frac{1}{2}(C_2H_2O_4)$, $M = 341{\cdot}33$. Triclinic, $a = 8{\cdot}183(4)$, $b = 14{\cdot}449(6)$, $c = 8{\cdot}879(4)$ Å, $\alpha = 125{\cdot}00(3)$, $\beta = 89{\cdot}32(3)$, $\gamma = 98{\cdot}30(3)°$, $U = 847{\cdot}8$ Å^3, $D_m = 1{\cdot}34$ (by flotation), $Z = 2$, $D_c = 1{\cdot}34$ g cm^{-3}. Space group $P1$ or $P\bar{1}$, subsequently shown to be the latter by successful refinement. Mo-K_α radiation, $\lambda = 0{\cdot}7107$ Å; μ(Mo-K_α) = 2·54 cm^{-1}.

Intensity Measurement.—Intensities with Bragg angles in the range θ 2·5—27·5° were measured by use of an automatic computer controlled [4] four-circle diffractometer with zirconium-filtered Mo-K_α radiation and a θ—2θ scan. The reflections were integrated over a peakwidth of 1·6° with steps of 0·04° in 2θ and a counting time of 5 s per step. The number of unique reflections measured was 3911, of which 1895 had $I \geqslant 3\sigma(I)$ and were classed as observed. The data were corrected for Lorentz-polarisation effects but not for absorption or extinction.

Structure Solution.—Several attempts were made to solve the structure by direct methods, but the results were highly dependent upon the method of calculating the normalised structure factors. The E values for oxotremorine were calculated by the K curve method,[5] which ensures that $\langle|E|^2\rangle \approx 1{\cdot}0$ within discrete spherical shells of reciprocal space, and avoids the anomalous distribution of $\langle|E|^2\rangle$ with respect to $\sin^2\theta$ frequently encountered with the older Wilson plot [6] method. However, a successful solution to the phase problem was only achieved when the reflections in each of the eight parity groups were normalised separately to ensure that $\langle|E|^2\rangle \approx 1{\cdot}0$ for each parity group. This was a rather unexpected result since, when the data were normalised in one batch, the values of $\langle|E|^2\rangle$ for the eight parity groups fell within the range 0·90—1·10 which would usually be considered satisfactory. However, renormalisation led to changes of up to 45% in the individual E values used for symbolic addition, and, clearly, differences of this magnitude could have a dramatic effect on the progress of phase determination. The overall E statistics, which were the same for both methods of normalisation, were $\langle|E|\rangle$ 0·782, $\langle|E|^2\rangle$ 0·997, and $\langle|E^2 - 1|\rangle$ 0·958, indicating that the structure was probably centrosymmetric.[7]

The structure was solved by direct methods with the LSAM symbolic addition programs,[8] and 499 reflections with E values $\geqslant 1{\cdot}5$. The origin was defined by reflections $2,\bar{1},\bar{1}$, $1,6,\bar{2}$, and $2,\bar{1},0$, and the symbols by $2,11,\bar{2}$, $2,4,\bar{2}$, $1,5,\bar{3}$, and $2,\bar{1}\bar{7},\bar{5}$. The successful combination of signs for the symbols was $(--++)$, and all non-hydrogen atom positions were revealed in the E map.

Structure Refinement.—The structure was refined by full-matrix least-squares, by use of observed reflections only and unit weights. Atomic scattering factors for carbon, oxygen, and nitrogen were taken from ref. 9 and for hydrogen from ref. 10. The initial R factor for 540 reflections with $\sin\theta/\lambda \leqslant 0{\cdot}35$ was 0·37. Refinement of scale factor, atomic co-

† *Present address:* Chemical Crystallography Laboratory, South Parks Road, Oxford OX1 3QR.

‡ *Present address:* Research Laboratories for Pharmaceutical Chemistry, Sandoz Ltd., Basle, Switzerland.

[1] B. Karlen, *Acta Pharm. Suecica*, 1970, **7**, 169.
[2] D. J. Jenden, 'Methods of Pharmacological Testing,' ed. A. Burger, Dekker, New York, 1967, p. 337.
[3] I. Hanin, D. J. Jenden, and A. K. Cho, *Mol. Pharmacol.*, 1966, **2**, 352.
[4] W. R. Busing, R. D. Ellison, H. A. Levy, S. P. King, and R. T. Roseberry, U.S. Atomic Energy Commission, Report ORNL 4143, 1968.
[5] J. Karle and H. Hauptman, *Acta Cryst.*, 1953, **6**, 473.
[6] A. J. C. Wilson, *Nature*, 1942, **150**, 152.
[7] I. L. Karle, K. S. Dragonette, and S. A. Brenner, *Acta Cryst.*, 1965, **19**, 713.
[8] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.
[9] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.
[10] 'International Tables for *X*-Ray Crystallography,' vol. 3, Kynoch Press, Birmingham, 1962.

ordinates, and eventually the overall isotropic temperature factor, whilst steadily increasing the sin θ/λ limit reduced R factor to 0·285 by the time all the data had been included. Two cycles of refinement of co-ordinates and individual isotropic temperature factors gave R 0·225 which could not be improved by further refinement. A difference-Fourier synthesis showed that the oxygen atoms of the oxalate and oxalic acid moieties were distributed over two or three sites in the unit cell, but there was no comparable indication of disorder for their carbon atoms. Such a situation might arise through rotation of the carboxy-groups about a vector close to that of the connecting carbon–carbon bond.

The disorder in the oxygen atoms was accounted for by placing partial atoms at each of the sites indicated by the difference-Fourier synthesis, and refining the site occupation factors in addition to the co-ordinates and temperature factors. The site occupation and temperature factors were refined on alternate cycles at first because of high correlation, but simultaneous refinement was successful in the later stages when the parameter shifts had become very small. The increase in the number of refined parameters due to the introduction of partial atoms meant that the oxotremorine cation had to be refined on separate cycles to the oxalic acid and oxalate anion. Further refinement reduced R to 0·178, and a second difference-Fourier synthesis revealed additional partial sites for atoms O(4) and O(5), and the positions of the hydrogen atoms for the protonated oxotremorine cation. Hydrogen atoms for the oxalic acid and oxalate moieties could not be located because of the disorder. The additional oxygen disorder was accounted for in the manner described, and the hydrogen atoms were included in the structure-factor calculation but their parameters were not refined. Subsequent refinement reduced R to 0·130 at which point there were no structurally significant peaks in the difference-Fourier map.

The temperature factors, with the exception of the hydrogen and disordered oxygen atoms, were converted to allow for anisotropic thermal motion, and refinement of co-ordinates, temperature factors, and, where appropriate, site-occupation factors reduced R to the final value of 0·104. The maximum peak-height in the final difference-Fourier synthesis was 0·54 eÅ^{-3}. The R factor for the structure is therefore larger than that commonly achieved for organic structures, principally because of the difficulty in accounting completely for the disorder in the oxalic acid and oxalate moieties, but there is little doubt that the molecular packing is correct, and the values of bond lengths and angles in the

TABLE 1

Fractional co-ordinates ($\times 10^4$) and anisotropic thermal parameters * ($\times 10^4$) for non-disordered atoms, with estimated standard deviations in parentheses

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	269(11)	−865(7)	2093(12)	539(54)	394(45)	688(58)	110(39)	98(45)	267(44)
C(2)	−479(9)	185(7)	2990(11)	301(42)	435(44)	701(53)	44(34)	22(37)	418(42)
C(3)	−1033(9)	1029(7)	3707(11)	381(44)	457(45)	529(47)	−31(36)	0(36)	355(39)
C(4)	−1711(9)	2113(6)	4666(10)	459(47)	277(36)	476(44)	−65(31)	−74(36)	201(34)
N(1)	−827(7)	−1855(5)	532(9)	406(37)	438(35)	657(43)	140(29)	161(32)	414(34)
C(5)	−1143(9)	−2851(6)	322(12)	372(44)	440(43)	700(55)	143(34)	170(40)	412(43)
O(1)	−635(7)	−3019(4)	1422(8)	708(41)	505(33)	783(41)	75(29)	33(32)	508(33)
C(6)	−2183(11)	−3718(8)	−1462(13)	591(59)	558(54)	701(61)	122(45)	−62(49)	301(50)
C(7)	−2393(16)	−3059(10)	−2310(15)	1230(104)	920(82)	721(71)	119(74)	−120(69)	482(65)
C(8)	−1506(13)	−1857(8)	−989(13)	974(77)	685(61)	647(60)	264(55)	154(55)	529(54)
N(2)	−3511(7)	1920(4)	4787(7)	426(35)	182(25)	289(29)	31(23)	19(25)	110(22)
C(9)	−3962(10)	1539(6)	6023(10)	556(49)	421(41)	416(42)	140(36)	143(36)	310(36)
C(10)	−5727(12)	1815(8)	6487(13)	724(66)	637(57)	698(62)	209(48)	256(51)	449(52)
C(11)	−5926(14)	2707(9)	6153(15)	948(83)	778(70)	937(79)	439(62)	412(66)	562(65)
C(12)	−4308(11)	2964(6)	5529(11)	722(62)	397(42)	536(49)	282(41)	185(45)	277(39)
C(13)	5428(8)	403(5)	−242(9)	397(41)	218(32)	291(36)	−20(28)	−14(31)	135(29)
C(14)	7842(13)	4633(7)	1237(16)	700(75)	386(48)	794(67)	162(48)	297(60)	319(50)
C(15)	7513(11)	3791(7)	1758(12)	626(57)	412(47)	487(50)	−90(40)	−9(45)	311(41)

* In the form: $\exp[-2\pi^2(h^2a^{*2}U_{11}\ldots + 2hka^*b^*U_{12}\ldots)]$.

TABLE 2

Site-occupation factors ($\times 10^3$), fractional co-ordinates ($\times 10^4$), and isotropic thermal parameters ($\times 10^4$) for the disordered oxygen atoms

Atom	s	x	y	z	U_{iso}
O(2A)	542(90)	5653(40)	0(16)	−1882(16)	411(53)
O(2B)	591(90)	5186(35)	158(14)	−1816(14)	391(48)
O(3A)	541(65)	6410(29)	1300(10)	1070(14)	289(44)
O(3B)	592(65)	5873(32)	1445(11)	1204(15)	391(41)
O(4A)	252(37)	7906(37)	4845(16)	418(28)	556(90)
O(4B)	135(37)	6384(48)	4659(22)	426(35)	193(100)
O(4C)	629(35)	6963(20)	4434(9)	−134(14)	698(51)
O(5A)	776(36)	8978(10)	5433(7)	2049(16)	581(42)
O(5B)	387(38)	9184(29)	5542(20)	3044(53)	1066(121)
O(6A)	489(37)	8451(31)	3898(14)	2966(24)	723(70)
O(6B)	287(37)	7691(36)	4125(15)	3396(27)	339(88)
O(6C)	291(26)	6570(43)	4208(21)	3273(35)	875(126)
O(7A)	450(77)	7123(47)	2752(15)	354(33)	316(74)
O(7B)	434(63)	6514(50)	2872(16)	542(27)	537(65)
O(7C)	212(47)	7716(58)	2866(22)	860(54)	357(108)

TABLE 3

Fractional co-ordinates ($\times 10^3$) for hydrogen atoms *

Atom	x	y	z	Atom	x	y	z
H(1,1)	50	−105	311	H(N2)	−400	125	380
H(1,2)	144	−73	158	H(9,1)	−400	75	580
H(4,1)	−160	225	380	H(9,2)	−320	200	700
H(4,2)	−120	275	580	H(10,1)	−640	125	580
H(6,1)	−320	−375	−100	H(10,2)	−600	225	820
H(6,2)	−140	−440	−220	H(11,1)	−640	225	500
H(7,1)	−373	−300	−200	H(11,2)	−600	365	760
H(7,2)	−160	−350	−340	H(12,1)	−440	325	460
H(8,1)	−217	−127	−10	H(12,2)	−360	350	660
H(8,2)	−40	−175	−140				

* U_{iso} 0·051 Å^2.

protonated oxotremorine cation indicate that the conformation derived in this analysis is completely reliable.

Final atomic parameters are given for the nondisordered atoms in Table 1, disordered oxygen atoms in Table 2, and hydrogen atoms in Table 3. Interatomic distances and angles [11] are presented in Table 4, torsion angles in Table 5, and least squares planes [12] in Table 6. Observed and calculated structure factors are listed in Supplementary Publication No. SUP 21290 (4 pp., 1 microfiche).†

TABLE 4

Interatomic distances (Å) and angles (°), with estimated standard deviations in parentheses

(*a*) Distances *

C(1)–C(2)	1·48(1)	C(13)–O(2A)	1·24(1)
C(1)–N(1)	1·47(1)	C(13)–O(2B)	1·24(1)
C(2)–C(3)	1·17(1)	C(13)–O(3A)	1·29(1)
C(3)–C(4)	1·48(1)	C(13)–O(3B)	1·30(1)
C(4)–N(2)	1·47(1)	C(14)–C(15)	1·52(1)
N(1)–C(5)	1·33(1)	C(14)–O(4A)	0·94(3)
N(1)–C(8)	1·46(1)	C(14)–O(4B)	1·42(2)
C(5)–O(1)	1·22(1)	C(14)–O(4C)	1·28(1)
C(5)–C(6)	1·50(1)	C(14)–O(5A)	1·21(1)
C(6)–C(7)	1·54(1)	C(14)–O(5B)	1·65(4)
C(7)–C(8)	1·50(1)	C(15)–O(6A)	1·25(2)
N(2)–C(9)	1·51(1)	C(15)–O(6B)	1·24(2)
N(2)–C(12)	1·51(1)	C(15)–O(6C)	1·39(3)
C(9)–C(10)	1·54(1)	C(15)–O(7A)	1·28(2)
C(10)–C(11)	1·51(1)	C(15)–O(7B)	1·14(2)
C(11)–C(12)	1·51(1)	C(15)–O(7C)	1·63(5)
C(13)–C(13[I])	1·54(1)		

(*b*) Angles

C(2)–C(1)–N(1)	111·5(7)	C(10)–C(11)–C(12)	106·8(8)
C(1)–C(2)–C(3)	178·4(10)	N(2)–C(12)–C(11)	104·5(6)
C(2)–C(3)–C(4)	178·5(11)	C(13[I])–C(13)–O(2A)	118·8(12)
C(3)–C(4)–N(2)	111·6(5)	C(13[I])–C(13)–O(2B)	120·1(12)
C(1)–N(1)–C(5)	121·6(7)	C(13[I])–C(13)–O(3A)	115·4(13)
C(1)–N(1)–C(8)	123·0(6)	C(13[I])–C(13)–O(3B)	112·6(12)
C(5)–N(1)–C(8)	115·2(7)	C(15)–C(14)–O(4A)	154·8(20)
N(1)–C(5)–O(1)	124·3(8)	C(15)–C(14)–O(4B)	111·3(15)
N(1)–C(5)–C(6)	109·4(7)	C(15)–C(14)–O(4C)	118·5(9)
C(6)–C(5)–O(1)	126·4(7)	C(15)–C(14)–O(5A)	119·7(12)
C(5)–C(6)–C(7)	104·2(7)	C(15)–C(14)–O(5B)	93·1(14)
C(6)–C(7)–C(8)	107·4(8)	C(14)–C(15)–O(6A)	120·0(10)
C(7)–C(8)–N(1)	103·8(7)	C(14)–C(15)–O(6B)	121·0(11)
C(4)–N(2)–C(9)	113·2(5)	C(14)–C(15)–O(6C)	110·9(13)
C(4)–N(2)–C(12)	114·0(5)	C(14)–C(15)–O(7A)	112·8(11)
C(9)–N(2)–C(12)	105·1(5)	C(14)–C(15)–O(7B)	112·1(10)
N(2)–C(9)–C(10)	103·2(6)	C(14)–C(15)–O(7C)	125·1(17)
C(9)–C(10)–C(11)	106·8(7)		

Roman numeral superscript denotes the following equivalent position: I $1-x, \bar{y}, \bar{z}$.

* Bond distances involving hydrogen are in the range 0·81—1·30 Å.

TABLE 5

Torsion angles (°), with estimated standard deviations in parentheses

C(1)–N(1)–C(5)–C(6)	−175·5(7)
C(1)–N(1)–C(5)–O(1)	3·7(11)
C(1)–N(1)–C(8)–C(7)	174·8(8)
C(2)–C(1)–N(1)–C(5)	−132·5(7)
C(2)–C(1)–N(1)–C(8)	53·9(10)
C(3)–C(4)–N(2)–C(9)	67·2(7)
C(3)–C(4)–N(2)–C(12)	−172·6(6)
C(4)–N(2)–C(9)–C(10)	160·3(6)
C(4)–N(2)–C(12)–C(11)	−160·8(7)
N(1)–C(5)–C(6)–C(7)	1·4(10)
N(1)–C(8)–C(7)–C(6)	0·1(32)
C(5)–C(6)–C(7)–C(8)	−0·9(11)
C(5)–N(1)–C(8)–C(7)	0·9(10)
C(6)–C(5)–N(1)–C(8)	−1·5(9)
C(7)–C(6)–C(5)–O(1)	−177·7(8)
C(8)–N(1)–C(5)–O(1)	177·7(8)
N(2)–C(9)–C(10)–C(11)	−21·1(9)
N(2)–C(12)–C(11)–C(10)	22·4(10)
C(9)–C(10)–C(11)–C(12)	−0·7(11)
C(9)–N(2)–C(12)–C(11)	−36·2(8)
C(10)–C(9)–N(2)–C(12)	35·2(7)
N(1)–C(1)–C(4)–N(4)	38·3(7)

TABLE 6

Equations of least-squares planes relative to crystallographic axes. Deviations (Å) from the plane are given in square brackets, and estimated standard deviations in parentheses

Plane (1): N(1), O(1), C(5), C(6)

$$-7{\cdot}1824x + 1{\cdot}4908y + 3{\cdot}4972z = 0{\cdot}5046$$

[N(1) −0·001(6), O(1) −0·001(6), C(5) 0·004(7), C(6) −0·002(10), C(1) −0·095(9), C(7) −0·050(13), C(8) −0·046(10)]

Plane (2): C(9)—(12)

$$-1{\cdot}8964x - 2{\cdot}5045y - 5{\cdot}8361z = -3{\cdot}1505$$

[C(9) 0·002(8), C(10) −0·004(10), C(11) 0·006(12), C(12) −0·002(9), N(2) 0·541(5)]

DISCUSSION

A perspective view with atomic numbering is given for the protonated oxotremorine cation in Figure 1 and for the disordered oxalic acid and oxalate anion in Figure 2.

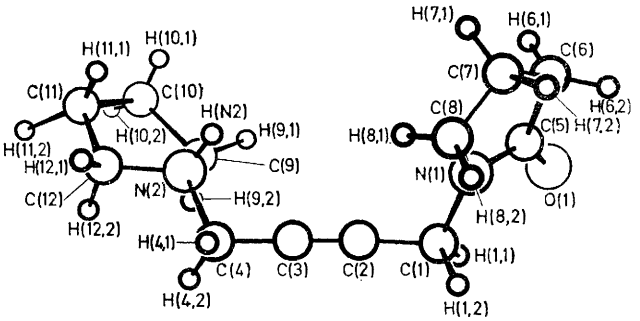


FIGURE 1 A perspective view of the protonated oxotremorine cation showing the atom numbering system used in the analysis

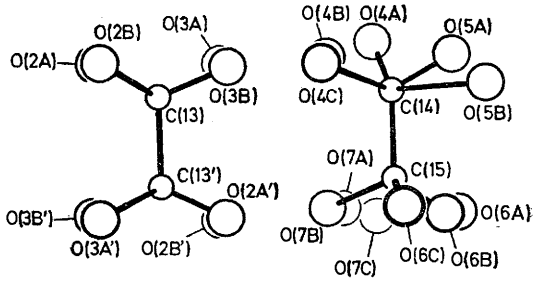


FIGURE 2 Atom numbering for the disordered oxalic acid molecule and oxalate anion

In the crystal, the oxalic acid is situated on the centre of symmetry at $(\frac{1}{2},0,0)$ whilst the oxalate anion is in a general

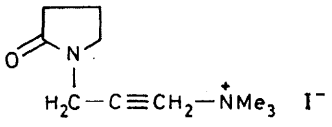
† See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1974, Index issue.

[11] W. R. Busing, K. O. Martin, and H. A. Levy, U.S. Atomic Energy Commission, Report ORNL TM 306, 1964.

[12] W. C. Hamilton, *Acta Cryst.*, 1961, **14**, 185.

position. These findings are in agreement with previous work [13,14] where the oxalic acid molecule was shown to be planar and centrosymmetric in crystals of the α-form, and the oxalate anion to be nonplanar in crystals of the hydrated ammonium salt. In the present investigation, however, little significance can be attached either to the conformation of the oxalate anion or to the bond lengths and angles in both the oxalic acid and oxalate moieties because of the considerable disorder in the oxygen positions. The unconstrained refinement of the oxygen site-occupation factors results in a non-unitary value for the sum of these factors over the partial sites for an individual atom. The difference between this sum and unity is $<1{\cdot}5\ \sigma$ for all atoms except O(5) where the difference is $3{\cdot}1\ \sigma$. However, this latter value may simply be a product of the assignment by least squares of a large temperature factor to O(5B).

The bond lengths and angles for the butyne and pyrrolidone groups are the same as for the oxotremorine analogue trimethyl-[4-(2-oxopyrrolidin-1-yl)but-2-ynyl]-ammonium iodide [15] (II). Bond lengths and angles for



(II)

the pyrrolidine ring are close to those found in the structures of DL-proline,[16] L-hydroxyproline,[17] and hexapyrronium.[18] The butyne group is linear within experimental error, and the pyrrolidine ring adopts the envelope conformation with the carbon atoms planar and the nitrogen atom 0·54 Å out of plane (Table 6). The substituent at the nitrogen atom is in the pseudo-equatorial position. The amide group of the pyrrolidone ring is planar (Table 6) as are those in (II), L-5-iodomethylpyrrolidin-2-one [19] and L-5-oxopyrrolidine-2-carboxamide hydrate,[19] but oxotremorine differs from these three compounds in the spatial distribution of atoms C(7) and C(8) relative to the amide plane. In oxotremorine, atoms C(7) and C(8) are on the same side of the amide plane and deviate from it by −0·050 and −0·046 Å respectively (Table 6), but in the three comparable structures the equivalent atoms are on opposite sides of the amide plane and the respective deviations lie in the ranges 0·18—0·26 and −0·06 to −0·18 Å. The pyrrolidone ring in oxotremorine is therefore much closer to planarity than in the other structures.

The conformation of the protonated oxotremorine cation may be compared with that of the structurally and pharmacologically related molecule (II). The torsion angles of principal interest are C(3)–C(4)–N(2)–C(12), N(1)–C(1)–C(4)–N(2), and C(2)–C(1)–N(1)–C(5). The respective τ values are for oxotremorine: −172·6(6), 38·3(7), and −132·5(7)°, and for (II) [15] 179, −143, and −99°. The essential differences between the two conformations are therefore a rotation of 181° about C(1)–C(4), and a rotation of 34° about C(1)–N(1). The observed conformation of the protonated oxotremorine cation is in poor agreement with that calculated by Kier [20] who predicted that τ[C(3)–C(4)–N(2)–C(12)] was *ca.* −125°, that τ[N(1)–C(1)–C(4)–N(2)] could not lie in the range 0—60°, and that τ[C(2)–C(1)–N(1)–C(5)] must lie in the range −60 to −120°. The energy difference between the crystal conformation and Kier's minimum energy conformation for an isolated cation is *ca.* 25 kJ mol^{-1}.

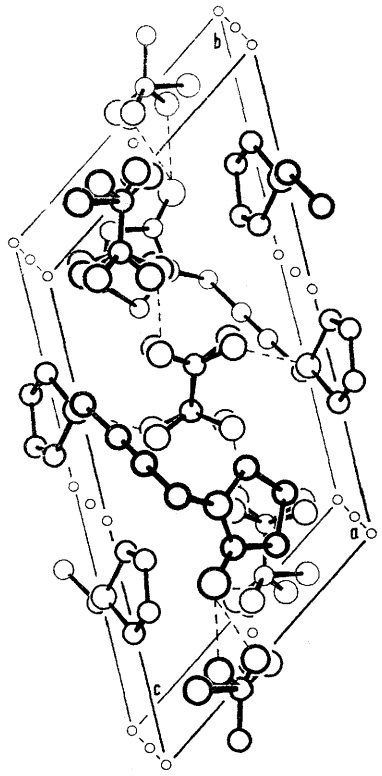


FIGURE 3 The molecular packing viewed normal to (100). Dashed lines represent hydrogen bonds

The molecular packing in (I) is shown in Figure 3. The protonated oxotremorine cation, oxalic acid, and oxalate anion are linked by a series of hydrogen bonds, denoted by dashed lines. Despite the disorder in the carboxy-groups, the hydrogen bonds may be identified, with only one ambiguity, from the relevant interatomic distances (Table 7). The ambiguity concerns the bonding to O(1) which is closer than the van der Waals distance

[13] E. G. Cox, M. W. Dougill, and G. A. Jeffrey, *J. Chem. Soc.*, 1952, 4854.
[14] G. A. Jeffrey and G. S. Parry, *J. Chem. Soc.*, 1952, 4864.
[15] R. W. Baker and P. J. Pauling, *J.C.S. Perkin II*, 1973, 1247.
[16] Y. Mitsui, M. Tsuboi, and Y. Iitaka, *Acta Cryst.*, 1969, **B25**, 2182.
[17] J. Dononhue and K. N. Trueblood, *Acta Cryst.*, 1952, **5**, 419.
[18] R. W. Baker, N. Datta, and P. J. Pauling, *J.C.S. Perkin II*, 1973, 1963.
[19] J. A. Molin-Case, E. Fleischer, and D. W. Urry, *J. Amer. Chem. Soc.*, 1970, **92**, 4728.
[20] L. B. Kier, *J. Pharm. Sci.*, 1970, **59**, 112.

TABLE 7

Selected intermolecular contact distances (Å). Distances may represent hydrogen bonds unless marked with an asterisk

N(2) · · · O(2A^{II})	2·81	O(1) · · · O(5B^{IV})	3·12 *
N(2) · · · O(2B^{II})	2·77	O(3A) · · · O(7A)	2·51
N(2) · · · O(3A^{III})	2·88 *	O(3A) · · · O(7B)	2·56
N(2) · · · O(3B^{III})	2·88 *	O(3A) · · · O(7C)	2·46
O(1) · · · O(4A^{IV})	2·75	O(3B) · · · O(7A)	2·50
O(1) · · · O(4B^{IV})	3·50 *	O(3B) · · · O(7B)	2·44
O(1) · · · O(4C^{IV})	3·39 *	O(3B) · · · O(7C)	2·53
O(1) · · · O(5A^{IV})	2·58		

Roman numeral superscripts denote the following equivalent position: II $\bar{x}, \bar{y}, \bar{z}$; III $x - 1, y, z$; IV $x - 1, y - 1, z$.

to both O(4A) and O(5A) of the oxalate anion. Because of the disorder, it is conceivable that there are hydrogen bonds to both partially occupied sites. That N(2) is hydrogen bonded to the oxalic acid through O(2A,B) and not O(3A,B) may be deduced from the N · · · H–O angles which are 163 and 175° for the former pair, and 107 and 108° for the latter.

We thank the M.R.C. for financial support, Professor D. J. Jenden for the crystals, and Miss Patricia Brennan for assistance.

[4/1881 *Received*, 16*th September*, 1974]