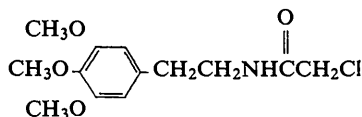# The Identification and Crystal Structure of 7-Hydroxy-1,9,10-trimethoxy-4-azabicyclo[5.2.2] undeca-8,10-dien-3-one, a Photolysis Product from *N*-Chloroacetylmescaline
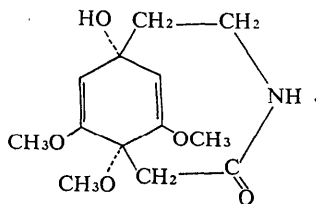
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Irradiation of the *N*-chloroacetyl derivative of mescaline,

produces a novel photocyclization product, m.p. 230–232°C, which has been identified by an X-ray analysis of its crystal structure to be


A nine-membered ring formed from four atoms of the six-membered ring and five atoms from the chain of the original molecule is folded into a boat conformation. The groups of atoms C–C=C–C and

$$\text{C–C–N–C}$$

are each planar. The central OCH$_3$ group and the OH group are *cis* with respect to each other. The material crystallizes in the orthorhombic space group *Aba*2, with cell parameters $a=25\cdot74\pm0\cdot03$, $b=13\cdot88\pm0\cdot02$, and $c=7\cdot49\pm0\cdot02$ Å and there are eight molecules in the unit cell. The structure was obtained by determining phases directly from the structure-factor magnitudes by use of the symbolic addition procedure for non-centrosymmetric space groups.

Introduction

Ultraviolet irradiation of *N*-chloroacetyl derivatives of aromatic amino acids and amines often results in very unusual polycyclic photoproducts. Since the end products vary considerably and are unpredictable, even though the starting materials may be closely related to each other, a suitable way to establish the structural formula as well as the molecular configuration is by X-ray analysis of the crystal structures. In previous investigations it was established by means of crystal structure analyses that

(Yonemitsu, Witkop & Karle, 1967; Karle, Karle & Estlin, 1967) and that

(2)

(1)
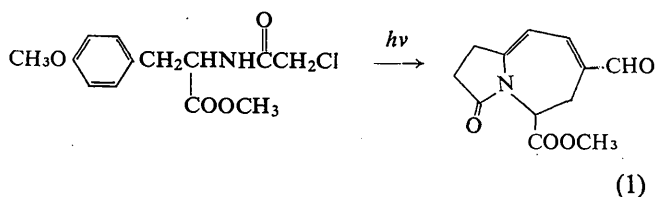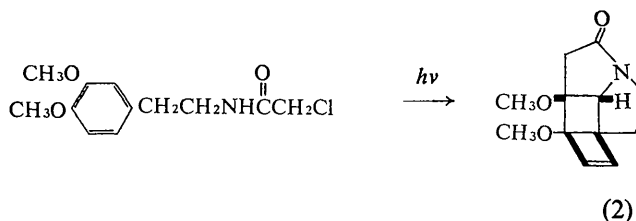
among several other products (Yonemitsu, Okuno, Kanaoka, Karle & Witkop, 1968; Karle, Gibson & Karle, 1969). In the present investigation we have identified one of the photoproducts of *N*-chloroacetylmescaline. The starting material differs from

$$hv \rightarrow$$

(3)
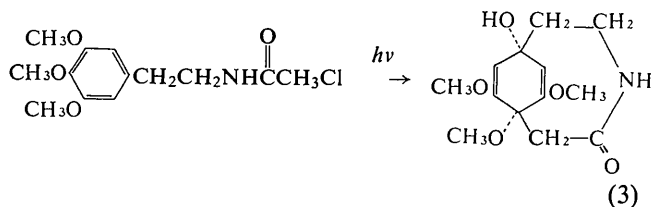
the starting material in (2) only by one additional methoxy group; the product, however, bears no resemblance to that in (2) (Yonemitsu, Nakai, Kanaoka, Karle & Witkop, 1969). The reaction mechanisms are obviously quite different in each of the three examples.

The photoproduct crystallizes in the noncentrosymmetric space group $Aba2$. This is the first application of the symbolic addition procedure to space group $Aba2$ and the special considerations involved will be described.

Experimental

Crystals of the photoproduct were supplied by Dr B. Witkop of the National Institutes of Health. They were colorless, diamond-shaped tablets with good optical extinctions along the diagonals of the face of the tablet. All the diffraction data were taken with the same crystal first mounted along the b and then along the c axis. The only reflections observed were hkl with $k + l = 2n$, $0kl$ with $k = 2n$ and $h0l$ with $h = 2n$. The space group is thus either the noncentric $Aba2(C_{2v}^{17})$ or the centric $Cmca(D_{2h}^{18})$. With eight molecules per unit cell the calculated density is 1·38 g.cm^{-3}. Other allowed Z values correspond to highly unreasonable densities. Since it appeared unlikely for the molecule to possess either a center of symmetry, a twofold axis or a mirror plane, the space group $Aba2$ was chosen, a conclusion in agreement with the statistical averages for the $|E|$ values (see below).

Intensity data were collected photographically with the multiple-film, equi-inclination Weissenberg technique and estimated visually by comparison with a calibrated film strip. Corrections were made for spot size and Lorentz and polarization factors. The data, $h0l-h6l$ and $hk0-hk1$, were cross-correlated and placed on an absolute scale by means of a K curve. Nor-

malized structure factors $|E|$ were obtained from the relation

$$|E_h|^2 = |F_h|^2/\varepsilon\sum_{j=1}^{N}f_{jh}^2 ,$$ (4)

where N is the number of atoms in the unit cell and f_j is the atomic scattering factor for the jth atom. For space group $Aba2$:

$\varepsilon=4$	for	$00l$	$(l=2n)$,
$\varepsilon=2$	for	$0k0$	$(k=2n)$
		$h00$	$(h=2n)$
		$h0l$	$(h=2n, l=2n)$
		$0kl$	$(k=2n, l=2n)$,
and $\varepsilon=1$	for	$hk0$	$(k=2n)$
		hkl	$(k+l=2n)$.

The values for the statistical averages for the normalized structure factors corresponding to non-centrosymmetric reflections were $\langle|E|\rangle=0\cdot850$ and $\langle||E|^2-1|\rangle=0\cdot795$, as compared with 0·886 and 0·736, the theoretical values for noncentrosymmetric space groups. Cell parameters were measured using precession photographs. These values along with other physical data are listed in Table 1.

Table 1. Physical constants

Molecular formula	$C_{13}H_{19}O_5N.\frac{1}{2}H_2O$
Molecular weight	278·3
Melting point	230–232 °C
Habit	Diamond plates
Crystal size	$\sim0\cdot2\times0\cdot6\times0\cdot6$ mm
Space group	$Aba2$
a	$25\cdot74\pm0\cdot03$ Å
b	$13\cdot88\pm0\cdot02$
c	$7\cdot49\pm0\cdot02$
V	2676 Å^3
ϱ_{calc}	1·381 g.cm^{-3}
Radiation	Cu $K\alpha$, 1·5418 Å
No. of independent reflections	1290
Molecules per unit cell	8

Structure analysis

Phases were derived directly from the normalized structure factor magnitudes $|E|$ by the symbolic addition procedure (Karle & Karle, 1964, 1966). For the non-primitive space group $Aba2$, the origin can be specified
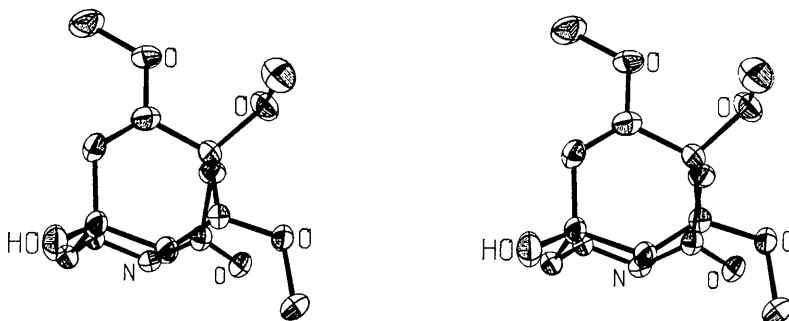

Fig. 1. Stereodiagram of one of the antipodes of the molecule. (Drawn by computer with a program written by Johnson, 1965.)

by assigning two phases (Karle & Hauptman, 1961): 0 or π to a $ug0$ reflection and an arbitrary phase value to a guu reflection. Since the origin in the z direction may be specified arbitrarily in this space group, it was convenient to assign a 0 phase to a $gu1$ reflection. The origin assignment and additional symbolic phase specifications for four additional reflections to implement the application of the sum of angles formula (Karle & Hauptman, 1950),

$$\varphi_\mathbf{h} \simeq \langle \varphi_\mathbf{k} + \varphi_\mathbf{h-k} \rangle_{\mathbf{k_r}},\qquad (5)$$

are shown in Table 2. Equation (5) was used to obtain an initial set of phases in terms of 0, π, a, b, p and m for about 50 reflections with $|E| > 1\cdot6$. These phases were used as input into the tangent formula (Karle & Hauptman, 1956)

$$\tan \varphi_\mathbf{h} \simeq \frac{\sum_k |E_k E_{\mathbf{h-k}}| \sin (\varphi_\mathbf{k} + \varphi_\mathbf{h-k})}{\sum_k |E_k E_{\mathbf{h-k}}| \cos (\varphi_\mathbf{k} + \varphi_\mathbf{h-k})},\qquad (6)$$

by which a total of 280 phases for reflections with $|E| > 1\cdot1$ were obtained. These 280 phases were used to compute E maps.

Table 2. *Phase assignments for specifying the origin in space group Aba2 and implementing equation (1)*

$|E|$	h	k	l	φ	
2·18	3	12	0	0	origin
2·20	20	5	1	0	assignment
4·00	18	6	0	a	
2·42	8	6	0	b	
2·07	23	4	6	p	
2·18	2	1	3	m	

Symbols a and b must be either 0 or π since they represent the phases of real structure factors. Either p or m or both must have complex or imaginary values, or else the phase determination would lead to all real phases. Space group $Aba2$ has glide planes which give mirror images of the molecules in the cell; hence the enantiomorphs are indistinguishable and no specification can be made. However, the *direction* of the axes must be chosen and this is accomplished in the same manner as specifying an enantiomorph, *i.e.* by choosing the sign of a phase whose magnitude is near $\pi/2$. Since in this case, as noted below, the magnitudes of p and m turned out to be near $\pi/2$ either $p = +\pi/2$ or $m = +\pi/2$ could specify the direction of the axes. From a $\sum_1$ relation (Karle & Hauptman, 1956) it appeared likely that the phase of 860 (assigned b) is zero. During the application of equation (5), it was found that $a + b$ is probably equal to zero; hence a is probably equal to zero. If m were chosen to be $+\pi/2$, then p could reasonably assume the values 0, π and $\pm\pi/2$ for some trial E maps. For the correct map, $p = +\pi/2$.

The constitution of the molecule was completely unknown and the hope was that either the whole molecule or parts of it could be recognized in an E map. Each of the four trial E maps computed had five to ten peaks which could represent groups of atoms with reasonable bond lengths and angles. Therefore, each one was considered as a possible partial structure. Phases derived from the partial structures were used as a basic set for application with the tangent formula, equation (6), to generate additional phases for new E maps (Karle, 1968). For the partial structure from the original E map with $a = b = 0$ and $p = m = +\pi/2$, the new E map revealed all the atoms in the molecule, which is
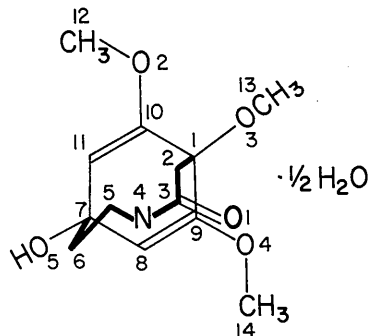
with the oxygen of the water molecule at $0,0,0\cdot192$. The partial structure was based on the two bonded group-
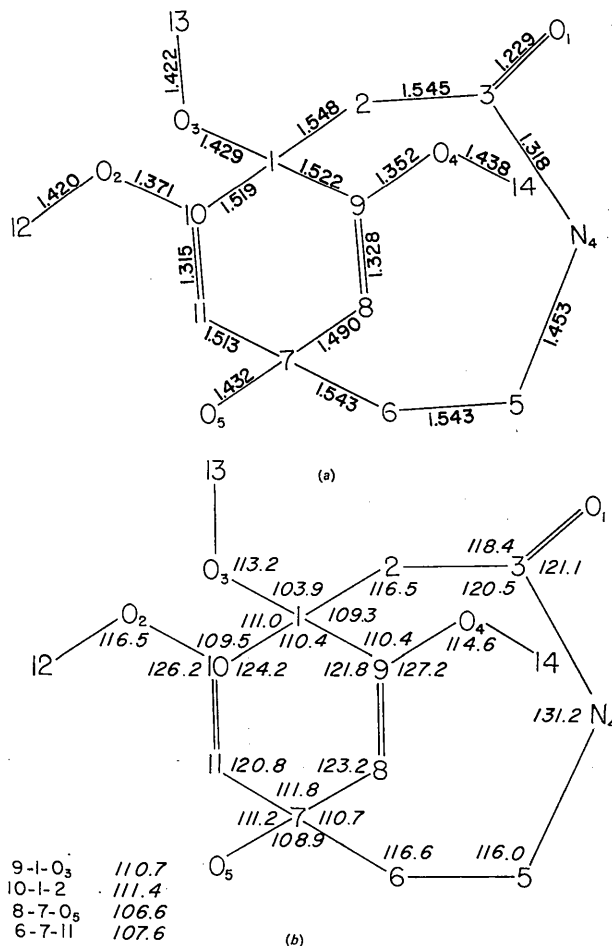

Fig. 2. (*a*) Bond lengths and (*b*) bond angles.

Table 3. *Observed and calculated structure factors*

The columns contain the index *h*, 10|*F*o|, 10|*F*c|, and the phase in centicycles.

ings of atoms O(3), C(10), C(1), C(9), C(8) and O(1), C(3), N(4), C(5). On re-examining the original E map, it was seen that there were additional weaker peaks which represented atoms as well as peaks of the same weak magnitude, which were extraneous. The oxygen atom of the water molecule appeared with a large maximum at 0,0,0·192 in the original E map but was left out of the partial structure since it was not immediately obvious that it was a meaningful peak. New E maps

based on partial structures from the incorrect E maps did not develop additional meaningful peaks.

The coordinates for the 20 heavy atoms as derived from the E map were refined, along with thermal factors, by full-matrix least squares. In space group $Aba2$, the origin along the z axis is not fixed by symmetry. In order to fix an origin along the z axis, the z coordinate of the water oxygen atom was held constant during the least-squares refinement. Since the water

Table 4. *Fractional atomic coordinates and thermal parameters for* $C_{13}H_{19}O_5N.\frac{1}{2}H_2O$

Thermal parameters are of the form

$$T = \exp\left[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)\right].$$

The β_{ij} values have been multiplied by 10^4.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	B^*
C(1)	0·1592	0·1439	0·6395	7	25	135	−3	0	−1	2·5
C(2)	0·1622	0·1654	0·8420	7	38	155	−2	−5	−8	2·7
C(3)	0·1112	0·1546	0·9488	9	28	104	1	−7	0	2·3
N(4)	0·0905	0·0689	0·9747	9	31	139	0	8	−2	2·0
C(5)	0·1075	−0·0264	0·9194	8	25	142	−1	2	−3	2·2
C(6)	0·0797	−0·0694	0·7554	8	24	162	−1	−1	4	2·1
C(7)	0·0944	−0·0271	0·5718	8	21	133	0	−5	−12	2·4
C(8)	0·0740	0·0728	0·5530	8	22	123	−1	−5	−11	2·3
C(9)	0·1030	0·1508	0·5783	8	21	103	0	2	3	2·7
C(10)	0·1813	0·0452	0·5962	7	40	114	2	2	6	2·3
C(11)	0·1529	−0·0304	0·5561	9	24	129	4	2	5	2·5
C(12)	0·2599	−0·0438	0·6109	8	58	206	9	4	17	3·6
C(13)	0·1905	0·2144	0·3702	13	47	182	−2	10	24	3·4
C(14)	0·0320	0·2562	0·5549	8	37	226	5	−4	18	3·2
O(1)	0·0910	0·2275	1·0111	13	29	195	4	11	−7	3·0
O(2)	0·2343	0·0467	0·6165	5	44	207	1	5	10	2·9
O(3)	0·1898	0·2184	0·5600	9	36	173	−7	1	10	2·9
O(4)	0·0870	0·2436	0·5780	7	20	168	0	−4	7	2·5
O(5)	0·0701	−0·0832	0·4349	12	23	174	0	−13	−6	3·3
W	0·0000	0·0000	0·1920	9	45	123	0	0	0	2·8

Standard deviations

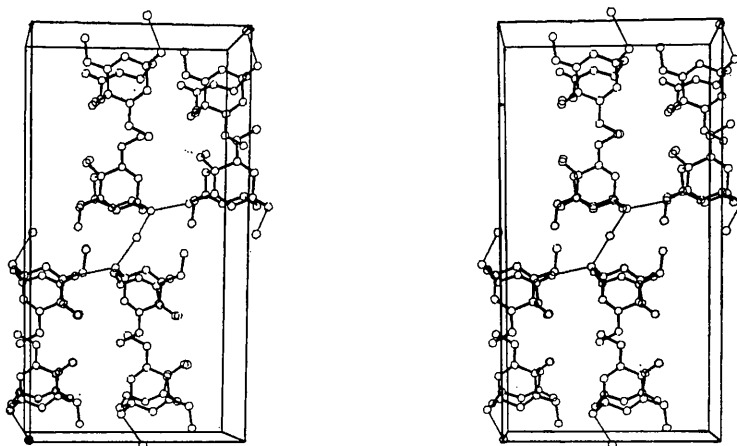|	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	B^*
C(1–11)	0·0002	0·0004	0·0010	1	3	11	1	2	6	0·2
C(12–14)	0·0002	0·0006	0·0012	1	4	15	2	3	8	0·2
O	0·0002	0·0003	0·0009	1	2	10	1	2	5	0·2

* Thermal factors from last cycle of isotropic refinement.

Fig. 3. The packing in a unit cell. The a axis is ↑, the b axis is → and the c axis is directed into the paper. The light lines indicate hydrogen bonding.

molecule occupies a special position in the lattice, *i.e.* $x = y = 0$ for the oxygen atom, these coordinates, as well as $\beta_{13} = \beta_{23} = 0$, were also kept constant in the refinement. The function minimized was $\sum w(|F_o| - |F_c|)^2$ with $w = 0.5$ for $F_o = 0$, $w = 1$ for $|F_o| < 25$ and $w = 25/|F_o|$ for $|F_o| \geq 25$. The scattering factors used were those listed *International Tables for X-ray Crystallography* (1962). Isotropic refinement ceased at $R = 11.9\%$. A difference map computed after an anisotropic refinement, $R = 8.9\%$, revealed the approximate positions of 18 of the 20 hydrogen atoms. Inclusion in the refinement of the hydrogen atoms as constant parameters with $B \sim 3.2$ Å^2, reduced the R value to 6.7%.

Observed and calculated structure factors and phase angles expressed in centicycles are listed in Table 3. The refined coordinates and thermal factors of the heavy atoms and the approximate coordinates for the hydrogen atoms are listed in Tables 4 and 5.

Table 5. *Approximate coordinates for* 18 *of the* 20 *hydrogen atoms*

	x	y	z
H(2a)	0·183	0·117	0·862
H(2b)	0·179	0·233	0·859
H(4)	0·063	0·075	1·055
H(5a)	0·096	−0·062	1·042
H(5b)	0·145	−0·025	0·892
H(6a)	0·037	−0·063	0·772
H(6b)	0·088	−0·142	0·750
H(8)	0·033	0·062	0·525
H(11)	0·162	−0·097	0·558
H(12a)	0·238	−0·092	0·692
H(12b)	0·254	−0·083	0·478
H(12c)	0·292	−0·045	0·637
H(13a)	0·207	0·142	0·317
H(13b)	0·207	0·272	0·342
H(14a)	0·027	0·245	0·433
H(14b)	0·007	0·227	0·673
H(14c)	0·031	0·327	0·542
H(0)	0·075	−0·157	0·433

Discussion

The starting material for the photoreaction, *N*-chloroacetylmescaline, was optically inactive. The photoproduct has two asymmetric carbon atoms and crystallizes in a noncentrosymmetric space group. However, the material exists as a racemate and is readily ac-

commodated in space group *Aba*2 which has glide planesrelating the mirror images of the molecule. One of the antipodes is illustrated in the stereodiagram in Fig. 1.

Except for the three atoms N(4), C(3), O(1), the molecule very nearly possesses a mirror plane through atoms O(5), C(7), C(6), C(5), C(2), C(1), O(3), C(13). These eight atoms are coplanar within ± 0.20 Å. Atoms N(4), C(3) and O(1) lie either to one side or the other of this plane to form the pair of racemates. The nine-membered ring formed from four atoms of the six-membered ring, C(7), C(8), C(9) and C(1), and five atoms from the chain of the original molecule assumes a boat conformation:
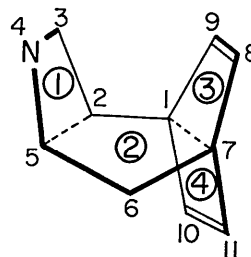
Atoms C(1), C(7), C(8) and C(9) are coplanar to within ± 0.015 Å while atoms C(2), C(3), N(4) and C(5) are coplanar to within ± 0.008 Å. Dihedral angles between planes (1) and (2) and between planes (2) and (3) are 118 and 105° respectively. Intraring distances between atoms separated by two other atoms are fairly short, *e.g.* C(3)$\cdots$C(9) is 2·78 Å and C(1)$\cdots$C(7) is 2·95 Å. There is another nine-membered ring containing C(10) and C(11) instead of C(8) and C(9) which has a chair conformation.

The orientation of the methoxy groups is of interest. The two OCH$_3$ groups adjacent to the double bonds of the six-membered rings lie so that each set of four heavy atoms in the grouping

$$\begin{array}{c} C{=}C \\ \diagdown \\ O \\ \diagup \\ CH_3 \end{array}$$

are coplanar to within ± 0.02 Å. The CH$_3$ groups are *cis* with respect to the double bonds resulting in the short C(11)$\cdots$C(12)
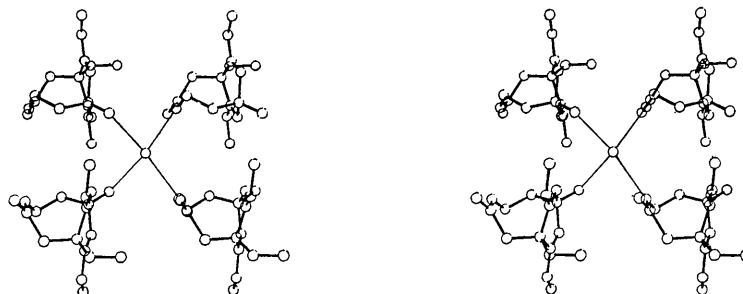

Fig. 4. Hydrogen bonding to the H$_2$O molecule. The *a* axis is ↑, the *c* axis is ← and the *b* axis is directed into the paper. Two OH$\cdots$O bonds and two NH$\cdots$O bonds are formed.

and C(8)···C(14) separations, which are only 2·79 and 2·77 Å respectively. The hydrogen atoms on the CH_3 groups are oriented so that one H atom is in the plane of the heavy atoms and directed away from the double bond. As a consequence, the other two H atoms are symmetrically disposed above and below the plane so as to maximize the distance of closest approach of a hydrogen atom to the carbon atoms in the double bond. The middle OCH_3 group lies in the approximate mirror plane [except for atoms N(4), C(3) and O(1)] of the molecule. This CH_3 group is equidistant from the other two OCH_3 groups. In the reserpine molecule (Karle & Karle, 1968), the OCH_3 groups in the moiety
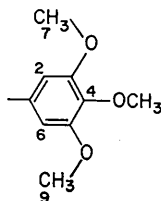
are disposed in a similar fashion as in the present molecule, that is, the middle OCH_3 group is approximately perpendicular to the ring while the other two OCH_3 groups are nearly coplanar with the ring, although the ring in the reserpine is a planar aromatic ring while the ring in the present molecule has a fold of 156° at C(1)···C(7). In reserpine the values for the C(2)···C(7) and C(6)···C(9) separations are similarly very low, 2·80 and 2·82 Å.

Bond lengths and angles are shown in Fig. 2. Standard deviations based solely on the least-squares fit are ~0·011 Å for the bond lengths and ~0·7° for the angles. There are no unusual values for the bond lengths. It is of interest to note that C(1)–O(3) and C(7)–O(5) are ~1·43 Å where the carbon atoms are saturated, whereas C(9)–O(4) and C(10)–O(2) are only ~1·36 Å where the carbon atoms are unsaturated. Values of ~1·36 Å for C–O bonds where the carbon atoms are part of a benzene ring have been found in reserpine, for example.

The oxygen atom of the water molecule occurs on a twofold axis at 00z and there are four H_2O molecules

in the unit cell while there are eight organic molecules* The packing in a unit cell is shown in Fig. 3. Each of the H_2O molecules is bonded in an approximately tetrahedral fashion to four organic molecules forming two OH···O bonds at 2·81 Å and two O···HN bonds at 3·00 Å, (Fig. 4). In addition, a hydrogen bond is formed between the C=O of one molecule and the HO– of another at 2·74 Å. Thus, the hydrogen bonds link a double layer of molecules into infinite sheets perpendicular to the a direction. Parallel sheets of molecules make van der Waals contacts near $x = \frac{1}{4}$ and $\frac{3}{4}$ between OCH_3 groups. The closest intermolecular approach is 3·19 Å between C(14), a carbon atom in a OCH_3 group, and O(1), the carbonyl oxygen atom, where the molecules are related by a screw axis, at $x = 0$, $y = \frac{1}{4}$, for example. All the other nearest approaches are between carbon and oxygen atoms and are greater than 3·4 Å.

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