

Crystal Structure of Triclinic Colchiceine Hemihydrate*

Maureen F. Mackay, James D. Morrison and Jacqueline M. Gulbis

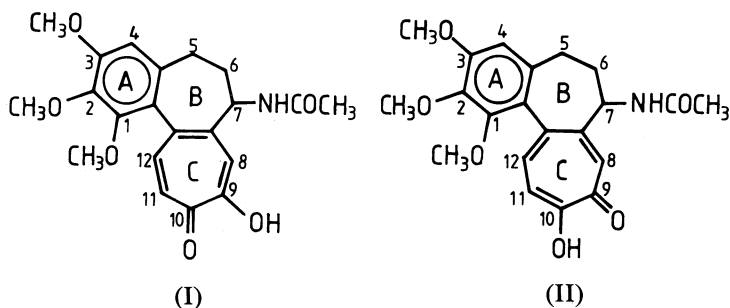
Department of Physical Chemistry,
La Trobe University, Bundoora, Vic. 3083.

Abstract

Triclinic crystals of colchiceine hemihydrate, $C_{21}H_{23}NO_6 \cdot \frac{1}{2}H_2O$, belong to the space group $P1$ with a 8.211(1), b 8.361(1), c 16.898(2) Å, α 92.35(1)°, β 93.93(1)°, γ 121.35(1)° and Z 2. The structure was solved by direct methods and successive difference syntheses with diffractometer data measured with Cu K α radiation. Refinement converged at R 0.053 for 2798 observed reflections. The two tautomers, one of the isocolchiceine and the other of the colchiceine form, exist as independent entities in the crystal; the angles between the normals to the plane of the benzene and troponoid rings are 44.5(4)° and 51.5(5)° respectively. The hydroxyl and N-acetyl groups are oriented to form channels along the a -axis which accommodate the water molecules.

1. Introduction

In view of the antimitotic properties of colchicine derivatives (Rösner *et al.* 1981) their molecular geometry is of considerable interest. For colchiceine, in which the methoxy substituent on the troponoid ring in cochicine has been replaced by a hydroxyl group, two tautomeric forms are possible. These are represented as (I) and (II),



* Dedicated to Dr A. McL. Mathieson on the occasion of his 65th birthday.

and correspond to the isocolchicine and colchicine forms respectively. In crystals of colchicine ethylacetate water solvate (Silverton 1979) and trimethylcolchicinic acid (Margulis 1982) the generally accepted colchicine form (II) was found to exist. However, in the solid state, Iorio *et al.* (1978) found 7-oxodeacetamidocolchicine to exist as an unusual 2 : 3 mixture of the tautomeric forms. More recently, Rius *et al.* (1984) have reported the crystal structure of 7-deacetamidocolchicine in which the molecules are in the isocolchicine form. From their results and those reported earlier by other authors, they suggested that the absence of any substituent at position 7 in colchicine derivatives may favour the isocolchicine form. We now report the crystal structure of colchicine hemihydrate in which there is a 1 : 1 mixture of the tautomers.

2. Experimental

Pale yellow needle-like crystals of colchicine hemihydrate are triclinic and belong to the space group *P*1. Accurate unit cell parameters were determined by the least-squares method from 2θ values for 25 reflections (2θ range 35° to 56°) measured on a diffractometer at 289(1) K with Cu K α radiation (λ 1.5418 Å). The crystal density was determined by flotation. Although the cell parameters are in reasonable agreement with those of Morrison (1951), his reported density 1.24 g cm^{-3} is too low.

Crystal Data

$\text{C}_{21}\text{H}_{23}\text{NO}_6 \cdot \frac{1}{2}\text{H}_2\text{O}$, *M* 394.4, triclinic, space group *P*1, *a* 8.211(1), *b* 8.361(1), *c* 16.898(2) Å, α 92.35(1)°, β 93.93(1)°, γ 121.35(1)°, *U* 984.4(2) Å³, *D*_m 1.33(1), *D*_c 1.33 g cm⁻³, *Z* 2, *F*(000) 418, μ 7.04 cm⁻¹ (Cu K α).

A crystal of approximate dimensions 0.30×0.14×0.095 mm with faces (010), (0 $\bar{1}$ 0), (001), (00 $\bar{1}$), (100) and ($\bar{2}$ 10) was used for the data collection. Intensity data were measured at 289(1) K on a Rigaku-AFC four-circle diffractometer with Cu K α radiation (graphite-crystal monochromator, λ 1.5418 Å). Intensities were recorded by an ω - 2θ scan, with scan rate 2° min^{-1} , scan range $\Delta\omega$ of $1.2^\circ + 1.5^\circ \tan \theta$ and 10 s stationary background counts. Three reference reflections monitored every 50 reflections showed no significant variation in intensity during data collection. Data to a $2\theta(\text{max})$ of 130° (*h* −9 to 9, *k* −9 to 9, *l* 0 to 19) yielded 3256 terms, and the 2798 for which $I \geq \sigma I_0$ were used for the structure refinement. The integrated intensities were corrected for Lorentz and polarization effects and analytical absorption corrections were made (transmission factors ranged from 0.902 to 0.941).

Attempts to solve the structure by vector superposition were unsuccessful, and the structure was solved by direct methods with MULTAN 78 (Main *et al.* 1978) and by successive difference syntheses. The molecular skeletons could not be depicted from any of the *E* maps although from most, the site of a plausible ≈ 10 -atom molecular fragment could be derived. A number of attempts were made to initiate structure solution, each based on one such fragment. Eventually, from the *E* map calculated with 324 phased terms with $|E| \geq 1.20$ (ABSFOU 1.96, PSIZERO 4.64, RESID 15.2%) peaks were assembled to correspond to sites feasible for a benzene ring and four associated atoms. Using this fragment, with the atoms included as C, structure solution

Table 1. Atomic coordinates for the non-hydrogen atoms and equivalent isotropic temperature factors (\AA^2)

The e.s.d. values for the atomic coordinates are given in parentheses and for B_{eq} are 0.1 \AA^2 ; B_{eq} is defined as $\frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$. Atoms in molecule (2) are denoted by the addition of 20 to their atomic numbers

Atom	$10^4 x$	$10^4 y$	$10^4 z$	B_{eq}	Atom	$10^4 x$	$10^4 y$	$10^4 z$	B_{eq}
C(1)	1179(0)	-262(0)	-154(0)	3.9	C(21)	4676(8)	514(6)	3112(3)	4.2
C(2)	-104(8)	-1600(6)	301(3)	4.4	C(22)	4397(8)	1736(6)	2662(3)	4.5
C(3)	-1710(8)	-1578(6)	502(3)	4.7	C(23)	2626(8)	1552(6)	2561(3)	4.6
C(4)	-2042(8)	-216(6)	238(3)	4.9	C(24)	1090(8)	142(6)	2909(3)	4.6
C(4a)	-737(6)	1150(6)	-212(3)	4.3	C(24a)	1346(6)	-1086(6)	3359(3)	4.2
C(5)	-1104(8)	2652(6)	-486(3)	4.8	C(25)	-321(6)	-2655(8)	3730(3)	5.3
C(6)	-1687(6)	2424(6)	-1373(3)	4.6	C(26)	-99(6)	-2215(8)	4638(3)	5.2
C(7)	-518(6)	1851(6)	-1855(3)	3.8	C(27)	1966(6)	-1367(6)	5005(3)	4.3
C(7a)	1617(6)	3070(6)	-1592(3)	3.5	C(27a)	2793(6)	-2537(6)	4729(3)	4.1
C(8)	2710(6)	4536(6)	-2067(3)	4.2	C(28)	2819(8)	-3765(6)	5240(3)	5.1
C(9)	4681(6)	5787(6)	-2054(3)	4.8	C(29)	3450(9)	-5026(6)	5198(3)	5.7
C(10)	6210(6)	5788(6)	-1580(3)	4.9	C(30)	4396(8)	-5270(6)	4538(4)	5.0
C(11)	5901(6)	4809(6)	-892(3)	4.8	C(31)	4648(8)	-4461(6)	3837(3)	5.2
C(12)	4219(6)	3521(6)	-595(3)	4.3	C(32)	4164(6)	-3177(6)	3564(3)	4.5
C(12a)	2297(6)	2660(5)	-889(3)	3.6	C(32a)	3384(6)	-2274(6)	3940(3)	4.0
C(12b)	875(6)	1164(6)	-418(3)	3.8	C(32b)	3131(6)	-928(6)	3461(3)	3.9
C(13)	-1171(6)	547(8)	-3243(3)	5.0	C(33)	3588(9)	398(9)	6303(3)	5.0
C(14)	-1570(9)	788(11)	-4103(3)	7.1	C(34)	3517(10)	431(11)	7183(4)	7.9
C(1M)	2443(9)	-1753(8)	-904(3)	6.3	C(21M)	7568(9)	1717(9)	3929(3)	6.1
C(2M)	1219(10)	-2671(8)	1256(4)	7.5	C(22M)	6205(9)	2791(9)	1565(3)	6.4
C(3M)	-4546(10)	-3043(9)	1168(4)	7.9	C(23M)	715(10)	2724(9)	2037(5)	8.4
O(1)	2759(5)	-284(4)	-328(2)	4.8	O(21)	6458(5)	751(4)	3192(2)	4.6
O(2)	140(5)	-3039(4)	525(2)	5.0	O(22)	5947(5)	3206(4)	2360(2)	5.4
O(3)	-2845(6)	-2960(5)	969(2)	6.5	O(23)	2490(6)	2801(5)	2109(2)	6.4
O(9)	5267(6)	7045(6)	-2577(3)	7.7	O(29)	3264(8)	-6057(6)	5761(3)	6.0
O(10)	7904(5)	6794(6)	-1779(3)	7.3	O(30)	5040(6)	-6405(5)	4656(3)	6.8
O(13)	-985(5)	-776(6)	-3066(2)	6.2	O(33)	4990(6)	1581(6)	5990(2)	6.3
N(1)	-1027(6)	1847(6)	-2703(2)	4.5	N(21)	2054(6)	-1086(6)	5869(3)	5.0
O(1s)	-1476(6)	5033(6)	6664(3)	8.2					

was initiated. After four successive difference syntheses, the sites of the non-hydrogen atoms in the two independent molecules, (1) and (2), were located. An isolated peak of significant height was assumed to be the site of an O atom of an unsuspected water molecule; this was proved correct on refinement. Although there were maxima in subsequent difference maps at the expected H-atom sites, not all were clearly resolved. The H atoms therefore, apart from those of the hydroxyl groups and water molecule which were omitted from the analysis, were included at idealized positions. For the final refinement, anisotropic temperature factors were given to the C, N and O atoms and common isotropic temperature factors were given to the methyl and non-methyl H atoms; the latter refined to the respective B values of $13.3(7)$ and $6.7(4) \text{ \AA}^2$. The parameters were refined in two blocks, each block containing parameters for one molecule. At convergence, we found $R = 0.053$ (defined as $\Sigma \Delta F / \Sigma |F_0|$ where $\Delta F = |F_0| - |F_c|$), $R_w = 0.052$ (defined as $(\Sigma w(\Delta F)^2 / \Sigma w|F_0|^2)^{1/2}$) and $S = 1.73$ (defined as $\{\Sigma w(\Delta F)^2 / (N_0 - N_v)\}^{1/2}$ for 513 variables (N_v) and 2798 data (N_0)). Refinement was made with SHELX 76 (Sheldrick 1976), and the function minimized was $\Sigma w(|F_0| - |F_c|)^2$, with $w = (\sigma^2 |F_0| + 0.0005 |F_0|^2)^{-1}$. The maximum parameter shift-to-error ratio at convergence was $0.05:1$, and the largest peaks on the final difference map were of heights $+0.24$ and $-0.24 e \text{ \AA}^{-3}$. Atomic scattering factors were taken from Ibers and Hamilton (1974).

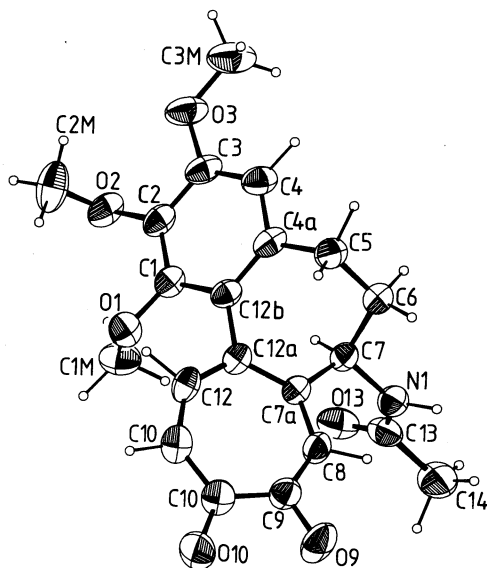


Fig. 1. Perspective view of the molecule (1) with thermal ellipsoids at the 40% probability level. The H atoms are represented by arbitrary spheres.

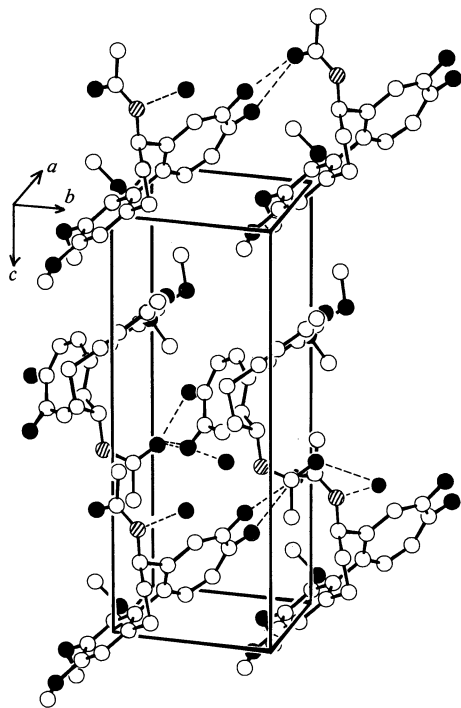


Fig. 2. Crystal packing showing the hydrogen bonds.

Final atomic positional coordinates are listed in Table 1. Fig. 1, which includes the numbering scheme, and Fig. 2 have been prepared from the output of ORTEP (Johnson 1965). Anisotropic thermal parameters, H-atom positional coordinates,

short intermolecular approaches and observed and calculated structure amplitudes have been deposited.*

3. Discussion of the Structure

The crystal structure of the title compound contains two crystallographically independent colchicine molecules of the same chirality, (1) and (2), in the asymmetric unit. Their conformation is similar in gross features, and also similar to that observed for colchicine in the ethylacetate–water solvate structure (EAWS) (Silverton 1979). There are, however, differences in the conformational detail of the two independent molecules (see Tables 2–4). Fig. 1 shows a perspective view of the molecule with the numbering scheme. The absolute skeletons in Figs 1 and 2, and for colchicine in the EAWS structure, are consistent with the configuration assigned to (+)-colchicine (Rösner *et al.* 1981).

Table 2. Bond lengths (Å) in the two independent molecules
The e.s.d. values are given in parentheses

Atoms	Molecule (1)	Molecule (2)	Atoms	Molecule (1)	Molecule (2)
C(1)–C(2)	1.381(5)	1.399(8)	C(7a)–C(12a)	1.408(7)	1.436(7)
C(1)–O(1)	1.359(4)	1.367(8)	C(8)–C(9)	1.395(8)	1.398(9)
C(1)–C(12b)	1.422(5)	1.407(7)	C(9)–C(10)	1.442(9)	1.467(9)
C(2)–C(3)	1.393(10)	1.378(10)	C(9)–O(9)	1.314(7)	1.274(7)
C(2)–O(2)	1.382(6)	1.380(6)	C(10)–C(11)	1.410(7)	1.363(8)
C(3)–C(4)	1.385(8)	1.391(8)	C(10)–O(10)	1.275(7)	1.320(8)
C(3)–O(3)	1.372(6)	1.365(7)	C(11)–C(12)	1.382(7)	1.407(8)
C(4)–C(4a)	1.393(7)	1.394(8)	C(12)–C(12a)	1.392(8)	1.380(8)
C(4a)–C(5)	1.518(8)	1.518(8)	C(12a)–C(12b)	1.500(7)	1.503(7)
C(4a)–C(12b)	1.386(9)	1.399(9)	C(13)–C(14)	1.512(7)	1.492(8)
C(5)–C(6)	1.515(7)	1.539(7)	C(13)–N(1)	1.340(7)	1.355(8)
C(6)–C(7)	1.539(8)	1.527(9)	C(13)–O(13)	1.238(7)	1.235(8)
C(7)–C(7a)	1.519(7)	1.527(8)	O(1)–C(1M)	1.435(7)	1.425(7)
C(7)–N(1)	1.466(6)	1.460(7)	O(2)–C(2M)	1.393(8)	1.431(7)
C(7a)–C(8)	1.410(7)	1.376(7)	O(3)–C(3M)	1.426(10)	1.421(11)

Ring A in both molecules (1) and (2) is planar within experimental error [$\chi^2 = \Sigma (\delta/\sigma^2) = 5.3$ for (1) and 2.5 for (2)]. Ring B adopts the expected boat conformation found in other colchicine derivatives; the sum of the torsional angles of this ring (see Table 4) is 296° for (1) and 297° for (2) similar to the values 296° for EAWS and 292° for 7-deacetamidocolchicine (Rius *et al.* 1984). In ring C the atoms are less coplanar in molecule (1) [r.m.s.d. = 0.076(5) Å, $\delta_{\max} = 0.100(5)$ Å for C(10)] than in molecule (2) [r.m.s.d. = 0.027(6) Å, $\delta_{\max} = 0.038(6)$ Å for C(9)]; the sum of the torsional angles for the ring is 63° for (1) and 27° for (2) compared with the value 15° for EAWS. The angles between the normals to rings A and C are 44.5(4)° for (1) and 51.5(5)° for (2) [cf. 54.7(3)° in EAWS]. The N-acetyl group has the conformation preferred by equatorial O-acetyl groups as first discussed by Mathieson (1965); the mean distance between the carbonyl oxygen, O(13), and the H atom at C(7) in the two molecules is 2.46 Å, and the atoms C(7), N(1), C(13), O(13) and C(14) are nearly coplanar [$\chi^2 = 74.2$, r.m.s.d. = 0.021(5) Å for (1) and $\chi^2 = 32.9$,

* Copies are available on application to the Editor-in-Chief, Editorial and Publications Service, CSIRO, 314 Albert Street, East Melbourne, Vic. 3002.

Table 3. Bond angles (degrees) in the two independent molecules

The e.s.d. values are given in parentheses

Atoms	Molecule		Atoms	Molecule	
	(1)	(2)		(1)	(2)
O(1)–C(1)–C(2)	119.7(3)	118.4(5)	C(8)–C(9)–C(10)	128.1(5)	124.9(6)
O(1)–C(1)–C(12b)	120.0(3)	119.8(5)	C(8)–C(9)–O(9)	117.5(5)	120.9(6)
C(2)–C(1)–C(12b)	120.3(3)	121.8(5)	O(9)–C(9)–C(10)	114.2(5)	114.2(6)
C(1)–C(2)–C(3)	120.7(5)	120.7(5)	C(9)–C(10)–C(11)	122.3(5)	126.6(6)
C(1)–C(2)–O(2)	120.0(4)	119.1(5)	C(9)–C(10)–O(10)	117.6(5)	114.7(6)
C(3)–C(2)–O(2)	119.2(5)	120.1(5)	O(10)–C(10)–C(11)	119.9(5)	118.7(6)
C(2)–C(3)–C(4)	120.0(5)	120.2(5)	C(10)–C(11)–C(12)	130.7(5)	130.8(5)
C(2)–C(3)–O(3)	114.8(5)	116.4(5)	C(11)–C(12)–C(12a)	132.7(5)	130.8(5)
O(3)–C(3)–C(4)	125.3(5)	123.4(5)	C(7a)–C(12a)–C(12)	124.9(5)	125.6(5)
C(3)–C(4)–C(4a)	119.5(5)	119.8(5)	C(12)–C(12a)–C(12b)	116.4(4)	115.6(5)
C(4)–C(4a)–C(5)	118.9(5)	120.6(5)	C(7a)–C(12a)–C(12b)	118.7(4)	118.9(5)
C(4)–C(4a)–C(12b)	121.7(5)	120.7(5)	C(1)–C(12b)–C(4a)	118.1(4)	118.8(5)
C(5)–C(4a)–C(12b)	119.4(5)	118.6(5)	C(1)–C(12b)–C(12a)	120.3(4)	120.9(5)
C(4a)–C(5)–C(6)	113.3(5)	110.7(5)	C(4a)–C(12b)–C(12a)	121.5(5)	120.2(5)
C(5)–C(6)–C(7)	111.8(5)	112.2(5)	O(13)–C(13)–C(14)	120.8(6)	122.6(6)
C(6)–C(7)–C(7a)	111.9(4)	111.2(5)	O(13)–C(13)–N(1)	123.4(5)	121.9(6)
C(6)–C(7)–N(1)	108.3(4)	109.4(5)	C(14)–C(13)–N(1)	115.8(5)	115.5(6)
C(7a)–C(7)–N(1)	114.0(4)	114.1(5)	C(7)–N(1)–C(13)	121.3(5)	121.8(5)
C(7)–C(7a)–C(8)	116.4(4)	117.3(5)	C(1)–O(1)–C(1M)	116.3(4)	114.4(4)
C(7)–C(7a)–C(12a)	117.0(4)	115.2(5)	C(2)–O(2)–C(2M)	115.0(4)	114.2(4)
C(8)–C(7a)–C(12a)	126.6(5)	127.4(5)	C(3)–O(3)–C(3M)	117.0(5)	117.7(5)
C(7a)–C(8)–C(9)	132.1(5)	133.5(6)			

r.m.s.d. = 0.018(6) Å for (2)]. The angles between the normals to this plane and rings A and C are 112.1(4)° and 84.6(4)° respectively for (1) and 110.2(5)° and 82.3(5)° for (2) [cf. values 108.6(3)° and 87.5(3)° in EAWS]. As in other colchicine derivatives, two of the methoxy groups, at C(1) and C(2), are approximately normal to ring A, pointing in opposite directions, while the methoxy group at C(3) is almost contained within the plane of the ring A. The angles between the normals to the methoxy planes and ring A for the substituents at C(1), C(2) and C(3) have the respective values 72.3(5)°, 89.4(5)° and 3.0(5)° for (1) and 100.1(6)°, 91.5(6)° and 4.1(1)° for (2) [cf. values 96.8(4)°, 85.1(4)° and 4.1(4)° in EAWS].

Apart from the tropolone systems, the bond lengths and angles (see Tables 2 and 3) are as expected and similar in value to those observed in related structures. It is however worth noting that at C(3), where the methoxy substituent lies nearly in the plane of ring A, the exocyclic angles are significantly distorted from the regular trigonal value. The angle enclosed by the methyl is the larger, the mean values for C(4)–C(3)–O(3) and C(2)–C(3)–O(3) in (1) and (2) being 124.3(5)° and 115.6(5)° respectively. This distortion does not occur in the exocyclic angles at C(1) and C(2), where the methoxy substituents are approximately normal to ring A. The two conformations for the methoxy groups (planar or normal to ring A) have been observed in numerous structures. In addition, the values found in these structures for the comparable exocyclic C–C–O angles are similar to those noted in the colchicine molecules (see Karle *et al.* 1984).

The most interesting features of the structure are the differing dimensions of the tropolone systems in the two independent molecules. The C–O bonds differ in length

Table 4. Selected torsional angles (degrees) in the two independent molecules
Values for EAWS (Silverton 1979) are included for comparison. The e.s.d. values are about 0.5°

Atoms	Molecule (1)	Molecule (2)	EAWS
C(1M)–O(1)–C(1)–C(2)	73.1	100.3	97.2
C(2M)–O(2)–C(2)–C(3)	–92.0	–90.4	–96.6
C(3M)–O(3)–C(3)–C(4)	2.9	4.4	3.1
C(4)–C(4a)–C(5)–C(6)	–108.8	–107.5	–108.9
C(4a)–C(5)–C(6)–C(7)	–40.6	–41.2	–35.6
C(5)–C(6)–C(7)–C(7a)	–47.9	–49.8	–53.7
C(6)–C(7)–C(7a)–C(12a)	78.4	77.8	75.2
C(7)–C(7a)–C(12a)–C(12b)	–4.4	–0.6	4.3
C(7a)–C(12a)–C(12b)–C(4a)	–49.7	–52.2	–56.5
C(12a)–C(12b)–C(4a)–C(5)	1.6	–0.9	1.8
C(12b)–C(4a)–C(5)–C(6)	70.9	74.1	68.8
C(12)–C(12a)–C(12b)–C(1)	–47.1	–53.3	–54.9
C(7a)–C(8)–C(9)–C(10)	7.4	3.0	–0.3
C(8)–C(9)–C(10)–C(11)	–18.4	–6.6	–3.8
C(9)–C(10)–C(11)–C(12)	10.0	2.3	3.3
C(10)–C(11)–C(12)–C(12a)	5.2	4.0	1.5
C(11)–C(12)–C(12a)–C(7a)	–5.0	–3.0	–3.4
C(12)–C(12a)–C(7a)–C(8)	–7.5	–2.7	0.2
C(12a)–C(7a)–C(8)–C(9)	9.0	3.2	2.6
O(9)–C(9)–C(10)–O(10)	–9.0	–5.1	–2.2
C(6)–C(7)–C(7a)–C(8)	–99.8	–99.7	–103.4
C(6)–C(7)–N(1)–C(13)	–142.4	–144.9	–152.4
C(7)–N(1)–C(13)–C(14)	–175.9	–176.5	175.6
C(7)–N(1)–C(13)–O(13)	3.7	–0.3	–4.2

by about 6σ ; in (1) it is C(10)–O(10) 1.275(7) Å which is the shorter with C(9)–O(9) 1.314(7) Å, whilst in (2) it is C(9)–O(9) 1.274(7) Å which is the shorter with C(10)–O(10) 1.320(8) Å. As the lengths reported for the C–O double and single bonds in an accurate tropolone structure are 1.232(2) and 1.359(2) Å respectively (Silverton *et al.* 1977), the values in the title compound indicate that there are two tautomeric forms for each independent molecule in the crystal to give an approximate 1:1 mixture. Consequently, molecules (1) have a larger proportion of the isocolchicine form (I) and molecules (2) have a larger proportion of the colchicine form (II). In molecule (1), apart from the C(9)–C(10) bond which has a length 1.442(9) Å, the other bonds of ring C have lengths within 2σ of the standard aromatic C–C bond length of 1.395 Å. This was also noted in 7-oxodeacetamido-colchiceine (Iorio *et al.* 1978). However, in molecule (2) there is bond alternation in ring C as is observed in EAWS. The carbon atom of the C–O bond which has the greater component of double bond character has the maximum deviation from the ring plane in each molecule, that is C(10) in (1) and C(9) in (2).

The crystal packing is illustrated in Fig. 2. The colchiceine molecules are oriented with their hydroxyl and N-acetyl groups forming channels parallel to the crystallographic *a*-axis which accommodate the water molecules. As the sites of the H atoms of the hydroxyl substituents and water molecules were not located in the analysis, only a brief description of the hydrogen bonding in the crystal can be given. The molecules (1) are linked by H bonds. These involve the hydroxyl substituent at C(9) or C(10), and the acetyl oxygen of an adjacent molecule related by a cell translation along *a* and *b*. The O(9)...O(13) and O(10)...O(13) distances are 2.848(7) and 2.897(7) Å

respectively. A similar mode of H bonding links the molecules (2) related by a cell translation along *b*, for which the O(9)...O(13) and O(10)...O(13) distances have the respective values 2.992(8) and 2.858(6) Å. In these interactions the acetyl oxygen, O(13), is the acceptor and the longer O...O spacings involve the oxygen of the C=O bond with the greater double bond component, that is O(10) in (1) and O(9) in (2). This H bonding scheme is also consistent with the presence of the two tautomers in each of the independent molecules (1) and (2). The latter are linked into layers perpendicular to the *c*-axis by H bonds with the water molecules. The water is H bonded to the N atom of molecule (1) by a weak interaction, the N(1)...O(1S) and HN(1)...O(1S) distances have the respective values 3.093(7) and 2.03 Å and the angle N(1)–HN(1)...O(1S) is 172°. It is the acetyl O atom which links molecules (2) to the water, the O(13)...O(1S) distance being 2.935(7) Å. Apart from two short intermolecular contacts, O(10)...O(1S) 3.160(7) Å and O(9)...C(13) 3.194(8) Å, both involving molecules (1), there are no other contacts less than 3.27(1) Å.

Acknowledgments

This work completes a project begun in 1947 by one of the authors (J.D.M.), when he and Dr A. McL. Mathieson were postgraduate students in the crystallography laboratory of Professor J. Monteath Robertson at the University of Glasgow. M.F.M. dedicates her contribution with gratitude and affection to Dr Mathieson who, since her postgraduate student days under his supervision, has maintained an interest in her work.

We are grateful to Professor J. W. Cook, and the late Dr J. D. Loudon, both formerly of the University of Glasgow, for providing the crystals used in the analysis, and we wish to thank Dr B. F. Hoskins of Melbourne University for making available the MULTAN 78 programs.

References

- Ibers, J. A., and Hamilton, W. C. (Eds) (1974). 'International Tables for X-ray Crystallography', Vol. 4 (Kynock Press: Birmingham).
- Iorio, M. A., Brossi, A., and Silverton, J. V. (1978). *Helv. Chim. Acta* **61**, 1213.
- Johnson, C. K. (1965). ORTEP: Thermal ellipsoid plot program. Oak Ridge National Laboratory Rep. No. ORNL-3794.
- Karle, I. L., Flippin-Anderson, J. L., Chiang, J. F., and Lowrey, A. H. (1984). *Acta Crystallogr. B* **40**, 500.
- Main, P., Hull, S. E., Lessinger, L., Germain, G., Declercq, J. P., and Woolfson, M. M. (1978). MULTAN 78: A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data. Univ. of York, England, and Louvain, Belgium.
- Margulis, T. N. (1982). *Cryst. Struct. Commun.* **11**, 1689.
- Mathieson, A. McL. (1965). *Tetrahedron Lett.* **46**, 4137.
- Morrison, J. D. (1951). *Acta Crystallogr.* **4**, 69.
- Rius, J., Molins, E., Miravittles, C., and Bladé-Font, A. (1984). *Acta Crystallogr. C* **40**, 839.
- Rösner, M., Caparo, H. G., Jacobson, A. E., Atwell, L., Brossi, A., Iorio, M. A., Williams, T. H., Sik, R. H., and Chignell, C. F. (1981). *J. Med. Chem.* **24**, 257.
- Sheldrick, G. M. (1976). SHELX 76: Program for crystal structure determination. Univ. of Cambridge, England.
- Silverton, J. V. (1979). *Acta Crystallogr. B* **35**, 2800.
- Silverton, J. V., Kabuto, C., Buck, K. T., and Cava, M. P. (1977). *J. Am. Chem. Soc.* **99**, 6708.