FUJII, S. (1979). *MOLCON. The Universal Crystallographic Computing System–Osaka*. The Computation Center, Osaka Univ., Japan.

HAISA, M. (1978). *Acta Cryst.* A**34**, 753–759.

HAISA, M., KASHINO, S. & MORIMOTO, M. (1980). *Acta Cryst.* B**36**, 2832–2834.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

PLANA, F., MIRAVITLLES, C., SOLANS, X. & GALÍ, S. (1977). *Cryst. Struct. Commun.* **6**, 387–392.

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Structure of 3-*O*-Demethylcolchicine Acetone Solvate, $C_{21}H_{23}NO_6.C_3H_6O$

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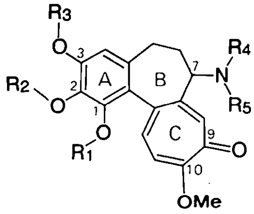
Abstract. $M_r = 443{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 8{\cdot}030\,(1)$, $b = 9{\cdot}700\,(1)$, $c = 30{\cdot}710\,(3)$ Å, $V = 2392{\cdot}0$ Å^3, $Z = 4$, $D_m = 1{\cdot}22\,(1)$, $D_x = 1{\cdot}231$ g cm^{-3}, $\lambda(\mathrm{Cu}\,K\alpha) = 1{\cdot}5418$ Å, $\mu = 7{\cdot}58$ cm^{-1}, $F(000) = 944$, $T = 293$ K, $wR = 0{\cdot}052$ for 2788 reflections. This biologically relatively active colchinoid compound crystallizes as an acetone solvate. The intensity data were not of very high quality and the structure was refined first with data processed by standard methods and then with Bayesian techniques which produced an improvement in the precision of the results. The molecular conformation bears considerable resemblance to those of previously reported active colchinoids.

Introduction. Colchicine and its analogs are thought to inhibit biological processes by blocking the polymerization of tubulin. While chemical manipulation of colchicine has indicated that aromatic substitution, proper chirality of the acetimido function and a carbonyl group at C(9) are necessary for effective tubulin binding (Capraro & Brossi, 1983), definite conclusions as to the role of these functionalities are lacking. The present structure is that of a chemically modified colchinoid compound which still possesses a biological activity not greatly diminished from that of colchicine itself (Capraro & Brossi, 1983). This investigation represents the second paper in an investigation of colchinoid compounds at the extremes of biological activity (the first was Silverton, Sharma & Brossi, 1985).

The general formula of the colchinoids is given as (I) and 3-*O*-demethylcolchicine has $R1$=$R2$=methyl, $R3$=$R4$=H, $R5$=acetyl.



(I)

Experimental. 3-*O*-Demethylcolchicine (crystallized from acetone): m.p. (uncorrected, acetone solvate), Fisher–Johns apparatus, 554 K optical rotation, Perkin–Elmer 241 polarimeter $[\alpha]_D^{20\,^\circ\mathrm{C}} = -157°$ ($c = 0{\cdot}4$ g dm^{-3}, $CHCl_3$). Literature (Rosner, Capraro, Jacobson, Brossi, Iorio, Williams, Sik & Chignell, 1981): m.p. 543 K, $[\alpha]_D^{20\,^\circ\mathrm{C}} = -151°$ ($CHCl_3$). $C_{21}H_{23}NO_6.CH_3COCH_3$; C, H, N calculated: 64·99, 6·59, 3·150; found (Microanalytical Section, Laboratory of Chemistry, NIADDK, NIH): 64·79, 6·70, 3·01%.

X-ray experimental data: Enraf–Nonius CAD-4 diffractometer; colorless prismatic crystals, 0·3 × 0·1 × 0·1 mm; $\sin\theta/\lambda(\max.) = 0{\cdot}6235$ Å^{-1}; 2788 reflections measured (max. time 90 s, $h\,0\rightarrow10$, $k\,0\rightarrow12$, $l\,0\rightarrow38$), 1092 reflections with $I \leq \sigma(I)$. 20 reflections ($20 \leq \theta \leq 30°$) used for measuring lattice parameters. No absorption correction.

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The crystals of this compound had been thought to be unsolvated and were stored for some time previous to the investigation. The measured X-ray intensities seemed surprisingly weak for the crystal size and the calculated crystal density was rather low, but since preparing suitable crystals had proven to be difficult, it was decided to continue the investigation with the few available crystals and the density was not measured until completion of data collection.

No interpretable E maps were produced by automatic and semi-automatic use of *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) with up to nine variable phases. The cause may have been inaccurate scaling due to the large fraction of unobserved reflections but it was possible to solve the phase problem by selection of planes occurring most frequently in negative quartets (Silverton, Kabuto & Akiyama, 1978) and use of nine of these as magic-integer variables in the multisolution technique. The reliability of the solutions was assessed both by a weighted figure of merit and the NQEST test (DeTitta, Edmonds, Langs & Hauptman, 1975). The solution with the best value of NQEST, which was also one of the best on the combined figure of merit, gave an E map showing most of the heavier atoms. All subsequent work used the programs of *XRAY*72 (Stewart, Kruger, Ammon, Dickinson & Hall, 1972) in the sequence: isotropic least-squares refinement of the trial model, finding missing heavy atoms from difference maps, anisotropic refinement, location of all H atoms and final refinement using isotropic refinement of H atoms. Difference maps indicated four large peaks not directly connected to the expected molecule which could be attributed to a molecule of acetone of solvation. R factors and final location of all expected H atoms confirmed the assignment. The thermal parameters of the atoms of the solvent molecule are rather large and, in retrospect, it is surprising that there was no decrease in intensity standards during data collection since the crystal was not protected from loss of solvent in any way. There was some difficulty in refining certain H atoms and, in such cases, only the positional parameters were refined. The solvent H atoms were included in the structure-factor calculations but not refined. Refinement: weighting scheme after Peterson & Levy (1957), function minimized: $\sum w\Delta^2$, final $R = 0{\cdot}048$ (observed reflections only), $wR = 0{\cdot}045$, $S = 1{\cdot}36$, $\langle \Delta/\sigma \rangle = 0{\cdot}05$, $|\Delta\rho_{\max}| = 0{\cdot}2$ e Å^{-3}; no correction for secondary extinction; scattering factors from *XRAY*72; anisotropic temperature factor expression: $\exp[2\pi^2\sum_i\sum_j(U_{ij}h_ih_ja^*_ia^*_j)]$.

Table 1. *Atomic parameters for the heavier atoms*

The equivalent isotropic temperature factor, U_{eq}, is the geometric mean of the diagonal terms of the vibration tensor. Positional parameters are multiplied by 10^4 and U_{eq} values by 10^3.

	x	y	z	U_{eq}(Å^2)
C(1)	8574 (4)	1122 (4)	1836 (1)	37 (1)
O(1)	6861 (3)	967 (3)	1839 (1)	44 (1)
C(1*m*)	6316 (6)	−334 (5)	1996 (2)	82 (2)
C(2)	9388 (4)	1468 (4)	2223 (1)	41 (1)
O(2)	8516 (3)	1589 (3)	2607 (1)	55 (1)
C(2*m*)	7707 (7)	2856 (6)	2664 (2)	105 (2)
C(3)	11089 (5)	1616 (4)	2229 (1)	45 (1)
O(3)	11945 (4)	1892 (3)	2601 (1)	58 (1)
C(4)	11984 (5)	1469 (4)	1849 (1)	41 (1)
C(4*a*)	11202 (4)	1126 (4)	1462 (1)	37 (1)
C(5)	12212 (5)	807 (4)	1061 (1)	43 (1)
C(6)	12367 (5)	−746 (4)	991 (1)	42 (1)
C(7)	10704 (4)	−1478 (4)	1086 (1)	35 (1)
C(7*a*)	9282 (4)	−779 (3)	838 (1)	34 (1)
C(8)	8798 (5)	−1348 (4)	454 (1)	40 (1)
C(9)	7566 (5)	−1001 (4)	131 (1)	45 (1)
O(9)	7493 (4)	−1722 (3)	−206 (1)	66 (1)
C(10)	6378 (5)	121 (4)	188 (1)	44 (1)
O(10)	5279 (3)	122 (3)	−148 (1)	64 (1)
C(10*m*)	3969 (6)	1149 (8)	−150 (2)	83 (2)
C(11)	6321 (5)	1058 (4)	513 (1)	45 (1)
C(12)	7344 (5)	1214 (4)	886 (1)	42 (1)
C(12*a*)	8644 (4)	447 (4)	1039 (1)	35 (1)
C(12*b*)	9471 (5)	935 (3)	1452 (1)	35 (1)
N	10837 (4)	−2953 (3)	1019 (1)	40 (1)
C(13)	10078 (5)	−3822 (4)	1296 (1)	43 (1)
O(13)	9140 (3)	−3401 (3)	1581 (1)	57 (1)
C(13*m*)	10424 (7)	−5329 (5)	1234 (2)	63 (2)
O(1*s*)	5067 (8)	4007 (5)	893 (2)	161 (3)
C(1*s*)	5264 (8)	4985 (7)	1117 (3)	104 (3)
C(2*s*)	5673 (8)	6322 (7)	923 (3)	147 (4)
C(3*s*)	5152 (10)	4898 (11)	1591 (3)	184 (5)

In view of the low quality of the X-ray data, the intensities of the weak reflections were evaluated using the Bayesian approach of French & Wilson (1978) by means of local programs (Cantrell & Silverton, 1979). Since no reflections are regarded as 'unobserved' and omitted from the refinement, the final conventional R factor was somewhat larger (0·096) although the weighted R factor was 0·052 and thus only slightly larger than that from the conventionally processed data. Since there was an improvement in the e.s.d.'s of the atoms (the average e.s.d. of a heavy-atom bond length was 0·0058 Å for conventional processing and 0·0049 Å for the Bayesian results), the numerical values given in this paper refer to the Bayesian intensity values. It is also interesting that the scale factor evaluated by the *NORMAL* component of *MULTAN* was much closer to the final refined value when the Bayesian data were used. The final scale factors were 1·614 and 1·611 and the *NORMAL* scale factors were 1·832 and 1·677 for the conventionally processed and Bayesian data respectively and possibly the use of the Bayesian data might have facilitated the direct methods.

Discussion. The atomic coordinates and equivalent isotropic thermal parameters for the heavier atoms are given in Table 1* and crystal conformation, bond lengths and angles are shown in Fig. 1. The bond lengths and angles appear to have values very similar to those in other comparable compounds.

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* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and bond distances and angles in the solvent molecule have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42110 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The molecular packing is shown in Fig. 2. The molecules are linked along screw axes by hydrogen bonds. There is an N···O(9) bond with dimensions: N···O 2·845 (4), H···O 2·06 (3) Å and N—H···O 157 (4)° along the *a* screw axis and such hydrogen bonds are common in colchinoid structures. The H atom on O(3) also forms a hydrogen bond along the *b* screw axis to the acetyl O atom of another molecule. The dimensions are: O(3)···O(13) 2·674 (4), H···O(13) 1·92 (5) Å and O(3)—H···O(13) 153 (5)°. The two bonds produce a network of molecules leaving holes filled by the acetone of solvation. The solvent does not appear to form hydrogen bonds and, although it is not readily released from the crystals, the atomic temperature factors are relatively large.

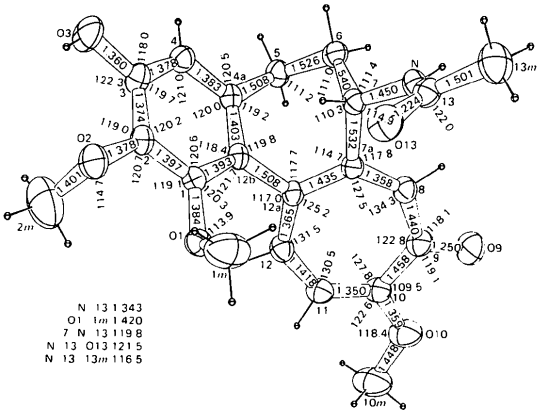

Fig. 1. Crystal conformation and dimensions of the molecule of 3-*O*-demethylcolchicine (distances in Å, angles in °). *ORTEP* drawing (Johnson, 1965); thermal ellipsoids are drawn at 40% probability and the H atoms are arbitrary. E.s.d.'s of bond lengths are ≤0·007 Å and e.s.d.'s of bond angles are ≤0·3° respectively.

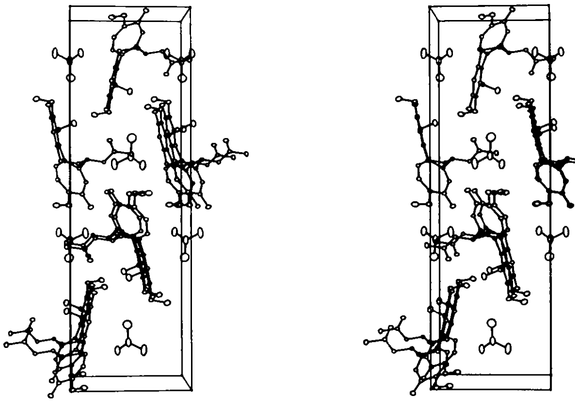

Fig. 2. Packing diagram; direction of projection **a**. The *b* axis is horizontal.

Table 2. *Torsion angles (°) for ring B in the solid-state conformations of colchinoids*

The values for the two independent molecules of compound (2) are indicated. E.s.d.'s for torsion angles in the present work are ≤1·0°.

	Torsion angle†						
Compound*	(1)	(2)	(3)	(4)	(5)	(6)	(7)
(1)	54 (3)	3 (7)	−78 (3)	48 (6)	41 (5)	−5 (4)	−70 (3)
(2)	53	3	−80	49	43	−3	−73
(2)	54	1	−79	50	41	−3	−72
(3)	49	1	−72	39	49	3	−79
(4)	53	3	−81	51	41	−1	−74

* The compounds and references are: (1) Average for colchicine acetate (Miravitlles *et al.*, 1982), colchicine (Lessinger & Margulis, 1978*a*), isocolchicine (Lessinger & Margulis, 1978*b*), colchiceine (Silverton, 1979): six independent molecules with parenthesized figures giving range limits. (2) *N*-Acetyldemecolcine (Silverton *et al.*, 1985). (3) 7-Deacetamidocolchiceine (Rius *et al.*, 1984). (4) 3-*O*-Demethylcolchicine (present paper).

† Torsion angles are: (1) C(4a)—C(12b)—C(12a)—C(7a), (2) C(12b)—C(12a)—C(7a)—C(7), (3) C(12a)—C(7a)—C(7)—C(6), (4) C(7a)—C(7)—C(6)—C(5), (5) C(7)—C(6)—C(5)—C(4a), (6) C(5)—C(4a)—C(12b)—C(12a), (7) C(6)—C(5)—C(4a)—C(12b).

Despite the perturbations introduced by the extra hydrogen bond formed by the 3-hydroxyl group, the molecular conformation observed in the present structure is very similar to that observed for all colchinoids previously reported and this is indicated in Table 2 which gives the average torsion-angle parameters of the flexible *B* ring for four previously reported colchinoid crystal structures and the actual values for two recent structures. [The table was originally given by Miravitlles, Solans, Bladé-Font, Germain & Declercq (1982) and was modified by Silverton *et al.* (1985).] In the table it is assumed that all published colchinoid structures have the *S* configuration as established chemically for natural colchicine by Corrodi & Hardegger (1955). The basic ring system of the colchinoids has much the same conformation even in the absence of an *N*-acetyl group. Rius, Molins, Miravitlles & Bladé-Font (1984) have reported the crystal structure of 7-deacetamidocolchiceine (compound 3 in Table 2) and the *B*-ring torsion angles will be seen to be very similar. It seems probable that the observed crystal conformation may represent a situation close to the global energy minimum. All such compounds possessing an *N*-carbonyl group (for references see Table 2) have it disposed on the same side of the molecule as in the present case. This similarity can be seen in the distances of the acetyl O atom from the least-squares planes of rings *A* and *C*, 4·15 and 2·73 Å respectively, to those reported for *N*-acetyldemecolcine by Silverton *et al.* (1985). Here the corresponding average distances are 3·60 and 2·70 Å respectively and, although this compound does not form hydrogen bonds, the distances are quite similar. The methoxy groups in the known colchinoid structures have different orientations but this is not surprising in view of the different forms of packing and the presence or absence of hydrogen bonds.

References

Cantrell, T. S. & Silverton, J. V. (1979). *J. Org. Chem.* **44**, 4477–4481.

Capraro, H.-G. & Brossi, A. (1983). *The Alkaloids,* Vol. XXIII, edited by A. Brossi, pp. 51–83. New York: Academic Press.

Corrodi, H. & Hardegger, E. (1955). *Helv. Chim. Acta,* **38**, 2030–2033.

DeTitta, G. T., Edmonds, J. W., Langs, D. A. & Hauptman, H. A. (1975). *Acta Cryst.* A**31**, 472–479.

French, S. & Wilson, K. (1978). *Acta Cryst.* B**34**, 517–525.

Johnson, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

Lessinger, L. & Margulis, T. N. (1978*a*). *Acta Cryst.* B**34**, 578–584.

Lessinger, L. & Margulis, T. N. (1978*b*). *Acta Cryst.* B**34**, 1556–1561.

Main, P., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1978). *MULTAN78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

Miravitlles, C., Solans, X., Bladé-Font, A., Germain, G. & Declercq, J.-P. (1982). *Acta Cryst.* B**38**, 1782–1786.

Peterson, S. W. & Levy, H. A. (1957). *Acta Cryst.* **10**, 70–75.

Rius, J., Molins, E., Miravitlles, C. & Bladé-Font, A. (1984). *Acta Cryst.* C**40**, 839–847.

Rosner, M., Capraro, H.-G., Jacobson, A. E., Brossi, A., Iorio, M. A., Williams, T. H., Sik, R. H. & Chignell, C. F. (1981). *J. Med. Chem.* **24**, 257–261.

Silverton, J. V. (1979). *Acta Cryst.* B**35**, 2800–2803.

Silverton, J. V., Kabuto, C. & Akiyama, T. (1978). *Acta Cryst.* B**34**, 588–593.

Silverton, J. V., Sharma, P. N. & Brossi, A. (1985). *Acta Cryst.* C**41**, 755–758.

Stewart, J. M., Kruger, G. J., Ammon, H. L., Dickinson, C. W. & Hall, S. R. (1972). The *XRAY72* system–version of June 1972. Tech. Rep. TR-192. Computer Science Center, Univ. of Maryland, College Park, Maryland.

Acta Cryst. (1985). C**41**, 1072–1075

Structures of (*E*)-Benzaldehyde Phenylhydrazone, $C_{13}H_{12}N_2$ (1), and (*E*)-Benzaldehyde 4′-Nitrophenylhydrazone, $C_{13}H_{11}N_3O_2$ (2)

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Abstract. (1) $M_r = 196\cdot3$, monoclinic, $P2_1/c$, $a = 6\cdot053\,(7)$, $b = 17\cdot643\,(13)$, $c = 15\cdot207\,(15)$ Å, $\beta = 92\cdot2\,(1)^\circ$, $V = 1622\cdot8$ Å^3, $Z = 6$, $D_m = 1\cdot20\,(1)$, $D_x = 1\cdot20$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0\cdot7107$ Å, $\mu = 0\cdot78$ cm^{-1}, $F(000) = 624$, room temperature, $R = 0\cdot077$ for 1069 independent reflections. The structure consists of an ordered molecule in a general position and a molecule disordered around a crystallographic centre of symmetry. Both molecules take up the *E* conformation; in the ordered molecule the angle between the two benzene rings is 8·1 (1)°. (2) $M_r = 241\cdot2$, monoclinic, Cc, $a = 6\cdot049\,(5)$, $b = 23\cdot320\,(11)$, $c = 8\cdot506\,(11)$ Å, $\beta = 96\cdot8\,(1)^\circ$, $V = 1191\cdot4$ Å^3, $Z = 4$, $D_m = 1\cdot34\,(1)$, $D_x = 1\cdot34$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0\cdot7107$ Å, $\mu = 1\cdot15$ cm^{-1}, $F(000) = 504$, room temperature, $R = 0\cdot071$ for 789 independent reflections. The molecule takes up the *E* conformation. There is a weak intermolecular hydrogen bond between the NH group and the *p*-nitro group, N···O 3·10 (1) Å.

Introduction. In a series of papers (Willey & Drew, 1985 and references therein), we have studied the structures of various phenylhydrazone derivatives. One of the main points to emerge is that the –NH group will participate in hydrogen bonding whenever possible, either intramolecular (for preference) or intermolecular (Willey & Drew, 1983; Drew, Vickery & Willey, 1984).

We now report the structures of the title compounds (1) and (2), which will provide two different arrangements. (1) can have no hydrogen bonding while (2) only contains a *p*-NO_2 group for possible intermolecular interaction with the NH group. These structures will also confirm the particular structural type (*E v Z*) adopted in such benzaldehyde derivatives.

[†] Deceased.

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