The acyclic S—O bond lengths of 1·41 (3) and 1·42 (3) Å agree well with reported values in the range 1·41 to 1·44 Å for similar compounds. The cyclic S—O bond length of 1·57 (4) Å compares with values in the range 1·55 to 1·63 Å in both saturated and partially unsaturated sultones. The S—C bond length of 1·78 (2) Å similarly falls in the middle of the range of previously reported values (1·73 to 1·82 Å).

There are no abnormal intermolecular contacts.

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Structure and Absolute Configuration, by Several Methods, of (*S*)-2-*O*-Acetyl-2-demethylthiocolchicine

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Abstract. 7-Acetamido-5,6,7,9-tetrahydro-1,3-dimethoxy-10-methylthio-9-oxobenzo[*a*]heptalen-2-yl acetate, $M_r = 501\cdot59$, monoclinic, $A2$, $a = 13\cdot721$ (2), $b = 10\cdot925$ (1), $c = 16\cdot795$ (1) Å, $\beta = 94\cdot97$ (1)°, $V = 2508\cdot14$ Å^3, $Z = 4$, $D_x = 1\cdot328$ g cm^{-3}, λ(Cu $K\alpha$) $= 1\cdot5418$ Å, $\mu = 14\cdot91$ cm^{-1}, $F(000) = 1064$ [M_r, D_x, μ and $F(000)$ based on the formula $C_{23}H_{25}NO_6S.C_3H_6O$], $T = 293$ K, $R = 0\cdot045$ for 2166 reflections with $I > \sigma(I)$. This colchicine derivative crystallizes as a solvate (possibly but not conclusively of acetone) and the structure reported represents the first X-ray determination of absolute configuration in this series of biologically active compounds. The absolute configuration was determined by several methods; all of which concur. The conformation of this compound resembles that of all previously reported colchicinoid compounds. The structure refinement was used as a test of a new vector processor.

Introduction. Colchicine and its analogs are thought to inhibit biological processes by blocking the polymerization of tubulin. For discussion and investigation of the biological action of colchicinoid compounds, it is important to know both conformation and configuration (Capraro & Brossi, 1983). Although a chemical determination was carried out by Corrodi & Hardegger (1955), no crystallographic determination of absolute configuration in this series has been reported in the literature. This investigation remedies the situation and adds a new colchicinoid crystal structure. In the preliminary stages of this work a large number of previously uninvestigated salts and derivatives of

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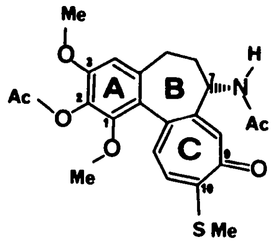
colchicine were prepared but all except the present compound proved to give crystals which were either too small for data collection or which diffracted very weakly. In some cases, the compounds showed evidence of various types of chemical decomposition both before and during X-ray measurements.



Experimental. 2-Acetyl-2-demethylthiocolchicine, crystallized from acetone: m.p. (uncorrected, acetone solvate), 459–461 K, Fisher–Johns apparatus, optical rotation $[\alpha]_D = -185°$ (C 0·42, $CHCl_3$), Perkin–Elmer 241 polarimeter. The negative optical rotation confirms that this compound belongs to the series of natural colchicinoids, as can be anticipated from its mode of preparation. (Previous literature and analytical data: Kerekes, Brossi, Flippen-Anderson & Chignell, 1985). X-ray experimental data: CAD-4 diffractometer; light yellow hexagonal plates, $(\sin\theta)/\lambda(\max.) = 0{\cdot}6228$ Å^{-1}. Two sets of X-ray intensity data: (*a*) hemisphere of data: 5354 reflections, 1764 with $I < \sigma(I)$, crystal size: 0·2 × 0·2 × 0·07 mm, max. time: 45 s, h: −17 to 17, k: −13 to 13 and l: 0 to 20 and (*b*) the unique set: 2675 reflections, 509 with $I < \sigma(I)$, crystal size: 0·15 × 0·20 × 0·25 mm, max. time: 120 s, h: −17 to 17, k: 0 to 13 and l: 0 to 20. 20 reflections ($20 \le \theta \le 25°$) used for measuring lattice parameters. No absorption correction. No measured density because of possibility of decomposition. 3 standard reflections ($35\bar{1}$, $02\bar{8}$, $50\bar{6}$) showed < 2% intensity variation.

Apart from the lattice extinction ($k + l \neq 2n$), there are no systematic absences and, of the possible space groups, only $A2$ is suitable for an optically active substance. The programs of *MITHRIL* (Gilmore, 1983) were used to solve the phase problem. The complete molecular structure was obtained after Fourier recycling and was further refined, using the *CRYLSQ* component of *XTAL* (Stewart, Hall, Alden, Olthof-Hazekamp & Doherty, 1985) in a local version designed to make use of the IBM 3090 vector processor. The refinement minimized $\sum w(F_o - F_c)^2$ with weights as given by Peterson & Levy (1957). The refinement employed isotropic thermal parameters for the H atoms and anisotropic thermal parameters for the heavier atoms of the form $\exp\{2\pi^2[\sum_i\sum_j(U_{ij}h_ih_ja_i^*a_j^*)]\}$. The modifications to *CRYLSQ* were carried out by JVS and John Eilart (IBM Research) and have been communicated to the editors of the *XTAL* system. Details of the modifications may be obtained from JVS. The modifications produce a twofold speed increase over the original program run on the same machine.

Refinement was essentially uneventful except that extra peaks were detected on and around the twofold axis. Despite the fact that the solvent of crystallization, acetone, possesses the necessary symmetry, the peaks could not be reconciled with an acetone molecule and positional disorder or some doubt as to the identity of the peaks must be assumed. The three 'atoms' (arbitrarily assigned C scattering factors) which appear to best fit the peaks are reported in the final results but no unique model of the disorder is proposed.

Because of the importance of checking the absolute configuration in the colchicine series, the determination was carried out by five different techniques.

1. The complete unaveraged hemisphere of data (set *a*) gave an R factor of 0·075 at convergence using anomalous-dispersion corrections (*International Tables for X-ray Crystallography*, 1974) and 3591 reflections with $I > \sigma(I)$. The model with the opposite configuration and the same data set gave an R factor of 0·079 and the ratio of R factors is 1·05, which is apparently significant since, at the 0·005 level (Hamilton, 1965), the theoretical ratio is 1·0007. However, at such small values, the R-factor ratio is a very non-robust statistic being very easily affected by systematic errors such as absorption or incomplete convergence and, as Rogers (1981) and Bernardinelli & Flack (1985) have mentioned, there are many practical and theoretical difficulties in its use.

2. The 87 measurements with the largest calculated differences between the two models were extracted and the R/R_e ratio of Engel (1972) was tested. With parameters corresponding to the accepted absolute configuration of colchicine as determined chemically by Corrodi & Hardegger (1955), R/R_e was 1·571 and the appropriate values for probability levels of 0·01 and 0·001 are 1·550 and 1·586, respectively, as derived by Hamilton (1965). The correctness of the determination is indicated at better than 1 chance in 100.

3. Refinement using the slowly collected unique set of data and scattering factors with anomalous-dispersion corrections converged at a conventional R factor of 0·045 and a weighted R factor of 0·043. The opposite enantiomorph was also refined and the conventional and weighted R factors were 0·047 and 0·046 respectively at convergence. The R-factor ratios are 1·04 and 1·07, either of which would be sufficient to determine the absolute configuration since the Hamilton (1965) ratio is 1·0020 at the 0·005 level although the previously mentioned objections to the robustness of this technique still apply. Table 1 and Fig. 1 are derived from the refinement of the accepted configuration which gave the R factor of 0·045. The goodness-of-fit parameter, S, is 1·39 for the best refinement.

Table 1. *Final atomic coordinates for the heavier atoms*

All parameters ×10⁴. The equivalent U values are the geometric means of the diagonal terms of the vibration tensors.

	x	y	z	U_{eq}(Å^2)
N	787 (3)	4231 (11)	6386 (2)	618 (18)
C1	4092 (3)	2115 (8)	7155 (2)	510 (13)
O1	4768 (2)	2555 (8)	6672 (2)	603 (12)
C2	4380 (3)	1929 (8)	7958 (2)	539 (13)
O2	5337 (2)	2169 (8)	8257 (2)	610 (12)
C3	3745 (3)	1393 (8)	8462 (2)	551 (14)
O3	4107 (2)	1226 (8)	9232 (2)	667 (12)
C4	2807 (3)	1047 (8)	8144 (3)	585 (14)
C4a	2518 (3)	1268 (8)	7341 (2)	547 (14)
C5	1491 (3)	975 (8)	7010 (3)	602 (16)
C6	872 (3)	2146 (8)	6893 (3)	628 (16)
C7	1444 (3)	3192 (9)	6539 (2)	513 (14)
C7a	1942 (3)	2756 (8)	5805 (2)	477 (13)
C8	1527 (3)	3108 (8)	5071 (2)	538 (14)
C9	1767 (3)	2947 (8)	4265 (2)	504 (13)
O9	1303 (2)	3524 (8)	3716 (2)	649 (12)
S10	2434 (1)	1868 (7)	3015 (1)	540 (5)
C10	2529 (3)	2084 (8)	4051 (2)	512 (13)
C101	4872 (6)	3830 (10)	6604 (5)	1202 (35)
C100	3287 (4)	658 (9)	2891 (3)	688 (17)
C11	3221 (3)	1530 (8)	4562 (2)	565 (14)
C12	3364 (3)	1547 (8)	5405 (2)	537 (14)
C12a	2812 (3)	2042 (8)	5976 (2)	489 (12)
C12b	3157 (3)	1809 (8)	6836 (2)	504 (12)
C13	1129 (4)	5349 (8)	6242 (2)	593 (16)
O14	1999 (2)	5544 (8)	6187 (2)	718 (13)
C14	384 (5)	6346 (9)	6160 (4)	910 (23)
C201	5530 (4)	3211 (9)	8672 (3)	735 (19)
O201	4894 (4)	3917 (8)	8810 (3)	1122 (21)
C202	6573 (5)	3342 (9)	8933 (4)	1034 (28)
C301	3483 (4)	643 (9)	9767 (3)	812 (21)
Disordered solvent				
C60	0	4057 (10)	0	907 (38)
C61	−1334 (11)	3934 (16)	781 (9)	1161 (63)
C62	−655 (12)	4595 (12)	423 (10)	940 (58)

4. The dispersion corrections were refined for both enantiomorphs and, while the R factors were 0·043 in both cases, the theoretical signs of the imaginary parts were preserved with the previously determined configuration and reversed for the opposite.

5. The Flack x parameter (Bernardinelli & Flack, 1985) was also evaluated by least-squares methods from the results of refinement 3 (*i.e.* the two enantiomorphs, the unique set of slowly collected data and unrefined anomalous-dispersion factors). Since its value was −0·084 (67), the absolute configuration is again in agreement. Overall, the Flack x parameter seems the most satisfactory statistic since the calculated standard deviation is such that it is highly improbable that x could have the value of 1·0 corresponding to the other enantiomorph. It is our opinion that the easily calculated Flack x parameter should always be evaluated in light-atom absolute-configuration determinations.

It was not possible to make any further deductions as to the details of the solvent disorder. The quoted final parameters, bond lengths in Fig. 1 and the short list of refinement parameters for the heavier atoms* in Table 1, are derived from refinement of the unique set of data with anomalous-dispersion corrections. Except in the region of the disordered solvent, all final difference densities do not exceed 0·2 e Å^{-3}. Differences as large as 0·5 e Å^{-3} exist near C60, C61 and C62. At completion of the refinement, all parameter shifts were $< 0{\cdot}02\sigma$ except in the disordered solvent region where some shifts were $0{\cdot}2\sigma$.

Discussion. Since, during chemical conversion of natural (−)-colchicine into the title compound the absolute configuration at C7 is not changed, the present investigation confirms the chemical determination of the absolute configuration of colchicine by Corrodi & Hardegger (1955) and is *S*(C7) as shown in Fig. 1.

A major influence in the packing of the molecules is an N···O9 hydrogen bond; a common occurrence in colchicinoids. The relevant dimensions are N···O9 2·959 (6), H···O9 2·06 (6)Å, N—H···O9 157 (3)° with the molecules related by the twofold axis. There is a moderately close contact between the S atom and an amide O atom related by the **a** lattice translation [3·398 (6) Å].

In general, the molecular conformation is very typical of colchicinoids. Proceeding clockwise around the *B* ring, starting with the C12b—C4a bond, the torsion angles are −2·0 (11), −73·4 (7), +42·0 (5), +48·9 (5), −76·8 (6), −0·9 (11) and +55·5 (11)° respectively and comparison with the collected values of Silverton, Sharma & Brossi (1985) indicates no significant differences and confirms the similarities

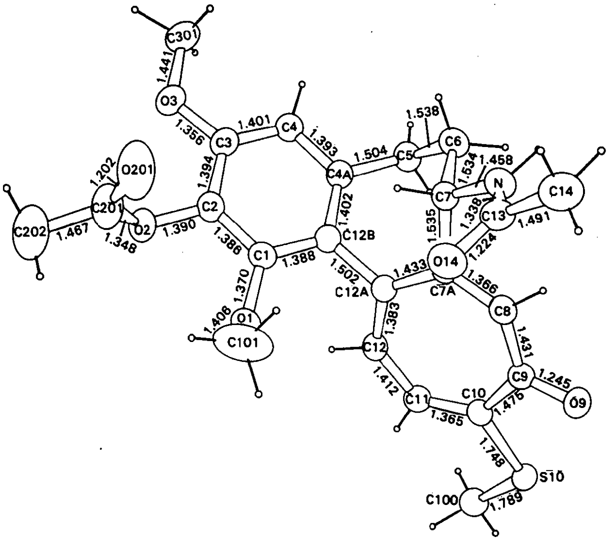


Fig. 1. *ORTEP* (Johnson, 1965) drawing of (*S*)-2-acetyl-2-demethylthiocolchicine in its crystal conformation and determined absolute configuration. E.s.d.'s of bond lengths vary from 0·005 Å near the center of the molecule to 0·013 Å at some methyl groups.

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* Lists of structure factors, all refinement parameters, supportive data for the Engel absolute-conformation determination and a table of bond angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44008 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

among the conformations reported in all colchicinoid crystal structures. The bond lengths and crystal conformation are shown in the *ORTEP* (Johnson, 1965) drawing, Fig. 1, and it will be observed that the amide group adopts the so-far universal conformation in colchicinoids. The bond angles are given in Table 2 (deposited) and no unusual values are apparent.

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Structure and Stereochemistry of Cacalol Methyl Ether, a Sesquiterpene*

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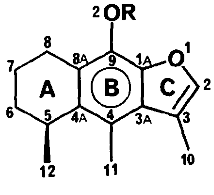
Abstract. 9-Methoxy-3,4,5-trimethyl-5,6,7,8-tetrahydronaphtho[2,3-*b*]furan, $C_{16}H_{20}O_2$, $M_r = 244\cdot3$, monoclinic, $P2_1$, $a = 8\cdot753\ (6)$, $b = 5\cdot338\ (4)$, $c = 14\cdot949\ (7)$ Å, $\beta = 105\cdot93\ (4)^\circ$, $V = 672\ (1)$ Å^3, $Z = 2$, $D_x = 1\cdot21$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0\cdot7107$ Å, $\mu = 0\cdot073$ mm^{-1}, $F(000) = 264$, $T = 293$ K, final $R = 0\cdot068$ for 905 reflections. (5*S*)-Stereochemistry is determined for the title compound and confirms the structure previously assigned on the basis of chemical and spectroscopic evidence. The *A* ring adopts a 1,2-diplanar conformation. The molecules in the crystal are packed at normal van der Waals distances.

Introduction. Cacalol (1) is a sesquiterpene which was isolated from the roots of *Cacalia decomposita* A. Gray, a shrub indigenous to northern Mexico (Romo & Joseph-Nathan, 1964). Following several revisions, structure (1) was proposed essentially simultaneously in three publications (Kakisawa, Inouye & Romo, 1969; Brown & Thomson, 1969; Ruiz, Correa & Maldonado, 1969) and this was confirmed by synthesis (Yuste & Walls, 1976; Huffman & Pandian, 1979).

It was of interest to determine the crystal structure of (2) in order to ascertain its conformation and molecular geometry.



(1) $R = H$

(2) $R = CH_3$

Experimental. Colourless crystal $0\cdot13 \times 0\cdot34 \times 0\cdot50$ mm. Nicolet *R*3 four-circle diffractometer. Lattice parameters from 25 machine-centred reflections with $6\cdot2 < 2\theta < 33\cdot6^\circ$. 1308 reflections with $3 < 2\theta < 50^\circ$, 905 independent with $I > 3\cdot0\sigma(I)$, index range h $-10 \rightarrow 10$, k $0 \rightarrow 6$, l $0 \rightarrow 17$, ω-scan mode, variable scan speed, scan width $1\cdot0^\circ$ (θ), two standard reflections (011, $\bar{1}\bar{1}0$) monitored every 50 measurements, no intensity variation, Lp correction, absorption ignored; structure solved by combination of direct methods and partial structure expansion by an iterative *E*–Fourier procedure

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