Crystal Structure of Euryopsonol

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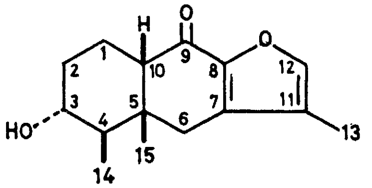
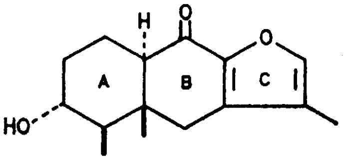
Euryopsonol, a furanoeremophilane sesquiterpene, has been studied by single-crystal *X*-ray diffraction and shown to be (2). Crystals are orthorhombic, space group $P2_12_12_1$, in a unit cell of dimensions a = 13.72(2), b = 11.65(2), c = 8.45(2) Å, with Z = 4. The crystal structure was determined by direct methods and the atomic parameters were refined by full-matrix least-squares to R 6.6% over 938 reflections. The A/B ring junction in (2) is *trans* di-axial; the cyclohexane ring adopts a $^4C_1$ chair conformation, whereas ring B is distorted halfway from an envelope E_1 towards a half-chair $^6H_1$. Strong intermolecular hydrogen bonding involving the 3-hydroxy- and 9-carbonyl-groups constitutes the major packing force.

EURYOPSONOL, a furanoeremophilane sesquiterpene, was isolated from the resin of *Euryops floribundus* NE.Br.[1,2] Chemical and spectroscopic studies[2] suggested *cis*-stereochemistry for the A/B ring junction shown in (1). A later comparison with kablicin,[3,4] a related furanoeremophilane, suggested a *trans* ring-junction (2).[5] Bohlman and his co-workers[6,7] have isolated the angelyl, isovaleryl, and isobutyryl esters of euryopsonol, and an n.m.r. study on these compounds suggested a *trans* A/B ring junction. Saponification of the angelyl ester, and re-esterification of the resulting euryopsonol with angeloyl chloride gave a product identical with the natural euryopsonol angelate,[7] indicating that no isomerisation had occurred at C(10) during isolation.[1,2] The synthesis of euryopsonol has been reported,[8] but the product had m.p. *ca.* 30° lower than that of the natural product.[1,2] An *X*-ray analysis of euryopsonol from *Euryops floribundus*, was undertaken to ascertain unequivocally the nature of the A/B ring junction, and to obtain details of the molecular conformation.



(1)



(2)

EXPERIMENTAL

Euryopsonol was recrystallized from ethyl acetate and a crystal mounted on a glass fibre. Preliminary oscillation and Weissenberg photographs established the quality of the crystal and the space group $P2_12_12_1$. Cell constants were refined and three-dimensional reflection data collected on a Phillips PW 1100 four-circle diffractometer equipped with a graphite monochromator. Reflections were scanned in the ω—2θ mode in steps of 0.04° s^{-1}, with $3 \leqslant \theta \leqslant 22$, to cover a total scan of 1.2°. The background reading was obtained by counting on both sides of each peak for the same period as the duration of the peak scan. Lorentz and polarization (L_p), as well as background corrections, were applied to the data leaving 938 reflections for structure refinement. Reflections with $|F| < \sigma|F|$ were considered unobserved.

Crystal Data.—$C_{15}H_{20}O_3$, M = 248, Orthorhombic, a = 13.72(2), b = 11.65(2), c = 8.45(2) Å, U = 1 351 Å^3, Z = 4, $F(000)$ = 536, μ = 0.48 cm^{-1}. Space group $P2_12_12_1$. Mo-K_α radiation, λ = 0.710 69 Å; μ(Mo-K_α) 0.48 cm^{-1}.

Structure Solution and Refinement.—The structure was solved by use of the programme SHELX 77[9] by a standard multisolution approach which revealed all the non-hydrogen atom positions on the first E map. The structure was

TABLE 1

Final fractional (× 10^4) estimated standard deviations in parentheses

Atom	x/a	y/b	z/c
O(1)	8 597(3)	3 002(5)	1 618(7)
O(2)	3 191(3)	4 608(4)	3 630(6)
O(3)	3 967(3)	3 624(4)	780(6)
C(1)	5 944(5)	3 085(6)	411(9)
C(2)	7 064(6)	3 140(7)	243(10)
C(3)	7 567(5)	2 823(6)	1 769(8)
C(4)	7 225(5)	3 563(6)	3 156(8)
C(5)	6 094(4)	3 490(5)	3 405(7)
C(6)	5 783(5)	4 380(6)	4 670(8)
C(7)	4 706(4)	4 582(5)	4 653(7)
C(8)	4 158(4)	4 356(5)	3 375(8)
C(9)	4 496(4)	3 891(5)	1 883(8)
C(10)	5 611(4)	3 841(5)	1 804(8)
C(11)	4 056(5)	5 001(6)	5 823(8)
C(12)	3 179(5)	5 005(6)	5 149(8)
C(13)	4 315(7)	5 381(8)	7 459(10)
C(14)	7 790(7)	3 251(8)	4 695(11)
C(15)	5 768(6)	2 268(7)	3 880(10)
H(1,1)	5 738(44)	2 289(56)	589(77)
H(1,2)	5 655(41)	3 434(51)	—631(76)
H(2,1)	7 293(45)	2 514(55)	—678(77)
H(2,2)	7 204(50)	3 776(58)	—56(78)
H(3)	7 369(4)	1 859(51)	2 043(73)
H(4)	7 353(42)	4 482(51)	2 864(72)
H(6,1)	6 151(42)	5 171(51)	4 359(75)
H(6,2)	5 879(45)	4 086(49)	5 630(79)
H(10)	5 837(41)	4 773(49)	1 493(73)
H(12)	2 476(47)	5 270(50)	5 482(74)
H(13,1)	4 735(44)	5 952(56)	7 482(77)
H(13,2)	4 491(43)	4 666(57)	7 975(70)
H(13,3)	3 745(48)	5 758(54)	7 843(73)
H(14,1)	8 259(47)	3 616(53)	4 441(76)
H(14,2)	7 628(44)	3 774(52)	5 727(76)
H(14,3)	7 658(47)	2 466(60)	5 107(83)
H(15,1)	5 993(43)	1 635(50)	2 984(73)
H(15,2)	5 942(49)	2 207(52)	4 829(82)
H(15,3)	5 069(44)	2 121(50)	4 025(74)
H(O1)	8 817(49)	2 612(56)	906(82)

further developed by difference-Fourier syntheses and eventually all hydrogen atoms positions were established. The oxygen atoms were subjected to anisotropic refinement and all hydrogen atoms refined with a common isotropic temperature factor. Unit-weight, full-matrix, least-squares refinement finally terminated at R 6.6%, with the unexplained electron density nowhere exceeding 0.27 Å^{-3}.

RESULTS AND DISCUSSION

Refined fractional co-ordinates are listed in Table 1. Figure 1 schematically illustrates the numbering scheme. Hydrogen atoms are numbered according to the carbon and oxygen atoms to which they are bonded. Interatomic bond lengths and angles are depicted in Figures 1 and 2, respectively. Torsion angles are listed in Table 2. Observed and calculated structure factors and atom thermal parameters are deposited as Supplementary Publication No. SUP 22479 (8 pp.).*

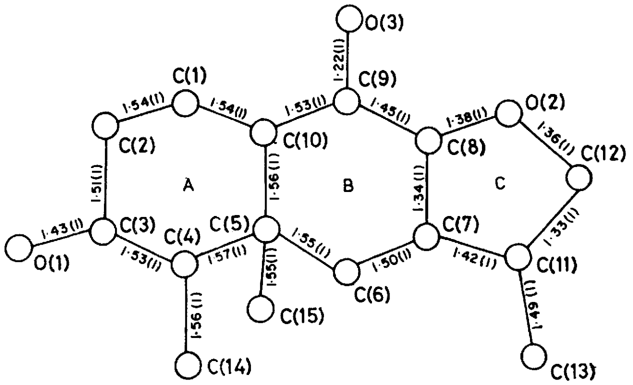


FIGURE 1 Schematic illustration of the numbering scheme and interatomic distances (Å) in euryopsonol

TABLE 2

Torsion angles (°) defined by non-hydrogen atoms

C(1)–C(2)–C(3)–C(4)	−55.3
C(1)–C(2)–C(3)–O(1)	−173.8
C(1)–C(10)–C(9)–O(3)	−17.4
C(2)–C(3)–C(4)–C(5)	57.0
C(3)–C(4)–C(5)–C(6)	−172.4
C(3)–C(4)–C(5)–C(10)	−56.0
C(4)–C(5)–C(6)–C(7)	164.6
C(4)–C(5)–C(10)–C(1)	57.2
C(5)–C(6)–C(7)–C(8)	−22.2
C(5)–C(10)–C(1)–C(2)	−57.6
C(6)–C(7)–C(8)–C(9)	0.6
C(6)–C(7)–C(11)–C(12)	179.8
C(6)–C(7)–C(11)–C(13)	0.9
C(7)–C(8)–C(9)–C(10)	−8.7
C(7)–C(11)–C(12)–O(2)	0.7
C(7)–C(6)–C(5)–C(10)	48.8
C(8)–C(9)–C(10)–C(1)	166.1
C(8)–C(9)–C(10)–C(5)	38.4
C(8)–C(7)–C(11)–C(12)	−0.7
C(9)–C(10)–C(1)–C(2)	174.3
C(9)–C(10)–C(5)–C(6)	−58.9
C(10)–C(1)–C(2)–C(3)	54.9
C(11)–C(12)–O(2)–C(8)	−0.4
C(12)–O(2)–C(8)–C(7)	−0.1
C(14)–C(4)–C(5)–C(15)	−60.6
C(14)–C(4)–C(5)–C(6)	62.6
C(15)–C(5)–C(6)–C(7)	−71.8
O(1)–C(3)–C(4)–C(5)	177.4
O(1)–C(3)–C(4)–C(14)	−57.2
O(2)–C(8)–C(7)–C(11)	0.5
O(2)–C(8)–C(9)–O(3)	−4.4
O(2)–C(12)–C(11)–C(13)	179.6
C(15)–C(5)–C(10)–H(10)	177.6

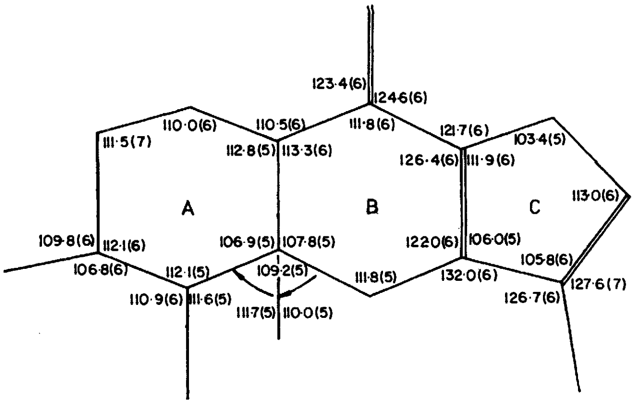


FIGURE 2 Schematic representation of the bond angles (°) in euryopsonol

A stereoscopic view of the structure of euryopsonol is shown in Figure 3. The X-ray diffraction study confirms the previous deductions [2,5] which had suggested structure (2) for euryopsonol.

The A/B *Ring Fusion*.—The X-ray crystallographic analysis of euryopsonol has revealed a *trans*-diaxial A/B ring-junction, and this is illustrated by the C(15)–C(5)–H(10) torsion angle of 177.6° (Table 2), compared with 180° for the perfect *trans*-junction. This system imposes a degree of ' planarity ' on the molecule with a preferred stable $^4C_1$ chair conformation for the cyclohexane ring A. A *cis* ring-junction would lead to multiple H · · · H van der Waals interactions. Although the latter system would be more flexible, it would lack the planarity of a *trans*-fusion.

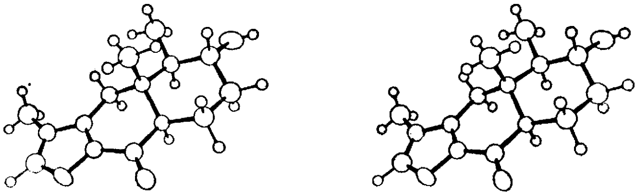


FIGURE 3 Stereoscopic view of euryopsonol

TABLE 3

Conformational analysis on the ring system in euryopsonol

	Ring A	Ring B	Ring C
Puckering amplitude Q/Å	0.584	0.487	0.006
$\phi(2)$/(°)	80.4	164.4	
θ/(°)	177.2	130.0	
Phase angle P(2)/(°)			104.3
Conformation	$^4C_1$	$E_1 \longleftrightarrow {}^6H_1$	E_3

Conformation of the A *and* B *Rings*.—The conformation of the A and B rings of euryopsonol in the solid state was quantitatively analysed according to the method of Cremer and Pople [10] and the nomenclature of Boeyens [11] as discussed previously.[12] Results are listed in Table 3.

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978, Index issue.

The cyclohexane ring exhibits a perfect $^4C_1$ chair conformation with a puckering amplitude of 0.588 Å. Ring B corresponds to a conformation which is distorted halfway from an envelope E_1 towards a half-chair $^6H_1$. The puckering amplitude of 0.48 Å is less than the calculated value (0.54) for a similar conformation of cyclohexane. The distortion in the B-ring suppresses π-electron delocalization in the system to such an extent that the observed bond lengths of C(7)–C(8) and C(11)–C(12) correspond to typical double bonds. The expected planarity of the C(6)—(10) carbon fragment in ring B is slightly distorted allowing more than one carbon atom in this ring to adjust according to the conformation of ring A.

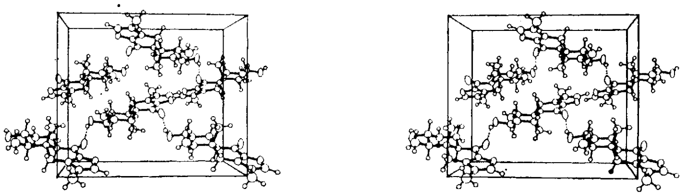

FIGURE 4 The unit cell, stereoscopically viewed along [001]. Intermolecular H(O1) · · · O(3) hydrogen bonding is indicated by broken lines

The 3-hydroxy-group in euryopsonol has been shown [2] to be α-orientated. The crystal structure reveals a β-*cis*-equatorial–axial relation between the C(14) and C(15) methyl groups. This conformation would, however, not be maintained in the molecule with a *cis* ring-junction. A puckering amplitude of $\phi = 0.006$ Å indicates that the five-membered furan ring is almost flat. The absolute stereochemistry of euryopsonol (2) has not been determined in this study.

Hydrogen Bonding.—Strong hydrogen bonding between the 3-hydroxy-group and the 9-carbonyl oxygen, constitutes the major intermolecular attraction and packing force. An interatomic distance of 2.04 Å pertaining to this interaction is shown by the broken lines in the stereoscopic drawing of the unit cell in Figure 4. The molecules are, through this attraction, interconnected in stacks a half *c* translation apart.

Eagle and co-workers [13] have suggested a greater deshielding of the C(12) proton by electron delocalization due to the introduction of a carbonyl group at C(9). This is in contrast to the results obtained from the crystal structure determination. The localized conjugated system in the structure, as discussed, is believed to arise from the strong intermolecular hydrogen bonding, by causing the deformation of ring B. The electron lone-pairs at the carbonyl oxygen atom, and possibly only one of these lone pairs, seem to be sufficient to cope with the strong hydrogen bonding in this structure.

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