Cyclonerotriol [6-(3-Hydroxy-2,3-dimethylcyclopentyl)-2-methylhept-2-ene-1,6-diol], a new Sesquiterpenoid Metabolite of *Fusarium culmorum*

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Cyclonerotriol has been shown to be (2*E*,6*S*)-6-[(1*R*,2*S*,3*R*)-3-hydroxy-2,3-dimethylcyclopentyl]-2-methylhept-2-ene-1,6-diol (1) by a combination of spectroscopic and *X*-ray methods. It has been related to a degradation product of cyclonerodiol.

In the course of investigations on the biosynthesis of the sesquiterpenoid metabolites of *Fusarium culmorum*, we have isolated a new crystalline metabolite, cyclonerotriol, $C_{15}H_{28}O_3$. Its i.r. spectrum contained hydroxy-absorption ($\nu_{max.}$ 3 380 and 3 290 cm^{-1}) and no carbonyl absorption. The off-resonance ^{13}C n.m.r. spectrum (Table 1) contained three singlets [one olefinic carbon

TABLE 1

^{13}C N.m.r. spectra of cyclonerotriol (1) and the lactone (2) in [$^2H_4$]methanol

δ_C (p.p.m.)	Multi-plicity	Calc. δ (p.p.m.)	Assign-ment *	Lactone δ_C (p.p.m.)	Multi-plicity
13.7	q	12.9 ^{a}	C-15		
15.3	q	17.8 ^{b}	C-1	13.7	q
23.2	t	23.7 ^{a}	C-9	31.1	t
24.6	q	25.4 ^{b}	C-13	24.6	q
25.1	t	21.7 ^{b}	C-5	25.8	t
26.1	q	26.3 ^{b}	C-14	25.2	q
41.3	t	34.9 ^{b}	C-4 †	40.0	t
41.6	t	43.0 ^{a}	C-8 †	29.1	t
45.4	d	47.2 ^{b}	C-2	45.2	d
55.3	d	56.5 ^{b}	C-6	53.4	d
68.8	t	68.1 ^{a}	C-12		
75.4	s	77.7 ^{c}	C-7	89.4	s
81.9	s	79.8 ^{b}	C-3	81.1	s
126.9	d	125.5 ^{a}	C-10	176.8	s
135.5	s	131.0 ^{a}	C-11		

^{a} Linalool used as model. ^{b} Methylcyclopentane used as model. ^{c} t-Butyl alcohol used as model.^{i}

* Numbering as in formula(1). † These assignments may be reversed.

(1) R = CH$_2$·OH
(3) R = Me
(4) R = CHO

(2)

(135.5 p.p.m.) and two fully substituted carbon atoms bearing oxygen functions (81.9 and 75.35 p.p.m.)], three doublets [one olefinic (126.9 p.p.m.) and two methine carbons (55.3 and 45.4 p.p.m.)], five triplets [one primary alcohol (68.8 p.p.m.) and four methylenes (41.6, 41.3, 25.1, and 23.2 p.p.m.)], and four methyl quartets (26.1, 24.5, 15.4, and 13.65 p.p.m.). Since there were two olefinic carbon atoms present, the remaining unsaturation was present as a carbocycle.

The ^{1}H n.m.r. spectrum, determined in [$^2H_5$]pyridine, showed that two of the methyl groups which (singlets at δ_H 1.41 and 1.46) were attached to fully substituted centres and one (doublet at δ 1.36, *J* 7 Hz) was attached to a methine carbon atom. The fourth methyl group (δ 1.82) was attached to a double bond. The olefinic proton resonance (δ 5.78) appeared as a broad triplet (*J* 7 Hz) corresponding to a =CH·CH$_2$- grouping. The CH$_2$·OH resonance appeared as a broad doublet (δ 4.28, *J* 5 Hz). When the solution was treated with deuterium oxide, this resonance collapsed to a singlet, and a triplet (δ 6.14, *J* 5 Hz) and two singlets (δ 5.08 and 5.12) disappeared. Oxidation of the primary alcohol group with manganese dioxide gave an oily αβ-unsaturated aldehyde [$\lambda_{max.}$ 231 nm (ϵ 8 000)] (4), reduction of which with sodium borohydride regenerated the parent triol. Hence the substituents on the trisubstituted double bond are a Me, CH$_2$·OH, and CH$_2$-. The double bond was assigned the *E* geometry since the aldehydic proton resonance appeared at δ 9.40 (*cf.* *E* δ 9.38, *Z* 10.11) [2] whilst the ^{13}C resonance of the primary alcohol appeared at 68.8 p.p.m. (*E* 68.1, *Z* 60.5 p.p.m.).[3]

Oxidation of the triol with 8N-chromium trioxide reagent gave a monohydroxy-γ-lactone ($\nu_{max.}$ 3 620, 3 520, and 1 775 cm^{-1}), $C_{12}H_{20}O_3$. The ^{1}H n.m.r. spectrum retained two three-proton singlets (δ 1.26 and 1.38) and a three-proton doublet (δ 1.04, *J* 7 Hz) but it lacked the resonances associated with the olefinic proton and hydroxymethyl groups. The ^{13}C n.m.r. spectrum contained three singlets [a carbonyl carbon resonance (176.8 p.p.m.), and signals for two fully substituted carbon atoms bearing oxygen atoms (89.4 and 81.05 p.p.m.)], two methine doublets (53.4 and 45.2 p.p.m.), four methylene triplets (40.0, 31.1, 29.1, and 25.8 p.p.m.), and three methyl quartets (25.2, 24.6, and 13.65 p.p.m.). Hence there is a 1,4-relationship between the tertiary hydroxy-group and the trisubstituted double bond. On the basis of the ' isoprene rule,' this tentatively led to the structures (1) for cyclonerotriol and (2) for the lactone. The calculated ^{13}C n.m.r, data based on methylcyclopentane and linalool as models,[1] were in good agreement (see Table 1). The mass spectrum of the metabolite can be interpreted in terms of the ready loss of two molecules of water followed by cleavage of the 6,7- and 7,8-bonds (the
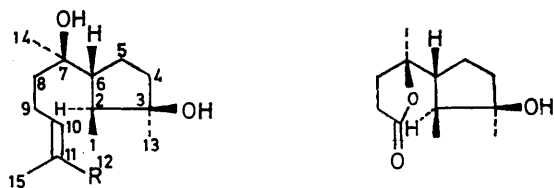
[1] J. T. Clerc, E. Pretsch, and S. Sternhell, ' ^{13}C-Kernresonanz-spektroskopie,' Akademishe Verlagsgesellschaft, Frankfurt am Main, 1973, pp. 46 and 58.

[2] K. C. Chan, R. A. Jewell, W. H. Nutting, and H. Rapoport, *J. Org. Chem.*, 1968, **33**, 3382.

[3] J. B. Stothers, ' Carbon-13 NMR Spectroscopy,' Academic Press, New York, 1972, p. 188.

sequences m/e 238 to 95, 99, and 139 and 220 to 125, 107, and 108).

The lactone (2) has been isolated [4,5] from degradation of cyclonerodiol (3) and the configuration around the five-membered ring has been correlated with that of plinol C, a cyclization product of linalool.[6] The lactone had an i.r. spectrum identical with one provided by Dr. B. E. Cross. Subsequently cyclonerodiol (3) was isolated from *Fusarium culmorum* and an authentic sample of the lactone (2) was prepared by ozonolysis and oxidation.

Biogenetically these sesquiterpenoids may be formally derived either by a novel cyclization of nerolidol (5) or of farnesyl pyrophosphate (6). In this context the stereochemistry of the tertiary hydroxy-group at C-7 and its relationship to the new C(2)–C(6) bond (see Scheme) became of interest. The stereochemistry about

SCHEME
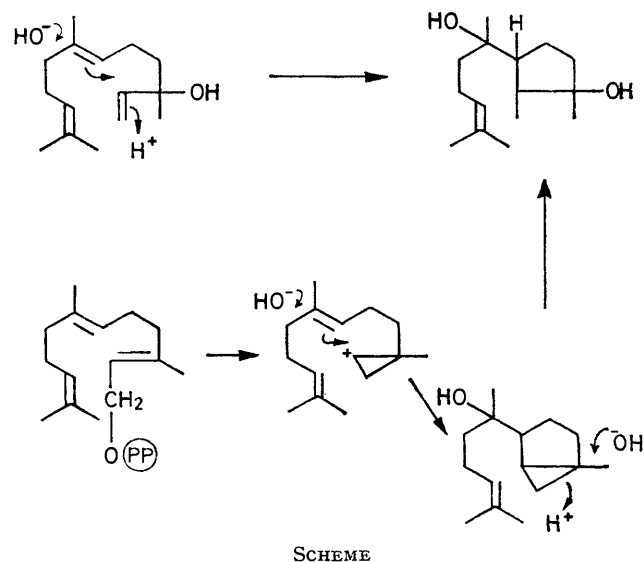
this centre was determined and the overall structure of the metabolite confirmed by a single crystal X-ray structure analysis.

The conformation of the molecule is shown in Figure 1. Of the two possible enantiomers from the crystal structure, that chosen was the one for which the asymmetric carbon atoms of the cyclopentane ring were the same as those deduced chemically.[6] The bond lengths and angles are listed in Table 3 and the torsion angles in Table 4. A projection of the crystal packing along the c axis is shown in Figure 2.

The list of short intermolecular contacts in Table 5 shows that the molecules are linked by hydrogen bonds O(1)–H(24) $\cdots$ O(2) along the 2_1 screw axis parallel to c and O(1) $\cdots$ H(27)–O(3) along the 2_1 screw axis parallel to b. No other contact distances are significantly shorter than the sum of the relevant van der

[4] S. Nozoe, M. Goi, and N. Morisaki, *Tetrahedron Letters*, 1970, 1293.

[5] B. E. Cross, R. E. Markwell, and J. C. Stewart, *Tetrahedron*, 1971, **27**, 1663.

Waals radii. The molecule itself has the cyclopentane ring in the envelope form with atoms C(2), C(3), C(5), and C(6) approximately coplanar and C(4) displaced by
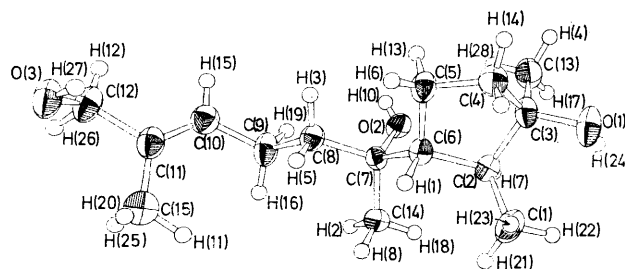
FIGURE 1   Molecular structure of cyclonerotriol

TABLE 2

Final atom co-ordinates ($\times 10^4$) with e.s.d.s in parentheses in units of the last significant figure

	x	y	z
O(1)	6 238(3)	5 309(2)	-5 551(3)
O(2)	6 953(2)	6 062(2)	-0 277(3)
O(3)	4 798(3)	10 720(2)	3 207(3)
C(1)	7 770(4)	6 732(3)	-4 707(5)
C(2)	7 087(3)	6 248(3)	-3 496(4)
C(3)	6 083(4)	5 643(3)	-4 072(4)
C(4)	5 106(4)	6 349(3)	-4 024(5)
C(5)	5 271(3)	6 868(3)	-2 555(5)
C(6)	6 553(3)	7 010(3)	-2 453(4)
C(7)	7 046(3)	7 013(3)	-0 888(4)
C(8)	6 423(4)	7 748(3)	0 066(4)
C(9)	6 926(4)	7 914(3)	1 592(4)
C(10)	6 163(4)	8 515(3)	2 539(5)
C(11)	6 229(4)	9 452(3)	2 784(5)
C(12)	5 409(4)	9 927(3)	3 805(5)
C(13)	5 856(4)	4 759(3)	-3 109(5)
C(14)	8 306(3)	7 226(3)	-0 947(5)
C(15)	7 103(4)	10 099(4)	2 156(7)
H(1)	6 737(26)	7 698(23)	-2 879(34)
H(2)	8 656(37)	7 280(32)	-0 031(52)
H(3)	5 626(29)	7 582(25)	0 204(40)
H(4)	5 170(41)	4 412(34)	-3 422(52)
H(5)	6 463(29)	8 374(23)	-0 425(40)
H(6)	4 906(28)	7 440(22)	-2 432(38)
H(7)	7 555(28)	5 774(23)	-3 029(36)
H(8)	8 516(32)	7 850(26)	-1 335(40)
H(9)	5 208(30)	6 813(26)	-4 816(40)
H(10)	6 565(27)	5 971(23)	0 250(37)
H(11)	7 650(43)	9 813(37)	1 396(52)
H(12)	4 967(33)	9 462(27)	4 184(40)
H(13)	4 937(32)	6 426(26)	-1 765(41)
H(14)	4 432(29)	6 053(25)	-4 043(39)
H(15)	5 570(27)	8 171(23)	2 916(37)
H(16)	7 693(34)	8234(28)	1 522(45)
H(17)	6 445(34)	4 358(28)	-3 178(45)
H(18)	8 694(30)	6 797(25)	-1 561(40)
H(19)	6 968(36)	7 205(31)	2 047(49)
H(20)	6 910(43)	10 537(37)	1 770(60)
H(21)	8 365(39)	7 130(33)	-4 374(52)
H(22)	8 098(40)	6 228(33)	-5 372(54)
H(23)	7 304(39)	7 166(33)	-5 308(51)
H(24)	6 738(24)	5 069(21)	-5 529(34)
H(25)	7 484(55)	10 330(46)	2 826(73)
H(26)	5 866(45)	10 274(38)	4 556(59)
H(27)	4 497(30)	10 564(28)	2 638(43)
H(28)	5 734(34)	4 959(29)	-2 189(47)

0.63 Å. This conformation minimises the nonbonded contacts along the C(2)–C(3) bond by bringing O(1) into an equatorial position with C-13 in an axial position

[6] S. Nozoe, M. Goi, and N. Morisaki, *Tetrahedron Letters*, 1971, 3701.

almost *trans* to C(1). The side-chain of the molecule is in an extended form with torsion angles of very near
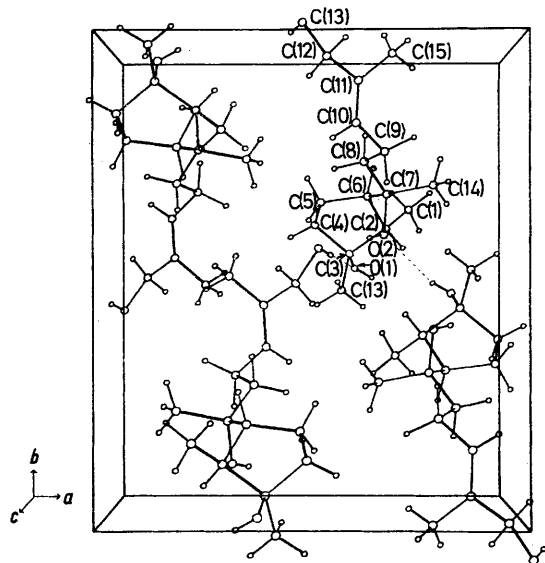

FIGURE 2   Crystal packing of cyclonerotriol

TABLE 3

Intramolecular distances and angles with e.s.d.s in parentheses in units of the last significant figure

(*a*) Bonds (Å)

C(3)–C(4)	1.514(6)	C(4)–H(9)	0.97(4)
C(2)–C(3)	1.546(6)	C(4)–H(14)	0.90(3)
C(2)–C(6)	1.552(5)	C(14)–H(2)	0.94(5)
C(5)–C(6)	1.536(5)	C(14)–H(8)	0.96(4)
C(4)–C(6)	1.530(6)	C(14)–H(18)	0.94(4)
C(3)–O(1)	1.437(5)	O(2)–H(10)	0.68(3)
C(3)–C(13)	1.526(6)	C(8)–H(3)	0.98(4)
C(1)–C(2)	1.523(6)	C(8)–H(5)	0.97(3)
C(6)–C(7)	1.541(5)	C(9)–H(19)	1.06(4)
C(7)–C(14)	1.525(5)	C(9)–H(16)	1.01(4)
C(7)–O(2)	1.429(4)	C(10)–H(15)	0.92(3)
C(7)–C(8)	1.526(5)	C(12)–H(12)	0.90(4)
C(8)–C(9)	1.531(6)	C(12)–H(26)	1.00(5)
C(9)–C(10)	1.499(6)	O(3)–H(27)	0.67(4)
C(10)–C(11)	1.314(6)	C(13)–H(4)	0.99(5)
C(11)–C(15)	1.482(7)	C(13)–H(17)	0.89(4)
C(11)–C(12)	1.497(6)	C(13)–H(28)	0.90(4)
C(12)–O(3)	1.420(5)	C(15)–H(11)	1.03(5)
O(1)–H(24)	0.68(3)	C(15)–H(20)	0.74(5)
C(2)–H(7)	0.96(3)	C(15)–H(25)	0.82(7)
C(6)–H(1)	1.05(3)	C(1)–H(21)	0.95(5)
C(5)–H(6)	0.91(3)	C(1)–H(22)	1.00(5)
C(5)–H(13)	1.02(4)	C(1)–H(23)	0.98(5)

(*b*) Angles (deg.)

O(1)–C(3)–C(13)	107.9(3)	C(5)–C(6)–C(7)	115.6(3)
C(4)–C(3)–C(2)	103.5(3)	C(6)–C(7)–C(8)	110.2(3)
C(4)–C(3)–C(13)	111.3(4)	C(6)–C(7)–O(2)	109.2(3)
O(1)–C(3)–C(2)	113.1(3)	C(6)–C(7)–C(14)	109.9(3)
C(4)–C(3)–O(1)	109.3(3)	O(2)–C(7)–C(8)	110.5(3)
C(13)–C(3)–C(2)	111.8(3)	O(2)–C(7)–C(14)	105.4(3)
C(3)–C(2)–C(1)	113.6(3)	C(7)–C(8)–C(9)	115.4(3)
C(6)–C(2)–C(1)	111.4(3)	C(8)–C(9)–C(10)	111.8(4)
C(3)–C(2)–C(6)	105.0(3)	C(9)–C(10)–C(11)	127.3(4)
C(2)–C(6)–C(5)	106.3(3)	C(10)–C(11)–C(15)	124.6(4)
C(6)–C(5)–C(4)	103.9(3)	C(10)–C(11)–C(12)	119.8(4)
C(3)–C(4)–C(5)	103.1(3)	C(11)–C(12)–O(3)	115.4(3)
C(2)–C(6)–C(7)	114.5(3)		

[7] L. E. Sutton, Interatomic Distances. Supplement, *Chem. Soc. Special Publ.*, No. 18, 1965.

180° for bonds between saturated carbon atoms. The mean bond lengths for $C(sp^3)$–$C(sp^3)$ of 1.536 Å within the ring and 1.529 Å outside the ring are not significantly different from each other nor from the accepted value of 1.537 Å,[7] and the average C–O(H) bond length of 1.429 Å

TABLE 4

Torsion angles in degrees

O(1)–C(3)–C(2)–C(6)	147	C(2)–C(6)–C(7)–O(2)	–55
O(1)–C(3)–C(2)–C(1)	25	C(2)–C(6)–C(7)–C(8)	–177
C(4)–C(3)–C(2)–C(6)	28	C(5)–C(6)–C(7)–C(14)	–176
C(4)–C(3)–C(2)–C(1)	–93	C(5)–C(6)–C(7)–O(2)	69
C(13)–C(3)–C(2)–C(6)	–91	C(5)–C(6)–C(7)–C(8)	–53
C(13)–C(3)–C(2)–C(1)	147	C(6)–C(5)–C(4)–C(3)	40
O(1)–C(3)–C(4)–C(5)	–163	C(6)–C(7)–C(8)–C(9)	–173
C(2)–C(3)–C(4)–C(5)	–42	C(14)–C(7)–C(8)–C(9)	–50
C(13)–C(3)–C(4)–C(5)	78	O(2)–C(7)–C(8)–C(9)	67
C(3)–C(2)–C(6)–C(5)	–4	C(7)–C(8)–C(9)–C(10)	–171
C(3)–C(2)–C(6)–C(7)	125	C(8)–C(9)–C(10)–C(11)	–98
C(1)–C(2)–C(6)–C(5)	119	C(9)–C(10)–C(11)–C(12)	–178
C(1)–C(2)–C(6)–C(7)	–112	C(9)–C(10)–C(11)–C(15)	–1
C(2)–C(6)–C(5)–C(4)	–21	C(10)–C(11)–C(12)–O(3)	–125
C(7)–C(6)–C(5)–C(4)	–150	C(15)–C(11)–C(12)–O(3)	57
C(2)–C(6)–C(7)–C(14)	60		

TABLE 5

Short intermolecular contact distances (Å)

$$\left.\begin{array}{l} O(1) \cdots O(2) \\ H(24) \cdots O(2) \end{array}\right\} (1.5 - x, 1 - y, -0.5 + z) \begin{cases} 2.87 \\ 2.21 \end{cases}$$

$$\left.\begin{array}{l} O(1) \cdots O(3) \\ O(1) \cdots H(27) \\ H(27) \cdots H(27) \end{array}\right\} (1 - x, -0.5 + y, 0.5 - z) \begin{cases} 2.77 \\ 1.90 \\ 2.33 \end{cases}$$

TABLE 6

Distances (Å) of atoms from the mean plane through C(3), C(2), C(6), C(5)

Distances: C(3) –0.02, C(2) 0.02, C(6) –0.02, C(5) 0.02, C(4) 0.63, O(1) 0.74, C(13) –1.44, C(1) 1.25

The equation to the plane is

$$-0.0592X + 0.6235Y - 0.7796Z = 0.2254$$

where X, Y, Z are the co-ordinates (Å) with respect to the axis set *a, b, c*

is in excellent agreement with the normal value [8] of 1.426 Å. As in other crystallographic studies, the average C–H and O–H bond lengths of 0.95 and 0.68 Å, respectively, are less than might be expected.[9]

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. U.v. spectra were measured with a Unicam SP 800 spectrometer, i.r. spectra with a Perkin-Elmer 257 spectrometer, mass spectra with a Hitachi RMU 6 spectrometer, [1]H n.m.r. spectra with a Varian HA-100 instrument, and [13]C n.m.r. spectra with a JEOL PFT 100 Fourier transform spectrometer operating at 25.15 MHz (spectral width 250 p.p.m.; 8 192 data points and 6—7 000 accumulations; pulse length was 6 μs at a pulse interval of 1.0 s). Tetramethylsilane was used as an internal standard and chemical shifts are estimated to be accurate to 0.1 p.p.m. Light petroleum refers to the fraction of b.p. 60—80°.

Isolation of Cyclonerotriol (1).—*Fusarium culmorum*

[8] W. C. Hamilton and J. A. Ibers, ' Hydrogen Bonding in Solids,' Benjamin, New York, 1968.
[9] International Tables for *X*-Ray Crystallography, Kynoch Press, Birmingham, vol. 1, 1962.

(ACC 1731) was grown on a Raulin Thom medium (60 l) for 21 days on surface culture or 10 days on shake culture. The mycelium was filtered and the broth acidified to pH 2 with dilute hydrochloric acid and extracted with ethyl acetate. The extract was washed with aqueous sodium hydrogen carbonate and aqueous sodium chloride, dried and evaporated. The residue was purified by repeated preparative layer chromatography on silica in chloroform–acetone–methanol (70 : 30 : 5). Cyclonerotriol had R_F 0.34 and gave a pink coloration on spraying and heating with ethanolic sulphuric acid. Cyclonerotriol [6-(3-*hydroxy*-2,3-*dimethylcyclopentyl*)-2-*methylhept*-2-*ene*-1,6-*diol*] (300 mg) crystallized from ethyl acetate–light petroleum as prisms, m.p. 113—114°, $[\alpha]_D$ −27.8° (c 0.2 in MeOH) (Found: C, 70.1; H, 10.5. $C_{15}H_{28}O_3$ requires C, 70.3; H, 10.9%), $\nu_{max.}$ (Nujol) 3 380 and 3 290 cm^{-1}; for ^{1}H and ^{13}C n.m.r. and mass spectra see text, Table 1, and Scheme.

Oxidation of Cyclonerotriol.—(a) *With manganese dioxide.* The triol (20 mg) in acetone (4 ml) was stirred with finely powdered active manganese dioxide (200 mg) at room temperature for 2 h. The manganese dioxide was filtered off and the solution evaporated. The residue was purified by preparative layer chromatography in chloroform–acetone–methanol (70 : 25 : 5) to afford 6-hydroxy-6-(3-hydroxy-2,3-dimethylcyclopentyl)-2-methylhept-2-enal (4) (18 mg) as an oil, $\nu_{max.}$ (CCl$_4$) 3 620, 1 695, and 1 645 cm^{-1}, $\lambda_{max.}$ (MeOH) 231 nm (ε 8 000), δ (CDCl$_3$) 1.1 (3 H, d, J 7 Hz), 1.25 (3 H, s), 1.30 (3 H, s), 1.80br (3 H, s), 6.5br (1 H, t, J 7 Hz), and 9.40 (1 H, s).

(b) *With chromium trioxide.* The triol (120 mg) in acetone (5 ml) was treated with 8N-chromium trioxide reagent until the orange colour persisted. After 20 min the solution was diluted with water and extracted with ether. The extract was dried and evaporated to give a residue which was purified by preparative layer chromatography in ethyl acetate–light petroleum (3 : 2) to afford the lactone (2) (55 mg), which crystallized from ether–light petroleum as needles, m.p. 66—68°, $[\alpha]_D$ −36° (c 0.2 in CHCl$_3$) (lit.,[4] m.p. 66—68°, $[\alpha]_D$ −52.5°; lit.,[5] m.p. 87—88°, $[\alpha]_D$ −38°) (Found: C, 65.4; H, 9.4. Calc. for $C_{12}H_{20}O_3,0.5H_2O$: C, 65.15; H, 9.5%), $\nu_{max.}$ (CHCl$_3$) 3 620, 3 520, and 1 775 cm^{-1}, δ 1.04 (3 H, d, J 7 Hz), 1.26 (3 H, s), and 1.38 (3 H, s); i.r. spectrum identical with one provided by Dr. B. E. Cross (University of Leeds). The product was identical with a sample obtained by ozonolysis and oxidation of cyclonerodiol.[5]

Reduction of the Aldehyde (4).—The aldehyde (10 mg) in methanol (5 ml) was treated with sodium borohydride (5 mg). After 30 min a few drops of acetic acid were added and the solution was concentrated and diluted with water. The product was recovered in ethyl acetate. Cyclonerotriol (6 mg) had m.p. 113—114° and was identical (i.r. spectrum and t.l.c.) with the sample described above.

The mass spectrum of cyclonerotriol showed m/e 39 (11.5%), 40 (3.6), 41 (47.3), 42 (7.9), 43 (100), 44 (10.9), 45 (6.1), 46 (4.2), 51 (2.4), 52 (1.8), 53 (9.7), 54 (3.6), 55 (23.6), 56 (8.5), 57 (6.7), 58 (9.1), 59 (7.9), 60 (2.4), 65 (3.0), 66 (1.8), 67 (21.8), 68 (7.9), 69 (12.1), 70 (6.1), 71 (11.5), 72 (8.5), 73 (1.8), 77 (3.0), 79 (4.8), 80 (3.0), 81 (30.9), 81 (30.9), 82 (16.4), 83 (7.9), 84 (7.9), 85 (6.7), 86 (3.0), 91 (3.0),

93 (6.7), 94 (3.0), 95 (19.4), 96 (23.6), 97 (9.1), 98 (6.7), 99 (4.8), 100 (1.8), 105 (1.8), 106 (1.8), 107 (14.5), 108 (7.2), 109 (7.2), 110 (2.4), 111 (3.6), 112 (1.8), 113 (1.8), 119 (1.8), 120 (1.2), 121 (6.7), 122 (5.5), 123 (7.9), 124 (7.2), 125 (67.3), 126 (9.0), 127 (1.8), 134 (3.0), 135 (4.8), 136 (3.0), 137 (3.6), 139 (18.8), 140 (11.5), 141 (3.0), 147 (2.4), 149 (3.6), 150 (2.4), 151 (1.2), 153 (1.8), 157 (1.8), 158 (2.4), 159 (1.8), 161 (1.2), 162 (3.0), 163 (1.8), 165 (1.2), 177 (1.2), 182 (1.2), 189 (1.2), 202 (1.2), 205 (3.6), 220 (1.8), 221 (1.2), 223 (2.3), 224 (2.4), 238 (1.8, M − 18), and 239 (1.2, M − 17), with metastable peaks at 203.5 (238/220), 188.5 (223/205), 91.6 (125/107), and 54.4 (85/68).

Crystal Data.—$C_{15}H_{28}O_3$, $M = 256.4$. Orthorhombic, $a = 11.864(2)$, $b = 13.783(3)$, $c = 9.116(2)$ Å, $U = 1490.7$ Å^3, $Z = 4$, $D_c = 1.142$ g cm^{-3}. Space group $P2_12_12_1$ (D_2^4, No. 19) [9] from the systematic absences 0k0 for k odd, h00 for h odd, 00l for l odd. λ(Mo-$K_{\alpha 1}$) 0.70926 Å. μ(Mo-K_α) 0.8 cm^{-1}, $F000$ 568.

Crystallographic Measurements.—A colourless prismatic crystal of dimensions ca. 0.5 × 0.2 × 0.15 mm was used for data collection. Unit cell dimensions and intensity data were measured on a Hilger and Watts Y 290 four-circle diffractometer. Accurate cell dimensions were calculated by least squares treatment of setting angles for 12 reflections. Intensity data were collected for the octant hkl in three consecutive shells with θ ranges of 2—20, 20—26, and 26—30° using the ω/2θ step scan technique with Mo-K_α radiation (graphite crystal monochromator). Each reflection was measured in 48 steps of 0.5 s each and background counts of 12 s were made at each end of the scan. Three standard reflections were remeasured after every 100 reflections and showed a gradual drop in intensity totalling about 10% over the data collection; no correction was made for this. After correction for Lorentz and polarisation effects but not for absorption, the data were classified as significant if $I > 3\sigma(I)$, based on counting statistics. After the averaging of equivalent reflections, there were 1 247 significant reflections out of a total of 2 013 measured.

Structure Determination.—The complete data set was used to calculate normalised structure factors ($|E|$) and phases were derived by the multiple start tangent formula procedure [10] using the 122 reflections with $|E| > 1.7$. The starting set of 5 reflections was chosen by convergence mapping [11] and a total of 16 sets of phases were derived. The correct set, which had a Karle residual [12] of 0.17 compared to >0.27 for the other sets, was used to phase a further 154 reflections with $|E| > 1.4$ and a subsequent Fourier synthesis on the 275 phased reflections showed 15 of the non-hydrogen atoms. The remaining atoms were found on a difference Fourier map.

These atom positions with isotropic temperature factors were refined by full matrix least-squares using the 1 247 significant reflections with unit weights. Ambiguities between oxygen and carbon atoms were resolved on the basis of temperature factors and bond lengths. Further refinement with anisotropic temperature factors reduced the residual R value to 0.09.* At this stage a difference Fourier synthesis revealed the positions of all 28 hydrogen atoms. The least-squares refinement of heavy atoms with anisotropic temperature factors and hydrogen atoms with isotropic temperature factors was continued with the data

* $R = \Sigma\Delta/\Sigma|F_o|$ and $R_\omega = [\Sigma\omega\Delta^2/\Sigma\omega|F_o|^2]^{\frac{1}{2}}$ where $\Delta = ||F_o| - |F_c||$.

[10] G. Germain and M. M. Woolfson, *Acta Cryst.*, 1968, **B24**, 91. The computer program used was TANF coded in Fortran by P. B. Hitchcock, University of Sussex.

[11] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1970, **B26**, 274.

[12] J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.

given individual weights (ω) defined empirically as $\omega = 1/\{1 + [(|F_0| - b)/a]^2\}$ where $a = 28$ and $b = 13$. Refinement was terminated at a residual $R = 0.041$ and $R_\omega = 0.041$, when the maximum value of shift/e.s.d. for any heavy atom parameter was 0.3. The e.s.d. of an observation of unit length was 1.1 and a final difference Fourier synthesis was everywhere less than ± 0.13 eÅ^{-3}.

Initial data processing was carried out with local programs and the structure solution and refinement were carried out by using the ' X-Ray '70 ' program system.[13] Scattering factors for neutral atoms were taken from ref. 14 and no allowance was made for anomalous scattering.

The choice of enantiomer for the structure was made on the basis of the chemical evidence only; no information about it was available from the crystal structure.

The final atom co-ordinates are listed in Table 2 and lists of final structure factors and isotropic temperature factors have been deposited as Supplementary Publication No. SUP 21415 (12 pp.).*

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1974, Index issue.

[13] J. M. Stewart, F. A. Rundell, and J. C. Baldwin ' X-Ray '70 System,' 1970 as implemented at the Atlas Computer Laboratory, Chilton, Didcot, Berkshire.

[14] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104; R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.