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STEREOCHEMISTRY AND CRYSTAL STRUCTURE OF DIHYDROXYSERRULATIC ACID

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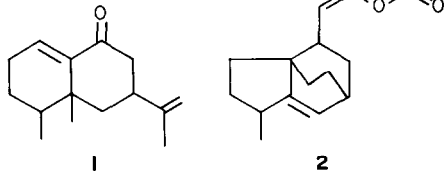
Abstract—The structure of the title compound has been shown to be (**6**), a diterpenoid analogue of the cadinene group. Standard degradation has given the naphthalene (**14**). The relative stereochemistry is established by crystal structure of dihydroxyserrulatic acid which has been determined by X-ray diffraction at 295 K, and refined by least squares to a residual of 0.059 for 1480 observed reflections. Crystals are orthorhombic, $P\ 2_12_12_1$, $a = 15.514$ (3), $b = 14.029$ (3), $c = 8.681$ (2)Å, $Z = 4$.

Since the discovery of the biogenetically aberrant eremophilone (**1**) and its congeners in *E. mitchelli*,[1] the genus which contains about a hundred species has attracted the attention of phytochemists and periodic reports of unusual structures have appeared. Thus the eremenes (e.g. **2**) from *E. freelingii*[2] and *E. fraseri*[3] and the decipiene (**3**) from *E. decipiens*[4] can be regarded as isoprenologues of highly evolved undescribed sesquiterpene systems. The acetylene (**4**) from *E. freelingii*[5] is another example of obscure biosynthesis and *E. opositifolia* is unusual in containing a large proportion of a branched chain conjugated acid (**5**).[6]



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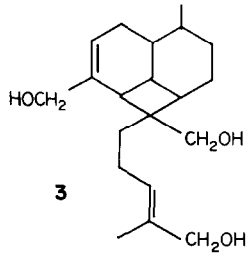

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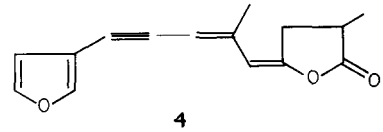
We now wish to describe the assignment of structure and stereochemistry (**6**) to dihydroxyserrulatic acid, an isoprenologue of the cadinene series, which has been obtained from the leaves of *E. serrulata* (F. Muell) Druce, a viscid shrub from the Eastern Goldfields of Western Australia. Dihydroxyserrulatic acid (**8**) was isolated in high yield (1%) as the main component of the acidic fraction of the ether extract.



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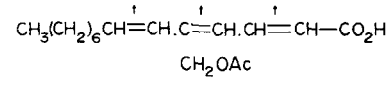

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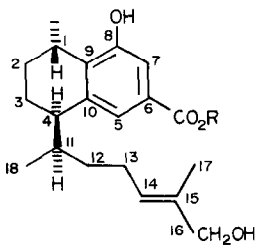
The functional groups were characterised by methylation with diazomethane which gave the ester (**7**), which was acetylated to give the diacetate (**8**). Methylation of **6** with MeI/K_2CO_3 gave the dimethoxy derivative (**9**). The UV spectrum of dihydroxyserrulatic acid (**6**) shows λ_{max} 213 (ϵ, 1200), 255 (4300) and 305 nm (ϵ, 1400) shifted in base to 220 (18,000) 265 (3200) and 320 (1500) indicating a benzenoid chromophore and consistent with a phenolic benzoic acid.[7] The NMR spectrum of the dihydroxy acid shows signals at δ 7.32 and 7.52 for two weakly coupled ($J = 1.5$ Hz) aromatic protons showing additional long range coupling. A broad triplet for an olefinic proton flanked by methylene appears at δ 5.21 and shows allylic couplings both to an olefinic Me group (δ 1.50) and to the methylene protons (δ 4.02) of an allylic hydroxymethyl group, thus identifying the part structure $-CH_2CH=C(CH_3)CH_2OH$. A secondary Me resonance (δ 1.20) shows its main coupling ($J = 7$ Hz) to a tertiary methine proton at δ 3.20. The downfield position of the latter signal suggests a benzylic proton which also follows from the long range coupling between this and both the aromatic protons. When the spectrum is measured in pyridine the benzylic proton signal and the coupled methyl are shifted downfield by δ 0.42 and 0.28

respectively, indicating they lie near the phenol or carboxyl group. The spectra also show resonances for a deshielded tertiary methine (δ 2.64) and another secondary methyl (δ 1.15) which are relatively insensitive to variation of the functional groups.

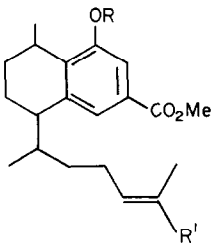
The presence of the primary allylic alcohol group, inferred from NMR data, was established by oxidation of the dimethoxy derivative (**9**) with manganese dioxide which gave the aldehyde (**10**) ν_{max} 1720, 1680 cm^{-1} in which the olefinic proton signal appears at δ 6.2 a shift $\sim\delta$ 1.0 from its position in **6**. Further evidence for the side chain functionality was obtained from the dimethoxy derivative (**9**) which after acetylation underwent ready hydrogenolysis and reduction to give **11**. Extension of the side chain to eight carbons followed from the MS. Thus the base peak in the spectra of the dihydroxy acid (**6**) and its dimethoxy derivative (**9**) arises from loss of $C_8H_{15}O$ (M-127) and both **7** and **11** have the same base peak at *m/e* 233 corresponding to loss of the different side chains.

The presence of an aromatic carboxyl in dihydroxyserrulatic acid (**6**) was established by reduction of the dimethoxy derivative (**11**) with Na–NH_3–EtOH which gave **12** showing a signal for aromatic Me at δ 2.28.

Six of the seven degrees of unsaturation in **6** are accounted for in the aromatic ring and the carboxyl and olefinic groups, requiring a bicarbocyclic system. Assuming normal biosynthesis the absence of tertiary methyls suggests a skeleton analogous to cadinane and in this case the data accumulated would require placing the functional groups as shown in **6**. Confirmation of the skeleton was obtained by mild dehydrogenation of **11** using DDQ leading to a naphthalene (**13**) which gave the crystalline acid (**14**) after hydrolysis. These compounds show consistent spectral properties. Thus the MS had base peaks for loss of C_6H_{13} from the side chain. The NMR spectra of **13** showed weakly coupled aromatic proton resonances at 8.42 and 7.26, shifts closely comparable with the calculated values[8] for 5-H and 7-H respectively. A singlet for 2-H and 3-H is expected as is the downfield position of the aromatic Me resonance and a benzyl proton resonance at δ 3.55 is coupled to a



6: R = H
7: R = Me

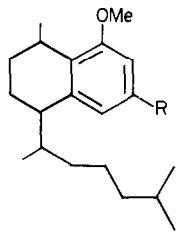


8: R = OAc R' = CH_2OAc
9: R = Me R' = CH_2OH
10: R = Me R' = CHO

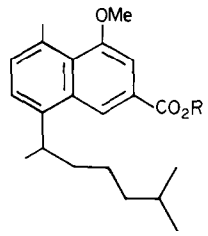
secondary Me group, consistent with its position on the side chain. Large NOE's were observed for the 7-H (34%) when the OMe group in **14** was irradiated and for the 2 H, 3 H singlet (23%) on irradiation of the aromatic Me group.

The carbon skeleton of serrulatic acid has been found previously in the quinone biflorin (**15**) from *Capraria biflora* (Scrophulariaceae),[9] but we are unaware of any other examples.

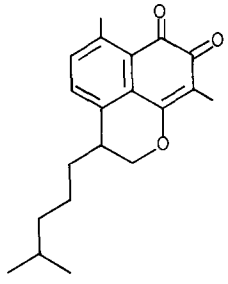
The outstanding problem is the assignment of stereochemistry at the 1-, 4- and 11-positions and their relative configuration were resolved by X-ray crystallography.



11: R = CO_2Me
12: R = CH_3



13: R = CH_3
14: R = H



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Crystallography

A prism 0.21 × 0.48 × 0.35 mm was used for the crystallographic work. Cell dimensions were determined from the angular parameters of 15 reflections with $2\theta \sim 25°$ centred in the counter aperture of a Syntex $P\bar{1}$ four-circle diffractometer; a unique set of data was then gathered using a conventional $2\theta/\theta$ scan within the limit $2\theta < 50°$ at 295(1)K yielding 1922 independent reflections; of these 1480 with $I > 2\sigma(I)$ were considered "observed" and used in the structure solution and refinement. No absorption correction was applied.

Crystal data. $C_{20}H_{28}O_4$, $M = 332.4$, orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19), $a = 15.514(3)$, $b = 14.029(3)$, $c = 8.681(2)$ Å. $D_m = 1.17(1)$, D_c ($Z = 4$) = 1.17 g cm^{-3}. $F(000) = 720$. Monochromatic Mo(K_α) radiation (λ = 0.71069 Å, μ 0.87 cm^{-1}. Neutral atom scattering factors.[10,11]

The structure was solved by direct methods using the MULTAN program[12] package; other computation was carried out using a local variant of the X-ray 72 program system[13] implemented on a CYBER 73 computer. Refinement was carried out, partitioning the parameters in three blocks comprising (i) the atoms of the phenyl/carboxylate system (ii) the molecular "tail" from C(13) onwards and (iii) the remainder; the non-hydrogen atom thermal motion was refined anistropically according to the form $\exp(-2\pi^2(U_{11}h^2a^{*2} + \cdots 2U_{23}klb^*c^*))$. In spite of the crystal size, the data was rather weak and, although all hydrogen atoms were located in a difference map, not all could be refined successfully having rather high thermal motion. Accordingly these atoms were constrained with positional coordinates fixed from the difference map, while the positional parameters of the remainder were refined, U(isotropic) for all hydrogen atoms being constrained at a value fixed by consideration of the thermal parameters of the neighbouring non-hydrogen atom. At convergence, non-hydrogen parameter shifts were $<0.3\sigma$ and hydrogen atom parameter shifts $<0.5\sigma$, the residual $R = \Sigma\|F_o| - |F_c\|/\Sigma|F_o|$ being 0.059 and $R' = (\Sigma w\|F_o| - |F_c\|^2/\Sigma w|F_o|^2)^{1/2}$ being 0.061; the appropriate value of n in a weighting scheme of the form $w = (\sigma^2(F_o) + n \times 10^{-4}(F_o)^2)^{-1}$ was found to be 7.

Table 1. Atomic fractional cell coordinates (x, y, z) (H, $\times 10^3$; C, O, $\times 10^4$) and thermal parameters ($10^3 U_{ij}$ Å^2), with least squares standard deviations in the final digit in parentheses

(a) the non-hydrogen skeleton

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	1419(4)	0932(4)	7478(7)	66(4)	40(3)	59(4)	4(3)	−23(4)	−6(3)
C(2)	2066(6)	0367(6)	8427(11)	155(8)	73(6)	164(9)	10(6)	−120(8)	−8(6)
C(3)	2101(6)	−0643(5)	8286(10)	116(7)	54(5)	102(6)	7(5)	−70(5)	−3(6)
C(4)	1319(4)	−1136(4)	7633(3)	58(4)	48(3)	44(3)	7(3)	1(3)	3(3)
C(5)	0651(4)	−1097(4)	4917(7)	45(3)	36(3)	46(3)	4(3)	−4(3)	−6(3)
C(6)	0331(3)	−0607(4)	3667(6)	43(3)	51(4)	44(3)	−2(3)	−3(3)	1(3)
C(7)	0392(4)	0390(4)	3627(7)	51(4)	57(4)	48(4)	−1(3)	−12(3)	7(3)
C(8)	0746(4)	0857(4)	4857(7)	55(4)	41(3)	56(4)	9(3)	−13(4)	−6(3)
O(8)	0822(3)	1842(3)	4868(5)	92(3)	35(2)	75(3)	1(2)	−27(3)	2(2)
C(9)	1048(3)	0374(4)	6155(7)	41(3)	48(4)	46(3)	5(3)	−4(3)	1(3)
C(10)	1004(3)	−0627(4)	6167(6)	42(3)	39(3)	42(3)	6(3)	−4(3)	4(3)
C(11)	1480(4)	−2212(4)	7408(4)	51(3)	58(4)	47(4)	4(3)	9(3)	9(3)
C(12)	2250(4)	−2422(4)	6381(8)	60(4)	47(4)	62(4)	0(3)	0(4)	16(3)
C(13)	2278(5)	−3454(5)	5868(9)	108(6)	57(4)	73(5)	2(4)	37(5)	−2(4)
C(14)	3007(4)	−3654(5)	4754(8)	69(4)	76(5)	69(5)	3(5)	10(4)	3(4)
C(15)	2924(4)	−3913(4)	3287(7)	59(4)	46(3)	58(4)	4(3)	6(4)	7(3)
C(16)	3718(5)	−4110(5)	2378(8)	81(5)	65(5)	72(5)	6(4)	17(4)	−4(5)
O(16)	3739(3)	−3614(3)	0947(5)	124(4)	68(3)	73(3)	−6(3)	43(3)	−8(3)
C(17)	2067(5)	−4030(6)	2534(9)	76(5)	126(7)	100(5)	−9(5)	1(5)	−18(6)
C(18)	1577(5)	−2716(6)	8987(9)	89(6)	81(6)	55(5)	8(5)	10(4)	17(5)
C(19)	−0063(4)	−1151(5)	2368(7)	51(3)	62(4)	42(3)	7(3)	−12(3)	−7(3)
O(19a)	−0150(3)	−2008(3)	2386(5)	117(4)	42(2)	70(3)	−8(3)	−26(3)	−9(3)
O(19b)	−0338(3)	−0613(3)	1240(5)	114(4)	66(3)	62(3)	2(3)	−42(3)	−5(2)
C(20)	0707(6)	1303(8)	8495(12)	92(7)	127(9)	100(7)	−6(6)	7(6)	−60(7)

(b) hydrogen atoms; distances to the parent non-hydrogen atom are also given (r_{X-H} Å).

Atom	x	y	z	U	r_{X-H}
H(1)	172(3)	157(4)	696(6)	70(–)	1.11(5)
H(2a)	260(–)	085(–)	875(–)	140(–)	1.10(–)
H(2b)	174(–)	028(–)	927(–)	140(–)	0.90(–)
H(3a)	253(4)	−040(5)	721(8)	100(–)	1.20(7)
H(3b)	236(4)	−095(5)	923(8)	100(–)	1.01(7)
H(4)	090(3)	−108(4)	865(6)	70(–)	1.10(5)
H(5)	056(3)	−175(3)	497(6)	50(–)	0.93(5)
H(7)	017(3)	074(4)	267(7)	60(–)	1.02(6)
H(8)	050(4)	201(5)	388(8)	100(–)	1.02(7)
H(11)	097(3)	−243(4)	693(6)	70(–)	0.95(5)
H(12a)	225(4)	−208(4)	552(6)	70(–)	0.89(6)
H(12b)	280(4)	−215(4)	677(6)	70(–)	1.00(6)
H(13a)	249(4)	−378(5)	694(7)	100(–)	1.09(6)
H(13b)	161(4)	−364(4)	522(7)	100(–)	1.21(6)
H(14)	356(4)	−361(5)	506(7)	80(–)	0.91(6)
H(16a)	429(4)	−398(5)	296(7)	100(–)	1.04(6)
H(16b)	367(4)	−488(5)	192(7)	100(–)	1.15(6)
H(16c)	394(–)	−286(–)	150(–)	100(–)	1.20(–)
H(17a)	188(–)	−452(–)	205(–)	120(–)	0.86(–)
H(17b)	160(–)	−370(–)	310(–)	120(–)	0.98(–)
H(17c)	227(–)	−392(–)	142(–)	120(–)	1.03(–)
H(18a)	161(4)	−340(5)	874(8)	100(–)	0.99(7)
H(18b)	116(4)	−255(5)	966(8)	100(–)	0.90(7)
H(18c)	212(4)	−253(5)	958(8)	100(–)	1.02(7)
H(19)	−066(4)	−098(5)	046(8)	100(–)	0.99(7)
H(20a)	023(4)	096(5)	877(10)	110(–)	0.92(7)
H(20b)	093(4)	164(5)	931(8)	110(–)	0.92(7)
H(20c)	036(5)	173(5)	794(8)	110(–)	0.94(7)

The results are given in the Tables and Fig. 1. Atom numbering follows the scheme below, the skeleton being numbered systematically: O and H atoms being denoted by the number of the C atom to which they are attached, suffixed by a, b, c, where necessary.

Certain aspects of the geometry appear to be affected by the lack of application of a thermal motion correction, the vibrational amplitudes within the lattice being high, e.g. C(2)–C(3) is found to have the unlikely value of 1.42(1) Å. Bearing this in mind there appear to be no geometrical abnormalities within the molecular skeleton. Planes within the skeleton about the π-bonded sections of the molecule are shown in Fig. 2. Strong hydrogen-bonding interactions are found between the phenol and

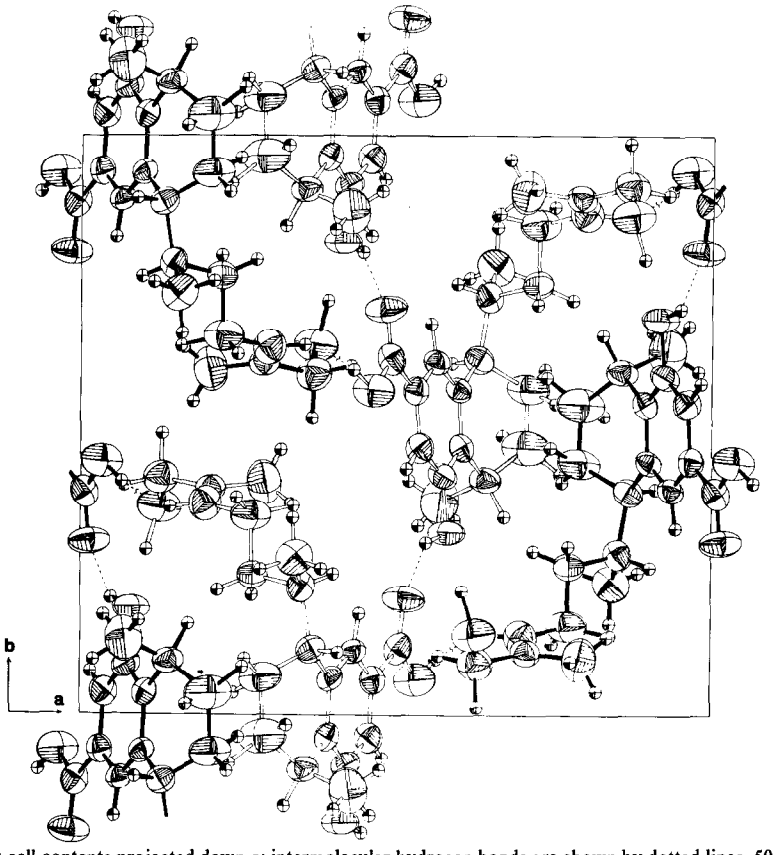


Fig. 1. Unit cell contents projected down c; intermolecular hydrogen bonds are shown by dotted lines. 50% thermal ellipsoids are shown; hydrogen atoms are assigned an arbitrary radius of 0.1 Å. *Note*: Chirality shown is arbitrarily assigned.

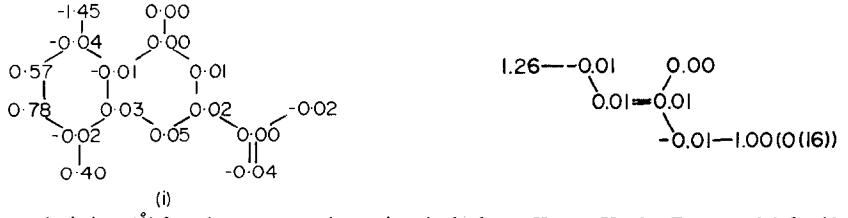
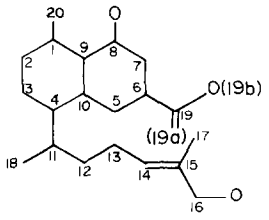


Fig. 2. Atom deviations (Å) from least squares planes given in the frame $X = ax$, $Y = by$, $Z = cz$, and defined by: (i) C(1, 4, 5, 6, 7, 8, 9, 10, 19)0(8, 19a, b)$0.9010X - 0.0733Y - 0.4275Z = -0.8510$ ($\chi^2 = 69$; $\sigma = 0.03$ Å); (ii) C(13, 14, 15, 16, 17) $0.0265X + 0.9615Y - 0.2734Z = -5.949$ ($\chi^2 = 4.9$; $\sigma = 0.01$ Å).

carboxylic acid groups; these are depicted in Fig. 1. Within the non-benzenoid ring, C(11) is pseudo-equatorial and C(20) pseudo-axial.



EXPERIMENTAL

General experimental details have been described.[14]

Isolation of dihydroxyserrulatic acid. Fresh leaves and terminal branches of *E. serrulata* (2 Kg), collected between Coolgardie and Kalgoorlie, Western Australia in 1974 were washed briefly in acetone and the washings concentrated, diluted with water and taken up in ether. Washing the latter with 8% $NaHCO_3$ aq gave a fraction (36 g) which was dissolved in ether and filtered through charcoal. Crystallisation of the filtrate residue from $CHCl_3$ gave *dihydroxyserrulatic acid* **6** (20 g) as prisms, m.p. 174–176°, $[\alpha]_D - 86°$ ($c = 1.57$, EtOH). Found: C, 72.1; H, 8.4. $C_{20}H_{28}O_4$ requires: C, 72.3; H, 8.5%). MS: *m/e* 314 ($M^+ - H_2O$ 75%), 232 (15), 206 (40), 205 (100), 188 (30), 187 (18), 161 (35), 145 (10), 109 (8), 69 (12); NMR ($CDCl_3$) δ, 7.32, 7.52 (5-H, 7-H, $J_{5,7} = 1.5$ Hz); 5.21 (14-H, br t, $J_{13,14} = 7$ Hz); 4.02 (16-H_2, br s); 3.20 (1-H, m); 2.64 (4-H, m); 1.50 (17-H_3, br s); 1.20 (20-H_3 d, J = 7 Hz); 1.15 (18-H_3, d, J = 7 Hz). (C_5D_5N) δ 8.04, 8.00 (5-H, 7-H, $J_{5,7} = 1.5$ Hz); 5.55 (14-H, br t, $J_{13,14} = 7$ Hz); 4.24 (16-H_2, br s); 3.62 (1-H, m); 2.75 (4-H, m); 1.74 (17-H_3, br s); 1.48 (20-H_3, d, J = 7 Hz); 1.04 (18-H_3, d, J = 7 Hz).

The *methyl ester* (**7**) was prepared by brief treatment of **6** with CH_2N_2 in ether (5 min) and purified by distillation b.p. 220°C/2 mm $[\alpha]_D - 32°$ ($c = 1.3$). (Found: C, 72.9; H, 8.6. $C_{21}H_{30}O_4$ requires: C, 72.8; H, 8.7). MS: *m/e* 346 (M^+, 15%), 328 (10), 314 (60), 219 (100), 188 (15), 187 (50%). NMR ($CDCl_3$) δ, 7.29, 7.38 (5-H, 7-H, $H_{5-7} = 1.5$ Hz); 5.22 (14-H, br t, $J_{13-14} = 7$ Hz); 3.96 (14 H_2, br s); 3.84 (OMe, s); 3.16 (1-H, m); 2.65 (4-H, m); 1.60 (17-H_3, br s); 1.19 (20-H_3, d, J = 7 Hz); 1.00 (18-H_3, d, J = 7 Hz).

The *diacetoxy methyl ester* (**8**) prepared from **7** with Ac_2O-pyridine was distilled at 190°/0.3 mm to give a viscous oil $[\alpha]_D - 17°$ ($c = 0.8$). (Found: C, 69.4; H, 7.7. $C_{25}H_{34}O_6$ requires: C, 69.7, H, 80%). MS: *m/e* 430 (M^+, 5%); 398 (10), 388 (8), 356 (20), 328 (15), 261 (25), 209 (100), 187 (30), 109 (35). NMR: ($CDCl_3$) δ

Table 2. Non-hydrogen interatomic distances and angles (Å, deg.); least squares estimated standard deviations in the final digit are given in parentheses

C(1)–C(2)	1.522(11)	C(19)–O(19b)	1.308(8)
C(1)–C(20)	1.507(12)	C(7)–C(8)	1.368(8)
C(1)–C(9)	1.504(8)	C(8)–C(9)	1.396(8)
C(2)–C(3)	1.423(11)	C(8)–O(8)	1.386(6)
C(3)–C(4)	1.507(10)	C(9)–C(10)	1.406(7)
C(4)–C(10)	1.539(8)	C(11)–C(12)	1.519(9)
C(4)–C(11)	1.542(8)	C(11)–C(18)	1.549(10)
C(5)–C(10)	1.382(8)	C(12)–C(13)	1.515(9)
C(5)–C(6)	1.377(8)	C(13)–C(14)	1.515(9)
C(6)–C(7)	1.402(8)	C(14)–C(15)	1.330(10)
C(6)–C(19)	1.492(9)	C(15)–C(16)	1.488(10)
C(19)–O(19a)	1.211(8)	C(16)–O(16)	1.425(9)
		C(15)–C(17)	1.492(10)
		C(8)–C(9)–C(10)	118.4(5)
		C(1)–C(9)–C(10)	122.2(5)
C(2)–C(1)–C(9)	113.3(5)	C(4)–C(10)–C(5)	123.75(5)
C(2)–C(1)–C(20)	110.2(7)	C(5)–C(10)–C(9)	119.3(5)
C(9)–C(1)–C(20)	110.3(6)	C(4)–C(10)–C(9)	117.0(5)
C(1)–C(2)–C(3)	119.8(8)	C(6)–C(19)–O(19a)	123.0(6)
C(2)–C(3)–C(4)	117.3(7)	C(6)–C(19)–O(19b)	113.9(5)
C(3)–C(4)–C(10)	110.7(5)	C(19a)–C(19)–O(19b)	123.1(6)
C(3)–C(4)–C(11)	111.5(5)	C(4)–C(11)–C(12)	112.0(5)
C(10)–C(4)–C(11)	113.6(5)	C(4)–C(11)–C(18)	110.5(5)
C(6)–C(5)–C(10)	121.6(5)	C(12)–C(11)–C(18)	110.8(5)
C(5)–C(6)–C(7)	119.5(5)	C(11)–C(12)–C(13)	112.4(6)
C(7)–C(6)–C(19)	121.3(5)	C(12)–C(13)–C(14)	112.8(6)
C(5)–C(6)–C(19)	119.2(5)	C(13)–C(14)–C(15)	126.1(6)
C(6)–C(7)–C(8)	119.0(5)	C(14)–C(15)–C(16)	118.9(6)
C(7)–C(8)–C(9)	122.1(5)	C(14)–C(15)–C(17)	122.4(6)
C(7)–C(8)–O(8)	121.1(5)	C(16)–C(15)–(17)	119.0(6)
C(9)–C(8)–O(8)	116.8(5)	C(15)–C(16)–O(16)	113.0(6)
C(8)–C(9)–C(1)	119.5(5)		

Interspecies hydrogen bonds; the angle subtended at the hydrogen is given in parentheses.

H(8) ...O(19a)($\bar{x}, \frac{1}{2}+y, \frac{1}{2}-z$)	1.84(6)(144(5))
H(19)...O(16c)($x-\frac{1}{2}, \bar{y}-\frac{1}{2}, \bar{z}$)	1.64(7)(169(6))

Table 3. Intramolecular non-hydrogen skeletal torsion angles, excluding the planar segments of the molecule

C(20)–C(1)–C(9)–C(8)	82.2	C(3)–C(4)–C(11)–C(18)	67.6
C(20)–C(1)–C(9)–C(10)	−98.6	C(10)–C(4)–C(11)–C(12)	68.7
C(20)–C(1)–C(2)–C(3)	108.1	C(10)–C(4)–C(11)–C(18)	−166.3
C(9)–C(1)–C(2)–C(3)	−16.2	C(4)–C(11)–C(12)–C(13)	−166.6
C(1)–C(2)–C(3)–C(4)	−20.2	C(18)–C(11)–C(12)–C(13)	68.6
C(2)–C(3)–C(4)–C(10)	47.1	C(11)–C(12)–C(13)–C(14)	176.0
C(2)–C(3)–C(4)–C(11)	174.7	C(12)–C(13)–C(14)–C(15)	−114.7
C(3)–C(4)–C(10)–C(9)	−38.0	C(14)–C(15)–C(16)–O(16)	−129.3
C(3)–C(4)–C(10)–C(5)	144.9	C(17)–C(15)–C(16)–O(16)	51.9
C(3)–C(4)–C(11)–C(12)	−57.3		

7.75, 7.53 (5-H, 7-H); 5.30 (14-H, m); 4.37 (16-H_2, s); 3.86 (OMe, s); 3.02 (1-H, m); 2.70 (4-H, m); 2.29, 2.02 (2 × $COCH_3$, s); 1.58 (17-H_3); 1.13 (20-H_3, d, J = 7 Hz); 0.99 (18-H_3, d, J = 7 Hz).

The *dimethoxy derivative* (**9**) was prepared from the acid (10 g) in acetone (100 ml) using excess MeI and K_2CO_3. After filtration through alumina in $CHCl_3$: light petroleum (1:1) the product was distilled, b.p. 160°/0.2 mm $[\alpha]_D$ − 30° (*c* = 1.4). (Found: C, 73.2; H, 9.0. $C_{22}H_{32}O_4$ requires: C, 73.3; H, 8.95%). IR ν_{max} 3550, 1710. MS: *m/e* 360 (M^+, 8%), 327 (28), 233 (100). NMR ($CDCl_3$): δ, 7.52 (5-H); 7.3 (7-H); 5.20 (14-H, br t, J = 7 Hz); 3.92 (16-H, s); 3.86, 3.90 (2 × OMe, s); 3.20 (1-H, m, $W_{1/2}$ = 18 Hz); 2.68 (4 H, m, $W_{1/2}$ = 10 Hz); 1.60 (16-H_3, br s); 1.13 (20-H_3, d, J = 7 Hz), 1.03 (18-H_3, d, J = 7 Hz).

MnO_2 *oxidation of the dimethoxy derivative* (**9**). Compound **9** (250 mg) and MnO_2 (1.0 g) were stirred in light petroleum (40 ml) for 2 hr. Filtration and evaporation gave **10** (220 mg) as an oil. MS: M^+ observed 358.211 ($C_{22}H_{30}O_4$ requires: 358.214) *m/e* 358 (15%), 326 (28), 297 (22), 233 (100). IR: ν_{max} 1720, 1680 cm^{-1}, NMR ($CDCl_3$), δ 9.30 (16-H, s); 7.52, 7.32 (5-H, 7-H); 6.20 (14-H, br t, J = 7 Hz); 3.90, 3.91 (2 × OMe, s); 3.20 (1-H, m); 2.65 (4 H, m); 1.69 (17-H_3, m); 1.20 (20-H_3, d, J = 7 Hz); 1.10 (18-H_3, d, J = 7 Hz).

Hydrogenation-hydrogenolysis of the dimethoxy derivative (**9**). Compound **9** (5 g) was acetylated with Ac_2O-pyridine and the product stirred under H_2 with 10% Pd/C in EtOH for 18 hr. Distillation gave an oil (**11**), b.p. 160°/0.5 mm, $[\alpha]_D$ − 57° (c = 0.6). (Found: C, 76.2; H, 9.6. $C_{22}H_{34}O_3$ requires: C, 76.3; H, 9.9%). MS: *m/e* 346 (M^+, 15%), 316 (4), 234 (55), 233 (100), 219 (12). NMR ($CDCl_3$) δ, 7.52, 7.32 (5-H, 7-H); 3.90 (2 × OMe), 3.20 (1-H, m); 2.65

(4-H, m); 1.15 (20-H_3, d, J = 7 Hz); 0.92 (18-H_3, d, J = 7 Hz); 0.80 (16-H_3, 17-H_3, d, J = 6 Hz).

Compound **11** (500 mg) in EtOH (20 ml) and NH_3 Liq. (200 ml) was reduced by the slow addition of Na (2 g). The mixture was stirred for a further hour and the products isolated after addition of 40% NH_4Cl (10 ml). Chromatography of the product on alumina (Act II) gave **11** (150 mg) and the less polar methyl ether **12** (200 mg) as an oil b.p. 140°/0.2 mm $[\alpha]_D$ − 27° (*c* = 1.2). (Found: C, 83.5; H, 11.2. $C_{21}H_{34}O$ requires: C, 83.4; H, 11.3%). MS: *m/e* 302 (M^+, 20%), 287 (4), 190 (50), 189 (100), 165 (25). NMR ($CDCl_3$): δ, 6.65, 6.55 (5 H, 7 H); 3.78 (OMe): 3.20 (1 H, $W_{1/2}$ 18 Hz); 2.58 (4 H, $W_{1/2}$ 10 Hz); 2.30 (19 H_3 s); 1.26–75 (16-, 17-, 18-, 20-H_3).

4 - (1,5 - *Dimethylhexyl*) - 8 - *methoxy* - 1 - *methylnaphth* - 6 - *oic acid* (**14**). Compound **11** (200 mg) was heated under reflux in benzene (20 ml) for 60 hr with DDQ (400 mg). After filtration the solvent was removed and the product chromatographed on alumina (Act II). Elution with 30% $CHCl_3$-light petroleum gave the naphthalene *ester* **13** (65 mg). MS: M^+ observed 342.219 ($C_{22}H_{30}O_3$ requires: 342.219), *m/e* 342 (50%), 312 (8), 260 (15), 257 (100), 227 (28). UV: λ_{max} (EtOH) 222 (ε, 29,500), 250 (46,300), 302 (5000), 345 (2300), 362 (3600). NMR: (CCl_4) δ 8.42 (5 H, br s); 7.26 (7 H, br s); 7.18 (2 H, 3 H, br s); 3.91, 3.95 (2 × OMe); 3.55 (11 H, m); 2.82 (2OCH_3, s); 1.33 (18 CH_3, d, J = 7 Hz), 0.84 (16 H, 17 H).

The *acid* **14** was prepared from **13** (50 mg) using boiling alcoholic 5% KOH aq under N_2. The acid was recovered with ether and purified by prep TLC and crystallisation from pentane to give clusters of prisms, m.p. 120–121° $[\alpha]_D$ − 60° (*c* = 0.75). (Found: C, 76.6; H, 8.5. $C_{21}H_{28}O_3$ requires: C, 76.8; H, 8.6%). MS: *m/e* 328 (M^+, 65%), 243 (100), 229 (10), 199 (12), 184 (15). NMR: δ(CCl_4), 8.59 (5 H); 7.36 (7 H); 7.21 (2-H, 3-H); 3.99 (OMe); 3.61 (11-H, m); 2.84 (20 H_3, s); 1.37 (18-H_3, d, J = 7 Hz); 0.85 (16-H_3, 17-H_3).

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