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ATTENUOL—STRUCTURE, STEREOCHEMISTRY AND SYNTHESIS†

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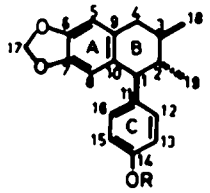
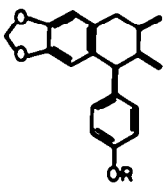
Abstract—A new lignan, attenuol, isolated from *Knema attenuata* (Wall.) Warb., has been assigned structure (1) on the basis of spectral data. Lignan (1) and the stereoisomer (4) (2-*epi*attenuol) have been synthesized and the structure assigned to attenuol has been confirmed.

From the hexane extract of the bark of *Knema attenuata* (Wall.) Warb. (Family: Myristicaceae), we isolated a new lignan, attenuol, $C_{19}H_{20}O_5$. In a preliminary communication[1] we had assigned structure (1) for the compound. We wish to report here full details of this work as well as the synthesis of 1 and the stereoisomer (4).

Attenuol, in its ^{1}H NMR spectrum (Fig. 1, Table 1), showed the presence of two secondary C–Me groups, a methylenedioxy group and a *p*-hydroxyphenyl residue. The ^{1}H NMR spectrum and the ^{13}C NMR spectrum (see experimental for assignments) of attenuol were in agreement with the structure (1). The presence of a hydroxyl was confirmed by the preparation of an acetate (2) and a methyl ether (3). The mass spectral fragmentation[1,2] of attenuol fitted well with the gross structure (1). The large coupling ($J = 9.5$ Hz) between C_1–H and C_2–H in the ^{1}H NMR spectrum of attenuol showed them to be *trans* to each other. The ORD[1,3] of attenuol shows the molecular amplitude ($a \times 10^{-2}$) of −347° leading to the assignment of the stereochemistry 1*S*, 2*S*, 3*R* as shown in 1.



1: R = H
2: R = CO·CH$_3$
3: R = CH$_3$
22: R = CH$_2$·Ph



4: R = H
16: R = CH$_2$·Ph

Attenuol is the sole example of a 1-aryltetralin lignan in which the ring C contains only one oxygen substituent. Its structure as well as relative stereochemistry have now been confirmed by the synthesis of 1 and the all-*cis* isomer (4) as follows:

Addition of bromine to methyl *p*-benzyloxycinnamate followed by alkaline hydrolysis yielded *p*-benzyloxyphenyl propiolic acid. The acid chloride of the latter was condensed with *trans*-3,4-methylenedioxycinnamyl alcohol to yield the ester (5) and the by-product (6) arising by addition of hydrogen chloride during the acid chloride formation. The latter (6) gave the chlorocinnamic acid (7) on hydrolysis. The ester (5) was cyclized, by heating in either DMF or acetic anhydride, to yield by an internal Diels–Alder reaction,[4,5] the 1-aryl-3,4-dihydronaphthalene lactone (8). Catalytic reduction of 8 with Raney nickel yielded the all-*cis* lactone 9 as in the case of γ-apopicropodophyllin.[6] The benzyloxy group underwent reductive cleavage during hydrogenation. A by-product obtained in the reduction was identified as the carbinol (10) arising by hydrogenation of the phenolic ring C. Catalytic reduction of 8 with Pd–C also yielded 9 and none of the ring A-reduced product as observed with γ-apopicropodophyllin.[6] The lactone (9) was rebenzylated to 11 and then reduced with LAH to yield the diol (12) and a minor by-product (13). Treatment of 12 with *p*-toluenesulfonyl chloride in pyridine gave the ditosylate (14) and the ether (15). The former was hydrogenolysed by LAH to yield the benzyl ether (16). Catalytic debenzylation of 16 yielded 2-*epi*attenuol (4) which was different from attenuol in its IR and NMR spectra.

Whereas benzylation of the lactone (9) with benzyl

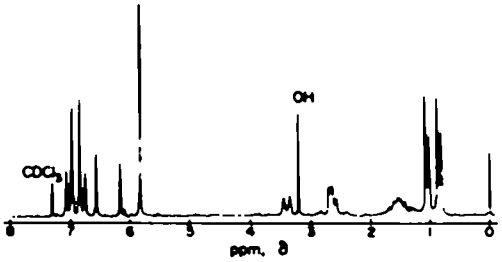


Fig. 1. ^{1}H NMR spectrum ($CDCl_3$, 90MHz) attenuol (1).

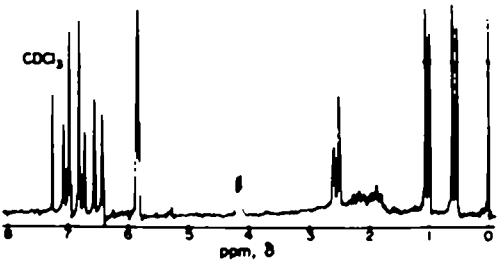


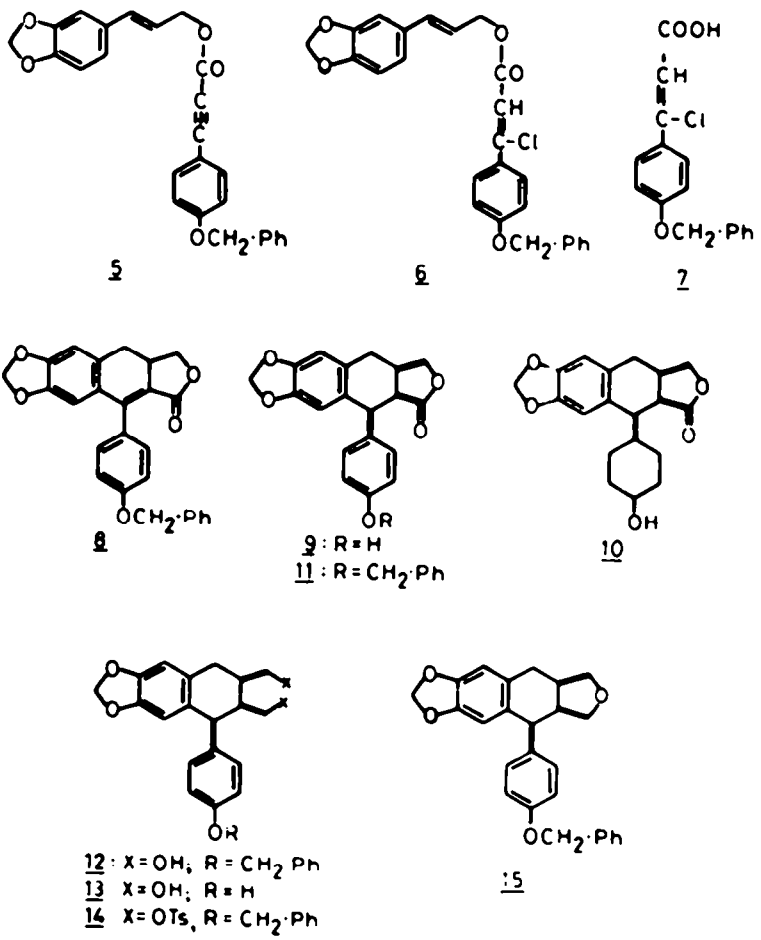
Fig. 2. ^{1}H NMR spectrum ($CDCl_3$, 90MHz) 2-*epi*attenuol (4).

†Contribution No. 538 from CIBA-GEIGY Research Centre.

Table 1. ^{1}H NMR (δ in ppm, J in Hz) in $CDCl_3$

Compd. No.	Assignments (numbering as in formula 1)										
	1	2,3	4	5	8	12,16	13,15	17	18	19	Others
1	3.39 (d, 9.5)	1.2-1.7 (m)	2.65 (m)	6.52 (s)	6.12 (s)	6.97 (d, 9)	6.75 (d, 9)	5.8 (s)	1.05 (d, 6)	0.85 (d, 6)	
2	3.5 (d, 9.5)	1.6 (m)	2.7 (m)	6.63 (s)	6.2 (s)	7.16 (s)		5.85 (s)	1.05 (d, 6)	0.85 (d, 6)	0.CO.CH_3, 2.28 (s)
3	3.41 (d, 9.5)	1.4 (m)	2.63 (m)	6.52 (s)	6.12 (s)	7.02 (d, 9)	6.82 (d, 9)	5.8 (s)	1.05 (d, 6)	0.85 (d, 6)	OMe, 3.8 (s)
4	4.19 (d, 4.4)	1.8-2.3 (m)	2.57 (d, 9)	6.56 (s)	6.43 (s)	7.02 (d, 9)	6.77 (d, 9)	5.86 (q,1.4)	0.58 (d, 7)	1.04 (d,6.5)	
8		3.0-3.9 (1H, m)	2.5-2.9 (m)	6.76 (s)	6.49 (s)	7.24 (d, 9)	7.02 (d, 9)	5.95 (s)	4.69 (t,8.5) 3.99 (t,8.5)		0.CH_2.Ph, 5.1 (s)
9	4.28-4.44 (m)			6.73 (s)	6.61 (s)	7.02 (d, 9)	6.73 (d, 9)	5.92 (s)	4.28-4.44 (m)		
10	4.2-4.5 (m)			6.75 (s)	6.75 (s)			5.92 (s)	4.2-4.5 (m)		
11	4.27-4.45 (m)			6.72 (s)	6.63 (s)	7.1 (d, 9)	6.86 (d, 9)	5.92 (q, 1.5)	4.27-4.45 (m)		0.CH_2.Ph, 5.02 (s)

Compd. No.	1	2,3	4	5	8	12,16	13,15	17	18	19	Others
12	4.28 (d, 4.2)			6.60 (s)	6.45 (s)			5.86 (q, 1.7)	3.82 (d, 5)	3.57 (d, 5)	O.CH_2.Ph, 5.07 (s)
13	4.29 (d, 5.5)			6.63 (s)	6.35 (s)	7.03 (d, 9)	6.81 (d, 9)	5.87 (q,1.7)			
14	3.8-4.2 (m)		2.6 (br, m)	6.48 (s)	6.33 (s)			5.85 (q,1.5)	3.8 - 4.2 (m)		O.CH_2.Ph, 5.06 (s) Ar-CH_3,2.46 (3H,s) 2.47 (3H,s)
15	3.7-4.1 (m)			6.66 (s)	6.43 (s)			5.84 (q,1.5)	3.7 - 4.1 (m)		O.CH_2.Ph, 5.07 (s)
16	4.2 (d, 4.7)	1.8-2.3 (m)	2.57 (d, 8)	6.56 (s)	6.44 (s)	7.08 (d, 9)	6.91 (d, 9)	5.84 (q,1.7)	0.57 (d, 7)	1.03 (d,6.5)	O.CH_2.Ph, 5.06 (s)
17	4.4 (m)			6.58 (s)	6.29 (s)	7.12 (d,8.5)	6.9 (d,8.5)	5.86 (s)	3.8-4.2 (m)		O.CH_2.Ph, 5.04 (s)
18	4.21 (d, 11)			6.58 (s)	6.18 (s)	7.04 (d, 8)	6.86 (d, 8)	5.83 (s)	3.64 (d,4)		O.CH_2.Ph, 5.04(s) O.CH_2.CH_3, 3.98 (q,7) 1.02 (t,7)
21				6.60 (s)	6.26 (s)	7.05 (d, 9)	6.9 (d, 9)	5.85 (s)			O.CH_2.Ph, 5.05 (s)
22	3.4 (d, 9)		2.7 (m)	6.52 (s)	6.12 (s)	7.03 (d, 9)	6.88 (d, 9)	5.8 (s)	1.09 (d, 6)	0.85 (d,6)	O.CH_2.Ph, 5.04 (s)



chloride and K_2CO_3 in acetone yielded the all-*cis* lactone (11), replacement of acetone by EtOH resulted in partial epimerisation at C_2. The desired *trans, trans*-stereochemistry was best achieved by treatment of 11 with NaOAc in EtOH which resulted in complete epimerisation at C_2 followed by opening of the lactone in the product[4-6] to give a mixture of the lactone (17) and the hydroxyester (18). The IR of the *cis*-lactone (11) shows the carbonyl peak at $\nu 1745\,cm^{-1}$ whereas the *trans*-lactone shows the peak at a higher frequency[4,5] $\nu 1770\,cm^{-1}$. The C_1-H in the hydroxy-ester (18) appears in the NMR spectrum as a doublet at δ 4.21 (J = 11 Hz) by *trans*-diaxial coupling with C_2-H. Reduction of 18 with LAH yielded the diol (19) which, with *p*-toluenesulfonyl chloride, gave the ditosylate (20) and the cyclic ether (21). Reduction of 20 with LAH gave the dimethyl compound (22) which, on debenzylation, gave the racemic phenol (1), identical with natural attenuol in its IR (in CH_2Cl_2) and NMR (in $CDCl_3$) spectra. This synthesis confirms the structure (1) and the *trans, trans*-stereochemistry assigned earlier to attenuol.

The NMR spectra of attenuol, its derivatives and the synthetic compounds are presented in Table 1.

The NMR spectra of attenuol (1) and 2-*epi*attenuol (4) (Figs. 1 and 2) show significant differences in the chemical shifts of H_6, H_1, C-methyls and the methylenedioxy groups. The conformation of attenuol (1) is best explained as shown in Fig. 3, the three substituents on ring B being pseudoequatorial. The pendant ring C which is orthogonal to ring B shields H_6 which appears at δ 6.12 as compared to H_5 which appears at δ 6.52. Ring C also shields the methyl on C_2 which appears at δ 0.85 as compared to the C_3-methyl at δ 1.05. H_1 is axial and coupled with the axial H_2 and appears as a doublet at δ 3.39 (J = 9.5 Hz). The methylenedioxy group appears as a singlet. A very similar picture is seen in the acetate (2), the methyl ether (3), and the benzyl ether (22). The methylenedioxy group is a singlet in compounds 17, 18 and 21 which all have the *trans, trans*-stereochemistry.

In comparison, 2-*epi*-attenuol (4) shows H_6 at δ 6.43 which is close to H_5 (δ 6.56) signifying lack of shielding by ring C. H_1 occurs at a lower field, δ 4.19 (d, J = 4.4 Hz), indicating that it is pseudoequatorial with a H-C_1-C_2-H dihedral angle of about 55°. The methy-

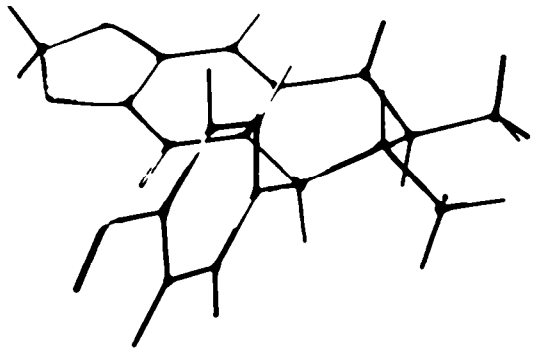
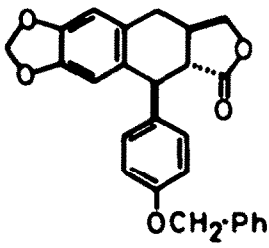


Fig. 3.



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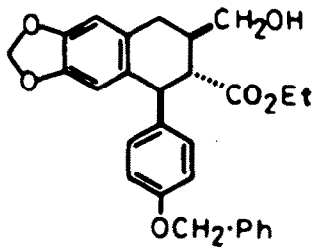

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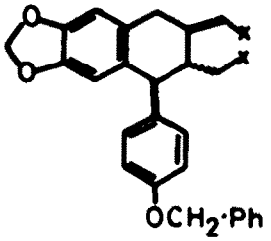
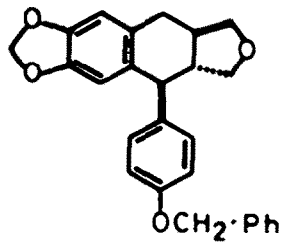


19 : X = OH
20 : X = OTs



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lenedioxy group appears as a quartet (J = 1.4 Hz) due to non-equivalence caused by the influence of the pseudoaxial ring C. These factors favour the conformation shown in Fig. 4 for 4 with the aryl and C_3-methyl groups being pseudoaxial. The C_3-methyl is shielded and occurs as a doublet at δ 0.58. The doublet at the normal value of δ 1.05 is assigned to the C_2-methyl. There have been no previous studies of the NMR spectra of all-*cis* 1-phenyltetralin lignans. The non-equivalence of the methylenedioxy group in ring A has previously been observed[10] when the group is located at C_7, C_8. When the group is present at C_6, C_7, generally they appear as a singlet. The non-equivalence of the methylenedioxy group at C_6, C_7 has however been observed in desoxypodophyllotoxin (23) in the presence of benzene.[11] It is significant that here also the ring C is axial.

In compounds 11, 12, 13, 14, 15 and 16 which all have the *cis, cis*-stereochemistry, H_5 and H_8 occur close to each other and the methylenedioxy group appears as a quartet. The conformation shown in Fig. 4 explains all the NMR spectral features of 2-epiattenuol. The preference of the diaxial conformation over the ring-inverted diequatorial one is evidently due to less non-bonded interactions in the former.

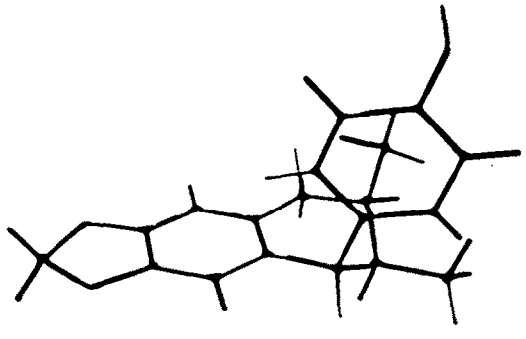
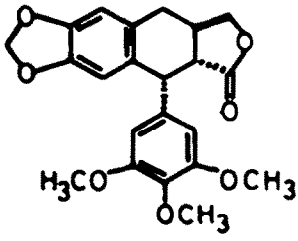


Fig. 4.



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EXPERIMENTAL

M.ps are uncorrected. UV and IR spectra were recorded on Beckman DK-2A and Perkin-Elmer 421 spectrophotometers respectively. NMR spectra were run on Varian A-60 and Bruker WH-90 instruments. Mass spectra were determined on an Atlas Varian Mat CH-7 spectrometer. ORD and CD measurements were carried out on Jasco J-20 spectropolarimeter.

Isolation of attenuol (1)

Powdered bark of *Knema attenuata* (collected at Agumbe) (2.4 kg) was extracted with hexane (2 × 20 l) and concentrated to a small volume. The solid that separated, on crystallisation from $CHCl_3$–hexane afforded colourless needles (150 mg) m.p. 160–161°. (Found: C, 76.8; H, 7.2. $C_{19}H_{20}O_5$ requires: C, 77.0; H, 6.8%); $[\alpha]_D^{25}$ − 20.5° (c, 1.16, $CHCl_3$); ORD (c 0.11, EtOH), $[\phi]_{350}$ − 89°; $[\phi]_{305}$ − 11,910°, $[\phi]_{295}$ + 22,760°, $[\phi]_{284}$ + 148°, $[\phi]_{272}$ + 3611°, $[\phi]_{258}$ + 18,740°, $[\phi]_{226}$ + 36,170°; CD (c 0.11, EtOH), $[\theta]_{315}$ 0, $[\theta]_{301}$ − 25,190, $[\theta]_{275}$ + 11,600, $[\theta]_{257}$ + 2546, $[\theta]_{245}$ + 12,050, $[\theta]_{231}$ − 26,250, $[\theta]_{210}$ + 50,860; λ_{max}^{EtOH} 223 (sh), 287, 294 (sh) nm (log ε 4.16, 3.69, 3.63); ν_{max}^{KBr} 3410, 2970, 2895, 1600, 1480, 1450, 1360, 1290, 1250, 1230, 1180, 1150, 1038, 970, 942, 898, 878, 866, 852, 828, 805, 787, 755 cm^{-1}; ^1H NMR ($CDCl_3$) (Table 1); ^{13}C NMR (in ppm in $CDCl_3$ at 25.155 MHz vs tetramethylsilane; assignments are tentative), C_{14}, 53.1 (s); C_6, C_7, 145.5, 145.3 (s); C_{11}, 139.0 (s); C_{10}, 133.8 (s); C_{12}, C_{16}, 130.5 (d); C_9, 130.1 (s); C_{13}, C_{15}, 115.2 (d); C_5, 109.7 (d); C_8, 107.6 (d); C_{17}, 100.4 (t); C_1, 54.1 (d); C_2, 44.0 (d); C_3, 39.5 (d); C_4, 35.5 (t); C_{19}, C_{20}, 19.9, 17.1 (q each). Mass spectrum, *m/e* (%), 296 (M^+, 100), 240 (85), 239 (95), 223 (50), 210 (60), 181 (30), 165 (18), 153 (20), 152 (25).

The bark was further extracted with MeOH (2 × 15 l) which on concentration gave a crystalline compound (500 mg) m.p. 223° identified as *meso*-inositol by comparison with an authentic sample. (Found: C, 40.6; H, 6.8. Calc. for $C_6H_{12}O_6$, C, 40.0; H, 6.7%).

Acetylattenuol (2)

To a soln of attenuol (65 mg) in pyridine (0.4 ml) was added Ac_2O (1 ml) and the soln kept at room temp. for 16 h. It was poured on crushed ice, the solid filtered, washed with H_2O and crystallised from hexane to afford colourless needles (50 mg), m.p. 110–111° (Found: C, 74.5; H, 6.8. $C_{21}H_{22}O_4$ requires: C, 74.5; H, 6.6%); ν_{max}^{Nujol} 1764, 1235, 1220, 1198, 1038, 936, 912 cm^{-1}. Mass spectrum, *m/e* (%), 338 (M^+, 72), 296 (72), 266 (3), 254 (3), 240 (69), 239 (60), 223 (100), 210 (48), 202 (21), 167 (27), 165 (18), 153 (12), 152 (12).

O-Methylattenuol (3)

Attenuol (30 mg) in acetone (15 ml), anhydrous K_2CO_3 (400 mg) and Me_2SO_4 (0.1 ml) were heated under reflux for 6 h. The soln was filtered and the filtrate evaporated *in vacuo*. Crystallisation of the product from aq. EtOH gave needles (18 mg), m.p. 114–115° (Found: C, 76.8; H, 7.4. $C_{28}H_{22}O_3$ requires: C, 77.4; H, 7.1%); Mass spectrum, *m/e* (%), 310 (M^+, 85), 254 (40), 253 (55), 224 (35), 223 (100), 202 (15).

p-Benzyloxycinnamic acid

A mixture of *p*-benzyloxybenzaldehyde (32 g), malonic acid (36 g), pyridine (80 ml) and piperidine (1 ml) was refluxed for 2 h and poured into H_2O. The solid was filtered and washed with MeOH to yield the cinnamic acid (31 g), m.p. 208–209°, M^+ 254. The acid, prepared by benzylation of *p*-hydroxycinnamic acid, is reported[12] to have m.p. 210–213°.

Methyl p-benzyloxycinnamate

A mixture of the above acid (32 g) in MeOH (500 ml) and conc H_2SO_4 (20 ml) was refluxed for 3 h, concentrated *in vacuo* and poured on ice. The solid was filtered and crystallised from $CHCl_3$–hexane to yield the ester (28 g), m.p. 135–136°. (Found: C, 76.0; H, 6.2. $C_{17}H_{16}O_3$ requires: C, 76.1; H, 6.0%).

Methyl α, β-dibromo-β-p-benzyloxyphenyl propionate

A soln of Br_2 (22 g) in $CHCl_3$ (80 ml) was added to a stirred, ice-cooled soln of the above ester (32 g) in $CHCl_3$ (300 ml). The soln was stirred for 1 h more, evaporated *in vacuo* and the residue crystallised from $CHCl_3$–hexane to yield the dibromo ester (39 g), m.p. 121–122°. (Found: C, 47.7; H, 3.9. $C_{17}H_{16}Br_2O_3$ requires: C, 47.7; H, 3.8%).

p-Benzyloxyphenyl propiolic acid

A soln of the above ester (39 g) and KOH (24 g) in 95% EtOH (200 ml) was refluxed with stirring for 6 h and cooled. The K salt that separated was filtered, dissolved in 1:1 aq MeOH and acidified at 10–15° with cold 20% H_2SO_4. The solid was filtered and crystallised from aq. EtOH to yield the propiolic acid (12 g), m.p. 158–160° (Found: C, 76.2; H, 5.1. $C_{16}H_{12}O_3$ requires: C, 76.2; H, 4.8%); ν_{max}^{Nujol} 2220, 1700, 1660, 1620 cm^{-1}.

Trans-3,4-methylenedioxycinnamyl alcohol

The alcohol was prepared by reduction[13] of methyl 3,4-methylenedioxycinnamate with LAH at −15° to −3°. The purity of the product, m.p. 70–72°, was checked by mass (M^+ 178) and NMR spectra.

3,4-Methylenedioxycinnamyl p-benzyloxyphenyl propiolate (5)

p-Benzyloxyphenyl propiolic acid (5 g) was stirred at 30° for 3 h with $SOCl_2$ (5 ml). Dry C_6H_6 was added and $SOCl_2$ and solvent evaporated *in vacuo*. The residue in C_6H_6 (100 ml) was refluxed for 5 h with *trans*-3,4-methylenedioxycinnamyl alcohol (4 g) and Py (3 ml). The soln was filtered to remove resinous material, washed (dil HCl, H_2O, dil $NaHCO_3$), dried and evaporated *in vacuo*. The residue was chromatographed over silica gel in CH_2Cl_2–hexane to yield the ester (5) (6.4 g) as a gum, $\nu_{max}^{CH_2Cl_2}$ 2200, 1705 cm^{-1}. Mass spectrum: *m/e* 412 (M^+). The later fractions in the chromatography yielded the β-chlorocinnamate (6) (0.7 g), m.p. 96–98° (from CH_2Cl_2–ether) (Found: C, 70.1; H, 5.1; Cl, 7.6. $C_{26}H_{21}ClO_5$ requires: C, 69.6; H, 4.7; Cl, 7.9%); $\nu_{max}^{CH_2Cl_2}$ 1720 cm^{-1}. Mass spectrum, *m/e* (%), 414 (M^+-HCl, 10), 357 (10), 288 (15), 271 (100). NMR ($CDCl_3$), δ 5.85 (2H, s, $-O.CH_2.O-$), 5.77 (2H, d, J = 5 Hz, C=CH–CH_2–O), 5.05 (2H, s, $-O.CH_2.Ph$).

Mild hydrolysis of the ester (6) with KOH yielded the acid (7), m.p. 196–198° (from EtOH) (Found: C, 66.5; H, 4.9. $C_{16}H_{13}ClO_3$ requires: C, 66.6; H, 4.5%). Mass spectrum, *m/e* (%), 290 (M^+33) 288 (M^+ 80), 208 (100).

1-(p-Benzyloxyphenyl)-3,4-dihydro-3-hydroxymethyl-6,7-methylene-dioxynaphthalene-2-carboxylic acid lactone (8)

(a) A soln of the crude ester (5) (8 g) in DMF (450 ml) was refluxed for 8 h, evaporated *in vacuo* and the residue crystallised from MeOH–ether to yield the lactone (8) (2.5 g), m.p. 228–230° (Found: C, 75.9; H, 5.1. $C_{26}H_{20}O_5$ requires; C, 75.7; H, 4.9%); ν_{max}^{KBr} 1735 cm^{-1}. Mass spectrum, *m/e* (%), 412 (M^+, 100), 321 (38), 277 (15), 263 (18), 247 (35), 219 (20).

(b) A soln of 5 (4 g) in Ac_2O (320 ml) was refluxed for 8 h, cooled and poured on ice (320 g). The soln was evaporated *in vacuo*, the residue taken up in CH_2Cl_2, washed ($NaHCO_3$ aq), dried and evaporated. The residue was chromatographed over silica gel in CH_2Cl_2–hexane to yield the lactone (8) (0.4 g), identical (mixed m.p., IR) with the above sample.

Cis, cis - 1 - (p-hydroxyphenyl) - 3 - hydroxymethyl - 6, 7 - methylenedioxy - 1, 2, 3, 4 - tetrahydronaphthalene - 2 - carboxylic acid lactone (9)

(a) The lactone (8) (2 g) in EtOH (300 ml) was heated at 70° for 18 h in an autoclave in presence of H_2 at 1000 psi over Raney Ni catalyst (2.5 g). The soln was filtered from the catalyst, evaporated and the product crystallised from MeOH to yield the lactone (9) (0.8 g), m.p. 235–237° (Found: C, 70.5; H, 5.4. $C_{19}H_{16}O_5$ requires: C, 70.4; H, 5.0%); ν_{max}^{KBr} 3380, 1745 cm^{-1}. Mass spectrum, *m/e* (%), 324 (M^+, 100), 279 (18), 265 (30), 264 (28), 252 (40), 240 (25), 239 (58). The yield of 9 was lower when the reduction was carried out at 100°. The mother liquor from this batch was evaporated and the product chromatographed over silica gel in C_6H_6 to yield the carbinol (10) (250 mg), m.p. 265–266° (from C_6H_6–acetone) (Found: C, 69.0; H, 7.3. $C_{19}H_{22}O_5$ requires C, 69.1; H, 6.7%); ν_{max}^{Nujol} 3350, 1750 cm^{-1}. Mass spectrum, *m/e* (%), 330 (M^+, 50), 232 (100), 231 (45), 187 (70), 157 (20), 129 (60).

(b) The lactone (8) (1.1 g) in AcOH (40 ml) was shaken in a Parr apparatus with H_2 at atm pr at room temp. in presence of 10% Pd–C catalyst (1.1 g). The catalyst was filtered, the filtrate evaporated *in vacuo* and the residue crystallised from MeOH to yield the lactone (9) (0.3 g), identical with the Raney Ni hydrogenation product.

Cis, cis - 1 - (p-benzyloxyphenyl) - 3 - hydroxymethyl - 6,7 - methylene - dioxy - 1,2,3,4 - tetrahydronaphthalene - 2 - carboxylic acid lactone (11)

A soln of 9 (2 g) in acetone (100 ml) was refluxed for 30 h with anhydrous K_2CO_3 (12 g), KI (0.2 g) and benzyl chloride (3.5 ml). The soln was evaporated, H_2O added and the solid filtered and washed with H_2O and finally with hexane to remove excess benzyl chloride. The solid was crystallised from CH_2Cl_2–MeOH to yield the lactone (11) (2 g), m.p. 183–185° (Found: C, 74.9; H, 5.6. $C_{26}H_{22}O_5$ requires: C, 75.3; H, 5.4%); ν_{max}^{KBr} 1740 cm^{-1}. Mass spectrum, *m/e* (%), 414 (M^+, 100), 342 (15), 323 (30), 239 (32).

Cis, cis - 1 - (p-benzyloxyphenyl) - 2,3 - bishydroxymethyl - 6,7 - methylenedioxy - 1,2,3,4 - tetrahydronaphthalene (12)

A soln of the lactone (11) (1 g) in dry THF (50 ml) was added to LAH (1.5 g) in THF (30 ml) at 15–20°. The soln was stirred at room temp. for 3 h and decomposed with EtOAc followed by saturated aq NH_4Cl. The soln was extracted with CH_2Cl_2 and the product chromatographed over silica gel in C_6H_6. Elution with C_6H_6 containing increasing amounts of MeOH yielded the diol (12) (0.6 g) as a gum, homogeneous by tlc. Mass spectrum, *m/e* (%), 418 (M^+, 100), 400 (30), 369 (42), 309 (52), 239 (85), 173 (51).

The later fractions in the chromatography yielded the triol (13) (40 mg), m.p. 252–254° (from acetone) (Found: C, 69·3; H, 6.3. $C_{19}H_{16}O_5$ requires: C, 69.5; H, 6.1%). Mass spectrum *m/e* (%), 328 (M^+, 90), 310 (25), 293 (12), 279 (100), 265 (14), 252 (38), 239 (85), 223 (36), 210 (35), 173 (40).

Reaction of diol (12) *with p-toluenesulphonyl chloride*

The diol (12) (0.6 g) in dry pyridine (25 ml) was treated with TosCl (2.5 g) and kept at room temperature for 48 h. The soln was poured on H_2O and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed (dil HCl, dil $NaHCO_3$, H_2O), dried and evaporated. The gummy product (0.8 g) was chromatographed over silica gel in C_6H_6–hexane (1:1). The earlier fractions yielded the ether (15) (0.3 g), m.p. 145–147° (from CH_2Cl_2–MeOH) (Found: C, 77.8; H, 6.3. $C_{28}H_{26}O_4$ requires: C, 78.0; H, 6.0%). Mass spectrum, *m/e* (%), 400 (M^+, 100), 369 (10), 343 (12), 309 (30), 291 (13), 239 (40).

The later fractions in the chromatography yielded the ditosylate (14) (150 mg), m.p. 163–165° (from CH_2Cl_2–MeOH) (Found: C, 66.2; H, 5.3. $C_{40}H_{36}O_9S_2$ requires: C, 66.1; H, 5.3%).

Cis, cis - 1- (*p-benzyloxyphenyl*) - 2,3 - *dimethyl*- 6,7 - *methylenedioxy* - 1,2,3,4 - *tetrahydronaphthalene* (16)

A soln of (14) (125 mg) in dry THF (10 ml) was added dropwise to a stirred suspension of LAH (200 mg) in THF (5 ml). The soln was refluxed for 3 h, cooled and decomposed with moist ether. The ether soln was washed (dil $NaHCO_3$, H_2O), dried and evaporated. The residual gum was chromatographed over silica gel in C_6H_6–hexane (1:1). The earlier fractions yielded the dimethyl derivative (16) (35 mg), m.p. 121–122° (from CH_2Cl_2–MeOH). Mass spectrum, *m/e* (%), 386 (M^+, 60), 240 (16), 239 (100), 223 (10), 211 (12), 202 (25), 187 (12), 181 (11), 153 (20).

2-Epi*attenuol* (4)

A soln of (16) (25 mg) in MeOH (8 ml) was shaken at room temp. with H_2 at atm pr in presence of 10% Pd–C catalyst (50 mg) for 45 min. The soln was filtered from the catalyst, evaporated and the product crystallised from CH_2Cl_2–hexane to yield 2-*epi*attenuol (4) (15 mg), m.p. 155–156°. Mass spectrum, *m/e* (%), 296 (M^+, 72), 240 (80), 239 (100), 223 (50), 210 (80), 182 (40), 181 (55), 165 (35), 153 (42), 152 (52).

Trans, trans - 1 - (*p-benzyloxyphenyl*) - 3 - *hydroxymethyl* - 6,7 - *methylenedioxy* - 1,2,3,4 - *tetrahydronaphthalene* - 2 - *carboxylic acid lactone* (17) *and* trans, trans - *ethyl* - 1 - (*p-benzyloxyphenyl*) - 3 - *hydroxymethyl* - 6,7 - *methylenedioxy* - 1,2,3,4 - *tetrahydronaphthalene* - 2 -*carboxylate* (18)

A soln of the lactone (11) (1 g) in EtOH (400 ml) was refluxed for 48 h with anhydrous NaOAc (5 g). The solvent was evaporated, H_2O added and the soln extracted with CH_2Cl_2. The product was chromatographed over silica gel in C_6H_6–hexane (1:1). The earlier fractions yielded the lactone (17) (70 mg), m.p. 198–201° (from CH_2Cl_2–hexane) (Found: C, 75.4; H, 5.6. $C_{26}H_{22}O_5$ requires: C, 75.3; H, 5.4%); ν_{max}^{KBr} 1770 cm^{-1}. Mass spectrum, *m/e* (%), 414 (M^+, 100), 342 (10), 324 (40), 323 (30), 239 (38). The later fractions yielded the hydroxy ester (18) (425 mg), m.p. 165–168° (from CH_2Cl_2–hexane) (Found: C, 73.1; H, 6.4. $C_{25}H_{26}O_6$ requires: C, 73.0; H, 6.1%); ν_{max}^{KBr} 3420, 1720 cm^{-1}. Mass spectrum, *m/e* (%), 460 (M^+, 10), 414 (100), 324 (38), 239 (55).

Trans, trans - 1 - (*p-benzyloxyphenyl*) - 2,3 - bis - *hydroxymethyl* - 6,7 - *methylenedioxy* - 1,2,3,4 - *tetrahydronaphthalene* (19)

A soln of the hydroxyester (18) (450 mg) in dry ether (50 ml) was added to LAH (1 g) in ether (20 ml), stirred at room temp. for 3 h and decomposed in the usual way to yield the diol (19) (275 mg), m.p. 153–154° (from EtOH) (Found: C, 74.9; H, 6.5. $C_{25}H_{26}O_5$ requires: C, 74.6; H, 6.3%). Mass spectrum, *m/e* (%), 418 (M^+, 100), 400 (10), 369 (33), 342 (15), 328 (20), 309 (40), 279 (25).

Trans, trans - 1 - (*p-benzyloxyphenyl*) - 2,3 - *dimethyl* - 6,7 - *methylene* - *dioxy* - 1,2,3,4 - *tetrahydronaphthalene* (22)

A soln of the diol (19) (250 mg) in dry pyridine (10 ml) was treated with TosCl (1 g) and kept at room temp for 24 h. Workup as usual gave the crude ditosylate (20) as a gum (220 mg) contaminated with the ether (21). This was reduced with LAH (0.8 g) in refluxing ether (30 ml) for 3 h. The product was chromatographed over silica gel in C_6H_6–hexane (1:1). The earlier fractions yielded the dimethyl compound (22) (55 mg), m.p. 100–101° (from MeOH). (Found: C, 80.6; H, 7.2. $C_{26}H_{26}O_3$ requires: C, 80.8; H, 6.8%). Mass spectrum, *m/e* (%), 386 (M^+, 100), 239 (65), 202 (32), 187 (18), 184 (22), 181 (20), 165 (15), 153 (25). The later fractions yielded the ether (21) (45 mg), m.p. 160–162°, (from CH_2Cl_2–MeOH) (Found: C, 77.8; H, 6.3. $C_{26}H_{24}O_4$ requires: C, 78.0; H, 6.0%). Mass spectrum, *m/e* (%), 400 (M^+, 100), 186 (22).

dl-Attenuol (1)

A soln of (22) (25 mg) in MeOH (10 ml) was shaken with 5% Pd–C catalyst in H_2 at atm pr to yield *dl*-attenuol (1) (15 mg), m.p. 165–166° (from CH_2Cl_2–hexane) (Found: C, 76.7; H, 7.1. $C_{19}H_{20}O_3$ requires: C, 77.0; H, 6.8%) Mass spectrum, *m/e* (%), 296 (M^+, 90), 240 (85), 239 (100), 223 (50), 210 (70), 181 (37), 165 (22), 153 (26), 152 (32). It was identical with natural attenuol in IR (in CH_2Cl_2) and NMR (in $CDCl_3$) spectra.

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