Ebenaceae Extractives. Part III.[1] Binaphthaquinones from Diospyros Species

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Diospyrin and isodiospyrin have been isolated from the bark of *Diospyros mespiliformis*. Isodiospyrin was also found in the bark and wood of *D. virginiana*. Isodiospyrin is optically active and, like diospyrin, is an unsymmetrical dimer of 7-methyljuglone, the two naphthaquinone moieties being coupled at C-6 and C-8′. The bark of *D. ellipti-folia* contains betulin, lupeol, plumbagin (2-methyljuglone), and another dimer, elliptinone, which is isomeric with diospyrin and isodiospyrin. Elliptinone has the structure 6,6′-biplumbagin.

EXTRACTION of the bark of *Diospyros mespiliformis* Hochst. with light petroleum gave a crude product which contained triterpenoid material (positive Liebermann–Burchard reaction), and gave a purple colour with alkali indicating the presence of a *peri*-hydroxynaphthaquinone of the juglone type. (Plumbagin has been reported [2] in the bark of this species.) Chromatography revealed the presence of two quinones and by comparison with known compounds one of these was identified as the biquinone, diospyrin (I), originally isolated from *D. montana* Roxb.[3] Neither plumbagin nor its isomer, 7-methyljuglone, could be detected.

The second quinone, orange-red prisms, m.p. 226—228° (decomp.) was isomeric with diospyrin, $C_{22}H_{14}O_6$. It showed very similar absorption both in the i.r. (ν_{CO} 1662 and 1640 cm.$^{-1}$, ν_{HO} absent) and the u.v.–visible region (see Table 1), and afforded a leuco-hexa-

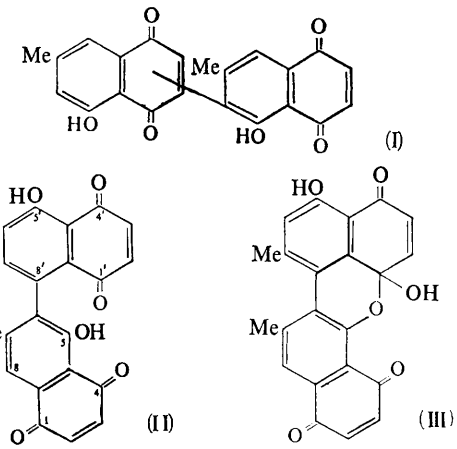
TABLE 1

U.v.–visible absorption of *Diospyros* quinones

Quinone	$\lambda_{max.}$ (EtOH) (log ε) (mμ)	$\lambda_{max.}$ (EtOH/HO$^-$) (log ε) (mμ)
7-Methyljuglone	218 (4·19), 253 (4·13), 424 (3·60)	223 (4·65), 264 (4·03), 292sh (4·01), 539 (3·85)
Plumbagin [a]	220 (3·87), 266 (4·12), 418 (3·61)	225 (4·18), 272 (4·05), 529 (3·65)
Diospyrin (I)	223 (4·59), 254 (4·43), 438 (3·99)	231 (4·64), 290 (4·19), 366 (3·51), 576 (4·08)
Isodiospyrin (II)	221 (4·57), 254 (4·39), 436 (3·98)	231 (4·61), 296 (4·02), 376 (3·49), 574 (4·10)
Elliptinone (VII) [a]	230 (4·45), 263 (4·29), 443 (3·96)	229 (4·51), 263 (4·28), 544 (3·94), 574 (3·94)

[a] In MeOH.

acetate and a dimethyl ether (*M*, 402). This evidence clearly indicates that the new compound is also a methyljuglone dimer and, like diospyrin, it must be unsymmetrical, as the n.m.r. spectrum shows signals from two aromatic methyl groups as a finely separated doublet at τ 7·98, while the *peri*-hydroxy-protons were revealed by two singlets at τ −2·46 and −2·08. Similarly, in the dimethyl ether the *O*-methyl protons resonate at τ 5·90 and 6·49, and the *C*-methyl protons at τ 7·92 and 7·98. The n.m.r. spectrum of the dimethyl ether also shows sharp singlets at τ 2·02 and 2·60 (τ 2·33 and 2·67 in the parent compound) which can be attributed to aromatic protons, and since they are unaffected by double irradiation they are evidently located in different rings.



By analogy with other juglone compounds, the signal at τ 2·33 in the n.m.r. spectrum of the parent compound may be ascribed [4] to a *peri*-hydrogen (8-H) in one methyljuglone moiety and that at τ 2·67 can be attributed to a β-proton (6′- or 7′-H) in the other half of the molecule. The four remaining protons are vinylic as revealed by a two-proton singlet at τ 3·02, and an AB quartet (intensity two protons) centred at τ 3·15. It follows that both quinone rings are unsubstituted and the two halves of the molecule must be linked by a bond from the *peri*-position of one to a β-position (C-6′ or C-7′) in the other. On this basis structure (II) may be assigned to the biquinone, the *meta*-relationship of the hydroxy- and methyl groups being assumed on biogenetic and phytochemical grounds, 3-methylnaphthalene-1,8-diol, present in *D. mollis* Griff.[5] being the likely precursor of all the dimeric compounds found in *Diospyros* spp. Despite the lack of symmetry, the two quinonoid protons in simple Bz-substituted 1,4-naphthaquinones usually have the same chemical shift and appear as an unresolved singlet.[4,6] This is true for one pair of vinylic protons in (II) but as the other pair gives rise to an AB quartet we were led to consider an alternative hemiacetal structure (III). This would account for the optical activity

[1] Part II, A. G. Brown and R. H. Thomson, *J. Chem. Soc.*, 1965, 4292.

[2] R. Paris and H. Moyse-Mignon, *Compt. rend.*, 1949, **228**, 2063.

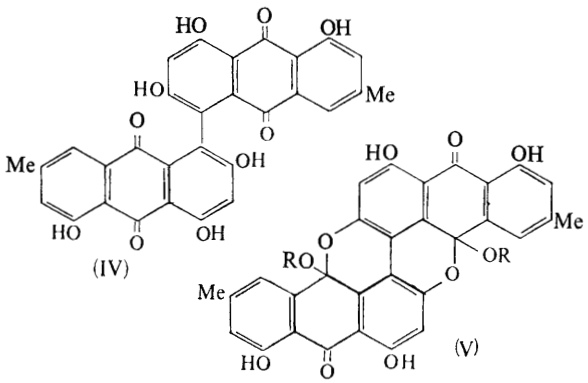
[3] (*a*) R. S. Kapil and M. M. Dhar, *J. Sci. Ind. Res. India*, 1961, **20***B*, 498; (*b*) G. S. Sidhu and M. Pardhasaradhi, *Tetrahedron Letters*, 1967, 1313.

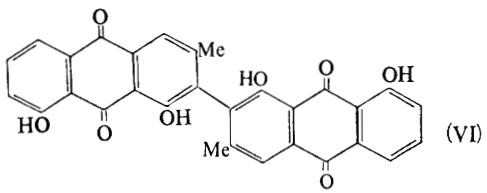
[4] R. E. Moore and P. J. Scheuer, *J. Org. Chem.*, 1966, **31**, 3272.

[5] Stang Mongolsuk and Chiravat Sdarwonvivat, *J. Chem. Soc.*, 1965, 1533.

[6] A. L. Fallas and R. H. Thomson, unpublished work.

of the compound and finds analogy in the conversion of skyrin (IV) into pseudoskyrin derivatives (V).[7] Structure (III) appeared to derive some support from an $M - 17$ peak (intensity 12% of the base peak) in the





mass spectrum (see Table 2). However, the latter observation was nullified when a similar, but more intense, peak was seen in the spectrum of diospyrin. Moreover, all attempts to racemise the compound under both acid and basic conditions were unsuccessful, starting material being recovered without loss of optical activity except on treatment with cold methanolic hydrogen chloride which gave a green polymeric product. Attempts to form a monomethyl ether under milder conditions also failed. We therefore abandoned structure (III), and since both the derived dimethyl ether and the leuco-hexa-acetate are also optically active, the chirality must be ascribed to restricted rotation about the central carbon–carbon bond. Examination of models shows that even when the two halves of structure (II) are at right angles to each other there is some overcrowding and free rotation is very severely restricted. A similar example is the optically active bianthraquinone, cassiamin (VI).[8] If the two halves of structure (II) are mutually at right angles this will account for the shielding of both aromatic methyl groups, and also for *one O*-methyl group in the dimethyl ether. With this degree of asymmetry it is not surprising that the vinylic protons of one naphthaquinone moiety exhibit an AB quartet in the n.m.r. spectrum but it is difficult to explain why the other pair does not.

Structure (II) has recently been advanced[9] for a compound, isodiospyrin, which accompanies diospyrin in the bark of *D. chloroxylon* Roxb. Sidhu and Prasad[9] were unable to separate isodiospyrin completely from diospyrin but the dimethyl ether was obtained pure. Direct comparison of isodiospyrin dimethyl ether with our dimethyl ether confirmed their identity. Accordingly, we regard the biquinone, m.p. 226—228°, as isodiospyrin although there remains a slight possibility that the Indian material may have structure (III).

Extraction of the bark of *D. virginiana* L. (persimmon) also yielded isodiospyrin and a small amount was present (t.l.c.) in the wood. This is of some local interest as the very hard wood of this species is used for the manufacture of golf clubs, and we were able to detect (t.l.c.) isodiospryin in the head of an old persimmon 'driver'. Purification of the isodiospyrin from *D. virginiana* bark yielded traces of another quinone, $C_{22}H_{14}O_7$, which, from its properties (see Experimental section) may be a hydroxy-isodiospyrin.

From the bark of *D. elliptifolia* Merr. we obtained, besides lupeol and betulin, plumbagin and a third binaphthaquinone, $C_{22}H_{14}O_6$, isomeric with diospyrin and isodiospyrin. The new compound, elliptinone, showed ν_{CO} 1667 and 1645 cm.$^{-1}$ (ν_{HO} absent) and had a u.v.–visible absorption curve consistent with a *peri*-hydroxy-1,4-naphthaquinone structure, giving a characteristic bathochromic shift in alkaline solution (see Table 1). The n.m.r. spectra of its derivatives show that this dimer is symmetrical and has structure (VII). The n.m.r. spectrum of the diacetate consists of a broad singlet at τ 7·87 arising from the acetate protons and the methyl protons at C-2 and C-2′, a quartet at τ 3·30 (J *ca.* 1·5 c./sec.) from the vinylic protons at C-3 and C-3′, and two doublets at τ 1·93 and 2·42 (J *ca.* 8 c./sec.) arising from the *ortho*-coupled aromatic protons. The signal at τ 1·93 is assigned to the *peri*-hydrogens since 8-H in juglone acetate also resonates at τ 1·93, and further comparison with the spectrum of this compound revealed that there were no signals from protons at C-6 and C-6′ in the spectrum of the dimer. The n.m.r. spectrum of elliptinone dimethyl ether is very similar to that of the diacetate except for the methoxy-signal which appears as a sharp singlet at τ 6·38. This upfield shift shows that the methoxy-groups are shielded by the adjacent benzene rings owing to rotation of the two halves of the molecule about the central carbon–carbon bond. A binaphthaquinone of structure (VII; OMe in place of OH) has recently been identified[10] as the product obtained on oxidation of diospyrol (VIII) tetramethyl ether. (Diospyrol occurs in the fruit of *D. mollis*.[10,11]) Direct comparison of this oxidation product with elliptinone dimethyl ether was not possible but the i.r. spectra of the two compounds are identical as are

[7] B. H. Howard and H. Raistrick, *Biochem. J.*, 1954, **56**, 56; S. Shibata, O. Tanaka, and I. Kitagawa, *Pharm. Bull. Japan*, 1955, **3**, 278; O. Tanaka, *Chem. Pharm. Bull. Japan*, 1958, **6**, 203.

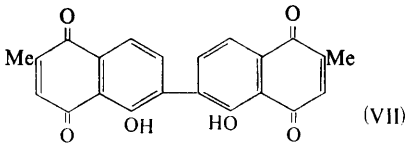
[8] N. L. Dutta, A. C. Ghosh, P. M. Nair, and K. Venkataraman, *Tetrahedron Letters*, 1964, 3023.

[9] G. S. Sidhu and K. K. Prasad, *Tetrahedron Letters*, 1967, 2905.

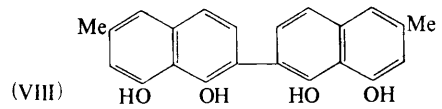
[10] K. Yoshihara, S. Natori, and Panida Kanchanapee, *Tetrahedron Letters*, 1967, 4857.

[11] J. W. Loder, Stang Mongolsuk, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1957, 2233.

their n.m.r. spectra, allowing for solvent shifts. We conclude that elliptinone is the dimer (VII).

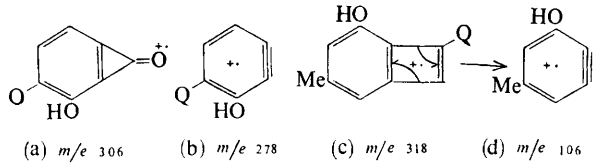


(VII)

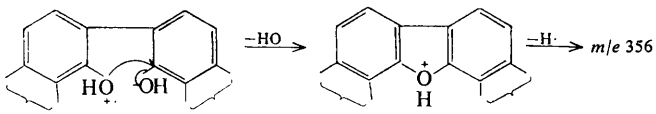


(VIII)

Mass Spectra.—The mass spectra of the dimeric naphthaquinones can be correlated with those of simple 1,4-naphthaquinones [12] but show a more complex pattern of mainly low-intensity peaks (see Table 2). $M + 2$ peaks are prominent, especially for diospyrin and its dimethyl ether which may have contained traces of the quinols. In diospyrin and isodiospyrin, initial loss of a methyl radical is dominant, followed by successive loss of CO but in elliptinone initial loss of CO is slightly more important and subsequent fragmentation in the manner of 2-methyl-1,4-naphthaquinone can be discerned leading to ions at *m/e* 306 and 278 postulated as (a) and (b) (Q = $C_{11}H_7O_3$), respectively, by analogy with the mass spectrum of plumbagin.[12] One quinonoid ring of diospyrin is linked to the benzenoid ring of the other moiety



(a) *m/e* 306 (b) *m/e* 278 (c) *m/e* 318 (d) *m/e* 106



(e) *m/e* 374 (f) *m/e* 357

and a relatively prominent peak in the spectrum at *m/e* 106 (12%) may be plausibly attributed to (d) arising by normal breakdown [12] of the molecular ion to (c) which fragments as indicated. The spectra of all three dimers show $M - 17$ and $M - 18$ peaks attributable to intramolecular elimination of HO· and H_2O represented, for elliptinone, as (e) ⟶ (f). (A similar elimination of MeO· from the molecular ions of the dimethyl ethers would account for a fragment ion at *m/e* 371 which is actually the base peak in the spectrum of elliptinone dimethyl ether.) In the lower mass region *m/2e* ions are relatively abundant; these are easily discerned at half-integral mass values and peaks at integral mass values *e.g.*, 187, 153, and 139 are possibly *m/2e* species derived from the molecular ion and fragment ions (a) and (b).

[12] J. H. Bowie, D. W. Cameron, and D. H. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 5094.

TABLE 2

Mass spectra of *Diospyros* quinones [a]

Compound								
7-Methyljuglone [b]	*m/e*	190	189	188	187	173	160	135
	I (%)	18	16	100	20	9	25	11
		134	133	132	131	106	105	104
		51	8	42	36	30	6	9
		103	85	83	78	77	63	57
		9	6	8	8	16	6	6
		52	51					
		6	10					
Plumbagin [d]	*m/e*	189	188	173	160	145	132	131
	I (%)	14	100	20·5	17	3	9·5	14
		121	120	92	77	64	63	51
		8·5	14	13	5	5·5	9	5
Diospyrin [b]	*m/e*	376	375	374	361	359	357	356
	I (%)	72	44	100	16	32	17	19
		346	345	331	329	328	319	318
		8	9	15	14	16	7	7
		317	303	302	301	300	292	275
		7	7	7	7	7	6	6
		189	187	186	185	178	165	163
		7	13	15	10	5	8	9
		153	152	147	135	134	131	115
		8	7	10	10	10	11	7
		106	104	103	97	95	91	83
		12	8	7	6	7	14	8
		81	77	76	69	57	55	50
		8	13	12	11	14	17	10
		45	44	43	41	39		
		12	14	14	17	12		
Isodiospyrin [c] ...	*m/e*	376	375	374	361	359	357	356
	I (%)	10	28	100	5	60	12	6
		346	345	341	339	331	329	328
		7	10	6	5	13	7·5	5
		319	318	303	292	275	189	187
		10	2	4·5	3·5	3	5	7·5
		165	163	152	139	115	89	80
		4	4	4	4	5	4	15
		79	78	77	76	69	63	57
		20	6·5	11	5	3	6	10
		56	55	51	43	41	39	
		7	4	6·5	10	11	11	
Elliptinone [c]	*m/e*	376	375	374	361	359	357	356
	I (%)	21	25	100	6	2·5	9	4·5
		346	345	331	329	328	318	306
		5	3	7·5	3	5	3	2·5
		303	278	187	165	153	139	126
		3	12	3·5	7·5	11	5	4
		97	73	71	69	60	57	55
		3	6	7·5	11	9	11	9
		43	41	39				
		11	12	9				

[a] Recorded with an AEI–MS9 instrument operating at 70 e.v. [b] Inlet temperature 200°. [c] Inlet temperature 160°. [d] See also ref. 12.

EXPERIMENTAL

Extraction of Diospyros mespiliformis.—The finely powdered bark (210 g.) was extracted (Soxhlet) with light petroleum (b.p. 60—80°), and the crude extract (3 g., 1·4%) was chromatographed on a column of acid-washed silica gel. An orange band was eluted with benzene–ether (95 : 5) and then separated into two components by p.l.c. (preparative-layer chromatography) on silica gel in n-heptane–ethyl acetate–acetic acid (70 : 30 : 10). The faster-moving zone yielded diospyrin (23 mg.) as orange-red prisms, m.p. 254—

256° (lit.,[3a] 258°) (from light petroleum, b.p. 60—80°) identical (i.r., u.v., R_F, mixed m.p.) with an authentic sample. The dimethyl ether (methyl iodide–silver oxide–chloroform) had m.p. 255—257°, mixed m.p. 254—256°. The second band gave isodiospyrin (17 mg.) identical with that isolated from *D. virginiana* (see below).

Extraction of Diospyros virginiana.—The finely milled bark (140 g.) was extracted with chloroform and the product (0·67 g., 0·48%) was chromatographed on acid-washed silica gel. Elution with chloroform gave an orange fraction which was further purified by p.l.c. on silica gel in chloroform–methanol (99 : 1). Crystallisation of the main component (R_F 0·8) from light petroleum (b.p. 100—120°) gave *isodiospyrin* as red prisms, m.p. 226—228° (30 mg., 0·02% dry wt. of bark) (Found: C, 70·7; H, 3·6. $C_{22}H_{14}O_6$ requires C, 70·6; H, 3·8%); $[\alpha]_D^{23}$ −16·6° ± 1° (*c* 0·27 in $CHCl_3$); $\nu_{max.}$ (KBr) 1662, 1640, 1600, 1585, 1371, 1360, 1336, 1277, 1200, 1105, 1096, and 848 cm.$^{-1}$. The n.m.r. spectrum (100 Mc./sec., $CDCl_3$) showed singlets (1H each) at τ −2·46 and −2·08 (which disappeared on deuteriation) and at 2·33 and 2·67 (Ar-*H*), and 3·02 (2H) (C*H*=C*H*), two doublets (C*H*=C*H*) at 3·04 and 3·26 (*J* 10 c./sec.), and a doublet (6H) at 7·98 (Ar-CH_3). Refluxing with methyl iodide and silver oxide in chloroform gave the dimethyl ether which was purified by t.l.c. (silica gel in chloroform) and crystallised from ether–light petroleum (b.p. 60—80°) as yellow needles, m.p. 233—234°, identical (mixed m.p., i.r., u.v., R_F) with a sample isolated from *D. chloroxylon*[9] [Found: C, 71·2; H, 4·7%, *M* (mass spectrum), 402. Calc. for $C_{24}H_{18}O_6$: C, 71·6; H, 4·5%; *M*, 402]; $\lambda_{max.}$ (EtOH) 218, 255, and 392 mμ (log ε 4·60, 4·58, and 3·86); $\nu_{max.}$ (KBr) 1658, 1610, 1588, 1450, 1400, 1330, 1302, 1287, 1250, 1230, 1107, 1097, 1052, and 846 cm.$^{-1}$. The n.m.r. spectrum (100 Mc./sec., $CHCl_3$) showed singlets at τ 2·02 and 2·60 (Ar-*H*), 3·02 (C*H*=C*H*), 5·90 and 6·49 (O-CH_3), 7·92 and 7·98 (Ar-CH_3), and two doublets (C*H*=C*H*) at 3·05 and 3·29 (*J* 10 c./sec.). The *leuco-hexa-acetate* crystallised from hexane–ethyl acetate as tablets, m.p. 133—134° (Found: C, 65·1; H, 4·8. $C_{34}H_{30}O_{12}$ requires C, 64·8; H, 4·8%); $[\alpha]_D^{23}$ −9·1° ± 1° (*c* 0·19 in $CHCl_3$); $\lambda_{max.}$ (EtOH) 237, 297, 318sh, and 333 mμ (log ε 4·81, 4·06, 3·76, and 3·50). The n.m.r. spectrum (60 Mc./sec., $CDCl_3$) showed singlets at τ 2·24 (1 Ar-*H*) and 2·90 (5 Ar-*H*), 7·60 (6H) (Ar-CH_3), and at 7·52, 7·76, 7·81, 8·04, 8·35, and 8·84 (3H each) (CH_3CO$_2$).

P.l.c. purification of isodiospyrin afforded a trace of a second quinone which showed $\lambda_{max.}$ (EtOH) 218, 262sh, 292sh, and 443 mμ, $\lambda_{max.}$ (EtOH/OH^-) 224, 288, 540 mμ; $\nu_{max.}$ (KBr) 3420, 1660, 1640, 1606, 1468, 1400, 1368, 1240, 1230, 1123, and 1072 cm.$^{-1}$ [Found: *M* (mass spectrum), 390. $C_{22}H_{14}O_7$ requires *M*, 390]. The pigment gave a violet solution in aqueous sodium carbonate but was insoluble in hydrogen carbonate solution.

Extraction of Diospyros elliptifolia.—(a) The finely milled bark (200 g.) was extracted with light petroleum (b.p. 60—80°) and the product (5·6 g.) was chromatographed on silica gel. Elution of an orange band with benzene–chloroform (75 : 25) gave a mixture of orange and colourless material. Crystallisation from light petroleum afforded lupeol, m.p. 215—216·5°, mixed m.p. 214—216°, *M* (mass spectrum), 426. The quinone in the mother liquor was separated by p.l.c. on silica gel in chloroform–ethyl acetate–acetic acid (90 : 10 : trace) and then sublimed at 70°/0·1 mm. to give plumbagin (20 mg.) as orange needles, m.p. 75° (from aqueous ethanol) identical (mixed m.p., i.r., u.v., R_F) with authentic material.

(b) The bark was then extracted with chloroform and the material (1·84 g.) so obtained was chromatographed on silica gel. Elution of an orange band with chloroform–methanol (95 : 5) gave a mixture which was triturated with acetone, warmed, and filtered free from the insoluble quinone. The soluble portion was identified as betulin, m.p. and mixed m.p. 250—252°, *M* (mass spectrum), 442. The insoluble material was further purified by t.l.c. in chloroform on silica gel to give *elliptinone* (16 mg.) as orange needles, subl. >290°, decomp. >310° (Found: C, 70·1; H, 3·9%; *M* (mass spectrum), 374. $C_{22}H_{14}O_6$ requires C, 70·6; H, 3·8%; *M*, 374); $[\alpha]_D^{23}$ = 0° (*c* 0·27 in $CHCl_3$); $\nu_{max.}$ (KBr) 1667, 1645, 1607, 1470, 1422, 1370, 1358, 1263, 1136, 1032, 990, 908, 845, 790, and 742 cm.$^{-1}$. Methylation with methyl iodide–silver oxide–chloroform gave the dimethyl ether which was crystallised from light petroleum (b.p. 60—80°)–chloroform and then sublimed at 200°/0·1 mm. to give yellow prisms, m.p. 273—275° (lit.,[10] 275°) (Found: C, 71·5; H, 4·6. Calc. for $C_{24}H_{18}O_6$: C, 71·6; H, 4·5%); $\lambda_{max.}$ (EtOH) 218, 255, and 370 mμ (log ε 4·62, 4·60, and 4·00); $\nu_{max.}$ (KBr) 1670, 1637, 1390, 1362, 1304, 1260, 1238, 1146, 1040, 967, 920, 875, 762, and 695 cm.$^{-1}$, identical with the i.r. spectrum of (VII; OMe in place of OH) from diospyrol tetramethyl ether.[10] The n.m.r. spectrum (60 Mc./sec., $CHCl_3$–CF_3CO_2H) showed doublets (each 2H) at τ 1·87 and 2·21 (Ar-*H*) (*J* 8 c./sec.), at 7·76 (6H) (CH=CCH_3) (*J* 1·5 c./sec.), a singlet (6H) at 6·38 (O–CH_3) and a quartet (2H) at 3·04 (C*H*=CCH$_3$) (*J* 1·5 c./sec.). The diacetate was obtained for n.m.r. study but was not prepared analytically pure.

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