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OBTUSASTYRENE AND OBTUSTYRENE, CINNAMYLPHENOLS FROM *DALBERGIA RETUSA**

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Key Word Index—*Dalbergia retusa*; Leguminosae–Lotoideae; isoflavonoids; neoflavonoids; cinnamylphenols; styryl-*para*-quinonemethide; 2-aryl-3-methyl-2,3-dihydrobenzofuran.

Abstract—The heartwood of *Dalbergia retusa* contains, in addition to 8-*O*-methylretusin, (*R*)-4-methoxydalbergione, (*R*)-obtusaquinol and (+)-obtusafuran [(2*R*,3*R*)-2-phenyl-3-methyl-2,3-dihydro-5-hydroxy-6-methoxybenzofuran], the cinnamylphenols obtusastyrene [*E*-1-(4-hydroxybenzyl)-2-phenylethylene], obtustyrene [*E*-1-(4-hydroxy-2-methoxybenzyl)-2-phenylethylene] and obtusaquinone [styryl-5-hydroxy-2-methoxy-4-quinonemethide]. The structural determination of compounds relied on spectra, degradations and syntheses.

INTRODUCTION

The central-American cocobolo, *Dalbergia retusa* Hemsley, has been studied by two groups of investigators. Misled by an error in the botanical literature which was rectified by Lecomte [2], we referred in our preliminary communications to this species wrongly as *D. obtusa* Lecomte [3] and named the previously unknown compounds accordingly. Table 1, which correlates our results with those obtained during subsequent studies by Jurd's group, shows the close chemical relationship of the analysed specimens. The differences in composition are hardly significant. Indeed, as obligatory precursors respectively to **1b** and **6a**, the intermediary presence of **1a** in specimen 1 and of **5b** in specimen 2 seems assured. The additional presence of the *S*-isomers of **2a**, **3a** and **4a** in specimen 2 may be due to chemical variation within the species. While (*R*)-4-methoxydalbergione (**2a**, α-3H, β-CH=CH_2) occurs additionally in several *Dalbergia* species [10–12] and 8-*O*-methylretusin was isolated also from *D. variabilis* Vog. [13], all other constituents have so far not been reported from any other source.

RESULTS

Obtusaquinol

Chromatography of a C_6H_6 extract gave fractions containing a coloured component [(±)-**2a**] and a colourless component (obtusaquinol). Attempted purification of obtusaquinol by TLC resulted only in the isolation of (*R*)-4-methoxydalbergione [(±)-**2a**], as a result of aerial oxidation. This indicates that obtusaquinol is (*R*)-3-(2,5-dihydroxy-4-methoxyphenyl)-3-phenylpropene (**3a**, α-CH=CH_2, β-H). Analogously, (*R*)-3,4-dimethoxydalbergione (**2b**, α-CH=CH_2, β-H) and the corresponding quinol **3b** co-occur in the heartwood of *Machaerium scleroxylon* Tul. [14], *M. kuhlmannii* Hoehne and *M. nictitans* (Vell.) Benth. [15]. Analytical data on (±)-obtusaquinol [rac-4-methoxydalbergiquinone] were reported [7].

Table 1. Constituents of cocobolo wood

	Presence (+)/Stereochemistry	
	Specimen 1	Specimen 2
Retusin (**1a**)		+[6]
8-*O*-Methylretusin (**1b**)	+	+[6]
4-Methoxydalbergione (**2a**)	+/R [4]	+/rac [7]
Obtusaquinol (**3a**)	+/R [4]	+/rac [7]
Obtusafuran (**4a**)	+/2R, 3R [3]	+/rac [8]*
Obtusastyrene (**5a**)	+ [4]	
Obtustyrene (**5b**)	+ [4]	
Obtusaquinone (**6a**)	+[5]	+ [7]

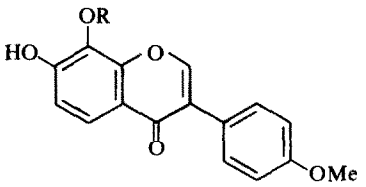
*Later reported to be an artificial rearrangement product of **4a** [9].

(+)-*Obtusafuran*

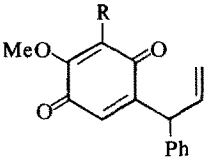
The absence of carbonyl groups and the presence of an oxygenated benzene chromophore without further conjugation were inferred, respectively, by IR and UV spectra. Singlets in the PMR spectrum were assigned to a methoxyl, a hydroxyl and two *para*-related protons on this benzene ring, and to a phenyl group. The spectrum, associated with appropriate spin decoupling experiments indicated furthermore the presence of an OCH—CH—Me unit. This evidence could best be accomodated by the alternative constitutions **4a** and **4b** for obtusafuran.

The relative positions of OH/OMe in obtusafuran were determined by hydrogenolysis to a dihydroxybenzene derivative which, on aerial oxidation, gave an optically active *para*-benzoquinone. The constitutional formula **7** for this compound was confirmed by the synthesis of the racemate. The olefin **8**, obtained by the appropriate Wittig reaction on 2-benzyloxy-4-methoxyacetophenone, was hydrogenated to **9a**, which was oxidized with Frémy's salt [16]. It follows that obtusafuran must be one of the stereoisomers of 5-hydroxy-6-methoxy-3-methyl-2-phenyl-2,3-dihydrobenzofuran (**4a**).

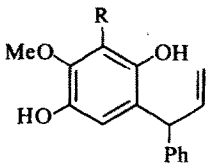
*Part 8 in the series 'The Neoflavonoid Group of Natural Products'. For Part 7 see ref. [1].



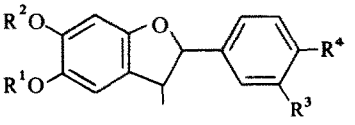
1a R = H
1b R = Me



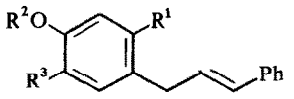
2a R = H
2b R = OMe



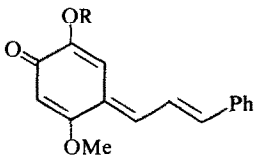
3a R = H
3b R = OMe



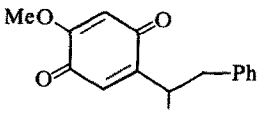
4a $R^1 = R^3 = R^4 = H$, $R^2 = Me$
4b $R^1 = Me$, $R^2 = R^3 = R^4 = Me$
4c $R^1 = Ac$, $R^3 = R^4 = H$, $R^2 = Me$
4d $R^1 = H$, $R^2 = Me$, $R^3 = OH$, $R^4 = OMe$



5a $R^1 = R^2 = R^3 = H$
5b $R^1 = OMe$, $R^2 = R^3 = H$
5c $R^1 = OMe$, $R^2 = Me$, $R^3 = H$
5d $R^1 = OMe$, $R^2 = H$, $R^3 = OH$



6a R = H
6b R = Me



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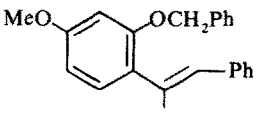

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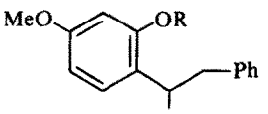
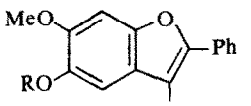
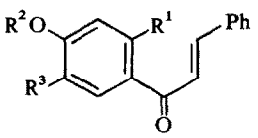


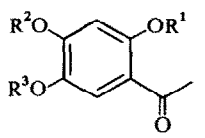
9a R = H
9b $R = CH_2Ph$



10a R = H
10b R = Ac



11a $R^1 = R^2 = R^3 = H$
11b $R^1 = OMe$, $R^2 = Me$, $R^3 = H$
11c $R^1 = OMe$, $R^2 = R^3 = H$
11d $R^1 = OMe$, $R^2 = CH_2Ph$, $R^3 = OCH_2Ph$



12a $R^1 = Me$, $R^2 = R^3 = CH_2Ph$
12b $R^1 = R^3 = H$, $R^2 = CH_2Ph$
12c $R^1 = R^2 = H$, $R^3 = Ac$
12d $R^1 = H$, $R^2 = Me$, $R^3 = Ac$
12e $R^1 = H$, $R^2 = R^3 = CH_2Ph$

The relative stereochemistry of obtusafuran was determined by comparison with the racemic *cis*-2,3-dihydrobenzofuran derivative (*cis*-**4a**), prepared by controlled catalytic hydrogenation of the benzofuran **10a**. This was synthesised by the reaction of 2,5-dihydroxyanisole with 1-bromo-1-phenylpropan-2-one in the presence of BF_3–Et_2O. The IR and PMR spectra of *cis*-**4a** and (+)-obtusafuran are very different, and the latter compound must thus be the 2,3-*trans*-isomer. Configuration of this assignment was obtained by the synthesis of *trans*-**4a** by heating of a DMSO solution of the acetate of the *cis*-isomer (*cis*-**4c**) with *t*-BuOH. The IR and PMR spectra of (±)-*trans*-**4a** and (+)-obtusafuran are identical. The PMR spectra of these *cis*- and *trans* isomers differ particularly with respect to the chemical shifts of H-2 and Me-3 (τ resp. 4.27 and 9.26 for *cis*-**4a** and 4.90 and 8.63 for *trans*-**4a**). Both isomers have the same vicinal $J_{H\text{-}2,H\text{-}3}$ (8 Hz), and this result is of general interest in relation to the considerable discussion [17] concerning the deduction of the relative stereochemistry of the 2,3-dihydrobenzofurans from PMR coupling constants.

The absolute stereochemistry of obtusafuran was determined by ozonolysis of (−)-**7**, derived from natural (+)-obtusafuran, to (*S*)-(−)-methylsuccinic acid [18]. The (−)-quinone therefore has the *S*-configuration (**7**, α-Me, β-H) and (+)-obtusafuran the 2*R*,3*R*-configuration (**4a**, α-Me, β-Ar).

Obtusastyrene and obtustyrene

Isolated as colourless oils, resp. $C_{15}H_{14}O$ and $C_{16}H_{16}O_2$, with UV, IR and PMR (ABX$_2$ system, J_{AB} = 16 Hz) spectra consistent with *E*-cinnamylphenol structures [19], comprising unsubstituted phenyl groups. An AA′BB′ system in the PMR spectrum of obtusastyrene was assigned to the aromatic protons of a *para*-oxygenated phenyl group, while analogous spectra did not provide information concerning the oxygenation pattern of obtustyrene and its methyl ether. These data, as well as biosynthetic considerations, based upon previously recognised structures of cinnamylphenols [1, 15, 20, 21] and our views concerning the biosynthetic relationship between cinnamylphenols and neoflavonoids [22], suggested structures **5a** and **5c** respectively for obtusastryene and for obtustyrene methyl ether.

The cinnamylphenol **5a** was prepared by the reduction of the chalcone **11a** with $LiAlH_4/AlCl_3$ [1, 20, 21] and found to be identical with obtusastyrene. Since double bond rearrangement has been shown to occur in some cases during similar reductions of chalcones [23], this process is unacceptable as structure proof. The unambiguous direct cinnamylation of phenol, however, either by the Claisen rearrangement [19, 24] or, more effectively, by the acid-catalysed condensation with cinnamyl alcohol [25], again gave obtusastyrene (**5a**).

The structural proposal for obtustyrene methyl ether was confirmed by its identity with the synthetic cinnamylphenol **5c** prepared by the reduction of the chalcone **11b** with $LiAlH_4/AlCl_3$, previous work [21] having shown that 2′-oxychalcones give products without rearrangement of the double bond. To distinguish between the alternative structures which thus emerged for obtustyrene, the chalcone **11c** was reduced to **5b**, and this cinnamylphenol proved indeed to be identical with the natural product. Obtustyrene was also synthesised by the direct cinnamylation of 3-methoxyphenol [25].

Obtusaquinone

Subsequently to the original preliminary communication on the structure elucidation and synthesis of this styryl-*para*-quinonemethide [5], a description of its properties [7], including an X-ray crystallographic study establishing the geometry of the trisubstituted double bond as shown in **6a** [26, 27] has become available. The compound can be synthesised either by Ag_2O oxidation of *C*-cinnamylated 4-methoxycatechol [28], or by PbO_2 oxidation of $LiAlH_4/AlCl_3$ reduced 2′-methoxy-4′,5′-dibenzyloxychalcone (**11d**).

The acetophenone **12a**, required for the preparation of this chalcone (**11d**) could be obtained by monobenzylation, followed by methylation of the acetophenone **12b**. The synthesis of **12b** by $K_2S_2O_8$ oxidation of 4-benzyloxy-2-hydroxyacetophenone gave a poor yield [29]. In contradistinction, the reaction of 1,2,4-triacetoxybenzene with BF_3–HOAc gave 5-acetoxy-2,4-dihydroxyacetophenone (**12c**) in high yield. Structure **12c** for this compound was confirmed by monomethylation which gave the known **12d** [30]. Benzylation of **12c** resulted in deacetylation and formation of the dibenzoyl derivative **12e** which, on methylation, gave the required acetophenone **12a**. This was condensed with benzaldehyde to the chalcone **11d**. Reduction of **11d** with $LiAlH_4/AlCl_3$ gave the cinnamylphenol **5d** which, on oxidation with PbO_2 gave the styryl-*para*-quinonemethide **6a**, identical in all respects with natural obtusaquinone.

DISCUSSION

Pyrolysis of (±)-obtusaquinol (**3a**) caused its abnormal Claisen rearrangement into (±)-obtusafuran (*trans*-**4a**). (±)-Obtusafuran, obtained by distillation of oily extracts of specimen 2 (Table 1) may thus be an artifact, and, indeed, chromatographic examination of a petroleum extract failed to reveal the presence of the compound [9]. The analysis of specimen 1, reported in the present paper, revealed the presence of (*R*)-obtusaquinol (**3a**, α-CH=CH$_2$, β-H) and (2*R*,3*R*)-obtusafuran (**4a**, α-Me, β-Ar). In connection with the consequent suspicion that (2*R*,3*R*)-obtusafuran and (2*S*,3*S*)-melanoxin (**4d**, β-Me, α-Ar) from *D. melanoxylon* Guill. et Perr. [31] may also be artifacts, it is to be noted that both were isolated from plant extracts under mild conditions, respectively by washing with hot benzene and chromatography, and by washing with ligroin and crystallization, and could, thus, conceivably, be derived by a variant of the general biogenetic route that gives rise to cinnamylphenols and neoflavonoids [22].

EXPERIMENTAL

Unless otherwise stated spectra were measured in EtOH (UV), $CHCl_3$ (IR), $CDCl_3$ (60 MHz PMR) and MeOH (ORD). All evapns of volatile material were performed under diminished pressure.

Isolation of the constituents. Ground heartwood (2.28 kg), collected in Central America, was continuously extracted with hot C_6H_6. Evapn of the solvent gave a residue (410 g). A portion (70 g) was chromatographed on Si gel (1.2 kg), eluting successively in 2 l. fractions with C_6H_6 (fractions 1–14), C_6H_6–$CHCl_3$ mixtures (fractions 15–62), $CHCl_3$ (fractions 63–90) and MeOH (fractions 90–93). Fractions 1–2 were fatty material. Fractions

3–6 were separated by TLC into **5a** (25 mg). Fractions 7–14 similarly gave (+)-**4a** (840 mg) and **5b** (95 mg). TLC indicated in fractions 15–27 the presence of (+)-**2a** (orange) and **3a** (colourless); attempted elution of the colourless spot, however, yielded only (+)-**2a** (53 mg). Fractions 28–63 were cryst. from EtOH to **6a** (2 g). Fractions 64–74 similarly gave **1b** (100 mg). From fractions 75–93 no pure compd could be isolated.

Identifications. 8-*O*-Methylretusin (**1b**) and (*R*)-4-methoxydalbergione [(+)-**2a**] were identified by direct comparison with authentic samples isolated resp. from *D. variabilis* [13] and *D. nigra* [10].

Obtusastyrene (**5a**). Oil, bp 180° (bath temp., 0.1 mm). [Found: C, 85.35; H, 7.09. $C_{15}H_{14}O$ requires: C, 85.68; H, 6.71%]. λ_{max} (nm): 256, 285, 294 (ε 13600, 4350, 3000). ν_{max} (cm^{-1}): 3550, 3300, 1600. PMR (τ): 2.74 (*s*, Ph), 2.95, 3.26 (A_2B_2 system, J_{AB} = 8 Hz, H-2, H-6 and H-3, H-5), 3.54, 3.64, 6.56 (ABX_2 system, J_{AB} = 15.9 Hz, J_{AX} −1.8 Hz, J_{BX} = 6.9 Hz, $CH_A{=}CH_B{-}CH_{2X}$), 5.0 (*br.s*, OH).

Obtustyrene (**5b**). Oil, bp 140° (bath temp., 0.1 mm). [Found: C, 79.70; H, 7.12. $C_{16}H_{16}O_2$ requires: C, 79.97; H, 6.71%]. λ_{max} (nm): 254, 285, 293 (ε 16800, 5700, 2500). ν_{max} (cm^{-1}): 3600, 1600. PMR (τ): 2.7–3.8 (*m*, 8 ArH), 3.55, 3.66, 6.55 (ABX_2 system; J_{AB} = 16 Hz, $CH_A{=}CH_B{-}CH_{2X}$), 4.0 (*br.s*, OH), 6.22 (*s*, OMe). *Methyl ether* (**5c**). MeI-methylation of **5b** gave **5c**, oil. [Found: M (HRMS), 254.1303. $C_{17}H_{18}O_2$ requires: M, 254.1307]. ν_{max} (cm^{-1}): 1600. PMR (τ): 2.77 (*s*, Ph), 2.6–3.8 (*m*, 3 ArH), 3.3–3.8 (*m*, 2 H), 6.55 (*m*, 2 H) (ABX_2 system, not analysed in detail, $CH_A{=}CH_B{-}CH_{2X}$), 6.18, 6.21 (2 *s*, 2 OMe).

Obtusaquinone (**6a**). Red needles, mp 174° with preliminary softening at 155–156° (cyclohexane). [Found: C, 75.58; H, 5.76. $C_{16}H_{14}O_3$ requires: C, 75.57; H, 5.55%]. λ_{max} (nm): 206, 253, 268, 399 (ε 17300, 7050, 7250, 43800). ν_{max} (cm^{-1}): 3400, 1605, 1600, 1580. PMR (τ): 2.4–2.8 (*m*, Ph), 2.4–3.0 (*m*, 3 H), 3.10 (*br. s*, OH), 3.16 (*s*, H-3), 4.13 (*s*, H-6), 6.15 (*s*, OMe). *Methyl ether* (**6b**). **6a** (95 mg), MeI (1 ml), K_2CO_3 (3 g), Me_2CO (20 ml), refl., 2 hr, gave **6b** (80 mg), dark orange micro-needles, mp 168–169° ($CHCl_3$–cyclohexane). [Found: M (HRMS), 268.1106. $C_{17}H_{16}O_3$ requires: M, 268.1099]. ν_{max} (cm^{-1}): 1640, 1605. 1-(2,4,5-*Trimethoxyphenyl*)-3-*phenylpropane*. Hydrogenation of **6a** in EtOH over 10% Pd/C (room temp., 1 atm.), followed by filtration, evapn of the EtOH and methylation of the residue gave crystals, mp 42–44°, identical with the methyl ether of dihydroviolastyrene [21].

(2R,3R)-*Obtusafuran* (**4a**, α-Me, β-Ar). Pale yellow microcrystals, mp 110–113° (EtOH), $[\alpha]_D^{25}$ +47° (*c* 0.86, MeOH). [Found: C, 74.85; H, 5.93 $C_{16}H_{16}O_3$ requires: C, 74.98; H, 6.29%]. λ_{max} (nm): 235 infl., 305 (ε 2950, 4600). ν_{max} (cm^{-1}): 3500, 1615. PMR (τ): 2.63 (*s*, Ph), 3.30 (*s*, H-4), 3.53 (*s*, H-7), 4.77 (*br.s*, OH), 4.90 (*d*), 6.4–6.9 (*m*), 8.63 (*d*) (AMX_3 system, J_{AM} = 8 Hz, J_{MX} = 7 Hz, J_{AX} = 0 Hz, $OCH_A{-}CH_M{-}CH_{3X}$). 6.15 (*s*, OMe) ORD (*c* 0.132): $[\phi]_{435}$ +340, $[\phi]_{345}$ +1130, $[\phi]_{333}$ +1580, $[\phi]_{312}$ +3150, $[\phi]_{303}$ +1690, $[\phi]_{294}$ −455, $[\phi]_{282}$ −2360, $[\phi]_{270}$ −1800, $[\phi]_{264}$ −1130.

Degradation to (−)-methylsuccinic acid. (a) *Hydrogenolysis and oxidation to (−)-2-methoxy-5-[(2S)-3-phenylpropan-2-yl]-1,4-benzoquinone* (**7**). Hydrogenation (room temp., 1 atm., 4 hr) of (+)-**4a** (270 mg) over 10% Pd/C (100 mg) in HOAc (50 ml) followed by filtration and evapn of the HOAc gave a residue. Purification by TLC permitted aerial oxidation to **7**, yellow needles, mp 118–120° (EtOH), $[\alpha]_D^{25}$ −11.0° (*c* 2.0, $CHCl_3$). [Found: M (MS), 256. $C_{16}H_{16}O_3$ requires: M, 256]. λ_{max} (nm): 207, 264, 325 (ε 13000, 12600, 920). ν_{max} (cm^{-1}): 1675, 1645, 1600. PMR (τ): 2.80 (*s*, Ph), 3.56 (*d*, *J* = 1 Hz, H-6), 4.10 (*s*, H-3), 6.20, 6.4–7.6 (*m*, CH_2—CH), 8.91 (*d*, *J* = 7 Hz, Me). ORD (*c* 0.054, MeOH) $[\phi]_{415}$ −275, $[\phi]_{400}$ −415, $[\phi]_{385}$ 0, $[\phi]_{358}$ +555, $[\phi]_{333}$ +1400, $[\phi]_{318}$ +1800, $[\phi]_{294}$ 0, $[\phi]_{286}$ −555, $[\phi]_{278}$ −2200, $[\phi]_{262}$ 0. (b) *Oxidation of (−)-7.* Ozonised oxygen was passed through (−)-**7** (125 mg) in HOAc (20 ml) (room temp., 15 hr). After evapn of the HOAc 3% H_2O_2 (10 ml) was added, followed by heating (100°, 10 min), acidification and evapn. The residue was triturated with Et_2O. Filtration and evapn of the H_2O gave a residue which was recryst. to (−)-methylsuccinic acid (11 mg), prisms, mp 105–110° (C_6H_6–Et_2O), $[\alpha]_D^{20}$ −7.8 ± 1.0° (*c* 0.6, H_2O) (lit. [32] mp 101–103°, $[\alpha]_D^{20}$ −8.7° (*c* 2.0, H_2O), lit. [33] mp 110–113°, $[\alpha]_D^{18}$ −14.9 ± 4.2° (*c* 0.6, EtOH).

Synthesis of 4′-hydroxy-2′-methoxychalcone (**11c**). 4-Hydroxy-2-methoxyacetophenone [34] (3.2 g), PhCHO (2 g), EtOH (10 ml) and KOH (5 g) in H_2O (10 ml) were stirred (room temp., 16 hr). The mixture was acidified and extracted with C_6H_6. Evapn of the C_6H_6 gave a residue which was recryst. to **11c** (2.6 g), mp 152–153° (EtOH). [Found: C, 75.61; H, 5.69. $C_{16}H_{14}O_3$ requires C, 75.57; H, 5.55%].

Synthesis of 4′,5′-dibenzyloxy-2′-methoxychalcone (**11d**). (a) *Acylation of 1,2,4-triacetoxybenzene* [35]. BF_3–HOAc (60 ml) was added to this compd (20 mg) and the mixture heated (100°, 10 min). Ice H_2O (250 ml) was then added and the ppt. (13 g) collected. A portion was sublimed (140°, 0.1 mm) giving 5-acetoxy-2,4-dihydroxyacetophenone (**12c**), microcrystals, mp 163°. [Found: C, 56.85; H, 4.91. $C_{10}H_{10}O_5$ requires: C, 57.14; H, 4.80%]. ν_{max} (cm^{-1}): 1760, 1630. PMR (τ): −2.62 (*s*, OH), 0.38 (*br. s*, OH), 2.37 (*s*, H-6), 3.55 (*s*, H-3). PMR (C_5H_5N, τ) 7.50 (*s*, Ac), 7.73 (*s*, OAc). *Monomethyl ether* (**12d**). **12c** (2 g), MeI (1 ml) and K_2CO_3 (5 g) in Me_2CO (20 ml) (reflux, 3 hr) gave **12d** (400 mg), needles, mp 104°. [Found: C, 59.23; H, 5.55. $C_{11}H_{12}O_5$ requires: C, 58.92; H, 5.40%], identical with an authentic sample, mp 104° [30]. (b) *Benzylation of* **12c**. **12c** (20 g), $PhCH_2Cl$ (30 g) and K_2CO_3 (30 g) in Me_2CO (300 ml) were heated under reflux (3 days). The product was purified by chromatography (Si gel, C_6H_6) to 4,5-dibenzyloxy-2-hydroxyacetophenone (**12e**, 17.1 g), needles, mp 96–97° (EtOH). [Found: C, 75.60; H, 5.49. $C_{22}H_{20}O_4$ requires: C, 75.84; H, 5.79%]. ν_{max} (cm^{-1}): 1630. PMR (τ): −2.52 (*s*, OH), 2.62, 2.65 (2 *s*, 2 Ph), 2.86 (*s*, H-6), 3.51 (*s*, H-3), 4.84, 4.95 (*s*, 2 CH_2), 7.58 (*s*, Ac). (c) *Methylation of* **12e**. **12e** (10 g), MeI (15 ml) and K_2CO_3 (20 g) in Me_2CO were heated under reflux (16 hr) giving 4,5-dibenzyloxy-2-methoxyacetophenone (**12a**, 14.6 g), needles, mp 76° (EtOH). [Found: C, 75.90; H, 6.08. $C_{23}H_{22}O_4$ requires: C, 76.22; H, 6.12%]. ν_{max} (cm^{-1}): 1660, 1600. PMR (τ): 2.46 (H-6), 2.60 (*s*, 2 Ph), 3.47 (*s*, H-3), 4.78, 4.88 (2 *s*, 2 CH_2), 6.21 (*s*, OMe), 7.46 (*s*, Ac). (d) *Condensation of* **12a** *with* PhCHO. **12a** (10 g), PhCHO (3 g), EtOH (40 ml) and KOH (20 g) in H_2O (20 ml) were stirred (room temp., 2 hr). The mixture was acidified, the ppt. collected and recryst. to 4′,5′-dibenzyloxy-2′-methoxychalcone (**11d**, 9.5 g), yellow microneedles, mp 113° (EtOH). [Found: C, 79.81; H, 5.93. $C_{30}H_{26}O_4$ requires: C, 79.98; H, 5.82%]. ν_{max} (cm^{-1}): 1650, 1600. PMR (τ): 2.3–2.9 (*m*, 2 Ph, PhCH=CH, H-6′), 3.48 (*s*, H-3′), 4.83, 4.92 (2 *s*, 2 CH_2), 6.25 (*s*, OMe).

Synthesis of E-cinnamylphenols. $LiAlH_4$ (resp. 1, 1, 1.3 and 1 g) in Et_2O (20 ml) was added to the chalcone (**11a** [36] 2.5 g, **11b** [37] 4 g, **11c** (see above) 3.2 g, **11d** (see above) 2 g) and the mixture was heated under reflux (30 min). $AlCl_3$ (resp. 10, 7.9, 10 and 10 g) in Et_2O (20 ml) was then added and the mixture further heated (30 min). Excess reagent was decomposed with H_2O, and the resulting mixture was acidified and extracted with Et_2O. Evapn of the Et_2O and TLC purification of the residue gave the cinnamylphenols resp **5a** (1.91 g) identical with natural obtusastyrene; **5c** (2.5 g) identical with obtustyrene monomethyl ether **5b** (1.75 g) identical with natural obtustyrene; **5d** (1.4 g) *E*-1-(4,5-dihydroxy-2-methoxybenzyl)-2-phenylethylene. Identities were established by elemental analysis or HRMS, IR and PMR.

Synthesis of obtusaquinone (**6a**) *and obtusaquinone methyl ether* (**6b**). PbO_2 (resp. 2 and 1 g) was added to the cinnamylphenol (**5d** [see above] 0.7 g, violastyrene [21] 0.2 g) in dry C_6H_6 (resp. 50 and 10 ml), the mixture shaken (resp. 1 and 10 min), filtered, and the product purified by TLC (Si gel, $CHCl_3$–MeOH) resp. to **6a** (100 mg) and **6b** (100 mg), identical (mp, mmp, IR and PMR) resp. with natural obtusaquinone and its methyl ether.

Synthesis of (±)-2-methoxy-5-(3-phenylpropan-2-yl)-1,4-benzoquinone (**7**). (a) *Preparation of Z- and E-1-(2-benzyloxy-4-methoxyphenyl)-1-methyl-2-phenylethylene* (**8**). Triphenylbenzylphosphonium chloride [38] (9 g) was added to EtONa (Na 1.4 g) in EtOH (50 ml) and the mixture was stirred (15 min). 2-Benzyloxy-4-methoxyacetophenone [39] (5 g) in EtOH (10 ml) was then added and the mixture heated under reflux (16 hr), poured

into H_2O and extracted with Et_2O. Chromatography (Si gel, C_6H_6) gave **8** (5.7 g), oil. [Found: C, 83.55; H, 6.87. $C_{23}H_{22}O_2$ requires: C, 83.60; H, 6.71%]. (b) *Hydrogenation of* **8** *into* (+)-1-(*2-hydroxy-4-methoxyphenyl*)-1-*methyl-2-phenylpropane* (**9a**). The ethylenes **8** (1.55 g) in HOAc (40 ml) were hydrogenated (room temp., 1 atm.) over 10% Pd/C (100 mg) until absorption of 250 ml H_2. The mixture was filtered and the HOAc evapd. The residue was separated by TLC (Si gel, $CHCl_3$) into **9a** (140 mg) and (±)-1-(2-benzyloxy-4-methoxyphenyl)-1-methyl-2-phenylethane (**9b**, 435 mg). **9a**, oil. [Found: M (HRMS), 242.1306. $C_{16}H_{18}O_2$ requires: M, 242.1307]. ν_{max} (cm^{-1}): 3250, 1600. PMR (τ): 2.81 (*s*, Ph), 3.56 (*dd*), 3.70 (*d*), 2.95 (*d*) (ABX system, J_{AB} = 2.5 Hz, J_{AX} = 8 Hz, H-5, H-3, H-6), 5.3 (*br. s*, OH), 6.26 (*s*, OMe), 6.5–7.5 (*m*, CH_2—CH), 8.78 (*d*, *J* = 7 Hz, Me). **9b**, oil, bp 165° (bath temp., 0.1 mm). [Found: C, 82.82; H, 7.38. $C_{23}H_{24}O_2$ requires: C, 83.10; H, 7.28%]. ν_{max} (cm^{-1}): 1600. PMR (τ): 2.68, 2.92 (2 *s*, 2 Ph), 3.58 (*dd*), 3.52 (*d*), 2.97 (*d*) (ABX system, J_{AB} = 2.5 Hz, J_{AX} = 8 Hz, H-5, H-3, H-6), 5.06 (*s*, CH_2), 6.30 (*s*, OMe), 6.3–7.6 (*m*, CH_2—CH), 8.82 (*d*, *J* = 7 Hz, Me). (c) *Oxidation of* **9a** *to* (±)-2-*methoxy*-5-(*3-phenylpropan-2-yl*)-1,4-*benzoquinone* (**7**). $ON(SO_3K)_2$ (1.2 g) in H_2O (3 ml) was added to **9a** (100 mg) in MeOH (20 ml). The mixture was stirred (1 hr) and extracted with $CHCl_3$. Evapn of the $CHCl_3$ gave a residue which was recryst. from EtOH to **7** identical (mp, elemental analysis, IR and PMR) with the degradation product of (+)-obtusafuran.

Synthesis of (±)-2,3-cis-5-*hydroxy*-6-*methoxy*-3-*methyl*-2-*phenyl*-2,3-*dihydrobenzofuran* (cis-**4a**). (a) *Preparation of* 5-*hydroxy*-6-*methoxy*-3-*methyl*-2-*phenylbenzofuran* (**10a**). Br_2 (32 g) was added dropwise to a stirred ice cold soln of benzyl methyl ketone (26.8 g) in HOAc (180 ml). The mixture was stirred (0°, 10 min), then heated (100°) until colourless, poured into H_2O, washed with H_2O, and distilled yielding 1-bromo-1-phenylpropan-2-one [40] (13 g), bp 90–94°, 1 mm. A mixture of this compd (2.5 g), 2,5-dihydroxyanisole [41] and BF_3–Et_2O (10 ml) was heated (100°, 30 min), poured into H_2O, and extracted with $CHCl_3$. Evapn of the $CHCl_3$ gave a residue which was purified by chromatography (Si gel, $CHCl_3$) and recryst. to **10a** (1.1 g) pale yellow microcrystals, mp 161° (EtOH). [Found: C, 75.19; H, 5.16. $C_{16}H_{14}O_3$ requires: C, 75.57; H, 5.55%]. ν_{max} (cm^{-1}): 3500, 1600. PMR (τ): 2.1–2.8 (*m*, Ph), 3.00 (*s*, H-4, H-7), 4.46 (*s*, OH), 6.10 (*s*, OMe), 7.60 (*s*, Me). (b) *Hydrogenation of* **10a** (350 mg) over 10% Pd/C (100 mg) in EtOAc (25 ml) (room temp., 1 atm., 16 hr), followed by filtration and evap. of the EtOAc gave a residue which was purified by TLC (Si gel, $CHCl_3$) and cryst. to *cis*-**4a** (72 mg), pale yellow microcrystals, mp 110–111° (EtOH). [Found: C, 74.71, H, 6.45. $C_{16}H_{16}O_3$ requires: C, 74.98; H, 6.29%]. λ_{max} (nm): 235 infl., 305 (ε 4800, 6400). ν_{max} (cm^{-1}): 3500, 1610. PMR (τ): 2.72 (*s*, Ph), 3.28 (*s*, H-4), 3.49 (*s*, H-7), 4.71 (*s*, OH), 4.27 (*d*), 6.2–6.6 (*m*), 9.26 (*d*) (AMX_3 system, J_{AM} = 8 Hz, J_{MX} = 7 Hz, OCH_A—CH_M—CH_{3X}), 6.16 (*s*, OMe).

Synthesis of (±)-*obtusafuran* (trans-**4a**) (a) *Acetylation of* **10a** *to* 5-*acetoxy*-6-*methoxy*-3-*methyl*-2-*phenylbenzofuran* (**10b**). A mixture of **10a** (450 mg), Ac_2O (5 ml) and C_5H_5N (10 ml) was kept at room temp. (16 hr), poured into H_2O and extracted with Et_2O. Evapn of the volatile material gave a residue which was recryst. to **10b** (400 mg), mp 120–121.5° ($MeOH$–H_2O). [Found: C, 73.21; H, 5.69. $C_{18}H_{16}O_4$ requires: C, 72.96; H, 5.44%]. (b) *Hydrogenation of* **10b** (1g) over 10% Pd/C (300 mg) in EtOH (25 ml) (room temp., 1 atm., 16 hr), followed by filtration and evapn gave *cis*-**4c** (0.8 g). (c) *Isomerization of* cis-**4c** *to* (±)-2,3-trans-5-*hydroxy*-6-*methoxy*-3-*methyl*-2-*phenyl*-2,3-*dihydrobenzofuran*. *Cis*-**4c** (0.2 g) in DMSO (25 ml) containing *t*-BuOH (3 g) was heated (100°, 16 hr) under N_2. The mixture was poured into H_2O, acidified, and extracted with C_6H_6. Purifications by TLC (Si gel, $CHCl_3$) gave (±)-*trans*-**4a** (15 mg), mp 90–95°, identical (IR and PMR) with natural (+)-obtusafuran (**4a**, α-Me, β-Ar).

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