Natural Benzofurans. Synthesis of Eupomatenoids-1, -3, -4, -5, -6, -7, and -13

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A group of eupomatenoids, natural lignans possessing 2-aryl-3-methyl-5-propenylbenzofuran structures. have been synthesized by short pathways which include the intramolecular Wittig reaction of an *o*-bromoethylaryl benzoate ester as a key step.

From the bark of *Eupomatia laurina* R. Br. there was isolated a benzofuran lignan, initially named eupomatene (subsequently eupomatenoid-1), which was shown to have structure (1) and was also synthesized.[1] In a more extensive examination of bark constituents,[2] six more benzofurans (eupomatenoids 2—7) and a dihydrobenzofuran (eupomatenoid-8, licarin B [3]) were isolated and identified. From the leaves, two further benzofurans (eupomatenoid-9 and -10), and from the wood an additional two (eupomatenoid-11 and -12) [4] were obtained. Most recently [5] eupomatenoid-13 and the related (±)-*trans*-dehydrodi-isoeugenol (2) (licarin-A[3]) have been reported as being present in the bark.

In short, of the assigned structures of these fourteen isolated natural products, nine are 2-aryl-3-methyl-5-[(*E*)-propenyl]-benzo[*b*]furans which may be represented by the general structure (3; R = H or OMe), two are related 2,3-dihydrobenzofurans [*e.g.* (2)], and three (eupomatenoid-9, -10, and -11) are 2-aryl-3-methylbenzofurans with their C-5 substituent formally derived by oxidation of the parent propenyl side-chain, *e.g.* eupomatenoid-9 (4). The pendent aryl rings have phenol or phenolic ether functionality (4-hydroxy-3-methoxyphenyl, 3,4-methylenedioxyphenyl, 3,4-dimethoxyphenyl, *p*-hydroxyphenyl) commonly found among lignans. Of these products, only eupomatenoid-1, -7, -8, and -12 have been previously synthesized,[1,6] by routes which are relatively lengthy or specific to individual members. We report here a procedure of general applicability which we have employed to synthesize eupomatenoid-1, -3, -4, -5, -6, -7, and -13.

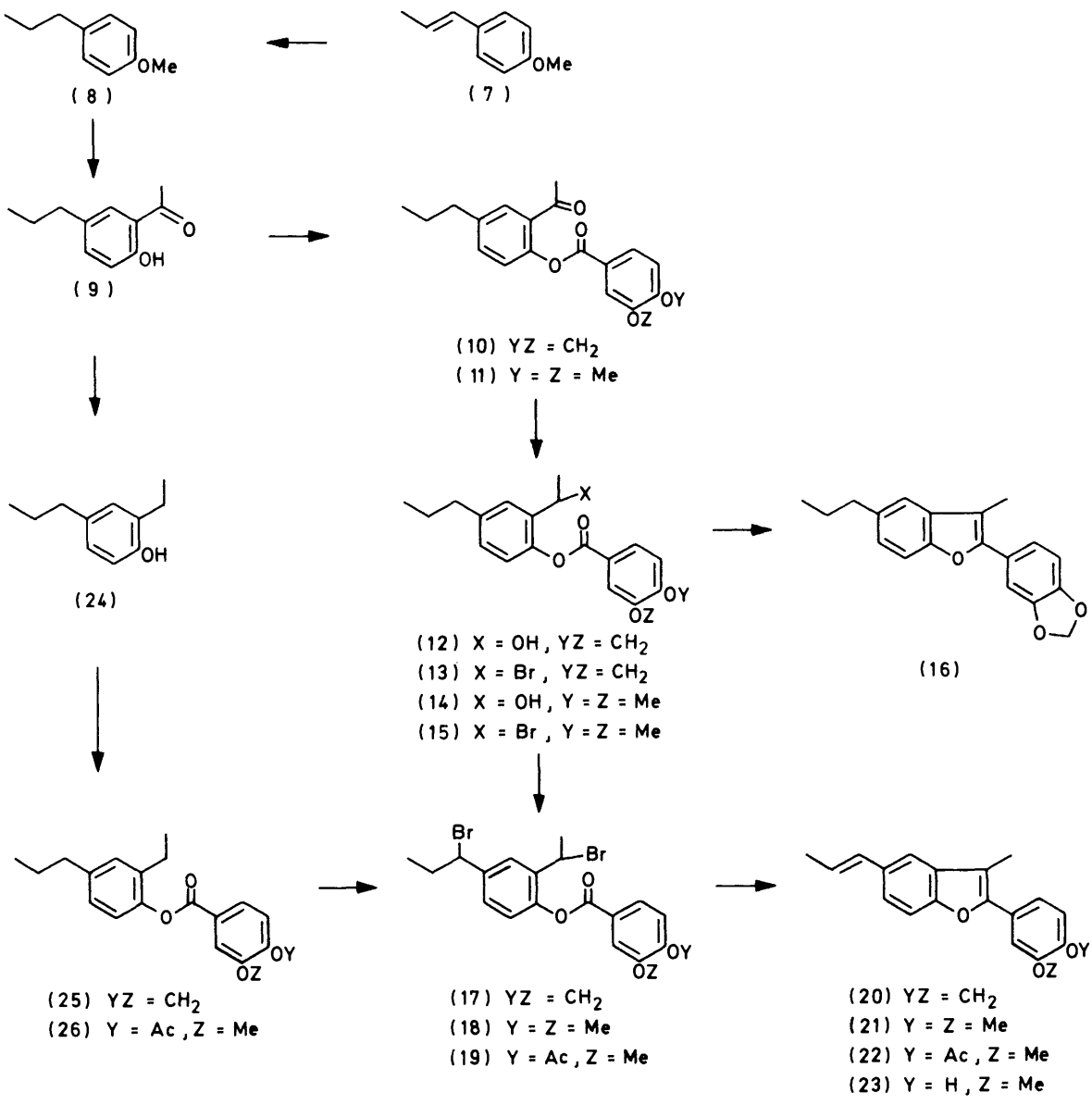
The formation of a cycloalkene by an intramolecular Wittig reaction, in which the ethylenic bond is formed from a carbonyl group and alkylidenephosphorane group within the same molecule, has been extensively examined and comprehensively reviewed.[7] Although an ester function is considered to be much less reactive than an aldehyde or ketone in Wittig carbonyl olefination, Hercouet and Le Corre [8] in a preliminary communication demonstrated a route to 2-arylbenzo[*b*]-furans (6) by the action of an arenecarboxylic acid chloride on *o*-hydroxybenzyltriphenylphosphonium bromide (5) in the presence of triethylamine [reaction (1)]. Significant extensions of this principle have recently been reported in their definitive paper.[9]

We initially examined an intramolecular Wittig procedure for the construction of a 2-aryl-3-methylbenzo[*b*]furan by attempting the synthesis of 3-methyl-2-(3,4-methylenedioxyphenyl)-5-propylbenzo[*b*]furan (dihydroeupomatenoid-3) (16), a known [2] derivative of eupomatenoid-3 (3; Ar = 3,4-methylenedioxyphenyl, R = H), *i.e.* (20). This procedure is outlined in Scheme 1.

Catalytic hydrogenation of anethole (7) at atmospheric pressure gave 4-propylanisole (8), which on acylation with acetyl chloride and aluminium chloride in methylene dichloride gave the known 2-hydroxy-5-propylacetophenone (9).[10] Conversion of this phenol into the substituted aryl benzoate (10) was followed by catalytic hydrogenation to yield the benzylic alcohol (12), which in turn afforded the benzylic bromide (13) on treatment with triphenylphosphine dibromide. Treatment of compound (13) with triphenylphosphine in acetonitrile to form the triphenylphosphonium bromide salt, followed by heating with triethylamine in toluene afforded, in 20—30% isolated yield, dihydroeupomatenoid-3 (16) with the expected ^{1}H n.m.r. spectrum, and a m.p. in agreement with that previously reported.[2]

We next examined the suitability of the α-bromoethyl compound (13) as an intermediate in the synthesis of the natural 5-[(*E*)-propenyl]benzofuran eupomatenoid-3 (20). Upon treatment with *N*-bromosuccinimide (NBS), compound (13) underwent benzylic bromination of the propyl side-chain, yielding the dibromide (17). This compound, upon treatment with two molar equivalents of triphenylphosphine followed by base treatment, underwent the desired simultaneous formation of the benzofuran heterocycle and side-chain dehydrobromination to afford eupomatenoid-3 (20) directly. The product was characterized by catalytic hydrogenation to give dihydroeupomatenoid-3 (16), identical with a sample prepared from the monobromide (13).

The success of our dibromide cyclization–elimination procedure suggested that the simple reagent 2-ethyl-4-propylphenol (24) would serve as an excellent starting material both for a short synthesis of eupomatenoid-3, and also for the analogous congeners eupomatenoid-4 (3; Ar = 3,4-dimethoxyphenyl, R = H), eupomatenoid-5 (3; Ar = 4-hydroxy-3-methoxyphenyl, R = H), and eupomatenoid-6 (3; Ar = *p*-hydroxyphenyl, R = H). This has proven to be the case. Thus the required phenol (24) was prepared by Clemmensen



Scheme 1.

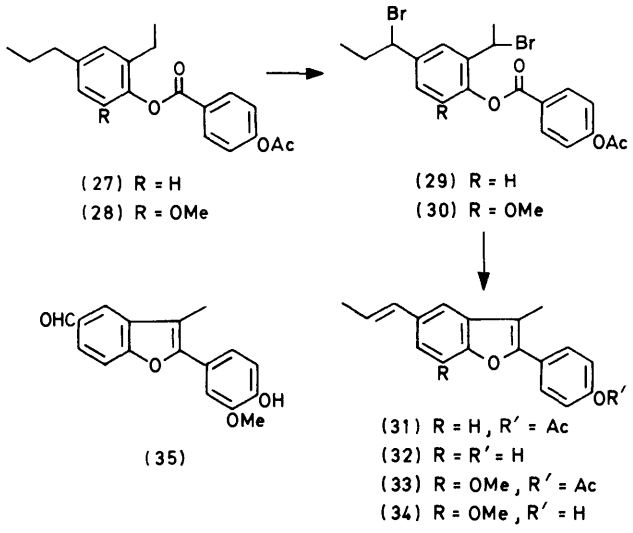
reduction of the acetophenone (9) already at hand. Esterification of the phenol (24) to give the piperonyloyl ester (25), followed by benzylic bromination of each alkyl chain with NBS, gave the same penultimate dibromide (17).

Eupomatenoid-4 (3; Ar = 3,4-dimethoxyphenyl, R = H) was similarly synthesized. Esterification of the phenolic acetophenone (9) with veratroyl chloride gave the ester (11) which, on catalytic hydrogenation, yielded the benzylic alcohol (14). The benzylic bromide (15) was obtained from the alcohol (14) by the action of triphenylphosphine dibromide and was converted into the dibromide (18) by bromination with NBS. Application of the Wittig procedure then yielded eupomatenoid-4 (21).

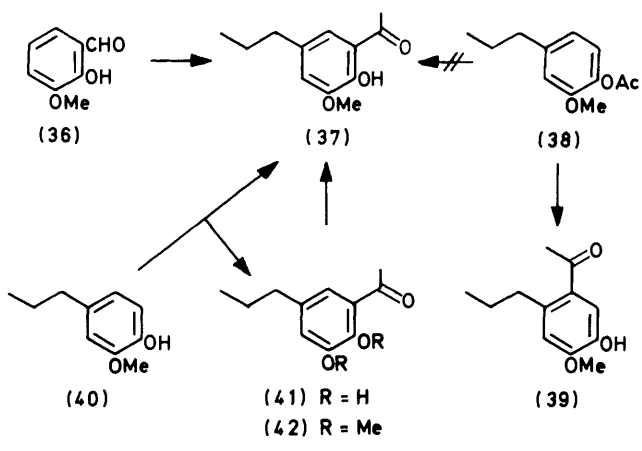
Eupomatenoid-5 (3; Ar = 4-hydroxy-3-methoxyphenyl, R = H) was synthesized by the abbreviated procedure starting from 2-ethyl-4-propylphenol (24). Esterification with 4-acetoxy-3-methoxybenzoyl chloride gave the ester (26) which, with two molar equivalents of NBS, gave the dibromide (19). Cyclization of compound (19) by the Wittig procedure gave eupomatenoid-5 acetate (22), and thence eupomatenoid-5 (23) by reductive hydrolysis with lithium aluminium hydride.

The same pathway readily led to eupomatenoid-6 (3; Ar = *p*-hydroxyphenyl, R = H). Thus, conversion of the phenol (24) into the ester (27) with *p*-acetoxybenzoyl chloride was followed by bis-benzylic bromination to give the dibromide (29) which, on Wittig cyclization, gave eupomatenoid-6 acetate (31) and thence eupomatenoid-6 (32) (Scheme 2).

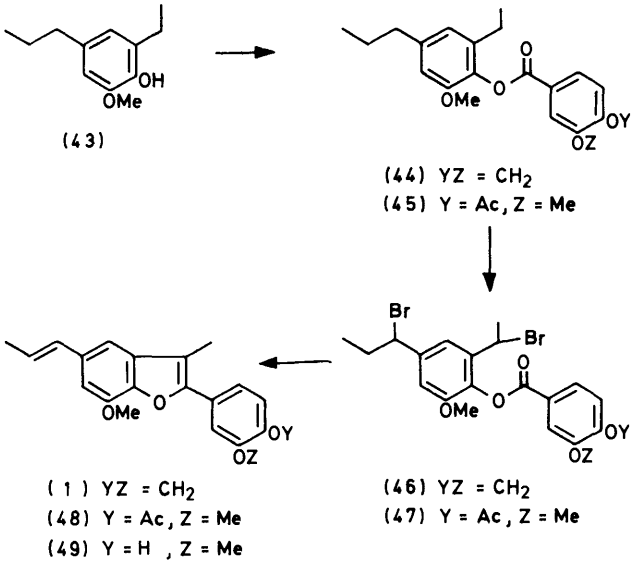
Eupomatenoid-1, -12, -7, and -13 are the respective 7-methoxy analogues (3; R = OMe) of eupomatenoid-3, -4, -5, and -6. In projecting syntheses of these analogues, the ready accessibility of 2-hydroxy-3-methoxy-5-propylacetophenone (37), the required starting material common to all four natural products, was of immediate concern. Although a synthesis of this compound from *o*-vanillin (36) has been reported,[11] it was deemed to be impracticable, since eight steps were required. An apparently attractive route to compound (37) by a Fries rearrangement of dihydroeugenol



Scheme 2.



Scheme 3.



Scheme 4.

acetate (38) was examined by Taylor and his co-workers,[1] but their route foundered when the *m*-acylphenol (39) was unexpectedly obtained. The same workers [1] did achieve a simplification of Pew's method [11] by reducing the number of steps from eight to five, but since this still appeared to be cumbersome, we sought an improved route.

The acylation of phenol derivatives by the action of carboxylic acids in the presence of boron trifluoride has been examined by both Meerwein [12] and Kindler [13] among others, and it is known that the ratio of the normal *ortho*/*para* isomers is temperature dependent. The abnormal formation of *meta*-acylphenols from guaiacol (2-methoxyphenol) derivatives by Fries rearrangement of phenolic esters was recognized many years ago by Reichstein.[14] In a re-examination of the Fries rearrangement using the Meerwein method, Da Re and Cimatoribus [15] showed that the formation of the *ortho*-isomer was favoured when the reaction was performed at temperatures >120 °C. We now find that by heating dihydroeugenol (40) with acetic acid and boron trifluoride at 150 °C, *ortho*-acetylation does indeed occur, accompanied by partial demethylation, to give a mixture of the required acyl phenol (37) and the catechol (41) (Scheme 3). Methylation of this phenolic mixture with dimethyl sulphate gave the dimethyl ether (42) which underwent selective demethylation on treatment with aluminium chloride. In this manner compound (37) was conveniently obtained from eugenol in 34% overall yield, and was in turn readily converted into 2-ethyl-6-methoxy-4-propylphenol (43) by Clemmensen reduction. This dialkylphenol served as the starting material for the syntheses of eupomatenoid-1 (1), eupomatenoid-7 (49), and eupomatenoid-13 (34).

The major *Eupomatia* constituent, eupomatenoid-1 (1), was obtained from compound (43) in three steps: formation of the piperonyloyl ester (44), benzylic bromination to give the dibromide (46), and Wittig intramolecular cyclization–dehydrohalogenation to give the required benzofuran (Scheme 4).

Similarly, esterification of the phenol (43) with 4-acetoxy-3-methoxybenzoyl chloride gave the ester (45) which on reaction with NBS yielded the dibromide (47). This, on cyclization–dehydrohalogenation, afforded eupomatenoid-7 acetate (48). Hydrogenolysis of this ester with lithium aluminium hydride then afforded eupomatenoid-7 (49) (Scheme 4).

The same approach led to eupomatenoid-13 (34) from the phenol (43) *via*, successively, the ester (28), the dibromide (30), and the benzofuran acetate (33) (Scheme 2).

Since eupomatenoid-5 (23) has been converted by methylation into eupomatenoid-4 (21),[2] and by oxidation of the acetate derivative into eupomatenoid-9 (4) and thence into eupomatenoid-10 (35),[3] the synthesis of compound (23) constitutes a total synthesis of the last three named natural products. Recently, there have been isolated [16] from the roots of *Ratanhiae radix* two benzofurans which were named ratanhiaphenol-I and -II. We note that the structure suggested for ratanhiaphenol-II is the same as that of eupomatenoid-6, and the close agreement in reported constants leaves little doubt regarding their identity.

Experimental

M.p.s were determined with a Gallenkamp apparatus and are uncorrected. Varian EM-390, Perkin-Elmer R-32, and Bruker FT/90-MHz spectrometers were employed for the determination of ^{1}H n.m.r. spectra, with tetramethylsilane (TMS) as internal reference and deuteriochloroform as solvent (unless otherwise stated). The silica gel used for chromatography was

J. T. Baker (40—400 mesh) and light petroleum refers to the fraction boiling in the range 80—95 °C.

1-*Methoxy*-4-*propylbenzene* (8).—A solution of anethole (7) (5.7 g) in ethyl acetate (50 ml) was stirred with 5% palladium–charcoal (1 g) under hydrogen at atmospheric pressure for 24 h. Removal of the catalyst and solvent gave 4-propylanisole (8) as a liquid, b.p. 50—54 °C at 0.7 mmHg (lit.,[17] 76.5 °C at 6 mmHg); δ 0.93 (3 H, t, *J* 7.5 Hz, CH_2Me), 1.4—1.8 (2 H, m, CH_2Me), 2.53 (2 H, t, *J* 7.5 Hz, $ArCH_2$), 3.76 (3 H, s, OMe), 6.78 (total 2 H, d, *J* 8 Hz, 2- and 6-H), and 7.08 (total 2 H, d, *J* 8 Hz, 3- and 5-H).

2-*Hydroxy*-5-*propylacetophenone* (9).—To a stirred suspension of aluminium chloride (4.17 g) in dichloromethane (40 ml) at 0 °C was added a solution of the ether (8) (1.95 g) in the same solvent (25 ml) followed by the dropwise addition of acetyl chloride (1.4 ml). The mixture was then heated under reflux under N_2 for 4 h and was then quenched by the addition of ice–water (50 ml). The organic layer was separated, washed with water, dried ($MgSO_4$), and evaporated to afford the ketone (9) as a yellow liquid (2.0 g), b.p. 98—105 °C at 1.2 mmHg (lit.,[10] 80—85 °C at 0.2 mmHg); δ 0.93 (3 H, t, *J* 7.5 Hz, CH_2Me), 1.4—1.8 (2 H, m, CH_2Me), 2.53 (2 H, t, *J* 7.5 Hz, $ArCH_2$), 2.60 (3 H, s, COMe), 6.84 (1-H, d, *J* 7.5 Hz, 3-H), 7.24 (1 H, dd, *J* 7.5 and 2 Hz, 4-H), 7.45 (1 H, d, *J* 2 Hz, 6-H), and 12.36 (1 H, s, OH).

2-*Acetyl*-4-*propylphenyl* 3,4-*Methylenedioxybenzoate* (10).—A mixture of the phenol (9) (1.0 g) and piperonyloyl chloride * (1.2 g) in pyridine (10 ml) was stirred at room temperature overnight. The solvent was then removed under pressure and the residue was extracted with dichloromethane and dilute hydrochloric acid (4%). The organic phase was washed (water), dried ($MgSO_4$), and evaporated, and the residual solid (1.9 g) was recrystallized from ethanol to give the *ester* (10) as prisms (1.68 g), m.p. 113—114 °C; $\nu_{max.}$ (CH_2Cl_2) 1 735 and 1 690 cm^{-1} (Found: C, 70.3; H, 5.7. $C_{19}H_{18}O_5$ requires C, 69.9; H, 5.6%); δ† 0.97 (3 H, t, *J* 7.5 Hz, CH_2Me), 1.48—1.80 (2 H, m, CH_2Me), 2.52 (3 H, s, COMe), 2.65 (2 H, t, *J* 7.5 Hz, $ArCH_2$), 6.08 (2 H, s, OCH_2O), 6.91 (1 H, d, *J* 8 Hz, 6- or 5′-H), 7.10 (1 H, d, *J* 8 Hz, 5′- or 6-H), 7.37 (1 H, dd, *J* 8 and 2 Hz, 5- or 6′-H), 7.61 (total 2 H, d, *J* 1.5 Hz, 2′- and 3-H), and 7.82 (1 H, dd, *J* 8 and 2 Hz, 6′- or 5-H).

2-(1-*Hydroxyethyl*)-4-*propylphenyl* 3,4-*Methylenedioxybenzoate* (12).—A solution of the ketone (10) (450 mg) in ethyl acetate (40 ml) was stirred with 5% palladium–charcoal (150 mg) under hydrogen at 1 atm pressure overnight. Removal of the catalyst and solvent gave a solid residue, which on crystallization from light petroleum–ethyl acetate yielded the *alcohol* (12) as prisms (450 mg), m.p. 81—82 °C; $\nu_{max.}$ (KBr) 3 520 and 1 715 cm^{-1} (Found: C, 69.6; H, 6.15. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.1%); δ 0.96 (3 H, t, *J* 7 Hz, CH_2Me), 1.45—1.79 (2 H, m, CH_2Me), 1.47 [3 H, d, *J* 6 Hz, CH(OH)*Me*], 2.02 (1 H, d, *J* 2.5 Hz, OH), 2.63 (2 H, t, *J* 7.5 Hz, $ArCH_2$), 4.89—5.13 [1 H, m, *J* 3 Hz, C*H*(OH)], 6.09 (2 H, s, OCH_2O), 6.91 (1 H, d, *J* 8.5 Hz, 6-H), 7.05—7.21 (total 2 H, m, 5- and 5′-H), 7.39 (1 H, d, *J* 2 Hz, 3-H), 7.60 (1 H, d, *J* 1.5 Hz, 2′-H), and 7.81 (1 H, dd, *J* 8 and 1.5 Hz, 6′-H).

2-(1-*Bromoethyl*)-4-*propylphenyl* 3,4-*Methylenedioxybenzoate* (13).—Triphenylphosphine (433 mg) and bromine (295 mg) were dissolved in acetonitrile (22 ml) and a solution of the alcohol (12) (440 mg) in the same solvent (25 ml) was added. The mixture was heated under reflux for 75 min and was then concentrated under reduced pressure. The residual orange oil was extracted with diethyl ether. The extracts were washed (water), dried ($MgSO_4$), and evaporated to give an amber oil. Purification by filtration of a solution in light petroleum through a short column of silica gel, and elution with light petroleum–dichloromethane gave the *benzylic bromide* (13) as an oil (Found: M^+, 390.0468. $C_{19}H_{19}BrO_4$ requires *M*, 390.0467); δ 0.93 (3 H, t, *J* 7 Hz, CH_2Me), 1.43—1.83 (2 H, m, CH_2Me), 1.99 (3 H, d, *J* 7 Hz, CHBr*Me*), 2.58 (2 H, t, *J* 8 Hz, $ArCH_2$), 5.20 (1 H, q, *J* 7 Hz, CHBr), 6.00 (2 H, s, OCH_2O), 6.85 (1 H, d, *J* 9 Hz, 6- or 5′-H), 7.0—7.43 (total 2 H, m, 5-H and 5′- or 6-H), 7.38br (1 H, s, 3-H), 7.62 (1 H, d, *J* 2 Hz, 2′-H), and 7.85 (1 H, dd, *J* 8 and 2 Hz, 6′-H).

This compound readily eliminated hydrogen bromide on attempted distillation and was consequently used without further purification.

3-*Methyl*-2-(3,4-*methylenedioxyphenyl*)-5-*propylbenzo*[b]*furan* [*Dihydroeupomatenoid*-3] (16).—Triphenylphosphine (225 mg) was added to a solution of the benzyl bromide (13) (278 mg) in acetonitrile (20 ml) and the mixture was heated under reflux under N_2 for 24 h. The oil obtained after removal of the solvent was dissolved in a mixture of toluene (50 ml) and triethylamine (0.6 ml) and the solution was heated under reflux under N_2 for 12 h. Filtration and removal of the solvent gave an oil which was dissolved in light petroleum–dichloromethane (1 : 9) and chromatographed on silica gel. Elution with the same solvent gave dihydroeupomatenoid-3 (16) as a solid which was crystallized from methanol as needles (42 mg), m.p. 84—85 °C (lit.,[2] 86—87 °C); δ‡ 0.97 (3 H, t, *J* 7 Hz, CH_2Me), 1.49—1.91 (2 H, m, CH_2Me), 2.42 (3 H, s, 3-Me), 2.70 (2 H, t, *J* 8 Hz, $ArCH_2$), 6.01 (2 H, s, OCH_2O), 6.91 (1 H, d, *J* 8.5 Hz, 5′- or 7-H), 7.08 (1 H, dd, *J* 8 and 2 Hz, 6- or 6′-H), and 7.23—7.40 (total 4 H, m, 4 × ArH); $\lambda_{max.}$ (EtOH) 317 nm (log ε 4.43).

2-(1-*Bromoethyl*)-4-(1-*bromopropyl*)*phenyl* 3,4-*Methylenedioxybenzoate* (17).—(*a*) A solution of the benzylic bromide (13) (550 mg) in tetrachloromethane (40 ml) was added to a suspension of NBS (300 mg) in the same solvent (40 ml) and the mixture was heated under reflux for 30 min. Evaporation of the cooled, filtered solution gave a yellow oil which rapidly darkened with time. Filtration of a light petroleum–dichloromethane (1 : 1) solution through silica gel gave the *dibromide* (17) as an oil (Found: M^+, 467.9596. $C_{19}H_{18}Br_2O_4$ requires *M*, 467.9573); δ§ 1.03 (3 H, t, *J* 7.5 Hz, CH_2Me), 2.02 (3 H, d, *J* 7 Hz, CHBr*Me*), 2.0—2.33 (2 H, m, $CHBrCH_2Me$), 4.86 (1 H, t, *J* 7.5 Hz, C*H*BrEt), 5.30 (1 H, q, *J* 7 Hz, C*H*BrMe), 6.08 (2 H, s, OCH_2O), 6.88 (1 H, d, *J* 8 Hz, 6-H), 7.15 (1 H, d, *J* 9 Hz, 5′-H), 7.40 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.56 (1 H, d, *J* 2 Hz, 3-H), 7.63 (1 H, d, *J* 1.5 Hz, 2′-H), and 7.85 (1 H, dd, *J* 8.5 and 1.5 Hz, 6′-H).

(*b*) Identical treatment of the ethylpropylphenyl ester (25) (see below) (1.15 g) with NBS (1.46 g) in tetrachloromethane (95 ml) yielded the dibromide (17) (1.99 g) with an identical ^1H n.m.r. spectrum.

2-*Ethyl*-4-*propylphenol* (24).—This was prepared from the ketone (9) as previously described,[10] and was purified by distillation, b.p. 104—110 °C at 0.55 mmHg (lit.,[10] 70—72 °C at 0.25 mmHg); δ 0.93 (3 H, t, *J* 7.5 Hz, CH_2CH_2Me), 1.23 (3 H, t, *J* 7.5 Hz, $ArCH_2Me$), 1.38—1.78 (2 H, m, CH_2CH_2-

* 3,4-Methylenedioxybenzoyl chloride.

† Primed numbers refer to the benzoate moiety for compounds (10), (12), and (13).

‡ Primed numbers refer to the 2-aryl substituent.

§ Primed numbers refer to the benzoate moiety.

Me), 2.4—2.73 (total 4 H, m, CH_2Et and CH_2Me), 4.58 (1 H s, OH), 6.62 (1 H, d, *J* 7.5 Hz, 6-H), and 6.80—6.90 (total 2 H, (m, 3- and 5-H).

2-*Ethyl*-4-*propylphenyl* 3,4-*Methylenedioxybenzoate* (25).—A solution of the phenol (24) (2.78 g) in pyridine (15 ml) was added to piperonyloyl chloride (3.35 g) in the same solvent (20 ml) and the mixture was stirred at room temperature for 36 h. After removal of the solvent, the residue was extracted with dichloromethane and water. The organic layer was washed successively with dilute sulphuric acid (5%; 100 ml), saturated aqueous sodium hydrogen carbonate, and water, and was then evaporated to give a solid (5.03 g), a solution of which in light petroleum–dichloromethane (3 : 2) was filtered through a short column of silica gel. Evaporation and crystallization from methanol gave the *ester* (25) as prisms, m.p. 41—42 °C (Found: C, 73.4; H, 6.6. $C_{19}H_{20}O_4$ requires C, 73.1; H, 6.45%); δ* 0.93 (3 H, t, *J* 7.5 Hz, CH_2CH_2Me), 1.17 (3 H, t, *J* 7.5 Hz, CH_2Me), 1.43—1.96 (2 H, m, CH_2CH_2Me), 2.43—2.70 (total 4 H, m, CH_2Et and CH_2Me), 6.04 (2 H, s, OCH_2O), 6.86 (1 H, d, *J* 9 Hz, 6-H), 7.02—7.06 (total 3 H, m, 3-, 5-, and 5′-H), 7.62 (1 H, d, *J* 1.5 Hz, 2′-H), and 7.82 (1 H, dd, *J* 8.5 and 1.5 Hz, 6′-H).

3-*Methyl*-2-(3,4-*methylenedioxyphenyl*)-5[(E)-*prop*-1-*enyl*]-*benzo*[b]*furan* [*Eupomatenoid*-3] (20).—A solution of the dibromide (17) (630 mg) and triphenylphosphine (840 mg) in acetonitrile (30 ml) was heated under reflux under nitrogen for 36 h. The solvent was then removed, toluene (60 ml) and triethylamine (2.4 ml) were added, and the mixture was refluxed for a further 20 h. The mixture was filtered, and evaporated to dryness and the residue was dissolved in light petroleum–dichloromethane (95 : 5) and the solution was filtered through silica gel. After elution of unchanged triphenylphosphine (240 mg), further elution afforded eupomatenoid-3 (20) (90 mg) as needles from benzene–light petroleum, m.p. 106—107 °C (lit.,[2] 111 °C); $\lambda_{max.}$ (EtOH) 239 (log ε 4.46), 257 (4.40), 299 sh (4.29), and 322 nm (4.37); $\nu_{max.}$ (Nujol) 1 238, 1 045, and 962 cm^{-1}; δ† 1.90 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.41 (3 H, s, 3-Me), 6.01 (2 H, s, OCH_2O), 6.07—6.62 (2 H, m, C*H*=C*HMe*), 6.91 (1 H, d, *J* 8.5 Hz, 7- or 5′-H), and 7.25—7.46 (total 5 H, m, 5 × ArH).

Catalytic hydrogenation (5% Pd–C) in ethyl acetate at atmospheric pressure yielded dihydroeupomatenoid-3(16), m.p. 83—84 °C, with a ^{1}H n.m.r. spectrum identical with that of the product obtained by the Wittig reaction on the monobromide (13) (see above).

2-*Acetyl*-4-*propylphenyl* 3,4-*Dimethoxybenzoate* (11).—This was prepared from the phenol (9) and veratroyl chloride ‡ as described for the analogous ester (10). Crystallization from ethanol yielded the *ester* (11) as fine needles, m.p. 94—95 °C (Found: C, 70.6; H, 6.7. $C_{20}H_{22}O_5$ requires C, 70.2; H, 6.5%); δ* 0.96 (3 H, t, *J* 8 Hz, CH_2Me), 1.46—1.80 (2 H, m, CH_2Me), 2.53 (3 H, s, COMe), 2.63 (2 H, t, *J* 8 Hz, ArCH_2), 3.96 (total 6 H, s, 2 × OMe), 6.92 (1 H, d, *J* 8 Hz, 6-H), 7.08 (1 H, d, *J* 8 Hz, 5′-H), 7.35 (1 H, dd, *J* 8 and 2 Hz, 5-H), 7.61 (1 H, d, *J* 2 Hz, 3- or 2′-H), 7.65 (1 H, d, *J* 2 Hz, 2′- or 3-H), and 7.85 (1 H, dd, *J* 8 and 2 Hz, 6′-H).

2-(1-*Hydroxyethyl*)-4-*propylphenyl*- 3,4-*Dimethoxybenzoate* (14).—This was prepared from the ketone (11) by catalytic hydrogenation as for the analogous ester (12). Crystallization from ethyl acetate–light petroleum gave the *alcohol* (14) as prisms, m.p. 99—100 °C (Found: C, 70.0; H, 7.3. $C_{20}H_{24}O_5$ requires C, 69.75; H, 7.0%); δ* 0.94 (3 H, t, *J* 6 Hz, CH_2Me), 1.33 [3 H, d, *J* 6 Hz, CH(OH)*Me*], 1.53—1.80 (2 H, m, CH_2Me), 2.56 (2 H, t, *J* 6 Hz, ArCH_2), 3.86 (total 6 H, s, 2 × OMe), 4.82 [1 H, q, *J* 6 Hz, C*H*(OH)], 6.77 (1 H, d, *J* 9 Hz, 6-H), 6.90—7.06 (total 2 H, m, 5- and 5′-H), 7.27 (1 H, d, *J* 1.5 Hz, 3-H), 7.49 (1 H, d, *J* 2 Hz, 2′-H), and 7.68 (1 H, dd, *J* 9 and 2 Hz, 6′-H).

2-(1-*Bromoethyl*)-4-*propylphenyl* 3,4-*Dimethoxybenzoate* (15).—This was prepared from the alcohol (14) by the action of triphenylphosphine dibromide in acetonitrile as for the analogous bromo-ester (13). The title compound was crystallized from benzene–light petroleum as small prisms, m.p. 127—130 °C (Found: M^+, 406.0789. $C_{20}H_{23}BrO_4$ requires *M*, 406.0780); δ* 0.97 (3 H, t, *J* 6 Hz, CH_2Me), 1.46—1.87 (2 H, m, CH_2Me), 1.98 (3 H, d, *J* 7 Hz, CHBr*Me*), 2.62 (2 H, t, *J* 6 Hz, ArCH_2), 3.97 (total 6 H, s, 2 × OMe), 5.33 (1 H, q, *J* 7 Hz, CHBr), 6.95 (1 H, d, *J* 9 Hz, 6-H), 7.10—7.17 (total 2 H, m, 5- and 5′-H), 7.40br (1 H, s, 3-H), 7.73 (1 H, d, *J* 1.5 Hz, 2′-H), and 7.92 (1 H, dd, *J* 9 and 1.5 Hz, 6′-H).

2-(1-*Bromoethyl*)-4-(1-*bromopropyl*)*phenyl* 3,4-*Dimethoxybenzoate* (18).—This was prepared from the monobromide (15) by treatment with NBS as for the analogous dibromo-ester (17). Crystallization from benzene–light petroleum gave the *dibromo-ester* (18) as rosettes of needles, m.p. 109—113 °C (Found: M^+, 483.9876. $C_{20}H_{22}Br_2O_4$ requires *M*, 483.9886); δ* 1.04 (3 H, t, *J* 6 Hz, CH_2Me), 2.00 (3 H, d, *J* 7 Hz, CHBr-*Me*), 2.17 (2 H, dq, *J* 6 and 4 Hz, CH_2Me), 3.98 (total 6 H, s, 2 × OMe), 4.89 (1 H, t, *J* 6 Hz, C*H*BrEt), 5.33 (1 H, q, *J* 7 Hz, C*H*BrMe), 6.96 (1 H, d, *J* 9 Hz, 6-H), 7.15—7.62 (total 3 H, m, 3-, 5-, and 5′-H), 7.72 (1 H, d, *J* 2 Hz, 2′-H), and 7.91 (1 H, dd, *J* 9 and 2 Hz, 6′-H).

2-(3,4-*Dimethoxyphenyl*)-3-*methyl*-5-[(E)-*prop*-1-*enyl*]-*benzo*[b]*furan*[*Eupomatenoid*-4] (21).—A solution of the dibromide (18) (555 mg) and triphenylphosphine (750 mg) in acetonitrile (30 ml) was heated under reflux under nitrogen for 23 h. The solvent was then removed, and toluene (45 ml), acetonitrile (2 ml), and triethylamine (2 ml) were added in turn; the mixture was then refluxed for a further 12 h. The mixture was then filtered, and the residue obtained on evaporation of the filtrate was dissolved in light petroleum–dichloromethane (1 : 1) and was chromatographed on silica gel. After elution of triphenylphosphine (350 mg), a mixture (210 mg) containing compound (21) was obtained. Purification by preparative t.l.c. (same solvent) gave pure eupomatenoid-4 (21), which was crystallized from methanol as prismatic needles (55 mg), m.p. 95—96 °C (lit.,[2] 96 °C); δ† 1.91 (3 H, d, *J* 5 Hz, CH=CH*Me*), 2.45 (3 H, s, 3-Me), 3.94 (3 H, s, OMe), 3.98 (3 H, s, OMe), 6.03—6.64 (2 H m, C*H*=C*HMe*), 6.96 (1 H, d, *J* 9 Hz, 7- or 5′-H), and 7.2—7.44 (total 5 H, m, 5 × ArH).

4-*Acetoxy*-3-*methoxybenzoic Acid.*—Vanillic acid (4-hydroxy-3-methoxybenzoic acid) (5.0 g) was heated on a steam-bath for 90 min with acetic anhydride (15 ml) and pyridine (10 ml); the mixture was then diluted with water (20 ml) and was then heated for an additional 10 min. The mixture was then poured onto ice [100 ml, acidified with concentrated hydrochloric acid (5 ml)] and was extracted with dichloromethane (250 ml). The extract was washed (water), dried ($MgSO_4$), and evaporated to dryness and the residue was crystallized from ethanol to yield the title acid (4.7 g) as small needles, m.p. 141—144 °C (lit.,[18] 141—142 °C); δ 2.33 (3 H, s, COMe), 3.92 (3 H, s, OMe), 7.13 (1 H, d, *J* 8 Hz, 5-H), 7.70—7.82 (total 2 H, m, 2- and 6-H), and 11.92br (1 H, s, CO_2H).

* Primed numbers refer to the benzoate moiety.
† Primed numbers refer to the 2-aryl substituent.
‡ 3,4-Dimethoxybenzoyl chloride.

2-Ethyl-4-propylphenyl 4-Acetoxy-3-methoxybenzoate (26).—Oxalyl chloride (2.2 ml) was added to a suspension of 4-acetoxy-3-methoxybenzoic acid (2.20 g) in benzene (20 ml) and the mixture was heated under reflux for 5 h. Removal of the solvent under reduced pressure gave the residual acid chloride [$\nu_{max.}$ ($CHCl_3$) 1 755 (OAc) and 1 804 cm^{-1} (COCl)], a mixture of which (1.25 g) and the phenol (24) (0.91 g) in pyridine (5 ml) was stirred at room temperature for 38 h. Removal of the solvent under reduced pressure gave a paste which was worked up in the usual way (diethyl ether extraction). Filtration of the product through silica gel (40 g) and elution with dichloromethane–tetrachloromethane (2 : 3) gave the ester (26) as an oil (1.50 g) which crystallized from aqueous ethanol as fine needles, m.p. 52.5—54 °C (Found: C, 70.7; H, 7.0. $C_{21}H_{24}O_5$ requires C, 70.8; H, 6.8%); δ* 0.95 (3 H, t, *J* 7 Hz, CH_2CH_2*Me*), 1.18 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.45—1.85 (2 H, m, CH_2CH_2Me), 2.33 (3 H, s, COMe), 2.43—2.70 total 4 H, m, ArCH_2Et and ArCH_2Me), 3.89 (3 H s, OMe), 7.02—7.27 (total 4 H, m, 3-, 5-, 6-, and 5′-H), and 7.78—7.90 (total 2 H, m, 2′- and 6′-H).

2-(4-Acetoxy-3-methoxyphenyl)-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-5 Acetate*] (22).—A mixture of the ester (26) (350 mg) and NBS (390 mg) in tetrachloromethane (25 ml) was heated under reflux for 25 min and was then cooled and filtered. The filtrate was evaporated under reduced pressure to give the dibromide (19) as a dark oil, δ* 1.05 (3 H, t, CH_2*Me*), 1.95—2.36 (2 H, m, CH_2Me), 2.04 (3 H, d, *J* 7 Hz, CHBr*Me*), 2.38 (3 H, s, COMe), 3.95 (3 H, s, OMe), 4.88 (1 H, t, *J* 7 Hz, *CH*BrEt), 5.31 (1 H, q, *J* 7 Hz, *CH*BrMe), 7.20 (total 2 H, d, *J* 9 Hz, 6- and 5′-H), 7.33—7.62 (total 2 H, m, 3- and 5-H), and 7.85—7.95 (total 2 H, m, 2′- and 6′-H).

A solution of the dibromide (19) (460 mg) and triphenylphosphine (510 mg) in acetonitrile (15 ml) was heated under reflux under nitrogen for 28 h. The solvent was then removed and the residue was redissolved in a mixture of toluene (40 ml) and triethylamine (0.8 ml), and the mixture was heated under reflux for a further 16 h. The product obtained after filtration and evaporation was chromatographed on silica gel; elution with dichloromethane–light petroleum yielded first, triphenylphosphine (60 mg), followed by the required eupomatenoid-5 acetate (22) (113 mg), which was crystallized from aqueous ethanol as needles, m.p. 113.5—114 °C (lit.,[2] 117 °C); δ 1.88 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.32 (3 H, s, COMe), 2.43 (3 H, s, 3-Me), 3.90 (3 H, s, OMe), 6.03—6.60 (2 H, m, *CH*=*CH*Me), 7.08 (1 H, d, *J* 9 Hz, ArH), and 7.20—7.42 (total 5 H, m, 5 × ArH).

2-(4-Hydroxy-3-methoxyphenyl)-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-5*] (23).—Lithium aluminium hydride (5 mg) was added to a solution of the acetate (22) (42 mg) in diethyl ether (20 ml); the mixture was heated under reflux for 30 min and was then worked up in the usual way after being quenched with ethyl acetate. Crystallization of the product from benzene–light petroleum gave eupomatenoid-5 (23) as rosettes of needles, m.p. 112—112.5 °C (lit.,[2] 114—115 °C); δ 1.88 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.42 (3 H, s, 3-Me), 3.95 (3 H, s, OMe), 5.68 (1 H, s, OH), 6.05—6.62 (2 H, m, *CH*=*CH*Me), 6.96 (1 H, d, *J* 9 Hz, ArH), and 7.22—7.40 (total 5 H, m, 5 × ArH).

2-Ethyl-4-propylphenyl 4-Acetoxybenzoate (27).—2-Ethyl-4-propylphenol (24) (1.23 g) and 4-acetoxybenzoyl chloride [19] (1.63 g) were dissolved in pyridine (15 ml) and the mixture was stirred at room temperature for 36 h. Removal of the solvent under reduced pressure and work-up in the usual way with diethyl ether extraction gave a coloured oil (2.44 g) which was distilled [140—160 °C (bath) at 0.5 mmHg] and the distillate was crystallized from aqueous ethanol to give the *ester* (27) as prisms, m.p. 49—51 °C (Found: C, 74.0; H, 7.1. $C_{20}H_{22}O_4$ requires C, 73.6, H, 6.8%); δ* 0.95 (3 H, t, *J* 7.5 Hz, CH_2CH_2*Me*), 1.18 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 1.43—1.85 (2 H, m, CH_2CH_2Me), 2.30 (3 H, s, COMe), 2.43—2.68 (total 4 H, m, CH_2Et and CH_2Me), 7.03—7.07 (total 3 H, m, 3-, 5-, and 6-H), 7.21 (total 2 H, d, *J* 9 Hz, 3′- and 5′-H), and 8.23 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

2-(4-Acetoxyphenyl)-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-6 Acetate*] (31).—A mixture of the ester (27) (1.10 g) and NBS (1.32 g) in tetrachloromethane (100 ml) was heated under reflux under nitrogen for 45 min, and was then worked up in the usual way to give the crude dibromide (29) as an oil, δ* 1.02 (3 H, t, *J* 7 Hz, CH_2*Me*), 2.00 (3 H, d, *J* 6 Hz, CHBr*Me*), 1.86—2.40 (2 H, m, CH_2Me), 2.30 (3 H, s, COMe), 4.86 (1 H, t, *J* 7 Hz, *CH*BrEt), 5.30 (1 H, q, *J* 6 Hz, *CH*BrMe), 7.10—7.63 (total 5 H, m, 3-, 5-, 6-, 3′-, and 5′-H), and 8.25 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

A solution of the dibromide (29) (1.25 g) and triphenylphosphine (1.49 g) in acetonitrile (20 ml) was heated under reflux for 26 h. The solvent was then removed, the residue was redissolved in a mixture of toluene (150 ml) and triethylamine (2.5 ml), and the solution was heated under reflux for a further 12 h. Work-up as for the analogous benzofurans and purification by filtration through silica gel (40 g) and elution with light petroleum–dichloromethane (1 : 1) gave eupomatenoid-6 acetate (31) as a solid (100 mg) which was crystallized from methanol as prismatic needles, m.p. 113.5—115 °C (lit.,[2] 113—115 °C); δ† 1.88 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.30 (3 H, s, COMe), 2.43 (3 H, s, 3-Me), 6.0—6.63 (2 H, m, *CH*=*CH*Me), 7.16 (total 2 H, d, *J* 9 Hz, 3′- and 5′-H), 7.30—7.43 (total 3 H, m, 4-, 6-, and 7-H), and 7.78 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

2-(4-Hydroxyphenyl)-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-6*] (32).—The acetate (31) was treated with lithium aluminium hydride in diethyl ether [as for eupomatenoid-5 (23)] to give compound (32) as a solid which was crystallized from benzene–light petroleum as fine needles m.p. 147.5—149 °C (lit.,[2] 148—150 °C); δ† 1.90 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.42 (3 H, s, 3-Me), 4.33br (1 H, s, OH) 5.98—6.60 (2 H, m, *CH*=*CH*Me), 6.88 (total 2 H, d, *J* 9 Hz, 3′- and 5′-H), 7.23—7.40 (total 3 H, m, 4-, 6-, and 7-H), and 7.65 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

2-Methoxy-4-propylphenol (40).—This was obtained by catalytic hydrogenation of eugenol with palladium–carbon in ethyl acetate and was distilled at 85—90 °C (bath) at 0.6 mmHg (lit.,[20] 129—131 °C at 13 mmHg); δ 0.92 (3 H, t, *J* 6 Hz, CH_2*Me*), 1.40—1.80 (2 H, m, CH_2Me), 2.50 (2 H, t, *J* 7.5 Hz, ArCH_2), 3.85 (3 H, s, OMe), 5.43 (1 H, s, OH), and 6.63—6.85 (3 H, m, 3 × ArH).

2-Hydroxy-3-methoxy-5-propylacetophenone (37).—Boron trifluoride was bubbled through a stirred solution of the methoxyphenol (40) (2.88 g) in acetic acid (2.2 ml) at 0 °C for 15 min; the dark-red, viscous solution was then heated at 150—155 °C (oil-bath temperature) for 1.5 h. The cooled mixture was then diluted with diethyl ether (200 ml) and the solution was washed successively with water, saturated aqueous sodium hydrogen carbonate, brine, and water. Evaporation of the dried ($MgSO_4$) organic phase gave a dark oil

* Primed numbers refer to the benzoate moiety.

† Primed numbers refer to the 2-aryl substituent.

(3.18 g) which on distillation [85—105 °C (bath) at 0.05 mmHg] gave a yellow oil (2.07 g), whose ^{1}H n.m.r. spectrum indicated it to be a mixture of compounds (41) and (37) in a *ca.* 6 : 1 ratio.

Anhydrous potassium carbonate (2.0 g) and dimethyl sulphate (1.5 ml) were added to a solution of this oil in acetone (50 ml), the mixture heated under reflux for 20 h and was then diluted with water and acidified with 10% hydrochloric acid. Work-up in the usual way with diethyl ether extract gave 2,3-dimethoxy-5-propylacetophenone (42) as an oil (1.91 g), δ 0.93 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.40—1.75 (2 H, m, CH_2Me), 2.55 (2 H, t, *J* 8 Hz, ArCH_2), 2.62 (3 H, s, COMe), 3.87 (6 H, s, 2 × OMe), 6.83 (1 H, d, *J* 2 Hz, 4-H), and 7.00 (1 H, d, *J* 2 Hz, 6-H).

Aluminium chloride (3.50 g) was added to a solution of compound (42) (1.91 g) in dichloromethane (100 ml), the mixture heated under reflux for 2 h and was then worked up after being washed in turn with water and dilute hydrochloric acid. Evaporation of the dried organic layer gave a residual dark oil which on distillation [105—120 °C (bath) at 0.2 mmHg] gave the title *o*-acetylphenol (37) as an oil (1.20 g), δ 0.95 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.42—1.77 (2 H, m, CH_2Me), 2.55 (2 H, t, *J* 8 Hz, ArCH_2), 2.62 (3 H, s, COMe) 3.90 (3 H, s, OMe), 6.87 (1 H, d, *J* 1.5 Hz, 4-H), 7.10 (1 H, d, *J* 1.5 Hz, 6-H), and 12.38 (1 H, s, OH).

2-*Ethyl*-6-*methoxy*-4-*propylphenol* (43).—Mossy zinc (14 g) was added to a solution of mercury(II) chloride (450 mg) in water (50 ml). The mixture was stirred for 30 min and the supernatant liquid was removed by decantation. The residue was washed with water (20 ml). 50% Hydrochloric acid (30 ml) was then added, followed by a solution of the acetophenone (37) (3.6 g) in ethanol (50 ml) and the mixture was heated under reflux under N_2 for 12 h. Extraction of this mixture with toluene (2 × 100 ml) and evaporation of the dried extract gave a dark liquid which was distilled [72—82 °C (bath) at 0.08 mmHg] to give compound (43) as a liquid (lit.,[20] 132—134 °C at 6 mmHg); δ 0.93 (3 H, t, *J* 7 Hz, CH_2CH_2*Me*), 1.20 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 1.40—1.83 (2 H, m, CH_2CH_2Me), 2.40—2.75 (total 4 H, m, CH_2Et and CH_2Me), 3.85 (3 H, s, OMe), 5.47 (1 H, s, OH), and 6.53br (2 H, s, 2 × ArH).

2-*Ethyl*-6-*methoxy*-4-*propylphenyl* 3,4-*Methylenedioxybenzoate* (44).—A solution of the methoxyphenol (43) (2.06 g) and piperonyloyl chloride (2.35 g) in pyridine (25 ml) was stirred at room temperature for 42 h. The mixture was worked up as for the analogous ester (25). Crystallization of the product from light petroleum gave the *ester* (44) as irregular prisms (1.83 g), m.p. 90—92 °C (Found: C, 70.1; H, 6.6. $C_{20}H_{22}O_5$ requires C, 70.2; H, 6.5%); δ* 0.96 (3 H, t, *J* 7.5 Hz, CH_2CH_2*Me*), 1.17 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 1.46—1.85 (2 H, m, CH_2CH_2Me), 2.40—2.63 (total 4 H, m, CH_2Et and CH_2Me), 3.77 (3 H, s, OMe), 6.03 (2 H, s, OCH_2O), 6.65br (total 2 H, s, 3- and 5-H), 6.85 (1 H, d, *J* 8 Hz, 5-H'), 7.62 (1 H, d, *J* 1.5 Hz, 2'-H), and 7.82 (1 H, dd, *J* 8 and 1.5 Hz, 6'-H).

7-*Methoxy*-3-*methyl*-2-(3,4-*methylenedioxyphenyl*)-5-[(E)-*prop*-1-*enyl*]*benzo*[b]*furan* [*Eupomatenoid*-1] (1).—A mixture of the ester (44) (210 mg) and NBS (240 mg) in tetrachloromethane (25 ml) was refluxed as in the preparation of the analogous compound (17). Purification by silica-gel chromatography gave the *dibromide* (46) in 67% yield as an oil, δ* 1.05 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 1.95—2.32 (total 5 H, m, CH_2Me and CHBr*Me*), 3.80 (3 H, s, OMe), 4.86 (1 H, t, *J* 6 Hz, *CH*BrEt), 5.27 (1 H, q, *J* 7 Hz, *CH*BrMe), 6.03 (2 H, s, OCH_2O), 6.92 (1 H, d, *J* 9 Hz, 5'-H), 6.99 (1 H, d, *J* 2 Hz, 3- or 5-H), 7.18 (1 H, d, *J* 2 Hz, 5- or 3-H), 7.66 (1 H, d, *J* 1.5 Hz, 2'-H), and 7.87 (1 H, dd, *J* 9 and 1.5 Hz, 6'-H).

Triphenylphosphine (230 mg) was added to a solution of the dibromide (46) (200 mg) in acetonitrile (15 ml) and the mixture was heated under reflux for 35 h. Removal of the solvent under reduced pressure gave a residue which was dissolved in a mixture of toluene (40 ml) and triethylamine (0.35 ml). Treatment and work-up as for the analogous benzofurans, with elution from silica gel with light petroleum–dichloromethane (3:2), gave eupomatenoid-1 (1) as a solid (50 mg) which was crystallized from ethanol as small prisms, m.p. 153—153.5 °C (lit.,[1] 154—156 °C); δ† 1.88 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.38 (3 H, s, 3-Me), 4.02 (3 H, s, OMe), 5.97 (2 H, s, OCH_2O), 6.10—6.57 (2 H, m, *CH*=*CH*Me), 6.77—6.90 (total 2 H, m, 5'-H- and 6- or 4-H), 6.98 (1 H, d, *J* 1 Hz, 4- or 6-H), and 7.20—7.30 (total 2 H, m, 2'- and 6'-H).

2-*Ethyl*-6-*methoxy*-4-*propylphenyl* 4-*Acetoxy*-3-*methoxybenzoate* (45).—This ester was prepared from the methoxyphenol (43) (1.03 g) and 4-acetoxy-3-methoxybenzoyl chloride (1.25 g) in pyridine (15 ml) as for the analogous ester (26). Crystallization from light petroleum gave the *ester* (45) as prisms (1.65 g), m.p. 94—95 °C (Found: C, 68.4; H, 7.0. $C_{22}H_{26}O_6$ requires C, 68.4; H, 6.8%); δ* 0.97 (3 H, t, *J* 7 Hz, CH_2CH_2*Me*), 1.17 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.43—1.77 (2 H, m, CH_2CH_2Me), 2.33 (3 H, s, COMe), 2.40—2.66 (total 4 H, m, CH_2Et and CH_2Me), 3.77 (3 H, s, 6-OMe), 3.90 (3 H, s, 3'-OMe), 6.66br (total 2 H, s, 3- and 5-H), 7.13 (1 H, d, *J* 7.5 Hz, 5'-H), and 7.80—7.92 (total 2 H, m, 2'- and 6'-H).

2-(4-*Acetoxy*-3-*methoxyphenyl*)-7-*methoxy*-3-*methyl*-5-[(E)-*prop*-1-*enyl*]*benzo*[b]*furan* [*Eupomatenoid*-7 *Acetate*] (48).—A mixture of the ester (45) (990 mg) and NBS (970 mg) in tetrachloromethane (100 ml) was heated under reflux under nitrogen for 30 min and the cooled, filtered solution was then evaporated under reduced pressure to give the crude dibromide (47) as a dark oil, δ* 1.07 (3 H, t, CH_2*Me*), 2.00 (3 H, d, *J* 6 Hz, CHBr*Me*), 2.00—2.40 (2 H, m, CH_2Me), 2.37 (3 H, s, COMe), 3.83 (3 H, s, OMe), 3.93 (3 H, s, OMe), 4.86 (1 H, t, *J* 7 Hz, *CH*BrEt), 5.27 (1 H, q, *J* 6 Hz, *CH*BrMe), 6.48—7.57 (total 3 H, m, 3-, 5-, and 5'-H), and 7.83—7.95 (total 2 H, m, 2'- and 6'-H).

Triphenylphosphine (250 mg) was added to a solution of the crude dibromide (47) (240 mg) in acetonitrile (15 ml) and the mixture was converted into products in a similar manner to the preparation of compound (22). Elution from silica gel with dichloromethane gave the acetate (48) which was crystallized from ethanol as small needles, m.p. 137—138.5 °C (lit.,[2] 144 °C; lit.,[6] 140—142 °C); δ† 1.90 (3 H, d, *J* 5.5 Hz, CH=CH*Me*), 2.34 (3 H, s, COMe), 2.43 (3 H, s, 3-Me), 3.92 (3 H, s, OMe), 4.04 (3 H, s, OMe), 6.06—6.60 (2 H, m, *CH*=*CH*Me), 6.84 (1 H, d, *J* 1 Hz, 6-H), 7.06 (1 H, d, *J* 1 Hz, 4-H), 7.20 (1 H, d, *J* 9 Hz, 5'-H), and 7.30—7.41 (total 2 H, m, 2'- and 6'-H).

2-(4-*Hydroxy*-3-*methoxyphenyl*)-7-*methoxy*-3-*methyl*-5-[(E)-*prop*-1-*enyl*]*benzo*[b]*furan* [*Eupomatenoid*-7] (49).—The acetate (48) (24 mg) was treated with lithium aluminium hydride (7 mg) as for the preparation of the analogue (23). Crystallization of the product from light petroleum gave eupomatenoid-7 (49) as a fine powder (18 mg) with m.p. 102—103 °C after recrystallization from aqueous ethanol (lit.,[2] 105—106 °C; gum [1]); δ† 1.91 (3 H, d, *J* 5 Hz, CH=CH*Me*), 2.41 (3 H, s, 3-Me), 3.98 (3 H, s, OMe), 4.04 (3 H, s, OMe), 5.70br (1 H, s, OH), 6.00—6.60 (2 H, m, *CH*=*CH*Me),

* Primed numbers refer to the benzoate moiety.

† Primed numbers refer to the 2-aryl substituent.

6.82 (1 H, d, *J* 1.5 Hz, 6-H), 6.94—7.04 (total 2 H, m, 4- and 5′-H), and 7.23—7.33 (total 2 H, m, 2′- and 6′-H).

2-Ethyl-6-methoxy-4-propylphenyl 4-Acetoxybenzoate (28) was prepared similarly to the analogue (27). The product was crystallized from ethanol to give the *ester* (28) as small prisms, m.p. 97—99 °C (Found: C, 70.9; H, 6.8. $C_{21}H_{24}O_5$ requires C, 70.8; H, 6.8%); δ* 0.96 (3 H, t, *J* 7 Hz, CH_2CH_2-*Me*), 1.16 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 1.43—1.77 (2 H, m, CH_2CH_2Me), 2.33 (3 H, s, COMe), 2.39—2.64 (total 4 H, m, CH_2Et and CH_2Me), 3.75 (3 H, s, OMe), 6.65br (total 2 H, s, 3- and 5-H), 7.20 (total 2 H, d, *J* 9 Hz, 3′- and 5′-H), and 8.23 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

2-(4-Acetoxyphenyl)-7-methoxy-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-13 Acetate*] (33).—The ester (28) (750 mg) was treated with NBS (820 mg) in tetrachloromethane (75 ml) as in analogous cases to give the crude dibromide (30) as a dark oil, δ* 1.04 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.98 (3 H, d, *J* 7 Hz, CHBr*Me*), 1.93—2.37 (2 H, m, CH_2Me), 2.33 (3 H, s, COMe), 3.79 (3 H, s, OMe), 4.85 (1 H, t, *J* 7 Hz, CHBrEt), 5.26 (1 H, q, *J* 7 Hz, CHBrMe), 6.93—7.33 (total 4 H, m, 3-, 5-, 3′-, and 5′-H), and 8.25 (total 2 H, d, *J* 9 Hz, 2′- and 6′-H).

Triphenylphosphine (790 mg) was added to a solution of the crude dibromide (30) (695 mg) in acetonitrile (20 ml) and the mixture was refluxed and worked up as for the analogue (22). Elution from silica gel with light petroleum–dichloromethane (1 : 3) gave the *acetate* (33) (*ca.* 20% yield) as small needles, m.p. 133—135 °C (from aqueous methanol) (Found: C, 74.7; H, 6.1. $C_{21}H_{20}O_4$ requires C, 75.0; H, 6.0%); δ† 1.91 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.32 (3 H, s, COMe), 2.43 (3 H, s, 3-Me), 4.04 (3 H, s, OMe), 6.03—6.61 (2 H, m, CH=CHMe), 6.83 (1 H, d, *J* 1.4 Hz, 6-H), 7.03 (1 H, d, *J* 1.4 Hz, 4-H), 7.18 (total 2 H, dd, *J* 7 and 2 Hz, 3′- and 5′-H), and 7.81 (total 2 H, dd, *J* 7 and 2 Hz, 2′- and 6′-H).

2-(4-Hydroxyphenyl)-7-methoxy-3-methyl-5-[(E)-prop-1-enyl]benzo[b]*furan* [*Eupomatenoid-13*] (34).—The acetate (33) was treated with lithium aluminium hydride in the usual way and the product was crystallized from benzene to yield eupomatenoid-13 (34) as fine needles, m.p. 193—195 °C (lit.,[5] 194—196 °C); δ† 1.89 (3 H, d, *J* 6 Hz, CH=CH*Me*), 2.39 (3 H, s, 3-Me), 4.04 (3 H, s, OMe), 4.73 (1 H, s, OH), 6.05—6.58 (2 H, m, CH=CHMe), 6.82 (1 H, d, *J* 1 Hz, 6-H), 6.90 (total 2 H, d, *J* 8.5 Hz, 3′- and 5′-H), 7.04 (1 H, d, *J* 1 Hz, 4-H), and 7.68 (total 2 H, d, *J* 8.5 Hz, 2′- and 6′-H).

* Primed numbers refer to the benzoate moiety.
† Primed numbers refer to the 2-aryl substituent.

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