Syntheses of the Natural Dibenzofuran, Ruscodibenzofuran

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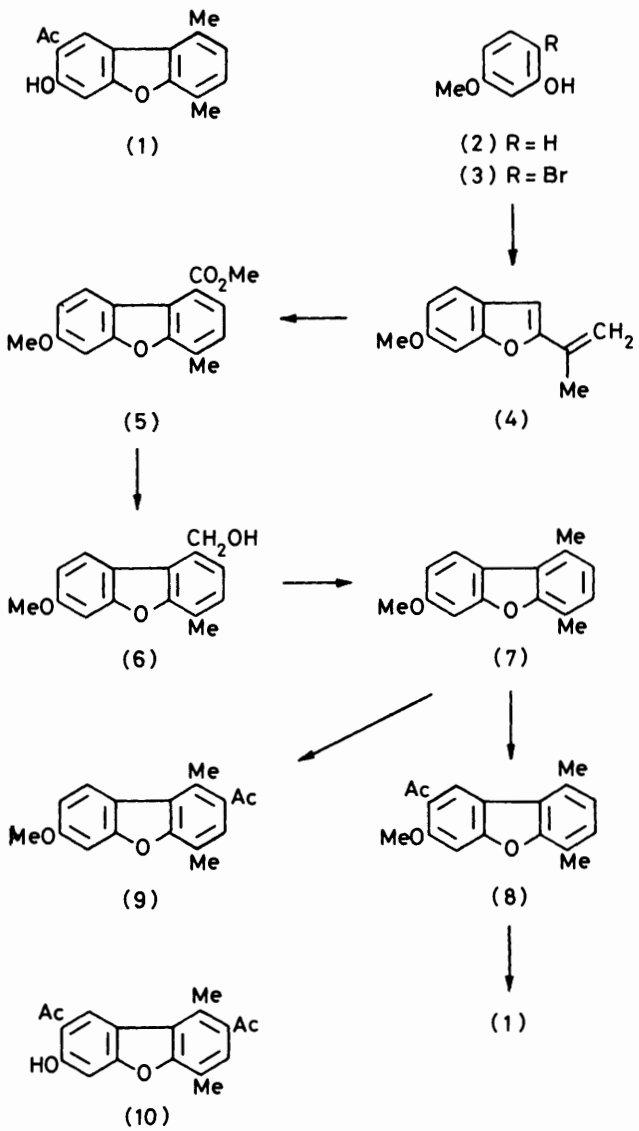
Short syntheses of the natural dibenzofuran, ruscodibenzofuran (1) from readily available phenols are described. The key steps involve initial formation of a 2-isopropenylbenzofuran by reaction of an *ortho*-halogenophenol with cuprous isopropenylacetylide followed by cycloaddition of methyl propiolate, to provide a functionalized dibenzofuran.

From the roots of *Ruscus aculeatus* L. (Liliaceae), an evergreen shrub yielding extracts for which a variety of medicinal effects have been claimed, ElSohly and co-workers isolated [1] a dibenzofuran which they subsequently named ruscodibenzofuran.[2] The natural occurrence of dibenzofurans, particularly within higher plants is comparatively rare.[3] Although these workers demonstrated from spectroscopic data and *X*-ray diffraction analysis that ruscodibenzofuran had the composition 8-acetyl-7-hydroxy-1,4-dimethyldibenzofuran (1), an attempted synthesis employing a mixed Ullmann reaction [2] was unsuccessful. Within a short period, however, three distinct syntheses were successfully completed. In the first, Högberg and Hjalmarsson employed a *p*-quinone–phenol condensation approach,[4] Brown and Jones subsequently applied methyleneketene technology [5] and we communicated a procedure involving Diels–Alder addition to an isopropenylbenzofuran generated by an *o*-halogenophenol–cuprous acetylide coupling.[6]

In Scheme 1, a synthesis of ruscodibenzofuran using this last procedure is outlined. The required *o*-halogenophenol, 2-bromo-5-methoxyphenol (3) was obtained from the action of dioxane dibromide on resorcinol monomethyl ether (2) [7] and on heating with cuprous isopropenylacetylide [8] yielded the rather unstable isopropenylbenzofuran (4) in *ca.* 25% yield. We chose to examine the thermal addition of methyl propiolate to (4) since the studies of Elix [9] and his co-workers on the synthesis of annelated furans suggested the likelihood of formation of the dibenzofuran (5), *i.e.* the Diels–Alder adduct oxidatively aromatized and with the desired regioselectivity. When heated together in toluene, the acetylenic ester and (4) yielded a complex mixture of products, two of which were readily isolated, each in *ca.* 20—25% yield. The ^{1}H n.m.r. spectrum of the first, revealing two pairs of *ortho* aryl protons, confirmed the desired dibenzofuran structure (5). The second product is an as yet unidentified 2 : 1 dienophile–diene adduct.

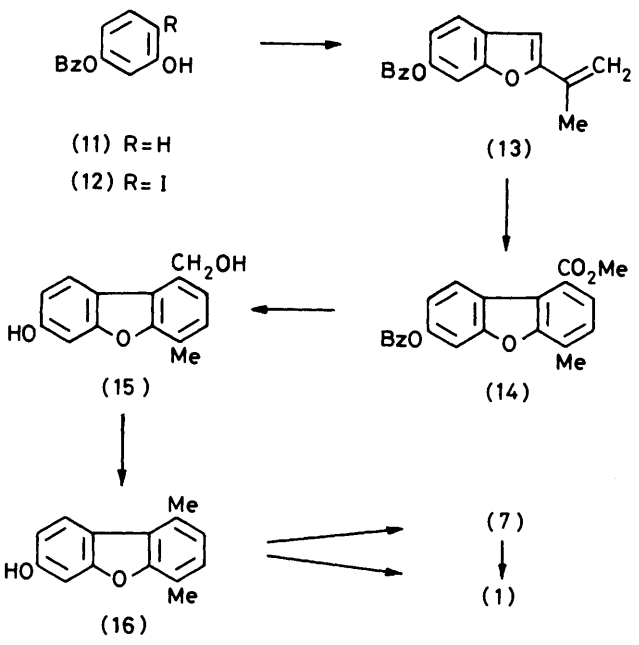
Lithium aluminium hydride reduction of the ester (5) readily yielded the benzylic alcohol (6) which underwent hydrogenolysis at atmospheric pressure to yield the methoxydimethyldibenzofuran (7). This formally completes a short total synthesis of ruscodibenzofuran (1), since (7) had been obtained in Högberg's synthesis [4] and converted into (1) in 60% yield by acetylation with acetyl chloride and aluminium chloride. Since we had also attempted this procedure, with however, a different and unsuccessful result, an alternative method for completion of the natural product synthesis was required.

In our hands, treatment of the dibenzofuran (7) with acetyl chloride and aluminium chloride yielded a readily separated mixture of two products, neither of which was the expected ruscodibenzofuran (1) or ruscodibenzofuran methyl ether (8). The major product, isolated in 38% yield, was a simple monoacetyl derivative, and the ^{1}H n.m.r. spectrum clearly indicated the alternative 2-acetyldibenzofuran structure (9). Professor

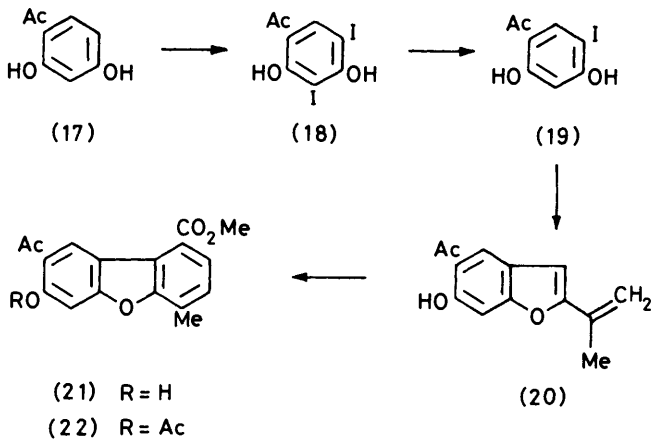


Scheme 1.

Högberg informed us that he had also isolated (9) in one experiment conducted at room temperature rather than 0 °C. The second product, isolated in 16% yield, proved to be a phenolic diacetyl derivative and is assigned structure (10). This compound had previously been reported [2] from Friedel–Crafts acetylation of ruscodibenzofuran and the reported spectrometric data was in excellent agreement. It is apparent that subtle differences in the experimental conditions cause con-



Scheme 2.



Scheme 3.

siderable variation in the nature of the isolated products. A third result was reported by Brown and Jones [5] wherein acetylation of (7) with aluminium chloride gave ruscodibenzofuran methyl ether (8) without the required demethylation.

We accordingly examined a variety of alternative conditions aimed at conversion of (7) into ruscodibenzofuran, and found that by replacing aluminium chloride with titanium tetrachloride, acetylation proceeded as desired to give ruscodibenzofuran methyl ether (8); demethylation of (8) by the action of boron tribromide in benzene at room temperature then cleanly afforded the natural product (1), identical with an authentic specimen.

Before we had solved satisfactorily this last difficulty, we examined an alternative approach (Scheme 2), employing a resorcinol mono-ester, instead of mono-ether as the starting phenol. The required iodophenol (12), readily obtained [7] from resorcinol monobenzoate (11), reacted with cuprous isopropenylacetylide to provide the isopropenylbenzofuran (13), which underwent Diels–Alder addition with methyl propiolate to give the dibenzofuran (14) in 22% yield. With lithium aluminium hydride, the ester (14) gave the phenolic benzyl alcohol (15) which was readily converted into the dimethyldibenzofuranol (16) by hydrogenolysis. Since this compound has been converted into (1),[5] an alternative synthesis of ruscodibenzofuran is accordingly completed. The phenol (16) was characterized by formation of the methyl ether derivative (7) identical with that obtained in Scheme 1.

To avoid the difficulty in effecting regioselective introduction of the acetyl function in the final step of the synthesis to intermediates such as (7), we considered the use of euparin (20), in which the requisite *o*-hydroxy methyl ketone group is initially incorporated, as a starting material. We had already established that this natural product was readily obtainable in *ca.* 40% yield by the cuprous acetylide coupling procedure with 5-bromo-2,4-dihydroxyacetophenone.[8] Since benzofurans are usually prepared by this procedure in higher yields from *o*-iodophenols, a convenient preparation of 2,4-dihydroxy-5-iodoacetophenone (19) was sought and obtained in a two-step sequence (Scheme 3). Whereas attempted monoiodination of 2,4-dihydroxyacetophenone (17) under a variety of conditions gave mixtures of the 3- and 5-mono-iodo and 3,5-di-iodo derivatives, the last, (18), could be readily obtained in excellent yield on di-iodination and underwent selective de-iodination by heating with stannous chloride in acetic acid [10] to give readily the required *o*-iodophenol (19). This was converted into euparin (20) by treatment with cuprous isopropenylacetylide (but with no yield improvement over the bromo analogue), and thence by heating with methyl propiolate in toluene to the dibenzofuran (21). Since the overall yield to this point in Scheme 3 provided no appreciable advantage over the earlier routes, and selective reduction of the methoxycarbonyl group was still required to complete a synthesis of ruscodibenzofuran, this route was not pursued beyond characterization of the dibenzofuran as the acetate derivative (22).

Experimental

M.p.s were determined with a Gallenkamp or Fisher-Johns apparatus and are uncorrected. Varian A-60, 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—140 mesh) and Merck (grade 60, 230—400 mesh).

2-*Isopropenyl*-6-*methoxybenzofuran* (4).—A mixture of copper(I) isopropenylacetylide (3.65 g) and 2-bromo-5-methoxyphenol [7] (5.66 g) in pyridine (125 ml) was heated under reflux (nitrogen atmosphere) for 12 h, and then cooled and stirred with concentrated ammonium hydroxide solution (500 ml). It was then extracted with ether (3 × 250 ml) and the extract washed successively with water (3 × 200 ml), and brine (3 × 200 ml), decolourized (charcoal) and dried. The residual amber oil (3.43 g) obtained on evaporation was dissolved in tetrachloromethane and filtered through a column of silica gel (230—400 mesh) to give the benzofuran (4) as an oil (1.35 g, 26% yield); δ(CCl_4) 2.06 (3 H, br s, Me), 3.77 (3 H, s, OMe), 5.03 (1 H, m, vinyl H), 5.66 (1 H, br s, vinyl H), 6.45 (1 H, br s, 3-H), 6.72 (1 H, dd, *J* 2 and 9 Hz, 5-H), 6.89 (1 H, d, *J* 2 Hz, 7-H), and 7.26 (1 H, d, *J* 9 Hz, 4-H). On storage at 0 °C, the oil freezes to a yellow solid, m.p. 32—33 °C. At room temperature, it rapidly resinified to a viscous mass. For subsequent reaction it was used immediately after preparation without further attempted purification.

Methyl 7-Methoxy-4-methyldibenzofuran-1-carboxylate (5).—A solution of isopropenylbenzofuran (4) (776 mg) and methyl propiolate (2 ml) in toluene (15 ml) was heated under reflux (nitrogen atmosphere) for 27 h. Removal of the solvent gave a dark yellow oil (1.22 g) which was dissolved in tetrachloromethane and chromatographed on silica gel. Elution with the same solvent gave *methyl 7-methoxy-4-methyldibenzofuran-1-carboxylate* as a solid (219 mg, 20% yield) which crystallized from methanol as colourless needles, m.p. 101.5—102 °C (Found: C, 71.2; H, 5.4. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%), δ 2.61 (3 H, s, ArMe), 3.91 (3 H, s, OMe), 4.02 (3 H, s, OMe), 6.97 (1 H, dd, *J* 3 and 9 Hz, 8-H), 7.10 (1 H, d, *J* 3 Hz, 6-H), 7.21 (1 H, d, *J* 9 Hz, 3-H), 7.91 (1 H, d, *J* 9 Hz, 2-H), and 8.64 (1 H, d, *J* 9 Hz, 9-H).

Continued elution with tetrachloromethane gave a crystalline solid (375 mg, 26% yield) which on recrystallization from methanol yielded a *bis-adduct* as small needles, m.p. 186—188 °C (Found: C, 67.5; H, 5.9. $C_{20}H_{20}O_6$ requires C, 67.4; H, 5.7%).

1-Hydroxymethyl-7-methoxy-4-methyldibenzofuran (6).—A solution of the dibenzofuran (5) (167 mg) in diethyl ether (15 ml) was added dropwise during 10 min to a stirred suspension of lithium aluminium hydride (243 mg) in the same solvent (10 ml). The mixture was then heated under reflux for 1 h, then worked up *via* ethyl acetate quenching and aqueous phase separation. Evaporation of the dried ether phase gave a solid (175 mg) which crystallized from methanol to give the *hydroxymethyldibenzofuran* (6) as prismatic needles, m.p. 126—127 °C (Found: C, 74.0; H, 5.8. $C_{15}H_{14}O_3$ requires C, 74.4; H, 5.8%), δ 2.56 (3 H, s, ArMe), 3.90 (3 H, s, OMe), 5.08 (2 H, s, ArCH_2OH), 6.94 (1 H, dd, *J* 2.3 and 8.5 Hz, 8-H), 7.12 (1 H, d, *J* 2.3 Hz, 6-H), 7.16 (2 H, br s, 2-H and 3-H), and 7.94 (1 H, d, *J* 8.5 Hz, 9-H). In $(CD_3)_2CO$ solution, the 2-H and 3-H signal was resolved as a pair of doublets at δ 7.22 (*J* 8.5 Hz) and 7.94 (*J* 8.5 Hz).

7-Methoxy-1,4-dimethyldibenzofuran (7).—A solution of the benzylic alcohol (6) (75 mg) in ethyl acetate (10 ml) was stirred with palladium–charcoal (10%; 123 mg) under hydrogen overnight. Removal of catalyst and solvent gave a colourless oil (61 mg) which crystallized from aqueous methanol to give the dimethylmethoxydibenzofuran as long irregular needles, m.p. 69.5—70.5 °C (lit.,[4] m.p. 69—70 °C); δ 2.54 (3 H, s, ArMe), 2.71 (3 H, s, ArMe), 3.89 (3 H, s, OMe), 6.85—7.04 (3 H, m, 2-H, 3-H, and 8-H), 7.14 (1 H, d, *J* 2 Hz, 6-H), and 7.86 (1 H, d, *J* 8 Hz, 9-H).

Action of Acetyl Chloride and Aluminium Chloride on 7-Methoxy-1,4-dimethyldibenzofuran.—A solution of the dibenzofuran (7) (51 mg) in dichloromethane (3 ml) was added dropwise during 10 min to a stirred mixture of aluminium chloride (284 mg) in the same solvent [20 ml at 0 °C (ice-bath)] under nitrogen. A solution of acetyl chloride in dichloromethane (0.1M; 3 ml) was then added dropwise during 45 min, with stirring continued at 0 °C for 4 h. The mixture was then stirred overnight at room temperature, after which hydrochloric acid (6 M; 50 ml) was added, and the layers separated. The aqueous phase was extracted with ether, and the combined organic phases washed, dried, and evaporated. T.l.c. examination (Whatman K5F silica gel; dichloromethane with a trace of acetic acid) of the residual yellow solid (93 mg) indicated the presence of two constituents (R_F 0.17 and 0.39). Separation by preparative t.l.c. gave *2-acetyl-7-methoxy-1,4-dimethyldibenzofuran* (9) as a yellow solid (R_F 0.39, 23 mg, 38% yield) which crystallized from methanol as small, yellow-orange needles, m.p. 111—112 °C (Found: C, 75.7; H, 6.1. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%), δ 2.57 (3 H, s, 4-Me), 2.64 (3 H, s, COMe), 2.89 (3 H, s, 1-Me), 3.91 (3 H, s, OMe), 6.96 (1 H, dd, *J* 2.3 and 8.7 Hz, 8-H), 7.13 (1 H, d, *J* 2.3 Hz, 6-H), 7.51 (1 H, s, 3-H), and 7.97 (1 H, d, *J* 8.7 Hz, 9-H). The second constituent (R_F 0.17) was isolated as a yellow solid (11 mg, 16% yield) which on recrystallization from acetone yielded *2,8-diacetyl-7-hydroxy-1,4-dimethyldibenzofuran* (10) as small yellow prisms, m.p. 223—224.5 °C (lit.,[2] m.p. 170 °C) (Found: C, 72.8; H, 5.4. $C_{18}H_{16}O_3$ requires C, 73.0; H, 5.4%), δ 2.55 (3 H, s, 4-Me), 2.65 (3 H, s, COMe), 2.75 (3 H, s, COMe), 2.87 (3 H, s, 1-Me), 7.08 (1 H, s, 6-H), 7.56 (1 H, s, 3-H), 8.37 (1 H, s, 9-H), and 12.81 (1 H, s, OH).

Action of Acetyl Chloride and Titanium Tetrachloride on 7-Methoxy-1,4-dimethyldibenzofuran.—A solution of acetyl chloride in dichloromethane (0.1 M; 1.8 ml) was added dropwise to a stirred solution of titanium tetrachloride (0.14 ml, 1.27 mmol) and the dibenzofuran (7) (40 mg) in the same solvent (20 ml) at 0 °C under nitrogen. Work-up as in the previous experiment gave a solid product (R_F 0.15 and 0.61). The faster-moving constituent proved to be unchanged dibenzofuran (15 mg). Separation of the slower-moving constituent gave 8-acetyl-1,4-dimethyl-7-methoxydibenzofuran (ruscodibenzofuran methyl ether) (8) as colourless needles (27 mg, 56% yield), m.p. 155.5—156 °C from methanol (lit.,[4] m.p. 155—156 °C; lit.,[2] m.p. 155 °C); δ 2.52 (3 H, s, 4-Me), 2.68 (3 H, s, COMe), 2.73 (3 H, s, 1-Me), 4.00 (3 H, s, ArOMe), 7.01 (1 H, d, *J* 8.1 Hz, 2-H or 3-H), 7.13 (1 H, d, *J* 8.1 Hz, 3-H or 2-H), 7.15 (1 H, s, 6-H), and 8.41 (1 H, s, 9-H).

Ruscodibenzofuran (1).—A solution of boron tribromide (0.03 ml) in benzene (5 ml) was added dropwise during 3 min to a stirred solution of ruscodibenzofuran methyl ether (20 mg) in the same solvent (3 ml) at 0 °C under nitrogen. The resultant black solution was warmed to room temperature overnight. Addition of water (10 ml) and washing, drying, and evaporation of the benzene extract gave a slightly yellow solid, which on purification by t.l.c. gave 8-acetyl-7-hydroxy-1,4-dimethyldibenzofuran (ruscodibenzofuran) as a solid (19 mg, 100% yield) which crystallized from ethanol as light yellow-green feathery needles, m.p. 173—174.5 °C undepressed on admixture with an authentic specimen (lit.,[4] m.p. 171—172 °C, lit.,[2] 168 °C); δ 2.52 (3 H, s, ArMe), 2.71 (3 H, s, ArMe), 2.74 (3 H, s, COMe), 7.01 (1 H, d, *J* 8 Hz, 2-H or 3-H), 7.06 (1 H, s, 6-H), 7.12 (1 H, d, *J* 8 Hz, 3-H or 2-H), 8.24 (1 H, s, 9-H), and 12.76 (1 H, s, OH).

6-Benzoyloxy-2-isopropenylbenzofuran (13).—A stirred mixture of 5-benzoyloxy-2-iodophenol [7,10] (7.26 g) and copper(I) isopropenylacetylide (2.74 g) in pyridine (120 ml) was heated under reflux (nitrogen atmosphere) for 19 h, then worked up as for the methyl ether (4). After chromatography, *6-benzoyloxy-2-isopropenylbenzofuran* (13) was isolated as an amorphous yellow solid (1.01 g, 18% yield) which crystallized from methanol containing a drop of pyridine as small colourless cubes, m.p. 90.5—92 °C (Found: M^+, 278.0943. $C_{18}H_{14}O_3$ requires *M*, 278.0943); δ (CCl_4) 2.10 (3 H, s, Me), 5.08—5.20 (1 H, m, vinyl H), 5.74—5.80 (1 H, m, vinyl H), 6.58 (1 H, s, 3-H), 7.01 (1 H, dd, *J* 2 and 9 Hz, 5-H), 7.29—7.59 (5 H, m, 4-, 7-, 3′-, 4′- and 5′-H), and 8.15—8.25 (2 H, m, 2′- and 6′-H).

Methyl 7-Benzoyloxy-4-methyldibenzofuran-1-carboxylate (14).—A solution of the benzofuran (13) (1.01 g) and methyl propiolate (0.8 ml) in toluene (25 ml) was heated under reflux (nitrogen atmosphere) for 9 days. Removal of the solvent under reduced pressure gave an amber viscous oil (1.3 g) of which unchanged benzofuran was shown by t.l.c. to be the principal constituent. The oil was redissolved in toluene (1 ml), more methyl propiolate (1 ml) was added, and the

reflux treatment continued for a further 4 days. Work-up by solvent removal and chromatography on silica gel yielded, by elution with tetrachloromethane, crude 6-benzoyloxy-2-isopropylbenzofuran as an oil (27 mg, 3% yield); δ 1.34 (6 H, d, *J* 7.2 Hz, $CHMe_2$), 3.10 (1 H, sept, *J* 7.2 Hz, $CHMe_2$), 6.38 (1 H, br s, 3-H), 7.05 (1 H, dd, *J* 1.8 and 9 Hz, 5-H), and 7.42—7.73 (7 H, m, ArH).

Elution with tetrachloromethane (2 : 1) then gave *methyl 7-benzoyloxy-4-methyldibenzofuran-1-carboxylate* (14) as a solid (294 mg, 22%) which crystallized from acetone as small cubes, m.p. 169.5—170 °C (Found: C, 73.4; H, 4.7. $C_{22}H_{16}O_5$ requires C, 73.3; H, 4.5%); δ 2.64 (3 H, s, 4-Me), 4.04 (3 H, s, CO_2Me), 7.20—7.33 (2 H, m, 3-H and 8-H), 7.54—7.69 (4 H, m, 6-, 3'-, 4'-, and 5'-H), 7.97 (1 H, d, *J* 9 Hz, 2-H), 8.22—8.33 (2 H, m, 2'- and 6'-H) and 8.95 (1 H, d, *J* 9 Hz, 9-H). Irradiation of the multiplet at δ 7.20—7.33 resulted in collapse of the doublets at δ 7.97 and 8.95 to singlets.

7-Hydroxy-1-hydroxymethyl-4-methyldibenzofuran (15).—A solution of the benzoate (14) (76 mg) in tetrahydrofuran (30 ml) was added dropwise during 15 min to a stirred suspension of lithium aluminium hydride (650 mg) in the same solvent (20 ml) under nitrogen. The mixture was then heated under reflux, and worked up *via* ethyl acetate quenching, aqueous acid addition, and phase separation. Evaporation of the washed and dried aqueous phase gave a residue (57 mg) which separated from benzene–tetrachloromethane as a flocculent solid (26 mg, 54%). The *phenol* (15) had m.p. 206—208 °C (decomp.) (Found: M^+, 228.0786. $C_{14}H_{12}O_3$ requires *M*, 228.0786); δ [$(CD_3)_2SO$] 2.50 (3 H, s, Me), 4.91 (2 H, d, *J* 5.3 Hz, CH_2OH), 5.36 (1 H, t, *J* 5.3 Hz, CH_2OH), 6.87 (1 H, dd, *J* 2.1 and 8.4 Hz, 8-H), 7.07 (1 H, d, *J* 2.1 Hz, 6-H), 7.16 (1 H, d, *J* 7.9 Hz, 2- or 3-H), 7.22 (1 H, d, *J* 7.9 Hz, 3- or 2-H), 7.86 (1 H, d, *J* 8.4 Hz, 9-H), and 12.67 (1 H, s, ArOH).

7-Hydroxy-1,4-dimethyldibenzofuran (16).—A solution of the alcohol (15) (52 mg) in ethyl acetate (10 ml) was stirred with palladium–charcoal (10%; 79 mg) under hydrogen overnight. Removal of catalyst and solvent gave a yellowish crystalline solid (64 mg) which on sublimation (119 °C at 0.9 mmHg) gave the phenol (16) as a powder, m.p. 153—154 °C (lit.,[5] m.p. 158 °C); δ 2.53 (3 H, s, ArMe), 2.70 (3 H, s, ArMe), 6.80 (1 H, dd, *J* 2.7 and 9. Hz, 8-H), 6.94—7.04 (3 H, m, 2-, 3-, and 6-H), and 7.08 (1 H, d, *J* 9 Hz, 9-H).

A stirred mixture of the phenol (16) (36 mg), potassium carbonate (490 mg), and methyl iodide (2 ml) in acetone (15 ml) was heated under reflux overnight, and then filtered and evaporated. Sublimation (145 °C at 0.2 mmHg) of the residue gave the methyl ether (7), m.p. 66—70 °C with ^1H n.m.r. spectrum identical with that obtained earlier.

2,4-Dihydroxy-3,5-di-iodoacetophenone (18).—This compound was prepared by a general procedure.[11] A solution of iodine (15.2 g) and potassium iodide (13.64 g) in water (45 ml) was added dropwise during 15 min to a stirred solution of 2,4-dihydroxyacetophenone (17) (5 g) in ammonium hydroxide solution (30%; 90 ml). The mixture was stirred at room temperature for 2 h, diluted with ice-cold sulphuric acid (15%), and cooled (ice-bath). The resultant precipitate was collected, washed with water, and dried to give a red solid (11.2 g, 93% yield) which, on recrystallization from methanol, gave the di-iodo derivative (18) as tiny prisms, m.p. 189—190 °C (lit.,[11] 180 °C); δ [$(CD_3)_2CO$] 2.56 (3 H, s, COMe) and 8.24 (1 H, s, 6-H).

2,4-Dihydroxy-5-iodoacetophenone (19).—A mixture of the di-iodoacetophenone (9.12 g) and stannous chloride dihydrate (11.5 g) in acetic acid (260 ml) and water (30 ml) was heated under reflux for 4.5 h and then cooled to room temperature, diluted with water (2 l), and extracted with ether (3 × 100 ml). Concentration under reduced pressure and addition of water to the red acetic acid solution precipitated the mono-iodo derivative as a pink solid (2.5 g, 40%), m.p. 181.5—184 °C. Recrystallization from aqueous methanol gave needles, m.p. 185—186 °C (lit.,[11] m.p. 184 °C); δ [$(CD_3)_2CO$] 2.58 (3 H, s, COMe), 6.52 (1 H, s, 3-H), 8.27 (1 H, s, 6-H), and 12.65 (1 H, s, OH).

5-Acetyl-6-hydroxy-2-isopropenylbenzofuran (*Euparin*) (20).—To a suspension of copper(I) isopropenylacetylide (1.29 g) in pyridine (50 ml) was added a solution of 2,4-dihydroxy-5-iodoacetophenone (2.42 g) in the same solvent (50 ml) and the mixture heated under reflux (nitrogen atmosphere) for 18 h. It was then cooled, diluted with ether (1.5 l), set aside at 0 °C overnight, and filtered. The washed and dried filtrate was evaporated under reduced pressure and the residual yellow-green solid recrystallized from methanol (containing a drop of pyridine) to give euparin (20) as orange prisms (700 mg, 32%), m.p. 118—121 °C identical with an authentic specimen.[8]

Methyl 8-Acetyl-7-hydroxy-4-methyldibenzofuran-1-carboxylate (21).—A stirred solution of euparin (20) (700 mg) and methyl propiolate (0.35 ml) in toluene (25 ml) was heated under reflux (nitrogen atmosphere) for 5 days. Removal of solvent under reduced pressure and chromatography of the residual solid (950 mg) on silica gel yielded the *dibenzofuran* (21) as a solid (313 mg, 33% yield), which crystallized from methanol, m.p. 163—164 °C (Found: C, 68.2; H, 4.8. $C_{17}H_{14}O_5$ requires C, 68.5; H, 4.7%); δ 2.60 (3 H, s, 4-Me), 2.81 (3 H, s, COMe), 4.05 (3 H, s, CO_2Me), 7.06 (1 H, s, 6-H), 7.29 (1 H, d, *J* 8 Hz, 3-H), 7.99 (1 H, d, *J* 8 Hz, 2-H), 9.30 (1 H, s, 9-H), and 12.85 (1 H, s, ArOH).

Methyl 7-Acetoxy-8-acetyl-4-methyldibenzofuran-1-carboxylate (22).—A solution of the phenol (21) (213 mg) in pyridine (15 ml) and acetic anhydride (15 ml) was heated under reflux for 1 h. After the solvent had been removed under reduced pressure, a solution of the residual beige solid in chloroform was filtered through a short column of silica gel, to give the *acetate* (22) as a colourless solid (78% yield) which crystallized from methanol as small needles, m.p. 170—171 °C (Found: C, 67.45; H, 4.8. $C_{19}H_{16}O_6$ requires C, 67.05; H, 4.8%).

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