Expedient Synthesis of Polyhydroxyisoflavones

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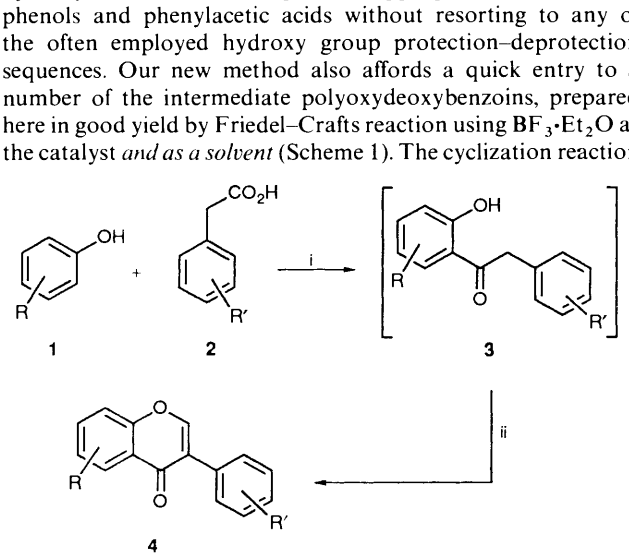
A general and direct synthesis of polyhydroxy isoflavones (3-phenyl-4*H*-1-benzopyran-4-ones) starting from the corresponding unprotected phenols and arylacetic acids is described. The aryl rings may carry additional alkyl, methoxy and/or halogeno groups. Intermediate polyhydroxy deoxybenzoins (1,2-diphenylethanones) can also be isolated in good yield.

Polyhydroxyisoflavanoids have been widely investigated during the last decade, owing to their range of biological properties of which anticancer activity[1–4] is an example. For their synthesis, several synthetic steps and the need for protection of free phenolic hydroxy groups are required in literature methods such as oxidative transformations of chalcone intermediates[5–7] or various ring closures of deoxybenzoins.[7] Polyhydroxydeoxybenzoins have widely been used as starting materials for isoflavones but only a few attempts have been made at carrying out the preparations using unprotected reactants. Bass[8] reported a single-stage synthesis of chromones from unprotected 2,4,6-trihydroxyphenyl alkyl ketones by treatment with boron trifluoride–diethyl ether and methanesulphonyl chloride in dimethylformamide (DMF). Pelter *et al.*[9,10] have studied the synthesis of isoflavones from unprotected hydroxydeoxybenzoins by using DMF dimethyl acetal alone or in conjunction with boron trifluoride–diethyl ether and DMF.

Whilst addition of a one-carbon unit to a protected polyhydroxydeoxybenzoin can be accomplished in a number of ways. Hoesch-reaction-based syntheses of polyoxydeoxybenzoins are often laborious, time-consuming and give poor yields.[11–14] Improved yields of phenolic deoxybenzoins have been obtained from resorcinol and arylacetic acids in the presence of boron trifluoride.[15]

We now introduce a direct, one-pot procedure for polyhydroxyisoflavones starting from appropriately substituted phenols and phenylacetic acids without resorting to any of the often employed hydroxy group protection–deprotection sequences. Our new method also affords a quick entry to a number of the intermediate polyoxydeoxybenzoins, prepared here in good yield by Friedel–Crafts reaction using BF_3·Et_2O as the catalyst *and as a solvent* (Scheme 1). The cyclization reaction



Scheme 1 *Reagents*: i, BF_3·Et_2O; ii, DMF, $MeSO_2Cl$

† Earnet/Bitnet: HASE(*a*)FINUHA or WAHALA(*a*)FINUHA

of the polyoxydeoxybenzoins is also catalysed by boron trifluoride. When the Friedel–Crafts acylation reaction is complete (by TLC) the C_1 source (dry DMF; 25 °C) and mesyl chloride (at 50 °C) are added and the mixture is heated on a water-bath. Excess of boron trifluoride–diethyl ether can be recovered by vacuum distillation from the reaction mixture. To illustrate the scope of the reaction, 19 hydroxyisoflavones (three of them new compounds, **4d**, **4i**, **4m** and nine known natural products **4a**, **4b**, **4e**, **4g**, **4j**, **4k**, **4p**, **4q**, **4r**) and 16 hydroxydeoxybenzoins (five of them new, **3c**, **3l**, **3m**, **3n**, **3p**) were synthesized, mostly in good yield (Table 1). 4′,8-Dihydroxyisoflavone **4b**, recently isolated from natural sources,[21] has now been synthesized for the first time.

A valuable aspect of the new procedural modification is that since free hydroxy groups are compatible with the reaction conditions, numerous mixed hydroxy/methoxy-substituted isoflavones, commonly encountered[44] as natural products, are directly accessible. This is fortunate because benzyl or silyl ethers or acyl groups are not stable under the reaction conditions while protection as the methyl ether, one of the very few phenol masks stable under these reaction conditions, is obviously not applicable either for any mixed hydroxy/methoxy substituted target. The same applies of course to the synthesis of polyoxygenated deoxybenzoins although these compounds occur much less frequently in Nature.

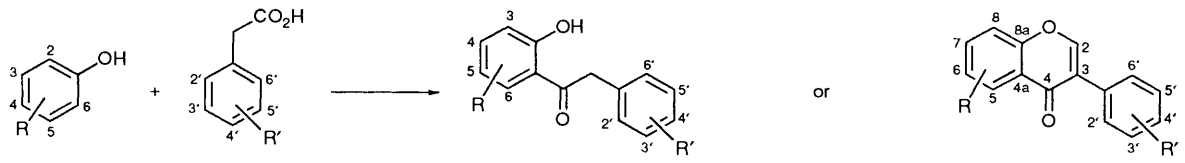
Monohydric phenols are usually acylated easily but the product is predominantly the *para* isomer because of the relatively large size of the acyl group and the *para*-directing effect of the catalyst.[45] *para*-Acylated phenols, obviously incapable of cyclizing to isoflavones, are only avoided when the phenolic *para* position is occupied to start with. Thus, *p*-cresol **1d** afforded, with 4-hydroxyphenylacetic acid **2b**, a 64% yield of 4′-hydroxy-6-methylisoflavone **4d**.

Among the dihydric phenols, resorcinol and substituted resorcinols react with variously substituted phenylacetic acids, giving excellent yields of isoflavones, or deoxybenzoins if required. Catechol **1b** undergoes mainly *para*-acylation which is why the 8-hydroxy-substituted isoflavone **4b** is produced in 15% yield only. Hydroquinone **1c** reacts somewhat sluggishly to give the *ortho*-acylation product **3d** in 68% yield and the corresponding isoflavone **4c** in 51% yield.

The trihydric phenols pyrogallol **1k** and phloroglucinol **1i** react cleanly to give deoxybenzoins or isoflavones as required. Hydroxyhydroquinone **1j** reacted very rapidly with boron trifluoride–diethyl ether to give unknown polar products of an intensely violet colour. Some starting material could be recovered but no deoxybenzoin or isoflavone derivatives are formed.

Hydroxy substituents at the *ortho*, *meta* or *para* position in the arylacetic acid moiety are similarly compatible. The presence of an *ortho* hydroxy group leads to the formation of the

Table 1

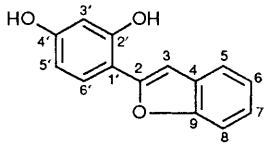


1 2 3 4

Substituents in phenol 1	Substituents in $ArCH_2CO_2H$ 2	Product and yield (%) Reaction time (t/h)[a]	Deoxybenzoin 3 (substituent)	Ref.	Reaction time (t/h)[a]	Isoflavone 4 (substituent)	Ref.
a H	**a** H	1.5	**a** 2-OH (23%)	16-18	1	**a** H (98%)[b]	18-20
a	**a**	1.5	**b** 4-OH (75%)	16, 17			
b 2-OH	**b** 4'-OH	2	**c** 3,4,4'-OH (78%)	*c*	1	**b** 4',8-OH (15%)	21
c 4-OH	**a**	6	**d** 2,5-OH (68%)	22	6	**c** 6-OH (51%)	22
d 4-Me	**b**	5			5	**d** 6-Me, 4'-OH (64%)	*c*
e 3-OH	**a**	1	**e** 2,4-OH (89%)	23	1	**e** 7-OH (93%)	24
e	**c** 3'-OH	1	**f** 2,3',4-OH (93%)	15	3	**f** 3',7-OH (91%)	15
e	**b**	1	**g** 2,4,4'-OH (98%)	25, 27	1.5	**g** 4',7-OH (98%)	28-31
e	**d** 2'-OMe	1	**h** 2,4-OH, 2'-OMe (98%)	32	1	**h** 7-OH, 2'-OMe (98%)	32
e	**e** 3'-OMe	1	**i** 2,4-OH, 3'-OMe (96%)	15	1	**i** 7-OH, 3'-OMe (84%)	
e	**f** 4'-OMe	1.5	**j** 2,4-OH, 4'-OMe (98%)	15, 26, 27, 33	1.5	**j** 7-OH, 4'-OMe (96%)	29, 31, 34, 35
e	**g** 3'-OMe,4'-OH	1	**k** 2,4,4'-OH, 3'-OMe (99%)	36	1.5	**k** 4',7-OH, 3'-OMe (94%)	37, 38
e	**h** 2'-OH	1			1	**l** 2',7-OH (72%)	32
f 3-OH, 4-Cl	**b**	1	**l** 2,4,4'-OH, 5-Cl (67%)	*c*	1	**m** 4',7-OH, 6-Cl (94%)	*c*
g 3-OH,2-Me	**b**	5	**m** 2,4,4'-OH, 3-Me (97%)	*c*	5	**n** 4',7-OH, 8-Me (91%)	39
h 3-OH,5-Me	**b**	2	**n** 2,4,4'-OH, 6-Me (86%)	*c*	2	**o** 4',7-OH, 5-Me (84%)	40
i 3,5-OH	**a**	1			1	**p** 5,7-OH (90%)	26, 41, 42
i	**f**	1			1	**q** 5,7-OH, 4'-OMe (90%)	26, 34, 35
i	**b**	5[d]	**o** 2,4,4',6-OH (83%)	27, 43	1	**r** 4',5,7-OH (53%)	26, 29, 34
j 3,4-OH	**b**		intractable complex mixture			intractable complex mixture	
k 2,3-OH	**b**	1	**p** 2,3,4,4'-OH (92%)	*c*	1	**s** 4',7,8-OH (83%)	14, 28

[a] Mixture heated on water-bath at 60–70 °C. [b] From isolated 2-hydroxydeoxybenzoin. [c] New compound. [d] At 0 °C.

benzofuran **5** as a minor by-product but even here the corresponding isoflavone **4l** is the main product. However, attempted isolation of the intermediate deoxybenzoin failed due to cyclization to the benzofuran during work-up.



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Experimental

M.p.s were determined in open capillary tubes with an Electrothermal apparatus, and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian GEMINI-200 FT NMR spectrometer using a standard $^1H/^{13}C$ dual probe (chemical shifts in δ). The assignments are based on chemical-shift data and DEPT and HETCOR measurements; assignments of peaks differing by δ 1 unit or less may be ambiguous. *J*-Values are given in Hz. Mass spectra were obtained with a JEOL JMS O1SG 2 mass spectrometer operating at 75 eV and HRMS spectra with a JEOL JMS SX102 mass spectrometer operating at 70 eV. Samples were introduced at 120–150 °C by a direct-inlet probe. TLC was conducted on Merck silica gel 60 F_{254} plates and Merck silica gel 60 (0.040–0.063 mm, 230–400 mesh) was used for flash column chromatography with CH_2Cl_2–EtOAc (7:2) elution for the purification of crude products. DMF and BF_3·Et_2O were dried and vacuum distilled over CaH_2 before use. All new compounds were fully characterized by ^1H, ^{13}C NMR, LRMS and HRMS analysis and they were homogeneous by TLC.

4-Hydroxy-3-methoxyphenylacetic Acid **2g**.—This was prepared according to Nakatsubo's method[46] from benzyloxyacetovanillone (0.01 mol) by treatment with thallium(III) nitrate (0.01 mol) in methanol (25 cm^3) containing 70% $HClO_4$ (5 cm^3) at room temperature. During the work-up procedure, namely evaporation of the solvent methanol from the reaction mixture, the product was found to be nitrated at the aromatic nucleus, giving a 98% yield of the methyl ester of 4-benzyloxy-3-methoxy-5-nitrophenylacetic acid. Therefore, the isolation procedure was changed to that used by McKillop.[47] After the oxidative rearrangement the precipitated thallium(I) nitrate was removed by filtration and the filtrate was diluted with water and extracted by chloroform. After hydrolysis of the ester with 10% KOH in MeOH–water (1:1) following the hydration with 10% Pd/C as a catalyst in aq. ethanol, 3-

methoxy-4-hydroxyphenylacetic acid was collected in 86% overall yield.

General Procedure for Isoflavones and Deoxybenzoins.—A phenol **1** (0.050 mol) and an arylacetic acid **2** (0.050 mol) were dissolved into freshly distilled BF_3·Et_2O (20 mol equiv.) under argon. The mixture was stirred and heated on a water-bath. For cyclization the reaction mixture was cooled to room temperature and dry DMF (77 cm^3) was added. The mixture was again heated to 50 °C and a solution of methanesulphonyl chloride (12 cm^3) in dry DMF (20 cm^3) was added slowly. After reaction at 60–70 °C the reaction mixture was cooled to room temperature and poured, without mechanical stirring, into a large volume of ice-cold aq. sodium acetate (12 g/100 cm^3). The crude product **4** was filtered off and recrystallized from a suitable solvent.

The intermediate deoxybenzoins **3** in many cases crystallized from the reaction mixture. They were isolated by washing of the collected material thoroughly with aq. NaOAc (12 g/100 cm^3) and recrystallization. If the reaction mixture was homogenous, deoxybenzoins were isolated by pouring of the mixture into a large volume of aq. NaOAc, extraction (Et_2O), drying and evaporation of the extract and recrystallization.

3,4,4′-*Trihydroxydeoxybenzoin* [1-(3,4-*dihydroxyphenyl*)-2-(4-*hydroxyphenyl*)*ethanone*] **3c**. Crystals, m.p. 211 °C (from aq. EtOH); δ_H([$^2H_6$]acetone) 4.12 (2 H, s, CH_2), 6.78 (2 H, d, *J* 8.7, 3′- and 5′-H), 6.91 (1 H, d, *J* 8.8, 5-H), 7.13 (2 H, d, *J* 8.7, 2′- and 6′-H), 7.54–7.60 (2 H, m, 2-and 6-H), 8.21 (1 H, s, OH), 8.35 (1 H, s, OH) and 8.70 (1 H, s, OH); δ_C([$^2H_6$]acetone) 44.70 (CH_2), 115.99 (C-5), 116.39 (C-3′, -5′), 116.55 (C-2), 123.60 (C-6), 127.70 (C-1′), 130.73 (C-1), 131.65 (C-2′, -6′), 146.16 (C-3), 151.35 (C-4′), 157.30 (C-4) and 197.47 (CO); *m*/*z* 244 (M^+, 48%), 138 (35), 187 (100), 109 (47), 107 (59), 81 (22) and 77 (23) (Found: M^+, 244.0742. $C_{14}H_{12}O_4$ requires M, 244.0736).

5-*Chloro*-2,4,4′-*trihydroxydeoxybenzoin* [1-(5-*chloro*-2,4-*dihydroxyphenyl*)-2-(4-*hydroxyphenyl*)*ethanone*] **3l**. Off-white crystals, m.p. 196–197 °C (from $CHCl_3$); δ_H([$^2H_6$]acetone) 4.25 (2 H, s, CH_2), 6.51 (1 H, s, 6-H), 6.81 (2 H, d, *J* 8.6, 3′- and 5′-H), 7.18 (2 H, d, *J* 8.6, 2′- and 6′-H), 8.07 (1 H, s, 3-H), 8.31 (1 H, s, OH), 10.11 (1 H, s, OH) and 12.60 (1 H, s, OH); δ_C([$^2H_6$]acetone) 44.49 (CH_2), 105.21 (C-3), 112.90 (C-5), 114.36 (C-1), 116.60 (C-3′, -5′), 126.67 (C-1′), 131.75 (C-2′, -6′), 133.66 (C-6), 157.76 (C-4′), 161.17 (C-2), 165.32 (C-4) and 204.25 (CO); *m*/*z* 278 (M^+, 14%), 173 (32), 171 (100), 107 (20) and 77 (7) (Found: M^+, 278.0355. $C_{14}H_{11}ClO_4$ requires M, 278.0346).

2,4,4′-*Trihydroxy*-3-*methyldeoxybenzoin* [1-(2,4-*dihydroxy*-3-*methylphenyl*)-2-(4-*hydroxyphenyl*)*ethanone*] **3m**. Off-white crystals, m.p. 187–188 °C (from propan-2-ol); δ_H([$^2H_6$]-acetone) 2.05 (3 H, s, *Me*Ar), 4.19 (2 H, s, CH_2), 6.50 (1 H, d, *J* 8.8, 5-H), 6.85 (2 H, d, *J* 8.6, 3′- and 5′-H), 7.24 (2 H, d, *J* 8.6, 2′- and 6′-H), 7.70 (1 H, s, OH), 7.81 (1 H, d, *J* 8.8, 6-H), 8.33 (1 H, s, OH) and 9.83 (1 H, s, OH); δ_C([$^2H_6$]acetone) 8.01 (*Me*Ar), 44.60 (CH_2), 108.19 (C-5), 112.22 (C-3), 113.40 (C-1), 116.43 (C-3′, -5′), 127.24 (C-1′), 131.32 (C-6), 131.54 (C-2′, -6′), 157.47 (C-2), 163.37 (C-4′), 164.84 (C-4) and 204.28 (CO); *m*/*z* 258 (M^+, 17%), 165 (4), 152 (16), 151 (100), 122 (5), 107 (11), 95 (5) and 77 (7) (Found: M^+, 258.0887. $C_{15}H_{14}O_4$ requires M, 258.0892).

2,4,4′-*Trihydroxy*-6-*methyldeoxybenzoin* [1-(2,4-*dihydroxy*-6-*methylphenyl*)-2-(4-*hydroxyphenyl*)*ethanone*] **3n**. Off-white crystals, m.p. 186–187 °C (from aq. EtOH); δ_H([$^2H_6$]acetone) 2.73 (3 H, s, *Me*Ar), 4.52 (2 H, s, CH_2), 6.35 (1 H, d, *J* 2.4, 3-H), 6.58 (1 H, d, *J* 2.4, 5-H), 6.88 (2 H, d, *J* 8.7, 3′- and 5′-H), 7.18 (2 H, d, *J* 8.7, 2′- and 6′-H), 8.50 (1 H, br s, OH), 10.82 (1 H, br s, OH) and 11.17 (1 H, s, OH); δ_C([$^2H_6$]acetone) 22.55 (*Me*Ar), 50.21 (CH_2), 101.61 (C-3), 111.57 (C-5), 115.96 (C-3′, -5′), 118.72 (C-1), 127.01 (C-1′), 131.44 (C-2′, -6′), 141.45 (C-6), 156.87 (C-4′), 161.76 (C-2), 162.49 (C-4) and 205.03 (CO); *m*/*z* (17 eV) 258 (M^+, 23%), 256 (20), 242 (18), 197 (12), 164 (17), 151 (100), 140 (12) and 134 (22) (Found: M^+, 258.0889. $C_{15}H_{14}O_4$ requires *M*, 2.58.0892).

2,3,4,4′-*Tetrahydroxydeoxybenzoin* [2-(4-*hydroxyphenyl*)-1-(2,3,4-*trihydroxyphenyl*)*ethanone*] **3p** (this compound has been mentioned in a Chinese article[48] but details of its characterization are lacking). Yellowish crystals, m.p. 208–209 °C (from 94% EtOH) (Found: C, 64.5; H, 4.6. $C_{14}H_{12}O_5$ requires C, 64.6; H, 4.6%); δ_H([$^2H_6$]acetone) 4.18 (2 H, s, CH_2), 6.48 (1 H, d, *J* 8.8, 5-H), 6.79 (2 H, d, *J* 8.6, 3′- and 5′-H), 7.17 (2 H, d, *J* 8.6, 2′- and 6′-H), 7.56 (1 H, d, *J* 8.8, 6-H), 7.83 (1 H, br s, OH), 8.22 (1 H, s, OH), 8.63 (1 H, br s, OH) and 12.77 (1 H, s, OH); δ_C([$^2H_6$]acetone) 44.41 (CH_2), 108.67 (C-5), 114.07 (C-1′), 116.51 (C-3′, -5′), 124.49 (C-6), 127.18 (C-1′), 131.69 (C-2′, -6′), 133.51 (C-3), 153.07 (C-2), 153.90 (C-4′), 157.65 (C-4) and 204.067 (CO); *m*/*z* 260 (M^+, 22%), 153 (100), 125 (3) and 107 (11) (Found: M^+, 260.0688. $C_{14}H_{12}O_5$ requires M, 260.0685).

4′,8-*Dihydroxyisoflavone* [8-*hydroxy*-3-(4-*hydroxyphenyl*)-4H-1-*benzopyran*-4-*one*] **4b**. Pale brownish crystals, m.p. 265 °C (from EtOH); δ_H([$^2H_6$]acetone) 6.90 (2 H, d, *J* 8.7, 3′- and 5′-H), 7.29 (2 H, d, *J* 5.4, 6- and 7-H), 7.50 (2 H, d, *J* 8.7, 2′- and 6′-H), 7.67 (1 H, d, *J* 5.4, 5-H), 8.27 (1 H, s, 2-H), 8.50 (1 H, s, OH) and 9.30 (1 H, s, OH); δ_C([$^2H_6$]acetone) 116.23 (C-3′, -5′), 116.93 (C-7), 119.89 (C-5), 124.65 (C-4a), 125.70 (C-3), 126.22 (C-6), 126.97 (C-1′), 131.53 (C-2′, -6′), 147.96 (C-8a), 153.70 (C-4′, -2), 158.77 (C-8) and 176.94 (C-4); *m*/*z* 254 (M^+, 100%), 253 ($M^+ - 1$, 12), 136 (37), 135 (16), 118 (17) and 108 (9) (Found: M^+, 254.0573. $C_{15}H_{10}O_4$ requires M, 254.0580).

4′-*Hydroxy*-6-*methylisoflavone* [3-(4-*hydroxyphenyl*)-6-*methyl*-4H-1-*benzopyran*-4-*one*] **4d**. Pale yellow crystals, m.p. 210–211 °C (from CH_2Cl_2–EtOAc); δ_H([$^2H_6$]acetone) 2.48 (3 H, s, Me), 6.89 (2 H, d, *J* 8.7, 3′- and 5′-H), 7.49 (3 H, d, *J* 8.7, 2′-6′- and 8-H), 7.61 (1 H, dd, *J* 9 and 2, 7-H), 8.00 (1 H, s, 5-H), 8.26 (1 H, s, 2-H) and 8.47 (1 H, s, OH); δ_C([$^2H_6$]acetone) 20.96 (Me), 116.22 (C-3′, -5′), 119.19 (C-8), 124.74 (C-4a), 125.49 (C-3), 125.74 (C-1′), 126.35 (C-5), 131.47 (C-2′, -6′), 136.04 (C-7), 136.30 (C-6), 154.18 (C-2), 155.79 (C-4′), 158.71 (C-8a) and 178.36 (C-4); *m*/*z* 252 (M^+, 93%), 251 ($M^+ - 1$, 43), 165 (4), 152 (3), 135 (16), 134 (17), 126 (4), 118 (14), 106 (8) and 89 (7) (Found: M^+, 252.0783. $C_{16}H_{12}O_3$ requires M, 252.0787).

7-*Hydroxy*-3′-*methoxyisoflavone* [7-*hydroxy*-3-(3-*methoxyphenyl*)-4H-1-*benzopyran*-4-*one*] **4i**. Crystals m.p. 218 °C (from 94% EtOH) (Found: C, 71.7; H, 4.5. $C_{16}H_{12}O_4$ requires C, 71.7; H, 4.5%); δ_H[$(CD_3)_2SO$] 3.80 (3 H, s, OMe), 6.90–7.01 (3 H, m, 4′-, 6- and 8-H), 7.12–7.26 (2 H, m, 2′- and 6′-H), 7.36 (1 H, t, *J* 8, 5′-H), 8.01 (1 H, d, *J* 8.7, 5-H), 8.39 (1 H, s, 2-H) and 10.88 (1 H, s, OH); δ_C[$(CD_3)_2SO$] 55.16 (OMe), 102.42 (C-8), 113.50 (C-6), 114.94 (C-4′), 115.54 (C-2′), 116.97 (C-4a), 121.48 (C-6′), 123.67 (C-3), 127.65 (C-5′), 129.43 (C-5), 133.81 (C-1′), 154.28 (C-2), 157.82 (C-8a), 159.43 (C-3′), 163.10 (C-7) and 174.82 (C-4); *m*/*z* 268 (M^+, 100%), 267 ($M^+ - 1$, 76), 253 (7), 239 (17), 238 (18), 225 (7), 136 (10), 132 (18), 108 (10), 102 (12) and 89 (11) (Found: M^+, 268.0730. $C_{16}H_{12}O_4$ requires M, 268.0735).

6-*Chloro*-4′,7-*dihydroxyisoflavone* [6-*chloro*-7-*hydroxy*-3-(4-*hydroxyphenyl*)-4H-1-*benzopyran*-4-*one*] **4m**. Off-white crystals, m.p. 324–325 °C (from aq. EtOH); δ_H[$(CD_3)_2SO$] 6.82 (2 H, d, *J* 8.4, 3′- and 5′-H), 7.07 (1 H, s, 8-H), 7.39 (2 H, d, *J* 8.4, 2′- and 6′-H), 8.00 (1 H, s, 5-H), 8.34 (1 H, s, 2-H) and 9.58 (1 H, s, OH); δ_C[$(CD_3)_2SO$] 103.79 (C-8), 115.22 (C-3′, -5′), 117.30 (C-6), 119.85 (C-4a), 122.43 (C-3), 123.69 (C-1′), 126.39 (C-5), 130.34 (C-2′, -6′), 153.50 (C-2), 155.94 (C-8a), 157.65 (C-4′), 158.24 (C-7) and 174.27 (C-4); *m*/*z* 288 (M^+, 100%), 287 ($M^+ - 1$, 45), 171 (32), 170 (6), 142 (8), 118 (40) and 89 (11) (Found: M^+, 288.0192. $C_{15}H_9ClO_4$ requires M, 288.0190).

4′,7-*Dihydroxy*-8-*methylisoflavone* [7-*hydroxy*-3-(4-*hydroxyphenyl*)-8-*methyl*-4H-1-*benzopyran*-4-*one*] **4n**. Off-white crystals, m.p. 319–320 °C (from $CHCl_3$) (lit.,[39] m.p. 236–237 °C from EtOH); δ_H[$(CD_3)_2SO$] 2.25 (3 H, s, Me), 6.82 (2 H, d, *J*

8.4, 3′- and 5′-H), 7.01 (1 H, d, *J* 8.6, 6-H), 7.40 (2 H, d, *J* 8.4, 2′- and 6′-H), 7.85 (1 H, d, *J* 8.6, 5-H), 8.38 (1 H, s, 2-H), 9.55 (1 H, s, OH) and 10.66 (1 H, s, OH); δ_C[$(CD_3)_2SO$] 7.85 (Me), 110.76 (C-8), 113.80 (C-6), 114.88 (C-3′, -5′), 116.65 (C-4a), 122.58 (C-3), 122.98 (C-1′), 123.68 (C-5), 129.95 (C-2′, -6′), 152.72 (C-2), 155.45 (C-4′), 157.05 (C-8a), 159.82 (C-7) and 175.04 (C-4); *m/z* 268 (M^+, 97%), 267 ($M^+ - 1$, 48), 256 (5), 239 (3), 151 (21), 150 (15), 129 (5), 122 (11), 118 (8) and 97 (6) (Found: M^+, 268.0738. $C_{16}H_{12}O_4$ requires M, 268.0736).

2-(2′,4′-*Dihydroxyphenyl*)*benzofuran* [4-(*benzofuran*-2-*yl*)*benzene*-1,3-*diol*] **5**. Pale brownish crystals, m.p. 144 °C (from PhH) (Found: C, 74.3; H, 4.5. $C_{14}H_{10}O_3$ requires C, 74.3; H, 4.5%); $\delta_H(CDCl_3)$ 6.34–6.41 (2 H, m, 3′- and 5′-H), 6.94–7.02 (3 H, m, 3-, 6- and 8-H), 7.21–7.38 (2 H, m, 5-and 7-H), 7.58 (1 H, d, *J* 8.3, 6′-H), 8.64 (1 H, s, OH) and 9.21 (1 H, s, OH); $\delta_C(CDCl_3)$ 102.97 (C-3), 104.10 (C-6′), 108.67 (C-3′), 110.18 (C-1′), 111.11 (C-5), 121.08 (C-7), 123.32 (C-6), 123.94 (C-8), 128.69 (C-5′), 130.27 (C-4), 154.29 (C-2′), 154.65 (C-4′), 156.08 (C-2) and 159.12 (C-9); *m/z* 226 (M^+, 100%), 197 (20), 181 (3), 169 (4), 141 (4) and 113 (5) (Found: M^+, 226.0624. $C_{14}H_{10}O_3$ requires M, 226.0630).

Acknowledgements

We thank Mr. Jorma Matikainen and Mr. Seppo Räisänen for running the mass spectra. Financial support to K. Wähälä from the Emil Aaltonen Foundation is gratefully acknowledged.

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Paper 1/02919C
Received 17*th June* 1991
Accepted 17*th July* 1991