Synthesis of α-methyldeoxybenzoins

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Reduction of hydroxy and/or methoxy-substituted isoflavones using $LiAlH_4$ in refluxing THF provides an easy access to a number of α-methyldeoxybenzoins, possible metabolites of phytoestrogens in man. The synthesis of *O*-demethylangolensin **2b**, 6′-hydroxyangolensin **2c**, angolensin **2d**, 1-(2,4-dihydroxyphenyl)-2-phenylpropan-1-one **2e**, 1-(2-hydroxy-4-methoxyphenyl)-2-(4-hydroxyphenyl)propan-1-one **2f**, 4′-*O*-methylangolensin **2g**, 1-(2-hydroxy-4-methoxyphenyl)-2-phenylpropan-1-one **2h**, and 1-(2-hydroxyphenyl)-2-phenylpropan-1-one **2i** is described.

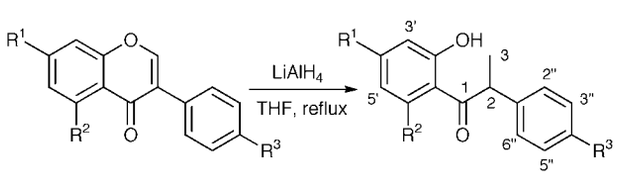
Recently, it has been established that α-methyldeoxybenzoins are likely metabolites of naturally occurring isoflavones such as genistein **1a**, daidzein **1b**, biochanin A **1c** and formononetin **1d**. The α-methyldeoxybenzoins as such are rare in the plant kingdom. The sole known example is angolensin **2d** which occurs in the heartwood of *Pterocarpus angolensis*, in *P. indicana* and in *Afromosia* species.[1–5] Angolensin methyl[1,2] and cadinyl (sesquiterpenoid) ethers[1,2] are also known to occur naturally.

Interest in the metabolism of the dietary isoflavones in man is now rapidly increasing. It is now known that formononetin **1d** is first converted to daidzein **1b** and thence to *O*-demethylangolensin (ODMA, **2b**),[6] a member of the α-methyldeoxybenzoin group of compounds. ODMA **2b** was first identified from the urine and plasma of sheep[7–9] and cattle.[6,9] Later it was isolated from the urine of chimpanzees[10] and humans,[11–13] human plasma,[14,15] human faeces,[16,17] and from cow milk.[18] Angolensin **2d**, the methylated analog of ODMA, has been found only in the urine of sheep.[19] The tentative identification of a new α-methyldeoxybenzoin, 6′-hydroxy-*O*-demethylangolensin **2a**, in human urine was recently announced.[20,21] We have since confirmed this by comparison with an authentic synthetic sample.[22]

Known syntheses of α-methyldeoxybenzoins mostly encompass numerous steps giving poor overall yields, as, for example, in the synthesis of 4″-hydroxy-2′,4′-dimethoxy-α-methyldeoxybenzoin by an 8-step route involving the photolysis of an α-hydroxydihydrochalcone.[5] Similarly, there is a multistep route to angolensin and ODMA by way of a Friedel–Crafts reaction of 1,3-dimethoxybenzene and 2-methoxypropionic acid.[11,23] More recently, α-methyldeoxybenzoins have been prepared by a base-catalysed C-methylation of deoxybenzoins, giving angolensin and its methylated analogs.[24] A free OH at C-2′ is compatible whereas a 4′-OH is methylated. Our experience is that 2′,4′-dihydroxydeoxybenzoins give complex mixtures of products, also by 4′- and α,α-dialkylation, with various procedures under basic conditions.[25]

O-Methylated and -benzylated analogs of angolensin have been prepared directly from angolensin by methylation[1,26,27] or benzylation.[1]

Certain reductions of isoflavones are reported to furnish α-methyldeoxybenzoins. Catalytic hydrogenation of the unsubstituted isoflavone in basic medium leads mainly to 2′-hydroxy-α-methyldeoxybenzoin presumably *via* the ring-opened α-methylene derivate.[28] Also, Birch reduction using lithium in liquid ammonia converts protected isoflavones to the corresponding α-methyldeoxybenzoins.[29] Some reductions of protected isoflavones with $LiAlH_4$ giving ring-opened ketones and further α-methyldeoxybenzoins as minor products have also been reported.[30] However, there are no mentions of hydride reductions of unprotected hydroxy-substituted isoflavones in the literature. The co-occurrence of α-methyldeoxybenzoins with various isoflavonoid derivatives, and their origin as reduced metabolites of the latter, prompted us to study the synthesis of α-methyldeoxybenzoins directly from isoflavone starting materials by reduction. This would be highly expedient as we already have an easy and general access to a number of isoflavones by a one-pot reaction.[31,32] Following our preliminary report of the first synthesis of 6′-hydroxy-*O*-demethylangolensin **2a**, by reduction of genistein with $LiAlH_4$ in refluxing THF,[33] we now describe an improved synthetic pathway and spectroscopic details for angolensin **2d**, *O*-demethylangolensin **2b** and for seven additional α-methyldeoxybenzoins, many of them new (Table 1) (see Scheme 1).

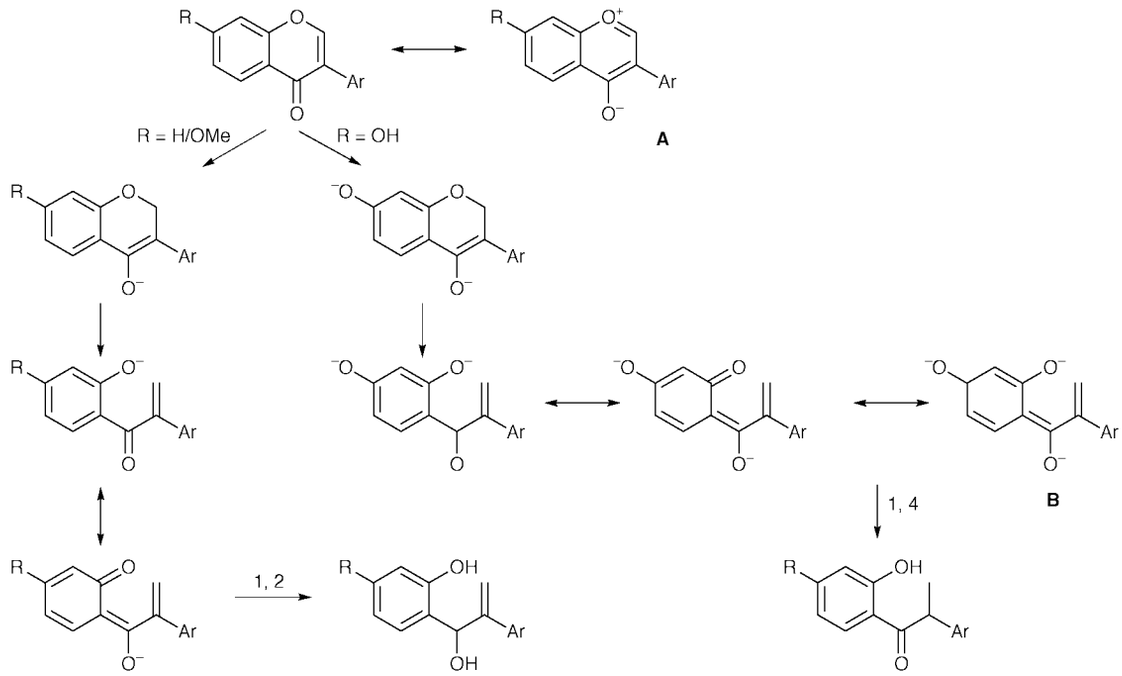


1a $R^1 = R^2 = R^3 = OH$
1b $R^1 = R^3 = OH$, $R^2 = H$
1c $R^1 = R^2 = OH$, $R^3 = OCH_3$
1d $R^1 = OH$, $R^2 = H$, $R^3 = OCH_3$
1e $R^1 = OH$, $R^2 = R^3 = H$
1f $R^1 = OCH_3$, $R^2 = H$, $R^3 = OH$
1g $R^1 = R^3 = OCH_3$, $R^2 = H$
1h $R^1 = OCH_3$, $R^2 = R^3 = H$
1i $R^1 = R^2 = R^3 = H$

2a $R^1 = R^2 = R^3 = OH$
2b $R^1 = R^3 = OH$, $R^2 = H$
2c $R^1 = R^2 = OH$, $R^3 = OCH_3$
2d $R^1 = OH$, $R^2 = H$, $R^3 = OCH_3$
2e $R^1 = OH$, $R^2 = R^3 = H$
2f $R^1 = OCH_3$, $R^2 = H$, $R^3 = OH$
2g $R^1 = R^3 = OCH_3$, $R^2 = H$
2h $R^1 = OCH_3$, $R^2 = R^3 = H$
2i $R^1 = R^2 = R^3 = H$

3a $R^1 = R^2 = OCH_3$
3b $R^1 = OCH_3$, $R^2 = H$
3c $R^1 = R^2 = H$
3d $R^1 = OCH_3$, $R^2 = OH$

Scheme 1 Reduction of isoflavones with $LiAlH_4$.



Scheme 2 Suggested reaction pathways for the LAH reduction of isoflavones.

Table 1 Reduction of isoflavones with $LiAlH_4$ in refluxing THF

Starting material	Amount of $LiAlH_4$ (mol equiv.)	Reaction time (*t*/h)	Products	Yield (%)
1a	5.5	2.5	**2a**[33]	66
1b	5.5	24	**2b**	42
1c	4.3	1	**2c**[a]	70
1d	3.3	2	**2d**	42
1e	3.3	1.5	**2e**[a]	60
1f	3.3	1.5	**2f**[a]	34
			3d[a]	17
1g	2.5	0.25	**3a**[a]	50
			2g	27
1h	2.5	0.25	**3b**[a]	50
			2h	29
1i	2.5	0.25	**3c**[a]	48
			2i	27

[a] New compound.

Results and discussion

As seen in the Table, the amount of reagent used was adjusted to take into account the number of free OH groups. It is also clearly seen how an increasing number of free OH groups requires a longer reaction time (in refluxing THF), presumably due to a combination of electronic and solubility effects.

The α-methyldeoxybenzoins are formed without complications except when there is no hydroxy substituent at the isoflavone 7-position. In such cases prop-2-en-1-ols are the main products. For example, the reduction of 4′,7-dimethoxyisoflavone **1g** gives 1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)prop-2-en-1-ol **3a** and 4′-*O*-methylangolensin **2g** in a ratio of 2 to 1. Contrary to some earlier proposals,[28] we assume that the initial step in these reductions is a 1,4-addition to the enone system, driven by the 4-oxypyrylium contributor (**A**) to the isoflavone structure. This is then followed by ring opening to a prop-2-en-1-one, in turn reduced by another 1,4-addition to give the deoxybenzoin enolates, or by a 1,2-addition to give the propenols (Scheme 2). We suggest that the effect of the 7-hydroxy substituent is to provide a further resonance contributor (**B**) where the propenone carbonyl is lacking, thus favouring conjugate hydride attack at the propene terminus. As the situation is somewhat different with the 7-H or 7-MeO analogs 1,2-attack at the propenone carbonyl predominates.

Experimental

Mps were determined in open capillary tubes with an Electrothermal apparatus and are uncorrected. IR spectra were recorded from KBr discs on a FTIR Biorad FTS-7 instrument. UV spectra were recorded in 94% ethanol solution with a CARY 5E UV-VIS-NIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian GEMINI-200 FT NMR spectrometer using the standard $^1H/^{13}C$ dual probe (chemical shifts in ppm). *J*-Values are given in Hz. LR and HR mass spectra were obtained with a JEOL JMS SX102 mass spectrometer operating at 70 eV. 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 chromatography. Tetrahydrofuran (THF) was dried by distilling over CaH_2 before use.

General procedure

In Table 1 there are collected the starting isoflavone **1a**–**i**, the amount of reducing agent used and the reaction time needed for the completion of reduction is judged by TLC monitoring. A solution of an isoflavone **1** (0.2 g) in THF (10 cm^3) was added over 0.5 h to a stirred slurry of lithium aluminium hydride (2.5–5.5 mol equiv., see Table 1) in refluxing THF (5 cm^3). After further refluxing (see Table 1), the reaction mixture was cooled and poured into saturated aq. NH_4Cl at 0 °C. The mixture was neutralized with 2 M HCl and extracted with EtOAc. The extract was washed with water, dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography.

O-Demethylangolensin 2b, 1-(2,4-dihydroxyphenyl)-2-(4-hydroxyphenyl)propan-1-one

Flash chromatography eluent: *n*-hexane–acetone (1 : 1). White crystals, mp 101 °C (from *n*-hexane–diethyl ether) (lit.,[34] 103 °C); λ_{max}(EtOH)/nm 214 (ε/dm^3 mol^{-1} cm^{-1} 21 700), 278 (15 300) and 318 (9600); ν_{max}/cm^{-1} 3303 (OH) and 1631 (CO); δ_H([$^2H_6$]acetone) 1.43 (3H, d, *J* 6.8, 3-H_3), 4.76 (1H, q, *J* 6.8, 2-H), 6.30 (1H, d, *J* 2.4, 3′-H), 6.37 (1H, dd, *J* 2.4 and 8.6, 5′-H), 6.78 (2H, d, *J* 8.6, 3″- and 5″-H), 7.20 (2H, d, *J* 8.5, 2″-H and 6″-H) and 7.89 (1H, d, *J* 8.8, 6′-H); δ_C([$^2H_6$]acetone) 18.1

(C-3), 44.8 (C-2), 102.3 (C-3′), 107.3 (C-5′), 111.6 (C-1′), 115.1 (C-3″ and -5″), 128.1 (C-2″ and -6″), 132.3 (C-1″), 132.7 (C-6′), 155.8 (C-4″), 164.0 (C-2′), 165.6 (C-4′) and 204.8 (C-1); *m*/*z* 258 (M^+, 14%), 138 (8), 137 (100) and 121 (17) (Found: M^+, 258.0894. $C_{15}H_{14}O_4$ requires *M*, 258.0892).

6′-Hydroxyangolensin 2c, 2-(4-methoxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one

Flash chromatography eluent: *n*-hexane–acetone (1:1). White crystals, mp 107 °C (from benzene); λ_{max}(EtOH)/nm 225 (ε/dm^3 mol^{-1} cm^{-1} 11 500) and 294 (11 100); ν_{max}/cm^{-1} 3347 (OH) and 1630 (CO); δ_H([$^2H_6$]acetone) 1.40 (3H, d, *J* 7.0, 3-H_3), 3.73 (3H, s, OCH_3), 5.27 (1H, q, *J* 6.9, 2-H), 5.89 (2H, s, 3′- and 5′-H), 6.8 (2H, d, *J* 8.8, 3″-H and 5″-H) and 7.23 (2H, d, *J* 8.8, 2″-H and 6″H); δ_C([$^2H_6$]acetone) 19.9 (C-3), 49.4 (C-2), 55.3 (OCH_3), 96.0 (C-3′ and -5′), 104.8 (C-1′), 114.4 (C-3″ and -5″), 130.0 (C-2″ and -6″), 135.3 (C-1″), 159.3 (C-4″), 165.3 (C-2′, -4′ and -6′) and 207.1 (C-1); *m*/*z* 288 (M^+, 18%), 270 (5), 167 (6), 153 (100) and 135 (45) (Found: M^+, 288.1000. $C_{16}H_{16}O_5$ requires *M*, 288.0998).

Angolensin 2d, 1-(2,4-dihydroxyphenyl)-2-(4-methoxyphenyl)-propan-1-one

Flash chromatography eluent: CH_2Cl_2–EtOAc (7:1). Pale yellowish crystals, mp 84 °C (from benzene) (lit.,[24] 86–87 °C); λ_{max}(EtOH)/nm 215 (ε/dm^3 mol^{-1} cm^{-1} 37 400), 280 (26 800) and 319 (17 000); ν_{max}/cm^{-1} 3353 (OH) and 1630 (CO); δ_H($CDCl_3$) 1.49 (3H, d, *J* 7.0, 3-H_3), 3.75 (3H, s, 4″-OMe), 4.57 (1H, q, *J* 6.8, 2-H), 6.27 (1H, d *J* 2.5, 3′-H), 6.32 (1H, dd, *J* 2.6 and 8.8, 5′-H), 6.84 (2H, d, *J* 8.6, 3″- and 5″-H), 7.20 (2H, d, *J* 8.7, 2″- and 6″-H), 7.68 (1H, d, *J* 8.8, 6′-H) and 12.00 (1H, br s, OH); δ_C($CDCl_3$) 19.2 (C-3), 45.9 (C-2), 55.3 (OMe), 103.5 (C-3′), 108.1 (C-5′), 112.8 (C-1′), 114.4 (C-3″ and -5″), 128.6 (C-2″ and -6″), 132.8 (C-6′), 133.5 (C-1″), 158.4 (C-4″), 162.8 (C-2′), 165.6 (C-4′) and 205.4 (C-1); *m*/*z* 272 (M^+, 36%), 151 (5), 149 (5), 138 (17), 137 (100), 136 (15), 135 (60), 105 (5) and 91 (5) (Found: M^+, 272.1047. $C_{16}H_{16}O_4$ requires *M*, 272.1048).

1-(2,4-Dihydroxyphenyl)-2-phenylpropan-1-one 2e

Flash chromatography eluent: CH_2Cl_2–EtOAc (7:2). White crystals, mp 137 °C (from *n*-hexane–Et_2O); λ_{max}(EtOH)/nm 213 (ε/dm^3 mol^{-1} cm^{-1} 22 200), 282 (15 300), 234 (8650) and 317 (9540); ν_{max}/cm^{-1} 3357 (OH) and 1631 (CO); δ_H([$^2H_6$]acetone) 1.48 (3H, d, *J* 6.8, 3-H_3), 4.88 (1H, q, *J* 6.6, 2-H), 6.30 (1H, d, *J* 2.2, 3′-H), 6.36 (1H, dd, *J* 2.4 and 8.8, 5′-H), 7.16–7.43 (5H, m, Ar-H) and 7.90 (1H, d, *J* 9.0, 6′-H); δ_C([$^2H_6$]acetone) 19.5 (C-3), 47.1 (C-2), 103.7 (C-3′), 108.8 (C-5′), 113.1 (C-1′), 127.8 (C-4″), 128.5 (C-2″ and -6″), 129.8 (C-3″ and -5″), 134.1 (C-6′), 143.1 (C-1″), 165.5 (C-2′), 167.1 (C-4′) and 205.8 (C-1); *m*/*z* 242 (M^+, 12%), 138 (10), 137 (100), 105 (13), 77 (5) and 58 (46) (Found: M^+, 242.0944. $C_{15}H_{14}O_3$ requires *M*, 242.0943).

1-(2-Hydroxy-4-methoxyphenyl)-2-(4-hydroxyphenyl)propan-1-one 2f

Flash chromatography eluent: *n*-hexane–acetone (1:1). White crystals, mp 142 °C (from *n*-hexane–diethyl ether); λ_{max}(EtOH)/nm 214 (ε/dm^3 mol^{-1} cm^{-1} 24 800), 227s (17 600), 276 (18 100) and 320 (10 400); ν_{max}/cm^{-1} 3465 (OH) and 1629 (CO); δ_H([$^2H_6$]-acetone) 1.43 (3H, d, *J* 6.8, 3-H_3), 3.83 (3H, s, OCH_3), 4.79 (1H, q, *J* 6.9, 2-H), 6.38 (1H, d, *J* 2.6, 3′-H), 6.41 (1H, dd, *J* 8.2 and 2.6, 5′-H), 6.78 (2H, d, *J* 8.6, 3″- and 5″-H), 7.20 (2H, d, *J* 8,6, 2″- and 6″-H) and 7.94 (1H, d, *J* 8.3, 6′-H); δ_C([$^2H_6$]acetone) 19.5 (C-3), 46.4 (C-2), 56.1 (OCH_3), 101.8 (C-3′), 108.1 (C-5′), 115.2 (C-1′), 116.7 (C-3″ and -5″), 129.6 (C-2″ and -6″), 133.7 (C-6′), 134.2 (C-1″), 157.5 (C-4″), 167.1 (C-2′ and -4′) and 207.1 (C-1); *m*/*z* 272 (M^+, 18%), 152 (15), 151 (100), 137 (14), 135 (8), 121 (8) (Found: M^+, 272.1052. $C_{16}H_{16}O_4$ requires *M*, 272.1048).

4′-*O*-Methylangolensin 2g, 1-(2-hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)propan-1-one

Flash chromatography eluent: *n*-hexane–acetone (7:4). White crystals, mp 67 °C (from *n*-hexane–Et_2O) (lit.,[24] 69–70 °C); λ_{max}(EtOH)/nm 215 (ε/dm^3 mol^{-1} cm^{-1} 25 500), 227s (18 700), 276 (18 400) and 319 (11 000); ν_{max}/cm^{-1} 3439 (OH) and 1637 (CO); δ_H($CDCl_3$) 1.50 (3H, d, *J* 6.8, 3-H_3), 3.75 (3H, s, 4″-OCH_3), 3.78 (3H, s, 4′-OCH_3), 4.59 (1H, q, *J* 7.0, 2-H), 6.33 (1H, dd, *J* 8.8 and 2.5, 5′-H), 6.38 (1H, d, *J* 2.3, 3′-H), 6.84 (2H, d, *J* 8.8, 3″- and 5″-H), 7.21 (2H, d, *J* 8.8, 2″- and 6″-H) and 7.69 (1H, d, *J* 8.8, 6′-H); δ_C($CDCl_3$) 19.2 (C-3), 46.0 (C-2), 55.2 (OCH_3), 55.5 (OCH_3), 101.0 (C-3′), 107.6 (C-5′), 112.7 (C-1′), 114.3 (C-3″ and -5″), 128.5 (C-2″ and -6″), 131.9 (C-6′), 133.5 (C-1″), 158.5 (C-4″), 165.8 (C-2′), 166.1 (C-4′) and 204.9 (C-1); *m*/*z* 286 (M^+, 30%), 284 (15), 269 (10), 151 (100), and 135 (40) (Found: M^+, 286.1202. $C_{17}H_{18}O_4$ requires *M*, 286.1205).

1-(2-Hydroxy-4-methoxyphenyl)-2-phenylpropan-1-one 2h

Flash chromatography eluent: *n*-hexane–acetone (7:4). White crystals, mp 109 °C (from *n*-hexane) (lit.,[29] 108 °C); λ_{max}(EtOH)/nm 213 (ε/dm^3 mol^{-1} cm^{-1} 18 100), 280 (13 300), 231 (7770) and 318 (7570); ν_{max}/cm^{-1} 3428 (OH) and 1630 (CO); δ_H($CDCl_3$) 1.53 (3H, d, *J* 7.0, 3-H_3), 3.79 (3H, s, 4′-OCH_3), 4.64 (1H, q, *J* 6.8, 2-H), 6.32 (1H, dd, *J* 2.6 and 8.8, 5′-H), 6.39 (1H, d, *J* 2.4, 3′-H), 7.19–7.32 (5H, m, Ar-H) and 7.69 (1H, d, *J* 8.8, 6′-H); δ_C($CDCl_3$) 19.2 (C-3), 47.0 (C-2), 55.6 (OMe), 101.1 (C-3′), 107.7 (C-5′), 112.8 (C-1′), 127.1 (C-4″), 127.6 (C-2″ and -6″), 129.1 (C-3″ and -5″), 132.1 (C-6′), 141.6 (C-1″), 165.9 (C-2′), 166.2 (C-4′) and 204.7 (C-1); *m*/*z* 256 (M^+, 7%), 162 (5), 152 (10), 151 (100), 117 (10) and 58 (40) (Found: M^+, 256.1090. $C_{16}H_{16}O_3$ requires *M*, 256.1099).

1-(2-Hydroxyphenyl)-2-phenylpropan-1-one 2i

Flash chromatography eluent: *n*-hexane–acetone (7:4). Colorless oil; λ_{max}(EtOH)/nm 213 (ε/dm^{-3} mol^{-1} cm^{-1} 19 100), 255 (9140) and 329 (4050); ν_{max}/cm^{-1} 2978 (OH) and 1638 (CO); δ_H($CDCl_3$) 1.54 (3H, d, *J* 7.0, 3-H_3), 4.73 (1H, q, *J* 6.6, 2-H), 6.78 (1H, t, *J* 8.3, 5′-H), 6.94 (1H, d, *J* 7.4, 3′-H), 7.19–7.42 (6H, m, Ar-H) and 7.79 (1H, d, *J* 8.0, 6′-H); δ_C($CDCl_3$) 19.3 (C-3), 47.3 (C-2), 118.7 (C-1′ and -3′), 118.9 (C-5′), 127.2 (C-4″), 127.6 (C-2″ and -6″), 129.1 (C-3″ and -5″), 130.5 (C-6′), 136.2 (C-4′), 141.2 (C-1″), 163.2 (C-2′) and 206.6 (C-1); *m*/*z* 226 (M^+, 11%), 194 (5), 122 (8), 121 (100), 105 (12), 77 (7) and 58 (35) (Found: M^+, 226.0996. $C_{15}H_{14}O_2$ requires *M*, 226.0994).

1-(2-Hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)prop-2-en-1-ol 3a

Flash chromatography eluent: *n*-hexane–acetone (7:4). Amorphous solid; λ_{max}(EtOH)/nm 205 (ε/dm^{-3} mol^{-1} cm^{-1} 13 100) and 254 (5130); ν_{max}/cm^{-1} 3350 (OH); δ_H($CDCl_3$) 3.70 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 5.21 (1H, s, 3-H), 5.43 (1H, s, 3-H), 5.80 (1H, s, 1-H), 6.32 (1H, dd, *J* 8.4 and 2.4, 5′-H), 6.41 (1H, d, *J* 2.4, 3′-H), 6.78–6.86 (3H, m, 6′-, 3″- and 5″-H), 7.30 (2H, d, *J* 6.7, 2″- and 6″-H) and 7.97 (1H, br s, OH); δ_C($CDCl_3$) 55.2 (2 × OCH_3), 75.4 (C-1), 102.4 (C-3), 105.8 (C-3′), 113.6 (C-5′), 113.9 (C-3″ and -5″), 117.6 (C-1′), 128.1 (C-2″ and -6″), 129.2 (C-6′), 131.0 (C-1″), 148.0 (C-2), 156.9 (C-2′), 159.2 (C-4′) and 160.5 (C-4″); *m*/*z* 286 (M^+, 2%), 282 (20), 269 (18), 268 (100, $M^+ - 18$), 267 (80), 253 (21), 239 (10), 224 (8), 153 (17) and 134 (10) (Found: M^+, 286.1219. $C_{17}H_{18}O_4$ requires *M*, 286.1176).

1-(2-Hydroxy-4-methoxyphenyl)-2-phenylprop-2-en-1-ol 3b

Flash chromatography eluent: *n*-hexane–acetone (7:4). Amorphous solid. λ_{max}(EtOH)/nm 205 (ε/dm^3 mol^{-1} cm^{-1} 27 300), 236 (10 200) and 282 (2670); ν_{max}/cm^{-1} 3449 (OH) and 3146 (OH); δ_H($CDCl_3$) 3.72 (3H, s, 4′-OCH_3), 5.31 (1H, s, 3-H), 5.51 (1H, s, 3-H), 5.85 (1H, s, 1-H), 6.34 (1H, dd, *J* 2.5 and 8.5,

5′-H), 6.44 (1H, d, *J* 2.6, 3′-H), 6.86 (1H, d, *J* 8.4, 6′-H) and 7.20–7.41 (5H, m, Ar-H); $\delta_C(CDCl_3)$ 55.8 (OMe), 75.8 (C-1), 103.0 (C-3), 106.4 (C-3′), 115.6 (C-5′), 118.3 (C-1′), 127.6 (C-2″ and -6″), 128.5 (C-4″), 129.0 (C-3″ and -5″), 129.8 (C-6′), 139.5 (C-1″), 149.5 (C-2), 157.5 (C-2′) and 161.1 (C-4′); *m*/*z* 254 (M^+, 5%), 239 (18), 238 ($M^+ - 18$, 100), 237 (68), 223 (13), 194 (7), 165 (12), 161 (22), 117 (11) and 58 (34) (Found: M^+, 256.1084. $C_{16}H_{16}O_3$ requires *M*, 256.1099).

1-(2-Hydroxyphenyl)-2-phenylprop-2-en-1-ol 3c

Flash chromatography eluent: *n*-hexane–acetone (7 : 4). Amorphous solid. λ_{max}(EtOH)/nm 205 (ε/dm³ mol^{-1} cm^{-1} 24 500), 240 (8680) and 278 (2680); ν_{max}/cm^{-1} 3497 (OH) and 3179 (OH); $\delta_H(CDCl_3)$ 5.27 (1H, s, 3-H), 5.51 (1H, s, 3-H), 5.91 (1H, s, 1-H), 6.79 (1H, dt, *J* 1.3 and 7.5, 5′-H), 6.89 (1H, dd, *J* 1.2 and 8.2, 3′-H), 6.98 (1H, dd, *J* 1.7 and 7.6, 6′-H), 7.18 (dt, 1H, *J* 1.7 and 7.7, 4′-H), 7.28–7.41 (5H, m, Ar-H) and 7.7 (1H, br s, OH); $\delta_C(CDCl_3)$ 76.3 (C-1), 115.5 (C-3), 117.2 (C-3′), 119.9 (C-5′), 124.7 (C-1′), 127.6 (C-2″ and -6″), 128.1 (C-4″), 128.5 (C-6′), 128.6 (C-3″ and -5″), 129.4 (C-4′), 138.7 (C-1″), 148.6 (C-2) and 155.8 (C-2′); *m*/*z* 226 (M^+, 3%), 222 (8), 209 (16), 208 ($M^+ - 18$, 100), 207 (93), 194 (10), 178 (26), 165 (10), 131 (30) and 104 (15) (Found: M^+, 226.0996. $C_{15}H_{14}O_2$ requires *M*, 226.0993).

1-(2-Hydroxy-4-methoxyphenyl)-2-(4-hydroxyphenyl)prop-2-en-1-ol 3d

Flash chromatography eluent: *n*-hexane–acetone (1 : 1) Amorphous solid. λ_{max}(EtOH)/nm 206 (ε/dm³mol^{-1} cm^{-1} 41 700), 237 (12 600) and 260 (15 400); ν_{max}/cm^{-1} 3354 (OH); δ_H([$^2H_6$]-acetone) 3.68 (3H, s, OCH_3), 5.35 (1H, s, 3-H), 5.39 (1H, s, 3-H), 5.99 (1H, s, 1-H), 6.30 (1H, dd, *J* 2.4 and 8.4, 5′-H), 6.36 (1H, d, *J* 2.6, 3′-H), 6.73 (2H, d, *J* 8.6, 3″-H and 5″-H), 7.01 (1H, d, *J* 8.4, 6′-H), 7.30 (2H, d, *J* 8.8, 2″-H and 6″-H); δ_C([$^2H_6$]-acetone) 55.4 (OCH_3), 72.1 (C-1), 102.4 (C-3), 105.7 (C-3′), 111.5 (C-5′), 115.8 (C-3″ and -5″), 121.4 (C-1′), 128.9 (C-2″ and -6″), 129.9 (C-6′), 132.2 (C-1″), 151.1 (C-2), 157.6 (C-2′), 157.9 (C-4′) and 161.1 (C-4″); *m*/*z* 272 (M^+, 8%), 268 (6), 255 (18), 254 (100), 253 (65), 239 (26), 161 (9), 153 (21), 127 (12) and 121 (16) (Found: M^+, 272.1047. $C_{16}H_{16}O_4$ requires *M*, 272.1048).

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