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ISOFLAVONES FROM *XANTHOCERCIS ZAMBESIACA*

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Key Word Index—*Xanthocercis zambesiaca*; Leguminosae; isoflavones; 7,3′-dihydroxy-8,4′-dimethoxyisoflavone.

Abstract—In addition to the previously described 7-hydroxy-8,4′-dimethoxy- and 7,3′-dihydroxy-8,4′-dimethoxyisoflavone the heartwood of *Xanthocercis zambesiaca* has been shown to contain 7-hydroxy-8,3′,4′-trimethoxy-, 3′,4′-dimethoxy-6,7-methylenedioxy- and 8,3′,4′-trimethoxy-6,7-methylenedioxy-isoflavone. A technique of determining isoflavone hydroxylation patterns by deuterium labelling is described.

Xanthocercis zambesiaca (Bak.) Dumaz-le-Grand, also known as *Pseudocadia zambesiaca* (Bak,) Harms [1,2] belongs to the tribe Sophoreae of the subfamily Lotoideae [3] of the Leguminosae. It occurs only in south tropical Africa as an evergreen tree [2,4], and is one of the two known species of *Xanthocercis*, the other, *X. madagascariensis*, occurring in Malagasy [2]. On exposure to the atmosphere, the pale grey-brown heartwood darkens markedly. The timber has been known to cause severe nose and throat irritation [4,5].

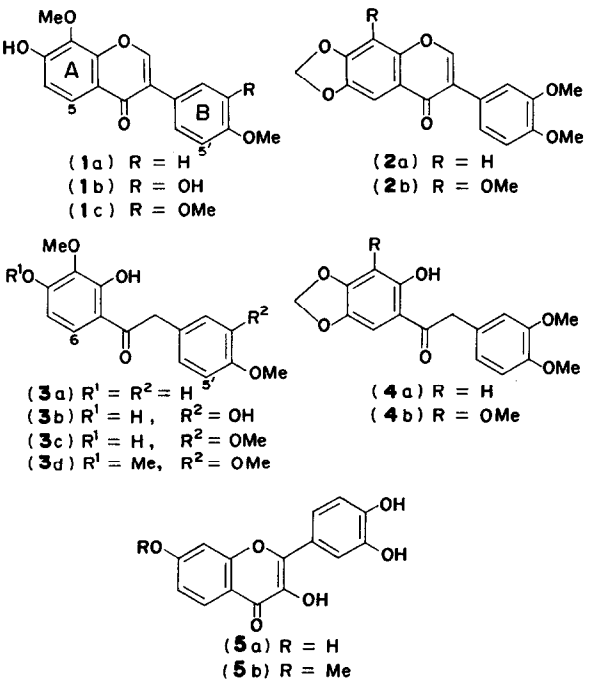
Milled heartwood on extraction with hexane gave 0.011% of 7-hydroxy-8,4′-dimethoxyisoflavone (8-*O*-methylretusin) [6] (**1a**), which together with its methylated and acetylated derivatives was identical (mmp, IR) with authentic samples. Mild base hydrolysis of **1a** gave the deoxybenzoin **3a**, which on alkali fusion gave 2-*O*-methylpyrogallol and 4-methoxyphenylacetic acid, identified by PC. The structure of **1a** was confirmed by a novel application of deuteration and MS (see below).

After extraction with Et_2O followed by EtOAc, which each yielded 0.3% material not further investigated, 6.8% as a red gum was obtained by MeOH extraction. After extensive PLC, five isoflavones including **1a** were isolated from this. One of these, 7,3′-dihydroxy-8,4′-dimethoxyisoflavone (3′-hydroxyretusin 8-methyl ether) [7] (**1b**) was independently and concurrently isolated, together with **1a**, from another source by Thomson [7].

The least polar isoflavone fraction was a *ca* 1:1 mixture of two compounds (0.07% of dry weight extracted) as a powder. Fractional crystallisation gave a compound $C_{18}H_{14}O_6$, mp 258–9°, the M^+ of which was 30 mu lower than the highest peak in the spectrum of the mixture. UV and IR were typical of an isoflavone with no free hydroxyl. The intensity of Band 1 in the UV suggested 6,7-dioxygenation [8–11]. Mild base hydrolysis of the mixture gave two separable deoxybenzoins. The NMR of the one corresponding to the isoflavone obtained pure showed a methylenedioxy and two methoxyl groups, *para* coupled (J = 1 Hz) protons at δ 7.05 and 6.35, suggesting a 2,4,5-trisubstituted phenacyl ring. A three-proton multiplet at δ 6.71 is consistent with a 3,4-disubstituted phenyl ring. The methylenedioxy group is assigned to the phenacyl ring, since cleavage α to the carbonyl group gives two appropriate fragments at *m/e* 165 and 151.

The absence of any $M^+ - 31$ peak from the spectrum of the isoflavone suggested [12] that neither of the methoxyl groups is at C-2′. From biogenetic considerations [13,14] one methoxyl is likely to be at C-4′, thus locating the other at C-3′. A comparison (mp, IR, NMR, UV) with 6,7-dimethoxy-3′,4′-methylenedioxyisoflavone [12] showed the two compounds to be different. Accordingly, the isoflavone is 3′,4′-dimethoxy-6,7-methylenedioxyisoflavone (**2a**) and its deoxybenzoin **4a**.

The second deoxybenzoin contained an additional methoxyl group and lacked the NMR signal for H-3, relative to **4a**, but the spectra were otherwise similar. Accordingly, the dioxybenzoin is assigned the structure **4b**, confirmed by fragments at *m/e* 195, and as before, 151, and the parent isoflavone, $C_{19}H_{16}O_7$ is thus 8,3′,4′-trimethoxy-6,7-methylenedioxyisoflavone (**2b**). An alternative structure, 6,3′,4′-trimethoxy-7,8-methylenedioxyisoflavone cannot be excluded rigorously, but the



co-occurrence of three other 8-methoxylated isoflavones suggests the former structure is more likely.

An isoflavone fraction of intermediate polarity was a mixture of two compounds (0.40% of dry weight extracted), as a powder. Fractional crystallisation gave **1a**, and the mother liquors provided a compound $C_{18}H_{16}O_6$, mp 185–7°, with the spectral characteristics of an isoflavone. The NMR showed the presence of three methoxyl groups and appropriate signals for H-2 and *ortho*-coupled H-5 at δ 7.88 (*s*) and 7.87 (*d*, $J = 9$ Hz) respectively. The IR absorption at 3140 cm^{-1} suggested a monohydroxytrimethoxyisoflavone, unsubstituted at C-5 and C-6. Acetylation and methylation gave a monoacetate and tetramethyl ether respectively.

A bathochromic shift was observed in the UV of the isoflavone on addition of sodium acetate, locating the hydroxyl at C-7 [8a,15]. Thus ring B could be di- or tri-methoxylated, depending on whether ring A bore a methoxyl at C-8. Isoflavones trioxygenated in the A ring absorb in the region 265-70 nm [8a]. The absorption at 256 nm in the present case compares with that of **1a** (257 nm) and favours a dioxygenated A ring. The presence of a peak at *m/e* 162 for the retro-Diels-Alder fragment [16] confirms the presence of a B ring with two methoxyl substituents. A methoxyl group can be excluded from C-2′ on the same grounds argued in the case of **2a**—lack of an $M^+ - 31$ peak. Thus the structure 7-hydroxy-8,3′,4′-trimethoxyisoflavone (**1c**) can be assigned to the compound. As expected, methylation gave a compound identical (mp, IR) with synthetic 7,8,3′,4′-tetramethoxyisoflavone (see below).

This assigment was confirmed by an unusual method. The crude mixture of **1a** and **1c** was heated under basic conditions with D_2O, affording after acidification deoxybenzoins **3a** and **3c** in which the methylene and unsubstituted ring positions *ortho* and *para* to hydroxyl are deuterium-enriched. MS of the mixture showed M^+ ions at *m/e* 291 and 321 (the latter accurately determined as $C_{17}H_{15}D_3O_6$), confirming that both deoxybenzoins were trideuterated. A 7-methoxy-8-hydroxyisoflavone would be expected to provide a tetradeuterated deoxybenzoin.

The most polar isoflavone (0.32% of dry weight extracted), $C_{17}H_{14}O_6$, mp 212–3°, was obtained pure by PLC of the crude methanol extract, and showed spectral characteristics similar to those of **1c**. NMR indicated two methoxyl groups and five aromatic protons, one of which, H-5, [8b] occurred as an *ortho*-coupled doublet ($J = 9$ Hz) at δ 7.67, showing that C-6 was unsubstituted. Absorptions for the remaining aromatic protons suggested a 3′,4′-, 2′,5′- or 2′,4′-oxygenation pattern. Acetylation gave a diacetate.

A hydroxyl group at C-7 was inferred from the UV shifts with sodium acetate (cf. **1c**). Lack of a shift with NaOAc/$B(OH)_3$, $AlCl_3$ or $AlCl_3$/HCl [8a] indicated that the second hydroxyl group was probably at C-8. Comparison with the spectra of **1a** and **1c** suggested the compound was a 7-hydroxy-8-methoxyisoflavone, leaving one hydroxyl and one methoxyl group to be placed in ring B. The absence of an $M^+ - 31$ peak excluded a 2′-methoxyl, so that the remaining possibilities for the oxygenation pattern of the B ring were 2′-hydroxy-4′-methoxy, 2′-hydroxy-5′-methoxy, 3′-hydroxy-4′-methoxy or 4′-hydroxy-3′-methoxy. Of these, the first would correspond to an isoflavone previously synthesised [17] and can be excluded on the basis of a wide mp discrepancy.

Alkali fusion of the deoxybenzoin derived from the isoflavone gave 2-*O*-methylpyrogallol as expected, but the phenylacetic acid fragment could not be positively identified owing to its close similarity on TLC to 2-hydroxy-5-methoxy-, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-phenylacetic acids. Partial methylation of the isoflavone gave a trimethyl ether the spectrum of which no longer shifted with NaOAc, implying that the 7-hydroxyl had been methylated and the B-ring hydroxyl was unreactive, possibly because of deactivation through H-bonding to the carbonyl, which would support placement at C-2′. However, it has been suggested [18] that the order of reactivity to methylation of the hydroxyl groups in the flavonol **5a** is 3′ < 4′ < 7. The monomethyl derivative **5b** was isolated using conditions identical to those employed for the partial methylation of the present isoflavone, If the 7-hydroxyl is most reactive even in such a case, where the B ring is activated by conjugation to the carbonyl, there is reason to suppose the same might be true for an isoflavone where the B ring is not so activated. It was also claimed [18] that this order of methylation is reversed using Me_2SO_4–Na_2CO_3, but it is not apparent why this should be so. A similar situation arose on acetylation of the isoflavone: a monoacetate with a free 7-hydroxyl resulted, so that arguments related to hydroxyl activity are untenable for structural assignment.

Permethylation of the isoflavone gave a tetramethyl ether whose mp was identical to that reported for synthetic 7,8,3′,4′-tetramethoxyisoflavone [19]. This compound was synthesised from trimethylpyrogallol and homoveratric acid. Selective monodemethylation of the deoxybenzoin obtained from their condensation was effected with $AlCl_3$ in refluxing ether to provide **3d.** This was converted to the isoflavone by the usual formylation with $HC(OEt)_3$/base followed by acid-catalysed dehydration.

The B ring of the natural isoflavone is thus 3′,4′-dioxygenated. Our observation that two of the B ring protons in the NMR of the diacetate are shifted more than the third, and to approximately equal extents [7,8b] suggested the presence of a 3′-hydroxyl. This was finally established using the deuteration procedure (see above) which gave a pentadeuterated deoxybenzoin, $C_{16}H_{11}D_5O_6$, showing only two aromatic one-proton singlets (H-5′ and H-6, cf. **3b**) in the NMR. Had the isoflavone B ring pattern been 2′-hydroxy-5′-methoxy or 4′-hydroxy-3′-methoxy, a tetradeuterated deoxybenzoin would be expected. Accordingly, the structure of the isoflavone is 7,3′-dihydroxy-8,4′-dimethoxyisoflavone (**1b**). The evidence for this structure extends that adduced by Thomson [7].

EXPERIMENTAL

Spectral data, except where otherwise indicated, are measured and presented as in Table 1. NMR spectra are run in $CDCl_3$ except where otherwise specified. Solvent petrol is a 50–75° boiling fraction. All PLC refers to SiO_2 plates.

Extraction. Dried, finely-milled *X. zambesiaca* heartwood (2.2 kg) was extracted (Soxhlet) successively with hexane, Et_2O, EtOAc and MeOH. On evaporation the hexane fraction gave 18.6 g oil from which a solid (300 mg) crystallised. The methanol fraction gave 150 g gum.

Purification. The crystals from the hexane extract were purified by PLC ($CHCl_3$–6% MeOH) yielding **1a** (244 mg). The MeOH extract (18.6 g) on PLC ($CHCl_3$–8% MeOH) gave 7

bands quenching 254 nm radiation. Of these, sequentially numbered, bands 1, 3 and 5, R_f's 0.98, 0.74 and 0.56, contained the most significant amounts of solid material on workup (2.86, 1.95 and 1.96 g respectively). Further PLC gave a mixture of **2a**/**2b** (200 mg, R_f 0.43, $CHCl_3$) from band 1, **1a**/**1c** (1.09 g, R_f 0.43, $CHCl_3$–3% MeOH) from band 2, and **1b** (880 mg, R_f 0.13, $CHCl_3$–3% MeOH) from band 3, as powders.

General procedures. Acetylation was carried with Ac_2O–pyridine for 18 hr at 15°. Methylation was with Me_2SO_4–K_2CO_3 NMe_2CO for 4 hr. Mild base hydrolysis was achieved by refluxing isoflavones for 30 min in 50% aq. EtOH containing 10% NaOH (0.5–1 ml). For alkali fusion, the deoxybenzoins obtained as above were heated for 1.5 min with KOH (2 molten pellets), the reaction air-cooled, acidified (6 N H_2SO_4), extracted (Et_2O) and separated into acidic and phenolic fractions [20]. These fractions were examined by PC using the organic phases of C_6H_6–$EtCO_2H$–H_2O (2/2/1) Am OH–xylene–H_2O–AcOH (4/6/5/4) and Bu^nOH–AcOH–H_2O (4/1/5). The papers were developed with diazotised sulphanilic acid [21]. For deuterium exchange, the isoflavone (50 mg), $KOBu^t$ (0.75 eq per active OH) and D_2O (0.4 ml) were heated in a sealed tube at 100° for 4 days. The mixture was cooled, acidified, extracted (Et_2O) and the deuterated deoxybenzoin purified by PLC ($CHCl_3$–6% MeOH).

3',4'-Dimethoxy-6,7-methylenedioxyisoflavone (**2a**) and *8,3',4'-trimethoxy-6,7-methylenedioxyisoflavone* (**2b**). Fractional crystallisation of the PLC fraction containing both compounds gave microcrystalline **2a** (3 mg) mp 258-9° from $CHCl_3$–petrol (Found: M^+ 326.0792. $C_{18}H_{14}O_6$ requires 326.0790), *m/e* 326, 311, 283, 240, 163, 147, 119 (100, 17, 7, 7, 13, 7, 7%), NMR, IR, UV—see Table 1. Mild base hydrolysis of the crude mixture (100 mg) gave *2-hydroxy-4,5-methylenedioxyphenyl-3',4'-dimethoxybenzyl ketone* (**4a**). (13 mg), mp 148–51° from EtOAc–petrol (Found: M^+ 316.0951. $C_{17}H_{16}O_6$ requires 316.0947), λ_{max} 236, 281, 349 nm (4.19, 3.90, 3.89), ν_{max} 1620, 1600, 1530, 1515, 940 cm^{-1}, δ 3.80 (6H, *s*, 2 × OMe), 4.02 (2H, *s*, $ArCH_2$), 5.87 (2H, *s*, CH_2O_2), 6.35 (1H, *d*, J = 1, H-3), 6.71 (3H, *m*, H-2',5',6'), 7.05 (1H, *d*, J = 1, H-6), 12.95 (1H, *bs*, OH), *m/e* 316 (M^+), 166, 165, 152, 151, 107 (23, 13, 100, 17, 12, 10%), R_f (in $CHCl_3$–3% MeOH) 0.67, and *2-hydroxy-3-methoxy-4,5-methylenedioxyphenyl-3',4'-dimethoxybenzyl ketone* (**4b**). (29 mg), mp 162–3° from EtOAc–petrol (Found: C, 62.26; H, 4.91. $C_{18}H_{18}O_7$ requires C, 62.42; H, 5.24%), λ_{max} 225, 289, 350(*sh*) nm (4.39, 4.03, 3.85), ν_{max} 1615, 1595, 1525, 1510, 963 cm^{-1}, δ 3.82 (6H, *s*, MeO-4,5), 3.98 (3H, *s*, MeO-3), 4.05 (2H, *s*, $ArCH_2$), 5.91 (2H, *s*, CH_2O_2), 6.75 (3H, *bs*, H-2',5',6'), 6.88 (1H, *s*, H-6), 13.09 (1H, *bs*, OH), *m/e* 346 (M^+), 196, 195, 180, 152, 151, 107, (33, 28, 100, 20, 9, 21, 8%), R_f 0.59.

7-Hydroxy-8,4'-dimethoxyisoflavone (**1a**). Fractional crystallisation of the PLC fraction containing **1a**/**1c** gave prisms of **1a** (200 mg) mp 229–32°, identical with an authentic sample [6,7]. The following data extends that already published: λ_{max} 257, 306(*sh*) nm (4.49, 3.90) (shifting to 269, 324(*sh*), 348 nm on addition of NaOMe and 267, 320(*sh*), 348 nm on addition of NaOAc), λ_{max} 3260, 1640, 1605, 1580, 1520 cm^{-1}, *m/e* 298 (M^+), 283, 255, 166, 138, 132, 123, 117 (100, 9, 10, 9, 17, 11, 7, 5%). *Monoacetate*, λ_{max} 256, 310(*sh*) nm (4.52, 3.80), ν_{max} 3260, 1640, 1605, 1580, 1520 cm^{-1}. *Permethyl derivative*, λ_{max} 255, 305(*sh*) nm (4.44, 3.87), ν_{max} 1650, 1620, 1510, 1570, 1520 cm^{-1}, *m/e* 312 (M^+), 297, 180, 156, 152, 137, 132, 117, (100, 5, 5, 9, 7, 7, 8, 4%). Mild base hydrolysis of **1a** (56 mg) gave *2,4-dihydroxy-3-methoxyphenyl-4'-methoxybenzyl ketone* (**3a**) (47 mg, 86%), mp 140–2° from EtOAc/petrol, λ_{max} 238(*sh*), 287, 321(*sh*) nm (4.01, 4.19, 3.89), ν_{max} 3200, 1630, 1590, 1520 cm^{-1}, δ 3.70 (3H, *s*, MeO-4'), 3.85 (3H, *s*, MeO-3), 4.05 (2H, *s*, $ArCH_2$), 6.39 (1H, *d*, J = 9, H-5), 6.74 (2H, *d*, J = 9, H-3', 5'), 7.09 (2H, *d*, J = 9, H-2', 6'), 7.44 (1H, *d*, J = 9, H-6), 12.73 (2H, *bs*, OH-2,4), *m/e* 288 (M^+), 168, 167, 152, 121 (15, 43, 100, 62, 44%). Microfusion of **3a** gave material with the same R_f's as 2-*O*-methylpyrogallol [22] and 4-methoxyphenylacetic acid (see below) on PC.

7-Hydroxy-8,3',4'-trimethoxyisoflavone (**1c**). Evaporation of the mother liquors from the crystallisation of **1a** and recrystallisation of the residue gave colourless needles of **1c**, mp 185–7° from EtOAc (Found; C, 65.47, H, 4.58. $C_{18}H_{16}O_6$ requires C, 65.85; H, 4.91%), *m/e* 328 (M^+), 313, 285, 166, 164, 162, 138, 123, 119 (100, 15, 5, 4, 6, 4, 12, 4, 5%), NMR, IR, UV—see Table 1. *Acetate*, mp 190–2° from EtOAc (Found; C, 64.55; H, 4.83. $C_{20}H_{18}O_7$ requires C, 64.86; H, 4.90%), λ_{max} 257,

Table 1. Spectral data of *Xanthocercis* isoflavones

IR spectra (KBr discs, cm^{-1})

Compound	OH		C=O	C=C				CH_2O_2
1b	3550,	3120	1630	1620,	1600,	1520		—
1c	3140		1633	1623,	1605,	1575,	1528,	—
2a	—		1635	1615,	1585,	1525,	1510	945

UV Spectra (in EtOH, nm (log ϵ), *sh* = shoulder)

Compound	Band 2	Band 1	Shifts
1b	254, 289	306(*sh*)	269, 292(*sh*), 350(*sh*) (NaOMe)
	(4.34), 4.05)	(3.93)	258(*sh*), 265, 292(*sh*), 348(*sh*) (NaOAc)
1c	256, 290(*sh*)	304(*sh*)	267, 341(*sh*) (NaOMe)
	(4.48, 4.15)	(4.02)	264, 344(*sh*) (NaOAc)
2a	264, 286(*sh*)	323, 330(*sh*)	—
	(4.35, 4.13)	(4.05, 4.02)	

NMR Spectra 60 MHz, δ (relative to TMS). All signals singlets except where indicated. A J value signifies a doublet. **1b** is run in $CDCl_3$–50% CD_3OD, **1c** and **2a** in $CDCl_3$

Compound	H-2	5	6	8	2'	5'	6'	CH_2O_2	MeO
1b	7.97	7.67	6.84	—	6.81	6.85	6.87	—	3.87, 3.87
		(J = 9)	(J = 9)		(*bs*)	(J = 8)	(J = 8)		
1c	7.88	7.87	6.94	—	6.90	6.90	6.90	—	3.97 (8)
		(J = 9)	(J = 9)		(*m*)	(*m*)	(*m*)		3.84, (3',4')
2a	7.85	7.51	—	6.78	7.15	7.15	7.15	6.02	3.87, 3.87
		(*bs*)		(*bs*)	(*m*)	(*m*)	(*m*)		

285(*sh*) nm (4.39, 4.08), ν_{max} 1750, 1650, 1610, 1590, 1530, 1505 cm^{-1}, δ 2.37 (3H, *s*, Ac), 3.85 (3H, *s*, MeO-4'), 3.86 (3H, *s*, MeO-3'), 3.97 (3H, *s*, MeO-8), 6.88 (1H, *bs*, H-5'), 6.91 (1H, *bs*, H-6'), 7.02 (1H, *d*, J = 9, H-6), 7.09 (1H, *bs*, H-2'), 7.92 (1H, *d*, J = 9, H-5), 7.96 (1H, *s*, H-2). *Permethyl derivative* mp 160–5° from PLC, identical with 7,8,3',4'-tetramethoxyisoflavone (see below). *Deuterated deoxybenzoins.* The crude mixture of **1a**/**1c** (50 mg) was deuterated to give a mixture of inseparable deoxybenzoins, $C_{16}H_{13}D_3O_5$ (Found; M^+ 291.1699. Requires 291.1186) and $C_{17}H_{15}D_3O_6$ (Found; M^+ 321.1283. Requires 321.1292) corresponding to trideuterated **3a** and **3c** respectively. The NMR of the mixture showed an absence of $ArCH_2$ and H-5 signals (cf. **3a**), whilst H-6 for both compounds appeared as δ 7.36 (*s*). The position of the other signals in the mixture was approximately the same as in **3a**, except that a diminished integral for H-3' was accompanied by a corresponding increase for MeO-4', on which MeO-3' of **3c** was superimposed.

7,3'-*Dihydroxy*-8,4'-*dimethoxyisoflavone* (**1b**). Recrystallisation of the pure PLC fraction containing **1b** gave material mp 212-3° from EtOH (208–10°)[7], *m/e* 314 (M^+), 299, 271, 167, 166, 148, 138, 133, 123, 105 (100, 23, 16, 13, 5, 5, 13, 10, 7, 10%), NMR, IR, UV—see Table 1. *Monoacetate*, (7-hydroxy-3'-acetoxy-8,4'-dimethoxyisoflavone) mp 205–6° from EtOAc/petrol (Found; M^+ 356.0972. $C_{19}H_{16}O_7$ requires 356.0896), λ_{max} 255, 305(*sh*) nm (4.54, 4.04) (shifting to 274, 354 nm on addition of NaOMe, and 273, 352 nm on addition of NaOAc). ν_{max} 3350, 1735, 1630, 1595, 1520 cm^{-1}. δ ($CDCl_3$–CD_3OD 1/1) 2.30 (3H, *s*, Ac), 3.84 (3H, *s*, MeO-4'), 3.97 (3H, *s*, MeO-8), 6.97 (1H, *d*, J = 9, H-6), 7.01 (1H, *d*, J = 8, H-5'), 7.27 (1H, *bs*, H-2'), 7.37 (1H, *d*, J = 8, H-6'), 7.80 (1H, *d*, J = 9, H-5), 8.03 (1H, *s*, H-2). Vigorous acetylation of the monoacetate gave the *diacetate*, mp 173–4.5° from EtOAc–petrol (163–5°)[7]. *Monomethyl derivative*, (3'-hydroxy-7,8,4'-trimethoxyisoflavone), mp 149–52° from EtOH (Found: C, 64.52; H, 4.93. $C_{18}H_{16}O_6$ requires C, 64.85; H, 4.91). λ_{max} 224, 254, 290 nm (4.47, 4.53, 4.23) (shifting to 250, 298 nm on addition of NaOMe), ν_{max} 3320, 1620, 1600, 1595, 1570, 1530, 1520 cm^{-1}, δ 3.87 (3H, *s*, MeO-4'), 3.96 (6H, *s*, MeO-7,8), 6.94 (1H, *d*, J = 5, H-5'), 6.97 (1H, *d*, J = 9, H-6), 7.01 (1H, *d*, J = 5, H-6'), 7.08 (1H, *bs*, H-2'), 7.92 (1H, *s*, H-2), 7.96 (1H, *d*, J = 9, H-5), *m/e* 328 (M^+), 313, 285, 181, 152, 148, 133, 105 (100, 35, 24, 6, 4, 6, 6, 5%). *Permethyl derivative* mp 167–9° from EtOH, identical with 7,8,3',4'-tetramethoxyisoflavone (see below). Mild base hydrolysis of **1b** (102 mg) gave, 2,4-*dihydroxy*-3-*methoxyphenyl*-3'-*hydroxy*-4'-*methoxybenzyl ketone* (**3b**) (70 mg, 71%), mp 127–9° from EtOAc (Found; C, 63.45; H, 5.14. $C_{16}H_{16}O_6$ requires C, 63.15; H, 5.30%), λ_{max} 231(*sh*), 289, 315(*sh*) nm (4.16, 4.21, 3.91), ν_{max} 3375, 1620, 1593, 1520 cm^{-1}, δ 3.78 (3H, *s*, MeO-4'), 3.82 (3H, *s*, MeO-3), 4.03 (2H, *s*, $ArCH_2$), 6.72 (3H, *bs*, H-2',5',6'), 6.38 (1H, *d*, J = 9, H-5), 7.39 (1H, *d*, J = 9, H-6), 12.80 (3H, *bs*, OH-2,3',4), *m/e* 304 (M^+), 167, 152, 149, 137, 113 (41, 100, 39, 78, 12, 29%), R_f 0.20. Microfusion of **3b** gave material with the same R_f's as 2-*O*-methylpyrogallol [22] and a variety of phenylacetic acids (see text and below). *Deuterated deoxybenzoin.* **1b** (50 mg) was deuterated to give the deoxybenzoin $C_{16}H_{11}D_5O_6$ (40 mg, 81%), (Found; M^+ 309.1263. Requires 309.1261), differing from **3b** as follows: δ 3.78 (3H, *s*, MeO-4'), 3.80 (3H, *s*, MeO-3), 6.74 (1H, *s*, H-5'), 7.45 (1H, *s*, H-6), 12.73 (3H, *bs*, OH-2,4,3'), *m/e* 310, 309, (M^+), 308, 169, 168, 167, 153, 141, (9, 27, 12, 40, 100, 19, 32, 15%).

Arylacetic acids. Veratric acid (2.0 g) was refluxed with $SOCl_2$ (6 ml) for 2 hr, the excess reagent evaporated under reduced pressure, the residue dissolved in dry C_6H_6 (25 ml) and added dropwise to an excess of CH_2N_2 in Et_2O at 0°. After 20 hr at 0°, the solvent was evaporated, the residue dissolved in dry C_6H_6 (50 ml), absolute MeOH (3 ml) added and the solution irradiated with a high-pressure Hg lamp for 21 hr. Evaporation of solvent gave homoveratric acid methyl ester, purified by PLC (C_6H_6) and saponified by reflux with 10% aq. KOH (25 ml). The mixture was acidified, extracted (Et_2O), the extract washed with 10% aq $NaHCO_3$, the washings acidified and homoveratric acid (3,4-*dimethoxyphenylacetic acid*) recovered on extraction (Et_2O) and workup, giving 1.0 g (46%) mp 88–92° (99–100)[23]. By similar Arndt-Eistert homologation utilising photo-Wolff rearrangement were prepared homovanillic acid (4-*hydroxy*-3-*methoxyphenylacetic acid*), mp 140–2° (142–3°)[24] (32% from acetyl vanillic acid), homoisovanillic acid (3-*hydroxy*-4-*methoxyphenylacetic acid*) mp 125–9° (131.5–2°)[25] (35% from acetyl isovanillic acid), and 4-*methoxyphenylacetic acid*, mp 80–4° (83–4°)[26] (46% from anisic acid).

7,8,3',4'-*Tetramethoxyisoflavone.* Tri-*O*-methylpyrogallol [27] (290 mg), homoveratric acid (340 mg, 1 eq) and polyphosphoric acid (12 g) were heated at 95° for 30 min, the mixture poured into iced water (75 ml) and extracted (Et_2O). The organic phase was dried and evaporated, and the residue purified by PLC (C_6H_6–40% EtOAc) to give 2,3,4-*trimethoxyphenyl*-3',4'-*dimethoxybenzyl ketone* (240 mg, 40%) as an oil, ν_{max} (film) 1673, 1593, 1520, 1500 cm^{-1}, δ 3.78 (12H, *bs*, 4 × OMe), 3.87 (3H, *s*, MeO-2), 4.12 (2H, *s*, $ArCH_2$), 6.57 (1H, *d*, J = 9, H-5), 6.69 (3H, *m*, H-2',5', 6'), 7.33 (1H, *d*, J = 9, H-6), *m/e* 345 (M^+), 195, 180, 165 (10, 100, 11, 30%). This material (235 mg) was refluxed 1 hr with anhydrous $AlCl_3$ in Et_2O, the reaction poured into iced dil HCl, and extracted ($CHCl_3$). The organic phase was dried and evaporated and the residue recrystallised (EtOAc) to give *2-hydroxy*-3,4-*dimethoxyphenyl*-3',4'-*dimethoxybenzyl ketone* (**3d**), mp 135–7° (134°)[19] (1150 mg, 67%). This material (150 mg) was refluxed 11 hr with $HC(OEt)_3$ (2 ml), Py (10 ml) and piperidine (10 drops). The reaction mixture was worked up as for **3d** to give 7,8,3',4'-*tetramethoxyisoflavone*, mp 164–6° from EtOH (168–70°)[19] (164–5°)[7], (110 mg, 71%). The following data extends that already published: [7,19] λ_{max} 256, 287(*sh*), 306(*sh*) nm (4.44, 4.15, 3.96), ν_{max} 1638, 1618, 1598, 1568, 1520 cm^{-1}, *m/e* 342 (M^+), 327, 299, 180, 171, 162, 152, 147, 137, 119 (100, 23, 7, 5, 5, 4, 8, 6, 6, 10%).

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