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α-HYDROXYDIHYDROCHALCONES AND RELATED 1,3-DIARYLPROPAN-2-ONES FROM *XANTHOCERCIS ZAMBESIACA*

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Key Word Index—*Xanthocercis zambesiaca*; Leguminosae; 7,8-dioxyisoflavonoids; α-hydroxydihydrochalcones; 1,3-diarylpropan-2-ones.

Abstract—In addition to some previously described 7,8-dioxy-isoflavonoids and 2-benzylbenzo[*b*]furan-3 (2H)-ones the heartwood of *Xanthocercis zambesiaca* has been shown to contain 7,8,3′-trihydroxy-4′-methoxyisoflavone. These are accompanied by the novel α,3,4,4′-tetrahydroxy-2′-methoxydihydrochalcone and its 3-deoxy analogue, the latter of which presumably served as biogenetic precursor for the unique 1-hydroxy-3-(4-hydroxyphenyl)-1-(4-hydroxy-2-methoxyphenyl) propan-2-one and its 1-deoxy analogue. Such possible biosynthetic relationship was demonstrated by the facile *in vitro* transformations of the appropriate α-hydroxydihydrochalcone into the different 1,3-diarylpropan-2-ones.

INTRODUCTION

Previous investigations [1, 2] of the heartwood extractives of *Xanthocercis zambesiaca* (Baker) Dumaz-le-Grand [3], the protected Nyala tree, revealed the presence of a variety of tri-, tetra-, and penta-oxygenated isoflavonoids. The 7,8-dioxy analogues amongst these may serve as precursors for xanthocercin A and B, the first members of the novel class of isoflavono-lignoids [2]. These compounds contain the 2-aryl-3-hydroxymethyl-1,4-benzodioxane moiety, a common feature of a variety of natural neolignans [4] and presumably originate by oxidative phenol coupling of substituted catechols with *p*-hydroxystyrenes. The potential implied by the versatile 7,8-dihydroxy functionality of the A-ring of the isoflavones thus prompted more detailed examination of heartwood metabolites related to the above classes of natural products.

RESULTS AND DISCUSSION

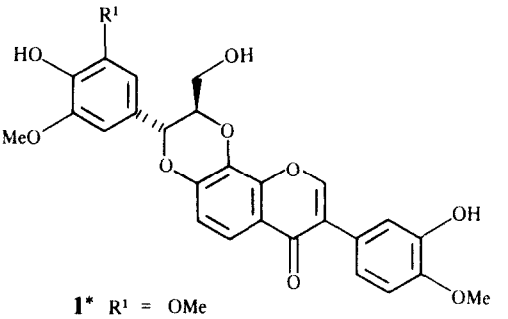
The methanol extract of the heartwood of *Xanthocercis zambesiaca* afforded xanthocercin A (**1**) and B (**2**) [2], the known 7-hydroxy-8,4′-dimethoxyisoflavone (8-*O*-methylretusin) [1, 5], 7-hydroxy-8,3′,4′-trimethoxyisoflavone [1], 7,3′-dihydroxy 8,4′-dimethoxyisoflavone [6], 7,3′,4′-trihydroxyflavonol (fisetin) [7], 2-benzyl-2,3′,4′,6-tetrahydroxybenzo[*b*]furan-3(2H)-one [8] and its 4-methoxy-3′-deoxy analogue [9, 10]—the latter three compounds being obtained from this natural source for the first time. These metabolites are accompanied by a novel derivative (**3**) of the 7,8,3′,4′-tetrahydroxyisoflavone, two novel α-hydroxydihydrochalcones (**5**) and (**7**), and two unique 1,3-diarylpropan-2-ones (**9**) and (**11**).

The ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of the tri-*O*-acetyl derivative (**4**) of the 7,8,3′-trihydroxy-4′-methoxyisoflavone (**3**) exhibited the diagnostic H-2 vinylic singlet in the low-field aromatic region (δ 8.35). The aromatic region of the spectrum additionally displayed an AB-system (δ 8.12, 7.40, both *d*, $J=9.0$ Hz), characteristic of the A-ring of 7,8-dioxygenated isoflavones [1] and an ABX-pattern (δ 7.50, *dd*, $J=2.0$, 8.5 Hz; 7.42, *d*, $J=2.0$ Hz; 7.16, *d*, $J=8.5$ Hz) consistent with a 3,4- or 2,4-disubstituted B-ring. Differentiation between these possibilities was effected by application of nuclear Overhauser effect (NOE) difference spectroscopy which indicated the selective association (12.3%) of methoxy protons with the *o*-doublet at δ7.16 only.

Comparison of ^{1}H NMR data of the *O*-acetyl derivatives **6** and **8** of racemic α,3,4,4′-tetrahydroxy-2′-methoxydihydrochalcone **5** and its 3-deoxy analogue **7** revealed their close structural resemblance. Both displayed AMX-systems [δ 2.91, *dd*, $J=9.4$, 14.5 Hz; 3.25, *dd*, $J=3.0$, 14.5 Hz; 6.10, *dd*, $J=3.0$, 9.4 Hz for **8**: δ 2.91, *dd*, $J=9.7$, 14 Hz; 3.26, *dd*, $J=3.0$, 14.6 Hz; 6.08, *dd*, $J=3.0$, 9.7 Hz for **6**] in the heterocyclic regions, as well as aromatic ABC-patterns for their respective A-rings. Differences between the spectra include replacement of the aromatic ABC-system (δ 7.23, *dd*, J = 2.0, 8.0 Hz; 7.19, *d*, $J=2.0$ Hz; 7.17, *d*, $J=8.0$ Hz) for the B-ring of **6** with an AA′BB′-pattern (δ 7.33, 7.06, both *d*, $J=8.8$ Hz) in the case of the trioxy derivative (**8**). The heterocyclic AMX-systems for both derivatives may, however, be indicative of the presence of a β-acetoxydihydrochalcone moiety for both these analogues. Detection of mutual benzylic coupling between H-2/6 (B-ring) and the methylene protons clearly defined these compounds **6** and **8** as α-hydroxydihydrochalcones (*cf.* refs [11 and 12]). Finally the unambiguous placement of the methoxy function at C-2′ in both **6** and **8** followed from the observed NOE association of these protons with H-3′ (15.2 and 22.9% resp.), H-α (1.9 and 2.1% resp.), H-6 (1.2 and 1.3*% resp.), and with H-2 (1.2 and 1.9*% resp.).

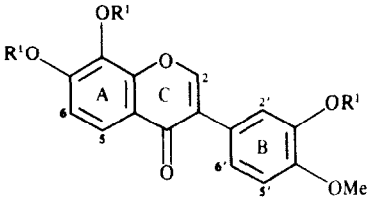
The α-hydroxydihydrochalcones (**5**) and (**7**) appropriately 'protected' at their 2′-oxygen functions and hence incapable of cyclization, should presumably be suscep-

*Approximate values due to signal overlap.

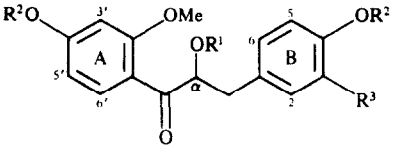


1* R^1 = OMe
2* R^1 = H

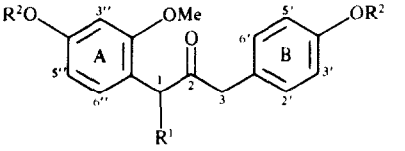
(*Single enantiomer for each racemate indicated)



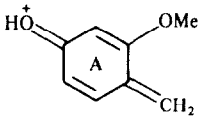
3 R^1 = H
4 R^1 = Ac



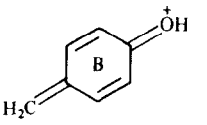
5 R^1 = R^2 = H, R^3 = OH
6 R^1 = R^2 = Ac, R^3 = OAc
7 R^1 = R^2 = H, R^3 = H
8 R^1 = R^2 = Ac, R^3 = H



9 R^1 = OH, R^2 = H
10 R^1 = OAc, R^2 = Ac
11 R^1 = R^2 = H
12 R^1 = H, R^2 = Ac



13 *m/z* 137 (100%)



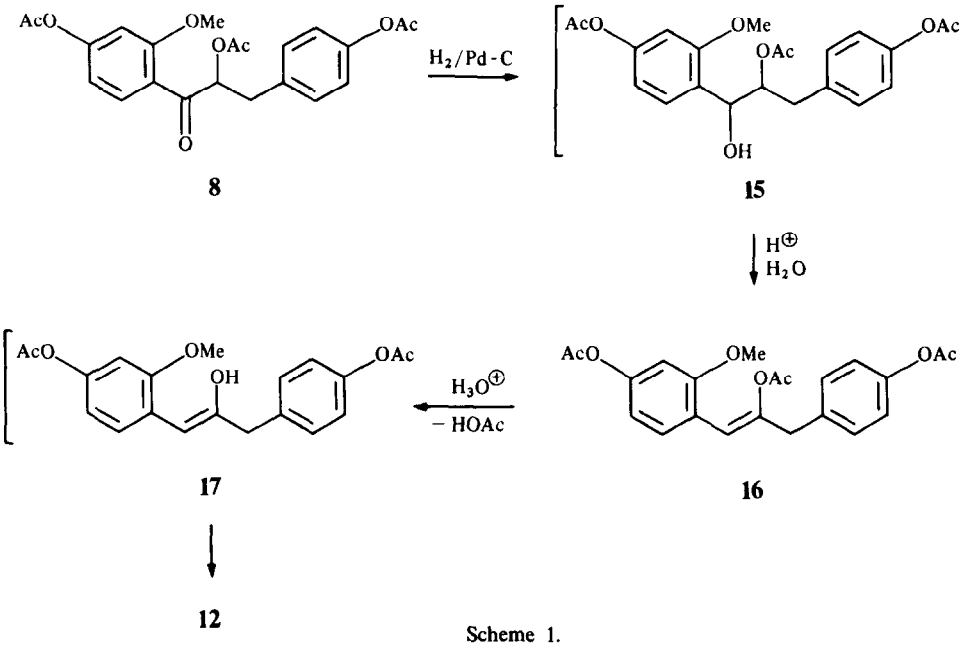
14 *m/z* 107 (24%)

tible to preferential modification of the aliphatic α-ketol moiety. Identification of the isomerized α-hydroxydihydrochalcone, 1-hydroxy-3-(4-hydroxyphenyl)-1-(4-hydroxy-2-methoxyphenyl)-propan-2-one (**9**) and its 1-deoxy analogue (**11**), the first members of the novel class of naturally occurring 1,3-diaryl-propan-2-ones could, therefore, be anticipated. These metabolites were characterized by the physical data of the phenols (**9** and **11**) and of those of their *O*-acetyl derivatives (**10** and **12**). ^{1}H NMR spectra revealed marked differences between the two α-ketols (**9** and **7**) in the heterocyclic regions. Whereas the spectrum of the α-hydroxydihydrochalcone (**7**) clearly exhibits an AMX-system (see above), the product of acyloin rearrangement (**9**) shows two doublets (δ 3.60 and 3.51, J = 15.4 Hz) for the diastereotopic methylene hydrogens, as well as vicinal coupling (J = 5.2 Hz) between H-1 (δ 5.36) and the C-1 hydroxyl proton (δ 4.36), the latter signal disappearing on D_2O exchange and acetylation. In the peracetate (**10**) H-1 is deshielded to δ 6.47 with the chemical shift of the acetoxy resonance (δ 2.13) indicative of its benzylic nature. The 1,3-diarylpropan-2-one arrangement for **9** was confirmed by appropriate spin-decoupling experiments which demonstrated association of the isolated proton at C-1 with the ABC-system of the A-ring and of the methylene protons with the AA′BB′-system of ring B. Location of the methyl group at the C-2″ oxygen in **10** was again verified by an NOE experiment which indicated strong association (15.1%) of the methyl protons and H-3″.

The ^{1}H NMR spectrum of 3-(4-hydroxyphenyl)-1-(4-

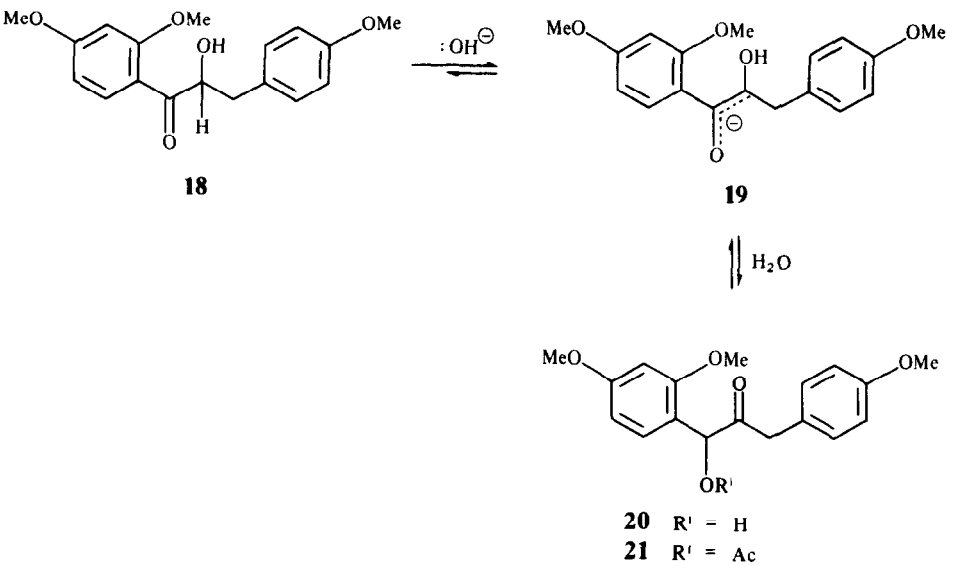
hydroxy-2-methoxyphenyl)propan-2-one (**11**) exhibited aromatic ABC- and AA'BB' spin systems, two isolated methylene singlets (δ 3.58, 3-CH_2; δ 3.54, 1-CH_2) and a single aromatic *O*-methyl resonance (δ 3.69), shown by its NOE association (17.5%) with H-3″ to be located at the C-2″ oxygen function. Spin decoupling of the methylene singlets clearly showed their adjacency to the respective aromatic rings and thus their benzylic nature (*cf.* refs [11, 12]). This, when taken in conjunction with the presence of a ^{13}C carbonyl resonance at δ206.2 and fragments (**13**) and (**14**) in the mass spectrum of diacetate (**12**) defined the constitution of the novel 1,3-diarylpropan-2-one (**11**).

The proposed structures (**9**) and (**11**) for the 2-propanones were unequivocally confirmed by synthesis [scheme 1 for (**9**) and 2 for (**11**)]. Thus, reduction of the α,4,4'-tri-*O*-acetyl-2'-*O*-methyldihydrochalcone (**8**) by means of catalytic hydrogenation afforded the benyzyl alcohol (**15**) which was not isolated but treated with *p*-toluenesulphonic acid in anhydrous benzene to give the propan-2-one (**12**) presumably *via* intermdiacy of the enol-acetate (**16**) and enol (**17**). The 1,3-diaryl-1-hydroxypropan-2-one was synthesized by utilization of the same protocol as was desbribed for base-catalysed α-ketol rearrangements of 3,3-diaryl-2-hydroxypropiophenones into isomeric 1-hydroxypropan-2-ones [13]. Thus, treatment of α-hydroxy-2',4,4'-trimethoxydihydrochalcone (**18**) with mild aqueous base under nitrogen afforded 1-hydroxy-1-(2,4-dimethoxyphenyl)-3-



8 **15** **17** **16** **12**

Scheme 1.



18 **19**

20 R' = H
21 R' = Ac

Scheme 2.

(4-methoxyphenyl)propan-2-one (**20**) *via* enolate (**19**). Acetylation of the α-ketol (**20**) afforded the monoacetate (**21**) with physical data identical to those of the corresponding derivative of the natural product.

In view of their identical phenolic substitution patterns the tri-oxygenated α-hydroxydihydrochalcone (**7**) presumably served as biogenetic precursor to both the 1,3-diarylpropan-2-ones (**9**) and (**11**). This contrasts with the suggested biosynthetic formation of reduced forms like (**22**–**25**) from flavan-3-ols and flavans [14–16]. The above facile *in vitro* transformations of α-hydroxydihydrochalcones (**8**) and (**18**) into the respective derivatives (**12**) and (**20**) of the natural products and the proven ease of conversion of α-hydroxydihydrochalcones to α-hydroxychalcones *via* the 1-hydroxy-1,3-diarylpropan-2-one of type (**20**) [17] may be taken as additional evidence for the presumed central role of the α-hydroxychalcone-α-hydroxydihydrochalcone pair in flavanoid biosynthesis.

EXPERIMENTAL

Mps: uncorr. ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ or Me_2CO-d_6 (19°) with the solvent signal (δ 7.24 or 2.04) as reference, unless otherwise stated, and mass spectral data on a Varian CH-5 instrument. Prep. TLC was carried out using 20 × 20 cm plates with 1.0 mm layers of silica gel PF_{254}. Zones were detected by UV and eluted with Me_2CO. CC was done with Kieselgel 60 (230–400 mesh) as stationary phase. Prep. PC comprised of 46 × 57 cm Whatman No. 3 sheets (100 mg/sheet), which were developed in 2% aq. HOAc. Bands were detected by UV and ammoniacal $AgNO_3$ solution and eluted with 80% EtOH. Acetylations were performed in Ac_2O–pyridine and methylations with MeI in Me_2CO/K_2CO_3.

Extraction and isolation of compounds. Drillings (2.1 kg) of the dried heartwood of *Xanthocercis zambesiaca* were extracted with MeOH (2 × 15 l) at room temp. (72 hr each). The combined extracts were evapd to 5 l, defatted with hexane (5 × 1 l) and evapd to give a dark-brown powder (135 g). A portion (2 × 40 g) of this material was subjected to counter-current distribution in a Quickfit Model 20 machine (25 ml lower phase; 103 transfers) in H_2O–*sec*-BuOH–hexane (5:4:1). The contents of tubes 66–103 (30 g) were resolved by means of paper chromatography to afford seven fractions. Fraction 1 (R_f 0.76, 2.0 g) and 6 (R_f 0.15, 0.4 g) were further fractionated by prep. TLC [C_6H_6–Me_2CO–MeOH (16:3:1) × 2 and C_6H_6–MeOH (9:1)] to yield subfractions 1.1–1.4 and 6.1–6.4 respectively.

3-(4-*Hydroxyphenyl*)-1-(4-*hydroxy*-2-*methoxyphenyl*) *propan*-2-*one* (**11**). TLC purification [C_6H_6–EtOAc–MeOH (7:2:1)] of subfraction 1.2 (R_f 0.37, 164 mg) afforded propan-2-one (**11**) (R_f 0.58) as a pale yellow amorphous solid (36 mg); ^{1}H NMR (Me_2CO-d_6): δ 8.30 and 8.23 (each 1H, each *s*, 2 × OH), 6.97 (2H, *d*, J = 8.5 Hz, H-2′, 6′), 6.88 (1H, *d*, $J_{5'',6''}$ = 8.1 Hz, H-6″), 6.75 (2H, *d*, J = 8.5 Hz, H-3′,5′), 6.44 (1H, *d*, $J_{3'',5''}$ = 2.5 Hz, H-3″), 6.36 (1H, *dd*, $J_{3'',5''}$ = 2.5 Hz, $J_{5'',6''}$ = 8.1 Hz, H-5″), 3.71 (3H, *s*, 2″-OMe), 3.58 (2H, *s*, 3-CH_2), 3.54 (2H, *s*, 1-CH_2); MS *m/z* (rel. int.): 272 $[M]^+$ (18), 137 (100), 107 (43).

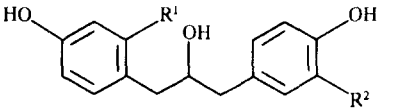
3-(4-*Acetoxyphenyl*)-1-(4-*acetoxy*-2-*methoxyphenyl*)-*propan*-2-*one* (**12**). Acetylation of ketone (**11**) (9 mg) yielded the diacetate (**12**) as an amorphous solid (8 mg). (Found: M^+, 356.1246. $C_{22}H_{20}O_6$ requires: M, 356.1260); ^{1}H NMR ($CDCl_3$): δ 7.13 (2H, *d*, J = 8.6 Hz, H-2′,6′), 7.06 (1H, *d*, $J_{5'',6''}$ = 8.0 Hz, H-6″), 7.00 (2H, *d*, J = 8.6 Hz, H-3′,5′), 6.64 (1H, *dd*, $J_{3'',5''}$ = 2.5 Hz, $J_{5'',6''}$ = 8.0 Hz, H-5″), 6.57 (1H, *d*, $J_{3'',5''}$ = 2.5 Hz, H-3″), 3.69 (3H, *s*, 2″-OMe), 3.68 and 3.66 (each 2H, each *s*, 2 × CH_2), 2.28 and 2.27 (each 3H, each *s*, 2 × OAc); MS *m/z* (rel. int.): 356 $[M]^+$ (8.6), 314 $[M-CH_2CO]^+$ (5.4), 179 (19), 137 (100), 107 (24).

(±)-1-*Hydroxy*-3-(4-*hydroxyphenyl*)-1-(4-*hydroxy*-2-*methoxyphenyl*)*propan*-2-*one* (**9**). The 1-hydroxy-2-propanone (**9**) (R_f 0.36) was obtained by TLC purification [$CHCl_3$–MeOH (47:3) × 2] of subfraction 1.3 (R_f 0.28, 156 mg) as a pale yellow amorphous solid (22 mg); ^{1}H NMR (Me_2CO-d_6): δ 8.65 and 8.30 (each 1H, each *br s*, 2 × OH), 7.05 (1H, *d*, $J_{5'',6''}$ = 8.2 Hz, H-6″), 6.88 (2H, *d*, J = 8.5 Hz, H-2′,6′), 6.70 (2H, *d*, J = 8.5 Hz, H-3′,5′), 6.51 (1H, *d*, $J_{3'',5''}$ = 2.1 Hz, H-3″), 6.43 (1H, *dd*, $J_{3'',5''}$ = 2.1 Hz, $J_{5'',6''}$ = 8.2 Hz, H-5″), 5.36 (1H, *d*, J = 5.2 Hz, H-1), 4.36 (1H, *d*, J = 5.2 Hz, 1-OH), 3. 79 (3H, *s*, 2″-OMe), 3.60 and 3.51 (each 1H, each *d*, J = 15.4 Hz) (3-CH_2).

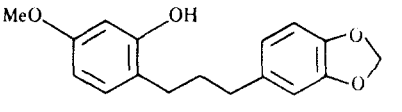
(±)-1-*Acetoxy*-3-(4-*acetoxyphenyl*)-1-(4-*acetoxy*-2-*methoxyphenyl*)*propan*-2-*one* (**10**). Acetylation of compound (**9**) (9 mg) yielded the triacetate (**10**) as an amorphous solid (7 mg).(Found: M^+, 414.1337. $C_{22}H_{22}O_8$ requires: M, 414.1315); 1H NMR ($CDCl_3$): δ 7.27 (1H, *d*, $J_{5'',6''}$ = 8.2 Hz, H-6″), 7.02 (2H, *d*, J = 9.0 Hz, H-2′,6′), 6.94 (2H, *d*, J = 9.0 Hz, H-3′,5′), 6.70 (1H, *dd*, $J_{3'',5''}$ = 2.1 Hz, $J_{5'',6''}$ = 8.2 Hz, H-5″), 6.66 (1H, *d*, $J_{3'',5''}$ = 2.1 Hz, H-3″), 6.47 (1H, *s*, H-1), 3.79 (3H, *s*, 2″-OMe), 3.72 and 3.63 (each 1H, each *d*, J = 16.0 Hz) (3-CH_2), 2.30 and 2.26 (each 3H, each *s*, 2 × OAc), 2.13 (3H, *s*, 1-OAc); MS *m/z* (rel. int.): 414$[M]^+$ (3.0), 237 (29), 195 (89), 153 (100), 135 (3.0), 107 (21).

(±)-1-*Acetoxy*-1-(2,4-*dimethoxyphenyl*)-3-(4-*methoxyphenyl*) *propan*-2-*one* (**21**). Methylation followed by acetylation and TLC separation [hexane–$CHCl_3$–Me_2CO (7:2:1)] of propan-2-one (**9**) (9 mg) gave derivative (**21**) (R_f 0.28) as a solid (5 mg); ^{1}H NMR ($CDCl_3$): δ 7.16 (1H, *d*, $J_{5'',6''}$ = 7.0 Hz, H-6″), 6.94 (2H, *d*, J = 8.8 Hz, H-2′,6′), 6.77 (2H, *d*, J = 8.8 Hz, H-3′,5′), 6.48 (1H, *dd*, $J_{3'',5''}$ = 2.0 Hz, $J_{5'',6''}$ = 7.0 Hz, H-5″), 6.47 (1H, *d*, $J_{3'',5''}$ = 2.0 Hz, H-3″), 6.43 (1H, *s*, H-1), 3.81, 3.80 and 3.75 (each 3H, each *s*, 3 × OMe), 3.63 and 3.56 (each 1H, each *d*, J = 16.0 Hz, 3-CH_2), 2.11 (3H, *s*, 1-OAc).

(±)-2-*Benzyl*-2,3′,4′,6-*tetra*-*acetoxybenzo*[*b*]*furan*-3(2H)-*one* [8]. Acetylation and prep. TLC separation [hexane–C_6H_6–1,2-dichloroethane–MeOH (9:6:4:1) × 2] of a portion (100 mg) of subfraction 1.4 (R_f 0.19, 172 mg) afforded two amorphous solids R_f 0.63 (12 mg) and 0.57 (16 mg) respectively. The former (R_f 0.63) was identified as 2-benzyl-2,3′,4′,6-tetra-acetoxybenzo[*b*]furan-3(2H)-one; ^{1}H NMR ($CDCl_3$): δ 7.59 (1H, *d*, $J_{4,5}$ = 8.4 Hz, H-4), 7.13 (1H, *dd*, $J_{2',6'}$ = 2.0 Hz, $J_{5',6'}$ = 8.1 Hz, H-6′), 7.09 (1H, *d*, $J_{2',6'}$ = 2.0 Hz, H-2′), 7.04 (1H, *d*, $J_{5',6'}$ = 8.1 Hz, H-5′), 6.81 (1H, *d*, $J_{5,7}$ = 2.0 Hz, H-7), 6.78 (1H, *dd*, $J_{5,7}$ = 2.0 Hz, $J_{4,5}$ = 8.4 Hz, H-5), 3.24 and 3.02 (each 1H, each *d*, J = 14.1 Hz)



22 R¹ = OH, R² = OMe
23 R¹ = R² = H
24 R¹ = OH, R² = H



25

(CH_2), 2.29, 2.25 and 2.24 (each 3H, each *s*, 3 × OAc), 2.07 (3H, *s*, 2-OAc); MS *m/z* (rel. int.): 456 $[M]^+$ (2.9), 414 $[M-CH_2CO]^+$ (7.9), 397 $[M-OAc]^+$ (1.9), 270 $[M-HOAc-3\times OAc]^+$ (23), 206 (30), 179 (46), 165 (33), 151 (7.4), 137 (100), 123 (83).

(±)-2-*Benzyl*-2,4',6-*triacetoxy*-4-*methoxybenzo*[*b*] *furan*-3(2H)-*one* (2,4',6-*tri*-O-*acetylcarpusin* [9, 10]. The second compound (R_f 0.57; *vide supra*) was identified as 2,4',6-tri-*O*-acetylcarpusin; ^{1}H NMR ($CDCl_3$): δ 7.25 (2H, *d*, *J* = 8.8 Hz, H-2',6'), 6.95 (2H, *d*, *J* = 8.8 Hz, H-3',5'), 6.37 (1H, *d*, $J_{5,7}$ = 1.8 Hz, H-7), 6.21 (1H, *d*, $J_{5,7}$ = 1.8 Hz, H-5), 3.87 (3H, *s*, 4-OMe), 3.25 and 3.04 (each 1H, each *d*, *J* = 14.0 Hz) (CH_2), 2.28 and 2.25 (each 3H, each *s*, 2 × OAc), 2.05 (3H, *s*, 2-OAc); MS *m/z* (rel. int.): 428$[M]^+$ (8.8), 386 $[M-CH_2CO]^+$ (2.6), 368 $[M-HOAc]^+$ (12), 237 (15), 209 (43), 195 (60), 167 (100), 107 (60).

(±)-α,4,4'-*Trihydroxy*-2'-*methoxydihydrochalcone* (**7**). Prep. TLC separation [$CHCl_3$–Me_2CO–MeOH (17:2:1) of fraction 3 from paper chromatography (R_f 0.57, 1.5 g) gave two compounds R_f 0.43 (172 mg) and 0.24 (150 mg) respectively. The first compound (R_f 0.43) comprised of the α-hydroxydihydrochalcone (**7**) as a yellow solid; ^{1}H NMR (Me_2CO-d_6): δ 7.74 (1H, *d*, $J_{5',6'}$ = 8.9 Hz, H-6'), 7.01 (2H, *d*, *J* = 8.7 Hz, H-2,6), 6.70 (2H, *d*, *J* = 8.7 Hz, H-3,5), 6.60 (1H, *d*, $J_{3',5'}$ = 2.0 Hz, H-3'), 6.56 (1H, *dd*, $J_{3',5'}$ = 2.0 Hz, $J_{5',6'}$ = 8.9 Hz, H-5'), 5.14 (1H, *dd*, *J* = 3.2, 8.0 Hz, H-α), 3.91 (3H, *s*, 2'-OMe), 2.97 (1H, *dd*, $J_{\alpha,\beta}$ = 3.2 Hz, $J_{\beta,\beta}$ = 13.9 Hz), 2.51 (1H, *dd*, $J_{\alpha,\beta}$ = 8.0 Hz, $J_{\beta,\beta}$ = 13.9 Hz) (β-CH_2).

(±)-α,4,4'-*Triacetoxy*-2'-*methoxydihydrodrochalcone* (**8**). Acetylation of α-hydroxydihydrochalcone (**7**) (72 mg) yielded the triacetate (**8**) as a solid (70 mg). (Found: C, 63.7; H, 5.4. $C_{22}H_{22}O_8$ requires: C, 63.8; H, 5.4%), ^{1}H NMR (Me_2CO-d_6, TMS as internal standard): δ 7.81 (1H, *d*, $J_{5',6'}$ = 8.6 Hz, H-6'), 7.33 (2H, *d*, *J* = 8.8 Hz, H-2,6), 7.06 (2H, *d*, *J* = 8.8 Hz, H-3,5), 7.02 (1H, *d*, $J_{3',5'}$ = 1.8 Hz, H-3'), 6.88 (1H, *dd*, $J_{3',5'}$ = 1.8 Hz, $J_{5',6'}$ = 8.6 Hz, H-5'), 6.10 (1H, *dd*, *J* = 3.0, 9.4 Hz, H-α), 4.03 (3H, *s*, 2'-OMe), 3.25 (1H, *dd*, $J_{\alpha,\beta}$ = 3.0 Hz, $J_{\beta,\beta}$ = 14.5 Hz), 2.91 (1H, *dd*, $J_{\alpha,\beta}$ = 9.4 Hz, $J_{\beta,\beta}$ = 14.5 Hz) (β-CH_2), 2.29 and 2.24 (each 3H, each *s*, 2 × OAc), 2.02 (3H, *s*, α-OAc); MS *m/z* (rel. int.): 354 $[M-HOAc]^+$ (13), 312 $[M-HOAc-CH_2CO]^+$ (10), 270 $[M-HOAc-2\times CH_2CO]^+$ (3.8), 151 (100), 119 (1).

(±)-α-*Hydroxy*-2',4,4'-*trimethoxydihydrochalcone* (**18**). Methylation of α-hydroxydihydrochalcone (**7**) (100 mg) followed by TLC purification [$CHCl_3$–Me_2CO (19:1)] gave the methyl ether (**18**) (R_f 0.64) as a yellow solid (90 mg). (Found: C, 68.5; H, 6.3. $C_{18}H_{20}O_5$ requires: C, 68.3; H, 6.4%); ^{1}H NMR ($CDCl_3$): δ 7.81 (1H, *d*, $J_{5',6'}$ = 8.8 Hz, H-6'), 7.03 (2H, *d*, *J* = 8.8 Hz, H-2,6), 6.72 (2H, *d*, *J* = 8.8 Hz, H-3,5), 6.56 (1H, *dd*, $J_{3',5'}$ = 2.2 Hz, $J_{5',6'}$ = 8.8 Hz, H-5'), 6.44 (1H, *d*, $J_{3',5'}$ = 2.2 Hz, H-3'), 5.25 (1H, *m*, H-α), 3.91 (1H, *s*, α-OH), 3.88, 3.84 and 3.72 (each 3H, each *s*, 3 × OMe), 3.06 (1H, *dd*, $J_{\alpha,\beta}$ = 3.8 Hz, $J_{\beta,\beta}$ = 13.8 Hz), 2.63 (1H, *dd*, $J_{\alpha,\beta}$ = 7.5 Hz, $J_{\beta,\beta}$ = 13.8 Hz) (β-CH_2); MS *m/z* (rel. int.): 298 $[M-H_2O]^+$ (60), 195 (69), 167 (90), 165 (100), 151 (31), 139 (40), 137 (49), 121 (79), 107 (22).

(±)-α-3,4,4'-*Tetra-acetoxy*-2'-*methoxydihydrochalcone* (**6**). Acetylation and TLC purification [hexane–Me_2CO–EtOAc (11:6:3)] of the second compound [R_f 0.24; *cf.* (**7**)] gave the title compound (**6**) (R_f 0.42) as a solid (64 mg). (Found: C, 60.8; H, 5.0. $C_{24}H_{24}O_{10}$ requires: C, 61.0; H, 5.1%); ^{1}H NMR (Me_2CO-d_6, TMS as int. standard): δ 7.82 (1H, *d*, $J_{5',6'}$ = 8.5 Hz, H-6'), 7.23 (1H, *dd*, $J_{2,6}$ = 2.0 Hz, $J_{5,6}$ = 8.0 Hz, H-6), 7.19 (1H, *d*, $J_{2,6}$ = 2.0 Hz, H-2), 7.17 (1H, *d*, $J_{5,6}$ = 8.0 Hz, H-5), 7.02 (1H, *d*, $J_{3',5'}$ = 2.1 Hz, H-3'), 6.87 (1H, *dd*, $J_{3',5'}$ = 2.1 Hz, $J_{5',6'}$ = 8.5 Hz, H-5'), 6.08 (1H, *dd*, *J* = 3.0, 9.7 Hz, H-α), 4.00 (3H, *s*, 2'-OMe) 3.26 (1H, *dd*, $J_{\alpha,\beta}$ = 3.0 Hz, $J_{\beta,\beta}$ = 14.6), 2.91 (1H, *dd*, $J_{\alpha,\beta}$ = 9.7 Hz, $J_{\beta,\beta}$ = 14.6 Hz) (β-CH_2), 2.28, 2.26 and 2.25 (each 3H, each *s*, 3 × OAc), 2.02 (2H, *s*, α-OAc); MS *m/z* (rel. int.): 412 $[M-HOAc]^+$ (7.0), 370 $[M-HOAc-CH_2CO]^+$ (6.6), 328 $[M-HOAc-2\times CH_2CO]^+$ (12), 286 $[M-HOAc-3\times CH_2CO]^+$ (4.3), 151 (100), 136 (2.0).

7-*Acetoxy*-8,4'-*dimethoxyisoflavone* (7-O-*acetyl*-8-O-*methylretusin* [1, 5]. Acetylation and subsequent TLC purification [hexane–Me_2CO–EtOAc (13:4:3)] of subfraction 6.1 (R_f 0.31, 19 mg) yielded 7-acetoxy-8,4'-dimethoxyisoflavone (R_f 0.41) as a solid (15 mg); ^{1}H NMR ($CDCl_3$, TMS as internal standard: δ 8.03 (1H, *d*, $J_{5,6}$ = 8.5 Hz, H-5) 8.02 (1H, *s*, H-2), 7.49 (2H, *d*, *J* = 9.0 Hz, H-2',6'), 7.12 (1H, *d*, $J_{5,6}$ = 8.5 Hz, H-6), 6.97 (2H, *d*, *J* = 9.0 Hz, H-3',5'), 4.01 (3H, *s*, 8-OMe), 3.83 (3H, *s*, 4'-OMe), 2.39 (3H, *s*, 7-OAc); MS *m/z* (rel. int.): 340 $[M]^+$ (49), 298 $[M-CH_2CO]^+$ (100), 166 (12), 132 (26).

7-*Acetoxy*-8,3',4'-*trimethoxyisoflavone* [1]. Acetylation and TLC purification [C_6H_6–MeOH (92:8)] of subfraction 6.2 (R_f 0.26, 22 mg) afforded the 7-acetoxy-8,3',4'-trimethoxyisoflavone (R_f 0.27) as a solid (16 mg); ^{1}H NMR ($CDCl_3$, TMS as int. standard: δ 8.07 (1H, *s*, H-2), 8.04 (1H, *d*, $J_{5,6}$ = 9.0 Hz, H-5), 7.20 (1H, *d*, $J_{2',6'}$ = 2.1 Hz, H-2'), 7.14 (1H, *d*, $J_{5,6}$ = 9.0 Hz, H-6), 7.06 (1H, *dd*, $J_{2',6'}$ = 2.1 Hz, $J_{5',6'}$ = 8.0 Hz, H-6'), 6.94 (1H, *d*, $J_{5',6'}$ = 8.0 Hz, H-5'), 4.03 (3H, *s*, 8-OMe), 3.94 and 3. 92 (each 3H, each *s*, 3' and 4'-OMe), 2.40 (3H, *s*, 7-OAc); MS *m/z* (rel. int.): 370 $[M]^+$ (91), 328 $[M-CH_2CO]^+$ (100), 167 (3.0), 166 (1.3), 162 (6.4).

7,3'-*Diacetoxy*-8,4'-*dimethoxyisoflavone* [6]. Acetylation follwed by TLC purification [hexane–Me_2CO–EtOAc (11:6:3)] of subfraction 6.3 (R_f 0.20, 41 mg) gave 7,3'-diacetoxy-8,4'-dimethoxyisoflavone (R_f 0.48) as a solid (23 mg); ^{1}H NMR (Me_2CO-d_6, TMS as int. standard): δ 8.43 (1H, *s*, H-2), 7.93 (1H, *d*, $J_{5',6'}$ = 9.0 Hz, H-5), 7.52 (1H, *dd*, $J_{2',6'}$ = 2.1 Hz, $J_{5',6'}$ = 8.7 Hz, H-6'), 7.43 (1H, *d*, $J_{2',6'}$ = 2.1 Hz, H-2'), 7.25 (1H, *d*, $J_{5,6}$ = 9.0 Hz, H-6), 7.17 (1H, *d*, $J_{5',6'}$ = 8.7 Hz, H-5'), 4.02 (3H, *s*, 8-OMe), 3.87 (3H, *s*, 4'-OMe), 2.38 and 2.27 (each 3H, each *s*, 2 × OAc); MS *m/z* (rel. int.): 398 $[M]^+$ (30), 356 $[M-CH_2CO]^+$ (64), 314 $[M-2\times CH_2CO]^+$ (100), 167 (2.9), 148 (2.3).

7,8,3'-*Triacetoxy*-4'-*methoxyisoflavone* (**4**). The title compound (**4**) (R_f 0.42) was obtained from subfraction 6.4 (R_f 0.10, 32 mg), after acetylation and TLC purification [hexane–Me_2CO–EtOAc (11:6:3)], as an amorphous solid (29 mg). (Found: M^+, 426.0975. $C_{22}H_{18}O_9$ requires: M, 426.0951); ^{1}H NMR (Me_2CO-d_6, TMS as int. standard): δ 8.35 (1H, *s*, H-2), 8.12 (1H, *d*, $J_{5,6}$ = 9.0 Hz, H-5), 7.50 (1H, *dd*, $J_{2',6'}$ = 2.0 Hz, $J_{5',6'}$ = 8.5 Hz, H-6'), 7.42 (1H, *d*, $J_{2',6'}$ = 2.0 Hz, H-2'), 7.40 (1H, *d*, $J_{5,6}$ = 9.0 Hz, H-6), 7.16 (1H, *d*, $J_{5',6'}$ = 8.5 Hz, H-5'), 3.86 (3H, *s*, 4'-OMe), 2.41, 2.36 and 2.26 (each 3H, each *s*, 3 × OAc); MS *m/z* (rel. int.): 426 $[M]^+$ (46), 384 $[M-CH_2CO]^+$ (92), 342 $[M-2\times CH_2CO]^+$ (68), 300 $[M-3\times CH_2CO]^+$ (100), 152 (2.9), 148 (2.6).

3,7,3',4'-*Tetra*-O-*acetylfisetin*. CC [$CHCl_3$-MeOH (19:1), RR_t 153 hr] of a portion (2 g) of fraction 7 (R_f 0.02, 9.5 g) followed by acetylation and TLC purification [hexane–Me_2CO–EtOAc (11:6:3)] yielded tetra-*O*-acetylfisetin (R_f 0:39) as a solid (9 mg); mp 194–196° (lit. [7] mp 196–198°).

Synthesis of (±)-3-(4-*acetoxyphenyl*)-1-(4-*acetoxy*-2-*methoxyphenyl*)*propan*-2-*one* (**12**). Catalytic hydrogenation [EtOH (20 ml), 10% Pd/C (13 mg), 6 hr] of α,4,4'-triacetoxy-2'-methoxydihydrochalcone (**8**) (50 mg) followed by TLC purification [C_6H_6–MeOH (19:1)] yielded an intermediate of R_f 0.31, which was refluxed (22 hr) in C_6H_6 (20 ml) containing *p*-toluenesulphonic acid (5 mg). Evapn of the solvent, followed by TLC separation [$CHCl_3$–EtOAc (9:1)] afforded the title propan-2-one (**12**) (R_f 0.65) as an amorphous solid (12 mg) identical to that obtained from the natural source.

Synthesis of (±)-1-*hydroxy*-1-(2,4-*dimethoxyphenyl*)-3-(4-*methoxyphenyl*)*propan*-2-*one* (**20**). 1 N aq. NaOH (5 ml) was added under N_2 to a solution of α-hydroxy-2',4,4'-trimethoxydihydrochalcone (**18**) in THF (80 mg in 5 ml) and the mixture stirred at room temperature for 22 hr. After stirring at 35° for

another 3 hr, ice was added, the reaction mixture acidified to pH 5 (1 N HCl) and extracted with EtOAc (3 × 20 ml). The combined extracts were washed with water (3 × 60 ml), until acid-free, dried (Na_2SO_4) and purified by TLC [hexane–$CHCl_3$–Me_2CO (7:2:1) × 2] to give the 1-hydroxy-2-propanone (**20**) (R_f 0.43) as a pale yellow solid (11 mg). (Found: M^+, 316.1372. $C_{18}H_{20}O_5$ requires: M, 316.1341); ^1H NMR (Me_2CO-d_6): δ 7.17 (1H, *d*, $J_{5'',6''}$ = 8.2 Hz, H-6''), 6.97 (2H, *d*, J = 8.6 Hz, H-2',6'), 6.80 (2H, *d*, J = 8.6 Hz, H-3',5'), 6.59 (1H, *d*, $J_{3'',5''}$ = 2.6 Hz, H-3''), 6.53 (1H, *dd*, $J_{3'',5''}$ = 2.6 Hz, $J_{5'',6''}$ = 8.2 Hz, H-5''), 5.39 (1H, *d*, J = 5.5 Hz, H-1), 4.43 (1H, *d*, J = 5.5 Hz, 1-OH), 3.83, 3.81 and 3.74 (each 3H, each *s*, 3 × OMe), 3.66 and 3.56 (each 1H, each *d*, J = 15.8 Hz, 3-CH_2); MS *m/z* (rel. int.): 316 $[M]^+$ (1.1), 195 (2.6), 167 (100), 149 (1.6), 121 (20).

(±)-1-*Acetoxy*-1-(2,4-*dimethoxyphenyl*)-3-(4-*methoxyphenyl*)-*propan*-2-*one* (**21**). Acetylation of 1-hydroxy-2-propanone (**20**) (8 mg) gave the monoacetate (**21**) (R_f 0.28, 5 mg) identical to that obtained from the natural product.

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