Oligomeric Isoflavonoids. Part 2.† Structure and Synthesis of Xanthocercin A and B, the First Isoflavono-lignoids

S. Catherine Bezuidenhout, Barend C. B. Bezuidenhoudt, E. Vincent Brandt, and Daneel Ferreira*
Department of Chemistry, University of the Orange Free State, P.O. Box 339, Bloemfontein, 9300 South Africa

The structures of xanthocercin A and B, the first isoflavono-lignoids, have been established as 2,3-*trans*-3-(4-hydroxy-3,5-dimethoxyphenyl)-8-(3-hydroxy-4-methoxyphenyl)-2-hydroxymethyl-2,3-dihydro-7*H*-1,4-dioxino[2,3-*h*]chromen-7-one (**1**) and 2,3-*trans*-8-(3-hydroxy-4-methoxyphenyl)-3-(4-hydroxy-3-methoxyphenyl)-2-hydroxymethyl-2,3-dihydro-7*H*-1,4-dioxino[2,3-*h*]chromen-7-one (**3**) respectively by spectroscopic methods. These structures have been confirmed by synthesis *via* phenol oxidative coupling of the appropriate 7,8-dihydroxyisoflavone and respectively sinapyl and coniferyl alcohol. The natural occurrence of xanthocercin A and B as single regioisomers and their regiospecific formation during synthesis presumably originate from marked differences in susceptibility to oxidation of the hydroxy functions in their 'catechol precursors'.

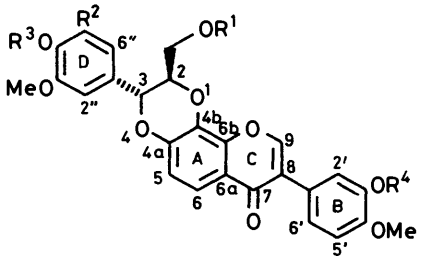
The 2-aryl-3-hydroxymethyl-1,4-benzodioxane moiety, presumably originating by oxidative phenol coupling of substituted catechols with *p*-hydroxystyrenes, is a common feature of a variety of natural neolignans.[1] The natural occurrence of these benzodioxane lignoids has recently been shown to include the catechol moieties of various other phenolic substrates, *e.g.* those in flavonoids,[2–4] xanthones,[5] and coumarins.[6–9] Owing to their claimed medicinal properties, *e.g.* antihepatotoxic effects,[10] the flavonolignans have been the subject of intensive recent investigations. We now report on the structure and synthesis of xanthocercin A (**1**) {2,3-*trans*-3-(4-hydroxy-3,5-dimethoxyphenyl)-8-(3-hydroxy-4-methoxyphenyl)-2-hydroxymethyl-2,3-dihydro-7*H*-1,4-dioxino[2,3-*h*]chromen-7-one} and its D-ring 3-demethoxy analogue, xanthocercin B (**3**), the first members of the novel class of isoflavono-lignoids.

Results and Discussion

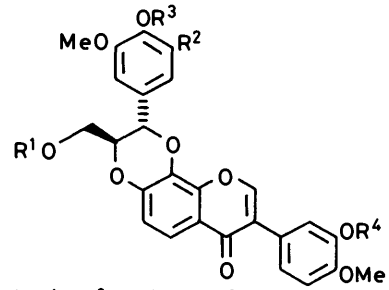
The methanol extract of the heartwood of *Xanthocercis zambesiaca* (Baker) Dumaz-le Grand,[11] the protected Nyala tree, contains a variety of 7,8-dioxygenated isoflavonoids.[12] These compounds are accompanied by α-hydroxydihydrochalcones,‡ 1,3-diarylpropan-2-ones,‡ 2-benzyl-2-hydroxybenzo[*b*]furan-3(2*H*)-ones,‡ and the novel lignoids, xanthocercin A (**1**) and B (**3**).

The presence of an isoflavone moiety in xanthocercin A (**1**) was obvious from its 300 MHz ^{1}H n.m.r. spectrum in $(CD_3)_2CO$ which exhibited the diagnostic 2-H [9-H in (**1**)] vinylic singlet at δ 8.27. The aromatic region of the spectrum displayed an AB-system (δ 7.05, 7.70, both d, both *J* 8.9 Hz), characteristic of the A-ring of 7,8-dioxygenated isoflavones,[12] an ABX-pattern (δ 7.00, d, *J* 8.4 Hz; δ 7.10, dd, *J* 2.1 and 8.4 Hz; δ 7.19, d, *J* 2.1 Hz) consistent with a 2,4-or 3,4-disubstituted B-ring, and a two-proton singlet at δ 6.89 indicative of a symmetrically tetrasubstituted aromatic ring. Besides three aromatic methoxy signals [δ 3.89, 3.86 (× 2)], the aliphatic region also displayed an AMXY-system (δ 5.16, d, *J* 8.0 Hz; δ 4.33, m; δ 3.93, dd, *J* 2.4 and 12.4 Hz; δ 3.62, dd, *J* 3.8 and 12.4 Hz). Comparison of the above data with those in the literature (*cf.* ref. 7) indicated that the structure of xanthocercin A (**1**) was composed of a 3,4,5-trioxygenated phenylpropanoid unit coupled *via* the *ortho*-dihydroxy functionality of a tetraoxygenated isoflavone moiety.

Acetylation of xanthocercin A (**1**) with acetic anhydride in



(**1**)* R^1 = R^3 = R^4 = H, R^2 = OMe
(**2**)* R^1 = R^3 = R^4 = Ac, R^2 = OMe
(**3**)* R^1 = R^2 = R^3 = R^4 = H
(**4**)* R^1 = R^3 = R^4 = Ac, R^2 = H
(**7**)* R^1 = R^3 = H, R^2 = OMe, R^4 = Me
(**8**)* R^1 = H, R^2 = OMe, R^3 = R^4 = Me
(**9**)* R^1 = R^2 = R^3 = H, R^4 = Me
(**10**)* R^1 = R^2 = H, R^3 = R^4 = Me
(**11**)* R^1 = R^3 = Ac, R^2 = H, R^4 = Me



(**5**)* R^1 = R^3 = R^4 = H, R^2 = OMe
(**6**)* R^1 = R^2 = R^3 = R^4 = H

* Single enantiomer for each racemate indicated.

† Part 1, B. C. B. Bezuidenhoudt, E. V. Brandt, J. A. Steenkamp, D. G. Roux, and D. Ferreira, *J. Chem. Soc., Perkin Trans. 1*, 1988, preceding paper.

‡ To be published elsewhere.

Table 1. ^{1}H N.m.r. δ-values for xanthocercin A (**1**) and B (**3**) and their derivatives (**2**), (**4**), (**8**), and (**10**) at 300 MHz. Splitting patterns and *J*-values (Hz) are given in parentheses

Proton	(**1**) in $(CD_3)_2CO$	(**2**) in $(CD_3)_2CO$	(**2**) in $CDCl_3$	(**8**) in $CDCl_3$	(**4**) in $CDCl_3$	(**4**) in $(CD_3)_2CO$	(**4**) in C_6D_6	(**10**) in $CDCl_3$
CH_2OR	3.93 (dd, 2,4, 12.4)	4.42 (dd, 3.0, 12.8)	4.45 (dd, 3.2, 12.5)	4.00 (dd, 2.5, 12.6)	4.47 (dd, 3.4, 12.4)	4.42 (dd, 3.0, 12.4)	3.81—3.91 (m)	3.60—3.70 (m)
	3.62 (dd, 3.8, 12.4)	4.17 (dd, 4.5, 12.8)	4.11 (dd, 4.5, 12.5)	3.65 (dd, 3.5, 12.6)	4.09 (dd, 4.4, 12.4)	4.12 (dd, 4.2, 12.4)		3.93—4.02 (m)
2-H	4.33 (ddd, 2.4, 3.8, 8.0)	4.69 (ddd, 3.0, 4.5, 8.0)	4.34 (ddd, 3.2, 4.5, 8.0)	4.12 (ddd, 2.5, 3.5, 8.3)	4.35 (ddd, 3.4, 4.4, 8.0)	4.68 (ddd, 3.0, 4.2, 7.9)	4.29—4.22 (m)	4.14(ddd, 2.8, 3,5. 8.2)
3-H	5.16 (d, 8.0)	5.26 (d, 8.0)	5.01 (d, 8.0)	5.08 (d, 8.3)	5.08 (d, 8.0)	5.29 (d, 7.9)	4.54 (d, 7.8)	5.12 (d, 8.2)
5-H	7.05 (d, 8.9)	7.11 (d, 9.0)	7.02 (d, 9.1)	7.05 (d, 9.1)	7.04 (d, 9.0)	7.10 (d, 9.0)	6.92 (d, 8.9)	7.05 (d, 9.1)
6-H	7.70 (d, 8.9)	7.74 (d, 9.0)	7.80 (d, 9.1)	7.83 (d, 9.1)	7.83 (d, 9.0)	7.73 (d, 9.0)	8.11 (d, 8.9)	7.83 (d, 9.1)
9-H	8.27 (s)	8.35 (s)	8.00 (s)	7.99 (s)	8.02 (s)	8.35 (s)	7.37 (s)	8.02 (s)
2′-H	7.19 (d, 2.1)	7.44 (d, 2.2)	7.31 (d, 2.1)	7.22 (d, 2.1)	7.32 (d, 2.1)	7.42 (d, 2.2)	7.51 (d, 2.1)	7.21 (d, 2.1)
5′-H	7.00 (d, 8.4)	7.17 (d, 8.5)	7.00 (d, 8.7)	6.91 (d, 8.0)	7.02 (d, 8.7)	7.16 (d, 8.7)	6.55 (d, 8.6)	6.93 (d, 8.2)
6′-H	7.10 (dd, 2.1, 8.4)	7.52 (dd, 2.2, 8.5)	7.40 (dd, 2.1, 8.7)	7.02 (dd, 2.1, 8.0)	7.41 (dd, 2.1, 8.7)	7.51 (dd, 2.2, 8.7)	7.44 (dd, 2.1, 8.6)	7.04 (dd, 2.1, 8.2)
2″- and 6″-H	6.89 (s)	6.98 (s)	6.62 (s)	6.67 (s)				
2″-H					6.98 (d, 1.9)	7.34 (m)	6.70 (d, 2.0)	6.95 (d, 2.0)
5″-H					7.10 (d, 8.7)	7.16 (m)	6.95 (d, 8.2)	6.92 (d, 8.3)
6″-H					6.98 (dd, 1.9, 8.7)	7.16 (m)	6.66 (dd, 2.0, 8.2)	7.03 (dd, 2.0, 8.3)
OMe	3.89, 3.86 (×2) (each s)	3.87, 3.85 (×2) (each s)	3.83, 3.80 (each s)	3.92, 3.90, 3.89 (×2), 3.86 (each s)	3.86, 3.85 (each s)	3.86 (×2) (s)	3.30, 3.27 (each s)	3.92, 3.91 (×2), 3.90 (each s)
OAc		2.28, 2.27 (each s)	2.33, 2.30 (each s)		2.32, 2.31 (each s)	2.26 (×2) (s)	1.91, 1.89 (each s)	
CH_2OAc		2.10 (s)	2.08 (s)		2.08 (s)	2.03 (s)	1.64 (s)	

Table 2. ^{13}C N.m.r. (75.432 MHz) δ-values for xanthocercin A and B derivatives (**2**) and (**11**) in $CDCl_3$ at 32 °C

Carbon	(**2**)	(**11**)
CH_2OAc	62.40	62.37
2	75.62	75.63
3	77.20	76.62
4a	146.94	146.91
4b	131.26	131.26
5	114.94	111.05
6	118.23	118.21
6a	119.36	119.40
6b	146.29	146.32
7	175.21	175.55
8	123.89	124.77
9	152.01	151.91
1′	124.17	124.25
2′	123.42	112.41
3′	139.42	148.60
4′	151.02	149.03
5′	112.23	110.97
6′	127.20	120.95
1″	132.94	133.46
2″	103.78	114.91
3″	152.55	151.60
4″	129.43	140.61
5″	152.55	123.30
6″	103.78	119.70
OMe	56.24, 55.95	55.91, 56.00
OCOMe	170.11, 168.85, 168.22	170.12, 168.51
OCO*Me*	20.69, 20.45	20.66, 20.70

pyridine afforded a triacetate (**2**). Besides confirmation of the presence of two phenolic (δ 2.27, 2.28) and a single alcoholic (δ 2.10) acetoxy group, the ^{1}H n.m.r. spectrum of compound (**2**) in $(CD_3)_2CO$ revealed large deshielding of the methylene portion of the aliphatic AMXY-system (δ 4.17, dd, *J* 4.5 and 12.8 Hz; δ 4.42, dd, *J* 3.0 and 12.8 Hz) when compared with that of the parent compound (**1**) (see above). Spin–spin decoupling of the heterocyclic doublet (δ 5.26), the coupling constant (*J* 8.0 Hz) of which is consistent with a *trans*-junction of substituents, led to sharpening of the aromatic two-proton singlet (δ 6.98). Equivalence of these protons and definition of the connectivities of the four aliphatic protons by a 2D-homonuclear COSY experiment confirmed the *trans*-2-acetoxymethyl-3-(4-acetoxy-3,5-dimethoxyphenyl)-1,4-benzodioxane moiety. The COSY experiment also defined the substitution pattern of the B-ring of the isoflavone moiety as 3-acetoxy-4-methoxy through long-range scalar coupling of the methoxy protons (δ 3.87) with the 5′-H doublet (δ 7.17, *J* 8.5 Hz) only. Based on these findings, the structure of xanthocercin A could be restricted to two alternative formulations (**1**) or (**5**).

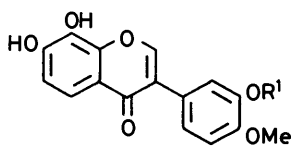
Distinction between these possibilities (**1**) or (**5**) was obtained by selective heteronuclear decoupling experiments according to the strategy developed by Ray *et al.*[7] towards solving similar problems with regard to coumarino-lignoids. Thus, irradiation of 3-H (δ 5.01 in $CDCl_3$) in the spectrum of the triacetate (**2**) led to significant sharpening of the C-4a signal (δ 146.94)* without affecting the appearance of that of C-4b. The structure of xanthocercin A could thus be formulated as (**1**).

Owing to its low concentration and accompanying problems regarding purification in the phenolic form (**3**), xanthocercin B was characterised as the triacetate (**4**) by means of spectroscopic methods. Structural similarity of xanthocercin A and B became evident from ^{1}H and ^{13}C n.m.r. spectral comparisons of their common derivatives (Tables 1 and 2 respectively). The ^{1}H n.m.r. spectra (300 MHz) of these compounds (**2**) and (**4**) were virtually superposable except for the presence of only two methoxy resonances (δ 3.86, 3.85 each s) and replacement of the two-proton aromatic singlet of the phenylpropanoid unit in (**2**) by an ABX-system (δ 6.98, d, *J* 1.9 Hz; δ 7.10, d, *J* 8.7 Hz; δ 6.98, dd, *J* 1.9 and 8.7 Hz) in the xanthocercin B derivative (**4**).

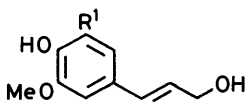
* Protonated carbons were identified by 2D-heteronuclear correlated spectroscopy, and non-protonated carbons by long-range 2D-heteronuclear correlated techniques.

Xanthocercin B thus differed from xanthocercin A with respect to the oxygenation pattern of the aromatic ring of the C_6–C_3 moiety only. The ABX-system of this ring was readily distinguished from that of the B-ring by utilisation of the 3-H doublet (δ 5.08, *J* 8.0 Hz) as reference signal in a spin–spin decoupling experiment. Confirmation of the 3′-acetoxy-4′-methoxy substitution pattern of the B-ring was obtained by observation of an n.O.e. effect (12.2%) between the methoxy hydrogens (δ 3.30) and the 5′-H doublet (δ 6.55, *J* 8.6 Hz) in C_6D_6. The n.O.e. (10.6%) between the remaining methoxy protons (δ 3.27) and the 2″-H doublet (δ 6.70, *J* 2.0 Hz) similarly characterised 4″-acetoxy-3″-methoxy substitution for the phenyl ring of the phenylpropanoid moiety. Distinction between the regioisomers (**3**) and (**6**), and thus confirmation of structure (**3**) for xanthocercin B, was again obtained by selective heteronuclear decoupling experiments; *i.e.* irradiation of 3-H (δ 5.07 in $CDCl_3$) in the synthetic 3′-*O*-methyl ether diacetate (**11**) (see below) led to significant sharpening of the C-4a signal (δ 146.91), but not that of C-4b.

The 3′-*O*-methyl ethers of xanthocercin A and B, (**7**) and (**9**), were synthesized by adoption of the biomimetic approach developed by Merlini *et al.*[13] for synthesis of the silybin/isosilybin regioisomers. Thus, oxidative coupling of 7,8-dihydroxy-3′,4′-dimethoxyisoflavone (**13**)[14] and sinapyl alcohol (**14**), both available *via* standard literature procedures,[15,16] in the presence of freshly prepared Ag_2O afforded 3′-*O*-methylxanthocercin A (**7**) in 40% yield. Methylation with methyl iodide/K_2CO_3 in anhydrous acetone gave the 3′,4″-di-*O*-methyl analogue (**8**) identical with the corresponding derivative of the natural product. In a similar procedure the dimethoxyisoflavone (**13**) and coniferyl alcohol (**15**) gave 3′-*O*-methylxanthocercin B (**9**) in 46% yield, the 4″-*O*-methyl ether (**10**) of which exhibited spectral properties identical with those of the partially methylated natural product. We could find no evidence for the formation of regioisomers of types (**5**) and (**6**) or of 2,3-*cis*-isomers in either of the synthetic sequences.

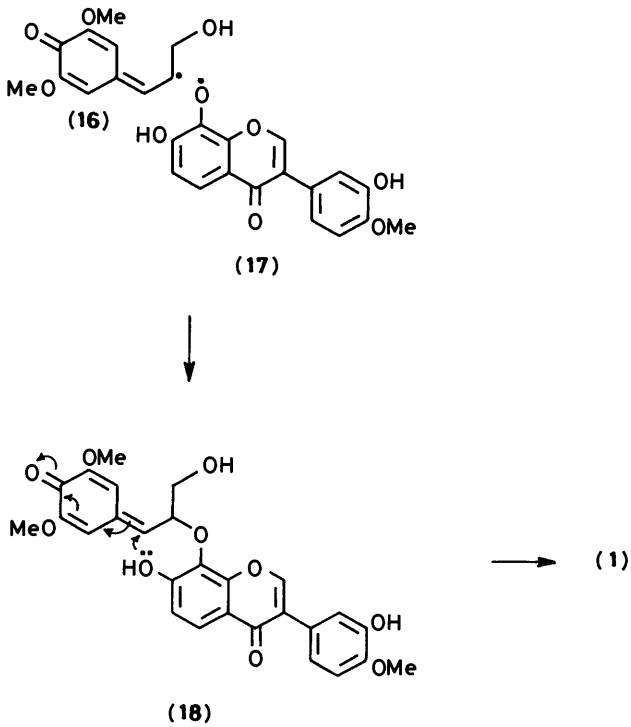


(**12**) R^1 = H
(**13**) R^1 = Me



(**14**) R^1 = OMe
(**15**) R^1 = H

The natural occurrence of xanthocercin A and B as single positional isomers, as well as their regiospecific formation during synthesis, are in contrast with the observation of the majority of flavono- and coumarino-lignoids being obtained from Nature and *via* synthesis as regioisomeric pairs, *e.g.* silybin/isosilybin[1,2] and cleomiscosin A and B.[7] Since these lignoids presumably originate from intermolecular *O*-β coupling of two phenoxy radicals, regiospecific formation of the xanthocercins, as well as the *ca.* 10:1 ratio of cleomiscosin A and B in *Cleome viscosa* Linné (syn. *C. icosanda* Linné),[7] may be explained in terms of the unique structural features of their 'catechol precursors', *i.e.* the 7,8-dihydroxyisoflavone (**12**) and 7,8-dihydroxy-6-methoxycoumarin.* While oxidation of the 7-hydroxy function in the coumarin would be partially disfavoured by the moderately electron-withdrawing α,β-unsaturated δ-lactone moiety, radical formation should occur preferentially at the 8-hydroxy group, thus leading to the predominant formation of cleomiscosin A.† In the case of the isoflavone (**12**) the strongly electron-withdrawing C-4 carbonyl group should render the 7-hydroxy group an even less attractive radical site, while simultaneously the 8-OH group will be activated towards radical formation by both electron-donating *ortho* oxygen functions. Intermolecular coupling of the oxygen radical (**17**) to the one (**16**) generated at the β-carbon of sinapyl alcohol (**14**) would then [*via* intermediate (**18**)] lead to



(**16**)
(**17**)
(**18**)
(**1**)

xanthocercin A (**1**). Similar factors should also govern the regiospecific genesis of xanthocercin B (**3**) from the isoflavone (**12**) and coniferyl alcohol (**15**). Predictions based on the above phenomena could, in principle, usefully contribute towards solving the problems surrounding distinction between regioisomeric forms amongst the aforementioned classes of lignoids.

Experimental

^1H and ^{13}C N.m.r. spectra were recorded on a Bruker AM-300 spectrometer with the solvent as internal standard, and mass spectral data on a Varian CH-5 instrument. M.p.s were obtained on a Reichert hot-stage apparatus and are uncorrected. Media used for the separation of compounds were: Whatman No. 3 for paper chromatography in 2% (v/v) aqueous HOAc, DC-Plastikfolin Kieselgel 60 F_{254} (0.25 mm; Merck) for t.l.c., Kieselgel PF_{254} (1 mm; 20 × 20 cm) for preparative t.l.c. (p.l.c.), and Merck Kieselgel 60 (230—400 mesh) for column chromatography. Methylations were performed with methyl

* *cf.* Observations[13] of regioselectivity being dictated by the nature of the catechol substituents, *i.e.* electron-donating substituents facilitating oxidation of *para*-hydroxy groups, and electron-withdrawing ones rendering the oxidation potential of the two hydroxy groups more even with mixtures of regioisomers being produced as a consequence.

† Such a prediction is, however, at variance with the reported *ca.* 1:1 formation of cleomiscosin A and B (g.l.c. of Me_3Si ethers) in a biomimetic synthesis (A. Arnoldi, A. Arnone, and L. Merlini, *Heterocycles*, 1984, **22**, 1537).

iodide in anhydrous acetone/K_2CO_3, and acetylations in acetic anhydride–pyridine. Analyses were performed by Analyitsche Laboratorien, Fritz-Pregl-strasse 24, 5270 Gummbersbach 1 Elbach, West Germany.

Isolation of Xanthocerin A (**1**) *and B* (**3**)

Drillings (2.1 kg) of the dried heartwood of *Xanthocercis zambesiaca* were extracted with methanol (3 × 5 l) at room temperature for 72 h. The combined extracts were evaporated to 5 l, defatted with hexane (5 × 1 l), and evaporated 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 water–butan-2-ol–hexane (5:4:1 v/v). The contents of tubes 66—103 (30 g) were resolved by paper chromatography to afford seven fractions. A portion (2 g) of the R_F 0.02 fraction (9.5 g) was further resolved by column chromatography in chloroform–methanol (19:1 v/v) into eight subfractions. Those with retention time 33—37 h were subjected to p.l.c. in benzene–acetone [9:1 v/v (× 2)] to give two bands, at R_F 0.29 (18 mg) and 0.21 (8 mg). The R_F 0.29 band consisted of 3′,7-dihydroxy-4′,8-dimethoxyisoflavone.[17]

Xanthocercin A (**1**) was obtained from the R_F 0.21 fraction as an amorphous solid, $[\alpha]_D$ ±0°; ^{1}H n.m.r. data in Table 1.

Tri-O-acetylxanthocercin A (**2**).—Acetylation of xanthocercin A (**1**) (8 mg) and subsequent p.l.c. in hexane–acetone–ethyl acetate (55:30:15 v/v) gave the *tri-O-acetyl derivative* (**2**) (7 mg) as a homogeneous solid, R_F 0.34, which crystallised from ethanol as white needles, m.p. 139 °C (Found: C, 62.6; H, 4.7. $C_{33}H_{30}O_{13}$ requires C, 62.5; H, 4.8%); ^{1}H and ^{13}C n.m.r. data in Tables 1 and 2 respectively; *m/z* 634 (M^+, 26%), 592 (46), 550 (30), 342 (22), 300 (56), 294 (1.2), 252 (100), 190 (1.2), 152 (2.9), and 148 (5.2).

3′,4″-*Di-O-methylxanthocercin A* (**8**).—Treatment of xanthocercin A (**1**) (7 mg) with methyl iodide followed by p.l.c. in hexane–acetone–ethyl acetate (55:30:15 v/v) afforded the 3′,4″-*di-O-methyl ether* (**8**) (4 mg) as a white, amorphous solid, R_F 0.23 (Found: M^+, 536.1663. $C_{29}H_{28}O_{10}$ requires *M*, 536.1683); ^{1}H n.m.r. data in Table 1; *m/z* 536 (M^+, 61%), 518 (3), 505 (6), 314 (2), 224 (100), 196 (11), 195 (20), 193 (11), 181 (30), 162 (4), and 152 (2).

The fraction (91 mg) with retention time 38—61 h from the above column chromatographic separation was further resolved by p.l.c. in benzene–acetone–methanol (8:1:1 v/v, × 2) into three subfractions, R_F 0.57 (35 mg), 0.46 (6 mg), and 0.42 (9 mg). The R_F 0.57 fraction gave 3′,7-dihydroxy-4′,8-dimethoxyisoflavone[17] and the R_F 0.42 fraction a further portion of xanthocercin A (**1**).

Xanthocercin B (**3**) was obtained from the R_F 0.46 fraction in a slightly impure form.

Tri-O-acetylxanthocercin B (**4**).—Acetylation of xanthocercin B (**3**) (6 mg), followed by p.l.c. in hexane–acetone–ethyl acetate (55:30:15 v/v), afforded the *tri-O-acetyl derivative* (**4**) (5 mg) as an amorphous, white solid, R_F 0.36 (Found: M^+, 604.1562. $C_{32}H_{28}O_{12}$ requires *M*, 604.1581); ^{1}H n.m.r. data in Table 1; *m/z* 604 (M^+, 48%), 562 (100), 520 (29), 502 (28), 460 (59), 384 (11), 342 (10), 300 (24), 270 (11), 260 (14), 230 (14), 222 (97), 180 (21), 179 (31), 162 (31), 151 (13), 148 (13), 147 (16), and 137 (13).

3′,4″-*Di-O-methylxanthocercin B* (**10**).—Methyl iodide methylation of xanthocercin B (**3**) (6 mg), followed by p.l.c. [hexane–benzene–acetone (4:4:2), × 2] afforded the 3′,4″-*di-O-methyl ether* (**10**) (2 mg) as a white, amorphous solid (R_F 0.16) (Found: M^+, 506.1635. $C_{28}H_{26}O_9$ requires *M*, 506.1648); ^{1}H n.m.r. data in Table 1; *m/z* 506 (M^+, 100%), 492 (4.1), 488 (5.4), 475 (4.1), 447 (4.9), 431 (5.8), 314 (27), 299 (6.9), 284 (16), 194 (99), 180 (5.1), 165 (18), 163 (15), 152 (15), 151 (89), 138 (55), 123 (7.8), 119 (15), and 107 (7.7).

Synthesis of the 3′-O-Methyl Ethers of Xanthocercin A and B

3′-O-*Methylxanthocercin A* (**7**).—7,8-Dihydroxy-3′,4′-dimethoxyisoflavone (**13**)[15] (314 mg) and sinapyl alcohol (**14**) (210 mg) were dissolved in a mixture of anhydrous benzene (200 ml) and methanol (100 ml). Freshly prepared silver(I) oxide (232 mg) was added and the mixture was stirred at room temperature for 20 h. Filtration and evaporation gave a crude mixture, which was resolved by p.l.c. [benzene–ethyl acetate–acetone–methanol (65:20:10:5)] to give 3′-*O*-methylxanthocercin A (**7**) (R_F 0.42) as a white, amorphous solid (210 mg); δ_H ([$^2H_6$]acetone; 297 K) 8.27 (s, 9-H), 7.68 (d, *J* 9.0 Hz, 6-H), 7.51 (br s, OH), 7.29 (d, *J* 2.1 Hz, 2′-H), 7.15 (dd, *J* 2.1 and 8.4 Hz, 6′-H), 7.03 (d, *J* 9.0 Hz, 5-H), 6.98 (d, *J* 8.4 Hz, 5′-H), 6.86 (s, 2″- and 6″-H), 5.12 (d, *J* 8.1 Hz, 3-H), 4.30 (ddd, *J* 2.6, 3.9, and 8.1 Hz, 2-H), 3.86—3.96 and 3.50—3.67 (each m, together CH_2OH), and 3.85 (× 2), 3.84, and 3.83 (each s, 4 × OMe).

3′,4″-*Di-O-methylxanthocercin A* (**8**).—Methylation (MeI) of 3′-*O*-methylxanthocercin A (**7**) (160 mg), followed by p.l.c. [hexane–acetone–ethyl acetate (55:30:15)], afforded the *methyl ether* (**8**) (R_F 0.23), identical with the corresponding natural derivative, as white needles (99 mg) from ethanol–methylene dichloride (minimum CH_2Cl_2), m.p. 214 °C (Found: C, 64.8; H, 5.2. $C_{29}H_{28}O_{10}$ requires C, 64.9; H, 5.3%).

3′-O-*Methylxanthocercin B* (**9**).—In a procedure similar to that for 3′-*O*-methylxanthocercin A, reaction of 7,8-dihydroxy-3′,4′-dimethoxyisoflavone (**13**)[15] (314 mg) and coniferyl alcohol (**15**)[16] (180 mg) yielded 3′-*O*-methylxanthocercin B (**9**) (R_F 0.58) as a white, amorphous solid (230 mg) after p.l.c. [benzene–acetone–methanol (7:2:1)].

3′,4″-*Di-O-methylxanthocercin B* (**10**).—Methyl iodide methylation of compound (**9**) (100 mg), followed by p.l.c. [hexane–benzene–acetone (4:4:2), × 2], afforded the 3′,4″-di-*O*-methyl ether (**10**) (R_F 0.16), identical with the natural derivative, as white cubes (44 mg) from ethanol, m.p. 191 °C (Found: C, 66.3; H, 5.2. Calc. for $C_{28}H_{26}O_9$: C, 66.4; H, 5.2%).

Di-O-acetyl-3′-O-methylxanthocercin B (**11**).—Acetylation of 3′-*O*-methylxanthocercin B (**9**) (100 mg) afforded the *diacetate* (**11**) as white needles (62 mg) from methanol, m.p. 173 °C (Found: C, 64.5; H, 4.9. $C_{31}H_{28}O_{11}$ requires C, 64.6; H, 4.9%); δ_H(C_6D_6) 8.02 (s, 9-H), 7.82 (d, *J* 9.0 Hz, 6-H), 7.19 (d, *J* 2.0 Hz, 2′-H), 7.09 (d, *J* 8.5 Hz, 5″-H), 7.02 (d, *J* 9.0 Hz, 5-H), 7.02 (dd, *J* 2.0 and 8.4 Hz, 6′-H), 6.97 (d, *J* 2.1 Hz, 2″-H), 6.96 (dd, *J* 2.1 and 8.5 Hz, 6″-H), 6.90 (d, *J* 8.4 Hz, 5′-H), 5.07 (d, *J* 7.8 Hz, 3-H), 4.46 (dd, *J* 3.2 and 12.3 Hz), and 4.07 (dd, *J* 4.2 and 12.3 Hz) (CH_2OAc), 4.34 (ddd, *J* 3.2, 4.2, and 7.8 Hz, 2-H), 3.90, 3.89, and 3.84 (each s, together 3 × OMe), 2.31 (s, 4″-OAc), and 2.07 (s, CH_2OAc); *m/z* 576 (M^+, 23%), 534 (14), 474 (92), 460 (4.8), 356 (7.2), 340 (5.4), 314 (100), 299 (22), 284 (15), 271 (12), 255 (5.6), 241 (7.8), 237 (8.0), 228 (8.6), 222 (65), 213 (8.0), 194 (4.4), 179 (33), 171 (4.4), 162 (87), 151 (18), 147 (45), 137 (17), 135 (10), 131 (54), 124 (18), 119 (68), 107 (12), and 103 (37).

Acknowledgements

Support by the South African Foundation for Research Development, C.S.I.R., Pretoria and the Sentrale Navorsingsfonds of this University is acknowledged. Wood samples of

Xanthocercis zambesiaca were supplied by the Director, Forestry Research, P.O. Box 727, Pretoria. Mass spectral data were recorded by Dr. J. M. Steyn, Department of Pharmacology of this University.

References

1 O. R. Gottlieb, *Fortschr. Chem. Org. Naturst.*, 1978, **35**, 1.
2 A. Pelter and R. Hänsel, *Chem. Ber.*, 1975, **108**, 790, and refs. therein.
3 R. Hänsel, J. Schultz, and A. Pelter, *Chem. Ber.*, 1975, **108**, 1482, and refs. therein.
4 M. R. Parthasarathy, K. R. Ranganathan, and D. K. Sharma, *Phytochemistry*, 1979, **18**, 506, and refs. therein.
5 H. Nielsen and P. Arends, *Phytochemistry*, 1978, **17**, 2040.
6 M. Das Gracas, B. Zoghbi, N. F. Roque, and O. R. Gottlieb, *Phytochemistry*, 1981, **20**, 180.
7 A. B. Ray, S. K. Chattopadhyay, S. Kumar, C. Konno, Y. Kiso, and H. Hikino, *Tetrahedron*, 1985, **41**, 209, and refs. therein.
8 P. Bhandari, P. Pant, and R. P. Rastogi, *Phytochemistry*, 1982, **21**, 2147.
9 Z. Lin-gen, O. Seligman, and H. Wagner, *Phytochemistry*, 1983, **22**, 617.
10 H. Hikino, Y. Kiso, H. Wagner, and M. Fiebig, *Planta Med.*, 1984, **50**, 248, and refs. therein.
11 J. B. Harborne, D. Boulter, and L. B. Turner, 'Chemotaxonomy of the Leguminosae,' Academic Press, London, 1971, vol. 14, p. 23.
12 S. H. Harper, D. B. Shirley, and D. A. Taylor, *Phytochemistry*, 1976, **15**, 1019.
13 L. Merlini, A. Zanarotti, A. Pelter, M. P. Rochefort, and R. Hänsel, *J. Chem. Soc., Perkin Trans. 1*, 1980, 775, and refs. therein.
14 A. S. Kukla and T. R. Seshadri, *Tetrahedron*, 1962, **18**, 1443.
15 L. Farkas, A. Gottsegen, M. Nógrádi, and S. Antus, *J. Chem. Soc., Perkin Trans. 1*, 1974, 305, and refs. therein.
16 A. Zanarotti, *Tetrahedron Lett.*, 1982, **23**, 3815.
17 T. Hayashi and R. H. Thomson, *Phytochemistry*, 1974, **13**, 1943.

Received 31*st March* 1987; *Paper* 7/567