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ENANTIOSELECTIVE SYNTHESIS OF FLAVONOIDS. PART 2. POLY-OXYGENATED α-HYDROXYDIHYDROCHALCONES AND CIRCULAR DICHROIC ASSESSMENT OF THEIR ABSOLUTE CONFIGURATION

JAN A.N. AUGUSTYN, BAREND C.B. BEZUIDENHOUDT*, ANNELIE SWANEPOEL, AND DANEEL FERREIRA

Department of Chemistry, University of the Orange Free State,
P.O. Box 339, Bloemfontein, 9300 South Africa

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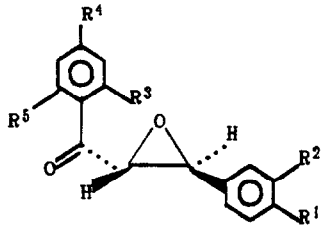
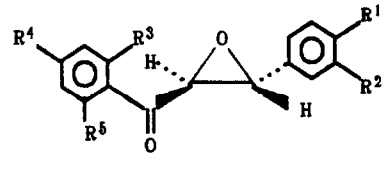
Abstract —— Chiral chalcone epoxides exhibiting the oxygenation patterns of naturally occurring flavonoids and isoflavonoids were transformed into the corresponding α-hydroxydihydrochalcones. The availability of both enantiomers permitted assessment of the absolute configuration at the single chiral centre by CD spectroscopy; such protocol being applicable to defining the configuration of some naturally occurring analogues, two of which are novel compounds.

α-Hydroxydihydrochalcones constitute a rare group of $C_6.C_3.C_6$ metabolites presumably sharing a close biogenetic relationship with the α-methyldeoxybenzoins and isoflavonoids[1-5]. Despite the ready availability of the α-hydroxydihydrochalcones *via* catalytic hydrogenation of chalcone epoxides[3,5], progress in the chemistry of these compounds is hampered by the lack of synthetic access to both enantiomers and also by the absence of a method for determination of the absolute configuration at the single chiral centre. The recent transformation of a non-oxygenated chiral chalcone epoxide to an aromatic deoxy α-hydroxydihydrochalcone[6] in conjunction with our synthesis and circular dichroic assessment of the absolute configuration of (α*R*)-α,2′,4′-trihydroxy-4-methoxydihydrochalcone[7], prompted extension of a similar protocol to a series of chalcone epoxides exhibiting the characteristic aromatic oxygenation patterns of naturally occurring α-hydroxydihydrochalcones.

The series of (-)-*trans*-(α*R*,β*S*) 1-7 and (+)-*trans*-(α*S*,β*R*)-chalcone epoxides 8-13 (Table 1), available[8] *via* epoxidation of the appropriate (*E*)-chalcones with H_2O_2 in the triphase system aqueous NaOH, poly-*L*- or *D*-alanine and CCl_4[9], were separately subjected to catalytic hydrogenation ($Pd/BaSO_4$ for 2, 3, 4, 8, 9, and 10; 5% Pd/C for 6 and 12; 10% Pd/C for 5,



(-)-(α*R*,β*S*): 1-7

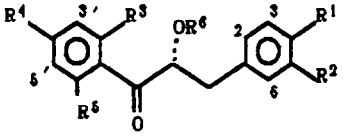


(+)-(α*S*,β*R*): 8-13

Table 1[8]. Oxygenation patterns and optical purities (% ee) of chalcone epoxides 1-13.

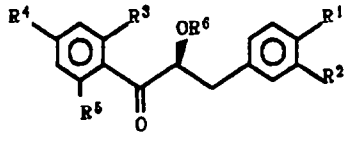
Epoxide, % ee	R^1	R^2	R^3	R^4	R^5	Epoxide, % ee
1 , 92	H	H	H	H	H	-
2 , 38	H	H	OMOM	H	H	8 , 53
3 , 66	OMe	H	OMOM	H	H	9 , 46
4 , 84	OMe	H	OMOM	OMe	H	10 , 53
5 , 62	OMe	OMe	OMOM	OMe	H	11 , 25
6 , 32	OMe	H	OMOM	OMe	OMe	12 , 20
7 , -	OMe	OMe	OMOM	OMe	OMe	13 , -

7, 11, and 13) to give the respective (+)-(*aR*) 14-19 and (-)-(*aS*)-*a*-hydroxydihydrochalcones 20-25. Enantiomeric purity was assessed by ^{1}H NMR in $CDCl_3$ with Pr(hfc)$_3$ as chiral shift reagent and is indicated in table 2. The ^{1}H NMR spectra (300 MHz) of the *a*-hydroxydihydrochalcones are characterized by the multiplet (δ5.43-4.94) of H-*a* (doublet of doublets, $J_{\alpha,\beta}$ 3.8-4.0 and 7.0-9.0 Hz, after deuterium exchange), two doublet of doublets ($J_{\alpha,\beta}$ 4.0, $J_{\beta,\beta}$ 14.0 Hz) of the *β*-methylene group (δ3.20-2.96, 2.80-2.65), and a doublet for the *a*-OH function (δ3.94-3.70).



(+)-*aR*,R^6=H: 14-19

R^6=*p*-OMe.C_6H_6.CO: 26-31



(-)-*aS*,R^6=H: 20-25

R^6=*p*-OMe.C_6H_4.CO: 32-37

Table 2. Oxygenation patterns and optical purities (% ee) of *a*-hydroxydihydrochalcones 14-25

Compound, % ee[a]	R^1	R^2	R^3	R^4	R^5	Compound, % ee[a]
14 , 27	H	H	OMOM	H	H	20 54
15 , 61	OMe	H	OMOM	H	H	21 , 48
16 , 76[b]	OMe	H	OMOM	OMe	H	22 , 52
17 , 61	OMe	OMe	OMOM	OMe	H	23 , 16
18 , 24	OMe	H	OMOM	OMe	OMe	24 , 19[b]
19 , 14	OMe	OMe	OMOM	OMe	OMe	25 , 16

(a) Determined with Pr(hfc)$_3$ as shift reagent unless specified to the contrary.
(b) Determined with Eu(tfc)$_3$ as shift reagent.

The CD spectra of the (+)-(*aR*) 14,15 and (-)-(*aS*)-*a*-hydroxydihydrochalcones 20 and 21 (*cf* Figure 1 for the spectra of the enantiomeric pair 14 and 20) exhibit weak negative and positive Cotton effects respectively in the 310-330 nm region for the n,π^* transition. The π,π^* transition shows a positive extremum in the 260-290 nm region and a negative extremum

Figure 1: CD curves of (+)–αR– and (–)–αS–hydroxydihydrochalcones 14 and 20

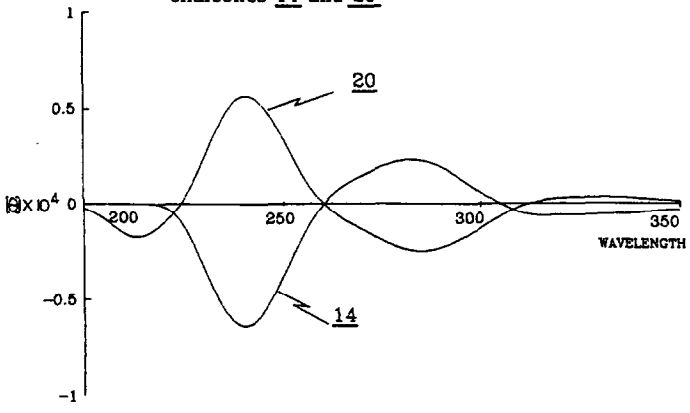


Figure 2: CD curves of (+)–αR– and (–)–αS–hydroxydihydrochalcones 16 and 22

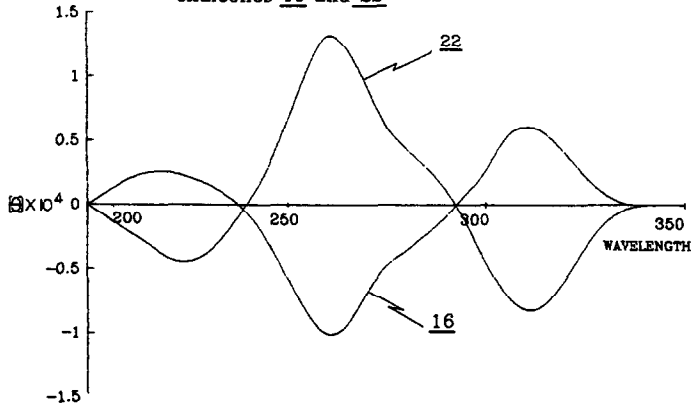
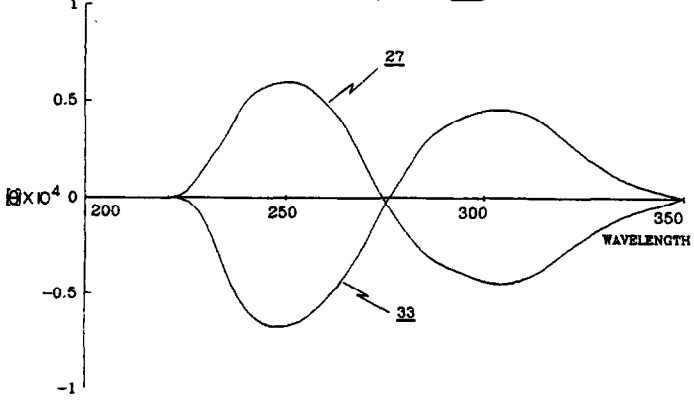


Figure 3: CD curves of αR– and αS–hydroxydihydrochalcone benzoates 27 and 33



in the 230-250 nm region for the (+)-*aR* analogues 14 and 15, with the signs of these Cotton effects being reversed for the (-)-*aS* isomers 20 and 21. Owing to the increased number of A-ring oxygen functions in the remaining *o*-hydroxydihydrochalcones, the high-amplitude Cotton effects resulting from π,π^* transitions are shifted to longer wave-lengths (225-270 and 305-315 nm respectively) thus presumably burying the weaker Cottons effects arising from n,π^* transitions[10]. Figure 2 depicts the circular dichroic characteristics of the enantiomeric pair of 4,4′-dimethoxy-2′-*O*-methoxymethyl-*o*-hydroxydihydrochalcones 16 and 22.

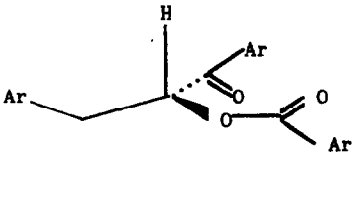
The nature of the chiral centre in the *o*-hydroxydihydrochalcones offered the opportunity to confirm the *aR* (for 14-19) and *aS* (for 20-25) absolute configurations by adoption of the CD exciton chirality approach of Nakanishi *et al*[10,11] for the *o*-*O*-(4-methoxybenzoyl) esters 26-37 of these analogues. The UV spectra of the *p*-methoxybenzoates indicate intramolecular CT or ^1L_a transitions in the 255-270 nm region (Table 3). The CD curves of the

Table 3. Oxygenation patterns, optical purities (% ee), and $\lambda_{max.}$ (UV) of the *o*-*O*-(4-methoxybenzoyl) esters 26-37

Ester	% ee[a]	$\lambda_{max.}$	R^1	R^2	R^3	R^4	R^5	Ester	% ee[a]	$\lambda_{max.}$
26	32	257.6	H	H	OMOM	H	H	32	56	257.6
27	56	257.6	OMe	H	OMOM	H	H	33	50	257.6
28	70	266.8	OMe	H	OMOM	OMe	H	34	52[b]	266.8
29	63[b]	269.2	OMe	OMe	OMOM	OMe	H	35	16	269.2
30	24	259.6	OMe	H	OMOM	OMe	OMe	36	10	259.6
31	4	260.4	OMe	OMe	OMOM	OMe	OMe	37	8	260.4

(a) Determined with Pr(hfc)$_3$ as shift reagent unless specified to the contrary.
(b) Determined with Eu(tfc)$_3$ as shift reagent.

(+)-*aR* esters 26-31 (*cf* Figure 3 for the spectra of the enantiomeric pair 27 and 33) exhibit intense sequential negative and positive Cotton effects in the 280-305 and 230-250 nm regions respectively (*eg* $\lambda_{ext.}$ 305 nm, Θ -4469 and 250 nm, Θ +5959, A = Θ_1-Θ_2 = -10428 for compound 27) which presumably indicates exciton interaction between the benzoate and benzoyl chromophores. The negative sign of the A-values is in agreement with negative chirality between the two long axes of these chromophores [presentation 39 based on preferred conformation 38 (Dreiding models)], thus confirming the *aR* absolute configuration for all members of the series 26-31. Intense positive first and negative second Cotton effects in the same CD regions for enantiomers 32-37 (*eg* $\lambda_{ext.}$ 305 nm, Θ +4563 and 250 nm, Θ -6806, A = +11369 for benzoate 33) similarly reflect positive chirality (presentation 41, conformation 40) and hence *S* absolute configuration at the single chiral centre of the benzoates 32-37.



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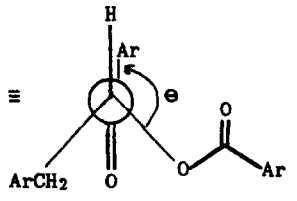

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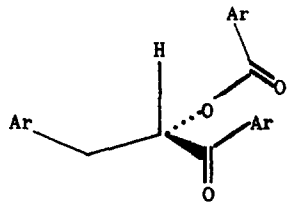

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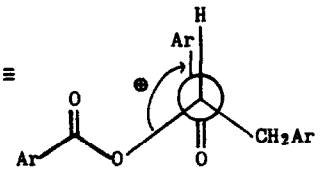

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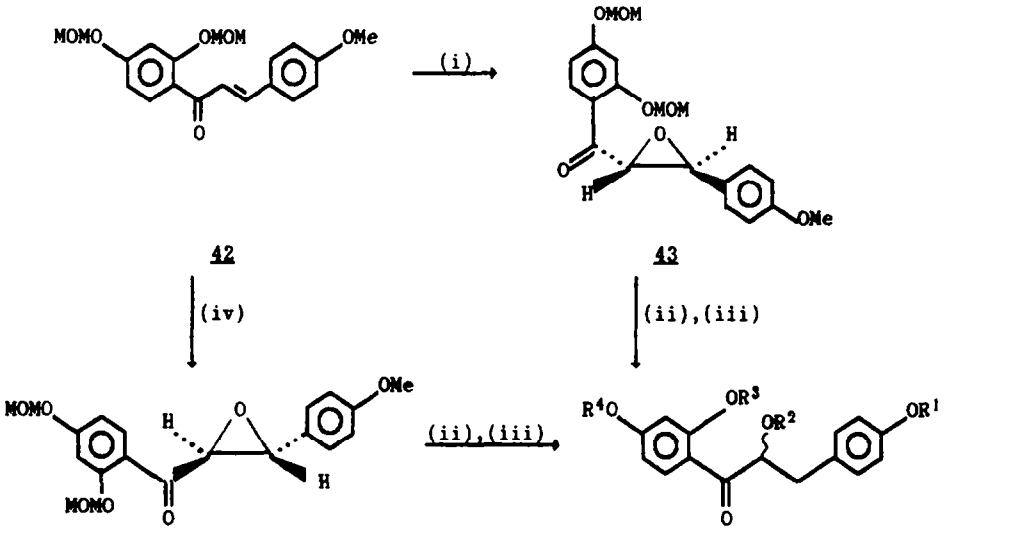
The circular dichroic approach towards definition of the absolute configuration of α-hydroxydihydrochalcones was applied to two novel analogues from the heartwood of *Pericopsis elata*, *i.e.* α,2′,4,4′-tetrahydroxydihydrochalcone 47 and the 4-*O*-methyl derivative 46, as well as the known[3] α,2′-dihydroxy-4,4′-dimethoxydihydrochalcone 48 to which an α*R* absolute configuration was assigned. Owing to the complexity of the phenolic mixture from *P. elata* metabolites 46 and 47 were characterized as their peracetates 49 and 50. Separate epoxidation of 4-methoxy-2′,4′-dimethoxymethyl-(*E*)-chalcone 42 as above using poly-*L*- and *D*-alanine respectively (Scheme), afforded the *trans*-(α*R*,β*S*)- and *trans*-(α*S*,β*R*)-epoxides 43 and 44 (70% and 36% ee respectively). Hydrogenolysis (H_2/Pd-$BaSO_4$) gave the respective α-hydroxydihydrochalcones 45 and 52 with 65% and 32% ee [Pr(hfc)$_3$ as chiral shift reagent] which were subsequently transformed to the α-*O*-(4-methoxybenzoyl) esters 51 and 53, the UV spectra of which again indicated intramolecular CT or ^1L_a transitions in the 260 nm region. Intense sequential negative and positive, and positive and negative Cotton effects in the CD spectra of benzoates 51 (73% ee; $\lambda_{ext.}$ 283 nm, Θ -11000 and 245 nm, Θ +14000, A = -25000) and 53 (38% ee; $\lambda_{ext.}$ 282 nm, Θ +6400 and 245 nm, Θ -10000, A = +16400) respectively, confirm their α*R* (51) and α*S* (53) absolute configurations. Removal of the protecting groups in synthetic analogue 45 and subsequent acetylation, afforded the triacetate 49 of the (*R*)-α-hydroxydihydrochalcone which exhibited a CD spectrum identical to that of the natural product. Comparison of the CD data of the α,2′,4,4′-tetra-acetoxydihydrochalcone 50 with those of the synthetic (*R*)-α,2′,4′-triacetoxy-4-methoxydihydrochalcone 49, and of those of the α,2′-dihydroxy-4,4′-dimethoxydihydrochalcone 48 from *Pterocarpus angolensis*[3] with CD data (Figures 4 and 5) of synthetic (*R*)-α,2′,4′-trihydroxy-4-methoxydihydrochalcone 46 simi-

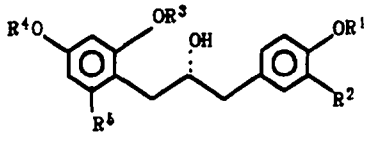
lary confirmed their *all* absolute configurations.



45 ~~~ = ⋮, R^1=Me, R^2=H, R^3=R^4=MOM
46 ~~~ = ⋮, R^1=Me, R^2=R^3=R^4=H
47 ~~~ = ⋮, R^1=R^2=R^3=R^4=H
48 ~~~ = ⋮, R^1=R^4=Me, R^2=R^3=H
49 ~~~ = ⋮, R^1=Me, R^2=R^3=R^4=Ac
50 ~~~ = ⋮, R^1=R^2=R^3=R^4=Ac
51 ~~~ = ⋮, R^1=Me, R^2=*p*-MeO.C_6H_4.CO, R^3=R^4=MOM
52 ~~~ = ▮, R^1=Me, R^2=H, R^3=R^4=MOM
53 ~~~ = ▮, R^1=Me, R^2=*p*-MeO.C_6H_4.CO, R^3=R^4=MOM

Scheme. Reagents and Conditions: (i) poly-*L*-alanine, CCl_4, soln. of NaOH in 30% H_2O_2, r.t.; (ii) H_2,Pd-$BaSO_4$, MeOH; (iii) *p*-MeO.C_6H_4.COCl, DMAP; (iv) similar to (i) except for replacement of poly-*L*- by poly-*D*-alanine.

Whereas assignment of configuration to metabolite 48 was previously done[3] by a dubious comparison of the CD data of the 1,3-diarylpropan-2-ols 54[a] and 55[b], the methodology developed here permits the assessment of absolute configuration by direct comparison of the



54 R^1=R^4=Me, R^2=R^3=R^5=H
55 R^1=R^4=Me, R^2=R^5=OMe, R^3=H

[a]Formed *via* deoxygenation of 48 with diborane

[b]Obtained by Birch-reduction of 3′,4′,5,7-tetra-*O*-methyl-(+)-catechin

chiroptical details of the natural product with those of the synthetic analogue.

Figure 4: CD curves of (αR)-α,2',4' trihydroxy-4-methoxydihydrochalcone 46 and its tri-O-acetyl derivative 49

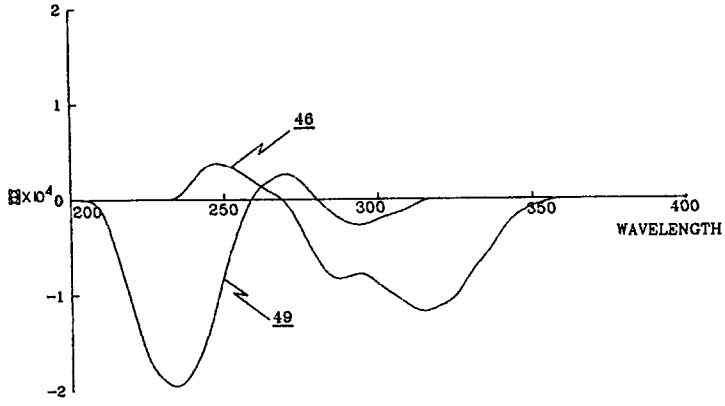
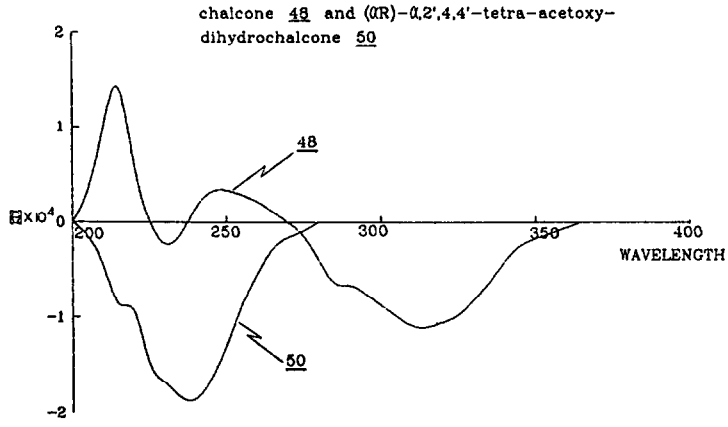


Figure 5: CD curves of (αR)-α,2'-dihydroxy-4,4'-dimethoxydihydrochalcone 48 and (αR)-α,2',4,4'-tetra-acetoxydihydrochalcone 50



The profound influence of intramolecular hydrogen bonding involving the α- and 2'-OH functions on the conformation and hence the sign of the Cotton effect in the CD spectra of α-hydroxydihydrochalcones, is demonstrated by comparison of the data of (α*l*)-α,2',4'-trihydroxy-4-methoxydihydrochalcone 46, its tri-*O*-acetyl derivative 49 and (α*l*)-4,4'-dimethoxy-2'-*O*-methoxymethyl-α-hydroxydihydrochalcone 16 (Figures 2 and 4). Conclusions regarding the absolute configuration of α-hydroxydihydrochalcones which are based on chiroptical data are thus reliable only for similarly derivatized α- and 2'-OH functionalities.

The results in this paper clearly demonstrate the utility of epoxychalcones as chirons

for naturally occurring α-hydroxydihydrochalcones. Detailed analysis of the CD data of the series of both *R* and *S* poly-oxygenated analogues should usefully contribute towards assessment of the absolute configuration of novel homologues from nature.

EXPERIMENTAL

TLC was performed on DC-Plastikfolin Kieselgel 60 PF_{254} (0.25 mm) and the plates sprayed with H_2SO_4-HCHO (40:1, v/v) after development. Preparative plates (PLC) [Kieselgel PF_{254} (1.0 mm)] were air-dried and used without prior activation. Acetylations were carried out with Ac_2O-anhydrous pyridine. ^1H NMR spectra were, unless specified to the contrary, recorded on a Bruker AM-300 spectrometer for solutions in $CDCl_3$ at 25°C with the solvent as internal standard. The enantiomeric excess (ee) of optical active compounds were determined by using tris(3-trifluoroacetyl-d-camphorato)-europium(III)[Eu(tfc)$_3$] or tris(3-heptafluoropropylhydroxymethylene-d-camphorato)-praseodymium(III)[Pr(hfc)$_3$] as chiral shift reagents in concentrations of 0.5-1 mg per 5 mg of compound. Mass spectral data were recorded on a Varian CH-5 instrument and m.p.s. (uncorrected) on a Reichert hot stage apparatus. CD measurements were obtained for solutions in MeOH on a Jasco J-20 spectropolarimeter and optical rotations measured with a Bendix-NPL automatic polarimeter for solutions in CH_2Cl_2.

Reductive cleavage of chalcone epoxides[3]

(±)-(α*R*)-2′-β-Methoxymethyl-α-hydroxydihydrochalcone **14**: The chalcone epoxide **2** (21 mg) was hydrogenated (1 atm) in MeOH (10 ml) at ambient temperatures for 4 h, utilizing freshly prepared[12] Pd-$BaSO_4$ (27 mg) as catalyst. Filtration (celite) and evaporation of the solvent followed by PLC ($CHCl_3$-Me_2CO, 97:3, v/v), yielded the α-hydroxydihydrochalcone **14** (Rf 0.6) as a colourless oil (18.5 mg, 92%). (Found: M^+-$C_2H_6O_2$, 224.0835. $C_{15}H_{12}O_2$ requires 224.0837). MS (EI) *m/z* 286 (M^+, 1%), 268(1), 224(7), 165(100), 135(44), 121(52); ^1H NMR δ7.75 (dd, J1.8 and 7.5 Hz, H-6′), 7.51 (ddd, J1.8, 7.8, and 7.8 Hz, H-4′), 7.27-7.10 (m, 7H), 5.43 (m, H-α), 5.31 (d, J6.8 Hz), and 5.23 (d, J6.8 Hz) (OCH_2OCH_3), 3.84 (br. d., J6.0 Hz, α-OH), 3.48 (s, OCH_2OCH_3), 3.15 (dd, J4.0 and 14.0 Hz, H-β), 2.76 (dd, J7.0 and 14.0 Hz, H-β); $[\alpha]_D^{25}$ + 37° (*c* 0.24); CD (*c* 0.0440) $[\Theta]_{215}$ 0, $[\Theta]_{240}$ -6703, $[\Theta]_{259}$ 0, $[\Theta]_{283}$ +2277, $[\Theta]_{305}$ 0, $[\Theta]_{325}$ -618, $[\Theta]_{345}$ -325.

(±)-(α*R*)-4-Methoxy-2′-β-methoxymethyl-α-hydroxydihydrochalcone **15**: Catalytic hydrogenation (3 h) of the chalcone epoxide **3** (41 mg) in MeOH (15 ml) over Pd-$BaSO_4$ (45 mg) and PLC ($CHCl_3$-Me_2CO, 96:4, v/v) gave the α-hydroxydihydrochalcone **15** (R_f 0.6) as a colourless oil (21 mg, 51%); (Found: M^+-H_2O, 298.1199. $C_{18}H_{18}O_4$ requires 298.1205). MS (EI) *m/z* 316 (M^+, 1%), 298(1), 254(1), 165(51), 152(12), 135(11), 121(100); ^1H NMR δ7.73 (dd, J1.8 and 7.0 Hz, H-6′), 7.51 (ddd, J1.8, 7.0, and 7.0 Hz, H-4′), 7.23 (dd, J1.0 and 7.5 Hz, H-3′), 7.10 (ddd, J1.0, 7.5, and 7.5 Hz, H-5′), 7.01 (d, 7.8, H-2,6), 6.76 (d, J7.8 Hz, H-3,5), 5.39 (ddd, J4.0, 6.8, and 7.0 Hz, H-α), 5.31 (d, J7.0 Hz), and 5.24 (d, J7.0 Hz) (OCH_2OCH_3), 3.80 (d, J6.8 Hz, α-OH), 3.75 (s, OCH_3), 3.49 (s, OCH_2OCH_3), 3.09 (dd, J4.0 and 14.0 Hz, H-β), 2.72 (dd, J7.0 and 14.0 Hz, H-β); $[\alpha]_D^{25}$ +53° (*c* 0.24); CD (*c* 0.0640) $[\Theta]_{210}$ 0, $[\Theta]_{235}$ -21255, $[\Theta]_{250}$ 0, $[\Theta]_{268}$ +13594, $[\Theta]_{305}$ 0, $[\Theta]_{315}$ -1730, $[\Theta]_{350}$ 0.

(±)-(α*R*)-4,4′-Dimethoxy-2′-β-methoxymethyl-α-hydroxydihydrochalcone **16**: Catalytic hydrogenation (5 h) of the chalcone epoxide **4** (25 mg) in MeOH (15 ml) over Pd-$BaSO_4$ (30 mg) and PLC ($CHCl_3$-Me_2CO, 97:3, v/v) gave the α-hydroxydihydrochalcone **16** (R_f 0.4) as a colourless oil (22 mg, 88%); (Found: M^+-H_2O, 328.1307. $C_{19}H_{20}O_5$ requires 328.1311); MS (EI) *m/z* 328 (M^+-18,4%), 284(5), 195(60), 165(26), 151(46), 121(100); ^1H NMR δ7.83 (d, J9.0 Hz, H-6′), 7.03 (d, J8.8 Hz, H-2,6), 6.77 (d, J8.8 Hz, H-3,5), 6.75 (d, J2.5 Hz, H-3′), 6.63 (dd, J2.5 and 9.0 Hz, H-5′), 5.35 (ddd, J3.8, 7.0, and 7.0 Hz, H-α), 5.31 (d, J7.0 Hz), and 5.23 (d, J7.0 Hz) (OCH_2OCH_3), 3.90 (d, J7.0 Hz, α-OH), 3.87 (s, OCH_3),

3.76 (s, OCH_3), 3.49 (s, OCH_2OCH_3), 3.10 (dd, J3.8 and 14.0 Hz, H-β), 2.70 (dd, J7.0 and 14.0 Hz, H-β; $[\alpha]_D^{25}$ +64^0 (*c* 0.24); CD (*c* 0.1430) $[\Theta]_{200}$ 0, $[\Theta]_{222}$ +2664, $[\Theta]_{242}$ 0, $[\Theta]_{260}$ -10452, $[\Theta]_{297}$ 0, $[\Theta]_{310}$ +6237, $[\Theta]_{335}$ 0.

(+)-(*αR*)-3,4,4′-Trimethoxy-2′-*O*-methoxymethyl-*α*-hydroxydihydrochalcone 17: Catalytic hydrogenation (20 min) of the chalcone epoxide 5 (31 mg) in EtOH (20 ml) over 10% Pd-C (30 mg) and PLC ($CHCl_3$-Me_2CO, 95:5, v/v) gave the *α*-hydroxydihydrochalcone 17 (R_f 0.5) as a colourless oil (13 mg, 42%); (Found: M^+, 376.1528. $C_{20}H_{24}O_7$ requires 376.1522); MS (EI) *m/z* 376 (M^+, 1%), 358(2), 313(2), 195(40), 165(24), 151(100); ^{1}H NMR δ7.83 (d, J9.0 Hz, H-6′), 6.75-6.60 (m, 5H), 5.37 (ddd, J4.0, 6.8, and 6.8 Hz, H-*α*), 5.31 (d, J7.0 Hz), and 5.24 (d, J7.0 Hz) (OCH_2OCH_3), 3.94 (d, J6.8 Hz, *α*-OH), 3.89 (s, OCH_3), 3.85 (s, OCH_3), 3.81 (s, OCH_3), 3.53 (s, OCH_2OCH_3), 3.11 (dd, J4.0 and 14.0 Hz, H-β), 2.74 (dd, J6.8 and 14.0 Hz, H-β); $[\alpha]_D^{25}$ +48^0 (*c* 0.23); CD (*c* 0.0911) $[\Theta]_{340}$ 0, $[\Theta]_{310}$ +5743, $[\Theta]_{285}$ 0, $[\Theta]_{260}$ -10740, $[\Theta]_{230}$ 0.

(+)-(*αR*)-4,4′,6′-Trimethoxy-2′-*O*-Methoxymethyl-*α*-hydroxydihydrochalcone 18: A mixture (52 mg) of the chalcone epoxide 6 and 4,4′,6′-trimethoxy-2′-*O*-methoxymethylchalcone (see ref. 8) was dissolved in EtOH (20 ml) and hydrogenated over 5% Pd/C (50 mg) (20 min) and the product 18 (R_f 0.5) obtained as a colourless oil (8 mg), after purification by PLC ($CHCl_3$-Me_2CO, 95:5, v/v); (Found: M^+, 376.1527). $C_{20}H_{24}O_7$ requires 376.1522; MS (EI) *m/z* 376 (M^+, 1%), 358(2), 225(67), 195(41), 181(52), 152(9), 121(100); ^{1}H NMR δ7.07 (d, J9.0 Hz, H-2,6), 6.76 (d, J9.0, Hz, H-3,5), 6.34 (d, J2.1 Hz, H-3′), 6.13 (d, J2.1 Hz, H-5′), 5.12 (d, J7.0 Hz) and 5.09 (d, J7.0 Hz) (OCH_2OCH_3), 4.94 (ddd, J4.0, 5.0, and 9.0 Hz, H-*α*), 3.83 (s, OCH_3), 3.78 (s, 2x OCH_3), 3.68 (d, J5.0 Hz, *α*-OH), 3.46 (s, OCH_2-OCH_3), 2.96 (dd, J4.0 and 14.0 Hz, H-β), 2.69 (dd, J9.0 and 14.0 Hz, H-β); $[\alpha]_D^{25}$ +24^0 (*c* 0.17); CD (*c* 0.0380) $[\Theta]_{330}$ 0, $[\Theta]_{308}$ +495, $[\Theta]_{298}$ 0, $[\Theta]_{260}$ -301, $[\Theta]_{220}$ 0.

(+)-(*αR*)-3,4,4′,6′-Tetramethoxy-2′-*O*-methoxymethyl-*α*-hydroxydihydrochalcone 19: A mixture (60 mg) of the chalcone epoxide 7 and 3,4,4′,6′-tetramethoxy-2′-*O*-methoxymethyl chalcone in EtOH (25 ml) was hydrogenated over 10% Pd/C (50 mg) (20 min) and the product 19 (R_f 0.5) obtained as a colourless oil (9 mg) following PLC ($CHCl_3$-Me_2CO, 95:5, v/v); (Found: M^+, 406.1635. $C_{21}H_{26}O_8$ requires 406.1627); MS (EI) *m/z* 406 (M^+, 1%) 388(2), 225(36), 195(30), 181(45), 151(100); ^{1}H NMR δ6.75-6.65 (m, 3H), 6.33 (d, J2.0 Hz, H-3′), 6.12 (d, J2.0 Hz, H-5′), 5.12 (d, J7.0 Hz) and 5.09 (d, J7.0 Hz) (OCH_2OCH_3), 4.95 (dd, J4.0 and 8.0 Hz, H-*α*), 3.81 (s, 3xOCH_3), 3.76 (s, OCH_3), 3.47 (s, OCH_2OCH_3), 2.97 (dd, J4.0 and 14.0 Hz, H-β), 2.71 (dd, J8.0 and 14.0 H-β); $[\alpha]_D^{25}$ +15^0 (*c* 0.16); CD (*c* 0.0830) $[\Theta]_{335}$ 0, $[\Theta]_{310}$ +294, $[\Theta]_{295}$ 0, $[\Theta]_{258}$ -1273, $[\Theta]_{225}$ 0.

(-)-(*αS*)-2′-*O*-Methoxymethyl-*α*-hydroxydihydrochalcone 20: Catalytic hydrogenation of the (*αS*,*βR*)-chalcone epoxide 8 (48 mg) as described for the (*αR*,*βS*)-enantiomer 2 gave the (*αS*)-*α*-hydroxydihydrochalcone 20 as a colourless oil (30 mg, 61%). MS and ^{1}H NMR data were identical to that of the (*αR*)-compound 14. $[\alpha]_D^{25}$ -47^0 (*c* 0.56); CD (*c* 0.1350) $[\Theta]_{225}$ 0, $[\Theta]_{240}$ +5938, $[\Theta]_{260}$ 0, $[\Theta]_{285}$ -2532, $[\Theta]_{312}$ 0, $[\Theta]_{333}$ +331, $[\Theta]_{360}$ +42.

(-)-(*αS*)-4-Methoxy-2′-*O*-methoxymethyl-*α*-hydroxydihydrochalcone 21: Catalytic hydrogenation of the (*αS*,*βR*)-chalcone epoxide 9 (36 mg) as described for the (*αR*,*βS*)-enantiomer 3 gave the (*αS*)-*α*-hydroxydihydrochalcone 21 as a colourless oil (26 mg, 72%). MS and ^{1}H NMR data were identical to that of the (*αR*)-compound 15. $[\alpha]_D^{25}$ -41^0 (*c* 0.40); CD (*c* 0.0400) $[\Theta]_{205}$ 0, $[\Theta]_{240}$ +15817, $[\Theta]_{253}$ 0, $[\Theta]_{270}$ -12654, $[\Theta]_{297}$ 0, $[\Theta]_{315}$ +6327, $[\Theta]_{385}$ 0.

(-)-(*αS*)-4,4′-Dimethoxy-2′-*O*-methoxymethyl-*α*-hydroxydihydrochalcone 22: Catalytic hydrogenation of the (*αS*,*βR*)-chalcone epoxide 10 (27 mg) as for the (*αR*,*βS*)-compound 4

gave the (*αS*)-*α*-hydroxydihydrochalcone 22 as a colourless oil (19 mg, 70%). MS and ^{1}H NMR data were identical to that of the (*αR*)-enantiomer 16. $[\alpha]_D^{25}$ -71° (*c* 0.18); CD (*c* 0.1430) $[\Theta]_{211}$ 0, $[\Theta]_{225}$ -4542, $[\Theta]_{240}$ 0, $[\Theta]_{260}$ +13770, $[\Theta]_{297}$ 0, $[\Theta]_{310}$ -8367, $[\Theta]_{340}$ 0.

(-)-(*αS*)-3,4,4′-Trimethoxy-2′-(*β*)-methoxymethyl-*α*-hydroxydihydrochalcone 23: Hydrogenation of the (*αS*,*βR*)-chalcone epoxide 11 (22 mg) as described for the (*αR*,*βS*)-compound 5 gave the (*αS*)-*α*-hydroxydihydrochalcone 23 as a colourless oil (9 mg, 40%). MS and ^{1}H NMR data identical to that of the (*αR*)-enantiomer 17. $[\alpha]_D^{25}$ -22° (*c* 0.26); CD (*c* 0.0960) $[\Theta]_{340}$ 0, $[\Theta]_{310}$ -1059, $[\Theta]_{285}$ 0, $[\Theta]_{260}$ +2431, $[\Theta]_{235}$ 0.

(-)-(*αS*)-4,4′,6′-Trimethoxy-2′-(*β*)-methoxymethyl-*α*-hydroxydihydrochalcone 24: Hydrogenation of a mixture (43 mg) of the (*αS*,*βR*)-chalcone epoxide 12 and corresponding chalcone as described for the (*αR*,*βS*)-compound 6, gave the (*αS*)-*α*-hydroxydihydrochalcone 24 as a colourless oil (11 mg). MS and ^{1}H NMR data identical to that of the (*αR*)-enantiomer 18. $[\alpha]_D^{25}$ -23° (*c* 0.20); CD (*c* 0.0500) $[\Theta]_{355}$ 0, $[\Theta]_{345}$ +151, $[\Theta]_{325}$ 0, $[\Theta]_{315}$ -301, $[\Theta]_{302}$ 0, $[\Theta]_{265}$ +2259, $[\Theta]_{215}$ 0.

(-)-(*αS*)-3,4,4′,6′-Tetramethoxy-2′-(*β*)-methoxymethyl-*α*-hydroxydihydrochalcone 25: Catalytic hydrogenation of a mixture (48 mg) of the (*αS*,*βR*)-chalcone epoxide 13 and corresponding chalcone as described for the (*αR*,*βS*)-enantiomer 7 gave the (*αS*)-*α*-hydroxydihydrochalcone 25 as a colourless oil (9 mg). MS and ^{1}H NMR data identical to that of the (*αR*)-compound 19. $[\alpha]_D^{25}$ -17° (*c* 0.10); CD (*c* 0.0670) $[\Theta]_{330}$ 0, $[\Theta]_{315}$ -182, $[\Theta]_{303}$ 0, $[\Theta]_{265}$ +1272, $[\Theta]_{225}$ 0.

Benzoylation of *α*-hydroxydihydrochalcones

General procedure: To a solution of the *α*-hydroxydihydrochalcone in dry pyridine (0.05 ml per mg of substrate) was added 4-methoxybenzoyl chloride (0.1-0.25 ml) and the mixture left at *ca* 40°C for 14 h. Crushed ice was added and the product as well as 4-methoxybenzoic acid recovered by filtration. Following PLC all esters were obtained as colourless oils.

(*αR*)-*α*-(*β*)-(4-Methoxybenzoyl)-2′-(*β*)-methoxymethyldihydrochalcone 26: Treatment of the *α*-hydroxydihydrochalcone 14 (30 mg) with 4-methoxybenzoyl chloride gave the ester 26 [R_f 0.6, $(ClCH_2)_2$-Me_2CO, 96:4; 19 mg, 44%]; (Found: M^+, 420.1566. $C_{26}H_{24}O_6$ requires 420.1573); MS (EI) *m/z* 420 (M^+, 1%), 268(3), 224(7), 165(24), 152(41), 135(100); ^{1}H NMR *δ*7.89 (d, J12.2 Hz, H-2",6"), 7.73 (dd, J2.3 and 10.5 Hz, H-6′), 7.43 (ddd, J2.3, 11.5, and 11.5 Hz, H-4′), 7.22 (m, 5H), 7.17 (dd, J1.1 and 11.5 Hz, H-3′), 7.04 (ddd, J1.1, 10.5, and 10.5 Hz, H-5′), 6.83 (d, J12.2 Hz, H-3",5"), 6.34 (dd, J5.0 and 12.3 Hz, H-*α*), 5.26 (d, J9.5 Hz) and 5.20 (d, J9.5 Hz) (OCH_2OCH_3), 3.79 (s, OCH_3), 3.43 (s, OCH_2OCH_3), 3.32 (dd, J5.0 and 20.0 Hz, H-*β*), 3.12 (dd, J12.3 and 20.0 Hz, H-*β*); CD (*c* 0.0581) $[\Theta]_{210}$ 0, $[\Theta]_{235}$ +2821, $[\Theta]_{253}$ 0, $[\Theta]_{265}$ -362, $[\Theta]_{287}$ 0, $[\Theta]_{295}$ +542, $[\Theta]_{271}$ 0, $[\Theta]_{305}$ -4123, $[\Theta]_{350}$ 0.

(*αR*)-4-Methoxy-*α*-(*β*)-(4-methoxybenzoyl)-2′-(*β*)-methoxymethyldihydrochalcone 27: Benzoylation of the *α*-hydroxydihydrochalcone 15 (15 mg) gave the ester 27 [R_f 0.6, $(ClCH_2)_2$-Me_2CO, 96:4, v/v; 7.5 mg, 35%]; (Found: M^+-$C_8H_7O_2$, 315.1222. $C_{18}H_{19}O_5$ requires 315.1232); MS (EI) *m/z* 298 (M^+-152, 4%), 254(3), 165(31), 152(12), 135(30), 121(100); ^{1}H NMR *δ*7.94 (d, J11.2 Hz, H-2",6"), 7.75 (dd, J2.2 and 9.5Hz, H-6′), 7.46 (ddd, J2.2, 9.5, and 10.7 Hz, H-4′), 7.20 (dd, J1.5 and 10.7 Hz, H-3′), 7.18 (d, J11.0 Hz, H-2,6), 7.07 (ddd, J1.5, 9.5, and 9.5 Hz, H-5′), 6.87 (d, J11.2 Hz, H-3",5"), 6.80 (d, J11.0 Hz, H-3,5), 6.34 (dd, J4.5 and 11.0 Hz, H-*α*), 5.30 (d, J8.5 Hz) and 5.24 (d, J8.5 Hz) (OCH_2OCH_3), 3.84 and 3.75 (each s, 2xOCH_3), 3.47 (s, OCH_2OCH_3), 3.29 (dd, J4.5 and 17.8 Hz, H-*β*), 3.10 (dd, J11.0 and 17.8 Hz, H-*β*); CD (*c* 0.0635) $[\Theta]_{220}$ 0, $[\Theta]_{250}$ +5959, $[\Theta]_{275}$ 0, $[\Theta]_{305}$ -4469, $[\Theta]_{355}$ 0.

(*aR*)-4,4′-Dimethoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 28: Benzoylation of the *α*-hydroxydihydrochalcone 16 (15 mg) gave the ester 28 [R_f 0.6, $(ClCH_2)_2$-Me_2CO, 95:5, v/v; 12 mg, 56%]; (Found: M^+-$C_8H_8O_3$, 328.1314. $C_{19}H_{20}O_5$ requires 328.1305); MS (EI) *m/z* 328 (M^+ -152, 13%), 283(18), 195(70), 165(30), 152(23), 135(100); ^1H NMR *δ*7.96 (d, J9.0 Hz, H-2",6"), 7.87 (d, J9.0 Hz, H-6′), 7.20 (d, J8.8 Hz, H-2,6), 6.87 (d, J9.0 Hz, H-3",5"), 6.80 (d, J8.8 Hz, H-3,5), 6.73 (d, J2.0 Hz, H-3′), 6.61 (dd, J2.0 and 9.0 Hz, H-5′), 6.34 (dd, J3.5 and 9.0 Hz, H-*α*), 5.31 (d, J6.8 Hz) and 5.26 (d, J6.8 Hz) (OCH_2OCH_3), 3.84 (2x) and 3.77 (each s, $3xOCH_3$), 3.48 (s, OCH_2OCH_3), 3.28 (dd, J3.5 and 14.5 Hz, H-*β*), 3.07 (dd, J9.0 and 14.5 Hz, H-*β*); CD (*c* 0.1010) $[\Theta]_{205}$ 0, $[\Theta]_{223}$ -6661, $[\Theta]_{232}$ 0, $[\Theta]_{245}$ +17365, $[\Theta]_{260}$ 0, $[\Theta]_{280}$ -16176, $[\Theta]_{320}$ 0.

(*aR*)-3,4,4′-Trimethoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 29: Benzoylation of the *α*-hydroxydihydrochalcone 17 (10 mg) gave the ester 29 [R_f 0.6, $(ClCH_2)_2$-Me_2CO, 95:5, v/v; 6 mg, 44%]; (Found: M^+-$C_8H_8O_3$, 358.1425. $C_{20}H_{22}O_6$ requires 358.1417); MS (EI) *m/z* 358 (M^+ -152, 8%), 313(15), 195(40), 165(15), 152(34), 135(100); ^1H NMR *δ*7.97 (d, J9.0 Hz, H-2",6"), 7.86 (d, J9.0 Hz, H-6′), 6.87 (d, J9.0 Hz, H-3",5"), 6.82 (dd, J2.0 and 8.8 Hz, H-5′), 6.82 (d, J2.0 Hz, H-3′), 6.76 (d, J9.0 Hz, H-5), 6.72 (d, J2.1 Hz, H-2), 6.62 (dd, J2.1 and 9.0 Hz, H-6), 6.37 (dd, J4.0 and 8.8 Hz, H-*α*), 5.30 (d, J7.0 Hz) and 5.26 (d, J7.0 Hz) (OCH_2OCH_3), 3.87 (s, $3xOCH_3$), 3.79 (s, OCH_3), 3.50 (s, OCH_2OCH_3), 3.24 (dd, J4.0 and 14.8 Hz, H-*β*), 3.09 (dd, J8.8 and 14.8 Hz), H-*β*); CD (*c* 0.0919) $[\Theta]_{220}$ 0, $[\Theta]_{245}$ +15278, $[\Theta]_{264}$ 0, $[\Theta]_{290}$ -14310, $[\Theta]_{310}$ 0, $[\Theta]_{320}$ +4861, $[\Theta]_{370}$ 0.

(*aR*)-4,4′,6′-Trimethoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 30: Benzoylation of the *α*-hydroxydihydrochalcone 18 (6 mg) gave the ester 30 [R_f 0.5, $(ClCH_2)_2$-Me_2CO, 95:5, v/v; 4 mg, 50%]; (Found: M^+-$C_8H_8O_3$, 358.1412. $C_{20}H_{22}O_6$ requires 358.1417); MS (EI) *m/z* 358 (M^+ -152, 4%), 313(4), 225(82), 195(27), 165(6), 152(20), 135(100); ^1H NMR *δ*7.85 (d, J9.0 Hz, H-2",6"), 7.12 (d, J8.8 Hz, H-2,6), 6.84 (d, J9.0 Hz, H-3",5"), 6.73 (d, J8.8 Hz, H-3,5), 6.29 (d, J2.0 Hz, H-3′), 6.08 (dd, J4.0 and 9.0, H-*α*), 6.07 (d, J2.0 Hz, H-5′), 5.08 (s, OCH_2OCH_3), 3.82, 3.76, 3.72, and 3.71 (each s, $4xOCH_3$), 3.40 (s, OCH_2OCH_3), 3.26 (dd, J4.0 and 15.0 Hz, H-*β*), 3.13 (dd, J9.0 and 15.0 Hz, H-*β*); CD (*c* 0.0950) $[\Theta]_{233}$ 0, $[\Theta]_{245}$ +2607, $[\Theta]_{263}$ 0, $[\Theta]_{278}$ -1666, $[\Theta]_{300}$ 0, $[\Theta]_{310}$ +161, $[\Theta]_{325}$ 0.

(*aR*)-3,4,4′,6-Tetramethoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 31: Benzoylation of the *α*-hydroxydihydrochalcone 19 (6 mg) gave the ester 31 [R_f 0.5, $(ClCH_2)_2$-Me_2CO, 95:5, v/v; 4 mg, 50%]; (Found: M^+-$C_8H_8O_3$, 388.1506. $C_{21}H_{24}O_7$ requires 388.1515); MS (EI) *m/z* 388 (M^+ -152, 1%), 343(3), 225(15), 195(80), 165(11), 152(37), 135(100); ^1H NMR *δ*7.86 (d, J9.0 Hz, H-2",6"), 6.83 (d, J9.0 Hz, H-3",5"), 6.75 (dd, J2.0 and 8.0 Hz, H-6), 6.72 (d, J2.0 Hz, H-2), 6.70 (d, J8.0 Hz, H-5), 6.29 (d, J2.1 Hz, H-3′), 6.10 (dd, J4.0 and 8.2 Hz, H-*α*), 6.07 (d, J2.1 Hz, H-5′), 5.06 (s, OCH_2OCH_3), 3.83, 3.80, 3.76, 3.71, and 3.70 (each s, $5xOCH_3$), 3.40 (s, OCH_2OCH_3), 3.27 (dd, J4.0 and 14.8 Hz, H-*β*), 3.14 (dd, J8.2 and 14.8 Hz, H-*β*); CD (*c* 0.0542) $[\Theta]_{230}$ 0, $[\Theta]_{250}$ +249, $[\Theta]_{262}$ 0, $[\Theta]_{280}$ -160, $[\Theta]_{320}$ 0.

(*aS*)-*α*-*O*-(4-Methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 32: Benzoylation of the *α*-hydroxydihydrochalcone 20 (18 mg) gave the ester 32 (13 mg, 49%). MS and ^1H NMR data identical to those of the (*aR*)-ester 26; CD (*c* 0.1225) $[\Theta]_{205}$ 0, $[\Theta]_{230}$ -1992, $[\Theta]_{250}$ 0, $[\Theta]_{255}$ +755, $[\Theta]_{262}$ 0, $[\Theta]_{265}$ -206, $[\Theta]_{270}$ 0, $[\Theta]_{300}$ +2643, $[\Theta]_{355}$ 0.

(*aS*)-4-Methoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 33: Benzoylation of the *α*-hydroxydihydrochalcone 21 (12 mg) gave the ester 33 (8 mg, 47%). MS and ^1H NMR data identical to those of the (*aR*)-ester 27; CD (*c* 0.0582) $[\Theta]_{220}$ 0, $[\Theta]_{250}$ -6806, $[\Theta]_{278}$ 0, $[\Theta]_{305}$ +4563, $[\Theta]_{350}$ 0.

(*aS*)-4,4′-Dimethoxy-*α*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 34: Benzoylation of the *α*-hydroxydihydrochalcone 22 (12 mg) gave the ester 34 (6 mg, 36%). MS and ^1H NMR data identical to those of the (*aR*)-enantiomer 28; CD (*c* 0.0838) $[\Theta]_{215}$ 0, $[\Theta]_{243}$ -6330, $[\Theta]_{261}$ 0, $[\Theta]_{280}$ +6445, $[\Theta]_{320}$ 0.

(*aS*)-3,4,4′-Trimethoxy-*a*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 35: Benzoylation of the *a*-hydroxydihydrochalcone 23 (6 mg) gave the ester 35 (4 mg, 49%). MS and ^{1}H NMR data identical to those of the (*aR*)-enantiomer 29; CD (*c* 0.0580) $[\Theta]_{215}$ 0, $[\Theta]_{250}$ -5194, $[\Theta]_{262}$ 0, $[\Theta]_{293}$ +4225, $[\Theta]_{355}$ 0.

(*aS*)-4,4′,6′-Trimethoxy-*a*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 36: Benzoylation of the *a*-hydroxydihydrochalcone 24 (9 mg) gave the ester 36 (7 mg, 57%). MS and ^{1}H NMR data identical to those of the (*aR*)-enantiomer 30; CD (*c* 0.0810) $[\Theta]_{230}$ 0, $[\Theta]_{253}$ -1513, $[\Theta]_{270}$ 0, $[\Theta]_{280}$ +347, $[\Theta]_{300}$ 0, $[\Theta]_{310}$ -126, $[\Theta]_{320}$ 0.

(*aS*)-3,4,4′,6′-Tetramethoxy-*a*-*O*-(4-methoxybenzoyl)-2′-*O*-methoxymethyldihydrochalcone 37: Benzoylation of *a*-hydroxydihydrochalcone 25 (6 mg) gave the ester 37 (4 mg, 51%). MS and ^{1}H NMR data identical to that of the (*aR*)-enantiomer 31; CD (*c* 0.0617) $[\Theta]_{230}$ 0, $[\Theta]_{245}$ -277, $[\Theta]_{258}$ 0, $[\Theta]_{285}$ +420, $[\Theta]_{345}$ 0.

Isolation of *a*-Hydroxydihydrochalcones from *Pericopsis elata*

Drillings (10 kg) of the heartwood of *P. elata* (Harms) were successively extracted with *n*-hexane (3x18 *l*, 24 h each) and Me_2CO (3x18 *l*, 24 h each) to give on evaporation of the solvents, an orange oil (12 g, 0.12%) and a dark brown resin (40 g, 0.4%), respectively. CC (Sephadex LH-20; EtOH; flow rate 15 ml h^{-1}) of the Me_2CO-extract yielded twelve crude fractions. One of these (fraction 6, RR_t 258 h, 2.1 g) contained the *a*-hydroxydihydrochalcones and was refractionated by PLC (C_6H_6-Me_2CO, 8:2, v/v) to give eight subfractions.

(*aR*)-*a*,2′,4′-Tri-*O*-acetyl-4-methoxydihydrochalcone 49: Acetylation followed by PLC (*n*-hexane-Me_2CO-EtOAc, 65:20:15, v/v) of subfraction 3 (R_f 0.6; 50 mg) gave the title compound 49 (R_f 0.4) as a yellow oil (10 mg); (Found: C, 63.9; H, 5.4. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.4%); MS (EI) *m/z* 414 (M^+, 1%), 354(34), 312(29), 270(18), 221(17), 179(51), 137(78), 134(12), 121(100); ^{1}H NMR (TMS internal std.) δ7.77 (d, J9.0 Hz, H-6′), 7.10 (d, J8.5 Hz, H-2,6), 7.09 (dd, J2.5 and 9.0 Hz, H-5′), 7.01 (d, J2.5 Hz, H-3′), 6.81 (d, J8.5 Hz, H-3,5), 5.91 (dd, J4.0 and 9.0 Hz, H-*a*), 3.78 (s, OCH_3), 3.07 (dd, J4.0 and 15.0 Hz, H-β), 2.93 (dd, J9.0 and 15.0 Hz, H-β), 2.30 (2x) and 2.08 (each s, 3xOAc); CD (*c* 0.0600) $[\Theta]_{210}$ 0, $[\Theta]_{233}$ -20000, $[\Theta]_{258}$ 0, $[\Theta]_{267}$ +3000, $[\Theta]_{281}$ 0, $[\Theta]_{295}$ -2000, $[\Theta]_{343}$ 0.

(*aR*)-*a*,2′,4,4′-Tetra-*O*-acetyldihydrochalcone 50: Acetylation followed by PLC (*n*-hexane-Me_2CO-EtOAc, 65:20:15, v/v) of subfraction 6 (R_f 0.3, 200 mg) gave the *a*-hydroxydihydrochalcone derivative 50 (R_f 0.3) as a yellow oil (110 mg); (Found: C, 62.2; H, 5.0. $C_{23}H_{22}O_9$ requires C, 62.3; H, 5.0%); MS (EI) *m/z* 442 (M^+, 1%), 382(33), 340(31), 298(28), 256(16), 221(49), 137(100); ^{1}H NMR δ7.78 (d, J8.5 Hz, H-6′), 7.21 (d, J8.5 Hz, H-2,6), 7.11 (dd, J2.0 and 8.5 Hz, H-5′), 7.02 (d, J2.0 Hz, H-3′), 7.00 (d, J8.5 Hz, H-3,5), 5.92 (dd, J4.0 and 9.0 Hz, H-*a*), 3.12 (dd, J4.0 and 15.0 Hz, H-β), 2.98 (dd, J9.0 and 15.0 Hz, H-β), 2.31, 2.30, 2.28, and 2.08 (each s, 4xOAc); CD (*c* 0.0640) $[\Theta]_{205}$ 0, $[\Theta]_{215}$ -10000, $[\Theta]_{219}$ -7000, $[\Theta]_{237}$ -19000, $[\Theta]_{281}$ 0.

(*aR*)-*a*,2′,4,4′-Tetrahydroxydihydrochalcone[13] 47: Deacetylation (KOH-MeOH, 1.2% m/v; 5 ml, r.t., 30 min) of the tetra-acetate 50 (100 mg) followed by PLC [$(CH_2Cl)_2$-Me_2CO, 8:2, v/v] gave the phenolic compound 47 (R_f 0.4) as a white solid (16 mg); $[a]_D^{25}$ -53° (*c* 0.32); ^{1}H NMR [$(CD_3)_2CO$, TMS internal std] δ9.79, 9.09, and 8.23 (each br. s, 3xOH), 7.90 (d, J9.0 Hz, H-6′), 7.04 (d, J9.0 Hz, H-2,6), 6.71 (d, J9.0 Hz, H-3,5), 6.46 (dd, J2.5 and 9.0 Hz, H-5′), 6.36 (d, J2.5 Hz, H-3′), 5.18 (ddd, J5.0, 8.0 and 8.0 Hz, H-*a*), 4.30 (d, J8.0 Hz, *a*-OH), 3.05 (dd, J5.0 and 14.0 Hz, H-β), 2.86 (dd, J8.0 and 14.0 Hz, H-β).

Enantioselective synthesis of both enantiomers of the *a*-hydroxydihydrochalcone from *P. elata*.

4-Methoxy-2′,4′-di-*O*-methoxymethylchalcone 42: Condensation of 2,4-di-*O*-methoxy-

methylacetophenone[14] (1.47 g) with 4-methoxybenzaldehyde (1.05 g) by the method described previously[8], gave the chalcone 42 (R_f 0.4) as a yellow oil (1.63 g, 74%) after PLC [*n*-hexane-$(CH_2Cl)_2$-Me_2CO, 65:20:15, v/v]; (Found: M^+, 358.3952. $C_{20}H_{22}O_6$ requires M^+, 358.3947); MS (EI) *m/z* 358 (M^+, 18%), 313(65), 285(85), 181(18), 165(100), 161(33), 149(53), 133(24); ^1H NMR (TMS internal std.) δ7.65 (d, J9.0 Hz, H-6′), 7.62 (d, J16.0 Hz, H-β), 7.54 (d, J9.0 Hz, H-2,6), 7.34 (d, J16.0 Hz, H-α), 6.91 (d, J9.0 Hz, H-3,5), 6.85 (d, J2.5 Hz, H-3′), 6.77 (dd, J2.5 and 9.0 Hz, H-5′), 5.24 (s, OCH_2OCH_3), 5.22 (s, OCH_2OCH_3), 3.84 (s, OCH_3), 3.50 (s, $2xOCH_2OCH_3$).

(αR,βS)-4-Methoxy-2′,4′-di-O-methoxymethylchalcone epoxide 43: Epoxidation (72 h) of chalcone 42 (400 mg) in CCl_4 (5 ml) with a NaOH-H_2O_2 solution (6 ml) catalysed by poly-*L*-alanine (200 mg) as described previously[8], gave the epoxide 43 [R_f 0.4; *n*-hexane-$(CH_2Cl)_2$-Me_2CO, 4:5:1, v/v] as a colourless oil (180 mg, 43%); (Found: M^+-$2xOCH_3$, 312.3267. $C_{18}H_{16}O_5$ requires 312.3251); MS (EI) *m/z* 374 (M^+, 3%), 255(100), 195(29), 165(27), 149(21), 121(48); ^1H NMR δ7.83 (d, J9.0 Hz, H-6′), 7.27 (d, J8.5 Hz, H-2,6), 6.89 (d, J8.5 Hz, H-3,5), 6.76 (d, J2.0 Hz, H-3′), 6.74 (dd, J2.0 and 9.0 Hz, H-5′), 5.18 (s, 4′-OCH_2OCH_3), 4.88 (d, J7.0 Hz) and 4.82 (d, J7.0 Hz) (2′-OCH_2OCH_3), 4.30 (d, J2.0 Hz, H-α), 3.91 (d, J2.0 Hz, H-β), 3.81 (s, OCH_3), 3.45 (s, OCH_2OCH_3), 3.11 (s, OCH_2OCH_3); CD (*c* 0.0625) $[\Theta]_{220}$ 0, $[\Theta]_{245}$ +25000, $[\Theta]_{270}$ 0, $[\Theta]_{293}$ -19000, $[\Theta]_{340}$ 0.

(αR)-4-Methoxy-2′,4′-di-O-methoxymethyl-α-hydroxydihydrochalcone 45: Catalytic hydrogenation (4 h) of the chalcone epoxide 43 (100 mg) in MeOH (50 ml) over Pd-$BaSO_4$ (60 mg) gave the α-hydroxydihydrochalcone 45 (R_f 0.5) as a colourless oil (50 mg, 50%), after PLC ($CHCl_3$-Me_2CO, 95:5, v/v); (Found: M^+ -H_2O, 358.3941. $C_{20}H_{22}O_6$ requires 358.3947); MS (EI) *m/z* 358 (M^+-H_2O, 2.4%), 227(31), 225(50), 181(18), 167(20), 151(12), 134(3), 121(100); ^1H NMR δ7.82 (d, J9.0 Hz, H-6′), 7.04 (d, J9.0 Hz, H-2,6), 6.87 (d, J2.5 Hz, H-3′), 6.77 (dd, J2.5 and 9.0 Hz, H-5′), 6.77 (d, J9.0 Hz, H-3,5), 5.35 (ddd, J4.0, 7.0, and 7.0 Hz, H-α), 5.31 (d, J7.0 Hz) and 5.24 (d, J7.0 Hz) (2′-OCH_2OCH_3), 5.22 (s, 4′-OCH_2OCH_3), 3.88 (d, J7.0 Hz, α-OH), 3.75 (s, OCH_3), 3.48 (s, $2xOCH_2OCH_3$), 3.10 (dd, J4.0 and 14.0 Hz, H-β), 2.70 (dd, J7.0 and 14.0 Hz, H-β); CD (*c* 0.0640) $[\Theta]_{233}$ 0, $[\Theta]_{258}$ -16000, $[\Theta]_{288}$ 0, $[\Theta]_{312}$ +9000, $[\Theta]_{342}$ 0.

(αR)-4-Methoxy-α-O-(4-methoxybenzoyl)-2′,4′-di-O-methoxymethyldihydrochalcone 51: Benzoylation of α-hydroxydihydrochalcone 45 (20 mg) as described above gave the ester 51 [R_f 0.6, *n*-hexane-$(CH_2Cl)_2$-Me_2CO, 5:4:1, v/v; 15 mg, 56%]; (Found: M^+-$C_8H_8O_3$, 358.3957. $C_{20}H_{22}O_6$ requires 358.3947); MS (EI) *m/z* 358 (M^+-$C_8H_8O_3$, 8%), 225(54), 165(26), 152(20), 135(100), 121(54); ^1H NMR δ7.96 (d, J9.0 Hz, H-2",6"), 7.85 (d, J9.0 Hz, H-6′), 7.21 (d, J9.0 Hz, H-2,6), 6.88 (d, J9.0 Hz, H-3",5"), 6.85 (d, J2.5 Hz, H-3′), 6.81 (d, J9.0 Hz, H-3,5), 6.75 (dd, J2.5 and 9.0 Hz, H-5′), 6.34 (dd, J4.0 and 9.0 Hz, H-α), 5.32 (d, J7.0 Hz) and 5.26 (d, J7.0 Hz) (2′-OCH_2OCH_3), 5.20 (s, 4′-OCH_2OCH_3), 3.83 and 3.75 (each s, $2xOCH_3$), 3.48 and 3.47 (each s, $2xOCH_2OCH_3$), 3.28 (dd, J4.0 and 14.5 Hz, H-β), 3.07 (dd, J9.0 and 14.5 Hz, H-β); CD (*c* 0.1000) $[\Theta]_{218}$ 0, $[\Theta]_{245}$ +14000, $[\Theta]_{260}$ 0, $[\Theta]_{288}$ -11000, $[\Theta]_{328}$ 0.

(αR)-α,2′,4′-Trihydroxy-4-methoxydihydrochalcone 46: Acid catalysed hydrolysis [3N HCl (1 ml), MeOH (5 ml), 50°C] of (αR)-4-methoxy-2′,4′-di-O-methoxymethyl-α-hydroxydihydrochalcone 45 (20 mg) followed by PLC (C_6H_6-Me_2CO, 9:1, v/v) gave the α-hydroxydihydrochalcone 46 (R_f 0.3) as a white solid (13 mg, 84%); (Found: M^+-H_2O, 270.2885. $C_{16}H_{14}O_4$ requires 270.2876); MS (EI) *m/z* 270 (M^+-H_2O, 5%), 152(3), 137(45), 121(100); ^1H NMR δ10.29 (s, OH), 7.55 (d, J9.0 Hz, H-6′), 7.03 (d, J9.0 Hz, H-2,6), 6.79 (d, J9.0 Hz, H-3,5), 6.40 (d, J2.5 Hz, H-3′), 6.40 (dd, J2.5 and 9.0 Hz, H-5′), 5.20 (ddd, J4.0, 7.0, and 7.0 Hz, H-α), 3.76 (s, OCH_3), 3.61 (d, J7.0 Hz, α-OH), 3.13 (dd, J4.5 and 14.0 Hz, H-β), 2.90 (dd, J7.0 and 14.0 Hz, H-β); CD (*c* 0.200) $[\Theta]_{237}$ 0, $[\Theta]_{245}$ +4000, $[\Theta]_{268}$ 0, $[\Theta]_{313}$ -12000, $[\Theta]_{359}$ 0.

(αR)-α,2′,4′-Tri-O-acetyl-4-methoxydihydrochalcone 49: Acetylation of the (αR)-α-hydroxydihydrochalcone 46 (10 mg) followed by PLC (*n*-hexane-Me_2CO-EtOAc, 65:20:15, v/v) gave the triacetate 49 (R_f 0.3) as a yellow oil (6 mg). MS and ^1H NMR data as well as Cotton effects were identical to those of the natural product.

(*αS,βR*)-4-Methoxy-2′,4′-di-*O*-methoxymethylchalcone epoxide **44**: Epoxidation (72 h) of chalcone **42** (400 mg) in CCl_4 (5 ml) with a $NaOH-H_2O_2$ solution (6 ml) catalysed by poly-*D*-alanine (200 mg) as described previously[8], gave the epoxide **44** [R_f 0.4; *n*-hexane-$(CH_2Cl)_2$-Me_2CO, 4:5:1, v/v] as a colourless oil (150 mg, 36%). MS and ^1H NMR data identical to those of the (*αR,βS*)-enantiomer **43**; CD (*c* 0.0500) $[\Theta]_{220}$ 0, $[\Theta]_{245}$ -11000, $[\Theta]_{268}$ 0, $[\Theta]_{294}$ +11000, $[\Theta]_{350}$ 0.

(*αS*)-4-Methoxy-2′,4′-di-*O*-methoxymethyl-*α*-hydroxydihydrochalcone **52**: Catalytic hydrogenation (4 h) of the chalcone epoxide **44** (50 mg) in MeOH (50 ml) over Pd-$BaSO_4$ (30 mg) gave the *α*-hydroxydihydrochalcone **52** (23 mg, 46%). MS and ^1H NMR data identical to those of the (*αR*)-enantiomer **45**; CD (*c* 0.0630) $[\Theta]_{234}$ 0, $[\Theta]_{258}$ +15000, $[\Theta]_{286}$ 0, $[\Theta]_{310}$ -9000, $[\Theta]_{345}$ 0.

(*αS*)-4-Methoxy-*α*-*O*-(4-methoxybenzoyl)-2′,4′-di-*O*-methoxymethyldihydrochalcone **53**: Benzoylation of *α*-hydroxydihydrochalcone **52** (20 mg) as described previously, gave the ester **53** (14 mg, 52%). MS and ^1H NMR data were identical to those of the (*αR*)-enantiomer **51**; CD (*c* 0.0500) $[\Theta]_{200}$ 0, $[\Theta]_{245}$ -10000, $[\Theta]_{261}$ 0, $[\Theta]_{282}$ +6000, $[\Theta]_{334}$ 0.

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