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ENANTIOSELECTIVE SYNTHESIS OF FLAVONOIDS. PART 1. POLY-OXYGENATED CHALCONE EPOXIDES

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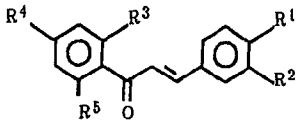
Abstract —— Epoxidation of a series of poly-oxygenated chalcones with H_2O_2 in the presence of poly-α-aminoacid catalysts afforded chiral aromatic oxygenated epoxides in moderate to high optical yields; their absolute configurations were determined by CD spectroscopy. These chalcone epoxides could, in principle, be used as chirons for enantiomerically enriched dihydroflavonols.

Despite the availability of non- and mono-oxygenated chalcone epoxides in moderate to high optical yields[1-9], utilization of these versatile precursors in enantioselective synthesis of flavonoids and isoflavonoids is limited to single transformations into respectively an aromatic deoxy α-hydroxydihydrochalcone[3] and a 3-hydroxyflavanone (dihydroflavonol)[7]. These conversions in conjunction with our recent[10] synthesis of enantiomerically enriched 4-methoxy-α*R*- and α*S*,2′,4′-trihydroxydihydrochalcones and assessment of their absolute configuration by circular dichroism, prompted extension of a similar protocol to a series of chalcones exhibiting the aromatic oxygenation patterns usually encountered in flavonoid/isoflavonoid chemistry. We thus now disclose our detailed results of relevance to the synthesis of poly-oxygenated chalcone epoxides and their possible use as chirons for enantiomerically enriched dihydroflavonols.

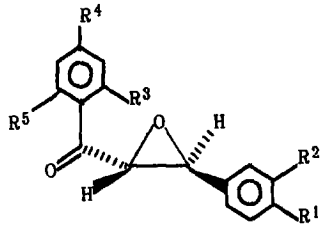
The *trans*(*E*)-chalcone methyl ethers 1-7 (J α,β 15.8-16.0 Hz) were protected at 2′-OH by the acid-labile methoxymethyl (MOM) group[11] and were available *via* base-catalyzed condensation of the appropriate oxygenated acetophenones and benzaldehydes. Owing to the high



(1) $R^1=R^2=R^3=R^4=R^5=H$
(2) $R^1=R^2=R^4=R^5=H, R^3=OMOM$
(3) $R^1=OMe, R^2=R^4=R^5=H, R^3=OMOM$
(4) $R^1=R^4=OMe, R^2=R^5=H, R^3=OMOM$
(5) $R^1=R^2=R^4=OMe, R^5=H, R^3=OMOM$
(6) $R^1=R^4=R^5=OMe, R^2=H, R^3=OMOM$
(7) $R^1=R^2=R^4=R^5=OMe, R^3=OMOM$

optical yields of aromatic deoxy chalcone epoxides using polyaminoacids in a triphase system[4,5], the polyalanines were selected as stereoselective catalysts for the epoxidation of 1-7.

Thus, treatment of the (*E*)-chalcones 1-7 at *ca* 20°C with hydrogen peroxide in the triphase system aqueous NaOH, poly-*L*-alanine {$[\alpha]_D^{25}$= -142.8° (*c* = 0.671 in CF_3COOH)}, and CCl_4[5,6,12,13], afforded the (-)-*trans*-epoxides 8-14 ($J\alpha,\beta$ = 1.5-2.2 Hz). The (+)-*trans* epoxides 15-20 ($J\alpha,\beta$ = 1.5-2.2 Hz) were similarly obtained by using poly-*D*-alanine {$[\alpha]_D$ = +102.2° (*c* = 0.314 in CF_3COOH)} in the same triphasic system. These conversions proceeded slowly with reaction times varying from 36 to 96 hours. Enantiomeric purity was assessed by ^1H NMR in $CDCl_3$ with Eu(tfc)$_3$ and Pr(hfc)$_3$ as chiral shift reagents and is indicated for the (-)- and (+)-enantiomers in tables 1 and 2 respectively. Four of these, 13, 14, 19, and 20 could, however, not be fully purified owing to decomposition caused by multiple development of preparative TLC plates. A low degree of contamination with the parent chal-



(*αR,βS*) enantiomers

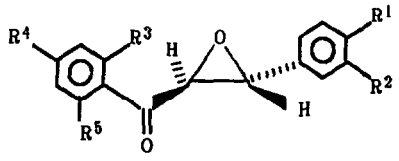
Table 1

Epoxide	R^1	R^2	R^3	R^4	R^5	$[\alpha]_D^{25}$ in CH_2Cl_2	% Yield	% ee
(8)	H	H	H	H	H	-200.5°	80	92[a]
(9)	H	H	OMOM	H	H	-50.3°	65	38[a]
(10)	OMe	H	OMOM	H	H	-76.0°	64	66[a]
(11)	OMe	H	OMOM	OMe	H	-122°	74	84[b]
(12)	OMe	OMe	OMOM	OMe	H	-79.4°	46	62[a]
(13)	OMe	H	OMOM	OMe	OMe	-[c]	-[c]	32[b]
(14)	OMe	OMe	OMOM	OMe	OMe	-[c]	-[c]	-[c]

(a) Determined with Eu(tfc)$_3$ as shift reagent.

(b) Determined with Pr(hfc)$_3$ as shift reagent.

(c) Not determined due to instability and purification difficulties.



($\alpha S,\beta R$) enantiomers

Table 2

Epoxide	R^1	R^2	R^3	R^4	R^5	$[\alpha]_D^{25}$ in CH_2Cl_2	% Yield	% ee
(15)	H	H	OMOM	H	H	$+74.8^0$	57	53[a]
(16)	OMe	H	OMOM	H	H	$+52.1^0$	38	46[a]
(17)	OMe	H	OMOM	OMe	H	$+76.5^0$	26	53[b]
(18)	OMe	OMe	OMOM	OMe	H	$+31.2^0$	34	25[a]
(19)	OMe	H	OMOM	OMe	OMe	-[c]	-[c]	20[b]
(20)	OMe	OMe	OMOM	OMe	OMe	-[c]	-[c]	-[c]

(a) Determined with Eu(tfc)$_3$ as shift reagent.

(b) Determined with Pr(hfc)$_3$ as shift reagent.

(c) Not determined due to instability and purification difficulties.

cones precluded assessment of optical purity by ^{1}H NMR for epoxides 14 and 20 as a result of overlap of the impurity signal with the methoxy resonance of the methoxymethyl group used as reference, such complicating factors being absent for 13 and 19. Owing to the high optical purity (92%) of the (-)-($\alpha R,\beta S$)-chalcone epoxide 8, its enantiomeric excess (ee) could only be determined by addition of a known weight of the racemate and subsequent integration of the reference signal. The reduced enantiomeric purity of the (+)-*trans*-epoxides 15-19 may partially be attributed to optically impure *D*-alanine {$[\alpha]_D^{25}$ -9.71^0 (*c*, 1.363 in 6N HCl; lit.[14] $[\alpha]_D^{30}$ -14.61^0 (*c*, 1.344 in 6N HCl]}.

The (-)-chalcone oxiranes 8-14 all exhibited negative Cotton effects in the 290-325 nm region (n,π^* transition) and positive Cotton effects in the 235-250 nm region (π,π^* transition) of their CD spectra. Comparison of the CD data with those of the aromatic deoxy (-)-*trans*-epoxychalcone 8 {$[\alpha]_D^{25}$ -200^0; 92% ee} with known[3] αR, βS absolute configuration and exhibiting negative and positive Cotton effects at 322 and 235 nm respectively, thus unequivocally confirmed similar absolute stereochemistry for the novel series 9-14. In the same regions of the CD spectra the (+)-*trans*-epoxychalcones 15-20 exhibit sequential positive and negative Cotton effects. Such a mirror-image relationship (*cf* Figure for comparison of 11 and 17) confirmed the enantiomeric connection between these series and hence $\alpha S,\beta R$ absolute configuration for 15-20.

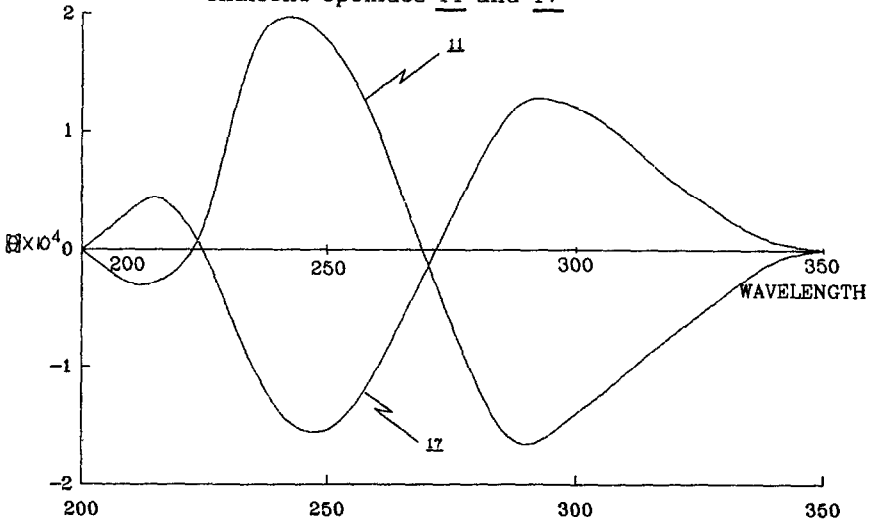
The following conclusions may be drawn from the results in tables 1 and 2:

(i) The oxygen functionalities influence the reaction in a complex and unpredictable manner. Stereoselectivity does not necessarily decrease with an increase in the number of substituents, *eg* 9 and 11 in table 1;

(ii) *Ortho*- and *meta*-substituents on both the A- and B-rings adversely affect stereoselectivity to a larger extent than those in *para*-positions, *eg* 11 and 12;

(iii) *o*-Substitution on the A-ring profoundly decreases stereoselectivity, *eg* 8 and 9, and 12 and 13. Such a decrease is presumably attributable to inhibition of hydrogen bonding of the carbonyl in *eg* chalcone 6 and the peptide group of the catalyst[6]. This hydrogen bond presumably also leads to a specific association of the chalcone and the catalyst surface hence allowing the selective delivery of 'oxygen' to one face of the double bond.

Figure: CD curves of the (−)−(αR,βS)− and (+)−(αS,βR) chalcone epoxides 11 and 17

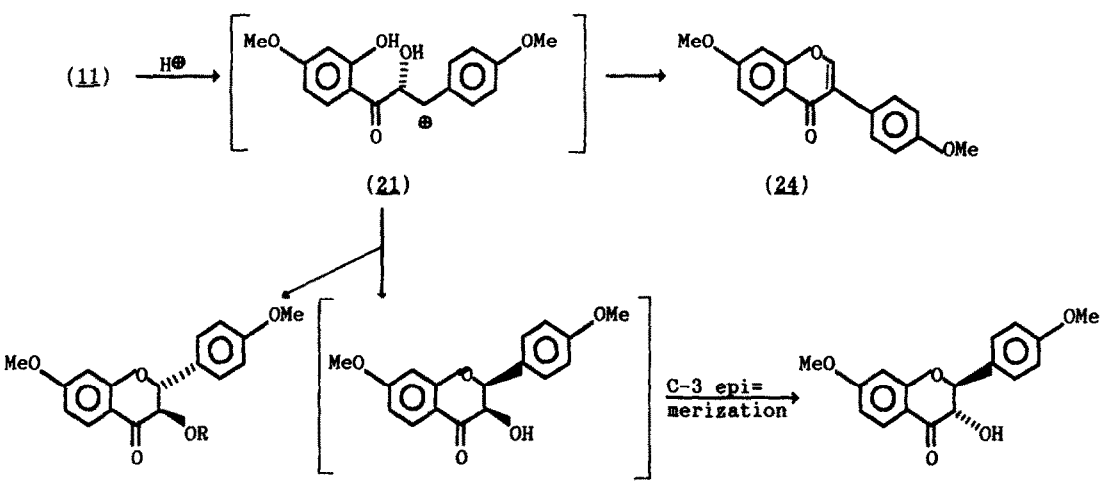


In view of the need for C-4-oxygenated flavonoids as incipient electrophiles in our programme of synthesis of condensed tannins, transformation of epoxychalcone 11 of highest optical purity to the dihydroflavonol 22 was investigated. With 1N HCl in methanol oxirane 11 is converted in low yields to the (-)-2,3-*trans*-dihydroflavonol 22 ($J_{2,3}$ = 12.0 Hz) and 4′,7-dimethoxyisoflavone 24 (Scheme). Assessment of optical purity (50% ee) and absolute

configuration (2*R*,3*R*) of the predominant enantiomer of the dihydroflavonol 22 were done by ^{1}H NMR using Eu(tfc)$_3$ as chiral shift reagent and CD[15] respectively of the *O*-acetyl derivative 23. The enantiomeric excess of the dihydroflavonol was increased to 53 and 56% in respectively trifluoroacetic acid/2,2,2-trifluoroethanol (TFE) and *p*-toluenesulphonic acid/TFE.

The 'loss' of optical purity in the conversion 11 → 22 indicates competition between protonation of the heterocyclic oxygen and hydrolysis of the 2′-*O*-acetal functionality hence leading to a considerable degree of S_N1 character for the cyclization step with concomitant racemization at C-*β* of a presumed carbocationic intermediate 21 hence leading to dihydroflavonols 22 and 25. The thermodynamically less stable (2*S*,3*R*)-2,3-*cis*-dihydroflavonol 25 will rapidly be epimerized at C-3 to 26 under the prevailing acidic conditions[16]. In order to enhance the S_N2 nature of the ring closure step and thus formation of 22, methods aimed at selective removal of the 2′-*O*-methylmethoxy group under mild conditions were explored. Whereas dimethylboron bromide[17] led to an intractable mixture, the yield (*ca* 10%) and purity of dihydroflavonol 22 from the reaction of epoxide 11 with diphosphorous tetraiodide[18] were insufficient for assessment of optical purity by the ^{1}H NMR method.

Although the protocol outlined above may be useful for the synthesis of enantiomerically enriched dihydroflavonols, the low chemical yields and the decrease in optical purity



Scheme. Proposed route to the formation of dihydroflavonols (22), (26) and isoflavone (24).

during generation of the six-membered heterocycle severely limit the merits of such an approach towards C-4-oxygenated flavonoids to be used as incipient electrophiles in condensed tannin synthesis. The utility of the epoxychalcones as chirons for naturally occurring *α*-hydroxychalcones and subsequent assessment of the absolute configuration of the latter group of compounds will be discussed separately.

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 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 optained 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.

General procedures

Methoxymethylations[19]: A solution of the 2-hydroxyacetophenone (2-5 g) in 15% (m/v) *aq.* KOH (20-50 ml) was stirred for 2 hours, CH_2Cl_2 (20-50 ml) and Adogen 464 [methyltrialkyl (C_8-C_{10}) ammonium chloride; 1.5-3.75 g] were added and stirring continued (10 min). Chloromethyl methyl ether (1.5-3.75 ml) was added dropwise and the mixture was stirred for 5-20 min at ambient temperatures. Removal of the organic phase and extraction of the aqueous layer with CH_2Cl_2 (2x15 ml) gave the crude products after drying (Na_2SO_4) and evaporation of the solvent. Flash chromatography yielded the pure products (91-98%).

Preparation of chalcones: To a solution of the appropriate acetophenone (1.4-2.8 g) in EtOH (20-40 ml) was added 50% (m/v) *aq* KOH (5-10 ml) and the mixture was stirred at room temperature for 30-40 min. Excess benzaldehyde (1.0-2.27 g, in 10 ml EtOH) was added dropwise and the reaction followed by TLC. After disappearance of the acetophenone (4-24 h), H_2O (20-40 ml) was added and the products extracted with ether (4x20 ml). Drying of the extracts (Na_2SO_4) followed by evaporation and flash column chromatography, gave the pure chalcones (62-71%). A detailed procedures is given for the novel analogue 7 only.

Epoxidation of chalcones: A solution of NaOH in 30% (m/v) H_2O_2 (0.08 g/ml) was added to a mixture of the polyalanine catalyst[4,5,6] and chalcones (*ca* 170 mg of catalyst/mmol chalcone) in CCl_4 (2-7 ml) and the mixture stirred at room temperature (32-96 h). Where necessary (TLC) a further addition of NaOH-H_2O_2 was made after 24 h. The catalyst was removed by filtration, rinsed with CH_2Cl_2 (50 ml) and the filtrate washed with water (3x20 ml). Drying (Na_2SO_4) of the solvent and evaporation at reduced pressure gave the crude product, which was crystallised from EtOH and/or purified by PLC (26-80%).

3,4,4′,6′-Tetramethoxy-2′-*β*-methoxymethylchalcone (7): Reaction of an ethanolic solution of 4,6-dimethoxy-2-*β*-methoxymethylacetophenone[20] (2.5 g in 40 ml) with *aq* KOH solution (10 ml) followed by 3,4-dimethoxybenzaldehyde (2.0 g) as described previously, gave the chalcone (7) (Rf 0.3; hexane-C_6H_6-Me_2CO, 4:5:1, v/v) as yellow needles (2.5 g, 62%) after flash chromatography (hexane-C_6H_6-Me_2CO, 35:60:5, v/v) and crystallization from EtOH; m.p. 88-90°C; (Found: M$^+$, 388.1513. $C_{21}H_{24}O_7$ requires 388.1522). ^1H NMR *δ*7.25 (d, J16.0 Hz, H-*β*), 7.06 (dd, J1.8 and 8.0, H-6), d, J1.8 Hz, H-2), 6.83 (d, J16.0

Hz, H-α), 6.82 (d, J8.0 Hz, H-5), 6.36 (d, J2.2 Hz, H-3′), 6.10 (d, J2.2 Hz, H-5′), 5.10 (s, OCH_2OCH_3), 3.88 (s, 4-OCH_3), 3.87 (s, 3-OCH_3), 3.82 (s, 4′-OCH_3), 3.74 (s, 6′-OCH_3), 3.36 (s, OCH_2OCH_3).

Synthesis of Epoxides. — (-)-($\alpha R,\beta S$)-Chalcone epoxide (8): Epoxidation (48 h) of chalcone[3] (1) (100 mg) with the triphasic system *i.e.* CCl_4 (2 ml), poly-(*L*)-alanine (80 mg), NaOH-H_2O_2 solution (1 ml followed by an additional 1 ml after 24 h), as described previously, gave the epoxide (8) (R_f 0.7; hexane-C_6H_6-Me_2CO, 5:4:1, v/v) as white needles (86 mg), m.p. 58-60°C [lit.[3,21] (racemate) 89-90°C]; (Found: M^+, 224.0841. $C_{15}H_{12}O_2$ requires 224.0834). ^1H NMR δ8.00 (dd, J1.2 and 8.3 Hz, H-6′), 7.33-7.65 (m, other aromatic resonances), 4.29 (d, J2.0 Hz, H-α), 4.07 (d, J2.0 Hz, H-β); CD (*c* 0.0056) $[\Theta]_{200}$ 0, $[\Theta]_{209}$ -12930, $[\Theta]_{212}$ 0, $[\Theta]_{230}$ +16628, $[\Theta]_{243}$ 0, $[\Theta]_{257}$ -12526, $[\Theta]_{275}$ -1919, $[\Theta]_{313}$ -7475, $[\Theta]_{360}$ 0.

(-)-($\alpha R,\beta S$)-2′-*O*-Methoxymethylchalcone epoxide (9): Reaction (48 h) of chalcone[22] (2) (500 mg) with the triphasic system *i.e.* CCl_4 (5 ml), poly-(*L*)-alanine (315 mg), NaOH-H_2O_2 solution (4.5 ml + 2 ml after 24 h); gave the epoxide (9) (R_f 0.5; hexane-C_6H_6-Me_2CO, 5:4:1, v/v) as white needles (340 mg); m.p. 79-82°C; (Found: M^+, 284.1043. $C_{17}H_{16}O_4$ requires 284.1049). ^1H NMR δ7.80 (dd, J1.8 and 7.8 Hz, H-6′), 7.46 (ddd, J1.8, 7.8, and 7.8 Hz, H-4′), 7.30-7.41 (m, B-ring protons), 7.13 (dd, J1.0 and 7.8 Hz, H-3′), 7.07 (ddd, J1.0, 7.8, and 7.8 Hz, H-5′), 4.90 (d, J6.8 Hz, OCH_2OCH_3), 4.80 (d, J6.8 Hz, OCH_2OCH_3), 4.28 (d, J2.0 Hz, H-α), 4.00 (d, J2.0 Hz, H-β), 3.06 (s, OCH_2OCH_3); CD (*c* 0.1310) $[\Theta]_{200}$ +2710, $[\Theta]_{230}$ +10600, $[\Theta]_{248}$ 0, $[\Theta]_{295}$ -6400, $[\Theta]_{355}$ 0.

(-)-($\alpha R,\beta S$)-4-Methoxy-2′-*O*-methoxymethylchalcone epoxide (10): Reaction (48 h) of chalcone[22] (3) (400 mg) in CCl_4 (5 ml) with NaOH-H_2O_2 solution (4.5 mg) catalysed by poly-(*L*)-alanine (300 mg) gave the epoxide (10) (R_f 0.4; hexane-C_6H_6-Me_2CO, 5:4:1 v/v) as white needles (270 mg); m.p. 75-78°C [lit.[22] (racemate) 78°C]; (Found: M^+, 314.1142. $C_{18}H_{18}O_5$ requires 314.1154). ^1H NMR δ7.81 (dd, J2.0 and 7.8 Hz, H-6′), 7.49 (ddd, J2.0, 7.8 and 7.8 Hz, H-4′), 7.30 (d, J7.8 Hz, H-2,6), 7.15 (dd, J1.1 and 7.8 Hz, H-3′), 7.10 (ddd, J1.1, 7.8, and 7.8 Hz, H-5′), 6.92 (d, J7.8 Hz, H-3,5), 4.95 (d, J7.0 Hz, OCH_2OCH_3), 4.88 (d, J7.0 Hz, OCH_2OCH_3), 4.31 (d, J2.2 Hz, H-α), 3.98 (d, J2.2 Hz, H-β), 3.85 (s, OCH_3), 3.15 (s, OCH_2OCH_3); CD (*c* 0.1050) $[\Theta]_{200}$ +3140, $[\Theta]_{210}$ +1730, $[\Theta]_{235}$ +10300, $[\Theta]_{267}$ 0, $[\Theta]_{300}$ -9700, $[\Theta]_{355}$ 0.

(-)-($\alpha R,\beta S$)-4,4′-Dimethoxy-2′-*O*-methoxymethylchalcone epoxide (11): Epoxidation (54 h) of chalcone[22] (4) (750 mg) in CCl_4 (7 mg) with the NaOH-H_2O_2 solution (4.5 ml + 2.5 ml after 24 h) catalysed by poly-(*L*)-alanine (400 mg) gave the epoxide (11) (R_f 0.3; hexane-C_6H_6-Me_2CO, 4:5:1; v/v) as white needles (580 mg); m.p. 59-62°C [lit.[22] (racemate) 78°C]; (Found: M^+, 344.1231. $C_{19}H_{20}O_6$ requires 344.1260). ^1H NMR δ7.85 (d, J8.3 Hz, H-6′), 7.27 (d, J9.0 Hz, H-3,5), 6.90 (d, J9.0 Hz, H-2,6), 6.64 (d, J2.0 Hz, H-3′), 6.61 (dd, J2.0 and 8.3 Hz, H-5′), 4.88 (d, J7.2 Hz, OCH_2OCH_3), 4.80 (d, J7.2 Hz, OCH_2OCH_3), 4.30 (d, J1.8 Hz, H-α), 3.92 (d, J1.8 Hz, H-β), 3.82 (s, 2xOCH_3), 3.11 (s, OCH_2OCH_3); CD (*c* 0.1680) $[\Theta]_{200}$ 0, $[\Theta]_{210}$ -3290, $[\Theta]_{222}$ 0, $[\Theta]_{240}$ +19900, $[\Theta]_{269}$ 0, $[\Theta]_{290}$ -17000, $[\Theta]_{350}$ 0.

(-)-($\alpha R,\beta S$)-3,4,4′-Trimethoxy-2′-*O*-methoxymethylchalcone epoxide (12)[22]: Treatment (96 h) of chalcone[22] (5) (99 mg) with the triphasic system *i.e.* CCl_4 (3 ml), poly-(*L*)-alanine (50 mg), NaOH-H_2O_2 solution (2.5 ml + 2 ml after 24 h) gave the epoxide[22] (12) (R_f 0.1; hexane-C_6H_6-Me_2CO, 25:70:5; v/v) as a white amorphous solid (48 mg) after prep. TLC; (Found: M^+, 374.1358. $C_{20}H_{22}O_8$ requires 374.1366). ^1H NMR δ7.85 (d, J9.0 Hz, H-6′), 6.95 (dd, J2.0 and 8.0 Hz, H-6), 6.85 (d, J8.0 Hz, H-5), 6.82 (d, J2.0 Hz, H-2), 6.64 (d, J2.2 Hz, H-3′), 6.61 (dd, J2.2 and 9.0 Hz, H-5′), 4.89 (d, J7.0 Hz, OCH_2OCH_3), 4.82 (d, J7.0 Hz, OCH_2OCH_3), 4.30 (d, J1.8 Hz, H-α), 3.92 (d, J1.8 Hz, H-β), 3.89, 3.86, and 3.83 (each s, 3xOCH_3), 3.13 (s, OCH_2OCH_3); CD (*c* 0.0220) $[\Theta]_{200}$ 0, $[\Theta]_{215}$ -2900, $[\Theta]_{229}$ 0, $[\Theta]_{257}$ +8700, $[\Theta]_{277}$ 0, $[\Theta]_{300}$ -12900, $[\Theta]_{350}$ 0.

(*αR,βS*)-4,4',6'-Trimethoxy-2'-*O*-methoxymethylchalcone epoxide (13): Treatment (32 h) of chalcone[20] (6) (430 mg) with the triphasic system *i.e.* CCl_4 (7 ml), poly-(*L*)-alanine (280 mg), NaOH-H_2O_2 solution (4.0 ml + 2 ml after 24 h) gave the epoxide[20] (13), which was not sufficiently stable to be purified by PLC or crystallisation. Despite the small amount of starting material left in the mixture, it was possible to obtain positive identification of the product by ^{1}H NMR δ7.22 (d, J8.8 Hz, H-2,6), 6.86 (d, J8.8 Hz, H-3,5), 6.31 (d, J2.0 Hz, H-3'), 6.12 (d, J2.0 Hz, H-5'), 5.08 (d, J7.7 Hz, OCH_2OCH_3), 5.06 (d, J7.7 Hz, OCH_2OCH_3), 3.93 (d, J1.8 Hz, H-β), 3.90 (d, J1.8 Hz, H-α), 3.79 (2x) and 3.73 (each s, $3xOCH_3$), 3.35 (s, OCH_2OCH_3).

(*αR,βS*)-3,4,4',6'-Tetramethoxy-2'-*O*-methoxymethylchalcone epoxide (14): Epoxidation (76 h) of chalcone (7) (98 mg) with the triphasic system *i.e.* CCl_4 (2 ml), poly-(*L*)-alanine (45 mg), NaOH-H_2O_2 solution (1.5 ml + 1 ml after 24 h) gave the epoxide (14), which was not sufficiently stable to be purified by PLC or crystallisation. Despite the fact that the product was contaminated by a small amount of starting material only, positive identification by ^{1}H NMR was possible. ^{1}H NMR δ6.90 (dd, J2.0 and 8.0 Hz, H-6), 6.87 (d, J8.0 Hz, H-5), 6.75 (d, J2.0 Hz, H-2), 6.31 (d, J2.0 Hz, H-3'), 6.13 (d, J2.0 Hz, H-5'), 5.09 (d, J8.5 Hz, OCH_2OCH_3), 5.06 (d, J8.5 Hz, OCH_2OCH_3), 3.94 (d, J1.5 Hz, H-β), 3.89 (d, J1.5 Hz, H-α), 3.86, 3.85, 3.79, and 3.74 (each s, $4xOCH_3$), 3.35 (s, OCH_2OCH_3).

(+)-(*αS,βR*)-2'-*O*-Methoxymethylchalcone epoxide (15): Epoxidation (48 h) of chalcone[22] (2) (225 mg) in CCl_4 (3 ml) with NaOH-H_2O_2 solution (2 ml + 1 ml after 24 h) and poly-(*D*)-alanine (175 mg) as catalyst, gave the epoxide (15) (R_f 0.5); hexane-C_6H_6-Me_2CO, 5:4:1; v/v) as white needles; m.p. 76-78°C. Ms and ^{1}H NMR data were identical to that of enantiomer (9); CD (*c* 0.0630) $[\Theta]_{213}$ 0, $[\Theta]_{230}$ -23500, $[\Theta]_{248}$ 0, $[\Theta]_{295}$ +13500, $[\Theta]_{360}$ 0.

(+)-(*αS,βR*)-4-Methoxy-2'-*O*-methoxymethylchalcone epoxide (16): Epoxidation (36 h) of chalcone[22] (3) (161 mg) in CCl_4 (3 ml) with NaOH-H_2O_2 solution (2 ml) and poly-(*D*)-alanine (120 mg) as catalyst, gave the epoxide (16) (R_f 0.4; hexane-C_6H_6-Me_2CO, 5:4:1; v/v) as white needles (65 mg); m.p. 76-78°C. Ms and ^{1}H NMR data were identical to that of enantiomer (10); CD (*c* 0.1130) $[\Theta]_{200}$ 0, $[\Theta]_{240}$ -7900, $[\Theta]_{272}$ 0, $[\Theta]_{300}$ +6600, $[\Theta]_{355}$ 0.

(+)-(*αS,βR*)-4,4'-Dimethoxy-2'-*O*-methoxymethylchalcone epoxide (17): Reaction (96 h) of chalcone[22] (4) (120 mg) in CCl_4 (3 ml) with NaOH-H_2O_2 (2.5 ml + 2 ml after 24 h) and poly-(*D*)-alanine (70 mg) as catalyst, gave the epoxide (17) (R_f 0.3; hexane-C_6H_6-Me_2CO, 4:5:1; v/v) as white needles (32 mg); m.p. 60-62°C. Ms and ^{1}H NMR data were identical to that of enantiomer (11); CD (*c* 0.0220) $[\Theta]_{200}$ 0, $[\Theta]_{210}$ +3440, $[\Theta]_{225}$ 0, $[\Theta]_{248}$ -15700, $[\Theta]_{272}$ 0, $[\Theta]_{290}$ +13200, $[\Theta]_{350}$ 0.

(+)-(*αS,βR*)-3,4,4'-Trimethoxy-2'-*O*-methoxymethylchalcone epoxide (18): Reaction (90 h) of chalcone[22] (5) (200 mg) in CCl_4 (3 ml) with basic H_2O_2 (4.0 ml + 2.0 ml after 24 h) and poly-(*D*)-alanine (150 mg) as catalyst, gave the epoxide (18) (R_f 0.1) as a white amorphous solid (72 mg) after purification by PLC (hexane-C_6H_6-Me_2CO, 25:70:5). Ms and ^{1}H NMR data were identical to that of its enantiomer (12); CD (*c* 0.3200) $[\Theta]_{200}$ 0, $[\Theta]_{215}$ +15200, $[\Theta]_{223}$ 0, $[\Theta]_{253}$ -2810, $[\Theta]_{277}$ 0, $[\Theta]_{300}$ +3740, $[\Theta]_{350}$ 0.

(*αS,βR*)-4,4',6'-Trimethoxy--2'-*O*-methoxymethylchalcone epoxide (19): Epoxidation (36 h) of chalcone[20] (6) (100 mg) in CCl_4 (2 ml) with basic H_2O_2 (1.5 ml + 1 ml after 24 h) and poly-(*D*)-alanine (49 mg) as catalyst gave the epoxide (19) which was not stable enough to be purified by PLC or crystallisation. ^{1}H NMR data were, however, identical to that of enantiomer (13).

(*αS,βR*)-3,4,4′,6-Tetramethoxy-2′-*O*-methoxymethylchalcone epoxide (20): Epoxidation (76 h) of chalcone (87 mg) in CCl_4 (2 ml) with basic H_2O_2 (1.5 ml + 1.0 ml after 24 h) and poly-(*D*)-alanine (41 mg) as catalyst gave the epoxide (20) which was not stable enough to be purified by PLC or crystallisation. ^{1}H NMR data were identical to that of enantiomer (14).

Acid catalysed cyclisation of (-)-(*αR,βS*)-4,4′-Dimethoxy-2′-*O*-methoxymethylchalcone epoxide (11): To a solution of epoxide (11) (51 mg) in 2,2,2-trifuoroethanol (5 ml) at -10^{0}C was added *p*-toluenesulphonic acid (28 mg) and the mixture stirred for 3 minutes. H_2O (10 ml) was added and the products extracted with ether. The ether extract was washed with water (3x10 ml), dried (Na_2SO_4), the ether evaporated and the residue separated by PLC (hexane-C_6H_6-Me_2CO, 4:5:1; v/v). Two main bands, R_f 0.3 (23 mg) and 0.4 (20 mg) were obtained.

(-)-(2*R*,3*R*)-4′,7-Dimethoxy-3-hydroxyflavanone (22): The former product (R_f 0.3) was identified as the title flavanone (22) {white needles (17 mg) from ethanol; m.p. 125-127^{0}C [lit.[22] (racemate) 126^{0}C]} $[\alpha]_D^{25}$-16.6^0 (*c* 0.1978 in CH_2Cl_2); (Found: M^+, 300.0995. $C_{17}H_{16}O_5$ requires 300.0998). ^{1}H NMR δ7.83 (d, J8.8 Hz, H-5), 7.49 (d, J9.0 Hz, H-2′,6′), 6.98 (d, J9.0 Hz, H-3′,5′), 6.65 (dd, J2.5 and 8.8 Hz, H-6), 6.46 (d, J2.5 Hz, H-8), 5.05 (d, J12.0 Hz, H-2), 4.56 (d, J12.0 Hz, H-3), 3.83 (s, 2xOCH$_3$), and 3.70 (s, OH); CD (*c* 0.0049) $[\Theta]_{200}$ 0, $[\Theta]_{210}$ +20070, $[\Theta]_{220}$ +2779, $[\Theta]_{232}$ +8893, $[\Theta]_{250}$ +2470, $[\Theta]_{262}$ 0, $[\Theta]_{290}$ -13741, $[\Theta]_{316}$ 0, $[\Theta]_{325}$ +5558, $[\Theta]_{345}$ 0.

Acetylation (acetic anhydride-pyridine) gave the acetate (23) as a colourless oil (16 mg; R_f 0.4; hexane-C_6H_6-Me_2CO, 5:4:1; v/v); ^{1}H NMR δ7.83 (d, J8.8 Hz, H-5), 7.40 (d, J9.0 Hz, H-2′,6′), 6.93 (d, J9.0 Hz, H-3′,5′), 6.64 (dd, J2.5 and 8.8 Hz, H-6), 6.46 (d, J2.5 Hz, H-8), 5.78 (d, J12.0 Hz, H-3), 5.34 (d, J12.0 Hz, H-2), 3.82 (s, 2xOCH$_3$), 2.00 (s, OAc).

4′,7-Dimethoxyisoflavone (24): The second band (R_f 0.4) gave 4′,7-dimethoxyisoflavone (24) as a cream amorphous solid (20 mg); m.p. 150^{0}C (lit.[23] 160^{0}C); ^{1}H NMR δ8.19 (d, J8.8 Hz, H-5), 7.90 (s, H-2), 7.48 (d, J9.0 Hz, H-2′,6′), 6.97 (dd, J2.5 and 9.0 Hz, H-6), 6.95 (d, J9.0 Hz, H-3′,5′), 6.84 (d, J2.5 Hz, H-8), 3.90 and 3.83 (each s, 2xOCH$_3$); *m/z* 282 (M^+, 100%).

Deprotection of 4,4′-dimethoxy-2′-*O*-methoxymethylchalcone epoxide (11) with P_2I_4[18]: P_2I_4 (13 mg) was added to a solution of the epoxide (11) (20 mg) in dry CH_2Cl_2 (5 ml) at 0^{0}C. After 25 minutes at 0^{0}C the temperature was raised to 25^{0}C and stirring continued for another 5 min. Evaporation of the solvent followed by PLC (hexane-C_6H_6-Me_2CO, 4:5:1; v/v) gave the 3-hydroxyflavanone (22) (R_f 0.3; 3 mg) and isoflavone (24) (R_f 0.4; 2 mg).

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