Enantioselective synthesis of flavonoids. Part 3.[1] *trans*- and *cis*-Flavan-3-ol methyl ether acetates

Hendrik van Rensburg, Pieter S. van Heerden * and Daneel Ferreira *

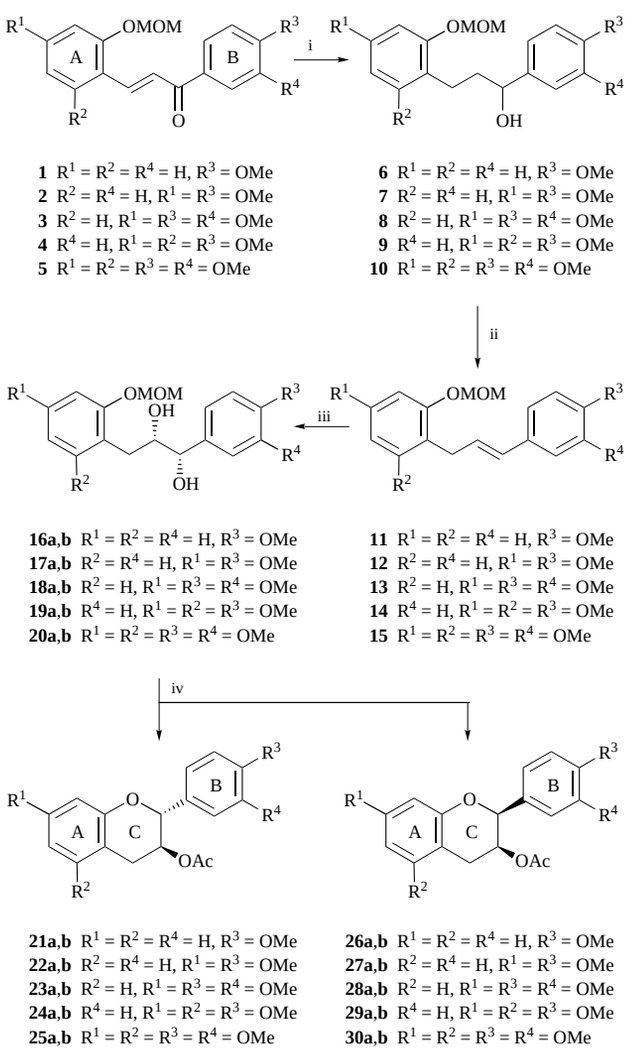
Department of Chemistry, University of the Free State, PO Box 339, Bloemfontein, 9300 South Africa

Asymmetric dihydroxylation of a series of polyoxygenated 1,3-diarylpropenes with AD-mix-α or AD-mix-β in the presence of methanesulfonamide and subsequent acid-catalysed cyclization, affords for the first time synthetic access to *trans*- and *cis*-flavan-3-ol derivatives, essentially enantiopure and in good yield.

Flavan-3-ols, the largest group of naturally occurring C_6–C_3–C_6 metabolites, have received considerable interest over the last few years on account of their importance as the constituent units of condensed tannins.[2] In addition, these compounds serve as the nucleophilic entities in the semi-synthesis of oligomeric proanthocyanidins,[3] natural products which are becoming increasingly important for their presumed health-promoting effects. Progress in the study of these complex phenolics is often hampered by the limited availability of naturally occurring flavonoid nucleophiles with 2,3-*trans*, and especially 2,3-*cis* stereochemistry. Surprisingly, the only synthetic access to monomeric flavan-3-ols involves the cumbersome process of hydrogenation and reduction of the corresponding dihydroflavonols.[4,5] In order to alleviate the restriction of studying only proanthocyanidins with substitution patterns exhibited by natural products that are available in quantities sufficient for preparative purposes, we embarked on a program[1] of synthesis of enantiomeric pure *trans*- and *cis*-flavan-3-ols. Our recent[6] transformation of the optically enriched oxygenated diols **20a**,**b** into the four catechin diastereoisomer derivatives **25a**,**b** and **30a**,**b**, prompted extension of this protocol to a series of diarylpropane-1,2-diols exhibiting the aromatic oxygenation patterns usually encountered in flavonoid chemistry. We thus now disclose results relevant to the synthesis of polyoxygenated diarylpropane-1,2-diols and their use as chirons for essentially enantiopure flavan-3-ols.

The series of (*E*)-*retro*-2-methoxymethylchalcone methyl ethers **1**–**5** ($J_{\alpha,\beta}$ 15.8–16.0 Hz) were prepared by base-catalysed condensation of the appropriate oxygenated acetophenones and benzaldehydes. Compounds **1**–**5** were transformed by consecutive reduction (Pd–H_2 and $NaBH_4$) and elimination {$SOCl_2$ and 1,8-diazabicyclo[5.4.0]undec-7-ene (1,8-DBU)} of the ensuing alcohols **6**–**10**, exclusively affording the (*E*)-1,3-diarylpropenes (deoxodihydrochalcones) **11**–**15** ($J_{1,2}$ 16 Hz) in good overall yield (65–73%) (Scheme 1, Table 1). Owing to the excellent results obtained by Sharpless *et al.*[7–10] (during asymmetric dihydroxylation of olefins) with AD-mix-α and AD-mix-β, these stereoselective catalysts were utilized for the introduction of chirality at C-3 in the flavan-3-ol framework.

Thus, treatment of the protected (*E*)-propenes **11**–**15** at 0 °C with AD-mix-α in the two-phase system Bu^{t}OH : H_2O (1 : 1), afforded the (+)-(1*S*,2*S*)-*syn*-diols **16a**–**20a** ($J_{1,2}$ 5.8–6.5 Hz) in high yields (80–86%) and optical purity (99% ee). The (−)-(1*R*,2*R*)-*syn*-diols **16b**–**20b** ($J_{1,2}$ 5.8–6.5 Hz) were similarly obtained by using AD-mix-β in the same two-phase system (82–87% yield, 99% ee). These conversions proceeded slowly with reaction times in the range 12–48 h. The enantiomeric purity of the diols was determined by observing the H-1 and H-2 spin systems of the corresponding mono and/or bis-MTPA esters,[11]



1 $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
2 $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
3 $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
4 $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
5 $R^1 = R^2 = R^3 = R^4 = OMe$

6 $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
7 $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
8 $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
9 $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
10 $R^1 = R^2 = R^3 = R^4 = OMe$

16a,**b** $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
17a,**b** $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
18a,**b** $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
19a,**b** $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
20a,**b** $R^1 = R^2 = R^3 = R^4 = OMe$

11 $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
12 $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
13 $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
14 $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
15 $R^1 = R^2 = R^3 = R^4 = OMe$

21a,**b** $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
22a,**b** $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
23a,**b** $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
24a,**b** $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
25a,**b** $R^1 = R^2 = R^3 = R^4 = OMe$

26a,**b** $R^1 = R^2 = R^4 = H$, $R^3 = OMe$
27a,**b** $R^2 = R^4 = H$, $R^1 = R^3 = OMe$
28a,**b** $R^2 = H$, $R^1 = R^3 = R^4 = OMe$
29a,**b** $R^4 = H$, $R^1 = R^2 = R^3 = OMe$
30a,**b** $R^1 = R^2 = R^3 = R^4 = OMe$

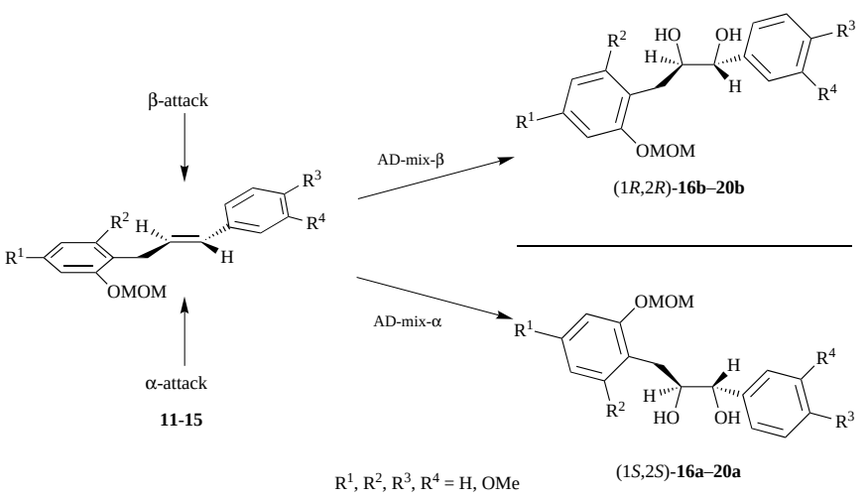
16-30a = configuration shown
16-30b = enantiomer

Scheme 1 *Reagents and conditions*: i, Pd–H_2, EtOH, then $NaBH_4$, EtOH; ii, $SOCl_2$, CH_2Cl_2, then 1,8-DBU, CH_2Cl_2, reflux; iii, AD-mix-α or AD-mix-β, Bu^{t}OH : H_2O (1 : 1, v/v), $MeSO_2NH_2$, 0 °C; iv, 3 M HCl, MeOH–H_2O (3 : 1, v/v), then Ac_2O, pyridine

which show different chemical shifts in the ^{1}H NMR spectra of the two diastereoisomers. The absolute configuration was tentatively assigned according to the Sharpless model[7,8] for AD-mix (Scheme 2).

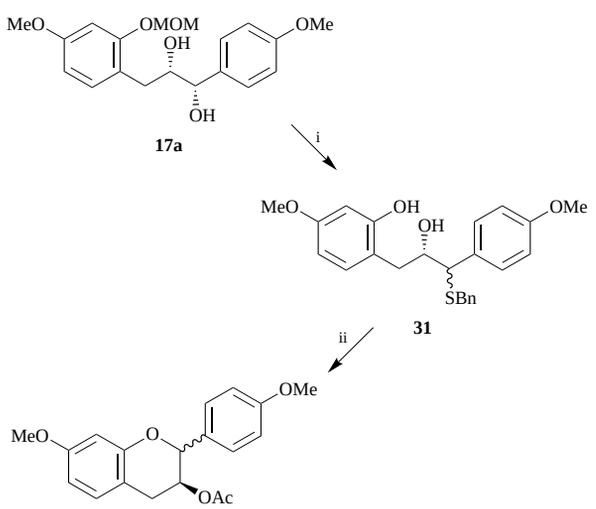
Table 1 Intermediate products in the conversion of the chalcones **1**–**5** into the flavan-3-ols **21a/b**–**30a/b**

Propan-1-ols	Yield (%)	Propenes	Yield (%)	1,2-Diols	Yield (%)	Ee (%)	Flavan-3-ols	Yield (%)	Ee (%)	*trans*:*cis*
6	99	**11**	73	**16a**	82	99	**21a/26a**	87	99	1:0.33
				16b	84	99	**21b/26b**	88	99	1:0.31
7	98	**12**	74	**17a**	86	99	**22a/27a**	88	99	1:0.36
				17b	82	99	**22b/27b**	90	99	1:0.33
8	99	**13**	70	**18a**	85	99	**23a/28a**	82	99	1:0.32
				18b	83	99	**23b/28b**	80	99	1:0.30
9	98	**14**	68	**19a**	80	99	**24a/29a**	71	99	1:0.32
				19b	83	99	**24b/29b**	70	99	1:0.33
10	99	**15**	66	**20a**	80	99	**25a/30a**	66	99	1:0.34
				20b	87	99	**25b/30b**	65	99	1:0.35



Scheme 2

The successful Lewis acid-catalysed phenylmethanethiol ring-opening and cyclization of chalcone epoxides in the synthesis of dihydroflavonols,[12] prompted evaluation of this protocol in the cyclization of the diols **16a**,**b**–**20a**,**b**. Thus, the Lewis acid, tin tetrachloride,[13] in the presence of the powerful nucleophilic phenylmethanethiol (BnSH) was utilized for selective substitution of the benzylic C(1)-OH (−20 °C) and subsequent removal of the methoxymethyl group (0 °C) in **17a**, to give the benzylthio derivative **31** (70%, mixture of *syn* and *anti*) (Scheme 3). Treatment of the benzylthio ether

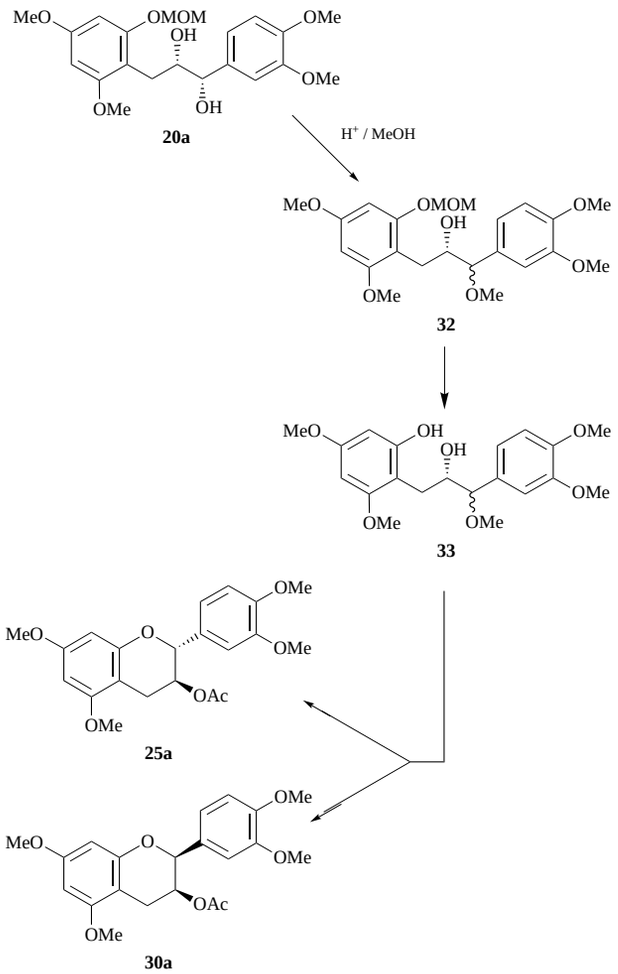


Scheme 3 *Reagents and conditions*: i, BnSH (4 equiv.), $SnCl_4$ (0.2 equiv.), −20 to 0 °C; ii, $AgBF_4$ (5 equiv.), CH_2Cl_2, 0 °C, then Ac_2O, pyridine

31 with the thiophilic Lewis acid, silver tetrafluoroborate ($AgBF_4$),[14] in CH_2Cl_2 at 0 °C, however, resulted in slow (24 h) and low % conversion (10–20%) into the flavan-3-ols **22a**,**27a**.

In order to transform the diols effectively into the corresponding flavan-3-ols, methods aimed at selective removal of the 2″-*O*-methoxymethyl group and subsequent ring closure under mild acidic conditions, were explored. Simultaneous deprotection and cyclization of diols **16a**,**b**–**20a**,**b** in the presence of 3 M HCl in MeOH, followed by acetylation, yielded 2,3-*trans*- (48–68%) **21a**,**b**–**25a**,**b** and for the first time 2,3-*cis*-flavan-3-ol methyl ether acetate derivatives (17–22%) **26a**,**b**–**30a**,**b** in excellent enantiomeric excesses (>99%) (Scheme 1, Table 1). The optical purity was assessed by ^{1}H NMR using [Eu(hfc)$_3$] as chiral shift reagent, which consistently indicated the presence of only one enantiomer, thus unequivocally confirming the fact that optical integrity was preserved in the transformation of the diols **16a**,**b**–**20a**,**b** into the corresponding *trans*- and *cis*-flavan-3-ols. The absolute stereochemistry of the naturally occurring *trans*- **23a**,**b**–**25a**,**b** and *cis*-flavan-3-ols **28a**,**b**–**30a**,**b** was assigned by comparison of CD data with those of authentic samples in the catechin,[15,16] fisetinidol[15,17] and afzelechin[15,18] series of compounds from our considerable collection of reference compounds. The absolute configuration of the *trans*-**21a**,**b**/**22a**,**b** and *cis*-flavan-3-ols **26a**,**b**/**27a**,**b** was assigned assuming that the stereochemistry of the reactions leading to those compounds is the same as for the natural products. Thus, the stereochemistry of the flavan-3-ol acetates confirm the assigned configuration of the diols as derived from the Sharpless model.

Cyclization of the highly oxygenated diol **20a** led to the formation of two separable intermediate products **32** and **33** (Scheme 4). Methanol thus initially acts as nucleophile in an S_N1-type acid-catalysed solvolysis of the C-1 benzylic hydroxy group, affording a *syn*:*anti* mixture of isomers **32**. Prolonged treatment (*ca.* 2 h) eventually led to deprotection of the acetal functionality to give the intermediate **33**, which is susceptible to cyclization to afford both the 2,3-*trans*- and 2,3-*cis*-flavan-3-ols



Scheme 4

25a and **30a**. Formation of both these isomers is explicable in terms of the generation of an incipient C-1 carbocation by protonation of the benzylic methoxy functionality, and subsequent S_N1 cyclization that leads to predominant formation of the thermodynamically more stable *trans*-isomer.[16,19] The aforementioned remarkable stability of the reputedly highly acid-labile methoxymethyl group towards acid hydrolysis was also observed during the enantioselective synthesis of isoflavans.[20]

We have thus developed the first and highly efficient synthesis of essentially enantiopure flavan-3-ols of both 2,3-*trans* and 2,3-*cis* configuration. These results abundantly demonstrate the utility of polyoxygenated diarylpropane-1,2-diols as chirons for naturally occurring flavanoids of this class. The potential of this protocol in the chemistry of the oligomeric proanthocyanidins and condensed tannins in general is evident, especially in view of its aptitude to the synthesis of free phenolic analogues. In addition, detailed analysis of CD data of the series of both 2*R*,3*S*-*trans*-, 2*S*,3*R*-*trans*-, 2*R*,3*R*-*cis*- and 2*S*,3*S*-*cis*-flavan-3-ol analogues should usefully contribute towards assessment of the absolute configuration of flavan-3-ols and will be discussed in an impending publication.

Experimental

^{1}H NMR spectra were recorded at ambient temperatures on a Bruker AM-300 spectrometer for solutions in $CDCl_3$ with Me_4Si as internal standard; *J* values recorded in Hz. High and low resolution EI-mass spectra were obtained on a VG70-70E mass spectrometer. Melting points were measured on a Reichert hot-stage apparatus and are uncorrected. CD measurements were obtained for solutions in MeOH on a Jasco J-710 spectropolarimeter and optical rotations measured with a Bendix-NPL automatic polarimeter for solutions in $CHCl_3$; the latter are recorded as 10^{-1} deg cm^2 g^{-1}. Thin layer chromatography (TLC) was performed on DC-Alufolien Kieselgel 60 F_{254} (0.25 mm) plates with visualisation by UV light and/or formaldehyde–sulfuric acid spray. Preparative plates (PLC) [Kieselgel PF_{254} (1.0 mm)] were air-dried and used without prior activation. Flash column chromatography (FLC) was on Merck Kieselgel 60 (230–400 mesh) under a positive pressure by means of compressed nitrogen.

General procedure for preparation of the (*E*)-*retro*-2-methoxymethylchalcones 1–5

To a solution of the appropriate acetophenone (1.4–2.8 g) in ethanol (20–40 cm^3) was added 50% (m/v) aq. KOH (5–10 cm^3) and the mixture was stirred at room temperature for 30–40 min. Excess of 2-*O*-methoxymethylbenzaldehyde (1.0–2.3 g, in 10 cm^3 ethanol) was added dropwise to the mixture and the reaction was followed by TLC. After disappearance of the acetophenone (4–24 h), water (20–40 cm^3) was added to the mixture which was then extracted with diethyl ether (4 × 20 cm^3). Drying of the combined extracts (Na_2SO_4) followed by evaporation and flash column chromatography, gave the pure *retro*-chalcones (50–70%).

4′-Methoxy-2-*O*-methoxymethyl-*retro*-chalcone 1. R_F 0.55 (hexane–benzene–acetone, 5:4:1); δ_H 8.15 (1H, d, *J* 16.0, H-β), 8.03 (2H, d, *J* 9.0, H-2′,6′), 7.66 (1H, dd, *J* 8.0 and 1.8, H-3), 7.59 (1H, d, *J* 16.0, H-α), 7.33 (1H, ddd, *J* 8.0, 8.0 and 1.8, H-5), 7.15 (1H, dd, *J* 8.0 and 1.2, H-6), 7.03 (1H, ddd, *J* 8.0, 8.0 and 1.2, H-4), 6.96 (2H, d, *J* 9.0, H-3′,5′), 5.26 (2H, s, OCH_2OCH_3), 3.87 (3H, s, OMe) and 3.49 (3H, s, OCH_2OCH_3) (Found: M$^+$, 298.1199. $C_{18}H_{18}O_4$ requires *M*$^+$, 298.1204).

4,4′-Dimethoxy-2-*O*-methoxymethyl-*retro*-chalcone 2. R_F 0.40 (hexane–benzene–acetone, 5:4:1); δ_H 8.10 (1H, d, *J* 16.0, H-β), 8.02 (2H, d, *J* 9.0, H-2′,6′), 7.60 (1H, d, *J* 9.0, H-6), 7.51 (1H, d, *J* 16.0, H-α), 6.96 (2H, d, *J* 9.0, H-3′,5′), 6.72 (1H, d, *J* 2.5, H-3), 6.58 (1H, dd, *J* 9.0 and 2.5, H-5), 5.25 (2H, s, OCH_2OCH_3), 3.86, 3.82 (2 × 3H, 2 × s, 2 × OMe) and 3.49 (3H, s, OCH_2OCH_3) (Found: M$^+$, 328.1310. $C_{19}H_{20}O_5$ requires *M*$^+$, 328.1310).

3′,4,4′-Trimethoxy-2-*O*-methoxymethyl-*retro*-chalcone 3. Mp 93 °C; R_F 0.21 (hexane–benzene–acetone, 5:4:1); δ_H 8.14 (1H, d, *J* 16.0, H-β), 7.70 (1H, dd, *J* 8.5 and 2.0, H-6′), 7.65 (1H, d, *J* 2.0, H-2′), 7.64 (1H, d, *J* 8.5, H-6), 7.56 (1H, d, *J* 16.0, H-α), 6.95 (1H, d, *J* 8.5, H-5′), 6.76 (1H, d, *J* 2.5, H-3), 6.64 (1H, dd, *J* 8.5 and 2.5, H-5), 5.30 (2H, s, OCH_2OCH_3), 4.00, 3.99, 3.87 (3 × 3H, 3 × s, 3 × OMe) and 3.54 (3H, s, OCH_2OCH_3) (Found: M$^+$, 358.1405. $C_{20}H_{22}O_6$ requires *M*$^+$, 358.1415).

4,4′,6-Trimethoxy-2-*O*-methoxymethyl-*retro*-chalcone 4. R_F 0.25 (hexane–benzene–acetone, 5:4:1); δ_H 8.27 (1H, d, *J* 16.0, H-β), 8.05 (2H, d, *J* 9.0, H-2′,6′), 7.94 (1H, d, *J* 16.0, H-α), 6.99 (2H, d, *J* 9.0, H-3′,5′), 6.42 (1H, d, *J* 2.5, H-3), 6.21 (1H, d, *J* 2.5, H-5), 5.30 (2H, s, OCH_2OCH_3), 3.94, 3.90, 3.86 (3 × 3H, 3 × s, 3 × OMe) and 3.53 (3H, s, OCH_2OCH_3) (Found: M$^+$, 358.1408. $C_{20}H_{22}O_6$ requires *M*$^+$, 358.1415).

3′,4,4′,6-Tetramethoxy-2-*O*-methoxymethyl-*retro*-chalcone 5. Mp 97 °C; R_F 0.18 (hexane–benzene–acetone, 5:4:1); δ_H 8.25 (1H, d, *J* 16.0, H-β), 7.94 (1H, d, *J* 16.0, H-α), 7.68 (1H, dd, *J* 8.0 and 2.0, H-6′), 7.66 (1H, d, *J* 2.0, H-2′), 6.94 (1H, d, *J* 8.0, H-5′), 6.41 (1H, d, *J* 2.5, H-3), 6.21 (1H, d, *J* 2.5, H-5), 5.30 (2H, s, OCH_2OCH_3), 3.99, 3.98, 3.94, 3.86 (4 × 3H, 4 × s, 4 × OMe) and 3.54 (3H, s, OCH_2OCH_3) (Found: M$^+$, 388.1521. $C_{21}H_{24}O_7$ requires *M*$^+$, 388.1520).

General procedure for preparation of the propanols 6–10

A solution of the *retro*-chalcone **1**–**5** (15 mmol) in ethanol (200 cm^3) was treated with 5% palladium-on-charcoal (10% mol) and hydrogenated at ambient temperature until a stoichiometric amount of H_2(g) had been consumed. The catalyst was filtered off, and $NaBH_4$ (60 mmol, 4 equiv.) was added to the

filtrate; the mixture was then stirred for 6–12 h, after which it was diluted with water (100 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated to afford the corresponding alcohols **6**–**10** in almost quantitative yields.

1-(4′-Methoxyphenyl)-3-(2″-methoxymethylphenyl)propan-1-ol 6. R_F 0.28 (hexane–benzene–acetone, 5:4:1); δ_H 7.32 (2H, d, *J* 8.5, H-2′,6′), 7.19 (1H, ddd, *J* 8.5, 8.5 and 1.5, H-5″), 7.18 (1H, dd, *J* 8.5 and 1.5, H-3″), 7.09 (1H, dd, *J* 8.5 and 1.5, H-6″), 6.97 (1H, ddd, *J* 8.5, 8.5 and 1.5, H-4″), 6.90 (2H, d, *J* 8.5, H-3′,5′), 5.22 (2H, s, OCH_2OCH_3), 4.64 (1H, m, H-1), 3.83 (3H, s, OMe), 3.49 (3H, s, OCH_2OCH_3), 2.75 (2H, m, 3-CH_2), 2.35 (1H, d, *J* 3.0, OH) and 2.09 (2H, m, 2-CH_2) (Found: M^+, 302.1509. $C_{18}H_{22}O_4$ requires M^+, 302.1518).

1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propan-1-ol 7. R_F 0.28 (hexane–benzene–acetone, 5:4:1); δ_H 7.30 (2H, d, *J* 9.0, H-2′,6′), 7.06 (1H, d, *J* 8.5, H-6″), 6.90 (2H, d, *J* 9.0, H-3′,5′), 6.70 (1H, d, *J* 2.5, H-3″), 6.51 (1H, dd, *J* 8.5 and 2.5, H-5″), 5.20 (2H, s, OCH_2OCH_3), 4.60 (1H, m, H-1), 3.82, 3.80 (2 × 3H, 2 × s, 2 × OMe), 3.48 (3H, s, OCH_2OCH_3), 2.68 (2H, m, 3-CH_2), 2.17 (1H, d, *J* 3.0, OH) and 2.02 (2H, m, 2-CH_2) (Found: M^+, 332.1620. $C_{19}H_{24}O_5$ requires M^+, 332.1624).

1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propan-1-ol 8. R_F 0.27 (hexane–benzene–acetone, 5:4:1); δ_H 7.07 (1H, d, *J* 8.0, H-5′), 6.95 (1H, d, *J* 2.0, H-3″), 6.89 (1H, dd, *J* 8.0 and 2.0, H-5″), 6.84 (1H, d, *J* 8.0, H-6″), 6.72 (1H, d, *J* 2.5, H-2′), 6.52 (1H, dd, *J* 8.0 and 2.5, H-6′), 5.20 (2H, s, OCH_2OCH_3), 4.60 (1H, m, H-1), 3.90, 3.89, 3.80 (3 × 3H, 3 × s, 3 × OMe), 3.48 (3H, s, OCH_2OCH_3), 2.70 (2H, m, 3-CH_2), 2.28 (1H, d, *J* 3.0, OH) and 2.03 (2H, m, 2-CH_2) (Found: M^+, 362.1730. $C_{20}H_{26}O_6$ requires M^+, 362.1729).

1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propan-1-ol 9. R_F 0.19 (hexane–benzene–acetone, 5:4:1); δ_H 7.28 (2H, d, *J* 8.5, H-2′,6′), 6.87 (2H, d, *J* 8.5, H-3′,5′), 6.40 (1H, d, *J* 2.2, H-5″), 6.22 (1H, d, *J* 2.2, H-3″), 5.20 (2H, s, OCH_2OCH_3), 4.48 (1H, m, H-1), 3.84, 3.82, 3.81 (3 × 3H, 3 × s, 3 × OMe), 3.48 (3H, s, OCH_2OCH_3), 3.01 (1H, d, *J* 3.0, OH), 2.78 (2H, m, 3-CH_2) and 1.94 (2H, m, 2-CH_2) (Found: M^+, 362.1721. $C_{20}H_{26}O_6$ requires M^+, 362.1729).

1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propan-1-ol 10. R_F 0.14 (hexane–benzene–acetone, 5:4:1); δ_H 7.00 (1H, d, *J* 2.0, H-2′), 6.87 (1H, dd, *J* 8.0 and 2.0, H-6′), 6.82 (1H, d, *J* 8.0, H-5′), 6.40 (1H, d, *J* 2.0, H-3″), 6.23 (1H, d, *J* 2.0, H-5″), 5.20 (2H, s, OCH_2OCH_3), 4.50 (1H, m, H-1), 3.90, 3.88, 3.84, 3.82 (4 × 3H, 4 × s, 4 × OMe), 3.48 (3H, s, OCH_2OCH_3), 3.06 (1H, d, *J* 3.0, OH), 2.80 (2H, m, 3-CH_2) and 1.90 (2H, m, 2-CH_2) (Found: M^+, 392.1831. $C_{21}H_{28}O_7$ requires M^+, 392.1835).

General procedure for preparation of the propenes 11–15

Freshly distilled thionyl chloride (24 mmol, 2 equiv.) was added dropwise to a solution of the alcohol **6**–**10** (12 mmol) in dry CH_2Cl_2 (15 cm^3) and the mixture was stirred at room temperature for 5 min. Dry benzene (20 cm^3) was added to the mixture which was then evaporated at 50 °C under reduced pressure. The resulting chloropropane was dissolved in dry benzene (15 cm^3) and 1,8-DBU (24 mmol, 2 equiv.) was added to the solution which was then refluxed for 12–18 h. After this, saturated aqueous NH_4Cl (40 cm^3) was added to the mixture which was then extracted with Et_2O (3 × 50 cm^3). The combined extracts were washed with water (50 cm^3), dried (Na_2SO_4) and evaporated. The resulting crude mixture was purified by FLC (hexane–acetone, 9:1).

(*E*)-1-(4′-Methoxyphenyl)-3-(2″-methoxymethylphenyl)propene 11. R_F 0.69 (hexane–benzene–acetone, 5:4:1); δ_H 7.26 (2H, d, *J* 9.0, H-2′,6′), 7.18 (1H, dd, *J* 8.5 and 1.8, H-5″), 7.16 (1H, ddd, *J* 8.5, 8.5 and 1.8, H-3″), 7.06 (1H, dd, *J* 8.5 and 1.8, H-6″), 6.95 (1H, ddd, *J* 8.5, 8.5 and 1.8, H-4″), 6.80 (2H, d, *J* 9.0, H-3′,5′), 6.35 (1H, d, *J* 16.0, H-1), 6.22 (1H, dt, *J* 16.0 and 6.2, H-2), 5.20 (2H, s, OCH_2OCH_3), 3.78 (3H, s, OMe), 3.53 (2H, d, *J* 6.2, 3-CH_2) and 3.46 (3H, s, OCH_2OCH_3); *m*/*z* 284 (M^+, 12%), 239 (18), 165 (15), 151 (9), 135 (30), 121 (48), 107 (15) and 91 (12) (Found: M^+, 284.1415. $C_{18}H_{20}O_3$ requires M^+, 284.1413).

(*E*)-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propene 12. R_F 0.64 (hexane–benzene–acetone, 5:4:1); δ_H 7.29 (2H, d, *J* 9.0, H-2′,6′), 7.12 (1H, d, *J* 8.2, H-6″), 6.84 (2H, d, *J* 9.0, H-3′,5′), 6.73 (1H, d, *J* 2.8, H-3″), 6.53 (1H, dd, *J* 8.2 and 2.8, H-5″), 6.37 (1H, d, *J* 16.0, H-1), 6.23 (1H, dt, *J* 16.0 and 6.3, H-2), 5.23 (2H, s, OCH_2OCH_3), 3.82, 3.81 (2 × 3H, 2 × s, 2 × OMe), 3.50 (3H, s, OCH_2OCH_3) and 3.48 (2H, d, *J* 6.5, 3-CH_2); *m*/*z* 314 (M^+, 18%), 269 (20), 195 (8), 181 (10), 135 (25), 121 (50) and 91 (14) (Found: M^+, 314.1507. $C_{19}H_{22}O_4$ requires M^+, 314.1518).

(*E*)-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propene 13. R_F 0.39 (hexane–benzene–acetone, 5:4:1); δ_H 7.13 (1H, d, *J* 8.5, H-5′), 6.93 (1H, d, *J* 2.2, H-3″), 6.88 (1H, dd, *J* 8.2 and 2.2, H-5″), 6.80 (1H, d, *J* 8.5, H-6″), 6.73 (1H, d, *J* 2.2, H-2′), 6.54 (1H, dd, *J* 8.5 and 2.2, H-6′), 6.36 (1H, d, *J* 16.0, H-1), 6.23 (1H, dt, *J* 16.0 and 6.2, H-2), 5.23 (2H, s, OCH_2OCH_3), 3.89, 3.88, 3.81 (3 × 3H, 3 × s, 3 × OMe), 3.51 (2H, d, *J* 6.5, 3-CH_2) and 3.50 (3H, s, OCH_2OCH_3); *m*/*z* 344 (M^+, 17%), 299 (18), 195 (8), 181 (50), 165 (30), 151 (80), 137 (40) and 121 (12) (Found: M^+, 344.1621. $C_{20}H_{24}O_5$ requires M^+, 344.1624).

(*E*)-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propene 14. R_F 0.55 (hexane–benzene–acetone, 5:4:1); δ_H 7.27 (2H, d, *J* 8.5, H-2′,6′), 6.83 (2H, d, *J* 8.5, H-3′,5′), 6.40 (1H, d, *J* 2.2, H-5″), 6.34 (1H, s, *J* 16.0, H-1), 6.24 (1H, d, *J* 2.2, H-3″), 6.21 (1H, dt, *J* 16.0 and 6.2, H-2), 5.23 (2H, s, OCH_2OCH_3), 3.84, 3.83, 3.80 (3 × 3H, 3 × s, 3 × OMe), 3.52 (2H, d, *J* 6.2, 3-CH_2) and 3.50 (3H, s, OCH_2OCH_3); *m*/*z* 344 (M^+, 20%), 299 (35), 225 (10), 211 (40), 167 (38), 151 (22), 135 (23) and 121 (80) (Found: M^+, 344.1620. $C_{20}H_{24}O_5$ requires M^+, 344.1624).

(*E*)-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propene 15. R_F 0.32 (hexane–benzene–acetone, 5:4:1); δ_H 6.89 (1H, d, *J* 2.0, H-2′), 6.85 (1H, dd, *J* 8.5 and 2.0, H-6′), 6.77 (1H, d, *J* 8.5, H-5′), 6.39 (1H, d, *J* 2.2, H-5″), 6.30 (1H, d, *J* 16.0, H-1), 6.23 (1H, d, *J* 2.2, H-3″), 6.18 (1H, dt, *J* 16.0 and 6.0, H-2), 5.21 (2H, s, OCH_2OCH_3), 3.88, 3.87, 3.83, 3.82 (4 × 3H, 4 × s, 4 × OMe), 3.51 (2H, d, *J* 6.0, 3-CH_2), 3.84 (3H, s, OCH_2OCH_3), *m*/*z* 374 (M^+, 70%), 329 (20), 225 (10), 211 (8), 167 (23), 151 (44) and 137 (12) (Found: M^+, 374.1723. $C_{21}H_{26}O_6$ requires M^+, 374.1729).

General procedure for asymmetric dihydroxylation of the propenes 11–15

A 50 cm^3 round-bottomed flask, equipped with a magnetic stirrer, was charged with *tert*-butyl alcohol (15 cm^3), water (15 cm^3) and AD-mix-α or -β (4.2 g). Stirring of the mixture at room temperature produced two clear phases; the lower aqueous phase appeared bright yellow. Methanesulfonamide (285 mg, 3 mmol, 1 equiv.) was added to the mixture which was then cooled to 0 °C and treated at once with the propene **11**–**15** (3 mmol). The resulting heterogeneous slurry was stirred vigorously at 0 °C for 12–24 h (progress was monitored by TLC). Sodium sulfite (4.5 g) was added to the mixture which was then allowed to warm to room temperature and stirred for 30–60 min. Ethyl acetate (30 cm^3) was added to the reaction mixture and organic layer was separated; the aqueous phase was then further extracted with the same solvent (3 × 15 cm^3). The combined organic layer and extracts were dried (Na_2SO_4) and evaporated and the crude extract was purified by PLC to give the corresponding diols **16a**,**b**–**20a**,**b**.

(1*S*,2*S*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethylphenyl)propane-1,2-diol 16a. R_F 0.15 (hexane–benzene–acetone, 5:4:1); δ_H 7.34 (2H, d, *J* 9.0, H-2′,6′), 7.20 (1H, ddd, *J* 8.0, 8.0 and 1.9, H-5″), 7.14 (1H, dd, *J* 8.0 and 1.9, H-3″),

7.07 (1H, dd, *J* 8.0 and 1.1, H-6″), 6.97 (1H, ddd, *J* 8.0, 8.0 and 1.1, H-4″), 6.93 (1H, d, *J* 9.0, H-3′,5′), 5.16 (2H, s, OCH_2OCH_3), 4.50 (1H, dd, *J* 6.5 and 3.0, H-1), 3.97 (1H, m, H-2), 3.84 (3H, s, OMe), 3.44 (3H, s, OCH_2OCH_3), 3.08 (1H, d, *J* 3.0, 1-OH), 2.82 (1H, dd, *J* 14.0 and 4.2) and 2.70 (1H, dd, *J* 14.0 and 8.5)(3-CH_2) and 2.66 (1H, d, *J* 4.5, 2-OH); *m*/*z* 318 (M^+, 22%), 165 (10), 151 (9), 137 (100), 121 (64), 107 (25) and 91 (20) (Found: M^+, 318.1467. $C_{18}H_{22}O_5$ requires M^+, 318.1467); $[\alpha]_D^{25}$ +15.1 (*c* 1.23); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+2.3 \times 10^3$ (268) and $+8.2 \times 10^3$ (233).

(1*R*,2*R*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethylphenyl)propane-1,2-diol 16b. $[\alpha]_D^{25}$ −12.6 (*c* 0.86); CD: $\Delta\varepsilon_{max}$ (λ/nm) -2.0×10^3 (267) and -6.5×10^3 (234); the R_F, ^{1}H NMR and MS data corresponded to those reported for **16a**.

(1*S*,2*S*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propane-1,2-diol 17a. R_F 0.08 (hexane–benzene–acetone, 5:4:1); δ_H 7.30 (2H, d, *J* 8.5, H-2′,6′), 6.99 (1H, d, *J* 8.5, H-6″), 6.88 (2H, d, *J* 8.5, H-3′,5′), 6.65 (1H, d, *J* 2.5, H-3″), 6.47 (1H, dd, *J* 8.5 and 2.5, H-5″), 5.11 (2H, s, OCH_2OCH_3), 4.45 (1H, dd, *J* 6.5 and 3.0, H-1), 3.90 (1H, m, H-2), 3.79, 3.75 (2 × 3H, 2 × s, 2 × OMe), 3.40 (3H, s, OCH_2OCH_3), 2.94 (1H, d, *J* 3.5, 1-OH), 2.72 (1H, dd, *J* 13.5 and 4.2) and 2.60 (1H, dd, *J* 13.5 and 9.0)(3-CH_2) and 2.50 (1H, d, *J* 4.2, 2-OH); *m*/*z* 348 (M^+, 11%), 181 (48), 165 (9), 151 (30), 137 (60) and 121 (50) (Found: M^+, 348.1571. $C_{19}H_{24}O_6$ requires M^+, 348.1572); $[\alpha]_D^{25}$ +18.3 (*c* 1.05); CD: $\Delta\varepsilon_{max}$ (λ/nm) -1.7×10^3 (274) and $+7.0 \times 10^3$ (236).

(1*R*,2*R*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propane-1,2-diol 17b. $[\alpha]_D^{25}$ −19.4 (*c* 1.27); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+1.9 \times 10^3$ (274) and -7.6×10^3 (236); the R_F, ^{1}H NMR and MS data corresponded to those reported for **17a**.

(1*S*,2*S*)-*syn*-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propane-1,2-diol 18a. R_F 0.05 (hexane–benzene–acetone, 5:4:1); δ_H 7.03 (1H, d, *J* 8.0, H-5′), 6.97 (1H, d, *J* 2.0, H-3″), 6.95 (1H, dd, *J* 8.0 and 2.0, H-5″), 6.86 (1H, d, *J* 8.0, H-6″), 6.69 (1H, d, *J* 2.8, H-2′), 6.53 (1H, dd, *J* 8.0 and 2.8, H-6′), 5.18 (2H, s, OCH_2OCH_3), 4.50 (1H, dd, *J* 6.5 and 3.0, H-1), 3.91 (1H, m, H-2), 3.92, 3.90, 3.79 (3 × 3H, 3 × s, 3 × OMe), 3.45 (3H, s, OCH_2OCH_3), 3.02 (1H, d, *J* 3.0, 1-OH), 2.77 (1H, dd, *J* 14.0 and 4.5) and 2.67 (1H, dd, *J* 14.0 and 9.0)(3-CH_2) and 2.55 (1H, d, *J* 4.0, 2-OH); *m*/*z* 378 (M^+, 13%), 195 (6), 181 (30), 167 (62), 151 (38), 137 (30) and 121 (18) (Found: M^+, 378.1677. $C_{20}H_{26}O_7$ requires M^+, 378.1678); $[\alpha]_D^{25}$ +8.3 (*c* 1.00); CD: $\Delta\varepsilon_{max}$ (λ/nm) -7.6×10^2 (275) and $+6.1 \times 10^3$ (236).

(1*R*,2*R*)-*syn*-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″-methoxyphenyl)propane-1,2-diol 18b. $[\alpha]_D^{25}$ −8.0 (*c* 0.86); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+7.7 \times 10^2$ (276) and -5.8×10^3 (236); the R_F, ^{1}H NMR and MS data corresponded to those reported for **18a**.

(1*S*,2*S*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propane-1,2-diol 19a. R_F 0.04 (hexane–benzene–acetone, 5:4:1); δ_H 7.33 (2H, d, *J* 9.0, H-2′,6′), 6.90 (2H, d, *J* 9.0, H-3′,5′), 6.35 (1H, d, *J* 2.2, H-5″), 6.20 (1H, d, *J* 2.2, H-3″), 5.13 (1H, d, *J* 7.0) and 5.11 (1H, d, *J* 7.0)(OCH_2OCH_3), 4.47 (1H, d, *J* 6.0, H-1), 3.88 (1H, m, H-2), 3.82, 3.79, 3.78 (3 × 3H, 3 × s, 3 × OMe), 3.43 (3H, s, OCH_2OCH_3), 3.36 (1H, br s, 1-OH), 2.85 (1H, dd, *J* 14.0 and 8.5) and 2.75 (1H, dd, *J* 14.0 and 5.5)(3-CH_2) and 2.64 (1H, d, *J* 5.5, 2-OH); *m*/*z* 378 (M^+, 50%), 241 (31), 211 (42), 197 (24), 179 (83), 167 (43), 151 (17), 137 (58) and 121 (24) (Found: M^+, 378.1678. $C_{20}H_{26}O_7$ requires M^+, 378.1679); $[\alpha]_D^{25}$ +20.6 (*c* 0.96); CD: $\Delta\varepsilon_{max}$ (λ/nm) -1.5×10^3 (276) and -1.6×10^3 (243).

(1*R*,2*R*)-*syn*-1-(4′-Methoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propane-1,2-diol 19b. $[\alpha]_D^{25}$ −19.1 (*c* 0.91); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+1.5 \times 10^3$ (276) and $+1.6 \times 10^3$ (243); the R_F, ^{1}H NMR and MS data corresponded to those reported for **19a**.

(1*S*,2*S*)-*syn*-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propane-1,2-diol 20a. R_F 0.03 (hexane–benzene–acetone, 5:4:1); δ_H 6.99 (1H, d, *J* 2.0, H-2′), 6.93 (1H, dd, *J* 8.2 and 2.0, H-5′), 6.36 (1H, d, *J* 2.1, H-5″), 6.20 (1H, d, *J* 2.1, H-3″), 5.13 (2H, s, OCH_2OCH_3), 4.47 (1H, dd, *J* 5.8 and 3.0, H-1), 3.90 (1H, m, H-2), 3.90, 3.88, 3.80 (4 × 3H, 3 × s, 4 × OMe), 3.43 (3H, s, OCH_2OCH_3), 3.37 (1H, d, *J* 3.0, 1-OH), 2.85 (1H, dd, *J* 13.0 and 8.5) and 2.77 (1H, dd, *J* 13.0 and 5.5)(3-CH_2) and 2.57 (1H, d, *J* 5.5, 2-OH); *m*/*z* 408 (M^+, 25%), 241 (19), 211 (52), 197 (23), 179 (81), 167 (86), 152 (23), 139 (21) (Found: M^+, 408.1785. $C_{21}H_{28}O_8$ requires M^+, 408.1784); $[\alpha]_D^{25}$ +10.7 (*c* 0.87); CD: $\Delta\varepsilon_{max}$ (λ/nm) -18.0×10^2 (276) and -6.0×10^2 (242).

(1*R*,2*R*)-*syn*-1-(3′,4′-Dimethoxyphenyl)-3-(2″-methoxymethyl-4″,6″-dimethoxyphenyl)propane-1,2-diol 20b. $[\alpha]_D^{25}$ −11.3 (*c* 1.00); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+16.0 \times 10^2$ (276) and $+8.1 \times 10^2$ (241); the R_F, ^{1}H NMR and MS data corresponded to those reported for **20a**.

General procedure for the preparation of the *trans*- and *cis*-3-*O*-acetylflavans

A solution of the corresponding diol **15a**,**b**–**20a**,**b** (1 mmol) and 3 M HCl (1.5 cm^3) in water–methanol (3:1; 20 cm^3) was refluxed at 60 °C for 5–9 h and then diluted with ice–water (20 cm^3). The aqueous phase was separated and extracted with ether (4 × 20 cm^3) and the combined organic phase and extracts were washed with water (4 × 20 cm^3), dried (Na_2SO_4) and evaporated. Subsequent acetylation (acetic anhydride/pyridine) of the residue and preparative TLC (hexane–benzene–acetone, 5:4:1) afforded the corresponding 2,3-*trans*- and 2,3-*cis*-flavan-3-ol derivatives **21a**,**b**–**30a**,**b**.

(2*R*,3*S*)-*trans*-4′-Methoxy-3-*O*-acetylflavan 21a. R_F 0.55 (hexane–benzene–acetone, 5:4:1); δ_H 7.32 (2H, d, *J* 9.0, H-2′,6′), 7.20 (1H, ddd, *J* 8.0, 8.0 and 2.0, H-6), 7.07 (1H, dd, *J* 8.0 and 2.0, H-8), 6.97 (1H, dd, *J* 8.0 and 2.0, H-5), 6.96 (1H, ddd, *J* 8.0, 8.0 and 2.0, H-7), 6.90 (2H, d, *J* 9.0, H-3′,5′), 5.37 (1H, m, H-3), 5.14 (1H, d, *J* 6.1, H-2), 3.82 (3H, s, OMe), 3.07 (1H, dd, *J* 16.0 and 5.0) and 2.89 (1H, dd, *J* 16.0 and 6.5)(4-CH_2) and 1.99 (3H, s, OAc); *m*/*z* 298 (M^+, 11%), 256 (10), 238 (61), 150 (64), 131 (10), 121 (99) and 107 (17) (Found: M^+, 298.1206. $C_{18}H_{18}O_4$ requires M^+, 298.1205); $[\alpha]_D^{25}$ +12.6 (*c* 0.98); CD: $\Delta\varepsilon_{max}$ (λ/nm) -6.8×10^3 (272) and $+8.2 \times 10^3$ (237).

(2*S*,3*R*)-*trans*-4′-Methoxy-3-*O*-acetylflavan 21b. $[\alpha]_D^{25}$ −10.8 (*c* 0.97); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+6.8 \times 10^3$ (272) and -7.6×10^3 (237); the R_F, ^{1}H NMR and MS data corresponded to those reported for **21a**.

(2*S*,3*S*)-*cis*-4′-Methoxy-3-*O*-acetylflavan 26a. Mp 142 °C; R_F 0.51 (hexane–benzene–acetone, 5:4:1); δ_H 7.40 (2H, d, *J* 9.0, H-2′,6′), 7.20 (1H, ddd, *J* 8.0, 8.0 and 2.0, H-6), 7.17 (1H, dd, *J* 8.0 and 2.0, H-8), 6.98 (1H, ddd, *J* 8.0, 8.0 and 2.0, H-7), 6.94 (1H, dd, *J* 8.0 and 2.0, H-5), 6.93 (2H, d, *J* 9.0, H-3′,5′), 5.43 (1H, m, H-3), 5.13 (1H, d, *J* 1.5, H-2), 3.84 (3H, s, OMe), 3.33 (1H, dd, *J* 17.0 and 4.5) and 3.00 (1H, dd, *J* 17.0 and 3.0)(4-CH_2) and 1.93 (3H, s, OAc); *m*/*z* 298 (M^+, 10%), 256 (19), 238 (51), 150 (69), 131 (25), 121 (79) and 107 (19) (Found: M^+, 298.1206. $C_{18}H_{18}O_4$ requires M^+, 298.1205); $[\alpha]_D^{25}$ +66.0 (*c* 0.72); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+6.8 \times 10^3$ (274) and -3.9×10^3 (236).

(2*R*,3*R*)-*cis*-4′-Methoxy-3-*O*-acetylflavan 26b. Mp 140 °C; $[\alpha]_D^{25}$ −72.4 (*c* 0.88); CD: $\Delta\varepsilon_{max}$ (λ/nm) -6.0×10^3 (274) and $+5.0 \times 10^3$ (235); the R_F, ^{1}H NMR and MS data corresponded to those reported for **26a**.

(2*R*,3*S*)-*trans*-7,4′-Dimethoxy-3-*O*-acetylflavan 22a. R_F 0.48 (hexane–benzene–acetone, 5:4:1); δ_H 7.30 (2H, d, *J* 8.8, H-2′,6′), 6.96 (1H, d, *J* 9.0, H-5), 6.90 (2H, d, *J* 8.8, H-3′,5′), 6.54 (1H, d, *J* 2.2, H-8), 6.53 (1H, dd, *J* 9.0 and 2.2, H-6), 5.34 (1H, m, H-3), 5.13 (1H, d, *J* 6.5, H-2), 3.83, 3.80 (2 × 3H, 2 × s, 2 × OMe), 2.99 (1H, dd, *J* 16.5 and 5.0) and 2.83 (1H, dd, *J* 16.5 and 6.5)(4-CH_2) and 2.00 (3H, s, OAc); *m*/*z* 328 (M^+, 14%), 286 (27), 268 (100), 180 (9), 161 (33), 150 (99), 137 (98) and 121 (99) (Found: M^+, 328.1311. $C_{19}H_{20}O_5$ requires M^+, 328.1311);

$[\alpha]_D^{25}$ −21.1 (*c* 0.99); CD: $\Delta\varepsilon_{max}$ (λ/nm) -10.0×10^3 (284) and $+15.0 \times 10^3$ (239).

(2*S*,3*R*)-*trans*-7,4′-Dimethoxy-3-*O*-acetylflavan 22b. $[\alpha]_D^{25}$ +18.4 (*c* 0.90); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+7.8 \times 10^3$ (283) and -13.0×10^3 (238); the R_F, ^{1}H NMR and MS data corresponded to those reported for **22a**.

(2*S*,3*S*)-*cis*-7,4′-Dimethoxy-3-*O*-acetylflavan 27a. Mp 156 °C; R_F 0.44 (hexane–benzene–acetone, 5:4:1); δ_H 7.40 (2H, d, *J* 9.0, H-2′,6′), 7.00 (1H, d, *J* 9.0, H-5), 6.93 (2H, d, *J* 9.0, H-3′,5′), 6.57 (1H, d, *J* 2.5, H-8), 6.56 (1H, dd, *J* 9.0 and 2.5, H-6), 5.40 (1H, m, H-3), 5.11 (1H, d, *J* 1.5, H-2), 3.84, 3.81 (2 × 3H, 2 × s, 2 × OMe), 3.26 (1H, dd, *J* 17.0 and 4.5) and 2.93 (1H, dd, *J* 17.0 and 3.0)(4-CH_2) and 1.93 (3H, s, OAc); *m*/*z* 328 (M^+, 9%), 286 (44), 268 (100), 180 (11), 161 (23), 150 (79), 137 (99) and 121 (90) (Found: M^+, 328.1311. $C_{19}H_{20}O_5$ requires M^+, 328.1311); $[\alpha]_D^{25}$ +94.4 (*c* 0.99); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+2.6 \times 10^3$ (273) and $+3.2 \times 10^3$ (233).

(2*R*,3*R*)-*cis*-7,4′-Dimethoxy-3-*O*-acetylflavan 27b. Mp 153 °C; $[\alpha]_D^{25}$ −100.2 (*c* 0.88); CD: $\Delta\varepsilon_{max}$ (λ/nm) -3.0×10^3 (273) and -2.8×10^3 (235); the R_F, ^{1}H NMR and MS data corresponded to those reported for **27a**.

(2*R*,3*S*)-*trans*-7,3′,4′-Trimethoxy-3-*O*-acetylflavan 23a. R_F 0.27 (hexane–benzene–acetone, 5:4:1); δ_H 6.97 (1H, dd, *J* 8.5 and 2.0, H-6′), 6.92 (1H, d, *J* 2.0, H-2′), 6.90 (1H, d, *J* 2.0, H-8), 6.85 (1H, d, *J* 8.5, H-5), 6.54 (1H, d, *J* 8.5, H-5′), 6.54 (1H, dd, *J* 8.5 and 2.0, H-6), 5.38 (1H, m, H-3), 5.10 (1H, d, *J* 6.0, H-2), 3.89, 3.87, 3.80 (3 × 3H, 3 × s, 3 × OMe), 3.01 (1H, dd, *J* 16.0 and 5.0) and 2.83 (1H, dd, *J* 16.0 and 7.0)(4-CH_2) and 1.98 (3H, s, OAc); *m*/*z* 358 (M^+, 9%), 316 (8), 298 (100), 210 (49), 180 (71), 167 (23), 151 (28) and 137 (23) (Found: M^+, 358.1417. $C_{20}H_{22}O_6$ requires M^+, 358.1416); $[\alpha]_D^{25}$ −15.2 (*c* 0.95); CD: $\Delta\varepsilon_{max}$ (λ/nm) -14.0×10^3 (286) and $+6.9 \times 10^3$ (241).

(2*S*,3*R*)-*trans*-7,3′,4′-Trimethoxy-3-*O*-acetylflavan 23b. $[\alpha]_D^{25}$ +16.9 (*c* 1.03); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+16.0 \times 10^3$ (286) and -7.4×10^3 (241); the R_F, ^{1}H NMR and MS data corresponded to those reported for **23a**.

(2*S*,3*S*)-*cis*-7,3′,4′-Trimethoxy-3-*O*-acetylflavan 28a. R_F 0.24 (hexane–benzene–acetone, 5:4:1); δ_H 7.05 (1H, d, *J* 2.0, H-8′), 7.00 (1H, dd, *J* 8.0 and 2.0, H-6′), 6.97 (1H, d, *J* 2.0, H-2′), 6.88 (1H, d, *J* 8.0, H-5), 6.57 (1H, d, *J* 8.0, H-5′), 6.56 (1H, dd, *J* 8.0 and 2.0, H-6), 5.43 (1H, m, H-3), 5.10 (1H, d, *J* 1.5, H-2), 3.93, 3.91, 3.80 (3 × 3H, 3 × s, 3 × OMe), 3.27 (1H, dd, *J* 17.0 and 4.5) and 2.93 (1H, dd, *J* 17.0 and 3.0)(4-CH_2) and 1.95 (3H, s, OAc); *m*/*z* 358 (M^+, 15%), 316 (5), 298 (100), 210 (56), 180 (61), 167 (42), 151 (31) and 137 (27) (Found: M^+, 358.1417. $C_{20}H_{22}O_6$ requires M^+, 358.1416); $[\alpha]_D^{25}$ +50.8 (*c* 0.80); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+2.1 \times 10^3$ (283) and $+9.1 \times 10^3$ (236).

(2*R*,3*R*)-*cis*-7,3′,4′-Trimethoxy-3-*O*-acetylflavan 28b. $[\alpha]_D^{25}$ −60.3 (*c* 0.86); CD: $\Delta\varepsilon_{max}$ (λ/nm) -2.8×10^3 (283) and -8.6×10^3 (237); the R_F, ^{1}H NMR and MS data corresponded to those reported for **28a**.

(2*R*,3*S*)-*trans*-5,7,4′-Trimethoxy-3-*O*-acetylflavan 24a. Mp 89 °C; R_F 0.45 (hexane–benzene–acetone, 5:4:1); δ_H 7.30 (2H, d, *J* 9.0, H-2′,6′), 6.89 (2H, d, *J* 9.0, H-3′,5′), 6.18 (1H, d, *J* 2.5, H-6), 6.11 (1H, d, *J* 2.5, H-8), 5.35 (1H, m, H-3), 5.06 (1H, d, *J* 6.5, H-2), 3.82, 3.79 (3 × 3H, 2 × s, 3 × OMe), 2.89 (1H, dd, *J* 17.0 and 5.5) and 2.68 (1H, dd, *J* 17.0 and 7.0)(4-CH_2) and 1.97 (3H, s, OAc); *m*/*z* 358 (M^+, 8%), 316 (8), 298 (100), 179 (10), 167 (40), 150 (59) and 121 (23) (Found: M^+, 358.1416. $C_{20}H_{22}O_6$ requires M^+, 358.1416); $[\alpha]_D^{25}$ −20.4 (*c* 0.70); CD: $\Delta\varepsilon_{max}$ (λ/nm) -2.5×10^3 (276) and $+4.5 \times 10^3$ (240).

(2*S*,3*R*)-*trans*-5,7,4′-Trimethoxy-3-*O*-acetylflavan 24b. Mp 88 °C; $[\alpha]_D^{25}$ +23.1 (*c* 0.77); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+2.9 \times 10^3$ (277) and -5.1×10^3 (240); the R_F, ^{1}H NMR and MS data corresponded to those reported for **24a**.

(2*S*,3*S*)-*cis*-5,7,4′-Trimethoxy-3-*O*-acetylflavan 29a. R_F 0.42 (hexane–benzene–acetone, 5:4:1); δ_H 7.40 (2H, d, *J* 9.0, H-2′,6′), 6.93 (2H, d, *J* 9.0, H-3′,5′), 6.21 (1H, d, *J* 2.5, H-6), 6.13 (1H, d, *J* 2.5, H-8), 5.43 (1H, m, H-3), 5.05 (1H, d, *J* 1.5, H-2), 3.84, 3.81, 3.80 (3 × 3H, 3 × s, 3 × OMe), 2.98 (1H, dd, *J* 17.0 and 4.5) and 2.92 (1H, dd, *J* 17.0 and 4.5)(4-CH_2) and 1.94 (3H, s, OAc); *m*/*z* 358 (M^+, 11%), 316 (16), 298 (100), 179 (15), 167 (30), 150 (79) and 121 (13) (Found: M^+, 358.1416. $C_{20}H_{22}O_6$ requires M^+, 358.1416); $[\alpha]_D^{25}$ +55.5 (*c* 0.77); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+1.3 \times 10^3$ (271) and $+3.9 \times 10^3$ (231).

(2*R*,3*R*)-*cis*-5,7,4′-Trimethoxy-3-*O*-acetylflavan 29b. $[\alpha]_D^{25}$ −60.3 (*c* 0.77); CD: $\Delta\varepsilon_{max}$(λ/nm) -1.8×10^3 (272) and -3.7×10^3 (232); the R_F, ^{1}H NMR and MS data corresponded to those reported for **29a**.

(2*R*,3*S*)-*trans*-5,7,3′,4′-Tetramethoxy-3-*O*-acetylflavan 25a. R_F 0.26 (hexane–benzene–acetone, 5:4:1); δ_H 6.93 (1H, dd, *J* 9.0 and 2.0, H-6′), 6.91 (1H, d, *J* 2.0, H-2′), 6.84 (1H, d, *J* 9.0, H-5′), 6.19 (1H, d, *J* 2.5, H-6), 6.12 (1H, d, *J* 2.5, H-8), 5.37 (1H, m, H-3), 5.04 (1H, d, *J* 7.0, H-2), 3.89, 3.87, 3.79, 3.78 (4 × 3H, 4 × s, 4 × OMe), 2.93 (1H, dd, *J* 17.0 and 5.5) and 2.68 (1H, dd, *J* 17.0 and 7.0)(4-CH_2) and 1.97 (3H, s, OAc); *m*/*z* 388 (M^+, 8%), 346 (7), 328 (100), 210 (5), 191 (11), 180 (58), 167 (38), 151 (18) and 137 (9) (Found: M^+, 388.1522. $C_{21}H_{24}O_7$ requires M^+, 388.1522); $[\alpha]_D^{25}$ +18.0 (*c* 0.85); CD: $\Delta\varepsilon_{max}$ (λ/nm) -5.1×10^3 (279) and $+3.7 \times 10^3$ (243).

(2*S*,3*R*)-*trans*-5,7,3′,4′-Tetramethoxy-3-*O*-acetylflavan 25b. $[\alpha]_D^{25}$ −16.3 (*c* 0.75); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+5.5 \times 10^3$ (279) and -3.6×10^3 (243); the R_F, ^{1}H NMR and MS data corresponded to those reported for **25a**.

(2*S*,3*S*)-*cis*-5,7,3′,4′-Tetramethoxy-3-*O*-acetylflavan 30a. R_F 0.23 (hexane–benzene–acetone, 5:4:1); δ_H 7.05 (1H, d, *J* 2.0, H-2′), 6.99 (1H, dd, *J* 8.0 and 2.0, H-6′), 6.88 (1H, d, *J* 8.0, H-5′), 6.23 (1H, d, *J* 2.5, H-6), 6.13 (1H, d, *J* 2.5, H-8), 5.45 (1H, m, H-3), 5.04 (1H, d, *J* 1.5, H-2), 3.93, 3.91, 3.81, 3.80 (4 × 3H, 4 × s, 4 × OMe), 2.98 (1H, dd, *J* 17.0 and 4.0) and 2.92 (1H, dd, *J* 17.0 and 3.5)(4-CH_2) and 1.96 (3H, s, OAc); *m*/*z* 388 (M^+, 21%), 346 (11), 328 (100), 210 (9), 191 (19), 180 (48), 167 (44), 151 (19) and 137 (13) (Found: M^+, 388.1523. $C_{21}H_{24}O_7$ requires M^+, 388.1522); $[\alpha]_D^{25}$ +55.5 (*c* 0.77); CD: $\Delta\varepsilon_{max}$ (λ/nm) $+1.1 \times 10^3$ (271) and $+10.9 \times 10^3$ (238).

(2*R*,3*R*)-*cis*-5,7,3′,4′-Tetramethoxy-3-*O*-acetylflavan 30b. $[\alpha]_D^{25}$ −60.3 (*c* 0.77); CD: $\Delta\varepsilon_{max}$ (λ/nm) -1.1×10^3 (271) and -10.6×10^3 (238); the R_F, ^{1}H NMR and MS data corresponded to those reported for **30a**.

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