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The novel flavan-3-ol, (2*R*,3*S*)-guibourtinidol and its diastereomers ☆

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Abstract

The novel (2*R*,3*S*)-guibourtinidol, representing the first flavan-3-ol with 4′,7-dihydroxy phenolic substitution pattern, was identified in the heartwood of *Cassia abbreviata*. Asymmetric dihydroxylation of (*E*)-1-(4′-*O*-methoxymethylphenyl)-3-(2″,4″-di-*O*-methoxymethylphenyl)-propene with AD-mix-α or AD-mix-β and subsequent acid-catalyzed cyclization afforded the four free phenolic guibourtinidol diastereomers, essentially enantiopure and in good yield. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *Cassia abbreviata*; Flavanoids; Phenolics; Asymmetric dihydroxylation

1. Introduction

Pro- and leucoguibourtinidins with their 4′,7-dihydroxy phenolic functionality represent a relatively rare group of proanthocyanidins which, while occurring as minor components in Australian *Acacia* species (Tindale & Roux, 1974), predominate in the Southern African species, *Guibourtia coleosperma* (Roux & De Bruyn, 1963; Saayman & Roux, 1965; Steynberg, Ferreira & Roux, 1983, 1987), *Julbernardia globiflora* (Pelter, Amenechi, Warren & Harper, 1969), *Acacia luederitzii* (Du Preez, Rowan & Roux, 1970; Ferreira, Du Preez, Wijnmaalen & Roux, 1985) and *Cassia abbreviata* (Malan, Swinny, Ferreira & Steynberg, 1996). A limited number of guibourtinidol derivatives were also found in *Cassia fistula* (Patil & Deshpande, 1982) and *Colophospermum mopane* (Malan et al., 1990).

Continuation of the work on *Cassia abbreviata* (Malan et al., 1996) revealed the presence of the novel (2*R*,3*S*)-4′,7-dihydroxyflavan-3-ol, guibourtinidol **1**, representing the first entry into the guibourtinidol series of diastereomeric flavan-3-ols. The structure of compound **1** and stereoselective synthesis of the free phenolic diastereomers **1** and **4**–**6** are described here.

2. Results and discussion

Guibourtinidol **1** was initially purified and identified as the 4′,7-di-*O*-methyl-3-*O*-acetyl derivative **2**. The ^{1}H NMR spectrum (Table 1) showed an ABMX spin system in the heterocyclic region and ABX and AA′BB′ spin patterns for two aromatic rings. When taken in conjunction with the presence of an *O*-acetyl (δ 1.98) and two *O*-methyl (δ 3.82, 3.80) resonances, these features were reminiscent of the protons of 4′,7-di-*O*-methyl-3-*O*-acetylflavan-3-ol (Van Rensburg, Van Heerden & Ferreira, 1997b). The aromatic spin sys-

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Table 1
^{1}H (300 MHz) and ^{13}C (75.46 MHz) NMR data for guibourtinidols **1**, **4**–**6** and derivative **2** at 296 K. Splitting patterns and *J*-values (Hz) are given in parentheses

Position	**2** ^{1}H($CDCl_3$)	**1**/**6** ^{1}H[$(CD_3)_2CO$]	**4**/**5** ^{1}H[$(CD_3)_2CO$]	**2** ^{13}C($CDCl_3$)	**1**/**6** ^{13}C[$(CD_3)_2CO$]	**4**/**5** ^{13}C[$(CD_3)_2CO$]
2	5.12 (d, 6.5)	4.66 (d, 8.0)	4.98 (d, 1.5)	78.6	82.4	79.1
3	5.30 (m)	4.02 (m)	4.20 (m)	69.8	67.7	66.4
4*eq*	2.99 (dd, 5.0, 16.0)	2.93 (dd, 5.0, 16.0)	3.09 (dd, 4.0, 16.0)	28.7	33.3	33.2
4*ax*	2.82 (dd, 7.0, 16.0)	2.74 (dd, 9.0, 16.0)	2.73 (dd, 3.5, 16.0)	28.7	33.3	
5	6.95 (d, 9.0)	6.88 (d, 9.0)	6.87 (d, 8.0)	130.5	130.5	130.9
6	6.53 (dd, 2.5, 9.0)	6.39 (dd, 2.5, 9.0)	6.37 (dd, 2.5, 8.0)	108.4	108.6	108.6
7				159.9	157.2	157.0
8	6.54 (d, 2.5)	6.30 (d, 2.5)	6.33 (d, 2.5)	101.6	102.8	103.0
9				154.8	155.6	155.8
10				111.4	111.9	111.0
1′				130.5	130.7	130.6
2′/6′	7.30 (d, 9.0)	7.24 (d, 9.0)	7.33 (d, 9.0)	128.0	129.0	128.6
3′/5′	6.90 (d, 9.0)	6.83 (d, 9.0)	6.82 (d, 9.0)	114.3	115.2	114.9
4′				159.9	157.6	157.2
OMe	3.82, 3.80 (each s)			55.7, 55.6		
OAc	1.98 (s)			21.4, 170.6		

tems were differentiated via the appropriate correlation experiments using the H-2(C) and H-4$_{eq}$(C) resonances as reference signals. The 2,3-*trans* relative configuration was evident from the $^3J_{2,3}$-value of 6.5 Hz, such a small coupling constant presumably reflecting significant contributions of A-conformers to the ensemble of conformers related to the C-ring (Tobiason & Hemingway, 1994). A high amplitude negative Cotton effect (−3864) at 283.9 nm in the CD spectrum of derivative **2** was in accordance with chiroptical data of flavan-3-ol derivatives with (2*R*,3*S*) absolute configuration (Korver & Wilkins, 1971; Van Rensburg et al., 1997b). The FAB mass spectrum showed a molecular ion at *m*/*z* 327 $[M\text{-}H]^+$, thus confirming the $C_{19}H_{20}O_5$ molecular formula for compound **2**.

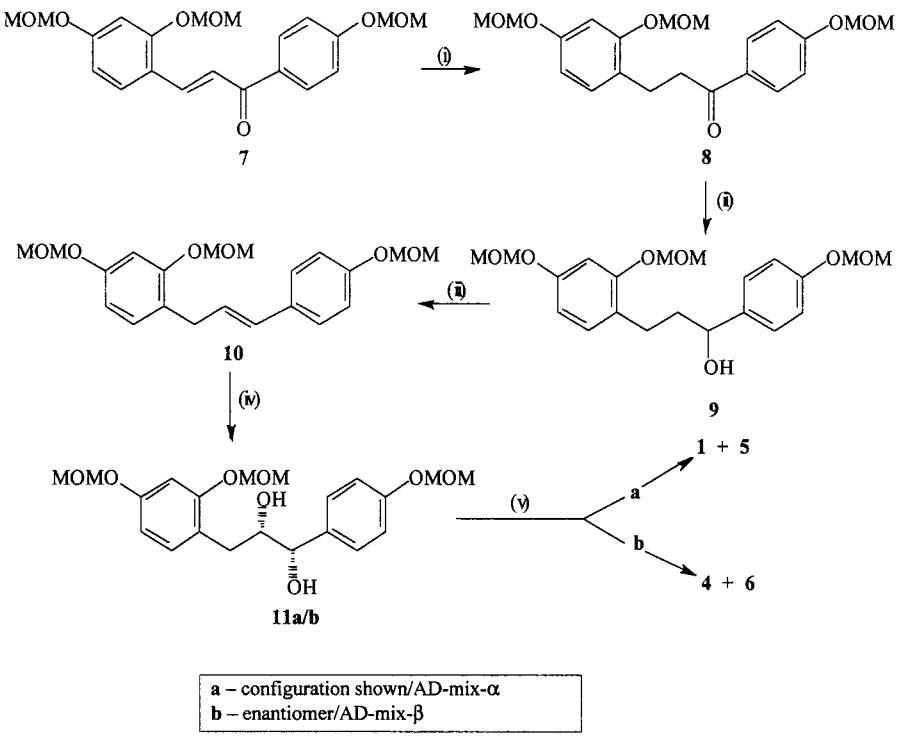
Guibourtinidol **1** was also purified as the peracetate **3** which afforded the free phenolic form via alkaline hydrolysis under an N_2 atmosphere, i.e. conditions which do not effect epimerization at C-2 of the thermodynamically more stable 2,3-*trans*-flavan-3-ol **1** (Kennedy, Munro, Powell, Porter & Foo, 1984). Assignment of the ^{13}C NMR spectra (Table 1) of derivative **2** and of the free phenols, (2*R*,3*S*)-guibourtinidol **1**, (2*S*,3*R*)-guibourtinidol **6** (*ent*-guibourtinidol), (2*R*,3*R*)-guibourtinidol **4** (epiguibourtinidol) and (2*S*,3*S*)-guibourtinidol **5** (*ent*-epiguibourtinidol) were based on HMBC and HMQC experiments.

The identification of guibourtinidol **1** as the first naturally occurring flavan-3-ol with 4′,7-dihydroxy phenolic substitution presented the opportunity to synthesize the four diastereomers **1** and **4**–**6** by adapting our recently developed protocol towards flavan-3-ol derivatives via asymmetric dihydroxylation of 1,3-diarylpropenes and subsequent acid-catalyzed cyclization (Van Rensburg, Van Heerden, Bezuidenhoudt & Ferreira, 1997a; Van Rensburg et al., 1997b) to the first synthesis of free phenolic flavan-3-ols. Owing to the acid lability of methoxymethyl derivative, the MOM functionality was used as a protecting group.

The (*E*)-*retro*-2,4,4′-tri-*O*-methoxymethylchalcone **7** (Scheme 1) was prepared in 72% yield by base-catalyzed condensation of 2,4-di-*O*-methoxymethylbenzaldehyde and 4-*O*-methoxymethylacetophenone. Hydrogenation of chalcone **7** in the presence of 5% Pd/C afforded the *retro*-dihydrochalcone **8** in quantitative yield. Subsequent reduction with $NaBH_4$ gave the 1,3-diarylpropan-1-ol **9** (99%) which was converted into the (*E*)-1,3-diarylpropene **10** (69%) using $SOCl_2$ and 1,8-diazabicyclo[5.4.0]undec-7-ene (1,8-DBU).

Treatment of the (*E*)-1,3-diarylpropene **10** with AD-mix-α in the two-phase system *t*BuOH:H_2O (1:1) (Jeong, Sjö & Sharpless, 1992; Kolb, Van Nieuwenhze & Sharpless, 1994; Sharpless et al., 1992; Wang, Zhang & Sharpless, 1993) afforded the (1*S*,2*S*)-*syn*-diol **11a** ($^3J_{1,2}$ = 6.3 Hz) in high yield (79%) and optical purity (99% ee). The (1*R*,2*R*)-*syn*-diol **11b** (78% yield, 99% ee) was similarly obtained by using AD-mix-β in the same two-phase system. The enantiomeric purity of the diols was determined by ^{1}H NMR using Eu(tfc)$_3$ as a chiral shift reagent while the absolute configuration was assigned according to the Sharpless model (Jeong et al., 1992; Sharpless et al., 1992; Van Rensburg et al., 1997b).

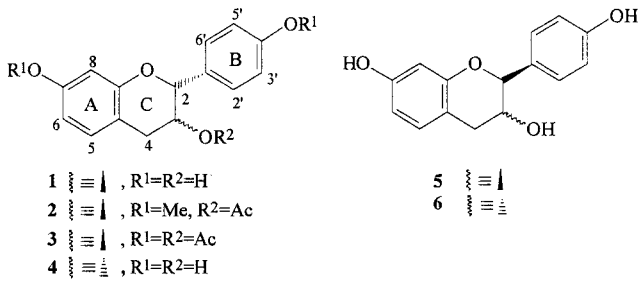
Simultaneous deprotection and cyclization of the (1*S*,2*S*)-*syn*-diol **11a** with 3M HCl in methanol at 60°C gave (2*R*,3*S*)-2,3-*trans*-4′,7-dihydroxyflavan-3-ol **1** (guibourtinidol, 60% yield, 99% ee) and the (2*S*,3*S*)-2,3-*cis*-4′,7-dihydroxyflavan-3-ol **5** (*ent*-epiguibourtinidol, 18% yield, 99% ee). The (1*R*,2*R*)-*syn*-diol **11b** similarly afforded the (2*S*,3*R*)- and (2*R*,3*R*)-4′,7-



Scheme 1. Reagents and conditions: (i) H_2/5% Pd–C; (ii) $NaBH_4$ in EtOH; (iii) $SOCl_2$ in CH_2Cl_2, then DBU; (iv) AD-mix-α or AD-mix-β, *t*-BuOH:H_2O (1:1), $MeSO_2NH_2$, 0°C; (v) 3M HCl, MeOH-H_2O (3:1), reflux.

dihydroxyflavan-3-ols **6** (*ent*-guibourtinidol, 61%, 99% ee) and **4** (epiguibourtinidol, 20%, 99% ee), respectively. The optical purity of the flavan-3-ols was assessed by ^{1}H NMR using Eu(tfc)$_3$ as a chiral shift reagent for the per-*O*-acetates, which consistently indicated the presence of a single enantiomer. Comparison of the CD data (see Experimental) of the synthetic 2,3-*trans*-(**1**/**6**; $^3J_{2,3}=8.0$ Hz) and 2,3-*cis*-(**4**/**5**; $^3J_{2,3}=1.5$ Hz) with published data (Korver et al., 1971; Van Rensburg et al., 1997b), confirmed the absolute stereochemistry of the flavan-3-ols and also the configuration at C-2 of the *syn*-diols **11a/b** as was derived from the Sharpless model (Jeong et al., 1992; Sharpless et al., 1992; Van Rensburg et al., 1997a, 1997b). ^{1}H and ^{13}C NMR data of the flavan-3-ols **1** and **4**–**6** are collated in Table 1.

We have thus demonstrated that the synthetic protocol to flavan-3-ol derivatives (Van Rensburg et al., 1997a, 1997b), i.e. asymmetric dihydroxylation of 1,3-diarylpropenes and subsequent acid-catalyzed cyclization of intermediate *syn*-diols, may be efficiently adapted to access for the first time free phenolic analogues of both 2,3-*trans*- and 2,3-*cis*-configuration in acceptable yields and in a highly stereoselective fashion. This method is currently being applied to include the full range of naturally occurring flavan-3-ols and of radio labelled analogues for much needed biosynthetic studies.



3. Experimental

^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer for solutions as indicated, with TMS as internal standard. FAB mass spectra were recorded on a VG 70-70E instrument with a VG 11-250J data system and an iontech saddlefield FAB gun. TLC was performed on precoated Merck plastic sheets (silica gel PF_{254}, 0.25 mm) and the plates were sprayed with H_2SO_4-HCHO (40:1, v/v) after development. Preparative plates (PLC) [20 × 20 cm, Kieselgel PF_{254} (1.0 mm)] were air dried and used without prior activation. Column chromatography was performed on Sephadex LH-20 in various columns, solvent systems and flow rates (to be specified in each instance). Flash column chromatography (FLC) was on Merck Kieselgel 60 (230–400 mesh) under a positive pressure

by means of compressed N_2. Methylations were performed with an excess of diazomethane in MeOH-Et_2O over a period of 48 h at −15°C, while acetylations were conducted in Ac_2O-pyridine at ambient temperature. Evaporations were done under reduced pressure at ambient temperature in a rotary evaporator, and freeze-drying of aqueous solutions on a Virtis 12 SL freezemobile.

3.1. Isolation of phenolic compounds.

Heartwood drillings (2.7 kg) were repeatedly extracted with Me_2CO (3 × 2.5 L) for 24 h periods at room temperature (25°C). The extract was concentrated by evaporation under vacuum at 35°C. The concentrate was dissolved in H_2O and then freeze-dried to give a pale-brown powder (340.0 g). Two portions (25 g) of the Me_2CO extract were separated on Sephadex LH-20/EtOH columns (5 × 160 cm) with flow rate of 1 ml/min, 32 min fractions. The fractions from columns A and B were combined as follows: C_1 (tubes 17–28, 594.9 mg), C_2 (29–40, 126 mg), C_3 (48–57, 232 mg), C_4 (69–77, 144 mg), C_5 (78–86, 132 mg), C_6 (91–103, 400 mg), C_7 (109–133, 2.72 g), C_8 (134–144, 1.34 g), C_9 (145–154, 3.67 g), C_{10} (155–189, 7.34 g), C_{11} (190–207, 1.69 g), C_{12} (208–237, 3.34 g), C_{13} (238–288, 2.33 g), C_{14} (289–341, 2.75 g), C_{15} (342–376, 508 mg), C_{16} (377–404, 432 mg), C_{17} (405–442, 615 mg), C_{18} (443–471, 235 mg), C_{19} (472–940, 614 mg) and C_{20} (942–1500, 802 mg). Only fraction C_6 will be dealt with here.

Methylation of a PLC purified portion (200 mg) [R_f 0.64, benzene-Me_2CO-MeOH (6:3:1)] of fraction C_6 followed by PLC separation in benzene-Me_2CO (9:1, ×1) afforded four bands [R_f 0.91 (4.7 mg), 0.71 (7 mg), 0.54 (10.4 mg), 0.42 (13 mg)] of which only the latter band was acetylated. Purification by PLC in benzene yielded the permethylaryl ether acetate **2**, R_f 0.22 (12.3 mg). The remaining bands still comprised mixtures and were not further investigated.

The remaining portion of fraction C_6 (200 mg) was acetylated and purified by PLC in benzene-Me_2CO (96:4, ×2) to afford a main band at R_f 0.54 (5.8 mg) which gave the full acetate **3** of guibourtinidol **1**. The acetylated compound was hydrolyzed in 1% KOH and MeOH for 5 min under N_2 at reflux temp. to give the free phenolic compound **1**, R_f 0.46 (5.7 mg).

The low yields of the permethylaryl ether acetate **2** and the full acetate **3** may be ascribed to the extremely complex phenolic mixture which permits the isolation of only those compounds which are visible as discrete bands on PLC.

3.1.1. 4′,7-Di-O-methyl-3-O-acetyl guibourtinidol **2**

Yellowish brown amorphous solid, δ_H and δ_C NMR (Table 1); CD: $\Delta\ \varepsilon_{max}$ [λ (nm)] −3864 (284), +5481 (239), −551 (230), +21.7 (227), +503 (217) (found: M^+, 328.1279. $C_{19}H_{20}O_5$ requires M^+, 328.1273).

3.1.2. Guibourtinidol **1**

Tan amorphous solid, ^1H and ^{13}C NMR spectral data (Table 1), CD — see below (Found: M^+, 258.0881. $C_{15}H_{14}O_4$ requires M^+, 258.0893).

3.2. Stereoselective Synthesis of Guibourtinidols **1** and **4–6**

3.2.1. 4,4′-Tri-O-methoxymethyl-retro-chalcone **7**

To a solution of 4-*O*-methoxymethylacetophenone (3 mmol) was added 50% *aq*. KOH (0.4 ml/mmol acetophenone) and the mixture was stirred at rt for 30 min. 2,4-Di-*O*-methoxymethylbenzaldehyde (3.6 mmol) was added and the mixture was stirred at rt until disappearance of the acetophenone. Water (50 ml) was added and the mixture was extracted with Et_2O (4 × 20 ml). Drying of the extracts with Na_2SO_4 followed by evaporation and FLC in hexane-benzene-Me_2CO (5:4:1) afforded the title compound **7** (R_f 0.34 in hexane-benzene-Me_2CO, 5:4:1) as light-yellow needles from EtOH (72% yield), m.p. 46–47°C; δ_H ($CDCl_3$) 8.13 (d, *J* 15.8. H-β), 8.04 (d, *J* 9.1, H-2′,6′), 7.62 (d, *J* 9.0, H-6), 7.55 (d, *J* 15.8, H-α), 7.13 (d, *J* 9.1, H-3′,5′), 6.87 (d, *J* 2.4, H-3), 6.76 (dd, *J* 9.0 and 2.4, H-5), 5.29, 5.27, 5.22 (3 × s, OCH_2OCH_3), 3.53, 3.52, 3.51 (3 × s, OCH_2OCH_3) (Found: M^+, 388.1517. $C_{21}H_{24}O_7$ requires M^+, 388.1522).

3.2.2. 2,4,4′-Tri-O-methoxymethyl-retro-dihydrochalcone **8**

A solution of the *retro*-chalcone **7** (16 mmol) in EtOH (200 ml) was hydrogenated over 5% Pd–C (1 mg/10 mg chalcone) until all the chalcone was consumed (TLC). The catalyst was filtered off and the EtOH evaporated to afford the title compound **8** (R_f 0.47 in hexane-benzene-Me_2CO, 5:4:1) as a colourless oil in quantitative yield: δ_H 7.97 (d, *J* 9.1, H-2′,6′), 7.12 (d, *J* 8.3, H-6), 7.08 (d, *J* 9.1, H-3′,5′), 6.81 (d, *J* 2.4, H-3), 6.66 (dd, *J* 8.3 and 2.4, H-5), 5.25, 5.21, 5.16 (3 × s, OCH_2OCH_3), 3.50, 3.49 (×2) (2 × s, OCH_2OCH_3), 3.22 (m, β–CH_2), 3.01 (m, α-CH_2) (Found: M^+, 390.1671. $C_{21}H_{26}O_7$ requires M^+, 390.1679).

3.2.3. 1-(4′-O-Methoxymethylphenyl)-3-(2″,4″-di-O-methoxymethylphenyl)-1-propanol **9**

To a solution of the *retro*-dihydrochalcone **8** (15 mmol) in EtOH (200 ml) was added $NaBH_4$ (60 mmol, 4 equiv.) and the mixture was stirred at rt for 12 h. It was diluted with H_2O (100 ml), extracted with Et_2O (3 × 100 ml), the combined extracts dried (Na_2SO_4) and the solvent evaporated to give the title alcohol **9** as a colourless oil in quantitative yield (R_f 0.21 in hex-

ane-benzene-Me_2CO, 5:4:1); δ_H 7.30 (d, *J* 8.8, H-2′,6′), 7.06 (d, *J* 8.2, H-6″), 7.03 (d, *J* 8.8, H-3′,5′), 6.80 (d, *J* 2.3, H-3″), 6.66 (dd, *J* 8.2 and 2.3, H-5″), 5.19 (×2), 5.16 (3 × s, OCH_2OCH_3), 4.63 (m, H-1), 3.50 (×2), 3.48 (3 × s, OCH_2OCH_3), 2.69 (m, 3-CH_2), 2.03 (m, 2-CH_2) (Found: M^+, 392.1841. $C_{21}H_{28}O_7$ requires M^+, 392.1836).

3.2.4. (*E*)-1-(4′-*O*-Methoxymethylphenyl)—3-(2″,4″-di-*O*-methoxymethylphenyl)-propene **10**

Freshly distilled $SOCl_2$ (24 mmol, 2 equiv.) was added dropwise to a solution of the alcohol **9** (12 mmol) in dry CH_2Cl_2 (15 ml), the mixture was stirred at rt for 5 min, dry benzene (20 ml) was added and the mixture evaporated to dryness at 50°C. The resulting chloropropane was dissolved in dry benzene (15 ml), 1,8-DBU (24 mmol, 2 equiv.) was added and the solution was refluxed for 12 h. Satd. *aq*. NH_4Cl was added and the mixture was extracted with Et_2O (3 × 50 ml), the combined extract washed with water (50 ml), dried (Na_2SO_4) and evaporated to dryness. The mixture was purified by PLC in hexane-benzene-Me_2CO (5:4:1) to give propene **10** as a clear oil (R_f 0.62, 69%); δ_H 7.28 (d, *J* 8.9, H-2′,6′), 7.10 (d, *J* 8.3, H-6″), 6.97 (d, *J* 8.9, H-3′,5′), 6.82 (d, *J* 2.4, H-3″), 6.68 (dd, *J* 8.3 and 2.4, H-5″), 6.37 (d, *J* 15.7, H-1), 6.23 (dt, *J* 15.7 and 6.6, H-2), 5.21, 5.18, 5.17 (3 × s, OCH_2OCH_3), 3.50, 3.49 (×2), (3 × s, OCH_3OCH_3), 3.48 (d, *J* 6.6, 3-CH_2) (Found: M^+, 374.1722. $C_{21}H_{26}O_6$ requires M^+, 374.1730).

3.2.5. (1*S*,2*S*)-*syn*-1-(4′-*O*-Methoxymethylphenyl)-3-(2″,4″-di-*O*-methoxymethyl-phenyl)-propane-1,2-diol **11a**

A 10 ml round-bottomed flask, equipped with a magnetic stirrer was charged with *t*BuOH (2.5 ml), water (2.5 ml) and AD-mix-α or -β (700 mg). Stirring of the mixture at rt produced two clear phases; the lower *aq*. phase appearing bright yellow. $MeSO_2NH_2$ (47.6 mg, 0.5 mmol, 1 equiv.) was added, the mixture was cooled to 0°C and treated with propene **10** (0.5 mmol) in Me_2CO (0.5 ml) in one batch. The resulting heterogeneous slurry was stirred vigorously at 0°C for 24 h, Na_2SO_3 (750 mg) was added and the mixture was allowed to warm to rt and stirred for 30 min. EtOAc (30 ml) was added and the organic layer was separated; the *aq*. phase was further extracted with EtOAc (3 × 15 ml), the combined extracts were dried (Na_2SO_4), evaporated to dryness and the mixture separated by PLC in benzene-Me_2CO (9:1) to give the *syn*-diol **11a** as a colourless oil (R_f 0.12, 79%); δ_H 7.33 (d, *J* 8.9, H-2′,6′), 7.05 (d, *J* 8.9, H-3′,5′), 7.04 (d, *J* 8.4, H-6″), 6.79 (d, *J* 2.3, H-3″), 6.67 (dd, *J* 8.4 and 2.3, H-5″), 5.19, 5.15, 5.13 (3 × s, OCH_2OCH_3), 4.49 (dd, J 4.4 and 3.0, H-1), 3.93 (m, H-2), 3.49, 3.48, 3.43 (3 × s, OCH_2OCH_3), 3.03 (d, *J* 4.4, 1-OH), 2.76 (dd, *J* 13.8 and 4.2) and 2.64 (dd, *J* 13.8 and 8.9) (3-CH_2), 2.57 (d, *J* 4.3, 2-OH); CD: Δ ε_{max} [λ (nm)] −230 (271), +4200 (232) (Found: M^+, 408.1791. $C_{21}H_{28}O_8$ requires M^+, 408.1784).

3.2.6. (1*R*,2*R*)-*syn*-1-(4′-*O*-Methoxymethylphenyl)-3-(2″,4″-di-*O*-methoxymethyl-phenyl)-propane-1,2-diol **11b**

CD: $\Delta\varepsilon_{max}$ [λ (nm)] +210 (272), −4300 (233); The ^1H NMR spectral data corresponded to those indicated for **11a** (Found: M^+, 408.1789. $C_{21}H_{28}O_8$ requires M^+, 408.1784.

3.3. General procedure for preparation of the flavan-3-ols

A solution of the diol **11a/11b** (100 mg, 0.25 mmol) and 3 M HCl (0.4 ml) in H_2O:MeOH [1:3 (0.6 ml)] was stirred at 60°C for 5 h and then diluted with ice water (10 ml). The *aq*. solution was extracted with Et_2O (4 × 20 ml), dried (Na_2SO_4) and the solvent evaporated. Purification by PLC in $CHCl_3$-MeOH (9:1) afforded the 2,3-*trans*-flavan-3-ols **1** (R_f 0.38, 60%) and **6** (61%) as well as the 2,3-*cis*-analogues **4** (R_f 0.33, 20%) and **5** (18%).

3.3.1. (2*R*,3*S*)-4′,7-Dihydroxyflavan-3-ol **1**

δ_H and δ_C (Table 1); CD: $\Delta\varepsilon_{max}$ [λ (nm)] = −1800 (275), +3000 (239) (Found: M^+, 258.0889. $C_{15}H_{14}O_4$ requires M^+, 258.0893).

3.3.2. (2*S*,3*R*)-4′,7-Dihydroxyflavan-3-ol **6**

CD: $\Delta\varepsilon_{max}$ [λ (nm)] +1700 (274), −3000 (239). The ^1H and ^{13}C NMR spectral data corresponded to those indicated for **1** (Found: M^+, 258.0883. $C_{15}H_{14}O_4$ requires M^+, 258.0893).

3.3.3. (2*S*,3*S*)-4′,7-Dihydroxyflavan-3-ol **5**

δ_H and δ_C (Table 1); CD: $\Delta\varepsilon_{max}$ [λ (nm)] +2500 (274), −1200 (238) (found: M^+, 258.0897. $C_{15}H_{14}O_4$ requires M^+, 258.0893).

3.3.4. (2*R*,3*R*)-4′,7-Dihydroxyflavan-3-ol **4**

CD: $\Delta\varepsilon_{max}$ [λ (nm)] = −2500 (272), +1000 (238). The ^1H and ^{13}C NMR spectral data corresponded to those indicated for **5** (Found: M^+, 258.0884. $C_{15}H_{14}O_4$ requires M^+, 258.0893).

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