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Synthesis of isoflavonoids. Enantiopure *cis*- and *trans*-6a-hydroxypterocarpans and a racemic *trans*-pterocarpan

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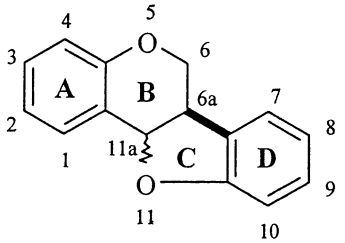
Abstract—Aldol condensation between phenylacetates and benzaldehydes affords 2,3-diaryl-3-hydroxypropanoates which serve as common precursors to both the first racemic *trans*-pterocarpan and enantiopure *cis*- and *trans*-6a-hydroxypterocarpans.

1. Introduction

Over the last few years pterocarpans, the second largest group of natural isoflavonoids,[1] have received considerable attention on account of their medicinal properties. These potent phytoalexins[2] are not only employed as antitoxins[3] but also display antifungal,[4,5] antiviral[3] and antibacterial[6] properties. Computational studies (AM1, molecular mechanics) concur that a *trans*-fused B/C-ring system **1** in pterocarpans is energetically less favorable than the *cis*-fused arrangement **2**,[7] hence confirming the phenomenon that all known naturally occurring pterocarpans possess the 6a,11a-*cis* relative configuration.[1,8]

Recent synthetic endeavors towards pterocarpans comprise Heck arylation,[9,10] the reduction and cyclization of the corresponding 2′-hydroxyisoflavanones,[11] cycloaddition reactions of 2*H*-chromenes with 2-alkoxy-1,4-benzoquinones,[12,13] and 1,3-Michael–Claisen annulation.[14,15] Only two methods, i.e. asymmetric dihydroxylation of an isoflav-3-ene followed by hydrogenative cyclization,[16] and 1,4-benzoquinone cyclo-addition reactions utilizing chiral Ti(IV) complexes,[17,18] permitted enantioselective access to this class of compounds. Here we report the first synthesis of a racemic 6a,11a-*trans*-pterocarpan as well as the stereoselective formation of *cis*- and *trans*-6a-hydroxypterocarpans by adapting not only our direct synthetic approach to *cis*-pterocarpans,[19,20] but also that of Pinard et al.[16] to address the issue of stereocontrol at C-6a and -11a of the pterocarpan framework **1**.



1 ≡ ⋮

2 ≡ ▌

2. Results and discussion

Despite identification of the first 6a-hydroxypterocarpan, (+)-pisatin, in 1960,[21] synthetic protocols to these potent phytoalexins are limited by lengthy multi-step routes and a lack of diversity as far as phenolic hydroxylation patterns are concerned.[1,2] These confinements are so restrictive that only two 6a-hydroxypterocarpans, i.e. pisatin and variabilin, have been synthesized.[2,16,22] Scheme 1 shows our proposed retro-synthetic approach towards 6a-hydroxypterocarpans **3** based on aldol condensation between benzaldehydes **8** and phenylacetates **9** to afford 2,3-diaryl-3-hydroxypropanoates **7**. Reduction and cyclization would then afford 3-benzylsulfanylisoflavans **6**. Oxidation of the latter and subsequent thermal elimination would yield isoflav-3-enes **5** which could give access to 6a-hydroxypterocarpans **3** following asymmetric dihydroxylation to diols **4** and subsequent deprotection and cyclization. Our approach thus shares the

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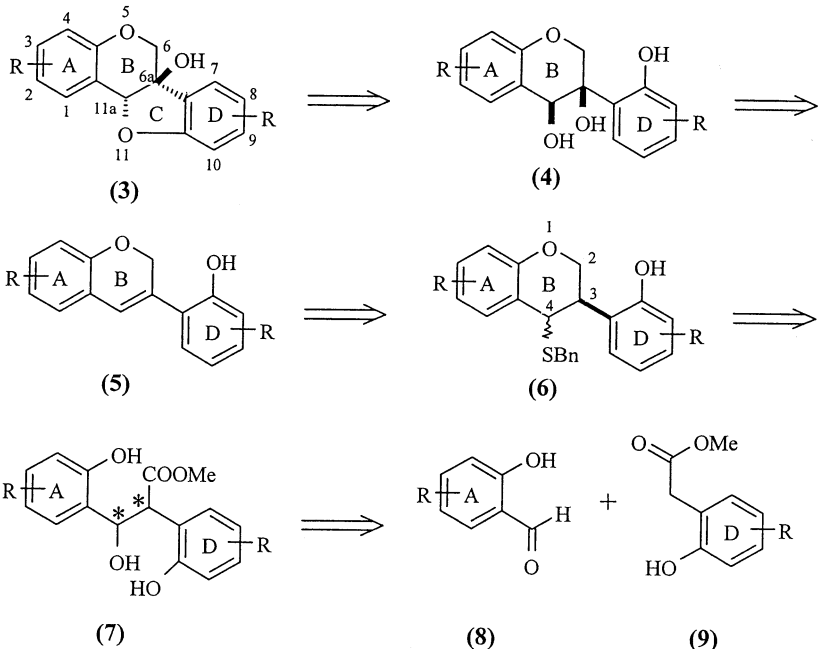


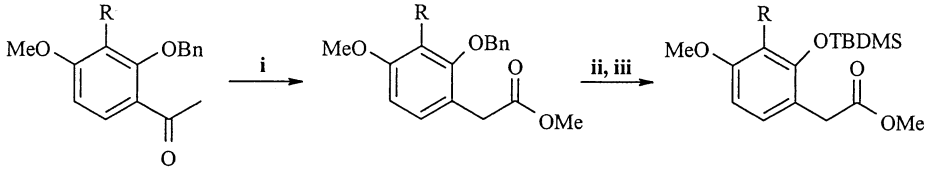
Scheme 1. Retro-synthesis of 6a-hydroxypterocarpans **3**.

key step of asymmetric dihydroxylation of isoflav-3-enes **5** with that of Pinard et al.[16]

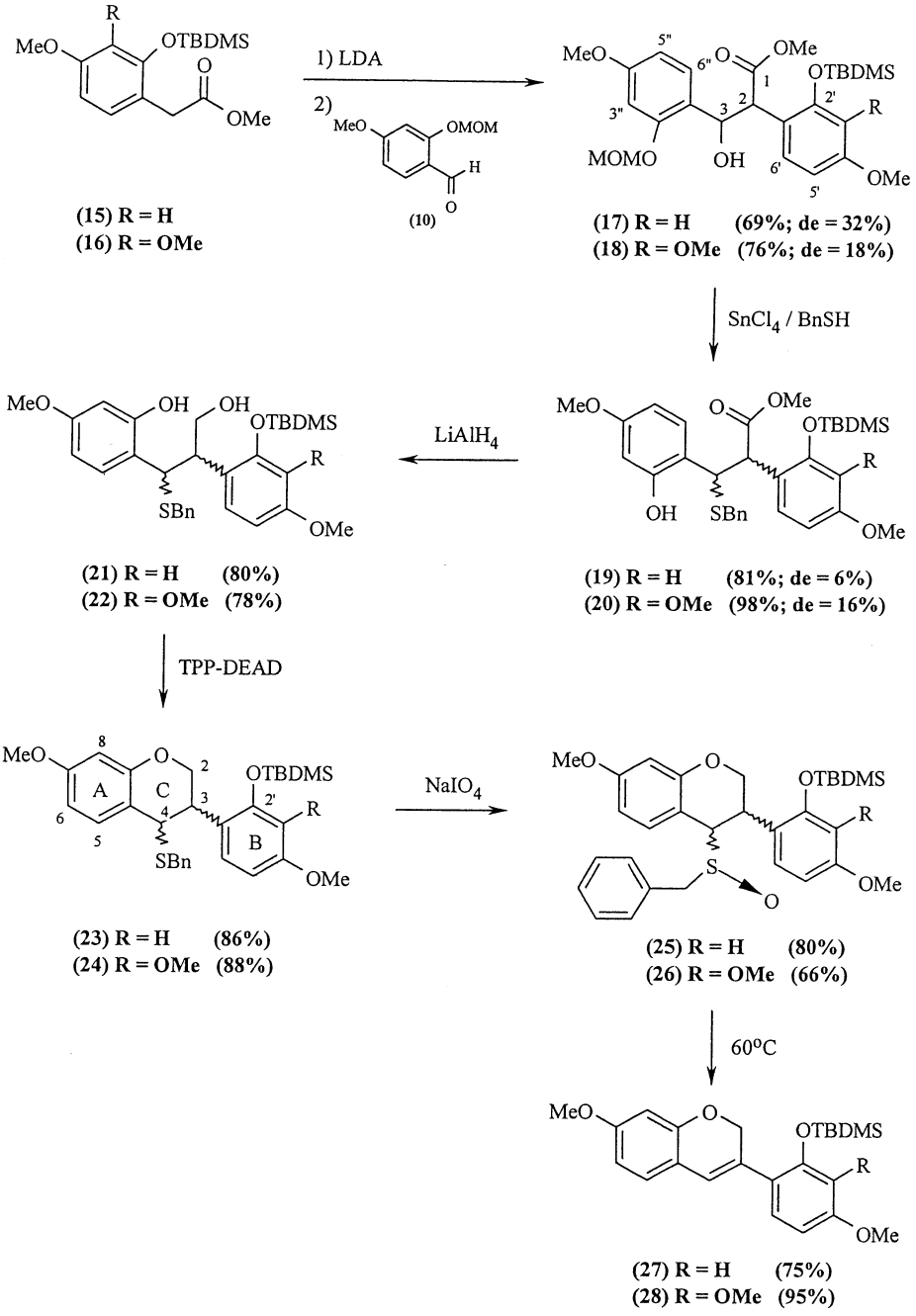
Methoxymethylation of 2-hydroxy-4-methoxybenzaldehyde[23] afforded compound **10** (Scheme 3) which possessed the requisite Lewis acid labile MOM group.[24] The phenylacetates **15** and **16**, in contrast, were protected as the Lewis acid stable *t*-butyldimethylsilyl ethers (TBDMS), hence permitting deprotection at a later stage.[20,25] Since 2-hydroxy-4-methoxy- and 2-hydroxy-3,4-dimethoxyphenylacetic acid are not commercially available, the phenylacetates **13** and **14** were prepared via a thallium(III)-nitrate (TTN) oxidative rearrangement[26] of 2-benzyloxyacetophenones **11** and **12** (Scheme 2). Debenzylation and silylation afforded the requisite acetates **15** and **16** in high yields.

Aldol condensation between phenylacetates **15** and **16**, and benzaldehyde **10** in the presence of lithium diisopropylamide (LDA),[27] afforded propanoates **17** and **18** which were selectively deprotected at the *O*-acetal functionality ($SnCl_4/PhCH_2SH$)[28] to yield 2,3-diaryl-3-benzylsulfanylpropanoates **19** and **20** (Scheme 3). Subsequent reduction ($LiAlH_4$) to propanols **21** and **22** and ensuing cyclization using triphenylphosphine-diethyl azodicarboxylate (TPP-DEAD)[29] afforded 4-benzylsulfanylisoflavans **23** and **24** in good overall yields. Isoflav-3-enes **27** and **28** were obtained via periodate oxidation of the *cis*- and *trans*-4-benzylsulfanylisoflavans **23** and **24** followed by thermal elimination of the sulfoxides **25** and **26**.[30–32]

Stereochemical assignment of the aldol diastereoisomers **17** and **18** was effected by comparing the observed ^1H NMR coupling constants ($^3J_{2,3}$) with the H–C_2–C_3–H dihedral angles of the predicted hydrogen bonded conformations.[20,33] The *erythro* product displayed an H–C_2–C_3–H dihedral angle of 60° which is smaller than the corresponding average dihedral angle of the *threo* conformations, hence leading to 'small' (5–7 Hz) and 'large' (ca. 10.0 Hz) $^3J_{2,3}$ values, respectively. The individual *threo*-($^3J_{2,3}$=10.0 Hz) and *erythro*-($^3J_{2,3}$=5.5–7.0 Hz) propanoates **17** and **18** gave mixtures of *threo*- and *erythro*-3-benzylsulfanylpropanoates **19** and **20**, thus implying an S_N1-type mechanism. Following reduction, *cis*- and *trans*-4-benzylsulfanylisoflavans **23** and **24** were obtained from the respective *threo*- and *erythro*-3-benzylsulfanylpropanols **21** and **22** via Mitsunobu cyclization.[29] ^1H NMR data facilitated identification of the *trans*-propanols and thus subsequent differentiation between the respective *cis*- and *trans* isoflavans **23** and **24**.[20,34] The reactivity of the diastereomeric compounds **19** and **20** was the same in all instances and the isoflav-3-enes **27** and **28** could be generated from both the 3,4-*cis*- and *trans*-benzylsulfanylisoflavans **23** and **24** in comparable yields.

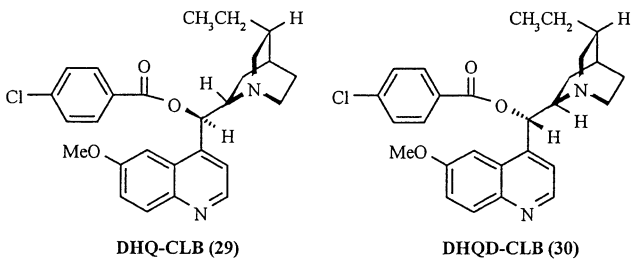


Scheme 2. *Reagents and conditions*: (i) TTN, $HClO_4$, MeOH, rt; (ii) H_2/Pt, acetone, rt; (iii) TBDMSCl, imidazole, DMF, rt.

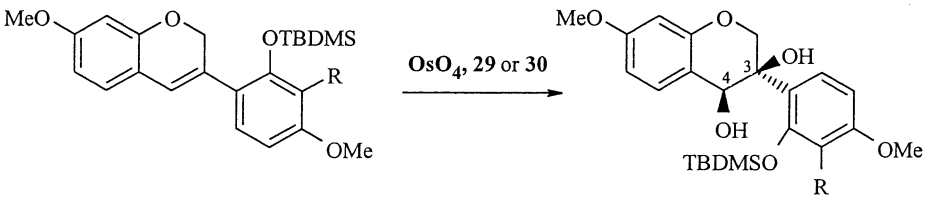


Scheme 3. Synthesis of isoflav-3-enes **27** and **28**.

Owing to the instability of isoflav-3-enes **27** and **28**, swift transformation to the corresponding isoflavan-3,4-diols was essential. The commercially available AD-mix-α or -β[35] was not reactive enough to affect asymmetric dihydroxylation. Therefore, treatment of isoflav-3-enes **27** and **28** in CH_2Cl_2 at −78°C with stoichiometric amounts of OsO_4 in the presence of the chiral catalyst dihydroquinine *p*-chlorobenzoate (DHQ-CLB) **29**, i.e. conditions similar to those employed by Pinard et al.[16] in the synthesis of (+)-pisatin, afforded (−)-(3*R*,4*S*)-*syn*-diols **31a** and **32a** in acceptable yields (63–68%) and excellent enantiomeric excesses (>99%). The (+)-(3*S*,4*R*)-*syn*-diols **31b** and **32b** were similarly obtained by using dihydroquinidine *p*-chlorobenzoate (DHQD-CLB) **30** as chiral ligand (Scheme 4).[16,36] The optical purity was assessed by ^1H NMR employing $Eu(hfc)_3$ as chiral shift reagent which consistently indicated the presence of only one enantiomer. The absolute configuration was tentatively assigned according to the Sharpless model[36,37] for asymmetric dihydroxylation reactions utilizing cinchona alkaloids as chiral ligands (Scheme 5).



DHQ-CLB (29) **DHQD-CLB (30)**



(27) R = H
(28) R = OMe

(31a) R = H
(32a) R = OMe
(31b, 32b) - enantiomers

isoflav-3-ene	ligand	diol	Configuration	yield (%)	ee (%)*	$[\alpha]_D$
27	29	31a	3*R*,4*S* (configuration shown)	65	>99	-28,7°
27	30	31b	3*S*,4*R* (enantiomer)	68	>99	+28.6°
28	29	32a	3*R*,4*S* (configuration shown)	66	>99	-25.8°
28	30	32b	3*S*,4*R* (enantiomer)	63	>99	+26.0°

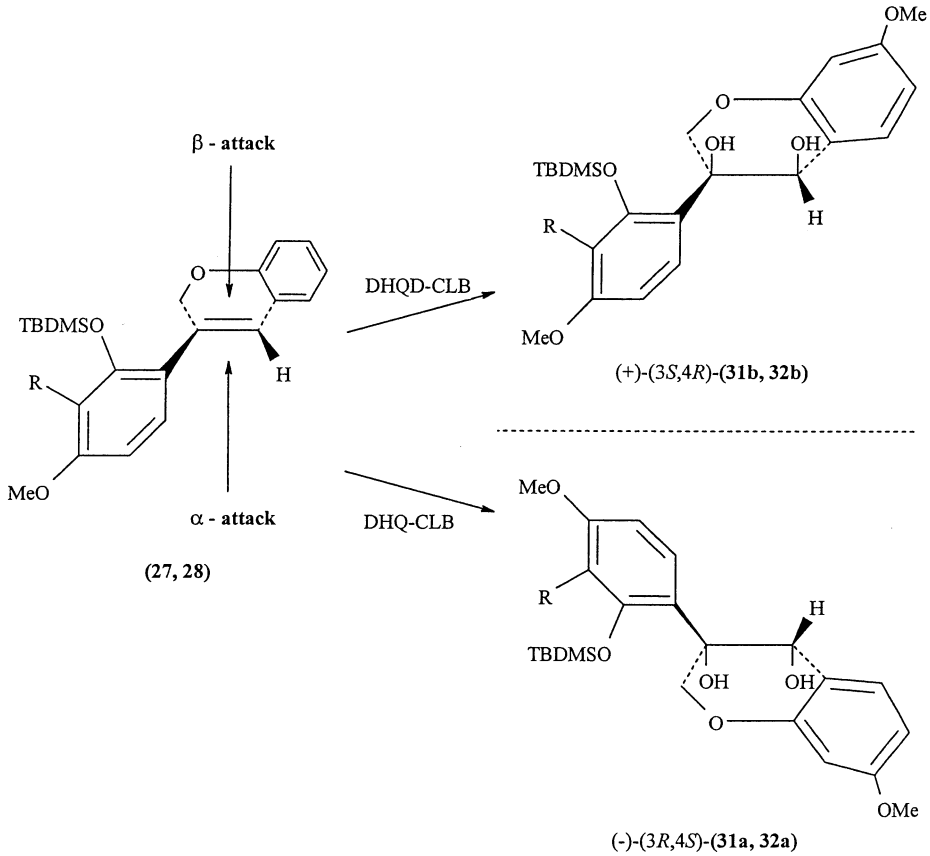
*determined by ^{1}H NMR employing Eu(hfc)$_3$ as chiral shift reagent

Scheme 4. Formation, yields and ee's for the asymmetric dihydroxylation of **27** and **28**.

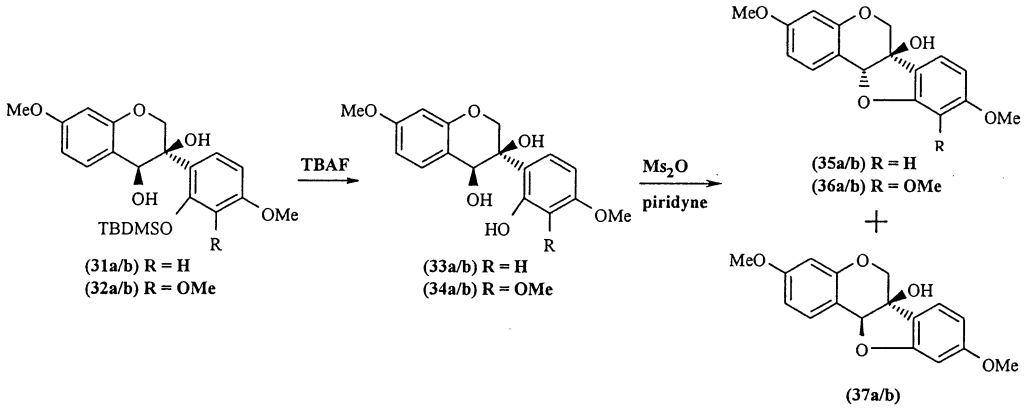
The CD curves of the (−)-(3*R*,4*S*)-diols **31a** and **32a** display sequential positive and negative Cotton effects in the 200–240 and 240–295 nm regions, respectively, the signs of these Cotton effects being reversed for the (+)-(3*S*,4*R*)-diols **31b** and **32b**. Comparison of this data with those of similar derivatives[38] corroborate the absolute stereochemistry as assigned.

Deprotection (TBAF suspended on silica)[39] of diols **31a/b** and **32a/b** afforded 2′-hydroxyisoflavan-3,4-diols **33a/b** and **34a/b** in quantitative yields which then served as precursors to the respective 6a-hydroxypterocarpans **35a/b** and **36a/b**. Attempted cyclization employing Mitsunobu reaction conditions was unsuccessful. However, selective mesylation (Ms_2O, pyridine) activated the secondary 4-hydroxy sufficiently to afford the requisite (6a,11a)-*cis*-6a-hydroxypterocarpans **35a/b** and **36a/b** in good yields and essentially optically pure form (Scheme 6).

It is interesting to note that diols **33a** (3*R*,4*S*) and **33b** (3*S*,4*R*) also afforded (6a*R*,11a*S*)- and (6a*S*,11a*R*)-*trans*-6a-hydroxypterocarpans **37a** and **37b**, respectively, as



Scheme 5. Asymmetric dihydroxylation of isoflav-3-enes **27** and **28**.



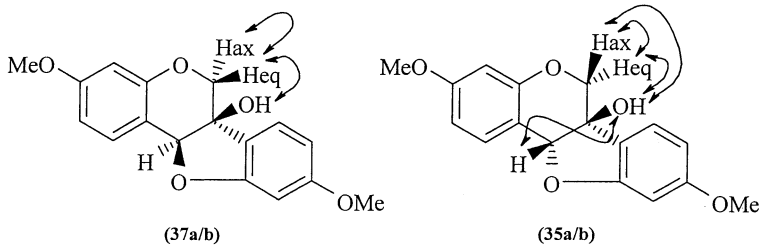
2'-hydroxy	yield (%)	pterocarpan	yield (%)	configuration	ee (%)	$[\alpha]_D$
33a	100	**35a**	70	6a*R*,11a*R* (as indicated)	>99	+223.6
33b	100	**35b**	75	6a*S*,11a*S* (enantiomer)	>99	-220.8
34a	100	**36a**	75	6a*R*,11a*R* (as indicated)	>99	+185.6
34b	100	**36b**	73	6a*S*,11a*S* (enantiomer)	>99	-186.2
33a	100	**37a**	10	6a*R*,11a*S* (as indicated)	>99	-128.6
33b	100	**37b**	9	6a*S*,11a*R* (enantiomer)	>99	-126.4

Scheme 6. Formation, yields and ee's for the transformation of diols **31** and **32**.

minor products (9–10% yield). The heterocyclic protons of both the *cis*- and *trans*-6a-hydroxypterocarpans **35a/b** and **37a/b** resonated in the ^{1}H NMR spectra as a geminal AB-system (δ 4.04, 6-H$_{ax}$, d, J=11.2 Hz; 4.24, 6-H$_{eq}$, dd, J=1.0, 11.2 Hz for **35a/b**, and δ 4.35, 6-H$_{ax}$, d, J=11.9 Hz; 3.99, 6-H$_{eq}$, dd, J=0.5, 11.9 Hz for **37a/b**), and broadened singlets for both 11a-H (δ 5.33 and 4.32 for **35a/b** and **37a/b**, respectively) and 6a-OH (δ 2.48–2.55, 3.22–3.26 for **35a/b** and **37a/b**, respectively). A notable feature is the conspicuous shielding of 11a-H ($\Delta\delta$ −1.01) in the *trans*-isomers **37a/b** relative to its chemical shift in the *cis*-analogues **35a/b**. Such shielding presumably results from the fact that 11a-H is axially orientated relative to both the aromatic A- and D-rings in the *trans*-isomers **37a/b**. Comparison of the NOESY interactions observed for **37** with those of the corresponding *cis*-analogue **35**, clearly indicated the selective interaction between 6a-OH and 11a-H for the latter compound only, thereby confirming a *trans* B/C-ring junction (Scheme 7) for **37**. The selective association of 6a-OH and 2-H$_{eq}$ additionally demonstrated the axial orientation of the 6a-hydroxyl group in the *trans*-analogue **37** as opposed to its equatorial position in the *cis*-isomer **35**. This is the first report on the formation of 6a,11a-*trans*-pterocarpans, in spite of their lower stability compared to those of 6a,11a-*cis*-analogues.[37]

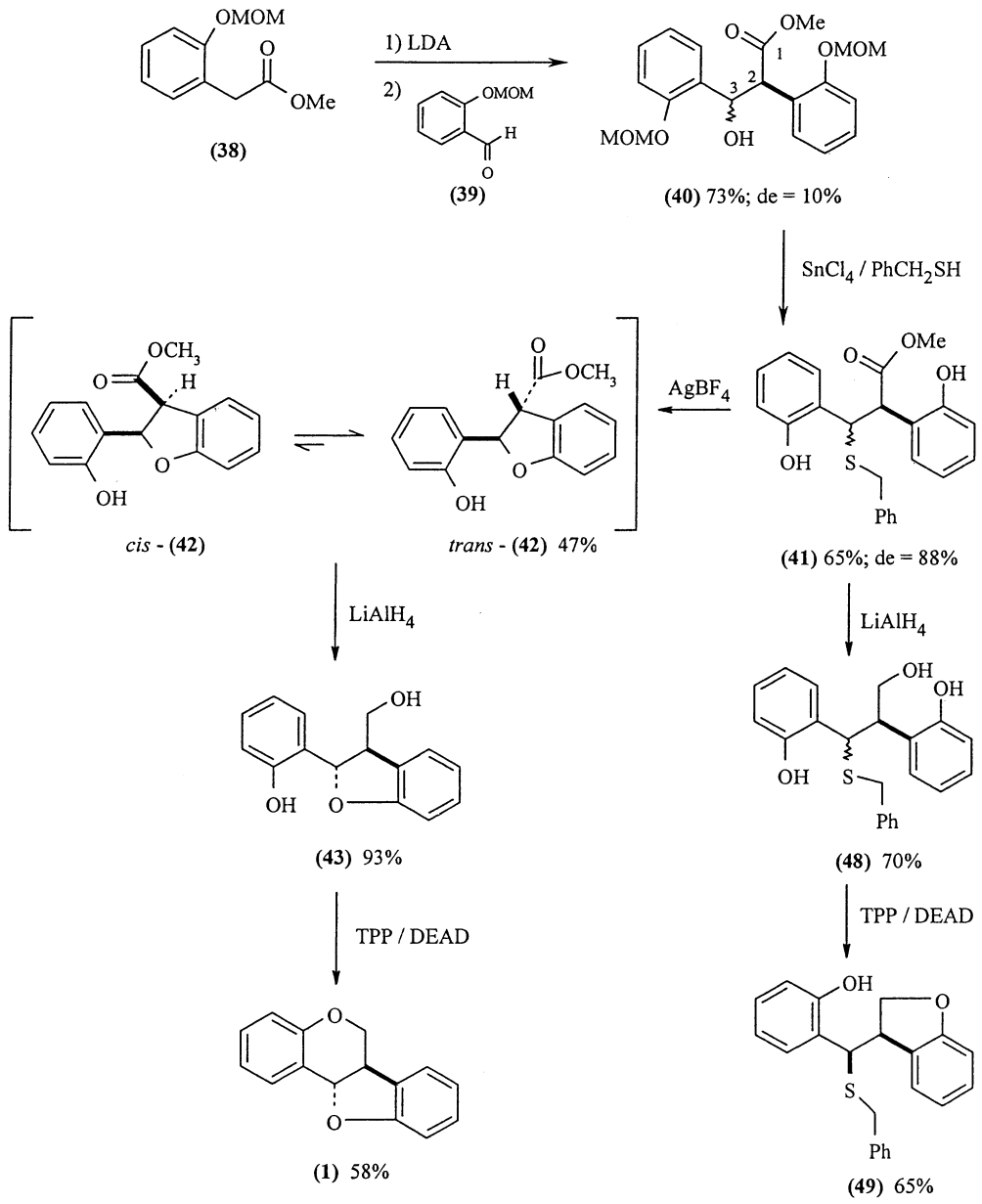
The (6a*R*,11a*R*)-isomers **35a** and **36a** exhibited sequential positive and negative Cotton effects in the 235–255 nm (n,π^* transition) and 275–300 nm (π,π^* transition) regions of their CD spectra, these Cotton effects being reversed in the same regions for the (6a*S*,11a*S*)-isomers **35b** and **36b**.

The absolute stereochemistry of the (+)-(6a*R*,11a*R*)- and (−)-(6a*S*,11a*S*)-*cis*-6a-hydroxypterocarpans **35a/b** and **36a/b** was derived from the corresponding diols **31a/b** and **32a/b**, respectively, as determined by the Sharpless model, assuming that optical integrity was preserved at C-6a during cyclization. The absolute configuration of (6a*R*,11a*S*)-*trans*-**37a** and (6a*S*,11a*R*)-*trans*-6a-hydroxypterocarpan **37b** was derived in a similar manner. However, final confirmation of the absolute stereochemistry and enantiomeric excess of (6a*R*,11a*R*)-**35a** was obtained by comparison of the CD and optical rotation data with those of authentic (+)-variabilin ($[\alpha]_D$=+211° [*c* 0.90, MeOH] vs $[\alpha]_D$=+224° [*c* 0.72, $CHCl_3$] for **35a**).[40–42] The mirror-image relationship of the two sets of isomers, confirmed their enantiomeric connection and hence served as proof of the (6a*S*,11a*S*)



a = configuration shown
b = enantiomer

Scheme 7. Comparison of NOESY interactions for **35a/b** and **37a/b**.



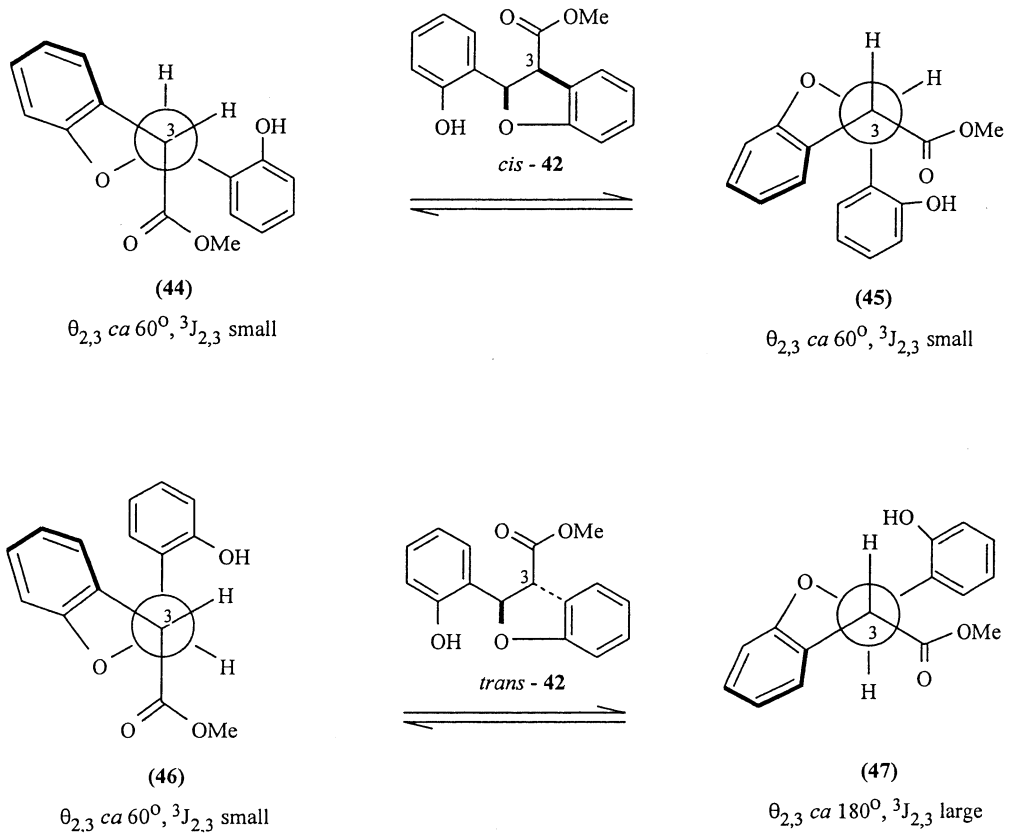
Scheme 8. Synthesis of *trans*-pterocarpan **1**.

absolute configurations of analogues **35b** and **36b**. This data should contribute towards correlating optical rotation and CD data with absolute stereochemistry of 6a-hydroxypterocarpans.

In all reported pterocarpan syntheses, formation of the six-membered B-ring invariably preceeds closure of the five-membered C-ring. Once the B-ring is formed Dreiding models indicate that it becomes virtually impossible to close the C-ring in a configuration other than the 6a,11a-*cis* form. However, we envisaged that reversal of the order of cyclization, i.e. initial C-ring formation followed by B-ring closure, may provide synthetic access to the hitherto unknown 6a,11a-*trans*-pterocarpans.

Thus, aldol condensation between the MOM-protected phenylacetate **38** and benzaldehyde **39**, using LDA for enolate generation,[27] afforded the 2,3-diaryl-3-hydroxypropanoate **40** (10% de) in 73% yield (Scheme 8). Such a low degree of diastereoselectivity is in accordance with previous observations where lithium was employed as the counter-ion.[43,44] Stereochemical assignment of the diastereoisomers of propanoate **40** was effected by comparing the ^{1}H NMR coupling constants ($^3J_{2,3}$=8.9 and 4.1 Hz for *threo*- and *erythro*-isomers, respectively) with the H–C_2–C_3–H dihedral angles of the predicted hydrogen bonded conformations.[20,33]

Deprotection of the acetal functionalities of the individual *threo*- and *erythro*-propanoates **40** using $SnCl_4$/$PhCH_2SH$ as above afforded mainly the *threo*-2,3-diaryl-3-benzylsulfanylpropanoate **41** (88% de; $^3J_{2,3}$=11.9 Hz) in 65% yield. Such a preference for the formation of the *threo*-diastereoisomers presumably reflects a predominant S_N1 mechanism for the thiolysis step. Cyclization ($AgBF_4$) of both the *threo*- and *erythro*-3-benzylsulfanylpropanoates



Scheme 9. Possible conformations for the *cis*-(**44**, **45**) and *trans*-(**46**, **47**) dihydrobenzofurans **42**.

41 to first form the pterocarpan C/D-ring system, afforded the thermodynamically more stable *trans*-fused 2,3-disubstituted dihydrobenzofuran **42** (47%; $^3J_{2,3}$=8.5 Hz, vide infra). Subsequent reduction ($LiAlH_4$) gave the primary alcohol **43** (93%), which was converted under Mitsunobu cyclization conditions into the 6a,11a-*trans*-pterocarpan **1** ($^3J_{6a,11a}$=13.5 Hz) in 58% yield.

In order to establish the relative configuration of the dihydrobenzofuran **42**, structures **44**–**47** were considered as the possible conformations of the *cis*-(**44**, **45**) and *trans*-(**46**, **47**) isomers (Scheme 9). The ^{1}H NMR spectrum of compound **42** exhibited a $^3J_{2,3}$-value of 8.5 Hz reminiscent of a 'large' dihedral angle between the vicinal protons, hence eliminating *cis*-conformers of types **44** and **45** and strongly supporting the presence of an *anti*-conformation of type **47**.

The ^{1}H NMR spectrum of 6a,11a-*trans*-pterocarpan **1** displayed two large couplings between 6a-,6-H_{ax} and 11a-H ($^3J_{6a,6ax}$=12.1; $^3J_{6a,11a}$=13.5 Hz) and a small coupling between 6a- and 6-H_{eq} ($^3J_{6a,6eq}$=4.9 Hz). The corresponding 6a,11a-*cis*-pterocarpan **2** displayed[20] a smaller coupling between 6a- and 11a-H ($^3J_{6a,11a}$=7.1 Hz) as well as W-coupling (J=0.8 Hz) of 6-H_{eq} with 11a-H. When taken in conjunction with the significant NOE association between 6a- and 11a-H in the *cis*-pterocarpan **2** and the conspicuous absence of similar association between the same protons in compound **1**, this was accepted as unequivocal evidence of the 6a,11a-*trans* configuration of the latter compound.

Availability of the free phenolic *threo*-2,3-diaryl-3-benzylsulfanylpropanoate **41** (Scheme 8) offered the opportunity to cut by one the number of steps in our direct synthetic protocol to 6a,11a-*cis*-pterocarpans.[20] However, treatment of the 2,3-diaryl-3-benzylsulfanylpropanol **48**, obtained in 70% yield by reduction ($LiAlH_4$) of propanoate **41**, with PPh_3/DEAD led to the exclusive formation of the 3-substituted 2,3-dihydrobenzofuran **49** in 65% yield. Such a preferential formation of the five- instead of six-membered ring is presumably expressed under the influence of steric interaction in the Mitsunobu cyclization intermediate.

We have thus succeeded in modifying the protocol developed for the synthesis of racemic *cis*-pterocarpans to permit access to the first *trans*-pterocarpan and enantiopure *cis*- and *trans*-6a-hydroxypterocarpans. The latter methodology, although broadly similar to that reported by Pinard et al.[16] for the synthesis of (+)-pisatin, permits the synthesis of 6a-hydroxypterocarpans exhibiting diverse oxygenation patterns and comparable overall yields. It should contribute significantly to advancing the chemistry of this important group of phytoalexins.

3. Experimental

^{1}H NMR spectra were recorded at ambient temperature on a Bruker AM-300 spectrometer for solutions in $CDCl_3$ with the solvent as internal standard. Infrared spectra were recorded in $CHCl_3$ on a Hitachi infrared model 270-50 spectrophotometer. High and low resolution EI-mass spectra

were obtained on a VG 70-70E mass spectrometer. CD data were recorded in MeOH on a Jasco-J710 spectrometer. Melting points (crystals from Me_2CO) were measured on a Reichert hot-stage apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on DC-Alufolien Kieselgel 60 F_{254} (0.25 mm) plates with visualisation by UV light and/or $HCHO–H_2SO_4$ spray. Preparative plates (PLC), Kieselgel PF_{254} (1.0 mm), were air-dried and used without prior activation. Flash column chromatography (FCC) was performed on Merck Kieselgel 60 (230–400 mesh) under a positive pressure by means of compressed N_2.

3.1. 2-Benzyloxyacetophenones 11[20] and 12

To a suspension of NaH (6 mmol) in dry DMF (50 mL) at 0°C, the 2-hydroxyacetophenone (3 mmol) was added in small portions over 20 min. After 5 min. benzyl chloride (12 mmol) was added dropwise. The reaction was stirred at 25°C for 3 h and the excess NaH was destroyed with ice. The mixture was extracted with EtOAc (3×50 mL), the combined EtOAc extract was washed with water (3×50 mL), dried (Na_2SO_4), evaporated to dryness and separated by FCC.

3.1.1. 2-Benzyloxy-4-methoxyacetophenone 11. 669 mg, (87%).[20]

3.1.2. 2-Benzyloxy-3,4-dimethoxyacetophenone 12. 747 mg, (87%); R_f 0.71 (benzene–Me_2CO 9:1) as a dark orange oil; ^1H NMR ($CDCl_3$) δ 2.54 (COCH_3, s, 3H), 3.90, 3.95 (2×OCH_3, 2×s, 2×3H), 5.16 (ArCH_2, s, 2H), 6.76 (6-H, d, J=9.0 Hz, 1H), 7.35–7.50 (ArH, m, 5H), 7.54 (5-H, d, J=9.0 Hz, 1H). δ 2.58; EI-MS found $[M+H]^+$, 287.1280; $C_{17}H_{19}O_4$ $[M+H]^+$ requires 287.1283.

3.2. Methyl 2-benzyloxyphenylacetates 13[20] and 14

A solution of the 2-benzyloxyacetophenones **11** and **12** (6.50 mmol) in MeOH (5 mL) was separately added dropwise to a solution of TTN (6.50 mmol) and 60% perchloric acid (6 mL) in MeOH (30 mL). After stirring at rt for 5 h the MeOH was decanted, water (50 mL) was added and the mixture extracted with $CHCl_3$ (3×100 mL). The combined $CHCl_3$ extract was washed with water (2×100 mL), dried (Na_2SO_4), evaporated and separated by FCC in benzene–Me_2CO (9:1).

3.2.1. Methyl 2-benzyloxy-4-methoxyphenylacetate 13. 1.54 g, (83%).[20]

3.2.2. Methyl 2-benzyloxy-3,4-dimethoxyphenylacetate 14. 1.79 g, (87%); R_f 0.71 (benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$): δ 3.56 (ArCH_2, s, 2H), 3.64, 3.89, 3.90 (3×OCH_3, 3×s, 3×3H), 5.10 (ArCH_2O, s, 2H), 6.67 (5-H, d, J=8.5 Hz, 1H), 6.92 (6-H, d, J=8.5 Hz, 1H), 7.34–7.50 (ArH, m, 5H); EI-MS found $[M+H]^+$, 317.1390; $C_{18}H_{21}O_5$ $[M+H]^+$ requires 317.1389.

3.3. 2-*t*-Butyldimethylsilyloxyphenylacetates 15[20] and 16

A solution of the methyl 2-benzyloxyphenylacetates **13** and **14** (5.4 mmol) in Me_2CO (20 mL) was separately treated with 15% Pd/C (10% m/m) and stirred under an H_2 atmosphere for 5 h. After filtering through Celite® the Me_2CO was evaporated and the product separated by FCC in benzene–Me_2CO (9:1) to give methyl 2-hydroxy-4-metoxyphenylacetate as a light yellow oil; 879 mg, (83%); R_f 0.42 (benzene–Me_2CO 9:1); ^1H NMR ($CDCl_3$) δ 3.64 (ArCH_2, s), 3.76 (COOCH_3, s), 3.77 (OCH_3, s), 6.46 (5-H, dd, J=2.2, 8.0 Hz), 6.51 (3-H, d, J=2.2 Hz), 7.00 (6-H, d, J=8.0 Hz), 7.64 (OH, s), and methyl 2-hydroxy-3,4-dimetoxyphenylacetate as a colourless oil; 1.22 g, (100%); R_f 0.32 (benzene–Me_2CO 9:1); ^1H NMR ($CDCl_3$): δ 3.63 (ArCH_2, s, 2H), 3.73, 3.86, 3.92 (3×OCH_3, 3×s, 3×3H), 6.07 (ArOH, bs, 1H), 6.46 (5-H, d, J=8.9 Hz, 1H), 6.87 (6-H, d, J=8.9 Hz, 1H).

A solution of the 2-hydroxyphenylacetates (6 mmol) in dry DMF (10 mL) was separately treated with imidazole (15 mmol) and TBDMSCl (9 mmol) and stirred at 25°C for 16 h. Et_2O (50 mL) was added and the mixture was washed with water (50 mL), brine (2×50 mL) and again with water (50 mL), dried (Na_2SO_4), evaporated and separated by PLC.

3.3.1. Methyl 2-*t*-butyldimethylsilyloxy-4-methoxyphenylacetate 15. 1.67 g, (90%).[20]

3.3.2. Methyl 2-*t*-butyldimethylsilyloxy-3,4-dimethoxyphenylacetate 16. 1.80 g, (88%); R_f 0.70 (benzene–Me_2CO 9:1) as a light yellow oil; ^1H NMR ($CDCl_3$): δ 0.21 (Si(CH_3)$_2$, s, 6H), 1.00 (^{t}Bu, s, 9H), 3.62 (ArCH2, s, 2H), 3.70, 3.76, 3.86 (3×OCH_3, 3×s, 3×3H), 6.55 (5-H, d, J=8.5 Hz, 1H), 6.89 (6-H, d, J=8.5 Hz, 1H); IR ($CDCl_3$) 1756(CO), 1470, 1338, 1297, 1178 cm^{-1}; EI-MS found $[M+H]^+$, 341.1784; $C_{17}H_{29}O_5Si$ $[M+H]^+$ requires 341.1784.

3.4. 2-*O*-Methoxymethyl-4-methoxybenzaldehyde 10

Prepared as a yellow oil in 94% yield as described earlier.[20]

3.5. 2,3-Diaryl-3-hydroxypropanoates 17[20] and 18

Diisopropylamine (1.1 mmol) in dry Et_2O (1 mL) at 0°C was treated with *n*-BuLi (1.1 mmol). The LDA mixture was cooled to −78°C and the propanoates **15** and **16** (1 mmol) in Et_2O (1 mL) were separately added. After stirring for 30 min the aldehyde **10** in Et_2O (1 mL) was added. The mixture was stirred at −78°C for 1 h and then heated to 0°C. After a further 2 h, phosphate buffer (pH 7.0) (30 mL) was added and the mixture was extracted with EtOAc (3×50 mL). The combined EtOAc layer was washed with water (2×100 mL), dried (Na_2SO_4), evaporated and separated by PLC to afford the aldol products **17** and **18**.

3.5.1. *erythro*- and *threo*-Methyl 2-(2′-*t*-butyldimethylsilyloxy-4′-methoxyphenyl)-3-hydroxy-3-(2″-*O*-methoxymethyl-4″-methoxyphenyl)propanoates 17. 349 mg, (69%); de, 32%.[20]

3.5.2. *erythro*- and *threo*-Methyl 2-(2′-*t*-butyldimethylsilyloxy-3′,4′-dimethoxyphenyl)-3-hydroxy-3-(2″-*O*-methoxymethyl-4″-methoxyphenyl)propanoates 18. 421mg, (76%); de, 18%;

erythro: R_f 0.59 (benzene–Me_2CO 9:1) as yellow needles (mp 76°C); ^1H NMR ($CDCl_3$) δ 0.14, 0.16 (2×SiCH_3, 2×s, 2×3H), 0.95 (^{t}Bu, s, 9H), 3.20 (3-OH, d, J=4.1 Hz, 1H), 3.50, 3.59, 3.61, 3.74, 3.87 (5×OCH_3, 5×s, 5×3H), 4.54 (2-H, d, J=5.5 Hz, 1H), 5.15, 5.25 (OCH_2OCH$_3$, 2×d, J=6.5 Hz, 2×1H), 5.60 (3-H, dd, J=4.1, 5.5 Hz, 1H), 6.36 (5′-H, dd, J=2.2, 8.5 Hz, 1H), 6.61 (5″-H, d, J=8.9 Hz, 1H), 6.64 (3′-H, d, J=2.2 Hz, 1H), 6.77 (6′-H, d, J=8.5 Hz, 1H), 7.24 (6″-H, d, J=8.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −3.9, −3.7 (Si(CH$_3$)$_2$), 19.0 (SiC(CH$_3$)$_3$), 26.5 (SiC(CH$_3$)$_3$), 48.7 (C-2), 52.3 (COOCH$_3$), 55.7 (4″-OCH$_3$), 56.2 (4′-OCH$_3$), 56.7 (OCH$_2$OCH$_3$), 60.7 (3′-OCH$_3$), 69.5 (C-3), 95.0 (CH$_2$OCH$_3$), 101.3 (C-3″), 105.0 (C-5′), 106.6 (C-5″), 119.9 (C-2′), 122.6 (C-1″), 124.2 (C-6″), 128.7 (C-6′), 140.0 (C-3′), 148.7 (C-1′), 153.2 (C-4′), 155.4 (C-2″), 160.4 (C-4″), 174.7 (COOCH$_3$); IR ($CHCl_3$) 2930, 1729 (CO), 1490, 1258 cm^{-1}; EI-MS found $[M+H]^+$, 537.2522; $C_{27}H_{41}O_9Si$ $[M+H]^+$ requires 537.2520.

threo: R_f 0.50 (benzene–Me_2CO 9:1) as yellow needles (mp 102°C); ^1H NMR ($CDCl_3$) δ 0.16, 0.18 (2×SiCH_3, 2×s, 2×3H), 1.04 (^{t}Bu, s, 9H), 3.26 (3-OH, d, J=5.0 Hz, 1H), 3.40, 3.42, 3.71, 3.74, 3.79 (5×OCH_3, 5×s, 5×3H), 4.54 (2-H, d, J=10.0 Hz, 1H), 4.85, 4.99 (OCH_2OCH$_3$, 2×d, J=6.5 Hz, 2×1H), 5.49 (3-H, dd, J=5.0, 10.0 Hz, 1H), 6.43 (5′-H, dd, J=2.2, 8.2 Hz, 1H), 6.45 (5″-H, d, J=8.9 Hz, 1H), 6.50 (3′-H, d, J=2.2 Hz, 1H), 7.11 (6″-H, d, J=8.9 Hz, 1H), 7.24 (6′-H, d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.0, −3.7 (Si(CH$_3$)$_2$), 19.2 (SiC(CH$_3$)$_3$), 26.6 (SiC(CH$_3$)$_3$), 50.3 (C-2), 52.4 (COOCH$_3$), 55.7 (4″-OCH$_3$), 56.2 (4′-OCH$_3$), 56.4 (OCH$_2$OCH$_3$), 60.6 (3′-OCH$_3$), 71.2 (C-3), 95.3 (CH$_2$OCH$_3$), 101.2 (C-3″), 104.9 (C-5′), 106.6 (C-5″), 121.0 (C-1′), 122.3 (C-1″), 123.4 (C-6′), 129.3 (C-6″), 140.1 (C-3′), 147.6 (C-2′), 152.9 (C-4′), 156.0 (C-2″), 160.4 (C-4″), 175.1 (COOCH$_3$); IR ($CHCl_3$) 2928, 1702(CO), 1496, 1242 cm^{-1}; EI-MS found $[M+H]^+$, 537.2520; $C_{27}H_{41}O_9Si$ $[M+H]^+$ requires 537.2520.

3.6. 2,3-Diaryl-3-benzylsulfanylpropanoates 19[20] and 20

3-(2′-*O*-Methoxymethylphenyl)propanoates **17** and **18** (0.4 mmol) in dry DCM (5 mL) at −15°C were separately treated with BnSH (1.6 mmol) followed by $SnCl_4$ (0.6 mmol) under an N_2 atm. The reaction mixture was stirred at −15°C for 15 min and then at 5°C for a further 15 min. Water (20 mL) was added and the mixture was extracted with EtOAc (3×25 mL). The combined EtOAc layer was washed with water (3×50 mL), dried (Na_2SO_4), evaporated and separated by PLC yielding the 3-benzylsulfanylpropanoates **19** and **20**.

3.6.1. *erythro*- and *threo*-Methyl 3-benzylsulfanyl-2-(2′-*t*-butyldimethylsilyloxy-4′-methoxyphenyl)-3-(2″-hydroxy-4″-methoxyphenyl)propanoates 19. 184 mg, (81%); de, 6%.[20]

erythro: ^{13}C NMR ($CDCl_3$) δ −3.8, −3.5 (Si(CH$_3$)$_2$), 18.8 (SiC(CH$_3$)$_3$), 26.3 (SiC(CH$_3$)3), 35.5 (ArCH$_2$S), 43.7 (C-2), 49.2 (C-3), 52.5 (4″-OCH$_3$), 55.6 (COOCH$_3$), 55.7 (4′-OCH$_3$), 103.7 (C-3′), 105.2 (C-3″), 106.7 (C-5″), 107.4 (C-5′), 119.4 (C-2″), 127.4 (Ar–C), 128.7 (2×Ar–C, C-6″), 129.4 (2×Ar–C, C-6′), 132.1 (C-2′), 137.6 (Ar–C), 155.2 (C-1″), 156.9 (C-1′), 160.3 (C-4″), 160.8 (C-4′), 174.0 (COOCH$_3$).

threo: ^{13}C NMR ($CDCl_3$) δ −3.9, −3.8 (Si(CH$_3$)$_2$), 18.8 (SiC(CH$_3$)$_3$), 26.3 (SiC(CH$_3$)$_3$), 35.8 (ArCH$_2$S), 47.1 (C-2), 48.3 (C-3), 52.5 (4″-OCH$_3$), 55.5 (COOCH$_3$), 55.6 (4′-OCH$_3$), 103.1 (C-3″), 105.0 (C-3′), 106.2 (C-5′), 106.4 (C-5″), 115.8 (C-2″), 119.5 (C-2′), 127.8 (Ar–C), 128.8 (C-6″), 128.9 (2×Ar–C), 129.4 (2×Ar–C), 129.8 (C-6′), 129.9 (C-1″), 131.8 (Ar–C), 137.5 (C-1′), 159.8 (C-4″), 160.4 (C-4′), 174.1 (COOCH$_3$).

3.6.2. *erythro*- and *threo*-Methyl 3-benzylsulfanyl-2-(2′-*t*-butyldimethylsilyloxy-3′,4′-dimethoxyphenyl)-3-(2″-hydroxy-4″-methoxyphenyl)propanoates 20. 262 mg, (98%); de, 16%;

erythro: R_f 0.58 (Benzene–Me_2CO 95:5) as light yellow flakes (mp 40°C); ^1H NMR ($CDCl_3$) δ 0.23 0.32 (2×SiCH_3, 2×s, 2×3H), 1.08 (^{t}Bu, s, 9H), 3.30, 3.42 (ArCH_2S, 2×d, J=13.1 Hz, 2×1H), 3.42, 3.77, 3.81, 3.89 (4×OCH_3, 4×s, 4×3H), 4.37 (2-H, d, J=11.5 Hz, 1H), 4.71 (3-H, d, J=11.5 Hz, 1H), 6.48 (5′-H, dd, J=2.9, 8.5 Hz, 1H), 6.52 (3′-H, d, J=2.9 Hz, 1H), 6.54 (5″-H, d, J=8.9 Hz, 1H), 6.99 (6′-H, d, J=8.5 Hz, 1H), 7.04–7.07 (ArH, m, 2H), 7.11 (6″-H, d, J=8.9 Hz, 1H), 7.21–7.27 (ArH, m, 3H), 7.34–7.36 (ArOH, m, 1H); EI-MS found $[M+H]^+$, 599.2500; $C_{32}H_{43}O_7SiS$ $[M+H]^+$ requires 599.2499.

threo: R_f 0.47 (Benzene–Me_2CO 95:5) as light yellow flakes (mp 40°C); ^1H NMR ($CDCl_3$) δ 0.16, 0.20 (2×SiCH_3, 2×s, 2×3H), 1.05 (^{t}Bu, s, 9H), 3.41, 3.69, 3.71, 3.79 (4×OCH_3, 4×s, 4×3H), 3.55, 3.64 (ArCH_2S, 2×d, J=12.9 Hz, 2×1H), 4.35 (2-H, d, J=11.0 Hz, 1H), 4.67 (3-H, d, J=11.0 Hz, 1H), 6.12 (5′-H, dd, J=2.5, 8.5 Hz, 1H), 6.34 (3′-H, d, J=2.5 Hz, 1H), 6.43 (5″-H, d, J=8.9 Hz, 1H), 7.48 (6′-H, d, J=8.5 Hz, 1H), 7.05 (6″-H, d, J=8.9 Hz, 1H), 7.16–7.32 (ArH, ArOH, m, 6H); EI-MS found $[M+H]^+$, 599.2597; $C_{32}H_{43}O_7SiS$ $[M+H]^+$ requires 599.2499.

3.7. 2,3-Diaryl-3-benzylsulfanylpropan-1-ols 21[20] and 22

Benzylsulfanylpropanoates **19** and **20** (0.4 mmol) in dry Et_2O (5 mL) at 10°C were separately treated with an excess of $LiAlH_4$ for 10 min. The $LiAlH_4$ was destroyed by the addition of moist Et_2O (20 mL) followed by aq. NH_4Cl (20 mL). The mixture was extracted with EtOAc (3×20 mL) and the combined organic layers washed with saturated $NaHCO_3$ (20 mL) and water (2×20 mL), dried (Na_2SO_4), evaporated and separated by PLC.

3.7.1. *erythro*- and *threo*-Methyl 3-benzylsulfanyl-2-(2′-*t*-butyldimethylsilyloxy-4′-methoxyphenyl)-3-(2″-hydroxy-4″-methoxyphenyl)propan-1-ol 21. 172mg, (80%).[20]

3.7.2. *erythro*- and *threo*-Methyl 3-benzylsulfanyl-2-(2′-*t*-butyldimethylsilyloxy-3′,4′-dimethoxyphenyl)-3-(2″-hydroxy-4″-methoxyphenyl)propan-1-ol 22; 180mg, (78%). *erythro*: R_f 0.57 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.22, 0.26 (2×SiCH_3, 2×s, 2×3H), 1.00 (^{t}Bu, s, 9H), 1.45–1.55 (C$_1$–OH, m, 1H), 3.35, 3.49 (ArCH_2S, 2×d, J=13.5 Hz, 2×1H), 3.38–3.56 (1-CH_2, m,

2H), 3.69–3.77 (2-H, m, 1H), 3.75, 3.84, 3.88 (3×OCH_3, 3×s, 3×3H), 4.27 (3-H, d, J=11.5 Hz, 1H), 6.51 (5″-H, d, J=9.0 Hz, 1H), 6.54 (5′-H, dd, J=2.5, 8.5 Hz, 1H), 6.55 (3′-H, d, J=2.5 Hz, 1H), 6.68 (6′-H, d, J=8.5 Hz, 1H), 7.10–7.14 (ArH, m, 2H), 7.19 (6″-H, d, J=9.0 Hz, 1H), 7.24–7.33 (ArH, m, 3H), 7.45–7.51 (ArOH, m, 1H); EI-MS found $[M+H]^+$, 571.2550; $C_{31}H_{43}O_6SiS$ $[M+H]^+$ requires 571.2550.

threo: R_f 0.57 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.12, 0.20 (2×SiCH_3, 2×s, 2×3H), 1.03 (^{t}Bu, s, 9H), 1.79–1.87 (C_1–OH, m, 1H), 3.45, 3.59 (ArCH_2S, 2×d, J=13.0 Hz, 2×1H), 3.55, 3.74, 3.80 (3×OCH_3, 3×s, 3×3H), 3.89–3.97 (1-CH_2;2-H, m, 3H), 4.20 (3-H, d, J=8.5 Hz, 1H), 6.25 (5′-H, dd, J=2.5, 8.5 Hz, 1H), 6.37 (3′-H, d, J=2.5 Hz, 1H), 6.42 (5″-H, d, J=8.9 Hz, 1H), 6.66 (6′-H, d, J=8.5 Hz, 1H), 6.67 (6″-H, d, J=8.9 Hz, 1H), 7.15–7.19 (ArH, m, 2H), 7.21–7.32 (ArH, ArOH, m, 4H); EI-MS found $[M+H]^+$, 571.2576; $C_{31}H_{43}O_6SiS$ $[M+H]^+$ requires 571.2550.

3.8. 4-Benzylsulfanylisoflavans 23[20] and 24

Benzylsulfanylpropanols **21** and **22** (0.2 mmol) in dry THF (2 mL) were separately treated with a solution of TPP-DEAD complex [TPP (2 mmol) and DEAD (1 mmol) in dry THF (1 mL)] at 25°C for 4 h. After evaporation of the THF the mixture was redissolved in DCM and separated by PLC affording isoflavans **23** and **24**.

3.8.1. *cis*- and *trans*-4-Benzylsulfanyl-2′-*t*-butyldimethylsilyloxy-4′,7-dimethoxyisoflavans 23. 89mg, (86%).[20]

cis: ^{13}C NMR ($CDCl_3$) δ −4.2, −3.3 (Si(CH_3)$_2$), 18.5 (SiC(CH$_3$)$_3$), 26.0 (SiC(CH_3)$_3$), 36.6 (C-3), 38.2 (ArCH$_2$S), 44.2 (C-4), 55.6, 55.7 (2×OCH$_3$), 66.2 (C-2), 101.2 (C-8), 105.4 (C-3′), 106.0 (C-5′), 108.4 (C-6), 115.9 (C-1′), 122.4 (C-4a), 127.2 (Ar–C), 128.7 (2×Ar–C), 128.9 (C-6′), 129.5 (2×Ar–C), 132.1 (C-5), 139.0 (Ar–C), 155.0 (C-2′, C-8a), 160.0 (C-4′, C-7).

trans: ^{13}C NMR ($CDCl_3$) δ −3.6 (Si(CH_3)$_2$), 18.8 (SiC(CH$_3$)$_3$), 26.3 (SiC(CH_3)$_3$), 36.0 (ArCH$_2$S), 37.6 (C-3), 43.7 (C-4), 55.5, 55.7 (2×OCH$_3$), 67.3 (C-2), 101.5 (C-8), 105.6 (C-3′), 106.0 (C-5′), 108.6 (C-6), 114.4 (C-4a), 123.8 (C-1′), 127.4 (Ar–C), 128.9 (2×Ar–C, C-6′), 129.4 (2×Ar–C), 132.0 (C-5), 138.3 (Ar–C), 154.4 (C-2′), 156.6 (C-8a), 159.5 (C-4′), 160.1 (C-7).

3.8.2. *cis*- and *trans*-4-Benzylsulfanyl-2′-*t*-butyldimethylsilyloxy-3′,4′,7-trimethoxyisoflavans 24. 98 mg, (88%).

cis: R_f 0.63 (Benzene) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.15, 0.35 (SiCH_3, 2×s, 2×3H), 0.86 (^{t}Bu, s, 9H), 2.76, 3.05 (ArCH_2S, 2×d, J=13.0 Hz, 2×1H), 3.75, 3.84, 3.91 (3×OCH_3, 3×s, 3×3H), 3.88 (3-H, ddd, J=3.0, 3.8, 11.5 Hz, 1H), 4.19 (4-H, dd, J=2.0, 3.8 Hz, 1H), 4.33 (2-H$_{eq}$, ddd, J=2.0, 3.0, 10.1 Hz, 1H), 4.65 (2-H$_{ax}$, dd, J=10.1, 11.5 Hz, 1H), 6.33 (8-H, d, J=2.5 Hz, 1H), 6.40 (6-H, dd, J=2.5, 8.2 Hz, 1H), 6.66 (5′-H, d, J=8.9 Hz, 1H), 6.67 (6′-H, d, J=8.9 Hz, 1H), 6.88 (5-H, d, J=8.2 Hz, 1H), 7.17–7.34 (ArCH$_2$S, m, 5H); EI-MS found $[M+H]^+$, 553.2441; $C_{31}H_{41}O_5SiS$ $[M+H]^+$ requires 553.2444.

trans: R_f 0.63 (Benzene) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.30, 0.32 (SiCH_3, 2×s, 2×3H), 1.07 (^{t}Bu, s, 9H), 3.70, 3.83 (ArCH_2S, 2×d, J=12.9 Hz, 2×1H), 3.78, 3.81, 3.82 (3×OCH_3, 3×s, 3×3H), 3.87 (3-H, ddd, J=3.0, 3.9, 4.5 Hz, 1H), 3.96 (4-H, dd, J=1.1, 3.9 Hz, 1H), 4.24 (2-H$_{eq}$, ddd, J=1.1, 4.5, 11.0 Hz, 1H), 4.55 (2-H$_{ax}$, dd, J=3.0, 11.0 Hz, 1H), 6.37 (8-H, d, J=2.5 Hz, 1H), 6.40 (5′-H, d, J=8.9 Hz, 1H), 6.50 (6′-H, d, J=8.9 Hz, 1H), 6.52 (6-H, dd, J=2.5, 8.5 Hz, 1H), 7.22 (5-H, d, J=8.5 Hz, 1H), 7.22–7.30 (ArCH$_2$S, m, 5H); EI-MS found $[M+H]^+$, 553.2445; $C_{31}H_{41}O_5SiS$ $[M+H]^+$ requires 553.2444.

3.9. 4-Benzylsulfonylisoflavans 25 and 26

4-Benzylsulfanylisoflavans **23** and **24** (0.30 mmol), dissolved in MeOH (5 mL), were separately treated with 4 M $NaIO_4$ (1.20 mmol) and stirred for 16 h at rt, after which a further portion of $NaIO_4$ (0.5 equiv.) was added and the mixture stirred for 30 min. After filtration the solvent was evaporated and the residue redissolved in EtOAc (50 mL). The organic layer was washed with water, dried (Na_2SO_4) and evaporated under reduced pressure. The products were purified by PLC.

3.9.1. *cis*- and *trans*-4-Benzylsulfonyl-2′-*t*-butyldimethylsilyloxy-4′,7-dimethoxyisoflavan 25. 128 mg, (80%).

cis: R_f 0.40 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.21, 0.33 (SiCH_3, 2×s, 2×3H), 0.92 (^{t}Bu, s, 9H), 3.25, 3.56 (ArCH_2SO, 2×d, J=13.0 Hz, 2×1H), 3.79, 3.84 (2×OCH_3, 2×s, 2×3H), 3.94 (3-H, ddd, J=3.5, 4.0, 12.0 Hz, 1H), 4.23 (4-H, dd, J=2.0, 4.0 Hz, 1H), 4.46 (2-H$_{eq}$, ddd, J=2.0, 3.5, 10.5 Hz, 1H), 4.91 (2-H$_{ax}$, dd, J=10.5, 12.0 Hz, 1H), 6.46–6.51 (6-,8-,3′-H, m, 3H), 6.57 (5′-H, dd, J=2.5, 8.5 Hz, 1H), 6.61 (5-H, d, J=8.5 Hz, 1H), 7.02 (6′-H, d, J=8.5 Hz, 1H), 7.07–7.12 (ArH, m, 2H), 7.28–7.32 (ArH, m, 3H); EI-MS found $[M+H]^+$, 539.2289; $C_{30}H_{39}O_5SiS$ $[M+H]^+$ requires 539.2288.

trans: R_f 0.44 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.34, 0.35 (SiCH_3, 2×s, 2×3H), 1.06 (^{t}Bu, s, 9H), 3.71–3.76 (3-H, m, 1H), 3.76, 3.80 (2×OCH_3, 2×s, 2×3H), 3.84, 4.08 (ArCH_2SO, 2×d, J=13.0 Hz, 2×1H), 3.95–3.97 (4-H, m, 1H), 4.24 (2-H$_{eq}$, dm, J=11.0 Hz, 1H), 4.43 (2-H$_{ax}$, dd, J=3.8, 11.0 Hz, 1H), 6.39 (5′-H, dd, J=2.5, 8.5 Hz, 1H), 6.45 (8-H, d, J=2.5 Hz, 1H), 6.49 (3′-H, d, J=2.5 Hz, 1H), 6.57 (6-H, dd, J=2.5, 8.5 Hz, 1H), 6.88 (6′-H, d, J=8.1 Hz, 1H), 7.09 (5-H, d, J=8.5 Hz, 1H), 7.21–7.26 (ArH, m, 2H), 7.30–7.35 (ArH, m, 3H); EI-MS found $[M+H]^+$, 539.2287; $C_{30}H_{39}O_5SiS$ $[M+H]^+$ requires 539.2288.

3.9.2. *cis*- and *trans*-4-Benzylsulfonyl-2′-*t*-butyldimethylsilyloxy-3′,4′,7-trimethoxyisoflavan 26. 103 mg, (60%).

cis: R_f 0.24 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.14, 0.34 (SiCH_3, 2×s, 2×3H), 0.89 (^{t}Bu, s, 9H), 3.10, 3.65 (ArCH_2SO, 2×d, J=13.1 Hz, 2×1H), 3.78, 3.80, 3.92 (3×OCH_3, 3×s, 3×3H), 4.00 (3-H, ddd, J=4.0, 4.0, 12.0 Hz, 1H), 4.28 (4-H, dd, J=2.5, 4.0 Hz, 1H), 4.46 (2-H$_{eq}$, ddd, J=2.5, 4.0, 10.9 Hz, 1H), 4.87 (2-H$_{ax}$, dd, J=10.9, 12.0 Hz, 1H), 6.45 (ArH, m, 3H), 6.61 (5-H, d,

J=8.5 Hz, 1H), 6.79 (6′-H, d, J=8.5 Hz, 1H), 7.15–7.20 (Ar*H*, m, 2H), 7.33–7.36 (Ar*H*, m, 3H); EI-MS found $[M+H]^+$, 569.2390; $C_{31}H_{41}O_6SiS$ $[M+H]^+$ requires 569.2393.

trans: R_f 0.47 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.28, 0.33 (SiCH_3, 2×s, 2×3H), 1.06 (^{t}Bu, s, 9H)), 3.79, 3.79, 3.82 (3×OCH_3, 3×s, 3×3H), 3.83 (3-H, ddm, J=2.5, 3.5 Hz, 1H), 3.84, 4.11 (ArCH_2S, 2×d, J=12.8 Hz, 2×1H), 3.92–3.95 (4-H, m, 1H), 4.24 (2-H_{eq}, ddd, J=1.2, 2.5, 11.1 Hz, 1H), 4.42 (2-H_{ax}, dd, J=3.5, 11.1 Hz, 1H), 6.43 (5′-H, d, J=8.9 Hz, 1H), 6.49 (8-H, d, J=2.5 Hz, 1H), 6.57 (6-H, dd, J=2.5, 8.5 Hz, 1H), 6.64 (6′-H, d, J=8.9 Hz, 1H), 7.06 (5-H, d, J=8.5 Hz, 1H), 7.23–7.27 (Ar*H*, m, 2H), 7.30–7.35 (Ar*H*, m, 3H); EI-MS found $[M+H]^+$, 569.2394; $C_{31}H_{41}O_6SiS$ $[M+H]^+$ requires 569.2393.

3.10. Isoflav-3-enes 27 and 28

The respective sulfoxides **25** and **26** (0.2 mmol) were dissolved in $CHCl_3$ (20 mL) and stirred for 24 h at 60°C. After evaporation of the solvent, separation by PLC afforded the isoflav-3-enes **27** and **28**.

3.10.1. 2′-*t*-Butyldimethylsilyloxy-4′,7-dimethoxyisoflav-3-ene 27. 79 mg, (75%); R_f 0.74 (benzene) as a yellow oil; ^1H NMR ($CDCl_3$) δ 0.24 (Si(CH_3)$_2$, s, 6H), 1.00 (^{t}Bu, s, 9H), 3.81, 3.81 (2×OCH_3, 2×s, 2×3H), 5.01 (2-H_2, s, 2H), 6.44 (3′-H, d, J=2.5 Hz, 1H), 6.47 (8-H, d, J=2.5 Hz, 1H), 6.49 (6-H, dd, J=2.5, 8.0 Hz, 1H), 6.54 (4-H, bs, 1H), 6.56 (5′-H, dd, J=2.5, 8.1 Hz, 1H), 6.98 (5-H, d, J=8.0 Hz, 1H), 7.19 (6′-H, d, J=8.1 Hz, 1H); EI-MS found $[M+H]^+$, 399.1955; $C_{23}H_{31}O_4Si$ $[M+H]^+$ requires 399.1960.

3.10.2. 2′-*t*-Butyldimethylsilyl-3′,4′,7-trimethoxyisoflav-3-ene 28. 106 mg, (95%); R_f 0.56 (benzene) as a light yellow oil; ^1H NMR ($CDCl_3$) δ 0.15 (Si(CH_3)$_2$, s, 6H), 0.98 (^{t}Bu, s, 9H), 3.80, 3.81, 3.89 (3×OCH_3, 3×s, 3×3H), 5.00 (2-H_2, s, 2H), 6.46 (3-H, d, J=2.2 Hz, 1H), 6.49 (6-H, dd, J=2.2, 8.0 Hz, 1H), 6.54 (4-H, bs, 1H), 6.59 (5′-H, d, J=8.5 Hz, 1H), 6.94 (6′-H, d, J=8.5 Hz, 1H), 6.96 (5-H, d, J=8.0 Hz, 1H); EI-MS found $[M+H]^+$, 429.2095; $C_{24}H_{33}O_5Si$ $[M+H]^+$ requires 429.2097.

3.11. Isoflavan-3,4-diols 31a/b and 32a/b

The respective isoflav-3-enes **27** and **28** (0.20 mmol) and chiral ligands DHQ-CLB **29** or DHQD-CLB **30** (0.30 mmol) were dissolved in anhydrous DCM (2 mL), cooled to −78°C and treated with OsO_4 (0.20 mmol) for 24 h. The resulting dark green solution was treated with aqueous 20% Na_2SO_3/20%–$NaHSO_4$ for 1 h at rt. Water (5 mL) was added and the mixture extracted with Et_2O (3×20 mL). The combined organic layer was washed with water (2×25 mL), dried (Na_2SO_4), evaporated and the products purified by PLC.

3.11.1. (−)-(3*R*,4*S*)-2′-*t*-Butyldimethylsilyloxy-4′,7-dimethoxyisoflavan-3,4-diol 31a. 56 mg, (65%); R_f 0.40 (benzene–Me_2CO 9:1) as a yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -3.02×10^3 (287), -5.06×10^3 (268), $+1.77\times10^3$ (238); $[\alpha]_D^{25}=-28.7$ (c 0.57, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.39, 0.40 (2×SiCH_3, 2×d, 2×3H), 1.04 (^{t}Bu, s, 9H), 2.84 (4-O*H*, d, J=6.0 Hz, 1H), 3.77, 3.79 (2×OCH_3, 2×s, 2×3H), 4.29, 4.39 (2-H_2, 2×d, J=11.1 Hz, 2×1H), 4.39 (3-O*H*, s, 1H), 5.18 (4-H, d, J=6.0 Hz, 1H), 6.42 (8-H, d, J=2.5 Hz, 1H), 6.46 (3′-H, d, J=2.2 Hz, 1H), 6.50 (5′-H, dd, J=2.2, 8.2 Hz, 1H), 6.57 (6-H, dd, J=2.5, 8.2 Hz, 1H), 7.36 (6′-H, d, J=8.2 Hz, 1H), 7.43 (5-H, d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −3.4, −3.3 (Si(*C*H$_3$)$_2$), 18.7 (Si*C*(CH$_3$)$_3$), 26.3 (SiC(*C*H$_3$)$_3$), 55.7 (2×O*C*H$_3$), 68.2 (C-4), 69.4 (C-2), 71.7 (C-3), 101.2 (C-8), 106.1 (C-3′), 106.2 (C-5′), 108.7 (C-6), 116.2 (C-4a), 122.0 (C-1′), 129.2 (C-6′), 130.8 (C-5), 154.7 (C-2′), 154.8 (C-8a), 160.6 (C-4′), 161.0 (C-7); EI-MS found $[M+H]^+$, 433.2043; $C_{23}H_{33}O_6Si$ $[M+H]^+$ requires 433.2047.

3.11.2. (+)-(3*S*,4*R*)-2′-*t*-Butyldimethylsilyloxy-4′,7-dimethoxyisoflavan-3,4-diol 31b. 55 mg, (68%); R_f 0.40 (benzene–Me_2CO 9:1) as a yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: $+3.10\times10^3$ (287), $+5.00\times10^3$ (268), -1.82×10^3 (238); $[\alpha]_D^{25}=+28.6$ (c 0.49, $CHCl_3$); ^1H- and ^{13}C NMR ($CDCl_3$) as for **31a**; EI-MS found $[M+H]^+$, 433.2046; $C_{23}H_{33}O_6$ Si $[M+H]^+$ requires 433.2047.

3.11.3. (−)-(3*R*,4*S*)-2′-*t*-Butyldimethylsilyloxy-3′,4′,7-trimethoxyisoflavan-3,4-diol 32a. 61 mg, (66%); R_f 0.49 (benzene–Me_2CO 9:1) as a yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -6.16×10^3 (281), $+1.69\times10^3$ (220); $[\alpha]_D^{25}=-25.8$ (c 0.58, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.34, 0.39 (2×SiCH_3, 2×d, 2×3H), 1.03 (^{t}Bu, s, 9H), 2.91 (4-O*H*, d, J=6.5 Hz, 1H), 3.79, 3.80, 3.86 (3×OCH_3, 3×s, 3×3H), 4.26, 4.32 (2-H_2, 2×d, J=11.5 Hz, 2×1H), 4.82 (3-O*H*, s, 1H), 5.15 (4-H, d, J=6.5 Hz, 1H), 6.42 (8-H, d, J=2.2 Hz, 1H), 6.54 (5′-H, d, J=8.9 Hz, 1H), 6.57 (6-H, dd, J=2.2, 8.5 Hz, 1H), 7.12 (6′-H, d, J=8.9 Hz, 1H), 7.37 (5-H, d, J=8.5 Hz, 1H); EI-MS found $[M+H]^+$, 463.2152; $C_{24}H_{35}O_7Si$ $[M+H]^+$ requires 463.2152.

3.11.4. (+)-(3*S*,4*R*)-2′-*t*-Butyldimethylsilyloxy-3′,4′,7-trimethoxyisoflavan-3,4-diol 32b. 54 mg, (63%); R_f 0.49 (benzene–Me_2CO 9:1) as a yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -6.00×10^3 (280), $+1.75\times10^3$ (220); $[\alpha]_D^{25}=+26.0$ (c 0.69, $CHCl_3$); ^1H NMR ($CDCl_3$) as for **32a**; EI-MS found $[M+H]^+$, 463.2150; $C_{24}H_{35}O_7$ Si $[M+H]^+$ requires 463.2152.

3.12. 2′-Hydroxyisoflavan-3,4-diols 33a/b and 34a/b

The 2′-*t*-butyldimethylsilyloxyisoflavan-3,4-diols **31a/b** and **32a/b** (0.12 mmol), dissolved in anhydrous THF (5 mL), were separately treated with TBAF suspended on silica (0.24 mmol) for 15 min at rt. After the addition of moist THF (5 mL), the solvent was evaporated and the products separated by PLC.

3.12.1. (3*R*,4*S*)-2′-Hydroxy-4′,7-dimethoxyisoflavan-3,4-diol 33a. 38 mg, (100%); R_f 0.59 (benzene–Me_2CO 7:3) as a light yellow oil; ^1H NMR ($CDCl_3$) δ 3.77, 3.80 (2×OCH_3, 2×s, 2×3H), 3.90–3.94 (4-O*H*, m, 1H), 4.21, 4.30 (2-H_2, 2×d, J=11.1 Hz, 2×1H), 5.14 (4-H, d, J=4.1 Hz, 1H), 5.53–5.56 (3-O*H*, m, 1H), 6.41 (5′-H, dd, J=2.5, 8.9 Hz, 1H), 6.45 (3′-H, d, J=2.5 Hz, 1H), 6.50 (8-H, d, J=2.5 Hz, 1H), 6.61 (6-H, dd, J=2.5, 8.5 Hz, 1H), 7.02 (6′-H, d, J=8.9 Hz, 1H), 7.36 (5-H, d,

J=8.5 Hz, 1H), 8.86–8.91 (ArO*H*, m, 1H); EI-MS found $[M+H]^+$, 319.1180; $C_{17}H_{19}O_6$ $[M+H]^+$ requires 319.1182.

3.12.2. (3*S*,4*R*)-2′-Hydroxy-4′,7-dimethoxyisoflavan-3,4-diol 33b. 37 mg, (100%); R_f 0.59 (Benzene–Me_2CO 7:3) as a light yellow oil; ^1H NMR ($CDCl_3$) as for **33a**; EI-MS found $[M+H]^+$, 319.1184; $C_{17}H_{19}O_6$ $[M+H]^+$ requires 319.1182.

3.12.3. (3*R*,4*S*)-2′-Hydroxy-3′,4′,7-trimethoxyisoflavan-3,4-diol 34a. 43 mg, (100%); R_f 0.74 (Benzene–Me_2CO 7:3) as a yellow oil; ^1H NMR ($CDCl_3$) δ 3.80, 3.86, 3.94 (3×OC*H*$_3$, 3×s, 3×3H), 4.28, 4.40 (2-H_2, 2×d, J=1.1 Hz, 2×1H), 5.27–5.32 (4-H, m, 1H), 6.44 (8-H, d, J=2.5 Hz, 1H), 6.49 (5′-H, d, J=9.0 Hz, 1H), 6.60 (6-H, dd, J=2.5, 8.1 Hz, 1H), 6.87 (ArO*H*, s, 1H), 7.16 (6′-H, d, J=9.0 Hz, 1H), 7.40 (5-H, d, J=8.1 Hz, 1H); EI-MS found $[M+H]^+$, 349.1291; $C_{18}H_{21}O_7$ $[M+H]^+$ requires 349.1287.

3.12.4. (3*R*,4*S*)-2′-Hydroxy-3′,4′,7-trimethoxyisoflavan-3,4-diol 34b. 41 mg, (100%); R_f 0.74 (Benzene–Me_2CO 7:3) as a yellow oil; ^1H NMR ($CDCl_3$) as for **34a**; EI-MS found $[M+H]^+$, 349.1288; $C_{18}H_{21}O_7$ $[M+H]^+$ requires 349.1287.

3.13. 6a-Hydroxypterocarpans 35a/b, 36a/b and 37a/b

Solutions of the 2′-hydroxyisoflavan-3,4-diols **33a/b** and **34a/b** (0.08 mmol) in anhydrous DCM (1 mL) were separately treated with Ms_2O (0.09 mmol) and pyridine (0.39 mmol). The reaction mixture was stirred at rt for 16 h. After dilution with moist Et_2O (5 mL), the organic layer was washed with water (3×25 mL), dried (Na_2SO_4), evaporated and the 6a-hydroxypterocarpans purified by PLC.

3.13.1. (+)-(6a*R*,11a*R*)-*cis*-6a-Hydroxy-3,9-dimethoxypterocarpan [(+)-variabilin] 35a. 17 mg, (70%); R_f 0.50 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -3.93×10^3 (294), $+2.45\times10^4$ (246); $[\alpha]_D^{25}$=+223.6 (*c* 0.72, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.48–2.55 (6a-O*H*, m, 1H), 3.78, 3.79 (2×OC*H*$_3$, 2×s, 2×3H), 4.04 (6-H_{ax}, d, J=11.2 Hz, 1H), 4.24 (6-H_{eq}, dd, J=1.0, 11.2 Hz, 1H), 5.33 (11a-H, bs, 1H), 6.43 (10-H, d, J=2.0 Hz, 1H), 6.47 (4-H, d, J=2.2 Hz, 1H), 6.55 (8-H, dd, J=2.0, 8.2 Hz, 1H), 6.67 (2-H, dd, J=2.2, 8.2 Hz, 1H), 7.27 (7-H, d, J=8.2 Hz, 1H), 7.42 (1-H, d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.8, 55.9 (2×O*C*H$_3$), 70.1 (C-6), 77.2 (C-6a), 85.3 (C-11a), 97.5 (C-10), 102.1 (C-4), 108.1 (C-8), 110.2 (C-2), 112.8 (C-11b), 120.4 (C-6b), 124.2 (C-7), 132.3 (C-1), 156.2 (C-4a), 161.3 (C-10a), 161.5 (C-3), 162.9 (C-9); EI-MS calcd for $C_{17}H_{16}O_5$ $[M+H]^+$ 301.1076; found 301.1076.

3.13.2. (−)-(6a*R*,11a*S*)-*trans*-6a-Hydroxy-3,9-dimethoxypterocarpan 37a. 2.3 mg, (10%); R_f 0.45 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$[λ (nm)]: $+2.95\times10^2$ (278), $+1.13\times10^3$ (222), $+7.98\times10^2$ (208); $[\alpha]_D^{25}$=−128.6 (*c* 0.28, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 3.22–3.26 (6a-O*H*, m, 1H), 3.70 (2×OC*H*$_3$, s, 6H), 3.99 (6-H_{eq}, d, J=11.9 Hz, 1H), 4.32 (11a-H, bs, 1H), 4.35 (6-H_{ax}, d, J=11.9 Hz, 1H), 6.45–6.50 (4-,8-,10-H, m, 3H), 6.62 (2-H, dd, J=2.5, 8.2 Hz, 1H), 7.22 (7-H, d, J=7.5 Hz, 1H), 7.28 (1-H, d, J=8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.9 (C-11a), 55.7, 55.9 (2×O*C*H$_3$), 69.3 (C-6), 97.5 (C-10), 102.8 (C-4), 108.0 (C-6a), 108.2 (C-8), 110.2 (C-2), 116.9 (C-10a), 121.8 (C-4a), 125.3 (C-1), 129.5 (C-7), 154.9 (C-6b), 158.7 (C-11b), 159.8 (C-9), 161.3 (C-3); EI-MS found $[M+H]^+$, 301.1070; $C_{17}H_{16}O_5$ $[M+H]^+$ requires 301.1076.

3.13.3. (−)-(6a*S*,11a*S*)-*cis*-6a-Hydroxy-3,9-dimethoxypterocarpan [(−)-variabilin] 35b. 17 mg, (75%); R_f 0.50 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: $+3.80\times10^3$ (294), -2.32×10^4 (246); $[\alpha]_D^{25}$=−220.8 (*c* 0.68, $CHCl_3$); ^1H- and ^{13}C NMR ($CDCl_3$) as for **35a**; EI-MS calcd for $C_{17}H_{16}O_5$ $[M+H]^+$ 301.1076; found 301.1079.

3.13.4. (+)-(6a*S*,11a*R*)-*trans*-6a-Hydroxy-3,9-dimethoxypterocarpan 37b. 2.2 mg, (9%); R_f 0.45 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -3.01×10^2 (278), -1.21×10^3 (222), -7.95×10^2 (208); $[\alpha]_D^{25}$=+126.4 (*c* 0.23, $CHCl_3$); ^1H- and ^{13}C NMR ($CDCl_3$) as for **37a**; EI-MS found $[M+H]^+$, 301.1075; $C_{17}H_{16}O_5$ $[M+H]^+$ requires 301.1076.

3.13.5. (+)-(6a*R*,11a*R*)-*cis*-6a-Hydroxy-3,9,10-trimethoxypterocarpan 36a. 23 mg, (75%); R_f 0.40 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: -8.24×10^3 (285), $+9.10\times10^3$ (245); $[\alpha]_D^{25}$=+185.6 (*c* 0.48, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.43–2.46 (6a-O*H*, m, 1H), 3.80, 3.87, 3.94 (3×OC*H*$_3$, 3×s, 3×3H), 4.05 (6-H_{ax}, d, J=11.5 Hz, 1H), 4.25 (6-H_{eq}, dd, J=1.0, 11.5 Hz, 1H), 5.36 (11a-H, bs, 1H), 6.48 (4-H, d, J=2.5 Hz, 1H), 6.57 (8-H, d, J=8.0 Hz, 1H), 6.67 (2-H, dd, J=2.5, 8.9 Hz, 1H), 7.04 (7-H, d, J=8.0 Hz, 1H), 7.48 (1-H, d, J=8.9 Hz, 1H); EI-MS found $[M+H]^+$, 331.1180; $C_{18}H_{19}O_6$ $[M+H]^+$ requires 331.1182.

3.13.6. (−)-(6a*S*,11a*S*)-*cis*-6a-Hydroxy-3,9,10-trimethoxypterocarpan 36b. 19 mg, (73%); R_f 0.40 (Benzene–Me_2CO 9:1) as a light yellow oil; CD (MeOH) $\Delta\epsilon_{max}$ [λ (nm)]: $+8.20\times10^3$ (285), -8.95×10^3 (245); $[\alpha]_D^{25}$=−186.2 (*c* 0.58, $CHCl_3$); ^1H NMR ($CDCl_3$) as for **36a**; EI-MS found $[M+H]^+$, 331.1183; $C_{18}H_{19}O_6$ $[M+H]^+$ requires 331.1182.

3.13.7. *erythro*- and *threo*-Methyl 3-hydroxy-2,3-di(2-*O*-methoxymethylphenyl)-propanoates 40. Diisopropylamine (2.59 mmol) in dry Et_2O (1 mL) at 0°C was treated with *n*-BuLi (2.59 mmol). The LDA mixture was cooled to −78°C and propanoate **38**[20] (2.35 mmol) in Et_2O (1 mL) was added. After stirring for 30 min the aldehyde **39**[20] (2.35 mmol) in Et_2O (1 mL) was added. The mixture was stirred at −78°C for 1 h and then heated to 0°C. After a further 2 h, phosphate buffer (pH 7.0) (30 mL) was added and the mixture was extracted with EtOAc (3×50 mL). The combined EtOAc layer was washed with water (2×100 mL), dried (Na_2SO_4), evaporated and separated by PLC to afford the aldol products **40**; 642mg, (73%); de, 10%;

erythro: R_f 0.60 (Benzene–Me_2CO 9:1) as a yellow oil; ^1H NMR ($CDCl_3$) δ 3.35, 3.57 (2×OCH$_2$OC*H*$_3$, 2×s, 2×3H), 3.69 (OC*H*$_3$, s, 3H), 3.70 (O*H*, d, J=4.1 Hz, 1H), 4.65, 4.76 (OC*H*$_2$OCH$_3$, 2×d, J=6.8 Hz, 2×1H), 4.70 (2-H, d,

J=4.1 Hz, 1H), 5.26, 5.31 (OCH_2OCH$_3$, 2×d, J=6.8 Hz, 2×1H), 5.75 (3-H, dd, J=4.1, 4.1 Hz, 1H), 6.80 (5′-H, ddd, J=1.1, 7.1, 7.1 Hz, 1H), 6.92 (3″-H, dd, J=1.1, 7.9 Hz, 1H), 6.97 (5″-H, ddd, J=1.1, 7.1, 7.1 Hz, 1H), 7.04 (6′-H, dd, J=1.9, 7.1 Hz, 1H), 7.07 (3′-H, dd, J=1.1, 8.1 Hz, 1H), 7.15 (4″-H, ddd, J=1.9, 7.1, 7.9 Hz, 1H), 7.21 (4′-H, ddd, J=1.9, 7.1, 8.1 Hz, 1H), 7.30 (6″-H, dd, J=1.9, 7.1 Hz, 1H); IR ($CHCl_3$) 2954, 1732 (CO), 1549, 1386 cm^{-1}; EI-MS found $[M+H]^+$, 377.4183; $C_{20}H_{25}O_7$ $[M+H]^+$ requires 377.4181.

threo: R_f 0.46 (Benzene–Me_2CO 9:1) as yellow needles (mp 80°C); ^{1}H NMR ($CDCl_3$) δ 3.41 (2×OCH$_2$OCH_3, 2×s, 2×3H), 3.71 (OCH_3, s, 3H), 3.96 (OH, d, J=5.9 Hz, 1H), 4.49 (2-H, d, J=8.9 Hz, 1H), 4.86, 4.87, 4.95, 4.98 (4×OCH_2OCH$_3$, 4×d, J=6.8 Hz, 4×1H), 5.58 (3-H, dd, J=5.9, 8.9 Hz, 1H), 6.83–7.00 (ArH, m, 4H), 7.09–7.15 (ArH, m, 2H), 7.24 (ArH, dd, J=1.9, 7.5 Hz, 1H), 7.31 (ArH, dd, J=1.9, 7.5 Hz, 1H); IR ($CHCl_3$) 2964, 1716 (CO), 1556, 1380 cm^{-1}; EI-MS found $[M+H]^+$, 377.4181; $C_{20}H_{25}O_7$ $[M+H]^+$ requires 377.4181.

3.13.8. *erythro*- and *threo*-Methyl 3-benzylsulfanyl-2,3-di(2-hydroxyphenyl)propanoates 41. *erythro*- and *threo*-2,3-di(2-*O*-Methoxymethylphenyl)propanoates **40** (0.74 mmol) in dry DCM (10 mL) at −15°C were separately treated with $PhCH_2SH$ (2.98 mmol) followed by $SnCl_4$ (1.12 mmol) under N_2 atmosphere.[28] The mixture was stirred at −15°C for 15 min and then at 5°C for a further 15 min. Water (20 mL) was added and the mixture was extracted with EtOAc (3×25 mL). The combined EtOAc layer was washed with water (3×50 mL), dried (Na_2SO_4), evaporated and separated by PLC yielding the 3-benzylsulfanylpropanoate **41**; 198 mg, (65%); de, 88%;

erythro: R_f 0.43 (Benzene–Me_2CO 9:1) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.39, 3.52 (ArCH_2S, 2×d, J=13.0 Hz, 2×1H), 3.52 (OCH_3, s, 3H), 4.52–4.68 (2-H, m, 1H), 4.79–4.93 (3-H, m, 1H), 6.80–7.12 (ArH, m, 6H), 7.18–7.30 (ArH; ArOH, m, 3H), 7.36–7.40 (ArH, m, 5H), 7.49–7.53 (ArOH, m, 1H); IR ($CHCl_3$) 1740(CO), 1630, 1510, 1468 cm^{-1}; EI-MS found $[M+H]^+$, 395.5011; $C_{23}H_{23}O_4S$ $[M+H]^+$ requires 395.5014.

threo: R_f 0.38 (Benzene–Me_2CO 9:1) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.62, 3.67 (ArCH_2S, 2×d, J=13.1 Hz, 2×1H), 3.83 (OCH_3, s, 3H), 4.23 (2-H, d, J=11.9 Hz, 1H), 4.77 (3-H, d, J=11.9 Hz, 1H), 6.56–6.65 (ArH, m, 2H), 6.71–6.83 (ArH, m, 4H), 6.90–6.95 (ArOH, m, 1H), 6.99–7.06 (ArH, m, 2H), 7.18–7.22 (ArH, m, 2H), 7.26–7.35 (ArH, m, 3H), 8.33–8.36 (ArOH, m, 1H); IR ($CHCl_3$) 1735(CO), 1620, 1502, 1460 cm^{-1}; EI-MS found $[M+H]^+$, 395.5012; $C_{23}H_{23}O_4S$ $[M+H]^+$ requires 395.5014.

3.13.9. *trans*-2-(2′-Hydroxyphenyl)-3-methoxycarbonyl-2,3-dihydrobenzofuran 42. A solution of *threo*-methyl 3-benzylsulfanyl-2,3-di(2-hydroxyphenyl)-propanoate **41** (0.36 mmol) in anhydrous DCM (5 mL) was treated with $AgBF_4$ (0.36 mmol) for 24 h at rt. When no more starting material could be detected (TLC), moist DCM (5 mL) was added, the solvent evaporated and the mixture separated by PLC to yield the benzofuran **42**; 45 mg, (47%); R_f 0.53 (benzene–Me_2CO 9:1) as a yellow oil; ^{1}H NMR ($CDCl_3$): δ 3.89 (OCH_3, s, 3H), 4.40 (2-H, d, J=8.5 Hz, 1H), 6.28 (3-H, d, J=8.5 Hz, 1H), 6.66–6.72 (ArOH, m, 1H), 6.90–7.01 (ArH, m, 4H), 7.21–7.42 (ArH, m, 4H); IR ($CHCl_3$) 1738 (CO), 1717, 1696, 1609 cm^{-1}; EI-MS found $[M+H]^+$, 271.0973; $C_{16}H_{15}O_4$ $[M+H]^+$ requires 271.0970.

3.13.10. *trans*-2-(2′-Hydroxyphenyl)-3-hydroxymethyl-2,3-dihydrobenzofuran 43. *trans*-2-(2′-Hydroxyphenyl)-3-methoxycarbonyl-2,3-dihydrobenzofuran **42** (0.15 mmol) in dry Et_2O (2 mL) at 25°C was treated with an excess of $LiAlH_4$ for 10 min. The $LiAlH_4$ was destroyed by the addition of moist Et_2O (20 mL) followed by aq. NH_4Cl (20 mL). The mixture was extracted with EtOAc (3×20 mL) and the combined organic layers washed with saturated $NaHCO_3$ (20 mL) and water (2×20 mL), dried (Na_2SO_4), evaporated and separated by PLC to afford **43**; 34 mg, (93%); R_f 0.27 (benzene–Me_2CO 9:1) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.51–2.62 (C1–OH, m, 1H), 3.64 (3-H, ddd, J=4.5, 5.1, 10.0 Hz, 1H), 3.95 (CH_2OH, dd, J=9.9, 10.0 Hz, 1H), 4.13 (CH_2OH, dd, J=4.5, 9.9 Hz, 1H), 5.92 (2-H, d, J=5.1 Hz, 1H), 6.89–6.96 (ArH, m, 3H), 6.99–7.03 (ArH, m, 1H), 7.14–7.34 (ArH; ArOH, m, 5H); EI-MS found $[M+H]^+$, 243.1021; $C_{15}H_{15}O_3$ $[M+H]^+$ requires 243.1021.

3.13.11. (±)-*trans*-Pterocarpan 1. *trans*-2-(2′-Hydroxyphenyl)-3-hydroxymethyl-2,3-dihydrobenzofuran **43** (0.14 mmol) in dry THF (1 mL) was treated with a solution of TPP-DEAD complex [TPP (1.40 mmol) and DEAD (0.70 mmol) in dry THF (1 mL)] at 25°C for 16 h. After evaporation of the solvent the mixture was redissolved in DCM and separated by PLC affording the *rac. trans*-pterocarpan **1**; 22 mg, (58%); R_f 0.75 (benzene) as white needles (mp 89°C); ^{1}H NMR ($CDCl_3$) δ 3.67 (6a-H, ddd, J=4.7, 11.9, 13.5 Hz, 1H), 4.55 (6-H$_{ax}$, dd, J=10.0, 11.9 Hz, 1H), 4.97 (6-H$_{eq}$, dd, J=4.7, 10.0 Hz, 1H), 5.24 (11a-H, d, J=13.5 Hz, 1H), 6.93 (4-H, d, J=8.2 Hz, 1H), 7.00 (3-H, dd, J=7.5, 8.2 Hz, 1H), 7.00 (9-H, dd, J=7.5, 8.0 Hz, 1H), 7.07 (10-H, d, J=8.0 Hz, 1H), 7.22 (7-H, d, J=7.3 Hz, 1H), 7.26 (2-H, dd, J=7.5, 7.5 Hz, 1H), 7.27 (8-H, dd, J=7.3, 7.5 Hz, 1H), 7.48 (1-H, d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 45.7 (C-6a), 69.3 (C-6), 84.2 (C-11a), 111.6 (C-10), 116.7 (C-4), 120.7 (C-3), 122.0 (C-9), 123.6 (C-1), 123.7 (C-7), 124.9 (C-4a), 127.9 (C-10a), 129.2 (C-8), 129.4 (C-2), 153.3 (C-11b), 161.9 (C-6b); EI-MS found $[M+H]^+$, 225.0916; $C_{15}H_{13}O_2$ $[M+H]^+$ requires 225.0916.

3.13.12. *threo*-3-Benzylsulfanyl-2,3-bis(2-hydroxyphenyl)-propan-1-ol 48. Benzylsulfanylpropanoate **41** (0.09 mmol) in dry Et_2O (2 mL) at 10°C was treated with $LiAlH_4$ (0.9 mmol) for 10 min. The $LiAlH_4$ was destroyed by the addition of moist Et_2O (20 mL) followed by aq. NH_4Cl (20 mL). The mixture was extracted with EtOAc (3×20 mL) and the combined organic layers washed with saturated $NaHCO_3$ (20 mL) and water (2×20 mL), dried (Na_2SO_4), evaporated and separated by PLC to yield **48**; 21 mg; (70%); R_f 0.27 (benzene–Me_2CO 9:1) as a yellow oil. ^{1}H NMR ($CDCl_3$): δ 2.51–2.59 (C$_1$–OH, m, 1H), 3.35 (2-H, ddd, J=2.0, 4.5, 11.2 Hz, 1H), 3.53, 3.65 (ArCH_2S, 2×d, J=13.1 Hz, 2×1H), 4.00 (1-H, d, J=2.0, 11.2 Hz, 1H), 4.45 (1-H, d, J=4.5, 11.2 Hz, 1H), 4.60 (3-H, d, J=11.2 Hz, 1H), 6.54 (ArH, ddd, J=1.1, 6.9, 7.0 Hz, 1H), 6.60 (ArH,

dd, *J*=1.9, 7.8 Hz, 1H), 6.68 (ArH, ddd, *J*=1.1, 7.2, 7.2 Hz, 1H), 6.77 (ArH, dd, *J*=1.1, 8.1 Hz, 1H), 6.81–6.86 (ArO*H*, m, 1H), 6.90 (ArH, dd, *J*=1.1, 8.1 Hz, 1H), 6.99 (ArH, ddd, *J*=1.9, 7.1, 8.0 Hz, 1H), 7.04 (ArH, ddd, *J*=1.5, 7.1, 8.0 Hz, 1H), 7.20–7.38 (ArH, m, 6H), 8.32–8.38 (ArO*H*, m, 1H); EI-MS found $[M+H]^+$, 367.4908; $C_{22}H_{23}O_3S$ $[M+H]^+$ requires 367.4908.

3.13.13. 3-(Benzylsulfanyl-2′-hydroxyphenylmethyl)-2,3-dihydrobenzofuran 49. Benzylsulfanylpropanol **48** (0.06 mmol) in dry THF (0.5 mL) was treated with a solution of TPP-DEAD complex [TPP (0.57 mmol) and DEAD (0.29 mmol) in dry THF (1 mL)] at 25°C for 4 h. After evaporation of the solvent the mixture was redissolved in DCM and separated by PLC affording the 3-substituted benzofuran **49**; 13 mg, (65%); R_f 0.67 (benzene) as a light yellow oil. ^{1}H NMR ($CDCl_3$): δ 3.53, 3.64 (ArCH_2S, 2×d, *J*=13.2 Hz, 2×1H), 3.86 α-H, d, *J*=11.0 Hz, 1H), 3.99 (3-H, ddd, *J*=5.5, 8.0, 11.0 Hz, 1H), 4.58 (2-H, dd, *J*=5.5, 9.5 Hz, 1H), 4.63 (2-H, dd, *J*=8.0, 9.5 Hz, 1H), 5.96–6.00 (4-H, m, 1H), 6.54 (5-H, ddd, *J*=1.0, 7.5, 7.5 Hz, 1H), 6.72–6.76 (3′-;5′-H, m, 2H), 6.85 (4′-H, ddd, *J*=1.1, 7.5, 7.5 Hz, 1H), 7.00 (7-H, dd, *J*=1.0, 7.5 Hz, 1H), 7.02 (ArO*H*, s, 1H), 7.05 (6-H, ddd, *J*=1.5, 7.5, 7.5 Hz, 1H), 7.18 (6′-H, dd, *J*=1.1, 7.5 Hz, 1H), 7.25–7.34 (ArH, m, 5H); EI-MS found $[M+H]^+$, 349.1260; $C_{22}H_{21}O_2S$ $[M+H]^+$ requires 349.1262.

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