THE DIRECT SYNTHESIS OF ISOFLAVANS *VIA* α-ALKYLATION OF PHENYLACETATES

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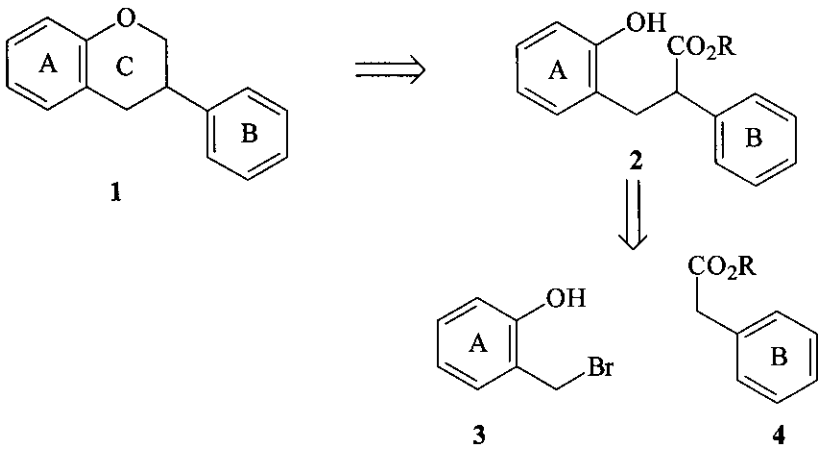
Abstract - Deprotonation of oxygenated phenylacetates and quenching of the enolates with oxygenated benzylic electrophiles, afforded 2,3-diarylpropanoates which served as precursors to the isoflavans following consecutive reduction and cyclization steps.

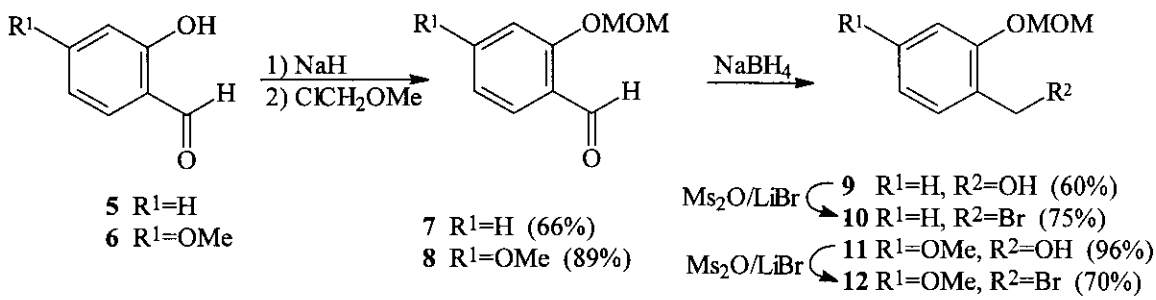
Although a large number of isoflavans with their relative simple structures are known, synthetic access to this class of phenolic metabolites[1] is restricted to the cumbersome process of hydrogenation of isoflavones[2] or pterocarpans.[3] Hitherto, the only direct synthesis[4] of isoflavans involves the coupling of a free phenolic A-ring moiety with a protected substituted styrene unit. These starting materials with appropriate oxygenation patterns are, however, not readily available. We have therefore opted for a more direct synthetic approach[5] towards racemic isoflavans that is based on the α-alkylation of phenylacetates and subsequent reduction and cyclization of the ensuing 2,3-diarylpropan-1-ols.

Consideration of the simple retro-synthetic sequence (**1**) ⇒ (**2**) ⇒ (**3**) + (**4**) indicates that our protocol for construction of the $C_6.C_3.C_6$ framework would involve the synthesis of oxygenated benzylic electrophiles of type (**3**), α-benzylation of phenylacetates (**4**) to give 2,3-diarylpropanoates of type (**2**) and subsequent reduction and cyclization of the latter compounds to give the isoflavans, *e.g.* (**1**). We thus now disclose our detailed results of relevance to the synthesis of a variety of isoflavans exhibiting the characteristic oxygenation patterns of naturally occurring analogues.

The MOM-protected phenolic benzyl bromides (**10**) and (**12**) [δ(CH_2) 4.57] were prepared *via* methoxymethylation of the *o*-hydroxybenzaldehydes (**5**) and (**6**) to give the *o*-methoxymethyl ethers (**7**) and (**8**) (Scheme 1) which were reduced with sodium borohydride ($NaBH_4$) to give the benzyl alcohols (**9**) and



(**11**). Treatment of these alcohols with methanesulfonic anhydride (Ms_2O) and 2,6-lutidine gave the labile intermediate sulfonates which were trapped in reasonable yields as the benzyl bromides using lithium bromide in anhydrous THF.[6] The bromide (**10**) could be preserved for up to five months at -25^{0}C, analogue (**12**), however, was unstable and had to be used immediately.



Scheme 1

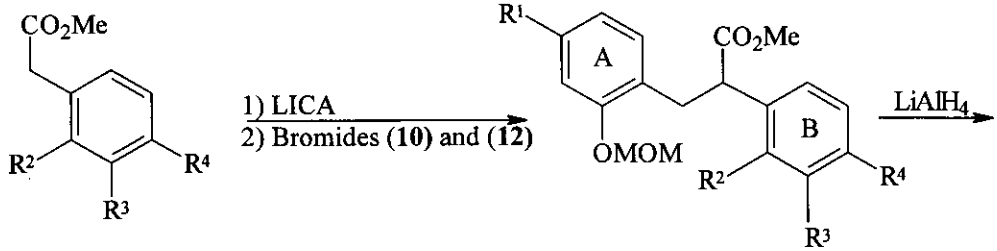
The consecutive steps of α-alkylation of the substituted phenylacetates [esters (**13**) - (**17**) were prepared by methylation of the phenylacetic acids] and the reduction and cyclization of the 2,3-diarylpropanoates were performed according to the sequence in Scheme 2. Owing to the excellent results reported for the α-alkylation of esters with lithium isopropylcyclohexylamide (LICA)[7,8] in the presence of hexamethylphosphoric triamide (HMPA),[9] this hindered base was selected for the deprotonation of esters (**13**) - (**17**). The efficiency of the LICA/HMPA system to produce the ester enolates within 15 min at -78^{0}C was demonstrated *via* quenching of the reaction with D_2O.[7,10] At elevated temperatures rapid decomposition of the enolates occurred which adversely affected yields.

The 2,3-diarylpropanoates (**18**) - (**27**) were obtained in moderate to good yields (20% - 96%) by trapping of the ester enolates with the benzylic electrophiles (**10**) and (**12**). A decrease in yield was observed for the more highly substituted benzyl bromide (**12**), presumably reflecting its instability due to a more labile C-Br bond. The 2,3-diarylpropanoates (**18**) - (**27**) were smoothly converted into the 2,3-diarylpropan-1-ols (**28**) - (**37**) in moderate to good yields (50 - 98%) by reduction with lithium aluminium hydride in ether at room temperature.

Our initial efforts at simultaneous deprotection of the 2-*O*-methoxymethyl group and cyclization with *p*-toluenesulphonic acid (PTSA) in refluxing benzene invariably failed. The 2-*O*-methoxymethyl group was then removed quantitatively with 3M HCl in refluxing methanol to afford the phenolic propan-1-ols (**38**) - (**45**)* which were subsequently subjected to cyclization using PTSA in refluxing benzene. Under these conditions the target racemic isoflavans (**46**) - (**54**) were, however, accompanied by various proportions of isomeric 2-benzyldihydrobenzo[*b*]furans (**55**) - (**62**). Formation of both the isoflavans and the 2-benzyldihydrobenzofurans is explicable in terms of the generation of an incipient carbocation *via* the protonated alcohol (**63**). The instability of such a species then induces a concerted 1,2-migration of the C-2 aryl group and cyclization of the transient C-2 carbocation, probably stabilized as a benzenonium ion of type (**64**) (Scheme 3). Confirmation for such a conjecture stems from the observation that the rate of formation of the dihydrobenzofurans is enhanced by increased hydroxylation of the B-ring in the 2,3-diarylpropan-1-ols of type (**38**) hence increasing the migratory aptitude of this phenolic moiety. This is most evident from comparison of the yields of cyclization products of the 2,3-diarylpropan-1-ols (**38**) [(**46**) (28%): (**55**) (28%)] and (**40**) [(**48**) (0%): (**57**) (60%)]. A notable exception to this phenomenon is prevalent in the 2,3-diarylpropan-1-ol (**39**) where the *o*-methoxy group presumably causes steric compression in the benzenonium ion intermediate of type (**64**), hence favouring the 6-Exo-Tet process[11] with predominant formation of the isoflavan series of compounds [(**47**) (65%): (**56**) (25%)].

The adverse influence of these acid-mediated aryl migrations on the yield of isoflavan formation, prompted us to effect the cyclization step under basic conditions. Owing to the excellent nucleofugic properties of sulfonates, the primary hydroxyl group was brosylated using 4-bromobenzenesulfonyl chloride (2.0 *eq.*) in pyridine containing dimethylaminopyridine (DMAP) and triethylamine. In view of their instability, the presumed primary *O*-brosylates were not isolated but treated directly with an excess

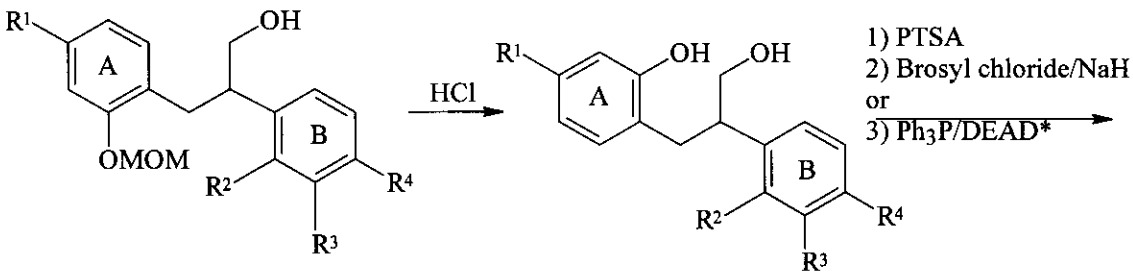
* Since the protected 2,3-diarylpropan-1-ols (**28**)-(**37**) were fully characterized, the diols (**38**)-(**45**) were identified by ^{1}H NMR data only.



13 $R^2=R^3=R^4=H$
14 $R^3=R^4=H$, $R^2=OMe$
15 $R^2=R^3=H$, $R^4=OMe$
16 $R^2=H$, $R^3=R^4=OMe$
17 $R^3=H$, $R^2=R^4=OMe$

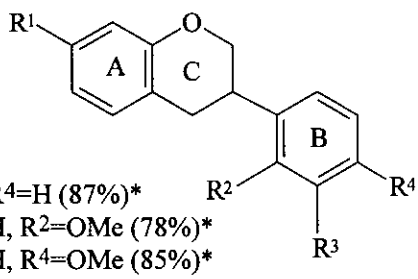
18 $R^1=R^2=R^3=R^4=H$ (80%)
19 $R^1=R^3=R^4=H$, $R^2=OMe$ (85%)
20 $R^1=R^2=R^3=H$, $R^4=OMe$ (83%)
21 $R^1=R^2=H$, $R^3=R^4=OMe$ (96%)
22 $R^1=R^3=H$, $R^2=R^4=OMe$ (75%)

23 $R^1=OMe$, $R^2=R^3=R^4=H$ (45%)
24 $R^1=R^2=OMe$, $R^3=R^4=H$ (47%)
25 $R^1=R^4=OMe$, $R^2=R^3=H$ (57%)
26 $R^1=R^3=R^4=OMe$, $R^2=H$ (20%)
27 $R^1=R^2=R^4=OMe$, $R^3=H$ (42%)

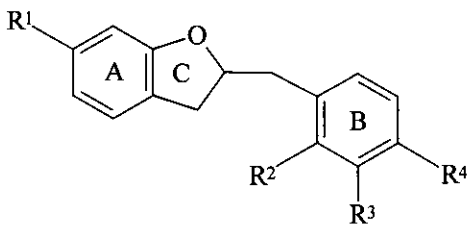


28 $R^1=R^2=R^3=R^4=H$ (98%)
29 $R^1=R^3=R^4=H$, $R^2=OMe$ (95%)
30 $R^1=R^2=R^3=H$, $R^4=OMe$ (92%)
31 $R^1=R^2=H$, $R^3=R^4=OMe$ (95%)
32 $R^1=R^3=H$, $R^2=R^4=OMe$ (98%)
33 $R^1=OMe$, $R^2=R^3=R^4=H$ (50%)
34 $R^1=R^2=OMe$, $R^3=R^4=H$ (85%)
35 $R^1=R^4=OMe$, $R^2=R^3=H$ (74%)
36 $R^1=R^3=R^4=OMe$, $R^2=H$ (72%)
37 $R^1=R^2=R^4=OMe$, $R^3=H$ (79%)

38 $R^1=R^2=R^3=R^4=H$ (98%)
39 $R^1=R^3=R^4=H$, $R^2=OMe$ (95%)
40 $R^1=R^2=R^3=H$, $R^4=OMe$ (99%)
41 $R^1=R^2=H$, $R^3=R^4=OMe$ (99%)
42 $R^1=R^3=H$, $R^2=R^4=OMe$ (98%)
43 $R^1=R^2=OMe$, $R^3=R^4=H$ (99%)
44 $R^1=R^4=OMe$, $R^2=R^3=H$ (99%)
45 $R^1=R^2=R^4=OMe$, $R^3=H$ (97%)



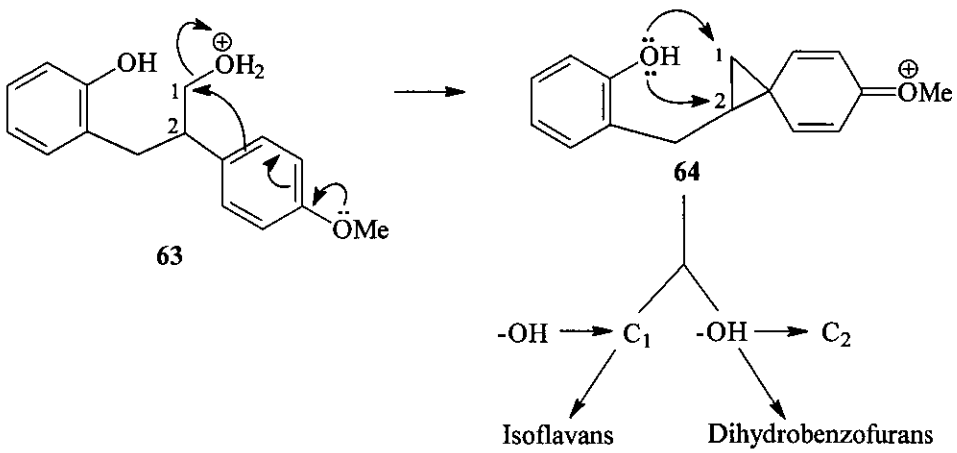
46 $R^1=R^2=R^3=R^4=H$ (87%)*
47 $R^1=R^3=R^4=H$, $R^2=OMe$ (78%)*
48 $R^1=R^2=R^3=H$, $R^4=OMe$ (85%)*
49 $R^1=R^2=H$, $R^3=R^4=OMe$ (84%)*
50 $R^1=R^3=H$, $R^2=R^4=OMe$ (75%)*
51 $R^1=OMe$, $R^2=R^3=R^4=H$
52 $R^1=R^2=OMe$, $R^3=R^4=H$ (90%)*
53 $R^1=R^4=OMe$, $R^2=R^3=H$ (81%)*
54 $R^1=R^2=R^4=OMe$, $R^3=H$ (88%)*



55 $R^1=R^2=R^3=R^4=H$
56 $R^1=R^3=R^4=H$, $R^2=OMe$
57 $R^1=R^2=R^3=H$, $R^4=OMe$
58 $R^1=R^2=H$, $R^3=R^4=OMe$
59 $R^1=R^3=H$, $R^2=R^4=OMe$
60 $R^1=R^2=OMe$, $R^3=R^4=H$
61 $R^1=R^4=OMe$, $R^2=R^3=H$
62 $R^1=R^2=R^4=OMe$, $R^3=H$

*Indicates yields for procedure 3

Scheme 2

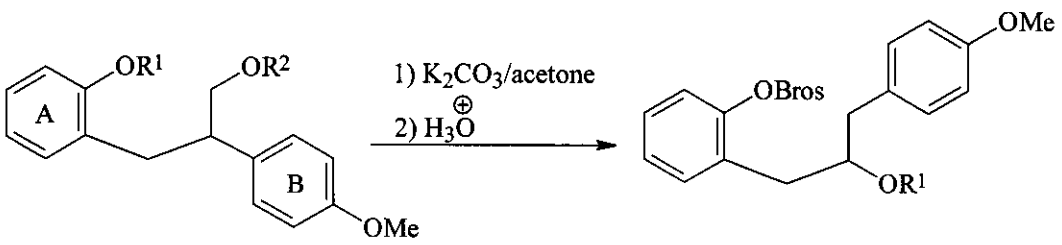


Scheme 3

of sodium hydride to effect cyclization. When applied to the 2,3-diarylpropan-1-ol (**40**) this procedure afforded the 4′-methoxyisoflavan (**48**) in a yield of only 35%. Since this poor yield may be attributable to dehydrobrosylation by the strong base, cyclization was subsequently attempted with potassium carbonate in anhydrous acetone which instead of the isoflavan, gave the 1,3-diarylpropan-2-ol derivatives (**65**) and (**66**) (Scheme 4). Careful isolation and identification of the brosylation product then indicated the presence of two *O*-brosyl functionalities and hence structure (**67**) for the compound that was wrongly assumed to be the primary mono-*O*-brosylate (**69**). The formation of the 1,3-diarylpropan-2-ol derivatives is then explicable in terms of the inhibition of cyclization resulting in a 1,2-aryl migration similar to the process depicted in Scheme 3. The intermediate benzenonium ion of type (**64**) is subsequently transformed into the secondary alcohol derivatives (**65**) and (**66**) by attack of brosylate ion and water, respectively, at C-2.

The observed cyclization of the dibrosylate (**67**) to the 4′-methoxyisoflavan (**48**) with sodium hydride clearly requires desulfonylation of the A-ring *O*-brosylate. This is presumably effected by the nucleophilic action of hydride ion,[12] hence generating 4-bromobenzenesulfinic acid and the A-ring phenoxide **71** which initiates intramolecular cyclization to the isoflavan (**48**) *via* substitution of the primary *O*-brosylate group.

Application of the above brosylation procedure on 2,3-diarylpropan-1-ol (**40**) but with 1.0 *eq*. of 4-bromobenzenesulfonyl chloride afforded the A-ring mono-*O*-brosylate (**68**) (60%) and the di-*O*-brosylate (**67**) (*ca*. 5%). Treatment of derivative (**68**) with sodium hydride in dichloromethane afforded 4′-

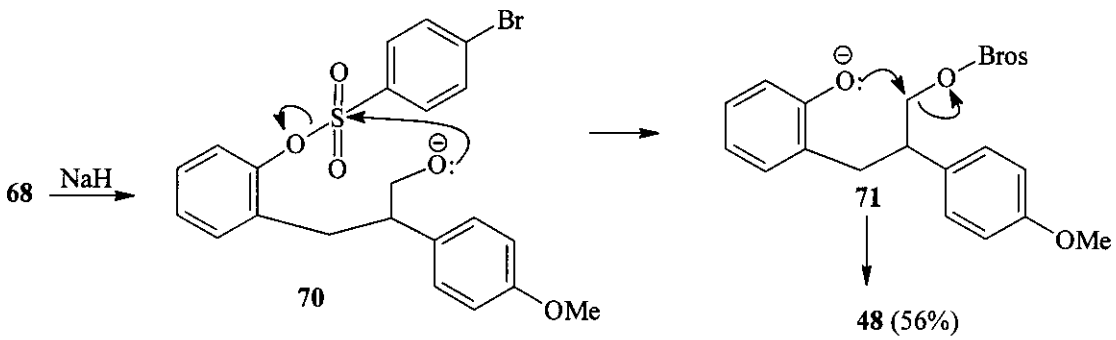


67 R^1=R^2=Bros
68 R^1=Bros, R^2=H
69 R^1=H, R^2=Bros

65 R^1=Bros
66 R^1=H

Scheme 4

methoxyisoflavan (**48**) in 56% yield. This transformation is presumably explicable in terms of deprotonation of the primary hydroxyl group by NaH. The primary alkoxide (**70**) then induces migration of the brosyl group to give the phenoxide ion (**71**) as precursor to the isoflavan (**48**) (Scheme 5).



Scheme 5

The consistent formation of the phenolic brosylate is presumably caused by the presence of the relatively strong base, triethylamine. When the brosylation was done in dichloromethane containing pyridine (1.2 *eq.*), the primary derivative (**69**) was obtained in low yield (21%), but with strong indications of severe decomposition during purification on silica gel. Direct cyclization using an excess of sodium hydride indeed led to the formation of the isoflavans in much improved yields [(*e.g.* 68% for (**48**)]. The 2,3-diarylpropan-1-ol (**42**) with its *o*-/*p*-disubstituted phenolic B-ring was an exception and gave the isoflavan (**50**) (30%) and the 2-benzyldihydrobenzofuran (**59**) (20%).

Finally, the cyclization was done under Mitsunobu conditions using an eight fold excess of a 1:1 triphenylphosphine/diethyl azodicarboxylate (DEAD)[4] complex in THF at 20-25^{0}C for 1 h. This protocol

gave the isoflavans in excellent yields (70-92%) and without the formation of the 2-benzyldihydrobenzofuran artefacts.

We have thus amply demonstrated the utility of this novel approach towards the first direct synthesis of racemic isoflavans.

EXPERIMENTAL

TLC was performed on DC-Plastikfolin Kieselgel 60 PF_{254} (0.25 mm) and the plates sprayed with H_2SO_4-HCHO (40:1, v/v) after development. ^1H NMR spectra were, unless specified to the contrary, recorded on a Bruker AM-300 spectrometer for solutions in $CDCl_3$ at 25°C with the solvent as internal standard. MS spectra were recorded on a Varian CH-5 instrument and mp (uncorrected) (crystallizations from acetone) on a Reichert hot-stage apparatus.

General procedures

Methoxymethylation. The phenol (0.036 mol) was added to a suspension of NaH (2 *eq*., 0.072 mol) in dry DMF (100 mL), followed by chloromethyl methyl ether (1.0 *eq*., 0.036 mol). After the reaction mixture was stirred for 30 – 60 min at rt, ice and 1.0 N HCl (50 mL) were added and the product was extracted with ether (3 x 300 mL). The ether extract was washed with saturated $NaHCO_3$ solution (100 mL) and water (100 mL), dried (Na_2SO_4) and evaporated. The product was purified by PLC or flash chromatography.

Alkylation. *n*-BuLi (15% in hexane, 1.6 M, 1.2 *eq*.) was added to a solution of isopropyl-cyclohexylamine (0.17 g, 1.2 mmol) in dry THF (2.0 mL) at 0°C under N_2 and the mixture was stirred for 15 min to give a cream coloured solution. The temperature was lowered to –78°C before the phenylacetate (1.0 mmol) in dry THF (0.5 mL) was added. The temperature was increased to –50°C or was stirred at –78°C for 30 min before the dry HMPA (0.54 g, 3 mmol) and the benzyl bromide (2.0 – 3.0 mmol) were added. After reaction time of 10 – 60 min, saturated ammonium chloride (3.0 mL) was added to the mixture before extraction with ether (3 x 5.0 mL). The ether extract was washed with saturated $NaHCO_3$ solution (5.0 mL) and water (5.0 mL), dried (Na_2SO_4) and evaporated at reduced pressure. The product was purified by PLC.

Reduction of methyl propanoates. A solution of propanoate (2.63 mmol) in dry ether (4 mL) was added to a suspension of $LiAlH_4$ (0.2 g, 5.26 mmol) in dry ether(2 mL) under N_2 atmosphere at rt and

stirred for 10 – 30 min. After the excess $LiAlH_4$ was quenched with ether (2 mL) and saturated ammonium chloride (3 mL), the reaction mixture was extracted with ether (3 x 10 mL), washed with saturated $NaHCO_3$ solution (5 mL) and water (5 mL), dried ($NaSO_4$) and the ether was removed *in vacuo* to give the product.

Acid hydrolysis and cyclization. The 2-methoxymethylphenylpropan-1-ols (0.30 mmol) were refluxed for 1 h in 3 N HCl (5 drops) and MeOH (2 mL), water was added and the reaction mixture was extracted with ether (3 x 10 mL). The extract was washed with saturated $NaHCO_3$ solution (5 mL) and water (10 mL), dried (Na_2SO_4) and the solvent was removed *in vacuo* to give the free phenolic propanols.

Method A. The free phenolic propanols (0.2 mmol) was refluxed with *p*-toluenesulfonic acid (10 mg) in benzene (3 mL) for 1 – 3 h, water (3 mL) was added and the mixture was extracted with ether (3 x 5 mL), neutralized with saturated $NaHCO_3$ solution (5 mL) and water (5 mL), and dried (Na_2SO_4). Separation on PLC gave the product.

Method B. The free phenolic propanols (0.24 mmol), brosyl chloride (0.064 g, 0.25 mmol), pyridine (0.02 g, 0.25 mmol) and dry dichloromethane (1.5 mL) were stirred at rt under N_2 atmosphere for 3 – 18 h. An excess of 60% NaH was added (until the gas evolution was finished) followed by heptane (5 mL), the excess NaH was filtered off and the solvent was removed *in vacuo*. PLC separation afforded the product.

Method C. A solution of Ph_3P (0.43 g, 1.64 mmol) and DEAD (0.12 g, 0.69 mmol) in THF (2.5 mL) was added to a solution of the free phenolic propanols (0.18 mmol) in dry THF (3.0 mL) and the reaction mixture was stirred for 1.5 h at rt. The THF was removed *in vacuo*, dichloromethane was added and the reaction mixture was separated by PLC to give the products.

Methoxymethylation

2-*O*-Methoxymethylbenzaldehyde (7).[13] Reaction of salicylaldehyde (0.87 mL, 8.2 mmol) with 60% NaH (0.80 g, 24.5 mmol) in dry DMF (25 mL) followed by chloromethyl methyl ether (0.7 mL, 8.2 mmol) as described previously, gave 7 (R_f 0.60, hexane-acetone, 8:2 v/y) as a light yellow oil (890 mg, 66%) after flash chromatography. *Anal.* Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.14; H, 6.14 ^{1}H-NMR δ: 10.48 (1H, s, CHO), 7.82 (1H, dd, J=8.0 and 2.0, 6-H), 7.54 – 7.47 (1H, m, 4-H), 7.19 (1H, dd, J=8.0 and 1.0, 3-H), 7.08 – 7.02 (1H, m, 5-H), 5.28 (2H, s, 2-OCH_2OCH$_3$) and 3.50 (3H, s, 2-OCH$_2$OCH_3).

4-Methoxy-2-*O*-methoxymethylbenzaldehyde (8). Reaction of 2-hydroxy-4-methoxybenzaldehyde (500 mg, 3.28 mmol) with NaH (160 mg, 6.56 mmol) in dry DMF (10 mL) followed by chloromethyl

methyl ether (0.25 mL, 3.28 mmol) gave **8** (R_f 0.40, hexane-acetone, 8:2. v/v) as a yellow oil (580 mg, 89%) after PLC. *Anal.* Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.38, H. 6.08. ^{1}H-NMR δ: 10.28 (1H, s, CHO), 7.77 (1H, d, J=8.5, 6-H), 6.66 (1H, d, J=2.0, 3-H), 6.57 (1H, dd, J=8.5 and 2.0, 5-H), 5.25 (2H, s, 2-OC*H*$_2$OCH$_3$), 3.82 (3H, s, 4-OMe) and 3.48 (3H, s, 2-OCH$_2$OC*H*$_3$).

Reduction of benzaldehydes

2-*O*-Methoxymethylbenzyl alcohol (9).[14] Compound (**7**) (220 mg, 1.32 mmol), dry THF-EtOH (1:1, 60 mL) and $NaBH_4$ (100 mg, 2.64 mmol) were stirred at rt for 24 h before acetone (100 mL) was added. The solvent was evaporated *in vacuo* whereafter water (50 mL) was added and the product was extracted with ether (3 x 40 mL). The ether extract was washed with water (30 mL), dried (Na_2SO_4) and evaporated at reduced pressure to give **9** (R_f 0.38, hexane-benzene-acetone, 7:2:1) as a light yellow oil (132 mg, 60%) after PLC. *Anal.* Calcd for $C_9H_{12}O_3$: C, 64.27, H, 7.19. Found: C, 64.16; H, 7.31. ^{1}H-NMR δ: 7.29 (1H, dd, J=7.5 and 2.0, 6-H), 7.21 (1H, ddd, J=7.5, 7.5 and 2.0, 5-H), 7.05 (1H, dd, J=7.5 and 1.5, 3-H), 6.97 (1H, ddd, J=7.5, 7.5 and 1.5, 4-H), 5.17 (2H, s, 2-OC*H*$_2$OCH$_3$), 4.66 (2H, s, C*H*$_2$OH), 3.44 (3H, s, 2-OCH$_2$OC*H*$_3$) and 2.85 – 2.81 (1H, br s, OH).

4-Methoxy-2-*O*-methoxymethylbenzyl alcohol (11). A mixture of $NaBH_4$ (230 mg, 5.6 mmol) and compound (**8**) (550 mg, 2.8 mmol) in THF-EtOH (70 mL) was stirred at rt for 45 min before acetone (100 mL) was added. The reaction mixture was evaporated at reduced pressure, before water (30 mL) was added whereafter the mixture was extracted with ether (3 x 30 mL). The extract was washed with water (30 mL), dried (Na_2SO_4) and evaporated at reduced pressure. PLC gave **11** (R_f 0.3, hexane-acetone 7:3) as a light yellow oil (536 mg, 96%). *Anal.* Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.71; H, 7.18. ^{1}H-NMR δ: 7.17 (1H, d, J=8.5, 6-H), 6.67 (1H, d, J=2.5, 3-H), 6.50 (1H, dd, J=8.5 and 2.5, 5-H), 5.18 (2H, s, 2-OC*H*$_2$OCH$_3$), 4.60 (2H, s, C*H*$_2$OH), 3.76 (3H, s, 4-OMe), 3.46 (3H, s, 2-OCH$_2$OC*H*$_3$) and 2.35 – 2.29 (1H, br. s, OH).

Bromination of benzyl alcohols

2-*O*-Methoxymethylbenzyl bromide (10). A mixture of compound (**9**) (591 mg, 3.51 mmol), LiBr (611 mg, 7.0 mmol) and 2,6-lutidine (0.82 mL, 7.0 mmol) in dry THF (3.0 mL) was stirred at 0^{0}C under N_2 atmosphere until all the LiBr was dissolved. Methanesulfonic anhydride (611 mg, 3.51 mmol) in dry THF (2.0 mL) was added and the reaction mixture was stirred for 2 h at 0^{0}C, followed by stirring at rt for 12 h (progress of the reaction was monitored by NMR). Pentane (5.0 mL) was added and after precipitation (15 min) and filtration of salts and polar by-products, the pentane/THF mixture was evaporated at reduced pressure to give a brown oil (608 mg, 75%). Compound (**10**) crystallized from dry

pentane at –25°C as white needles* which was stored in a dry THF solution at –25°C under N_2 (2.0 M). ^{1}H-NMR δ: 7.31 (1H, dd, J=7.5 and 2.0, 3-H), 7.29 – 7.22 (1H, m, 4- or 5-H), 7.08 (1H, dd, J=8.0 and 1.5, 6-H), 6.95 (1H, ddd, J=8.0, 8.0 and 1.0, 4- or 5-H), 5.26 (2H, s, 2-OCH_2OCH$_3$), 4.57 (2H, s, CH_2) and 3.51 (3H, s, 2-OCH$_2$OCH_3).

4-Methoxy-2-*O*-methoxymethylbenzyl bromide (12). Compound (**11**) (1.0 g, 5.05 mmol), LiBr (0.88 mg, 10.1 mmol) and 2,6-lutidine (1.18 mL, 10.1 mmol) in dry THF (4.0 mL) were stirred at 0°C under N_2 until all the LiBr was dissolved. Methanesulfonic anhydride (0.87 g, 5.05 mmol) in dry THF (2.0 mL) was added and the reaction mixture was stirred under N_2 for 30 h at rt (progress was monitored by NMR) After precipitation (15 min) and filtration of the salts and polar by-products by pentane (10 mL), the pentane/THF was evaporated *in vacuo*. Compound (**12**) (1.0 g, 70%) was unstable and used immediately as a 2.0 M solution in THF. ^{1}H-NMR δ: 7.28 (1H, d, J=8.0, 6-H), 6.70 (1H, d, J=2.0, 3-H), 6.46 (1H, dd, J=8.0 and 2.0, 5-H), 5.25 (2H, s, 2-OCH_2OCH$_3$), 4.57 (2H, s, CH_2), 3.78 (3H, s, 4-OMe) and 3.56 (3H, s, 2-OCH$_2$OCH_3).

Synthesis of 2,3-diarylpropanoates.

Methyl 3-(2-*O*-methoxymethylphenyl)-2-phenylpropanoate (18). Methyl phenylacetate (**13**) (500 mg, 3.3 mmol) in THF (3.0 mL) was added to a mixture of isopropylcyclohexylamine (0.66 mL, 4.0 mmol), *n*-BuLi (2.27 mL, 4.0 mmol) and THF (3.0 mL), followed by HMPA (1.74 mL, 9.9 mmol) and (**10**) (5.0 mL, 9.9 mmol) as was previously described. After 30 min at -78°C the general work up procedure was followed. Compound (**18**) was obtained as a light yellow oil (800 mg, 80%) after PLC. (R_f 0.48, hexane-benzene-acetone 8:1:1). *Anal.* Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.09; H, 6.83. ^{1}H-NMR δ: 7.36 – 7.20 (5H, m, ArH), 7.15 [1H, dd, J=8.0, 7.0 and 1.0, 4- or 5-H(A)], 7.09 – 7.04 [2H, m, 3,6-H(A)], 6.86 [1H, ddd, J=8.0, 7.0 and 1.0, 4- or 5-H(A)], 5.21 (1H, d, J=6.0) and 5.18 (1H, d, J=6.0, 2-OCH_2OCH$_3$), 4.04 (1H, dd, J=8.5 and 6.0, 2-H), 3.59 (3H, s, COOMe), 3.50 (3H, s, 2-OCH$_2$OCH_3), 3.41 (1H, dd, J=13.5 and 8.5, 3-H) and 3.15 (1H, dd, J=13.5 and 6.0, 3-H).

Methyl 2-(2-methoxyphenyl)-3-(2-*O*-methoxymethylphenyl)propanoate (19). Methyl 2-methoxyphenylacetate (**14**) (190 mg, 1.1 mmol) in THF (2.0 mL) was added to a mixture of isopropylcyclohexylamine (0.21 mL, 1.3 mmol), *n*-BuLi (0.69 mL, 1.3 mmol) and THF (1.0 mL), followed by HMPA (1.55 mL, 3.2 mmol) and **10** (1.56 mL, 3.2 mmol). After 60 min at –78°C the general work up procedure gave **19** as a light yellow oil (297 mg, 85%) after PLC (R_f 0.45, hexane-benzene-acetone 7:2:1) *Anal.* Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.19; H, 6.63. ^{1}H-NMR δ: 7.23 [1H, dd, J=7.0 and 1.5, 6-H(B)], 7.19 [1H, dd, J=8.0 and 2.0, 3-H(A)], 7.11 (1H, ddd, J=8.0, 8.0 and 2.0,

* Owing to decomposition during drying, the mp could not be determined accurately.

4-H(B)], 7.04 [1H, dd, J=8.0 and 2.0, 6-H(A)], 6.95 – 6.86 [2H, m, 4-H(A), 5-H(B)], 6.81 [1H, dd, J=8.0 and 1.0, 3-H(B)], 6.79 [1H, dd, J=8.0 and 1.0, 5-H(A)], 5.19 (1H, d, J=6.0) and 5.16 (1H, d, J=6.0, 2-OCH_2OCH_3), 4.43 (1H, dd, J=7.0 and 7.0, 2-H), 3.69 [3H, s, 2-OMe(B)], 3.61 (3H, s, COOMe), 3.51 (3H, s, 2-OCH_2OCH_3), 3.43 (1H, dd, J=13.5 and 7.0, 3-H) and 3.03 (1H, dd, J=13.5 and 7.0, 3-H).

Methyl 2-(4-methoxyphenyl)-3-(2-*O*-methoxymethylphenyl)propanoate (20). Methyl 4-methoxyphenylacetate (**15**) (310 mg, 1.7 mmol) in THF (2.0 mL) was added to a mixture of isopropylcyclohexylamine (0.34 mL, 2.1 mmol), *n*-BuLi (1.29 mL, 2.1 mmol) and THF (1.0 mL), followed by HMPA (0.90 mL, 5.2 mmol) and **10** (2.5 mL, 5.2 mmol). After 60 min at –78^{0}C the general work up procedure gave **20** as a light yellow oil (470 mg, 83%) after PLC (R_f 0.48, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.21; H, 6.58.. ^{1}H-NMR δ: 7.19 [2H, d, J=8.5, 2,6-H(B)], 7.13 (1H, ddd, J=8.0, 7.0 and 5.0, 4- or 5-H(A)], 7.03 [1H, dd, J=8.0 and 1.5, 3- or 6-H(A)], 6.99 [1H, dd, J 8.0 and 1.5, 3- or 6-H(A)], 6.82 [1H, ddd, J=7.0, 7.0 and 2.0, 4- or 5-H(A)], 6.81 [2H, d, J=8.5, 3,5-H(B)], 5.17 (2H, s, 2-OCH_2OCH_3), 3.92 (1H, dd, J=8.5 and 7.0, 2-H), 3.76 [3H, s, 4-OMe(B)], 3.58 (3H, s, COOMe), 3.48 (3H, s, 2-OCH_2OCH_3), 3.32 (1H, dd, J=13.5 and 8.5, 3-H) and 3.05 (1H, dd, J=13.5 and 7.0, 3-H).

Methyl 2-(3,4-dimethoxyphenyl)-3-(2-*O*-methoxymethylphenyl)propanoate (21). Methyl 3,4-dimethoxyphenylacetate (**16**) (500 mg, 2.4 mmol) in THF (3.0 mL) was added to a mixture of isopropylcyclohexylamine (0.47 mL, 2.9 mmol), *n*-BuLi (1.77 mL, 2.9 mmol) and THF (1.5 mL), followed by HMPA (1.24 mL, 7.1 mmol) and **10** (2.38 mL, 4.8 mmol). After 10 min at –78^{0}C the general work up procedure afforded **21** as a light yellow oil (825 mg, 96%) after PLC (R_f 0.60, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{20}H_{24}O_6$; C, 66.65; H, 6.71. Found: C, 66.84; H, 6.59. ^{1}H-NMR δ: 7.15 – 7.09 (1H, m, ArH), 7.04 – 6.95 (2H, m, ArH), 6.84 – 6.73 (4H, m, ArH), 5.17 (2H, s, 2-OCH_2OCH_3), 3.91 (1H, dd, J=8.0 and 6.5, 2-H), 3.82 [6H, s, 3,4-OMe(B)], 3.59 (3H, s, COOMe), 3.47 (3H, s, 2-OCH_2OCH_3), 3.34 (1H, dd, J=13.0 and 8.0, 3-H) and 3.05 (1H, dd, J=13.0 and 6.5, 3-H).

Methyl 2-(2,4-dimethoxyphenyl)-3-(2-*O*-methoxymethylphenyl)propanoate (22). Methyl 2,4-dimethoxyphenylacetate (**17**) (500 mg, 2.4 mmol) in THF (4.0 mL) was added to a mixture of isopropylcyclohexylamine (0.47 mL, 2.9 mmol), *n*-BuLi (1.77 mL, 2.9 mmol) and THF (1.5 mL), followed by HMPA (1.24 mL, 7.1 mmol) and **10** (2.38 mL, 4.8 mmol). After 15 min at –78^{0}C the general work up procedure gave **22** as a light yellow oil (643 mg, 75%) after PLC (R_f 0.45, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{20}H_{24}O_6$; C, 66.65; H, 6.71. Found: C, 66.79; H, 6.81. ^{1}H-NMR δ: 7.10 [1H, d, J=8.0, 6-H(B)], 7.08 (1H, ddd, J=7.0, 7.0 and 1.0, 4- or 5-H(A)], 7.01 [1H, dd, J=8.0 and 1.0, 6-H(A)], 6.90 [1H, dd, J=7.5 and 1.5, 3-H(A)], 6.77 [1H, ddd, J=7.0, 7.0 and 1.0, 4- or 5-H(A)], 6.40 [1H, dd, J=8.0 and 2.0, 5-H(B)], 6.36 (1H, d, J=2.0, 3-H(B)], 5.16 (2H, s, 2-OCH_2OCH_3), 4.30 (1H, dd, J=7.5

and 7.5 Hz, 2-H), 3.76 [3H, s, OMe(B)], 3.64 [3H, s, OMe(B)], 3.58 (3H, s, COOMe), 3.48 (3H, s, 2-OCH_2OCH_3), 3.36 (1H, dd, J=13.0 and 7.0, 3-H) and 2.95 (1H, dd, J=13.0 and 7.5, 3-H).

Methyl 2-phenyl-3-(4-methoxy-2-*O*-methoxymethylphenyl)propanoate (23). Compound (**13**) (163 mg, 1.08 mmol) in THF (1.0 mL) was added to a mixture of isopropylcyclohexylamine (0.2 mL, 1.2 mmol), *n*-BuLi (0.9 mL, 1.26 mmol) and THF (1.1 mL), followed by HMPA (0.56 mL, 3.08 mmol) and **12** (1.1 mL, 2.2 mmol). After 15 min at -78^0C the general work up procedure gave **23** as a light yellow oil (160 mg, 45%) after PLC (R_f 0.80, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.22; H, 6.87. ^{1}H-NMR δ: 7.29 – 7.19 (5H, m, ArH), 6.90 [1H, d, J=8.0, 6-H(A)], 6.65 [1H, d, J=2.0, 3-H(A)], 6.37 [1H, dd, J=8.0 and 2.0, 5-H(A)], 5.16 (1H, d, J=6.5) and 5.13 (1H, d, J=6.5, 2-OCH_2OCH_3), 3.93 (1H, dd, J=9.0 and 6.5, 2-H), 3.74 [3H, s, 4-OMe(A)], 3.58 (3H, s, COOMe), 3.47 (3H, s, 2-OCH_2OCH_3), 3.28 (1H, dd, J=13.5 and 9.0, 3-H) and 3.01 (1H, dd, J=13.5 and 6.5, 3-H).

Methyl 2-(2-methoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)propanoate (24). Compound (**14**) (142 mg, 0.79 mmol) in THF (0.75 mL) was added to a mixture of isopropylcyclohexylamine (0.16 mL, 0.97 mmol), *n*-BuLi (0.7 mL, 0.98 mmol) and THF (1.5 mL), followed by HMPA (0.40 mL, 2.2 mmol) and **12** (0.8 mL, 1.6 mmol) as previously described. After 45 min at -78^0C the general work up procedure afforded **24** as a light yellow oil (135 mg, 47%) after PLC (R_f 0.60, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.49; H, 6.59. ^{1}H-NMR δ: 7.19 [1H, d, J=7.0, 6-H(B)], 7.21 – 7.15 [1H, m, 4- or 5-H(B)], 6.87 [1H, ddd, J=8.0, 8.0 and 1.5, 4- or 5-H(B)], 6.81 [1H, d, J=8.0, 6-H(A)], 6.79 [1H, dd, J=8.5 and 1.5, 3-H(B)], 6.63 [1H, d, J=2.0, 3-H(A)], 6.32 [1H, dd, J=8.0 and 2.0, 5-H(A)], 5.14 (1H, d, J=7.0) and 5.11 (1H, d, J=7.0, 2-OCH_2OCH_3), 4.34 (1H, dd, J=8.0 and 7.0, 2-H), 3.72 [3H, s, 4-OMe(A)], 3.69 [3H, s, 2-OMe(B)], 3.59 (3H, s, COOMe), 3.47 (3H, s, 2-OCH_2OCH_3), 3.30 (1H, dd, J=14.0 and 7.0, 3-H) and 2.93 (1H, dd, J=14.0 and 8.0, 3-H).

Methyl 2-(4-methoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)propanoate (25). Derivative (**15**) (157 mg, 0.87 mmol) in THF (0.80 mL) was added to a mixture of isopropylcyclohexylamine (0.17 mL, 1.03 mmol), *n*-BuLi (0.75 mL, 1.05 mmol) and THF (1.5 mL), followed by HMPA (0.44 mL, 2.42 mmol) and **12** (1.08 mL, 2.16 mmol, 2.0 *eq.*). After 20 min at -78^0C the general work up procedure afforded **26** as a clear oil (178 mg, 57%) after PLC (R_f 0.40, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.78; H, 6.83. ^{1}H-NMR δ: 7.21 [2H, d, J=8.5, 2,6-H(B)], 6.90 [1H, d, J=8.5, 6-H(A)], 6.83 [2H, d, J=8.5, 3,5-H(B)], 6.66 [1H, d, J=2.0, 3-H(A)], 6.38 [1H, dd, J=8.5 and 2.0, 5-H(A)], 5.17 (1H, d, J=6.5) and 5.15 (1H, d, J=6.5, 2-OCH_2OCH_3), 3.89 (1H, dd, J=8.5 and 7.0 H, 2-H), 3.78 (3H, s, OMe), 3.75 (3H, s, OMe), 3.59 (3H, s, COOMe), 3.48 (3H, s, 2-OCH_2OCH_3), 3.26 (1H, dd, J=13.0 and 8.5, 3-H) and 2.99 (1H, dd, J=13.0 and 7.0, 3-H).

Methyl 2-(3,4-dimethoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)propanoate (26). Compound (**16**) (130 mg, 0.62 mmol) in THF (1.0 mL) was added to a mixture of isopropylcyclohexylamine (0.14 mL, 0.85 mmol), *n*-BuLi (0.60 mL, 0.84 mmol) and THF (0.7 mL), followed by HMPA (0.4 mL, 2.2 mmol) and **12** (0.7 mL, 1.4 mmol). After 20 min at -78^0C the general work up procedure gave **26** as a clear oil (48 mg, 20%) after PLC (R_f 0.30, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.79; H, 6.87. ^{1}H-NMR δ: 6.87 [1H, d, J=8.0, 6-H(A)], 6.81 – 6.73 (3H, m, 2,5,6-H(B)], 6.64 [1H, d, J=2.0 Hz, 3-H(A)], 6.36 [1H, dd, J=8.0 and 2.0, 5-H(A)], 5.15 (2H, s, 2-OC*H*$_2$OCH$_3$), 3.88 – 3.83 (1H, m, 2-H), 3.83 (6H, s, OMe), 3.73 (3H, s, OMe), 3.59 (3H, s, COOMe), 3.46 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.25 (1H, dd, J=13.5 and 8.0, 3-H) and 2.97 (1H, dd, J=13.5 and 7.0, 3-H).

Methyl 2-(2,4-dimethoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)propanoate (27). Derivative (**17**) (161 mg, 0.77 mmol) in THF (2.0 mL) was added to a mixture of isopropylcyclohexylamine (0.14 mL, 0.85 mmol), *n*-BuLi (0.70 mL, 0.85 mmol) and THF (0.7 mL), followed by HMPA (0.4 mL, 2.2 mmol) and **12** (0.8 mL, 1.6 mmol). After 30 min at -78^0C the general work up procedure gave **17** as yellow needles (124 mg, 42%) after PLC (R_f 0.50, hexane-benzene-acetone 6:2:2). mp 98^0C. *Anal.* Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C 64.79; H, 6.79. ^{1}H-NMR δ: 7.10 [1H, d, J=8.0, 6-H(A)], 6.81 [1H, d, J=8.0, 6-H(A)], 6.62 [1H, d, J=2.0, 3-H(A)], 6.40 [1H, dd, J=8.0 and 2.0, 5-H(B)], 6.36 [1H, d, J=2.0, 3-H(B)], 6.33 [1H, dd, J=8.0 and 2.0, 5-H(A)], 5.14 (1H, d, J=7.0) and 5.13 (1H, d, J=7.0, 2-OC*H*$_2$OCH$_3$), 4.25 (1H, dd, J=7.5 and 7.5, 2-H), 3.76 (3H, s, OMe), 3.72 (3H, s, OMe), 3.66 (3H, s, OMe), 3.58 (3H, s, COOMe), 3.46 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.27 (1H, dd, J=14.0 and 7.5, 3-H) and 2.89 (1H, dd, J=14.0 and 7.5, 3-H).

Synthesis of 2,3-diarylpropan-1-ols

3-(2-*O*-methoxymethylphenyl)-2-phenyl-1-propanol (28). Propanoate (**18**) (88 mg, 0.3 mmol) in ether (2.5 mL) was added to $LiAlH_4$ (16 mg, 0.4 mmol) in ether (0.8 mL) and the mixture was stirred for 10 min to give **28** (78 mg, 98%) as a light yellow oil (R_f 0.24, hexane-benzene-acetone 8:1:1). *Anal.* Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.83; H, 7.53. ^{1}H-NMR δ: 7.33 – 7.18 (5H, m, ArH), 7.13 [1H, ddd, J=8.0, 8.0 and 1.5, 4- or 5-H(A)], 7.06 [1H, dd, J=8.0 and 1.5, 3- or 6-H(A)], 6.99 [1H, dd, J=8.0 and 1.5, 3- or 6-H(A)], 6.86 [1H, ddd, J=8.0, 8.0 and 1.5, 4- or 5-H(A)], 5.17 (1H, d, J=6.0) and 5.14 (1H, d, J=6.0, 2-OC*H*$_2$OCH$_3$), 3.77 (2H, d, J=6.0, 1-CH$_2$), 3.48 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.17 – 3.10 (1H, m, 2-H), 3.11 – 3.04 (1H, m, 3-H), 2.96 – 2.86 (1H, m, 3-H) and 1.79 – 1.65 (1H, br s, OH).

2-(2-Methoxyphenyl)-3-(2-*O*-methoxymethylphenyl)-1-propanol (29). Compound (**19**) (290 mg, 0.9 mmol) in ether (3.0 mL) was added to $LiAlH_4$ (66 mg, 1.8 mmol) in ether (1.0 mL). After stirring for 10 min the propanol (**29**) (252 mg, 95%) was obtained as a light yellow oil (R_f 0.20, hexane-benzene-acetone

7:2:1). *Anal.* Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.29; H, 7.24. ^{1}H-NMR δ: 7.24 [1H, dd, J=7.0 and 2.0, 6-H(B)], 7.22 – 7.08 (1H, m, Ar. H), 7.04 [1H, dd, J=6.5 and 1.5, 3-H(A)], 7.03 [1H, dd, J=6.5 and 1.5, 6-H(A)], 6.95 – 6.88 (2H, m, Ar. H), 6.85 [1H, dd, J=7.0 and 1.5, 3-H(B)], 5.19 (1H, d, J=7.0) and 5.16 (1H, d, J=7.0, 2-OCH_2OCH$_3$), 3.77 – 3.72 (2H, m, 1- CH$_2$), 3.75 [3H, s, 2-OMe(B)], 3.65 – 3.56 (1H, m, 2-H), 3.50 (3H, s, 2-OCH$_2$OCH_3) , 3.13 (1H, dd, J=13.0 and 8.0, 3-H), 2.89 (1H, dd, J=13.0 and 6.0, 3-H) and 1.92 – 1.85 (1H, br s, OH).

2-(4-Methoxyphenyl)-3-(2-*O*-methoxymethylphenyl)-1-propanol (30): Compound (**20**) (204 mg, 0.6 mmol) in ether (3.0 mL) was added to LiAlH$_4$ (35 mg, 1.0 mmol) in ether (1.5 mL). Stirring for 30 min afforded **30** (172 mg, 92%) as a light yellow oil (R$_f$ 0.15, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.61; H, 7.45. ^{1}H-NMR δ: 7.14 [2H, d, J=9.0, 2,6-H(B)], 7.16 – 7.09 [1H, m, 4- or 5-H(A)], 7.04 [1H, dd, J=8.0 and 1.5, 3- or 6-H(A)], 6.97 [1H, dd, J=8.0 and 1.5, 3- or 6-H(A)], 6.88 – 6.81 [1H, m, 4- or 5-H(A)], 6.83 [2H, d, J=8.5, 3,5-H(B)], 5.18 (1H, d, J=6.5) and 5.15 (1H, d, J=6.5, 2-OCH_2OCH$_3$), 3.76 [3H, s, 4-OMe(B)], 3.76 – 3.70 (2H, m, 1-CH$_2$), 3.47 (3H, s, 2-OCH$_2$OCH_3), 3.11 – 2.99 (2H, m, 2,3-H), 2.91 – 2.80 (1H, m, 3-H) and 1.90 – 1.83 (1H, br s, OH).

2-(3,4-Dimethoxyphenyl)-3-(2-*O*-methoxymethylphenyl)-1-propanol (31). Methyl ester (**21**) (775 mg, 2.2 mmol) in ether (2.0 mL) was added to LiAlH$_4$ (164 mg, 4.3 mmol) in ether (2.0 mL). Stirring for 30 min gave **31** (678 mg, 95%) as a clear oil (R$_f$ 0.16, hexane-benzene-acetone 6:3:1). *Anal.* Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.81; H, 7.39. ^{1}H-NMR δ: 7.13 [1H, ddd, J=8.0, 6.5 and 1.5, 4- or 5-H(A)], 7.05 [1H, dd, J=8.5 and 1.5, 3- or 6-H(A)], 6.97 [1H, dd, J=7.5 and 1.5, 3- or 6-H(A)], 6.85 [1H, ddd, J=8.0, 6.5 and 1.5, 4- or 5-H(A)], 6.80 [1H, d, J=8.0, 5-H(B)], 6.76 [1H, dd, J=8.0 and 2.0, 6-H(B)], 6.69 [1H, d, J=2.0, 2-H(B)], 5.17 (2H, s, 2-OCH_2OCH$_3$), 3.84 [3H, s, OMe(B)], 3.83 [3H, s, OMe(B)], 3.77 – 3.71 (2H, m, 1-CH$_2$), 3.48 (3H, s, 2-OCH$_2$OCH_3), 3.11 – 3.00 (2H, m, 2,3-H), 2.90 – 2.77 (1H, m, 3-H) and 1.70 – 1.63 (1H, br s, OH).

2-(2,4-Dimethoxyphenyl)-3-(2-*O*-methoxymethylphenyl)-1-propanol (32). Propanoate (**22**) (88 mg, 0.3 mmol) in ether (2.5 mL) was added to LiAlH$_4$ (24 mg, 0.44 mmol) in ether (1.0 mL). Stirring for 10 min yielded **32** (78 mg, 98%) as a light yellow oil (R$_f$ 0.24, hexane-benzene-acetone 8:1:1). *Anal.* Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.79; H, 7.41. ^{1}H-NMR δ: 7.13 [1H, d, J=7.5, 6-H(B)], 7.13 [1H, dd, J=7.5 and 2.0, 3- or 6-H(A)], 7.08 [1H, ddd, J=7.5, 7.5 and 1.5, 4- or 5-H(A)], 7.01 [1H, dd, J=7.5 and 2.0, 3- or 6-H(A)], 6.85 [1H, ddd, J=7.5, 7.5 and 1.5, 4- or 5-H(A)], 6.44 [1H, dd, J=7.5 and 1.5, 5-H(B)], 6.42 [1H, d, J=1.5, 3-H(B)], 5.19 (1H, d, J=7.0) and 5.17 (1H, d, J=7.0, 2-OCH_2OCH$_3$), 3.78 [3H, s, OMe(B)], 3.73 [3H, s, OMe(B)], 3.75 – 3.69 (2H, m, 1-CH$_2$), 3.56 – 3.45 (1H, m, 2-H), 3.49 (3H, s, 2-OCH$_2$OCH_3), 3.07 (1H, dd, J=13.0 and 8.0, 3-H), 2.84 (1H, dd, J=13.0 and 6.5, 3-H) and 1.85 – 1.76 (1H, br s, OH).

2-Phenyl-3-(4-methoxy-2-*O*-methoxymethylphenyl)-1-propanol (33). Compound (**23**) (80 mg, 0.24 mmol) in ether (2 mL) was added to $LiAlH_4$ (14 mg, 0.37 mmol) in ether (0.7 mL). Stirring for 30 min gave **33** (36 mg, 50%) as a light yellow oil (R_f 0.40, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.69; H, 7.42. ^{1}H-NMR δ: 7.32 – 7.17 (5H, m, ArH), 6.87 [1H, d, J=8.5, 6-H(A)], 6.66 [1H, d, J=2.5 Hz, 3-H(A)], 6.41 [1H, dd, J=8.5 and 2.5, 5-H(A)], 5.14 (1H, d, J=7.0) and 5.12 (1 H, d, J=7.0, 2-OC*H*$_2$OCH$_3$), 3.77 – 3.74 (2H, m, 1-CH$_2$), 3.74 [3H, s, 4-OMe(A)], 3.46 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.10 – 3.03 (1H, m, 2-H), 2.98 (1H, dd, J=13.0 and 8.0, 3-H), 2.83 (1H, dd, J=13.0 and 6.0, 3-H) and 1.69 – 1.64 (1H, br s, OH).

2-(2-Methoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)-1-propanol (34). Ester (**24**) (84 mg, 0.23 mmol) in ether (3 mL) was added to $LiAlH_4$ (21 mg, 0.46 mmol) in ether (1 mL). Stirring for 20 min afforded **34** (66 mg, 85%) as a light yellow oil (R_f 0.36, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.51; H, 7.16. ^{1}H-NMR δ: 7.22 [1H, dd, J=7.0 and 2.0, 3- or 6-H(B)], 7.18 [1H, ddd, J=7.0, 7.0 and 1.5, 4- or 5-H(B)], 6.94 – 6.83 (2H, m, ArH), 6.91 [1H, d, J=8.0, 6-H(A)], 6.66 [1H, d, J=3.0, 3-H(A)], 6.41 [1H, dd, J=8.0 and 3.0, 5-H(A)], 5.15 (2H, s, 2-OC*H*$_2$OCH$_3$), 3.80 – 3.71 (2H, m, 1-CH$_2$), 3.76 (3H, s, OMe), 3.74 (3H, s, OMe), 3.59 – 3.51 (1H, m, 2-H), 3.47 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.03 (1H, dd, J=14.0 and 8.0, 3-H), 2.81 (1H, dd, J=14.0 and 6.0, 3-H) and 1.89 – 1.80 (1H, br s, OH).

2-(4-Methoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)-1-propanol (35). Compound (**25**) (114 mg, 0.32 mmol) in ether (1.5 mL) was added to $LiAlH_4$ (21 mg, 0.48 mmol) in ether (1 mL) and stirred for 15 min to give **35** (78 mg, 74%) as a clear oil (R_f 0.4, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Found: C, 68.53; H, 7.18. ^{1}H-NMR δ: 7.12 [2H, d, J=9.0, 2,6-H(B)], 6.86 [1H, d, J=8.0, 6-H(A)], 6.83 [2H, d, J=9.0, 3,5-H(B)], 6.66 [1H, d, J=3.0, 3-H(A)], 6.40 [1H, dd, J=8.0 and 3.0, 5-H(A)], 5.15 (1H, d, J=7.0) and 5.12 (1H, d, J=7.0, 2-OC*H*$_2$OCH$_3$), 3.77 (3H, s, OMe), 3.74 (3H, s, OMe), 3.76 – 3.70 (2H, m, 1-CH$_2$), 3.47 (3H, s, 2-OCH$_2$OC*H*$_3$), 3.08 – 2.98 (1H, m, 2-H), 2.95 (1H, dd, J=13.0 and 8.0, 3-H), 2.79 (1H, dd, J=13.0 and 6.5, 3-H) and 1.80 – 1.74 (1H, br s, OH).

2-(3,4-Dimethoxyphenyl)-3-(4-methoxy-2-*O*-methoxymethylphenyl)-1-propanol (36). Propanoate (**26**) (50 mg, 0.13 mmol) in ether (2.0 mL) was added to $LiAlH_4$ (13 mg, 0.26 mmol) in ether (1 mL). Stirring for 30 min gave **36** (30 mg, 72%) as a light yellow oil (R_f 0.28, hexane-benzene-acetone 6:2:2). *Anal.* Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.39; H, 7.35. ^{1}H-NMR δ: 6.84 [1H, d, J=8.5, 6-H(A)], 6.79 [1H, d, J=8.0, 5-H(B)], 6.77 [1H, dd, J=8.0 and 2.0, 6-H(B)], 6.69 [1H, d, J=2.0, 2-H(B)], 6.66 [1H, d, J=2.5, 3-H(A)], 6.36 [1H, dd, J=8.5 and 2.5, 5-H(A)], 5.14 (2H, s, 2-OC*H*$_2$OCH$_3$), 3.84 (3H, s, OMe), 3.83 (3H, s, OMe), 3.74 (3H, s, 4-OMe), 3.75 – 3.70 (2H, m, 1-CH$_2$), 3.46 (3H, s, 2-

OCH_2OCH_3), 3.05 – 2.99 (1H, m, 2-H), 2.95 (1H, dd, J=13.0 and 7.5, 3-H), 2.78 (1H, dd, J=13.0 and 6.0, 3-H) and 1.80 – 1.70 (1H, br s, OH).

2-(2,4-Dimethoxyphenyl-3-(4-methoxy-2-*O*-methoxymethylphenyl)-1-propanol (37). The ester (**27**) (133 mg, 0.34 mmol) in ether (3.0 mL) was added to $LiAlH_4$ (35 mg, 0.68 mmol) in ether (2 mL). Stirring for 20 min gave **37** (97 mg, 79%) as a light yellow oil (R_f 0.20, hexane-benzene-acetone 7:2:1). *Anal.* Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.16; H, 7.09. ^{1}H-NMR δ: 7.11 [1H, d, J=9.0, 6-H(B)], 6.90 [1H, d, J=9.0, 6-H(A)], 6.66 [1H, d, J=2.5, 3-H(A)], 6.45 – 6.39 [3H, m, 3-(B), 5-(B), 5-H(A)], 5.15 (2H, s, 2-OCH_2OCH_3), 3.77 (3H, s, OMe), 3.74 (3H, s, OMe), 3.73 (3H, s, OMe), 3.79 – 3.70 (2H, m, 1-CH_2), 3.48 (3H, s, 2-OCH_2OCH_3), 3.54 – 3.39 (1H, m, 2-H), 2.99 (1H, dd, J=14.0 and 8.5, 3-H), 2.78 (1H, dd, J=14.0 and 6.5, 3-H) and 1.86 – 1.79 (1H, br s, OH).

Cyclization of free phenolic propanols

Isoflavan (46)[15] and 2-Benzyldihydrobenzo[*b*]furan (55).[16] 2-Phenyl-3-(2-hydroxyphenyl)-1-propanol (**38**) was obtained from acid hydrolysis of **28** and was cyclised according to method A to give **46** (R_f 0.6, dichloromethane-hexane 85:15) as a clear oil (10 mg, 28%) and **55** (R_f 0.5, dichloromethane-hexane 85:15) as a clear oil (10 mg, 28%). Isoflavan (**46**): Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.81; H, 6.84. ^{1}H-NMR δ: 7.38 – 7.21 (5H, m, ArH), 7.15 – 7.06 (2H, m, ArH), 6.90 – 6.84 (2H, m, ArH), 4.35 (1H, ddd, J=11.0, 3.5 and 2.0, 2-H), 4.03 (1H, dd, J=11.0 and 11.0, 2-H), 3.30 – 3.19 (1H, m, 3-H), 3.12 – 2.95 (2H, m, 4-CH_2). Dihydrobenzofuran (**55**): Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.79; H, 6.83. ^{1}H-NMR δ: 7.35 – 7.20 (5H, m, ArH), 7.15 – 7.06 (2H, m, ArH), 6.84 – 6.75 (2H, m, ArH), 5.05 – 4.95 (1H, m, 2-H), 3.21 (1H, dd, J=8.0 and 8.0, 3-H), 3.18 (1H, dd, J=14.0 and 6.5) and 2.92 (1H, dd, J =14.0 and 6.5, CH_2Ph) and 2.95 (1H, dd, J=8.0 and 8.0, 3-H). Propanol (**38**) cyclised by Method B: The propanol (138 mg, 0.61 mmol), BrsCl (170 mg, 0.67 mmol), pyridine (0.06 mL, 0.73 mmol) and dichloromethane (2.0 mL) were stirred for 3 h. The general work up procedure gave isoflavan (**46**) (79 mg, 62%). Propanol (**38**) cyclised by Method C: The propanol (33 mg, 0.14 mmol) in THF (2.8 mL), Ph_3P (189 mg, 0.72 mmol), DEAD (0.22 mL, 0.69 mmol) and THF (2.2 mL) were stirred for 1.25 h. Workup gave isoflavan (**46**) (26 mg, 87%).

2'-Methoxyisoflavan (47) and 2-(2'-Methoxybenzyl)-dihydrobenzo[*b*]furan (56). 3-(2-Hydroxyphenyl)-2-(2-methoxyphenyl)-1-propanol (**39**) was obtained from acid hydrolysis of **29** and was cyclised according to method A to give isoflavan (**47**) (R_f 0.7, hexane-benzene 7:3) as a clear oil (32 mg, 65%) and dihydrobenzofuran (**56**) (R_f 0.6, hexane-benzene 7:3) as a clear oil (11 mg, 25%). **47**: *Anal.* Calcd for $C_{16}H_{16}O_{22}$: C, 79.97; H, 6.71. Found: C, 79.89; H, 6.64. ^{1}H-NMR δ: 7.27 – 7.21 (1H, m, ArH), 7.15 – 7.06 (3H, m, ArH), 6.96- 6.83 (4H, m, ArH), 4.36 (1H, ddd, J=10.0, 3.0 and 2.0, 2-H), 4.06 (1H, dd,

J=10.0 and 10.0, 2-H), 3.84 (3H, s, 2'-OMe), 3.76 – 3.64 (1H, m, 3-H), 3.09 (1H, dd, J=16.0 and 10.5, 4-H) and 2.96 (1H, ddd, J=16.0, 5.0 and 2.0, 4-H). **56**: *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.83; H, 6.59. ^{1}H-NMR δ: 7.26 – 7.05 (4H, m, ArH), 6.92 – 6.74 (4H, m, ArH), 5.12 – 5.02 (1H, m, 2-H), 3.82 (3H, s, 2'-OMe), 3.17 (1H, dd, J=9.0 and 16.0, 3-H), 3.15 (1H, dd, J=13.0 and 7.0) and 2.94 (1H, dd, J=13.0 and 7.0, C*H*$_2$Ar) and 2.98 – 2.90 (1H, m, 3-H) Propanol (**39**) cyclised by Method B: The propanol (**39**) (74 mg, 0.29 mmol), BrsCl (77 mg, 0.30 mmol), pyridine (0.03 mL, 0.32 mmol) and dichloromethane (2.0 mL) were stirred for 18 h to give isoflavan (**47**) (41 mg, 60%) after the general work up procedure. Propanol (**39**) cyclised by Method C: The propanol (**39**) (104 mg, 0.41 mmol) in THF (6.6 mL), Ph_3P (821 mg, 3.14 mmol), DEAD (0.50 mL, 1.64 mmol) and THF (5.0 mL) were stirred for 1 h to give isoflavan (**47**) (73 mg, 78%).

4'-Methoxyisoflavan (48). 3-(2-Hydroxyphenyl)-2-(4-methoxyphenyl)-1-propanol (**40**) (61 mg, 0.24 mmol) was obtained from acid hydrolysis of **30** and was stirred with BrsCl (73 mg, 0.28 mmol), pyridine (0.02 mL, 0.28 mmol) and dichloromethane (1.5 mL) for 21 h to give **48** (39 mg, 68%) as white needles after PLC (R_f 0.78, hexane-benzene-acetone 6:2:2), mp 80^{0}C *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 78.05; H, 6.83. ^{1}H-NMR δ: 7.17 (2H, d, J=8.0, 2',6'-H), 7.15 – 7.07 (2H, m, ArH), 6.89 (2H, d, J=8.0, 3',5'-H), 6.92 – 6.84 (2H, m, ArH), 4.32 (1H, ddd, J=10.0, 3.5 and 2.0, 2-H), 3.98 (1H, dd, J=10.0 and 10.0, 2-H), 3.80 (3H, s, 4'-OMe), 3.26 – 3.15 (1H, m, 3-H) and 3.04 – 2.95 (2H, m, 4-CH_2). Propanol (**40**) cyclised by Method C: The propanol (100 mg, 0.33 mmol) in THF (6.6 mL), Ph_3P (820 mg, 3.14 mmol), DEAD (0.50 mL, 1.64 mmol) and THF (5.0 mL) were stirred for 1 h to give **48** (79 mg, 85%) after the general work up procedure.

2-(4'-Methoxybenzyl)-dihydrobenzo[*b*]furan (57). 3-(2-Hydroxyphenyl)-2-(4-methoxyphenyl)-1-propanol (**40**) was cyclised according to method A to give **57** (R_f 0.7, hexane-benzene-acetone 6:2:2) as clear oil (38 mg, 60%). *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 78.13; H, 6.89. ^{1}H-NMR δ: 7.19 (2H, d, J=9.0, 2',6'-H), 7.20 – 7.07 (2H, m, ArH), 6.86 (2H, d, J=9.0, 3',5'-H), 6.91 – 6.76 (2H, m, ArH), 5.01 – 4.91 (1H, m, 2-H), 3.80 (3H, s, 4'-OMe), 3.19 (1H, dd, J=15.5 and 9.0 Hz, 3-H), 3.12 (1H, dd, J=14.0 and 7.0) and 2.87 (1H, dd, J=14.0 and 7.0, C*H*$_2$Ar) and 2.94 (1H, dd, J=15.5 and 8.0, 3-H).

3',4'-Dimethoxyisoflavan (49). 3-(2-Hydroxyphenyl)-2-(3,4-dimethoxyphenyl)-1-propanol (**41**) (300 mg, 1.04 mmol) (obtained by acid hydrolysis of **31**), BrsCl (279 mg, 1.1 mmol), pyridine (0.10 mL, 1.25 mmol) and dichloromethane (3.0 mL) were stirred for 48 h, the temperature was lowered to –20^{0}C and the excess of NaH was added. Standard work up procedure gave isoflavan (**49**) as white needles (185 mg, 66%) after PLC (R_f 0.62, hexane-benzene-acetone 6:2:2) mp 69^{0}C. *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.41; H, 6.59. ^{1}H-NMR δ: 7.15 – 7.06 (2H, m, ArH), 6.89 – 6.75 (5H, m, ArH), 4.33

(1H, ddd, J=11.0, 3.5 and 1.5, 2-H), 3.99 (1H, dd, J=11.0 and 11.0, 2-H), 3.24 – 3.14 (1H, m, 3-H) and 3.04 – 2.99 (2H, m, 4-CH_2). Propanol (**41**) cyclised by method C: The propanol (130 mg, 0.45 mmol) in THF (8.0 mL), Ph_3P (1.12 g, 4.28 mmol), DEAD (0.60 mL, 1.64 mmol) and THF (6.0 mL) were stirred for 1.5 h to afford isoflavan (**49**) (102 mg, 84%).

2-(3',4'-Dimethoxybenzyl)-dihydrobenzo[*b*]furan (58). 3-(2-Hydroxyphenyl)-2-(3,4-dimethoxyphenyl)-1-propanol (**41**) was cyclised according to method A to give **58** (R_f 0.88, hexane-benzene-acetone 6:2:2) as a clear oil (10 mg, 60%). *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.68; H, 6.89. ^{1}H-NMR δ: 7.14 – 7.05 (2H, m, ArH), 6.84 – 6.74 (5H, m, ArH), 5.04 – 4.94 (1H, m, 2-H), 3.85 (6H, s, OMe), 3.20 (1H, dd, J=15.0 and 9.0, 3-H), 3.09 (1H, dd, J=14.0 and 7.0) and 2.88 (1H, dd, J=14.0 and 7.0, CH_2Ar) and 2.93 (1H, dd, J=15.0 and 8.0, 3-H).

2',4'-Dimethoxyisoflavan (50). The 3-(2-hydroxyphenyl)-2-(2,4-dimethoxyphenyl)-1-propanol (**42**) (280 mg, 0.96 mmol) (obtained by acid hydrolysis of **32**), BrsCl (281 mg, 1.1 mmol) and pyridine (0.09 mL, 1.1 mmol) were stirred for 17 h before the temperature was lowered to 0^0C to add the excess of NaH. After PLC (R_f 0.75, hexane-benzene-acetone 6:2:2) the isoflavan (**50**) was isolated as white needles (95 mg, 36%), mp 75^0C. *Anal.* Calcd for $C_{17}C_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.68; H, 6.86. ^{1}H-NMR δ: 7.14 – 7.06 (2H, m, Ar. H), 7.02 (1H, d, J=8.0, 6'-H), 6.89 – 6.83 (2H, m, ArH), 6.50 – 6.44 (2H, m, ArH), 4.32 (1H, ddd, J=10.0, 3.5 and 2.0, 2-H), 4.02 [1H, dd, J=10.0 and 10.0, 2-H(*ax*)], 3.81 (3H, s, OMe), 3.80 (3H, s, OMe), 3.65 – 3.54 (1H, m, 3-H), 3.06 (1H, dd, J=16.0 and 10.5, 4-H) and 2.93 (1H, ddd, J=16.0, 5.0 and 2.0, 4-H). Propanol (**42**) cyclised by Method C: The propanol (100 mg, 0.35 mmol) in THF (6.0 mL), Ph_3P (865 mg, 3.30 mmol), DEAD (0.46 mL, 0.69 mmol) and THF (4.4 mL) were stirred for 1.5 h to afford **50** (70 mg, 75%).

2-(2',4'-Dimethoxybenzyl)-dihydrobenzo[*b*]furan (59). 3-(2-Hydroxyphenyl)-2-(2,4-dimethoxyphenyl)-1-propanol (**42**) was cyclised according to method A to give **59** (R_f 0.76, hexane-benzene-acetone 6:2:2) as white needles (27 mg, 70%), mp 83^0C. *Anal.* Calcd for $C_{17}C_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.67; H, 6.80. ^{1}H-NMR δ: 7.15 – 7.06 (3H, m, ArH), 6.85 – 6.75 (2H, m, ArH), 6.46 (1H, d, J=2.0, 3'-H), 6.44 (1H, dd, J=10.0 and 2.0, 5'-H), 5.09 – 4.98 (1H, m, 2-H), 3.81 (3H, s, OMe), 3.80 (3H, s, OMe), 3.16 (1H, dd, J=15.5 and 9.0, 3-H), 3.09 (1H, dd, J=13.5 and 7.0) and 2.88 (1H, dd, J=13.5 and 7.0, CH_2Ar) and 2.94 (1H, dd, J=15.5 and 7.0, 3-H).

7-Methoxyisoflavan (51).[17] 3-(2-Hydroxy-4-methoxyphenyl)-2-phenyl-1-propanol was obtained from acid hydrolysis of **33** and was cyclised according to method A to give **51** (R_f 0.7, hexane-benzene-acetone 6:2:2) as white needles (10 mg, 35%), mp 98^0C (lit.,[17] 98^0C). ^{1}H-NMR δ: 7.37 – 7.21 (5H, m, ArH), 6.97 (1H, d, J=8.0, 5-H), 6.47 (1H, dd, J=8.0 and 2.5, 6-H), 6.41 (1H, d, J=2.5, 8-H), 4.33 (1H, ddd, J=11.0, 3.5 and 2.0, 2-H), 4.01 (1H, dd, J=10.5 and 10.5, 2-H), 3.76 (3H, s, 7-OMe), 3.26 – 3.16 (1H, m, 3-H) and

3.00 – 2.91 (2H, m, 4-CH_2).

2',7-Dimethoxyisoflavan (52)[18] and 2-(2'-Methoxybenzyl)-6-methoxydihydrobenzo[*b*]furan (60): 3-(2-Hydroxy-4-methoxyphenyl)-2-(2-methoxyphenyl)-1-propanol (**43**) was obtained from acid hydrolysis of (**34**) and was cyclised according to method A to give **52** (R_f 0.9, dichloromethane-hexane 6:4) as white needles (7 mg, 22%), mp 80^{0}C (lit.,[18] 81^{0}C) and **60** (R_f 0.8, dichloromethane-hexane 6:4) as a clear oil (6 mg, 18%). Isoflavan (**52**). ^{1}H-NMR δ: 7.23 (1H, ddd, J=7.0, 7.0 and 1.0, 4'- or 5'-H), 7.11 (1H, dd, J=8.0 and 2.0, 6'-H), 6.97 (1H, d, J=8.0, 5-H), 6.92 (1H, ddd, J=7.0, 7.0 and 1.0, 4'- or 5'-H), 6.88 (1H, dd, J=7.0 and 1.0, 3'-H), 6.46 (1H, dd, J=8.0 and 2.5, 6-H), 6.41 (1H, d, J=2.5, 8-H), 4.33 (1H, ddd, J=10.0, 3.5 and 2.0, 2-H), 4.03 (1H, dd, J=10.0 and 10.0, 2-H), 3.82 (3H, s, OMe), 3.76 (3H, s, OMe), 3.70 – 3.58 (1H, m, 3-H), 3.00 (1H, dd, J=16.0 and 10.0, 4-H) and 2.88 (1H, ddd, J=16.0, 6.0 and 2.0, 4-H). **60.** *Anal.* Calcd for $C_{17}C_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.91; H, 6.84. ^{1}H-NMR δ: 7.25 – 7.16 (2H, m, ArH), 6.98 (1H, d, J=9.0, 4-H), 6.92 – 6.84 (2H, m, ArH), 6.36 (1H, d, J=2.0, 7-H), 6.35 (1H, dd, J=9.0 and 2.0, 5-H), 5.14 – 5.04 (1H, m, 2-H), 3.82 (3H, s, OMe), 3.74 (3H, s, OMe), 3.13 (1H, dd, J=13.5 and 7.0) and 2.94 (1H, dd, J=13.5 and 7.0, C*H*$_2$Ar), 3.09 (1H, dd, J=7.5 and 7.5, 3-H) and 2.85 (1H, dd, J=7.5 and 7.5, 3-H). Propanol (**43**) cyclised by Method C: The propanol (170 mg, 0.60 mmol) in THF (10.0 mL), Ph_3P (1.55 g, 5.7 mmol), DEAD (0.94 mL, 5.7 mmol) and THF (8.3 mL) were stirred for 1.5 h to give isoflavan (**52**) (143 mg, 90%).

4',7-Dimethoxyisoflavan (53).[17] 3-(2-Hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-1-propanol (**44**) (126 mg, 0.44 mmol) (obtained by acid hydrolysis of **35**) in THF (7.5 mL), Ph_3P (1.09 g, 4.18 mmol), DEAD (0.66 mL, 1.76 mmol) and THF (5.8 mL) were stirred for 1 h to give **53** (96 mg, 81%) as white needles, mp 103^{0}C (lit.,[17] 105-107^{0}C) after PLC (0.24, hexane-acetone 9:1). ^{1}H-NMR δ: 7.16 (2H, d, J=8.5, 2',6'-H), 6.98 (1H, d, J=9.0, 5-H), 6.89 (2H, d, J=8.5, 3',5'-H), 6.47 (1H, dd, J=9.0 and 2.5, 6-H), 6.42 (1H, d, J=2.5, 8-H), 4.30 (1H, ddd, J=10.0, 3.5 and 2.0, 2-H), 3.96 (1H, dd, J=10.5 and 10.5, 2-H), 3.80 (3H, s, OMe), 3.76 (3H, s, OMe), 3.22 – 3.11 (1H, m, 3-H) and 2.95 – 2.88 (2H, m, 4-CH_2).

2-(4'-Methoxybenzyl)-6-methoxydihydrobenzo[*b*]furan (61). 3-(2-Hydroxy-4-methoxyphenyl)-2-(4-methoxyphenyl)-1-propanol (**44**) was cyclised according to method A to give **61** (R_f 0.6, hexane-benzene-acetone 6:2:2) as a yellow oil (11 mg, 50%). *Anal.* Calcd for $C_{17}C_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.41; H, 6.63. ^{1}H-NMR δ: 7.17 (2H, d, J=9.0, 2',6'-H), 6.99 (1H, d, J=7.0, 4-H), 6.85 (2H, d, J=9.0, 3',5'-H), 6.37 (1H, d, J=2.0, 7-H), 6.36 (1H, dd, J=7.0 and 2.0, 5-H), 5.02 – 4.92 (1H, m, 2-H), 3.78 (3H, s, OMe), 3.74 (3H, s, OMe), 3.13 (1H, dd, J=7.5 and 7.5, 3-H), 3.07 (1H, dd, J=7.0 and 7.0, C*H*$_2$Ar) and 2.89 – 2.81 (2H, m, 3-H, C*H*$_2$Ar).

2',4',7-Trimethoxyisoflavan (54).[19] 3-(2-Hydroxy-4-methoxyphenyl)-2-(2,4-dimethoxyphenyl)-1-propanol (**45**) (90 mg, 0.28 mmol) (obtained by acid hydrolysis of **37**) in THF (4.7 mL), Ph_3P (696 mg, 2.66

mmol), DEAD (0.18 mL, 1.12 mmol) and THF (3.9 mL) were stirred for 1 h to give **54** as white needles, mp 63^{0}C (lit.,[19] 61^{0}C (75 mg, 88%) after PLC (R_f 0.34, hexane-acetone 9:1). ^{1}H-NMR δ: 7.01 (1H, d, J=8.5, 6'-H or 5-H), 6.97 (1H, d, J=8.5, 6'-H or 5-H), 6.49 – 6.40 (4H, m, Ar. H), 4.30 (1H, ddd, J=10.0, 3.0 and 2.0, 2-H), 3.99 (1H, dd, J=10.0 and 10.0, 2-H), 3.81 (3H, s, OMe), 3.79 (3H, s, OMe), 3.76 (3H, s, OMe), 3.61 – 3.51 (1H, m, 3-H), 2.97 (1H, ddd, J=16.0, 11.0 and 1.5, 4-H) and 2.86 (1H, ddd, J=16.0, 5.5 and 2.0, 4-H).

2-(2',4'-Dimethoxybenzyl)-6-methoxydihydrobenzo[*b*]furan (62). 3-(2-Hydroxy-4-methoxyphenyl)-2-(2,4-dimethoxyphenyl)-1-propanol **45** was cyclised according to method A to give **62** (R_f 0.64, hexane-benzene-acetone 6:2:2) as light yellow oil (18 mg, 53%). *Anal.* Calcd for $C_{18}C_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.11; H, 6.89. ^{1}H-NMR δ: 7.09 (1H, d, J=9.0, 6'-H), 7.00 (1H, d, J=9.0, 4-H), 6.45 (1H, d, J=2.0, 3'-H), 6.43 (1H, dd, J=9.0 and 2.0, 5'-H), 6.37 (1H, d, J=2.0, 7-H), 6.36 (1H, dd, J=9.0 and 2.0, 5-H), 5.09 – 4.99 (1H, m, 2-H), 3.80 (3H, s, OMe), 3.79 (3H, s, OMe), 3.74 (3H, s, OMe), 3.09 (1H, dd, J=15.0 and 9.0, 3-H), 3.06 (1H, dd, J=14.0 and 7.0) and 2.87 (1H, dd, J=14.0 and 7.0, C*H*$_2$Ar) and 2.84 (1H, dd, J=15.0 and 7.0, 3-H).

2-(4-Bromobenzenesulfonyloxy)-3-(2-[4-bromobenzenesulfonyloxy]phenyl)-1-(4-methoxyphenyl)-propane (65). The dibrosylate (**67**) (40 mg, 0.084 mmol), K_2CO_3 (35 mg, 0.25 mmol) and dry acetone (10 mL) were refluxed for 48 h. Water was added to dissolve the K_2CO_3 and the mixture was extracted with ether (3x5.0 mL), dried (Na_2SO_4) and separated by PLC (hexane-benzene-acetone 6:2:2) to give two bands at R_f 0.67 (2 mg, 30%) and 0.47 (13 mg, 32%). The former band gave **65** as a white powder. IR (KBr) cm^{-1} 1468, 1158 (SO_2) and 1053. *Anal.* Calcd for $C_{28}H_{24}O_7Br_2S_2$: C, 48.30; H, 3.47; Br, 22.95; S, 9.19. Found: C, 48.19; H, 3.38; Br, 22.81; S, 9.08. ^{1}H-NMR δ: 7.63 (2H, d, J=9.0) and 7.54 (2H, d, J=9.0) [2,3,5,6-H(D)], 7.36 (2H, d, J=9.0) and 7.31 (2H, d, J=9.0) [2,3,5,6-H(C)], 7.21-7.16 (1H, m, ArH), 7.11-7.01 (3H, m, ArH), 6.95 [2H, d, J=8.5, 2,6-H(B)], 6.74 [2H, d, J=8.5, 3,5-H(B)], 4.86-4.76 (1H, m, 2-H), 3.82 [3H, s, 4-OMe(B)], 2.92 (1H, dd, J=14.0 and 6.5, 1-H or 3-H) and 2.82-2.65 (3H, m, 1-H, 3-H, 1-H or 3-H). The R_f 0.47 band gave 3-(2-[4-*bromobenzenesulfonyloxy*]*phenyl*)-2-*hydroxy*-1-(4-*methoxyphenyl*)-*propane* (**66**) as a yellow oil (*Anal.* Calcd for $C_{22}C_{21}O_5BrS$: C, 55.36; H, 4.43; Br, 16.74; S, 6.70. Found: C, 55.21; H, 4.09; Br, 16.61; S, 6.59. ^{1}H-NMR δ: 7.66 [4H, s, ArH(D)], 7.33-7.05 (4H, m, ArH), 7.12 [2H, d, J=9.0, 2,6H(B)], 6.87 [2H, d, J=9.0, 3,5-H(B)], 4.08-3.99 (1H, m, 2-H), 3.81 [3H, s, 4-OMe(B)], 2.78-2.65 (3H, m, 1-H, 3-H, 1-H or 3-H), 2.57 (1H, dd, J=14.0 and 9.0, 1-H or 3-H) and 1.67-1.58 (1H, br s, 2-OH).

1-(4-Bromobenzenesulfonyloxy)-3-(2-[4-bromobenzenesulfonyloxy]phenyl)-2-(4-methoxyphenyl)-propane (67). The propanol (**40**) (40 mg, 0.15 mmol), BrsCl (77 mg, 0.30 mmol), Et_3N (0.05 mL, 0.30 mmol), DMAP (2 mg) and pyridine (1.0 mL) were stirred for 4 h. 3M HCl (5 drops) and ice were added

and the mixture was extracted with ether (3x10 mL), washed with saturated $NaHCO_3$ solution (5.0 mL) and water (5.0 mL), dried (Na_2SO_4) and evaporated. Separation on PLC (hexane-benzene-acetone 6:2:2) gave **67** (R_f 0.48) as brown oil (72 mg, 70%). IR (KBr) cm^{-1} 1468, 1158 (SO_2), 1089 and 1032. *Anal.* Calcd for $C_{28}H_{24}O_7Br_2S_2$: C, 48.30; H, 3.47; Br, 22.95; S, 9.19. Found: C, 48.60; H, 3.41; Br, 23.08; S, 9.34. ^{1}H-NMR δ: 7.75 [2H, d, J=9.0, ArH(D)], 7.69 [2H, d, J=9.0, ArH(D)], 7.59 [4H, s, 2,3,5,6-H(C)], 7.14 (1H, ddd, J=7.5, 7.5 and 2.0, ArH), 7.08-7.01 (3H, m, ArH), 6.90-6.82 (2H, m, ArH), 6.84 [2H, d, J=9.0, 2,6-H(B)], 6.71 [2H, d, J=9.0, 3,5-H(B)], 4.11-4.01 (2H, m, 1-CH_2), 3.77 [3H, s, 4-OMe(B)], 3.21-3.11 (1H, m, 2-H), 2.91 (1H, dd, J=14.0 and 6.5, 3-H) and 2.62 (1H, dd, J=14.0 and 9.0, 3-H).

3-(2-[4-Bromobenzenesulphonyloxy]phenyl)-2-(4-methoxyphenyl)-1-propanol (68). The propanol (**40**) (89 mg, 0.35 mmol), BrsCl (88 mg, 0.35 mmol), Et_3N (70 mg, 0.69 mmol), DMAP (42 mg, 0.35 mmol) and pyridine (1.0 mL) were stirred for 48 h. Ice and 3M HCl (1.0 mL) were added and the mixture was extracted with ether (3x5 mL), washed with saturated $NaHCO_3$ solution (5.0 mL) and water (50 mL) and dried (Na_2SO_4). After separation on PLC (hexane-benzene-acetone 6:2:2) brosylate **68** (R_f 0.4) was isolated as a light yellow oil (98 mg, 60%). IR (KBr) cm^{-1} 1468, 1158 (SO_2) and 1038 cm^{-1}. *Anal.* Calcd for $C_{22}H_{21}O_5BrS$: C, 55.36; H, 4.43; Br, 16.74; S, 6.70. Found: C, 55.16; H, 4.28; Br, 16.59; S, 6.58. ^{1}H-NMR δ: 7.75 [2H, d, J=9.0, ArH(D)], 7.66 [2H, d, J=9.0, ArH(D)], 7.15-6.96 (6H, m, ArH), 6.81 [2H, d, J=9.0, 3,5-H(B)], 3.77 [3H, s, 4-OMe(B)], 3.70-3.65 (2H, br s, 1-CH_2), 3.07-2.95 (1H, m, 2-H), 2.94 (1H, dd, J=14.0 and 7.0, 3-H), 2.65 (1H, dd, J=14.0 and 7.0, 3-H) and 1.48-1.40 (1H, b s, OH).

1-(4-Bromobenzenesulphonyloxy)-3-(2-hydroxyphenyl)-2-(4-methoxyphenyl)propane (69). The propanol (**40**) (100 mg, 0.39 mmol), pyridine (1.0 mL) and brosyl chloride (99 mg, 0.39 mmol) were stirred in dichloromethane (10 mL) at rt for 3 h. 3M HCl (3 drops) was added, the mixture was extracted with ether (3x10 mL), washed with saturated $CuSO_4$ (10 mL) and water (10 mL), dried (Na_2SO_4) and evaporated. Separation on PLC (hexane-benzene-acetone 6:2:2) gave brosylate (**69**) (38 mg, 21%) (R_f 0.47) as a light yellow oil. *Anal.* Calcd for $C_{22}H_{21}O_5BrS$: C, 55.36; H, 4.43; Br, 16.74; S, 6.70. Found: C, 55.49; H, 4.57; Br, 16.91; S, 6.89. ^{1}H-NMR δ: 7.55 [2H, d, J=7.0, ArH(C)], 7.50 [2H, d, J=7.0, ArH(C)], 7.04 (1H, ddd, J=6.0, 6.0 and 1.5, ArH), 6.96 [2H, d, J=8.0, 2,6-H(B)], 6.87 (1H, dd, J=6.0 and 1.5, ArH), 6.79-6.67 (4H, m, ArH), 4.23-4.11 (1H, m, 1-CH_2), 3.79 [3H, s, 4-OMe(B)], 3.30-3.20 (1H, m, 2-H), 3.00 (1H, dd, J=11.0 and 6.0, 3-H) and 2.81 (1H, dd, J=11.0 and 6.0, 3-H).

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