Stereoselectivity in Benzyl 1,2-Diaryl Ether Cleavage by Bromotrimethylsilane

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Lignin model benzyl 1,2-diaryl ether compounds such as 3-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-3-(4-hydroxymethyl-2-methoxyphenoxy)propanol are cleaved cleanly and selectively with bromotrimethylsilane, *anti*-isomers producing *anti*-bromides with high (*ca.* 95%) diastereoselectivity, presumably *via* anchimerically assisted displacement. Bromination of *anti* lignin model benzyl alcohols proceeds with 85% retention of configuration when other hydroxy groups in the molecule are protected, and *ca.* 75% retention when they are free. In both ether-cleavages and brominations, *syn*-isomers show notably lower stereoselectivity with marginal inversion.

The natural complexity of lignin provides a challenge to chemists interested in quantitative aspects of lignin structure and the chemical reactivity of specific subunits. A common approach to obtain this information is *via* the synthesis of lignin model compounds which are used as the basis of chemical and spectroscopic studies. Our investigations [1] into the structure and cleavage of the benzyl aryl ether **1** and the benzyl alcohol **2** lignin models (Scheme 1) have revealed an interesting diastereoselectivity exhibited by bromotrimethylsilane (TMSBr) for the α-ether cleavage of compounds **1** as well as the conversion of benzylic alcohols **2** into bromides.

The conversion of benzyl alcohols (including lignin models **2**) into bromides by TMSBr is a facile route to benzyl bromides.[2–5] Treatment of 4-hydroxybenzyl alcohols such as **2a** with TMSBr and subsequent HBr elimination *via* aqueous or organic bases provides a convenient preparation of important quinone methide intermediates for lignin investigations.[4–6] Jung and Hatfield [2] previously noted that bromination with TMSBr proceeded predominantly with inversion of configuration, observing a 94% inversion in the case of (−)-octan-2-ol. A similar level of kinetic stereoselectivity was noted [3] in the bromination of *anti*-**2d** but the bromide stereochemistry was not characterized.

In the course of developing a selective benzyl aryl ether cleavage method for α-etherified lignin model compounds such as **1a** and **1e** the use of TMSBr was explored. TMSBr had been previously shown to cleave methoxymethyl ethers under mild conditions [7] as well as 3-, 4- and 5-membered cyclic ethers.[2,8] It was assumed that benzyl aryl ethers, particularly those with strongly electron-releasing *para* substituents, would also be readily cleaved.

Results and Discussion

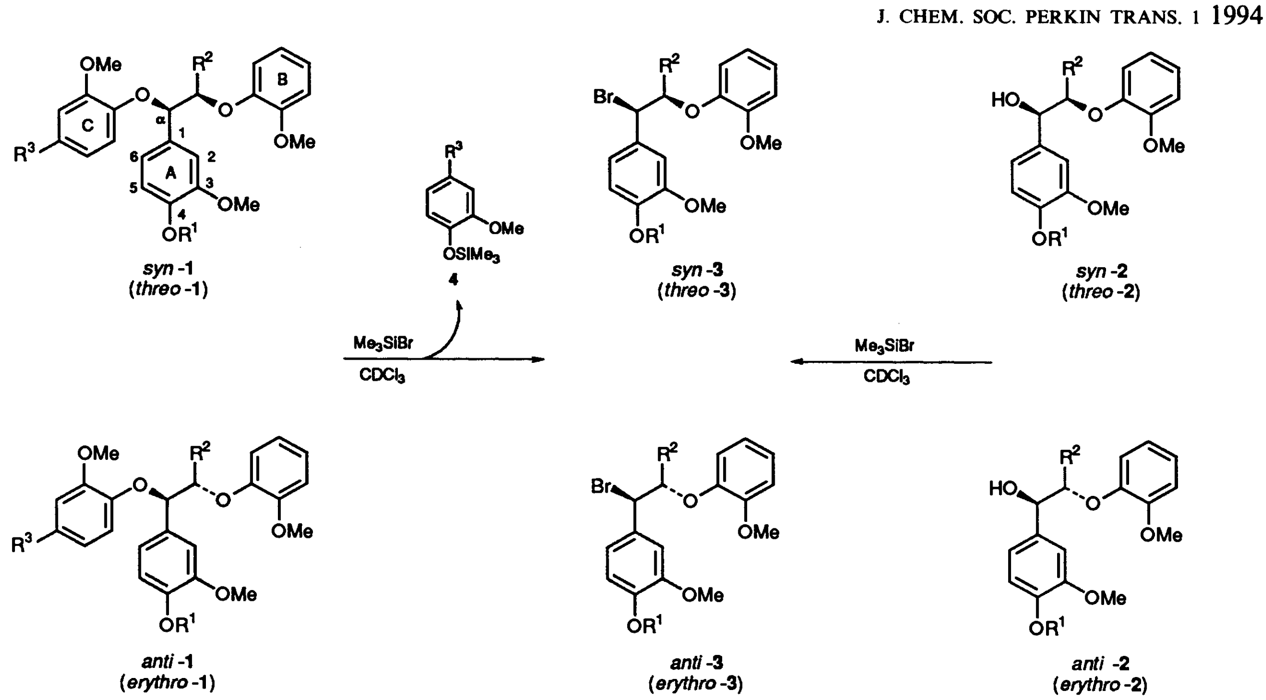
NMR-tube α-aryl ether cleavage of models **1a** and **1e** (Scheme 1) was extremely rapid and selective; the β-aryl ether linkage remained intact over a period of days at room temperature. We planned to gain further insight into the stereochemistry of these α-aryl ethers since the *syn*/*anti* assignment is currently based on chemical shifts of the γ-protons [1,9] and on the *anti*-selectivity of addition of phenols to quinone methides.[1,10] However, the cleavage reaction of free-phenolic benzyl aryl ethers **1a** and **1e** was too fast at room temperature and stereochemical scrambling occurred before NMR measurements could be completed.

We had previously noted slow scrambling of the α-bromide of *anti*-**2d** [3] which possessed a 4-methoxy rather than a 4-hydroxy substituent in ring A. Thus, methylation to compounds **1b** and **1f** and subsequent exposure to TMSBr provided the α-bromides **3b** which also showed an improved stability. Further improvement in bromide stability was obtained by acetylation of the remaining hydroxy group (compounds **1d** and **1g**)—we assume that the isomerization is aided by the presence of HBr released from reaction with alcohols. Benzyl aryl ether cleavage of the phenolic acetate **1c** was not detectable in the course of a 2-day exposure to TMSBr at room temperature. This indicates that the benzyl ring must be electron rich for the benzyl aryl ether cleavage reaction to occur under these conditions. Using 2–5 mg of compound and *ca.* 2 equiv. of TMSBr in 400 mm^3 † $CDCl_3$ in an NMR tube, ethers *anti*-**1d** and *anti*-**1g** (Fig. 1) were completely cleaved to bromides **3c** within 10 min at 300 K, whereas ethers *syn*-**1d** and *syn*-**1g** required 12 and 30 min, respectively, for complete conversion. Isomerization of bromides **3c** to the thermodynamic equilibrium mixture was complete in 24 h, giving 56 ± 2:44 ± 2 *anti*:*syn* **3c** in all cases (Fig. 2). The bromides **3a** (derived from models **1a**, **1e** or **2a**) equilibrated to a 44:56 *anti*:*syn* mixture.

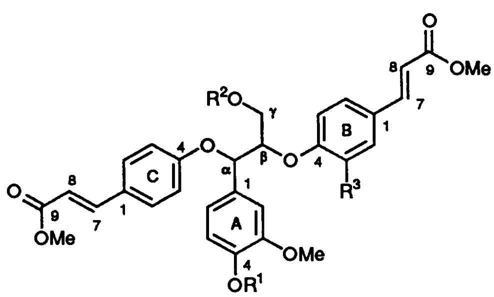
The *anti*:*syn* ratios were determined directly from ^1H NMR spectra using α-proton doublets and β- or γ-resonances as a further check (Table 1). The bromide **3** isomers were assigned from their γ-proton shifts. As has been observed in all compounds and derivatives of this type, the *syn* (*threo*) γ-proton chemical shifts are at higher field than their *anti* (*erythro*) counterparts, and the two *syn* γ-resonances are more dispersed [1,9] (*e.g.* $\Delta\delta$ = 0.33 *vs.* 0.07 ppm in *syn*- *vs.* *anti*-**1g**). The cleaved products **4** underwent slow reactions with TMSBr or HBr present in the system. Thus, **4a** gave **4b** by HBr addition, and the *p*-hydroxy- (or *p*-trimethylsiloxy-) benzyl ester in **4d** was cleaved slowly to yield the bromide **4e**, the reaction being complete in *ca.* 24 h.

The plot in Fig. 2 shows the initial bromide *anti*:*syn* ratios and indicates the equilibration rates of the bromides **3**. It is clear that bromination of *anti*-**2c** and, more dramatically, cleavage of *anti* ethers of **1d** or **1g** yield bromides **3c** with high *retention* of configuration. The *syn* isomers of **1d** and **1g** undergo predominantly an inversion of configuration but with a significantly lower degree of selectivity. Finally, bromination of

† 1 mm^3 = 1 μl.



Compd.	R^1	R^2	R^3
1a	H	CH_2OH	CH = $CHCO_2Me$
1b	Me	CH_2OH	CH = $CHCO_2Me$
1c	Ac	CH_2OAc	CH = $CHCO_2Me$
1d	Me	CH_2OAc	CH = $CHCO_2Me$
1e	H	CH_2OH	CH_2OH
1f	Me	CH_2OH	CH_2OH
1g	Me	CH_2OAc	CH_2OAc
2a, 3a	H	CH_2OH	
2b, 3b	Me	CH_2OH	
2c, 3c	Me	CH_2OAc	
2d, 3d	Me	Me	
4a			CH = $CHCO_2Me$
4b			$CH(Br)CH_2CO_2Me$
4c			CH_2OH
4d			CH_2OAc
4e			CH_2Br
5a	H	H	H
5b	Me	H	H
5c	Me	Ac	H
6a	H	H	OMe
6b	Me	H	OMe
6c	Me	Ac	OMe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Scheme 1 Action of TMSBr on the benzyl aryl ethers **1** and benzyl alcohols **2**. Side-chain labelling (α, β, γ) follows standard conventions used by lignin chemists.

the less-reactive γ-acetate *anti*-**2c** is more diastereoselective than *anti*-**2a**, and the equilibration of the bromides **3c** is slower than **3a**. The similar behaviour of *anti*-**2c** and the *anti* ethers of **1d** and **1g** in giving retention of configuration is consistent with the stereochemical assignments.

Molecular modelling and determination of the cleavage characteristics of additional benzyl aryl ether models provided insight into the source of the high degree of stereoselectivity observed for *anti*-isomers. It is clear that retention of configuration must arise from an anchimerically assisted displacement reaction.[11] Assistance from β-substituent groups (CH_2OH or CH_2OAc) were discounted because high retention was also observed with a β-Me group (*e.g.* **2d**) although ether cleavage reactions were not examined. Of the two other neighbouring groups capable[11] of providing the assistance, the β-aryloxy substituent (rather than the B-ring methoxy) was suggested by molecular modelling studies and confirmed experimentally to be responsible even though cases of such aryloxy participation are rare.[11,12] Thus semi-empirical molecular orbital (MO) calculations showed the oxonium ion intermediates from B-ring methoxy participation to be *ca.* 30–75 kJ higher in energy than the 3-membered ring oxonium ions (such as **7**) for β-aryloxy participation (Scheme 2) and the oxonium ions from the *anti*-isomers to be more stable than from *syn*-isomers. Experimentally, compounds *anti*-**5c** (no B-ring methoxyl) and *anti*-**6c** were each cleaved by TMSBr to give bromides **3c** with high retention (*ca.* 95%). Additionally, enthalpies of formation for ground-state conformers of **1d** and **1e**, determined from molecular mechanics with complete vibrational and torsional annealing to establish the validity of the minima, showed that the *anti*-rotamer required for anchimerically assisted displacement of the benzyl aryl ether was the major rotamer for the *anti*-isomer by a factor of 8–15 times but was a minor or negligible contributor to the *syn*-isomer conformation. A combination of greater ground-state populations for the reacting conformers coupled with a greater

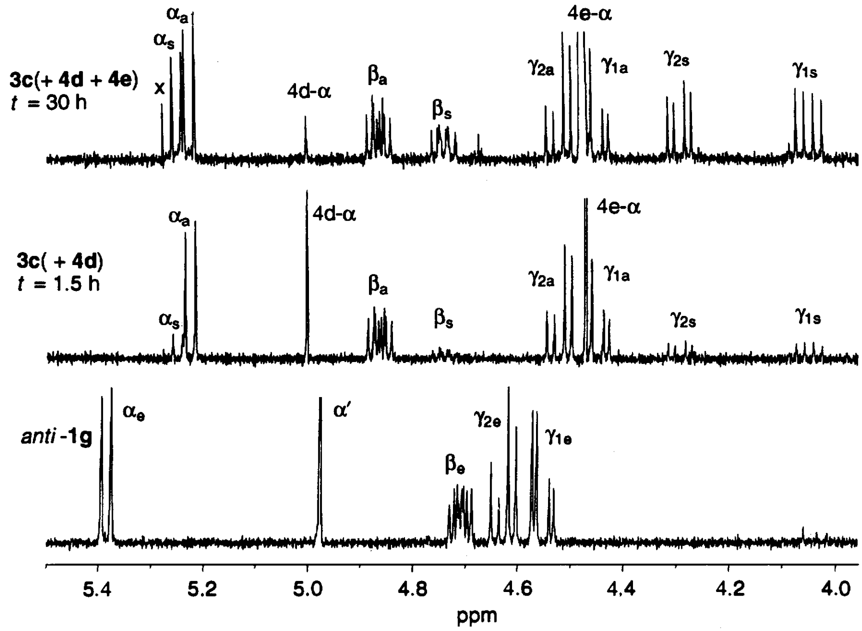


Fig. 1 Partial ^{1}H NMR spectra from NMR tube reaction between the benzyl aryl ether *anti*-**1g** and TMSBr. The lower trace shows *anti*-**1g** before addition of TMSBr; the middle trace is 1.5 h after addition of *ca.* 2 equiv. TMSBr and shows bromides **3c**: *syn*-**3c** has grown to 15% from its initial value of *ca.* 5% *via* isomerization; the upper trace is 30 h after addition to the TMSBr when bromides **3c** have reached their thermodynamic ratio, 56:44 *anti*:*syn*. In this case, the released compound **4d** is also cleaved slowly with TMSBr to form the bromide **4e**. (a = *anti*, *s* = *syn*).

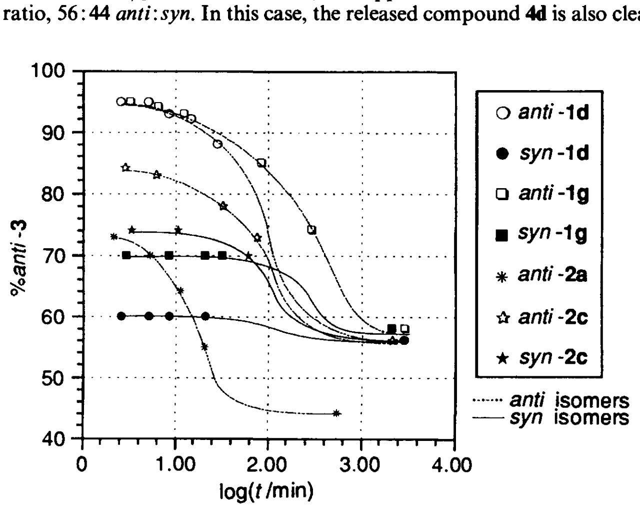


Fig. 2 Bromination of the alcohols **2** or cleavage of the ethers **1** gives the bromides **3** which isomerize. Percent *anti*-**3** is plotted against time (on a log scale) showing the stereoselectivity of the reaction (short time) and the isomerization rate and final equilibrium ratios of the bromides **3**.

stability of the oxonium ion intermediate **7** presumably allows the *anti*-benzyl aryl ethers to be cleaved and brominated by a concerted anchimerically assisted mechanism whereas *syn*-isomers react by a process which may include both concerted and non-concerted pathways. The retention of configuration for *anti*-isomers is in contrast to the observation of inversion made in the case of conversion of (−)-octan-2-ol using TMSBr.[2]

In summary, lignin model benzyl 1,2-diaryl ethers are cleaved cleanly and selectively with TMSBr, *anti*-isomers producing *anti*-bromides with high (*ca.* 95%) diastereoselectivity.

Experimental

General.—^{13}C and ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as internal standard, or [$^2H_6$]acetone where the central solvent peak served as internal standard (δ_H 2.04, δ_C 29.8). Assignments were by the usual complement of NMR experiments.[1,13] Benzyl aryl ethers were synthesized as described previously.[1] Syntheses of model compounds **2a–d** have been described elsewhere.[14,15] Acetylations were performed with 4-dimethylaminopyridine–acetic anhydride in methylene dichloride.[6] Methylations were performed with diazomethane in ethyl ether. Diazomethane was generated as needed by the cautious addition of *N*-nitroso-*N*-methylurea (750 mg) to an immiscible mixture of 40% aq. KOH (3 cm^3) and ethyl ether (10 cm^3) which was kept in an ice–water bath. The compound to be methylated (0.1 mmol) was dissolved in MeOH (1 cm^3) and the ethereal diazomethane (3 cm^3) was added using suitable precautions. The reaction was monitored by TLC and additional diazomethane was added if necessary. The solution was washed with brine and processed in the usual way to afford syrups which were further purified by flash chromatography or preparative TLC if necessary (70–92% yields). Molecular mechanics calculations were performed with PCModel, from Serena Software, Bloomington, IN. All structures were repeatedly annealed to establish the validity of the minima located. Changes in ΔH_f with annealing were less than 0.8 kJ mol^{-1}. AM1 calculations were performed with the Spartan program, from WaveFunction, Inc., Irvine CA. Computations employed a Gateway 66 MHz DX2 microcomputer and a Silicon Graphics Indigo workstation.

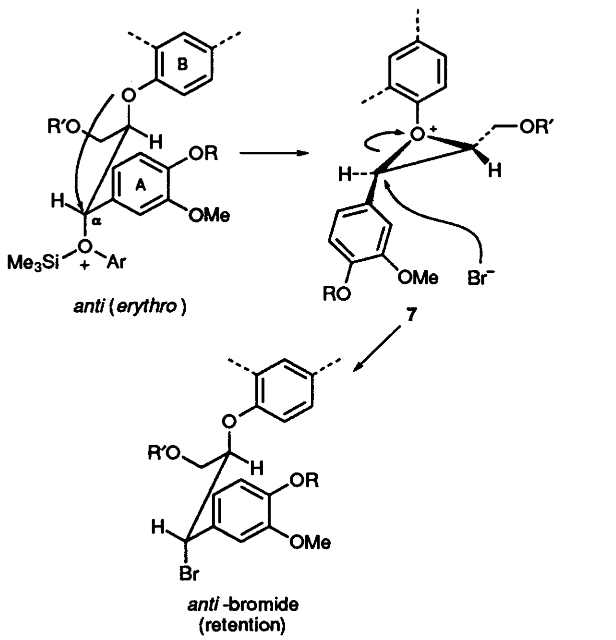
Bromination/Ether Cleavage.—Benzyl aryl ethers **1** (or **5**) or benzyl alcohols **2** (2–5 mg) were dissolved in $CDCl_3$ (400 mm^3) in a 5-mm NMR tube. TMSBr (1–2 mm^3, *ca.* 2 equiv.) was added to the tube which was then shaken and transferred to the NMR probe at 300 K within 1 min. An initial spectrum (t = 2–3 min after TMSBr addition) was taken and further spectra acquired at selected intervals. The bromides **3** from the ethers **1** were spectroscopically identical with those produced by bromination of the alcohols **2**. Isomer ratios were measured from integration of the α-proton doublets.

Methyl 3-{4-[3-*Acetoxy*-1-(3,4-*dimethoxyphenyl*)-2-(2-*methoxyphenoxy*)*propoxy*]-3-*methoxyphenyl*} *acrylate* **1d**.—The purified *syn* and *anti* isomers of **1a**[1] were methylated with diazomethane to afford *syn*-**1b** and *anti*-**1b**; *syn*-**1b** δ_C([$^2H_6$]acetone) 61.83 (γ), 81.22 (α) and 86.45 (β); *anti*-**1b** δ_C([$^2H_6$]acetone) 61.56 (γ), 80.71 (α) and 85.32 (β). Acetylation

Table 1 ^{1}H NMR data for the side-chain protons of selected benzyl ether, benzyl alcohol and benzyl bromide compounds[a]

Compound (solvent)	Chemical shifts (ppm)				Coupling constants (Hz)			
	α	β	γ_1	γ_2	$J_{\alpha,\beta}$	J_{β,γ_1}	J_{β,γ_2}	J_{γ_1,γ_2}
anti-**1d** (C)	5.440	4.709	4.534	4.628	6.5	3.0	5.4	11.7
syn-**1d** (C)	5.495	4.790	4.062	4.380	5.6	6.3	3.7	11.8
anti-**1e** (A)	5.451	4.551	3.835	3.934	5.7	3.6	5.0	11.8
syn-**1e** (A)	5.515	4.528	3.537	3.723	5.9	6.1	3.8	11.7
anti-**1g** (A)	5.547	4.839	4.437	4.533	5.4	3.6	6.1	11.8
syn-**1g** (A)	5.597	4.843	4.088	4.339	5.5	3.8	6.4	11.7
anti-**2c** (C)	4.900	4.445	4.126	4.384	*b*	3.2	7.5	11.6
syn-**2c** (C)	4.871	~4.2[b]	4.031	~4.2[b]	*b*	*b*	*b*	*b*
anti-**3a** (C)	5.244	4.557	4.017	4.088	8.8	3.1	4.3	12.3
syn-**3a** (C)	5.327	4.399	3.300	3.542	9.1	3.2	3.2	12.4
anti-**3b** (C)	5.265	4.565	4.017	4.097	8.9	3.1	4.1	12.3
syn-**3b** (C)	5.345	4.407	3.284	3.546	9.1	3.2	3.1	12.4
anti-**3c** (C)	5.180	4.820	4.407	4.475	7.1	3.9	5.0	11.8
(A)	5.422	5.056	4.303	4.400	6.7	4.4	5.3	11.8
syn-**3c** (C)	5.205	4.696	4.005	4.247	6.3	5.4	4.4	11.8
(A)	5.428	4.953	4.055	4.214	6.3	5.0	4.2	11.8
anti-**5a** (A)	5.603	4.881	*b*	*b*	5.5	*b*	*b*	*b*
anti-**5b** (A)	5.603	4.881	3.954	3.954	5.5	*b*	*b*	*b*
anti-**5c** (A)	5.629	5.084	4.460	4.507	5.8	6.2	3.8	11.9
anti-**6a** (A)	5.621	4.791	~3.95[b]	~3.95[b]	5.3	*b*	*b*	*b*
anti-**6b** (A)	5.640	4.787	*b*	*b*	5.3	*b*	*b*	b
anti-**6c** (A)	5.659	4.988	4.428	4.487	5.3	3.8	6.2	11.9

[a] Values were determined at 300 K in $CDCl_3$ (C) with TMS as internal reference or [$^2H_6$]acetone with the central solvent peak as internal reference (2.04 ppm). The numbering system is based on lignin nomenclature (see Scheme 1); *anti* = *erythro*, *syn* = *threo*. [b] Coupling to the OH protons and exchange lead to broadened or unresolved signals.



Scheme 2 Anchimeric assistance from aryloxy B-ring rationalizing retention of *anti* stereochemistry for *anti* isomers

of the methylated isomers gave the desired *syn*-**1d** and *anti*-**1d**; *syn*-**1d** (Found: M^+, 566.2169. $C_{31}H_{34}O_{10}$ requires *M*, 564.2152); δ_C([$^2H_6$]acetone) 64.09 (γ), 81.26 (α) and 81.92 (β); *anti*-**1d** δ_C([$^2H_6$]acetone) 63.72, (γ), 80.76 (α) and 81.90 (β).

3-(4-*Hydroxy*-3-*methoxyphenyl*)-2-(2-*methoxyphenoxy*)-3-(4-*hydroxymethyl*-2-*methoxyphenoxy*)*propanol* **1e**.—A *syn*/*anti* mixture of **2a** (377 mg, 1.18 mmol) was converted into the quinone methide *via* the TMSBr method.[1,4] To this solution (75 cm^3) was added a freshly prepared suspension of 4-hydroxy-3-methoxybenzyl alcohol (385 mg, 2.5 mmol) and DBU (15 mm^3, 0.1 mmol) in CH_2Cl_2 (10 cm^3). The yellow colour indicative of the quinone methide disappeared during the course of the addition. The mixture was stirred overnight and subsequently evaporated to a syrup. Purification of this by silica gel chromatography [40 g silica; $CHCl_3$–EtOAc, 2:1 (200 cm^3); then $CHCl_3$–EtOAc, 1:1] afforded **1e** as a *syn*/*anti* mixture (178.8 mg, 33%, 32:68 t:e); *syn*-**1e** δ_C([$^2H_6$]acetone) 61.83 (γ), 81.18 (α) and 86.22 (β); *anti*-**1e** δ_C([$^2H_6$]acetone) 61.67 (γ), 81.18 (α) and 85.23 (β).

3-*Acetoxy*-1-(4-*acetoxymethyl*-2-*methoxyphenoxy*)-1-(3,4-*dimethoxyphenyl*)-2-(2-*methoxyphenoxy*)*propane* **1g**.—Methylation of **1e** with diazomethane gave 1-(3,4-dimethoxyphenyl)-3-hydroxy-1-(4-hydroxymethyl-2-methoxyphenoxy)-2-(2-methoxyphenoxy)propane **1f** as a *syn*/*anti* mixture; *syn*-**1f** δ_C([$^2H_6$]acetone-d_6): 61.98 (γ), 81.20 (α), 86.26 (β); *anti*-**1f** δ_C([$^2H_6$]acetone) 61.81 (γ), 81.20 (α) and 85.32 (β). Acetylation and purification by silica gel chromatography ($CHCl_3$–EtOAc, 19:1) gave the purified *anti*-**1g** (> 95% purity) and *syn*-**1g** (90%) (Found: M^+, 554.2152. $C_{30}H_{34}O_{10}$ requires *M*, 554.2152); *syn*-**1g** δ_C([$^2H_6$]acetone) 64.22 (γ), 81.78 (α) and 81.87 (β); *anti*-**1g** δ_C([$^2H_6$]acetone) 63.86 (γ), 80.94 (α) and 81.88 (β).

3-*Acetoxy*-1-*bromo*-1-(3,4-*dimethoxyphenyl*)-2-(2-*methoxyphenoxy*)*propane* **3c**.—The bromides **3c** were generated by the action of TMSBr on the benzyl alcohol **2c** or ethers **1d** or **1g**. The pure isomeric bromides **3c** were isolated in essentially quantitative yield from the alcohols **2c**[4] after the reaction product had been extracted into ethyl acetate and the extract washed with aqueous $NaHCO_3$ to remove HBr, dried ($MgSO_4$), and evaporated to dryness (Found: M^+, 440.0651/438.0628. $C_{20}H_{23}BrO_6$ requires *M*, 440.0661/438.0678); *anti* isomer, δ_C($CDCl_3$) 52.33 (α), 81.45 (β) and 64.32 (γ); δ_C([$^2H_6$]acetone) 53.94 (α), 81.35 (β) and 64.46 (γ); *syn* isomer, δ_C($CDCl_3$) 54.13 (α), 81.61 (β) and 63.68 (γ); δ_C([$^2H_6$]acetone) 56.34 (α), 81.84 (β) and 64.02 (γ).

The bromides **3a** and **3b** have been described previously[3,16] and were not isolated. ^{1}H NMR data is given in Table 1.

Compounds anti-**5a** *and* anti-**5b**.—These derivatized benzyl aryl ethers were synthesized in order to establish the nature of the anchimeric assistance by schemes similar to those used to produce compounds **1**.

The *erythro*- or *anti*-isomers of methyl 3-{4-[1,3-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yloxy]-3-methoxyphenyl}acrylate and methyl 3-{4-[1,3-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-2-yloxy]phenyl}acrylate were prepared as previously described.[1] Etherification of the benzylic alcohol with methyl *p*-hydroxycinnamate, as described previously,[1] produced the *erythro* (*anti*) isomers of **5a** and **6a** in 67 and 63% yields following purification by flash chromatography (2:1, $CHCl_3$–EtOAc as eluent). Compound **5a**, methyl 3-(4-{3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-[4-(2-methoxycarbonylvinyl)-phenoxy]propoxy}phenyl)acrylate, was a white foamy solid (Found: M^+, 534.1861. $C_{30}H_{30}O_9$ requires *M*, 534.1889); δ_C([$^2H_6$]acetone) 51.52 (C9-OMe), 51.53 (B9-OMe), 56.26 (A3-OMe), 61.42 (γ), 79.32 (α), 82.67 (β), 112.00 (A2), 115.55 (A5), 116.15 (B8), 116.25 (C8), 117.23 (C2), 117.23 (C6), 117.34 (B2), 117.34 (B6), 121.43 (A6), 128.19 (C1), 128.22 (B1), 129.37 (A1), 130.46 (B3), 130.46 (B5), 130.48 (C3), 130.48 (C5), 144.87 (C7), 144.94 (B7), 147.35 (A4), 148.23 (A3), 160.49 (C4), 161.67 (B4), 167.67 (C9), 167.72 (B9). Compound **6a**, methyl 3-(4-{3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-[2-methoxy-4-(2-methoxycarbonylvinyl)-phenoxy]propoxy}phenyl)acrylate, was a white foamy solid (Found: M^+, 564.2048. $C_{31}H_{32}O_{10}$ requires *M*, 564.1995); δ_C([$^2H_6$]acetone) 51.52 (B9-OMe), 51.56 (C9-OMe), 56.22 (A3-OMe), 56.32 (B3-OMe), 61.31 (γ), 79.44 (α), 84.21 (β), 112.14 (B2), 112.21 (A2), 115.38 (A5), 116.16 (C8), 116.59 (B8), 117.23 (C2), 117.23 (C6), 117.54 (B5), 121.53 (A6), 123.04 (B6), 128.13 (C1), 129.21 (B1), 129.39 (A1), 130.42 (C3), 130.42 (C5), 144.89 (C7), 145.23 (B7), 147.29 (A4), 148.17 (A3), 151.24 (B4), 151.54 (B3), 160.57 (C4), 167.68 (C9) and 167.71 (B9). Methylation with diazomethane and purification gave extremely low (*ca.* 12–15%) yields of the required phenol-methylated products **5b** and **6b**. The source of losses in the methylation were not further investigated. Compound **5b**, methyl 3-(4-{1-(3,4-dimethoxyphenyl)-3-hydroxy-2-[4-(2-methoxycarbonylvinyl)phenoxy]-propoxy}phenyl)acrylate, was a pale yellow oil, δ_C([$^2H_6$]-acetone) 51.52 (C9-OMe), 51.52 (B9-OMe), 55.97 (A4-OMe), 56.12 (A3-OMe), 61.38 (γ), 79.21 (α), 82.64 (β), 112.38 (A2), 112.47 (A5), 116.21 (B8), 116.33 (C8), 117.26 (C2), 117.26 (C6), 117.38 (B2), 117.38 (B6), 121.02 (A6), 128.26 (C1), 128.32 (B1), 130.51 (B3), 130.51 (B5), 130.52 (C3), 130.52 (C5), 130.56 (A1), 144.87 (C7), 144.96 (B7), 150.25 (A4), 150.26 (A3), 160.50 (C4), 161.69 (B4), 167.66 (C9) and 167.72 (B9). Compound **6b**, methyl 3-(4-{1-(3,4-dimethoxyphenyl)-3-hydroxy-2-[2-methoxy-4-(2-methoxycarbonylvinyl)phenoxy]-propoxy}phenyl)acrylate, was a pale yellow oil, δ_C([$^2H_6$]acetone) 51.52 (B9-OMe), 51.55 (C9-OMe), 55.98 (A4-OMe), 56.07 (A3-OMe), 56.37 (B3-OMe), 61.29 (γ), 79.37 (α), 84.19 (β), 112.19 (B2), 112.24 (B5), 112.70 (A2), 116.27 (C8), 116.67 (B8), 117.29 (C2), 117.29 (C6), 117.60 (B5), 121.14 (A6), 123.10 (B6), 128.25 (C1), 129.30 (B1), 130.49 (C3), 130.49 (C5), 130.59 (A1), 144.91 (C7), 145.25 (B7), 150.20 (A4), 150.23 (A3), 151.31 (B4), 151.65 (B3), 160.63 (C4), 167.68 (C9) and 167.71 (B9). Finally, acetylation using Ac_2O–DMAP gave the derivatives required for determination of the effect of the B-ring methoxy group on the stereoselectivity of the ether cleavage reactions. Compound **5c**, methyl 3-(4-{3-acetoxy-1-(3,4-dimethoxyphenyl)-2-[4-(2-methoxycarbonylvinyl)phenoxy]propoxy}phenyl) acrylate, was a pale yellow oil, δ_C([$^2H_6$]acetone) 20.58 (γ-OAc), 51.54 (C9-OMe), 51.57 (B9-OMe), 55.97 (A4-OMe), 56.14 (A3-OMe), 63.49 (γ), 79.32 (α), 79.81 (β), 112.17 (A2), 112.47 (A5), 116.49 (B8), 116.55 (C8), 117.27 (C2), 117.27 (C6), 117.41 (B2), 117.41 (B6), 120.88 (A6), 128.55 (C1), 128.74 (B1), 130.09 (A1), 130.53 (B3), 130.53 (B5), 130.61 (C3), 130.61 (C5), 144.81 (C7), 144.81 (B7), 150.38 (A4), 150.43 (A3), 160.24 (C4), 161.18 (B4), 167.66 (C9), 167.69 (B9) and 170.79 (γ-OAc). Compound **6c**, methyl 3-(4-{3-acetoxy-1-(3,4-dimethoxyphenyl)-2-[2-methoxy-4-(2-methoxycarbonylvinyl)phenoxy]propoxy}phenyl)-acrylate, was a pale yellow oil, δ_C([$^2H_6$]acetone) 20.61 (γ-OAc), 51.54 (B9-OMe), 51.58 (C9-OMe), 55.99 (A4-OMe), 56.09 (A3-OMe), 56.35 (B3-OMe), 63.49 (γ), 79.62 (α), 81.21 (β), 112.24 (A2), 112.38 (B5), 112.38 (B2), 116.42 (C8), 116.98 (B8), 117.28 (C2), 117.28 (C6), 118.21 (B5), 120.82 (A6), 122.93 (B6), 128.46 (C1), 129.89 (B1), 130.14 (A1), 130.52 (C3), 130.52 (C5), 144.85 (C7), 145.14 (B7), 150.33 (A4), 150.37 (A3), 150.72 (B4), 151.80 (B3), 160.44 (C4), 167.67 (C9), 167.67 (B9) and 170.79 (γ-OAc).

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