ortho-Regioselective Arylation of Phenols: New General Synthesis of *ortho*-Hydroxyarylhydroquinone Bis(methyl Ethers)

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The ortho-regioselective synthesis of unsymmetrical hydroxylated biaryls is accomplished *via* metal-template arylation of different titanium and bromomagnesium phenolates with benzoquinone bis(dimethyl ketals). The results are interpreted in terms of the complex-induced proximity effect.

Hydroxylated biaryls are not only fundamental synthons in the preparation of podands and spherands,[1] but are also useful synthetic precursors to naturally occurring polycyclic compounds.[2]

Oxidative coupling of phenols represents a well established method for the preparation of hydroxylated and symmetrical biaryls.[3]

A great deal of effort has been devoted to chemoselective synthesis of unsymmetrical biaryls and significant results have been obtained by the coupling of different transition metal arenes with convenient aryl halides.[4]

A special route to hydroxylated biaryls is represented by the reaction of electron-rich aromatic substrates with benzoquinone bis(dimethyl ketal) in the presence of zinc chloride.[5] The process is a typical Lewis acid-promoted electrophilic substitution and mixtures of regioisomers have been obtained on reaction with phenols.

Results and Discussion

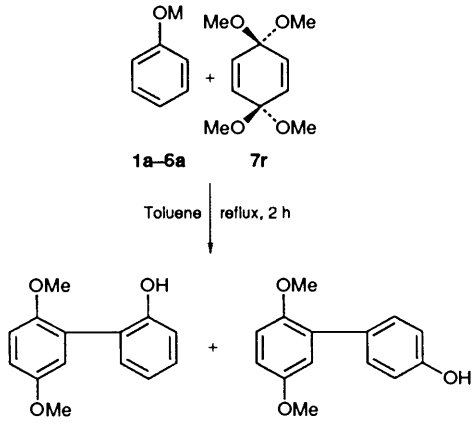
In connection with our interest in the metal-template electrophilic substitution on phenol systems,[6] we recently investigated the reaction of metal phenolates with benzoquinone bis(dimethyl ketals) and we found specific reaction conditions for the preparation of unsymmetrical hydroxylated biaryls in good yield and with a high degree of regiochemical control.

Initially, we studied the effect of the metal promoter M with the intent of obtaining a regioselective process. We chose the phenol and the bisketal **7r** as model reagents in order to avoid side-co-ordinative and steric effects due to the presence of additional groups on the aromatic nucleus. Moreover, in the light of our previous results on the regiochemical outcome of reactions with compounds showing some chemical analogy with the reagent **7r** (*i.e.*, vinylcyclopropanedicarboxylates[7] and ketals[8]), and because the reagent **7r** decomposes at room temperature, producing resinous materials in the presence of hard Lewis acids like $AlCl_3$, $ZnCl_2$ or $TiCl_4$, we utilized metal phenolates with moderate Lewis acidity.[6b]

Reactions were carried out in toluene in order to favour the formation of a reactive phenol–bisketal complex which is responsible for the *ortho*-regioselective process in accordance with our original strategy.[6] Significative results are reported in Table 1.

As shown in Table 1, formation of both *ortho*- and *para*-biaryls **8ar** and **9ar** was observed in all cases. Variable amounts of triaryls, due to reaction of the substrates **1a**–**6a** with two molecules of the reagent **7r**, were detected as by-products, depending on the nature of the metal utilized. In addition, results from Table 1 suggest that titanium is the metal of choice, being the most *ortho*-regioselective promoter. We interpreted these results as being due to the specific oxygenophilic cation's capacity to give the pentaco-ordinate reactive complex **10** involving the phenol and the reagent (Scheme 1).

Table 1 Cation effect in the reaction of different metal phenolates **1a**–**6a** with benzoquinone bis(dimethyl ketal) **7r**



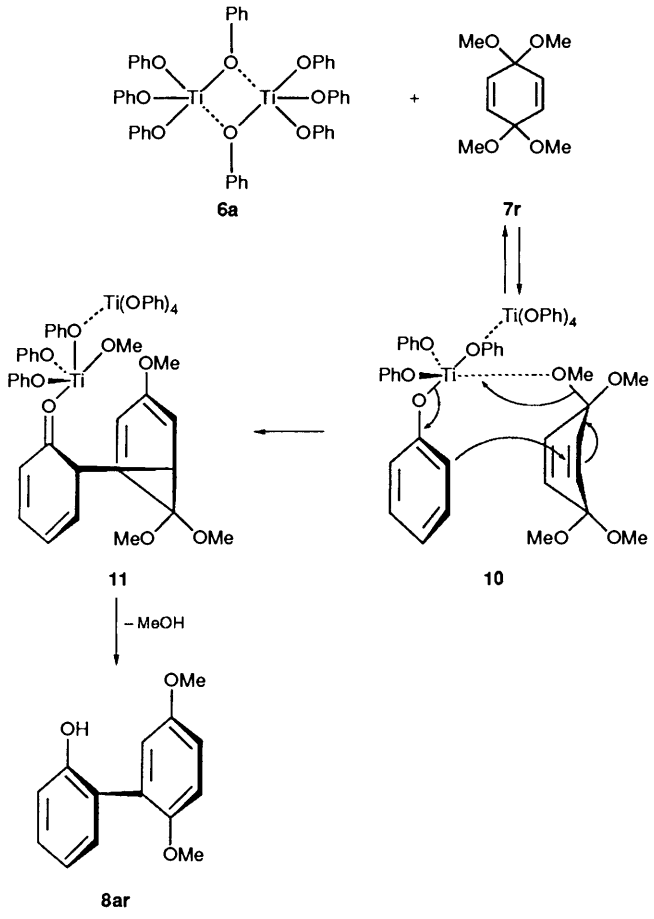
Phenolate	M	Unchanged phenol recovered (%)	Products and yields 8ar (%)	9ar (%)
1a	MgBr	37	20	21
2a	Mg	55	16	20
3a	Zn	48	33	11
4a	B	60	25	13
5a	Al	40	30	18
6a	Ti	57	35	3

The titanium phenolate exists in non-polar solvents as the dimeric structure **6a** in which the metal co-ordinates to five oxygen atoms.[9] The donor reagent **7r** can interact with the titanium, breaking the oxygen bridge and giving rise to the complex **10** in which the cation assembles the phenol and the bisketal in an ordered structure capable of directing the electrophilic attack to the proximate *ortho*-position *via* a complex-induced proximity effect (CIPE).[10,†]

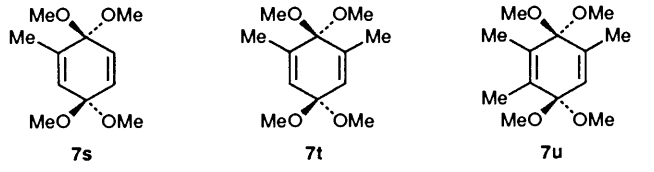
The next point to investigate was the influence of steric hindrance around the metal centre in the reactive complex **10**. To this end, experiments were conducted in which different titanium phenolates were treated with the increasingly substituted benzoquinone bisketals **7s**, **7t** and **7u**.

Not surprisingly the bulkiness of the reactive complex influences the regiochemical behaviour of the process. Indeed, in the reaction with the bisketal **7s**, two isomeric biaryls, **8** and **8′**, were obtained (molecular ratio ≈ 2:1) arising from complexes **12** and **13** with different geometries (Fig. 1).

† The present reaction exhibits some analogy with the arylation recently developed by Barton and co-workers.[11]



Scheme 1



Benzoquinone bis(dimethyl ketals) utilized in the investigation of the steric effect

Moreover, results from Table 2 show that a single methyl group attached to the 2-position of the bisketal ring provides enough steric hindrance to favour the preferential co-ordination of the titanium phenolate with the less hindered acetal group (complex **12**). Consequently, the electrophilic attack preferentially occurs at the more hindered position.

This was confirmed by the results obtained with the bisketals **7t** and **7u**. Attempts to achieve reaction of these substrates with titanium and bromomagnesium phenolates were unsuccessful, no reaction being observed at 80 °C over a period of 10 h. We therefore extended the synthesis to different phenols and bisketals, carrying out the reactions under the best conditions previously found. Synthetic results are reported in Table 3.

As shown in Table 3, the process is of general applicability with respect to the phenol affording the products in satisfactory to good yield under good regiochemical control. The requisite bisketals **7r**, **7s**, **7t**, **7u**, **7v** and **7w** can be readily prepared from the corresponding and easily accessible hydroquinones.[12]

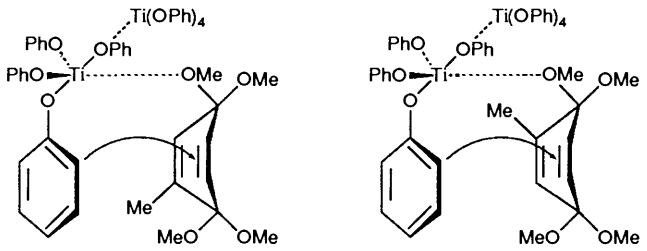
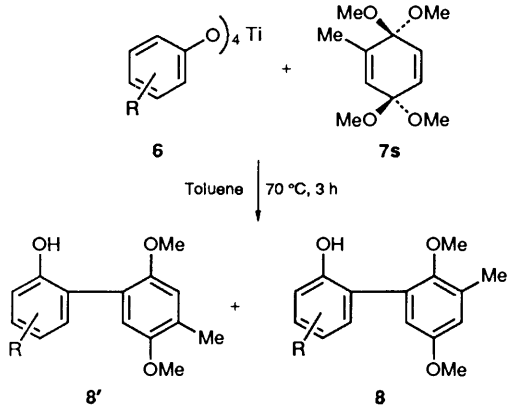


Fig. 1 Isomeric complexes involved in the reaction between titanium phenolate and the reagent **7s**

Table 2 Steric effect in the reaction of variously substituted titanium phenolates **6** with 2-methylbenzoquinone bis(dimethyl ketal) **7s**



Phenol	R	Product 8	Yield (%)	Product 8'	Yield (%)
6b	3-Bu^t	**8bs**	20	**8'bs**	12
6c	3-Me	**8cs**	18	**8'cs**	9
6d	4-Me	**8ds**	25	**8'ds**	13
6e	3,4-(OCH_2O)	**8es**	40	**8'es**	17

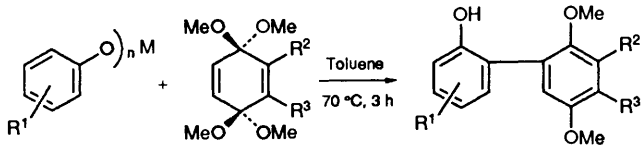
In conclusion, the above reported unsymmetrical *ortho*-hydroxylated biaryl synthesis is an interesting example of a new methodology for *ortho*-regioselective arylation of phenol systems. Moreover, since the hydroxybiaryl moiety is present in a large number of natural and biologically active compounds, this reaction may offer new synthetic opportunities.

Experimental

M.p.s were obtained on Electrothermal melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC100 spectrometer at 100 MHz, on a Bruker CXP200 spectrometer at 200 MHz, or on a Bruker AMX400 spectrometer at 400 MHz. Chemical shifts are expressed in ppm relative to $SiMe_4$ as internal standard; *J*-values are given in Hz. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. Mass spectra were obtained on a Finnigan 1020 instrument at 70 eV. Microanalyses were carried out by Istituto di Chimica Generale ed Inorganica dell'Università di Parma, Italy. Chlorine content was determined by combustion in an oxygen-filled flask. All the phenolates were prepared as previously described.[6b] All the bisketals were prepared as reported in the literature.[12]

Synthesis of Hydroxylated Biaryls. General Procedure.—A solution of the selected bisketal (0.01 mol) in dry toluene (25 cm^3) was added to a stirred solution of the appropriate phenolate (0.01 mol) in dry toluene (25 cm^3) under nitrogen.

Table 3 Regioselective synthesis of unsymmetrical hydroxylated biaryls **8** *via* metal-template arylation of titanium and bromomagnesium phenolates **1**. **6** with benzoquinone bisdimethyl ketals **7r, v, w**



1, 6 **7r, v, w** **8**

Phenolate	M	R^1	Reagent	R^2	R^3	Product	Yield (%)
6a	Ti^{IV}	H	**7r**	H	H	**8ar**	45
6c	Ti^{IV}	3-Me	**7r**	H	H	**8cr**	48
6f	Ti^{IV}	3-OMe	**7r**	H	H	**8fr**	60
6b	Ti^{IV}	3-Bu^t	**7r**	H	H	**8br**	61
6e	Ti^{IV}	3,4-(OCH_2O)	**7r**	H	H	**8er**	100
6g	Ti^{IV}	3,4-(CH=CH)$_2$	**7r**	H	H	**8gr**	85
6h	Ti^{IV}	4-Cl	**7r**	H	H	**8hr**	55
6d	Ti^{IV}	4-Me	**7r**	H	H	**8dr**	30
6i	Ti^{IV}	4-OMe	**7r**	H	H	**8ir**	70
6j	Ti^{IV}	4-Bu^t	**7r**	H	H	**8jr**	39
1b	MgBr	3-Bu^t	**7v**	Me	Me	**8bv**	30
1e	MgBr	3,4-(OCH_2O)	**7v**	Me	Me	**8ev**	56
1g	MgBr	3,4-(CH=CH)$_2$	**7v**	Me	Me	**8gv**	40
1b	MgBr	3-Bu^t	**7w**	CH=CH–CH=CH		**8bw**	68
1e	MgBr	3,4-(OCH_2O)	**7w**	CH=CH–CH=CH		**8ew**	72
1g	MgBr	3,4-(CH=CH)$_2$	**7w**	CH=CH–CH=CH		**8gw**	62
1i	MgBr	4-OMe	**7w**	CH=CH–CH=CH		**8iw**	50

The mixing was continued for 3 h at 70 °C; 2 mol dm^{-3} aq. HCl (50 cm^3) was then rapidly added. The resulting mixture was extracted with methylene dichloride (3 × 50 cm^3). The organic phase was dried (Na_2SO_4), the methylene dichloride was distilled off, and the residue was chromatographed on silica gel plates with 7–20% hexane–EtOAc mixtures or CH_2Cl_2 to give the products.

2′,5′-Dimethoxybiphenyl-2-ol **8ar**. Foam (Found: C, 72.9; H, 6.15. $C_{14}H_{14}O_3$ requires C, 73.02; H, 6.13%); ν_{max}(NaCl)/cm^{-1} 3401 (OH); δ_H(200 MHz; C_6D_6) 3.07 (3 H, s, OMe), 3.29 (3 H, s, OMe), 6.46 (1 H, d, *J* 8.9, 3′-H), 6.71 (1 H, s, OH), 6.74 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.88 (1 H, d, *J* 3.1, 6′-H), 6.88 (1 H, td, *J* 7.5 and 1.5, 4- or 5-H), 7.14 (1 H, td, *J* 7.5 and 1.7, 5- or 4-H), 7.24 (1 H, dd, *J* 7.5 and 1.5, 3- or 6-H) and 7.27 (1 H, dd, *J* 7.5 and 1.7, 6- or 3-H); *m/z* 230 (M^+, 100%), 215 (39) and 200 (26).

2′,5′-Dimethoxybiphenyl-4-ol **9ar**. A pale yellow solid, m.p. 158–161 C (from benzene) (Found: C, 72.95; H, 6.2%); ν_{max}(KBr)/cm^{-1} 3378 (OH); δ_H(200 MHz; C_6D_6) 3.29 (3 H, s, OMe), 3.38 (3 H, s, OMe), 4.55 (1 H, br s, OH), 6.61 (2 H, d, *J* 8.6, 3- and 5-H), 6.64 (1 H, d, *J* 8.6, 3′-H), 6.74 (1 H, dd, *J* 8.6 and 3.0, 4′-H), 7.00 (1 H, d, *J* 3.0, 6′-H) and 7.47 (2 H, d, *J* 8.6, 2- and 6-H); *m/z* 230 (M^+, 100%), 215 (68) and 200 (20).

2′,4,5′-Trimethoxybiphenyl-2-ol **8fr**. Foam (Found: C, 69.1; H, 6.15. $C_{15}H_{16}O_4$ requires C, 69.21; H, 6.20%); ν_{max}(NaCl)/cm^{-1} 3401 (OH); δ_H(200 MHz; C_6D_6) 3.11 (3 H, s, OMe), 3.32 (6 H, s, 2 × OMe), 6.49 (1 H, d, *J* 8.9, 3′- or 6-H), 6.60 (1 H, dd, *J* 8.6 and 2.6, 5- or 4′-H), 6.73 (1 H, dd, *J* 8.9 and 3.1, 4′- or 5-H), 6.88 (1 H, d, *J* 2.6, 3- or 6′-H), 6.92 (1 H, d, *J* 3.1, 6′- or 3-H), 7.01 (1 H, s, OH) and 7.19 (1 H, d, *J* 8.6, 6- or 3′-H); *m/z* 260 (M^+, 100%), 245 (70), 230 (23) and 213 (30).

4-t-Butyl-2′,5′-dimethoxybiphenyl-2-ol **8br**. A pale yellow solid, m.p. 89–93 °C (from benzene) (Found: C, 75.6; H, 7.8. $C_{18}H_{22}O_3$ requires C, 75.49; H, 7.74%); ν_{max}(KBr)/cm^{-1} 3373 (OH); δ_H(200 MHz; C_6D_6) 1.25 (9 H, s, Bu^t), 3.09 (3 H, s, OMe), 3.32 (3 H, s, OMe), 6.48 (1 H, d, *J* 8.9, 3′-H), 6.75 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.78 (1 H, s, OH), 6.95 (1 H, d, *J* 3.1, 6′-H), 7.00 (1 H, dd, *J* 8.1 and 2.0, 5-H), 7.29 (1 H, d, *J* 8.1, 6-H) and 7.38 (1 H, d, *J* 2.0, 3-H); *m/z* 286 (M^+, 100%) and 271 (79).

5-Chloro-2′,5′-dimethoxybiphenyl-2-ol **8hr**. Foam (Found: C, 63.4; H, 5.0; Cl, 13.3. $C_{14}H_{13}ClO_3$ requires C, 63.52; H, 4.95; Cl, 13.40%); ν_{max}(NaCl)/cm^{-1} 3367 (OH); δ_H(200 MHz; C_6D_6) 3.05 (3 H, s, OMe), 3.23 (3 H, s, OMe), 6.41 (1 H, d, *J* 10.0, 3′-H), 6.64 (1 H, s, OH), 6.71 (1 H, d, *J* 2.8, 6′-H), 6.73 (1 H, dd, *J* 10.0 and 2.8, 4′-H), 6.94 (1 H, d, *J* 8.6, 3-H), 7.08 (1 H, dd, *J* 8.6 and 2.5, 4-H) and 7.31 (1 H, d, *J* 2.5, 6-H); *m/z* 266 (M + 2, 31%), 264 (M^+, 100), 249 (20) and 214 (69).

2′,5′-Dimethoxy-5-methylbiphenyl-2-ol **8dr**. A pale brown solid, m.p. 73–77 °C (from benzene) (Found: C, 73.7; H, 6.7. $C_{15}H_{16}O_3$ requires C, 73.75; H, 6.60%); ν_{max}(KBr)/cm^{-1} 3396 (OH); δ_H(400 MHz; C_6D_6) 2.14 (3 H, s, Me), 3.10 (3 H, s, OMe), 3.31 (3 H, s, OMe), 6.48 (1 H, d, *J* 8.9, 3′-H), 6.58 (1 H, s, OH), 6.74 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.92 (1 H, d, *J* 3.1, 6′-H), 6.97 (1 H, dd, *J* 8.2 and 2.0, 4-H), 7.11 (1 H, d, *J* 2.0, 6-H) and 7.19 (1 H, d, *J* 8.2, 3-H); *m/z* 244 (M^+, 100%), 229 (50), 214 (25) and 197 (22).

2′,5,5′-Trimethoxybiphenyl-2-ol **8ir**. A pale brown solid, m.p. 91–93 °C (from benzene) (Found: C, 69.35; H, 6.3. $C_{15}H_{16}O_4$ requires C, 69.21; H, 6.20%); ν_{max}(KBr)/cm^{-1} 3466 (OH); δ_H(200 MHz; C_6D_6) 3.10 (3 H, s, OMe), 3.29 (3 H, s, OMe), 3.34 (3 H, s, OMe), 6.40 (1 H, br s, OH), 6.48 (1 H, d, *J* 8.8, 3′- or 3-H), 6.73 (1 H, dd, *J* 8.8 and 3.0, 4′- or 4-H), 6.77 (1 H, dd, *J* 8.7 and 3.1, 4- or 4′-H), 6.92 (1 H, d, *J* 3.0, 6′- or 6-H), 6.97 (1 H, d, *J* 3.1, 6- or 6′-H) and 7.16 (1 H, d, *J* 8.7, 3- or 3′-H); *m/z* 260 (M^+, 100%), 245 (31), 230 (15) and 213 (19).

5-t-Butyl-2′,5′-dimethoxybiphenyl-2-ol **8jr**. A pale brown solid, m.p. 94–99 °C (from benzene) (Found: C, 75.4; H, 7.7. $C_{18}H_{22}O_3$ requires C, 75.49; H, 7.74%); ν_{max}(KBr)/cm^{-1} 3361 (OH); δ_H(400 MHz; C_6D_6) 1.24 (9 H, s, Bu^t), 3.08 (3 H, s, OMe), 3.31 (3 H, s, OMe), 6.49 (1 H, d, *J* 8.9, 3′-H), 6.57 (1 H, s, OH), 6.74 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.99 (1 H, d, *J* 3.1, 6′-H), 7.23 (1 H, dd, *J* 8.5 and 2.1, 4-H), 7.25 (1 H, dd, *J* 8.5 and 0.8, 3-H) and 7.44 (1 H, dd, *J* 2.1 and 0.8, 6-H); *m/z* 286 (M^+, 63%), 271 (100), 256 (9) and 241 (12).

1-(2′,5′-Dimethoxyphenyl)naphthalen-2-ol **8gr**. A pale brown solid, m.p. 127–129 °C (from benzene) (Found: C, 77.0; H, 5.9. $C_{18}H_{16}O_3$ requires C, 77.12; H, 5.75%); ν_{max}(KBr)/cm^{-1} 3497 (OH); δ_H(400 MHz; C_6D_6) 3.07 (3 H, s, OMe), 3.23 (3 H, s, OMe), 5.46 (1 H, s, OH), 6.60 (1 H, d, *J* 8.7, 3′-H), 6.81 (1 H, d, *J* 3.0, 6′-H), 6.87 (1 H, dd, *J* 8.7 and 3.0, 4′-H), 7.1–7.3 (2 H, m, 6- and 7-H), 7.34 (1 H, d, *J* 8.9, 3-H), 7.55 (1 H, d, *J* 8.9, 4-H), 7.60 (1 H,

d, *J* 8.1, 5- or 8-H) and 7.61 (1 H, d, *J* 7.4, 8- or 5-H); *m/z* 280 (M^+, 100%), 265 (34), 248 (33) and 233 (26).

2′,5′-*Dimethoxy*-4-*methylbiphenyl*-2-*ol* **8cr**. Foam (Found: C, 73.6; H, 6.5. $C_{15}H_{16}O_3$ requires C, 73.75; H, 6.60%); ν_{max}(NaCl)/cm^{-1} 3367 (OH); δ_H(400 MHz; C_6D_6) 2.14 (3 H, s, Me), 3.09 (3 H, s, OMe), 3.31 (3 H, s, OMe), 6.47 (1 H, d, *J* 8.9, 3′-H), 6.75 (1 H, dd, *J* 7.7 and 0.8, 5-H), 6.75 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.80 (1 H, s, OH), 6.94 (1 H, d, *J* 3.1, 6′-H), 7.11 (1 H, d, *J* 0.8, 3-H) and 7.21 (1 H, d, *J* 7.7, 6-H); *m/z* 244 (M^+, 100%), 229 (42), 213 (26) and 197 (24).

2′,5′-*Dimethoxy*-4,5-*methylenedioxybiphenyl*-2-*ol* **8er**. Foam (Found: C, 65.5; H, 5.3. $C_{15}H_{14}O_5$ requires C, 65.69; H, 5.15%); ν_{max}(NaCl)/cm^{-1} 3378 (OH); δ_H(100 MHz; C_6D_6) 3.08 (3 H, s, OMe), 3.28 (3 H, s, OMe), 5.31 (2 H, s, CH_2), 6.44 (1 H, d, *J* 8.9, 3′-H), 6.68 (1 H, s, OH), 6.71 (1 H, dd, *J* 8.9 and 3.1, 4′-H), 6.81 (1 H, s, 3- or 6-H), 6.83 (1 H, d, *J* 3.1, 6′-H) and 6.86 (1 H, s, 6- or 3-H); *m/z* 274 (M^+, 100%), 257 (15), 241 (16) and 229 (78).

2-(1′,4′-*Dimethoxynaphthalen*-2′-*yl*)-4,5-*methylenedioxyphenol* **8ew**. A pale brown solid, m.p. 148–150 °C (from benzene) (Found: C, 70.5; H, 5.1. $C_{19}H_{16}O_5$ requires C, 70.36; H, 4.98%); ν_{max}(KBr)/cm^{-1} 3252 (OH); δ_H(200 MHz; C_6D_6) 3.29 (3 H, s, OMe), 3.34 (3 H, s, OMe), 5.38 (2 H, s, CH_2), 6.48 (1 H, s, 3′-H), 6.98 (2 H, s, 3- and 6-H), 7.32 (2 H, m, 5′- and 8′-H), 7.72 (1 H, s, OH), 8.00 (1 H, m, 7′- or 6′-H) and 8.46 (1 H, m, 6′- or 7′-H); *m/z* 324 (M^+, 100%), 308 (36), 293 (18) and 277 (53).

5-*t*-*Butyl*-2-(1′,4′-*dimethoxynaphthalen*-2′-*yl*)*phenol* **8bw**. A solid, m.p. 120–122 °C (from benzene) (Found: C, 78.5; H, 7.1. $C_{22}H_{24}O_3$ requires C, 78.54; H, 7.19%); ν_{max}(KBr)/cm^{-1} 3508 (OH); δ_H(400 MHz; C_6D_6), 1.31 (9 H, s, Bu^t), 3.28 (3 H, s, OMe), 3.41 (3 H, s, OMe), 6.60 (1 H, s, 3′-H), 7.15 (1 H, dd, *J* 8.1 and 2.1, 5-H), 7.34 (2 H, m, 5′- and 8′-H), 7.45 (1 H, d, *J* 8.1, 6-H), 7.51 (1 H, d, *J* 2.1, 3′-H), 7.81 (1 H, s, OH), 8.03 (1 H, m, 7′- or 6′-H) and 8.47 (1 H, m, 6′-or 7′-H); *m/z* 336 (M^+, 100%), 265 (51) and 250 (19).

2-(1′,4′-*Dimethoxynaphthalen*-2′-*yl*)-5-*methoxyphenol* **8iw**. A pale brown solid, m.p. 141–143 °C (from benzene) (Found: C, 73.4; H, 5.7. $C_{19}H_{18}O_4$ requires C, 73.53; H, 5.85%); ν_{max}(KBr)/cm^{-1} 3300 (OH); δ_H(200 MHz; C_6D_6), 3.29 (3 H, s, OMe), 3.33 (3 H, s, OMe), 3.44 (3 H, s, OMe), 6.57 (1 H, s, 3′-H), 6.80 (1 H, dd, *J* 8.8 and 3.1, 4′-H), 7.16 (1 H, d, *J* 3.1, 6′-H), 7.29 (1 H, d, *J* 8.8, 3′-H), 7.33 (2 H, m, 5′- and 8′-H), 7.37 (1 H, s, OH), 8.01 (1 H, m, 7′- or 6′-H) and 8.44 (1 H, m, 6′- or 7′-H); *m/z* 310 (M^+, 100%), 295 (36), 278 (18) and 263 (34).

1′,4′-*Dimethoxy*-1,2′-*binaphthyl*-2-*ol* **8gw**. A pale brown solid, m.p. 134–135 °C (from benzene) (Found: C, 80.2; H, 5.6. $C_{22}H_{18}O_3$ requires C, 79.98; H, 5.49%); ν_{max}(KBr)/cm^{-1} 3496 (OH); δ_H(400 MHz; C_6D_6) 3.20 (3 H, s, OMe), 3.24 (3 H, s, OMe), 6.17 (1 H, s, OH), 6.47 (1 H, s, 3′-H), 7.22 (2 H, m, 6- and 7-H), 7.38 (2 H, m, 5′- and 8′-H), 7.45 (1 H, d, *J* 8.7, 3-H), 7.63 (1 H, d, *J* 8.7, 4-H), 7.66 (2 H, m, 5- and 8-H), 8.16 (1 H, m, 7′- or 6′-H) and 8.52 (1 H, m, 6′- or 7′-H); *m/z* 330 (M^+, 95%), 315 (66), 298 (42) and 283 (100).

4-*t*-*Butyl*-2′,5′-*dimethoxy*-3′,4′-*dimethylbiphenyl*-2-*ol* **8bv**. A pale brown solid, m.p. 109–111 °C (from benzene) (Found: C, 76.55; H, 8.3. $C_{20}H_{26}O_3$ requires C, 76.40; H, 8.34%); ν_{max}(KBr)/cm^{-1} 3333 (OH); δ_H(200 MHz; C_6D_6) 1.31 (9 H, s, Bu^t), 2.01 (3 H, s, Me), 2.17 (3 H, s, Me), 3.13 (3 H, s, OMe), 3.33 (3 H, s, OMe), 6.59 (1 H, s, 6-H), 7.11 (1 H, dd, *J* 8.1 and 2.0, 5-H), 7.40 (1 H, d, *J* 8.1, 6-H), 7.46 (1 H, d, *J* 2.0, 3-H) and 7.86 (1 H, s, OH); *m/z* 314 (M^+, 100%), 299 (50), 243 (60) and 228 (40).

1-(2′,5′-*Dimethoxy*-3′,4′-*dimethylphenyl*)*naphthalen*-2-*ol* **8gv**. A pale yellow solid, m.p. 109–111 °C (from benzene) (Found: C, 77.8; H, 6.6. $C_{20}H_{20}O_3$ requires C, 77.90; H, 6.54%); ν_{max}(KBr)/cm^{-1} 3311 (OH); δ_H(400 MHz; C_6D_6) 2.11 (3 H, s, Me), 2.24 (3 H, s, Me), 3.04 (3 H, s, OMe), 3.17 (3 H, s, OMe), 6.26 (1 H, s, OH), 6.51 (1 H, s, 6′-H), 7.19 (1 H, t, *J* 7.8, 6- or 7-H), 7.26 (1 H, t, *J* 8.0, 7- or 6-H), 7.46 (1 H, d, *J* 8.8, 3-H), 7.62 (1 H, d, *J* 8.8, 4-H), 7.66 (1 H, d, *J* 7.8, 5- or 8-H) and 7.77 (1 H, d, *J* 8.0, 8- or 5-H); *m/z* 308 (M^+, 100%), 293 (16), 278 (27) and 263 (33).

2′,5′-*Dimethoxy*-3′,4′-*dimethyl*-4,5-*methylenedioxybiphenyl*-2-*ol* **8ev**. A pale yellow solid, m.p. 113–115 °C (from benzene) (Found: C, 67.4; H, 6.1. $C_{17}H_{18}O_5$ requires C, 67.54; H, 6.00%); ν_{max}(KBr)/cm^{-1} 3300 (OH); δ_H(100 MHz; C_6D_6) 1.99 (3 H, s, Me), 2.15 (3 H, s, Me), 3.14 (3 H, s, OMe), 3.27 (3 H, s, OMe), 5.38 (2 H, s, CH_2), 6.50 (1 H, s, 6′-H), 6.95 (1 H, s, 3- or 6-H), 6.96 (1 H, s, 6- or 3-H) and 7.78 (1 H, s, OH); *m/z* 302 (M^+, 100%), 288 (13), 270 (38) and 255 (56).

2′,5′-*Dimethoxy*-3′,4-*dimethylbiphenyl*-2-*ol* **8cs**. A solid, m.p. 86–88 °C (from benzene) (Found: C, 74.5; H, 7.1. $C_{16}H_{18}O_3$ requires C, 74.39; H, 7.02%); ν_{max}(KBr)/cm^{-1} 3311 (OH); δ_H(400 MHz; C_6D_6) 2.06 (3 H, s, 3′-Me), 2.16 (3 H, s, 4-Me), 3.11 (3 H, s, OMe), 3.30 (3 H, s, OMe), 6.66 (1 H, d, *J* 3.2, 4′-H), 6.76 (1 H, d, *J* 3.2, 6′-H), 6.77 (1 H, dd, *J* 7.8 and 1.8, 5-H), 7.15 (1 H, m, 3-H), 7.26 (1 H, d, *J* 7.8, 6-H) and 7.71 (1 H, s, OH); *m/z* 258 (M^+, 100%), 243 (41) and 228 (32).

2′,5′-*Dimethoxy*-4,4′-*dimethylbiphenyl*-2-*ol* **8′cs**. Foam (Found: C, 74.3; H, 7.1%); ν_{max}(NaCl)/cm^{-1} 3367 (OH); δ_H(400 MHz; C_6D_6) 2.18 (3 H, s, 4′-Me), 2.27 (3 H, s, 4-Me), 3.14 (3 H, s, OMe), 3.29 (3 H, s, OMe), 6.51 (1 H, s, 3′- or 6′-H), 6.72 (1 H, s, 6′- or 3′-H), 6.82 (1 H, dd, *J* 7.8 and 1.0, 5-H), 6.92 (1 H, s, OH), 7.16 (1 H, d, *J* 1.0, 3-H) and 7.30 (1 H, d, *J* 7.8, 6-H); *m/z* 258 (M^+, 100%), 242 (21), 227 (18) and 212 (17).

2′,5′-*Dimethoxy*-3′,5-*dimethylbiphenyl*-2-*ol* **8ds**. Foam (Found: C, 74.3; H, 6.95%); ν_{max}(NaCl)/cm^{-1} 3322 (OH); δ_H(400 MHz; C_6D_6) 2.06 (3 H, s, Me), 2.18 (3 H, s, Me), 3.11 (3 H, s, OMe), 3.29 (3 H, s, OMe), 6.68 (1 H, d, *J* 3.1, 4′-H), 6.75 (1 H, d, *J* 3.1, 6′-H), 6.99 (1 H, dd, *J* 8.2 and 2.2, 4-H), 7.17 (1 H, d, *J* 2.2, 6-H), 7.24 (1 H, d, *J* 8.2, 3-H) and 7.55 (1 H, s, OH); *m/z* 258 (M^+, 100%), 242 (38), 228 (22) and 211 (19).

2′,5′-*Dimethoxy*-4′,5-*dimethylbiphenyl*-2-*ol* **8′ds**. Foam (Found: C, 74.5; H, 7.1%); ν_{max}(NaCl)/cm^{-1} 3378 (OH); δ_H(400 MHz; C_6D_6) 2.20 (3 H, s, Me), 2.27 (3 H, s, Me), 3.15 (3 H, s, OMe), 3.29 (3 H, s, OMe), 6.52 (1 H, s, 3′- or 6′-H), 6.72 (1 H, s, OH), 6.72 (1 H, s, 6′- or 3′-H), 7.00 (1 H, dd, *J* 8.2 and 2.0, 4-H), 7.19 (1 H, d, *J* 2.0, 6-H) and 7.24 (1 H, d, *J* 8.2, 3-H); *m/z* 258 (M^+, 100%), 243 (22) and 228 (28).

2′,5′-*Dimethoxy*-3′-*methyl*-4,5-*methylenedioxybiphenyl*-2-*ol* **8es**. Foam (Found: C, 66.7; H, 5.7. $C_{16}H_{16}O_5$ requires C, 66.66; H, 5.59%); ν_{max}(NaCl)/cm^{-1} 3279 (OH); δ_H(100 MHz; C_6D_6), 2.03 (3 H, s, Me), 3.10 (3 H, s, OMe), 3.26 (3 H, s, OMe), 5.34 (2 H, s, CH_2), 6.64 (1 H, s, 4′- or 6′-H), 6.65 (1 H, s, 6′- or 4′-H), 6.87 (1 H, s, 3- or 6-H), 6.91 (1 H, s, 6- or 3-H) and 7.67 (1 H, s, OH); *m/z* 288 (M^+, 100%), 273 (22), 256 (26) and 242 (81).

2′,5′-*Dimethoxy*-4′-*methyl*-4,5-*methylenedioxybiphenyl*-2-*ol* **8′es**. Foam (Found: C, 66.5; H, 5%); ν_{max}(NaCl)/cm^{-1} 3344 (OH); δ_H(100 MHz; C_6D_6) 2.25 (3 H, s, Me), 3.12 (3 H, s, OMe), 3.25 (3 H, s, OMe), 5.35 (2 H, s, CH_2), 6.48 (1 H, s, 3′-H), 6.63 (1 H, s, 6′-H), 6.86 (1 H, s, OH), 6.92 (1 H, s, 3- or 6-H) and 6.94 (1 H, s, 6- or 3-H); *m/z* 288 (M^+, 22%), 257 (6) and 241 (18).

4-*t*-*Butyl*-2′,5′-*dimethoxy*-3′-*methylbiphenyl*-2-*ol* **8bs**. Foam (Found: C, 75.8; H, 8.0. $C_{19}H_{24}O_3$ requires C, 75.97; H, 8.05%); ν_{max}(NaCl)/cm^{-1} 3306 (OH); δ_H(400 MHz; C_6D_6) 1.28 (9 H, s, Bu^t), 2.06 (3 H, s, Me), 3.10 (3 H, s, OMe), 3.31 (3 H, s, OMe), 6.68 (1 H, d, *J* 3.0, 4′-H), 6.77 (1 H, d, *J* 3.0, 6′-H), 7.06 (1 H, dd, *J* 8.1 and 2.0, 5-H), 7.36 (1 H, d, *J* 8.1, 6-H), 7.45 (1 H, d, *J* 2.0, 3-H) and 7.82 (1 H, s, OH); *m/z* 300 (M^+, 100%), 285 (40), 228 (38) and 214 (20).

4-t-*Butyl*-2′,5′-*dimethoxy*-4′-*methylbiphenyl*-2-*ol* **8′bs**. A pale yellow solid, m.p. 99–101 °C (from benzene) (Found: C, 75.8; H, 8.0%); ν_{max}(KBr)/cm^{-1} 3311 (OH); δ_H(200 MHz; C_6D_6) 1.28 (9 H, s, Bu^t), 2.28 (3 H, s, Me), 3.15 (3 H, s, OMe), 3.32 (3 H, s, OMe), 6.52 (1 H, s, 3′- or 6′-H), 6.73 (1 H, s, 6′- or 3′-H), 6.95 (1 H, s, OH), 7.07 (1 H, dd, *J* 8.1 and 1.9, 5-H), 7.37 (1 H, d, *J* 8.1,

6-H) and 7.44 (1 H, d, *J* 1.9, 3-H); *m/z* 300 (M^+, 98%), 285 (62) and 252 (10).

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