An Electron Spin Resonance Study of Radicals produced by Oxidation of *ortho*-Mono- and -Di-hydroxybiphenyls

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The e.s.r. spectra obtained by oxidation of biphenyl-2,2′-diols in neutral solution showed the formation of a monoaryloxyl radical in which the unpaired electron is shared equally by both rings. In the spectra of radicals from unhindered 2,2′-diols variation of the temperature produced small changes in *g* value, which appeared to have a periodic character. Hyperfine splitting constants varied with temperature in both hindered and unhindered radicals. Splitting constants were also unambiguously assigned to the spectra obtained from substituted biphenyl-2-ols.

In a preliminary communication [1] we reported that radicals of sufficient stability for e.s.r. examination by stationary methods were obtained when symmetrically substituted biphenyl-2,2′-diols were oxidized in non-polar solvents with silver oxide. More detailed examination of the temperature dependence of these spectra has revealed some interesting features, and we now report this work in full, together with the interpretations of the spectra from some related biphenyl-2-ols.

Biphenyl-2,2′-*diols*.—Two groups of diols were examined, a hindered series with 3,3′-di-t-butyl substitution, and an unhindered series with 4,4′-di-t-butyl substitution. The striking feature of ring equivalence, common to both groups, was first established using the hindered diol (1). When this compound was ring-deuteriated and oxidized in chloroform solution with silver oxide in the presence of D_2O, a simple septet spectrum was observed (Table 1), clearly indicating the equivalence of the six methoxy-protons. In the absence of D_2O samples gave rise to a doublet of septets showing that one hydroxy-proton still remained; the symmetry of the spectrum indicating that this proton was either rapidly exchanged between the 2,2′-oxygens or equally shared between them. In either case a *cis*-configuration about the central bond is necessary, and free rotation apparently does not occur. As the undeuteriated diol (1) gave a doublet of septets spectrum on oxidation, with a linewidth only slightly broader, a *meta*-hydrogen splitting too small to be resolved was also assumed to be present.

With this information it was a straightforward matter to solve the more complex spectrum from the unhindered diol (4) as a doublet of triplets of septets (Table 1). It was found that the same spectra were produced by chloroform solutions of the diols that had been shaken with aqueous alkaline ferricyanide. This not only demonstrates the homogeneity of the radical solutions, but also indicates that the dissociation constant for the second proton must be quite low.

Although good signals could be obtained over a wide range of temperatures, that from the unhindered diol (4) showed an unusual variation. At −65 °C the spectrum could be accurately simulated, but as the sample was heated marked changes, including loss of symmetry, occurred until at 60 °C the spectrum again approached symmetry, and showed considerable reduction in hydroxy-splitting. To simplify the spectra the oxidations were repeated in the presence of D_2O, thus eliminating hydroxy-splitting. Both low temperature and high temperature spectra (Figure 1) exhibited minimal complexity as the splitting constants fell into integral ratios $a_{\text{H-OMe}}/a_{\text{H-3,3'}}$ = 2 : 3 and 1 : 2, respectively.

It was possible to obtain approximate computer simulations of the spectra recorded at intermediate temperatures by mixing the low and high temperature radicals in appropriate proportions, using *g* values which differed by 2×10^{-5}, and giving the lower temperature spectrum the lower *g* value, as shown in Figure 2. This procedure assumes the existence of two distinct states of the radical with different *g* values. The possibility that one of these may have been a secondary radical arising from an irreversible chemical change was rejected on noting that the sequence could be reversed repeatedly by reversing the temperature change. Reversible dimerization to an acetal was also rejected as the radical formed by oxidation of such a dimer would exhibit a quartet rather than a septet splitting. All the radicals from the biphenyldiols studied were estimated to have *g* values of $2.00423 \pm 5 \times 10^{-5}$ at room temperature by reference to Frémy's salt, measured concurrently.

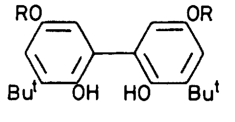
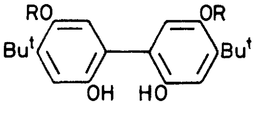
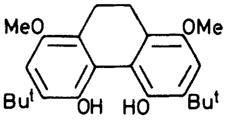
Similar behaviour was observed on oxidizing the isopropoxybiphenyldiol (6). A symmetrical spectrum was obtained at 20 °C and almost achieved at −65 °C. Again, asymmetric spectra were obtained at intermediate temperatures, which could be simulated as mixtures of the low and high temperature radicals, using *g* values which differed by 3×10^{-5}. This compound differed from diol (4) in that some asymmetry reappeared at temperatures higher than 20 °C. In the radical from the ethoxybiphenyldiol (5) asymmetry was observed at both low and high temperatures, while the room temperature spectrum could be simulated as that of a single radical.

None of the hindered diols (1)—(3) gave spectra showing significant asymmetry when the temperature was varied from −65 to +60 °C. Spectra recorded for the radical obtained from (2) at 10° intervals between these limits showed a linear increase in both hydroxy- and alkoxy-hydrogen splittings with decreasing temperature of the same overall size as those in the unhindered series.

In both series three factors may influence the spectra, namely the dihedral angle between the rings, the freedom of rotation of the alkoxy groups, and the O–H bond lengths and orientation. While variation of splitting constant with temperature is not so unusual, variations in *g* value have rarely been observed, one of the few examples being *p*-benzosemiquinone where the increase in *g* value from 2.00450 at −66 °C to 2.00468 at 23 °C has been ascribed to temperature dependent solvent interactions.[2] It has also been shown that temperature variation in the dihedral angle in twisted hydrocarbon radicals can cause variation in *g* values, attributed to changes in the ratio of σ to π contributions to the delocalization of the unpaired electron.[3,4]

The gradual reduction in the splitting constant of the alkoxy-group with rising temperature observed in the hindered series (Table 1) suggests a simple increase in thermal motion such that the lone pair orbitals of the alkoxy-oxygen become less accessible to the free electron.

Table 1. Radicals from partial oxidation of biphenyldiols in chloroform solution. Hyperfine splitting constants are quoted in mT, followed by multiplicities in parentheses

Compound	Number	R	Temp. (°C)	$a_{H\text{-}OR}$	$a_{H\text{-}3,3'}$	$a_{H\text{-}OH}$
 (1)-(3)	(1)	Me	−58	0.089 (7)		0.060 (2)
	(1)	Me	20	0.083 (7)		0.054 (2)
	(1)	Me	60	0.080 (7)		0.050 (2)
	(2)	Et	−28	0.105 (5)		0.0575 (2)
	(2)	Et	20	0.098 (5)		0.054 (2)
	(2)	Et	40	0.095 (5)		0.0525 (2)
	(3)	Pr^i	20	0.059 (3)		0.054 (2)
 (4) - (6)	(4)	Me	−65	0.094 (7)	0.140 (3)	OD
	(4)	Me	60	0.078 (7)	0.156 (3)	OD
	(5)	Et	20	0.104 (5)	0.147 (3)	OD
	(6)	Pr^i	−65	0.067 (3)	0.147 (3)	OD
	(6)	Pr^i	20	0.060 (3)	0.150 (3)	OD
 (7)	(7)		20	0.080 (7)		0.080 (2)

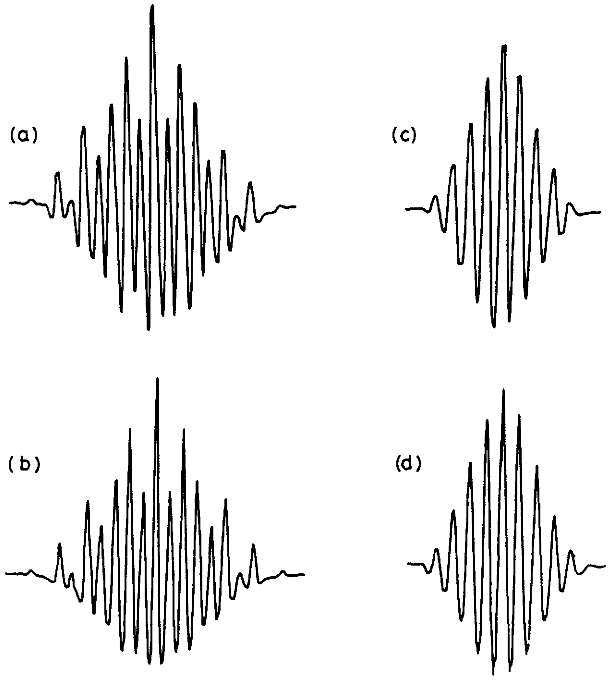


Figure 1. Second derivative e.s.r. spectrum obtained from 5,5′-dimethoxy-4,4′-di-t-butylbiphenyl-2,2′-diol (4) in $CHCl_3$ with D_2O and Ag_2O, (a) at -65 C°, (b) simulated, (c) at $+60$ °C, and (d) simulated

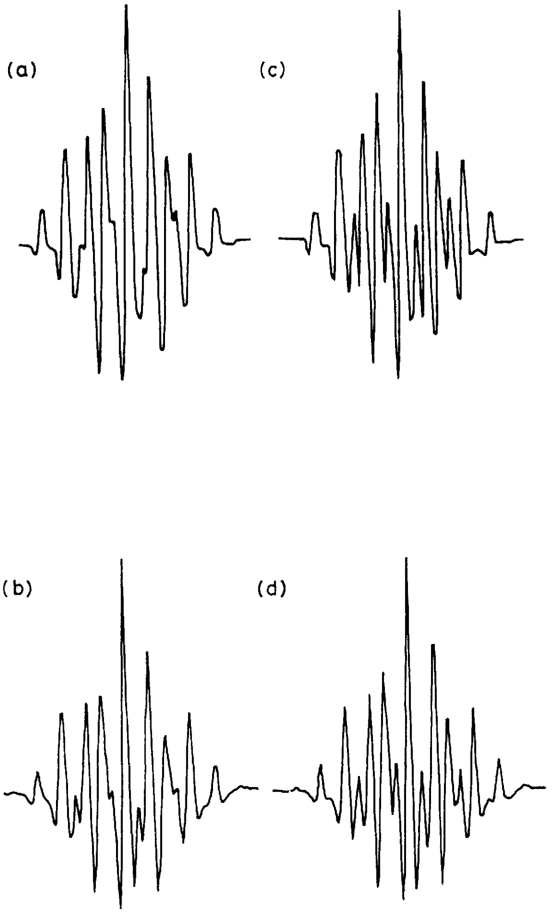
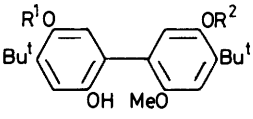
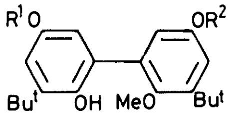


Figure 2. As for Figure 1, (a) at $+10$ °C, (b) simulated, (c) at -10 °C, and (d) simulated

In the unhindered series it is possible that at one extreme of temperature the radical may be exhibiting fast exchange between left- and right-handed twist conformations and at the other, slow exchange or remaining fixed. In the former case the average size of the dihedral angle would be less than in the latter. The difference in g value observed is appropriate for an out-of-plane effect.[3]

The observation that increasing the size of the alkoxy-substitutent does not produce a straightforward progressive change in behaviour suggests that the temperature change may alter vibrational frequencies differently in various parts of the

Table 2. Radicals from the oxidation of biphenylols in carbon tetrachloride solution at 20 °C. Hyperfine splitting constants are quoted in mT, followed by multiplicities in parentheses, except for doublets

Compound	Number	R^1	R^2	a_{H-OR^1}	a_{H-3}	a_{H-6}	$a_{H-6'}$	$a_{H-3'}$
 (8) -(10)	(8) (9) (10)	Me Et Pr^i	Me Et Pr^i	0.150 (4) 0.170 (3) 0.110 (2)	0.453 0.447 0.445	0.112 0.118 0.110	0.075 0.072 0.070	0.040 0.037 0.037
					Phenolic ring		Ether ring	
 (11) - (13)	(11) (12) (13)	Me Et Pr^i	Me Et Pr^i	0.152 (4) 0.171 (3) 0.093 (2)	0.092 (3) 0.094 (3) 0.093 (3)		0.046 (3) 0.049 (3) 0.051 (3)	

molecule so that at certain temperatures an integral frequency relationship, that is to say resonance, will exist. In such a situation periodicity rather than progression would be expected.

It is of interest that the hindered biphenyldiols behave in a fashion similar to the even more hindered dihydrophenanthrenediol (7), both showing the same gradual change in splitting constants throughout the temperature range. It seems that the buttressing effect of the t-butyl groups adjacent to hydroxy-oxygen is sufficient to prevent fast conformational interchange in this series.

Biphenyl-2-ols.—On oxidation with silver oxide in carbon tetrachloride the trimethoxybiphenylol (8) gave a strong and stable signal (Figure 3) of 31 lines with g 2.00494 $\pm 5 \times 10^{-5}$ which could not be directly interpreted. A stepwise approach was therefore adopted in which initially the hindered trialkoxy-compound (12) was prepared and the four ring protons were replaced by deuterium. On oxidation this gave a simple triplet spectrum, showing that splitting by the 2′- and 4′-ethoxy-methylene groups was too small to be observed. Oxidation of the undeuteriated compound (12) gave a spectrum which could now be interpreted as a triplet of triplets of triplets. In this the largest triplet was assigned to the 5-ethoxy-group by comparison with the spectrum of the deuteriated compound. The remaining two triplet splittings must therefore belong to hydrogens at C(4), C(6), C(4′), and C(6′), comprising two pairs of equivalent or nearly equivalent hydrogens. Assignment of splitting constants to these pairs was not straightforward, as the hydrogens of the phenolic ring are at positions of expected low spin density while those of the phenolic ring are not, which may compensate for their greater removal from the aryloxy-oxygen.

The relative size of these triplet splittings was settled by returning to the unhindered phenol series. Compound (9) was prepared and selectively deuteriated at C(6) (9a). The spectrum obtained on oxidation of the undeuteriated compound consisted of four doublets of triplets. The triplet was assigned to the 5-ethoxy-group. The largest doublet was clearly due to the *ortho*-hydrogen at C(3), and the *meta*-splitting was allocated by comparison with the reduction in overall width of the spectrum of the deuteriated compound. The remaining two doublet splittings were allocated by assigning a higher spin density at C(6′) than at C(3′) on the basis of resonance delocalization of the unpaired electron. The relative size of the splittings for hydrogens at C(6) (0.118 mT) and C(6′) (0.072 mT) in the radical from compound (9) is assumed to be general, and on this basis the splittings of all the radicals studied can be satisfactorily assigned (Table 2). Although the splitting constants varied with temperature a detailed study was not attempted.

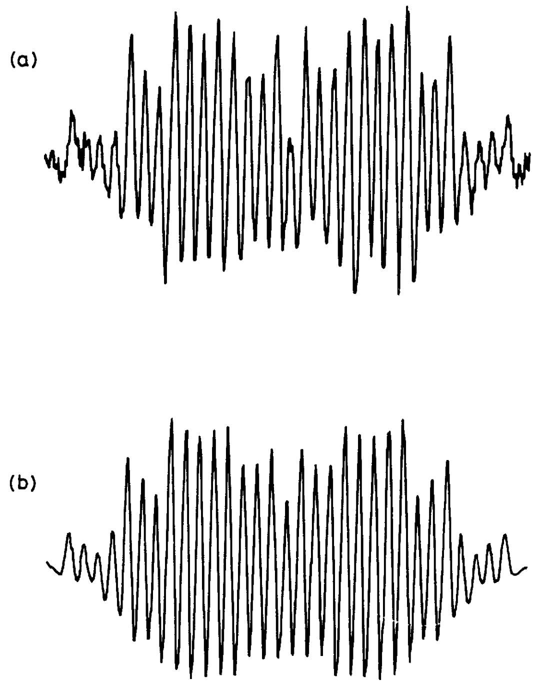
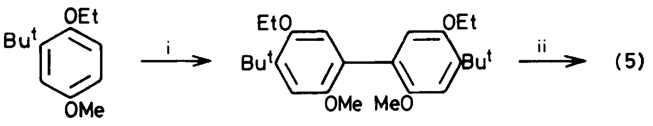
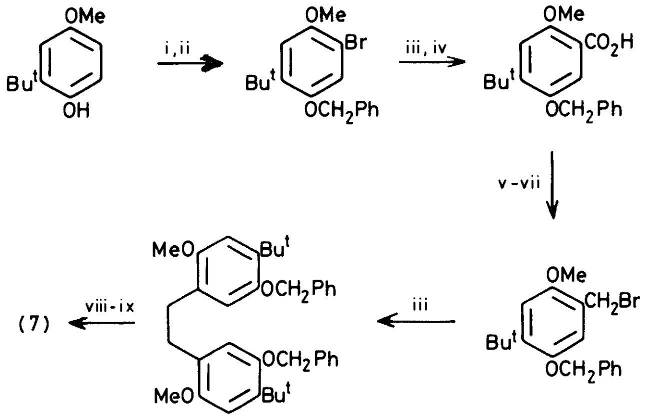


Figure 3. (a) Second derivative e.s.r. spectrum obtained from 2-hydroxy-4,4′-di-t-butyl-2′,5,5′-trimethoxybiphenyl (8) in CCl_4 at 20 °C, (b) simulated

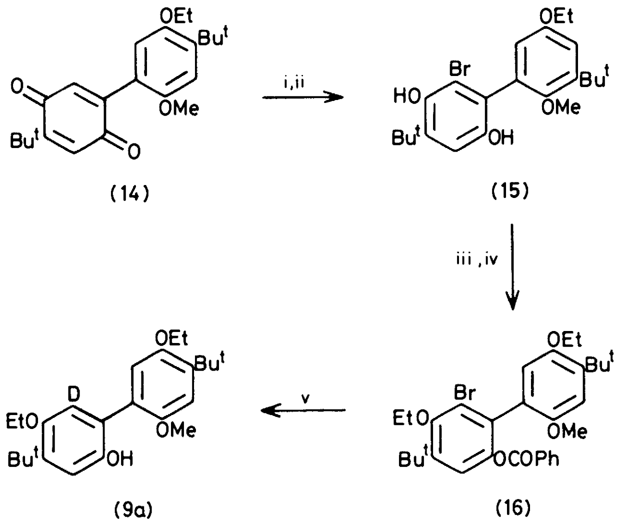
Preparation of Compounds.—For hindered biphenyldiols oxidation of the monomeric phenol with one equivalent of alkaline ferricyanide was found to be the simplest method. For the unhindered diols acid hydrolysis of the dibenzo[*d*,*f*][1,3]-dioxepinspirocyclohexadienone oxidation product of the monomeric phenol was most convenient when the phenol was at hand; [5] otherwise useful alternatives were oxidative coupling with vanadium oxytrifluoride or Ullmann coupling of iodides, followed by treatment with one equivalent of boron tribromide. This reagent was surprisingly selective in cleaving the 2,2′-alkoxy-groups (Scheme 1). If the 2,2′-oxygens are protected as isopropyl ethers, these may be selectively cleaved with titanium tetrachloride.[6]



Scheme 1. *Reagents:* i, VOF_3; ii, BBr_3



Scheme 2. *Reagents:* i, $PhCH_2Br$; ii, Br_2–Na_2CO_3; iii, Mg; iv, CO_2; v, MeOH–H^+; vi, $LiAlH_4$; vii, HBr; viii, H_2, Pd–C; ix, $K_3Fe(CN)_6$



Scheme 3. *Reagents:* i, $NaBH_4$; ii, Br_2; iii, PhCOCl; iv, Et_2SO_4; v, Na–Bu^tOD

Grignard coupling of benzyl bromides provides a convenient route to dihydrophenanthrenes such as (7) as shown in Scheme 2. As this reaction is not as rapid as formation of the Grignard reagent, it is necessary to use just half an equivalent of magnesium.

In the preparation of trialkoxybiphenylols from the corresponding diols it was found that dimethyl sulphate could be limited to monoalkylation by using one equivalent of aqueous sodium hydroxide in acetone at low temperature. Some problems were encountered in the selective deuteriation of phenol (9) at C(6). It was hoped that the undeuteriated compound could be brominated at this position, but it was found that bromine oxidatively dealkylated the compound to the quinone (14).[7] The route eventually used involved bromination of the hydroquinone, and subsequent replacement of bromine by deuterium. Attempts to displace the bromine by catalytic deuteriation failed: dissolving sodium in t-butyl [^{2}H]alcohol was effective (Scheme 3).

Experimental

E.s.r. spectra were recorded with a Varian V-4500 spectrometer equipped with a 9 in magnet, and a TCM20 Deltron temperature controller. Samples were prepared by adding solutions of the phenols to silver oxide, and degassing with nitrogen. Splitting constants are estimated to have a maximum error of 0.002 mT. N.m.r. spectra were recorded with a Hitachi–Perkin-Elmer R-24B spectrometer. M.p.s are uncorrected. Combustion analyses were by the Australian Microanalytical Service.

5,5′-Dimethoxy-3,3′-di-t-butylbiphenyl-2,2′-diol (1) had m.p. 228—229 °C (lit.,[8] 229—230 °C), 5,5′-diethoxy-3,3′-di-t-butylbiphenyl-2,2′-diol (2) had m.p. 185—186 °C (lit.,[9] 185.5—186 °C), 2-hydroxy-4,4′-di-t-butyl-2′,5,5′-trimethoxybiphenyl (8) had m.p. 130—131 °C (lit.,[10] 129—130 °C), and 2-hydroxy-3,3′-di-t-butyl-2′,5,5′-trimethoxybiphenyl (11) had m.p. 102—104 °C (lit.,[11] 103—105 °C).

Ring Deuteriation of 5,5′-*Dimethoxy*-3,3′-*di-t-butylbiphenyl*-2,2′-*diol* (1).—Acetyl chloride (distilled) (12 ml) was mixed with dry dioxan (10 ml) and cooled to 10°. D_2O (4 ml) was added very slowly while stirring. A portion of this solution (10 ml) was added to a solution of the biphenyldiol (1 g) in dry dioxan (5 ml) and boiled under reflux for 9 h. The biphenyldiol was extracted with hexane, which was washed with water, aqueous sodium hydrogencarbonate, and water, and evaporated. After repetition of this deuteriation the biphenyldiol showed no detectable aromatic protons in the n.m.r. spectrum.

5,5′-*Di-isopropoxy*-3,3′-*di-t-butylbiphenyl*-2,2′-*diol* (3).—A solution of t-butylhydroquinone (16.6 g) and 2-bromopropane (28 g) was stirred with sodium iodide (5 g) in dimethyl sulphoxide (DMSO) (50 ml) under nitrogen for 1 h. Sodium hydroxide (4.4 g) in water (5 ml) was added and stirring was continued overnight. Water (100 ml) was added and the mixture was extracted with hexane. This was washed with water and evaporated. On crystallization from hexane 4-isopropoxy-2-t-butylphenol (10.9 g) was obtained which on recrystallization had m.p. 78—79 °C (Found: C, 75.0; H, 9.8. Calc. for $C_{13}H_{20}O_2$: C, 75.1; H, 9.6%); δ (CCl_4) 1.30 (d, 2 Me, J 6.0 Hz), 1.45 (Bu^t), 4.25 (sept, CH, J 6.0 Hz), 5.1 (OH), and 6.2—6.7 (3 ArH); M^+ 208. A solution of this phenol (4.7 g) in acetone (50 ml) was stirred under nitrogen with potassium ferricyanide (8.2 g) in water (80 ml) and sodium hydroxide (0.95 g) in water (10 ml) was added. After stirring for 2 h the mixture was extracted with hexane. The residue after evaporation of solvent was crystallized from methanol to give the *product* (3) (3.1 g), m.p. 140—141 °C (Found: C, 75.5; H, 9.2. $C_{26}H_{38}O_4$ requires C, 75.4; H, 9.1%); δ (CCl_4) 1.28 (d, 4 Me, J 6 Hz), 1.40 (2 Bu^t), 4.31 (sept, 2 CH, J 6 Hz), 4.8 (2 OH), 6.43, and 6.73 (d, 4 ArH, J 4 Hz); M^+ 414.

5,5′-*Dimethoxy*-4,4′-*di-t-butylbiphenyl*-2,2′-*diol* (4) *using Vanadium Oxytrifluoride*.—A solution of 4-isopropoxy-2-t-butylphenol (10.4 g), prepared as described previously, and dimethyl sulphate (7.5 g) in acetone (50 ml) was refluxed under nitrogen while stirring with sodium hydroxide (3 g) in water (7 ml) for 1.5 h. Water (50 ml) was added and the mixture was extracted with hexane. This was washed with water and evaporated to give 4-*isopropoxy*-2-*t-butylanisole*, an oil. A small sample prepared in the same way was purified by silica t.l.c. (Found: C, 75.5; H, 9.9. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%); δ (CCl_4) 1.24 (d, 2 Me, J 6.0 Hz), 1.31 (Bu^t), 3.64 (OMe), 4.24 (sept, CH, J 6.0 Hz), and 6.2—6.7 (3 ArH); M^+ 222. Without purification this anisole and chloroacetic acid (5.2 g) were dissolved in carbon tetrachloride which was evaporated to dry the materials. These were redissolved in dry dichloromethane (30 ml) and vanadium oxytrifluoride (6.7 g) was added while stirring at 0 °C. After 20 min water was added and the mixture was extracted with hexane. This was washed with water, sodium hydrogencarbonate solution, and water, then evaporated. The residue was crystallized twice from methanol; the second time sufficient sodium borohydride was added to decolourize the solution, which was then acidified and cooled to give 2,2′-*di-isopropoxy*-5,5′-*dimethoxy*-4,4′-*di-t-butylbiphenyl* (7.9 g), m.p. 106 °C (Found: C, 75.9; H, 9.8. $C_{28}H_{42}O_4$ requires C, 75.0; H, 9.6%); δ (CCl_4) 1.1 (d, 4 Me, *J* 7 Hz), 1.35 (2 Bu^t), 3.71 (2 OMe), 4.02 (sept, 2CH_2, *J* 7 Hz), 6.71, and 6.76 (4 ArH); M^+ 442. A solution of this biphenyl (3.5 g) in carbon tetrachloride (15 ml) was stirred at 0 °C, and titanium tetrachloride (2 ml) in cold carbon tetrachloride (10 ml) was added. The mixture was allowed to come to room temperature while stirring for 20 min. After addition of water, the product was extracted with ether which was washed with water, dried, and evaporated. The residue was dissolved in methanol and decolourized with sodium borohydride. The solution was acidified, then diluted with water giving the biphenyldiol (4) (2.2 g), m.p. 167—168 °C (lit.,[10] 169—170 °C).

5,5′-*Diethoxy*-4,4′-*di-t-butylbiphenyl*-2,2′-*diol* (5).—A solution of 4-ethoxy-3-t-butylanisole (36 g) in chloroform (144 ml) was stirred with iodine (44 g) and silver trifluoroacetate (49 g) for 1 h. The solution was filtered from the silver iodide residue which was washed with acetone. The combined solutions were washed with water and evaporated to give 4-*ethoxy*-2-*iodo*-5-*t-butylanisole* (44 g), m.p. 100 °C (from ethanol) (Found: C, 46.9; H, 5.7; I, 38.0. $C_{13}H_{19}IO_2$ requires C, 46.8; H, 5.7; I, 38.0%); δ (CCl_4) 1.35 (Bu^t), 1.42 (t, Me, *J* 7 Hz), 3.72 (OMe), 3.93 (q, CH_2, *J* 7 Hz), 6.60, and 7.00 (ArH); M^+ 334. This iodide (8.1 g) was heated with treated [12] copper bronze (15 g) in an oil-bath. When the reactants reached 200° a rapid rise to 236° occurred. The oil-bath was held at 220° for a further 30 min. The solids were extracted with hot chloroform and the residue on evaporation was crystallized from ethanol–acetone to give 5,5′-*diethoxy*-2,2′-*dimethoxy*-4,4′-*di-t-butylbiphenyl* (3.5 g), m.p. 147—147.5 °C (Found: C, 75.1; H, 9.4. $C_{26}H_{38}O_4$ requires C, 75.3; H, 9.2%); δ ($CDCl_3$) 1.34 (Bu^t), 1.34 (t, Me, *J* 6 Hz), 3.75 (OMe), 4.03 (q, CH_2, *J* 6 Hz), 6.84, and 6.96 (ArH); M^+ 414.

A solution of this biphenyl (2 g) in hexane (10 ml) was cooled in an ice-bath while stirring under nitrogen. A solution of boron tribromide (6.6 ml) (1 g per 5 ml of dichloromethane) was added and the mixture was allowed to come to room temperature overnight. Water was added dropwise while stirring till the vigorous reaction had ceased. After separation of the organic layer and evaporation of solvents the residue was dissolved in methanol. The solution was decolourized with a little sodium borohydride, acidified, diluted with water till cloudy, warmed, and cooled to crystallize the *diol* (5) (1.2 g), m.p. 208—209.5 °C (Found: C, 74.5; H, 8.8. $C_{24}H_{34}O_4$ requires C, 74.6; H, 8.8%); δ ($CDCl_3$) 1.40 (Bu^t), 1.45 (t, Me, *J* 7 Hz), 4.04 (q, CH_2, *J* 7 Hz), 5.2 (OH), 6.79, and 7.01 (ArH); M^+ 386.

5,5′-*Di-isopropoxy*-4,4′-*di-t-butylbiphenyl*-2,2′-*diol* (6).—Sodium hydroxide (12 ml of 50%) was added to a solution of 2-t-butyl-4-methoxyphenol (18 g) and 2-bromopropane (18.4 g) in DMSO (30 ml) and acetone (50 ml) while stirring under nitrogen. After stirring for 1 h and refluxing for 1 h water (160 ml) was added and the mixture was extracted with hexane. This was washed thoroughly with water and evaporated to give the 4-*isopropoxy*-3-*t-butylanisole* (21.4 g), an oil (Found: C, 75.4; H, 9.8. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%); δ ($CDCl_3$) 1.33 (d, 2 Me, *J* 6.0 Hz), 1.37 (Bu^t), 3.68 (OMe), 4.50 (sept, 1 H, *J* 6.0 Hz), and 6.4—6.9 (m, 3ArH); M^+ 222.

This diether (15 g) was dissolved in chloroform (100 ml) and stirred with silver trifluoroacetate (19.4 g) and iodine (18 g). After 1 h the mixture was filtered and the silver iodide was washed with acetone. The combined solutions were evaporated to give 4-*isopropoxy*-2-*iodo*-3-*t-butylanisole* (17.7 g), m.p. 60° (from methanol) (Found: C, 48.3; H, 6.1; I, 36.7. $C_{14}H_{21}IO_2$ requires C, 48.3; H, 6.1; I, 36.7%); δ (CCl_4) 1.32 (Bu^t), 1.35 (t, 2 Me, *J* 6.0 Hz), 3.73 (OMe), 4.50 (sept., CH, *J* 6.0 Hz), 6.65, and 7.00 (ArH); M^+ 348. This anisole (17 g) was heated with copper bronze (20 g) as described previously to give 5,5′-*di-isopropoxy*-2,2′-*dimethoxy*-4,4′-*di-t-butylbiphenyl* (6.8 g), m.p. 131 °C (from methanol) (Found: C, 76.0; H, 9.5. $C_{28}H_{42}O_4$ requires C, 76.0; H, 9.6%); δ (CCl_4) 1.35 (d, 4 Me, *J* 6.0 Hz), 1.40 (2 Bu^t), 3.60 (2 OMe), 4.50 (sept, CH, *J* 6.0 Hz), 6.62 (2 ArH), and 6.76 (2 ArH); M^+ 442.

Boron tribromide (9.4 ml of a 1 g in 5 ml dichloromethane solution) was added to a solution of this biphenyl (3.3 g) in dry dichloromethane (30 ml) while stirring at 0 ° under nitrogen, and the mixture was allowed to come to room temperature with stirring overnight. Water was added dropwise, then sufficient hexane to invert the layers. The organic layer was separated and evaporated and the *diol* (6) (1.7 g) was crystallized from methanol, m.p. 226 °C (Found: C, 75.1; H, 9.2, $C_{26}H_{38}O_4$ requires C, 75.3; H, 9.2%); δ ($CDCl_3$) 1.35 (d, Me. *J* 6.0 Hz), 1.38 (Bu^t), 4.50 (sept, *J* 6.0 Hz), 5.2 (OH), 6.60, and 6.85 (ArH); M^+ 414.

4-*Benzyloxy*-3-*t-butylanisole*.—A solution of 3-t-butyl-4-methoxyphenol (72 g) and benzyl chloride (51 g) in acetone (150 ml) and DMSO (80 ml) was stirred under nitrogen and a solution of sodium hydroxide (30 g) in water (50 ml) was added. After refluxing overnight, water (300 ml) was added and the mixture was extracted with hexane, washed with water, and evaporated to give the *product* (97 g), m.p. 57 °C, which crystallized on addition of hexane (Found: C, 80.0; H, 8.1. $C_{18}H_{22}O_2$ requires C, 80.0; H, 8.2%); δ ($CDCl_3$) 1.36 (Bu^t), 3.67 (OMe), 4.96 (CH_2), 6.4—6.9 (3 ArH), and 7.1—7.4 (5 ArH); M^+ 270.

4-*Benzyloxy*-2-*bromo*-5-*t-butylanisole*.—The benzyl ether above (108 g) was dissolved in carbon tetrachloride (108 ml) and stirred vigorously while cooling in an ice–salt-bath with a solution of sodium carbonate (23.5 g) in water (100 ml). Bromine (65.3 g) in carbon tetrachloride (70 ml) was added dropwise so that the temperature stayed below 3° C. After stirring a further 15 min the organic layer was separated, washed with water, and evaporated. On crystallization from hexane the *product* (130 g) was obtained, m.p. 76 °C (Found: C, 61.7; H, 5.9. $C_{18}H_{21}BrO_2$ requires C, 61.9; H, 6.1%); δ ($CDCl_3$) 1.35 (Bu^t), 3.77 (OMe), 4.93 (CH_2), 6.80, 6.99 (ArH), and 7.1—7.4 (5 ArH); M^+ 348/350.

5-*Benzyloxy*-2-*methoxy*-4-*t-butylbenzoic Acid*.—Magnesium (10 g) was placed in a 1 l three neck round-bottomed flask with magnetic stirrer. A few crystals of iodine were added and the flask was flamed under a slow stream of nitrogen until the iodine was seen to vaporize. The bromide above (95.5 g) and 1,2-dibromomethane (10 g) were dissolved in dry tetrahydrofuan (distilled from sodium hydride) (400 ml). Enough of this solution was run into the flask to cover the magnesium, then 1,2-dibromoethane (1 ml) was added, and reaction was seen to commence. The stirrer was then turned on and the main solution was added dropwise at such a rate that 50 °C was maintained. When the addition was complete the solution was refluxed for a further 30 min, then cooled to −40 °C in an acetone–dry ice-bath. Carbon dioxide was passed over the surface of the vigorously stirred solution, at such a rate that the temperature approached −25 °C. When the temperature started to fall again the cooling bath was removed without delay and stirring was continued under the carbon dioxide stream for a further 1 h. The mixture was then poured onto crushed ice (100 ml) and acidified with hydrochloric acid. The *product* was extracted with ethyl acetate, which was washed with water, dried, and evaporated to give an *oil* which crystallized (72.2 g), m.p. 134—136 °C, on addition of hexane (Found: C, 72.3; H, 7.2. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.1%); δ ($CDCl_3$) 1.38 (Bu^t), 3.96 (OMe), 5.02 (CH_2), 6.86, 7.54 (2 ArH), 7.2 (5 ArH), and 9.3 (OH); *M*$^+$ 314.

Methyl 5-Benzyloxy-2-methoxy-4-t-butylbenzoate.—The acid above (113 g) was stirred and refluxed overnight in methanol (500 ml) with concentrated hydrochloric acid (10 ml). The *ester* (110 g), m.p. 105—106 °C, crystallized from this solution on cooling (Found: C, 73.0; H, 7.2. $C_{20}H_{24}O_4$ requires C, 73.0; H, 7.5%); δ ($CDCl_3$) 1.37 (Bu^t), 3.76 (2 Me), 4.96 (CH_2), 8.83 (1 ArH), and 7.28 (6 ArH); *M*$^+$ 328.

4-*Benzyloxy*-2-*hydroxymethyl*-5-*t*-*butylanisole*.—Lithium aluminium hydride was added in portions to a solution of the ester above (24 g) in dry tetrahydrofuran (75 ml) while stirring, until vigorous effervescence was no longer observed (*ca*. 2 g). Ethyl acetate (200 ml) was added, then magnesium sulphate (6 g) and water (2 ml). The mixture was filtered and the solids were washed several times with ethyl acetate. On evaporation of the solvent and crystallization from hexane the *product* (19.7 g) was obtained, m.p. 89—89.5 °C (Found: C, 75.9; H, 8.4. $C_{19}H_{24}O_3$ requires C, 75.9; H, 8.1%); δ ($CDCl_3$) 1.38 (Bu^t), 2.15 (OH), 3.79 (OMe), 4.57 (CH_2OH), 5.02 (OCH_2Ph), 6.82, 6.86, (ArH), and 7.33 (5ArH); *M*$^+$ 300.

4-*Benzyloxy*-2-*bromomethyl*-5-*t*-*butylanisole*.—The benzyl alcohol above (70 g) was dissolved in benzene (210 ml) and cooled to 4 °C in an ice-bath. While stirring, aqueous hydrobromic acid (46—49%) (175 ml) was added slowly so that the temperature did not rise. Stirring was continued for 3 h while the ice-bath was maintained, then the temperature was allowed to rise overnight. Ether and water were added then the organic layer was separated, washed with water, sodium hydrogencarbonate solution, and water, dried, and evaporated at room temperature. The *bromide* (68 g), crystallized from hexane, had m.p. 100 °C (Found: C, 62.8; H, 6.1; Br, 22.3. $C_{19}H_{23}BrO_2$ requires C, 62.8; H, 6.4; Br, 22.0%); δ ($CDCl_3$) 1.37 (Bu^t), 3.41 (OMe), 4.46 (CH_2Br), 4.99 (CH_2Ph), 6.79, 6.83 (ArH), and 7.3 (5 ArH); *M*$^+$ 362/364.

1,2-*Bis*-(5-*benzyloxy*-2-*methoxy*-4-*t*-*butylphenyl*)*ethane*.—The benzyl bromide above (68.3 g) was dissolved in dry THF (250 ml) and added to magnesium (2.3 g), previously flamed under nitrogen with a crystal of iodine. When a little of the solution had been added, the mixture was warmed to initiate reaction, then the remainder of the solution was added while stirring at a rate sufficient to sustain a temperature of 55 °C. After addition was complete the mixture was refluxed for 2.5 h. The solution was washed with water and on cooling gave the *coupled product* (36 g), m.p. 161—162 °C (Found: C, 80.5; H, 7.9. $C_{38}H_{46}O_4$ requires C, 80.5; H, 8.2%); δ ($CDCl_3$) 1.37 (Bu^t), 2.76 (CH_2), 3.81 (OMe), 4.88 ($PhCH_2$), 6.56, 6.75 (ArH), and 7.27 (ArH); *M*$^+$ 566.

1,2-*Bis*-(5-*hydroxy*-2-*methoxy*-4-*t*-*butylphenyl*)*ethane*.—The dibenzyloxy-ether above (3 g) was hydrogenated in ethanol (45 ml) over palladium charcoal for 3 h, then filtered. Water (10 ml) was added and on partial evaporation of the ethanol and cooling, the *product* (1.8 g), m.p. 197—198 °C, crystallized (Found: C, 74.4; H, 8.8. $C_{24}H_{34}O_4$ requires C, 74.6; H, 8.9%); δ ($CDCl_3$) 1.39 (Bu^t), 2.71 (CH_2), 3.72 (OMe), 4.6 (OH), 6.43, and 6.62 (ArH); *M*$^+$ 386.

4,5-*Dihydroxy*-1,8-*dimethoxy*-3,6-*t*-*butyl*-9,10-*dihydrophenanthrene* (7).—A solution of the above biphenylethane (1.1 g) in ether (100 ml) was stirred and refluxed with a solution of potassium ferricyanide (1.9 g) and sodium hydroxide (1 g) in water (20 ml) overnight. The ether layer was separated, washed with water, and evaporated to a blue glass. This was dissolved in methanol giving a red solution which was decolourized with sodium borohydride, acidified with dilute hydrochloric acid, warmed, and cooled to crystallize the *diol* (7) (0.5 g), m.p. 208—212 °C (Found: C, 71.5; H, 8.6. $C_{20}H_{32}O_4.H_2O$ requires C, 71.6; H, 8.5%); δ ($CDCl_3$) 1.43 (Bu^t), 2—3 (CH_2), 3.75 (OMe), 6.3 (OH), and 6.80 (ArH); *M*$^+$ 384.

5,5′-*Diethoxy*-2-*hydroxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl* (9).—A solution of diol (5) (200 mg) and dimethyl sulphate (70 mg) in acetone (5 ml) was stirred under nitrogen in an ice-bath while aqueous sodium hydroxide (1 ml of 2.5%) was added. After stirring overnight the mixture was extracted with hexane and a portion was purified by t.l.c. on silica to give the *product* (9), m.p. 111—113 °C, δ ($CDCl_3$) 1.40 (2 Bu^t), 1.43 (t, 2 OEt, *J* 7 Hz), 3.76 (OMe), 3.95 (q, 2 OEt, *J* 7 Hz), 6.34 (OH), 6.62, 6.71, and 6.87 (2 H) (ArH); *M*$^+$ 400.

2-*Hydroxy*-5,5′-*di*-*isopropoxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl* (10).—In a procedure similar to that above, the diol (6) gave the *monomethylated product* (10), m.p. 60—63 °C, δ ($CDCl_3$) 1.35 (d, 4 Me, *J* 7 Hz), 1.39 (2 Bu^t), 3.77 (OMe), 4.55 (sept, 2CH, *J* 7 Hz), 6.4 (OH), 6.65, 6.73, 6.90, and 6.92 (ArH); *M*$^+$ 428.

5,5′-*Diethoxy*-2-*hydroxy*-2′-*methoxy*-3,3′-*di*-*t*-*butylbiphenyl* (12).—With the diol (2) a procedure similar to that for the unhindered compound (9) gave the *product* (12), m.p. 102—103.5 °C (Found: C, 75.0; H, 9.1. $C_{25}H_{36}O_4$ requires C, 75.0; H, 9.0%); δ (CCl_4) 1.12, 1.36 (t, Me, *J* 7 Hz), 1.41 (2 Bu^t), 3.37 (OMe), 3.91, 3.93 (q, CH_2, *J* 7 Hz), 6.3 (OH), 6.53 (d, 2 ArH, *J* 3 Hz), and 6.74 (d, 2 ArH, *J* 3 Hz).

2-*Hydroxy*-5,5′-*di*-*isopropoxy*-2′-*methoxy*-3,3′-*di*-*t*-*butylbiphenyl* (13).—A solution of 5,5′-di-isopropoxy-3,3′-di-t-butylbiphenyl-2,2′-diol (3) (1 g) in DMSO (10 ml) was stirred under nitrogen with methyl iodide (1 g). Sodium hydroxide (0.11 g) in water (1 ml) was added and the mixture was stirred overnight. The temperature was then raised to 45° and stirring continued for a further 2 h. Water (20 ml) was added and the mixture was extracted with hexane. The residue on evaporation of solvent was purified on alumina to yield the *product* (12) (0.6 g) as an oil (Found: C, 75.8; H, 9.5. $C_{27}H_{40}O_4$ requires C, 75.7; H, 9.4%); δ (CCl_4) 1.30 (d, 4 Me, *J* 7 Hz), 1.40 (2 Bu^t), 3.34 (OMe), 4.29, 4.32 (sept., CH, *J* 7 Hz), 6.2 (OH), 6.46, and 6.65 (d, 4 ArH, *J* 3 Hz); *M*$^+$ 428. This material crystallized after 18 months, m.p. 84 °C.

5′-*Ethoxy*-3,6-*dihydroxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl*.—A suspension of 2-t-butyl-5-(5-ethoxy-2-methoxy-4-t-butylphenyl)-1,4-benzoquinone (14)[13] (2 g) in methanol (20 ml) was treated with sodium borohydride until colourless and fully dissolved. On acidification and cooling the *hydroquinone* (1.6 g) was deposited as crystals, m.p. 152 °C (Found: C, 74.0; H, 8.9. $C_{23}H_{32}O_4$ requires C, 74.2; H, 8.7%); δ ($CDCl_3$) 1.40 (2 Bu^t), 1.42 (t, Me, *J* 7 Hz), 3.76 (OMe), 3.97 (q, CH_2, *J* 7 Hz), 4.5, 6.4 (OH), 6.51, 6.69, and 6.87 (2 H), (ArH); *M*$^+$ 372.

2-*Bromo*-5′-*ethoxy*-3,6-*dihydroxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl* (15).—Bromine (0.7 g) in carbon tetrachloride (10 ml) was slowly added to a stirred suspension of the previous hydroquinone (1.6 g) in carbon tetrachloride (60 ml). The resulting solution was washed with water and evaporated. The residue crystallized from methanol to give the *bromo-compound* (15) (1.6 g), m.p. 147—149 °C (Found: C, 61.3; H, 7.0. $C_{23}H_{31}BrO_4$ requires C, 61.2; H, 6.9%); δ ($CDCl_3$) 1.4 (Bu^t), 1.4 (t, Me, *J* 7 Hz), 3.67 (OMe), 3.91 (q, CH_2, *J* 7 Hz), 5.0, 5.5 (OH), 6.57, 6.81, and 6.87 (ArH); M^+ 450/452.

6-*Benzoyloxy*-2-*bromo*-5′-*ethoxy*-3-*hydroxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl*.—Benzoyl chloride (0.81 g) was added to a solution of the hydroquinone (15) (2 g) in dichloromethane (10 g) and pyridine (0.46 g) and stirring was continued for 2 h. Hexane was added and the mixture was washed with dilute hydrochloric acid, water, aqueous sodium hydrogencarbonate, and water. The solvent was evaporated and crystallization of the residue from acetone gave the *monobenzoate* (2 g), m.p. 163—165 °C (Found: C, 64.7; H, 6.7. $C_{30}H_{35}BrO_5$ requires C, 64.9; H, 6.4%); δ ($CDCl_3$) 1.29 (t, Me, *J* 7 Hz), 1.32, 1.46 (Bu^t), 3.62 (OMe), 3.89 (q, CH_2, *J* 7 Hz), 5.9 (OH), 6.63, 6.80, 7.22 (3 ArH), and 7.2—7.8 (m, 5 ArH); M^+ 554/556.

2-*Deuterio*-3,5′-*diethoxy*-6-*hydroxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl*.—The previous benzoate (1.5 g) was dissolved in dimethylformamide (10 ml) and stirred with diethyl sulphate (0.6 g) and potassium carbonate (0.6 g) for 1.5 h. Water (20 ml) was added and the mixture was extracted with hexane, which was washed five times with water and evaporated to give 6-*benzoyloxy*-2-*bromo*-3,5′-*diethoxy*-2′-*methoxy*-4,4′-*di*-*t*-*butylbiphenyl* (16), an oil, M^+ 582/584. Without purification this oil (16) (0.17 g) in tetrahydrofuran (15 ml) was stirred and heated under reflux under nitrogen with sodium (1 g), t-butyl [^{2}H]-alcohol (3 ml of a 60% solution in tetrohydrofuran) and D_2O (0.5 ml). Sufficient D_2O and sodium were added periodically so that sodium metal was always present and the mixture was fluid enough to stir. After 2 days water was added cautiously and the mixture was extracted with hexane. On evaporation and crystallization of the residue from methanol the *deuteriated product* (9a) (0.09 g), m.p. 108—111 °C, was obtained, δ (CCl_4) 1.37 (2 Bu^t), 1.44 (t, 2 Me, *J* 7 Hz), 3.72 (OMe), 3.95, 3.99 (q, 2 CH_2, *J* 7 Hz), 5.9 (OH), 6.62, 6.72, and 6.82 (ArH); M^+ 401. The undeuteriated material prepared similarly using t-butyl alcohol was identical with material prepared by monomethylation of 5,5′-diethoxy-4,4′-di-t-butylbiphenyl-2,2′-diol (5) and had an additional aromatic proton resonance at δ 6.50 (Found: C, 75.0; H, 9.1. $C_{25}H_{36}O_4$ requires C, 75.0; H, 9.0%); M^+ 400. Attempted replacement of the bromine by catalytic absorption of deuterium gas was unsuccessful.

t-Butyl [^{2}H]alcohol solution was prepared by hydrolysis of t-butyl acetate with sodium metal and D_2O. In a subsequent preparation it was found that t-butyl [^{2}H]alcohol could be prepared in this way *in situ*.

Acknowledgement

We are grateful to the Australian Research Grants Committee for financial assistance.

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Received 27*th July* 1982; *Paper* 2/1286