Phenol Oxidation and Biosynthesis. Part 27.† Reactions of Relevance to the Formation of Erysodienone *in vitro*

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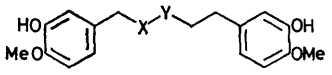
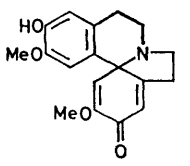
Potassium hexacyanoferrate(III) oxidation of *N*-(2-arylethyl)-2-arylacetamide and arylmethyl arylpropyl ketone gave the corresponding nine-membered ring derivatives formed by *p,p*-phenol oxidative coupling (where aryl was 3-hydroxy-4-methoxyphenyl). This strongly supports the previously reported mechanism for the *in vitro* formation of erysodienone. The required ketone was prepared from *O*-benzylisovanillin by homologation with toluene-4-sulphonylmethyl isonitrile.

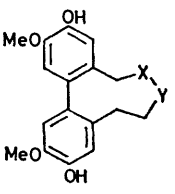
THE potassium hexacyanoferrate(III) oxidation of the bisarylethylamine (1a) has been shown to give erysodienone (2).[1] Model studies [2] showed the oxidation to



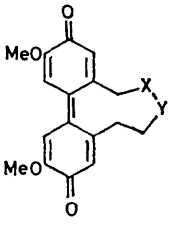
(1) a; X = CH_2, Y = NH
b; X = CO, Y = NH
c; X = CO, Y = CH_2
d; X = Y = CH_2
e; X = Y = CH_2, *OO'*-diacetyl



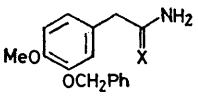
(2)



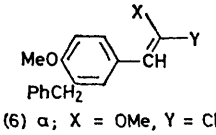
(3) a; X = CH_2, Y = NH
b; X = CO, Y = NH
c; X = CO, Y = CH_2
d; X = Y = CH_2



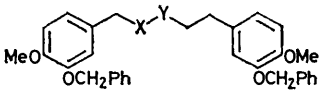
(4) a; X = CH_2, Y = NH
b; X = CO, Y = NH
c; X = CO, Y = CH_2



(5) a; X = O
b; X = H_2
c; X = H_2, HCl salt



(6) a; X = OMe, Y = CN
b; X = 4-$MeC_6H_4SO_2$, Y = NHCHO
c; X = 4$MeC_6H_4SO_2$, Y = NC
d; X = Y = H
e; X = H, Y = CO_2Et



(7) a; X = CO, Y = NH
b; X = C(NC)$SO_2C_6H_4$-4-Me, Y = CH_2
c; X = CO, Y = CH_2
d; X = C(NCO)$SO_2C_6H_4$-4-Me, Y = CH_2
e; X = C = NNH$SO_2C_6H_4$-4-Me, Y = CH_2
f; X = Y = CH_2

proceed *via* an initial C–C coupling giving the dibenzazonine derivative (3a). Subsequent oxidation to the diphenoquinone (4a) and cyclisation gave erysodienone (2). The reaction proceeds in high yield (30%) [2] and thus, unexpectedly, formation of the nine-membered ring (3a) must readily occur. Further model studies on the structural requirements for formation of the intermediate (3a) or an analogue are clearly required. This paper describes the preparation and phenol oxidative coupling of the amide (1b), ketone (1c), and alkane (1d).

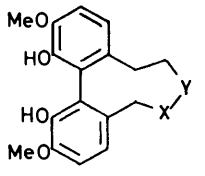
Methoxyacetonitrile has been used in a novel preparation of β-arylethylamines by aryl aldehyde homologation.[3] In a modification of this reaction, the primary amide (5a) was prepared from the methoxycinnamonitrile derivative (6a) [3] by reaction with toluene-α-thiol, sodium hydride, and ammonia. Subsequent reduction with diborane and reaction of the derived amine (5b) with the methoxycinnamonitrile derivative (6a), toluene-α-thiol, and sodium hydride [3] gave the known [4] amide (7a). Hydrogenation of this amide (7a) over palladium–charcoal removed the benzyl protecting groups giving the bisphenolic amide (1b). Formulation as amide (1b) was in full agreement with all spectral data and microanalysis.

The bisphenol (1b) was subjected to oxidations by potassium hexacyanoferrate(III), vanadium oxychloride, manganese dioxide, and the iron(III) chloride–DMF complex $\{[Fe(DMF)_3Cl_2]^+ [FeCl_4]^-\}$. Oxidation with alkaline potassium hexacyanoferrate(III) in chloroform and water gave the azoninone derivative (3b) in 10—12% yield allowing for recovered starting material. The yield was not significantly increased by the addition of benzyltriethylammonium chloride, lithium perchlorate, or glycine. Benzyltriethylammonium chloride has been reported to increase the yield (to 44%) of erysodienone (2) from the bisphenol (1a).[5] Vanadium oxychloride [6] oxidation of the bisphenol (1b) gave the azoninone derivative (3b) in 16% yield. The bisphenol (1b) was only slowly oxidised by the iron(III) chloride–DMF complex.[7] Manganese dioxide [8] was too powerful an oxidant even in the presence of silica [9] as a diluent. In each case microanalyses, mass (M^+ 329.126 5), and n.m.r. and i.r. spectra were all in excellent agreement with the structure (3b). The aromatic signals in the n.m.r. spectrum at δ 6.35 and 6.38 were in agreement with the absence of *ortho*-coupling. Thus, the alternative structure (8a) for the product was excluded. In addition, a dimeric product was also formed; the structure, however, was not determined. Formation of the azoninone derivative (3b) in comparable yield to erysodienone (2) from the bisphenol (1a) strongly supports the intermediacy of the

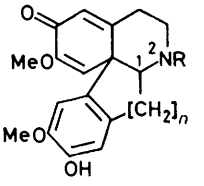
† Part 26, ref. 15 (preceding paper).

dibenzazonine (3a) in the formation of erysodienone (2) *in vitro*. Prolonged reaction of the bisphenol (1b) with potassium hexacyanoferrate(III) gave only very polar materials. Presumably, the amide function was insufficiently nucleophilic to trap the diphenoquinone (4b).

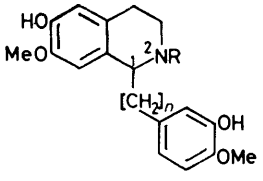
Since the azoninone derivative (3b) was readily available, Bischler–Napieralski cyclisation as a synthesis of the spirodienone (9a) and thus proerysodienone (9b) was examined. As a model system the free bisphenolic amide (1b) was allowed to react with phosphoryl chloride



(8) a; X = CO, Y = NH
b; X = CO, Y = CH_2



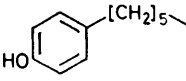
(9) a; *n* = 1, R = H, 1,2-didehydro
b; *n* = 1, R = H
c; *n* = 1, R = CO_2Et
d; *n* = 2, R = $COCF_3$
e; *n* = 1, R = $COCF_3$
f; *n* = 1, R = SO_2Me



(10) a; *n* = 1, R = H, 1,2-didehydro, HCl salt
b; *n* = 1, R = CO_2Et
c; *n* = 2, R = $COCF_3$
d; *n* = 1, R = $COCF_3$
e; *n* = 1, R = SO_2Me
f; *n* = 1, R = SO_2Me; *OO'*-dibenzyl

in acetonitrile [10] to give the derived dihydroisoquinoline isolated as its hydrochloride (10a) (92%). Under the same mild Bischler–Napieralski reaction conditions, the azoninone derivative (3b) gave an intractable mixture lacking dienone characteristics (i.r.). As an alternative pathway to the spirodienone (9b) Bischler–Napieralski cyclisation and subsequent phenol oxidative coupling of the amide (1b) was examined. Such a route has precedence in the formation of the spirodienones (9c) [11] and (9d) [12] from the bisphenols (10b) and (10c), respectively. The nitrogen atom was protected by electron withdrawing substituents in order to minimise complications arising from its nucleophilicity. The dihydroisoquinoline (10a) was converted into the *N*-trifluoroacetyltetrahydroisoquinoline derivative (10d) by reaction with sodium borohydride and subsequently with trifluoroacetic anhydride. Bischler–Napieralski cyclisation of the amide (7a), followed by reduction with sodium borohydride, methanesulphonylation, and hydrogenolysis of the benzyl protecting groups gave the tetrahydroisoquinoline derivative (10e). Oxidations of bisphenols (10d) and (10e) were unsuccessful (see Experimental section); either the reactions were sluggish or overoxidations rapid. A minor non-dienone compound was isolated in each case on oxidation with potassium hexacyanoferrate(III); structural assignments were not possible. Presumably the spirodienones (9e or f), if formed, were unstable to the reaction conditions.

Having established that the azoninone derivative (3b) was readily obtained from the bisphenol (1b), the phenol oxidative coupling of the nitrogen-free analogues (1c) and (1d) was examined. 1,5-Bis-(4-hydroxyphenyl)-pentane (11) has previously been prepared from 4-anisaldehyde by reaction with acetone followed by catalytic hydrogenation, Clemmensen reduction, and demethylation with hydriodic acid.[13] Such a pathway is inapplicable to the unsymmetric ketone (1c) and thus an alternative route was sought. Toluene-4-sulphonylmethyl isonitrile has been monoalkylated under basic phase transfer conditions.[14] The required ketone (1c) could conceivably be prepared *via* alkylation of the isonitrile (12a) with the bromide (12b) and subsequent



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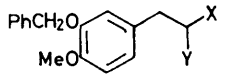
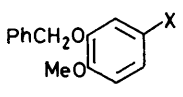


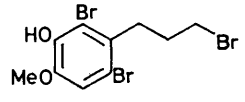
(12) a; X = NC, Y = 4-$MeC_6H_4SO_2$
b; X = H, Y = CH_2Br
c; X = H, Y = CH_2OH
d; X = H, Y = CH_2OCS_2Me
e; X = H, Y = CH_2I
f; X = H, Y = $CH_2OC(S)NEt_2$

hydrolysis. The use of toluene-4-sulphonylmethyl isonitrile as a CNC synthon in the preparation of β-arylethylamines from aryl aldehydes has recently been described.[15]

The anion derived from toluene-4-sulphonylmethyl isonitrile was readily generated using potassium t-butoxide.[15] Addition of *O*-benzylisovanillin (13a) gave



(13) a; X = CHO
b; X = $C{\equiv}CSO_2C_6H_4$-4-Me



(14)

the expected [15] vinylformamide derivative (6b). Subsequent dehydration with phosphorus oxychloride gave the vinyl isonitrile derivative (6c). Structural assignments of both the amide (6b) and isonitrile (6c) were in full agreement with microanalyses and spectral data. Both were obtained as single isomers and were, by analogy,[15] assigned *E* stereochemistry. Reduction with sodium borohydride [15] of the isonitrile (6c) gave the saturated analogue (12a). A minor by-product was also isolated when the intermediates (6b) and (6c) were not purified. Spectral data and microanalysis showed this to be the styrene derivative (6d) formed, presumably, *via* the acetylenic sulphone (13b).

The required bromide (12b) should be available from *O*-benzylisovanillin (13a) by an appropriate Wittig reaction, lithium aluminium hydride reduction, and replacement of the hydroxy-group by bromine. Reaction of *O*-benzylisovanillin (13a) with ethoxycarbonylmethylenetriphenylphosphorane, prepared *in situ* using propylene oxide as an acid scavanger,[16] gave the expected *trans*-acrylate (6e) (n.m.r.). Subsequent prolonged reaction with lithium aluminium hydride gave the propanol derivative (12c) in high yield. Structural assignments of both the acrylate (6e) and alcohol (12c) were in full agreement with microanalyses and spectral data.

Reaction of the alcohol (12c) with phosphorus tribromide [17] gave a poor yield of the bromide (12b). Formation of alkyl halides from reaction of alcohol *S*-methyl dithiocarbonates with soft halide electrophiles has recently been described.[18] Using standard methods alcohol (12c) was converted into the *S*-methyl dithiocarbonate (12d). Reaction of this derivative (12d) with bromine gave a crystalline compound with composition $C_{10}H_{11}Br_3O_2$. Clearly the compound was phenolic (i.r., n.m.r.) and was assigned the structure (14), being formed by cleavage of the benzyl ether followed by bromination of the aryl group. Reaction, however, of the dithiocarbonate (12d) with iodomethane at 90 °C or with diethylamine followed by iodomethane gave the required iodide (12e). The latter reaction proceeded *via* the more nucleophilic [18] thiocarbamate (12f).

Addition of iodide (12e) to the anion derived from the isonitrile (12a) and potassium t-butoxide gave the expected pentane derivative (7b). The reaction was improved by the addition of 18-crown-6, presumably due to increased nucleophilicity [19] of the metallated isonitrile. Although the pentane derivative (7b) could not be crystallised, its structural assignment was consistent with spectral data and subsequent transformations. Oxidation of the pentane derivative (7b) with mercury(II) nitrate [20] or peracetic acid gave the ketone (7c). The reaction probably proceeds *via* the isocyanate (7d) followed by hydrolysis. Hydrogenation of this ketone (7c) over palladium–charcoal removed the benzyl protecting groups to give the bisphenol (1c).

Huang–Minlon [21] reduction of the ketone (7c) or reduction of the derived toluene-4-sulphonylhydrazone (7e) with sodium cyanoborohydride [22] or catecholborane [23] gave the corresponding alkane (7f). Hydrogenolysis of the benzyl protecting groups of the pentane derivative (7f) required acetic acid–perchloric acid as solvent and gave the expected diacetate (1e) which was saponified to form the bisphenol (1d). The structures of both bisphenols (1c) and (1d) were in full agreement with microanalyses and spectral data.

Phenol oxidative coupling of the ketobisphenol (1c) using alkaline potassium hexacyanoferrate(III) with or without benzyltriethylammonium chloride gave mostly polar material and a minor product that was clearly dimeric (*m/e* 686, 658, 346, and 344). The use of 18-crown-6 as phase transfer catalyst increased the rate of reaction and formed traces of an additional compound. Alternatively, cetyltriethylammonium bromide gave consistently good results: both the dimeric product (10—14%) and a new product ($C_{19}H_{20}O_5$) (7—11%) were formed. Prolonged reaction drastically reduced the yield of isolable material. The new product was assigned the structure (3c); the absence of *ortho*-coupling in the n.m.r. spectrum excluded the alternative structure (8b).

In contrast, the alkane bisphenol (1d) on oxidation with potassium hexacyanoferrate(III) gave mostly an intractable polar mixture. Possibly unfavourable phase transfer or steric congestion prevented formation of the cyclononane derivative (3d). Clearly *in vitro* cyclisations of bisphenols to analogues of the erysodienone precusor (3a) do not require a basic nitrogen function with a possible chelating or electron transfer role. Unlike precursor (3a), the intermediate cyclononane derivatives (3b and c) were isolated and gave polar tars on further oxidation. Presumably neither amide nor ketone functions were sufficiently nucleophilic to attack the diphenoquinones (4b or c) and thus prevent competing intermolecular reactions.

Formation of the cyclononane derivatives (3b and c) during oxidation of the bisphenols (1b and c) using hexacyanoferrate(III) is further strong evidence in favour of the intermediacy of the azonine derivative (3a) in the *in vitro* formation of erysodienone (2). Toluene-4-sulphonylmethyl isonitrile should find further application in aldehyde homologation.*

EXPERIMENTAL

General experimental methods have been described.[15,25]

2-(3-Benzyloxy-4-methoxyphenyl)acetamide (5a).—The methoxycinnamonitrile derivative (6a) (0.74 g), toluene-α-thiol (0.31 g), and sodium hydride (80%; 76 mg) in DMF (5 ml) were heated to 90 °C (N_2). Ammonia was bubbled through the solution for 1 h and the mixture added to water. The precipitated amide (5a) was recrystallised from benzene to give needles (0.58 g, 86%), m.p. 153° (lit.,[26] 153°).

2-(3-Benzyloxy-4-methoxyphenyl)ethylammonium Chloride (5c).—Diborane in THF (1.12M; 1.83 ml) was added to the amide (5a) (0.50 g) in THF (5 ml) (N_2). After refluxing for 10 h, water (1 ml) was added and the mixture was poured into water and acidified with dilute hydrochloric acid. The precipitate was recrystallised from ethanol to give the salt (5c) (425 mg, 78%), m.p. 164° (lit.,[4] 164°).

2-(3-Benzyloxy-4-methoxyphenyl)-N-[2-(3-benzyloxy-4-methoxyphenyl)ethyl]acetamide (7a).—The methoxycinnamonitrile derivative (6a) (7.35 g), amine (5b) (6.38 g), toluene-α-thiol (3.09 g), and sodium hydride (0.75 g) in DMF (25 ml) were heated at 90 °C for 15 min (N_2). The mixture was cooled, added to water, and the precipitate recrystallised from benzene to give the amide (7a) (10.4 g, 82%), m.p. 110—112° (lit.,[4] 118°), $\nu_{max.}$ ($CHCl_3$) 3 450, 1 660, 1 610, 1 600, and 1 520 cm^{-1}, δ 2.6, 3.3 (4 H, 2t, *J* 7 Hz, CH_2CH_2), 3.4 (2 H, s, $ArCH_2$), 3.83 (6 H, s, OMe), 5.1 (4 H, s, $ArCH_2$), 5.4br (1 H, s, NH), 6.2—6.8 (6 H, m, ArH), and 7.1—7.5 (10 H, m, Ph).

* *Note added in proof.* Attention is drawn to the recent homoerythrina alkaloid syntheses reported by McDonald.[24] The intramolecular phenol oxidative coupling of oxygenated 1-phenylethyltetrahydroquinoline derivatives has been shown to be dramatically improved by the introduction of sp^2 centres.

(3-*Hydroxy*-4-*methoxyphenyl*)-N-[2-(3-*hydroxy*-4-*methoxyphenyl*)*ethyl*]*acetamide* (1b).—The amide (7a) (5.11 g) and 60% aqueous perchloric acid (1 drop) in ethanol (100 ml) were hydrogenated at 1 atm. over 10% palladium–charcoal (200 mg) for 10 h. Filtration, evaporation, work-up (chloroform–water), and crystallisation from benzene gave the *phenolic amide* (1b) (3.21 g, 97%) as prisms, m.p. 120—121°, $\nu_{max.}$ ($CHCl_3$) 3 550, 3 420, 2 900, 1 660, and 1 600 cm^{-1}, δ 2.53 (2 H, t, *J* 6.5 Hz, CH_2), 3.3 (2 H, t, *J* 6.5 Hz, CH_2), 3.36 (2 H, s, $ArCH_2$), 3.83 (6 H, s, OMe), 5.6br (1 H, s, NH), 6.15br (2 H, s, OH), and 6.4—6.9 (6 H, m, ArH), *m/e* 331 (M^+) 181, 166, 137, and 122 (Found: C, 65.25; H, 6.15; N, 4.05. $C_{18}H_{21}NO_5$ requires C, 65.25; H, 6.4; N, 4.25%).

Phenol Oxidative Coupling of the Amide (1b).—(*a*) The amide (1b) (662 mg) and benzyltriethylammonium chloride (100 mg) in chloroform (1 l) were added with rapid stirring to potassium hexacyanoferrate(III) (3.95 g) in 5% aqueous sodium hydrogen carbonate (100 ml). After 25 min, normal work-up (chloroform–water), chromatography on silica (chloroform–methanol 20 : 1), and crystallisation from chloroform–ethanol gave 5,6,8,9-*tetrahydro*-3,11-*dihydroxy*-2,12-*dimethoxy*-7H-*dibenz*[d,f]*azonin*-6-*one* (3b) (51 mg, 12%) as needles, m.p. 263—264°, $\nu_{max.}$ 3 200, 1 642, 1 595, and 1 515 cm^{-1}, δ 2.56 (2 H, t, *J* 7 Hz, CH_2), 2.85 (2 H, s, $ArCH_2$), 2.8—3.2 (2 H, m, CH_2), 3.5 (6 H, s, OMe), 6.35 (2 H, s, ArH), 6.38 (2 H, s, ArH), 3.83br (1 H, s, NH), and 7.33br (2 H, s, 2-OH), *m/e* 329.126 5 (M^+ requires 329.126 3), 300, 272, 257, and 241 (Found: C, 65.5; H, 5.75; N, 4.1. $C_{18}H_{19}NO_5$ requires C, 65.65; H, 5.8; N, 4.25%); starting material (1b) (240 mg); and a dimer (19 mg), m.p. 115—116° (from chloroform–ethanol), $\nu_{max.}$ ($CHCl_3$) 1 670 cm^{-1}, *m/e* 658. (*b*) To the amide (1b) (662 mg) in dry dichloromethane (500 ml) was added vanadium oxychloride (870 mg). After 0.5 h the solution was washed with saturated aqueous potassium hydrogen carbonate, aqueous sodium sulphate, and aqueous disodium EDTA. After drying and evaporation, p.l.c. gave the azoninone (3b) (86 mg, 16%). Oxidations by manganese dioxide with or without silica, or $[Fe(DMF)_3Cl_2]^+FeCl_4^-$ gave no azoninone (3b).

Reaction of Azonin-6-*one Derivative* (3b) *and Phosphoryl Chloride*.—Reaction of the azonin-6-one derivative (3b) 1.2 mg) and phosphoryl chloride as for the amide (1b) gave no dienone (i.r., u.v.) although the amide absorption (1 640 cm^{-1}) disappeared in 40 min.

6-*Hydroxy*-1-(3-*hydroxy*-4-*methoxybenzyl*)-7-*methoxy*-3,4-*dihydroisoquinoline Hydrochloride* (10a).—The amide (1b) (0.50 g) and phosphoryl chloride (1.4 ml) in acetonitrile (6 ml) were stirred for 50 h at room temperature. The product (10a) was filtered off, washed with acetonitrile, and recrystallised from 0.5M-ethanolic hydrogen chloride to give the hydrochloride (10a) (485 mg, 92%), m.p. 186°.

N-*Trifluoroacetyl*-N-*norprotosinomenine* (10d).—Dihydroisoquinoline (10a) (1.0 g) and sodium borohydride (0.2 g) in methanol (25 ml) were stirred until reduction was complete (t.l.c.). The methanol was evaporated and 1M-sodium hydroxide (10 ml) was added followed by dilute hydrochloric acid (to neutrality). Work-up (chloroform–water) gave a residue which was dissolved in pyridine (10 ml). Trifluoroacetic anhydride (2.8 ml) was added with cooling. After 24 h, the mixture was poured into water and the solid recrystallised from carbon tetrachloride–methanol to give the *trifluoroacetamide derivative* (10d) (0.81 g, 69%), m.p. 152—152.5°, $\nu_{max.}$ 3 520, 2 940, 1 685, and 1 595 cm^{-1}, δ 2.68, 3.57 (4 H, 2t, *J* 6 Hz, CH_2CH_2), 3.0 (2 H, d, *J* 7 Hz, $CHCH_2$), 3.7 (3 H, s, OMe), 3.86 (3 H, s, OMe), 5.33 (1 H, t, *J* 7 Hz, $CHCH_2$), 5.4—5.8br (2 H, m, OH), 6.26 (1 H, s, ArH), and 7.66 (3 H, s, ArH), *m/e* 411 (M^+), 274, and 137 (Found: C, 58.65; H, 5.15; N, 3.55. $C_{20}H_{20}F_3NO_5$ requires C, 58.4; H, 4.9; N, 3.4%).

6-*Benzyloxy*-1-(3-*benzyloxy*-4-*methoxybenzyl*)-2-*methylsulphonyl*-7-*methoxy*-1,2,3,4-*tetrahydroisoquinoline* (10f).—The amide (7a) (2.5 g) and phosphoryl chloride (2.5 ml) in chloroform (10 ml) were heated to reflux for 1 h. After evaporation and work-up (chloroform–water) the residue was dissolved with sodium borohydride (0.91 g) in methanol (100 ml) (N_2). After complete reduction (t.l.c.) 1M-sodium hydroxide (100 ml) was added. Work-up (chloroform–water) gave an oil which was dissolved in pyridine and methanesulphonyl chloride (1.2 ml) was added dropwise. After 32 h at room temperature, the mixture was added to water and the solid recrystallised from methanol to give the *tetrahydroisoquinoline derivative* (10f) (1.98 g, 72%), m.p. 146—147°, $\nu_{max.}$ 3 020 and 1 605 cm^{-1}, δ 2.36 (3 H, s, SO_2Me), 2.6, 3.6 (4 H, 2t, *J* 8.5 Hz, CH_2CH_2), 2.98 (2 H, d, *J* 7 Hz, $CHCH_2$), 3.7 (3 H, s, OMe), 3.85 (3 H, s, OMe), 4.92 (1 H, t, *J* 7 Hz, $CHCH_2$), 5.1 (4 H, s, $ArCH_2$), 6.4 (1 H, s, ArH), 6.6—6.9 (3 H, m, ArH), and 7.2—7.6 (10 H, m, Ph), *m/e* 573 (M^+), 572, 494, and 346 (Found: C, 69.35; H, 6.25; N, 2.35; S, 5.7. $C_{23}H_{35}NO_6S$ requires C, 69.1; H, 6.15; N, 2.45; S, 5.6%).

N-*Methylsulphonyl*-N-*norprotosinomenine* (10e).—The benzyl ether (10f) (1.6 g) and perchloric acid (60%; 1 drop) in ethanol (40 ml) were hydrogenated over 10% palladium–charcoal (100 mg). Evaporation, work-up (chloroform–water), and crystallisation from methanol gave the *bisphenol derivative* (10e) (1.06 g, 97%), m.p. 140—141°, $\nu_{max.}$ 3 540, 2 900, 1 595, and 1 500 cm^{-1}, δ 2.46 (3 H, s, SO_2Me), 2.69, 3.52 (4 H, 2t, *J* 8 Hz, CH_2CH_2), 3.0 (2 H, d, *J* 7 Hz, $CHCH_2$), 3.74 (3 H, s, OMe), 3.86 (3 H, s, OMe), 4.98 (1 H, t, *J* 7 Hz, $CHCH_2$), 5.7br (2 H, s, OH), 6.32 (1 H, s, ArH), and 6.6—6.9 (3 H, m, ArH), *m/e* 314, 312, 274, and 137 (Found: C, 58.2; H, 5.8; N, 3.5; S, 8.1. $C_{19}H_{23}NO_6S$ requires C, 58.0; H, 5.9; N, 3.55; S, 8.15%).

Attempted Oxidations of the N-*Norprotosinomenine Derivatives* (10d *and* e).—Potassium hexacyanoferrate(III) oxidation of the bisphenols (10d or e) in the presence of 5% aqueous sodium hydrogen carbonate or ammonium acetate–ammonia buffer [11] in chloroform–water gave mostly polar tars. From the bisphenol (10d) a minor product (<5%) was isolated by p.l.c. (chloroform–methanol 20 : 1), $\nu_{max.}$ 3 540, 1 685, 1 635, and 1 595 cm^{-1}. The biphenol (10e) gave a minor product (<5%), $\nu_{max.}$ 3 520, 2 910, 2 840, 1 675, and 1 595 cm^{-1}, *m/e* 312, 298, and 137. Oxidation of either biphenol (10d or e) with vanadium oxychloride in dichloromethane gave only polar tar and starting material. Both phenols (10d and e) reacted only slowly with manganese dioxide–silica [8] in chloroform or with cerium(IV) sulphate in aqueous methanol to give only polar tars.

1-(3-*Benzyloxy*-4-*methoxyphenyl*)-2-*formamido*-2-(4-*tolylsulphonyl*)*ethene* (6b).—Toluene-4-sulphonylmethyl isonitrile (5.4 g) in THF (26 ml) was added over 3 min with stirring to potassium t-butoxide (15.2 g) in THF (260 ml) at 7 °C (Ar). The mixture was immediately cooled to −20 °C and 3-benzyloxy-4-methoxybenzaldehyde (13a) (6.58 g) in THF (28 ml) added followed by glacial acetic acid (7.8 ml). Evaporation at room temperature, work-up (dichloromethane–water), and chromatography on silica (methanol–

dichloromethane 1 : 49) gave the crude *enamide* (6b) (10.5 g, 90%). Crystallisation from acetone–hexane gave the enamide (6b) (8.75 g, 75%) as needles, m.p. 188—189° (from acetone–hexane), $\nu_{max.}$ 3 260, 1 695, 1 630, 1 310, and 1 140 cm^{-1}, $\lambda_{max.}$ 208 (ε 34 500), 234 (25 500), 294 (18 700), and 321 nm (23 800), δ 2.4 (3 H, s, ArMe), 3.88 (3 H, s, OMe), 5.12 (2 H, s, $ArCH_2$), and 6.7—8.0 (15 H, m, ArH, vinyl-H, and NHCO) (Found: C, 65.65; H, 5.2; N, 3.15; S, 7.45. $C_{22}H_{23}NO_5S$ requires C, 65.9; H, 5.3; N, 3.2; S, 7.35%).

1-(3-*Benzyloxy*-4-*methoxyphenyl*)-2-*isocyano*-2-(4-*tolylsulphonyl*)*ethene* (6c).—Phosphoryl chloride (1.7 ml) was added over 45 min with stirring to the enamide (6b) (4.43 g) in triethylamine (28 ml) and dichloromethane (45 ml) at −30 °C (N_2). The mixture was stirred overnight at room temperature. Work-up (dichloromethane–saturated aqueous sodium hydrogen carbonate, water), and chromatography on alumina (benzene) gave the *vinyl isonitrile derivative* (6c) (3.82 g, 90%). Recrystallisation from benzene–light petroleum gave needles, m.p. 124—125°, $\nu_{max.}$ 2 110, 1 615, 1 330, and 1 150 cm^{-1}, $\lambda_{max.}$ 248 (ε 13 300), 320 (10 700), and 345 nm (18 200), δ 2.47 (3 H, s, ArMe), 3.97 (3 H, s, OMe), 5.2 (2 H, s, $ArCH_2$), and 6.9—8.0 (13 H, m, ArH and vinyl-H) (Found: C, 68.85; H, 4.75; N, 3.3. $C_{24}H_{21}NO_4S$ requires C, 68.7; H, 5.05; N, 3.35%).

1-(3-*Benzyloxy*-4-*methoxyphenyl*)-2-*isocyano*-2-(4-*tolylsulphonyl*)*ethane* (12a).—The isonitrile (6c) (3.82 g) in THF (55 ml) was added with stirring to sodium borohydride (1.2 g) in ethanol (55 ml) (N_2). The mixture was warmed slowly to 40 °C and then cooled to room temperature. Evaporation, work-up (dichloromethane–water), and chromatography on alumina (benzene) gave the crude product (12a) (3.71 g, 97%). Recrystallisation from benzene–light petroleum gave the *isonitrile* (12a) (2.8 g, 75%) as white prisms, m.p. 137—138°, $\nu_{max.}$ 2 160, 1 335, and 1 140 cm^{-1}, $\lambda_{max.}$ 227 (ε 16 100) and 274 nm (2 400), δ 2.5 (3 H, s, ArMe), 2.65—3.6 (2 H, m, $ArCH_2$), 3.86 (3 H, s, OMe), 4.5 (1 H, dd, *J* 8 and 3 Hz, CH), 5.14 (2 H, s, $ArCH_2$), 6.8br (3 H, s, ArH), 7.38br (5 H, s, Ph), 7.4 and 7.9 (4 H, ABq, *J* 10 Hz, ArH), *m/e* 421 (M^+), 382, 164, 132, and 91 (100%) (Found: C, 68.5; H, 5.55; N, 3.45; S, 7.4. $C_{24}H_{23}NO_4S$ requires C, 68.3; H, 5.5; N, 3.3; S, 7.6%). In addition, the *styrene derivative* (6d) was isolated as a minor by-product, m.p. 63—65° (from hexane), $\nu_{max.}$ 1 625w, 1 240, 1 140, and 1 005 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 218 (ε 17 300), 259 (10 400), 266sh (9 900), and 285sh nm (3 300), δ 3.84 (3 H, s, OMe), 5.07 (1 H, dd, *J* 9 and 1 Hz, vinyl-H), 5.1 (2 H, s, $ArCH_2$), 5.47 (1 H, dd, *J* 17, 1 Hz, vinyl-H), 6.57 (1 H, dd, *J* 17, 9 Hz, vinyl-H), 6.8—7.06 (3 H, m, ArH), and 7.1—7.6 (5 H, m, Ph), *m/e* 240 (M^+), 149, and 91 (100%) (Found: C, 80.15; H, 6.75. $C_{16}H_{16}O_2$ requires C, 79.95; H, 6.7%).

Ethyl 3-(3-*Benzyloxy*-4-*methoxyphenyl*)*acrylate* (6e).—3-Benzyloxy-4-methoxybenzaldehyde (13a) (9.7 g), triphenylphosphine (10.5 g), and propylene oxide (5.6 ml) in dichloromethane (12 ml) were cooled to 0 °C and ethyl bromoacetate (4.5 ml) was slowly added. After 5 days at room temperature the mixture was evaporated (0.5 mmHg pressure) and the residue chromatographed on silica (benzene) to give the crude product (6e) (100%). Recrystallisation from diethyl ether gave the *acrylate derivative* (6e) (10.2 g, 82%) as needles, m.p. 96—97.5°, $\nu_{max.}$ 1 705 and 1 635 cm^{-1}, $\lambda_{max.}$ 237 (ε 11 600), 295 (12 600), and 322 nm (15 000), δ 1.2—1.4 (3 H, t, *J* 6 Hz, OCH_2CH_3), 3.94 (3 H, s, OMe), 4.1—4.4 (2 H, q, *J* 6 Hz, OCH_2CH_3), 5.2 (2 H, s, $ArCH_2$), 6.36 (1 H, d, *J* 16 Hz, vinyl-H), and 6.8—7.78 (9 H, m, ArH), *m/e* 312 (M^+), 277, 238, 224, and 91 (100%) (Found: C, 73.25; H, 6.4. $C_{19}H_{20}O_4$ requires C, 73.05; H, 6.45%).

3-(3-*Benzyloxy*-4-*methoxyphenyl*)*propan*-1-*ol* (12c).—The acrylate (6e) (7.5 g) in dry THF (55 ml) was added over 75 min to lithium aluminium hydride (5.3 g) in diethyl ether (80 ml). After 24 h saturated aqueous sodium sulphate was added to destroy the hydride and the solids were filtered off and leached with hot THF. Evaporation and crystallisation from aqueous methanol gave the *alcohol* (12c) (4.9 g, 75%) as needles, m.p. 98—100°, $\nu_{max.}$ 3 500br cm^{-1}, $\lambda_{max.}$ 208 (ε 13 200), 225sh (5 400), and 278 nm (1 800), δ 1.6—2.1 (3 H, m, CH_2 and OH), 2.4—2.7 (2 H, m, $ArCH_2$), 3.4—3.7 (2 H, t, *J* 6 Hz, CH_2OH), 3.85 (3 H, s, OMe), 5.14 (2 H, s, $ArCH_2$), 6.6—7.0br (3 H, m, ArH), and 7.2—7.6br (5 H, m, Ph), *m/e* 272 (M^+), 181, 149, 137, and 91 (100%) (Found: C, 75.1; H, 7.3. $C_{17}H_{20}O_3$ requires C, 74.95; H, 7.4%).

1-(3-*Benzyloxy*-4-*methoxyphenyl*)-3-*bromopropane* (12b).—Phosphorus tribromide (70 μl) and pyridine (30 μl) in toluene (2 ml) were cooled to −10 °C and the alcohol (12c) (0.54 g) with pyridine (10 μl) in toluene and dichloromethane (3 : 2, 5 ml) was added with stirring over 4 h. After a further 1 h at −10 °C the solution was warmed to room temperature. During 2 days pyridine (80 μl) and phosphorus tribromide (50 μl) were added in two portions. Methanol (0.5 ml) was added at −10 °C and the mixture evaporated. Work-up (toluene–water, saturated aqueous sodium hydrogen carbonate) and chromatography on silica (benzene) gave the *bromide* (12b) (0.20 g, 30%). Recrystallisation from ethanol gave prisms, m.p. 62—63°, $\nu_{max.}$ 1 230, 1 150, and 1 010 cm^{-1}, $\lambda_{max.}$ 207 (ε 16 700), 226sh (6 400), and 279 nm (2 000), δ 1.8—2.3 (2 H, m, $C-CH_2-C$), 2.45—2.8 (2 H, t, *J* 6 Hz, $ArCH_2$), 3.1—3.45 (2 H, t, *J* 6 Hz, CH_2Br), 3.85 (3 H, s, OMe), 5.1 (2 H, s, $ArCH_2$), 6.6—6.9br (3 H, s, ArH), and 7.1—7.5 (5 H, m, Ph), *m/e* 336, 334 (M^+), 245, 243, and 91 (Found: C, 60.8; H, 5.8. $C_{17}H_{19}BrO_2$ requires C, 60.9; H, 5.7%).

O-[3-(3-*Benzyloxy*-4-*methoxyphenyl*)*propyl*]-S-*methyldithiocarbonate* (12d).—The alcohol (12c) (5.7 g) and imidazole (0.15 g) in THF (130 ml) were heated to reflux with sodium hydride (1g) for 6 h, with carbon disulphide (11.4 ml) for 0.5 h, and with iodomethane (6.9 ml) for 0.5 h (N_2). After cooling to room temperature, glacial acetic acid (4.2 ml) was added and the mixture evaporated. Work-up (diethyl ether–saturated aqueous sodium hydrogen carbonate, water) and chromatography on silica (benzene) gave the *dithiocarbonate* (12d) (7.3 g, 96%). Recrystallisation from diethyl ether–methanol gave prisms, m.p. 59—60°, $\nu_{max.}$ 1 240, 1 220, and 1 055 cm^{-1}, $\lambda_{max.}$ 211 (ε 13 900), 225sh (12 800), and 277 nm (11 800), δ 1.8—2.27 (2 H, m, CH_2), 2.55 (3 H, s, SMe), 2.55—2.8 (2 H, m, $ArCH_2$), 3.84 (3 H, s, OMe), 4.44—4.68 (2 H, t, *J* 6 Hz, OCH_2), 5.1 (2 H, s, $ArCH_2$), 6.64—6.85 (3 H, m, ArH), and 7.2—7.5br (5 H, s, Ph), *m/e* 362 (M^+), 329, 315, 254, 227, 164, 135, and 91 (100%) (Found: C, 63.0; H, 6.05; S, 17.65. $C_{19}H_{22}O_3S_2$ requires C, 62.95; H, 6.1; S, 17.7%).

1-*Bromo*-3-(2,6-*dibromo*-3-*hydroxy*-4-*methoxyphenyl*)-*propane* (14).—Bromine (0.16 ml) was added over 0.5 h to the dithiocarbonate (12d) (0.28 g) and pyridine (6 μl) in dichloromethane (3 ml) at 0 °C. The mixture was allowed to react for 2 h at room temperature. Work-up (dichloromethane–saturated aqueous sodium thiosulphate, sodium hydrogencarbonate, water) and chromatography on silica (benzene) gave the *tribromide* (14) (100%). Recrystallisation from diethyl ether–light petroleum gave needles, m.p.

97—98°, $\nu_{max.}$ 3 400 cm^{-1}, δ 1.9—2.3 (2 H, m, CH_2), 2.95—3.2 (2 H, m, $ArCH_2$), 3.4—3.65 (2 H, t, *J* 6 Hz, $BrCH_2$), 3.9 (3 H, s, OMe), 6.0 (1 H, s, OH), and 7.07 (1 H, s, ArH), *m/e* 405, 403 (M^+), and 295 (100%) (Found: C, 29.9; H, 3.0. $C_{10}H_{11}Br_3O_2$ requires C, 29.8; H, 2.75%).

1-(3-*Benzyloxy*-4-*methoxyphenyl*)-3-*iodopropane* (12e).—(*a*) Dithiocarbonate (12d) (2.72 g) in iodomethane (30 ml) was heated to 85—90 °C (sealed tube) for 40 h. Work-up (dichloromethane–saturated aqueous sodium thiosulphate, water) and crystallisation from ethanol gave the *iodide* (12e) (2.3 g, 80%). (*b*) Diethylamine (60 ml) and dithiocarbonate (12d) (8.2 g) were left at room temperature for 5 h. The amine was evaporated and the residue heated to reflux in iodomethane (80 ml). Evaporation (80 °C at 10^{-4} mmHg), work-up (dichloromethane–water) and crystallisation from ethanol gave the iodide (12e) (6.3 g). Evaporation (80 °C at 10^{-4} mmHg pressure) of the mother liquor and recrystallisation gave a second crop (0.4 g, 82% total). Recrystallisation gave plates, m.p. 53—55°, $\nu_{max.}$ 1 230, 1 140, and 1 010 cm^{-1}, $\lambda_{max.}$ 209 (ε 20 000), 226 sh (8 500), and 278 nm (3 000), δ 1.8—2.24 (2 H, m, CH_2), 2.4—2.47 (2 H, m, $ArCH_2$), 2.96—3.2 (2 H, t, *J* 7 Hz, ICH_2), 3.84 (3 H, s, OMe), 5.15 (2 H, s, $ArCH_2$), 6.65—6.95 (3 H, m, ArH), and 7.2—7.6br (5 H, s, Ph), *m/e* 382 (M^+), 291, 136, 107, and 91 (100%) (Found: C, 53.35; H, 5.2. $C_{17}H_{19}IO_2$ requires C, 53.4; H, 5.0%).

1,5-*Bis*-(3-*benzyloxy*-4-*methoxyphenyl*)-2-*isocyano*-2-(4-*tolylsulphonyl*)*pentane* (7b).—To potassium t-butoxide (1.74 g) and 18-crown-6 (0.33 g) in THF (20 ml) at −10 °C was added the isonitrile (12a) (5g) in THF (25 ml) (over 3 min) followed by the iodide (12e) (4.1 g) in THF (10 ml) (Ar). After slowly warming to room temperature the excess of base was destroyed with dry ice and the solvent was evaporated off. Work-up (dichloromethane–water) gave the crude pentane derivative (7b) (100%), $\nu_{max.}$ ($CHCl_3$) 2 120, 1 320, and 1 130 cm^{-1}, δ 1.2—2.05 (4 H, m), 2.2—2.56 (2 H, m, $ArCH_2$), 2.46 (3 H, s, ArMe), 3.1br (2 H, s, $ArCH_2$), 3.9 (6 H, s, OMe_2), 5.1 (4 H, s, $ArCH_2$), 6.54—6.84 (6 H, m, ArH), and 7.2—7.95 (14 H, m, ArH).

1,5-*Bis*-(3-*benzyloxy*-4-*methoxyphenyl*)*pentan*-2-*one* (7c).—(*a*) Mercury(II) nitrate (0.58 g) was added with vigorous stirring to the isonitrile (7b) (1g) in THF (7.5 ml). After 7 h, evaporation and chromatography on alumina (benzene) gave the *ketone* (7c) [0.46 g, 68% based on iodide (12e)]. (*b*) Peracetic acid (1 ml, 8.4 mmol) and the isonitrile (7b) (2 g) in THF (15 ml) were heated to reflux for 20 h. Work-up (diethyl ether–saturated aqueous potassium iodide/sodium thiosulphate, water) and chromatography on alumina (benzene) gave the ketone (7c) (1.16 g, 85%). Crystallisation from acetone–hexane gave prisms, m.p. 84—86°, $\nu_{max.}$ 1 710 cm^{-1}, $\lambda_{max.}$ 208 (ε 45 000), 225sh (16 600), and 280nm (5 600), δ 1.6—2.0 (2 H, m), 2.18—2.5 (4 H, m), 3.5 (2 H, s, $ArCH_2CO$), 3.88 (6 H, s, OMe), 6.68—7.5 (6 H, m, ArH), and 7.3—7.5br (10 H, s, Ph), *m/e* 510 (M^+), 419, 227, 193, 137, and 91 (100%) (Found: C, 77.35; H, 6.7. $C_{33}H_{34}O_5$ requires C, 77.62; H, 6.7%).

1,5-*Bis*-(3-*benzyloxy*-4-*methoxyphenyl*)*pentane* (7f).—(*a*) Potassium hydroxide (1.23 g) and hydrazine hydrate (2.25 ml) in diethylene glycol (7.25 ml) were heated to 155 °C to effect solution, cooled, and the ketone (7c) (0.37 g) added (N_2). After 1.5 h at 155 °C the excess of hydrazine and the water were distilled off by raising the temperature to 200 °C (vapour temperature) and after 0.5 h the mixture was cooled to room temperature. Work-up (dichloromethane–brine) and chromatography on alumina (benzene) gave the *pentane derivative* (7f) (0.17 g, 50%). (*b*) The ketone (7c) (60 mg) and 4-tolylsulphonylhydrazine (34.5 mg) in methanol (2 ml) were heated to reflux for 3 h and then evaporated. The residue and toluene-4-sulphonic acid monohydrate (3 mg) were heated to 105 °C under nitrogen in DMF (0.3 ml) and sulpholane (0.3 ml). Sodium cyanoborohydride (30 mg) was added and after 1 h at 105 °C (N_2) the mixture was cooled to room temperature. Work-up (diethyl ether–water) and chromatography gave the pentane derivative (7f) (30 mg, 50%). (*c*) Catecholborane [23] (0.28 ml, 2.6 mmol) was added to the crude 4-tolylsulphonyl hydrazone (7e) [from ketone (7c) (0.5 g), dried over phosphorus pentaoxide at 1 mmHg] in chloroform (2 ml) at −10 °C (N_2). After vigorously stirring for 20 min, sodium acetate trihydrate (0.8 h) was added and the mixture was allowed to reach room temperature, and then heated to reflux for 1 h. Work-up (chloroform–water) and chromatography on silica (benzene) gave the pentane derivative (7f) (0.35 g, 70%). Crystallisations from ethanol gave needles (0.28 g, 56%), m.p. 79—80° (from diethyl ether–light petroleum); $\nu_{max.}$ 1 240, 1 140, and 1 010 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 207 (ε 30 600), 225sh (10 300), and 278 nm (3 200), δ 1.0—1.9 [6 H, m, $(CH_2)_3$], 2.2—2.7 (4 H, m, $ArCH_2$), 3.85 (6 H, s, OMe), 5.1 (4 H, s, $ArCH_2$), 6.6—6.8 (6 H, m, ArH), and 7.1—7.6 (10 H, m, Ph), *m/e* 496 (M^+), 405, 227, 137, and 91 (100%) (Found: C, 79.75; H, 7.25. $C_{33}H_{36}O_4$ requires C, 79.8; H, 7.3%).

1,5-*Bis*-(3-*hydroxy*-4-*methoxyphenyl*)*pentane* (1d).—The pentane derivative (7f) (132 mg) was hydrogenated at 1 atm in glacial acetic acid (5 ml) containing 60% aqueous perchloric acid (1 drop) over 10% palladium–charcoal (25 mg) for 4 h. Filtration and work-up (chloroform–saturated aqueous sodium hydrogen carbonate, water) gave the diacetate (1e) (90 mg, 88%), $\nu_{max.}$ ($CHCl_3$) 1 750 cm^{-1}, δ 1.1—1.9 [6 H, m, $(CH_2)_3$], 2.24 (6 H, s, OAc), 2.2—2.7 (4 H, m, $ArCH_2$), 3.8 (6 H, s, OMe), and 6.7—7.0 (6 H, m, ArH). Potassium hydroxide (0.11 g) was added to the diacetate (1e) (90 mg) in methanol (1 ml) (N_2). After 6 h the solution at 0 °C was neutralised with 2N-hydrochloric acid. Work-up (dichloromethane–saturated aqueous sodium hydrogen carbonate, water) and chromatography on silica (benzene–ethyl acetate 10 : 1) gave the *bisphenol* (1d) (70 mg, 83%). Crystallisation from aqueous methanol gave needles (50 mg, 60%), m.p. 125—127 °C (from chloroform), $\nu_{max.}$ ($CHCl_3$) 3 540 cm^{-1}, $\lambda_{max.}$ 207 (ε 11 600), 220 (7 700), and 281 nm (3 600), $\lambda_{max.}$ (EtOH–KOH) 211 (ε 33 000), 243 (9 300), and 294 nm (4 900), δ 1.2—1.9 (6 H, m), 2.3—2.7 (4 H, m, $ArCH_2$), 3.85 (6 H, m, OMe), 5.6br (2 H, s, OH), and 6.6—6.85 (6 H, m, ArH), *m/e* 316 (M^+), 137 (100%), and 122 (Found: C, 72.05; H, 7.45. $C_{19}H_{24}O_4$ requires C, 72.1; H, 7.65%).

1,5-*Bis*-(3-*hydroxy*-4-*methoxyphenyl*)*pentan*-2-*one* (1c).—The ketone (7c) (2g) in ethyl acetate (40 ml) was hydrogenated at 1 atm. over 10% palladium–charcoal (0.48 g) for 2 days. Filtration, evaporation, and crystallisation from acetone–hexane gave the *bisphenol* (1c) (1.0 g, 77%) as rosettes of needles, m.p. 124—126°, $\nu_{max.}$ 3 400 and 1 700 cm^{-1}, $\lambda_{max.}$ 210 (ε 20 000), 225sh (14 000), and 281 nm (7 100), $\lambda_{max.}$ (EtOH–KOH) 216 (25 000), 239sh (14 000), and 296 nm (7 900), δ 1.65—2.05 (2 H, m), 2.2—2.75 (4 H, m, $ArCH_2$ and $COCH_2$), 3.55br (2 H, s, $ArCH_2CO$), 3.85 (6 H, 2s, OMe), 4.8—5.4br (2 H, OH), and 6.7 (6 H, m, ArH), *m/e* 330 (M^+), 193 (100%), and 137 (Found: C, 69.1; H, 6.7. $C_{19}H_{22}O_5$ requires C, 69.05; H, 6.7%).

Dibenzcyclononane Derivative (3c).—(*a*) The bisphenol (1c) (100 mg) in chloroform (160 ml) was added (N_2) with rapid stirring to potassium hexacyanoferrate(III) (0.62 g), sodium hydrogen carbonate (0.8 g), and cetyltriethylammonium bromide (24 mg) in water (15 ml). After 1 h, work-up (chloroform–water) and p.l.c. gave the *bisphenol* (3c) (7.3 mg, 10% allowing for recovered starting material) (R_F 0.39; light petroleum–ethyl acetate 2 : 3), m.p. 171—174° (from benzene–light petroleum), $\nu_{max.}$ ($CHCl_3$) 3 530 and 1 690 cm^{-1}, $\lambda_{max.}$ 210 (ε 35 000) and 289 nm (8 000), $\lambda_{max.}$ (KOH–EtOH) 213 (ε > 43 000), 248sh (16 000), and 308 nm (7 200), δ 1.7—2.72 (6 H, m), 3.19, 3.40 (2 H, ABq, *J* 16 Hz, $ArCH_2CO$), 3.8 (3 H, s, OMe), 3.87 (3 H, s, OMe), 5.54 (1 H, s, OH), 5.62 (1 H, s, OH), 6.5 (1 H, s, ArH), 6.72 (2 H, s, ArH), and 6.9 (1 H, s, ArH), *m/e* 328 (M^+, 100%), 300, 271, and 241 (Found: C, 69.7; H, 6.2. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.15%); and a by-product (R_F 0.57). Larger scale reactions (300—600 mg) gave the bisphenol (3c) (7—11%), and the by-product (10—14%), *m/e* 686, 658, 346, and 344. (*b*) Reaction of the bisphenol (1c) (100 mg) as (*a*) using benzyltriethylammonium chloride (15 mg), instead of cetyltriethylammonium chloride, for 0.5 h gave only the by-product (5.2 mg). (*c*) Reaction as (*a*) using 18-crown-6 (8 mg), instead of the quaternary ammonium salt, for 0.5 h gave the by-product (7 mg) and only traces of bisphenol (3c).

Phenol Oxidative Coupling of Bisphenol (1d).—The bisphenol (1d) (100 mg) in chloroform (157 ml) was added (N_2) with rapid stirring to potassium hexacyanoferrate(III) (1.24 g), sodium hydrogen carbonate (1.6 g), and benzyltriethylammonium chloride (31 mg) in water (30 ml). Work-up as above after 0.5 h gave a complex mixture (t.l.c.). Repeated p.l.c. (benzene–ethyl acetate 19 : 1, acetone–1,2-dichloroethane 3 : 50) gave an oil (2 mg), $\nu_{max.}$ 3 515 cm^{-1}, *m/e* 332 316, 153, and 137 (100%).

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