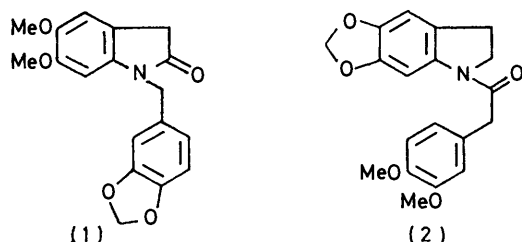


Electrochemical Oxidation of Aromatic Ethers. Part 5.¹ Further Studies of the Coupling Reactions of Alkoxyated Aralkyl- and Aryl-amides

By Malcolm Sainsbury* and John Wyatt, School of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY

An electrochemical conversion of 5,6-dimethoxy-1-(3,4-dimethoxybenzyl)indoline into 6-hydroxy-5-methoxy-1-(3,4-dimethoxybenzyl)indole is described and some examples of the electro-oxidative intra- and inter-molecular coupling reactions of indoles, oxindoles and aralkyl- and aryl-amides are examined. Mechanisms are advanced to account for the products of electrolysis and the probable cause of electrode filming. The latter phenomenon often encountered in such oxidations is discussed and the structural element responsible (a benzylic methylene group adjacent to a nitrogen or oxygen atom) is identified. For certain substrates an alternative mechanisms of aryl-aryl coupling, not involving two radical cations, is proposed.

We have reported that electrochemical oxidation of the oxindole (1) leads to an intractable tar rather than an intramolecularly aryl-aryl coupled product as had been expected.² In an attempt to effect the desired type of cyclisation we have now examined the related compound



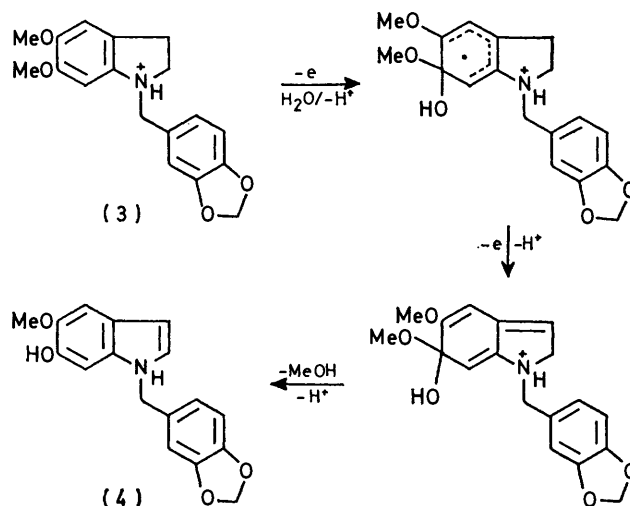
(2), the cyclic voltammogram of which shows anodic peaks (*versus* s.c.e.) of 0.7, 1.15, and 1.25 V, each due to the loss of one electron.

In the 0.1M-sodium perchlorate in acetonitrile electrolyte system which we employ customarily dialkoxyated aryl rings lose an electron to a platinum anode at +1.1–1.2 V.³ However, the substrate (2) gave only tar when a preparative experiment was carried out at this potential; on the other hand at +0.7 V some homoveratric acid (5%) was formed as well as tar. This result suggests that at the lower anode potential a radical cation is formed from the heterocyclic system, and fragmentation of the N-substituent then occurs at a rate which exceeds that of an intramolecular coupling reaction between the radical cation and the un-ionized nonfused aryl ring.

Such a conclusion is supported by the fact that the indolinium salt (3) is not oxidized below +1.3 V; but interestingly, at an anodic potential of 1.3 V a preparative electrolysis of this compound proceeded without tar formation until 2F mol⁻¹ of current were consumed. Instead of a tetracyclic product, however, work-up of the anolyte afforded the indole (4) and we suggest the following scheme for its production, noting at the same time that it may only exist in a protonated form during the electrolysis for as the parent indole (4) it is oxidised destructively at +0.6 V. The participation of water in this sequence may at first appear unusual but, although the acetonitrile electrolyte was dried before use, we¹ and others^{4,5} observe that the water concentration may still

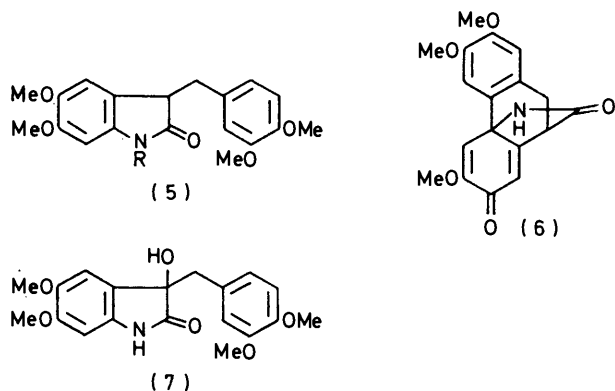
be 10 mM or higher. Unfortunately the yield in this reaction was only 10%, but with more careful control of conditions it may prove to be of some synthetic utility.

Earlier we stated that the 1-acetyloxindole (5; R = Ac) when electrolysed at an anode potential of +1.1 V afforded the dienone (6) and commented that de-*N*-acetylation probably occurred during work-up.² We now wish to amend this suggestion and propose that the N-substituent is eliminated as a result of the electrochemistry and in a similar manner to that described for the *N*-acylindoline (2). The oxindole (5; R = H) and its *N*-acetyl derivative both show very similar cyclic voltammograms with anodic peaks at +0.75 (5; R = H) or +0.86 (5; R = Ac) and +1.1 V (both compounds). A preparative electrolysis of the parent structure (5; R = H) at an anode potential of +0.75 V gave, after the consumption of 2 F mol⁻¹ of current, two products: m.p. 172–175 °C and m.p. 270–275 °C. The mass spectrum of the first exhibits a very weak molecular ion peak at *m/e* 359 with major fragmentation peaks at *m/e* 343, 341, and 151. In the i.r. spectrum bands at



3 350w (OH), 3 210s (NH), 1 710, 1 690, and 1 670 cm⁻¹ are observed; whereas the ¹H n.m.r. spectrum shows five aromatic proton resonances, very similar in form to those of the starting material, but now the benzylic methylene protons give rise to a simple AB pattern at

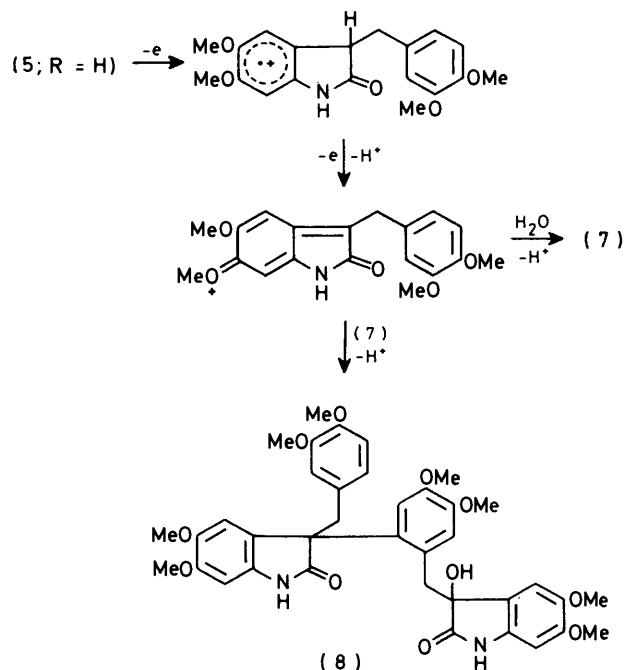
δ 3.35 (d, $J = 13$ Hz) and 4.12 (d, $J = 13$ Hz) instead of an ABX system, demonstrating that the structure no longer bears a proton at C-3. Indeed, the only other difference between the ^1H n.m.r. spectra is the presence of an extra 1H singlet peak at δ 2.89 in the product which is removed by the addition of deuterium oxide. On this basis we consider this product to be simply the 3-hydroxy-derivative (7) of the parent oxindole. The second product shows bands at 3 500, 3 360, and 3 160 cm^{-1} in the i.r. spectrum, together with carbonyl bands at 1 705 and 1 695 cm^{-1} . The mass spectrum shows a peak at highest mass of m/e 682 and major fragment ions at m/e 531, 341 (base peak), 310, 272, and 151. An intermolecularly coupled structure is indicated and in the ^1H n.m.r. spectrum signals for nine aromatic protons are recognized (see Experimental section). Moreover, the pattern of signals shows that one of the 3,4-dimethoxybenzyl rings is involved in the point of linkage. Additionally one set of benzylic methylene proton signals forms a broad singlet at δ 3.3, whereas another appears as an AM system at δ 2.78 (d, $J = 15$ Hz) and δ 3.50, the last signal being partly obscured by the methoxy-resonances. One singlet peak, due to the



hydrogen atom of a hydroxy-group occurs at δ 1.71; this, together with two NH resonances at δ 7.15 and 7.60, is removed when deuterium oxide is added. This data, together with our conclusion concerning the structure of the first product, prompt the structural assignment (8) and we presume that a ready loss of water prevents the clear observation of the true molecular ion peak in the mass spectrum (a metastable peak at m/e 664.5 is suggestive of the loss of 18 m.u. from an extremely weak molecular ion peak at m/e 700). A scheme for the formation of the products (7) and (8) may then be as shown (next column).

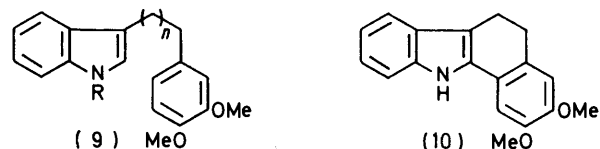
Substrates which contain a simple indole nucleus show the first anodic peak at *ca.* 0.8 V in cyclic voltammetric experiments. However, attempts to cyclise electrochemically the 3-phenethylindole (9; $n = 1$, R = H) to the dihydrobenzo[*a*]carbazole (10) either at +0.8 V, or at 'forced' potentials of +1.1–1.3 V, were unproductive and lead to resins. The 1-acetyl derivative (9; $n = 1$, R = Ac) is more difficult to oxidise, $E_{\frac{1}{2}} + 1.1$ V (first wave), and a preparative electrolysis at this potential

affords a very small amount of an unstable product which gives rise to a poorly resolved ^1H n.m.r. spectrum which



has an 'aromatic' to 'aliphatic' proton integral ratio of 4 : 5. The mass spectrum exhibits a weak molecular ion at m/e 560 and on this basis we speculate reservedly that this product is the bisindolenine (11) which may form as shown on the next page.

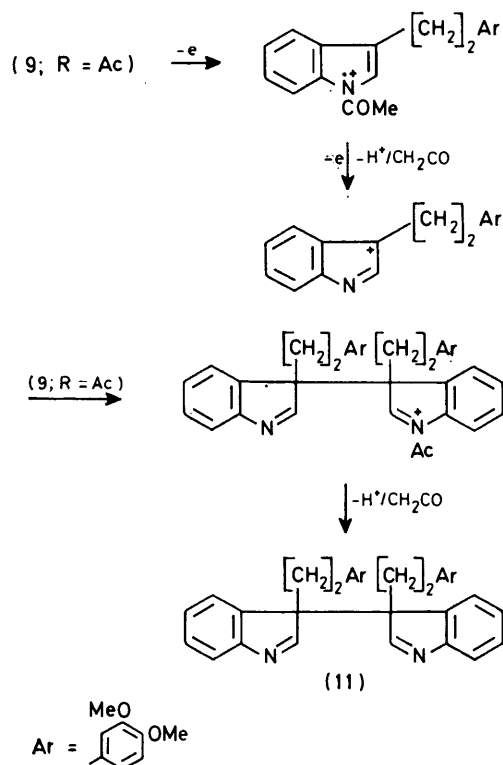
In the case of the homologue (9; $n = 2$, R = Ac) only a tar was obtained, but an electrolysis of the enamido-ketone (12; $n = 2$) at an anode potential of 1.1 V proceeded relatively smoothly * until *ca.* 6 F mol $^{-1}$ of current had been used. Work-up of the anolyte afforded a high-melting black solid which gives rise to a molecular ion peak at m/e 279 in the mass spectrum. The ^1H n.m.r. spectrum exhibits signals quite typical of a 2,3-disubstituted indole or indolenine and, additionally, two



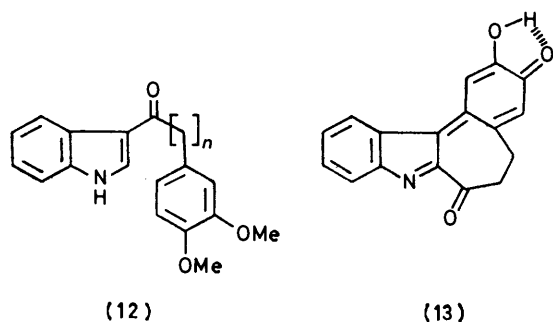
singlet 1 H peaks at δ 6.56 and 6.80 are observed. There are no methoxy hydrogen resonances, but the presence of a CH_2CH_2 unit is established by the appearance of a 4H A_2B_2 multiplet centred at δ 2.90. This product does not react with 1,2-diaminobenzene and we propose that it has the hydroxyquinonoid structure (13). Interestingly, the lower homologue (12; $n = 1$) does not form a similar derivative although cyclic voltammetry shows

* The product tends to adhere to the surface of a platinum anode thus increasing cell resistance, but if a carbon felt anode is used instead of platinum, potential control can be more easily exercised and a higher yield of product (68% versus 15%) is obtained. (We thank Mr. Mark Powell for conducting this last experiment).

that it undergoes reversible one electron oxidation at 1.2 V. After preparative electrolysis, some intermolecular products result but the bulk of the substrate



is recovered unchanged. These facts suggest that in order to give a 2,3-disubstituted indole such as that which leads to the hydroxyquinone (13) the radical

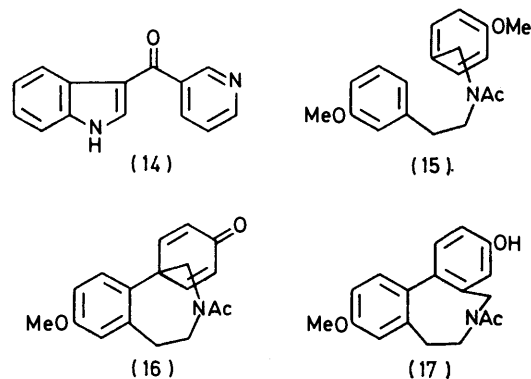


cation formed initially from the dimethoxylated benzene ring must react at the indole 3-position yielding a spiro-intermediate; this then undergoes *selective* bond breaking and rearrangement. The difference between the two reactants (12; $n = 1$ and 2) simply reflects the relatively high energetics of a reaction requiring a five-membered transition state compared to that involving a six-membered system.^{6,7}

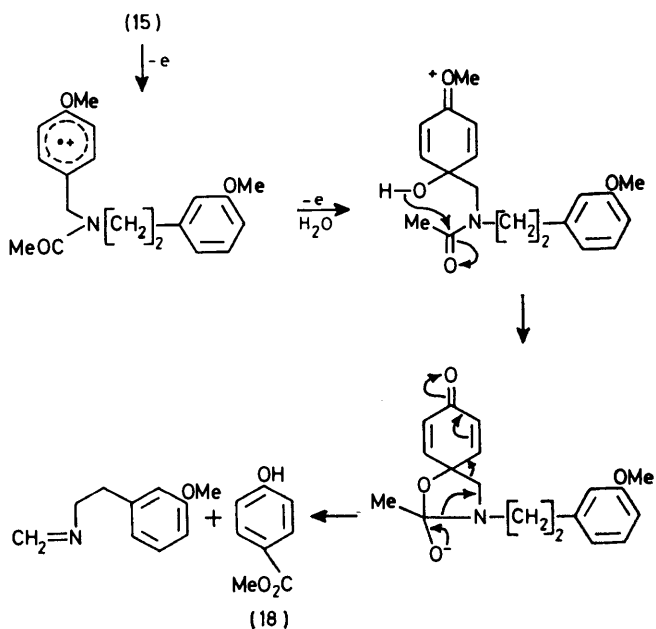
Structure (13) is selected for the product from the electrolysis of (12; $n = 2$) rather than the alternative, in which the substituents joined to the indole 2- and 3-positions are interchanged, since the rearrangement process leading to the latter would require a developing

positive centre next to a carbonyl group. It is noteworthy that 3-nicotinoylindole (14)⁸ is not oxidized below +1.5 V.

Where intramolecular aryl-aryl coupling is possible, through either *ortho*- or *para*-positions, the latter course is preferred; thus the amide (15) should afford the dienone (16), which on acid treatment should give the tricyclic phenol (17) through rearrangement.

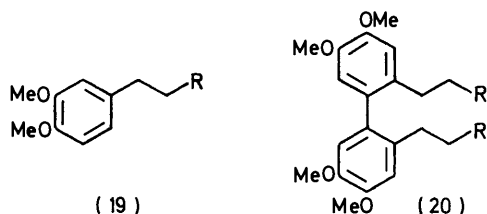


An electrochemical oxidation of the amide was attempted at an anode potential of +1.35 V, a value equal to that of the first anodic peak in the cyclic voltammogram; however, electrode fouling occurred. Since current-voltage curves for this substrate show that a carbon anode is less susceptible to fouling than platinum a second preparative experiment was conducted using a graphite felt electrode. Although the colour of the anolyte immediately darkened anode potential control was now possible and the experiment was continued at +1.35 V until 2 F mol⁻¹ of current had been used. Instead of the anticipated phenol (17) 4-hydroxyphenyl acetate (18) was obtained; this may form as follows:



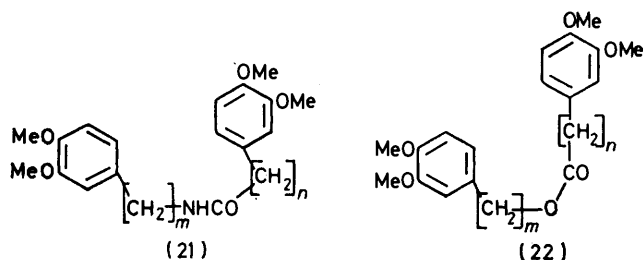
Previously, whenever we have encountered electrode filming we have considered that a contributory cause is unspecific intermolecular coupling.^{1,2} However, we have no evidence in terms of products to support this view since the reactions have always been prematurely terminated. This deficiency prompted us to examine the extent of intermolecular coupling in some relatively simple monoaryl derivatives. Interestingly the electrochemical oxidation of β -(3,4-dimethoxyphenyl)propionic acid (19; R = CO₂H) took place at an anode potential of 1.1 V to give the biaryl (20; R = CO₂H), without electrode fouling. The yield was increased from 30 to 55% by substituting trifluoroacetic acid for the usual acetonitrile-sodium perchlorate electrolyte system.⁹ This and the coulometry of the process strongly favours the initial formation of a radical cation.

Similarly when *N*-acetylhomoveratrylamine (18; R = NHAc) was electrolysed the biaryl (20; R = NHAc)



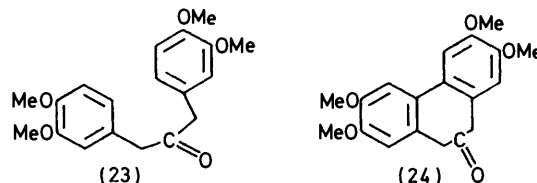
was produced without complications, although in this case the best yield obtained was only 26%.

In an earlier paper² we speculated that in the case of secondary amides, *e.g.* (21) where filming problems are severe electron loss and deprotonation at nitrogen may give rise to a radical which may then oxidise further and cause electrode coating. The evidence of the previous experiment argues against this proposal and in fact cyclic voltammetric analysis of *N*-benzylbenzamide shows that it is not oxidised below +1.8 V, an anode potential far higher than we have ever used. Furthermore in a parallel study with the analogous esters (22) we have also encountered electrode fouling problems.¹

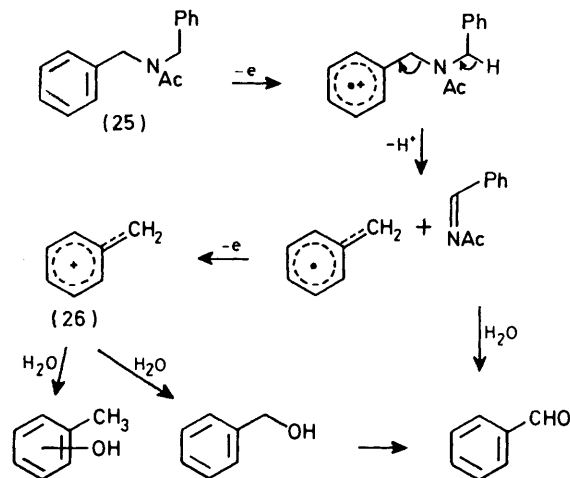


An analysis of all of the compounds for which we observe electrode filming during oxidation shows that the majority contain a benzylic methylene group adjacent to an oxygen or nitrogen atom. Moreover, the latent acidity of the methylene protons (as deduced from chemical-shift measurements) provides a rough guide to the ease of fouling; thus esters of the type (22; $m = 1, n = 0$), δ_{CH_2} 5.2, cause electrode coating almost twice as fast as their amide counterparts (21; $m = 0$,

$n = 1$), δ_{CH_2} 4.3. Whereas the electrolysis of bis-1,3-(3,4-dimethoxyphenyl)propan-2-one (23), δ_{CH_2} 3.6, proceeds, without filming, to give the tricyclic ketone (24) in high yield.



In all of our previous work we have sought to control the anode potential to values corresponding to those of anodic peaks in the cyclic voltammograms of the starting materials. When filming occurs this is often difficult, or impossible, to achieve and the experiments were abandoned. However, Lund¹⁰ and others¹¹⁻¹³ have shown that in 'uncontrolled' electrolyses benzyl alcohols, ethers and esters may give rise to the corresponding benzaldehydes. In order to determine whether such processes are possible with amides we next carried out an oxidation with *N,N*-dibenzylacetamide (25). Initially the anode potential was set at +1.9 V but this was allowed to rise to *ca.* +2.3 during the course of the experiment which lasted until *ca.* 2 F mol⁻¹ of current had been consumed. Work-up afforded a dark resinous material which was partly refined by elution in chloroform:ethanol (9:1) through a column of silica. Early fractions were analysed by vapour phase chromatography and a comparison of retention times with a number of possible products (a choice aided by mass spectrometric studies) shows that benzaldehyde, benzoic acid, *ortho*- and *para*-cresol were formed. The presence of the last three compounds was confirmed by their isolation as pure components from the anolyte of a second electrolysis by base extraction, *etc.* These represent only a small proportion of the total product but, unfortunately, the rest is of a resinous nature.

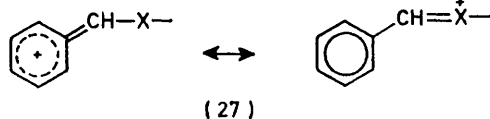


The formation of benzaldehyde may be rationalized by the following sequence which embodies as the crucial

step the deprotonation of one of the benzylic hydrogen atoms and further oxidation of the product radical to give a cation (26).¹⁴ The formation of the cresols may also be derived from the cation (26) or the radical cation of the amide (25) by attack of water not at the benzylic site but now at a ring position. This type of breakdown is well known and similar mechanistic schemes have been advanced to explain, for example, the anodic debenzyl-ation of aryl benzyl ethers.¹⁵

It may be that the extra yields observed in aryl-aryl coupling reactions conducted in trifluoroacetic acid by Parker⁹ and ourselves simply reflects the repression of the deprotonation of radical cations in the acidic media. Clearly, however, many mechanisms may be advanced for the actual coupling reaction and the requirement for the union of two radical cations¹⁶ is not always necessary,^{9,17} indeed one may easily postulate that an interaction between a cation such as (27) and an un-ionized aryl nucleus may also occur where appropriate stabilizing factors exist, thus it is obvious that cations of the type (27) will be especially favoured when the neighbouring group or atom X may assist delocalisation of the positive charge.

We suggest that when intramolecular coupling is precluded for steric or other reasons the formation of such cations frequently allows the formation of diverse compounds many of which are more easily oxidized than the original substrate and it is the breakdown products of these compounds which often cause electrode fouling. In this way it is then easy to account for filming in the case of benzylic amides, esters and ethers, whereas benzyl ketones, for example (24), are oxidised cleanly.



EXPERIMENTAL

All preparative electrolyses were conducted with an H-type cell of 200 cm³ capacity, with 'dry' acetonitrile as solvent and anhydrous sodium perchlorate as supporting electrolyte, unless stated otherwise. The anode was of platinum gauze (area 80 cm²) and the cathode a mercury pool. Current was provided by a Farnell stabilized power supply and the potential of the anode was monitored with a digital voltmeter *via* an agar bridge and a standard calomel electrode (s.c.e.).

Cyclic voltammetry was carried out under the same electrolyte conditions, but using a platinum wire anode and a 'home-made' waveform generator, the design and circuit diagram of which are due to Dr. J. H. P. Utley, Queen Mary College, London.

U.v. spectra were recorded for solutions in aqueous 95% ethanol; i.r. spectral data refer to Nujol mulls; ¹H n.m.r. spectra were recorded at 100 MHz with tetramethylsilane as internal standard.

Standard Procedure.—All preparative experiments were conducted in the following manner: after the utilization of a specified amount of current, the contents of the anode compartment (the anolyte) were poured into water and extracted with chloroform. The combined and dried

extracts were evaporated and the residue refined either by fractional crystallisation or column/layer chromatography.

5,6-Dimethoxy-1-(3,4-methylenedioxybenzyl)indoline (3).—5,6-Dimethoxy-1-(3,4-methylenedioxybenzyl)indol-2(3H)-one (1)² (3.0 g) in tetrahydrofuran (30 cm³) was added at 0 °C to a solution of diborane in the same solvent (1M; 27 cm³) and then heated at reflux for 90 min. The excess of reagent was destroyed by the addition of ethanol, followed by hydrochloric acid (10 cm³). After 1 h, water (50 cm³) was added and the solution basified with ammonia. Extraction with chloroform (2 × 25 cm³) and removal of the solvent from the combined extracts, afforded a pale yellow solid which was triturated with diethyl ether. In this way colourless prisms of the indoline were obtained (0.92 g), m.p. 70–72 °C; *m/e* 313 (*M*⁺), 161, and 151; δ(CDCl₃) 2.90 (2 H, t, *J* = 6 Hz), 3.28 (2 H, t, *J* = 6 Hz), 3.84 (6 H, s, 2 × OMe), 4.12 (2 H, s), 5.95 (2 H, s), 6.30 (1 H, s), and 6.70–7.00 (4 H, m) (Found: C, 68.6; H, 6.0; N, 4.3. C₁₈H₁₉NO₄ requires C, 69.0; H, 6.1; N, 4.5%).

6-Hydroxy-5-methoxy-1-(3,4-methylenedioxybenzyl)indole (4).—The indoline (3) (0.8 g) in ether (30 cm³) was treated with hydrogen chloride, the solvent was then removed and the salt so obtained oxidized at an anode potential of +1.3 V until 2 F mol⁻¹ of current had been used. The analyte was poured into 5% aqueous sodium carbonate (250 cm³) and extracted with dichloromethane (3 × 50 cm³). The combined extracts were dried and evaporated to give a gum which was chromatographed on silica, using an ethyl acetate–light petroleum (b.p. 60–80 °C) elution system. The indole (4) was obtained as colourless prisms (0.11 g, 15%), m.p. 90–91 °C (diethyl ether); *m/e* 297 (*M*⁺), 178 (4%), 148 (6%), and 135 (100%); *v*_{max} 3 360, 1 610w, and 1 580 cm⁻¹; δ(CDCl₃) 3.82 (3 H, s), 5.14 (2 H, s), 5.45br (1 H, s), 5.87 (2 H, s, OCH₂O), 6.40 (1 H, d, *J* = 3.5 Hz), 6.50–6.70 (4 H, m), 6.96 (1 H, d, *J* = 3.5 Hz), and 7.16 (1 H, s) (Found: C, 68.6; H, 5.1; N, 4.6. C₁₇H₁₅NO₄ requires C, 68.7; H, 5.1; N, 4.7%).

3-Hydroxy-5,6-dimethoxy-3-(3,4-dimethoxybenzyl)indolin-2(3H)-one (7) and 3-Hydroxy-5,6-dimethoxy-3-{2-[3-(3,4-dimethoxybenzyl)-5,6-dimethoxy-2-oxindolin-3-yl]-4,5-dimethoxybenzyl}indolin-2(3H)-one (8).—5,6-Dimethoxy-3-(3,4-dimethoxybenzyl)indolin-2(3H)-one² (5; R = H) (1.5 g) was electrolysed at +0.86 V until 2F mol⁻¹ of current had been consumed, removal of the solvent after work-up afforded an oil (7) which slowly crystallized as prisms (0.44 g), m.p. 172–175 °C, *m/e* 359 (*M*⁺), 343 (15%) and 341 (33%); *v*_{max} 3 350w, 3 210, 1 710, 1 690, and 1 670 cm⁻¹; δ(CDCl₃) 2.80 (1 H, s), 3.36 (1 H, d, *J* = 13 Hz), 3.54 (3 H, s, OMe), 3.75 (9 H, s, 3 × OMe), 4.1 (1 H, d, *J* = 13 Hz), 6.25 (1 H, s), 6.38 (1 H, s), 6.5–6.6 (3 H, m), and 9.06 (1 H, s, NH) (Found: C, 63.6; H, 6.0; N, 3.9. C₁₉H₂₁NO₆ requires C, 63.5; H, 5.8; N, 3.9%).

The mother-liquor from which this product was obtained was evaporated and chromatographed on silica (ethyl acetate–light petroleum, b.p. 60–80 °C) affording (8) as colourless prisms (0.06 g), m.p. 270–275 °C (ethanol), *m/e* 682 (*M*⁺ – 18), 531 (20%), and 341 (100%); *v*_{max} 3 500, 3 350, 3 160, 1 700, and 1 622 cm⁻¹; δ(CDCl₃) 1.63* (1 H, s), 2.80 (1 H, d, *J* = 16 Hz), 3.26 (2 H, s), 3.66 (1 H, d, *J* = 16 Hz), 3.72 (12 H, s, 4 × OMe), 3.89 (12 H, s, 4 × OMe), 6.0–6.6 (6 H, m), 6.65 (1 H, s), 6.76* (1 H, s), 7.12 (1 H, s), 7.41 (1 H, s), and 7.53* (1 H, s) (Found: C, 65.0; H, 6.0; N, 3.8. C₃₈H₄₀N₂O₁₁ requires C, 65.1; H, 5.75; N, 4.0%).

3-[β-(3,4-Dimethoxyphenyl)ethyl]indole (9; n = 1, R =
* Removed on addition of D₂O.

H).—This compound was prepared from 3-(3,4-dimethoxyphenylacetyl)indole, m.p. 174—176 °C, by reduction with sodium borohydride in boiling n-propanol; yield 79%, m.p. 114 °C; m/e 281 (M^+) and 151 (100%); λ_{\max} 223, 283, and 335 nm; ν_{\max} 3 380, 1 597, and 1 580 cm^{-1} ; $\delta(\text{CDCl}_3)$ 2.96br (4 H, s), 3.73 (3 H, s), 3.79 (3 H, s), 6.6—6.8 (3 H, m), 6.95—7.25 (4 H, m), 7.46—7.60 (1 H, m), and 7.86br (1 H, s). The *N*-acetyl derivative (9; R = Ac) has m.p. 108—110 °C (Found: C, 74.1; H, 6.6; N, 4.0. $\text{C}_{20}\text{H}_{21}\text{NO}_3$ requires C, 74.3; H, 6.55; N, 4.3%).

Oxidation of (9; n = 1, R = Ac).—The oxidation of this compound was conducted at an anode potential of +1.1 V and terminated after 2 F mol^{-1} of current had been passed. Work-up gave a black resinous material, but when this was subjected to column chromatography on silica using 1 : 1 ethyl acetate–light petroleum (b.p. 60—80 °C) a small quantity of a semicrystalline solid was obtained. This darkened rapidly and decomposed on exposure to light, but initially showed m/e 560 (M^+) and 151 (100%); ν_{\max} 1 615 cm^{-1} . Attempts to purify this compound further failed and repetitions of the oxidation reaction with other electrode and electrolyte systems were unproductive.

6-Hydroxy-2,3-dihydrobenzo[6,7]cyclohept[1,2-b]indole-1,5-dione.—3-(3,4-Dimethoxyphenylpropionyl)indole (12; $n = 2$), m.p. 137—138 °C prepared from 3,4-dimethoxyphenylpropionyl chloride and indolylmagnesium bromide, was oxidized at an anode potential of +1.5 V until 6 F mol^{-1} of current had been used. A dark purple coloured residue was obtained after work-up which when triturated with ethanol afforded prisms of the quinone (13); yield 15% (when a carbon anode was used the yield was increased to 68%). The quinone may be recrystallized from ethanol but has an indefinite m.p. ca. 230—240 °C; m/e 277 (M^+ , 100%), 251 (30%), 250 (95%), and 249 (33%); λ_{\max} 215, 241, 310, and 350sh nm; ν_{\max} 3 340, 1 670, 1 658, 1 640, and 1 630 cm^{-1} ; $\delta[(\text{CD}_3)_2\text{SO}]$ 12.6br (1 H, s, removed by addition of D_2O), 2.0br (1 H, d), 7.72—7.25 (3 H, m), 6.81 (1 H, s), 6.56 (1 H, s), and 2.95 (4 H, m) (Found: C, 73.5; H, 3.6; N, 5.0. $\text{C}_{17}\text{H}_{11}\text{NO}_3$ requires C, 73.6; H, 4.0; N, 5.05%).

4-Hydroxyphenyl Acetate (18).—*N*-(4-Methoxybenzyl)-*N*-(3-methoxyphenylethyl)acetamide (15) (1 g) was oxidized using a graphite felt anode at +1.35 V until 2 F mol^{-1} of current had been used. Work-up (column chromatography) gave 4-hydroxyphenyl acetate (150 mg) as an oil; m/e 152 (M^+), 110 (100%), and 81 (10%); ν_{\max} 3 400, 1 730, and 1 600 cm^{-1} ; $\delta(\text{CDCl}_3)$ 2.20 (3 H, s), 6.00—6.82br (1 H, s, OH), 6.6 (2 H, d, $J = 9$ Hz), and 6.8 (2 H, d, $J = 9$ Hz) (Found: C, 63.0; H, 5.4. Calc. for $\text{C}_8\text{H}_8\text{O}_3$: C, 63.15; H, 5.3%).

Bis-4,4',5,5'-tetramethoxybiphenyl-2,2'-dipropionic Acid (20; R = CO₂H).— β -(3,4-Dimethoxyphenyl)propionic acid (1.5 g) was electrolysed at +1.1 V in acetonitrile–trifluoroacetic acid–sodium perchlorate as electrolyte (4 : 1 : 0.1, by weight) until 1 F mol^{-1} of current had been used. This gave eventually an oil which slowly crystallised to the biphenyl (20; R = CO₂H) (0.82 g), m.p. 145 °C (ethanol); m/e 418 (M^+), 299, and 286; λ_{\max} 228sh and 287 nm; ν_{\max} 3 500, 3 300, 2 650—2 400, 1 682, and 1 602 cm^{-1} ; $\delta(\text{CDCl}_3)$ 2.36 (4 H, t, $J = 7$ Hz), 2.65 (4 H, t, $J = 7$ Hz), 3.81 (6 H, s, 2 \times OMe), 3.89 (6 H, s, 2 \times OMe), 6.30—5.60br (4 H, s, $\text{H}_2\text{O} + 2 \times \text{CO}_2\text{H}$), 6.64 (2 H, s), and 6.83 (2 H, s). When the sample is heated at 60 °C under reduced pressure for 10 h water is lost and the anhydrous acid is obtained (Found: C, 63.1; H, 6.4. $\text{C}_{22}\text{H}_{26}\text{O}_8$ requires C, 63.15; H, 6.3%).

2,2'-Bis-(N-acetylaminoethyl)-4,4',5,5'-tetramethoxybiphenyl

(20; R = NHAc).—*N*-Acetyl-3,4-dimethoxyphenethylamine was oxidised as in the previous experiment to give the biphenyl derivative (20; R = NHAc) in 26% yield. The product has m.p. 188—190 °C (ethanol), m/e 444 (M^+), 385, 299, and 151; ν_{\max} 3 280, 3 080w, and 1 650 cm^{-1} ; $\delta(\text{CDCl}_3)$ 1.84 (6 H, s, 2 \times Ac), 2.50 (4 H, m), 3.20 (4 H, m), 3.75 (6 H, s, 2 \times OMe), 3.82 (6 H, s, 2 \times OMe), 6.0br (2 H, s), 6.52 (2 H, s), and 6.71 (2 H, s) (Found: C, 64.9; H, 7.3; N, 6.1. $\text{C}_{24}\text{H}_{32}\text{N}_2\text{O}_6$ requires C, 64.8; H, 7.3; N, 6.3%).

Bis-1,3-(3,4-dimethoxyphenyl)propan-2-one (23).—Dry tetrahydrofuran (30 cm^3) was added to a mixture of *NN'*-carbonyldiimidazole (8.2 g) and dimethoxyphenylacetic acid (10 g). Carbon dioxide was evolved and when this had subsided dry nitrogen was bubbled through the solution for 30 min. The solution was then cooled to –10 °C and lithium aluminium hydride (0.5 g) added in portions. The reaction mixture was allowed to warm to room temperature during 3 h, water added (50 cm^3) and some solvent removed by distillation under reduced pressure; the residue was extracted with chloroform (2 \times 50 cm^3) and the combined, dry extracts evaporated to give the ketone (23) as an oil which slowly crystallized; yield (3.6 g, 43%), m.p. 103—105 °C (ethanol) (lit.¹⁸ 84—86 °C); m/e 330 (M^+), $\delta(\text{CDCl}_3)$ 3.64 (4 H, s), 3.82br (12 H, s), and 6.75—6.84 (6 H, m) (Found: C, 69.0; H, 6.8. Calc. for $\text{C}_{19}\text{H}_{22}\text{O}_5$: C, 69.1; H, 6.7%).

6,7-Dihydro-2,3,9,10-tetramethoxy-5H-dibenzo[a,c]cyclohepten-6-one (24). The ketone (23) (1.5 g) was electrolysed at an anode potential of +1.1 V until 2 F mol^{-1} of current had been used. Work-up afforded a viscous oil which crystallized when triturated with ethanol and recrystallized from this solvent as colourless prisms (0.68 g, 45%), m.p. 240—241 °C (decomp.) (lit.¹⁹ 259 °C), m/e 328 (M^+), 300 (10%), 285 (15%), and 151 (100%); ν_{\max} 1 705, 1 600, and 1 585 cm^{-1} ; $\delta(\text{CDCl}_3)$ 3.52 (4 H, s), 4.03br (12 H, s), 6.8 (2 H, s), and 7.10 (2 H, s) (Found: C, 69.4; H, 6.0. Calc. for $\text{C}_{19}\text{H}_{20}\text{O}_5$: C, 69.5; H, 6.1%).

Oxidation of NN-Dibenzylacetamide (25).—The amide (1.5 g) was oxidised at an initial anode potential of +1.9 V. However, this rose rapidly to +2.3 V and remained at this value until 2 F mol^{-1} of current had been used. No attempt was made to reset the potential at the lower value during this experiment. The anolyte was worked-up in the usual way but after column chromatography on silica (chloroform–ethanol 9 : 1) the fractions were combined and analysed by v.p.c. using two column systems: 2.5% OV1 on Chromasorb W at 150 °C and 15.0% Apiezon L on Universal B at 130 °C linked to an MS12 AE1 mass spectrometer. From comparisons with the retention times of a number of possible compounds, together with mass spectrometric fragmentation patterns benzaldehyde, benzoic acid, and 2- and 4-cresols were identified. In addition a repeated electro-oxidation was carried out but this time the combined fractions were washed first with sodium hydrogencarbonate solution, and then with sodium hydroxide. In this way individual components were obtained in obvious ways although in the case of the sodium hydroxide extract, after acidification, the cresols were isolated as a mixture which required further column chromatography [SiO_2 , light petroleum (b.p. 60—80 °C)–diethyl ether] for resolution.

J. W. is supported by a S.R.C. CASE studentship in collaboration with Allen and Hanbury Research Ltd. We thank Dr. R. Newton of that organisation for his constant interest and encouragement.

[7]2238 Received, 21st December, 1977

REFERENCES

- ¹ Part 4, M. Sainsbury and J. Wyatt, *J.C.S. Perkin I*, 1977, 1750.
- ² M. Sainsbury and J. Wyatt, *J.C.S. Perkin I*, 1976, 661.
- ³ V. D. Parker, *Chem. Comm.*, 1970, 1567.
- ⁴ S. Ikenoya, M. Masui, H. Ohmori and S. Sayo, *J.C.S. Perkin II*, 1974, 571.
- ⁵ A. J. Fry in 'Synthetic Organoelectrochemistry', Harper and Row, New York, p. 88.
- ⁶ J. E. Baldwin, *J.C.S. Chem. Comm.*, 1976, 734.
- ⁷ M. Sainsbury, *Heterocycles*, 1978, in the press.
- ⁸ K. N. Kilminster and M. Sainsbury, *J.C.S. Perkin I*, 1972, 2264.
- ⁹ V. D. Parker and A. Ronlán, *J. Amer. Chem. Soc.*, 1975, **97**, 4717.
- ¹⁰ H. Lund, *Acta. Chem. Scand.*, 1957, **11**, 491.
- ¹¹ R. F. Garwood, Naser-ud-din, and B. C. L. Weedon, *J.C.S. Chem. Comm.*, 1969, 923.
- ¹² L. Gherson and K. Nyberg, *Accounts Chem. Res.*, 1972, 106.
- ¹³ O. R. Brown, S. Chandra, and J. A. Harrison, *J. Electroanalyt. Chem.*, 1972, **34**, 505.
- ¹⁴ M. Matsui, H. Ohmori, H. Sayo, A. Ueda, and C. Ueda, *J.C.S. Perkin II*, 1976, 1180.
- ¹⁵ S. M. Weinreb, G. A. Epling, R. Comi, and M. Reitano, *J. Org. Chem.*, 1975, **40**, 1356.
- ¹⁶ A. Ronlán, O. Hammerich, and V. D. Parker, *J. Amer. Chem. Soc.*, 1973, **95**, 7132.
- ¹⁷ K. Nyberg, *Acta. Chem. Scand.*, 1971, **25**, 2499.
- ¹⁸ S. Chiavarelli, G. Settimj, and H. M. Alves, *Gazzetta*, 1957, **87**, 109.
- ¹⁹ E. M. Tchiroukhine, *Ann. Chim. (France)*, 1958, **3**, 405.