Electrochemical Oxidation of Aromatic Ethers. Part 9.[1] Proof of the Mode of Aryl–Aryl Coupling in 4-Benzylisochroman-3-ones, and the Oxidative Reactions of 2-and 3-Aralkyl-1,2,3,4-tetrahydroisoquinolines

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The influence of the solvent upon the coupling reactions of 4-(3,4-dimethoxybenzyl)-6,7-dimethoxyisochroman-3-one has been studied and it is shown that formation of the product, 7a,8-dihydro-3,10,11-trimethoxy-2*H*-phenanthro[9,8a-*b*]furan-2,7(5*H*)-dione, proceeds through a six-membered ring transition state. Anodic oxidation of 2-aralkyl-1,2,3,4-tetrahydroisoquinolines leads to cleavage of the aralkyl substituent, whereas 1,2,3,4-tetrahydro-6,7-dimethoxy-3-(3,4-dimethoxybenzyl)-2-methylisoquinoline cyclises to yield 1,2,3,4-tetrahydro-7,10,11-trimethoxy-3-methyl-2,8a-methanodibenzo[*c,e*]azocin-6-one and its 1-hydroxy derivative.

We have shown recently[2] that anodic oxidation of the 4-benzylisochromanone (**1**; R = Me) affords the γ-lactone (**2**; R = Me). This product may arise in two ways (see Scheme 1): by coupling to C-4a, followed by rearrangement and demethylation (route a), or by coupling to C-8a and migration of the 6'-8a bond (route b). Should the latter sequence operate then it is surprising that none of the δ-lactone (**4**; R = Me) is formed since its production simply requires *O*-demethylation of the intermediate species (**3**; R = Me).

An analogous situation has been encountered with the tetrahydroisoquinoline (**5**),[3] here, however, anodic oxidation in acetonitrile solution yields the neospirodienone (**7**) indicating that the first product of reaction is the six-membered ring cation (**6**) which is equivalent to the species (**3**) above. However, when methanol is added to the electrolysis medium, *O*-demethylation of the cation (**6**) occurs giving the morphinedienone (**8**).

The balance between the two competitive pathways in this latter reaction is changed by the addition of a latent nucleophile, and thus we hoped to effect a similar control over the oxidation of the isochromanone (**1**; R = Me). However, when methanol was added anodic oxidation of our substrate afforded the methoxylated derivative (**11**; Nu = OMe), together with a reduced yield of the γ-lactone (**2**; R = Me). The expected δ-lactone (**4**; R = Me) was not formed.

We consider that the methoxylated isochromanone (**11**; Nu = OMe) arises from the radical cation (**9**) which readily deprotonates to give a radical: further oxidation yields the cation (**10**) and this then reacts with methanol as indicated in Scheme 2. Similar results were obtained when pyridine was added instead of methanol. Here the final product, after aqueous work-up, was the hydroxyisochromanone (**11**; Nu = OH) which is formed by hydrolysis of the pyridinium salt (**11**; Nu = $C_5H_5N^+$). The hydroxyisochromanone (**11**; Nu = OH) was also produced during an electrolysis experiment in which water was deliberately added, together with some of the γ-lactone (**2**; R = Me). However, the main products here were veratraldehyde, veratric acid, and 5,6-dimethoxyisobenzofuran-1(3*H*)-one (**13**).[4]

This last compound was most unexpected and we believe that it is formed by debenzylation of the radical cation (**9**) (or its equivalent), in competition with the deprotonation reaction [(9) ⟶ (10)] already described. This is then followed by oxidative ring contraction, *possibly via* the species (**12**). Evidence in favour of this hypothesis is provided by the fact that the simple isochromanone (**14**) also yields 5,6-dimethoxyisobenzofuran-1(3*H*)-one when it is oxidised in aqueous acetonitrile, whereas in dry acetonitrile it is recovered unchanged. Hence, in the absence of a suitable nucleophile the radical cation derived from the isochromanone (**14**) fails to react further, but in the presence of water deptrotonation occurs to give ultimately the same cation (**15**) as that produced by debenzylation of the 4-benzylisochromanone (**2**; R = Me) (see Scheme 2).

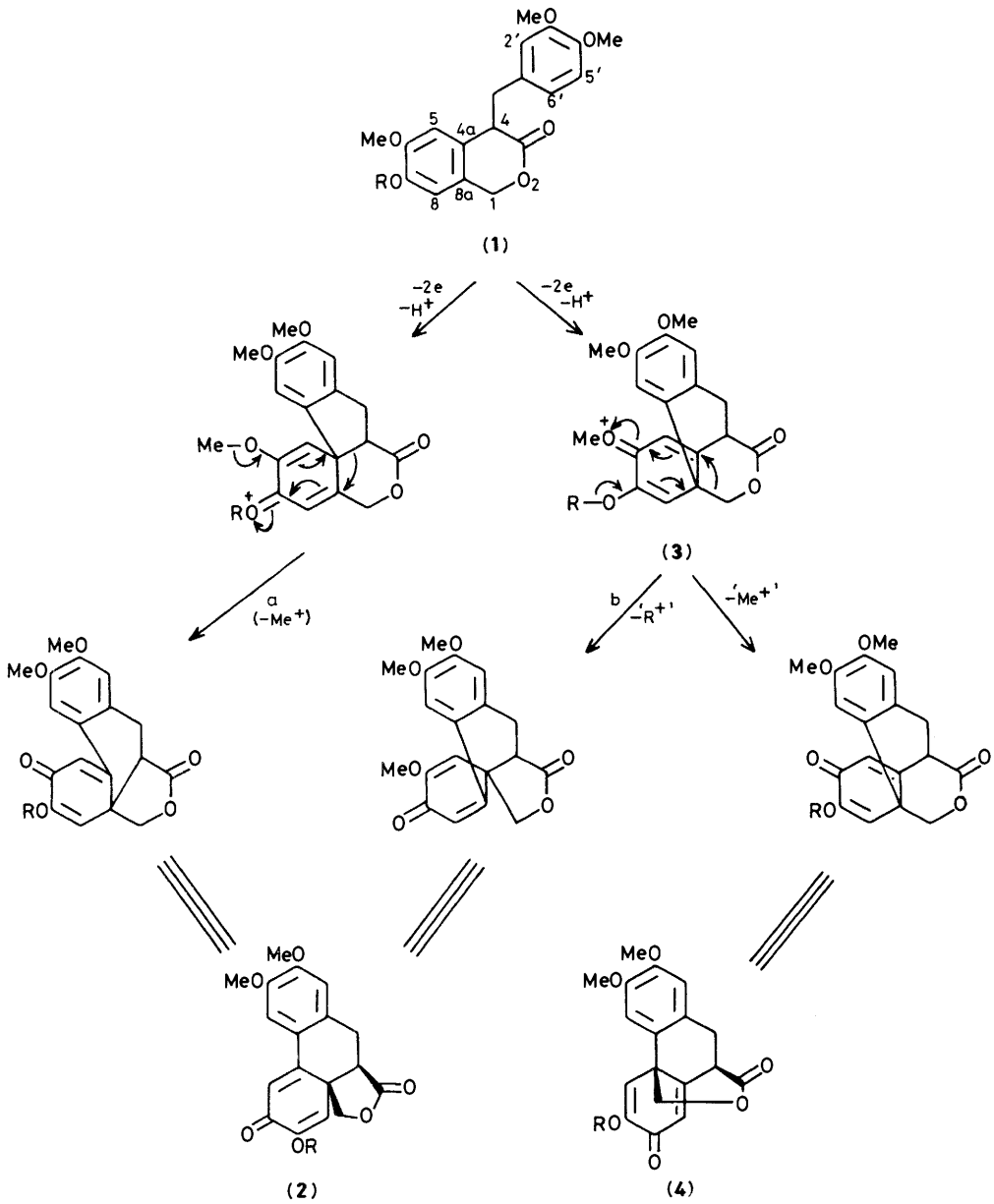
The mother-liquor from which the methoxylated isochromanone (**11**; Nu = OMe) crystallised contained traces of another lactonic product ($\nu_{max.}$ 1 785, 1 660, and 1 645 cm^{-1}). This same compound, shown to have the structure (**16**; X = O), was also formed when the methoxylated isochromanone was oxidised in a separate experiment, and it is clear that it is an over-oxidation product of the methoxylated γ-lactone (**16**; X = H_2) although this compound was not isolated.

This was another unanticipated result, for the ^1H n.m.r. spectrum of the methoxylated isochromanone shows that in order to reduce non-bonded interactions the 4-benzyl substituent of this compound is forced more closely towards C-8a than it is in the parent.

Thus, in the spectrum of the isochromanone (**1**; R = Me) the resonances of the C-1 protons form an AB spin–spin system at δ 4.95 and 4.55 (*J* 15 Hz), but in that of its methoxylated derivative the δ 4.55 doublet is shifted upfield to δ 3.80 (the other half of this pattern is virtually unchanged and resonates at δ 4.93). In addition, the signal due to 8-H, which occurs at δ 6.56 in the spectrum of the parent, is shifted to δ 6.95 in the spectrum of the methoxylated derivative.

These changes may be interpreted as being due to an increased population of the conformer (**17**) when R = OMe. Consequently, we thought that coupling to C-8a would be preferred in the methoxylated derivative and thus a product containing a δ-lactone system might have been favoured. However, the facts that in practice it is not and that the δ-lactone (**4**; R = Me) is not formed from the isochromanone (**1**; R = Me) in the presence of nucleophiles suggested to us that here we were dealing with a rare example of a 5-*endo-trig* electrochemical aryl–aryl coupling reaction,[5] *i.e.* bond formation direct to C-4a.

To establish this hypothesis we next prepared the 7-ethoxyisochromanone (**1**; R = Et) and electrolysed it in acetonitrile solution under standard conditions. The only product isolated was the γ-lactone (**2**; R = Me) (67%), identical in every respect with that obtained from the isochromanone (**1**;



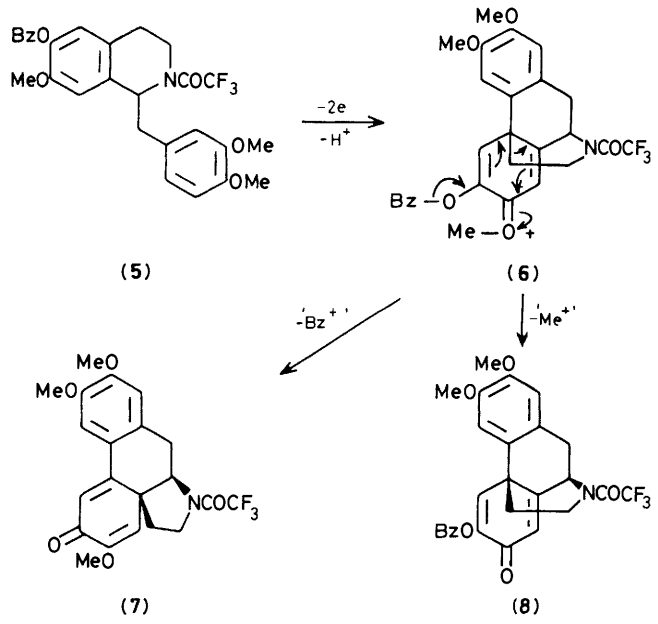
Scheme 1. Alternative coupling pathways for 4-benzylisochroman-3-ones. (R = Me or Et)

R = Me), showing that our initial premise was incorrect since this compound can only arise through direct coupling to C-8a and the operation of route b (Scheme 1).

It is now clear that the coupling reactions of 4-benzylisochromanones and 1-benzyltetrahydroisoquinolines are similar; both take place through six-membered ring forming reactions formally of the 6-*endo-trig* type, but since there is an acidic proton at C-4 in the former group of compounds, the presence of a nucleophile in the electrolysis medium serves to bring about deprotonation (or debenzylation) rather than aryl–aryl coupling. In this event the reaction is diverted at a very early stage so that the addition of reagents such as methanol during the oxidation of isochromanones is inoperative in promoting δ-lactone formation.

Hartenstein *et al.*,[6] have shown that the 3-benzyltetrahydroisoquinoline (**18**)[7] also undergoes cyclisation *via* a six-membered ring-forming process; the products are the tetracycles (**19**; R = H) and (**19**; R = OH). In this case the oxidant used was vandium oxytrifluoride, but since we[2] and others[8] have shown that occasionally the results of coupling reactions using this reagent differ from those which employ electrochemical methods, we considered it necessary to examine the anodic oxidation of the isoquinoline (**18**). In practice, however, the same two compounds were formed and there was no sign of the salt (**20**) which might have been considered as an alternative product.

As a simple means of examining the effect of increasing the length of the side-chain in reactions of this type we have made and electrochemically oxidised the *N*-aralkyltetrahydroisoquinolines (**21**; $n = 1$) and (**21**; $n = 2$). Unfortunately, neither compound afforded ring-coupled products; instead the *N*-substituent was cleaved off. In the case of the lower homologue the products were veratric acid, veratraldehyde, and 6,7-dimethoxy-3,4-dihydroisoquinoline, and with the *N*-phenethyl



derivative, veratric acid, veratraldehyde, and 6,7-dimethoxy-2-methyl-3,4-dihydroisoquinolinium perchlorate (**22**) were obtained.

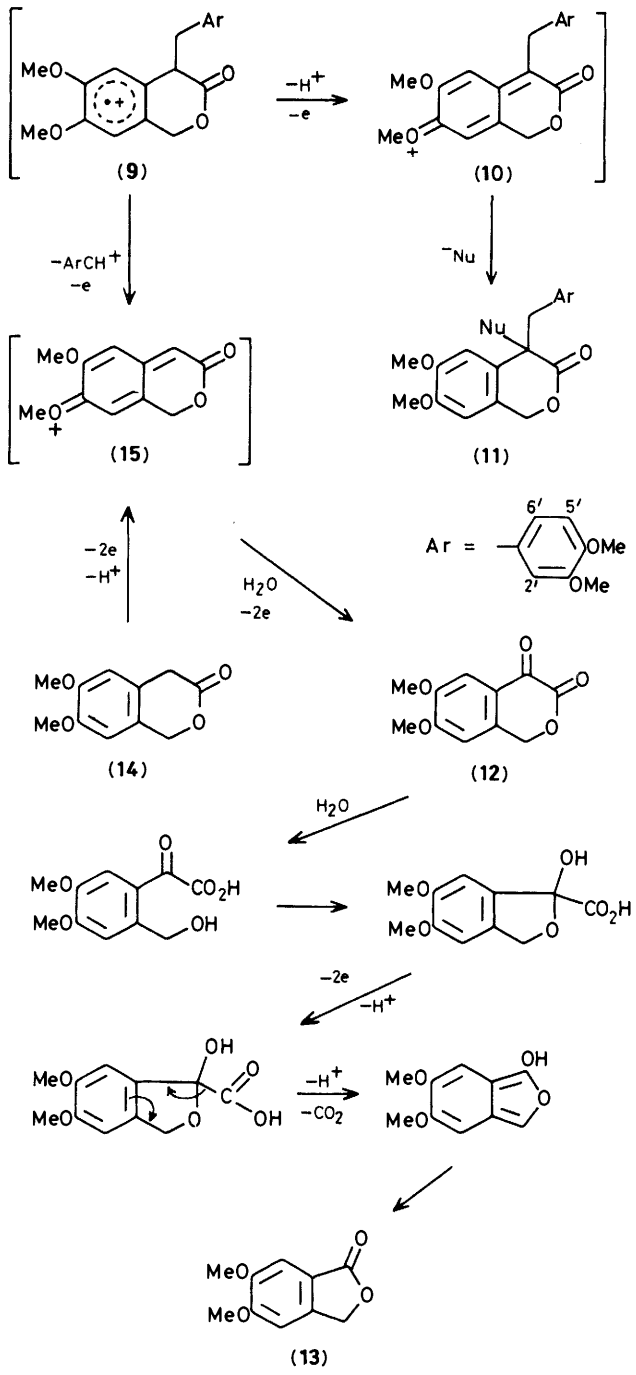
Experimental

U.v. spectra were recorded as solutions in 95% ethanol. I.r. spectra refer to Nujol mulls. ^{1}H N.m.r. spectra were recorded at 100 MHz and at 400 MHz using tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were recorded at 90 MHz. Yields refer to pure samples of products.

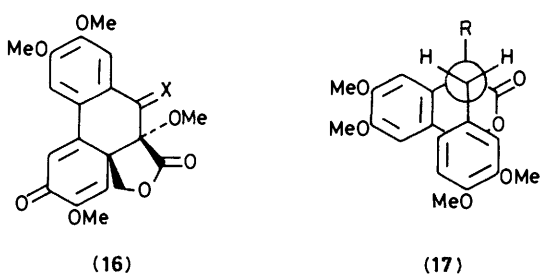
General Electrolysis Procedure.—The substrate (1 g) in the appropriate solvent (150 cm^2) containing sodium perchlorate (3 g) as supporting electrolyte was added to the anode compartment of a H-type cell. Similar amounts of solvent and electrolyte were also added to the cathode compartment. Platinum gauze electrodes were used and the anodic potential monitored by the use of a standard calomel electrode (s.c.e.) *via* an Agar/salt bridge. After the passage of 2 F mol^{-1} of current the contents of the anode compartment were poured into water (20 cm^3) and the mixture evaporated to *ca.* 20 cm^3.

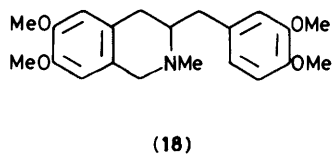
The residue was treated with dichloromethane (50 cm^3), the organic phase washed with water (3 × 10 cm^3), dried (Na_2SO_4), and evaporated. Final purification was achieved by column chromatography on silica eluting with light petroleum (40—60 °C) and ethyl acetate, and then where appropriate by crystallisation–recrystallisation. The products are listed in order of elution from the column.

Oxidation of 4-(3,4-*Dimethoxybenzyl*)-6,7-*dimethoxyisochroman*-3-*one* (**1**; R = Me).—(i) In acetonitrile–methanol (1:1) at an anode potential of +1.15 V the following products were obtained: (a) 7a,8-dihydro-3,10,11-trimethoxy-2*H*-phenanthro-[9,8a-*b*]furan-2,7(5*H*)-dione (**2**; R = Me) (0.078 g, 8%), m.p. 256—267 °C (lit.,[2] 256—257 °C); (b) 4,6,7-*trimethoxy*-4-(3,4-*dimethoxybenzyl*)*isochroman*-3-*one* (**11**; Nu = OMe) (0.27 g, 25%, m.p. 137 °C; $\nu_{max.}$ 1 735 cm^{-1}; *m/z* (%) 388 (M^+, 4), 237 (71), and 151 (100); δ_H($CDCl_3$) 6.95 (s, 1 H, 8-H), 6.80 (d, 1 H, *J* 8 Hz, 5′-H), 6.44 (d, d, 1 H, *J* 8, 2 Hz, 6′-H), 6.42 (s, 1 H, 5-H), 6.14 (d, 1 *H*, *J* 2 Hz, 2′-H), 4.93, 3.80 (AM system, 2 H, *J* 15 Hz, 1-H_2), 3.92, 3.88, 3.84, 3.60 (4 × s, 12 H, 4 × ArOCH_3), 3.40, 3.04 (AB system, 2 H, *J* 7 Hz, Ar-CH_2), and 3.22 (s, 3 H, 4-OCH_3);



Scheme 2. Anodic oxidation of the 4-benzylisochromanones in the presence of nucleophiles





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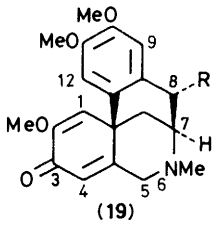

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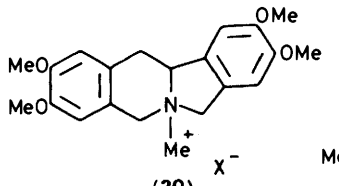

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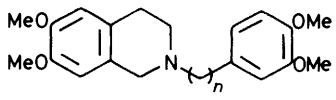

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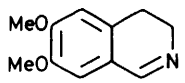

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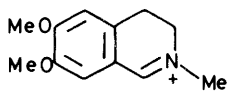

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Oxidation of 6,7-*Dimethoxyisochroman*-3-*one* (**14**).—In acetonitrile–water (10:1) with an anode potential of +1.1 V, the product 5,6-dimethoxyisobenzofuran-1(3*H*)-one (61%) was obtained.

Oxidation of 4,6,7-*Trimethoxy*-4-(3,4-*dimethoxybenzyl*)*isochroman*-3-*one* (**11**; Nu = OMe).—In acetonitrile with an anode potential of +1.15 V the product 7a,8-*dihydro*-3,7a,10,11-*tetramethoxy*-2H-*phenanthro*[9,8a-b]*furan*-2,7,8-*trione* (**16**; X = O) (67%) was obtained, m.p. *ca.* 232 °C (decomp); $\nu_{max.}$ 1 785, 1 660, 1 645, and 1 610 cm^{-1} $\lambda_{max.}$ 255, 296, and 365 nm; *m*/*z* (%) 386 (M^+, 58), 355 (46), and 327 (100); $\delta_H(CDCl_3)$ 7.62 (s, 1 H, 9-H), 7.26 (s, 1 H, 12-H), 7.11 (s, 1 H, 1-H), 6.08 (s, 1 H, 4-H), 4.20 (s, 2 H, 5-H_2), 4.03 (s, 3 H, 11-OCH_3), 4.01 (s, 3 H, 10-OCH_3), 3.81 (s, 3 H, 3-OCH_3), and 3.34 (s, 3 H, 7a-OCH_3); n.O.e. experiments: irrad. at δ 4.01, enhancements at δ 7.62 (7.2%) and 4.03 (16.3%); irrad. at δ 4.03, enhancements at δ 4.01 (15.7%) and 7.26 (5%); irrad. at δ 7.26, enhancement at δ 7.11 (5%); irrad. at δ 3.81, enhancements at δ 6.08 (6%) and 3.34 (10%). (This spectrum and the n.O.e. experiments were recorded at 400 MHz.) (Found: C, 62.1; H, 4.6. $C_{20}H_{18}O_8$ requires C, 62.2; H, 4.7%).

Oxidation of 7-*Ethoxy*-6-*methoxy*-4-(3,4-*dimethoxybenzyl*)-*isochroman*-3-*one* (**1**; R = Et).—In acetonitrile with an anode potential of +1.1 V, the product 7a,8-dihydro-3,10,11-trimethoxy-2*H*-phenanthro[9,8a-*b*]furan-2,7(5*H*)-dione (**2**; R = Me) (67%), was obtained, m.p. 256—257 °C, identical with the sample previously obtained from the isochromanone (**1**; R = Me).

$\delta_C(CDCl_3)$ 170.9 (s, CO), 150.0, 149.5, 148.4, 148.3 (4 s, C-7, C-6, C-4′, C-3′), 125.8 (s, C-1′), 125.1 (d, C-6′), 124.6 (d, C-8), 122.8 (s, C-8a), 113.5 (s, C-4a), 110.8, 108.2, 105.6 (3 × d, C-5, C-5′, C-2′), 80.7 (s, C-4), 69.1 (5, C-1), 56.3, 56.1, 55.8 (5 × q, 5 × OCH_3), and 48.4 p.p.m. (t, ArCH_2) (Found: C, 64.85; H, 6.1. $C_{21}H_{24}O_7$ requires C, 64.9; H, 6.2%).

(ii) In acetonitrile–pyridine (10:1) with an anode potential of +0.9—1.0 V, the following products were obtained: (a) 3,4-dimethoxybenzaldehyde (10%), m.p. and mixed m.p. 42—45 °C (comparison with commercially available sample); (b) 4-*hydroxy*-6,7-*dimethoxy*-4-(3,4-*dimethoxybenzyl*)*isochroman*-3-*one* (**11**; Nu = OH) (25%), m.p. 148—150 °C; $\nu_{max.}$ 3 490, 1 740, 1 615, and 1 600 cm^{-1}; $\lambda_{max.}$ 225sh and 276 nm; *m*/*z* (%) 357 (M^+ − 18, 11), 223 (M^+ − 151, 23), and 151 (100); $\delta_H(CDCl_3)$ 6.98 (s, 1 H, 8-H), 6.65 (1 H, d, *J* 8 Hz, 5′-H), 6.43 (1 H, dd, *J* 8 Hz, *J* 2 Hz, 6′-H), 6.45 (1 H, s, 5-H), 6.26 (1 H, d, *J* 2 Hz, 2′-H), 3.82 (s, 9 H, 3 × OCH_3), 3.64 (s, 3 H, OCH_3), and 3.20 (s, 2 H, CH_2Ar); $\delta_C(CDCl_3)$ 177.2 (s, 3-C), 148.6, 148.4, 147.8, 147.6 (4 × s, C-3′, C-4′, C-6, C-7), 128.0 (s, C-1′), 126.3 (s, C-8a), 122.5 (d, C-6′), 121.7 (s, C-4a), 113.7, 111.0, 108.2, 106.5 (4 × d, C-2′, C-5, C-5′, C-8), 73.7 (s, C-4), 69.9 (t, C-1), 56.1, 55.8 (4q, 4 × OCH_3), and 47.2 p.p.m. (t, ArCH_2) (Found: C, 64.1; H, 6.0. $C_{20}H_{22}O_7$ requires C, 64.2; H, 5.9%).

(iii) In acetonitrile–water (10:1) with an anode potential of +1.1 V, the following products were obtained: (a) γ-lactone (**2**; R = Me)[2] (8%), (b) 3,4-dimethoxybenzaldehyde (6%); and (c) 5,6-dimethoxyisobenzofuran-1(3*H*)-one (**13**) (12%), m.p. 154—156 °C (lit.,[4] m.p. 154—156 °C); $\nu_{max.}$ 1 756 and 1 600 cm^{-1}; $\lambda_{max.}$ 250, 285, and 295sh nm; *m*/*z* (%) 194 (M^+, 10), 165 (100); $\delta_H(CDCl_3)$ 7.28 (s, 1 H, 7-H), 6.92 (s, 1 H, 4-H), 5.20 (s, 2 H, 1-H_2), and 3.94, 3.85 (2 × s, 6 H, 2 × OCH_3); $\delta_C(CDCl_3)$ 171.5 (s, C-1), 155.0, 150.5 (2 × s, C-5, C-6), 141.2, 141.1 (2 × s C-3a, C-7a), 106.2, 103.6 (2 × d, C-4, C-7), 69.2 (t, C-3), and 56.4, 56.3 p.p.m. (2 × q, 2 × OCH_3) (Found: C, 61.7; H, 5.4. Calc. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.2%).

Oxidation of 1,2,3,4-*Tetrahydro*-6,7-*dimethoxy*-3-(3,4-*dimethoxybenzyl*)-2-*methylisoquinoline* (**18**).[7]—In acetonitrile with an anode potential of +1.1 V, the following products were obtained: (a) 5,6,7,8-tetrahydro-2,10,11-trimethoxy-6-methyl-7,12b-methanodibenz[*c*,*e*]azocin-3-one (**19**; R = H) (65%), m.p. and mixed m.p. 168.5—170 °C (methanol) (lit.,[8] 168.5—170 °C); (b) 5,6,7,8-tetrahydro-8-hydroxy-2,10,11-trimethoxy-6-methyl-7,12b-methanodibenz[*c*,*e*]azocin-6-one (**19**; R = OH) 5%), m.p. 187—188 °C (lit.,[8] 188—189 °C).

Oxidation of 1,2,3,4-*Tetrahydro*-6,7-*dimethoxy*-2-(3,4-*dimethoxybenzyl*)*isoquinoline* (**20**; *n* = 1).—In acetonitrile with an anode potential of +0.95 −1.1 V the following products were obtained: (a) 3,4-dimethoxybenzaldehyde (isolated as an oil) (10%); (b) 3,4-dimethoxybenzoic acid (8%), m.p. and mixed m.p. 179—182 °C; and (c) 3,4-dihydro-6,7-dimethoxyisoquinoline (**21**) (16%) (isolated as an oil), *m*/*z* (%) 191 (M^+, 8) and 189 (100). This product was shown to be identical with an authentic sample prepared by the method of Späth and Polgar.[9]

Oxidation of 1,2,3,4-*Tetrahydro*-6,7-*dimethoxy*-2-(3,4-*dimethoxyphenethyl*)*isoquinoline* (**20**; *n* = 2).—In acetonitrile with an anode potential of +1.0—1.1 V, the following products were obtained: (a) 3,4-dimethoxybenzaldehyde (15%); (b) 3,4-dimethoxybenzoic acid (4%); (c) 3,4-dihydro-6,7-dimethoxy-2-methylisoquinolinium perchlorate (**22**), which was not isolated as such but converted into 1,2,3,4-tetrahydro-6,7-dimethoxy-2-methylisoquinoline by reduction with sodium borohydride in aqueous acetonitrile–ethanol solution. After treatment with warm dilute hydrochloric acid and basification, removal of the solvents gave the tetrahydroisoquinoline as a pale brown oil (overall yield 18%). This compound was authenticated by comparison with a sample of 1,2,3,4-tetrahydro-6,7-dimethoxy-2-methylisoquinoline prepared from 3,4-dihydro-6,7-dimethoxyisoquino-

line (**21**) by *N*-methylation with methyl iodide and reduction of the product with sodium borohydride. This product was also obtained as an oil, but slowly crystallised on standing, m.p. 82—84 °C (lit.,[10] 83—84 °C).

4-*Ethoxy*-3-*methoxyphenylacetic Acid*.—Tetraethyl dimethylaminomethylenediphosphonate (2 g) was prepared according to the method of Gross and Costisella.[11] This reagent was dissolved in dry dioxane (5 cm^3) and added dropwise to a suspension of sodium hydride (0.16 g) in dioxane (5 cm^3). When the liberation of hydrogen had subsided (*ca.* 2 h), 4-ethoxy-3-methoxybenzaldehyde[12] (1 g) in dioxane (5 cm^3) was added and the reaction mixture heated at 80 °C for 2—3 h. It was then cooled and poured into water (50 cm^3) and extracted with diethyl ether (3 × 25 cm^3). The combined extracts were then evaporated to leave an oil; this was heated on a water-bath with conc. hydrochloric acid (5 cm^3) for 20—25 min, and the reaction mixture was then allowed to cool, diluted with water (15 cm^3), and extracted with chloroform (3 × 10 cm^3). The combined and dried extracts were then evaporated to give the title acid as colourless prisms (0.4 g, 36%) (recrystallised from water), m.p. 156—157 °C (lit.,[13] 158 °C); $\delta_H(CDCl_3)$ 6.70 (s, 3 H, 2-H, 5-H, 6-H), 4.21 (q, 2 H, *J* 7 Hz, CH_3CH_2O), 3.85 (s, 3 H, CH_3O), 3.55 (s, 2 H, $ArCH_2$), and 1.55 (t, 3 H, *J* 7 Hz, CH_2CH_2O) (Found: C, 62.6; H, 6.75. Calc. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.7%).

7-*Ethoxy*-6-*methoxyisochroman*-3-*one*.—4-Ethoxy-3-methoxyphenylacetic acid (1 g) in glacial acetic acid (3 cm^3) was heated to 60 °C, and conc. hydrochloric acid (0.8 cm^3) followed by 37% formaldehyde in water (0.8 cm^3) were added. The solution was then heated on a water-bath for 1.25 h and left to cool with stirring for 4 days. After this time it was poured into water (50 cm^3) and extracted with chloroform (3 × 25 cm^3). The combined extracts were washed with 10% sodium carbonate solution (2 × 10 cm^3), dried and evaporated to give the *title compound* (0.86 g, 82%), m.p. 106—107 °C; $\nu_{max.}$ 1 740 cm^{-1}; $\delta_H(CDCl_3)$ 6.66, 6.62 (2s, 2 × 1 H, 5-H, 8-H), 5.15 (s, 2 H, 1-H_2), 4.01 (q, 2 H, *J* 7.5 Hz, OCH_2CH_3), 3.80 (s, 3 H, OCH_3), 3.55 (s, 2 H, 4-H_2), and 1.4 (t, 3 H, *J* 7.5 Hz, OCH_2CH_3); *m/z* 222 (M^+, 100%) (Found: C, 64.7; H, 6.3. $C_{12}H_{14}O_4$ requires C, 64.85; H, 6.35%).

7-*Ethoxy*-6-*methoxy*-(3,4-*dimethoxybenzylidene*)*isochroman*-3-*one*.—7-Ethoxy-6-methoxyisochroman-3-one (0.5 g), 3,4-dimethoxybenzaldehyde (0.4 g), and pyrrolidine (0.1 cm^3) were heated together at 140 °C for 2.5 h under nitrogen. When cool the reaction mixture was dissolved in 1:1 glacial acetic acid and methanol (5 cm^3) and added to the top of a silica gel column. Elution with chloroform gave the title compound as a gum which slowly crystallised and was recrystallised from methanol to give pale yellow *prisms* (0.5 g, 60%), m.p. 168—170 °C; $\nu_{max.}$ 1 710, 1 602, and 1 598 cm^{-1}; $\lambda_{max.}$ 245sh, 375 cm^{-1}; *m/z* (%) 370 (M^+, 100) 341 (15); $\delta_H(CDCl_3)$ 7.62 (s, 1 H, =C*H*Ar), 7.10—6.68 (m, 5 H, ArH), 5.19 (s, 2 H, 1-H_2), 4.02 (q, 2 H, *J* 7.5 Hz, OCH_2CH_3), 3.85, 3.70, 3.50 (3 × s, 9 H, 3 × OCH_3), and 1.45 (t, 3 H, *J* 7.5 Hz, OCH_2CH_3) (Found: C, 68.0; H, 5.9. $C_{21}H_{22}O_6$ requires C, 68.1; H, 6.0%).

7-*Ethoxy*-6-*methoxy*-4-(3,4-*dimethoxybenzyl*)*isochroman*-3-*one* (**1**; R = Et).—7-Ethoxy-6-methoxy-4-(3,4-dimethoxybenzylidene)isochroman-3-one (2 g) in ethyl acetate (150 cm^3) was hydrogenated at 60 lb cm^{-2}) over a platinum oxide catalyst (0.17 g). After 10 h, the solvent and catalyst were removed to give the title compound as an oil which slowly crystallised. Recrystallisation from ethanol gave a colourless *solid* (0.98 g, 47%), m.p. 113—115 °C; $\nu_{max.}$ 1 740 and 1 615 cm^{-1}; $\lambda_{max.}$ 235 and 283 nm; *m/z* (%) 372 (M^+, 5), 151 (100); $\delta_H(CDCl_3)$ 6.80—6.35 (m, 5 H, ArH), 4.75 (q, 2 H, *J* 15 Hz, 1-H_2), 4.12 (q, 2 H, *J* 7 Hz, OCH_2CH_3), 3.80, 3.68, 3.60 (3 × s, 9 H, 3 × OCH_3), *ca.* 3.7 (t, 1 H, 4-H), 3.20 (d, 2 H, *J* 5 Hz, CH_2Ar), and 1.51 (t, 3 H, *J* 7 Hz, OCH_2CH_3) (Found: C, 67.6; H, 6.3. $C_{21}H_{24}O_6$ requires C, 67.7; H, 6.5%).

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