Anodic Oxidation of 1,2,3,4-Tetrahydronaphthalene and Isochroman Analogues of 1-Benzyl- and 1-Phenethylisoquinoline Alkaloids. Products and Mechanism of the Intramolecular Cyclization

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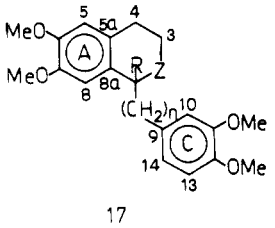
The anodic oxidation of 1-(3′,4′-dimethoxybenzyl)-6,7-dimethoxy- (**17a**), 1-(3′,4′-dimethoxybenzyl)-1-methyl-6,7-dimethoxy- (**17b**), and 1-(3′,4′-dimethoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (**17e**), and 1-(3′,4′-dimethoxybenzyl)- (**17c**) and 1-(3′,4′-dimethoxybenzyl)-1-methylisochroman (**17d**) was studied by preparative electrolyses, cyclic voltammetry, and second harmonic ac measurements. With **17a,b**, three different intramolecular coupling reactions were observed. The major reaction involved coupling between C-5a and C-14 leading, after demethylation, to a dienone of structure **18**. The other cyclization reactions involved coupling between C-8a and C-14 with formation of an isomeric dienone (**19**) and coupling between C-4 and C-14 with formation of a 2,3:6,7-bis(4′,5′-dimethoxybenzo)bicyclo[3.2.2]nonane derivative (**21**). For **17e** the only reaction was coupling between C-8a and C-14 leading to the dienone **19c**. With **17c–d** there was intramolecular coupling between C-5a and C-14 giving the dienones **18c,d** and between the heteroatom and C-14 giving, after hydrolysis, the hydroxylated compounds **24a,b**. Second harmonic ac measurements indicated that all coupling reactions involved a very fast initial ECE reaction leading to a relatively stable cationic intermediate. The products observed can be rationalized readily in terms of known rearrangements and substitution reactions of these cations.

The intramolecular, oxidative coupling of phenols[1–3] and phenol ethers[4–15] of structures **1** or **2** has been studied in great detail (see Schemes I and II). As can be seen, a wide variety of products are formed depending on solvent, oxidant, and substitution pattern. In order to determine the importance of the heteroatom Z in structure **2** (Scheme II) for the intramolecular coupling reaction and to find out whether or not ring B (structure **2**) puts any steric restrictions on the cyclization reaction as compared to structure **1** we decided to investigate the carbon and oxygen analogues, **17a–e**, of compounds **2a–d**. The compounds **17b** and **17e** were included in this study in order to determine the reactivity of the benzylic position (C-1 in formula **17**).



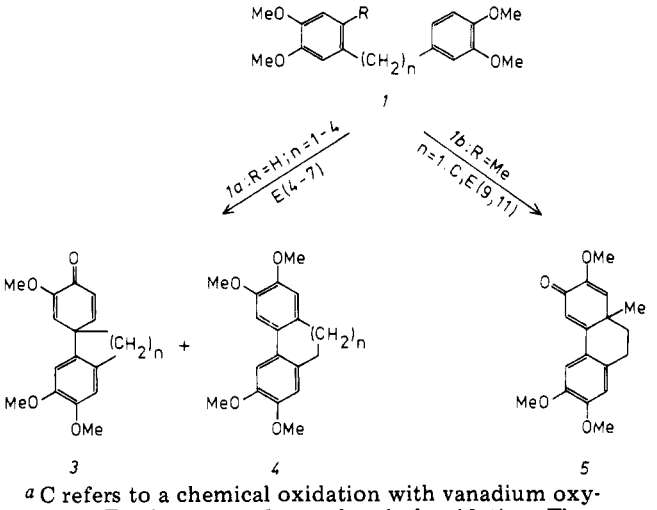
17

a: Z = CH_2; R = H; n = 1
b: Z = CH_2; R = Me; n = 1
c: Z = O; R = H; n = 1
d: Z = O; R = Me; n = 1
e: Z = CH_2; R = H; n = 2

Results

The results of the preparative experiments are given in Table I. The syntheses of the starting compounds **17a–e** are outlined in Scheme III. The identity of the electrolysis products **18–28** was established by spectroscopic methods. In the electrolysis of **17a** three different dienones were isolated. Dienones obtained by coupling between positions 5 or 8 and 9 (formula **17**) can be ruled out as none of the dienones isolated showed the required AB quartet (protons 13 and 14) in their NMR spectra. Furthermore, the protons of ring C always appear as two singlets in the spectra of the coupled products, showing that ring C always couples at carbon 14 (formula **17**).

Scheme I[a]



[a] C refers to a chemical oxidation with vanadium oxyfluoride. E refers to an electrochemical oxidation. The numbers in parentheses are literature references.

Only two different dienones can be formed by *direct* coupling, namely **18** (coupling between positions 5a and 14 in structure **17**) and **19** (coupling between positions 8a and 14). However, it has been shown[11,15] that intermediates giving dienones of structure **19** (Z = NCHO or Z = O) undergo acid-catalyzed rearrangement followed by demethylation to the dienones **20** and **20b**. It therefore seems reasonable to assume that the three dienones obtained by electrolysis of **17a** are **18a**, **19a**, and **20a**, an assumption which is supported by all spectroscopic data. Definite assignment of structure was achieved by analysis of the NMR data, in particular the signals from the protons on carbons 9 and 13 (14) (structures **18–20**). In compound **18a** H-9 is allylic and the two H-13 are aliphatic, in **19a** H-9 is aliphatic whereas the two H-13 are allylic, and in **20a** both H-9 and the two H-13 are aliphatic (see Experimental Section for detailed assignments of NMR peaks). The structures of the other dienones were established in a similar way by comparison of NMR and IR data with those of compounds **18a–20a**.

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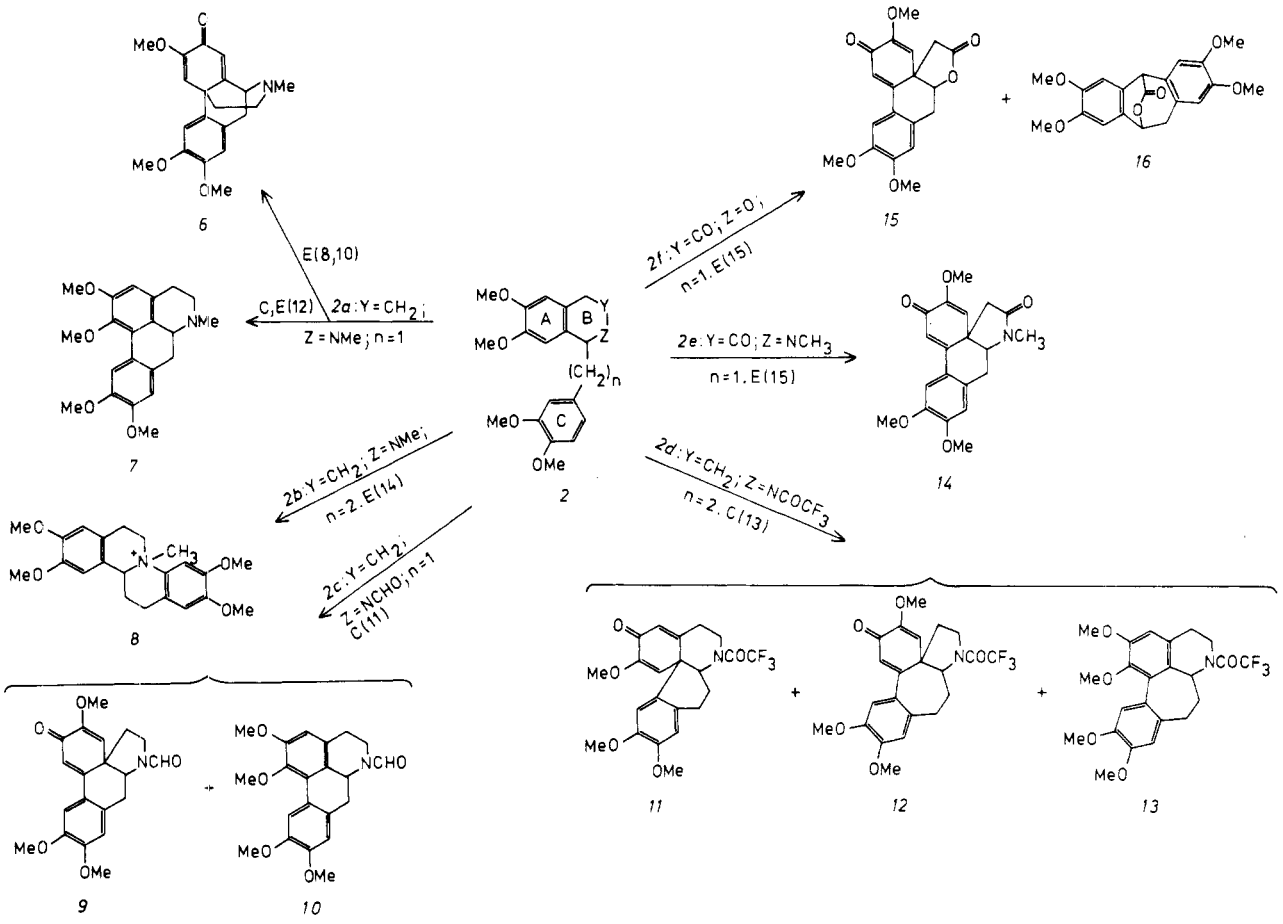
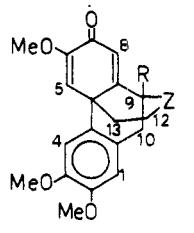
Scheme II[a]

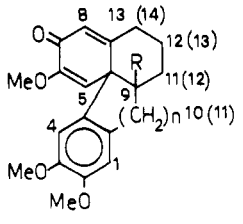


[a] C refers to a chemical oxidation with vanadium oxyfluoride in TFA. E refers to an electrochemical oxidation. The numbers in brackets are literature references.



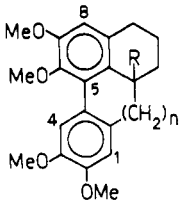
18

a: Z=CH2; R=H
b: Z=CH2; R=Me
c: Z=O; R=H
d: Z=O; R=Me

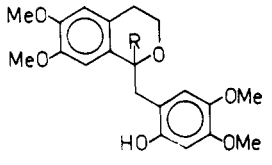


19

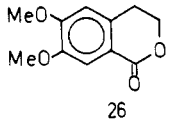
a: R=H; n=1
b: R=Me; n=1
c: R=H; n=2



23 a: R=H; n=1
b: R=Me; n=1
c: R=H; n=2



24 a: R=H
b: R=Me



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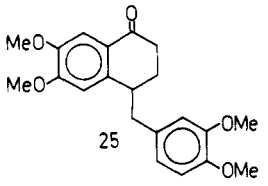

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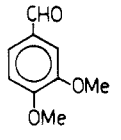

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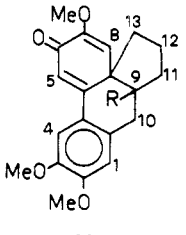
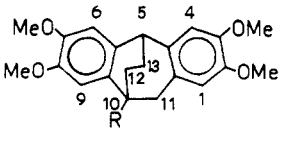


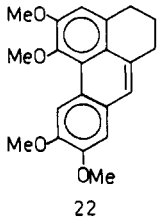
20

a: R=H
b: R=Me

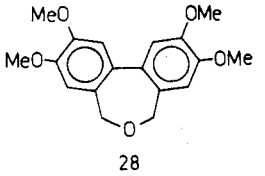


21

a: R=H
b: R=Me



22



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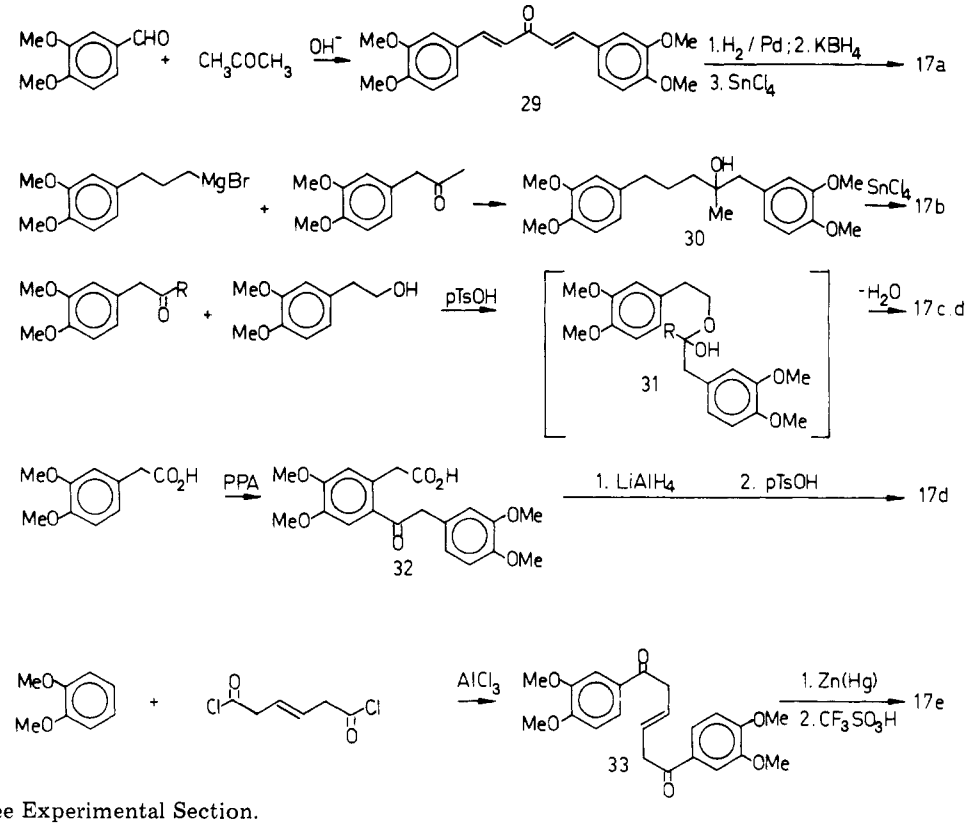
Scheme III. Syntheses of 17a–e[a]



[a] For details see Experimental Section.

Table I. Preparative Anodic Oxidations of Compounds 17a–e[a]

entry	compd	electrolyte	temp, °C	E, V[b]	C, %[c]	products (yield, %)[d]
1	**17a**	MeCN, $LiBF_4$[e]	−35	0.85	93	**18a** (33); **19a** (29); **20a** (6); **21a** (>0)
2	**17a**	MeCN, HBF_4[f]	−35	0.85	100	**18a** (48); **20a** (6); **21a** (>0)
3	**17a**	MeCN, H_2SO_4, H_2O[g]	−35	0.85	95	**18a** (30); **19a** (11); **20a** (3); **21a** (>0)
4	**17a**	EtCN, $LiBF_4$[e]	−81	0.85	100	**18a** (41); **19a** (21); **20a** (2); **21a** (13)
5	**17a**	MeOH, K_2CO_3	+10	1.2	30	**25** (62)
6	**17a**	DCM–TFA, Bu_4NBF_4[h]	0	0.90	74	**22** (13)
7	**17b**	MeCN, Me_4NBF_4[i]	+10	1.1	70	**18b** (34)
8	**17b**	DCM–TFA, Bu_4NBF_4[h]	+10	0.90	65	**23b** (45)
9	**17b**	MeCN, HBF_4[f]	−35	0.85	92	**18b** (71); **20b** (3); **21b** (>0)
10	**17b**	MeCN, $LiBF_4$[e]	−35	0.85	100	**18b** (33); **19b** (28); **20b** (9); **21b** (>0)
11	**17c**	MeCN, HBF_4[f]	−35	1.35	79	**18c** (26); **24a** (49); **26** (19); **27** (>0); **28** (3)
12	**17c**	MeCN, $LiBF_4$[e]	−35	1.00	76	**24a** (34); **26** (>0)
13	**17c**	MeCN, HBF_4[f]	−35	0.80	79	**18c** (16); **24a** (64); **26** (18)
14	**17c**	MeCN, H_2O, $LiBF_4$[i]	−35	0.90	67	**18c** (13); **24a** (28); **26** (6)
15	**17d**	MeCN, HBF_4[f]	−35	1.00	66	**18d** (56); **24b** (26); **26** (18)
16	**17d**	MeCN, $LiBF_4$[e]	−35	1.00	80	**24b** (49); **26** (14)
17	**17d**	MeCN, H_2O, $LiBF_4$[i]	−35	1.00	75	**18d** (35); **24b** (33); **26** (13)
18	**17e**	MeCN, HBF_4[f]	−35	0.85	100	**19c** (79)
19	**17e**	DCM–TFA, Bu_4NBF_4[h]	−22	1.00	100	**23e** (69)
20	**17e**	MeCN, $LiBF_4$[e]	+10	0.85	100	**19c** (72)

[a] The electrolyses were carried out under nitrogen in a one-compartment cell at controlled potential with platinum as anode. In all experiments 1.5 mmol of the substrate was dissolved in 60 mL of electrolyte. The amount of current, Q, passed through the cell was 3 faradays/mol in experiment 6. In all other experiments Q = 2 faradays/mol. At first the electrolyses of **17a** were carried out at 10 °C. However, at this temperature the conversion after 2 faradays/mol was very low and no product could be isolated. [b] The anode potential, E, was measured relative to a saturated calomel electrode (SCE) in experiments 5 and 7. In all the other experiments the reference was Ag/Ag^+. The SCE potential can be converted to the (Ag/Ag^+) potential by subtraction of 0.0 V. [c] The conversion, C, is calculated from the amount of unchanged starting material *isolated* after workup. [d] The yields are based on converted starting material. The usual chemical yield based on total amount of starting material is obtained by multiplication of the yield with the conversion. [e] 0.5 g of $LiBF_4$ in 60 mL of acetonitrile (MeCN). [f] 2 mL of 35% aqueous HBF_4 in 60 mL of MeCN. [g] 0.5 mL of concentrated H_2SO_4 and 1.5 mL of H_2O in 60 mL of MeCN. [h] 60 mL of 5:1 dichloromethane (DCM)–trifluoroacetic acid (TFA) and 0.5 g of *n*-Bu_4NBF_4. [i] 2 mL of H_2O and 0.5 g of $LiBF_4$ in 60 mL of MeCN.

Voltammetry Results. Voltammetric data were obtained for the oxidation of compounds **17a, 17c, 17d,** and **17e** and also for all the products from the preparative scale electrolyses. The data in Table II were derived from results of cyclic voltammetry as well as fundamental and second harmonic ac measurements. A typical[23] cyclic voltammogram is that shown in Figure 1 from the oxidation of **17d.** The oxidation is an initial two-electron process which shows no indication of re-

Table II. Voltammetric Data for the Oxidation of Compounds 17a and 17c,d and the Products Obtained on Electrolysis of These Compounds[a]

substrate/ electrolysis products	E_{rev}, V[b]	substrate/ electrolysis products	E_{rev}, V[b]
17a	0.800; 0.930; 1.050; 1.185	**17c**	0.915; 1.200
18a	0.955	**18c**	0.955
19a	0.970	**24a**	0.90 (irreversible)
21a	0.795; 0.920	**17d**	0.885; 1.205
22	0.595	**18d**	1.000
25	0.855		
17e	0.790; 1.065		
19c	0.905		
23c	0.855		

[a] See Table I. [b] Estimated reversible potentials from second harmonic measurements relative to an Ag/Ag^+–acetonitrile reference electrode in acetonitrile containing n-Bu_4NBF_4 (0.2 M). These values can be converted to the saturated calomel reference scale by adding 0.345 V.

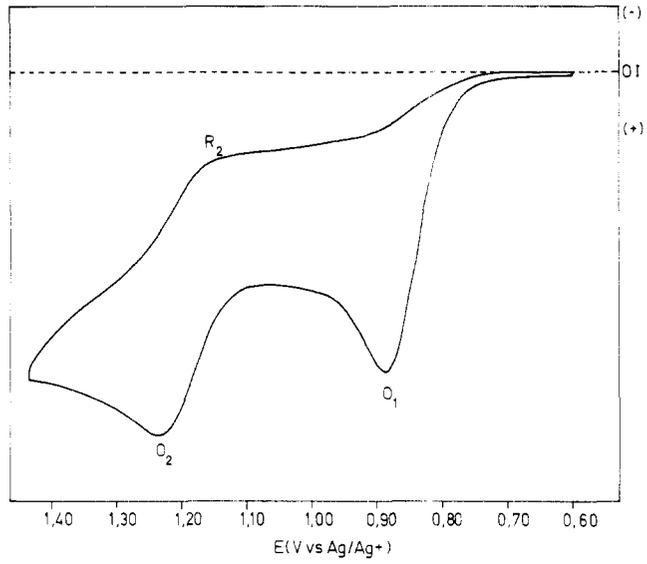


Figure 1. Cyclic voltammogram for the oxidation of **17d** in acetonitrile containing n-Bu_4NBF_4 (0.2 M). Voltage sweep rate 50 mV s^{-1}. Ag/Ag^+ reference electrode.

versibility even at scan rates as high as 1000 V s^{-1} and a second quasireversible one-electron process at a potential about 300 mV more positive. The initial two-electron process is probably of the ECE[24] type, since the second harmonic ac voltammograms were those expected for a reversible one-electron transfer, i.e., about 68 mV peak to peak separation.[16]

The quasireversible redox couple O_2–R_2 (Figure 1) also involves a one-electron transfer, since the peak-to-peak separation in the second harmonic ac voltammogram was found to be close to 68 mV. The potentials for the quasireversible couples, O_2–R_2, for the reactive intermediates from oxidation of **17a–e** were in all cases substantially greater than those of any of the products isolated from preparative electrolysis (see Table II). The major products were the corresponding dienones (structures **18–20**), which are oxidized at a potential approximately 100 mV more positive than for the substrates. The more positive potential associated with the oxidation of the reactive intermediates can thus be explained by assuming that they are positively charged. It is well known that cations derived from aromatic compounds are oxidized at more positive potentials than the substrates, usually 300 mV or more.[17,18]

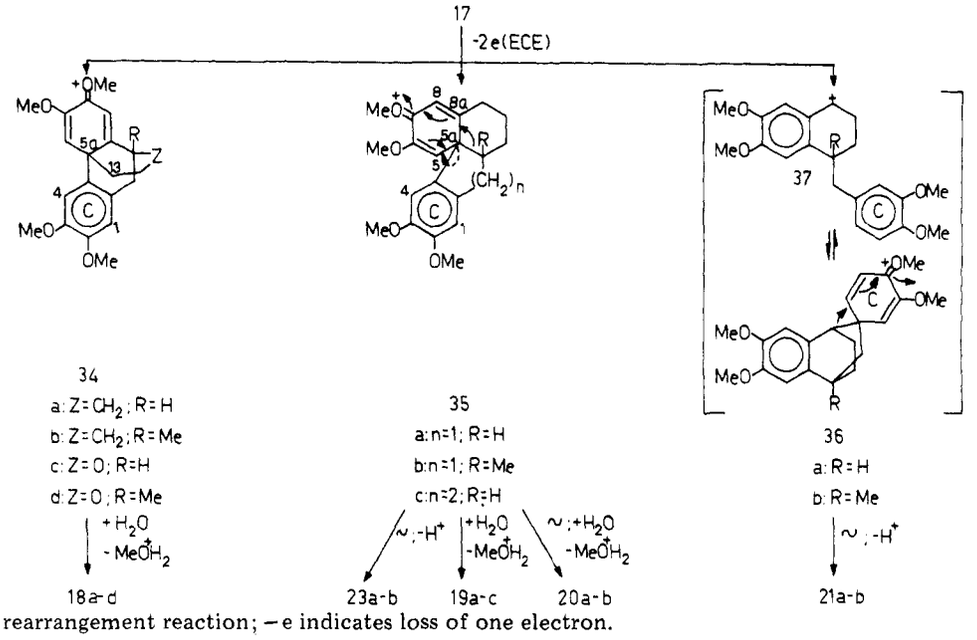
The voltammetric behavior and the product distribution from preparative electrolysis of compound **17a** was found to be considerably more complicated than that from the other substrates. The voltammograms indicated that the initial two-electron ECE process produces three different intermediates with reversible potentials more positive than the substrate (Table II). None of the oxidation potentials of the products correspond to those observed during the voltammetric study of the oxidation of the substrate. It is thus quite likely that in this case there are three different ECE processes taking place and producing three different cationic intermediates, which then react further to give the various products.

Coulometry. Coulometric oxidations[2] of 1 mM solutions of compounds **17b–e** either in $MeCN/LiClO_4$ or $MeCN/HBF_4$ gave n values close to 2. Compound **17a** invariably gave coulometric n values higher than 2.

Discussion

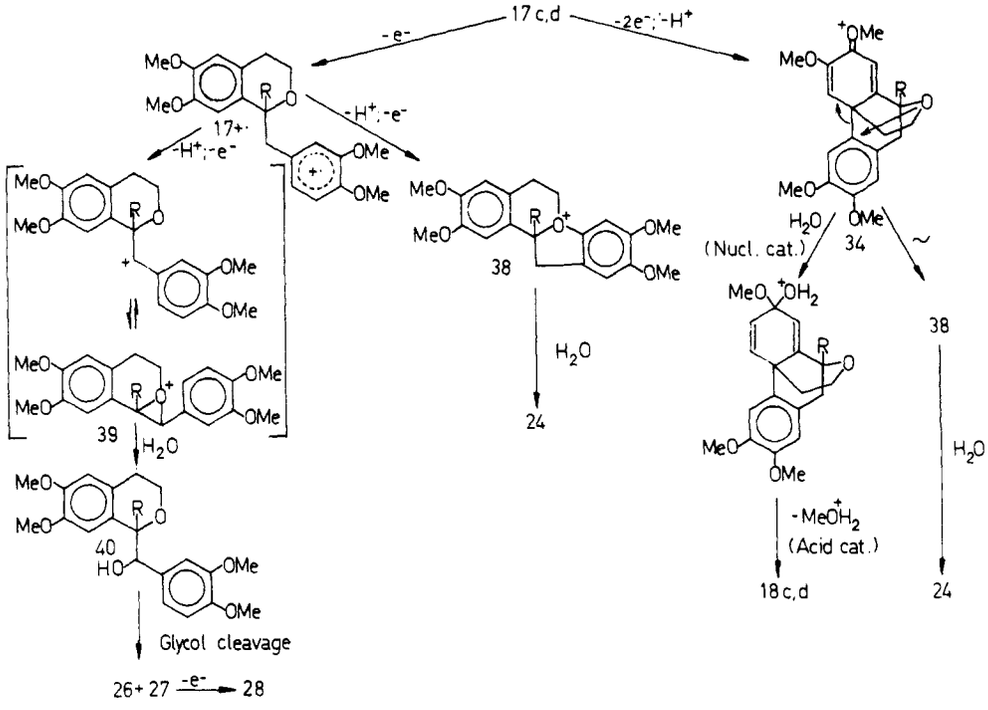
The voltammetric data in Table II indicate that three different cationic intermediates are formed on anodic oxidation of compound **17a.** In view of our product studies (Table I) and earlier studies of related compounds[1–15] it appears reasonable to ascribe the structures **34a, 35a,** and **36a** to these cationic intermediates. The observed reversible couples at 0.930, 1.050, and 1.185 V correspond to a one-electron oxidation of ring C to give a dication radical. The products observed can be rationalized in terms of the reactions shown in Scheme IV. The dienone **18a** is formed via nucleophilic attack of water, when present,[25] followed by elimination of $MeOH_2^+$. In the same manner the dienone **19a** is obtained from the cation **35a.** The cation **35a** can also rearrange in two different ways. One rearrangement (indicated with fully drawn arrows in structure **35**) leads to dienone **20a** (via nucleophilic attack of water and elimination of $MeOH_2^+$). The other (indicated with a dotted arrow) leads to the aromatic structure **23a** after loss of a proton. The latter product is observed only in solvents of low nucleophilicity and in the presence of acid (experiment 6 in Table I), in accordance with our previous observations[4–7] of similar rearrangements during anodic cyclization of compounds with structure **1.** The highest yield of the dienone **19a** was obtained in neutral solution (experiments 1 and 4 in Table I). In the presence of HBF_4/H_2O **19a** was not observed (experiment 2) and in the presence of H_2SO_4/H_2O the yield of **19a** was less than half (experiment 3). This decrease in the yield of **19a** is not accompanied by any considerable increase in the yield of any of the other products. This indicates that the acid catalyzes the rearrangement of **35a** to **23a** at the expense of rearrangement leading to **20a** (the yield of this product is fairly constant). **23a** is more easily oxidized than the substrate and is converted to its cation radical, which is stable only in TFA/DCM. In the other electrolytes the cation radical probably undergoes nucleophilic substitution followed by further oxidation with formation of intractable tars.[26] A decrease of the electrolysis temperature from −35 °C (experiment 1) to −81 °C (experiment 4) resulted in a drastic increase of the yield of **21a** and an improvement in the current yield. This probably depends on a lower H_2O concentration and activity in EtCN at −81 °C and an increased stability of the cation radical formed by oxidation of **21a** (this compound is more easily oxidized than **17a**) or of the cation **36a.** In general the improvements in yield at lower temperatures are in part dependent on the increased stability of the products. The results from experiments 1 and 4 do not indicate any effect of the temperature on the relative rates of the cyclization reactions leading to **18a, 19a,** and **20a.** In contrast the addition of H_3O^+

Scheme IV. Possible Mechanisms for the Formation of 18a–d, 19a–c, 20a,b, 21a,b, and 23a,b[a]



[a] ~ signifies a rearrangement reaction; −e indicates loss of one electron.

Scheme V. Possible Mechanisms for the Anodic Formation of 18c,d, 24, 27, and 28



[a] ~ signifies a rearrangement; −e indicates loss of one electron.

(as 35% aqueous HBF_4) seems to affect the relative rates of the cyclization reactions. Comparison of experiments 1 and 2, 9 and 10–12, and 15 and 16 clearly shows that the rate of the cyclization reaction leading to dienones of structure **18** increases more than the other cyclization reactions in going from acetonitrile/$LiBF_4$ to the acetonitrile/HBF_4 as electrolyte. In Scheme IV we have suggested that the cyclization product **21** is formed via rearrangement of the cation **36**, which is formed by coupling between the benzylic C-4 carbon and C-9 in ring C (structure **17**).[27] Structure **21** could also arise by rearrangement of the cation **34** (bond shift from C-5a to C-13). However, in that case only two cationic intermediates should be observed in the second harmonic ac measurements (Table II). Furthermore the oxidation of **17a** in methanol (experiment 5, Table I) shows that the benzyl cation **37** is formed during anodic oxidation of **17a–b**. The results of the anodic oxidations of compounds **17c,d** can be rationalized in terms of the mechanisms in Scheme IV in a similar way as for **17a**. It is interesting that the yield of the dienone **18b** is much better than that of **18a** in the presence of HBF_4 (experiments 2 and 9 in Table I) and that coupling in the phenethyl analogue **17d** only occurs between C-8a and C-10 (structure **17**).

No dienones (**18c,d**) are formed on electrolysis of compounds **17c,d** in the absence of water (experiments 16 and 17). Only the hydroxylated compound **24**, the tetralone **26**, veratric aldehyde (**27**), and the oxidation product (**28**) of veratric aldehyde are observed. Two possible mechanisms for the formation of these products are outlined in Scheme V. In the first

the radical cation $17^{+\cdot}$ is formed by selective oxidation of ring C. Nucleophilic attack of the oxygen in ring B on the cation radical moiety followed by further oxidation and deprotonation gives the cation **38**, which on hydrolysis yields **24**. Deprotonation of $17^{+\cdot}$ followed by further oxidation yields a benzylic cation, which undergoes intramolecular nucleophilic attack to give the cation **39**, which is then hydrolyzed to the glycol **40**. Further oxidation of **40** results in the usual glycol cleavage to form veratric aldehyde (**27**) and **26**. In the second mechanism, **24** is formed via the cation **34** by intramolecular nucleophilic substitution as in Scheme V. However, it is difficult to explain the formation of **26** and **27** from **34**. Possibly both mechanisms are operative and in the absence of external nucleophiles **34** only undergoes intramolecular nucleophilic substitution to give **38**. If an external nucleophile such as water is added the reaction leading to **18** becomes fast enough to compete with the reaction leading to **24** (Scheme V). However, the present data do not allow any definite assignment of mechanisms.

Synthetic Applications. It should be noted firstly that the coupling to ring C always occurs at C-14; no coupling at C-10 was observed. In contrast, coupling in ring A occurs directly at both C-5a and C-8a and indirectly at C-8 (**17**), giving structures **18–20** and **23**. The yields of the dienones **18–19** and of the compound **23** are good and our experiments indicate that it should be possible to achieve fairly selective formation of either **18** or **19** (**20** is always a minor product) or **23** by simple changes in the electrolysis conditions (pH, addition of TFA, etc.). Of more special interest is the possibility of introducing a hydroxy group in the C-14 position of benzyl- or phenethylisochromans similar to **17c,d** via the indirect oxidation in Scheme V.

Conclusions

Ring B in structure **17** does not appear to put any steric restraints on the coupling between rings A and C, since the same types of products and similar yields are obtained as in the anodic coupling of compounds of structure **1**. The heteroatom Z in **2** and **17** appears to be without effect on the coupling between rings A and C. However, due to the nucleophilicity of oxygen and nitrogen[14] a competing intramolecular cyclization reaction can occur. This involves nucleophilic attack of Z (= O or N) on ring C after oxidation to the cation radical or the cation at the anode (see Scheme V). It is of interest to note that this intramolecular nucleophilic reaction can be inhibited completely by addition of strong acid when Z = N (protonation of nitrogen; see **2** → **8** in Scheme II). The C-1 methyl group in structure **17** does not affect the product pattern or voltammetry compared with that of the compounds without a C-1 methyl, indicating that the reactivity of the C-1 position is low compared to that of the C-4 position.

Experimental Section

General procedures and apparatus used for voltammetry and coulometry and for the purification of solvents were conventional and have been described previously.[2] The NMR spectra were recorded in deuteriochloroform with Me_4Si as internal reference. IR spectra were recorded using KBr tablets (solids) or thin films (liquids). High resolution mass spectra were recorded with a Varian MAT 311 instrument.

Synthesis of 1-(3′,4′-Dimethoxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17a). 1,5-Bis(3,4-dimethoxyphenyl)-3-pentanone (41). 3,3′,4,4′-Tetramethoxybenzalacetone (**29**)[19] (mp 124–125 °C, 70.8 g, 0.2 mol) was dissolved in ethanol (300 mL) and submitted to catalytic hydrogenation at 1 atm with Pd/C (10%, 5 g) as catalyst. When the theoretical amount of hydrogen had been consumed, the catalyst was filtered off and the filtrate was evaporated to yield pure **41**: 80.2 g (100%); mp 83–84 °C; NMR δ 6.77 (6 H, m, ArH), 3.90 (12 H, s, OCH_3), 2.80 (8 H, m, CH_2).

1,5-Bis(3,4-dimethoxyphenyl)-3-pentanol (42). **41** (46.3 g, 0.129 mol) was dispersed in methanol (150 mL) and KBH_4 (3.5 g, 0.065 mol) dissolved in a 1:3 mixture of 0.1 M aqueous NaOH and methanol was added with stirring during 0.5 h. Stirring was continued at room temperature for 4 h and then water (250 mL) was added to precipitate **42**: yield 45.3 g (97%); mp 89–91 °C; NMR δ 6.75 (6 H, s, ArH), 3.83 (12 H, s, OCH_3), 2.75 (5 H, m, $ArCH_2$, CHOH), 1.70 (4 H, m, CH_2).

17a. 42 (9.90 g, 27.5 mmol) dissolved in dry nitromethane (100 mL) was heated to 90 °C and $SnCl_4$ (14.30 g, 55 mmol) was added dropwise with stirring. The reaction mixture was kept at 90 °C (dry atmosphere) for 2 h and then poured on a mixture of ice (200 g) and concentrated HCl (60 mL). This mixture was stirred until no further color changes occurred and then extracted with ether (2 × 100 mL). The combined ether extracts were washed with saturated bicarbonate solution and water, dried over sodium sulfate, and evaporated to yield a yellow oil (8.00 g), which was purified by filtration through alumina (methylene chloride eluent) to yield 7.50 g (80%) of a colorless oil which crystallized after standing several months. The oil was identified as from spectroscopic data for a crystalline sample obtained by chromatography on silica gel (diisopropyl ether eluent): mp 80–81 °C; NMR δ 6.83 (3 H, m, *C*-ArH[28]), 6.50 (1 H, s, *A*-ArH), 6.45 (1 H, s, *A*-ArH, 3.80 (9 H, s, OCH_3), 3.70 (3 H, s, OCH_3), 2.73 (5 H, m, $ArCH_2$, ArCH), 1.70 (4 H, m, *B*-CH_2).

Anal. Calcd for $C_{21}H_{26}O_4$: 342.1766. Found: 342.1798.

Synthesis of 1-(3′,4′-Dimethoxybenzyl)-1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17b). 1,5-Bis(3,4-dimethoxyphenyl)-2-methyl-2-pentanol (30). 1-Bromo-3-(3,4-dimethoxyphenyl)propane (5.18 g, 20 mmol) dissolved in dry tetrahydrofuran (THF) (25 mL) was added slowly to magnesium filings (5 g preactivated with 5–10 drops of 1,2-dibromoethane) covered with THF in a carefully dried three-neck flask (nitrogen atmosphere). The reaction mixture was refluxed for 0.5 h and after cooling 1-(3,3-dimethoxyphenyl)-2-propanone (3.88 g, 20 mmol) dissolved in dry THF (15 mL) was added slowly. After refluxing for 2 h under N_2 the mixture was allowed to cool and poured on ice (150 g), neutralized with dilute HCl, and extracted with ether (2 × 75 mL). The combined ether extracts were washed with water, dried over sodium sulfate, and evaporated to yield a yellowish oil (6.10 g), which according to its NMR spectrum was a mixture of **30** and the propane and propanone starting materials. The two latter compounds were removed by distillation at 0.1 mm. The residue (4.91 g) was identified as **30** by its NMR: δ 6.72 (6 H, s, ArH), 3.87 (12 H, s, OCH_3), 2.70 (2 H, s, $ArCH_2$), 2.60 (2 H, m, $ArCH_2$), 1.62 (4 H, m, CH_2), 1.17 (3 H, s, CH_3). Yield 65%.

17b. 30 (3.74 g, 10 mmol) was dissolved in dry methylene chloride (100 mL) contained in a flask fitted with a magnetic stirring bar and a drying tube. With stirring trifluoromethanesulfonic acid (TFMS) (3.00 g, 20 mmol) was added dropwise. After stirring for 2 h at room temperature the solution was extracted with water (50 mL), saturated $NaHCO_3$ (50 mL), and water (50 mL), dried over sodium sulfate, and evaporated to give a yellow oil (3.30 g), which was purified by filtration through alumina (20 g, methylene chloride eluent) to yield 3.06 g (86%) of a colorless oil identified as **17b** from the spectroscopic data below, obtained from a crystalline sample made by rechromatography of the oil on silica gel (diisopropyl ether eluent) followed by recrystallization from ethanol: mp 90–91 °C; NMR δ 6.63 (5 H, m, ArH), 3.93 (6 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 3.75 (3 H, s, OCH_3), 2.87 (2 H, m, *C*-$ArCH_2$), 2.63 (2 H, m, *A*-$ArCH_2$), 1.70 (4 H, m, CH_2), 1.33 (3 H, s, CH_3).

Anal. Calcd for $C_{22}H_{28}O_4$: 356.1987. Found: 356.1975.

Synthesis of 1-(3′,4′-Dimethoxybenzyl)-6,7-dimethoxyisochroman (17c). Alternative A. 2-(Carboxymethyl)-3′,4,4′,5-tetramethoxydeoxybenzoin (32). 3,4-Dimethoxyphenylacetic acid (19.6 g, 0.1 mol) and polyphosphoric acid (PPA) (150 g) were thoroughly mixed and heated to 80 °C for 30 min.[20] Then the mixture was slowly poured on ice and stirred until the red color had disappeared (this sometimes required gentle warming) and extracted with methylene chloride (3 × 150 mL). The combined extracts were washed with water (2 × 100 mL), dried over sodium sulfate, and evaporated to give a yellow oil (16.72 g), which after crystallization from ethanol afforded **32**: 13.71 g (73%); mp 153–155 °C; NMR δ 7.37 (1 H, s, ArH_6), 6.80 (4 H, s, ArH), 4.20 (4 H, s, $ArCH_2CO$), 3.90 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3).

17c. 32 (13.22 g, 35.3 mmol) was added in small portions to a stirred mixture of $LiAlH_4$ (4.50 g, 132 mmol) in dry THF (250 mL) kept under nitrogen. After the addition stirring was continued for 2 h more at room temperature. The reaction mixture was then cooled and water (100 mL) was added slowly, followed by 2 M HCl to acidic reaction. A further 300 mL of water was added and the mixture was extracted with ether (6 × 100 mL). The combined ether extracts were washed with water (100 mL), dried over sodium sulfate, and evaporated to give a viscous, colorless oil (12.17 g), which NMR indicated to contain

50% of **17c**. This oil was dissolved in chloroform (100 mL) contained in a round-bottom flask fitted with a magnetic stirring bar and a Soxhlet extractor containing molecular sieves (3A, 4 g). *p*-Toluenesulfonic acid (250 mg, 1.54 mmol) was added and the mixture was refluxed for 1 h, cooled, extracted with saturated $NaHCO_3$ (75 mL) and water (75 mL), dried over sodium sulfate, and evaporated to give an oil (11.57 g), which crystallized upon standing overnight. Recrystallization from ethanol gave **17c** (9.97 g, 82%), identified by its: mp 91–92 °C; NMR δ 6.80 (3 H, s, *C*-ArH), 6.60 (1 H, s, *A*-ArH_5), 6.53 (1 H, s, *A*-ArH_8), 4.93 (1 H, t, J = 6 Hz, ArCH), 3.93 (2 H, q, J = 5 Hz, OCH_2), 3.88 (9 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 3.08 (2 H, d, J = 6 Hz, *C*-$ArCH_2$), 2.72 (2 H, q, J = 5 Hz, *A*-$ArCH_2$).

Anal. Calcd for $C_{20}H_{24}O_5$: 344.1623. Found: 344.1602.

Alternative B. 17c. A mixture[21] of homoveratryl alcohol (1.82 g, 10 mmol), dicyclohexylcarbodiimide (DCC) (6.30 g, 30 mmol), dimethyl sulfoxide (Me_2SO) (15 mL), TFA (0.4 mL, 10 mmol), pyridine (0.8 mL, 10 mmol), and dry methylene chloride (35 mL) was stirred for 24 h and then poured into ether (200 mL), and oxalic acid (2.70 g, 30 mmol) was added in small portions. The precipitated crystals were filtered off and the filtrate was washed with saturated $NaHCO_3$ (50 mL) and water (2 × 75 mL), dried over sodium sulfate, and evaporated to give a yellow oil (1.88 g), which according to its NMR contained homoveratrum aldehyde (66%) and homoveratryl alcohol (30%). This oil was dissolved in methylene chloride (100 mL) contained in a round-bottom flask fitted with a magnetic stirring bar and a Soxhlet extractor containing molecular sieves (3A, 3 g). Homoveratryl alcohol (0.65 g, 3.6 mmol) and *p*-toluenesulfonic acid (0.1 g, 0.6 mmol) were added and the mixture was refluxed for 2 h, cooled, extracted with saturated $NaHCO_3$ (75 mL) and water (75 mL), and evaporated to give a yellow oil (2.51 g), which on crystallization from ethanol yielded **17c** (1.76 g, 75%), identical with the product obtained by alternative A.

Synthesis of 1-(3′,4′-Dimethoxybenzyl)-1-methyl-6,7-dimethoxyisochroman (17d). Homoveratryl alcohol (9.10 g, 50 mmol), (3,4-dimethoxyphenyl)-2-propanone (9.80 g, 50 mmol), and *p*-toluenesulfonic acid (1.00 g, 6.1 mmol) were dissolved in chloroform (150 mL) contained in a round-bottom flask fitted with a magnetic stirring bar and a Soxhlet extractor and refluxed for 20 h. After cooling the reaction mixture was extracted with saturated $NaHCO_3$ (100 mL) and water (100 mL), dried, and evaporated to give a yellow oil (17.83 g), which crystallized upon standing. Recrystallization from methanol afforded **17d** (16.68 g, 93%), identified by its: mp 80–81 °C; NMR δ 6.63 (5 H, m, ArH), 3.90 (2 H, t, OCH_2), 3.88 (9 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 3.03 (2 H, d, *C*-$ArCH_2$), 2.55 (2 H, t, J = 6 Hz, *A*-$ArCH_2$).

Anal. Calcd for $C_{21}H_{26}O_5$: 358.1779. Found: 358.1786.

Synthesis of 1-(3′,4′-Dimethoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (17e). 1,6-Bis(3,4-dimethoxyphenyl)-hex-3-ene-1,6-dione (33). *trans*-β-Hydromuconic acid (43.2 g, 0.3 mol) and freshly distilled $SOCl_2$ were refluxed together for 2 h. Excess $SOCl_2$ was distilled off and the residue was dissolved in dry chloroform (150 mL) and slowly mixed with $AlCl_3$ (120 g, 0.9 mol) and dry chloroform (400 mL). With mechanical stirring veratrole (91 mL, 0.6 mol) was added dropwise. The resulting slurry was stirred for 1–2 h with reflux and then poured on a mixture of ice (1000 g) and concentrated HCl (200 mL). The organic phase was separated and the aqueous phase was extracted several times with chloroform. The combined organic phases were washed with saturated $NaHCO_3$ and water, dried over sodium sulfate, and evaporated to give a semicrystalline mass (65 g). Recrystallization from methyl ethyl ketone yielded **33**: 52.4 g (52%); mp 159–160 °C; NMR δ 7.50 (2 H, d, J = 8 Hz, ArH), 7.42 (2 H, s, ArH), 6.78 (2 H, d, J = 8 Hz, ArH), 5.80 (2 H, m, olephinic-H), 3.87 (12 H, s, OCH_3), 3.68 (4 H, m, CH_2).

1,6-Bis(3,4-dimethoxyphenyl)-3-hexene (43). 33 (76.8 g, 0.22 mol), zinc amalgam made from Hg_2Cl_2 (17.1 g) and zinc (171 g) as described in ref 22, concentrated HCl (140 mL), water (105 mL), and toluene (140 mL) were refluxed together with vigorous stirring for 24 h. Every sixth hour concentrated HCl (70 mL) was added. After cooling the organic phase was separated and the aqueous phase was extracted with ether (2 × 250 mL). The combined organic phases were washed with water (250 mL), dried over sodium sulfate, and evaporated to give a colorless oil (57.3 g), which on crystallization from methanol yielded the hexene: 52.0 g (73%); mp 80–82 °C; NMR δ 6.73 (6 H, m, ArH), 5.50 (2 H, m, olephinic-H), 3.87 (12 H, s, OCH_3), 2.50 (8 H, m, CH_2).

17e. 43 (2.50 g, 7.0 mmol) and TFMSA (0.25 g, 1.7 mmol) were dissolved in dry methylene chloride (100 mL), stirred for 2 h at room temperature (dry atmosphere), and then washed with saturated $NaHCO_3$ (50 mL) and water (50 mL), dried over sodium sulfate, and evaporated to give **17e** as a yellowish oil (2.50 g, 100%), which crystallized slowly on standing. This product was used in the electrolyses experiments. An analytical sample of **17e** was obtained by chromatography on alumina (activity 2–3 according to Brockman, ether/methylene chloride = 1:1 as eluent) followed by recrystallization from ethanol: mp 59–61 °C; NMR δ 6.67 (5 H, m, ArH), 3.85 (12 H, s, OCH_3), 2.70 (5 H, m, ArCH, $ArCH_2$), 1.83 (6 H, m, CH_2).

Anal. Calcd for $C_{22}H_{28}O_4$: 359.1986. Found: 359.1961.

Electrolysis. General. The electrolyses were conducted in a closed one-compartment cell fitted with a cooling mantle and a magnetic stirring bar. The anode was a platinum cylinder (50 cm^2), the cathode was a coiled nickel wire (diameter 1.25 mm, length 40 cm), and the reference electrode was either a saturated calomel electrode or a Ag/Ag^+ electrode. The compound to be electrolyzed (1.5 mmol) was dissolved in the electrolyte[29] (60 mL) and submitted to constant potential electrolysis. After the electrolysis the electrolyte was poured into water (or saturated $NaHCO_3$ when the electrolyte contained acid) (300 mL). The organic phase was separated and the aqueous phase was extracted with methylene chloride (2 × 100 mL). The combined organic phases were washed with water, dried over sodium sulfate, and evaporated. The residue was filtered through alumina (activity 2–3, methylene chloride eluent) when dienones were to be isolated and through silica gel (methylene chloride eluent) when phenols were to be isolated. The product obtained after evaporation of the methylene chloride was analyzed as described below.

Analysis of Electrolysis Products. Isolation Procedure. The cyclized products (ortho–para coupling), **22** and **23b,** from electrolysis of **17a** and **17b** were isolated by chromatography on silica gel with diisopropyl ether as eluent. The other oxidation products from **17a** and **17b** were isolated by rechromatography on alumina (activity 2–3) with ether/methylene chloride = 1:1 as eluent. The products were eluted in the following order: **21a, 17a, 20a,** and **18a + 19a.** The products from **17b** appeared in a similar way. **18a** and **19a** were separated by chromatography on a Celite/activated carbon column (1:1, methylene chloride eluent). Once **19a** had been obtained in crystalline form it became possible to crystallize the compound from the crude electrolysis product dissolved in ethanol by seeding (the same was the case with **18b**).

Compound **25** was isolated by chromatography on alumina with ether as eluent. Compound **23c** was isolated by direct crystallization of the residue (vide supra) from ethanol.

The isolation of the products from oxidation of **17c** and **17d** was quite troublesome. The hydroxylated products **24a,b** do not survive chromatography on alumina and the dienones **18c,d,** and to some extent also **24a,b,** decompose on silica gel. We found it necessary to run separate experiments in order to isolate all products.

In the first experiment the electrolysis product was chromatographed on alumina (ether/methylene chloride = 1:1 as eluent) and the dienones **18c** and **18d** were isolated while the hydroxylated products were lost. In the second the dienone was precipitated from the electrolysis product dissolved in ethanol by seeding with pure, crystalline dienone from the first experiment. After evaporation of the ethanol the residue was chromatographed on silica gel at −15 °C with ether/methylene chloride (1:1) as eluent and **23a** and **23b** were obtained in a pure state.

Product 22 from 17a: mp 99–100 °C; NMR δ 9.27 (1 H, s, ArH), 7.30 (1 H, s, ArH), 7.13 (1 H, s, ArH), 7.07 (1 H, s, ArH), 4.05 (3 H, s, OCH_3), 4.02 (6 H, s, OCH_3), 3.93 (3 H, s, OCH_3), 3.12 (4 H, m, $ArCH_2$), 2.07 (2 H, m, CH_2); IR ν 2940, 2840, 1620, 1600, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{22}O_4$: 338.1517. Found: 338.1496.

Dienone 18a from 17a: mp 99–101 and 138–139 °C; NMR δ 6.87 (1 H_8, s), 6.65 (1 H_4, s), 6.40 (1 H_1, s), 6.30 (1 H_5, s), 3.92 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 3.10 (3 H, m, H_9 and H_{10}), 2.00 (2 H, m, H_{13}), 1.57 (4 H, m, H_{11} and H_{12}); IR ν 2940, 2850, 1666, 1640, 1620, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1518. Found: 326.1521.

Dienone 19a from 17a: mp 168–171 °C; NMR δ 6.98 (1 H_8, s), 6.68 (1 H_4, s), 6.45 (1 H_1, s), 5.98 (1 H_5, s), 3.93 (6 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 2.67 (4 H, m, H_{10} and H_{13}), 1.73 (5 H, m, H_9, H_{11}, and H_{12}); IR ν 3090, 2985, 2840, 1665, 1640, 1595, 1520, 1460 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1517. Found: 326.1478.

Dienone 20a from 17a: mp 166–167 °C; NMR δ 6.86 (1 H_5, s), 6.42 (1 H_4, s), 6.27 (1 H_1, s), 5.80 (1 H_8, s), 3.92 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3), 3.60 (3 H, s, OCH_3), 2.48 (3 H, m, H_9 and H_{10}), 1.78 (2 H, m, H_{13}), 1.20 (4 H, m, H_{11} and H_{12}).

Anal. Calcd for $C_{20}H_{22}O_4$: 326.1518. Found: 326.1534.

Product 21a from 17a: mp 161–163 °C; NMR δ 6.82 (1 H, s, ArH), 6.77 (1 H, s, ArH), 6.73 (1 H, s, ArH), 6.53 (1 H, s, ArH), 3.90 (9 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 3.75 (1 H_5, m), 3.16 (1 H_{10}, m), 2.10 (4 H, m, H_{12} and H_{13}); IR ν 3000, 2940, 2840, 1615, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 346.1675.

Tetralone 25 from 17a: mp 127–128.5 °C; NMR δ 7.55 (1 H, s, ArH), 6.70 (3 H, m, ArH), 6.40 (1 H, s, ArH), 3.92 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 2.87 (5 H, m, H_1, H_3, and $ArCH_2$), 2.13 (2 H, m, H_2); IR ν 2930, 2840, 1670, 1600, 1510 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_5$: 356.1623. Found: 356.1596.

Dienone 18b from 17b: mp 169–170 °C; NMR δ 6.80 (1 H_8, s), 6.57 (1 H_4, s), 6.40 (1 H_1, s), 6.30 (1 H_5, s), 3.88 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 2.93 (2 H, s, H_{10}), 1.95 (2 H, m, H_{13}), 1.48 (4 H, m, H_{11} and H_{12}), 1.28 (3 H, s, CH_3); IR ν 3000, 2940, 2840, 1670, 1640, 1620, 1520, 1465 cm^{-1}; ^{13}C NMR δ 181.16 (s), 169.63 (s), 150.80 (s), 148.04 (2 s, overlapping), 130.51 (s), 129.38 (s), 120.45 (2 s, overlapping), 110.06 (d), 108.27 (d), 56.33 (q), 55.84 (q), 54.87 (q), 46.26 (t), 45.13 (s), 44.48 (t), 43.34 (t), 37.98 (s), 27.43 (q), 19.64 (t).

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1655.

Dienone 19b from 17b: mp 81–83 and 142–145 °C; NMR δ 7.10 (1 H_8, s), 6.73 (1 H_4, s), 6.57 (1 H_1, s), 6.00 (1 H_5, s), 3.90 (6 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 2.81 (2 H, q, J = 16 Hz, H_{10}), 2.00 (6 H, m, H_{11} and H_{13}), 0.98 (3 H, s, CH_3); ^{13}C NMR δ 181.48 (s), 158.92 (s), 151.43 (s), 151.13 (s), 148.04 (s), 129.54 (s), 123.53 (d), 123.37 (s), 118.50 (d), 110.87 (d), 107.30 (d), 56.00 (q, two overlapping), 55.03 (q), 53.89 (s), 49.83 (s), 40.23 (t), 39.28 (t, two overlapping), 22.56 (q), 21.59 (t); IR ν 3000, 2960, 2840, 1660, 1640, 1595, 1520, 1670 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1636.

Dienone 20b from 17b: mp 112–114 °C; NMR δ 6.82 (1 H_5, s), 6.38 (1 H_4, s), 6.22 (1 H_1, s), 5.68 (1 H_8, s), 3.87 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 3.55 (3 H, s, OCH_3), 2.88 (2 H, q, J = 16 Hz, H_{10}), 2.27 (2 H, m, H_{13}), 1.60 (4 H, m, H_{11} and H_{12}), 1.10 (3 H, s, CH_3); IR ν 3000, 2940, 2860, 1670, 1640, 1620, 1505, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1671.

Product 23b from 17b: mp 103–105 °C; NMR δ 8.02 (1 H, s, ArH), 6.70 (1 H, s, ArH), 6.56 (1 H, s, ArH), 3.93 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.65 (3 H, s, OCH_3), 2.78 (4 H, m, $ArCH_2$), 1.73 (4 H, m, CH_2), 0.88 (3 H, s, CH_3); IR ν 2920, 2840, 1610, 1600, 1575, 1510, 1470 cm^{-1}.

Anal. Calcd for $C_{22}H_{26}O_4$: 354.1825. Found: 354.1828.

Dienone 18c from 17c: mp 184–186 °C; NMR δ 6.85 (1 H_8, s), 6.67 (1 H_4, s), 6.42 (1 H_1, s), 6.32 (1 H_5, s), 4.38 (1 H_9, t, J = 4 Hz), 3.85 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 3.73 (2 H_{12}, m), 3.33 (2 H_{10}, d, J = 4 Hz), 1.98 (2 H_{13}, m); IR ν 3010, 2980, 2960, 2920, 2875, 1680, 1660, 1640, 1630, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{19}H_{20}O_5$: 328.1311. Found: 328.1324.

1-(3′,4′-Dimethoxy-6′-hydroxybenzyl)-6,7-dimethoxyisochroman (23a). Obtained as an oil which NMR and TLC indicated to be a single compound: NMR δ 6.88 (1 H, s, C-ArH_2), 6.77 (2 H, s, ArH), 6.63 (1 H, s, ArH), 3.93 (3 H, s, OCH_3) 3.90 (1 H_1, m), 3.85 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.68 (2 H_3, t, J = 6.5 Hz), 3.47 (2 H, d, J = 2.5 Hz, C-$ArCH_2$), 2.62 (2 H_4, t, J = 2.5 Hz); IR ν 3000, 2940, 2840, 1610, 1510, 1470 cm^{-1}; mass m/e 360 (M^+). If **23a** was dissolved in CD_3OD/D_2O (1:1) and left for 1 h the mass of the molecular ion of the residue obtained on evaporation of the solvent changed to 361.

Product 28 from 17c: mp 251–253 °C; NMR δ 7.03 (2 H, s, ArH), 6.93 (2 H, s, ArH), 4.30 (4 H, sAA, $ArCH_2$), 4.00 (6 H, s, OCH_3), 3.97 (6 H, s, OCH_3).

Anal. Calcd for $C_{18}H_{20}O_5$: 316.1311. Found: 316.1299.

Compound 26 from 17c or 17d: mp 138–140 °C; NMR δ 7.53 (1 H, s, ArH), 6.70 (1 H, s, ArH), 4.53 (2 H, t, J = 6 Hz, OCH_2), 3.97 (3 H, s, OCH_3), 3.95 (3 H, s, OCH_3), 3.00 (2 H, t, J = 6 Hz, $ArCH_2$); mass m/e 208 (M^+).

Dienone 18d from 17d: mp 162–164 °C; NMR δ 6.90 (1 H_8, s), 6.65 (1 H_4, s), 6.47 (1 H_1, s), 6.38 (1 H_5, s), 3.93 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.77 (2 H_{12}, t, J = 5.5 Hz), 3.25 (2 H_{10}, s, br), 1.95 (2 H_{13}, t, J = 5.5 Hz), 1.55 (3 H, s br, CH_3); IR ν 3000, 2950, 2880, 2850, 1675, 1650, 1625, 1525, 1460 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}O_5$: 342.1466. Found: 342.1460.

1-(3′,4′-Dimethoxy-6′-hydroxybenzyl)-1-methyl-6,7-dimethoxyisochroman (24b): mp 57–59 °C; NMR δ 6.85 (1 H, s, ArH_2), 6.73 (2 H, s, ArH), 6.63 (1 H, s, ArH), 3.95 (3 H, s, OCH_3), 3.92 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 3.67 (2 H_3, t, J = 7 Hz), 3.47 (2 H, s, C-$ArCH_2$), 2.58 (2 H_4, t, J = 7 Hz), 1.98 (3 H, s, CH_3).

Anal. Calcd for $C_{21}H_{26}O_6$: 374.1729. Found: 374.1757.

Product 23c from 17e: mp 131–133 °C; NMR δ 7.13 (1 H, s, ArH), 6.77 (1 H, s, ArH), 6.67 (1 H, s, ArH), 3.93 (3 H, s, OCH_3), 3.88 (6 H, s, OCH_3), 3.45 (3 H, s, OCH_3), 2.80–1.70 (11 H, m); IR ν 3000, 2930, 2860, 1610, 1600, 1580, 1520, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 354.1831. Found: 354.1806.

Dienone 19c from 17e: mp 134–136 °C; NMR δ 6.63 (1 H_8, s), 6.42 (1 H_4, s), 6.22 (1 H_1, s), 6.13 (1 H_5, s), 3.88 (3 H, s, OCH_3), 3.68 (3 H, s, OCH_3), 3.60 (3 H, s, OCH_3), 3.10–1.40 (11 H, m); IR ν 3000, 2940, 2860, 1670, 1640, 1615, 1515, 1470 cm^{-1}.

Anal. Calcd for $C_{21}H_{24}O_4$: 340.1674. Found: 340.1699.

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Registry No.—**17a,** 68080-86-4; **17b,** 68080-87-5; **17c,** 68080-88-6; **17d,** 68080-89-7; **17e,** 68080-90-0; **18a,** 68080-91-1; **18b,** 68080-92-2; **18c,** 68080-93-3; **18d,** 68080-94-4; **19a,** 68080-95-5; **19b,** 68080-96-6; **19c,** 68080-97-7; **20a,** 68080-98-8; **20b,** 68080-99-9; **21a,** 68081-00-5; **21b,** 68081-01-6; **22,** 68081-02-7; **23a,** 68081-09-4; **23b,** 68081-03-8; **23c,** 68081-04-9; **24a,** 68081-05-0; **24b,** 68081-06-1; **25,** 68081-07-2; **26,** 14174-13-1; **27,** 120-14-9; **28,** 68081-08-3; **29,** 38552-39-5; **30,** 68081-10-7; **32,** 26954-85-8; **33,** 68081-11-8; **41,** 68081-12-9; **42,** 68081-13-0; **43,** 68081-14-1; 1-Bromo-3-(3,4-dimethoxyphenyl)propane, 3945-85-5; 1-(3,4-dimethoxyphenyl)-2-propanone, 776-99-8; 3,4-dimethoxyphenylacetic acid, 93-40-3; homoveratryl alcohol, 7417-21-2; homoveratrumaldehyde, 5703-21-9; *trans*-β-hydromuconic acid, 29311-53-3; veratrole, 91-16-7; *trans*-β-hydromuconic acid chloride, 58823-57-7.

References and Notes

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(23) The same general pattern is observed for substrates **17a–c** and **17e**.
(24) E signifies a one-electron transfer process and C a chemical reaction such as deprotonation, demethylation, nucleophilic attack, etc.
(25) In acetonitrile there are usually trace amounts of water present. However, it is also possible that acetonitrile itself functions in a similar manner as a nucleophile and in this case will give a nitrilium ion, which undergoes hydrolysis to **18a** during workup.
(26) It is possible that the dienone **19a** undergoes acid-catalyzed rearrangement to a phenol of similar structure as **23a** (OH group on C-7), which is destroyed by further oxidation.
(27) Direct coupling between C-4 and C-14 in **37** followed by deprotonation also gives **21.** However, in all our previous studies of similar couplings[4–7] the initial electrophilic attack has always occurred in the substituted ortho position with formation of a charged intermediate, which rearranges to give the final product.
(28) *C*-ArH indicates the protons on ring *C* in structures **17–21;** *A*-ArH indicates the protons on ring *A* in structures **17–21,** etc.
(29) Commercial, p.a. quality solvents stored over molecular sieves were used.