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Anodic Oxidation of 1,4-Dimethoxy Aromatic Compounds. A Facile Route to Functionalized Quinone Bisketals

Daniel R. Henton,[1a] Richard L. McCreery, and John S. Swenton*[1b,2]

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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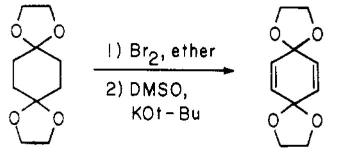
The anodic oxidation of 12 functionalized 1,4-dimethoxybenzene derivatives and 8 functionalized 1,4-dimethoxynaphthalenes has been studied under a variety of conditions. Many substituted 1,4-dimethoxy aromatics afford high yields of the respective quinone bisketals by single-cell anodic oxidation without accurate control of the electrode potential. Oxidizable groups often complicate the anodic oxidation; however, in some cases protected derivatives of these functionalities can be converted to the bisketals in good yields. Aromatics containing reducible functions can often be smoothly oxidized to quinone bisketals by the use of a divided cell. The current efficiencies and the effect of electrode material on selected systems are reported and discussed.

Several years ago our synthetic efforts in anthracyclinone synthesis required a protected quinone system stable toward organometallic reagents and accessible in high yield from readily available precursors.[3] In view of the importance of the quinone entity in organic and biological chemistry, it was initially surprising that a general method for protection of this reactive moiety had not been developed. Dreiding prepared the bisketal **2** in a classical two-step sequence from 1,4-cyclohexanedione in 52% overall yield.[4] The modest overall yield, the dependence of the route on the availability of the requisite 1,4-dione, and the direct inapplicability to naphthoquinone bisketals caused us to reject this route for our purposes. Trimethylsilyl cyanide has been shown to efficiently yield protected cyanohydrins with ketones (see **3** → **4**),[5] and this has been extended to monoprotection of quinones.[6]



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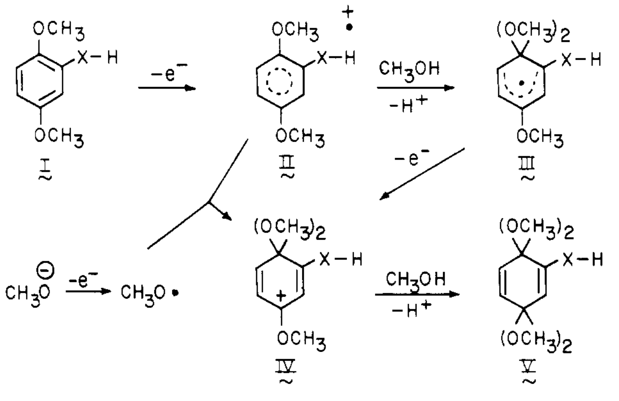
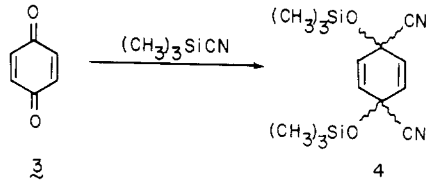
Scheme I. Mechanistic Considerations in the Anodic Oxidative Addition of Methanol to 1,4-Dimethoxy Aromatics





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[1] (a) Eastman Kodak Graduate Fellow, 1978–1979; (b) Camille and Henry Dreyfus Teacher-Scholar, 1972–1977.

[2] Part of this research has been presented in preliminary form: (a) Henton, D. R.; Chenard, B. L.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1979**, 326–7. (b) Manning, M. J.; Henton, D. R.; Swenton, J. S. *Tetrahedron Lett.* **1977**, 1679–82.

[3] (a) Manning, M. J.; Raynolds, P. W.; Swenton, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 5008–10. (b) Swenton, J. S.; Jackson, D. K.; Manning, M. J.; Raynolds, P. W. *Ibid.* **1978**, *100*, 6182–8. (c) Raynolds, P. W.; Manning, M. J.; Swenton, J. S. *Tetrahedron Lett.* **1977**, 2383–6. (d) Swenton, J. S.; Raynolds, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 6188–95. (e) Jackson, D. K.; Narasimhan, L.; Swenton, J. S. *Ibid.*, in press.

[4] Heller, J. E.; Dreiding, A. S.; O'Connor, B. R.; Simmons, H. E.; Buchanan, G. L.; Raphael, R. A.; Taylor, R. *Helv. Chim. Acta* **1973**, *56*, 272–80.

[5] (a) Lidy, W.; Sundermeyer, W. *Chem. Ber.* **1973**, *106*, 587–93; (b) Neef, H.; Muller, R. *J. Prakt. Chem.* **1973**, *315*, 367–74. (c) Evans, D. A.; Truesdale, L. K.; Carroll, G. L. *J. Chem. Soc., Chem. Commun.* **1973**, 55–6.

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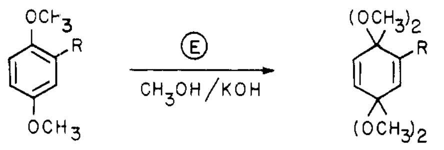
However, blocking of both quinone carbonyls would seemingly afford a cis–trans mixture[5c] which would complicate further synthetic steps. Furthermore, we were uncertain as to the stability of protected cyanohydrins in the presence of organometallic species.

Whereas conventional methodology did not offer a viable solution to preparing protected quinone derivatives, electroorganic synthesis was more encouraging. Belleau and Weinberg[7-9] had reported two simple examples (1,4-dimethoxy- and 1,2,4-trimethoxybenzene, **5** and **6**) of electrochemical bisketal formation.



5 R = H
6 R = OCH₃
7

While the details for this oxidative electrochemical addition reaction have not been rigorously established, two mechanistic possibilities are outlined in Scheme I. The first involves an ECEC[10] sequence I → II → III → IV → V, whereas the second proceeds via the pathway I → II → IV → V.[9c] In the first mechanism, the radical cation II is attacked by nucleophile (CH_3OH or CH_3O^-) followed by a second oxidative step to yield IV. However, in the second pathway, a methoxy radical generated concurrently at the anode reacts with II to yield IV. Regardless of the mechanism, we were particularly concerned first with the possible complication of benzylic substituents which could lose a proton from an intermediate such as IV, resulting in side-chain substitution or oxidation. Second, there was the effect of more remote substituents on the course of these reactions. The extension of this reaction to functionalized aromatic systems was then dependent upon the relative ease of this anodic addition reaction vs. oxidative reactions on the aromatic ring substituents. The chemical literature attests to the rich chemistry associated with a variety of functional groups in anodic oxidation processes. Thus, benzylic methylene groups,[11] benzylic secondary[11a] and tertiary alcohols,[12] dimethyl ketals,[9c] aldehydes,[13] amides,[14] and conjugated esters[15] have been reported to undergo electrochemical oxidation at potentials and under conditions similar to those we would be using. Furthermore, other moieties (aromatic bromides,[16] carbonyl groups, and conjugated double bonds[15]) have been reduced electrochemically. Since our efforts required the synthesis of highly functionalized systems, it became essential to know the limitation(s) of this anodic addition relative to substituent groups on the ring. We report here an extensive study of the effects of substituents on the formation of bisketals, the current efficiencies for selected reactions, and the influence of electrode material on the oxidations. While our choice of substituted 1,4-dimethoxy aromatics for study was dictated largely by substituents of concern in the anthracyclinone synthetic work, the results demonstrate the versatility as well as the limitation of anodic oxidation as a route to protected quinones.

Preparative Electrolyses

Single-cell electrolysis without accurate potential control is the most convenient method for electroorganic synthesis since the equipment is readily available and the reactions can easily be performed on a laboratory scale (≤0.3 mol). Thus, we first studied the anodic oxidations of a variety of substituted 1,4-dimethoxy aromatics in a single cell. In these electrolyses, both the substrate and the product are in contact with the cathode; thus, a difficulty associated with this method is the reduction of susceptible functional groups. This situation can be remedied by the use of a divided cell wherein the catholyte and anolyte are separated. Here we employed an H-cell with a glass frit as the cell divider. However, the frit introduces a resistance in the cell which results in lower currents unless a higher voltage power supply is available. Subject to this limitation on scale, we have found that a number of systems can be smoothly oxidized to bisketals in a divided cell when the compounds do not undergo clean reaction in a single-cell electrolysis (vida infra). Thus, the electrolyses reported herein are grouped into single-cell (Table I) and divided-cell processes (Table II). A discussion of the particular features of the individual systems will be deferred to the section after the general reaction conditions have been noted.

The anodic oxidation of 1,4-dimethoxy aromatics to quinone bisketals is fortunately insensitive to many reaction variables. The majority of the reactions were performed in 2% methanolic potassium hydroxide, the presence of water in the potassium hydroxide and adventitious water in the methanol having little effect on the reaction. For systems wherein base hydrolysis of a functional group could be a problem (i.e., methyl esters), anhydrous methanolic sodium methoxide can be utilized, albeit with some loss in conductivity of the solution. For less soluble compounds, anodic oxidation has been successfully performed in a methanolic slurry.[17] Whereas all of our initial oxidations were performed with a platinum gauze anode and a platinum sheet cathode, recent electrolyses utilizing reticulated vitreous carbon as the anode material also proceeded satisfactorily, the current efficiency (Table I, entry 15) and chemical yields being comparable, and in selected cases (vida infra) better, with the carbon electrode. We have not extensively studied the effect of temperature, current, or electrode potential on the yield

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(6) Evans, D. A.; Hoffman, J. M.; Truesdale, L. K. *J. Am. Chem. Soc.* **1973**, *95*, 5822–3.

(7) (a) Belleau, B.; Weinberg, N. L. *J. Am. Chem. Soc.* **1963**, *85*, 2525–6. (b) Weinberg, N. L.; Belleau, B. *Tetrahedron* **1973**, *29*, 279–85.

(8) See also: (a) Buchanan, G. L.; Raphael, R. A.; Taylor, R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 373–5. (b) Margaretha, P.; Tissot, P. *Helv. Chim. Acta* **1975**, *58*, 933–6. (c) Bornatsch, W.; Vegel, E. *Angew Chem., Int. Ed. Engl.* **1975**, *14*, 420–1. (d) Svensson, L.-K. *Acta Chem. Scand.* **1972**, *26*, 2372–84.

(9) For leading references and an extensive discussion of anodic oxidations and methoxylation of substituted benzenes, see: (a) Ross, S.; Finkelstein, M.; Rudd, E. F. "Anodic Oxidation"; Academic Press: New York, 1975. (b) Weinberg, N. "Technique of Electroorganic Synthesis Part 1"; Wiley-Interscience: New York, 1974; Vol. V, Chapter IV. (c) Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlan, A. *J. Chem. Soc., Perkin Trans 1* **1978**, 708–15.

(10) In this notation an E stands for an electrochemical step and a C stands for a chemical step.

(11) (a) Juday, R. E. *J. Org. Chem.* **1957**, *22*, 532–5. (b) Parker, V. D.; Burgert, B. E. *Tetrahedron Lett.* **1968**, 2415–6.

(12) Maruyama, K.; Murakami, K. *Bull Chem. Soc. Jpn.* **1968**, *41*, 1401–4.

(13) Anodic oxidation of benzaldehyde in methanolic sodium methoxide affords methyl benzoate: Tatsumi, M. Japanese Patent 6814,683, 1968; *Chem. Abstr.* **1969**, *71*, P70336.

(14) For a discussion of amide oxidations, see ref 9b, pp 452–3.

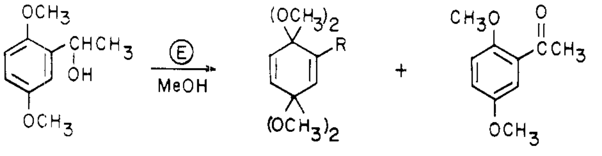
(15) Conjugated esters are subject to both electrochemical reduction and oxidation: Ingersoll, A. W. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, pp 311–4. Baltes, H.; Stork, L.; Schafer, H. J. *Chem. Ber.* **1979**, *112*, 807–17.

(16) For a discussion of the debromination of 1-bromonaphthalene, see: Fry, A. J. "Synthetic Organic Electrochemistry"; Harper and Row: New York, 1972; Chapter 5.

(17) Electrolysis in a methanolic slurry was also found to proceed smoothly for 1,5-dimethoxynaphthalene: Jackson, D. K.; Swenton, J. S. *Synth. Commun.* **1977**, *7*, 333–7.

of these processes; however, within the range we have operated, no apparent dependence on these variables was noted. Electrolyses were performed at 4–30 °C with potentials sufficient to afford a starting current of 1–4 A for single-cell and 0.4–0.6 A for divided-cell operations. Reactions carried out under controlled potential or constant current gave the product bisketals in comparable yields.

As evidenced by Table I, a variety of substituted 1,4-dimethoxybenzenes and 1,4-dimethoxynaphthalenes undergo anodic oxidation to their respective bisketals in good yield. In the benzene series (Table I), bromo (entries 1,2), trimethylsilyl (entry 4), allyl (entry 17), and alkyl substituents (entry 5) do not interfere with the course of the oxidation. As anticipated from the aforementioned mechanistic consideration of the anodic oxidation, certain substituents do complicate the reaction. Thus, a benzylic hydroxyl group suffers competitive oxidation to the ketone as illustrated for **15**. Although the yield of **15a** is acceptable (50%), contaminated bisketals are often difficult to isolate as pure compounds since chromatography on neutral alumina often does not allow clean separation of the desired bisketal whereas silica gel chromatography invariably causes some monohydrolysis of the product. Oxidation of the side chain also complicates the electrolysis of the benzaldehyde **28** (Table II, entry 6) at platinum since the bisketal of the ester is formed in poor yield with other unidentified products. When the electrolysis was performed with half the number of coulombs being passed, **34** was isolated as its acid in 34% yield, establishing that oxidation of the aldehyde function (presumably via its hemiacetal) is occurring at least as fast as bisketal formation. For this system, the reaction was markedly improved by the use of the reticulated vitreous carbon anode whereupon the bisketal **35** was formed in 59% distilled yield. In this instance and in the anodic oxidation of **16**, the carbon anode is preferred to the platinum one. Whereas complications arise in oxidations of benzylic alcohols and aldehydes, protection of the alcohol as its methyl ether (**13**, Table I, entry 6) and the aldehyde as its ethylene glycol ketal (**14**, Table I, entry 7) allows anodic oxidation to their respective bisketals in excellent yields (i.e., 92 and 88%). Interestingly, anodic oxidation of aldehyde dimethyl acetals has been reported to afford ortho esters.[10c] As the anodic oxidation of **16** illustrates, nucleophilic substituents capable of trapping a carbonium ion can lead to cyclized products.[8b] Thus, **16** affords a mixture of its bisketal, **16a**, and the bicyclic system **36** in addition to some uncharacterized minor products.

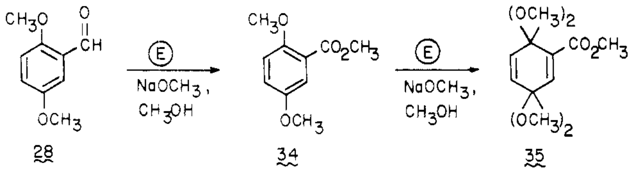


15

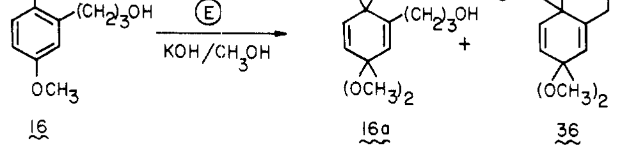
15a R = CH(OH)CH3, 50%

32 R = -C(O)CH3,

33



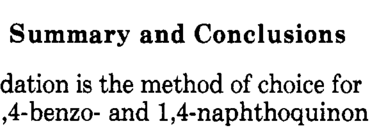
28 **34** **35**



16 **16a** **36**

As noted earlier, certain substituents are subject to reduction in single-cell electrolyses because they come in contact with the cathode. Although the reductive removal of bromo substituents from benzenoid systems is slow enough to allow such compounds to be electrolyzed satisfactorily in a single cell (Table I, entries 1 and 2), removal of the bromo substituents in naphthalene compounds (Table II, entries 7 and 9) occurs much more readily, causing some concern. However, anodic oxidation of **29** and **30** in a divided cell produces the naphthoquinone bisketals in excellent yields. The reduction problem was also encountered with amide **26** and aldehyde **28**. Thus, electrolysis of **26** in a single cell afforded <5% of the desired bisketal, while **28** under similar conditions afforded alcoholic materials as major products. With these results, the remaining carbonyl-containing compounds, including the easily reducible cinnamate derivative **27**, were electrolyzed in a divided cell. As shown in Table II (entries 4 and 5), bisketals were formed in acceptable yields under these conditions. The lower yields for these divided-cell electrolyses relative to the single-cell processes are due to some diffusion of the compound through the glass frit during the course of electrolysis ($\sim$10% of the material diffuses to the cathode chamber). Furthermore, for these particular systems, loss was entailed in the short-path distillations required to completely purify the liquid or low-melting products. The yields of crude products having spectroscopic properties nearly identical with the fully purified materials were 15–20% higher than those recorded in Table II. Thus, while divided-cell electrolyses are not so convenient to perform as the single-cell reactions, this technique considerably expands the scope of the reaction, allowing the electrolysis reaction to be performed on molecules containing reducible functions.

The nature of the alcohol component of the bisketal was not of concern to us in our projected studies; however, we did briefly examine the electrolysis of 1,4-diethoxybenzene, **37**, in ethanolic potassium hydroxide. The bisketal **38** was formed, but the yield (63%), current efficiency (21%), and complexity of the crude reaction mixture demonstrated that formation of the ethyl ketal is not so facile under these reaction conditions as for the methoxy derivatives.

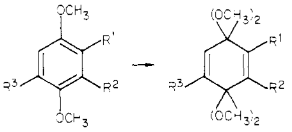


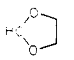
37 **38**

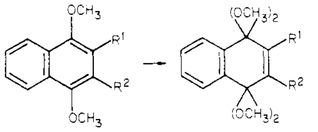
Summary and Conclusions

Anodic oxidation is the method of choice for preparation of ketals of 1,4-benzo- and 1,4-naphthoquinones. Readily oxidized substituents on the ring must be in protected form, while reducible substituents can be accommodated by the use of a divided cell. The reaction itself is easily performed by using apparatus commonly available in a chemical laboratory and is not critically dependent on electrode potential, current, temperature, or electrode material (Pt vs. C) in most cases. Future papers will concern the synthetic application of these bisketals and the regioselective hydrolysis of these compounds to the synthetically valuable monoketals.

Table I. Anodic Oxidations in a Single Cell



entry	compd	R^1	R^2	R^3	yield, %	current efficiency[a]	$E_{p/2}$, V[c]
1^{3a}	**8**	Br	H	H	78	55	1.44
2[d]	**9**	Br	H	Br	58		1.53
3	**10**	CH_3	H	H	80	74	1.22
4	**11**	$(CH_3)_3Si$	H	H	93	39	1.25
5	**12**	CH_3	CH_3	CH_3	63	66	1.26
6	**13**	$CH(OCH_3)CH_3$	H	H	92	43	1.28
7	**14**		H	H	88	34	1.35
8	**15**	$CH(OH)CH_3$	H	H	50[b]	32	1.26
9	**16**	$(CH_2)_3OH$	H	H	48[b]	38	1.21
10[d]	**17**	$CH_2CH{=}CH_2$	H	H	81	71	1.24



entry	compd	R^1	R^2	yield, %	current efficiency[a]	$E_{p/2}$, V[c]
11	**18**	H	H	74	33	1.05
12	**19**	CH_3	H	75	74	1.14
13	**20**	OCH_3	H	83		0.92
14	**21**	CH_3	OCH_3	82	49	1.18
15	**22**	CH_3	$Si(CH_3)_3$	80	25 (49)[e]	1.19

[a] Current efficiency for complete two-electron oxidation of the aromatic compound. [b] Other products formed; see text and Experimental Section. [c] $E_{p/2}$ vs. SCE. [d] See accompanying paper for experimental details. [e] Current efficiency for reticulated vitreous carbon anode.

Experimental Section[18]

Single-Cell Electrolyses. Most of the anodic oxidations were performed by using a circular platinum gauze (33 mm in diameter × 28 mm high) anode and a platinum sheet (8 × 8 mm) cathode. For electrolyses at uncontrolled potential, the cathode was centered in the circular gauze anode. For electrolyses at controlled potential, an assembly similar to that previously described was utilized,[3d] except that a Ag/AgCl reference electrode was placed inside the cylindrical anode as close to it as possible, and the cathode was placed outside the anode. In selected oxidations, a 1.5 × 2 × 4.5 cm piece of reticulated vitreous carbon, 1RVC 2X1-10-S (available from Chemotronics International, Inc.), attached to a piece of Pt wire was used as the anode. The cell was a jacketed beaker through which a cooling solution was circulated to maintain the desired temperature. All reactions were rapidly stirred magnetically. Our initial studies employed an Electro Model EC-2 (power supply A) from Electro Labs., Inc. The more recent studies employed a Model JQE36-3M power supply (power supply B) from Kepco, Inc. For divided-cell electrolyses at constant current, a Model JQE75-1.5M was used (power supply D). For electrolyses at constant potential, a potentiostat constructed from a Kepco Model BOP72-5M bipolar operational amplifier capable of a maximum output of 5.5 A at 80 V was employed (power supply C). The only significant difference between the power supplies is the time of the electrolysis. After electrolysis, the solution was concentrated on the rotary evaporator at <35 °C, the residual oil partitioned between water and ether (or methylene chloride), and the water layer extracted several times with organic solvent. After the organic layer was washed with saturated brine solution and dried over Drierite or sodium carbonate, concentration in vacuo afforded the crude product.

2-Methyl-1,1,4,4-tetramethoxy-2,5-cyclohexadiene, 10a. A stirred solution of 3.5 g (23 mmol) of the aromatic compound[19] in 175 mL of 2% sodium methoxide in methanol was electrolyzed by using power supply C at 0.99–1.2 V relative to a Ag/AgCl electrode at 15 °C. The current ranged from a maximum of 2 A to a minimum of 60 mA at the conclusion of the electrolysis (5960 C passed, 74% current efficiency). Workup afforded 4.57 g of a yellow oil which crystallized in the freezer. Two recrystallizations at low temperature from ether gave 3.93 g (80%) of the bisketal in two crops as a pale yellow oil at room temperature: IR (neat) 2940 (s), 2832 (m), 1454 (m), 1403 (m), 1382 (w), 1316 (w), 1299 (w), 1206 (m), 1154 (m), 1170–1000 (br envelope, s), 964 (s), 691 cm^{-1} (w); NMR τ 4.05 (AB q, J = 10.7 Hz, $\Delta\nu$ = 13.2 Hz, "A" meta coupled, J = 2.1 Hz) and 4.24 (m) (3 H total), 6.82 (s, 6 H), 6.92 (s, 6 H), 8.32 (d, J = 1.6 Hz, 3 H); exact mass for $C_{11}H_{18}O_4$ calcd m/e 214.1205, obsd m/e 214.1210, difference 0.0005.

2-(Trimethylsilyl)-1,1,4,4-tetramethoxy-1,4-cyclohexadiene, 11a. A stirred solution of 1.0 g (4.75 mmol) of the aromatic compound in 100 mL of 2% methanolic potassium hydroxide was

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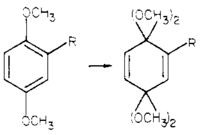
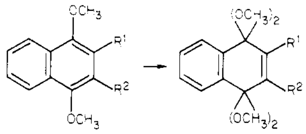
[18] All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Measurements of standard samples indicated that the observed melting points were probably 1–2 °C lower than the corrected value. Infrared spectra were recorded on a Perkin-Elmer Model 467 grating spectrometer. ^1H NMR spectra were taken at 60 MHz with Varian EM-360 or A-60A instruments. ^{13}C NMR spectra (Me_4Si reference) were recorded on a Bruker HX-90 instrument by Dr. Charles Cottrell. Mass spectra and exact mass measurements were obtained by Mr. C. R. Weisenberger on a Consolidated Electronics MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Micronolyticol Laboratory, Herlev, Denmark. Aluminum oxide and silica gel were obtained from E. Merck Co. Tetrahydrofuran was distilled from benzophenone ketyl directly into the reaction flask. Butyllithium in hexane (Ventron) was titrated in tetrahydrofuran with 1,10-phenanthroline as the indicator. Workup as usual refers to extraction with ether, washing of the ether layers with saturated brine solution, drying over calcium sulfate, and concentration in vacuo. In chromatography, E refers to ether, while PE refers to petroleum ether, bp 35–50 °C.

[19] Kun, K.; Cassidy, H. J. Org. Chem. 1960, 25, 3223–6.

Table II. Anodic Oxidations in a Divided Cell



entry	compd	R	yield of bisketal, %	current efficiency^a	$E_{p/2}$, V^d
1	23	$NHC(O)CH_3$	17	78	1.09
2	24	$(CH_2)_2CO_2CH_3$	61	80	1.26
3	25	$(CH_2)_2C(O)N(CH_3)_2$	68	67	1.24
4	26	$(CH_2)_2C(O)NH_2$	50	67	1.23
5	27	$CH=CHCO_2CH_3$	46	49	1.35
6	28	C(O)H	26,^{b} 59^c	71,^{b} 59^c	1.51



entry	compd	R^1	R^2	yield of bisketal, %	current efficiency^a	$E_{p/2}$, V^d
7	29	Br	H	84		1.34
8	30	Br	CH_3	85	57	1.42
9	31	Br	Br	50	7	1.50

^{a} Current efficiency for complete two-electron oxidation of the aromatic compound. ^{b} Reaction at platinum anode, current efficiency calculated for four-electron oxidation to 35. ^{c} Reaction at reticulated vitreous carbon anode. ^{d} $E_{p/2}$ vs. SCE.

electrolyzed for 35 min at 1 A (power supply B) with the temperature held below 30 °C. The reaction was monitored by the disappearance of the UV absorption at 290 nm. Workup afforded 1.29 g of pale yellow liquid which gave on molecular distillation (bath temperature 80 °C, 0.1 mm) 1.2 g (93%) of the analytically pure bisketal: IR (neat) 2946 (s), 2902 (s), 2834 (s), 1465 (m), 1403 (s), 1349 (m), 1251 (s), 1207 (m), 1118 (s, br), 1070 (s, br), 1048 (s, br), 973 (s), 860 (s), 845 (s), 768 (m), 700 cm^{-1} (m); NMR τ 3.82 (m, 1 H), 3.97 (m, 2 H), 6.80 (s, 6 H), 6.90 (s, 6 H), 9.87 (s, 9 H).

Anal. Calcd for $C_{13}H_{24}O_4Si$: C, 57.32; H, 8.88. Found: C, 57.29; H, 8.76.

1,1,4,4-Tetramethoxy-2,3,5-trimethyl-2,5-cyclohexadiene, 12a. A solution of 2.00 g (11.1 mmol) of the aromatic compound[20] in 95 mL of 2% methanolic potassium hydroxide was electrolyzed for 1 h (power supply C), the solution being stirred and cooled below 5 °C. The initial current was 1.6 A at 1.19 V, the final current being 75 mA at 1.54 V. A total of 3235 C was passed (66% efficiency), the reaction being monitored by UV at 295 nm. Workup gave 2.62 g of a pale yellow oil which solidified in the freezer (mp 34–42 °C). One recrystallization from 10 mL of petroleum ether at low temperature gave 1.702 g (63%, mp 45–60 °C, >90% pure by NMR) of a pale yellow solid. The mother liquors (0.85 g) appeared to be 60–70% of the desired bisketal; the impurities were not readily characterizable, though spectra (NMR, IR) exclude monohydrolysis product(s) as major components ($\leq$5%). Further purification of this bisketal was accomplished only at the expense of losing roughly half of the material through repeated recrystallization. A sample which was homogeneous by IR and NMR (^{1}H and ^{13}C) had a melting point of 67.5–69.5 °C: IR (KBr) 3010 (m), 2950 (m), 2846 (m), 1456 (m), 1250 (m), 1220 (m), 1080 (vs), 1058 (m), 1035 (m), 964 cm^{-1} (m); NMR τ 4.10 (m, 1 H), 6.90 (s, 6 H), 7.16 (s, 6 H), 8.3–8.5 (m, 9 H); ^{13}C NMR ($CDCl_3$) 139.7, 137.5, 133.1, 129.8, 98.9, 95.8, 50.7, 15.9, 11.6, 11.3.

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.53; H, 9.11.

1-(2,2,5,5-Tetramethoxycyclohexadienyl)-1-methoxyethane, 13a. A solution of 1.02 g (5.17 mmol) of the aromatic compound in 100 mL of 2% sodium methoxide in methanol was cooled (15 °C) and the magnetically stirred solution electrolyzed with power supply C (1.07–1.25 V vs. Ag/AgCl) with an initial current of 2.0 A and a final current of 25 mA (2314 C utilized, 43% efficiency). All glassware used in the workup was washed with aqueous ammonia. The colorless solution was concentrated in vacuo below 30 °C and the residue added to a separatory funnel containing saturated sodium chloride (20 mL) and ether (20 mL). The aqueous phase was then extracted with additional ether (3 × 10 mL). The ether/methanol was concentrated in vacuo, the residue dissolved in 10 mL of ether, and the ether solution washed with 1 mL of saturated sodium chloride. After the ether solution was dried and concentrated, 1.31 g (98%) of a nearly colorless oil was obtained, which was molecularly distilled (bath temperature 110 °C, 0.1 torr) to give 1.23 g (92%) of analytically pure material: IR (neat) 2976 (s), 2945 (s), 2912 (s), 2840 (s), 1463 (m, br), 1405 (m), 1315 (m), 1216 (m), 1158 (m), 1130–1050 (s), 975 cm^{-1} (s); NMR τ 3.75–4.21 (m, 3 H), 6.30 (q, J = 6.5 Hz, 1 H), 6.77, 6.79, 6.82, 6.83, and 6.87 (overlapping singlets, 15 H), 8.77 (d, J = 6.5 Hz, 3 H).

Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.58; H, 8.54.

2,2,5,5-Tetramethoxy-2,5-dihydrobenzaldehyde Ethylene Ketal, 14a. A solution of 3.9 g (18.3 mmol) of the aromatic compound in 200 mL of 2% methanolic sodium methoxide at 15 °C was electrolyzed by using power supply C, the electrolysis being followed by the decrease in the UV absorption at 295 nm. The initial current was 4–5 A (1.10 V vs. Ag/AgCl), and after passage of 10 445 C (34% efficiency) the current was 60 mA (1.15 V vs. Ag/AgCl). Workup afforded 4.75 g of a thick yellow oil which was molecularly distilled in a base-washed apparatus to give 4.36 g (88%) of analytically pure product: IR (neat) 2946 (m), 2900 (m), 2836 (m), 1467 (m), 1398 (m), 1166 (m), 1116 (s), 1060 (s, br), 973 cm^{-1} (s); NMR τ 3.66 (d, J = 2.8 Hz, 1 H), 4.04 (AB q, J = 10.7 Hz, $\Delta\nu$ = 15.3 Hz, "A" meta coupled, J = 2.8 Hz, 2 H), 4.77 (s, 1 H), 6.12 (m, 4 H), 6.79 (s, 6 H), 6.90 (s, 6 H).

Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.63; H, 7.50.

1-(2,2,5,5-Tetramethoxycyclohexadienyl)ethanol, 15a. A stirred solution of 1.00 g (5.5 mmol) of the aromatic compound[21] in 100 mL of 2% methanolic potassium hydroxide was electrolyzed at 1 A (power supply B) until the UV absorption at 290 nm decreased to <5% of its initial value. Standard workup afforded 1.18 g of a yellow oil which appeared to be primarily the bisketal 15a by ^{1}H NMR. Chromatography on activity III neutral alumina

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(20) Smith, L. I. *J. Am. Chem. Soc.* **1934**, *56*, 472–4.

(21) Williams, J. *J. Org. Chem.* **1954**, *19*, 1205–14.

(50% ether/petroleum ether) separated only a minor amount of 2,5-dimethoxyacetophenone (10 mg) from the mixture, and the remaining material (~1 g) was chromatographed on a Merck Lobar "B" silica gel column. Elution proceeded as follows (E = ether and PE = petroleum ether): 50% E/PE (80 mL), nil; E (80 mL), nil; E (40 mL), 10 mg of pure **33**; 1% CH_3OH/E (20 mL), 29 mg of **33** and **32**; 1% CH_3OH/E (20 mL), 32 mg of pure **32**; 1% CH_3OH/E (80 mL), monoketals and other impurities (93 mg); 1% CH_3OH/E (140 mL), 0.482 g of **15a**; 1% CH_3OH/E (180 mL), 0.318 g of a mixture of **15a** and a fourth product. The estimated yield of bisketal **15a** was ~50%, with the material being about 95% pure (contaminated with monoketal(s) hydrolysis products). The bisketal **15a** showed the following: NMR τ 3.80 and 3.97 (m and AB q, J = 11.4 Hz, $\Delta\nu$ = 12.6 Hz, "A" meta coupled, J = 2.4 Hz, 3 H total), 5.54 (q, J = 7 Hz, 1 H), 6.76, 6.81, and 6.90 (overlapping singlets, 12 H), 7.03 (br s, 1 H), 8.72 (d, J = 7 Hz, 3 H).

3-(2,2,5,5-Tetramethoxycyclohexadienyl)propanol, 16a, and 6,6,9-Trimethoxy-6,9-dihydrochroman, 36. A solution of 1.0 g (5.10 mmol) of **16**[26] in 95 mL of 1% sodium methoxide in methanol was electrolyzed by using power supply B at 0.75 A with a reticulated vitreous carbon anode until 2600 C was passed (38% current efficiency). Workup afforded 1.27 g of a yellow oil which was chromatographed on 200 g of activity III neutral alumina slurry-packed in 25% E/PE. Elution proceeded as follows: 25% E/PE (200 mL), 50 mg of unidentified product; 25% E/PE (100 mL), 35% E/PE (100 mL), 50% E/PE (70 mL), 0.24 g of **36**; 50% E/hexane (20 mL), 18 mg of a mixture of **36** and a third component; 50% E/PE (90 mL), 0.11 g of an unidentified product; 50% E/PE (320 mL), 75% E/PE (100 mL), E (140 mL), 0.16 g of an unidentified mixture; E (160 mL), 1% CH_3OH/E (200 mL), 3% CH_3OH/E (35 mL), 0.632 g of **16a**. Compound **36**, 0.24 g (21%), was homogeneous by IR, NMR, and TLC. The analytical sample was short-path distilled (0.1 mm, bath temperature 85–90 °C); IR (neat, NaCl) 2936 (s), 2824 (m), 1463 (m), 1430 (m), 1400 (m), 1372 (m), 1301 (m), 1202 (m), 1149 (s), 1100 (vs), 1070 (vs, br), 1015 (s), 959 (vs), 921 (m), 885 cm^{-1} (m); NMR τ 4.13 (s, 2 H), 4.43 (m, 1 H), 6.14–6.54 (m, 2 H), 6.82 (s, 6 H), 6.89 (s, 3 H), 7.40–8.54 (m, 4 H); exact mass for $C_{12}H_{18}O_4$ calcd m/e 226.1205, obsd m/e 226.1210, difference 0.0005.

Compound **16a**, 0.63 g (48%), could not be obtained analytically pure. The spectroscopic data are reported for material directly off the chromatography column: IR (neat) 3490 (m, br), 2956 (s, br), 2848 (m), 1657 and 1611 (impurities, w), 1466 (m), 1455 (m), 1445 (m), 1400 (m), 1315 (m), 1301 (m), 1208 (m), 1170–1010 (br envelope, vs), 972 cm^{-1} (s, br); NMR τ 4.00 (AB q, J = 10.9 Hz, $\Delta\nu$ = 12.3 Hz, "A" meta coupled, J = 1.8 Hz) and 4.17 (m) (3 H total), 6.27 (s, impurities), 6.29–6.59 (m, 2 H), 6.79 (s, 6 H), 6.89 (s, 6 H), 7.16 (br s, 1 H), 7.64–8.6 (m, 4 H).

1,1,4,4-Tetramethoxy-1,4-dihydronaphthalene, 18a. A slurry of 4.0 g (21.3 mmol) of 1,4-dimethoxynaphthalene[22] in 120 mL of 1% methanolic potassium hydroxide was oxidized by using power supply A at 8 °C for 2 h. The slurry gradually changed into a homogeneous solution as the electrolysis proceeded. Removal of the methanol afforded a purple solid which was taken up in 60 mL of 50:50 E/PE and washed with water (2 × 10 mL) and saturated brine solution (10 mL). After the mixture was dried over calcium sulfate and concentrated, 4.9 g of yellow oil was obtained which crystallized in the refrigerator (mp 37–42 °C). Recrystallization of this material from PE gave 3.95 g (74%) of white crystals: mp 43.0–44.5 °C (lit.[8d] mp 35–38 °C); IR (KBr) 2946 (m), 2835 (m), 1456 (m, br), 1393 (s), 1309 (m), 1293 (s), 1247 (m), 1206 (m), 1139 (m), 1074 (vs, br), 1038 (m), 1018 (s), 984 (m), 976 (m), 967 (m), 785 (s), 778 (s), 710 cm^{-1} (m); NMR τ 2.38–2.85 (m, 4 H), 3.78 (s, 2 H), 6.92 (s, 12 H); exact mass for $C_{14}H_{18}O_4$ calcd m/e 250.120 50, obsd m/e 250.120 99, difference 0.000 49.

2-Methyl-1,1,4,4-tetramethoxy-1,4-dihydronaphthalene, 19a. A solution of 3.50 g (0.017 mol) of the naphthalene[23] in 100 mL of 1% methanolic potassium hydroxide was electrolyzed at 6 °C for 2.5 h by using power supply A, the progress of the reaction being monitored by observing the UV absorption at 320 nm. Workup afforded 4.44 g of a light yellow solid. Three low-temperature recrystallizations from methanol gave 3.42 g (75%) of white solid, mp 64.5–66.5 °C. Repeated crystallization of this material from PE gave a constant melting point of 65.5–66.8 °C: IR (KBr) 2935 (m), 2832 (m), 1456 (m), 1358 (m), 1307 (m), 1262 (s), 1129 (m), 1080 (vs), 1046 (s), 1036 (m), 975 (m), 960 (m), 939 (m), 780 (s), 769 cm^{-1} (m); NMR τ 2.36–2.83 (sym m, 4 H), 3.87 (q, J = 1 Hz, 1 H), 6.88 (s, 6 H), 7.18 (s, 6 H), 8.17 (d, J = 1 Hz, 3 H); exact mass for $C_{15}H_{20}O_4$ calcd m/e 264.136 148 4, obsd m/e 264.136 78, difference 0.0006.

1,1,2,4,4-Pentamethoxy-1,4-dihydronaphthalene, 20a. The anodic oxidation of 1,2,4-trimethoxynaphthalene[24] (0.779 g, 3.57 mmol) was carried out in 70 mL of 2% potassium hydroxide (by weight) in methanol at 5 °C in 50 min by using power supply C while the solution was flushed with nitrogen. The disappearance of a UV absorption at 305 nm indicated the completion of the electrolysis. Workup afforded 1.009 g of a nearly white solid, mp 89–94 °C. One recrystallization from E/PE containing a small amount of methanol gave 0.828 g (83%) of product: mp 94–95.5 °C; IR (KBr) 2942 (m), 2833 (m), 1668 (s), 1451 (m), 1365 (w), 1315 (m), 1260 (m), 1240 (m), 1212 (m), 1120 (sh), 1100–1060 (vs), 1034 (m), 962 (m), 927 (m), 791 cm^{-1} (s); NMR τ 2.42–2.91 (m, 4 H), 4.90 (s, 1 H), 6.29 (s, 3 H), 6.95 (s, 12 H).

Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.42; H, 7.17.

2-Methyl-1,1,3,4,4-pentamethoxy-1,4-dihydronaphthalene, 21a. 2-Methyl-1,3,4-trimethoxynaphthalene[25] (3.50 g, 0.0151 mol) was dissolved in 150 mL of 2% (by weight) potassium hydroxide in methanol in a 250-mL jacketed beaker. The electrolysis was carried out below 10 °C by using power supply C (voltage set at 1.3 V) for 80 min. The reaction was followed by current drop and UV absorption (293 nm). Workup afforded 4.32 g of a yellowish solid, mp 74–84 °C. Recrystallization from high-boiling PE gave 3.83 g of white solid, mp 80–86 °C; a second recrystallization afforded 3.66 g (82%), mp 84–89 °C. A small amount was recrystallized twice more to give material with a constant melting point of 88–89.5 °C: IR (KBr) 2951 (m, br), 2831 (m), 1660 (m), 1455 (m), 1315 (m), 1281 (m), 1265 (m), 1237 (s), 1080 (vs), 1046 (m), 1032 (s), 954 (m), 919 (m), 786 cm^{-1} (s); NMR τ 2.3–2.8 (m, 4 H), 6.09 (s, 3 H), 6.97 and 7.13 (2 s, 12 H), 8.28 (s, 3 H); exact mass for $C_{16}H_{22}O_5$ calcd m/e 294.146 711 7, obsd m/e 294.147 36, difference 0.000 65.

2-Methyl-1,1,4,4-tetramethoxy-3-(trimethylsilyl)-1,4-dihydronaphthalene, 22a. To a cooled (≤20 °C), stirred solution of 2% methanolic sodium methoxide in methanol (100 mL) was added 1.085 g (3.95 mmol) of 1,4-dimethoxy-2-methyl-3-(trimethylsilyl)naphthalene. This was electrolyzed for 1 h (power supply C), starting at 1.15 V (2.04 A), the final current being 20 mA at 1.35 V. The total current passed was 3100 C (25% efficiency). The reaction was monitored by the disappearance of UV absorptions at 334, 318, and 290 nm. The pale yellow methanol solution was worked up as usual to give 1.259 g of a faintly yellow solid, mp 56–62 °C. Two recrystallizations from PE gave 0.704 g of product, mp 62–64 °C; a second crop (mp 53–60 °C, 0.359 g) giving good spectra was also obtained, for a total of 1.063 g (80%). The analytical sample had mp 66–67 °C: IR (KBr) 2946 (m), 2932 (m), 1449 (w), 1263 and 1268 (m), 1255 (s), 1226 and 1218 (w), 1137 (w), 1077 (vs), 1046 (m), 1013 (w), 872 (m), 848 (m), 785 cm^{-1} (s); NMR τ 2.32–2.80 (m, 4 H), 7.08 and 7.15 (2 s, 12 H total), 8.07 (s, 3 H), 9.71 (s, 9 H).

Anal. Calcd for $C_{18}H_{28}SiO_4$: C, 64.25; H, 8.39. Found: C, 64.31; H, 8.33.

Double-Cell Electrolyses. These electrolyses were performed in an H-cell, as previously described,[3d] in which the anode and cathode compartments were separated by a medium-porosity sintered glass frit. Only the anode compartment was stirred magnetically. The cell was immersed in a cold bath and the temperature monitored by a thermistor placed in the anode

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[22] Inoue, A.; Kuroski, N.; Konishi, K. *Bull. Univ. Osaka Perfect. Ser. A* **1959**, *8*, 31–55; *Chem. Abstr.* **1961**, *55*, 13853e.

[23] Ansbacher, S.; Fernholz, E.; Dolliver, M. A. *J. Am. Chem. Soc.* **1940**, *62*, 155–8.

[24] A compound reported to be 1,2,4-trimethoxynaphthalene (see ref 24a) has the same melting point and an analysis in agreement with 1-hydroxy-2,4-dimethoxynaphthalene (see ref 24b). (a) Brunner, O.; Hauke, P. *Monatsh. Chem.* **1954**, *85*, 88–91. (b) Baldwin, J. E.; Basson, H. H. *J. Org. Chem.* **1969**, *34*, 2788–90.

[25] Carrara, G.; Bonacci, G. *Gazz. Chim. Ital.* **1943**, *738* 225–40.

[26] Kabalka, G. *Tetrahedron* **1973**, *29*, 1159–62.

compartment when the Kepco BOP supply was used; otherwise, a thermometer was used. The anode compartment was filled with the material to be electrolyzed in the indicated solvent and the cathode compartment with the electrolysis solvent plus electrolyte. Diffusion through the frit was sufficiently slow that <10% of the solute diffused to the cathode compartment during the time of the electrolysis. The anode was a cylindrical platinum gauze electrode (25 mm in diameter × 50 mm high) while the cathode was a platinum sheet (8 × 8 mm).

2-Acetamido-1,1,4,4-tetramethoxy-2,5-cyclohexadiene, 23a. The 2,5-dimethoxyacetanilide[27] (1.0 g, 5.12 mmol) was dissolved in 60 mL of 2% methanolic potassium hydroxide and electrolyzed (power supply C) from 1.05 to 1.35 V (current 0.8–0.04 A) below 10 °C until 1272 C was passed (78% efficiency). Disappearance of starting material was ascertained by TLC on silica gel (ether eluent). The reddish brown solution was concentrated in vacuo and the residue partitioned between 25 mL each of ether and saturated brine solution. The aqueous phase was back-extracted with methylene chloride (4 × 15 mL), and the organic extracts were combined and dried. Concentration afforded 1.2 g of a red-brown oil which was filtered through 40 g of activity III neutral alumina (ether eluent), collecting 20-mL fractions. Fractions 3–6 contained 0.36 g of yellowish crystals of impure bisketal. One recrystallization from E/PE gave 0.23 g (17%) of pure bisketal: mp 133–136 °C (analytical sample melted at 137.5–138.5 °C); IR (KBr) 3275 (s), 2946 (m), 2836 (m), 1692 (s), 1678 (s), 1535 (vs), 1399 (s), 1349 (m), 1261 (s), 1103 (s), 1080 (vs), 1048 (s), 995 (m), 690 cm^{-1} (m); NMR τ 2.87 (d, J = 2.4 Hz, superimposed on NH, 2 H), 3.99 (AB q, J = 10.6 Hz, $\Delta\nu$ = 31 Hz, "A" meta coupled, J = 2.4 Hz, 2 H), 6.70 (s, 6 H), 6.83 (s, 6 H), 7.93 (s, 3 H); exact mass for $C_{12}H_{19}O_5N$ calcd *m/e* 257.1263, obsd *m/e* 257.1270, difference 0.0007.

Methyl-3-(2,2,5,5-tetramethoxy-1,4-cyclohexadienyl)-propionate, 24a. Methanol (freshly distilled from magnesium) was converted to 1% sodium methoxide in methanol by addition of sodium. The dimethoxy aromatic compound[28] (1.0 g, 4.5 mmol) was dissolved in 65 mL of the electrolysis solvent and transferred via syringe to the electrolysis cell maintained under a positive pressure of nitrogen. The material was electrolyzed by using power supply C, with the potential being raised from 1.3 V (0.25 A) to a final potential of 1.80 V (36 mA). The current efficiency was about 80% (1086 C passed). The methanol solution was poured into a mixture of 1:2 saturated salt solution/water (60 mL) and extracted with methylene chloride (2 × 20 mL) and ether (2 × 20 mL). The organics were combined and washed with saturated sodium chloride (2 × 15 mL), and the aqueous material was back-extracted with ether (2 × 20 mL). The organics were partially dried by passing them through Drierite and concentrated to a watery oil. The ether solution (10 mL) was then washed with 5 mL of saturated salt solution, dried over Drierite, and removed to give 0.87 g of a yellow oil with the expected IR and NMR spectra. Mechanical loss reduced this yield about 10–15%. Short-path distillation (0.1 mm, bath temperature 120–125 °C) gave 0.78 g of a colorless oil (61%): IR (neat) 2949 (m), 2838 (m), 1734 (s), 1465 (sh, m), 1442 (m), 1403 (m), 1363 (m), a range of overlapping absorptions from 1330 to 1020 (m to s), 970 cm^{-1} (s); NMR τ 4.06 (AB q, J = 11.1 Hz, $\Delta\nu$ = 11.9 Hz, "A" meta coupled, J = 2 Hz) and 4.24 (m) (3 H total), 6.42 (s, 3 H), 6.84 (s, 6 H), 6.92 (s, 6 H), 7.60 (br s, 4 H); exact mass for $C_{14}H_{22}O_6$ calcd *m/e* 286.1416, obsd *m/e* 286.1422, difference 0.0006.

3-(2,2,5,5-Tetramethoxy-1,4-cyclohexadienyl)-*N*,*N*-dimethylpropionamide, 25a. A solution of 0.976 g (4.11 mmol) of the aromatic compound in 65 mL of 2% methanolic potassium hydroxide was electrolyzed by using power supply C. The potential was set at 0.95 V (0.7 A) and was raised to 1.15 V (30 mA) near the completion of the electrolysis (1179 C, 67% current efficiency). The yellow solution was concentrated to ~30 mL and poured into 30 mL of 1:1 saturated salt solution/water and the organic material extracted with 20 mL of 1:1 E/methylene chloride. The aqueous phase was further extracted with methylene chloride (4 × 10 mL), and the organic phases were combined, dried, and concentrated to afford 1.027 g of oil whose NMR spectrum indicated this to be almost entirely the bisketal. Attempted short-path distillation (bath temperature 140–155 °C, 0.1 mm) afforded at first a liquid which then solidified on the cold finger: 0.84 g (68%), mp 50–53 °C. Recrystallization of this material at low temperature from 1:1 E/PE gave 0.742 g of white needles, mp 51–52.5 °C. A second recrystallization afforded the analytical sample: mp 52–53.5 °C; IR (KBr) 2945 (br, m), 2845 (m), 1641 (s), 1403 (m), 1394 (m), 1113 (sh), 1105 (s), 1083 (s), 1067 (sh), 997 cm^{-1} (m); NMR τ 4.01 (AB q, J = 10.7 Hz, $\Delta\nu$ = 12.0 Hz, "A" meta coupled, J = 2.3 Hz) and 4.16 (m) (3 H total), 6.80 (s, 6 H), 6.87 (s, 6 H), 6.98 (s, 3 H), 7.13 (s, 3 H), 7.59 (s, 4 H).

Anal. Calcd for $C_{15}H_{25}NO_5$: C, 60.18; H, 8.42. Found: C, 60.10; H, 8.35.

3-(2,2,5,5-Tetramethoxy-1,4-cyclohexadienyl)propionamide, 26a. A solution of the amide[29] (0.999 g, 4.78 mmol) in 65 mL of 2% methanolic sodium methoxide was cooled to ≤15 °C and electrolyzed by using power supply C. The initial current of 0.6 A (1.05 V) dropped throughout the electrolysis to 10 mA (1.25 V), and the UV absorption at 290 nm cleanly disappeared. Workup (extraction with methylene chloride) afforded 1.016 g of yellow solid, mp 85–91 °C, which was recrystallized from chloroform/E twice to give 0.65 g (50%) of white solid, mp 97.5–99 °C. One additional recrystallization gave the analytical sample: 0.55 g; mp 98.5–100 °C; IR (KBr) 3378 (br, s), 3192 (s), 2934 (m), 2824 (m), 1682 (sh, s), 1668 (s), 1625 (s), 1451 (br, m), 1399 (m), 1321 (m), 1222 (m), 1181 (m), 1146 (m), 1128 (m), 1073 (br, s), 1038 (s), 954 cm^{-1} (s); NMR τ 3.94 (AB q, J = 10.3 Hz, $\Delta\nu$ = 15.7 Hz, "A" meta coupled, J = 2.2 Hz) and 4.07 (m, vinyl and NH_2) (5 H total), 6.75 (s, 6 H), 6.85 (s, 6 H), 7.53 (s, 4 H); exact mass for $C_{13}H_{21}NO_5$ calcd *m/e* 271.1419, obsd *m/e* 271.1425, difference 0.0006.

Methyl (*E*)-3-(2,2,5,5-Tetramethoxy-1,4-cyclohexadienyl)propenoate, 27a. A solution of 1.00 g (3.25 mmol) of the aromatic in 65 mL of 2% methanolic sodium methoxide was electrolyzed by using power supply C with an initial current of 0.67 A (1.07 V) and a final current of 10 mA (1.45 V). Workup as usual afforded 1.07 g of yellow oil which was induced to crystallize, and the resulting solid was recrystallized twice from 30% E/PE at low temperature, followed by a low-temperature ether recrystallization. There resulted 0.61 g of light yellow solid, mp 55–61 °C. The NMR of the mother liquors showed the desired bisketal to be the major component; thus, they were chromatographed on 100 g of activity III neutral alumina. Elution proceeded as follows: 30% E/PE (125 mL), nil; 50% E/PE (100 mL), nil; 50% E/PE (125 mL), 120 mg of nearly pure bisketal. This material was combined with the previously obtained bisketal and recrystallized from 1:1 E/PE (at low temperature) to give 0.58 g (46%) of the pure bisketal: mp 60–62 °C; IR (KBr) 2950 (br, m), 2846 (m), 1717 (s), 1638 (m), 1620 (m), 1440 (m), 1412 (m), 1305 (s), 1255 (m), 1230 (m), 1199 (m), 1184 (m), 1170 (s), 1093 (vs), 1046 (m), 1011 (m), 972 cm^{-1} (m); NMR τ 3.26 (AB q, J = 16 Hz, $\Delta\nu$ = 34.9 Hz, 2 H), 3.71 (m, 1 H), 4.01 (AB q, J = 10.8 Hz, $\Delta\nu$ = 15.6 Hz, "A" meta coupled, J = 2.5 Hz, 2 H), 6.31 (s, 3 H), 6.76 (s, 6 H), 6.90 (s, 6 H); exact mass for $C_{14}H_{20}O_6$ calcd *m/e* 284.1260, obsd *m/e* 284.1267, difference 0.0007.

Continued elution with 100 mL of 50% E/PE, 225 mL of 75% E/PE, and 225 mL of pure ether gave ~50 mg of an uncharacterized mixture of compounds.

2-Bromo-1,1,4,4-tetramethoxy-1,4-dihydronaphthalene, 29a. A solution of 1.40 g (5.2 mmol) of 2-bromo-1,4-dimethoxynaphthalene[31] in 60 mL of 1% methanolic potassium hydroxide was anodically oxidized by using power supply A. The reaction was followed by UV spectroscopy, and the naphthalene absorption at 302 nm was decreased by >95% of its initial value in 5 h. Workup afforded a solid which was crystallized from E/PE to yield 1.46 g (84%) of pure, white, crystalline product: mp 65–67 °C; IR (KBr) 2946 (m), 2840 (m), 1453 (m), 1330 (m), 1250 (m), 1240 (m), 1094 (vs), 1078 (vs), 988 (m), 785 (s), 740 cm^{-1} (m); NMR τ 2.3–2.8 (m, 4 H), 3.22 (s, 1 H), 6.82 (s, 6 H), 7.05 (s, 6 H); exact

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mass for $C_{14}H_{17}O_4Br$ calcd *m/e* 328.0310646, obsd *m/e* 328.03142, difference 0.0004.

2-Bromo-3-methyl-1,1,4,4-tetramethoxy-1,4-dihydronaphthalene, 30a. A slurry of 3.0 g (10.7 mmol) of 2-bromo-3-methyl-1,4-dimethoxynaphthalene[32] in 65 mL of 2% methanolic potassium hydroxide solution was anodically oxidized by using power supply D. The reaction was followed by UV spectroscopy, and the naphthalene absorption at 293 nm was decreased by >95% of its initial value in 2 h. The initial heterogeneous reaction mixture became homogeneous as the reaction proceeded and then became heterogeneous again as the product precipitated. Workup (methylene chloride as extraction solvent) afforded a solid which was crystallized from E/PE to yield 2.96 g (81%) of pure, white, crystalline product: mp 147–149 °C; IR (KBr) 2998 (m), 2962 (m), 2934 (m), 2838 (m), 1456 (m), 1262 (s), 1225 (s), 1081 (vs), 816 (m), 791 (m), 734 cm^{-1} (m); NMR τ 2.3–2.7 (m, 4 H), 6.99 (s, 6 H), 7.05 (s, 6 H), 7.91 (s, 3 H).

Anal. Calcd for $C_{15}H_{19}O_4Br$: C, 52.50; H, 5.58; Br, 23.28. Found: C, 52.52; H, 5.57; Br, 23.40.

2,3-Dibromo-1,1,4,4-tetramethoxy-1,4-dihydronaphthalene, 31a. A slurry of the aromatic compound (1.0 g, 2.89 mmol) in 60 mL of 2% sodium methoxide in methanol was placed in the anode compartment of the H-cell and electrolyzed at 15 °C by using power supply C. The potential was gradually raised from 1.1 to 2.05 V (1970 C passed). A second 1.0-g sample was electrolyzed as above at 40 °C (2500 C passed). The two electrolytes were combined and the methanol removed in vacuo. The residue was diluted with 150 mL of water and the resulting solid collected by filtration. An NMR spectrum of this material indicated approximately 30% conversion to the bisketal (~7% current efficiency). The solid obtained above was boiled with ether (20–30 mL) and the bisketal removed by filtration. This material, mp 202–205 °C, was dissolved in chloroform, filtered, and then recrystallized from chloroform/E to give 0.65 g (50% based on reacted starting material) of the bisketal: mp 204–206 °C; IR (KBr) 2988 (m), 2952 (m), 2824 (m), 1607 (m), 1470 (m), 1454 (m), 1434 (m), 1240 (s), 1235 (s), 1209 (m), 1201 (m), 1183 (m), 1129 (m), 1111 (s), 1084 (vs), 1022 (m), 785 (s), 746 (s), 634 cm^{-1} (m); NMR τ 2.18–2.60 (m, 4 H), 6.94 (s, 12 H).

Anal. Calcd for $C_{14}H_{16}Br_2O_4$: C, 41.21; H, 3.95. Found: C, 41.21; H, 3.98.

Methyl 2,2,5,5-Tetramethoxy-1,4-cyclohexadienecarboxylate, 32. A solution of 1.0 g (6.02 mmol) of 2,5-dimethoxybenzaldehyde in 60 mL of 2% methanolic potassium hydroxide was electrolyzed under nitrogen below 20 °C with power supply C and the platinum gauze anode. The initial potential of 1.2 V (0.6 A) was slowly raised to 1.5 V (60 mA) as the reaction proceeded (3250 C). Standard workup gave 1.21 g of a yellow oil which was chromatographed on 40 g of activity III neutral alumina slurry-packed in 10% E/PE. Elution proceeded as follows: 10% E/PE (25 mL), 20% E/PE (50 mL), nil; 20% E/PE (50 mL), mixture of starting aldehyde and the bisketal methyl ester; 30% E/PE (125 mL), 0.45 g of the bisketal methyl ester. Further elution gave only small amounts of oil; thus, a majority of the material placed on the column was not eluted. Short-path distillation of the major component (bath temperature 105 °C, 0.1 mm) gave 0.43 g (28%) of the pure bisketal 32, identical with the known material.[3b]

In a second experiment, the electrolysis was carried out with 2% methanolic sodium methoxide and interrupted after 1800 C had been passed. The methanol was removed in vacuo, 20 mL of water was added to the warm solid to hydrolyze the ester, and the mixture was extracted with ether (3 × 15 mL). The ethereal layer contained 0.24 g of an oil which was primarily starting aldehyde by NMR. Acidification of the aqueous layer afforded, after workup and recrystallization, 0.37 g (34%) of white crystals of 2,5-dimethoxybenzoic acid, mp 74.5–76.5 °C (lit.[30] mp 76–77 °C), which showed an IR spectrum identical with that of an authentic sample.

Methyl 2,2,5,5-Tetramethoxy-1,4-cyclohexadienecarboxylate, 32. A solution of 2,5-dimethoxybenzaldehyde (1.01 g, 6.08 mmol) in 70 mL of 2% potassium hydroxide in methanol in one arm of an ice-cooled H-cell was stirred vigorously and electrolyzed for 2.25 h by using power supply D and the reticulated vitreous carbon anode. The initial current was 0.5 A at a total applied voltage of 45 V; this remained constant the first 45–50 min, and then the total voltage climbed to 60–70 V to maintain the current. Shortly thereafter, no aldehyde was visible by TLC (25% E/PE, silica gel), though the aromatic ester was still visible. Toward the end of the electrolysis, the current dropped as low as 0.35 A as the power supply output voltage maximized. Roughly 4000 C were passed (59% efficiency). When stopped, only a trace of the aromatic ester was visible by TLC. Workup afforded 1.08 g of a yellow oil which was the nearly pure bisketal of the ester. Short-path distillation (0.1 mm, bath temperature 100–120 °C) gave 0.92 g (59%) of a pale yellow oil having the expected spectral characteristics.

1,4-Dimethoxy-2-(trimethylsilyl)benzene, 11. A solution of 3.00 g (13.8 mmol) of bromo-1,4-dimethoxybenzene and 3.51 mL (3.00 g, 27.6 mmol) of trimethylsilyl chloride containing 1% triethylamine in 25 mL of dry tetrahydrofuran under a nitrogen atmosphere was cooled to −65 °C and magnetically stirred. A 10.2-mL portion of 1.66 M *n*-butyllithium (16.9 mmol) was then slowly syringed in over a 10-min period, the temperature being maintained below −60 °C. Gas chromatography (0.125 in. × 25 ft, 5% SE-30 on 60/80 Chromosorb G, column temperature 185 °C) indicated nearly quantitative conversion to the product. The reaction was quenched by adding 5 mL of saturated sodium bicarbonate and worked up as usual to give 2.987 g of a nearly colorless oil which contained only a small amount of protonated starting material as an impurity (GLC). This material was filtered through 30 g of silica gel with 5% E/PE as the eluent as follows: 40 mL, nil; 60 mL, 2.68 g of product (trace of solvent); 60 mL, 0.303 g of a mixture of the silyl compound and *p*-dimethoxybenzene. The mixture was filtered through the same column: 80 mL, nil; 20 mL, 0.188 g of product; 20 mL, 0.043 g of a mixture. The pure fractions were combined and molecularly distilled (70 °C, 0.1 mm) to give 2.59 g (89%) of pure product as a clear musty-smelling liquid: NMR τ 3.25 (m, 1 H), 3.39 (m, 2 H), 6.32 and 6.35 (2 s, 6 H), 9.77 (s, 9 H); IR (neat, NaCl) 2950 (m), 2832 (w), 1581 (w), 1473 (s, br), 1438 (s), 1404 (s), 1276 (s), 1226 (vs, br), 1183 (m), 1152 (m), 1079 (w), 1053 (m), 1030 (m), 888 (m), 840 (s, br), 768 (m), 730 (m), 688 (m), 628 cm^{-1} (m); exact mass for $C_{11}H_{18}O_2Si$ calcd *m/e* 210.1076, obsd *m/e* 210.1080, difference 0.0004.

1-(2,5-Dimethoxyphenyl)-1-methoxyethane, 13. A slurry of 3.0 g of 2,5-dimethoxybenzaldehyde in 30 mL of tetrahydrofuran at −55 °C was treated with 12.5 mL of 1.6 M methyllithium in ether. After 15 min at −50 °C, GLC (25 ft × 0.125 in., 5% SE-30 on 60/80 Chromosorb G, column temperature 185 °C) showed that only a trace of aldehyde remained. Methyl iodide was then added (1.2 mL, 19.3 mmol), and after an induction period, the temperature suddenly climbed to 0 °C. The mixture was then refluxed gently for 1 h, but little of the desired ether was formed (GLC), so 100 mg of sodium hydride and an additional 1.2 mL of methyl iodide were added. After the mixture was refluxed for 0.5 h, approximately 50% of the ether had formed. An additional 0.8 mL of methyl iodide was added (7.75 g, 54.6 mmol total), and the reaction was complete within 4 h. Standard workup, decolorization with charcoal, and short-path distillation gave 3.27 g (92%) of the ether as a clear oil: IR (neat) 2976 (m), 2934 (m), 2836 (m), 1590 (w), 1496 (vs), 1466 (s), 1430 (m), 1421 (m), 1374 (m), 1355 (m), 1300 (m), 1281 (s), 1252 (m), 1223 (vs), 1185 (s), 1165 (m), 1118 (s), 1085 (s), 1055 (s), 1032 (m), 1015 (m), 810 (m), 716 (m), 700 cm^{-1} (m); NMR τ 3.20 (m, 1 H), 3.44 (m, 2 H), 5.44 (q, $J = 6.5$ Hz, 1 H), 6.33 (s, 6 H), 6.86 (s, 3 H), 8.73 (d, $J = 6.5$ Hz, 3 H); exact mass for $C_{11}H_{16}O_3$ calcd *m/e* 196.10993, obsd *m/e* 196.11034, difference 0.0004.

2,5-Dimethoxybenzaldehyde Ethylene Glycol Ketal, 14. The ketal was formed by azeotropic distillation of water from a mixture of 2.45 g (14.7 mmol) of the aldehyde, 11.3 g (182 mmol) of ethylene glycol, 0.25 g of *p*-toluenesulfonic acid monohydrate, and 100 mL of benzene using a Dean–Stark trap. After collection of about 5 mL of an ethylene glycol/water mixture, the reaction mixture was treated with 0.5 g of sodium hydroxide pellets and stirred overnight. Standard workup and short-path distillation (0.1 mm, bath temperature 105 °C) gave 2.99 g (97%) of the ketal containing <2% aldehyde by NMR: IR (neat) 2953 (s), 2885 (s), 2837 (s), 1594 (m), 1502 (s), 1468 (s), 1435 (m), 1405 (m), 1285

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(s), 1227 (s, br), 1202 (sh), 1185 (s), 1173 (s), 1075 (s, br), 1053 (s, br), 1033 (m), 968 (m, br), 890 (m), 821 (m), 737 (m), 716 (m), 704 cm^{-1} (m); NMR τ 3.08 (t, J = 1.6 Hz, 1 H), 3.37 (d, J = 1.6 Hz, 2 H), 4.09 (s, 1 H), 6.11 (rough d, $\Delta\nu$ = 2.4 Hz, 4 H), 6.33 (2 s, $\Delta\nu \simeq$ 1.4 Hz, 6 H); exact mass for $C_{11}H_{14}O_4$ calcd *m/e* 210.089 20, obsd *m/e* 210.089 60, difference 0.0004.

1,2,4-Trimethoxynaphthalene, 20. A solution of 15 g of sodium dithionite in 80 mL of water was shaken with a slurry of 10.00 g (0.0574 mol) of lawsone, 2-hydroxy-1,4-naphthoquinone, in 160 mL of ether for several minutes. Additional sodium dithionite (7 g, 0.126 mol total) was added in small portions with shaking until all of the solids went into solution and both layers were colorless or pale yellow. The ether layer was washed with 35 mL of saturated brine containing 0.5 g of sodium dithionite and then dried by being passed through magnesium sulfate into a 500-mL Erlenmeyer flask flushed with nitrogen. The ether was boiled off, and 90 mL of methanol was added, followed by addition of 44 mL of dimethyl sulfate (58.5 g, 0.464 mol). A solution of 37.2 g (0.93 mol) of sodium hydroxide in 40 mL of water was added to this stirred mixture at a rate which kept the solution boiling. After the addition was complete, the mixture was refluxed on the steam bath for 5 min, diluted with 100 mL of water, and extracted with ether (5 × 75 mL). Washing the ether with saturated sodium chloride solution containing some sodium hydroxide (2 × 50 mL), drying over magnesium sulfate, and removing the solvent gave 10.8 g of a reddish oil which was passed through an alumina column (0.75 in. × 6 in., eluted with PE) to give 10.25 g of a very pale yellow oil which crystallized when seeded (mp 36.5–39.6 °C). Dissolving the oil in 16.5 mL of 94% methanol/water at 40 °C and cooling the solution with seeding gave 9.70 g (77.6%) of product: mp 38.5–40 °C; IR (KBr) 2931 (w), 2837 (w), 1624 (m), 1595 (s), 1464 (s, br), 1378 (vs), 1359 (s), 1279 (m), 1225 and 1211 (s), 1171 (m), 1107 (vs), 1072 (m), 1029 (m), 1006 (m), 773 cm^{-1} (s); NMR τ 1.80–2.20 (m, 2 H), 2.50–2.97 (m, 2 H), 3.58 (s, 1 H), 6.14 (s, 3 H), 6.24 (s, 6 H); exact mass for $C_{13}H_{14}O_3$ calcd *m/e* 218.094 29, obsd *m/e* 218.094 60, difference 0.0003.

1,4-Dimethoxy-2-methyl-3-(trimethylsilyl)naphthalene, 22. To a solution of 5.0 g (17.8 mmol) of 2-bromo-1,4-dimethoxy-3-methylnaphthalene in 50 mL of dry tetrahydrofuran at –65 °C was slowly added 11.0 mL of 1.63 M *n*-butyllithium in hexane. After the reaction mixture was stirred for ca. 5 min, trimethylsilyl chloride containing some triethylamine (4.0 mL, 31.5 mmol) was slowly added via syringe. After being stirred for 0.5 h at –65 °C and 2 h at room temperature, the solution was poured into 20 mL of 10% sodium carbonate solution. Workup as usual gave 4.55 g of a yellow oil which was approximately an 85:15 mixture of the desired silyl compound and the debrominated starting material. Chromatography on 100 g of silica gel slurry-packed in 5% E/hexane proceeded as follows: 175 mL, nil; 125 mL, 2.61 g of pure silyl compound; 200 mL, 1.83 g of mixture. Rechromatography of the latter material afforded 1.1 g of the pure silyl compound. Short-path distillation (0.1 mm, bath temperature 105–120 °C) gave 3.53 g (72%) of the pure silyl compound: IR (neat) 3066 (m), 2980 (m), 2942 (s), 2898 (m), 2836 (m), 1576 (m), 1562 (m), 1451 (m), 1340 (vs), 1268 (s), 1256 (s), 1196 (m), 1170 (m), 1108 (m), 1090 (s), 1020 (m, br), 978 (m), 946 (m), 863 (s), 845 (s), 763 (s), 693 (s), 628 cm^{-1} (s); NMR τ 1.90–2.30 (m, 2 H), 2.47–2.93 (m, 2 H), 6.23 (s, 6 H), 7.58 (s, 3 H), 9.57 (s, 9 H); exact mass for $C_{16}H_{22}O_2Si$ calcd *m/e* 274.138 89, obsd *m/e* 274.139 51, difference 0.0006.

3-(2,5-Dimethoxyphenyl)-*N*,*N*-dimethylpropionamide, 25. To a stirred solution of the acid[33] (2.0 g, 9.51 mmol) in 5–6 mL of methylene chloride was quickly added 1.37 mL (19.1 mmol) of thionyl chloride via syringe. After 2 h of being stirred under nitrogen, this solution was transferred in small portions to a rapidly stirred solution of 40% aqueous dimethylamine (25 mL). After standard workup and short-path distillation (0.1 mm, bath temperature 150 °C), 1.74 g (77%) of a colorless oil was obtained: IR (neat) 2992 (w), 2938 (m), 2834 (m), 1642 (s, br), 1589 (m), 1500 (vs), 1467 (m, br), 1417 (m), 1401 (m), 1285 (m), 1267 (m), 1227 (vs), 1184 (m), 1145 (m, br), 1054 (s), 1033 (m), 807 (m), 719 (m), 708 cm^{-1} (m); NMR τ 3.27–3.69 (m, 3 H), 6.30 (s, 3 H), 6.36 (s, 3 H), 7.16 and 7.20 (2 s, 6 H), 7.24–7.93 (m, 4 H); exact mass for $C_{13}H_{19}NO_3$ calcd *m/e* 237.136 48, obsd *m/e* 237.137 11, difference 0.0006.

Methyl 3-(2,5-Dimethoxyphenyl)propenoate, 27. A slurry of 3.1 g (14.9 mmol) of the acid in 40 mL of methanol was heated to reflux and 0.4 mL of sulfuric acid added, whereupon the acid dissolved. After the mixture was refluxed for 18–20 h, standard workup and short-path distillation gave 2.99 g (90%) of the ester as a yellow oil; further purification can be accomplished by a low-temperature recrystallization from ether: mp 37.5–40 °C; IR (neat) 2998 (m), 2950 (m), 2838 (m), 1712 (vs), 1632 (s), 1582 (m), 1499 (vs), 1467 (s), 1435 (s), 1327 (s), 1295 (s), 1266 (s), 1243 (s), 1228 (s), 1197 (s), 1176 (vs), 1053 (s), 1031 (s), 994 (m), 868 (m), 814 (m), 715 (m), 709 cm^{-1} (d, m); NMR τ 2.21 (d, J = 16.2 Hz, 1 H), 3.09 (t, J = 1.8 Hz, 1 H), 3.30 (d, $J \approx$ 1.8 Hz, 2 H), 3.69 (d, J = 16.2 Hz, 1 H), 6.23 (s, 3 H), 6.31 (s, 6 H); exact mass for $C_{12}H_{14}O_4$ calcd *m/e* 222.089 20, obsd *m/e* 222.089 74, difference 0.0005.

2,3-Dibromo-1,4-dimethoxynaphthalene, 31. A slurry of 2,3-dibromo-1,4-naphthoquinone[34] (7.16 g, 22.7 mmol) in 160 mL of ether was shaken with a solution of 15 g (86.1 mmol) of sodium dithionite in 80 mL of water until the quinone had dissolved. The tan ether solution was washed with saturated brine (25 mL), dried, and concentrated in a stream of nitrogen. Methanol (35 mL) and dimethyl sulfate (17.2 mL, 0.182 mol) were added to the tan residue, and the solution was rapidly stirred as a solution of 15 g (0.38 mol) of sodium hydroxide in 15 mL of water was added at a rate to maintain a gentle reflux. Upon addition of alkali, the solution turned black and stayed that way. The mixture was then diluted with 150 mL of water and cooled in ice, and the red-brown solid was collected. Sublimation (0.1 mm, bath temperature 105 °C) overnight gave several grams of a yellow-orange solid which was then passed through 40 g of silica gel (10% E/PE eluent). Recrystallization of this material from ether afforded 2.2 g (29%) of colorless crystals: mp 119.5–121 °C; IR (KBr) 3066 (w), 2996 (w), 2972 (m), 2940 (m), 2848 (w), 1554 (s), 1497 (m), 1457 (s), 1447 (s), 1442 (s), 1422 (s), 1356 (vs), 1322 (m), 1312 (m), 1254 (m), 1197 (m), 1162 (m), 1084 (vs), 990 (vs), 963 (m), 866 (m), 797 (s), 771 (vs), 693 (s), 622 (m), 357 (m), and 342 cm^{-1} (m); NMR ($CDCl_3$) τ 1.78–2.13 (m, 2 H), 2.30–2.67 (m, 2 H), 6.60 (s, 6 H); exact mass for $C_{12}H_{10}O_2{}^{79}Br_2$ calcd *m/e* 343.9049, obsd *m/e* 343.9055, difference 0.0006.

1,1,4,4-Tetraethoxy-1,4-dihydrobenzene, 38. A solution of *p*-diethoxybenzene (1.00 g, 6.02 mmol) in 95 mL of absolute ethanol containing 1.75 g of potassium hydroxide pellets was cooled to below 10 °C, stirred vigorously, and electrolyzed for 140 min at a current of roughly 1 A and a potential ranging from 1.13 to 1.34 V by using power supply C. A total of 5500 C was passed (21% efficiency), the solution acquiring a reddish orange color which made it necessary to monitor the electrolysis by GLC (0.125 in. × 1 ft, 5% SE-30 on 60/80 Chromosorb G, column temperature 130 °C). The ethanol was removed at room temperature on the rotoevaporator; the dark red-orange residue was washed with 20 mL of water and then extracted with ether (3 × 15 mL). The ether was washed with 10 mL of saturated salt solution and filtered through Drierite. The ether was removed in vacuo, and the oil remaining was triturated three or four times with 5–10 mL of PE. The PE extracts were concentrated to give 1.67 g of an orange oil which crystallized in the freezer. This was filtered through 30 g of activity III neutral alumina with PE as the eluent. The first 200 mL of eluent contained 1.074 g (69%) of the nearly pure bisketal as an oily yellow crystalline solid. One recrystallization from 5 mL of PE at low temperature gave 0.974 g (63%) of a pale yellow solid, mp 39–41 °C. Two additional recrystallizations gave 0.914 g (59%) of a nearly white solid, mp 40–41.7 °C, with a pronounced spicy odor: IR (KBr) 2980 (s), 2930 (m), 2885 (m), 1414 (m), 1396 (sh, m), 1122 (s), 1099 (s), 1067 (s), 1052 (s), 1000 cm^{-1} (s); NMR τ 4.13 (s, 4 H), 6.54 (q, J = 7 Hz, 8 H), 8.82 (t, J = 7 Hz, 12 H); exact mass for $C_{14}H_{24}O_4$ calcd *m/e* 256.1675, obsd *m/e* 256.1680, difference 0.0005.

Determination of Oxidation Potentials. The oxidation potentials were determined by cyclic voltammetry using a Ag/AgCl electrode (0.4 M KCl as supporting electrolyte) which was –0.025

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to −0.05 V relative to a saturated calomel electrode. The appropriate correction factor was applied to the experimentally determined $E_{p/2}$ [$E_{p/2}$ is the potential on the oxidation wave where the current is half the maximum (peak) current]. The reference electrode was inserted in a salt bridge (1.0 M tetramethylammonium chloride) which tapered to a capillary tip. This was placed within 0.5 mm of the platinum disk (Beckman Instruments) working electrode. A short piece of platinum wire was used as the auxiliary electrode. Solutions were prepared by using acetonitrile distilled successively from calcium hydride and phosphorus pentoxide and stored under nitrogen over molecular sieves. Tetra-*n*-butylammonium perchlorate (0.05 M) was used as the supporting electrolyte, and the compound was (1–2) $\times 10^{-3}$ M. The potentials reported are those obtained with a scan rate of 0.1 V/s. The oxidations were not completely reversible at this scan rate, and for certain compounds, other oxidation waves were seen at higher potentials ($\leq$2.0 V). Accuracy of the $E_{p/2}$ values reported is estimated to be ±0.05 V.

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Registry No. **8**, 25245-34-5; **8a**, 60316-51-0; **9**, 2674-34-2; **9a**, 65400-01-3; **10**, 24599-58-4; **10a**, 60736-94-9; **11**, 72054-75-2; **11a**, 72054-78-5; **12**, 4537-09-1; **12a**, 72205-69-7; **13**, 72054-77-4; **13a**, 72054-80-9; **14**, 72054-76-3; **14a**, 72054-79-6; **15**, 41038-40-8; **15a**, 72205-70-0; **16**, 33538-81-7; **16a**, 72205-71-1; **17**, 19754-22-4; **17a**, 72054-81-0; **18**, 10075-62-4; **18a**, 37972-49-9; **19**, 53772-19-3; **19a**, 64648-82-4; **20**, 60683-53-6; **20a**, 72205-72-2; **21**, 35896-55-0; **21a**, 72214-02-9; **22**, 72205-73-3; **22a**, 72205-74-4; **23**, 3467-59-2; **23a**, 72205-75-5; **24**, 62397-61-9; **24a**, 72205-75-5; **25**, 72205-76-6; **25a**, 72205-77-7; **26**, 72205-78-8; **26a**, 72205-79-9; **27**, 28689-10-3; **27a**, 72205-80-2; **28**, 93-02-7; **28a**, 72205-81-3; **29**, 64648-81-3; **29a**, 64648-84-6; **30**, 53772-33-1; **30a**, 64648-85-7; **31**, 72214-03-0; **31a**, 72214-04-1; **32**, 72205-82-4; **33**, 1201-38-3; **36**, 72205-83-5; **38**, 72205-84-6; 2,5-dimethoxybenzoic acid, 2785-98-0; trimethylsilyl chloride, 75-77-4; methyl iodide, 74-88-4; ethylene glycol, 107-21-1; 2-hydroxy-1,4-naphthoquinone, 83-72-7; 3-(2,5-dimethoxyphenyl)propionic acid, 10538-49-5; 2,3-dibromo-1,4-naphthoquinone, 13243-65-7; *p*-diethoxybenzene, 122-95-2.

Organocopper Chemistry of Quinone Bisketals. Application to the Synthesis of Isoprenoid Quinone Systems

Bertrand L. Chenard,[1a] Michael J. Manning, Peter W. Raynolds, and John S. Swenton*[1b,2]

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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The reactions of organocuprates of 1,4-benzoquinone and 1,4-naphthoquinone bisketals are reported. These reagents, formed from the corresponding lithium reagent, cuprous iodide, and dimethyl sulfide react efficiently with allylic bromides (allyl, prenyl, geranyl, and phytyl), often with utilization of greater than one R group of the R_2CuLi. Their reactions with acid chlorides and benzyl bromide proceed with acceptable efficiency, but they are unreactive toward a number of other substrates. The utility of this chemistry in the synthesis of menaquinone-2, phylloquinone, cymopol, and cymopol methyl ether is described.

Whereas the quinone moiety is present in numerous natural-product systems, methods for carbon–carbon bond formation to quinones[3] have been limited to alkylation via a radical addition–oxidation sequence,[4] arylation using diazonium salts,[5] and functionalization of hydroquinone ethers followed by oxidation.[6] Recently there has been renewed interest in synthetic procedures for carbon–carbon bond formation at the quinone nucleus. Sequences involving allylation via π-allylnickel complexes[7] and allyltin reagents[8] and isoprenylation via protected quinones[9] and the utility of 2,5-dimethoxybenzoquinone[10] in effecting this objective have been published. Several years ago we noted that lithioquinone bisketals, readily available from the corresponding bromo derivatives by metal–halogen exchange, allowed introduction of carbon functionality into protected quinones.[2,11] Acid hydrolysis could be controlled to afford either the quinone or its monoketal in most cases.[12] Whereas 1 gave functionalized quinone bisketals in good yields with difficultly enolized ketones, aryl esters, and aryl aldehydes, it gave either no yields or poor yields

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