

Product and Mechanistic Studies of the Anodic Oxidation of Methoxylated Naphthalenes. The EEC_rC_p Mechanism

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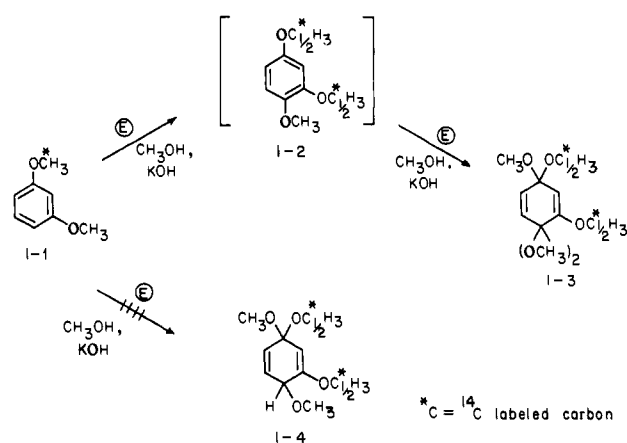
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Abstract: The anodic oxidations of 1- and 2-methoxy- and 1,2-, 1,3-, 1,4-, 1,5-, 1,6-, 1,7-, 2,3-, 2,6-, and 2,7-dimethoxynaphthalenes have been studied in methanolic potassium hydroxide. At lower temperatures (0–20 °C) the major process in 1-methoxynaphthalene and 1,5-, 1,6-, and 1,7-dimethoxynaphthalenes is two-electron oxidation resulting in addition of methoxy groups across the 1,4-positions followed by loss of methanol on workup to afford the methoxylated naphthalene. In contrast, 2-methoxynaphthalene and 1,3-, 2,3-, 2,6-, and 2,7-dimethoxynaphthalenes give major amounts of products derived from four-electron oxidation under these conditions. When the anodic oxidation of this first class of compounds was conducted in refluxing methanol, increased amounts of four-electron oxidation products were isolated. While 1-methoxynaphthalene and naphthalene also undergo anodic oxidation under these conditions, these unactivated systems react less selectively and efficiently. Mechanistic studies are most consistent with the key step of the anodic oxidation under these conditions being the reaction of methoxy radical with the aromatic radical cation. This reaction sequence is termed the EEC_rC_p mechanism, and the results of the oxidation of the methoxylated naphthalenes above are discussed in this format.

Direct methods for introduction of oxygenated substituents into aromatic rings are often quite limited. Classically, this has been achieved by the hydrolysis of aryldiazonium salts,³ alkali fusion of arylsulfonic acids,⁴ the Elb's persulfate oxidation of aromatic alcohols,⁵ the Dakin reaction,⁶ and Baeyer–Villiger oxidation of aryl aldehydes and ketones.⁷ Some recent methods for oxygenation of unactivated aromatics include routes via aryl organometallic species,^{8–10} peroxides and Lewis acids,¹¹ oxidations with cobalt(III) trifluoroacetate,¹² and a method employing hydrogen peroxide and super acid.¹³ Many of these methods lack generality and/or have shortcomings such as low yields, multistep sequences, and overoxidation problems. Thus, new methods for directly introducing oxygenated substituents into aromatic substrates are of continuing interest.

Anodic oxidation is potentially an excellent procedure for direct introduction of oxygen functionalities into aromatics.¹⁴ This reaction, which has been extensively studied in benzenoid systems, is often complicated by overoxidation of the aromatic compound.¹⁵ Thus, anodic oxidation of 1,3-dimethoxybenzene afforded the bisketal, I-3, in 66% yield (Scheme I). To establish the mechanism of this conversion, electrolysis of 1,3-dimethoxybenzene labeled with $-O^{14}CH_3$ in one of the methoxy groups gave I-3 with

Scheme I. Anodic Oxidative Pathways for 1,3-Dimethoxybenzene



complete retention of radioactivity.^{15c} This established that the oxidation of 1,3-dimethoxybenzene to 1,2,4-trimethoxybenzene proceeded without loss of an original methoxy group and supported the anodic substitution mechanism I-1 → I-2 → I-3. The involvement of an anodic addition compound (i.e., I-4) is ruled out by the published work since loss of methanol from I-4 would have eventually yielded I-3 with some loss of total radioactivity.^{15d} The problem of overoxidation as noted above is especially important in reactions involving replacement of hydrogen by an alkoxy group since introduction of this oxygen substituent decreases the oxidation potential of the product. Thus, the product formed in the initial substitution reaction is more reactive than the starting compound toward oxidation. Similar anodic oxidations have not been extensively studied in substituted naphthalenes. Anodic oxidation of a series of 1,4-dimethoxynaphthalenes afforded the respective 1,4-naphthoquinone bisketals in high yield,¹⁶ while naphthalene, 1-methoxynaphthalene, and 2-methoxynaphthalene on anodic oxidation in methanolic potassium hydroxide afforded the product mixtures shown in eq 1.^{17a}

Anodic methoxylation of aromatic hydrocarbons has recently been of considerable interest as an entry to quinone bisketals,^{16c} quinone monoketals,¹⁸ and methoxylation reaction of aromatic

(1) National Science Foundation undergraduate research student 1977, Conoco Predoctoral Fellow, 1980–1981.

(2) For preliminary reports of some of this work, see: Jackson, D. K.; Swenton, J. S. *Synth. Commun.* 1977, 7, 333–337. Dolson, M. G.; Jackson, D. K.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* 1979, 327–329.

(3) "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, pp 453–455.

(4) "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, pp 175–176.

(5) Sethna, S. M. *Chem. Rev.* 1951, 49, 91–101.

(6) Dakin, H. D. *Am. Chem. J.* 1909, 42, 477–498.

(7) Friess, S. L.; Soloway, A. H. *J. Am. Chem. Soc.* 1951, 73, 3968–3972.

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(9) Lewis, N. L.; Gabhe, S. Y.; DeLaMeter, M. R. *J. Org. Chem.* 1977, 42, 1479–1480.

(10) (a) Buck, P.; Koblrich, G. *Tetrahedron Lett.* 1967, 1563–1565. (b) Wiriyachitra, P.; Cava, M. P. *J. Org. Chem.* 1977, 42, 2274–2277.

(11) Kurz, M. E.; Johnson, G. *J. Org. Chem.* 1971, 36, 3184–3187 and references cited therein.

(12) Kochi, J. K.; Tang, R. T.; Bernath, T. *J. Am. Chem. Soc.* 1973, 95, 7114–7123.

(13) Olah, G. A.; Ohnishi, R. *J. Org. Chem.* 1978, 43, 865–867.

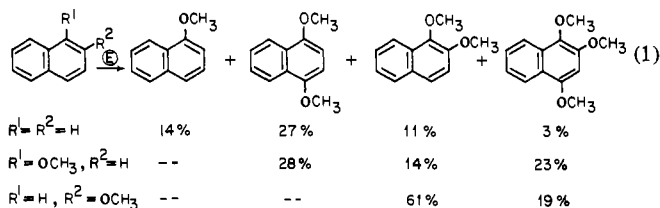
(14) (a) Ebersson, L.; Nyberg, K. *Tetrahedron* 1976, 32, 2185–2206. (b) Blum, Z.; Cedheim, L.; Nyberg, K. *Acta Chem. Scand. Ser. B* 1975, B29, 715–716. (c) So, Y.; Miller, L. L. *Synthesis* 1976, 468–469.

(15) (a) Ebersson, L.; Nyberg, K. *Acc. Chem. Res.* 1973, 6, 106–112. (b) Belleau, B.; Weinberg, N. L. *J. Am. Chem. Soc.* 1963, 85, 2525–2526. (c) Weinberg, N. L.; Belleau, B. *Tetrahedron* 1973, 29, 279–285. (d) The possibility that I-4 is formed and then oxidized directly to I-3 in a second step is unlikely. Compound 2 (vide infra), a compound with a similar activated hydrogen, can be isolated with no difficulty from the anodic oxidation of 1.

(16) (a) Svensson, L. *Acta Chem. Scand.* 1972, 26, 2372–2384. (b) Manning, M. J.; Henton, D. R.; Swenton, J. S. *Tetrahedron Lett.* 1977, 1679–1682. (c) Henton, D. R.; McCreery, R. L.; Swenton, J. S. *J. Org. Chem.* 1980, 45, 369–378.

(17) (a) Bockmair, G.; Fritz, H. P. *Electrochim. Acta* 1976, 21, 1099–1100. (b) See also Ebersson, L.; Helgee, B. *Chem. Scr.* 1974, 5, 47–48.

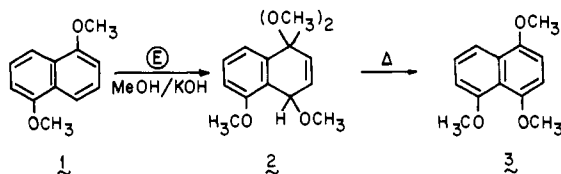
(18) Henton, D. R.; Anderson, K.; Manning, M. J.; Swenton, J. S. *J. Org. Chem.* 1980, 45, 3422–3433.



systems.¹⁹ For full exploitation and extension of this type of anodic oxidation, a detailed knowledge of the mechanism of the reaction is essential. Of special interest is the initial position of attack of the methanol-derived fragment on the aromatic ring and the nature of the species (methoxide or methoxy radical) involved in the anodic addition steps. While 1,4-dimethoxyaromatics afford no information of the initial position of attack on the aromatic ring, product studies from anodic oxidation of less symmetrical species could afford an answer to this question. We report here product studies of the anodic methoxylation of a series of methoxynaphthalenes and the utilization of mechanistic results from 1- and 2-methoxynaphthalene investigations to explain the course of these and related reactions.

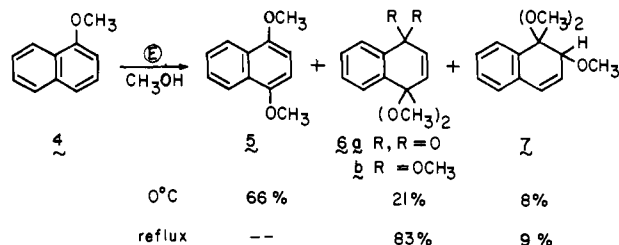
Product Studies

1,5-Dimethoxynaphthalene (1). Anodic oxidation of a slurry of 1,5-dimethoxynaphthalene in 1% methanolic potassium hydroxide at 0–20 °C led to formation of the 1,4-addition product **2** in nearly quantitative yield.² Even performing the anodic ox-



idation in refluxing methanol gave only **2**. Thus, in contrast to earlier studies in benzenoid systems, anodic addition is nearly the exclusive process here. The structure of **2** rests on its NMR spectrum and its conversion to 1,4,5-trimethoxynaphthalene. While the elimination of **2** to yield **3** was previously effected in a second acid-catalyzed step,² a more synthetically expedient procedure involves heating the crude electrolysis mixture to ca. 60 °C while removing the solvent. The concentrated basic solution generated in this step apparently effects elimination of **2** to give **3**; thus, 1,4,5-trimethoxynaphthalene is obtained in a one-step operation in 85% yield. Since the intermediacy of a 1,4-addition product in this system was rigorously demonstrated, in subsequent work no attempt was made to isolate all of the initial electrolysis product(s). Ultraviolet analysis indicated that for most of the work reported below, only small amounts of naphthalene chromophore were present at the termination of the electrolysis. Thus, the crude electrolysis mixture was either heated and/or treated with dilute acid prior to product isolation and identification.

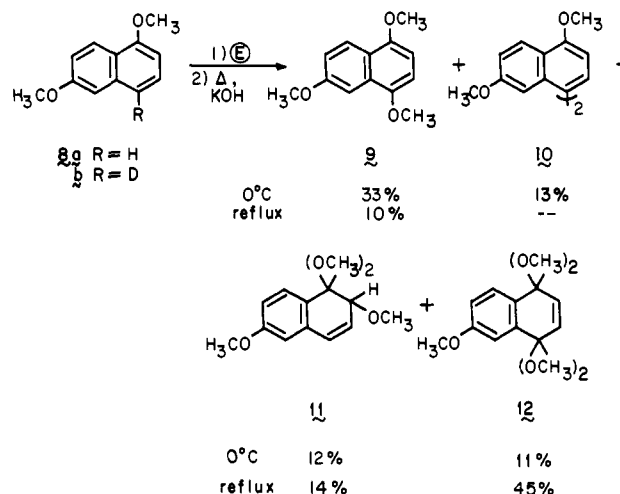
1-Methoxynaphthalene (4). The electrolysis of **4** at 0 °C was



continued until UV analysis indicated virtually no naphthalene chromophore remained. The products obtained after silica gel chromatography were **5**, **6a**, and **7**. Compounds **5** and **6a** were identified by comparison of their spectra with those of authentic samples, while **7** was assigned as the 1,2-addition product from

its spectroscopic properties and its conversion to the 1,2-dimethoxynaphthalene (98%) upon treatment with acid. Since only a small residual naphthalene type of UV absorption was present after electrolysis, **5** must have arisen from elimination of methanol from the 1,4-addition product analogous to **2**. Indeed, careful workup of the 0 °C anodic oxidation of **4** gave a mixture (NMR) of **6b**, **7**, and a labile anodic addition product. With use of the known spectra of **6b** and **7**, the NMR signals assigned to the 1,4-addition product (vide infra, **42**) are as follows: δ 7.67–6.95 (m, aryl), 6.20 (m, vinyl), 4.88 (br s, methine), and 3.13, 3.05, and 3.00 (s, methoxy). The formation of **6a** derives from monohydrolysis of the *p*-quinone bisketal, **6b**, during silica gel chromatography. A marked temperature effect on the product ratio was also noted.²⁰ Thus, performing the electrolysis in refluxing methanol followed by chromatography of the product mixture on neutral alumina resulted in the high-yield formation of **6b** to the exclusion of **5**, with the yield of **7** being unchanged.

1,6-Dimethoxynaphthalene (8). The anodic oxidation of **8**



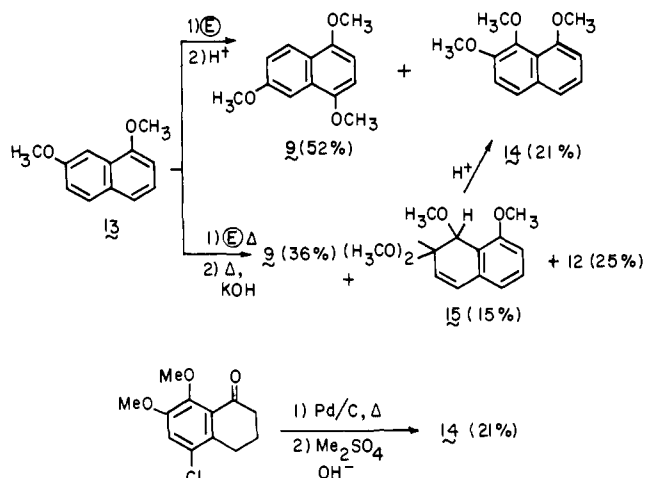
resulted in a lower accounting of material and the characterization of the following four products: the known compound **9**, the dimer **10**, the 1,2-addition product **11**, and the bisketal **12**. To rigorously establish the position of dimerization in **10**, the monodeuterio compound **8b** was electrolyzed. The dimer obtained from electrolysis of **8b** showed no deuterium by mass or NMR spectroscopy. The structure **11** is assigned on the basis of its spectroscopic properties and its conversion to the known 1,2,6-trimethoxynaphthalene upon treatment with acid. Likewise, the structure of **12** was assigned on the basis of its spectroscopic properties and confirmed by its conversion to the known 6-methoxy-1,4-naphthoquinone upon acid hydrolysis. Performing the electrolysis in refluxing methanol results in an increased amount of **12** and a reduced amount of **9**; the dimer was not detected in this higher temperature reaction.

1,7-Dimethoxynaphthalene (13). Electrolysis of **13** at 20 °C followed by treatment of the crude product mixture with trifluoroacetic acid afforded after chromatography the known **9** and an unknown trimethoxynaphthalene which has been assigned as **14**. The formation of the sterically congested **14** was quite unexpected; however, this structural assignment was rigorously established by its synthesis from 5-chloro-7,8-dimethoxy-1-tetralone²¹ as outlined below. Since neither **9** nor **14** could have been present in the crude electrolysis product (UV analysis), they most reasonably result from elimination of methanol from products derived from anodic addition across the 1,4- and 7,8-positions of **13**. Performing the electrolysis of **13** in refluxing methanol followed by removal of solvent at elevated temperature in the rotary evaporator and alumina chromatography showed the presence of some four-electron oxidation product, **12**, in addition

(19) (a) Konz, E.; Pistorius, R. *Synthesis* 1979, 603–605. (b) Groebel, B. T.; Konz, E.; Millauer, H.; Pistorius, R. *Ibid.* 1979, 605–607.

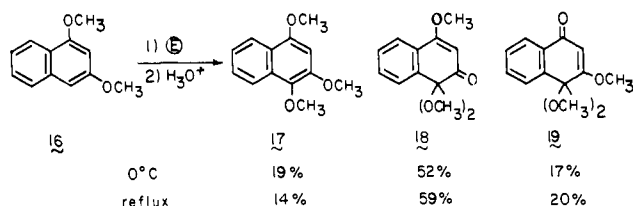
(20) A temperature effect on two- vs. four-electron products was first noted in benzo[*b*]thiophene anodic oxidations: Chenard, B. L.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* 1979, 1172–1173.

(21) Ghosh, R.; Robinson, R. *J. Chem. Soc.* 1944, 506–510.



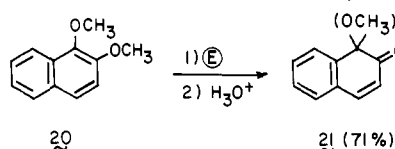
to a decreased amount of **9**. Again, the formation of the 1,2-addition product **15** (or **14**) was rather insensitive to the temperature of the anodic oxidation.

1,3-Dimethoxynaphthalene (16). The anodic oxidation of **16**



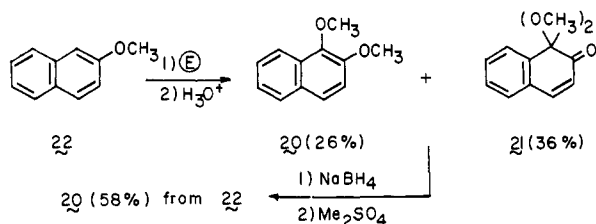
followed by aqueous acetic acid hydrolysis afforded the known **17**, derived from the 1,4-anodic addition process, and the known monoketals **18** and **19**, which have been shown to arise from hydrolysis of the respective bisketal.¹⁸ Performing the electrolysis at reflux temperatures produces very similar results. Therefore, unlike the systems we have seen thus far, **16** gives an exceedingly large amount of four-electron oxidation product with respect to the two-electron oxidation product, even in the low-temperature reaction.

1,2-Dimethoxynaphthalene (20). In this system anodic ox-



idation followed by oxalic acid hydrolysis produced a 71% yield of a quinone monoketal which was assigned structure **21** on the basis of spectroscopic and analytical data. Comparison of the UV spectrum of **21** with related systems in the literature suggested the orthoquinone monoketal chromophore (see Table I). Definite proof for **20** was obtained by a reduction-elimination sequence affording the known 1-methoxy-2-naphthol as described in the experimental section. Thus, in this system, a high preference for 1,2-anodic addition was observed.

2-Methoxynaphthalene (22). The anodic oxidation of **22**,



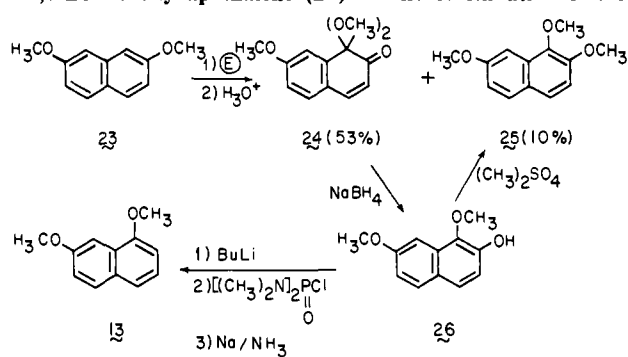
followed by oxalic acid hydrolysis, afforded, after chromatography, the following two products: **20** and **21**. Again in the anodic oxidation of **22** an intermediate could be detected. This compound which was obtained ca. 75% pure (contaminated with the bisketal **49**) showed an NMR spectrum consistent with **48** (vide infra):

Table I. UV Spectra of Orthonaphthoquinone Monoketals

compd						λ_{nm} (log ϵ)		
	R ¹	R ²	R ³	R ⁴	R ⁵			
--22a	H	H	H	CH ₃	Ac	233 (4.26)	241 (4.27)	319 (3.94)
--22b	CH ₃	H	H	Ac	Ac	237 (4.26)	330 (3.90)	
--22a	OCH ₃	H	H	Ac	Ac	234 (4.22)	357 (3.77)	
21	H	H	H	CH ₃	CH ₃	233 (4.30)	322 (3.84)	
24	H	H	OCH ₃	CH ₃	CH ₃	228 (4.17)	246 (4.28)	358 (3.96)
30	H	OCH ₃	H	CH ₃	CH ₃	252 (4.32)	314 (3.85)	

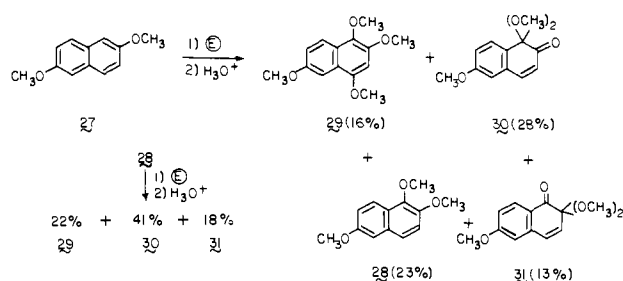
δ 7.25–6.95 (m, aryl), 6.19 (AB q, $\Delta\nu = 37$ Hz, $J = 10$ Hz with the upfield component split into a doublet, $J = 1.4$ Hz, vinyl), 3.92 (d, $J \approx 1.4$ Hz, methine), and 3.32, 3.15, and 3.07 (s, methoxy). The small coupling constant of 1.4 Hz between the vinyl group and the methine hydrogen was absent in the electrolysis product from 1-deuterio-2-methoxynaphthalene. Treatment of this material with acid afforded 1,2-dimethoxynaphthalene, **20**. Compound **20** is undoubtedly produced by loss of methanol from a 1,2-addition product (i.e., **48**). The monoketal **21** derives from secondary oxidation of an initially produced 1,2-dimethoxynaphthalene to an orthoquinone bisketal (**49**) followed by monohydrolysis. When the anodic oxidation was performed in refluxing methanol, the results were unchanged. The synthetic utility of this particular anodic oxidation is demonstrated by the conversion of the crude electrolysis mixture from **22** to 1,2-dimethoxynaphthalene in 58% overall yield.

2,7-Dimethoxynaphthalene (23). Anodic oxidation of this



system followed by acid hydrolysis again afforded a quinone monoketal, **24**—the product of four-electron oxidation—together with a two-electron oxidation product, **25**. Compound **25** exhibited spectroscopic and physical properties of 1,2,7-trimethoxynaphthalene. The monoketal again exhibited a UV spectrum (Table I) as well as other spectroscopic properties suggesting it was **24**. The oxygen substitution pattern was established by conversion to 1,2,7-trimethoxynaphthalene, while the location of the carbonyl was confirmed by conversion to **13**, as shown. Therefore, as for 2-methoxynaphthalene itself, **23** exhibits as a major process oxygen substitution at the α -position. As for 2-methoxynaphthalene, no temperature dependence of the product mixture was observed.

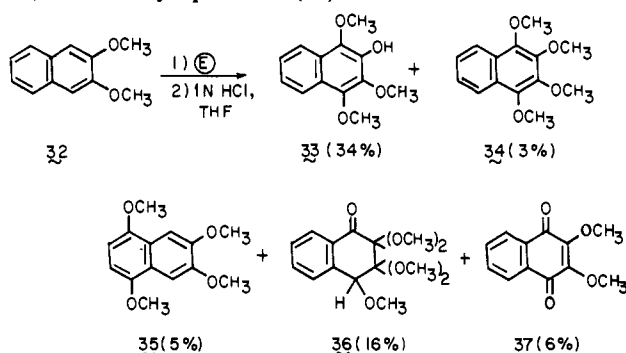
2,6-Dimethoxynaphthalene (27). Electrolysis of **27** followed



by acid hydrolysis afforded a four-component mixture of **28**–**31**.

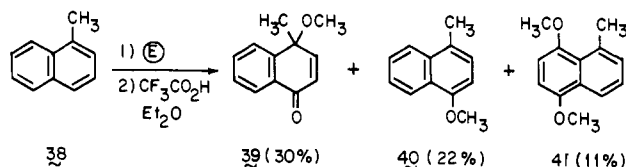
Compound **28** is known, and silver(II) oxide oxidation of **29** gave the known 2,6-dimethoxy-1,4-naphthoquinone. The structures of the monoketals **30** and **31** were established by a sequence of reactions identical with that used for **24** (see supplementary material for details). The more complex product mixture observed for **27** reflects the general problem attendant with many anodic oxidations: secondary oxidation of an initially formed product (i.e., **28**). Independent anodic oxidation of **28** followed by hydrolysis afforded **29–31** in the yields specified. As for the two other β -methoxy-substituted systems, no temperature dependence on the product ratio was observed.

2,3-Dimethoxynaphthalene (32). The anodic oxidation of 32



is quite complicated and appears to be of minimal synthetic value under these reaction conditions. Five products have been isolated, accounting for 64% of starting **32**. The structures of these products have been established by conversion to known systems as detailed in the supplementary material.

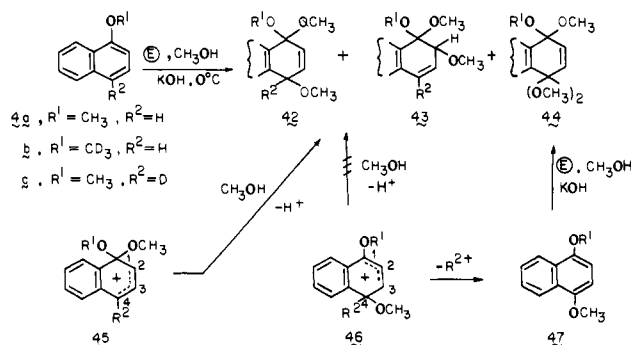
1-Methylnaphthalene (38) and Naphthalene. The anodic oxidation of 1- and 2-methoxynaphthalene gave products involving reaction in the methoxy-activated ring. Thus, we examined a system having only a methyl substituent to evaluate the selectivity of oxidation here and the parent system, also. Anodic oxidation of **38** gave a somewhat complex product mixture from which



39–41 were isolated and characterized. Compounds **40** and **41** are known, and the structure of **39** was established by conversion to 4-methyl-1-naphthol. Unfortunately, the modest accounting of material (ca. 63%) prevents a rigorous statement; however, it appears that the mildly activating methyl group directs reaction into the more substituted ring. Even naphthalene undergoes four-electron oxidation in refluxing methanol to give 1,4-naphthoquinone bisketal in 42% yield.

Mechanistic Studies

1-Methoxynaphthalene. As already noted the primary products formed in the anodic oxidation of **4** at 0 °C are the two-electron



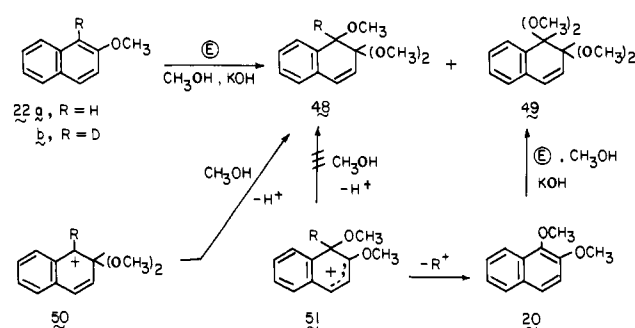
oxidation products **42** (66%) and **43** (8%) and the four-electron oxidation product **44** (21%). Of major interest are the inter-

mediates which lead to the major products **42** and **44**. Since anodic oxidation of **47** gives **44** (74%), **44** in this reaction undoubtedly derives from oxidation of **47** generated in situ. While control experiments strongly suggested that **42a** does not undergo elimination to **47** under these conditions, demanding evidence was desired for excluding this possibility. Accordingly, the anodic oxidation of **4b** was examined. Since **44b** formed in this reaction had one CD₃ group per molecule (NMR and mass spectral analyses), this *excludes* methanol elimination from **42** to give **47** and the sequence of reactions **42** → **47** → **44** as the source of **44** in the anodic oxidation of **4**.²³

Having now established that **44** is not formed via a trivial process from **42**, two mechanistic pathways are attractive to rationalize the anodic oxidation of **4**. First, **42** and **44** could arise from a common intermediate, **46**, which is formed from addition of a methanol-derived fragment at C-4 of oxidized **4**. Intermediate **46** would partition itself between methanol attack to give **42** and proton loss to afford **47** (thence **44**). Second, these two products could arise from different intermediates. The 1,4-addition product, **42**, would come from cation **45** which is formed by addition of a methanol-derived fragment at C-1, while **46** would be the precursor of **44**. If the first mechanistic pathway prevailed, i.e., **46** partitioning itself to **42** and **47**, the product ratio **42:44** should be isotope dependent. Thus, for the 4-deuterio compound, **4c**, the rate of the reaction **46** → **42** should be isotope independent, whereas the **46** → **47** process should be subject to a primary isotope effect. If the second mechanistic scheme prevailed with **46** undergoing exclusive conversion to **47** and **45** yielding **42**, the use of the 4-deuterio compound would afford virtually no change in the **42:44** product ratio. Anodic oxidation of **4c** gave **42** (as **5**), **43**, and **44** in the exact ratio as from anodic oxidation of **4**, thus excluding the intervention of solely the intermediate **46** in this reaction.

The 1,2-addition product **43** is formed in virtually the same yield either upon electrolysis at 0 °C or at the reflux temperature. This is undoubtedly due to the greater stability of **43** relative to **42** toward loss of methanol. While we favor **43** being formed by methanol attack at C-2 of **45**, an initial attack at C-2 of oxidized **4** followed by solvent attack at C-1 of this intermediate cannot be excluded.

2-Methoxynaphthalene (22). In contrast to 1-methoxy-



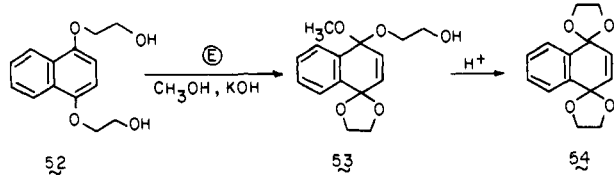
naphthalene, the anodic oxidation of 2-methoxynaphthalene afforded a minor amount of the two-electron oxidation product **48** (26%) and a major amount of the four-electron oxidation product **49** (36%). Anodic oxidation of **20** gives **49** in high yield; thus, the amount of **49** produced in the reaction of **22** comes from oxidation of **20** formed in situ. Since **48** is indefinitely stable under the anodic oxidation conditions, methanol elimination from **48** is not the source of the in situ formed **20**. The mechanistic arguments here are similar to those used in the 1-methoxynaphthalene anodic oxidation. The formation of **48** and **49** from

(22) (a) Hewgill, F. R.; Middleton, B. S. *J. Chem. Soc. C* **1967**, 2316–2321. (b) Ebnother, A.; Meijer, T. M.; Schmid, H. *Helv. Chim. Acta* **1952**, *35*, 910–928.

(23) An argument that **44** could be produced without loss of a OCD₃ group by a stereospecific 1,4-addition of methanol to give **42** followed by a stereospecific 1,4-elimination can be ruled out. The anodic oxidation of 1,4-diethoxybenzene in methanol gives ca. 50:50 cis/trans mixture of the mixed 1,4-benzoquinone bisketal.

22 could proceed from a common intermediate **51** which partitions itself between proton loss (forming **20**) and solvent addition (forming **48**) or via the independent pathways $50 \rightarrow 48$ and $51 \rightarrow 20 \rightarrow 49$. The route involving **51** as a common intermediate should have a different ratio of **48:49** depending upon whether $R = H$ or $R = D$ while the $50 \rightarrow 48$ and $51 \rightarrow 20 \rightarrow 49$ sequences would exhibit no product isotope effect. Anodic oxidation of **22b** gave **48** (isolated as **20**) and **49** (isolated as **21**) in the same ratio as it did **22a**.

1,4-Bis(2-hydroxyethoxy)naphthalene (52). While the product isotope effect studies afford information on the positions of initial attack in the anodic oxidation, they give no information on the nature of the attacking species. To examine this aspect of the mechanism, we studied the anodic oxidation of **52**. This system



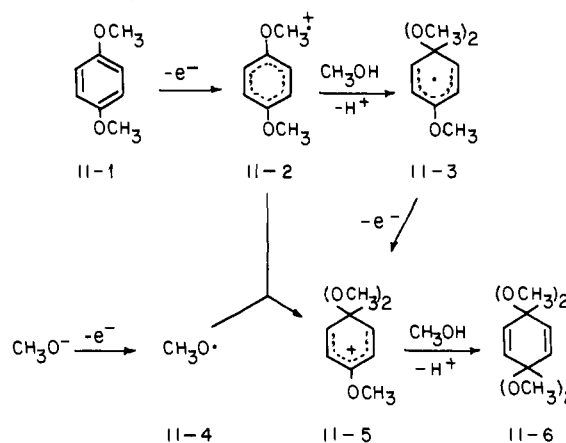
was chosen in preference to a 1- or 2-substituted naphthalene so that possible steric effects would not complicate interpretation of the results. Furthermore, interesting results had been obtained with the benzene analogue of **52** (vide infra); thus, a comparison of the mechanism of naphthalene vs. benzene anodic oxidation could be examined. Anodic oxidation of **52** gave **53** in 85% yield, no **54** being detected in the reaction. As noted in the analogous benzene system, **53** did undergo acid-catalyzed isomerization to **54**. The exclusive formation of **53** indicates a unique role for methanol in this reaction which is discussed below.

Discussion

Comparison with Previous Work. The products and product ratios from anodic oxidation of 1- and 2-methoxynaphthalene reported previously^{17a} (vide infra) and those given here are markedly different. The experimental conditions for both this and the earlier work appear similar except that (1) higher current densities were used here (10 mA·cm² vs. ~30 mA·cm²) and (2) the latter group distilled the crude electrolysis mixture and apparently analyzed the products by vapor-phase chromatography while the products here were isolated by adsorption chromatography. Especially striking is the large amount of 1,2-dimethoxynaphthalene reported from anodic oxidation of 2-methoxynaphthalene utilizing 9.4 faradays/mol of reactant. At a lesser number of coulombs (5.3 faradays/mol), we observed a major amount of the four-electron oxidation product. Furthermore, we observed no appreciable amount of 1,2,4-trimethoxynaphthalene in the reaction of either the 1- or 2-methoxy systems. We surmised that the 1,2,4-trimethoxynaphthalene of the earlier work formed via a thermal rearrangement in the distillation used to isolate the products. However, vacuum distillation of 1,4-naphthoquinone bisketal afforded no 1,2,4-trimethoxynaphthalene. Thus, we cannot satisfactorily account for the different product ratios observed in the anodic oxidation of 1- and 2-methoxynaphthalene in our studies and the earlier work.²⁴

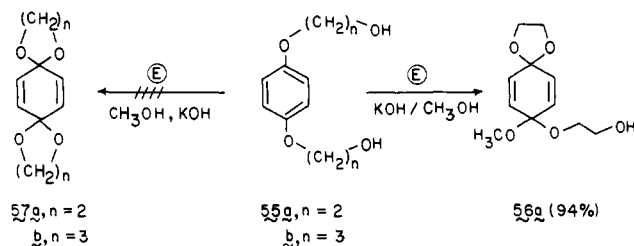
Temperature Effect on Products. As noted in the text the temperature of the anodic oxidation may alter the relative ratio of two- vs. four-electron oxidation products. While the oxidation of **1** at either 0 °C or reflux gave only the addition product **2**, due to the stability of **2** toward elimination of methanol to give **3**, naphthalenes **4**, **8**, and **13** gave increased amounts of four-electron oxidation product at the higher temperature. The nature of this temperature dependence was examined in more detail for **4**. Anodic oxidation of **4** in refluxing methanol gave an 83% yield of the four-electron oxidation product **6b**, with no **5** being detected. When the electrolysis of **4** at 0 °C was carried out until the UV absorption maximum disappeared, refluxing the electrolysis so-

Scheme II. Possible Mechanistic Pathways for Anodic Oxidation of 1,4-Dimethoxybenzene



lution for a time span equal to the initial electrolysis caused a reemergence of the naphthalene chromophore in the UV. Therefore, it is likely that the increased amount of four-electron product is due to in situ elimination of the 1,4-addition product followed by subsequent oxidation. Performing the electrolysis of **8** and **13** in refluxing methanol showed intermediate results; an increased amount of the four-electron oxidation product was observed but the two-electron oxidation product was still present in appreciable amounts. In contrast to naphthalenes **4**, **8**, and **13**, little temperature effect on product ratio was noted in the anodic oxidation of compounds **16**, **22**, **23**, and **27**. It appears that the increased amount of four-electron oxidation products observed at reflux temperatures in some of the systems is due to in situ elimination of 1,4-anodic addition products. Somewhat surprisingly some 1,2-anodic addition products (e.g., **7**) are quite stable under reflux conditions and the basic conditions present during product isolation.

The Basic Reaction Mechanism. Since the anodic methoxylation of naphthalenes has all of the characteristics of the earlier studied anodic methoxylation of 1,4-dimethoxybenzene, it is instructive to note mechanistic proposals for the latter reaction. Early workers favored a mechanistic scheme wherein anodically generated methoxy radical reacted with the neutral aromatic as a key step in the reaction.^{25a} Recent studies were again interpreted as supporting this route since anodic oxidation of **55a** in methanolic



potassium hydroxide gave **56a**, not **57a**.^{25b} These latter workers surmised that **56a** could only arise if methoxy radical attacked the neutral aromatic **55a**.^{25c} What apparently has been the most favored mechanism is the classical ECEC sequence, II-1 \rightarrow II-2 \rightarrow II-3 \rightarrow II-5 \rightarrow II-6 (Scheme II).²⁶ A third, more recent proposal favors a sequence involving methoxy radical attack on the aryl radical cation, II-1 \rightarrow II-2 and then II-2 + II-4 \rightarrow II-5 \rightarrow II-6.^{27,28} We term this sequence the EEC₁C_p pathway in which

(24) Acid-catalyzed (boron trifluoride) rearrangement of 1,4-naphthoquinone bisketal does afford 1,2,4-trimethoxynaphthalene (Henton, D. R., unpublished results).

(25) (a) For a discussion, see: Mann, C. K.; Barnes, K. K. "Electrochemical Reactions in Nonaqueous Systems"; Marcel Dekker: New York, 1970; pp 163-172. (b) Margaretha, P.; Tissot, P. *Helv. Chim. Acta* 1975, 58, 933-936. (c) We have verified the experiment of Margaretha and have also briefly studied the anodic oxidation of **55b** to establish that this result was not unique to the two-carbon side chain. Oxidation of **55b** yielded less than 5% of **57b** (see Experimental Section for details).

(26) Weinberg, N. L.; Belleau, B. *Tetrahedron* 1973, 29, 279-285.

(27) Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlan, A. *J. Chem. Soc., Perkin Trans. 1* 1978, 708-715.

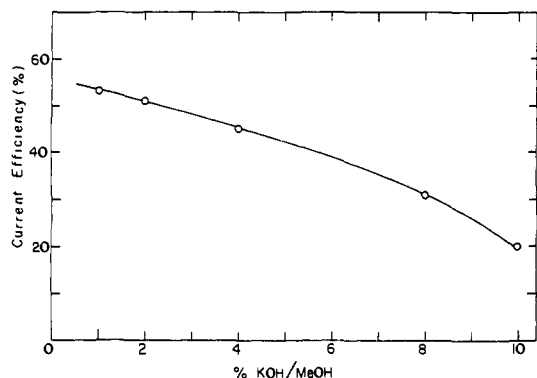


Figure 1. Current efficiency for anodic oxidation of 1-methoxynaphthalene as a function of base concentration.

the first two symbols denote the electrochemical steps required to form the methoxy radical and radical-cation species and C_r and C_p refer to chemical steps involving radical and polar intermediates, respectively.

Concerning the three mechanisms outlined above, the process involving methoxy radical attack on the neutral naphthalene can be excluded. If a solution of 1-methoxynaphthalene ($E_p = 1.38$ V) in 2% methanolic potassium hydroxide was electrolyzed at 1.03 V vs. SCE with 8 equiv of current relative to the aromatic compound, no oxidation of 1-methoxynaphthalene was noted. Under these conditions, methoxide oxidation occurs but not oxidation of the aromatic compound. In fact, methoxide discharge undoubtedly accounts for the less than 100% (i.e., 32–84%) of current efficiencies for anodic oxidation of 1,4-dimethoxybenzenes and -naphthalenes.^{16c} Furthermore, the importance of methoxide discharge should be a function of the base concentration. Indeed, as illustrated in Figure 1, the current efficiency for anodic methoxylation of 1-methoxynaphthalene decreases regularly with increasing base concentration. This decrease would be due to increasing amounts of methoxide discharge at the anode and indicates that optimum conditions for anodic oxidations of this type require the use of minimum base concentrations consistent with the required current flow in the reaction.

The choice between the ECEC and the EEC_rC_p mechanism is difficult. However, the oxidations $52 \rightarrow 53$ and $55a \rightarrow 56a$ indicate a unique role for a methanol residue. If an ECEC mechanism is operative, it is difficult to believe external attack by solvent on the aromatic radical cation could occur to the exclusion of intramolecular five-membered ring formation; it would seem some 54 and 57 should have been formed in the anodic methoxylation of 52 and 55 . While the above results strongly suggest the methoxy radical is involved in the reaction, we prefer to implicate its reaction with the aromatic radical cation rather than with the neutral aromatic as the unique aspect of the mechanism. The EEC_rC_p mechanistic scheme is undoubtedly a simplification, the key step of which is the reaction of an anodically generated methoxy radical with the aromatic radical cation. While the reaction of a transient species with a second transient species is generally of low probability in homogeneous reactions, the high concentration of such transient molecules in the vicinity or on the surface of the electrode makes this a more acceptable step in an electrochemical reaction. All mechanistic proposals are necessarily simplified; however, the EEC_rC_p mechanism is a convenient working hypothesis useful in predicting and explaining new anodic oxidation reactions of this type.

Two- vs. Four-Electron Oxidation Products of Methoxylated Naphthalenes. An interesting aspect of the product studies is the competition between oxidative addition and oxidative substitution reaction pathways for the methoxylated naphthalenes. For the α -methoxylated naphthalenes ($1, 4, 8, 13$), a two-electron process resulting in the formation of the 1,4-addition product (e.g., 2) is

the major oxidative pathway. Minor products formed during the anodic oxidation of the α -substituted naphthalenes are varied; however, commonly seen are products resulting from 1,2-anodic addition (e.g., $7, 11, 15$) and products resulting from a four-electron oxidation (e.g., $6, 12$). In contrast to the α -substituted naphthalenes, the major oxidation pathway of the β -methoxylated naphthalenes ($16, 22, 23, 27$) involves four-electron oxidation to yield the bis-ketal of the orthoquinone. In competition with the four-electron process is a two-electron oxidative addition pathway leading to the 1,2-addition product. Acid-catalyzed hydrolysis of these products affords the monoketals $21, 24, 30$, and 31 and the fully functionalized naphthalenes $17, 20, 25$, and 28 , respectively.

The mechanistic studies of 1- and 2-methoxynaphthalene offer a rationale as to why certain naphthalene derivatives give predominantly two-electron oxidation products and others give major amounts of four-electron oxidation products. It appears that attack of methoxy radical on the aromatic radical cation at a position bearing hydrogen on the ring will result in loss of a proton to give a substituted naphthalene which undergoes further oxidation. This is nicely demonstrated for 2-methoxynaphthalene in which cation 51 gives 20 which is subsequently oxidized to 49 . However if attack of methoxy radical occurs at the ipso position of the radical cation, the cation generated cannot aromatize readily and undergoes reaction with solvent to give the anodic addition product. Anodic oxidation of 1-methoxynaphthalene illustrates this case wherein 45 is formed which gives the anodic addition product 42 , and perhaps 43 . While space limitations prevent a thorough discussion of this point with all of the methoxylated naphthalenes studied, the results of the other systems are nicely accommodated by this rationale.

Positional Selectivity of Methoxy Radical Reaction with Methoxylated Naphthalenes. One of the initial goals of the extensive study of the anodic methoxylation of substituted naphthalenes was to develop a reliable criterion for the initial position of attack by methoxy radical on the naphthalene radical cation. This would not only serve as a predictive tool for the expected position of methoxylation in unknown systems but could aid in understanding the divergent behavior of methoxylated naphthalenes regarding the two- vs. four-electron oxidation processes. The studies outlined earlier strongly indicate that 1-methoxynaphthalene radical cations competitively react at the C_1 (major) and C_4 (minor) positions, while in the 2-methoxy system, methoxy radical reacts at the C_1 (major) and C_2 (minor) carbons. Several molecular orbital parameters have been utilized to correlate the position of anodic substitution reactions in aromatic systems. Most of these studies have assumed an ECEC mechanism (nucleophilic attack on the aromatic radical cation) and have correlated the position of attack with the charge density of the radical cation.²⁹ However, in aromatic cyanations, the spin density has been utilized to rationalize the position of cyanation in several benzenoid systems.³⁰ Here, too, an ECEC-type of mechanism was assumed. With use of the mechanistic reasoning of the previous section and the product and temperature studies noted earlier, the position of methoxy radical attack in a variety of methoxylated naphthalenes can now be ascertained. The data in Table II were constructed with one approximation: four-electron oxidation products derive from methoxy radical addition at a carbon-bearing hydrogen, while two-electron oxidation products result from methoxy radical attack at a carbon substituted with a methoxy group. Since quantitative accounting of material in these reactions was not possible, the data of Table I which are based on product studies must be considered approximate. Only four compounds

(29) (a) Cedheim, L.; Ebersson, L. *Acta Chem. Scand. Ser. B* **1975**, B29, 969–974. (b) Yoshida, K. *J. Am. Chem. Soc.* **1979**, 101, 2116–2121.

(30) Andreades, S.; Zahnaw, E. W. *J. Am. Chem. Soc.* **1969**, 91, 4181–4190.

(31) The HMO charge densities and coefficients were similar with use of either standard Hückel Theory or the ω technique.³²

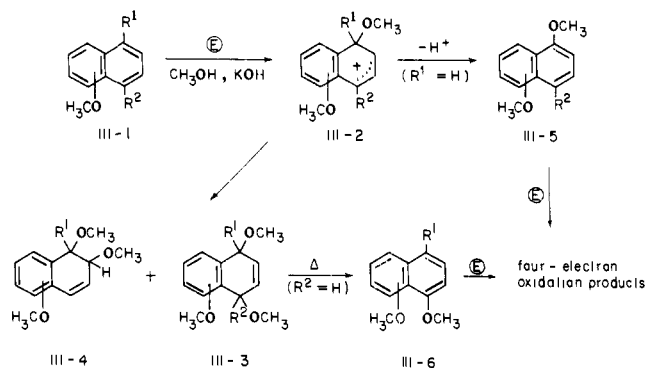
(32) Streitwieser, A. "Molecular Orbital Theory for Organic Chemists"; Wiley: New York, 1961. The parameters used were those recommended in Chapter 5: $h_O = 2.0$, $k_{C-O} = 0.8$, $\delta = 0.1$, $\omega = 1.4$.

(28) For an interesting discussion of aromatic nitration proceeding via radical attack on an aromatic radical cation, see: Perrin, C. L. *J. Am. Chem. Soc.* **1977**, 99, 5516–5518.

Table II. Positions of Methoxy Radical Attack on Methoxylated Naphthalene Radical Cations and Associated HMO Parameters of the Respective Radical Cations³¹

compd	methoxy radical attack	position of	
		highest charge density	highest spin density
1,5-(OCH ₃) ₂ , 1	C-1	C-1	C-4
1-OCH ₃ , 4	C-1 (74%), C-4 (21%)	C-1	C-4
1,6-(OCH ₃) ₂ , 8	C-1 (45%), C-4 (11%)	C-1	C-4
1,7-(OCH ₃) ₃ , 13	C-1 (52%), C-7 (21%)	C-1	C-1
1,3-(OCH ₃) ₂ , 16	C-1 (19%), C-4 (69%)	C-1	C-4
2-OCH ₃ , 22	C-1 (36%), C-2 (26%)	C-1	C-1
2,7-(OCH ₃) ₂ , 23	C-1 (53%), C-2 (10%)	C-1	C-1
2,6-(OCH ₃) ₂ , 27	C-1 (57%), C-2 (23%)	C-2	C-1

Scheme III. Generalized Scheme for Anodic Oxidation of Substituted Naphthalenes

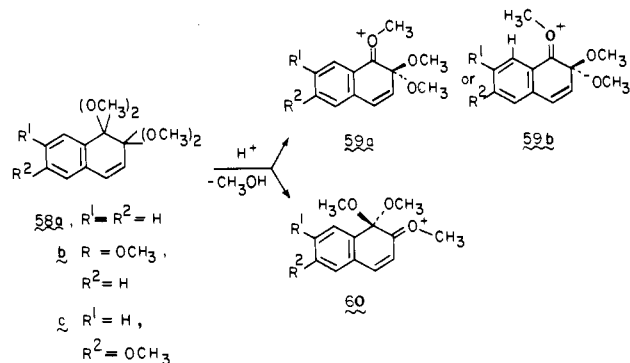


(1-methoxy, 1,6-, 2,6-, and 1,3-dimethoxy) have different centers of highest charge and spin density. In two of these cases [1-OCH₃ and 1,6-(OCH₃)₂] the center of highest charge density reacts with methoxy radical while for the two other compounds (1,3- and 2,6-dimethoxy), reaction of methoxy radical occurs at the center of highest spin density.³³ In all cases the major position for reaction of methoxy radical is at the α -position of the naphthalene, and unfortunately, neither spin nor charge densities give a reliable measure of which α -position is preferred. Other factors in the transition state for the reaction are undoubtedly of importance. A final point is the use of charge density as a criterion for predicting the site of substitution in electrochemical oxidations and as indirect support for the ECEC mechanism. As noted here the position of highest reactivity based on charge density is often the same as that predicted by spin density.

While simple HMO parameters do not afford reliable criteria on the major position of methoxy radical attack, simple resonance considerations offer a better guide. Two examples are instructive: 1-methoxy- and 2-methoxynaphthalene. From the product stability view, methoxy radical addition at C₁ (i.e., 45) affords a carbonium ion apparently less stable than that formed by addition at C₄ (i.e., 46). However, the ion 45 has the added stabilization of ~13 kcal/mol which derives from a carbon bearing two oxygen substituents.³⁴ If this stabilization is partially manifested in the transition state, then formation of 45 may be preferred over 46. For a system having a β -methoxy group (i.e., 2-methoxynaphthalene), the stabilization gained from having a carbon bearing two oxygen substituents can be partially offset by the linear conjugation present in an ion such as 51 vs. the cross-conjugation of ion 50. These product stability considerations for the possible carbonium ion intermediates rationalize the major product(s) from

anodic oxidations of the other naphthalenes studied.

Monohydrolyses of the Ortho Bisketals. A final point of interest concerns the highly regioselective formation of ketals 21 and 24 and the absence of such selectivity in the case of 30 and 31. The monoketals arise from the acid labile bisketals 58a-c. The



preferential hydrolysis of the β -ketal in 58a and 58b could be ascribed to the preferential formation of the linearly conjugated cation 60 relative to the cross-conjugated cation 59. A second consideration is based on the stereoelectronics of ketal hydrolysis:^{35,36} as the transition state for conversion to the cation is approached, most effective stabilization of charge requires the methoxy group to be in the plane of the ring. For 59a and 59b this planarity would generate steric congestion while for 60 this planar arrangement is quite acceptable sterically. Either rationale would explain the preferential hydrolysis of the β -ketal group. For bisketal 58c the formation of a mixture of monoketals 30 and 31 (28:13 with hydrolysis of the β -ketal favored) is apparently due to additional stabilization of the *p*-methoxy group of cations 59a and/or 59b.

Summary

Mechanistic and product studies indicate that anodic oxidation of methoxylated naphthalenes involves preferential or exclusive addition of a methoxy residue at the α -position of the naphthalene to give an intermediate such as III-2. When R¹ = OCH₃, reaction of III-2 with solvent affords the two-electron addition products (i.e., III-3 and III-4) which are reasonably stable if the anodic oxidation is carried out at 0 °C. If the anodic oxidation is performed in refluxing methanol, 1,4-adducts such as III-3 (R² = H) may eliminate methanol to give a substituted naphthalene III-6 which is further oxidized; 1,2-addition compounds (i.e., III-4) are much more stable toward loss of methanol. By contrast, if the α -position attacked is substituted with hydrogen (R¹ = H in III-2), loss of a proton gives a substituted naphthalene which is further oxidized under the reaction conditions to afford four-electron oxidation products. Reactions of this latter type show little temperature dependence of product ratios since no 1,4-addition compounds are available for in situ elimination of methanol. Thus, four-electron oxidation products can be formed via two reaction sequences depending upon the position of initial substitution and the temperature of the anodic oxidation. This then explains the difference in two- vs. four-electron oxidation of the various substituted naphthalenes. The major amounts of two-electron oxidation products formed in the low-temperature anodic oxidation of 1-methoxynaphthalene and 1,5-, 1,6-, and 1,7-dimethoxynaphthalene arise because the initial addition of the methanol residue is primarily at a methoxy-bearing carbon. By contrast, 2-methoxynaphthalene and 1,3-, 2,3-, 2,6-, and 2,7-dimethoxynaphthalenes yield four-electron products because the initial addition of the methoxy residue is at a carbon bearing a hydrogen. The preferred mechanism for formation of III-2, while necessarily simplistic, is termed an EEC_rC_p process and involves reaction of

(33) Good correlations have been demonstrated between spin density distributions calculated from the ESR spectra of radical cations and spin density distributions calculated from the Hückel theory: Zweig, A.; Hodgson, W. G.; Juva, W. H. *J. Am. Chem. Soc.* **1964**, *86*, 4124-4129.

(34) (a) Hine, J. "Structural Effects on Equilibria in Organic Chemistry"; Wiley: New York, 1975; p 9. (b) Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press: New York, 1970; pp 593-594.

(35) (a) Deslongchamps, P. *Tetrahedron* **1975**, *31*, 2463-2490. (b) Cordes, E. H.; Bull, H. G. *Chem. Rev.* **1974**, *4*, 581-603. Fife, T. H. *Acc. Chem. Res.* **1972**, *5*, 264-272.

(36) See, for example: Kirby, A. J.; Martin, R. J. *J. Chem. Soc., Chem. Commun.* **1978**, 803-804.

anodically generated methoxy radical with the aromatic radical cation. Finally, anodic methoxylation of substituted naphthalenes serves as a convenient method for preparation of selected methoxylated naphthalenes and orthonaphthoquinone monoketals.

Experimental Section³⁷

Anodic Oxidations. All of the preparative anodic methoxylations were performed in a single-cell apparatus under nitrogen using a circular platinum gauze anode (33-mm diameter \times 28-mm height) and a platinum sheet (8 \times 2 mm) as cathode with 1% methanolic potassium hydroxide as solvent. For controlled potential work, the previously described potentiostat¹⁶ was employed by using platinum wire, placed as close as possible to the interior wall of the cylindrical anode, as the reference electrode. These controlled potential reactions were performed at 1.7–1.9 V relative to the platinum wire with ca. 1 A of current. Larger preparative electrolyses were performed at constant current (1 A) by using a Keppo Model JQE 36-3M power supply. There was no noticeable difference in product ratios using the different electrolytic conditions. Current efficiencies reported are corrected for the relative amounts of two- and four-electron oxidation products. Unless otherwise stated, structures were confirmed by comparison of their IR and NMR spectra with authentic samples.

1,5-Dimethoxynaphthalene (1). A slurry of 5.0 g (26.6 mmol) of freshly recrystallized 1,5-dimethoxynaphthalene and 450 mL of solvent was electrolyzed at 20–25 °C until the UV absorption at 325 nm was no longer discernible in the end absorption (3.5 h at ca. 1 A). Evaporation of the methanol on the rotary evaporator (60–65 °C final bath temperature) gave a reddish solid. Water (100 mL) was added; the solid was filtered and washed with water (2 \times 25 mL); and then the light yellow solid was dried under vacuum to give 4.94 g (85%) of 1,4,5-trimethoxynaphthalene as a light yellow solid, mp 113–116 °C (lit.² 116–118 °C). This material showed IR and NMR spectra identical² with those of the analytically pure material and could be used directly for conversion to 5-methoxy-1,4-naphthoquinone.²

1-Methoxynaphthalene (4). A solution of 3.0 g (19.0 mmol) of 4 in 400 mL of solvent was electrolyzed (1.75 h, 4987 coulombs, 73% current efficiency) at 0 °C until the absorption maximum at 320 nm decreased to 5% of its initial value. Evaporation of the methanol and cooling afforded a crude solid which was filtered, and the solid was washed with 10 mL of cold methanol/water (7:3) to afford 1.98 g of 1,4-dimethoxynaphthalene, mp 84–85 °C (lit.³⁸ 85 °C). The mother liquors were diluted with 30 mL of water and extracted with ether (4 \times 40 mL), and the concentrated ether extract (blue oil) was chromatographed on silica gel (1.8 \times 20 cm column slurry packed with 5% E/PE). Elution proceeded as follows: 60 mL of PE, nil; 100 mL of 2% E/PE, 0.37 g of 5 (total yield 66%); 120 mL of 3% E/PE, 0.33 g (8%) of 7 as a light yellow oil [IR (neat) 2941 (s), 2830 (s), 1201 (s), 1144 (s), 1103 (s), 1080 (s), 1062 (s), 1001 (s), 928 (s), 762 (s) cm^{-1} ; NMR δ 7.7–7.4 (m, 1 H), 7.25–6.83 (m, 3 H), 6.2 (AB of ABX, $J_{AB} = 9.5$ Hz, $\Delta\nu = 35$ Hz, the higher field component coupled to X, $J_{AX} = 5.0$ Hz, 2 H), 3.93 (d, $J = 5.0$ Hz, 1 H), 3.43 (s, 3 H), 3.00 (s, 3 H), 2.78 (s, 3 H)]. When 0.091 g (0.41 mmol) of the compound was stirred for 1 h in 5 mL of methanol/concentrated hydrochloric acid (10:1), workup as usual gave 77 mg of 1,2-dimethoxynaphthalene.

Elution was continued as follows: 30 mL of 3% E/PE, 0.027 g of a mixed fraction; 100 mL of 5% E/PE, 0.80 g (21%) of 6a.

A solution of 1.5 g (9.5 mmol) of 1 in 80 mL of solvent was heated to reflux and electrolyzed until the UV absorption at 320 nm had decreased to 7% of its initial value (1.8 h, current range 1.35–0.50 A, 6242 coulombs, 56% current efficiency correcting for two-electron processes). The methanol was removed at reduced pressure, 20 mL of water was

added, and the residue was extracted with ether (3 \times 10 mL). The ethereal solution was washed with brine and dried through calcium sulfate. Removal of solvent at reduced pressure afforded 2.26 g of a light green oil which was chromatographed on activity III neutral alumina (2.5 \times 30 cm, slurry packed with 5% E/PE). Elution proceeded as follows: 40 mL of 5% E/PE, nil; 60 mL, 0.18 g (9%) of 7 as a colorless oil.

Elution was continued: 20 mL of 5% E/PE, 0.01 g of a mixed fraction; 300 mL of 5% E/PE, 2.00 g (84%) of 6b as a colorless oil which crystallized upon trituration with PE [mp 43–45 °C (lit.¹⁶ 43–44.5 °C)].

For isolation of 42, the anodic oxidation was performed at 0 °C as described above, and the solution was poured into an equal volume of cold brine. Extraction of the organic material into methylene chloride gave a mixture of 6b, 7, and 42 with the NMR spectrum reported in the text.

1,6-Dimethoxynaphthalene (8a). A solution of 1.0 g (5.3 mmol) of 8a in 80 mL of solvent was electrolyzed at 20 °C until the absorption at 329 nm had decreased to 20% of its initial value (0.75 h, 2540 coulombs, 45% current efficiency). The methanol was removed in vacuo (60 °C bath), the residue diluted with water (20 mL), and the organic product extracted with ether (3 \times 15 mL). Workup gave a blue-green oil which was chromatographed on activity III neutral alumina (100 g, 2.5 \times 25 cm column, slurry packed in 4% E/PE). Elution was performed with the above solvent and proceeded as follows: 80 mL, nil; 60 mL, 0.38 g (33%) of 9 as a colorless oil which solidified upon cooling. Recrystallization from hexane/methylene chloride gave 9 as white needles; mp 43–44 °C, picrate mp 148–149 °C (lit.³⁹ 148–149 °C). Elution was continued as follows: 20 mL, 0.01 g of a mixed fraction; 80 mL, 0.13 g (13%) of 10 as a white solid [mp 183–184 °C; IR (KBr) 1623 (s), 1592 (s), 1445 (s), 1422 (s), 1297 (s), 1247 (s), 1214 (s), 1076 (s), 1030 (s), 813 (s) cm^{-1} ; NMR (CDCl₃) δ 8.26 (d, $J = 9$ Hz, 2 H), 7.34 (d, $J = 8$ Hz, 2 H), 7.09 (center of d of d, $J = 9, 2$ Hz, 2 H), 6.76 (d, $J = 8$ Hz) overlapping with 6.73 (d, $J = 2$ Hz) for a total of 4 H, 4.03 (s, 6 H), 3.51 (s, 6 H); ¹³C NMR (CDCl₃) δ 158.12, 155.26, 135.40, 130.06, 128.85, 123.85, 120.94, 117.10, 105.55, 101.86, 55.54, 55.15; exact mass calcd for C₂₄H₂₂O₄ m/e 374.1528, obsd m/e 374.1523, difference 0.0005].

Elution was continued as follows: 80 mL, nil; 120 mL, 0.16 g (12%) of 11 as a light yellow oil [IR (neat) 2958 (m), 2857 (w), 1592 (w), 1562 (m), 1481 (m), 1447 (m), 1321 (m), 1309 (m), 1271 (m), 1247 (s), 1179 (m), 1155 (m), 1117 (s), 1087 (s), 1064 (s), 1039 (s), 1023 (s), 980 (m), 961 (m), 909 (m), 893 (m), 833 (m), 813 (w), 806 (w), 781 (m, br), 757 (w) cm^{-1} ; NMR δ 7.09 (AB, $J = 8$ Hz, $\Delta\nu = 51$ Hz, 2 H, with higher field component partially obscured and further split $J = 2$ Hz), 6.52 (br s of overlapping absorptions), 6.26 (partially obscured AB, $J = 10$ Hz, $\Delta\nu = 34$ Hz, with the higher field component further split into a d, $J = 5$ Hz, 2 H), 3.89 (d, $J = 5$ Hz, 1 H), 3.69 (s, 3 H), 3.38 (s, 3 H), 3.01 (s, 3 H), 2.77 (s, 3 H)].

Elution was continued as follows: 40 mL, 0.01 g of a mixed fraction; 200 mL, 0.15 g (11%) of 12 as a pale blue oil, which could be obtained in a colorless state upon molecular distillation [IR (neat) 2985 (s), 2865 (w), 1605 (s), 1484 (s), 1453 (s), 1368 (m), 1319 (s), 1292 (s), 1279 (s), 1235 (s), 1219 (s), 1187 (s), 1116 (s), 1099–1036 (s, br), 1024 (s), 1000 (m), 990 (m), 962 (s), 877 (m), 855 (m), 819 (m) cm^{-1} ; NMR δ 7.35 (half of AB, $J = 8$ Hz, 1 H), 6.97–6.62 (m, 2 H), 6.14 (s, 2 H), 3.78 (s, 3 H), 3.07 (s, 6 H), 3.05 (s, 6 H); exact mass calcd for C₁₅H₂₀O₅ m/e 280.1311, obsd m/e 280.1317, difference 0.0006].

Elution was continued as follows: 200 mL, 0.19 g of an unidentified blue oil thought to be polymeric due to its NMR spectrum.

The electrolysis at reflux was conducted as for 4 on 1.0 g of 8 in 80 mL of solvent (0.8 h, 1.0–0.5 A, 2597 coulombs, 69% current efficiency). Workup gave a light green oil which was chromatographed as above to afford 9 (10%), 11 (14%), and 12 (45%).

1,7-Dimethoxynaphthalene (13). A solution of 4.0 g (21 mmol) of 13 in 400 mL of solvent was electrolyzed (1.8 h, 8400 coulombs, 47% current efficiency) at 10 °C until the UV absorption at 333 nm decreased to 5% of its initial value. The methanol was removed in vacuo, 100 mL of brine added, and the solution continuously extracted with 150 mL of ether. Concentration of the ether afforded a light green oil which was dissolved in 100 mL of anhydrous ether, the solution cooled to 0 °C under nitrogen, and 1.7 mL of trifluoroacetic acid added. After 2 h at 0 °C, the ethereal solution was washed with water (2 \times 15 mL) and saturated sodium bicarbonate solution (2 \times 15 mL) and concentrated to afford a dark blue-green oil; this residue was chromatographed on silica gel (2.5 \times 25 cm column slurry packed with 5% E/PE). Elution was performed with 6% E/PE: 100 mL, nil; 160 mL, 2.5 g (52%) of 9 as a colorless oil which crystallized on cooling (mp 42–44 °C with IR and NMR spectra identical with those of the authentic sample).

Elution was continued as follows: 40 mL, nil; 360 mL, 1.28 g of 14 as an orange oil which was further purified by passage through a short alumina column (10% E/PE eluant) to afford 0.96 g (21%) of 14 as

(37) 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 (CCl₄) with Varian EM-360 instrument. ¹³C NMR spectra (Me₄Si 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 Electronic MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Micro-analytical Laboratory, Herlev, Denmark. Aluminum oxide and silica gel were from E. Merck Co. Tetrahydrofuran was distilled from benzophenone ketyl directly into the reaction flask. Butyllithium in hexane (Ventrol) 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.

(38) *Beilstein's Handb. Org. Chem.* 1918, 6, 975.

(39) Grob, C. A.; Jundt, W. *Helv. Chim. Acta* 1948, 31, 1691–1706.

white crystals from E/PE: mp 52–53 °C; IR (KBr) 1602 (s), 1574 (s), 1515 (s), 1462 (s), 1432 (s), 1377 (s), 1360 (s), 1333 (s), 1285 (s), 1265 (s), 1086 (s), 1052 (s), 1004 (s), 820 (s), 760 (s) cm^{-1} ; NMR δ 7.38–6.87 (str m, 4 H), 6.58 (center of d of d, $J = 6, 2$ Hz, 1 H), 3.86 (s, 6 H), 3.76 (s, 3 H); UV (EtOH) λ_{max} 228 (ϵ 72 000), 292 (ϵ 8020), 302 (ϵ 8360), 328 (ϵ 3800), 339 nm (ϵ 3620).

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$: C, 71.56; H, 6.42. Found: C, 71.35; H, 6.49.

The reaction at reflux was performed as for **4** on 1.0 g (5.3 mmol) of **13** (0.8 h, 1.1–0.4 A, 2349 coulombs, 54% current efficiency). The light green oil resulting from workup was chromatographed on 115 g of activity III neutral alumina (2.8 \times 18 cm column slurry packed with 4% E/PE). Elution performed with the above solvent gave the following: 80 mL, nil; 240 mL, 0.41 g (36%) of **9** as a colorless oil which solidified on cooling. Elution was continued as follows: 100 mL, nil; 300 mL, 0.21 g (15%) of **15** as a colorless oil which gave 0.15 g (13% overall) of **14** upon reaction with 10% methanolic hydrochloric acid for 1 h. Elution was continued as follows: 140 mL, 35 mg of a mixed fraction; 540 mL, 0.37 g (25%) of **12** as a pale blue oil.

1,3-Dimethoxynaphthalene (16). A solution of 1.0 g (5.3 mmol) of **16** in 100 mL of solvent was maintained at 20 °C and electrolyzed until the UV absorption maximum at 341 nm had decreased to 7% of its initial value (0.8 h, 2210 coulombs, 75% current efficiency). The methanol was removed at reduced pressure, 20 mL of water added, and the residue extracted with ether (3 \times 15 mL). Workup afforded a light green oil which was dissolved in 5 mL of acetone, 5 mL of 10% acetic acid was added, and the mixture was stirred for 20 min, after which time 10 mL of saturated bicarbonate solution was added. The organic portion was separated, and the aqueous portion was extracted with ether (2 \times 10 mL). The combined organic layers were washed with brine (20 mL) and dried through calcium sulfate. Removal of solvent at reduced pressure afforded 1.26 g of an orange oil which was chromatographed on 50 g of silica gel (slurry packed with 45% E/PE) as follows: 100 mL of 45% E/PE, nil; 80 mL of 45% E/PE, 0.22 g (19%) of **17** as a colorless oil which crystallized upon standing [mp 37–39 °C (lit.¹⁷ 38 °C)]. Elution was continued as follows: 20 mL of 45% E/PE, nil; 80 mL of 50% E/PE, 0.645 g (52%) of **18** as a white, crystalline solid [mp 101–102 °C (lit.^{16c} mp 102–103 °C)]. Elution was continued as follows: 20 mL of 50% E/PE, nil; 140 mL of 50% E/PE and 160 mL of 60% E/PE, 0.21 g (17%) of **19** as a crystalline, white solid [mp 101–103 °C (lit.^{16c} 100.5–101.5 °C)].

1,2-Dimethoxynaphthalene (20). A solution of 3.0 g of **20** in 300 mL of solvent was electrolyzed (1.75 h, 4202 coulombs, 73% current efficiency) at 20 °C until the UV absorption at 333 nm had decreased to 25% of its initial value. The methanol was removed in vacuo, 30 mL of brine added, and the residue extracted with ether (4 \times 40 mL). Workup afforded a yellow oil which was dissolved in 70 mL of tetrahydrofuran, and 14 mL of 2% aqueous oxalic acid was added. After 1 h at room temperature, 30 mL of saturated sodium bicarbonate solution was added, the product worked up, and the 3.3 g of orange oil chromatographed on neutral alumina (activity III, 2.5 \times 37 cm column slurry packed with 2% E/PE). Elution with 5% E/PE proceeded as follows: 150 mL, nil; 900 mL, 2.33 g (71%) of **21** as a yellow oil whose IR and NMR spectra agree with those reported herein. In a larger run, 10 g of **20** in 400 mL of 1% methanolic potassium hydroxide was electrolyzed as before and the orange-brown oil distilled [bp 116–120 °C (0.7 mm)] to afford 7.0 g (65%) of **21** as a light yellow oil.

When the anodic oxidation reaction of **20** was conducted as above, concentrated, and filtered through a short neutral alumina column (10% E/H eluant), the pure bisketal **49** was obtained: IR (neat) 2951 (m), 2838 (m), 1463 (m), 1451 (m), 1249 (m), 1233 (m), 1215 (m), 1192 (m), 1138 (m), 1124 (m), 1108 (s), 1084 (s), 1073 (s), 1012 (m), 988 (m), 933 (m), 782 (m), 751 (m) cm^{-1} ; NMR δ 7.64–7.42 (m, 1 H), 7.23–6.84 (m, 3 H), 6.25 (AB q, $\Delta\nu = 32$ Hz, $J = 10$ Hz, 2 H), 3.32 (s, 6 H), 3.18 (s, 6 H); exact mass calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$ m/e 250.12050, obsd m/e 250.12099, difference 0.00049.

2-Methoxynaphthalene (22). A slurry of 6.0 g (0.038 mol) of **22** in 450 mL of solvent was electrolyzed (14 h, 19491 coulombs, 75% current efficiency) at 20 °C. Standard workup afforded a light yellow oil which was dissolved in 125 mL of tetrahydrofuran and treated with 25 mL of 2% oxalic acid. After the mixture was stirred for 1 h, 30 mL of saturated bicarbonate solution was added to the reaction mixture and the reaction worked up to afford 7.33 g of an orange oil. Vacuum distillation [bp 125–165 °C (10 mm)] gave 4.88 g of a mixture of **20** and **21**. Chromatography of 1 g of the product mixture on neutral alumina (activity III, 2.5 \times 31 cm column slurry packed in 4% E/PE) proceeded as follows: 100 mL, nil; 100 mL, 0.38 g (26%) of **20** as a light yellow oil which crystallized from PE [mp 30–31 °C (lit.⁴⁰ 31 °C)]. Elution was con-

tinued as follows: 120 mL, nil; 280 mL, 0.6 g (36%) of **21** as a yellow oil [IR (neat) 2940 (m), 2835 (m), 1690 (s), 1675 (s), 1619 (m), 1570 (m), 1453 (m), 1290 (s), 1242 (s), 1203 (m), 1189 (m, sh), 1140 (m, sh), 1130 (m), 1080 (vs), 1048 (m, sh), 1000 (m), 830 (s), 768 (s) cm^{-1} ; NMR δ 7.7–7.0 (m, 5 H), 5.91 (d, $J = 10$ Hz, 1 H), 3.20 (s, 6 H); UV (EtOH) λ_{max} 233 (ϵ 20 000), 322 nm (ϵ 6910); exact mass calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$ m/e 204.0786, obsd m/e 204.0790, difference 0.0004].

A sample of **48** (75% pure, contaminated with **49**) was obtained by chromatography on activity III basic alumina (1% E/H eluant), giving the NMR spectrum reported in the text.

2,7-Dimethoxynaphthalene (23). A slurry of 3.0 g (16 mmol) of **23** in 300 mL of solvent was electrolyzed (2.75 h, 8089 coulombs, 58% current efficiency) at 25 °C until the UV maximum at 325 nm decreased to 5% of its original value. Workup afforded 4.4 g of a yellow-orange oil which was dissolved in 60 mL of tetrahydrofuran, and 12 mL of 2% oxalic acid solution was added. After the solution was stirred for 2.75 h, 60 mL of saturated sodium bicarbonate solution was added and the material worked up to afford 4.1 g of an orange oil which was chromatographed on silica gel (2.5 \times 45 cm column slurry packed with 5% E/H). Elution performed with 5% E/H proceeded as follows: 640 mL, nil; 260 mL, 0.35 g (10%) of **25** as a colorless oil which crystallized on standing [mp 37–38.5 °C (lit.⁴¹ 38.5–39.5 °C)]. Elution proceeded as follows: 320 mL, nil; 1780 mL, 2.13 g of **24** as a yellow, crystalline solid. Trituration with hexane afforded 1.97 g (53%): mp 77.5–78.5 °C; IR (KBr) 1665 (s), 1608 (s), 1568 (s), 1557 (s), 1502 (s), 1451 (s), 1438 (s), 1292 (s), 1250 (s), 1230 (s), 1082 (s), 1070 (s), 849 (s) cm^{-1} ; NMR δ 7.15–6.98 (str m, 3 H) 6.69 (d of d, $J = 9, 2$ Hz, 1 H), 5.77 (d, $J = 10$ Hz, 1 H), 3.83 (s, 3 H), 3.20 (s, 6 H); UV (EtOH) λ_{max} 228 (ϵ 14 700), 246 (ϵ 19 250), 358 nm (ϵ 9063)].

Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_4$: C, 66.67; H, 5.98. Found: C, 66.74; H, 5.99.

2,6-Dimethoxynaphthalene (27). A slurry of 4.0 g (21 mmol) of **27** in 400 mL of solvent was electrolyzed (3.5 h, 7665 coulombs, 75% current efficiency) at 30 °C until the UV absorption at 344 nm had decreased to 20% of its initial value. Workup afforded an orange oil which was dissolved in 80 mL of tetrahydrofuran, 16 mL of 2% oxalic acid solution was added, and the mixture was stirred for 1.5 h. After addition of 60 mL of saturated bicarbonate solution, workup afforded a brown oil which was chromatographed on neutral alumina (activity III, 2.5 \times 48 cm column slurry packed with 5% E/PE). Elution (5% E/PE) proceeded as follows: 270 mL, nil; 160 mL, 1.08 g (23%) of **28** as a crystalline white solid [mp 55–56 °C (lit.⁴¹ 55 °C)].

Elution was continued as follows: 55 mL, nil; 450 mL, 0.87 g (16%) of **29** as a crystalline white solid [mp 87–88 °C; IR (KBr) 1610 (s), 1442 (m), 1370 (m), 1360 (m), 1252 (m), 1220 (s), 1108 (m), 1038 (m) cm^{-1} ; NMR δ 7.44 (AB, $J = 9$ Hz, $\Delta\nu = 50$ Hz, with higher field component split into a doublet, $J = 2$ Hz, 2 H), 7.28 (d, $J = 2$ Hz, 1 H), 6.45 (s, 1 H), 3.86 (s, 6 H), 3.84 (s, 6 H); exact mass calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$ m/e 248.1049, obsd m/e 248.1055, difference 0.0006].

Elution was continued: 90 mL, nil; 920 mL, 1.42 g (28%) of **30** as a yellow oil which crystallized [mp 74–75 °C; IR (KBr) 1685 (s), 1568 (s), 1275 (s), 1262 (s), 1182 (m), 1084 (s), 1062 (s), 1040 (s), 830 (m); NMR δ 7.12 (AB, $J = 8$ Hz, $\Delta\nu = 41$ Hz; the higher field component is partially obscured and coupled to a second proton, $J = 3$ Hz, 2 H), 6.68 (partially obscured s, 1 H), 6.48 (AB, $J = 10$ Hz, $\Delta\nu = 66$ Hz, 2 H), 3.77 (s, 3 H), 3.17 (s, 6 H); UV (EtOH) λ_{max} 252 (ϵ 20 700), 314 nm (ϵ 7060); exact mass calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ m/e 234.0892, obsd m/e 234.0899, difference 0.0007].

Elution was continued: 70 mL, 0.8 g of a mixed fraction; 1135 mL, 0.67 g (13%) of **31** as a colorless oil [IR (neat) 1680 (s), 1590 (s), 1279 (s), 1080 (s) cm^{-1} ; NMR δ 7.82 (d, $J = 9$ Hz, 1 H), 6.80–6.42 (m, 3 H), 6.02 (d, $J = 11$ Hz, 1 H), 3.80 (s, 3 H), 3.32 (s, 6 H); UV (EtOH) λ_{max} 227 (ϵ 12 600), 253 (ϵ 11 100), 317 (ϵ 3130); exact mass calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ m/e 234.0892, obsd m/e 234.0899, difference 0.0007].

2,3-Dimethoxynaphthalene (32). A solution of 5.0 g (27 mmol) of **32** in 450 mL of solvent was electrolyzed (5.2 h, 16 231 coulombs, 83% current efficiency) at 30 °C until the UV absorption at 322 nm decreased to 5% of its original value. Workup afforded 8.0 g of a yellow oil which was dissolved in 125 mL of tetrahydrofuran and treated with 42 mL of 1 M hydrochloric acid. After 3 h at 85 °C the black solution was cooled and then neutralized with 150 mL of 5% sodium hydroxide. The now basic reaction mixture was extracted with ether (3 \times 125 mL). The aqueous phase was acidified with concentrated hydrochloric acid and extracted with ether (4 \times 100 mL) and the ether layer dried and concentrated to afford 3.4 g of brown oil. Filtration of this material through a plug of neutral alumina with 10% E/PE gave 2.3 g of **33** as an off-white solid which was recrystallized from PE to give 2.1 g (33%) of **33**: mp 82–83 °C; IR (KBr) 3280 (m, br), 1470 (m, sh), 1460 (m), 1421 (m),

1419 (m), 1370 (m), 1080 (s), 1010 (m) cm^{-1} ; NMR δ 7.95–7.78 (m, 2 H), 7.31–7.12 (m, 2 H), 5.66 (s, 1 H), 4.02 (s, 3 H), 3.92 (s, 6 H); exact mass calcd for $\text{C}_{13}\text{H}_{14}\text{O}_4$ m/e 234.0892; obsd m/e 234.0897, difference 0.0005.

Workup of the initial ether extract afforded 3.2 g of a brown oil which was chromatographed on neutral alumina (activity III, 2.5×53 cm column slurry packed with 2% E/PE). Elution proceeded as follows: 320 mL of 2% E/PE, nil; 160 mL of 2% E/PE, 0.21 g (3%) of **34** as a white crystalline solid [mp 53–54 °C (lit.⁴² 52–53 °C)]. Elution was continued as follows: 100 mL of 2% E/PE, nil; 1720 mL of 2% E/PE, 1.30 g (16%) of **36** as a colorless oil [IR (neat) 2940 (s), 2838 (s), 1717 (br, s), 1602 (s), 1454 (s, br), 1200 (s, br), 1160 (s, br), 1110–1050 (vs, br), 1027 (s), 910 (s), 745 (s) cm^{-1} ; NMR δ 7.94–7.78 (m, 1 H), 7.51–7.08 (m, 3 H), 4.64 (s, 1 H), 3.73 (s, 3 H), 3.58 and 3.54 (2 s, 6 H), 3.28 (s, 2 H), 3.16 (s, 3 H); ^{13}C NMR (CDCl_3) δ 192.06, 140.94, 133.66, 130.21, 127.93, 127.49, 126.62, 103.99, 101.32, 82.53, 61.85, 52.92, 51.89, 51.80, 51.70; exact mass calcd for $\text{C}_{15}\text{H}_{20}\text{O}_6$ m/e 296.1260, obsd m/e 296.1257, difference 0.0003].

Elution was continued with 4% E/PE as follows: 160 mL, 0.06 g of a mixed fraction; 560 mL of 4% E/PE, 0.32 g (5%) of **35** as a white crystalline solid [mp 125–126 °C; IR (KBr) 1601 (s), 1511 (m), 1488 (s), 1465 (m), 1455 (m), 1438 (s), 1338 (s), 1268 (s), 1208 (s), 1180 (s), 1020 (m), 980 (s), 867 (m), 790 (m) cm^{-1} ; NMR (CDCl_3) δ 7.44 (s, 2 H), 6.54 (s, 2 H), 3.98 (s, 6 H), 3.90 (s, 6 H); exact mass calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$ m/e 248.1048, obsd m/e 248.1055, difference 0.0007].

Elution was continued as follows: 280 mL of 4% E/PE, 0.08 g of a mixed fraction; 740 mL of 4% E/PE, 0.39 g of **37** as a dark yellow solid. Trituration with PE afforded 0.37 g (6%) of the known quinone, mp 113–114 °C (lit.⁴³ 115 °C).

1-Methylnaphthalene (38). A solution of 3.0 g (21 mmol) of **38** in 300 mL of 1% methanolic potassium hydroxide was electrolyzed (6 h, 17950 coulombs, 50% current efficiency) at 20 °C until the UV absorption at 282 nm decreased to 20% of its initial value. The methanol was removed at reduced pressure, 30 mL of brine added, and the residue extracted with ether (4×30 mL). Workup afforded a bluish oil which was dissolved in 100 mL of ether and maintained under a nitrogen atmosphere, and 1.65 mL of trifluoroacetic acid was added. This solution was stirred for 16 h, at which time the solution was washed with water (2×30 mL), saturated NaHCO_3 (3×20 mL), and 30 mL of brine. Workup afforded a blue oil which was chromatographed on silica gel (2.5×50 cm column slurry packed with 3% E/H) as follows: 140 mL of 3% E/H, nil; 80 mL of 3% E/H, 0.79 g (22%) of **40** as a colorless oil [picrate mp 145–147 °C (lit.⁴⁴ 148–149 °C)].

Elution was continued as follows: 60 mL of 3% E/H, 0.05 g of a mixed fraction; 80 mL of 3% E/H, 0.50 g (11%) of **41** as a white crystalline solid [mp 50–51 °C (lit.⁴⁵ 49 °C)].

Elution was continued as follows: 220 mL of 3% E/H, 0.14 g of a brown oil which was not identified; 300 mL of 3% E/H, nil; 180 mL of 5% E/H, nil; 880 mL of 5% E/H, 1.21 g (30%) of **39** as a colorless oil [IR (neat) 2988 (w), 2940 (w), 2830 (w), 1670 (s), 1628 (w), 1603 (s), 1459 (m), 1388 (m), 1369 (w), 1307 (s), 1153 (w), 1106 (s), 1083 (m), 1059 (m), 1040 (w), 858 (w), 785 (s) cm^{-1} ; NMR ($\text{CCl}_4/60$ MHz) δ 8.18–7.94 (m, 1 H), 7.66–7.12 (m, 2 H), 6.68 (AB, $J = 9.5$ Hz, $\Delta\nu = 28$ Hz, 2 H), 2.93 (s, 3 H), 1.52 (s, 3 H); exact mass calcd for $\text{C}_{12}\text{H}_{12}\text{O}_2$ m/e 118.0837, obsd m/e 188.0842, difference 0.0005].

Preparative Scale Oxidation of 2-Methoxynaphthalene (22). A slurry of 20 g (0.127 mol) of **22** in 450 mL of 1% methanolic potassium hydroxide was electrolyzed at 20 °C at a constant current of 1.2 A, until the UV absorption at 327 nm had decreased to ~5% of its initial value (13.5 h). The methanol was removed at reduced pressure, 100 mL of brine added, and the residue extracted with ether (3×100 mL). The ethereal solution was washed with 75 mL of brine and dried through CaSO_4 . Workup afforded an orange oil which was dissolved in 250 mL of tetrahydrofuran, and 50 mL of 2% aqueous oxalic acid was added. This solution was allowed to stir for 1.5 h at which time 100 mL of saturated bicarbonate solution was added. Workup (extraction with 2×40 mL of ether) gave an orange oil. This oil was dissolved in 150 mL of methanol and cooled to 0 °C. To this was added 2.0 g of sodium borohydride, and this solution was allowed to stir until hydrogen evolution ceased at which time 100 mL of water was added. Workup (extraction with 3×75 mL of ether) gave a dark brown oil. A mixture of this oil, 20 mL of dimethyl sulfate, 50 g of potassium carbonate, and 200 mL of acetone was stirred at reflux under a nitrogen atmosphere for 20 h. The

acetone was removed at reduced pressure, and a mixture of 200 mL of methanol and 15 g of potassium hydroxide was added. After this solution was stirred for 1 h, the methanol was removed at reduced pressure, and 200 mL of water was added. The product was extracted with ether (3×80 mL) and worked up to yield a dark oil which was vacuum distilled (0.6 mm), collecting the fraction from 102 to 109 °C, affording 14.2 g (59%) of 1,2-dimethoxynaphthalene as a colorless oil which crystallized upon refrigeration; mp 30–31 °C.

1,2,6-Trimethoxynaphthalene (28). A solution of 630 mg (2.8 mmol) of **28** in 100 mL of solvent was electrolyzed (0.4 h, 672 coulombs, 86% current efficiency) at 30 °C until the UV absorption maximum at 338 nm decreased to 5% of its initial value. The methanol was removed at reduced pressure, 20 mL of brine added, and the residue extracted with ether (2×20 mL). Workup afforded a slightly yellow oil which was dissolved in 10 mL of tetrahydrofuran, and 2 mL of 2% oxalic acid was added. This solution was allowed to stir for 1.5 h at which time 15 mL of saturated sodium bicarbonate was added. The organic layer was separated, and the aqueous portion was extracted with ether (2×15 mL). Workup of the combined organic portions afforded an orange oil which was chromatographed on neutral alumina (activity III, 2.5×28 cm column, slurry packed with 5% E/H) as follows: 500 mL of 5% E/H, nil; 300 mL of 5% E/H, 0.15 g (22%) of **29** as a white crystalline solid [mp 87–88 °C; IR (KBr) and NMR spectra were identical to those already specified].

Elution was continued as follows: 125 mL of 8% E/PE, nil; 220 mL of 8% E/H, 0.27 g (41%) of **30** as a yellow crystalline solid [mp 73–74 °C; IR (KBr) and NMR spectra were identical to those already specified].

Elution was continued as follows: 20 mL of 8% E/H, 0.027 g of a mixed fraction; 350 mL of 8% E/H, 0.12 g (18%) of **31** as a colorless oil [IR (neat) and NMR spectra were identical to those already specified].

Naphthalene. A solution of 1.0 g (7.8 mmol) of naphthalene in 80 mL of solvent was electrolyzed at 20 °C until the UV absorption maximum at 311 nm decreased to 50% of its initial value. The solution was then heated to reflux without interrupting the electrolysis. After a total of 10000 coulombs (22% current efficiency) was passed at 1.35–1.0 A, the reaction was stopped. The solvent was removed in vacuo from the black reaction mixture, 20 mL of water added, and the product extracted with ether (4×20 mL). After workup the resulting dark blue oil was chromatographed on neutral alumina (activity III, 2.5×27 cm column slurry packed with 3% E/PE). Elution proceeded as follows: 110 mL of 3% E/PE, nil; 70 mL of 3% E/H, 0.14 g of a mixture of naphthoquinone bisketal and a blue oil; 450 mL of 3% E/PE, 0.82 g (42%) of the bisketal as a colorless oil which crystallized upon cooling.

1-Methoxynaphthalene-*OCD*₃ (4b). A mixture of 2.0 g (0.014 mol) of α -naphthol, 2.0 g of potassium carbonate, 1.5 mL (0.022 mol) of methyl-*d*₃ iodide (Aldrich) was heated at 60 °C for 20 h. The reaction mixture was cooled, filtered, and concentrated in vacuo. The residue was partitioned between 20 mL of ether/water (1:1). Workup and short-path distillation [60 °C bath (2.0 mm)] gave 2.13 g (95%) of **4b** which was shown to be greater than 95% *d*₃ by NMR and mass spectroscopy. The electrolysis and product separation were as described for the nondeuterated system.

1-Methoxynaphthalene-4-*d*₁ (4c). To a solution of 2.0 g (0.0084 mol) of 4-bromo-1-methoxynaphthalene in 60 mL of anhydrous ether, stirring under nitrogen at –23 °C, was slowly added 5.41 mL (0.0086 mol) of 1.59 M *n*-butyllithium in hexane. This solution was warmed to 0 °C for 15 min and quenched with 4 mL of deuterium oxide. The ethereal solution was washed with water (20 mL) and brine (20 mL) and then dried through Drierite. Workup afforded the product as a bluish oil which was molecularly distilled [60 °C (2.0 mm)] to afford 1.21 g (91%) of **4c** which was shown to be >95% *d* by mass spectroscopy. The electrolysis and product isolation studies for this system were described for the parent.

2-Methoxynaphthalene-1-*d*₁ (22b). A slurry of 2.0 g (0.0084 mol) of 1-bromo-2-methoxynaphthalene in 60 mL of anhydrous ether was stirred at –23 °C under a nitrogen atmosphere. To this slurry was slowly added 5.41 mL (0.0086 mol) of 1.59 M *n*-butyllithium in hexane. The reaction mixture was then warmed to 0 °C for 30 min and quenched with 3 mL of deuterium oxide. The ethereal solution was washed with water (20 mL) and brine (20 mL) and dried through Drierite. Removal of ether afforded **22b** as a white crystalline solid, which was recrystallized from methanol/water to afford 1.30 g (97%); mp 70–71 °C. The anodic oxidation and product isolation were as described for the parent system.

1,4-Bis(2-hydroxyethoxy)naphthalene (52). To a 250-mL separatory funnel containing 65 mL of water and 100 mL of ether was added 5.5 g of 1,4-naphthoquinone (~90% purity, ~32 mmol) and 5.5 g of sodium dithionite. This mixture was vigorously shaken, another 4.5 g of sodium dithionite was added, and the mixture was vigorously shaken again.

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Another 3 g of sodium dithionite was added in 1-g portions, shaking after each addition. The aqueous layer was removed, and the ethereal solution was washed with brine (40 mL) and dried through Drierite. Removal of solvent afforded a brownish solid which was combined with 6.6 g (75 mmol) of ethylene carbonate, 2.0 g of tetraethylammonium bromide, and 5 mL of dimethylformamide and stirred at 150 °C for 8 h. The mixture was then poured into 40 mL of water; the product crystallized overnight. The product was collected and sublimed [150 °C (0.07 mm)] to afford 5.02 g (63%) of **52** as white crystals: mp 125–127 °C; IR (KBr) 3413 (s), 2976 (m), 1629 (w), 1590 (s), 1443 (s), 1420 (m), 1383 (m), 1366 (m), 1351 (m), 1261 (s), 1229 (s), 1150 (m), 1093 (s), 1066 (s), 1030 (m), 901 (s), 893 (m), 885 (m), 794 (m), 763 (s), 742 (m) cm^{-1} ; NMR (CD_3COCD_3) δ 8.38–8.11 (m, 2 H), 7.56–7.30 (m, 2 H), 6.79 (s, 2 H), 4.30–3.81 (m, 8 H), 2.81 (s, 2 H); exact mass calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$ m/e 248.1048, obsd m/e 248.1055, difference 0.0003.

Electrolysis of 52. A solution of 0.50 g (2.0 mmol) of **52** in 70 mL of 1% methanolic potassium hydroxide was maintained at 20 °C and electrolyzed until the UV absorption maximum at 329 nm had decreased to 2% of its initial value (1515 coulombs, 25% current efficiency, 0.75 h). The electrolysis mixture was poured into 200 mL of brine and continuously extracted with ether. The ethereal solution was washed with brine and dried through calcium sulfate. Removal of solvent at reduced pressure afforded 496 mg of a light yellow oil. Chromatography of this oil on neutral alumina (activity III, 1.8×10 cm slurry packed with 20% E/H) proceeded as follows: 100 mL of 20% E/H, 100 mL of 30% E/H, and 40 mL of 40% E/H, nil; 180 mL of 40% E/H, 0.472 g (85%) of **53** as a colorless oil [IR (neat) 3571 (m), 3012 (m), 2932 (m), 1449 (m), 1381 (m), 1302 (m), 1238 (m), 1133 (s), 1110–1000 (s, br), 962 (s), 943 (s), 877 (w), 763 (s) cm^{-1} ; NMR δ 7.67–7.13 (m, 4 H), 6.11 (AB, $J = 10$ Hz, $\Delta\nu = 14$ Hz, 2 H), 4.03 (s, 4 H), 3.66–2.86 (m, 5 H), 2.97 (s, 3 H); exact mass calcd for $\text{C}_{15}\text{H}_{18}\text{O}_5$ m/e 278.1154, obsd m/e 278.1162, difference 0.0008].

Treatment of 53 with Acid. To a stirred solution of 133 mg (0.48 mmol) of **53** in 5 mL of ether was added ~10 mg of anhydrous *p*-toluenesulfonic acid. A white precipitate formed almost immediately. After 5 min, the reaction mixture was cooled to ~0 °C, and the white crystals were collected by vacuum filtration to afford 75 mg (63%) of the bisethylene glycol ketal of 1,4-naphthoquinone: mp 160–162 °C; IR (KBr) 3049 (w), 2967 (w), 1451 (w), 1389 (m), 1307 (m), 1291 (m), 1238 (m), 1150 (s), 1139 (s), 1103 (s), 1047 (s), 1019 (m), 1000 (w), 962 (s), 943 (s), 763 (s) cm^{-1} ; NMR δ 7.67–7.17 (m, 4 H), 6.08 (s, 2 H), 4.12 (s, 8 H); exact mass calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4$ m/e 246.0892, obsd m/e 246.0893, difference 0.0001.

1,4-(3-Hydroxypropoxy)benzene (55b). A mixture of 1.0 g (9.1 mmol) of hydroquinone, 2.7 g (19.4 mmol) of 3-bromo-1-propanol, 4.5 g of potassium carbonate, and 10 mL of acetone was refluxed overnight under a nitrogen atmosphere. The resulting product mixture was par-

tioned between 50 mL of water and 50 mL of dichloromethane. Conventional extraction and workup gave a white crystalline solid which was recrystallized from ether/hexane to give 1.73 g (84%) of **55b**: mp 95.5–97 °C; IR (KBr) 3311 (m), 2959 (w), 2890 (w), 1490 (s), 1453 (m), 1370 (w), 1271 (m), 1212 (s), 1103 (w), 1046 (s), 1031 (s), 942 (m), 821 (s) cm^{-1} ; NMR (CDCl_3 , D_2O) δ 6.81 (s, 4 H), 4.07 (t, $J = 6.5$ Hz) overlapping with 3.84 (t, $J = 6.5$ Hz) with a total area of 8 H, 1.99 (pent, $J = 6.5$ Hz, 4 H); exact mass calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4$ m/e 226.1206, obsd m/e 226.1212, difference 0.0006.

Electrolysis of 55b. A solution of 500 mg (2.21 mmol) of **55b** in 80 mL 1% methanolic potassium hydroxide was electrolyzed at ambient temperature until the UV absorption maximum at 288 nm had decreased to ~5% of its initial value (40 min, 1203 coulombs, 35% current efficiency). The methanol was removed in vacuo, 30 mL of brine was added, and the residue was extracted with 3×15 mL of dichloromethane. Workup afforded 510 mg of a yellowish oil. To a solution of 100 mg of the electrolysis product in 5 mL of anhydrous ether was added 2 mg of anhydrous *p*-toluenesulfonic acid. A white precipitate formed immediately, and the reaction was quenched with 5% NaHCO_3 after 10 s. The reaction was extracted with 3×10 mL of dichloromethane. Normal workup afforded 73 mg of an oily white solid. Trituration with ether afforded 33 mg of **57b** as a white crystalline solid. Passage of the mother liquors through a short activity III neutral alumina column with 45% ether/hexane afforded an additional 22 mg of **57b** (63% total yield): mp 201–202 °C; IR (KBr) 3003 (w) 2915 (w), 1420 (w), 1408 (m), 1229 (m), 1106 (s), 1074 (s), 1035 (m), 979 (s), 970 (s), 922 (s), 885 (w), 855 (m) cm^{-1} ; NMR (CDCl_3) δ 6.42 (s, 4 H), 4.05 (t, $J = 6$ Hz, 8 H), 1.83 (broadened pent, $J \approx 6$ Hz, 4 H); exact mass calcd for $\text{C}_{12}\text{H}_{16}\text{O}_4$ m/e 224.1048, obsd m/e 224.1055, difference 0.0007.

Attempted purification and identification of the electrolysis product was hampered by its instability to molecular distillation and to chromatography (neutral or basic alumina and fluorosil). The addition of pure **57b** to an NMR sample of the crude electrolysis product shows that **57b** comprises less than 5% of the electrolysis product.

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Supplementary Material Available: A table of charged densities and coefficients squared for methoxylated naphthalenes and structure proofs for compounds **10**, **11**, **12**, **14**, **21**, **24**, **29**, **30**, **31**, **33**, **35**, **36**, and **39** (9 pages). Ordering information is given on any current masthead page.