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Electroreductive Dimerization of Coumarin and Coumarin Analogues at Carbon Cathodes

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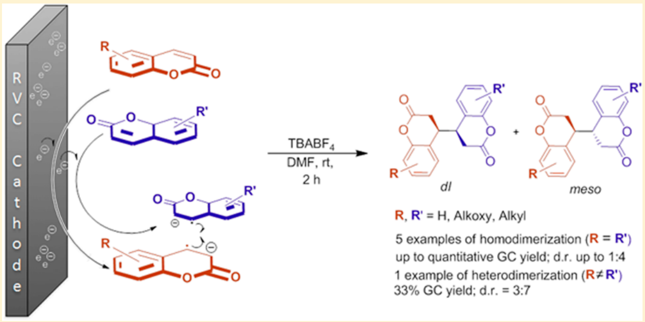
Supporting Information



ABSTRACT: Electrochemical reduction of coumarin (**1**), 6-methylcoumarin (**2**), 7-methylcoumarin (**3**), 7-methoxycoumarin (**4**), and 5,7-dimethoxycoumarin (**5**) at carbon cathodes in dimethylformamide containing 0.10 M tetra-*n*-butylammonium tetrafluoroborate has been investigated by means of cyclic voltammetry and controlled-potential (bulk) electrolysis. Cyclic voltammograms for reduction of **1**−**5** exhibit two irreversible cathodic peaks: (a) the first peak arises from one-electron reduction of the coumarin to form a radical−anion intermediate, which is protonated by the medium to give a neutral radical; (b) although most of this radical undergoes self-coupling to yield a hydrodimer, reduction of the remaining radical (ultimately to produce a dihydrocoumarin) causes the second cathodic peak. At a potential corresponding to the first voltammetric peak, bulk electrolysis of **1**−**5** affords the corresponding hydrodimer as a mixture of *meso* and *dl* diastereomers. Although the *meso* form dominates, the *dl*-to-*meso* ratio varies, due to steric effects arising from substituents on the aromatic ring. Electroreduction of an equimolar mixture of **1** and **4** gives, along with the anticipated symmetrical hydrodimers, an unsymmetrical product derived from the two coumarins. A mechanistic scheme involving both radical−anion and radical intermediates is proposed to account for the formation of the various products.

INTRODUCTION

Coumarin and its derivatives are widely utilized as pharmaceutical compounds because of their numerous applications as anticoagulants,[1] antibiotics,[2] and antidepressants[3] together with their use as anti-HIV-1,[2] antidiabetes,[3] antitumor,[4] and anti-inflammation[5] agents. Two of the most used coumarin-based drugs are (*RS*)-4-hydroxy-3-(3-oxo-1-phenylbutyl)-2*H*-chromen-2-one (Warfarin) and its sodium salt (Coumadin), both of which are employed as anticoagulants. Due to their optical properties, coumarins have been employed in laser devices, light-emitting diodes, and fluorescent markers for biomedical imaging.[6]

Reduction of coumarins has been studied extensively by means of polarography[7−9] as well as other electrochemical techniques such as cyclic voltammetry and controlled-potential (bulk) electrolysis.[10−28] On the basis of this body of work, it has been established generally that these compounds undergo a one-electron reduction to form a radical−anion intermediate that can be protonated by the solvent-supporting electrolyte to give a neutral radical; the latter species can (a) couple with itself to afford a hydrodimer or (b) gain another electron, followed by protonation, to give a dihydrocoumarin (chroman-2-one). In a study of the reduction of several coumarins at a mercury cathode in the presence of adsorbed alkaloids, Gourley and co-workers[10,11] found that hydrodimers and dihydrocoumarins can be obtained in substantial and moderate yields, respectively; closely related research was carried out by the group of Schäfer.[16,17] Sarrazin et al.[14] conducted a thorough examination by means of polarography and cyclic voltammetry of the reduction of 3- and 4-carboxycoumarins in both protic and aprotic media, and a mechanistic picture for the electrochemical behavior of these compounds was developed with the aid of bulk electrolyses and EPR studies. In an investigation of the electroreduction of coumarin at a mercury cathode in a methanol−water medium, Horner and Franz[15] reported that the use of lithium salts as supporting electrolytes enhances the yield of the hydrodimer. Nielsen et al.[19] studied the mechanism of the electrochemical reduction of 4-methylcoumarin at mercury in acidic methanol−water containing yohimbine; yields of dihydrocoumarin and the hydrodimer were found to depend on pH, supporting electrolyte identity, electrode potential, and reagent concentration. Electroreductive hydrodimerization of coumarin at a lead cathode in acetonitrile has been probed by Kise and co-workers;[20,23] computations based on the use of density functional theory were employed to elucidate the nature of the transition states involved in formation of the *dl* and *meso* diastereomers. A review article

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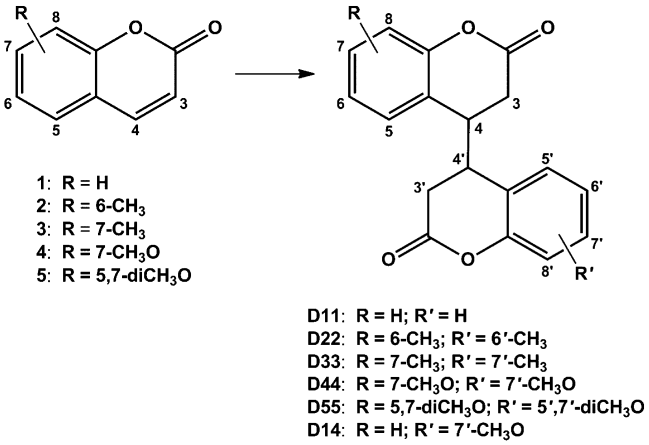
by Semeniuchenko et al.[26] includes a section pertaining to the electrochemical reduction of coumarins. A recent publication by Batanero and co-workers[28] has identified coumarin as one of the products arising from electrochemical reduction of 1,2-naphthoquinone at mercury in oxygen-containing acetonitrile.

As a consequence of our ongoing interest in both the electrosynthesis and electroreduction of coumarins,[29−31] we became interested in the behavior of coumarin and several of its derivatives at glassy carbon cathodes, with particular emphasis on the formation of hydrodimers. As is evident from the preceding paragraph, most earlier research pertaining to the electrochemistry of coumarins has entailed the use of mercury cathodes in aqueous media. In the present work, cyclic voltammetry and controlled-potential electrolysis, along with GC and GC−MS as means to identify and quantitate the electrolysis products, have been utilized to investigate the electroreduction of coumarin (**1**) and four of its derivatives (**2**−**5**), identified in Scheme 1, at glassy carbon cathodes in dimethylformamide (DMF) containing tetra-*n*-butylammonium tetrafluoroborate ($TBABF_4$) as supporting electrolyte. In particular, the electrochemical behavior of coumarins **2**−**5** has not, to the best of our knowledge, been studied previously, nor have the synthesis and characterization of their corresponding hydrodimers (consisting of mixtures of *dl* and *meso* diastereomers) been reported. Electroreduction of an equimolar mixture of two different coumarins (**1** and **4**) yields, among other products, an unsymmetric hydrodimer.

Scheme 1. Structures of Coumarins 1−5 and Coumarin-Derived Dimers D11, D22, D33, D44, D55, and D14



■ RESULTS AND DISCUSSION

Cyclic Voltammetric Behavior of Coumarins 1−5. Shown in Figure 1 are cyclic voltammograms recorded at 100 mV s^{-1} for the reduction of 3.0 mM solutions of coumarins **1**−**5** at a glassy carbon cathode in DMF containing 0.10 M $TBABF_4$. These voltammograms display two irreversible cathodic peaks: (a) the first peak is due to one-electron reduction of the double bond between carbon-3 and carbon-4 to form a radical−anion intermediate which is protonated (most likely by residual water in the solvent−electrolyte) to yield a neutral radical that undergoes self-coupling to afford a hydrodimer; and (b) the second, much smaller peak, seen at more negative potentials, can be attributed to further one-electron reduction of any neutral radical that remains in the diffusion layer to a carbanion, followed by protonation, to give a dihydrocoumarin.

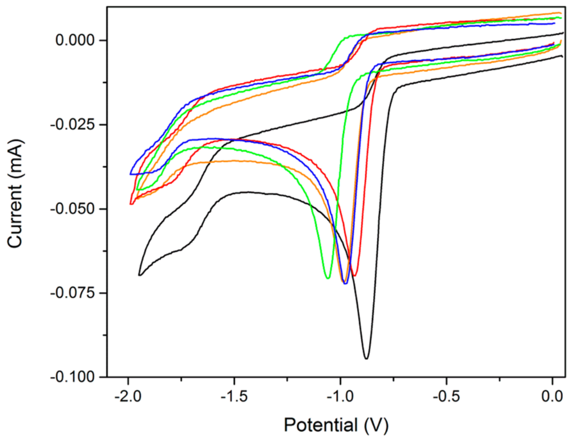


Figure 1. Cyclic voltammograms recorded at 100 mV s^{-1} for the reduction of 3.0 mM solutions of coumarin (**1**, black curve), 6-methylcoumarin (**2**, red curve), 7-methylcoumarin (**3**, blue curve), 7-methoxycoumarin (**4**, orange curve), and 5,7-dimethoxycoumarin (**5**, green curve) at a glassy carbon electrode in oxygen-free DMF containing 0.10 M $TBABF_4$. Potentials are given with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam, in contact with DMF saturated with both cadmium chloride and sodium chloride; this electrode has a potential of −0.76 V versus an aqueous saturated calomel electrode at 25 °C. Each scan goes from 0 to −2.0 to 0 V.

It is interesting to compare the cathodic peak potentials (E_{pc1}) for the first stage of reduction for coumarins **1**−**5**, as seen in Figure 1; the pertinent values, in order, are −0.88, −0.93, −0.98, −0.99, and −1.06 V, respectively. Qualitatively, the negative shift in these peak potentials, as a function of the various substituents, is in accord with relatively recent theoretical calculations, carried out by Fry and co-workers,[32,33] that pertain to the effects of various substituents on the reduction potentials for a number of benzalacetophenones at glassy carbon cathodes. In the case of compounds **2**−**5** of the present study, the methyl and methoxy substituents on the aromatic ring are both electron-donating moieties, which cause reduction of these species to occur, as observed (Figure 1), at slightly more negative potentials than coumarin **1**.

In addition, we took interest in a comparison of the relative currents for the two cathodic peaks (i_{pc1} and i_{pc2}) for reduction of each of the five coumarins as a function of scan rate over the range from 25 to 1000 mV s^{-1}. Although precise measurement of the peak height for the second stage of reduction is complicated by uncertainty in the decaying current for the first cathodic peak, the ratio of the two cathodic peak currents (i_{pc2}/i_{pc1}) was found approximately to double as the scan rate was increased over the specified range. Thus, we conclude that some of the aforementioned radical−anion intermediate generated during the first stage of reduction survives protonation by the medium for a longer time when a faster scan rate is employed; this observation supports the mechanism for reduction of coumarins **1**−**5** that is proposed later.

Controlled-Potential (Bulk) Electrolyses of Coumarins 1−5. Controlled-potential reductions of 5.0 mM solutions of coumarins **1**−**5** were carried out at reticulated vitreous carbon (RVC) cathodes in DMF containing 0.10 M $TBABF_4$. Coulometric data and product distributions are compiled in Table 1. For all of these experiments, the coulometric *n* value

Table 1. Coulometric Data and Product Distributions for Electrochemical Reduction of Coumarins 1−5 at Reticulated Vitreous Carbon Cathodes in DMF Containing 0.10 M TBABF$_4$

entry	substrate	*E* (V)	concentration (mM)	*n*[a]	product information[b]		
1	**1**	−0.98	5.0	1.01	**D11** [103] (*30/70*)		
2	**2**	−1.34	5.0	0.99	**D22** [108] (*43/57*)		
3	**3**	−1.34	5.0	0.97	**D33** [94] (*21/79*)		
4	**4**	−1.26	5.0	1.03	**D44** [76] (*24/76*)		
5	**5**	−1.45	5.0	1.00	**D55** [92] (*41/59*)		
6	**1** and **4**	−1.50	10.0[c]	1.01	**D11** [33] (*22/78*)	**D14** [34] (*27/73*)	**D44** [38] (*30/70*)

[a] Average number of electrons per molecule of substrate. [b] Boldface symbols designate the product as shown in Scheme 1; numbers in brackets indicate the percentage of substrate incorporated into the product; numbers in parentheses give the *dl*/*meso* ratio. [c] A one-to-one mixture of **1** and **4**, each at a concentration of 5.0 mM.

was very close to 1.0, demonstrating that **1**−**5** undergo reduction to form an intermediate radical−anion (**6**, as displayed in Scheme 1). When any one of coumarins **1**, **2**, **3**, and **5** is electrolyzed by itself (Table 1, entries 1−5), a symmetrical hydrodimer (actually present as a mixture of *dl* and *meso* diastereomers) is obtained in virtually quantitative yield, as observed by means of GC and GC−MS. However, the average yield of hydrodimer **D44** for several electrolyses of coumarin **4** was only 76%, but none of the dihydrocoumarin was observed. On the other hand, when an equimolar mixture of **1** and **4** is electrolyzed (Table 1, entry 6), two symmetric hydrodimers (**D11** and **D44**) and one unsymmetric hydrodimer (**D14**) are produced, and the yields of the three species are approximately equal. Although statistically the ratio of these three species should be 1:2:1 (or 25:50:25), we do not yet know why the observed and theoretical ratios differ. It is noteworthy that, for electrochemical reductions of **1**−**5** at potentials corresponding to the second voltammetric peak, we sometimes observed the formation of very small amounts of the respective chroman-2-one.

Chromatograms reveal the diastereomers (*dl* and *meso*) as separate peaks, with the first peak always being smaller than the second peak. Using high-performance liquid chromatography, we isolated one diastereomer of the unsymmetric hydrodimer (*meso*-**D14**, Figure 2), and with the aid of X-ray crystallography, we found that the second peak is for the *meso* compound. If it is assumed that the properties dictating the order of elution of the diastereomers for **D14** in our GC experiments exist for all of the other hydrodimers, one can conclude that the *dl*/*meso* ratio is close to 25/75, which is in accord with previous literature.[20,23] However, there are two exceptions—substrate **2** (Table 1, entry 2) and substrate **5** (Table 1, entry 5)—for which the *dl*/*meso* ratio is closer to 50/50, an observation that will be explained further when we discuss the mechanistic picture for reduction of coumarins. Additional support for the various *dl*/*meso* ratios was obtained by means of ^{1}H NMR spectrometry. For example, the α-protons for **D22** are observed as a pair of distinct signals (corresponding to the two diastereomers) at δ 2.58 and 2.60 ppm, which (after integration) reveal a diastereomeric ratio of 1/1; results of these measurements are compiled in the Supporting Information.

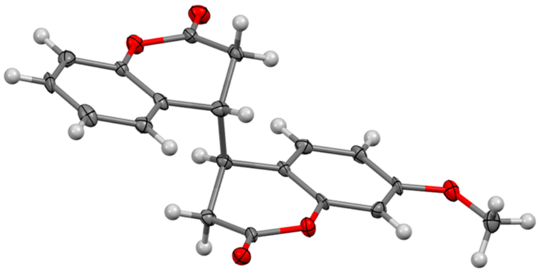
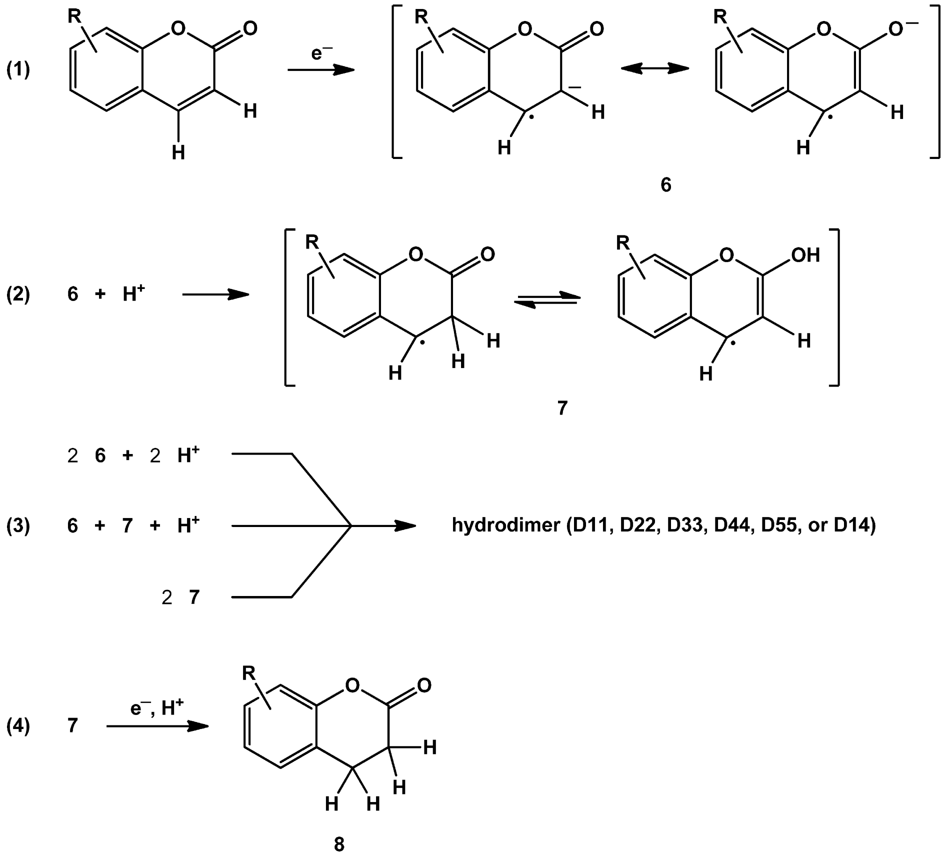


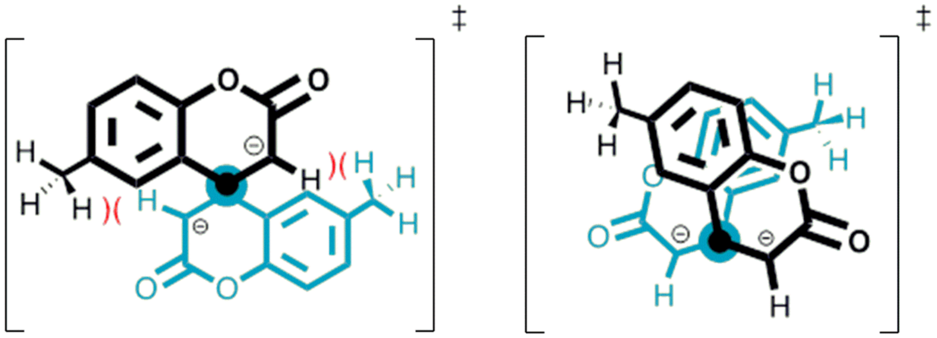
Figure 2. Crystal structure of *meso*-**D14**.

As additional support of our mechanism (proposed in the next section of this paper) for electrochemical reductions of **1**−**5**, we carried out a single bulk electrolysis of a 5.0 mM solution of coumarin **1** at a reticulated vitreous carbon cathode in DMF−0.10 M TBABF$_4$ at a potential (−1.80 V) slightly more negative than the second cathodic peak for **1**. Although GC−MS analysis of the catholyte revealed the presence of the hydrodimer (**D11**) as a major product, we did detect the presence of chroman-2-one, which provides evidence for a chroman-2-one-4-yl radical intermediate.

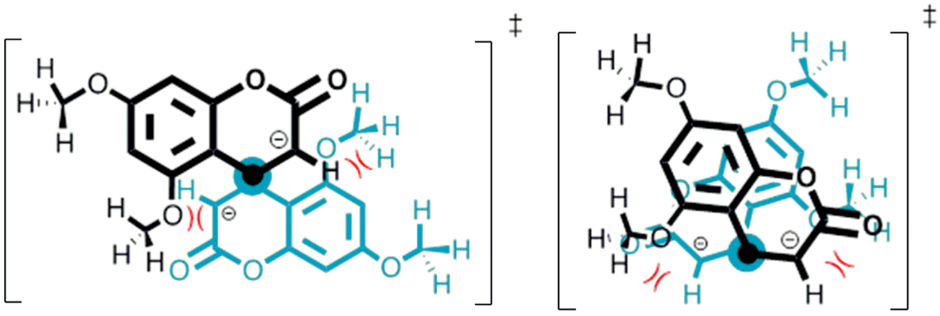
Proposed Mechanism for Electroreduction of Coumarins. Depicted in Scheme 2 is a mechanistic picture with a plausible set of pathways to explain the electrochemical behavior of coumarins **1**−**5**. As shown in reaction (1), addition of a single electron to a coumarin results in the formation of radical−anion **6**, which bears a negative charge at the 3-position and an unpaired electron at the 4-position. Protonation of **6** by adventitious water present in the solvent−electrolyte (typically at concentrations ranging from 40 to 50 mM)[34,35] leads to radical **7** [reaction (2)]. Coupling to afford both *dl*- and *meso*-

Scheme 2. Mechanistic Pathways for Electrochemical Reduction of Coumarins and for the Formation of Dimeric and Monomeric Products




D22 *meso* transition state

D22 *dl* transition state


D55 *meso* transition state

D55 *dl* transition state

Figure 3. Possible transition states, adapted from Kise et al.,[20,23] for homocoupling of intermediates **7** derived from separate electroreductions of **2** and **5**, demonstrating the proposed high-energy transition-state configurations arising from steric clashes.

hydrodimers can occur via three distinct routes: (a) two radical−anions (**6**) can react, with uptake of two protons; (b) **6** and **7** can react, with uptake of a single proton; or (c) two radicals (**7**) can react [reaction (3)]. Findings obtained by means of ^{13}C and ^{1}H NMR spectrometry, as well as by X-ray crystallography, confirm that the 4,4′-hydrodimer is obtained. To account for the small amount of a chroman-2-one seen in electrolyses of **1**−**5** at potentials corresponding to the second voltammetric peak, we propose that **7** accepts an electron from the cathode to form a carbanion which is rapidly protonated by the medium [reaction (4)].

Kise and co-workers[20,23] reported two optimized transition-state structures for hydrocoupling of the radical−anion **6** of coumarin **1**, one for the *meso*- and the other for the *dl*-hydrodimer. On the basis of calculations, these authors predicted a lower-energy transition state for the *meso* compound, in good agreement with their experimental results (25/75 *dl*/*meso* ratio). In the present work, compounds **D11**, **D14**, **D33**, and **D44**, follow this general model, exhibiting (as shown in Table 1) a diastereoselectivity on the order of 25/75 *dl*/*meso* (based on ^{1}H NMR spectrometry and GC peak areas). However, compounds **D22** and **D55** display a substantial erosion of this selectivity, with *dl*/*meso* ratios approaching 50/50. We propose that this difference might be attributable to a new steric interaction between the "large" sp^3 groups (6-methyl and 5-methoxy) for **D22** and **D55**, respectively, along with α-protons of their coupling partners as shown in Figure 3. Thus, we suggest that, due to these steric clashes (denoted by red symbols), the *meso* transition state is now energetically closer to the *dl* transition state of Kise et al.[20,23] As indicated in Scheme 2, we have not ruled out the possibility that radical **7** can be involved in the production of hydrodimers; computational and experimental efforts toward obtaining a comprehensive model are underway.

■ CONCLUSIONS

Cyclic voltammograms for the reduction of coumarins at glassy carbon cathodes in a DMF−TBABF$_4$ medium reveal a two-step process. Bulk electrolyses at potentials corresponding to the first stage of reduction of a single coumarin afford a hydrodimer (a mixture of *dl* and *meso* diastereomers) in virtually quantitative yield, as determined by means of GC and GC−MS. Electrolysis of equimolar amounts of two different coumarins gives a mixture of two symmetric hydrodimers and one unsymmetric hydrodimer, with corresponding diastereomers. When coumarins are electrolyzed at a potential corresponding to the second stage of reduction, the main product is the hydrodimer, but small quantities of a chroman-2-one are also formed.

■ EXPERIMENTAL SECTION

Reagents. Each of the following chemicals was obtained from commercial sources and was used as received without further purification: anhydrous diethyl ether (absolute), *n*-hexadecane (99%), chloroform (98%), chloroform-*d* (99.8%), coumarin (**1**, ≥99%), 6-methylcoumarin (**2**, ≥99%), 7-methylcoumairn (**3**, ≥98%), 7-methoxycoumarin (**4**, ≥98%), 5,7-dimethoxycoumarin (**5**, 98%), dimethylformamide (99.9%), and acetonitrile (99.9%). Tetra-*n*-butylammonium tetrafluoroborate (>99%), which served as the supporting electrolyte, was recrystallized from water−methanol and stored in a vacuum oven at 70−80 °C prior to use. All deaeration procedures were accomplished with zero-grade argon.

Cells, Electrodes, Procedures, and Instrumentation. A description of the cell used for cyclic voltammetry can be found in a previous publication.[36] We constructed a planar, circular glassy carbon cathode (with a geometric area of 0.071 cm^2) by press-fitting a short piece of glassy carbon cylinder (grade GC-20, 3.0 mm diameter, Tokai Electrode Manufacturing Company, Tokyo, Japan) into the end of a machined Teflon tube. Electrical connection to the working electrode was made via a 3.0 mm diameter stainless-steel rod that contacted the cathode material and extended upward through the tube. A coil of platinum wire served as the auxiliary (counter) electrode for cyclic voltammetry. Prior to each scan, the glassy carbon working electrodes were cleaned with an aqueous suspension of 0.05 μm alumina on a polishing pad, followed by a rinse with DMF in an ultrasonic bath. All potentials in the present work are reported with respect to a reference electrode consisting of a cadmium-saturated mercury amalgam, in contact with DMF saturated with both cadmium chloride and sodium chloride;[37−39] this electrode has a potential of −0.76 V versus an aqueous saturated calomel electrode at 25 °C. Cyclic voltammetric experiments were performed as described in a previous paper.[40]

Information about the two-compartment (divided) cell, instrumentation, and procedures used for controlled-potential (bulk) electrolysis is provided elsewhere.[41,42] For bulk electrolyses, we employed RVC cathodes, the fabrication and cleaning of which have been previously described;[42] the aforementioned cadmium-saturated mercury amalgam reference electrode was utilized, and the auxiliary anode was a graphite rod immersed in a DMF−0.10 M TBABF$_4$ solution separated from the cathode compartment by a sintered-glass disk backed by a methyl cellulose−DMF−0.10 M TBABF$_4$ plug.

Electrosynthesis of Symmetric Hydrodimers. Each of the five symmetrical hydrodimers in this investigation was synthesized via electrochemical reduction of the corresponding coumarin monomer. A 100 mM solution of the chosen coumarin, dissolved in DMF containing 0.10 M TBABF$_4$, was placed in the electrochemical cell mentioned above.[41] To conduct the electrosynthesis, the RVC working electrode was held at −1.5 V until the current decayed to less than 1 mA (about 2 h), and the electrolysis was allowed to continue for an additional 30 min to ensure full reduction. Then the catholyte was poured into a separatory funnel containing diethyl ether and 10% aqueous HCl; the ether phase was separated, washed twice with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure with the aid of a rotary evaporator. Then the resulting solid (a mixture of diastereomers) was allowed to remain under vacuum overnight. Finally, the dominant diastereomer (*meso* compound) was obtained via recrystallization from hot ethanol and chloroform. By means of this procedure, the following crystalline compounds were synthesized and characterized spectroscopically.

*[4,4′-Bichroman]-2,2′-dione (**D11**):* ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.69−2.74 (m, 2H), 2.83−2.91 (m, 4H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 28.7 (CH), 33.0 (CH$_2$), 117.7 (CH), 123.4 (C), 124.8 (CH), 129.6 (CH), 129.8 (CH), 151.3 (C), 167.7 (C); HRMS (ESI−TOF) *m*/*z* calcd for $C_{18}H_{14}O_4Na$ [M + Na]$^+$ 317.0790, found 317.0800.

*6,6′-Dimethyl-[4,4′-bichroman]-2,2′-dione (**D22**):* ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.38 (s, 6H), 2.65−2.70 (m, 2H), 2.82−2.86 (m, 4H), 7.01 (d, *J* = 8.5 Hz, 2H), 7.06 (s, 2H), 7.15 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 20.9 (CH$_3$), 33.1 (CH), 38.7 (CH$_2$), 117.3 (CH), 123.2 (C), 129.0 (CH), 130.0 (CH), 134.6 (C), 149.2 (C), 168.0 (C); HRMS (ESI−TOF) *m*/*z* calcd for $C_{20}H_{18}O_4Na$ [M + Na]$^+$ 345.1103, found 345.1099.

*7,7′-Dimethyl-[4,4′-bichroman]-2,2′-dione (**D33**):* ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.38 (s, 6H), 2.65−2.69 (m, 2H), 2.82−2.85 (m, 4H), 6.94 (s, 2H), 7.01 (d, *J* = 7.5 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 21.2 (CH$_3$), 33.1 (CH), 38.5 (CH$_2$), 118.0 (CH), 120.4 (C), 125.6 (CH), 129.4 (CH), 139.9 (C), 151.2 (C), 168.1 (C); HRMS (ESI−TOF) *m*/*z* calcd for $C_{20}H_{18}O_4Na$ [M + Na]$^+$ 345.1103, found 345.1104.

*7,7′-Dimethoxy-[4,4′-bichroman]-2,2′-dione (**D44**):* ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.67−2.70 (m, 2H), 2.80−2.85 (m, 4H), 3.82 (s, 6H), 6.67 (s, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 33.2 (CH), 38.5 (CH$_2$), 55.6 (CH$_3$), 103.3 (CH), 110.6 (CH), 115.3 (C), 130.2 (CH), 152.1 (C), 160.5 (C), 167.8 (C); HRMS (ESI−TOF) *m*/*z* calcd for $C_{20}H_{18}O_6Na$ [M + Na]$^+$ 377.1001, found 377.0997.

5,5′,7,7′-Tetramethoxy-[4,4′-bichroman]-2,2′-dione (**D55**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.67−2.71 (m, 2H), 3.01 (d, J = 16.5 Hz, 2H), 3.43−3.44 (m, 2H), 3.48 (s, 6H), 3.74 (s, 6H), 5.99 (d, J = 2.7 Hz, 2H), 6.12 (d, J = 1.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.9 (CH), 33.5 (CH_2), 55.1 (CH_3), 55.5 (CH_3), 93.6 (CH), 94.0 (CH), 104.0 (C), 153.4 (C), 157.6 (C), 160.7 (C), 167.9 (C); HRMS (ESI−TOF) m/z calcd for $C_{22}H_{22}O_8Na$ $[M + Na]^+$ 437.1212, found 437.1208.

Electrosynthesis of Unsymmetric Hydrodimer (D14). Synthesis of unsymmetric hydrodimer **D14** was accomplished via reduction of a mixture of coumarin **1** and 7-methoxycoumarin **4**, each at an initial concentration of 50 mM in DMF containing 0.10 M $TBABF_4$, in the electrochemical cell referred to earlier.[41] We held the potential of the RVC working electrode at −1.5 V until the current decayed to less than 1 mA (about 2 h), after which the electrolysis was continued for an additional 30 min to ensure complete reduction of the coumarins. Then the catholyte was poured into a separatory funnel containing diethyl ether and 10% aqueous HCl; the organic phase was separated and washed twice with water, dried over anhydrous sodium sulfate, and filtered; most of the solvent was removed via rotary evaporation. Preparative-scale high-performance liquid chromatography was used to isolate and purify the *meso* diastereomer, which was characterized spectroscopically.

7-Methoxy-[4,4′-bichroman]-2,2′-dione (**D14**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.73−2.67 (m, 2H), 2.87−2.81 (m, 4H), 3.83 (s, 3H), 6.68 (d, J = 1.3 Hz, 1H), 6.76 (d, J = 4.0 Hz, 1H), 7.13 (d, J = 4.1 Hz, 1H), 7.17 (d, J = 4.1 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 3.7 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.0 (CH), 33.2 (CH), 38.1 (CH_2), 39.1 (CH_2), 55.6 (CH_3), 103.3 (CH), 110.6 (CH), 115.1 (CH), 117.6 (CH), 123.6 (C), 124.8 (CH), 129.5 (CH), 129.7 (CH), 136.3 (C), 151.3 (C), 152.2 (C), 160.6 (C), 167.7 (C), 167.8 (C); HRMS (EI) m/z calcd for $C_{19}H_{16}O_5$ $[M]^+$ 324.0992, found 324.0998.

Separation, Identification, and Quantitation of Electrolysis Products. At the end of each controlled-potential (bulk) electrolysis, the catholyte was partitioned between diethyl ether and 10% aqueous HCl, and the organic layer was washed twice with brine. Then the ether phase was dried over anhydrous sodium sulfate and concentrated with the aid of rotary evaporation. Products were separated and identified by means of gas chromatography (GC) and gas chromatography−mass spectrometry (GC−MS). Each chromatograph was equipped with a 30 m × 0.25 mm capillary column with a DB-5 stationary phase; the GC system utilized a flame-ionization detector, whereas the GC−MS system contained an inert mass-selective detector operating in electron ionization mode (70 eV). Gas chromatographic retention times and mass spectral data for the electrolysis products were compared with those of commercially available or chemically synthesized authentic samples. Identities of all synthesized materials were confirmed by means of both ^{1}H and ^{13}C NMR spectrometry (500 MHz instrument) as well as high-resolution GC−MS. Procedures used for the quantitation of electrolysis products have been described in an earlier publication.[43] Peak areas for the different products were determined with respect to an internal standard (n-hexadecane) added in a known amount to the electrolysis cell prior to the start of a controlled-potential reduction. All product yields are reported as the percentage of starting material incorporated into each product.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for compounds **11**, **22**, **33**, **44**, **55**, and **14**, as well as X-ray crystallographic data for compound **14**. This material is available free of charge via the Internet at http://pubs.acs.org. In addition, files containing supplementary crystallographic data (CCDC 1015743) can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44) 1223-336-033 or e-mail deposit@ccdc.cam.ac.uk.

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Notes

The authors declare no competing financial interest.

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