(245 mg, 0.89 mmol) and Et_3N (247 mL, 1.78 mmol) sequentially. The mixture was stirred at 0 °C for 10 h and then warmed up to room temperature. After the solution was stirred for an additional 6 h, the mixture was stripped of solvent under reduced pressure and worked up as described for **33b**. The product was obtained as a pair of diastereoisomers, **33a** and **33b** in an 83% yield. The ratio of **33a** and **33b** was about 7:13 as determined by measuring either the methyl ester or Gly αCH_2 resonances of the two compounds in ^1H NMR. Isomer **33a** was separated from **33b** by using flash chromatography (EtOAc/hexane = 2:1, R_f = 0.51): ^1H NMR ($CDCl_3$) δ 0.96 (d, J = 6.2 Hz, 6 H, Leu δCH_3), 1.40–1.76 (m, 1 H, Leu γCH), 1.95 (d, J = 7.5 Hz, 3 H, Ala βCH_3), 2.00–2.32 (m, 1 H, Leu βCH), 2.58–2.96 (m, 1 H, Leu βCH), 3.74 (s, 3 H, OCH_3), 4.09 (d, J = 5.72 Hz, Gly αCH_2), 5.38 (q, J = 7.5 Hz, 1 H, Ala αCH), 5.69 (dd, J = 5.7, 10.1 Hz, 1 H, Leu αCH), 7.23 (br t, J = 5.7 Hz, 1 H, NH), 7.56–7.88 (m, 4 H, Pht); ^{13}C NMR ($CDCl_3$) δ 17.54 (Ala βC), 21.35, 22.52 (Leu δCH_3), 24.95 (Leu γC), 38.52 (Leu βC), 41.42 (Gly αC), 42.72 (Leu αC), 52.21 (OCH_3), 57.45 (Ala αC), 123.67, 131.26, 134.55 (Pht), 153.93 (CN_4), 167.28, 167.62, 169.31 (C=O).

Synthesis of 13a and 13b from 2 Using PCl_5 and Different Azide Reagents. When PCl_5/Me_3SiN_3 or $PCl_5/(n\text{-}Bu)_3SnN_3$ were the reagents used for synthesis of the tetrazoles **13a** and **13b** the general procedure described above was applied except HN_3 was replaced with Me_3SiN_3 or $(n\text{-}Bu)_3SnN_3$. When the reagents $PCl_5/NaN_3/NH_4Cl$ were used, the reaction was carried out in DMF at 90 °C for 4 h and worked up as described in the general procedure.

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The Influence of Ion Pairing on the Electroreductive Cleavage of Substituted 9,10-Anthraquinones in DMF Solution

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A variety of substituted 9,10-anthraquinones with acetate and trifluoroacetate leaving groups at the 2-methyl position were synthesized from 2-methyl-9,10-anthraquinones containing 0–2 methoxy substituents. Cyclic voltammograms of the acetates in DMF containing $LiClO_4$ as supporting electrolyte exhibited two reduction waves, the first resulting from the formation of Li^+ ion pairs of their radical anions and the second from Li^+ ion pairs of their dianions. Constant potential reduction of the acetates to their dianions followed by air oxidation gave high yields (78–88%) of their reductive cleavage products, the 2-methyl-9,10-anthraquinones. In contrast, reduction of the acetates to their radical anions led to high yields of their alcohols (the 2-(hydroxymethyl)-9,10-anthraquinones) as a result of saponification. Reduction of the trifluoroacetates in DMF/$LiClO_4$ produced comparable yields of their corresponding reductive cleavage products and alcohols via ion pairs of their radical anions or dianions.

Reductive cleavage has been used to deprotect 9,10-anthraquinone esters of amino acids,[1a] peptides,[1a] carboxylic acids,[1b] and primary amines.[1b] Bioreductive cleavage of the antitumor anthracyclines, which possess a substituted 9,10-anthraquinone, has been proposed as a possible mechanism whereby these drugs function as antineoplastic agents.[2,3] There is uncertainty, however, regarding the precise mechanism of this in vivo reaction of anthracyclines.[3b,c] Koch and co-workers[2b] have provided evidence that suggests that a hydroquinone intermediate is the actual species that undergoes cleavage whereas other workers[2c] favor a semiquinone. A third intermediate, which has not been seriously considered in the literature, is a radical anion. This could be an oversight since hydrophobic environments exist in the cell wherein this intermediate could be relatively long-lived.

It was our long-range goal to prepare a variety of substituted anthraquinones with good leaving groups and examine substituent effects upon the cleavage reactions of their hydroquinones in aqueous electrolytes and their radical anions or dianions in nonaqueous electrolytes by using electrochemical techniques. Redox potentials of these compounds, which would serve as models for the anthracyclines, could be useful in the design and synthesis of new anthracyclines that have low cardiotoxicity.[4] In this paper we report the synthesis of anthraquinones **1–4** and their electrochemistry in DMF electrolytes.

Results and Discussion

Synthesis of Anthraquinones 1–4. The synthetic route to anthraquinones **1–4** is outlined in Scheme I with **2**. Bromination of **2a** with *N*-bromosuccinimide gave **2b** in 75% yield. Compound **2b** was converted to **2c** with AgOAc (91%), **2d** with AgO_2CCF_3 (92%), and **2e** with

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(2) (a) Moore, H. W.; West, K. F.; Srinivasacher, K.; Czerniak, R. In *Structure–Activity Relationships of Anti-Tumour Agents*; Reinhoudt, D. N., Connors, J. A., Pinedo, H. M., van de Poll, K. W., Eds.; Martinus Nijhoff: Boston, 1983; pp 93–110. (b) Kleyer, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1983**, *105*, 2504. (c) Komiyama, T.; Oki, J.; Inui, T. *J. Antibiot.* **1979**, *32*, 1219. (d) Ramakrishnan, K.; Fisher, J. *J. Am. Chem. Soc.* **1983**, *105*, 7187. (e) Sinha, B. K. *Biochem. Pharmacol.* **1981**, *30*, 2626. (f) Donehower, R. C.; Meyers, C. E.; Chabner, B. A. *Life Sci.* **1979**, *25*, 1.

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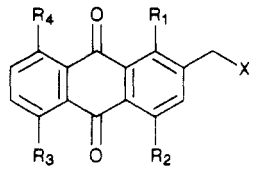

1: $R_1 = R_2 = R_3 = R_4 = H$
2: $R_1 = OCH_3$, $R_2 = R_3 = R_4 = H$
3: $R_1 = R_4 = OCH_3$, $R_2 = R_3 = H$
4: $R_1 = R_4 = H$, $R_2 = R_3 = OCH_3$

a: X = H
b: X = Br
c: X = O_2CCH_3
d: X = O_2CCF_3
e: X = OH

aqueous $AgNO_3$ (90%). Similar yields were obtained with 1, 3, and 4. The trifluoroacetates **1d–4d** could also be prepared from the alcohols **1e–4e** by treatment with trifluoroacetic anhydride in the presence of a catalytic amount of trifluoroacetic acid. In this manner, **4d** was synthesized from **4e** in 93% yield. An alternate route to the alcohols is the acid-catalyzed hydrolysis of acetates **1c–4c**. Heating **4c** in aqueous 1-propanol in the presence of H_2SO_4 led to an 82% yield of **4e**. Satisfactory spectral data and elemental analyses were obtained for all new compounds.

Cyclic Voltammetry of Anthraquinones 1a–4a. In aprotic media such as DMF a quinone is typically reduced in two separate one-electron steps to its radical anion and dianion.[5] Such is the case for **2a** in DMF/$LiClO_4$ at a glassy carbon (GC) electrode which exhibits two reduction waves in its cyclic voltammogram (CV) at −0.996 and −1.197 V (vs. Ag/AgCl/0.10 M Cl^-) as shown in Figure 1a. Constant potential reduction of **2a** at −1.300 V produced a wine-red solution of its dianion with an n value of 2. Exposure of the catholyte to oxygen followed by workup led to a nearly quantitative recovery of **2a**. Compounds **1a** and **3a** give two closely separated reduction waves like **2a**, but **4a** displays only one broad reduction wave presumably from two overlapping waves. Peak potentials (E_p) for **1a–4a** in DMF/$LiClO_4$ are given in Table I.

The reduction of **1a–4a** in DMF/TBAP (tetrabutylammonium perchlorate) is considerably more complex. The CV of **2a** in this electrolyte (Figure 1b) shows a reversible wave at −1.034 V for the formation of its radical anion and at least two irreversible waves at more negative potentials. Constant potential reduction of **2a** at −1.900 V gave several products that were not identified and only a 16% recovery of **2a** upon workup. The peak potentials from the CVs of **1a–4a** in DMF/TBAP are given in Table I. In each case a poorly defined reduction wave precedes $E_p(2)$. Since the dianions of **1a–4a** are not stable in DMF/TBAP, this electrolyte was not used in the electroreductive cleavage studies of **1c–4c** and **1d–4d**. Peak potentials of these compounds were measured by using CV and are given in Table I.

The differences in the CVs of **2a** in Figure 1 can be explained by ion pairing. The first reduction waves of **2a** in DMF/$LiClO_4$ and DMF/TBAP, which result from the reduction of **2a** to $\mathbf{2a}^{\bullet-}$, are reversible and occur at about the same potential (E_p = −1.0 V). In contrast, the second wave, which results from the reduction of $\mathbf{2a}^{\bullet-}$, occurs at a much less negative potential in DMF/$LiClO_4$ and is more reversible. This suggests that the actual species that is reduced in DMF/$LiClO_4$ is not $\mathbf{2a}^{\bullet-}$ but its neutral ion pair, $Li^+\ \mathbf{2a}^{\bullet-}$. Undoubtedly, $\mathbf{2a}^{2-}$ is also associated with one or more Li^+ ions stabilizing the dianion in this medium. There is even evidence that **2a** is associated with Li^+. Solutions of **2a** are pink in DMF/$LiClO_4$ and yellow in DMF/TBAP. Also, E_p for **2a** is 38 mV less negative in the presence of Li^+. A comparison of $E_p(1)$ and $E_p(2)$ for **1a–4a** in Table I shows that the strength of the ion pair increases as methoxy groups are introduced on the anthraquinone. In DMF/$LiClO_4$ ΔE_p is 300 mV for **1a**, 200 mV for **2a**, 60

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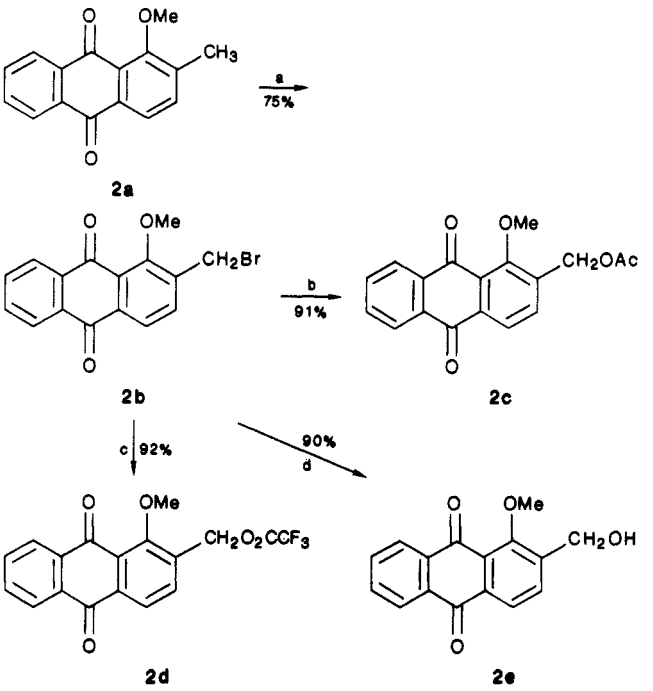
Scheme I[a]



[a] (a) NBS, CCl_4, benzoyl peroxide; (b) AgOAc, $HCCl_3$, HOAc; (c) AgO_2CCF_3, $HCCl_3$, HO_2CCF_3; (d) $AgNO_3$, H_2O, dioxane.

Table I. Cathodic Peak Potentials (V) in DMF Measured by Cyclic Voltammetry[a]

	0.10 M $LiClO_4$			0.10 M TBAP		
compd	$E_p(1)$	$E_p(2)$	$E_p(3)$	$E_p(1)$	$E_p(2)$	$E_p(3)$
1a	−1.040	−1.348		−0.991	−1.689	
2a	−0.996	−1.197		−1.034	−1.713	
3a	−1.113	−1.191		−1.178	−1.783	
4a	−1.1[d]			−1.148	−1.682	
1c	−0.909	−1.235		−1.018	−1.714	−1.790
2c	−0.938	−1.174		−1.039	−1.667	−1.775
3c	*b*	−1.123		−1.069	−1.660	−1.830
4c	*b*	−1.112		−1.148		−1.811
1d	−0.8	−0.932	−1.246	−0.937	−1.079	−1.9
2d	−0.842	−0.993	−1.155	−0.900	−1.098	−1.680
3d	−0.885	−1.1[d]		−0.896	−1.116	*c*
4d	−1.0	−1.1[d]		−0.997	−1.159	−1.724

[a] Reference is Ag/AgCl (0.10 M Cl^-), sweep rate = 100 mV s^{-1}. [b] Shoulder. [c] Several overlapping waves. [d] Broad.

Table II. Products and Yields from Constant Potential Reductions in DMF with $LiClO_4$ as Supporting Electrolyte[a]

compd	E_{app}, V[b]	products (% yield)[c]
1c	−1.05	1a (8), 1e (65)
1c	−1.75	1a (78), 1e (6)
2c	−0.90	2a (6), 2e (58)
2c	−1.50	2a (78), 2e (2)
3c	−1.60	3a (88), 3e (3)
4c	−1.00	4a (16), 4e (80)
4c	−1.50	4a (83), 4e (15)
1d	−1.10	1a (36), 1e (37)
1d	−1.30	1a (34), 1e (45)
2d	−1.00	2a (26), 2e (18)
2d	−1.30	2a (16), 2e (16)
3d	−1.60	3a (29), 2e (37)
4d	−1.60	4a (40), 4e (57)

[a] Working electrode—carbon felt. [b] Vs. Ag/AgCl (0.10 M Cl^-). [c] HPLC analysis using reverse-phase column.

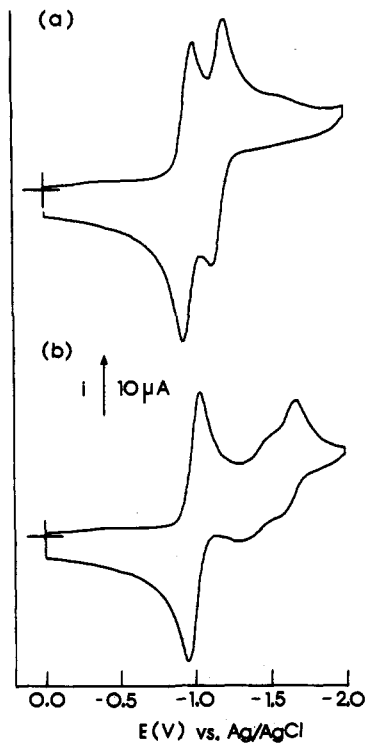
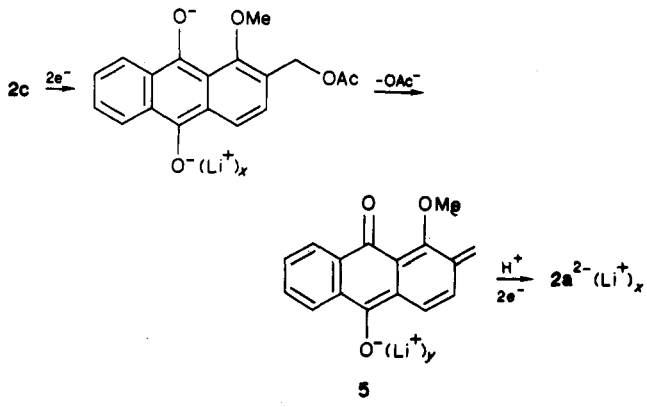


Figure 1. (a) Cyclic voltammogram of 1.0 mM **2a** in DMF (0.10 M $LiClO_4$) at a sweep rate of 100 mV s^{-1}. (b) Cyclic voltammogram 1.0 mM **2a** in DMF (0.10 M TBAP) at a sweep rate of 100 mV s^{-1}.

Scheme II



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mV for **3a**, and <50 mV for **4a**.

Electroreduction of Acetates 1c–4c in DMF/$LiClO_4$. A CV of 1.0 mM **2c** in DMF/$LiClO_4$ is shown in Figure 2a. As with anthraquinone **2a**, two reduction waves are observed, although the diffusion-controlled current is considerably higher. Plots of $\nu^{1/2}$ vs. i_p (ν = scan rate and i_p = peak current) for both waves are linear, demonstrating that the reduction processes are diffusion-controlled. $E_p(1)$ and $E_p(2)$ do not change with varying concentrations of **2c** (0.50–4.0 mM), which is consistent with a rate-determining step that is first order in **2c**. Acetates **1c**, **3c**, and **4c** also exhibit two waves. The first wave of **3c** and **4c** appears as a shoulder on the second wave at faster scan rates (ν > 50 mV s^{-1}). $E_p(1)$ and $E_p(2)$ for **1c–4c** are given in Table I.

Constant-potential reduction of **2c** at −1.500 V in DMF/$LiClO_4$ gave a 78% yield of the expected cleavage product **2a** with an n value of 4. Some alcohol (**2e**) was also formed, but in low yield (see Table II). The sequence of reactions in Scheme II is consistent with these data. A $2e^-$ reduction of **2c** produces the Li^+ ion pair of its dianion $\mathbf{2c}^{2-}$, which undergoes cleavage to the vinylogous quinone methide **5**. A reaction pathway involving $2e^-$ and H^+ then converts **5** to the dianion of **2a**. The source of H^+ is presumably water even though DMF was distilled from CaH_2 and $LiClO_4$ was dried at 150 °C under reduced pressure (0.2 mmHg) for several hours prior to use. The number of Li^+ ions in each ion pair in Scheme II is not known. Constant-potential reduction of **1c**, **3c**, and **4c** at potentials more negative than their $E_p(2)$ values, which converts these acetates to ion pairs of their dianions, also gave their corresponding cleavage products (**1a**, **3a**, and **4a**, respectively) in high yields (see Table II).

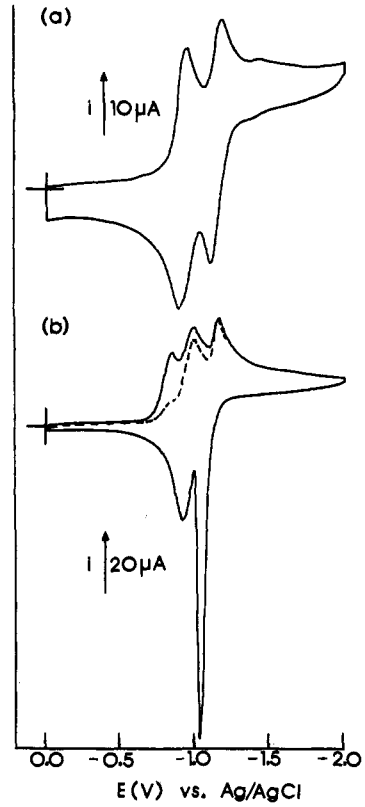

Figure 2. (a) Cyclic voltammogram of 1.0 mM **2c** in DMF (0.10 M $LiClO_4$) at a sweep rate of 100 mV s^{-1}. (b) Cyclic voltammogram of 1.0 mM **2d** in DMF (0.10 M $LiClO_4$) at a sweep rate of 100 mV s^{-1}. Dashed curve is the second scan.

Anthraquinones **1c–3c** were also reduced at or near their $E_p(1)$ values which generates ion pairs of their corresponding radical anions. The results are strikingly different (Table II). At these potentials **1e–3e** are the major products. We believe the alcohols result from saponification of their esters. Support for this postulate comes from a series of experiments performed on **1c** which can be reduced cleanly to its radical anion. Reduction of 3.8 mM **1c** at −0.950 V for 72 min in DMF/$LiClO_4$, either with no added compounds or with varying small amounts of water or in 0.10 M $CH_3CH_2OCS_2^-$ (a strong nucleophile that has been used to trap quinone methides such as **5**[2d]) gave approximately 30% **1c**, 3% **1a**, and 45% **1e** in each instance. Thus, it appears that the alcohols are not produced by the reaction of quinone methide intermediates with H_2O or OH^-. In contrast, when 0.10 M $PhCH_2OAc$ was added to the medium, 61% **1c**, 6% **1a**, and 13% **1e** were obtained under identical conditions and time. The added $PhCH_2OAc$, which is not reduced at potentials less negative than −2.0 V, presumably competes with **1c** for OH^- and thereby increases the ratio of **1a** to **1e**. Finally, it should be noted that esters **1c–4c** are hydrolyzed to their alcohols in DMF/$LiClO_4$ solutions containing LiOH.

Regardless of whether saponification is the competing reaction or not, the high yields of the reductive cleavage

products **1a–4a** from the dianion ion pairs of **1c–4c** and the low yields of **1a–4a** from the radical anion ion pairs of **1c–4c** show that the dianions cleave at a faster rate than the radical anions. Since radical anions can undergo bimolecular disproportionation to a neutral quinone and dianion, it is possible that **1a–4a** form exclusively from the dianions of **1c–4c** even at the less negative potentials.

Electroreduction of Trifluoroacetates 1d–4d in DMF/$LiClO_4$. Trifluoroacetates **1d–4d** were prepared to study the effect of this better leaving group on reductive cleavage. A CV of **2d** in DMF/$LiClO_4$ is shown in Figure 2b. Three reduction waves are observed at −0.900, −1.098, and −1.680 V. All three waves give plots of $\nu^{1/2}$ vs. i_p that are linear and peak potentials are constant over a wide range of concentrations of **2d** (0.50–4.0 mM). Reduction of the trifluoroacetate group can be ruled out as a source of one of these waves since $PhCH_2O_2CCF_3$ is not reduced between 0 and −2.0 V. The first wave, which results from reduction of **2d** to its radical anion ion pair, is 139 mV less negative than $E_p(1)$ for **2c**. This demonstrates that **2d** is more easily reduced than **2c**, a result that would be expected upon replacing acetate with the more electron-withdrawing trifluoroacetate group. The first wave for **2d** is completely irreversible and nearly absent in the second scan (dashed curve) showing that the radical anion is short-lived. At scan rates of 20–500 mV s^{-1} and without IR compensation, a plot of $E_p(1)$ vs. log ν is nearly linear with a slope of −60 mV/decade (r = 0.995) which is consistent with a one-electron reduction followed by a rapid chemical reaction (e.g., an EC process).[6] $E_p(2)$ and $E_p(3)$ shift considerably less to more negative potentials with increasing scan rate (approximately −20 mV decade). The large anodic peak at −1.1V in Figure 2b is likely due to an adsorbed species.

Constant potential reduction of **1d–4d** either to their radical anions or dianions in DMF/$LiClO_4$ gave comparable amounts of **1a–4a** and **1e–4e** in combined yields ranging from 42% to 97% (Table II). It is apparent that reductive cleavage from the ion pair of the radical anion or dianion occurs faster with the trifluoroacetate leaving group, but so does saponification with the more electron deficient ester.

Conclusion

In summary then, our results show that reductive cleavage of anthraquinones **1c–4c** in DMF/$LiClO_4$ occurs in high yields via their dianion ion pairs with Li^+ but in low yields via their radical anion ion pairs since reductive cleavage of the latter occurs more slowly allowing a saponification process to predominate. The trifluoroacetate leaving group enhances the reductive cleavage process such that cleavage of the radical anion ion pairs is rapid, but the saponification process is also accelerated. Work is in progress aimed at measuring rate constants for the reductive cleavage and extending these studies to other substituents and aqueous media.

Experimental Section

General. Melting points were determined in open capillary tubes with a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. IR spectra were obtained with a Sargent-Welch Pye Unicam 3-200 IR spectrometer. ^1H NMR spectra were recorded at 60 MHz (JEOL JNM-PMX60). Mass spectra were obtained with a Finnegan OWA Model 1020 GC-MS. HPLC analyses were performed with a Waters Associate C-18 Bondapak reverse-phase column, a Varian Vari-Chrom detector, and an Altex Model 100 metering system. The temperature was approximately 25 °C, the eluant was 65:35 methanol–water, the flow rate was 1.15 mL/min, and the wavelength was 260 nm.

Electrochemical Measurements. Electrochemical experiments were performed with a Princeton Applied Research (PAR) potentiostat, Model 273, in conjunction with a PAR 175 universal programmer. Voltammograms were recorded on a Linseis LY 18100 x–y recorder. All potentials in the text are referred to Ag/AgCl (0.10 M KCl).

Cyclic Voltammetry. A 25-mL three-necked round-bottom flask was used to prepare a one-compartment cell. The working electrode was a glassy carbon disk (A = 0.090 cm^2) set in a Teflon tube. Prior to measurements on each solution this electrode was cleaned and polished with 0.30 and 0.050 μm α-alumina (Buehler), wiped with a tissue, and sonicated in water for 3–5 min. A graphite rod served as a counter electrode. The Ag/AgCl reference electrode was separated from the DMF electrolyte to keep the latter as dry as possible. This was accomplished by using in sequence a course glass frit, a 10-cm tube (0.5-cm diameter) containing a DMF (0.50 M $LiClO_4$)/methyl cellulose gel, and then directly an aqueous agar (1.0 M NaCl) which was in contact with the reference electrode.

General Procedure for Constant Potential Electrolyses in DMF. A three-compartment cell was used for the electrolyses. The center compartment, containing Carborundum carbon felt (pretreated by soaking in concentrated HNO_3 for 5–10 min, washing thoroughly with deionized water, and drying in an oven at 100 °C), was separated from the reference electrode on one side and the counter electrode on the other side by a glass frit (medium) and DMF (0.20 M $LiClO_4$ or n-Bu_4NClO_4)/methyl cellulose agar. The counter electrode was a graphite rod in DMF electrolyte, and the reference compartment contained the Ag/AgCl electrode (described above) in DMF electrolyte. Approximately 10 mL of DMF electrolyte was introduced into the center compartment, and the solution was deoxygenated with N_2 or Ar. After the background current was measured, 10–20 mg of the compound to be reduced was added, and the resulting solution was again deoxygenated. After the electrolysis was complete, the contents of the center compartment were transferred to a separatory funnel by using CH_2Cl_2 for rinsing. Approximately 50 mL of deionized water was added, and the resulting mixture was extracted with CH_2Cl_2 (3 × 20 mL). The CH_2Cl_2 extracts were combined, washed with water (3 × 20 mL), and dried over Na_2SO_4. After filtering, the bulk of the CH_2Cl_2 was removed in a rotary evaporator and the residue, which contained a small amount of DMF, was dried with a stream of N_2, leaving a yellow solid that was dissolved in methanol and analyzed by using HPLC.

Solvents and Electrolytes. DMF was dried by heating spectrophotometric grade DMF (Aldrich) at 60 °C over CaH_2 for 6–10 h followed by distillation at 50–60 °C under reduced pressure. Further drying was accomplished by stirring the distillate over neutral Al_2O_3 (dried under vacuum at 170–180 °C) for several hours prior to redistillation at 50–60 °C. The dry DMF was stored under N_2. Tetra-n-butylammonium perchlorate (Eastman) was purified according to the literature method.[7] $LiClO_4$ (Aldrich) was heated at 125–150 °C under vacuum (0.2 mmHg) for several hours prior to use.

2-(Bromomethyl)-9,10-anthracenedione (1b) was prepared from commercially available 2-methyl-9,10-anthracenedione (**1a**) as previously described,[1b] mp 199–201 °C [lit.[1a] mp 198–201 °C].

2-[(Ethanoyloxy)methyl]-9,10-anthracenedione (1c). A mixture of **1b** (2.07 g, 6.88 mmol), AgOAc (2.93 g, 17.6 mmol) in 75 mL of $CHCl_3$–HOAc (1:2) was heated to reflux under N_2 for 5 h. After the mixture was cooled, the silver salts were removed by filtration and washed with CH_2Cl_2. The combined filtrates were washed with water (2 × 100 mL) and saturated $NaHCO_3$ (50 mL) and dried over $MgSO_4$. Removal of solvent gave 1.80 g of a yellow solid. Chromatography of this material on silica gel followed by elution with CH_2Cl_2–CH_3OH (25:1) gave 1.48 g (77%) of **1b** as a light yellow solid: mp 150–151 °C; IR (Nujol) 1739, 1667, 1586, 1328, 1290, 1250, 1171, 1146, 1099, 1046, 971, 934, 837, 707 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.16 (s, 3 H), 5.20 (s, 2 H),

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7.54–8.27 (m, 7 H); MS, *m/e* (relative intensity) 280 (1), 238 (94), 209 (46), 193 (16), 164 (20), 163 (15), 152 (15), 43 (100). Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.50; H, 4.34.

2-[((Trifluoroethanoyl)oxy)methyl]-9,10-anthracenedione (1d). A mixture of **1b** (1.00 g, 3.32 mmol), silver trifluoroacetate (2.18 g, 9.87 mmol), and 15 mL of $CHCl_3$–CF_3CO_2H (1:2) was heated to reflux for 5.5 h. After the mixture was cooled, the silver salts were removed by filtration and washed with CH_2Cl_2. The combined filtrates were washed with cold water (2 × 25 mL) and saturated $NaHCO_3$ (25 mL) and dried over $MgSO_4$. Removal of solvent gave a yellow solid residue that was recrystallized from heptane/toluene to give 1.64 g of light yellow crystals: mp 163–164 °C; IR (Nujol) 1784, 1671, 1591, 1353, 1328, 1295, 1207, 1165, 930, 897, 855, 774, 712 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 5.48 (s, 2 H), 7.66–8.32 (m, 7 H); MS, *m/e* (relative intensity) 334 (41), 237 (100), 221 (49), 209 (19), 193 (75), 192 (23), 165 (52), 164 (59), 163 (42), 152 (22), 151 (22), 82 (63), 76 (23), 69 (58). Anal. Calcd for $C_{17}H_9O_4F_3$: C, 61.09; H, 2.72. Found: C, 60.62; H, 3.25.

1-Methoxy-2-methyl-9,10-anthracendione (2a) was prepared by the method of Savard and Brassard:[8] mp 164–165 °C [lit.[9] mp 166–167 °C]. Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.00; H, 5.08.

2-(Bromomethyl)-1-methoxy-9,10-anthracenedione (2b). A mixture of **2a** (1.80 g, 7.15 mmol), recrystallized *N*-bromosuccinimide (1.40 g, 7.86 mmol), benzoyl peroxide (200 mg), and 100 mL of CCl_4 was heated to reflux for 10 h. The reaction mixture was allowed to cool slowly overnight, resulting in the formation of yellow needles of **2b** (1.58 g, 67%), which were collected by filtration and used without further purification in the preparation of **2c** and **2d**. The filtrate was washed with water (3 × 100 mL), dried over $MgSO_4$, and evaporated to dryness, giving 0.80 g of a yellow solid consisting of **2a**, bromide **2b**, and dibromide. These compounds could be separated by chromatography on silica gel followed by elution with CH_2Cl_2. An analytically pure sample of **2b** was obtained by recrystallization from heptane–toluene: mp 190–191 °C; IR (Nujol) 1664, 1575, 1326, 1278, 1212, 1156, 1047, 965, 858, 774, 717 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 4.05 (s, 3 H), 4.56 (s, 2 H), 7.56–8.24 (m, 6 H); MS, *m/e* (relative intensity) 252 (100), 237 (20), 234 (31), 223 (58), 209 (24), 206 (31), 178 (48), 165 (95), 152 (69), 151 (28), 82 (33), 76 (53). Anal. Calcd for $C_{16}H_{11}BrO_3$: C, 58.03; H, 3.35; Br, 24.12. Found: C, 57.66; H, 3.72; Br, 23.89.

2-[(Ethanoyloxy)methyl]-1-methoxy-9,10-anthracenedione (2c). A mixture of **2b** (0.302 g, 0.913 mmol), AgOAc (0.455 g, 2.74 mmol), and 30 mL of $CHCl_3$–HOAc (1:2) was heated to reflux for 6 h. After the mixture was cooled, the silver salts were removed by filtration using CH_2Cl_2 for rinsing. The filtrate was washed with water (4 × 25 mL) and saturated $NaHCO_3$ (2 x 25 mL) and dried over $MgSO_4$. Removal of solvent in a rotary evaporatory gave 265 mg of a yellow solid. Chromatography on silica gel and elution with CH_2Cl_2–EtOAc (96:4) gave 257 mg (91%) of **2c**. An analytically pure sample of **2c** as yellow needles was obtained by recrystallization from heptane–toluene: mp 130–131 °C; IR (CCl_4) 1740, 1668, 1576, 1370, 1320, 1249, 1218, 1049, 1001, 970, 732 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.14 (s, 3 H), 3.93 (s, 3 H), 5.22 (s, 2 H), 7.56–8.24 (m, 6 H); MS, *m/e* (relative intensity) 310 (tr), 268 (23), 238 (86), 165 (33), 152 (24), 76 (14), 43 (100). Anal. Calcd for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found: C, 69.56; H, 4.85.

2-[((Trifluoroethanoyl)oxy)methyl]-1-methoxy-9,10-anthracenedione (2d). A mixture of **2b** (83.7 mg, 0.253 mmol), AgO_2CCF_3 (231 mg, 1.05 mmol), 10 mL of $CHCl_3$, and 17 mL of CF_3CO_2H was heated to reflux for 2 h. After the mixture was cooled, the silver salts were removed by filtration using CH_2Cl_2 for rinsing. The filtrate was cooled in an ice bath, washed with cold water (2 × 50 mL), and dried over Na_2SO_4. Removal of solvent in a rotary evaporator left a yellow solid. Recrystallization from heptane gave 84.7 mg of **2d** (92%) as light yellow plates: mp 137–138 °C; IR (Nujol) 1780, 1661, 1568, 1356, 1327, 1277, 1228, 1162, 1046, 1013, 975, 874, 851, 821, 774, 752, 718 cm^{-1}; ^1H NMR (60 MHz, $CHCl_3$) δ 3.97 (s, 3 H), 5.48 (s, 2 H), 7.60–8.21 (m, 6 H); MS, *m/e* (relative intensity) 364 (13), 267 (29), 251 (28), 250 (38), 237 (38), 222 (54), 221 (29), 207 (22), 194 (68), 193 (28), 166 (39), 165 (100), 164 (25), 163 (26), 152 (56), 151 (51), 150 (27), 139 (31), 82 (24), 76 (51), 75 (29), 69 (71). Anal. Calcd for $C_{18}H_{11}O_5F_3$: C, 59.35; H, 3.04. Found: C, 59.73; H, 3.38.

2-(Hydroxymethyl)-1-methoxy-9,10-anthracenedione (2e). To a solution of **2b** (50.00 mg, 0.151 mmol) in 15 mL of THF was added a solution of $AgNO_3$ (300 mg, 1.76 mmol) in 5 mL of water. The resulting mixture was heated at reflux for 3 h. After the mixture was cooled, the AgBr was removed by filtration using acetone for rinsing. The filtrate was diluted with an equal volume of water and extracted with CH_2Cl_2 (3 × 25 mL). The CH_2Cl_2 extracts were combined, dried over Na_2SO_4, and evaporated to dryness. The yellow residue was recrystallized from heptane–toluene, giving 20.0 mg (50%) of **2e** as yellow needles: mp 180–181 °C; IR (Nujol) 3220, 1672, 1572, 1328, 1278, 1246, 1190, 1155, 1070, 1049, 1027, 1000, 959, 900, 880, 863, 800, 718 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.26 (br s, 1 H), 3.97 (s, 3 H), 4.85 (br s, 2 H), 7.60–8.26 (m, 6); MS, *m/e* (relative intensity) 268 (5), 254 (10), 253 (77), 251 (24), 239 (18), 238 (100), 237 (41), 225 (17), 223 (10), 222 (18), 221 (16), 209 (24), 207 (14), 194 (23), 181 (19), 166 (16), 165 (41), 153 (22), 152 (50), 151 (41), 150 (22), 139 (26), 115 (14), 105 (21), 82 (18), 77 (28), 76 (37), 75 (29), 74 (11), 70 (15), 63 (20), 51 (14), 50 (17), 39 (17). Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51. Found: C, 71.74; H, 4.93.

2-Methyl-1,8-dimethoxy-9,10-anthracenedione (3a). Anthraquinone **3a** was prepared from isochrysophanic acid (2-methyl-1,8-dihydroxy-9,10-anthracenedione)[8] by the method of Kelly and Ghoshal[10] and was obtained as yellow needles in 85% yield by recrystallization from heptane: mp 146–147 °C; IR (CCl_4) 2920, 1670, 1580, 1468, 1318, 1270, 1250, 1220, 1065, 987 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 3.81 (s, 3 H), 3.86 (s, 3 H), 7.01–7.67 (m, 5 H); MS, *m/e* (relative intensity) 282 (50), 268 (17), 267 (100), 265 (30), 264 (26), 250 (10), 165 (22), 152 (18), 139 (10). Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 71.91; H, 4.98.

2-(Bromomethyl)-1,8-dimethoxy-9,10-anthracenedione (3b). A mixture of **3a** (3.12 g, 11.0 mmol), *N*-bromosuccinimide (2.25 g, 12.7 mmol), benzoyl peroxide (250 mg), and 175 mL of CCl_4 was heated to reflux for 12 h. The reaction mixture was cooled, extracted with water (3 × 100 mL), and dried over $MgSO_4$. The solvent was removed in a rotary evaporator, giving 3.96 g of a yellow solid. Chromatography of this residue on silica gel followed be elution with CH_2Cl_2 gave a small amount of dibromide followed by slightly impure **3b**. Recrystallization of **3b** from heptane–toluene produced 3.02 g (76%) of yellow needles: mp 166–167 °C; IR (CCl_4) 2915, 1670, 1565, 1464, 1440, 1315, 1270, 1255, 1220, 990 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.95 (s, 3 H), 4.03 (s, 3 H), 4.55 (s, 2 H), 7.11–7.85 (m, 5 H); MS, *m/e* (relative intensity) 362 (27), 360 (24), 347 (19), 345 (21), 282 (34), 281 (100), 280 (67), 267 (43), 266 (40), 265 (44), 252 (24), 237 (20), 165 (20), 152 (32). Anal. Calcd for $C_{17}H_{14}O_6Br$: C, 56.53; H, 3.63; Br, 22.12. Found: C, 56.51; H, 3.76; Br, 22.35.

2-[(Ethanoyloxy)methyl]-1,8-dimethoxy-9,10-anthracenedione (3c). With the procedure described above for preparing **2c**, **3c** was obtained from **3b** as yellow needles in a yield of 93%: mp 162–163 °C; IR (CCl_4) 2950, 1740, 1670, 1580, 1468, 1440, 1315, 1270, 1250, 1220, 1055, 1045, 1010, 980 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.08 (s, 3 H), 3.92 (s, 6 H), 5.23 (s, 2 H), 7.30–7.93 (m, 5 H); MS, *m/e* (relative intensity) 340 (1), 298 (12), 297 (15), 283 (13), 280 (12), 268 (44), 267 (28), 253 (11), 251 (11), 250 (20), 237 (10), 165 (12), 152 (18), 151 (12), 139 (11), 76 (12), 43 (100). Anal. Calcd for $C_{19}H_{13}O_6$: C, 67.05; H, 4.74. Found: C, 66.81; H, 4.85.

2-[((Trifluoroethanoyl)oxy)methyl]-1,8-dimethoxy-9,10-anthracenedione (3d). With the procedure described above for preparing **2d**, **3d** was obtained from **3b** as yellow needles in 85% yield: mp 116–117 °C; IR (CCl_4) 2910, 2841, 1780, 1708, 1667, 1570, 1450, 1370, 1307, 1268, 1257, 1212, 1169, 1131, 1067, 1046, 1000, 980, 695 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.97 (s, 6 H), 5.45 (s, 2 H), 7.11–7.98 (m, 5 H); MS, *m/e* (relative intensity) 394 (16), 379 (80), 297 (44), 281 (50), 280 (100), 265 (86), 252 (35), 251 (34), 250 (54), 237 (64), 223 (34), 209 (33), 165 (62), 152 (74), 151 (45), 139 (42), 76 (53), 69 (64), 63 (30). Anal. Calcd for $C_{19}H_9O_6F_3$: C, 57.88; H, 3.32. Found: C, 58.58; H, 3.49.

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2-(Hydroxymethyl)-1,8-dimethoxy-9,10-anthracenedione (3e). With the above procedure for **2e**, **3e** was prepared from **3b** as yellow crystals in 79% yield: mp 148–149 °C; IR (CCl_4) 3305, 1720, 1663, 1530, 1350, 1315, 1268, 1245, 1210, 1000, 970, 905, 663 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.95 (s, 6 H), 4.78 (br s, 2 H), 7.30–7.96 (m, 5 H); MS, *m/e* (relative intensity) 298 (17), 283 (100), 268 (57), 267 (32), 251 (34), 250 (77), 240 (30), 237 (36), 223 (31), 165 (35), 152 (69), 151 (49), 139 (51), 76 (45), 63 (33). Anal. Calcd for $C_{17}H_{14}O_5$: C, 68.44; H, 4.74. Found: C, 68.41; H, 5.23.

3-Methyl-1,8-dimethoxy-9,10-anthracenedione (4a). A mixture of commercially available chrysophanic acid (1.29 g, 5.08 mmol), $(CH_3)_2SO_4$ (8.4 mL, 87 mmol), and anhydrous K_2CO_3 (12.6 g, 91 mmol) in 150 mL of acetone was heated to reflux for 6 h. After the reaction mixture was cooled, the potassium salts were removed by filtration, and the solvent was removed in a rotary evaporator, giving a yellow solid. Recrystallization from heptane–toluene gave 1.23 g (89%) of **4a** as yellow spurs: mp 192–193 °C [lit.[8] mp 196–197 °C]; IR (Nujol) 1655, 1580, 1328, 1282, 1235, 1170, 1030, 1068, 1011, 954, 912, 881, 852, 790, 756 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.43 (s, 3 H), 3.95 (s, 6 H), 6.97–7.77 (m, 5 H). Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.18; H, 4.89.

3-(Bromomethyl)-1,8-dimethoxy-9,10-anthracenedione (4b). A mixture of **4a** (1.21 g, 4.30 mmol), *N*-bromosuccinimide (0.84 g, 4.72 mmol), benzoyl peroxide (120 mg), and 100 mL of CCl_4 was heated to reflux for 7 h. An aliquot of the reaction mixture was analyzed by NMR and found to contain a 1:5:1 mixture of **4a**/**4b**/dibromide. The reaction mixture was cooled, washed with water (2 × 250 mL), and dried over $MgSO_4$. Removal of CCl_4 in a rotary evaporator gave a yellow solid. Recrystallization from heptane–toluene gave 1.36 g of a 1:8:1 mixture of **4a**/**4b**/dibromide. Chromatography of the mother liquor on silica gel followed by elution with CH_2Cl_2–EtOAc (95:5) gave in order 120 mg of fairly pure dibromide, 250 mg of a 2:8:1 mixture of **4a**/**4b**/dibromide, and 100 mg of mostly **4a**. The 250-mg second fraction was combined with the above crystals (1.36 g) and recrystallized from heptane–toluene, giving 85% pure **4b** (0.90 g), which was used in the preparation of **4c–4e**. Further purification was achieved by chromatography on silica gel (twice) and recrystallization (twice) to give an analytically pure sample of **4b** as yellow needles: mp 174–175 °C; IR (Nujol) 1650, 1577, 1329, 1280, 1225, 1062, 1013, 963, 896, 870, 840, 794, 754 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.96 (s, 6 H), 4.47 (s, 2 H), 7.11–7.79 (m, 5 H); MS, *m/e* (relative intensity) 282 (27), 267 (100), 265 (20), 239 (12), 223 (12), 181 (11), 166 (12), 165 (48), 153 (17), 152 (34), 139 (17), 82 (13), 76 (25), 63 (18). Anal. Calcd for $C_{17}H_{13}BrO_4$: C, 56.53; H, 3.63; Br, 22.12. Found: C, 56.53; H, 3.83; Br, 21.99.

3-[(Ethanoyloxy)methyl]-1,8-dimethoxy-9,10-anthracenedione (4c). Impure (85%) **4b** (0.84 g, 1.98 mmol) was reacted with AgOAc as described above for **2c** to give 0.65 g (97%) of **4c** (mp 169–171 °C). Chromatography on silica gel and elution with CH_2Cl_2–EtOAc (9:1) followed by recrystallization from heptane–toluene gave analytically pure **4c** as yellow needles: mp 171–172 °C; IR (Nujol) 1720, 1654, 1577, 1323, 1275, 1225, 1166, 1126, 1058, 1037, 960, 916, 880, 848, 786, 750 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 2.14 (s, 3 H), 4.00 (s, 6 H), 5.12 (s, 2 H), 7.08–7.83 (m, 5 H); MS, *m/e* (relative intensity) 340 (16), 325 (36), 280 (31), 209 (29), 207 (57), 152 (22), 96 (22), 43 (100). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 66.85; H, 4.77.

3-(Hydroxymethyl)-1,8-dimethoxy-9,10-anthracenedione (4e). A solution of **4c** (35.6 mg, 0.105 mmol) in 5 mL of 0.75 N H_2SO_4 and 3 mL of 1-propanol was heated to reflux for 2.5 h. The reaction mixture was diluted with 50 mL of cold water and extracted with CH_2Cl_2 (2 × 25 mL). The CH_2Cl_2 extracts were combined, dried over Na_2SO_4, and evaporated to dryness, giving a yellow solid. Chromatography of this material on silica gel and elution with CH_2Cl_2–EtOAc–EtOH (91:6:3) gave 25.6 mg (82%) of **4e** as a yellow solid: mp 223–225 °C [lit.[11] mp 227–229 °C]; MS, *m/e* (relative intensity) 298 (tr), 296 (26), 281 (100), 235 (18), 153 (13), 152 (25), 151 (32), 150 (17), 139 (33), 76 (20), 75 (14), 63 (17). Anal. Calcd for $C_{17}H_{14}O_5$: C, 68.44; H, 4.74. Found: C, 68.17; H, 5.31.

3-[((Trifluoroethanoyl)oxy)methyl]-1,8-dimethoxy-9,10-anthracenedione (4d). To a mixture of **4e** (25.6 mg, 0.0858 mmol) in 5 mL of trifluoroacetic anhydride was added 10 drops of trifluoroacetic acid. After warming for 10–15 min, a yellow solid separated from the reaction mixture. With N_2, the excess reagents were removed by evaporation, leaving a yellow solid. Recrystallization from heptane–toluene gave 31.6 mg (93%) of **4e** as yellow needles: mp 156–157 °C; IR (Nujol) 1781, 1651, 1580, 1326, 1276, 1236, 1152, 1066, 1030, 1020, 1002, 966, 953, 910, 894, 840, 792, 776, 750, 734 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 3.98 (s, 6 H), 5.38 (s, 2 H), 7.12–7.75 (m, 5 H); MS, *m/e* (relative intensity) 394 (29), 379 (100), 280 (23), 266 (23), 237 (18), 209 (19), 193 (19), 165 (22), 152 (27), 133 (19), 76 (24), 69 (49). Anal. Calcd for $C_{19}H_{13}O_6F_3$: C, 57.88; H, 3.32. Found: C, 58.10; H, 3.63.

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