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Selective Oxidation of an Electronically Unsymmetrical Distyrylbenzene at Either of Two Sites

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A p-distyrylbenzene bearing electron-withdrawing groups on one terminal ring and electron-supplying groups on the other was synthesized and one ring was found to be significantly more electron rich than the other. Electrochemical oxidative cleavage was shown to take place predominantly at the electron-rich double bond. Selective protection of that double bond followed by anodic oxidation and deprotection afforded the product of overall anodic cleavage of the electron-deficient double bond, thus expanding the range of possible transformations of the distyrylbenzene.

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It is an article of faith in synthetic electrochemistry, amply justified by precedent, that a substance with two electroactive sites of different redox potential undergoes preferential electrochemical conversion at the site of lower potential. This is an inherent advantage in operational electrochemistry over reduction or oxidation processes carried out using chemical agents, which are often insufficiently selective. Yet sometimes it might be desired to carry out an electrochemical transformation at the site of higher potential without affecting the lower potential site. We describe here the synthesis of an electronically unsymmetric molecule and a strategy for selective anodic cleavage at either of its two potentially electroactive sites.

The anodic oxidation of alkenes can produce a wide variety of products, depending upon the alkene structure and the experimental conditions.^{1–3} Depending upon conditions, a variety of products are typically formed, e.g., cleavage of the carbon-carbon bond competes with rearrangement of a phenyl group, affording diphenylacetalde-hyde, which is then quickly oxidatively converted to benzophenone.⁴ However, a number of other products can also be produced including dimeric and rearranged substances and products of nucleophilic attack upon cationic intermediates. We have previously described the anodic cleavage of stilbenes (1,2-diphenylethylenes) into two molecules of aldehyde (Equation 1) in the presence of water.^{5,6}

$$ArCH = CHAr' \xrightarrow{-4e^{-}} ArCH = O + O = CHAr'$$
[1]

We observed that oxidation potentials increase greatly as one or more electron-withdrawing groups are attached to the stilbene nucleus. Compound (1) containing a stilbene unit at one end and another at the other end with the ends connected by a saturated chain (Scheme 1) would surely undergo oxidation at the end bearing electron-donating substituents. But it was not obvious whether selective oxidation might be possible when the two units are connected such that the central benzene ring is part of both two stilbene subunits, because such a molecule, a so-called 1,4-distyrylbenzene (2), constitutes a single extended electronic system. It was decided to construct such a system and determine whether its electron density is unsymmetrical. If so, the next questions would be (a) whether the more electron rich end could be selectively protected from oxidation, permitting electrochemistry at the other end and (b) the feasibility of removal of the protecting group.

Results and Discussion

Synthesis of alkenes.— The synthesis of the desired distyrylbenzene is straightforward (Scheme 2). A Wittig reaction between 3,5*bis*-[trifluoromethyl]benzyltriphenylphosphonium bromide (**3**) and an equimolar amount of terephthaldehyde under phase transfer conditions afforded stilbene **4** in 58% yield together with a smaller amount (<9%) of 3,3,5',5'-*tetrakis*[trifluoromethyl]stilbene. A second Wittig condensation of **4** with 3,5-dimethylbenzyltriphenylphosphonium bromide (**5**) afforded the desired unsymmetrical distyrylbenzene **6**. Both Wittig steps afforded mixtures of *cis* and *trans* isomers, which could be converted completely to the *trans* form by overnight reflux in toluene containing a trace of I₂. This was particularly convenient with the distyryl compound **6**, which was initially produced as a mixture of *E*,*E*, *Z*,*E*, *E*,*Z*, and *Z*,*Z* isomers by gc-mass spectrometric analysis and immediately converted to the *E*,*E* isomer by iodine-catalyzed equilibration.

Charge distribution in 6.- The first issue to be addressed was whether the different substituents on the two terminal rings of 6 are likely to result in significantly different reactivity between its two double bonds. The electrostatic potential map of 6 (Figure 1) computed at the DFT/6–31G(d) level with full geometry optimization, shows the highest electron density to be in the dimethylated ring and its adjacent double bond. A natural population analysis⁷ (NPA) computation of the charges on each atom confirmed the electrostatic potential map in showing that the carbon atoms in the dimethylated ring carry a higher degree of negative charge than the corresponding ring atoms at the other end of the molecule (Table I). This is borne out further in the ¹H NMR spectra of **6**, in which the proton resonances of the dimethyl substituted ring as well as the adjacent double bond appear at higher fields than those of the ring and double bond at the other end of the molecule (Table II). In short, the data all lead to the conclusion that the electron density in 6 is highly unsymmetrical and therefore that anodic oxidation should take place at the dimethylated end.



Figure 1. Electrostatic potential map of distyrylbenzene 6. Color code: red: highly negative; yellow: slightly negative; green: slightly positive; blue: highly positive.

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Scheme 1. Distilbenes bearing both electron-withdrawing (EWG) and electron-donating (EDG) groups.



Scheme 2. Synthesis of an electronically unsymmetrical distyrylbenzene and a derivative with the more electron-rich double bond protected.

Selective protection of the more electron rich double bond of 6.— The next steps in the overall plan were to protect the more electron rich double bond of **6**, carry out the electrolytic anodic cleavage of the remaining double bond, and finally remove the protecting group. It was decided to synthesize **9**, a derivative of **6** in which the more electron rich double bond of unsymmetrical distyrylbenzene **6** is



^aAtomic charges computed by the Natural Population Analysis procedure at the density functional B3LYP/6–31G(d) level. protected against oxidation by dibromination, since the *vic*-dibromo functionality could be easily removed cathodically. Synthesis of **9** was straightforward: Wittig synthesis of stilbene aldehyde **7**, followed by



^aChemical shifts measured at 400 MHz in CDCl₃. ^bProtons E and E' appear as a slightly broadened singlet.



Figure 2. Cyclic voltammogram of unsymmetrical distyrylbenzene 6.

bromination of the double bond of 7 using pyridinium perbromide⁸ (Scheme 2) and a final Wittig reaction to produce **9**.

Voltammetry.— The oxidation potentials of compounds **6** (+0.90 V), **9** (+1.44 V), and the parent molecule stilbene (+1.45 V) were measured by cyclic voltammetry at a glassy carbon electrode in acetonitrile/0.1 M Bu₄NBF₄ relative to Ag/0.1 M AgNO₃ in acetonitrile (Figures 2–4). As a consequence of its greater degree of conjugation, distyrylbenzene **6** is about 0.5 V easier to reduce than **9**, whose reduction potential (ca. 1.45 V) is close to that of stilbene itself.

Electrocatalytic oxidation of 6.— We had previously employed *tris*[4-methyl-2-nitro]triphenylamine (**10a**) as an electrocatalyst (more properly, mediator of electron transfer) for the anodic cleavage of stilbenes bearing as many as four electron-withdrawing substituents (Scheme 3).^{4,5} However, the oxidation potential of **10a** is too high to be used in similar fashion for the anodic oxidation of the distryrylbenzene **6**. The most widely used anodic mediator is tri-4-bromotriphenylamine (**10b**), introduced for this purpose by Steckhan.⁹ However, we were aware that the cation radical of **10b** has since been found to undergo slow decomposition.¹⁰ We therefore decided to use the corresponding trichloro derivative **10c**, which we synthesized (by a modification of an earlier literature procedure¹¹) in the expectation



Figure 3. Cyclic voltammogram of dibromodihydrodistyrylbenzene 9.



Figure 4. Cyclic voltammogram of 1,2-diphenylethylene (stilbene).

that the stronger carbon-chlorine bond and lesser leaving group ability of chlorine under electrophilic conditions¹² would confer greater stability upon the cation radical of 10c. The oxidation potential of 10c is $+0.73 \text{ V}^{13}$ and lower than that of 6 (+0.90 V). In the event, controlled potential anodic oxidation of a solution of 6 in acetonitrile/water solution containing 10 mol% of **10c** was carried out at +0.75 V vs Ag/Ag⁺. The initial blue solution of the cation radical of 10c immediately began to stream from the anode as expected, but the solution quickly began to develop a purple color, suggesting that 10c was decomposing. Well before 6 had been consumed, the current passing through the cell had dropped to zero and the color had become light pink, indicating that the cation radical of **10c** had completely decomposed. Analysis by GC-MS indicated the presence of two major components: unreacted 6 (48%) and 4-formyl-3',5'-bis[trifluoromethyl]stilbene (4) (36% crude yield of a 5:1 mixture of the stilbene aldehydes 4 and 7; 72% yield based upon unreacted starting material). Workup and flash chromatography afforded a mixture of 4 and 7, which was separated by preparative thin layer chromatography resulted in isolation of pure 4 and 7 in 5:1 ratio, confirming our expectation that the double bond nearer the dimethyl substituted ring would be the preferred site of cleavage of 6 (Scheme 4). The rapid decrease in current, coupled with the change in color, suggested that the catalyst was decomposing during electrolysis. Peters has reported similar decomposition of metal salen complexes during attempted electrocatalytic reduction of alkyl halides.¹⁴ Addition of fresh catalyst to the solution was unsuccessful because decomposition of the catalyst appeared to take place faster as electrolysis proceeded. The nature of the decomposition of 10c is under investigation.

Anodic oxidation and deprotection of 9.— Because of the decomposition of mediator **10c** during the anodic oxidation of **6**, it was decided to carry out the oxidation of **9** directly, i.e., without mediator. Because of the readily reducible vicinal dibromide functionality of **9**, the oxidation was carried out in a divided cell at a platinum anode. After passage of the calculated⁴ 4 Faradays/mol of current, gc-mass spectrometric analysis indicated that the expected cleavage of the

A

10a, Ar = 4-Methyl-2-nitrophenyl
b, Ar = 4-Bromophenyl
c, Ar = 4-Chlorophenyl

Scheme 3. Triphenylamines bearing electron-withdrawing groups.



Scheme 4. Anodic oxidation of an unsymmetrical distyrylbenzene at the more electron-rich double bond.

double bond had taken place. Workup afforded the expected cleavage product (8) together with a small amount of debrominated material (7) (Scheme 5). Finally, cathodic deprotection of 8 occurred smoothly at a carbon cathode under controlled potential to afford the deprotected aldehyde 7 in 75% yield, identical with a previously synthesized (see Scheme 2) sample.

Experimental

Tri-4-chloro-triphenylamine (10c).— was prepared using a procedure described by Patil et al.¹¹ 1-Chloro-4-iodobenzene (2.73 g, 11.5 mmol) and 4-chloroaniline (0.696 g, 5.5 mmol) were dissolved in dry toluene (35 mL). Copper(I) iodide (38.1 mg, 3.6 mol%) and 2,2'-bipyridyl (31.5 mg, 3.6 mol%) were added to the solution, and the reaction vessel was placed in an oil bath heated to 115°C. Potassium tert-butoxide (1.85 g, 16.5 mmol) was added, and then the vessel was sealed and purged with N₂. After 5 hr, the reaction was allowed to cool to RT. Solids were removed by vacuum filtration, and solvent was removed by rotary evaporation. The crude product was dissolved in CH₂Cl₂ (30 mL) and washed with 0.1 M aqueous NaHSO₃ (2.3 mL), followed with H₂O (1.3 mL). Purification by flash chromatography over silica with hexane as the eluent, followed by recrystallization from 95% EtOH, yielded 853 mg of **10c** (44% yield): mp 144–146°C (lit.¹⁶ mp 148–149°C).

3,5-Bis[trifluoromethyl]benzyltriphenylphosphonium bromide (3).— 3,5-bis[trifluoromethyl]-benzyl bromide (3.07 g, 10.0 mmol) and triphenylphosphine (3.70 g, 14.0 mmol) were dissolved in 100 mL of benzene and heated to reflux overnight to produce a white precipitate. The mixture was cooled in ice and the precipitate was removed by vacuum filtration and dried at 90°C to yield 5.60 g (98% yield) of the phosphonium salt, mp (dec) 314–320°C; ¹H NMR (400 MHz, DMSO- d_6): 8.10 (s, 1H), 7.92–7.96 (m, 3H), 7.67–7.85 (m, 12H), 7.58 (s, 2H), 5.39 (d, J = 15.6 Hz, 2H).

(*E*)-4-Formyl-3',5'-bis[trifluoromethyl]stilbene (4).— 3,5-bis [trifluoromethyl]benzyltriphenyl-phosphonium bromide (3.42 g, 6.0 mmol) and terephthalaldehyde (0.87 g, 6.5 mmol) were reacted in 120 mL of 50/50 vol% CH_2Cl_2/H_2O in the presence of Na_2CO_3 (30.0 g, 40 equiv) and tetrabutylammonium iodide (0.30 g, 10%) equiv)and the mixture was stirred vigorously overnight. 25 ML of water was added and the organic layer was removed by evaporation. The aqueous layer was extracted with 3 15-mL portions of CH₂Cl₂. The combined organic layers were dried over MgSO4 and evaporated to afford a vellow liquid, that mostly crystallized upon standing overnight. Analysis by GC-MS showed a 45:55 mixture of stereoisomers. The mixture was purified by flash chromatography with toluene as eluent. A trace amount of I₂ was added to the combined product fractions and the solution stirred overnight at reflux to obtain (E)-isomer (99%) in toluene. The solvent was evaporated and the residue recrystallized from 95% EtOH to afford 1.17 g of fine white needles (58% yield): mp 140–142°; ¹H NMR (400 MHz, CH₃CN): 9.96 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.30/7.24 (q_{AB}, J = 12.3 Hz, 2H), 7.24 (s, 2H), 6.98 (s, 1H), 2.32 (s, 6H); ¹³C NMR (CDCl₃): 191.7, 143.8, 138.5, 136.6, 135.4, 132.6, 130.5, 130.4, 127.1, 127.0, 125.0, 21.5; MS m/z (relative intensity): 236 (100), 192 (38), 178 (31).

3,5-Dimethylbenzyltriphenylphosphonium bromide (5).— 3,5-Dimethylbenzyl bromide (1.99 g, 10.0 mmol) and triphenylphosphine (3.70 g, 14.0 mmol) were dissolved in 100 mL of benzene and heated to reflux overnight to produce a white precipitate. The mixture was cooled in ice and the precipitate was removed by vacuum filtration and dried at 90°C to yield 4.40 g (95% yield) of the phosphonium salt, mp (dec) 313–315°C; ¹H NMR (400 MHz, DMSO-*d*₆): 7.88–7.93 (m, 3H), 7.60–7.8 (m, 12H), 6.93 (s, 1H), 6.50 (s, 2H), 5.03 (d, *J* = 15.6 Hz, 2H), 2.06 (s, 6H).

(E,E)-1-(3,5-Dimethylstyryl)-2-4-(3'5'bis[trifluoromethyl]styryl)benzene (6).— The crude product from the synthesis of**4a**wasdissolved in 25 mL CH₂Cl₂. Tetrabutylammonium iodide (124 mg,10 mole%) and Na₂CO₃ (12.9 g, 40 equiv) were added, followedby**yy**(1.28 g, 2.78 mmol) and 25 mL H₂O. The flask was cappedand stirred vigorously overnight. Water (100 mL) was added andthe organic layer separated by separatory funnel. The aqueouslayer was extracted with CH₂Cl₂ (3 × 30 mL) and the combinedorganic layers were dried over Na₂SO₄ and evaporated to afford2.97 g of crude product. The product mixture was analyzed byGC-MS and found to consist of unreacted**4a**, three stereoisomersof 1,4-*bis*[trifluoromethyl)styrylbenzene, and four stereoisomers



Scheme 5. Anodic oxidation of the protected distyrylbenzene at the more electron-deficient double bond.

of 6. The crude product and a few crystals of I_2 were dissolved in 50 mL xylene and refluxed for three days. GC-MS showed that the bis[trifluoromethyl)styrylbenzene and 6 were now present as single stereoisomers, presumably E,E. The mixture was cooled, extracted with thiosulfate solution, separated, dried over Na₂SO₄ and evaporated to afford 3.0 g crude product. Purification by flash chromatography over silica gel beginning with hexanes followed by 2% EtOAc in hexanes as eluent, followed by recrystallization from EtOH, yielded 600 mg (48% yield) of **6**, mp 177–181°C; IR ν (cm⁻¹): 3031 (w), 2919 (w), 1599)m), 1511 (w), 1466 (w), 1379 (s), 1278 (s), 1119 (s), 999 (w), 952 (s), 941 (s), 887 (s), 850 (s), 836 (m) 802 (w), 682 (s); ¹H NMR (300 MHz, CD₃CN, δ): 8.11 (s, 2H),7.85 (s, 1H), 7.59 (s, 4H), 7.44/7.32 (q_{AB} , J = 16.8 Hz, 2H), 7.20 (s, 2H), 7.18 (s, 2H), 6.94 (s, 1H), 2.30 (s, 6H); ¹³C NMR (CDCl₃, ppm): 139.7, 138.4, 138.3, 137.2, 135.3, 132.3, 132.2 (q, J = 131.3 Hz), 129.9, 129.8, 127.8, 127.5, 127.1, 126.3 (q), 125.4, 124.8, 121.8, 120.9 (m), 21.5; MS m/z (% relative intensity): 447 (29), 446 (100); Anal. Calcd for C₂₆H₂₀F₆: C, 69.95; H, 4.51. Found: C, 69.72; H, 4.50.

(E)-4-Formyl-3,5-dimethylstilbene (7).— 3,5-Dimethylbenzyltriphenylphosphonium bromide (1.85 g, 4.0 mmol) and terephthalaldehyde (0.58 g, 4.3 mmol) were reacted in 80 mL of 50/50 vol% CH₂Cl₂/H₂O in the presence of Na₂CO₃ (20.0 g, 0.19 mmol) and tetrabutylammonium iodide (0.20 g, 0.5 mmol). After 20 hr, 25 mL of water was added and the organic layer was removed. The aqueous layer was extracted with 3 15-mL portions of CH₂Cl₂. The combined organic layers were dried over MgSO4 and evaporated to afford a yellow liquid that mostly crystallized upon standing overnight. Analysis by GC-MS showed a 45:55 mixture of stereoisomers. The mixture was purified by flash chromatography with toluene as eluent. A trace amount of I2 was added to the combined product fractions and the solution stirred overnight at reflux to obtain the pure (E)-isomer in toluene. The solution was decolorized with NaHSO3 and the solvent evaporated to afford 0.829 g of tan solid (83% crude yield), which was recrystallized from 95% EtOH to afford 0.617 g of tan crystals (62% yield): mp 76–77°; ¹H NMR (400 MHz, CH₃CN): 9.96 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.30/7.24 (q_{AB}, J = 12.3 Hz, 2H), 7.24 (s, 2H), 6.98 (s, 1H), 2.32 (s, 6H); ¹³C NMR (CDCl₃): 191.7, 143.8, 138.5, 136.6, 135.4, 132.6, 130.5, 130.4, 127.1, 127.0, 125.0, 21.5; MS m/z (relative intensity): 236 (100), 192 (38), 178 (31).

1,2-Dibromo-1-(4-formylphenyl)-2-(3',5'-dimethylphenyl)ethane (8).— (E)-4-Formyl-3',5'-dimethylstilbene (7) (100 mg, 0.4 mmol) was dissolved in CH₂Cl₂ and cooled to 0°C. Pyridinium tribromide (186 mg, 1.3% molar xs) was added and the solution was allowed to stir overnight while gradually warming to room temperature, during which time it turned from light orange to yellow. It was washed with 35 mL aq. sodium thiosulfate. The colorless organic layer was washed with water, dried over Na₂SO₄, and evaporated to afford 164 mg (97% yield): mp 168–172°C; ¹H NMR (400 MHz, CH₃CN): 10.03 (s, 1H), 7.96 (d, J = 7.8 Hz, 2H), 7.80 (d, J = 7.8 Hz, 2H), 7.25 (s, 2H), 7.06 (s, 1H), 5.85/5.73 (q_{AB}, J = 9.0 Hz, 2H), 2.34 (s, 6H). Anal. Calcd for C₁₇H₁₆OBr₂: C, 51.55; H, 4.07. Found: C, 51.66: H, 3.90.

(E)-1-(1,2-Dibromo-2–3,5-dimethylphenyl)ethyl-4-(3'5'-bis[trifluoromethyl]styryl)-benzene (9).— Dibromide **8** (ca. 1.3 mmol) was dissolved in 15 mL CH₂Cl₂ and 15 mL was added. Na₂CO₃ (5.5 g) and TBAI (335 mg) were added and stirred to dissolve. Phosphonium bromide **3** was added and the mixture was stirred vigorously for two days. the orange solution was then transferred to a separatory funnel with 40 mL CH₂Cl₂, decolorized by washing with 15 mL aq. sodium thiosulfate, and washed with H₂O. The organic layer was separated, the aqueous layer was extracted with CH₂Cl₂, and the combined organic layers dried over Na₂SO₄. Evaporation afforded 900 mg of yellow-orange waxy solid, which was purified by flash chromatography, beginning with hexane and gradually increasing to 5% EtOAc as eluents. TLC analysis indicated the presence of four products in the eluate; two were stereoisomers of **6** and the other were stereoisomers of **9**. Recrystallization from ether afforded 219 mg (28% yield) of **9** as fine white crystals, mm 164–166°C; ¹H NMR (300 MHz, CD³CN): 7.83 (s, 1H), 7.77 (s, 2H), 7.50 (d, J = 8.3 Hz, 2H), 7.27 (J = 8.3 Hz, 2H), 7.22 (s, 2H), 7.03 (s, 1H), 6.93 /6.78 (q_{AB}, J = 12.3 Hz, 2H), 5.75 (d, J = 12.2 Hz, 1H), 5.66 (d, J = 12.2 Hz, 1H), 2.33 (s, 6H). Anal. Calcd for C₂₆H₂₀Br₂F₆: C, 51.51; H, 3.33. Found: C, 52.17; H, 3.40.

Electrocatalytic oxidation of 6.- Controlled potential anodic oxidation of a solution of 58 mg (0.13 mmol) of 6 was carried out in 25 mL of 84:16 v/v acetonitrile/water solution containing 10 mol% of 10c at +0.75 V vs Ag/Ag⁺ reference. The initial blue solution of the cation radical of 10c immediately began to stream from the anode, but the solution quickly began to develop a purple color, suggesting that it was decomposing to a different substance. Well before 6 had been consumed, the current passing through the cell had dropped to zero and the color had become light pink, indicating rapid decomposition of 10c under the electrolysis conditions. Analysis by GC-MS indicated the presence of two major components: unreacted 6 (48%) and 4-formyl-3',5'-bis[trifluoromethyl]stilbene (4) (36% crude yield of a mixture of the stilbene aldehydes 4 and 7; 72% yield based upon unreacted starting material). Workup and flash chromatography afforded a mixture of 4 and 7, which was separated by preparative thin layer chromatography resulted in isolation of pure 4 (24 mg; 50%) and 7 (4.5 mg; 10%). The rapid decrease in current, coupled with the change in color, suggested that the catalyst was decomposing throughout the electrolysis. Addition of fresh catalyst to the solution was unsuccessful because decomposition of the catalyst appeared to take place faster as electrolysis proceeded.

Direct electrochemical oxidation of protected alkene 9.- Methylcellulose (1 gm) was dissolved in 20 mL of hot DMF containing 0.1 M LiBF₄. A small amount of the solution was added to the cathode side of the frit and allowed to set to produce gel, thus preventing mass transit from the two sides of the cell. Alkene 9 (55 mg; 0.09 mmol) was dissolved in 20 mL of 95:5 acetonitrile:water containing 0.1 M containing 0.1 M LiBF4 and added to the the anode side of the cell. An additional amount of the electrolyte solution was added to the cathode side of the cell until the liquid levels on both sides of the cell were approximately equal. A graphite carbon cloth (6 cm^2) was placed in the cathode compartment and a platinum mesh electrode (2 cm^2) was added on the anode side. The solution was purged of oxygen by passing a slow stream of acetonitrile-saturated nitrogen through the cell for 20 min. A fixed current of 10 mA was then passed through the cell until an amount of current equal to 4 Faradays/mol of 9 had passed. The contents of the anode compartment were washed with 10 mL of brine, then evaporated to dryness. The remaining solids were extracted with ether, leaving the supporting electrolyte behind. The ether solution was dried over Na2SO4 and evaporated. Preparative thin layer chromatographic separation of the residue resulted in isolation of the cleavage product, aldehyde 8 (11 mg, 30% yield) together with a small amount of debrominated aldehyde (4); the yield is 33% yield if the isolated 4 is included.

Cathodic debromination of 8.— Dibromoaldehyde (100 mg; 0.25 mmol) was dissolved in 25 mL of 0.1 Bu₄NBF₄ in acetonitrile in the cathode compartment of the divided electrochemical cell used in the preceding experiment. The solution was degassed by passing nitrogen through the solution for 20 minutes while stirring magnetically. Controlled potential electrolysis was carried out at -1.75 V, during which time the current decreased from 40 mA to less than 5 mA. Most of the catholyte was evaporated and the residual oily mixture was filtered through a silica plug using CH₂Cl₂ to remove most of the electrolyte. The filtrate was then separated by flash chromatography over silica using CH₂Cl₂ as eluent to afford aldehyde **7** (47 mg, 80% yield), identical with a previously synthesized sample.

Conclusions

These experiments demonstrate the feasibility of effecting electrochemical oxidation at the site of higher oxidation potential of a substance containing two oxidizable sites by first protecting the lower potential site. The site of lower potential, the dimethylbenzene end of the molecule, was shown to be more electron rich by spectroscopic and computational methods. Because it is more electron rich, the double bond nearer the dimethylbenzene group reacts selectively with pyridinium bromide, protecting it from anodic transformation, leaving the remaining double bond as the only site susceptible to anodic cleavage. On the other hand, anodic cleavage was only selective by a factor of 5:1.

Searches for useful electrocatalysts (more properly, electron transfer mediators) frequently begin with cyclic voltammetric studies. Criteria often applied in such studies are:

- The mediator must have a potential lower than that of the substrate of interest, but not too much lower: a difference of 400–600 mV is often quoted.¹⁵
- The mediator must exhibit reversible cyclic voltammetric behavior.
- 3. Electron transfer from the substrate (for oxidations, the cation radical of the mediator must exchange more or less rapidly with the substrate).

However, a point brought out clearly by these studies is the fact that a mediator that satisfies all of these criteria may still not be adequate if it is unstable electrochemically on the longer time scale of a preparative electrolysis. A less obvious problem, in our experience, takes place when one synthesizes a redox catalyst to have the high reactivity toward substrates of high oxidation potential. For example, we recently reported the synthesis of several high redox potential mediators^{5,13} intended for catalyzing the even higher oxidation potentials we encountered in a series of stilbenes bearing several electron-withdrawing groups.^{5,6} As we found in the present study, the higher redox reactivity aimed for in such substances often means that their cation radicals are correspondingly more reactive toward chemical decomposition. We suspect that the same may be true of mediators intended for cathodic use. In fact, as we noted above, Peters et al., have found that metal salen complexes intended to mediate the reduction of alkyl halides often are destroyed by reaction with the free radical products of the electron transfer that they mediate.¹⁴

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