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Electrocatalytic Oxidative Cleavage of Electron-Deficient Substituted Stilbenes in Acetonitrile–Water Employing a New High Oxidation Potential Electrocatalyst. An Electrochemical Equivalent of Ozonolysis

Xin Wu, Anthony P. Davis, and Albert J. Fry*

Chemistry Department, Wesleyan University, Middletown, Connecticut 06459

afry@wesleyan.edu

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ABSTRACT

$$\mathrm{ArCH{=}CHAr'} \xrightarrow[\mathrm{CH_3CN/H_2O,\ LiClO_4}]{-4\,e^-,\ \mathrm{Ar_3N\ (cat)}} \mathrm{ArCH{=}O\ +\ Ar'CH{=}O}$$

93-98%

A series of symmetrical and unsymmetrical stilbenes bearing two or more strong electron-withdrawing groups were oxidatively cleaved to the corresponding aldehydes in high yield by electrocatalytic anodic oxidation in aqueous acetonitrile employing a new high oxidation potential triphenylamine electrocatalyst. The oxidations apparently involve the corresponding 1,2-diols, which are also converted to aldehydes in high yield under the same conditions.

Although simple alkyl-substituted olefins are directly oxidizable only under extreme conditions,[1,2] or at chemically reactive electrodes such as PbO_2,[3] aryl substitution renders the double bond much more susceptible to anodic oxidation. Typical reactions of the initial alkene cation radical involve reaction at the double bond or allylic position with a nucleophilic component of the medium and/or dimerization, followed by proton loss or, again, nucleophilic attack.[4] Such reactions have only rarely[5] involved clean formation of a single product. Cyclization processes can also occur, sometimes via further oxidation of the cation radical to a dication with highly arylated alkenes.[6] We reported several years ago a study of the synthesis and anodic oxidation in methanol of stilbenes bearing strong electron-withdrawing groups.[7] The oxidation potentials of these substances are close to that of the solvent. Consequently, very large excesses of current, as much as forty or more times the calculated amount, had to be passed in order to completely consume the starting material.[7] Apart from the practical consequence of such electrolysis inefficiency (long reaction times), the large amount of current consumed by side reactions raises the possibility of interaction of reaction intermediates with side products formed by oxidation of the solvent. It would clearly be desirable to carry out the reaction more efficiently. We felt that it should be possible in general to mitigate the high oxidation potentials of these and many other electronegatively substituted substances through so-called indirect oxidation by mediated electron transfer.[8] In this type of electrocatalysis (Figure 1), one employs an electron-transfer catalyst

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(1) This paper is dedicated to the memory of Yoshihiro Matsumura.

(2) Bertram, J.; Fleischmann, M.; Pletcher, D. *Tetrahedron Lett.* **1971**, *12*, 349.

(3) Möller, K.-C.; Schäfer, H. J. *Electrochim. Acta* **1996**, *42*, 1971.

(4) (a) Steckhan, E. *J. Am. Chem. Soc.* **1978**, *100*, 3526. (b) Steckhan, E.; Schäfer, H. J. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 472. (c) Bäumer, U.-St.; Schäfer, H. J. *Electrochim. Acta* **1996**, *42*, 1971.

(5) Möller, K.-C.; Schäfer, H. J. *Electrochim. Acta* **1997**, *42*, 1971.

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(8) (a) Steckhan, E. *Top. Curr. Chem.* **1987**, *142*, 1. (b) Simonet, J.; Pilard, J.-F. *Organic Electrochemistry*; Lund, H., Hammerich, O., Eds.; Dekker: New York, 2001; p 1164 ff. (c) Torii, S. *Organic Electrochemistry*; Schäfer, H. J., Ed.; Wiley-VCH: Weinheim, Germany, 2004; Chapter 15, pp 503−505.

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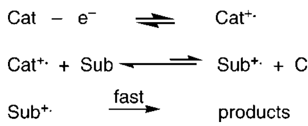


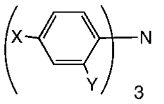
Figure 1. Electrocatalytic oxidation of a substrate Sub by electrocatalyst Cat.

(Cat) whose oxidation potential is lower than that of the substrate (Sub). The catalyst is chosen such that its oxidation affords a stable cation radical intermediate ($Cat^{+\bullet}$). In favorable cases, $Cat^{+\bullet}$ may in turn abstract an electron from the substrate, initiating a reaction cascade resulting ultimately in conversion to products and regenerating Cat to be reoxidized by the electrode to continue the catalytic cycle. This can occur even though the oxidation potential of the substrate may be as much as 500 mV or more higher than that of the catalyst.[8] For successful electrocatalysis to take place, the thermodynamically unfavorable second step must be compensated kinetically by a rapid following reaction of $Sub^{+\bullet}$.

Processes not involving mediated electron transfer but rather reaction of the alkene with an electrochemically generated reagent have been reported. Several metal ions, e.g., Mn(III), Pd(II), and Os(VIII), have been shown to effect the electrocatalytic oxidation of alkenes,[9] but such reactions have rarely been observed to proceed cleanly to a single product. Schäfer and Bäumer reported an exception to this generalization.[10] They carried out the anodic oxidation of a number of 1,2-disubstituted alkenes using a mixture of an IO_4^- salt and $RuCl_3$ in an acetonitrile−water−CCl_4 mixture. The alkenes were converted to carboxylic acids in good yields by a complex sequence in which periodate first oxidizes ruthenium to RuO_4, which then effects *bis*-hydroxylation of the alkene. Periodate then oxidatively cleaves the diol to two molecules of aldehyde, which are oxidized further to carboxylic acids by RuO_4. In this cleverly designed sequence, RuO_4 is used for two separate conversions and periodate also performs two functions: to oxidatively regenerate RuO_4 and to cleave the intermediate diol. The overall sequence is rendered catalytic by regeneration of periodate at the anode. Alkene cleavages to afford carboxylic acids can also be carried out by using ozone generated anodically at a PbO_2 anode; yields are good but current efficiencies were low (5−6%).[11] There are few chemical methods other than ozonolysis which can effect cleavage of a carbon−carbon double bond into two molecules of aldehyde in this fashion, but the aldehydes formed in this process are oxidized further to acids under these conditions. Anodic cleavage of alkenes into aldehydes can be effected by a IO_4^-−ruthenium−tungsten system, using an unusual cell in which the anode is immersed in an aqueous solvent while the alkene is in a separate organic layer not in contact with the anode.[12] This avoids over-oxidation of the aldehyde to carboxylic acid. But once again, applications were limited to unsubstituted arenes or those bearing electron-donating groups.

Concerns about toxicity and expense of metal catalysts, their solubility in organic media, and the attraction of carrying out such conversions in a simpler and more conventional undivided cell led us to examine mediated electron transfer as a possible method for effecting the electrocatalytic equivalent of ozonolysis of electronegatively substituted alkenes.

Steckhan and co-workers introduced the use of substituted triphenylamines (**1**) as convenient electrocatalysts[8a,13] and pointed out their advantages for a variety of anodic chemical conversions: they are soluble in a variety of common organic solvents, the cation radicals are long-lived if all three para-positions are substituted, and the oxidation potential of the compound can be adjusted by variation in the ring substituents. The triphenylamines most widely used as electrocatalysts have been 4,4′,4″-tribromotriphenylamine (**1a**) and to a much lesser extent its hexabromo analogue (**1b**). A preliminary experiment established the fact that **1a** is completely ineffective at promoting the electrocatalytic oxidation of electronegatively substituted stilbenes; its oxidation potential is too low. The higher oxidation potential of **1b** has sometimes been used to carry out conversions of substances that are unaffected by **1a**, but its synthesis requires tedious separations from polybromo congeners.[13a] We recently found a more convenient electrocatalyst, 4,4′,4″-trimethyl-2,2′,2″-trinitrotriphenylamine (**1c**), which is easily prepared in pure form by room temperature nitration of commercially available tri-*p*-tolylamine by $Cu(NO_3)_2$ in acetic anhydride.[14] **1c** is readily soluble in organic solvents, affords a stable cation radical upon one-electron oxidation, and, most importantly, has an oxidation potential 0.5 V higher than that of **1a** (Figure 2).



1a, X = Br; Y = H; E_{ox} = +0.82 V
b, X = Y = Br; E_{ox} = +1.26 V
c, X = CH_3; Y = NO_2; E_{ox} = +1.32 V

Figure 2. Oxidation potentials of triarylamine electrocatalysts vs $Ag/AgNO_3$.

We report here the **1c**-electrocatalyzed anodic oxidation of a number of stilbenes (**2a**−**f**) bearing two or more electron-withdrawing groups and suggest a possible mechanism for the observed conversions. Several possible reaction intermediates (**3a**−**c**) were also subjected to the electrolysis

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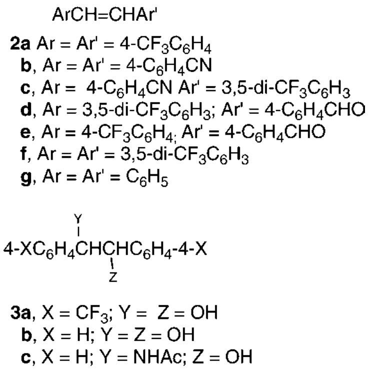
conditions to test whether they might be considered viable intermediates. Stilbenes **2a** and **2f** were synthesized by reductive coupling of the appropriate substituted benzaldehyde, using a mixture of $TiCl_4$ and zinc.[15] Stilbenes **2b**−**e** were prepared by Wittig coupling of an aromatic aldehyde with the appropriate benzyltriphenylphosphonium salt. Diol **3a** was prepared by Sharpless dihydroxylation of **2a**.[7] Diol *meso*-**3b** was a commercial sample. The acetamido alcohol **3c** was prepared by acetylation of (1*R*,2*S*)-2-amino-1,2-diphenylethanol (Ac_2O, pyridine).


ArCH=CHAr'

2a Ar = Ar' = 4-$CF_3C_6H_4$
b, Ar = Ar' = 4-C_6H_4CN
c, Ar = 4-C_6H_4CN Ar' = 3,5-di-$CF_3C_6H_3$
d, Ar = 3,5-di-$CF_3C_6H_3$; Ar' = 4-C_6H_4CHO
e, Ar = 4-$CF_3C_6H_4$; Ar' = 4-C_6H_4CHO
f, Ar = Ar' = 3,5-di-$CF_3C_6H_3$
g, Ar = Ar' = C_6H_5

$$\mathrm{4\text{-}XC_6H_4CH\overset{Y}{C}H\underset{Z}{C}HC_6H_4\text{-}4\text{-}X}$$

3a, X = CF_3; Y = Z = OH
b, X = H; Y = Z = OH
c, X = H; Y = NHAc; Z = OH

Figure 3. Substrates for electrocatalytic oxidations in aqueous acetonitrile.

Preparative Electrolyses. Controlled potential oxidations[16] were carried out in an undivided cell equipped with platinum cathode, carbon anode, and coulometer, at a potential (+1.30 V vs Ag/$AgNO_3$ reference) at which the triphenylamine **1c** is oxidized without significant oxidation of the substrate stilbene. The electrolysis was carried out in 10−20 mL of a 0.1 M solution of $LiClO_4$ in acetonitrile containing a small amount (0.5 mL) of added water together with 0.1−0.5 mmol of the stilbene and 5−15 mol % of **1c**. (The electrolysis procedure and cell are described in the Supporting Information.) The electrolyzed solution was first analyzed by gas chromatography−mass spectrometry (GC-MS) and then worked up and the products isolated by preparative scale TLC. Electrocatalytic oxidation of stilbenes **2a**−**f** was found in every case to lead very cleanly and in high yield (≥93% isolated) to a single substituted benzaldehyde from symmetrical alkenes or an equimolar mixture of two aldehydes from unsymmetrical alkenes (Table 1 and Figure 4). Coulometric *n*-values (the ratio of the number of Faradays of current passed to the number of moles of alkene consumed) ranged from 4 to ca. 12. The proton NMR and mass spectra and TLC R_f of the product aldehydes were compared with those of samples of the known substances and were identical.

Table 1. Electrocatalytic Cleavage of Substituted Stilbenes by the Action of 4,4′,4″-Trimethyl-2,2′,2″-trinitrotriphenylamine in Acetonitrile/H_2O

stilbene	oxidation potential of stilbene[a]	yield of aldehyde(s) (%)[b]	n^c	current efficiency (%)[d]
2a	1.50	96	6.0	68
2b	1.55	95	5.9	68
2c	1.70	93	7.5	53
2d	1.59	95	7.5	54
2e	1.46	96	8.5	47
2f	1.73	95	11.8	34
2g	1.1	95	4.0	100

[a] Potentials measured relative to Ag/0.1 M $AgNO_3$. [b] Isolated; GC yields were 100%. [c] Ratio of number of Faradays of current consumed to number of moles of stilbene. [d] Current efficiency = 100 × 4/*n*.

Coulometry and Mechanism. Cleavage of an alkene into two aldehyde molecules formally requires removal of four electrons from the alkene, i.e., a coulometric *n*-value of 4. An *n*-value of this magnitude strongly suggests the formation of a discrete intermediate in the process. All electrolyses were sampled and analyzed by GC-MS throughout the course of the electrolysis. Even in the early stages of electrolysis, the only constituents of the solution (apart from the catalyst) are the stilbene and the product aldehyde(s), demonstrating that any intermediate in the electrolysis is more easily oxidized than the alkene itself. The electronegatively substituted diol **3a** was found to be catalytically oxidized by **1c** substantially faster (and with consumption of two electrons per molecule) than the corresponding alkene **2a**, suggesting that it is a reasonable (actually likely) intermediate. Replacement of **1c** by **1a** resulted in isolation of the unchanged alkenes **2a**−**f** from control experiments. However, the lower potential catalyst **1a** was found to oxidize *trans*-stilbene (**2g**), and as expected, cleavage into two molecules of benzaldehyde did take place. The electrocatalytic oxidation of *meso*-hydrobenzoin (**3b**) and the hydroxyamide **3c** to 2 equiv of benzaldehyde by **1a** was also successful and in fact proceeded to completion much faster than did the oxidation of **2g**. Finally, direct anodic electrolyses of compounds **3b** and **3c** were carried out under the same conditions except without catalyst and found to afford the same product (benzaldehyde) as in the electrocatalyzed process, although, as expected, considerably higher potentials were required.

$$\mathrm{ArCH{=}CHAr'} \xrightarrow[\mathrm{CH_3CN/H_2O,\ LiClO_4}]{-4\,e^-,\ \mathrm{Ar_3N\ (cat)}} \mathrm{ArCH{=}O} + \mathrm{Ar'CH{=}O}$$

Figure 4. Products of electrocatalytic oxidation of stilbenes catalyzed by triphenylamine derivatives **1a** and **1c**.

A possible mechanism for the catalyzed process is presented in Scheme 1. The simplest interpretation of the

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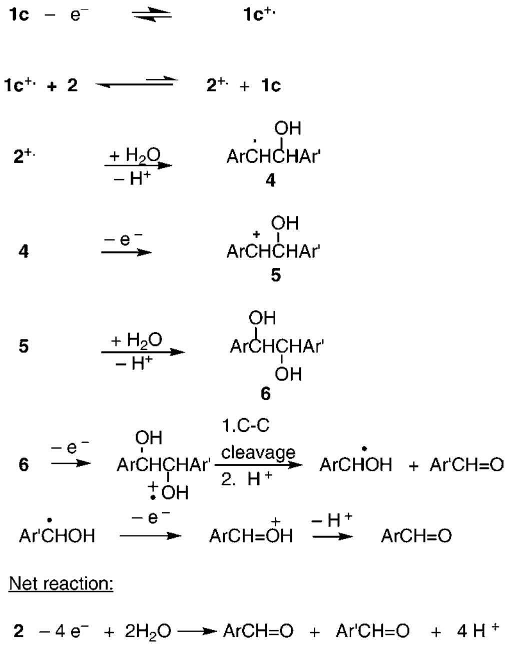
(15) (a) McMurry, J. E.; Fleming, M. P. *J. Am. Chem. Soc.* **1974**, *96*, 4708. (b) McMurry, J. E. *Acc. Chem. Res.* **1974**, *7*, 281. (c) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513.

(16) A reviewer suggested that it would be experimentally simpler to carry the reactions out at constant current. Under constant current conditions, several as yet unidentified low-yield byproducts accompany the desired aldehydes. The reasons for this behavior are being investigated.

Scheme 1. Proposed Mechanism for the Triarylamine-Catalyzed Electrochemical Oxidation of Stilbenes



observed cleavage reaction is that the reaction proceeds in two separate two-electron steps. The first step in both the direct and catalyzed oxidations is undoubtedly removal of an electron from the π-bond of the alkene to afford a radical cation ($\mathbf{2}^{+\bullet}$). Attack by a nucleophilic component of the medium, either acetonitrile or water, followed by proton loss would then afford the neutral benzylic radical **4**. Water is shown as the attacking nucleophile in Scheme 1 because it is more nucleophilic than acetonitrile. Oxidation of **4** followed by a second nucleophilic attack would produce the intermediate diol **6**. Since nucleophilic attack takes place twice during this sequence, one cannot rule out a certain proportion of attack by acetonitrile at one of the stages to ultimately produce a hydroxyamide akin to **3c**. We find, though, that this compound, like **4**, is also cleaved into aldehydes under the reaction conditions.

Cleavage of **2** into two aldehyde molecules corresponds to a four-electron oxidation, i.e., a theoretical coulometric n-value of 4. Coulometry indicated that, although the electrocatalyzed experiments proceed with much better current efficiency than in the direct electrolyses in methanol, most electrolyses still required more than the theoretical quantity of electricity. Catalytic anodic oxidation of **2a**, for example, proceeded with an n-value of 6.0, i.e., a 50% excess of current. This is not because of competitive solvent oxidation. Rather, the equilibrium between **2a**−**f** and the cation radical of **1c** ($\mathbf{1c}^{+\bullet}$) (second step in Scheme 1) is undoubtedly highly thermodynamically unfavorable because of the much higher oxidation potential of **2**.[7,8] Although the rate constant for reaction of the cation radical $\mathbf{2}^{+\bullet}$ with water is undoubtedly large, the bimolecular reaction rate, i.e., $k[H_2O][\mathbf{2}^{+\bullet}]$, must be limited by the very low concentration of $\mathbf{2}^{+\bullet}$. This allows time for $\mathbf{1c}^{+\bullet}$ to migrate to the cathode and be reduced to the neutral catalyst, thus interrupting the catalytic cycle. In support of this interpretation, the intensely blue-green $\mathbf{1c}^{+\bullet}$ can be observed to build up in solution and than decay by reaction with **2** on a time scale of several seconds. The equilibrium between $\mathbf{1c}^{+\bullet}$ and **2** will be even more unfavorable with stilbenes of higher oxidation potential, increasing the proportion of competitive reduction of $\mathbf{1c}^{+\bullet}$ taking place. We are now developing catalysts of higher oxidation potential than **1c**, which should eliminate this problem.

High potential electrocatalysts such as **1c** should be generally useful for facilitating the anodic oxidation of a wide variety of relatively difficultly oxidizible substances. We are pursuing several attractive applications.

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Supporting Information Available: Synthesis and characterization of stilbenes and cell and experimental electrolysis procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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