Paired Electrosynthesis at the Femtoliter Scale: Formation of 9,10-Anthracenedione from the Oxidation of Anthracene and Reduction of Dioxygen

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Abstract: A system is described in which the unique properties of a pair of microband electrodes are exploited both to initiate and to probe the products of a paired electrosynthesis using short-lived species. In particular, the oxidation of anthracene is coupled with the simultaneous reduction of dioxygen in acetonitrile to yield the anthracene radical cation and the superoxide anion. These latter react within a femtoliter scale volume to form initially 9,10-dihydro-9,10-epidioxyanthracene, which rearranges into 9,10-anthracenedione and, presumably, dihydrogen *via* an electron transfer catalyzed process.

Introduction

The reactions between strong nucleophiles and strong electrophiles, though of profound fundamental and presumably synthetic interest, have been little studied. This is due largely to the difficulty of generating such powerful reagents together, conditions favorable for the formation of one generally being inimical to the other. There are however a few circumstances under which such a combination becomes feasible. For instance, photoinitiated electron transfer through excitation of a charge transfer complex[1] can lead to the formation of a strong electrophile−nucleophile pair, which may or may not react chemically.[2] Evidently, the scope of this technique is limited by the need to form a sizable concentration of the charge transfer complex in the first place. A second alternative, also based on the activation of inert precursors through electron transfer, consists in pulsing the potential of an electrode alternately to anodic and cathodic potentials to generate in turn an electrophile and a nucleophile.[3] However, the need to perform a series of independant electrolyses implies that the solution used must be of reasonable conductivity, which again may limit the scope of the method. It occurred to us that this and other problems could be resolved by employing, as before, two electrogeneration potentials, separated not in time, but in space. The activated products formed at each separated electrode could then react together thanks to the merging of the diffusion layers extending at each electrode. A similar notion has been applied previously to studies at a rotating ring−disc electrode, where the products of the separated electrode reactions are mixed by hydrodynamic forces[4] rather than by diffusion. In order that the highly reactive and thus short-lived species which we wished to employ should meet by diffusion and then react, the distance between the sites where they are generated should be as small as possible. To this end, the ultramicroelectrode seemed the tool of choice.

The analytical uses of these electrodes are numerous and well documented,[5] while their synthetic applications remain rather scarce. This fact stems from the normal practice of using such electrodes for which the characteristic dimensions are less than the width of the convection-free layer under the experimental conditions used. The concomitant small total charge passed, and thus chemical change wrought, has led to little enthusiasm from synthetic chemists. Perhaps the most notable exception has been in the use of colloidal suspensions of conducting particles in an externally applied electric field,[6] effectively as a randomly dispersed array of spherical microelectrodes. It must be borne in mind though, that the extraordinary properties of microelectrodes can be exploited with an electrode of which only one of the characteristic dimensions is small, leaving open the possibility of bringing about macroscopic change in a solution. There would be little point in performing a conventional electrolysis at an electrode which was effectively an ornate conventional electrode, but we propose that the system described above can be achieved through the use of ultramicroelectrodes to carry out a coupled electrosynthesis.[7] Previously, the distance between the anode and cathode in the undivided cells employed and thus the distance which the electrogenerated reagents must cross unchanged has been in the order of at least tens of millimeters. Using a pair of closely spaced microband electrodes for such a reaction leads to the definition of a reaction volume where the diffusion layers of these two electrodes overlap, as in previous studies involving the simultaneous reduction and oxidation of a single compound on adjacent microbands leading to electrochemically generated luminescence.[8]

The whole is then effectively a microreactor of only several femtoliters volume, the bulk solution serving solely as a store of reagents and products. Thus, starting from a mother liquor containing suitably unreactive precursors, powerful nucleophiles and electrophiles, or super-acidic and super-basic species, which would normally react with the electrolyte solution before

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meeting, may be generated simultaneously in close proximity, and so combine chemically. It is the purpose of the present work to demonstrate the feasibility of such a synthesis. For this reason we have limited ourselves to the simple case of a single pair of band electrodes. In order to bring about the bulk transformation of a solution of large volume the use of an electrode such as an interdigitated array with the same interelectrode gap but greater overall active length needs to be envisaged, but was not required for the present investigation.

The synthetic reaction attempted was the coupling of the anthracene radical cation with the superoxide anion to form, at least initially, 9,10-dihydro-9,10-epidioxyanthracene (**1**). This reaction was chosen on the grounds that the required oxidation and reduction are both well known, as is the putative product (**1**), although there appears to be no previous published electrochemical study of the compound. The oxidation of anthracene in the chosen solvent, acetonitrile, is chemically irreversible on the normal voltammetric time scale due to a reaction between the initially formed radical cation and the solvent, although some doubt remains about the relevant pseudo-first-order rate constant.[9] The reduction of oxygen in acetonitrile has long been known to give rise to the superoxide ion, which is stable in dry acetonitrile on a time scale of minutes. The apparent degree of reversibility depends strongly on the electrode material used,[10] hence the choice in the present investigation of a gold cathode in the electrode assembly.

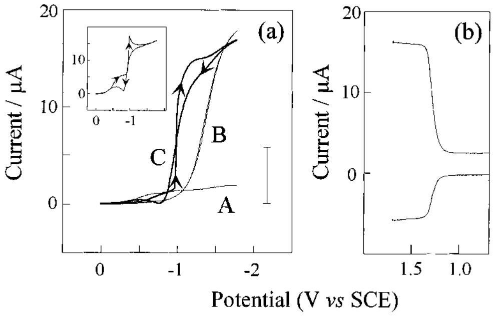

Figure 1. (a) Response to cyclic voltammetry at 200 mV s^{-1} of the cathode (Au) of the double band array, the potential of the anode (Pt) being fixed at +1.6 V: (curve A) anthracene 1.0 mM in argon saturated solution; (curve B) dioxygen saturated solution; (curve C) anthracene 1.0 mM in dioxygen saturated solution (8.2 mM). The inset shows the response of the system for a concentration of anthracene of 8.2 mM, conditions being otherwise identical to those for curve C, while the bar in the lower right-hand quadrant shows the height of the wave for the oxidation of anthracene under the same conditions. Solvent was MeCN, NBu_4BF_4 0.2 M, at ambient temperature. (b) Responses of the anode (lower trace) and cathode (upper trace) to linear sweep voltammetry at the anode with the cathode being held at −1.2 V and the conditions being otherwise identical to those for curve C in part (a).

Experimental Section

The electronic electrochemical equipment used was of an entirely conventional nature, the bipotentiostat being constructed in house. All potentials are quoted relative to an aqueous SCE reference electrode, and all voltammograms were recorded at a potential sweep rate of 200 mV s^{-1}. Unless otherwise indicated, positive currents are cathodic. The double band array used in the present study was constructed using published techniques,[11] as a "sandwich" of window glass, platinum foil (Goodfellow, 99.95%), Mylar (Energy Beam Sciences, 2 μm thickness), gold foil (Goodfellow, 99.95%), and a second layer of glass, bonded with epoxy resin (Epon, type 828), hardened with 10% triethylamine-tetramine (Aldrich, technical grade). The whole then consisted of a platinum anode and a gold cathode, each of 5 μm thickness, separated by 2.5 μm over a length of 4 mm. The array was polished using 1200 grit abrasive paper followed by 300 nm alumina suspension (both Presi) on a felt cloth. The dimensions and correct mutual alignment of the elements of the array were respectively determined and assured voltammetrically[12,13] and optically. Experiments were carried out in a conventional electrochemical cell designed for use on a vacuum line, the solution volume being 10 mL. A large platinum wire served as counter electrode.

Tetrabutylammonium tetrafluoroborate was obtained from the reaction of aqueous solutions of tetrabutylammonium hydrogen sulfate and sodium tetrafluoroborate (both Aldrich) and recrystallized twice from a methanol−water mixture before being dried under vacuum and used at a concentration of 0.2 M as supporting electrolyte in all experiments described. Solutions were saturated with dioxygen unless otherwise stated. Double band experiments were carried out in the presence of a small quantity of neutral alumina (Aldrich) previously heated under vacuum to remove residual water. Acetonitrile (Aldrich, HPLC Grade) was distilled over CaH_2 under an atmosphere of dinitrogen before use. Dioxygen and argon (both Air Liquide) were passed over $CaCl_2$ and anhydrous $CuSO_4$ before use. Anthracene (Aldrich, Gold Label) was used as received, while 9,10-anthracenedione (Rhône-Poulenc) was recrystallized from chloroform. 9,10-Dihydro-9,10-epidioxyanthracene was synthesized by literature methods[14] and its identity and purity confirmed by NMR spectroscopy.

Results and Discussion

Figure 1a shows three voltammograms, all produced by holding the anode of the array at +1.6 V, a potential beyond that required for the oxidation of anthracene, and performing cyclic voltammetry at the cathode, thus simultaneously setting in train synthetic reactions and probing the diffusion layer above the array. Curve A shows the response in the presence of anthracene and the absence of dioxygen, curve B that in the presence of dioxygen and the absence of anthracene, and curve C the result of the presence of both anthracene and dioxygen. Curve C is in no way the resultant of the superposition of curves A and B. The response of the system to the presence of dioxygen and anthracene in equimolar quantities (8.2 mM) is shown in an inset, the sharp peak shown on the forward scan being present whenever the ratio of hydrocarbon to dioxygen is high. The presence of such a feature in a steady-state voltammogram can in no way result from a diffusional effect, and must be due to a chemical reaction. A voltammogram recorded under the same conditions as those for curve C but with the anode held at +1.3 V, a potential at which anthracene is not oxidized, was identical to curve B.

Perusal of curve C in Figure 1a shows that it contains three interesting features, a plateau between −0.4 and −0.8 V, a sharp rise in current at around −1 V, and an apparent return wave at −0.73 V. The initial plateau occurs before the formal reduction potential for dioxygen in acetonitrile, and is therefore not due to an interaction with the superoxide ion and has been largely neglected in this work, other than being subtracted when quoting the height of the following wave. That the occurrence of this second wave depends on the simultaneous oxidation of anthracene at the anode may be seen from Figure 1b, and it is also worthwhile to note that the current recorded at the cathode is approximately two and a half times that due to the oxidation which gives rise to it. Similarly, that the superoxide ion may

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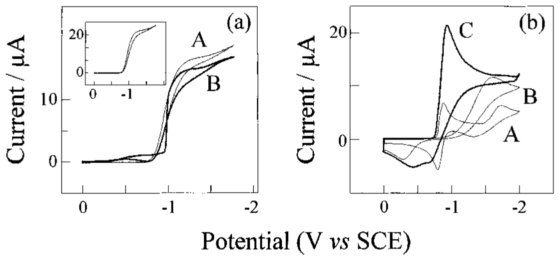


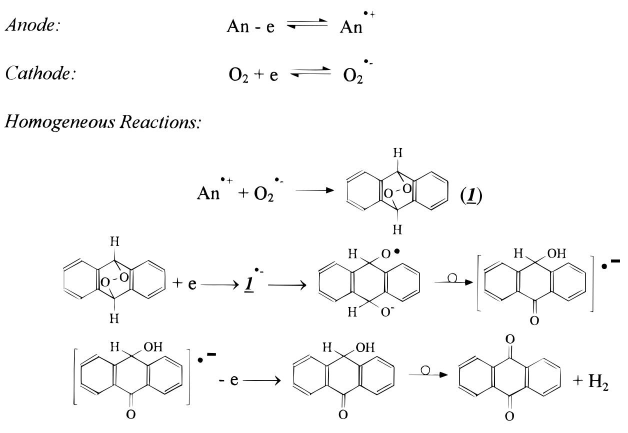
Figure 2. (a) Curve C of Figure 1a is repeated (curve B) for comparison with a voltammogram (curve A, top left inset) recorded under the same conditions, other than that anthracene was replaced by 9,10-anthracenedione, also at a concentration of 1.0 mM. (b) Voltammetric response at a 500 μm diameter platinum disc of A, an argon saturated 5 mM solution of **1**, B a dioxygen saturated solution, and C a dioxygen saturated 5 mM solution of **1** to cyclic voltammetry at 200 mV s^{-1}.

be involved is shown by a careful examination of curve B in Figure 1a which shows that the potentials concerned correspond to the very foot of the reduction wave of dioxygen. There is then a very small concentration of superoxide present in the diffusion layer of the electrode.

Figure 2a shows the comparison of curve C from Figure 1a (noted as curve B in Figure 2a) with the steady state wave for the reduction of anthraquinone (9,10-anthracenedione, noted ANQ) in the presence of dioxygen. The two waves are almost identical, except for the previously noted sharp rise in current in curve B. Such a feature is strongly suggestive of the involvement of an electrocatalytic mechanism[15] in which ANQ is produced quantitatively in the diffusion layer as soon as a threshold potential[15] is reached. The expected product from the reaction of the anthracene radical cation and superoxide is **1**. This expectation together with the results detailed above suggested that **1** was converted electrocatalytically into ANQ, for which reaction we tentatively propose the mechanism[16] reported in Scheme 1.

The sharp rise in current referred to earlier is greater than would be expected on the basis of the reduction of a product formed stoichiometrically from anthracene (see also Figure 1b). We ascribe this effect to the presence of a redox catalysis mechanism[17] in which ANQ$^{\bullet -}$ formed by reduction of ANQ which is generated electrocatalytically from **1** (Scheme 1) mediates the reduction of dioxygen. This suggestion is further supported by the data presented in Figure 2b, which show the voltammetric response at a 500 μm diameter platinum disc electrode of **1** in argon saturated solution, curve A, of a saturated solution of dioxygen alone, curve B, and of **1** in a saturated dioxygen solution, curve C. At low concentrations of **1**, both the wave in this last curve and that due to the direct reduction of dioxygen are visible. In brief, the response shown in curve B in Figure 2a is very close to that obtained from an authentic sample of 9,10-anthracenedione under the same conditions. We propose that these observations come about as a result of an electrocatalytic mechanism, the overall reaction being as shown in Scheme 2 (where An$^{\bullet +}$ is formed at the anode).

Scheme 1



Scheme 2

Initiation:

$$O_2 + e \longrightarrow O_2^{\bullet -}$$

$$O_2^{\bullet -} + An^{\bullet +} \longrightarrow \underline{1} \dashrightarrow ANQ \qquad \textit{(see Scheme 1)}$$

Propagation:

$$ANQ + e \longrightarrow ANQ^{\bullet -}$$

$$ANQ^{\bullet -} + O_2 \rightleftharpoons ANQ + O_2^{\bullet -}$$

$$O_2^{\bullet -} + An^{\bullet +} \longrightarrow \underline{1} \dashrightarrow ANQ \qquad \textit{(see Scheme 1)}$$

Thus the wave in curve C of Figure 2b at around −1.00 V is assigned to the reduction of dioxygen, mediated by 9,10-anthraquinone formed itself *via* the electron transfer catalyzed reorganization of **1**. This explains why the plateau of wave C in Figure 1a and the cathodic current in Figure 1b are greater than expected given the concentration of anthracene and therefore the maximum concentration of anthraquinone formed. In addition, the presence of a double return wave at −0.68 and −0.44 V may be noted.

The peak at around −1 V in curve C of Figure 2b was found to grow progressively as the concentration of **1** was increased. The upper data set (open circles) in Figure 3a shows the variation of this peak with the concentration of **1** added, as measured at the gold electrode of the double band array, operated in the single electrode mode. The lower set of data (open triangles) shows the variation with the concentration of anthracene of the height of the plateau following the sharp rise in current at around −1.00 V (see Figures 1a and 2a), for voltammograms recorded at the cathode under the same conditions as those for curve C in Figure 1a. The nonlinear dependance of the heights of these waves with respectively the concentration of **1** (circles) or anthracene (triangles) present is clear. A small quantity of anthracene gives rise to currents far greater than would be predicted on the basis of the reduction of a product formed from the anthracene radical cation and the superoxide ion. The similarity, both in magnitude and form, of these two sets of data, obtained from very different experiments, is striking.

The dependance of the height of the second plateau in the forward scan of curve C of Figure 1a with the concentration of dioxygen in the solution, for three concentrations of anthracene, is shown in Figure 3b. The amount of dioxygen present was

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(15) Amatore, C.; Pinson, J.; Savéant, J-M.; Thiébault, A. *J. Electroanal. Chem.* **1980**, *107*, 59−74.

(16) Further evidence for the occurrence of such a mechanism was obtained from the electrochemistry of (**1**) at a platinum electrode. The results obtained, which are not presented here, indicate that this compound is quantitatively converted into ANQ ($E°_{ANQ}$ = 0.86 V *vs* SCE) within the diffusion layer following its one-electron reduction, provided that the potential sweep rate used is less than 2 V s^{-1}. This reaction is completely frozen at much shorter time scales (>200 Vs^{-1}), allowing the real voltammogram of **1** ($E°_1$ = 0.90 V *vs* SCE) to be recorded. For intermediate scan rates, the voltammetry of **1** shows trace crossings characteristic of electron transfer catalyzed reactions.[15] The response recorded at low sweep rate (see Figure 2a, curve A) is then superficially similar to that obtained from an authentic sample of ANQ itself, the apparent reversibility of the reduction then being due to the reversibility of the reduction of this compound.

(17) For straightforward electrochemical redox catalysis see: (a) Andrieux, C. P.; Dumas-Bouchiat, J. M.; Savéant, J-M. *J. Electroanal. Chem.* **1978**, *87*, 39−54. For a mechanism involving redox catalysis through a mediator generated in an electrocatalytic reaction, as in the present case, see: (b) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J-M.; Thiébault, A. *J. Am. Chem. Soc.* **1984**, *106*, 6318.

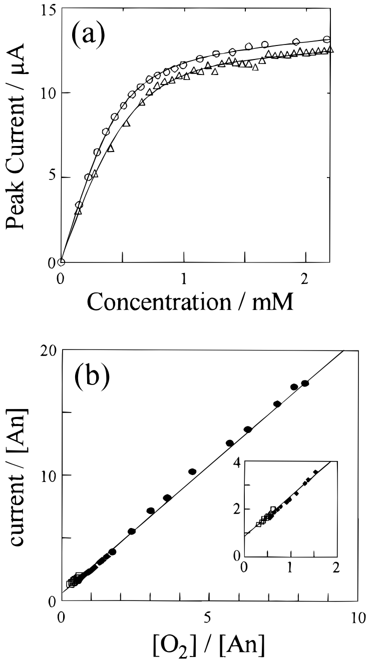
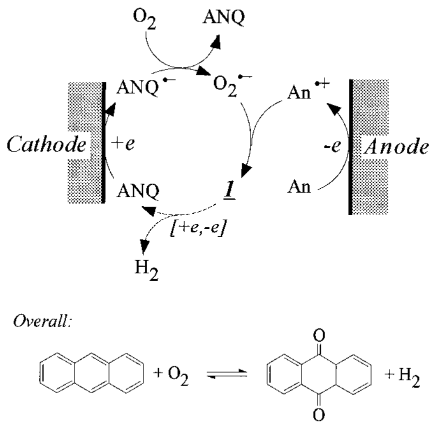


Figure 3. (a) Variation of peak current measured at the gold electrode of the double band electrode as a function of the concentration of the analytes; **1** + O_2 (circles) or anthracene + O_2 (triangles). (b) Variation of plateau height (current in μA) of curve C in Figure 1a with the concentration (in mM) of dioxygen in solution for the three concentrations of anthracene: 1 (solid circles); 5 (solid diamonds), or 10 mM (open squares).

varied by the partial degassing of a dioxygen saturated solution. For each point the concentration was determined voltammetrically by comparison with the height of the wave obtained on a single band for the saturated solution. The anode was then reconnected and the voltammogram re-recorded in double band mode. The data have been presented without subtracting the height of the preceding plateau. This procedure may be justified if it is assumed that the process giving rise to this plateau is suppressed as the mechanism causing the following sharp front is triggered, then the height of this peak should be measured from the baseline. The apparent return wave in curve C of Figure 1a or 2a may then be interpreted as the point at which the mechanism responsible for the sharp current rise is supressed and the system attempts to return to steady-state behavior. This interpretation is further justified by the fact that this "return wave" was never observed to pass below the zero current line under any circumstances. The data presented demonstrate that both dioxygen and anthracene play a large part in the response of the array. It can be seen that the behavior of the system is consistent over the concentration ranges studied for dioxygen and anthracene, which spanned a large part of the total solubility range for each compound. Furthermore, although due to the scale the data sets in Figure 3a appear to reach a plateau, in fact the limiting currents continue to increase with the concentration of anthracene or **1** present.

Scheme 3



The arguments outlined above allow a coherent picture to be drawn of the processes involved in the response of the double band. Curves A and B of Figure 2a are almost certainly due to the same electrochemical reaction. The forms of the voltammograms are very close, and the similarity of the dependencies of the forward peak heights on the concentration of either anthracene or **1** as shown in Figure 3 is remarkable. This is explained, in the case of the double band results, by the successful synthesis of **1**. Since reactions between aromatic cation radicals and electron-rich species are known[18] to be predominantly electron transfer in nature, this most likely occurs *via* an intermediate complex of excited neutral species formed upon electron transfer from the superoxide ion and anthracene cation radical. Subsequent to the easy reduction of **1**, 9,10-anthracenedione is formed electrocatalytically and mediates the reduction of dioxygen.

One objection that could be raised is the fact that the reductive process on the cathode of the double band appears to be triggered at potentials where the reduction of dioxygen is only incipient. However, once a single molecule of **1** has been formed it will itself be reduced, leading catalytically *via* the formation of the radical anion of 9,10-anthracenedione to the further reduction of dioxygen to superoxide. This superoxide is then available to react with the anthracene radical cation, and a catalytic cycle is established, leading to a sharp rise in current. Such autocatalytic mechanisms are well known experimentally and their theoretical kinetics well documented.[19] The overall reaction is shown in Scheme 3 in which the reactions detailed in Schemes 1 and 2 are implicit. The close resemblance between the curves in Figure 2a may now be seen in terms of the reactions outlined in Scheme 3. In curve B, the "explosive" rise in current is triggered at around −1 V. Following this, the response tracks that for 9,10-anthraquinone at a similar concentration as almost all the anthracene is converted to the quinone form. Comparison of the plateau heights of the two curves in Figure 2a indicates a yield of around 90%.

Conclusion

The use of paired microband electrodes allows the coupling of a strong nucleophile with a strong electrophile, something which has, up to now, been difficult, due to the instability of such species and the incompatibility of the conditions required

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(18) Koike, K.; Thomas, J. K. *J. Chem. Soc., Faraday Trans.* **1992**, *88 (2)*, 195−200.

(19) Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1981**, *103*, 6930−6937.

(20) One of the referees pointed out the similarity between the proposed technique and photoinitiated intermolecular electron transfer. Indeed, as noted in the Introduction section, here a reactive ion pair is "constructed" from individual ionic components created at each electrode, while in CT photochemistry, the ion pair results from direct photochemical activation of the CT complex. The advantage of the electrochemical method described here is the obviation of the need to form an initial charge transfer complex between acceptor and donor. Such complexes are, in most cases, only weakly bound, and thus exist at low concentration. In passing the electron instead by an external circuit considerable gains in conversion rate and efficiency may be expected. Also, the use of electrochemical conditions vs photochemical ones may lead to different overall reactions because of different followup reactions of the initial product, as evidenced here by the electron transfer catalyzed conversion of **1** into ANQ.

to generate them. Anthracene and dioxygen have been directly coupled to form 9,10-anthracenedione, something which would be difficult to achieve by conventional chemical techniques.[20] Moreover, a chemical reaction has been carried out uniquely through the imposition of a spatially structured reactivity in solution.

The technique of paired electrosynthesis may now be extended beyond the present realm, where the requirement that the electrogenerated reagents be sufficiently unreactive to cross a conventional electrochemical cell unchanged is a major constraint. In addition, although we used an arrangement where current was passed through a distant counter electrode the technique would be equally applicable were the current to be passed uniquely between adjacent microbands, in a way very reminiscent to what occurs in pit corrosion. Since the associated Ohmic drop would then be much reduced, solutions of low conductivity[11] could then be exploited.

The present work was developed to test and establish the principle of the spatial segregation of chemical reactions based on the small diffusion layers that are inherent to microelectrodes. The results presented are directly transposable to interdigitated arrays (IDA)[21,22] as the diffusional regime is similar at these devices. This promising technique will thus be brought to maturity, allowing the use of electrodes of greater overall active area, and so lead to preparative scale reactions.

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(21) Such large electrode arrays have been produced through a variety of methods[5] for analytical purposes, the most robust and thus those most suited to an eventual preparative application probably being those produced by photolithographic techniques[22] where interelectrode spacers of silicon dioxide as slim as 0.5 μm have been reported.

(22) See *e.g.*: (a) Aoki, K.; Morita, M.; Niwa, O.; Tabei, H. *J. Electroanal. Chem.* **1988**, *256*, 269. (b) Chidsey, C. E.; Feldman, B. J.; Lundgren, C.; Murray, R. W. *Anal. Chem.* **1986**, *58*, 601.