Mediated electron transfer from lithium investigated voltammetrically in tetrahydrofuran: why are some mediators more effective reducing reagents than others?

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ABSTRACT: A study of a range of aromatic molecules is investigated electrochemically to determine what makes an effective reducing mediator. With the aim of developing a better understanding of electron transfers (ETs) mediated from lithium in functional group reduction, a series of single ET reactions are reported in this paper. Typical reaction conditions involved the use of aromatic mediators such as naphthalene, anthracene, 4,4′-di-*tert*-butyl-1,1′-biphenyl (DBB) with lithium metal in tetrahydrofuran (THF) at −78 °C. The results of these experiments showed that some mediators were more effective reducing reagents than others. Cryoelectrochemical procedures are used to mimic the conditions of the SET reactions in order to investigate the exact nature and role of the mediator formed upon ET. It is demonstrated that electro-generated and stabilized radical anions of anthracene at −78 °C mediate the reduction of organic substrates, whereas the more reactive dianion is quickly protonated and therefore unable to act as an ET reagent; direct electrochemical reduction of the sulfide, phenyl 3-phenylpropylsulfide (RSPh) gives the thiol, thiophenol, and propyl benzene whereas mediated reduction gives the dimer, diphenyl disulfide and propyl benzene. The possibility to selectively reduce a substrate with either a single electron or with two electrons is possible by using either the radical anion (mediated) or via the direct electroreduction. DBB and naphthalene (both single electron accepting species only) have been found to be the most effective reducing reagents in this study. Anthracene and other two-electron accepting species only showed effective reducing ability when a stoichiometric amount of lithium was used therefore preventing the 'over-reduction' to the dianion. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: mediator; cryoelectrochemistry; anthracene; single electron transfer (SET); tetrahydrofuran (THF)

INTRODUCTION

The role of mediators as homogeneous electron-transfer (ET) reagents for the reductive cleavage of functional groups is widely employed in synthetic organic chemistry. Typically, lithium metal is reacted with an arene electron-transferring catalyst and substrate, the aromatic radical anion being generated *in situ* (Scheme 1).

In particular, 4,4′-di-*tert*-butyl-1,1′-biphenyl (DBB) and naphthalene have attracted much interest as being the most effective mediators. In the past few decades many examples of the use of these mediators has been reported. For example, a range of functional groups which include thioethers, allylic and benzylic thiols, acetals, disulfides, tertiary alkyl chlorides, and heterocycles have been

reduced employing DBB and naphthalene[1] as the mediators;[2–4] the reductive ring opening of oxygen-containing benzo-fused heterocycles,[5] structural modification of carbohydrates,[6] the reductive decyanation of nitriles,[7] and the coupling of carbonyl compounds[8] have also been reported. In addition, Donohoe *et al.*[9,10] have investigated a number of applications of mediated syntheses including the total synthesis of cylindricine A,[11] the formation of enantiopure pyrroline building blocks for natural product synthesis,[12] and in the partial reduction of heterocycles.[13,14] From an electrochemical perspective, redox catalysis is gaining wide popularity particularly in biosensor research, environmental applications, and in biological investigations (proteins, DNA, etc.). The work of Savéant[15–17] and Parker,[18] in particular, has significantly developed the area of redox catalysis.

With a range of mediators available, both in synthetic and in homogeneous redox catalysis, it is recognized that some mediators are more 'effective' reducing reagents

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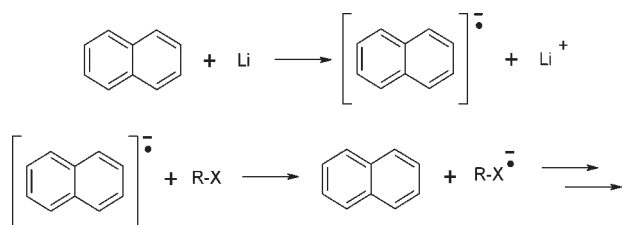
Scheme 1.

than others. Given the structural similarities between many of these mediators (polyaromatic compounds in particular) the question arises of why this should be? What makes a mediator effective as a reducing reagent? Furthermore, the ability of some mediators to accept more than one electron raises the interesting question of whether it is possible to 'selectively' mediate with either (a) a monoanion or (b) a dianion to yield, for example, a monomeric or dimeric product, respectively. Finally, how does a synthetic-mediated ET reaction compare to that of a direct electrochemical reaction whereby the electrode serves as the electron source? The aim of this investigation is to answer these fundamental questions which have been raised frequently in the literature,[1,4,5,7] and to provide an insight into what makes a mediator 'effective'.

Herein, a series of mediated reactions are reported in this paper. Typical reaction conditions involved the use of aromatic mediators such as naphthalene, anthracene, DBB with lithium metal in tetrahydrofuran (THF) at $-78\,^{\circ}$C. The results of these experiments showed that some mediators were more effective reducing reagents than others. For example, DBB and naphthalene gave >70% yields of reduced phenyl 3-phenylpropylsulfide and *trans*-1-(3-iodopropoxy)-4-(methoxymethoxy)cyclohexane compared with anthracene and 2,2′-dimethoxy-1,1′-binaphthyl which did not reduce the substrates but did yield 9,10-dihydroanthracene in the former case. These interesting observations raised the question as to why this should be the case for a series of structurally similar aromatic mediators?

Herein, we used cyclic voltammetry (CV) in an experimental setup designed to mimic the conditions of the SET reactions in order to investigate the exact nature and role of the mediator formed upon ET. Developing our previous work with naphthalene[19] we show, as a case example, that electro-generated and stabilized radical anions of anthracene at $-78\,^{\circ}$C mediate the reduction of organic substrates, whereas the more basic dianion is quickly protonated and therefore unable to act as an ET reagent. For example, reductive mediation of the sulfide, phenyl 3-phenylpropylsulfide (RSPh) yields the dimer, diphenyl disulfide and the propyl benzene, whereas the direct electrochemical reduction gives the thiol, thiophenol, and propyl benzene. Therefore the possibility to selectively reduce a substrate with either a single electron or with two electrons becomes possible. DBB and

naphthalene (both single electron accepting species only) have been found to be the most effective reducing reagents in this study. Anthracene and other two-electron accepting species only showed effective reducing ability when a stoichiometric amount of lithium was used therefore preventing the 'over-reduction' to the dianion. In these cases, the formation of dimers was feasible.

EXPERIMENTAL

Reagents

Tetra-*n*-butylammonium perchlorate (TBAP) and tetra-*n*-butylammonium hexafluorophosphate (TBAF) (Fluka), anthracene, ferrocene, ferrocenium hexafluorophosphate, and phenyl 3-phenylpropylsulfide (Aldrich) were used as received and without any further purification. Anhydrous THF was purified by filtration through two columns of activated alumina (grade DD-2) as supplied by Alcoa, employing the method of Grubbs and coauthors.[20] Acetonitrile (ACN) (Fisher Scientific) was dried over molecular sieves (BDH Laboratory Reagents) and kept under argon before use. DBB and naphthalene (Aldrich) were recrystallized from methanol before use. 2,2′-Dimethoxy-1,1′-binaphthyl was synthesized from the corresponding alcohol (Aldrich) by methylation (MeI, K_2CO_3, DMF). Using the corresponding carboxylic acids (Aldrich), methyl naphthalene-2-carboxylate and methyl naphthalene-1-caboxylate were prepared by esterification (MeOH, H_2SO_4).

The halides, *trans*-1-(3-iodopropoxy)-4-(methoxymethoxy)cyclohexane (R-I), *trans*-1-(3-bromopropoxy)-4-(methoxymethoxy)cyclohexane (R-Br), and *trans*-1-(3-chloropropoxy)-4-(methoxymethoxy)cyclohexane (R-Cl) were prepared from a general precursor which has been described previously.[21,22]

Voltammetry

Voltammetric measurements were carried out on an Autolab PGSTAT 20 (Eco-Chemie, Utrecht, Netherlands) potentiostat. A three-electrode arrangement was used in an air-tight, three-necked electrochemical cell. The cell with solid electrolyte was dried *in vacuo* overnight before solvent addition and electrochemical experiments. The working electrodes employed were 5 and 12.5 µm (radius) platinum disk-electrodes (Cypress Systems, Inc., Kansas, US) and a 1 mm (diameter) platinum disk-electrode housed in Teflon™, with a large area, shiny platinum wire (Goodfellow Cambridge Ltd, Cambridge, UK) as the counter electrode. The working electrodes were carefully polished before use on a clean polishing pad (Kemet, UK) using 3, 1, and 1/10 µm diamond spray (Kemet, UK). All working electrodes were carefully dried prior to use. Before carrying out electrochemical

experiments, the microdisk radius was electrochemically calibrated using literature methodology.[23] A Fc/Fc$^+$PF$_6^-$ reference electrode was developed for use in THF and at low temperatures.[24] The temperature was monitored and controlled by an external system (Julabo FT902, JULABO Labortechnik GmbH, D-77960 Seelbach/Germany). Typically the solutions were degassed vigorously for 1 min using impurity-free argon (BOC gases, Guildford, Surrey, UK) to remove any trace oxygen and an inert atmosphere was maintained throughout all analyses. All solutions were prepared under an atmosphere of argon using oven-dried glassware such as syringes and needles used for the transfer of moisture sensitive reagents and where required all mediator solutions were prepared and stored at $-78\,°C$. All voltammetric measurements were performed inside a Faraday cage in order to minimize any background noise.

Controlled-potential electrolyses

Controlled-potential, bulk electrolyses were carried out in a two-compartment cell, the catholyte and anolyte being separated by a sintered glass frit. The cathode was a rectangular platinum plate (area $= 2\,cm^2$) (Goodfellow, UK), and the anode a platinum mesh housed within the separate compartment with 0.1 M TBAP in THF. A Fc/Fc$^+$PF$_6^-$ reference electrode was used as the reference electrode. All electrolyses were vigorously stirred using a magnetic stirrer bar and the temperature maintained using an external cooling system (Julabo FT902, JULABO Labortechnik GmbH, D-77960 Seelbach/Germany). The potential was held constant at the required reduction potential of the electron transfer (ET) reagent (*vs.* Fc/Fc$^+$PF$_6^-$) determined from microdisk-cyclic voltammograms.

Saturated aqueous ammonium chloride (2 ml) followed by water (10 ml) was added to the electrolyzed solution upon reaction completion. Diethyl ether (20 ml) was then added and the two fractions separated. The organic fraction was then washed with aqueous hydrochloric acid (1 M, 8×10 ml), saturated sodium bicarbonate (10 ml), and saturated aqueous sodium chloride (10 ml). The organic layer was dried over magnesium sulfate and then carefully evaporated under reduced pressure. The products were identified by ^{1}H NMR, ^{13}C NMR, and, where necessary, LC-MS.

Single electron transfer (SET) reaction for functional group reduction: general procedure

To a two-neck flask containing the mediator under investigation dry THF was added (typical concentration, 0.1 M) under argon, the solution was then cooled to $0\,°C$.

Fresh lithium was prepared by submerging the wire in pentane while scraping the oxidized surface with a knife. The lithium metal was then cut directly into the mediator solution under a stream of argon. The resulting blue–green solution was cooled to $-78\,°C$ and allowed to stir for 4 h. The starting material (0.50 mmol) in dry THF (10 ml) was cooled to $-78\,°C$ and the mediator solution (2 equiv.) added rapidly. The reaction was allowed to stir at $-78\,°C$ for a further 10 min and quenched by the dropwise addition of saturated aqueous ammonium chloride (5 ml). The solution was allowed to warm to ambient temperature, poured into brine (20 ml), and extracted with diethyl ether (2×30 ml). The organic extracts were combined, dried over MgSO$_4$, and evaporated under reduced pressure.

Microdisk chronoamperometry

The current observed at a microdisk electrode can be described in terms of the dimensionless current function and time function:

$$f = \frac{I}{4FnDrc} \quad (1)$$

$$\tau = \frac{4Dt}{r^2} \quad (2)$$

where I is the current, F is the Faraday constant, n the number of electron(s) transferred, D the diffusion coefficient, r the disk radius, c the bulk concentration, and t the time. Microdisk chronoamperometry permits the simultaneous determination of D and n provided no coupled chemistry operates on the timescale of the experiment. The time-dependent current response, I, resulting from a diffusion-controlled reductive (or oxidative if required) current after a potential step at a microdisk electrode is given in Eqn (3):

$$I = -4nFDcrf(\tau) \quad (3)$$

where Eqn (4) defines $f(\tau)$:

$$f(\tau) = 0.7854 + 0.8862\tau^{-1/2} + 0.2146e^{-0.7823\tau^{-1/2}} \quad (4)$$

The above approximations [Eqns (1–4)] were derived by Shoup and Szabo[25] and describe the current response to within an accuracy of 0.6% over all τ. Experimentally, the chronoamperometric experiment is run over a time scale incorporating a transition from planar diffusion, with a $I \propto D^{1/2}$ dependence, to steady-state hemispherical diffusion with a $I \propto D$ dependent behavior.[26] Accordingly, deconvolution of the parameters D and n is possible from a single scan. Fitting is achieved using ORIGIN 6.0 (Microcal Software, Inc.) whereby inputting accurate values for r and c, the software iterates through values of D and n until the fit of the experimental data is optimized.

Tafel analysis

Mass transport-corrected Tafel analysis of a voltammetric wave is a method that may be used under certain conditions for studying the kinetic nature of a heterogeneous ET.[27] When these conditions are met, a plot of $(F/RT)(E - E_f^o)$ versus $\ln[(I_{lim}/I) - 1]$ will be linear in both the limits of electrochemical reversibility and irreversibility, where I is the steady-state current and I_{lim} is the steady-state current in the limit of mass-transport. For an electrochemically reversible ET this plot will have a gradient of 1 and for an electrochemically irreversible ET this plot will have a gradient of $1/\alpha$.[28]

Analytical techniques

^{1}H NMR spectra were recorded using a Bruker AV400 (400 MHz) spectrometer in CDCl$_3$ and referenced to tetramethylsilane (Si(Me)$_4$) as an internal standard. Signal positions were recorded in δ (ppm) with the abbreviations s, d, t, q, quint., sept., br, app., and m denoting singlet, doublet, triplet, quartet, quintet, septet, broad, apparent, and multiplet, respectively. All coupling constants, J, are quoted in Hz.

Crude electrolysis mixture was analyzed by thin-layer chromatography (TLC). TLC was performed on Merck Kieselgel 60 F$_{254}$ 0.25 mm precoated aluminium-backed silica plates. Compounds were visualized with UV light and/or by staining with basic potassium permanganate solution.

Flash chromatography was used to separate the products following electrolysis and carried out according to the method described by Still et al.[29] using Merck Kieselgel 60 (40–63 µm). Column fractions were monitored by TLC.
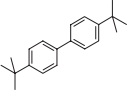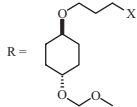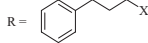
RESULTS AND DISCUSSION

A series of SET reactions were performed using various mediators as the ET reagents. The results, which are discussed in the first section, showed that some mediators were more effective reducing reagents than others. The aim of the subsequent sections therefore was to answer three key questions. First, why are some mediators more effective than others? Second, is it possible to reduce a substrate using either the monoanion or dianion form of a mediator generated to transfer one or two electrons selectively? Thirdly, how do the mediated and direct electrolyses of mediation compare?

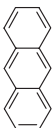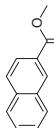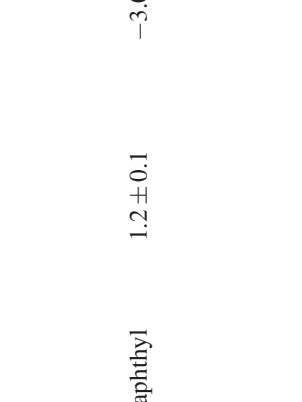### Single electron transfer experiments

A series of SET reactions were performed using halides and sulfides as the organic substrates and with a range of polyaromatic compounds as mediators. The structures of the compounds used and the results of the reduction reactions are given in Tables 1 and 2. The exact experimental details have been described above and in previous work.[30] It was observed that DBB and naphthalene (Table 1) used as the mediators gave the best percentage yields of reduced products. For example, the sulfide, phenyl 3-phenylpropylsulfide (RSPh), gave propylbenzene (RH) in 74% yield with naphthalene and [(3-{[trans-4-(methoxymethoxy)cyclohexyl]oxy}propyl)-thio]benzene (R'SPh) gave trans-1-(methoxymethoxy)-

Table 1. Voltammetric data for single electron transfer (SET) reagents with $n = 1$ obtained at $-78\,°C$ in THF (0.1 M TBAP) using a Pt microelectrode

ET reagent	$E_{1/2}$ (V) versus Fc/Fc$^+$PF$_6^-$	n	$D \times 10^{-10}$ (m^2 s^{-1})	Tafel value (mV)	SET experimental results[a]; percentage yield of reduced product (%)
DBB	-3.34	1 ± 0.1	2.3 ± 0.1	132	R-I $\rightarrow$ R-H (60%) + R-R (6%) R'SPh $\rightarrow$ R'-H (90%) R-Cl $\rightarrow$ R-H (92%) R-Br $\rightarrow$ R-H (81%)
Naphthalene	-3.11	1 ± 0.1	2.4 ± 0.1	115	R-I $\rightarrow$ R-H (62%) RSPh $\rightarrow$ R-H (74%) R-Cl $\rightarrow$ R-H (68%) R-Br $\rightarrow$ R-H (72%)

[a] SET experiments performed using an excess of lithium.

Table 2. Voltammetric data for SET reagents with $n = 2$ (overall) obtained at $-78\,^\circ$C in THF (0.1 M TBAP) using a Pt microelectrode

ET reagent	$D \times 10^{-10}$ (m^2 s^{-1})	1st reduction wave			2nd reduction wave			SET experimental results[a]
		$E_{1/2}$ (V) versus Fc/Fc$^+$PF$_6^-$	n	Tafel Value (mV)	$E_{1/2}$ (V) versus Fc/Fc$^+$PF$_6^-$	n	Tafel value (mV)	Percentage yield of reduced product/%
Anthracene	2.9 ± 0.1	-2.47	1 ± 0.1	57	-3.14	2 ± 0.1	94	RSPh → No reduction R-Cl → No reduction[b] R-I → R-R (70%)[b] R-Br → R-R (70%)[b]
Methyl naphthalene-2-carboxylate	2.0 ± 0.1	-2.56	1 ± 0.1	98	-3.25	2 ± 0.1	230	R-I → No reduction
Methyl naphthalene-1-carboxylate	1.8 ± 0.1	-2.45	1 ± 0.1	110	-3.14	2 ± 0.1	201	RSPh → No reduction
2,2′-Dimethoxy-1,1′-binaphthyl	1.2 ± 0.1	-3.00	1 ± 0.3	91	-3.30	2 ± 0.1	129	R-I → No reduction R′SPh → No reduction

[a] Experiments performed using an excess of lithium unless otherwise stated.
[b] Experiments performed with 1 equivalent of lithium.

4-propoxycyclohexane (R′H) in 90% yield with DBB (Table 1). Similar percentage yields of reduction were also observed for iodides, bromides, and chlorides (Table 1). In contrast to these results, all of the mediators in Table 2 gave no reduction products under the general conditions used (excess lithium, $-78\,^{\circ}$C). For example, anthracene when used as a mediator for the reduction of the sulfides and iodides described above did not act as an ET reagent and gave only the partially reduced aromatic compound: 9,10-dihydroanthracene as the product.

Following these data, an electrochemical procedure was developed to mimic the conditions used in the SET reactions and ultimately, investigate the properties of the mediators.

Voltammetric analyses

Steady-state voltammetry, cyclic voltammetry, and microdisk chronoamperometry of the mediators.
Using microdisk voltammetry,[31] the steady-state voltammograms for the mediators used in the SET reactions were obtained. Figures 1–3 show the voltammograms for DBB, anthracene, and methyl naphthalene-1-carboxylate, respectively, in THF (0.1 M TBAP) at $-78\,^{\circ}$C. The half-wave potential, $E_{1/2}$, and Tafel slope[27,28,31] for each compound are given in Tables 1 and 2. DBB and naphthalene showed a single wave (Table 1) whereas the mediators in Table 2 all showed double waves. Tafel analysis for anthracene (Table 2) showed that the first wave was reversible (electrochemically) ($E_{1/2} = -2.47$ vs. Fc/Fc^{+}PF$_{6}^{-}$; 57 mV) whereas the second wave is quasi-irreversible ($E_{1/2} = -3.14$ vs. Fc/Fc^{+}PF$_{6}^{-}$; 94 mV). Voltammetry performed at low temperatures ($-78\,^{\circ}$C) in THF allowed the full resolution of the voltammetric waves for some mediators in Table 2 and also for DBB (Table 1) from the solvent breakdown.[22,30,32–34]
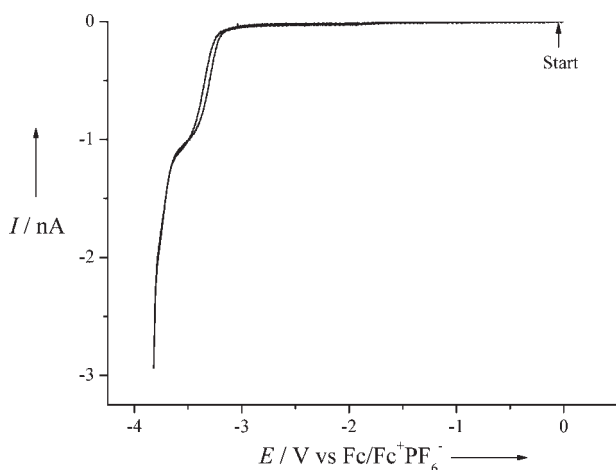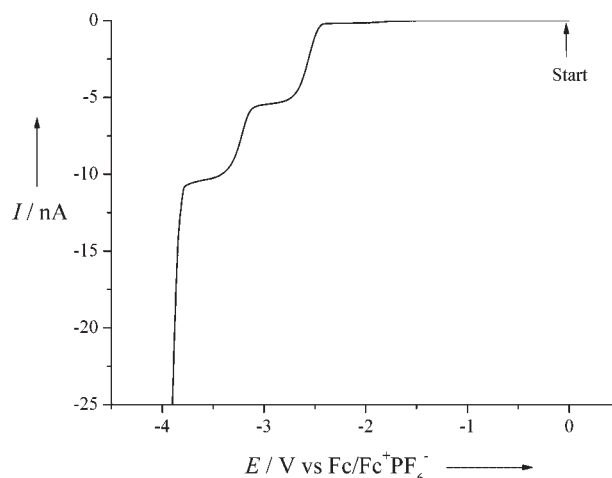

Figure 2. Voltammetric response of anthracene (3 mM) in THF (0.1 M TBAP) using a 12.5 μm (radius) platinum microelectrode recorded at a scan rate of 10 mV s^{-1} (at $-78\,^{\circ}$C)

Microdisk chronoamperometry[26] was used to simultaneously determine the number of electron(s) transferred, n, to each mediator and the diffusion coefficient, D in THF at $-78\,^{\circ}$C. The results are shown in Tables 1 and 2 for each mediator. DBB and naphthalene are $n = 1$ ET reagents (Table 1) while anthracene and 2,2′-dimethoxy-1,1′-binaphthyl, for example (Table 2), are $n = 2$ ET reagents.

It was hypothesized at this stage that the dianions in Table 2 were unable to act as mediators due to instability of the reactive intermediate towards protonation. Further investigations using CV at a macrodisk electrode were performed. Figure 4 shows the voltammogram for anthracene at $-78\,^{\circ}$C in THF (0.1 M TBAP). The first peak is electrochemically reversible ($E_{p} = -2.72$ V vs. Fc/Fc^{+}PF$_{6}^{-}$) while the second peak, as expected, was chemically irreversible ($E_{p} = -3.43$ V vs. Fc/Fc^{+}PF$_{6}^{-}$). These results suggested that the dianion was being

Figure 1. Voltammetric response of DBB (2.1 mM) in THF (0.1 M TBAP) using a 13 μm (radius) platinum microelectrode recorded at a scan rate of 10 mV s^{-1} (at $-78\,^{\circ}$C)
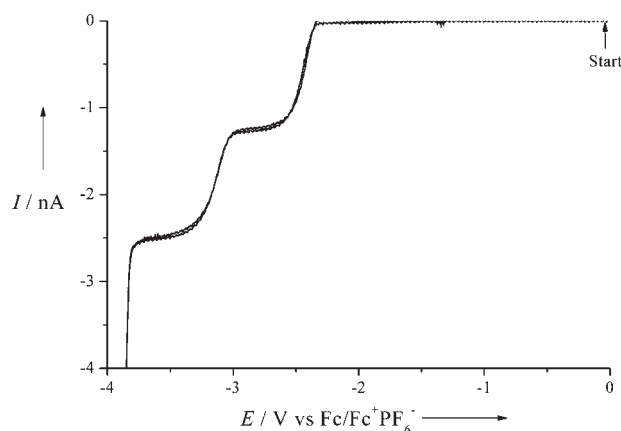

Figure 3. Voltammetric response of methyl naphthalene-1-carboxylate (3.3 mM) in THF (0.1 M TBAP) using a 5 μm (radius) platinum microelectrode recorded at a scan rate of 10 mV s^{-1} (at $-78\,^{\circ}$C)

protonated by the solvent and supported the results obtained from both the SET reactions where anthracene gave 9,10-dihydroanthracene as the only product (Table 2).

Steady-state voltammetry, cyclic voltammetry, and microdisk chronoamperometry of the organic substrates.

In order to compare fully the synthetic experiments electrochemically, the reduction of various organic substrates by electro-generated mediators was required and under the same experimental conditions (THF, $-78\,°C$). As above, the steady-state voltammetry of the iodide (*trans*-1-(3-iodopropoxy)-4-(methoxymethoxy)cyclohexane) (R-I), (*trans*-1-(3-bromopropoxy)-4-(methoxymethoxy)cyclohexane) (R-Br), and (*trans*-1-(3-chloropropoxy)-4-(methoxymethoxy)cyclohexane) (R-Cl) was recorded and is shown in Fig. 4. The order of ease of reduction was found to be: R-I > R-Br > R-Cl. The sulfide, phenyl 3-phenylpropylsulfide (RSPh) was also analyzed voltammetrically and the voltammogram recorded is shown in Fig. 5. The sulfide, [(3-{[*trans*-4-(methoxymethoxy)cyclohexyl]oxy}propyl)-thio]benzene (R′SPh) has been previously analyzed.[22] Table 3 summarizes the half-wave potential data and where applicable Tafel slope data are given. Finally, microdisk chronoamperometry was used to determine both n and D. For all of these organic substrates $n = 2$. For all of these compounds it can be observed that their reduction potentials are all $> -3.2\,V$ *versus* $Fc/Fc^+PF_6^-$ and so mediation using aromatic molecules at lower potentials is advantageous.

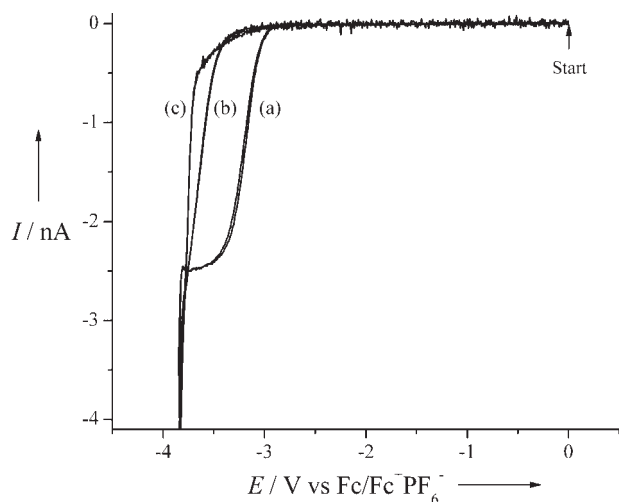Next, mediation by anthracene and coulometric experiments was required in order to confirm the theory

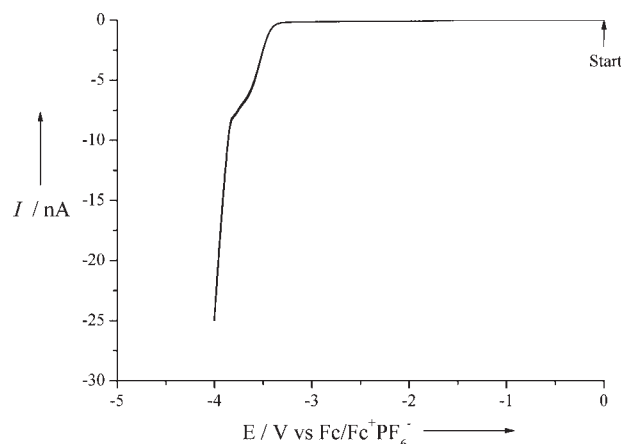**Figure 5.** Voltammetric response of phenyl 3-phenylpropylsulfide (8.2 mM) in THF (0.1 M TBAP), using a 5 µm (radius) platinum microelectrode and recorded at a scan rate of 10 mV s^{-1} ($-78\,°C$)

that radical anion mediators in THF ($-78\,°C$) are able to act as ET reagents in contrast to dianions which rapidly protonate. By using voltammetry, the potential at the working electrode can be controlled accurately and therefore an assessment of the anion and dianion separately can be made. Moreover, each organic substrate being an $n = 2$ species allows the possibility for different products based on direct *versus* mediated electrochemistry[19] to be obtained.

Mediated electrochemistry and simulations

Using a similar procedure to our work involving naphthalene as a mediator in THF ($-78\,°C$)[19] experiments involving the sulfide, phenyl 3-phenylpropylsulfide (RSPh) and anthracene as the mediator were

Figure 4. Voltammetric response of (a) *trans*-1-(3-iodopropoxy)-4-(methoxymethoxy)cyclohexane (R-I) (3 mM); (b) *trans*-1-(3-bromopropoxy)-4-(methoxymethoxy)cyclohexane (R-Br) (3 mM); and (c) *trans*-1-(3-chloropropoxy)-4-(methoxymethoxy)cyclohexane (R-Cl) (3 mM) in THF (0.1 M TBAP) using a 5 µm platinum electrode. Scan rate: 10 mV s^{-1} ($-78\,°C$)
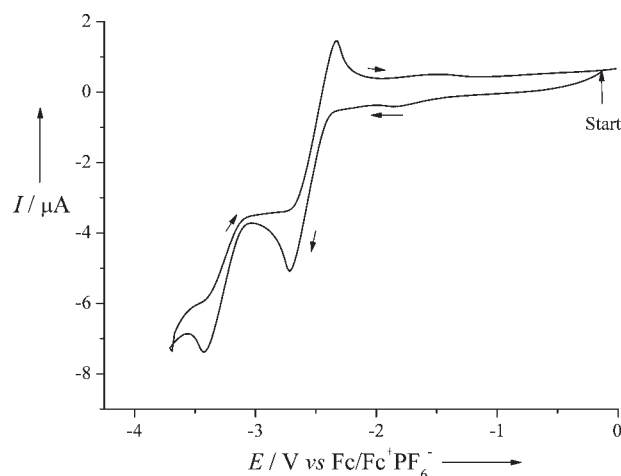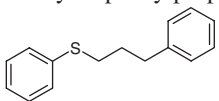
Figure 6. Cyclic voltammetry of anthracene (2.5 mM), at $-78\,°C$ in THF (0.1 M TBAP) using a platinum electrode (1 mm) recorded at a scan rate of 250 mV s^{-1}

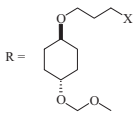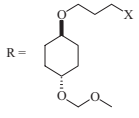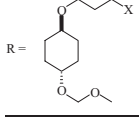**Table 3.** Organic substrates used in electrochemical analyses: Electrochemical parameters obtained from voltammetric experiments performed at $-78\,°C$

ET reagent	$E_{1/2}$ (V) *versus* Fc/Fc$^+$PF$_6^-$	n	$D \times 10^{-10}$ (m^2 s^{-1})	Tafel value (mV)
Phenyl 3-phenylpropyl sulfide	-3.53	2 ± 0.3	3.6 ± 0.2	128
R-I	-3.25	2 ± 0.2	2.0 ± 0.1	207
R-Br	-3.6	2 ± 0.3	2.1 ± 0.2	—
R-Cl	-3.7	2 ± 0.2	1.9 ± 0.3	—

performed. If our theory above was correct, then the first wave should mediate whereas the second wave would not. The steady-state voltammetry for anthracene with and without RSPh (at various concentrations) in THF ($-78\,°C$) is shown in Fig. 7(A). It was observed that the wave height ($E_{1/2} = -2.47$ V *vs*. Fc/Fc$^+$PF$_6^-$) corresponding to the first ET increased upon additions of the sulfide. These data are recorded in Table 4. In an analogous experiment the mediation was performed at $-50\,°C$ in THF and the results are shown in Fig. 7(B). As for the $-78\,°C$ case, the wave increased upon addition of the sulfide (Table 4).

If the proposed mechanism for the mediated ET follows the well-established electrochemical EC mechanism, it may be successfully simulated by DIGISIM software. The data used in the simulations (as for previous investigations using naphthalene)[19] were obtained from the electrochemical analyses described above: $E_{1/2}$, n, c, and D values (Tables 2 and 3). For the $-50\,°C$ simulations, the diffusion coefficient, D, for anthracene was determined from the limiting current at a given temperature on the steady-state voltammogram of anthracene reduction using $I_{lim} = 4nFDrc$, where I_{lim} is the limiting current, F is Faraday's constant ($96\,485$ C mol^{-1}), r the electrode radius, and c the concentration. D for the sulfide was determined by calculating the activation energy, E_a, for diffusion from a plot of $\ln I_{lim}$ *vs*. $1/T$ at a range of temperatures followed by an Arrhenius-type calculation

to obtain D at $-50\,°C$. Using these parameters, which also included the radius r of the electrode ($5\,\mu$m), initial concentrations of species (1 mM anthracene, fixed initial concentration RSPh), temperature T ($-78\,°C$, $-50\,°C$), transfer coefficient α values of 0.5, and scan rate v equal to that of the experimental scan rate, simulations were performed in order to obtain the kinetic parameters: k_s and k_f (heterogeneous and homogenous rate constants, respectively). The fits obtained at -78 and $-50\,°C$ are shown in Fig. 8(A) and 8(B), respectively.

From these simulations, k_s and k_f values of *ca*. 1 cm s^{-1} and 60 L mol^{-1} s^{-1} were obtained for mediation by anthracene at $-78\,°C$. At $-50\,°C$, k_s and k_f values of 1 cm s^{-1} and 100 L mol^{-1} s^{-1} were determined. The limiting currents obtained by simulations are shown in Table 4 and show excellent agreement to those obtained experimentally. At higher temperatures, mediation was not observed and no catalytic increases in the current wave height were observed.

Coulometric experiments

To support the simulation and synthetic evidence that anthracene mediates as the monoanion but not as the dianion a number of electrolyses were performed.

Phenyl 3-propylsulfide (RSPh) was reduced in the presence of anthracene on a preparatory scale using
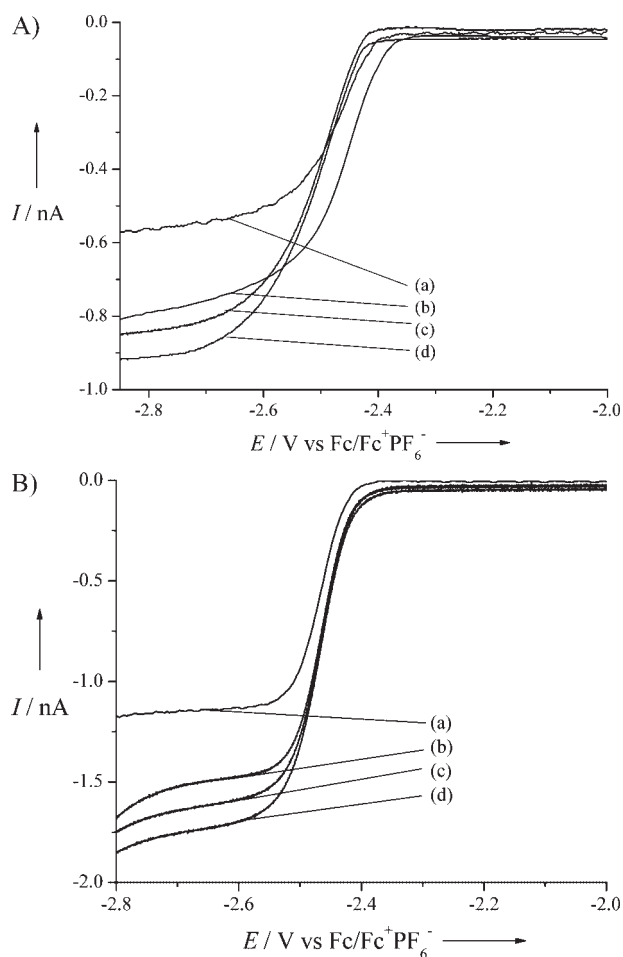
Figure 7. A: Voltammetric response of (a) anthracene (1 mM) in THF (0.1 M TBAP), using a 5 μm (radius) platinum microelectrode recorded at a scan rate of 10 mV s^{-1} and with phenyl 3-phenylpropylsulfide (b) 12 mM (5 mV s^{-1}), (c) 16 mM (2 mV s^{-1}), and (d) 31 mM (2 mV s^{-1}) at −78 °C. B: Voltammetric response of (a) anthracene (1 mM) in THF (0.1 M TBAP), using a 5 μm (radius) platinum microelectrode recorded at a scan rate of 10 mV s^{-1} and with phenyl 3-phenylpropylsulfide (b) 9.4 mM (5 mV s^{-1}) (c) 18.3 mM (5 mV s^{-1}), and (d) 26.8 mM (5 mV s^{-1}) at −50 °C
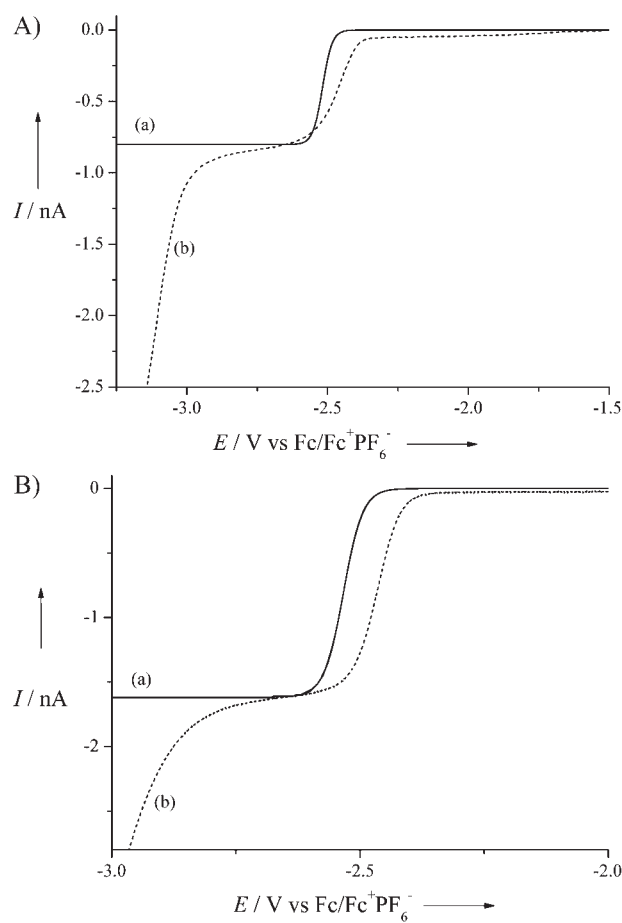

Figure 8. A: Overlay of (a) the theoretical simulation result (solid line) with (b) (dashed line) the RSPh response (23 mM, scan rate 5 mV s^{-1}, 5.0 μm (radius)). Parameters used for the simulations were as follows: $T = -78\,^\circ$C, $\alpha = 0.5$, $D_{\text{anthracene}} = 2.9 \times 10^{-6}$ cm^2 s^{-1}, $D_{\text{RSPh}} = 3.6 \times 10^{-6}$ cm^2 s^{-1}, $k_{\text{s}} = 1$ cm s^{-1}, $k_{\text{f}} = 60$ L mol^{-1} s^{-1}. B: Overlay of (a) the theoretical simulation result (solid line) with (b) (dashed line) the RSPh response (18 mM, scan rate 5 mV s^{-1}, 5.0 μm (radius)). Parameters used for the simulations were as follows: $T = -50\,^\circ$C, $\alpha = 0.5$, $D_{\text{anthracene}} = 5.7 \times 10^{-6}$ cm^2 s^{-1}, $D_{\text{RSPh}} = 8 \times 10^{-6}$ cm^2 s^{-1}, $k_{\text{s}} = 1$ cm s^{-1}, $k_{\text{f}} = 95$ L mol^{-1} s^{-1}

Table 4. Comparison of limiting currents observed at different temperatures and concentrations of RSPh with simulated currents

Temperature (K)	k_{f} (L mol^{-1} s^{-1})	[RSPh] (mM)	I_{lim} (experimental) (nA)	I_{lim} (simulated) (nA)
−78 °C	60	0	0.58	0.58
		12.01	0.67	0.73
		16.12	0.75	0.76
		23.16	0.82	0.80
		30.79	0.84	0.84
−50 °C	95	0	1.13	1.13
		9.37	1.48	1.48
		18.3	1.61	1.62
		26.83	1.73	1.72
		34.94	1.79	1.81

Table 5. Controlled-potential, bulk electrolyses in THF (0.1 M) at $-78\,^{\circ}$C

Starting material	Mediator	Number of electron(s), n	Potential *versus* Fc/Fc$^+$PF$_6^-$ (V)	Product(s) isolated
Phenyl 3-phenylpropylsulfide (RSPh)	Anthracene	1	-2.7	Phenyl disulfide (PhS-SPh)[a]
RSPh	Anthracene	2	-3.5	No reduction
Anthracene	None	2	-3.3V	9,10-Dihydroanthracene
RSPh	None	2	-3.7	Thiophenol; propylbenzene (PhSH; Ph(CH$_2$)CH$_3$)[a]
trans-1-(3-Iodopropoxy)-4-(methoxymethoxy)cyclohexane (R-I)	None	2	-3.2	*trans*-1-(Methoxymethoxy)-4-propoxycyclohexane (R-H)[a]

Products isolated.
[a] Characterization of PhS-SPh and RH has been described previously.[19,30]

controlled-potential electrolysis. For electro-generation of the radical anion of anthracene the potential was held at -2.7 V (*vs*. Fc/Fc$^+$PF$_6^-$) (Table 2). Notably, this value is lower than the value for the direct reduction of the sulfide, Table 3. The results of the electrolysis are shown in Table 5. The indirect reduction of RSPh gave the product diphenyl disulfide (PhS-SPh) as obtained using naphthalene[19] as the mediator and distinct from the thiol which is obtained from direct reductions of the sulfide, RSPh (Table 5).

Following this, a second electrolysis was performed whereby the potential was held constant at -3.7 V (*vs*. Fc/Fc$^+$PF$_6^-$) corresponding to the formation of the dianion of anthracene. No reduction products were obtained from this experiment.

Finally, the potential of a solution of anthracene only was held constant at -3.7 V (*vs*. Fc/Fc$^+$PF$_6^-$). The results are shown in Table 5. The formation of 9,10-dihydroanthracene was evident with the protons likely to be coming from both the supporting electrolyte and solvent. These data support our finding above in that the dianion is too reactive within the timescale required for mediation, whereas the radical anion is stabilized to some extent by the lower temperature, enough to mediate.

The SET reactions were repeated using the iodide and sulfides listed in Tables 1–3 using a stoichiometric amount of lithium. The results showed that, although not a high percentage yield of reduced product, anthracene and 2,2′-dimethoxy-1,1′-binaphthyl, for example, can mediate at the monoanion level.

CONCLUSIONS

We posed three questions at the outset of this paper. First, what makes a mediator effective as a reducing reagent? Second, is it possible to 'selectively' mediate with either (a) a monoanion or (b) a dianion to yield, for example, a monomeric or dimeric product, respectively. Third, how does a synthetic-mediated ET reaction compare to that of

a direct electrochemical reaction whereby the electrode serves as the electron source?

First, in regard to the behavior of the different mediators, naphthalene and DBB are known to be by far the most effective mediators. Table 1 shows that the radical anions of these species are thermodynamically more powerful reducing reagents than the aromatic arenes of all the other mediators investigated as shown by their formal potentials (Tables 1 and 2). It is likely that this is a reason for their greater effectiveness. Second, the use of a dianion to bring about a mediated two-electron process appears to be synthetically of no use since the dianions are much more basic species than the monoanion, so that attempts at mediation at the dianion level result in the abstraction of protons from the solvent in preference to the reduction. Third, direct electroreduction of iodides and sulfides is a two-electron process, contrasting to the one ET seen using mediators. This complementarity of direct and mediated reduction is a potentially useful synthetic strategy.

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