Electrochemical Reduction of Activated Olefins in Deuteriated Solvents. II. A Regioselective Deuteriation Catalytic Process from α,β-Ethylene Aryl Sulfones

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Dedicated to Professor Lennart Eberson on the occasion of his 65th birthday


The title compounds were electrochemically reduced in aprotic dimethyl sulfoxide-d6, acetone-d6 or organic solvents containing heavy water. When a catalytic amount of charge passed through the cell, α-deuteriation of olefins occurred in high yield. Since both chemical and electrochemically formed bases were found to be totally inefficient in the performance of such deuteriation, a radical chain process is tentatively proposed. During attempted total reduction of substrates, tetradeuteriated dimers were isolated, from which information on the reduction mode and coupling process can be obtained.

The electrochemical reactivity of sulfones and sulfoxides is now a rather well documented field. More specifically, cathodic coupling and electrocatalytic electrodimerization of α,β-ethylenic sulfones in aprotic solvents have been achieved. With regard to the cathodic behaviour of α,β-ethylenic sulfoxides 1, it has recently been shown that ‘activation by means of electron transfer’ in deuterated solvents (DS) such as dimethyl sulfoxide-d6 (DMSO) and acetone-d6 (AN) leads quantitatively to α-mondeuteriated compounds according to the following eqn. (1).

The aim of the present paper is to study similarly the cathodic behaviour of α,β-ethylenic sulfones 2 and 3 both in deuteriated solvents and in DMSO with heavy water added, in order to check whether deuteriation, already found with sulfoxides 1, was also relevant to the behaviour of unsaturated sulfones.

Experimental

Sulfones synthesis. The synthesis of sulfones 2H and 3H is fully described in the literature: sulfone 2H was prepared according to Ref. 5, sulfone 3aH according to Ref. 6 and substrate 3b–eH according to Ref. 7. 1H NMR spectra were recorded on a JEOL GSX 270 WB (270 MHz) in CDCl3 or CD2Cl2 with Me4Si as an internal reference. Mass spectra were obtained with a Varian MAT 311 spectrometer.

Ar–SO2–CH=CH2

2H

Ar=phenyl

p–CH3–C6H4SO2–CH=CH–Ar

3H

a Ar=phenyl
b Ar=2-phenyl
c Ar=2-naphthyl
da Ar=9-anthryl
e Ar=4-Cl–C6H4

Electrolytes. DMF and DMSO were distilled and kept over molecular sieves 3 Å. DMSO-d6 (99.8%), AN-d5 (99.8%) and D2O (100%) were purchased from Solvents-

ArSO–CH=CHR → ArSO–CD=CHR

Cathodic activation [??0.1 F mol–1]

DS-tetraalkylammonium salt

(1)

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Documentation—Syntheses’ (SDS). Salts such as Et₂NClO₄ (TEAP) and Bu₄NBF₄ (TRATFB) were easily prepared; they were recrystallized from water and then dried under vacuum. LiClO₄ (95%) was bought from Aldrich and used without further purification.

Voltammetry. Current–voltage curves were obtained by use of a PAR model 362 potentiostat equipped with a X-Y Kipp–Zonen recorder. The three electrode Metrohm cell was furnished with a hanging mercury drop as working electrode (cathode), a counter electrode made of platinum (Pt wire or gauze) and a reference system: Ag/AgCl|KCl 0.1 M in DMF. This reference was the only one used throughout the described work.

Coulometry and macroelectrolysis. Potentiostatic electrolyses were achieved in a two-compartment Metrohm cell (separator: glass frit of porosity 5). The working electrode was a mercury pool (area: ca. 10 cm²), the counter electrode being a platinum gauze. The electrolysis cell was connected to a Tacussel PRT 40–1X potentiostat equipped with a Tacussel I5G5-LN integrator.

Work-up and purification. At the end of the electrolyses conducted in deuteriated solvents (DMSO-d₆ and AN-d₁) the products were not isolated; results given in Table 2 correspond to ¹H NMR analysis achieved directly from electrolytic solution. In contrast, when heavy water was used as the deuteron donor (by addition to DMSO), the typical procedure was as follows: 1 g of 3H was dissolved in 40 ml of DMSO containing 0.1 M LiClO₄ and 2 ml D₂O. The working electrode was, in all cases, a stirred mercury pool (area: 10 cm²). Applied working potentials are all listed in Table 3. Experimentally, electrolyses were stopped when 0.1 F mol⁻¹ of sulfone had passed. Afterwards, the catholyte solution was extracted with methylene chloride and then washed with water. Dried extracts were chromatographed on silica gel (Merck 60 H) using cyclohexane-ethyl acetate as the eluent for products 3D, and methylene chloride-ethyl acetate mixture for dimers 4D according to the product solubility.

Results of electrolyses. (A) Electrochemical activation. 2H reduced at 0.1 F mol⁻¹ in CD₃CN or DMSO-d₆ to give (1-deuterioethenyl)phenyl sulfone 2-d₁, lit.⁸

3H gave (E)-4-methylphenyl 1-deutério-2-phenyl-ethenyl sulfone 3aD, m.p. (isopropyl ether) 120 °C. ¹H NMR: δ 2.40 (s, 3 H), 7.20 (d, 2 H, J=8.2 Hz), 7.26 (m, 3 H), 7.33 (dd, 2 H, J=7.5 Hz), 7.62 (t, 1 H, J=2 Hz), 7.82 (d, 2 H, J=8.2 Hz).

3H gave (E)-4-methylphenyl 1-deutério-2-(2-pyridyl)-ethenyl sulfone 3bD, m.p. (isopropyl ether) 100 °C. ¹H NMR: δ 2.40 (s, 3 H), 7.20 (d, 2 H, J=8.2 Hz), 7.30–7.50 (m, 3 H), 7.70 (t, 1 H, J=2 Hz), 7.90 (d, 2 H, J=8.2 Hz), 8.60 (dd, 1 H, J=8 Hz, pyridyl).

3H gave (E)-4-methylphenyl 1-deutério-2-(2-naphthyl)ethenyl sulfone 3cD, m.p. (ethanol) 160 °C. ¹H NMR: δ 2.40 (s, 3 H), 7.35 (d, 2 H, J=8.2 Hz), 7.55–7.65 (m, 7 H, naphthyl). 7.80 (t, 1 H, J=2 Hz), 7.9 (d, 2 H, J=8.2 Hz).

3H gave (E)-4-methylphenyl 1-deutério-2-(2-anthryl)-ethenyl sulfone 3D, m.p. (ethanol) 171 °C. ¹H NMR: δ 2.40 (s, 3 H), 7.30–7.60 (m, 7 H), 7.90–8.10 (m, 5 H), 8.40 (s, 1 H, H₁₀ anthryl), 8.60 (t, 1 H, J=2 Hz).

3H gave (E)-4-methylphenyl 1-deutério-2-(4-chlorophenyl)ethenyl sulfone 3D, m.p. (ethanol) 150 °C. ¹H NMR: δ 2.40 (s, 3 H), 6.67 (t, 1 H, J=2 Hz), 7.30 (d, 2 H, J=8.2 Hz), 7.50 (s, 4 H, chlorophenyl), 7.9 (d, 2 H, J=8.2 Hz).

(B) Exhaustive reduction of 3aH. Hydrodimer (±)-4aD, m.p. (ethanol) 172 °C. ¹H NMR: δ 2.40 (s, 6 H), 3.78 (s, 2 H, C₃H₂CH), 6.65 (dd, 4 H, J=7.5 Hz), 7.03–7.16 (m, 6 H), 7.22 (d, 4 H, J=8.2 Hz), 7.58 (d, 4 H, J=8.2 Hz). MS: m/z 416 (M–C₅H₅–CH–CD₂), 261 (M/2).

Hydrodimer novo-4aD, m.p. (CHCl₃) 297 °C. ¹H NMR (CD₂Cl₂): δ 2.35 (s, 6 H), 3.15 (s, 2 H), 6.95 (dd, 4 H, J=7.5 Hz), 7.12 (d, 4 H, J=8.2 Hz), 7.27 (m, 10 H). MS: m/z 367 (M–H₃C–C₅H₂–SO₂), 261 (M/2).

Results

Sulfones 2H and 3H are readily reducible at a mercury cathode, especially when conventional aprotic solvents containing tetraalkylammonium salts are used. Substrates 3H generally exhibit at least three steps (see Table 1). The two first steps are monoelectronic (consecutive formation of the anion radical – reversible step at a sweep rate v≥0.5 V s⁻¹ – and of the dianion – irreversible peak as depicted in Fig. 1). When a proton donor like phenol was added to excess in the solution, two main reduction steps were observed, the first one accounting for the two-electron cleavage of the C–S bond, and the second for the bielectronic saturation of the transient olefin.

The electrochemical behaviour of sulfone 2H has already been discussed elsewhere and was found to correspond to a very fast [2⁺2] cyclodimerization catalyzed at the level of the anion radical by electron transfer. Therefore, the electrochemical step (low sweep rates) does not account for the ethylenic sulfone but for its cyclodimer.

There was no change in the voltammetric behaviour of sulfones 2H and 3H when deuteriated solvents were used instead of more conventional aprotic solvent/electrolyte couples. However, some discrepancies were observed when macroelectrolyses were stopped when a very limited amount of electricity (i.e., 0.1 mol of electrons per mole of sulfone) had passed through the cell. Thus with sulfone 2H, electrolysis results in DMSO-d₆ and AN-d₁ are gathered in Table 2. In deuteriated acetonitrile containing tetraalkylammonium salt, deuteriation of 2H occurred but in moderate yields. In contrast when DMSO-d₆ containing lithium perchlorate was used, deuteration was not observed but previously reported
Table 1. Voltammetry of some unsaturated sulfones 3H and 3D (concentration: $2 \times 10^{-3}$ M) in aprotic (DMF containing 0.1 M Bu$_4$NBF$_4$) and protic (addition of phenol) media. Mercury microelectrodes. Sweep rate: 100 mV s$^{-1}$. Reference: Ag/AgI/1$^{-}$0.1 M–DMF. N.B.: in the presence of 5% water or 5% D$_2$O, no significant change in peak potentials toward values found for aprotic solvent was found.

| Substrates | Aprotic solvent | | Protic solvent | |
|-----------|----------------|-----------------|-----------------|
|           | $E_1$/V | $E_2$/V | $E_3$/V | $E’$/V | $E_1$/V | $E_2$/V |
| 3aH (Z) | −1.29 (1e) | −1.87 (1e) | −2.06 | −1.26 | −1.17 (2e) | −2.03 (2e) |
| 3aH (E) | −1.31 (1e) | −1.91 (1e) | −2.10 | −1.28 | −1.22 (2e) | −2.02 (2e) |
| 3bH     | −1.10 (1e) | −1.85 (1e) | −2.01 | −1.07 | −1.19 (2e) | −2.02 (2e) |
| 3aD (E) | −1.25 (1e) | −1.82 (1e) | 2.04 | −1.22 | −1.05 (2e) | −1.76 (2e) |
| 3bD     | −1.08 (1e) | −1.57 (1e) | −1.81 | −1.05 | −1.12 (2e) | −1.72 (2e) |
| 3cD     | −1.16 (1e) | −1.55 (1e) | −1.82 | −1.13 | −1.12 (2e) | −1.72 (2e) |

Fig. 1. Cyclic voltammetry of 3aH (E) and 3aD (E) at a stationary mercury microelectrode. Reference electrode: Ag/AgI/1$^{-}$0.1 M. Electrolyte: DMF–0.1 M Bu$_4$NBF$_4$; (A1) and (A2) for compound 3aH (E) ($2 \times 10^{-3}$ M); (B1) and (B2) for compound 3aD (E) ($2 \times 10^{-3}$ M). (A1) and (B1) sweep rate: 0.1 V s$^{-1}$, (A2) and (B2) sweep rate: 0.5 V s$^{-1}$. ⬤, in aprotic solution. ⬤⬤, in a solution containing $4 \times 10^{-3}$ M phenol.

cyclodimerization was found to occur in quantitative yield.

With sulfones 3H, the deuteration reaction could not be specifically achieved in only deuterated solvents. When stopped after a small amount of electricity had been consumed, macroelectrolysis of 3H with (Z + E) mixtures in DMSO or DMF, showed the total disappearance of the Z isomer due to the cathodic conversion of Z into E as already described for a number of olefins.$^{9–11}$ Deuteration was found to occur in high yield (Table 3) only when macroelectrolytic activation of sulfones 3H (on either the starting isomer) was accomplished in DMSO containing an amount (5%) of heavy water (D$_2$O) in addition to the supporting electrolyte. The regioselectivity of the deuteration reaction appeared to be very good. Moreover, the E isomer was always the only isolated isomer after cathodic treatment of all tested sulfones 3H. In addition, results with sulfone 3D (Table 1, Figs. 1 and 2) showed very similar behaviour with the parent protonated sulfones 3H. It is worth noting, however, that a clear potential shift towards less negative values was found for the first reduction step.

When 3aH was reduced (potentiostatic exhaustive reduction in this case) in DMSO with 5% D$_2$O added,
### Table 2. Cathodic activation with sulfone 2H in deuteriated solvents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate concentration</th>
<th>Solvent (Electrolyte)</th>
<th>Working potential(^a) /V</th>
<th>Electrical consumption / F mol(^{-1})</th>
<th>Products</th>
</tr>
</thead>
</table>
| 1     | 5 × 10\(^{-2}\) M        | CD\(_3\)CN (Bu\(_4\)NBF\(_4\) 0.1 M) | −1.4                        | 0.1                                    | C\(_6\)H\(_6\)-SO\(_2\)-CD=CH\(_2\) 45%  
C\(_6\)H\(_5\)-SO\(_2\)-CH=CH\(_2\) 55% |
| 2     | 5 × 10\(^{-2}\) M        | CD\(_3\)SO\(_3\)D (LiClO\(_4\) 0.1 M) | −1.4                        | 0.1                                    | 95%      |

\(^a\)Reference electrode Ag/Agl\(^+\)/1\(^-\) 0.1 M – DMF.

### Table 3. Electrolys of α,β-ethylenic sulfones 3H in DMSO–0.1 M LiClO\(_4\) with 5% D\(_2\)O added. The electrolyses were stopped after 0.1 F mol\(^{-1}\) of electricity had passed; two-compartment cell; mercury pool cathode (area: 10 cm\(^2\)).

<table>
<thead>
<tr>
<th>Starting sulfone (isomer)</th>
<th>Working potential(^a) /V</th>
<th>Product deuteriated sulfones 3D</th>
<th>Isolated yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3aH (E+Z or E)</td>
<td>−1.15</td>
<td>3aD</td>
<td>95 (E)</td>
</tr>
<tr>
<td>3bH (E)</td>
<td>−0.95</td>
<td>3bD</td>
<td>97 (E)</td>
</tr>
<tr>
<td>3cH (E)</td>
<td>−1.00</td>
<td>3cD</td>
<td>97 (E)</td>
</tr>
<tr>
<td>3dH (E)</td>
<td>−0.90</td>
<td>3dD</td>
<td>85 (E)</td>
</tr>
<tr>
<td>3eH (E)</td>
<td>−1.05</td>
<td>3eD</td>
<td>95 (E)</td>
</tr>
</tbody>
</table>

\(^a\)Reference electrode: Ag–Agl\(^+\)/1\(^-\) 0.1 M in DMF.

The total consumption of electricity was 1.1 F mol\(^{-1}\). Two compounds 4aD were isolated (crystallization from chloroform and ethanol). They were identified as the (+)-dimer (75% of isolated yield) and meso dimer (5%). The stereochemistry of each isomer was established by comparison with fully protonated analogues (+) meso and (+)-4aH as described in a previous paper.\(^3\)

Finally, it was checked that the reduction of 3aD in DMSO + 5% D\(_2\)O (coulometric measurement: 1.05 F mol\(^{-1}\) produced dimers 4aD [(±)-meso in mixture ratio: 90:10].

### Discussion

The cathodic activation and exhaustive reduction of compounds 2H and 3H have already been fully investigated.\(^{12}\) Series 2H was found (probably for structural reasons) to undergo catalytically unexpected cathodic
cycloaddimerization, often in very high yield and under very simple experimental conditions. In contrast, compounds 3H, when principally reduced in DMSO–LiClO₄, produced only acyclic dimeric forms [with a very large proportion of (±)-isomer]. Such a coupling reaction seemed surprising because previous work with α,β-ethylenic sulfoxides under similar experimental conditions resulted mostly in the cleavage of the C–S bond, by means of a β-elimination (E-protonation–E-elimination process).

\[
\begin{align*}
\text{Ar}^+\text{SO}_2\text{CH}=\text{CH}^+\text{Ar}^2 & \rightarrow \text{Ar}^+\text{SO}_2\text{CH}OH\text{CH}^+\text{Ar}^2 \\
\text{Ar}^+\text{SO}_2\text{CH}OH\text{CH}^+\text{Ar}^2 & \rightarrow \text{dimeric products (± mixture)} \\
& \rightarrow \text{Ar}^+\text{SO}_2\text{CH}=\text{CH}^+\text{Ar}^2 \\
& \rightarrow \text{s (fast)} \\
& \rightarrow \text{Ar}^+\text{SO}_2\text{CH}OH\text{CH}=\text{CH}^+\text{Ar}^2 \\
& \rightarrow \text{Ar}^+\text{SO}_2\text{CH}=\text{CH}^-\text{Ar}^2 \\
& \rightarrow \text{Ar}^+\text{SO}_2^- + \text{CH}_2OH\text{CH}^-\text{Ar}^2 \\
\end{align*}
\]

Scheme 1.

The present work also demonstrates that deuteration reactions achieved electrochemically with α,β-ethylenic sulfoxides, could also be applied to the parent sulfoxides by using specific experimental conditions.

The most suitable conditions for a substitution of this kind were shown to be DMSO + 0.1 M LiClO₄ with 5% D₂O added. However, the use of tetrabutylammonium tetrafluoroborate also led to deuteration. Whatever the stereochemistry of the starting material, regioselective deuteration could occur in very good yield, leading exclusively to E isomer. Note that the synthesis of such deuteriated sulfoxides (i.e., phenyl 1-deutero-2-phenylethenyl sulfoxide) has been mentioned in the literature from a more complicated reaction pathway.

What kind of mechanism could explain this deuteration process? It should be recalled first that methyl aryl sulfoxides are very weakly acidic. It is then expected that vinylc and styryl sulfoxides can react specifically with very strong bases. With sulfoxides such as 3H in particular, a base-catalysis process could be assumed. In fact, the formation at low temperature of lithium salts 3Li, which are able to react regioselectively with many kinds of electrophiles (like D₂O), has been described. More particularly at the cathode interface, very small amounts of electrogenerated bases produced during the activation phase (low electricity consumption) might trigger hydrogen–deuterium exchange catalyst in compounds 3H. In order to check the possible effect of all kinds of bases, two series of experiments were run.

(i) With chemical bases (without current). A typical procedure to test the possible action of these bases is as follows: 26 mg of 3aH in 3 ml of DMSO–0.5 M LiClO₄ + 0.1 ml D₂O were reacted with strong bases such as tetrabutylammonium hydroxide (0.2 equiv.) or potassium tert-butoxide (0.2 equiv.). After 24 h at room temperature, absolutely no reaction with 3aH was noted (and especially no visible H–D exchange in the NMR spectrum).
(ii) With strong electrogenerated bases. The chosen pro-base was azobenzene (AZ). In dry DMSO, the first voltammetric step of azobenzene (formation of the anion radical) was not disturbed by addition of 3aH (E) in large excess (tenfold), meaning that base AZ is not strong enough to rapidly deprotonate styryl sulfones. Furthermore, no changes were observed when heavy water was added (first 2% and then 5%). In order to check the voltammetric data, macroelectrolyses were carefully carried out with 3aH (E) and 3eH as substrates according to the following procedure. Azobenzene (0.012 g, 0.06 mmol) was reduced in 4 ml DMSO + 0.1 M LiClO₄ + 0.2 ml D₂O in the presence of 0.1 g (about 0.4 mmol) of sulfone. The working potential of the mercury pool cathode (2 cm²) was fixed at −0.8 V (the level of the first step of AZ). After passage 0.1 F mol⁻¹, electrolysis was stopped. After extraction according to the usual work-up, ³H NMR analysis of both reaction products showed that neither sulfone suffered any chemical transformation.

Thus, it seems reasonable to assume that the key reaction, whatever the electrolyte cation present (Li⁺ or N⁺ Bu₄), is the neutralization of 3H anion radical by D₂O. In the presence of a large excess of heavy water, 3H would be hydrated similarly to most other anion radicals of compounds (such as aromatic compounds and activated olefins) with a suitable LUMO (see work by Savéant’s group¹ in this field). Deuteron–proton exchange might then occur at this level, based on the relative acid–base strength of 3H⁻ and 3D⁻ inside the heavy water shell as shown in Scheme 2, and followed by eqn. (2).

\[
(3D^-)_{\text{acid}} + 3H \rightleftharpoons 3D + (3H^-)_{\text{acid}}
\]  

(2)

Since voltammetric curves of compounds 3H did not present any significant discrepancies in the absence and the presence of heavy water, it seems reasonable that the propagation reaction is, in this case, rather slow and displaced toward the right-hand side by a change of solvation energy. Intrinsically, propagation should not occur since \(E_{3H} < E_{3D}\). It is recalled here (in contrast with sulfoxides) that the conditions under which sulfones undergo deuteration are with added D₂O, deuterated solvents being unable to bring about the exchange by themselves. Deuterated E-isomers were obtained in all cases whatever the structure of the starting compound. However, the fast transformation \(Z \rightarrow E\) via electron transfer (even in the absence of D₂O) has already been noted, and here the stereochemistry of deuteriated struc-

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References


16. The addition of D$_2$O to α-sulfonylvinylcubium derivatives has been also mentioned: Eisch, J. J. and Galle, J. E. J. Org. Chem. 44 (1978) 3279.

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