

The Influence of Solvent on the Mechanism and Stereochemistry of Electrohydrodimerization. The Reduction of Cinnamic Acid Esters in Methanol

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Dedicated to Professor Hans J. Schäfer on the occasion of his 60th birthday.

Fussing, I., Hammerich, O., Hussain, A., Nielsen, M. F., and Utley, J. H. P., 1998. The Influence of Solvent on the Mechanism and Stereochemistry of Electrohydrodimerization. The Reduction of Cinnamic Acid Esters in Methanol. – Acta Chem. Scand. 52: 328–337. © Acta Chemica Scandinavica 1998.

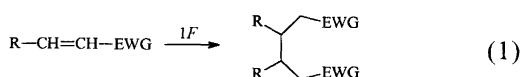
The kinetics and mechanisms of reactions following electrochemical reduction of members of a series of cinnamic acid esters, Ph-CH=CH-COOR, R=alkyl or aryl, in methanol (MeOH) have been studied. The results are compared with those previously obtained for reduction of the same compounds in *N,N*-dimethylformamide (DMF). The change from DMF to MeOH gives rise to important differences which are related to the higher acidity and the hydrogen-bond donating capabilities of MeOH. The changes include: (i) anodic shifts of the formal reduction potentials, in MeOH, by 80–130 mV; (ii) increased rates of reaction of the radical anions in MeOH by 2–3 orders of magnitude; (iii) in contrast with clean 1 F processes for the entire series in DMF, reduction in MeOH gave a 1 F process for the aryl cinnamates and a ≈ 1.5 F process for the alkyl cinnamates; (iv) the products of preparative scale reduction of methyl cinnamate in MeOH were a mixture of the saturated ester (2 F) and the *meso* and (\pm) isomers of the linear hydrodimer (1 F), whereas reduction in DMF gave exclusively the cyclized 1 F product, all-*trans*-2-methoxycarbonyl-3,4-diphenylcyclopentanone [corresponding to (\pm) coupling]; (v) the stereochemistry of the product of coupling changes from exclusively (\pm), in DMF, to equal amounts of *meso* and (\pm) in MeOH. The changes may be rationalized in a mechanism which crucially involves initial formation of a radical anion hydrogen-bonded (at the carbonyl oxygen) to MeOH. Linear sweep voltammetric experiments reveal an important dependence of reaction order upon the type of ester reduced, which is strong evidence of competition between dimerization of the hydrogen-bonded radical anion in a rate-determining second-order reaction (favored for the aryl esters) and rate-determining protonation in a first-order reaction of the carbonyl oxygen (favored for alkyl esters). It is also shown that the neutral radicals formed by protonation of the radical anions at oxygen are more difficult to reduce than the parent ester and may either dimerize (1 F) or tautomerize to the more easily reduced carbon protonated radical (2 F). The change in mechanism and stereoselectivity of electroreduction on going from DMF to MeOH electrolyte seems to be general for hydrodimerizations.

The electrohydrodimerization (EHD) of olefins activated by the presence of an electron-withdrawing group (EWG), such as -CN, -CHO, -COR, -COOH or -COOR, eqn. (1), is an important electrosynthetic reaction,^{1–3} the most spectacular example being the Monsanto process for the conversion of acrylonitrile

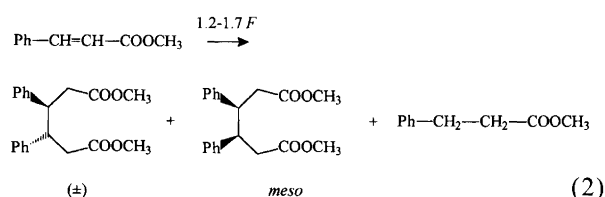
(R = H and EWG = CN) to adiponitrile in the production of Nylon 66.^{1,4,5}

Cinnamic acid and its derivatives (R = Ph and EWG = COOH, COOR or CONR₂) have been widely used for studies of synthetic, mechanistic and stereochemical aspects of the EHD process.^{6–23} Phenyl substitution at the position of coupling (C-3) means that both (\pm) and *meso* isomers may be formed. This is illustrated for the

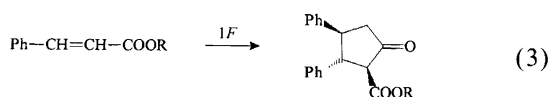
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electrochemical reduction of methyl cinnamate in methanol (MeOH), eqn. (2),²² the subject of the present paper. In addition to the (\pm) and *meso* isomers of dimethyl 3,4-diphenyladipate, which in MeOH are formed in a 1 F process with a ratio close to one, the product mixture also contains methyl 3-phenylpropionate resulting from saturation of the carbon-carbon double bond in a 2 F process. The overall consumption of charge is typically between 1.2 and 1.7 F.



In contrast, when the reduction of methyl cinnamate or other cinnamates is carried out in aprotic solvents, such as *N,N*-dimethylformamide (DMF), the initial coupling is followed by a cyclization of the Dieckmann-type leading, after work-up, to the corresponding 2-alkoxycarbonyl-3,4-diphenylcyclopentanones, eqn. (3).^{8,9,16-19,21-23} The yields from such 1 F reduction in DMF are often close to 100% and the reaction is highly stereoselective, giving^{16,23} exclusively the all-*trans* isomer corresponding to (\pm) coupling at C-3.

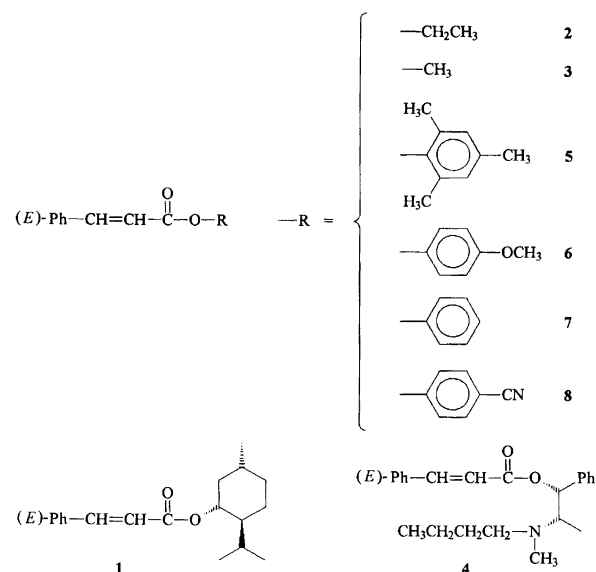


Thus, it is a feature of the coupling reaction of cinnamic acid esters that the (\pm) isomer is favored in aprotic solvents (e.g. DMF), whereas in hydroxylic solvents (e.g. MeOH), a nearly statistical distribution of (\pm) and *meso* isomers is found. This pattern is also a feature of the EHD reactions of other activated olefins.²⁴⁻³¹

Recently, we have reported on the kinetics and mechanism for the stereoselective coupling-cyclization reaction observed for the cinnamic acid esters in DMF,²³ eqn. (3). In the context of an apparently qualitative dependence of the course of these reactions in aprotic *vis-à-vis* hydroxylic solvents we now present the results from a study of the reduction in MeOH designed to elucidate the apparent differences in mechanism. This question has not previously been rigorously addressed. The experimental work concerns the electrochemical reduction of the eight esters, 1-8, shown in Scheme 1.

Results and discussion

Reductive coupling-cyclization in DMF. Initially it is useful to review briefly some of the kinetic and mechan-



Scheme 1.

istic aspects of the reductive coupling-cyclization of the cinnamic acid esters in DMF.²³

The results obtained by cyclic voltammetry (CV) and linear sweep voltammetry (LSV) at low voltage sweep rates (ν) in solvent containing a moderate concentration (0.28 M) of water were in agreement with a mechanism including the initial formation of the radical anion in a reversible one-electron transfer step followed by the essentially irreversible coupling of two radical anions. Typical voltammograms obtained for methyl cinnamate (3) and phenyl cinnamate (7) at $\nu = 1 \text{ V s}^{-1}$ are shown in Fig. 1. The reduction peak, R^1 , corresponds to the

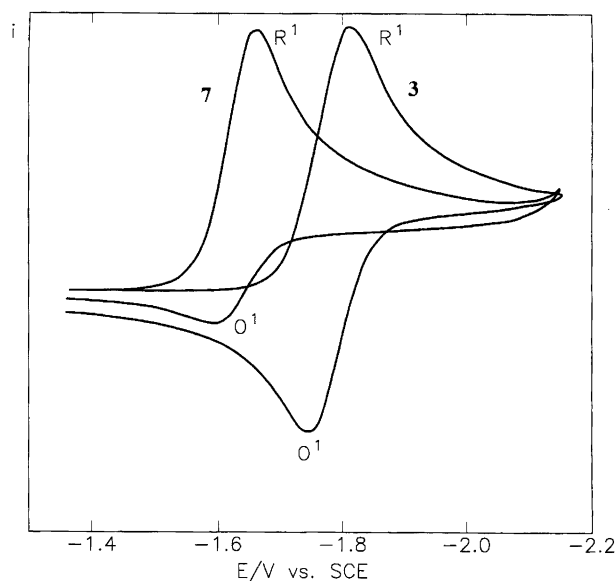
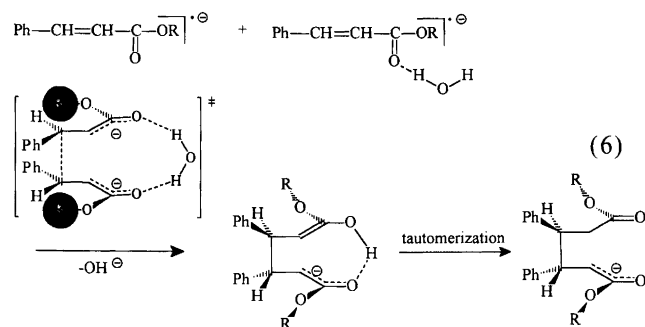
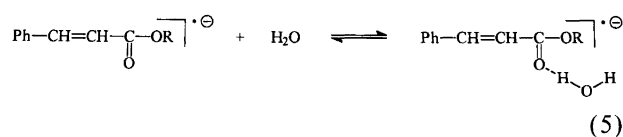


Fig. 1. Cyclic voltammograms of methyl cinnamate (3) and phenyl cinnamate (7) recorded in DMF- Et_4NBr (0.1 M) containing water (0.28 M) at an Hg working electrode; $C_A = 2 \text{ mM}$, $\nu = 1 \text{ V s}^{-1}$; $T = 295 \text{ K}$.

formation of the radical anion and current corresponding to the oxidation of the radical anion back to the starting material, O^1 , is clearly seen in both cases during the back sweep indicating that the rates of the coupling processes are only moderate.

The rate constants, k , for the coupling process varied between $4.1 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$ (*tert*-butyl cinnamate) and $5.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ (4-cyanophenyl cinnamate, **8**). By comparison of the two voltammograms in Fig. 1 it is seen also that the more reactive radical anion is that derived from the more easily reduced substrate, **7**. This relationship between the reactivity of the radical anion and the formal potential for the substrate–radical anion redox couple is a general feature of the reaction and a plot of $\log k$ vs. the formal potential, E° , for the substrate–radical anion redox couple was found to be linear with a slope of 7.2 V^{-1} . In agreement with earlier work^{10,11,15,32–34} it was observed also that the rate of the coupling process increased by increasing the concentration of water in the DMF. These and other results led to the proposal of a mechanism the early steps of which are shown as eqns. (4)–(6).



Stereochemically the role of water is to serve as a template that lowers the activation energy for coupling in the (\pm) fashion as illustrated by eqn. (6). Another stereochemical consequence of the proposed transition state is the interaction between the alcohol/phenol part of the ester and the phenyl substituents at C-3, which is believed to be the origin of the high enantioselectivity observed in several cases when R is a chiral auxiliary.²¹ An important mechanistic aspect of the coupling mechanism is the fast transfer of one of the hydrogen-bonded protons from water to a carbonyl oxygen in the dimeric dianion, eqn. (6). This causes the coupling process to be kinetically irreversible.

Cyclic voltammetry in MeOH. The cyclic voltammograms obtained for **3** and **7** in MeOH at $\nu = 50 \text{ V s}^{-1}$ are shown in Fig. 2. The most noteworthy feature of the two voltammograms, in comparison with those obtained in DMF (Fig. 1), is the total absence of oxidation current during the back sweep. Considering that the sweep rate applied is 50 times higher than that used for Fig. 1 it is evident that the rate of the chemical reaction following the initial electron transfer is much faster in MeOH than in DMF. Another observation of interest is that the reduction of **7** results in two closely spaced peaks, R^1 and R^3 , that have merged into one broad peak.

When the sweep rate is increased to 500 V s^{-1} (Fig. 3) a reverse current, O^1 , due to the reoxidation of the radical anion of **7** is clearly observed; reoxidation of the radical anion of **3** is barely visible. Thus, compared with DMF the order of reactivity of the radical anions in MeOH is reversed, that is, the more reactive radical anion is now that derived from the less easily reduced substrate, **3**. This feature in itself is sufficient to allow for the conclusion that the mechanism for the reaction in MeOH of at least one of the two radical anions differs from that in DMF. It is also seen that the merged peaks, R^1 and R^3 , observed for **7** at $\nu = 50 \text{ V s}^{-1}$ are now almost resolved in two separate reduction peaks, whereas a broad peak similar to that for **7** at $\nu = 50 \text{ V s}^{-1}$ is observed for **3**. The origin of R^3 , which is not observed during voltammetry in DMF (Fig. 1), will be discussed in a later section.

Constant current coulometry. The number of electrons exchanged per molecule of cinnamic acid ester in the time domain of a microscale preparative electrolysis was determined by constant current coulometry.³⁵ The decay

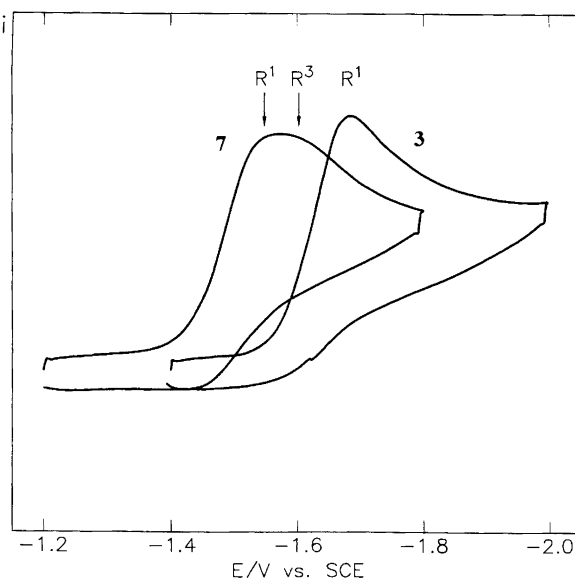


Fig. 2. Cyclic voltammograms of methyl cinnamate (**3**) and phenyl cinnamate (**7**) recorded in MeOH– Et_4NBr (0.1 M) at an Hg working electrode; $C_A^0 = 1 \text{ mM}$, $\nu = 50 \text{ V s}^{-1}$; $T = 295 \text{ K}$.

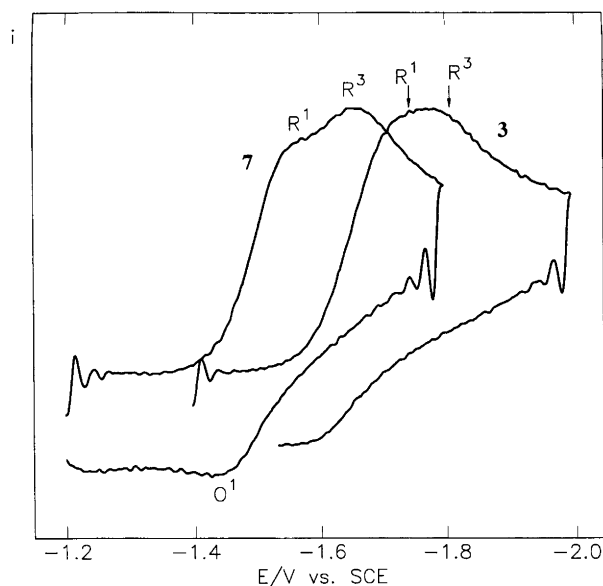


Fig. 3. Cyclic voltammograms of methyl cinnamate (**3**) and phenyl cinnamate (**7**) recorded in MeOH-Et₄NBr (0.1 M) at an Hg working electrode; $C_A = 1$ mM, $v = 500$ V s⁻¹; $T = 295$ K.

in concentration of substrate was monitored through measurements of the voltammetric peak current, i_p , as illustrated in Fig. 4A for the reduction of methyl cinnamate (**3**). It is seen that the concentration of **3** decays linearly with time and thus the time required for the complete conversion of **3** into products could be determined by extrapolation of i_p to $i = 0$. For compound **3** this procedure resulted in $n = 1.55$. This is considerably higher than the value of one observed in DMF and reflects most likely that 1 F and 2 F processes occur simultaneously in MeOH. Similar results were observed for the other alkyl cinnamates, **1**, **2** and **4**, and the 2,4,6-trimethylphenyl ester, **5** (Table 1).

Somewhat different behavior was observed for the three remaining aryl cinnamates, **6–8**, as illustrated in Fig. 4B by the coulometry for **7**. It is seen that after electrolysis for approximately 3 min a new reduction peak appears at a potential 120 mV negative of the peak for **7** and the intensity of the new peak was found to increase with electrolysis time. When the electrolysis was stopped after 7 min and the solution allowed to stand for 10 more min with the current interrupted, the height of the new peak increased further at the expense of that for **7** as seen by comparison of the two voltammograms labeled '7' and '7+10' in Fig. 4B. This shows that the product giving rise to the new peak is formed in a reaction that does not consume charge. The new peak was found to increase even further after addition of an authentic sample of **3** to the solution indicating that the product was methyl cinnamate, obviously formed by transesterification of the labile aryl ester³⁶ catalyzed by the base formed during the coulometric reduction. However, it is seen also that it required electrolysis for

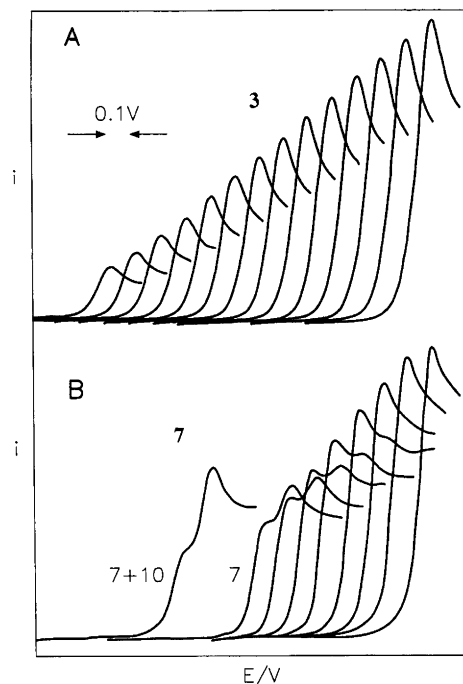


Fig. 4. Results from constant current coulometry for **3** (A) and **7** (B) in MeOH-Et₄NBr (0.1 M). The amount of substrate was 0.2 mmol and the current was 30 mA. The voltammograms were recorded at 1 min intervals, beginning at $t = 0$ min, and are, for clarity, displaced horizontally by a distance corresponding to 0.1 V for each minute. The voltammograms labeled '7' and '7+10', respectively, for the reduction of **7** were recorded after electrolysis for a total of 7 min ('7') after which the solution was allowed to stand for an additional 10 min without the passage of charge ('7+10').

Table 1. Coulometric n -values in MeOH and formal potentials, E° , in DMF and MeOH for the reduction of alkyl and aryl cinnamates, Ph-CH=CH-COOR.^a

R (Compound)	n	E° (DMF) ^b	E° (MeOH) ^c
Methyl (1)	1.50	-1.794	-1.683
Ethyl (2)	1.53	-1.789	-1.673
Methyl (3)	1.55	-1.778	-1.668
Bu(Me)NCH(Me)CHPh (4)	1.51	-1.767	-1.639
2,4,6-Trimethylphenyl (5)	1.2–1.4 ^d	-1.674 ^e	-1.566
4-Methoxyphenyl (6)	1.0–1.2 ^f	-1.654	-1.547
Phenyl (7)	0.95 ^g	-1.631	-1.524
4-Cyanophenyl (8)	0.93 ^g	-1.521	-1.438

^aIn solvent containing Et₄NBr (0.1 M). The formal potentials are given in V vs. SCE at $T = 295$ K. ^bFrom Ref. 23. ^cThis work; determined as the midpoint potential, $\frac{1}{2}(E_p^{\text{ox}} + E_p^{\text{red}})$, at $v = 1000$ V s⁻¹. ^dUncertain value owing to a slightly non-linear decay of the substrate concentration. ^eThis work. ^fUncertain value owing to merging reduction peaks for the substrate and the transesterification product (see the text). ^gValue obtained after approximately 20% conversion in order to minimize the effect of transesterification (see the text).

approximately 3 min before the base concentration was sufficient for the transesterification to proceed at a rate comparable to that for the coulometric experiment, and thus it was possible to determine the n -values for **6–8** by

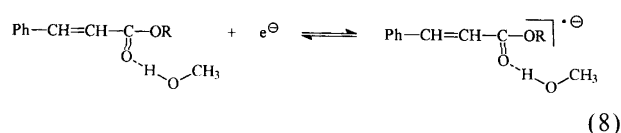
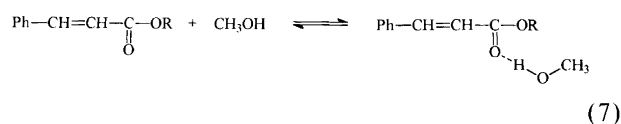
using data obtained at low conversion during the first approximately 3 min. For that reason the values obtained for these three compounds are less precise than those obtained for the other five cinnamates, but the precision is sufficient to conclude that n for all three compounds, **6–8**, is close to one (Table 1).

Products from the electrochemical reduction of methyl cinnamate in MeOH. The transesterification accompanying the electrochemical reduction of the cinnamic acid esters will obviously complicate the interpretation of the product distribution observed after preparative electrolysis and for that reason reduction on a preparative scale was studied only for methyl cinnamate, **3**. Several electrolyses were carried out at constant current as described in the Experimental section. In addition to unconverted starting material (5–20%) the major products were methyl 3-phenylpropionate (25–55%), resulting from saturation of the C–C double bond, and the two diastereomeric forms of the hydrodimer, dimethyl 3,4-diphenyladipate (total yield 22–53%), with the (\pm)-to-*meso* ratio being close to one. There was no indication of the formation of the cyclic product, eqn. (3), observed when the electrolysis was carried out in DMF.

Formal potentials for the substrate–radical anion redox couple in MeOH. The formal potentials, E° , for the substrate–radical anion redox couples were recorded at $\nu = 1000 \text{ V s}^{-1}$ as the average of the peak potentials, E_p^{red} and E_p^{ox} , corresponding to R^1 and O^1 . The results are summarized in Table 1 together with the corresponding values obtained in DMF. The observed dependence of E° on the alcohol/phenol part of the esters observed in both solvents may obviously be rationalized in terms of the electron-withdrawing properties of R, that is, the more electron-withdrawing R results in the more easily reduced substrate. It is seen also that the cinnamates are easier to reduce in MeOH than in DMF by 80–130 mV. This may be attributed to the higher solvation energy, primarily for the radical anions, in MeOH caused by hydrogen-bonding. The smaller difference is observed for **8**. Owing to the presence of the strongly electron-withdrawing cyano group in the 4-position of the phenyl ring the radical anion of this compound has a more delocalized negative charge than the radical anions of the other cinnamates and is for that reason expected to be a less powerful hydrogen-bond acceptor.

In hydroxylic solvents the formation of hydrogen-bonds also contributes significantly to the solvation of uncharged substrates if these contain highly polarized functional groups.³⁷ Examples are aldehydes, ketones and acid derivatives and compounds of this type exist predominantly in, e.g., MeOH, as the hydrogen-bonded species. These are expected to be easier to reduce than the non-specifically solvated substrates owing to the electron-withdrawing effect of the hydrogen-bond and, accordingly, electron transfer leads directly to the hydrogen-bonded radical anion, eqns. (7) and (8). This is in

contrast with the behavior in aprotic solvents, e.g., DMF and acetonitrile, containing small amounts of water or alcohols. It is widely agreed that in these solvent systems the heterogeneous electron transfer involves the substrate in a non-specifically solvated state and that the formation of the hydrogen-bonded radical anion may be treated as a follow-up equilibrium.³⁸



Kinetics and mechanism studies by LSV. The observation that the chemical reaction following the heterogeneous electron transfer is indeed very fast in MeOH makes the series of cinnamic acid esters potential candidates for a kinetics and mechanism study by LSV at low sweep rates.^{35,39,40} However, the peak separations, $E_p^{\text{ox}} - E_p^{\text{red}}$, observed during CV at $\nu = 1000 \text{ V s}^{-1}$ were in the range 120–150 mV, which corresponds⁴¹ to an approximate value of the heterogeneous electron transfer rate constant, k_s , of only 0.2 cm s^{-1} and the results should for this reason be interpreted with care.^{39,40} (In the evaluation of k_s it was assumed that the value of D , the diffusion coefficient, was $1 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ and that α , the transfer coefficient, was close to 0.5).

The variation of the peak potential for R^1 (from now on referred to as E_p) with ν and the substrate concentration, C_A° , was recorded for the entire series of cinnamates together with values of the half-peak width, $E_{p/2} - E_p$. The results are summarized in Table 2 as values of $-dE_p/d \log \nu$, $dE_p/d \log C_A^\circ$, $E_{p/2} - E_p$ and $E_p - E^\circ$ together with theoretical data^{39,40} for the first- and second-order rate laws, eqns. (9)–(11), associated with common radical ion mechanisms. The mechanism abbreviations are those frequently used for radical ion reactions^{39,40} and k_1 and k_2 are the corresponding first- and second-order rate constants.

$$\begin{aligned} \text{EC/ECE: } & -d[\text{Ph-CH=CH-COOR}^\ominus]/dt \\ & = k_1[\text{Ph-CH=CH-COOR}^\ominus] \end{aligned} \quad (9)$$

$$\begin{aligned} \text{DISP1: } & -d[\text{Ph-CH=CH-COOR}^\ominus]/dt \\ & = 2k_1[\text{Ph-CH=CH-COOR}^\ominus] \end{aligned} \quad (10)$$

$$\begin{aligned} \text{DIM1: } & -d[\text{Ph-CH=CH-COOR}^\ominus]/dt \\ & = 2k_2[\text{Ph-CH=CH-COOR}^\ominus]^2 \end{aligned} \quad (11)$$

From the data in Table 2 it is immediately seen that the reaction mechanism followed by the alkyl cinnamate radical anions, does not give rise to the same rate law as that followed by the aryl cinnamate radical anions with

Table 2. Linear sweep voltammetry data at $T=273.7$ K for the reduction of alkyl and aryl cinnamates, Ph-CH=CH-COOR , in $\text{MeOH-Et}_4\text{NBr}$ (0.1 M).

R (Compound)	$-dE_p/d \log v^a$	$dE_p/d \log C_A^{\circ b}$	$E_{p/2} - E_p^c$	$E_p - E^{o/d}$	k_{12}^e	k_{13}^f
Experimental data						
Menthyl (1)	26.5	-0.7	47.5	32	1.2×10^3	—
Ethyl (2)	26.3	-1.7	44.0	44	3.5×10^3	—
Methyl (3)	26.9	3.2	44.5	38	2.0×10^3	—
Bu(Me)NCH(Me)CHPh (4)	24.0	-1.0	54.0 ^g	15	2.9×10^2	—
2,4,6-Trimethylphenyl (5)	22.8	10.5	43.0	-4	—	5.7×10^4
4-Methoxyphenyl (6)	20.1	17.7	39.0	11	—	3.9×10^5
Phenyl (7)	23.5	19.6	39.0	16	—	7.3×10^5
4-Cyanophenyl (8)	21.7	19.6	37.5	24	—	2.0×10^6
Theoretical data ^h						
EC/ECE, rate law (9)	27.2	0	43.6			
DISP1, rate law (10)	27.2	0	43.6			
DIM1, rate law (11)	18.1	18.1	35.7			

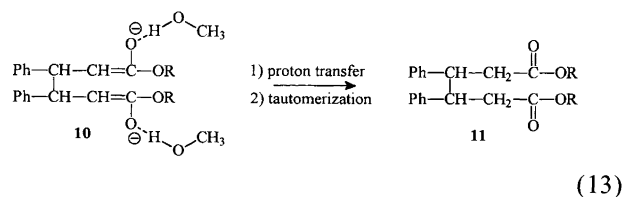
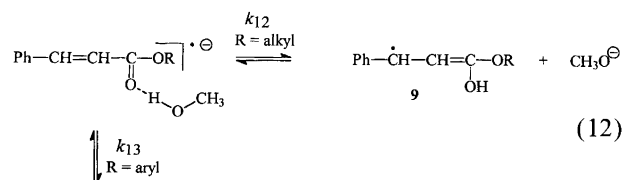
^aIn mV at $C_A^{\circ}=1.0$ mM; $v=0.2$ and 2.0 V s⁻¹. ^bIn mV at $v=0.2$ V s⁻¹; $C_A^{\circ}=1-9$ mM. ^cIn mV at $C_A^{\circ}=9.0$ mM and $v=0.2$ V s⁻¹. ^dIn mV at $C_A^{\circ}=1.0$ mM and $v=0.2$ V s⁻¹. ^eIn s⁻¹; from eqn. (17). ^fIn M⁻¹s⁻¹; from eqn. (18). ^gSlightly distorted peak, presumably due to adsorption. ^hAt $T=273.7$ K. From Refs. 39 and 40. The mechanism abbreviations refer to the nomenclature used in Refs. 39,40.

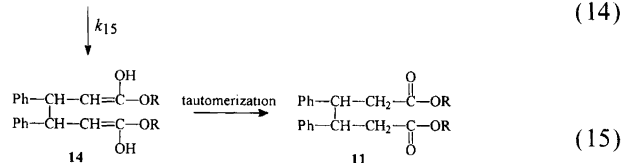
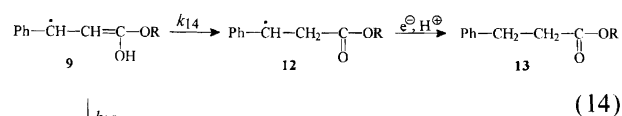
the radical anion of 2,4,6-trimethylphenyl cinnamate being a borderline case. For the alkyl cinnamates the values of $-dE_p/d \log v$ are in the range 24–27 mV and together with the observations that E_p is essentially independent of C_A° and that $E_{p/2} - E_p$ is between 44 and 48 mV this indicates that the kinetics are described by a *first-order* rate law, eqns. (9) or (10). For the aryl cinnamates the values of $-dE_p/d \log v$ and $dE_p/d \log C_A^{\circ}$ are both close to 20 mV, which together with $E_{p/2} - E_p$ values in the range 37–39 mV indicates a *second-order* rate law, eqn. (11). The data for 2,4,6-trimethyl cinnamate would then reflect a reaction order in radical anion between one and two. A general feature of the data is that the values of $E_{p/2} - E_p$ are slightly larger than the theoretical values. The reason for this is most likely that the voltammetric response, due to the only moderate heterogeneous electron transfer rate, is not controlled completely by the kinetics of the follow-up reaction.^{39,40} However, the deviations are small and do not affect the conclusions made above.

The clue to the understanding of the result that the reaction mechanism for the alkyl cinnamate radical anions gives rise to a first-order rate law is the reduction peak, R^3 , observed during CV at high voltage sweep rates (Figs. 2 and 3). The fact that the species giving rise to R^3 is formed in MeOH, but not in DMF, and is observed to be only slightly more difficult to reduce than the starting material indicates that this species is indeed the *O*-protonated radical anion, **9**, in agreement with what has been observed in related cases.^{42,43} Thus, the major pathway for the alkyl cinnamate radical anions appears to include rate-determining protonation (at oxygen) by MeOH resulting in a pseudo first-order rate law. In contrast, the second-order rate law, eqn. (11), observed for the aryl cinnamate radical anions indicates that the mechanism in these cases includes the rate-

determining coupling of two hydrogen-bonded radical anions as the major pathway.

With these results at hand the complete mechanism may be described as follows. For the alkyl cinnamates the major pathway after the formation of the radical anion, eqns. (7) and (8), includes protonation at oxygen, eqn. (12), leading to the neutral free radical, **9**, which rapidly undergoes further reaction. The radical anions of the aryl cinnamates react preferentially by coupling, eqn. (13), resulting in the formation of the dimer dianion, **10**. Protonation and tautomerization finally lead to the hydrodimer, **11**. The reaction of the radical intermediate, **9**, may follow either of two routes. The first of these, eqn. (14), involves tautomerization of **9** to the *C*-protonated form, **12**, which in contrast with the *O*-protonated form is easier to reduce than substrate.^{42,44} Further reduction at the potential of R^1 and protonation then leads to the 2 F product, the saturated ester, **13**. The second route, eqn. (15), involves dimerization of **9** to **14**, which tautomerizes to the 1 F product, the hydrodimer, **11**.





The reactions of the radical anion, protonation [eqn. (12)] or coupling [eqn. (13)], are purposely formulated as equilibrium processes. In particular, it is has been observed in several cases that the dimerizations of radical anions are reversible in the absence of follow-up reactions and may, under such conditions, be characterized both kinetically and thermodynamically.^{45,46} The same is without doubt true for protonation reactions as long as the proton donor is a weak acid such as MeOH. However, the rapid follow-up reactions of the neutral free radical, **9**, and the dimer dianion, **10**, both compete effectively with the backward reactions of equilibrium (12) and equilibrium (13) and for that reason the forward reactions become kinetically irreversible and rate-determining.

The rates of the protonation (alkyl cinnamates) and coupling (aryl cinnamates) are reflected by the values of the peak potential shift, $E_p - E^{\circ}$ (Table 2), and from these it is possible to obtain estimates of the corresponding rate constants via the theoretical relationships between $E_p - E^{\circ}$ and k .^{39,40} These are given by eqns. (16)–(18) for the three mechanisms corresponding to the rate laws (9)–(11). Thus, the evaluation of the rate constants from values of $E_p - E^{\circ}$ is, in principle, a simple matter once the mechanism (rate law) is known. However, it is easily seen from eqns. (16)–(18) that the approach requires experimental data of high precision as a change in k by one order of magnitude would result in a change in $E_p - E^{\circ}$ of only approximately 20 or 30 mV depending of the mechanism.

$$\text{EC/ECE: } k_{12} = \frac{nFv}{RT} \exp \left[\frac{2nF}{RT} (E_p - E^{\circ}) + 2 \times 0.783 \right] \quad (16)$$

DISP1:

$$k_{12} = \frac{nFv}{RT} \exp \left[\frac{2nF}{RT} (E_p - E^{\circ}) + 2 \times 0.783 + \ln 2 \right] \quad (17)$$

$$\text{DIM1: } k_{13} = \frac{3nFv}{4RTC_A} \exp \left[\frac{3nF}{RT} (E_p - E^{\circ}) + 3 \times 0.902 \right] \quad (18)$$

Before the calculations can be made, one more problem needs attention and this concerns the rate constants, k_{12} , for protonation, eqn. (12). It is seen that the pathway that leads to the hydrodimer, eqns. (12) and (15), is overall an EC-type process with rate-determining protonation, whereas the pathway that results in the forma-

tion of the saturated ester, eqns. (12) and (14), again with rate-determining protonation, will be either an overall ECE or DISP1 type depending on whether the second electron transfer takes place at the electrode (ECE) or in solution (DISP1). However, since significant reverse current was observed by CV during the back sweep at $v = 500 \text{ V s}^{-1}$ (Fig. 3) it seems most likely that the reaction proceeds predominantly by the DISP1 pathway.⁴⁷ The competition between the formation of the hydrodimer, **11**, via an EC mechanism and the saturated ester, **13**, via a DISP1 mechanism introduces an additional uncertainty in the calculation of k_{12} since eqns. (16) and (17) differ by the term $\ln 2$ in eqn. (17). In other words, for a given value of $E_p - E^{\circ}$ we have $k_{12}(\text{DISP1}) = 2k_{12}(\text{EC})$. Since the major product isolated after preparative electrolysis of **3** is the saturated ester, **13**, the DISP1 pathway seems to predominate over the EC pathway and for this reason eqn. (17) was used for the evaluation of k_{12} . It should be kept in mind, however, that the maximum absolute error in k_{12} amounts to only a factor of two; the relative error is likely to be smaller than that.

The rate constants obtained by using eqn. (17) for the proton transfer process (alkyl cinnamates) and eqn. (18) for the coupling process (aryl cinnamates) are summarized in Table 2.

The importance of hydrogen-bonding for the kinetics and the mechanism. As already mentioned the electrochemical reduction of the cinnamic acid esters in MeOH involves most likely the hydrogen-bonded substrate leading directly to the radical anion in a hydrogen-bonded state. Thus, the proton transfer, eqn. (12), occurs as a unimolecular reaction within the hydrogen-bonded complex and the kinetics are for that reason most adequately described by first-order rate constants, k_{12} (Table 2).

As seen from Table 2 the magnitudes of k_{12} and k_{13} are strongly dependent on the nature of R. The values of k_{12} cover more than one order of magnitude, from $2.9 \times 10^2 \text{ s}^{-1}$ (**4**) to $3.5 \times 10^3 \text{ s}^{-1}$ (**2**), and those for k_{13} cover almost two orders of magnitude, from $2.3 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ (**5**) to $2.0 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ (**8**). It is also seen that there is a tendency for the rate constants observed for the proton transfer reaction, k_{12} (R = alkyl), to *increase*, whereas the rate constants for the coupling reaction, k_{13} (R = aryl), *decrease* when the cinnamate becomes more difficult to reduce. These opposite trends observed for the reaction with an electrophile (protonation) and the coupling reaction are in agreement with the general reactivity pattern observed for radical ions⁴⁸ and would be expected to encompass the entire series of compounds if it had been possible also to determine k_{12} for the aryl cinnamates and k_{13} for the alkyl cinnamates. This expectation is supported by the fact that a linear relationship between $\log k$ and E° , including data for *both* R = alkyl and R = aryl, was indeed observed for the coupling of the cinnamate radical anions in DMF.²³ Seen in this context it is not a surprise that

a change in mechanism from coupling to protonation occurs on going from the most to the least easily reduced substrate. Under our experimental conditions, $C_A^\circ \geq 1$ mM, this change coincides with the change from alkyl to aryl esters. However, although the coupling reaction appears to be the predominant pathway for the aryl cinnamates, it is still possible to detect the product resulting from protonation, **9**, as reflected by the observation of the reduction peak, R^3 , e.g. for $R = \text{Ph}$ (Figs. 2 and 3).

It is of interest to compare the values of k_{13} for **6–8** with the rate constants for coupling observed in DMF. For all three compounds the rate constant for coupling is increased by nearly two orders of magnitude on going from DMF to MeOH. This reflects without doubt that MeOH (in MeOH) is a much more powerful hydrogen-bond donor than water (in DMF), in good agreement also with the observation that the cinnamates are 80–130 mV easier to reduce in MeOH.

Stereochemical aspects and conclusions. A major goal of this study was to uncover the mechanistic details behind the observation that the coupling reaction in DMF containing small amounts of water is highly stereoselective, whereas (\pm) and *meso* hydrodimers are formed in small but equal amounts in MeOH.

As already pointed out, the relatively slow and stereoselective coupling in DMF involves two *radical anions*, which, owing to the templating effect of the hydrogen-bonded water molecule, are held in a configuration favorable for coupling in the (\pm) fashion. The present study has demonstrated that the coupling reaction resulting in the formation of the (\pm) and *meso* diastereomers of dimethyl 3,4-diphenyladipate in nearly equal amounts in MeOH involves the coupling of the *neutral radical*, **9**. The lack of charge in **9** not only reduces the electrostatic repulsion in the transition state, but also has the effect that the hydrogen-bond complexes with MeOH are structurally less organized than the complex between the radical anion and water in DMF. These two effects are believed to be the major factors behind the fast and non-selective coupling observed for **9**.

The role of water as a template during the reductive coupling–cyclization of cinnamic acid esters in DMF is not unique. A similar templating effect has been suggested to explain the exclusive formation of (\pm) diastereomers during the EHD of unsaturated sulfones in the presence of lithium ion⁴⁹ and may well be the origin of the high (\pm)-to-*meso* ratios observed in other cases, where the reductive dimerization of activated olefins has been carried out in aprotic solvents the presence of metal ions.^{24–29} It is important to point out, however, that the effect of templating species, water or metal ions, relies entirely on the presence of, e.g., a carbonyl group close to the coupling center and on the absence of steric effects that may prevent the otherwise favorable transition state for coupling in the (\pm) fashion. In fact, if a template cannot be formed the *meso* isomer might be expected to

be formed in a slight excess, since the *meso* form in the absence of special effects is expected to be the more stable isomer.⁵⁰ The predominance of the *meso* isomer has indeed been reported in a few cases, e.g., for the EHD of 2,6-di-*tert*-butyl-4-benzylidene-2,5-cyclohexadienone in DMF containing an excess of MeI,⁵¹ which results in the formation of 1,2-bis(3,5-di-*tert*-butyl-4-methoxyphenyl)-1,2-diphenylethane with a (\pm)-to-*meso* ratio close to 0.5. In this case it appears likely that the formation of the *meso* isomer in excess is caused by steric hindrance of the formation of the radical anion–water template by the *tert*-butyl groups close to the carbonyl function.

The observation that the electrochemical reduction of cinnamic acid esters in MeOH leads to the hydrodimer with a (\pm)-to-*meso* ratio close to one is not unique either. In fact, we are not aware of studies where it has been demonstrated that the reductive dimerization of an activated olefin carried out in a hydroxylic solvent is stereoselective. Thus, it is tempting to conclude that the mechanism suggested for the formation of hydrodimers during the reduction of cinnamic acid esters in MeOH may be of a general nature and that the coupling in all these cases takes place between neutral free radicals formed by proton transfer within the radical anion–solvent hydrogen-bond complexes.

The conclusions drawn in this study concerning the stereochemistry of the EHD of activated olefins may then be summarized as follows.

(A) Aprotic solvents containing small amounts of a hydroxylic co-solvent (e.g., water) or metal ions (e.g., Li^+ or Ce^{3+}) result in product mixtures with the (\pm) diastereomer present in excess (or exclusively) if the structure of the substrate allows for the interaction with the template in the transition state. Substrates that are unable to form suitable hydrogen-bonded or ion-paired transition state structures result in the formation of significant amounts of the *meso* diastereomer.

(B) Hydroxylic solvents result in the the formation of product mixtures containing similar amounts of the (\pm) and *meso* diastereomers in addition to the product resulting from saturation of the C–C double bond.

Experimental

Chemicals. Methanol (HPLC grade) was obtained from Lab-Scan and was used without further purification. Tetraethylammonium bromide (Aldrich, 98%) was stored in a desiccator prior to use. Methyl and ethyl cinnamates were obtained from Fluka (*purum*), the methyl cinnamate being recrystallized from MeOH before use. The synthesis of the aryl cinnamates and the esters derived from (–)-menthol and *N*-butylephedrine have been described previously.^{21,23}

Cyclic and linear sweep voltammetry. The cells and instrumentation were essentially the same as earlier described.^{52,53} A platinum disc ($d = 0.6$ mm) electroplated

with mercury acted as the working electrode, the counter electrode was a platinum wire and the reference electrode consisted of a silver wire immersed in MeOH-Et₄NBr (0.1 M), which was also the solvent-electrolyte system for all measurements. Substrate concentrations were typically 1.0–10.0 mM. All LSV experiments were performed with the cell placed in an ice-water bath in order to reduce evaporation of the solvent and to ensure that the measurements were carried out at a uniform and easily reproducible temperature. Peak potentials, E_p , were determined as an average of 10 measurements at each sweep rate and concentration. Formal potentials, E° , were determined as the midpoint between the reduction and the oxidation peak at a voltage sweep rate of 1000 V s⁻¹. The values reported are the average of four such measurements. Ferrocene was used as an external reference. The standard deviations were typically ± 2 mV.

Constant current coulometry. Coulometric n -values were determined by constant current coulometry³⁵ (30 mA) using 0.2 mmol of substrate dissolved in approximately 50 ml of the MeOH-Et₄NBr (0.1 M) solution. Dissolved oxygen was removed by purging with nitrogen saturated with MeOH for at least 20 min and a stream of nitrogen was maintained over the solution surface during the experiment. A two compartment cell was used; the cathode being a mercury pool ($A = 12.6$ cm²) magnetically stirred during electrolysis, and the anode a graphite rod. The anode compartment consisted of a glass tube with a sintered bottom. A layer of neutral alumina (1–2 mm thick) covered the sinter to reduce seepage between the compartments. The decay in substrate concentration was monitored through recordings of the CV peak current at one minute intervals using the same working and reference electrodes as described above.

Preparative electrolyses. The controlled current electrolysis of methyl cinnamate in MeOH was carried out a number of times, the general procedure being as follows. Methyl cinnamate (1.7–3.0 g, 10.5–18.5 mmol) was dissolved in approximately 100 ml of MeOH-Et₄NBr (0.1 M) solution and placed in a divided cell with an Hg pool cathode ($A = 23.8$ cm²). The solution was subjected to constant current (100 mA) until the passage of charge corresponding to 1.0–1.2 F was complete. The catholyte was then acidified to pH 5–6 with dilute hydrochloric acid after which the volume was reduced *in vacuo* to 10–20 ml. The resulting solution was extracted with either diethyl ether or dichloromethane and the organic extracts were dried over MgSO₄ after which the solvent was removed *in vacuo* leaving a white solid (70–80% yield by mass). Analysis of this material by ¹H NMR spectroscopy showed that the supporting electrolyte had been effectively removed by the extraction procedure. The products (see below) were identified by ¹H NMR spectroscopy (CDCl₃) by comparison with the spectra of authentic samples.^{23,54} The relative yields were obtained

from the intensity of the singlet for the methoxycarbonyl group. The major components were (only the chemical shifts for the methoxycarbonyl group are given): methyl 3-phenylpropionate [25–55%, δ 3.64 (s, 3 H)], (\pm)-dimethyl 3,4-diphenyladipate [12–28%, δ 3.54 (s, 6 H)] and *meso* dimethyl 3,4-diphenyladipate [10–25%, δ 3.35 (s, 6 H)]. In all cases the (\pm) and *meso* isomers were present in nearly equal amounts. In addition, the spectra showed the presence of unconverted starting material, methyl cinnamate [5–20%, δ 3.80 (s, 3 H)].

Acknowledgements. This work was carried out as part of a project within the EU Human Capital and Mobility Program (Activation of Organic Molecules by Electron Transfer, ERBCHRXCT 920073). O.H. and M.F.N. thank the Danish Natural Science Research Council for financial support.

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Received May 8, 1997.