Influence of magnesium(II) ions on cathodic reactions in aprotic solvents—carboxylation of methyl aryl ketones

Derek Pletcher and Louise Slevin

Department of Chemistry, The University, Southampton, UK SO17 1BJ

The presence in the medium of free Mg^{II} leads to a complete change in the voltammetry for the reduction of 2-acetylnaphthalene in DMF–Bu$_4$NBF$_4$ saturated with carbon dioxide. The mechanism for these changes has been investigated and it is confirmed that the Mg^{II} interacts with the radical anions formed in the initial electron transfer reaction. The relevance of these conclusions to electrocarboxylations carried out in undivided cells with a sacrificial Mg anode is discussed. It is concluded that all the Mg^{II} formed at the anode is complexed strongly by the final carboxylated products from the cathode reaction and therefore the cathode reaction occurs in an environment where no free Mg^{II} ions are available. On the other hand, the complexation of the carboxylated products stabilises them to unwanted further reactions, thereby improving the selectivity of the electrosynthesis.

Introduction

The concept of using Mg or Al anodes in an undivided cell for cathodic reactions in aprotic media is of increasing importance in organic electrosyntheses.[1-2] The influence of the Mg^{II} or Al^{III} formed in the anode reaction on the chemistry at the cathode remains uncertain; the metal ions could (*a*) complex the radical anion/carbanion intermediates close to the cathode surface leading to a change in product or (*b*) stabilise anionic products in the bulk solution. Alternatively, the dissolving anode could merely provide clean and non-interfering chemistry. A recent paper[3] confirmed that the use of a Mg anode or the presence of Mg^{II} in solution totally changed the products from the reduction of benzoate esters in DMF and the mechanism for this change in product was defined. It was, however, emphasised that the mechanism proposed would only be applicable when the radical anion formed initially at the cathode has significant stability in the electrolysis medium.

It was therefore considered of interest to extend the study to the other limiting case where the radical anion formed at the cathode is not stable. The system chosen for study was the carboxylation of 2-acetylnaphthalene. The cathodic carboxylation of substituted alkyl halides[4-8] and of aryl ketones[9-12] are examples of reactions where cells with Mg or Al anodes have been used on a pilot scale because the carboxylic acid products are intermediates in the synthesis of a family of anti-inflammatory drugs. Indeed, a recent paper[12] has described the successful electrosynthesis of an intermediate in the manufacture of the drug Naproxen® by the cathodic carboxylation of 6-methoxy-2-acetylnaphthalene using a sacrificial anode in an undivided cell.

Experimental

The equipment, cells and procedures as well as the source of many of the chemicals have been described previously.[3] The 2-acetylnaphthalene was supplied by Aldrich Chemicals and the carbon dioxide gas by Distillers MG. The latter was dried with a column of molecular sieves before entering the cell.

All the voltammetry was carried out with a carefully polished vitreous carbon disc electrode (area 0.07 cm^2). In all experiments, the practical reference electrode was a Ag wire in the electrolyte medium. At the end of each set of experiments, a voltammogram was recorded after the addition of a small sample of ferrocene to the solution and all potentials have been converted to the Cp$_2$Fe/Cp$_2$Fe$^+$ scale.

The electrochemical reduction of 2-acetylnaphthalene in the presence of excess carbon dioxide was carried out in an undivided, enclosed beaker cell fitted with a magnesium rod anode placed down the middle of a cylindrical steel gauze cathode (area ≈ 50 cm^2). The cell was filled with 40 cm^3 of 25 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu$_4$NBF$_4$ and this solution was saturated with carbon dioxide. The CO$_2$ flow was maintained throughout the duration of the electrolysis which was carried out at room temperature.

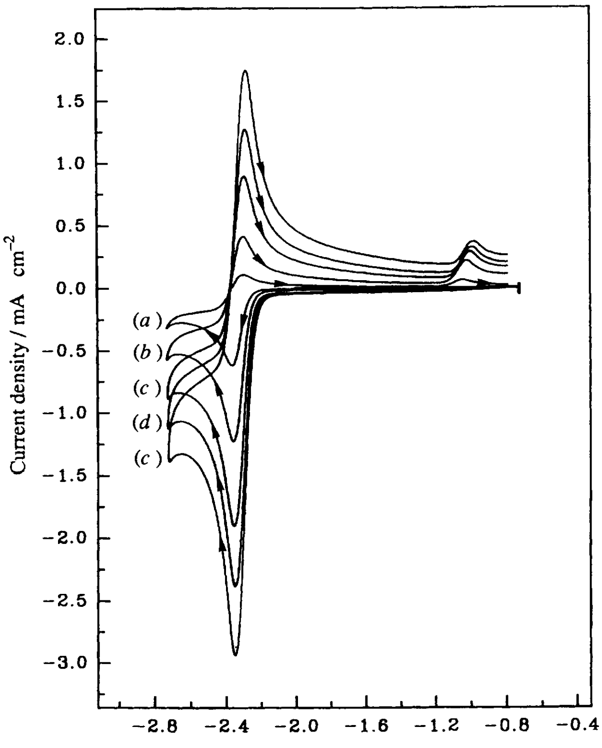


Fig. 1 Cyclic voltammograms recorded at a vitreous carbon disc electrode (area 0.08 cm^2) for a solution of 5 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu$_4$NBF$_4$. The potential scan rates are: (*a*) 20; (*b*) 80; (*c*) 200; (*d*) 320; and (*e*) 500 mV s^{-1}.

Results

Fig. 1 reports a set of voltammograms recorded at a vitreous carbon disc electrode for a solution of 5 mmol dm^{-3} 2-

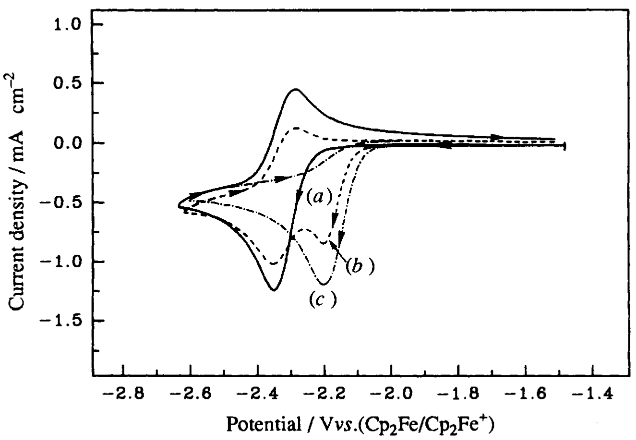
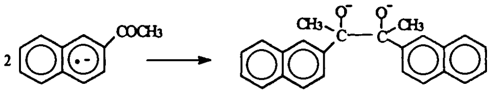


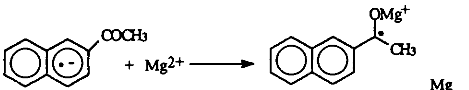
Fig. 2 Cyclic voltammograms recorded at 80 mV s^{-1} using a vitreous carbon disc electrode (area 0.08 cm^2) for a solution of 5 mol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu_4NBF_4 containing (*a*) 0; (*b*) 2.5 and (*c*) 5.24 mmol dm^{-3} $Mg(CF_3SO_3)_2$

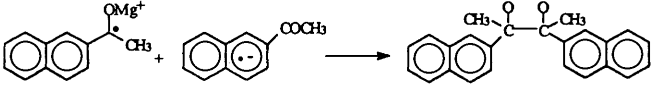
acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu_4NBF_4 at a series of potential scan rates. All the voltammograms show a well formed cathodic peak at $E_p = -2.35$ V *vs.* the Cp_2Fe/Cp_2Fe^+ couple as well as two coupled anodic peaks at $E_p = -2.29$ and -0.99 V. While the anodic peak at -2.29 V can only just be observed at the slowest scan rates, it is clear that the ratio $I_p{}^A/I_p{}^C$ approaches one at 500 mV s^{-1}. It can further be seen that the cathodic peak current density is proportional to the square root of the potential scan rate. Therefore, the response appears to be consistent with a reversible 1e^- reduction of the ketone where the radical anion is not completely stable.[13] The diffusion coefficient estimated from the cathodic peak current densities using the Randles Sevcik equation is 1.06×10^{-5} cm^2 s^{-1}, close to the value expected in DMF as the solvent. Certainly, the cathodic current function is almost independent of the potential scan rate and the reduction remains a 1e^- whether or not the radical anion is stable. The product of the chemical reaction is likely to be the pinacol and the voltammograms may be fitted to a reaction scheme where the rate constant for the dimerisation is 47 dm^3 mol^{-1} s^{-1}.[14] When the negative potential limit was extended to -3.30 V, two further reduction peaks were observed and the reverse scan also became more complex. These processes were, however, not studied in this programme.


(1)

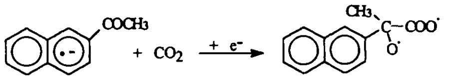

(2)

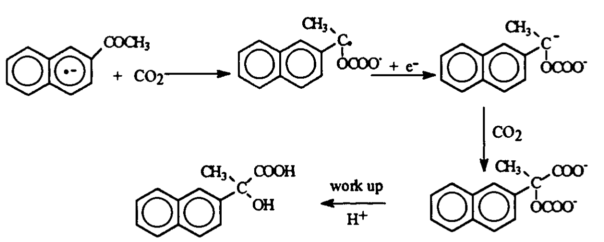
When $\mathrm{Mg^{II}}$ was added to the solution of 5 mmol dm^{-3} 2-acetylnaphthalene either as the magnesium trifluoromethanesulfonate salt or as a solution of magnesium tetrafluoroborate prepared by the anodic dissolution of Mg in DMF–0.1 mol dm^{-3} Bu_4NBF_4, the voltammetry changes significantly, see Fig. 2. With an equimolar concentration of the ketone and $\mathrm{Mg^{II}}$, the reduction of the ketone has become completely irreversible and the cathodic peak has shifted positive by 150 mV to -2.20 V *vs.* the Cp_2Fe/Cp_2Fe^+ couple: the peak current is again proportional to the square root of potential scan rate. With a deficiency of $\mathrm{Mg^{II}}$, the intermediate situation is observed; two cathodic peaks are seen and the coupled anodic peak is diminished. It should be emphasised that there is only a small change to the cathodic peak current density. Therefore, while the reaction between the radical anion and $\mathrm{Mg^{II}}$ is rapid, the overall reduction of the ketone remains a 1e^- reaction. This contrasts with the influence of $\mathrm{Mg^{II}}$ on the reduction of benzoate esters which changed from a 1e^- to a 2e^- process.[3] On the other hand, it seems reasonable to assume that the interaction of the $\mathrm{Mg^{II}}$ with the radical anion, whether viewed as ion pairing, Lewis acid–Lewis base interaction or the formation of a Mg–O bond, again catalyses the formation of dimer. Hence, the initial electron transfer, reaction (1), is followed by the reactions such as (3) and (4) where the $\mathrm{Mg^{II}}$ may be considered as accelerating the dimerisation of the radical anions by mediating the interaction between the two negatively charged intermediates. Reaction (4) is written in a way where the charge interaction can be seen to drive the dimerisation step; in fact, there are several ways of formally writing this step. A Japanese group has concluded that lithium ions had a similar effect on the chemistry of the radical anions formed from the reduction of methyl aryl ketones in similar conditions.[15] They investigated several ketones including 2-acetylnaphthalene and concluded that the yield of dimer was enhanced by the presence of Li^+ in the catholyte; also, the rate of dimerisation of the radical anions was found to increase with the concentration of Li^+.


(3)


(4)

The radical anion of 2-acetylnaphthalene also reacts rapidly with carbon dioxide. When the voltammograms were recorded for 5 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu_4NBF_4 saturated with carbon dioxide, a single irreversible cathodic peak was observed at $E_p \approx -2.24$ V *vs.* the Cp_2Fe/Cp_2Fe^+ couple. Now, however, at all potential scan rates, the peak current density is twice that in the absence of CO_2. On the other hand, the peak current density is proportional to the square root of the potential scan rate. Since carbon dioxide does not start to reduce until ≈ 3 V and the reduction of methyl aryl ketones in these conditions has been reported to give the carboxylated product,[15–18] the reduction of the ketone must occur by the ece mechanism, where reaction (1) is followed by (5). In fact, it has been proposed[15–18] that the reaction scheme is more correctly written as Scheme 1.


(5)



Scheme 1

The voltammetry of a solution of 5 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu_4NBF_4 saturated with carbon dioxide and containing 5 mmol dm^{-3} $\mathrm{Mg^{II}}$ also shows a single irreversible cathodic peak. The cathodic peak is observed at $E_p = -2.20$ V *vs.* the Cp_2Fe/Cp_2Fe^+ couple and its height is clearly that for a 1e^- reduction. When the $\mathrm{Mg^{II}}$ is added in small aliquots to the solution saturated with CO_2, two overlapping reduction peaks, $E_p \approx -2.20$ and -2.30 V, are

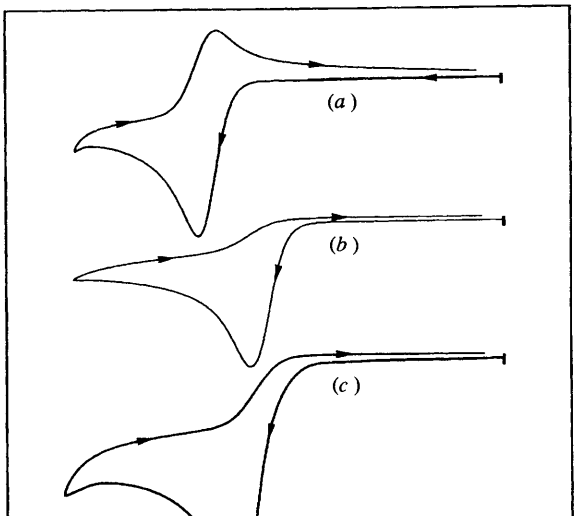
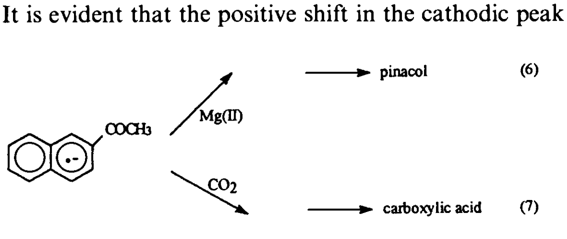


Fig. 3 Cyclic voltammograms recorded at 80 mV s^{-1} using a vitreous carbon disc electrode (area 0.08 cm^2) for solutions in DMF–0.1 M Bu_4NBF_4 of: (*a*) 5 mmol dm^{-3} 2-acetylnaphthalene; (*b*) 5 mmol dm^{-3} 2-acetylnaphthalene + 5.24 mmol dm^{-3} $Mg(CF_3SO_3)_2$; (*c*) 5 mmol dm^{-3} 2-acetylnaphthalene + saturated CO_2; and (*d*) 5 mmol dm^{-3} 2-acetylnaphthalene + 5.24 mmol dm^{-3} $Mg(CF_3SO_3)_2$ + saturated CO_2

seen on the voltammogram while the total cathodic peak current density decreases smoothly from the value for a 2e$^-$ reduction to half its initial value.

The influence of Mg^{II} and CO_2 on the voltammetry of 2-acetylnaphthalene recorded at 80 mV s^{-1} is summarised in Fig. 3. In a solution containing both Mg^{II} and CO_2, the chemistry of the radical anion and hence the voltammetric response, as well as the final products, will be determined by the competition (6) *vs.* (7). It is evident that the positive shift in the cathodic peak for 2-acetylnaphthalene, on addition to the solution of equimolar quantity of Mg^{II}, is significantly larger than that caused by saturating the medium with CO_2. Moreover, the voltammetry in the presence of both Mg^{II} and CO_2 resembles that in the presence of Mg^{II} alone. Both these observations are clear indications that the kinetics of pathway (6) are much faster than those of pathway (7) and that pinacol would be the expected product even when the solution is saturated with CO_2.



(6)

(7)

At first sight, this conclusion contrasts sharply with the knowledge that a good yield of carboxylated product can be obtained from an electrolysis in an undivided cell with a sacrificial magnesium or aluminium anode.[9–12] Hence, the voltammetry was recorded at intervals during such an electrolysis. The electrolysis was carried out with a solution of 25 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^{-3} Bu_4NBF_4 saturated with CO_2 and using a constant current of 100 mA, until a charge of 154 C had been passed. This is 80% of the theoretical charge for a 2e$^-$ reduction. At this time, it was found that the solution contained ≈5 mmol dm^{-3} unconverted 2-acetylnaphthalene, confirming that the reduction does, indeed, involve 2e$^-$/2-acetylnaphthalene molecule. It was also found that the cathode potential only changed by ≈300 mV during the electrolysis, ruling out the possibility that the cathode is passivated or undergoes marked changes during the electrolysis. Fig. 4 illustrates the voltammetric response for this final electrolysis solution in the presence of excess carbon dioxide, curve (*a*), and following removal of the carbon dioxide, curve (*b*). In the presence of CO_2, a single, irreversible reduction peak was observed at $E_p = -2.27$ V *vs.* the Cp_2Fe/Cp_2Fe^+ couple. On removal of the dissolved CO_2 from solution, a single, partially reversible reduction peak was observed at $E_p = -2.35$ V. It can also be seen that the cathodic peak in the presence of CO_2 is much larger than after its removal from solution (in fact, by a factor of 1.6). Overall, the electrochemistry of this solution is much closer to that for 2-acetylnaphthalene in the absence of Mg^{II}. On the other hand, the magnesium anode is certainly dissolving and its weight loss was equivalent to a Faradaic yield for the reaction, Mg ⟶ Mg^{II}, of 130%. This is typical for such electrolyses and the excess Mg loss may result from physical erosion of the anode to form very fine Mg powder or the involvement of Mg^I in the dissolution process.[19] Hence, Mg^{II} is certainly present in the medium during and after electrolysis. The conclusion must be that the electrode reactions are (8) and (9) and that a reaction such as (10) occurs in the bulk solution so that the Mg^{II} formed

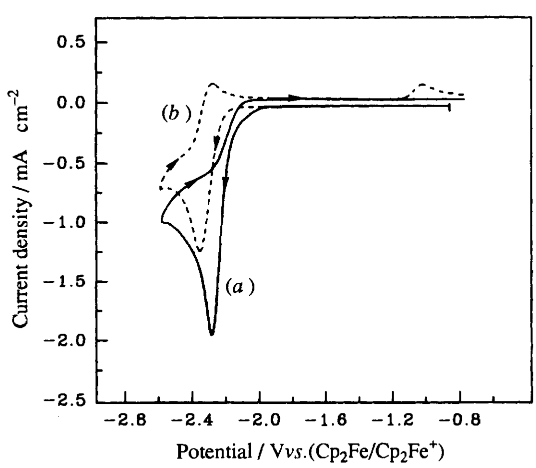
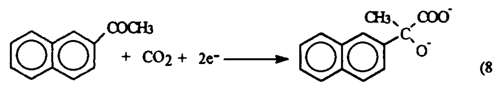
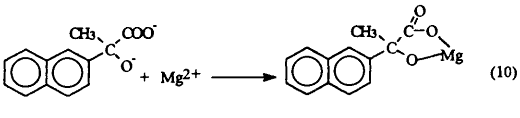


Fig. 4 Cyclic voltammograms of a solution after an electrolysis in an undivided cell with a Mg anode and steel cathode. The electrolysis solution was 25 mmol dm^{-3} 2-acetylnaphthalene in DMF–0.1 mol dm^3 Bu_4NBF_4 saturated with CO_2 and the electrolysis was carried out for 154 C (80% conversion of the ketone) using a cathode current density of 2 mA cm^{-2}. The voltammograms were recorded at 80 mV s^{-1} using a vitreous carbon disc electrode (area 0.08 cm^2) with the solution (*a*) saturated with CO_2 and (*b*) free of CO_2.



(8)

$$Mg - 2e^- \longrightarrow Mg^{2+} \qquad (9)$$



(10)

at the anode is all strongly complexed by the products of the cathode reaction. Because the stoichiometry of both the anode and cathode reactions are controlled by Faraday's laws, in such an electrolysis cell there will be no free Mg^{II} available in the electrolyte medium to interact with the radical anions formed at the cathode surface. On the other hand, the carboxylated products are stabilised by the interaction with Mg^{II} and this prevents unwanted further reactions, thereby improving the selectivity of the electrosynthesis.

It should be noted that the voltammetry of 2-acetylnaphthalene in the solution at the end of the electrolysis does not have exactly the characteristics predicted from the results with fresh solutions. In the solution without CO_2, the reduction is not as reversible as expected while when the solution is saturated with CO_2, the positive shift in the cathodic peak potential is not as large as expected (the shift is only 80 mV compared to 110 mV in the clean solution) and the cathodic peak current does not fully double. On the other hand, it must be recognised that the solution may be significantly different after electrolysis; it certainly contains a high concentration of electrolysis products (which, for example, increase the viscosity) and these could include some free Mg^{II} since there is some evidence that the yield of Mg^{II} at the anode may be higher than expected. This, however, does not change the conclusion that the carboxylated product will not be formed if free Mg^{II} is available close to the cathode surface.

Conclusions

It has been demonstrated that the addition of free Mg^{II} ions to the solution influences strongly the mechanism of reduction of 2-acetylnaphthalene in the aprotic medium saturated with CO_2. Indeed, an equimolar amount of Mg^{II} causes the reaction to change from a $2e^-$ process, leading to carboxylation of the ketyl group to a $1e^-$ process probably leading to the pinacol. This arises because of rapid interaction of the 2-acetylnaphthalene radical anion with Mg^{II} close to the cathode which prevents reaction of the radical anion with CO_2.

It is therefore clear that when the electrocarboxylation is carried out in an undivided cell with a dissolving Mg anode, the cathode reaction must still occur in an environment free from Mg^{II} able to interfere with the desired cathode chemistry. It is, however, also apparent that the carboxylated products from the cathode are species capable of complexing the Mg^{II} formed at the anode. Hence, we conclude that the free Mg^{II} is removed from the electrolyte by this complex formation in the bulk solution. Because of the balanced stoichiometry of the electrode reactions, there need never be free Mg^{II} in the electrolyte close to the cathode and this is critical to the success of such undivided cells with dissolving anodes. At the same time, the stabilisation of the carboxylated products by the interaction with Mg^{II} prevents unwanted, further reactions and this increases the selectivity of the electrosynthesis.

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