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Electrochemical carboxylation of cinnamate esters in MeCN

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Abstract

Electrochemical carboxylation of cinnamate esters has been carried out by cathodic reduction of C=C bond in an undivided cell equipped with Mg sacrificial anode and using MeCN saturated with CO_2 as solvent. The yields and the ratio of mono- and dicarboxylic acids are strongly affected by various factors: cathodic material, current, charge, and temperature. The highest yield (78.9%) was obtained starting from ethyl cinnamate. Cyclic voltammograms have been measured and reaction pathways have been proposed.

Keywords: Carboxylation; Electrochemical; Cinnamate esters; Carbon dioxide

1. Introduction

CO_2 is the largest contributor to the green house effect, which may increase the earth average temperature to such a value that may cause catastrophic events. Therefore great effort has been placed toward the reduction of CO_2 at atmospheric loading.[1] On the other hand, CO_2 can be proposed as a C_1 building block in organic synthesis. Its low cost and its facile reaction with carbanions explain why many efforts have been made in order to obtain speciality chemicals by CO_2 insertion to organic molecules.[2–5]

Carbanions can easily be generated by the electrochemical reduction of organic halides,[6–9] aromatic ketones,[10–13] and activated olefins.[14–16] Hence, the electrocarboxylation of these compounds is potentially an easy way to prepare carboxylated products, some of them of industrial interest, particularly for the production of anti-inflammatory drugs.

Electrocarboxylation of olefins has been studied in the past decades; however, the results are not very efficient. Mono- and dicarboxylation of simple activated olefins (CH_2=CHX with X=CO_2CH_3, CN, and acetyl) have been prepared in moderate or low yields by electroreduction at mercury cathode in MeCN by Tyssee and Baizer.[17] Saveant et al. studied the cathodic reduction of some activated olefins (α,β-unsaturated esters, ketones, nitriles), carried out under potentiostatic control in CO_2-saturated DMF solutions with moderate yields.[18] 2-Arylsuccinates have been prepared in good yields by electrochemcial reduction of styrene, yet it should be catalyzed by Ni–PMDTA,[19] in the presence of *N*-carboalkoxyimidazoles,[20] or using expensive Pt as cathode.[21]

Herein, we wish to report electrochemical carboxylation of cinnamate esters in MeCN. To optimize the yield, the effects of various synthetic parameters on the electrocarboxylation process, such as the electrode material, the current, the charge, and the temperature, have been studied. The voltammetry and kinetics have been examined without and with CO_2 in MeCN. The reaction pathways for the present electrochemical carboxylation are discussed.

2. Results and discussion

2.1. Constant current electrocarboxylation of methyl cinnamate

Since a constant current electrolysis is a much more convenient procedure than a constant potential electrolysis, the reaction conditions for the constant current electrolysis of

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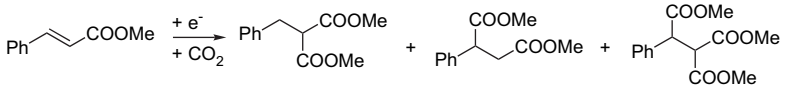
Table 1
Electrocarboxylation of methyl cinnamate under various synthetic parameters[a]



1a **2a** **3a** **4a**

Entry	Cathode	*I*/mA	*Q*/F mol^{-1}	*T*/°C	Yield[b]/%	Ratio **2a**:**3a**:**4a**
1	Stainless steel	100	2	25	64.4	21:13:66
2	Ni	100	2	25	41.6	48:13:39
3	Cu	100	2	25	53.6	50:11:39
4	Ti	100	2	25	75.2	31:19:50
5	Ti	60	2	25	60.2	40:15:45
6	Ti	80	2	25	66.8	30:15:55
7	Ti	110	2	25	68.6	29:18:53
8	Ti	120	2	25	64.9	37:17:46
9	Ti	140	2	25	65.8	55:17:28
10	Ti	160	2	25	67.1	37:16:47
11	Ti	100	1.2	25	44.3	80:12:8
12	Ti	100	1.6	25	62.2	56:12:32
13	Ti	100	2.4	25	67.8	49:17:34
14	Ti	100	2.8	25	66.1	62:15:23
15	Ti	100	3.2	25	59.2	63:15:22
16	Ti	100	2	35	66.0	64:15:21
17	Ti	100	2	10	76.5	47:12:41
18	Ti	100	2	0	77.2	24:13:63
19	Ti	100	2	−10	77.4	17:10:73

[a] General conditions: methyl cinnamate=0.1 M, Et_4NBF_4=0.1 M, MeCN=10 mL, P_{CO_2}=1 atm.
[b] GC yields.

methyl cinnamate (**1a**) were surveyed as summarized in Table 1. The yields of mono- and dicarboxylic acids were affected by the choice of cathode material, current, charge, and temperature.

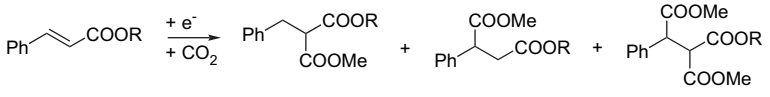
The nature of the cathodic material strongly determined the yields or reactivity in CO_2 fixation. Ti was the most efficient as a cathode material, which resulted in good electrocarboxylation yield reaching the value of 75.2% (Table 1, entry 4). Other cathode materials such as stainless steel, Ni, and Cu gave moderate yields (Table 1, entries 1–3).

The yields are also strongly affected by the current (Table 1, entries 4–10). The larger the current is, the more negative the electrode potential will be. So there will be other reactions on the electrode surface, such as the reduction of CO_2 or Mg^{2+}, which will decrease the carboxylation yield. On the other hand, the lower the current density is, the more positive the electrode potential will be. So the proportion of the Faradaic current will be declined, which will also decrease the carboxylation yield. Therefore, the optimized current is 100 mA on the electrodes of Mg–Ti.

The effect of the amount of electricity supplied to the electrodes (Table 1, entries 4 and 11–15) is consistent with a two-electron transfer process in which the current yield is not 100%. Increasing the number of Faradays per mole of **1a**, the yields in carboxylated products increase linearly before 2 F mol^{-1}, however, after which the yields decrease. So the best choice is 2 F mol^{-1} of **1a**.

Although a strong decrease in the yields was observed at higher temperature (Table 1, entry 16), only a slight increase of the yields was observed at lower temperature (Table 1, entries 17–19).

Table 2
Electrocarboxylation of cinnamate esters[a]



1 **2** **3** **4**

Entry	R	**1**	Yield[b]/%	Ratio **2**:**3**:**4**
1	Me	**1a**	77.2[c]	24:13:63
2	Et	**1b**	78.9	33:11:56
3	Pr	**1c**	61.9	35:11:54
4	Bu	**1d**	73.1	30:5:65

[a] General conditions: cinnamate esters=0.1 M, Et_4NBF_4=0.1 M, MeCN=10 mL, stainless steel cathode, Mg anode, *T*=0 °C, *I*=100 mA, electric charge=2 F mol^{-1}, P_{CO_2}=1 atm.
[b] GC yields.
[c] This experiment (the same of entry 18, Table 1) was repeated here for clarity.

2.2. Electrochemical carboxylation of cinnamate esters

To test the applicability of this electrochemical carboxylation, the investigation was extended to other cinnamate esters.

The results of these electrolyses under the conditions described above (Table 1, entry 18) are reported in Table 2. In all cases, two monocarboxylic acids and one dicarboxylic acid were obtained. The good yields were obtained with ethyl ester and methyl ester (Table 2, entries 1 and 2). Moderate yields were achieved with propyl ester and butyl ester (Table 2, entries 3 and 4). These indicate that this electrochemical synthesis works well for cinnamate esters.

2.3. Cyclic voltammetry of cinnamate esters

The cyclic voltammograms of **1a–d** (MeCN–0.1 M Et_4NBF_4, GC cathode, v=0.1 V s^{-1}) exhibit a one-electron reduction peak in the potential range −1.40 to −1.50 V vs Ag/AgI/I^- and a second chemically irreversible reduction at low potentials. An example of the voltammetric behavior of the compounds is shown in Figure 1 (curve b). When the scan rate was increased, the first peak became partially reversible, while the second remaining irreversible, showing for a chemical reaction followed the first one-electron transfer reaction. The radical anion generated by the electroreduction of the activated alkene is involved in several competitive reactions, which lead to the formation of hydrodimers and saturated esters.[22]

When the cyclic voltammograms were recorded in MeCN saturated with CO_2, different behaviors were observed (Fig. 2). The first reduction peak potential moved more positively and current increased. The peak current ratios i_p/i_p^0 measured in the presence of CO_2 are included in the data presented in Table 3. The current enhancements show the reactions between CO_2 and electrogenerated radical anions.

The similar behaviors have been observed to other cinnamate esters. The relative data were shown in Table 3.

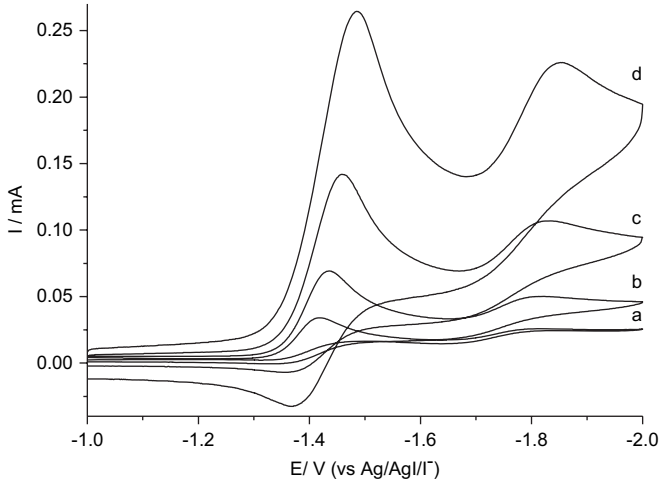


Figure 1. Cyclic voltammograms of methyl cinnamate in MeCN–0.1 M Et_4NBF_4 at different scan rates: (a) 0.02 V s^{-1}, (b) 0.1 V s^{-1}, (c) 0.5 V s^{-1}, (d) 2 V s^{-1}, reference: Ag/AgI/I^-; T=25 °C.

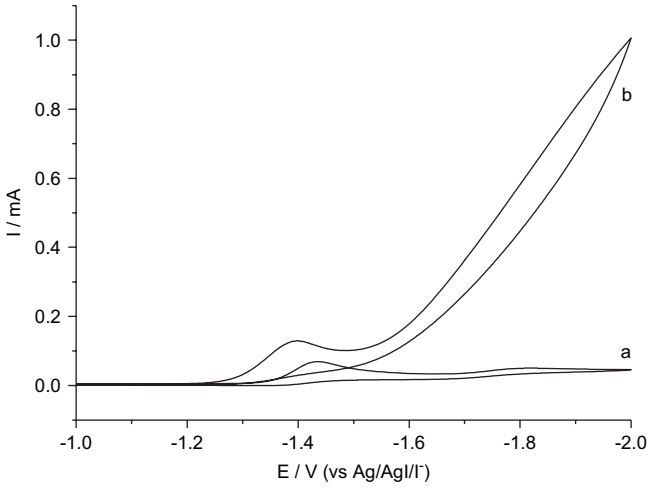
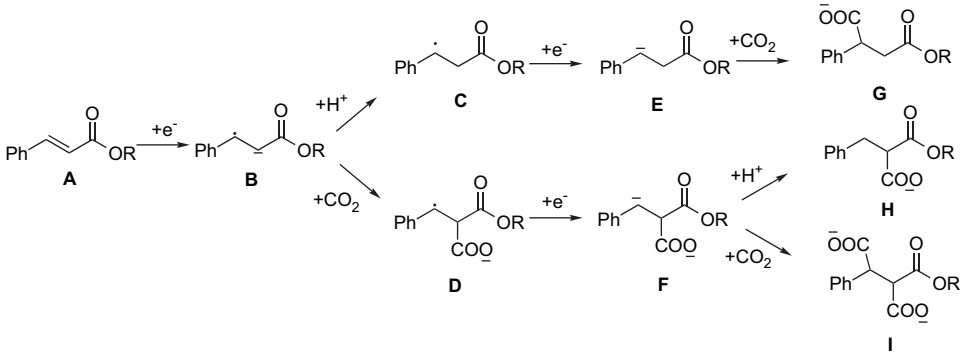


Figure 2. Cyclic voltammograms of methyl cinnamate in MeCN–0.1 M Et_4NBF_4 in the (a) absence and (b) presence of saturated CO_2.

Table 3
Peak potentials and peak currents of cinnamate esters in MeCN–0.1 M Et_4NBF_4[a]

R	1	E_p^{0b}/V	i_p^{0b}/mA	E_p^{c}/V	i_p^{c}/mA	i_p/i_p^0
Me	**1a**	−1.44	0.0640	−1.40	0.1226	1.92
Et	**1b**	−1.43	0.0775	−1.40	0.1434	1.85
Pr	**1c**	−1.42	0.0716	−1.39	0.1259	1.76
Bu	**1d**	−1.42	0.0736	−1.39	0.1446	1.96

[a] GC working electrode, T=25 °C, C=2 mM, v=0.1 V s^{-1}.
[b] Measured in the absence of CO_2.
[c] Measured in the presence of CO_2.



Scheme 1.

2.4. Reaction pathway

According to the electrosynthesis results and cyclic voltammograms, proposed reaction pathways for the present electrocarboxylation are shown in Scheme 1. One-electron reduction of cinnamate esters **A** would give the radical anion **B**. As the solvent is dried and saturated with CO_2, most of **B** undergoes a nucleophilic attack on CO_2 to give the radical anion **D**, while only a little of **B** is protonated to radical **C**. Further one-electron reduction of **D** affords the carbanion **F**, which also would react with CO_2 or H^+. Carbanion **F** is spatially rigid and sterically hindered, so that it is easier to react with H^+ to afford monocarboxylic acid **H** and then CO_2 to afford dicarboxylic acid **I**. On the other hand, the radical **C** involves further reduction and nucleophilic reaction to afford another monocarboxylic acid **G**.

3. Conclusion

In conclusion, CO_2 fixation has been carried out, under mild conditions, in good yields by electrocarboxylation of cinnamate esters. It is shown that various conditions, such as the nature of the electrode, the current, the passed charge, and the temperature, could affect the yields of mono- and dicarboxylic acids. Under the optimized condition, electrocarboxylation of methyl cinnamate achieved 77.4% of global carboxylic acids. Several cinnamate esters were electrochemically reduced in the presence of CO_2 to the corresponding carboxylic acids in satisfactory yields (61.9–78.9%).

The cyclic voltammograms of cinnamate esters in MeCN showed two successive reduction waves. Comparison of the electrochemical behaviors in the absence and presence of saturated of CO_2 can be used as one criterion of the reaction pathway. The radical anion generated by the electroreduction is involved in several competitive reactions, which lead to formation of the monocarboxylic acids and dicarboxylic acid.

4. Experimental section

4.1. General

^{1}H NMR spectra were recorded on AVANCE 500 (500 MHz) spectrometer in $CDCl_3$ with Me_4Si as an internal standard. Mass spectra were obtained on a 5973N spectrometer connected with a HP 6890 gas chromatograph. HRMS was measured on a CONCEPT 1H. Cyclic voltammograms were measured with CHI650 electrochemical analyzer (CHI, USA). Glassy carbon (GC) electrode (d=2 mm) was used as a working electrode. The counter electrode and the reference electrode were a platinum wire and Ag/AgI/0.1 M n-Bu_4NI in DMF, respectively. Galvanostatic electrolysis was carried out using a dc regulated power supply QJ 12001X (1 A, 120 V) in an undivided cell equipped by two-electrode.

Acetonitrile (MeCN) and dimethylformamide (DMF) was kept over 4 Å molecular sieves. Tetraethylammonium tetrafluoroborate (Et_4NBF_4) was prepared according to the literature.[23] Propels cinnamate and butyl cinnamate was prepared by the reaction of alcohols with cinnamate acid. Other reagents were used as received.

4.2. Electrocarboxylation of cinnamate esters (typical procedure)

The galvanostatic electrolysis was carried out in a mixture of methyl cinnamate (0.1 M) and Et_4NBF_4 (0.1 M) in 10 mL dry MeCN under a slow stream of CO_2 in a one-compartment electrochemical cell equipped with a magnesium rod sacrificial anode and a metallic ring cathode until 2 F mol^{-1} of charge was passed. The reaction mixture was distilled under reduced pressure. The residue was esterified in DMF by adding anhydrous K_2CO_3 (1 mmol) and MeI (3 mmol) and the mixture was stirred at 50 °C for 5 h. The solution was hydrolyzed and extracted with Et_2O, and the organic layers was washed with H_2O, dried over $MgSO_4$, and evaporated. The methyl esters corresponding to acids were isolated by column chromatography with petroleum ether/ethyl acetate mixtures as eluent. After isolation and identification of the products, working curves were used with biphenyl as internal standard for analysis of the electrochemical carboxylation.

4.2.1. Dimethyl benzylmalonate **2a**

GC–MS (*m*/*z*, %) 222 (M^+, 36), 131 (100), 162 (83), 91 (55), 159 (28), 103 (26), 161 (26), 163 (20), 77 (14), 133 (10), 93 (9); ^{1}H NMR ($CDCl_3$) δ 7.30–7.17 (5H, m), 3.70 (6H, s), 3.68 (1H, d, J=8 Hz), 3.23 (2H, d, J=8 Hz); HRMS *m*/*z* (M^+) calcd for $C_{12}H_{14}O_4$ 222.0892, found 222.0890.

4.2.2. Ethyl methyl benzylmalonate **2b**

GC–MS (*m*/*z*, %) 236 (M^+, 32), 131 (100), 91 (59), 162 (51), 159 (34), 176 (29), 103 (24), 161 (18), 77 (14), 163 (13), 164 (13); ^{1}H NMR ($CDCl_3$) δ 7.32–7.19 (5H, m), 4.15 (2H, q, J=7 Hz), 3.70 (3H, s), 3.66 (1H, d, J=5 Hz), 3.22 (2H, d, J=5 Hz), 1.19 (3H, t, J=7 Hz); HRMS *m*/*z* (M^+) calcd for $C_{13}H_{16}O_4$ 236.1049, found 236.1052.

4.2.3. Methyl propyl benzylmalonate **2c**

GC–MS (*m*/*z*, %) 250 (M^+, 34), 131 (100), 162 (83), 91 (73), 148 (54), 159 (39), 103 (26), 147 (24), 32 (23), 163 (22), 161 (21); ^{1}H NMR ($CDCl_3$) δ 7.32–7.12 (5H, m), 4.10–4.02 (2H, m), 3.69 (3H, s), 3.67 (1H, d, J=4 Hz), 3.24 (2H, d, J=4 Hz), 1.64–1.57 (2H, m), 0.86 (3H, t, J=8 Hz); HRMS *m*/*z* (M^+) calcd for $C_{14}H_{18}O_4$ 250.1205, found 250.1213.

4.2.4. Butyl methyl benzylmalonate **2d**

GC–MS (*m*/*z*, %) 264 (M^+, 37), 162 (100), 131 (76), 91 (56), 148 (55), 159 (26), 147 (25), 163 (21), 161 (20), 103 (19), 204 (14); ^{1}H NMR ($CDCl_3$) δ 7.32–7.19 (5H, m), 4.11–4.05 (2H, m), 3.69 (3H, s), 3.67 (1H, d, J=7 Hz), 3.22 (2H, d, J=8 Hz), 1.57–1.53 (2H, m), 1.31–1.26 (2H, m), 0.88 (3H, t, J=7 Hz); HRMS *m*/*z* (M^+) calcd for $C_{15}H_{20}O_4$ 264.1362, found 264.1370.

4.2.5. 2-Methoxycarbonyl-3-phenyl-succinic acid dimethyl ester ***4a***

GC–MS (*m/z*, %) 280 (M^+, 1), 121 (100), 248 (92), 189 (82), 131 (46), 161 (40), 103 (37), 216 (32), 77 (28), 59 (21), 177 (19); ^{1}H NMR ($CDCl_3$) δ 7.33–7.26 (5H, m), 4.32 (1H, d, J=12 Hz), 4.24 (1H, d, J=11 Hz), 3.78 (3H, s), 3.68 (3H, s), 3.46 (3H, s); HRMS *m/z* (M^+) calcd for $C_{14}H_{16}O_6$ 280.0947, found 280.0948.

4.2.6. 2-Ethoxycarbonyl-3-phenyl-succinic acid dimethyl ester ***4b*** *(mixture of four isomers)*

GC–MS (*m/z*, %) 294 (M^+, 0.5), 262 (100), 131 (94), 189 (77), 121 (61), 103 (51), 203 (38), 161 (34), 77 (31), 175 (25), 216 (19); ^{1}H NMR ($CDCl_3$) δ 7.26–7.20 (5H, m), 4.25 (1H, d, J=12 Hz), 4.18 (1H, d, J=12 Hz), 4.16–3.82 (2H, m), 3.71–3.40 (6H, m), 1.23–0.85 (3H, m); HRMS *m/z* (M^+) calcd for $C_{15}H_{18}O_6$ 294.1103, found 294.1117.

4.2.7. 2-Phenyl-3-propoxycarbonyl-succinic acid dimethyl ester ***4c*** *(mixture of four isomers)*

GC–MS (*m/z*, %) 308 (M^+, 1), 131 (100), 276 (96), 234 (75), 121 (58), 189 (57), 202 (56), 103 (49), 161 (40), 162 (37), 175 (30); ^{1}H NMR ($CDCl_3$) δ 7.30–7.25 (5H, m), 4.24 (1H, d, J=12 Hz), 4.21 (1H, d, J=12 Hz), 4.13–3.78 (2H, m), 3.75–3.44 (6H, m), 1.68–1.18 (2H, m), 0.94–0.67 (3H, m); HRMS *m/z* (M^+) calcd for $C_{16}H_{20}O_6$ 308.1260, found 308.1263.

4.2.8. 2-Butoxycarbonyl-3-phenyl-succinic acid dimethyl ester ***4d*** *(mixture of four isomers)*

GC–MS (*m/z*, %) 322 (M^+, 0.1), 140 (100), 131 (94), 202 (69), 290 (67), 121 (57), 189 (52), 103 (46), 162 (43), 161 (38), 210 (38); ^{1}H NMR ($CDCl_3$) δ 7.27 (5H, d, J=6 Hz), 4.30 (1H, d, J=12 Hz), 4.23 (1H, d, J=12 Hz), 4.18–3.84 (2H, m), 3.75–3.41 (6H, m), 1.61–1.35 (2H, m), 1.28–1.08 (2H, m), 0.93–0.76 (3H, m); HRMS *m/z* (M^+) calcd for $C_{17}H_{22}O_6$ 322.1416, found 322.1420.

Acknowledgements

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