

Efficient Electrochemical Dicarboxylation of Phenyl-substituted Alkenes: Synthesis of 1-Phenylalkane-1,2-dicarboxylic Acids

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Abstract: Electrochemical dicarboxylation of phenyl-substituted alkenes in the presence of atmospheric pressure of carbon dioxide with a platinum plate cathode and a magnesium rod anode readily took place efficiently in a DMF solution containing 0.1 M Et₄NClO₄ to give the corresponding 1,2-dicarboxylic acids in high yields.

Key words: carboxylic acids, magnesium, phenyl-substituted alkenes, electrochemical carboxylation, electrochemistry

One of useful methods for preparation of carboxylic acids is one carbon elongation reaction of organic halides or alkenes using a cyanide ion of KCN or NaCN, carbon monoxide, and carbon dioxide. 2-Phenylsuccinic acids, useful compounds as synthetic intermediates or as antitumor agents,¹ have been prepared by several methods: i.e., addition of NaCN to ethyl α -cyano- β -phenylacrylate,^{2a} addition of HCN to α -phenylcinnamionitrile,^{2b} addition of 1,1-diaminoethene to β -nitrostyrene,^{2c} reductive addition of arenediazonium salts to maleic or fumaric acid,^{2d} condensation of benzaldehyde, phenylacetone, and NaCN,^{2b} and oxidative coupling of carboxylic acid dianions.^{2e,2f} In these preparations, however, there are several drawbacks: the use of hazardous or complex reagents, the requirement of a long reaction time, and limitation to a preparation of symmetrical dicarboxylic acids in the case of oxidative coupling. Carboxylic acids can also be prepared by chemical fixation of carbon dioxide to alkenes, but severe reaction conditions are required in these reactions.³ On the other hand, an electrochemical fixation of carbon dioxide to organic halides or carbonyl compounds can be readily carried out efficiently even in an atmospheric pressure of CO₂ under neutral and mild conditions to give carboxylic acids in high yields.^{4,5} We have already reported that electrochemical carboxylation of allylic halides,⁶ propargylic bromides,⁷ 1,4-dibromo-2-bromomethylbut-2-ene,⁸ vinyl bromides,⁹ and vinyl triflates¹⁰ proceeds efficiently by using magnesium as a reactive-metal anode to give the corresponding carboxylic acids in high yields. As one of our continuing studies on electrochemical carboxylation, we recently succeeded in an efficient electrochemical fixation of two CO₂ molecules to the C=C bond of phenyl-substituted alkenes to give the corresponding 2-phenylsuccinic acids in moderate to high yields. In this paper, we report such a convenient and efficient method for synthesizing various 2-phenylsuccinic acids by electrochemical dicarboxylation. Although electrochemical carboxylation of phenyl-substituted alkenes



Scheme 1

Table 1 Electrochemical Dicarboxylation of Phenyl-substituted Alkenes^a

Entry	Alkene	R ¹	R ²	R ³	Conversion (%)	Yield ^b (%)
1 ^c	1a	H	H	H	73	66 (90)
2	1b	Me	H	H	98	68 (69)
3	1c	H	Me	H	98	77 (79) ^d
4	1d	H	H	Me	98	70 (71) ^d
5	1e	Ph	H	H	93	91 (98)
6	1f	H	Ph	H	84	84 (>99) ^e
7	1g	H	H	Ph	84	84 (92) ^e

^a Alkene **1** (3.5 mmol) in DMF (20 ml) containing 0.1 M Et₄NClO₄ was electrolyzed in the presence of an atmospheric pressure of CO₂ using a one-compartment cell equipped with a Pt plate cathode (2 × 3 cm²) and an Mg rod anode (∅ 3 mm).

^b Isolated yields. The yields based on a reacted starting alkene **1** are shown in parentheses.

^c Electrolysis was carried out in the presence of 4-methoxyphenol (3 mg).

^d Isomer ratio (*threo:erythro*); 2.7:1 (entry 3), 2.5:1 (entry 4).

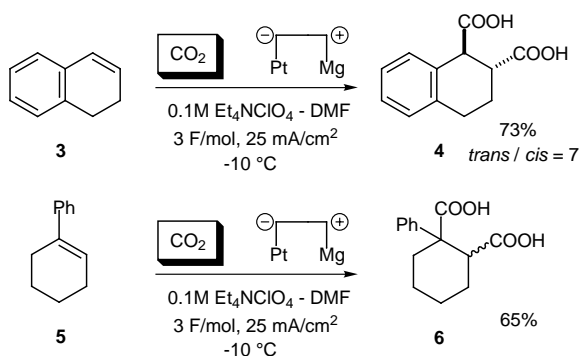
^e Isomer ratio (*dl:meso*); 1.8:1 (entry 6), 1.9:1 (entry 7).

has been reported by several workers, a mixture of mono- and dicarboxylated acids has been obtained,^{11,12} and dicarboxylic acids have only been formed in low conversions by using an Ni(II) catalyst.¹²

A general procedure of the present electrochemical dicarboxylation is as follows: Alkene (3.5 mmol) in 20 mL of DMF containing 0.1 M Et₄NClO₄ was electrolyzed at -10 °C with a constant current (25 mA/cm²) under an atmospheric pressure of carbon dioxide. A one-compartment cell equipped with a platinum plate cathode (2 × 3 cm²) and a magnesium rod anode (∅ 3 mm) was used for electrolysis. The electricity passed was 3 F/mol. After electrolysis, the electrolyzed solution was acidified with 2N HCl and extracted with diethyl ether. The ethereal solution was washed successively with H₂O and saturated

NaHCO₃. The aqueous solution was again acidified with 2N HCl, and the resulting carboxylic acid was extracted with ether. The combined ethereal solution was washed with saturated brine and dried over MgSO₄. Evaporation of the solvent gave an almost pure 1,2-dicarboxylic acid.

The results of the electrochemical dicarboxylation are summarized in Table 1. Electrochemical dicarboxylation of phenyl-substituted alkenes proceeded in high conversions (73–98%) to give the corresponding 1,2-dicarboxylic acids in high yields. For instance, electrochemical dicarboxylation of styrene (**1a**) gave 2-phenylsuccinic acid in 66% isolated yield (entry 1). The conversion of styrene was 73% and the yield based on the converted **1a** was 90%. Electrochemical dicarboxylation of other substituted styrenes using our method was also found to occur efficiently. Thus, electrochemical dicarboxylation of α -methylstyrene (**1b**) and 1,1-diphenylethylene (**1e**) gave the corresponding 2,2-disubstituted succinic acids **2b** and **2e** in 68% and 91% yields, respectively (entries 2 and 5). When (*E*)- (**1c**) and (*Z*)- β -methylstyrenes (**1d**) were subjected to the present dicarboxylation, a mixture of *threo*- and *erythro*-2-methyl-3-phenylsuccinic acids¹³ was obtained in 77% and 70% yields, respectively (entries 3 and 4). Isomer ratios of *threo*- and *erythro*-2-methyl-3-phenylsuccinic acids, determined by ¹H NMR, were 2.7:1 (entry 3) and 2.5:1 (entry 4), respectively, and the *threo*-isomer was preferentially obtained in each case. Furthermore, similar electrochemical carboxylations of (*E*)- (**1f**) and (*Z*)-stilbenes (**1g**) gave 2,3-diphenylsuccinic acid,^{2f} both in 84% yields, which contains a *dl*-isomer as a major product (*dl*:*meso* = 1.8:1 in entry 6, 1.9:1 in entry 7). The present dicarboxylation also took place efficiently when cycloalkenes were used as substrates. Thus, a similar electrochemical carboxylation of 1,2-dihydronaphthalene (**3**) gave naphthalene-1,2-dicarboxylic acid (**4**) in 73% isolated yield. A similar electrochemical reaction of 1-phenylcyclohexene (**5**) gave 1-phenylcyclohexane-1,2-dicarboxylic acid (**6**) in 65% yield (Scheme 2). This dicarboxylic acid **6** was not produced in the nickel catalyzed electrochemical carboxylation.¹²



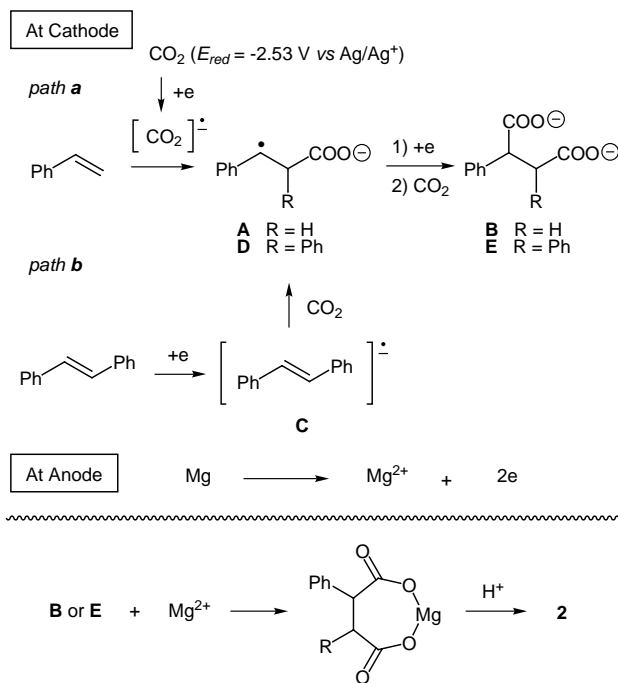
Scheme 2

Cyclic voltammetry of phenyl-substituted alkenes **1** was carried out, and the observed reduction peak potentials (E_{red}) are summarized in Table 2.

Table 2 Reduction Peak Potentials of Phenyl-substituted Alkenes **1**

Alkene	R ¹	R ²	R ³	E_{red} (V vs Ag/Ag ⁺) ^a
1a	H	H	H	-2.91
1b	Me	H	H	< -3.0
1c	H	Me	H	< -3.0
1d	H	H	Me	< -3.0
1e	Ph	H	H	-2.58
1f	H	Ph	H	-2.44
1g	H	H	Ph	-2.50

^a Reduction peak potentials were determined with a gold disk electrode at the scan rate of 0.1 Vs⁻¹ and are shown in V vs Ag/Ag⁺.



Scheme 3

From these results and the reduction potential of CO₂ (-2.53 V vs Ag/Ag⁺), two possible reaction pathways shown in Scheme 3 may be considered.^{11b} One is the pathway *a*, in which alkenes **1** have more negative reduction potentials than that of CO₂ (entries 1, 2, 3, and 4 in Table 1). In these cases, a one-electron reduction of carbon dioxide preferentially occurs to generate its anion radical, since the reduction potentials of alkenes **1** are more negative than that of carbon dioxide. The addition of CO₂ anion radical to alkenes **1** would result in the formation of an intermediate **A**. Further one-electron reduction followed by reaction with CO₂ gives rise to dicarboxylate ion **B** (path *a*). On the other hand, in the reaction of alkenes **1** whose reduction potentials are almost the same or slightly more positive than that of CO₂ (entries 5, 6, and 7 in Table 1), a direct or CO₂-mediated one-electron reduction of alkenes **1** takes place to generate their anion radicals **C**. Reaction of **C** with CO₂ gives monocarboxylated intermediate **D**. Further one-electron reduction followed by reac-

tion with CO₂ leads to the formation of dicarboxylate ion **E** (path **b**). At an anode, on the other hand, a dissolution of magnesium metal takes place to give magnesium ion in both of the electrochemical pathways described above. The magnesium ion readily captures carboxylate ions **B** or **E** to form stable magnesium carboxylates, which upon an acid treatment give dicarboxylic acids **2**.

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