

ELECTROSYNTHESIS OF ARYL-CARBOXYLIC ACIDS FROM  
CHLOROBENZENE DERIVATIVES AND CARBON DIOXIDE

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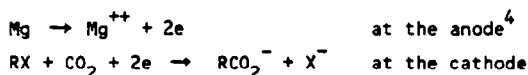
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**Abstract** - The electrocarboxylation of a large variety of chlorobenzene compounds is achieved in *N,N*-dimethylformamide by constant current electrolysis between a stainless steel cathode and a sacrificial magnesium anode in a diaphragmless cell. Substituted benzoic acids are obtained in high yield in simple conditions thus avoiding the usual preparation of organometallic intermediates.

Attempts to achieve the synthesis of carboxylic acids by electroreduction of organic halides (RX) have been numerous in the recent years<sup>1</sup>. However the required means (divided cells with organic media, necessity of catalytic additives, potentiostatic technique...) did not let hope for a growth up to a preparative scale.

Quite recently a new efficient method allowing the electrocarboxylation of a wide range of halocompounds has been proposed. It is based on the use of sacrificial anodes of aluminium<sup>2</sup> or magnesium which offers the significant advantage of working with diaphragmless cells. As we have reported<sup>3</sup> the electrolyses are achieved by setting a constant current between a magnesium anode and any cathode such as nickel, graphite or stainless steel. The solvent may be an usual aprotic one, such as *N,N*'dimethylformamide and only a low concentration of supporting electrolyte (Bu<sub>4</sub>NBr, Bu<sub>4</sub>NI...) is required to settle the initial conductivity since ionic species are produced during the reaction.

The electrochemical balance is expressed as follows :



Thus, the overall reaction consists in an one-pot electroassisted synthesis very similar to the conventional carboxylation of Grignard reagents without needing preparing the organometallic intermediate. The method is efficient even at high concentration of RX (0,5 to 1 M) and high current densities (20 mA/cm<sup>2</sup>).

In this paper, we present the results of the electrocarboxylation of easily available chloro and polychlorobenzene derivatives which are suitable starting materials for the synthesis of benzoic acids derivatives.

The electrolyses at the laboratory scale have been performed in an electrochemical device, as depicted in figure 1, with a cylindrical stainless steel gauze surrounding a rod of magnesium, at about 5° C, under atmospheric pressure of carbon dioxide. In most cases, the concentration of RX decreases during the reaction as delineated in figure 2. At the end of the electrolysis the carboxylic acid is recovered from its magnesium salt as detailed in the experimental section. The results are summarized in table I.

Table 1 : Electrocarboxylation of substituted chlorobenzenes

Entry	reagent <sup>a</sup>	eE <sup>b</sup>	$\tau$ (%) <sup>c</sup>	Yield (%) <sup>d</sup>	acidic products <sup>a</sup> and relative distribution (%) PhCO <sub>2</sub> H	Neutral by-products (%) <sup>e</sup>
1	PhCl	(2) 3	(60) 78	85	PhCO <sub>2</sub> H	PHH (10)
2	2-Cl	(2) 4	(70) 90	65	2-Cl (95)/PhCO <sub>2</sub> H (5)	PhCl (5)
3	3-Cl	2	70	65	3-Cl (99)/PhCO <sub>2</sub> H (1)	PhCl (traces)
4	4-Cl	2	70	65	4-Cl (95)/PhCO <sub>2</sub> H (5)	PhCl (traces)
5	2,3-Cl <sub>2</sub>	2	70	74	2,3-Cl <sub>2</sub> (46)/2,6-Cl <sub>2</sub> (48)/2+3-Cl (6)	1,2+1,3-Cl <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (6)/PhCl (traces)
6	3,5-Cl <sub>2</sub>	(2) 4	(70) 90	50	3,5-Cl <sub>2</sub> (95)/3-Cl (5)	1,3-Cl <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (10)/PhCl (3)/PHH (traces)
7	2,4-Cl <sub>2</sub>	(2) 4	(60) 85	60	2,5-Cl <sub>2</sub> (95)/2,4+3,4-Cl <sub>2</sub> (5)	1,2+1,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>4</sub> (10)/PhCl (traces)
8,9	2 or 4-CO <sub>2</sub> H	3 <sup>f</sup>	30		no diacid, only PhCO <sub>2</sub> H	
10	4-F	2	80	80	4-F	PhF (10)
11	4-CH <sub>3</sub>	2	80	78	4-CH <sub>3</sub>	PhCH <sub>3</sub> (15)
12	2-CF <sub>3</sub>	2	70	80	2-CF <sub>3</sub>	PhCF <sub>3</sub> (5)
13	3-CF <sub>3</sub>	2	95	85	3-CF <sub>3</sub>	PhCF <sub>3</sub> (traces)
14	4-CF <sub>3</sub>	2	75	80	4-CF <sub>3</sub>	PhCF <sub>3</sub> (3)

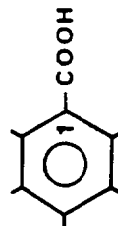
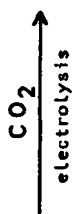
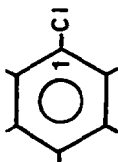


Table 1 : continued

15	4-OCH <sub>3</sub>	2	75	60	4-OCH <sub>3</sub>	PhOCH <sub>3</sub> (35)
16	4-COCH <sub>3</sub>	2	50	50	4-COCH <sub>3</sub>	PhCOCH <sub>3</sub> (45)
17	4-COOCH <sub>3</sub>	2	80	0		PhCOOCH <sub>3</sub> (100)
18	2-CN	2	60	65	2-CN	PhCN (10)
19	4-Br	2	95	85	4-Cl (80)/4-Br(15)/PhCO <sub>2</sub> H (5)	PhBr + PhCl (15)
20	3-Cl 4-CH <sub>3</sub>	(2) 4	(70) 95	70	3-Cl 4-CH <sub>3</sub> (75)/2-CH <sub>3</sub> 5-Cl (15) 2+4-CH <sub>3</sub> (10)	2+4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Cl (10)/PhCH <sub>3</sub> (traces)
21	3-Cl 4-COCH <sub>3</sub>	(2) 3	(70) 80	80	3-Cl 4-COCH <sub>3</sub> (70)/2-COCH <sub>3</sub> 5-Cl (30)	2+4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Cl (10)/PhCOCH <sub>3</sub> (traces)
22	2-Cl 4-COCH <sub>3</sub>	2	70	60	2-Cl 4-COCH <sub>3</sub> (70)/2-Cl 5-COCH <sub>3</sub> (30)	3+4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Cl <sup>g</sup> /PhCOCH <sub>3</sub> (traces)
23	2-Cl 3-OCH <sub>3</sub>	2	50	80	2-Cl 3-OCH <sub>3</sub> (80)/2-Cl 6-OCH <sub>3</sub> (20)	2+3-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> Cl <sup>g</sup> /PhOCH <sub>3</sub> (traces)
24	2,3-Cl <sub>2</sub> 4-OCH <sub>3</sub>	2	75	60	2,3-Cl <sub>2</sub> 4-OCH <sub>3</sub> (60)/others (40)	) various chloro and ) dichloro anisole <sup>g</sup>
25	2,4-Cl <sub>2</sub> 3-OCH <sub>3</sub>	2	55	80	2,4-Cl <sub>2</sub> 3-OCH <sub>3</sub> (70)/others (30)	

a : H if no indication

b : Electric charge (electron-mol. per mol. of RX). Values in brackets indicate intermediate nE and τ (G.C. titration of samples).

c : Consumed RX (G.C. titration).

d : Yields of isolated acids vs. consumed RX.

e : Yields (G.C. titration) vs. consumed RX.

f : One electron-mol. is firstly involved in the reduction of the acidic proton.

g : Not calculated.

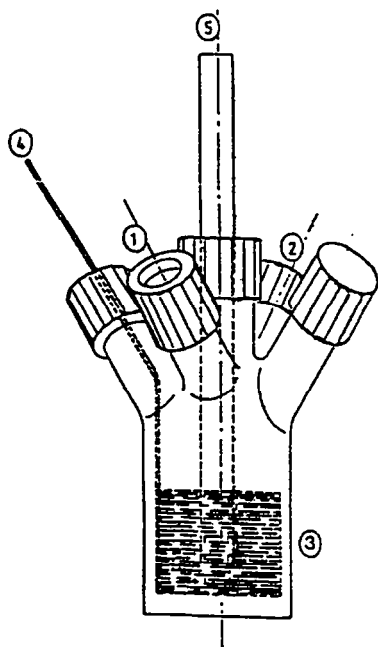


Figure 1

## Electrochemical cell

- (1) and (2) Input and output of CO<sub>2</sub>  
 (3) Stainless steel gauze cathode and  
 (4) its connection (20 cm<sup>2</sup>)  
 (5) Magnesium rod as anode (8 cm<sup>2</sup>).

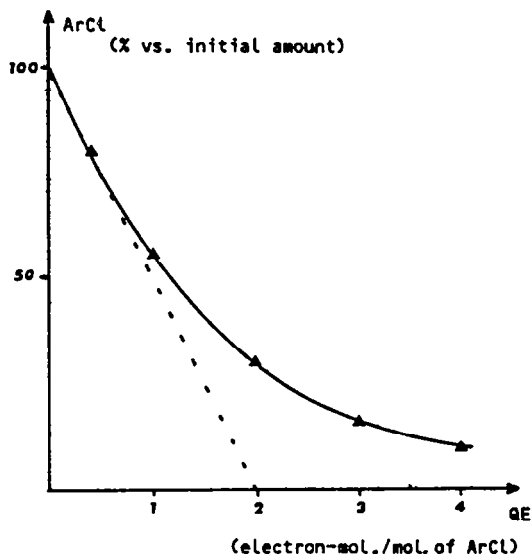


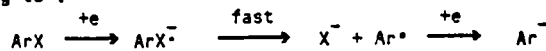
Figure 2

Consumption of ArCl during electrolysis  
(ex. of 1,2-dichlorobenzene)

Dashed line represents the theoretical curve for a 100 % faradic yield.

It is noticeable that polyacids were never obtained from polychlorobenzenes (entries 2 to 7 and 20 to 25) even if the electrolyses were continued after a large consumption of the starting material. This only led to the reduction of the remaining C-Cl bonds into C-H bonds. Two hypotheses can be considered. In the first one, the reductive dechlorination would precede the carboxylation since even chlorobenzene can be reduced into benzoic acid. Nevertheless, the evolution of the products distribution rather suggests an opposite reaction sequence which is in keeping with the fact that only benzoic acid is formed from the 2-chloro or 4-chlorobenzoic acids (entry 8 or 9). Similar behaviours are encountered with alkyl chlorobenzoates (entry 17) and to a smaller extent with 4-chloroacetophenone (entry 16).

The electronic reduction of aromatic halides (ArX) can be assumed to proceed via an ECE mechanism<sup>5</sup> according to :



If electron-withdrawing groups are present on the aromatic ring, the rate of the splitting of the radical anion ArX<sup>-</sup> may become slow enough<sup>6</sup> to control the rate of electrogeneration of the ion Ar<sup>-</sup>. A competition can then arise between an electrophilic attack of Ar<sup>-</sup> by CO<sub>2</sub> or a capture of H atom<sup>7</sup>. To support this, new experiments carried out with bromo compounds in which the life time of ArX<sup>-</sup> is shorter than with chloro compounds<sup>7</sup>, have shown that the electrocarboxylation is widely improved. For instance, 4-bromoacetophenone is almost wholly converted into 4-acetylbenzoic acid. In addition, when electrolyses are conducted in a solvent which is a better H donor than N,N-dimethylformamide (eg. tetrahydrofuran) the yield of ArCO<sub>2</sub><sup>-</sup> from ArCl is widely reduced and ArH becomes the main product. Conversely in tetramethylurea as solvent methyl 4-chlorobenzoate and 1,4-dichlorobenzene are converted into terephthalic acid with respectively 30 and 20 % yield. Nevertheless magnesium ions arising from the anode very likely affect this

mechanism. Indeed, our results are quite different from those obtained in classical divided cells, where electrocarboxylation of aryl chlorides is not effective<sup>8</sup>. This positive effect of Mg(II) may involve interaction with either  $ArX^-$  or  $Ar^-$  but this point is not clearly understood.

From trichlorobenzenes (entries 5 to 7) and substituted polychlorobenzenes (entries 20 to 25) the distribution of the mono carboxylated isomers is hardly foreseeable. However, it can be noted that the ratio of isomeric dichlorobenzoic acids arising from entries 5 or 7 are identical to those corresponding to the electroreduction into dichlorobenzenes when  $CO_2$  is absent<sup>9</sup>.

In conclusion the electrocarboxylation of a wide range of chlorobenzene derivatives can be achieved in a very simple manner except for the case of compounds substituted by strong electron-withdrawing (eg  $CO_2R$ ) or too easily reducible (eg  $NO_2$ ) groups. The experimental conditions, using an undivided cell, a common and safe solvent, cheap electrode materials and constant current electrolysis seem to be suitable for an industrial process.

For this purpose, experiments are at present performed on a preindustrial scale from batches employing 30 l solutions and allowing the synthesis of 2 to 4 kg per day of carboxylic acids. The solution maintained at room temperature under an overpressure (4 bars) of carbon dioxide is flowed by a pump through an electrolytic cell with a stainless steel cathode and sacrificial magnesium blocks as the anode<sup>10</sup>. Results quite similar to those presented in this paper have been obtained especially for the preparation of some valuable synthetic intermediates in pharmaceutical and agrochemical fields, such as 4-fluorobenzoic, 3,4-dichlorobenzoic, 4-trifluoromethylbenzoic acids, ... Consequently, it can be expected that this novel one-stage synthesis will compete in some cases with the usual way employing hazardous organometallic intermediates<sup>11</sup>.

## EXPERIMENTAL

The solvent *N,N* dimethylformamide (DMF) was distilled over anhydrous copper sulfate, under reduced pressure, just before use. Tetrabutylammonium bromide ( $NBu_4Br$ ) as supporting electrolyte and the chlorobenzene derivatives ( $ArCl$ ) were available grade.

**Electrolysis.** In a typical experiment DMF (30 ml),  $NBu_4Br$  (300 mg),  $ArCl$  (3 g for a solid or 3 ml for a liquid) were introduced in the electrochemical cell (Fig. 1). The cell was then immersed in cold water to dissipate the heat evolved by the electrolysis and to keep the temperature near 5° C. After bubbling of  $CO_2$  for a few minutes allowing to expel residual air, a low overpressure (0.1 bar) of  $CO_2$  was applied. Electrodes are connected to a power supply and a constant current of  $I = 0.4$  A was settled to the stirred mixture. The analysis of samples allows to follow up the decrease of  $ArCl$  in relation to the time, that is to say to the electric charge (QE) (see Fig. 2) which is expressed as :

$$QE \text{ (electron-mol. per mol. of } ArCl) = \frac{I(A) \times t(s) \times n_{ArCl} \text{ (g)}}{9.65 \cdot 10^4 \times FW_{ArCl} \text{ (g)}}$$

**Recovery of the carboxylic acids.** After electrolysis most of the solvent and eventually at the same time volatile starting materials and neutral by products were evaporated. The residue was acidified with 6 N aqueous hydrochloric acid (10 ml) and extracted with diethyloxide (3 x 10 ml). The organic extract was treated by 2 N aqueous sodium hydroxide (2 x 10 ml) to separate acidic and neutral products. The aqueous layer was again acidified until pH became readily acid and extracted with diethyloxide (3 x 30 ml) which was then evaporated so leading to the aromatic acid or a mixture of acids.

**Analysis.** Samples taken during and after electrolysis were acidified with 6 N aqueous hydrochloric acid and extracted with diethyloxide containing an appropriate internal standard. Unreacted starting materials and neutral by-products were titrated by gas chromatography (SE30 15 %, 2 m at different temperatures). Identification of the isolated acids was done by  $^1H$  NMR,  $^{13}C$  NMR and control of the melting point. In the case of mixtures of acids, identification and titration was performed by gas chromatography on a capillary column (Superox AT1000, 11 m) by comparison

with authentic samples when available. If not, analyses were effected by mass spectroscopy coupled with gas chromatography from methyl ester derivatives prepared (except for diorthosubstituted benzoic acids which do not react) as follows : the acid (500 mg) and sulfuric acid (0.5 ml) were added to methanol (10 ml), then the mixture was refluxed overnight. After evaporation of most of the solvent, the residue was extracted with dichloromethane (2 x 20 ml), washed with 5 % aqueous sodium hydrogen carbonate (20 ml), water (20 ml), dried with magnesium sulfate and evaporated.

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