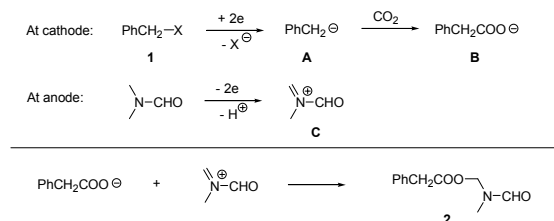


Three Component Coupling Reaction of Benzyl Halides,
CO₂, and DMF by Using Paired Electrosynthesis;
Sacrificial Anode Free Electrochemical Carboxylation of
Benzyl halides

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Electrochemical carboxylation (EC) is one of useful and attractive methods for a fixation of carbon dioxide into organic molecules. Carboxylic acids can readily be obtained in high yields under mild conditions even in an atmospheric pressure of CO₂ when a reactive metal, such as magnesium and aluminum, is used as an anode in the electrolysis using an undivided cell.^{1,2} In other words, the use of a reactive-metal anode (sacrificial anode) is crucial for efficient electrochemical fixation of CO₂ into organic molecules when electrolysis is carried out in an undivided cell. A number of EC of organic compounds in an undivided cell have already been demonstrated by the use of a sacrificial reactive-metal anode. We have also successfully carried out EC of various organic molecules to afford useful carboxylic acids,³⁻¹³ including α -fluorinated non-steroidal anti-inflammatory drugs,¹⁴ in good yields. However, sacrificial reactive-metal anode is consumable, and exchange of consumed anode material to new one is necessary in successive electrolysis. This would become problem, especially both in large scale synthesis and in electrolysis using flow system. Sacrificial anode free EC with high efficiency would be desirable. We have tried this subject and successfully carried out sacrificial anode free EC of benzyl halides by the use of paired electrolysis.

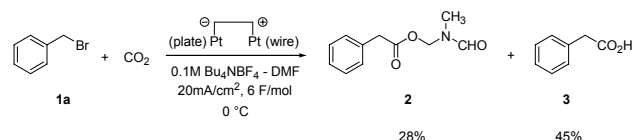


Aimed reaction system is as follows; at cathode, reduction of benzyl halide **1** generates benzyl anion **A**, which captures CO₂ to produce carboxylate ion **B**. At anode, oxidation of DMF occurs to generate iminium ion **C** and proton. Coupling reaction of **B** and **C** achieves efficient EC of **1** to obtain product **2**. If this reaction system would work well, efficient EC without a reactive-metal anode can be realized.

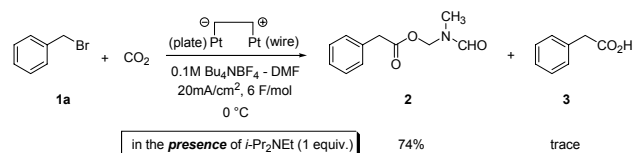
Electrolysis of benzyl halides was carried out with a constant current at 0 °C in DMF containing 0.1 M Bu₄NBF₄ under an atmospheric pressure of carbon dioxide with bubbling through the solution. Quasi-divided cell,¹⁵ a one-compartment cell equipped with a platinum plate cathode (2 x 2 cm²) and a platinum wire anode (0.5 mm ϕ), was used for the electrolysis. After electrolysis, the reaction mixture was diluted with ether and the resulting organic solution was washed with saturated brine. Aqueous layer was extracted with ether, and combined organic layer was washed with saturated NaHCO₃ solution and two layers were separated. From the aqueous layer, carboxylic acid was obtained by acidification with

3N HCl followed by extraction with ether. From the organic layer, three component coupling product was obtained after purification of the resulting crude product by column chromatography.

When EC of benzyl bromide **1a** was carried out under the conditions as shown below, carboxylation could surprisingly take place efficiently even without the use of magnesium anode to afford three component coupling product **2** in 28% yield along with 45% of carboxylic acid **3**.



Because formation of coupling product **2** was not efficient and protonation product **3** was obtained as a major product, the reaction was tried to carry out in the presence of a proton acceptor such as amine. It was found that exclusive formation of coupling product **2** could be achieved when EC was carried out in the presence of 1 equiv. of *i*-Pr₂NEt.



Other results of three component coupling and role of amine as an additive will be also discussed.

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