

Electrochemical generation of aryl and vinyl radicals and their radical cyclization followed by fixation of carbon dioxide

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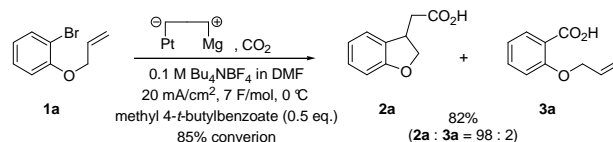
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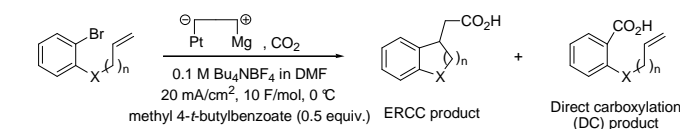
Electroreductive generation of carbon radicals from organic halides is one of the useful and eco-friendly alternatives to conventional radical generation using toxic organotin reagents such as tributyltin hydride. Successful electroreductive generation of carbon-centered radicals without Bu₃SnH has been carried out by direct, metal complex-catalyzed, or mediated (indirect) electrochemical reduction of organic halides and diazonium salts, and its application to radical cyclization reactions has also been performed to synthesize carbo- and heterocycles.¹ However, most of the termination steps in electroreductive radical reactions are merely protonation of the resulting anion, yielding protonated cyclic compounds, and little attention has been given to the use of the resulting anion for further reactions, especially carbon-carbon bond-forming reactions. To the best of our knowledge, Ni-catalyzed tandem cyclization-carboxylation of unsaturated haloaryl ethers is the only example in electroreductive “radical-type” cyclization followed by C-C bond formation with carbon dioxide.² During the course of our studies in electro-organic synthesis,³ we recently succeeded in selective generation of aryl radicals from 2-allyloxybromobenzenes by electrochemical reduction using methyl 4-*t*-butylbenzoate as an electron transfer mediator. We also found that thus-generated aryl radicals were applicable to radical cyclization, and after further one-electron reduction of the resulting cyclized radical, the resulting anion efficiently captured carbon dioxide to yield 3,4-dihydrobenzofuran-3-ylacetic acids in high selectivities and good yields.⁴ Moreover, this protocol was successfully applied to vinyl radical cyclization followed by fixation of carbon dioxide. Herein, we report electrochemical generation of aryl and vinyl radicals from the corresponding bromides and their radical cyclization followed by fixation of carbon dioxide affording carbo- and heterocycle-substituted acetic acids in moderate to good yields.

Firstly, screening of reaction conditions, including an additive as an electron transfer mediator, for electrochemical radical cyclization-carboxylation was carried out by using 2-allyloxybromobenzene **1a** as a substrate. We found that when 7 F/mol of electricity was passed in constant current electrolysis of **1a** at 20 mA/cm² in the presence of carbon dioxide and 0.5 equiv. of methyl 4-*t*-butylbenzoate as a mediator at 0 °C, conversion of **1a** reached 85% and the desired radical cyclization-carboxylation product, 2,3-dihydrobenzofuran-3-ylacetic acid (**2a**), was obtained in 82% yield with high selectivity. It is noteworthy that methyl 4-*t*-butylbenzoate using as an electron transfer mediator could be recovered quantitatively, and after purification by column

chromatography, the recovered mediator was reusable for the present reaction.



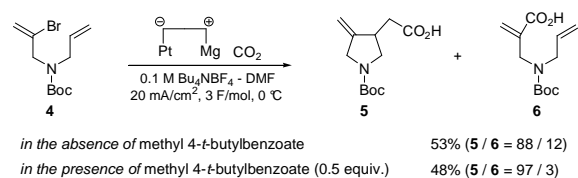
Under the similar conditions, the scope of the present electrochemical radical cyclization-carboxylation (ERCC) reaction was investigated and a part of the results are shown. In all cases, ERCC products **2** were obtained selectively in moderate to good yield. Benzopyranylacetic acid **2d** could also be obtained by 6-exo cyclization of the aryl radical generated from **1d** followed by carboxylation.



Entry	Substrate	ERCC Product	Yield [%] ^{a)} and ratio (ERCC / DC) ^{b)}	Conversion [%] ^{b)}
1 ^{c)}			40 [67] (> 99 / 1)	60
2			68 [74] (94 / 6)	92
3			58 [91] (98 / 2)	64

a) Isolated yields. The yields based on reacted substrate are shown in brackets. b) Determined by ¹H NMR. c) 5.7 F/mol of electricity was passed with 10 mA/cm² of current density.

We also found that the present ERCC reaction was applicable to vinyl bromides.



References

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