

CO₂ anion–radical in organic carboxylations

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Abstract—This letter shows a first approximation to the use of CO₂ anion–radical in the obtention of α -methyl and α -ethylcyanoacetic acids from propionitrile and butyronitrile, respectively, through a paired electrochemical reaction with CO₂. The electrosynthesis of α -chloro-phenylacetic acid from benzyl chloride and phenylacetic acid from toluene by another proposed pathway is also discussed.

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The CO₂ reduction is a very important aim in the development of alternative fuel sources and as possible means of energy storage.¹ However, the use of CO₂ as a source of carbon for the synthesis of organic molecules has not yet been developed. Few papers on this topic have been published, for instance, the preparation of *cis*- and *trans*-1,2-cyclohexanedicarboxylate by reaction of cyclohexene and CO₂ anion–radical obtained by photo-reduction of CO₂;² the nucleophilic addition of CO₂ anion–radical (from gamma-irradiated formate ions) to the C₅–C₆ double bond of N-substituted thymines;³ the reaction of CO₂ anion–radical, also obtained by irradiation of aqueous solutions containing formate, with substituted benzenes;⁴ or the obtention of cyanoacetic acid via a paired electrosynthesis carried out in our research group.⁵ At this paired reaction process takes place the anodic oxidation of electrolyte anions and subsequent reaction with solvent molecules (acetonitrile). The obtained $\cdot\text{CH}_2\text{CN}$ radicals are coupled with cathodic CO₂-reduced species, proceeding through the medium-porosity glass-fritt diaphragm, to afford the desired product.

Numerous chemical,^{6–8} electrochemical,^{9–15} photoelectro-chemical,^{16,17} direct photochemical¹⁸ and photocatalytic¹⁹ systems have been developed for the reduction of CO₂ to a variety of products.

In this present letter, we extend the use of CO₂ anion–radical to the preparation of different carboxylic acids.

Keywords: CO₂ anion–radical; Carboxylation; Paired electrosynthesis.

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When acetonitrile is replaced as the solvent by propionitrile or butyronitrile, α -methyl-cyanoacetic acid or α -ethyl-cyanoacetic acid are, respectively, obtained. The α -propionitrile or α -butyronitrile radicals are formed by anodic oxidation of the supporting-electrolyte anion with further H⁺ abstraction from the solvent, and are coupled with CO₂ anion–radical molecules, produced in the cathodic compartment.⁵ The α -position attack in propionitrile and butyronitrile was determined by ¹H NMR.

Adjacent functional groups appear to weaken C–H bonds: radicals next to carbonyl, nitrile or ether functional groups, or centred on a carbonyl carbon atom, are more stable than even tertiary alkyl radicals. Whether the functional group is electron-withdrawing or electron-donating is clearly irrelevant here: both types seem to stabilize radicals.²⁰

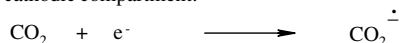
The obtained yields and current efficiencies on the desired carboxylic acids are summarized in Table 1.

These electrolyses were carried out²¹ under constant current conditions (300 mA, current density of 22 mA/cm²). The facility of H⁺ abstraction, from the radical electrogenerated when the supporting electrolyte anion is oxidized, was observed by electrolysis of a mixture

Table 1.

Solvent	Faradays circulated through the cell	Yield (g/F)	Current efficiency (%)
Propionitrile	0.021	17.4	19.5
Butyronitrile	0.021	15.2	14.75

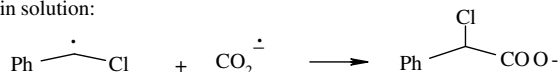
cathodic compartment:



anodic compartment:



in solution:



Scheme 1.

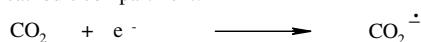
of acetonitrile/propionitrile (1:1) and acetonitrile/butyronitrile (1:1). The obtained experimental results showed that in the first case the ratio of cyanoacetic acid/ α -methyl-cyanoacetic acid was 3:1, however, in the second one the ratio of cyanoacetic acid/ α -ethyl-cyanoacetic acid was 7.8:1. It means that the H[•] abstraction in acetonitrile is easier than the abstraction in the α -position of propionitrile and the latter easier than H[•] abstraction in butyronitrile.

The anodic oxidation of benzyl chloride²² at Pt anode was performed under constant potential conditions (+2.5 V(vs Ag/Ag⁺)) in acetonitrile/Bu₄NBF₄ as SSE (solvent-supporting electrolyte). When, simultaneously to this oxidation, the reduction of cathodically bubbled CO₂ is effected by using a medium-porosity glass-fritt diaphragm, α -chloro- α -phenylacetic (36%) and α -phenylacetic (47%) acids are anodically obtained as the main products. The formation of the first compound could be rationalized, through a paired reaction similar to those previously described by us (Scheme 1).^{23,24}

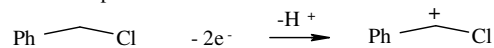
However, cyclic voltammetry of benzylchloride only shows an oxidation peak, corresponding to a 2e⁻ process, meaning that both 1e⁻ processes take place almost simultaneously, and the electrogenerated chlorobenzyl radicals are immediately oxidized at the electrode surface to chlorobenzyl cations, which are desorbed into the homogeneous solution. On the other hand, CO₂ anion-radicals proceeding from the cathode can react, in the anolyte solution, with the electrogenerated dichlorobenzyl cations to afford, as shown in Scheme 2, an unstable radical.

This unstable radical can undergo homolytic fragmentation²⁵ leading another more stable radical (see Scheme 3) in a similar manner to the decarbonylation of acyl radicals²⁶ or the extremely facile decarboxylation pro-

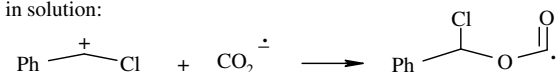
cathodic compartment:



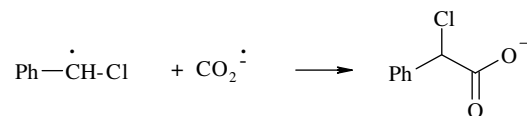
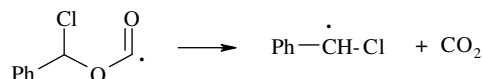
anodic compartment:



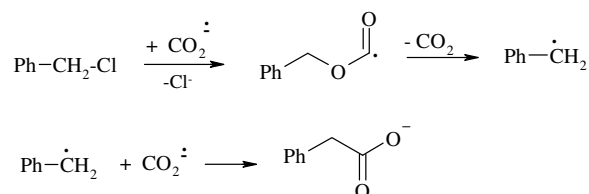
in solution:



Scheme 2.



Scheme 3.



Scheme 4.

cess of acyloxy radicals, particularly derived from aliphatic acids.

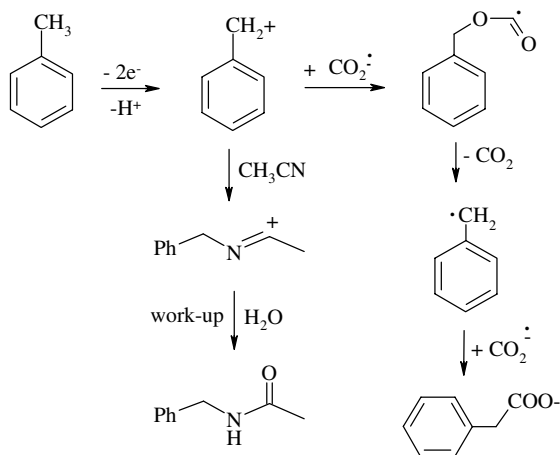
The coupling of this new stable radical with another CO₂ anion-radical molecule also affords α -chloro- α -phenylacetic acid.

The formation of α -phenylacetic acid can be explained as indicated in Scheme 4. The CO₂ anion-radical can act as a nucleophile towards benzyl chloride affording another unstable radical, similarly to previously proposed, which evolves to a benzyl radical and further couples with a new CO₂ anion-radical molecule leading to the carboxylate.

α -Phenylacetic acid is obtained in small amounts in the cathodic compartment, especially if the diaphragm has a very big pore. Some benzyl chloride molecules diffuse to the cathodic compartment to be reduced (easier than CO₂) to the corresponding anion, which reacts with a CO₂ molecule to afford α -phenylacetate. The diffusion of benzyl chloride causes two problems, the first is the consumption of the substrate and the second is the fact that, due to the more negative reduction potential of CO₂, it is not reduced in the presence of benzyl chloride. In order to minimize this diffusion phenomenon, the substrate was slowly added into the anodic compartment during the reaction to avoid high concentration of substrate in solutions. Under dilute conditions the substitution reaction does not take place, whereas the oxidation of benzyl chloride, in which we are interested, is favoured.

The anodic oxidation of toluene, under the same experimental conditions, has also been performed. In this case *N*-benzylacetamide is obtained as the main product but α -phenylacetic acid is also formed as a secondary product (11%).

Cyclic voltammetry of toluene shows an oxidation peak corresponding to a 2e⁻ process. The electrochemical formation of benzyl cations is supported by a Ritter



Scheme 5.

reaction with the solvent, acetonitrile, to give *N*-benzylacetamide. The formation of α -phenylacetic acid is rationalized in Scheme 5, and is similar to the formation of α -chloro- α -phenylacetic acid.

The possibility of an electron-transfer in solution, in the last step of the carboxylations described in this letter, is not discarded.

We can conclude that these processes, once optimized, open a new and interesting alternative to the use of carbon dioxide in organic synthesis.

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References and notes

1. Stevens, G. B.; Reda, T.; Raguse, B. *J. Electroanal. Chem.* **2002**, *526*, 125.
2. Morgenstern, D. A.; Wittrig, R. E.; Fanwick, Ph. E.; Kubiak, C. P. *J. Am. Chem. Soc.* **1993**, *115*, 6470.
3. Ito, T.; Hatta, H.; Nishimoto, S. *Int. J. Radiat. Biol.* **2000**, *76*, 683.
4. Rosso, J. A.; Bertolutti, S. G.; Braun, A. M.; Martire, D. O.; Gonzalez, M. C. *J. Phys. Org. Chem.* **2001**, *14*, 300.
5. Batanero, B.; Barba, F.; Sánchez-Sánchez, C. M.; Aldaz, A. *J. Org. Chem.* **2004**, *69*, 2423.
6. Bryan, J. C.; Geib, S. J.; Rheingold, A. L.; Meyer, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 2826.

7. DeLaet, D. L.; del Rosario, R.; Fanwick, P. E.; Kubiak, C. P. *J. Am. Chem. Soc.* **1987**, *109*, 754.
8. Wu, J.; Fanwick, P. E.; Kubiak, C. P. *Organometallics* **1987**, *6*, 1805.
9. Simon-Manso, E.; Cúbica, C. P. *Organometallics* **2005**, *24*, 96.
10. Hori, Y.; Ito, H.; Okano, K.; Nagasu, K.; Sat, S. *Electrochim. Acta* **2003**, *48*, 2651.
11. Isaacs, M.; Canales, J. C.; Aguirre, M. J.; Estiu, G.; Caruso, F.; Ferraudi, G.; Costamagna, J. *Inorg. Chim. Acta* **2002**, *339*, 224.
12. Schreiber, R.; Cury, P.; Herrera, F.; Gomez, H.; Cordova, R. *J. Electroanal. Chem.* **2001**, *516*, 23.
13. Chiericato, G., Jr.; Arana, C. R.; Casado, C.; Cuadrado, I.; Abruña, H. D. *Inorg. Chim. Acta* **2000**, *300*, 32.
14. DuBois, D. L.; Miedaner, A.; Haltiwager, R. C. *J. Am. Chem. Soc.* **1991**, *113*, 8753; Lehn, J.-M.; Ziessel, R. *J. Organomet. Chem.* **1990**, *382*, 157.
15. Hammouche, M.; Lexa, D.; Momenteau, M.; Saveant, J.-M. *J. Am. Chem. Soc.* **1991**, *113*, 8455.
16. Memming, R. In *Topics in Current Chemistry*; Steckhan, E., Ed.; Springer: Berlin, 1988; Vol. 143, p 79, and references cited herein.
17. Zheng, J.; Lu, T.; Cotton, T. M.; Chumanov, G. *J. Electroanal. Chem.* **2002**, *518*, 6.
18. Lemke, F. R.; DeLaet, D. L.; Gao, J.; Kubiak, C. P. *J. Am. Chem. Soc.* **1988**, *110*, 6904.
19. Dey, G. R.; Belapurkar, A. D.; Kishore, K. *J. Photochem. Photobiol. A: Chem.* **2004**, *163*, 503.
20. *Organic Chemistry*; Clayden, J., Greeves, N., Warren, S., Wothers, P., Eds.; Oxford University Press, 2001; p 1027.
21. A concentric cell with two compartments, separated by a porous (D3) glass-frit diaphragm, and equipped with a magnetic stirrer, was employed. The catholyte was saturated by bubbling CO_2 . A platinum plate was used as cathode and a platinum net as anode. The solvent-supporting electrolyte system (SSE) was a nominally anhydrous 0.05 M solution of tetrabutylammonium tetrafluoroborate in acetonitrile. The volumes of catholyte and anolyte were 15 and 45 mL, respectively.
22. Benzyl chloride was electrolyzed under controlled potential conditions at +2.5 V, using the separated cell described in Ref. 21. When the reaction was finished the solvent in the anolyte chamber was removed under reduced pressure. The residue was extracted with ether/(5% NaHCO_3 solution) and the aqueous phase neutralized with 5% HCl solution and further extracted with ether. This second organic phase was dried over Na_2SO_4 and concentrated by evaporation. The obtained yields (36% α -chloro- α -phenyl acetic and 47% α -phenylacetic acid) are relative to the alkaline aqueous phase.
23. Batanero, B.; Barba, F.; Martín, A. *J. Org. Chem.* **2002**, *67*, 2369.
24. Otero, M. D.; Batanero, B.; Barba, F. *Tetrahedron Lett.* **2005**, *46*, 8681.
25. Greene, F. D.; Savitz, M. L.; Osterholtz, F. D.; Lav, H. H.; Smith, W. N.; Zanet, P. M. *J. Org. Chem.* **1963**, *28*, 55.
26. Appleguist, D. E.; Kaplan, B. I. *J. Am. Chem. Soc.* **1965**, *87*, 2194.