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Electrosynthesis of Imidazolium Carboxylates

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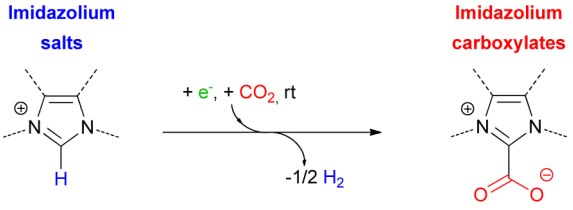
ABSTRACT



Synthesis of imidazolium carboxylate compounds was efficiently achieved by electrochemical reduction of imidazolium precursors under very mild conditions.

Although thermodynamically stable, N-heterocyclic carbenes (NHCs) are very reactive species and, thus, need to be stored under exclusion of air and moisture generally at low temperatures. They are commonly used in many applications such as ligands for organometallic catalysts, organic catalysis, material and drug syntheses, therapeutics, and electrochemistry.[1] Currently, a large majority of NHCs are synthesized from their corresponding imidazolium salts by deprotonation with a strong base (*n*-BuLi, tBuOK, NaH), which usually requires special conditions (low temperature, inert atmosphere).[2] Numerous works are devoted to the synthesis of stable masked carbenes such as imidazolium-2-carboxylate,[3,4] hydrogen carbonate,[5] 2-alkoxy,[6] 2-cyano,[7] 2-trichloromethyl,[8,9] 2-pentafluorobenzene,[7,10] 2-thioisocyanates,[11] and metal-stabilized NHCs[8,12] which can regenerate *in situ* free carbenes by thermal activation. Among these protected carbenes, synthesis of imidazolium-2-carboxylate is of particular interest due to the almost free cost of CO_2. These zwitterionic compounds react with numerous transition metals[3c,e,4] and electrophiles[3a,c,13] and are also useful building blocks to generate halide-free ionic liquids or imidazolium salts.[3] Two different pathways are currently described for the synthesis of imidazolium-2-carboxylate compounds. The first one

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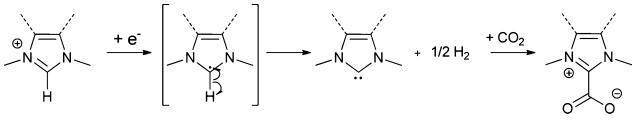
(named "B" as basic pathway) consists of deprotonation of an imidazolium salt at low temperature under an inert atmosphere generating the free carbene intermediate.[3a,c] After filtration and removal of NaX or KX salts (with X = halides) on Celite, passing CO_2 into the carbene containing solution generally leads to precipitation of the carboxylate adduct. The second method (named "DMC") lies on the direct one-pot N-methylation and C-carboxylation of N-monoalkylated imidazole precursors using dimethylcarbonate (DMC) as the reactant.[3b] In contrast to route B, this 7 h procedure requires a high temperature and pressure, typically 130 °C at 10 bar, and is limited to the methylation of the remaining unsubstituted nitrogen. Given the weak acidity of the NCHN proton of the imidazolium ring (pK_a ~20−24),[14] an interesting alternative toward the formation of the carboxylate may arise from its electrochemical reduction leading to the carbene and finally, after CO_2 addition, to the desired adduct (Scheme 1). Numerous reports have demonstrated the possibility to electrogenerate the carbene intermediate from its imidazolium salt. These carbenes have been trapped with different electrophiles[15] or metals[11] produced by anodic dissolution.

Scheme 1. Plausible Formation Mechanism of Imidazolium Carboxylate



Despite several publications reporting on the potential electrogeneration of transient carboxylate species,[16] to the best of our knowledge, their preparative isolation has never been reported although electrochemistry usually allows working under mild conditions.[17] Thus, we report here a new pathway (named "E" as electrochemical) toward the formation of imidazolium-2-carboxylate compounds or their bicarbonate evolution product by electroreduction of the corresponding imidazolium salts **1H$^+$,I$^-$**, **2H$^+$,I$^-$**, **3H$^+$,BF$_4^-$**, and **4H$^+$,BF$_4^-$** (Figure 1). Furthermore this original approach will be confronted with the above-mentioned chemical methods.

After **1H$^+$,I$^-$**, **2H$^+$,I$^-$**, **3H$^+$,BF$_4^-$**, and **4H$^+$,BF$_4^-$** were synthesized according to known procedures,[18] voltammetric studies were undertaken in DMF (Figure 2).

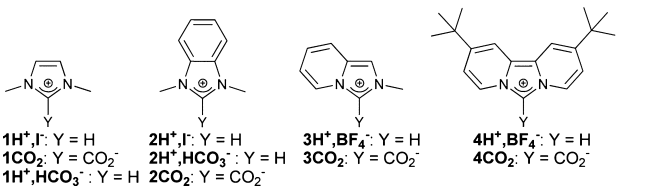


Figure 1. Molecular structure of the investigated imidazolium salts.

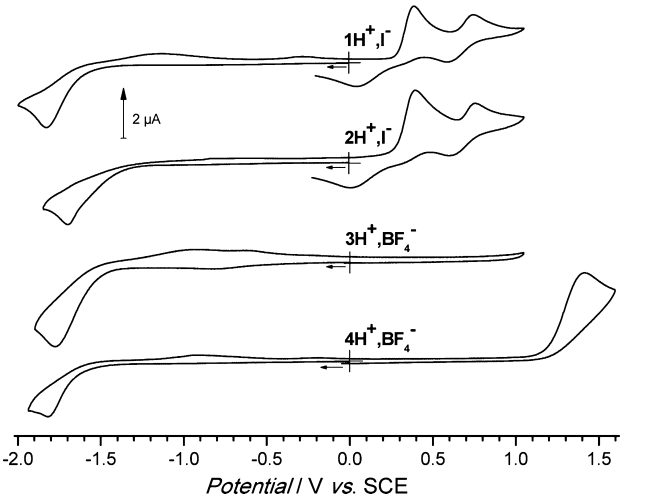


Figure 2. CVs of imidazolium salts in DMF containing 0.1 M $TBAPF_6$ (under Ar, WE: Pt, Ø = 1 mm, $\nu = 0.1\ V\ s^{-1}$, $c = 2.0 \times 10^{-3}$ M).

Cyclic voltammograms (CV) of these four imidazolium salts reveal one irreversible monoelectronic reduction at E_{pc} = −1.83, −1.70, −1.77, and −1.82 V/SCE, respectively. A similar potential, *i.e.* −2.2 V/SCE, has been previously reported by Clyburne and co-workers for the monoelectronic reduction of 1,3-bis(2,4,6-trimethylphenyl) imidazolium chloride. These authors have previously ascribed the irreversibility of this reduction process to a consecutive reaction which leads to the formation of H_2 and free carbene.[19] For **1H$^+$,I$^-$** and **2H$^+$,I$^-$**, two successive anodic oxidations are observed at E_{pa} = 0.39 (−1e) and 0.75 V/SCE (−0.5e) as expected for iodide salts. Additionally, **4H$^+$,BF$_4^-$** exhibits one irreversible oxidation at E_{pa} = 1.42 V/SCE. The higher intensity of this peak as compared to the monoelectronic reduction one (i_{pa}/i_{pc} = 1.56) implies that more than 1 F mol^{-1} is abstracted during this oxidation process, in agreement with an electrochemical−chemical−electrochemical (ECE) mechanism. However, the oxidation product(s) was-(were) not studied further. Similarly, in acetonitrile, a solvent allowing higher oxidation potentials to be reached compared

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to DMF, additional irreversible oxidation processes are observed at E_{pa} = 2.43, 2.26, 2.01 V/SCE for **1H$^+$,I$^-$**, **2H$^+$,I$^-$**, and **3H$^+$,BF$_4^-$**, respectively (see Supporting Information).

Electrosyntheses of imidazolium carboxylates were carried out at rt in DMF or CH_3CN (0.1 M $TBAPF_6$ or $TEAPF_6$) on a large area platinum electrode. As for the chemical deprotonation pathway, electrolyses were first conducted in two steps, *i.e.* reduction of the imidazolium salts under Ar and then bubbling of CO_2 into the solution at atmospheric pressure. However, following this procedure no carboxylate was obtained. Indeed, working at rt drastically increases the reactivity of carbenes or radicals which might be able to react during the time scale of the electrolysis with themselves, the supporting electrolyte, and/or the solvent. Nevertheless, in the particular case of **2H$^+$,I$^-$**, the imidazolium salt with a hydrogen carbonate counterion **2H$^+$,HCO$_3^-$** was produced. The latter is known to be the product of hydrolysis of the desired carboxylated material (**2CO$_2$**).[5]

With the hope of preventing side product formation, electrolyses were then performed directly under a CO_2 atmosphere by setting the working electrode at a potential corresponding to the first reduction step of imidazolium salts under these conditions. The current dropped to the residual current after an uptake of 1.1−1.5 mol equiv of electrons, in agreement with a one-electron transfer mechanism. Then, the CVs of the electrolyzed solutions no longer show the initial reduction peaks, which gives evidence for complete conversion of the reactants. After evaporation of the solvent, the solid residues were washed with THF to remove the supporting electrolyte, I^- or BF_4^-, and were dried under vacuum. Good to high yields were obtained (Table 1), validating the high interest of the electrochemical route. Indeed, this procedure is easy and highly selective, works at ambient temperature and atmospheric pressure, and is thus safe and energy-saving. Besides, workup is very simple, and though not experienced, the supporting electrolyte from the cathodic compartment could be potentially recycled. In the case of **1H$^+$,I$^-$** and **2H$^+$,I$^-$**, the carboxylate adducts consecutively react to the respective bicarbonate salts upon workup under nonabsolute conditions. This hydrolysis was also observed for "DMC" and "B" chemical pathways in the particular case of **2H$^+$,I$^-$**. The absence of oxidation peaks at E_{pa} = 0.39 and 0.75 V/SCE proves that these products are not contaminated by iodide impurities which are known to inhibit certain organometallic catalysts.

Indeed, after keeping the electrolyzed solution under a CO_2 atmosphere during the night, single crystals of **2H$^+$, HCO$_3^-$** suitable for X-ray diffraction analysis were obtained (Figure 3).

Table 1. Comparison of the Efficiency of the Three Different Methods for Carboxylate Synthesis (See Experimental Details in Supporting Information)

		product isolated yield (%)	
starting product	method[a]	CO_2^-	HCO_3^-
1H$^+$,I$^-$	E (1.50)	**1CO$_2$** 77[b]	**1H$^+$,HCO$_3^-$** 17[b]
1H$^+$,I$^-$	B	**1CO$_2$** 81	
1-methyl-imidazole	DMC	**1CO$_2$** 90	
2H$^+$,I$^-$	E		**2H$^+$,HCO$_3^-$** 56 (1.50), 57[d] (1.25), 66[c,d] (1.25)
2H$^+$,I$^-$	B	**2CO$_2$** 23[b]	**2H$^+$,HCO$_3^-$** 70[b]
1-methyl-benzimidazole	DMC	**2CO$_2$** 27[b]	**2H$^+$,HCO$_3^-$** 55[b]
3H$^+$,BF$_4^-$	E (1.14)	**3CO$_2$** 66	
3H$^+$,BF$_4^-$	B	**3CO$_2$** 55	
imidazo[1,5-*a*]pyridine	DMC	**3CO$_2$** 53	
4H$^+$,BF$_4^-$	E (1.50)	**4CO$_2$** 84	
4H$^+$,BF$_4^-$	B	**4CO$_2$** 83	

[a] E: Electrochemical (rt, 1 atm CO_2); values in brackets correspond to number of Faradays consumed per mole of imidazolium salts; B: deprotonation with a strong base; DMC: N-methylation and C-carboxylation using dimethylcarbonate. [b] Mixture of CO_2^- and HCO_3^-. [c] Electrolysis performed at −40 °C. [d] Performed in two steps (reduction then bubbling of CO_2).

Very few X-ray structure analyses of imidazolium bicarbonate salts have been reported to date.[4,20] Numerous short contacts (< sum of van der Waals radii) are observed in the crystal. In particular, HCO_3^- interacts with the slightly acidic H1, H8A, and H9A protons of the benzimidazolium moiety (C1−H1···O3 = 3.094(2), 142°; C8−H8A···O1 = 3.343(2), 160°; C9−H9A···O1 = 3.181(2), 122°) and forms a common H-bridged dimer with a second bicarbonate molecule (not shown).

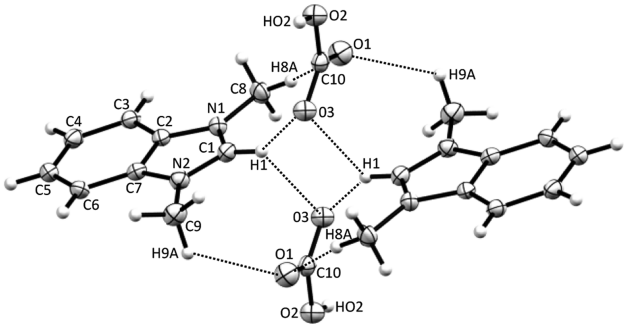

Figure 3. Ortep view of **2H$^+$,HCO$_3^-$**. Thermal ellipsoids are scaled to the 50% probability level.

Due to the absence of **2CO$_2$** upon electrochemical reduction of **2H$^+$,I$^-$** under CO_2 at rt, the same reaction was performed at −40 °C. Under these conditions, **2CO$_2$** was still not detected but **2H$^+$,HCO$_3^-$** was produced in

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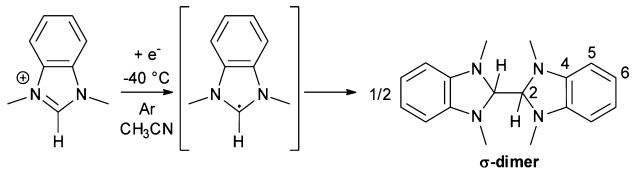
Scheme 2. Electrochemical Formation of the Neutral σ-Dimer



66% yield along with a white deposit which covered the platinum working electrode. This intriguing solid was directly dissolved in deuterated benzene for further NMR analyses. Its initial ^{1}H NMR spectrum was very simple, denoting the high symmetry of this compound. Its molecular structure can be unambiguously attributed to the ***σ*-dimer** depicted in Scheme 2.[21] Noteworthy, this compound corresponds to the bis-aminal of glyoxal with *N*,*N*′-dimethyl-1,2-phenylenediamine. Two multiplets centered at 6.80 (4 *H6*, see attribution in Scheme 2) and 6.33 ppm (4 *H5*) and two singlets located at 4.17 (2 *H2*) and 2.48 ppm (12 *H(Me)*) are observed.

The ^{1}H,^{13}C HSQC experiment reveals a correlation between the *H2* signal at 4.17 ppm and the *C2* signal at 91.1 ppm proving that this proton is bound to a C-atom. Moreover, the ^{1}H−^{1}H NOESY experiment confirms the spacial proximity of this *H2* proton (4.17 ppm) and the *N*-methyl group (2.48 ppm) as well as that of the proton H5 (6.33 ppm) and the *N*-methyl group (2.48 ppm). Additionally, the doublet ($^4J(Me/H2)$ = 0.4 Hz, 4.28 ppm) initially observed for methyl protons of $\mathbf{2H^+,I^-}$ is absent on this electrogenerated product which indicates a disruption of the conjugation between these protons. This rare radical−radical coupling product has been predicted to exhibit the lowest energy conformation by quantum chemical calculations.[22] Thus the absence of $\mathbf{2CO_2}$ stems from its subsequent hydrolysis to $\mathbf{2H^+,HCO_3^-}$ and also from the direct coupling of the electrogenerated intermediate radical. The ***σ*-dimer** is not stable under air over a longer period (< 1 h) and thus underwent a consecutive oxidation reaction in $CDCl_3$, finally providing $\mathbf{2H^+,Cl^-}$ as the major product which crystallized in the NMR tube and was identified by X-ray diffraction analyses. The chloride counteranion necessarily comes from the deuterated solvent which is known to contain a significant level of free chloride anion.

Common chemical "B" and "DMC" pathways were then undertaken to compare the efficiency of these well-known methods with the electrochemical pathway (Table 1). It should be mentioned that the "DMC" method cannot be performed with compound $\mathbf{4H^+,BF_4^-}$ due to the presence of fully substituted N-atoms, demonstrating in this particular case its limitation. Comparable yields were obtained supporting the high interest in electrosynthesis. Moreover, deprotonation of imidazolium salts with *t*BuOK only works with $\mathbf{2H^+}$–$\mathbf{4H^+}$. With $\mathbf{1H^+}$, a stronger base such as NaH is needed to generate the intermediate carbene demonstrating the lack of universality for the chemical method.

In conclusion, electrosynthesis of imidazolium carboxylates has been achieved for the first time. This very simple, versatile, environmentally benign (recycling of the supporting electrolyte provided), safe, and novel route proceeds at room temperature and atmospheric pressure of CO_2. It leads to the synthesis of pure carboxylate or hydrogenocarbonate compounds in yields comparable to those of the common DMC or the basic deprotonation pathway, but with a broader substrate spectrum. We now want to extend the scope of this method to more unusual azolium salts.

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Supporting Information Available. Copies of ^{1}H, ^{13}C, and 2D NMR spectra for all new compounds, details on experimental procedures, characterization data, HR-ESI mass spectra, IR spectra, X-ray structures of $\mathbf{2H^+}$, $\mathbf{HCO_3^-}$ and $\mathbf{2H^+,Cl^-}$. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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