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***N*-heterocyclic carbenes with negative-charge tags: direct sampling from ionic liquid solutions†**Priscila M. Lalli,^a Thyago S. Rodrigues,^b Aline M. Arouca,^b Marcos N. Eberlin*^a and Brenno A. D. Neto*^b

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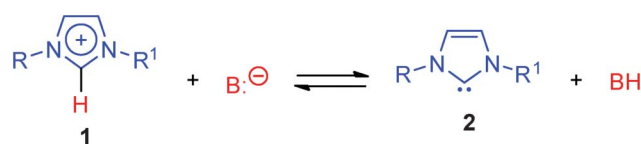
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Herein we report on the sampling and characterization *via* electrospray ionization (tandem) mass spectrometry of free, long-lived *N*-heterocyclic carbenes (NHC) bearing negative-charge tags. To facilitate electrospray “ion fishing” *via* electrostatic ejection directly to the gas phase, negative-charge tagged NHC were formed in imidazolium-based ionic liquid solutions *via* double deprotonation of imidazolium cations bearing acid side groups, *viz.* CH₂CO₂H or (CH₂)₃SO₃H. *Via* ESI-MS/MS experiments, the gaseous *N*-heterocyclic carbenes were found to display structurally diagnostic dissociations and bimolecular reactions. In perfect parallel to solution chemistry, the gaseous negative-charge tagged NHC were found to react promptly with CO₂ by carboxylation to form negative-charge tagged imidazolium carboxylates. Neutral carbenes were inaccessible for mass spectrometry, but the charge tag strategy opens many new possibilities to explore the intrinsic chemistry of these key but elusive species.

Introduction

Carbenes¹ are key but elusive chemical entities. Many reactions are known to involve carbenes as their pivotal intermediates but such highly reactive and fascinating hypervalent species were for a long time inaccessible to experimental observation. *N*-heterocyclic carbenes (NHC) such as those of the imidazolidene type **2** (Scheme 1) were the first carbenes to be isolated,² and these “bottleable” carbenes have since found many applications.³

Ionic liquids (IL)⁴ are of great academic, industrial and technological importance, and are used in many applications such

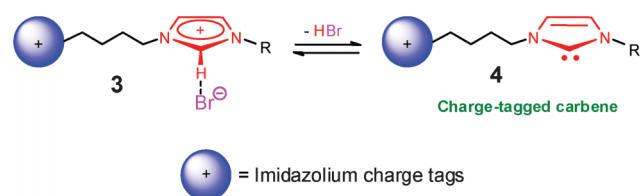
Scheme 1 NHC (**2**) formation from imidazolium-based IL (**1**).

as green solvents, catalysts and media for nanoparticle growth. Due to the relative acidity of the C2–H hydrogen (p*K*_a in the range of 21–23),⁵ imidazolium (**1**)-based IL coexist with NHC (**2**);⁶ hence **2** have been shown to have a major influence on IL properties, such as stabilizing metal complex derivatives and metal nanoparticles and acting as catalysts for reactions performed in these “noninnocent” IL.⁷

Mass spectrometry (MS) is inherently blind to neutral species,⁸ hence neutral carbenes have been investigated *via* gas phase MS experiments mainly in their ionized forms⁹ or indirectly *via* neutralization–reionization MS (NRMS) experiments.¹⁰ Using the “charge tag” strategy,¹¹ however, MS was made capable of handling “neutrals” and then, with the arrival of electrospray ionization (ESI),¹² charge tagged species have been formed in solution and “fished”¹³ directly into the isolated gas phase environment for MS measurements and intrinsic reactivity investigations.¹⁴

Via ESI-MS of solutions of bromine salts of doubly, triply and quadruply charged imidazolium ions,¹⁵ ionic pairs of NHC bearing positive-charge tags (**3**) have been “fished” to the gas phase and dissociated to form free positive-charge tagged NHC (**4**). It also appeared that **4** was concurrently fished presumably due to the **3** ⇌ **4** solution equilibrium (Scheme 2).

Herein we report a negative-charge version of the “charge tag” approach which we apply to the direct and efficient fishing from ionic liquid solutions of free and long-lived NHC with negative-charge tags (Scheme 3).

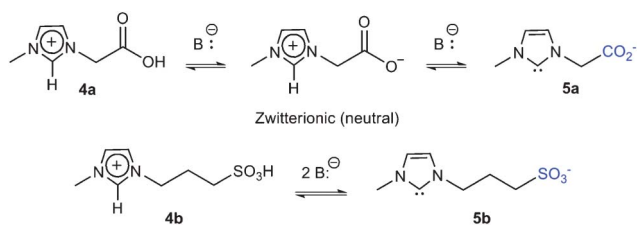


Scheme 2 Positive-charge tagged NHC.

^aThomson Mass Spectrometry Laboratory, Institute of Chemistry, University of Campinas, UNICAMP, Campinas, SP, Brazil, 13083-970. E-mail: eberlin@iqm.unicamp.br; Fax: +55 (19) 35213073

^bUniversity of Brasilia, Chemistry Institute, IQ-UnB Campus Universitário Darcy Ribeiro, CEP, Brazil, 70904-970, P.O. Box 4478, Brasilia, DF, Brazil. E-mail: brenno.ipi@gmail.com; Fax: +55 (61) 32734149; Tel: + 55 (61) 31073867

† Experiments were performed using a QTOF (Waters Manchester, UK) mass spectrometer with a hybrid quadrupole/orthogonal acceleration time-of-flight (oa-TOF) geometry. Instrument ESI source conditions were as follows: capillary voltage 2.5 kV, sample cone 30 V, extraction cone 3 V, source temperature 100 °C, desolvation temperature 100 °C, and desolvation flow rate 300 mL min⁻¹ of nitrogen. Ion/molecule reactions were performed by selecting the desired reactant at the quadrupole analyzer and by adding CO₂ to the collision cell at a pressure of *ca.* 1 mbar.



Scheme 3 Negative-charge tagged NHC formation in IL solutions from deprotonation of imidazolium ions bearing acidic side groups.

Results and discussion

To form NHC with negative-charge tags and to facilitate their ESI ejection in free, naked forms, we used imidazolium ions **4a,b** with acid side groups attached to one of the ring nitrogens as precursors (Scheme 3).

We postulated that double-deprotonation in solution of both acidic hydrogens of **4a,b** by the action of a base should form the desired long-lived free charge-tagged NHC **5a,b** in sufficient amounts for ESI fishing and MS detection and further manipulation in the gas phase. Fortunately, the mono-deprotonated zwitterionic species are neutral and therefore undetectable by ESI-MS, avoiding undesirable ion suppression effects from these intermediate species.

The chloride salts of **4a,b**¹⁷ were therefore diluted in methanol to form 100 μ M solutions and submitted to ESI-MS in the negative ion mode after addition of excess of KOtBu. Fortunately, the resulting ESI(-)-MS (Fig. 1) displayed predominant and abundant ions of m/z 139 (139.0529) and m/z 203 (203.0388) corresponding to the intact, free and long-lived negative-charge tagged NHC **5a,b**. ESI¹⁶ is known to be a technique that does not form ions, but transfers those already present in solution directly to the gas phase; hence, **5a,b** were,

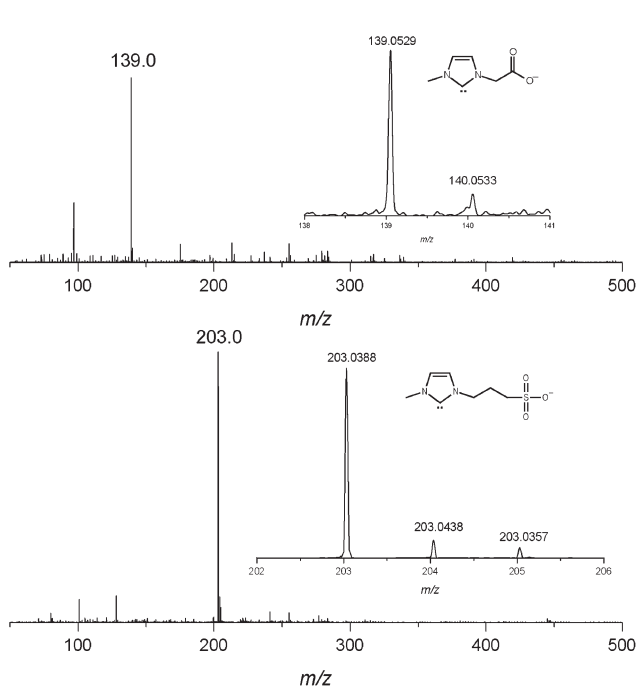


Fig. 1 ESI(-)-MS of methanolic solutions of IL **4a** and **4b** after addition of KOtBu. Note the detection of the negative-charge tagged NHC **5a** (m/z 139) and **5b** (m/z 203).

most likely, directly fished *via* electrostatic ion ejection¹⁸ from the IL solution.

To confirm the formation and interception of the unprecedented **5a,b**, these anions were isolated and subjected to dissociation and structurally diagnostic ion/molecule reactions¹⁷ with CO₂. The resulting spectra after dissociation (Fig. 2) reveal structurally diagnostic chemistries that support the negative-charge tagged NHC structures **5a,b** (Scheme 4).

NHC are known to display rich reactivity,³ acting mostly as strong electrophiles or nucleophiles depending on the nature of the counter reactant.¹⁸ Recently, it was reported that NHC in IL solutions freely react with CO₂ to form imidazolium carboxylates.¹⁹ The gaseous **5a,b** were therefore reacted with CO₂ (Fig. 3) and, in perfect parallel with the solution chemistry, found to react promptly with CO₂ (Scheme 5) to form abundant negative-charge tagged imidazolium carboxylates **6a** of m/z 183 (183.0432) and **6b** of m/z 247 (247.0299).

Conclusions

Both the structurally diagnostic unimolecular dissociation chemistry upon collision with argon as well as the bimolecular ion/molecule reactivity towards CO₂ provided evidence that, *via* ESI, long-lived

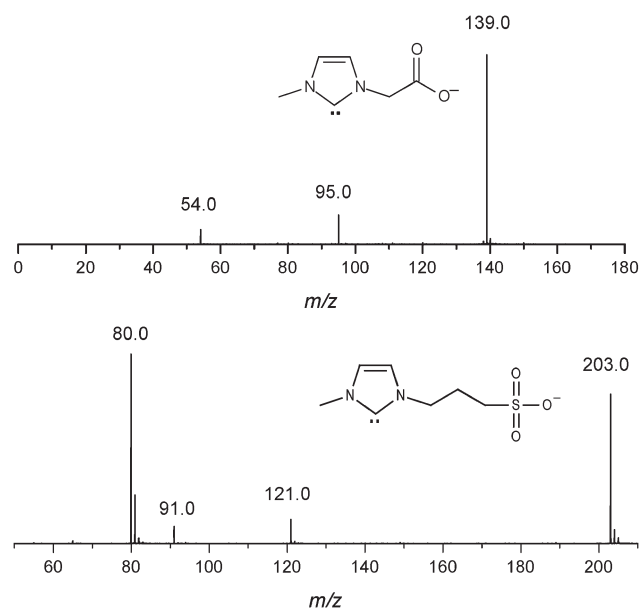
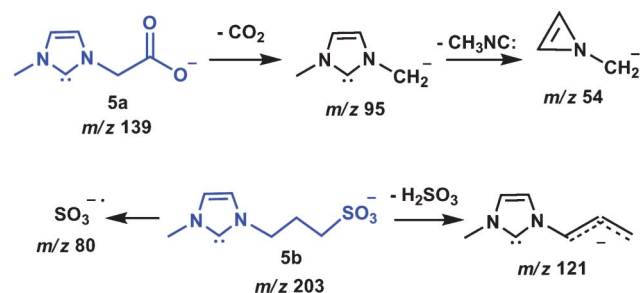


Fig. 2 ESI(-)-MS/MS for collision-induced dissociation of the negative-charge tagged NHC **5a,b**.



Scheme 4 Proposed routes and structures for the collision induced dissociation of the gaseous negative-charge tagged NHC **5a,b**.

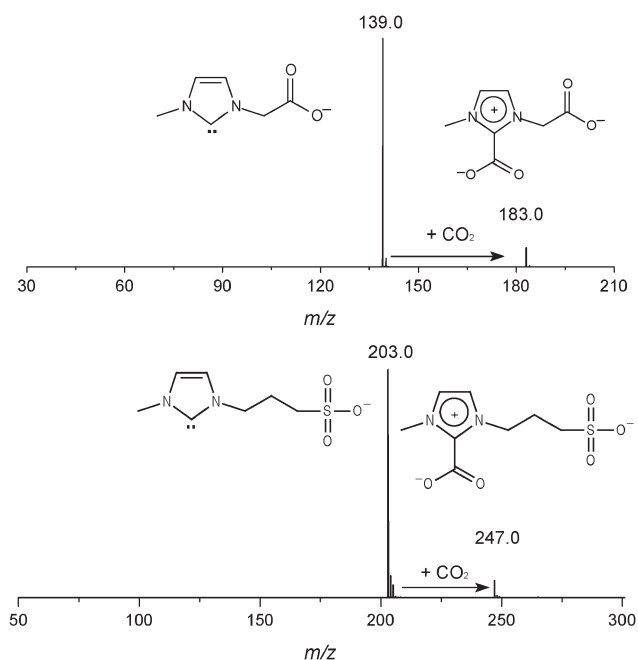
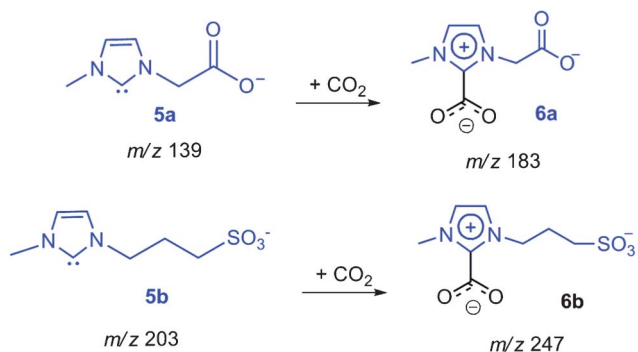


Fig. 3 ESI(-)-MS/MS for ion/molecule reactions of the negative-charge tagged NHC **5a,b** with CO_2 generating **6a** (m/z 183) and **6b** (m/z 247).



Scheme 5 Gas-phase carboxylation (ion/molecule reaction) of **5a,b**.

free negative-charge tagged NHC can be efficiently fished from solutions of imidazolium ions bearing acid side groups directly to the isolated gas phase environment of a mass spectrometer. The gentle transfer of these “naked” NHC to the gas phase and the finding of the prompt addition of these ions to CO_2 , which perfectly parallels solution chemistry, opens unique opportunities to investigate, *via* MS experiments, the intrinsic physico-chemical properties and the solvent and counter-ion free reactivity of many types of reactants with gaseous NHC. These pivotal species can now be efficiently prepared in solution, gently ejected to the gas phase by ESI and properly manipulated inside mass spectrometers with the assistance of either positive¹⁵ or negative-charge tags.

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