

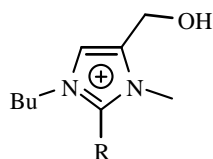
Imidazolium Ionic Liquids: C2 Substitution and Acidity

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Room temperature ionic liquids (RTILs) are continuing to attract a great deal of attention, particularly as solvent alternatives for a wide range of organic reactions.¹ In examining the RTILs employed in virtually all of these efforts, the core structure is most frequently a dialkylimidazolium cation. Although rather robust to a wide range of chemical conditions, this species is readily able to undergo deprotonation at the 2 position, resulting in the formation of a carbene. This carbene can be very useful, serving as a ligand for many transition metal complexes and even as a nucleophilic catalyst itself. At the same time, the reactivity of this carbene can be detrimental in other situations as has been observed by Aggarwal and ourselves.² To that end, we have begun a study both of the acidity of the 2 position as well as convenient methods for substituting this position to avoid base-induced complications.

The acidity of dialkylimidazolium salts has been reported before in the literature by Streitwieser. In his studies, the pK_a of this position in 1,3-di-*tert*-butylimidazol-2-ylidene was determined to be 23 in DMSO.³ This is surprisingly high, considering that many reports have noted the generation of imidazole carbene modified palladium species in the presence of no base stronger than triethylamine. Further, in Aggarwal's work, the strongest base was DABCO, while in our earlier studies the base was sodium hydroxide or methoxide. In all of these cases, one would not necessarily expect significant deprotonation of the 2 position.

To examine this acidity more carefully, a series of deuterium exchange reactions have been conducted in D₂O. Although it was expected that the C2 position would be relatively acidic, it was surprising to note that dicyanamide salt **1** underwent exchange quite rapidly in the absence of any added base (rate = 3.0 x 10⁻⁵ min⁻¹). Indeed, a similar result was obtained for the corresponding butyl,methylimidazolium dicyanamide salt (4.1 x 10⁻² min⁻¹). One possible explanation for these observations is the fact that aqueous solutions of sodium dicyanamide are reported to be slightly basic (pH of roughly 8). As a result, the anion may be serving as the base in these salts. To test this hypothesis, a similar exchange experiment was conducted on butyl,methylimidazolium tetrafluoroborate. In this case, no exchange was observed for up to 72 hours without the addition of base.

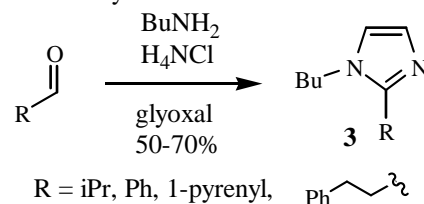


- 1** R = H
2 R = Me

Given this high degree of acidity, 2-methyl substituted compounds were also investigated. They were expected to be much less susceptible to exchange, so it was not surprising that these salts failed to undergo any detectable exchange in the absence of added base. What was more

surprising was the observation that even a very mild base such as triethylamine was sufficient to induce a slow but measurable exchange at the C2 methyl group. Thus, the fructose-derived dicyanamide salt **2** underwent complete, though slow, exchange of the three protons at this position (4.0 x 10⁻⁵ min⁻¹). The presence of a stronger base such as potassium hydroxide greatly increased this rate (2.3 x 10⁻³ min⁻¹). The simple butyl,methylimidazolium salts behaved similarly.

As a result, it appears that basic stability may require even more highly substituted groups at the 2 position. To study this possibility, we have begun exploring a three step synthesis of the substituted products outlined below. An additional source of interest in these compounds is the growing attention focused on functionalized or "task-specific" RTILs, which can serve a number of diverse functions, including homogeneous supports or chelating agents for specific metals or compounds.⁴ Thus, condensation of an aldehyde with equimolar amounts of butylamine, ammonium chloride, and glyoxal affords the substituted products **3** in generally good (60-70%) yield. Alkylation, followed by anion metathesis completes the synthesis of the 2-substituted RTILs. Rather conveniently, this procedure works with alkyl and aromatic aldehydes. With these compounds in hand, the study of the acidity and exchange of these various new RTILs is underway.



¹ *Ionic Liquids in Synthesis*; Wasserscheid, P.; Welton, T., Eds.; Wiley-VCH: Weinheim, Germany, 2003.

² Aggarwal, V.K.; Emme, I.; Mereu, A. *Chem. Commun.* **2002**, 1612-1613. Handy, S.T. Okello, M. *Tetrahedron Lett.* **2003**, *44*, 8399-8402.

³ Kim, Y.-J.; Streitwieser, A. *J. Am. Chem. Soc.* **2002**, *124*, 5757-5761.

⁴ Davis, Jr., J.H.; Fox, P.A. *Chem. Commun.* **2003**, 1209-1212. Handy, S.T. Okello, M. *Tetrahedron Lett.* **2003**, *44*, 8399-8402.