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Proton Affinities of *N*-Heterocyclic Carbene Super Bases

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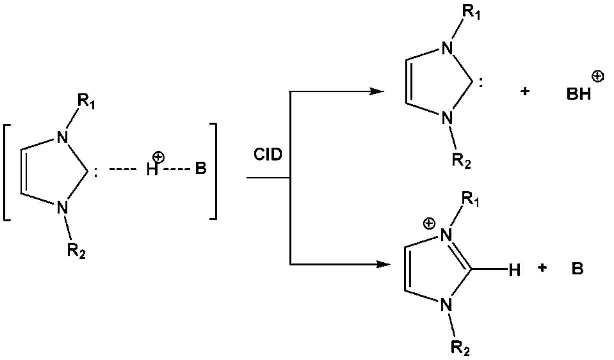
ABSTRACT

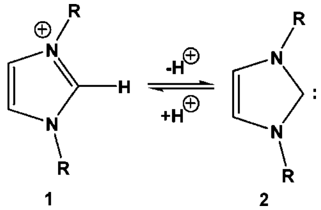


The gas-phase proton affinity of the *N*-heterocyclic carbene, 1-ethyl-3-methylimidazol-2-ylidene, was determined to be 251.3 ± 4 kcal/mol using the kinetic method, a value which makes the carbene one of the strongest bases reported thus far. Density functional theory calculations have been carried out at the B3LYP/6-31+G(d) level to compare the high experimental value with that estimated theoretically. Experimental results also show that two other *N*-heterocyclic carbenes with larger substituents have even higher proton affinities.

The thermochemical properties of carbenes, including their proton affinities (PAs, the negative of the enthalpies of their protonation reactions), are of fundamental interest since carbenes play key roles as reactive intermediates in many organic reactions.[1] However, due to their transient nature, limited accessibility, and the special experimental techniques required for their detection, the measurement of the PAs of carbenes is extremely challenging. Previous measurements are limited to very few carbenes such as difluorocarbene $:CF_2$ (172 ± 2 kcal/mol)[2] and dichlorocarbene $:CCl_2$ (208.3 ± 2 kcal/mol),[3] as well as to related compounds such as silylene SiH_2: (201 ± 3 kcal/mol),[4] and were made using proton-transfer bracketing methods.

A breakthrough[5] in organic structural chemistry is the successful isolation of a stable singlet *N*-heterocyclic carbene, 1,3-di-1-adamantylimidazol-2-ylidene **2** (R = 1-adamantyl), simply by the deprotonation of an imidazolium salt (Scheme 1).[6] This appears to provide a general method for the formation of various *N*-heterocyclic carbenes. The most striking application of electron-rich *N*-heterocyclic carbenes occurs in organometallic catalysis where they serve as novel metal ligands to enhance catalytic activity (e.g., the second-generation Grubbs ruthenium olefin metathesis catalyst).[7]

Scheme 1. Formation of Carbene from Imidazolium Ion



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1,3-Dialkylimidazolium salts are among the most thoroughly investigated classes of room-temperature ionic liquids (ILs).[8] They are used as novel solvents for organic synthesis due to their extraordinary solubilizing power and negligible vapor pressure.[9] However, it has been observed that ILs having an imidazolium structure are unstable in the presence of base.[10] This instability would prevent imidazolium ILs from being used as a general medium to perform base-catalyzed reactions. These considerations make information on the acidity of the imidazolium ions or the PA values of the corresponding *N*-heterocyclic carbenes highly significant. The basicity of *N*-heterocyclic carbenes and the acidity of the C2 hydrogen of the imidazolium nuclei in solution have been studied by several groups.[11] However, the gas-phase PAs of *N*-heterocyclic carbenes have not been investigated experimentally, although both theoretical[12] and experimental evidence[13] for the existence of *N*-heterocyclic carbenes in the gas phase has been obtained.

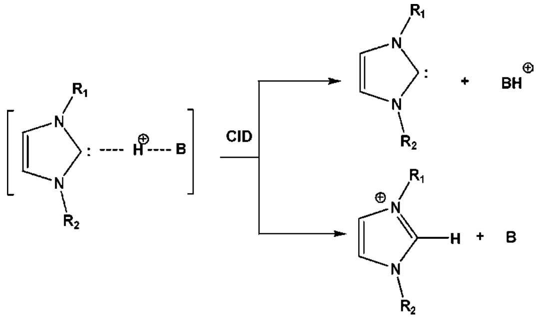
Thermochemical properties of nonvolatile compounds including their PAs can be estimated by the mass spectrometric kinetic method.[14] The method relies on the isolation of a proton-bound cluster which dissociates primarily through two competitive pathways as shown in eq 1 below.

$$B_1H^+ + B_2 \leftarrow [B_1HB_2^{\,+}] \rightarrow B_2H^+ + B_1 \tag{1}$$

Thermochemical information may be obtained from the product ion spectrum of the mass selected cluster ion using the relationship $\ln(I_1/I_2) = (\Delta[\Delta G])/RT_{\mathrm{eff}} = (\Delta[\Delta H])/RT_{\mathrm{eff}} - (\Delta[\Delta S])/R$. In this equation, I_X ($x = 1, 2$) is the relative abundance of the product ion B_XH^+, R is the ideal gas constant, T_{eff} is the effective temperature of the excited cluster ion, and $\Delta(\Delta G)$, $\Delta(\Delta H)$, and $\Delta(\Delta S)$ are the differences in the free energy, enthalpy, and entropy of protonation between the two bases, B_X.

Herein, we report the gas-phase PAs of *N*-heterocyclic carbenes, as measured by the extended version of the kinetic method.[15] In this study, the proton-bound dimer ions of the *N*-heterocyclic carbene with the reference bases (Scheme 2) were generated by electrospray ionization (ESI) of a methanol/water solution containing an imidazolium salt (e.g., a room-temperature IL, 1-ethyl-3-methyl-1*H*-imidazolium tetrafluoroborate), and one of the commercially available reference super bases (SB, compounds characterized by PAs above 1000 kJ/mol or 239 kcal/mol).[16] The two super bases used were 1,5-diazabicyclo[4.3.0]non-5-ene (**DBN**, PA = 248.16 kcal/mol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (**DBU**, PA = 250.45 kcal/mol). The dimer subsequently fragments into the protonated reference SB by loss of the *N*-heterocyclic carbene and competitively to the imidazolium ion by loss of the reference SB upon collision-induced dissociation (CID) (Scheme 2). The two SBs were chosen for three reasons: (i) they contain imino functional groups and are structurally similar to the analyte; under these circumstances, the difference in the entropy of protonation between the reference base and the carbene remains constant, providing the basis for the application of the extended version of the kinetic method to obtain PA values;[15] (ii) they have self-consistent thermochemical values as reported by Hunter and Lias;[17] and (iii) their cognate carbenes are expected to have extremely high gas-phase basicities, as indicated by experimental results in solution[11] and by theoretical calculations.[18] Determination of their gas-phase PAs therefore requires reference compounds with very high PAs in order to obtain accurate peak ratios. (Note that the kinetic method ideally requires at least three references for good accuracy. In this study, accessibility to three good references was difficult. Phosphazenes failed to form clusters with imidazolium ions; instead, they generated predominantly protonated molecules during electrospray ionization, even in aprotic solvents such as CH_2Cl_2. We also considered guanidine derivatives as the reference bases, but their multiple basic sites could result in high entropy effects in kinetic method measurements).

Scheme 2. Fragmentation Pathway of Dimer Ions



Collision-induced dissociation of the mass-selected cluster ion was effected, and the abundance ratio of the resulting protonated monomers was measured. As an example, Figure

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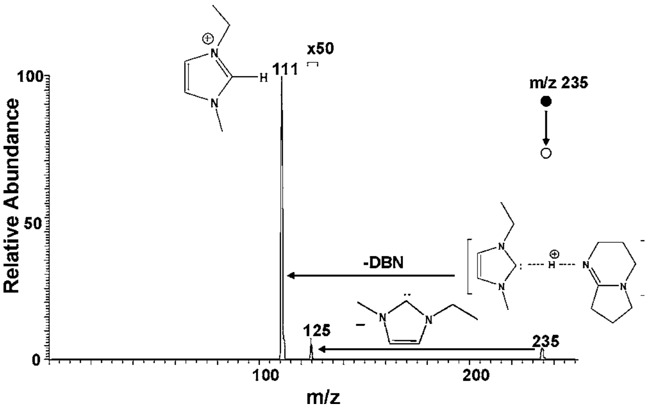

Figure 1. Product ion mass spectrum of the mass-selected **[3- - -H- - -DBN]**$^+$ cluster ion at 10 eV collision energy under multiple collision CID conditions showing formation of two competitive fragment ions.

1 shows the product ion spectrum of the proton-bound cluster ion of 1-ethyl-3-methylimizadol-2-ylidene **3** with **DBN** yielding two products corresponding to the individual protonated monomers, the imidazolium cation (*m*/*z* 111, i.e., the protonated carbene) and **[DBN + H]**$^+$ (*m*/*z* 125).

The predominance of the peak of *m*/*z* 111 relative to that at *m*/*z* 125 strongly suggests that **3** has a higher gas-phase PA than **DBN**. This tentative conclusion was tested further by performing CID experiments on the cluster ion generated from the two SBs each complexed with the imidazolim ion at five different collision energies. The results are summarized in Table 1.

Table 1. Natural Logarithm of Product Ion Abundance Ratios *R* for CID of the Proton-Bound Dimers

	CID energies (eV)	**DBN**	**DBU**	T_{eff} (K)
ln *R*	10	−6.66 ± 0.16	−3.30 ± 0.60	344
	15	−6.50 ± 0.08	−3.26 ± 0.63	357
	20	−6.43 ± 0.55	−3.24 ± 0.61	362
	40	−6.22 ± 0.22	−3.03 ± 0.48	363
	50	−5.58 ± 0.18	−2.99 ± 0.69	447

The natural logarithm of the ratio R of the product ion abundances ($R = I_{\mathrm{ref}}/I_{\mathrm{carbene}}$) is first plotted versus the known gas-phase PAs of the reference SBs (plot 1, Figure 2). This treatment provides straight lines at each collision energy with different slopes and intercepts. Then, the negative intercepts were plotted against the slopes of each of these plots to obtain a second plot, from which the PA of 1-ethyl-3-methylimizadol-2-ylidene **3** was determined as 251.3 ± 4 kcal/mol (assuming no error in the PAs of the references) and the difference in entropy of the two competitive fragmentation channels was found to be 4.1 cal/mol K. The effective temperature, T_{eff}, derived from the kinetic method plots varied from 344 to 447 K as the collision energy was increased from 10 to 50 eV. Density functional theory (DFT) calculations at the B3LYP/6-31+G(d) level were carried out to estimate the PA of the carbene **3**, which gives a value of 260.8 kcal/mol, including a thermal correction (298.15 K, 1 atm). This calculated value is higher than the above experimental value by 9.5 kcal/mol. The phenomenon that calculated thermochemical values using DFT are higher than the experimental values was observed previously. For instance, the theoretical value of the gas-phase basicity of tetra-*tert*-butyltetrahedrane obtained from the B3LYP/6-31G(d) was reported to be 23 kcal/mol higher than the experimental data meaured by the equilbrium method,[19] and a very large basis set was therefore suggested for the computation. Our calculated PA for the carbene **3** is close to the PA of its parent carbene, imidazol-2-ylidene (258.4 kcal/mol), calculated at the B3LYP/6-31G* level by Alder.[18a]

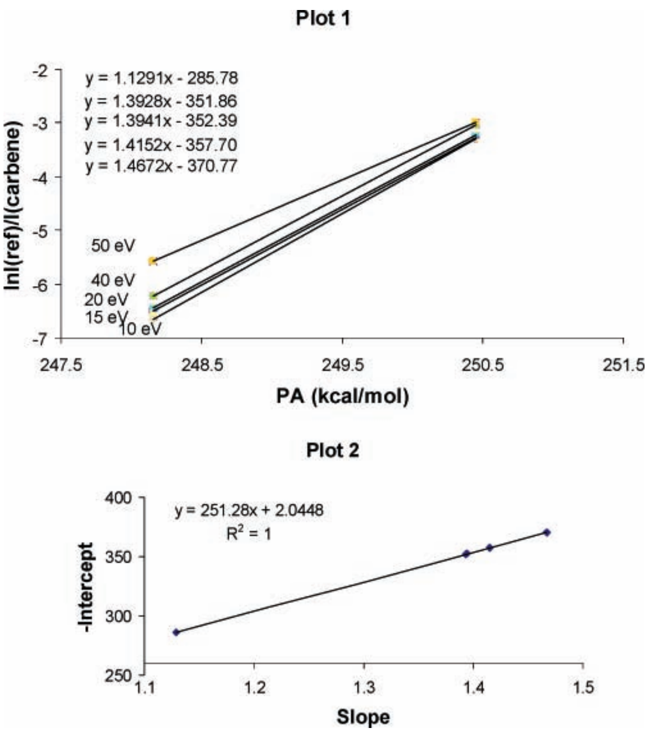

Figure 2. Plots of the extended version of the kinetic method (error bars in plot 1 are not shown for clarity).

Figure 3 displays the B3LYP/6-31+G(d)-optimized structures of the planar singlet carbene (a), its precursor imidazolium ion (b), and its cluster ion with **DBN** (c). Several different rotational isomers of the carbene **3** were tested, and the one shown in Figure 3a is the best rotamer. The calculation also shows that the singlet−triplet splitting for this carbene is very large, 82.8 kcal/mol, and thus the chemistry will be dominated by the ground-state singlet. The singlet stablity stems from the π-donor, σ-acceptor nature of the amino substituents in the carbene. In addition, in the cluster ion, the distance between the C2 hydrogen of the imidazo-

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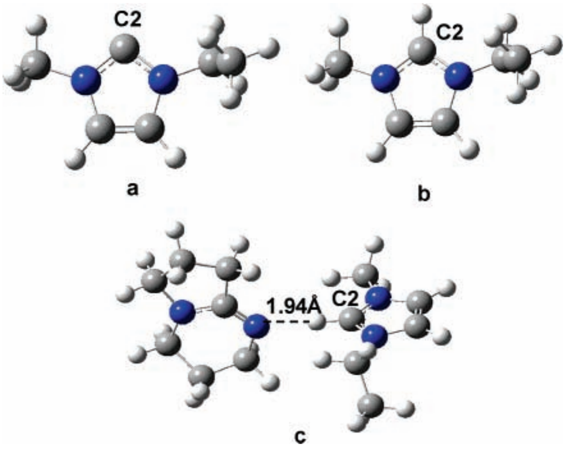

Figure 3. Optimized structures of **3** (a), its precursor imidazolium ion (b), and its cluster ion with **DBN** (c) calculated by DFT at the B3LYP/6-31+G(d) level.

lium ion and the nitrogen of the imino group of **DBN** is 1.94 Å.

Other *N*-heterocyclic carbenes examined included 1,3-di-*tert*-butylimizadol-2-ylidene **4** and 1,3-di-(2,6-isopropylphenyl)imizadol-2-ylidene **5**. Using **DBU** as the reference base, the natural logarithm of the ratio R of the product ion abundances ($I_{\mathrm{ref}}/I_{\mathrm{carbene}}$) under the same CID conditions (collision energy and pressure) follows the order: **3** > **4** > **5** (see the table in the Supporting Information), indicating the PA order **3** < **4** < **5**. This is in agreement with the expected substituent effect, assuming large substituents can stabilize the imizadolium ion. This observed substituent effect is also consistent with the computational results by Lee[18b] which show an increase in PA with increasingly bulky substituents.

In conclusion, we present the first experimental measurements of gas-phase PAs of *N*-heterocyclic carbene super bases. This fundamental information on these species may lead to greater insight into their reactivity. The measured PA of 1-ethyl-3-methylimidazol-2-ylidene (251.3 ± 4 kcal/mol) places it as one of the most basic neutral compounds as well as the most basic carbene species measured thus far. This study also extends the application of the kinetic method to the measurement of thermochemical values of exotic species in the gas phase.

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Supporting Information Available: Experimental details and data on substituent effects are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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