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Assessing the Proton Affinities of *N,N′*-Diamidocarbenes

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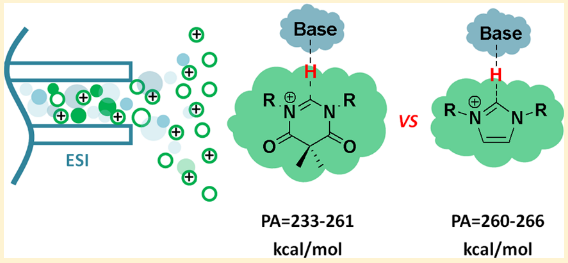
Supporting Information

ABSTRACT: The gas-phase proton affinities (PAs) of a series of novel diamidocarbenes (DACs) were assessed and compared to various imidazolylidene-based *N*-heterocyclic carbenes (NHCs) through experimental and computational methods. Apart from a perfluorinated-phenyl derivative (PA = 233 kcal/mol), the calculated and measured PAs for a range of DACs (256−261 kcal/mol) were comparable to those of the NHCs (260−266 kcal/mol). Proton transfer from the protonated carbene to various reference bases, as observed by mass spectrometry, was inhibited by steric bulk and precluded the direct measurement of the PA for the known DACs, *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene and *N,N′*-diisopropylphenyl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene. However, DACs featuring less hindered *N*-aryl substituents facilitated proton transfer, and the measured PA values were found to be consistent with density functional theory calculations (B3LYP/6-31+G(d)). Notably, the PAs of the DACs studied were similar to those of the NHCs, indicating that the former retain many of the nucleophilic characteristics intrinsic to their parent diaminocarbenes and that the observed differences in chemical reactivity may be primarily attributed to an enhanced electrophilicity.



INTRODUCTION

Traditional carbenes (e.g., methylene) are typically electrophilic and display commensurate chemical reactivity profiles including abilities to insert into C−H bonds, activate H_2, cyclopropanate olefins, and couple to carbon monoxide to form ketenes.[1−4] However, the transiency of methylene and other electrophilic carbenes also requires in situ generation methods, which can be problematic and avoided through the use of isolable analogues. Following the first report of a stable carbene by Bertrand over two decades ago,[5] Arduengo and co-workers isolated the first crystalline carbene through incorporation into an *N*-heterocyclic scaffold.[6] The carbenoid character (or lack thereof) of the *N*-heterocyclic carbenes (NHCs, Figure 1) has been a topic of some controversy.[7−10] Regardless, when compared to traditional carbenes, NHCs are relatively nucleophilic and often display different reactivities. For example, NHCs do not activate H_2 nor fix carbon monoxide to make ketenes;[11] they do, however, bind to transition metals, a process that often results in catalysts with superior activities,[12−14] and react with elemental sulfur and electrophilic heteroallenes.[15]

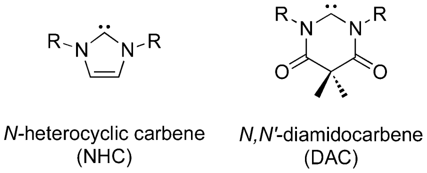


Figure 1. General structures for an *N*-heterocyclic carbene (NHC) and an *N,N′*-diamidocarbene (DAC).

Recently, we developed the *N,N′*-diamidocarbenes (DACs, Figure 1) which are not only stable but feature enhanced electrophilic properties due to the strategically placed carbonyl groups that draw electron density from the adjoining nitrogen atoms away from the carbene center.[16−20] The reactivity profile of the DACs is similar to that of traditional carbenes, and examples of C−H insertions,[16] CO fixation,[16,17,21] and NH_3 activation[17] have been reported. Using computational methods, the unique reactivities of the DACs have been attributed to the relatively low-lying lowest unoccupied molecular orbital (LUMO) in conjunction with a highest occupied molecular orbital (HOMO) energy level similar to that of prototypical NHCs.[22] Thus, while the DACs are relatively electrophilic, they are still nucleophilic and coordinate to a broad range of transition metals as well as couple to a range of electrophilic compounds.[16,23,24] Since basicity often correlates with nucleophilicity, we reasoned that measuring the proton affinity (PA) of the DACs would facilitate quantitative comparisons to other carbenes and guide the development of new classes of DACs and potentially other stable, electrophilic carbenes.

Several strategies have been developed to study the affinities of carbenes for protons, including both pK_a and PA measurements. The former largely involve monitoring the exchange of isotopes in water[25−28] or the reaction of the free

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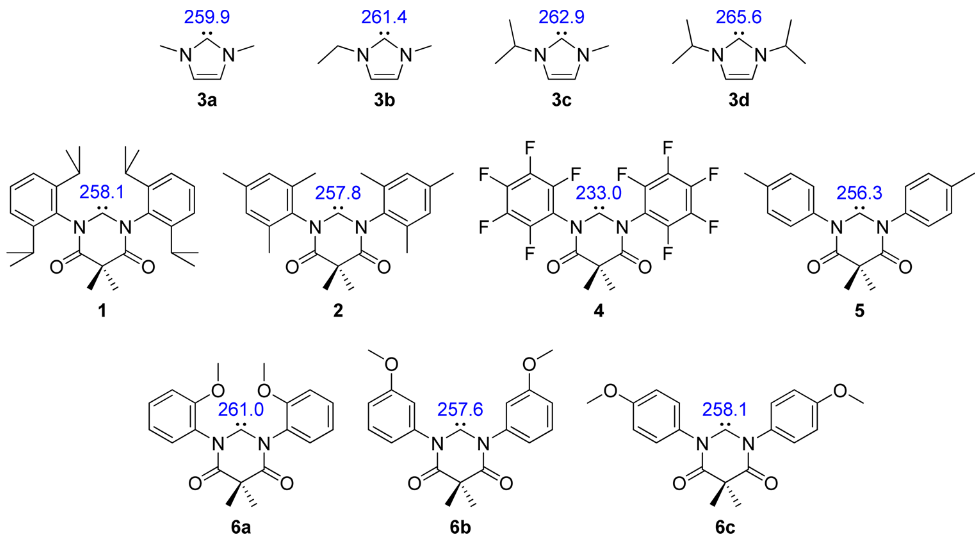
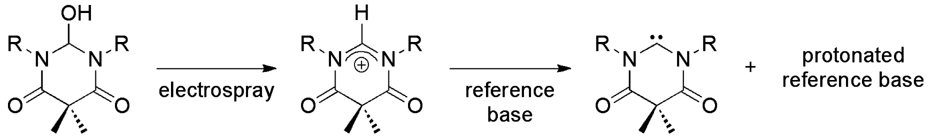


Figure 2. Calculated proton affinities in kcal/mol at 298 K for selected NHCs and DACs using B3LYP/6-31+G(d).

Scheme 1



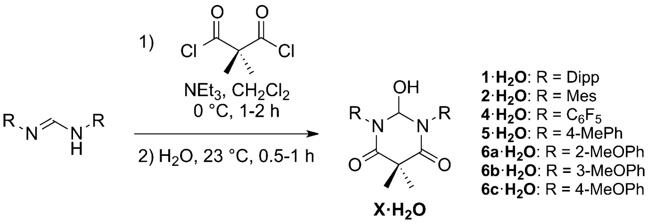
carbene with hydrocarbon indicators in THF or DMSO.[29−31] While these methods enable solution-state determination, solvent incompatibility can arise, and the resultant values are highly solvent dependent. In comparison, proton affinity values are intrinsic to the chemical entity and may be measured in the gas phase through mass spectrometry.[32,33] Recently, we reported the reaction of reference bases with cationic carbene precursors in the gas phase which enabled the bracketing of PA values for the corresponding carbenes.[34,35]

In this paper, we describe experimental and computational PA studies of known as well as new DACs in the gas phase. We found that, despite the incorporation of electron-withdrawing carbonyl groups adjacent to the nitrogen atoms, the DACs display PA values similar to the NHCs studied herein. Collectively, these results, which are consistent with density functional theory calculations and observed chemical reactivity, indicate that the DACs display similar basicities and nucleophilic characteristics as the NHCs and provide a means to quantitatively compare these classes of stable carbenes.

■ RESULTS AND DISCUSSION

Our initial efforts were directed toward determining the PAs of the known DACs **1** and **2** which were calculated by density functional theory to be similar (ca. 258 kcal/mol); by comparison, the calculated PA values of the NHCs **3a**−**d** were only modestly higher (260−266 kcal/mol) than those of the DACs (Figure 2).[36] To experimentally measure the PAs of the **1** and **2**, attention shifted to mass spectrometry and proton-exchange reactions between the protonated carbene precursors (i.e., **1H**$^+$ and **2H**$^+$) and various bases in the gas phase which had previously been utilized for determining the PA values of various NHCs.[34,35,37] Whereas the prior studies of the NHCs had been conducted directly with the air-stable salt precursors, the tendency to form covalent rather than ionic carbene precursors as well as the high water sensitivity of the DAC precursors necessitated a modified introduction method. Fortunately, electrospray ionization of the formally hydrated version of the DAC (e.g., **1·H$_2$O**; Scheme 1, R = 2,6-diisopropylphenyl) dissolved in formic acid solution was found to successfully yield **1H**$^+$ as the major signal. The synthesis of the water adduct of **1** (and other derivatives reported in this paper) was carried out as shown in Scheme 2.[17]

Scheme 2



Dipp = 2,6-diisopropylphenyl; Mes = 2,4,6-trimethylphenyl

As summarized in Table 1, **1H**$^+$ was exposed to various strong bases in the gas phase to test for the occurrence of proton transfer. Given the calculated PA of DAC **1** (258.1 kcal/mol), we were surprised that bases as strong as 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP; PA = 263.8 kcal/mol) failed to deprotonate **1H**$^+$. Similarly, attempts to bracket the PA of DAC **2** were also unsuccessful. As we had previously bracketed the PAs of NHCs **3a** and **3b** (which have relatively small substituents) experimentally through analogous gas-phase measurements,[34,35] sterics were envisioned to inhibit proton transfer. Subsequent efforts were directed toward two bulkier NHC derivatives, **3c** and **3d**. For **3cH**$^+$, we observed proton transfer to BEMP (PA = 263.8 kcal/mol) but not to *tert*-octyliminotris(dimethylamino)phosphorane (tOctP$_1$(dma); PA

Table 1. Summary of the PA Bracketing Results for DACs 1, 2 and NHCs 3c, 3d

		proton transfer to reference base[b]			
ref base[a,39]	PA (kcal/mol)	**1H**$^+$	**2H**$^+$	**3cH**$^+$	**3dH**$^+$
BEMP	263.8 ± 2.0	−	−	+	−
tOctP$_1$(dma)	262.0 ± 2.0	−	−	−	−
tBuP$_1$(dma)	260.6 ± 2.0	−	−	−	−
HP$_1$(dma)	257.4 ± 2.0	−	−	−	−

[a] BEMP = 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine; tOctP$_1$(dma) = *tert*-octyliminotris-(dimethylamino)phosphorane; tBuP$_1$(dma) = *tert*-butylimino-tris-(dimethylamino)phosphorane; HP$_1$(dma) = iminotris-(dimethylamino)phosphorane. [b] The "+" symbol indicates the observation of proton transfer, and the "−" symbol indicates the lack of observed proton transfer.

= 262.0 kcal/mol; Table 1). Thus, the PA of **3c** was determined to be between 262.0 and 263.8 kcal/mol, consistent with the computationally predicted PA of 262.9 kcal/mol. BEMP did not effect proton transfer with **3dH**$^+$ (Table 1), and reference bases with PAs higher than BEMP were not practical due to their nonvolatility.[38] We therefore assigned the PA for the corresponding carbene as >263.8 kcal/mol, in agreement with the calculated value of 265.6 kcal/mol.

In light of our success with the PA measurement of the NHCs,[34,35] we re-examined potential steric inhibition of proton transfer for DACs **1** and **2**. In addition to the relatively large *N*-aryl substituents of the aforementioned DACs, the strong bases needed for our studies were sterically encumbered, which may further inhibit proton transfer.[40−42] Efforts were thus directed toward the synthesis and study of the perfluorophenyl DAC derivative **4** (calculated PA = 233.0 kcal/mol) as this substrate should be less bulky than DACs **1** and **2**, and the corresponding conjugate acid should be more acidic. As such, less basic and less sterically demanding reference bases would be needed to bracket the PA of this carbene.

Using the aforementioned mass spectrometric methodology, the PA of **4** was measured. While *N*-methylpiperidine (PA = 232.1 ± kcal/mol did not deprotonate **4H**$^+$, proton transfer was observed when triethylamine (PA = 234.7 ± kcal/mol) was used as the reference base (Table 2). The experimental PA of **4** was therefore established to be 233 kcal/mol, in agreement with the calculated value of 233.0 kcal/mol.

Building upon the aforementioned results obtained for **4**, we sought to expand the PA measurements to include relatively basic DAC derivatives. Considering the lack of proton transfer with **1** and **2**, a less sterically encumbered DAC featuring a 4-methylphenyl *N*-substituent with a calculated PA value (256.3 kcal/mol) similar to that of **1** and **2** was envisioned (i.e., **5**). In a manner analogous to **1·H$_2$O**, the formally hydrated derivative (i.e., **5·H$_2$O**) was synthesized. Electrospray of a formic acid solution of **5·H$_2$O** and the gas-phase introduction of reference bases to bracket the PA value were explored. Reference bases with PA values of 260.6 kcal/mol and higher effectively deprotonated **5H**$^+$; in contrast, proton transfer was not observed for reference bases with PAs below 260.6 kcal/mol. Instead, when the base HP$_1$(dma) (PA = 257.4 kcal/mol), 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD; PA = 254.0 kcal/mol), or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; PA = 250.5 kcal/mol) was introduced, ions with mass-to-charge ratios corresponding to the adducts of the protonated DAC and the reference base (or, alternatively, the protonated reference base and the DAC) were observed. This result was consistent with the susceptibility of DACH$^+$ to react with nucleophiles such as water and the splitting of N−H bonds by free DACs,[17] though the actual nature of the complex (e.g., a covalent versus a noncovalent ion−molecule adduct) has not been probed. Regardless of its structure, proton transfer cannot be ascertained when such complexation occurs. However, a lack of proton transfer with *N,N,N′,N′*-tetramethyl-1,3-propanediamine (PA = 247.4 kcal/mol) as the reference base did indicate that the PA of the tolyl DAC **5** was between 247.4 and 260.6 kcal/mol (Table 3). Thus, unlike with DACs **1** and **2**, the PA of the less sterically hindered tolyl DAC **5** was successfully bracketed, indicating that the conjugate acids of DACs **1** and **2** feature sterically inaccessible protons under the conditions studied.

Table 2. Summary of Results for Proton Affinity Bracketing of Perfluorophenyl DAC 4

ref base[43]	PA (kcal/mol)	proton transfer (between protonated **4H**$^+$ and ref base)[a]
N,*N*-dimethylcyclohexylamine	235.1 ± 2.0	+
triethylamine	234.7 ± 2.0	+
N-methylpiperidine	232.1 ± 2.0	−
N-methylpyrrolidine	230.8 ± 2.0	−
piperidine	228.0 ± 2.0	−

[a] The "+" symbol indicates the observation of proton transfer, and the "−" symbol indicates the lack of observed proton transfer.

Table 3. Summary of Results for Proton Affinity Bracketing of Tolyl DAC 5

ref base[39,43]	PA (kcal/mol)	Proton transfer (between **5H**$^+$ and ref base)[a]
BEMP	263.8 ± 2.0	+
tOctP$_1$(dma)	262.0 ± 2.0	+
tBuP$_1$(dma)	260.6 ± 2.0	+
N,N,N′,N′-tetramethyl-1,3-propanediamine	247.4 ± 2.0	−

[a] The "+" symbol indicates the observation of proton transfer, and the "−" symbol indicates the lack of observed proton transfer.

To further probe how aryl substitution influences the PAs of the DACs, attention shifted to the anisidyl series **6**, as installing a methoxy group was calculated to increase the PA of the DAC, with a relative PA order of **6a** > **6c** > **6b**. The DACs **6** were synthesized in an analogous manner to the other formally hydrated DAC adducts (Scheme 2) and then subjected to electrospray analysis and PA bracketing (Table 4). For the relatively basic DAC **6a**, tOctP$_1$(dma) (PA = 262.0 kcal/mol) effected deprotonation of **6aH**$^+$ although tBuP$_1$(dma) (PA = 260.6 kcal/mol) did not. The experimental PA for **6a** was therefore bracketed between 260.6 and 262.0 kcal/mol, consistent with the calculated value (261.0 kcal/mol). Proton transfer from the protonated, yet less basic, *meta* and *para* derivatives **6b** and **6c** was observed with tBuP$_1$(dma) (PA = 260.6 kcal/mol; Table 4, third row). As with the tolyl DAC **5**, the *m*/*z* ratios indicated adduct formation between the protonated reference base and the DAC when employing reference bases HP$_1$(dma) and MTBD. The lack of proton transfer with *N,N,N′,N′*-tetramethyl-1,4,-butanediamine (PA = 250.1 kcal/mol) placed the PA values of **6b** and **6c** above 250.1

Table 4. Summary of Proton Affinity Bracketing Results for the Anisidyl-Based DACs 6

ref base[39,43]	PA (kcal/mol)	proton transfer (between protonated **6H**$^+$ and ref base)[a]		
		6a	**6b**	**6c**
BEMP	263.8 ± 2.0	+	+	+
tOctP$_1$(dma)	262.0 ± 2.0	+	+	+
tBuP$_1$(dma)	260.6 ± 2.0	−	+	+
HP$_1$(dma)	257.4 ± 2.0	complex	complex	complex
MTBD[b]	254.0 ± 2.0	complex	complex	complex
N,*N*,*N*′,*N*′-tetramethyl-1,4-butanediamine	250.1 ± 2.0	−	−	−

[a]The "+" symbol indicates the observation of proton transfer, and the "−" symbol indicates the lack of observed proton transfer. [b]MTBD = 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene.

kcal/mol and below 260.6 kcal/mol, consistent with the theoretical calculations.

The observance of proton transfer with **6a-cH**$^+$ suggested to us that the absence of proton transfer between **1H**$^+$ and **2H**$^+$ with BEMP was a kinetic effect due to sterics. Electrostatic potential (ESP) calculations, which enable a visual representation of the accessibility of the C2 proton, supported our hypothesis (Figure 3). In the cases where experimental bracketing was not possible (i.e., **1H**$^+$ and **2H**$^+$), strong shielding of the C2 proton was observed. In contrast, when smaller aryl substituents were employed, the C2 proton became more exposed and susceptible to deprotonation even by sterically bulky bases.

Finally, we calculated the HOMO and LUMO energies for the DACs and NHCs studied herein. Given the similar PAs yet dissimilar electrophilicities, we expected that the HOMO energies would be similar, but not the LUMO energies.[22] Indeed, DAC **1** was calculated to display a HOMO that was only 7 kcal/mol lower than that of **3a**; the LUMO of the former carbene, in contrast, was 54 kcal mol^{-1} lower than that of the latter. Likewise, the DAC **2** was calculated to display a HOMO energy level that was similar to that of NHC **3a** (within 6 kcal/mol) whereas the energy level of the LUMO of the DAC was 51 kcal/mol lower than that of the NHC.

CONCLUSIONS

In summary, for the first time, the gas-phase proton affinities of the diamidocarbenes were assessed both computationally and experimentally. The inability to bracket the PAs of **1** and **2** was attributed to steric hindrance at the carbene center by the *N*-aryl substituents and supported by electrostatic potential surface calculations. Moreover, protonated DAC variants with decreased steric demands, including perfluorophenyl, *p*-tolyl, and various anisidyl derivatives, prepared by electrospray of the formally hydrated carbene precursors in formic acid solution, were found to undergo deprotonation in the gas phase upon exposure to appropriate bases. Bracketed PA values were in good agreement with theory which underscored the ability to accurately calculate PAs via this method. Except in the case of the perfluorophenyl derivate **4**, which possessed a very low PA (233.0 kcal/mol), the proton affinities of the DACs studied herein were similar in value to the PAs of various NHCs (256.3−261.0 kcal/mol). Collectively, the calculations and the mass spectrometry data obtained for the carbenes described herein indicate that the DACs display similar basicities as the NHCs. Thus, we conclude that the observed reactivity differences between the two classes of carbenes may be attributed to the enhanced electrophilic characteristics of the DACs, as evidenced by their relatively low-lying LUMOs and abilities to react with a broad range of nucleophiles.[16,17,44,45] Moreover, having ascertained the PAs of various DACs, the results described above may be utilized to determine the compatibility of DACs with various acidic functional groups (e.g., electron-deficient terminal alkynes or ketones)[22,44,45] as well as to contribute to the design and understanding of new carbene scaffolds.

EXPERIMENTAL SECTION

For NHCs **3a**, **3b**, and **3d**, the corresponding precursors (1,3-dimethylimidazolium tetrafluoroborate, 1-ethyl-3-methylimidazolium tetrafluoroborate, and 1,3-diisopropylimidazolium tetrafluoroborate) were used as received. The precursor to **3c**, 1-methyl-3-isopropylimidazolium iodide, was synthesized according to a literature procedure.[46] Bis(4-methylphenyl)formamidine,[47] bis(2-methoxyphenyl)formamidine,[48] bis(perfluorophenyl)formamidine,[49] 2-chloro-1,3-bis-(2,6-diisopropylphenyl)-4,6-diketo-5,5-dimethylpyrimidine (**1·HCl**),[17] and the formally hydrated carbene adduct **2·H$_2$O**[17] were synthesized according to literature procedures. All other commercial substrates were used as received. All reference bases were used as received.

To generate the protonated carbene species via electrospray, the formally hydrated DACs were dissolved in formic acid or a mixture of formic acid/water (1:10 v/v) ([DAC]$_0$ ~10^{-4} M). Standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glovebox were used for the condensation reactions needed to prepare **1,2,4−6·H$_2$O**. Benzene and dichloromethane were dried and degassed using a solvent purification system. Chemical shifts (δ) are reported in ppm relative to the residual chloroform (^{1}H: 7.24 ppm, ^{13}C: 77.0 ppm) as reference. Melting points were obtained at a 1 °C·min^{-1} ramp rate and are uncorrected.

Synthesis of Bis(3-methoxyphenyl)formamidine. A 100 mL round-bottom flask was charged with *m*-anisidine (20.0 g, 162 mmol, 2 equiv), triethyl orthoformate (12.0 g, 81 mmol, 1 equiv), five drops of formic acid, and a stir bar. The flask was equipped with a short-path distillation head and heated to 110 °C for 2 h, distilling off ethanol. The temperature was increased to 140 °C for 2 h and then cooled to room temperature whereupon the reaction mixture crystallized. The crude product was ground with a glass rod, triturated with pentane, and filtered through a medium porosity glass frit. Washing with pentane until the filtrate was colorless followed by drying the collected solid under reduced pressure afforded the desired compound as a tan solid (19.3 g, 75 mmol, 93%). Mp: 108−109 °C. ^{1}H NMR (CDCl$_3$, 400.09 MHz): δ 3.66 (s, 6H), 6.56 (bs, 2H), 6.61−6.66 (m, 4H), 7.18 (t, ^3J = 8.0 Hz, 2H), 8.26 (s, 1H), 10.29 (bs, 1H). ^{13}C NMR (CDCl$_3$, 100.50 MHz): δ 55.0, 104.9, 109.3, 111.0, 130.1, 146.6, 150.2, 160.5. IR (KBr): ν = 3003.9, 2960.5, 2833.7, 1672.9, 1590.1, 1485.6, 1295.2, 1149.6, 1050.2, 1034.9, 779.1 cm^{-1}. HRMS (CI): [M]$^+$ calcd for $C_{15}H_{16}N_2O_2$ 256.1212, found 256.1212. Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.26; H, 6.31; N, 11.29.

Synthesis of Bis(4-methoxyphenyl)formamidine. A 100 mL round-bottom flask was charged with *p*-anisidine (20.0 g, 162 mmol, 2 equiv), triethyl orthoformate (12.0 g, 81 mmol, 1 equiv), five drops of formic acid, and a stir bar. The flask was equipped with a short path distillation head and heated to 110 °C for 2 h, distilling off ethanol. The temperature was increased to 140 °C for 2 h and then cooled to room temperature whereupon the reaction mixture crystallized. The crude product was ground with a glass rod, triturated with pentane, and filtered through a medium porosity glass frit. Washing with pentane until the filtrate was colorless followed by drying the collected solid under reduced pressure afforded the desired compound as a dark red-brown solid (19.95 g, 78 mmol, 96%). Mp: 118−119 °C. ^{1}H NMR (CDCl$_3$, 400.09 MHz): δ 3.77 (s, 6H), 6.82 (d, ^3J = 9.0 Hz, 4H), 6.95 (d, ^3J = 9.0 Hz, 4H), 8.07 (s, 1H), 9.93 (bs, 1H). ^{13}C NMR (CDCl$_3$, 100.50 MHz): δ 55.4, 114.5, 120.3, 138.8, 150.0, 155.8. IR (KBr): ν =

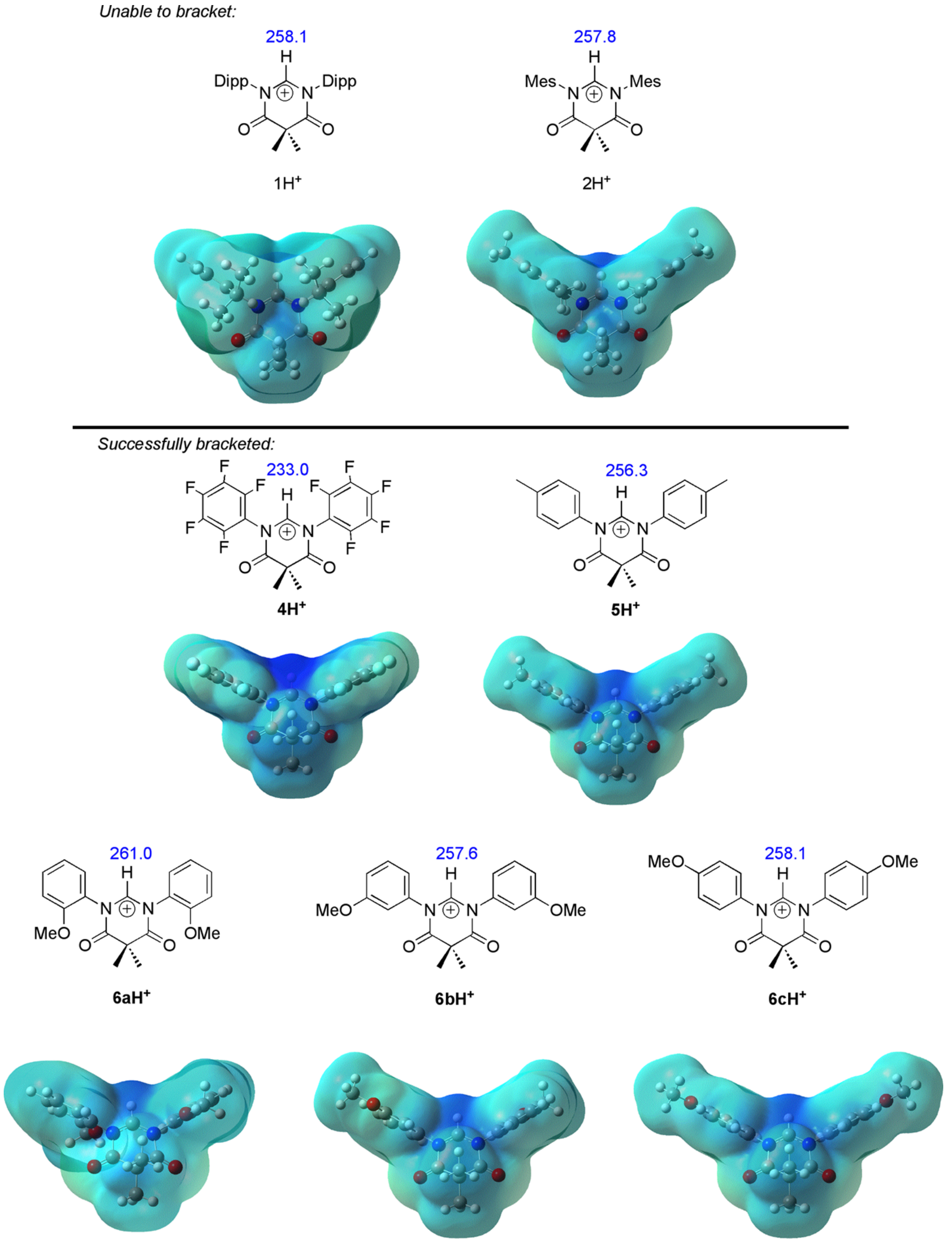


Figure 3. Calculated electrostatic potential surfaces for various protonated DACs. Values in blue are calculated proton affinities for the corresponding carbenes (B3LYP/6-31+G(d), kcal/mol).

2907.6, 2832.2, 1669.2, 1518.0, 1441.8, 1295.1, 1249.0, 1205.6, 1028.2, 823.3, 719.3, 526.3 cm^{-1}. HRMS (CI): [M]$^+$ calcd for $C_{15}H_{16}N_2O_2$ 256.1212, found 256.1212. Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.14; H, 6.32; N, 11.09.

Synthesis of 1·H_2O. A 20 mL vial was charged with 2-chloro-1,3-bis(2,6-diisopropylphenyl)-4,6-diketo-5,5-dimethylpyrimidine (0.150 g, 0.302 mmol) and a stir bar. To this vial open to the atmosphere was added benzene (5 mL) and stirred at ambient temperature until the solvent evaporated. Washing with pentane and drying under reduced pressure afforded the desired product as a white solid (0.127 g, 0.265 mmol, 88%). Mp: 205−206 °C dec. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 1.13−1.16 (overlapping d, 12H), 1.19 (d, ^3J = 6.8 Hz, 6H), 1.29 (d, ^3J = 6.8 Hz, 6H), 1.58 (s, 3H), 1.80 (s, 3H), 2.97−3.07 (d overlapping sept, 3H), 3.24 (sept, ^3J = 6.8 Hz, 2H), 5.78 (d, ^3J = 4.1 Hz, 1H), 7.18−7.23 (m, 4H), 7.35 (t, ^3J = 7.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 22.8, 23.3, 23.6, 24.3, 25.2, 27.1, 28.7, 29.3, 46.5, 89.6, 123.9, 124.9, 129.5, 132.4, 145.6, 149.2, 171.7. IR (KBr): ν = 3351.9, 2968.0, 2930.9, 2868.5, 1679.4, 1640.4, 1464.1, 1446.2, 1320.6, 1128.5, 1049.8, 805.7 cm^{-1}. HRMS (CI): [M + H]$^+$ calcd for $C_{30}H_{43}N_2O_3$ 479.3274, found 479.3269. Anal. Calcd for $C_{30}H_{42}N_2O_3$: C, 75.28; H, 8.84; N, 5.85. Found: C, 74.87; H, 8.96; N, 5.92.

Synthesis of 4·H_2O. A 25 mL Schlenk flask was charged with bis(perfluorophenyl)formamidine (0.100 g, 0.266 mmol), dichloromethane (10 mL), triethylamine (56 μL, 0.399 mmol, 1.5 equiv), and a stir bar. The mixture was cooled to 0 °C in an ice bath, and then dimethylmalonyl dichloride (0.047 g, 0.279 mmol, 1.05 equiv) was added dropwise. The ice bath was then removed, and the reaction was stirred at ambient temperature for 1.5 h, whereupon the volatiles were removed under reduced pressure. The solid residue was extracted with benzene (20 mL) and filtered through a medium frit funnel under nitrogen. The filtrate was concentrated to dryness, redissolved in 1 mL $CHCl_3$, and stirred open to the atmosphere for 1 h. Removal of volatiles under reduced pressure, washing with pentane (3 × 1.5 mL), and drying under reduced pressure afforded the desired product as a white solid (0.106 g, 0.216 mmol, 81%). Mp: 85−87 °C dec. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.58 (s, 3H), 1.82 (s, 3H), 3.65 (bs, 1H), 5.99 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 21.0, 27.2, 48.6, 87.9, 112.3, 138.0, 138.1, 142.1, 144.1, 145.1, 170.9. The aryl ^{13}C signals (112−145 ppm) were determined via ^{19}F decoupled ^{13}C NMR spectroscopy. ^{19}F NMR ($CDCl_3$, 376.46 MHz): δ −141.33 (m, 2F), −145.9 (m, 2F), −150.87 (t, J = 21.8 Hz, 2F), −160.24 to −160.45 (m, 4F). IR (KBr): ν = 3262.9, 1724.2, 1708.5, 1761.2, 1651.7, 1520.7, 1410.5, 1109.8, 994.7, 635.9 cm^{-1}. HRMS (CI): $[M + H]^+$ calcd for $C_{18}H_9F_{10}N_2O_3$ 491.0453, found 491.0464. Anal. Calcd for $C_{18}H_8F_{10}N_2O_3$: C, 44.10; H, 1.64; N, 5.71. Found: C, 43.78; H, 1.75; N, 5.34.

Synthesis of 5·H_2O. A 25 mL Schlenk flask was charged with *N,N′*-bis(4-methylphenyl)formamidine (0.100 g, 0.446 mmol, 1 equiv), dichloromethane (15 mL), triethylamine (93 μL, 0.668 mmol, 1.5 equiv), and a stir bar. The mixture was cooled to 0 °C in an ice bath, and then dimethylmalonyl dichloride (0.079 g, 0.468 mmol, 1.05 equiv) was added dropwise. The ice bath was then removed, and the reaction was allowed to stir at ambient temperature for 1 h whereupon the volatiles were removed under reduced pressure. The solid residue was extracted with benzene (25 mL) and filtered through a medium frit funnel under nitrogen. Concentration of the filtrate to dryness followed by the addition of 5 mL wet benzene and stirring open to the atmosphere for 30 min resulted in a precipitate that was collected over a medium frit funnel. Further purification of the crude solid by column chromatography (eluent =1:1 v/v hexanes/ethyl acetate) afforded the desired product as a white solid (0.063 g, 0.186 mmol, 42%). Mp: 133−134 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.42 (s, 3H), 1.67 (s, 3H), 2.32 (s, 6H), 4.69 (bs, 1H), 5.89 (s, 1H), 7.05 (d, ^3J = 8.6 Hz, 4H), 7.13 (d, ^3J = 8.2 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 21.1, 21.8, 27.2, 47.5, 90.2, 127.3, 130.0, 136.3, 138.0, 172.7. IR (KBr): ν = 3318.3, 2983.1, 2923.1, 1691.8, 1652.5, 1513.9, 1428.2, 1230.6, 1124.2, 1106.8, 1032.1, 753.6, 522.7 cm^{-1}. HRMS (CI): $[M - H]^+$ calcd for $C_{20}H_{21}N_2O_3$ 337.1552, found 337.1548. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.96; H, 6.05; N, 8.18.

Synthesis of 6a·H_2O. A 25 mL Schlenk flask was charged with *N,N′*-bis(2-methoxyphenyl)formamidine (0.100 g, 0.390 mmol, 1 equiv), dichloromethane (15 mL), triethylamine (82 μL, 0.585 mmol, 1.5 equiv), and a stir bar. The mixture was cooled to 0 °C in an ice bath, and then dimethylmalonyl dichloride (0.069 g, 0.410 mmol, 1.05 equiv) was added dropwise. The ice bath was then removed, and the reaction was allowed to stir at ambient temperature for 1 h whereupon the volatiles were removed under reduced pressure. The solid residue was extracted with benzene (25 mL) and filtered through a medium frit funnel under nitrogen. Concentration of the filtrate to dryness followed by the addition of 5 mL wet benzene and stirring open to the atmosphere for 30 min resulted in a precipitate that was collected over a medium frit funnel. Further purification of the crude solid by column chromatography (eluent =1:3 v/v hexanes/ethyl acetate) afforded the desired product as an off-white solid (0.074 g, 0.200 mmol, 51%). Mp: 161−162 °C dec. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.57 (s, 3H), 1.83 (s, 3H), 3.84 (s, 6H), 4.40 (bs, 1H), 5.92 (s, 1H), 6.97−7.05 (m, 4H), 7.20−7.35 (m, 4H). ^{13}C NMR ($CDCl_3$, 100.65 MHz): δ 21.8, 27.4, 48.2, 56.1 (b), 90.0 (b), 112.3 (b), 121.2 (b), 127.7 (b), 129.9 (b), 154.7, 172.6. IR (KBr): ν = 3244.2, 2943.0, 2840.0, 1689.4, 1645.2, 1504.6, 1431.5, 1272.2, 1128.5, 1044.7, 806.2, 770.8 cm^{-1}. HRMS (CI): $[M]^+$ calcd for $C_{20}H_{22}N_2O_5$ 370.1529, found 370.1528. Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.59; H, 5.93; N, 7.75.

Synthesis of 6b·H_2O. A 100 mL Schlenk flask was charged with *N,N′*-bis(3-methoxyphenyl)formamidine (0.500 g, 1.95 mmol, 1 equiv), dichloromethane (75 mL), triethylamine (0.4 mL 2.92 mmol, 1.5 equiv), and a stir bar. The mixture was cooled to 0 °C in an ice bath, and then dimethylmalonyl dichloride (0.346 g, 2.05 mmol, 1.05 equiv) was added dropwise. The ice bath was then removed, and the reaction was allowed to stir at ambient temperature for 1.5 h, whereupon the volatiles were removed under reduced pressure. The solid residue was extracted with benzene (100 mL) and filtered through a medium frit funnel under nitrogen. Concentration of the filtrate to dryness followed by the addition of 25 mL of wet benzene, and stirring open to the atmosphere for 30 min resulted in a precipitate that was collected over a medium frit funnel. Concentration of the filtrate and purification of the crude solid by silica gel column chromatography (eluent =1:1 v/v hexanes/ethyl acetate) afforded the desired product as a white solid (0.108 g, 0.292 mmol, 15%). Mp: 63−65 °C dec. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.46 (s, 3H), 1.69 (s, 3H), 3.75 (s, 6H), 4.64 (bs, 1H), 5.97 (s, 1H), 6.77−6.85 (m, 6H), 7.24 (t, ^3J = 8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 21.8, 27.3, 47.7, 55.4, 90.1, 113.5, 133.7, 119.6, 130.1, 139.9, 160.3, 172.5. IR (KBr): ν = 3291.3, 2941.3, 2837.0, 1699.5, 1652.2, 1603.3, 1495.4, 1288.5, 1221.4, 1038.7 cm^{-1}. HRMS (CI): $[M]^+$ calcd for $C_{20}H_{22}N_2O_5$ 370.1529, found 370.1525. Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.64; H, 6.10; N, 7.68.

Synthesis of 6c·H_2O. A 25 mL Schlenk flask was charged with *N,N′*-bis(4-methoxyphenyl)formamidine (0.100 g, 0.390 mmol, 1 equiv), dichloromethane (15 mL), triethylamine (82 μL, 0.585 mmol, 1.5 equiv), and a stir bar. The mixture was cooled to 0 °C in an ice bath, and then dimethylmalonyl dichloride (0.069 g, 0.410 mmol, 1.05 equiv) was added dropwise. The ice bath was removed, and the reaction was allowed to stir at ambient temperature for 1 h whereupon the volatiles were removed under reduced pressure. The solid residue was extracted with benzene (25 mL) and filtered through a medium frit funnel under nitrogen. Concentration of the filtrate to dryness followed by the addition of 5 mL of wet benzene and stirring open to the atmosphere for 30 min resulted in a precipitate that was collected over a medium frit funnel. Further purification of the crude solid by column chromatography (eluent = 1:2 v/v hexanes/ethyl acetate) afforded the desired product as a white solid (0.069 g, 0.186 mmol, 48%). Mp: 147−148 °C dec. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.54 (s, 3H), 1.76 (s, 3H), 3.79 (s, 6H), 3.81 (s, 1H), 6.05 (s, 1H), 6.91 (d, ^3J = 8.6 Hz, 4H), 7.20 (d, ^3J = 9.0 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 21.8, 27.5, 47.6, 55.5, 90.5, 114.8, 115.3, 120.9, 129.0, 131.6, 159.3, 172.7. IR (KBr): ν = 3213.1, 2953.9, 2837.2, 1713.1, 1697.6, 1642.6, 1512.3, 1249.6, 1029.6, 833.5 cm^{-1}. HRMS (CI): $[M]^+$ calcd for $C_{20}H_{22}N_2O_5$ 370.1529, found 370.1524. Anal. Calcd for $C_{20}H_{22}N_2O_5$: C, 64.85; H, 5.99; N, 7.56. Found: C, 64.47; H, 5.89; N, 7.83.

Gas-Phase Experiments and Calculations. Bracketing experiments were conducted using a house-modified quadrupole ion trap mass spectrometer as previously described.[35] Protonated carbene ions were generated by electrospray ionization (ESI) from a ∼10^{-4} M solution using a flow rate of 15−25 μL/min. The analyzed solutions were prepared by dissolving the conjugate acids of NHCs **3a**, **3b**, **3c**, and **3d** in methanol; dissolving the formally hydrated DACs **1**, **4**, and **5** in pure formic acid; or dissolving the formally hydrated DACs **2** and **6** in pure formic acid followed by ten-fold dilution using DI water.

The capillary temperature was 150 °C. Neutral reference bases were added with the helium gas flow. The protonated carbene ions were allowed to react with neutral reference bases for 0.03−1000 ms. The unreactive DACs **1** and **2** were allowed to react up to 10000 ms with BEMP to ensure that proton transfer was not occurring. The occurrence of proton transfer was regarded as evidence that the reaction was exothermic ("+" in tables); otherwise, the reaction was regarded as endothermic ("−" in tables). The typical electrospray needle voltage was ∼4.5 kV. A total of 10 scans were collected and averaged.

All calculations were performed using density functional theory (B3LYP/6-31+G(d))[50−54] as implemented in Gaussian 09.[55] All of the geometries were fully optimized, and frequencies were calculated; no scaling factor was applied. The optimized structures had no negative frequencies. The temperature for the calculations was set to 298 K. GaussView 5.0 was used to generate the electrostatic potential maps of the protonated carbenes based on their optimized structures in the gas phase. Density isovalues for the surfaces were set to 0.0004. The color range for the surfaces was set to −0.19 to +0.19.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Cartesian coordinates for all calculated species and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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Due to a production error, the last sentence in the Results and Discussion section was truncated in the version published on October 3, 2013. The sentence is completed in the version reposted on October 4, 2013.