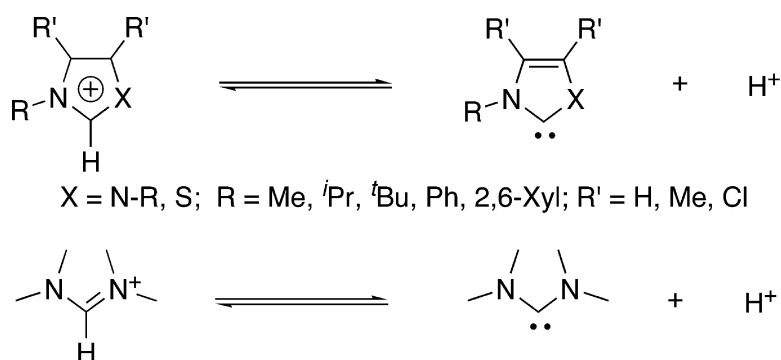


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Basicity of Nucleophilic Carbenes in Aqueous and Nonaqueous Solvents—Theoretical Predictions

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Abstract: The complete basis set method CBS-QB3 was used in conjunction with the CPCM solvation model to predict both the absolute and relative pK_a 's of 12 nucleophilic carbenes in dimethyl sulfoxide (DMSO), acetonitrile (MeCN), and water. Average absolute pK_a values in DMSO ranged from 14.4 ± 0.16 for 3-methylthiazol-2-ylidene (**12**) to 27.9 ± 0.23 in the case of bis(dimethylamino)carbene (**11**), while values in MeCN were determined to be between 25.7 ± 0.16 (**12**) and 39.1 ± 0.25 (**11**). Relative pK_a calculations yielded similar results. Calculations in aqueous solution gave pK_a 's between 21.2 ± 0.2 (**12**) and 34.0 ± 0.3 (**11**). Excellent agreement between calculated and experimental pK_a 's was obtained for the few cases where experimental numbers are available, confirming that this theoretical approach may be used to calculate highly accurate pK_a values.

Introduction

The discovery of a stable nucleophilic carbene by Arduengo et al.¹ in 1991 ignited a flurry of interest in the field of carbene research. While much research has focused on the isolation of novel carbenes^{2,3} and their use as ligands in transition-metal-based catalysts, there has been comparatively less work performed looking at fundamental properties of the carbenes themselves.

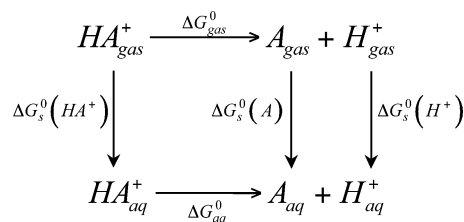
There have been many reports detailing the use of imidazole-based carbenes as ligands in ruthenium-based olefin metathesis.^{3–5} Initially, these carbenes were the unsaturated imidazol-2-ylidenes, but the incorporation of saturated imidazolin-2-ylidenes into the catalyst (or pre-catalyst) has since been shown to result in higher catalytic activity.^{5,6} It has been suggested that this may be due to the increased basicity of the ligand system.⁶

Ring substituents may also play a part in determining catalytic activity. Substitution of the imidazole ring by chlorine at the 4 and 5 positions results in a dramatic down-turn in activity when carbenes are applied as catalysts in ring-opening polymerization.⁷ In the same study, thiazole-based carbenes were found to be significantly less active than their imidazole-based analogues.

If these effects could be correlated with carbene basicity, it would assist in the design of better catalysts. It is therefore of interest to determine the basicity of carbenes based on imidazole and related species.

There have only been two reports dealing with the experimental basicity of imidazol-2-ylidenes. Alder et al.⁸ measured the pK_a of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene in DMSO-*d*₆ as 24.0. More recently, Kim and Streitwieser⁹ noted that the pK_a of 1,3-di-*tert*-butylimidazol-2-ylidene in DMSO was 22.7.

While a number of reports have appeared in the past 15 years dealing with the calculation of pK_a ,^{10,11} until recently there have been no methods for determining *highly accurate* pK_a values from computational chemistry. In principle, it is possible to determine theoretically the pK_a for an imidazolium salt/carbene system (HA^+/A) using the following thermodynamic cycle:



where ΔG_{gas}^0 and ΔG_{aq}^0 represent the free energy of deprotona-

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- (1) Arduengo, A. J., III; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361–363.
- (2) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–91.
- (3) Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2162–2187.
- (4) (a) Angeletakis, C.; Chen, M. US Patent 6455029, 2002. (b) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035–4037. (c) Connon, S. J.; Dunne, A. M.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 3835–3838. (d) Bell, A.; Grubbs, R. H.; Morgan, J. P.; Moore, J. L. International Patent WO02076613, 2002.
- (5) Scholl, M.; Trnka, T. M.; Morgan, J. P.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 2247.
- (6) Denk, K.; Sirsch, P.; Herrmann, W. A. *J. Organomet. Chem.* **2002**, *649*, 219–224.

- (7) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046–3056.
- (8) Alder, R. W.; Allen, P. R.; Williams, S. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1267–1268.
- (9) Kim, Y.-J.; Streitwieser, A. *J. Am. Chem. Soc.* **2002**, *124*, 5757–5761.
- (10) Lim, C.; Bashford, D.; Karplus, M. *J. Phys. Chem.* **1991**, *95*, 5610–5618.
- (11) (a) Jorgensen, W. L.; Briggs, J. M.; Gao, J. *J. Am. Chem. Soc.* **1987**, *109*, 6857. (b) Jorgensen, W. L.; Briggs, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 4190. (c) Guissani, Y.; Guillot, B.; Bratos, S. *J. Chem. Phys.* **1988**, *88*, 5850.

tion in the gas and aqueous phases, respectively, and $\Delta G_s^0(X)$ represents the free energy of solvation of species X .

Given that

$$pK_a = -\log K_a$$

and

$$\Delta G_{aq}^0 = -2.303RT \log K_a$$

it may be seen that

$$pK_a = \Delta G_{aq}^0 / 2.303RT$$

where

$$\begin{aligned} \Delta G_{aq}^0 &= G^0(A_{aq}) + G^0(H_{aq}^+) - G^0(HA_{aq}^+) \\ &= G^0(A_{gas}) + \Delta G_s^0(A) + G^0(H_{gas}^+) \\ &\quad + \Delta G_s^0(H^+) - G^0(HA_{gas}^+) - \Delta G_s^0(HA^+) \end{aligned}$$

This relationship implies that an error in calculating ΔG_{aq}^0 of just 1.36 kcal/mol results in an error of 1 pK_a unit. High-level energy calculations are therefore required. Previous groups have used many such calculations to determine the value of ΔG^0 , including DFT calculations (B3LYP/aug-cc-pVTZ),¹² post-HF methods with large basis sets (MP2/6-311+G(2df,2p)),¹³ complete basis set methods (e.g. CBS-QB3, CBS-APNO), and Gaussian methods (e.g. G2).^{14–16} The free energies of solvation for A and HA^+ have been most often determined using the conductor-like polarizable continuum model (CPCM); however, other methods have been applied, including an alternate continuum–solvation approach,¹² a cluster–continuum model,¹³ and SM5.42R.¹⁴ Taken together, these approaches for calculating pK_a have met with varying degrees of success. However, the landmark paper by Liptak and Shields in 2001¹⁵ described a procedure for obtaining highly accurate pK_a values with a minimal amount of experimental input.

Herein, we describe our use of the Liptak–Shields method to estimate the pK_a of 12 heterocyclic carbenes, shown in Figure 1. Compounds **1**,¹⁷ **2**,¹⁷ **5**,¹⁸ **6**,¹⁹ and **10**²⁰ are isolable carbenes, and reports detailing the in situ generation of **3**,⁷ **4**,²¹ **9**,²² and **11**^{20,23} have been published. Compounds **9**²² and **11**²³ have both been found to dimerize slowly in solution at room temperature. Compounds **7**, **8**, and **12** are cut-down versions of the experimentally isolable 1,3-bis(4-methylphenyl)imidazol-2-

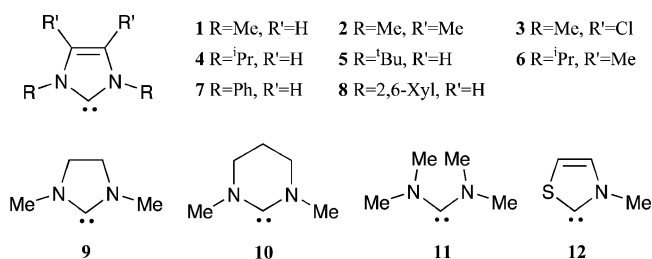


Figure 1. Imidazole- and thiazole-based carbenes for which pK_a 's have been determined in the course of this study.

ylidene,¹⁷ 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene,¹⁷ and 3-(2,6-diisopropylphenyl)-4,5-dimethylthiazol-2-ylidene,²⁴ respectively.

In this study, a variety of computational methods for the calculation of pK_a are considered and the results compared with available experimental data. We have chosen to focus on the basicity of the carbenes in two nonaqueous solvents, namely dimethyl sulfoxide and acetonitrile. It should be noted that N-heterocyclic carbenes are known to undergo rapid deuterium–hydrogen exchange at the 4 and 5 positions in DMSO- d_6 ,²⁵ while some imidazol-2-ylidenes undergo C–H insertion reactions with MeCN.²⁶ Nevertheless, these solvents were chosen because reliable thermodynamic parameters, particularly for the free energy of proton transfer (vide infra), were readily available.²⁷ Such reliable data are unavailable for solvents more commonly used to study carbenes (e.g., THF).

Computational Methods

Level of Theory. As pK_a determinations are so dependent on accuracy, the choice of theory becomes critical. Liptak et al. have performed several studies^{14–16,28} in which they apply different levels of theory, both in solution and in the gas phase, to pK_a determinations. They concluded that, for gas-phase energies, the CBS-QB3 method gives the most accurate results.¹⁵ Additionally, the CPCM model could be used to predict solvation free energy. In the determination of the pK_a of some substituted phenols, it was found to be necessary to perform a geometry optimization in solution in order to obtain accurate results.²⁸ Several basis sets were also assessed, with those bearing diffuse functions shown to be the most accurate for geometry optimizations.¹⁴ In contrast to what might be expected on the grounds of basis set improvements, single-point calculations at CPCM/HF/6-31G(d)/CPCM/HF/6-31+G(d) were found to give the best correlation between calculated and experimental pK_a 's.

In light of these findings, we chose to perform gas-phase energy calculations at the CBS-QB3 level, while solution-phase geometries were calculated using CPCM/HF/6-31+G(d) or CPCM/B3LYP/6-31+G(d,p). Single-point energy calculations in solution were then carried out at different levels of theory, as described below.

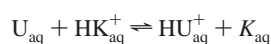
Thermodynamic Parameters. In the determination of absolute pK_a 's, $G^0(H^+)_{gas}$ was taken as -4.39 kcal/mol. This number is derived from the value of $G^0(H^+)_{gas}$ obtained in the Sackur–Tetrode equation (-6.28 kcal/mol), but it takes into account a change of reference state (from atmospheres to moles per liter).²⁸ The value for the free energy of solvation of the hydrogen ion ($\Delta G_s^0(H^+)_{aq}$) is subject to much

- (12) Jang, Y. H.; Sowers, L. C.; Çagin, T.; Goddard, W. A. *J. Phys. Chem. A* **2001**, *105*, 274–280.
 (13) Pliego, J. R.; Riveros, J. M. *J. Phys. Chem. A* **2002**, *106*, 7434–7439.
 (14) Toth, A. M.; Liptak, M. D.; Phillips, D. L.; Shields, G. C. *J. Chem. Phys.* **2001**, *114*, 4595–4606.
 (15) Liptak, M. D.; Shields, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 7314–7319.
 (16) Liptak, M. D.; Shields, G. C. *Int. J. Quantum Chem.* **2001**, *85*, 727–741.
 (17) Arduengo, A. J., III; Dias, H. V. R.; Harlow, R. L.; Kline, M. J. *Am. Chem. Soc.* **1992**, *114*, 5530–5534.
 (18) Arduengo, A. J., III; Bock, H.; Chen, H.; Denk, M. K.; Dixon, D. A.; Green, J. C.; Herrmann, W. A.; Jones, N. L.; Wagner, M.; West, R. *J. Am. Chem. Soc.* **1994**, *116*, 6614–6649.
 (19) Kuhn, N.; Steimann, M.; Weyers, G. Z. *Kristallogr.—New Cryst. Struct.* **2001**, *216*, 315.
 (20) Otto, M.; Conejero, S.; Canac, Y.; Romanenko, V. D.; Rudzhevitch, V.; Bertand, G. *J. Am. Chem. Soc.* **2004**, *126*, 1016–1017.
 (21) Weskamp, T.; Schattenmann, W. C.; Spiegler, M.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 2490–2493.
 (22) Denk, M. K.; Thadani, A.; Hatano, K.; Lough, A. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2607–2609.
 (23) Alder, R. W.; Blake, M. E.; Oliva, J. M. *J. Phys. Chem. A* **1999**, *103*, 11200–11211.

- (24) Arduengo, A. J., III; Goerlich, J. R.; Marshall, W. J. *Liebigs Ann.* **1997**, 365–373.
 (25) Denk, M. K.; Rodezno, J. M. *J. Organomet. Chem.* **2000**, *608*, 122–125.
 (26) Arduengo, A. J., III; Calabrese, J. C.; Davidson, F.; Dias, H. V. R.; Goerlich, J. R.; Krafczyk, R.; Marshall, W. J.; Tamm, M.; Schmutzler, R. *Helv. Chim. Acta* **1999**, *82*, 2348–2364.
 (27) Marcus, Y. *Pure Appl. Chem.* **1983**, *55*, 977–1021.
 (28) Liptak, M. D.; Gross, K. C.; Seybold, P. G.; Feldgus, S.; Shields, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 6421–6427.

debate, as it remains difficult to either measure or predict accurately²⁹ (a brief literature search uncovered values between -251 and -264.6 kcal/mol, see later). A value of -261.85 kcal/mol was used for $\Delta G_s^0(\text{H}^+)_{\text{aq}}$ in this work (see Discussion). An additional problem arises when nonaqueous solvents are considered. Specifically, the estimation of the free energy of proton transfer to nonaqueous solvents ($\Delta G_t^0(\text{H}^+)$) is frequently performed using the tetraphenylarsonium tetraphenylborate (TATB) assumption.²⁷ The basic premise of this assumption is that the ΔG_t^0 of the Ph_4As^+ ion from water to any solvent is equal to the ΔG_t^0 of the BPh_4^- ion from water to the same solvent.²⁷ The reliability of this assumption has recently been questioned,³⁰ but the lack of alternative reliable data means that figures obtained by this method were applied in this study. $\Delta G_t^0(\text{H}^+)$ was taken to be -4.64 kcal/mol for DMSO and 11.09 kcal/mol for MeCN.²⁷ Final values for $\Delta G_s^0(\text{H}^+)$ of -266.49 and -250.76 kcal/mol were thereby obtained for DMSO and MeCN, respectively.

This variability, in both $\Delta G_s^0(\text{H}^+)_{\text{aq}}$ and $\Delta G_t^0(\text{H}^+)$, can lead to large errors in the $\text{p}K_a$ values obtained. This problem may be circumvented by determining $\text{p}K_a$'s in a relative manner.¹⁴ Consider the following two species in equilibria:



The unknown $\text{p}K_a$ of acid HU^+ may be determined from the known $\text{p}K_a$ of acid HK^+ :

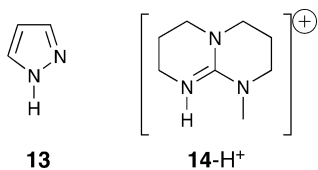
$$\text{p}K_a(\text{HU}^+) = \text{p}K_a(\text{HK}^+) + \Delta \text{p}K_a$$

Therefore:

$$\begin{aligned} \Delta \text{p}K_a &= \text{p}K_a(\text{HU}^+) - \text{p}K_a(\text{HK}^+) \\ &= \frac{\Delta G_{\text{aq}}^0(\text{HU}^+) - \Delta G_{\text{aq}}^0(\text{HK}^+)}{2.303RT} \\ &= \frac{G^0(\text{U}_{\text{aq}}) - G^0(\text{HU}_{\text{aq}}^+) - G^0(K_{\text{aq}}) + G^0(\text{HK}_{\text{aq}}^+)}{2.303RT} \end{aligned}$$

The need to estimate $\Delta G_t^0(\text{H}^+)_{\text{aq}}$ is thus eliminated, and $\text{p}K_a$ may be more accurately determined.³¹

In this work, relative $\text{p}K_a$'s were calculated using pyrazole (**13**) as a standard in DMSO ($\text{p}K_a = 19.8$)³² and MHPP- H^+ (**14**- H^+ , 9-methyl-3,4,6,7,8,9-hexahydro-2H-pyrimido[1,2-*a*]pyridin-1-ium) in MeCN ($\text{p}K_a = 25.43$).³³



Gas-Phase Calculations. Nucleophilic carbenes and the corresponding azolium salts were initially optimized in the gas phase at the B3LYP density functional level of theory using the CBSB7³⁴ basis set. High-level gas-phase free energies (G^0) were then calculated using the CBS-QB3 model chemistry.³⁴ This method performs an initial geometry optimization and frequency calculation using the B3LYP/CBSB7 level, followed by single-point calculations at the CCSD(T)/6-31+G(d⁺),

MP4SDQ/CBSB4, and MP2/CBSB3 levels. The final single-point calculation includes a complete basis set extrapolation. The CBS-QB3 method includes a zero-point vibrational energy (ZPVE) correction from the B3LYP/CBSB7 frequency calculation scaled by 0.9899. Reference standards and their respective ions were treated in an analogous fashion.³⁵

Solution-Phase Calculations. Geometry optimizations in solution were performed using the polarized continuum model of Barone and Cossi (CPCM)³⁶ at the CPCM/HF/6-31+G(d) and CPCM/B3LYP/6-31+G(d,p) levels. Initial geometries were taken from the gas-phase B3LYP/CBSB7 optimizations. Standard free energies of solvation in DMSO, MeCN, and water were then calculated by performing single-point calculations at the CPCM/HF/6-31G(d), CPCM/HF/6-31+G(d), and CPCM/MP2/6-311+G(d,p) levels for the HF optimizations and at the CPCM/B3LYP/6-311+G(d,p) level for the B3LYP optimized structures. These four different solvation regimes are referred to as **S1**, **S2**, **S3**, and **S4**, respectively, in the Results section. In all solvation calculations, the variables TSNUM and TSARE, representing the number of tesserae on each sphere and the area of each tesserae (in Å²), were set at 240 and 0.3, respectively. To determine solution-phase proton affinities, ZPVE and thermodynamic corrections were taken from the CBS-QB3 calculations and scaled by 0.9899.

To achieve convergence in the case of compound **12**, the convergence criteria were loosened at the CPCM/B3LYP/6-31+G(d,p) level in both DMSO and MeCN. Additionally, loose convergence criteria were needed for **6**- H^+ (MeCN/CPCM/HF/6-31+G(d)), **3**- H^+ (MeCN/CPCM/B3LYP/6-31+G(d,p)), and **2**- H^+ (H₂O/CPCM/HF/6-31+G(d)). This loosening of the convergence criterion has previously been found to be necessary by other workers.²⁸

All calculations were performed using the Gaussian98³⁷ or Gaussian03³⁸ suite of programs.

Results

Geometries. Compounds **1**–**12** each exhibit a number of different conformations. For example, compound **4** may exist as one of two C_{2v} symmetric conformers (**4** or **4'**) or in a C_s symmetric state (**4''**).

- (35) It is worth noting that these calculations require a large amount of computational resources. For example, the gas-phase calculations for **8** and **8**- H^+ (by far the largest systems studied) were performed on an SGI Origin 3400. In total, 59 days of continuous computing time across two processors were required, using a total of 600 MW of memory and 100 GB of scratch space.
- (36) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995–2001.
- (37) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11.3; Gaussian, Inc.: Pittsburgh, PA, 2002.
- (38) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; J. A. Montgomery, J.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A., *Gaussian 03*, Revision B.04; Gaussian, Inc.: Pittsburgh, PA, 2003.

(29) Tawa, G. J.; Topol, I. A.; Burt, S. K.; Caldwell, R. A.; Rashin, A. A. *J. Chem. Phys.* **1998**, *109*, 4852–4863.

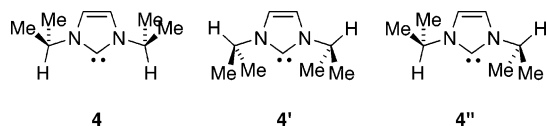
(30) (a) Schurhammer, R.; Wipff, G. *J. Mol. Struct. (THEOCHEM)* **2000**, *500*, 139. (b) Schurhammer, R.; Wipff, G. *J. Phys. Chem. A* **2000**, *104*, 11159.

(31) As noted by a reviewer, the determination still depends on the accuracy of the $\text{p}K_a$ of the reference standard.

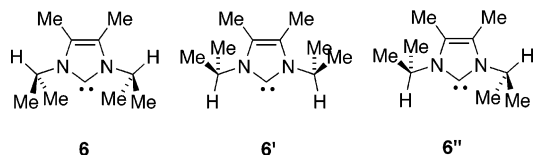
(32) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(33) Kovacevic, B.; Maksic, Z. B. *Org. Lett.* **2001**, *3*, 1523–1526.

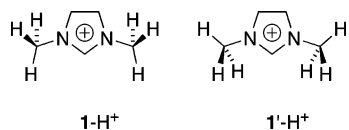
(34) Montgomery, J. A., Jr.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **1999**, *110*, 2822–2827.



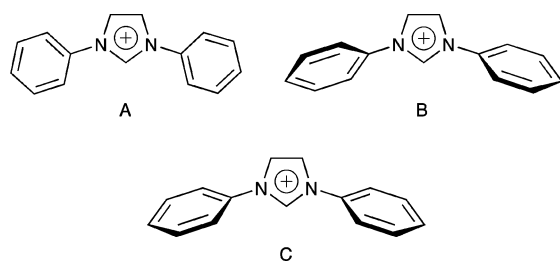
Calculations at the B3LYP/CBSB7 level showed that conformer **4** is 0.085 kcal/mol lower in energy than **4''**, which in turn is 0.072 kcal/mol lower in energy than **4'**. The corresponding imidazolium salts show a similar trend, with **4**-H⁺ being 0.43 kcal/mol lower in energy than **4''**-H⁺, which in turn is 0.44 kcal/mol lower in energy than **4'**-H⁺. All conformers exhibit no imaginary frequencies at this level of theory. Compound **6** can exhibit similar conformers. Previously reported calculations⁸ at the AM1 level of theory have shown **6** to be 0.45 kcal/mol higher in energy than **6'**, and 0.50 kcal/mol higher than **6''**. Conformers **4** and **6** were used in this study.



The conformations of **1**, **2**, **3**, **5**, **9**, **10**, and **12** used are based on the findings of Turner et al.,³⁹ who reported that **1**-H⁺ is a minimum compared with **1'**-H⁺, which exhibits imaginary frequencies.



The conformations of compounds **7** and **8** are dependent upon the orientation of the phenyl rings relative to the imidazole core, shown below as A, B, and C.



The conformation of compound **7** resembles that of the C₂ symmetric structure B, with the phenyl rings exhibiting a propeller-type arrangement and twisted approximately 35° relative to the plane of the imidazole core. The C_{2v} symmetric structure C, in which the phenyl rings are orthogonal to the imidazole core, is not a minimum for **7**—attempts to minimize the geometry in this symmetry group resulted in imaginary frequencies corresponding to a twisting of the phenyl rings.

The minimum energy structure of compound **8** corresponds to structure C. This is not unexpected given the methyl substituents at the 2 and 6 positions of the phenyl rings. Structure A is not a minimum in either case.

Compound **11** has been the subject of an extensive study by Alder et al.,²³ who demonstrated that singlet **11** is almost planar

Table 1. NCN Bond Angles for Carbenes **1–12**

	N ₁ -C ₂ -N ₃ ^a			expt ^d
	CBS-QB3	HF ^b	B3LYP ^c	
1	102.0	103.2	102.4	
2	102.0	103.3	102.3	101.5(1) ^e
3	103.0	103.9	103.2	
4	102.4	103.7	102.8	
5	103.0	103.9	103.0	102.2(5) ^f
6	102.7	103.7	102.8	
7	102.3	103.0	102.2	101.2(1) ^{e,g}
8	101.8	102.9	102.0	101.4(2) ^{e,h}
9	105.9	106.4	106.2	
10	115.9	116.4	116.1	
11	120.0	119.2	119.7	
12	105.3	106.3	105.7	

^a Bond angles in degrees. ^b MeCN/CPCM/HF/6-31+G(d). ^c MeCN/CPCM/B3LYP/6-31+G(d,p). ^d Chemically equivalent positions in experimental crystal structures have been averaged. ^e Experimental data from ref 17. ^f Experimental data from ref 18. ^g 1,3-Bis(4-methylphenyl)imidazol-2-ylidene. ^h 1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene.

Table 2. CBS-QB3 Free Energies, G⁰ (hartree)

	carbene		imidazolium salt	
	carbene	symmetry	imidazolium salt	symmetry
1	-304.273224	C _{2v}	-304.685734	C _{2v}
2	-382.742475	C _{2v}	-383.165316	C _{2v}
3	-1222.595440	C _{2v}	-1222.995015	C _{2v}
4	-461.199904	C _{2v}	-461.620041	C _{2v}
5	-539.663258	C _{2v}	-540.087787	C _{2v}
6	-539.666998	C _{2v}	-540.096110	C _{2v}
7	-687.071027	C ₂	-687.486516	C ₂
8	-844.006171	C _{2v}	-844.425705	C _{2v}
9	-305.452052	C ₂	-305.865430	C _{2v}
10	-344.678862	C _s	-345.105260	C _s
11	-306.615309	C ₂	-307.043198	C ₂
12	-607.522502	C _s	-607.917911	C _s

Table 3. Absolute pK_a for Carbenes **1–12** in DMSO and MeCN^a

	dimethyl sulfoxide						acetonitrile					
	S1	S2	S3	S4	av	dev ^b	S1	S2	S3	S4	av	dev ^b
1	21.3	20.9	20.9	21.4	21.1	0.23	32.5	32.2	32.1	32.6	32.4	0.22
2	24.0	23.5	23.4	23.8	23.7	0.21	35.3	34.8	34.7	35.0	34.9	0.21
3	16.3	16.1	16.0	16.2	16.2	0.10	27.6	27.3	27.2	27.4	27.4	0.10
4	22.3	21.9	21.8	22.2	22.0	0.21	33.6	33.2	33.0	33.5	33.3	0.21
5	22.8	22.6	22.5	22.6	22.6	0.09	34.1	33.9	33.8	33.9	33.9	0.09
6	24.8	24.4	24.4	24.4	24.5	0.15	36.1	35.8	35.7	35.7	35.8	0.14
7	16.2	16.1	16.1	16.0	16.1	0.05	27.4	27.3	27.3	27.5	27.4	0.07
8	16.9	16.8	16.7	16.6	16.8	0.09	28.2	28.1	28.0	28.3	28.2	0.12
9	22.8	22.3	22.3	21.9	22.3	0.25	34.1	33.6	33.5	33.1	33.6	0.25
10	27.6	27.1	27.1	26.7	27.1	0.23	38.9	38.4	38.3	38.0	38.4	0.23
11	28.3	27.9	27.9	27.5	27.9	0.23	39.6	39.2	39.1	38.7	39.1	0.25
12	14.7	14.4	14.4	14.1	14.5	0.16	25.9	25.6	25.6	25.4	25.6	0.15

^a S1 = CPCM/HF/6-31G(d)//CPCM/HF/6-31+G(d), S2 = CPCM/HF/6-31+G(d)//CPCM/MP2/6-311+G(d,p)//CPCM/MP2/6-311+G(d,p), S3 = CPCM/MP2/6-311+G(d,p)//CPCM/MP2/6-311+G(d,p), and S4 = CPCM/B3LYP/6-311+G(d,p)//CPCM/B3LYP/6-31+G(d,p). ^b Mean unsigned deviation from average pK_a.

(C₂ symmetric), with a small degree of pyramidalization at nitrogen. Our results mirror these findings.

Table 1 shows experimental and calculated NCN bond angles for compounds **1–12**. As shown below, this angle can have a dramatic effect on basicity. A full table of calculated and experimental geometrical parameters for compounds **1–12** and **1**-H⁺ to **12**-H⁺ is available as Supporting Information.

Energies and pK_a Values. Table 2 shows the symmetry and CBS-QB3 energies of the carbenes and their corresponding imidazolium salts. The absolute pK_a's calculated for carbenes **1–12** are outlined in Table 3. These results are obtained from the gas-phase CBS-QB3 energies and four different solvation

(39) Turner, E. A.; Pye, C. C.; Singer, R. D. *J. Phys. Chem. A* **2003**, *107*, 2277–2288.

Table 4. Relative pK_a for Carbenes **1–12**^a in DMSO and MeCN

	dimethyl sulfoxide ^b						acetonitrile ^c					
	S1	S2	S3	S4	av	dev ^d	S1	S2	S3	S4	av	dev ^d
1	21.3	21.0	21.1	21.9	21.3	0.29	32.2	32.1	32.0	32.3	32.2	0.09
2	24.1	23.7	23.6	24.3	23.9	0.28	34.9	34.6	34.7	34.7	34.7	0.10
3	16.4	16.2	16.2	16.7	16.4	0.16	27.2	27.3	27.2	27.1	27.2	0.06
4	22.4	22.0	22.0	22.7	22.3	0.28	33.2	33.1	33.0	33.2	33.1	0.08
5	22.9	22.7	22.7	23.1	22.8	0.15	33.7	33.9	33.7	33.6	33.7	0.07
6	24.8	24.6	24.5	24.9	24.7	0.18	35.7	35.7	35.6	35.5	35.6	0.11
7	16.2	16.2	16.3	16.5	16.3	0.11	27.1	27.3	27.2	27.2	27.2	0.07
8	17.0	16.9	16.9	17.1	17.0	0.08	27.9	28.0	27.9	28.0	28.0	0.06
9	22.9	22.5	22.4	22.4	22.5	0.16	33.7	33.6	33.4	32.8	33.4	0.27
10	27.6	27.2	27.3	27.2	27.3	0.15	38.5	38.4	38.3	37.7	38.2	0.25
11	28.4	28.0	28.0	28.0	28.1	0.14	39.2	39.1	39.0	38.4	38.9	0.29
12	14.8	14.5	14.6	14.6	14.6	0.07	25.6	25.6	25.6	25.1	25.5	0.20

^a **S1** = CPCM/HF/6-31G(d)//CPCM/HF/6-31+G(d), **S2** = CPCM/HF/6-31+G(d)//CPCM/HF/6-31+G(d), **S3** = CPCM/MP2/6-311+G(d,p)//CPCM/HF/6-31+G(d), and **S4** = CPCM/B3LYP/6-311+G(d,p)//CPCM/B3LYP/6-31+G(d,p). ^b Relative to pyrazole (**13**). ^c Relative to MHPP (**14**) (see text). ^d Mean unsigned deviation from average pK_a .

Table 5. Proton Affinity^a Both in the Gas Phase and in MeCN

	gas phase ^b				gas phase ^b		
	S3	S4	S4		S3	S4	
1	258.3	299.0	299.4	7	260.1	293.1	293.8
2	264.9	302.3	303.1	8	264.1	303.4	304.9
3	250.7	292.3	292.2	9	259.0	300.1	300.4
4	263.5	300.2	301.5	10	267.3	306.8	307.0
5	266.8	302.3	303.3	11	268.2	308.0	307.9
6	268.7	304.0	305.1	12	247.9	290.7	287.6

^a In kcal/mol. ^b CBS-QB3 enthalpy.

regimes, as described previously. In DMSO, average pK_a 's are between 14.5 and 27.9. Mean unsigned deviations (MUD) from the average pK_a are, at all times, less than 0.25 pK_a unit, with an average value of 0.17 pK_a unit. pK_a 's in MeCN (^{MeCN} pK_a) are in the range 25.7–39.1, with MUDs below 0.25, averaging 0.17 unit.

Relative pK_a values are given in Table 4. It may be seen that the relative pK_a values are slightly more variable than the absolute values, with MUDs up to 0.29 unit in both solvents, with the average of all MUDs being 0.15.

Table 5 shows the proton affinities for carbenes **1–12**. These values have been determined both in the gas phase (using the CBS-QB3 methodology) and in acetonitrile solution by applying the **S3** and **S4** solvation schemes.

Discussion

We begin the discussion by noting that, strictly speaking, the pK_a 's referred to here are acidity constants of the conjugate acids of the carbenes, i.e., the imidazolium salts. However, as ligand basicity is an important concept in organometallic and catalytic chemistry, particularly in relation to phosphines, it is common practice to refer to the pK_a of a base and we will continue to use this convention.

Geometry Changes in Solution. Given our decision to optimize geometries in solution, it is interesting to observe the changes that occur upon solvation. It should initially be stated that the precise comparison of gas-phase geometries (or solvated geometries) with those obtained from solid-state measurements (i.e., crystal structures) is not possible. In the case of ions, solid-state measurements are dependent upon the counterion.⁴¹

(40) Hehre, W. J.; Yu, J.; Klunzinger, P. E.; Lou, L. *A Brief Guide to Molecular Mechanics and Quantum Chemical Calculations*; Wavefunction, Inc.: Irvine, CA, 1998.

Upon solvation, the CPCM/HF/6-31+G(d) optimization scheme generally predicted an increase in the carbene valence angle for both carbenes and salts (up to 1.3° for **2** and **4** and 0.85° for **2–H**⁺, see Supporting Information), although a decrease is noted for **11** and **11–H**⁺. Similarly, bond lengths are predicted to decrease in both the carbenes and their associated salts. It is known that bond lengths calculated using Hartree–Fock may be shorter than expected due to the neglect of electron correlation in the Hartree–Fock wave function.⁴⁰ It is therefore difficult to predict whether this shortening may truly be expected upon solvation, or whether it is an artifact of the methodology used.

In contrast, the CPCM/B3LYP/6-31+G(d,p) methodology predicted an increase in the carbene valence angle upon solvation, but it predicted a decrease in the $\angle N_1–C_2–N_3$ in the salts. Bond lengths, however, remained almost the same as the gas-phase values in both types of compounds. This might strengthen the argument that the changes observed at the CPCM/HF level of theory are due more to the use of Hartree–Fock than to solvation effects.

Overall, the geometrical changes appear to be fairly minor, but they may have a more significant effect on the solvation energies.²⁸ Thus, as a safety precaution, it seems sensible to perform the solvation optimization in order to ensure accurate prediction of pK_a 's.

Determination of $\Delta G_s^0(H^+)_{aq}$. As mentioned previously, the value for $\Delta G_s^0(H^+)_{aq}$ is the subject of much conjecture. This can have a dramatic effect on the accuracy and reliability of pK_a calculations. Recently, Tissandier et al. reported an experimental finding of -263.98 ± 0.07 kcal/mol.⁴² This value has been applied in the computational determination of pK_a as performed by Chipman.⁴³ Liptak et al. use a similar value of -264.61 kcal/mol in their work on determining absolute pK_a 's,^{15,16,28} with highly accurate results, while Topol et al.⁴⁴ apply a value of -262.5 kcal/mol to give an average absolute difference of 0.8 pK_a unit between experiment and theory for a series of imidazoles. In the determination of pK_a values for some 5-substituted uracils, the value of $\Delta G_s^0(H^+)_{aq}$ was taken as -258.32 kcal/mol.¹² This value was chosen to minimize the rms deviation between the calculated and experimental pK_a values. In an early paper describing the computational determination of absolute pK_a 's, Lim et al.¹⁰ applied a value of -259.5 kcal/mol, obtained by averaging a range of available experimental data. Tawa et al.²⁹ calculated the hydration free energy to be -262.23 kcal/mol, while the application of a primitive quasi-chemical model by Grabowski et al. yielded a value between -251 and -256 kcal/mol.⁴⁵

(41) This is particularly noticeable in the case of **11–H**⁺. The four N–CH₃ bonds in the perchlorate salt (**11–H**⁺ClO₄⁻) are reported as 1.457, 1.457, 1.413, and 1.413 Å (Prick, P. A. J.; Beurskens, P. T. *Cryst. Struct. Commun.* **1979**, *8*, 293). In the case of the 2,6-dinitro-4-(trifluoromethyl)benzenesulfonate salt, however, these same four bonds are reported to be 1.453, 1.457, 1.467, and 1.476 Å (Benetollo, F.; Polo, A.; Conte, L.; Guerrato, A. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1987**, *43*, 928). In the context of Table S1, the first two bond lengths of each set are combined to give N–Me, while the last two pairs give N–Me'.

(42) Tissandier, M. D.; Cowen, K. A.; Feng, W. Y.; Gundlach, E.; Cohen, M. H.; Earhart, A. D.; Coe, J. V.; Tuttle, T. R. *J. Phys. Chem. A* **1998**, *102*, 7787–7794.

(43) Chipman, D. M. *J. Phys. Chem. A* **2002**, *106*, 7413–7422.

(44) Topol, I. A.; Tawa, G. J.; Burt, S. K.; Rashin, A. A. *J. Phys. Chem. A* **1997**, *101*, 10075–10081.

(45) Grabowski, P.; Riccardi, D.; Gomez, M.; Asthagiri, D.; Pratt, L. R. *J. Phys. Chem. A* **2002**, *106*, 9145–9148.

In the current study, $\Delta G_s^0(\text{H}^+)_{\text{aq}}$ was taken as -261.85 kcal/mol. This value was chosen to minimize the absolute difference between the calculated absolute and relative $\text{p}K_a$'s.

Calculated Absolute $\text{p}K_a$'s. Given the variability in $\Delta G_s^0(\text{H}^+)_{\text{aq}}$ and the uncertainty in determining $\Delta G_s(\text{H}^+)$ for a given solvent, it should be noted that the values described herein may not be firm numbers, but they may be subject to an unknown shift that is characteristic of each solvent.⁴³ It is still instructive, however, to compare values obtained in the same solvent, as these comparisons are independent of the value of $\Delta G_s^0(\text{H}^+)_{\text{solvent}}$.⁴³

Average $\text{p}K_a$'s in both DMSO and MeCN follow the series $\mathbf{11} \approx \mathbf{10} \gg \mathbf{6} > \mathbf{2} > \mathbf{5} \approx \mathbf{9} \geq \mathbf{4} > \mathbf{1} \gg \mathbf{8} > \mathbf{3} \approx \mathbf{7} > \mathbf{12}$. If we compare the carbenes that contain methyl substituents at nitrogen (i.e., **1**, **2**, **3**, **9**, **10**, **11**, and **12**), we can determine some of the factors that render a carbene ligand more basic. While substitution at the 4 and 5 positions of the imidazol-2-ylidene ring with halogens (as in **3**) does produce air-stable⁴⁶ carbenes,⁴⁷ it also drastically reduces the basicity relative to the parent 1,3-dimethylimidazol-2-ylidene (**1**). This is presumably due to the electron-withdrawing nature of chlorine. Analogously, the addition of an electron-donating group at the 4 and 5 positions (as in **2**) increases the basicity by 2.6 $\text{p}K_a$ units compared to the parent, **1**. Interestingly, a comparison of **4** and **6** shows an almost identical trend, with the $\text{p}K_a$ increasing by 2.5 units upon substitution at the backbone carbons.

Substitution at nitrogen may also have a dramatic influence on basicity. If we compare carbenes that differ only at nitrogen (i.e., **1**, **4**, **5**, **7**, and **8**), we see that substitution at nitrogen dramatically reduces the $\text{p}K_a$ in the cases of both **7** and **8**, while **4** and **5** are only slightly more basic than the parent, **1**. This decrease in basicity most likely occurs in a manner similar to that seen for **3**, i.e., as a result of the electron-withdrawing inductive effect of the aryl rings.⁴⁸ The slightly decreased basicity of **7** as compared to **8** likely results from additional electron withdrawal through the π system; this is possible in **7**, as the phenyl rings are twisted only slightly relative to the imidazole core, but impossible in **8**, as the methyl groups force the phenyl ring to adopt an orientation orthogonal to the plane of the imidazole ring. It is also possible that the electron-donating methyl groups in **8** moderate the degree to which the phenyl rings withdraw electrons.

The most basic carbene of the methyl series is **11**, with a predicted absolute $\text{p}K_a$ of 27.9 in DMSO and 39.1 in MeCN. The basicity of this carbene is almost matched by **10**, with a $^{\text{DMSO}}\text{p}K_a$ of 27.1 and a $^{\text{MeCN}}\text{p}K_a$ of 38.4. The saturated carbene **9** also exhibits a slightly higher $\text{p}K_a$ compared to **1**. Although it is initially tempting to attribute this increase in basicity to a decrease in electron delocalization compared to the parent carbene **1**, it may be envisaged that the degree of delocalization in **9** and **10** would be similar. Electron delocalization therefore does not appear to be a key factor in determining basicity.

Inspection of Table 1 reveals that the NCN bond angle of carbenes **9** and **10** is very similar and is much larger than that observed for the other compounds. It therefore seems likely that, in the absence of other influences (such as electron-withdrawing/donating groups), it is the NCN angle that has the strongest influence on basicity. This finding is similar to that of Alder,⁴⁹ who noted that proton affinity was strongly influenced by NCN bond angle. The high basicity calculated for **11** supports the suggestion that bis(diisopropylaminocarbene) is the most basic carbene ligand known to date.⁶

The thiazole-based carbene, **12**, is the least basic of all carbenes considered. This finding is not unexpected. Despite the fact that nitrogen is more electronegative than sulfur,⁵⁰ it has long been known that imidazolium ions are more basic (less acidic) than thiazolium ions.^{51–54} This appears to be due to the greater polarizability of sulfur and its ability to absorb electron density.^{53,55}

The variability in $\text{p}K_a$ values for each carbene calculated using **S1–S4** may be attributed to specific aspects of the levels of theory used. For example, in previous work on acids and their anions, it was found that the use of a diffuse basis set in the wave function of the CPCM calculation (as in **S2**, **S3**, and **S4**) lowers (overestimates) ΔG_s values for the acids more so than the anions.^{28,36} This results in a higher overall solvation energy ($\Delta G_{s(\text{overall})} = \Delta G_s^0(\text{A}) + \Delta G_s^0(\text{H}^+) - \Delta G_s^0(\text{HA}^+)$ in eq 4) and, therefore, a higher $\text{p}K_a$. Similarly, the use of correlated methods (**S3** and **S4**) is also known to lead to an underestimation in the overall solvation energy,³⁶ and hence, one would expect lower predicted $\text{p}K_a$ values. These factors should operate in opposing directions for **S3** and **S4**; however, **S2** might overestimate $\text{p}K_a$ relative to the other schemes. In our case, Tables 3 and 4 clearly show that the **S2** and **S3** methods consistently yield very similar results; the **S1** scheme overestimates the $\text{p}K_a$ relative to the average in all cases, while the **S4** method varies between under- and overestimation. There does not appear to be a simple explanation for the behavior of each solvation scheme.

Comparison with Relative $\text{p}K_a$'s. The magnitude of the difference between absolute and relative $\text{p}K_a$'s depends highly on the value chosen for $\Delta G_s^0(\text{H}^+)_{\text{aq}}$. We were able to obtain an overall difference of 0.0 $\text{p}K_a$ unit by using -261.6 kcal/mol for the proton solvation free energy in the DMSO calculations and -262.1 kcal/mol in the MeCN calculations. The average of these two values was taken as $\Delta G_s^0(\text{H}^+)_{\text{aq}}$. The use of this average value results in an average difference of 0.2 $\text{p}K_a$ unit in the case of both solvents; however, in MeCN, the relative $\text{p}K_a$ is consistently lower, while in DMSO the relative $\text{p}K_a$ is always higher. As the difference arises from a constant scaling factor in the absolute calculations (i.e., $\Delta G_s^0(\text{H}^+)_{\text{aq}}$), the $\text{p}K_a$ series that the carbenes follow remains identical to that described previously.

Comparison with Available Literature Data. The limited number of experimental studies performed on carbene basicity

- (46) Imidazol-2-ylidenes have been found to be stable with respect to dry oxygen (Denk, M. K.; Rodezno, J. M.; Gupta, S.; Lough, A. J. *J. Organomet. Chem.* **2001**, *617–618*, 242–253). Used here, “air-stable” may be more accurately described as “moisture-stable”.
- (47) (a) Arduengo, A. J., III; Davidson, F.; Dias, H. V. R.; Goerlich, J. R.; Khasnis, D.; Marshall, W. J.; Prakasha, T. K. *J. Am. Chem. Soc.* **1997**, *119*, 12742–12749. (b) Cole, M. L.; Jones, C.; Junk, P. C. *New J. Chem.* **2002**, *26*, 1296–1303.
- (48) (a) Streitwieser, A., Jr.; Caldwell, R. A.; Granger, M. R. *J. Am. Chem. Soc.* **1964**, *86*, 3578–3579. (b) Streitwieser, A., Jr.; Ziegler, G. R. *J. Am. Chem. Soc.* **1969**, *91*, 5081–5084.

- (49) Alder, R. W. Personal communication, 2003.
- (50) Atkins, P. W.; Jones, L. L. *Chemistry: Molecules, Matter, and Change*, 3rd ed.; W. H. Freeman and Co.: New York, 1997.
- (51) Haake, P.; Bausher, L. P. *J. Phys. Chem.* **1968**, *72*, 2213–2217.
- (52) Haake, P.; Bausher, L. P.; Miller, W. B. *J. Am. Chem. Soc.* **1969**, *91*, 1113–1119.
- (53) Aldrich, H. S.; Alworth, W. L.; Clement, N. R. *J. Am. Chem. Soc.* **1978**, *100*, 2362–2366.
- (54) Sauers, R. R. *Tetrahedron Lett.* **1996**, *37*, 149–152.
- (55) (a) Scheffers-Sap, M. M. E.; Buck, H. M. *J. Am. Chem. Soc.* **1979**, *101*, 4807–4811. (b) Geijo, F.; López-Calahorra, F.; Olivella, S. *J. Heterocycl. Chem.* **1994**, *21*, 1781–1784.

Table 6. Basicity of Carbenes 1–12 and Common Phosphines in Aqueous Solution

compound	pK _a (H ₂ O)	compound	pK _s (H ₂ O)
1	27.4 ± 0.4	11	34.0 ± 0.3
2	29.5 ± 0.3	12	21.2 ± 0.2
3	23.4 ± 0.2	P(<i>p</i> -ClPh) ₃	1.03 ^a
4	28.2 ± 0.3	PPh ₃	2.73 ^b
5	28.3 ± 0.1	P(<i>p</i> -MePh) ₃	3.84 ^b
6	30.4 ± 0.3	PMe ₃	8.65 ^b
7	22.0 ± 0.1	PEt ₃	8.69 ^b
8	22.6 ± 0.1	PCy ₃	9.70 ^b
9	28.5 ± 0.4	P(<i>t</i> -Bu) ₃	11.40 ^b
10	33.7 ± 0.3		

^a Reference 61b. ^b Reference 61a.

precludes extensive comparison with literature data. The basicity of 1,3-di(*tert*-butyl)imidazol-2-ylidene (**5**) in DMSO was derived as 22.7.⁹ This is in excellent agreement with our predicted values of 22.6 ± 0.09 (absolute) and 22.8 ± 0.15 (relative).

Similarly, the basicity of 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene (**6**) was measured as 24.0 in DMSO.⁸ Our calculated values of 24.5 ± 0.15 (absolute) and 24.7 ± 0.18 (relative) are in reasonable agreement. Kim and Streitwieser⁹ made the suggestion that this reported value might have been an overestimate based on the measurement of both ion pair and free ions in solution and that the pK_a of **6** should be directly comparable to that of **5**, as they are closely related species. We have seen, however, that the inclusion of methyl groups in the backbone of the ring can dramatically enhance the basicity of a carbene. Thus, the value of 24.0 reported by Alder may not be an overestimate.

Haake and co-workers⁵² estimated the approximate aqueous pK_a's of 1,3,4-trimethylimidazolium iodide, 3,4-dimethylthiazolium iodide, and 3,4-dimethylloxazolium iodide as 17, 14, and 12, respectively. This fits with our findings that imidazole-based carbenes are stronger bases than those which are thiazole-based. Other workers⁵⁶ have measured the aqueous pK_a of the 3,4-dimethylthiazolium ion as 18.9.

In acetonitrile, the most basic carbene (**11**) exhibits a pK_a of 39.2. This value is higher than that reported for some strong neutral organic bases (for example, the pentacyclic vinamidinium-type bases that have reported ^{MeCN}pK_a's up to 32.9)⁵⁷ and the well-known neutral organic base DBU (^{MeCN}pK_a = 24.13).⁵⁸ It is, however, no match for some of the reported phosphazene bases which have pK_a's up to 46.9.⁵⁹

Carbene vs Phosphine Basicity. Given the tendency to consider carbenes as potential replacements for phosphine ligands in many catalytic reactions, it is of interest to compare the relative basicities of the two types of ligands. Since much of the available experimental data for phosphines is based on aqueous solution, the average absolute pK_a's of carbenes 1–12 were calculated in water, using the method described above. The results are given in Table 6,⁶⁰ together with the pK_a's of

some common phosphines experimentally determined in water.⁶¹ We note in passing that the order of basicity of the carbenes in water is almost identical to that in DMSO or MeCN. From Table 6, it may be seen that even the most basic phosphine shown, P(*t*-Bu)₃, is still ~10 pK_a units less basic than the least basic carbene (**12**). It is also interesting to note that if one compares the basicity of P(*p*-ClPh)₃, PPh₃, and P(*p*-MePh)₃, a trend identical to that observed for carbenes 1–3 is found, i.e., pK_a(Cl) < pK_a(H) < pK_a(Me).

In addition to allowing comparison with common phosphines, these aqueous calculations allow us to compare the pK_a's of the carbenes with those of many other common organic bases, for example, triethylamine, which has an aqueous pK_a of 11.01, and pyrrolidine (^{H₂O}pK_a = 11.27).⁶²

Solvent Effects. The dependence of pK_a on solvent has long been recognized and may be attributed to the differing ability of each solvent to solvate the carbene, the salt, and the liberated proton.³² Our results show that the order of basicities of the carbenes is ^{MeCN}pK_a > ^{H₂O}pK_a > ^{DMSO}pK_a. The higher basicity of the compounds in MeCN as compared to DMSO is not unexpected. This trend has been reported for several diimine heterocyclic bases, including imidazole.⁶³ Other classes of compounds also exhibit this behavior;⁴³ in many cases, the ^{MeCN}pK_a values may be extrapolated from ^{DMSO}pK_a values by adding 10–13 units.⁵⁹ In this work, ^{MeCN}pK_a's are, on average, 11.2 units higher than the corresponding ^{DMSO}pK_a.

The ^{MeCN}pK_a of many amines may be extrapolated from the ^{H₂O}pK_a values by adding 7–8 units,⁶⁴ and indeed, a similar trend is observed here, albeit with an average difference of 5.0 pK_a units. The average difference between ^{H₂O}pK_a and ^{DMSO}pK_a values is 6.2 units. While it has previously been reported that the pK_a of imidazole is lower in DMSO than in water,^{63,65} this trend is not universal and appears to depend strongly on the structure of the species in question.⁶⁵

Proton Affinity. The PA of imidazol-2-ylidene has previously been reported as 262.1 kcal/mol at the MP2(FC)/6-31G** level,⁵⁴ 257.3 kcal/mol at the MP2 level with an extended basis set,⁶⁶ and 258.4 kcal/mol at the B3LYP/6-31G* level.²³ The reported PAs of thiazol-2-ylidene and oxazol-2-ylidene are 254.7 and 247.2 kcal/mol, respectively.⁵⁴ The PAs of the substituted carbenes 1,3-dimethylimidazol-2-ylidene (**1**) and 3-methylthiazol-2-ylidene (**12**) have been calculated at the B3LYP/6-311+G(2d,p) level and found to be 259.5 and 248.8 kcal/mol, respectively.⁶⁷ **11** has a reported PA of 275.0 kcal/mol (B3LYP/6-31G*).²³ The PA of the aryl-substituted carbene 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene, which is closely related to **8**, has been calculated as 275.7 kcal/mol at the B3LYP/6-31G* level.²³ All these previous calculations have been in the gas phase.

It may be seen from Table 5 that the gas-phase PAs obtained in this study are between 248.2 and 268.5 kcal/mol, while those

(56) Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 683–692.

(57) Schwesinger, R.; Missfeldt, M.; Peters, K.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1165–1167.

(58) Kaljurand, I.; Rodima, T.; Leito, I.; Koppel, I. A.; Schwesinger, R. *J. Org. Chem.* **2000**, *65*, 6202–6208.

(59) Schwesinger, R.; Schlemper, H.; Hasenfratz, C.; Willaredt, J.; Dambacher, T.; Breuer, T.; Ottaway, C.; Fletschinger, M.; Boele, J.; Fritz, H.; Putzas, D.; Rotter, H. W.; Bordwell, F. G.; Satish, A. V.; Ji, G.-Z.; Peters, E.-M.; Peters, K.; von Schnering, H. G.; Walz, L. *Liebigs Ann.* **1996**, 1055–1081.

(60) Average pK_a's are given. Calculated pK_a's for each solvation scheme are available as Supporting Information (Table S2).

(61) (a) Rahman, M. M.; Liu, H.-Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1989**, *8*, 1–7. (b) Allman, T.; Goel, R. G. *Can. J. Chem.* **1982**, *60*, 716–722.

(62) *CRC Handbook of Chemistry and Physics*, 1st student ed.; CRC Press: Boca Raton, 1988.

(63) El-Gyar, S. A.; Hamed, M. M. A.; Abdalla, E. M.; Mahmoud, M. R. *Monatsh. Chem.* **1993**, *124*, 127–133.

(64) (a) Foroughifar, N.; Leffek, K. T.; Lee, Y. G. *Can. J. Chem.* **1992**, *70*, 2856–2858. (b) Coetzee, J. F.; Padmanabhan, G. R. *J. Am. Chem. Soc.* **1965**, *87*, 5005–5010.

(65) Crampton, M. R.; Robotham, I. A. *J. Chem. Res., Synop.* **1997**, 22–23.

(66) Dixon, D. A.; Arduengo, A. J., III. *J. Phys. Chem.* **1991**, *95*, 4180–4182.

(67) Graham, D. C.; Cavell, K. J.; Yates, B. F. *J. Phys. Org. Chem.* **2004**, in press.

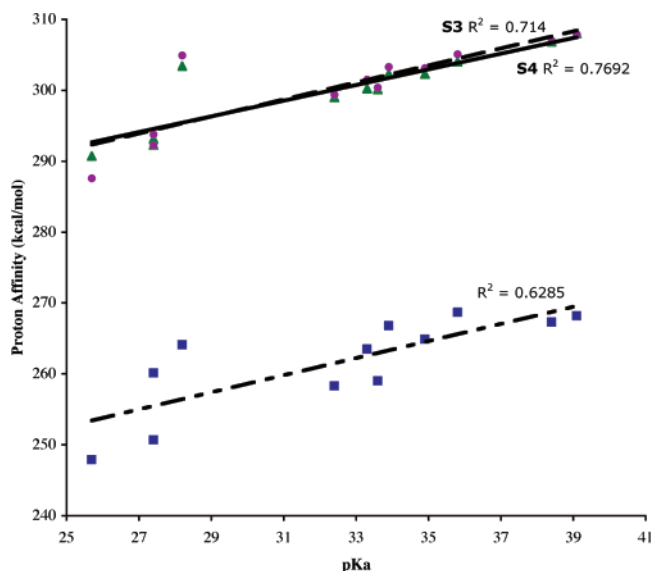


Figure 2. Correlation between pK_a and proton affinity, calculated with CBS-QB3 (squares, broken line), **S3** (MeCN) (triangles, solid line), and **S4** (MeCN) (circles, broken line).

obtained in solution span the range 298.0–320.9 kcal/mol. PAs of this magnitude in MeCN have previously been reported for some organic (super)bases.³³

The previously reported gas-phase PA for **11**²³ is significantly higher than that reported here. This difference probably arises as a result of the differences in the levels of theory used. Complete basis set methods are state-of-the-art in determining accurate thermochemical data,¹⁵ and therefore the value given in Table 5 could be expected to more accurately reflect the true number. It may be seen that there is good agreement between the previously reported PAs of **1** and **12** and the values calculated here.

Proton affinity has previously been shown to directly correlate with pK_a .³³ The correlation between pK_a and PAs calculated using CBS-QB3, **S3**, and **S4** is shown in Figure 2. For solution-phase PAs the correlation is, in general, excellent; however, in the case of **8**, it no longer holds (it is interesting to note that, in the absence of **8**, R^2 values of 0.99 and 0.97 are obtained for **S3** and **S4**, respectively). We had initially thought that the **S3** solvation scheme may provide a rapid method for determining accurate relative basicities within a series of compounds; however, it now appears that when a slightly broader cross-section of compounds is studied, high-level calculations are indeed required to ensure correct predictions.

Conclusions

The pK_a 's of 12 nucleophilic carbenes have been calculated using the CBS-QB3 model chemistry in conjunction with the CPCM solvation methodology. Carbene **11** was found to be the

most basic, with a $^{DMSO}pK_a$ of 27.9 ± 0.23 , a $^{MeCN}pK_a$ of 39.1 ± 0.25 , and a $^{H_2O}pK_a$ of 34.0 ± 0.3 . The least basic carbene was found to be the thiazole-based **12**, whose $^{DMSO}pK_a$, $^{MeCN}pK_a$, and $^{H_2O}pK_a$ were 14.5 ± 0.16 , 25.6 ± 0.15 , and 21.2 ± 0.2 , respectively. When ranked according to basicity, the carbenes follow an identical pattern independent of solvent.

Substitution at the 4 and 5 positions of the imidazole ring was found to significantly alter the pK_a of the carbenes. For example, substitution by chlorine resulted in a dramatic decrease in pK_a , while the inclusion of methyl groups at $C_{4/5}$ increases the pK_a by approximately 2.5 units. Altering the substituents at nitrogen had a similar effect on basicity, with the addition of electron-withdrawing phenyl rings decreasing the pK_a by up to 5.4 units.

In the absence of other factors, such as electron-donating or -withdrawing substituents, the NCN angle has the most dramatic effect on basicity, with an increase in valence angle leading to a rise in the pK_a . Additionally, imidazole-based carbenes are significantly more basic than those based on thiazole.

The solution-phase proton affinities, calculated using CPCM/MP2/6-311+G(d,p)//CPCM/HF/6-31+G(d), were found to give the best correlation with calculated pK_a 's, and may provide a rapid method for determining relative basicities.

The theoretical approach described in this paper is essentially an ab initio one, with little recourse to experimental data. The good agreement between calculated and available experimental pK_a values confirms that, provided a reliable estimate of the heat of solvation of the proton can be determined, the theoretical approach used here^{14–16} can be employed to calculate useful chemical results of very high accuracy.

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Supporting Information Available: Absolute $^{H_2O}pK_a$'s calculated using **S1–S4** for **1–12** and free energies of solvation of compounds **1–12** using solvation models **S1–S4** in MeCN, DMSO, and water; optimized geometries of compounds **1–14** in the gas phase, acetonitrile, dimethyl sulfoxide, and water. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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