J|A|C|S
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

ARTICLE

pubs.acs.org/JACS

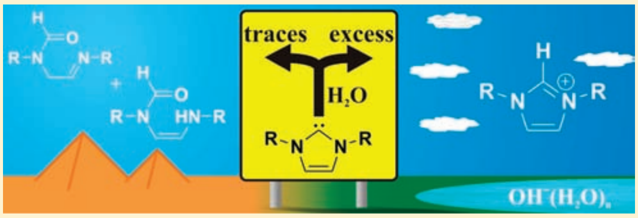
Hydrolysis of Imidazole-2-ylidenes

Oldamur Hollóczki,[†,‡] Péter Terleczky,[†] Dénes Szieberth,[†] Georgios Mourgas,[§] Dietrich Gudat,[*,§] and László Nyulászi[*,†,‡]

[†]Department of Inorganic and Analytical Chemistry and [‡]Materials Structure and Modeling Research Group of the Hungarian Academy of Sciences, Budapest University of Technology and Economics, Szt. Gellért tér 4., Budapest, H-1111 Hungary

[§]Institut für Anorganische Chemie, Universität Stuttgart, Pfaffenwaldring 55, 70550 Stuttgart, Germany

Supporting Information



ABSTRACT: The direct reaction of an imidazole-2-ylidene in a predominantly aqueous environment [about 0.1 M solution in a H_2O (>60%)/THF solvent system] was investigated for the first time. The reaction yielded a stable solution of the corresponding imidazolium-hydroxide of pH 13, which is in agreement with results from an *ab initio* molecular dynamics simulation. In contrast, hydrolysis of the carbene in a mainly aprotic environment (>80% THF) gives a hydrogen-bridged carbene—water complex which could be detected by NMR and IR spectroscopies for the first time. This complex converts slowly to two isomeric ring opened products and is at higher water concentration in dynamic equilibrium with the imidazolium hydroxide. A computational mechanistic study of the carbene hydrolysis with a gradually increasing number of water molecules revealed that the imidazolium—hydroxide structure can only be optimized with three or more water molecules as reactants, and with the increasing number of water molecules its stability is increasing with respect to the carbene—water complex. In agreement with the experimental results, these findings point out that solvent stabilization and basicity of the hydroxide ion plays a crucial role in the reaction. With increasing number of water molecules the barriers connecting the reaction intermediates are getting smaller, and the ring opened hydrolysis products can be derived from imidazolium—hydroxide type intermediates. Computational studies on the hydrolysis of a nonaromatic imidazolidine-2-ylidene analogue clearly indicated the analogous ring-opened product to be by 10—12 kcal/mol more stable than the appropriate ion pair and the carbene—water complex, in agreement with the known aromatic stabilization of imidazol-2-ylidenes. Accordingly, these molecules hydrolyze with exclusive formation of the ring-opened product.

INTRODUCTION

In the last few decades stable singlet carbenes[1] have become one of the most widely examined groups of compounds in chemistry. The interest is generated by their catalytic applicability either as transition metal complexes[2] or metal free organocatalysts,[3] having often outstanding selectivity and stability.[2e,3b] Derivatives of the remarkably stable imidazole-2-ylidenes[4] are perhaps the most frequently used species. Still, although their transition metal complexes can be resistant to moisture, and some reactions can even be performed in aqueous media,[5] free carbenes are usually considered to be particularly sensitive against hydrolysis.[1,6] As this property makes their handling difficult and expensive,[7] a better understanding and prevention of this reaction could seriously improve their applicability. It is thus strange that only a few attempts were made to investigate this hydrolysis, and although it was noticed that different hydrolysis products were obtained under different conditions,[8,9] no explanation for this behavior has been sought.

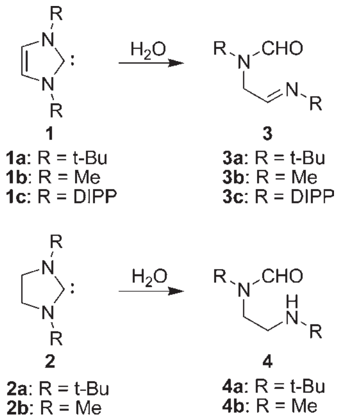
The hydrolysis of the (free) 1,3-ditert-butylimidazole-2-ylidene **1a** differs from that of the saturated 1,3-ditert-butylimidazolidine-2-ylidene[10] **2a**.[8] In the presence of air or moisture, **1a** converts to **3a** (Scheme 1),[7] and it has been reported that the same product (**3a**) was also deliberately formed in a very slow reaction (for the full conversion 3 months were needed!) with an equimolar amount of water in THF.[8]Compound **2a** under the same conditions hydrolyzes to **4a** (Scheme 1) instantaneously.[8] The sluggish reactivity of **1a** is in clear contrast with the expected high sensitivity of carbenes against even traces of humidity. The proposed mechanism of this reaction was a concerted insertion into the O—H bond,[11] rather than a stepwise protonation—hydroxide addition, since addition of catalytic amounts of OH^- or H^+ sources to the reaction mixture did not increase the rate of hydrolysis. Furthermore, the imidazolium salt formed in the reaction with the added acid aimed for catalysis was found to be resistant against any further decomposition. The difference between the reaction rate of **1** and **2** was rationalized by the known difference in their stability.[12,13]

The proton/deuteron exchange of the imidazolium cation **5b** in the presence of large excess of water has also been investigated in buffered solutions in the pH range 5—8.[9] Even though in these experiments no other product than the imidazolium cation **5b** could be detected,[9] the presence of carbene **1b** was concluded from the proton/deuteron exchange reaction (Scheme 2) followed

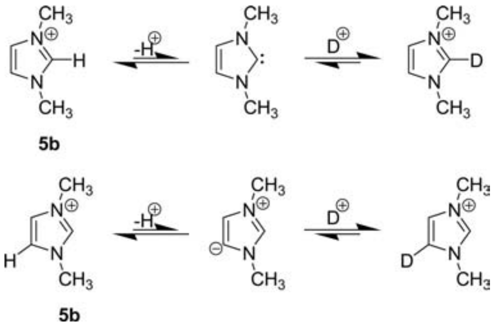
Received: April 27, 2010
Published: December 21, 2010

ACS Publications © 2010 American Chemical Society

Scheme 1. Hydrolysis of Imidazole-Derived Carbenes (DIPP = 2,6-Diisopropylphenyl)



Scheme 2. Hydrogen/Deuterium Exchange of Imidazolium Cation



by NMR spectroscopy.[9,14,15] We note that similar exchange at positions 4 and 5 has also been reported (Scheme 2).[14b]

Facile protonation of a carbene to give an imidazolium cation is in accordance with the reported extremely strong basicity of carbenes.[16] Imidazolium cations as cationic components of "ionic liquids" are used in a variety of applications in the presence of water or air moisture without considerable decomposition.[17] Nevertheless, while these findings suggest a reversible protonation/deprotonation reaction instead of a ring-opening in the presence of large excess of water, it remains unclear at which water to carbene ratio, and at which pH range, the mechanism of the hydrolytic reaction will switch from ring-opening to protonation.

In this context it should be mentioned that water molecules may play multiple roles in hydrolysis reactions. First, water can be a proton donor; the result of this simple reaction would result in formation of an imidazolium−hydroxide[18] from a carbene. The acidity of a water molecule is influenced by the environment, and it is greatly increased if the resulting hydroxide ion is stabilized by several hydrogen bonds (possibly from other water molecules).[19] It has been reported, for example, that in a dodecahedral water cluster an autoprotonation reaction can take place with a very low barrier.[19] Second, a series of water molecules may act as a relay channel to transfer the proton from its original to the final position,[19] giving a possible explanation for the well-known high electric conductivity of proton (and hydroxide ion). Such proton relay is also known to greatly reduce the activation barrier for otherwise hindered bond cleavage reactions.[20−22] Third, water molecules may stabilize ionic systems either as an electron pair donor or by forming a hydrogen bond. Thus, the number of water molecules can indeed have a significant effect on the mechanism and energetics of the hydrolysis.

Interestingly, no computational studies have been devoted to understand this apparently complex behavior of the hydrolysis properties of imidazole-2-ylidenes, despite the significance of this reaction. Only the reaction of less stable[12] H, Me, CN, Cl, and F substituted carbenes with one and two water molecules providing the corresponding O−H inserted product alcohol has been examined by Restrepo et al., showing a decrease in gaps by the addition of the second molecule of water, due to its proton relay behavior.[21] Furthermore, the low rate of the reaction of imidazol-2-ylidene with an equimolar amount of water raises the question of how moist the solvent can be for the carbene to remain intact. In the present work, the hydrolysis of 1,3-dimethylimidazole-2-ylidene **1b**, and 1,3-ditertbuthylimidazole-2-ylidene **1a**, together with that of the nonaromatic 1,3-dimethylimidazolidine-2-ylidene **2b** will be discussed with different numbers of neighboring water molecules, to model the reaction in the gas phase, in nonpolar organic solvents containing traces of water, and in aqueous solution. In addition, these studies will be backed by experimental investigations of the hydrolysis of 1,3-bis(2,6-diisopropyl-phenyl)imidazole-2-ylidene **1c**.

■ MODELS AND METHODS

Although the carbene to water molar ratio does not provide direct information about the microenvironment of the carbene, increasing concentration of water will result in larger water networks,[22] containing two, three, or more water molecules. Thus, to account for the different amounts of water we have first computed the reaction between the carbenes and one, two, and three water molecules.

To model the decomposition in the aqueous phase we used a microsolvation approach, considering a water monolayer, with the assumption that a primary solvate shell contains most of the favorable (e.g., hydrogen bond with the solute) and unfavorable (such as between an unpolar chain and a polar solvent) interactions.[23] The explicit model chosen consists of 30 water molecules in the primary shell, providing full coverage for the solvated molecule, and one water molecule as a reactant. The principles to form the starting geometries of the clusters were to keep linear hydrogen bonds, and keep the tetrahedral structure around the oxygen of each water molecule. This resulted in a shell consisting of water pentamers and hexamers.[23] To use a different approach for the description of the aqueous phase reaction, *ab initio* molecular dynamic simulations have also been performed for **1b** surrounded by 102 water molecules (equivalent to a ca. 0.5 M concentration).

Full geometry optimizations and the subsequent verification of the Hessian have been performed by the Gaussian 03 program package.[24a] For the reaction of one, two, and three water molecules with **1b** the intermediates and transition states have been optimized with different DFT functionals (B3LYP, B3PW91, PW91PW91, B97−1, MPW1K, MPWB1K, BMK, M05−2X, TPSSh) and also at the MP2 level with the 6-311+G** and 6-311++G** basis sets. To further test the reliability of the geometries and relative energies B3LYP/aug-cc-pVTZ, B3LYP/6-311+G**//B3LYP/6-31+G*, RI-MP2/def2-TZVPP//B3LYP/6-31+G*,[24b] RI-B97-D/def2-TZVPP,[24b] and, for certain systems, CCSD(T)/cc-pVTZ//B3LYP/6-31+G* and CCSD(T)/cc-pVTZ//MP2/6-311+G** calculations have also been performed. To make coupled cluster single point calculations accessible, the convergence criteria has been set to 10^{-5} on the energy and 10^{-7} on the wave function in case of these calculations. Since the relative energies of each point calculated at the B3LYP/6-311+G** and B3LYP/6-311+G**//B3LYP/6-31+G* level were found to be in reasonable agreement with those at all other levels (for details see Supporting Information), we applied B3LYP/6-311+G** for the reaction of **1a** and **2b** with one, two, and three water molecules, and B3LYP/6-311+G**//B3LYP/6-31+G* for that of **1b** and **2b** in the solvate shell. For the intermediates of the reaction of **1b** in the solvate shell, M05−2X/6-311+G**//M05−2X/6-31+G* energies and further ωB97X-D/6-311++G** and MOS(ω600)-RI-MP2/cc-pVTZ single point energies[24c] at the B3LYP/6-31+G* level geometries have been calculated. For the visualization of the optimized structures the MOLDEN program has been used.[25]

For the *ab initio* molecular dynamics calculations the VASP code has been applied.[26] Gamma point calculations were carried out using the PW91PW91 GGA exchange-correlation functional and hard PAW pseudopotentials provided with the VASP package. 500 eV was used as cutoff energy for the plane wave basis set.

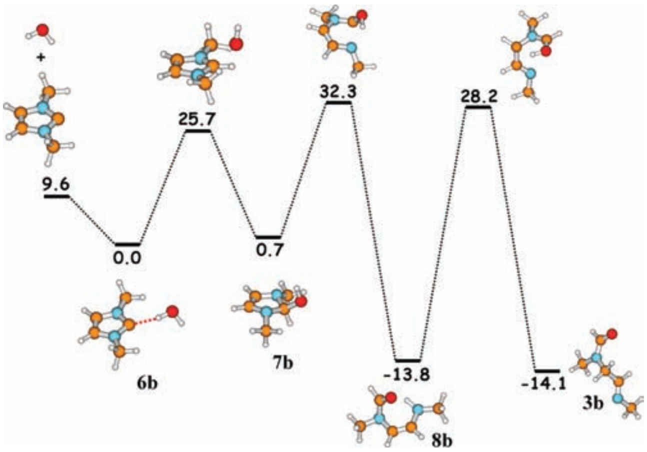
Experimental manipulations were performed under an atmosphere of dry argon using either Schlenk techniques or a glove box. For the experimental studies, 1,3-bis-(2,6-diisopropylphenyl)imidazole-2-ylidene **1c** was prepared according to the procedure previously described by Dible and Sigman.[27] The crude product was purified by recrystallization from hexane and its purity checked by elemental analysis and ^{1}H NMR spectroscopy. Studies of the hydrolysis were carried out by either adding a defined amount of deionized and degassed water with a microliter syringe to solutions of the carbene (30 mg) in anhydrous C_6D_6 or THF-d_8 (0.5 mL) or, alternatively, treating a suspension of solid **1c** (30 mg) in water (0.4 mL) with THF-d_8 (0.1−0.2 mL) to ensure formation of a homogeneous solution. The reactions were followed by ^{1}H and ^{13}C NMR spectroscopy. Products were identified and characterized in the reaction mixtures by one-dimensional (^{1}H, ^{13}C{^{1}H}) and two-dimensional (^{1}H-gs-NOESY, ^{1}H,^{13}C-gsHSQC, ^{1}H,^{13}C-gsHMBC) NMR spectra; no attempts toward isolation of any of the products was made. For a titration of a carbene solution with water, specified amounts of water were added by means of a microliter syringe to a precooled (−35 °C) solution of **1c** (30 mg) in THF-d_8 (0.5 mL). The reaction was monitored by recording ^{1}H and ^{13}C NMR spectra at −35 °C immediately after homogenization of the solution. All NMR spectra were recorded on a Bruker AV400 spectrometer (^{1}H 400.1 MHz, ^{13}C 100.6 MHz) at 303 K. The WET technique was used to suppress the water signal in aqueous solution. Chemical shifts are referenced to external TMS (^{1}H, ^{13}C); *i, o, m, p* denote the positions in N-aryl rings. IR spectra of reaction mixtures of **1c** and H_2O in C_6D_6 were measured on a Nicolet 6700 FT-IR spectrometer equipped with a diamond ATR unit. A complete listing of available ^{1}H and ^{13}C NMR data including the assignment of individual resonances is included in the Supporting Information.

Spectroscopic data. Data for **1c** − H_2O follow. ^{1}H NMR (C_6D_6): δ = 7.27 (m, 2 H, *p*-CH), 7.17 (m, 4 H, *m*-CH), 6.57 (s, 2 H, $C_{4/5}$H), 2.90 (sept, $^{3}J_{HH}$ = 7 Hz, 4 H, CH), 1.53 (s, 2 H, H_2O), 1.28 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3), 1.16 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3). ^{1}H NMR (THF-d_8): δ = 7.36 (m, 2 H, *p*-CH), 7.26 (m, 4 H, *m*-CH), 7.19 (s, 2 H, $C_{4/5}$H), 2.81 (sept, $^{3}J_{HH}$ = 7 Hz, 4 H, CH), 2.59 (s, H_2O), 1.20 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3), 1.17 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3).

Data for for **3c** follow. ^{1}H NMR (C_6D_6; signals of aromatic protons in *N*-aryl substituents omitted as no unambiguous assignment feasible): δ = 8.20 (s, 1 H, CHO), 7.83 (t, $^{3}J_{HH}$ = 4 Hz, 1 H, CH=N), 4.50 (d, $^{3}J_{HH}$ = 4 Hz, 2 H, NCH_2), 3.00 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 2.98 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 1.17 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3), 0.97 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3), 0.93 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3). ^{1}H NMR (THF-d_8; signals of aromatic protons in *N*-aryl substituents omitted as no unambiguous assignment feasible): δ = 8.17 (s, 1 H, CHO), 7.76 (t, $^{3}J_{HH}$ = 3.9 Hz, 1 H, CH=N), 4.52 (d, $^{3}J_{HH}$ = 3.9 Hz, 2 H, NCH_2), 3.23 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 2.87 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 1.26 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3), 1.11 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3).

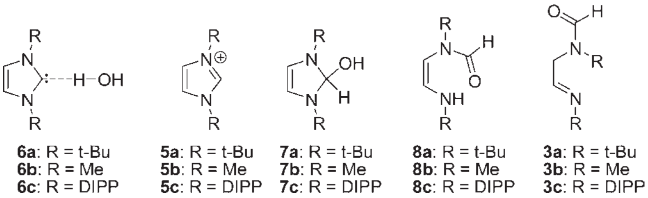
Data for **8c** follow. ^{1}H NMR (C_6D_6): δ = 8.04 (s, 1 H, CHO), 7.2−7.1 (m, 6 H, *p,m*-CH), 7.14 (m, 1 H, *p*-CH), 7.00 (m, 2 H, *m*-CH), 6.75 (br, 1 H, NH), 5.56 (d, $^{3}J_{HH}$ = 7 Hz, 1 H, =CH—N), 4.66 (d, $^{3}J_{HH}$ = 7 Hz, 1 H, =CH—N), 3.73 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 3.20 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 1.31 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3), 1.12 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3), 1.03 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3). ^{1}H NMR (THF-d_8; signals of the aromatic protons in *N*-aryl substituents omitted as no unambiguous assignment feasible): δ = 8.02 (d, $^{4}J_{HH}$ = 0.9 Hz, CHO), 6.39 (br d, $^{3}J_{HH}$ = 9 Hz, 1 H, NH), 5.63 (dd, $^{3}J_{HH}$ = 7.8, 9.1 Hz, 1 H, CH=N), 4.84 (ddd, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ = 0.9, 0.9 Hz, 1 H, CH=N), 3.55 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 3.25 (sept, $^{3}J_{HH}$ = 7 Hz, 2 H, CH), 1.25 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3), 1.21 (d, $^{3}J_{HH}$ = 7 Hz, 12 H, CH_3).

Scheme 3. B3LYP/6-311+G** Energy Profile[a,b] of the Reaction of 1b and One Water (Relative Energies in kcal mol^{-1})



[a] M05−2X/6-311+G** relative energies are 10.4, 0.0, 27.5, −3.3; 33.6, −10.6, 30.5, −14.1 kcal mol^{-1}, respectively.
[b] MP2/6-311+G** relative energies are 10.3, 0.0, 28.2, −1.0, 33.8, −7.4, 30.2, −7.1 kcal mol^{-1}, respectively. CCSD(T)/cc-pVTZ/6-311+G** relative energies are 10.5, 0.0, 35.2, 2.9, 33.1, −10.3, 30.2, −12.6 kcal mol^{-1}, respectively.

Chart 1. Chemical Structures of the Molecules Involved in the Hydrolysis of 1a−c (DIPP = 2,6-Diisopropylphenyl)

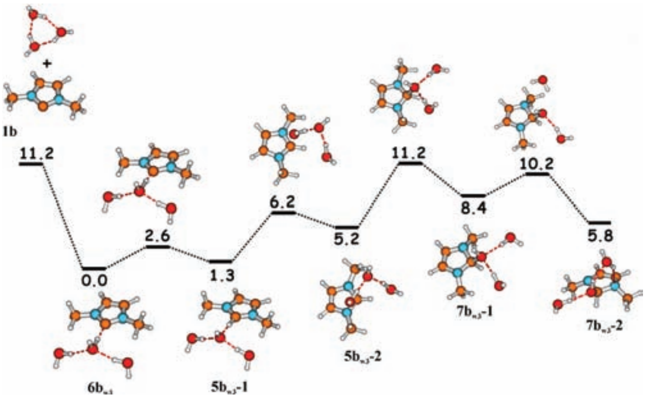


Data for **5c** follow. ^{1}H NMR (H_2O/THF-d_8 4:1): δ = 7.98 (s, 2 H, $C_{4/5}$H), 7.64 (m, 2 H, *p*-CH), 7.47 (m, 4 H, *m*-CH), 2.41 (sept, $^{3}J_{HH}$ = 7 Hz, 4 H, CH), 1.22 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3), 1.15 (d, $^{3}J_{HH}$ = 7 Hz, 6 H, CH_3).

RESULTS AND DISCUSSION

Reaction with One Water Molecule. The energy profile of the proposed mechanism, with the relative energies of the intermediates and transition states, is shown in Scheme 3, and Chart 1 summarizes the chemical structures of the molecules involved in the hydrolysis of **1a**−**c**. The initial step of this reaction is the formation of a hydrogen-bonded structure **6b**,[28] in which one of the hydrogen atoms of the water molecule is coordinated to the hypovalent carbon atom.[18] The oxygen is apparently oriented to the methyl groups, indicating C−H···O interaction that could be verified by localizing the corresponding bond critical point.[29] The electron density at that point (ρ = 0.008)

Scheme 4. B3LYP/6-311+G Energy Profile[a] for the Reaction of 1b with Three Water Molecules (Relative Energies in kcal mol^{-1})**



[a] M05−2X/6-311+G** relative energies are 11.5, 0.0, 3.1, 2.2, 2.5, 2.4, 7.5, 1.9, 2.4, 0.3 kcal mol^{-1}, respectively. RI-MP2/def2-TZVPP//B3LYP/6-311+G**: 12.6, 0.0, 3.0, 2.8, 5.3, 4.5, 10.5, 6.5, 7.2, 3.1 kcal mol^{-1}, respectively.

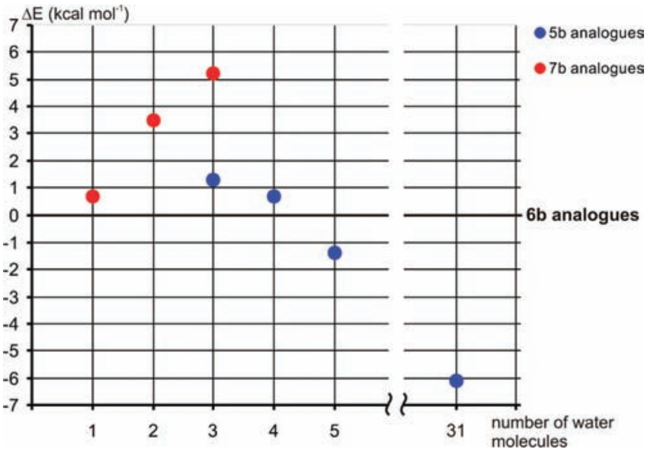


Figure 1. Relative energy of **5b** and **7b** with respect to **6b**, in the presence of 1−5 and 31 water molecules at the B3LYP/6-311+G** level.

was about 20% of that between two hydrogen bonded water molecules, indicating a weak interaction only. It is noteworthy that the $C_{carbene}$−O_{water} bonded intermediate, which was reported[21] to have a key role in the hydrolysis of the less stabilized[11] carbenes, could not be located, in agreement with the stabilized nature of imidazol-2-ylidenes. Similarly, no imidazolium−hydroxide type structure could be optimized; attempts to locate such structures resulted in **6b**, as had recently been shown for the 1,3-dimethylimidazolium hydroxide ion pair.[18]

From the hydrogen bonded structure **6b** the concerted insertion of the carbene into the O−H bond is possible (as suggested by Denk et al.[8]), yielding a nonaromatic 2,3-dihydro-1,3-dimethylimidazole-2-ol **7b** with a saturated carbon atom.[30] The transition state of this step is quite polarized, as suggested by the −0.95 Mulliken charge on the oxygen in comparison to the corresponding values of −0.57 and −0.28 for **6b** and **7b**, and is therefore destabilized, and the negatively charged OH moiety is tilted away from the vertical symmetry plane of the ring due to the aforementioned interaction with the hydrogen of the alkyl group. This transition structure can also be considered as a close contact imidazolium−hydroxide ion pair, based on the 1.079 Å C(2)−H bond and the 1.864 Å O−H and 2.312 Å C−O distances. Interestingly, the B3LYP/6-311+G** H-bonded structure **6b** is somewhat more stable than **7b** (for results at other levels of the theory see Table S1 in the Supporting Information). It should be noted that in a recent computational study[18] a significantly (by ca. 3 kcal mol^{-1}) larger energy difference between **6b** and **7b** has been reported. The difference is due to the fact that we have located an isomer of **7b** which is more stable than the previously reported[18] one.

The transition state of the direct rearrangement of **7b** to **3b** by proton transfer could not be found; however, a rearrangement yielding **8b** (that is a Schiff base isomer of the experimentally found product) could be obtained.[31] The final isomerization from **8b** to the thermodynamically more stable **3b**[32] is apparently aided by the formyl group, or alternatively by another water or solvent molecule acting as a proton relay. The relative energies of **7b** and **3b** show that the stability of the products provides indeed the driving force of the reaction, which is, however, kinetically hindered by the substantial barriers both for the insertion (25.7 kcal mol^{-1} at the B3LYP/6-311+G** level) and the rate determining ring-opening step (32.3 kcal mol^{-1} at the B3LYP/6-311+G** level).

To have a better comparison with the experimental work of Denk et al., the hydrolysis of the *tert*-butyl derivative has also been examined. For the analogous reaction path, similar relative energies were obtained for intermediate **7a** (1.9 kcal mol^{-1}), products (−12.8 kcal mol^{-1} for both **8a** and **3a**[33]), and the ring-opening transition state (30.9 kcal mol^{-1}) compared to those for the methyl analogue, but the barrier of the OH insertion is considerably decreased (18.6 kcal mol^{-1}), presumably due to the increased number of the stabilizing nearby methyl groups. Accordingly, for the more heavily substituted carbenes it is reasonable to expect that the **6** and **7** type structures are in dynamic equilibrium with each other, while the subsequent ring-opening is hindered by the substantial, rate determining barrier.

Reaction with Two and Three Water Molecules. The reaction of **1b** with two water molecules exhibits a similar energy profile as that with one water molecule (for the corresponding scheme see Supporting Information), but the barrier of the insertion of the carbene into the O−H bond is significantly lower (14.5 kcal mol^{-1}) due to the coordination of the second water to the passing OH^{-} moiety. Apparently, the second water molecule alleviates the proton transfer also in the ring-opening step, resulting in a barrier of 24.6 kcal mol^{-1}.[34] The reaction of **1b** with a water cluster of three water molecules (Scheme 4) results in a hydrogen bonded assembly. Among these structures, $\mathbf{6b}_{w3}$ was found to be the most stable one, which can be attributed to the weak hydrogen bonds between the methyl hydrogens and oxygen, as shown by the presence of bond critical points.[29] Most interestingly, in the presence of three waters an imidazolium−hydroxide $\mathbf{5b}_{w3}$ structure could also be optimized. $\mathbf{5b}_{w3}$ is connected to the slightly more stable $\mathbf{6b}_{w3}$ by a low barrier proton shift. Expectedly, ionic **5b** can be stabilized with respect to **6b** by the presence of more water. (In the presence of four and five water molecules, the relative energy of **5b** decreases to 0.7 and −1.4 kcal mol^{-1}, respectively, see Figure 1.) Polar solvents also stabilize the imidazolium hydroxide, type **5b** structures, as shown by single point PCM energy calculations in THF which predict $\mathbf{5b}_{w3}$ to be more stable than $\mathbf{6b}_{w3}$ by 1.6 kcal mol^{-1}. There are several $\mathbf{5b}_{w3}$ structures with different hydrogen bond arrangements, which are connected by low energy barriers. **7b**$_{w3}$ is formed from **5b**$_{w3-2}$. Thus, in the presence of three water molecules a stepwise protonation/deprotonation mechanism is operative rather than a concerted carbene insertion into the O−H bond via a contact ion pair-like transition structure.

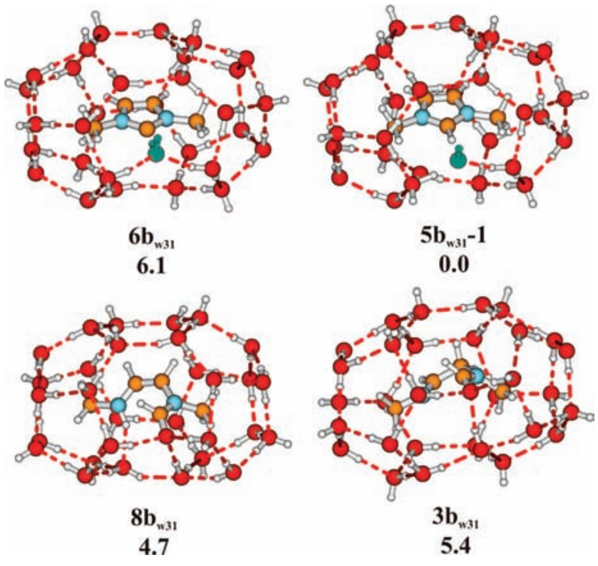
The destabilization of the insertion products **7b**$_{w2}$ and **7b**$_{w3}$, with respect to **6b**$_{w2}$ and **6b**$_{w3}$, is 4.7 and 8.4 kcal mol^{-1}, respectively. These values are significantly larger than the 0.7 kcal mol^{-1} energy difference in case of the single water molecule. Likewise, for **5b**$_{w3}$, several **7b**$_{w3}$ type structures are conceivable; those in Scheme 4 are obtained by IRC calculations started from the corresponding transition states. Nevertheless, the aforementioned trend still holds if we compare the energy of our most stable isomers of **7b**-like structures: their energy rises from 0.7 to 3.5 and 5.2 kcal mol^{-1}, respectively, when one or two additional water molecules are added. These data suggest that, with the increasing number of water molecules, the barrier between the **5**, **6**, and **7** type structures is reduced, alleviating their rearrangement to each other. On the other hand the **5** type structures are simultaneously stabilized by excess of water, and imidazolium hydroxide (stabilized by an appropriately large cluster of water molecules) might be the only product of the reaction (Figure 1). It should be noted here that by other functionals (such as M05−2X, see footnote in Scheme 4 and Supporting Information) somewhat smaller relative energies have been obtained for **7b** compounds. Nevertheless, the gradual destabilization of type **7b** structures compared to the analogue **5b** by the increasing number of water molecules could be observed with all applied methods.

The stability of the open chain products (**3** and **8**) provides also the driving force for the reaction in the presence of two and three water molecules. The barrier for the ring-opening step is somewhat reduced to 21.6 kcal mol^{-1} (with respect to the reactants) in the presence of three reactant water molecules (see Schemes S2 and S3 in the Supporting Information), and is still the rate limiting step. **8b**$_{w2}$ and **8b**$_{w3}$ are somewhat more stable than **3b**$_{w2}$ and **3b**$_{w3}$ in the gas phase. Modeling the presence of the THF solvent by PCM calculation of the t-Bu analogues, both **3a**$_{w2}$ and **3a**$_{w3}$ are by 0.6 kcal mol^{-1} more stable than **8a**$_{w2}$ and **8a**$_{w3}$, respectively, in agreement with Denk's result,[8] who observed only **3a** as reaction product.

Employing a First Solvate Shell To Model the Effect of Water as a Solvent. Thirty water molecules provide a full coverage for the carbene and a "reactant" water molecule (Scheme 5, **6b**$_{w31}$) that forms a H-bond with the hypovalent carbon atom. Proton transfer from the reactant to the carbene yields 1,3-dimethylimidazolium-hydroxide solvated by 30 water molecules (**5b**$_{w31}$), being more stable by 6.1 kcal mol^{-1}. The migration of the hydroxide ion within the solvate shell yields several minima, having similar energies to **5b**$_{w31}$ (see Supporting Information). At this point it must be noted that the hydrate shell may have numerous hydrogen-bond orientations, which have some influence on the shell's stability.[35] Thus, all structures have been optimized using starting geometries with the same hydrogen bond orientations, which have remained unchanged during the relaxed optimization, except for **5b**$_{w31}$**-2** (see Supporting Information), where the migration of the hydrogen bonds follows the movement of the hydroxide ion.

The possible adduct of the hydroxide ion and the imidazolium cation (**7b**$_{w31}$) could not be obtained; the C−O bond always opened up during the optimization, despite our efforts to find a minimum containing an intact **7b** type structural unit.[36] Consequently, it is very likely that the elimination of a hydroxide anion (stabilized by hydratation) from a **7b**-like structure would take place without any barrier in aqueous media. As a further indication for the lack of OH$^-$ addition in the presence of an excess of water is that although the possible open chain reaction products (**8b**$_{w31}$ and **3b**$_{w31}$) have been obtained, their energy has been found to be significantly higher than that of **5b**$_{w31}$**-1** (4.7 and 5.4 kcal mol^{-1}, respectively). It is worth mentioning here that all DB-RI-MP2/cc-pVTZ//B3LYP/6-31+G*, ωB97X-D/6-311++G**//B3LYP/6-31+G*, DB-ωB97X-D/cc-pVTZ//B3LYP/6-31+G*, and M05−2X/6-311+G**//M05−2X/6-31+G* single point energies have been found to be in reasonable agreement with the B3LYP/6-311+G**//B3LYP/6-31+G* ones, while MOS(ω600)-RI-MP2/cc-pVTZ//B3LYP/6-31+G* relative energies are similar for **5b**$_{w31}$ and **3b**$_{w31}$ (for more information see Supporting Information). Thus, it is apparent that solvation stabilizes **5b** to such an extent that the ring-opening process (yielding the nonionic, and thus not so well solvated, **8b**$_{w31}$ and **3b**$_{w31}$) becomes unfavorable.

Scheme 5. Optimized Geometries for the Steps of Carbene Hydrolysis in a Primary Solvate Shell with Their Relative Energies[a] (in kcal mol^{-1})



[a] The reacting water molecule/resulting OH$^-$ group is green. M05−2X/6-311+G**//M05−2X/6-31+G* relative energies are (in kcal mol^{-1}) **6b**$_{w31}$, 6.4; **5b**$_{w31}$, 0.0; **8b**$_{w31}$, 3.6; **3b**$_{w31}$, 4.2.

In order to investigate the feasibility of the OH$^-$ addition in more dilute aqueous solutions, *ab initio* molecular dynamic calculations (using the PW91PW91 functional) were carried out on a **1b**−water system, using a cubic unit cell with 15 Å edges containing one **1b** and 102 water molecules. The unit cell was constructed by placing the carbene in a box of water having the appropriate density and removing the overlapping water molecules. Geometry optimization was carried out keeping the unit cell parameters fixed, and then random velocities corresponding to the zero-point vibrations were assigned to the individual atoms. The system was warmed up to 300 K in 3000 steps using a 1 fs time step, then kept at 300 K for 5000 time steps.

Protonation of the carbene happened early in the simulation (at 700 fs), and the carbene remained protonated during the entire simulation process. The hydroxide ion formed was tracked, and the distance of the O atom of the hydroxide ion (identified by having only one proton within 1.3 Å) from the C(2) atom of the imidazolium cation was plotted against time in Figure 2. The plot displays a generally increasing trend (jumps on

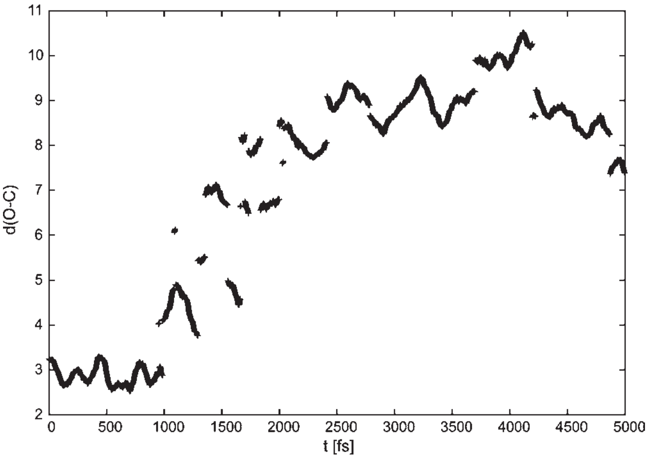


Figure 2. Distance of the OH^- ion from the C(2) atom of the imidazolium moiety plotted against time in the molecular dynamics simulation.

the graph are caused by proton transfer from the nearby water to the hydroxide ion) from the point of protonation until the distance of the OH^- ion reaches the 7−9 Å interval where it oscillates until the end of the simulation. Apparently the solvation of the protonated carbene and the hydroxide ion keeps the hydroxide well apart from the carbene, thus preventing further reaction, in agreement with the aforementioned relative energies of **5b**$_{\mathbf{w31}}$**-2** and the possible open chain derivatives.

Hydrolysis of Imidazolidine-2-ylidene. Since aromaticity has an effect on the stability of imidazole-2-ylidenes,[13] the energy profile of the hydrolysis is presumably also influenced significantly by aromatic properties, in agreement with the experimentally found differences in the rate of decomposition. To explore the extent of this effect we investigated the hydrolysis of **2b**. The reaction paths were found to be analogous to that of **1b**. For the energy profile of the reaction with one and two water molecules see Supporting Information; for the one with three waters, see Scheme 6. Chart 2 summarizes the chemical structures of the molecules involved in the hydrolysis of **2b**.

The interaction energy between the carbene and the water or water cluster is 9.4, 13.4, and 14.8 kcal mol^{-1} in **9b**, **9b**$_{\mathbf{w2}}$, and **9b**$_{\mathbf{w3}}$, respectively. The analogous values for **1b**, **1b**$_{\mathbf{w2}}$, and **1b**$_{\mathbf{w3}}$ are 9.6, 13.9, and 11.2 kcal mol^{-1}, respectively, showing that the strength of the hydrogen bond is only slightly influenced by the change in aromatic properties. Furthermore, **11b**$_{\mathbf{w3}}$, the hydroxide salt derivable from the carbene, could also be optimized in the case of at least three interacting water molecules. The water adduct intermediates **10b**, **10b**$_{\mathbf{w2}}$, **10b**$_{\mathbf{w3}}$ and the reaction products **4b**, **4b**$_{\mathbf{w2}}$, **4b**$_{\mathbf{w3}}$, however, are by about 10 kcal mol^{-1} more stabilized with respect to the corresponding **9b** structure than the analogous intermediates (**7b**, **7b**$_{\mathbf{w2}}$, **7b**$_{\mathbf{w3}}$) and products (**3b**, **3b**$_{\mathbf{w2}}$, **3b**$_{\mathbf{w3}}$) with respect to the corresponding **6b**, **6b**$_{\mathbf{w2}}$, and **6b**$_{\mathbf{w3}}$, respectively. This energy difference, which compares favorably with the 13−15 kcal mol^{-1} aromatic stabilization energy of **1b**,[13c,d] makes the insertion into the O−H bond (yielding intermediate **10b**) exothermic in the presence of both two or three water molecules.

Interestingly, the barrier of the water addition was found to be similar for **1b** and **2b** (25.7 and 23.3 kcal mol^{-1}, respectively), indicating that this TS is for both molecules destabilized by the same effect, which is apparently the cleavage of the O−H bond of the water molecule rather than the change in aromaticity. This is in good agreement with the planar, thus presumably aromatic, structure of the imidazole ring in the O−H insertion TS of **1b**. However, with an increasing number of neighboring waters, the barrier of the formation of the **2b**-derived adducts drops faster than that of the aromatic **1b** derivatives; thus, in the case of three involved water molecules the gap is ca. 10 kcal mol^{-1} lower for the nonaromatic carbene, in good agreement with the observed difference in reaction rates of **1a** and **2a** by Denk et al.[8] This finding indicates that, with this extended stabilization of the polarized transition state, aromaticity contributes significantly to the kinetic stabilization of **1b** in the hydrolysis reaction.

The energy of the ring-opening TS (the rate determining step) is apparently also influenced by the backbone, since in the case of a single water it is considerably higher for **2b** than for **1b** with respect to the corresponding water adduct. Since in this step the initial rupture of the C−N bond results in a negatively charged amide moiety which instantaneously rearranges to **8b** by a proton migration, this difference can be explained by the stabilizing effect of conjugation in the TS between the backbone double bond and the amide. However, an additional water molecule can also stabilize the amide moiety with respect to **7b** by hydrogen bond formation, resulting in a reduced barrier.

2b has also been examined in a solvate shell using a water monolayer consisting of 30 molecules, which provided full coverage for **2b** (Scheme 7). Interestingly, **9b**$_{\mathbf{w31}}$ could not be optimized; all attempts gave **11b**$_{\mathbf{w31}}$ by a proton transfer from the H-bonding water molecule to the carbene during optimization. The O−H adduct **10b**$_{\mathbf{w31}}$, however, could be optimized, having somewhat higher energy (3.9 kcal mol^{-1}) than **11b**$_{\mathbf{w31}}$. This is in clear contrast with the unsuccessful attempts to optimize **7b**$_{\mathbf{w31}}$, the analogous derivative of the aromatic **1b**. Furthermore, the energy of the open chain product **4b**$_{\mathbf{w31}}$ was found to be lower than that of **11b**$_{\mathbf{w31}}$ by 10.4 kcal mol^{-1}, indicating that **2b** in water can decompose by ring-opening. Thus, solvation alone does not provide enough stability for the ionic azolium salt **11b**$_{\mathbf{w31}}$, while for the stability of **5b**$_{\mathbf{w31}}$ aromaticity contributes significantly. Consequently, the integrity of the ring of imidazole derived carbenes in the presence of water, and also that of imidazolium salts in basic aqueous solution, is attributable to both aromatic properties and solvation.

Experimental Studies of Carbene Hydrolysis. NMR spectroscopic monitoring of the hydrolysis of carbene **1c** in both C_6D_6 and THF-d_8 with different amounts of water ranging from a substoichiometric quantity (0.5 equiv of water) to a slight excess (4 equiv) allowed us to identify as the first directly detectable products the formyl derivative **8c** and its Schiff base tautomer **3c**, respectively. The ratio of both products depended on the solvent used; whereas in C_6D_6 only traces of **3c** were observed, it constituted the major isomer in the more polar THF (the isomer ratio varied with the amount of water present but ratios of **3c**:**8c** of up to 2:1 were observed). Although no ene−diamine tautomer (**8a**) had been observed by Denk and co-workers during the hydrolysis of carbene **1a**,[8] a similar tautomerization had also been reported for *N*-t-butyl and *N*-aryl substituted α-amino-imines[37] and was assumed to reflect the different electron releasing properties of the substituents present. The formyl derivatives **3c** and **8c** were found to be stable in C_6D_6 solution whereas in THF a further partial hydrolysis to give small amounts of formic acid and 1,2-bis(2,6-diisopropylphenyl)ethane[37] was observed. NMR spectroscopic monitoring of the progress of the reaction indicated that carbene **1c** was in both solvents hydrolyzed at a much higher rate as had been reported for **1a**[8] since small amounts of the hydrolysis products were detectable

Scheme 6. B3LYP/6-311+G Energy Profile of the Reaction of 2b with Three Water Molecules (Relative Energies in kcal mol^{-1})**

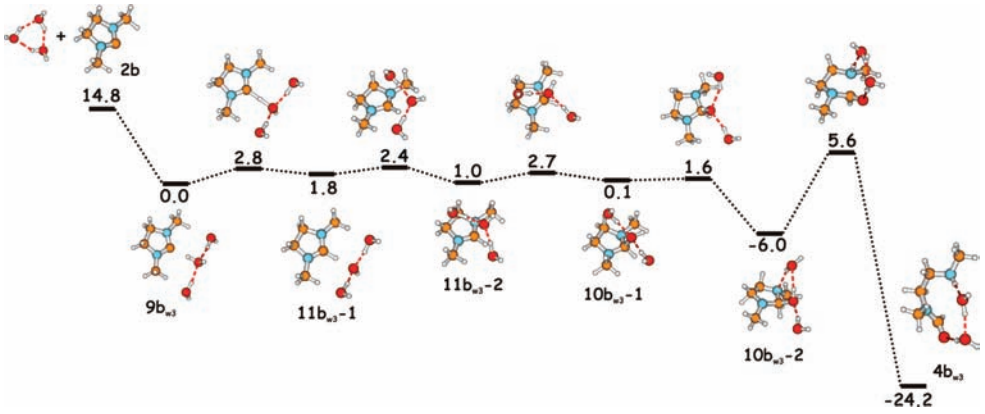
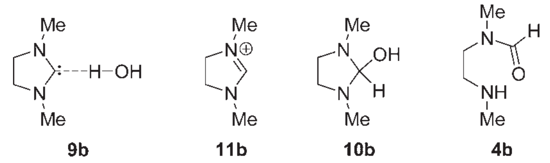
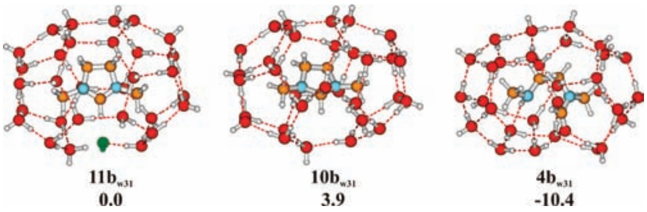


Chart 2. Chemical Structures of the Molecules Involved in the Hydrolysis of 2b



Scheme 7. Optimized Geometries for the Steps of Carbene Hydrolysis in a Primary Solvate Shell and Their Relative Energies (in kcal mol^{-1})[a]



[a] The OH^- ion formed in the reaction is green.

immediately after mixing all reagents, and cleavage of the imidazole ring was completed within a few hours. Although no quantitative kinetic measurements were made, the reaction became faster at increased water concentrations. Even if the presence of any reaction intermediates preceding the formation of **3c** and **8c** was not directly detectable, thorough analysis of the observed spectral data allowed us to derive some further information on the initial stages of the reaction. Thus, ^{1}H NMR spectra of reaction mixtures in both solvents showed beside the resonances of carbene **1c** and hydrolysis products **3c** and **8c** a signal attributable to unreacted water. The chemical shift of this signal differed from the known value of the water signal in the pure solvent[38] and moved to increasingly lower field when the molar ratio of **1c**:H_2O increased. The spectra of solutions in C_6D_6 were special as in this case a second water signal appeared when more than 1 equiv of water (with respect to **1c**) was present. As we also observed in these cases the formation of a two phase system, we attribute one signal (δ = 1.53) to water dissolved in the organic phase and the second one (δ = 4.7) to the aqueous phase.[38] Integration of the spectra confirmed that the organic phase contained approximately equal molar amounts of carbene and water, and allowed us thus to deduce that the absolute water concentration of approximately 0.15 mmol mL^{-1} (as calculated from the relative signal intensities and the known initial carbene concentration) is far larger than the maximum concentration of water in pure benzene at the same temperature (0.042 mmol mL^{-1} at 30 °C[39]). Comparison of the NMR data of **1c** in anhydrous solvents or in the presence of water disclosed further small but significant changes in chemical shifts of all signals, with the largest deviation being observed for the ^{13}C NMR resonance of the divalent carbon atom which moved from a value of 220.4 ppm in anhydrous C_6D_6 to 217.2 ppm in a carbene–H_2O 1:1 mixture.

Inspection of 2D ^{1}H EXSY spectra of the reaction mixtures indicated the presence of reversible dynamic exchange between the protons in H_2O and the hydrogen atoms on the imidazole ring. Similar isotope scrambling had previously been noted to occur between carbene **1a** and solvents with kinetically acidic protons like DMSO, methanol, or water.[40] Although the exchange mechanism was not satisfactorily established, it had been suggested that the H/D-exchange may proceed via a stepwise protonation–deprotonation involving both an imidazolium cation and an "abnormal" (4-deprotonated) carbene isomer[41] as key intermediates. NMR signals of imidazolium cations are not directly detectable in the presence of carbenes as both species interconvert rapidly by exchange of the acidic proton at C_2,[42] and the spectra of mixtures display thus only a single set of NMR signals which represents the population weighted average of the true NMR spectra of both components. However, due to the large shift difference for the ring protons at $C_{4(5)}$ in both species,[42] the position of the averaged signal can still serve as sensitive probe of the composition of a given solution. In this regard, the observation that addition of small amounts of water to solutions of carbene **1c** in anhydrous solvents produces only very small displacements (−0.04 ppm in C_6D_6 and +0.02 ppm in THF-d_8) allows us to rule out that a significant amount of the carbene was converted into the corresponding imidazolium cation. Therefore, the presence of considerable amounts of a bis(carbene)–proton complex[42] may also be ruled out under these circumstances. Instead, we prefer to explain the observed NMR spectral changes by assuming the presence of a carbene–water complex in which both components are connected by hydrogen bonding. The formation of such a complex has precedence in the characterization of an isolable H-bridged adduct of a carbene with diphenylamine,[28b] and is also supported by IR studies of a solution of **1c**:H_2O (1:1) in C_6D_6. The spectrum showed weak absorption bands at 3660, 3151, and 3121 cm^{-1}, respectively, which are in reasonable agreement with the scaled[43]

B3LYP/6-311+G** values (3737 and 3300 cm^{-1}). These bands are absent in both a solution of **1c** in anhydrous C_6D_6 and in H_2O-saturated C_6D_6, respectively, and have similar frequencies as had been established for the vibrational modes of water-clusters in benzene (C_6H_6) where individual water molecules may exhibit hydrogen-bridging interactions with either the π-system of the solvent or other water molecules in the cluster.[44] The presence of three bands in the investigated region suggests that more than one complex might be involved (possibly an equilibrating mixture of free carbene and assemblies of a carbene with different numbers of water molecules), which might also explain that the observed upfield shift of the ^{13}C NMR signal of C_2 upon addition of 1 equiv of water ($\Delta\delta$ −3.2 ppm) is much lower than the difference in B3LYP/IGLO-III NMR shifts for **1b** and **6b** (**1b**, 243.6 ppm; **6b**, 228.9 ppm).

In contrast to the results discussed so far, studies of the hydrolysis of **1c** in H_2O−THF-d_8 mixtures (containing <40% THF and >290 equiv of H_2O) produced a totally different picture. ^1H and ^{13}C NMR studies of the strongly alkaline solutions (pH 12−13) indicated that the hydrolysis of the starting material was complete immediately after mixing. The spectra showed a single set of signals which were attributable to the imidazolium cation **5c** whereas no indication for the formation of the ring cleaved products **3c** and **8c** was obtained. Unequivocal identification of **5c** was straightforward from the observed ^{13}C chemical shifts of 126.1 (C_2) and 132.3 ($C_{4,5}$) ppm for the carbon atoms, and the strong deshielding of the signal of the 4,5-protons in the imidazole ring (δ = 8.0−8.1 as compared to δ = 7.19 in THF-d_8). Quite remarkably, a signal for the proton at C_2 was not detectable, which we explain as a consequence of dynamic exchange with the solvent that is known to occur at a high rate[45] and is considered to induce merging of the signal of this proton with the H_2O signal. Monitoring the reaction for an extended time indicated that **5c** was stable and gave no evidence for the occurrence of ring cleavage, suggesting that conversion of the imidazolium salt to the formyl derivatives **3c** or **8c**, respectively, is under these conditions indeed unfavorable, as it was predicted for **5b** in the microsolvation study and by our molecular dynamics investigation.

Having verified that hydrolysis of **1c** in predominantly aqueous or predominantly organic solvent systems (THF, benzene, <4 equiv of H_2O) follows obviously different pathways, we reckoned that monitoring the reaction in solvent mixtures with intermediate amounts of water (between 4 and 300 equiv) might allow us to observe at which point the change in reaction pathways occurs. To this end, we performed a stepwise titration of a solution of **1c** with water under NMR control. Starting with a solution of the carbene in anhydrous THF-d_8, a specified amount of water was added at each step and the resulting mixture analyzed by ^1H and ^{13}C NMR. The experiment was carried out at −35 °C in order to slow down the hydrolysis process and allow sufficient time for the NMR characterization, and covered solvent mixtures containing from 0 up to 20% of water.

Inspection of the NMR spectra recorded during the initial stages of the titration revealed that the solution contained unreacted **1c** as major species beside small amounts of the ring opened products **3c** and **8c** which were formed from the very beginning. During the progress of the titration the signals attributable to **3c** and **8c** grew slowly in intensity with increasing reaction time but showed hardly any variation in chemical shift. In contrast, the signals of **1c** showed very pronounced displacements after each addition of H_2O which were largest for the $H_{4,5}$ protons and the hypovalent carbon C_2. Analysis of the titration curves (Figure 3) reveals that the change in δ^1H and $\delta^{13}C$ following the addition of the first equivalent of H_2O is first cut back when more water (up to approximately 10 equiv) is added. A second, substantially larger jump is observed when the ratio of H_2O:**1c** is further raised from about 20:1 to 60:1, and finally the curve flattens out when the excess of water grows still larger. Considering that the final chemical shifts come close to those of the imidazolium cation **5c**, the signal displacement during the later stages of the titration is readily explained by assuming that the solution contains a rapidly exchanging mixture of free carbene **1c**, its protonated product **5c**, and probably the corresponding bis-(carbene)−proton complex,[42] respectively. The observed resonances represent then the population weighted average of all species, and the observed trends imply that the relative population of **5c** increases with the water content of the solution, and that **5c** represents the dominant species during the last stages of the titration. The curvature of the titration curves during the initial titration steps cannot be explained by a simple equilibrium between **1c** and **5c** [probably also a bis-(carbene)−proton complex[42] is involved] but indicates that one (or more) further species must be involved in the exchange process. As the rather small absolute chemical shift changes in this regime suggest that this species exhibits presumably similar spectral characteristics as **1c**, we interpret these findings as further experimental evidence in support of the presence of a hydrogen-bridged carbene−water complex.

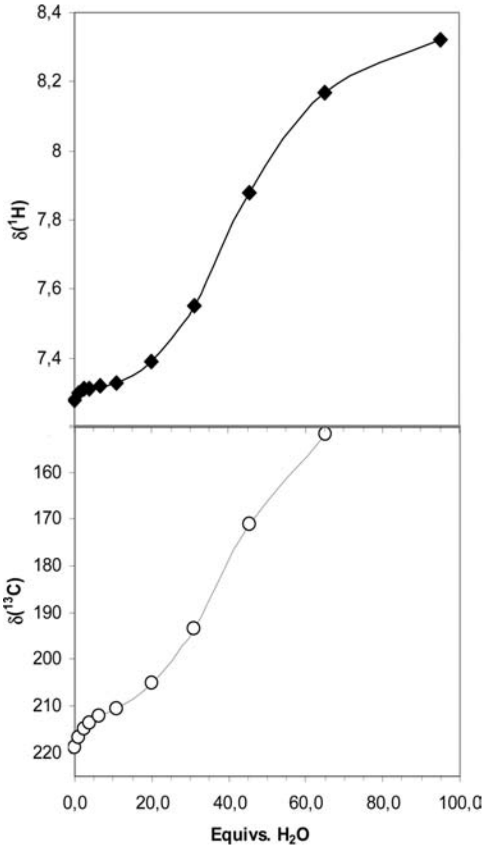


Figure 3. Titration curves showing the evolution of the chemical shifts for the $H_{4,5}$ protons (top) and the C_2 carbon atom (bottom) during titration of a THF solution of carbene **1c** with water at −35 °C.

A further aspect worth mentioning is the fact that we found that the solution which is obtained at the end of the titration and contains approximately 20% water is not stable, but that conversion of the equilibrium mixture of carbene **1c** and its conjugate acid **5c** into the ring opened products **3c** and **8c** continues upon prolonged storage at ambient temperature even if no more water was added. This behavior is in marked contrast to the long-term stability of the imidazolium hydroxide solutions obtained by hydrolysis of **1c** in a predominantly aqueous solvent system with <40% THF.

SUMMARY AND CONCLUSION

The experimental and computational study of the hydrolysis of imidazol-ylidenes at different carbene/water ratios reveals a complex mechanistic picture. The first step of the hydrolysis of **1c** is the immediate formation of a dynamic mixture of water−carbene complexes (e.g., **6c**). The next reaction step is determined by the amount of water present, which affects the basicity of the hydroxide ion in the solution: at low water content, the isolated OH^- is a stronger base (the pK_a of water in DMSO is 32)[46] than the carbene (pK_a of imidazolium ions is approximately 22 in DMSO[16]), thus preventing the formation of an ionic imidazolium hydroxide, whereas in the presence of a large amount of water the basicity of the hydroxide ion is significantly reduced (pK ca. 16) but the basicity of the carbene remains unchanged.[9,16] As a consequence, under these conditions the carbene is protonated, and the imidazolium (**5c**) hydroxide solvated ion pair is the sole reaction product, in agreement with results from the microsolvation model calculations and the molecular dynamics study for **1b**. At intermediate water content, the imidazolium hydroxide **5c**[OH] is in dynamic equilibrium with the carbene **1c** and probably an imidazolium−carbene complex.[42] The ratio **1c**:**5c** is controlled by the solvent environment and increases strongly with decreasing water content, reflecting presumably both the concentration dependence of the equilibrium **1c** + $H_2O \leftrightarrows$ **5c** + OH^- and the stabilizing effect of a more and more hydrophilic environment on the imidazolium hydroxide. Under these circumstances, also a slow and irreversible transformation to the ring opened products **3c** and **8c** is observed. Apparently, decreasing water concentration imposes a destabilizing effect on the hydroxide ion so that the ring opened products may now provide the thermodynamic sink for the reaction. This is in agreement with the results of the computational study of the reaction between **1b** and 3 mol of water which shows that although an imidazolium hydroxide structure indeed exists, the imidazolium ion can be attacked by the (solvated) OH^- to give the ring opened products **3c** and **8c** via an energetically accessible transition structure. Finally, the reaction mixtures with the smallest water concentrations clearly showed the presence of a **1c**−water complex, which was experimentally detected for the first time. In agreement with this observation, calculations depicted complexes of carbene **1b** with one or two water molecules as stable compounds whereas a tautomer **5b**(OH^-) could not be located as a local minimum but rather as a transition state connecting the carbene−water complex with **7**. These findings led us to conclude that in the presence of the smallest water concentrations the imidazolium−hydroxide ion pair does not play a role in the conversion to the ring opened products **3** and **8**, in full agreement with the report of Denk et al.[8] who did not observe an appreciable change in the rate of the hydrolysis of **1a** upon addition of acid or base. A quantitative understanding of the energetics and kinetics of the individual interconnected reactions would require a still more precise modeling of the solvation effects that includes also the possibility of mixed solvation of the carbene and solvent−water interactions.

A further important aspect of our study is the difference between the reactivity of the aromatic imidazolium-derived system and its saturated nonaromatic counterpart which yielded exclusively ring-opened products, independent from the amount of the reacting water. This underlines the importance of aromatic stabilization for the robustness of imidazolium derived carbenes and also their salts. Altogether, our investigations show clearly that imidazolium-based carbenes are much less sensitive against humidity (i.e., traces of water) than is generally considered.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Complete refs 24a and 24c, Schemes S1−S6, geometries (in Cartesian coordinates), total energies of the optimized structures, and relative energies of the structures involved in the reaction of **1b** with 1−3 and 31 water molecules at different levels of theory, as well as comprehensive listings of ^1H and ^{13}C NMR data including signal assignments. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

nyulaszi@mail.bme.hu

ACKNOWLEDGMENT

Financial support from the DFG-HAS travel grant, calculations of Tibor Höltzl by the Q-Chem 3.2 program package, and the comments of an anonymous referee are gratefully acknowledged. This work is supported by the New Hungary Development Plan (Project ID: TÁMOP-4.2.1/B-09/1/KMR-2010-0002).

REFERENCES

(1) Recent reviews: (a) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39–91. (b) Kirmse, W. *Angew. Chem., Int. Ed.* **2004**, *43*, 1767–1769. (c) Bertrand, G. *React. Intermed. Chem.* **2004**, 329–373. (d) Canac, Y.; Soleilhavoup, M.; Conejero, S.; Bertrand, G. *J. Organomet. Chem.* **2004**, *689*, 3857–3865. (e) Arduengo, A. J., III; Bertrand, G. L. *Chem. Rev.* **2009**, *109*, 3209–3210.

(2) (a) Anderson, D. R.; Lavallo, V.; O'Leary, D. J.; Bertrand, G.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 7262–7265. (b) Crabtree, R. H. *J. Organomet. Chem.* **2005**, *690*, 5451–5457. (c) Perry, M. C.; Burgess, K. *Tetrahedron: Asymmetry* **2003**, *14*, 951–961. (d) Leuthäusser, S.; Schwarz, D.; Plenio, H. *Chem.—Eur. J.* **2007**, *13*, 7195–7203. (e) Arnold, P. L.; Pearson, S. *Coord. Chem. Rev.* **2007**, *251*, 596–609.

(3) Recent reviews: (a) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534–541. (b) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. (c) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed. Engl.* **2007**, *46*, 2988–3000. (d) Moore, J. L.; Rovis, T. *Top. Curr. Chem.* **2009**, *291*, 77–144.

(4) Arduengo, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361–363.

(5) (a) Csabai, P.; Joó, F. *Organometallics* **2004**, *23*, 5640–5643. (b) Fekete, M.; Joó, F. *Catal. Commun.* **2006**, *7*, 783–786.

(6) Arduengo and co-workers also reported "an air stable carbene", see the following: Arduengo, A. J.; 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.

(7) Recently, different imidazole-2-ylidene derivatives have been dissolved in silicone oils, and this mixture has been found to be stable in air for months. This finding has been rationalized considering a stabilizing effect by formation of pentacoordinate silicon compounds, see the following: Bonette, F.; Kato, T.; Destarac, M.; Mignani, G.; Cossío, F. P.; Baceiredo, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8632–8635.

(8) Denk, K. D.; Rodezno, J. M.; Gupta, S.; Lough, A. *J. Organomet. Chem.* **2001,** *617*−*618*, 242–253.

(9) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Tóth, K. *J. Am. Chem. Soc.* **2004**, *126*, 4366–4374.

(10) (a) Arduengo, A. J.; Goerlich, J.; Marshall, W. *J. Am. Chem. Soc.* **1995,** *117*, 11027–11028. (b) Denk, M. K.; Thadani, A.; Hatano, K.; Lough, A. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2607–2609.

(11) Insertion of carbenes into O−H bonds is also known with alcohols (see ref 1a), and in the case of highly stabilized carbenes this reaction was found to be reversible. See the following: Enders, D.; Breuer, K.; Raabe, G.; Runsink, J.; Teles, J. H.; Melder, J. P.; Ebel, K.; Brode, S. *Angew. Chem., Int. Ed. Engl.* **1995,** *34*, 1021.

(12) Forró, A.; Veszprémi, T.; Nyulászi, L. *Phys. Chem. Chem. Phys.* **2000**, 3127–3129.

(13) Imidazole-2-ylidene has aromatic properties, see the following: (a) Boeme, C.; Frenking, G. *J. Am. Chem. Soc.* **1996**, *118*, 2039–2046. (b) Heinemann, C.; Müller, T.; Apeloig, Y.; Schwartz, H. *J. Am. Chem. Soc.* **1996,** *118*, 2023–2038. (c) Cheng, M.-J.; Hu, C.-H. *Chem. Phys. Lett.* **2001,** *349*, 477–482. (d) Hollóczki, O.; Nyulászi, L. *J. Org. Chem.* **2008,** *73*, 4974–4979.

(14) (a) Teles, J. H.; Melder, J. P.; Ebel, K.; Schneider, R.; Gehrer, E.; Harder, W.; Brode, S.; Enders, D.; Breuer, K.; Raabe, G. *Helv. Chim. Acta* **1996,** *79*, 61–83. (b) Giernoth, R.; Bankmann, D. *Tetrahedron Lett.* **2006,** *47*, 4293–4296.

(15) It is worthy to note that, in the case of thiazolium salts apart from the proton exchange, the addition of the hydroxide to the C(2), followed by the ring opening, has also been observed, and has also been suggested as the possible reason for the facile absorption of thiamine into the cells. See the following: (a) Duclos, J. M.; Haake, P. *Biochemistry* **1974,** *13*, 5358. (b) Zoltewicz, J. A.; Uray, G. *J. Org. Chem.* **1980,** *45*, 2104.

(16) (a) Alder, R. W.; Allen, P. R.; Williams, S. J. *J. Chem. Soc., Chem. Commun.* **1995,** *12*, 1267–1268. (b) Kim, Y.-J.; Streitwieser, A. *J. Am. Chem. Soc.* **2002,** *124*, 5757–5761. (c) Magill, A. M.; Cavell, K. J.; Yates, B. F. *J. Am. Chem. Soc.* **2004**, *126*, 8717–8724. (d) Chu, Y.; Deng, H.; Cheng, J.-P. *J. Org. Chem.* **2007**, *72*, 7790–7793.

(17) (a) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002,** *102*, 3667–3692. (b) de Kort, M.; Tuin, A. W.; Kuiper, S.; Overkleeft, H. S.; van der Marel, G. A.; Buijsman, R. C. *Tetrahedron Lett.* **2004,** *45*, 2171–2175.

(18) Song, Z.; Wang, H.; Xing, L. *J. Solution Chem.* **2009,** *38*, 1139–1154.

(19) Kuo, J.; Ciobanu, C. V.; Ojamäe, L.; Shavitt, I.; Singer, S. J. *J. Chem. Phys.* **2003**, *118*, 3583–3588.

(20) Cypryk, M.; Apeloig, Y. *Organometallics* **2002,** *21*, 2165–2175.

(21) Orregeno, J. F.; Cano, H.; Restrepo, A. *J. Phys. Chem. A* **2009**, *113*, 6517–6523.

(22) Cramer, C. J.; Truhlar, D. G. *Chem. Rev.* **1999,** *99*, 2161–2200.

(23) This methodology has recently been successfully used to model the hydrolysis of silyl-ethers. For more detailed discussion of the model, and the accuracy of the B3LYP method compared to MP2, see the following: Terleczky, P.; Nyulászi, L. *J. Phys. Chem. A* **2009**, *113*, 1096–1104.

(24) (a) Frisch, M. J.; *Gaussian 03, Revision C.02*; Gaussian, Inc.: Wallingford CT, 2004.(b) RI-MP2 and RI-B97-D single point energies have been calculated by the Turbomole 5.10 program package: Ahlrichs, R.; Bär, M.; Häser, M.; Horn, H.; Kölmel, C. *Chem. Phys. Lett.* **1989**, *162*, 165. (c) DB-RI-MP2/cc-pVTZ//B3LYP/6-31+G*, ωB97X-D/6-311++G**//B3LYP/6-31+G*, DB-ωB97X-D/cc-pVTZ//B3LYP/6-31+G* and MOS(ω600)-RI-MP2/cc-pVTZ//B3LYP/6-31+G* single point energies have been calculated by the Q-Chem 3.2 program package “Advances in methods and algorithms in a modern quantum chemistry program package”: Y. Shao, L.; et al. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172.

(25) Schaftenaar, G.; Nordik, J. H. *J. Comput.-Aided Mol. Des.* **2000**, *14*, 123.

(26) (a) Kresse, G.; Hafner, J. *Phys. Rev. B* **1993,** *48*, 13115. (b) Kresse, G.; Furthmüller, J. *Comput. Mater. Sci.* **1996,** *6*, 15. (c) Kresse, G.; Furthmüller, J. *Phys. Rev. B* **1996,** *54*, 11169.

(27) Dible, B. R.; Sigman, M. S. *J. Am. Chem. Soc.* **2003,** *125*, 872.

(28) (a) Similar H-bonded structures with alcohols and amines has been investigated computationally, see the following: De Sarkar, S.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2010,** *132*, 1190–1191. (b) Similar H-bonded structure between diphenylamine and an imidazole-2-ylidene has been characterized by x-ray crystallography, see the following.: Cowan, J. A.; Clyburne, J. A. C.; Davidson, M. G.; Harris, R. L. W.; Howard, J. A. K.; Kupper, P.; Leech, M. A.; Richards, S. P. *Angew. Chem., Int. Ed.* **2002,** *41*, 1432.

(29) Bader, R. W. F. *Acc. Chem. Res.* **1985,** *18*, 9.

(30) Similar insertion with comparable barrier has been suggested in case of the reaction of a cyclic(alkyl)(amino)carbene and ammonia, see the following: Frey, G. D.; Lavallo, V.; Donnadieu, B.; Schoeller, W. W.; Bertrand, G. *Science* **2007**, *316*, 439.

(31) It should also be mentioned that the ring opening OH inserted product can proceed via a different, less favorable path (35.8 kcal mol^{-1} barrier), yielding a zwitterionic structure [Me—N—CH═CH—N-(Me)—C(H)═OH] that can isomerize to a rotamer of the same Schiff base in a multistep reaction. The last step of this mechanism having a 61.9 kcal mol^{-1} barrier is likely to proceed via a bimolecular process and with a small barrier. For more information, also see Supporting Information.

(32) Although the isomerization of **8b** to **3b** provides only 0.2 kcal mol^{-1} energy in gas phase calculations, single point PCM calculations with THF as solvent showed 1.5 kcal mol^{-1} energy benefits, in better agreement with the experiments. We also note that there are many possible isomeric structures of both **8b** and **3b**; those in the schemes are the most stable ones.

(33) Although **8a** and **3a** have identical energy in gas phase calculations, single point PCM calculations with THF as solvent indicated **3a** to be more stable by 0.8 kcal mol^{-1}, in better agreement with the experiments.

(34) Although in the case of two and three waters the TS of the direct **7b**$_{\mathbf{w2-1}}$ to **3b**$_{\mathbf{w2}}$ and **7b**$_{\mathbf{w3}}$**-1** to **3b**$_{\mathbf{w3}}$ rearrangement has also been found (37.4 and 36.6 kcal mol^{-1} B3LYP/6-311+G** barriers, respectively), the formation of **8b** is easier (the **7b**$_{\mathbf{w2}}$**-2** to **8b**$_{\mathbf{w2}}$ and **7b**$_{\mathbf{w3}}$**-2** to **8b**$_{\mathbf{w3}}$ barriers being 24.5 and 21.6 kcal mol^{-1}, respectively, at the same level). Thus, the reaction presumably proceeds via **8b**$_{\mathbf{w2}}$ and **8b**$_{\mathbf{w3}}$.

(35) (a) Kirov, M. V. *J. Struct. Chem.* **2002,** *43*, 790. (b) Terleczky, P.; Nyulászi, L. *Chem. Phys. Lett.* **2010,** *488*, 168–172.

(36) We have applied several different starting geometries as well as initial optimizations with different fixed C2 carbon−hydroxide oxygen distances, and reduced step sizes to locate this minimum.

(37) Gans-Eichler, T.; Gudat, D.; Nättinen, K.; Nieger, M. *Chem.—Eur. J.* **2006,** *12*, 1162.

(38) For a reference to the chemical shift of water in different NMR solvents, see the following: Budavari, S.; O'Neil, M. J.; Smith, A.; Heckelman, P. E. *The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals*, 11th ed.; Merck Co., Inc.: Rahway, NJ, 1989.

(39) Karlsson, R. *J. Chem. Eng. Data* **1973,** *18*, 290.

(40) Denk, M. K.; Rodezno, J. M. *J. Organomet. Chem.* **2000**, *608*, 122.

(41) A stable derivative has recently been isolated: Aldeco-Perez, E.; Rosenthal, A. J.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Science* **2009**, *326*, 556.

(42) Arduengo, A. J.; Gamper, S. F.; Tamm, M.; Calabrese, J. C.; Davidson, F.; Craig, H. A. *J. Am. Chem. Soc.* **1995**, *117*, 572.

(43) A B3LYP/6-31+G* scaling factor of 0.9679 was suggested: Andersson, M. P.; Uvdal, P. *J. Phys. Chem. A* **2005**, *109*, 2937–2941.

(44) Pribble, N. R.; Zwier, T. S. *Science* **1994**, *265*, 75. Gruenloh, C. J.; Carney, J. R.; Arrington, C. A.; Zwier, T. S.; Fredericks, S. Y.; Jordan, K. D. *Science* **1997**, *276*, 1678.

(45) Giernoth, R.; Bankmann, D. *Tetrahedron Lett.* **2006,** *47*, 2493.

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