Gas phase protonation of diazirines: a route to N-protonated diazomethanes

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N-Protonated diazomethanes have been generated successfully *via* gas phase protonation of the corresponding diazirines.

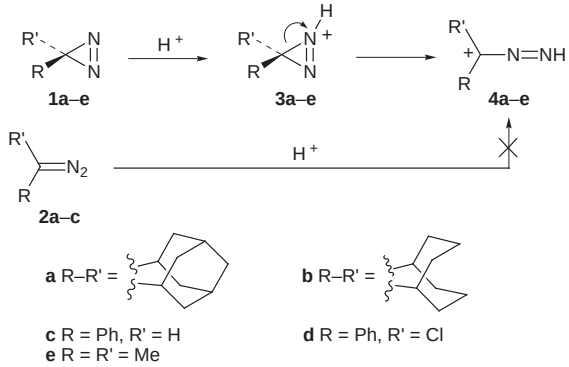
The electronic distribution in diazoalkanes is usually represented by the resonance forms **I**–**IV**. The reactivities of diazo-

I **II** **III** **IV**

alkanes with acids and electrophiles are dominated by forms **II** and **III**; forms **I** and **IV** play no role at all. An early study by Wiberg[1] postulated N-protonation, which was subsequently revised in the light of more extensive data.[2–4] Conventionally, protonation occurs at the C atom of the diazoalkanes. Since their discovery in 1966, the diazirines, cyclic diazo compounds with three-membered rings, have been added to the ranks of the well-known aliphatic diazo compounds.[5] Herein we report the successful generation of the N-protonated diazoalkanes **4a**–**d** *via* the protonation of the corresponding diazirines **1a**–**d** (Scheme 1).

The gas phase protonation of diazirines **1a**–**d** and the equilibrium constant experiments were performed on an Extrel FTMS 2001 Fourier transform mass spectrometer equipped with a 3.0 T superconducting magnet with an inlet system described in previous studies.[6] The experiment was initiated by a pulsed electron beam (electron energy of 20 eV). The detectable intermediates in the cell are evidently either the protonated diazirines **3a**–**d** or the N-protonated diazoalkanes **4a**–**d**. Since the spectra gave only the masses of the protonated species, it is not possible to distinguish whether the protonated species appear in the closed (**3**) or open form (**4**).

In order to clarify this process, we determined the gas phase basicity (GB) of diazirines **1a**–**d** and proceeded with high-level *ab initio* computations of proton affinities of diazirines **1c**,**d** and their open forms **2c**,**d** (Scheme 1). In the case of the large molecules **1a**,**b** and **2a**,**b**, proton affinities for model com-



Scheme 1

pounds, 3,3-dimethyldiazirine **1e** and 2-diazopropane **2e** were calculated.

The GB of diazirine (D) was determined by measuring the equilibrium constants of the proton-transfer reactions between D and a reference base (B_0) of known basicity [eqn. (1)].[7]

$$D + B_0H^+ \rightleftharpoons DH^+ + B_0 \quad (1)$$

The equilibrium constants are given by the ratio of pressures for a reference base to a diazirine, $[B_0]/[D]$, and the ratio of intensities of spectra for the corresponding conjugate acid, $[DH^+]/[B_0H^+]$ [eqn. (2)]. In most cases, equilibrium was

$$K = \frac{[DH^+][B_0]}{[D][B_0H^+]} \quad (2)$$

attained after a reaction period of several hundred milliseconds to 1 s. The observed free energy changes [eqn. (3)] for

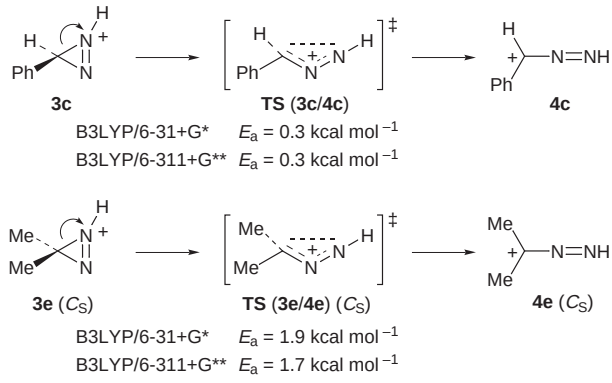
$$\Delta G° = -RT \ln K \quad (3)$$

respective proton transfer equilibria and the selected GB values are summarized in Table 1. For the case of **1d**, we adopted the threshold technique[8] instead of the equilibrium method because the amount of the conjugate acid ion formed in the cell was too small to be measured quantitatively. When bases having lower basicity than butyronitrile (GB = 184.4 kcal mol^{-1}) were used as reference bases, the proton transfer reaction from the protonated reference base to the neutral **1d** occurred to give the protonated **1d**. On the other hand, when reference bases with higher basicity than acetone (GB = 187.9 kcal mol^{-1}) were used, the proton transfer reaction from the protonated reference base to the neutral **1d** was not observed. The results suggest that the basicity of **1d** would be intermediate between those of acetone and butyronitrile, *i.e.* GB = 186.4 ± 1 kcal mol^{-1}. The ΔGB values are provided for comparison. The basicities of

Table 1 Gas phase basicities[a] and proton affinities[b] of ammonia, diazirines **1a**–**e** and diazoalkanes **2c**–**e**

Species	GB/ kcal mol^{-1}	ΔGB/ kcal mol^{-1}	PA/ kcal mol^{-1}	ΔPA/ kcal mol^{-1}
NH_3	195.6	0.0	202.4	0.0
			(202.5)	(0.0)
1a	194.2	1.4		
1b	193.7	1.9		
1c	187.6	8.0	176.7	25.7
			(178.7)	(23.8)
1d	186.3	9.3	171.0	31.4
1e			177.1	25.3
			(179.6)	(22.9)
2c			192.8	9.6
			(193.7)	(8.8)
2d			194.1	8.3
2e			197.2	5.2
			(199.0)	(3.5)

[a] Experimental data. [b] Derived with B3LYP/6-31 + G* and B3LYP/6-311 + G** (in parenthesis).

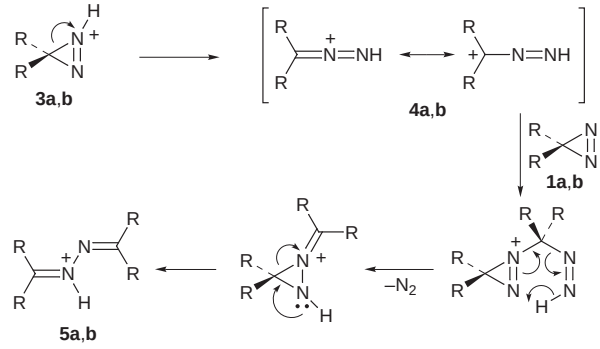


Scheme 2

diazirines **1a** and **1b** are stronger than **1c** and **1d** by approximately 6 kcal mol^{-1}.

The geometry optimizations and frequency calculations were carried out at the B3LYP hybrid density functional theoretical level with the internal 6-31 + G* and 6-311 + G** basis sets, using procedures implemented in the GAUSSIAN 94 system of programs.[9] Zero-point vibrational energy (ZPVE) corrections were scaled by a 0.98 factor. The proton affinities of diazirines **1c**–**e** and diazoalkanes **2c**–**e** obtained as the differences in the total energies of the neutral and the protonated forms, including the ZPVE corrections, are given in Table 1. The differences (ΔPA) in the calculated proton affinities (PA) between species **1c**–**e**, **2c**–**e** and a reference compound (NH_3) are also provided. Because the measured ΔGB values of the 3,3-dialkyldiazirines **1a** and **1b**, of 1.4 and 1.9 kcal mol^{-1}, and of the 3-aryldiazirines **1c** and **1d**, of 8.0 and 9.3 kcal mol^{-1}, are in much closer agreement with the ΔPA values calculated (B3LYP/6-31 + G*) for model diazoalkane **2e** (5.2 kcal mol^{-1}), and the aryldiazoalkanes **2c** (9.6 kcal mol^{-1}) and **2d** (8.3 kcal mol^{-1}) than for diazirines, we deduce that the detected species in the cell are the N-protonated diazoalkanes. As expected, the calculated PA for C-protonation of 2-diazopropane is higher (217.2 kcal mol^{-1}, B3LYP/6-311 + G**) than the PA for its N-protonation (199.0 kcal mol^{-1}). Moreover, the low calculated activation barriers for the conversion of N-protonated diazirines **3c**,**e** into the corresponding N-protonated diazoalkanes **4c**,**e** (Scheme 2) confirm the ease of the ring opening in the N-protonated diazirines under the experimental conditions.

The chemistry of the N-protonated diazoalkane in the cell is interesting due to the following observations. In particular, protonation of **3a** leads to an ion with the mass of the protonated azine **5a**, and this could occur by ring opening of the protonated diazirine **3a** into N-protonated 2-diazoadamantane **4a**, which reacts with neutral diazirine **1a** to yield the expected the protonated azine **5a**. The N-protonated 2-diazoadamantane **4a**, *m*/*z* 163, decays with the concomitant growth of the protonated azine **5a**, *m*/*z* 297, in the time frame of the experiment (1 s). A plausible mechanism of this reaction is the nucleophilic displacement by the neutral diazirine **1a** of the activated N-protonated 2-diazoadamantane **4a**. This is followed by proton transfer in concert with nitrogen extrusion to yield the protonated azine, as depicted in Scheme 3.



Scheme 3

The diazoalkane **2b** (*m*/*z* 151) has a gas phase basicity similar to that of **2a** but the formation of the protonated azine **5b** (*m*/*z* 273) occurs at a slower rate, possibly resulting from the steric effects of the flexibility on the bicyclo ring in **4b**. In contrast, the N-protonated diazoalkanes **4c**,**d** remain unreactive with their respective neutral diazirine parents even after 3 s. This may be so because the phenyl substituent in these species decreases the electrophilicity of the targeted carbon owing to the π-donor ability of the phenyl ring.

In conclusion, we have shown that N-protonated diazomethanes can be generated *via* protonation of the corresponding diazirines. Our experiments also indicate that some of the N-protonated species are reactive and can undergo further reaction with neighbouring molecules.

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Notes and References

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