Site of Protonation of Alkyl- and Arylhydrazines Probed by ^{14}N, ^{15}N, and ^{13}C NMR Relaxation and Quantum Chemical Calculations

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The protonation site of some alkyl- ($MeNHNH_2$ and Me_2NNH_2) and aryl- ($ArNHNH_2$, Ar = Ph, 4-$OMeC_6H_4$, 4-$NO_2C_6H_4$) hydrazines has been investigated in water, methanol, and dimethyl sulfoxide as solvents by measuring the change in the relaxation rate of ^{14}N, ^{15}N, and ^{13}C between the neutral and protonated forms. The relative stability of the two protonated forms was also investigated theoretically by means of semiempirical and ab initio calculations. The preferred protonation site of 1,1-dimethylhydrazine is the alkylated nitrogen, whereas methylhydrazine may also undergo protonation at the unsubstituted nitrogen. Phenylhydrazine and 4-nitrophenylhydrazine are protonated at the primary amine nitrogen, whereas 4-methoxyphenylhydrazine undergoes protonation at both nitrogens.

Unsymmetrical hydrazines $R^1R^2NNH_2$ (R = hydrogen, alkyl, or aryl) have two sites available for protonation, i.e., the substituted (N-1) and unsubstituted (N-2) nitrogen,[1] and can give rise to two conjugate acids, $R^1R^2NNH_3^+$ (**a**) and $R^1R^2NH^+$-NH_2 (**b**).

The commonly accepted view,[1] based on substituent effects[2] and IR[3] and NMR[4] evidence, is that protonation at N-2 (**a**) predominates when R is an aryl group, and the opposite (**b** favored) when R is an alkyl group.[5] However, Condon et al.[6] argued that alkylhydrazines undergo protonation at both nitrogens to a comparable extent. Moreover, the nucleophilic reactivity of hydrazines points out that the substituted nitrogen may in some cases act as the nucleophile.[7] These circumstances prompted us to investigate the site of protonation of hydrazines through the analysis of ^{14}N and ^{15}N NMR relaxation rates in the neutral and ionized forms, because, as we have recently reported,[8] the change in the NMR relaxation rate of the nuclei that can act as basic site is a selective probe of ionization taking place at that atom. In fact, the addition of a proton to a spin-$^1/_2$ nucleus (like ^{15}N or ^{13}C) will cause an increase in its dipolar relaxation rate $1/T_1^{DD}$ because it depends on the NH distance, as in eq 1,[9] where γ_N and γ_H are the magnetogyric ratios of

$$\frac{1}{T_1^{DD}} = \frac{N\hbar^2\gamma_N^2\gamma_H^2}{r_{NH}^6}\tau_c \qquad (1)$$

^{15}N and ^1H, respectively, τ_c is the correlation time, N is the number of protons, and r_{NH} is the N−H distance. The distance dependence ($1/r^6$) is so strong that a directly bonded proton will be much more effective in promoting relaxation than any other, more distant, proton nucleus in the molecule. The dipolar relaxation rate $1/T_1^{DD}$ is determined through the combination of a T_1 and NOE measurement as $1/T_1^{DD} = (1/T_1)(\eta/\eta_{max})$, where $\eta_{max} = \gamma_H/2\gamma_N = -4.93$. Conversely, the line width ($W_{1/2}$) of amine ^{14}N ($I = 1$) signals decrease upon protonation, owing to the small electric field gradient (efg) at a tetrahedral nitrogen.[8a,10,11]

The calculation of the stability of both protonated forms (**a** and **b**) by quantum chemical methods gives data comparable only to gas-phase basicity data, which to the best of our knowledge are available only for the parent compound. Any comparison with solution basicities should therefore include the solvent effect on the proton-transfer equilibrium. To this effect, we have also carried out calculations for both isolated and solvated species.

Results

We have studied some representative alkyl- and arylhydrazines, i.e., $MeNHNH_2$ (**1**), Me_2NNH_2 (**2**); 4-X−$C_6H_4NHNH_2$, X = H (**3**), NO_2 (**4**), OCH_3 (**5**) at 0.5 M concentration in DMSO, methanol, and water. Alkylhydrazine hydrochlorides reacted with DMSO and were studied only in methanol and water.

NMR Measurements. ^1H spectra of neutral arylhydrazines[12] in DMSO-d_6 exhibit the NH and NH_2 protons at δ 6−8 and ca. 4, respectively. In **3**·HCl and **4**·HCl one of the signals is strongly deshielded (to ca. δ 10), whereas the other one undergoes a much smaller deshielding. The relative intensities of about 3:1 indicate the formation of $ArNHNH_3^+$ in this solvent. However, the spectrum of **5**·HCl exhibits a peak at δ 10.1 and an extremely broad, nonintegrable hump at δ ca. 8.

N-1 and N-2 ^{14}N signals of alkylhydrazines ($W_{1/2}$ = 0.5−1 kHz) are poorly resolved especially in the case of neutral $MeNHNH_2$, and only T_1 values are reported. The protonation of $PhNHNH_2$ could not be investigated by ^{14}N NMR because only one very broad signal could be observed ($W_{1/2}$ = 7 and 0.9 kHz for neutral and protonated form, respectively). The larger line width of hydrazo nitrogens compared to that of simple amines agrees with efg calculations for NH_2NH_2;[11] however, the enhanced effect on phenylhydrazine shows that its longer correlation time also plays a role. ^{14}N data are collected in Table 1.

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TABLE 1: Values of ^{14}N Chemical Shift (ppm) and T_1 (ms) for Neutral and Protonated Alkylhydrazines

	N-1				N-2			
	B		BH^+		B		BH^+	
hydrazine	δ	T_1	δ	T_1	δ	T_1	δ	T_1
$MeNHNH_2$[a]	−319	*c*	−328	0.74	−309	0.22	−309	0.22
$MeNHNH_2$[b,d]	∼−325	*c*	−327	0.48	−310	0.29	∼−315	*c*
Me_2NNH_2[a]	−310	0.18	−319	0.76	−289	0.26	−287	0.32
Me_2NNH_2[b]	−320	0.23	−318	0.30	−286	0.31	−289	0.24

[a] In water. [b] In MeOH. [c] Not available because of poor resolution. [d] Spectrum of B showed one poorly resolved signal, whose T_1 is reported under N-2 for convenience.

Upon protonation in DMSO, ^{15}N N-1 signals are slightly shielded ($\Delta\delta < 1$) except for **4**, for which $\Delta\delta = 12$, and N-2 signals are deshielded by 5−6 ppm. In methanol and water chemical shifts change by <2 ppm, and especially in the case of N-2 the values are barely outside experimental error. ^{15}N data are collected in Table 2.

^{15}N NMR results in DMSO show a major T_1 and T_1^{DD} shortening for both N-1 and N-2 upon protonation. According to eq 1, if the correlation time is the same for both B and BH^+ this result would imply that protonation takes place at both nitrogen atoms. However, because τ_c is proportional to $1/T_1^{DD}$ and $W_{1/2}$ (eq 1), an increase of τ_c leads to a decrease in ^{15}N T_1 (the same direction expected for protonation) and also in ^{14}N T_1 (the opposite of what is expected for protonation).

An estimate of τ_c for arylhydrazines can be obtained by measuring the ^{13}C dipolar relaxation rate of C-1 or C-4 (such a τ_c value is an upper limit, because the reorientation of the N-1−H vector may be faster than that of the ring). The motion of N-2 is expected to be largely independent of the ring; accordingly, the arguments that follow will apply only to N-1. The correlation time of N-1 or N-2 in $MeNHNH_2$ and Me_2NNH_2 cannot be reliably inferred from that of the methyl groups, owing to their fast rotation, and such measurements were not carried out. ^{13}C relaxation times are collected in Table 3.

The values of ^{13}C T_1^{DD} in DMSO and MeOH become shorter on going from neutral to protonated form, whereas in water they undergo small changes. An increase of τ_c in the same solvent may be due to an increase in the hydrodynamic volume, possibly because of ion pairing in the salts. Hence, before interpreting T_1 changes in terms of a preferred protonation site, we have to take into account the changes in correlation time, as follows (for simplicity we will omit the DD superscript).

C-1 is an unsuitable probe because its relaxation is also affected by the N−H proton(s). On the other hand, the relaxation of C-4 is due to H-3 and H-5, as well as by H-4 in **3**. Because the C-4−H and C-3(5)−H distances (calculated by ab initio methods; see below) are the same in **3** and its ions (ca. 1.07 and 2.13 Å, respectively), the dipolar relaxation rate of ^{13}C ($1/T_1^C$) is proportional to τ_c, and the change in correlation time $\tau_c(B)/\tau_c(BH^+)$ is given by $T^C = T_1^C(BH^+)/T_1^C(B)$. Therefore, the ratio of ^{15}N T_1's for N-1 is $T^N = T_1^N(BH^+)/T_1^N(B) = (N_B/N_{BH^+})T^C$. If N-1 does *not* undergo protonation, then the change in ^{15}N T_1 should be the same as that of ^{13}C T_1's, and $T^N = T^C$. Conversely, protonation occurring to some extent on N-1 will cause $N_B < N_{BH^+}$ and correspondingly $T^N < T^C$. In the limit of complete protonation at N-1, $N_B/N_{BH^+} = 1/2$ and $T^N = T^C/2$ (Table 3).

Quantum Chemical Calculations. Because both basic sites belong to the same functional type, solvation will play a decisive role in determining the preferred site of protonation in solution. Therefore, calculations were carried out both for the isolated and solvated species, modeling the solvent by means of continuum methods. Semiempirical calculations (Table 4) were carried out with the AM1[13] method, and the solvent water was treated by the Cramer−Truhlar method (AM1−SM2).[14] Ab initio calculations[15] (Table 5) were performed at the MP2(FC)/6-31G(d) level. The solvent was modeled by the SCRF method[16] (Table 6). The main geometrical parameters are collected in Table 7 and graphically presented in Figures 1 and 2.

Discussion

NMR Results. First, we remark that changes in ^{15}N chemical shifts or $^1J_{NH}$ (often used to probe protonation sites) do not offer a clearcut answer to the problem under investigation, because these either change very little or in the same direction for both alkyl- and arylhydrazines, which have different protonation sites. Likewise, changes in $^1J_{NH}$ are often comparable with those induced by different solvents,[17] and in aqueous solutions proton exchange would remove all such couplings.

(a) Alkylhydrazines. For **2**, the ^{14}N T_1 of N-1 increases, as expected for protonation at an amino nitrogen,[8a,10,11] which indicates that N-1 is the preferred protonation site. Conversely, the T_1 of N-2 remains constant or increases. With regard to **1**, protonation at N-1 is easily inferred by the increase in its T_1. However, owing to the scarce resolution of the two signals, it is difficult to confirm this by comparison with N-2. In fact, upon protonation in water the T_1 of N-2 also increases; hence, the possibilities remain that the correlation time of BH^+ is shorter than that of B, or protonation at N-2 occurs too, probably to a minor extent.

For **1** and **2**, the ^{15}N T_1^{DD} values of both nitrogens in MeOH decrease. This is consistent with N-1 protonation, but the decrease at N-2 requires further explanation. ^{14}N results for **2** do not support protonation at N-2; therefore, the decrease at N-2 should be due to a larger correlation time of BH^+ relative to B. Assuming that all changes in T_1^{DD} of N-2 are due to dynamics, and correcting the data for N-1 by the appropriate factor, they remain consistent with N-1 protonation. On the other hand, for **1** the T_1^{DD}'s of both nitrogens decrease by the same factor upon protonation, which is probably due to N-2 protonation to some extent.

In water, the values for N-1 and N-2 increase except for the N-1 of **2**. The results for **1** are compatible with protonation only if τ_c also changes. Assuming that protonation of **2** occurs at N-1 (see ^{14}N results), the increase in T_1 at N-2 is due to a decrease in τ_c; if this correction is applied to the data for N-1, the net decrease observed is still consistent with protonation at N-1. With regard to **1**, the data for N-2 can be corrected as above, which confirms N-1 as the preferred protonation site. The results obtained for N-2 via ^{14}N and ^{15}N are consistent with a decrease in τ_c; however, in light of the results in MeOH the possibility that protonation at N-1 is partially occurring cannot be ruled out. In summary, the data are consistent with protonation at N-1 (the alkylated nitrogen) of both **1** and **2**, but protonation at N-2 for **1** cannot be ruled out.

(b) Arylhydrazines. The ^{15}N T_1^{DD}'s of arylhydrazines in DMSO undergo a large shortening at both N-1 and N-2. For **3** and **4** $T^N \approx T^C$, i.e., the T_1 shortening observed is due to correlation time changes, and protonation is not occurring at N-1. This conclusion supports protonation at N-2, which agrees with ^{1}H spectra and other existing data.[1−4] On the contrary, for **5** $T^N < T^C$, which indicates that the slower molecular motion is not sufficient to account for the observed decrease of T_1, i.e., protonation takes place at N-1 as well as at N-2. This

TABLE 2: Values of Chemical Shift (ppm), T_1 (s), NOE, and T_1^{DD} (s) of ^{15}N Nuclei for Neutral and Protonated Hydrazines

	N-1								N-2							
	B				BH^+				B				BH^+			
X	δ	T_1	η	T_1^{DD}	δ	T_1	η	T_1^{DD}	δ	T_1	η	T_1^{DD}	δ	T_1	η	T_1^{DD}
(a) Arylhydrazines (4-X-$C_6H_4NHNH_2$) in DMSO-d_6																
H	−294.8	8.8	−4.9	8.8	−295.5	2.4	−4.7	2.5	−321.1	4.5	−4.0	5.5	−315.7	0.7	−3.5	1.0
NO_2	−277.7	4.1	−4.4	4.5	−289.6	1.6	−4.4	1.8	−321.7	3.2	−4.1	3.8	−315.6	0.5	−3.6	0.8
OMe	−298.2	6.7	−4.4	7.4	−298.0	1.8	−4.3	2.0	−318.6	3.2	−4.6	3.5	−313.9	0.6	−3.7	0.8
(b) In CH_3OH/CD_3OD 8:2																
$PhNHNH_2$	−297.1	24.3	−4.6	25.7	−296.7	11.7	−3.7	15.3	−321.6	13.0	−4.6	14.0	−321.1	3.7	−4.3	4.3
$MeNHNH_2$	−327.8	25.7	−4.6	27.7	−326.0	14.1	−4.6	15.2	−308.4	14.6	−4.5	16.2	−308.1	8.0	−4.5	8.9
Me_2NNH_2	−320.9	190	−4.7	201.8	−317.0	25.1	−4.0	30.8	−285.4	24.0	−4.9	24.0	−286.7	10.0	−4.0	12.0
(c) In H_2O/D_2O 8:2																
$PhNHNH_2$	−297.4	17.9	−4.4	20.5	−297.1	20.8	−4.3	23.7	−319.3	8.5	−4.4	9.6	−319.1	8.5	−3.5	12.0
$MeNHNH_2$	−327.8	32.8	−4.6	35.4	−327.8	42.8	−4.4	47.9	−308.6	19.1	−4.9	19.1	−308.0	44.2	−4.4	50.1
Me_2NNH_2	−320.8	124	−4.6	132.6	−319.9	69.9	−4.4	78.3	−285.6	12.4	−3.6	16.9	−285.1	32.8	−4.9	33.2

TABLE 3: Values of ^{13}C T_1 (s) and NOE of C-4 in Neutral and Protonated Arylhydrazines (4-X-$C_6H_4NHNH_2$)[a]

	B			BH^+				
X	T_1	η	T_1^{DD}	T_1	η	T_1^{DD}	T_N[d]	T_C[d]
H	1.7	1.4	2.3	0.4	1.5	0.5	0.28	0.24
H[b]	2.7	1.6	3.3	1.6	1.7	1.8	0.59	0.54
H[c]	2.2	1.9	2.3	2.0	1.9	2.1	1.15	0.91
NO_2	16.6	0.6	51.7	6.0	0.4	26.7	0.40	0.51
OMe	15.7	0.4	72.3	6.2	0.3	42.8	0.27	0.59

[a] In DMSO-d_6, except where noted. [b] CH_3OH/CD_3OD 8:2. [c] H_2O/D_2O 8:2. [d] See text; data from Table 2.

TABLE 4: Heats of Formation (ΔH_f, kcal/mol) and Values Relative to the Most Stable Ion ($\Delta\Delta H_f$, kcal/mol) of the Protonated Forms of Hydrazines from Semiempirical Calculations

	AM1[a]		AM1−SM2[a,b]	
species	ΔH_f	$\Delta\Delta H_f$	ΔH_f	$\Delta\Delta H_f$
1a	181.681	(0.0)	99.683	(0.0)
1b	184.689	3.0	108.997	9.3
2a	182.797	(0.0)	119.373	(0.0)
2b	186.199	3.4	131.194	11.8
3a	210.142	(0.0)	135.559	6.4
3b	209.368	0.8	141.916	(0.0)
4a	224.982	(0.0)	134.629	(0.0)
4b	226.167	1.2	142.834	8.2
5a	170.115	1.0	96.722	(0.0)
5b	169.126	(0.0)	101.646	4.9

[a] AM1//AM1. [b] Cramer−Truhlar solvation model for water; AM1−SM2//AM1.

conclusion is supported by ^{1}H spectra and is consistent with an enhanced basicity of N-1 due to the electron-releasing effect of the 4-OMe substituent.

In MeOH and water ^{15}N T_1's decrease slightly or increase. The analysis of ^{13}C T_1's again indicates that the observed effect on ^{15}N relaxation is due to dynamics changes, and protonation takes place at N-2.

Quantum Chemical Calculations. *(a) Geometries.* Protonation of **3** at any site causes a major twisting of the hydrazo moiety with respect to the aromatic ring; in fact, the $C_2-C_1-N_1-N_2$ dihedral angle increases from 25.3° in neutral **3** to 82.6° and 89.4° in **3a** and **3b**, respectively (Figure 2). The geometry of forms **a**, as well as of neutral **3**, features a gauche arrangement of the N−H hydrogen atoms (as in hydrazine)[11] only in the case of $MeNH_2NH_2^+$, whereas in $Me_2NHNH_2^+$ and $ArNH_2$-NH_2^+ they are arranged in a typical anti fashion, probably to avoid eclipsing with the bulkier methyl or aryl groups (Figures 1 and 2). Forms **b** do not present peculiar structural features.

TABLE 5: Absolute (E, au) and Relative (ΔE, kcal/mol) Energies of the Protonated Forms of Hydrazines from ab Initio Calculations[a]

species	E(HF)	ΔE(HF)	E(MP2)[a]	ΔE(MP2)
1a	−150.555 929	4.7	−151.010 138	4.3
1b	−150.563 417	(0.0)	−151.017 060	(0.0)
2a	−189.592 785	7.2	−190.179 027	6.9
2b	−189.604 214	(0.0)	−190.190 018	(0.0)
3a	−341.074 194	2.7	−342.150 946	2.9
3b	−341.078 466	(0.0)	−342.155 539	(0.0)
4a	−544.516 442	0.3	−546.144 724	1.0
4b	−544.516 959	(0.0)	−546.146 262	(0.0)
5a	−454.953 274	3.0	−456.339 924	3.3
5b	−454.958 072	(0.0)	−456.345 252	(0.0)

[a] MP2(FC)/6-31G(d)//HF/6-31G(d) for **1a**−**b**, **2a**−**b**, **3a**−**b**; MP2(FC)/6-31G(d)//HF/3-21G for **4a**−**b** and **5a**−**b**.

TABLE 6: Molecular Radii (a_0, Å), Absolute (E, au), and Relative (ΔE, kcal/mol) Energies of the Protonated Forms of Hydrazines from ab Initio SCRF Calculations in Water and DMSO[a]

		H_2O[b]		DMSO[c]	
species	a_0	E	ΔE	E	ΔE
1a	3.32	−150.562 505	2.3	−150.562 408	2.4
1b	3.30	−150.566 237	(0.0)	−150.566 198	(0.0)
2a	3.59	−189.598 120	4.2	−189.598 041	4.3
2b	3.61	−189.604 875	(0.0)	−189.604 865	(0.0)
3a	4.08	−341.090 611	(0.0)	−341.090 351	(0.0)
3b	4.08	−341.081 570	5.7	−341.081 520	5.5
4a	4.30	−544.579 320	(0.0)	−544.578 281	(0.0)
4b	4.31	−544.552 977	16.5	−544.552 388	16.2
5a	4.33	−454.977 781	(0.0)	−454.977 380	(0.0)
5b	4.34	−454.966 706	6.9	−454.966 565	6.8

[a] SCRF/6-31G(d)//HF/6-31G(d) calculations. [b] $\epsilon = 78.5$. [c] $\epsilon = 46.7$.

(b) Energetics of Protonation in the Gas Phase. For arylhydrazines, the energy difference between **a** and **b** does not exceed 3 kcal/mol at all levels of theory employed, N-1 being more basic. The difference in stability is maximum for **5**, which can better stabilize the positive charge at N-1, and minimal for **4**, where the form protonated at N-1 (**b**) is destabilized. The results for alkyl derivatives depend on the method used: thus, AM1 calculations predict N-2 to be slightly more basic, whereas ab initio calculations indicate a more definite preference for N-1 ($\Delta E = 4-7$ kcal/mol). Hence, ab initio results for arylhydrazines, although favoring protonation at N-1, do not allow a reliable prediction of the relative stability of **a** and **b** in solution, whereas those for alkylhydrazines indicate a preferred protonation at N-1.

(c) Energetics of Protonation in Continuum Solvents. At the AM1−SM2 level, **a** is predicted to be more stable by 5−12

TABLE 7: Main Geometrical Parameters of Neutral and Protonated Hydrazines[a]

(a) Alkylhydrazines $MeRNNH_2$; R = H, Me

R	$r(N_1N_2)$	$r(N_1C(Me))$	$r(N_1R)$	$r(N_2H_2)$	$\angle(C(Me)N_1R)$	$\angle(RN_1N_2H_2)$
			$RNMeNH_3^+$			
H	1.432	1.463	1.003	1.015	111.99	65.7
Me	1.434	1.462	1.462	1.017	114.18	62.6
			$RNMeHNH_2^+$			
H	1.425	1.498	1.011	1.003	108.37	178.6
Me	1.425	1.493	1.496	1.004	112.84	176.5

(b) Arylhydrazines 4-X-$C_6H_4NHNH_2$; X = H, 4-OMe, 4-NO_2[b]

X	$r(N_1N_2)$	$r(N_1H_1)$	$r(N_1C_1)$	$r(N_2H_2)$	$\angle(H_1N_1C_1)$	$\angle(H_1N_1N_2H_2)$
			$ArNHNH_2$			
H	1.395	0.995	1.398	1.004	113.69	99.2
			$ArNHNH_3^+$			
H	1.444	1.000	1.444	1.011	112.52	175.0
4-NO_2	1.503	1.011	1.456	1.017	115.56	172.7
4-OMe	1.515	1.000	1.452	1.018	115.48	173.9
			$ArNH_2NH_2^+$			
H	1.435	1.010	1.473	1.004	110.50	177.5
4-NO_2	1.495	1.017	1.488	1.010	111.56	175.3
4-OMe	1.496	1.016	1.485	1.010	111.41	174.6

[a] HF/6-31G(d) calculations. Distances in angstroms, angles in degrees. See Figures 1 and 2 for atom numbering. [b] Nitro and methoxy groups are coplanar with the aromatic ring.

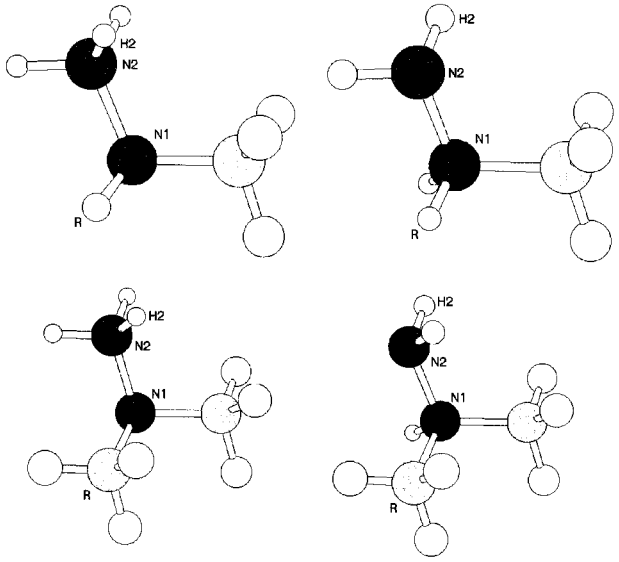

Figure 1. Structures of protonated alkylhydrazines ($MeNHNH_2$ and Me_2NNH_2) from HF/6-31G(d) geometry optimization. N black, C gray, H white. R represents a hydrogen atom or a methyl group for the purpose of reporting geometrical parameters in Table 7.

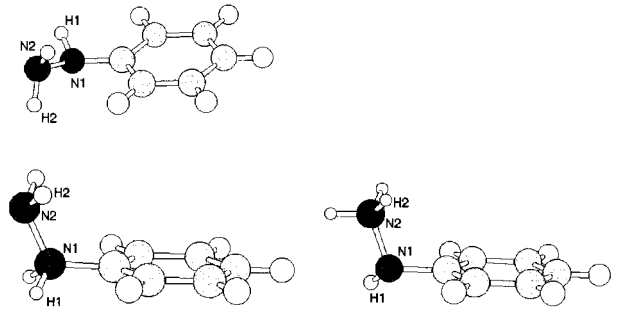

Figure 2. Structures of phenylhydrazine and its protonated forms from HF/6-31G(d) geometry optimization. N black, C gray, H white.

kcal/mol for both alkyl- and arylhydrazines. Conversely, SCRF results in water and DMSO (their small difference has been previously noted[8c,16]) indicate the preferred protonation site to be N-2 for arylhydrazines and N-1 for alkylhydrazines. The extent of preference varies between 5−7 kcal/mol (**3** and **5**) and 16 kcal/mol for **4**, where the electron-withdrawing effect of the substituent is a large destabilization of **b**. For alkyl derivatives, the preference is less marked. Hence, the SCRF method correctly predicts an enhanced stabilization in solution of ion **a** for arylhydrazines and of ion **b** for alkylhydrazines. In this respect the AM1−SM2 method performs significantly worse. However, the peculiar behavior of **4** (protonation at both sites) is not borne out by these calculations.

Summary and Conclusions

Protonation substantially affects ^{14}N and ^{15}N relaxation of arylhydrazines, largely through changes in correlation time; NMR results are consistent with protonation taking place exclusively at N-2 except for 4-methoxyphenylhydrazine, for which protonation at N-1 has also been found. Alkylhydrazines **1** and **2** undergo protonation at N-1, although for **1** protonation at N-2 may also occur. Calculations on the isolated molecules indicate that the intrinsic basicity of N-1 and N-2 is very similar; the inclusion of the solvent predicts the preferred protonation site to be N-1 for the alkyl- and N-2 for arylhydrazines studied herein.

Experimental Section

All compounds used are commercially available. NMR measurements were carried out with degassed samples at 20 or 25 °C on Varian Gemini 300 (^{15}N, ^{13}C) or Bruker AM 400 (^{14}N) instruments, operating at 7.0 and 9.4 T, respectively. ^{14}N and ^{15}N chemical shifts are referred to external neat nitromethane. ^{15}N and ^{13}C relaxation times were determined by inversion−recovery or saturation−recovery; NOEs were determined by nonselective proton irradiation during 2−4 T_1. ^{14}N relaxation times were determined by inversion−recovery with acoustic ringing suppression.[18] All calculations were run with the programs *Spartan 3.0*[19] and *Gaussian 92*,[20] running on an IBM RS/6000 workstation.

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