

A Study of Solvent Polarity and Hydrogen Bonding Effects on the Nitrogen NMR Shielding of Isomeric Tetrazoles and *ab Initio* Calculation of the Nitrogen Shielding of Azole Systems

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High-precision nitrogen NMR shieldings, bulk susceptibility corrected, are reported for the *N*-methyl derivatives of the two existing isomeric tetrazoles (I, II) in a variety of solvents which represent a wide range of solvent properties from the point of view of polarity as well as hydrogen bond donor and acceptor strength. The observed range of solvent-induced nitrogen shielding variations of I and II is significant for the pyrrole-type nitrogens (*N*-Me), up to 9 ppm, and even more so for pyridine-type nitrogen atoms, where it can attain a value of 20 ppm. There is a clear distinction between the two types of nitrogen atoms in that the former exhibit a deshielding effect with increasing polarity of the medium while the latter experience an increase in the magnetic shielding of their nuclei. The latter effect is significantly augmented by solvent-to-solute hydrogen-bond formation where the pyridine-type nitrogens are involved directly. It is also quite diversified throughout the pyridine-type nitrogen atoms and seems to constitute a measure of relative basicity with respect to hydrogen-bond formation of the nitrogens concerned. This basicity seems to parallel that with respect to a full transfer of a proton, as can be reckoned from *ab initio* calculations of the relevant protonation energies reported in the present study. The experimental data for the tetrazoles in cyclohexane solutions are combined with those obtained in our earlier extensive studies on azole, diazole, and triazole ring systems, for a comparison with *ab initio* calculations of the nitrogen shieldings concerned. The latter were carried out using the coupled Hartree–Fock/GIAO/6–31++G** approach and geometry optimizations employing the same basis set; they show a good linear correlation with the experimental data and reproduce not only major changes but also most of the subtle variations in the experimental nitrogen shieldings of the azole systems as a whole. © 1998 Academic Press

Key Words: nitrogen NMR; nitrogen shieldings; nitrogen chemical shifts; tetrazoles; triazoles; diazoles; azoles; solvent effects; calculations.

INTRODUCTION

We have already presented the results of our extensive studies of solvent-induced effects on the nitrogen NMR shielding (chemical shift) of azole (1), diazole (2), triazole (3), oxazole (4), oxadiazole (4), thiazole (5), and thiadiazole (5) five-membered heteroaromatic ring systems which

included all of the existing isomeric structures of the latter in a wide range of solvents encompassing a broad spectrum of polarity and hydrogen-bonding properties. It was shown there that the solvent effects concerned are quite significant and span a range of about 30 ppm, on the average, for pyridine-type nitrogens, and about 10 ppm for pyrrole-type nitrogen atoms. They can be rationalized in terms of nonspecific interactions of the solutes with the medium polarity/polarizability as well as of specific, site-oriented interactions like hydrogen bonding where the solutes provide acceptor centers at their imino- or pyridine-type nitrogens and, in the case of oxazole and thiazole systems, also at the oxygen or sulfur atoms concerned. The only structures missing from our earlier investigations were those of the two isomeric tetrazoles in the form of their *N*-methyl derivatives (I) and (II) (Fig. 1) where one avoids complications which result from a prototropic tautomeric equilibrium between the parent structures involved, i.e., those containing NH rather than NMe moieties. Compounds (I) and (II) provide interesting examples of competition between basic centers within a given molecule in solution since each of them contains three nonequivalent pyridine-type nitrogens which can act as hydrogen bond acceptors with respect to protic solvent molecules. This problem has already been raised in our earlier studies on triazoles (3) and six-membered heteroaromatic azine systems (6–8), which showed that the basicity toward hydrogen bonding estimated from solvent-induced nitrogen shielding variations for a given nitrogen atom parallels the basicity toward a complete proton transfer as reckoned from gas-phase protonation energies calculated by *ab initio* methods. Thus, the aim of the present work is to extend our studies over (I) and (II) with due attention paid to distinguishing between medium polarity and hydrogen bonding effects on the nitrogen shielding of both pyrrole-type (NMe) and pyridine-type (—N=) atoms, and to the relative basicity of the latter as hydrogen-bond acceptors, and any relationships between the latter and the corresponding protonation energies. Finally, the present work combined with our earlier studies on azole systems provides a complete set

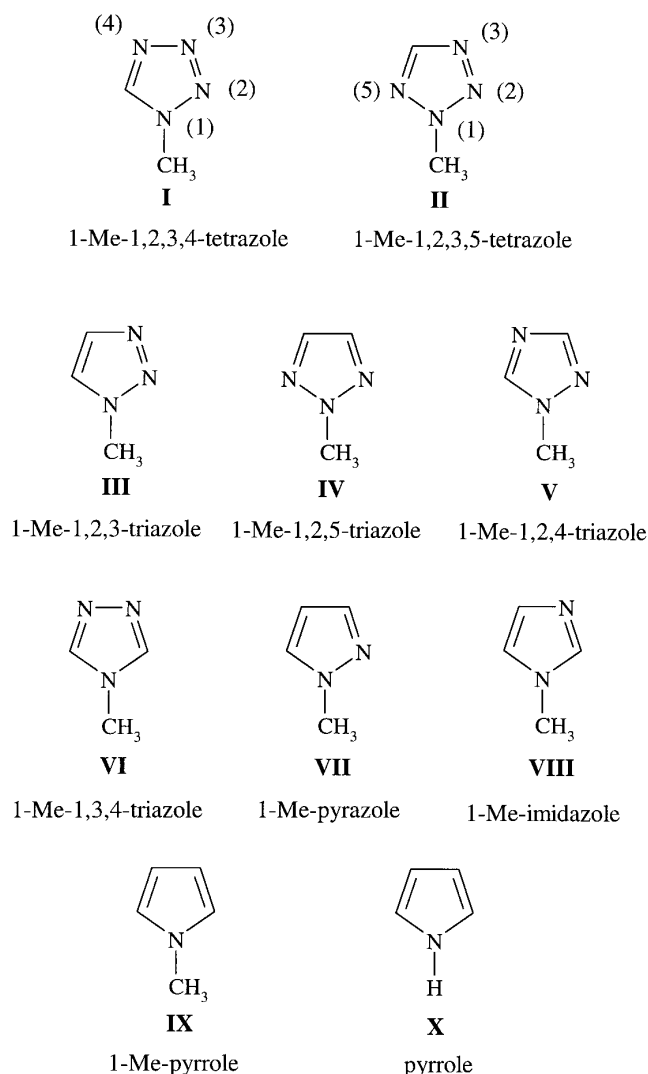


FIG. 1. Structures of compounds (I)–(II) studied experimentally in the present work, and additional structures of compounds (III)–(X) whose shieldings were measured in our earlier work (1–3) under the same conditions, and calculated in the present study. Attention is drawn to the numbering scheme employed where the pyrrole-type nitrogen is marked invariably as *N*-1. A confusing, albeit popular numbering system in the literature would name (I) “1-methyltetrazole” and (II) “2-methyltetrazole.” The origin of the latter stems from the fact that the parent structures, those with NH instead of NMe groups, are involved in a tautomeric equilibrium in solution, but such a numbering system not only is confusing, but also is incompatible with the generally accepted numbering of atoms in oxazole, thiazole, and related ring structures, where number 1 is invariably assigned to the oxygen or sulfur atom involved.

of nitrogen shieldings of the molecules concerned in dilute solutions in cyclohexane, where molecular interaction effects on the shieldings are likely to be weak, and this seems to be a suitable experimental basis for a comparison with *ab initio* calculations of the shieldings of isolated molecules. As far as the calculations are concerned, we have chosen the Hartree–Fock approach using the 6–31++G** basis

set which places both polar and diffuse functions on hydrogens as well as on heavy atoms (see Experimental). This seems to be a reasonable choice for polar molecules which include nitrogen atoms bearing lone pair electrons.

RESULTS AND DISCUSSION

Tables 1 and 2 report the high-precision ^{14}N NMR shieldings measured for (I) and (II), respectively, in 13 solvents which represent a wide range of solvent properties from the point of view of hydrogen bonding and polarity effects. A word of comment is necessary here regarding the assignments of the shieldings. Essentially, they are based on earlier reports (9) which in turn relied on the relevant ^1H – ^{15}N spin–spin couplings and the fact that the pyrrole-type nitrogen nuclei in five-membered heteroaromatics are significantly more shielded than the corresponding pyridine-type nitrogens. However, there has still been some uncertainty about the assignment of N-2 and N-3 in I, since the couplings were not sufficiently informative. It will be shown later that the assignments in Table 1 are correct from the point of view of *ab initio* calculation of the shieldings and also the relevant protonation and hydrogen bonding effects reported in the present work. Actually they differ from those of Ref. (9) only in that the assignments of N-2 and N-3 in (I) are reversed. A scrutiny of the data in Tables 1 and 2 shows that solvent effects on the nitrogen shieldings in tetrazoles (I) and (II) are quite significant and diversified, depending on the position of a given nitrogen atom in the ring system involved. Generally, the directions of the effects are opposite for the pyrrole type nitrogens (N-1) as compared with those for pyridine-type nitrogen atoms (N-2, N-3, N-4, N-5, where applicable); thus, there is a deshielding

TABLE 1
Nitrogen NMR Shielding of 1-Methyl-1,2,3,4-tetrazole
in 0.1 M Solutions

Solvent	Nitrogen shielding in ppm ref. to neat liquid nitromethane corrected for bulk susceptibility			
	N(1)	N(2)	N(3)	N(4)
Cyclohexane (0.005 M)	+159.55	+8.42	–23.31	+43.23
Et ₂ O (0.01 M)	+156.47	+9.42	–19.11	+45.94
CCl ₄ (0.03 M)	+157.47	+9.29	–18.82	+45.63
Benzene	+155.94	+9.37	–17.96	+46.62
Dioxane	+153.99	+10.06	–16.40	+47.96
Acetone	+153.10	+9.93	–15.27	+48.61
DMSO	+150.92	+10.35	–13.00	+50.18
CH ₂ Cl ₂	+154.28	+9.81	–14.46	+49.24
CHCl ₃	+154.63	+9.91	–14.61	+49.71
EtOH	+152.71	+10.96	–8.78	+55.63
MeOH	+151.99	+10.35	–8.28	+56.35
CF ₃ CH ₂ OH	+151.87	+14.1	–1.8	+62.2
H ₂ O	+150.34	+14.06	–1.75	+60.33

TABLE 2
Nitrogen NMR Shielding of 1-Methyl-1,2,3,5-tetrazole
in 0.1 M Solutions

Solvent	Nitrogen shielding in ppm ref. to neat liquid nitromethane corrected for bulk susceptibility			
	N(1)	N(2)	N(3)	N(5)
Cyclohexane	+106.99	−3.41	+41.30	+73.09
Et ₂ O	+105.08	−1.95	+43.27	+73.39
CCl ₄	+106.63	−1.89	+42.96	+73.18
Benzene	+104.97	−1.64	+43.76	+73.27
Dioxane	+103.34	−0.53	+44.94	+73.43
Acetone	+102.93	−0.50	+45.47	+72.86
DMSO	+101.51	+0.38	+46.14	+72.58
CH ₂ Cl ₂	+104.00	−0.12	+46.90	+73.63
CHCl ₃	+104.52	−0.28	+47.31	+73.66
EtOH	+103.47	+0.30	+49.50	+73.42
MeOH	+102.78	+0.68	+51.41	+73.35
CF ₃ CH ₂ OH	+104.08	+1.7	+61.0	+77.0
H ₂ O	+102.34	+6.00	+56.36	+77.56

effect on N-1 accompanied with a shielding effect on the other nitrogens with the increasing polarity and hydrogen bond donor strength of the solvent employed. This is in accord with analogous observations from our earlier work on other azole systems (1–3), and such effects can be rationalized in terms of a conventional picture (Fig. 2) which invokes the increasing delocalization of the lone pair electrons of N-1 into the π -electron system of the aromatic ring, as a result of either polarity of the medium or the effect of an engagement of the lone pair electrons of pyridine-type nitrogens in solvent-to-solute hydrogen bonding. The latter effects are likely to draw electron charge away from N-1 and augment delocalization. On the average, the magnitudes of the opposing effects are larger for (I), where the pyrrole-type nitrogen (N-1) occupies a position at an end of the chain of four nitrogens, than for (II), where N-1 is located inside the chain, and the electron-withdrawing effect of N-5 competes with those exerted by N-2 and N-3 (Fig. 2); this is also in accord with the foregoing. We have already observed analogous differences in the magnitude of solvent-induced effects on the nitrogen shielding of 1-Me-1,2,3-triazole as compared with 1-Me-1,2,5-triazole (3).

More detailed insight into the various site-specific and nonspecific contributions to the solvent induced nitrogen shielding variations of (I) and (II) can be obtained by making use of the empirical scheme represented by the master equation (10, 11)

$$\sigma(i, j) = \sigma_0(i) + a(i)\alpha(j) + b(i)\beta(j) + s(i)[\pi^*(j) + d(i)\delta(j)], \quad [1]$$

where i and j denote the solute and solvent, respectively, σ

is the nitrogen shielding, α represents the hydrogen bond donor strength of the solvent as a bulk medium, β gives its hydrogen bond acceptor strength, π^* is its polarity/polarizability, and δ is a correction for polychlorinated solvents ($\delta = 0.5$) and aromatic solvents ($\delta = 1$). The corresponding response of the solute nitrogen shielding to a given solvent property is represented by the solute terms a , b , s , and d , respectively. The nitrogen shielding in the reference state, cyclohexane solution, is given by σ_0 ; the latter is a least-squares fit of the data obtained for all of the solvents employed rather than the experimental value concerned.

Table 3 shows the solvent parameter sets employed in the present work (10, 11) as well as the results of a multiple regression analysis performed over the corresponding sets of master equations [1] for the compounds and nitrogen atoms involved. The least-squares fitted values of the relevant solute/atom terms σ_0 , a , b , s , and d are reported together with their standard deviations. The terms d are not significant, and the magnitudes of the b terms, which probably represent some weak interactions of the CH groups with basic centers in the solvent molecules involved, do not exceed 3 ppm; the most interesting are the terms a (nitrogen shielding response to solvent-to-solute hydrogen bonding) and s (nitrogen shielding response to solvent polarity).

The magnitudes of the s terms are, on the average, about the same (ca. 5 ppm) for both pyrrole-type nitrogens (N-1) and pyridine-type nitrogen atoms, but their signs are opposite for the two groups of atoms, negative for N-1, and positive for the other group; this means that the increasing polarity of the solvent induces a significant deshielding effect on the N-1 nuclei, while those in pyridine-type nitrogens experience a significant shielding increase. This is in accord with the picture of the increasing delocalization of the lone pair electrons of N-1 with the increasing polarity of the medium, and also with analogous observations for other azole systems (1–5). However, there are some significant deviations from

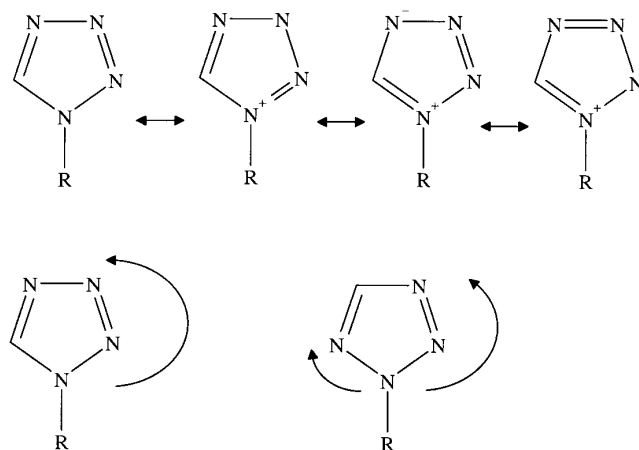


FIG. 2. Conventional representation of lone pair electron delocalization in (I), and a comparison of electron charge migration paths in (I) and (II).

TABLE 3
Solvent Parameters Used and Least-Squares Fitted Solute Parameters for a Set of Master Equations [1]

Solvent	α	β	π^*	δ		
Cyclohexane	0	0	0	0		
Et ₂ O	0	0.47	0.27	0		
CCl ₄	0	0	0.29	0.5		
Benzene	0	0.10	0.59	1		
Dioxane	0	0.37	0.55	0		
Acetone	0.07	0.48	0.72	0		
DMSO	0	0.76	1.00	0		
CH ₂ Cl ₂	0.22	0	0.80	0.5		
CHCl ₃	0.34	0	0.76	0.5		
EtOH	0.86	0.77	0.54	0		
MeOH	0.98	0.62	0.60	0		
H ₂ O	1.13	0.18	1.09	0		
CF ₃ CH ₂ OH	1.51	0	0.73	0		

Compound/nitrogen atom	σ_0 (ppm)	a (ppm/unit scale)	b (ppm/unit scale)	s (ppm/unit scale)	d (dimensionless)	Correlation coefficient r
I/N-1	+159.2 ± 0.3	−1.5 ± 0.3	−2.6 ± 0.4	−6.4 ± 0.4	−0.1 ± 0.1	0.993
I/N-2	+8.9 ± 0.6	+2.0 ± 0.5	−1.3 ± 0.9	+2.4 ± 0.8	−0.1 ± 0.1	0.947
I/N-3	−22.3 ± 0.7	+9.2 ± 0.7	+1.2 ± 1.2	+8.4 ± 1.1	−0.1 ± 0.3	0.992
I/N-4	+43.8 ± 0.5	+9.3 ± 0.4	+1.4 ± 0.7	+5.2 ± 0.7	−0.1 ± 0.1	0.996
I/N-1	+107.0 ± 0.3	0.0 ± 0.2	−2.2 ± 0.4	−4.1 ± 0.4	−0.2 ± 0.1	0.982
II/N-2	−3.3 ± 0.8	+1.7 ± 0.7	−1.0 ± 1.2	+5.1 ± 1.1	−0.3 ± 0.2	0.933
II/N-3	+42.3 ± 0.8	+8.5 ± 0.7	−2.9 ± 1.3	+5.5 ± 1.2	−0.3 ± 0.2	0.987
II/N-5	+73.4 ± 0.6	+1.7 ± 0.5	−2.9 ± 0.9	+1.6 ± 0.8	−0.9 ± 0.6	0.916

the average of the s terms for pyridine-type nitrogens, N-2 in (I) and N-5 in (II) show a weak response ($s = ca. +2$) while the shielding of N-3 in (I) reveals a remarkable sensitivity ($s = +8$) to solvent polarity effects. This seems to reflect a significant differentiation among the pyridine-type nitrogens concerned in their electron-acceptor strength such as that depicted in Fig. 2 by means of the conventional resonance structures where a formal negative charge is placed on a given pyridine-type nitrogen and a formal positive charge on N-1. Generally, in view of the fact that the values of π^* for the set of solvents employed span a range from 0 (cyclohexane) to about 1 (DMSO, water), the effects of solvent polarity on the nitrogen shieldings of N-1 can reach -5 ppm, while those relating to the pyridine-type nitrogens concerned can attain a value of $+8$ ppm.

Even more pronounced and diversified are effects of solvent-to-solute hydrogen bonds which engage the pyridine-type nitrogens of the solute concerned. These are represented by the least-squares fitted values of the a term in Eq. [1] as reported in Table 3. For N-1 nitrogens, the terms are barely significant with some bias towards negative values, i.e., a weak deshielding of N-1 upon the formation of a hydrogen bond at a pyridine-type nitrogen as an acceptor where a solvent molecule acts as a donor. This is intuitively correct in view of the foregoing discussion of solvent polarity effects (the s terms in Eq. [1]) on the nitrogen shielding of N-1, since in such instances elec-

tron charge should be drawn away from N-1 in the direction of the pyridine-type nitrogen concerned. As far as the pyridine-type nitrogens are concerned, those which are directly affected by the hydrogen bond formation, the relevant a terms attain much higher magnitudes and are invariably positive, approximately $+2$ to $+10$ ppm per unit scale of α ; this means a significant increase in the nitrogen shielding upon the formation of a solvent-to-solute hydrogen bond at the nitrogen atom involved. Since the corresponding α terms, characterizing the solvents employed from the point of view of their hydrogen bond donor strength, assume values ranging from zero (aprotic solvents) to 1.5 (2,2,2-trifluoroethanol), the relevant contribution to the nitrogen shielding variation upon the formation of hydrogen bonds can reach values from $+3$ to $+15$ ppm for the pyridine-type nitrogens in (I) and (II). Generally, both the sign and magnitudes of the effects are consistent with those observed by us for other azole systems, and also for six-membered azine-type heteroaromatics such as pyridine, diazines, triazines, and 1,2,4,5-tetrazine (1–8). This is also in accord with analogous effects found in other molecular systems where nitrogen atoms participate in double, aromatic, or triple bonds and also bear lone pair electrons which are not a part of the corresponding π -electron system (9). However, the isomeric tetrazole structures examined are especially interesting in view of the fact that each contains three nonequivalent acceptors of hydrogen bonds (the corresponding pyridine-type nitrogens, N-

2, N-3, and N-4 or N-5) which can compete with each other. We have already shown that the a terms obtained for pyridine-type nitrogen shieldings of azine heteroaromatics (6–8) and for triazole ring systems (3) provide a sensitive probe for relative affinities of these nitrogens as acceptors of hydrogen bonds; the latter affinities may be termed an exhibition of variations in “soft” basicity, while analogous affinities with respect to a complete proton transfer should then be termed “hard” basicity. We have also found indications that the affinity of the nitrogen atoms concerned to accepting hydrogen bonds from solvent molecules, measured by the a terms for the relevant nitrogen shieldings, parallels that with respect to gas-phase protonation, as reckoned from *ab initio* calculated protonation energies (3, 6–8). The tetrazole systems examined in the present work should provide a rigorous test for such a correlation, in view of the fact that each contains three non-equivalent pyridine-type nitrogen atoms which can enter competition with respect to hydrogen bond or proton acceptance.

We estimated the protonation energies (Table 4) for (I) and (II) and each of the basic centers involved using RHF/6–31++G** calculations which included geometry optimization for the neutral molecules and all of the cations involved; these are compared with the corresponding a terms obtained from the nitrogen shielding data by means of master equations [1]. There is a clear-cut distinction, from the point of view of the affinity towards accepting hydrogen bonds from solvent (the magnitude of the a terms) as well as that with respect to protonation (the computed protonation energies) between pyridine-type nitrogens that are adjacent to N-1 (these are N-2 or N-5, where applicable) and those which occupy the more remote positions (N-3 and N-4); the latter reveal a remarkably pronounced basicity, in both its aspects, as compared with the former (Fig. 3). Moreover, even within each of the two groups of pyridine-type nitrogens, the more subtle variations in the a terms seem to parallel those in the protonation energies (Table 4). In view

*the most basic centers with respect
to both protonation and hydrogen bonding*

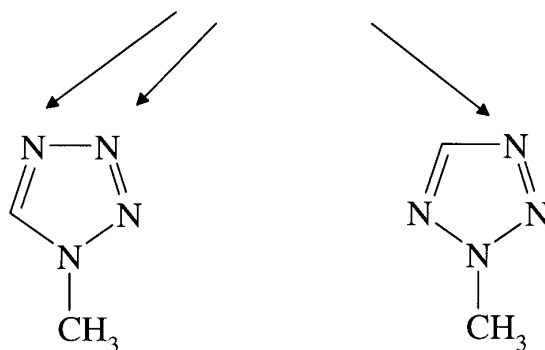


FIG. 3. Assessment of the most basic centers within compounds (I) and (II). Basicity with respect to hydrogen bonding is shown to be parallel with that relating to protonation.

of the foregoing, tetrazoles (I) and (II) provide a crucial argument in favor of the existence of parallel trends in “hard” and “soft” basicities of pyridine-type nitrogen atoms in heteroaromatic ring systems.

Now, since the present work combined with our earlier studies on azole systems (1–3) provides a comprehensive set of nitrogen shielding data which includes measurements for dilute solutions of the solutes concerned in cyclohexane, we endeavored to calculate the relevant absolute nitrogen shieldings using *ab initio* methods (Table 5). The saturated hydrocarbon solvent employed is likely to enter rather weak molecular interactions with the solutes, and therefore the experimental data are suitable for a comparison with theoretical values of the nuclear shieldings calculated for isolated molecules. Attention is drawn to the fact that the calculations of the shieldings were based on optimized geometries using the same basis set, 6–31++G**, for both the optimization and the nitrogen shieldings. There is a good linear relationship between the experimental data and the theoretical shieldings (Fig. 4), as expressed by the equation

$$\sigma_{\text{exp.}} = (0.8804\sigma_{\text{calcd.}} + 112.56) \pm 5.76 \text{ ppm} \quad [2]$$

with a linear correlation coefficient $r = 0.997$. The slope coefficient shows that the calculations overestimate the magnitudes of the absolute shieldings by about 12%, and the free term yields an estimate of the absolute shielding of the reference employed, neat liquid nitromethane, as about -112 ppm. The latter value is in reasonable agreement with the current estimates of nitrogen shielding in nitromethane (9). The experimental nitrogen shieldings of the azole systems concerned in dilute solutions in cyclohexane (Table 5) cover a range of about 262 ppm, from -23 ppm for (I)/(N-3) through $+239$

TABLE 4

Relationship between Nitrogen NMR Shielding Variations Induced by Solvent-to-Solute Hydrogen Bonding Effects and *ab initio* Calculated Gas-Phase Protonation Energies

Compound/acceptor site for protonation or hydrogen bonding	RHF/6-31++G** calcd. protonation energy for optimized geometries concerned (kJ/mol)	Nitrogen NMR shielding variation induced by hydrogen bonding at the acceptor site (term a , Eq. [1], ppm/unit scale of α)
I/N(2)	843.53	+2.0
I/N(3)	916.50	+9.2
I/N(4)	921.84	+9.3
II/N(2)	814.06	+1.7
II/N(3)	890.75	+8.5
II/N(5)	816.99	+1.7

ppm for (X)/(N-1) with respect to neat liquid nitromethane; thus, the standard deviation of the linear fit, ± 5.76 ppm, amounts to only about 2% of the range of shieldings concerned, and does not exceed even the weakest of the solvent-induced variations observed in the nitrogen shieldings of azole systems. Needless to say, we compare here calculations relating to isolated molecules with experimental data obtained for solutions in cyclohexane rather than with those for low-pressure gas phase, and thus we neglect any gas-to-solution shifts of the shieldings involved or, more precisely, any differentiation therein throughout the set of the nitrogen shieldings considered. In view of the good linear relationship obtained (Eq. [2]) such a differentiation for solutions in cyclohexane seems to be small, particularly if we take into account the limitations set by a finite basis set and the neglect of electron correlation effects by the Hartree–Fock approach.

The calculations seem to solve any doubts about the assignments of nitrogen shieldings in compound (I), those concerning the N-2 and N-3 nitrogen atoms there. They show that

TABLE 5

Ab initio Coupled-Hartree–Fock (CHF) Calculations of Nitrogen NMR Shielding of Tetrazoles and Other Azole Systems

Compound/ nitrogen atom	Experimental values of nitrogen shielding (ppm, dilute solutions in cyclohexane, ref. to neat nitromethane)	CHF/6-31++G**/GIAO calculated nitrogen NMR shielding (ppm, referred to a bare nucleus)
I/N(1)	+159.55	+57.4
I/N(2)	+8.42	–115.8
I/N(3)	–23.31	–152.6
I/N(4)	+43.23	–64.0
II/N(1)	+106.99	–3.6
II/N(2)	–3.41	–145.0
II/N(3)	+41.30	–73.3
II/N(5)	+73.09	–41.4
III/N(1)	+149.50 ^a	+43.0
III/N(2)	+7.51 ^a	–130.8
III/N(3)	+20.58 ^a	–108.4
IV/N(1)	+133.07 ^a	+22.5
IV/N(2,5)	+47.97 ^a	–79.8
V/N(1)	+176.07 ^a	+76.7
V/N(2)	+78.95 ^a	–30.9
V/N(4)	+122.91 ^a	+17.0
VI/N(1)	+226.00 ^a	+127.2
VI/N(3,4)	+47.00 ^a	–69.5
VII/N(1)	+181.28 ^b	+76.9
VII/N(2)	+65.69 ^b	–52.5
VIII/N(1)	+225.02 ^b	+124.6
VIII/N(3)	+111.50 ^b	+2.1
IX/N(1)	+235.19 ^c	+132.4
X/N(1)	+238.77 ^c	+137.1

^a Experimental data from our earlier work (3) obtained under the same experimental conditions.

^b As above, ref. (2).

^c As above, ref. (1).

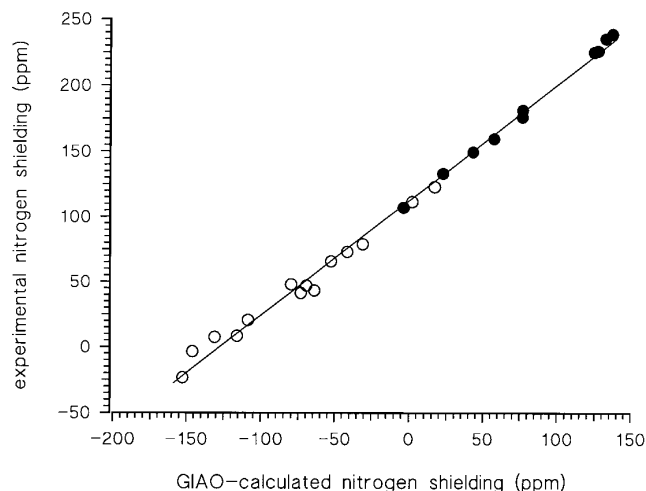


FIG. 4. A plot of experimental nitrogen shieldings, referenced to neat liquid nitromethane, against GIAO/CHF-calculated absolute nitrogen shieldings for the azole systems considered which include all of the existing parent structures. ○, pyridine-type nitrogen; ●, pyrrole-type nitrogens.

N-2 is significantly more shielded than N-3, by about 30 ppm according to Eq. [2], and this amounts to more than five times the standard deviation of the linear fit concerned. Actually, the calculations confirm equally well all of the remaining assignments throughout the set of nitrogen shieldings of azole systems. Moreover, many subtle points of experimentally observed differences in the nitrogen shieldings are reproduced precisely by the computations. These include the remarkable differences between the shieldings of the pyrrole-type nitrogen (N-1) with respect to the corresponding pyridine-type nitrogen atoms within a given molecule; the unusually high shielding of N-4 in (V) and of N-3 in (VIII) as compared with all of the remaining pyridine-type nitrogens; essentially all differences, large or subtle ones, throughout the set of pyrrole-type nitrogens; the slight overlap of the range of shieldings of pyridine-type nitrogens with that of N-1 atoms. Actually, the calculated absolute shieldings indicate that all the N-1 nuclei concerned are magnetically shielded ($\sigma > 0$) while those in the pyridine-type nitrogens are deshielded or anti-shielded ($\sigma < 0$) with respect to a bare nucleus, with a slight exception of N-4 in (V) and of N-3 in (VIII) which enter the low-end range of N-1 shieldings.

Generally, it seems that the Hartree–Fock approach at the level of sophistication employed in the present work yields good results in confrontation with experimental nitrogen shieldings provided that one accounts for the slight but systematic exaggeration of the calculated magnitudes, that shown in Eq. [2]; this is corroborated by our earlier results obtained for six-membered azine-type heteroaromatic rings (6–8) including pyridine and all of the existing isomeric diazine, triazine, and tetrazine systems. Attention is drawn to the fact that the experimental and theoretical datasets compared in the present work are internally consistent. All

of the experimental values of the nitrogen shieldings were obtained under the same conditions and relate to dilute solutions in cyclohexane; measurements for such solutions are likely to provide the closest approximation to gas-phase nitrogen shieldings, and even more so with respect to relative shieldings. On the other side, the *ab initio* theoretical values were obtained using a fairly large basis set for molecular geometries which were optimized using the same set, so that there is no arbitrariness involved like that when one employs "experimental" geometries of various and often dubious quality or when the optimization is carried out using a different, usually much smaller basis set.

EXPERIMENTAL

The compounds studied, (I) and (II), were prepared by published procedures (13). Particular care was taken in the NMR measurements to use very pure and dry solvents as reported previously (1–6). The NMR samples concerned were prepared and handled under a dry argon atmosphere in glove bags. The ^{14}N NMR shielding measurements were taken on a Bruker AM500 spectrometer (11.7 T) at $35 \pm 0.2^\circ\text{C}$, as maintained by a VT unit, at a frequency of 36.14 MHz. Random and systematic errors were reduced to below 0.1 ppm for the solute nitrogen shieldings in different solvents. External neat liquid nitromethane was employed as a reference by means of 10 mm/4 mm o.d. coaxial tubes. The inner tube contained 0.3 M nitromethane in acetone- d_6 as a reference and a source of deuterium lock; the nitrogen shielding of this solution is +0.77 ppm with respect to that of neat liquid nitromethane (9). The latter value is obtained from measurements using concentric spherical sample/reference containers in order to eliminate bulk susceptibility effects. The value of +0.77 ppm is used as a correction upon a conversion to the neat nitromethane reference scale of nitrogen NMR shieldings. Bulk susceptibility corrections for the shieldings measured with respect to the actual reference employed (0.3 M nitromethane in acetone- d_6) were made as described previously (9), and since dilute solutions were used, their magnetic volume susceptibilities are assumed to be equal to those of the corresponding solvents at $+35^\circ\text{C}$. In our measurements, the exact resonance frequency of the ^{14}N signal of neat nitromethane was 36.141524 MHz, from which a value of 36.136826 MHz is obtained for the bare nitrogen nucleus (9). The latter value is used in conjunction with the relevant resonance frequency differences to calculate the nitrogen shieldings relative to that of neat nitromethane. Lorentzian lineshape fitting of the ^{14}N signals was used to produce values for the precise resonance frequencies of both the samples used and of the external standard, as well as the relevant standard deviations of the variables fitted. The latter included not only the resonance frequencies con-

cerned, but also the phases of the signals, their linewidths and intensities, and the linear baseline drift. The standard deviations of the resonance frequencies concerned were, in all cases, below 2 Hz, and this corresponds to an error of less than 0.05 ppm for the nitrogen shieldings; the latter are reported such that the last digit is uncertain.

The *ab initio* calculations were carried out using the Gaussian 94 (Revision D.3) software package (12) which was implemented on a Pentium 120 MHz-based ESCOM system equipped with 64 MB RAM. The restricted Hartree–Fock (RHF) approach combined with the 6–31++G** basis set was employed for full optimizations of the relevant geometries, and then for computations of the corresponding energies and nitrogen NMR shieldings; the latter were evaluated using the coupled Hartree–Fock (CHF) approach and the gauge-included atomic orbital (GIAO) method.

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