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Journal of Magnetic Resonance 164 (2003) 212–219

JMR Journal of Magnetic Resonance

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Solvent polarity and hydrogen-bonding effects on the nitrogen NMR shieldings of *N*-nitrosamines and DFT calculations of the shieldings of *C*-, *N*-, and *O*-nitroso systems

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Received 23 January 2003; revised 8 July 2003

Abstract

High-precision nitrogen NMR shieldings, bulk susceptibility corrected, are reported for dimethyl-*N*-nitrosamine (**I**) and diethyl-*N*-nitrosamine (**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 amino-type nitrogens, up to about 16 ppm, and originates essentially from the deshielding effect of the increasing polarity of solvent. On the other side, the nitroso nitrogen shieldings reveal an even stronger response to solvent effects, within about 20 ppm, but in this case the increasing polarity and hydrogen bond donor strength of solvent produce enhanced shielding. DFT quantum-mechanical calculations using the GIAO/B3PW91/6-311++G** approach and geometry optimizations employing the same basis set and hybrid density functionals show an excellent correlation with the experimental data on *C*-, *N*-, and *O*-nitroso moieties and reproduce not only major changes but also most of the subtle variations in the experimental nitrogen shieldings of the nitroso systems as a whole. A combination of the calculations involving the corresponding *N* and *O*-protonated species and the trends observed in the solvent-induced nitrogen shielding variations shows clearly that the prime acceptor site for hydrogen bonding is the nitroso oxygen atom.

Keywords: ^{14}N NMR; Nitrogen shieldings; Nitrogen chemical shifts; Nitrosamines; Nitroso groups; Solvent effects; Calculations; Density functional theory

1. Introduction

We have already presented the results of our extensive studies of solvent-induced effects on the nitrogen NMR shieldings (chemical shifts) of *C*-nitroso groups in nitrosoalkanes [1–5] and nitrosobenzenes [6], and the *O*-nitroso group in *tert*-butyl nitrite [7], 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 6–12 ppm for the nitroso group nitrogen atoms. They can be rationalized in terms of contributions from non-specific interactions of the solutes with the medium polarity/polarizability as well as specific interactions like hydrogen bonding.

The aim of the present work is to extend our studies over the *N*-nitroso groups in *N*-nitrosamines with due attention paid to the relevant amino moieties. This approach has not yet been attempted regarding *N*-nitrosamines in spite of a considerable body of data on the nitrogen NMR shieldings of such molecular systems that has been accumulated over past years [1]. However, there is an even more important aspect of the present work, that concerning site oriented preferences in solvent-to-solute hydrogen bonding. A novel approach is presented here which makes use of solvent induced variations in the nitrogen NMR shieldings of at least two nonequivalent nitrogen atoms within a solute molecule; needless to say, *N*-nitrosamines provide a good molecular model for this purpose, since there are two

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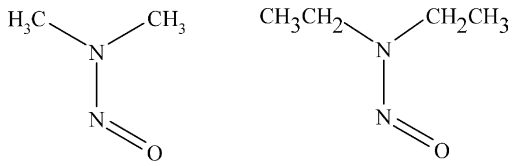
doi:10.1016/S1090-7807(03)00267-2

nonequivalent nitrogens (those of amino and nitroso moieties) while there are two potential acceptor centers of hydrogen bonds, the nitrogen and oxygen atoms of the nitroso group involved. Attention is drawn to the fact that the search for the preferred acceptor center(s) is not confined to nitrogenous sites, in the present case it encompasses nitrogen and oxygen atoms in the solute. Moreover, the nitrogen atoms whose nuclear magnetic shieldings are employed as a probe in the search for the acceptor site(s) do not have to be directly engaged in hydrogen bonding. Actually, it will be demonstrated here that the behavior of the nitrogen shieldings of *N*-nitrosamines in solutions shows clearly that the prime acceptor site for hydrogen bonding is the oxygen atom of the nitroso group. Obviously, this approach is not confined to *N*-nitrosamines, and can be employed in any cases where at least two nonequivalent nitrogen atoms show a substantial and diversified response of their nuclear magnetic shieldings to solvent-to-solute hydrogen bonding.

We have selected for this purpose two simple nitrosamines (**I**) and (**II**) (Fig. 1) whose amino nitrogens bear two alkyl groups as substituents, in order to avoid complications that may arise from the possibility of solute-to-solvent hydrogen-bond effects on the nitrogen shieldings in the case of NH(R)NO nitrosamines. The compounds studied presently, (**I**) and (**II**), have sufficient solubility in the wide range of solvents, including cyclohexane, employed in our previous work on other nitroso systems [1–7]. Additionally, it should be interesting to compare the behavior of the nitrogen shieldings, as a function of solvent, of *N*-nitrosamines (**I**) and (**II**) with that of the corresponding *N*-nitramines, R_2N–NO_2; the latter have already been examined in our previous study [8], under experimental conditions which were the same as those employed in the present work. The barrier to internal rotation about the N–N bond in *N*-nitrosamines, about 92 kJ/mol [9], is significantly higher than that for *N*-nitramines, about 40 kJ/mol.

Finally, the present work combined with our earlier studies on nitroso systems provide a large set of nitrogen shieldings for dilute solutions of the molecules concerned in cyclohexane where molecular interaction effects on the nitrogen shieldings are likely to be weak.



Dimethyl-N-nitrosamine **I** *Diethyl-N-nitrosamine* **II**

Fig. 1. Structures of compounds (**I**) and (**II**) studied experimentally in the present work.

This seems to be a suitable experimental basis for a comparison with DFT calculations of the shieldings of isolated molecules. As far as the calculations are concerned, we have chosen the density functional approach in order to account for electron correlation effects, and the large 6-311++G** basis set of wavefunctions which places both polar and diffuse functions on hydrogens as well as on heavy atoms (see Section 3). This seems to be a reasonable choice for polar molecules which include nitrogen atoms bearing lone pair electrons and direct nitrogen–oxygen and nitrogen–nitrogen bonds.

In common with our earlier reports [1–8], we present our results in terms of $\Delta\sigma$ which represents the differences in the nitrogen nuclear shielding constants σ of the compounds studied and that of neat liquid nitromethane used as external reference, with due corrections for bulk magnetic susceptibility differences. Thus, we use the expression 'nitrogen shielding' for $\Delta\sigma$, since a positive sign corresponds to an increase in magnetic shielding. Hence $\Delta\sigma = -\delta$, where the latter is commonly termed as the chemical shift. Consequently, 'nitrogen shieldings' and 'nitrogen chemical shifts' differ only in their sign.

2. Results and discussion

Table 1 reports the high-precision ^{14}N NMR shieldings measured for (**I**) and (**II**) (Fig. 1), respectively, in 13 solvents which represent a wide range of solvent properties from the point of view of hydrogen-bonding and polarity effects. The nitrogen shieldings of the amino moieties of nitrosamines (**I**) and (**II**), as a function of solvent effects, span a considerable range of about 16 ppm within the set of solvents employed. At first glance, the shielding variation seems to follow the

Table 1
Nitrogen NMR shieldings of dimethyl-*N*-nitrosamine and diethyl-*N*-nitrosamine in 0.1 M solutions at +35 °C

Solvent	Nitrogen shielding in ppm ref. to neat liquid nitromethane corrected for bulk susceptibility			
	$(CH_3)_2N$–N=O		$(CH_3CH_2)_2N$–N=O	
	Me_2N	N=O	Et_2N	N=O
Cyclohexane	+156.46	−164.08	+129.04	−163.85
CCl_4	+154.46	−161.73	+127.76	−161.45
Et_2O (+30 °C)	+153.92	−161.61	+127.38	−162.19
Benzene	+152.98	−160.50	+126.15	−160.70
Dioxane	+150.33	−158.87	+124.55	−159.08
Acetone	+149.31	−157.92	+123.44	−158.64
DMSO	+145.48	−155.12	+120.85	−156.31
CH_2Cl_2	+149.03	−157.08	+123.00	−157.22
$CHCl_3$	+149.17	−157.62	+123.24	−156.94
EtOH	+148.00	−155.36	+122.32	−155.63
MeOH	+146.77	−154.02	+121.21	−154.24
CF_3CH_2OH	+144.20	−148.50	+118.81	−147.47
H_2O	+139.27	−143.20	+114.47	−143.11

polarity of solvent in the sense of enhanced deshielding with the increasing polarity, and this point will be discussed in detail in conjunction with Eq. (1). This behavior of nitrogen shieldings is typical of amino moieties whose lone pairs of electrons are engaged in a delocalized π-electron system, and the delocalization of the lone pair is augmented by solvent polarity or any other effects [1]. Thus, in the present case of nitramines, the latter process would involve a gradual shift of the actual structure from (**Ia**) to that represented by (**Ib**) (Fig. 2).

On the other side, the nitrogen shieldings of the nitroso groups concerned seem to follow an analogous, albeit reverse sequence. The polarity of the solvent employed, and possibly its hydrogen bond donor strength, seem to significantly enhance the magnetic shielding of the nitroso nitrogen nucleus (Table 1), by up to +21 ppm with respect to the solutions of (**I**) and (**II**) in cyclohexane, while the analogous, but opposite effect on the shieldings of the amino moieties of the nitrosoamines examined is up to about −16 ppm. The behavior of the nitroso nitrogen shieldings of the nitrosoamines, as a function of solvent effects, provides an independent indication of the delocalization of the lone pair electron of the amino moiety (Fig. 2), by analogy with our earlier study of nitrosobenzenes [6]. The *para*-methoxy derivative of nitrosobenzene shows a remarkable increase in the magnetic shielding of nitrogen with respect to that of nitrosobenzene; the methoxy substituent is a putative donor of π-electrons in delocalized π-electron systems, and as such should induce changes in the electronic structure of the nitroso group involved, in the direction of that represented by (**Ib**) in Fig. 2. Moreover, changes induced in the nitrogen shieldings of nitrosobenzenes by solvent polarity and solvent-to-solute hydrogen bonds

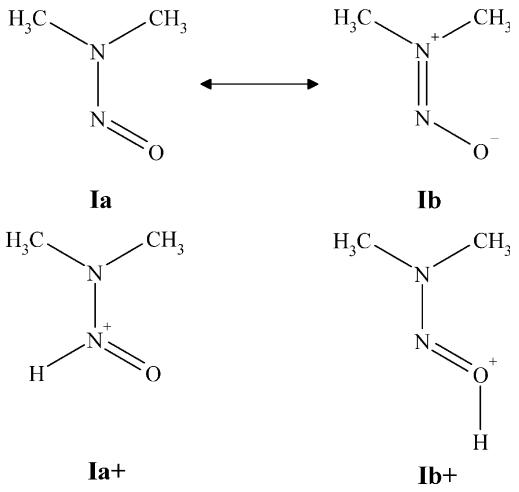


Fig. 2. Conventional representation of the electronic structure of (**I**) in terms of resonance structures (**Ia**) and (**Ib**). The significant barrier, ca. 92 kJ/mol (23 kcal/mol), to rotation about the N–N bond suggests an appreciable contribution of (**Ib**) to the actual structure. Cations (**Ia+**) and (**Ib+**) represent results of *N*-protonation and *O*-protonation, respectively, of nitrosamine (**I**).

match closely those reported here for the nitrosoamines (**I**) and (**II**).

The significant difference between the amino nitrogen shieldings of (**I**) and (**II**) in a given solvent, about 26 ppm (Table 1), is an example of the so-called β-effect of alkyl groups. It has already been established [1] that nitrogen magnetic shielding decreases significantly in the following sequence of alkyl substitution at a nitrogen atom for a given X residue

$$CH_3N(X) \rightarrow RCH_2N(X) \rightarrow R_2CHN(X) \rightarrow R_3CN(X)$$

where R is an alkyl group and X represents any atom or group of atoms. This is called the β-effect [1] as each step involves the introduction of a carbon atom to the β-position with respect to the nitrogen atom concerned, and produces a deshielding effect, $\Delta\sigma = -6$ to -13 ppm. In the present case, the replacement of the two methyl groups in (**I**) with two ethyl groups, which yields the structure of (**II**), produces a double β-effect and a concomitant deshielding of the amino nitrogen, ca. $\sigma = -26$ ppm, just within the range expected. Needless to say, such comparisons make sense only in the case of solutions in the same solvent.

A more detailed insight into the various site-specific and nonspecific contributions to the solvent induced variations of the amino nitrogen shieldings of (**I**) and (**II**) can be obtained by making use of the empirical scheme represented by [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 2 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 equation (1) for the compounds and the 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 b and d are not significant, but the s term (nitrogen shielding response to solvent polarity) is highly significant for both (**I**) and (**II**) and shows that the increasing polarity results in an appreciable deshielding

Table 2
Solvent parameters used and least-squares fitted solute parameters for a set of master equation (1)

Solvent	α	β	π^*	δ
Cyclohexane	0	0	0	0
Et_2O	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_2Cl_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_2O	1.13	0.18	1.09	0
CF_3CH_2OH	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 (dimension less)	Correlation coefficient r
(I)/NMe_2	+156.77	−3.35	+0.22	−11.34	−0.27	0.99
	±0.58	±0.50	±0.91	±0.84	±0.08	
(I)/NO	−164.15	+5.75	−2.43	+10.97	−0.33	0.98
	±1.17	±1.02	±1.84	±1.72	±0.16	
(II)/NE_2	+129.45	−3.15	+0.75	−9.27	−0.27	0.99
	±0.55	±0.48	±0.87	±0.81	±0.10	
(II)/NO	−163.83	+6.45	−3.77	+10.43	−0.34	0.98
	±1.10	±0.96	±1.74	±1.62	±0.16	

of the amino nitrogen nuclei. It is the only term that counts in the case of **(I)**, but for **(II)** there is some contribution of the term a (nitrogen shielding response to solvent-to-solute hydrogen bonding) which reveals that the increasing hydrogen bond donor strength of solvent produces a moderate deshielding effect on the amino nitrogen.

This is in accord with the picture of the increasing delocalization of the lone pair electrons of the amino nitrogen with the increasing polarity of the medium, and also with our analogous observations for pyrrole-type nitrogen atoms in azole ring systems [12–16]. Generally, in view of the fact that the values of π^* for the set of solvents employed span a range from 0 (cyclohexane) to 1.09 (water), the effects of solvent polarity on the nitrogen shielding of the amino nitrogen can reach a value of −12 ppm for compound **(I)** thus accounting for about 2/3 of the entire range of the solvent effects observed. There is also some additional deshielding effect of solvent-to-solute hydrogen bonding (see the a term in Table 2), up to about −5 ppm. This suggests the nitroso group in the nitrosamine concerned as the acceptor site for the hydrogen bonds; the hydrogen bondings seems to augment the delocalization of the lone pair electrons of the amino moiety. This point will be discussed further, in conjunction with DFT calculations.

The same applies to the nitrogen shieldings of the nitroso moieties of **(I)** and **(II)**, as can be reckoned from the corresponding a and s terms (Table 2), but in this case the increasing polarity and hydrogen bond donor strength of the solvent concerned enhance the magnetic shielding of nitrogen, by up to about +12 and +7 ppm, respectively. This also suggests a concomitant increase in the delocalization of the lone pair electrons of the amino moieties involved, but a question arises about the acceptor site(s) for hydrogen bonding. This problem will be solved in conjunction with the following discussion of ab initio calculations of the nitrogen shieldings.

Now, since the present work combined with our earlier studies on nitroso systems [1–7] provides a 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 DFT methods (Table 3). 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, 6-311++G**, for both the optimization and the nitrogen shieldings.There is a good linear relationship between the experimental data and the theoretical shieldings (Fig. 3), as expressed by the following equation which includes the relevant standard deviations of the linear fit

$$\sigma_{\text{exp.}} = [0.7953(\pm 0.0223)\sigma_{\text{calcd.}} + 122.38(\pm 11.83)] \pm 22.25 \text{ ppm} \quad (2)$$

Table 3
DFT calculations of nitrogen NMR shieldings of *C*-, *N*-, and *O*-nitroso systems

Compound	Experimental values of nitrogen shielding (ppm, dilute solutions in cyclohexane, ref. to neat nitromethane, bulk susceptibility corrected)	B3PW91/6-311++G** calculated nitrogen NMR shielding (ppm, referred to a bare nucleus)
CH_3NO_2	+9.50[a]	−138.90
$(CH_3)_3C$–NO	−590.86[b]	−902.94
Nitrosobenzene	−532.46[b]	−852.97
p-Nitrosoanisole	−499.69[b]	−783.95
$(CH_3)_2N$–NO		
(NO)	−164.08	−326.27
(Me_2N)	+156.49	+11.41
$(CH_3)_2N$–NH^+=O		
(NH=O)	–	−81.30
(Me_2N)	–	−2.60
$(CH_3)_2N$–N=OH^+		
(N=OH)	–	−249.17
(Me_2N)	–	−38.03
$(CH_3CH_2)_2N$–NO		
(NO)	−163.85	−332.57
(Et_2N)	+129.04	−18.36
$(CH_3)_3C$–O–NO	−201.77 (in *n*-hexane)[c]	−376.57

[a] Experimental data from our earlier work [5] obtained under the same experimental conditions as those employed in the present study.
[b] As above, Ref. [6].
[c] As above, Ref. [7].

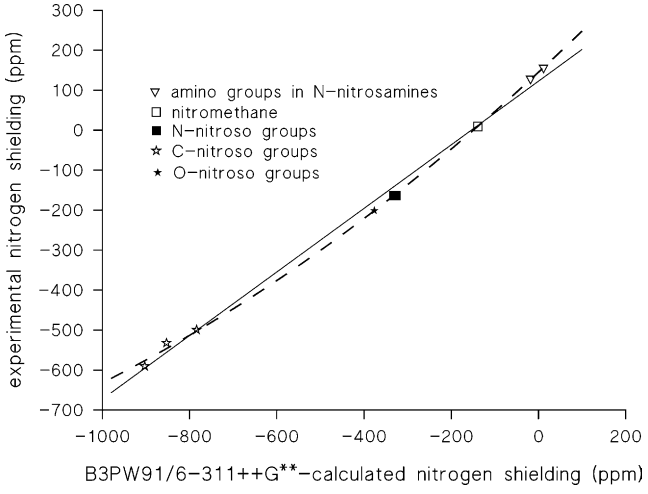


Fig. 3. A plot of experimental nitrogen shieldings, referenced to neat liquid nitromethane, against GIAO/B3PW91/6-311++G**//B3PW91/6-311++G** calculated absolute nitrogen shieldings for the nitrosamines (**I**) and (**II**) as well as for some examples of *C*- and *O*-nitroso groups. The relevant values of the shieldings are reported in Table 3, and the linear regression (solid straight line) concerned is represented by Eq. (2), while the parabolic regression (dashed curve) is represented by Eq. (3). The experimental shieldings, bulk susceptibilty corrected, are taken on dilute solutions in cyclohexane.

with a linear correlation coefficient $r = 0.998$. The slope coefficient of 0.7953 shows that the calculations systematically overestimate the magnitudes of the absolute shieldings, by about 20%, and the free term yields an estimate of the absolute shielding of the reference employed, neat liquid nitromethane, as about −122 ppm. The experimental nitrogen shieldings of the nitroso systems concerned in dilute solutions in cyclohexane (Table 5) cover a range of about 750, from −591 ppm for $(CH_3)_3C$–NO through +156 ppm for the amino moiety in nitrosamine (**I**) with respect to neat liquid nitromethane; thus, the standard deviation of the linear fit, ±22.25 ppm, amounts to only about 3% of the range of the shieldings concerned. The deviations of the datapoints from the linear regression appear to be random, at least at the 95% confidence level, as they pass the so-called sign test; there is no statistically significant preponderance of either plus or minus signs, and there is no significant clustering of like signs. Nevertheless, the slope (scaling) coefficient of 0.7953 deviates significantly from the ideal value of unity, in contrast with those obtained in our analogous studies on oxazole and oxadiazole ring systems [17] as well as on *C*-, *N*-, and *O*-nitro systems [8]; the latter were carried out under experimental conditions which were the same as those in the present work, and the same level of sophistication of DFT calculations was employed. This apparent discrepancy seems to stem out from the fact that the present calculations relate to magnetic shielding constants σ which span a very large range, that of about 750 ppm. A parabolic regression which yields Eq. (3)

$$\sigma_{\text{exp.}} = [2.2950(\pm 0.359) \times 10^{-4}\sigma^2_{\text{calcd.}} + 1.0064(\pm 0.0340)\sigma_{\text{calcd.}} + 145.04(\pm 5.77)] \pm 8.57 \text{ ppm} \quad (3)$$

shows a major improvement from the point of the standard deviation concerned; now, the latter amounts to only 1.1% of the range of shieldings considered. The sign test shows that the deviations are random, and the coefficient of $\sigma_{\text{calcd.}}$ becomes insignificantly different from the ideal value of unity which means that there is no systematical exaggeration or underestimation of the magnitudes of σ. This and the value of the free term, about $+145 \pm 6$ ppm, are in accord with our earlier results on experimental vs. computed nitrogen shieldings of other molecular systems [8,17] where the level of sophistication of DFT/ab initio calculations was the same as that employed presently. The meaning of the quadratic term in Eq. (3) is quite straightforward as the latter is independent of the sign of σ. The term represents a correction to the calculated value of σ, and if the latter is, e.g., −200 ppm (or +200 ppm), the correction amounts to about +9 ppm. The latter is just within the limits outlined by the overall standard deviation of the least squares fit which means that the correction is

insignificant within the range of −200 to +200 ppm for the nuclear magnetic shielding constants σ involved, where $\sigma = 0$ for a bare nucleus. This range of σ covers nitrogen NMR shieldings of a large majority of diamagnetic molecules and ions, while *C*-nitroso group shieldings fall far outside. Thus, the quadratic correction in Eq. (3) suggests that the DFT computations at the level employed in the present work systematically underestimate the nitrogen magnetic shielding as such (not the magnitude of σ), and that the effect becomes apparent only in the case of unusually large magnitudes of σ. A word of comment is required about nonlinear regressions like that represented by Eq. (3). The latter equation is correct if one tacitly assumes that the magnetic shielding constants σ are expressed in parts per million (ppm) as physical pseudo-units. Then the coefficient of σ^2 is in ppm^{-1}, that of σ is dimensionless, and the free term is in ppm. Actually, the σ constants are dimensionless numbers, ppm is simply a factor of 10^{-6} so that ppm^{-1} is a factor of 10^6, and ppm squared is a factor of 10^{-12}. Thus one can rewrite Eq. (3) using these factors in order to obtain its precise form, but the latter would be unwieldy to use.

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 relationship obtained, Eqs. (2) and (3), such a differentiation for solutions in cyclohexane seems to be small, particularly if we take into account the limitations effected by a finite basis set of wavefunctions and by the density functional theory (DFT) in accounting for electron correlation effects. Moreover, many subtle points of experimentally observed differences in the nitrogen shieldings are reproduced precisely by the computations. These include the increasing magnetic shielding in the following sequence: *C*- ≪ *O*- < *N*-nitroso groups, the difference in the nitrogen shielding between the amino groups in (**I**) and (**II**) which is a manifestation of the so-called β-effect, and the large differences between the shieldings of the nitroso and amino groups concerned.

In view of the foregoing relationship between the computed and experimental nitrogen shieldings, we endeavored to obtain a theoretical estimate of solvent-to-solute hydrogen-bonding effects on the nitrogen shielding of both amino and nitroso moieties of (**I**), using simple model structures (**Ia+**) and (**Ib+**) (Fig. 2) which are obtained from (**I**) by protonation of the nitroso nitrogen or oxygen atom, respectively. These can be considered as limiting stages of hydrogen bonding, involving a full proton transfer to the acceptor molecule. The results of the calculation are given in Tables 3 and 4, and show that both the *N*- and *O*-protonation produce in a significant decrease in the magnetic shielding of nitrogen in the NMe_2 moiety, and a significant increase in the case of NO. However, the NO/NMe_2 ratio of the effects computed for the *O*-protonation, −1.6, is vastly different from that for the *N*-protonation, −17.5. Now we turn to the experimental values for (**I**), from which effects of solvent-to-solute hydrogen bonding on the nitrogen shieldings are retrieved by means of Eq. (1); the analogous NO/NMe_2 ratio of effects on the shieldings of solvent-to-solute hydrogen bonding is given by the ratio of the corresponding solute terms *a* (Table 2), which amounts to −1.7. The latter value matches closely that computed for the *O*-protonation of (**I**), and shows that the oxygen atom of the nitroso moiety of (**I**) is the prime acceptor site for hydrogen bonds (Table 4).

The experimental as well as computational results obtained in the present work for the *N*-nitrosamines (**I**) and (**II**) fit neatly into a simple scheme which is shown in Fig. 4. The latter depicts the enhancement of the amino lone pair electron delocalization with the increasing polarity of solvent and hydrogen-bonding effects, and the concomitant response of the nitrogen shieldings of the amino and nitroso moieties involved; the structures remain planar as suggested by the computed and experimental geometries shown in Table 5. If we compare this with analogous results obtained for *N*-nitramines [8], some significant differences are revealed. Similar patterns are observed for solvent induced effects on the nitrogen shielding of the amino moieties in both

Table 4
Calculated gas phase protonation shifts of nitrogen shieldings of $(CH_3)_2N–N=O$ *versus* observed effects of hydrogen bonding

Protonation or hydrogen bonding acceptor site	Calcd. gas phase protonation shift of nitrogen shielding (ppm) [a]		Calcd. NO/NMe_2 nitrogen shielding shift ratio	Observed ratio of hydrogen-bonding effects on nitrogen shieldings[b]
	for N=O	for NMe_2		
Nitrogen in N=O	+194.8	−11.1	−17.5	
Oxygen in N=O	+62.9	−39.3	−1.6	−1.7

[a] These values are computed as differences between the calculated shieldings for the relevant ion and the neutral molecule (**I**) (Table 3), multiplied by the scaling factor of 0.7953 taken from Eq. (2).

[b] Calculated from the relevant *a* terms for NO and NMe_2 moieties of nitrosamine (**I**) (Table 2); the result fits neatly the ratio calculated for the *O*-protonation, thus pointing at the nitroso oxygen as the prime acceptor site for solvent-to-solute hydrogen bonds.

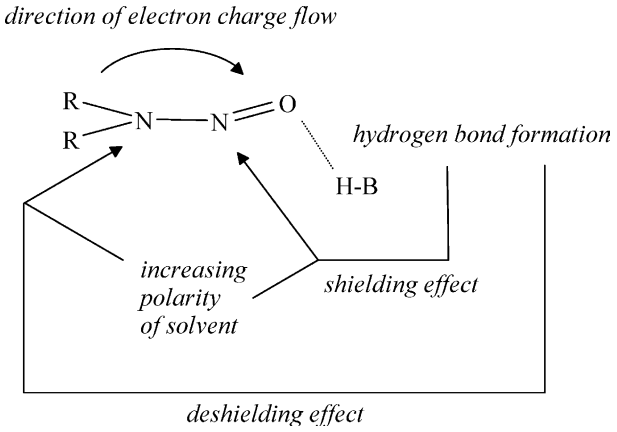


Fig. 4. A plausible explanation of the observed solvent effects on the nitrogen shieldings of nitrosamines (**I**) and (**II**) in terms of electron charge migration toward the nitroso moiety which is enhanced by solvent polarity as well as hydrogen bonding of the nitroso moiety as an acceptor site. The present study shows clearly that the nitroso oxygen atom is the prime acceptor site.

$R_2N–N=O$ and $R_2N–NO_2$, and this suggests enhanced delocalization of the lone pair electrons with the increasing polarity of the surrounding medium; however, the behavior of the nitro nitrogen shieldings of $R_2N–NO_2$ as well as relevant ab initio calculations indicate that the *N*-nitramine geometry changes gradually, from nonplanar, in nonpolar solvents, to planar, in strongly polar media [8].

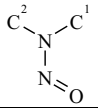
Generally, it seems that the density functional approach at the level of sophistication employed in the present work yields good results in confrontation with experimental nitrogen shieldings; this is corroborated by our earlier results [17] obtained for *N*-methylsydnone and all isomeric oxazoles and oxadiazoles. 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 DFT/ab initio theoretical values of the shieldings were obtained using a large basis set, for molecular geometries which were optimized using the same combination of density functional/basis 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.

A word of comment about the geometries of nitrosamines (**I**) and (**II**) is necessary here. Our calculations (Table 5) show a planar structure of the amino moieties in (**I**) and (**II**) (the latter is not reported in the table). This is in accord with gas-phase electron diffraction measurements for (**I**) [18] as well as with the relevant X-ray data in the solid state [19].

3. Experimental

The compounds studied experimentally, (**I**) and (**II**), were prepared by a published procedure [20]. Particular care was taken in the NMR measurements to use very pure and dry solvents as reported previously [2–7]. 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 Avance DRX-500 system (11.7 T) at 35 ± 0.2 °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

Table 5
Calculated and experimental geometries of dimethylnitrosamine (**I**)



Bond length (in pm)[a] or bond angle (°)	B3PW91/ 6-311++G** calcd. (present work)	Solid state, X-ray [19]	Gas phase, electron diffraction [18]
C^1N	144.3	146.1	146.0
C^2N	144.8	146.5	146.0
NN	133.3	132.0	134.4
NO	121.5	126.0	123.4
$\angle C^1NC^2$	120.6	120.0	123.2
C^1NN	123.2	122.6	120.4
$\angle C^2NN$	116.2	117.4	116.4
∠NNO	116.4	114.3	113.5

[a] In picometers (100 pm = 1 angstrem); the geometry was fully optimized, including hydrogen atoms, but results reported in the table relate only to the heavy atoms concerned. The optimized structure is planar, as indicated by the sum $\angle C^1NC^2 + \angle C^1NN + \angle C^2NN$ which amounts to 360°; the same holds for the experimental geometries concerned.

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 [1]. 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 [1], and since dilute solutions were used, their magnetic volume susceptibilities are assumed to be equal to those of the corresponding solvents at +35 °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 [1]. 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 concerned, 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. Typically, the spectral width was about 21 kHz, with a digital resolution of 5 Hz/point.

The DFT calculations were carried out using the Gaussian 94 (revision D.3) software package [21]. Both the full geometry optimization and the nitrogen shielding calculations were performed with a 6-311++G** basis set of wavefunctions using the density functional theory (DFT) with the hybrid B3PW31 functionals and the GIAO method (gauge included atomic orbitals) for computing the magnetic shieldings concerned. Thus, the method can be described, in a shorthand notation, as GIAO/B3PW91/6-311++G**//B3PW91/6-311++G**. The large set of wavefunctions employed uses both diffuse and polar functions on hydrogen and the heavy atoms concerned and appears to be a satisfactory choice for polar molecules containing lone pairs of electrons, and particularly those containing direct nitrogen–oxygen and nitrogen–nitrogen bonds.

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