ELSEVIER

Hydrogen-bond and solvent polarity effects on the nitrogen NMR shielding of urea systems

Michal Witanowski[a], Wanda Sicinska[a], Zenobia Biedrzycka[a], Graham A. Webb[b,*]

[a]*Institute of Organic Chemistry, Polish Academy of Sciences, 01-224, Warsaw, Poland*
[b]*Department of Chemistry, University of Surrey, Guildford, Surrey, GU2 5XH, UK*

Abstract

High precision ^{14}N NMR measurements of the nitrogen shieldings of tetramethylurea, **1**, and urea, **2**, are reported for dilute solutions in a set of solvents which represent a wide spectrum of properties from the point of view of hydrogen-bonding and solvent polarity/polarisability. It is shown that solvent induced nitrogen shielding changes are appreciable and can be attributed to solute-to-solvent, solvent-to-solute hydrogen-bonding and solvent polarity effects. All of these interactions produce deshielding of the nitrogen nuclei of **1** and **2**. This is in accord with an enhanced delocalisation of the nitrogen lone-pair electrons into the π systems of **1** and **2** due to the solute–solvent interactions. GIAO-CHF ab Initio molecular orbital calculations, using a 6-31^{++}G** basis set, are reported for the nitrogen shieldings of the isolated molecules **1** and **2**. These reproduce quite well the position of the urea nitrogen resonance obtained in a dilute solution in cyclohexane, with respect to some model compounds which include amino and amido moieties. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Nitrogen Shieldings; Urea; Tetramethylurea; Hydrogen-bonding; Solvent polarity effects

1. Introduction

We have previously shown that solvent effects on nitrogen NMR shieldings (chemical shifts) can both be large and provide an insight into solute–solvent interactions arising from solvent polarity and hydrogen-bonding influences. Our earlier work has involved nitrogen NMR measurements on triply bonded nitrogen atoms, such as those found in cyano and isocyano groups [1, 2] and doubly bonded nitrogen in a variety of imino-like C=N moieties [3–5] including those found in nitrogenous aromatic heterocycles, such as azines [6, 7] and azoles [8–13], covalent isocyanates [14], azides [15], cyanides [16], nitro compounds [17, 18] and nitroso compounds [19, 20].

We propose to extend our studies to include nitrogen atoms in amido-like moieties, starting with the symmetrical structures of tetramethylurea, **1**, and urea, **2**, shown in Fig. 1. In these compounds the dipole moment lies along the C_{2v} axis containing the carbonyl group. The electronic structures of such systems can be depicted in terms of the conventional resonance structures given in Fig. 2. These show some delocalisation of the nitrogen lone-pair electrons to the carbonyl group resulting in some partial double bond character of the C–N bond. Evidence for this proposal is provided by ^{13}C NMR data [21] which shows that there is hindered rotation about the C–N bond in **1**.

Due to steric hindrance there is a degree of
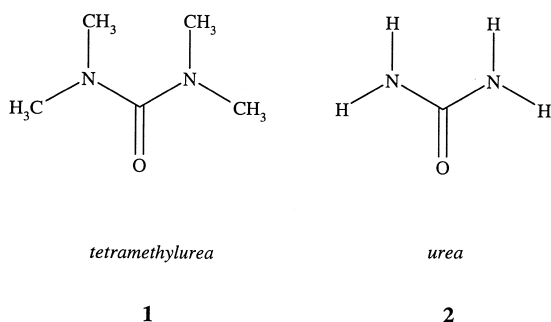
* Corresponding author.

Fig. 1. Structures of the Compounds studied, **1** and **2**.

non-planarity in the structure of compound **1**, as indicated by X-ray measurements [22], electron diffraction data [23], photoelectron spectroscopy and semi-empirical MNDO calculations [24] and ab initio molecular orbital calculations [25]. Analogous results are obtained in the present work using ab initio molecular orbital calculations at the Hartree–Fock level with a 6-31^{++}G** basis set. The same basis set is used to calculate the nitrogen NMR shieldings by the GIAO-CHF procedure, described in Section 3, the results of which are given in Table 1. The electron delocalisation from the nitrogen atom, as shown in Fig. 2, is expected to result in a deshielding of the nitrogen nuclei involved [27].

Some possible solute–solvent interactions for compound **2** are shown in Fig. 3. We expect that the extent of the nitrogen lone-pair delocalisation should be enhanced by three solvent related factors. These

are an increase in solvent polarity, solute-to-solvent hydrogen-bond formation by the NH moieties of urea, and solvent-to-solute hydrogen-bonding involving the urea carbonyl group. All, or any, of these interactions is expected to result in an increase in the extent of the nitrogen deshielding, as witnessed by its NMR spectrum. In compound **1** the solute to solvent hydrogen-bonding, of which compound **2** is capable, will be absent since compound **1** does not have any NH moieties. Hence solvent effects on the nitrogen shielding of **1** are expected to be smaller than those observed for **2**.

As in our previous publications [1–20, 27] we use the expression ''Nitrogen NMR Shielding'' rather than ''Nitrogen Chemical Shift''. Hence we employ a sign convention for the nitrogen shielding data which has a positive sign to denote an increase in the shielding. This is opposite to that used with the chemical shift scale.

2. Results and discussion

High precision ^{14}N NMR measurements of the nitrogen shieldings of compounds **1** and **2** are reported in Table 2 for solutions in a variety of solvents.

Unfortunately, due to poor solubility, it was not possible to perform NMR measurements on **2** in the full range of solvents. The set of solvents chosen represent a large number of properties regarding hydrogen-bond formation and polarity/polarisability.
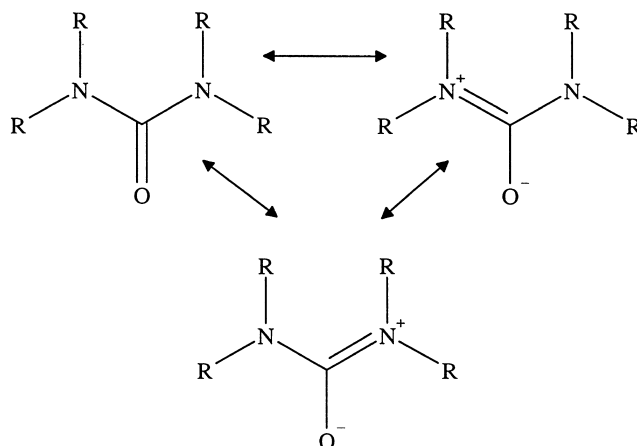

Fig. 2. Conventional representation of the electronic structure of urea systems in terms of resonance structures.
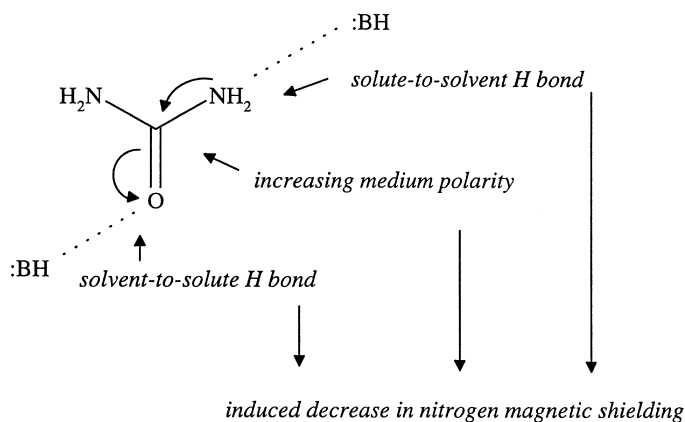
Fig. 3. Possible contribtions of solvent effects to the nitrogen nuclear shielding of urea systems. Such contributions are observed in the present work.

Section 3 contains details of the methods used to produce the results given in Table 2. The NMR shielding data are corrected for bulk susceptibility effects and have a precision such that the final digit given is uncertain.

We use the empirical scheme represented by the master Eq. (1) in order to separate the various specific and non-specific contributions to the solvent induced nitrogen shielding variations [28, 29].

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

$$+ d(i)\delta(j)] \tag{1}$$

In Eq. (1) i and j represent the solute and solvent

respectively a gives the hydrogen-bond donor strength of the solvent, β is the solvent hydrogen-bond acceptor strength, π^* is the solvent polarity/polarisability, and δ is a correction for polychlorinated solvents ($\delta = 0.5$) and aromatic solvents ($\delta = 1$). The solute terms a, b, s and d give the corresponding response of the solute nitrogen shielding to a given solvent property. The symbol σ_0 represents the nitrogen shielding for the solute in a cyclohexane solution taken as a reference state.

Table 3 contains a list of the solvent parameters, used in conjunction with Eq. (1), and the least-squares fitted solute parameters for a set of master equations. As shown in Table 3 the values obtained for the

Table 1

Experimental and ab intio calculated magnetic shielding of nitrogen in urea systems and in some model compounds and reference substances

Compound	Experimental NMR shielding of nitrogen for dilute solutions in cyclohexane, ref. to neat liquid nitromethane (ppm)	CHF/GIAO calcd. absolute shielding, 6-31^{++}G** basis set, optimized geometries (present work)
Tetramethylurea (**1**)	+ 319.60[a]	+ 219.0
Urea (**2**)	+ 317[b]	+ 211.9
Ammonia	+ 386.7 (in Me$_4$C)[c]	+ 267.8
Aniline	+ 328.60[a]	+ 229.8
N,N-Dimethylformamide	+ 282.90[a]	+ 197.0
Acetonitrile	+ 125.81[a]	+ 6.8
Nitromethane	+ 9.05[a]	− 159.9

[a] Experimental data from the present work obtained under the same experimental conditions as used for compounds **1** and **2**.

[b] Compound is virtually insoluble in cyclohexane, but Eq. (1) yields this estimate as a result of analysis of the experimental data for polar solvents, Table 2.

[c] Data from ref. [26], and references cited therein.

Table 2
Solvent effects on the nitrogen NMR shieldings of urea systems

| Solvent | Nitrogen NMR shielding (ppm) referred to neat liquid nitromethane[a] | |
	1	2
Cyclohexane	+ 319.60	–[b]
CCl$_4$	+ 318.57	–[b]
Et$_2$O (+ 30°C)	+ 319.59	–[b]
Benzene	+ 318.70	–[b]
Dioxane	+ 318.58	–[b]
Acetone	+ 318.26	+ 307.84
DMSO	+ 317.28	+ 304.09
CH$_2$Cl$_2$	+ 317.16	+ 307.60
CHCl$_3$	+ 316.10	+ 306.55
EtOH	+ 315.97	+ 305.39
MeOH	+ 315.22	+ 307.42
CF$_3$CH$_2$OH	+ 313.80	+ 306.77
H$_2$O	+ 312.26	+ 303.17

[a] All data are corrected for bulk susceptibility effects and related to 0.01 M solutions at + 35 ± 0.2°C.
[b] Compound is insoluble in the solvent concerned.

parameter d are insignificant for both compounds studied. For compound **1** the most significant terms are a and s, which are both negative in sign indicating a decrease in nitrogen nuclear shielding with an increase in solute to solvent hydrogen-bond formation and with an increase in solvent polarity/polarisability.

The b term, which represents the nitrogen shielding response to solvent to solute hydrogen-bond formation, is insignificant. This is expected since compound **1** does not contain any NH moieties. Hence the analysis of the observed nitrogen shielding results for compound **1** in a variety of solvents is in accord with the intuitive predictions presented in Fig. 3

For compound **2**, urea, the nitrogen shielding data are limited by its lack of solubility in some of the chosen solvents. However, although the results given in Table 3 are less precise for compound **2** they are still significant. The a, b and s terms are significant and negative in sign. This shows that the formation of both solute to solvent and solvent to solute hydrogen-bonds and solvent polarity/polarisability effects all produce nitrogen deshielding as depicted in Fig. 3. The results given in Table 3 for compound **2** allow us to estimate the unmeasurable nitrogen shielding of urea in cyclohexane. For this we obtain a value of 317 ppm. Thus the overall range of

Table 3
Solvent parameters used and least-squares fitted solute parameters for a set of master equations Eq. (1)

Solvent	α	β	π^*	δ	Dielectric constant[a]
Cyclohexane	0	0	0	0	1.87
Et$_2$O	0	0.47	0.27	0	3.89
CCl$_4$	0	0	0.29	0.5	2.21
benzene	0	0.10	0.59	1	2.25
Dioxane	0	0.37	0.55	0	2.19
Acetone	0.07	0.48	0.72	0	19.75
DMSO	0	0.76	1.00	0	45.80
CH$_2$C$_{12}$	0.22	0	0.80	0.5	8.54
CHCl$_3$	0.34	0	0.76	0.5	4.55
EtOH	0.86	0.77	0.54	0	24.20
MeOH	0.98	0.62	0.60	0	30.71
H$_2$O	1.13	0.18	1.09	0	76.70
CF$_3$CH$_2$OH	1.51	0	0.73	0	–

Compound	σ_0 (ppm)	a (ppm/unit scale)	b (ppm/unit scale)	s (ppm/unit scale)	d (ppm/unit scale)	Correlation coefficent r
1	+319.8 ± 0.4	−3.1 ± 0.4	−0.8 ± 0.7	−3.1 ± 0.6	−0.1 ± 0.2	0.98
2	+317 ± 3	−2 ± 1	−5 ± 2	−9 ± 2	+0.4 ± 0.3	0.93

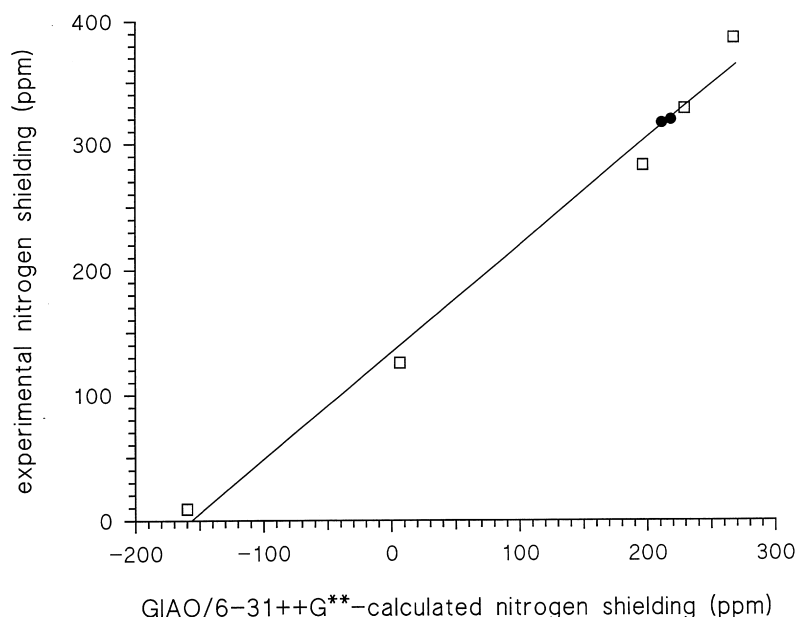[a] The constants were recalculated for a temperature of 35°C from the data available in ref. [30].

Fig. 4. A plot of the experimental and GIAO-CHF calculated (Table 1) nitrogen shieldingsof urea systems and some model molecules. The relevant linear correlation is expressed by Eq. (2).

solvent effects on the nitrogen shielding for compound **1** is about 7 ppm and about 14 ppm for compound **2.** This difference arises from the fact that in the case of **2** there is an additional influence of hydrogen-bonding between the solute NH moieties and solvent acceptor centres, which is absent for compound **1**.

Hence the overall picture of solvent effects on the nitrogen shieldings of compounds **1** and **2** is in good accord with the enhancement of lone-pair electron delocalisation due to solvent polarity/polarisability, solute-to-solvent and solvent-to-solute hydrogen-bond formation.

Table 1 contains the results of some GIAO-CHF ab initio molecular orbital calculations of the nitrogen shieldings for the ureas studied here and for some model compounds and reference substances. We note that the ab initio calculated nitrogen shieldings are compared with the measured nitrogen shieldings for these compounds in cyclohexane as an inert solvent. The relationship between the calculated and observed nitrogen shielding data (Fig. 4) is given by Eq. (2), the corresponding linear correlation coefficient is 0.995 and the standard deviation is about 4% of the range of nitrogen

shieldings considered.

$$\sigma_{\text{exp}} = (0.8556\sigma_{\text{calc}} + 133.95) \pm 16.0 \text{ ppm} \qquad (2)$$

The ab initio GIAO-CHF nuclear shielding calculations reproduce neatly the position of the nitrogen shieldings of compounds **1** and **2** with respect to amido and amino nitrogen moieties. The nitrogen atoms of **1** and **2** are more shielded than the former and less shielded than the latter. From the slope we deduce that the calculations systematically exagerate the magnitude of the observed shieldings by about 15%.

3. Experimental

The compounds studied are commercially available. Very pure and dry solvents were used in the NMR measurements as previously reported [1–20]. A dry argon atmosphere, in glove boxes, was used for the solution preparations. The ^{14}N shielding measurements were taken on a Bruker AM500 spectrometer operating at 36.14 MHz and a temperature of $35 \pm 0.2°$C maintained by a VT unit. Random and systematic errors were reduced to less than 0.1 ppm for the solute nitrogen shieldings in different solvents.

External neat liquid nitromethane was used as a reference by means of 10 mm/4 mm o.d. coaxial tubes. A solution of 0.3 M nitromethane in acetone-d_6 was placed in the inner tube; this has a nitrogen shielding of + 0.77 ppm from that of neat liquid nitromethane [27]. This value is obtained from measurements using concentric sherical sample/reference containers in order to eliminate bulk susceptibility effects. Consequently the contents of the inner tube act both as a reference, with respect to neat nitromethane as standard, and as a deuterium lock for the NMR spectrometer. The exact resonance frequency of the ^{14}N signal of neat nitromethane is 36.141524 MHz, from which a value of 36.136826 MHz is obtained for the bare nitrogen nucleus [27]. This value is employed in conjuction 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 the external standard and of the samples used. Dilute solutions were used in the present investigation, hence their susceptibilities are assumed to be equal to those of the corresponding solvent at 35°C.

The GIAO-CHF ab initio nitrogen shielding calculations were performed on a Pentium-S (200MHz) based system using the Gaussian 94 suite of programs [31].

The 6-31^{++}G** basis set was used for both the geometry optimisation and nitrogen shielding calculations.This basis set employs both polar and diffuse functions on hydrogen and the heavy atoms and appears to be a satisfactory choice for polar molecules containing lone-pairs of electrons.

References

[1] M. Witanowski, W. Sicinska, G.A. Webb, Mag. Res. Chem. 27 (1989) 380.

[2] M. Witanowski, W. Sicinska, G.A. Webb, Mag. Res. Chem. 30 (1992) 169.

[3] M. Witanowski, W. Sicinska, G.A. Webb, Spectroscopy Int. J. 10 (1992) 25.

[4] M. Witanowski, Z. Biedrzycka, W. Sicinska and G.A. Webb, J. Chem. Soc Perkin II (1997) 533.

[5] M. Witanowski, W. Sicinska, Z. Biedrzycka, Z. Grabowski, G.A. Webb, J. Mol. Struct. 404 (1997) 267.

[6] M. Witanowski, W. Sicinska, S. Biernat, G.A. Webb, J. Magn. Res. 91 (1991) 289.

[7] M. Witanowski, Z. Biedrzycka, W. Sicinska, Z. Grabowski, G.A. Webb, J. Magn. Res. (A) 124 (1997) 127.

[8] M. Witanowski, W. Sicinska, Z. Grabowski, G.A. Webb, Mag. Res. Chem. 28 (1990) 988.

[9] M. Witanowski, W. Sicinska, Z. Grabowski, G.A. Webb, J. Magn. Res. (A) 104 (1993) 310.

[10] M. Witanowski, W. Sicinska, Z. Biedrzycka, G.A. Webb, J. Magn. Res. (A) 109 (1994) 177.

[11] M. Witanowski, W. Sicinska, Z. Biedrzycka, Z. Grabowski, G.A. Webb, J. Magn. Res. (A) 112 (1995) 66.

[12] M. Witanowski, Z. Biedrzycka, W. Sicinska, Z. Grabowski, G.A. Webb, J. Magn. Res. (A) 120 (1996) 148.

[13] M. Witanowski, W. Sicinska, Z. Biedrzycka, Z. Grabowski, G.A. Webb, J. Chem. Soc., Perkin II (1996) 619.

[14] M. Witanowski, Z. Biedrzycka, W. Sicinska, G.A. Webb, J. Mol. Struct. 328 (1995) 253.

[15] M. Witanowski, W. Sicinska, G.A. Webb, Spectroscopy Int. J. 12 (1994) 25.

[16] M. Witanowski, W. Sicinska, Z. Biedrzycka, G.A. Webb, J. Mol. Struct. 380 (1996) 133.

[17] M. Witanowski, W. Sicinska, S. Biernat, Spectroscopy Int. J. 7 (1989) 305.

[18] M. Witanowski, W. Sicinska, Z. Biedrzycka, G.A. Webb, Mag. Res. Chem. 31 (1993) 916.

[19] M. Witanowski, Z. Biedrzycka, G.A. Webb, Mag. Res. Chem. 34 (1996) 233.

[20] M. Witanowski, Z. Biedrzycka, W. Sicinska, G.A. Webb, Mag. Res. Chem. 35 (1997) 262.

[21] F.A.L. Anet, M. Ghiaci, J. Amer. Chem. Soc. 101 (1979) 6857.

[22] C.S. Frampton, K.E.B. Parkes, Acta Cryst. C52 (1996) 3246.

[23] L. Fernholt, S. Samdal, R. Seip, J. Mol. Struct. 72 (1981) 217.

[24] L. Treschanke, P. Rademacher, J. Mol. Struct. 131 (1985) 61.

[25] T. Strassner, J. Mol. Modeling (Electronic Publication) 2 (1996) 217.

[26] M. Witanowski, L. Stefaniak, G.A. Webb, in:Ann. Rep. NMR Spectuosc., Vol. 7, Academic Press, London, 1977.

[27] M. Witanowski, L. Stefaniak, G.A. Webb, in: G.A. Webb (Ed.), Ann. Rep. NMR Spectrosc., Vol. 25, Academic Press, London, 1993.

[28] M.H. Abraham, P.L. Grellier, J.L.M. Abboud, R.M. Doherty, R.W. Taft, Cart. J. Chem. 66 (1988) 2673.

[29] Y. Marcus, Chem. Soc. Rev. (1993) 409.

[30] R.C. Weast (Ed.), Handbook of Chemistry and Physics, 64th edn., p E-49, Chemical Rubber Co., Cleveland OH, 1984.

[31] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.P. Cheeseman, T. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V.G. Zakrzewski, J.V. Ortiz, J.B. Foreman, J. Cioslowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, M.W. Wong, J.L. Andres, E.S. Replogle, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. Defrees, J. Baker, J.P. Stewart, M. Head-Gordon, C. Gonzalez, J.A. Pople, Gaussian, Inc., Pittsburgh PA, 1995.