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Nitrogen NMR shieldings of thiourea systems as a function of solvent polarity and hydrogen bond effects

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Abstract

Tetramethylthiourea, **1**, and thiourea, **2**, have been studied in a wide variety of solvents by high-precision ^{14}N NMR measurements. The chosen solvents exhibit a wide range of hydrogen-bonding and polarity/polarisability properties. The observed nitrogen shielding variations of the solutes, due to solvent change, are significant and are attributed to solvent polarity, solute to solvent and solvent to solute hydrogen-bonding effects. Nitrogen deshielding of **1** and **2** is produced by all these interactions, due to an enhanced delocalisation of the nitrogen lone-pair electron into the π systems of **1** and **2**. The nitrogen NMR shieldings of **1** and **2** are calculated by the CHF–GIAO ab initio molecular orbital procedure using a $6\text{-}31^{++}G^{**}$ basis set. The calculations are for isolated molecules, and their results satisfactorily reproduce the position of the thiourea nitrogen resonance obtained in a dilute solution in cyclohexane with respect to that of urea systems and nitromethane. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Thiourea systems; Hydrogen-bonding; Solvent polarity; ^{14}N NMR; Ab initio molecular orbital calculations

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1. Introduction

In our earlier work, we have reported that solvent effects on NMR shieldings (Chemical Shifts) can produce an insight into the nature of solute–solvent interactions. Such interactions may be produced by hydrogen-bonding and solvent polarity effects. Previously we have investigated, by means of nitrogen NMR, various types of bonding involving nitrogen atoms. We have measured the NMR spectra of triply-bonded nitrogen atoms, such as those found in cyano and isocyano compounds [1,2], and doubly-bonded nitrogen atoms in various imino-like –C=N moieties [3–5], as well as those found in nitrogenous aromatic heterocycles such as azines [6,7] and azoles [8–14], covalent isocyanates [15], azides [16], cyanates [17], nitro groups [18,19] and nitroso compounds [20,21]. In addition we have studied the effects of solute–solvent interactions on the nitrogen NMR shielding of urea systems [22].

The purpose of the present study is to extend our investigations to include tetramethylthiourea, **1**, and thiourea, **2**, as shown in Fig. 1. As in the case of urea [22], the dipole moments in **1** and **2** lie along the C_{2v} axis which also contains the –C=S group. As shown in Fig. 2 the electronic structures of these molecules can be depicted by means of conventional resonance structures. Such structures show some partial double bond character of the C–N bond due to delocalisation of the nitrogen lone-pair electrons to the –C=S group. Support for this suggestion is provided by means of

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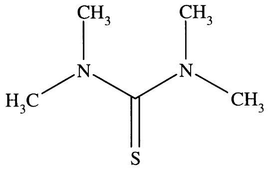

tetramethylthiourea *thiourea*

1 **2**

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

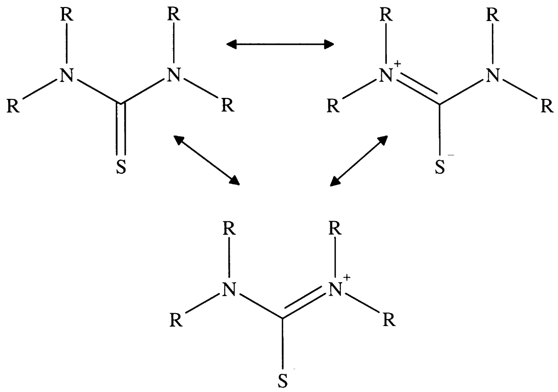

Fig. 2. Resonance structures for a conventional representation of the electronic structure of thiourea systems.

some ^{13}C NMR data for **1** [23], which give an estimate of about 6 kcal/mol for the C–N rotation barrier. Similarly, for **2** the barrier is estimated to be about 14 kcal/mol from a ^{1}H NMR study [24].

The structure of **1** is non-planar due to steric hindrance. It has a shallow pyramidal configuration at the nitrogen atom [25], as shown by electron diffraction measurements in the gas phase, and X-ray data for the solid state. In contrast, **2** is planar in the solid phase but microwave measurements reveal it to be non-planar in the gas phase [25]. Similar conclusions are reached in the present work using ab initio molecular orbital calculations at the Hartree–Fock level with a 6-31^{++}G** basis set on an isolated molecule of **1** and of **2**. We use the same basis set to calculate the nitrogen NMR shieldings, which are reported in Table 1 as a result of some CHF–GIAO calculations.

As shown in Fig. 2, electron delocalisation from the nitrogen atoms in **1** and **2** to the π system is predicted to take place, which is expected to result in a deshielding of the nitrogen nuclei [26,27].

As regards the possibility of hydrogen-bonding interactions, some ab initio molecular orbital calculations at the MP2/6-31G*/HF/6-31G* level on the interaction of **1** with a water molecule show that only the sulphur atom of **1** is involved in hydrogen-bonding [28]. It is reported that this hydrogen bonding results in a greater electron density at the sulphur atom. Consequently, the charge separated structures given in Fig. 2 are favoured. This electronic rearrangement should result in a deshielding of the nitrogen nuclei in **1**.

As far as the solute to solvent hydrogen-bond interactions are concerned, we take compound **2** as an example, as shown in Fig. 3. In this case the presence of $-NH_2$ groups provides an additional opportunity for hydrogen bonding, as the $-NH_2$ groups can act

Table 1
Experimental and ab initio calculated magnetic shielding of nitrogen in thiourea systems and in some reference substances

Compound	Experimental NMR shielding of nitrogen for dilute solutions in cyclohexane, reference to neat liquid nitromethane (ppm)	CHF/GIAO calcd. Absolute shielding, 6-31^{++}G** basis set, optimised geometries (present work)
Tetramethylthiourea (1)	+290.06	+189.5
Thiourea (2)	+285[a]	+183.9
Tetramethylurea	+319.60[b]	+219.0
Urea	+317[a,b]	+211.9
Nitromethane	+9.05[b]	−159.9

[a] 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 for thiourea, and Ref. [22] for urea.

[b] Data from our earlier work, Ref. [22], obtained under the same experimental conditions as those for compounds **1** and **2**.

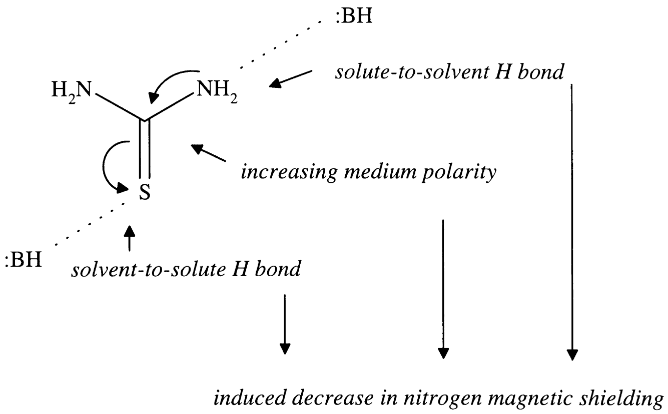

Fig. 3. The observed contributions of solvent effects to the nitrogen nuclear shielding of thiourea systems.

as hydrogen-bond donors to basic centres in the solvent molecules. Thus, in the case of compound **2** there are three solvent related factors, which enhance the degree of nitrogen lone-pair delocalisation. Namely, solute to solvent hydrogen bond formation by the $-NH_2$ moieties, solvent to solute hydrogen bonding involving the $-C{=}S$ group and an increase in solvent polarity. All of these interactions are expected to result in an increase in the extent of nitrogen deshielding. Clearly in the case of compound **1** solute to solvent hydrogen bonding is absent as this compound does not contain any $-NH_2$ moieties.

We use the expression “Nitrogen NMR Shielding” rather than “Nitrogen Chemical Shift”, as in our previous investigations [1–22,26,27]. Consequently, we employ a positive sign to denote an increase in shielding which is opposite to that used with the chemical shift scale.

2. Results and discussion

Table 2 contains the results of some high precision ^{14}N NMR measurements of the nitrogen shieldings of compounds **1** and **2** in a variety of solvents. The set of solvents chosen exhibits a large range of polarity/polarisability, and hydrogen-bond formation properties. Due to poor solubility it was, unfortunately, not possible to perform NMR measurements on **2** in the full set of solvents employed in this study. The results given in Table 2 were obtained by the methods described in Section 3. The NMR data given are corrected for solvent bulk susceptibility effects and are quoted with a precision such that only the final digit given is uncertain.

The range of solvent effects observed for the nitrogen nuclear shielding of **1**, in the full set of solvents employed, is about 11 ppm. For compound **2** the range of solvents used is incomplete, but if we extrapolate the experimental data to include a cyclohexane solution (Table 1) the range of solvent effects on the nitrogen shielding is comparable to that observed for **1**. This is in sharp contrast with the conclusions based upon solutions of both **1** and **2** in two polar solvents, namely DMSO and pyridine [29]. The solutions used were 2 M and the results were not corrected for bulk susceptibility effects [29].

In order to separate the various specific and non-specific contributions to the solvent-induced nitrogen shielding variations, we use the master Eq. (1) [30,31]

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

where i and j represent the solute and solvent, respectively, α 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 ($\delta = 0.5$) 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 $\sigma_0(i)$ represents the nitrogen shielding for

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

Solvent	Nitrogen NMR shielding (ppm) referred to neat liquid nitromethane[a]	
	1	**2**
Cyclohexane	+290.06	–[b]
CCl_4	+288.43	–[b]
Et_2O (+30°C)	+289.66	+278.02
Benzene	+288.69	–[b]
Dioxane	+288.06	+280.45
Acetone	+286.99	+278.06
DMSO	+284.45	+272.16
CH_2Cl_2	+285.71	+279.51
$CHCl_3$	+285.01	+278.58
EtOH	+285.29	+275.02
MeOH	+284.83	+276.36
H_2O	+279.92	+272.06
CF_3CH_2OH	+278.73	+277.92

[a] All data are corrected for bulk susceptibility effects and related to 0.05 M solutions at +35 ± 0.2°C.

[b] Compound is insoluble in the solvent concerned.

the solute in a cyclohexane solution taken as a reference state.

Table 3 contains a list of 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 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 solvent to solute hydrogen bond formation and an increase in solvent polarity/polarisability.

The **b** term, which represents the nitrogen shielding response of solute to solvent hydrogen bond formation, is found to be fairly small for compound **1**. This probably represents some interaction of the methyl groups of **1** with the solvents employed. Hence, the analysis of the observed nitrogen shielding results for compound **1** in a variety of solvents is in accordance with the intuitive predictions presented in Fig. 3. This is comparable to the results obtained earlier on urea systems [22].

For compound **2** (thiourea), the nitrogen shielding data are limited because of its lack of solubility in some of the chosen solvents. However, although the results given in Table 2 are less precise for compound **2**, they remain significant. All of the **a**, **b** and **s** terms are significant and negative in sign. This shows that the formation of both the solute to solvent and solvent to solute hydrogen bonds and solvent polarity/polarisability effects all produce nitrogen deshielding as shown in Fig. 3. Thus, the overall view of the solvent effects on the nitrogen shieldings of compounds **1** and

Table 3
Solvent parameters used and least-squares fitted solute parameters for a set of master equations [1]

Solvent	α	β	π^*	δ	Dielectric constant[a]	
Cyclohexane	0	0	0	0	1.87	
Et_2O	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_2Cl_2	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_2O	1.13	0.18	1.09	0	76.70	
CF_3CH_2OH	1.51	0	0.73	0	–	
Compound	σ_0 (ppm)	a (ppm/unit scale)	b (ppm/unit scale)	s (ppm/unit scale)	d (dimensionless)	Correlation coefficient, r
1	+ 290.1 ± 0.6	− 3.8 ± 0.5	+ 2.5 ± 0.9	− 6.3 ± 0.8	− 0.3 ± 0.1	0.98
2	+ 285 ± 3	− 2 ± 1	− 5 ± 3	− 8 ± 3	− 0.2 ± 0.6	0.89

[a] The constants were recalculated for a temperature of 35°C from the data available in Ref. [32].

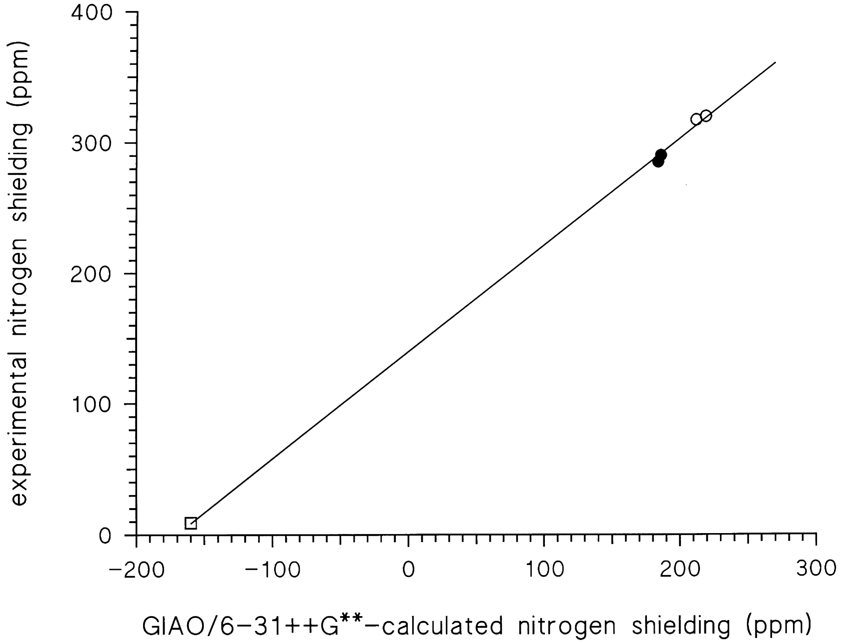

Fig. 4. A plot of the experimental and CHF–GIAO calculated (Table 1) nitrogen shieldings of thiourea systems (●), urea systems (○) and nitromethane (□). The linear correlation is expressed by Eq. (2).

2 is in good agreement with the enhancement of lone-pair electron delocalisation due to solvent polarity/polarisability, solute to solvent and solvent to solute hydrogen bond formation.

The results of some CHF–GIAO ab initio molecular orbital calculations of the nitrogen shieldings for the thioureas studied here and for the corresponding ureas and nitromethane as reference standard are given in Table 1. 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 0.9997 and the standard deviation is given by

$$\sigma_{\mathrm{exp}} = (0.8178\sigma_{\mathrm{calc}} + 139.34) + 3.9\ \mathrm{ppm} \qquad (2)$$

about 1% of the range of nitrogen shieldings considered.

From the slope given by Eq. (2), we deduce that the calculations systematically exaggerate the magnitude of the observed shieldings by about 18%.

We note from Fig. 4 that not only are the nitrogen shielding differences between the urea and thiourea systems well reproduced by the calculations reported in the present work, but also the subtle shielding variations between the urea and thiourea bases and their tetramethyl derivatives accounted for.

3. Experimental

The compounds studied are commercially available. Very pure and dry solvents were used in the NMR measurements as previously reported [1–22]. A dry argon atmosphere, in glove boxes, was used for the solution preparations. The ^{14}N shielding measurements were taken on a Bruker AVANCE 500 spectrometer operating at 36.14 MHz and maintained at a temperature of 35 + 0.2°C 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 [26,27]. This value is obtained from measurements made using concentric spherical 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 [26,27]. This value is employed in conjunction with the relevant resonance frequency differences to calculate the nitrogen shieldings relative to that of neat nitromethane.

We employed Lorentzian lineshape fitting of the ^{14}N signals to produce precise values for the resonance frequencies of the external standard and of the samples used. Dilute solutions were used in the present investigation. Consequently, their susceptibilities were assumed to be equal to those of the corresponding solvents at 35°C.

The CHF–GIAO ab initio nitrogen shielding calculations were performed on a Pentium-S (200 MHz) based system using the GAUSSIAN 94 suite of programs [33] The 6-31^{++}G** basis set was used for both the geometry optimisation and nitrogen shielding calculations. This basis set employed both the polar and diffuse functions on hydrogen and the heavy atoms, and appears to be a satisfactory choice for polar molecules containing lone-pair of electrons.

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