PERKIN 2

Solvent induced variations in nitrogen NMR shieldings of some oxime systems as a test of the Solvaton model of non-specific molecular interactions

Michal Witanowski,[a] **Zenobia Biedrzycka,**[a] **Wanda Sicinska**[a] **and 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, UK GU2 5XH*

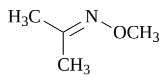
High precision ^{14}N NMR measurements are reported for three oxime systems in a variety of solvents. Both hydrogen bonding and solvent polarity effects are found to make significant contributions to the observed range of nitrogen shieldings. For a non-conjugated oxime moiety the solvent induced nitrogen shielding variations are found to be of opposite sign to those found for oximes which have a strongly conjugated carbonyl group. These shielding variations are interpreted in terms of solute–solvent specific and non-specific interactions. The analysis of the shielding data results in the view that, in these two cases of carbonyl group conjugation, there are opposing directions of electronic charge migration as a function of an increase in solvent polarity. There appears to be a change in the preference of the solute hydrogen bond acceptor site from the oxime to the carbonyl moiety in the case of *p*-benoquinone mono oxime derivatives. Medium polarity effects on the solute nitrogen shielding are adequately accounted for by INDO/S parametrised molecular orbital calculations of nitrogen shieldings as a function of solvent relative permittivity (ε) by means of the Solvaton model. This model describes satisfactorily the effects of a change in solvent polarity on the nitrogen shielding of a variety of nitrogen containing solutes.

Introduction

We have previously demonstrated[1–19] that solvent induced effects on nitrogen NMR shieldings are a very reliable way of estimating the extent, and direction, of electronic charge migration in a wide range of solute molecules due to non-specific solute–solvent interactions. Such effects can arise from solvent polarity/polarizability. In addition we have shown the importance of specific solute–solvent interactions, such as hydrogen bonding, on solvent induced variations in nitrogen NMR shieldings.

Our present investigation involves oxime systems **1**–**3** as model compounds. The structure of a simple oxime, like that of compound **1**, is analogous to that of an imine in which an N–C bond has been replaced by an N–O bond. However if the oxime moiety is strongly conjugated with an electron sink, such as the carbonyl group in compound **2**, a significant disturbance in electronic structure can occur with respect to that of compound **1**. Such a change can result in a variation in solute–solvent interactions and thus upon solute nitrogen shieldings as a function of solvent. Thus a comparison of the solvent effects on the nitrogen shieldings of compounds **1** and **2** should be a demanding test of the predictive abilities of the Solvaton model.[20] Our earlier work has revealed that the Solvaton model can provide a reliable estimate of both the signs and magnitudes of non-specific solvent effects on nitrogen NMR shieldings. Such effects include those due to solvent polarity/polarizability. Concomitantly the Solvaton calculations provide a measure of the direction of the electronic charge migration in the solute molecules as a function of an increase in solvent polarity.

Our major current aim is to investigate the structures of the oxime methyl ethers, compounds **1** and **2**, rather than those of the parent oximes, such as **3**. Consequently we hope to avoid potential complications which could arise from the hydrogen bond donor ability of the parent oximes. In addition we obviate the possibility of solvent induced changes in the position of the isomerisation equilibria found for the parent oximes, such as that between **3** and **3a**.



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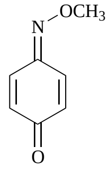

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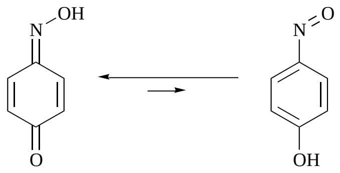

3 **3a**

As in our previous work[1–19] we use the term ‘nitrogen NMR shielding’ rather than ‘nitrogen chemical shift’. Thus our sign convention for the nitrogen shielding data is opposite to that associated with the chemical shift scale since we employ a positive sign to denote an increase in shielding.

Results and discussion

The results of high precision ^{14}N NMR measurements of the nitrogen shieldings of compounds **1**–**3** are given in Table 1. Restricted solubility has resulted in compound **3** being measured in only three solvents. The selection of solvents used corresponds to a large range of properties with respect to hydrogen bonding and polarity effects. The experimental section contains a description of the procedures used to obtain these results which are corrected for bulk susceptibility effects and have a precision such that the last digit quoted is uncertain.

The data reported in Table 1 show that the effects of solvents on the nitrogen shieldings of the compounds studied are large, for compound **1** the range is *ca.* 25 ppm and for compound **2** it is *ca.* 13 ppm. However it is interesting to note that in changing from non-polar to highly polar and hydrogen bonding solvents the induced nitrogen shielding changes for these two compounds are in opposite directions. For compound **1** a strong increase in shielding occurs while compound **2** experiences a nitrogen deshielding effect.

In order to obtain more detailed information on the factors producing these nitrogen shielding variations we employ the empirical scheme represented by eqn. (1).[22,23] To separate the various specific and non-specific contributions to the solvent induced nitrogen shielding variations, we have made use of the empirical scheme represented by eqn. (1),[8,9] where *i* and *j* denote

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

the solute and solvent, respectively; σ is the nitrogen shielding, α represents the hydrogen bond donor strength of the solvent, 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 given by the solute terms *a*, *b*, *s* and *d*. The nitrogen shielding in the reference state, cyclohexane solution, is given by σ_0.

Table 1 Solvent effects on the nitrogen NMR shieldings of some oxime systems

	Nitrogen NMR shielding (ppm) referred to neat liquid nitromethane[a]		
Solvent	Compound **1**	Compound **2**	Compound **3**
Cyclohexane	+7.73	−32.88	—
Et_2O	+9.21	−35.52	−25.81(0.05 M)
CCl_4	+9.77	−34.21	—
Benzene	+10.05	−35.73	—
Dioxane	+11.18	−36.08	—
Acetone	+11.28	−37.24	—
DMSO	+11.69	−38.60	—
CH_2Cl_2	+13.24	−37.59	—
$CHCl_3$	+14.73	−38.81	—
EtOH	+17.15	−41.91	−53.3
MeOH	+20.12	−42.46	−83.1
H_2O	+30.25	—	—
CF_3CH_2OH	+32.78	−45.3	—

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

Table 2 contains the parameter sets employed in the present work together with the least-squares fitted estimates of the solute nitrogen shielding responses, and the linear correlation coefficients, for comparison of the experimental and calculated nitrogen shieldings. The results given in Table 2 show that the values obtained for the parameter *d* are insignificant. The most important parameters are *a* and *s*. These correspond to the effects on the solute nitrogen shielding of the hydrogen bond acceptor ability of the solute and of solvent polarity/polarizability effects, respectively. For compound **1** the values of *a* and *s* obtained are both significant and positive in sign. This result is typical for nitrogenous moieties containing a CN double or triple bond and a lone pair of electrons on the nitrogen atom such as those found in imines and their heteroaromatic analogues[1–7,10,11,24] and nitriles.[18] The value for *s* shows that an increase in solvent polarity leads to a migration of electronic charge towards the nitrogen atom involved. While the value for *a* shows that the nitrogen lone pair of electrons acts as a potent acceptor of hydrogen bonds from the solvent molecules.

The results obtained for compound **1** show that the unconjugated oxime moiety behaves similarly, with respect to both specific and non-specific molecular interactions in solution, to imino type structures and their analogues. The values of *a* and *s* for compound **2** provide a very interesting example which shows substantial deviations from the behaviour of imino type functions; including the present case of the unconjugated oxime, **1**. The values of the *a* and *s* terms for compound **2** are both significant in magnitude but are negative in sign. This situation is just the opposite to that found for compound **1**.

The negative sign for the *a* term of compound **2** is the first one reported for imino moieties and their analogues. Such values are usually large and positive in sign corresponding to hydrogen bonding from the solvent to the lone pair electrons of the solute molecule. The fact that compound **2** has a negative *a* term suggests that the preferred site of hydrogen bonding is the carbonyl group as shown in Fig. 1.

This hydrogen bonding should result in the migration of electronic charge away from the oxime moiety and towards the carbonyl group in compound **2**. The same direction of charge migration, upon increasing solvent polarity, is suggested by the negative value of the *s* term. These observations are in agreement with intuition which suggests that the oxygen atom of the carbonyl group forms the negative end of the dipole in this dipolar molecule (Fig. 1). The conformation of the OCH_3

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

Solvent	α	β	π^*	δ	Relatively permittivity[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*	Correlation coefficient *r*
1	+8.4 ± 0.5	+9.4 ± 0.6	−1.3 ± 1.1	+4.6 ± 0.9	−0.2 ± 0.2	0.990
2	−33.1 ± 0.2	−6.0 ± 0.2	−1.8 ± 0.3	−4.2 ± 0.3	0.0 ± 0.1	0.998

[a] The constants were recalculated for a temperature of 35 °C from the data available in ref. 21.

group given in Fig. 1 is in accord with both experimental and theoretical results for oxime systems.[25]

Molecular orbital calculations, at the INDO/S level, of the nitrogen shielding of solute molecules are able to include the effects of non-specific solute–solvent interactions on the shielding by means of the Solvaton model.[20] The results so obtained give values of the nitrogen shielding as a function of the relative permittivity (ε) of the solvent treated as a continuous medium.

The results of the Solvaton calculations, reported in Table 3, show that the calculated effects of non-specific solute–solvent interactions on the nitrogen shieldings of compounds **1** and **2** are in opposite directions. These results are in very good agreement with the observed values of *s* for compounds **1** and **2**. This provides a very demanding test of the reliability of the Solvaton model to predict accurately the changes in nitrogen nuclear shielding, and the concomitant electronic charge migration, induced by changes in solvent polarity.

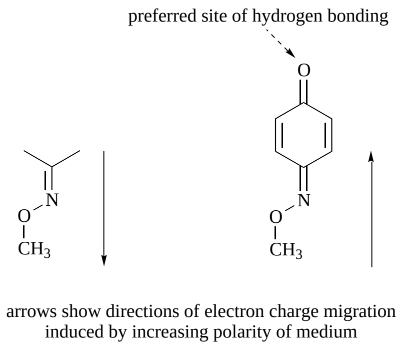

Fig. 1 Effect of solvent–solute interactions in oximes

Table 3 Nitrogen shielding increments induced by varying the relative permittivity (ε) of the medium as calculated by the Solvaton model

	Nitrogen shielding increment (in ppm) with respect to that for $\varepsilon = 2$	
ε	Compound **1**	Compound **2**
4	+1.7	−0.7
8	+2.5	−0.9
10	+2.7	−1.0
20	+2.8	−1.1
40	+2.9	−1.1
80	+2.9	−1.1

Table 4 contains a survey of the directions of medium polarity effects on nitrogen NMR shieldings, both those observed experimentally and those predicted by Solvaton calculations, for a large variety of nitrogenous moieties including the present case of conjugated and non-conjugated oximes. The results presented show that the Solvaton calculations are successful in all cases considered.

For compound **3**, Table 1 shows that the solvent induced nitrogen shielding variation is in the same direction as that found for the methyl ether **2**. However, the large nitrogen deshielding observed for compound **3** in a methanol solution very probably contains a large contribution due to a shift in the equilibrium towards *p*-nitrosophenol, **3a**. The nitrogen shielding of **3a** is expected to be *ca.* −500 ppm with respect to nitromethane.[26]

Experimental

The compounds studied, **1**–**3**, were prepared by published procedures.[27–29] Very pure and dry solvents were used in the NMR measurements as reported previously.[1–19] The solutions were prepared and handled under a dry argon atmosphere in glove bags. The ^{14}N shielding measurements were taken on a Bruker AM500 Spectrometer at 35 + 0.2 °C, as maintained by a variable temperature 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 used as a reference by means of 10 × 4 mm o.d. coaxial tubes. The inner tube contained 0.3 M nitromethane in [^{2}H$_6$]acetone; the nitrogen shielding of this solution is +0.77 ppm from that of neat liquid nitromethane.[24] This 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 conversion constant. Thus 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 36.141 524 MHz, from which a value of 36.136 826 MHz is obtained for the bare nitrogen nucleus.[24] This latter value is used in conjuction with the relevant resonance frequency differ-

Table 4 Direction of medium polarity effects on nitrogen NMR shielding (shielding increase '+', deshielding '−')

Structure	Experimental	Predicted by Solvaton model	Ref.
Pyridine-type nitrogen			
six-membrane ring	+	+	1, 2
five-membrane ring	+	+	3, 4, 5, 6, 7
Pyrrole-type nitrogen	−	−	3, 4, 7, 8
imino-nitrogen			
$R_2C{=}N{-}R$	+	+	9
Imine-*N*-oxide nitrogen			
$R_2C{=}N(O){-}R$	+	+	10,11
Oxime nitrogen			
$R_2C{=}N{-}OR$	+	+	Present work
Oxime nitrogen			
conjugated with C=O	−	−	Present work
Carbodiimide nitrogen			
$R{-}N{=}C{=}N{-}R$	−	−	12
Isocyanate nitrogen			
$R{-}N{=}C{=}O$	−	−	13
Nitro nitrogen			
$R{-}NO_2$	−	−	14, 15, 16
Nitroso nitrogen			
$R{-}N{=}O$	−	−	17
Cyano nitrogen			
$R{-}CN$	+	+	18
Isocyanide nitrogen			
$R{-}NC$	−	−	19

ences 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. Dilute solutions were used in the present study hence their susceptibilities are assumed to be equal to those of the corresponding solvent at 35 °C.

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