N, N′-Dicyclohexylcarbodiimide as a model for solvent polarity effects on nitrogen NMR shielding

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Abstract

Variations in the nitrogen NMR shieldings of N,N′-dicyclohexylcarbodiimide under the influence of solvents span a range of about 7 ppm and are shown to be mostly governed by solvent polarity, with a rather negligible contribution of hydrogen-bonding effects. The apparently anomalous direction of the effect, operating in the deshielding direction upon increasing the polarity of the medium, as compared with the opposite effect observed generally in C=N moieties, is shown to be typical of R–N=C=X systems, and corroborated by quantum-mechanical calculations based on the so-called solvaton model. The sign and magnitude of the effect obtained from the experimental data and the calculations provide a rigorous test for the latter model of solute–solvent interactions.

Introduction

Nitrogen NMR shieldings (chemical shifts) seem to provide a deep insight into molecular interactions that take place in solutions containing nitrogenous solutes, in view of the sensitivity of the shieldings to such interactions [1–13]. We use here, as before [1–13], the sign convention which attributes the plus sign to the increasing magnetic shielding of the

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TABLE 1
Solvent parameters used and least-squares fitted solute parameters for a set of master equations (1)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>α</th>
<th>β</th>
<th>π*</th>
<th>δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>0.00</td>
<td>0.47</td>
<td>0.27</td>
<td>0.5</td>
</tr>
<tr>
<td>Et₂O</td>
<td>0.00</td>
<td>0.10</td>
<td>0.59</td>
<td>1</td>
</tr>
<tr>
<td>CCl₄</td>
<td>0.00</td>
<td>0.29</td>
<td>0.55</td>
<td>0</td>
</tr>
<tr>
<td>Benzene</td>
<td>0.00</td>
<td>0.37</td>
<td>0.10</td>
<td>0.59</td>
</tr>
<tr>
<td>Dioxane</td>
<td>0.00</td>
<td>0.07</td>
<td>0.76</td>
<td>0.72</td>
</tr>
<tr>
<td>Acetone</td>
<td>0.00</td>
<td>0.34</td>
<td>0.76</td>
<td>0.55</td>
</tr>
<tr>
<td>DMSO</td>
<td>0.00</td>
<td>0.86</td>
<td>0.76</td>
<td>0.54</td>
</tr>
<tr>
<td>CH₂Cl₂</td>
<td>0.00</td>
<td>0.98</td>
<td>0.76</td>
<td>0.60</td>
</tr>
<tr>
<td>Ethanol</td>
<td>0.00</td>
<td>1.51</td>
<td>1.02</td>
<td>0</td>
</tr>
<tr>
<td>Methanol</td>
<td>0.00</td>
<td>1.61</td>
<td>1.01</td>
<td>0.22</td>
</tr>
<tr>
<td>CF₃CH₂OH</td>
<td>0.00</td>
<td>1.68</td>
<td>3.73</td>
<td>0.88</td>
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</table>

nitrogen nuclei, and therefore we employ the term "nitrogen shielding" rather than "nitrogen chemical shift" since the latter is usually associated with a reverse sign convention. It is usually feasible to estimate various contributions to solvent-induced variations in nitrogen NMR shieldings using an empirical scale of solvent properties, that are described in refs. 14–17. The scale can be described by means of eqn. (1):

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

(1)

where \(i\) and \(j\) stand for solute and solvent, respectively; \(\sigma\) is the relevant nitrogen shielding, \(\alpha\) represents hydrogen-bond donor strength of the solvent, \(\beta\) represents its hydrogen-bond acceptor strength, \(\pi^*\) is its polarity–polarizability, and \(\delta\) is a correction for polychlorinated solvents (\(\delta = 0.5\)) and aromatic solvents (\(\delta = 1\)). The solute terms, \(a\), \(b\), \(s\), and \(d\), represent the corresponding responses of the nitrogen shielding to a given property of the solvent employed, and \(\sigma_0\) is the nitrogen shielding in the reference state which is approximated by a solution in cyclohexane. The relevant characteristics of a number of selected solvents, that are expressed in terms of the \(\alpha\), \(\beta\), \(\pi^*\), and \(\delta\) scales, are presented in Table 1.

So far, there seem to exist some regularities in the direction of nitrogen shielding changes effected by increasing solvent polarity–polarizability; the latter is expressed by the \(\pi^*\) scale employed here, and the corresponding response of the nitrogen shielding is described by the \(s\) term in eqn. (1). As
a rule for, C=N and C≡N moieties, where the increasing solvent polarity is likely to induce a shift of the electron charge towards the nitrogen atom involved, the experimentally found σ terms are positive, i.e., the nitrogen nucleus becomes more shielded with the increasing polarity of the medium:

\[
\begin{align*}
\sigma > 0 \\
\text{C=N} \\
\sigma < 0
\end{align*}
\]

An opposite trend is observed when the nitrogen atom is attached to more electron-attracting atoms, like those of oxygen, or when the delocalization of lone pair electrons leaves the nitrogen atom with some positive net charge:

\[
\begin{align*}
\sigma > 0 \\
\text{O} \\
\sigma < 0
\end{align*}
\]

A notable exception is found [9] in the isothiocyanato moiety

\[
\text{CH}_3\text{C=S} \\
\sigma < 0
\]

where the contribution of solvent polarity to nitrogen shielding variation operates in the deshielding direction, in spite of the fact that the nitrogen atom should be the most attractive centre for electron charge.

The latter example includes a structure which may be conventionally described as that containing an sp²-hybridized nitrogen atom attached to an sp-hybridized carbon atom. Since the exception described above seems to break down the simple rationalization of solvent-induced effects on nitrogen NMR shielding which attributes an increased shielding to the accumulation of electron charge at the nitrogen atom concerned, we decided to seek for another model molecule belonging to that structural type, and to examine solvent effects on its nitrogen NMR shielding.

**Results and discussion**

The carbodiimide structure, R-N=C=N-R, which may be considered as a nitrogenous analogue of the allene structure, R₂C=C=CR₂, seems to
TABLE 2
Solvent effects on nitrogen NMR of N,N'-dicyclohexylcarbodiimide
All data are corrected for bulk susceptibility effects, and relate to 0.2 M solutions at +35.0 ± 0.2°C

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Nitrogen NMR shielding (ppm) referred to neat nitromethane</th>
<th>Experimental</th>
<th>Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane</td>
<td>281.60</td>
<td>281.54</td>
<td></td>
</tr>
<tr>
<td>Et₂O</td>
<td>281.20</td>
<td>281.34</td>
<td></td>
</tr>
<tr>
<td>CCl₄</td>
<td>280.35</td>
<td>280.89</td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>280.25</td>
<td>280.35</td>
<td></td>
</tr>
<tr>
<td>Dioxane</td>
<td>280.21</td>
<td>280.13</td>
<td></td>
</tr>
<tr>
<td>Acetone</td>
<td>280.03</td>
<td>279.56</td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>279.31</td>
<td>279.40</td>
<td></td>
</tr>
<tr>
<td>CH₃Cl₂</td>
<td>279.25</td>
<td>278.62</td>
<td></td>
</tr>
<tr>
<td>Methanol</td>
<td>279.22</td>
<td>279.72</td>
<td></td>
</tr>
<tr>
<td>CHCl₃</td>
<td>278.67</td>
<td>278.57</td>
<td></td>
</tr>
<tr>
<td>DMSO</td>
<td>278.56</td>
<td>279.10</td>
<td></td>
</tr>
<tr>
<td>CF₃CH₂OH</td>
<td>274.82</td>
<td>275.22</td>
<td></td>
</tr>
</tbody>
</table>

provide a good example of the R-N=C=X system, where one can assign the sp² and sp hybridization to the nitrogen and carbon orbitals, respectively. The two R-N=C planes should be approximately perpendicular, but there is a twofold symmetry axis which passes through the central carbon atom. A stable molecule of this kind is N,N'-dicyclohexylcarbodiimide

and this one was chosen by us for nitrogen NMR investigations.

A set of 12 solvents was employed, which covers a wide range of solvent properties from the point of view of polarity and hydrogen-bonding effects on solutes (Tables 1 and 2). The nitrogen shieldings of the carbodiimide in dilute solutions (Table 2) were obtained from high-precision ¹⁴N NMR measurements (see Experimental section) at a controlled temperature, with all precautions possible taken against systematic errors that can appear in comparisons of NMR shieldings obtained from independent measurements.
The experimental data (Table 2) show that the nitrogen shieldings of N,N'-dicyclohexylcarbodiimide span a range of about 7 ppm for the set of solvents employed, and that the highest magnetic shielding takes place in its solution in cyclohexane, while polar and protic solvents seem to induce low-field shifts of the nitrogen resonance with respect to the latter. A regression analysis according to eqn. (1) yielded the corresponding responses of the nitrogen shielding to polarity–polarizability and hydrogen-bonding properties of the solvents which are presented as terms a, b, s and d in Table 1, together with their standard deviations. Retrieving the nitrogen shieldings by means of eqn. (1) and the estimates of the latter terms gave calculated values (Table 2) which show a linear correlation coefficient of 0.97 with respect to the experimental values, and this is quite satisfactory in view of the fact that if CF₃CH₂OH as a solvent is excluded from consideration, the range of solvent effects on the shielding drops to about 3 ppm.

While the terms a and b, those representing responses of the shieldings to hydrogen-bond donor and acceptor properties of the solvents, respectively, seem to be hardly significant (Table 2), and the same holds for the term d, the response to solvent polarity–polarizability (s = 3.73 ppm per unit scale of $\pi^*$) seems to account for most of the observed range of solvent effects on the nitrogen shielding of the carbodiimide. The minus sign means that the effect of the increasing polarity of the solvent employed operates in the deshielding direction, and this is in accord with the direction observed [9] for the isothiocyanato structure mentioned, R–N=C=S. This is quite an important discovery, since it seems to suggest that the isocyanato structure is not an exception in the response of its nitrogen NMR shielding to solvent polarity effects, and that the deshielding direction is likely to be a rule for R–N=C=X structures. Moreover, the symmetry of the carbodiimide structure suggests that the foregoing response to solvent polarity should result primarily from a polarization within the R–N bonds concerned, with an electron-charge shift towards the nitrogen atoms. The latter effect can be propagated as a $\pi$-electron charge shift from nitrogen to carbon in the N=C=N moiety of the carbodiimide. This could explain the apparently anomalous response to solvent polarity of the nitrogen shielding of R–N=C=X, as compared with other C=N moieties where the polarization of the double bond should involve a charge shift from carbon to nitrogen.

The data and the regression analysis by means of eqn. (1) should also provide a rigorous test for solvaton-model quantum-mechanical calculations of solvent effects on solutes. The solvaton model employs semi-empirical methods, like INDOS/S-SOS [18], combined with the generation of electric charges in the surroundings of a solute molecule, and including
interactions of the latter with these charges which are mediated by a given dielectric constant; in the present case, the calculations also included the relevant magnetic shielding of the nitrogen nuclei concerned. The most important point here is the predicted sign of the effect on the calculated nitrogen shielding, which may be compared with the sign of the term $s$ obtained from the relevant experimental data and the regression analysis by means of eqn. (1). So far, the solvaton model has invariably predicted correct signs of the effect on nitrogen NMR shielding of solvent polarity [3–10], and this also included the case for the isothiocyanato structure considered [9].

The results of our calculations for the carbodiimide structure concerned, using the INDOS/S-SOS approach and the solvaton model, are reported in Table 3. The model predicts a deshielding effect on the nitrogen nucleus in the carbodiimide upon increasing the dielectric constant of the medium, and this is in accord with the experimental data and with the sign and magnitude of the $s$ term obtained from eqn. (1). This result provides a strong argument in favour of the solvaton-model calculations of perturbations in the electron charge distribution induced by solvents in solute molecules in cases where solvent polarity effects on the latter are either dominant or can be extracted from experimental data by some methods, like that represented by eqn. (1) and the associated characteristics of solvent properties.

The experimental and theoretical results obtained for the nitrogen NMR shieldings in the carbodiimide structure strongly suggest that the deshielding effect of solvent polarity on the nitrogen nucleus in R–N=C=X solutes is a general phenomenon, while an opposite effect is typical for imino-type C=N moieties and the cyano groups in nitriles. So far, the deshielding effect seemed to be associated only with structures where solvent-induced polarization was likely to leave a positive net charge at the nitrogen atom concerned.
Experimental

N,N'·Dicyclohexylcarbodiimide was available commercially, and its purification was carried out, prior to use, by distillation under a dry atmosphere and a pressure of 3 mm mercury. Special attention was paid to the use of pure and dry solvents. All solutions were prepared and handled under dry argon atmosphere in glove bags. The nitrogen NMR shieldings of 0.2 M N,N'-dicyclohexylcarbodiimide in a set of 12 solvents, that are characterized by a large diversity of solvent properties (Table 2), were measured by high-precision $^{14}$N NMR at 36.14 MHz (Bruker AM-500 spectrometer) and 35 ± 0.2°C; the temperature was maintained by a variable temperature unit. Care was taken in order to bring the possible random and systematic errors to below 0.1 ppm upon following the nitrogen shieldings variation for the carbodiimide upon the influence of the solvents employed. The shieldings were referenced externally to neat liquid nitromethane, using 10 mm/4 mm O.D. coaxial tubes. The inner tube contained 0.3 M nitromethane in acetone-$d_6$ whose nitrogen shielding is +0.77 ppm from that of neat liquid nitromethane [1–3], under conditions where bulk susceptibility difference effects vanish (in concentric spherical sample/reference containers); the latter value was employed as a conversion constant. Thus, the content of the inner tube served as a precise reference to the neat nitromethane standard, and also provided a source of deuterium lock for the system. The exact resonance frequency of the $^{14}$N signal of neat nitromethane was 36.141524 MHz, and recalculations which were carried out by methods outlined in ref. 1 yielded a value of 36.136826 MHz for a bare nitrogen nucleus. The latter value was used in conjunction with the relevant resonance frequency differences in order to calculate the nitrogen NMR shieldings relative to that of the primary standard, neat nitromethane. The resonance frequencies of the samples and the external standard were found by Lorentzian line shape fitting of the relevant $^{14}$N NMR signals. The nitrogen shieldings obtained were then corrected for bulk susceptibility effects, according to procedures described in ref. 1; since dilute solutions were employed, their susceptibilities were assumed to be equal to those of the respective solvents at 35°C.

References