Variable temperature $^1$H and $^{13}$C NMR study of restricted rotation in $N,N$-bis(2-hydroxyethyl)acetamid

R. Alan Aitken, Melanja H. Smith, Heather S. Wilson

$^*$EaStCHEM School of Chemistry, University of St Andrews, North Haugh, St Andrews, Fife, KY16 9ST, U. K.

Abstract

$N,N$-bis(2-hydroxyethyl)acetamide shows restricted rotation about the amide bond in both $^1$H and $^{13}$C NMR spectra rendering the two hydroxyethyl groups non-equivalent. A variable temperature study in CD$_2$SOCD$_3$ allowed estimation of the free energy barrier to rotation as 75.6 ± 0.2 kJ mol$^{-1}$. Previously published data in CDCl$_3$ appears to be erroneous.

Keywords: Variable temperature NMR; Restricted rotation; Amide bond

1. Introduction

The simple compound $N,N$-bis(2-hydroxyethyl)-acetamide or $N$-acetylidiethanolamine 1 (Scheme 1) was first described in a patent some 75 years ago [1] and has since found a wide variety of applications including as a component of surfactants [1], and of radiation curable polymers [2]. It has also been mentioned both as a product and a reference compound in a series of recent studies on selective acyl transfer reactions in which acylating agents such as $N$-acetyl-4,6-dimethylpyrimidine-2-thione [3] and 3-($N,N$-diacetylamin)quinazolin-4-ones [4] were reacted with various amines including diethanolamine.

![Scheme 1](Image)

In view of the well-known restricted rotation about the amide bond, the NMR spectra of this compound are expected to exhibit interesting dynamic effects due to interconversion of the two (degenerate) conformations as a function of temperature, which should allow estimation of the free energy barrier to rotation [5].

Previous NMR characterisation of this simple compound is poor and various conflicting and erroneous data have been published. A correct low-resolution $^1$H spectrum was published in D$_2$O in 1987 [6] but this only showed a singlet for the methyl group ($\delta$ 2.27) and all eight other CH protons occurring together as a multiplet ($\delta$ 3.45–4.03). In 2013 the $^1$H spectrum was reported in CDCl$_3$ at 500 MHz [7] showing a singlet for methyl ($\delta$ 2.15) and two triplets ($\delta$ 4.23, 4.21) assigned to CH$_2$O and two triplets ($\delta$ 3.62, 3.61) assigned to CH$_2$N but with mismatched coupling constants in the latter case.

Again in 2014 [4], $^1$H data in CDCl$_3$ at 500 MHz appeared with chemical shift ranges similar to those above but with the CH$_2$O signal reported as a singlet. In addition, these authors reported $^{13}$C NMR data for the first time (125 MHz, CDCl$_3$) but this includes two separate carbonyl signals ($\delta$ 170.8, 171.25) with the remaining three environments each reported as a chemical shift range: $\delta$ 20.76–22.02 for Me, $\delta$ 45.33–49.63 for CH$_2$N and $\delta$ 50.38–62.23 for CH$_2$O. In view of the serious problems with this data we have re-determined the $^1$H and $^{13}$C NMR spectra of 1 both in CDCl$_3$ and in CD$_2$SOCD$_3$ and, by means of a variable temperature study in the latter solvent, obtained several consistent values for the free energy barrier to rotation about the amide bond.

2. Experimental

Preparation of $N,N$-bis(2-hydroxyethyl)acetamide 1 [2]

To a solution of diethanolamine (10 g, 95 mmol) in THF (20 cm$^3$) stirred and cooled below 5 $^\circ$C was added dropwise acetic anhydride (10 g, 98 mmol). After the addition the mixture was heated to 100 $^\circ$C for 1 h and then evaporated using a rotary evaporator followed by a high vacuum pump until all traces of acetic acid and acetic anhydride had been removed. The product was obtained as a faintly yellow oil (12.5 g, 99%).

NMR spectra were determined at 300 MHz for $^1$H and at 75 MHz for $^{13}$C using a Bruker instrument. Chemical shift values are given in ppm relative to Me$_2$Si and spectra are referenced either to internal Me$_2$Si or to residual solvent peaks. Coupling constants are given in Hz. For data obtained see Tables 1 and 2.

3. Results and Discussion

Compound 1 has been prepared by reaction of diethanolamine with methyl acetate [1] or ethyl acetate [8] or base mediated reaction of acetamide with ethylene oxide [9], but the most widely used method is reaction of diethanolamine with acetic anhydride. This has been performed
in water [7], in acetonitrile in the presence of a zeolite catalyst [10], and in methanol with one equivalent of triethylamine [11]. However we used the direct reaction of equimolar amounts of diethanolamine and acetic anhydride in THF at 100 °C followed by evaporation under high vacuum [2] and obtained compound 1 in 90% yield.

NMR spectra of the product were first recorded in CDCl$_3$ at 300 MHz and this showed two slightly non-equivalent triplets for each of CH$_2$N and CH$_2$O (Table 1). However these were all in the range $\delta$ 3.4–3.8, which is at odds with both the previous spectra reported in CDCl$_3$[4,7]. By moving to CD$_3$SOCD$_3$ separate clearly defined triplets were observed in the range $\delta$ 3.3–3.5. A comparison of the CH$_2$ signals in the two solvents is shown in Figure 1.

Table 1: $^1$H NMR data for 1

<table>
<thead>
<tr>
<th>Solvent</th>
<th>CDCl$_3$</th>
<th>CD$_3$SOCD$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>2.15 (s)</td>
<td>2.00 (s)</td>
</tr>
<tr>
<td>CH$_3$N</td>
<td>3.50 (d, J 5.3)</td>
<td>3.30 (d, J 6.2)</td>
</tr>
<tr>
<td></td>
<td>3.52 (d, J 5.3)</td>
<td>3.36 (d, J 5.8)</td>
</tr>
<tr>
<td>CH$_3$O</td>
<td>3.77 (d, J 5.3)</td>
<td>3.45 (d, J 6.2)</td>
</tr>
<tr>
<td></td>
<td>3.78 (d, J 5.3)</td>
<td>3.51 (d, J 5.8)</td>
</tr>
<tr>
<td>OH</td>
<td>5.69 (br s)</td>
<td>5.52 (v br s)</td>
</tr>
</tbody>
</table>

Figure 1: CH$_3$N and CH$_3$O $^1$H NMR signals for 1

When $^{13}$C NMR spectra were run in both solvents, the expected pattern was observed with a single carbonyl signal, two widely separated signals for CH$_3$N and two slightly non-equivalent signals for CH$_3$O (Table 2). The clearly defined patterns obtained (Figure 2) give no hint as to origin of the erroneous literature data [4].

Table 2: $^{13}$C NMR data for 1

<table>
<thead>
<tr>
<th>Solvent</th>
<th>CDCl$_3$</th>
<th>CD$_3$SOCD$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>21.71</td>
<td>21.61</td>
</tr>
<tr>
<td>CH$_3$N</td>
<td>49.99</td>
<td>48.13</td>
</tr>
<tr>
<td></td>
<td>52.80</td>
<td>51.46</td>
</tr>
<tr>
<td>CH$_3$O</td>
<td>60.07</td>
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</tr>
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<td></td>
<td>60.44</td>
<td>59.08</td>
</tr>
<tr>
<td>CO</td>
<td>173.05</td>
<td>170.14</td>
</tr>
</tbody>
</table>

Figure 2: CH$_3$N and CH$_3$O $^{13}$C NMR signals for 1

Having established the expected pattern of non-equivalence of the two hydroxyethyl groups at RT due to restricted rotation of the acetyl group, CD$_3$SOCD$_3$ was chosen as the preferred solvent for a variable temperature study and spectra were obtained for both $^1$H and $^{13}$C over the range 25–100 °C. As shown in Figure 3, upon moving from RT to 100 °C, the separate $^{13}$C signals for CH$_3$O were replaced by a single peak and the pairs of triplets for CH$_3$O and CH$_3$N were each replaced by a single triplet. By coincidence the coalescence temperature in each case was 77 °C.

Figure 3: Variable temperature results for 1
The free energy barrier to rotation $\Delta G^*$ can be calculated using the equation:

$$\frac{\Delta G^*}{R \times T_c} = 22.96 + \ln\left(\frac{T_c}{\delta \nu}\right)$$

where $R$ is the gas constant, $T_c$ is the coalescence temperature in K and $\delta \nu$ is the low temperature chemical shift difference in Hz. The corresponding calculated values are: from $^{13}$C of CH$_2$O 75.74 kJ mol$^{-1}$, from $^1$H of CH$_2$O 75.40 kJ mol$^{-1}$ and from $^1$H of CH$_2$N 75.50 kJ mol$^{-1}$. These values compare well with those previously reported for similar systems such as $N,N$-diethylacetamide (71.0 kJ mol$^{-1}$) and $N,N$-dipropylacetamide (71.4 kJ mol$^{-1}$) [12].

4. Conclusions
As expected, the restricted rotation about the amide bond in compound 1 leads to non-equivalence of the two hydroxyethyl groups at room temperature and doubling of the signals due to CH$_2$N and CH$_2$O in both $^1$H and $^{13}$C NMR spectra. The spectra obtained in CDCl$_3$ are not in agreement with the data recently published by two separate groups [4,7], which appear to be erroneous. Quantification of the barrier to rotation by means of a variable temperature study in CD$_3$SOCD$_3$ gives values well within the normal range for such amides.

**Supplementary information**
Copies of $^1$H and $^{13}$C NMR spectra for 1 in CDCl$_3$ at 25 °C and in CD$_3$SOCD$_3$ at 25, 77 and 100 °C.

**References**