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

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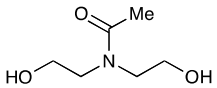
Abstract
N,N-bis(2-hydroxyethyl)acetamide shows restricted rotation about the amide bond in both ^{1}H and ^{13}C NMR spectra rendering the two hydroxyethyl groups non-equivalent. A variable temperature study in CD_3SOCD_3 allowed estimation of the free energy barrier to rotation as 75.6 ± 0.2 kJ mol^{-1}. 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*-acetyldiethanolamine **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 acetylating agents such as *N*-acetyl-4,6-dimethylpyrimidine-2-thione [3] and 3-(*N,N*-diacetylamino)quinazolin-4-ones [4] were reacted with various amines including diethanolamine.



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Scheme 1

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_2O in 1987 [6] but this only showed a singlet for the methyl group (δ 2.27) and all eight other CH protons occurring together as a multiplet (δ 3.45–4.03). In 2013 the ^{1}H spectrum was reported in $CDCl_3$ at 500 MHz [7] showing a singlet for methyl (δ 2.15) and two triplets (δ 4.23, 4.21) assigned to CH_2O and two triplets (δ 3.62, 3.61) assigned to CH_2N but with mismatched coupling constants in the latter case.

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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_2O 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 (δ 170.8, 171.25) with the remaining three environments each reported as a chemical shift range: δ 20.76–22.02 for Me, δ 45.33–49.63 for CH_2N and δ 50.38–62.23 for CH_2O. 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_3SOCD_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 °C was added dropwise acetic anhydride (10 g, 98 mmol). After the addition the mixture was heated to 100 °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, 90%).

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_4Si and spectra are referenced either to internal Me_4Si 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_2N and CH_2O (Table 1). However these were all in the range δ 3.4–3.8, which is at odds with both the previous spectra reported in $CDCl_3$ [4,7]. By moving to CD_3SOCD_3 separate clearly defined triplets were observed in the range δ 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**

Solvent	$CDCl_3$	CD_3SOCD_3
Me	2.15 (s)	2.00 (s)
CH_2N	3.50 (d, *J* 5.3)	3.30 (d, *J* 6.2)
	3.52 (d, *J* 5.3)	3.36 (d, *J* 5.8)
CH_2O	3.77 (d, *J* 5.3)	3.45 (d, *J* 6.2)
	3.78 (d, *J* 5.3)	3.51 (d, *J* 5.8)
OH	5.69 (br s)	5.52 (v br s)

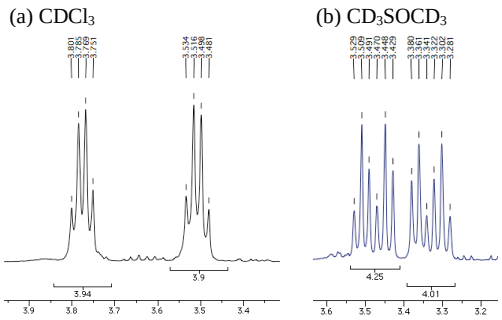

Figure 1: CH_2N and CH_2O ^{1}H NMR signals for **1**

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_2N and two slightly non-equivalent signals for CH_2O (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**

Solvent	$CDCl_3$	CD_3SOCD_3
Me	21.71	21.61
CH_2N	49.99	48.13
	52.80	51.46
CH_2O	60.07	58.86
	60.44	59.08
CO	173.05	170.14

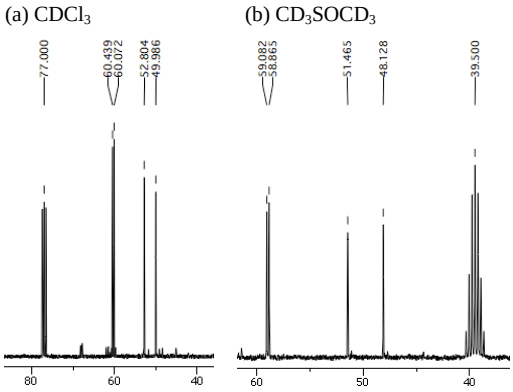

Figure 2: CH_2N and CH_2O ^{13}C NMR signals for **1**

Having established the expected pattern of non-equivalence of the two hydroxyethyl groups at RT due to restricted rotation of the acetyl group, CD_3SOCD_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_2O were replaced by a single peak and the pairs of triplets for CH_2O and CH_2N were each replaced by a single triplet. By coincidence the coalescence temperature in each case was 77 °C.

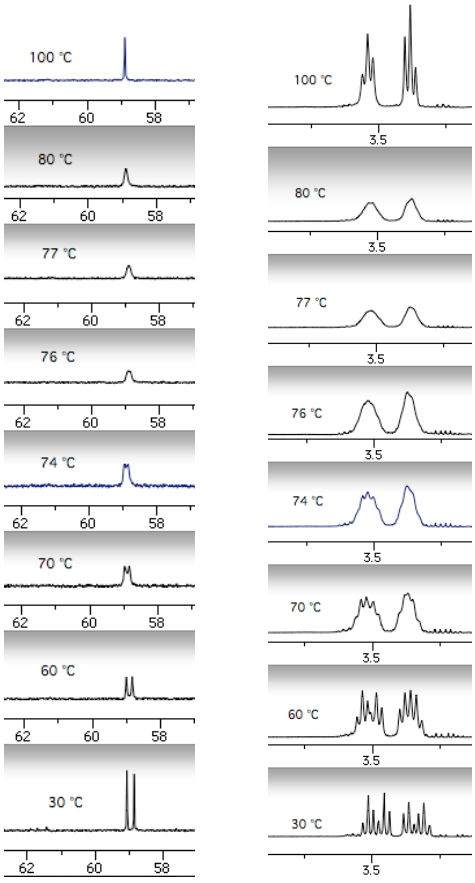

Figure 3: Variable temperature results for **1**

The free energy barrier to rotation $\Delta G^{\neq}$ can be calculated using the equation:

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

where R is the gas constant, T_c is the coalescence temperature in K and δ_ν is the low temperature chemical shift difference in Hz. The corresponding calculated values are: from ^{13}C of CH_2O 75.74 kJ mol^{-1}, from ^{1}H of CH_2O 75.40 kJ mol^{-1} and from ^{1}H of CH_2N 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_2N and CH_2O 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_3SOCD_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_3SOCD_3 at 25, 77 and 100 °C.

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