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A ^{13}C and ^{15}N experimental NMR and theoretical study of the structure of linear primary aliphatic amines and ammonium salts: from C1 to C18

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ABSTRACT

Eighteen aliphatic linear amines, from methylamine to stearylamine, have been experimentally studied by NMR and theoretically calculated at the GIAO/B3LYP/6-311++G(d,p) level. A partial exploration of their conformation has been carried out, mainly to determine the effect on the chemical shifts. In solution and for neutral amines, ^{15}N chemical shifts indicate a mixture of two conformations. In the solid state (CPMAS NMR) only the subset of solid amines has been studied (from C14 to C18). The ^{15}N signals of the corresponding ammonium salts in the solid state depend on the counteranions, Cl^- and $CF_3CO_2^-$, a result that is theoretically proven.

1. Introduction

Although for most functional groups and ring systems it can be said that they are part of bioactive compounds and materials,[1] this is only partly true for linear aliphatic amines (alkylamines or alkane-1-amines according to IUPAC nomenclature). The influence of the chain length (methyl, ethyl, butyl) of 8-alkylamino analogues of an adenosine derivative was studied in haemodynamic response.[2] The fact that aliphatic amines decrease the hERG binding affinity has been reported.[3] We should note that this family of compounds has been the subject of NMR studies almost from the beginning of each nucleus, in particular ^{13}C[4–6] and ^{15}N.[7] We have devoted during the years some papers to these compounds: effect on the ^{13}C chemical shifts produced by the protonation of amines;[8] comparison of ^{13}C chemical shifts of amines and *N*-alkyl pyridinium salts;[9] influence of the conformation of amines (mainly cyclic) on ^{1}H, ^{13}C and ^{15}N chemical shifts;[10] determination of the structure of fatty amines with 16 and 18 carbon atoms by NMR.[11,12] We have also studied by NMR the protonation of 2-pyrazolines using amines as models.[13,14]

None of these NMR publications being comprehensive, we decided to study the following 18 amines and their cations: methylamine (**1**), ethylamine (**2**), propylamine (**3**), butylamine (**4**), pentylamine (amylamine) (**5**), hexylamine (**6**), heptylamine (**7**), octylamine (caprylamine) (**8**), nonylamine (**9**), decylamine (**10**), undecylamine (**11**), dodecylamine (laurylamine) (**12**), tridecylamine (**13**), tetradecylamine (myristylamine) (**14**), pentadecylamine (**15**), hexadecylamine (palmitylamine) (**16**), heptadecylamine (margarylamine) (**17**) and octadecylamine (stearylamine) (**18**). Actually, data for **1** and **2** come from the literature and no experimental data will correspond to **17**, a non-commercial product, although it has been approached theoretically.

2. Results and discussion

We will discuss first the calculated energies (36 compounds) and then the NMR results (34 compounds) both in solution and in the solid state. The energy calculations were carried out at the B3LYP/6-311++G(d,p) level and the obtained optimized geometries served for the GIAO calculations of absolute shieldings (see Computational details).

2.1. Energies

For the 18 compounds we have calculated four conformations (for the simplest derivatives some of them are identical). This is only a very minor part of the total conformational space even considering only 60° rotations of staggered situations. We have reported previously[10] that the calculated absolute shieldings (σ, ppm) of the adjacent methylene group are dependent on their orientation

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relative to the N lone pair. So we have explored two conformations of the amino group (Fig. 1), the C_s and the C_1, maintaining the fully extended all-trans structure for the aliphatic chain.[15]

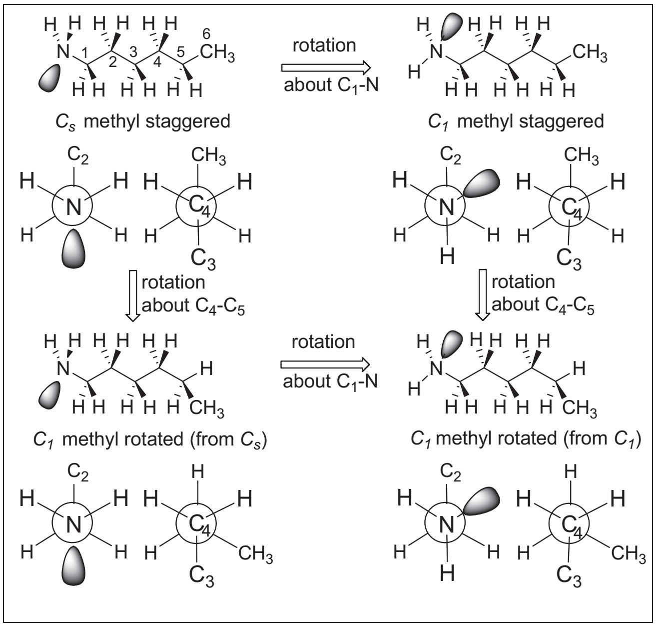

Fig. 1. The four studied conformations in the case of hexylamine (**6**). They correspond to the rotation of the amino group (C_1–N bond) and to the rotation of the C_4–C_5 bond.

We have pointed out, in our work on long-chain fatty amines,[11] that the chemical shifts of the terminal methyl groups are not well reproduced by the calculations of the C_s structure; for this reason, we decided to rotate 60° the methyl group about the $n-1$ bond (C_{16}–C_{17} for **18** and C_{15}–C_{16} for **17** and so on). The resulting structures are of C_1 symmetry. The energetic results are reported in Tables 1 and 2.

Table 1
Absolute (hartree) and relative energies (kJ mol^{-1}) calculated at the B3LYP/6-311++G(d,p) level for amines

Amine	C_s		C_1		C_s Me rotated		C_1 Me rotated	
	Absolute	Relative	Relative	Absolute	Absolute	Relative	Absolute	Relative
1	−95.89389	0.00	−95.89389	0.00	−95.89389	0.00	−95.89389	0.00
2	−135.22152	0.00	−135.22154	−0.04	−135.22152	0.00	−135.22154	−0.04
3	−174.54597	0.00	−174.54581	0.43	−174.54526	1.86	−174.54513	2.20
4	−213.87019	0.00	−213.87004	0.39	−213.86876	3.75	−213.86879	3.69
5	−253.19457	0.00	−253.19442	0.39	−253.19325	3.44	−253.19312	3.81
6	−292.51891	0.00	−292.51875	0.42	−292.52018	3.51	−292.51741	3.95
7	−331.84325	0.00	−331.84309	0.41	−331.84190	3.53	−331.84175	3.94
8	−371.16760	0.00	−371.16743	0.44	−371.16625	3.54	−371.16609	3.98
9	−410.49193	0.00	−410.49177	0.42	−410.49060	3.51	−410.49043	3.95
10	−449.81628	0.00	−449.81611	0.45	−449.81494	3.53	−449.81477	3.97
11	−489.14061	0.00	−489.14045	0.43	−489.13928	3.51	−489.13911	3.96
12	−528.46496	0.00	−528.46479	0.46	−528.46362	3.53	−528.46344	3.99
13	−567.78929	0.00	−567.78912	0.45	−567.78795	3.51	−567.78778	3.97
14	−607.11363	0.00	−607.11346	0.45	−607.11228	3.54	−607.11211	3.98
15	−646.43795	0.00	−646.43780	0.42	−646.43662	3.51	−646.43645	3.95
16	−685.76231	0.00	−685.76213	0.45	−685.76096	3.54	−685.76079	3.99
17	−725.08664	0.00	−725.08647	0.45	−725.08530	3.53	−725.08513	3.98
18	−764.41098	0.00	−764.41081	0.46	−764.40964	3.53	−764.40947	3.98

Table 2
Absolute energies (hartree) and proton affinities (kJ mol^{-1}) calculated at the B3LYP/6-311++G(d,p) level for ammonium cations

Ammonium	Absolute	PA	PA+ZPE	Experimental PA
NH_{4+}	−56.58272	886.5	846.5	853.6
1H^+	−96.249058	932.5	892.2	899.0
2H^+	−135.58203	946.5	906.8	912.0
3H^+	−174.90843	951.6	911.8	917.8
4H^+	−214.23389	954.9	915.1	921.5
5H^+	−253.55891	956.6	916.9	923.5
6H^+	−292.88362	957.5	917.9	927.5
7H^+	−332.20819	958.2	918.4	923.2
8H^+	−371.53267	958.5	918.9	928.9
9H^+	−410.85711	958.8		
10H^+	−450.18151	958.9	919.3	930.4
11H^+	−489.50590	959.1		
12H^+	−528.83026	959.1		
13H^+	−568.15464	959.2		
14H^+	−607.47898	959.2		
15H^+	−646.80334	959.3		
16H^+	−686.12767	959.3		
17H^+	−725.45204	959.3		
18H^+	−764.77637	959.3		

Besides the data reported in Tables 1 and 2, we have calculated the dipole moments that are comprised between 1.41 (**1**) and 1.54 D (**18**) for the C_s and 1.21 (**18**) and 1.33 D (**5**) for the C_1. There is a linear variation of the dipole moment with the inverse of the number of carbons (1/C) if even and odd numbers are separated (this is similar to odd/even dichotomy in alkanes boiling and melting points):[16]

$$\mu_{\text{even}} = (1.466 \pm 0.001) - (0.169 \pm 0.003) 1/\text{C}, n = 9, R^2 = 0.998 \quad (1)$$

$$\mu_{\text{odd}} = (1.520 \pm 0.001) - (0.184 \pm 0.001) 1/\text{C}, n = 9, R^2 = 1.000 \quad (2)$$

The dipole moment of methylamine (**1**) has been measured in the gas phase to be between 1.24 and 1.35 D[17] that compares well with the value we have calculated, 1.41 D.

Having calculated all amine/ammonium pairs, we have obtained the proton affinities, PA in kJ mol^{-1} (Table 2), and compared them with the ten available experimental values found in the NIST database.[18] The values are linearly related,

$$\text{PA}_{\text{exp}} = -(53 \pm 32) + (1.02 \pm 0.03)\text{PA}_{\text{calc}}, n = 10, R^2 = 0.991 \quad (3)$$

the large intercept is partly due to our values not having been corrected for ZPE effects. With this correction, the intercept become not significant and the correlation slightly improves,