Tetrahedron 67 (2011) 4633–4639

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

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

Dionisia Sanz [a,*], Rosa M. Claramunt [a,*], M. Ángeles García [a], Ibon Alkorta [b], José Elguero [b]

[a] *Departamento de Química Orgánica y Bio-Orgánica, Facultad de Ciencias, UNED, Senda del Rey 9, E-28040 Madrid, Spain*
[b] *Instituto de Química Médica, CSIC, Juan de la Cierva 3, E-28006 Madrid, Spain*

ARTICLE INFO

Article history:
Received 24 February 2011
Received in revised form 12 April 2011
Accepted 15 April 2011
Available online 21 April 2011

Keywords:
Amines
^{13}C NMR
^{15}N NMR
CPMAS
GIAO
DFT study

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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* Corresponding authors. E-mail addresses: dsanz@ccia.uned.es (D. Sanz), rclaramunt@ccia.uned.es (R.M. Claramunt).

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doi:10.1016/j.tet.2011.04.067

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]

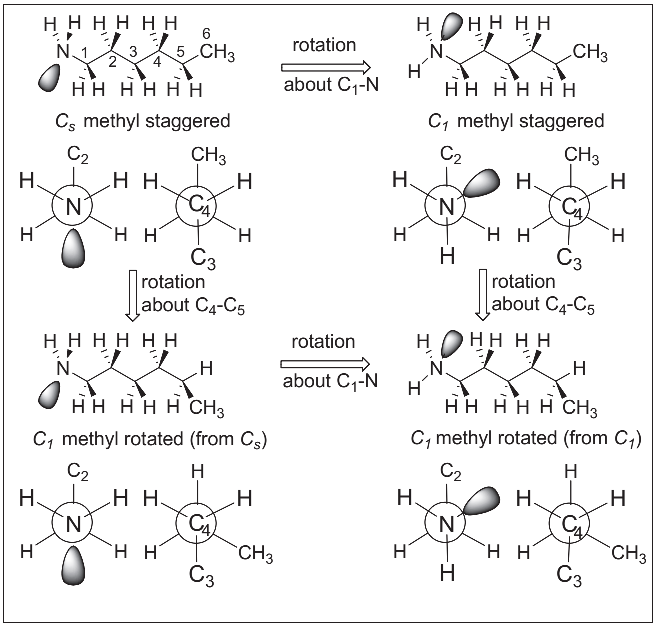


Fig. 1. The four studied conformations in the case of hexylamine (**6**). They correspond to the rotation of the amino group (C_1–N bond) and to the rotation of the C_4–C_5 bond.

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

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]

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		

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

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

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,

$$\mathrm{PA_{exp}} = -(7.5 \pm 29.9) + (1.02 \pm 0.03)\mathrm{PA_{calc}} + \mathrm{ZPE},$$
$$n = 10, R^2 = 0.992 \qquad (4)$$

Note that the experimental value for the C_7 amine, 923.2 kJ mol^{-1}, is certainly wrong (a value about 928 kJ mol^{-1} is expected from the calculations and from internal consistency). We have observed that $\mathrm{PA_{calc}}$ increases linearly with 1/C,

$$\mathrm{PA_{calcd}} = (961.6 \pm 0.2) - (29.1 \pm 0.5)1/\mathrm{C}, n = 18, R^2 = 0.994 \qquad (5)$$

Eq. 5 means that for large number of carbon atoms, the PA of the amine will be close to 961 kJ mol^{-1}.

High-level calculations of the proton affinities of some amines have been carried out by Maksic and Vianello[19] [MP2(fc)/6-311+G(d,p)//B3LYP/6-31G*+ZPVE(B3LYP/6-31G(d))] for NH_{4^+}, **1**H^+, **2**H^+ and **3**H^+=854.0, 897.9 and 908.8 kJ mol^{-1}, by Raabe et al.[20] [ZPE+MP2/6-311++G(d,p)//HF/6-311++G(d,p)] for NH_{4^+}, **1**H^+, **2**H^+, **3**H^+, **4**H^+ and **5**H^+=856.5.0, 900.8 and 912.1, 916.3 and 918.8 kJ mol^{-1}, and by Vianello et al.[21] [ROMP2(fc)/6-311+G(d,p)//B3LYP/6-31G(d)] for NH_{4^+} and **1**H^+, **2**H^+=853.5 and 899.1 kJ mol^{-1}.

Note finally that the rotation of the amino group from C_s to C_1 produces a very low increase in energy, about 0.4 kJ mol^{-1}, but that the rotation of the C–C(methyl) bond increases the energy by about 3.5–4 kJ mol^{-1}, i.e., the first one should be able to compete with the C_s but not so, or much less, the second one.

2.2. NMR in solution. Neutral molecules (amines)

The GIAO/B3LYP/6-311++G(d,p) calculated absolute shieldings (σ, ppm) have been transformed into chemical shifts (δ, ppm) by means of two empirical equations that we have established using a large and diversified collection of data:[22]

$$\delta^{13}\mathrm{C(ppm)} = 175.7 - 0.963\sigma^{13}\mathrm{C\,ppm} \qquad (6)$$

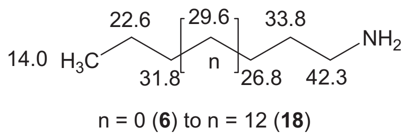
$$\delta^{15}\mathrm{N(ppm)} = -152.0 - 0.946\sigma^{15}\mathrm{N\,ppm} \qquad (7)$$

2.2.1. ^{15}N NMR. We have tried a multiple regression to determine the contributions of the C_s and C_1 conformations to the experimental chemical shifts (Table 3), of the form:

$$\delta^{15}\mathrm{N_{exp.}} = a\delta^{15}\mathrm{N_{calc}}C_s + b\delta^{15}\mathrm{N_{calc}}C_1 \qquad (8)$$

The result is highly satisfactory since we found a=0.755 and b=0.245 (n=17, R^2=1.000), that is, $a+b$=1.000. Having tried this kind of models many times, in general, $a+b$ are, at the best, close to 1 but sometimes one of them is negative, which is devoid of physical meaning. Eq. 8 means that the all-trans C_s conformation is predominant but that there is about 25% of a conformation where the amino group is rotated (see Fig. 1). Actually, since there are two C_1 conformers (*gauche* and *gauche′*) it results that there is 75.5% C_s, 12.25% C_1 *gauche*, 12.25% C_1 *gauche′*, which is fairly consistent with the energy results (Table 1).

2.2.2. ^{13}C NMR. Our attempts to use equations similar to Eq. 8 but with four terms corresponding to the four conformations represented in Fig. 1 failed. Table 3 results show that from **6** to **18** there is a regular trend that can be summarized like this (values in ppm):



n = 0 (**6**) to n = 12 (**18**)

Table 3

^{15}N and ^{13}C NMR chemical shifts of neutral amines in $CDCl_3$ (δ, ppm). Homologies: yellow near the NH_2; blue near the CH_3

Comp.	N	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}	C_{16}	C_{17}	C_{18}
1	−377.3	28.3 (Me)																	
2	−355.4	36.3	18.9 (Me)																
3	−358.0	44.12	26.85	11.22 (Me)															
4	−357.5	41.88	35.98	19.91	13.85 (Me)														
5	−357.5	42.21	33.54	29.04	22.49	14.00 (Me)													
6	−357.5	42.23	33.82	26.51	31.66	22.58	13.96 (Me)												
7	−357.5	42.23	33.86	26.80	29.11	31.79	22.55	13.99 (Me)											
8	−357.5	42.18	33.81	26.80	29.19	29.37	31.73	22.54	13.95 (Me)										
9	−357.5	42.19	33.82	26.78	29.16	29.48	29.40	31.76	22.53	13.93 (Me)									
10	−357.5	42.22	33.85	26.82	29.24	29.50	29.56	29.44	31.82	22.58	13.99 (Me)								
11	−357.5	42.24	33.88	26.85	29.28	29.57	29.46	29.57	29.59	31.85	22.62	14.03 (Me)							
12	−357.5	42.25	33.88	26.85	29.29	29.47	29.57	29.58	29.62	29.59	31.86	22.62	14.03 (Me)						
13	−357.5	42.25	33.88	26.85	29.29	29.57	29.59	29.61	29.59	29.63	29.47	31.86	22.62	14.03 (Me)					
14	−357.5	42.25	33.89	26.85	29.30	29.62	29.60	29.58	29.63	29.60	29.64	29.47	31.87	22.63	14.03 (Me)				
15	−357.5	42.22	33.83	26.85	29.30	29.62	29.47	29.60	29.63	29.60	29.64	29.58	29.63	31.87	22.63	14.03 (Me)			
16	−357.5	42.29	33.92	26.88	29.33	29.60	29.65	29.62	29.62	29.64	29.66	29.66	29.66	29.49	31.89	22.65	14.06 (Me)		
18	−357.5	42.29	33.93	26.88	29.33	29.60	29.62	29.66	29.64	29.63	29.65	29.66	29.66	29.66	29.66	29.50	31.89	22.65	14.06 (Me)

^{15}N and ^{13}C data for compounds **1** and **2** are from literature.[4–7,23,24]

The best fit was obtained using dummies (0 absent, 1 present) for carbons C_1, C_2, C_3, C_4 and for the methyl group:

$$\delta^{13}C_{exp.} = -(3.0 \pm 0.3) + (0.940 \pm 0.009)\delta^{13}C_{calc} + (1.04 \pm 0.14)C_1 - (3.51 \pm 0.11)C_2 + (0.61 \pm 0.08)C_3 - (0.23 \pm 0.08)C_4 + (3.09 \pm 0.19)Me, n = 154, R^2 = 0.998 \quad (9)$$

The fact that this equation has a significant intercept, 3.0±0.3 ppm and a slope different from 1.000, means that Eq. 6 is not totally adequate. This is due to the fact that this equation was established using 461 sp, sp^2, sp^3 and aromatic carbon atoms linked to other carbons but also to oxygen and nitrogen atoms, while now we have only sp^3 carbon atoms linked to other sp^3 carbon atoms and one of them to an sp^3 nitrogen atom.

The α (C_1), β (C_2), γ (C_3) and δ (C_4) effects (alternate signs) mean that the C_s conformation alone is not enough to describe this part of the molecule. It is known that the effects of the amino group along an alkyl chain are important and affect the four or five first positions: 29.3 (α), 11.3 (β), −4.6 (γ) and 0.6 ppm (δ).[4,5]

To describe correctly the methyl signal a large correction of +3.1 ppm is necessary. This correction cannot be avoided by introducing the calculation with the rotated methyl group (Fig. 1). However, the differences between experimental values and calculated ones (excluding **1** and **2**) are −0.84 (75% C_s to 25% C_1), +1.15 (75% C_s Me rotated to 25% C_1 Me rotated) and 0.16 ppm (an average of the two preceding ones). Thus, the rotation of the methyl is implicated in the anomaly of the chemical shifts for the terminal methyl groups.

The two worse points are carbons C_1 of methylamine (**1**), exp. 28.30, fitted 28.85, residual −0.55 ppm and C_2 of ethylamine (**2**), exp. 18.90, fitted 17.98, residual +0.92 ppm, both methyl groups and both from the literature (DMSO-d_6 instead of $CDCl_3$).[4–6,23]

2.3. NMR in solution. Protonated molecules (ammonium cations in CF_3CO_2H solution)

In the case of protonated amines (Table 4), there is only a possible conformation for the $-NH_3^+$ group, but it remains the problem of the methyl group as in neutral amines.

2.3.1. ^{15}N NMR. We have tried two models, one using C_s (the major conformation), Eq. 10, and another using a linear combination of 75.5% of C_s and 24.5% of C_1 for the amines, Eq. 11, together with a dummy (0 for amines, 1 for ammonium cations) both yielding similar results in what R^2 is concerned:

$$\delta^{15}N_{exp} = (1.002 \pm 0.004)\delta^{15}N_{calc} - (1.55 \pm 0.20)cation, n = 34, R^2 = 1.000 \quad (10)$$

$$\delta^{15}N_{exp} = (1.000 \pm 0.004)\delta^{15}N_{calc} - (2.31 \pm 0.19)cation, n = 34, R^2 = 1.000 \quad (11)$$

Note that the values for **1** and **2** are from the literature (hydrochlorides in methanol solution).[7,24]

2.3.2. ^{13}C NMR. We have tried an equation (Eq. 12) similar to that used for neutral amines (Eq. 9):

$$\delta^{13}C_{exp} = -(6.0 \pm 0.6) + (1.00 \pm 0.02)\delta^{13}C_{calcd} - (4.8 \pm 0.3)C_1 + (0.1 \pm 0.1)C_2 + (1.5 \pm 0.2)C_3 - (0.4 \pm 0.1)C_4 + (3.3 \pm 0.3)Me, n = 154, R^2 = 0.996 \quad (12)$$

Table 4
^{15}N and ^{13}C NMR chemical shifts of protonated amines in TFA (*δ*, ppm). Homologies: yellow near the NH_3^+; blue near the CH_3

Comp.	N	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}	C_{16}	C_{17}	C_{18}
1H^+	−361.4	24.4 (Me)																	
2H^+	−346.7	35.0	12.9 (Me)																
3H^+	−349.7	42.63	19.66	7.96 (Me)															
4H^+	−349.1	40.74	28.15	17.88	10.66 (Me)														
5H^+	−349.1	41.02	26.83	25.92	20.54	11.04 (Me)													
6H^+	−349.1	41.39	26.56	24.81	30.11	21.22	11.60 (Me)												
7H^+	−349.1	41.07	26.26	24.75	27.28	30.19	21.04	11.43 (Me)											
8H^+	−349.1	40.92	26.37	24.86	27.70	27.62	30.46	21.24	11.77 (Me)										
9H^+	−349.1	41.03	26.25	24.77	27.83	27.60	27.93	30.55	21.22	11.60 (Me)									
10H^+	−349.1	40.99	26.22	24.75	27.95	27.57	28.10	27.95	30.62	21.24	11.62 (Me)								
11H^+	−349.1	40.96	26.19	24.73	28.00	27.55	27.93	28.12	28.22	30.65	21.24	11.62 (Me)							
12H^+	−349.1	41.09	26.32	24.86	28.19	27.69	28.40	28.43	28.26	28.07	30.81	21.39	11.77 (Me)						
13H^+	−349.1	41.00	26.25	24.79	28.15	27.63	28.33	28.41	28.41	28.20	28.01	30.77	21.33	11.72 (Me)					
14H^+	−349.1	41.00	26.25	24.81	28.19	27.65	28.23	28.36	28.47	28.43	28.47	28.04	30.81	21.36	11.72 (Me)				
15H^+	−349.1	41.08	26.34	24.90	28.13	27.74	28.30	28.32	28.46	28.53	28.57	28.57	28.60	30.90	21.46	11.85 (Me)			
16H^+	−349.2	41.00	26.27	24.85	28.09	27.69	28.27	28.28	28.42	28.55	28.55	28.55	28.55	28.55	30.87	21.42	11.82 (Me)		
18H^+	−349.2	40.98	26.28	24.87	28.33	27.73	28.33	28.48	28.57	28.62	28.62	28.62	28.64	28.64	28.64	28.64	30.92	21.47	11.90 (Me)

^{15}N and ^{13}C data for compounds **1** and **2** are from literature.[4–7,23,24]
4H^+: $^1J_{NH}$=74.4 Hz, from $^1H-^{15}N$ HMBC spectrum.
6H^+: $^1J_{NH}$=77.9 Hz, from $^1H-^{15}N$ HMBC spectrum.
8H^+: $^1J_{NH}$=74.2 Hz, from $^1H-^{15}N$ HMBC spectrum.

The coefficients are rather different and again a similar correction corresponds to the methyl group. The two worse points are carbons C_1 and C_2 of ethylamine (**2**), exp. 35.0, fitted 37.0, residual −2.0 ppm and exp. 12.9, fitted 11.1, residual +2.8 ppm, both from the literature (hydrochloride in methanol instead of CF_3CO_2H).[23]

2.4. Comparison between neutral and protonated amines

The protonation chemical shift effects, $\Delta\delta=\delta$ (ammonium cations)−δ (neutral amines), obtained using the data of Tables 3 and 4 are reported in Supplementary data. The experimental ^{15}N NMR signals of the cations (compare Tables 3 and 4) are shifted +8.4 ppm from those of the corresponding amines save in the case of methylamine (**1**) where the effect is much larger, +15.9 ppm.[7] These values include the solvent effect, in our case, trifluoroacetic acid, that has been estimated in +2.3 ppm.[14] For phenethylamine and homoveratrylamine effects of +9.9 and 8.8 ppm have been, respectively, reported, when comparing the ^{15}N chemical shifts obtained in $CDCl_3$ with those found in a solution of 5% of CF_3CO_2H in $CDCl_3$.[25]

Concerning ^{13}C chemical shifts, the effect on the methyl group is about −2/−3 ppm save for methylamine (**1**, −3.9 ppm) and ethylamine (**2**, −6.0 ppm). These values agree with previous results.[23] Average values for chain carbons are −1.2 (C_1 α carbon), −7.5 (C_2 β carbon) and −2.2 (C_3 γ carbon), the remaining carbons have always negative and small $\Delta\delta$ values that are mainly due to solvent effects (from $CDCl_3$ to CF_3CO_2H), as were reported for other amines.[8,23,26] The signal of the methyl group in protonated amines, about 11–12 ppm for most of them, is not explained by the GIAO calculations where the effect of the protonation on the methyl group is positive and almost negligible from **5** to **18** ($\leq$1 ppm).

2.5. NMR. Solid-state studies (CPMAS)

We have carried out a search in the Cambridge Structural Database (CSD, refcodes)[27] for the structure of ammonium salts from **14**H^+ to **18**H^+ (Table 5) excluding organometallic anions.

Table 5
X-ray structures and refcodes[27] of ammonium salts from **14**H^+ to **18**H^+ (no data about **17**H^+). Rotation about the indicated bond (the rest all-trans)

Comp.	All-trans[a]	Non all-trans structures
14	Anion: 4-bromocinnamate JEPZAG Anion: 1-carbocyclobutanecarboxylate TOKVAR	Anion from a cholic acid, XIQBAB Torsion in the middle, between C4 and C5
15	Anion: 1-carbocyclobutanecarboxylate TOKVEV	—
16	—	Anion from a cholic acid, XIQBEF Torsion in the middle, between C4 and C5
18	—	Anion: diiodoplumbate,[b] WOLPAP Rotation about two bonds: $C-C-C-NH_3^+$

[a] The all-trans conformations are usually distorted in a kind of corkscrew.
[b] No examples with a non organometallic anion.

None of the data involves trifluoroacetate or hydrochloride anions, so we carried out crystallization experiments without succeeding in obtaining single crystals useful for X-ray determinations. The data reported in Table 5 indicate that for the studied anions both all-trans and rotated conformations in different parts of the alkyl chain were found.

Ammonium trifluoroacetates **14**H^+, **15**H^+, **16**H^+ and **18**H^+ were prepared by dissolving the amine in trifluroacetic acid and evaporating the excess of acid; ammonium hydrochlorides **4**H^+ and **18**H^+ were prepared by adding the stoichiometric amount of aqueous hydrochloric acid (37%) to a methanol solution of **4** and **18**. The CPMAS results are gathered in Table 6.

The ^{13}C $\Delta\delta$ values are similar to those obtained in solution (see Supplementary data) although less regular in part because some signals are splitted, a common phenomenon in CPMAS NMR.[28] The most curious feature is that observed on ^{15}N, while in solution the effect is about +6 ppm [8.4−2.3(solvent effect)≈6 ppm], in the solid state is about +4 ppm for the trifluoroacetates but +15 ppm for the **18**H^+Cl^-.

To understand this apparent anomaly we have prepared **4**H^+Cl^- and recorded its ^{15}N and ^{13}C CPMAS NMR spectra: −332.6 ppm (^{15}N) and 40.16 (C_1), 29.77 (C_2), 20.42 (C_3) and 13.95 ppm (CH_3). The ^{15}N signal is very close to that of **18**H^+Cl^- (−333.2) and in order to explain such large effect, we decided to calculate the absolute shieldings of butylammonium **4**H^+ trifluoroacetate and hydrochloride salts (Fig. 2).

As it can be seen, the counteranion plays an important role and satisfactorily explains the experimental results.

3. Conclusions

For the first time a set of linear aliphatic amines, from C1 to C18, has been studied experimentally by NMR, mainly ^{15}N but also ^{13}C, and theoretically using DFT calculations. The conjunction of both techniques is necessary to reach conclusions about the conformation of neutral amines (75% of C_s and 25% of C_1 conformations), the anomaly of the terminal methyl groups and the protonation effects. GIAO theoretical calculations reproduce fairly well the influence of the counteranion on the ^{15}N chemical shifts of ammonium salts in the solid state.

4. Experimental part

4.1. General

Melting points were determined under a microscope *Axiolab Zeiss* with a *TMS-92-Linkan* heating stage and are uncorrected. Samples of linear amines C3–C15 were purchased from Aldrich and used without further purification: propylamine (bp 48 °C), butylamine (bp 78 °C), amylamine (bp 104 °C), hexylamine (bp 131–132 °C), heptylamine (bp 154–156 °C), octylamine (bp 175–177 °C), nonylamine (bp 201 °C), decylamine (mp 12–14 °C), undecylamine (mp 15–17 °C), dodecylamine (mp 27–29 °C), tridecylamine (mp 30–32 °C), tetradecylamine (mp 38–40 °C) and pentadecylamine (mp 35–37 °C).

The ammonium trifluoroacetates **14**H^+, **15**H^+, **16**H^+ and **18**H^+ were prepared by dissolving 300 mg of the amine in 2 mL of trifluroacetic acid and then the excess of acid was evaporated at normal pressure at room temperature: **14**H^+ (mp 78–81 °C), **15**H^+ (mp 81–82 °C), **16**H^+ (mp 85–86 °C) and **18**H^+ (mp 88–89 °C). Two hydrochlorides **4**H^+ (mp 214 °C, lit. Mp 214 °C[29]) and **18**H^+ (mp 161.5–162.5 °C, lit. Mp 159–161 °C[30]) were prepared by adding the stoichiometric amount of aqueous hydrochloric acid (37%) to a methanol solution of **4** and **18**. Compound **18**H^+Cl^- precipitated from the solution as a crystalline solid and was used without further purification. Compound **4**H^+Cl^- was obtained as a white solid only after evaporation under reduced pressure of the methanolic solution, redissolved again three times in methanol and the solvent evaporated to dryness.

4.2. NMR

Solution NMR spectra were recorded on a Bruker DRX 400 (9.4 T, 400.13 MHz for ^1H, 100.62 MHz for ^{13}C and 40.56 MHz for ^{15}N) spectrometer with a 5-mm inverse-detection H-X probe equipped

Table 6
^{15}N and ^{13}C NMR chemical shifts of neutral amines,[a] ammonium trifluoroacetates and $\Delta\delta$ protonation effects in the solid state

Comp.	N	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}	C_{16}	C_{17}	C_{18}
Neutral																			
14	−348.7	43.3	38.9	29.0	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	33.6	24.0	14.3 (Me)				
15	−348.8	43.4	39.0	29.1	29.7	32.7	32.7	32.7	32.7	32.2	32.2	32.7	32.2	33.9	24.1	14.5 (Me)			
		42.8														14.0 (Me)			
16[b]	−347.7	43.4	39.0	29.0	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	33.7	24.0	14.4 (Me)		
18[b]	−347.8	43.4	39.0	29.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	32.2	33.7	24.0	14.4 (Me)
Cations																			
14H^+	−343.9	39.8	30.6	28.4	28.9	33.0	33.0	33.0	33.0	33.0	33.0	33.0	34.5	24.7	13.9 (Me)				
	−345.0			27.7										24.2					
15H^+	−343.4	39.8	31.6	28.4	29.1	32.6	32.6	32.6	32.6	32.6	32.6	32.6	32.6	34.4	24.1	14.6 (Me)			
	−345.1			27.6												14.2 (Me)			
16H$^+$	−344.0	40.0	32.4	28.6	29.4	33.4	33.4	33.4	33.4	33.4	33.4	33.4	33.4	33.4	34.7	25.1	14.4 (Me)		
	−345.1	39.1		27.8												24.4	14.1 (Me)		
	−345.9																13.6 (Me)		
18H^+	−343.8	39.9	32.2	28.4	29.2	33.2	33.2	33.2	33.2	33.2	33.2	33.2	33.2	33.2	33.2	33.2	34.6	24.9	14.2 (Me)
	−345.0	38.8		27.7															13.8 (Me)
	−345.9																		13.3 (Me)
18H^{+}[c]	−333.2	39.6	30.9	28.9	33.7	33.7	33.7	33.7	33.7	33.7	33.7	33.7	33.7	33.7	33.7	33.7	34.9	24.9	15.3 (Me)
				28.1															
Protonation effects[d]																			
14	+4.3	−3.5	−8.3	−1.0	−3.3	+0.8	+0.8	+0.8	+0.8	+0.8	+0.8	+0.8	+0.9	+0.5	−0.4 (Me)				
15	+4.6	−3.3	−7.4	−1.1	−0.6	−0.1	−0.1	−0.1	−0.1	−0.1	−0.1	−0.1	+0.4	+0.5	0.0	+0.2 (Me)			
16	+2.7	−3.9	−6.6	−0.8	−2.8	+1.2	+1.2	+1.2	+1.2	+1.2	+1.2	+1.2	+1.2	+1.2	+1.0	+0.8	−0.4 (Me)		
18	+2.9	−4.0	−6.8	−1.2	−3.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+1.0	+0.9	+0.9	−0.6 (Me)
18[c]	+14.6	−3.8	−8.1	−0.7	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.5	+1.2	+0.9	+0.9 (Me)

[a] Amines **1**–**13** are or become liquids into the zirconia rotor at 298 K.
[b] Values taken from Ref. 11.
[c] Hydrochloride.
[d] $\Delta\delta=\delta$(ammonium cations)$-\delta$(neutral amines), when several values were observed in the spectrum $\Delta\delta$ has been calculated from the average value.

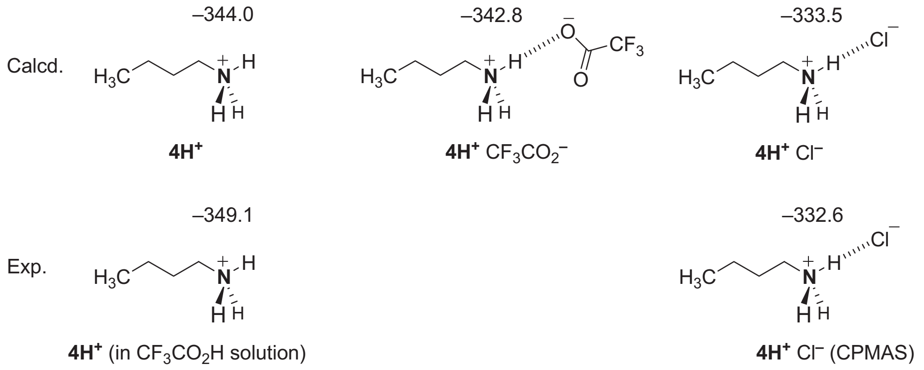


Fig. 2. Protonation and phase effects in butylammonium salts.

with a z-gradient coil, at 300 K. Chemical shifts (δ in ppm) are given from internal solvent, $CDCl_3$ 7.26 for ^1H and 77.0 for ^{13}C, and for ^{15}N NMR nitromethane (0.00) was used as external standard. The spectra done in TFA solution was recorded with a lock capillary with DMSO-d_6 2.49 for ^1H and 39.5 for ^{13}C. Typical parameters for ^1H NMR spectra were spectral width 3500 Hz and pulse width 7.5 µs at an attenuation level of 0 dB. Typical parameters for ^{13}C NMR spectra were spectral width 7 kHz, pulse width 10.6 µs at an attenuation level of −6 dB and relaxation delay 2 s; WALTZ-16 was used for broadband proton decoupling; the FIDS were multiplied by an exponential weighting (lb=2 Hz) before Fourier transformation. 2D inverse proton detected heteronuclear shift correlation spectra, (^1H–^{13}C) gs-HMQC, (^1H–^{13}C) gs-HMBC, (^1H–^{15}N) gs-HMQC, (^1H–^{15}N) gs-HMBC were acquired and processed using standard Bruker NMR software and in non-phase sensitive mode. Gradient selection was achieved through a 5% sine truncated shaped pulse gradient of 1 ms. Selected parameters for (^1H–^{13}C) gs-HMQC and gs-HMBC spectra were spectral width 3500 Hz for ^1H and 7000 Hz for ^{13}C, 1024×256 data set, number of scans 2 (gs-HMQC) or 4 (gs-HMBC) and relaxation delay 1 s. The FIDs were processed using zero filling in the F1 domain and a sine-bell window function in both dimensions was applied prior to Fourier transformation. In the gs-HMQC experiments GARP modulation of ^{13}C was used for decoupling. Selected parameters for (^1H–^{15}N) gs-HMBC and (^1H–^{15}N) gs-HMQC spectra were spectral width 3500 Hz for ^1H and 12.5 kHz for ^{15}N, 1024×256 data set, number of scans 4, relaxation delay 1 s, 37–60 ms delay for the evolution of the ^{15}N–^1H long-range coupling. The FIDs were processed using zero filling in the F1 domain and a sine-bell window function in both dimensions was applied prior to Fourier transformation.

Solid-state ^{13}C (100.73 MHz) and ^{15}N (40.60 MHz) CPMAS NMR spectra have been obtained on a Bruker WB 400 spectrometer at 300 K using a 4 mm DVT probehead. Samples were carefully packed in a 4-mm diameter cylindrical zirconia rotor with Kel-F end-caps. Operating conditions involved 3.2 µs 90° 1H pulses and decoupling field strength of 78.1 kHz by TPPM sequence. ^{13}C spectra were originally referenced to a glycine sample and then the chemical shifts were recalculated to the Me_4Si [for the carbonyl atom

δ(glycine)=176.1 ppm] and ^{15}N spectra to $^{15}NH_4Cl$ and then converted to nitromethane scale using the relationship: $\delta\ ^{15}N(MeNO_2)=\delta ^{15}N(NH_4Cl)-338.1$ ppm. Typical acquisition parameters for ^{13}C CPMAS were: spectral width, 40 kHz; recycle delay, 5–15 s; acquisition time, 30 ms; contact time, 2 ms; and spin rate, 12 kHz. Typical acquisition parameters for ^{15}N CPMAS were: spectral width, 40 kHz; recycle delay, 15 s; acquisition time, 30 ms; contact time, 2–5 ms; and spin rate, 6 kHz.

4.3. Computational details

Calculations were carried out at the B3LYP/6-31G* level[31,32] using the Gaussian 03 programs.[33] Frequency calculations at the same level were carried out to verify that the structures correspond to energy minima (no imaginary frequencies). A further geometry optimization has been carried out at B3LYP/6-311++G(d,p) computational level. These geometries have been used for the calculations of the absolute chemical shieldings with the GIAO method[34] at the same computational level. No other computational methods were used since GIAO/B3LYP/6-311++G(d,p) afforded convenient results in previous works,[22,25,35] but we are aware that depending on the nucleus other possibilities could be preferable.[36]

Acknowledgements

This work was carried out with financial support from the Ministerio de Ciencia e Innovación (CTQ2010-16122 and CTQ2009-13129-C02-02) and Comunidad Autónoma de Madrid (Project MADRISOLAR2, ref. S2009/PPQ-1533). Thanks are given to the CTI (CSIC) for allocation of computer time.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.04.067.

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