CMST 9(1) 147-161 (2003)
DOI:10.12921/cmst.09.01.147-161

COMPUTATIONAL METHODS IN SCIENCE AND TECHNOLOGY **9(1-2)**, 147-161 (2003)

THEORETICAL STUDIES OF ^{1}H, ^{13}C AND ^{15}N NMR SPECTRA FOR MODEL STRUCTURES OF N-METHYLMORPHOLINIUM AND N-METHYLPIPERIDINIUM BETAINES*

DARIA WIECZOREK[1], ZOFIA DEGA-SZAFRAN[2], MIROSŁAW SZAFRAN[2],
HENRYK SZYMUSIAK[1], RYSZARD ZIELIŃSKI[1], RENATA GŁEMBALSKA[2]

[1] Department of Technology and Environmental Protection, Poznan University of Economics,
Aleja Niepodległości 10, 60-967 Poznan, Poland
e-mail: ktos@novci1.ae.poznan.pl

[2] Faculty of Chemistry, Adam Mickiewicz University
Grunwaldzka 6, 60-780 Poznan, Poland
e-mail: degasz@amu.edu.pl

(Rec. 7 November 2003)

Abstract: Screening constants for model structures of linear and twisted conformers of N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MPBn) with the alkyl spacer (n) containing 1-5 methylene groups calculated by the GIAO/B3LYP/6-31+G(d, p) are reported and analyzed. Linear correlations between the experimental ^{1}H and ^{13}C chemical shifts and computed absolute shielding constants have been obtained. These results suggest that in solution twisted conformers dominate. The linear correlations between the calculated ^{15}N absolute shielding constants for MMBn and MPBn suggest that the two kinds of betaines have similar structures.

1. INTRODUCTION

Nuclear magnetic resonance (NMR) is a very important tool in studying microscopic phenomena in physics, chemistry, material science, biology, and medicine. Determination of spectral parameters using the quantum-chemistry methods helps in the assignment and interpretation of the experimental data. Electronic structure calculations provide experimentally unavailable information, allow detailed studies of microscopic mechanisms, verification of difficult experiments, and *a priori* examination of "what if" situations [1]. Calculations of NMR parameters are essential in areas ranging from high T_c superconductors to the hydrogen bonded systems and backbone conformation of proteins. The NMR shielding tensor $\boldsymbol{\sigma}_K$ can be reliably computed even for large molecules, whereas calculations of the spin-spin coupling tensor $\mathbf{J}_{KL}$ are still limited to small systems. These quantities are easily computable with *ab initio* theories and density functional theory (DFT) methods [2-4]. However, when using quantum-chemical calculations, three important features that complicate the comparison with experiment [1,4,5] are neglected: (a) electron-nucleus hyperfine interactions that take place in the region close to the nuclei, where the electrons move fast, make the NMR parameters particularly susceptible to relativity, both scalar and spin-orbit interactions; (b) thermal averaging over rovibrational motion that should be made to allow a direct comparison with experiment and (c) such phenomena as

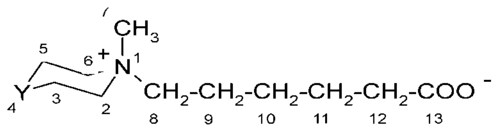
---

* Dedicated to the memory of Professor Jacek Rychlewski

intermolecular interactions, solvation and matrix effects that influence molecular properties of the species studied.

Betaine compounds are zwitterions with two formally charged carboxylate and ammonium groups separated by at least one sp^3 carbon atom. The term betaine, which initially denoted trimethylated derivative of glycine, $[Me_3N^+\text{-}CH_2\text{-}COO^-]$, actually referes to all the internal quaternary ammonium, sulphonium and phosphonium zwitterions. Betaines are widely used in biology, medicine and pharmacy [6]. It is also known that some crystals of many betaine complexes exhibit phase transitions with ferroelectric, antiferroelectric and ferroelastic behavior [7]. Most of the physical properties exhibited by surfactant molecules in aqueous solutions depends on the dominant conformers. Therefore, theoretical studies on possible geometry of surfactant molecules provide a valuable source of information that allows a confirmation of the experimentally suggested structure of the molecules in a given medium.

In this work we report results of theoretical studies on NMR spectroscopy of some model structures of N-methylmorpholinium betaines (MMBn) and N-methylpiperidinium betaines (MPBn) in which carboxylate and ammonium groups are separated by a spacer (*n*) containing 1-5 methylene groups. Chemical structures and the numbering system of the betaines with 5 methylene groups (MMB5 and MPB5) are given in Scheme 1. We compare the results of our theoretical studies with the experimental ^{1}H and ^{13}C NMR spectra recorded for these compounds. The problem of prediction of accurate NMR chemical shifts and interpretion of the data using quantum chemical calculations has attracted considerable attention in recent years. It should be noted, however, that these NMR parameters are considerably affected by the chemical environment, i.e., the molecular conformation and the interactions with solvent molecules [4]. There are only a few publications, to our knowledge, on successful application of the GIAO approach to dipolar molecules such as cationic surfactants or betaines [8]. Therefore, in this work we apply this technique as a tool to compute theoretical values of shielding constants for model structures and correlate the values obtained in such a way with the experimental ones determined for two series of amphoteric surfactants: MMBn and MPBn having the carboxyalkyl spacer (n) containing from 1 to 5 methylene groups.



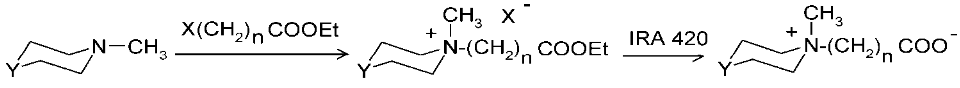
MMB5, Y=O
MPB5, Y=CH_2

Scheme 1.

2. EXPERIMENTAL

Compounds

N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts having carboxyalkyl groups of methyl, propyl, butyl and pentyl (MMBn) were obtained from N-methylmorpholine by the method described for N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MPBn) [9] (Scheme 2).



Y= O or CH_2, X = Cl or Br, n = 1-5

Scheme 2.

Measurements

NMR spectra were recorded using a Varian Gemini 300 VT spectrometer operating at 300.07 and 75.46 MHz for ^1H and ^{13}C, respectively. For the proton spectra the pulse width 32°, acquisition time 5 s, FT size 32 K and digital resolution 0.3 Hz per point and for the carbon spectra pulse width 60°, FT size 64 K and digital resolution 0.6 Hz per point were used. The ^1H and ^{13}C spectra were measured in D_2O relative to internal dioxane and recalculated relative to TMS by adding 3.55 ppm and 67.40 ppm, respectively. The 2D spectra were obtained with standard Varian software and the concentration of the sample was 0.3 mol/dm^3.

Computational method

The Becke's three-parameter hybrid functional correlation functional (B3LYP) [10] and two split-valence 6-31G(d) and 6-31+G(d, p) basis sets were employed for full geometry optimizations and NMR isotropic shielding calculations. From several stable model conformers only two of them were taken into further considerations. One of them is the linear conformer in which alkyl chain is strained, which ensures that charged groups are maximally separated and the second one is a nonlinear conformer with twisted alkyl chain where the two charged groups are located at a relatively short distance from each other. In the case of the linear conformers, the geometry optimization procedure was performed using a fixed linear conformation of the alkyl chain, while for twisted conformations the optimization procedure was applied without any geometric restrictions. To spare computer time, the zero-point-energy values were not calculated, assuming negligible error in estimation of relative stability in the pair of model conformers. For each optimized conformers geometry obtained in such a way the NMR shielding tensors were calculated by means of the GIAO approach. The computed GIAO ^1H and ^{13}C isotropic magnetic shielding NMR data were empirically scaled following the procedure given by Forsyth and Sebag [2, 3] to achieve good agreement with experimentally observed δ_H and δ_C chemical shifts. Such a procedure allows elimination of the systematic error in comparing experimental and computed values of shielding constants for TMS. All calculations were performed with the Gaussian 98 program package [11]. Experimental values of both ^1H and ^{13}C NMR chemical shifts used in this work for MPBn were previously published [12], while the corresponding data for MMBn were determined in our laboratory.

3. RESULTS

3.1. Geometry

The geometry, molecular shape and conformation of the molecule studied are determined by equilibration forces operating through covalent bonds (i.e. 'skeletal' structure) and the so-called 'non-bonded interactions' (i.e. short-range and long-range through space interactions between groups of atoms or local charges within the molecules) as well as through interactions of the molecules with their local environment [13,14]. In the case of betaines, which are zwitterionic molecules, the electrostatic interactions between the charged groups of atoms are particularly important. Due to nonspecific and nondirectional character of coulombic interactions the conformations of a single free betaine molecule and that in crystals are usually different [15].

From crystallographic studies it is known that in anhydrous MPB1, the piperidine ring appears in chair conformation with CH_3 group in the axial position and CH_2COO" group in the equatorial position [16]. The same experimental data for the morpholine analogue are not known. Good quality DFT calculations are the only source of molecular structures for the series of MMBn and MPBn with different spacers. In our previous study we have compared the X-ray data to those calculated at B3LYP/6-311++G(d, p) level for MPB1 and the PM3 method for MPB4, finding avery good agreement [13, 17]. In this work we have found that our geometry optimizations performed in a lower 6-31+G(d, p) basis set give very similar results and, therefore they are more practical for calculations for larger molecules. We consider only chair conformations of the morpholine ring with the CH_3 group in the axial position, as it was found experimentally for MPB1 [16] and for MMB1 HCl [18], and $CH_2CH_2CH_2CH_2CH_2COO$~ group in the equatorial position.

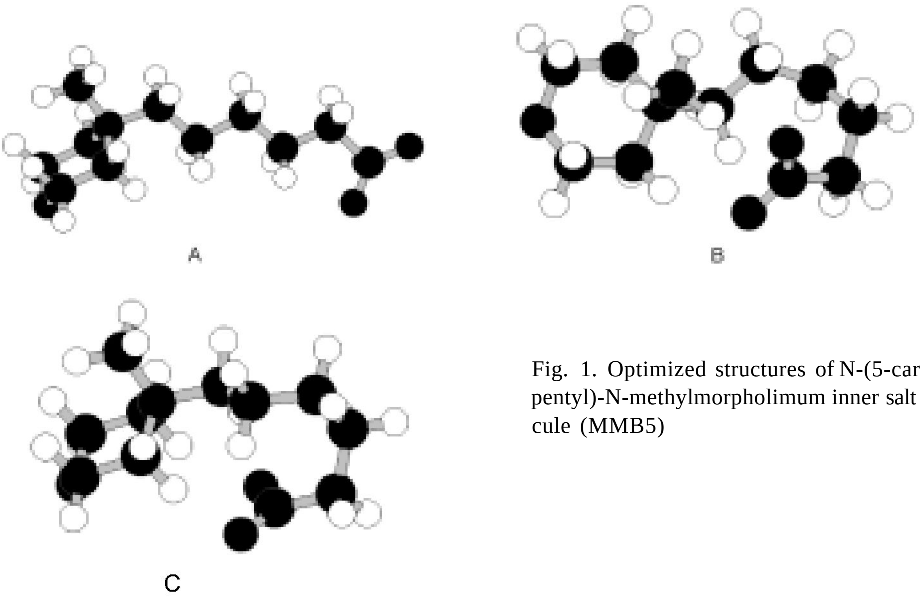


Fig. 1. Optimized structures of N-(5-carboxypentyl)-N-methylmorpholimum inner salt molecule (MMB5)

It was found that the optimization of the geometry of betaines leads to two types of stable conformers depending on the number of CH_2 groups between the nitrogen center of the molecule and the carboxy group. Figure 1 shows the structures of the three conformers, one linear (A) and two twisted (B, C) of MMB5. Generally, in the linear structures A the charged parts of molecule are separated by the longest distance between them. In the structures B, the terminal carboxy group approaches the ammonium group in the plane parallel to the ring plane, while in the structures C, from the side opposite to the N-CH_3 group. The B and C conformers are nearly equal in energy, but B one is the mostly stabile due to the nearest distance between charged parts of the molecule (Table 1).

Table 1. Selected properties of optimized structures of MMBn and MPBn computed by the B3LYP/6-31+G(d, p) method. Symbols: n - number of carbon atoms in the spacer, μ - dipole moment [D], N-C7, N-C8 - bond length [Å], N...O - interatomic distance between N atom and the nearest O atom in the COO group [Å], C7-N-C8-C9 torsion angle [deg]; E-energy [a.u]; E (rel), [kcal/mol]

n	Conformer	E	E (rel)	μ	N···O	N-C7	N-C8	C7-N-C8-C9
				MMBn				
1	Linear	–554.980926	1.6	11.86	2.903	1.500	1.543	180
1	Twisted #	–554.983362	0	11.08	2.866	1.509	1.539	60.7
2	Linear	–594.273259	10.6	17.31	4.168	1.501	1.571	180
2	Twisted	–594.290164	0	11.86	3.296	1.510	1.552	44.3
3	Linear	–633.572476	18.7	23.03	5.177	1.502	1.562	180
3	Twisted	–633.602020	0	12.35	3.663	1.512	1.543	44.3
4	Linear	–672.874170	27.7	29.20	6.543	1.505	1.554	180
4	Twisted	–672.918184	0	11.66	3.680	1.514	1.541	49.6
5	Linear	–712.180410	38.9	35.16	7.693	1.505	1.552	180
5	Twisted	–712.242381	0	9.91	3.403	1.514	1.543	40.2
5	Twisted #	–712.240608	1.2	11.42	3.444	1.499	1.545	87.7
				MPBn				
1	Linear	–519.097321	0	11.98	2.903	1.499	1.540	180
1	Twisted #	–519.097140	0.1	12.53	2.885	1.508	1.539	60.8
2	Linear	–558.389196	8.6	18.36	4.180	1.500	1.565	180
2	Twisted	–558.403532	0	12.18	3.472	1.500	1.553	43.2
3	Linear	–597.689815	16.8	23.36	5.181	1.500	1.564	180
3	Twisted #	–597.716559	0	12.32	3.696	1.502	1.542	161.2
4	Linear	–636.990538	25.7	29.37	6.312	1.504	1.550	180
4	Twisted #	–637.032876	0	11.98	3.636	1.497	1.544	89.8
5	Linear	–676.298555	36.9	35.61	7.678	1.504	1.548	180
5	Twisted #	–676.357413	0	10.72	3.453	1.497	1.548	89.1

Note: (#) - twisted conformer C (see Fig. 1).

The relationships between relative electronic energies [ΔE] computed for morpholinium and piperidinium betaines and the number of methylene groups in the spacer are shown in Fig. 2. Two parallel straight lines with positive slopes indicate that the increase in the number of carbon atoms in the spacer leads to more stable structures in both series. We have found that the twisted forms of betaines with morpholinium moiety are less stable by ca. 2.0 kcal/mol than the corresponding piperidinium ones. Basic molecular characteristics of the optimized structures of MMBn and MPBn in both linear and twisted forms are given in Table 1.

We can regard the numerical value of the torsion angle C7-N1-C8-C9 (Table 1) as indicative of the geometry of the molecules. It is seen that for both MMBn and MPBn series the value of the torsion angle strongly depends on the spatial conformation of the betaine molecules. For the twisted conformer B (Fig. 1) with $n > 1$ the value of the torsion angle oscillates around ca. 45°, while for conformers C it is close to 90°, being independent of the structure of the heterocyclic ring (Y = O for MMBn and Y = CH_2 for MPBn). Comparison of other geometry data for MMBn and MPBn indicates a similar spatial structure of the compounds belonging to the two series. The only difference is predicted for the value of the dipole moment (μ) of the molecules with slightly higher values of μ for piperidinium derivatives than for morpholinium ones, as long as the same spatial conformations of the compounds are compared.

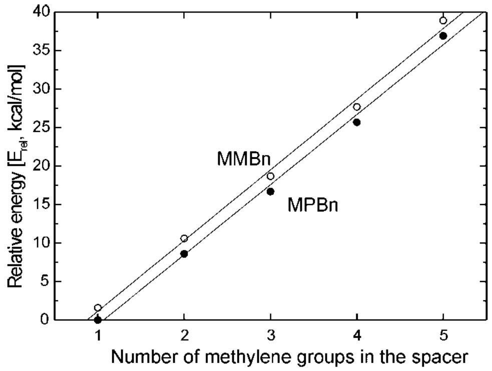


Fig. 2. Reative stability of the twisted and linear conformer of MMBn (o) and MPBN (• symbols) as computed by the GIAO/B3LYP/6-31+G(d, p) method

3.2. Comparison of computed shieldings with experimental data

3.2.1. Carbon-13 chemical shifts

In most studies of theoretical shieldings, a comparison is made either of experimental absolute shieldings to calculated absolute shieldings are compared, or experimental chemical shifts to chemical shifts calculated from absolute shieldings, by subtraction of a calculated reference. An inherent problem of using a shielding calculated for a reference compound for prediction of chemical shifts was reported in Ref. [19]. The problem is that any error in the calculated shift of the reference compound will be reflected in all of the derived shifts. The second possibility is that the relative order of shifts can be predicted accurately, but the shifts may need scaling in order to achieve quantitative agreement with experimental data. Forsyth and Sebag [2] proposed an empirical scaling procedure for the GIAO shielding calculations and used linear regression data to provide empirical scaling for theoretical isotropic shieldings in order to achieve more closely the level of predictable accuracy needed for practical applications of computed ^{13}C chemical shifts. The scaled calculations yield a much more practical level of error in computed chemical shifts than direct calculations where the only adjustment is subtraction of a fixed reference. Taking into account the electron correlation in the B3LYP calculations should lead to better relative NMR shieldings than those obtained by much simpler Hartree-Fock calculations. The set of compounds chosen by us includes 10 derivatives times two conformations, altogether 20 calculations. The experimental ^{13}C chemical shifts were compared here with the theoretical shieldings obtained by means of the GIAO B3LYP calculations performed at the 6-31+G(d, p) level.

Table 2. The experimental (ppm, in D_20) and computed ^{13}C chemical shifts (ppm) for linear and twisted conformers of N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MMBn)

n		C2,6	C3,5	C4	C7	C8	C9	C10	C11	C12	COO
						MMBn					
1	Exp	61.34	60.84	–	48.51	65.14	–	–	–	–	169.4
	Linear	64.5	57.5	–	44.2	71.7	–	–	–	–	167.6
	Twisted #	63.3	61.2	–	38.7	73.6	–	–	–	–	166.1
3	Exp	61.22	60.43	–	47.74	65.19	34.27	19.96	–	–	181.3
	Linear	62.4	56.3	–	43.9	82.3	30.2	20.4	–	–	176.6
	Twisted	62.5	59.7	–	37.3	77.0	25.0	23.0	–	–	177.2
4	Exp	61.25	60.43	–	47.67	65.59	21.63	23.39	37.55	–	183.2
	Linear	62.2	56.2	–	44.1	80.8	20.7	23.4	37.4	–	179.4
	Twisted	59.55	58.2	–	38.2	73.3	16.2	16.8	35.1		178.9
5	Exp	60.38	61.23	–	47.64	65.83	21.54	26.07	26.23	38.06	184.2
	Linear	56.2	61.5	–	43.8	78.4	20.9	26.1	29.6	38.1	182.1
	Twisted #	56.4	62.6	–	43.1	73.4	19.6	27.6	24.4	39.0	181.9
						MPBn					
1	Exp[1]	62.45	20.40	21.40	49.16	64.20	–	–	–	–	177.30
	Linear	62.8	20.3	19.6	46.6	73.9	–	–	–	–	175.1
	Twisted #	64.6	18.8	21.8	40.4	76.2	–	–	–	–	172.7
2	Exp[1]	62.17	20.38	21.34	48.22	59.71	39.01	–	–	–	177.55
	Linear	59.9	20.6	21.5	47.1	82.9	28.5	–	–	–	169.8
	Twisted	59.6	20.6	18.2	46.6	73.8	39.6	–	–	–	174.6
3	Exp[1]	63.32	20.32	21.38	48.60	62.27	28.28	34.50	–	–	181.27
	Linear	60.3	20.1	20.4	46.9	83.8	23.8	33.5	–	–	174.4
	Twisted #	61.0	20.5	16.1	46.7	75.5	22.5	38.9	–	–	177.5
4	Exp[1]	63.76	20.32	21.40	48.51	62.43	31.23	23.21	37.53	–	183.09
	Linear	59.0	18.6	19.0	45.5	79.2	23.6	24.2	41.5	–	179.2
	Twisted #	58.5	21.3	20.9	43.0	74.7	19.9	21.3	39.6	–	180.2
5	Exp[1]	63.97	20.32	21.42	48.48	62.59	31.18	26.00	26.00	38.11	184.04
	Linear	60.2	18.3	18.5	46.8	78.8	24.2	28.9	32.6	40.2	179.4
	Twisted #	61.3	21.3	20.9	43.0	73.8	39.2	19.6	28.2	24.2	182.0

[1] data taken from Ref. [12],# — twisted conformer C (see Fig. 1)

Table 3. ${}^{13}C$ screening constants (ppm) for N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MMBn)

n	Conformer	C2,6	C3,5	C4	C7	C8	C9	C10	C11	C12	COO
						MMBn					
1	Linear	135.9 136.0	129.9 129.9	–	147.5	123.6	–	–	–	–	40.4
	Twisted #	129.7 133.4	129.0 130.3	–	151.1	120.8	–	–	–	–	40.5
2	Linear	136.11 136.13	130.4 130.4	–	146.4	114.1	162.9	–	–	–	38.9
	Twisted	128.8 130.9	128.7 129.9	–	152.8	115.7	153.1	–	–	–	29.1
3	Linear	135.8 135.8	130.6 130.6	–	146.2	113.9	165.9	157.7	–	–	34.9
	Twisted	126.7 127.1	128.9 130.2	–	149.6	114.0	162.6	150.8	–	–	23.8
4	Linear	135.4 135.5	130.4 130.4	–	145.6	114.8	165.1	162.9	151.1	–	32.3
	Twisted	129.6 131.3	129.3 129.9	–	148.7	117.0	168.5	168.0	151.5	–	21.7
5	Linear	135.1 135.1	130.8 130.8	–	145.4	116.7	164.3	160.0	157.2	150.1	31.1
	Twisted	128.7 130.1	128.9 130.1	–	149.6	119.2	167.4	162.1	159.5	149.3	18.3
	Twisted #	129.2 134.7	129.8 130.4	–	149.5	119.6	170.1	161.6	165.4	151.5	18.0
						MPBn					
1	Linear	134.2 134.4	167.7 167.8	168.3	146.1	123.5	–	–	–	–	39.9
	Twisted #	128.3 133.1	168.8 169.2	166.5	150.9	121.0	–	–	–	–	40.2
2	Linear	134.6 134.7	168.9 169.0	168.2	145.9	114.9	162.1	–	–	–	38.6
	Twisted	127.0 129.8	167.8 168.8	167.1	152.6	116.8	152.5	–	–	–	29.0
3	Linear	134.1 134.1	169.0 169.0	168.8	145.7	113.7	165.8	157.4	–	–	35.1
	Twisted #	128.7 131.6	166.9 167.6	170.8	143.2	116.8	163.2	150.4	–	–	23.2
4	Linear	133.3 133.7	168.6 168.9	168.4	145.2	115.6	164.3	163.8	148.7	–	28.1
	Twisted #	127.1 133.7	167.9 168.3	168.0	147.9	118.7	169.2	167.9	151.1	–	21.7
5	Linear	133.3 133.3	169.3 169.3	168.1	144.7	117.3	164.2	160.1	157.0	150.4	30.8
	Twisted #	127.6 134.1	167.6 167.7	168.4	147.9	120.0	169.6	161.6	165.4	151.4	18.5

Note: (#) - twisted conformer C (see Fig. 1)

Table 4. Parameters of the regression equation describing the linear correlation between experimental ^{13}C and ^{1}H chemical shifts (ppm) and screening constants (ppm) computed by the GIAO/B3LYP/6-31+G(d, p) method for MMBn and MPBn (r - correlation coefficient, ND - number of data points)

n	Conformer	A_C	B_C	r	ND	A_H	B_H	r	ND
				MMB					
1	Linear	-1.153	214.2	-0.9948	7	-0.138	7.34	-0.9750	5
1	Twisted #	-1.153	212.8	-0.9906	7	-0.382	14.27	-0.9587	5
3	Linear	-1.180	216.6	-0.9795	9	-0.932	29.78	-0.9709	6
3	Twisted	-1.191	218.0	-0.9885	9	-0.979	33.41	-0.9524	6
4	Linear	-1.195	218.0	-0.9919	10	-1.108	34.85	-0.9846	7
4	Twisted	-1.109	203.0	-0.9953	10	-0.818	26.16	-0.9178	7
5	Linear	-1.210	219.5	-0.9943	11	-1.115	35.05	-0.9747	8
5	Twisted #	-1.095	204.1	-0.9971	11	-0.780	25.39	-0.9471	8
				MPB					
1	Linear	-1.211	223.4	-0.9969	8	-0.778	25.24	-0.8113	6
1	Twisted #	-1.195	220.8	-0.9926	8	-0.706	23.17	-0.7987	6
2	Linear	-1.144	214.0	-0.9808	9	-0.999	31.72	-0.9528	6
2	Twisted	-1.116	207.5	-0.9933	9	-0.655	21.53	-0.8081	6
3	Linear	-1.153	214.9	-0.9866	10	-1.059	33.37	-0.9895	7
3	Twisted #	-1.090	202.8	-0.9938	10	-0.596	19.63	-0.7465	7
4	Linear	-1.143	211.4	-0.9909	11	-1.277	39.76	-0.9989	8
4	Twisted #	-1.087	203.8	-0.9945	11	-0.670	21.74	-0.9123	8
5	Linear	-1.163	215.2	-0.9903	12	-1.201	37.54	-0.9757	9
5	Twisted #	-1.075	201.9	-0.9949	12	-0.890	20.82	-0.8903	9

- twisted conformer C (see Fig. 1)

The computed values of ^{13}C isotropic absolute shieldings, σ_{calc}, were correlated with experimental values of ^{13}C chemical shifts (Tables 2 and 3), δ_{exp}, according to the following equation:

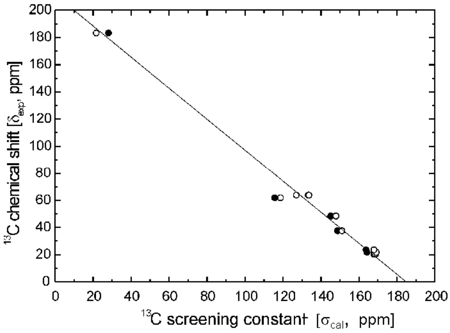
$$\delta_{exp} = A_C \sigma_{calc} + B_C \qquad (1)$$

The values of the slope (A_C) and intercept (B_C) of the least-squares correlation line for Eq. (1) are listed in Table 4. They were further used to scale GIAO isotropic absolute shieldings, a, to obtain the predicted ^{13}C chemical shifts.

Figure 3 illustrates the correlation between the experimental ^{13}C chemical shifts and the screening constants for MPB4 in the linear (A) and twisted (B) structures.

It is seen in Fig. 3 that the experimental values of ^{13}C chemical shift exhibit a very good linear correlation with the computed data of ^{13}C screening constant for the linear conformation of MPB4. Similar good correlations were found for other compounds. It should be noted, however, that the only point located out of the regression line in Fig. 3 is the signal assigned to the C8 atom. It is the α-carbon atom of the alkyl chain of the molecules located in the vicinity of the N-atom.

Fig. 3. Relationship between the experimental ^{13}C chemical shifts (δ) and the ^{13}C screening constants (σ) computed by the GIAO/B3LYP/6-31+G(d, p) method for linear conformer (•) and twisted conformer (o) of MPB4. Regression line drawn for the linear conformer



Comparison of the experimental and computed values of ^{13}C NMR leads to the following conclusions: 1) The value of the correlation coefficient in each case is close to -1, showing a slightly better correlation for the twisted B structure as compared to the linear A structure. 2) The absolute value of the slope tends to decrease with increasing number of carbon atoms in the spacer. For both series betaines the results of GIAO shieldings from B3LYP/6-31+G(d, p)//B3LYP/6-31+G(d, p) calculations plotted versus the number of CH_2 groups give a straight line of the slope of -1.08. 3) The absolute values of the correlation coefficients are between 0.98 and 0.99, and are slightly higher for the B-type structures. 4) One can conclude that for betaines having $n > 1$, a possibility of their existence in the twisted structure (with the small distant ammonium and carboxyl groups) has to be considered.

3.2.2. Proton chemical shifts

Tables 5 and 6 list the experimental and calculated values of ^{1}H chemical shifts and ^{1}H screening constants for MMBn and MPBn, respectively. Regression equations parameters for the correlation between the experimental values of proton chemical shifts and the calculated GIAO shielding constants for MMBn and MPBn are listed in Table 4. Figure 4 illustrates correlations between the experimental values of the ^{1}H chemical shifts and the calculated screening constants for MPB4 in A and B structures. The experimental values of the proton chemical shifts cover a range from 1.2 to 3.2 ppm. The computed values of the ^{1}H isotropic absolute shieldings, σ_{calc}, are correlated with the experimental values of the ^{1}H chemical shifts, δ_{exp}, according to the following equation:

$$\delta_{exp} = A_H \cdot \sigma_{calc} + B_H \qquad (2)$$

The numerical values of the slope (A_H) and intercept (B_H) of Eq. (2) were obtained by means of the least-square method. The values of A_H and B_H coefficients obtained in such a way can be used to scale the GIAO isotropic absolute shieldings, σ, to obtain the predicted ^{1}H chemical shifts. The corresponding correlation coefficients, r, are collected in Table 4. It is seen that the values of the r coefficient are slightly higher for the linear conformers. The value of A_H vary from -0.138 to -1.201. The correlation found for protons is less satisfactory in comparison to that for carbon-13 and leads to the opposite conclusion, that the linear conformers dominate in aqueous solutions.

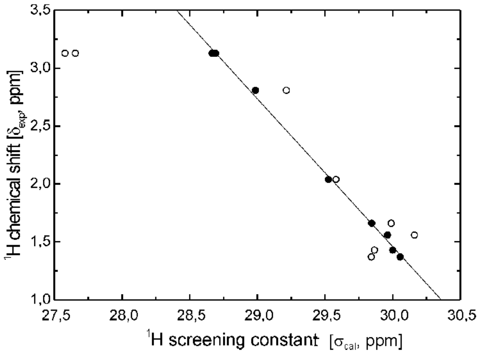


Fig. 4. Relationship between the experimental proton chemical shifts and the ^{1}H screening constants (a) computed by the GIAO/B3LYP/6-31+G(d, p) method for linear conformer (•) and twisted conformer (o) of MPB4. Regression line drawn for the linear conformer

Table 5. The experimental (ppm, in D_2O) and computed ^{1}H chemical shifts (ppm) for linear and twisted conformers of N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MMBn)

n		H-C2,6	H-C3,5	H-C4	H-C7	H-C8	H-C9	H-C10	H-C11	H-C12
					MMBn					
	Exp	3.84; 3.58	3.45	-	3.19	3.29	-	-	-	-
1	Linear	3.87; 3.51	3.40	-	3.24	3.32	-	-	-	-
	Twisted #	3.77; 3.65	3.48	-	3.16	3.30	-	-	-	-
	Exp	3.84	3.29	-	3.00.	3.29	1.83	2.07	-	-
3	Linear	3.99	3.23	-	2.76	3.22	1.85	2.27	-	-
	Twisted	3.94	3.61	-	2.61	3.51	1.88	2.35	-	-
	Exp	3.83	3.29	-	2.98	3.29	1.60	1.42	2.05	-
4	Linear	4.09	3.19	-	2.80	3.12	1.63	1.57	2.07	-
	Twisted	3.70	3.58		2.64	3.38	1.71	1.51	1.98	
	Exp	3.84	3.30	-	2.98	3.30	1.60	1.18	1.43	2.00
5	Linear	4.13	3.11	-	2.78	3.06	1.85	1.07	1.67	1.95
	Twisted #	3.81	3.62	-	2.26	3.22	1.86	1.36	1.53	1.97
					MPBn					
	Exp[1]	3.24; 3.42	1.69	1.46	3.03	3.68	-	-	-	-
1	Linear	2.28; 3.46	1.91	1.94	2.95	3.87	-	-	-	-
	Twisted #	2.54; 3.90	2.03	1.90	3.20	2.94	-	-	-	-
	Exp[1]	3.16	1.68	1.39	2.84	3.42	2.61	-	-	-
2	Linear	3.06	1.78	1.65	3.06	3.67	2.67	-	-	-
	Twisted	3.01	1.98	1.84	2.43	3.71	2.17	-	-	-
	Exp[1]	3.12	1.71	1.46	2.84	3.12	1.80	2.06	-	-
3	Linear	3.11	1.72	1.62	2.89	3.08	1.62	2.05	-	-
	Twisted #	3.38	1.76	2.05	2.47	2.25	2.17	2.00	-	-
	Exp[1]	3.13	1.66	1.43	2.81	3.13	1.56	1.37	2.04	-
4	Linear	3.13	1.66	1.46	2.76	3.16	1.51	1.39	2.06	-
	Twisted #	3.20	1.64	1.72	2.16	3.25	1.52	1.73	1.91	-
	Exp[1]	3.11	1.65	1.44	2.81	3.11	1.56	1.18	1.44	1.99
5	Linear	3.14	1.74	1.58	2.72	3.00	1.57	0.92	1.75	1.87
	Twisted #	3.31	1.58	1.69	2.06	3.14	1.76	1.46	1.67	1.81

[1] data taken from Ref. [12], # — twisted conformer C (see Fig. 1)

In the betaines having the alkyl spacer containing one methylene group (n = 1) one can distinguish two optimized spatial structures with a very similar energy minimum as computed by the B3LYP/6-31+G(d, p) method for both MMB1 and MPB1. One of them is the A structure in which the plane of the COO group of the betaine is located perpendicularly to the plane of the heterocyclic ring of the molecule. The other one is the C structure in which the plane of the COO group is located parallel to the plane of the heterocyclic ring of the betaine considered. Comparison of the theoretical and computed 'HNMR data (Table 4) indicates that the C structure is preferred, especially for the MPB1. For betaines with n > 1 a better correspondence between the calculated results and the experimental data occurs for the linear structure. As can be seen in Fig. 4, a big discrepancy can be observed between the computed and the experimental signal for protons of α-CH_2 group of the alkyl chain in the twisted conformation. Similar discrepancies can be also found for some other twisted conformers of higher members of both series. Therefore, it is reasonable to suppose that the conclusions obtained from the correlations obtained for ^{13}C NMR data suggesting a close distance between the ammonium and carboxyl groups result from

Table 6. Average ^1H screening constants (ppm) for N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MPBn)

n	Conformer	H-C2,6	H-C3,5	H-C4	H-C7	H-C8	H-C9	H-C10	H-C11	H-C12
					MMBn					
1	Linear	25.13 29.76	27.81	–	29.15	28.61	–	–	–	–
	Twisted #	27.54 29.19	27.81	–	28.19	28.61	–	–	–	–
2	Linear	28.71	27.86	–	29.00	28.01	29.44	–	–	–
	Twisted	28.68	27.82	–	27.78	27.18	29.31	–	–	–
3	Linear	28.55	27.87	–	29.01	28.54	29.93	29.51	–	–
	Twisted	27.98	27.82	–	27.94	28.85	29.12	29.61	–	–
4	Linear	27.93	27.77	–	28.93	28.58	30.05	29.98	29.59	–
	Twisted	28.75	27.84	–	27.65	27.46	29.88	30.13	29.56	–
5	Linear	27.75	27.72	–	28.93	28.69	29.93	30.47	29.77	29.68
	Twisted	28.18	27.84	–	27.58	27.66	29.75	30.34	29.61	29.60
	Twisted #	28.56	27.78	–	29.11	27.26	29.64	30.08	29.74	29.54
					MPBn					
1	Linear	26.42 29.49	29.97	29.94	29.20	28.63	–	–	–	–
	Twisted #	27.32 29.24	29.96	30.11	28.34	28.66	–	–	–	–
2	Linear	28.68	29.96	30.09	29.07	28.07	29.48	–	–	–
	Twisted	28.45	29.95	30.13	27.89	28.46	29.33	–	–	–
3	Linear	28.53	29.87	29.97	29.06	28.59	29.56	29.97	–	–
	Twisted #	27.25	29.93	29.49	29.14	28.79	29.29	29.56	–	–
4	Linear	28.66	29.84	30.00	28.99	28.67	30.06	29.96	29.53	–
	Twisted #	27.68	29.99	29.87	29.22	27.58	29.94	30.16	29.58	–
5	Linear	28.63	29.80	29.93	28.98	28.75	29.95	30.48	29.79	29.69
	Twisted #	24.23	29.96	29.75	29.17	27.50	29.64	30.11	29.78	29.56

Note: (#) - twisted conformer C (see Fig. 1) intermolecular interaction between two neighboring molecules leading to formation of polymolecular ionic pairs. The interaction (electrostatic and hydrogen bonding) with water molecules cannot be neglected.

3.2.3. Nitrogen-15 chemical shifts

Table 7 lists the values of ^{15}N screening constants computed by means of the B3LYP/6-31+G(G,_p) method for both linear and twisted structures of MMBn and MPBn. It is seen that for a given betaine the value of ^{15}N screening constant strongly depends on the spatial structure of the compound. Figure 5 shows a correlation between the calculated screening constants of ^{15}N for the optimized linear structures of MMBn and MPBn. A good linear correlation shown in Fig. 5 suggests that the spatial structure of the two series of betaine surfactants primarily depends on the number of carbon atoms in the alkyl chain. For a given alkyl chain the structure of the two kinds of betaines seems to be similar as long as the ^{15}N NMR data are considered.

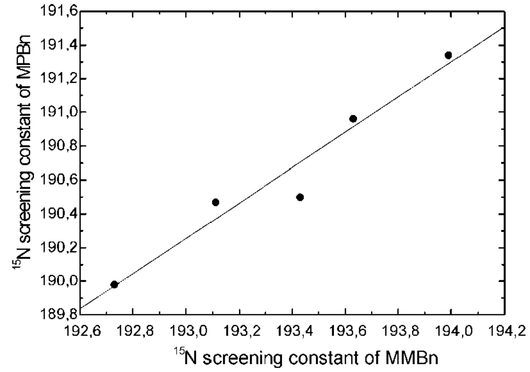


Fig. 5. Plot of the ^{15}N screening constants (σ) computed by the B3LYP/6-31+G(d, p) method of MPBn *versus* MMBn

Table 7. ^{15}N screening constants (ppm) for N-(ω-carboxyalkyl)-N-methylmorpholinium inner salts (MMBn) and N-(ω-carboxyalkyl)-N-methylpiperidinium inner salts (MPBn)

n	Conformer	MMBn	MPBn
1	Linear	193.43	190.50
1	Twisted #	192.28	189.39
2	Linear	193.99	191.34
2	Twisted	191.01	189.43
3	Linear	192.73	189.98
3	Twisted	191.14	191.11
4	Linear	193.63	190.96
4	Twisted #	193.38	192.38
5	Linear	193.11	190.47
5	Twisted #	194.41	192.14

- twisted conformer C (see Fig. 1)

4. CONCLUSIONS

The screening constants (σ_{calc}) calculated for the linear and twisted conformers for MMBn and MPBn, where n = 1-5 denote number of the CH_2 groups between charged N^+ and COO^- groups, by the GIAO B3LYP/6-31+G(d,p) method are correlated with the experimental carbon-13 and proton chemical shifts. The correlations between the experimental chemical shifts in D_2O solutions and the calculated screening constants, are better for carbon-13 than proton (compare correlation coefficients and slopes listed in Table 4). The calculated carbon-13 chemical shifts suggest the twisted conformers while the results of the proton chemical shifts - the linear one.

Acknowledgments
The financial support for this work was provided by Adam Mickiewicz University and Poznań University of Economics within the research project 'Synthesis and physicochemical properties of heterocyclic surface active agents with ester substituents'. Grant UAM-AE No. 51102-204 (2001).

References

[1] J. Vaara, *Theory and calculations of NMR and EPR parameters. CSC Report on Scientific Computing 1999-2000.* S. Kotila and J. Haataja, eds. CSC - Scientific Computing Ltd., Finland, 118-121 (2001).

[2] D. A. Forsyth and A. B. Sebag, *Computed ^{13}C NMR chemical shifts via empirically scaled GIAO shieldings and molecular mechanics geometries. Conformation and configuration from ^{13}C shifts,* J. Am. Chem. Soc. **119,** 9483-9494 (1997).

[3] A. B. Sebag, D. A. Forsyth, and M. A. Plante, *Conformation and configuration of tertiary amines via GIAO-derived (13)C NMR chemical shifts and a multiple independent variable regression analysis,* J. Org. Chem. **66,** 7967-7973 (2001).

[4] J. Casanovas, A. M. Namba, S. León, G.L.B. Aquino, G.V. J. da Silva and C. Alemán, *Calculated and experimental NMR chemical shifts of p-menthane-3,9-diols. A combination of molecular dynamics and quantum mechanics to determine the structure and the solvent effects,* J. Org. Chem. **66,** 3775-3782 (2001).

[5] M. Barfield and P. Fagerness, *Density functional theory/GIAO studies of the ^{13}C, ^{15}N and ^1H NMR chemical shifts in aminopirymidines and aminobenzenes: relationships to electron densities and amine group orientations,* J. Am. Chem. Soc. **119,** 8699-8711 (1997).

[6] X. Domingo, in E. G. Lomax, ed, *Amphoteric Surfactants,* p. 75 (Marcel Dekker, New York, 1996).

[7] G. Schaack, *Experimental results on phase transitions in betaine compounds,* Ferroelectrics **104,** 147-158 (1990).

[8] Z. Dega-Szafran, I. Gąszczyk, D. Maciejewska, M. Szafran, E. Tykarska and I. Wawer, *^{13}C CP MAS NMR, FTIR, X-ray diffraction and PM3 studies of some N-(ω-carboxyalkyl)morpholine hydrohalides.* J. Mol. Struct. **560,** 261-273 (2001).

[9] P. Barczyński, Z. Dega-Szafran, E. Dulewicz, M. Petryna, and M. Szafran, *Aqueous basicity and proton affinity of zwitterionic ω-(N-methylpiperidine)-alkanocarboxylates and ω-(N-piperidine)-alkanocarboxylic acids,* Polish J. Chem. **74,** 1149-1161 (2000).

[10] A. D. Becke, *Density-functional thermochemistry. III. The role of exact exchange,* J. Chem. Phys. **98,** 5648-5655 (1993).

[11] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts,

R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian 98, Revision A.6. Gaussian, Inc., Pittsburgh PA, 1998.

[12] Z. Dega-Szafran, E. Dulewicz, and M. Szafran, *^1H and ^{13}C NMR spectra of betaines, $>N^+(CH_z)_nCOO$, and their hydrogen halides. Additivity rules for carbon-13 chemical shifts*. Magn. Reson. Chem. **38,** 43-50 (2000).

[13] M. Szafran and Z. Dega-Szafran, *Conformational preferences of isostructural N-methylpiperidine betaine and (1-methylcyclohexyl)acetic acid studies by PM3 and B3LYP calculations. The effect of electrostatic interactions on the rotation barrier.* J. Mol. Struct. **598,** 251-260 (2001).

[14] E. L. Eliel, S. H. Wilen, and L. M. Mander, *Stereochemistry of Organic Compounds,* Wiley, New York, 1994 (and references therein).

[15] Z. Dega-Szafran, A. Katrusiak, and M. Szafran, *Molecular structure of bis(pyridiniumvalerate) hydrogen perchlorate studied by X-ray diffraction, FTIR spectroscopy, PM3 and SAM1 calculations,* J. Mol. Struct. **555,** 203-212 (2000).

[16] Z. Dega-Szafran, Z. Kosturkiewicz, E. Dulewicz, and M. Szafran, *Conformational analysis of N-methylpiperidine betaine studied by X-ray diffraction, FTIR spectroscopy and ab initio calculations,* J. Mol. Struct. **478,** 49-55 (1999).

[17] M. Szafran, Z. Dega-Szafran, E. Dulewicz, Z. Kosturkiewicz, M. Nowakowska, W. Orwat, and M. Ratajczak-Sitarz, *Conformational analysis of 5-piperidinevaleric acid, 5-(N-methylpiperidine)-valerate and their hydrogen halides by MO calculations, X-ray diffraction and FTIR spectroscopy.* J. Mol. Struct. **484,** 125-138 (1999).

[18] Z. Dega-Szafran, M. Szafran, A. Antkowiak, M. Grundwald-Wyspianska, E. Nowak, M. Gdaniec, and Z. Kosturkiewicz, *Structure of and hydrogen bonding in a 3:2 inclusion compound of N-methylmorpholine betaine hydrochloride with acetonitrile,* J. Mol. Struct. **605,** 325-330 (2002).

[19] W. Kutzelnigg, U. Fleischer and M. Schindler, in P. Diehl, E. Fluck, H. Gunther, R. Kosfeld, and J. Seelig, eds, *NMR Basic Principles and Progress,* vol. 23, p. 165 (Springer-Verlag, Berlin, 1991).