

Quantum Chemical Computational Study on Chlorocholine Chloride and Bromocholine Bromide

M. KARAKAYA* and F. UCUN

Department of Physics, Faculty of Arts & Sciences, Süleyman Demirel University, 32260 Isparta, Turkey

*Corresponding author: Fax: +90 246 2371106; Tel: +90 246 2113801; E-mail: mkarakayafizik@hotmail.com

(Received: 29 May 2012;

Accepted: 8 March 2013)

AJC-13092

This study deals with the conformational and spectral analysis of chlorocholine chloride and bromocholine bromide by means of theoretical calculations. The optimized molecular structures and vibrational frequencies and also ^1H and ^{13}C NMR shift values of the compounds have been calculated using density functional theory method with 6-311++G(d,p) basis set. The comparison of their experimental and calculated IR, Raman and NMR spectra of the compounds has indicated that the spectra of two optimized conformers can simultaneously exist in one experimental spectrum. Thus, it was concluded that the compounds simultaneously exist in two conformations in the ground state. The natural bond orbital (NBO) analysis has also supported the simultaneous existing of two conformers for the both compounds. All the assignments of the theoretical frequencies were performed by potential energy distributions using VEDA 4 program.

Key Words: Chlorocholine chloride, Bromocholine bromide, IR, Raman, NMR, DFT.

INTRODUCTION

Choline is a required compound to make essential membrane phospholipids. The neurotransmitter acetylcholine is a precursor for the biosynthesis and also is an important source of labile methyl groups. The determination of the minimum energy conformers of acetylcholine has been subject by many theoretical works¹⁻³. The conformational behaviour and molecular motion of acetylcholine in vacuum and aqueous solution have investigated by Marino *et al.*⁴. The authors have calculated five low lying conformations by molecular mechanics computing. The *ab initio* data of acetylcholine has indicated that the most stable conformation is the *trans*-gauche arrangement of the two essential torsion angles (τ_1 ; C-C-O-C and τ_2 ; N-C-C-O)^{5,6}. The observed conformation of acetylcholine is *trans*-gauche ($\tau_1 = -166.9$ and $\tau_2 = 84.7^\circ$) in the crystal of its chloride^{7,8}, *gauche*-gauche ($\tau_1 = 78.9$ and $\tau_2 = 78.4^\circ$) in the crystal of its bromide⁹ and *gauche*-gauche ($\tau_1 = \pm 83$ and $\tau_2 = \pm 89^\circ$) in the crystal of its iodide¹⁰.

In this study the optimized molecular structures and vibrational frequencies and ^1H and ^{13}C NMR chemical shifts of chlorocholine chloride [(2-chloroethyl) trimethylammonium chloride] and bromocholine bromide [(2-bromoethyl) trimethylammonium bromide] have been calculated using density functional theory (DFT/B3LYP) method with 6-311++G(d,p) basis set and compared with the corresponding experimental data.

COMPUTATIONAL METHOD

The optimized structure parameters and vibrational frequencies of chlorocholine chloride (ClChCl) and bromocholine bromide (BrChBr) have been calculated by density functional theory B3LYP method with 6-311++G(d,p) basis set level. The computations were performed by using Gaussian 03 package¹¹ and Gauss-View molecular visualization programs¹² on the personal computer. The calculated vibration frequencies were scaled with a scale factor of 0.9614¹³ and assignment by using VEDA 4 program¹⁴. The chemical shifts of ^1H and ^{13}C NMR in water and IEFPCM model were calculated by GIAO method¹⁵ using the same set level of the theory, routinely used for NMR chemical shift calculations on fairly large molecules^{16,17}. In the chemical shift calculations tetramethylsilane (TMS) was used as reference molecule. So, the theoretical chemical shift ^1H and ^{13}C values were obtained by subtracting the GIAO isotropic magnetic shielding (IMS) values^{18,19}. For instance, the average ^{13}C IMS value of TMS was taken into account for the calculation of ^{13}C chemical shift of any X carbon atom by considering the following equation, $CS_x = IMS_{\text{TMS}} - IMS_x$.

RESULTS AND DISCUSSION

Ground state conformers: The optimized molecular structures of the two low energy conformers of chlorocholine chloride (ClChCl) and bromocholine bromide (BrChBr) were shown in Fig. 1. As initial geometry the position of halide

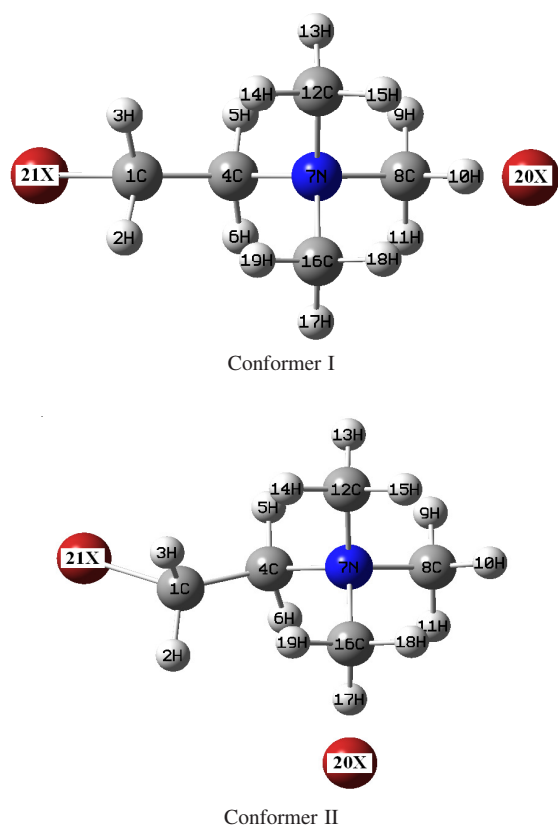


Fig. 1. Molecular structures of optimized lowest energy conformers of ClChCl and BrChBr (X = Cl, Br)

anion (X) was taken with an torsion angle X(20)-C(8)-N(7)-C(4) and an X...N distance of around 3.50 Å and scanned around this torsion angle from 180° to -180° at increments of 20°. Potential energy surface (PES) scan of the compounds showed two minimum-energy structures. These structures were chosen further optimized. The two conformers are defined by essential torsion angles as given in Table-1. The electronic and relative energy values are given in Table-2. As seen the relative energy values between the conformers of the compounds are fairly low.

Vibrational frequencies: The conformers I of the compounds belong to the C_s point group and the conformers II to the C_1 point group (Fig. 1). So, for the conformers I of the compounds have 32 vibrational modes of the symmetry and 25 modes of anti symmetry. All the vibrations are active

both in infrared (IR) and Raman (R). The resulting vibrational frequencies for the both conformers of the compounds are given in Table-3. For comparison the tables also show the experimental vibrational frequencies (IR and R) of powder ClChCl and BrChBr²⁰. The assignments of all the vibrational modes in the tables were obtained by using VEDA 4 program and calculated for conformer I of ClChCl. The symmetry species of all the vibrational modes for the conformers I are written in the second column of Table-3. The correlation values (R^2) and root mean square errors (RMSE) between the experimental and calculated frequencies can be seen in the last two lines of the tables. The RMSE is defined by

$$\text{RMSE}(w_i) = \sqrt{\sum \frac{(w_i^{\text{calc}} - w_i^{\text{exp}})^2}{n}}$$

where w_i^{calc} and w_i^{exp} are the calculated and experimental frequencies of i , respectively and n denotes the number of considering frequencies. As seen from these values the calculated results show a good agreement with the experimental ones for both the conformers of the compounds.

Geometric structures: The calculated and experimental optimized structure parameters for the conformers of ClChCl and BrChBr are summarized in Table-4, in accordance with the atom numbers in Fig. 1. Since the X-ray analysis of the compounds could not be reached in the literature the calculated optimized structure parameters (bond lengths and bond angles) were compared with those of choline chloride^{21,22} and dihedral angles with those of acetylcholine chloride^{6,7} and acetylcholine bromide⁸. The R^2 and RMSE values in the table are seen to be fairly good for the both conformers of the compounds.

Chemical shifts: The experimental and calculated ^1H and ^{13}C NMR chemical shifts (with respect to TMS) for the conformers of ClChCl and BrChBr are given in Table-5. The experimental chemical shifts of ClChCl in $\text{D}_2\text{O}-d_6$ solvent have been obtained from Spectral Database for Organic Compounds Web Page²³. But, those of BrChBr are not obtained in the literature thus, all the calculated chemical shifts were compared with those of ClChCl. Since the experimental ^1H chemical shift values of individual hydrogens are not available we have also found the average values of ^1H chemical shifts for the CH_2 and CH_3 hydrogen atoms and they are shown as bold in

TABLE-1
ESSENTIAL TORSION ANGLES FOR CONFORMERS OF ClChCl AND BrChBr

	ClChCl		BrChBr	
	Conformer I	Conformer II	Conformer I	Conformer II
$\tau_1[\text{X}(21)-\text{C}(1)-\text{C}(4)-\text{N}(7)]$	-180.00	163.16	180.00	164.83
$\tau_2[\text{C}(1)-\text{C}(4)-\text{N}(7)-\text{C}(8)]$	-180.00	166.41	180.00	167.12
$\tau_3[\text{C}(1)-\text{C}(4)-\text{N}(7)-\text{X}(20)]$	-180.00	104.13	180.00	104.70
$\tau_4[\text{X}(20)-\text{C}(8)-\text{N}(7)-\text{C}(4)]$	180.00	-60.32	-180.00	-60.50

TABLE-2
ELECTRONIC ENERGIES AND RELATIVE ENERGIES
BETWEEN CONFORMERS OF ClChCl AND BrChBr

	ClChCl		BrChBr	
	Conformer I	Conformer II	Conformer I	Conformer II
Energy (Hartree/part)	-1173.431707	-1173.431455	-5401.280650	-5401.280371
Relative energy (kcal/mol)	0.00	0.158027	0.00	0.174958

TABLE-3
EXPERIMENTAL AND CALCULATED VIBRATIONAL FREQUENCIES FOR CONFORMERS OF ClChCl AND BrChBr

Mode No.	Symmetry ^a	Assignments ^b (PED % ^c)	Experimental frequencies (cm ⁻¹)		Experimental frequencies (cm ⁻¹)		Calculated frequencies (cm ⁻¹)			
			ClChCl ²⁰		BrChBr ²⁰		B3LYP 6-311++G(d,p)			
			IR	R	IR	R	ClChCl		BrChBr	
						Conformer I	Conformer II	Conformer I	Conformer II	
57	A''	CH ₂ [vCH(93) _{asym}]	–	–	–	–	3049	3038	3061	3044
56	A'	CH ₃ [vCH(76) _{asym}]	–	–	–	–	3035	3033	3037	3038
55	A''	CH ₃ [vCH(72) _{asym}]	–	–	3025sh	–	3031	3032	3033	3032
54	A''	CH ₃ [vCH(94) _{asym}]	–	3023sh, 3011s	–	3024sh	3026	3027	3031	3028
53	A''	CH ₂ [vCH(97) _{asym}]	3011m	–	3012, 3001m	3011s, 3003sh	3005	3025	3007	3025
52	A'	CH ₃ [vCH(75) _{asym}]	–	–	–	–	2992	2994	2996	2994
51	A'	CH ₂ [vCH(76) _{sym}]+ CH ₃ [vCH(20) _{asym}]	–	–	–	–	2986	2988	2991	2988
50	A''	CH ₃ [vCH(51) _{asym}]	–	–	–	–	2982	2986	2983	2987
49	A'	CH ₃ [vCH(63) _{asym}]	–	–	–	2971s	2982	2966	2983	2976
48	A'	CH ₂ [vCH(65) _{sym}]	2954vs, 2923vs	2972s, 2956sh	2954vs, 2925vs	2928br	2957	2948	2958	2948
47	A'	CH ₃ [vCH(51) _{sym}]	2871sh, 2855s	2897	2871sh, 2855vs	2888br	2863	2882	2865	2880
46	A'	CH ₃ [vCH(59) _{sym}]	–	2880sh	–	–	2836	2862	2841	2861
45	A''	X ₂₀ ...CH ₃ [vXH(25)] + CH ₃ [δXHC(13)]	–	2827	–	2816br	2831	2840	2836	2843
44	A'	CH ₃ [δHCH(38)] + τHCHX ₂₀ (19)	1486m, 1468m	1502sh	1482s	1496sh	1474	1475	1471	1472
43	A''	CH ₃ [δHCH(48)]	–	1483sh, 1471m	1467s	1478w	1470	1460	1467	1459
42	A'	(CH ₃ +CH ₂)[δHCH(35)]	1459m	–	1461s	1461vw	1459	1454	1457	1453
41	A'	τHCHX ₂₀ (31)+ τHCCN(10)	–	1454m	–	1444w	1448	1445	1446	1444
40	A''	CH ₃ [δHCH(52)]	–	–	–	–	1444	1441	1442	1441
39	A'	(CH ₂ +CH ₃)[δHCH(77)]	–	–	–	–	1438	1437	1435	1435
38	A'	(CH ₂ +CH ₃)[δHCH(47)]+ τHCHX ₂₀ (17)	1425vw	1425w, 1411w	–	–	1431	1432	1430	1429
37	A''	CH ₃ [δHCH(49)] + τHCHX ₂₀ (26)	–	–	–	–	1419	1424	1419	1422
36	A'	(CH ₃ +CH ₂)[δHCH(61)]	1414vw	–	1415m	1417w	1416	1416	1416	1414
35	A''	τHCHX ₂₀ (62)	–	–	1378m	1388w	1384	1392	1386	1391
34	A'	CH ₃ [δHCH(22)] + τHCHX ₂₀ (22)	1379m	–	1361sh	–	1381	1382	1384	1383
33	A'	τHCCN(58)	1366sh	1359vw	1343sh	1346w	1361	1374	1355	1371
32	A''	CH ₂ -C[δHCC(49)]	1303w	1346vw	–	–	1312	1320	1312	1315
31	A'	τHCCN(55)	–	1306w	1272m, 1264	1284w, 1272w	1260	1268	1242	1248
30	A'	N-(CH ₃) ₃ [γNCCC(12)]	1246vw	1272w	1236w	1262sh	1239	1249	1233	1236
29	A''	CH ₂ -X ₂₁ [δHCX(27)] + CH ₂ -C[δHCC(16)] + τHCCN(15)	–	–	–	–	1237	1232	1227	1227
28	A'	τHCCN(25)+ τHCHX ₂₀ (13) + τX ₂₀ HCCN(10)	–	–	1193vw	–	1210	1210	1196	1200
27	A''	δHCX ₂₁ (23)	1141vw	1154sh	1145w	1146w	1159	1172	1154	1162
26	A'	τHCNC(19)+ δHCH(12) +N-CH ₃ [δNCH(10)]	–	1067	1128vw	1126vw	1115	1112	1114	1108
25	A''	CH ₃ -N[δHCN(40)] + δHCX ₂₁ (18)	–	–	–	1079vw	1103	1095	1092	1084
24	A''	τHCNC(33) + CH ₃ [δHCH(13)]	1065vw	–	1056w	1058m	1047	1043	1046	1041
23	A'	CH ₂ [vCC(78)]	1043vw	–	1020w	974m	1022	1025	1021	1023
22	A''	τHCCX ₂₁ (56) + CH ₂ - X ₂₁ [δHCX(10)]	978br	979br	972m	950m	1009	1016	976	988
21	A'	vNC(55)	953br	947br	950m	913m	928	933	923	931

20	A''	vNC(66) + τ HCCX ₂₁ (10)	922br	920br	914m	–	893	915	890	910
19	A'	vNC(74)	810br	813br	–	–	879	856	875	845
18	A''	τ HCCN(50) + δ HCC(20) + δ HCX ₂₁ (15)	769br	769m	794vw	766s	757	786	746	769
17	A'	vX ₂₁ C(43) + vNC(20) + δ CCN(14) + δ X ₂₁ CC(13)	731br	736	725br	–	747	729	725	709
16	A'	vNC(63) + vX ₂₁ C(36)	–	–	671w	673s	705	702	642	637
15	A'	N-(CH ₃) ₃ [γ NCCC(45)]	–	510	457w	501m	494	485	479	470
14	A'	δ CNC(36)+N- (CH ₃) ₃ [γ NCCC (45)] + vNC(11)	–	464	–	458m	434	442	432	436
13	A''	δ CNC(39)	–	451sh	–	–	430	437	431	433
12	A''	δ CNC(18)	–	379vw	–	379w	355	359	354	353
11	A'	δ CNC(57)	–	370sh	–	365w	352	350	347	346
10	A'	τ HCHX ₂₀ (51)+ τ HCNC(12) + τ X ₂₀ HCN(10)	–	–	–	–	320	329	313	320
09	A''	τ HCHX ₂₀ (30)+ τ HCNC(14)	–	–	–	–	316	304	310	298
08	A''	τ HCHX ₂₀ (40)+ τ HCNC(30)	–	279m	–	–	276	259	271	241
07	A'	δ X ₂₁ CC(11)	–	–	–	231s	274	234	227	210
06	A'	δ X ₂₁ CC(28)+ δ CCN(20)	–	–	–	179w	192	197	172	176
05	A'	δ X ₂₀ HC(15)+vX ₂₀ H(13) + δ CNC(10)	–	–	–	153vw	153	171	134	133
04	A''	τ CCNC(27)+ τ X ₂₁ CCN(15) + vX ₂₀ H(15) + δ X ₂₀ HC(13)	–	–	–	129vw	144	143	101	121
03	A'	δ CCN(26)+ τ HX ₂₀ HC(23) + δ X ₂₁ CC(14)	–	–	–	–	76	115	67	103
02	A''	τ CCNC(67)	–	–	–	–	69	73	58	68
01	A'''	τ X ₂₁ CCN(61)+ τ HCCN(20)	–	–	–	–	52	46	42	32
–	–	–	–	–	–	R ² =	0.9993	0.9995	0.9998	0.9998
–	–	–	–	–	–	RMSE=	22.52204	19.34691	14.39313	14.88696

^aSymmetries for conformer I of ClChCl. ^bVibrational modes assignments for conformer I of ClChCl. ^cPotential energy distribution (PED), less than 10 % are not shown. v: stretching, δ : bending, γ : out of plane bending, τ : torsion modes, sym: symmetric, asym: anti symmetric w: weak, m: medium, s: strong, v: very, sh: shoulder, br: broad.

Table-5. For comparison in the table are also given the average values of the chemical shifts of each atom in the both conformers of the compounds. The R² and mean absolute error (MAE) values are written in the last two lines of the table. According to these values, one important observation is that the calculated results for the average chemical shifts of the two conformers of the compounds have a better agreement with the experimental data relative to the individual conformers.

Natural bond orbital analysis: The role of hyper conjugative interactions in the stabilization of conformers of compounds is investigated by natural bond orbital (NBO) analysis²⁴⁻²⁷. Table-6 summarizes the hyper conjugative interactions (kcal mol⁻¹) representing the transfer of an electron from the lone pair (LP Cl and LP Br) to an antibonding orbital since the molecular structures of the two conformers are only different by the location of the Cl anion for ClChCl and the Br anion for BrChBr. For instance, the strongest interactions for the conformer I of ClChCl are identified for the interaction of lone pair orbital localized on Cl₂₀ with the adjacent σ^* C₈-H₁₀, σ^* C₁₂-H₁₅, σ^* C₁₆-H₁₈ bonds. From the table the total hyper conjugative energies determined relative to only the location

of the X₂₀ anions for the two conformers are very close. This supports that the two conformers of ClChCl and BrChBr should have close optimized energies.

Frontier molecular orbitals, UV-visible analysis and molecular electrostatic potentials: Frontier molecular orbitals (FMOs) are important in determining such properties as molecular reactivity and the ability of a molecule to absorb light. Frontier molecular orbitals are also very important for optical and electric properties²⁸. The highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are the main orbital taking part in chemical reaction. The HOMO energy characterizes the ability of electron giving, the LUMO energy characterizes the ability of electron accepting and the gap between HOMO and LUMO energies characterizes the molecular chemical stability²⁹. The HOMO and HOMO-1 are mainly localized on the chlorine atom for ClChCl and on the bromide atom for BrChBr. The LUMO orbitals are localized on the C(1) and X(21) atoms and the LUMO+1 orbitals are localized on the choline group. The energy values of the HOMO-1, HOMO, LUMO and LUMO+1 levels calculated at B3LYP/6-311++G(d,p) level for both the conformers of the compounds are given in Table-7. As an example, the energy

TABLE-4
CALCULATED OPTIMIZED GEOMETRIC PARAMETERS FOR CONFORMERS OF ClChCl AND BrChBr

Parameters	Exp. ChCl ²¹	Exp. ChCl ²²	Calculated B3LYP[6-311++G(d,p)]			
			ClChCl		BrChBr	
			Conformer I	Conformer II	Conformer I	Conformer II
Bond lengths (Å)						
N(7)-C(8)	1.509	1.50	1.515	1.512	1.514	1.511
N(7)-C(12)	1.491	1.53	1.512	1.496	1.511	1.497
N(7)-C(16)	1.506	1.52	1.512	1.512	1.511	1.511
N(7)-C(4)	1.559	1.60	1.512	1.533	1.516	1.537
C(1)-C(4)	1.461	1.56	1.525	1.524	1.523	1.521
C(1)-H(2)	1.040	–	1.087	1.088	1.086	1.087
C(1)-H(3)	1.000	–	1.087	1.089	1.086	1.088
C(4)-H(5)	1.100	–	1.091	1.090	1.090	1.090
C(4)-H(6)	1.090	–	1.091	1.097	1.090	1.097
C(8)-H(9)	1.120	–	1.090	1.090	1.090	1.090
C(8)-H(10)	1.100	–	1.097	1.090	1.097	1.096
C(8)-H(11)	1.100	–	1.090	1.096	1.090	1.096
C(12)-H(13)	1.000	–	1.090	1.089	1.090	1.089
C(12)-H(14)	1.040	–	1.088	1.088	1.088	1.088
C(12)-H(15)	1.090	–	1.098	1.089	1.099	1.089
C(16)-H(17)	1.050	–	1.090	1.098	1.090	1.098
C(16)-H(18)	1.150	–	1.098	1.090	1.098	1.090
C(16)-H(19)	0.970	–	1.088	1.089	1.088	1.089
X(21)-C(1)	–	–	1.808	1.808	1.969	1.969
X(20)...N(7)	–	–	3.573	3.539	3.762	3.733
–	–	R ² =	0.9496	0.9494	0.9506	0.9510
–	–	RMSE =	0.050762	0.050763	0.050264	0.050262
Bond angles (°)						
C(8)-N(7)-C(12)	–	–	108.13	109.39	108.16	109.41
C(8)-N(7)-C(16)	106.8	–	108.13	108.29	108.16	108.37
C(12)-N(7)-C(16)	109.6	–	109.10	109.87	109.18	109.85
C(4)-N(7)-C(8)	104.2	–	107.95	106.96	107.96	106.93
C(4)-N(7)-C(12)	110.9	–	111.70	110.66	111.62	110.64
C(4)-N(7)-C(16)	115.2	–	111.70	111.59	111.62	111.54
N(7)-C(4)-C(1)	114.6	–	115.32	114.08	115.05	114.04
C(4)-C(1)-X(21)	–	–	107.85	108.27	108.17	108.42
X(21)-C(1)-H(2)	–	–	106.54	106.53	105.72	105.68
C(1)-C(4)-H(5)	–	–	109.73	110.95	110.09	111.43
N(7)-C(4)-H(5)	–	–	106.78	105.76	106.54	105.50
N(7)-C(8)-H(9)	–	–	108.32	108.33	108.40	108.43
N(7)-C(8)-H(10)	–	–	107.02	108.24	107.22	108.26
N(7)-C(8)-H(11)	–	–	108.32	107.11	108.40	107.34
N(7)-C(12)-H(15)	–	–	106.74	108.77	107.01	108.75
N(7)-C(16)-H(18)	–	–	106.74	107.75	107.01	107.81
X(20)..C(8)..N(7)	–	–	85.35	82.97	86.53	84.26
–	–	R ² =	0.7341	0.8733	0.7431	0.8707
–	–	RMSE =	2.216972	1.969378	2.224893	1.989853
Dihedral angles (°)						
	Exp. AChCl ⁶	Exp. AChBr ⁸				
C(8)-N(7)-C(4)-C(1)	171.4	175.49	-180.00	166.41	180.00	167.12
N(7)-C(4)-C(1)-X(21)	84.7	78.44	-180.00	163.16	180.00	164.83
C(1)-C(4)-N(7)-C(16)	53.0 ^a	–	61.25	48.14	61.25	48.80
C(1)-C(4)-N(7)-C(12)	-70.02 ^a	–	-61.25	-74.52	-61.25	-73.81
X(20)-N(7)-C(4)-C(1)	–	–	-180.00	104.13	180.00	104.70
C(1)-C(4)-N(7)-C(8)	170.8 ^a	–	-180.00	166.41	180.00	167.12
X(20)-C(8)-N(7)-C(4)	–	–	180.00	-60.32	-180.00	-60.50
X(20)-C(16)-N(7)-C(4)	–	–	177.76	55.74	177.90	55.82

^aTaken from Ref.⁷.

diagram of HUMOs and LUMOs for the conformer I of ClChCl are drawn in Fig. 2.

Electronic values, such as absorption wavelengths, excitation energies and oscillator strengths were computed by Time-Dependent Density Functional Theory (TD-DFT)

method at 6-311++G(d,p) basis set level as UV visible spectra analysis and tabulated in Table-8. Also the major contributions of the transitions in the table were designated with the aid of SWizard program³⁰.

TABLE-5
CALCULATED AND EXPERIMENTAL ^{13}C AND ^1H NMR ISOTROPIC CHEMICAL SHIFTS
(WITH RESPECT TO TMS, ALL VALUES IN ppm) FOR CONFORMERS OF ClChCl AND BrChBr

Atom	Experimental (ppm) (in D_2O - d_6) ClChCl ²³	Calculated B3LYP 6-311++G(d,p) GIAO/IEFPCM model (Solvent: water)					
		ClChCl			BrChBr		
		Conformer I	Conformer II	Average	Conformer I	Conformer II	Average
C1	36.59	46.263	46.127	46.195	39.552	39.283	39.418
C4	67.40	70.341	67.818	69.080	71.088	68.692	69.890
C8	54.66	58.195	57.977	58.086	58.109	57.760	57.935
C12	54.51	52.646	53.965	53.306	52.543	53.885	53.214
C16	54.36	52.643	51.999	52.321	52.539	51.793	52.166
	R ² =	0.8210	0.8571	0.8406	0.9355	0.9535	0.9464
	MAE =	3.946	3.236	3.5908	2.7774	2.0554	2.4166
H2		3.901	3.959	3.930	3.728	3.813	3.771
H3		3.902	3.833	3.868	3.728	3.703	3.716
H(X21-CH ₂)	3.812	3.902	3.896	3.899	3.728	3.758	3.743
H5		3.238	2.857	3.048	3.288	3.014	3.151
H6		3.239	6.514	4.877	3.289	6.509	4.899
H(N-CH ₂)	4.044	3.239	4.686	3.963	3.289	4.762	4.026
H9		2.596	2.691	2.644	2.653	2.726	2.690
H10		6.124	2.595	4.360	6.098	2.642	4.370
H11		2.597	5.743	4.170	2.654	5.726	4.190
H(N-CH ₃)	3.243	3.772	3.676	3.724	3.802	3.698	3.750
H13		2.430	2.693	2.562	2.455	2.677	2.566
H14		2.564	3.151	2.858	2.645	3.147	2.896
H15		6.112	2.754	4.433	6.079	2.767	4.423
H(N-CH ₃)	3.243	3.702	2.866	3.284	3.726	2.864	3.295
H17		2.431	6.197	4.314	2.456	6.180	4.318
H18		6.112	2.401	4.257	6.079	2.439	4.259
H19		2.564	2.395	2.480	2.645	2.491	2.568
H(N-CH ₃)	3.243	3.702	3.664	3.683	3.727	3.703	3.715
	R ² =	0.2806	0.6770	0.5750	0.6231	0.6064	0.4756
	MAE =	0.4684	0.3914	0.2260	0.4730	0.4132	0.2236

TABLE-6
HYPERCONJUGATIVE INTERACTIONS (kcal mol^{-1}) FOR CONFORMERS OF ClChCl AND BrChBr

Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol ClChCl		E(2) kcal/mol BrChBr		
		Conformer I	Conformer II	Conformer I	Conformer II	
LP(X ₂₀)	$\sigma^* \text{C}_1\text{-H}_2$	–	0.13	–	0.13	
	$\sigma^* \text{C}_4\text{-H}_5$	–	0.47	–	0.40	
	$\sigma^* \text{C}_4\text{-H}_6$	–	8.37	–	7.99	
	$\sigma^* \text{C}_4\text{-N}_7$	–	0.05	–	–	
	$\sigma^* \text{N}_7\text{-C}_{12}$	0.05	–	–	–	
	$\sigma^* \text{N}_7\text{-C}_{16}$	0.05	0.08	–	0.06	
	$\sigma^* \text{C}_8\text{-H}_9$	0.09	0.07	0.08	0.07	
	$\sigma^* \text{C}_8\text{-H}_{10}$	8.60	0.09	7.86	0.08	
	$\sigma^* \text{C}_8\text{-H}_{11}$	0.09	6.76	0.08	6.26	
	$\sigma^* \text{C}_{12}\text{-H}_{13}$	0.12	–	0.12	–	
	$\sigma^* \text{C}_{12}\text{-H}_{14}$	0.07	–	0.06	–	
	$\sigma^* \text{C}_{12}\text{-H}_{15}$	8.90	–	8.18	–	
	$\sigma^* \text{C}_{16}\text{-H}_{17}$	0.12	9.71	0.12	9.07	
	$\sigma^* \text{C}_{16}\text{-H}_{18}$	8.90	0.11	8.18	0.10	
	$\sigma^* \text{C}_{16}\text{-H}_{19}$	0.07	0.11	0.06	0.10	
	Total		27.06	25.95	24.74	24.26
	Relative energy		1.11	0.00	0.48	0.00

X: Cl, Br.

To predict the reactive sites of electrophilic and nucleophilic attacks for the investigated compounds, molecular electrostatic potentials (MEP) of the conformers of the compounds were calculated and molecular electrostatic potential maps were given in Fig. 3. In the figure the negative (blue and

yellow) regions are related to electrophilic reactivity and the positive (red) regions are related to nucleophilic reactivity.

Spectral analysis: The calculated IR and R spectra of the conformers I and II of ClChCl and BrChBr are given in Fig. 4A and B, respectively. The experimental spectra of the

TABLE-7
CALCULATED HOMO-LUMO ENERGY VALUES (a.u) FOR CONFORMERS OF ClChCl AND BrChBr

Parameters	B3LYP 6-311++G(d,p)			
	ClChCl		BrChBr	
	Conformer I	Conformer II	Conformer I	Conformer II
HOMO	-0.19690	-0.20122	-0.18667	-0.18774
LUMO	0.05489	-0.04578	0.00378	0.02790
HOMO-LUMO energy gap (ΔE)	0.25179	0.15544	0.19045	0.21564
HOMO-1	-0.19706	-0.20162	-0.18682	-0.18899
LUMO+1	0.18923	-0.02563	0.18209	0.17698
(HOMO-1)-(LUMO + 1) energy gap (ΔE)	0.38629	0.17599	0.36891	0.36597

TABLE-8
CALCULATED WAVELENGTHS λ (nm), EXCITATION ENERGIES (eV),
OSCILLATOR STRENGTHS (f) FOR CONFORMERS OF ClChCl AND BrChBr

TD-DFT/B3LYP/6-311++G(d,p)							
	Wavelengths λ (nm)	Excitation energies (eV) major contribution	Oscillator strengths (f)		Wavelengths λ (nm)	Excitation energies (eV) Assignment	Oscillator strengths (f)
	351.39	3.5284	0.0020		333.02	3.7230	0.0021
ClChCl conformer I	351.07	HOMO \rightarrow LUMO (98 %) 3.5316	0.0013	ClChCl conformer II	331.96	HOMO \rightarrow LUMO (97 %) 3.7349	0.0030
	343.34	HOMO-1 \rightarrow LUMO (99 %) 3.6111	0.0274		326.72	HOMO-1 \rightarrow LUMO (96 %) 3.7948	0.0257
		HOMO-2 \rightarrow LUMO (97%)				HOMO-2 \rightarrow LUMO (97 %)	
BrChBr conformer I	459.04	2.7010	0.0021	BrChBr conformer II	399.11	3.1065	0.0016
	458.68	HOMO \rightarrow LUMO (99 %) 2.7031	0.0002		396.54	HOMO \rightarrow LUMO (97 %) 3.1266	0.0013
	442.65	HOMO-1 \rightarrow LUMO (100 %) 2.8010	0.0146		384.51	HOMO-1 \rightarrow LUMO (98 %) 3.2244	0.0199
		HOMO-2 \rightarrow LUMO (99 %)				HOMO-2 \rightarrow LUMO (96 %) HOMO-2 \rightarrow LUMO+1	

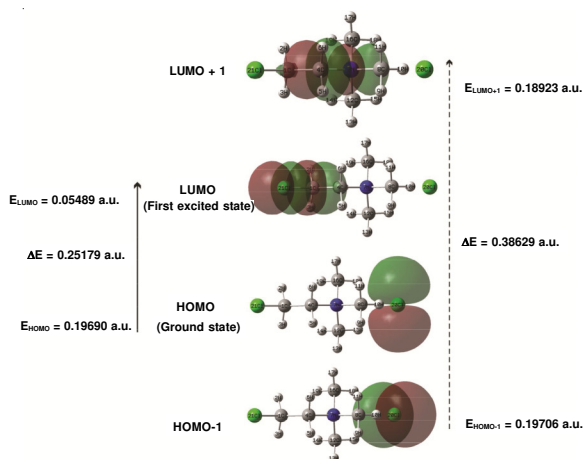


Fig. 2. Energy diagram of HUMOs and LUMOs for conformer I of ClChCl

compounds are also given in the figure, as labeled D's. As seen the experimental IR or R spectra do not fit well to the calculated spectra for the two conformers, individually. The experimental spectra show the peaks splinted doublets or triplets and thus, have more spectral lines than the calculated ones. Since the relative energy values between the two conformers of the compounds are very low we think that the spectra of the two conformers of can simultaneously exist in one experimental spectrum. So, we have drawn the superposition of the calculated spectra (IR or R) of the two conformers and obtained the spectra in Fig. 4 C's. By confronting them to the experimental ones (Fig. 4 D's) it can be seen that they fit very well to each other.

Taking into account the experimental and calculated chemical shifts, as discussed before, the agreement between them are best for the average chemical shift values of the two conformers relative to the individual conformers (Table-5). This also confirms the simultaneous presence of the two conformers regarding one experimental NMR spectrum for the both conformers since of their fast motions in the liquid phase.

Conclusion

The optimized molecular structures (bond lengths and bond angles), vibrational frequencies and corresponding vibrational assignments for the optimized conformers of chlorocholine chloride and bromocholine bromide have been calculated by using DFT/B3LYP method with 6-311++G(d,p) basis set, for the first time. The calculated results were seen to be in a good agreement with the experimental data. The assignments of all the fundamental vibrational modes have been clarified by using VEDA 4 program. Gauge including atomic orbital (GIAO) ^1H and ^{13}C NMR shift values for the conformers of the compounds have been calculated by using B3LYP method with the same basis set. Molecular electrostatic potentials (MEP), natural bond orbitals (NBO), frontier molecular orbitals (FMOs) were analyzed. As a conclusion the comparison of the experimental and calculated IR, Raman and NMR spectra of the compounds have shown that the compounds simultaneously exist in two optimized conformers in the ground state. This is may be because of highly deliquescent of choline compounds.

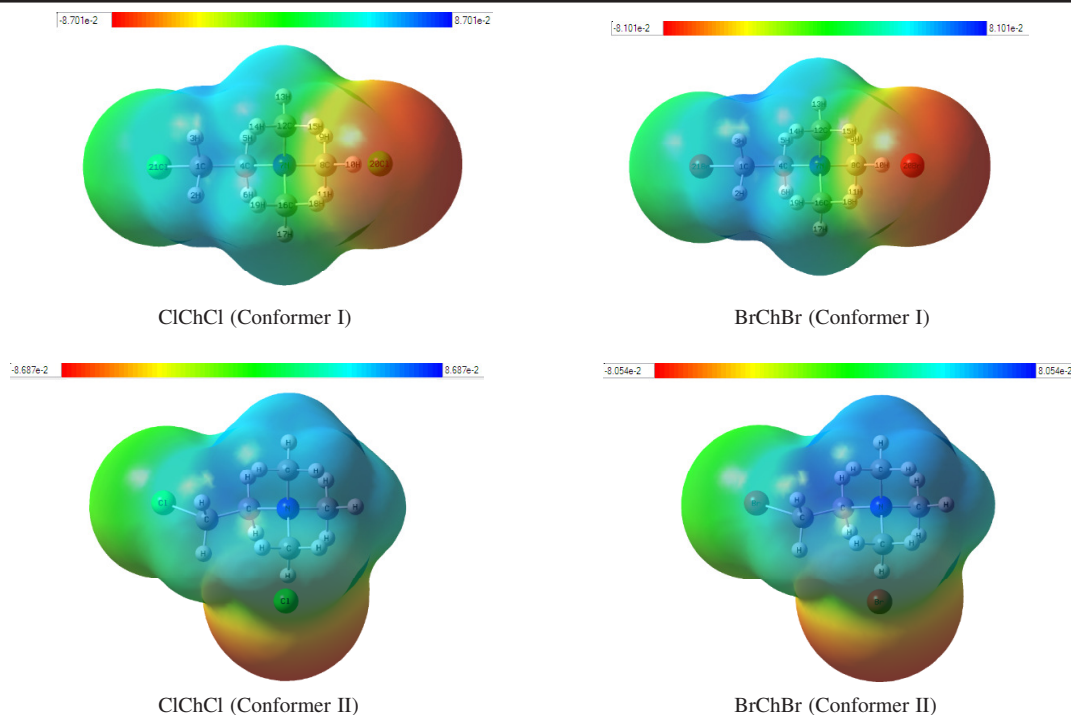


Fig. 3. Electron density surface painted according to value of electrostatic potential for conformers of ClChCl and BrChBr

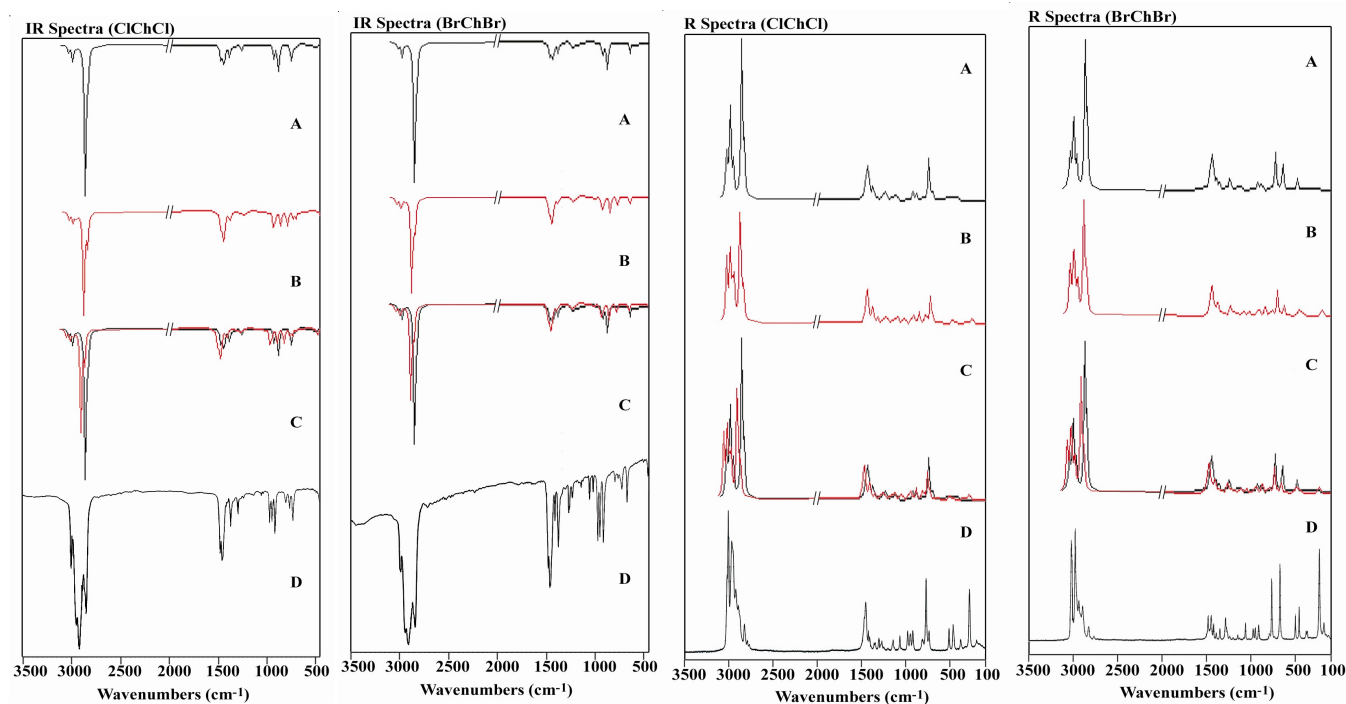


Fig. 4. Calculated IR and R spectra of conformer I (A) and conformer II (B) of ClChCl and BrChBr; C's show the superposition of A and B; D's, experimental spectra

REFERENCES

- M.D. Segall, M.C. Payne and R.N. Boyes, *Mol. Phys.*, **93**, 365 (1998).
- A.S. Davies, W.O. George and S.T. Howard, *Phys. Chem. Chem. Phys.*, **5**, 4533 (2003).
- J. Song, M.S. Gordon, C.A. Deakynne and W. Zheng, *J. Phys. Chem.*, **A108**, 11419 (2004).
- T. Marino, N. Russo, E. Tocci and M. Toscano, *Theor. Chem. Acc.*, **107**, 8 (2001).
- J. Cailliet, P. Claverie and B. Pullman, *Acta Cryst.*, **B34**, 3266 (1978).
- J.K. Herdtklotz and R.L. Sass, *Biochem. Biophys. Res. Commun.*, **40**, 583 (1970).
- K. Frydenvang and B. Jensen, *Acta Cryst.*, **B52**, 184 (1996).
- T. Svinning and H. Sorum, *Acta Cryst.*, **B31**, 1581 (1975).
- S. Jagner and B. Jensen, *Acta Cryst.*, **B33**, 2757 (1977).
- B. Pullman and P. Courriere, *Mol. Pharmacol.*, **8**, 612 (1972).
- M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheesman, 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, J. Mennucci, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, N. Rega, P. Salvador, J.J. Dannenberg, D.K. Malich, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, A.G. Baboul, B.B. Stetanov, G. Liu, A. Liashenko, P. Piskorz, J. Komaromi, R.

- Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, 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 03, Revision C.02, Gaussian, Inc., Pittsburgh PA (2003).
12. A. Frisch, A.B. Nielsen and A.J. Holder, Gauss View User Manual, Gaussian Inc., Pittsburg PA (2001).
13. Computational Chemistry: A Practical Guide for Applying Techniques to Real-World Problems (Electronics), D.C. Young, John Wiley & Sons, Inc, New York (2001).
14. M.H. Jamroz, Vibrational Energy Distribution Analysis, VEDA 4, Warsaw (2004).
15. R.F.W. Bader, Atoms in Molecules, A Quantum Theory, Oxford University Press, Oxford, UK (1990).
16. J.R. Cheeseman, G.W. Trucks, T.A. Keith and M.J. Frisch, *J. Chem. Phys.*, **104**, 5497 (1996).
17. T.A. Keith and R.F.W. Bader, *Chem. Phys. Lett.*, **210**, 223 (1993).
18. R. Ditchfield, *Mol. Phys.*, **27**, 789 (1974).
19. C.M. Rohlfing, L.C. Allen and R. Ditchfield, *Chem. Phys.*, **87**, 9 (1984).
20. <http://www.sigmaaldrich.com/european-export.html>, Sigma-Aldrich Electronic Web Page, Sigma-Aldrich Coop., New York (2006).
21. J. Hjortas and H. Sorum, *Acta Cryst.*, **B27**, 1320 (1971).
22. M.E. Senko and D.H. Templeton, *Acta Cryst.*, **13**, 281 (1960).
23. http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng Spectral Database for Organic Compounds Web Page, National Institute of Advanced Industrial Science and Technology, Japan (2001).
24. A.E. Reed, L.A. Curtis and F. Weinhold, *Chem. Rev.*, **88**, 899 (1988).
25. J.P. Foster and F. Weinhold, *J. Am. Chem. Soc.*, **102**, 7211 (1980).
26. A.E. Reed and F. Weinhold, *J. Chem. Phys.*, **83**, 1736 (1985).
27. A.D. Becke, *J. Chem. Phys. Rev.*, **98**, 5648 (1993).
28. Frontier Orbitals and Organic Chemical Reactions, I. Fleming, Wiley, London (1976).
29. K. Fukui, *Science*, **218**, 747 (1982).
30. S.I. Gorelsky, SWizard Program, Revision 4.5., <http://www.sg.chem.net/>, University of Ottawa, Ottawa, Canada (2010).