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Correlation Analysis for the Determination of the Steric Effect on N-15 Chemical Shift Depending on Quantum Mechanical Parameters

Emad A. S. Al-Hyali[1] , Yosef Othman Al-Jobure[2]
Department of Chemistry, College of Education for pure Science, Mosul University, Mosul, Iraq
Department of Chemistry, College of Science, Mosul University, Mosul, Iraq
emadabd2006@yahoo.com , yousefottman@gmail.com

ABSTRACT

This study is aimed to develop a new set of additive variables for calculating the N15 chemical shift based on quantum mechanical methods for a number of saturated aliphatic amine compounds using the Chem. Office program. Correlation analysis between the experimental N-15 chemical shift with selected variables from two quantum mechanical methods by employing SPSS program were carried out. The relationship between the theoretically calculated chemical shift values of the N15 atom nuclei with the practical values found in the literature were investigated. The two quantum mechanical methods employed to derive parameters used for calculating the N-15 chemical shift, one of them is the semi-empirical Austin method, AM1, and the other representing the ab initio method, density functional theory DFT. The success of the method is determined in terms of the values of correlation coefficient (R) and standard error (SE) as well as the physical meaning of the selected parameters. Good agreement is seen between the practical and theoretical values. A comparison between the two methods was performed to find out the best in calculating chemical shift. The DFT method gave better results.

Keywords: Correlation analysis, AM1, DFT method, N-15 chemical shift

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1- Introduction

Nitrogen is one of the essential elements that form the backbone of organic and bio- organic compounds. The effective groups containing nitrogen atoms are of great importance, since they can react with most elements and have an oxidation number from 3 to 5, coordination number from 1 to 4 and a bonding order up to 3. Nitrogen is found in nature in two isotopes N14 and N15 and in relative abundance (99.635 and 0.365), respectively. They both give a nuclear magnetic spectrum. The nucleus of N14 gives a quadrupole moment which was proved to be unstable when studying large molecules those have several non-equivalent nitrogen atoms, and this in fact arises from the increase in the width of the N14 signal, which is equal to several KHz of frequencies.

Although the natural abundance of N-15 is smaller than that of N14, there are at least two factors enhancing the intensity of the NMR-N15 spectrum. The first is that, the signal width of the spectrum line in N14-NMR is not present in the N-15 NMR. The second factor is the large Nuclear Overhauser Effect (NOE= 4.93) that enhances the signal intensity of the N15-NMR spectrum compared to the nuclei of proton bound to the N15 atoms when the spin population is inverted during the process of proton de-coupling when measuring the N15-NMR spectrum. Moreover, some times the relaxation time of the nitrogen atom can be shortened by using a higher magnetic field strength. The chemical shift is one of the important indications that clarify the application of nuclear resonance. The presence of similar nuclei those having the same frequency but differs in their chemical environment, their spectra will be completely different depending on the electronic environment.

There are many common features in the chemical shift of the N15-NMR and the C13-NMR spectra [1]. The most common feature is the large contribution of the paramagnetic factor to the chemical shift arises from the asymmetric distribution of electrons around the nucleus. This factor is responsible for the wide range of chemical shifts of both nuclei, which extends over a range of hundreds of ppm.

The presence of a free pair of electron on the nitrogen atom of the free amines makes these groups more susceptible to the effect of solvent. This feature is very important, especially in the study of reactions those involving molecular interactions. At the same time, the presence of the electron pair makes the task of comparing the chemical shifts obtained from different sources difficult and not possible. Therefore, the chemical shift measured in the same medium can only be used for the purposes of structural elucidation, meaning that when measuring the chemical shift of a N15 nucleus, it should be referred to the medium in which the measurements were made. Theoretical treatment of N-15 NMR chemical shift have been attempted by several authors. One of the most detailed study appeared in the literature is that carried out by Dauthaler and Robert [2] in which they tried to derive variables for aliphatic amine compounds in a similar way to the method of Grant and Paul [3] when calculated the chemical shift of C13. Because of the high influence of the medium on the chemical shift of N15, the medium in any study must be determined. It was found that the chemical shift of N15 was very inconsistent with the practical results, and these variables did not have physical meaning in terms of the theory of the N15-NMR.

The method of calculations and theoretical treatment of nuclei other than proton, such as (N15 and C13) [1,4],are very important that stimulated the interest of many researchers over many years. In 1964, Grant and Paul developed additive parameters to predict chemical shift of C13 nuclei. These variables were developed and refined by another group of researchers [3,4], which played an essential role in diagnosing organic molecules with low molecular weights [5]. and macromolecules [6,7]. Despite the practical importance of these variables, no effort was made to give them any physical meaning in terms of the theory of the C13 NMR. Similarly, Duthaler and Roberts [1] developed additive variables to calculate the chemical shift of the N15 atomic nucleus.

Later in 1988, Shehab and Abdel Wahab [8] proposed practical additive variables to calculate the chemical shift of C13 nuclei, aiming to give a physical meaning to get a better understanding of the factors that affecting the chemical shift of the C13 nuclei. In 1994, Al-Hyali [9] and Khalil [10] carried out two separate studies to refine and developing the Abdul-Wahab and Shehab variables to calculate the chemical shift of C13 and N15 nuclei, respectively.

In a more recent studies Khalil and Shehab [11] developed additive parameters to calculate the chemical shift aiming to be with a physical meaning consistent with the theory of the N15 NMR technique. Then, in 2007-2008, Al-Hyali [12] used new variables to study the structural distortion of cyclic compounds by studying the nuclear magnetic resonance spectrum of the C13 and N15 nuclei. In 2011, Al-Hyali [13] developed new variables using quantum mechanics methods to calculate the chemical shift of the C13 nucleus. Theoretical calculation of N-15 NMR were not treated adequately, only very few studies were found in the literature.

In this study, additive parameters were suggested to calculate the N-15 chemical shifts for a number of aliphatic amine compounds using two quantum mechanical methods. One of them is a semi-empirical, AM1 method. The other one represent the ab-initio methods DFT. The best set of these two methods in achieving this study is determined by comparing the experimental and calculated chemical shift values in terms of the correlation coefficient (R), standard error (SE) and the physical meaning of the considered variables.The nature of the relationship between the proposed variables those calculated theoretically and the chemical shift values of the N15 nuclei were investigated. Simple and multiple regression analysis is used for this purposes by employing SPSS program. Such kind of studies have become common for various applications [14-16].

2- Theoretical calculations of the compounds under study

This study included calculating the chemical shift of the nitrogen atom (N15) nuclei theoretically by using different variables calculated by quantum mechanics. Statistical analysis was achieved to derive equations for the determination of the chemical shift of nitrogen. The work was carried out using two theories, one of them is a semi-empirical method, Austin1 (AM1), and the other is an ab initio method (DFT). The treatment was carried out for each method separately.

The chemical shift of nitrogen-15 is affected by two factors. One of them is electronic represented by the inductive effect and the other is resulted from the spatial congestion represented by the steric effect (when using the same solvent). These factors were formulated as parameters to describe these variables in the theoretical study. 20 compounds (listed in Table (1) were collected for performing this study[1].

The theoretical parameters were calculated by Chem. Office program (v.12, 2010) as follow: The structural formula of the compound under study was drawn using the Chem. Draw program as a two dimensions. Using the Chem 3D program, the molecule is converted into a three-dimension.

In order to obtain the most stable form (lowest energy) Molecular Mechanic,MM2, is carried out, by which the total energy and its details can be obtained: Stretch, Bend, Stretch-Bend (S-B), Torsion, 1,4 VDW, Non1,4VDW , Dipole-Dipole (D-D) , and. Total Energy (TE). Starting from the formula of minimum energy, quantum mechanics calculations is performed. The basic calculation of DFT is carried out using the method of B3LYP and basis set (3-21G) [17-21].

Additional variables such as bond lengths and angles (C-N-C) in the molecules were calculated, atomic charge on the nitrogen atom represented by Muliken Charges. Molecular Orbital Energy (HOMO-LUMO), Hardness (ŋ), μ (Electronic Chemical Potential) and Global Electrophilic Index (W) were evaluated.

2-1 Statistical Analysis:

The (SPSS V.19 Ibm) program is employed for achieving this study. The first step in the statistical analysis, is performing simple regression (equation 1) analysis which is carried out to find the nature of the relationship between the chemical shift of N15 for each molecule with all the variables determined by the AM1 and DFT methods by employing the Chem. Office program.

$Y = b + aX$ …………(1)

Where b is a reference value. This step helps to get the best way for selecting parameters for doing the multiple regression analysis for deriving the equation required for calculating N-15 chemical shift.

Applying the multiple linear regression analysis (MLR) [22], the values of the selected parameters were considered as independent variables (X_1, X_2, X_3,….X_n), and the experimental chemical shift values are the dependent variable (Y) as in equation(2).

$Y = b + a_1X_1 + a_2 X_2 + …… + a_n X_n$ ……….(2)

Table 1: Compounds selected for this study

No	Name	**No**	Name
1	Ethanamine	11	Dipropylamine
2	Propan-2-amine	12	Methanamine
3	Propan-1-amine	13	Dimethylamine
4	butan-1-amine	14	Dibutylamine
5	butan-2-amine	15	Diisobutylamine
6	2-methylpropan-2amine	16	di-sec-butylamine
7	2-methylpropan-2-amin	17	Dipentylamine
8	N-methylethanamine	18	Diisopentylamine
9	N-methylbutan-1-amine	19	Dihexylamine
10	Diethylamine	20	N-isopropyl-2-methylpropan-2amine

3- Results and Discussion

It is well known that, the organic molecules with linear and branched chains are flexible and thus can change their stereoscopic shapes and geometric dimensions to reduce the tension that, resulting from crowding due to the distribution of substituents at more location at the molecule [23]. Such variation can affect the electronic distribution on the studied molecules, which in turn affect the chemical shift in the NMR studies. This kind of effect cannot be recognized or estimated quantitatively by the common techniques. This is what distinguishes this type of study from traditional laboratory methods.

Twenty compounds [1] were chosen for doing this study. The work was carried out using a number of physical variables derived by AM1 and the DFT was conducted at (B3LYP) at basis set (3-21G). The variables were selected depending on their relationship with the chemical shifts of N-15 [24-27]. The chemical shift is affected by the substituted groups on the reaction centers, through the steric and inductive effects. In addition, the energy functions were calculated.

The values of the parameters estimated by AM1 and DFT are listed in Table (2).

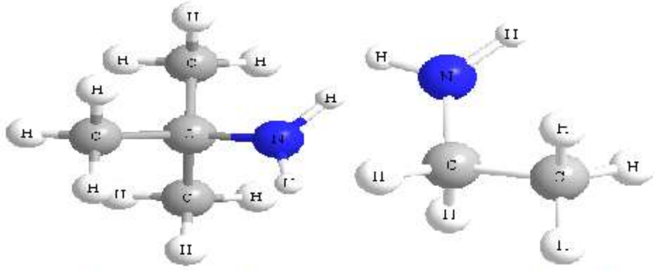
Table 2: The values of the physical variables calculated theoretically using (AM1) method

Angel	Energy-tot	1,4non-VDW	Torsion	Bend	Stretch	Density	W	N	M	LUMO	HOMO
111.264	0.579	-0.1816	-0.15	0.147	0.04	5.3518	0.0069	0.2923	-0.064	0.229	-0.356
110.025	1.065	-0.598	-0.2	0.216	0.11	5.3345	0.0265	0.2473	-0.115	0.133	-0.362
112.964	1.924	-0.3774	0.354	0.342	0.111	5.3513	0.025	0.2445	-0.111	0.134	-0.355
113.138	2.789	-0.5731	0.293	0.653	0.184	5.3493	0.0257	0.2431	-0.112	0.131	-0.355
111.119	2.617	-0.743	0.239	0.585	0.203	5.3354	0.0271	0.246	-0.115	0.131	-0.361
113.574	3.075	-0.7305	0.896	0.549	0.249	5.3496	0.0249	0.2443	-0.11	0.134	-0.355
109.766	1.254	-1.1028	-0.34	0.282	0.259	5.3287	0.0273	0.2456	-0.116	0.13	-0.362
112.422	1.696	-0.3839	-0.14	0.348	0.109	5.3106	0.0259	0.2326	-0.11	0.123	-0.342
113.195	5.734	-1.0627	1.711	1.225	0.288	5.309	-0.051	0.0071	-0.109	0.123	-0.342
109.11	3.409	-0.5154	0.315	0.9	0.182	5.3014	-0.053	0.0053	-0.111	0.122	-0.344
110.108	7.237	-1.1987	2.064	1.815	0.346	5.3067	-0.053	0.0048	-0.111	0.12	-0.341
113.906	0.004	0	0.005	0.052	0.002	5.3499	-0.047	0.0156	-0.109	0.14	-0.359
113.501	1.109	-0.1224	0.002	0.315	0.048	5.3063	-0.049	0.0098	-0.109	0.128	-0.345
113.453	9.203	-1.4513	2.23	2.294	0.505	5.3064	-0.051	0.0062	-0.109	0.121	-0.338
113.219	12.97	-2.1457	4.288	3.458	0.923	5.3025	-0.051	0.0057	-0.109	0.12	-0.337
108.153	10.14	-2.0284	2.89	2.679	0.689	5.3039	-0.055	0.0012	-0.112	0.114	-0.339
114.122	10.73	-1.6963	2.161	2.623	0.646	5.304	-0.052	0.0057	-0.109	0.121	-0.339
113.201	10.46	-3.3844	2.824	2.908	0.806	5.3203	-0.052	0.0049	-0.109	0.118	-0.335
113.977	13.1	-2.1945	2.799	3.232	0.846	5.3073	-0.052	0.0056	-0.109	0.12	-0.338
108.696	9.347	-1.4409	1.469	3.712	0.781	5.3009	-0.058	-0.001	-0.114	0.111	-0.34

Table 3: The values of the physical variables calculated theoretically using (DFT) method

Angel	Energy-tot	1,4non-VDW	Torsion	Bend	Sterch	Density	W	N	M	LUMO	HOMO
109.64	0.5815	-0.182	-0.15	0.1451	0.0395	5.36	0.5167	0.07	-0.268	-0.199	-0.337
108.34	1.0663	-0.598	-0.19	0.6148	0.1091	5.36	0.0075	0.152	-0.047	0.1046	-0.201
110.28	1.9234	-0.378	0.354	0.5424	0.111	5.36	0.0066	0.156	-0.045	0.1103	-0.209
109.92	2.7895	-0.573	0.293	0.3529	0.184	5.36	0.0053	0.157	-0.040	0.1163	-0.197
107.16	2.6167	-0.743	0.239	0.5843	0.2029	5.35	0.0071	0.154	-0.046	0.1074	-0.208
110.97	3.0735	-0.718	0.897	0.8308	0.2454	5.36	0.0083	0.152	-0.050	0.1013	-0.201
107.24	1.2538	-1.103	-0.34	0.682	0.2592	5.35	0.0097	0.148	-0.053	0.094	-0.20
110.13	1.6955	-0.384	-0.14	0.3471	0.1098	5.27	0.0048	0.154	-0.038	0.1156	-0.192
110.16	5.7341	-1.063	1.711	1.227	0.2871	5.28	0.006	0.147	-0.042	0.1052	-0.189
108.88	3.4065	-0.803	0.298	0.9137	0.1809	5.28	0.005	0.151	-0.038	0.1125	-0.190
110.77	7.2185	-1.188	1.76	1.7692	0.347	5.21	0.0049	0.15	-0.038	0.1118	-0.188
108.54	0.0038	0	0.915	0.0523	0.0019	5.36	0.0052	0.157	-0.040	0.1163	-0.197
111.19	1.1115	-0.123	0.514	0.3134	0.0484	5.27	0.0048	0.153	-0.038	0.1148	-0.191
111.08	9.1964	-1.449	2.622	2.2959	0.504	5.26	0.0055	0.152	-0.04	0.1105	-0.192
111.01	12.869	-2.217	4.195	3.4518	0.9138	5.27	0.0076	0.143	-0.046	0.0963	-0.189
108.59	10.137	-2.016	1.872	2.6897	0.6915	5.27	0.007	0.148	-0.045	0.1023	-0.19
111.68	10.729	-1.405	2.167	2.6204	0.6476	5.27	0.0054	0.151	-0.040	0.1103	-0.190
113.29	10.458	-3.28	2.823	2.9003	0.8105	5.56	0.008	0.149	-0.048	0.0999	-0.197
111.01	12.98	-2.178	2.584	2.0775	0.8114	5.27	0.0052	0.15	-0.039	0.1103	-0.188
105.63	9.137	-1.526	1.451	3.6444	0.7798	5.55	0.0082	0.143	-0.048	0.0943	-0.191

Looking at Tables (2 and 3), there is a clear difference between the two methods. These variations are due to the basic principle and the way of calculation of each model when treating the molecule, this is agree with a previous study[18, 25-27]. Referring to Tables (2 and 3) differences among the values of the angles of the two compounds (1,2) are noticed (see Figure 1), where the angle values of the first compound are higher than the second. This is due to the effect of the spatial arrangement of the second compound resulting from branching (higher steric effect), while the first compound is linear. The effect of spatial arrangement is clear on the values of each compound. It is clear that, the angle values in the branched compounds are less than the linear and straight compounds. This applies to all the studied compounds, and increases the accuracy of this theoretical study. This is agree with the basic concepts of the theoretical study and the treatment by the first method (AM1). The basic calculations of the considered molecules by the DFT method, is carried out through solving the Schrodinger equation with a clear treatment of the electronic arrangement [25].



Compound No.1 Compound No.7

Fig. 1: three dimension picture of linear (No.1) and branched (No.7) compounds

3-1 Statistical analysis

In this study, simple and multiple linear regression analysis was conducted in order to reach better understanding of the nature of the relationship between the N-15 chemical shifts [15-16] and the selected parameters[28]. The nature of the relationship between the proposed variables those calculated by AM1 and DFT methods with the N-15 chemical shift in addition to the relation among the parameters themselves were investigated. Simple regression analysis is used for this purposes. The results obtained are listed in tables (4 and 5) for AM1 and DFT respectively

Table 4: R value for the simple regression results between N-15 chemical shift and variables determined by AM1

	$^{\delta}$\Exp	HOMO	LUMO	M	N	W	Stretch	Bend	Torsion	1,4non-VDW	TE	Angel	Density
$^{\delta}$\Exp	1												
HOMO	0.271	1											
LUMO	0.335	0.46	1										
M	0.252	0.08	0.921	1									
N	0.182	0.78	0.521	0.24	1								
W	0.187	0.78	0.356	0.06	0.981	1							
Stretch	0.563	0.74	0.467	0.2	0.59	0.58	1						
Bend	0.558	0.81	0.471	0.17	0.689	0.69	0.97	1					
Torsion	0.48	0.79	0.422	0.13	0.67	0.66	0.9	0.89	1				
1,4non-VDW	0.29	0.68	0.439	0.17	0.513	0.5	0.92	0.88	0.847	1			
TE	0.453	0.83	0.474	0.17	0.677	0.67	0.97	0.97	0.951	0.9	1		
Angle	0.453	0.11	0.027	0.08	0.063	0.03	0	0.03	0.151	0	0.09	1	
Densit	0.481	0.82	0.586	0.3	0.758	0.73	0.6	0.67	0.577	0.5	0.66	0.2	1

Table 5: R value for the simple regression results between N-15 chemical shift and variables determined by DFT

	$^{\delta}$\Exp	HOMO	LUMO	M	N	W	Stretch	Bend	Torsion	1,4non-VDW	TE	Angel	Density
$^{\delta}$\Exp	1												
HOMO	0.153	1											
LUMO	0.064	0.986	1										
M	0.093	0.994	0.999	1									
N	0.014	0.952	0.99	0.981	1								
W	0.129	-0.99	-1	0.997	-0.98	1							
Stretch	0.567	0.315	0.196	0.235	0.089	-0.25	1						
Bend	0.612	0.322	0.195	0.236	0.08	-0.25	0.955	1					
S-B	0.437	0.325	0.217	0.252	0.118	-0.25	0.957	0.891					
Torsion	0.143	0.331	0.225	0.26	0.127	-0.26	0.852	0.833	1				
1,4non-VD	0.521	-0.3	0.2	-0.23	-0.11	0.25	-0.92	-0.85	-0.778	1			
TE	0.45	0.336	0.217	0.256	0.109	-0.25	0.962	0.925	0.909	-0.877	1		
Angle	0.502	0.052	0.046	0.46	0.04	-0.02	0.216	0.144	0.495	-0.33	0.374	1	
Density	0.274	-0.14	-0.12	-0.13	-0.11	0.08	0.169	0.187	-0.076	-0.239	-0.036	-0.23	1

The importance of studying the simple relations between the N15 chemical shift and the parameters determined by AM1 and DFT methods (as in Tables 4 and 5) is to find out the nature of the relation whether these relationships were direct (positive values of the coefficient (a) or inverse relations(negative values of the coefficient (a) in addition to the strength of these relations. This method also helps to make the best choice of the parameters when applying the equation of multiple regression analysis (Tables 6-9).

The results listed in Table 4 indicate that the best linear relationship between the N-15 chemical shift and the variables found by the method AM1 were torsion, bending, Van der Waals forces and electronic density. While in the case of DFT (Table 5), the best relationship was found with torsion, bend, torsion-bend, and angle. Some of the relationships between the variables with each other were excluded since they are calculated one from the other and could be linearly combined and may provide misleading results.

The obtained relationships are relatively good, but they are not sufficient as a simple analysis to describe the system accurately to calculate the chemical shift in this way. For this reason, other variables were used and the process of multi-parameter regression analysis was conducted with two up to five variables. The analysis was stopped at this number of variables due to the lack of degrees of Freedom to perform statistical analysis

The best obtained results in the multiple regression are when using five variables. These results were indicated by correlation coefficient (R) close to unity and standard error (SE) close to zero in both methods (AM1, DFT), as shown in Tables (6 and7) respectively.

Table 6: Example of the correlation results (R and SE) for the theoretical calculation of chemical shift by using up to five variables determined by the (AM1) method.

Variables	R	S.E
Angle, Stretch	0.864	10.31
S-B, W, Angle	0.954	6.86
Angle, Stretch, W, Density	0.962	5.91
Angle, Stretch, Torsion, 1,4 VDW, HOMO	0.987	3.67
Angle, Stretch, Torsion, 1,4 VDW, n	0.988	3.53
Angle, Stretch, Torsion, 1,4 VDW, Bend	0.986	3.73
Angle, Stretch, Torsion, 1,4 VDW, SB	0.988	3.533
Angle, Stretch, W, Torsion ,SB	0.985	3.88
Angle, Stretch, W, Torsion,1,4 VDW	0.988	3.538
Angle, Stretch, W, Torsion ,Density	0.985	3.93
Angle, Stretch, HOMO, Torsion, Density	0.982	4.27
Angle, Stretch, Torsion, TE,M	0.986	3.78
Angle, Stretch, Torsion, TE, n	0.987	3.67
Angle, Stretch, Torsion, TE, W	0.988	3.49
Angle Stretch, W, Density, Bend	0.972	5.5
Angle 1,4 VDW,SB ,Torsion , W	0.964	5.99
Stretch 1,4 VDW,SB ,Torsion , n	0.984	3.98
Angle HOMO, Torsion, 1,4 VDW, SB	0.987	3.62
Angle, W, Torsion, 1,4 VDW, SB	0.988	3.53

Table 7: Examples of the correlation results (R and SE) for the theoretical calculation of chemical shift using up to five variables by applying the (DFT) method.

Variables	R	S.E
Non1,4VDW, Angle	0.884	9.54
Bend, Torsion, Non1,4 VDW	0.936	8.34
Bend, Torsion, Non1,4 VDW, Angle	0.969	5.399
Bend, Torsion, Non1,4 VDW, Angle, Stretch	0.976	4.93
Bend, Torsion, Non1,4 VDW,Angle,1,4 VDW	0.978	4.68
Bend, Torsion, Non1,4 VDW ,Angle, TE	0.98	4.45
TE, Torsion, Density, Bend, Angle	0.961	6.204
Bend, Torsion, Non1,4 VDW ,Angle, Density	0.995	2.21
Bend, Torsion, Non1,4 VDW, Angle ,SB	0.976	4.93
Bend, Torsion, Non1,4 VDW ,Angle, HOMO	0.969	6.712
Bend, Torsion, 1,4 VDW, Angle, Density	0.971	5.34
TE, Torsion, 1,4 VDW, Angle, Density	0.926	8.53
TE, Torsion, 1,4 VDW ,Angle ,SB	0.94	7.71
TE, Torsion, 1,4 VDW ,Bend ,SB	0.934	8.03
Bend, Torsion, Stretch, TE ,Angle	0.962	6.15
Bend, Torsion, Stretch, HOMO ,Angle	0.953	6.85
Bend, Torsion, Stretch ,Angle, non-1,4 VDW	0.969	5.58
Bend, Torsion, Stretch,Angle,1,4 VDW	0.969	5.58

Observing tables 6 and 7, the best sets of correlating N-15 chemical shifts with up to five variables, when applying the AM1 model is when (R = 0.988), while for the DFT method, the best value is at R = 0.995. These results are listed in table (8). And could be formulated as in equations 3 and 4 for both method respectively.

Table 8: Results of multiple regression analysis for both methods AM1and DFT

AM1		DFT	
Var.	Coef.	Var.	Coef.
Torsion	-11.520	Bend	17.857
Angle (C-N-C)	-6.858	Torsion	-17.840
Stretch	44.045	Angle	-4.118
TE	2.979	Density	-58.296
W	62.776	Non1,4VDW	-16.179
R	0.988	R	0.995
SE	5.49	SE	2.21
No of observation	20	No of observation	20
Constant =	785.782	Constant =	776.749

The best results obtained from multiple regression analysis for both methods AM1 and DFT are listed in table (8). Two multi-parametric equations (eq. 3 and 4) were derived for the theoretical calculation of N-15 chemical shift depending on the parameters evaluated by AM1 and DFT. The DFT gave better results in terms of consistency and agreement between the observed and calculated N15 chemical shifts. Table(8) indicate that, the most effective parameters on the N-15 chemical shift are the electronic density, Van Der Waals forces, and the geometrical dimension such as the CNC angle and the torsion which results from stress upon a part of molecule leading to twisting it away from standard dimension. The increase of the negative value of the coefficient of the variable decreasing the value of the chemical shift causing shielding effect. These results agree with the physical meaning of the principles of NMR [29].

AM1

Shift N-15= (785.782-11.520*Torsion-6.858*Angle 44.045*Stretch+2.979*TE +62.776*W)**......... (3)**

DFT

Shift N-15=**(**776.749+17.857*Bend-17.840*Torsion-16.179*Non1,4VDW-58.296*
Density -4.118*Angle) **--------(4)**

Comparing the calculated N-15 chemical shift estimated by AM1 and DFT with the practical values [1] were carried out. The obtained results are given in tables 9 and 10 respectively.

Table 9: Calculation of the theoretical chemical shift values by AM1 method and comparing them with the practical values.

W	TE	Angle	Stretch	Torsion	Shift Theory	Shift exp	Different
0.0069	0.5793	111.26	0.0398	-0.1547	28.457	24.6	3.857
0.0265	1.065	110.02	0.1098	-0.1954	43.187	43.6	-0.412
0.025	1.9235	112.96	0.1109	0.3542	19.213	19.8	-0.586
0.0257	2.7894	113.14	0.184	0.2928	24.569	21	3.569
0.0271	2.6167	111.12	0.2029	0.239	39.441	40.4	-0.958
0.0249	3.0752	113.57	0.2487	0.8964	18.275	18.4	-0.124
0.0273	1.2539	109.77	0.2591	-0.341	53.829	58.4	-4.570
0.0259	1.6955	112.42	0.1092	-0.1432	27.963	27.7	0.2636
-0.0511	5.7342	113.2	0.2878	1.7112	16.359	24.1	-7.74
-0.0529	3.4088	109.11	0.1821	0.3151	48.761	47.9	0.861
-0.0528	7.2366	110.11	0.3459	2.0636	40.403	38.9	1.503
-0.0468	0.0038	113.91	0.002	0.0046	1.7554	1.3	0.455
-0.0494	1.1092	113.5	0.0476	0.0018	9.7021	6.7	3.002
-0.0512	9.2027	113.45	0.5048	2.2295	28.505	29.7	-1.194
-0.0514	12.9746	113.22	0.9231	4.2883	36.043	34.8	1.243
-0.0554	10.1418	108.15	0.6885	2.89	67.869	67.1	0.769
-0.0518	10.7327	114.12	0.6464	2.1612	35.466	40.3	-4.833
-0.0518	10.4604	113.2	0.8063	2.8239	40.373	40	0.373
-0.0516	13.1003	113.98	0.8462	2.7991	44.976	40.3	4.676
-0.0578	9.3467	108.7	0.7805	1.469	82.0461	82.2	-0.153

Table 10: Calculation of the theoretical chemical shift values by DFT method and comparing them with the practical values.

Torsion	Bend	1,4nonVDW	Density	Angel	Shift Theory	Shift Exp	Different
-0.1544	0.1451	-0.1821	5.36	109.643	21.006	24.6	-3.59
-0.1946	0.6148	-0.5977	5.36	108.343	42.189	43.6	-1.41
0.3543	0.5424	-0.3776	5.36	110.2791	19.569	19.8	-0.23
0.2925	0.3529	-0.5727	5.36	109.9223	21.914	21	0.914
0.239	0.5843	-0.7427	5.35	107.1601	41.71	40.4	1.310
0.8972	0.8308	-0.7177	5.36	110.971	17.68	18.4	-0.712
-0.341	0.682	-1.1029	5.35	107.2354	59.31	58.4	0.919
-0.1433	0.3471	-0.3839	5.27	110.1321	30.913	27.7	3.21
1.7111	1.227	-1.0627	5.28	110.1571	23.83	24.1	-0.26
0.2984	0.9137	-0.8029	5.28	108.875	44.524	47.9	-3.37
1.7601	1.7692	-1.1878	5.21	110.765	36.24	38.9	-2.65
0.9147	0.0523	0	5.36	108.543	1.861	1.3	0.56
0.5139	0.3134	-0.1225	5.27	111.1852	10.02	6.7	3.32
2.6221	2.2959	-1.4491	5.26	111.0817	30.28	29.7	0.584
4.1953	3.4518	-2.2166	5.27	111.0082	34.99	34.8	0.196
1.8723	2.6897	-2.0164	5.27	108.593	69.53	67.1	2.438
2.1674	2.6204	-1.4054	5.27	111.6801	40.43	40.3	0.136
2.8229	2.9003	-3.2795	5.56	113.2939	40.509	40	0.509
2.5844	2.0775	-2.1782	5.27	111.0081	38.57	40.3	-1.72
1.4508	3.6444	-1.5263	5.55	105.6304	82.054	82.2	-0.14

Table 11: Comparison between the theoretical and practical chemical shift values for the compounds under study in the two methods (AM1, DFT)

	AM1			DFT		
No	Shift theory	Shift exp	Different	Shift theory	Shift exp	Different
1	28.46	24.6	3.857	21.01	24.6	-3.59
2	43.19	43.6	-0.412	42.19	43.6	-1.41
3	19.21	19.8	-0.586	19.57	19.8	-0.23
4	24.57	21	3.569	21.91	21	0.914
5	39.44	40.4	-0.958	41.71	40.4	1.31
6	18.28	18.4	-0.124	17.68	18.4	-0.712
7	53.83	58.4	-4.57	59.31	58.4	0.919
8	27.96	27.7	0.264	30.91	27.7	3.21
9	16.36	24.1	-7.74	23.83	24.1	-0.26
10	48.76	47.9	0.861	44.52	47.9	-3.37
11	40.4	38.9	1.503	36.24	38.9	-2.65
12	1.755	1.3	0.455	1.861	1.3	0.56
13	9.702	6.7	3.002	10.02	6.7	3.32
14	28.51	29.7	-1.194	30.28	29.7	0.584
15	36.04	34.8	1.243	34.99	34.8	0.196
16	67.87	67.1	0.769	69.53	67.1	2.438
17	35.47	40.3	-4.833	40.43	40.3	0.136
18	40.37	40	0.373	40.51	40	0.509
19	44.98	40.3	4.676	38.57	40.3	-1.72
20	82.05	82.2	-0.153	82.05	82.2	-0.14

Looking at the results in Table (11), differences between the calculated N-15 chemical shifts in the two methods, were noticed depending on the basic principle of the method of calculation for each model. Also difference were seen between the theoretical and practical values of N-15 chemical shifts of the studied compounds such as compound numbers (1,4,7,9,11,17, and 19) when estimated by the AM1 method (R= 0.988, SE=3.49). The highest shift between the practical and calculated values is noted in the compound number (9) in the same table. When applying the ab initio method (DFT), better results are obtained in terms of (R=0.995, and SE=2.21). The DFT theory showed better agreement (figure 2) between the calculated and experimental N-15 chemical shift values (R=0.9904 for DFT and R=0.976 for AM1). This method proved to be the best for performing such calculations. The results obtained are in agreement with other findings seen in the literature [30].

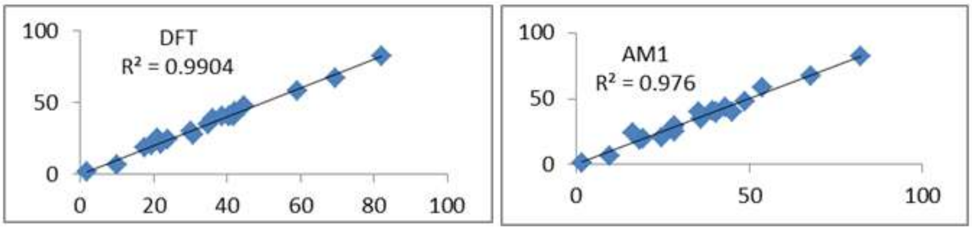


Fig. 2: The relationship between the practical and theoretical values of the chemical shifts of the studied compounds (AM1, DFT)

4- Conclusion

Results revealed, this study can provide researchers with valuable information about geometry and stereochemistry in a quantitative manner. Twenty compounds were selected for achieving this investigation. The work was carried out using a number of physical variables derived by AM1 and DFT (B3LYP) at basis set (3-21G). The variables were selected depending on their relationship with the chemical shifts of N-15. The results showed that, chemical shift is affected by the substituted groups on the reaction centers, through the steric and inductive effects. These data cannot be provided by traditional laboratory methods. It gives an idea about the structural distortion that can be obtained from the calculation of the difference between the experimental and calculated chemical shift of the nuclei of nitrogen-15 atoms. The differences between the calculated and the practical chemical shift were found to be a good measure of the amount of structural distortions. Additive parameters were suggested to calculate the N-15 chemical shifts for a number of aliphatic amines using AM1 and DFT methods. The best set of these two methods in achieving this study is determined by comparing the experimental and calculated chemical shift values in terms of the correlation coefficient (R), and standard errors (SE). The DFT gave better results in terms of consistency and agreement between the observed and calculated N15 chemical shifts.

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