How to Cite:
Al-Hyali, E. A. S., & Othman, Y. (2022). Multiple linear regression for the estimation of steric effect in cyclic systems from calculation of C-13 chemical shifts and employing parameters derived using DFT method. *International Journal of Health Sciences*, *6*(S4), 1630–1650.
https://doi.org/10.53730/ijhs.v6nS4.6314

Multiple linear regression for the estimation of steric effect in cyclic systems from calculation of C-13 chemical shifts and employing parameters derived using DFT method

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***Abstract*---**In this work, differences between C-13 chemical shift calculated by the linear addition method (LAM) and the practical values is used as a measure of the steric effects. The C-13NMR chemical shift of a number of saturated and aromatic cyclic organic compounds were selected for achieving this study. The results obtained exhibited high agreement between the calculated and practical values, deviation is only noticed on locations exhibited steric hindrance caused by the substitution of methyl groups on two neighboring carbon atoms. The study proved that the amount of shift resulting from the spatial effect is of an additive character. The amount of shift due steric effect noticed was similar in both aromatic or saturated systems unless other factor is interfered. Density functional theory (DFT) methods is applied to calculate the bond lengths, of the aromatic molecules (toluenes), electronic densities, and the heat of formation using the method B3LYP at basis set 3-21G by (Chem office V.12,2010). Their relationship to space interference were investigated. The results obtained indicated that, the steric resulting from the spatial interference, heat of formation, and distortions in the geometric dimensions of the ring (the bond lengths) are well related to the values of chemical shift. The study showed that, there is no linear relationship between the values of chemical shift and electronic density.

***Keywords*---**Linear addition method, DFT method, Regression analysis, C-13 NMR.

Introduction

The carbon-13 nuclear magnetic resonance plays a major role in the process of organic diagnosis of different compounds due to the ease and simplicity of its spectrum, which is free from the complications resulting from the coupling [1-2]. The additive property of the chemical shift of the substituted groups, created a great chance in theoretical studies. Many theoretical methods have been used to calculate the chemical shifts of the carbon-13 nuclei and studying the effects caused by the geometrical structures of different organic compounds. The results of the applied methods were somewhat far from the experimental values [3].

Other methods succeeded in calculating the chemical shifts of the carbon-13 nuclei theoretically through the development of variables of an additive character. A Number of these methods depended on the basic principles on C-13 NMR[3], while others used statistical method such as the regression analysis [4,5] or mathematical methods such as simultaneous equations [4]. These studies have been applied in different fields for the development of various information in the related subjects [5]. The proposed variables in all of these studies were based on two factors: the first one is electronic in nature and representing the inductive effect that generated by the substituted groups (due to difference in their electro-negativities) on the carbon atom under study, and the second one is the steric interactions between the protons of the studied carbon atom with the protons on the neighboring carbon. These two factors were formulated in various ways. Grant [7] and Al-Hyali [4] described the first factor by the number of carbon atoms in the positions (α, β, γ... etc.) with respect to the carbon atom under consideration. Shehab [8] used the number of carbon atoms in the alpha position of a primary, secondary and tertiary types. Others [6] described the effect of the substituted groups in the positions (α, β, γ... etc.) of different types in terms of their ability to push and withdraw electrons. This effect is working through the participation of the electrons of the substituted groups with the electrons in the P orbital of the carbon atom under consideration. Any additional sharing of electrons by the substituted groups leading to the departure of the electronic distribution of the studied atom from the spherical symmetry and leads the chemical shift to a lower field (de-shielding).

The second factor has been formulated in various ways. Grant [9,10] described the protons interactions in terms of the number of protons in the positions (α, β, γ... etc.) with respect to the carbon atom under study. Lindemann and Adams [11] used correction factors to express the deviation in the spatially crowded positions in the molecule. Al-Hyali [4,5] thought that only protons located in the same side of the molecule can interfere, while protons in opposite side are not affected by each other. Interferences between the electronic density of the atoms concerned occurs in a way that has not been understood so far. It should be noted that, observations recorded in practice in most cases shift into a higher field (shielding), only a few observations exhibited shift to lower field [12].

In the aromatic compounds, the steric effect is studied by considering the size of the substituent and the hydrogen bonding. The LAM is one of the common methods used to calculate the chemical shift of the carbon-13 nuclei of the organic molecules [15,16]. This method is based on extracting the effects of the

substituents, which were mentioned previously, from subtracting the value of the chemical shift of a reference compound (un-substituted) from the chemical shift of a single substituted compound, then adding this extracted value to the practical chemical shift of the reference compound and using it in calculating the chemical shift of other compounds (as shown in the practical part). The deviation between the calculated and experimental values indicates the presence of other factors that affecting the chemical shift, such as the steric and other interferences.

To the best of our knowledge, this method has not been applied by any researcher in the literature to calculate the chemical shift of carbon-13 of saturated compounds. Due to the lack of literature concerning the existence of studies of this type, only very limited studies those used the linear addition method to estimate the steric effect of monocyclic aromatic compounds [17,18] and some naphthalenes [19]. In this study, the amount of the steric hindrance resulting from the presence of adjacent methyl groups by calculating the chemical shift of methyl cyclohexane and methyl decalin using cyclohexane and un-substituted decalin as reference compounds were estimated quantitatively which is not possible to calculate by the common methods. The steric hindrance caused by adjacent methyl groups in aromatic systems were also evaluated.

This study also included the use of quantum mechanical methods to calculate some geometric dimensions and electronic densities to estimate the changes caused by the steric interferences in the molecular structures of the studied aromatic compounds and to compare these changes with the values of chemical shift.

Experimental Part

Calculation of the chemical shift of cyclohexane and decalin compounds

The deviation of chemical shift caused by substitution of a methyl group on the carbon atoms of the cyclohexane ring was calculated by subtracting the practical values of chemical shift (σc-13) obtained from previous studies [9] (relative to the TMS compound) of the methyl cyclohexane compound from the un-substituted cyclohexane compound, as follows:

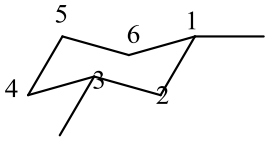
The practical values of methyl cyclohexane are as follows:

C. No.	δ C – 13 ppm
1 (ε)	33.06
2,6 (α)	35.77
3,5 (β)	26.55
4 (γ)	26.40

The practical chemical shift values for the carbon nuclei of the cyclohexane compound were (27.06) ppm. Thus, the amount of the effects can be calculated as follows:

ε	C1	33.06-27.06 = 6
α	C2,6	35.77-27.06 = 8.71
β	C3,5	26.55-27.06 = 0.51
γ	C4	26.40-27.06 = 0.66

The value of the chemical shift of any other compound can be calculated by adding these values to the practical chemical shift of the un-substituted cyclohexane compound. To illustrate this, calculation of the chemical shift of the carbon atoms of 1,3-cis dimethyl cyclohexane, is taken as an example:



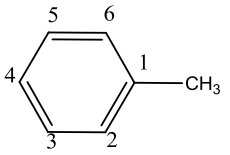
C-1,3	δ_{C-13} = 27.06+1 β = 27.06 + 6-0.51 = 32.55
C-2	δ_{C-13} = 27.06+2 β = 27.06 + 2(8.71) = 44.48
C-4,6	δ_{C-13} = 27.06 + 1 α + 1 γ
C-5	δ_{C-13} = 27.06 + 2 β

When calculating the chemical shift of decalin compounds in this way, the values of the methyl group affecting the cyclohexane compounds mentioned above were used, in addition to the amount of the following two effects:

- The effect of merging two rings in the decalin (17.16ppm), which was calculated from the difference between the value of the practical chemical shift of the bridge atoms in the decalin [27] and the chemical shift of cyclohexane.
- The effect of fusion on the carbon atoms in the alpha position to the bridge carbon was found to be equal to (7.68ppm) when the value of the chemical shift of these atoms is subtracted from the value of the cyclohexane ring.

Calculating the chemical shift of methyl benzene

The effect of substitution of a methyl group on the benzene ring was determined by the difference between the practical values of the chemical shift of the carbon nuclei of the toluene compound and the benzene ring (128.7ppm), which were obtained from previous studies [1]. The calculated effects values were determined as follows:



C1	δ_{C-13} = 137.8-128.7 = 9.1
C2,6	δ_{C-13} = 129.31-128.7 = 0.61
C3,5	δ_{C-13} = 128.5-128.7 = 0.2
C4	δ_{C-13} = 125.6-128.7 = 3.1

Calculating the chemical shift of different compounds in the same way that was used in cyclohexane and decalin .It is worth mentioning that the effect of the calculated values resulted from substitution on the rings are equivalent to the

inductive effect of the substituent and not the effects of proximity to the neighboring substituted groups because they were calculated from a single-substituted compound.

These calculations were performed using the DFT using the method B3LYP at basis set 3-21G [20]. The molecule with minimum energy were obtained by the process of energy minimization. The bond lengths and angles were compared with the standard bonds found in the literature [22] as well as the dihedral angles of the particle were obtained. The electronic density on each atom and the heat of formation of the molecules were determined.

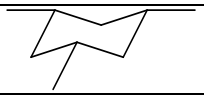
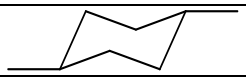
Results and Discussion

The use of LAM in calculating the chemical shift of carbon-13 nuclei is more common in aromatic compounds, and calculating the chemical shift of aliphatic compounds is rarely used. The LAM is deduced from a practical values by comparison with a mono-substituted compound used as a reference value representing the effect of the substituted groups, which were found to be of an additive character, inductively by influencing the electronic distribution on the atom under study and sterically through proton interactions on the neighboring carbons on the same molecule.

Saturated compounds

The effect of substitution of the methyl group on the chemical shift of the ring carbon atoms of cyclohexane and decalin compounds were calculated as a model for saturated cyclic compounds. Tables (1 and 2) show the chemical shift values for the practical carbon-13 nuclei and those calculated by applying LAM to a group of cyclohexane and decalin compounds respectively.

Table (1)
Observed and calculated (by LAM) chemical shift of C-13 nuclei for cyclohexane compounds

Item	Compounds	CNo	δ(obs) ppm	δ (cal)	Res
1		13	32.28	33.06	0.24
		2	44.7	44.48	- 0.22
		4.6	35.37	35.77	0.40
		5	26.45	26.55	0.10
2		1,3,5	32.68	32.04	- 0.64
		2,4,6	44.2	44.48	0.28
3		1	33.06	33.06	0.00
		2,6	35.77	35.77	0.00
		3,5	26.55	26.55	0.00
		4	26.4	27.06	0.66
4		1,4	32.61	33.06	0.45
		2,3,5,6	35.63	35.26	- 0.37

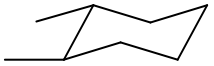
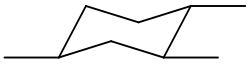
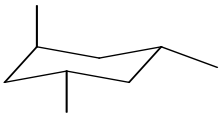
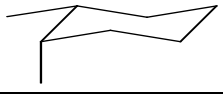
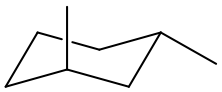
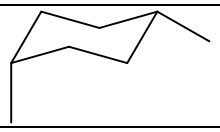
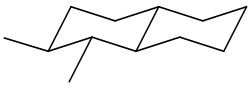
5		1,2	39.55	41.77	2.22
		3,6	36.03	35.77	- 0.26
		4,5	26.85	26.55	- 0.30
6		2	46.22	50.48	4.26
		1,3	39.15	41.26	2.11
		4,6	36.45	35.25	- 1.2
		5	26.43	26.04	- 0.39
7		3	45.08	43.98	- 1.10
		1	39.19	41.77	2.58
		2	38.87	41.77	2.39
		5	35.43	35.26	- 0.67
		6	35.74	36.79	1.05
		4	32.89	35.55	- 0.34
8		2	44.99	44.48	- 0.51
		4,6	40.92	44.48	3.56
		5	28.6	32.04	3.44
		1,3	26.44	32.04	5.6
9		1,2	34.43	41.77	7.34
		3,6	31.51	35.77	4.26
		4,5	23.67	26.55	2.88
10		1,3	27.05	33.06	6.01
		2	41.42	44.48	3.06
		4,6	33.88	37.77	3.89
		5	20.75	26.55	5.8
11		1,4	30.13	33.06	2.39
		2,3,5,6	30.89	35.26	4.37
12		1	38.82	41.77	2.95
		2	33.58	41.26	7.68
		3	40.73	43.98	3.25
		4	27.97	32.55	4.58
		5	31.82	35.26	3.44
		6	29.47	36.79	7.32

Table (2)
Practical chemical shifts and calculated by LAM of decalin compounds

Item	Compounds	CNo	δ (obs) ppm	δ (cal)	res
1		9	50.60	53.04	2.44
		10	44.05	43.82	- 0.23
		1	38.42	40.85	2.43
		2	37.12	35.88	- 1.24
		4,5	35.39	34.85	- 0.54
		8	31.02	34.85	3.83
		3	27.45	26.66	- 0.79

		6	27.16	27.17	0.01
		7	2682	27.17	0.35
2		9	43.49	44.33	0.84
		10	43.39	44.33	0.94
		1	43.31	43.56	0.25
		3	35.66	35.88	0.22
		4,5	34.3	34.34	0.04
		8	34.15	34.34	0.19
		2	33.06	33.17	0.11
		6,7	27.02	27.17	0.15
3		9	49.44	53.04	3.6
		2	45.42	44.59	- 0.83
		10	43.67	44.33	0.66
		4	42.99	43.56	0.57
		1	37.71	41.36	3.65
		5	34.63	34.85	0.22
		3	32.44	33.17	0.73
		8	30.63	34.85	4.22
		6	27.16	27.17	0.01
		7	26.91	27.17	0.26
4		1,8	43.05	43.56	0.51
		9,10	42.84	44.33	1.49
		3,6	35.6	35.88	0.28
		4.5	34.05	34.34	0.29
		2,7	32.89	33.17	0.28
5		9,10	44.18	44.18	0.00
		1,4	44.18	43.05	- 1.13
		2,3	39.78	41.88	2.1
		5,8	34.32	34.85	0.53
		6,7	27.14	27.17	0.03
6		9	49.36	52.42	3.06
		1	44.34	49.56	5.22
		10	43.3	43.82	0.52
		2	39.27	41.88	2.61
		3	35.82	35.37	- 0.45
		4	35.8	34.34	- 1.46
		5	34.51	34.85	0.34
		8	30.96	34.34	3.38
		6	27.14	27.17	0.03
		7	26.58	27.17	0.59

Examining the differences between the values of the practical carbon-13 chemical shift and the values calculated by using LAM in Table (1), the following can be noted:

- Isolated methyl groups in the equatorial positions, do not generate any steric tension and therefore has no significant effect on the chemical shift of the cyclic carbon atom whether attached or far from them (the substituted carbon atoms in compounds number 1-5 and in C-5 in compound No. 7)

- The methyl groups at positions (1and 2) affect the connected carbon ring with approximately (2.22) ppm, as in (C-1,2) in compound No.5, (C-1,2) in compound 7, (C-1,2) in compound No.9 and (C-1) in compound 12, while the carbon atom attached to a methyl group that is in the α position to other two methyl groups show deviation twice the value resulted from the effect of having one group in position ∝, note (C-2) in compound No. 6. These results indicate that the effect of adding a methyl group is of additive character.
- When there are large steric interferences resulting from increased substitution on the ring, the deviation in the value of the chemical shift moves to the carbon atoms in position α to the substitution location. (C-4,6) in compound 7 and (C-3,6) in compound 8. This deviation represents a medium value and it doubled increased when one of the substituted groups is in the axial position, (C-4,6) in compound No.10 and (C-3,5) in compound No.12. The reason for this deviation may due to the ring flattening that occurs as a result of the high steric interference, which leading to distortion in the tetrahedral symmetry of the carbon atoms [23].
- The axial methyl groups shift the absorption of the carbon atoms in position 3 and 5 as well as the adjacent carbon by approximately (5.0) ppm due to the γ-gaush interactions as in the atoms (C-1,3) in compound No. 9, (C–4,5) in compound No.10, (C–1,3) in compound No. 11 and (C–2,3,4,5,6) in compound No. 12 and this is quite similar to what was observed in previous studies [24].
- The additive characteristic of the different effects caused by the methyl groups in carbon (C-1,2) in compound 9 can be observed, where the deviation from the practical values is equal to (7.34) ppm, which is equal to the sum of the effect of the axial methyl group (5.0) and the effect of methyl groups existed in positions 1and 2 (which is equal to 2.2). Also, the amount of deviation in the carbon atom (C-2) in compound No.12 is equal to the summation of the effect of the γ-gauch interference with the protons on the carbon atom of the axial methyl group (5.7 ≅) ppm, and the effect of the presence of two methyl groups in the position 1, 2 (2.2 ≅) ppm .

The chemical shift of decalin compounds are calculated by LAM deduced from cyclohexane compounds as well as those calculated from the merging of two cyclohexane rings (decalin) as mentioned previously. The results showed tendencies indicated by the differences between the practical and the calculated chemical shifts from the LAM listed in Table (2) which refers to the following:

- The substitution of the methyl group on the decalin ring on position ∝ to the bridge atoms causes a deviation in the chemical shift from the practical value similar to that caused by substitution of the two methyl groups of positions 1, 2 on the cyclohexane ring and by approximately the same amount as in (C-1,9) in compound No.1 and (C-1,9) in compound No.3 and (C-9) in compound No.6. This effect represents the sum of two effects, the first one is the presence of a substitution on the ∝ position of the bridge atoms as well as the presence of a methyl group on the carbon atom (2). This represents an additional effect similar to that of the compound 1,2-dimethylcyclohexane (the substituent effect is transmitted from the alpha position of the bridge atoms to the analogous carbon atom in the other ring (C-8) and about the same amount.

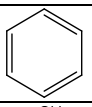
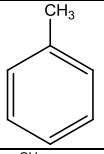
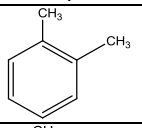
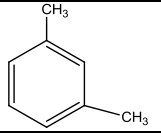
- The presence of two methyl groups on the two alpha carbon atoms to each other (1,2) and far from the fusion site of the two rings gives a direct effect that is completely similar to that of 1,2-dimethylcyclohexane and in exactly the same shift (2.2)ppm for the substituted ring atoms. The two bridge carbon atoms, show small deviation, as in (C-9,10) in compound No.2, and sometimes this deviation disappears as in (C-9,10) in compound No.5.

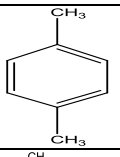
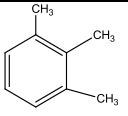
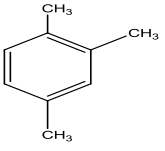
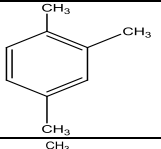
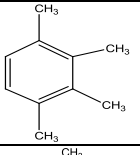
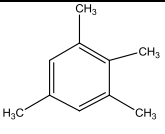
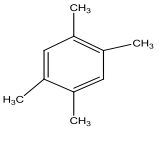
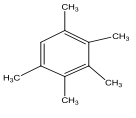
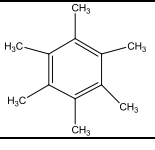
Aromatic compounds

The effect of the methyl groups substituted on the aromatic rings occurs through the electronic rearrangement of the pi system generated by the effect of these groups on the aromatic ring leading to variation in the electronic density on the ring atoms and the molecular dimensions of the molecule as a results, such as the bond lengths and angles among different atoms. This in turn affecting the activities of these atoms towards different chemical reactions. Carbon-13NMR spectroscopy is one of the most important methods those can detect these changes. The effect of electronic density and molecular geometry are reflected through variation in chemical shift. Since the effect of the substituted groups on the chemical shift is of additive nature, the LAM could be used for calculating the chemical shift of the aromatic systems [18].

This research included the estimation of the effect of methyl substitution on the chemical shifts of toluene compounds calculated by the LAM and comparing these shifts with the practical values obtained from the literature. The deviation between the two mentioned values are correlated with various variables obtained from quantum mechanical methods represented by the electronic density values and the bond lengths obtained using the DFT method.

Table (3)
The chemical shifts of toluene compounds calculated by the LDM and compared with practical values

Item	Compounds	C_{No}	δ(obs) ppm	δ (cal) ppm	Res
1		1 – 6	128.7	128.7	0.0
2		1	137.8	137.8	0.0
		2,6	129.3	129.3	0.0
		3,5	128.5	128.5	0.0
		4	125.6	125.6	0.0
3		1,2	136.4	138.4	2
		3,6	129.9	129.1	- 0.8
		4,5	126.1	125.4	- 0.7
4		1,3	137.5	137.6	0.1
		2	130.1	129.9	- 0.2
		4,6	126.4	126.2	- 0.2
		5	128.3	128.3	0.0

5		1,4	134.5	134.7	- 0.2
		2,3,6,5	129.1	129.1	0.0
6	 1,2,3-trimethylbenzene	1,3	136.1	138.2	2.1
		2	134.8	139	4.2
		4,6	127.9	126	- 1.9
		5	125.5	125.2	- 0.3
7		1	133.4	135.3	1.9
		2	136.3	138.2	1.9
		3	130.5	129.7	- 0.8
		4	135.2	134.5	- 0.7
		5	126.7	126.0	- 0.7
		6	129.8	128.9	- 0.9
8		1,3,5	137.6	137.4	-0.2
		2,4,6	127.4	126.8	- 0.6
9		1,4	133.5	135.1	1.6
		2,3	134.5	138.8	4.4
		5,6	127.3	125.8	- 1.5
10		1,3	136.0	138.0	2
		2	131.6	135.9	4.3
		5	134	134.3	0.3
		4,6	128.9	126.6	- 2.3
11		1,2,4,5	133.8	135.1	1.3
		3,6	131.2	129.5	- 1.7
12		1,5	133.0	134.9	1.9
		2,4	132.1	135.7	3.6
		3	134.5	132.6	4.1
		6	131.5	126.4	- 5.1
13		1 – 6	132.3	135.5	3.2

Observing the differences between the practical chemical shift and those calculated by LAM in Table (3), the following appears:

- Substitusion of two methyl groups on the aromatic ring in positions (1 and 2) shifts the absorption to a lower field by approximately (2.0) ppm, and this is similar to what was found in the saturated compounds in Tables (3and 4) and this indicates that the effect of the presence of two methyls in positions (1 and 2) on the ring is almost constant regardless of the nature of the compounds, whether was aromatic or aliphatic, provided that the two groups lie in the same plane of the ring, and this is consistent with the definition of Taft [13] for the steric factor of the substituents attached to carbon atoms of (sp3) hybridization, which is a function of Van der Waals radii or is a measure of the effective volume of the ortho substituent in aromatic compounds.
- When a methyl group is located between two other methyl groups, i.e. when the substitution is in the (1, 2, 3) positions, the (C-2) ring carbon atom suffers from a shift approximately twice that observed when the methyl is ortho for only one methyl group as (C–2) in compound No.9, (C–2) in compound No.10, (C– 2, 3,4) in compound No.12 and all the ring carbon atoms in compound No.13.
- The cyclic carbon atoms in the ortho positions with respect to both sides substituted carbon atoms in compounds with substitution of the type (1, 2, 3) such as (C-4,6) in compound No.6, (C-5,6) in the compound No.9, (C-4, 6) in compound No.10 and (C-6) in compound No.12 are shifted to a higher field. The reason is due to two factors, the first is these atoms are located in the ortho or para position to one or more methyl groups. The electronic donation of these groups, is directed towards these sites, increases the amount of shielding (diamagnetic factor) on the carbon atoms under consideration.

The other reason is, the large steric interference between the protons of the methyl group and carbon No.2 increasing the possibility of leaving the level of the ring and generating interaction similar to the type γ-gaush [24] leading to deviation in the values of the chemical shift from the practical value approximately equal to (2) ppm as (C–1,2) in compound No.3, (C–1,3) in compound No.6, (C–1,2) in compound No.7, (C–1,3) in compound No.10, (C-1,5) in compound No.11. The amount of deviation in the carbon atoms that are ortho to two methyl groups is shifted approximately by (4)ppm, such as (C-2) in compound No. 6, compound No. 10, (C – 2, 3) in compound No.9, and (C-3) in compound No. 12.

The departure of the two methyl groups from the ring level could be resulted in decreasing the deviation from the mentioned rates, it becomes (1.6) ppm as seen in carbon atoms (C-1,4) in compound No. 9 (3.6) ppm in carbon atoms (C–2,4) in compound No.12 and (3.2) ppm for all ring atoms in compound No. 13. The amount of deflection in the last compound (hexa methyl benzene) represents the rate of steric interactions caused by the six methyl groups which take certain positions that maintaining the symmetry of the type (C-6) [25].

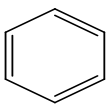
The presence of methyl groups in the ortho-sterically obstructed site restricting their free rotation forcing these groups, to take certain shapes resulting from ring

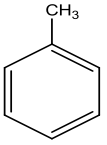
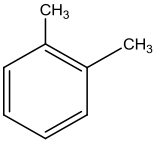
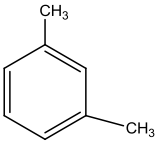
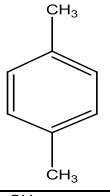
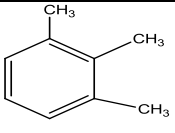
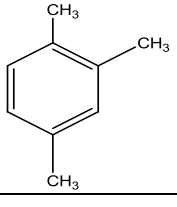
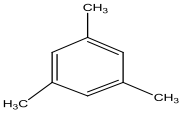
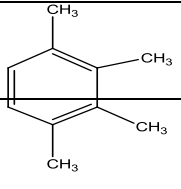
departure from planarity. It was previously explained, these deviation values can also be indicated by the change in the geometric dimensions of the aromatic ring as shown in the calculations of the bond lengths of (C-C) those were accomplished using quantum mechanics methods (DFT method). The bonds located among the substituted cyclic carbon atoms are longer than the rest of the bonds. They approach the length of the single bond due to the low electronegativity resulting from the electron pushing of the methyl groups away from these sites (Table 5, 4). The methyl groups are electron donating, so it changes the distribution of the electron density on the aromatic ring upon substitution and thus has a clear effect on the chemical shift values of the ring carbon atoms.

The electronic effects on the chemical shift values of carbon-13 for toluene compounds have been investigated by calculating the change in electronic density (Table No. 4) and bond lengths (Table No. 5) resulting from the substitution of methyl groups on the benzene ring .Observation of Table (4) indicates that, the highest electronic density in the toluene compound is on the carbon atoms ortho to the methyl group followed by the carbon in the para position (4.003) due to the effect of proximity (3.996). The electronic density is lowest on the carbon atom connected to the methyl group (3.984), while the electronic density on the carbon atom in the meta position is similar to that of the benzene ring (3.988).

The values of the chemical shift of the aromatic ring carbon atoms are consistent with the values of the electron density, unless there is an additional factor affecting their values. The ring carbon attached to the methyl group is more de-shielded (137.8) ppm as a result of its connection to a methyl group with hybridization (sp3) in the ortho position, the carbon atom in the para location is more shielded than the carbon atoms (125.6 ppm) due to the repulsion between the proton in the para position with the protons of the methyl group, which shift the absorption of carbon atoms in the ortho position to a lower field compared with the carbon atom in the para position. This explains the substitution effect of a methyl group on the un-substituted benzene ring in the ortho (0.6) and para (-3.2) positions, which was calculated by LAM that were previously addressed. While the chemical shift of carbon atoms (C-3,5) in the meta position are similar to the chemical shift of un-substituted benzene due to the absence of electronic and steric effects on these atoms.

Table (4)
Practical chemical shift, electronic densities and heat of formation calculated by applying, the DFT method for toluene compounds

Item	Compounds	C_{No}	δ (obs)	Electron density	Heat of Formation (ΔHf)
1		1	128.7	4.185639	28.6665
		2	128.7	4.185849	
		3	128.7	4.185741	
		4	128.7	4.185793	
		5	128.7	4.185766	
		6	128.7	4.185802	

2		1	138.8	4.190363	23.947
		2	129.3	4.182182	
		3	128.5	4.189567	
		4	125.6	4.182286	
		5	128.5	4.188232	
		6	129.3	3.98454	
3		1	136.4	4.185259	22.333
		2	136.4	4.186473	
		3	129.9	4.186407	
		4	126.1	4.185343	
		5	126.1	3.989935	
		6	129.9	3.990003	
4		1	137.5	4.193744	18.336
		2	130.1	4.179141	
		3	137.5	4.195817	
		4	126.4	3.981396	
		5	128.3	4.191718	
		6	126.4	3.980805	
5		1	134.5	4.187564	18.778
		2	129.1	4.185863	
		3	129.1	3.986855	
		4	134.5	4.187577	
		5	129.1	4.185836	
		6	129.1	3.986642	
6		1	136.1	4.189206	24.645
		2	134.8	4.183969	
		3	136.1	4.185766	
		4	127.9	4.012489	
		5	125.5	4.003749	
		6	127.9	4.016332	
7		1	133.4	4.17914	17.982
		2	136.3	4.191915	
		3	130.5	3.985222	
		4	135.2	4.185798	
		5	127.6	3.98797	
		6	129.8	4.000711	
8		1	137.6	4.198088	13.278
		2	127.4	3.977985	
		3	137.6	4.198126	
		4	127.4	3.977953	
		5	137.6	4.198149	
		6	127.4	3.977949	
9		1	133.5	4.176007	23.119
		2	134.4	4.184564	
		3	134.4	3.988528	

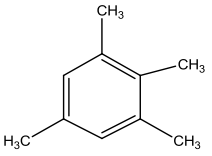
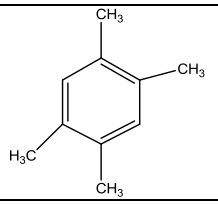
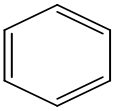
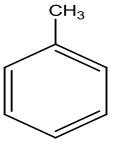
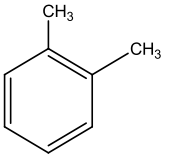
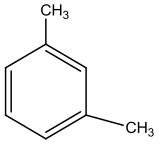
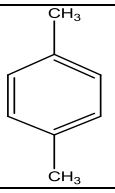
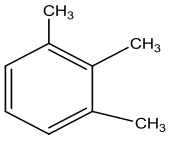
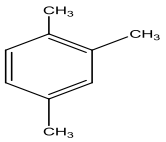
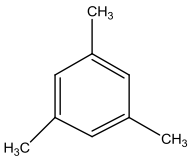
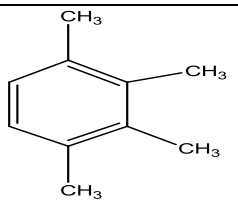
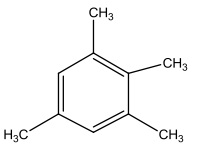
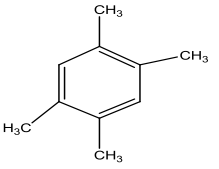
		4	133.5	3.99326	
		5	127.3	4.003949	
		6	127.3	3.999886	
10		1	136.0	4.193914	18.430
		2	131.6	3.980506	
		3	136.0	4.191184	
		4	128.9	3.983713	
		5	134.3	4.008654	
		6	128.9	3.980447	
11		1	133.8	4.173038	19.851
		2	133.8	3.993003	
		3.6	131.2	3.999246	
		4	133.8	4.17068	
		5	133.8	4.002242	

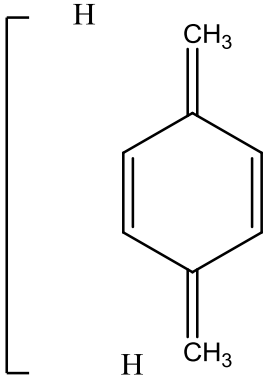
Table (5)
Bond lengths calculated by the DFT method for toluene compounds

Item	Compounds	Bond No.	Bond Length (A°)	Bond No.	Bond Length(A°)
1		$C_1 - C_2$	1.3976	$C_4 - C_5$	1.3975
		$C_2 - C_3$	1.3974	$C_5 - C_6$	1.3974
		$C_3 - C_4$	1.3975	$C_6 - C_1$	1.3976
2		C_1 -C_2	1.3983	$C_4 - C_5$	1.3941
		C_2 - C 3	1.3957	$C_5 - C_6$	1.3957
		C_3 - C_4	1.3981	$C_6 - C_1$	1.3999
3		$C_1 - C_2$	1.3962	$C_4 - C_5$	1.4005
		$C_2 - C_3$	1.3945	$C_5 - C_6$	1.4005
		$C_3 - C_4$	1.3962	$C_6 - C_1$	1.4005
4		$C_1 - C_2$	1.3927	$C_4 - C_5$	1.4034
		$C_2 - C_3$	1.3986	$C_5 - C_6$	1.4034
		$C_3 - C_4$	1.3989	$C_6 - C_1$	1.4034
5		$C_1 - C_2$	1.3956	$C_4 - C_5$	1.3947
		$C_2 - C_3$	1.4002	C_5 –	1.3948

				C_6	
		$C_3 - C_4$	1.4018	$C_6 - C_1$	1.4011
6		$C_1 - C_2$	1.3927	$C_4 - C_5$	1.4112
		$C_2 - C_3$	1.3925	$C_5 - C_6$	1.4125
		$C_3 - C_4$	1.4025	$C_6 - C_1$	1.3995
7		$C_1 - C_2$	1.3941	$C_4 - C_5$	1.4022
		$C_2 - C_3$	1.3995	$C_5 - C_6$	1.4109
		$C_3 - C_4$	1.3993	$C_6 - C_1$	1.4001
8		$C_1 - C_2$	1.3962	$C_4 - C_5$	1.4039
		$C_2 - C_3$	1.4039	$C_5 - C_6$	1.3964
		$C_3 - C_4$	1.3963	$C_6 - C_1$	1.4039
9		$C_1 - C_2$	1.3854	$C_4 - C_5$	1.4206
		$C_2 - C_3$	1.4006	$C_5 - C_6$	1.4088
		$C_3 - C_4$	1.4068	$C_6 - C_1$	1.4025
10		$C_1 - C_2$	1.3971	$C_4 - C_5$	1.4115
		$C_2 - C_3$	1.3971	$C_5 - C_6$	1.4084
		$C_3 - C_4$	1.3997	$C_6 - C_1$	1.3995
11		$C_1 - C_2$	1.3969	$C_4 - C_5$	1.4037
		$C_2 - C_3$	1.4091	$C_5 - C_6$	1.4062
		$C_3 - C_4$	1.395	$C_6 - C_1$	1.405

The bond lengths of these compounds, are calculated using the Chem. Office program and shown in Table (5), agree with the results shown previously, where the bonds (C1-C2) and (C1-C6) are longer than the rest of the bonds of (C-C) in the aromatic ring. It approaches the single bond due to the low electronic density resulting from the electronic pushing of the methyl group away from these

locations. This is consistent with previous studies [26]. These effects are evident in the rest of the toluene compounds addressed in this study. In the ortho xylene compound, it is noted that the values of the chemical shifts of the carbon atoms in the contact location (C-1,2) with the substituted methyl groups is less shielded than the rest of the ring atoms (136.4) ppm and this agrees with the values of the electronic density on these atoms (3.995), as well as the length of the bond (C1-C2) (1.4356), which represent the length of the (C-C) ring bonds. While the electron density on the carbon atoms (C-4,5) is approximately (3.99), the absorption of the first atom is shifted to a lower field due to the proton interference between the protons on the carbon atoms (C-3,6) with the protons of the methyl group in the ortho position to them. The carbon atoms (C-4,5) are shifted to a higher field compared to the benzene molecule because it located para to a methyl group in the meta xylene and the electron density is as low as possible in the two carbon atoms (C-1,3) (3.981) and as much as possible on the carbon atom (C-2) (4.013) which is in an ortho position to a two methyl groups, and the two carbon atoms (C-4,6) those are ortho for two methyl groups and para for another methyl group. When looking at the values of the chemical shifts of the cyclic carbon atoms in this compound, it is found that the two carbon atoms attached to a methyl group (C-1,3) are less shielded. Although the electron density on the carbon atom (C-2) is high, it shifts to a lower field (130.1) compared to the benzene molecule (128.7) due to the steric obstruction as a result of its existence in the ortho position to a methyl group. The two carbon atoms (C-4,6) are shifted to a higher field (126.4) as a result of being ortho to a methyl group and para to another group. The carbon atom (C-5), has a chemical shift (128.3 ppm), close to the value of the chemical shift of the benzene molecule since its distant from electronic and steric effects. In the compound p-xylene, the electron density is high on the carbon atoms (C-2,3,5,6) because each is ortho to the two methyl groups, while the electronic density on the two carbon atoms (C-1,2) is low due to the direction of the electron donation of the methyl group towards the ortho and the para positions. This is consistent with the geometric dimensions of the ring so that the bonds (C4-C5, C4-C3, C1-C6, C1-C3) are longer than the bonds (C5-C6, C2-C3) due to the increase in the electronic density in the last locations resulting from the effect of hyper conjugated resonance effect caused by the methyl groups in the para positions as shown below:

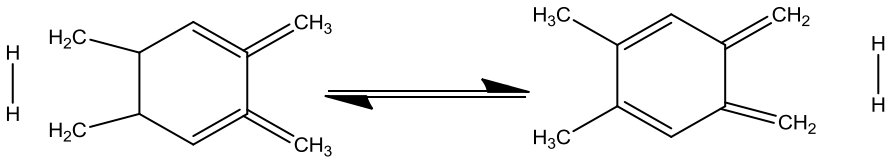


The chemical shift values for this compound agree with what was previously mentioned, where the ring atoms in this compound give two absorptions, one for

the two carbon atoms at the contact location with the methyl groups (134.5) and the other four carbon atoms (C–2,3,5,6) are at higher field (129.1). The matter becomes more complicated when increasing the number of substituted groups on the ring. From observing the values of the electronic density on the carbon atoms of the aromatic ring in the Hemillitene compound, it is found that the electronic density on the carbon atom (C-2) is high (4.007) because it is located in the ortho position to the two methyl groups. However, the value of its chemical shift (134.8) is at a lower field due to the steric interactions of the protons of the methyl group connected to it with the protons of the methyl groups on the neighboring carbon atoms. For the same reason the carbon atoms (C-1,3) are appeared at a low field and their interferences effect on the geometric dimensions of the ring is evident by observing the lengths of the bonds (C1-C2), (C2-C3)(Table No.(5)) where these bonds are long (1.4312) compared to the rest of the bonds in the ring due to the electron pushing character of the methyl groups as well as the effect of proton interference on the carbon atoms of the substituted methyl groups. When comparing the chemical shift of carbon atoms (C-4,6) in this structure (127.9) with its value for atoms (C-3,6) (129.9) in the ortho xylene compound (where all the atoms are in the ortho position of a methyl group, it was noticed that the absorption of carbon atoms (C-3,6) in the last compound are shifted to a lower field when compared with the chemical shift of the benzene molecule (128.7), while the absorption of the same carbon (C-4,6) shifts to a higher field, and this can be explained by the fact that the carbon atoms (C-3,6) suffer from steric interference (repulsion) with protons of the methyl group in ortho-position that shifts towards a lower field. Whereas, the carbon atoms (C-4,6) in the Hemillitene compound may suffer from γ-gaush interactions resulting from the methyl group on the carbon atom (C-2) leading to the departure of the aromatic ring from the planarity. The value of the chemical shift of the carbon atom (C-5) in the last compound is at a high field (125.5) compared to the benzene molecule despite its low electronic density (3.986), and this is consistent with the electronic effect resulting from its para location with respect to one of the methyl group.

When comparing the chemical shift values of the pseudo cumene compound with the electron density values on the ring atoms, all the explanations and reasons mentioned for discussing the previous compounds also applies. It is noted that the carbon atoms (C-1,2,4) appear at low field because of their connection to methyl groups, in addition to the steric interferences caused by the protons of the methyl group with the protons on the neighboring atoms. It is noticed that, despite the high electronic density on the carbon atom (C-3)(4.010), it appears at a low field (130.5ppm), due to the spatial interference resulting from its location in the ortho position for two methyl groups. In order to clarify the role of steric effect, it can be noted that the carbon atom (C-5) shows absorption at (126.7) and it is located ortho to a methyl group and para to another one. The role of the steric effect can be highlighted by comparing the absorption of (C-5) in hemillitene, pseudo-cumene and mesitylene, where (C-5) appears in the first compound at (125.5) ppm, and it is located para to a methyl group free of steric effect, while the absorption in the second compound is shifted to a lower field (126.7) as a result of its existence ortho to methyl group and para to another, despite the fact that the electron density on (C-5) in the second compound (4.002) which is higher than the first (3.986), while the carbon atoms (C-2,4,6) appear in the mesitylene at (127.4) ppm which is para to methyl group and ortho to two

methyl groups despite that the electron density on them(4.015) is higher than that on (C-5) in the other two compounds. This is a good evidence for the Van der Waals repulsion occurred between C-5 and protons of the methyl group which shift to a lower field by (1.52 ppm). Looking at Table (5), the pseudo cummene showed largest variation in the bond length (C1-C2)(1.4316) which got closer to the length of single bond due to electron pushing of the methyl groups which decreasing the electron density on these locations. The ring carbon of mesitylene exhibit two absorption, one of them at low field (137.6ppm) and low electron density (3.978) for the substituted carbon atoms (C-1,3,5) and the other at (127.4 ppm) of the carbon atoms (C-2,4,6). The pernnitene compound agrees with the rest of the compounds those, substituted by more than two groups such as the carbon atoms attached to methyl groups in the ortho position of two other methyl groups (C-2,3) have the largest electron density (4.004), but the chemical shift of these atoms is less shielded than the carbon atoms substituted on the both sides (C-1,4) and this is different from what was observed in the compound Hemillitene and isodurene compound (C-2 is larger than C-1,3). The chemical shift of the two carbon atoms (C-6,5) (127.3) ppm, which are ortho to a methyl group and para to another one, as was observed in the carbon atoms (C-2,4,6) in the mesitylene compound and (C-4,6). Measurements of bond lengths in Table (5) show that the change in the bond length values and its distance from the bond length of the benzene molecule is as large as possible in the bonds (C1-C2) (1.4330), (C2-C3) (1.4297) and (C3-C4), (1.4221).The experimental chemical shift values represent an average value of the shapes taken by different molecules, so each of the carbon atoms (C-1,4) and (C-2,3) have similar chemical shift values due to symmetry. Whatever applied to the compounds discussed above is applicable to the isodurene compound, while it is noted that, in the durene compound, the chemical shift of the two carbon atoms (C-3,6) is at a lower field compared to its counterparts in other compounds (C-6,4) in the isodurene (C-3,6), and in the pseudo-cumene compound ... etc. The reason is the steric interactions with the two methyl groups in the ortho positions, in addition to the presence of the durene compound in the two forms shown later due to the effect of hyper conjugation resonance which limit the movement of the protons of the methyl groups. Protons of the methyl those suffers from this effect is restricted and the substituted cyclic carbon atoms are shifted to a lower field (133.8) compared to that observed in the ortho-xylene compound (129.9) ppm.



The measurements of the bond lengths showed a noticeable change in the bond lengths of (C4-C5, C1-C2) which are longer than the rest of the bonds in the ring carbon atoms. This agrees with the electronic density values. The bond lengths of penta methyl benzene and hexa methyl benzene are expected to be identical to what was observed in the previous compounds. The steric effect caused by the substitution of methyl groups on the benzene ring through the heat of formation can be predicted as shown in Table (4), which were calculated using the DFT method. If the heat of formation of the benzene ring is taken (28.665 kcal / mol)

as a reference and then following the effect of adding methyl groups on the ring, the following will be noticed:
When a methyl group is added to the ring (toluene), the value of the heat of formation energy decreases by approximately (5 kCal/mol) (the heat of formation is 23.947 kcal/mol). Adding a second methyl to the ring decreases the heat of formation value by approximately (10 kcal / mol) as shown in the meta- and para-xylene compound, whose heat of formation (18,336, 18.778 kcal / mol) respectively. The value of the heat of formation for both compounds is close due to absence of the spatial effect in both. The ortho-xylene compound, is less stable by (4 kcal/mol) than both, due to the steric obstruction resulting from the presence of two methyl groups in the ortho site.

When a third methyl group is added to benzene, the heat of formation value will decrease by approximately (15 kcal/mol) in the absence of the effect of the steric hindrance factor, and this was actually observed in the compound of mesitylene (13.278 kcal/mol). And when two of these three groups are in ortho position will reduce the stability of the compound by (4 kcal/mol), and this is what happens in the pseudo-cumene compound, which was found to have a heat of formation value (17.982 kcal/mol), but in the case of the presence of the three methyl groups in the location (1,2,3) on the ring, as in the Hemillitene compound, the stability of the compound will decrease by more than double (24.645 kcal / mol). When the number of substituents increases on the aromatic ring, things become more complicated, and there may be other factors in addition to the steric effect, which may be caused by the exit of a methyl group from the plain of the aromatic ring, which leads to a distortion in the geometric dimensions of the ring. The steric effect remains clear and this can be seen when comparing the compounds predinitene, isodurene and durene which is caused by the presence of two methyl groups in the ortho position.

Conclusion

Throughout the foregoing discussion, it can be concluded that the spatial effect has a significant impact on the stability of the considered compounds, and to the distortions caused in their geometrical dimensions of the aromatic ring . This has been proven through the values of the bond lengths, Table (5), which in turn affects the values of chemical shift of the nuclei of carbon-13 atoms, and the effect of adding a methyl group on the heat of formation has an additive character in the absence of the steric factor. The C-13 NMR and could be used for the estimation of steric factor quantitatively which could not be undertaken by common methods.

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