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Abstract: The quantum chemical PMR (Proton magnetic resonance) chemical shift calculation, inherently, has the information on the induced field values not only within the molecular system, but also in the neighborhood of the molecule, to the extent, which is significant. Within the molecule the locations of the protons are specified by the way of the complete description of coordinate of all the atoms in the molecule. If the information about the induced fields in the neighborhood is to be known, then it is necessary to place protons at appropriate locations in the neighborhood irrespective of whether the proton is part of the molecule and or bonded to any other atom of the molecule. Such a stand-alone proton in the neighborhood is specified by the coordinates with reference to the molecular axes system, which would sense this induced field and in the result would be reported as proton chemical shift. Such induced field contributions are usually calculated using a classical dipole model for reasons that the protons are not part of the molecule and is at extraneous locations when the molecular magnetic susceptibilities can be used conveniently for calculating induced fields and thus chemical shifts. Such a QM (Quantum mechanical) calculation of chemical shifts and comparison with values from classical equations is being reported.

Key words: Aromatic ring current, induced fields, chemical shifts, inter molecular, classical dipole model, comparison QM (Quantum mechanical) and classical calculation.

1. Introduction

Chemical shifts that observable in NMR (Nuclear magnetic resonance) spectra are the consequences of the changes in the circulation characteristics of molecular electrons due to the force exerted by the externally applied magnetic fields on these electrons that are in motion in their assigned molecular orbital [1-5]. These magnitudes of such changes are of the order in parts per million of the externally applied fields. In the classical description, these changes in the electron motions indicate the degree to which the external fields can influence the electron within the frame work of a given molecular electronic structure. A measure of this tendency of the electrons to respond to the external magnetic fields is the

physical quantity molecular magnetic susceptibility [6, 7]. This magnetic susceptibility induces a magnetic moment (primary magnetic field contribution for change in electron circulation), the magnitude of which depends on the intensity of the applied magnetic field.

This induced moment is usually located at the electrical center of gravity. Depending on the symmetry of the molecule, the electrical center of gravity may coincide with mass center of gravity of the molecule. When a nucleus is placed at this point where the induced magnetic moment arises, then the magnetic field strength experienced by the nucleus is different (in ppm units) from the magnitude of the external magnetic field, and this difference is the (shielding constant) chemical shift observable in NMR. The induced magnetic moment, in turn, can induce fields (secondary magnetic fields) in the

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neighborhood. Hence, depending upon the magnitudes of the secondary fields, it is possible to observe chemical shift contributions

Due to the delocalized pi-electrons, the aromatic ring currents result in large diamagnetic susceptibility and hence contribute to shifts particularly in adjacent proton locations, even if these protons are not bonded to atoms within the given aromatic molecule in which the ring currents arise [6]. Thus typically in solid state, and if the material is a single crystal of aromatic organic molecule, then the PMR (Proton magnetic resonance) chemical shifts observed would have contributions from within the molecule itself at a proton and can also have contributions from large currents from aromatic rings present in adjacent molecules [7, 8]. In fluids such contributions are possible, but they would be subjected to time dependence due to fluctuations in the various degrees of freedom of the molecules. Fig. 1 illustrates the possible ways in which a non-bonded proton can be located with respect to an aromatic molecule, typically the benzene molecule. Thus, there is an induced magnetic field generated in the neighboring points around a molecule due to electron currents, and these fields become observable only when a proton nucleus is placed at these neighboring locations. Usually when classical equations are used for calculating induced secondary field values, the location of the induced magnetic moment is at the centre of the electron current loop, and the equation is expressed in terms of the x, y and z coordinates of the points where the induced field value is necessary and this calculation inherently does not to require a proton to be placed know the value of the induced field. The classical equation for induced field at a point near the magnetic dipole has been derived using a point dipole approximation. This approximation considers the finite distance "d" of separation between the magnetic pole-pair (responsible for the dipole moment) compared to the distance "R_i". The magnetic dipole can be considered as point dipole, when the distance "d" is negligibly small compared to the "R_i".

It is to be remarked at this stage that for calculating by the methods of quantum mechanical computational chemistry, only when a proton is present at a specified point, the corresponding chemical shift value would not be available as output. Hence the methods of QM (Quantum mechanical) computational chemistry are usually for calculating shielding (chemical shifts) values for intra molecular protons.

The known inter molecular chemical shift (long-range shielding effects) contributions are evaluated on the basis of the equations derived with classical point dipole approximation. Thus estimating the induced field values (for chemical shift) at points located outside the aromatic molecule, but closer to the aromatic ring is beset with errors for reasons that the point dipole approximation may not be valid. The consideration in





Case 1: Proton position in the laboratory fixed system is unaltered; the aromatic ring changes orientation in the laboratory frame of reference. Obviously, the angle of the proton position vector with respect to the molecular symmetry axis (Z_M) varies. This makes the conventional equations (used for isotropic ring current shifts) not applicable.

Fig. 1 Non-bonded proton placed near the aromatic ring.

this paper is how to make the best use of QM method to estimate the induced field (chemical shift) values for locations in the vicinity of a molecule and not merely within the molecule at the proton locations. In fact, the classical dipole field equation of Fig. 3 has been shown [2] to be a particular case from the general equation for shielding derived on the basis of Quantum Mechanical considerations [9] for the effect of magnetic field on the electrons in molecule.

The induced field within a molecule at a given nuclear site is an electronic property of the nuclei, which is a measure of the shielding of the nuclei from



A = Avagadro number

Fig. 2 A benzene ring, aromatic current, induced magnetic moment at the centre of the ring, a distant neighboring point where the induced field is to be calculated and the corresponding classical equation.

the externally applied magnetic field. This means the field at the nuclei can be less or more than the applied field depending on the sign of the induced field which would be added to the external field value. This shielding of the nuclei can be measured with reference to a bare nucleus surrounding which no electrons would present. Such values of the shielding, referring to the bare nucleus value as "zero", are absolute shifts observable in spectra of actual molecules. When these shifts are referenced to a spectral line position of a standard chemical, then all the absolute shift values can be subjected to a change in the reference value, and the resulting values are referred to as chemical shifts. In the context of calculations using classical equations, if the resulting induced values are added to chemical shift values, then the result would also be chemical shift including the ring current effect. If the calculated values are added to absolute shift values, then the result would be absolute shifts and includes ring current effects.

2. Considerations for the QM Approach

As it was mentioned in the introduction, if the ring current contribution to chemical shift (induced field) values was to be calculated at points outside the benzene molecule in its vicinity, it would be necessary to place a proton nucleus at the required point, and provide the list of coordinates of all atoms in the benzene molecule and the extraneous proton for the calculation of the chemical shift values with the computational soft ware. For such an extraneous proton, it is may convenient to include a molecule like methane and ensure that at least one of the four protons of the methane was placed at the required point extraneous to the benzene molecule.

Fig. 3 displays such a configuration of the two molecules with proper disposition. If the set of seven carbon atoms and ten hydrogen atoms are well specified by the coordinates, then the calculation would return result consisting of the chemical shift values of all the protons. The chemical shift value of



Fig. 3 Methane molecule placed in the vicinity of benzene ring: (left) methane at a point along the symmetry axis of benzene and (right) methane carbon placed coplanar with the ring plane.

the methane protons would be different from the corresponding values isolated methane molecule due to the ring current contributions from the benzene molecule present. Even though this way of calculating long-range ring current effect seems simple enough, the following criteria must be ascertained before getting inferences from such results.

If a comparison is to be made exclusively for the ring current effect, then the geometry of the two molecules in terms of the bond lengths and bond angles must be the same as it is for the optimized isolated molecule. If a calculation of the optimized energy of the two isolated molecules results in values E_A and E_B , then for a combined structure the E_T would be equal to $E_A + E_B$, if and only if electrostatic perturbation (bonding interactions) is absent on one molecule due to the presence of the other. As can be seen from Fig. 4, the interaction energy between the two molecules $(E_T - (E_A + E_B))$ is near zero value when the distance between the molecules are changed from about 15 Å till 4.5 Å, and for the smaller distances there is significant interaction energy. When the distance between the molecules is changed, the molecular geometry of each of the molecule keep intact as the independently optimized geometry. The ring current due to the delocalized pi electrons can be so large for the aromatic molecules that the induced secondary magnetic fields can be present even at such distances where there is no significant interaction energy indicating the absence of any electron-electron, electron-nuclear electrostatic interactions. When the



-20.0 -30.0 -40.0 -50.0 -60.0 0.0 5.0 10.0 15.0

Fig. 4 Benzene & Methane; interaction energy of the molecules as a function of the distance of separation between the two molecules.

distances get smaller, there is significant interaction energy and hence localized electron circulations in one molecule may contribute to shielding in the other. Thus in such proximities of the molecules, the chemical shift values calculated may differ not only because of the ring current effect, but also due to the localized electron circulations.

Since the aromatic ring current effects can induce secondary magnetic fields at distances much larger than the distances at which electrostatic interactions are significant, there seems a possibility to estimate these fields as different from the local electron circulation effects. Such a disentangling can provide the way to compare quantitatively the estimates by classical dipole equation and the QM calculations, so that techniques like interpolations and extrapolations may be yielding the ring current effects when the effects of local electron circulations are intricately present simultaneously. Such possibilities are highly useful in Solid State materials [7, 8] and bio-inspired materials [10-12] in general, and in particular the biological macromolecular 3-D structure determinations. In such contexts to relate the material properties from the single molecule physical properties and design appropriate molecules for the desired material properties – molecules to materials could be the outlook.

In this study combined system of molecules are (i) Benzene & Methane and (ii) Benzene & Hydrogen. The first set is convenient for reasons that both benzene and methane are symmetric molecules with all the protons in the respective molecules are equivalent. Thus in liquid medium the molecules give a single line PMR spectrum, for benzene 6 protons resonate and for methane 4 protons resonate. Each molecule is subjected to a geometry optimization and the stable minimum-energy equilibrium-structure is secured. Next, these two structures of the respective molecules are placed at appropriate distance of separations as measured from the distance between the mass centers of gravity of the molecules. For each distance of separation a single point energy calculation yields the total energy of these combined structures at that distance. This combined energy at larger distances can be equal to the sum of the total independent molecular energies, and at the smaller distances the energy of the combined system may not be equal to the sum of individual molecular energies. At such instances the difference in the energy can termed as an interaction energy, apparently be notwithstanding the fact that each molecule had unalterably the same equilibrium geometry all through.

For an extraneous proton, it may be convenient to include a molecule like methane and ensure that at least one of the 4 protons of the methane gets placed at the required point in the neighborhood of the benzene molecule. Fig. 4 displays such a configuration of the two molecules with proper disposition. If the set of 7 carbon atoms and 10 hydrogen atoms are well specified by the coordinates, then the calculation would return result consisting of the chemical shift values of all the protons. The chemical shift value of the methane protons would be different from the corresponding values isolated methane molecule due to the ring current contributions from the benzene molecule present. Even though this way of calculating long-range ring current effect seems simple enough, the following criteria must be ascertained before getting inferences from such results.

Since the electrons in a neighboring molecule ("neighboring" could be, in general, up to a distance of about 8-12 Å distance for small molecules) can experience electrostatic interactions from the benzene ring, would it be necessary to optimize the geometry of the two molecules placed together as in Fig. 3. If a comparison is to be made exclusively for the ring current effect, then the geometry of the two molecules in terms of the bond lengths and bond angles must be the same as it is for the optimized isolated molecule. If a calculation of the optimized energy of the two isolated molecules results in values E_A and E_B , then for a combined structure the E_T would be equal to $E_A + E_B$ if and only if electrostatic perturbation (bonding interactions) is absent on one molecule due to the presence of the other. As can be seen from Fig. 4, the interaction energy between the two molecules $(E_T - (E_A + E_B))$ is near zero value when the distance between the molecules are changed from about 15 Å till 4.5 Å, and for the smaller distances there is significant interaction energy. When the distance between the molecules is changed, the molecular geometry of each of the molecule was kept intact as the independently optimized geometry. The ring current due to the delocalized pi electrons can be so large for the aromatic molecules that the induced secondary magnetic field can be present even at such distances where there is no significant interaction energy indicating the absence of any electron-electron, electron-nuclear electrostatic interactions between the two molecules. When the distances get smaller, there

is significant interaction energy and hence localized electron circulations in one molecule may contribute to shielding in the other. Thus in such proximities of the molecules, the chemical shift values calculated may differ not only because of the ring current effect, but also due to the localized electron circulations.

Classical equation is for estimating only the induced magnetic field values irrespective of whether there is electrostatic interactions are present or not. On the other hand, the QM method would changes in the chemical shifts due to electrostatic interactions as well as the long-range induced magnetic fields at such distances when there are no electrostatic interactions. Hence it is the intention in this paper to infer on the trends of chemical shift values as a function of intermolecular distance between a pair of molecules all through with the same equilibrium geometry.

3. Methods of Calculation

The classical equation as expressed in the Fig. 2 is used for the calculation of chemical shift tensor value with the molar susceptibility tensor values given in Fig. 5.

For the *ab initio* QM calculation of the chemical shifts [3, 4], it was found convenient to use the computational-chemistry remote-server which can be accessed as the "working demo" of the internet portal http://www.webmo.net. Even though at this demo portal only one-minute jobs can be run, the molecular systems chosen and the Gaussian computational soft ware available at the portal were found satisfactory to get illustrative results. The SCF (Self consistent field) procedure with STO-3G (Slater type orbital, expressed by linear combination of 3 Gaussian functions: contracted Gaussian basis function set-3G) minimal basis set was enough to infer the possible trends from such study. This "webmo" demo portal has features to plot the results in the conventional spectra formats to view the spectral patterns for the listed out calculated spectral parameter values. The structure editor at this portal is a Java applet feature convenient for structure



 $-85 - (-35) = -50 \ge 10^{-6} =$ Anisotropy Fig. 5 Benzene: susceptibility tensor values in the PAS (Principal axes system).

editing and viewing at any stage during the calculation, and the same Java feature also has the option for data viewing after the calculation. Typically the PMR spectra in Fig. 7 have been obtained by opting to view the calculated data (printed out as absolute shift values for a numerical read out) in a tabular form. DFT (Density functional theory) methods were also available as options at this portal which can be availed if the job can be completed in CPU time duration of one-minute. The results are presented in the following sections with discussions.

Both by the Classical model and from the QM methods, the full shielding tensor (chemical shift tensor) is obtained. By proper diagonalization of the tensor of 9 elements, it is possible to get the diagonal elements of the tensor in the principal axes system. The trace calculated as the average of the diagonal elements would give the isotropic value for the chemical shift applicable to liquid medium. Equations for the isotropic value have also been derived algebraically by the theoretical formalisms.

4. Results and Discussions

4.1 Classical Dipole Field and Chemical Shifts

The chemical shift values are calculated, with the classical dipole model and the susceptibility tensor values of benzene, typically at two points with distances 20 Å and 5 Å along Z-axis and also along Y-axis from the center of the ring. This calculation is

typical of what is possible with classical dipole model and is simple to implement. The results of the calculations are reproduced in the tabular form as in Table. 1. When another molecule containing proton is placed near the benzene molecule, what is necessary is to know the proton coordinate so that the induced field (chemical shift) can be calculated at the proton location.

4.2 Benzene & Methane Combined

To illustrate the typical results of QM calculation of chemical shifts, when the two molecules benzene and methane are at distances 13.328 Å and 9.01 Å, no significance difference is noticeable. Moreover by the distance dependent energy calculation, no electrostatic interaction is evident.

Thus the two PMR lines are respectively at the isolated benzene value appearing in the left side down-field line and at the methane value at the right side up-field value. In Fig. 7 the distances of separation are much less. Consequently, it can be seen that the up-field methane proton lines appear differently – not as single line for all the 4 protons. As the distance gets closer the methane lines are much better seen as 4 lines. However, the benzene protons absorb at the same chemical shift value and all the six proton NMR lines appear at the same down-field location in the spectrum.

Table. 1Calculated chemical shift values at points nearthe benzene ring.

Calculated ring current shifts ppm			
Proton distance from ring centre	Trace angle with mol-Z = 90	Field parallel to Y	
		YY-component	
		Proton Y	Proton perpendicular to Y
20 Å	-0.000334402779	0.001404	-0.000702
5 Å	-0.021401777856	0.089856	-0.044928
Calculated ring current shifts ppm			
Proton stance from ring centre	Trace angle with mol-Z = 0	Field parallel to Z	
		ZZ component	
		Proton on Z-axis	Proton in ring plane
20 Å	0.000668806839	0.003411	-0.001705
5 Å	0.042803637696	0.218304	-0.10912



Fig. 6 Benzene & Methane: Methane is placed at 13.328 Å and 9.01 Å and this set of coordinates at the respective distances results in PMR spectra as above.



Fig. 7 Benzene & Methane: Methane is placed at 6.27 Å and 2.78 Å and this set of coordinates at the respective distances results in PMR spectra as above.

Since the benzene aromatic ring can have ring current effect at larger distances this effect is seen at methane protons. No such large induced fields can be produced by the methane molecule at the benzene protons. Note that the carbon atom of methane molecule is located along the symmetry axis of the benzene ring, which is different from the disposition in Fig. 4.

In Fig. 3, on the left side image if the benzene molecule is rotated by an axis perpendicular to the paper without altering the methane configuration, then the relative orientation of the image as on the right side would be the result. Thus if QM calculations can be

made at such distance of separation when it yields the ring current contribution to chemical shift of methane protons, a rotation pattern would be generated as a consequence.

A similar calculation of NMR spectra by QM methods for combined benzene & methane placed in different disposition gives more conspicuous effects on the benzene protons also (for comparable distances of separation) due to the presence of nearby methane, as it is shown in Fig. 8.

Such rotation patterns are reproduced in the Figs. 9 and 10. Note the consequence of the symmetry of the methane molecule reflecting in the rotation pattern of Fig. 9. The methane molecule has its three protons downwards to face the benzene molecule and one of the protons is away upwards. Three of the traces in the graph start at a point and when rotated by 90° these

three traces intersect at a single point with different chemical shift value compared to the starting point for 0° . In these graphs, the vertical axis zero value corresponds to the chemical shift value of methane proton calculated for the geometry optimized isolated methane molecule, in which all the four protons are equivalent and have the same chemical shift. One of the lines corresponding to the upward oriented proton traces distinctly different path through the rotation. In Fig. 10, lines corresponding to two of the protons (downwards to face benzene) have similar path like the three protons of the Fig. 9. The other two protons in Fig. 10, facing upwards away from the ring, trace the same path all through. When the contribution to changes in chemical shifts, which are mainly from the ring current effects these trends of the proton line traces, should be obvious.



Fig. 8 Benzene & Methane: Note the relative disposition to be same as in Fig. 4 placed at 3.087 Å (above) and 2.78 Å (below). The benzene protons differ in chemical shift values.



QM Chemical Shift Calculations to Infer on the Long-Range Aromatic Ring Current-Induced Field Contributions

Fig. 9 Benzene & Methane: referring to top left side image, the benzene is rotated at intervals of 10° so that when rotated by 90° the relative orientation equivalent to the top right image results.



Fig. 10 Benzene & Methane: Rotation pattern for a rotation of benzene similar to that in Fig. 9, with methane molecule oriented differently compared to that in Fig. 9.

4.3 Benzene & Hydrogen Combined

Having considered ring current effects calculated by QM method for the protons of methane placed nearby to the benzene molecule, for a quantitative comparison of the ring current contributions, calculated by classical equation and QM method, the protons of Hydrogen molecule are considered (Fig. 11). Protons 13 and 14 are of the hydrogen molecule with bond along the symmetry axis of benzene ring. 14 and 15 are protons of hydrogen molecule with bond placed coplanar with the ring (90° with benzene symmetry axis). A hydrogen

molecule (protons 15 & 16) is placed at the remotest location of 25 Å from the benzene ring, at such distance the ring current contribution would be insignificant. The hydrogen molecules are placed at distances ranging from 8 Å to 9 Å along the respective axes.

Chemical shift values were obtained by QM method as described in Section 3 (The zero value on the vertical axis refers to the chemical shift in the isolated molecule). The graphical plot of the calculated values appears as if it is linear with distance which is only apparently so considering the smaller range of 1 Å (at





Proximity distance dependence of chemical shift difference



In the two figures on the Lefthand column (Seved from Structure editor) find the Benzene molecule rotated as indicated by the red arrow perpendicular to the palne. This rotation in steps of 15 degrees interval resulted in 12 distinct disposition of the benzene ring with respect to the fixed Hydrogen molecules with respect to the axes system. QM results of this orientation dependent shielding effect is plotted (a rotation pattern) in RHS column lower figure.

(b)

Fig. 11 (a) Three hydrogen molecules with optimized geometry placed near the Benzene molecule; (b) Rotation pattern obtained for the variation of ring current shifts of hydrogen molecules. The benzene ring is rotated at 15° intervals from 0° to 180° .

intervals of 0.2 Å). It would be strictly linear if the graph displayed the chemical shift dependence with inverse cube of the distance. These traces for the protons of the hydrogen molecules are to stand in comparison with the trends obtained for methane as in Figs. 9 and 10. For the relative orientations of hydrogen

molecules and benzene illustrated in Fig. 11, the variation of ring current contribution to the shifts calculated by QM and classical methods are presented in the Figs. A more convincing quantitative comparison is possible by considering the calculated values presented in the graphical plots of Figs. 12 and 13.

QM results

At hydrogen 15 (25 Angstroms away from center), no significant cahnge with distance and the shielding is the same as it would be for an isolated hydrogen molecule in the absence of benzene.

13 & 14 Protons of Hydrogen Molecule along the C6 Symmetry axis:15 and 16 as well as 17 perpendicular to symmetry axis in molecular plane



Fig. 12 For the relative orientations of hydrogen molecules and benzene as in Fig. 11, the values of the ring current contributions (obtained by QM calculations) are displayed as graphical plots for a variation in distances in the range 5 Å to 12 Å.

For the classical method, results of calculated values for only one of the two protons for each hydrogen molecule have been presented in graph.

Since the other proton of the hydrogen molecule is at one bond length away, the difference was not much in the chemical shift, as can be seen in the graph for the results from QM method.

It is generally known that for such aromatic ring current shift magnitudes, the protons along the symmetry axis (perpendicular to the ring plane) would

Classical Dipole model

Since it is merely a secondary field without any specific orbital interactions (for energy considerations), these QM results must be the same as the Classical dipole model where the Magnetic dipole is placed at the ring center of optimized benzene. Possilts of the Two methods seem to compare well.

ene. Results of the Two methods seem to compare well to be able to use the results of calssical model confidently with the QM results as a transferable quantity

This classical equation was used for calculating secondary field at one point corresponding to the distance on the x-axis. Hence only one point is plotted for each of diamagnetic and diamagnetic locations





Fig. 13 For the configuration of molecules in Fig. 12 the plotted results are obtained by classical dipole model. The shift axes values (Y-axis) and the distance axes (X-axis) values can be found convenient for direct comparison.

have larger effect than the proton at the same distance in the plane of the ring. Quantitatively, distance from the center of the ring being the same, the contributions in the plane of the ring are opposite in sign and only half the magnitude of the ring current shift along the perpendicular to the ring plane. The results in Figs. 12 and 13 characterize the shifts as that due to ring current effect on the basis of the general criterion described in the previous paragraph.

4.3 Inferences on Intra Molecular and Inter Molecular (Long-Range Contributions) by the QM Computations.

As it was pointed out in Introduction with regard to the point dipole approximation, the classical equations may be applicable mainly for the case of long-range, inter molecular contributions.

The QM method, unlike the use of classical equation, has inherently the totality of all the contribution at a proton coordinate. When a OM calculation is made at a possible proton location close to a molecule, even if the proton is extraneous to the molecular structure, there can be contributions of the intermolecular nature as if the proton is a bonded to some atom in the molecule. This contribution has to be reckoned as described because this contribution would not be amenable for calculation by equations of classical dipole model. Since the proton coordinate has to be specified for QM calculations, at those specified coordinate values, the ring current contribution of long-range nature can be calculated. By a comparison of results in Figs. 12 and 13 it can be reliably inferred that the QM method and classical equation give the same result for the contribution recognizable as a long-range contribution.

When the QM calculations for such cases where there may be a long-range part in the total calculated value, this must be the contribution at the extraneous proton. Then the remote current contribution can be calculated by classical equation and this value can be subtracted out. The remaining part would be the local shielding contribution in intra molecular sense.

If the classical equation value is insignificant, it may be concluded that the proton which is in the proximity truly is not to be considered for any contributions from the interior of the molecule. Typically for the type of QM results depicted in Fig. 8, the methane molecule is a molecular entity not as a part within the benzene molecule. But the calculated spectra seem to have contributions also by mutual electrostatic interactions between the molecules and hence the situation is not as simple as the only intermolecular, or only the long-range induced magnetic field contributions.

5. Conclusions

The result reported in Ref. [7] is one of the instances when a QM method for remote atom has been resorted to while considering the shielding contributions in a unit cell of single crystal. This is similar to the considerations in this paper. Taking into account the comparison of classical and QM results for long range shielding contributions can bring in more confidence into such efforts. In the context of biological macromolecules, some of the amino acid peptide residues have side chains containing phenyl rings. The biological macromolecules [13-15], in particular peptides and proteins, with the given sequence of amino acid residues as primary structure, can have bends, turns and folds resulting in secondary and tertiary structures. Thus, it is not unusual to find the side chain phenyl ring of one residue has non-bonded contact distances with proton containing groups from remotely located residue of the same molecule. In such contexts the kind of long range shielding contributions are significant and can be accounted for with classical equations [16]. When such non bonded complexes undergo time dependent fluctuations (in solution state and biological conditions) the relevant groups would be moving relative to one another at faster rates [12]. The question arises then, as to what would be the geometry at any instant for the groups? Does energy optimization of structures occur at these rates and equilibrium geometry follows the time scales of fluctuations all the time to new geometry every instance? On the other hand, if equilibrium geometry prevails unaltered then the ring current shielding would be only a matter of distance, though the electrostatic interactions can follow these time scales as much as the magnetic fields that are induced. Rearrangement of atoms to quickly be changing at every instance for

energy considerations is a matter of time scales [17] of chemical changes during reactions. For such critical details a QM method would be the appropriate procedure rather than the classical equations for induced magnetic fields. The possibility

is significant that, from QM calculations and calculations with classical model and the derived equations yield the same results for ring current contributions, and application of this result would be helpful though with an awareness of the situations for validity of both methods. When the molecules have (even when it is not a single complex molecule) strong electrostatic interaction affecting the molecular structures, it should be possible to disentangle the aromatic ring current part from the total proton shielding values from the QM methods. Verification of this possibility should be by trying out from the structures of macromolecules from a data base [13, 18, 19] of chemical shifts and the corresponding proton coordinates.

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