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Chemical Reactivity Profiles of Two Selected Polychlorinated Biphenyls

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Global reactivity and local selectivity profiles such as electronegativity, hardness, polarizability, electrophilicity index, condensed Fukui function, and local electrophilic power of a selected polychlorinated biphenyl, viz., 2,2′,5,5′-tetrachlorobiphenyl have been calculated using the B3LYP/6-31G* method in gas and solution phases in order to gain insight into the toxic nature of this compound and a comparison is also made with 3,3′,4,4′,5-pentachlorobiphenyl. It is seen that both global and local electrophilicity helps in understanding the overall toxic nature of the system. The significance of the planarity and electron affinity in determining the toxic nature of the polychlorinated biphenyls is now better understood.

1. Introduction

Polychlorinated biphenyls (PCB) are found at an appreciable level in the polar regions as a result of long-range atmospheric transport. The pollution caused by PCB has attracted a widespread concern. The PCBs have been used as lubricating agents, fire retardants, transformer oils, hydraulic fluids, and insulating and impregnating agents. They are also environmental contaminants due to their capacity of persistence and lipophilicity, biological accumulation into the food chain, and concentration in fatty tissues, including breast tissues.[1−9] The noninflammability and chemical stability associated with the PCBs have contributed to the widespread environmental problems. It is possible to observe from the toxicity data that there are only 12 PCBs, which have been identified as toxic, out of 209 PCB congeners. These compounds exhibit toxicity similar to that of polychlorinated dibenzo-*p*-dioxin (PCDD). This information on PCB has prompted several investigators to understand the toxic nature of PCB and their interaction with cellular components.[10] The origin of toxicity of PCDDs has been attributed to the electron accepting nature in the charge transfer complex with a receptor in living cells. The oxidative DNA damage induced by PCB and their implication in breast cancer has been addressed. Hence, the electron affinity of PCBs is used as an important quantity in understanding their toxic effects. Accordingly the calculation of electron affinity of various PCBs has attracted recent theoretical interests.

Three-dimensional structure−property correlations for the prediction of thermodynamic properties of PCBs have been recently made to predict the enthalpy of vaporization and enthalpy of sublimation. Recently, Arulmozhiraja et al. using density functional theory calculations have obtained structure, potential energy, and torsional barrier heights for selected polychlorinated biphenyls.[11] Rotational energy barrier, electron affinity, and planarity of various PCBs have been calculated in that study to rationalize the nontoxic nature of ortho-substituted PCBs. Rotational energy barriers of biphenyls and substituted biphenyls have been calculated using the B3LYP/6-311+G* method by Grein.[12] Similar calculations on the torsional barrier of biphenyl (BP) and PCB using various theoretical methods ranging from semiempirical AM1 to Hartree−Fock methods have also been reported.[13] It is evident from these calculations that the toxicity mainly arises from the electron affinity and inherent nature of the planar geometry of the biphenyls and substituted biphenyls. It is well-known in the gas phase that BP is twisted (torsional angle between two phenyl rings) with a twist angle of about 45°. This twist in BP is usually explained as arising from the competition between the repulsion of the ortho-hydrogens favoring 90° twists (torsional angle ϕ) and the electron delocalization effect preferring a coplanar arrangement.[14] In chlorinated biphenyls, this balance in interactions is still perturbed by the chlorine atoms, which influences the geometrical parameters of biphenyls, specifically the torsional angle between the phenyl rings. It is evident from previous theoretical studies that the torsional angle is not influenced by the chlorine substituents at the para and meta positions.[10,11] However, the torsional angle between two phenyl rings with ortho substitution is nearly 90°. In real life systems, PCBs are known to interact with the cellular components, and hence, the addition and the removal of an electron during the formation of the complex are significant events. The electron acceptance as well as electron removal to PCBs lead to changes in the torsional angle ϕ of PCBs and hence their geometry.

Development of appropriate descriptors for the quantitative structure−activity relationship is an important area of research. Popular qualitative chemical concepts such as electronegativity and hardness have been widely used in understanding various aspects of chemical reactivity.[15−19] Density functional theory (DFT) provides a rigorous theoretical basis for these concepts. These reactivity indices are better appreciated in terms of the associated electronic structure principles such as the electronegativity equalization principle, the hard−soft acid base (HSAB) principle,[20] the maximum hardness principle (MHP),[21,22] the minimum polarizability principle (MPP),[23] etc. Local reactivity descriptors such as density, Fukui function, local softness, etc. have been used successfully in the studies of the site selectivity

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in a molecule. It is reported in the earlier study that the rotational freedom of PCBs allows them to orient with any torsional angle in the protein field and provides the pathway for easy interaction with receptors in living cells and hence their toxicity.[11] An attempt has been made in our present investigation to observe how various chemical reactivity and selectivity indices and their associated electronic structure principles manifest themselves when PCBs rotate in the realistic environment so that an appropriate descriptor could be selected to explain the toxicity of various compounds.

2. Theoretical Background

Chemical hardness (η) has been identified as a useful global reactivity index in atoms, molecules, and clusters.[24,25] The theoretical definition of chemical hardness has been provided by DFT as the second derivative of electronic energy with respect to the number of electrons N, for a constant external potential $V(r)$

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{V(r)} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{V(r)} \tag{1}$$

The corresponding global softness is expressed as

$$S = \frac{1}{2\eta} = \left(\frac{\partial^2 N}{\partial E^2}\right)_{V(r)} = \left(\frac{\partial N}{\partial \mu}\right)_{V(r)} \tag{2}$$

Using a finite difference method, a working equation for the calculation of chemical hardness can be given by

$$\eta = \frac{\mathrm{IP} - \mathrm{EA}}{2} \tag{3}$$

where IP and EA are the ionization potential and electron affinity of the atom or molecule, respectively. If ϵ_{HOMO} and ϵ_{LUMO} are the energies of the highest occupied and lowest unoccupied molecular orbitals, respectively, then the above equation can be rewritten using Koopmans' theorem[25] as

$$\eta = \frac{\epsilon_{\mathrm{LUMO}} - \epsilon_{\mathrm{HOMO}}}{2} \tag{4}$$

Validation of the maximum hardness principle associated with atoms and molecules and their excited states has been reported recently.[26−28] It is known that the polarizability is inversely proportional to the third power of hardness.[29−31] Based on this inverse relationship, a minimum polarizability principle has been proposed as a companion to MHP.[23] The electric dipole polarizability is a measure of the linear response of the electron density in the presence of an infinitesimal electric field F and it represents a second-order variation in energy

$$\alpha_{a,b} = -\left(\frac{\partial^2 E}{\partial F_a \partial F_b}\right) \quad a \text{ and } b = x, y, \text{ and } z \tag{5}$$

The polarizability α is calculated as the mean value as given in the following equation:

$$\langle \alpha \rangle = {}^1/_3(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \tag{6}$$

For a better understanding of the site selectivity in a chemical system, suitable local descriptors of selectivity need to be defined. An appropriate definition of local softness $s(r)$ is given by[31]

$$s(r) = \left(\frac{\partial \rho(r)}{\partial \mu}\right)_{v(r)} \tag{7}$$

such that

$$\int s(r)\, \mathrm{d}r = S \tag{8}$$

Combining eqs 7 and 8

$$s(r) = \left(\frac{\partial \rho(r)}{\partial N}\right)_{v(r)}\left(\frac{\partial N}{\partial \mu}\right)_{v(r)} = \left(\frac{\partial \mu}{\partial v(r)}\right)_N S = f(r)S \tag{9}$$

where $f(r)$ is termed as the Fukui function (FF).[32] It is obvious that the local softness contains the same information as the FF (i.e., the sensitivity of the chemical potential of a system to a local external potential) as well as additional information about the molecular softness. Using left and right derivatives with respect to the number of electrons, electrophilic and nucleophilic FF and the associated local softness can be defined. To describe the reactivity of an atom in a molecule, it is necessary to condense the values of $f(r)$ and $s(r)$ around each atomic site into a single value that characterizes the atomic contribution in a molecule. Thus, for an atom k in a molecule, depending upon the types of electron transfer, three kinds of condensed FF on the atom k can be obtained. For an N − electron system, independent calculations have been made on $N - 1$, N, and $N + 1$ electronic systems with the same molecular geometry. Various population schemes yield $q_k(N - 1)$, $q_k(N)$, and $q_k(N + 1)$ for all of the atoms. Then these values were substituted in the following equations, and the corresponding FF values for f_k^+, f_k^-, and f_k° were obtained.[30−32] In a finite difference approximation, the f_k values are defined as[33−35]

$$f_k^{+} = q_k(N+1) - q_k(N) \text{ for a nucleophilic attack} \tag{10a}$$

$$f_k^{-} = q_k(N) - q_k(N-1) \text{ for an electrophilic attack} \tag{10b}$$

$$f_k^{\circ} = [q_k(N+1) - q_k(N-1)]/2 \text{ for a radical attack} \tag{10c}$$

where q_k is the gross electronic population of atom k in the molecule. Parr and Yang have proposed that larger FF values indicate more reactivity. Hence, the greater the value of the condensed FF, the more reactive the particular atomic center in the molecule is.

Parr et al. have introduced a global electrophilicity index ω as[36]

$$\omega = \frac{\mu^2}{2\eta} \tag{11}$$

According to this definition, ω measures the ability of a molecular species to soak up electrons and is used in understanding the reactivity of the human immunodeficiency virus type 1 (HIV-1) nucleocapsid protein p7 (NCp7) when reacted with a variety of electrophilic agents.[37−40] Similar to this global quantity, the local (regional) electrophilic power can be defined as[41,42]

$$\omega_k = \omega f_k^{+} \tag{12}$$

The site which has the maximum value of the ωf_k^+ can be considered as the active site for the electrophilic attack, and

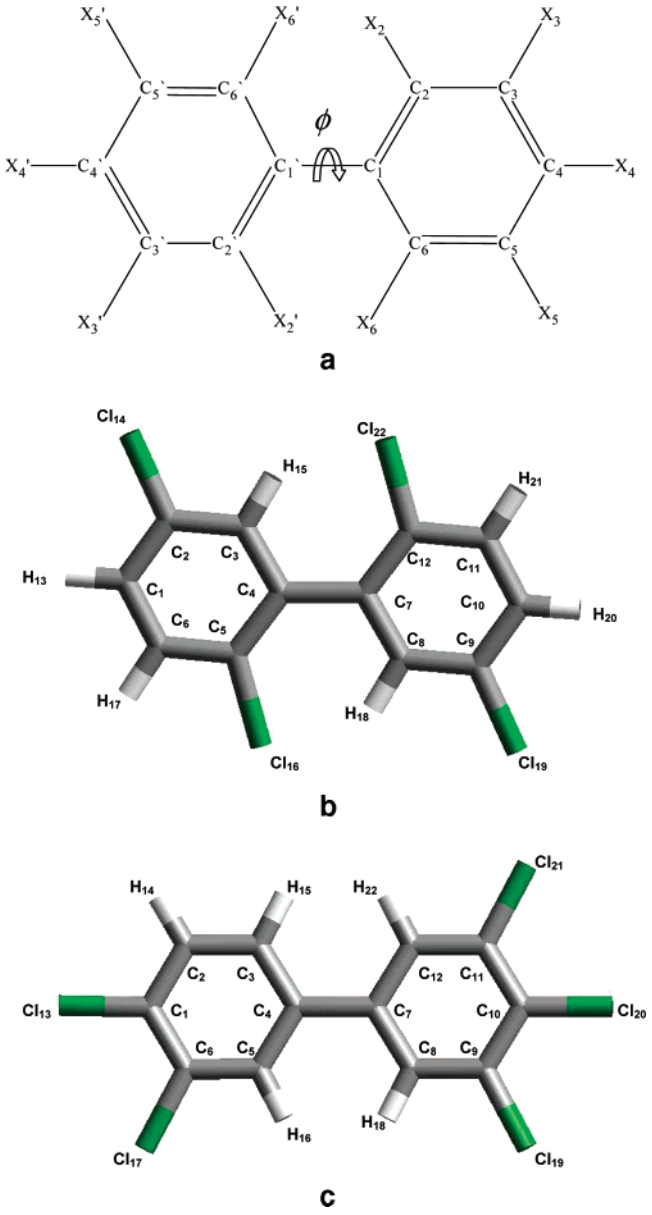

Figure 1. (a) General atom-numbering scheme for PCB model. The optimized geometries of (b) 2,2′,5,5′-tetrachlorobiphenyl (TCBP) and (c) 3,3′,4,4′,5-pentachlorobiphenyl (PCBP) with different atom numbering scheme used for Fukui function analysis.

this site also coincides with the softest site (nucleophilic) in a molecule, and hence, it is highly reactive.

3. Computational Details

The general atom-numbering scheme of the PCB is shown in Figure 1a. The geometry of 2,2′,5,5′-TCBP is optimized by using Becke's three parameter hybrid density functional, B3LYP/6-31G*, which includes both Hartree−Fock exchange and DFT exchange correlation functionals.[43−46] The above calculations are carried out using the Gaussian 98 package.[47] The optimized geometries are characterized by harmonic vibrational frequencies which confirmed that the structure of 2,2′,5,5′- TCBP is a minimum on the potential energy surface. The relative energy of 2,2′,5,5′-TCBP is calculated as a function of the torsional angle (rotation through the bond C_1-C_1'). To calculate the relative energy, the geometries at various ϕ values are optimized at B3LYP/6-31G*. The relative energy for 2,2′,5,5′-TCBP is calculated as $\Delta E(\phi) = [E(\phi) - E(\phi = 90.0)]$ using the total energies of the respective optimized conformations. To select the proper electronic descriptor based on DFT, for the possible toxicity of 2,2′,5,5′-TCBP, the various reactivity and selectivity descriptors such as chemical hardness, chemical potential, polarizability, electrophilicity index, and local electrophilic power are calculated for all of the rotated conformations. The condensed FF is calculated using the natural population analysis (NPA).[48] Because, the Hirschfeld[49] population scheme (Stockholder partitioning scheme) is known to provide nonnegative FF values, it has also been used to calculate FF values as implemented in the DMOL^3 package[50] employing BLYP/DN method.

TABLE 1: Calculated Relative Energy, Chemical Hardness, Chemical Potential, Polarizability, and Electrophilicity Index of 2,2′,5,5′-TCBP

torsional angle (degrees)	relative energy[a]	chemical hardness[b]	chemical potential[b]	polarizabilty[c]	electrophilicity index[b]
−30	18.74	2.505	−4.187	168.392	3.500
0	69.52	2.405	−4.278	171.671	3.804
30	18.92	2.505	−4.187	168.315	3.500
60	1.01	2.696	−4.078	165.014	3.085
90	0	2.911	−3.915	163.196	2.632
120	2.30	2.709	−4.053	164.966	3.032
150	26.86	2.531	−4.166	167.808	3.428
180	122.69	2.333	−4.266	171.065	3.900
210	26.86	2.531	−4.166	167.841	3.428

[a] In kJ/mol. [b] In eV. [c] In au.

4. Results and Discussion

The interaction between the π orbitals of phenyl rings favors planarity of the PCBs, whereas the repulsion between the ortho hydrogen atoms tends to force the molecule to be nonplanar. The delicate balance of these two interactions results in a twisted arrangement. Hence, the torsional angle for rotation of the C_1-C_1' bond of the polychlorinated biphenyl is the important geometrical parameter. The rotational freedom allows these compounds to freely interact with the cellular components in the realistic environment and hence their toxic nature. Previous studies[11] on the PCBs revealed that the rotational energy barrier of these molecules provides the information about the possible toxicity of these molecules. The flexible planarity is the essential descriptor for the toxicity of PCBs. Electron affinity is the other parameter considered as the descriptor for the toxicity of these compounds. The simple analysis of the definition of the global and local reactivity indices reveals that the role of the electron affinity of the molecule is incorporated in the formal definitions based on the density functional theory. It is interesting to probe how various global and local descriptors vary with the torsional angle. The comparison of the variation of reactivity descriptors with the torsional angle and rotational barrier leads to the selection of the appropriate reactivity descriptor for quantification of toxicity of PCBs. Recently Arulmozhiraja et al.[51] have carried out high quality DFT calculations on selected PCBs, and the study highlighted the role played by the torsional angle and rotational freedom in the proteins with realistic conditions.[11]

The optimized geometry of 2,2′,5,5′-tetrachlorobiphenyl (TCBP) is depicted in Figure 1b along with different atom numbering for FF calculation. Table 1 presents the values of the relative energy, chemical hardness, chemical potential, polarizability, and the electrophilicity index[52−55] for different torsional angle values for 2,2′,5,5′ -TCBP. The variation of rotational energy with the torsional angle for this molecule is shown in Figure 2a. It is seen that the 2,2′,5,5′-TCBP has got large energy barriers at the planar orientations. The rotational

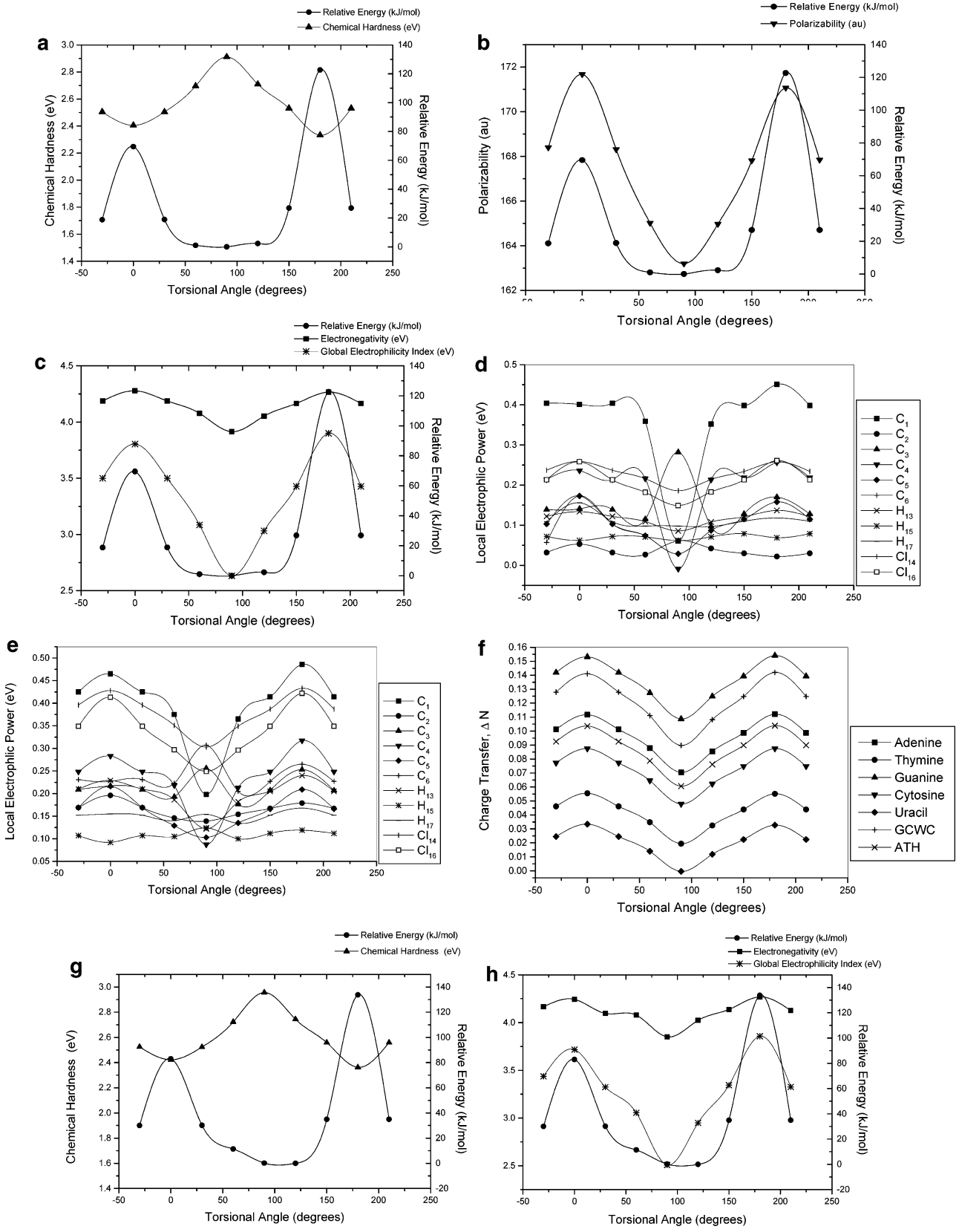

Figure 2. a. Variation of relative energy (kJ/mol) and chemical hardness (eV) with the torsional angle (degrees) for 2,2′,5,5′-TCBP. b. The variation of polarizability and relative energy (kJ/mol) with the torsional angle (degrees) for 2,2′,5,5′-TCBP. c. The variation of relative energy (kJ/mol), electronegativity (eV) and global electrophilicity index (eV) with the torsional angle (degrees) for 2,2′,5,5′-TCBP. d. The variation of local electrophilic power (eV) with the torsional angle (degrees) for C atoms, H atoms and Cl atoms in 2,2′,5,5′-TCBP. e. The variation of local electrophilic power (eV) with the torsional angle (degrees) for C atoms, H atoms and Cl atoms in 2,2′,5,5′-TCBP using Hirshfeld partioning scheme. f. Charge Transfer between 2,2′,5,5′-TCBP with various torsional angle (degrees) and bases/base pairs. g. The variation of relative energy (kJ/mol) and chemical hardness (eV) with the torsional angle (degrees) for 2,2′,5,5′-TCBP in the solution phase. h. The variation of relative energy (kJ/mol), electronegativity (eV) and global electrophilicity index (eV) with the torsional angle (degrees) for 2,2′,5,5′-TCBP in the solution phase.

energy variation is similar to the typical potential wells with a relatively small barrier on the left and a large barrier on the right side, and the relative energy difference between these two barriers is calculated to be 53.17 kJ/mol. Due to dominant Cl−H interactions, the minimum energy conformation corresponds to 90°. As reported in the earlier theoretical investigations, strong Columbic repulsion between Cl−Cl atoms tend to increase the torsional barrier at 180° and 0°, and ΔE^{180} {$=E(\phi = 180°) - E$(equilibrium)} is found to be 122.69 kJ/mol in our case, which is closer to 112.40 kJ/mol, as reported in the literature.[11] These high torsional barriers prevent this molecule from attaining a near planar structure by inhibiting free rotation around the C−C single bond, whereas in the case of 3,3′,4,4′,5-pentachlorobiphenyl (PCBP)[56] (with its numbering scheme in Figure 1 c), it has got a very small energy barrier of 7.36 kJ/mol at the planar orientation, which implies that this molecule can adopt planar conformation easily than 2,2′,5,5′-TCBP and hence its toxicity. It is evident from the previous calculation as well as from the present investigation on the variation of rotational energy with the torsional angle for 2,2′,5,5′ -TCBP that it has two energy minima. The first one is very shallow and the difference between two minima is about 1.29 kJ/mol. It is possible to observe that the profile of the rotational energy in the range from 60° to 120° is flat indicating that 2,2′,5,5′ -TCBP can freely change from one conformer to another. It has been shown that 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) which is very flexible is a highly toxic molecule.[51] This gives strong evidence that 3,3′,4,4′,5-PCBP which is a nonortho substituted PCB must be a toxic molecule. Because of the very large torsional barrier at the planar orientation for 2,2′,5,5′-TCBP, it is difficult for the same to attain planar geometry easily and hence less toxic in nature. However, at the same time, it can rotate freely between 60° and 120° because of the relative flatness in the potential energy surface in these regions thereby switching its conformation between these two energy minima. In the case of 3,3′,4,4′,5-PCB, though rotational motion seems to be confined to a narrow region at 30° and 120°, energy barriers are small which can be easily over come by these molecules and attain planarity in the biological systems thereby leading to a high toxicity of the molecule.[56] Further, the rotational freedom of PCBs gives greater opportunities for it to orient with any torsional angle in a protein field and provides ways and means for an easy interaction with a receptor in living cells, which ultimately lead to their higher toxicity.

The changes in the rotational energy barrier and chemical hardness with torsional angle for 2,2′,5,5′-TCBP are depicted in the same figure (Figure 2a). It is found that the maximum global hardness coincides with the minimum energy conformation ($\phi = 90°$). Minimum global hardness values coincide with $\phi = 180°$ and 0°, respectively. According to the principle of maximum hardness, both these conformations are highly reactive when compared to the twisted conformation as observed in earlier studies.[11] This evidence reinforces the role played by the planarity of the PCBs in determining the toxicity of various congeners of PCBs. The higher the planarity, the higher the toxic potential of PCBs.[51] The plot of the rotational energy barrier and polarizability presented in Figure 2b reveals that $\phi = 180°$ and 0° are the two structures having high polarizabilities vis-á-vis their high relative energy values, and hence, these conformations are highly reactive. Again, the minimum polarizability principle supports the decisive role played by the planarity of the PCBs. It is possible to observe the validity of both MHP and MPP in the context of determining the toxicity of PCBs vis-à-vis their rotational energy profiles.

The plot of the rotational energy barrier and the global electrophilicity index with ϕ is shown in Figure 2c. It is interesting to note that high electrophilicity values have been obtained for the conformations corresponding to $\phi = 180°$ and 0°. It is evident from the electrophilicity profile that the $\phi = 180°$ conformation has a very high ω and ΔE values. The high electrophilicity value can be used as a criterion for the high toxic nature in the case of PCBs. It is clear that ω can be used as a proper descriptor for toxicity in PCBs. In this plot, we also present the electronegativity profile, which mimics the corresponding profiles of ω and ΔE, as expected.

Figure 2d depicts the local electrophilicity profiles calculated using the natural population analysis scheme (NPA), as a function of the torsional angle ϕ for C, H, and Cl atoms, respectively. Corresponding quantities calculated using Hirshfeld partitioning, which gained importance due to its unique nature of providing nonnegative FF values are presented in Figure 2e. Only one representative atom center each from a given symmetry class is presented. It is heartening to note that in both sets of plots the local electrophilicity of chlorine atoms mimics the relative energy as well as the global electrophilicity plots. This fact corroborates with the results of Poland and Glover, who found that the number and site of the chlorine atoms govern the toxicity and biological activity of dioxins.[57] This confirms that the local electrophilicity bears the signature of toxicity in the Cl centers and accordingly the whole molecule of PCBs. The Cl_{14} center is more toxic than the Cl_{16} center at $\phi = 90°$ configuration. Toxicity of C_1 and H_{13} centers are also more pronounced than the other C and H centers. It may be noted that centers placed in symmetric location will be in the similar environments and accordingly will have same local electrophilicity values. Local electrophilicity sharply pin-points at the $\phi = 90°$ configuration than the corresponding relative energy plots. The local electrophilicity profiles of 3,3′,4,4′,5-PCB calculated using NPA and also corresponding quantities calculated using Hirshfeld partitioning scheme as a function of torsional angle for the C, H, and Cl atoms show that Cl_{20} center is more toxic than other Cl center for the $\phi = 30°$ conformation.[56] It is also interesting to observe that the Cl_{20} center has got higher local electrophilic power (ω_k) values for all conformations compared to other Cl centers showing it as a pronounced toxicity site. The C_{10} and H_{14} centers also show high ω_k values compared to other C and H centers for most of the conformations and expected to be toxic.

Oakley and co-workers have demonstrated that there is a definite mechanistic pathway for the PCB induced oxidative DNA damage. Possible interaction of PCB with DNA involves free radical generation and increased oxidative DNA base damage in the presence of lower chlorinated biphenyls.[58] To assess the oxidation of lower chlorinated biphenyls, the amount of charge transfer between PCBs and nucleic acid (NA) bases/DNA base pairs have been computed.[58] We have calculated the amount of charge transfer between 2,2′,5,5′-TCBP and various bases, viz., adenine, guanine, thymine, cytosine, uracil, and DNA base pairs GCWC and ATH by applying the formula[59]

$$\Delta N = \frac{\mu_B - \mu_A}{2(\eta_A + \eta_B)} \tag{13}$$

As it is expected the planar (Figure 2f) geometry of the TCBP allows the maximum amount of electron transfer for all of the bases and it is the minimum for the $\phi = 90°$ configuration. Among the bases, guanine and uracil have the maximum and minimum value for ΔN respectively, whereas for the selected

TABLE 2: Calculated Density Functional Descriptors for 2,2′,5,5′-TCBP Using BLYP/DN Method

torsional angle (degrees)	chemical hardness[a]	chemical potential[a]	electrophilicity index[a]
−30	1.775	−4.386	5.419
0	1.703	−4.462	5.845
30	1.775	−4.386	5.419
60	1.93	−4.276	4.737
90	2.093	−4.134	4.083
120	1.949	−4.245	4.623
150	1.800	−4.367	5.298
180	1.599	−4.448	6.187
210	1.800	−4.367	5.298

[a] In eV.

TABLE 3: Calculated Chemical Hardness and Chemical Potential of the Bases and Selected Base Pairs in Gas Phase

bases/base pairs	chemical hardness[a]	chemical potential[a]
adenine	2.850	−3.103
thymine	2.894	−3.689
guanine	2.916	−2.648
cytosine	2.785	−3.370
uracil	2.962	−3.919
GCWC	2.018	−3.030
ATH	2.526	−3.256

[a] In eV.

TABLE 4: Effect of Explicit Solvation on the Various Density Functional Descriptors for 2,2′,5,5′-TCBP Using Polarizable Continuum Model

torsional angle (degrees)	relative energy[a]	chemical hardness[b]	chemical potential[b]	electrophilicity index[b]
−30	30.09	2.524	−4.166	3.438
0	82.99	2.422	−4.243	3.717
30	30.17	2.523	−4.096	3.325
60	11.43	2.722	−4.078	3.055
90	0.21	2.957	−3.851	2.508
120	0	2.744	−4.023	2.949
150	34.89	2.559	−4.137	3.344
180	133.79	2.363	−4.269	3.857
210	34.98	2.559	−4.126	3.326

[a] In kJ/mol. [b] In eV.

base pairs, GCWC has the maximum at $\phi = 90°$ conformation. If two systems X and Y are brought together, as in a reaction they must form a single system with the constant values of chemical potential. The negative chemical potential can be called the absolute electronegativity and there is always a transfer of electron from less electronegative system to more electronegative system. The ΔN calculation for determining electron transfer between selected PCBs and bases/selected base pairs is reported showing clearly the electron accepting nature of PCBs. Charge transfer calculation shows that the transfer of charge between NA bases/DNA base pairs and 3,3′,4,4′,5-PCBP is more compared with that of 2,2′,5,5′-TCBP which clearly indicates the higher toxic nature of 3,3′,4,4′,5-PCBP.[56] Table 3 reports the global reactivity descriptors (η and μ) for these bases and base-pairs for completeness.

5. Solvation Analysis of PCBs

The values of the relative energy, chemical hardness, chemical potential, and electrophlicity index for different torsional angle values in solution phase are presented in Table 4. The variation of rotational energy with torsional angle for 2,2′,5,5′-TCBP is shown in Figure 2g. The minimum energy conformation corresponds to $\phi = 120°$, and the relative energy variation looks like a typical potential well with relatively small barrier on the left and large barrier on the right side with the energy difference of 50.8 kJ/mol. The large rotational barrier prevents this molecule from attaining planarity and hence the molecule is less toxic in solution too. The presence of an implicit solvent environment for 3,3′,4,4′,5-PCBP shifts the minimum energy conformation to $\phi = 60°$, and the relative energy variation is between 0 and 8.83 kJ/mol[56] which is small compared to nontoxic 2,2′,5,5′-TCBP, which has the variation between 0 and 133.79 kJ/mol. We see that the 3,3′,4,4′,5-PCBP reduces its maximum relative energy values from 9.7 to 8.83 kJ/mol. Hence, this molecule has more toxic potentials in the solvent environment.

The variation in rotational energy and chemical hardness with torsional angle for 2,2′,5,5′-TCBP is given in the same Figure 2g. It is found that the global hardness does not coincide with the minimum energy conformation $\phi = 120°$. However, the minimum global hardness coincides with the $\phi = 180°$ and 0° conformation, as expected. The plot of the rotational energy barrier and global electrophilicity index with ϕ is depicted in Figure 2h. It is interesting to find that the high ω values are obtained for conformations corresponding to $\phi = 180°$ and 0°. It is evident from the ω profile that the $\phi = 180°$ conformation has very high ω and ΔE values. The high ω values could be used as the criterion for the high toxic nature of PCB. In this plot, we also present the electronegativity profile, which more or less mimics the corresponding profiles of ω and ΔE. Local electrophilicity profiles calculated using NPA as function of torsional angle for C, H, and Cl atoms reveal that the Cl_{16} center is more toxic than Cl_{14} at the $\phi = 120°$ conformation. The toxicities of the C_1 and H_{13} centers are also more pronounced than that of other C and H centers for most of the conformations. We have also calculated the amount of charge transfer in the solution phase between PCB and various bases, viz., adenine, guanine, thymine, cytosine, uracil, and DNA base pairs GCWC and ATH, by using eq 13, and the planar geometry allows the maximum amount of electron transfer for all of the bases and considered base pairs even in the solution phase. We find that the electron transfer for planar geometry remains a minimum for bases thymine and uracil.

6. Concluding Remarks

The chemical reactivity and selectivity profiles for 2,2′,5,5′-TCBP are computed and compared with those of 3,3′,4,4′,5-PCBP. It has been found that 2,2′,5,5′-TCBP has a very large rotational energy barrier at $\phi = 0°$ and 180°. Because of the large rotational barrier, this molecule cannot adopt a planar conformation, and hence, it is less toxic. In the case of 3,3′,4,4′,5-PCBP with a very small rotational energy barrier, it is shown to have a flexible planarity so that it changes its conformation while moving in biological systems, thereby interacting readily, exhibiting its toxic properties. On the other hand, the comparison between the chemical reactivity and selectivity profiles of 3,3′,4,4′,5-PCBP with 2,2′,5,5′-TCBP reveals that 3,3′,4,4′,5-PCBP is a highly toxic system as evident from the previous reports. Solvation of those systems also provides the same information with only a shift in their minimum relative energy conformation. The local electrophilic power of the individual atom and possible active reactive sites are reported for 2,2′,5,5′-TCBP and compared with those of 3,3′,4,4′,5-PCBP. The calculated charge transfer between the 2,2′,5,5′-TCBP and NA bases/DNA pairs shows that the charge

transfer takes place from NA bases/DNA pairs to 2,2′,5,5′-TCBP. A similar calculation provided a clue that charge transfer is more in the case of 3,3′,4,4′,5-PCBP. This calculation provides an interesting clue that 2,2′,5,5′-TCBP is less toxic when compared to the 3,3′,4,4′,5-PCBP. The clear electron accepting nature of PCB is evident from the charge-transfer calculation.

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Note Added after ASAP Posting. This article was posted ASAP on 11/6/2003. Due to a production error, in Figure 2, Thymine was misspelled as Thyamine. This has been corrected and was reposted on 11/17/2003.

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