On the Charge Transfer Between a Toxin and a Biosystem

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Abstract

Chemical potential and hardness of Benzidine, 3,3'- Dimethoxybenzidine, 3,3'- Dichlorobenzidine, 2,2',5,5'- Tetrachlorobiphenyl, 3,3',4,4',5,- Pentachlorobiphenyl, Dibenzofuran and adenine, thymine, guanine, cytocin, uracil, GCWC and ATH are calculated through DFT/6-31G(d), B3LYP method. It is shown that benzidines act as electron donors whereas polychlorinated biphenyls and dibenzofuran act as electron acceptors during their interaction with biosystems.

Motivation. To understand the nature of charge transfer between a toxin and a biosystem.

Method. Calculation of μ, η, η_{PQ} and ΔN for several toxins and NA bases and DNA base pairs using B3LYP/6-31G(d) method.

Results. Benzidines donate electrons to and PCBs ,dibenzofuran accepts electrons from a biological system simulated by NA bases and DNA base pairs

Conclusions. Benzidine, 3,3'- Dimethoxybenzidine and 3,3'- Dichlorobenzidine are electron donors and 2,2',5,5'- Tetrachlorobiphenyl, 3,3',4,4',5,- Pentachlorobiphenyl, Dibenzofuran are electron acceptors during their interactions with biosystems. Among the toxins benzidine is the best donor and 3,3',4,4',5- PCBP is the best acceptor where as among the bases/ base pairs guanine is the best acceptor and uracil is the best donor.

Keywords. DFT, Toxicity, Electron Transfer, Electronegativity, Hardness.

Abbreviations and notations

DFT, Density Functional Theory	NA, Nucleic Acid
TCBP, Tetrachlorobiphenyl	PCBP, Pentachlorobiphenyl

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1 INTRODUCTION

An understanding of the interaction between a toxin like a halogenated aromatic hydrocarbon and a biosystem often through a protein called AhR is the crucial step in the corresponding toxicological study [1-10]. This interaction is through a charge transfer process in addition to π- stacking in most cases. Therefore knowledge of the amount and the direction of the charge transfer is crucial in analyzing the respective toxic potential. In the present work an attempt has been made towards that goal in terms of density functional theory (DFT) based reactivity descriptors [11-13] and the associated electronic structure principles.

Electronegativity (χ) [14, 15] and hardness (η) [16, 17] are two cardinal indices [18] of chemical reactivity and selectivity. Electronegativity [19] (negative of chemical potential,μ the Lagrange multiplier associated with the normalization constraint of DFT [11]) and hardness [20] are respectively the following first order and second order derivatives,

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_{v(\vec{r})} \tag{1}$$

and

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

where E and $v(\vec{r})$ are the total energy and the external potential respectively for an N- electron system.

Within a finite difference approximation the above derivatives take the following forms in terms of the ionization potential (I) and electron affinity (A) as [11]

$$\chi = \frac{I + A}{2} \tag{3}$$

and

$$\eta = \frac{I - A}{2} \tag{4}$$

The corresponding joint hardness η_{PQ} is defined as [21]

$$\eta_{PQ} = \frac{I_P - A_Q}{2} \tag{5}$$

The amount of charge transfer may be calculated [20] as follows using these descriptors,

$$\Delta N = \frac{\mu_Q - \mu_P}{2\left(\eta_P + \eta_Q\right)} \tag{6}$$

These reactivity descriptors are better appreciated in terms of the associated electronic structure principles. According to Sanderson's electronegativity equalization principle [22] "There will be electron flow from a system of lower electronegativity (higher chemical potential) to that of higher electronegativity (lower chemical potential) until the electronegativity values get equalized to a value roughly equal to the geometric mean of the individual electronegativities". Two important hardness related structure principles are hard- soft acid- base (HSAB) principle [16, 20, 23] and maximum hardness principle (MHP) [24]. While the former states that. "For the partners of comparable electronegativity values hard acids prefer to coordinate with hard bases and soft acids

with soft bases for both their kinetic and thermodynamic considerations", the statement of the latter is, "There seems to be a rule of nature that molecules arrange themselves so as to be as hard as possible". In the present work we try to gain insights into the nature of charge flow between a toxin and a biosystem in terms of the above reactivity descriptors and the corresponding electronic structure principles. We select benzidine, 3,3'- dimethoxybenzidine, 3,3'- Dichlorobenzidine, 2,2',5,5'- Tetrachlorobiphenyl, 3,3',4,4',5,- Pentachlorobiphenyl, Dibenzofurans as toxins interacting with nucleic acid (NA) bases adenine, thymine, guanine, cytocin, uracil, and selected DNA base pairs GCWC and ATH. Section 2 presents the computational details, section 3 provides results and discussion and finally section 4 contains some concluding remarks.

2 COMPUTATIONAL DETAILS

All the geometries of the molecules studied here have been optimized using GAUSSIAN 03 program [25]. DFT level calculations with B3LYP exchange- correlation functional and 6-31G(d) basis set are used. The chemical potential (μ) and chemical hardness (η) are calculated using Koopman's theorem,

$$\mu = \left(\frac{\varepsilon_{LUMO}+\varepsilon_{HOMO}}{2}\right) \tag{7}$$

and

$$\eta = \frac{\varepsilon_{LUMO}-\varepsilon_{HOMO}}{2} \tag{8}$$

We have studied toxins like benzidine, 3,3'- dimethoxybenzidine, 3,3'- Dichlorobenzidine, 2,2',5,5'- Tetrachlorobiphenyl, 3,3',4,4',5,- Pentachlorobiphenyl, Dibenzofurans and nucleic acid (NA) bases like adenine, thymine, guanine, cytocin, uracil and DNA base pairs like GCWC and ATH.

3 RESULTS AND DISCUSSION

Figure 1 presents the optimized structures with the atom- numbering schemes of various toxins while some of their relevant geometrical parameters are given in Table1.

The chemical potential and hardness values of various toxins, NA bases and DNA base pairs are provided in Table 2. According to Sanderson's electronegativity equalization principle electron flow will take place from a system of lower electronegativity (higher chemical potential) to that of higher electronegativity (lower chemical potential). Comparing the chemical potential values of the toxins and bases/ base pairs we see that benzidine, 3,3'- dimethoxybenzidine and 3,3'- Dichlorobenzidine (except for interaction with guanine) act as electron donors whereas 2,2',5,5'- TCBP, 3,3',4,4',5 PCBP and Dibenzofuran (except during its interaction with uracil) behave as electron acceptors while interacting with biosystems.

In Table 3 we present various joint hardness values and also the amount of electron transfer. According to maximum hardness principle a flow of electron will take place from A to B if $\eta_{AB} \langle \eta_{BA}$ and vice versa. Comparison of these two joint hardness values (Table 3) provides identical results as that obtained from their chemical potential values.

It may be noted that the sign of ΔN also provides the identical trends to show the inherent consistency of all three approaches. For all the electron donor toxins, the maximum amount of

charge transfer takes place during their interaction with uracil and the minimum amount of charge transfer takes place when they react with guanine (actually the situation gets reversed for 3,3'-dichlorobenzidine). On the other hand for the electron acceptor toxins, a completely opposite trend is observed, *viz.,* maximum charge transfer with guanine and minimum charge transfer with uracil (in the reverse direction when uracil interacts with dibenzofuran). Among the studied toxins benzidine is expected to be the most toxic from the donor class whereas 3,3',4,4',5- PCBP is expected to be the most toxic from the acceptor class, by comparing their relative ΔN values.

4 CONCLUDING REMARKS

Three different approaches, *viz.,* Sanderson's electronegativity equalization principle, maximum hardness principle and the amount of charge transfer calculation show that toxins like benzidine, 3,3'- dimethoxybenzidine and 3,3'- dichlorobenzidine act as electron donors whereas 2,2',5,5'- TCBP, 3,3',4,4',5 PCBP and dibenzofuran act as electron acceptors when they interact with most of the biosystems. Guanine is shown to be the best donor whereas Uracil is found to be the best acceptor.

Acknowledgment

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5 References

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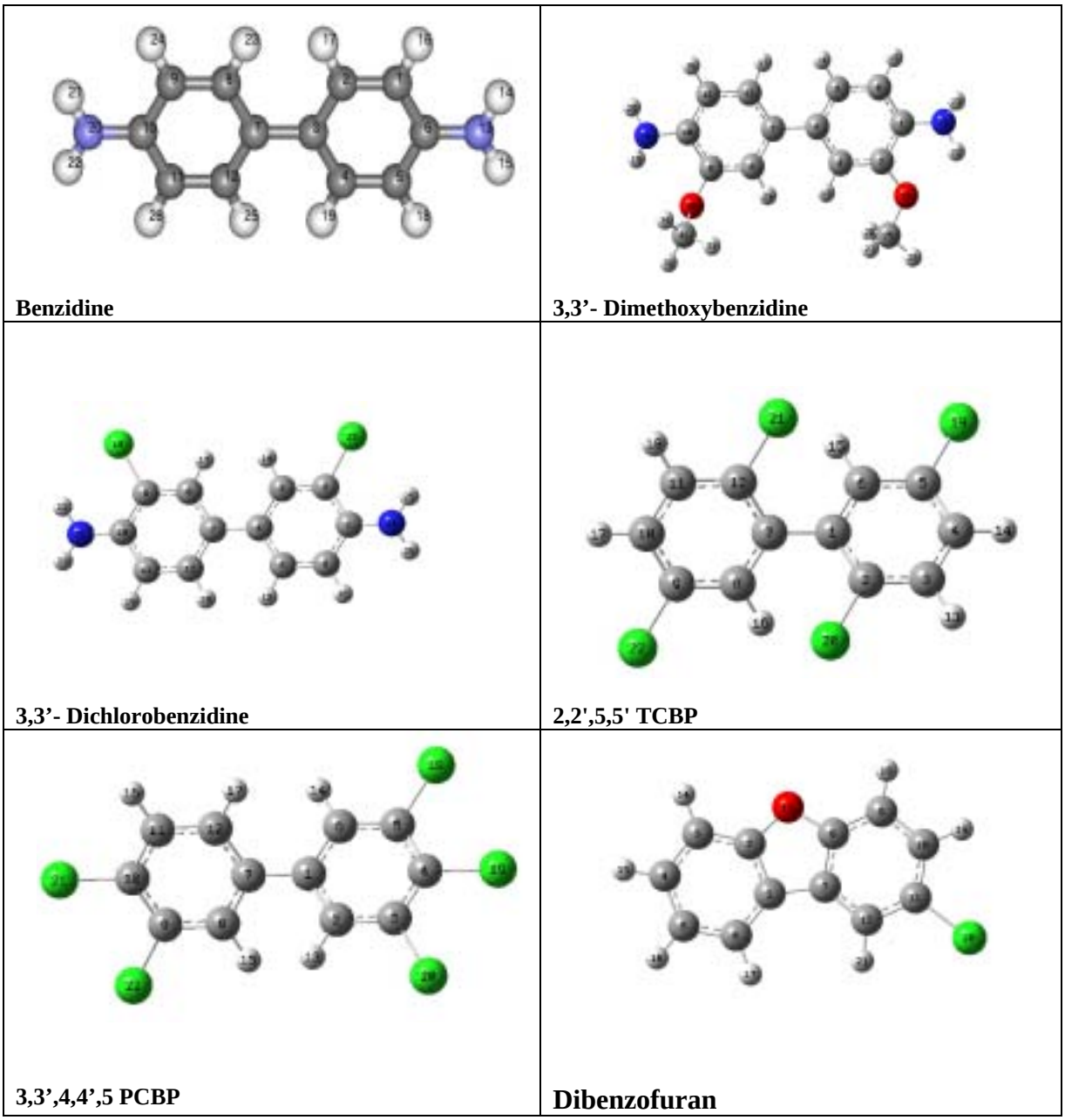

Figure 1: Structures with atom numbering schemes of the selected toxins.

Table 1: Selected geometrical parameters for the toxins

Molecule	Bond Length (Å)	Bond Angle (Degree)
Benzidine	C3-C7= 1.482 C3-C4=1.406 C4-C19=1.087 C6-N13=1.401 N13-H14=1.013	C4-C3-C7=121.528 C3-C4-C5=121.793 C3-C4-H19=119.353 C5-C6-N13=120.926 C6-N13-H14=119.597
3,3'- Dimethoxybenzidine	C4-C7=1.488 C2-O24=1.376 C1-N21=1.395 O24-C25=1.416 C9-O30=1.389 C10-N18=1.397 O30-C31=1.429	C3-C4-C7=121.314 C1-C2-O24=114.095 C2-C1-N21=119.687 C2-O24-C25=118.366 C9-C10-N18=119.693 C8-C9-O30=120.287 C9-O30-C31=113.665
3,3'- Dichlorobenzidine	C4-C7= 1.487 C1-N24=1.387 C10-N21=1.387 C2-Cl13=1.768 C9-Cl18=1.768	C3-C4-C7=121.787 C2-C1-N24=122.540 C1-C2-Cl13=118.894 C8-C9-Cl18=118.701 C9-C10-N21=122.540
2,2',5,5' TCBP	C1-C7= 1.494 C1-C2=1.403 C1-C6=1.402 C2-C3=1.395 C3-H13=1.085 C5-Cl19=1.756	C1-C7-C12=122.686 C1-C2-C3=121.237 C1-C2-Cl20=120.54 C2-C3-H13=119.608 C4-C5-Cl19=119.597
3,3',4,4',5 PCBP	C1-C7= 1.484 C1-C2=1.401 C2-C3=1.392 C2-H13=1.084 C5-Cl18=1.747 C4-Cl19=1.735	C7-C1-C2=120.887 C1-C2-C3=120.788 C1-C2-H13=120.515 C2-C3-Cl20=118.157 C4-C5-Cl18=120.776
Dibenzofuran	C8-O13=1.375 C2-O13=1.378 C1-C7=1.452 C2-C8=2.197 C11-Cl20=1.762	C1-C7-C8=105.408 C2-O13-C8=105.928 C2-C1-C7=105.294 C10-C11-Cl20=118.650

Table 2: Chemical potential (μ) and hardness (η) of selected toxins and NA bases/ DNA base pairs

Molecule	μ (eV)	η (eV)
Benzidine	-2.130	2.220
3,3'- Dimethoxybenzidine	-2.389	2.163
3,3'- Dichlorobenzidine	-2.861	2.210
2,2',5,5' TCBP	-4.462	1.703
3,3',4,4',5 PCBP	-4.513	1.663
Dibenzofuran	-3.712	2.493
Adenine	-3.103	2.850
Thymine	-3.689	2.894
Guanine	-2.648	2.916
Cytocin	-3.370	2.785
Uracil	-3.919	2.962
GCWC	-3.030	2.018
ATH	-3.256	2.526

Table 3: Joint hardness (η_{AB}) and amount of charge transfer between toxins (*A*) and NA bases /DNA base pairs (*B*)

NA bases /DNA base pairs	η_{AB}	η_{BA}	ΔN
Benzidine			
Adenine	2.0485	3.0215	-0.0960
Thymine	1.7775	3.3365	-0.1524
Guanine	2.3090	2.8270	-0.0504
Cytocin	1.8825	3.1225	-0.1239
Uracil	1.6965	3.4855	-0.1726
GCWC	1.6690	2.5690	-0.1062
ATH	1.8100	2.9360	-0.1186
3,3'- Dimethoxybenzidine			
Adenine	2.1525	2.8665	-0.0711
Thymine	1.8815	3.1815	-0.1284
Guanine	2.4130	2.6720	-0.0255
Cytocin	1.9865	2.9675	-0.0990
Uracil	1.8005	3.3305	-0.1491
GCWC	1.7730	2.4140	-0.0765
ATH	1.9140	2.7810	-0.0923
3,3'- Dichlorobenzidine			
Adenine	2.4090	2.6510	-0.0239
Thymine	2.1380	2.9660	-0.0811
Guanine	2.6695	2.4565	0.0208
Cytocin	2.2430	2.7520	-0.0509
Uracil	2.0570	3.1150	-0.1023
GCWC	2.0295	2.1985	-0.0200
ATH	2.1705	2.5655	-0.0417
2,2',5,5' TCBP			
Adenine	2.9560	1.5970	0.1492
Thymine	2.6850	1.9120	0.0841
Guanine	3.2165	1.4025	0.1964
Cytocin	2.7900	1.6980	0.1217
Uracil	2.6040	2.0610	0.0582
GCWC	2.5765	1.1445	0.1924
ATH	2.7275	1.5115	0.1426
3,3',4,4',5 PCBP			
Adenine	2.9615	1.5515	0.1562
Thymine	2.6905	1.8665	0.0904
Guanine	3.2220	1.3570	0.2036
Cytocin	2.7955	1.6520	0.1285
Uracil	2.6095	2.0155	0.0642
GCWC	2.5820	1.0990	0.2014
ATH	2.7230	1.4660	0.1500
Dibenzofuran			
Adenine	2.9758	2.3671	0.0570
Thymine	2.7048	2.6821	0.0021
Guanine	3.2363	2.1726	0.0983
Cytocin	2.8098	2.4681	0.0324
Uracil	2.6238	2.8311	-0.0190
GCWC	2.5963	1.9146	0.0756
ATH	2.7373	2.2816	0.0454