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Quantum Chemical Descriptors Based QSTR Study of Nitrobenzene Derivatives against Tetrahymena Pyriformis

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Abstract

Eight quantum chemical descriptors namely molecular weight, molar refractivity, HOMO energy, electronegativity, electron affinity, ionization potential, total energy and Log P of fifty four nitrobenzene derivatives have been calculated with the help of CAChe Pro of Fujitsu software using DFT methods and the semiemperical PM3 methods. Observed toxicities of all compounds are in terms of -log (IGC_{50}), mM, which is the inverse logarithm of the concentration causing 50% growth inhibition of Tetrahymena pyriformis after 40 hours. These eight descriptors have been used in the development of QSTR models. The QSTR model developed from descriptors molecular weight, molar refractivity, electron affinity and total energy have very high predictive power and can be used to find out the toxicity of any new derivative of nitrobenzene. Reliable QSTR models have been obtained from single descriptors namely electron affinity and total energy. The quality of regression has been adjudged by correlation coefficient, cross validation coefficient and statistical parameters like standard error, standard error of estimate, p-value, t-value, degrees of freedom etc.

Keywords: Nitrobenzene derivatives, tetrahymena pyriformis, DFT, electron affinity, total energy.

Introduction

The toxicity of nitrobenzenes against *Tetrahymena pyriformis* has been extensively studied by using 2D and 3D QSAR methodologies[1-4]. Hydrophobicity and electrophilic reactivity appeared the most important structural factors contributing to the toxic action of nitrobenzene[5]. Nitrobenzene and their numerous derivatives are of use as explosives and propellants in the military and in industry[6,7]. Waste from nitro compounds are easily disseminated leading to a potential hazard for humans and the environment[8]. A number of studies have shown that nitro compounds, as well as their metabolites of environmental transformation, by-products of synthesis, or incomplete combustion are harmful for the biosphere due to their toxicity[9-11]. For instance, toxic effects in humans include gastrointestinal, neurological and reproductive disorders, cirrhosis of the liver, hepatitis, cataracts, respiratory and skin irritation, nephrotoxicity, and hematological defects. Moreover, nitrobenzene derivatives are widely used in medicine, industry and agriculture. Nitroaromatic pesticides as well as the explosive residues are considered as toxic environmental pollutants. Some of these compounds have mutagenic or carcinogenic activity and may accumulate in the food chain (bioaccumulation). Therefore, the presence of aromatic and nitroaromatic xenobiotics in the environment may present serious public health and environmental problems. Both nature and degree of aromatic substitutions may have effects on the chemical toxicity of nitroaromatic compounds[12].

In recent years various descriptors like quantum chemical, topological and energy descriptors have been successfully employed for QSTR and QSAR studies of different compunds[13-19]. In this paper, Quantum chemical descriptors have been used for the development of QSTR models for Fifty four nitrobenzene derivatives. The descriptors that have been used are molecular weight, molar refractivity, HOMO energy, electronegativity, electron affinity, ionization potential, total energy and Log P. The predicted toxicities obtained from developed QSTR models were found close to reported observed toxicities.

Material and Methods

Fifty four substituted nitrobenzene derivatives given in table-1 have been taken as study material. The toxicity of these compounds was measured in terms of -log (IGC_{50}), mM, which is the inverse logarithm of the concentration causing 50% growth inhibition of *Tetrahymena pyriformis* after 40 hours. The 3D modeling and geometry optimization of all the compounds and evaluation of values of descriptors have been done with the help of CAChe Pro software of Fujitsu, using the DFT Methods[20-22] and semiemperical PM3 Hamiltonian[23]. The Project Leader program has been used for multi linear regression (MLR) analysis. The statistical parameters have been calculated by Smith's Statistical Package (version 2.80). The descriptors that have been used are described below.

Water/Octanol Partition coefficient (Log P)[24]: The Water/Octanol partition coefficient is the ratio of concentrations of un-ionized compound between the two solutions. To measure the partition coefficient of ionizable solutes, the pH of the aqueous phase is adjusted such that the predominant form of the

compound is un-ionized. The logarithm of the ratio of the concentrations of the un-ionized solute in the solvents is called log P

$$log\ P_{oct/wat} = log\left(\frac{[solute]_{octanol}}{[solute]^{un-ionized}_{water}}\right)$$

Molar Refractivity[25]: It is a constitutive-additive property that is calculated by the Lorenz-Lorentz formula,

$$MR = \frac{n^2-1}{n^2+1} * \frac{M}{\rho}$$

where M is the molecular weight, n is the refraction index and ρ is the density. For a radiation of infinite wavelength, the molar refractivity represents the real volume of the molecules. Molar refractivity is related, not only to the volume of the molecules but also to the London dispersive forces that act in the drug-receptor interaction.

Molecular Weight: It is the sum of atomic weights of all the atoms of the compound.

Total energy: Total energy (TE) of a molecular system is sum of the total electronic energy (Eee) and the energy of internuclear repulsion (Enr)[26].

$$TE = Eee + Enr$$

The total electronic energy of the system is given by

$$Eee = 1/2\ P\ (H + F)$$

Where P is the density matrix, H is the one-electron matrix, and F is the Fock matrix.

HOMO Energy: The energy required to remove an electron from the highest occupied molecular orbital (HOMO) is called HOMO energy.

Electronegativity, Ionisation Potential and Electron Affinity[27,28]: Parr et al define the electronegativity as the negative of chemical potential,

$$\chi = -\mu = -(\partial E/\partial N)\ \nu\ (r) \quad (1)$$

The operational definition of absolute hardness, global softness and electronegativity is as

$$\chi = -\mu\ 1/2\ (IP+EA) \quad (2)$$

where IP and EA are the ionization potential and electron affinity respectively, of the chemical species. According to the Koopman's theorem, the IP is simply the eigen value of HOMO with change of sign and EA is the eigen value of LUMO with change of sign, hence we have

$$\chi\ 1/2\ (\varepsilon\ LUMO + \varepsilon\ HOMO) \quad (3)$$

Table-1
Nitrobenzene Derivatives used in our study along with their Observed toxicity

S. No.	Compounds	Observed Toxicity –log(IGC_{50})
1	Nitrobenzene	0.14
2	2-Chloronitrobenzene	0.68
3	2-Bromonitrobenzene	0.75
4	3-Chloronitrobenzene	0.73
5	4-Ethylnitrobenzene	0.80
6	4-Chloronitrobenzene	0.43
7	4-Bromonitrobenzene	0.38
8	4-Fluoronitrobenzene	0.25
9	2,4,6-Trimethylnitrobenzene	0.86
10	2,4-Dichloronitrobenzene	0.99
11	3-Bromonitrobenzene	1.03
12	2,3-Dichloronitrobenzene	1.07
13	3-Methyl-4-bromonitrobenzene	1.16
14	3,4-Dichloronitrobenzene	1.16
15	1,2-Dinitrobenzene	1.25
16	1,4-Dinitrobenzene	1.30
17	2,5-Dibromonitrobenzene	1.37
18	4-Butoxynitrobenzene	1.42
19	2,4,6-Trichloronitrobenzene	1.43
20	2,3,4-Trichloronitrobenzene	1.51
21	5-methyl-1,2-dinitrobenzene	1.52
22	2,4,5-Trichloronitrobenzene	1.53
23	2,3,4,5-Tetrachloronitrobenzene	1.78
24	2,3,5,6-Tetrachloronitrobenzene	1.82
25	6-Iodo-1,3-dinitrobenzene	2.12
26	2,4,6-Trichloro-1,3-dinitrobenzene	2.19
27	1,2-Dinitro-4,5-dichlorobenzene	2.21
28	6-Bromo-1,3-dinitrobenzene	2.31
29	2,4,5-Trichloro-1,3-dinitrobenzene	2.59
30	4,6-Dichloro-1,2-dinitrobenzene	2.42
31	2,3,5,6-Tetrachloro-1,4-dinitrobenzene	2.74
32	1,3-Dimethyl-2-nitrobenzene	0.30
33	2,3-Dimethylnitrobenzene	0.56
34	3,5-Dichloronitrobenzene	1.13
35	3-Chloro-4-fluoronitrobenzene	0.80
36	2.5-Dichloronitrobenzene	1.13
37	1,2,3-Trifluoro-4-nitrobenzene	1.89
38	2,3,4,6-Tetrafluoronitrobenzene	1.87
39	1-Chloro-2,4-dinitrobenzene	2.16
40	2,4-Dinitro-1-fluorobenzene	1.71
41	Pentafluoronitrobenzene	2.43
42	1,5-Difluoro-2,4-dinitrobenzene	2.08
43	1,2-Dimethyl-4-nitrobenzene	0.59
44	1-Fluoro-3-iodo-5-nitrobenzene	1.09
45	1-Fluoro-2-nitrobenzene	0.23
46	1,2,3-Trichloro-5-nitrobenzene	1.55
47	1,3-Dichloro-4,6-dinitrobenzene	2.72
48	2,6-Dimethylnitrobenzene	0.30
49	2-Methyl-3-chloronitrobenzene	0.68
50	2-Methylnitrobenzene	0.05
51	2-Methyl-5-chloronitrobenzene	0.82
52	6-Chloro-1,3-dinitrobenzene	1.98
53	3-Methylnitrobenzene	0.05
54	4-Methylnitrobenzene	0.17

Results and Discussion

Fifty four derivatives of nitrobenzene are given in table-1 along with their observed toxicity in terms of -log (IGC_{50}). The values of eight descriptors of compounds, which have been calculated, are given in table-2. For the development of QSTR models multi linear regression (MLR) analysis has been performed using different combinations of descriptors. The MLR analysis has indicated that the toxicity of nitrobenzene can be successfully modeled even in mono-parametric regression using descriptors electron affinity and total energy. The mono-parametric QSTR model obtained by using descriptor total energy is given by following regression equation,

$^{Mono-}PT1 = -0.0346854*E_T - 2.22073$

$r^2 = 0.842424$, $rCV^2 = 0.817187$, Std. Error = 0.0600, SEE = 0.3029, t-value = 16.6692, p-value = 0, DOF = 0.8393, N = 54, VC = 1.

and the mono-parametric QSTR model obtained by using descriptor electron affinity is given by following regression equation,

$^{Mono-}PT2 = 1.44437*E_A - 1.04585$

$r^2 = 0.736855$, $rCV^2 = 0.708911$, Std. Error = 0.0829, SEE = 0.3913, t-value = 12.0659, p-value = 0, DOF = 0.7318, N = 54, VC = 1.

In the above regression equations, r^2 is correlation coefficient, rCV^2 is cross-validation coefficient, Std. Error is standard error, SEE is standard error of estimate, DOF is degrees of freedom, N is data points (compounds), and VC is variable count. Total energy and electron affinity appear important descriptor for this set of nitrobenzene derivatives. The trends of observed toxicity and predicted toxicity obtained from $^{Mono-}$PT1 and $^{Mono-}$PT2 are shown in figure-1 and figure-2. The predicted toxicities, obtained from above two mono-parametric QSTR models $^{Mono-}$PT1 and $^{Mono-}$PT2, are listed in table-3.

The addition of other descriptor in the above mono-parametric model yields a model with improved predictability. The resulting bi-parametric QSTR model obtained by using descriptors molecular weight and total energy is given by following regression equation,

$^{Bi-}PT1 = 0.00498977*MW - 0.0271056*E_T - 2.44255$

$r^2 = 0.891916$, $rCV^2 = 0.869526$ Std. Error = 0.0483, SEE = 0.2508, t-value = 20.7132, p-value = 0, DOF = 0.8898, N = 54, VC = 2.

and the bi-parametric QSTR model developed from descriptors molar refractivity and electron affinity is given by following regression equation,

$^{Bi-}PT2 = 0.0480157*MR + 1.26113*E_A - 2.86509$

$r^2 = 0.87697$, $rCV^2 = 0.849372$, Std. Error = 0.0519, SEE = 0.2675, t-value = 19.2554, p-value = 0, DOF = 0.8746, N = 54, VC = 2.

The trends of observed toxicity and predicted toxicity obtained from $^{Bi-}$PT1 and $^{Bi-}$PT2 are shown in figure-3 and figure-4. The predicted toxicities, obtained from above two bi-parametric QSTR models $^{Bi-}$PT1 and $^{Bi-}$PT2, are listed in table-3.

Using combination of three descriptors, the tri-parametric QSTR models are obtained with improved predictive power. The best two are discussed here,

$^{Tri-}PT1 = 0.0346058*MR + 0.675744*E_A - 0.0162879*E_T - 2.97539$

$r^2 = 0.908686$, $rCV^2 = 0.866198$, Std. Error = 0.0439, SEE = 0.2304, t-value = 22.7567, p-value = 0, DOF = 0.9070, N = 54, VC = 3.

This QSTR model involves molar refractivity as first descriptor, electron affinity as second descriptor and total energy as third descriptor.

$^{Tri-}PT2 = 0.00491374*MW + 0.361497*E_A - 0.0200948*E_T - 2.3013$

$r^2 = 0.902500$, $rCV^2 = 0.877689$, Std. Error = 0.0456, SEE = 0.2382, t-value = 21.9356, p-value = 0, DOF = 0.9006, N = 54, VC = 3.

This QSTR model involves molecular weight as first descriptor, electron affinity as second descriptor and total energy as third descriptor. The trends of observed toxicity and predicted toxicity obtained from $^{Tri-}$PT1 and $^{Tri-}$PT2 are shown in figure-5and figure-6. The predicted toxicities, obtained from above two tri-parametric QSTR models $^{Tri-}$PT1 and $^{Tri-}$PT2, are listed in table-3.

By the combination of four descriptors, tetra-parametric QSTR models are obtained with excellent predictive power. The best two are discussed here,

$^{Tetra-}PT1 = 0.00228773*MW + 0.0232587*MR + 0.569215*E_A - 0.0165772*E_T - 2.78577$

$r^2 = 0.913259$, $rCV^2 = 0.875215$, Std. Error = 0.0427, SEE = 0.2247, t-value = 23.3928, p-value = 0, DOF = 0.9116, N = 54, VC = 4.

This QSTR model is obtained by using the descriptors molecular weight, molar refractivity, electron affinity and total energy. The values of correlation coefficient and cross validation coefficient indicate that this model has excellent predictive power and can be used to find out the toxicity of any nitrobenzene derivative.

$^{Tetra-}PT2 = 0.00385828*MW + 0.0230104*MR - 0.389962*\chi - 0.0203582*E_T - 4.88179$

$r^2 = 0.91214$, $rCV^2 = 0.886503$, Std. Error = 0.0430, SEE = 0.2261, t-value = 23.2320, p-value = 0, DOF = 0.9104, N = 54, VC = 4.

This QSTR model is obtained by using the descriptors molecular weight, molar refractivity, electronegativity and total energy. The values of correlation coefficient and cross validation coefficient indicate that this model has excellent predictive power and can be used to find out the toxicity of any nitrobenzene derivative. The trends of observed toxicity and predicted toxicity obtained from $^{Tetra-}$PT1 and $^{Tetra-}$PT2 are shown in figure-7 and figure-8. The predicted toxicities, obtained from above two tetra-parametric QSTR models $^{Tetra-}$PT1 and $^{Tetra-}$PT2, are listed in table-3.

Table-2
Values of descriptors and observed toxicity of Nitrobenzene Derivatives

C. No.	MW	MR	E_{HOMO}	χ	EA	IP	E_T	LogP	$-\log(IGC_{50})$
1	123.111	33.383	-10.603	-1.134	1.134	10.603	-69.403	2.000	0.14
2	157.556	38.188	-9.944	-1.267	1.267	9.944	-81.165	2.518	0.68
3	202.007	41.006	-10.396	-1.286	1.286	10.396	-79.285	2.792	0.75
4	157.556	38.188	-10.063	-1.306	1.306	10.063	-81.168	2.518	0.73
5	151.165	43.025	-10.410	-1.087	1.087	10.410	-83.750	2.864	0.80
6	157.556	38.188	-10.219	-1.356	1.356	10.219	-81.172	2.518	0.43
7	202.007	41.006	-10.702	-1.389	1.389	10.702	-79.290	2.792	0.38
8	141.101	33.599	-10.845	-1.415	1.415	10.845	-85.318	2.140	0.25
9	165.191	48.506	-9.946	-1.020	1.020	9.946	-90.951	3.402	0.86
10	192.001	42.992	-10.049	-1.471	1.471	10.049	-92.934	3.036	0.99
11	202.007	41.006	-10.524	-1.354	1.354	10.524	-79.290	2.792	1.03
12	192.001	42.992	-9.788	-1.396	1.396	9.788	-92.930	3.036	1.07
13	216.034	46.047	-10.418	-1.323	1.323	10.418	-86.474	3.259	1.16
14	192.001	42.992	-9.971	-1.486	1.486	9.971	-92.938	3.036	1.16
15	168.109	40.707	-11.323	-1.967	1.967	11.323	-101.181	1.954	1.25
16	168.109	40.707	-11.305	-2.253	2.253	11.305	-101.204	1.954	1.30
17	280.903	48.628	-10.395	-1.493	1.493	10.395	-89.171	3.584	1.37
18	195.218	53.719	-10.013	-1.006	1.006	10.013	-110.252	2.955	1.42
19	226.446	47.797	-9.888	-1.567	1.567	9.888	-104.692	3.554	1.43
20	226.446	47.797	-9.852	-1.564	1.564	9.852	-104.700	3.554	1.51
21	182.135	45.749	-11.040	-1.923	1.923	11.040	-108.372	2.421	1.52
22	226.446	47.797	-9.768	-1.596	1.596	9.768	-104.700	3.554	1.53
23	260.891	52.602	-9.741	-1.683	1.683	9.741	-116.464	4.072	1.78
24	260.891	52.602	-9.523	-1.614	1.614	9.523	-116.451	4.072	1.82
25	294.005	53.116	-9.723	-1.980	1.980	9.723	-110.008	3.211	2.12
26	271.444	55.122	-10.298	-2.171	2.171	10.298	-136.479	3.508	2.19
27	236.999	50.317	-10.440	-2.241	2.241	10.440	-124.716	2.990	2.21
28	247.005	48.330	-11.150	-2.100	2.100	11.150	-111.085	2.746	2.31
29	271.444	55.122	-10.072	-2.173	2.173	10.072	-136.481	3.508	2.59
30	236.999	50.317	-10.467	-2.166	2.166	10.467	-124.700	2.990	2.42
31	305.889	59.927	-9.798	-2.489	2.489	9.798	-148.227	4.026	2.74
32	151.165	43.465	-9.981	-1.044	1.044	9.981	-83.760	2.935	0.30
33	151.165	43.465	-10.036	-1.047	1.047	10.036	-83.769	2.935	0.56
34	151.165	43.465	-10.091	-1.036	1.036	10.091	-83.780	2.935	1.13
35	175.547	38.404	-10.176	-1.551	1.551	10.176	-97.084	2.658	0.80
36	192.001	42.992	-9.740	-1.429	1.429	9.740	-92.929	3.036	1.13
37	177.082	34.032	-11.025	-1.932	1.932	11.025	-117.150	2.419	1.89
38	195.073	34.248	-10.864	-2.181	2.181	10.863	-133.057	2.558	1.87
39	202.554	45.512	-10.656	-2.087	2.087	10.656	-112.970	2.472	2.16
40	186.099	40.924	-11.544	-2.194	2.194	11.544	-117.123	2.093	1.71
41	213.063	34.465	-11.157	-2.435	2.435	11.157	-148.983	2.698	2.43
42	204.090	41.140	-11.822	-2.421	2.421	11.822	-133.041	2.233	2.08
43	151.165	43.465	-10.165	-1.055	1.055	10.165	-83.777	2.935	0.59
44	266.998	46.007	-9.662	-1.534	1.534	9.662	-94.124	3.397	1.09
45	141.101	33.599	-10.629	-1.386	1.386	10.629	-85.318	2.140	0.23
46	226.446	47.797	-10.038	-1.608	1.608	10.038	-104.703	3.554	1.55
47	236.999	50.317	-10.694	-2.191	2.191	10.694	-124.735	2.990	2.72
48	151.165	43.465	-9.980	-1.043	1.043	9.980	-83.760	2.935	0.30
49	171.583	43.229	-9.923	-1.258	1.258	9.923	-88.350	2.985	0.68
50	137.138	38.424	-10.238	-1.091	1.091	10.238	-76.587	2.467	0.05
51	171.583	43.229	-9.839	-1.259	1.259	9.840	-88.351	2.985	0.82
52	202.554	45.512	-10.656	-2.086	2.086	10.656	-112.970	2.472	1.98
53	137.138	38.424	-10.271	-1.082	1.082	10.271	-76.591	2.467	0.05
54	137.138	38.424	-10.472	-1.109	1.109	10.472	-76.594	2.467	0.17

where MW = molecular weight, MR = Molar Refractivity, E_{HOMO} = Energy of HOMO, χ = Electronegativity, EA = Electron Affinity, IP = Ionization Potential, E_T = Toatl Energy

Table-3
Predicted Toxicities ^{Mono}PT1 to ^{Tetra}PT2 of the Nitrobenzene Derivatives

C. No.	^{Mono}PT1	^{Mono}PT2	^{Bi}PT1	^{Bi}PT2	^{Tri}PT1	^{Tri}PT2	^{Tetra}PT1	^{Tetra}PT2
1	0.187	0.593	0.053	0.168	0.077	0.108	0.069	0.063
2	0.594	0.784	0.544	0.566	0.524	0.562	0.53	0.443
3	0.529	0.812	0.714	0.726	0.604	0.749	0.676	0.733
4	0.595	0.84	0.544	0.615	0.55	0.576	0.552	0.474
5	0.684	0.524	0.582	0.572	0.612	0.517	0.568	0.638
6	0.595	0.913	0.544	0.679	0.585	0.594	0.58	0.514
7	0.529	0.96	0.715	0.855	0.674	0.787	0.735	0.813
8	0.739	0.997	0.574	0.532	0.533	0.618	0.538	0.563
9	0.934	0.428	0.847	0.751	0.874	0.707	0.809	0.862
10	1.003	1.078	1.035	1.054	1.02	1.041	1.031	0.986
11	0.529	0.91	0.715	0.812	0.65	0.774	0.715	0.771
12	1.003	0.971	1.034	0.96	0.97	1.014	0.989	0.921
13	0.779	0.865	0.979	1.014	0.921	0.976	0.966	1.061
14	1.003	1.101	1.035	1.074	1.03	1.047	1.04	0.974
15	1.289	1.795	1.139	1.57	1.411	1.269	1.343	1.355
16	1.29	2.209	1.139	1.931	1.604	1.373	1.506	1.407
17	0.872	1.111	1.376	1.353	1.169	1.411	1.316	1.454
18	1.603	0.407	1.52	0.983	1.359	1.237	1.31	1.501
19	1.411	1.217	1.525	1.406	1.442	1.481	1.471	1.457
20	1.411	1.214	1.525	1.403	1.441	1.481	1.47	1.449
21	1.538	1.732	1.404	1.757	1.672	1.467	1.586	1.607
22	1.411	1.26	1.525	1.443	1.463	1.492	1.488	1.439
23	1.819	1.385	2.016	1.783	1.879	1.929	1.923	1.934
24	1.818	1.286	2.016	1.697	1.833	1.904	1.884	1.878
25	1.595	1.814	2.006	2.182	1.992	2.07	2.073	1.996
26	2.513	2.09	2.611	2.52	2.622	2.56	2.616	2.644
27	2.105	2.191	2.121	2.377	2.311	2.179	2.27	2.202
28	1.632	1.988	1.801	2.104	1.926	1.904	1.94	2.028
29	2.513	2.093	2.611	2.523	2.624	2.561	2.617	2.6
30	2.105	2.083	2.12	2.282	2.261	2.152	2.227	2.192
31	2.921	2.549	3.102	3.151	3.194	3.08	3.182	3.091
32	0.685	0.462	0.582	0.538	0.598	0.502	0.554	0.556
33	0.685	0.467	0.582	0.543	0.601	0.503	0.556	0.568
34	0.685	0.451	0.583	0.529	0.594	0.5	0.55	0.577
35	1.147	1.195	1.065	0.935	0.983	1.073	1.001	0.942
36	1.003	1.019	1.034	1.002	0.992	1.026	1.008	0.918
37	1.843	1.744	1.616	1.205	1.416	1.621	1.452	1.496
38	2.394	2.105	2.137	1.53	1.851	2.119	1.904	1.911
39	1.698	1.968	1.63	1.952	1.85	1.718	1.797	1.732
40	1.842	2.123	1.661	1.867	1.831	1.76	1.782	1.841
41	2.947	2.471	2.659	1.861	2.289	2.62	2.359	2.417
42	2.394	2.452	2.182	2.164	2.251	2.25	2.222	2.338
43	0.685	0.478	0.583	0.553	0.606	0.506	0.56	0.595
44	1.044	1.17	1.441	1.279	1.186	1.457	1.329	1.306
45	0.739	0.956	0.574	0.496	0.513	0.607	0.522	0.515
46	1.411	1.277	1.525	1.458	1.471	1.497	1.495	1.494
47	2.106	2.119	2.121	2.314	2.278	2.162	2.242	2.242
48	0.685	0.461	0.582	0.538	0.598	0.502	0.553	0.556
49	0.844	0.771	0.808	0.797	0.809	0.772	0.793	0.754
50	0.436	0.531	0.318	0.356	0.339	0.306	0.313	0.3
51	0.844	0.773	0.808	0.798	0.81	0.772	0.794	0.738
52	1.698	1.968	1.63	1.951	1.849	1.718	1.796	1.731
53	0.436	0.517	0.318	0.344	0.333	0.303	0.307	0.304
54	0.436	0.556	0.318	0.378	0.351	0.313	0.323	0.349

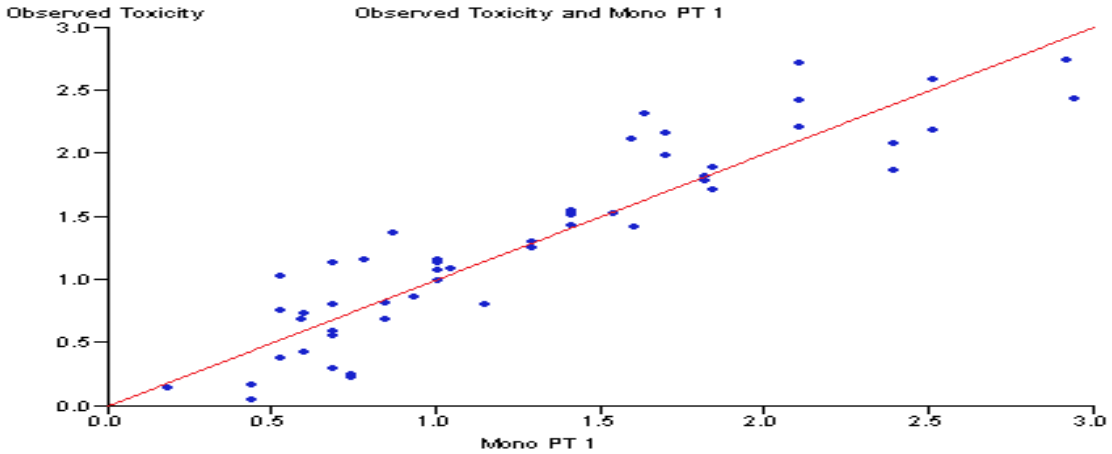

Figure-1

Trend of observed toxicity and predicted toxicity (obtained from ^{Mono}PT1) of the Nitrobenzene derivatives

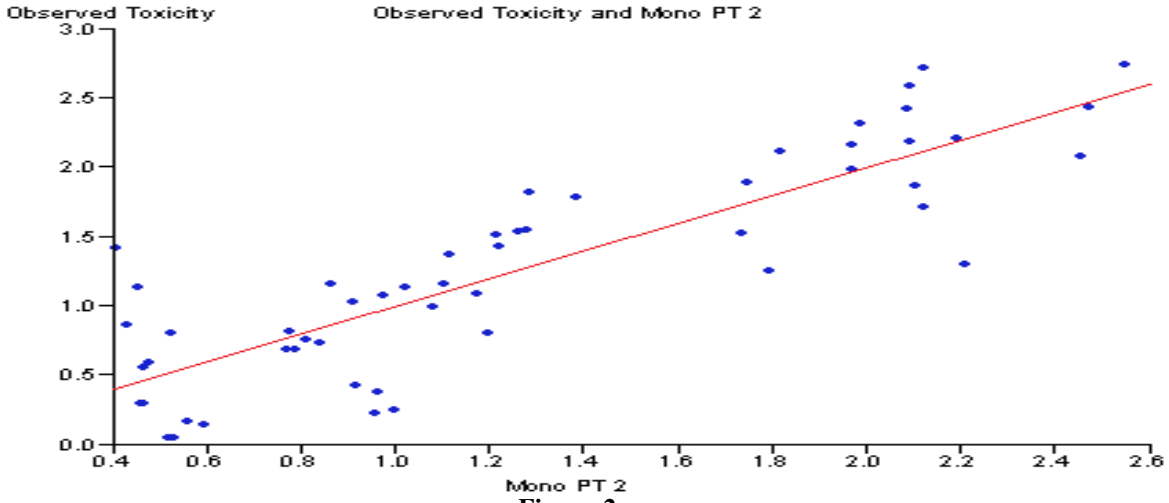

Figure-2

Trend of observed toxicity and predicted toxicity (obtained from ^{Mono}PT2) of the Nitrobenzene derivatives

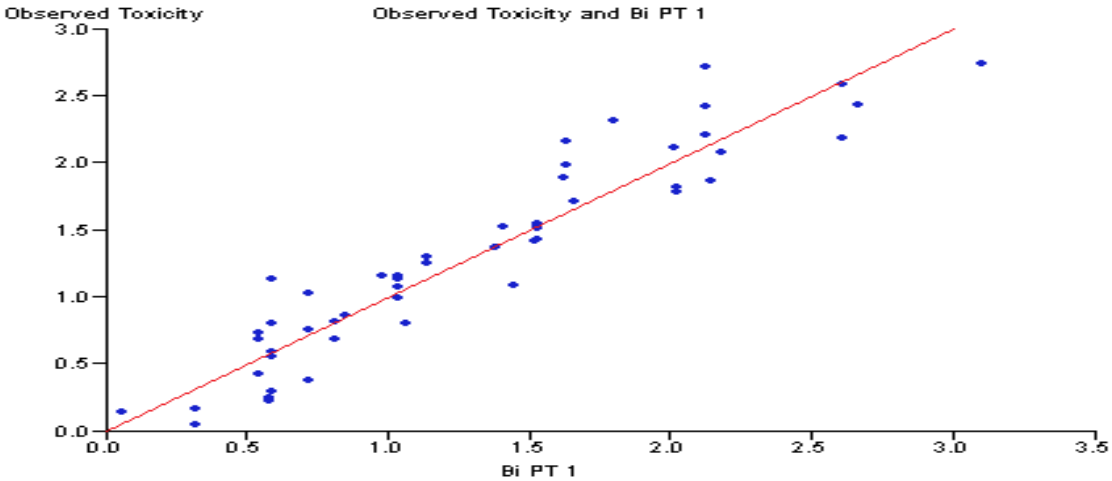

Figure-3

Trend of observed toxicity and predicted toxicity (obtained from ^{Bi}PT1) of the Nitrobenzene derivatives

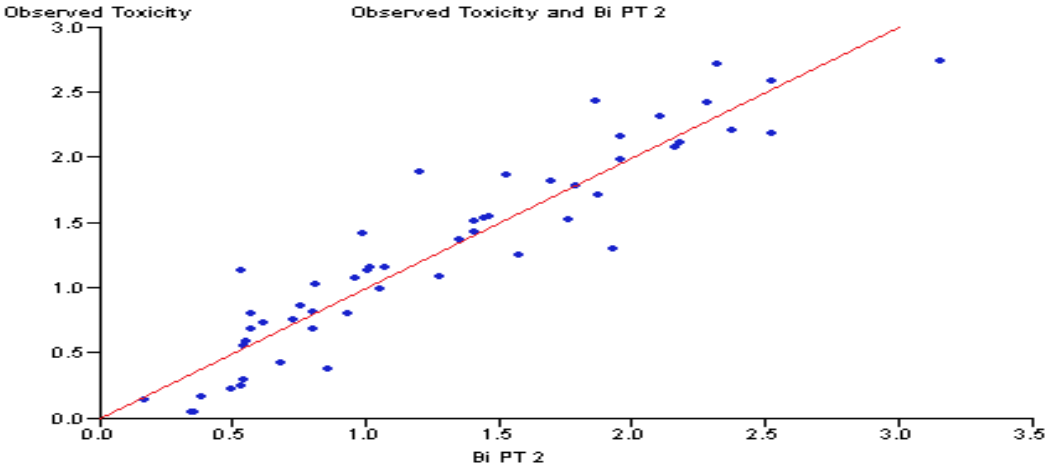

Figure-4

Trend of observed toxicity and predicted toxicity (obtained from ^{Bi}PT2) of the Nitrobenzene derivatives

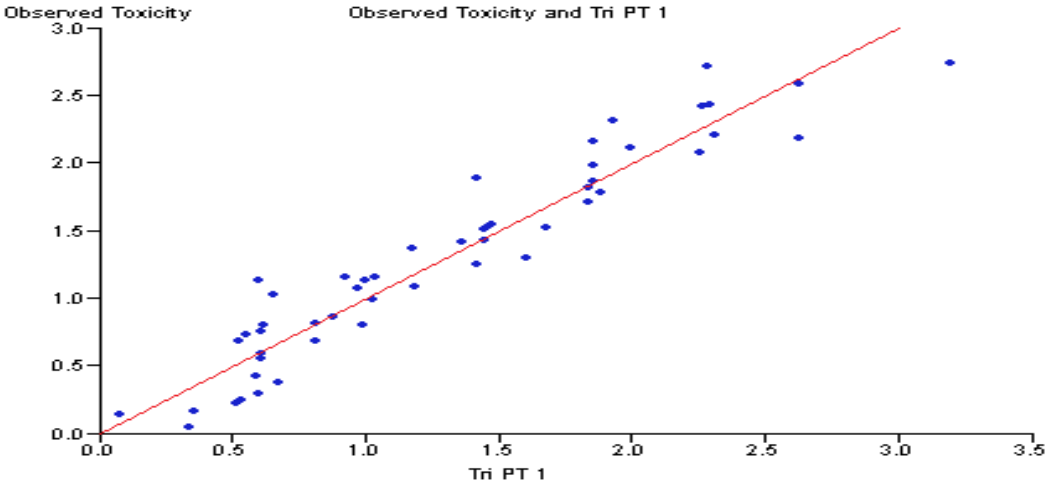

Figure-5

Trend of observed toxicity and predicted toxicity (obtained from ^{Tri}PT1) of the Nitrobenzene derivatives

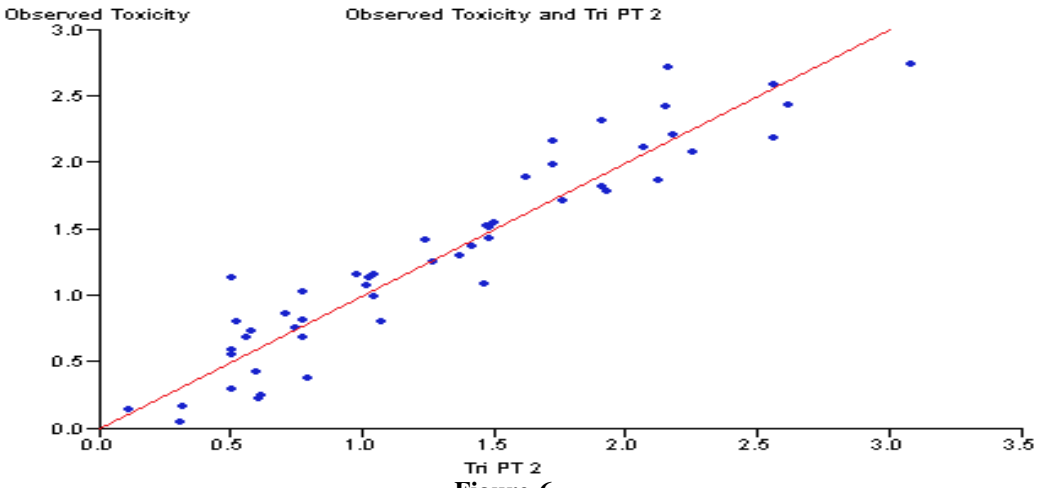

Figure-6

Trend of observed toxicity and predicted toxicity (obtained from ^{Tri}PT2) of the Nitrobenzene derivatives

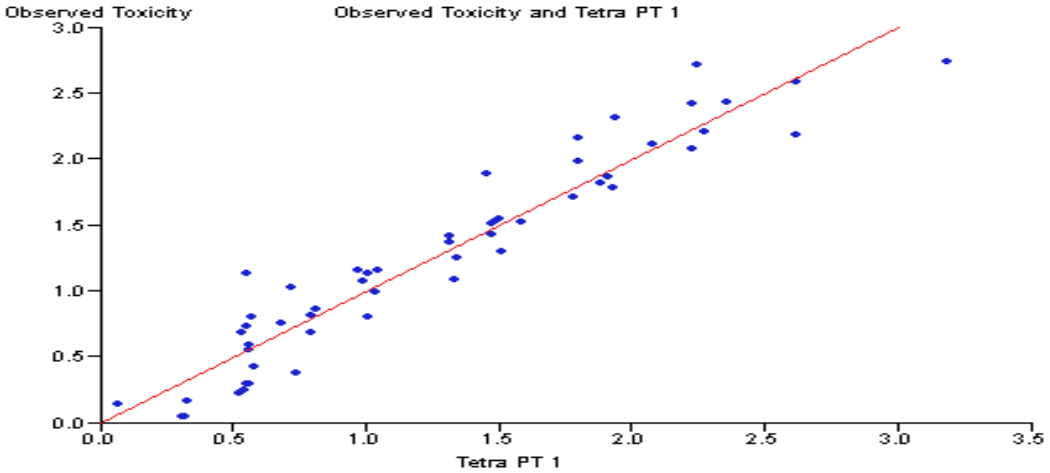

Figure-7

Trend of observed toxicity and predicted toxicity (obtained from ^{Tetra}PT1) of the Nitrobenzene derivatives

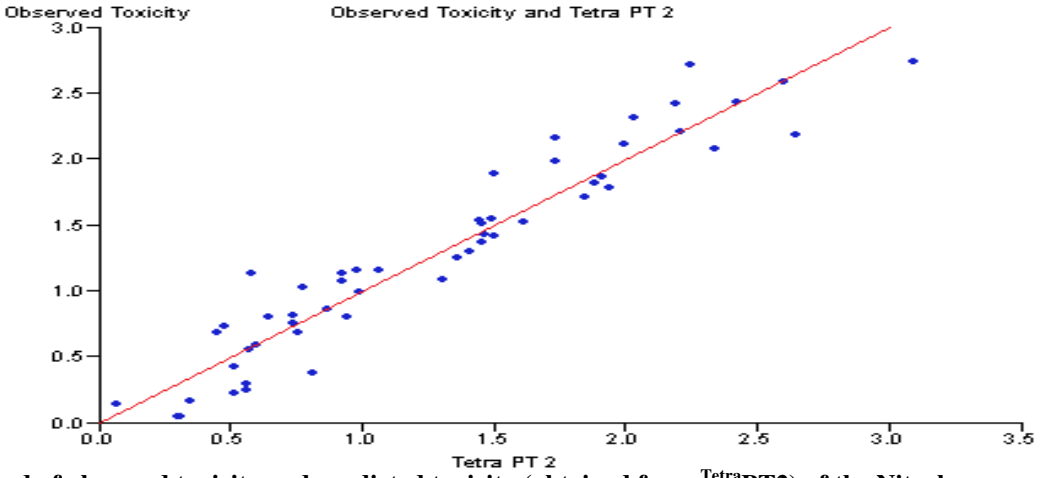

Figure-8: Trend of observed toxicity and predicted toxicity (obtained from ^{Tetra}PT2) of the Nitrobenzene derivatives

Conclusion

It is clear from the above study that, the best combination of Quantum chemical descriptors is molecular weight, molar refractivity, electron affinity and total energy for the QSTR study of nitrobenzene derivatives against *Tetrahymena pyriformis.* Reliable QSTR models have been obtained from single descriptors namely electron affinity and total energy. Therefore, electron affinity and total energy appear good descriptors for QSTR study of nitrobenzene derivatives.

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