Available on line www.jocpr.com

Journal of Chemical and Pharmaceutical Research

ISSN No: 0975-7384
CODEN(USA): JCPRC5

J. Chem. Pharm. Res., 2010, 2(5): 193-205

Quantum chemical and energy descriptors based QSAR study of triazine derivatives

P. P. Singh*, S. B. Sharma, Kalpana Singh

Department of Chemistry, M. L. K. (P. G.) College, Balrampur, U. P., India

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ABSTRACT

QSAR models have been developed to predict the activities in terms of log 1/C for 62 triazine derivatives synthesized by Baker with the help of quantum chemical and energy descriptors viz. heat of formation, steric energy, total energy, HOMO energy, LUMO energy, absolute hardness and electronegativity. Best QSAR has been developed using the descriptors heat of formation, steric energy, total energy and LUMO energy with regression coefficient 0.971913 and cross-validation coefficient 0.788624. Descriptors which are alone capable to produce good QSAR models are heat of formation, steric energy and total energy. QSAR model developed using heat of formation or steric energy or total energy in any combination provides very reliable QSAR model.

Keywords: Heat of formation, Multilinear regression, QSAR, Steric energy, Total energy, PM3, Triazine.

INTRODUCTION

QSAR is a process whereby the structures of a set of compounds are quantified and then compared to the numerical values of a biological activity or a physical property. The challenge here has been to find some numerical code for a molecule or a fragment that is information-rich. This structure information and the measured property or activity are then processed into a mathematical model of relationship. From a quality model it is possible to predict and to design compounds for synthesis and testing that have a good possibility for activity. Techniques such as pattern recognition, [1,2] discriminate analysis, [3] cluster analysis, [2,4] and regression analysis, [5] which have been developed and used heavily out side of chemistry are now beginning to be used by those working with structure- activity relationship. In this paper, the multilinear regression analysis has been applied for QSAR study. The relationship has been worked out between the Log1/C values of a series of compounds and certain quantum chemical and energy

descriptors. The compounds chosen for study are derivatives of triazines and shown in Fig.-1.

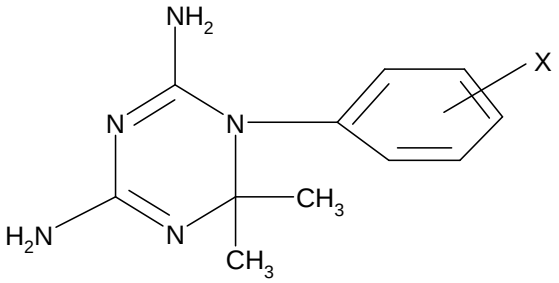


Fig.-1: Compound-1[4,6-diamino-1, 2, dihydro-2, 2,dimethyl-1-1 (x-phenyl)-s-triazines]

Baker and few graduate students [6] synthesized variations of compound-1, a drug now in clinical trials against cancer. Baker's group synthesized 256 variations of compound-1 and studied their inhibiting effect on dihydrofolate reductase isolated from Walker 256 and L1210 leukemia tumors. He did demonstrate vividly that starting at the enzyme level rather than with whole animals constitutes a powerful technique for drug development. This approach has also been brilliantly exploited by Hitching and his group[7,8] in the development of allopurinol for gout and the new antibacterial agent, trimethoprim. Out of 256 compounds synthesized by Baker the QSAR study of 50 compounds has recently been reported [9]. The remaining compounds have been divided into three groups as detailed below.

1- The X substituents of compound-1 have SO_2F at position –3 of the phenyl ring.
2- The X substituents of compounds –1 have SO_2F at position –4 of the phenyl rings.
3- The X substituents of compounds –1 have no -SO_2F.

The work of the paper has been limited to the QSAR study of compounds of serial–1 using quantum chemical and energy descriptors [10-12]. We have used the following quantum chemical and energy descriptors for developing QSAR models-

1.	Heat of Formation	(ΔHf)
2.	Steric Energy	(SE)
3.	Total Energy	(TE)
4.	HOMO Energy	($\in$HOMO)
5.	LUMO Energy	($\in$LUMO)
6.	Absolute Hardness	(η)
7.	Electronegativity	(χ)

EXPERIMENTAL SECTION

Sixty two derivatives of compound-1 have been taken as study material. They are listed in Table-1 along with their biological activity in terms of Log 1/C, where C is molar concentration of inhibitor causing 50% reversible inhibitions of enzyme and defined as

$$\text{Log}(1/C) = -k_1 (\log P)^2 + k_2 (\log P) + k_3 \sigma + k_4 \quad (1)$$

Where

k1, k2, k3, k4 = constants
C = concentration having a standard response in a standard time
P = octanol/water partition coefficient
Log P = pharmacokinetic influence on activity
σ = pharmacodynamic influence on activity

Enzyme dihydrofolate reductase isolated from Leukemia tumor forms covalatent bond with highly reactive derivatives of triazines. The compounds are strongly electrophilic, react through carbonium ion intermediate and form covalent bonds with amino, hydroxyl, carboxyl groups. Consequences are (i) bifunctional agents (ii) DNA-DNA strand and DNA protein cross links.

The values of quantum chemical and energy descriptors [15-18] have been evaluated by solving the equations given below-

Parr et al [19] define the electronegativity as the negative of chemical potential :-

$$\chi = -\mu = -(\partial E/\partial N)_v \quad (2)$$

The absolute hardness η is defined as [20]

$$\eta = 1/2(\delta\mu/\delta N)v_{(r)}$$
$$= 1/2\,(\delta^2 E/\delta^2 N)v_{(r)} \quad (3)$$

where E is the total Energy, N the number of electrons of the chemical species and $v_{(r)}$ the external potential.

The corresponding global softness S, which bears an inverse relationship with the global hardness is defined as-

$$S = 1/2\eta = (\partial N/\partial\mu)v_{(r)} \quad (4)$$

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

$$\eta = (IP-EA)/2 \quad (5)$$
$$S = 1/(IP-EA) \quad (6)$$
$$\chi = -\mu = (IP+EA)/2 \quad (7)$$

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 [20], hence, eqns. 5-7 can be written as

$$\eta = (\varepsilon\,LUMO - \varepsilon\,HOMO)/2 \quad (8)$$
$$S = 1/(\varepsilon\,LUMO - \varepsilon\,HOMO) \quad (9)$$
$$\chi = -(\varepsilon\,LUMO + \varepsilon\,HOMO)/2 \quad (10)$$

The quantum chemical and energy descriptors [21-24] are useful parameters for describing QSAR of a chemical system. A more useful quantity is the heat of formation of the compound and is defined as

$$\Delta H_f = E_{elect} + E_{nuc} - E_{isol} + E_{atom} \quad (11)$$

where E_{elect} is the electronic energy, E_{nuc} is the nuclear-nuclear repulsion energy, E_{isol} is the energy required to strip all the valence electrons of all the atoms in the system and E_{atom} is the total heat of atomization of all the atoms in the system.

Total energy of a molecular system is the sum of the total electronic energy (E_{ee}) and the energy of internuclear repulsion (E_{nr}).

For QSAR prediction, the 3D modeling and geometry optimization of all the derivatives of triazines have been done with the help of CAChe software using the semiempirical PM3 [25] hamiltonian.

Table-1: Log1/C data for reversible inhibition of dihydrofolate reductase by 4,6-diamino-1, 2, dihydro-2, 2,dimethyl-1-1 (x-phenyl)-s-triazines

No.	X	Log 1/C (Observed)
1	3-Cl, 4 -$(CH_2)_4C_6H_3$-2'-Cl, 4'- SO_2F	7.77
2	3-Cl, 4 -$CH_2NHCONH$-C_6H_4-3'-Me, 4'- SO_2F	7.80
3	3-Cl, 4 -O $(CH_2)_2$- NHCONH-C_6H_3-3'-Me, 4'- SO_2F	7.82
4	3 -O $(CH_2)_2OC_6H_4$-4'-SO_2F	7.82
5	3-Cl, 4 -$(CH_2)_4C_6H_3$-4'-Cl, 2'- SO_2F	7.82
6	3-Cl, 4 -$(CH_2)_2C_6H_4$-4'-SO_2F	7.85
7	3-Cl, 4 -$(CH_2)_2$ C_6H_3-5'-Cl, 2'- SO_2F	7.85
8	3-Cl, 4 -$(CH_2)_2$ C_6H_3-3'-Cl, 4'- SO_2F	7.85
9	3-Cl, 4 -$CH_2NHCONH$-C_6H_4-4'-SO_2F	7.92
10	3-Cl, 4 -O $(CH_2)_2$NH-$CONHC_6H_4$-3'-SO_2F	7.92
11	3 -$(CH_2)_4C_6H_3$-5'-Cl, 2'- SO_2F	7.96
12	3-Cl, 4 -$OCH_2C_6H_3$-4'-Cl, 3'- SO_2F	8.00
13	3 -$(CH_2)_4C_6H_3$-2'-Cl, 4'- SO_2F	8.00
14	3-Cl, 4 -$(CH_2)_4C_6H_4$-3'-SO_2F	8.03
15	3-Cl, 4 -$(CH_2)_2$ C_6H_3-4'-Cl, 2'- SO_2F	8.05
16	3-Cl, 4 -O $(CH_2)_3$NH-CONH C_6H_3-4'-Me, 3' -SO_2F	8.06
17	3 -$(CH_2)_4C_6H_4$-4'-SO_2F	8.10
18	3 -$(CH_2)_4C_6H_4$-3'-SO_2F	8.10
19	3 -$(CH_2)_2C_6H_4$-4'-SO_2F	8.10
20	3-Cl, 4 -$(CH_2)_4$ C_6H_3-4'-Cl, 3'-SO_2F	8.11
21	3-Cl, 4 -$(CH_2)_4$ C_6H_4-4'-SO_2F	8.14
22	3-Br, 4-OCH_2CONH- C_6H_4-4' -SO_2F	8.14
23	3-Cl, 4 -$(CH_2)_4C_6H_3$-3'-Cl, 2' -SO_2F	8.20
24	3-Cl, 4 -$(CH_2)_2$ C_6H_3-4'-Cl, 3' -SO_2F	8.27
25	3-Cl, 4 -$(CH_2)_2$ C_6H_3-3'-Cl, 2' -SO_2F	8.30
26	3-Cl, 4 -$(CH_2)_2$ C_6H_3-2'-Cl, 4' -SO_2F	8.33
27	3-$(CH_2)_4$ C_6H_3-4'-Cl, 3' -SO_2F	8.37
28	4 -CH_2CH (Ph-4"-Me)-$CONHC_6H_4$-4'-SO_2F	7.24
29	4 -CH_2CH (Ph-2"-CH_3)-$CONHC_6H_4$-4'-SO_2F	7.24
30	4 -Cl, 3 -O $(CH_2)_2OC_6H_4$-4'-SO_2F	7.27
31	4 –CH (CH_3) CH_2 -$CONHC_6H_4$-4'-SO_2F	7.29

No.	X	Log 1/C (Observed)
32	4 –O $(CH_2)_2$- NHCONH-C_6H_4-3'-SO_2F	7.32
33	4 -CH_2NHCONHC_6H_4-4'-SO_2F	7.35
34	4 -$(CH_2)_2$ C_6H_4-4'-SO_2F	7.41
35	4 -$(CH_2)_2$NHS$O_2C_6H_4$-4'-SO_2F	7.41
36	4 - $(CH_2)_2$- CONHC_6H_3-3'-OMe, 4'-SO_2F	7.46
37	4 -SCH_2 CONHC_6H_4-4'-SO_2F	7.52
38	4 -CH_2CH (Me) CONHC_6H_4-4'-SO_2F	7.55
39	4 -$(CH_2)_2$ CONHC_6H_4-4' -SO_2F	7.60
40	4 -$(CH_2)_2$NH SO_2 C_6H_4-3- SO_2F	7.64
41	4 -$(CH_2)_3$ CONHC_6H_4-4' -SO_2F	7.66
42	4 -$(CH_2)_4$ C_6H_4-4' -SO_2F	7.70
43	4 -CH_2-CONHC_6H_4-4'-SO_2F	7.70
44	4 -OCH_2CONHC_6H_4-4'-SO_2F	7.72
45	4 -CH_2NHCONHC_6H_3-3'-Me, 4'-SO_2F	7.72
46	4 -$(CH_2)_2$CONHC_6H_4-3'- SO_2F	7.74
47	4 -O $(CH_2)_2$OC_6H_4-4'-SO_2F	7.80
48	4 -$(CH_2)_3$CONHC_6H_4-2'- SO_2F	7.80
49	4 -$(CH_2)_2$CONHC_6H_3-3'-Me, 4'-SO_2F	7.89
50	4 -$(CH_2)_3$CONHC_6H_4-3'- SO_2F	7.92
51	4 -$(CH_2)_4C_6H_3$-2'-Cl, 4'-SO_2F	7.96
52	4 -OCH_2CONHC_6H_4-3' -SO_2F	8.00
53	4 -$(CH_2)_2$CONHC_6H_3-4'-Me, 3' -SO_2F	8.02
54	4 -CH_2NHCONHC_6H_4-3' -SO_2F	8.04
55	4 -$(CH_2)_2$CON(Me)- C_6H_4-4' -SO_2F	8.04
56	4 -CH_2CONHC_6H_4-3' -SO_2F	8.06
57	4 -$(CH_2)_2$CONHC_6H_3-6'-Me, 3' -SO_2F	8.08
58	4 -$(CH_2)_2$ NHCOC_6H_4-4'-SO_2F	8.11
59	3-Cl, 4 -$(CH_2)_4$ C_6H_3-4'-Cl, 3'-SO_2F	8.11
60	4 -$(CH_2)_4$OC_6H_4-4'-SO_2F	8.14
61	4 -$(CH_2)_2$CONHC_6H_3-2'-Me, 4' -SO_2F	8.24
62	4 -$(CH_2)_2$CONHC_6H_3-4'-OMe, 3' -SO_2F	8.24

RESULTS AND DISCUSSION

Values of the descriptors of the triazine derivatives have been calculated using PM3 method and are given in Table-2. With the help of these values of descriptors, ninety QSAR models have been developed using MLR analysis in different combinations of descriptors. Best five QSAR models are listed below-

Table-2: Values of descriptors used in QSAR models of triazine derivatives

Compound	Heat of Formation (kcal/mole)	Steric Energy (kcal/mole)	Total Energy (Hartree)	HOMO Energy (eV)	LUMO Energy (eV)	Absolute Hardness	Electronegativity	Activity
1	-87.544	-45.475	-255.231	-8.828	-1.008	3.849	4.961	7.770
2	-86.982	-45.021	-249.669	-8.891	-1.012	3.995	4.919	7.800
3	-87.735	-44.718	-246.812	-8.801	-1.011	3.870	4.886	7.820
4	-86.731	-44.718	-249.387	-8.882	-1.012	3.937	4.871	7.820

Compound	Heat of Formation (kcal/mole)	Energy Steric (kcal/mole)	Energy Total (Hartree)	HOMO Energy (eV)	LUMO Energy (eV)	Absolute Hardness	Electronegativity	Activity
5	-86.996	-45.211	-247.131	-8.898	-1.061	3.856	4.904	7.820
6	-86.259	-44.263	-248.964	-8.792	-1.004	3.923	4.886	7.850
7	-86.952	-44.263	-246.713	-8.791	-1.004	3.828	4.904	7.850
8	-86.250	-44.263	-245.123	-8.799	-1.091	3.862	4.947	7.850
9	-86.897	-45.234	-247.977	-8.795	-1.002	3.960	4.971	7.920
10	-85.992	-43.203	-247.977	-8.795	-1.002	3.935	4.879	7.920
11	-84.475	-42.597	-247.413	-8.793	-1.000	3.812	4.880	7.960
12	-84.835	-43.671	-246.848	-8.799	-0.998	3.750	4.974	8.000
13	-83.839	-41.991	-247.123	-8.789	-0.998	3.802	4.935	8.000
14	-83.349	-41.537	-246.425	-8.782	-0.997	3.956	4.848	8.030
15	-83.993	-41.234	-248.333	-8.781	-0.996	3.784	4.936	8.050
16	-84.868	-41.082	-247.985	-8.787	-0.991	4.022	4.812	8.060
17	-82.923	-41.912	-241.234	-8.781	-0.994	3.902	4.861	8.100
18	-83.456	-40.476	-241.345	-8.711	-0.994	3.894	4.822	8.100
19	-82.215	-42.772	-245.438	-8.785	-0.991	3.913	4.904	8.100
20	-82.054	-40.325	-248.112	-8.712	-0.994	3.886	4.899	8.110
21	-81.579	-39.871	-244.874	-8.783	-0.999	3.946	4.881	8.140
22	-81.570	-39.871	-244.874	-8.783	-0.993	3.928	4.944	8.140
23	-81.762	-38.962	-244.028	-8.780	-0.990	3.864	4.875	8.200
24	-79.471	-35.354	-243.041	-8.776	-0.981	3.875	4.949	8.270
25	-78.980	-37.447	-248.114	-8.774	-0.986	3.835	4.895	8.300
26	-78.589	-36.993	-242.194	-8.772	-0.981	3.842	5.010	8.330
27	-78.561	-38.332	-248.134	-8.770	-0.984	3.852	4.890	8.370
28	-99.452	-53.503	-257.567	-8.833	-1.029	3.976	4.907	7.240
29	-96.987	-53.503	-257.567	-8.839	-1.029	3.979	4.914	7.240
30	-97.678	-53.048	-257.144	-8.832	-1.027	4.002	4.899	7.270
31	-95.291	-54.876	-256.862	-8.832	-1.027	3.902	4.926	7.290
32	-94.012	-52.291	-258.345	-8.829	-1.025	3.904	4.814	7.320
33	-90.654	-51.837	-256.016	-8.827	-1.024	3.941	4.942	7.350
34	-93.354	-53.765	-255.169	-8.822	-1.022	3.899	4.900	7.410
35	-93.354	-50.928	-255.169	-8.822	-1.022	3.547	5.244	7.410
36	-92.006	-50.170	-254.464	-8.821	-1.029	3.995	4.836	7.460
37	-91.961	-49.262	-253.618	-8.812	-1.017	3.868	4.979	7.520
38	-91.094	-48.807	-250.334	-8.816	-1.016	3.927	4.898	7.550
39	-90.287	-48.050	-252.490	-8.800	-1.019	3.891	4.934	7.600
40	-89.641	-47.444	-254.781	-8.811	-1.013	3.570	5.049	7.640
41	-89.318	-47.141	-251.644	-8.819	-1.019	3.861	4.878	7.660
42	-88.672	-46.535	-251.991	-8.877	-1.010	3.903	4.851	7.700
43	-88.672	-44.654	-251.079	-8.802	-1.010	3.993	4.947	7.700
44	-88.997	-42.854	-250.790	-8.822	-1.010	3.898	4.938	7.720
45	-88.350	-46.232	-250.797	-8.844	-1.010	3.964	4.911	7.720
46	-88.027	-45.929	-250.515	-8.805	-1.009	3.960	4.835	7.740
47	-87.058	-45.021	-249.669	-8.802	-1.006	3.924	4.864	7.800
48	-88.913	-40.567	-245.234	-8.802	-1.099	3.872	4.804	7.800
49	-85.605	-43.657	-248.400	-8.797	-1.009	3.917	4.891	7.890
50	-85.121	-43.203	-247.977	-8.795	-1.009	3.965	4.834	7.920

Compound	Heat of Formation (kcal/mole)	Energy Steric (kcal/mole)	Energy Total (Hartree)	HOMO Energy (eV)	LUMO Energy (eV)	Absolute Hardness	Electronegativity	Activity
51	-80.876	-42.597	-247.413	-8.791	-1.009	3.799	4.934	7.960
52	-86.863	-41.991	-246.848	-8.791	-0.990	3.937	4.859	8.000
53	-83.500	-45.688	-246.566	-8.790	-0.991	3.980	4.811	8.020
54	-83.184	-41.385	-248.231	-8.789	-0.997	4.007	4.851	8.040
55	-86.561	-46.456	-246.284	-8.789	-0.997	3.975	4.869	8.040
56	-82.866	-41.082	-246.991	-8.787	-0.996	3.999	4.859	8.060
57	-82.530	-44.885	-245.720	-8.781	-0.995	3.906	4.870	8.080
58	-80.543	-40.325	-245.991	-8.785	-0.994	3.729	5.045	8.110
59	-82.051	-40.325	-245.297	-8.733	-0.994	3.967	4.798	8.110
60	-81.578	-39.871	-244.874	-8.712	-0.993	3.961	4.798	8.140
61	-78.831	-36.567	-246.345	-8.712	-0.989	3.900	4.918	8.240
62	-79.013	-38.356	-243.464	-8.771	-0.981	3.934	4.814	8.240

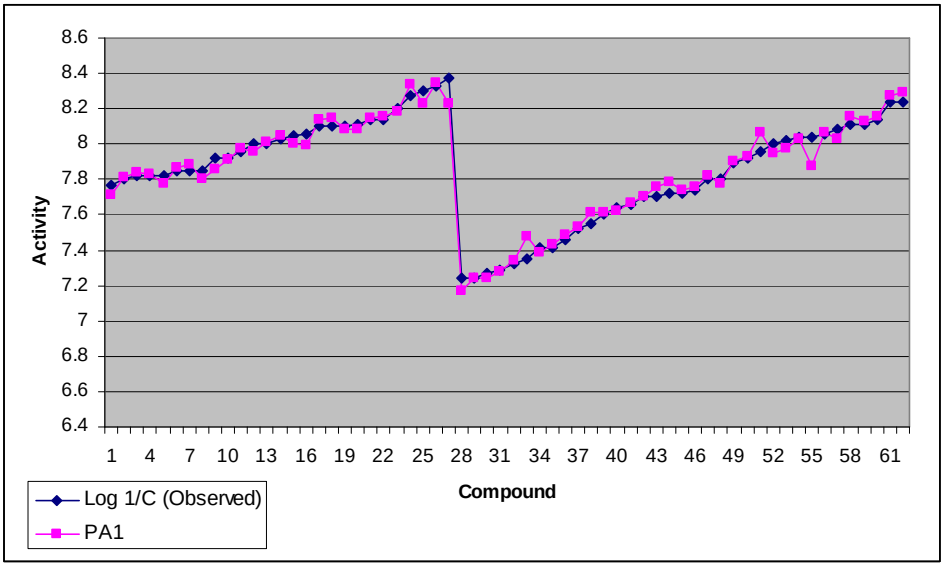
First QSAR model

This is the best QSAR model and has been developed using heat of formation, steric energy, total energy and LUMO energy. MLR equation is given by-

PA1=0.0282435*ΔHf+0.0171513*SE+0.0151976*TE+1.41916*∈LUMO+16.2739
rCV^2=0.788624
r^2=0.971913

Value of regression coefficient is 0.971913 and cross-validation coefficient is 0.788624 which indicate the ability of predictive power of this QSAR model. QSAR model PA1 can efficiently be used for the prediction of activity of any derivative of compound-1. Predicted activities PA1 of triazine derivatives are given in Table-3. Graph between observed and predicted activities PA1 is shown in Graph-1 which clearly illustrates the high predictive power of the QSAR model.

Graph-1: Graph between observed activities in terms of log 1/C and predicted activities calculated by QSAR model PA1



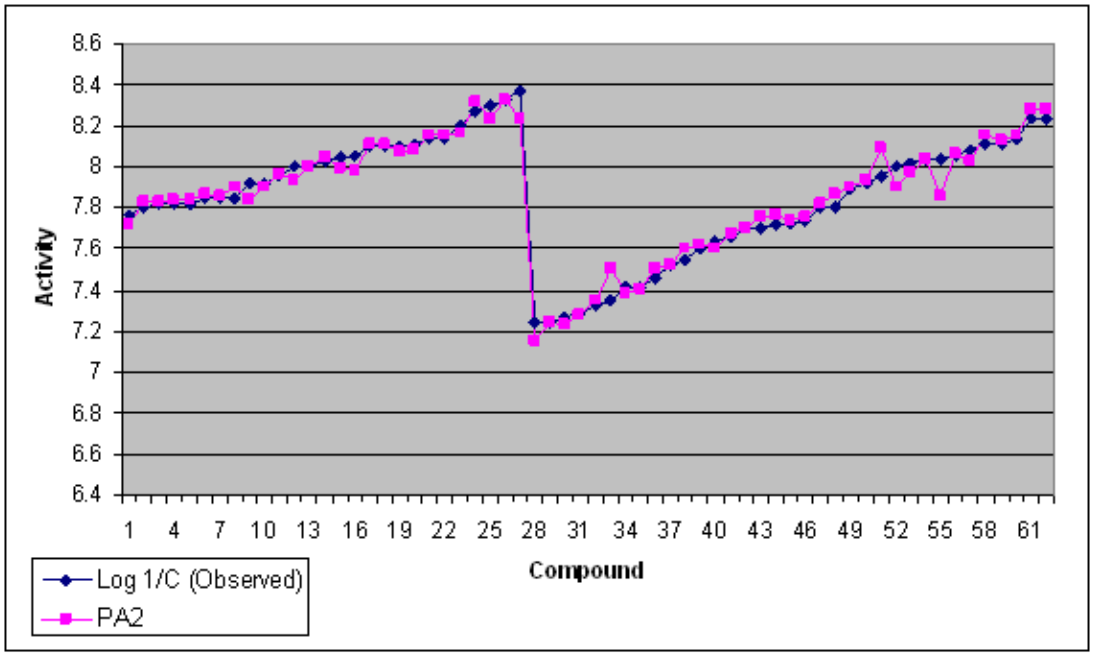
Second QSAR model

Second best QSAR model PA2 has been developed using heat of formation, steric energy, total energy and absolute hardness as the descriptors. MLR equation is as under-

PA2=0.0358547*ΔHf+0.0158545*SE+0.0116698*TE+0.076711*η+14.2656
rCV^2=0.94973
r^2=0.965889

Values of regression and cross-validation coefficients indicate its good predictive power. Graph between observed and predicted activities PA2 is shown in Graph-2.

Graph-2: Graph between observed activities in terms of log 1/C and predicted activities calculated by QSAR model PA2



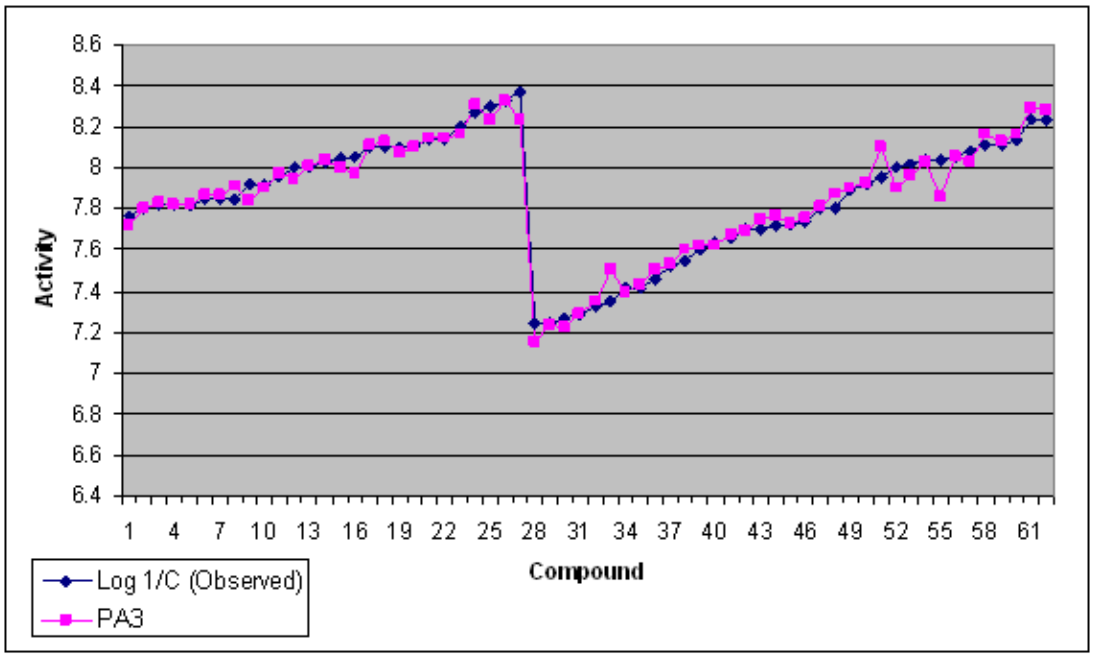
Third QSAR model

MLR equation of this QSAR model PA3 is given by-

PA3=0.0349129*ΔHf+0.0153468*SE+0.0119722*TE+0.225111*∈HOMO+16.5168
rCV^2=0.954087
r^2=0.965857

Descriptors used in this QSAR model are heat of formation, steric energy, total energy and HOMO energy. Value of regression coefficient is above 0.95 which indicates good predictive power of QSAR model. Graph between observed and predicted activities PA3 is shown in Graph-3 which clearly illustrates the good predictive power of the QSAR model.

Graph-3: Graph between observed activities in terms of log 1/C and predicted activities calculated by QSAR model PA3



Fourth QSAR model

This QSAR model has been developed using heat of formation, steric energy, total energy and electronegativity. Value of regression coefficient is 0.965739; hence, the predictive power is very reliable. MLR equation is given by-

PA4=0.0356873*ΔHf+0.0157999*SE+0.0115728*TE-0.0835273*χ+14.9329
rCV^2=0.951124
r^2=0.965739

Fifth QSAR model

This QSAR model is given by PA5 and has heat of formation, steric energy and total energy as the descriptors. MLR equation is as under-

PA5=0.0354168*ΔHf +0.0158098*SE+0.0121804*TE+14.6519
rCV^2=0.953071
r^2=0.965359

Value of regression coefficient indicates that the predictive power of the QSAR model is very reliable.

QSAR model developed using single descriptor

QSAR models developed using single descriptor viz. heat of formation, steric energy and total energy are also reliable. Good QSAR models obtained by using single descriptor are discussed below-

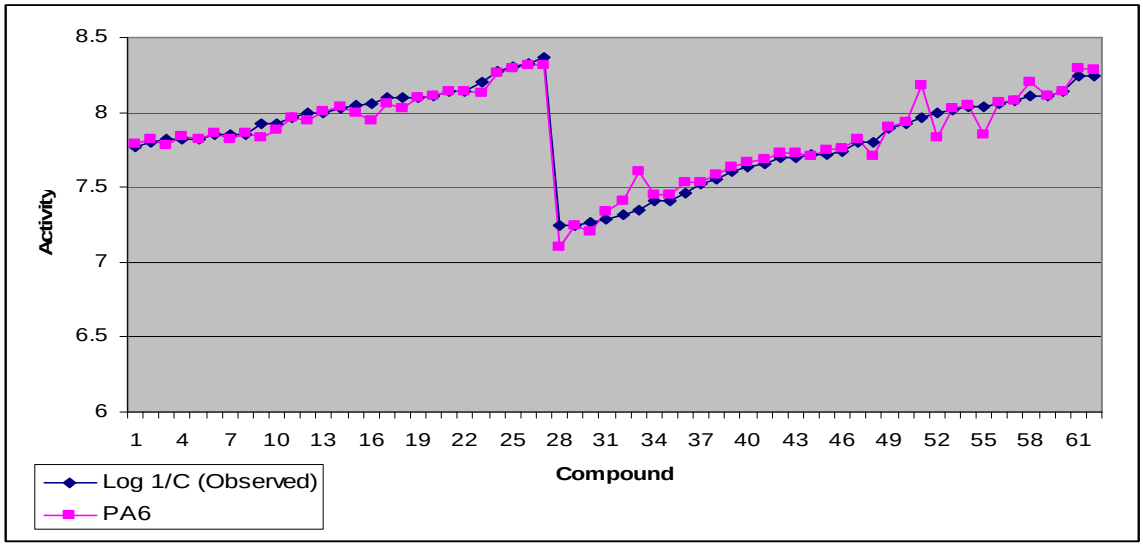
QSAR model developed using heat of formation

This QSAR model has 0.942564 regression coefficient and 0.940848 cross-validation coefficient. MLR equation is given by-
PA6=0.0582874*ΔHf+12.8932
rCV^2=0.940848

r^2=0.942564

Graph-4 represents the predicted activities PA6 and observed activities which indicates that the QSAR model PA6 obtained by heat of formation is sufficient to predict the activity of any triazine derivative.

Graph-4: Graph between observed activities in terms of log 1/C and predicted activities calculated by QSAR model PA6



QSAR model developed using steric energy

QSAR model developed using steric energy as descriptor has 0.89943 regression coefficient and 0.891342 cross-validation coefficient as indicated by its MLR equation-

PA7=0.0604619*SE+10.5412
rCV^2=0.891342
r^2=0.89943

Evidently, the activity of any triazine derivative can be predicted by this QSAR model.

QSAR model developed using total energy

Total energy alone form the reliable QSAR model whose MLR equation is as follows-

PA8=0.0615215*TE+23.1787
rCV^2=0.783133
r^2=0.79526

Values of activities of triazine derivatives have been calculated by substituting the values of descriptors in MLR equations PA1-PA8 and given in Table-3.

Table-3: Values of predicted activities PA1-PA8 of triazine derivatives

Comp.	PA1	PA2	PA3	PA4	PA5	PA6	PA7	PA8
1	7.713	7.722	7.720	7.722	7.724	7.790	7.792	7.476
2	7.814	7.826	7.799	7.817	7.818	7.823	7.819	7.819
3	7.843	7.828	7.831	7.831	7.831	7.779	7.837	7.994
4	7.831	7.839	7.817	7.838	7.836	7.838	7.837	7.836
5	7.780	7.841	7.824	7.844	7.846	7.822	7.808	7.975
6	7.870	7.867	7.866	7.866	7.865	7.865	7.865	7.862
7	7.884	7.861	7.869	7.866	7.867	7.825	7.865	8.001
8	7.805	7.907	7.911	7.906	7.912	7.866	7.865	8.098
9	7.854	7.843	7.840	7.832	7.839	7.828	7.806	7.923
10	7.914	7.905	7.903	7.904	7.903	7.881	7.929	7.923
11	7.978	7.967	7.972	7.974	7.973	7.969	7.966	7.957
12	7.961	7.938	7.949	7.943	7.950	7.948	7.901	7.992
13	8.013	8.002	8.008	8.005	8.009	8.006	8.002	7.975
14	8.047	8.046	8.042	8.045	8.042	8.035	8.030	8.018
15	8.006	7.993	8.002	7.998	8.000	7.997	8.048	7.901
16	7.997	7.986	7.976	7.983	7.976	7.946	8.057	7.922
17	8.136	8.112	8.114	8.114	8.114	8.060	8.007	8.338
18	8.144	8.114	8.132	8.119	8.117	8.029	8.094	8.331
19	8.082	8.076	8.074	8.073	8.074	8.101	7.955	8.079
20	8.084	8.087	8.102	8.087	8.086	8.110	8.103	7.914
21	8.147	8.153	8.148	8.150	8.150	8.138	8.131	8.114
22	8.156	8.152	8.148	8.145	8.150	8.139	8.131	8.114
23	8.182	8.165	8.166	8.168	8.168	8.127	8.185	8.166
24	8.337	8.317	8.314	8.312	8.318	8.261	8.404	8.226
25	8.230	8.239	8.239	8.242	8.240	8.290	8.277	7.914
26	8.347	8.330	8.331	8.322	8.334	8.312	8.305	8.279
27	8.231	8.241	8.241	8.244	8.241	8.314	8.224	7.913
28	7.173	7.151	7.151	7.148	7.146	7.096	7.306	7.333
29	7.243	7.239	7.236	7.235	7.234	7.240	7.306	7.333
30	7.239	7.229	7.226	7.224	7.222	7.200	7.334	7.359
31	7.281	7.281	7.284	7.281	7.281	7.339	7.223	7.376
32	7.340	7.350	7.352	7.360	7.349	7.413	7.380	7.285
33	7.480	7.508	7.504	7.503	7.503	7.609	7.407	7.428
34	7.387	7.387	7.392	7.390	7.387	7.452	7.290	7.480
35	7.436	7.405	7.435	7.406	7.432	7.452	7.462	7.480
36	7.487	7.508	7.502	7.508	7.501	7.530	7.508	7.524
37	7.533	7.524	7.530	7.522	7.527	7.533	7.563	7.576
38	7.617	7.606	7.606	7.605	7.605	7.584	7.590	7.778
39	7.616	7.619	7.623	7.617	7.619	7.631	7.636	7.645
40	7.619	7.600	7.625	7.614	7.624	7.668	7.673	7.504
41	7.672	7.675	7.677	7.681	7.678	7.687	7.691	7.697
42	7.708	7.707	7.692	7.712	7.706	7.725	7.728	7.676
43	7.754	7.755	7.748	7.744	7.747	7.725	7.841	7.732
44	7.781	7.768	7.764	7.765	7.768	7.706	7.950	7.750
45	7.741	7.742	7.729	7.737	7.737	7.744	7.746	7.749
46	7.761	7.762	7.757	7.763	7.757	7.762	7.764	7.767
47	7.820	7.818	7.816	7.819	7.816	7.819	7.819	7.819
48	7.780	7.870	7.873	7.880	7.874	7.711	8.088	8.092
49	7.900	7.906	7.904	7.905	7.904	7.903	7.902	7.897
50	7.928	7.939	7.933	7.939	7.934	7.932	7.929	7.923
51	8.067	8.095	8.098	8.098	8.100	8.179	7.966	7.957
52	7.944	7.907	7.906	7.907	7.905	7.830	8.002	7.992
53	7.978	7.975	7.970	7.976	7.969	8.026	7.779	8.010
54	8.028	8.037	8.027	8.032	8.028	8.045	8.039	7.907

Comp.	PA1	PA2	PA3	PA4	PA5	PA6	PA7	PA8
55	7.875	7.856	7.855	7.853	7.852	7.848	7.732	8.027
56	8.062	8.068	8.058	8.062	8.059	8.063	8.057	7.983
57	8.027	8.027	8.028	8.028	8.026	8.083	7.827	8.062
58	8.158	8.154	8.163	8.153	8.165	8.199	8.103	8.045
59	8.126	8.126	8.131	8.128	8.121	8.111	8.103	8.088
60	8.156	8.155	8.164	8.157	8.150	8.138	8.131	8.114
61	8.273	8.284	8.293	8.280	8.281	8.298	8.330	8.023
62	8.292	8.285	8.280	8.287	8.282	8.288	8.222	8.200

CONCLUSION

Best descriptor of activity of triazine derivative is the combination of heat of formation, steric energy, total energy and LUMO energy with regression coefficient 0.971913 and cross-validation coefficient 0.788624. Any combination of descriptors, in which either heat of formation or steric energy or total energy is present, gives very good QSAR model.

Heat of formation provides the reliable QSAR model with 0.942564 regression coefficient and 0.940848 cross-validation coefficient. Steric energy and total energy both are also capable to produce reliable QSAR models separately. Reliability of QSAR models developed using single descriptor is in the following order-
Heat of formation > Steric energy > Total energy

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