

Quantitative Structure-Activity Relationship (QSAR) Study of New Fluorovinyloxyacetamides

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Quantitative Structure-Activity Relationship (QSAR) have been established of 57 fluorovinyloxyacetamides compounds to correlate and predict EC₅₀ values. Genetic algorithm (GA) and multiple linear regression analysis were used to select the descriptors and to generate the equations that relate the structural features to the biological activities. This equation consists of three descriptors calculated from the molecular structures with molecular mechanics and quantum-chemical methods. The results of MLR and GA show that dipole moment of z-axis, radius of gyration and logP play an important role in growth inhibition of barnyard grass.

Keywords : QSAR, Genetic algorithm (GA), Fluorovinyloxyacetamides

Introduction

Oxyacetamide has been developed as a herbicide, which shows good herbicidal activity for annual weeds through inhibition of cell division and amino acid biosynthesis.¹ Especially, the excellent selectivity between crop (rice) and weeds (barnyard grass), an important weed in paddy fields, is a merit of oxyacetamide herbicide.² To exploit a new and highly active herbicide, fluorovinyloxyacetamides, which was introduced fluorovinyl group into oxyacetamide, were synthesized and evaluated their herbicidal activities. In this research, we tried to describe the synthetic method and QSAR study of fluorovinyloxyacetamides.

Synthesis of fluorovinyloxyacetamides³⁻⁵ is as follows (Figure 1). The chloroacetamides (**e**) were prepared from the substitution reaction of amines (**g**) with chloroacetyl chloride (**f**) using sodium hydroxide as a base in THF. The reaction of (**e**) with sodium acetate in DMF gave acetates (**d**) in high yields. The hydroxyacetamides (**b**) were obtained from base catalyzed hydrolysis of (**d**). On the other hand, the vinyl fluorides (**c**) were provided by the Wittig reaction of trifluoromethyl ketones (**h**) with dibromodifluoromethane, triphenylphosphine in THF. Finally, addition-elimination reaction of (**b**) with (**c**) in the basic condition gave the fluorovinyloxyacetamides (**a**). The structures of new fluorovinyloxyacetamides (**a**) are summarized in Table I.

Quantitative Structure-Activity Relationship (QSAR)⁶⁻¹¹ is a powerful method for the design of bioactive compounds and the prediction of corresponding activity with physical and chemical properties. Usually there are two major approaches to analyze QSAR data : i) the property (or activity) of a series of compounds is expressed as a multiple linear regression of descriptors, and ii) the non-linear regression method represents the property (or activity) with artificial neural network (ANN).^{12,13} ANN is an information-processing paradigm inspired by the densely interconnected, parallel structure of the mammalian brain processes information.

This study was based on a Genetic Function Approxima-

tion (GFA) algorithm.^{14,15} GFA can not only automatically select the optimum number of descriptors in regression analysis but also construct Multiple Linear Regression (MLR) models through the use of linear, higher order polynomials, splines and gaussians. The GFA algorithm method was used to select the optimum number of descriptors for use in regression analysis. The GFA algorithm could be a useful technique for searching the large probability space with a large number of descriptors for a small number of molecules.

The purpose of this research was to determine predictive QSAR models¹⁶⁻¹⁹ by analysis of training set containing 57 molecules. If the models are reasonable, it is possible to predict biological activity of non-tested molecules. Finally, the successful models of QSAR certainly decrease the number of compounds to be synthesized, by making it possible to select the most promising compounds.

Methods

Experimental; Chemicals. 1-Piperidino-2-[(*E*)-1,3,3,3-tetrafluoro-2-(3-methylphenyl)-1-propenyloxy]-1-ethanone (compound 1): A solution of 286 mg (2 mmol) of *N*-2-hydroxyacetyl piperidine in 10 mL THF was added to 444 mg (2 mmol) of 1,1,3,3,3-pentafluoro-2-(3-methylphenyl)-1-propene at room temperature. The reaction mixture was treated with 0.2 mL of 10 M-NaOH solution and stirred for 30 min. The mixture was washed with 10 mL of water and extracted with ethyl acetate. The extract was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The 310 mg (90%) of compound 1 (an *E* and *Z* isomeric mixtures on silica gel) was extracted with mixture of solvents (ethyl acetate/*n*-hexane = 1 : 2). The separation of geometrical isomers by silica gel chromatography (ethyl acetate/*n*-hexane = 1 : 4) was provided by 230 mg of *E*-isomer. oil; ¹H-NMR (300 MHz, CDCl₃, TMS) δ: 7.31-7.04 (m, 4H), 4.78 (*E*) 4.66 (*Z*) (s, 2H), 3.64-3.03 (m, 4H), 2.37 (s, 3H), 1.74-1.38 (m, 6H); ¹⁹F-NMR (200 MHz, CDCl₃, CFCl₃) δ:

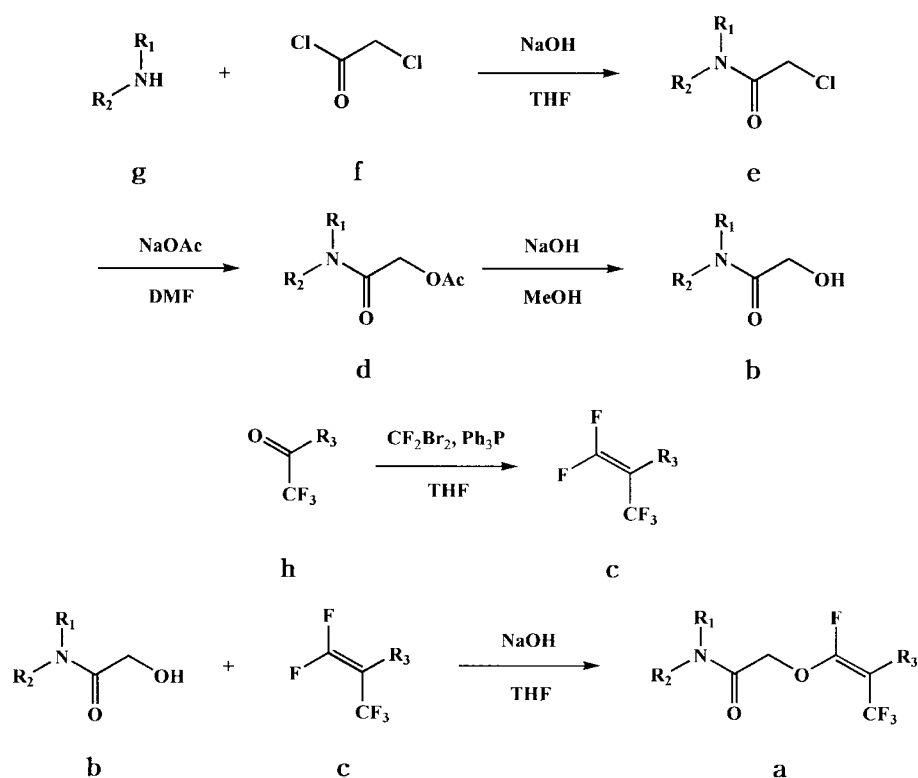


Figure 1. Synthesis of fluorovinyl oxyacetamides.

-57.83 (d, 3F), -82.24 (q, 1F): MS m/z (rel. int.) 345 (26), 126 (71), 98 (70), 84 (100).

The other compounds (2 to 57) were obtained about 70 to 90% yields from the same reaction condition using corresponding hydroxyacetamides (b) and vinyl fluorides (c).

Computations; Data Construction. A series of 57 fluorovinyl oxyacetamides derivatives was used in this work (Table 1). These molecules consisted of mixture of *E* and *Z* isomer, but the energy of all molecules was minimized at *E* isomer configuration. A grid search procedure was performed with core structure ($R_1=\text{CH}_3$, $R_2=\text{phenyl}$, $R_3=\text{phenyl}$) to identify their lowest energy conformation. The conformational energy of each conformer was generated by increasing the torsional angle ψ_1 and ψ_2 by 30 degrees. Geometry optimization was performed to obtain fixed core structure using the results of this conformational search (the minimum energy conformations have 30-130° angle range of ψ_1 and 150-200° angle range of ψ_2) by *ab initio* calculation with 4-31G basis set of Gaussian 94 program (see Figure 2).²⁰ After geometry optimization, functional groups were added to the core structure and the full geometry optimization was performed by Merck Molecular Force Field (MMFF)^{21,22} method. After minimization, all molecules were aligned in the orientation that they were assumed to bind to the putative receptor. The method for performing the alignment was Maximum Common Sub Group (MCSG).^{23,24} The MCSG was carried out rigid fit to superimpose each structure to overlays the shape reference compound (compound 45).

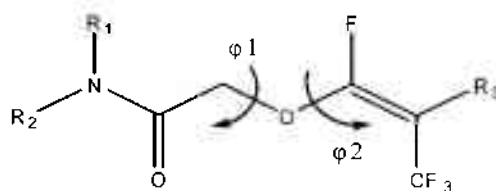
The activity was expressed in terms of 50%-growth-inhibition concentration (EC_{50}) of barnyard grass. The EC_{50} val-

ues were estimated by fitting data to sigmoidal type function (1) because the experiments were performed in a range of concentration (1.000, 0.2500, 0.0625, 0.0156, 0.0040 kg/ha) and activities were represented by 10 percent unit. In the equation (1), the initial and final value were fixed. Activities were demonstrated to 100 percent, and other variables were changed to fit. The concentration and EC_{50} value were converted by -log function to fit scale.

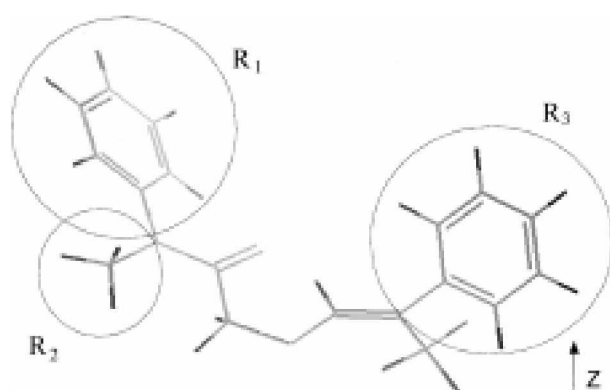
$$y = \frac{A_1 - A_2}{1 + e^{(x - x_0)/dx}} + A_2 \quad (1)$$

(A_1 : initial value = 0, A_2 : final value = 100, x_0 : center, dx : time const.)

Selection of the Descriptors and the Activity Description. It is necessary to construct a numerical descriptors of a set of molecule in order to build QSAR models. A descriptor can be a quantitative property that depends on the structure of molecule. In this study, all 118 descriptors such as topological, spatial, electronic, quantum mechanical, and thermodynamic descriptors were calculated by Cerius2²⁵ program. Genetic Function Approximation (GFA) technique was utilized to select descriptors and to generate different QSAR models from various descriptors. GFA technique began with a population of 100 random models and 10000 iterations to evolution. The descriptors were selected by a few steps using GFA method: i) 118 descriptors were divided by four or five groups which were randomly selected, ii) GFA allowed the selection of some descriptor that is frequently used from each group of descriptors. Repeating this step,

Table 1. Structures of Fluorovinylloxyacetamides in Training Set

No.	R ₁	R ₂	R ₃	No.	R ₁	R ₂	R ₃
1	-(CH ₂) ₅ -		3-CH ₃ -C ₆ H ₄	31	4-CH ₃ O-C ₆ H ₄	C ₂ H ₅	C ₆ H ₅
2	-(CH ₂) ₅ -		4-C ₂ H ₅ -C ₆ H ₄	32	3-CF ₃ -C ₆ H ₄	C ₂ H ₅	4-CH ₃ -C ₆ H ₄
3	-(CH ₂) ₅ -		3,5-Cl ₂ -C ₆ H ₃	33	4-Cl-C ₆ H ₄	C ₂ H ₅	4-CH ₃ -C ₆ H ₄
4	-CH(CH ₃)(CH ₂) ₄ -		4-CH ₃ -C ₆ H ₄	34	4-CH ₃ O-C ₆ H ₄	<i>n</i> -C ₃ H ₇	4-CH ₃ -C ₆ H ₄
5	-CH(C ₂ H ₅)(CH ₂) ₄ -		4-CH ₃ -C ₆ H ₄	35	C ₆ H ₅	<i>i</i> -C ₃ H ₇	3,5-(CH ₃) ₂ -C ₆ H ₃
6	-CH(CH ₃)(CH ₂) ₃ CH(CH ₃)-		3-Cl-C ₆ H ₄	36	C ₆ H ₅	<i>i</i> -C ₃ H ₇	4-CH ₃ O-C ₆ H ₄
7	-(CH ₂) ₆ -		3-CH ₃ -C ₆ H ₄	37	C ₆ H ₅	<i>i</i> -C ₃ H ₇	4-C ₂ H ₅ O-C ₆ H ₄
8	-(CH ₂) ₆ -		4-C ₂ H ₅ -C ₆ H ₄	38	3-CH ₃ -C ₆ H ₄	<i>i</i> -C ₃ H ₇	C ₆ H ₅
9	-(CH ₂) ₆ -		3,4-(CH ₃) ₂ -C ₆ H ₃	39	3-CH ₃ -C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-C ₂ H ₅ -C ₆ H ₄
10	-(CH ₂) ₆ -		3,5-(CH ₃) ₂ -C ₆ H ₃	40	3-CH ₃ -C ₆ H ₄	<i>i</i> -C ₃ H ₇	3-CH ₃ O-C ₆ H ₄
11	-(CH ₂) ₆ -		3-CH ₃ O-C ₆ H ₄	41	3-CH ₃ -C ₆ H ₄	<i>i</i> -C ₃ H ₇	3-F-C ₆ H ₄
12	-(CH ₂) ₆ -		4-Cl-C ₆ H ₄	42	3-CH ₃ O-C ₆ H ₄	<i>i</i> -C ₃ H ₇	C ₆ H ₅
13	C ₂ H ₅	<i>n</i> -C ₄ H ₉	4-CH ₃ -C ₆ H ₄	43	3-CH ₃ O-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-CH ₃ -C ₆ H ₄
14	C ₆ H ₅	CH ₃	C ₆ H ₅	44	4-CH ₃ O-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-CH ₃ -C ₆ H ₄
15	C ₆ H ₅	CH ₃	3-CH ₃ -C ₆ H ₄	45	4-CH ₃ O-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-CH ₃ O-C ₆ H ₄
16	C ₆ H ₅	CH ₃	4-CH ₃ -C ₆ H ₄	46	4-CH ₃ O-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-F-C ₆ H ₄
17	C ₆ H ₅	CH ₃	4-C ₂ H ₅ -C ₆ H ₄	47	4-F-C ₆ H ₄	<i>i</i> -C ₃ H ₇	3-CF ₃ -C ₆ H ₄
18	C ₆ H ₅	CH ₃	4-C ₂ H ₅ O-C ₆ H ₄	48	4-F-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-F-C ₆ H ₄
19	C ₆ H ₅	CH ₃	3-CF ₃ -C ₆ H ₄	49	3-Cl-C ₆ H ₄	<i>i</i> -C ₃ H ₇	4-F-C ₆ H ₄
20	C ₆ H ₅	CH ₃	3-F-C ₆ H ₄	50	4-CH ₃ -C ₆ H ₄	CH ₃	C ₆ H ₅
21	C ₆ H ₅	CH ₃	4-Cl-C ₆ H ₄	51	3,4-(CH ₃) ₂ -C ₆ H ₃	CH ₃	4-CH ₃ -C ₆ H ₄
22	4-CH ₃ O-C ₆ H ₄	CH ₃	3-CH ₃ -C ₆ H ₄	52	3-Cl-C ₆ H ₄	CH ₃	3,4-(CH ₃) ₂ -C ₆ H ₃
23	4-CH ₃ O-C ₆ H ₄	CH ₃	3,4-(CH ₃) ₂ -C ₆ H ₃	53	3-Cl-C ₆ H ₄	CH ₃	4-C ₂ H ₅ -C ₆ H ₄
24	4-CH ₃ O-C ₆ H ₄	CH ₃	3,4-OCH ₃ O-C ₆ H ₃	54	3-Cl-C ₆ H ₄	CH ₃	4-CH ₃ O-C ₆ H ₄
25	4-F-C ₆ H ₄	CH ₃	C ₆ H ₅	55	4-Cl-C ₆ H ₄	CH ₃	C ₆ H ₅
26	4-F-C ₆ H ₄	CH ₃	4-CH ₃ -C ₆ H ₄	56	4-Cl-C ₆ H ₄	CH ₃	3-CH ₃ O-C ₆ H ₄
27	4-F-C ₆ H ₄	CH ₃	4-CH ₃ O-C ₆ H ₄	57	4-Cl-C ₆ H ₄	CH ₃	4-CH ₃ O-C ₆ H ₄
28	2,4-F ₂ -C ₆ H ₃	CH ₃	3-Cl-C ₆ H ₄				
29	2,4-Cl ₂ -C ₆ H ₃	CH ₃	4-F-C ₆ H ₄				
30	C ₆ H ₅	C ₂ H ₅	4-F-C ₆ H ₄				

**Figure 2.** Geometry optimized core structure.

finally 16 descriptors (Table 2) were selected. These descriptors have high divergency and good representation of biological activity.

Results and Discussion

In this study, we screened 16 preselected descriptors for 57 fluorovinylloxyacetamides compounds using GFA method. Finally, we generated 100 QSAR equations that consist of four descriptors among QSAR random models. As a rule of thumb,²⁶ data set should be approximately 5 times more than the number of selected descriptors for good results. The results of the best QSAR model using 1-4 descriptors are given in Table 3. Regression models are all significant at *p*-

Table 2. List of Descriptors Used in This Study

Abbreviation	Definition
Dipole-X, Y, Z	X, Y, Z component of the dipole moment
LUMO-MOPAC	The energy of Lowest Unoccupied Molecular Orbital (LUMO) by MOPAC AM1 calculation
HOMO-MOPAC	The energy of Highest Occupied Molecular Orbital (HOMO) by MOPAC AM1 calculation
RadOfGyration	Radius of Gyration
PMI-X, Y, Z	X, Y, Z component of principle moment of inertia
logP	Calculated LogP (the partition coefficient) by Desolvation free energy of water (Fh2o) and octanol (Foct)
Vm	Molecular volume
Foct	Desolvation free energy of octanol
ShapeRMS	RMS value to shape reference
Dipole-MOPAC	Dipole moment by MOPAC AM1 calculation
Density	Density
MolRef	Molar refractivity by Ghose and Crippen calculation

Table 3. The best QSAR equation using 1-4 descriptors and their regression statistics

No. of descriptor	Equation	r^2	r^2_{cv}	SE	F	p-value
1	5.415-0.0109 (Vm)	0.627	0.598	0.190	92.357	2.27E-13
2	5.477-0.355 (logP)	0.810	0.789	0.137	115.021	3.41E-20
	-0.545 (RadOfGyration)					
3	5.365-0.350 (logP)	0.853	0.832	0.121	102.684	4.52E-22
	-0.524(RadOfGyration)					
	+0.0577 (Dipole-Z)					
4	5.600-0.341 (logP)	0.859	0.829	0.120	79.317	1.71E-21
	-0.560 (RadOfGyration)					
	+0.0581 (Dipole-Z)					
	-0.122 (ShapeRMS)					

r^2 : correlation coefficient, r^2_{cv} : cross-validated r^2 , SE: standard error, F: Fisher test value, p-value: significance level

value < 0.001 using the F statistics. The p-value is the observed significance probability of obtaining a greater F value by chance alone if a model fits no better than the overall response mean. The lower the p-value, the more significant the QSAR equation. As a result of the lowest p-value and the highest cross-validated r^2 , an optimum fit was found to require three descriptors. This equation produces the best description for the activity of the fluorovinyloxyacetamides.

$$\begin{aligned} \text{Activity} = & 5.365 \\ & -0.350 (\text{Log P}) \\ & -0.524 (\text{RadOfGyration}) \\ & +0.0577 (\text{Dipole-Z}) \end{aligned} \quad (2)$$

($r^2=0.853$, Cross-validated $r^2=0.832$, $F=102.684$, p-value=4.52E-22)

The good relationship between the observed and the GFA predicted $-\log EC_{50}$ for training set is shown in Table 4 and Figure 3. The residual of those values was 0.003-0.284 and mean residual is 0.09095. The test set (Table 5) which is composed of 14 compounds were used to prove prediction ability of this equation. The prediction results of test set using equation (2) are depicted in Figure 4 and Table 6. These have also small error value that represents the prediction ability of final QSAR equation.

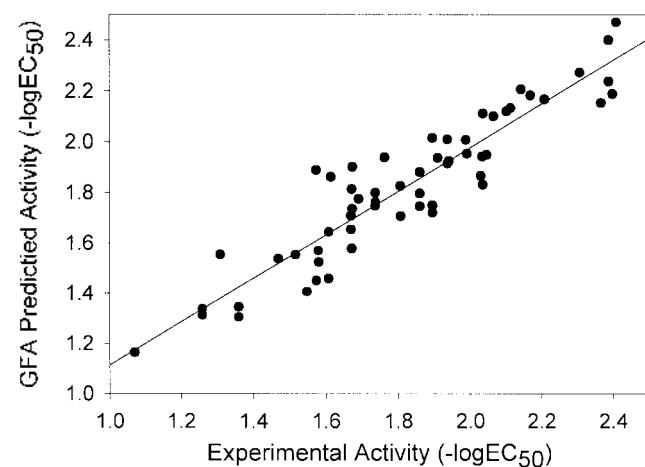
The Figure 5 represents the descriptors selected in the elite population of this models in the GFA calculation. Each

curve of descriptor usage versus crossover operation number reaches a plateau after about 1000 crossovers in the GFA procedure which indicate a convergent optimization of QSAR equations. The most often used descriptor is clearly logP, which is found in about 30% of all QSAR models. It is considered that logP played an important role on the biological activity of molecule that might be concerned with herbicides distribution. That is, herbicides should be solved in water environment to penetrate into plant. Generally, LogP value is inversely proportional to solubility of water environment. Other descriptors, radius of gyration and dipole-Z in equation (2), were rarely selected in the elite population. However, they were effective descriptors combined with logP in equation (2). Radius of gyration confirms the significance of steric hinderance caused by the size of functional groups (R_1 , R_2 , R_3). Dipole-Z accounts for dipole-dipole interaction of functional group R_1 . They may be related to bind between drug and receptor because drug size and charge distributions are essential factors to bind active site of receptor molecule.

The multicollinearity of three descriptors in equation (2) is represented by variance inflation factor (VIF). The effect of multicollinearity is to inflate the variance of the least squares estimator and possibly any predictions made, and also to restrict the generality and applicability of the QSAR model. VIF value is calculated from $1/(1-r^2)$, where r^2 is the multiple

Table 4. Observed and GFA predicted $-\log EC_{50}$ for Training Set

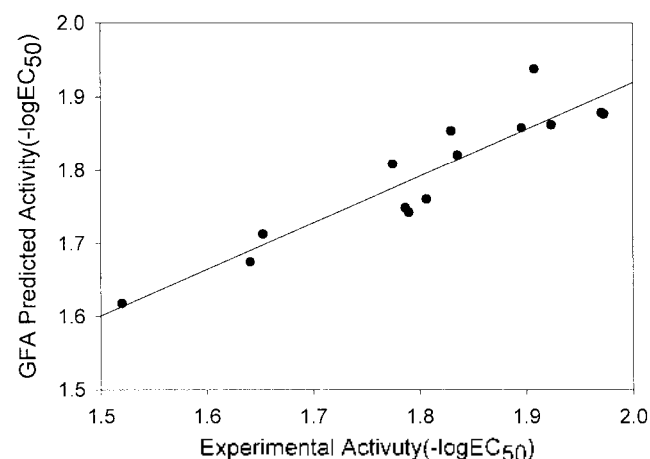
No.	Observed Activity ($-\log EC_{50}$)	GFA prediction	GFA residual	No.	Observed Activity ($-\log EC_{50}$)	GFA prediction	GFA residual
1	2.114	2.132	-0.019	31	1.937	2.009	-0.072
2	1.738	1.798	-0.061	32	1.259	1.311	-0.052
3	1.674	1.901	-0.227	33	1.517	1.552	-0.035
4	1.574	1.888	-0.315	34	1.360	1.345	0.015
5	1.807	1.706	0.101	35	1.309	1.553	-0.244
6	1.738	1.762	-0.024	36	1.860	1.796	0.065
7	2.102	2.119	-0.017	37	1.608	1.457	0.151
8	1.867	1.746	0.115	38	2.036	1.830	0.205
9	1.992	1.954	0.038	39	1.070	1.164	-0.093
10	1.910	1.936	0.026	40	1.470	1.537	-0.067
11	2.036	2.111	-0.075	41	1.673	1.735	-0.062
12	2.066	2.101	-0.035	42	1.806	1.925	-0.019
13	1.614	1.862	-0.247	43	1.581	1.524	0.057
14	2.408	2.470	-0.062	44	1.574	1.449	0.125
15	2.366	2.153	0.213	45	1.259	1.336	-0.078
16	2.398	2.188	0.210	46	1.618	1.643	-0.035
17	1.860	1.880	-0.020	47	1.360	1.304	0.056
18	1.937	1.914	0.023	48	1.896	1.749	0.147
19	2.046	1.949	0.098	49	1.672	1.577	0.095
20	2.387	2.400	-0.013	50	2.143	2.207	-0.063
21	2.169	2.183	-0.013	51	1.672	1.813	-0.141
22	2.030	1.866	0.165	52	1.579	1.569	0.010
23	1.737	1.746	-0.009	53	1.548	1.406	0.142
24	1.896	2.014	-0.118	54	1.670	1.708	-0.038
25	2.387	2.238	0.150	55	1.988	2.006	-0.018
26	1.941	1.924	0.017	56	1.691	1.774	-0.083
27	1.763	1.938	-0.175	57	1.670	1.653	0.017
28	2.034	1.942	0.092				
29	1.896	1.719	0.176				
30	2.209	2.167	0.042				

**Figure 3.** Activity values predicted by GFA Model of Training Set.

correlation coefficient of one descriptor's effect regressed on the remaining molecular descriptors. If VIF value is larger than 5, information of descriptors can be hidden by correla-

Table 5. Structures of Fluorovinylloxyacetamides in Test Set

No.	R ₁	R ₂	R ₃
1	4-CH ₃ O-C ₆ H ₄	CH ₃	3,5-(CH ₃) ₂ -C ₆ H ₃
2	4-CH ₃ O-C ₆ H ₄	CH ₃	4-CH ₃ O-C ₆ H ₄
3	4-CH ₃ O-C ₆ H ₄	CH ₃	4-Cl-C ₆ H ₄
4	4-F-C ₆ H ₄	CH ₃	3-CH ₃ -C ₆ H ₄
5	4-F-C ₆ H ₄	CH ₃	3,5-(CH ₃) ₂ -C ₆ H ₃
6	4-F-C ₆ H ₄	CH ₃	3-CH ₃ O-C ₆ H ₄
7	C ₆ H ₅	C ₂ H ₅	4-CF ₃ -C ₆ H ₄
8	4-CH ₃ -C ₆ H ₄	C ₂ H ₅	4-F-C ₆ H ₄
9	4-CH ₃ O-C ₆ H ₄	C ₂ H ₅	4-F-C ₆ H ₄
10	2-Cl-C ₆ H ₄	C ₂ H ₅	4-CH ₃ -C ₆ H ₄
11	3-Cl-C ₆ H ₄	C ₂ H ₅	C ₆ H ₅
12	4-Cl-C ₆ H ₄	C ₂ H ₅	C ₆ H ₅
13	C ₆ H ₅	<i>i</i> -C ₃ H ₇	4-CH ₃ -C ₆ H ₄
14	C ₆ H ₅	<i>i</i> -C ₃ H ₇	3,4-OCH ₂ O-C ₆ H ₄

**Figure 4.** Activity values predicted by GFA Model of Test Set.**Table 6.** Observed and GFA Predicted $-\log EC_{50}$ for Test Set

No.	Observed Activity ($-\log EC_{50}$)	GFA prediction	GFA residual	No.	Observed Activity ($-\log EC_{50}$)	GFA prediction	GFA residual
1	1.641	1.675	-0.034	8	1.836	1.821	0.015
2	1.924	1.862	0.062	9	1.830	1.854	-0.024
3	1.807	1.761	0.046	10	1.520	1.678	-0.158
4	1.971	1.879	0.092	11	1.973	1.877	0.096
5	1.653	1.713	-0.060	12	1.775	1.809	-0.034
6	1.908	1.938	-0.030	13	1.790	1.743	0.047
7	1.787	1.749	0.038	14	1.896	1.858	0.038

tion of descriptors. In this model, the VIF value of these descriptors are 1.0155 (dipole-Z), 1.0292 (radius of gyration), 1.0229 (logP). Therefore, these descriptors showed no intercorrelation.

Relations between descriptors and activity can be seen from Figure 6. Solid and Dot lines in Figure 6 depict respectively regression line and 95% confidence level of regression line. The molecules 12, 27, 45, 54 show great deviation in

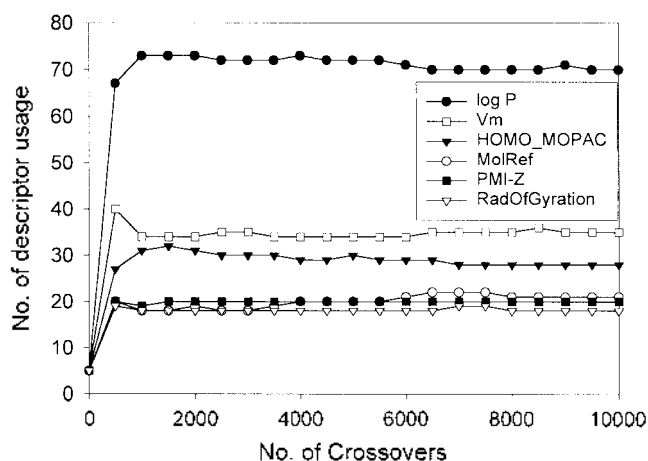


Figure 5. Population of GFA Selected Descriptors.

correlation between $\log P$ and $-\log EC_{50}$ (Figure 6(a)). On the other hands, these molecules show good correlations between RadOfGyration and $-\log EC_{50}$ or dipole-Z and $-\log EC_{50}$ (Figure 6(b) and (c)). In the case of the molecules 14, 22, 32, 39, they express great deviation with RadOfGyration (Figure 6(b)) while they express good correlations with $\log P$ (Figure 6(a)). This correlation patterns represent that these descriptors can describe biological activities effectively.

According to these descriptors, this fluorovinloxyacetamide herbicides have important characteristics such as great plant penetration ability and molecular size. The highly active molecules might have smaller $\log P$, smaller radius of gyration and larger dipole moment than less active molecules.

Further analysis of this data indicated that simple calculation of $\log P$, radius of gyration, dipole moment might predict the biological activity of this herbicides.

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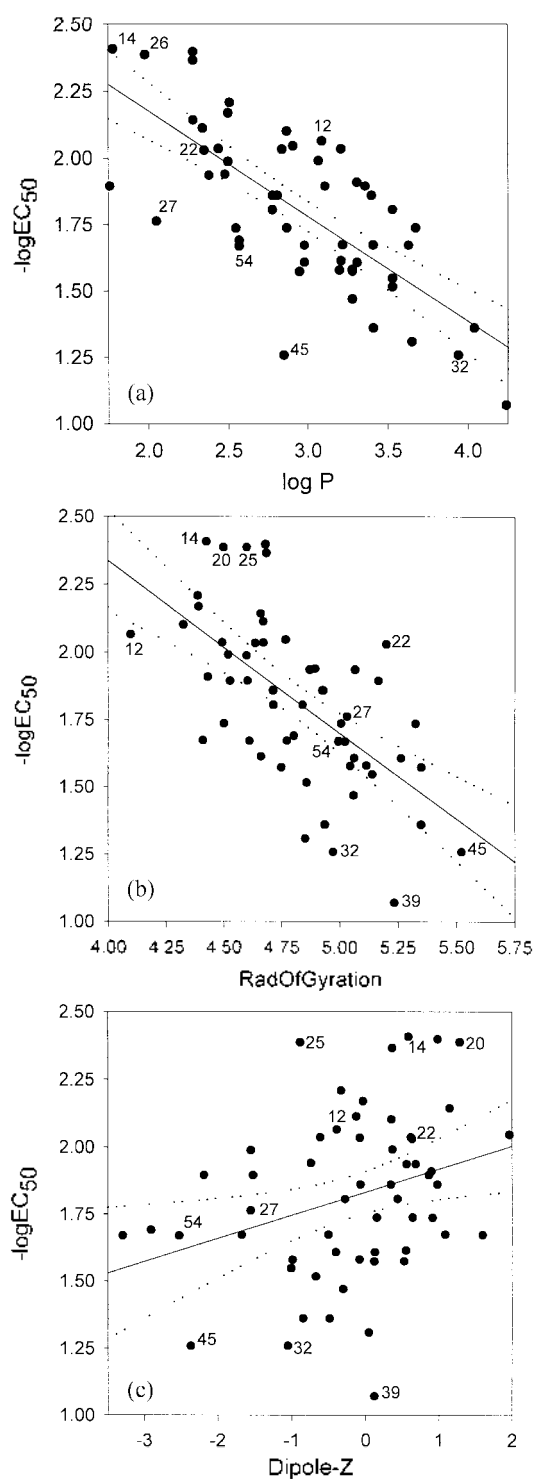


Figure 6. Plots of $-\log EC_{50}$ vs. (a) $\log P$, (b) radius of gyration and (c) dipole-Z.

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