January 2001

Chem. Pharm. Bull. **49**(1) 5—9 (2001)

5

Solute–Stationary Phase Interaction in Gas Liquid Chromatography. Thermodynamic Parameters for Substituted Halogenobenzene Derivatives

Hideko Kawaki

School of Pharmaceutical Sciences, Kinki Uiversity, 3–4–1 Kowakae, Higashi-Osaka 577–8502, Japan.
Received February 3, 2000; accepted September 18, 2000

Thermodynamic parameters were determined by variable temperature experiments on the gas liquid chromatography (GLC) relative retention values, $\log \gamma$, of 3- and 4-substituted halogenobenzene derivatives under non-polar condition. These $\Delta\Delta H_s^{\circ}(R,X)$ had a compensational relation with the $\Delta\Delta S_s^{\circ}(R,X)$ values. The free energy change $\Delta\Delta G_s^{\circ}(R,X)$ which is estimated from the $\Delta\Delta H_s^{\circ}(R,X)$ and the $\Delta\Delta S_s^{\circ}(R,X)$ at 298 K is less than $-23\,\mathrm{kJ \cdot mol^{-1}}$. The $\Delta\Delta S_s^{\circ}(R)$ values could be explained by translational entropy change for the adsorbed active complex between the solute and stationary phase. It is suggested that the interaction could be mainly expressed by the physical adsorption exclusive of hydrogen bonding. The $\Delta\Delta G_s^{\circ}(R,X)$ values for each halogen derivative have been the excellent linear lines taking the same slopes for the monosubstituted benzene derivatives, $\Delta\Delta G_s^{\circ}(R)$. The regression analyses of their intercepts were given using the descriptor evaluated as the molecular volume $\sigma_a(X)$ rather than $\sigma_M(X)$. The regression analysis for polyhalogenobenzene was also given successfully using $\sigma_a(X_n)$.

Key words gas liquid chromatography; retention value $\log \gamma$; entropy change $\Delta\Delta S_s^{\circ}$; substituted halogenobenzene derivative; adsorbed active complex; descriptor σ_a

A halogen compound is generally known to have higher reactivity than others and to be useful for many fields as a medicine, an agricultural chemical, *etc*. The interaction energy between a halogen compound and an enzyme was often found on the outside where they were related with Hammett type substituent constant. This suggests in general that the dispersion energy depends on a large molecular size. We will consider the nature of the reaction in halogen. The enthalpy $\Delta\Delta H_s^{\circ}(R,X)$ and entropy $\Delta\Delta S_s^{\circ}(R,X)$ changes were estimated from variable temperature experiments for the relative retention values, $\log \gamma$, of 3- and 4-substituted halogenobenzene derivatives as well as monosubstituted benzene ones.[1] The $\Delta\Delta H_s^{\circ}(R,X)$ values were consistent with $T\Delta\Delta S_s^{\circ}(R,X)$ under a standard condition. The $\Delta\Delta S_s^{\circ}$ values may correspond to the translational activated entropy changes, $\Delta\Delta S_{ABC}^{\ddagger}$ introduced by Eyring's adsorption model[2] for monosubstituted benzene derivatives. This also suggests that this interaction is weak similar to those of a non-bonding complex.

Experimental
Relative Retention Value $\log \gamma$ and Experimental Conditions for GLC The $\log \gamma$ is defined by Eq. 1.[3]

$$\log \gamma = \log[t_R(B)/t_R(A)] = -[\Delta H_s^{\circ}(B) - \Delta H_s^{\circ}(A)]/2.303RT + [\Delta S_s^{\circ}(B)$$
$$- \Delta S_s^{\circ}(A)]/2.303R = -[\Delta G_s^{\circ}(B) - \Delta G_s^{\circ}(A)]/2.303RT \quad (1)$$

Here, $t_R(A)$ and $t_R(B)$ are the retention times of benzene and substituted halogenobenzenes respectively. ΔG_s°, ΔH_s° and ΔS_s° denote the free energy, enthalpy and entropy of dissolution of the sample and stationary liquid phase. Measurements were obtained using a Shimadzu 8A type gas liquid chromatograph.

Measurement Conditions: Sample, 3- and 4-substituted halogenobenzene derivatives; reference, benzene; mobile phase, nitrogen (N$_2$); stationary phase, Chromosorb W (AW-DMCS)+20% squalane; column temperature, 338—418 K; temperature is measured with a precision of ± 0.1 K using a CA thermocouple.

Regression Analysis: The regression analyses of the interaction energy change were carried out using the program MVA.[4]

Descriptor for Regression Analyses σ_a: Polarizability $\alpha/\times 10^{-24}\,\mathrm{cm^3}$ is given by the Clausius–Mosotti equation, using the reference indices ob-

served using the sodium D line at 293 K.[5] The descriptor σ_a is derived as follow,

$$\sigma_a \equiv \log[\alpha(B)/\alpha(A)] \quad (2)$$

where A and B represent methane or benzene and its derivatives, respectively.

σ_v: Van der Waals volume/cm^3 is cited from the literature values[6]:

$$\sigma_v \equiv \log[V_{vdw}(B)/V_{vdw}(A)] \quad (3)$$

where A and B represent reference methane and others.

The correlation between σ_a and σ_v was good in Eq. 4 and σ_a has been useful as σ_v.

$$\sigma_a = 0.825(0.061)\sigma_v + 0.017(0.034) \quad (4)$$

$n=12$ (methane, propane, n-pentane, cyclohexane, benzene, toluene, methanol, n-butanol, tetrahydrofuran, tetrahydropyran, N-Me pyrrolidine and camphor),

$$r=0.995, \quad F=910.4, \quad \text{S.D.}=0.022$$

where n, r, F and S.D. denote the number of data, correlation coefficent, variance ratio and standard deviation, respectively. The values within parenthess of regression equations denote the 95% confidence intervals.

Results and Discussion
Temperature-Dependence of $\log \gamma$ Data on the temperature-dependence of $\log \gamma$, in 3- and 4-substituted halogenobenzene derivatives, summarized in Table 1, gave the linear lines with the positive slope by plotting to $1/T \times 10^3/\mathrm{K^{-1}}$ in Fig. 1, namely $\Delta\Delta H_s^{\circ}(R,X)$ were negative. The values of $\Delta\Delta H_s^{\circ}(R,X)$, $\Delta\Delta S_s^{\circ}(R,X)$, and $\Delta\Delta G_s^{\circ}(R,X)$ at 298 K are summarized in Table 2. The $\Delta\Delta H_s^{\circ}(R,X)$ was compensatory for $\Delta\Delta S_s^{\circ}(R,X)$, and they gave the same linear line on monosubstituted benzene derivatives (Fig. 2). All the $\Delta\Delta G_s^{\circ}(R,X)$ values were smaller than $-23\,\mathrm{kJ \cdot mol^{-1}}$ under non-polar conditions. These results suggest that they can be analyzed by using the descriptor expressed from either $\Delta\Delta H_s^{\circ}(R,X)$ or $\Delta\Delta S_s^{\circ}(R,X)$.

**Evaluation of Thermodynamic Parameters. a) Entropy Change $\Delta\Delta S_s^{\circ}(R)$ in Monosubstituted Benzene De-

Table 1. Substituted Halogenobenzene Derivatives and Their Observed log γ Values at Several Temperatures

R, X		$1/T \times 10^3 \mathrm{K}^{-1}$					
		2.39	2.42	2.45	2.48	2.51	2.54
1	1,3-F,Me	0.175	0.185	0.194	0.205	0.216	0.226
2	1,3-F,OMe	0.402	0.423	0.444	0.466	0.489	0.512
3	1,3-F,NO$_2$	0.643	0.670	0.699	0.728	0.761	0.790
4	1,3-Cl,Me	0.567	0.591	0.618	0.647	0.673	0.705
5	1,3-Cl,OMe	0.826	0.859	0.895	0.935	0.970	1.012
6	1,3-Cl,NO$_2$	1.091	1.139	1.173	1.219	1.261	1.310
7	1,3-Br,H	0.516	0.540	0.565	0.588	0.612	0.638
8	1,3-Br,Me	0.774	0.808	0.842	0.876	0.908	0.944
9	1,3-Br,OMe	1.037	1.078	1.121	1.164	1.206	1.250
10	1,3-Br,NO$_2$	1.323	1.371	1.417	1.464	1.514	1.564
11	1,3-Br,COMe	1.313	1.363	1.413	1.463	1.513	1.565
12	1,3-Br,CN	1.059	1.100	1.138	1.181	1.223	1.266
13	1,3-I,H	0.779	0.809	0.841	0.873	0.907	0.939
14	1,3-I,Me	1.047	1.085	1.125	1.165	1.206	1.250
15	1,3-I,NO$_2$	1.620	1.671	1.726	1.780	1.838	1.894
16	1,4-F,Me	0.172	0.181	0.190	0.201	0.210	0.221
17	1,4-F,OMe	0.394	0.415	0.435	0.458	0.480	0.501
18	1,4-F,NO$_2$	0.659	0.691	0.718	0.750	0.779	0.820
19	1,4-F,COMe	0.654	0.687	0.718	0.750	0.782	0.813
20	1,4-F,CO$_2$Et	0.878	0.921	0.959	1.001	1.042	1.080
21	1,4-Cl,Me	0.555	0.582	0.605	0.634	0.661	0.688
22	1,4-Cl,OMe	0.827	0.866	0.898	0.938	0.976	1.013
23	1,4-Cl,OEt	1.000	1.045	1.083	1.130	1.174	1.217
24	1,4-Cl,NO$_2$	1.115	1.155	1.195	1.241	1.281	1.331
25	1,4-Cl,COMe	1.098	1.146	1.186	1.234	1.281	1.331
26	1,4-Cl,CN	0.866	0.900	0.934	0.965	1.005	1.043
27	1,4-Br,Me	0.776	0.808	0.842	0.876	0.908	0.944
28	1,4-Br,OMe	1.049	1.092	1.124	1.171	1.216	1.261
29	1,4-Br,OEt	1.226	1.274	1.312	1.365	1.417	1.467
30	1,4-Br,NO$_2$	1.326	1.376	1.415	1.470	1.523	1.574
31	1,4-Br,COMe	1.313	1.363	1.413	1.463	1.513	1.565
32	1,4-Br,CO$_2$Me	1.382	1.434	1.476	1.532	1.588	1.642
33	1,4-I,Me	1.042	1.085	1.117	1.157	1.204	1.249
34	1,4-I,OMe	1.334	1.386	1.426	1.475	1.529	1.585
35	1,4-I,NO$_2$	1.630	1.689	1.735	1.790	1.849	1.913
36	1,4-I,CO$_2$Et	0.847	0.879	0.911	0.950	0.983	1.023
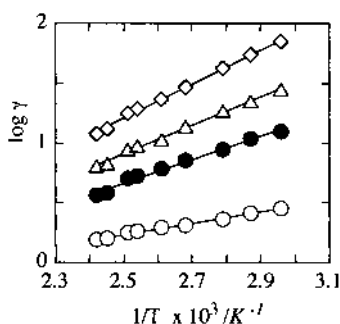
Fig. 1. Correlations between $\log \gamma$ and $1/T \times 10^3/\mathrm{K}^{-1}$ in 3-Methyl Halogenobenzene Derivatives under Non-polar Condition

○=F; ●=Cl; △=Br; □=I.

rivatives The interaction energy will be discussed in entropy term, since $\Delta\Delta H_s^\circ(R)$ values were compensated by $\Delta\Delta S_s^\circ(R)$ and $\Delta\Delta G_s^\circ(R)$ values became about the same as weak hydrogen bonded energy. When we will consider the adsorption on a nonuniform surface to the interaction of the gaseous sample (A or B) and the stationary liquid (C=constant in the system), the activated translational entropy change $\Delta S^\ddagger$ for Eyring's adsorption model[2] is expressed as in Eqs. 5 and 6:

$$\Delta S_{AC}^\ddagger = -\boldsymbol{R}\ln\frac{(2\pi m_A \boldsymbol{k} Te)^{3/2}}{\boldsymbol{h}^3} \tag{5}$$

where $\boldsymbol{R}$, $\boldsymbol{k}$, T and $\boldsymbol{h}$ are gas constant, Boltzmann constant, absolute temperature and Planck constant, respectively.

$$\Delta S_{BC}^\ddagger = -\boldsymbol{R}\ln\frac{(2\pi m_B \boldsymbol{k} Te)3/2}{\boldsymbol{h}^3} \tag{6}$$

The difference of Eqs. 5 and 6 is given by,

$$\Delta\Delta S_{ABC}^\ddagger = -\boldsymbol{R}\left(\ln\frac{(2\pi m_B \boldsymbol{k} Te)^{3/2}}{\boldsymbol{h}^3} - \ln\frac{(2\pi m_A \boldsymbol{k} Te)^{3/2}}{\boldsymbol{h}^3}\right)$$

$$= -\frac{3}{2}\boldsymbol{R}\ln\frac{2\pi m_B \boldsymbol{k} Te}{2\pi m_A \boldsymbol{k} Te} \tag{7}$$

when T is constant, Eq. 7 is given by,

$$\Delta\Delta S_{ABC}^\ddagger = -\frac{3}{2}\boldsymbol{R}\ln\frac{m_B}{m_A} \tag{8}$$

when m_A and m_B take the relative molecular mass (M_A, M_B) and $\Delta\Delta S_{ABC}^\ddagger$ becomes the linear relation to $\ln M_B/M_A$ (Table 3). The $\ln M_B/M_A$ is now replaced with σ_M in the following;

$$\ln M_B/M_A = 2.303 \log M_B/M_A \equiv \sigma_M \tag{9}$$

Table 2. Thermodynamic Parameters of Solute at 298 K in GLC for Substituted Halogenobenzene Derivatives

	X, R	$-\Delta\Delta H_s^\circ$/kJ·mol^{-1}	$-\Delta\Delta S_s^\circ$/J·mol^{-1}·K^{-1}	$-\Delta\Delta G_s^\circ$/kJ·mol^{-1}
1	1,3-F,Me	6.55±0.27	12.31±0.67	2.9±0.1
2	1,3-F,OMe	14.04±0.42	25.89±1.05	6.3±0.1
3	1,3-F,NO$_2$	18.92±0.75	32.92±1.84	9.1±0.2
4	1,3-Cl,Me	17.60±0.96	31.25±2.36	8.3±0.3
5	1,3-Cl,OMe	23.76±1.13	41.03±2.78	11.5±0.3
6	1,3-Cl,NO$_2$	27.94±1.09	45.94±2.68	14.2±0.3
7	1,3-Br,H	15.49±0.33	27.13±0.80	7.1±0.1
8	1,3-Br,Me	21.60±0.36	36.78±0.88	10.6±0.1
9	1,3-Br,OMe	27.21±0.33	45.19±0.80	13.7±0.1
10	1,3-Br,NO$_2$	30.68±0.57	47.99±1.42	16.4±0.1
11	1,3-Br,COMe	32.09±0.29	51.57±0.73	16.7±0.1
12	1,3-Br,CN	26.39±0.71	42.82±1.76	13.6±0.2
13	1,3-I,H	20.53±0.50	34.18±1.23	10.3±0.1
14	1,3-I,Me	26.02±0.80	42.18±1.99	13.5±0.2
15	1,3-I,NO$_2$	35.10±0.94	52.93±2.30	19.3±0.3
16	1,4-F,Me	6.26±0.31	11.66±0.77	2.8±0.1
17	1,4-F,OMe	13.73±0.34	25.29±0.86	6.2±0.1
18	1,4-F,NO$_2$	20.09±1.67	35.40±4.10	9.5±0.4
19	1,4-F,COMe	20.28±0.23	35.94±0.54	9.6±0.1
20	1,4-F,CO$_2$Et	25.81±0.59	44.85±1.44	12.4±0.5
21	1,4-Cl,Me	16.98±0.61	29.97±1.53	8.0±0.2
22	1,4-Cl,OMe	23.71±0.80	40.82±1.99	11.5±0.2
23	1,4-Cl,OEt	27.71±0.86	47.07±2.13	13.7±0.2
24	1,4-Cl,NO$_2$	27.44±1.38	44.25±3.41	14.3±0.4
25	1,4-Cl,COMe	28.72±0.82	47.94±0.54	14.5±0.2
26	1,4-Cl,CN	22.44±1.21	37.49±4.27	11.4±0.4
27	1,4-Br,Me	20.83±1.72	35.14±0.80	10.4±0.1
28	1,4-Br,OMe	26.98±1.91	44.42±4.71	13.7±0.5
29	1,4-Br,OEt	30.77±1.99	50.11±4.92	15.8±0.5
30	1,4-Br,NO$_2$	30.69±1.24	47.85±3.08	16.4±0.3
31	1,4-Br,COMe	31.65±1.97	50.32±4.86	16.7±0.2
32	1,4-Br,CO$_2$Me	33.15±1.97	52.83±4.84	17.4±0.5
33	1,4-I,Me	26.12±2.09	42.49±5.13	13.5±0.6
34	1,4-I,OMe	31.59±2.22	50.03±5.50	16.7±0.6
35	1,4-I,NO$_2$	35.56±2.34	53.81±5.76	19.5±0.6
36	1,4-I,CO$_2$Et	40.77±2.18	61.75±5.40	22.4±0.6
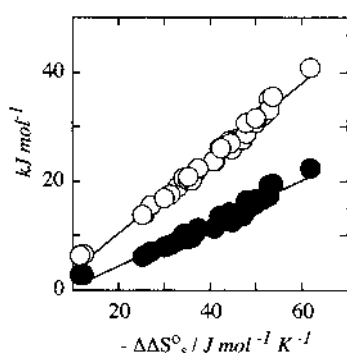
Fig. 2. Correlations between $-\Delta\Delta H_s^\circ$ or $-\Delta\Delta G_s^\circ$ and $-\Delta\Delta S_s^\circ$ in 3 and 4-Substituted Halogenobenzene Derivatives

○ = $-\Delta\Delta H_s^\circ$; ● = $-\Delta\Delta G_s^\circ$.

The relation with $\Delta\Delta S_s^\circ$ values and σ_M were in Fig. 3 and the regression analysis except for bromo- and iodobenzenes is given by,

$$-\Delta\Delta S_s^\circ = 148.15(24.99)\sigma_M - 0.01(4.50) \qquad (10)$$

$n=15$, $r=0.963$, $F=164.0$, S.D.=3.22

The $\Delta\Delta S_{ABC}^\ddagger$ is dependent on σ_M with the linear relation by Eyring's model. The $\Delta\Delta S_s^\circ$ values showed the deviation of Br and I. This deviation would come from the change in lin-

Table 3. Entropy Changes $-\Delta\Delta S_s^\circ$/J·mol^{-1}·K^{-1} under Non-polar Condition and the Descriptors σ_M and σ_a on Monosubstituted Benzene Derivatives

	R	$-\Delta\Delta S_s^\circ$/J·mol^{-1}·K^{-1}	σ_M	σ_a
1	H	0.00	0.000	0.000
2	Me	11.66	0.072	0.074
3	Et	20.07	0.133	0.135
4	n-Pr	27.46	0.187	0.189
5	n-Bu	34.95	0.235	0.236
6	OMe	22.96	0.141	0.103
7	OEt	29.89	0.194	0.158
8	COMe	30.75	0.187	0.147
9	COEt	37.68	0.235	0.193
10	CO$_2$Me	33.34	0.241	0.166
11	CO$_2$Et	39.12	0.284	0.211
12	CN	23.15	0.121	0.080
13	NO$_2$	29.68	0.198	0.097
14	F	5.6[1]	0.090	−0.002
15	Cl	20.5[2]	0.159	0.076
16	Br	27.13	0.202[3]	0.113
17	I	34.18	0.278[4]	0.175

1 and 2 are estimated from the linear relation to monosubstituted benzene and halogenobenzene derivatives. 3 and 4 are modified from σ_M.

ear relation between the molecular weight and volume for a large size activated complex. This idea must be verified in future.
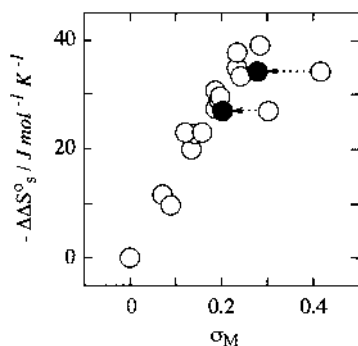
Fig. 3. Plots of $-\Delta\Delta S_s^\circ$ *vs.* σ_M in Monosubstituted Benzene Derivatives under Non-polar Condition

● indicates the modified values for Br and I.

If the activated complex increases the degree of freedom for one dimension, since bromo- and iodobenzenes have large molecular size, the $\Delta\Delta S_{ABC}^\ddagger$ values may decrease. As σ_M values of bromo- and iodobenzenes could be modified to $(2/3)\sigma_M$, a good linear relationship shown by closed circles (Fig. 3). The modified regression analysis is given by

$$-\Delta\Delta S_s^\circ = 135.08(20.11)\sigma_M + 2.08(3.79) \quad (11)$$

$n=17$, $r=0.965$, $F=204.9$, S.D.$=2.84$

(b) Free Energy Change $\Delta\Delta G_s^\circ(R,X)$ in Monosubstituted Halogenobenzene Derivatives In a previous report,[7] the $\Delta\Delta G_s^\circ(R)$ values were expressed using two descriptors, σ_{s° and μ^2/α for monosubstituted benzene derivatives except halogenobenzenes. The σ_{s° comes from evaluation of the force constants determined by the modified Lennard–Jones (12,6) potential equation and represents E_{dis} and repulsion E_{rep} energies. The μ^2/α was introduced by the classical equations of the orientation E_{ori} and induction E_{ind} energies, when $\alpha_A\alpha_B$ values were proportional to r_{AB}^6.

The correlations between $\Delta\Delta G_s^\circ(R)$ and $\Delta\Delta G_s^\circ(R,X)$ were good linear lines in each halogen compound (Table 4, Fig. 4).

$$\Delta\Delta G_s^\circ(R,F) = 0.96(0.05)\Delta\Delta G_s^\circ(R) - 0.14(0.42) \quad (12)$$

$n=8$, $r=0.999$, $F=2200.8$, S.D.$=0.19$

$$\Delta\Delta G_s^\circ(R,Cl) = 0.91(0.08)\Delta\Delta G_s^\circ(R) + 5.36(0.62) \quad (13)$$

$n=9$, $r=0.995$, $F=717.4$, S.D.$=0.26$

$$\Delta\Delta G_s^\circ(R,Br) = 0.93(0.05)\Delta\Delta G_s^\circ(R) + 7.43(0.39) \quad (14)$$

$n=12$, $r=0.997$, $F=1748.7$, S.D.$=0.25$

$$\Delta\Delta G_s^\circ(R,I) = 0.91(0.05)\Delta\Delta G_s^\circ(R) + 10.53(0.41) \quad (15)$$

$n=7$, $r=0.999$, $F=2033.0$, S.D.$=0.23$

Their slopes were consistent in value and the intercepts of bromo- and iodobenzenes were in agreement with the experimental values. The $\Delta\Delta G_s^\circ(X)$ values in halogen are proportional to σ_M except fluorobenzenes shown in Fig. 5.

We discussed that $\Delta\Delta S_s$ values depended on $\Delta\Delta S_{ABC}^\ddagger$ by the adsorption in the solute–stationary interaction. As we pointed out before,[7] CH/π (squarane CH of stationary phase and benzene π of solute) interaction was estimated to monosubstituted benzene derivatives except halogenobenzene. Weiss *et al.*[8] suggested that F and the others (Cl, Br, I) took

Table 4. Free Energy Values of Solute at 298 K in GLC for 3- and 4-Substituted Halogenobenzene, and Monosubstituted Benzene Derivatives and Their Descriptor

|	R, X	$-\Delta\Delta G_s^\circ$ kJ·mol^{-1}	$-\Delta\Delta G_s^\circ(R)$ kJ·mol^{-1}	$\sigma_a(X)$
1	1,3-F,Me	2.9	3.1	−0.002
2	1,3-F,OMe	6.3	6.6	−0.002
3	1,3-F,NO$_2$	9.1	10.0	−0.002
4	1,3-Cl,Me	8.3	3.1	0.076
5	1,3-Cl,OMe	11.5	6.6	0.076
6	1,3-Cl,NO$_2$	14.2	10.0	0.076
7	Br	7.1	0.0	0.113
8	1,3-Br,Me	10.6	3.1	0.113
9	1,3-Br,OMe	13.7	6.6	0.113
10	1,3-Br,NO$_2$	16.4	10.0	0.113
11	1,3-Br,COMe	16.7	9.9	0.113
12	1,3-Br,CN	13.6	7.0	0.113
13	I	10.3	0.0	0.175
14	1,3-I,Me	13.5	3.1	0.175
15	1,3-I,NO$_2$	19.3	10.0	0.175
16	1,4-F,Me	2.8	3.1	−0.002
17	1,4-F,OMe	6.2	6.6	−0.002
18	1,4-F,NO$_2$	9.5	10.0	−0.002
19	1,4-F,COMe	9.6	9.9	−0.002
20	1,4-F,CO$_2$Et	12.4	12.9	−0.002
21	1,4-Cl,Me	8.0	3.1	0.076
22	1,4-Cl,OMe	11.5	6.6	0.075
23	1,4-Cl,OEt	13.7	8.7	0.075
24	1,4-Cl,NO$_2$	14.3	10.0	0.075
25	1,4-Cl,COMe	14.5	9.9	0.075
26	1,4-Cl,CN	11.4	7.0	0.075
27	1,4-Br,Me	10.4	3.1	0.113
28	1,4-Br,OMe	13.7	6.6	0.113
29	1,4-Br,OEt	15.8	8.7	0.113
30	1,4-Br,NO$_2$	16.4	10.0	0.113
31	1,4-Br,COMe	16.7	9.9	0.113
32	1,4-Br,CO$_2$Me	17.4	10.8	0.113
33	1,4-I,Me	13.5	3.1	0.175
34	1,4-I,OMe	16.7	6.6	0.175
35	1,4-I,NO$_2$	19.5	10.0	0.175
36	1,4-I,CO$_2$Et	22.4	12.9	0.175
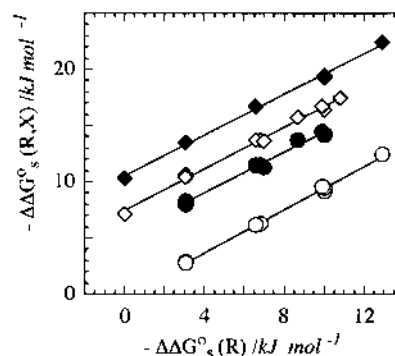
Fig. 4. Correlations between $-\Delta\Delta G_s^\circ(R,X)$ and $-\Delta\Delta G_s^\circ(R)$ in each Halogenobenzene Derivative

○$=$F; ●$=$Cl; ◇$=$Br; ◆$=$I.

different crystal structures for the 4-halogenoethynylbenzenes. The former was predominantly CH/F and the latter was T-shaped CH/π hydrogen bridge, but the crystal structure of chlorine was ordered and those of bromine and iodine were disordered. This suggested that the CH/F distance was shorter than the sum of the van der Waals radii (d).[9]

Howard *et al.*[10] concluded that the interaction energy estimated by *ab initio* calculation of C_{sp^2}–F/H–C (methane)

Table 5. The $\log\gamma$ Values for Halogenobenzene Derivatives at 453 K and the Descriptor

	X	$\log\gamma$	σ_a
1	F	−0.025	−0.002
2	Cl	0.537	0.076
3	Br	0.782	0.113
4	I	1.105	0.175
5	1,2-F$_2$	0.000	−0.006
6	1,2-Cl$_2$	1.026	0.138
7	1,2-Br$_2$	1.472	0.200
8	1,2-I$_2$	2.023	0.291
9	1,3-F$_2$	−0.051	−0.005
10	1,3-Cl$_2$	0.980	0.140
11	1,3-Br$_2$	1.445	0.203
12	1,4-F$_2$	−0.109	−0.004
13	1,4-Cl$_2$	0.980	0.140
14	1,4-Br$_2$	1.438	0.203
15	1,4-I$_2$	2.000	0.300
16	1,2-Cl,F	0.523	0.072
17	1,3-Cl,F	0.469	0.073
18	1,4-Cl,F	0.469	0.082
19	1,2-Br,F	0.794	0.110
20	1,3-Br,F	0.704	0.111
21	1,4-Br,F	0.722	0.118
22	1,2-Br,Cl	1.369	0.170
23	1,3-Br,Cl	1.213	0.171
24	1,4-Br,Cl	1.203	0.170
25	1,2,4-Cl$_3$	1.394	0.180
26	F$_6$	−0.477	−0.047
27	Cl$_6$	2.529	0.337
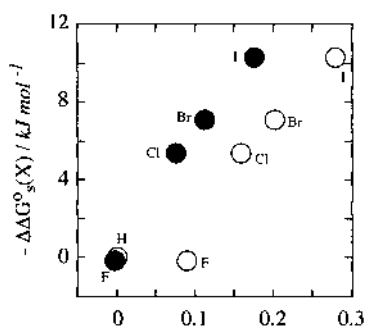
Fig. 5. Correlations between $-\Delta\Delta G_s^\circ(X)$ and Both Descriptors σ_M (○) and σ_a (●).

would be weak and consistent with that of a van der Waals complex rather than a hydrogen bond. In this paper, we also suggest that there are CH/F for fluorobenzene and CH/π for others. The two type interactions were thought to take the van der Waals complex rather than charge transfer interaction energy, E_{CT} by hydrogen bonding. The correlation between $\Delta\Delta G_s^\circ$ and σ_M deviated from the linear line in fluorobenzene but σ_a depended on van der Waals volume and showed a good fit (Fig. 5). These regression analyses are given by,

$$\text{intercept}=26.86(14.63)\sigma_M(X)-0.57(3.58) \tag{16}$$

$$n=5,\ r=0.959,\ F=34.1,\ \text{S.D.}=1.53$$

$$\text{intercept}=61.47(9.29)\sigma_a(X)+0.19(0.92) \tag{17}$$

$$n=5,\ r=0.997,\ F=443.1,\ \text{S.D.}=0.44$$

The $\sigma_a(X)$ values were a much more efficient descriptor than $\sigma_M(X)$ for halogen.

Regression Analyses of $\log\gamma$ in Polysubstituted Halogenobenzene Derivatives We previously concluded[11] that the interaction between polyhalogenobenzene derivatives and the stationary phase was expressed using two descriptors σ_{s° and ΣR. The substituent constant of resonance effect R was derived from proton transfer equilibria by Swain et al.[12] and represented E_{CT}. When we reconsider the above conclusion, the regression analyses of $\log\gamma$ values are given by excluding E_{CT} as discussed in the 2nd section. The $\log\gamma$ values of polyhalogenobenzene derivatives[11] were carried out using $\sigma_a(X_n)$ and are given by,

$$\log\gamma=7.303(0.301)\sigma_a(X_n)-0.045(0.049) \tag{18}$$

$$n=27,\ r=0.995,\ F=2490.2,\ \text{S.D.}=0.072$$

These results suggest that the active complex between solute (even fluorine compound) and stationary phase is van der Waals interaction excluding charge transfer interaction under nonpolar condition.

References
1) Kawaki H., *Chem. Pharm. Bull.*, **41**, 797—803 (1993).
2) Glasstone S., Laidler K. J., Eyring H., "The Theory of Rate Processes—The Kinetics of Chmical Reactions, Viscosity, Diffusion and Electrochemical Phenomena—," McGraw-Hill Book Company, Inc., New York and London, Capter VII, 1941.
3) Littlewood A. B., Phillips C. S. G., Price D. T., *J. Chem. Soc.*, **1955**, 1480.
4) Takagi T., Tanaka T., Iwata N., Shindo Y., Iwara A., Katayama T., Izawa H., Fujii S., Sasaki Y., Proceedings of 4th Software Conference, Osaka, 1988, pp. 285—288.
5) Weast R. C. (ed.), "Handbook of Chemistry and Physics," 70th, CRC Press. Inc., 1989—1990, pp. C4—C551.
6) Gavezzotti A., *J. Am. Chem. Soc.*, **105**, 5220—5225 (1983).
7) Kawaki H., Sasaki Y., Takagi T., Fujii S., Masuda F., *Chem. Pharm. Bull.*, **37**, 3268—3271 (1989).
8) Weiss H.-C., Boese R., Smith H. L., Haley M. M., *Chem. Commun.*, **1997**, 2403—2404.
9) Scott R. R., Taylor R., *J. Phys. Chem.*, **100**, 7384—7391 (1996).
10) Howard J. A. K., Hoy V. J., O'Hagan D., Smith G. T., *Tetrahedron*, **52**, 12613—12622 (1996).
11) Sasaki Y., Fujii S., Takagi T., Kawaki H., *Chem. Pharm. Bull.*, **37**, 1554—1555 (1989).
12) Swain C. G., Unger S. H., Rosenquist N. R., Swain M. S., *J. Am. Chem. Soc.*, **105**, 492—502 (1983).