634 © 1985 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 58, 634—637 (1985) [Vol. 58, No. 2

Solvent Effects on Chemical Reactivities II. Aromatic Substitution Reactions

Takayuki Ohmae
Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980

(Received September 21, 1984)

The propagator method is applied to the study of solvent effects on reactivities of aromatic substitution reactions. We obtain the following set of results: (1) The influence of nonpolar solvent on electrophilic reactions is opposite to that on nucleophilic reactions; (2) the solvent which has the large dielectric constant weakens the directive power of a substituent group; (3) frontier orbitals control solvent effects on the chemical reactivities of aromatic substitution reactions.

Several theories have been proposed to explain experimental results of aromatic substitution reactions.[1-3] Fukui *et al.* have proposed the frontier electron theory.[4,5] Their theory was first introduced in discussing the orientation in electrophilic substitution reactions. Afterward, the theory has been applied not only to electrophilic, but also to radical and nucleophilic substitution reactions as well as addition reactions in conjugated molecules, showing its utility, through a satisfactory agreement of theory with experiment.[6,7]

In a previous work, we have successfully studied solvent effects on selectivities of pericyclic reactions using the propagator method.[8] In this paper, we investigate influences of nonpolar solvent on reactivities of aromatic substitution reactions.

Propagator

The reaction system in question is assumed to be well described by the following hamiltonian in the second quantized representation:[8]

$$\mathbf{H}_0 = \sum_s \alpha_s \mathrm{a}_s{}^\dagger \mathrm{a}_s + \sum_{s,t} \beta_{st} \mathrm{a}_s \mathrm{a}_t + \sum_q \mathrm{h}\omega \mathrm{b}_q{}^\dagger \mathrm{b}_q + \sum_q \sum_{s,t} (g_{st}^{q*} \mathrm{b}_q{}^\dagger + g_{st}^q \mathrm{b}_q) \mathrm{a}_s{}^\dagger \mathrm{a}_t, \tag{1}$$

where $\mathrm{a}_s^\dagger$ and a_s are respectively the creation and annihilation operators for the π-electron at the s th atom of a solute molecule, $\mathrm{b}_q^\dagger$ and b_q are the creation and annihilation operators for the phonon with mode q, respectively, α_s is the coulomb integral, β_{st} the resonance integral, ω the phonon energy and g_{st}^q the electron-phonon interaction constant. In this model, the solvent is replaced by a phonon gas and solvent-solute interaction by the electron-phonon interaction.[8,9] This model is realistic for nonpolar solvents.

The electron-phonon interaction constant is related with the dielectric constant, ε, of a solvent:

$$g_{st}^q \propto \left(\frac{1}{\varepsilon_\infty} - \frac{1}{\varepsilon}\right)^{1/2}, \tag{2}$$

where ε_∞ is the dielectric constant of the solvent measured at the optical mode.

The propagator, $\mathbf{G}^0(z) \equiv (z - \mathbf{H}_0)^{-1}$, which describes the electronic structure of the solute molecule interacting with solvents, is easily obtained with some approximations:[8,10]

$$\mathbf{G}^0(z) = [(z-\mathbf{h}) - \sum_q \boldsymbol{g}^{q*} n_q (z-\mathbf{h}+\omega)^{-1} \boldsymbol{g}^q - \sum_q \boldsymbol{g}^q (n_q+1)(z-\mathbf{h}-\omega)^{-1} \boldsymbol{g}^{q*}]^{-1}, \tag{3}$$

where

$$\mathbf{h} = \sum_s \alpha_s \mathrm{a}_s{}^\dagger \mathrm{a}_s + \sum_{s,t} \beta_{st} \mathrm{a}_s{}^\dagger \mathrm{a}_t. \tag{4}$$

Once the propagator is known we can obtain the eigenvalues and eigenvectors of $\mathbf{H}_0$.

Frontier Electron Density

Let us consider the frontier electron density:

$$f_r^{\mathrm{E}} \equiv \frac{1}{2\pi \mathbf{i}} \int_{\mathrm{H}} \mathrm{d}z \mathrm{G}_{rr}^0(z), \tag{5a}$$

$$f_r^{\mathrm{N}} \equiv \frac{1}{2\pi \mathbf{i}} \int_{\mathrm{L}} \mathrm{d}z \mathrm{G}_{rr}^0(z), \tag{5b}$$

where f_r^{E} and f_r^{N} are respectively the electron density of the highest occupied molecular orbital, HOMO, and the that of the lowest unoccupied molecular orbital, LUMO, and the contours H and L respectively enclose the poles ε_{H} and ε_{L} (see Fig. 1).

It is well known that the chemical reactivity is well correlated with the frontier electron density:[5] 1) in case of reactions with electrophilic reagents, that position having the higher density of HOMO is more susceptible to attack; 2) in case of reactions with nucleophilic reagents, that position having the higer density of LUMO is reactive.

Now, it is well known that the variation of solvent can change the rate and/or the reaction products. In case of aromatic substitution reactions, the variation of solvent changes the isomer ratio of products. In order to study this problem, it is sufficient for us to examine the solvent effects on the frontier electron density.

It is said that the interaction between the solute and the solvent is small, *i.e.*, $|g_{ij}^q| \ll 1$, in the aromatic substitution reaction.[12] Therefore, the propagator in Eq. 3 is well approximated as follows;

$$\mathbf{G}^0(z) \cong (z-\mathbf{h})^{-1} + (z-\mathbf{h})^{-1} \sum_q \boldsymbol{g}^{q*} n_q (z+\omega-\mathbf{h})^{-1} \boldsymbol{g}^q (z-\mathbf{h})^{-1} + (z-\mathbf{h})^{-1} \sum_q \boldsymbol{g}^q (n_q+1)(z-\omega-\mathbf{h})^{-1} \boldsymbol{g}^{q*} (z-\mathbf{h})^{-1}. \tag{6}$$

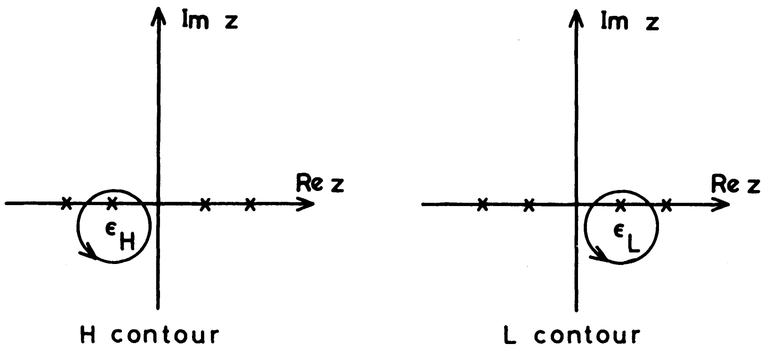

Fig. 1. Contours H and L.
ε_H is the energy of HOMO.
ε_L is the energy of LUMO.

Substituting Eq. 6 into Eqs. 5a and 5b, we obtain the frontier electron density including the solvent effect. For f_r^E,

$$\begin{aligned}
f_r^E &\equiv \frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\mathrm{G}^0_{rr}(\mathrm{z}) \\
&= \frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z<r|\{(z-\mathbf{h})^{-1} \\
&\quad + (z-\mathbf{h})^{-1}\sum_q \boldsymbol{g}^{q*}n_q(z-\mathbf{h}+\omega)^{-1}\boldsymbol{g}^q(z-\mathbf{h})^{-1} \\
&\quad + (z-\mathbf{h})^{-1}\sum_q \boldsymbol{g}^q(n_q+1)(z-\mathbf{h}-\omega)^{-1}\boldsymbol{g}^{q*}(z-\mathbf{h})^{-1}\}|\mathrm{r}> \\
&= f_r^{0E} + \sum_q\sum_{i,j} n_q|<r|i>|^2|g^q_{ij}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_i)^2(z-\varepsilon_j+\omega)} \\
&\quad + \sum_q\sum_{i,j}(n_q+1)|<r|i>|^2|g^q_{ij}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_i)^2(z-\varepsilon_j-\omega)} \\
&\cong f_r^{0E} + \sum_q n_q|<r|\mathrm{H}>|^2|g^q_{\mathrm{HL}}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_H)^2(z-\varepsilon_L+\omega)} \\
&\quad + \sum_q n_q|<r|\mathrm{L}>|^2|g^q_{\mathrm{HL}}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_L)^2(z-\varepsilon_H+\omega)} \\
&\quad + \sum_q(n_q+1)|<r|\mathrm{H}>|^2|g^q_{\mathrm{HL}}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_H)^2(z-\varepsilon_L-\omega)} \\
&\quad + \sum_q(n_q+1)|<r|\mathrm{L}>|^2|g^q_{\mathrm{HL}}|^2\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_L)^2(z-\varepsilon_H-\omega)} \\
&\cong f_r^{0E} + \sum_q(2n_q+)1|g^q_{\mathrm{HL}}|^2\frac{f_r^{0N}-f_r^{0E}}{(\varepsilon_H-\varepsilon_L)^2},
\end{aligned} \tag{7}$$

where we assume that the electron-phonon interaction constant has a dominant value between HOMO and LUMO. Moreover, we can approximate

$$\frac{1}{2\pi\mathbf{i}}\int_H \mathrm{d}z\frac{1}{(z-\varepsilon_L)^2(z-\varepsilon_H+\omega)} \cong \frac{1}{(\varepsilon_H-\varepsilon_L)^2}, \tag{8}$$

since $|\omega/\varepsilon| \ll 1$. Similarly f_r^N is obtained as

$$f_r^H \cong f_r^{0N} - \sum_q(2n_q+1)|g^q_{\mathrm{HL}}|^2\frac{f_r^{0N}-f_r^{0E}}{(\varepsilon_H-\varepsilon_L)^2} \tag{9}$$

In Eqs. 7 and 9, f_r^{0E} f_r^{0N} are respectively the usual density of HOMO and LUMO.

It should be noted here that the sign of the second term of Eq. 7 is opposete to that of Eq. 9. This shows that the solvent effect on electrophilic reactions is opposite to that on nucleophilic reactions.

Solvent Effect Index

We define a solvent effect index, τ_r,

$$\tau_r \equiv \frac{f_r^{0N}-f_r^{0E}}{(\varepsilon_H-\varepsilon_L)^2}. \tag{10}$$

In kindred reactions, the factors in Eqs. 7 and 9 which depend on the phonon mode q can be assumed to be of the same order. So the solvent effects on chemical reactivities are classified by the above index: in case of reactions with electrophilic reagent, that position having the large value of τ_r becomes susceptible to attack; in case of reactions with nucleophilic reagent, that position having the negative value of τ_r becomes more reactive.

The solvent effect indexes of several monosubstituted benzenoids (see Fig. 2) are listed in Table 1. Calcula-

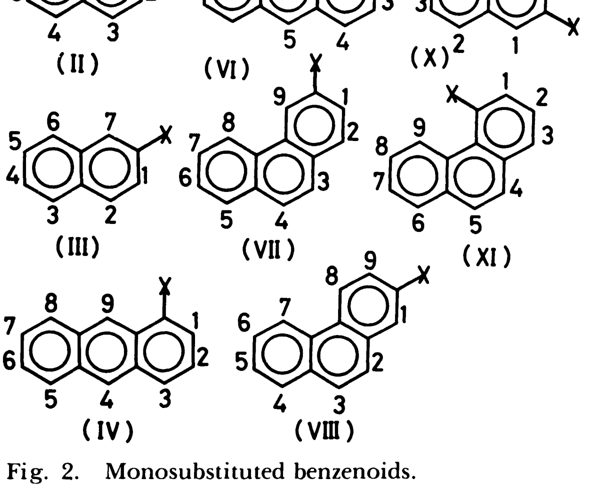

Fig. 2. Monosubstituted benzenoids.

tions are performed within the simple Hückel approximation. The parameters are taken from reference 2.

Table 1 shows the characteristic of the solvent effects on aromatic substitution reactions: 1) Substituent groups have a material effects; for example, at the sites 1 and 2 of molecule I with *ortho-*, *para-*directors, *e.g.*, OH, CH_3, Cl, and OCH_3, electrophilic reactions become favorable: on the contrary at the site 3 of molecule I with a *metha-*director, *e.g.*, NO_2, electrophilic reactions becomes favorable; this fact conclusively shows that solvent effects depend on the nature of the solute molecule only; 2) the stronger the directive power of *ortho-*, *para-*directors, the larger absolute value τ_r.

In conclusion, it should be noted that the solvent which has the large dielectric constant weakens the directive power of a substituent group. If we use the solvent which have the large dielectric constant, we can obtain the reaction products which are minor in the usual reaction conditions. For example, we can obtain the resolcinol using the substitution reaction of the

TABLE 1. SOLVENT EFFECT INDEXES OF MONOSUBSTITUTED BENZENOIDS

Molecule	Site X	OH	CH_3	Cl	OCH_3	NO_2
I	1	0.147	0.072	0.083	0.177	−0.037
	2	0.243	0.120	0.120	0.259	−0.145
	3	−0.121	−0.182	−0.157	−0.099	0.122
II	1	−0.215	−0.141	−0.054	−0.171	0.234
	2	0.113	0.035	0.019	0.123	−0.145
	3	−0.075	−0.133	−0.042	−0.010	0.035
	4	0.262	0.095	0.048	0.288	−0.318
	5	0.141	0.063	0.029	0.146	−0.164
	6	0.026	−0.013	−0.001	0.047	−0.047
	7	0.348	0.144	0.068	0.366	−0.416
III	1	0.171	0.115	0.059	0.164	−0.158
	2	0.296	0.038	0.026	0.326	−0.398
	3	0.325	0.063	0.038	0.350	−0.421
	4	−0.021	−0.051	−0.024	0.011	−0.014
	5	0.156	0.055	0.030	0.160	−0.185
	6	0.189	−0.005	0.003	0.234	−0.280
	7	−0.111	−0.122	−0.055	−0.026	0.056
IV	1	−0.443	−0.196	−0.088	−0.394	0.569
	2	0.099	0.016	0.009	0.112	−0.160
	3	−0.415	−0.229	−0.101	−0.343	0.478
	4	0.218	0.015	0.018	0.280	−0.376
	5	0.235	0.079	0.041	0.255	−0.333
	6	0.160	0.059	0.029	0.166	−0.218
	7	0.060	0.009	0.006	0.075	−0.099
	8	0.323	0.120	0.059	0.334	−0.438
	9	0.516	0.150	0.079	0.556	−0.755
V	1	0.237	0.062	0.054	0.237	−0.276
	2	0.205	0.009	0.010	0.205	−0.323
	3	0.500	0.046	0.046	0.500	−0.740
	4	0.272	0.031	0.031	0.272	−0.392
	5	0.026	−0.012	−0.009	0.026	−0.051
	6	0.150	0.021	0.019	0.150	−0.212
	7	0.164	0.004	0.007	0.164	−0.252
	8	0.126	−0.039	−0.027	0.126	−0.229
	9	−0.396	−0.101	−0.088	−0.396	0.568
VI	1	0.322	0.138	0.070	0.327	−0.399
	2	−0.104	−0.071	−0.030	−0.077	0.112
	3	0.177	0.083	0.041	0.179	−0.216
	4	0.075	0.010	0.011	0.101	−0.103
	5	−0.412	−0.289	−0.116	−0.307	0.450
VII	1	−0.053	0.012	0.004	−0.055	0.094
	2	0.187	0.034	0.022	0.217	−0.260
	3	0.327	0.090	0.052	0.363	−0.426
	4	0.116	−0.028	−0.006	0.174	−0.205
	5	0.169	0.032	0.022	0.198	−0.232
	6	0.002	−0.001	−0.001	0.002	−0.004
	7	0.144	0.030	0.019	0.168	−0.196
	8	0.101	0.026	0.016	0.114	−0.132
	9	−0.197	−0.090	−0.043	−0.164	0.225

Table 1. Continued

VIII	1	−0.091	−0.057	−0.026	−0.030	0.069
	2	0.287	−0.019	−0.009	0.317	−0.384
	3	0.342	0.018	0.008	0.362	−0.439
	4	0.232	0.025	0.012	0.246	−0.298
	5	−0.048	0.003	0.002	−0.037	0.042
	6	0.191	0.001	0.000	0.205	−0.249
	7	0.069	0.028	0.014	0.083	−0.100
	8	0.064	−0.025	−0.012	0.082	−0.111
	9	0.112	0.029	0.014	0.130	−0.129
IX	1	0.265	0.042	0.038	0.286	−0.083
	2	0.178	0.023	0.024	0.209	−0.265
	3	0.242	0.105	0.058	0.242	−0.303
	4	0.021	0.015	0.004	0.016	−0.018
	5	0.145	0.033	0.026	0.157	0.203
	6	0.185	0.109	0.053	0.170	−0.209
	7	−0.250	−0.165	−0.084	−0.196	0.271
	8	0.163	0.035	0.026	0.173	−0.231
	9	−0.198	−0.054	−0.035	−0.177	0.274
X	1	−0.199	−0.146	−0.062	−0.124	0.199
	2	0.104	0.021	0.014	0.126	−0.138
	3	0.018	0.013	0.003	0.014	−0.014
	4	0.021	−0.030	−0.007	0.053	−0.059
	5	0.150	0.072	0.032	0.144	−0.167
	6	0.033	−0.012	0.002	0.051	−0.064
	7	0.210	0.081	0.045	0.218	−0.258
	8	−0.024	−0.011	−0.007	−0.023	0.032
	9	0.162	0.025	0.027	0.190	−0.237
XI	1	−0.117	−0.089	−0.042	−0.067	0.111
	2	−0.023	−0.024	−0.013	−0.017	0.013
	3	−0.184	−0.177	−0.089	−0.114	0.146
	4	0.267	0.018	0.015	0.301	−0.367
	5	0.358	0.096	0.056	0.378	−0.455
	6	0.296	0.129	0.072	0.299	−0.353
	7	−0.017	0.006	0.003	−0.014	0.019
	8	0.195	0.042	0.026	0.208	−0.252
	9	0.159	0.113	0.061	0.157	−0.176

hydroxyl group.

References

1) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemistry," John Wiley (1961).

2) T. Yonezawa, C. Nagata, H. Kato, A. Imamura, and K. Morokuma, "Introduction to Quantum Chemistry," (in Japanese), Kagaku dohjin (1983).

3) K. Higashi, H. Baba, and A. Rembaum, "Quantum Organic Chemistry," John Wiley (1965).

4) K. Fukui, T. Yonezawa, and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952).

5) K. Fukui, T. Yonezawa, C. Nagata and H. Shingu, *J. Chem. Phys.*, **22**, 1433 (1954).

6) I. Fleming, "Frontier Orbitals and Organic Chemical Reactions," John Wiley (1976).

7) K. Fukui, "Chemical Reactions and Electron Orbital," (in Japanese), Maruzen (1976).

8) T. Ohmae, to be published.

9) R. D. Connon, "Electron Transfer Reactions," Butterworth (1980).

10) T. Ohmae, K. Nishikawa, K. Deguchi, and S. Aono, *Bull. Chem. Soc. Jpn.*, **54**, 3296 (1981).

11) C. Reichart, *Pure & Apple. Chem.*, **54**, 1867 (1982).