Transmission of Substituent Effects through Five-Membered Heteroaromatic Rings. III.
Addition Equilibria of Hydroxide Anion to Benzaldehyde Analogues

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Transmission of substituent effects through 5-membered heteroaromatic rings is investigated theoretically at the RHF/6-31+G* and B3LYP/6-31+G* levels using the equilibria for the OH⁻ addition to five-membered heteroaromatic aldehydes (5MHA). The transmission efficiency (S) in 5MHA(**A**) increases in the order NH > O > S > PH but the order exactly reverses in 5MHA(**T**⁻). This is originated by the delocalizability of the π lone-pair on Y, n_π(Y). A better correlation is obtained with σ_p than with σ_p^- in the Hammett plots with positive slope. $\rho_Z > 0$, indicating that the substituent (Z) effects are not transmitted by a direct conjugation. The magnitude of ρ_Z for Y=NH is the largest among the heteroaromatic systems. which is consistent with the largest transmission efficiency change (ΔS). The equilibria for the addition processes are favorable in the gas phase ($\Delta G° < 0$). which reverses to unfavorable in aqueous solution ($\Delta G° > 0$) due to the relatively large solvation energy of OH⁻ in the initial state in aqueous solution. The orders of $\Delta G°$ and ρ_Z in the gas phase are almost maintained in solution.

Introduction

In previous works.[1] we have reported transmission of substituent effects through five-membered heteroaromatic rings involved in the protonation equilibria of benzaldehyde analogues. Eq. (1).[1a] and the deprotonation equilibria of phenol analogues. Eq. (2)[1b] where Y = NH. O. PH and S. The transmission of substituent effects in the benzaldehyde ana-


5MHA(A)   P5MHA(AH⁺)

(1)

P(OH)   PA(O⁻)   + H⁺

(2)
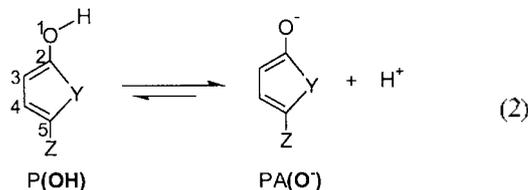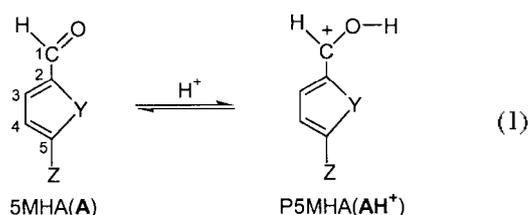
logues. 5MHA(**A**) of Eq. (1). was found to vary in parallel with the delocalizability of the π lone-pair on the heteroatom (n_π(Y)). Y = NH > O > S > PH. In contrast. the transmission of substituent effects in the protonated form. P5MHA(**AH**⁺). is dominantly influenced by the amount of cationic charge on C¹ and the para-delocalizability of the cationic charge on C¹ through the ring as a result of *competing resonance*⁻

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between n_π(Y) and substituent Z. On the other hand. for both **P(OH)** and **PA(O**⁻**)** states in Eq. (2). the transmission of substituent effects decrease in the order NH > O > PH > S.[1b] which is exactly the same order as that of π-delocalization ability of n_π(Y).[3]

Since in the reaction series of Eqs. (1) and (2) the transmission of substituent effects involves direct conjugation between substituent (Z) and a cationic functional center (C¹) and an anionic functional center (O¹) respectively. it would be of much interest to explore the transmission behaviors in the systems where such direct conjugation is absent.

In this work we have investigated theoretically the transmission of substituent effects in the addition equilibria of OH⁻ to benzaldehyde analogues Eq. (3). where Y = O. NH. PH. S and CHCH and Z = NH₂. CH₃. H. Cl. CN and NO₂. using the *ab initio* Hartree-Fock SCF and the Density Functional Theory (DFT) methods.[4] As noted in the previous works. the transmission behaviors of a heteroaromatic ring derivative depend strongly on the nature of the heteroatom (Y). *i.e.*. the transmission of substituent (Z) effect is dependent upon the availability of π lone-pair electrons on Y in the 2,5-conjugation.

5MHA(A)   + OH⁻   5MHA(T⁻)

(3)
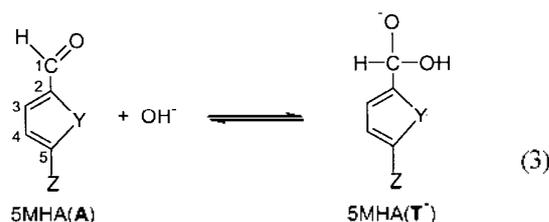
Y = O, NH, PH, S and CHCH

Z = NH₂, CH₃, H, Cl, CN and NO₂

Calculations

In order to obtain the structures and energies for the reactants and the tetrahedral addition intermediates in the gas phase, all the geometrical parameters were fully optimized without any geometrical constraints using Restricted Hartree-Fock (RHF) and DFT method of Becke's 3-parameter hybrid functional[5] using the Lee, Yang and Parr correlation functional[6] (B3LYP) with 6-31+G* basis set,[7] RHF/6-31+G*//RHF/6-31+G* and B3LYP/6-31+G*//B3LYP/6-31+G*. To confirm the stationary point species.[8] frequency calculations were also carried out at the RHF level.

The calculated electronic energy change (ΔE_{el}) in the gas phase was converted to enthalpy change (ΔH) at 298 K by correcting for the zero point vibrational energy (ΔE_{ZPVE}) with applying a scaling factor of 0.9153,[9] thermal energy (ΔE_{T_l} and PDV (=ΔnRT) terms. The Gibbs free energy change (ΔG) was then obtained using the calculated entropy changes (-TΔS) as Eq. (4).[10] The ΔE_{el} at B3LYP level was converted to the ΔH or ΔG using the thermochemical data calculated at the RHF level.

$$\Delta G = \Delta E_{el} + \Delta E_{ZPVE} + \Delta E_T + \Delta nRT - T\Delta S$$
$$= \Delta H - T\Delta S \qquad (4)$$

The solvation energies in aqueous solution with dielectric constant (ε) of 78.5 were calculated using the Polarizable Continuum Model (PCM)[11] and the Isodensity Polarizable Continuum Model (IPCM).[12] In the PCM and IPCM methods. the solvation Gibbs free energy (ΔG_s) was obtained at the B3LYP level using the geometries optimized at the same level. PCM-B3LYP/6-31+G*//B3LYP/6-31+G* and IPCM-B3LYP/6-31+G*//B3LYP/6-31+G*. The Gibbs free energy change (ΔG_{aq}) in aqueous solution is defined by Eq. (5) where $\delta \Delta G_s$ denotes the difference of ΔG_s between 5MHA (T$^-$) and sum of 5MHA(A) and OH$^-$. Gausian 98 program package[13] was used throughout this work.

$$\Delta G_{aq} = \Delta G_{gas} + \delta \Delta G_s \qquad (5)$$

Results and Discussion

Energetics in the Gas Phase. In this work, we have focused on the transmission of substituent effects involved in the addition equilibria of OH$^-$ to 5MHA(A) forming tetrahedral adducts (T$^-$) as shown in Eq. (3). Ion-dipole complexes and a transition state (TS) should exist on the potential energy surface (PES) along the reaction coordinate. if the addition processes were to occur through a double-well PES. However, the addition processes in the gas phase are found to have a single-well PES without any intervening species. We have tried to locate a TS for the reaction with Z = H, however we could not locate the TS because 5MHA (T$^-$) was directly formed without any ion-dipole complexes. Accordingly we can safely assume that Eq. (3) proceeds through a single-well PES irrespective of Y and Z.

The calculated energetics for the gas-phase addition of OH$^-$ to the 2-substituted heteroaromatic aldehydes with Z =

Table 1. The calculated energetics (in kcal mol^{-1}) for the addition equilibria of OH$^-$ to the 2-substituted heteroaromatic aldehydes with Z = H, Eq. (3), in the gas phase

Y	Method	ΔE^{ea}	ΔH^{ob}	-TΔS^{ob}	ΔG^{ob}
CHCH		-31.45	-32.68	9.97	-22.71
NH		-28.64	-29.86	10.02	-19.84
O	RHF/6-31+G*	-33.43	-34.70	10.19	-24.51
PH		-32.47	-33.69	10.08	-23.62
S		-33.67	-34.88	9.92	-24.96
CHCH		-32.99	-34.22	9.97	-24.25
NH		-28.61	-29.83	10.02	-19.81
O	B3LYP/6-31+G*	-32.69	-33.95	10.19	-23.76
PH		-33.12	-34.35	10.08	-24.27
S		-33.41	-34.62	9.92	-24.70

^{a}Electronic energy changes are corrected for zero-point vibration energies. ^{b}At 298.15 K.

H are summarized in Table 1. Examination of Table 1 shows that the reaction energies (ΔE°) at both the RHF and B3LYP levels are similar within 1.5 kcal mol^{-1}. However the orders of ΔE° calculated by the two methods are slightly different. *i.e.*, $-\Delta E^\circ$ increases in the order Y = NH (< CHCH) < PH < O < S by RHF but Y = NH < O (< CHCH) < PH < S at the B3LYP level. We will mainly discuss using the results of the B3LYP level since electron correlation effect is accounted for in the DFT method.[14]

Table 1 shows that the enthalpy (ΔH°) and/or Gibbs free energy changes (ΔG°) are exoergic. though ΔG° is unfavorable by *ca.* 10 kcal mol^{-1} compared to ΔH° due to positive contribution of entropy changes (-TΔS°). This indicates that the gas-phage equilibria are much more favorable toward the formation of the 5MHA(T$^-$) species. We find that ΔG° for the heteroaromatic derivatives are comparable to that of benzaldehyde (Y = CHCH) within *ca.* ± 0.5 kcal mol^{-1} except for the pyrrole derivative (Y = NH) which is much more unfavorable by 4.43 kcal mol^{-1} (Table 1).

The Gibbs free energy change (ΔG°) is in the same order as that of ΔE°: NH < O < PH ($\cong$ CHCH) < S. This order is in line with the result previously reported for the deprotonation equilibria. Eq. (2).[1b] However abolute changes of ΔG relative to Y = NH, $|\delta \Delta G|$ (= $|\Delta G(Y) - \Delta G(Y=NH)|$). for Eq. (3) are much smaller than those for Eq. (2); 3.95 (Y = O) ~4.89 (Y = S) kcal mol^{-1} for Eq. (3). 7.88 (Y = O) ~12.50 (Y = S) kcal mol^{-1} for Eq. (2). This is caused by the structural differences between products, PA(O$^-$) and 5MHA(T$^-$). *i.e.*, the transmission behavior of heteroaromatic rings of in PA(O$^-$) represents the direct conjugation between the heteroaromatic ring and reaction center, O^1. which is absent in 5MHA(T$^-$).

Since in the adduct. (T$^-$), the anionic charge of OH$^-$ should be accommodated. the ring charge increases in the adduct formation due to partial dispersion of the anionic charge. The greater the charge dispersion the more stable will be the adduct, and hence the greater will be the exothermicity. ΔE° (and ΔG°), of the reaction. Although the differences in ΔE° (or ΔG°) are small. the order of increasing exothermicity of the reaction (or stability of T$^-$), -ΔG. is Y = NH < O < PH < S at the B3LYP level. This is exactly the

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same order found for the deprotonation energies of phenol analogues, or the order of the $-\Delta G^0$ values for Eq .(2). Since in both processes, *i.e.*, deprotonation equilibria (Eq. (2)) and adduct (T^-) formation equilibria (Eq. (3)), the anionic charge dispersion of products determines the stability of products or free energy changes of the reaction, ΔG^0, the electron acceptor properties of Y, which was found as NH < PH < O < S, should be important. This is reflected indeed in the exothermicity if we exclude the anomalous heterocyclic compound with Y = PH.[15]

Transmission of Substituent Effects. The bond length change, Δd_{12}, can be regarded as a measure of the extent of transmission of substituent effects to the reaction center, carbonyl carbon, and is manifested in the form of contraction or stretching. The slope of the plot of d_{12} against σ_P (or σ_P^-)[16] of substituent Z, Eqs. (6), gave susceptibility parameter, *S*, as a measure of the transmission efficiency of the substituent effect of the reactant and the product. In the 5MHA(**A**), the d_{12} is better correlated with σ_P^+ than with σ_R since direct conjugation between the substituent (Z) and carbonyl center (C^1) is possible. However, in the 5MHA(**T**$^-$), the d_{12} is better correlated with σ_P rather than with σ_P^-, since there is no

$$d_{12} = S\,\sigma_P^- \qquad (6a)$$

$$d_{12} = S\,\sigma_P \qquad (6b)$$

direct conjugation as discussed above. The values of *S* determined using Eqs. (6) are summarized in Table 2. Examination of Table 2 reveals that the magnitude of *S* for 5MHA(**A**) decreases in the order NH > O > S > PH (>> CHCH).

This is the same order as that of the delocalizability of $n_\pi(Y)$, and the lowest value obtained for benzaldehyde (Y = CHCH) is a consequence of the longer chain involved as already discussed.[1a] The magnitude of *S* for 5MHA(**T**$^-$) is, however, in the reverse order NH < O < S, except for Y = PH[15] due to increased anionic charge densities in carbonyl moiety of 5MHA(**T**$^-$). We note in Table 2 that the sign of *S* is positive for both states but that of ΔS (= $S(T^-) - S(A)$) is negative. The positive, small *S* values for T^- indicate that there is very low resonance donation effect of the substituent (Z) is left still in the adduct (T^-), which is very much reduced compared to that in the reactants (**A**). As a result, in the adduct formation, an electron acceptor substituent, *e.g.* Z = *p*-NO$_2$, leads to a shorter d_{12}, and hence to a more stabilized adduct, **T**$^-$. The greater stability of **T**$^-$ with a stronger electron acceptor substituent (Z) should lead to a positive

Hammett reaction constant, $\rho_z > 0$, as we have obtained (*vide infra*).

To examine the substituent effects of the equilibrium, Eq. (3), the Hammett correlation, Eq. (7),[17] for the variation of substituent Z at C^5 was tested and the gas-phase ρ_Z values

$$-\frac{\Delta G}{2.303RT} = \rho\sigma \qquad (7)$$

obtained at RHF and B3LYP levels of theory are collected in Table 3. Since the Z-substituent is para to the reaction center, three types of para substituent constants, σ_P, σ_P^- or σ_P^-, have been tried.[18] The best correlation is obtained with s_P (rather than σ_P^-), which indicates that there is no direct conjugation in the transmission of substituent effects in Eq. (3), as expected from $\delta\Delta G$ values.

Reference to Table 3 reveals that the gas-phase ρ_Z values are positive and quite large (≥ 12) but the differences between two levels of theory, RHF and B3LYP, are very small and the trend is also similar. *e.g.*, at both the RHF and DFT levels, the ρ_Z values of all the heteromatics are much larger, by *ca.* 2-3 times than that of benzaldehyde and magnitude of the ρ_Z for 2-pyrrolyl system is the largest among the heteroaromatics. The smallest ρ_Z values for Y = CHCH can be ascribed to the longer chain involved with Y = CHCH as discussed in the susceptibility constant, *S*. The largest ρ_Z value for the 2-pyrrolyl system reflects the largest change of the transmission efficiency, ΔS, between 5MHA(**A**) and 5MHA(**T**$^-$) species as shown in Table 2.

Similar analyses were also performed using Swain-Lupton dual substituent parameters (DSP).[19] Eq. (8), where F and R represent field and resonance substituent constants and *f* and *r* are the susceptibility to F and R, respectively. The ratio of two susceptibilities. *f*/*r*, are also collected in Table 3. The magnitudes of *f*/*r* decrease in the order NH > O > S > PH. Since the resonance contribution is relatively small in 5MHA(**T**$^-$) compared with 5MHA(**A**), the lost resonance component of substituent effect is the largest for Y = NH and

$$-\frac{\Delta G}{2.303RT} = f\mathrm{F} + r\mathrm{R} \qquad (8)$$

Table 2. Susceptibility Constants, $S.^a$

Y	$S_{5MHA(A)}$	$S_{5MHA(T^-)}^b$	ΔS^c
CHCH	0.85	0.17	-0.68
NH	1.40	0.46	-0.94
O	1.16	0.60	-0.56
PH	1.02	$-^d$	$-$
S	1.04	0.67	-0.37

^{a}Values are $S \times 100$ and regression coefficients, $r > 0.93$. ^{b}Z = NO$_2$ was excluded. $^c\Delta S = S_{5MHA(T^-)} - S_{5MHA(A)}$. ^{d}Anomolous.

Table 3. Calculated Hammett type reaction constants (ρ_z) and the ratio of *f* and *r* (*f*/*r*) in the DSP analyses

Y	ρ_z				f/r^e
	RHF/3-21+G*^{a}	RHF/6-31+G*^{a}	B3LYP/6-31+G*^{a}	PCM^b	
CHCH	13.9	12.6	12.6	4.0^c	2.6
NH	18.0	15.4	16.2	10.9	3.5
O	16.1	14.2	15.1	5.6^d	3.4
PH	15.9	14.1	15.5	8.0	2.4
S	18.5	14.5	15.4	8.1^c	2.8

^{a}Regression coefficients. $r > 0.98$. ^{b}Regression coefficients. $r > 0.92$. ^{c}Z = NO$_2$ was excluded. ^{d}Z = NH$_2$ and Cl were excluded. ^{e}Regression coefficients. $r > 0.95$.

Table 4. The calculated ΔG_s and ΔG_{aq} (in kcal mol^{-1}) for the addition equilibria of OH$^-$ to the 2-substituted heteroaromatic aldehydes with Z = H, Eq. (3)

Y	Method	ΔG_s(5MHA (A) + OH$^-$)^a	ΔG_s(5MHA (T$^-$))	$\delta\Delta G_s^b$	ΔG_{aq}
CHCH		-110.60	-75.97	+34.63	+10.38
NH		-111.54	-75.48	+36.06	+16.25
O	PCM	-109.60	-78.49	+31.11	+7.35
PH		-108.68	-71.88	+36.80	+12.53
S		-109.71	-73.52	+36.19	+11.48
CHCH		-85.44	-64.24	+21.20	-3.05
NH		-87.12	-63.44	+23.68	+3.87
O	IPCM	-86.29	-65.38	+20.91	-2.85
PH		-86.59	-65.07	+21.52	-2.75
S		-86.18	-64.45	+21.73	-2.97

^{a}Sum of ΔG_s(5MHA(A)) and ΔG_s(OH$^-$). $^b\delta\Delta G_s = \Delta G_s$(5MHA(T$^-$)) – ΔG_s(5MHA(A)).

the smallest for Y = PH. Therefore the order of f/r is the same as that of S for 5MHA(A). because the order of S for 5MHA(A) represents the degree of delocalizability of n_π(Y) (*vide supra*).

Solvent Effects. The Gibbs free energy of solvation (ΔG_s) in aqueous solution for Eq. (3) are calculated using the PCM and IPCM methods. and the Gibbs free energy changes (ΔG_{aq}) obtained using Eq. (5) are summarized in Table 4. As can be seen in Table 4. the $\delta\Delta G_s$ values obtained by the PCM method are much larger (10-15 kcal mol^{-1}) than those obtained by the IPCM method, and hence the ΔG_{aq} obtained by PCM method are unfavorable compared to those obtained by IPCM method. These are mainly caused by the difference in the ΔG_s of nucleophile, OH$^-$. between two solvation models. PCM and IPCM, *i.e.*, the calculated ΔG_s was -104.5 kcal mol^{-1} by the PCM method but -80.4 kcal mol^{-1} by the IPCM method. Therefore it is expected that the solvent effect of OH$^-$ can be better reproduced by the PCM method than the IPCM method, since the experimental ΔG_s of OH$^-$ (104-107 kcal mol^{-1}) agrees well with that of the PCM method.[20] The continuum models neglect specific solvation such as hydrogen bonding to OH$^-$ so that anyone of the two models can not reproduce correctly the experimental solvation energy of OH$^-$ ion in water. Therefore the agreement of ΔG_s^o for OH$^-$ between experiment and PCM seems fortuitous. The Gibbs free energy (ΔG_{aq}) changes for Eq. (3) in aqueous solution are much more unfavorable than those in the gas phase. ΔG^o (Table 1), due mainly to the large initial state solvation energy of OH$^-$.

Analyses of NBO[21] charges have shown that negative charges on the aldehydic oxygen and ring increases by *ca.* -0.37 and 0.20 respectively in the adduct formation. In particular. the negative charge increase on the oxygen atom is in the order NH < PH < S < O but that on the ring is O < S < PH ≤ NH. Thus the negative charge increment for Y = O is the largest on the oxygen but is the smallest on the ring. Conversely the increment for Y = NH is the smallest on the oxygen but is the largest on the ring. This charge increment on the oxygen should lead to the solvation energy increase in

T$^-$ accordingly (Table 4). *i.e.*, the solvation energy of T$^-$ is the largest with Y = O and the smallest with Y = NH. However, examination of the ΔG_s(T$^-$) values in Table 4 reveals that this prediction is borne out with the IPCM model but is not with the PCM. for which the ΔG_s(T$^-$) for Y = NH is not the smallest. More specifically the order of charge increment of the oxygen agrees with that of the solvation energies of T$^-$ (ΔG_s(T$^-$)), NH < PH < S < O. by the IPCM method. but not with the PCM model which is PH < S < NH < O for ΔG_s(T$^-$). These analyses suggest that the solvation energies are better accounted for by the IPCM than PCM model.

The ΔG_{aq} value of Y = NH is the highest (+3.9 kcal mol^{-1}) with the rest of values (for Y = CHCH, O, PH and S) being very similar (~ -3.0 kcal mod^{-1}). This trend is the same as that found for the gas-phase free energy changes. ΔG^o in Table 1: the ΔG^o value is the highest with Y = NH (-19.8 kcal mol^{-1}) but the rest of values (for Y = CHCH. O. PH and S) are similar (~ -24.0 kcal mol^{-1}). This means that the solvent effect is almost uniform among the various heteroaromatics. as expected form the continuum solvation models.

Conclusion

The transmission efficiency (S) in the 5MHA(A) form decreases in the order NH > O > S > PH. On the contrary, the S in the 5MHA(T$^-$) is exactly in the reverse order. These are originated by the delocalizability of the π lone-pair on Y. n_π(Y). Accordingly the magnitude of ρ_Z for the reaction is the largest for 2-pyrrolyl system among the heteroaromatics due to the largest change in the S on going from 5MHA(A) to 5MHA(T$^-$). This is nearly the same results as that for the deprotonation equilibria of Eq. (2). The magnitudes of ρ_Z is however much smaller than that of Eq. (2) since the substituent (Z) effects can not be transmitted by direct conjugation in 5MHA(T$^-$). The equilibria of 5MHA(T$^-$) formation by OH$^-$ to addition heteroaromatic aldehydes are favorable in the gas phase with exothermic reaction energies, ΔG^o < 0. In contrast the equilibria in aqueous solution become unfavorable due to relatively large initial state solvation energy of OH$^-$. The solvent effects are, however, nearly uniform so that the gas-phase order of free energy changes. ΔG^o. is almost maintained in solution.

References

1. (a) Lee, I.; Rhee, S. K.; Kim, C. K.; Chung, D. S.; Kim, C. K. *Bull. Korean Chem Soc.* **2000**, *21*, 882. (b) Sohn, C. K.; Lim, S. H.; Rhee, S. K.; Kim, C. K.; Kim, C. K.; Lee, I. *Bull. Korean Chem Soc.* **2000**, *21*, 891.
2. (a) Yukawa, Y.; Tsuno, Y.; Sawada, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 2274. (b) London, G. M.; Berke, C. *J. Am. Chem. Soc.* **1974**, *96*, 4508.
3. Streitwieser, A.; Heathcock, C. H. *Introduction to Organic Chemistry*, 2nd ed.; Collier MacMillan: London, 1981; p 1069.
4. (a) Hohenberg, P.; Kohn, W. *Phys. Rev.* **1964**, *136*, B864.

(b) Kohn, W.; Sham, L. *J. Phys Rev.* **1965**, *140*, A1133.

5. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

6. (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B37*, 785. (b) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200.

7. Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986; Chapter 4.

8. (a) Pople, J. A.; Krishnan, R.; Schlegel, H. B.; Binkley, J. S. *Int. J. Quantum Chem.* **1979**, *S13*, 225. (b) Pople, J. A.; Schlegel, H. B.; Krishnan, R.; DeFree, D. J.; Binkley, J. S.; Frisch, M. J.; Whiteside, R. A.; Haut, R. F.; Hehre, W. *ibid.* **1979**, *S15*, 269.

9. Scott, A. P.; Radom, L. *J. Phys. Chem.* **1966**, *100*, 16502.

10. Foresman, J. B.; Frisch, A. E. *Exploring Chemistry with Electronic Structure Methods*, 2nd ed.; Gaussian Inc.: Pittsburg, 1996; p 166.

11. (a) Miertus, S.; Tomasi, J. *J. Chem. Phys.* **1982**, *65*, 239. (b) Miertus, S.; Scrocco, E.; Tomasi, J. *J. Chem. Phys.* **1981**, *55*, 117.

12. (a) Foresman, J.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. *J. Phys. Chem.* **1996**, *100*, 16098. (b) Wiberg, K. B.; Rablen, P. R.; Rush, D. J.; Keith, T. A. *J. Am. Chem. Soc.* **1995**, *117*, 4261. (c) Rablen, P. R.; Pearlman, S. A.; Miller, D. A. *J. Am. Chem. Soc.* **1999**, *121*, 227.

13. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98, Revision A.6*. Gaussian, Inc.: Pittsburgh, PA, 1998.

14. *Encyclopedia of Computational Chemistry*; Schleyer, P. v. R., Ed.; John Wiley & Sons: New York, 1998; vol. 1, p 664.

15. The structures of 5MHA(**A**) and 5MHA(**T**$^-$) with Y = PH show that the molecules are not coplanar with pyramidal angle of *ca.* 95-98° at the P atom. This non-planarity should lead to the anomalous behaviors of this compound and this anomalous behavior was also appeared for the deprotonation equilibria of Eq. (2).

16. Substitent constants, σ and σ^-, are taken from: Issacs, N. S. *Physical Organic Chemistry*, Longman Scientific & Technical, Harlow, 1987. Chapter 4.

17. Hammett, L. P. *Physical Organic Chemistry*; McGrawhill; New York, 1940.

18. The reaction system of Eq. (1) is considered as a formal analogue of para-substituted benzene derivatives; Chapman, N. B.; Shorter, J. Eds. Correlation Analysis in Chemistry, Plenum, New York, 1978. Chapter 5.

19. (a) Swain, C. G.; Lupton, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 4328. (b) Swain, C. G.; Unger, S. H.; Rosenquist, N. R.; Swain, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 492.

20. (a) Florián, J.; Warshel, A. *J. Phys. Chem. A* **1997**, *101*, 5583. (b) Chamber, C. C.; Hawkins, G. D.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem.* **1996**, *100*, 16385.

21. (a) Brunck, T. K.; Weinhold, F. *J. Am. Chem. Soc.* **1979**, *101*, 1700. (b) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899. (c) Glendening, E. D.; Weinhold, F. *J. Comput. Chem.* **1988**, *19*, 593, 610. (d) Glendening, E. D.; Badenhoop, J. K.; Weinhold, F. *J. Comput. Chem.* **1998**, *19*, 628.