

## Ab Initio Molecular Orbital Study on a Linear Relationship between Activation Energies of Menshutkin Reactions and Proton Affinities of Nitrogen Bases

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Received September 12, 1997

In a previous paper (*J. Am. Chem. Soc.* **1991**, *113*, 4738), we reported that there was a linear relationship between the activation free energies  $\Delta G^\ddagger$  of the Menshutkin reaction of  $\text{CH}_3\text{I}$  and the proton affinities for the corresponding nitrogen donor bases ( $\delta\text{PA}_{\text{obs}}$ , relative to  $\text{PA}_{\text{obs}}$  of ammonia). The  $\Delta G^\ddagger$  is dependent on the hybridization of the nitrogen, which means that a plot,  $\delta\text{PA}_{\text{obs}}$  vs  $\Delta G^\ddagger$  for the  $\text{N}(\text{sp}^2)$  donors, yielded a straight line that was different from a corresponding line for the  $\text{N}(\text{sp}^3)$  donors. Although *N,N*-dimethylaniline and its 4-substituted derivatives have formally  $\text{sp}^3$  nitrogen donors, their  $\delta\text{PA}_{\text{obs}} - \Delta G^\ddagger$  points were observed to be neither on the  $\text{sp}^3$  nor on the  $\text{sp}^2$  line. In the present study, ab initio molecular orbital (MO) calculations are adopted to explain why there are different linear relationships between the two energies of the three types of bases. Our calculations show that at the MP2/6-31+G\*/RHF/6-31+G\* level of theory the calculated  $\delta\text{PA}_{\text{calc}}$  values have a linear correlation with the  $\delta\text{PA}_{\text{obs}}$ . Differences of calculated activation energies ( $\delta E_a$ , relative to that of  $\text{NH}_3$ ) also show a good linear relationship with the  $\delta\text{PA}_{\text{calc}}$ . The C–X distances (X = N or Cl) at the TS structures are also closely correlated with the  $\delta E_a$ , i.e., the Menshutkin reaction with a shorter C–N distance in the TS has to overcome a higher activation energy. The  $\delta\text{PA}_{\text{calc}}$  values should be reduced when we use the  $\delta\text{PAs}$  of the  $\text{sp}^2$  bases as indices of nucleophilicity in Menshutkin reactions in the gas phase.

### Introduction

The quantitative study of substituent effects, which is one of the most important issues in organic chemistry, has been carried out for many reactions. The complete and detailed surveys were conducted in the reaction of the  $\text{S}_{\text{N}}1$ -type solvolysis.<sup>1</sup> The basic concepts in physical organic chemistry are best analyzed by using the simple reaction systems. The Menshutkin reaction (MR)<sup>2</sup> expressed by eq 1 is also one of the systems that have been used for analyzing the substituent effect in detail.



Rates of MRs are dependent on nucleophilicity of Y. To test this fact, one of us correlated the observed proton affinities ( $\text{PA}_{\text{obs}}$ ) and activation free energies  $\Delta G^\ddagger_{\text{obs}}$  of MRs with  $\text{CH}_3\text{I}$  and bases in acetonitrile. The  $\delta\text{PA}_{\text{obs}}$  and  $\delta\Delta G^\ddagger_{\text{obs}}$  energies were used for a correlation analysis; both of them are referred to the corresponding values of ammonia. Two linear relationships, which are dependent on hybridization of the donor atoms in nucleophiles, were observed in  $\delta\text{PA}_{\text{obs}}$  vs  $\delta\Delta G^\ddagger_{\text{obs}}$  plots.<sup>3</sup> On the other hand,  $\delta\Delta G^\ddagger_{\text{obs}}$  of *N,N*-dimethylaniline and its 4-substituted derivatives, which have formally  $\text{sp}^3$  nitrogen donors,

locate neither on the  $\text{sp}^3$  nor on the  $\text{sp}^2$  line. These facts led to the conclusion that the gas-phase PA of nucleophiles has a close relation to their reactivity, i.e., nucleophilicity, in solution. A similar relation was also observed in the charge-transfer association of bases and  $\text{I}_2$ .<sup>4</sup>

Many theoretical investigations have been performed to study  $\text{S}_{\text{N}}2$  mechanism of small systems in detail.<sup>5</sup> Some of them dealt with substitution or leaving-group effects for the reaction mechanism.<sup>6</sup> The mechanism of the MR as a typical  $\text{S}_{\text{N}}2$  reaction has been investigated by using ab initio molecular orbital (MO) calculations.<sup>7</sup> Gao et al. investigated the potential energy profile, including solvent effect.<sup>8</sup> A new approach for characterizing the TS in the MR was performed by Shaik et al.<sup>9</sup> However, these theoretical studies analyzed only small systems.

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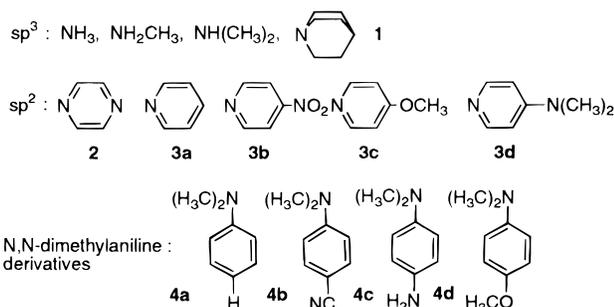
Table 1. Calculated Energies of Reactants, Transition States and Protonated Forms.

		Nu	TS	Nu <sup>+</sup>	NuCH <sub>3</sub> <sup>+</sup>	PA	MA	E <sub>a</sub>
NH <sub>3</sub>	RHF	-56.189 50	-555.225 98	-56.531 28	-95.574 16	214.5	96.5	36.2
	MP2	-56.362 66	-555.660 24	-56.700 41	-95.869 17	211.9	113.5	37.4
	MP4	-56.379 38	-555.712 95	-56.718 73		212.9		36.4
NH <sub>2</sub> CH <sub>3</sub>	RHF	-95.210 69	-594.255 35	-95.574 16	-134.614 27	228.1	108.4	31.1
	MP2	-95.511 32	-594.821 05	-95.869 15	-135.038 75	224.5	126.7	29.8
	MP4	-95.544 54	-594.890 52	-95.904 09		225.6		28.6
NH(CH <sub>3</sub> ) <sub>2</sub>	RHF	-134.242 64	-633.285 81	-134.614 27	-173.651 61	233.2	111.7	32.0
	MP2	-134.673 94	-633.986 17	-135.038 73	-174.209 14	228.9	131.5	28.2
	MP4	-134.723 44	-634.071 96	-135.090 07		230.1		27.0
1	RHF	-327.082 75	-826.130 32	-327.477 00	-366.510 62	247.4	123.6	29.2
	MP2	-328.168 67	-827.490 19	-328.551 35	-367.723 62	240.1	143.9	22.4
2	RHF	-262.690 48	-761.720 16	-263.036 47	-302.076 53	217.1	97.4	40.5
	MP2	-263.517 08	-762.814 44	-263.854 88	-303.029 01	212.0	117.0	37.6
3a	RHF	-246.703 49	-745.740 84	-247.073 67	-286.110 20	232.3	110.3	35.6
	MP2	-247.496 07	-746.800 54	-247.855 00	-287.026 37	225.2	128.5	33.1
3b	RHF	-450.174 37	-949.201 43	-450.516 46	-489.555 10	214.7	94.0	42.1
	MP2	-451.509 18	-950.805 35	-451.845 57	-491.018 41	211.1	115.3	38.3
3c	RHF	-360.589 99	-859.629 98	-360.972 11	-400.006 74	239.8	116.6	34.0
	MP2	-361.692 51	-860.998 96	-362.061 50	-401.231 07	231.5	133.7	31.9
3d	RHF	-379.789 62	-878.833 80	-380.187 92	-419.221 30	249.9	126.0	31.4
	MP2	-381.016 26	-880.326 56	-381.401 66	-420.569 85	241.8	143.1	29.4
4a	RHF	-363.790 34	-862.823 90	-364.167 30	-403.192 47	236.5	107.5	38.0
	MP2	-364.986 81	-864.297 06	-365.355 91	-404.521 28	231.6	131.1	29.5
4b	RHF	-455.527 73	-954.555 45	-455.887 80	-494.913 66	225.9	97.3	41.7
	MP2	-456.998 94	-956.306 14	-457.354 47	-496.520 52	223.1	123.0	31.4
4c	RHF	-418.818 51	-917.855 31	-419.203 21	-458.228 47	241.4	112.4	36.0
	MP2	-420.182 37	-919.496 86	-420.560 07	-459.725 48	237.0	136.5	26.8
4d	RHF	-477.670 75	-976.707 07	-478.052 70	-517.078 09	239.7	102.5	36.3
	MP2	-479.179 10	-978.492 39	-479.552 95	-518.718 39	234.6	134.1	27.6

<sup>a</sup> Total energies are given in hartrees and PA, E<sub>a</sub> and MA in kcal mol<sup>-1</sup>. MP2 and MP4 mean energies at the MP2/6-31+G\*//RHF/6-31+G\* and MP2(SDTQ)/6-31+G\*//RHF/6-31g\* levels of theory.

From the experimental viewpoint of physical organic chemistry, these studies are important and very attractive. However, substituent effects of the MRs have been well investigated and discussed in much larger systems. In substrates and in nucleophiles, they have one or more aromatic rings to which we can introduce many types of substituents. Therefore, large substituents and nucleophiles are essential to investigation into substituent effect on the MRs in order to compare experimental results with theoretical ones.

In the present study, our attention is focused on the observed  $\delta\text{PA}_{\text{obs}} - \delta\Delta G_{\text{obs}}^{\ddagger}$  relation depending on hybridization of nitrogen donors and the substituent effect of nucleophiles. Therefore, we used relatively large bases to make the following calculations. Methyl chloride instead of its iodine analogue, i.e., X = Cl in eq 1, was adopted as a model reactant for the simplicity of calculations.



To confirm the origin of the observed linear relationship, we estimated and correlated PA<sub>calc</sub> and the activation energies (E<sub>a</sub>) of the MRs at the MP2/6-31+G\*//RHF/

6-31+G\* level of theory. The relationship between the proton affinity and the activation energies of Y was analyzed in detail by using results of ab initio MO calculations. According to the Leffler–Hammond principle,<sup>10,11</sup> we have to compare  $\delta\Delta G_{\text{obs}}^{\ddagger}$  with the methyl cation affinities (MA) instead of the PA values since the products of the reactions are CH<sub>3</sub>Y<sup>+</sup> in the present study. Therefore, we also estimated the MAs at the MP2/6-31+G\*//RHF/6-31+G\* level of theory for all the nucleophiles and investigated the  $\delta\text{MA} - \delta E_a$  relationship.

### Method of Calculations

Ab initio MO calculations were performed by using the GAUSSIAN94 program<sup>12</sup> to optimize stable and transition-state (TS) structures at the RHF/6-31+G\* level of theory. Vibrational frequency calculations showed all the TSs to have only one imaginary frequency as listed in Table 2.

PA<sub>calc</sub>(Y) or MA<sub>calc</sub>(Y), the energy differences between a base Y and YH<sup>+</sup> or YCH<sub>3</sub><sup>+</sup>, are defined by eqs 2 and 3

$$\text{PA}_{\text{calc}}(\text{Y}) = E_{\text{Y}} - E_{\text{YH}^+} \quad (2)$$

$$\text{MA}_{\text{calc}}(\text{Y}) = E_{\text{Y}} - E_{\text{YCH}_3^+} \quad (3)$$

where E<sub>Y</sub>, E<sub>YH<sup>+</sup></sub> and E<sub>YCH<sub>3</sub><sup>+</sup></sub> are the total energies of Y, YH<sup>+</sup>, and YCH<sub>3</sub><sup>+</sup>. To ascertain what level of theory is required for quantitative discussions about the substituent effect, the PA<sub>calc</sub>

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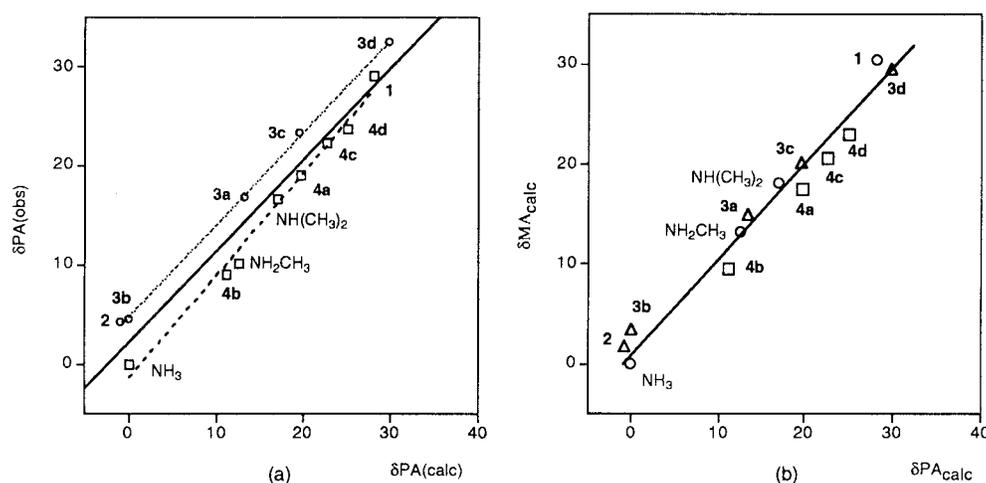
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**Table 2.** C–Cl, C–N Lengths, Mulliken Charges, and Energetic Parameters for the Menshutkin Reactions Depending on Nucleophiles

	C–Cl <sup>a</sup> (Å)	N–C <sup>a</sup> (Å)	$\nu^b$ (cm <sup>-1</sup> )	Cl <sup>c</sup>	CH <sub>3</sub> <sup>c</sup>	amine	$\delta E_a^d$	$\delta PA_{\text{calc}}^{d,e}$	$\delta PA_{\text{obs}}^d$	$\delta MA_{\text{calc}}^{d,e}$
CH <sub>3</sub> Cl <sup>f</sup>	1.785			-0.062	0.062					
NH <sub>3</sub>	2.474	1.900	559.1i	-0.700	0.494	0.206	0.0	0.0	0.0	0.0
NH <sub>2</sub> Me	2.422	1.943	595.7i	-0.664	0.435	0.229	7.6	12.6	10.1	13.1
NHMe <sub>2</sub>	2.394	1.965	584.8i	-0.643	0.409	0.235	9.2	17.0	16.6	18.0
N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> CH	<b>1</b>	2.358	593.0i	-0.589	0.341	0.248	15.0	28.2	29.0	30.4
NC <sub>4</sub> H <sub>4</sub> N	<b>2</b>	2.463	561.1i	-0.671	0.337	0.334	-0.1	0.0(0.0)	4.5	3.4(2.4)
NC <sub>5</sub> H <sub>5</sub>	<b>3a</b>	2.432	570.6i	-0.664	0.365	0.299	4.3	13.3(6.8)	16.8	14.9(10.5)
NC <sub>5</sub> NO <sub>2</sub>	<b>3b</b>	2.469	562.3i	-0.677	0.352	0.325	-0.9	-0.9(-0.4)	4.2	1.7(1.2)
NC <sub>5</sub> OCH <sub>3</sub>	<b>3c</b>	2.419	574.7i	-0.661	0.366	0.296	5.6	19.6(10.1)	23.3	20.1(14.1)
NC <sub>5</sub> H <sub>4</sub> NMe <sub>2</sub>	<b>3d</b>	2.402	578.6i	-0.650	0.363	0.287	8.0	29.9(15.4)	32.4	29.5(20.7)
NMe <sub>2</sub> Ph	<b>4a</b>	2.411	593.1i	-0.632	0.390	0.242	8.0	19.7	19.0	17.5
NMe <sub>2</sub> PhCN	<b>4b</b>	2.425	594.2i	-0.626	0.397	0.229	6.0	11.2	9.0	9.5
NMe <sub>2</sub> PhNH <sub>2</sub>	<b>4c</b>	2.402	594.9i	-0.630	0.431	0.198	10.6	25.1	23.7	23.0
NMe <sub>2</sub> PhOCH <sub>3</sub>	<b>4d</b>	2.422	594.0i	-0.630	0.473	0.157	9.9	22.7	22.3	20.6

<sup>a</sup> C–X (X = Cl, N) lengths (Å) in the TS structure. <sup>b</sup> Imaginary frequencies of TS structures. <sup>c</sup> Mulliken charges of Cl, CH<sub>3</sub>, and amine fragments. <sup>d</sup> Energies in kcal mol<sup>-1</sup>. <sup>e</sup> Values in parentheses are the reduced  $\delta PA_{\text{calc}}$ . <sup>f</sup> For CH<sub>3</sub>Cl, the values are those for the stable structure.

**Figure 1.** Linear relationships between (a)  $\delta PA_{\text{calc}}$  and  $\delta PA_{\text{obs}}$  (b)  $\delta PA_{\text{calc}}$  and  $\delta MA_{\text{calc}}$ . The solid, broken and dotted lines in (a) are the relation for all,  $sp^2$  and  $sp^3$  bases.

(Y) up to the MP4/6-31+G\*\*/RHF/6-31+G\* level of theory were estimated for small bases and compared with the corresponding values observed. Table 1 lists calculated total energies, PAs, and  $E_a$ 's of the MRs for the bases shown above.

The  $PA_{\text{calc}}(\text{NH}_3)$  is 211.9(212.9) kcal mol<sup>-1</sup> at the MP2/6-31+G\*\*/RHF/6-31+G\* (MP4/6-31+G\*\*/RHF/6-31+G\*) level of theory, while the  $PA_{\text{obs}}(\text{NH}_3)$  is 203.5 kcal mol<sup>-1</sup>.<sup>13</sup> The ab initio MO calculation overestimated the  $PA_{\text{calc}}(\text{NH}_3)$  by 8.4 (9.4) kcal mol<sup>-1</sup>, which corresponds to only 3.9% (4.6%) of the  $PA_{\text{obs}}$ . It is very difficult to directly reproduce absolute values for the PA of bases by using ab initio MO calculations even at the MP2/6-31+G\*\*/RHF/6-31+G\* level of theory.<sup>14</sup> Zhang et al. showed that the MP4/6-31+G\*\*/RHF/6-31+G\*\* level of theory was required in order to obtain the correct PA value for the nitrogen atom of glycine.<sup>15</sup>

The  $\delta PA$  was defined as the difference of the proton affinity relative to that of NH<sub>3</sub> (eq 4) estimated by ab initio MO calculations.

$$\delta PA = PA(Y) - PA(\text{NH}_3) \quad (4)$$

$$\delta MA = MA(Y) - MA(\text{NH}_3) \quad (5)$$

The  $\delta MA$  defined by eq 5 is similarly calculated from MA-(Y) and MA(NH<sub>3</sub>). Table 2 summarizes these relative energy parameters. A positive value of  $\delta PA(Y)$  means that the proton affinity of Y is larger than that of NH<sub>3</sub>. The  $\delta PA_{\text{calc}}$  was compared with  $\delta PA_{\text{obs}}$ , the observed  $\delta PA$  for the small  $sp^3$  bases. The  $\delta PA_{\text{calc}}$  values for NH<sub>2</sub>CH<sub>3</sub> and NH(CH<sub>3</sub>)<sub>2</sub> are 12.6-(12.7) and 17.0(17.2) kcal mol<sup>-1</sup> at the MP2/6-31+G\*\*/RHF/6-31+G\* level of theory, and those observed are 10.1 and 16.6 kcal mol<sup>-1</sup>, respectively.<sup>2</sup> The MP4/6-31+G\*\*/RHF/6-31+G\* level of theory gave  $\delta PA_{\text{calc}}$  similar to those of the lower level of theory. According to the results as well as the size of molecules investigated here, the energies mentioned below were used at the MP2/6-31+G\*\*/RHF/6-31+G\* level of theory unless otherwise noted.

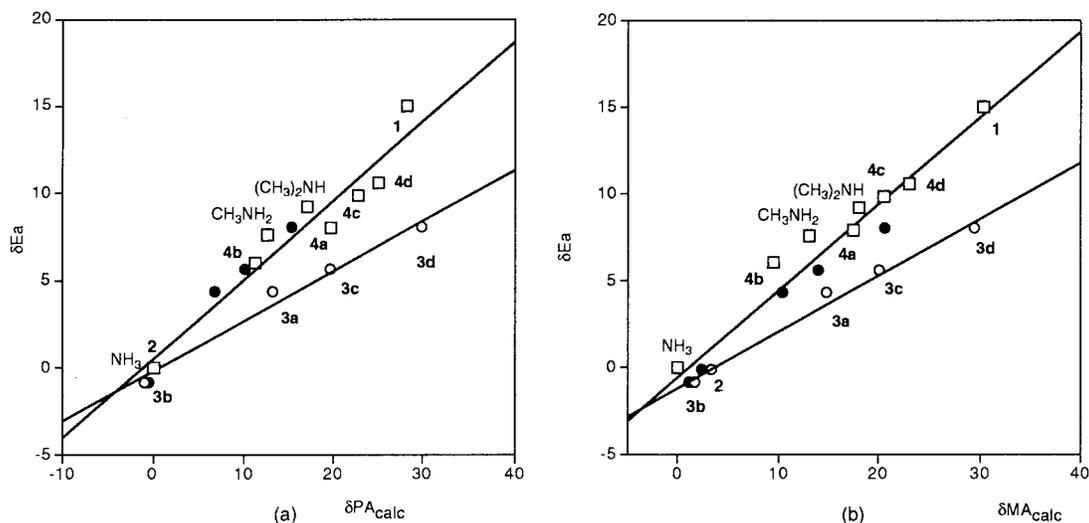
## Results and Discussion

**Comparison of  $\delta PA_{\text{obs}}$  and  $\delta PA_{\text{calc}}$ .** To check the reliability of  $\delta PA_{\text{calc}}$  for all the bases calculated in the present study, the  $\delta PA_{\text{obs}} - \delta PA_{\text{calc}}$  relation was first examined. Figure 1a displays calculated vs observed  $\delta PAs$ . The  $\delta PA_{\text{calc}}$  correlates well with the  $\delta PA_{\text{obs}}$ , and the slope of the line is 0.925 with the correlation coefficient of 0.969 (the solid line). However, we can see individual dependencies of the  $sp^3$  and  $sp^2$  bases. For example, all the  $\delta PA_{\text{calc}}$  points of the  $sp^3$  bases appear below the solid line. The  $\delta PA_{\text{calc}}$  of the  $sp^3$  bases is linearly related with those observed, and its slope is

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**Figure 2.** Plots of (a)  $\delta\text{PA}_{\text{calc}}$  vs.  $\delta E_a$  and (b)  $\delta\text{MA}_{\text{calc}}$  vs.  $\delta E_a$  of the bases. Closed circles in both figures show the points of the reduced  $\delta\text{PA}_{\text{calc}}$  of the  $\text{sp}^2$  bases.

almost unity (slope 1.031, intercept  $-1.375$ , correlation coefficient 0.993, the broken line). It means that the present level of theory is reliable enough to quantitatively discuss the  $\delta\text{PA}_{\text{calc}}$  of the  $\text{sp}^3$  bases. It is important to point out that  $\delta\text{PAs}$  of all the *N,N*-dimethylaniline derivatives were also included in making the  $\text{sp}^3$  line. They seem to rank as  $\text{sp}^3$  bases.

All the  $\delta\text{PA}_{\text{obs}}$  for  $\text{sp}^2$  bases are over the solid line in Figure 1a. A plot  $\delta\text{PA}_{\text{obs}}$  vs  $\delta\text{PA}_{\text{calc}}$  only for the  $\text{sp}^2$  bases is also linear with a correlation coefficient of practically 1.0 (the dotted line). The slope and the intercept of the obtained line are 0.928 and 4.752, respectively. It means that the present level calculations systematically slightly underestimate the  $\delta\text{PA}_{\text{calc}}$  in comparison with the  $\delta\text{PA}_{\text{obs}}$ . A more sophisticated level of theory should be adopted to estimate the correct  $\delta\text{PA}$  values of the  $\text{sp}^2$  bases.

Although one has to keep in mind that the computed  $\delta\text{PA}_{\text{calc}}$  values of the  $\text{sp}^2$  bases are associated with a small systematic error, it is nevertheless possible to investigate the substituent effect quantitatively via correlation of the proton affinity difference  $\delta\text{PA}_{\text{calc}}$  with the calculated properties such as activation energies, bond lengths, or Mulliken charges at the TS.

**Relation between  $\delta\text{MA}_{\text{calc}}$  and  $\delta\text{PA}_{\text{calc}}$ .** According to the Leffler–Hammond principle,<sup>10,11</sup> free energies of activation  $\Delta G^\ddagger$  are expected to have the relation to free energy difference between reactants and products,  $\Delta G_r$  and  $\Delta G_p$ , as follows,

$$G^\ddagger - \Delta G_r = \alpha(\Delta G_p - \Delta G_r) \quad (6)$$

or

$$\delta\Delta G^\ddagger/\delta\Delta G = \alpha \quad (7)$$

It is possible to relate the calculated  $\delta E_a$  to  $\delta\Delta G^\ddagger$  ( $= \Delta G^\ddagger - \Delta G_r$ ) and the calculated MA to the free energy difference  $\delta\Delta G$  ( $= \Delta G_p - \Delta G_r$ ), although we have to consider entropic effect. The MA rather than the PA should be used for analyzing the selectivity–reactivity relationship in the present study.

As mentioned above, our previous work<sup>3</sup> confirmed that  $\delta\text{PAs}$  show a clear linear relationship with  $\delta\Delta G^\ddagger$ . Therefore, there should be a linear relationship between  $\delta\text{PA}$

and  $\delta\text{MA}$ . The MA value of  $\text{NH}_3$  was calculated to be  $113.5 \text{ kcal mol}^{-1}$ , which is smaller by  $98.4 \text{ kcal mol}^{-1}$  than that of  $\text{PA}_{\text{calc}}(\text{NH}_3)$ . The other  $\text{MA}_{\text{calc}}$  are also smaller by  $100\text{--}120 \text{ kcal mol}^{-1}$  than the PAs. Despite the large differences among PAs and MAs, the relative values are very similar as listed in Table 2. Figure 1b, which displays the  $\delta\text{PA} - \delta\text{MA}$  plot, has a straight line with the relation

$$\delta\text{MA}_{\text{calc}} = 0.9872\delta\text{PA}_{\text{calc}} \quad (r = 0.981) \quad (8)$$

This relation between the two energies makes it possible to use  $\delta\text{PA}_{\text{calc}}$  instead of  $\delta\text{MA}_{\text{calc}}$  when we analyze the reactivity–selectivity relation in the present investigation.

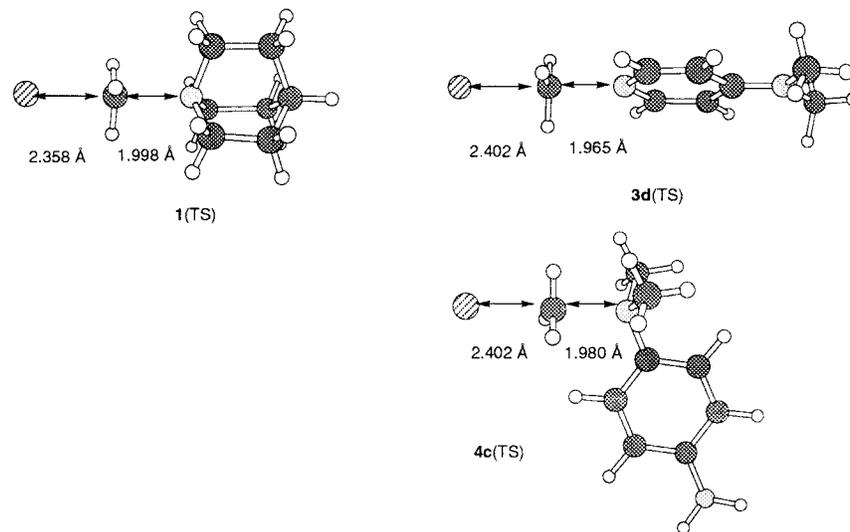
**Relation between  $\delta\text{PA}_{\text{calc}}$  and  $\delta E_a$ .** It was observed that the  $\delta\Delta G^\ddagger_{\text{obs}}$  of the MR is linearly correlated with the  $\delta\text{PA}_{\text{obs}}$ . Therefore, the TS structures with the nucleophiles shown above were next searched, and their activation energies were estimated. The  $E_a$  of the MR in the gas phase was estimated as the energy difference between the total energy of a TS and the sum of total energies of reactants,  $\text{CH}_3\text{Cl}$  and Y

$$E_a(\text{Y}) = E_{\text{TS}} - (E_{\text{CH}_3\text{Cl}} + E_{\text{Y}}) \quad (9)$$

The differences of the  $E_a$  ( $\delta E_a$ ) relative to that of  $\text{NH}_3$  was also estimated as follows

$$\delta E_a(\text{Y}) = E_a(\text{NH}_3) - E_a(\text{Y}) \quad (10)$$

A positive  $\delta E_a(\text{Y})$  means that a base Y is more reactive than  $\text{NH}_3$  in MRs. Figure 2a displays a correlation between  $\delta\text{PA}_{\text{calc}}$  and  $\delta E_a$ . In Figure 2, there are two linear relationships, i.e., one for the  $\text{sp}^3$  bases including the *N,N*-dimethylaniline derivatives and the other for the  $\text{sp}^2$  bases. There are no points distinctly deviating from the line consisting of the  $\delta\text{PA}_{\text{calc}} - \delta E_a$  points of the  $\text{sp}^3$  bases as well as **4a** and its derivatives. The slope of the  $\text{sp}^3$  line is 0.453, which is larger than that (0.287) of the  $\text{sp}^2$  bases. The correlation coefficients of the two lines are 0.984 and 0.993. This trend was seen in the observed  $\delta\text{PA} - \delta\text{GA}^\ddagger_{\text{obs}}$  plot.<sup>3</sup> The  $\text{sp}^3$  slope (0.156) experimentally obtained was also larger than the  $\text{sp}^2$  slope (0.143),



**Figure 3.** Comparison of TS geometries with the lowest activation energies of the  $sp^3$ , the  $sp^2$  bases and the  $N,N$ -dimethylaniline derivatives as nucleophiles.

although the difference between the slopes is not as large as that from the MO calculations.

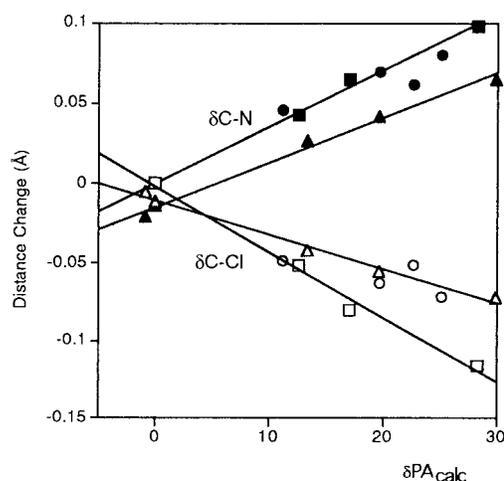
The  $\delta PA_{\text{calc}} - \delta E_a$  points of **4a** and its derivatives locate on the  $sp^3$  lines in Figures 1 and 2. It is, therefore, concluded that  $N,N$ -dimethylaniline derivatives act as the  $sp^3$ -type bases in the gas phase. The solvent effect may explain the strange behavior of these bases observed in the experiments.<sup>3</sup>

Figure 2b, showing the  $\delta MA - \delta E_a$  plot, is very similar to Figure 2a except for the slopes of straight lines. The slopes for  $sp^3$  and  $sp^2$  bases were estimated to be 0.461 ( $r = 0.986$ ) and 0.323 ( $r = 0.994$ ).

**Relation of  $\delta PA_{\text{calc}}$  and  $\delta C-X$  Distances in TS Structures.** Geometrical parameters, especially the C-N and the C-Cl distances at TSs, are considered to be one of the indices that specify the position of a TS along the reaction coordinate. As the  $E_a$  correlates well with the  $\delta PA_{\text{calc}}$ , we next analyzed the relation between  $\delta PA_{\text{calc}}$  and the two bond parameters in the TS structures listed in Table 2. Figure 3 displays the TS structures with the lowest  $E_a$  in the  $sp^3$ ,  $sp^2$  bases and  $N,N$ -dimethylaniline derivatives. It is important to point out that **4c(TS)** takes a pyramidal geometry around the N donor atom in the  $N(\text{CH}_3)_2$  fragment.

A nucleophile with a larger  $\delta PA_{\text{calc}}$ , i.e., a strong nucleophile, is expected to have a longer C-N distance and a shorter C-Cl length in the TS structure. The calculated results were consistent with the expectation. For example, the  $\delta PA_{\text{calc}}$  of **1** is larger by 28.2 kcal mol<sup>-1</sup> than that of  $\text{NH}_3$ . The C-N and the C-Cl distances of **1** in the TS were calculated to be 1.998 and 2.358 Å, respectively, while those lengths for  $\text{NH}_3$  are 1.900 and 2.474 Å. If these lengths change parallel to the reaction coordinates, the TS of **1** locates at an earlier position than that of  $\text{NH}_3$  along the reaction coordinate.

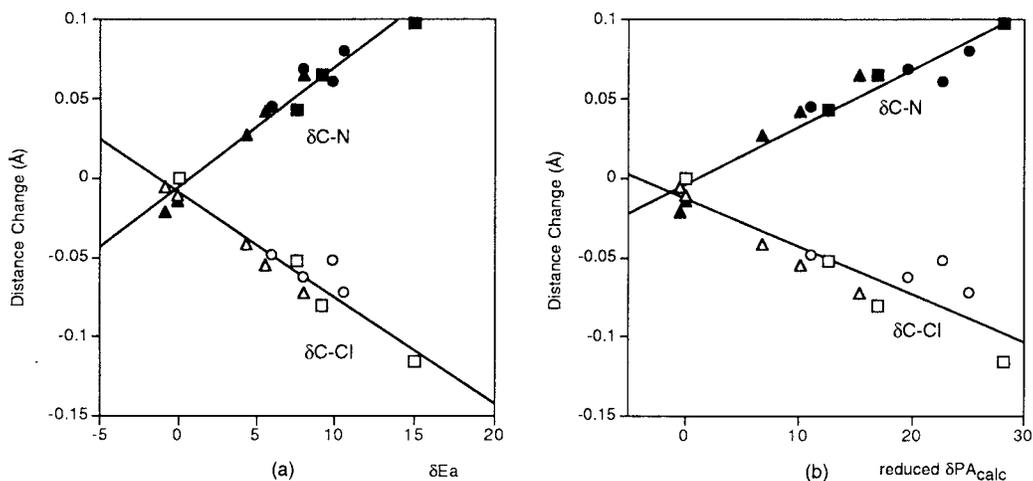
We also calculated the  $\delta C-X$  ( $X = \text{Cl}, \text{N}$ ) in the TS structure, the difference in the C-X distance relative to the corresponding length for the  $\text{NH}_3$  system. Figure 4 displays the  $\delta C-X$  distance against the  $\delta PA_{\text{calc}}$ . All the correlation coefficients of the four lines in the figure are more than 0.995. The  $\delta C-\text{Cl}$  of the  $sp^3$  bases (open squares) shows a completely different dependence from that of the  $sp^2$  bases (open circles), while the largest  $\delta C-$



**Figure 4.** Linear Relationship of  $\delta PA_{\text{calc}}$  vs. the  $\delta C-X$  distance ( $X = \text{Cl}, \text{N}$ ) in the TS structures. Squares, circles, and triangles indicate points of  $sp^3$ ,  $sp^2$  bases and the  $N,N$ -dimethylaniline derivatives.

Cl is 0.098 Å of **1** for the  $sp^3$  bases. The difference of the  $\delta C-\text{Cl}$  for the  $sp^2$  bases is 0.067 Å and that for  $N,N$ -dimethylaniline derivatives only 0.023 Å. The range of the  $\delta C-\text{N}$  length of the latter two bases is narrower than that for the  $sp^3$  bases.

**Relation of  $\delta E_a$  and  $\delta C-X$  Distances in TS Structures.** According to the Hammond postulate,<sup>10</sup> a TS with a low  $E_a$  is expected to have a long C-N distance and a short C-Cl distance since a low  $E_a$  indicates the position of a TS along IRC to be early. For example, these distances for **3d** were estimated to be 1.965 and 2.402 Å and those for **2** were 1.886 and 2.463 Å. The  $E_a$  of **3d** is smaller by 8.1 kcal mol<sup>-1</sup> than that of **2**. Therefore, the present results were consistent with the postulate. All the  $\delta C-X$  should correlate well with  $\delta E_a$  since the energy is one of the indices that exactly define the nucleophilicity of bases. This is true as shown in Figure 5a, which displays the relationship between the  $\delta C-X$  and the  $\delta E_a$ . This relation is completely different from that between the  $\delta C-X$  and  $\delta PA_{\text{calc}}$ . Points not only for the  $sp^3$  but for the  $sp^2$  bases make a single line in Figure 5, although there are a few points slightly deviating from the lines.



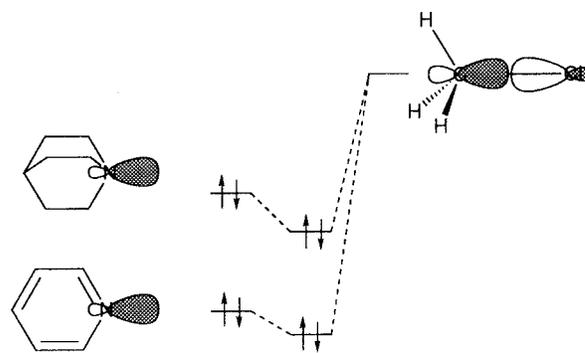
**Figure 5.** Linear Relationship of (a)  $\delta E_a$  or (b) reduced  $\delta PA_{\text{calc}}$  vs. the  $\delta C-X$  distance in the TS structures. Squares, triangles, and circles indicate points of  $sp^3$ ,  $sp^2$  bases and the  $N,N$ -dimethylaniline derivatives.

The slopes of the  $\delta C-Cl$  and the  $\delta C-N$  lines are  $-0.007$  and  $0.008$ , and the correlation coefficients are  $0.956$  and  $0.975$ .

**Reduced  $\delta PA$  as a Scale of Nucleophilicity of the  $sp^2$  Bases.** As the activation energy is an exact index of nucleophilicity of a nucleophile, we cannot always obtain the values, and therefore,  $\delta PAs$  could perhaps be appropriate as another index of the nucleophilicity of bases. However, this index is dependent on hybridization of nitrogen donors in the present case. For example, the  $\delta PA_{\text{calc}}$  for **1** turned out to be  $28.2 \text{ kcal mol}^{-1}$ , which differs only by  $1.7 \text{ kcal mol}^{-1}$  from that of **3d** ( $29.9 \text{ kcal mol}^{-1}$ ). It is likely that the nucleophilicity of **1** is almost the same as that of **3d**, and the two nucleophiles are expected to have similar  $E_a$ 's. However, the  $E_a$  of the former was calculated to be  $22.4 \text{ kcal mol}^{-1}$ , which is smaller by  $7.0 \text{ kcal mol}^{-1}$  than that of the latter ( $29.4 \text{ kcal mol}^{-1}$ ). These results tell us that the nucleophilicity of **1** is larger than that of **3d** although they have similar PAs. This trend is confirmed about all the  $sp^2$  bases by the result that the slope for the  $sp^2$  bases in Figure 2 is smaller than that of the  $sp^3$  bases.

To use the  $\delta PA$  as the index of the nucleophilicity of all bases, we have to introduce a scale factor, which should be  $0.5446 = 0.287/0.527$ , the ratio of slopes of the  $\delta PA_{\text{calc}} - \delta E_a$  plots of the  $sp^2$  and  $sp^3$  bases in Figure 2. The closed circles in Figure 2a are the points of the reduced  $\delta PA_{\text{calc}}$  of the  $sp^2$  bases. The slope, intercept, and correlation coefficient were calculated to be  $0.531$ ,  $-0.147$  and  $r = 0.990$  for the lines including all the  $\delta PA_{\text{calc}}$  of the  $sp^3$  bases and  $N,N$ -dimethylaniline derivatives as well as the reduced  $\delta PA_{\text{calc}}$  of the  $sp^2$  bases. A similar result was obtained for the  $\delta MAs$  as shown in Figure 2b. In the methyl cation case, the scale factor of the  $sp^2$  bases is  $0.647$ , which is estimated by the slopes of the  $\delta E_a - \delta MA$  plots. The slope, intercept, and correlation coefficient were calculated to be  $0.499$ ,  $-0.543$ , and  $r = 0.975$  for the lines including all the points with the reduced  $\delta PA_{\text{calc}}$ .

The reduced  $\delta PA_{\text{calc}} - \delta CX$  plot in Figure 5b also showed straight lines, although the correlation coefficient for the  $\delta C-Cl$  is a little low. The correlation coefficients of  $\delta C-Cl$  and  $\delta C-N$  were calculated to be  $0.899$  and  $0.963$ . Therefore, it is considered that the nucleophilicity of the  $sp^2$  bases in the gas phase is almost half as large



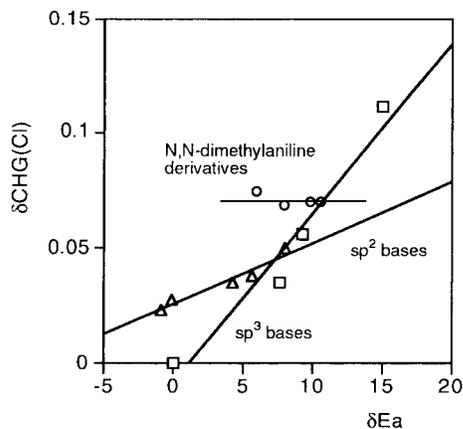
**Figure 6.** Schematic representations for orbital interactions between the LUMO of  $CH_3Cl$  and lone pair orbitals of  $sp^2$  and  $sp^3$  bases.

as that expected from the  $\delta PA_{\text{calc}}$  values. This trend originates from the lower energy of the lone pair orbitals of the  $sp^2$  bases.

**Relation of Nucleophilicity and Energy Level of Lone Pair Orbital.** It is easy to explain why the nucleophilicity of an  $sp^2$  base is weaker than that of an  $sp^3$  base, even though both have similar PAs. The  $E_a$  for the MR closely relates to the energy level of the lone pair orbital in a base. That is, in the beginning of the MR, the LUMO of  $CH_3Cl$  interacts with lone pair orbital of a nucleophile as shown in Figure 6. The  $s$ -orbital character in lone pair orbitals of **3a** and the other  $sp^2$  bases are larger than the  $sp^3$  bases since the former orbital takes the  $sp^2$  hybridization and the latter the  $sp^3$  hybridization. In general, the larger  $s$ -character of the  $sp^2$  bases lets the lone pair orbitals locate at lower positions than those of the  $sp^3$  bases. According to the Frontier orbital theory,<sup>16</sup> the smaller the energy gap between interacting orbitals is, the lower the activation energy is. Therefore, the nucleophilicity of an  $sp^2$  base is lower than that of  $sp^3$  bases when they have similar  $\delta PAs$ . Therefore,  $\delta PA_{\text{calc}}$  values should be reduced when we use the  $\delta PAs$  of the  $sp^2$  bases as indices of nucleophilicity.

**Relation of  $\delta PA_{\text{calc}}$  with Mulliken Charges in the TS Structures.** It is quite interesting to see how much

(16) (a) Fukui, K.; Yonezawa, T.; Shingu, H. *J. Chem. Phys.* **1952**, *20*, 722 (b) Fukui, K.; Yonezawa, T.; Nagata, C.; Shingu, H. *J. Chem. Phys.* **1954**, *22*, 1433.



**Figure 7.** The plots of relation between the  $\delta\text{CHG}(\text{Cl})$  and the  $\delta E_a$ .

charge in the leaving group, the Cl anion in the present case, is developed at a TS. The largest negative charge of  $-0.700$  was obtained for the TS with the  $\text{NH}_3$  fragment (Table 2). As the Mulliken charge of the Cl atom in  $\text{CH}_3\text{-Cl}$  is only  $-0.062$ , the halogen atom gets  $0.638$  from the  $\text{CH}_3$  and the  $\text{NH}_3$  fragments. The smallest negative charge ( $-0.589$ ) is obtained in the TS of **1**. The difference of the charges between the TS for  $\text{NH}_3$  and **1** is as large as  $0.111$ . As a larger  $E_a$  indicates the later position of a TS along the reaction coordinate, a larger charge is developed in the Cl at the TS for  $\text{NH}_3$  as expected. Figure 7 displays correlations between the  $\delta E_a$  and the  $\delta\text{CHG}(\text{Cl})$ , the difference between the Mulliken charge of the Cl atom in a TS(Y) and that in the TS( $\text{NH}_3$ ). The  $\delta\text{CHG}(\text{Cl})$  of the  $\text{sp}^3$  bases increases as the  $\delta E_a$  values increases.

We can see different dependences of the  $\delta\text{CHG}(\text{Cl})$  in the system with aromatic fragments in the figure. Although there is a clear linear relationship with the  $\text{sp}^2$  bases, its slope ( $0.003$ ) is less than half of the corresponding value of the  $\text{sp}^3$  bases ( $0.007$ ). The largest change in the Mulliken charges is only  $0.027$  at the  $\text{sp}^2$  bases. The  $\delta\text{CHG}(\text{Cl})$  shows no clear dependence on the  $\delta E_a$  with the *N,N*-dimethylaniline derivatives, i.e., the largest difference of values is  $0.0015$ . The effect of the aromatic

moiety in the nucleophiles is to produce a nearly constant charge in the leaving group at the TS. We could not extract any correlations between the  $\delta E_a$  and  $\delta\text{CHG}$  in the  $\text{CH}_3$  and the amine fragments.

### Concluding Remarks

It is quite important to determine nucleophilicity of nucleophiles in a reaction without estimating their activation energies because the molecules employed at experiments are, in general, too large for ab initio MO calculations to estimate the values even at the MP2/6-31+G\*\*/RHF/6-31+G\* level of theory. The  $\delta\text{PA}$  seems suitable for this purpose, and in the case of  $\text{sp}^3$  bases, all the calculated properties of the TS linearly correlate with the  $\delta\text{PA}_{\text{calc}}$  values. However, the present calculations suggested that we have to scale the  $\delta\text{PA}$  of the  $\text{sp}^2$  bases, which means that the order of nucleophilicity of bases can be treated uniformly in the gas phase by using the scaled  $\delta\text{PA}_{\text{calc}}$  for the  $\text{sp}^2$  bases as shown in Figures 2 and 5. However, there should be many other factors for the MR in solution. Although both the  $\text{sp}^2$  bases and the *N,N*-dimethylaniline derivatives possess the fragment consisting of a hydrophobic aromatic ring and a substituent, the  $\text{sp}^3$  bases do not have such a moiety. To explain the observed the  $\delta\text{PA}_{\text{obs}}$  and  $\Delta G^\ddagger$  relation in solution, we have to include solvent effects within theoretical calculations.

**Acknowledgment.** The authors owe thanks to the Computer Center, Institute for Molecular Science at the Okazaki National Research Institutes for the use of the NEC HSP computer and the Library Program GAUSSIAN94. This work was supported by the Grant-in-Aid for Scientific Research from the Ministry of Education of Japan.

**Supporting Information Available:** Z-matrices and energies of all structures (50 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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