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Nucleophilic Substitution at Unactivated Vinylic Carbon. Factors Conducive to the Energetic Preference for the In-Plane S_N2 Pathway

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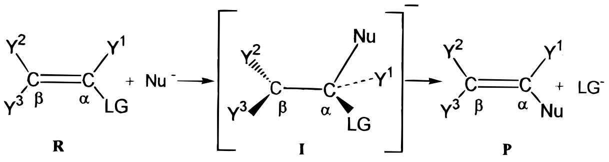
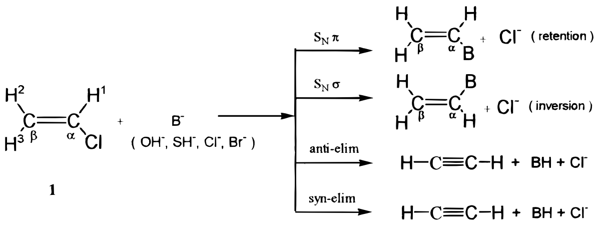
Abstract: The gas-phase nucleophilic bimolecular substitutions at unactivated vinylic carbon ($CH_2{=}CHCl$, **1**) by four nucleophiles (OH^-, SH^-, Cl^-, and Br^-) are investigated theoretically at the G2(+)(MP2) level. The results show that the stronger nucleophiles (OH^- and SH^-) substitute by an out-of-plane S_N2 path with retention ($S_N\ \pi$) but an in-plane S_N2 path ($S_N\ \sigma$) with inversion of configuration is preferred for the substitution by the weaker bases, Cl^- and Br^-. However, the elimination pathway is much more facile for OH^- than any substitution process. We have considerd three factors, (i) the LUMO symmetries (σ^*, or π^*), (ii) the proximate $\sigma-\sigma^*$ charge-transfer interactions, and (iii) the electrostatic interactions in the transition state, as possible causes for preferred pathway for each nucleophile. The stability of the $S_N\ \pi$ transition state is predominantly influenced by the proximate $\sigma-\sigma^*$ type interactions, whereas electrostatic interactions are the major factor conducive to the energetic preference for the $S_N\ \sigma$ over the $S_N\ \pi$ processes for Cl^- and Br^-. Solvent effect raises the barrier height but the mechanism and preferred path are not affected.

Nucleophilic vinylic substitution can proceed via an intermediate carbanion, or concertedly with concurrent bond formation and cleavage,[1] eq 1. In the former process, **I** is a stable intermediate in which the negative charge is delocalized by conjugation in systems activated by electron-withdrawing groups at C_β (Y^2 and/or Y^3 = NO_2, RCO, CO_2R, etc). In the single-step, concerted process, **I** is a transition state (TS). In the stepwise mechanism through a carbanion intermediate retention of configuration is normally observed, although partial or complete stereoconvergence may result when the intermediate has a long lifetime.[1] Exclusive inversion has rarely been observed for simple vinylic systems. However, the vinyl analogue of the aliphatic S_N2 mechanism, in which the backside attack of the nucleophile occurs concertedly with leaving group expulsion within the molecular plane, has been proposed experimentally, mostly for the reactions proceeding with highly S_N1 character.[2] Recently, this type of in-plane S_N2 route with inversion of configuration has been predicted to be theoretically feasible at an unactivated vinylic carbon in the gas phase and in solution.[3] This unexpected theoretical result of energetic preference for the in-plane σ-attack ($S_N\ \sigma$) over the out-of-plane π-attack ($S_N\ \pi$) in unactivated vinylic systems leads us to a further quest: what is the real nature of, or the driving force behind, such preference?



(1)

In this work we investigated the mechanism of the gas-phase nucleophilic vinylic substitution using reactions of vinyl chloride (**1**; Y^1 = Y^2 = Y^3 = H and LG = Cl in eq 1) with four nucleophiles (Nu^- = OH^-, SH^-, Cl^-, and Br^-) at the G2(+)(MP2) level of theory. For strong bases, elimination−addition processes are also possible, in which consecutive addition of the nucleophile and hydrogen to the elimination product (acetylene) finally yields a vinylic substitution product, and hence four types of reaction paths are considered, eq 2.



(2)

The primary goal of this work is to elucidate the mechanism of nucleophilic substitutions at unactivated vinyl carbon, in particular to examine various factors which are conducive to the energetic preference for the in-plane σ-attack ($S_N\ \sigma$ route) over the out-of-plane π-attack ($S_N\ \pi$ route).

Calculations

The Gaussian 98 program package[4] with standard Pople-type basis sets was used throughout in this work. Energies (*E*) were calculated at three levels, RHF/6-311+G** (RHF), MP2/6-311+G** (MP2), and G2(+)(MP2) levels with MP2/6-311+G** geometries for the latter two levels. The G2(+)(MP2)[4,5] method is a modified G2(MP2) version[5] in which geometries are determined with an extra diffuse function (+) added. In the original G2 theory,[6] the energies are calculated with MP2/

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Table 1. Proton Affinities of Bases

base	calcd (kcal mol^{-1})[a] MP2	calcd (kcal mol^{-1})[a] G2(+)(MP2)	exptl (kcal mol^{-1})[b]
OH$^-$	389.4	389.1 (389.8)[c]	390.5
SH$^-$	353.9	351.1 (352.1)[c]	351.4
Cl$^-$	334.5	333.2 (334.1)[c]	333.5
Br$^-$	322.8	323.4 (323.9)[c]	322.6[d]

[a] $\Delta H = H(B^-) - H(BH)$. [b] Gronert, S. *J. Am. Chem. Soc.* **1993**, *115*, 10258. [c] Values in parentheses are at the G2 level: Morgon, N. H. *J. Chem. Phys. A* **1998**. *102*, 2050. [d] Curtiss, L. A; McGrath, M. P.; Blaudeau, J.; Davis, N. E.; Binning, R. C., Jr.; Radom, L. *J. Chem. Phys.* **1995**. *103*, 6104.

6-31G* geometries. The stationary points were verified by calculation of the vibrational frequencies at the RHF/6-311+G** level (scaled by 0.9051). The gas-phase standard free energy changes and activation free energies $\Delta G_g°$ and $\Delta G_g^‡$ (relative to the separated reactants, **1** + Nu$^-$) were then obtained by applying zero-point (ZPE) and thermal energy corrections and entropy changes, $\Delta S°$ and $\Delta S^‡$. The solvation energies ($\Delta G_{sol}°$) were calculated using the isodensity polarized continum model (IPCM) with an isodensity level of 0.001 au.[7]

Results and Discussion

To test the performance of our G2(+)(MP2) calculation, we compared the proton affinities (PAs) of the four nucleophiles, OH$^-$, SH$^-$, Cl$^-$, and Br$^-$, calculated at the MP2 and G2(+)(MP2) levels with the experimental values in Table 1.

We note quite an improvement in the calculated PAs with the G2(+)(MP2) theory relative to those at the simple MP2 level especially for SH$^-$ and Cl$^-$. The performance of the G2(+)(MP2) calculation is quite comparable to that of the higher level calculation at the G2(+) theory (Table 1) as judged by the PA results.

Reactant (RC) and Product (PC) Complexes. Approaching and departing nucleophiles Cl$^-$ and Br$^-$ form loose electrostatic complexes (RC and PC) with the most positive hydrogen, H_1 (the Mulliken charges are, H_1 (0.195), H_2 (0.161), and H_3 (0.151) for **1**), in the substitution processes, $S_N\pi$ and $S_N\sigma$ paths in eq 2. For nucleophiles OH$^-$ and SH$^-$, the RCs are formed with H_2 (anti-elimination) and H_3 (syn-elimination), whereas the PCs are formed with the departing group, Cl$^-$. The structures of these complexes are shown in **S1** (Supporting Information) together with the energies of the complexes.

Transition-State Structures and Energetics. The structures of the transition states (TSs) are shown in Figure 1 together with those of reactants and products, and the energetics are summarized in Tables 2 and 3.

Nucleophilic Substitution. Reference to Tables 2 and 3 reveals that the in-plane σ-attack is favored over the out-of-plane π-attack for all the nucleophiles except B$^-$ = OH$^-$ at the RHF level. However, this trend is reversed at the MP2 level and exhibits energetic preference for the π-attack over the σ-attack with all the nucleophiles except B$^-$ = Br$^-$ for which the barrier heights are quite similar for the two types of substitution processes. The highest level results with the G2(+)(MP2) theory in Table 3 show that the σ-attack is energetically preferred to the π-attack for the Cl$^-$ and Br$^-$ nucleophiles while the reverse is true for the OH$^-$ and SH$^-$. Thus the correct energetic preference for the σ-attack over the π-attack for Cl$^-$ and Br$^-$ predicted at the RHF level must be fortuitous. These changes in the energetic preference for the σ-attack over the π-attack for the Cl$^-$ and Br$^-$ from RHF to MP2 and G2(+)(MP2) can be rationalized as follows.

It has been shown that resonance delocalization tends to reduce the electron correlation energy, so that a more resonance delocalized structure has a lower correlated energy than a less delocalized form.[8] The large lowering of the correlated activation energies, $\Delta E^‡$, for the $S_N\pi$ processes at the MP2 level is therefore an indication that the $S_N\pi$ TSs are stabilized largely by delocalization. However, this correlated energy lowering of the more resonance delocalized form by 11−23 kcal mol^{-1} seems to be overestimated with a low level correlated MO (MP2 level) since at the more sophisticated [G2(+)(MP2)] level, the $\Delta E^‡$ values are slightly raised again (except for Br$^-$). The $S_N\sigma$ and $S_N\pi$ processes of SH$^-$ are competitive with a marginally lower barrier for the latter ($\delta\Delta G^‡ = \Delta G^‡(S_N\pi) - \Delta G^‡(S_N\sigma) = -2.1$ kcal mol^{-1}). Now with Cl$^-$, the $S_N\sigma$ route is favored over the $S_N\pi$ route by $\delta\Delta G^‡ = 4.7$ kcal mol^{-1}; this trend is consistent with the G2(+) results of Glukhovtsev et al.[3] A greater difference in the $\Delta E^‡$ values, for chloride (Cl$^-$) exchange, $\delta\Delta E^‡ = \Delta E^‡(S_N\pi) - \Delta E^‡(S_N\sigma) = 10.1$ kcal mol^{-1}, is predicted at the G2(+) level[3] than at the G2(+)(MP2) level (4.3 kcal mol^{-1}). We therefore think that convergence is reached at the G2(+)(MP2) level and there will be no more inversion of the order of preferred reaction routes at any higher level calculations. The substitution reactions of OH$^-$ and SH$^-$ are exothermic, whereas that of Br$^-$ is endothermic. In the gas phase, the $S_N\sigma$ substitution of **1** by OH$^-$ is not feasible. We failed to locate the in-plane σ-attack TS for OH$^-$; in fact the $S_N\pi$ route for OH$^-$ has an extremely low barrier ($\Delta G^‡ = 2.2$ kcal mol^{-1}) with a high reaction exothermicity ($\Delta G° = -53.2$ kcal mol^{-1}).

For substitution by Br$^-$, the barrier heights are higher, 39.5 and 32.1 kcal mol^{-1} for the π- and σ-attack processes, due largely to the endothermicity of the reaction ($\Delta G° = 9.1$ kcal mol^{-1}). The reverse reaction (Cl$^-$ + $CH_2CHBr \rightarrow CH_2CHCl$ + Br$^-$) should, however, be exothermic (−9.1 kcal mol^{-1}) and has a low barrier height ($\Delta G^‡ = 30.4$ and 23.0 kcal mol^{-1} respectively for the $S_N\pi$ and $S_N\sigma$ path). Thus the order of increasing barrier heights ($\Delta G^‡$) for the reactions with the Nu:(LG) pair is Cl$^-$:(Br$^-$) < SH$^-$:(Cl$^-$) < Cl$^-$:(Cl$^-$) < Br$^-$:(Cl$^-$) for the σ-attack and OH$^-$:(Cl$^-$) < SH$^-$:(Cl$^-$) < Cl$^-$:(Br$^-$) < Cl$^-$:(Cl$^-$) < Br$^-$:(Cl$^-$) for the π-attack.

Reference to Figure 1 reveals that the TSs for the $S_N\sigma$ paths are quite loose with a small degree of bond formation and a large degree of bond cleavage, in contrast those for the $S_N\pi$ paths are relatively tight with a large extent of bond making and a small amount of leaving group departure. To see this more clearly we have calculated percentage bond-order changes in

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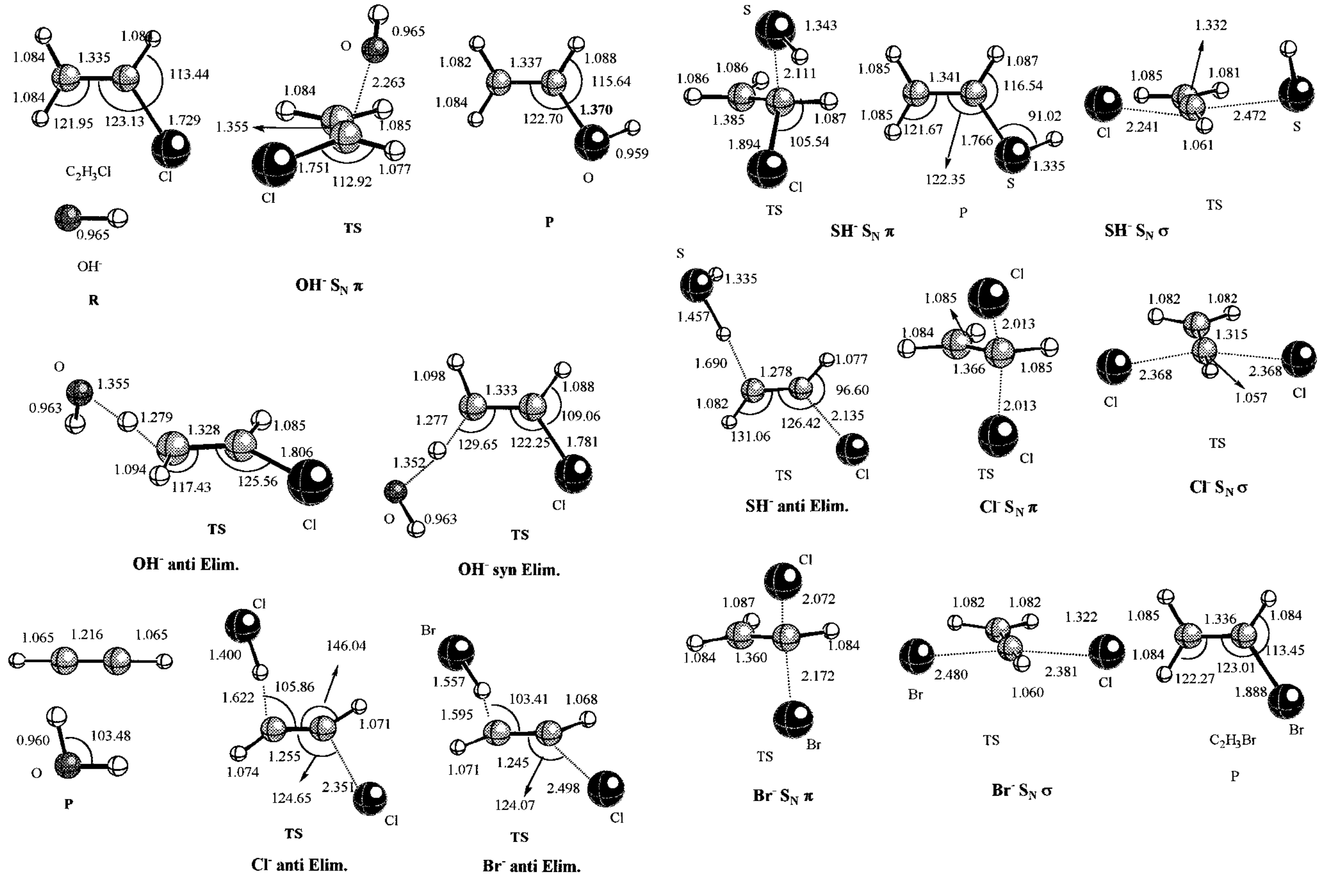

Figure 1. Structures of reactant, products, and transition states.

Table 2. Energetics (in kcal mol^{-1} relative to the separated reactants) for Nucleophilic Substitution (S_N π and S_N σ) and Elimination (anti and syn) Reactions of Vinyl Chloride at RHF and MP2 Levels[a]

reaction path	base	RHF/6-311+G** $\Delta E^{\ddagger}$	RHF/6-311+G** $\Delta E°$	MP2/6-311+G** $\Delta E^{\ddagger}$	MP2/6-311+G** $\Delta E°$	MP2/6-311+G** $\Delta G^{\ddagger}_g$	MP2/6-311+G** $\Delta G°_g$
S_N π	OH^-	4.56	−73.86	−6.70	−54.64	0.56	−50.51
	SH^-	34.95	−25.05	11.65	−24.89	20.32	−22.06
	Cl^-	48.38	0.00	26.80	0.00	35.62	0.00
	Br^-	54.68	10.95	33.37	11.12	39.39	10.85
S_N σ	SH^-	26.03	−25.05	22.72	−24.89	29.65	−22.06
	Cl^-	29.36	0.00	30.89	0.00	36.68	0.00
	Br^-	32.67	10.95	33.25	11.12	38.14	10.85
elim							
anti	OH^-	−11.32	−46.02	−16.28	−29.59	−11.01	−37.17
syn	OH^-	−8.88	−46.02	−13.52	−29.59	−8.17	−37.17
anti	SH^-	30.97	4.21	16.46	8.37	20.20	−2.09
anti	Cl^-	40.24	27.27	26.83	29.14	27.02	16.90
anti	Br^-	38.52	50.11	37.23	41.27	36.34	28.30

[a] Reactant (B^- + **1**) energies in hartrees: OH^- (−612.38719), SH^- (−935.11700), Cl^- (996.54690), and Br^- (−3109.42534) at the MP2/6-311+G** level.

the TS, % $\Delta n^{\ddagger}$,[9] for d_1 (C_α−Nu bond), d_2 (C_α−LG bond), and d_4 (C_β=C_α) as shown in Table 4. We note that except for OH^-, the bond-making and cleavage are ca. 55−60 and 25−40% for the S_N π and 30−35 and 55−65% for the S_N σ routes. In the S_N π TS, the π bond of C_β=C_α is partially broken (to a single bond in the limit) and in the S_N σ a second π-bond is partially formed (to a triple bond in the limit). These π-bond changes are in general large in the S_N π TS, but also substantial in the S_N σ TS. For example, in the identity reaction of Cl^- with **1**, ca. 14% of the triple bond is formed in the in-plane σ-attack, which is greater than that for the reaction of Br^- with **1** (ca. 9%). Thus the S_N π TSs are characterized by a relatively tighter bond formation (closer approach of the nucleophile to the vinylic carbon) than in the S_N σ TSs, which is in line with the large proximate σ−σ^* delocalization stabilization within the S_N π TSs. It has been shown that when there are intermolecular delocalizations due to the proximate σ−σ^* (including n−σ^*, π−σ^*, and σ−π^*) charge transfer interactions electron correlation allows the two interacting molecules to approach each other more closely by overcoming a significant amount of exclusion repulsion.[10]

The greater degree of bond cleavage than bond formation in the in-plane σ-attack routes should require a large amount of deformation energy[11] (ΔE_{def}, which is the energy required to transform the reactant, **1**, into its transition structure, Table 4) and hence should lead to high activation barriers. The difference in the deformation energy between the S_N π and S_N σ TSs ($\delta\Delta E_{\mathrm{def}} = \Delta E_{\mathrm{def}}(\sigma) - \Delta E_{\mathrm{def}}(\pi)$ in kcal mol^{-1}) increases as the S_N π route becomes increasingly more favorable, Br^- (14.93 kcal mol^{-1}), Cl^- (19.71 kcal mol^{-1}), and SH^- (22.92 kcal mol^{-1}). For the OH^- nucleophile, perhaps this difference becomes so great that the S_N σ attack is not feasible compared to the much lower S_N π path (as we found). Based on the greater deformation energies for the S_N σ than S_N π path, the in-plane σ-attack should be considered less favorable than the out-of-plane π-attack, as has long been accepted by many organic

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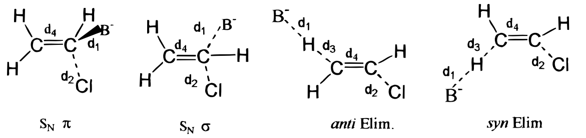
Table 3. Reaction and Activation Parameters (relative to the separated reactants, $CH_2CHCl + Nu^-$) in the Gas Phase at the G2(+)(MP2) Level and Solvation ($\Delta G^{\ddagger}_{sol}$, kcal mol^{-1}) and Activation Free Energies ($\Delta G^{\ddagger}_{AN}$, kcal mol^{-1}) in Acetonitrile

reaction path	base	$\Delta E^{\ddagger\ a}$	$\Delta H^{\ddagger}$	$\Delta H°$	$\Delta G^{\ddagger}_{g}$	$\Delta G°_{g}$	$\Delta G^{\ddagger}_{sol}$	$\Delta G^{\ddagger}_{AN}{}^{b}$
$S_N\pi$	OH^-	−6.16	−7.16	−54.65	2.15	−53.20	15.21	17.36
	SH^-	15.33	14.51	−21.47	24.36	−19.04	14.07	38.43
	Cl^-	27.25	26.04	0.0	34.53	0.0	15.69	50.22
	Br^-	32.30	31.81	9.23	39.50	9.14	13.60	53.10
$S_N\sigma$	SH^-	18.55	18.32	−21.47	26.46	−19.04	14.55	41.01
	Cl^-	23.01	22.83	0.0	29.76	0.0	16.34	46.10
	Br^-	25.62	25.43	9.23	32.11	9.14	14.46	46.57
elim								
anti	OH^-	−18.34	−18.79	−27.34	−11.03	−34.83	17.19	6.16
syn	OH^-	−15.38	−16.03	−27.34	−7.90	−34.83	14.04	6.14
anti	SH^-	15.69	15.55	10.61	22.70	2.70	14.84	36.74
anti	Cl^-	21.96	22.19	28.53	27.68	19.82	15.93	43.61
anti	Br^-	31.30	31.68	38.36	36.77	29.54	7.61	44.38

[a] Reactant ($B^- + \mathbf{1}$) energies in hartrees: OH^- (−613.26785), SH^- (−935.92276), Cl^- (−997.35824), and Br^- (−3110.28653) at the G2(+)(MP2) level. [b] $\Delta G^{\ddagger}_{AN} = \Delta G^{\ddagger}_{g} + \Delta G^{\ddagger}_{sol}$.

Table 4. Percentage Changes of Bond Order, % $\Delta n^{\ddagger}$,[a] Deformation Energies (ΔE_{def})



base	path	d$_1$	d$_2$	d$_3$	d$_4$	ΔE_{def}	$\delta\Delta E_{def}{}^{b}$
OH^-	π	22.5	3.5		13.5	2.84	
SH^-	π	56.3	24.0		32.0	25.92	22.92
	σ	30.8	57.4		2.1	48.84	
Cl^-	π	62.3	37.7		20.5	39.42	19.71
	σ	34.5	65.5		14.2	59.13	
Br^-	π	62.3	43.5		16.7	46.74	14.93
	σ	37.3	66.2		9.1	61.67	
OH^-	anti elim	51.7	12.0	27.7		13.86	
	syn elim	51.9	8.2	27.5		14.14	
SH^-	anti elim	81.4	49.1	63.6		83.35	
Cl^-	anti elim	80.9	64.5	59.2		94.34	
Br^-	anti elim	78.5	72.2	57.3		103.84	

[a] % $\Delta n^{\ddagger} = \{[\exp(-r^{\ddagger}/a) - \exp(-r_R/a)]/[\exp(-r_P/a) - \exp(-r_R/a)]\} \times 100$, where $r^{\ddagger}$, r_R, and r_P are the bond length in the TS, reactant, and product, respectively. We adopted $a = 0.6$ for d$_1$, d$_2$, and d$_3$, and $a = 0.3$ for d$_4$.[9,11a] [b] $\delta\Delta E_{def} = \Delta E_{def}(\sigma) - \Delta E_{def}(\pi)$ at the MP2 level of theory.

chemists. What other factors are then responsible for reversing this trend of ΔG_{def} to the energetic preference for the $S_N\sigma$ over the $S_N\pi$ path?

First, we looked into the frontier MO levels. Lucchini et al.[12] have shown that there is an almost complete correspondence between the symmetry (π^* or σ^*) of the lowest unoccupied (LU) MO and the stereochemical outcome of nucleophilic substitution (π-attack or σ-attack) on the corresponding real substrates. However, as they have reported, the LUMO of vinyl chloride, **1**, is a π^* orbital although the lowest σ^* orbital is quite nearby with an energy difference of $\Delta E = 0.037$ au (calculated at the RHF/6-31G*//RHF/3-21G* level). Our results are also in agreement with this π^*-LUMO (0.0964 au), and the lowest σ^* MO is at 0.1138 au with a difference of 0.017 au between the two (calculated at the RHF/6-311+G**//RHF/6-311+G** level). If the $S_N\sigma$ route were FMO energy gap controlled, the $S_N\pi$, not $S_N\sigma$, path should have been preferred. So, this indicates that the substitution of **1** by Cl^- is not FMO energy gap controlled. In contrast, the $S_N\sigma$ (σ^* level is at 0.0623 au) preference over the $S_N\pi$ (π^* level is at 0.0882 au) path is correctly predicted for the substitution reaction of vinyl bromide, CH_2CHBr, with Cl^-. The energy gap between the two is in this case large $\Delta E = 0.026$ au (compared to that of **1**, 0.017 au). In any case, the π^*-LUMO obtained at the two levels of theory for **1** is not compatible with the G2(+)(MP2) results of $S_N\sigma$ preference for the nucleophilic substitution of **1** by Cl^-. We therefore conclude that the ground-state LUMO symmetry at the α-carbon of the vinyl system cannot be the predominant factor determining the mechanistic preference in the nucleophillic vinylic substitution.

As a next candidate for the factor conducive to the energetic preference for the in-plane S_N2 pathway, we examine the intramolecular geminal and first-neighbor vicinal $\sigma-\sigma^*$ type (including $\pi-\sigma^*$ and $\sigma-\pi^*$) charge-transfer interactions in the TS. These types of second-order perturbation interaction energies, $\Delta E^{(2)}$, have provided valuable insights into the stereoelectronic effects involved in many equilibrium and dynamic processes.[8,10,13] To see them more clearly, we have subjected the TSs to natural bond orbital (NBO) analysis.[8,10,13b,d,e,f] The results for our four main reaction paths are summarized in **S2**. The energy lowering is given by

$$\Delta E^{(2)}{}_{\sigma\sigma^*} = \frac{\langle\sigma|\hat{F}|\sigma^*\rangle^2}{\epsilon_{\sigma^*} - \epsilon_{\sigma}} \tag{3}$$

where F is the Fock operator and ϵ_{σ} (or ϵ_{π}) and ϵ_{σ^*} (or ϵ_{π^*}) are NBO orbital energies. Examination of the results in **S2** reveals that such TS stabilizing, second-order proximate $\sigma-\sigma^*$ interactions are large in the $S_N\pi$ path ($\sum\Delta E^{(2)}{}_{\sigma\sigma^*}$ for $S_N\pi$ with Br^-, Cl^-, and SH^- is ca. 557, 196, and 164 kcal mol^{-1}, respectively), but are much smaller in the $S_N\sigma$ path ($\sum\Delta E^{(2)}{}_{\sigma\sigma^*}$ for $S_N\sigma$ with Br^-, Cl^-, and SH^- is ca. 32, 33, and 15 kcal mol^{-1}, respectively). This is not unexpected since, as we have noted earlier, the $S_N\sigma$ TSs are much looser than the $S_N\pi$ TSs so that the matrix elements, $\langle\sigma|\hat{F}|\sigma^*\rangle$ in eq 3 are much smaller due to small overlap between σ and σ^* orbitals.

Given the much smaller charge-transfer stabilization energies for the $S_N\sigma$ than $S_N\pi$ processes, such $\sigma-\sigma^*$ proximate delocalization in the TS cannot be responsible for the energetic preference of the $S_N\sigma$ path in the substitution of unactivated vinyl chloride by Cl^- and Br^- (Table 3). Obviously, we have

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Table 5. Electrostatic Energies (ΔE_{es} in kcal mol^{-1}) for the Major Electrostatic Interactions of C_α and H with Nu and LG

		ΔE_{es}				
base	path	C_α–Nu	C_α–LG	H_1–Nu	H_1–LG	total
OH^-	π	−2.4	−0.2	−39.5	−2.4	−44.5
SH^-	π	7.2	5.3	−8.0	−5.5	−1.0
	σ	−4.9	−4.5	−25.4	−21.5	−56.3
Cl^-	π	0.1	0.1	−8.3	−8.3	−16.4
	σ	−17.7	−17.7	−28.2	−28.2	−91.8
Br^-	π	1.7	2.3	−7.0	−9.6	−12.6
	σ	−11.1	−12.2	−23.5	−26.2	−73.0

to look for another factor to rationalize the lower activation barrier for the $S_N\ \sigma$ than $S_N\ \pi$ path.

In the NBO theory, the energy changes, $\Delta E = E$(associated) $-$ E(separated), accompanying association of two interacting molecules (as in the water dimer, in the TS for bimolecular substitution etc.) are given in two terms, charge-transfer (ΔE_{CT}) and other " no-charge-transfer" (ΔE_{NCT}) energy changes[10]

$$\Delta E = \Delta E_{NCT} + \Delta E_{CT} \tag{4}$$

The latter is due to exclusion repulsion and electrostatic (including induction and polarization) interactions. For example, for a water dimer, the high level results gave −4.1, +2.4, and −6.5 kcal mol^{-1} for ΔE, ΔE_{NCT}, and ΔE_{CT}, respectively.[10] In this case, the ΔE_{NCT} term is destabilizing and the charge-transfer energy, ΔE_{CT}, provides the major part of the water dimer formation energy. Obviously our quest after a conducive factor for the energetic preference of the $S_N\ \sigma$ over the $S_N\ \pi$ path should now be directed to the ΔE_{NCT} term. A common feature found in the experimentally observed $S_N\ \sigma$ processes is the development of a strong cationic charge on the vinyl carbon in a loose S_N1-like TS.[2] The in-plane $S_N\ \sigma$ processes are often observed experimentally with vinyl substrates which are prone to react with a strong S_N1 character.[2] For example, the acetolysis of alkyl-substituted vinyl iodonium salts proceeds with a TS in which strong cationic charge is left behind as the leaving group, neutral iodobenzene, has nearly completely departed.[2d] When, however, the vinyl cationic charge is delocalized to an electron donor or conjugative substituent, like a β-phenyl group, the exclusive in-plane $S_N\ \sigma$ mechanism is no longer observed. It is therefore important to recognize that the strong positive charge development is required in the TS for an $S_N\ \sigma$ process to be preferred to the $S_N\ \pi$ process.

Thus the cationic vinyl carbon and an anionic nucleophile in a loose TS are bound to interact electrostatically to stabilize the TS. We have collected atomic charges for each TSs in **S3**, and significantly large electrostatic interaction energies (ΔE_{es} > 5.0 kcal mol^{-1}) are calculated as shown in Table 5. Surprisingly, the negative (and hence stabilizing) ΔE_{es} values for the $S_N\ \sigma$ with Cl^- and Br^- are much larger than those for other processes. In fact, the ΔE_{es} values are much smaller for the $S_N\ \pi$ paths (except for OH^-) than for the $S_N\ \sigma$ paths. The stabilizing ΔE_{es} (<0) values for the $S_N\ \sigma$ path with Cl^- and Br^- exceed the greater destabilizing deformation energies for the $S_N\ \pi$ path ($\Delta\Delta G_{def}$ = 13.7 and 9.6 kcal mol^{-1} for Cl^- and Br^-, respectively, Table 4) and more than compensate for the large deformation energies in favor of the $S_N\ \sigma$ over the $S_N\ \pi$ process. The lower exclusion repulsion energies in the loose $S_N\ \sigma$ TS than in the tight $S_N\ \pi$ TS should also contribute to the energetic preference of the $S_N\ \sigma$ path.

We can therefore conclude that the tight $S_N\ \pi$ TSs are primarily stabilized by the proximate σ–σ* type charge-transfer interactions, $\Delta E^{(2)}_{\sigma-\sigma^*}$ (ΔE_{CT} control), whereas the loose $S_N\ \sigma$ TSs are mainly stabilized by the electrostatic interactions, ΔE_{es} (ΔE_{NCT} control). The electrostatic energies are stronger and more stabilizing in the $S_N\ \sigma$ TSs than the charge-transfer interaction energies in the $S_N\ \pi$ TSs for the weak nucleophiles, Cl^- and Br^-, and the reverse is true for the strong nucleophiles, OH^- and SH^-.

Elimination Reaction. The gas-phase β-elimination of vinyl chloride with a strong base, OH^-, is a very facile process with negative $\Delta G^\ddagger$ values (−11.0 and −7.9 kcal mol^{-1} relative to the separated reactants for anti- and syn-eliminations in Table 3). The percentage bond order changes in Table 4 show that the elimination with OH^- proceeds via a highly E1cb-like E2 TS with a large degree of deprotonation (> 50%) but only small degree of leaving group departure. In contrast, the elimination with SH^-, Cl^-, and Br^-, weaker bases than OH^-, is a typical E2 reaction with a large degree of deprotonation and leaving group departure. This is why the deformation energies, ΔE_{def}, are so large (83−104 kcal mol^{-1}) for these process (Table 4). For bases SH^-, Cl^-, and Br^-, the syn elimination was not feasible. The activation energies, $\Delta G^\ddagger$, show that the elimination and substitution may proceed competively for SH^-, Cl^-, and Br^- in the gas phase and also in acetonitrile solution. However, the elimination with OH^- is so facile ($\Delta G^\ddagger$ < 0) that the $S_N\ \pi$ substitution route cannot compete and the reaction of OH^- with **1** should take place exclusively via the elimination route. The TSs for these processes are also shown in Figure 1. The syn-elimination by OH^- is somewhat sterically hindered and for this reason the anti-elimination is favored over the syn-elimination.

Solvent Effect. Since the nucleophilic vinylic substitution reactions are conducted often in dipolar aprotic solvents,[14] solvent effects are investigated with acetonitrile using a continuum model, isodensity polarizable continuum model (IPCM).[7] The theoretical estimation of entropy changes in solution is a difficult problem. However, the entropy changes are found to be essentially constant of the medium,[15] so that we used the gas-phase entropies in the estimation of free energy changes, $\Delta G^\ddagger$ and $\Delta G°$, in acetonitrile. The results in Table 3 reveal that, although the barrier heights are raised by the solvent almost uniformly, the preference between the $S_N\ \pi$ and $S_N\ \sigma$ pathways is not altered. The elimination by OH^- now has positive activation barriers ($\Delta G^\ddagger$ > 0). The elevation of $\Delta G^\ddagger$ in acetonitrile is consistent with the strong solvation of the anionic nucleophile in the initial state which is more stabilizing in the solvent (MeCN) (by ca. 16 kcal mol^{-1} for Cl^-) relative to the more charge delocalized TS. Since acetonitrile is a dipolar aprotic solvent, solvation of a more localized charge in the loose activated complex ($S_N\ \sigma$ TS) should be smaller so that solvation stabilization is somewhat lower for the $S_N\ \sigma$ path (by ca. 0.5−0.9 kcal mol^{-1}). The high activation barriers in solution may well be the reason for the relative difficulty of observing an in-plane S_N2 process with unactivated vinyl systems.

Conclusion

Our G2(+)(MP2) results indicate that in the gas-phase substitution of the unactivated vinyl system ($CH_2{=}CHCl$, **1**) by strong nucleophiles, OH^- and SH^-, the out-of-plane, S_N2 path with retention ($S_N\ \pi$) is favored, whereas the in-plane S_N2 path with inversion ($S_N\ \sigma$) is energetically preferred by weak

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nucleophiles, Cl^- and Br^-. The $S_N\pi$ TSs are relatively tight with a large degree of bond formation and a low extent of bond cleavage, and the TSs are predominantly stabilized by the geminal and first-neighbor vicinal $\sigma-\sigma^*$ charge-transfer interactions. In contrast, the $S_N\sigma$ TSs are relatively loose and stabilized primarily by the electrostatic interactions. The E2 elimination is extremely facile for OH^- with strong E1cb character. Solvent, CH_3CN, causes the activation barriers to elevate uniformly so that the mechanism and the preferred path ($S_N\pi$ or $S_N\sigma$) are not altered.

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Supporting Information Available: Structures of reactant and product complexes and tables of genimal and first-neighbor vicinal charge transfer interaction energies and calculated Milliken and NBO charges (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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