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The α-Effect in Gas-Phase S_N2 Reactions Revisited

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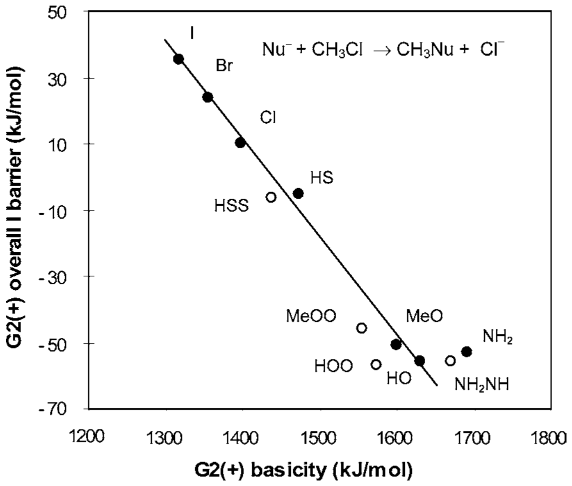
ABSTRACT



This paper re-examines gas-phase S_N2 reactions at saturated carbon for model reactions $Nu^- + CH_3Cl \rightarrow CH_3Nu + Cl^-$ ($Nu^- = HO^-, MeO^-, NH_2^-, HS^-, Cl^-, Br^-, I^-, HOO^-, MeOO^-, HSS^-$, and NH_2NH^-) using the G2(+) theory. The calculated results show that the α-effect does exist in the gas-phase S_N2 reaction at the sp^3 carbon, contrary to the currently accepted notion of the absence of the α-effect in the gas phase.

A class of nucleophiles, which have an electronegative atom containing one or more unshared lone-pair electrons adjacent to the nucleophilic atom, is called α-nucleophiles[1] and shows enhanced reactivity compared to that expected from a Brønsted-type correlation (log *k* vs p*K*a).[2] The α-effect has been reported in many different types of reactions in solution.[3] Several interpretations have been given including differential ground state (GS) destabilization, transition state (TS) stabilization, and solvent effect.[4,5] Among these, the interpretation in terms of the GS destabilization cannot be the origin, since the GS destabilization not only enhances the reactivity but also makes the equilibrium favorable, as pointed out explicitly in the literature.[4] The α-effect should arise from a factor that stabilizes specifically the TS but not the product state. It has widely been considered that the α-effect does not exist in the gas phase and that solvent

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effects play an important role.[5a−c] However, the real picture of that factor is not clear yet.

Experimental evidence against the α-effect in the gas phase was reported in 1985 by Depuy and co-workers,[5a] who showed that the branching ratios among the proton transfer, carbonyl addition, and substitution channels for the reaction of methyl acetate with HO^- and HOO^- did not change with the base (nucleophile). However, the conclusion based on the direct comparison of the branching ratios is not exclusive since the base (nucleophile) dependence could be different for the different reaction channels.[4] Furthermore, the basic assumption behind the argument, namely, the absence of the α-effect for the proton-transfer reaction, is also questionable.[1] The most cited computational evidence against the α-effect was given in 1987 by Jorgensen et al.,[5c] who reported that, for the gas-phase S_N2 reaction of CH_3Cl, the TS with HOO^- was less stable than that with HO^-. However, the level of calculations was not high, and the TS was not thoroughly examined in this pioneering study.

In the present study, we have calculated a series of gas-phase anionic S_N2 reactions (eq 1) of CH_3Cl with seven normal (HO^-, MeO^-, NH_2^-, HS^-, Cl^-, Br^-, and I^-) and four α-nucleophiles (HOO^-, $MeOO^-$, HSS^-, and NH_2NH^-), and found that the level of computation is important to obtain reliable results. Furthermore, HOO^- is conformationaly more flexible than HO^-, and we could obtain a new and more stable TS not considered previously. All of these results require modification of the conclusion based on the previous calculations as well as on the gas-phase experiment and clearly show that the α-effect exists in the gas-phase S_N2 reactions at an saturated carbon (sp^3 hybridization).

$$\mathrm{Nu^- + CH_3Cl \rightarrow CH_3Nu + Cl^-} \qquad (1)$$

$$(\mathrm{Nu^- = HO^-, MeO^-, NH_2^-, HS^-,}$$
$$\mathrm{Cl^-, Br^-, I^-, HOO^-, MeOO^-, HSS^-, and\ NH_2NH^-})$$

A modified form of G2 theory, G2(+),[6a,7] introduced by Radom et al. and successfully applied in the study of S_N2 reactions at saturated carbon,[6] nitrogen,[8] and oxygen,[9] was used in our calculations. Relative energies correspond to enthalpy changes at 298.15 K in kJ/mol. All optimized structures involved in the reactions are given in Supporting Information. The key energetic quantities are presented in Table 1. The data in Table 1 indicate that the calculated G2(+) basicities are in good agreement with the experimental values.[10]

Table 1. Calculated Basicities of Nucleophiles and Overall Barriers, $\Delta H^{\ddagger}_{ovr}$ (kJ/mol), for Equation 1

Nu^-	basicity (calcd)[a]	basicity(expt)[c]	$\Delta H^{\ddagger}_{ovr}$[d]
HO^-	1631.8	1633.0	−55.5
HOO^-	1573.1	1575.3 ± 2.1	−56.6
NH_2^-	1692.0	1687.8 ± 0.42	−52.2
NH_2NH^-	1671.6		−55.5
HS^-	1473.1	1468.0 ± 12.0	−5.6
HSS^-	1438.8	1448.0 ± 13.0	−6.3
MeO^-	1599.0	1596.0 ± 4.0	−50.6
$MeOO^-$	1554.8	1567.3 ± 3.3	−45.8
Cl^-	1398.4[b]	1395.0	9.8[b]
Br^-	1354.9[b]	1353.5 ± 0.42	23.9[e]
I^-	1317.8[b]	1315.0	35.1[e]

[a] $\Delta H = H(\text{Nu-H}) - H(\text{Nu}^- - H(\text{H}^+)$. [b] From ref 6a. [c] From ref 10. [d] $\Delta H^{\ddagger}_{ovr} = H[\text{Nu}\cdots\text{CH}_3\cdots\text{Cl}]^{-\ddagger} - H(\text{CH}_3\text{Cl}) - H(\text{Nu}^-)$. [e] From ref 6b.

Figure 1 shows that a good correlation ($R^2 = 0.995$) exists between the overall barriers ($\Delta H^{\ddagger}_{ovr}$) and the basicities of six normal nucleophiles (HO^-, MeO^-, HS^-, Cl^-, Br^-, and I^-). The observed correlation reinforces the generally accepted view that the nucleophilic reactivity is basically controlled by the basicity of nucleophile if the substrate is fixed. It is worth noticing that the points for three α-nucleo-

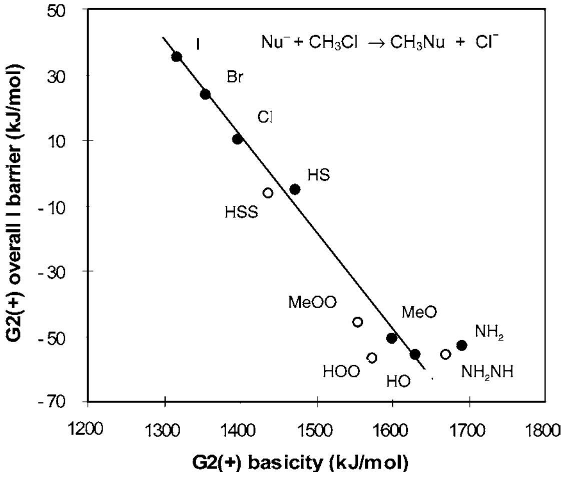

Figure 1. Plots of the G2(+) overall barriers ((H(ovr) vs the basicities of normal nucleophiles (●) and α-nucleophiles (○) for eq 1 at 298.15 K.

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philes out of the four examined deviate downward from the correlation line, displaying detectable α-effect in the S_N2 reaction. The point for NH_2NH^- is slightly above the line, but this nucleophile is more reactive than NH_2^- despite its smaller basicity, as can be seen in Figure 1. It should also be noted that both MeO^- and HO^- behave normally, whereas HOO^- deviates downward from the correlation line. The results indicate that the deviation of HOO^- is not due to the size effect, namely, an extra stability due to a polarizability effect, often observed in the gas-phase calculations for a large species. The four pairs of the normal and corresponding α-nucleophiles are compared in detail below.

HO^- vs HOO^-. The reaction of $HO^- + CH_3Cl$ has been extensively studied experimentally[11] and computationally.[12] The reaction of $HOO^- + CH_3Cl$ is less studied theoretically and only calculated at a lower level.[5c] The calculations by Jorgensen et al. at the MP_n(n = 2 and 3)//HF/6-31+G* level of theory suggested that the $\Delta H^{\ddagger}_{\mathrm{ovr}}$ for $HO^- + CH_3Cl$ is lower than that for $HOO^- + CH_3Cl$ by more than 10 kJ/mol. However, the present study revealed that the TSs for reactions of $HO^- + CH_3Cl$ and $HOO^- + CH_3Cl$ are 55.5 and 56.6 kJ/mol below the reactants at the G2(+) level, respectively, thus indicating that HOO^- is more reactive than HO^-, even though HOO^- is a much weaker base than HO^-. The different results can be attributed to the different TS geometries for the reaction of HOO^-; we found a new TS with a skew conformer (Figure 2, C−O−O−H = 108.5°), in addition to the trans conformer (C−O−O−H = 180.0°) reported previously.[5c] The skew conformation is more stable (by 8.7 kJ/mol) than the trans one probably due to the favorable electrostatic interaction between the α-atom (O) in HOO^- and the positively charged methyl moiety at the TS. Such interaction is weaker in the trans conformer.

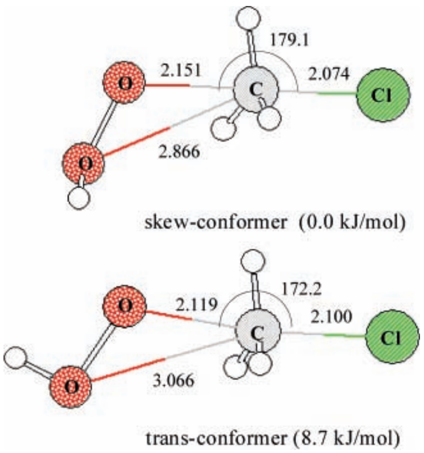

Figure 2. Two different TSs in the reaction of $HOO^- + CH_3Cl$. All atomic distances are in angstroms and angles are in degrees. The values in parentheses are relative enthalpies at 298.15 K.

NH_2^- vs NH_2NH^-. In these two cases the attacking atoms are nitrogen. The calculated gas-phase basicity of NH_2NH^- is smaller than NH_2^- by 20.4 kJ/mol, whereas the $\Delta H^{\ddagger}_{\mathrm{ovr}}$ for the reaction of $NH_2NH^- + CH_3Cl$ is lower than that for $NH_2^- + CH_3Cl$ by 3.3 kJ/mol. This leads to the expectation that the reaction efficiency for the gas-phase reaction should be higher for NH_2NH^- than for NH_2^-.

HS^- vs HSS^-. The attacking atoms are sulfur in these two nucleophiles. The calculated G2(+) $\Delta H^{\ddagger}_{\mathrm{ovr}}$ values in Table 1 show that the $\Delta H^{\ddagger}_{\mathrm{ovr}}$ is −6.3 kJ/mol for the reaction of α-nucleophile HSS^- with CH_3Cl, slightly lower than that for HS^- with CH_3Cl by 0.7 kJ/mol, even though HSS^- is less basic than HS^- by 34.3 kJ/mol. Thus, the α-effect is clearly observed.

MeO^- vs $MeOO^-$. The calculated overall barrier for $MeO^- + CH_3Cl$ is −50.6 kJ/mol, which is higher than that for $HO^- + CH_3Cl$ by 4.9 kJ/mol, consistent with the smaller basicity of MeO^- in the gas phase. Although the $\Delta H^{\ddagger}_{\mathrm{ovr}}$ for α-nucleophile $MeOO^-$ is slightly higher than that for MeO^- by 4.8 kJ/mol due to its smaller basicity and steric effects, there is still a obvious downward deviation for $MeOO^-$ in Figure 1. This result again confirms the α-effect in the gas-phase S_N2 reaction. The TS prefers the skew conformation (C−O−O−C = 103.8°) due to the favorable interaction between the α-atom with the methyl moiety as in the case of HOO^-.

In summary, the high level G2(+) calculations show that three out of the four α-nucleophiles examined exhibit downward deviation from the plot of overall barrier vs basicity and accelerate the reaction through the stabilization of the transition structures. The other α-nucleophile (NH_2NH^-) clearly shows an enhanced reactivity compared to that of the corresponding normal nucleophile (NH_2^-). The α-effect does exist in the gas-phase S_N2 reaction at saturated carbon, contrary to the currently accepted notion of the absence of the α-effect in the gas phase.

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Supporting Information Available: Optimized geometries and G2(+) enthalpies at 298.15 K of all species in eq 1. This material is available free of charge via the Internet at http://pubs.acs.org.

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