Double-Inversion Mechanisms of the $X^- + CH_3Y [X,Y = F, CI, Br, I] S_N2$ Reactions

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Supporting Information

ABSTRACT: The double-inversion and front-side attack transition states as well as the proton-abstraction channels of the X^- + CH₃Y [X,Y = F, Cl, Br, I] reactions are characterized by the explicitly correlated CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory using small-core relativistic effective core potentials and the corresponding augcc-pVTZ-PP bases for Br and I. In the X = F case the double-inversion classical(adiabatic) barrier heights are 28.7(25.6), 15.8(13.4), 13.2(11.0), and 8.6(6.6) kcal mol⁻¹ for Y = F, Cl, Br, and I, respectively, whereas the barrier heights are always above the double-inversion saddle points. For X = F, the front-side attack classical(adiabatic) barrier heights, 45.8(44.8), 31.0(30.3), 24.7(24.2), and 19.5(19.3) kcal mol⁻¹ for Y = F, Cl, Br, and I, respectively, are higher than the corresponding double-inversion ones, whereas for the other systems the front-side attack saddle points are in the 35–70 kcal mol⁻¹ range. The double-inversion transition states have XH···



 CH_2Y^- structures with C_s point-group symmetry, and the front-side attack saddle points have either C_s (X = F or X = Y) or C_1 symmetry with XCY angles in the 78–88° range. On the basis of the previous reaction dynamics simulations and the minimum energy path computations along the inversion coordinate of selected XH…CH₂Y⁻ systems, we suggest that the double inversion may be a general mechanism for S_N2 reactions.

1. INTRODUCTION

The back-side attack Walden inversion mechanism of the bimolecular nucleophilic substitution (S_N2) reactions is one of the best-known stereospecific reaction pathways in organic chemistry. The simplest $S_N 2$ reactions are $X^- + CH_3 Y$ type, where X and Y are halogens (F, Cl, Br, I). Walden inversion occurs when X⁻ attacks the back side of CH₃Y, the system goes through a central transition state, and the umbrella motion of the CH₃ group inverts the configuration around the carbon center while a new CX bond forms and the CY bond breaks, thereby resulting in $XCH_3 + Y^-$ products (Figure 1). There is also a less-known front-side attack retention pathway (Figure 1), which goes over a high-energy barrier.¹⁻⁶ Very recently, we have uncovered a new double-inversion mechanism for the F⁻ + $CH_3Cl S_N^2$ reaction, in which a proton-abstraction-induced inversion is followed by a second inversion, thereby resulting in retention of configuration, as shown in Figure 1.⁶ The first step of the double inversion is the formation of a XH…CH2Ycomplex, in which an inversion can occur. Then, either the reaction produces an inverted CH₃Y molecule or the first inversion is followed by a second inversion via the usual [X… CH₃…Y]⁻ transition state, resulting in a CH₃X product with retention of the initial configuration. For the F⁻ + CH₃Cl reaction, we have found a FH…CH2Cl⁻ transition state (firstorder saddle point) of C_s point-group symmetry, in which the CH_2Cl^- group is almost planar and FH is in the C_s plane.⁶ The electronic energy of this so-called double-inversion transition



Figure 1. Different mechanisms of the X^- + CH₃Y reactions. Blue background denotes an inverted configuration relative to that of the reactant (yellow).

state is just above the reactants asymptote by 16.4 kcal mol^{-1} , whereas the classical barrier height of the front-side attack is as high as 31.3 kcal $mol^{-1.6}$. Thus, the double inversion opens a

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Figure 2. Classical and zero-point vibrational energy corrected (adiabatic) energies of the double-inversion and front-side attack saddle points and abstraction-channel products ($HX + CH_2Y^-$) relative to the energies of the reactants, X^- (color coded) + CH_3Y (columns), obtained at the CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory.

significantly lower energy retention pathway for the F^- + CH_3Cl reaction than the front-side attack. Reaction dynamics simulations on an accurate global ab initio analytical potential energy surface⁶ showed that the dominant mechanism of the F^- + CH_3Cl reaction is the back-side attack substitution. At a collision energy of ~10 kcal mol⁻¹ the double-inversion pathway opens, and this is the mechanism that is responsible for retention in the collision energy of the front-side attack is ~40 kcal mol⁻¹. Furthermore, at a collision energy of ~20 kcal mol⁻¹ the HF + CH_2Cl^- abstraction channel opens as well. As expected, the reactant's CH stretching excitation enhances the double inversion and the abstraction channel, whereas it does not significantly affect the back-side attack reactivity.

After revealing this novel double-inversion mechanism for the F^- + CH₃Cl reaction an obvious and important question comes to everyone's mind. Is the double inversion a general pathway for S_N2 reactions? In the present study we aim to investigate the possibility of double inversion in 16 S_N2 reactions of the X⁻ + CH₃Y type, where X and Y are F, Cl, Br, and I. Six reactions, where the atomic number of X is less than that of Y, are exothermic, the six reverse reactions are endothermic, and there are four isoenergetic identity reactions, where X and Y are the same. Many previous theoretical studies investigated the Walden inversion pathway involving the preand postreaction ion-dipole complexes and the central transition states;⁷⁻¹⁸ therefore, here we focus on the lessknown retention pathways and the abstraction channel. We use high-level ab initio methods to characterize the double-inversion saddle points as well as the front-side attack transition states and the proton-abstraction channels of the previously mentioned 16 reactions. The present ab initio results provide guidance for future dynamical investigations of the retention pathways in $S_{\rm N}2$ reactions.

2. COMPUTATIONAL DETAILS

We have computed the structures and harmonic vibrational frequencies of the stationary points using the explicitly correlated coupled-cluster singles, doubles, and perturbative triples CCSD(T)-F12b (ref 19) method with the augmented correlation-consistent polarized valence *n*-zeta aug-cc-pV*n*Z [*n* = D and T] basis sets.²⁰ For Br and I, small-core energy-consistent relativistic effective core potentials and the corresponding aug-cc-pV*n*Z-PP [*n* = D and T] basis sets are used.²¹ The constrained optimizations, where one of the internal coordinates is fixed, have been carried out at the CCSD(T)-F12b/aug-cc-pVDZ(-PP) level of theory. The electron correlation computations are performed using the ab initio program package Molpro.²²

3. RESULTS AND DISCUSSION

The classical and zero-point energy (ZPE)-corrected adiabatic relative energies of the double-inversion and front-side attack saddle points and the HX + CH_2Y^- products obtained at the

CH₃CI CH₃Br CH₃I CH₃F 1.519 1.926 2.093 2.274 Bı 60.1 62.2 61 2.184 2.640 2.405 2.481 1 1.666 1.661 1.663 1.658 1.925 2.094 2.276 1.513 Br 58.0 61.5 62.6 62.3 2.396 2.665 2.169 2.478 Br⁻ 1.465 1.460 1.458 1.455 Br Br Rı B 1.50 1.923 2.093 2.15 Br 63.0 63. 91.2 1.815 2.496 2.405 CI[−] 1.413 1.317 1.311 1.309 2.113 Br 96.9 95.1 1.766 1.807 1.810 1.839 F 0.987 0.988 0.981 1.007

Figure 3. Structures of the double-inversion saddle points obtained at the CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory. The distances and the H_bCY angles are given in angstroms and degrees, respectively, where H_b denotes the abstracted hydrogen atom in the C_s plane.

CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory are given in Figure 2. In Tables S1–S3 in the Supporting Information (SI) the corresponding aug-cc-pVDZ(-PP) energies are given as well. The ZPE values and the harmonic vibrational frequencies of all the stationary points are given in Tables S4–S6 in the SI. The aug-cc-pVDZ(-PP) and aug-cc-pVTZ(-PP) basis sets give the same relative energies within ~0.5 kcal mol⁻¹, or in many cases the agreement is much better. This shows the fast basis set convergence of the explicitly correlated F12 method and suggests that the aug-cc-pVTZ(-PP) basis provides wellconverged results with about ± 0.1 kcal mol⁻¹ uncertainty relative to the complete-basis-set results. For F⁻ + CH₃Cl, the benchmark relative energies are also available,⁶ obtained by the focal-point analysis (FPA) approach,^{23,24} which considers extrapolation to the complete-basis-set limit, electron correlation beyond CCSD(T), core electron correlation, and scalar relativistic effects. The FPA classical barrier heights and reaction endothermicity are 16.4, 31.3, and 29.2 kcal mol⁻¹ (ref 6) for double inversion, front-side attack, and abstraction, respectively, whereas the corresponding CCSD(T)-F12b/augcc-pVTZ values are 15.8, 31.0, and 28.7 kcal mol⁻¹. These results suggest that the present relative energies are well within chemical accuracy (uncertainties <1 kcal mol⁻¹). In the cases of double-inversion barrier height and endothermicity of the abstraction channel, the deviations between the CCSD(T)-F12b/aug-cc-pVTZ and FPA energies are mainly due to the

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Figure 4. Structures of the front-side attack saddle points obtained at the CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory. The CX and CY distances and the XCY angles are given in angstroms and degrees, respectively.

core electron correlation effects. For front-side attack, the large core correlation effect is almost canceled by the substantial post-CCSD(T) correlation and scalar relativistic effects.

As Figure 2 shows, the double-inversion barrier heights and the endothermicity of the abstraction channels of the X^- + CH₃Y reactions increase as X goes from F to I and decrease as Y goes from F to I. Thus, the I⁻ + CH₃F reaction has the highest double-inversion barrier height and abstraction endothermicity, whereas the F⁻ + CH₃I reaction has the lowest ones. In all cases the double-inversion saddle point is below the HX + CH₂Y⁻ asymptote. This indicates that the proton-inducted inversion, the first step of double inversion, can happen even if the system does not have enough energy to break apart to form the HX + CH₂Y⁻ products. The F⁻ + CH₃Y reactions have significantly lower classical doubleinversion barrier heights of 28.7, 15.8, 13.2, and 8.6 kcal mol⁻¹ for Y = F, Cl, Br, and I, respectively, than the other 12 reactions that have barrier heights in the 45–90 kcal mol⁻¹ range. On the basis of these results we can conclude that the F⁻ + CH₃Cl reaction, where the double-inversion mechanism was discovered,⁶ is a good candidate for double inversion, but the F⁻ + CH₃I reaction might be even better. The special role of F⁻ among the halide nucleophiles may be explained by its high proton affinity. Furthermore, the hydrogen-bonded complexes were only discovered in the entrance channels of the F⁻ + CH₃Y reactions.^{14,25,6,16}

For the front-side attack there are only 10 distinct saddle points because the forward and backward reactions have the same transition states. Of course, the barrier heights of the nonidentity $X^- + CH_3Y$ and $Y^- + CH_3X$ reactions are different because the same saddle-point energy is relative to different reactant energies. As Figure 2 shows, some trends can be observed for the energy order of the front-side attack barrier heights. Similar to the double-inversion, the front-side attack barrier heights of $X^- + CH_3Y$ increase as X goes from F to I and decrease as Y goes from F to I. Among all reactions investigated

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in this study, the I⁻ + CH₃F reaction has the highest front-side attack barrier (66.8 kcal mol⁻¹), whereas F^- + CH₃I has the lowest one (19.5 kcal mol⁻¹). For the X⁻ + CH₃X identity reactions the front-side attack barrier height increases from F (45.8 kcal mol⁻¹) to Cl (48.6 kcal mol⁻¹) and then decreases as Br (43.9 kcal mol⁻¹) and I (41.5 kcal mol⁻¹).

Comparing the double-inversion and front-side attack barrier heights, we can conclude that in the case of the $F^- + CH_3Y$ [Y = F, Cl, Br, I] reactions the double-inversion saddle points are well below the front-side attack ones. Thus, for the four $F^- + CH_3Y$ systems we can expect retention of configuration at collision energies below the front-side attack barrier height. In the case of the other 12 reactions the double-inversion classical barrier heights are higher than the front-side attack ones.

The ZPE corrections have substantial effects on the doubleinversion barrier heights and the endothermicity of the protonabstraction channel, whereas the ZPE effects on the front-side attack barrier heights are less significant. As Figure 2 shows, the ZPE correction decreases the double-inversion barrier heights by about 2–3 kcal mol⁻¹ for F⁻ + CH₃Y and by about 4–6 kcal mol⁻¹ for the other 12 reactions. For the abstraction channels, the ZPE effects are even larger; the adiabatic product relative energies are below the classical ones by 3–5 kcal mol⁻¹ for HF + CH₂Y⁻ and by 5–7 kcal mol⁻¹ for the other 12 systems. The ZPE correction also decreases the front-side attack barriers, but the effects are only in the 0.2 to 2.1 kcal mol⁻¹ range. Although some of the ZPE effects are large, the adiabatic relative energies are qualitatively similar to the classical ones.

The geometries and the most important structural parameters of the double-inversion and front-side attack saddle points are shown in Figures 3 and 4, respectively. The structural parameters of the saddle points are also listed in Tables S7 and S8 in the SI and the structures of CH₃Y, CH₂Y⁻, and HX are given in Table S9 in the SI. The interested reader can also find the Cartesian coordinates of the double-inversion and frontside attack saddle points in Tables S10 and S11, respectively, in the SI. As Figure 3 shows, all double-inversion saddle points have C_s point-group symmetry and consist of an XH and a CH₂Y⁻ group. The XH saddle-point distances are slightly stretched relative the isolated HX molecule. The most significant stretching effects of 0.06 to 0.09 Å are seen for the FH distances and for ClH…CH₂I⁻, where the ClH distance is 0.14 Å larger than the bond length of the HCl molecule. In the case of X = Cl, Br, and I, the structure of the CH_2Y^- group is very similar to that of the free CH₂Y⁻; for example, the CY distances are just 0.001 to 0.004 Å shorter at the saddle point than in the isolated CH_2Y^- if Y = Cl, Br, and I and 0.013 to 0.025 Å longer in the case of Y = F. The sole exemption is ClH…CH₂I⁻, where the CI distance is significantly contracted by 0.127 Å. In the case of the $FH\cdots CH_2Y^-$ saddle points, the structure of the CH₂Y⁻ group is significantly distorted, the CY distances are contracted by 0.062, 0.134, 0.154, and 0.165 Å for Y = F, Cl, Br, and I, respectively, and the CH_2Y^- group is close to a planar structure. The similarity of the FH_{h} ... $CH_{2}Y^{-}$ [Y = F, Cl, Br, I] and the ClH_b \cdots CH₂I⁻ saddle-point structures is also seen in the case of the H_bCY angles, which are in the 90–100° range for these five structures, whereas the H_bCY angles are in the $55-65^{\circ}$ range for the other 11 systems. The H_bC distances, ~1.8 Å, are also similar for the FH_b ... CH_2Y^- and the ClH_b ... CH₂I⁻ saddle points, whereas the corresponding values are in the 2.2 to 2.7 Å range for the other reactions. (Among these the shortest values, ~2.2 Å, are for XH_{b} ... $CH_{2}F^{-}$ [X = Cl, Br, I].)

As Figure 4 shows, at the front-side attack saddle points, two halogens are connected to the carbon atom and both the CX and CY distances are substantially stretched relative to the corresponding bond lengths in the isolated methyl-halides. Because both the forward and backward reactions go over the same front-side attack barrier, six-six saddle-point structures are the same. The $FYCH_3^-$ structures, where Y = Cl, Br, and I, are special because in this case the transition state has C_{c} symmetry, where four atoms, F, Y, C, and H, are in the C_s plane. All of the other systems have saddle-point structures without having four atoms in a plane. The identity reactions also have C_s point-group symmetry, but here the two identical halogens and two hydrogen atoms are out of the plane. The ClBrCH₃⁻, ClICH₃⁻, and BrICH₃⁻ systems have structures similar to the identity reactions; however, because of the different halogen ligands these saddle points have C_1 symmetry. The XCY angles are $\sim 80^{\circ}$ if X or Y is F; otherwise, the angles are $\sim 85^{\circ}$. These bond angles suggest significant sideways scattering, which was found in the case of the front-side attack trajectories of the F⁻ + CH₃Cl reaction.⁶ The CY distances are stretched by ~0.5 Å for the $FYCH_3^-$ saddle points relative to corresponding CY bond lengths in the CH₃Y molecules. In the case of the $XYCH_3^-$ saddle points, where X = Cl, Br, and I, the CF, CCl, CBr, and CI distances are about 0.10 to 0.14, 0.14 to 0.19, 0.16 to 0.21, and 0.20 to 0.26 Å larger, respectively, than the corresponding values for FYCH₃⁻.

The key step of the double-inversion mechanism is the inversion of the CH_2Y^- group via a $XH\cdots CH_2Y^-$ saddle point. Let us first investigate the inversion of the isolated CH_2Y^- system. The double-well potential energy curves of CH_2Y^- [Y = F, Cl, Br, I] along the inversion coordinate are shown in Figure 5. The minima correspond to pyramidal equilibrium structures



Figure 5. Potential energy curves for CH_2Y^- [Y = F, Cl, Br, I] obtained by constrained optimizations at the CCSD(T)-F12b/aug-cc-pVDZ(-PP) level of theory. α is defined as the ZCH angle, where Z is a dummy atom in the C_i plane with ZCY angle of 90°.

with C_s symmetry, whereas at the top of the barrier CH_2Y^- is planar with C_{2v} symmetry. The inversion classical (adiabatic) barrier heights are 13.2(13.0), 12.4(12.2), 14.3(13.9), and 13.8(13.4) kcal mol⁻¹ for Y = F, Cl, Br, and I, respectively, at the CCSD(T)-F12b/aug-cc-pVDZ(-PP) level of theory, and the corresponding aug-cc-pVTZ(-PP) values are 13.0(12.8), 12.7(12.3), 14.4(14.0), and 13.8(13.4) kcal mol⁻¹. These relatively small barriers indicate that a proton-abstractioninduced inversion can happen in the X⁻ + CH₃Y systems. To investigate the minimum energy path of the induced inversion, we performed constrained optimizations starting from the



Figure 6. Potential energy paths for the proton-abstraction-induced inversion of selected $X^- + CH_3Y$ (X = F, Cl, Br; Y = Cl, Br, I) reactions obtained by constrained optimizations at the CCSD(T)-F12b/aug-cc-pVDZ(-PP) level of theory. α is defined as the ZCH angle, where Z is a dummy atom in the C_s plane with ZCY angle of 90° and H is one of the out-of-plane H atoms. The energies are relative to $X^- + CH_3Y$ (equilibrium).

double-inversion saddle points fixing the α inversion coordinate and relaxing the other internal coordinates. We define angle α (ZCH) using a dummy atom Z in the C_s plane with ZCY angle of 90° and one of the out-of-plane H atoms. The potential energy curves as a function of α are given in Figure 6 for the F^- + CH₃Cl, F^- + CH₃I, Cl⁻ + CH₃I, and Br⁻ + CH₃Br systems. Reaction dynamics simulations performed recently⁶ for F^- + CH₃Cl showed that after F^- abstracts a proton, the system typically rotates into a double-inversion saddle-pointlike configuration, which corresponds to $\alpha > 100^{\circ}$ in Figure 6. Then, the configuration around the carbon center can invert (α decreases below 90°) while the FH bond breaks and a CH bond forms. As Figure 6 shows, along this inversion reaction path the potential energy decreases rapidly apart from a small barrier in some cases. These potential energy paths clearly show that the inversion can occur for various systems; the main difference is in the energy of the saddle-point-like structure relative to that of the reactants. For F⁻ + CH₃Cl and F⁻ + CH_3I , the relative energies go up to about 16 and 8 kcal mol⁻¹, respectively, whereas for Cl⁻ + CH₃I and Br⁻ + CH₃Br the ClH and BrH have to climb up to as high as 46 and 62 kcal mol^{-1} . Of course, reaction dynamics simulations should be performed to verify these reaction pathways.

4. SUMMARY AND CONCLUSIONS

Recent reaction dynamics simulations on an analytical ab initio potential energy surface revealed a novel double-inversion mechanism for the F⁻ + CH₃Cl S_N2 reaction.⁶ We also found an FH…CH₂Cl⁻ double-inversion saddle point, which has significantly lower energy than that of the front-side attack

transition state.⁶ In the present study we performed high-level explicitly correlated CCSD(T)-F12b computations with triple- ζ basis sets for 16 reactions of X^- + CH₃Y type, where X and Y are halogens, and showed that XH…CH₂Y⁻-type doubleinversion saddle points exist for all 16 reactions. The doubleinversion barrier heights are the smallest for the X = F systems and increase as X goes from F to I and decrease as Y goes from F to I. Thus, the F^- + CH₃I reaction has the lowest doubleinversion classical(adiabatic) barrier height of 8.6(6.6) kcal mol^{-1} , which is about the half of the barrier height of the F⁻ + CH_3Cl reaction. For the X⁻ + CH_3X identity reactions the double-inversion classical(adiabatic) barrier heights are 28.7(25.6), 54.8(50.3), 61.9(56.8), and 67.8(62.3) kcal mol⁻¹ for X = F, Cl, Br, and I, respectively. These results demonstrate that the barrier heights in the case of F^- nucleophile are significantly less than the others. It is also seen that the ZPE corrections have substantial effects on the double-inversion barrier heights. The energy levels of the HX + $CH_2Y^$ abstraction channels are always above the corresponding XH…CH₂Y⁻ saddle points. The front-side attack saddle points are above the double-inversion ones for the $F^- + CH_3Y$ [Y = F, Cl, Br, I] reactions and the reverse holds for the other systems. Thus, the double inversion is likely to play a more important role in the $S_N 2$ reactions with F⁻ nucleophile.

All double-inversion saddle points have C_s point-group symmetry. The FH…CH₂Y⁻ [Y = F, Cl, Br, I] and ClH…CH₂I⁻ saddle points have similar structures, H_bC distances are ~1.8 Å, and H_bCY angles are in the 90–100° range. For the other systems the H_bC separations are larger, 2.2 to 2.7 Å, and the H_bCY angles are 55–65°. The front-side attack saddle points have C_s symmetry with four atoms, FYCH, in a plane for the FYCH₃⁻ [Y = Cl, Br, I] systems, whereas for the other reactions the saddle-point structures are twisted, resulting C_s symmetry with only two atoms, CH, in the plane for the identity reactions and C_1 symmetry for the XYCH₃⁻ [X/Y = Cl/Br, Cl/I, Br/I] systems. Both the CX and CY distances are substantially stretched by 0.5 to 0.8 Å relative to the corresponding bond lengths in the isolated methyl-halide molecules. The XCY angles are in the 78–88° range, which suggests the dominance of sideways scattering for the front-side attack reactive collisions.

Reaction pathways along the inversion coordinate of the XH…CH₂Y⁻ systems are investigated. On the basis of the present results and the typical double-inversion trajectories found previously for the F⁻ + CH₃Cl reaction, we can conclude that the proton-abstraction-induced inversion, which is the first step of the double-inversion mechanism, may be a general mechanism, where first the XH…CH₂Y⁻ system forms a double-inversion saddle-point-like structure and second the inversion occurs while the XH bond breaks and a new CH bond forms. The present work may inspire and guide future reaction dynamics studies to investigate the retention mechanisms in S_N2 reactions.

ASSOCIATED CONTENT

S Supporting Information

Classical relative energies of the stationary points obtained at the CCSD(T)-F12b/aug-cc-pV*n*Z(-PP) [n = D and T] levels of theory. Structures and harmonic vibrational frequencies of all the stationary points investigated in this study and Cartesian coordinates of the double-inversion and front-side attack saddle points obtained at the CCSD(T)-F12b/aug-cc-pVTZ(-PP) level of theory. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Glukhovtsev, M. N.; Pross, A.; Schlegel, H. B.; Bach, R. D.; Radom, L. Gas-Phase Identity $S_N 2$ Reactions of Halide Anions and Methyl Halides with Retention of Configuration. *J. Am. Chem. Soc.* **1996**, *118*, 11258–11264.

(2) Li, G.; Hase, W. L. Ab Initio Direct Dynamics Trajectory Study of the Cl⁻ + CH₃Cl S_N 2 Reaction at High Reagent Translational Energy. *J. Am. Chem. Soc.* **1999**, *121*, 7124–7129.

(3) Angel, L. A.; Ervin, K. M. Dynamics of the Gas-Phase Reactions of Fluoride Ions with Chloromethane. *J. Phys. Chem. A* 2001, *105*, 4042–4051.

(4) Bento, A. P.; Bickelhaupt, F. M. Nucleophilicity and Leaving-Group Ability in Frontside and Backside $S_N 2$ Reactions. J. Org. Chem. 2008, 73, 7290–7299.

(5) Yang, Z.-Z.; Ding, Y.-L.; Zhao, D.-X. Theoretical Analysis of Gas-Phase Front-Side Attack Identity $S_N 2(C)$ and $S_N 2(Si)$ Reactions with Retention of Configuration. J. Phys. Chem. A **2009**, 113, 5432–5445.

(6) Szabó, I.; Czakó, G. Revealing a Double-Inversion Mechanism for the $F^- + CH_3Cl S_N 2$ Reaction. *Nat. Commun.* **2015**, *6*, 5972.

(7) Glukhovtsev, M. N.; Pross, A.; Radom, L. Gas-Phase Identity $S_N 2$ Reactions of Halide Anions with Methyl Halides: A High-Level Computational Study. J. Am. Chem. Soc. **1995**, 117, 2024–2032.

(8) Glukhovtsev, M. N.; Pross, A.; Radom, L. Gas-Phase Non-Identity S_N2 Reactions of Halide Anions with Methyl Halides: A High-Level Computational Study. *J. Am. Chem. Soc.* 1996, 118, 6273–6284.
(9) Raugei, S.; Cardini, G.; Schettino, V. An Ab Initio Molecular

Dynamics Study of the $S_N 2$ Reaction $Cl^- + CH_3Br \rightarrow CH_3Cl + Br^-$. J. Chem. Phys. 1999, 111, 10887–10894. (10) Chabinyc, M. L.; Craig, S. L.; Regan, C. K.; Brauman, J. I. Gas-

Phase Ionic Reactions: Dynamics and Mechanism of Nucleophilic Displacements. *Science* **1998**, *279*, 1882–1886.

(11) Parthiban, S.; de Oliveira, G.; Martin, J. M. L. Benchmark ab Initio Energy Profiles for the Gas-Phase $S_N 2$ Reactions $Y^- + CH_3 X \rightarrow$ $CH_3 Y + X^- (X,Y = F,Cl,Br)$. Validation of Hybrid DFT Methods. *J. Phys. Chem. A* **2001**, *105*, 895–904.

(12) Gonzales, J. M.; Cox, R. S.; Brown, S. T.; Allen, W. D.; Schaefer, H. F. Assessment of Density Functional Theory for Model $S_N 2$ Reactions: $CH_3X + F^-$ (X = F, Cl, CN, OH, SH, NH_2 , PH_2). J. Phys. Chem. A **2001**, 105, 11327–11346.

(13) Gonzales, J. M.; et al. Definitive Ab Initio Studies of Model $S_N 2$ Reactions $CH_3X + F^-(X = F, Cl, CN, OH, SH, NH_2, PH_2)$. *Chem.*— *Eur. J.* **2003**, *9*, 2173–2192.

(14) Zhang, J.; Hase, W. L. Electronic Structure Theory Study of the $F^- + CH_3I \rightarrow FCH_3 + I^-$ Potential Energy Surface. J. Phys. Chem. A **2010**, 114, 9635–9643.

(15) Manikandan, P.; Zhang, J.; Hase, W. L. Chemical Dynamics Simulations of $X^- + CH_3Y \rightarrow XCH_3 + Y^-$ Gas-Phase S_N2 Nucleophilic Substitution Reactions. Nonstatistical Dynamics and Nontraditional Reaction Mechanisms. *J. Phys. Chem. A* **2012**, *116*, 3061–3080.

(16) Szabó, I.; Császár, Á. G.; Czakó, G. Dynamics of the F⁻ + $CH_3Cl \rightarrow Cl^- + CH_3F S_N^2$ Reaction on a Chemically Accurate Potential Energy Surface. *Chem. Sci.* **2013**, *4*, 4362–4370.

(17) Zhang, J.; Xu, Y.; Chen, J.; Wang, D. Y. A Multilayered-Representation, Quantum Mechanical/Molecular Mechanics Study of the $CH_3Cl + F^-$ Reaction in Aqueous Solution: the Reaction Mechanism, Solvent Effects and Potential of Mean Force. *Phys. Chem. Chem. Phys.* **2014**, *16*, 7611–7617.

(18) Xie, J.; Otto, R.; Mikosch, J.; Zhang, J.; Wester, R.; Hase, W. L. Identification of Atomic-Level Mechanisms for Gas-Phase X^- + CH₃Y S_N2 Reactions by Combined Experiments and Simulations. *Acc. Chem. Res.* **2014**, *47*, 2960–2969.

(19) Adler, T. B.; Knizia, G.; Werner, H.-J. A Simple and Efficient CCSD(T)-F12 Approximation. J. Chem. Phys. 2007, 127, 221106.

(20) Dunning, T. H., Jr. Gaussian Basis Sets for Use in Correlated Molecular Calculations. I. The Atoms Boron Through Neon and Hydrogen. J. Chem. Phys. **1989**, *90*, 1007–1023.

(21) Peterson, K. A.; Figgen, D.; Goll, E.; Stoll, H.; Dolg, M. Systematically Convergent Basis Sets with Relativistic Pseudopotentials. II. Small-Core Pseudopotentials and Correlation Consistent Basis Sets for the Post-*d* Group 16–18 Elements. *J. Chem. Phys.* **2003**, *119*, 11113–11123.

(22) Werner, H.-J.; Knowles, P. J.; Knizia, G.; Manby, F. R.; Schütz, M.; et al. *Molpro, A Package of Ab Initio Programs,* version 2012.1.http://www.molpro.net.

(23) Allen, W. D.; East, A. L. L.; Császár, A. G. In *Structures and Conformations of Non-Rigid Molecules*; Laane, J., Dakkouri, M., van der Veken, B., Oberhammer, H., Eds.; Kluwer: Dordrecht, The Netherlands, 1993; p 343.

(24) Császár, A. G.; Allen, W. D.; Schaefer, H. F. In Pursuit of the Ab Initio Limit for Conformational Energy Prototypes. *J. Chem. Phys.* **1998**, *108*, 9751–9764.

(25) Xie, J.; Zhang, J.; Hase, W. L. Is There Hydrogen Bonding for Gas Phase $S_N 2$ Pre-Reaction Complexes? *Int. J. Mass Spectrom.* DOI: 10.1016/j.ijms.2014.04.002.