

Revealing a new mechanism feature of $F^- + CH_3Cl \rightarrow Cl^- + CH_3F$ reaction by using ab initio molecular dynamics

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Abstract. S_N2 reaction gained much attention because of its vital role in biomolecular and organic chemistry. In the past decades, great progress on mechanism understanding of S_N2 reaction has been made by a lot of papers. However, atomic details of the reaction are complicated and hard to explore without precise potential energy surface. In this report, an ab initio molecular dynamics method shed light on the reaction explorations. Although a potential energy surface is disable, we can still make contributions on the mechanism study. Here, we found a novel mechanism in $F^- + CH_3Cl \rightarrow Cl^- + CH_3F$ that shared common transition state with abstract mechanism but avoid the proton transfer channel. It is a combination of proton roundabout and classical back-side attack mechanism, which is never observed in previous papers. Interestingly, a hydrogen bond transfer process exists in the novel mechanism which simultaneously involved in both C-H-F and Cl-H-F hydrogen bond. It provides another channel of proton transfer in low collision energy, and shows that more explorations have to be carried out even though various mechanism of S_N2 reaction have been reported.

1. Introduction

It takes decades for researchers to explore and understand the S_N2 reaction mechanism. Since these mechanisms play a vital role on revealing dynamics of biomolecular reaction and a large amount of papers on S_N2 reaction pathway have been reported. [1-21] Especially these involved in halogen atoms, which explored frequently because of their strong electronegativity. There is a classical mechanism called “back-side attack” in the textbook that the nucleophile attack the C atom and make the bond between C atom and leaving group weaken. The back-side attack mechanism has a central barrier connected by two minima, which is considered as direct mechanism. However, various indirect mechanisms contained pre-complex and non-covalent interaction has been revealed gradually in last decade. For instance, indirect mechanisms, such as hydrogen-bond in $F^- + CH_3Cl$ reaction mainly results from electrostatic interaction between one H atom in CH_3Cl complex and F atom, which impelled by the significant electronegativity. Besides, the so-called “roundabout” mechanism is predominantly caused by initial angular momentum and Van del Waals. Very recently, a double inversion mechanism observed by Gabor et al has a long-lived hydrogen bond before the Walden inversion, which is a special hydrogen-bond mechanism to some extent. [6,7]

So far there are two mainly mechanisms revealed in S_N2 reaction, direct and indirect pathway. [8] Direct mechanism typically contains both rebound and stripping. In rebound mechanism, a bond between nucleophile and C atom come

into being along with leaving group getting most translational energy. On the contrary, the nucleophile take the CH_3 away and left the leaving group nearby initial position in stripping mechanism. And the indirect one consist of different pathway in which pre-reaction complexes existed. Hase et al summarized principal mechanism of S_N2 reaction in a previous paper. In retrospect, all indirect mechanisms were attributable to the complex formation. Since the descriptions of pre-reaction complex are complicated so as to Hase et al argued that much explorations to describe features of S_N2 pathway need to be done. As is known, F atom has significant orientation in S_N2 reaction, besides, chlorine is supported by much basis sets. Thus, in this paper, we reported a novel reaction pathway of $F^- + CH_3Cl$ as well as $F^- + CH_3I$ with an ab initio molecular dynamics method which is capable of visualizing the initio coordinate conditions.

Traditionally, molecular dynamics simulations required a potential energy surface prepared in advance, which is hard to fit in polyatomic system. Here we apply an ‘on the fly’ method to carry out the dynamics simulations where an accurate potential surface is disabled. A module performing adiabatic ab initio molecular dynamics is implemented recently in nwchem.[22] The integration of nuclei and electronic potential calculated by using velocity-Verlet algorithm and Gaussian basis set based methods, respectively.[23] We found a novel pathway that the non-covalent interaction not only exists between HF and C atom but also HF and Cl atom. Briefly, the attacking atom F get a H atom and form hydrogen-bond complex with C atom at the beginning, then the bond between H atom and C would be break along with a new hydrogen-bond between Cl and HF formed. At the end of pre-reaction complex, a hydrogen-bond between HF and C reformed, that process is never observed in previous reports. And the rest of

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part is known as back-side attack pathway. Interestingly, the C-Cl bond has nearly rotated a whole circle in the entire pre-reaction, as shown in Figure 1.1. That results from the convenience provided by visible initio conditions. On the basis of trajectories, we have indeed verified a series of pattern that the indirect mechanism occurred on certain range of alpha along with impact parameter changed from 0 to b_{max} in where the reaction possibility reduced to zero.

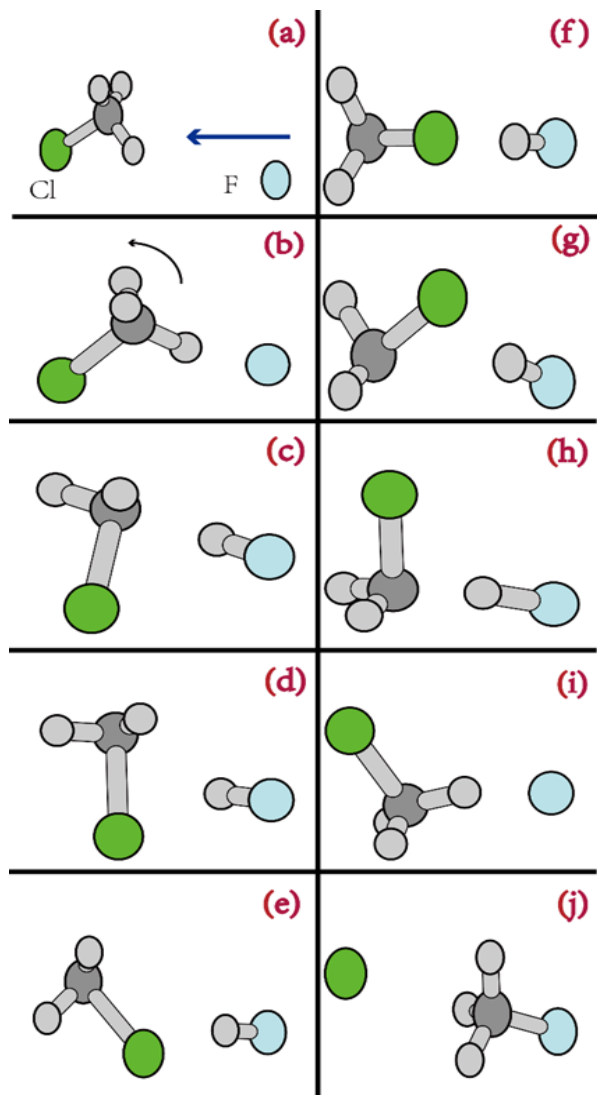


Figure 1.1: The evolution pathway of novel mechanism presented as proton transfer then come back to back-side attack. (PTCB).

In this work, we observed a novel reaction pathway that has never been found in any S_N2 reactions before: a reaction mechanism which is mixture of a proton-abstracted mechanism and a backside attack mechanism, also called proton transfer then come back (PTCB): the nucleophile F^- attacks the side of CH_3Cl and forms a hydrogen bond with one H atom, and the nucleophile then abstracts the proton (proton-abstracted) inducing the rotational of the rest of substrate, CH_2Cl^- (roundabout); after one rotation of the CH_2Cl nucleophile releases the proton and forms the hydrogen-bond complex again; the following part of reaction is the traditional,

back-side attack process. This reaction mechanism (proton-abstracted roundabout and back-side attack) is a new reaction mechanism not seen before. Furthermore, the proton-abstracted roundabout mechanism is different from the roundabout mechanism, where the nucleophile attacks the side of the substrate to cause the rotation of the whole substrate; here the nucleophile attracts proton and the HF induces part of the substrate rotated (CH_2Cl^-). The new findings of this study shows, on one hand, that some mechanisms of the S_N2 at C center should also observed by BOMD method without a precise potential energy surface, for example the new found double-inversion mechanism; on the other hand, the new finding of this study, the proton-abstracted roundabout and backside attack mechanism, shows, so far, the S_N2 mechanisms have not been completely discovered. Additional work needs to be done to probe the reaction mechanism and dynamics of the S_N2 reaction in general.

2. Theoretical methods

2.1 ab initio molecular dynamics (AIMD)

Ab initio calculations combine classical molecular dynamics simulations with electronic structure calculations on the fly. To perform AIMD simulations where the only assumptions are the validity of classical mechanics to describe ionic motion and the Born-Oppenheimer (BO) approximation to separate nuclear and electronic coordinates. Car and Parrinello kick started and dominated the AIMD field and their methods stays at the beginning of all new developments in this field.[24] The vast majority AIMD is to propagate the nuclei classically and solve Schrödinger equation for every step 'on the fly' with using a updated orbital stem from last step. As a state-of-art in BOMD, a module to perform BOMD in any of the Gaussian basis sets based methods in nwchem package is implemented. In view of F^- has significant orientation impact on CH_3Cl , we have to deal with the initio coordinates conditions cautiously. The initio conditions will be discussed in next part, but briefly, we exert two different settings to the beginning position and velocity. First things first, we build a frame of axes with the original point is the mass-center of CH_3Cl optimized in DFT level (m06-2x/mg3s), in that case, there is no necessary to move or change the CH_3Cl complex. Our aim is to find novel pathway of $CH_3Cl + F^-$, therefore no-limitations on impact parameter (called b) as well as beginning position of F^- ion make sense indeed, which means we rotate the F^- randomly along the axes and give it different impact parameter in a variety of collision energy from 0.68eV to 2.49 eV. From these thousands of trajectories, we gain a general view of mechanisms that might happen. Calculating potential energy in every step makes BOMD a costly method. Thus, the value of using mg3s basis set to carry out the trajectories is considering the cost and efficiency simultaneously. Another setting for initio conditions is fix the impact parameter and rotate the CH_3Cl complex along axis crossing the mass-center. That calculation was performed in DFT level (m06-2x/cc-pvtz). Based on the results, we pick up the novel pathway considered and clarify the existence of their

transition states and barrier. That coordinates setting is for the cross section calculations, since it requires a series of possibilities corresponding certain impact parameters.

2.2 Initio coordinate conditions and trajectory

In a recent work, C atom was chosen as the original point of coordinate system and the attack angle changed from 0 to 180 degrees.[7] However, the C atom is definitely not the mass-center of CH_3Cl , even it might be nearby the center. Instead of mainly concerned 0-180 degrees over rotation angle of CH_3Cl in former work, where glossed over nearly half orientations, we take account of whole orientations of the CH_3Cl along the axis as well as paralleled velocity direction. As key point of classical part in AIMD, the nuclei's motion hinged on the accuracy of barycenter. Therefore, in our work, we exert velocity-Verlet method to perform trajectory integrations. For the best accuracy and computational cost, we set the time step as 10 au, about 0.24 fs, and the number of steps in the nuclear dynamics is 5000 default. Based on simulation results, we can continually increase step number when it comes to the indirect mechanism especially those own long-lived ion-complex or hydrogen-bond complex needed much more steps to observed whole process. Besides, the temperature is fixed at 298.15k. As touched on introduction above, we employee two different beginning settings to carry out the simulations. Firstly, the CH_3Cl is frozen with center of mass as the original point. The distance between barycenter and F ion is measured to exceed 15\AA which is generally considered the formation of reactant. At the first setting, the F^- rotate along with not only one axis but also other two axes in order to get sufficient perspectives in attacking directions. We set up a wide range of collision energy to exert the AIMD, which the lower limit is fix at 0.68 eV, since that height is capable of covering all known transition states. Hence theoretically, we can observe all saddle points presented in previous works. Secondly, we aim to calculate the probability of the reaction and that is required simulations in series impact parameters increasing gradually at certain collision energy, 1 eV, the interval of impact parameter is 0.05\AA . The results will discuss in next section.

2.3 Nudged Elastic Band method

Given that the trajectories of AIMD simulations cannot represent the minimum energy path (MEP), we exert a nudged elastic band method to find MEP. Nudged Elastic Band method can be used to perform minimum energy path optimizations. Here, we use the climbing image nudged elastic band method, which is a modified version of regular NEB.[25,26] The reaction pathway was mapped out using dozens of images from the reactant to the product state. The structure of the top images on the reaction pathway was isolated for a transition state search. The obtained transition state was confirmed by a frequency calculation in the gas phase with only one imaginary frequency. The first transition state found in DFT/aug-cc-pvtz/m06-2x [27,28] of novel mechanism has a barrier 10.0 kcal/mol, which is competitive with the double-inversion mechanism.[6]

3. Results and discussion

The impact parameter of reactants plays a key role in $\text{S}_{\text{N}}2$ reaction, especially the $\text{F}^- + \text{CH}_3\text{Cl}$, because of the significant orientation of F ion. [8] The maximum of impact parameter at which reaction occurs called b_{max} should be identified firstly. Given that costliness of BOMD especially in cc-pvtz level, 150 trajectories were calculated in each b changed from 0 to 8\AA . We found that reaction still occurs in b of 5\AA , and no more happened in b of 6\AA . Hence, the value of b_{max} is larger than 5\AA and less than 6\AA . To confirm the precise number of b_{max} , we exert dichotomy to carry out the simulations. For instance, if reaction still occurs in b of 5.5\AA , it indicates that b_{max} is between b of 5.5\AA and b of 6\AA , and so forth. There are no more reactions higher than b of 5.95\AA , which is the b_{max} . As shown in Figure 3.1, three mechanisms presented by different colors. The classical back-side attack pathway has a double well potential energy surface with one negative transition state (TS3) of -13.4 kcal/mol. On the contrary, abstraction mechanism obtained a positive transition state (TS1) of 10.0 kcal/mol and the minimum is slight lower than the saddle point. Interestingly, the novel pathway shared a common transition state and a minimum (min3) but avoided the proton transfer pathway eventually. The complex come back to back-side attack (so called PTCB) through a positive saddle point (TS2) of 10.1 kcal/mol which is a bit higher than transition state of abstraction mechanism, which means it becomes significantly competitive with abstraction mechanism. As a consequence, the novel mechanism provides a new sight into the $\text{S}_{\text{N}}2$ reaction pathway which is generally considered that roundabout is not facile to appear in low collision energy.

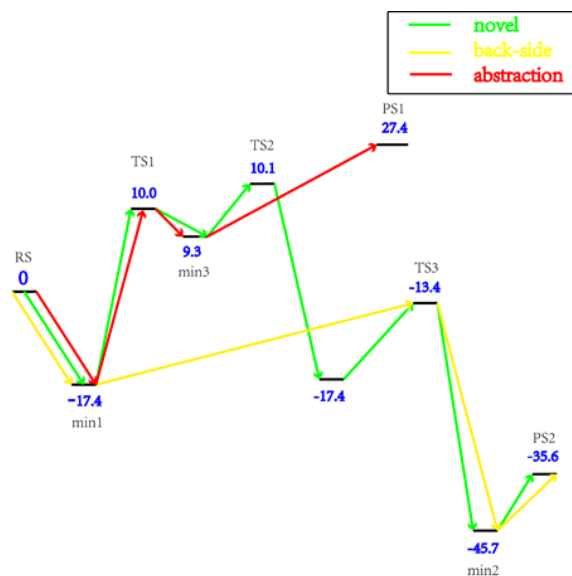


Figure 3.1: Stationary points of three mechanisms in DFT/aug-cc-pvtz/m06-2x theory level. The green, yellow, red curve represent novel, back-side and abstraction mechanisms, respectively. The structure information were presented in supplement.

The possibilities of reaction mechanisms are shown in Figure 3.2, indicating that total probability rapidly decrease after b of 4\AA . The direct rebound mechanism is concentrated

in small b , and reduced linearly to zero after b of 1 Å. Similar with rebound pathway, the direct stripping mechanism declined linearly after b of 2 Å and reached zero at b of 4 Å. Interestingly, indirect mechanism contained hydrogen mechanism, ion-dipole mechanism etc, through an up and down procedure. The peak of curve appears at b of 3 Å, nearly equal to the total probability. These curves show that the atomistic mechanisms are extremely rely on impact parameters. The reaction cross section σ is calculated by integrating the reaction probability versus b , $P(b)$ over b ; i.e. $\sigma = 2\pi \int P(b)b db$. The total reaction cross section is 1.57 Å². The rebound, stripping, indirect and total percentages of all trajectories are 10.3, 6, 13.8 and 30.6%, respectively. Thus, rebound mechanism is more dominant than stripping mechanism for chlorine reaction.

However, possibilities of indirect mechanisms is higher than we expected, especially hydrogen-bond mechanism. As shown in Figure 3.3, hydrogen-bond mechanism dominant the most to indirect trajectories. Its percentage of all trajectories is 7.5%, even bigger than stripping mechanism. The curve reaching vertex at large impact parameter shows that F ion orients CH₃Cl efficiently and was easily trapped by hydrogen atom owing to its significant electronegativity. This feature produced an unusual reaction pathway via a pullback mechanism as detailed below. The F ion attacks CH₃Cl from the front side at large b , driven a semicircle at space through non-covalent interaction caused by CH₃ umbrella, then coming back along another semicircle. And in every round F ion is closer to CH₃ umbrella than last until a back-side transition state formed. Non-covalent interactions play key role in that procedure.

Here, we report a novel mechanism both involved in non-covalent and covalent interaction before classical back-side attack. As shown in Figure 1.1 (a), the F ion attacks CH₃Cl to form hydrogen complex then translates the kinetic energy to CH₃Cl. As a result, the CH₃Cl complex rotates to the opposite direction of velocity of F ion. However, with the strong electronegativity of F ion, a hydrogen atom on the CH₃Cl was taken away by hydrogen bond, which is shown in Figure 1.1 (c). Then, with the rotation of CH₂Cl, hydrogen bond between C-H-F was broken along the increasing of distance between C and F, as shown in Figure 1.1 (d) which is transition state of abstraction mechanism. Yet unlike the behavior in abstraction mechanism in where the CH₂Cl and HF apart away from each other, HF was attracted by Cl and formed another hydrogen bond of Cl-H-F, as shown in Figure 1.1 (e). Moreover, CH₂Cl and HF would formed a head to head structure which is unstable, then the CH₂Cl kept rolling and the persistence of hydrogen bond of Cl-H-F makes the process smooth. As shown in Figure 1.1 (g), the structure looks like the Figure 1.1 (d) because both of them is the beginning and ending of hydrogen bond of Cl-H-F, respectively. A hydrogen bond between C-H-F reformed shown in Figure 1.1 (h) along the rotation of CH₂Cl, then a hydrogen complex reported by previous papers came into being shown in Figure 1.1 (i). The rest part of the reaction pathway is the textbook backside attack pathway.

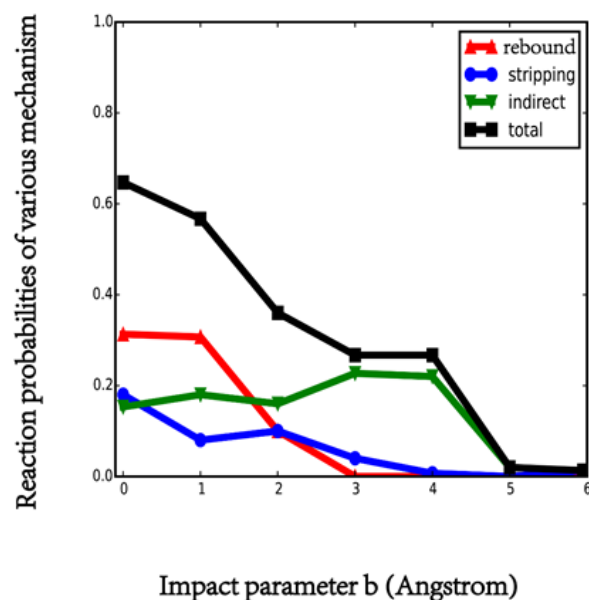


Figure 3.2: Reaction probabilities of various mechanisms contained four elements including rebound, stripping, indirect and total mechanisms.

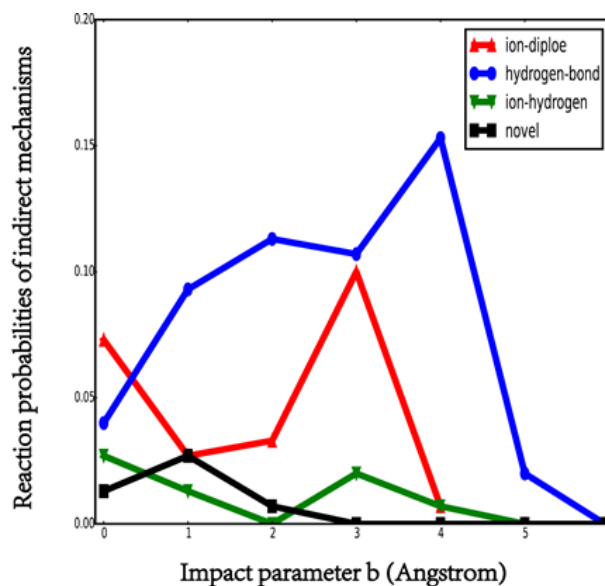


Figure 3.3: Indirect mechanisms of trajectories calculations contain four elements including ion-dipole, hydrogen-bond, ion-hydrogen-bond hybrid and novel mechanisms. An obvious conclusion draw that the hydrogen-bond mechanism makes dominant contributions to indirect reaction pathway.

4. Conclusion

A novel reaction mechanism, a proton-abstracted roundabout with back-side attack reaction, was discovered for the S_N2 reaction at C center, F⁻ + CH₃Cl. This new PTCB mechanism has not been observed before in any S_N2 reactions: the first half is a proton-abstracted induced part of the substrate roundabout mechanism followed a second half backside attack mechanism. The PT (proton transfer) part of the new mechanism shares the same transition state as the proton abstraction mechanism. However, from this transition state, the PTCB mechanism is a

downhill process as the PT mechanism is an uphill process. Therefore, the PT mechanism results in the reaction avoiding the PT channel at low collision energy. Indeed, the PT channel was not open at 0.7 eV from our calculation, whereas the PT mechanism contributes 3% to the total reactive trajectories. It is understandable that the PT mechanism has the smallest percentage of the whole reactive trajectories because it has the highest barrier height among all the mechanisms.

Our study tells that the majority of the reaction mechanisms of the S_N2 reaction can be observed by AIMD method, such as the backside attack, the hydrogen-complex, the roundabout and the proton-abstraction. Most importantly, S_N2 at C for the title reaction has one unique mechanism, PT mechanism, which was not found in any S_N2 reactions before. The current study, on one hand, shed new spotlight on the S_N2 reaction mechanism and dynamics; on the other hand, it indicates the current knowledge on the reaction mechanism of the S_N2 reactions might not be complete. More studies, both experimental and theoretical studies, need to be done to extend our knowledge on the S_N2 reactions both in gas phase and solution phase.

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