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Roundabout Mechanism of Ion–Molecule Nucleophilic Substitution Reactions

Xiangyu Wu, Fei Ying, Hongyi Wang, Li Yang, Jiaxu Zhang, and Jing Xie*

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ABSTRACT: Roundabout (RA) is an important indirect mechanism for gas-phase $X^- + CH_3Y \rightarrow XCH_3 + Y^- S_N^2$ reactions at a high collision energy. It refers to the rotation of the CH₃-group by half or multiple circles upon the collision of incoming nucleophiles before substitution takes place. The RA mechanism was first discovered in the Cl⁻ + CH₃I S_N² reaction to explain the energy transfer observed in crossed molecular beam imaging experiments in 2008. Since then, the RA mechanism and its variants have been observed not only in multiple C-centered S_N² reactions, but also in N-centered S_N² reactions, proton transfer reactions, and elimination reactions. This work reviewed recent studies on the RA mechanism and summarized the characteristics of RA mechanisms in terms of variant types,



product energy partitioning, and product velocity scattering angle distribution. RA mechanisms usually happen at small impact parameters and tend to couple with other mechanisms at relatively low collision energy, and the available energy of roundabout trajectories is primarily partitioned to internal energy. Factors that affect the importance of the RA mechanism were analyzed, including the type of leaving group and nucleophile, collision energy, and microsolvation. A massive leaving group and relatively high collision energy are prerequisite for the occurrence of the roundabout mechanism. Interestingly, when reacting with CH_3I , the importance of RA mechanisms follows an order of $CI^- > HO^- > F^-$, and such a nucleophile dependence was attributed to the difference in proton affinity and size of the nucleophile.

KEYWORDS: direct dynamics simulations, ion—molecule nucleophilic substitution reaction, indirect mechanisms, roundabout mechanisms, elimination, proton transfer, product energy distribution, nucleophile

INTRODUCTION

Nucleophilic substitution reactions (the S_N2 reaction) of ions in the gas phase are fundamental organic reactions that have been widely studied by both experimental and theoretical chemists.¹⁻⁶ In chemistry, it is important to understand the reaction dynamics and mechanisms. For a representative gas phase ion-molecule $S_N 2$ reaction, $X^- + CH_3 Y \rightarrow XCH_3 + Y^-$ (1), the reactive event usually begins with a nucleophile (X^{-}) approaching the carbon atom of the substrate (CH₃Y) from the back-side, forming a prereaction complex X⁻…CH₃Y (RC). Then, the system goes through a transition state (TS) with an umbrella inversion of the CH₃ unit. As the new X-C bond continues to shorten and the old C-Y bond elongates, a postreaction complex XCH₃…Y⁻ (PC) is formed before its dissociation to products. This traditional model corresponds to a well-known double-well shaped potential energy profile, being supported by experiments and electronic structure calculations for many reactions.^{5,7-10} However, in the last two decades, with the advances in dynamics simulation and crossed molecular beam ion imaging experiments, studies continuously discovered new dynamical mechanisms. The

actual dynamics of the prototypical $S_N 2$ reactions (1) are found to be more complex.¹¹

Computational methods used for simulating the gas phase $S_N 2$ reactions mainly include direct dynamics simulations,^{12–15} where the energy and forces were computed on-the-fly, and the quasi classical trajectory simulation^{16–18} on the prefitted potential energy surfaces. Based on the motions of the atoms during the simulated trajectories, the dynamic mechanisms of ion–molecule $S_N 2$ reactions are classified into direct and indirect mechanisms. Direct mechanisms occur by rebound, stripping and frontside attack.¹¹ Multiple indirect mechanisms have been identified, including the formation of ion-dipole complex,¹² hydrogen-bonded complex,^{120–22} central barrier

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Figure 1. (A–D) Center-of-mass images of I⁻ velocities at four different collision energies. The image intensity is proportional to $[(d^3\sigma)/(dv_x dv_y dv_z)]$: Isotropic scattering results in a homogeneous ion distribution on the detector. (E–H) Energy transfer distributions extracted from the images in (A–D) with a phase space theory calculation (red curve). The arrows in (H) indicate the average Q value obtained from the simulations. Adapted with permission from ref 4. Copyright 2008 American Association for the Advancement of Science.

recrossing,^{23,24} double inversion,^{25,26} roundabout,⁴ and composites of these features.²⁷ The relative importance of the indirect and direct mechanisms depends on the nature of the reactants and the collision energy. In this review, we focused on the indirect roundabout mechanism that has been reported in many S_N2 reactions since its proposal in 2008.⁴ This is the first review of the roundabout mechanism.

The roundabout mechanism was first reported for the Cl⁻ + $CH_3I \rightarrow CH_3Cl + I^-$ gas-phase S_N2 reaction in a combined study of an ion-molecule crossed beam imaging experiment and direct dynamics simulation by the Wester and Hase group.⁴ According to the scattering plots of the I⁻ product, the reaction dynamics were found to transit from isotropic scattering to backward scattering as the collision energy $E_{\rm rel}$ increases (Figure 1, A to D). The resulting distribution of energy transfer $(Q = E_{kin, final} - E_{kin, initial})$ displays a double-peak shape at a broad range of energy at collision energies of 0.76, 1.07, and 1.90 eV (Figure 1, F to H). On the contrary, the phase space theory (PST), which assumes a statistical distribution of the available energy among all degrees of freedom of the reaction products, predicts a single-peak distribution of Q within a narrow range of energy (Figure 1, F to H). Such disagreement between PST and experimentally observed dynamics at high E_{rel} , albeit there is good agreement at a low collision energy of 0.39 eV, led to the discovery of the roundabout mechanism.

Direct dynamics simulation at the MP2(fc)/ECP/aug-ccpVDZ level of theory was thus performed at E_{rel} of 1.90 eV. Direct rebound mechanisms were observed and these trajectories give rise to one peak of the distribution of energy transfer Q (Figure 1H, right arrow). Besides, a distinctive indirect mechanism, named a roundabout, was observed. As depicted in Figure 2, during the reaction, Cl^- first strikes the side of the CH_3 group, causing it to rotate around the more



Figure 2. View of a typical roundabout trajectory at 1.9 eV for Cl⁻ + CH₃I \rightarrow CH₃Cl + I⁻ S_N2 reaction. Color code: Cl, green; I, purple; C, blue; H, white. Adapted with permission from ref 4. Copyright 2008 American Association for the Advancement of Science.

massive I atom. Then, after one or two CH_3 revolutions, Cl^- attacks the C atom backside and displaces I⁻. The product energy is primarily partitioned to CH_3Cl internal modes with ~60% to vibration and ~20% to rotation for the roundabout mechanism. This is in approximate agreement with PST (Figure 1H, left arrow), assuming statistical dynamics even though a long-lived reaction complex is not formed. Reactions occur via this mechanism produce the two symmetric low-

velocity peaks in the scattering pattern of the I⁻ product ion (Figure 1D), and they give rise to the other peak of the distribution of energy transfer Q (Figure 1H, left arrow). This combined experimental and computational study identified the previously unknown mechanism involving CH₃ rotation at high collision energy and called the roundabout mechanism. The roundabout mechanism represents an example of nontraditional pathway that does not follow the conventional reaction path paradigm that underlies conventional transition state theory.

Since the first report, the roundabout mechanism has been observed in many chemical reaction systems.^{20,27-41} Hence, in this work, we review the research progresses on roundabout mechanisms from 2008 to date. In the "Roundabout Mechanism in C-Centered S_N2 Reactions" section, we discuss the roundabout mechanism in C-centered $S_N 2$ reactions with respect to some key features, including its variant types, product energy partitioning, and velocity scattering angle distribution. We analyze the factors that affect the importance of the RA-involved mechanisms, including the nucleophile and the leaving group, the collision energy, and the effect of microsolvation. In the "Roundabout Mechanisms in Other Reactions" section, we summarize the roundabout mechanisms in other reactions like N-centered S_N2 reactions, proton transfer reactions, and elimination reactions. Animations of some roundabout-involved mechanisms that were not provided in previous reports are present in this contribution. This review shows that the roundabout mechanism is a general mechanism in ion-molecular collision events, especially at high collision energies.

ROUNDABOUT MECHANISM IN C-CENTERED S_N2 REACTIONS

Types of Leaving Group

From dynamics simulations, multiple mechanisms have been identified for a series of ion-molecule $S_N 2$ reactions,¹¹ but the roundabout mechanism was only reported for a few of them. In Table 1, we have summarized, to the best of our knowledge, the simulation works that reported a roundabout mechanism on ion-molecule $S_N 2$ reactions from 2008.

The roundabout mechanism was mainly observed when the leaving group is the most massive I atom, including CH_3I reacting with F^{-28} HO^{-,20,29} Cl^{-,4,30,38,42} CN^{-,43} and

 Table 1. Roundabout Mechanism Reported in Simulation

 Studies^a

	Substrate						
Nu	CH ₃ Cl	CH3I	NH ₂ Cl	$\rm NH_2I$	CH ₃ ONO ₂		
\mathbf{F}^{-}	Yes ⁵⁵	Yes ²⁸	Yes ^{33,36}	Yes ³⁹			
$F^{-}(H_2O)$		Yes ^{35,44}					
Cl ⁻		Yes ^{4,30,38,42}					
$Cl^{-}(H_2O)$		Yes ³⁷					
HO ⁻		Yes ^{20,29}			Yes ⁵⁶		
$HO^{-}(H_2O)$		Yes ²⁷					
$HOO^{-}(H_2O)$		Yes ⁴⁵					
CN ⁻		Yes ⁴³					
NH ₂ ⁻		Yes ⁵⁷					

^{*a*}Note: For the F⁻ + $C_2H_5Cl/Br/I$ and F⁻(CH₃OH) + C_2H_5Br systems, the roundabout mechanism has only been observed in the elimination E2 path so far.^{32,40,41}

microhydrated nucleophile $F^{-}(H_2O)$,^{35,44} HO⁻(H₂O),²⁷ Cl⁻(H₂O),³⁷ HOO⁻(H₂O);⁴⁵ and NH₂I + F⁻³⁹ reactions. In principle, when the leaving group is Br, it is sufficiently heavy to cause a roundabout mechanism. However, due to the lack of simulation works on reactions involving Br,^{41,46-48} such reports are lacking for S_N2 reactions, but the RA mechanism was observed for the elimination mechanism for the $F^{-}(CH_3OH)_{0,1}$ + CH_3CH_2Br system.⁴¹ When the leaving group is Cl, the roundabout mechanism is observed for reactions F^- + CH₃Cl (Wang group),³⁴ F^- + NH₂Cl,^{33,36} but was not reported for reaction $HO^- + CH_3Cl^{49}$ or $HOO^{-}(H_2O)_{0.1} + CH_3CI^{50}$ under the condition of room temperature simulation, corresponding to a collision energy of 0.04 eV. This is largely due to the low collision energy, the dependence of RA mechanism on collision energy will be discussed later. Czakó group performed quasi classical trajectories simulations for F^- + CH₃Cl reaction at a broad range of collision energy of 0.04 to 2.6 eV, but the RA mechanism was not reported in these studies. This is probably because identifying the RA mechanism is not straightforward for a large amount of trajectories (over millions of trajectories), or is not the focus of these work.^{16,25,51} Of note, the RA mechanism shares similarities with the double-inversion mechanism, where the latter was observed in the simulations of F^- + CH₃Cl reaction.²⁵ When the leaving group becomes F, simulations were performed for $HO^- + CH_3F^{52-54}$ and $F^- +$ CH₃F¹⁷ reactions, and identifying the RA mechanism was not the focus of the studies.

Taken together, the roundabout mechanism is quite general in ion-molecule S_N2 reactions. A massive leaving group and relatively high collision energy are prerequisite for the occurrence of the roundabout mechanism.

Variant of Roundabout Mechanisms in S_N2 Reactions

In the prototype of roundabout mechanism,⁴ nucleophile Cl⁻ first strikes CH₃, causing it to rotate around the massive I atom for one or two circles, before substitution takes place (Figure 2). If the nucleophile first strikes the leaving group, like the I atom, instead of CH₃, it may also cause the CH₃ to rotate for half or one-and-a-half circles and, finally, substitution happens. This latter case was first reported in F⁻ + CH₃I S_N2 reaction simulations and was called the half-roundabout (h-RA) mechanism.²⁸ Later, in HO⁻(H₂O)₀₋₁ + CH₃I systems, CH₃group was found to rotate more than one-half circle.²⁷ These h-RA trajectories may witness a transient [CH₃-I-Y-(H₂O)_{0,1}]⁻ intermediate before CH₃ rotates (Figure 3a and supplementary movies).

Normally, in a roundabout mechanism, the nucleophile will approach the backside of the rotated CH₃ and produce a CH₃-inverted product such as CH₃F or CH₃OH. However, there were rare HO⁻ + CH₃I trajectories led to stereochemistry retained product at $E_{\rm rel}$ of 2.0 eV. As shown in Figure 3b and supplementary movies, after rotating for a circle, the CH₃-group reaches the just right position so that the nucleophile HO⁻ can attack its frontside. Similar to the direct frontside attack (FSA) mechanism, the stereogeometry of the CH₃-group was not inverted in the CH₃OH product. It was known that frontside attack is a high-barrier path and it usually happens in a direct and fast manner. Here, the roundabout induced frontside attack mechanism is novel and expands our understanding of the FSA mechanism.

The roundabout mechanism usually occurs in the early stage of a trajectory. Hence, it may couple to other mechanisms



Figure 3. View of representative trajectories for the (a) half-roundabout, (b) roundabout + frontside attack, and (c) roundabout + proton exchange mechanisms for $OH^-(H_2O)_{0,1} + CH_3I S_N 2$ reactions that form $CH_3OH + I^-$ products. Color code: O, red; I, purple; C, blue; H, white.



Figure 4. Percentage of different roundabout mechanisms in all roundabout-involved trajectories for the (a) $HO^{-}(H_2O) + CH_3I$, (b) $F^{-} + CH_3I$, (c) $CI^{-} + CH_3I$, and (d) $CI^{-}(H_2O) + CH_3I$ S_N^2 reactions.

before the substitution takes place. These coupled mechanisms mainly include the formation of hydrogen- or halogen-bonded complexes and proton exchange. Figure 4 shows the types of RA-coupled mechanisms and their ratio over all the RA-involved trajectories for some S_N2 reactions. Table 2 lists the ratio of the roundabout-involved trajectories for ion-molecule S_N2 reactions over the indirect trajectories ($r_{RA/Ind}$) and the total trajectories ($r_{RA/Total}$). The ratios were computed based on the cross sections.

For the HO⁻ + CH₃I S_N2 reaction, only a small percent of trajectories couples the RA and/or h-RA mechanism with the formation of a hydrogen-bonded prereaction complex [HO–HCH₂I]⁻ (denoted as 0RC) at low collision energies. For the RA-involved trajectories, the percentage of the RA + 0RC coupled mechanism is 7% at $E_{\rm rel}$ of 0.05 eV and 4% at $E_{\rm rel}$ of 0.5 eV; the others are pure RA or h-RA mechanisms. See Figure S2 and the Supporting Information for representative trajectory. Introducing a water molecule to the system opens several new mechanisms and makes RA-coupled mechanisms prevalent. For HO⁻(H₂O) + CH₃I S_N2 reactions, among the RA-involved trajectories the percentage of RA-coupled mechanisms are 96%, 65%, 50%, and 3% at $E_{\rm rel}$ of 0.05, 0.5, 1.0, and 2.0 eV, respectively. The coupled mechanisms include

(1) RA + 0PC: RA coupling with postreaction complex $[CH_3OH-I]^-$ (0PC); (2) RA + 1RC: RA coupling with $(H_2O)HO^-$ —HCH₂I prereaction complex (1RC); (3) RA + PE: RA coupling with proton exchange between the (H_2O) -HO⁻-HCH₂I and CH₂I⁻-H₂O(H₂O) complexes, and/or proton exchange between HO⁻-HCH₂I and CH₂I⁻-H₂O complexes (Figure 3c and supplementary movies); (4) RA + 0RC + 1RC; (5) RA + 1RC + PE; (6) RA + 1RC + C2: C2 is the halogen-bonded [CH₃-I-OH(H₂O)]⁻ complex. Snapshots of trajectories are present in Figure S6. The percentages of these mechanisms are present in Figure 4a. Clearly, coupled mechanisms become more important as the collision energy decreases. Among the six types of RA-coupled mechanisms, four of them involve the formation of 1RC, and they constitute 96%, 48%, 47% at $E_{\rm rel}$ of 0.05 0.5, and 1.0 eV, respectively. Hence, except the highest $E_{\rm rel}$ of 2.0 eV, 1RC is the most important complex that coupled with roundabout mechanism, consistent with that 1RC dominates the S_N2 mechanisms of the singly hydrated $OH^{-}(H_2O) + CH_3I$ reactions.²²

For the F^- + CH₃I reaction,²⁸ the RA or h-RA mechanisms are coupled with either the F^- —HCH₂I prereaction complex (0RC) or the FCH₃—I⁻ postreaction complex (0PC). As shown in Figure 4b, five types of coupling mechanisms were

		Percentage (%)				
Method	$E_{\rm rel}~({\rm eV})$	^a RA-pure/Ind	^b RA-couple/Ind	^c RA-all/Ind	^d Ind/Total	reference
B97-1/ECP/d	0.32	1.0	1.0	2.0	58.9	ref 28
	1.53	4.7	1.4	6.1	63.6	
M06-2X/aug-cc-pVDZ	0.7	-	6.7	6.7	45	ref 34
B3LYP/ECP/d	1.53	3.5	3.5	7.0	57	ref 35
B97-1/ECP/d	0.05	2.6	-	2.6	38	ref 29
	0.5	9.7	0.2	9.9	41	
	1.0	26.3	-	26.3	19	
	2.0	100.0	-	100.0	3	
B97-1/ECP/d	0.05	-	1.6	1.6	76	ref 27
	0.5	3.4	6.3	9.6	80	
	1.0	8.1	8.1	16.2	52	
	2.0	35.8	1.2	37.0	44	
MP2(fc)/ECP/d	0.2	-	20.5	20.5	83	ref 30
	0.39	0	0	0	1	
	0.76	23.1	38.5	61.5	13	
	1.07	0	0	0	0	
	1.9	94.4	5.6	100	17	
BhandH/ECP/d	0.2	-	5.7	5.7	70	
	0.39	-	25.0	25.0	12	
B97-1/ECP/d	1.9	71.2	23.5	94.7	17	ref 37
PM7	0.3	0	-	0	13.3	^e ref 43
	0.7	5.3	-	5.3	5.8	
	1.1	50.0	-	50.0	1.6	
CAM-B3LYP/ECP/d	0.04	0.7	-	0.7	89	ref 45
M06-2X/6-31+G(d)	0.43	one traj.	-	-	-	ref 56
	Method B97-1/ECP/d M06-2X/aug-cc-pVDZ B3LYP/ECP/d B97-1/ECP/d B97-1/ECP/d MP2(fc)/ECP/d BhandH/ECP/d B97-1/ECP/d CAM-B3LYP/ECP/d M06-2X/aug-cc-pVDZ B97-1/ECP/d BhandH/ECP/d B97-1/ECP/d M06-2X/aug-cc-pVDZ B97-1/ECP/d B97-1/ECP/d </td <td>Method E_{rel} (eV) B97-1/ECP/d 0.32 1.53 1.53 M06-2X/aug-cc-pVDZ 0.7 B3LYP/ECP/d 1.53 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 B97-1/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP3 0.76 1.07 1.9 BhandH/ECP/d 0.2 M07 0.3 0.7 1.1 CAM-B3LYP/ECP/d 0.04 M06-2X/6-31+G(d) 0.43</td> <td>Method E_{rel} (eV) "RA-pure/Ind B97-1/ECP/d 0.32 1.0 1.53 4.7 M06-2X/aug-cc-pVDZ 0.7 - B3LYP/ECP/d 1.53 3.5 B97-1/ECP/d 0.05 2.6 0.5 9.7 1.0 26.3 2.0 100.0 0 0 B97-1/ECP/d 0.05 - 0.5 B97-1/ECP/d 0.05 - 0.05 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.2 - 0.39 0 0.76 23.1 1.07 0 1.9 94.4 BhandH/ECP/d 0.2 - 0.39 - 0.39 - B97-1/ECP/d 1.9 71.2 PM7 0.3 0 0.7 5.3 1.1 S0.0 CAM-B3LYP/ECP/d 0.</td> <td>Method Erel (eV) "RA-pure/Ind %R-couple/Ind B97-1/ECP/d 0.32 1.0 1.0 1.53 4.7 1.4 M06-2X/aug-cc-pVDZ 0.7 - 6.7 B3LYP/ECP/d 1.53 3.5 3.5 B97-1/ECP/d 0.05 2.6 - 0.5 9.7 0.2 1.0 1.0 26.3 - - 2.0 100.0 - - B97-1/ECP/d 0.05 - 1.6 0.5 9.7 0.2 - 1.0 26.3 - - 2.0 100.0 - - B97-1/ECP/d 0.05 - 1.6 0.5 3.4 6.3 - 1.0 8.1 8.1 - 2.0 35.8 1.2 - MP2(fc)/ECP/d 0.2 - 5.7 0.39 0 0 - 1.9 <td< td=""><td>Method Erel (eV) Precentage (%) B97-1/ECP/d 0.32 1.0 1.0 2.0 1.53 4.7 1.4 6.1 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 B3LYP/ECP/d 1.53 3.5 3.5 7.0 B97-1/ECP/d 0.05 2.6 - 2.6 0.5 9.7 0.2 9.9 1.0 26.3 - 26.3 2.0 100.0 - 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 0.5 9.7 0.2 9.9 1.0 26.3 2.0 100.0 - 100.0 100.0 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 1.6 0.5 3.4 6.3 9.6 1.0 8.1 16.2 1.0 8.1 8.1 16.2 2.0 35.8 1.2 37.0 MP2(fc)/ECP/d 0.2<</td><td>Method E_{rel} (eV) 10RA-pure/Ind 10RA-couple/Ind 10RA-all/Ind 4Ind/Total B97-1/ECP/d 0.32 1.0 1.0 2.0 \$8.9 1.53 4.7 1.4 6.1 63.6 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 45 B3LYP/ECP/d 1.53 3.5 3.5 7.0 57 B97-1/ECP/d 0.05 2.6 - 2.6 38 0.5 9.7 0.2 9.9 41 1.0 26.3 - 26.3 19 2.0 100.0 - 100.0 3 B97-1/ECP/d 0.05 - 1.6 1.6 76 0.5 3.4 6.3 9.6 80 1.0 8.1 8.1 16.2 52 2.0 35.8 1.2 37.0 44 MP2(fc)/ECP/d 0.2 - 20.5 20.5 83 0.39</td></td<></td>	Method E_{rel} (eV) B97-1/ECP/d 0.32 1.53 1.53 M06-2X/aug-cc-pVDZ 0.7 B3LYP/ECP/d 1.53 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 B97-1/ECP/d 0.05 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 B97-1/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP2(fc)/ECP/d 0.2 MP3 0.76 1.07 1.9 BhandH/ECP/d 0.2 M07 0.3 0.7 1.1 CAM-B3LYP/ECP/d 0.04 M06-2X/6-31+G(d) 0.43	Method E_{rel} (eV) "RA-pure/Ind B97-1/ECP/d 0.32 1.0 1.53 4.7 M06-2X/aug-cc-pVDZ 0.7 - B3LYP/ECP/d 1.53 3.5 B97-1/ECP/d 0.05 2.6 0.5 9.7 1.0 26.3 2.0 100.0 0 0 B97-1/ECP/d 0.05 - 0.5 B97-1/ECP/d 0.05 - 0.05 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.05 - 0.010.0 B97-1/ECP/d 0.2 - 0.39 0 0.76 23.1 1.07 0 1.9 94.4 BhandH/ECP/d 0.2 - 0.39 - 0.39 - B97-1/ECP/d 1.9 71.2 PM7 0.3 0 0.7 5.3 1.1 S0.0 CAM-B3LYP/ECP/d 0.	Method Erel (eV) "RA-pure/Ind %R-couple/Ind B97-1/ECP/d 0.32 1.0 1.0 1.53 4.7 1.4 M06-2X/aug-cc-pVDZ 0.7 - 6.7 B3LYP/ECP/d 1.53 3.5 3.5 B97-1/ECP/d 0.05 2.6 - 0.5 9.7 0.2 1.0 1.0 26.3 - - 2.0 100.0 - - B97-1/ECP/d 0.05 - 1.6 0.5 9.7 0.2 - 1.0 26.3 - - 2.0 100.0 - - B97-1/ECP/d 0.05 - 1.6 0.5 3.4 6.3 - 1.0 8.1 8.1 - 2.0 35.8 1.2 - MP2(fc)/ECP/d 0.2 - 5.7 0.39 0 0 - 1.9 <td< td=""><td>Method Erel (eV) Precentage (%) B97-1/ECP/d 0.32 1.0 1.0 2.0 1.53 4.7 1.4 6.1 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 B3LYP/ECP/d 1.53 3.5 3.5 7.0 B97-1/ECP/d 0.05 2.6 - 2.6 0.5 9.7 0.2 9.9 1.0 26.3 - 26.3 2.0 100.0 - 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 0.5 9.7 0.2 9.9 1.0 26.3 2.0 100.0 - 100.0 100.0 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 1.6 0.5 3.4 6.3 9.6 1.0 8.1 16.2 1.0 8.1 8.1 16.2 2.0 35.8 1.2 37.0 MP2(fc)/ECP/d 0.2<</td><td>Method E_{rel} (eV) 10RA-pure/Ind 10RA-couple/Ind 10RA-all/Ind 4Ind/Total B97-1/ECP/d 0.32 1.0 1.0 2.0 \$8.9 1.53 4.7 1.4 6.1 63.6 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 45 B3LYP/ECP/d 1.53 3.5 3.5 7.0 57 B97-1/ECP/d 0.05 2.6 - 2.6 38 0.5 9.7 0.2 9.9 41 1.0 26.3 - 26.3 19 2.0 100.0 - 100.0 3 B97-1/ECP/d 0.05 - 1.6 1.6 76 0.5 3.4 6.3 9.6 80 1.0 8.1 8.1 16.2 52 2.0 35.8 1.2 37.0 44 MP2(fc)/ECP/d 0.2 - 20.5 20.5 83 0.39</td></td<>	Method Erel (eV) Precentage (%) B97-1/ECP/d 0.32 1.0 1.0 2.0 1.53 4.7 1.4 6.1 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 B3LYP/ECP/d 1.53 3.5 3.5 7.0 B97-1/ECP/d 0.05 2.6 - 2.6 0.5 9.7 0.2 9.9 1.0 26.3 - 26.3 2.0 100.0 - 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 0.5 9.7 0.2 9.9 1.0 26.3 2.0 100.0 - 100.0 100.0 100.0 B97-1/ECP/d 0.05 - 1.6 1.6 1.6 0.5 3.4 6.3 9.6 1.0 8.1 16.2 1.0 8.1 8.1 16.2 2.0 35.8 1.2 37.0 MP2(fc)/ECP/d 0.2<	Method E_{rel} (eV) 10 RA-pure/Ind 10 RA-couple/Ind 10 RA-all/Ind 4 Ind/Total B97-1/ECP/d 0.32 1.0 1.0 2.0 \$8.9 1.53 4.7 1.4 6.1 63.6 M06-2X/aug-cc-pVDZ 0.7 - 6.7 6.7 45 B3LYP/ECP/d 1.53 3.5 3.5 7.0 57 B97-1/ECP/d 0.05 2.6 - 2.6 38 0.5 9.7 0.2 9.9 41 1.0 26.3 - 26.3 19 2.0 100.0 - 100.0 3 B97-1/ECP/d 0.05 - 1.6 1.6 76 0.5 3.4 6.3 9.6 80 1.0 8.1 8.1 16.2 52 2.0 35.8 1.2 37.0 44 MP2(fc)/ECP/d 0.2 - 20.5 20.5 83 0.39

Table 2. Ratio of Roundabout Involved Mechanisms for Ion-Molecule S_N2 Reactions from Dynamics Simulations

"Ratio of RA and/or h-RA trajectories to indirect trajectories. ^bRatio of RA-coupled trajectories to indirect trajectories. ^cRatio of all the RAinvolved trajectories to the indirect trajectories. ^dRatio of indirect trajectories to all the reacted S_N^2 trajectories. ^cThe ratio of Table 2 were computed based on cross section, except data from ref 43, which were computed based on the number of trajectories.

observed. The proportions of the RA-coupled mechanism in RA-involved states are 50% and 23% at $E_{\rm rel}$ values of 0.32 and 1.53 eV, respectively. For the singly hydrated F⁻(H₂O) + CH₃I S_N2 reaction, simulations were performed at $E_{\rm rel}$ of 1.53 eV, and both pure RA and RA-coupled mechanisms account for 3.5% of the indirect mechanisms. For the F⁻ + CH₃Cl reaction, the roundabout mechanism was also found to couple with the proton exchange mechanism (Figure 1.1 in ref 34), which was observed previously in the HO⁻(H₂O) + CH₃I S_N2 reaction.²⁷

For the Cl⁻ + CH₃I reaction,³⁰ in a good number of trajectories, the CH₃ group was found to rotate more than once, denoted as RA(n). The RA or RA(n) mechanisms were coupled to the formation of Cl⁻—CH₃I (0aRC) and ClCH₃— l⁻ (0aPC) complexes (Figure 4c). The portion of RA-coupled mechanisms decreases from 100%, to 63% and 6% as $E_{\rm rel}$ increases from 0.2 to 0.76 and 1.0 eV. As for the Cl⁻(H₂O) + CH₃I reactions, the RA mechanism can happen either before or after the H₂O molecule leaves the anionic nucleophile Cl⁻. The RA mechanism couples with the RC and/or PC complexes as well as barrier-recrossing mechanisms. At $E_{\rm rel}$ of 1.9 eV, pure RA mechanisms dominate, taking 75%.

For the $NH_2^- + CH_3I$ reaction,⁵⁷ both RA and h-RA mechanisms were observed, although the authors did not call the mechanisms RA mechanisms. One may check the animations provided in supplementary movies 2 and 6 of ref 57.

Dependence on Collision Energy

It is known that increasing the collision energy decreases the percentage of overall indirect mechanisms.²⁷ On the contrary,

though roundabout is a type of indirect mechanism, increasing the $E_{\rm rel}$ actually increases the frequency of its occurrence. Consequently, the ratio of the RA-involved mechanism to the indirect mechanism $(r_{RA/Ind})$ increases as E_{rel} increases (Figure 5a). This trend can be found for the HO⁻ + CH₃I $S_N 2$ reaction, where the $r_{RA/Ind}$ ratio increases from 2.6% to 9.9%, 26.3%, and 100% as $E_{\rm rel}$ increases from 0.05 to 0.5, 1.0, and 2.0 eV_{2}^{20} and for the HO⁻(H₂O) + CH₃I S_N2 reaction, where the respective $r_{RA/Ind}$ ratio is 1.6%, 9.6%, 16.2%, and 37.0%;²⁷ and for F^- + CH₃I and CN⁻ + CH₃I S_N2 reactions (Table 2).^{28,43} An outlier is found for the Cl^- + CH_3I S_N2 reaction.³⁰ Simulations from the MP2 method suggested that roundabout mechanisms were not observed at $E_{\rm rel}$ values of 0.39 and 1.07 eV. But at $E_{\rm rel}$ values of 0.2, 0.76, and 1.9 eV, the roundabout mechanisms were observed and the $r_{\text{RA/Ind}}\xspace$ ratio follows an increasing order of 20.5%, 61.5%, and 100%. There was a discrepancy in the simulation results between MP2 and BHandH methods, since the latter reported the $r_{\text{RA/Ind}}\xspace$ ratio to be 25.0% at $E_{\rm rel}$ of 0.39 eV. Despite this inconsistent result for the Cl^- + CH_3I reaction, it can be concluded that the roundabout mechanism becomes more important among the indirect mechanism as $E_{\rm rel}$ increases.

Effect of Microsolvation

At the same $E_{\rm rel}$ adding one water molecule to the ionic nucleophile barely affects the portion of the roundabout mechanism (Figure 5). For example, at $E_{\rm rel}$ of 1.53 eV, the $r_{\rm RA/Ind}$ ratio is 6.1% for the F⁻ + CH₃I S_N2 reaction and 7.0% for the F⁻(H₂O) + CH₃I S_N2 reaction. Similar $r_{\rm RA/IND}$ values have also been observed for HO⁻ and HO⁻(H₂O) reacting



Figure 5. Percentage of RA trajectories to (a) indirect mechanisms and (b) all reacted S_N2 trajectories for multiple anionic nucleophiles reacting with CH_3I .

with CH₃I at the same $E_{\rm rel}$ of 0.05, 0.5, and 1.0 eV, but not for 2.0 eV (Figure 5). As discussed in the "Variant of Roundabout Mechanisms in S_N2 Reactions" section, adding a water molecule adds complexity to the type of RA-coupled mechanisms for the HO⁻ and Cl⁻ + CH₃I system. A decrease in the $E_{\rm rel}$ makes the RA-coupled mechanism more prevalent. Effect of Nucleophile

Figure 5 also conveys interesting information that the importance of RA mechanisms raises as the nucleophile changes from F^- to HO^- to Cl^- as react with CH_3I . This is coincident with the fact that the RA mechanism was first discovered in $Cl^- + CH_3I$ reaction. But why is there such a nucleophile dependence?

We believe there are at least two types of reasons. First, the proton affinity of Cl⁻ (334.8 kcal/mol) is smaller than that of F- (373.2 kcal/mol) and HO⁻(391.9 kcal/mol).⁵⁸ Hence, once HO^{-}/F^{-} anions collide with the CH_3 -group, they tend to interact strongly with the H-atom and become trapped within the prereaction complexes (RC) well. This is reflected on the potential energy profile that the RC well is shallower in the Cl⁻-system (-11.7 kcal/mol) than in the F⁻-system (-19.5 kcal/mol) and HO⁻-system (-20.5 kcal/mol).²¹ The difference in the importance of the RC-involved mechanism from dynamics simulation provides additional support. For the F⁻ + CH_3I S_N2 reaction, the formation of the $[F^--HCH_2I]$ complex contributes 91% and 92% of indirect mechanisms at $E_{\rm rel}$ of 0.32 and 1.53 eV.²⁸ The RC-involved mechanisms also dominate the HO⁻ + CH₃I $S_N 2$ reaction.²⁰ In comparison, for the Cl⁻ + CH₃I S_N^2 reaction, the formation of the [Cl⁻- $CH_3I]\ RC$ complex only contributes 20% and 38% of indirect mechanisms at $E_{\rm rel} = 0.2$ and 0.76 eV.³⁰ In other words, the competing RC mechanisms in HO⁻/F⁻-systems suppressed

the RA mechanisms, but this competition has less effect on the Cl⁻-system.

However, it cannot explain why the HO⁻-system prefers the RA mechanism compared to F⁻-system. We propose that the second reason is that Cl⁻ is bulkier and heavier than HO⁻, and HO⁻ is bulkier than F⁻. A bulky nucleophile faces a larger steric hindrance when interacting with the CH₃-group. This causes a repulsion between the incoming nucleophile and CH₃-group, which in turn drives the translational energy to transfer to the rotational mode of CH₃, thus promoting the RA mechanisms.

It faces difficulties to extend the above dependence of the RA mechanism on the mass, size, and proton affinity of nucleophiles to the case of CN⁻ (proton affinity is 351 kcal/ mol).⁵⁹ First, different simulation methods gave different results. In specific, no RA mechanisms were reported for the $CN^- + CH_3I S_N 2$ trajectories at E_{rel} of 0.3 and 1.1 eV using B3LYP/aug-cc-pVDZ/ECP level of theory (Gutal et al.),⁴³ and at $E_{\rm rel}$ of 0.04 eV using M06/ECP/d level of theory (Liu et al).⁶⁰ But RA mechanisms were observed at E_{rel} of 0.7 eV (1 trajectory) and 1.1 eV (2 trajectories) using PM7 method (Gutal et al.).⁴³ Because the PM7 simulation work only gives the numbers of trajectories, these results cannot be directly compared to the results based on the cross section, which are used for $HO^{-}/F^{-}/Cl^{-} + CH_{3}I$ systems. Anyway, we include these points in Figure 5 for readers' reference. The points of the CN⁻-system are supposed to lie between Cl⁻ and HO⁻ systems. Clearly, most of the plotted data are not. Second, CN⁻ is an ambident nucleophile, meaning either C or N can be the reactive center. How would this feature affect the occurrence of RA mechanism remains unclear. Future simulations under high collision energy may give us more information.

Product Energy Partitioning

For X⁻ + CH₃Y \rightarrow CH₃X + Y⁻ S_N2 reactions, the indirect mechanisms are found to partition more energy to the internal energy (i.e., vibration and rotation) of product CH₃X than the direct mechanisms,^{14,30} because there are more interactions and energy exchange for the indirect mechanisms.⁶¹ This is also the case for the roundabout mechanisms.

Take the Cl⁻ + CH₃I S_N2 reaction for illustration.³⁰ For $E_{\rm rel}$ of 0.76, 1.07, and 1.9 eV, the product energy partitioning is primarily to relative translation for the direct reactions, but to CH₃Cl internal energy for the indirect reactions. The roundabout mechanism transfers substantial energy to CH₃Cl rotation; for the other indirect mechanisms, the energy partitioning is primarily to CH₃Cl vibration. The energy transfer dynamics of the roundabout trajectories at an $E_{\rm rel}$ of 1.9 eV were studied by determining the C-I and C-Cl bond stretch energies and the CH₃I and CH₃Cl rotational energies versus time. As shown in Figure 6, during the initial collision of the reactants, a large amount of the available energy is transferred to the C-I bond stretch and CH₃ rotation about the massive I atom. After one CH₃ rotation, Cl⁻ again collides with CH₃ and the substitution occurs with the C-I bond excited. The excited C-I bond results in a high C-Cl stretch energy, and the large CH₃ angular velocity about the I atom leads to a high rotational energy for CH₃Cl. The high vibrational and rotational energies of the excited CH₃I reactant are transferred to the CH₃Cl product. For all the roundabout trajectories at $E_{rel} = 1.9 \text{ eV}$, the CH₃Cl internal modes receive \sim 80% of the available energy, close to the PST prediction of



Figure 6. (a) C-X (X = I and Cl) distances versus time for a representative roundabout trajectory involving one CH₃ rotation of Cl⁻ + CH₃I S_N2 reaction. (b) C-X (X = I and Cl) bond stretch potential energies as a function of time for the roundabout trajectory in (a). Adapted with permission from ref 30. Copyright 2013 American Institute of Physics.

88%. Moreover, increasing the reactant rotational temperature from 75 to 300 K for the 1.9 eV collisions resulted in more rotational energy in the CH_3Cl product and a larger fraction of roundabout trajectoriegens.

For the roundabout trajectories in HO⁻ and HO⁻(H₂O) + $CH_3I S_N^2$ reaction, the CH_3OH internal modes receive about ~90% of the available energy. Figure 7a is a scattering plot of



Figure 7. Scattering plot of the internal energy fractions at various $E_{\rm rel}$ for the roundabout trajectories of (a) HO⁻ + CH₃I, and (b) F⁻ + CH₃I S_N2 reaction.

the internal energy fractions at various $E_{\rm rel}$ values for the roundabout trajectories of the HO⁻ + CH₃I S_N2 reaction. It shows that for the roundabout trajectories over 80% available energies are partitioned to the internal energies. As for the roundabout trajectories in the F⁻ + CH₃I S_N2 reaction (Figure 7b), the percentage of internal energy in products ranges from 60% to 96%, giving an average of ~80%.

Figure 7 also shows that the roundabout mechanism mainly happens at a small impact factor that is no greater than 4 Å. This guarantees an effective collision to make the CH₃-group rotate. The maximum impact parameter leading to the RA mechanisms, $b_{\max,RA}$, is no greater than half of the maximum impact parameter (b_{max}) of the S_N2 reaction. Note that indirect mechanisms like prereaction complexes usually can occur at a full range of the impact parameter. At $E_{\rm rel}$ of 0.05, 0.5, 1.0, and 2.0 eV, the respective value of $b_{\text{max,RA}}/b_{\text{max}}$ are 4/8, 2/6.5, 3/6, and 2/5 Å for HO⁻ + CH₃I S_N 2 reactions, and the respective values are 4/10, 2/7, 3/6, and 3/4.5 for HO⁻(H₂O) + CH₃I S_N2 reactions. At $E_{\rm rel}$ values of 0.32 and 1.53 eV, these values are 3/8.5 and 3/5.75 for the F^- + CH_3I S_N2 reactions (Table S1). In general, for $F^-/HO^ /HO^-(H_2O)$ + CH_3I $S_{\rm N}2$ reactions, the RA mechanisms are most likely to happen at b of 0 to 2 Å (Table S2 and Figure S6).

Velocity Scattering Angle Distribution

Experimentally, the velocity scattering angle (VSA) θ was defined as the angle between the velocity vector of the CH₃I reactant and the velocity vector of the I⁻ product (Figure 1). In simulations, the VSA was defined in a similar manner but was computed between the velocity vectors of the X⁻ reactant and CH₃X product. Both definitions give the same value of θ . According to this definition, for $\theta = 0^{\circ}$ the velocity vector of the CH₃X product is pointing in the same direction as that for the X⁻ reactant. For $\theta = 180^{\circ}$, these vectors are pointing in opposite directions. When θ is greater than 90°, the event is forward scattering; when θ is greater than 90°, the event is backward scattering. For an indirect mechanism, the velocity vectors of products are random, thus the VSA distribution is usually isotropic.³⁰

As shown in Figure 7, the VSA of the roundabout trajectories of $HO^{-}/F^{-} + CH_{3}I S_{N}2$ reactions spans across the 0° to 180° and has a roughly even distribution. This is in accordance with the expectation of an indirect mechanism.

ROUNDABOUT MECHANISMS IN OTHER REACTIONS

Roundabout Mechanism in Proton Transfer Reactions

The RA mechanisms are not unique to $S_N 2$ reactions. Table 3 lists the other reactions that reported roundabout mechanisms. They were observed in the proton transfer (PT) reactions of $X^- + CH_3I \rightarrow CH_2I^- + HX (X = OH, F)$.^{29,31} The importance of the roundabout-involved mechanism at high collision energy for the proton transfer pathway is the same as the $S_N 2$ reaction.

During the RA mechanism of the PT reaction, the nucleophile X⁻ collides with the CH₃-group or the leaving group like the I-atom, and then the CH₃-group rotates around the massive I-atom before grabbing a proton from CH₃ to form HX (for animations, see Supporting Information). In some cases, the formed CH₂I⁻ keeps rotating around the I-atom before it separates from the HX-moiety.

For the HO⁻ + CH₃I PT reaction, the pure RA mechanism is the most important indirect mechanism at E_{rel} of 1.0 and 2.0 eV, contributing 76% and 100%, respectively (Figure 5 in ref

			Percentage (%)				
Reactants	Method	$E_{\rm rel}({\rm eV})$	RA-pure/Ind ^a	RA-couple/Ind ^b	RA-all/Ind ^c	Ind/Total ^d	reference
Proton transfer reactions							
$F^- + CH_3I$	B97-1/ECP/d	1.53	9.1	9.1	18.2	33	ref 31
$HO^- + CH_3I$	B97-1/ECP/d	300 K	2.1	-	2.1	71	ref 29
		400 K	3.9	-	3.9	64	
		500 K	4.6	-	4.6	65	
N-centered S _N 2 reactions							
$F^- + NH_2Cl$	B3LYP/aug-cc-pVDZ	300 K	0	-	0	91	ref 33
		1.73	2.9	-	2.9	69	
$F^- + NH_2Cl$	M06/aug-cc-pVDZ	0.3	-	10.5	10.5	56	^e ref 36
$F^- + NH_2I$	M06-2X/ECP/d	0.03	-	20.3	20.3	77	^e ref 39
		0.1	-	19.4	19.4	75	
		0.5	-	44.4	44.4	100	
E2 reactions							
$F^- + CH_3CH_2Cl$	M06/aug-cc-pVDZ	1.9	10.0	-	10.0	10	ref 40
$F^- + CH_3CH_2Br$	M06/ECP/d	0.04	0	-	0	41	ref 41
		1.9	8.3	-	8.3	21	
$F^{-}(CH_{3}OH) + CH_{3}CH_{2}Br$	M06/ECP/d	0.04	0	-	0	55	
		1.9	2.9	-	2.9	64	
$F^- + CH_3CH_2I$	M06/ECP/d	1.9	8.7	-	8.7	21	ref 32

Table 3. Ratio of Roundabout Involved Mechanisms for Other Ion-Molecule Reactions from Dynamics Simulations

^{*a*}Ratio of RA and/or h-RA trajectories to indirect trajectories. ^{*b*}Ratio of RA-coupled trajectories to indirect trajectories. ^{*c*}Ratio of all the RA-involved trajectories to the indirect trajectories. ^{*d*}Ratio of indirect trajectories to all the reacted trajectories. ^{*e*}The ratios of Table 3 were computed based on cross section, except data from refs 36, 39, which were computed based on the number of trajectories.

20). As $E_{\rm rel}$ decreases to 0.5 and 0.05 eV, the RA mechanisms begin to couple with pre- and postreaction complexes, and the halogen-bonded complex $[CH_3-I-OH]^-$. For the singly hydrated OH⁻(H₂O) + CH₃I \rightarrow CH₂I⁻ + 2H₂O proton transfer reactions, the RA-involved mechanisms dominate the indirect mechanisms with a fraction of 56% at the highest $E_{\rm rel}$ of 2.0 eV.²⁷ As $E_{\rm rel}$ decreases, the probability of CH₂I⁻(H₂O) + H₂O product channels increases, and the roundabout mechanism also participates in this product channel. For the F⁻ + CH₃I \rightarrow HF + CH₂I⁻ proton transfer reaction under 1.53 eV collision, the roundabout-involved mechanism contributes ~18% of the indirect mechanisms.^{31,62}

Roundabout Mechanism in N-Centered S_N2 Reactions

N-Centered S_N^2 reactions are less studied or understood compared to the C-centered S_N^2 reactions. To the best of our knowledge, the RA mechanism was mentioned only for F⁻ + NH₂I or NH₂Cl S_N^2 reactions.^{33,36,39} The RA mechanisms occur as a part of the composite mechanisms and are slightly different from the prototypical RA mechanisms of C-centered S_N^2 reactions.

For the $F^- + NH_2I \rightarrow NH_2F + I^- S_N2$ reaction, the Wang group reported two RA-involved mechanisms. One is the proton-abstraction roundabout and backside-attack mechanism, in which F^- first abstracts one proton to form HF, but HF does not have enough energy to drift from the NHI⁻ fragment, and the HF-group rotates around the massive I atom, then releases the abstracted proton at the end of the roundabout process, followed by the classical backside attack. This mechanism accounts for 5%, 2%, and 22% of the indirect trajectories at $E_{\rm rel} = 0.03$, 0.1, and 0.5 eV, respectively. The other is proton-abstraction induced inversion and proton-abstraction roundabout and backside attack mechanism. The only difference to the former mechanism is that F^- abstracts one proton after the upside-down inversion of the two protons as F^- attacks NH₂I. This mechanism contributes 11%, 13%,

and 22% of the indirect trajectories at $E_{\rm rel} = 0.03 \ 0.1$, and 0.5 eV, respectively. Of note, these percentages are evaluated based on the number of trajectories. We also noticed that, in the above RA-involved mechanisms, the HF-moiety that contains the incoming F-atom rotates instead of the NH₂-moiety that belongs to the substrate rotates.

The aforementioned proton-abstraction and roundabout mechanism was also observed in the F⁻+NH₂Cl S_N2 reaction,^{33,36} and the NH₂-group was reported to rotate. In one work, this composite mechanism was observed at $E_{\rm rel}$ of 40 kcal/mol and accounted for ~2% of the reactive trajectories.³³ In another work, it was observed at $E_{\rm rel} = 0.3$ eV and accounted for ~6% of the reactive trajectories.³⁶ In comparison, the RA-involved mechanism is favored as reacting with NH₂I than NH₂Cl.

Roundabout Mechanism in Elimination Reactions

Changing the substrate from CH₃Y to C₂H₅Y not only increases the steric hindrance of the Walden inversion during the S_N2 reaction but also opens up new product channels, the elimination E2 reaction. Making the heavier ethyl group rotate is more difficult than making the methyl group rotate, so the RA mechanisms may be even rarer in X⁻ + C₂H₅Y reactions. So far, the dynamics simulations have been performed mostly for the F⁻ nucleophile as it reacts with C₂H₅Y (Y = Cl, Br, I).^{32,40,41,63} No RA mechanisms were reported for the S_N2 reactions of these systems. This is somewhat in accord with the finding in section Effect of Nucleophile that the RA mechanism is least favored when F⁻ is the nucleophile. However, we anticipate that when the nucleophile changes RA mechanisms may be observed in the S_N2 reactions with C₂H₅Y.

However, the RA mechanisms were observed in the E2 reactions, $X^- + C_2H_5Y \rightarrow HX + C_2H_4 + Y^-$, partly due to their high reaction probabilities. In a roundabout E2 trajectory, the nucleophile X^- collides the C_2H_5 -group, either the CH₂-moiety or the CH₃-moiety, or the leaving group, followed with

the rotation of the C_2H_5 -group, then X⁻ takes a proton from the CH₃-moiety and forms HX, along with the separation of C_2H_4 and Y⁻. At E_{rel} of 1.9 eV, the E2 reactions contribute 80% and 71% of the reactive trajectories of the $F^- + C_2H_5I$ and F^- + C_2H_5Cl reactions.^{32,40} And the RA mechanisms contribute to $\sim 1\%$ of the E2 trajectories. As for the $F^{-}(CH_{3}OH)_{0.1} + CH_{3}CH_{2}Br E2$ reactions, the RA mechanism was not observed at $E_{\rm rel} = 0.04$ eV, but was observed at $E_{\rm rel} =$ 1.9 eV, accounting for $\sim 5\%$.⁴¹ Again, high collision energy is a prerequisite for the occurrence of RA mechanism in the E2 reaction, similar to the case of S_N2 reactions. Interestingly, the RA mechanism was found in both anti-E2 and syn-E2 trajectories of the F^- + C_2H_5I reaction, but only in anti-E2 trajectories of F^- + C_2H_5Cl or C_2H_5Br reactions. The animation of anti-E2 trajectories is available in ref 40. Figure 8 presents the snapshots of a syn-E2 trajectory of $F^- + C_2H_5I$



Figure 8. View of a representative trajectory of the $F^- + C_2H_3I \rightarrow HF + C_2H_4 + I^-$ elimination reaction that follows the roundabout mechanism and syn-E2 path. Color code: F, yellow; I, purple; C, blue; H, white.

reaction (animation is provided in the Supporting Information). F⁻ first collides with I-atom, then the C_2H_5 -group rotates for a circle. At the point when F and I atoms are on the same side of the C–C bond, F⁻ grabs a proton from the CH₃moiety to form HF, along with the formation of C_2H_4 and I⁻.

The syn-E2 path has a higher barrier than that of the anti-E2 path. For F^- + C_2H_5I E2 reactions, the respective barrier height is -4.9 and -16.0 kcal/mol relative to reactants.^{32,40} However, the roundabout mechanism leads to both anti-E2 and syn-E2 pathways. This is similar to the case of S_N2 reactions, where the frontside attack has a much higher barrier than the backside attack, and the roundabout mechanism can couple with both pathways. Not surprisingly, the high barrier pathways, i.e. syn-E2/frontside attack S_N2 , have a lower probability than the lower barrier pathways, i.e., anti-E2/backside attack S_N2 , with or without roundabout mechanisms.

CONCLUSION

Roundabout (RA) has evolved to become a general type of indirect dynamical mechanism, which does not follow the intrinsic reaction coordinates, for gas-phase ion—molecule $S_N 2$ reactions, especially at high collision energy. Since its discovery in 2008 while studying the $Cl^- + CH_3I \rightarrow ClCH_3 + I^-$ reaction, the RA mechanism and its variants were observed not only in multiple C-centered $S_N 2$ reactions, but also in N-centered $S_N 2$ reactions, proton transfer reactions, and elimination reactions.

For a typical RA mechanism of the $S_N 2$ reaction, the anionic nucleophile first hits the CH₃-moiety. In the later reported half-roundabout (h-RA) mechanism, the nucleophile first hits the leaving group, like the I-atom. Then the CH3-moiety rotates for half and multiple circles before the substitution takes place. Though most of the RA trajectories were followed by a backside attack of nucleophiles, a few trajectories were followed by a frontside attack that led to the CH₃Y product with stereo geometry retained. RA and h-RA mechanisms occur at an early stage of a trajectory, so it can be with other mechanisms, such as the formation of hydrogen-bonded complex and proton exchange processes. Especially, when the collision energy is small, the fraction of RA-coupled mechanisms may exceed the pure (h-)RA mechanisms. Although adding a water molecule to the ionic nucleophile barely changes the weight of RA-involved mechanisms over indirect mechanisms, it adds complexities to the types of RAcoupled mechanisms.

The RA mechanisms were mainly observed when the leaving group was the most massive I-atom, partly due to the abundance of simulation studies on CH₃I and C₂H₅I. For a trajectory undergoing the RA mechanism, the majority of collision energies are transferred to the internal energy. As an indirect mechanism, the products velocity scattering angle displays isotropic distribution. RA mechanisms occur more frequently at low impact parameters and high collision energies. This is opposite to the trend of overall indirect mechanisms, which become less important as the collision energy increases. Interestingly, there is a nucleophile dependence on the importance of RA mechanisms, which raises as the nucleophile changes from F⁻ to HO⁻ to Cl⁻ and reacts with CH₃I. The preference of the Cl⁻-system to RA mechanisms is attributed to the relatively smaller proton affinity of Cl⁻, which avoids the competition with the prereaction complex involved mechanism, and the bigger size of Cl⁻ that induces larger repulsion of CH₃-group and promotes its rotation.

As far as we know, the identification of RA mechanisms is based on observing the animation movies of each reactive trajectory. This procedure is not suitable for analyzing a large number of trajectories. According to this review, RA or hRA mechanisms usually happen at an early stage and display a special feature of substrate rotation. Hence, an algorithm that tracks the angle of the nucleophile, leaving group, and substituents, e.g., $F-I-CH_3$, and critical bond distances can be created to help identifying the RA-involved mechanisms in the future.

So far, the roundabout mechanism has been reported only for ion-molecule bimolecular reactions at the ground state. Can this happen between two neutral molecules? How about changing the substrate to propyl or butyl halides? What if the reactants are in excited states? All of these questions await to be explored by the experimental and theoretical communities.

ASSOCIATED CONTENT

9 Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsphyschemau.4c00061.

Experimental and theoretical methods, supplementary experimental and theoretical results, and computational raw data (PDF)

h-RA, OH⁻ + CH₃I \rightarrow CH₃OH + I⁻ S_N2 reaction (MP4)

h-RA, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4) RA + FSA, OH⁻ + CH₃I \rightarrow CH₃OH + I⁻ S_N2 reaction (MP4) h-RA + 0RC, OH⁻ + CH₃I \rightarrow CH₃OH + I⁻ S_N2 reaction (MP4) RA + 0PC, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4) RA(n) + 1RC, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4) RA + PE, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4) RA + PE, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4) RA + 1RC + C2, OH⁻(H₂O) + CH₃I \rightarrow CH₃OH + I⁻ + H₂O S_N2 reaction (MP4)

h-RA, OH⁻ + CH₃I \rightarrow CH₂I⁻ + H₂O proton transfer reaction (MP4)

RA(n), OH⁻ + CH₃I \rightarrow CH₂I⁻ + H₂O proton transfer reaction (MP4)

RA, F⁻ + C₂H₅I \rightarrow CH₂CH₂ + HF + I⁻ elimination reaction (MP4)

AUTHOR INFORMATION

Corresponding Author

Jing Xie – Key Laboratory of Cluster Science of Ministry of Education, Beijing Key Laboratory of Photoelectronic/ Electrophotonic Conversion Materials, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, China; orcid.org/0000-0001-9676-5734; Email: jingxie@bit.edu.cn

Authors

- Xiangyu Wu Key Laboratory of Cluster Science of Ministry of Education, Beijing Key Laboratory of Photoelectronic/ Electrophotonic Conversion Materials, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, China; ⊙ orcid.org/0000-0001-9866-7812
- Fei Ying Key Laboratory of Cluster Science of Ministry of Education, Beijing Key Laboratory of Photoelectronic/ Electrophotonic Conversion Materials, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, China; ◎ orcid.org/0000-0001-6465-2778
- Hongyi Wang State Key Laboratory of Urban Water Resource and Environment, MIIT Key Laboratory of Critical Materials Technology for New Energy Conversion and Storage, School of Chemistry and Chemical Engineering, Harbin Institute of Technology, Harbin 150001, China
- Li Yang State Key Laboratory of Urban Water Resource and Environment, MIIT Key Laboratory of Critical Materials Technology for New Energy Conversion and Storage, School of Chemistry and Chemical Engineering, Harbin Institute of Technology, Harbin 150001, China; School of Chemistry and Chemical Engineering, Yili Normal University, Yining 835000, China; Orcid.org/0000-0002-0143-3524
- Jiaxu Zhang State Key Laboratory of Urban Water Resource and Environment, MIIT Key Laboratory of Critical Materials Technology for New Energy Conversion and Storage, School of Chemistry and Chemical Engineering, Harbin Institute of Technology, Harbin 150001, China; School of Chemistry and Chemical Engineering, Yili Normal University, Yining 835000, China; © orcid.org/0000-0002-3125-7824

Complete contact information is available at:

https://pubs.acs.org/10.1021/acsphyschemau.4c00061

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Author Contributions

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Notes

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