nature portfolio

Peer Review File

A dynamic isotope effect in the nucleophilic substitution reaction between F- and CD3I

Corresponding Author: Professor Roland Wester

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Attachments originally included by the reviewers as part of their assessment can be found at the end of this file.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
Please see attached report

Reviewer #2

(Remarks to the Author)
This paper describes an experimental and computational study of the F- + CD3I reaction. The authors employ crossed molecular beam methods coupled with velocity map ion imaging. Ion images are presented for the I- products of the S_N2 nucleophilic substitution reaction, and for the CD2I- products of the deuteron abstraction reactions. The ion image data are analysed to determine the angular scattering and internal energy distributions in the two reaction channels. The results for the deuterated system are compared with previous experimental results obtained by the same group for the hydrogenated reactions, and also with computational results obtained using full-dimensionality quasi-classical trajectory (QCT) and reduced-dimensionality quantum mechanical (QM) dynamical methods employing a recent ab initio potential energy surface (PES). Whilst the QCT calculations are shown to reproduce the experimental results for both channels of the deuterated reaction and the hydrogenated abstraction reaction, the QCT calculations fail to reproduce significant forward scattering observed for the hydrogenated substitution reaction. On the basis of the reduced-dimensional QM calculations the authors suggest the enhanced forward scattering in the latter case may be due to enhanced reactivity at high total angular momentum and the role of quantum mechanical tunnelling, which is expected to be most significant in the hydrogenated substitution reaction. The authors also note, however, that differences in IVR in the hydrogenated and deuterated reactions, and the accuracy with which these are described in the QM and QCT calculations, may also play a role.

Overall, the paper is well-written and the results clearly presented. In my view the authors present novel results on the title reaction, which merit publication in Nature Communications. Whilst I am supportive of publication, I have a number of comments which the authors should address prior to acceptance of the manuscript, which I list below.

1. The role of QM effects in molecular scattering is a longstanding issue in molecular reaction dynamics, and I feel the authors somewhat overplay the significance of the work described in the current manuscript, albeit as interesting as it is. I think some reference should be made to seminal studies of simpler systems, such as F + H2 or H + H2, which were the first to identify some of the issues raised by the authors.

2. I found the subdivision of the scattering into the different 'mechanisms', as shown in Table 1 of the main paper and described in the Supplementary Information, somewhat arbitrary. If the authors are simply using this information as a means of quantifying scattering into different directions, or distinguishing isotropic from anisotropic scattering, that seems fine to me, but labelling them as different reaction mechanisms is quite a strong statement, and one which is perhaps not fully established in the manuscript.

3. Further to point 2, perhaps Table 1 is redundant in the main text anyway? It doesn't seem to contain information that isn't clearly derived, albeit more qualitatively, from the figures.

4. I have a concern about how trustworthy are the reduced-dimensionality QM calculations. What is striking is that the QM calculations show enhanced reactivity at high total angular momentum, compared with the QCT calculations, for both the deuterated and hydrogenated S_N2 reactions. However, the QCT data are in good agreement with the experimental data for the deuterated reaction. Furthermore, in the deuterated case, there is little experimental evidence of forward scattering, which one might expect to see based on the QM results. This raises a concern that the reduced-dimensionality QM calculations don't describe the dynamics accurately, particularly at low collision energy, where forward scattering is most prominent in the hydrogenated S_N2 reaction.

5. Following on from point 4, the results of the reduced-dimensionality QM calculations raise quite a few questions in my mind which are yet to be fully resolved. It seems to me that comparison of the QCT and QM data indicate that the reduced-dimensionality of the QM calculations could be a significant limitation. The authors do mention this in the context of the description of IVR in the hydrogenated versus deuterated systems, and perhaps that issue needs to be brought out more in the discussion, with less emphasis placed on the role of high total angular momentum and QM tunnelling, which are largely drawn from consideration of the reduced-dimensionality QM calculations, about which there may be some questions raised about the their reliability.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
See attached report.

Reviewer #2

(Remarks to the Author)
The authors have satisfactorily addressed my concerns regarding the manuscript. I think the paper is now suitable for publication in Nature Communications.

Response to Reviewer #1

This manuscript presents a combined experimental and theoretical study of the F- + CD3I SN2 reaction and of the D- abstraction reaction, for which the angle-velocity differential cross sections have been measured at collision energies ranging from 0.7 eV to 2.3 eV in the case of the SN2 reaction and 1.7 eV to 2.3 eV for the D-abstraction. The experimental results are of remarkable quality for anion-neutral reactions. QCT calculations were performed on an accurate high level ab initio by the Czakó and coworkers ref. [30] at the same collision energies.

The main topic of this manuscript is the study of the isotopic substitution effects and, indeed, the manuscript presents a thorough comparison of the two reactions at the same or very close collision energies. Interesting differences are found in the experimental scattering angle recoil velocity polar maps for the two isotopic variants. Forward scattering is larger for the reaction with CH3I, while backward scattering is larger for the reaction with the CD3I isotopologue. The agreement between the QCT calculated separate angle (DCS) and velocity distributions and the corresponding experimental results for the H- and D- reactions is reasonably good in both cases. However, it underestimates the magnitude of the forward scattering in the case of the reaction with CH3I. The manuscript also includes some TD QM scattering calculations, but only the total reaction probabilities as a function of the total angular momentum are shown. It is found that the QM reaction probability at high values of J is much larger than that found in the QCT calculations, especially at the lowest collision energies. This effect is found in the reaction with the two isotopologues, but it is more pronounced in the case of the reaction with CH3I. Although no QM DCSs are shown, the authors implicitly assume that the much larger contribution from high J would lead in an enhanced forward scattering. Whether this will bring the future (?) QM results in better agreement with the experimental data is not clear. The authors conclude from these two pieces of evidence that perhaps QM dynamical effect may be important in describing the SN2 reactions.

I found the manuscript interesting with valuable content, but its interest is not greater than that of previous articles by the teams of the main authors of the present manuscript. I would have some reservations about publishing this manuscript in a general-science journal. For one thing, its subject matter is quite specific, and although SN2 reactions are of great importance in Chemistry, the reaction mechanism in gas phase has been extensively studied in the literature over the last 20 years or so. On the other hand, articles of similar content have been published in Nat. Comm. So I think the manuscript can published there.

We are happy about the positive view of the reviewer on the quality of the presented data. We agree that it is unfortunate that only QCT simulations, but no quantum scattering calculations can be carried out in the full 12-dimensional space of the relative motion of the atoms in the reaction. Since this will likely remain the case for many years to come, we are happy that we could include 6-dimensional calculations, which are at the forefront of what is numerically possible for ion-neutral reactive scattering. The caveat is that we cannot directly compare experiment and quantum scattering calculations.

However, the absence of agreement between QCT and experiment for the particular case of SN2 reactions of hydrogenated molecules, and the excellent agreement for SN2 reaction of deuterated molecules and for proton transfer and deuteron transfer highlights that a non-classical aka quantum effect must be at work in the hydrogenated SN2 reaction.

This finding is a major step forward compared to any of the previous detailed presentations of results on substitution and elimination reactions that the reviewer is alluding to. We are therefore strongly convinced that the present results are of interest for a wide scientific community. Our detailed answers to the reviewers comments show this in more detail.

Be that as it may, I think that the manuscript should be carefully revised before its final acceptance. My comments and criticisms are as follow:

1. I am missing a lot of information about the experiments and the theoretical calculations that should be included at the least in the Supplementary Information.

We have added additional details to the experimental methods in the supplementary information. Additional details on the QCT computations are given in the Methods section. We also provide a more detailed description on the centrifugal sudden (CS) approximation employed in the quantum dynamics calculations, the formulae on how to calculate the reaction probability and the integral cross section, and more numerical parameters in the supplementary information. We think that the quantum dynamics results can be well reproduced based on these parameters.

2. I have several doubts about the experimental polar maps shown in this manuscript. As I understand the impact position and arrival time are measured simultaneously in these experiments and under these conditions, 3-D velocity distributions can be extracted. What is represented in Fig. 1 are the raw signals or they have been elaborated to account for 2-D → 3-D reconstruction? Should the reader assume that what is shown is the equatorial polar map of the Newton sphere at each collision energy? Those details should be explained in some more detail.

We apologize to the reviewer that an explanation was missing how the presented two-dimensional images are obtained from the product velocity vectors. This information is now added to the methods section, it is the same procedure used in our previous studies.

3. In the polar maps I miss the drawing of the circle of the nominal maximum velocity that for the I− product compatible with the energy conservation.

This is surprising, as these circles were included in our submitted manuscript. Possibly the line strength was too small. This has been changed with the revised figure 1.

4. I believe that Fig. S1 is very relevant and should be included in the main paper.

We are fine with this suggestion and have replaced figure 1 with figure S1. We have updated the main text and the text in the first section of the supplementary information accordingly.

5. The assignment of the regions in the polar maps of Fig S1 seems to be topographical, based on the angle-velocity at which the product appears. However, I wonder whether the assignment of the various mechanisms, as shown in Table I, has made use of the information that can be extracted from the QCT calculations. Incidentally, I suggest that, as in Fig. 1 and 3, Fig. S1 should show the top row for D- and the bottom for H- reactions.

Yes, this assignment has been carried out empirically based on the measured scattering images. This assignment has not used the QCT simulations.

The previous figure S1 and the new figure 1 show the results for deuterated reactants in the top row and the results hydrogenated molecules in the bottom row.

6. Can the relative cross section at the different energies be estimated from the integration of the experimental differential cross sections?

No, this is something our experimental setup has never been designed to achieve. It is difficult, because the absolute calibration of the ion and neutral beam densities and their overlap can not be reliably performed in the experiment. In particular, this overlap is expected to drift over a time scale of hours due to slight movements of the ion beam. This is not relevant for detecting single events for differential measurements, but would be an issue for absolute cross section determinations.

7. As for the QCT calculations, the Method section should include b_{max} at each energy. If the calculations have been performed with the Venus code, this should be mentioned. I do not understand why the authors do not use the simple recipe of sampling the impact parameter for each trajectory such that $b = (Rnd)^{1/2} b_{max}$. It would be more precise for high impact parameters.

Following the Reviewer's suggestion, we have added the b_{max} values to the Methods section. We did not use the Venus code, as it has been clarified in the revised manuscript. The new text reads as

"Quasiclassical trajectory (QCT) computations were performed for the F^- + CH_3I and F^- + CD_3I reactions at 0.71, 1.20, 1.57, and 2.33 eV and 0.76, 1.10, 1.50, and 2.24 eV collision energies, respectively, ~~on~~ using our own dynamics code and a recently-developed full-dimensional high-level ab initio analytical potential energy surface (PES) [30]."

"The b_{max} values are 13.5(13.0), 11.5(11.5), 11.0(10.5), and 9.5(9.0) bohr for the F^- + CH_3I(CD_3I) reactions at the above collision energies, respectively."

We prefer to compute the same number of trajectories at fixed equidistant *b* values, because it allows us plotting the *P*(*b*) function straightforwardly and provides statistically accurate reaction probabilities even at low impact parameters. The use of $(Rnd)^{1/2}b_{max}$ could be practical for integral cross section computations, but requires binning to obtain the opacity functions.

8. In Figs. 2 and 4 the authors label the QCT results as "Simulation", but I believe that what is shown are the purely theoretical angular and velocity distributions without including any experimental aspects that would make of them a true simulation directly comparable with the experimental data. In particular, the spread in collision energy, which is not negligible (0.18 eV), should have been taken into account.

Numerical QCT calculations have been referred to as "simulations" in many previous publications by various research groups in the field, we assume in parts also due to the random sampling of the initial conditions of each trajectory. We therefore prefer to concur with this nomenclature.

The QCT simulations are not folded by the collision energy spread because the internal energy distributions are so broad that the finite experimental resolution is estimated not to modify these distributions in a significant way.

9. I would suggest the authors to use an absolute scathe for the DCSs ($Å^2$ sr^{-1}). This is more informative than "Normalized Counts".

The absolute intensity scale of the differential scattering distributions is not known as the absolute calibration of the ion and neutral beam densities can not be reliably performed in the experiment (see also our answer to comment 6 above). The measurements yield ion counts per velocity intervals, but its absolute value has no significant meaning. We therefore use "Normalized Counts" to label the intensity.

10. A proper comparison of the experimental data would have require the calculation of the QCT polar maps. This is perfectly feasible in QCT calculations and I would suggest that the authors do this.

Motivated by the Reviewer's suggestion, we have now computed the QCT polar maps and include them now in the supplementary information for comparison with the experiment.

11. Relatively few details are given about the methodology used in the QM calculations. In particular, are the calculation done under the CS approximation?

Yes, to save computational cost, the CS approximation is implemented when calculating the reaction probabilities for non-vanishing partial waves. In the CS approximation, the projection of the total angular momentum on the body-fixed z axis, *K*, becomes a good quantum number and is conserved. As also stated above, we have added the description of the CS approximation in the supplementary information.

12. What are the initial rotational quantum numbers used in the QM and QCT calculations?

The initial rotational state used in both the QM and QCT calculation is taken to be J=0. We have added the following sentence to the QCT part of the Methods section: "The initial rotational angular momentum of the reactants is set to zero by standard modification of the velocities."

We have also added the following sentence below equation S11 in the supplementary information: "In this study, we focus on the quantum dynamics from the reactant ground ro-vibrational states, *i.e.* $n_0=J_0=0$.".

13. As long as the reaction probability, P(J), has been calculated with QM and QCT, there is sufficient information to plot in both cases the total reaction cross section at the calculated collision energies. This should be plotted and included in the SI.

We agree and have added a plot of the integral cross sections to the supplementary information and compare it with previously measured experimental cross sections.

14. By inspection of the P(J), I believe that the QM cross sections are much larger that the QCT ones, especially at low energies. Can there be any explanation for this?

The total cross sections, which are now reported in the revised supplementary information, are actually only about a factor of two different. As we discuss in the manuscript, one possible reason for this is quantum tunneling through the Walden inversion barrier, which is not included in the the QCT simulations. However, since tunneling is suppressed for reactions of the heavier deuterium atoms, this probably does not explain all of the difference.

Another important reason is likely the reduced dimensionality of the QD model. Specifically, the QD calculation does not describe proton transfer (PT), which competes with SN2 in the present reaction, due to the limitations of the employed QD model. The PT reaction probability is smaller, but still of a significant magnitude compared to the SN2 channel at all but the lowest studied collision energies. Therefore, reactants that would undergo PT are enforced to some extend to enter into the SN2 product channel, enhancing unphysically the reactivity of the SN2 reaction. In a previous study by some of us [Wang et al. J. Phys. Chem. Lett (2016), Ref. 48] this effect was also present and it certainly accounts for part of the enhancement. We have added this to the discussion section in the manuscript.

15. I believe that the main difference between the reaction with H- and D- species lies in the different ZPE. The plot of the MEP for the vibrationally adiabatic potential would be very illustrative. It is not clear to me how tunneling through the effective barrier can be an explanation.

In fact near the barrier the ZPE does not modify the potential substantially. We have added a new figure to the supplementary information showing the classical and the ZPE-corrected vibrationally adiabatic relative energies of the stationary points. As this Figure shows, the ZPE has only a minor effect (< 0.01 eV) on the Walden-inversion barrier height.

In summary, I think that this manuscript deserves to be published, but it should be revised along the lines indicated above.

We have taken great care to revise the manuscript along the reviewer's comments.

Response to Reviewer #2

This paper describes an experimental and computational study of the F- + CD3I reaction. The authors employ crossed molecular beam methods coupled with velocity map ion imaging. Ion images are presented for the I- products of the S_N2 nucleophilic substitution reaction, and for the CD2I- products of the deuteron abstraction reactions. The ion image data are analysed to determine the angular scattering and internal energy distributions in the two reaction channels. The results for the deuterated system are compared with previous experimental results obtained by the same group for the hydrogenated reactions, and also with computational results obtained using full-dimensionality quasi-classical trajectory (QCT) and reduced-dimensionality quantum mechanical (QM) dynamical methods employing a recent ab initio potential energy surface (PES). Whilst the QCT calculations are shown to reproduce the experimental results for both channels of the deuterated reaction and the hydrogenated abstraction reaction, the QCT calculations fail to reproduce significant forward scattering observed for the hydrogenated substitution reaction. On the basis of the reduced-dimensional QM calculations the authors suggest the enhanced forward scattering in the latter case may be due to enhanced reactivity at high total angular momentum and the role of quantum mechanical tunnelling, which is expected to be most significant in the hydrogenated substitution reaction. The authors also note, however, that differences in IVR in the hydrogenated and deuterated reactions, and the accuracy with which these are described in the QM and QCT calculations, may also play a role.

Overall, the paper is well-written and the results clearly presented. In my view the authors present novel results on the title reaction, which merit publication in Nature Communications. Whilst I am supportive of publication, I have a number of comments which the authors should address prior to acceptance of the manuscript, which I list below.

We thank the reviewer for the careful analysis of our manuscript and the positive recomendation. Our specific answers to the reviewer's comments are presented in the following text.

1. The role of QM effects in molecular scattering is a longstanding issue in molecular reaction dynamics, and I feel the authors somewhat overplay the significance of the work described in the current manuscript, albeit as interesting as it is. I think some reference should be made to seminal studies of simpler systems, such as F + H2 or H + H2, which were the first to identify some of the issues raised by the authors.

We did not intend to create the false impression that little research was performed on quantum effects in molecular scattering prior to our work or the last few years. In the second paragraph of our manuscript we already refer to several publications from the last ten years on quantum effects in three- and four-atom systems and cite five papers that have revealed quantum effects in chemical dynamics (including a reference to F + HD and to H + HD). We now have added a new reference [Althorpe and Clary, Annu. Rev. Phys. Chem. (2003), Ref. 20] to introduce the many earlier achievements on this topic.

2. I found the subdivision of the scattering into the different 'mechanisms', as shown in Table 1 of the main paper and described in the Supplementary Information, somewhat arbitrary. If the authors are simply using this information as a means of quantifying scattering into different directions, or distinguishing isotropic from anisotropic scattering, that seems fine to me, but labelling them as different reaction mechanisms is quite a strong statement, and one which is perhaps not fully established in the manuscript.

In several cases a clear correspondence was found in previous studies between patterns of the angular scattering distribution and reaction mechanisms calculated by direct dynamics or PES-based quasiclassical trajectory simulations. We used this notion also in the present

work to empirically differentiate the scattering distribution to reaction mechanisms. In our view this is not arbitrary, in particular given that small changes of the boundaries do not affect the overall fraction of a mechanism much (as discussed in the manuscript). Nevertheless, we are happy to rename the direct stripping and sideways stripping to forward scattering and sideways scattering to not over-interpret these patterns. We prefer to keep the names of the very characteristic direct rebound S_N2 mechanism and also to the indirect mechanisms.

3. Further to point 2, perhaps Table 1 is redundant in the main text anyway? It doesn't seem to contain information that isn't clearly derived, albeit more qualitatively, from the figures.

We think Table 1 is very important for the manuscript, as it contains the concentrated information from the differential scattering images and shows the significance of the enhanced forward scattering probability for hydrogenated compared to deuterated reactants. We have therefore kept it in the revised manuscript.

4. I have a concern about how trustworthy are the reduced-dimensionality QM calculations. What is striking is that the QM calculations show enhanced reactivity at high total angular momentum, compared with the QCT calculations, for both the deuterated and hydrogenated S_N2 reactions. However, the QCT data are in good agreement with the experimental data for the deuterated reaction. Furthermore, in the deuterated case, there is little experimental evidence of forward scattering, which one might expect to see based on the QM results. This raises a concern that the reduced-dimensionality QM calculations don't describe the dynamics accurately, particularly at low collision energy, where forward scattering is most prominent in the hydrogenated S_N2 reaction.

We acknowledge that there are limitations about the reduced-dimensionality model used in the QM calculations, especially that the model cannot describe the other important channel in this reaction, proton transfer (PT), which competes with the SN2 reaction channel in the studied collision energy range (see also our response to comment 14 of reviewer 1). We have added this to the discussion section in the manuscript.

However, it should also be emphasized that the current QD model includes important degrees of freedom relevant to the SN2 reaction path. To our best knowledge, the employed QD model is also the most accurate model that can be dealt with in the frame of quantum mechanics currently. As can be seen from the supplementary information, some numerical parameters employed in the quantum scattering calculations are very large, resulting in extremely large computational costs. We hope that in the future all degrees of freedom can be included, when the quantum scattering method will be revolutionized or the computers will provide a large numerical advantage.

5. Following on from point 4, the results of the reduced-dimensionality QM calculations raise quite a few questions in my mind which are yet to be fully resolved. It seems to me that comparison of the QCT and QM data indicate that the reduced-dimensionality of the QM calculations could be a significant limitation. The authors do mention this in the context of the description of IVR in the hydrogenated versus deuterated systems, and perhaps that issue needs to be brought out more in the discussion, with less emphasis placed on the role of high total angular momentum and QM tunnelling, which are largely drawn from consideration of the reduced-dimensionality QM calculations, about which there may be some questions raised about the their reliability.

As stated in our answer to comment 4, there are unfortunately limitations in that full-dimensional quantum scattering calculations are not feasible for six-atom nucleophilic substitution reactions, and will likely not be for many years to come. We think that they nevertheless provide important additional insight into the studied reaction. As stated above, we discuss this in more detail in the revised manuscript.

Response to Reviewer

The authors have incorporated most of the reviewers' corrections/suggestions. In general terms, I deem the manuscript ready for its publication, especially after the inclusion of a supplementary material and some more details in the Methods section. However, I disagree with the authors on a few points in their rebuttal letter.

1. I understand that no absolute value of the ICS or DCS can be measured in these experiments. I also understand that not even relative cross sections at different energies or from different channels or for the two isotopologues can be inferred from the experimental data. But this is certainly not the case for QCT calculations for which there is no constraint to express the results in absolute units. Since the QCT and the experimental DCSs and product's relative energy distributions are plotted in separate plots, I see no problem in expressing the theoretical results in Å 2 (or a 20). It would certainly be more informative than using "Normalized counts" (there is not such unit in any theoretical treatment). Meanwhile the experimental data could be expressed in Normalized counts. The reader would benefit from getting an idea of how the DCS evolves with the collision energy or the relative importance of the two main channels.

We think that the normalized distributions carry all the relevant informative when comparing theory and experiment. Furthermore, it would be confusing if we showed absolute values of the calculated DCS, since we would need different color ranges for each panel as the SN2 reactivity decreases fast with collision energy. Since calculated absolute integral cross sections are given in Figure S2 of the SI, one can easily get a picture of the magnitude also of the DCS and how it changes with collision energy.

2. I also concur with reviewer #2 in that Table 1 is unnecessary insofar the information is already included in the angle-recoil velocity polar maps.

We do not think that Table 1 is unnecessary, as the values for the branching ratios for the different reaction scattering mechanisms are not shown in the scattering images. Also their estimated accuracies are only shown in the Table.

3. I am sorry, but from Fig. 5 I fail to see any (relative) enhancement of the reaction probability of the hydrogenated reaction at large angular momenta compared to the deuterated reaction. It seems to me that the ratio forward/backward is similar if not greater for the reaction with CD3I. These are relatively minor considerations, but they must be considered by the authors. Apart from that, I found the article worthy of publication in Nat. Comm.

We agree that the effect is indeed minor, but it can be seen at 1.2 eV collision energy and also at the highest two collision energies. To account for this we have slightly rephrased the statements on page 7 and page 8 of the manuscript.

Manuscript Number: NCOMMS-23-57980-T

Title: "A dynamic isotope effect the nucleophilic substitution reaction F^- + CD_3I"

Author: Atilay Ayasli et al.

This manuscript presents a combined experimental and theoretical study of the F^- +CD_3I S_N2 reaction and of the D- abstraction reaction, for which the angle-velocity differential cross sections have been measured at collision energies ranging from 0.7 eV to 2.3 eV in the case of the S_N2 reaction and 1.7 eV to 2.3 eV for the D-abstraction. The experimental results are of remarkable quality for anion-neutral reactions. QCT calculations were performed on an accurate high level ab initio by the Czakó and coworkers ref. [30] at the same collision energies.

The main topic of this manuscript is the study of the isotopic substitution effects and, indeed, the manuscript presents a thorough comparison of the two reactions at the same or very close collision energies. Interesting differences are found in the experimental scattering angle recoil velocity polar maps for the two isotopic variants. Forward scattering is larger for the reaction with CH_3I, while backward scattering is larger for the reaction with the CD_3I isotopologue. The agreement between the QCT calculated separate angle (DCS) and velocity distributions and the corresponding experimental results for the H- and D- reactions is reasonably good in both cases. However, it underestimates the magnitude of the forward scattering in the case of the reaction with CH_3I. The manuscript also includes some TD QM scattering calculations, but only the total reaction probabilities as a function of the total angular momentum are shown. It is found that the QM reaction probability at high values of J is much larger than that found in the QCT calculations, especially at the lowest collision energies. This effect is found in the reaction with the two isotopologues, but it is more pronounced in the case of the reaction with CH_3I. Although no QM DCSs are shown, the authors implicitly assume that the much larger contribution from high J would lead in an enhanced forward scattering. Whether this will bring the future (?) QM results in better agreement with the experimental data is not clear. The authors conclude from these two pieces of evidence that perhaps QM dynamical effect may be important in describing the S_N2 reactions.

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subject matter is quite specific, and although S_N2 reactions are of great importance in Chemistry , the reaction mechanism in gas phase has been extensively studied in the literature over the last 20 years or so. On the other hand, articles of similar content have been published in Nat. Comm. so I think the manuscript can published there.

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4. I believe that Fig. S1 is very relevant and should be included in the main paper.

5. The assignment of the regions in the polar maps of Fig S1 seems to be topographical, based on the angle-velocity at which the product appears. However, I wonder whether the assignment of the various mechanisms, as shown in Table I, has made use of the information that can be extracted from the QCT calculations. Incidentally, I suggest that, as in Fig. 1 and 3, Fig. S1 should show the top row for D- and the bottom for H- reactions.

6. Can the relative cross section at the different energies be estimated from the integration of the experimental differential cross sections?

7. As for the QCT calculations, the Method section should include $b_{\max}$ at each energy. If the calculations have been performed with the Venus code, this should be mentioned. I do not understand why the authors do not use the simple recipe of sampling the impact parameter

for each trajectory such that $b = (Rnd)^{1/2} b_{\max}$. It would be more precise for high impact parameters.

8. In Figs. 2 and 4 the authors label the QCT results as "Simulation", but I believe that what is shown are the purely theoretical angular and velocity distributions without including any experimental aspects that would make of them a true simulation directly comparable with the experimental data. In particular, the spread in collision energy, which is not negligible (0.18 eV), should have been taken into account.

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12. What are the initial rotational quantum numbers used in the QM and QCT calculations?

13. As long as the reaction probability, $P(J)$, has been calculated with QM and QCT, there is sufficient information to plot in both cases the total reaction cross section at the calculated collision energies. This should be plotted and included in the SI.

14. By inspection of the $P(J)$, I believe that the QM cross sections are much larger that the QCT ones, especially at low energies. Can there be any explanation for this?

15. I believe that the main difference between the reaction with H- and D- species lies in the different ZPE. The plot of the MEP for the vibrationally adiabatic potential would be very illustrative. It is not clear to me how tunneling through the effective barrier can be an explanation.

In summary, I think that this manuscript deserves to be published, but it should be revised along the lines indicated above.

Manuscript Number: NCOMMS-23-57980A (revised)

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Author: Ayasli et al.

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1. I understand that no absolute value of the ICS or DCS can be measured in these experiments. I also understand that not even relative cross sections at different energies or from different channels or for the two isotopologues can be inferred from the experimental data. But this is certainly not the case for QCT calculations for which there is no constraint to express the results in absolute units. Since the QCT and the experimental DCSs and product's relative energy distributions are plotted in separate plots, I see no problem in expressing the theoretical results in $Å^2$ (or a_0^2). It would certainly be more informative than using “Normalized counts” (there is not such unit in any theoretical treatment). Meanwhile the experimental data could be expressed in Normalized counts. The reader would benefit from getting an idea of how the DCS evolves with the collision energy or the relative importance of the two main channels.

2. I also concur with reviewer #2 in that Table 1 is unnecessary insofar the information is already included in the angle-recoil velocity polar maps.

3. I am sorry, but from Fig. 5 I fail to see any (relative) enhancement of the reaction probability of the hydrogenated reaction at large angular momenta compared to the deuterated reaction. It seems to me that the ratio forward/backward is similar if not greater for the reaction with CD_3I.

These are relatively minor considerations, but they must be considered by the authors. Apart from that, I found the article worthy of publication in Nat. Comm.