Quantitative Dynamics of the N$_2$O + C$_2$H$_2$ → Oxadiazole Reaction: A Model for 1,3-Dipolar Cycloadditions

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ABSTRACT: The reaction N$_2$O + C$_2$H$_2$ → oxadiazole has been considered as a prototype for 1,3-dipolar cycloadditions. Here, we report a comprehensive dynamical study of this important reaction on a full-dimensional potential energy surface, which is fitted to about 64 000 high-level ab initio data by a machine learning approach. Comprehensive dynamical simulations are carried out to provide quantitative chemical insight into its reaction dynamics. In addition to confirming the enhancement effect of the N$_2$O bending mode on the reactivity, intricate mode specificity effects of other vibrational modes in reactants are revealed for the first time. The asymmetric stretching mode of N$_2$O and the C–C–H bending mode of C$_2$H$_2$ show no effect. All remaining modes can enhance the reactivity. In particular, the vibrational excitation of the N$_2$O symmetric stretching mode shows similar enhancement effect on the title reaction, compared to its bending mode excitation. Detailed analysis reveals that the concerted mechanism dominates with the reactants propelled sufficiently close to each other to yield product. This study advances our understanding of the chemical dynamics of the title reaction.

1. INTRODUCTION

The reaction between nitrous oxide (N$_2$O) and acetylene (C$_2$H$_2$) to form oxadiazole (C$_2$H$_2$N$_2$O) is an important prototype and a proving ground for understanding the 1,3-dipolar cycloadditions.1-3 Many 1,3-dipolar cycloadditions have been classified as “click reactions”.4 In contrast to the stepwise mechanism with a diradical intermediate,5,6 most experimental and theoretical investigations concluded that 1,3-dipolar cycloadditions often take place via a concerted way without an intermediate,7-9,10 although exceptions do exist.11-12 The reactivity, regioselectivity, and substituent effects of these 1,3-dipolar cycloadditions have been studied extensively.13,14,15-21 Recently, Houk and co-workers found that the excitation of the dipolar bending mode (N$_2$O for the title reaction) can promote the reactivity significantly based on direct dynamical calculations.22,23 They concluded that the N$_2$O bending mode must be excited to make the reaction possible.24-25 Their discoveries24-25 suggest that dynamical effects are important in organic reactions.26-28

Due to the expensive electronic structure calculations and complicated potential energy surfaces (PESs) with many degrees of freedom, Houk and co-workers generated only a small number of trajectories (64-128) with electronic energies and forces computed at the level of B3LYP/6–31G(d) for the title reaction.22,23 In addition, initial coordinates and momenta were sampled at the transition state (TS) region according to a normal mode sampling with only the zero-point vibrational energy (ZPE) in each normal mode, 0.6 kcal mol$^{-1}$ in the reaction coordinate, and zero rotational energy.22,23 It has been argued that this sampling does not correspond to realistic situations.23 Further, as it started from TS, the impact parameters cannot be sampled. Nonetheless, these rare dynamical studies of organic reactions provide valuable information about the mechanism and kinetics/dynamics.32 However, quantitative information is still lacking, in particular, due to the challenge in developing a reliable PES, which inhibits our full understanding of its dynamics. Herein, we report a comprehensive investigation of dynamics of the title reaction on an accurate full-dimensional PES, which is fitted by the permutation invariant polynomial-neural network (PI-PNN) method33-35 based on ca. 64 000 points calculated at the explicitly correlated (F12a) version of CASSD(T) with the augmented correlation-corrected valence double zeta (AVDZ) basis set.39,40 Detailed theoretical methods are given in the next section (Section 2), including ab initio calculations, potential energy surface, and QCT calculations. Section 3 presents the results and discussions. Conclusions are given in Section 4.

2. THEORY

2.1. Ab Initio Calculations. The title reaction N$_2$O + C$_2$H$_2$ → oxadiazole concerts with a cyclic transition state (TS),
as shown in Figure 1. The geometries of all stationary points were first optimized at the levels of CCSD(T)-F12a/AVnZ, n = D, T. CCSD(T)-F12 converges faster with respect to the size of the basis set than the standard CCSD(T) calculations. Therefore, it can be employed to develop full-dimensional accurate PESs effectively. All ab initio calculations were carried out using the MOLPRO 2015.1 program package in the current work. The inner orbitals of the nonhydrogen atoms (C, N, O) were kept frozen in the CCSD(T) calculations. For each single-point energy calculation with four cores, it takes about 10–30 min using the Intel Xeon CPU E5–2680 v3 @ 2.50 GHz.

2.2. Potential Energy Surface. All dynamically relevant regions should be well described by the PES. Following our previous strategy, the ranges of configurations and energies were first inspected. Then, different grids with appropriate coordinates were used in different regions to sample dynamically relevant configurations. Notice that changes in the intramolecular coordinates result in significant energy changes. Therefore, dense grids should be used for intramolecular coordinates of N2O and C2H2 (the reactant region), and all internal coordinates of the TS and product regions. On the other hand, the intermolecular coordinates between the two species in the reactant region were sampled with relatively sparse grids. Further, direct dynamical calculations at a low level of theory, e.g., B3LYP/6–31+G(d), were performed to sample additional relevant points if they are not close to the point that already existed in the data set according to the generalized Euclidean distance, \[ \chi_2(\{r\}) = \sqrt{\sum_{i=1}^{21} |r_i - \bar{r}_i|^2} < 0.2 \text{ Å} \] defined in terms of the intermolecular distances between two points, \( \{\bar{r}\} \) and \( \{\bar{r}'\} \). All permutationally equivalent points \( 2!2!2! = 8 \) were included in such screenings. Finally, roughly 15 000 points were selected as the initial set of points.

Then, the initial set of points was computed at a selected ab initio level, and a raw PES was obtained by fitting. Starting from various initial conditions, trajectory calculations were carried out on this PES to further explore the configuration space and to generate new points. The above generalized Euclidean distance was used for efficient sampling. Further, if key properties of the system, including geometries, frequencies, and energies of the stationary points, as well as the minimum energy path (MEP) were not reproduced well by the PES, points were added in relevant regions. The procedure was repeated, and the PES was improved gradually until convergence.

These sampled ab initio points were then used to fit the PES according to the permutation invariant polynomial-neural network (PIP-NN) form,

\[ E_{\text{fit}} = b^{(3)}_i + \sum_{k=1}^{K} \omega^{(3)}_{i,k} f_j \left( b^{(2)}_k + \sum_{j=1}^{l} \omega^{(2)}_{j,k} G_j \right) f_j \left( b^{(3)}_i + \sum_{j=1}^{l} \omega^{(1)}_{j,i} G_j \right) \]

where \( l \) denotes the size of the input layer; \( J \) and \( K \) stand for the sizes of the neurons of the two hidden layers, respectively; for the two hidden layers, the hyperbolic tangent function is used as the transfer function; \( \omega^{(1)}_{j,i} \), the weighting parameter, connects the \( j \)th neuron of the \((l-1)\)th layer and the \( i \)th neuron of the \( l \)th layer; \( b^{(0)}_j \) is the bias parameter of the \( j \)th neurons of the \( l \)th layer; and \( E_{\text{fit}} \) is the fitted potential energy. Fitting parameters \( \omega \) and \( b \) were determined by optimal fitting of NN with the root-mean-square deviation (RMSD) as the performance function:

\[ \text{RMSD} = \sqrt{\frac{1}{N_{\text{data}}} \sum_{i=1}^{N_{\text{data}}} (E_{\text{fit}} - E_{\text{target}})^2} \]

In this work, all 456 PIPs with the maximum order of 3 were used as the input layer of the NN. These PIPs are symmetrized monomials of Morse-like variables of intramolecular distances, \( G = S H \sqrt{p_i p_j} \), \( p_i = \exp(-\lambda r_i) \) (\( \lambda = 1.05 \text{ Å}^{-1} \)), \( i, j = 1-7 \) and \( i \neq j \). The symmetrization operator, \( S \), contains all of the permutations among like atoms and guarantees the rigorous permutation invariance with respect to the exchange of like atoms in the PIP-NN approach. This approach has succeeded in fitting accurate PESs for many polyatomic reactions with up to 7 atoms, for instance, OH + CH4 and F/Cl + CH3OH.

For each NN fitting, the entire data were divided randomly into three data sets, i.e., the training (90%), validation (5%), and test (5%) sets. The learning of each NN was halted when errors of the validating set started to increase. Only fits with similar RMSDs for three sets were adopted. The maximum deviation was also a criterion for choosing the final PIP-NN PES. We tested several NN structures with different numbers of neurons in the two hidden layers. For each structure, 100–200 different NN training calculations were carried out with different initial fitting parameters, and different training, validation, and test sets. The PES can be obtained from the authors upon request.

2.3. Quasi-Classical Trajectory Calculations. The VENUS program was used for the full-dimensional QCT calculations. At the collision energies of 40, 50, and 60 kcal mol\(^{-1}\), the initial vibrational states of the reactants included the ground state (\( \nu = 0 \)), excitations in the reactant vibrational states, the bending mode (\( \nu_9(N_2O) = 1, 5 \)), the symmetric stretching mode (\( \nu_9(N_2O) = 1 \)), the asymmetric stretching mode (\( \nu_9(N_2O) = 1 \)) of N2O, the C–C–H bending mode (\( \nu_9(C_2H_2) = 1 \)), and the H–C–C–H wagging mode (\( \nu_9(C_2H_2) = 1, 5 \)) of C2H2. The initial rotational energies of both reactants were zero. For each initial condition, 1.5 × 10\(^4\) trajectories were calculated to make the statistical errors all less than 2.7%. The standard error was estimated by

\[ \Delta = \sqrt{\frac{N_{\text{total}} - N}{N_{\text{total}} N}} \]

The QCT method has been discussed extensively in the literature, so only a brief outline is given here. The reactive...
integral cross-section (ICS) of the title reaction was computed by

$$\sigma(E_c) = \pi b_{\text{max}}^2 P(E_c)$$  \hspace{1cm} (2)$$

where the reaction probability $P(E_c)$ at the collision energy $E_c$ is given by $P(E_c) = N_r/N_{\text{total}}$ with $N_r$ and $N_{\text{total}}$ being the number of the reactive or the total trajectories, respectively.

For each trajectory, the impact parameter $b$ was sampled according to $b = b_{\text{max}} \zeta^{1/2}$, where $\zeta$ is a random number ranging from 0.0 to 1.0, and the maximal impact parameter ($b_{\text{max}}$) was determined using small batches (104) of trajectories with trial values. The trajectories were initiated at a separation of 8.0 Å and terminated when reactants were separated by 8.2 Å. These initial and termination criteria are sufficiently long so that the interactions between reactants are negligible.

For cycloaddition reactions, the trajectories were halted when the distances of the two forming bond distances C–N and C–O arrived at 1.6 Å, which were similar to those used in a previous direct dynamical study by Houk and co-workers.23 In addition, the title reaction generally takes place in a solution. As shown in Figure 2, the potential energies along with the MEP on the PIP-NN PES as a function of the reaction coordinate $s$ (amu$^{-1/2}$bohr). The symbols represent the ab initio energies at the CCSD(T)-F12a/AVDZ level. For comparison, the potential diagram of this reaction in various solvents at the level of B3LYP/6–31+G(d,p) is plotted in this figure.

Other scattering parameters such as the spatial orientation of the initial reactants and vibrational phases were determined according to the Monte Carlo approach as implemented in VENUS.53 The propagation time step was selected to be 0.05 fs, which is much smaller than that used in the direct dynamic calculations (1 fs).23 The gradient of the PES with respect to atomic coordinates was calculated numerically. The combined fourth-order Runge–Kutta and sixth-order Adams–Moulton algorithms are used for the integration of the trajectories. Almost all trajectories conserve energy within a chosen criterion (10$^{-4}$ kcal mol$^{-1}$).

It should be noted that the zero-point vibrational energies (ZPEs) of the reactants are included at the reactant asymptote. However, the QCT treatment allows leakage of ZPE during the reaction process. The final product energies are much higher than their ZPEs for this exothermic cycloaddition reaction. Furthermore, the tunneling effect, which might play significant roles at low energies/temperatures, is not considered within the QCT framework. It is thus highly desirable to perform exact quantum dynamic computation, which is, however, very difficult for the current system with seven atoms, namely, fifteen degrees of freedom. Fortunately, QCT computations often yield qualitative and even quantitative results, compared to the quantum dynamical calculated outcome$^{57–59}$ and available experiments.60 In addition, the simulations were computed at high collision energies, 40, 50, 60 kcal mol$^{-1}$, in this work. Therefore, the trajectory is very fast, which typically finished within 200 fs. Consequently, for short-time QCTs at high collision energies, it is reasonably assumed that the tunneling effect is irrelevant and the contributions of ZPE-violating trajectories during the evolution process are minimal.

### 3. RESULTS AND DISCUSSION

#### 3.1. Ab Initio Calculations.

As shown in Figure 1 and Table 1, the structural parameters and harmonic frequencies at the CCSD(T)-F12a/AVDZ and CCSD(T)-F12a/AVTZ levels are almost identical. In general, the B3LYP/6–31G(d) calculated geometric parameters by Lan et al.61 are consistent with the current high-level calculations, with deviations being 0.05 and 0.04 Å for the two forming bonds at TS, respectively. The activation energies are 25.1 (26.3, ZPE corrected) and 27.1 (28.1) kcal mol$^{-1}$ at levels of CCSD(T)-F12a/AVDZ and CCSD(T)-F12a/AVTZ, respectively. The reaction energies are −44.5 (−39.6) and −42.3 (−37.7) kcal mol$^{-1}$ at AVDZ and AVTZ, respectively. Both are comparable to previous ZPE corrected CBS-QB3 values, 27.9 and −37.1 kcal mol$^{-1}$.$^{12,61}$

![Figure 2. Potential profile of the MEP on the PIP-NN PES as a function of the reaction coordinate s (amu$^{-1/2}$bohr). The symbols represent the ab initio energies at the CCSD(T)-F12a/AVDZ level.](image)

#### Table 1. Energies (kcal mol$^{-1}$) and Vibrational Harmonic Frequencies (cm$^{-1}$) of the Stationary Points Along with the Reaction N$_2$O + C$_2$H$_2$ → Oxadiazole

| species   | method | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12 | 13 | 14 | 15 |
|-----------|--------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| N$_2$O + C$_2$H$_2$ (0; 0; 0) | PES$^a$ | 582 | 582 | 1291 | 2272 | 572 | 572 | 729 | 729 | 2004 | 3403 | 3498 |
|           | AVDZ$^b$ | 584 | 584 | 1295 | 2276 | 552 | 552 | 730 | 730 | 2001 | 3401 | 3493 |
|           | AVTZ$^c$ | 600 | 600 | 1301 | 2284 | 616 | 616 | 752 | 752 | 2005 | 3408 | 3501 |
| Oxadiazole (−44.54; −44.49; −42.26) | PES$^a$ | 584 | 611 | 686 | 781 | 833 | 942 | 967 | 1085 | 1131 | 1147 | 1356 | 1427 | 1547 | 3280 | 3303 |
|           | AVDZ$^b$ | 608 | 615 | 679 | 765 | 797 | 938 | 966 | 1091 | 1132 | 1142 | 1356 | 1423 | 1543 | 3279 | 3302 |
|           | AVTZ$^c$ | 595 | 632 | 680 | 733 | 781 | 942 | 972 | 1093 | 1135 | 1143 | 1360 | 1429 | 1548 | 3283 | 3306 |
| TS (25.00; 25.05; 27.14) | PES$^a$ | 585 | 267 | 283 | 486 | 587 | 632 | 704 | 711 | 731 | 820 | 1285 | 1807 | 1890 | 3372 | 3437 |
|           | AVDZ$^b$ | 593 | 281 | 298 | 482 | 566 | 593 | 705 | 706 | 730 | 809 | 1289 | 1815 | 1898 | 3367 | 3436 |
|           | AVTZ$^c$ | 606 | 285 | 305 | 495 | 559 | 619 | 717 | 718 | 761 | 824 | 1265 | 1819 | 1912 | 3372 | 3443 |

$^a$This work, fitted PIP-NN PES. $^b$This work, CCSD(T)-F12a/AVDZ. $^c$This work, CCSD(T)-F12a/AVTZ.
kcal mol\(^{-1}\) deviation for the activation energy at the level of CCSD(T)-F12a/AVDZ, compared to that of CCSD(T)-F12a/AVTZ, is neglected compared to the high barrier, 25.1 kcal mol\(^{-1}\), and should have no effect on the dynamics and reactivity. As a compromise between efficiency and calculation cost, CCSD(T)-F12a/AVDZ was selected for developing the PES of the title reaction.

3.2. Potential Energy Surface. The PIP-NN fitting approach is employed to fit the PES base on ca. 64,000 points at the level of CCSD(T)-F12a/AVDZ. After several testing, 20 and 80 neurons were selected in the two hidden layers, respectively. The final PES has a total of 10,901 parameters, making the evaluation of the PIP-NN slow. The RMSDs for the training/validation/test/total sets are 0.33/0.59/0.61/0.37 kcal mol\(^{-1}\), respectively. Note these 64,000 points correspond to 512,000 points because of the permutation invariances with respect to the identical atoms, namely, the two carbon/hydrogen/nitrogen (2!2!2!) atoms in the title system. Thanks to the ultraflexible PIP-NN approach with rigorous permutation invariance among like atoms, energies, geometries (Figure 1), and harmonic frequencies (Table 1) of the stationary points are well reproduced. As shown in Figure 2, the potential energy along with the MEP on the PES is also in excellent agreement with the ab initio calculations. Initially, reactant species C\(_2\)H\(_2\) and N\(_2\)O (both linear) are parallel to each other. Along with the MEP, they approach each other with the bond configuration. As shown in Figure 3a,b, small fitting errors (most less than 0.07 kcal mol\(^{-1}\)) are evenly distributed within the entire energy range up to 100 kcal mol\(^{-1}\), which is sufficient for high energy or temperature dynamic studies.

Figure 4 presents a two-dimensional (2-D) contour plot (with other coordinates relaxed) of the PIP-NN PES as a function of the ab initio energy up to 100.0 kcal mol\(^{-1}\) and \(E_C\) (in kcal mol\(^{-1}\)) as a function of \(E_C\) (in kcal mol\(^{-1}\)) from diifferent initial conditions.

3.3. Dynamics. Comprehensive dynamics calculations were carried out at \(E_C\) = 40, 50, and 60 kcal mol\(^{-1}\), respectively, without rotational energies in the two reactants. As shown in Figure 5 and Table S1, for ground-state reactants (\(v = 0\)), the reactivities of the title reaction are very minimal, with the reactive integral cross-sections (ICSs) being only 0.002, 0.012, and 0.028 \(\text{Å}^2\), respectively, at \(E_C\) = 40, 50, and 60 kcal mol\(^{-1}\), which are much higher than the barrier height (25.0 kcal mol\(^{-1}\)). As demonstrated below, the narrow cone of acceptance and the requirement of the concerted formation of the two bonds come in as the steric factor that can be attributed to the entropy in the Arrhenius equation. Statistically, the chance to access the TS is hindered, leading to minimal reactivities. Indeed, the entropic loss upon bond formation is prevailing in cycloaddition reactions.\(^{62}\)

When the energy is deposited in different reactant vibrational modes, its efficiency in promoting reactions may vary accordingly. This so-called mode specificity is thus defined by the differences in reactivity due to excitations in various reactant vibrational modes and has been extensively investigated in both gaseous reactions\(^ {57,58,63}\) and reactions at gas–solid interfaces.\(^ {66,67}\) For vibrationally excited reactants, N\(_2\)O or C\(_2\)H\(_2\), the ICS trends all increase along with increasing \(E_C\) consistent with the activation nature of the title reaction. The excitations of different vibrations show different influences...
on the reactivities. For excitations in the N₂O bending mode, ν(N₂O) = 1, 5, the ICSs are increased by 50–800% within 40–60 kcal mol⁻¹. This is consistent with the findings from previous direct post transition state dynamics 68 by Houk and co-workers, 22,23 and the predictions 69 by the sudden vector projection (SVP) model, which attributes the enhancement of reactivity to the coupling of a reactant mode with the reaction coordinate at the TS. 70 As shown in Figure S1, the reaction coordinate vector at the TS largely involves the N₂O bending mode, 22,23 whose normal mode vector is shown in Figure S2. As seen in Figure S5, the mode specificity is rather complicated for the title reaction, while Houk and co-workers concluded that no other mode (except the N₂O bending mode) should have much effect on its reactivity. 22 Clearly, the excitations in the N₂O asymmetric stretching mode (ν(N₂O) = 1) and the C−C−H bending mode (ν(C(C₂H₂)) = 1) of C₂H₂ essentially show no effect except for ν(N₂O) = 1 at Eᵣ = 50 kcal mol⁻¹. According to the normal mode vectors in Figures S2 and S3, the ν(N₂O) mode leads to one elongated and one shortened N−N and N−O distances, and the ν(C(C₂H₂)) mode results in C₂H₂ trans-like configuration. This is in contrast to the concerted TS in Figure 2, which requires both N−N̅ and N̅−O bond distances to elongate simultaneously and both angles HCC' and H'C'C of C₂H₂ to bend in the same direction. 59

All other vibrational modes of the reactants show promotion effects on the title reaction, albeit different in magnitude. The excitation of the N₂O symmetric stretching mode (ν(N₂O) = 1) shows a significant boost effect, only slightly smaller than ν(N₂O) = 1, as seen in Figure S5. This is because ν(N₂O) = 1 leads to elongated N−N and N−O distances simultaneously, consistent with the geometric requirement at the TS. According to the SVP predictions, 69 the reactivity can be promoted by excitations of the H−C−C−H wagging mode (ν(N₂O) = 1) and the C−H symmetric stretching mode (ν(C(C₂H₂)) = 1) of C₂H₂. They are in line with the current QCT results, which show that the ICSs are marginally increased by ca. 10%. As shown in Figure S5, similar effects can be found for the excitations of the C₂H₂ C−H symmetric stretching mode (ν(C−H(N₂O)) = 1). A remarkable increase of the ICS (40–110%) is found for ν(C(C₂H₂)) = 5, slightly higher than ν(N₂O) = 1, and smaller than ν(N₂O) = 1. For the excitation of the C−C stretching mode (ν(C(C₂H₂)) = 1) of C₂H₂, its ICS is larger than ν(N₂O) = 1, and ν(C−H(N₂O)) = 1, and increased by 20–30% compared to ν = 0. In addition, if the C₂H₂ or N₂O rotations are sampled according to a Boltzmann distribution at 300/1000 K, the ICSs are not affected, 0.011/0.010 or 0.012/0.012 Å², at Eᵣ = 50 kcal mol⁻¹ and ν = 0. This is consistent with the deduction from direct dynamical results by Houk and co-workers; starting from the TS region, only 0–1% of the available energy was partitioned into the rotations of N₂O or C₂H₂. 23

Figure 6 presents the ICSs as a function of the total energy, which provides the energy efficacies among various vibrational excitations and the translational energies. One can see that in the total energy scale, the N₂O bending mode excitations (ν(N₂O) = 1, 5) are more effective than the translational energy in promoting the title reaction. For other vibrational excitations in the reactants, the translational energy is more effective in promoting the reaction.

The dynamics of the title reaction can be explored further in detail. Figure 7a presents the distribution of the time gap between the two forming bonds, C−N and C−O, in the reactive QCTs at 50 kcal mol⁻¹ and ν = 0. Following the criteria used by Xu et al. 23 the first bond length is chosen to be 1.6 Å with the second one being 2.0 Å. Clearly, most (66%) of the time gaps fall in the range of 0–2 fs, and the remaining 34% are all within 2–30 fs. The average time gap is 4.7 fs. In the direct dynamics starting from the TS region, the calculated time gaps are all under 30 fs with a larger average 6–12 fs, 23 compared to the current calculations. Both time gaps are under the C−N or C−O vibrational period of ca. 30 fs. Therefore, the concerted mechanism is highly dominant for the title reaction, and the stepwise mechanism with a diradical intermediate can be safely ruled out.

During the reaction, the first forming bond can be either C−N or C−O bond. At Eᵣ = 50 kcal mol⁻¹ and ν = 0, the corresponding ratio is 0.80:1 for CN:CO. As shown in Figures S4–S6 of the Supporting Information (SI), at other initial conditions, the ratios for CN:CO are all around 1:1 (0.80:1), consistent with the nearly equal amplitudes for both forming bonds (Figure S1 of SI) at the TS. 23 The distribution of the reactive impact parameters, as shown in Figure 7b, possesses peaks within 0.4–0.6 Å with a maximum impact parameter of 1.2 Å. The distributions of the forming angles OC'C and NCC' at initial configurations and TS in the reactive QCTs are displayed in Figure 7c,d, respectively.
Clearly, for most reactive QCTs, the initial OC–C and NCC bond angles fall in a large range, 50–125°. At the TS, their distributions become much narrower, mainly within 95–105°, which are close to 101.7 and 106.4° of the ab initio TS. Figures S4–S6 show similar statistical analyses at other initial conditions. Besides, the bending angles NN‘O of N₂O are all nearly 180° at initial configurations and are significantly bent at TS in the reactions, as shown in Figure 8. In other words, the dipole bending mode is excited during the reaction process.

**Figure 8.** Distributions of the bending angle NN‘O at initial configurations and TS in reactive trajectories from different initial conditions: (a) $E_c = 50$ kcal mol$^{-1}$, $v = 0$; (b) $E_c = 50$ kcal mol$^{-1}$, $v_{b(N_2O)} = 1$; (c) $E_c = 40$ kcal mol$^{-1}$, $v = 0$; and (d) $E_c = 60$ kcal mol$^{-1}$, $v = 0$.

In addition to the time gap between the forming bonds, we measured the average asynchronicity as the difference between the two forming bonds at the transition state for $E_c = 50$ kcal mol$^{-1}$ and $v = 0$. The average asynchronicity is 0.071 Å and they are all within 0.0–0.303 Å. These values are shorter than those determined in previous direct dynamical studies, confirming the concerted mechanism for the title reaction.

Regarding the microscopic mechanism of the title reaction, three reactive trajectories are plotted in Figure 4, with their trajectory movies provided in the SI. The trajectory in a solid black line corresponds to $E_c = 50$ kcal mol$^{-1}$ and $v = 0$. First, two reactants approach each other, namely, to hit the repulsive wall. Therefore, a large amount of translational energy is required to propel the separate reactants sufficiently close to each other to reach the repulsive wall. Second, the trajectories squeeze out with the NN‘O angle bent significantly to form the product through a very narrow region, as discussed above. The overall physical picture is consistent with previous direct dynamical calculations, with one such representative trajectory included in Figure 4 for direct visualization and comparison. The reactive trajectory took place mildly on the B3LYP/6–31G(d) surface without hitting the repulsive wall. This is because only 0.6 kcal mol$^{-1}$ was deposited into the reaction coordinate in previous direct dynamics, and the slow velocity allows the reaction to follow the MEP. In addition, they concluded that only those N₂O molecules with vibrationally excited bending modes can turn the corner and pass through the TS without hitting the wall. This is consistent with Figure 8a, namely, the bending angles NN‘O of N₂O must be bent at the TS region for reactions, although they are linear at the reactant asymptote. In Figure 4, the red and blue solid lines represent trajectories starting from $v_{b(N_2O)} = 1$ and $S$, respectively. One can see that with more and more energy deposited into the N₂O bending mode, the trajectories can turn to the corner earlier, even without hitting the repulsive wall. This confirms the important bending excitation of N₂O in the reaction dynamics.

### 4. SUMMARY AND CONCLUSIONS

The first accurate full-dimensional PES of the N₂O + C₂H₂ → oxadiazole reaction in the gas phase is developed by a machine learning approach. Comprehensive QCT calculations are performed to provide a quantitative and full understanding of the dynamics for this important reaction, which is a model for 1,3-dipolar cycloadditions. It has been found that all excitations in the reactant vibrations can enhance the reactivity, except for the asymmetric stretching mode of N₂O and the C–C–H bending mode of C₂H₂, which essentially show no effect since they lead to configuration conflict with the concerted TS. The title reaction takes place via a concerted mechanism, supported by the short time gaps (the average is 4.7 fs) between the two forming bonds. Detailed statistical analysis on the geometries of the initial and TS in reactive trajectories has also been performed to confirm the concerted nature of the 1,3-dipolar cycloaddition of the title reaction. This work undoubtedly helps to shed more light on the full understanding of the reaction dynamics in this important system. It should be noted that in this work, the reaction is studied in the gas phase. Most organic reactions take place in the liquid phase associated with some solvent, in which the reactivity and reaction dynamics can be significantly affected by the solvent–solute complexes, solvent caging, the coupling of the product motions to the solvent bath, thermalization of internally excited reaction products, hydrogen bond, etc. The mode specificity effect is thus expected to be minimal, especially when diffusion is the limiting factor. In this situation, the energy deposited into a specific mode is dissipated to the solution environment before it is transformed into the reaction coordinate.

### ASSOCIATED CONTENT

**Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c03210.

QCT calculated ICS values (Table S1), the normal mode vectors of the reaction coordinate at the transition state (Figure S1), the normal mode vectors of vibrations in two reactants (Figures S2 and S3), and additional analysis resembling Figure 7 but at other initial conditions (Figures S4–S6) (PDF)

Representative trajectory movies (ZIP)

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