First Principles Computational Investigation of Chiral Enantiomers of H_2O_2

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Abstract

The chirality amongst molecules can be examined through molecular dynamics and simulations. Chemists investigate the chirality of molecules with computational protocols and density functional theory calculations (DFT). An *ab initio* molecular dynamics (AIMD) calculation demonstrates the convergence in dihedral angles and allows for the visualization of a molecule's potential and kinetic energy fluctuating at a high temperature. Nudged elastic band (NEB) calculations show the energetics of interconverting the enantiomers in a molecule with a dihedral angle. The results from these calculations help to further analyze the molecular structure and chirality within molecules such as Hydrogen peroxide (H_2O_2).

Introduction

H_2O_2 is one of the simplest chiral molecules to investigate because it is a four-atom molecule with two stable conformers. An example of chiral objects are left and right hands on top of one another; the hands are distinguishable because they cannot be superimposed [2]. Chirality is an important phenomenon studied in chemistry, biochemistry, and the pharmaceutical industry. Chirality is investigated in the drug design and development industry due to the enantiomers of chiral compounds having a significant effect on the behavior of pharmaceutical drugs [4]. Computational chemists investigate chirality through molecular simulation to understand the properties of chiral enantiomers and the energetic barriers to interconverting them. In the biochemical field, homochirality is investigated with respect to the functional properties of biomolecules [5]. Chirality is therefore an essential topic in modern molecular science.

To study the chirality of H_2O_2, we characterized the configurational landscape, including the chiral enantiomers, of the H_2O_2 molecule with DFT calculations. We found that manipulating the structure of the H_2O_2 molecules changed its internal energy and we characterized these changes using the dihedral angle to demonstrate the chirality of the molecule. We ran geometry optimization calculations to find the H_2O_2 molecules' local and global minimum configurations. We performed an AIMD calculation to simulate the dynamics of the H_2O_2 molecule at high temperature, including the exploration of the torsional landscape. This trajectory was analyzed along the lines of the molecule's potential and kinetic energy as well as the dihedral angle versus time. Two NEB calculations were carried out to interconvert the lowest energy configurations, i.e. the chiral enantiomers, found from the optimizations. These NEB calculations used metastable configurations as initial guesses for the transition states and were characterized by both the configurations' internal energies and dihedral angles. Furthermore, we computed the barriers to interconverting the two chiral enantiomers.

Methods

To perform DFT calculations, we used the CP2K software, the PBE functional, double zeta basis set, and GTH pseudopotentials. Single-point energy and geometry optimizations were performed for several configurations of an isolated H_2O_2 molecule in a 12 $Å^3$ box [3]. We executed AIMD calculations with CP2K-Quickstep at 1 femtoseconds (fs) time step at 800 K. Velocity rescaling was employed to maintain a consistent temperature within 100 K of the target (800 K). The AIMD calculation accumulated a more than 40 ps trajectory. Two NEB paths were computed between the lowest energy configurations of H_2O_2. These paths are herein denoted “cis” and “trans” for the transition states given as initial guesses. Each NEB calculation used the climbing image method used to find the TS [6]. The "cis" and "trans" metastable configurations were used as guesses for the TS in the two paths. A band of 9 replicas were computed for the “cis” path. A band of 5 replicas were computed for the “trans” path. In order to visualize the molecule we utilized Xcrysden, Avogadro, and Ovito. For plotting, we utilized Gnuplot, Matplotlib, and Google sheets.

Results

I. *Geometry optimization*

For the geometry optimizations of H_2O_2, we found four (meta)stable configurations which were found with dihedral angles of -0.01° (“cis”) , 180.67° (“trans”), 114.94°(“L”), 246.64° (“R”). The lowest energy configurations had dihedral angles of 114.937° (“L”) and 245.36° (“R”). These lowest energy configurations are illustrated in Fig. 1.

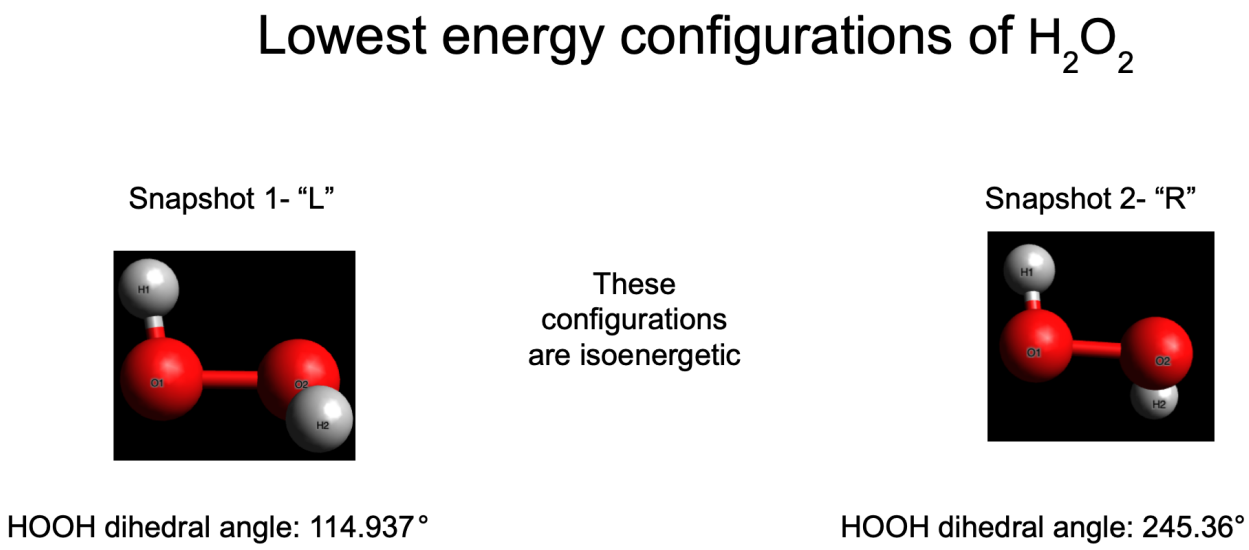


Figure 1: The lowest energy configurations from the geometry optimizations of H_2O_2.

These lowest energy configurations are demonstrative of *chiral enantiomers:* The dihedral angle of "R" has the same magnitude as that of "L", but the opposite sign due to the rotation of the other OH bond. The snapshots in Fig. 1 of the H_2O_2 molecule demonstrate the different dihedral angles of the two conformers. Not only do the lowest energy configurations have exactly opposite dihedral angles, but they also have the same energy. Because these conformers are isoenergetic and cannot be superimposed due to their opposite dihedral angles, the H_2O_2 molecule is chiral.

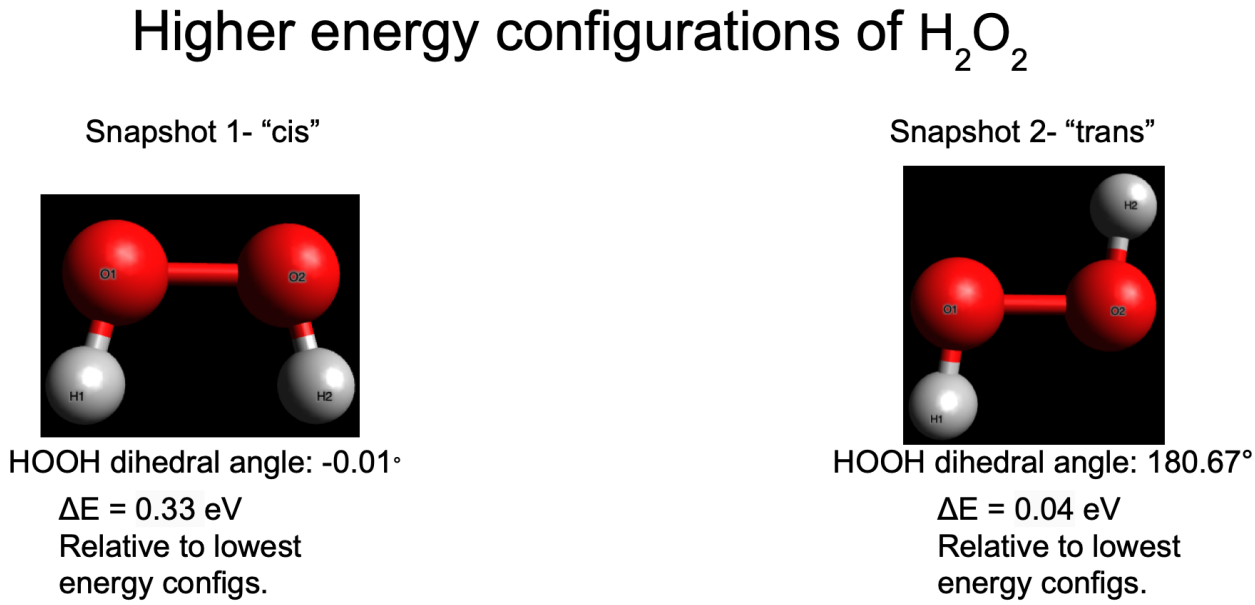


Figure 2: The higher energy configurations from the geometry optimization of H_2O_2.

Fig. 2 illustrates two metastable configurations of H_2O_2 that were higher in energy by 0.33 eV ("cis") and 0.04 eV ("trans"). The "cis" configuration has a higher energy than the "trans" energy configuration (Table 1). As shown in Fig. 2, the higher energy configurations differ in both their energy values and dihedral angles. The "cis" energy configuration has both hydrogens oriented in the same direction while the "trans" configuration has its hydrogens pointing in opposite directions. The repulsion of the closely positioned H atoms in the "cis" configuration is likely the origin of its higher energy.

Table 1: Absolute energies and energies relative to the lowest energy configurations of eight configurations of H_2O_2.

Config.	L	R	cis	trans	B	C	D	E
Abs. energy (eV)	-901.42 eV	-901.42 eV	-901.09 eV	-901.38 eV	-901.38 eV	-901.38 eV	-901.38 eV	-901.38 eV
Rel. energy (eV)	0 eV	0 eV	0.33 eV	0.04 eV	0.04 eV	0.04 eV	0.04 eV	0.04 eV

As shown in Table 1, the absolute energies of all the configurations do not differ by much. The relative energy values, relative to the lowest energy value, reflect the similarities of the energies across configurations. The cis configuration has a higher relative energy value relative to the lowest energy values than the trans configuration does. The cis configuration is 0.29 eV higher than the trans energy configuration. The last four configurations have the same absolute energy values as well as relative energy values as the trans configurations. Therefore, these configurations relaxed to the metastable trans configuration.

II. AIMD results

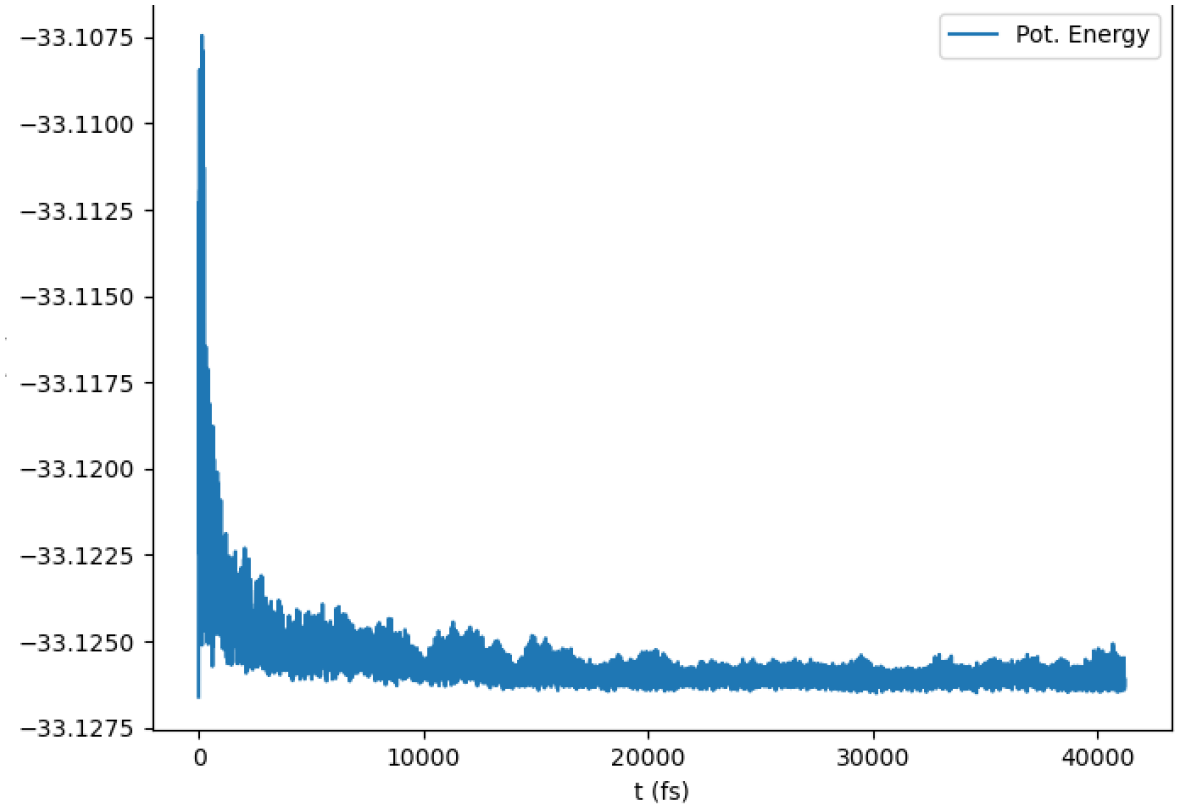


Figure 3A: Potential energy evolved over time from AIMD calculation

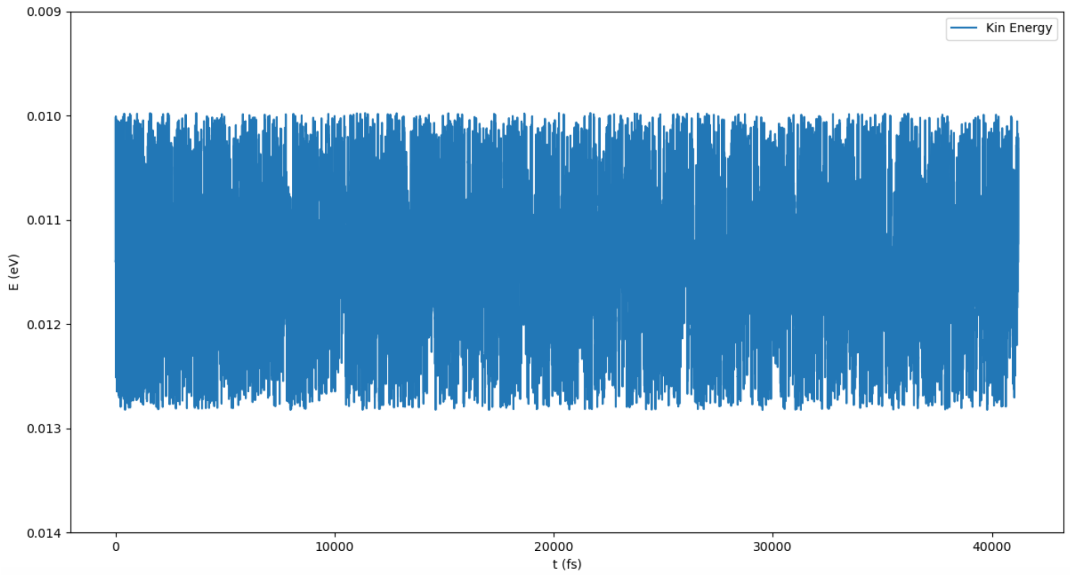


Figure 3B: Kinetic energy evolved over time from AIMD calculation

The AIMD calculation ran for 42.0 picoseconds (ps). Performing a high temperature AIMD calculation of H_2O_2 at 800 K yielded large fluctuations in the kinetic energy, but a potential energy that ultimately fluctuated around a converged average between -901.38 eV and -901.41 eV. Fluctuations in the kinetic energy correlate with fluctuations in the temperature around the target value of 800 K. If the temperature strays too far from 800 K the velocities were rescaled accordingly. The molecule is constantly vibrating and rotating throughout the trajectory. As shown in Figure 3A, the potential energy largely fluctuates in the first 30000 fs and as time goes on, the potential energy converges and reaches a lower energy point with smaller fluctuations. As shown in Figure 3B, the kinetic energy fluctuates all around a converged average between 0.013 eV and 0.010 eV through the entirety of the calculation.

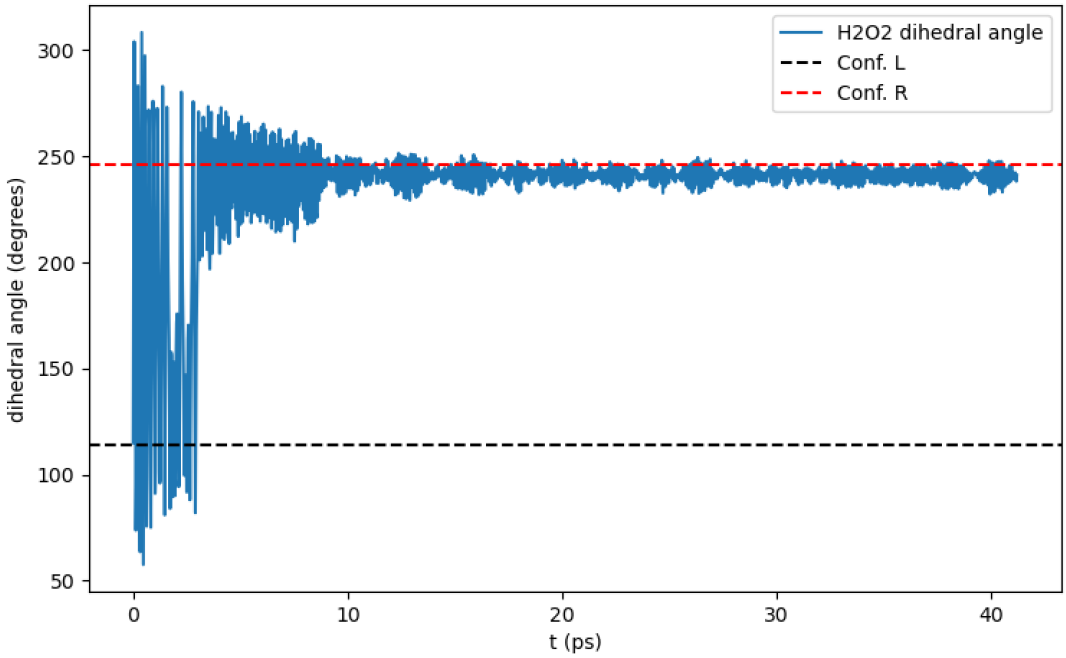


Figure 4: Dihedral angle throughout the AIMD calculation.

The dihedral angle vs time, as depicted in Figure 4, exhibits an exploration of multiple configurations initially in the trajectory, including one of the low energy conformers "L", followed by a gradual convergence to the other low energy configuration "R". Throughout the calculation, the dihedral angle fluctuated over a wide range. Early in the calculation ($t < 4$ ps) the H_2O_2 molecule's dihedral angle fluctuates significantly around 114 degrees, the dihedral angle of one of the lowest energy configurations. After four ps, the dihedral angle converges near 250°, close to the dihedral angle of the other lowest energy configuration determined via geometry optimizations. The molecule mostly demonstrates that these two dihedral angles are consistent with the observation that these configurations are lowest in potential energy. The H_2O_2 molecule explores two distinct configurations. The convergence of the dihedral angle coincides with the convergence of the potential energy during the trajectory. The H_2O_2 molecule spends most of the time in the second configuration. Based on the difference in configurations throughout the calculation, both chiral enantiomers are visible. The convergence of the potential energy shown in Fig. 3A corresponds to the convergence of the dihedral angle in Fig. 4 to that of one of the lowest energy configurations of the molecule. While AIMD at high temperature demonstrated H_2O_2 in a wide range of configurations as quantified by the dihedral angle, we will need to do NEB calculations to determine the potential energy barrier to interconvert these chiral enantiomers.

III. NEB results

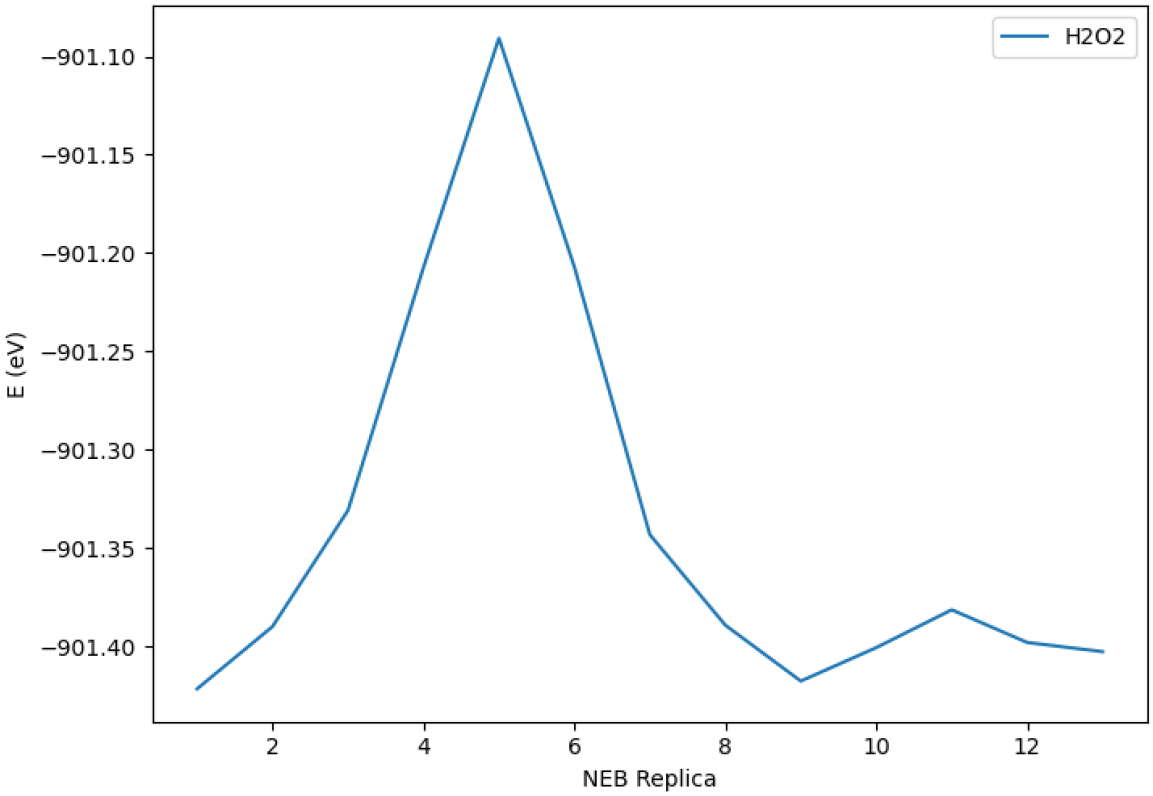


Figure 5: Energy configurations of both paths from NEB calculation concatenated in one plot.

In Figure 5, replica numbers one through nine represent the “cis” path configurations. Replica numbers nine to thirteen represent the “trans" path configurations. Step nine represents the optimized coordinates of the R enantiomer of H_2O_2. Replicas one and thirteen represent the coordinates of the L enantiomer. The cis path potential energy barrier is 0.35 eV. This is much larger as compared to the trans path potential energy barrier of 0.04 eV. Since the cis pathway has a larger barrier, the cis pathway is less favorable for interconverting the chiral enantiomers.

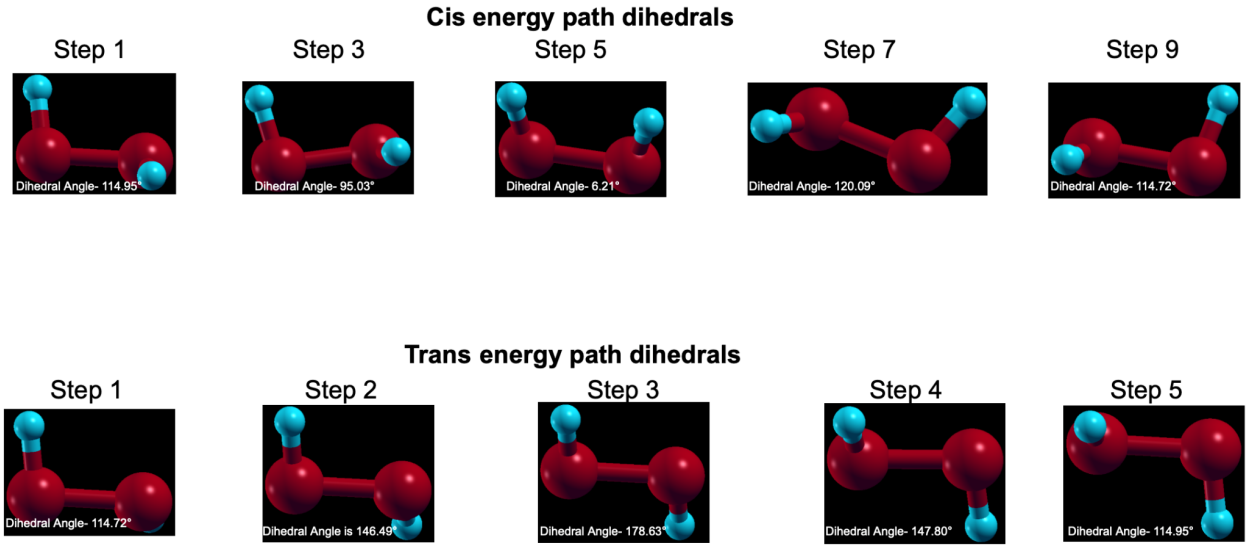


Figure 6: Dihedral angles of both paths from NEB calculation.

As shown in Figure 6, in each path the dihedral angle began at ±114° and finished at approximately the same value but opposite in sign The differences between the paths can be seen, however, from the intermediates connecting the initial and final replica. As shown in Figure 6, the hydrogen in the cis path begins facing up-right above the oxygen atoms, while the other hydrogen faces almost the center of the rightmost oxygen atom. This is the same observation that can be made for the first step in the trans path, except the second hydrogen atom is leveled behind the oxygens atoms. In the last step of the cis path, the position of the hydrogen atoms were interchanged. In the last step of the trans path, Figure 6 appears to rotate one hydrogen atom facing the oxygen atoms while the other hydrogen rests below the oxygen atoms. As both calculations ran, the dihedral angles changed drastically, but finished at the same angle it started at, as was designed.

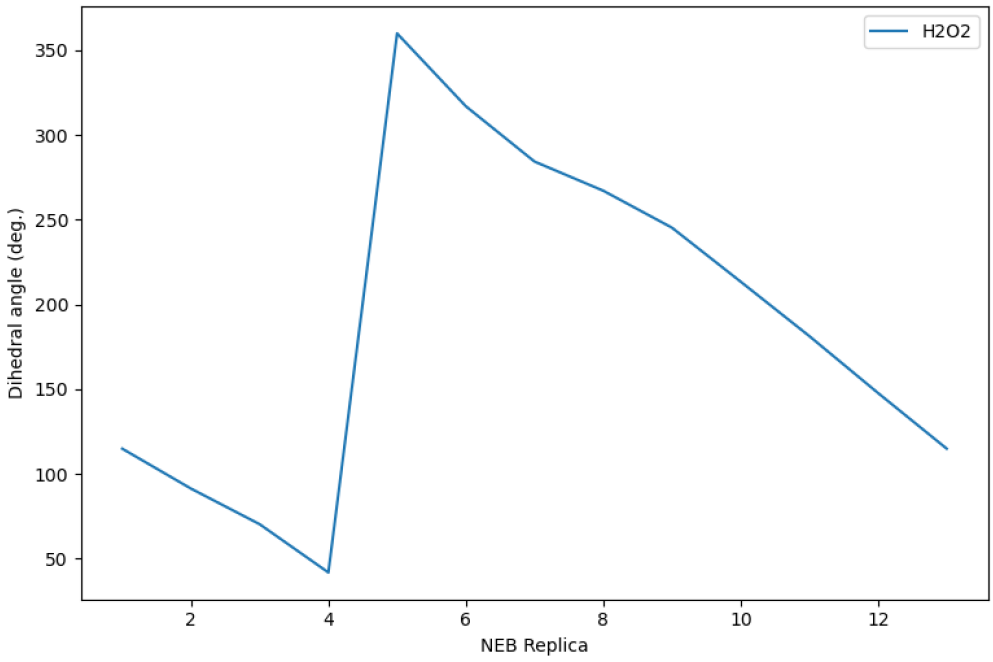


Figure 7: Dihedral angles of both paths from NEB calculation.

Both NEB paths' dihedral angles throughout the calculations are shown in Figure 7. The cis path began at replica number one and finished at replica number nine. The trans path dihedral angle began at replica number nine and finished at replica number thirteen. The dihedral angle for the cis energy path minimizes between replica number one and four and drastically increases at replica number five. The degrees in the angle of the cis energy path gradually decreases as the line plot transitions to the dihedral of the trans energy path. The progression of the dihedral angles through these two paths correspond to a full rotation of the hydrogen peroxide dihedral angle. In other words, these NEB paths sampled the full torsional landscape of the molecule.

Conclusion

The two lowest energy configurations from the geometry optimizations of H_2O_2 demonstrate that the molecule is chiral in that its dihedral angles are equal in magnitude and opposite in sign. Because the lowest energy configurations from the geometry optimization were isoenergetic, that further proved the chirality of the molecule. The AIMD calculation demonstrated the convergence in the dihedral angle, as well as allowing for the visualization of the H_2O_2 molecules potential and kinetic energy fluctuating at a high temperature. Furthermore, NEB calculations showed the energetics of interconverting the enantiomers. Since the cis pathway has a larger barrier, the pathway is less favorable for the molecule. The softwares chemists utilize to perform these calculations help chemists analyze the molecular structure, chirality, and energy forces within and between molecules.

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