

Abstract

The purpose of this research was to study the Cannizzaro reaction of 5-Hydroxymethylfurfural (HMF) using Density Theory Function (DFT). This research has applications to future environmental projects as HMF is a biomass-derived platform chemical and has the potential as an alternative commodity chemical for fossil fuel-based platform chemicals such as terephthalic acid. DFT calculations were used to probe the reaction mechanism. The transition structures (TS) for the first and second steps were found as well as their associated energies. A machine learning (ML) model was made using SchNet to predict energies for the second TS that will be used in future methodology that involves explicit modeling of the solvent medium. The figure below shows the proposed mechanism for this Cannizzaro reaction, the first three steps were completed computationally.



Computational Methods

The DFT calculations were performed using Gaussian09 software. Geometry optimizations for each molecule were performed at the B3LYP level of theory with the 6-311+G(d,p) basis set and the Self-Consistent Reaction Field set to water with the Polarizable Continuum Model. GaussView was used analyze the molecule and frequency calculations confirmed stationary points. Use GaussView to compose Z-matrix



Coordinate (IRC) calculation was done to create many structures over the potential energy surface. Using this IRC data, a Single Point (SP) calculation was done to get the energies for each geometry. This data was all compiled into a single .db file that SchNet could read and be able to test and validate from for its deep learning model.

Investigation into the Cannizzaro Reaction of HMF Utilizing Computational Chemistry Methods Bruno Mochi, Dr. Orlando Acevedo Department of Chemistry University of Miami, FL

Cannizzaro Transition Structures

The first transition state (TS1) was found using both the B3LYP and MP2 methods simulated in PCM water and methanol. The second transition state (TS2) was found at the B3LYP level of theory in water only. There were two different geometries for TS2 with one being the two-center hydride transfer (as seen on the right) and the other being the one-center hydride transfer. ΔG^{\dagger} and ΔH^{\dagger} were calculated by subtracting the reactant energies (at ground state) from the transition state energy.



TS2 Two-Center Hydride Transfer

Cannizzaro Potential Energy Surface

The QM calculation showed the proposed mechanism favored the 2nd TS as the rate-determining step. Given the small energy difference between the one- and two-centered TS2, (TS2 1C and TS2 2C) it is difficult to confirm which one is ultimately favored. Therefore, the SchNet model was trained using both TS2 geometries for ML predictions. To the left is a figure of the reaction energy diagram of the studied Cannizzaro reaction featuring HMF.

P2



Reaction Coordinate



TS1 Nucleophilic Attack



TS2 One-Center Hydride Transfer

	ΔG (kcal/mol)	ΔH (kcal/mol)
TS1	10.0	1.48
P1	-6.56	-7.34
TS2 (2C)	16.7	3.06
TS2 (1C)	17.8	5.26
P2	-10.3	-11.9

SchNet Machine Learning

increase in speed. embedding, 64 interaction, 64 interaction, 64 atom-wise, 32 shifted softplus atom-wise, 1 sum pooling

MODEL ra

RMSE

Now that we have done the QM calculations of the structures from this mechanism using implicit PCM water as the solvent, the next step is to compute this reaction in explicit water using a quantum mechanical and molecular mechanical mixed (QM/MM) approach. To reduce the cost of the calculations we trained the QM region (which is the Cannizzaro reaction – the water is the MM) using SchNet to use in our new ML/QM/MM methodology. Once we can reproduce properly the reaction in water, we will shift our attention running the reaction in ionic liquids. Experimentally, six ILs have been tested, the highest yields of BHMF (100%) and HMFA (84%) were found using [EMIM][TFSI] and 5 equivalents of NaOH. We propose studying this system using our ML/QM/MM methodology to examine additional ILs, alternative bases, and different conditions to improve the rate of reaction.

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SchNet is a deep learning architecture for molecules that makes use of continuous-filter convolutional layers to help model atomistic systems. It allows for chemically and spacially resolved insight into quantum-mechanistical observables of atomistic systems. In our case, SchNet was trained to reproduce the QM-derived TS energies with an over 10,000-fold



The .db file contained 1,141 structures with their energies. The SchNet model was trained using 70:30, 80:20, and 90:10 training to validating ratios. The models took about 6 hours to train.

atio	70:30	80:20	90:10
-	0.0136	0.0096	0.0118

Future work

Acknowledgments