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Acidic Sugar Degradation Pathways

An Ab Initio *Molecular Dynamics Study*

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Abstract

Ab initio molecular dynamics (MD) simulations were employed to elucidate xylose and glucose degradation pathways. In the case of xylose, a 2,5-anhydride intermediate was observed leading to the formation of furfural through elimination of water. This pathway agrees with one of the mechanisms proposed in the literature in that no open chain intermediates were found. In the case of glucose, a series of intermediates were observed before forming the 2,5-anhydride intermediate that eventually leads to hydroxymethylfurfural (HMF). One of these intermediates was a very short-lived open-chain form. Furthermore, two novel side-reaction pathways were identified, which lead to degradation products other than HMF.

Index Entries: Degradation; pathway; acidic, intermediate, sugar.

Introduction

Loss of fermentable sugars to acidic degradation is one of the primary concerns for the chemical prehydrolysis of lignocellulosic biomass. The decrease in yield of xylose and glucose during prehydrolysis could significantly affect the economic viability of these processes *(1–3)*. In order to improve the yields of sugar products, particularly during dilute-acid prehydrolysis, understanding the sugar degradation pathways at the molecular level is critical. Today, review of the literature reveals numerous studies of sugar-degradation mechanisms in acidic media based on experiments, but few using kinetic modeling *(4–13)*. It was commonly thought that furfural and hydroxymethylfurfural (HMF) are by far the principal acidic degradation products for xylose and glucose, respectively. However, furfural and HMF production only account for a portion of the sugar loss observed during pretreatment *(11,13,14)*. Some parasitic degradation pathways leading to the formation of noncellulosic polymeric materials

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were also suggested *(12,13)*. However, the detailed mechanisms for these parasitic reactions are not known. For furfural and HMF formation, some researchers *(6,7)* have proposed degradation pathways that proceed via a series of open-chain intermediates. In contrast, Antal and coworkers *(8)* have proposed a mechanism based on a 2,5-anhydride intermediate for xylose degradation leading to furfural. Nevertheless, the precise mechanism for the formation of furfural and HMF remains an open question.

Computational Method

Ab initio molecular dynamics (MD) code (CPMD) *(15)* based on Car–Parrinello approach *(16)* was used in the calculations. The CPMD code is based on density-functional theory and is capable of simulating chemical reaction pathways for systems of up to several hundred atoms. The code adopts a frozen core approximation during the simulation, because the cores generally do not affect chemical reactions. In the case of H, there is no core electron. For C and O, the core electrons are 1*s* orbital electrons. Wave functions for valence and semi-core electrons are linear combinations of plane-wave basis functions. The cut-off for the wave functions is 70 Ry, which was found to be sufficient. The cut-off was determined by varying the cut-off value until the atomic structure and total energy are no longer affected by this value, and a good agreement between calculated atomic structure and experimental data was obtained. The electron mass of 1100 a.u. and a time-step of 0.125 fs were used in these calculations. The BLYP pseudo-potential with gradient correction was used. Only the energy at Γ-point was calculated. Γ-point is the origin in reciprocal *k*-space. The calculations were carried out with three-dimensional periodic boundary conditions. Each unit cell ($12 \times 12 \times 12$ Å^3) contains one protonated sugar molecule surrounded by sufficient vacuum space to separate the interactions between the sugar molecules. A total of 2 ps simulation time was carried out on a high-speed Linux Pc machine. Each step takes about 60 s cpu time. The simulated time may not correspond with the actual time for the reactions.

Results and Discussion

Ab initio MD simulation was used to investigate acidic xylose and glucose degradation pathways at 500 K, conditions known to result in severe sugar degradation during prehydrolysis *(14)*. Although the energetic height of the reaction barrier may not be affected by temperature, temperature may affect the reaction rate according to kinetic reaction theory. It is therefore advantageous to simulate the reaction at the highest temperature possible, where the reaction mechanism remains unchanged, as it will take less computing time. The basic idea employed in the simulation is that

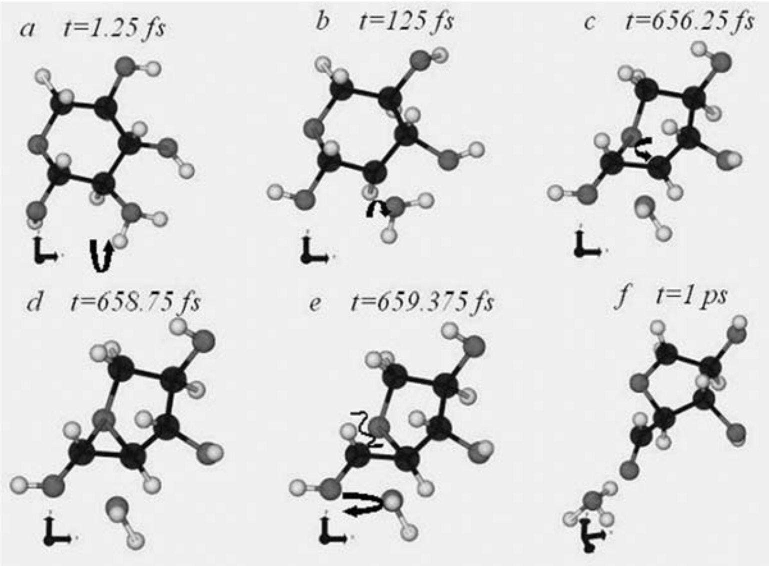

Fig. 1. The transformation of a protonated β-xylose (C2-OH) into a 2,5-anhydride furfural precursor at 500 K. Each subfigure ***(a–f)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** Protonation of C2-OH; ***(b)*** water molecule leaves positively charged xylose molecule; ***(c)*** the ring structure deforms due to the presence of positive charge, C2 and ring O move closer to each other; ***(d)*** ring O forms bonds with C1, C2, and C5 resulting in a very short-lived intermediate; ***(e)*** the bond between ring O and C1 breaks; ***(f)*** water molecule carries away the excess H^+ from the OH at C1. No open-chain form is observed during the reaction. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

the first step in sugar degradation under acidic media is the protonation of the OH groups on the xylose and glucose rings. Because there are four and five OH groups on the xylose and glucose rings, respectively, it is not known which OH groups will be most prone to attack by a proton. Thus, simulations were conducted for probable protonation of all of the OH groups. It is found that only protonation of the OH group on position C2 (C2–OH) leads to a 2,5-anhydride intermediate, which eventually forms furfural and HMF via further elimination of water molecules shown in Figs. 1 and 2 for xylose and glucose, respectively. Protonated glucose and xylose at other OH positions are either stable or degraded to other by-products, which will be discussed in detail below.

In the case of xylose, this study confirms the mechanism proposed by Antal and coworkers *(8)* in that no open-chain intermediates to form furfural were present. The oxolane ring in xylose is very stable and does not open up after protonation of the C2–OH. The formation of the 2,5-anhydride intermediate (furfural precursor) is very fast and will take less than a picosecond. A recent Gaussian calculation *(17)* shows that the reaction barrier for the formation of this intermediate is only 13 kcal/mol, which accounts for the rapidity of the reaction. The protonations of the C1–OH and

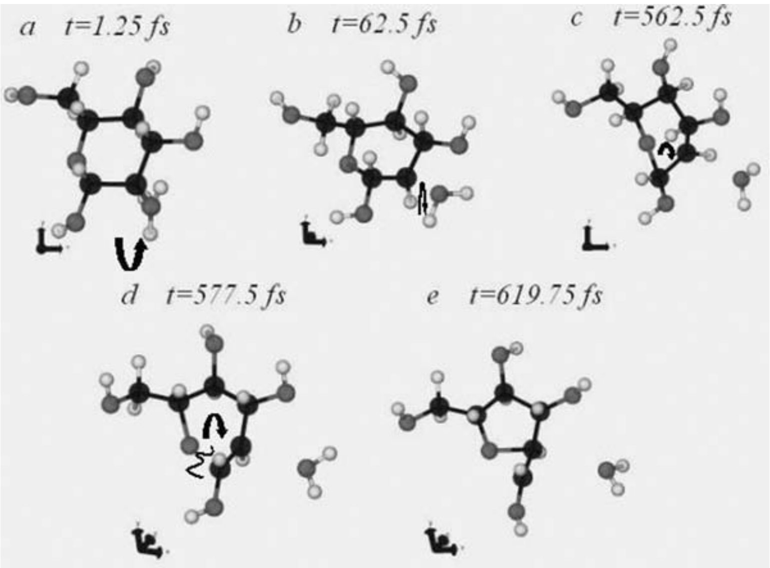

Fig. 2. The transformation of a protonated β-glucose (C2–OH) to HMF precursor at 500 K. Each subfigure ***(a–e)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** Protonation of C2–OH; ***(b)*** water molecule leaves positively charged glucose molecule; ***(c)*** the ring structure deforms due to the presence of positive charge, C2 and ring O move closer to each other; ***(d)*** ring O breaks the bond with C1; ***(e)*** a new bond between ring O and C2 forms. An open-chain form with a very short life-time (<100 fs) ***(d)*** is observed during the reaction. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

C3–OH do not lead to xylose degradation; at least in the time scale simulated, which was a few picoseconds. The attack of a proton on the C4–OH leads to the fragmentation of the xylose molecule (shown in Fig. 3), which may account for the other degradation products observed, such as formic acid. Further study to clarify the products will be conducted.

In the case of glucose, an open-chain form that has a very short life time (<100 fs) was observed before the formation of 2,5-anhydride intermediate (HMF precursor) as a result of the protonation of the C2–OH (see Fig. 2). The differences in reaction pathways between protonated glucose and xylose at C2–OH could perhaps be explained by the stability of their respective positively charged residues. Because glucose has one extra OH group, this six-member ring is more positively charged than xylose, considering that oxygen is an electron-withdrawing element compared to carbon. Thus, when the protonated OH group (i.e., water molecule) leaves the ring, the extra positive charge left behind destabilizes the entire ring structure. In the case of glucose, the ring opens up briefly before forming a furan ring, leaving the extra positive charge to the side methyl group. In the case of xylose, because the ring is less positively charged compared to glucose, the ring structure is maintained during the formation of furfural precursor.

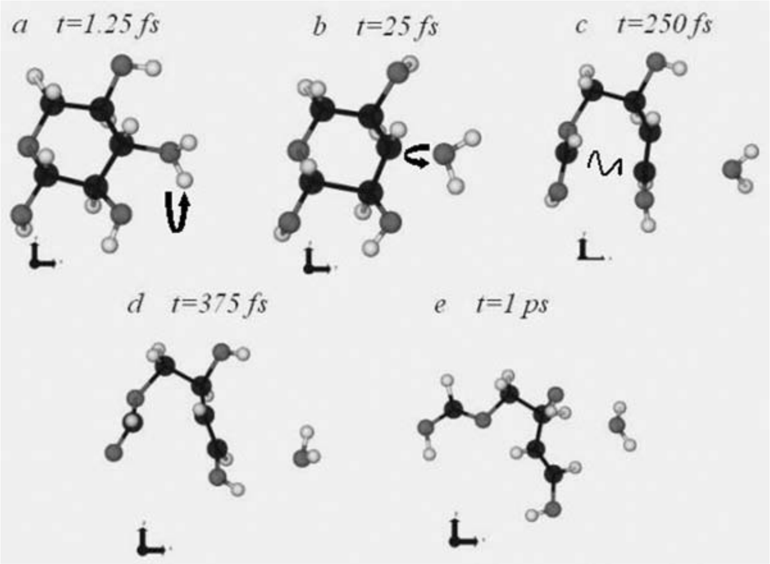

Fig. 3. The fragmentation of protonated β-xylose (C3–OH) at 500 K. Each subfigure ***(a–e)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** protonation of C3–OH; ***(b)*** water molecule leaves positively charged xylose molecule; ***(c)*** the ring structure opens up due to the breakage of C1–C2 bond; ***(d)*** and ***(e)*** the structure becomes more of a linear chain as time progresses. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

Proton attack of the C3–OH and C4–OH in glucose leads to two other five-member ring intermediates shown in Figs. 4 and 5. The formation of these two furan rings is also very rapid, on the time scale of <1 ps. These two intermediates may further polymerize to form the non-cellulosic material observed in laboratory experiments. This agrees with the conclusions of a recent carbon-labeling NMR study by Johnson and Davis *(13)*. However, protonation of the C1–OH does not lead to glucose degradation during the simulation period conducted. A very interesting phenomenon occurred for the protonation of the C6–OH. This proton was very quickly transferred to the O-5 (the ring oxygen). This process is shown in Fig. 6. Equilibrium was then reached between the open-chain and the ring forms. These two structures are relatively stable and no further degradation was observed in the computer simulation.

All these reactions were simulated *in vacuo*, because water is not required to participate in these ring-arrangement reactions. Furthermore, because the formation of 2,5-anhydride intermediate is very rapid, and water molecules appear to leave the ring after protonation (see Figs. 1–6), it is justifiable that the essential mechanism for first stages of sugar degradation under acidic media is captured without the solvent molecules. Further support for our approach comes from evidence that deuterium (D) was not incorporated into furfural from D_2O solution *(18,19)*. However, water undoubtedly plays an important role in other

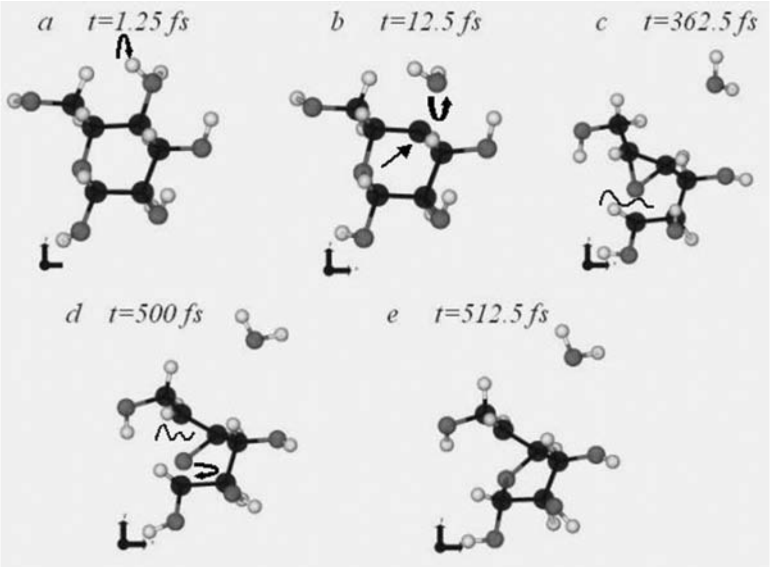

Fig. 4. The transformation of protonated β-glucopyranose (at C4–OH) to β-glucofuranose at 500 K. Each subfigure ***(a–e)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** Protonation of C4–OH; ***(b)*** water molecule leaves positively charged glucose molecule; ***(c)*** the ring structure opens up and O forms bonds with both C4 and C5; ***(d)*** ring O breaks the bond with C5; ***(e)*** the ring closes between ring O and C4 to form a β-glucofuranose structure. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

aspects of the overall degradation process, such as stabilizing some of the intermediates, and/or reducing/increasing the reaction barriers. Specifically, bulk water structure may be important in the subsequent elimination of two water molecules from xylose and glucose to form furfural and HMF, respectively. Our simulations of these reactions in aqueous solutions with explicit water molecules are in progress.

We propose that the additional elimination of two water molecules from the 2,5-anhydride intermediate under acidic condition without explicit solvent water molecules was not successfully simulated for the following reasons: (1) it may take a longer time (>5 ps) for this reaction to occur, (2) water molecules may play an important role in abstraction of the proton from the intermediate to form the double bond, and (3) the elimination of water in alcohol under acidic media may take two steps as suggested in literature. The first step is the protonation of OH and the departure of water molecule. The second step is the abstraction of H^+ from the neighboring carbon atom, which requires assistance from the solvent water molecule. However, calculations *(17)* using a continuum solvation model show that the solvent in these reactions does not affect the barriers and show that the reaction barriers for elimination of water are around 20 kcal/mol, which is relatively low and thus feasible for simulatation by MD calculations with explicit water solvent.

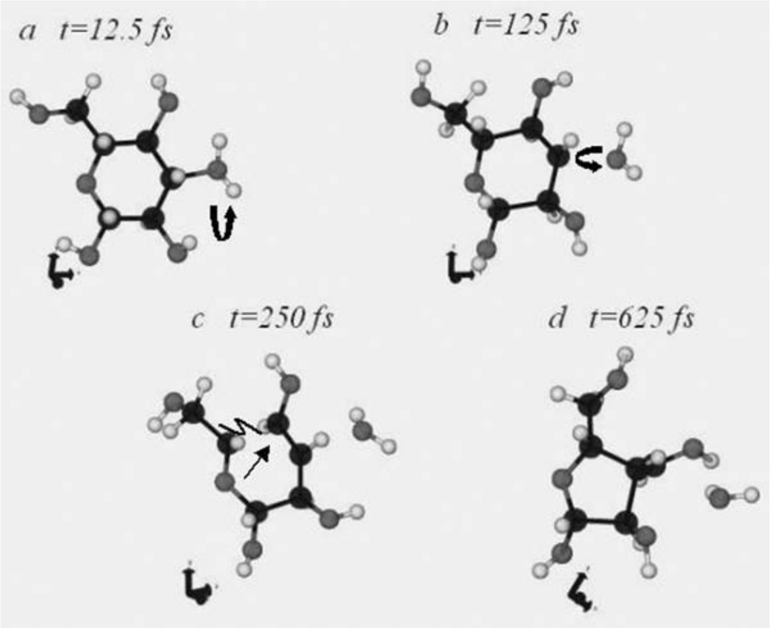

Fig. 5. Conversion of protonated β-glucopyranose (at C3–OH) to a five-member ring intermediate at 500 K. Each subfigure ***(a–d)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** Protonation of C3–OH; ***(b)*** water molecule leaves positively charged glucose molecule; ***(c)*** the ring structure opens up due to the breakage of C4–C5 bond ; ***(d)*** the ring closes between C5 and C3 forming a furanose structure. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

Summary

In conclusion, we have simulated the essential biomass sugars' (xylose and glucose) degradation pathways using *ab initio* MD. Multiple reaction pathways were observed for glucose and xylose degradation. These multiple reaction pathways could explain some of the previously puzzling experimental observations [e.g., NMR carbon-labeling results *(13)* and the mysterious disappearance of glucose during dilute-acid cellulose hydrolysis under some conditions *(11,14)*]. Understanding the sugar degradation mechanism is essential for the prevention or minimization of the loss of sugar during prehydrolysis. Earlier studies indicated that a very small amount of ethanol could increase glucose yield dramatically in dilute acid hydrolysis *(20)*. Ethanol may interfere with or minimize glucose degradation in several ways. One possible scenario is that ethanol interacts more strongly with glucose, thus shielding it from protonation (in effect reducing acid concentration). Another possibility is that ethanol destabilizes the intermediate state, thus preventing it from forming (in effect increasing the reaction barrier). We intend to pursue the simulation of these possible reaction pathways in future work.

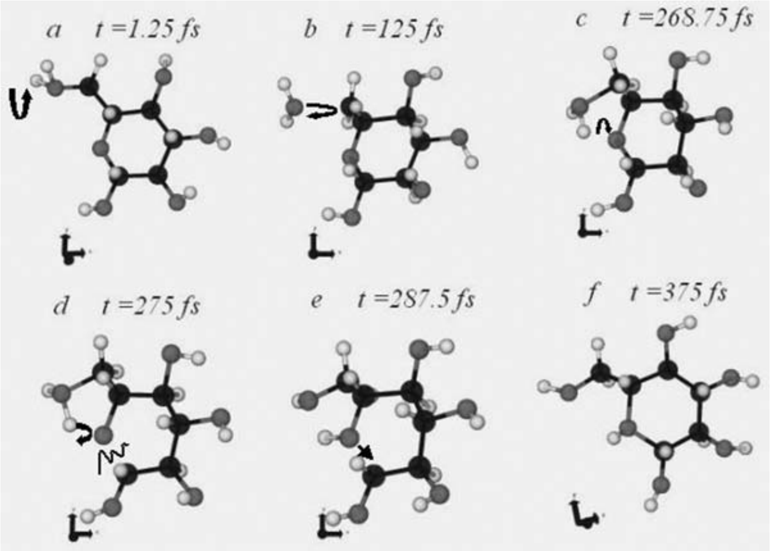

Fig. 6. Proton hopping from C6–OH on the β-glucose to the ring O. Each subfigure ***(a–f)*** is a snapshot of the atomic structures at various reaction times shown. ***(a)*** Protonation of C6–OH; ***(b)*** water molecule leaves positively charged glucose molecule; ***(c)*** rotation of protonated C6–OH; ***(d)*** the ring opens up due to the interaction between the ring O and the proton on C6–OH. ***(e)*** the proton on C6–OH moves to the ring O; ***(f)*** the ring closes with the protonated ring O. The whole series of structures shown are simulated in less than 500 fs. [Symbols: C (black sphere); O (grey sphere); H (white sphere)].

Acknowledgments

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