Determining the Best Situation, E1 or E2, to Thermodynamically Promote Hydration

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ABSTRACT

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Description automatically generated**The purpose of this experiment was to explore two possible mechanisms for the dehydration of 2(1*H*)-Naphthalenone, octrahydroxy-3-hydroxy-4a,8a-dimethyl. Our goal was to compare the thermodynamics of an E1 and an E2 mechanism to see which one is more favorable. According to literature, the E1 mechanism is ideally more favorable because water is a weak base. An E2 reaction would require a stronger base to displace the polar leaving group. Our results proved the E2 mechanism to be, in fact, more thermodynamically stable. This shows the usefulness and importance of running simulations because they visualize exceptions to what was previously known as true in literature.

INTRODUCTION and THEORY

Our goal for this experiment was to investigate the dehydration of 2(1*H*)-Naphthalenone octrahydroxy-3-hydroxy-4a,8a-dimethyl-. We explored two possible mechanisms for the reaction. The first of which is an E1, a unimolecular, two-step reaction consisting of ionization to form a carbocation intermediate then deprotonation of the carbocation. The second is a E2 reaction, which is a one-step, biomolecular elimination. Both mechanisms break single carbon-carbon and carbon-hydrogen bonds to form a double bond.

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| **Figure 1-** E1 mechanism for the dehydration of the compound. | **Figure 2-** E2 mechanism for the dehydration for the compound. |

For an E1 mechanism, the more stable the carbocation is, the faster the reaction. E1 reactions do not require a strong base, because there is no leaving group that would need to be replaced. It can occur in this 2° carbons(even though it prefers tertiary carbons). It also does not require specific stereochemistry for the starting material. The same cannot be said for an E2 reaction. The proton removed must be in the anti-position to the leaving group. E2 reactions also requires a strong base to displace the polar leaving group.1 Since E2 reactions require a strong base, and water is a weak base, the hypothesis for this experiment was the reaction will be more favorable thermodynamically stable following the E1 mechanism, as it is in literature.

COMPUTATIONAL DETAILS

The electronic structure modeling of the compounds were done using Gaussian 16.2 The molecules that we analyzed (all steps in Figures 1 and 2 including the water and hydronium ion) were first optimized for their minimum energy using the Hartree-Fock (HF) method, then the energy scans were recorded using the DFT with a B3LYP correlation functional. The following basis sets were used for this experiment: 3-21G, 6-31G, 6-311G, 6-311G(2d), and 6-311G(2d,2p). Each scan used the optimization of the prior scan to increase accuracy.

RESULTS and DISCUSSION

The structure of the molecules in Figures 1 and 2 chosen to analyze had the alcohol and the two methyl groups in their equatorial positions.

**Table 1-** The change in internal energy, U, enthalpy, H, free energy G, and entropy, S, for the individual steps in the reaction mechanisms and the individualized steps.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **E1** |  |  |  | **E2** |  |  |
|  | B1-A1 | C1-B1 | D1-C1 | D1-A1 | B2-A2 | D2-B2 | D2-A2 |
| ∆ H (kcal/mol\*K) | -32.70 | -2.41 | 38.17 | 3.06 | -32.70 | 35.76 | 3.06 |
| ∆ S  (kcal/mol\*K) | -0.0043 | 0.0481 | -0.0057 | 0.0382 | -0.0043 | 0.0425 | 0.0382 |
| ∆ G  (kcal/mol\*K) | -31.40 | -16.77 | 39.87 | -8.30 | -31.40 | 23.10 | -8.30 |
| ∆ U  (kcal/mol\*K) | -32.44 | -15.86 | 37.91 | -10.38 | -31.40 | 23.10 | -8.30 |

The changes in U, H, G, and S are found in Table 1. Note the final values for D-A for E1 and C’-A for E2 have the same numbers, but values their intermediates vary.

**Table 2-** The status of the individual steps and the overall reaction being entropically or enthalpically driven.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **E1** |  |  |  | **E2** |  |  |
|  | B1-A1 | C1-B1 | D1-C1 | D1-A1 | B2-A2 | D2-B2 | D2-A2 |
| T∆ S (kcal/mol) | -1.28 | 14.3 | -1.70 | 11.39 | -1.28 | 12.67 | 11.39 |
| G  (kcal/mol) | -31.40 | -16.77 | 39.87 | -8.30 | -31.40 | 23.10 | -8.30 |
| Enthalpically or Entropically Driven | Entropic | Entropic | Enthalpic | Entropic | Entropic | Enthalpic | Entropic |

The formula for Gibbs free energy is G = H- T∆S. Free energy is more thermodynamically stable when it is negative. In cases where T∆S is greater than H, the reaction is entropically driven. Inversely, if the H is greater than T∆S, the reaction is enthalpically driven. It is shown in Table 2 that the overall mechanism is entropically driven, and one of the intermediates from each mechanism is enthalpically driven.

Figure 3- A comparison of the free energy of the mechanism for E1 and E2.

According to the data from Gaussian, the mechanism for E2 is more thermodynamically stable, as it has a lower average ∆G than that of the E1 mechanism. This was the opposite of the hypothesis that E1 was the most favorable.

CONCLUSION

This experiment proved the usefulness of molecular modeling. The hypothesis that E1 would be the more favorable mechanism was proven wrong because it did not obey the knowledge found in literature. Using molecular modeling software such as Gaussian 16 would save time and resources for many reasons. In this case, it helped in predicting the path reactions can take. Further research could be done on different structures (changing chirality, switching leaving group, etc.) to see other instances of E1 being favored by thermodynamics.

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