

DFT Augmented Exploration of Rearrangement of Imidazole *N*-Oxides to Imidazole-2-ones in Aqueous Media

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The 2-unsubstituted imidazole *N*-oxides and oxazole *N*-oxides have a strong tendency to rearrange into corresponding 2-keto compounds. A three step mechanism was formulated and subjected to computational study. The key idea behind selecting the water molecule instead of external acid, originated from amphoteric character of water depending upon the relative pH of the medium. As a consequence, initial step of the reaction is expected to be a simple proton transfer from water to *N*-oxide. The heterolytic cleavage of water molecule is accompanied with synchronous protonation of oxide as well as hydroxylation of the C-2 carbon. The resulting 2,3-diol is expected to be relatively unstable on grounds of stereoelectronic factors inducing strong polarity on C-2 hydrogen. This would result in intramolecular dehydration of the diol to form the 2-hydroxy imidazole product. During proton transfer step-1, the proposed transition state is extensively stabilised by the formation of a five-membered H-bonded ring. The step-2 is proposed to involve a four membered cyclic transition state for intramolecular dehydration. In the final step-3, there is again a proton transfer from the C-2 (OH) to the N atom of the ring at C-3 position. This is consistent with relative acid-base strength of the -OH group at C-2 and the tertiary N-atom of the ring at position-3. The final step-3 is proposed to involve a four membered transition state for the required proton transfer.

For the gas phase modeling of proposed rearrangement, the DFT calculations were carried out using the B3LYP exchange-correlation functional, together with the 6-31G(d) basis set. Earlier reports have demonstrated the excellent ability of the B3LYP/6-31G(d) method in computing reliable geometrical parameters for reactants, products and the transition states in similar studies. The potential energy surface (PES) for the entire reaction mechanism was scanned systematically for all possible intermediates and transition structures. Geometry optimisations were carried out without any symmetry constraints. Vibrational frequencies were evaluated at optimised geometries, to verify the nature of stationary points. The transition structures were characterised by one imaginary frequency, whereas all the intermediates, reactants and products have all real frequencies. Intrinsic reaction coordinate (IRC) calculations were performed in forward and reverse directions, by following the eigenvector associated with the unique negative eigenvalue of the Hessian matrix to unambiguously establish the transition state connectivity.