Nmr Investigation of Energy Barriers for Hydrogen-Bond Breakage of Protein Side-Chain NH\textsubscript{3}\textsuper{\#} Groups

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Hydrogen bonds and ion pairs involving charged side chains are important for protein function. However, their dynamic properties are not well understood. Recently we demonstrated that lysine side-chain NH\textsubscript{3}\textsuper{\#} groups are extremely useful probes for NMR investigations of the hydrogen-bond/ion-pair dynamics. Previously we found that bond rotations of protein side-chain NH\textsubscript{3}\textsuper{\#} groups are nearly as rapid as those of side-chain CH\textsubscript{3} groups, we determined or-
barrier reorganizations of the protein backbone is a key determinant of pH dependence of the internal motions of lysine side-chain NH\textsubscript{3}\textsuper{\#} groups forming intermolecular ion pairs with DNA. For these NH\textsubscript{3}\textsuper{\#} groups, we determined or-
parameters and correlation times for bond rotations and reorientations at four temperatures. The order parameters were virtually independent of temper-
atures in this range. In contrast, the NH\textsubscript{3}\textsuper{\#} bond-rotation correlation times were found to depend strongly on temperature. Based on transition state theory, the energy barriers for NH\textsubscript{3}\textsuper{\#} rotations were analyzed and compared to those for CH\textsubscript{3} rotations. Enthalpies of activation for NH\textsubscript{3}\textsuper{\#} rotations were found to be significantly higher than those for CH\textsubscript{3} rotations, which can be attributed to the requirement of hydrogen-bond breakage. However, the transition states in which hydrogen bonds with water molecules should be transiently broken are entropically favorable, and the overall free energies of activation for NH\textsubscript{3}\textsuper{\#} rotations are as low as those for CH\textsubscript{3} rotations. This entropic reduction in energy barriers can accelerate molecular processes requiring hydrogen bond breakage and may be kinetically important for protein function. This work was supported by Grant CHE-1307344 from the National Science Foundation.