

The Catalytic Cleavage of RNA Models by a Dinuclear Zn(II) Complex

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RNA cleavage, as catalyzed by self-cleaving ribozymes, is dependent on metal ions involved in the active sites. In order to better understand the roles of the metal ions and to develop efficient artificial RNA-cleaving agents, small-molecule-metal- complex mimics are being studied. Among the metal complexes studied in our group, a dinuclear Zn(II) complex was shown to exhibit extraordinary catalytic activity toward the minimal RNA analog, 2-hydroxypropyl-4-nitrophenyl phosphate (HPNP). To further characterize this catalyst, the cleavage of uridine 3'-4-nitrophenyl phosphate (UPNP) and uridylyl(3',5')uridine (UpU), was also examined. The pH profiles of second-order rate constants were obtained on all three substrates. Surprisingly, a lower rate enhancement was observed for the catalytic cleavage of UPNP and UpU compared to that of HPNP in our kinetic studies. This difference in catalytic activity reveals that using HPNP as a model substrate for RNA cleavage study might overestimate the capability of the catalyst. In addition, the deuterium solvent isotope effect on the cleavage of UPNP was measured to elucidate the catalytic mechanism. The lack of significant kinetic isotope effect ($k^H/k^D \sim 0.8$) rules out the presence of concerted Brønsted acid/base catalysis and indicates the relevance of electrostatic interactions between transition state and the two zinc cations. Furthermore, the binding of this catalyst to monomethylphosphate dianion as a transition state analog was measured to study the stabilization contributed from the cation-anion interaction. The pH dependence of the binding supports the zinc aquo complex as the active catalytic species in this system.

