Metal-dependent Stabilization of DNA Duplexes Containing 2-Oxo-imidazole-4-carboxylate/carboxamide as Nucleobases

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Keywords: Metal-mediated base pair; Cu(II) ion; 2-Oxo-imidazole-4-carboxylate; 2-Oxo-imidazole-4-carboxamide; Artificial DNA.

The versatility and programmability of DNA structures have intrigued researchers to design and incorporate novel unnatural base pairs into DNA in a bid to enrich its structural diversity. Among several categories, metal-mediated base pairs, consisting of two ligand-type artificial nucleobases and a bridging metal ion, have gained increasing attention due to its unique coordination binding mode.\(^1\) In addition to thermal stabilization of the duplexes, metal-mediated base pairing also allows for metal-dependent control of functional DNAs such as DNAzymes.\(^2,3\) Finding suitable ligand-type nucleobases that can specifically and strongly bind to a certain metal ion within a DNA structure is thus important for achieving such functions.

In this study, we synthesized DNA duplexes containing a pair of 2-oxo-imidazole-4-carboxylate (X) nucleobases (Fig. 1a) and its carboxamide derivatives (Y).\(^4\) Melting analysis in the presence of various transition metal ions revealed that the duplex containing an X–X pair was very unstable on its own, but was stabilized by the addition of 1 equiv of Cu\(^{II}\) (\(\Delta T_m = +20 ^\circ C\)) (Fig. 1b). This result indicates the formation of a Cu\(^{II}\)-mediated X–Cu\(^{II}\)–X base pair in the duplex, which was also confirmed by ESI-TOF mass spectrometry. It is likely that the X nucleobases coordinated to the Cu\(^{II}\) ion via the carboxylate O\(^–\) and the endocyclic N atoms to form a neutral complex. In contrast, the duplex containing a Y–Y pair showed no significant stabilization upon metal addition (\(\Delta T_m = −1 ^\circ C\)), showing that the replacement of the O\(^–\) with NH\(_2\) loses such coordination affinity. Furthermore, the X base was found to form a Hg\(^{II}\)-mediated base pair in a Cl\(^–\)-free buffer (\(\Delta T_m = +11 ^\circ C\)). The highly stable X–Cu\(^{II}\)–X base pair is promising for applications in the development of metal-responsive DNA materials.