

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

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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} ($\Delta T_m = +20$ °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 ($\Delta T_m = -1$ °C), showing that the replacement of the O[−] with NH₂ loses such coordination affinity. Furthermore, the **X** base was found to form a Hg^{II}-mediated base pair in a Cl[−]-free buffer ($\Delta T_m = +11$ °C). The highly stable **X–Cu^{II}–X** base pair is promising for applications in the development of metal-responsive DNA materials.

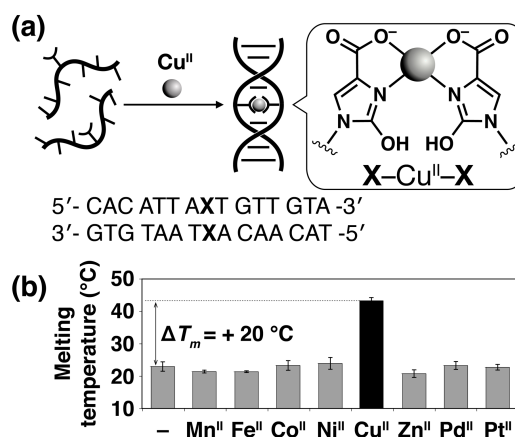


Figure 1. (a) Scheme of metal-mediated base pairing. (b) Duplex melting temperatures (T_m) in the presence of various metal ions. [DNA duplex] = 2 μ M, [metal ion] = 2 μ M, in 10 mM HEPES buffer (pH 7.0), 100 mM NaCl. $N = 3$. Error bars: S. D.

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