A Bulky Rhodium Complex Bound to an Adenosine-Adenosine DNA Mismatch: General Architecture of the Metalloinsertion Binding Mode

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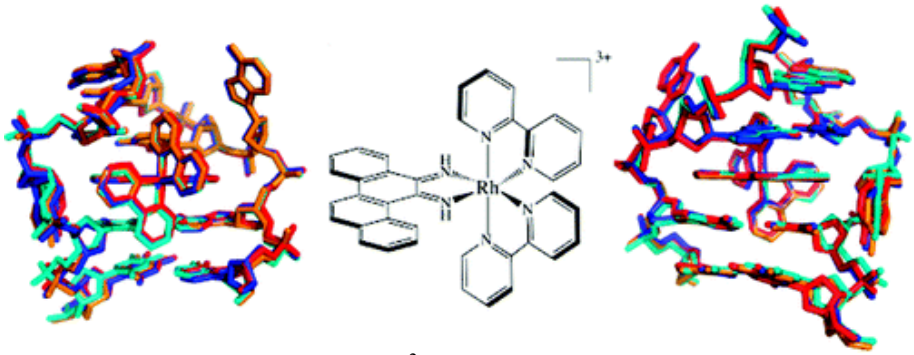
Abstract



Two crystal structures of Δ-Rh(bpy)$_2$(chrysi)$^{3+}$ (chrysi is 5,6-chrysenequinone diimine) bound to the oligonucleotide duplex 5′-CGG*AA*ATT*AC*CG-3′ containing two adenosine-adenosine mismatches (italics) through metalloinsertion were determined. Diffraction quality crystals with two different space groups ($P3_221$ and $P4_32_12$) were obtained under very similar crystallization conditions. In both structures, the bulky rhodium complex inserts into the two mismatched sites from the minor groove side, ejecting the mismatched bases into the major groove. The conformational changes are localized to the mismatched site; the metal complex replaces the mismatched base pair without an increase in base pair rise. The expansive metal complex is accommodated in the duplex by a slight opening in the phosphodiester backbone; all sugars retain a C2′-endo puckering, and flanking base pairs neither stretch nor shear. The structures differ, however, in that in one of the structures, an additional metal complex is bound by intercalation from the major groove at the central 5′-AT-3′ step. We conclude that this additional metal complex is intercalated into this central step because of crystal packing forces. The structures described here of Δ-Rh(bpy)$_2$(chrysi)$^{3+}$ bound to thermodynamically destabilized AA mismatches share critical features with binding by metalloinsertion in two other oligonucleotides containing different single-base mismatches. These results underscore the generality of metalloinsertion as a new mode of noncovalent binding by small molecules with a DNA duplex.

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