J. Am. Chem. Soc., **128** (17), 5654 -5655, 2006. 10.1021/ja061409c S0002-7863(06)01409-0
Web Release Date: April 7, 2006

A Mismatch-Selective Bifunctional Rhodium-Oregon Green Conjugate: A Fluorescent Probe for Mismatched DNA

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Received February 28, 2006

Abstract:

A fluorescent metallointercalator conjugate that selectively targets DNA base mismatches has been synthesized by coupling an organic fluorophore to a bulky Rh intercalator containing the chrysenequinone diimine ligand. Ion pairing between the cationic Rh and anionic fluorophore moieties dramatically quenches the fluorescence of the conjugate in solution and in the presence of matched DNA. However, in the presence of mismatched DNA, the fluorescence of the conjugate is increased >300%. This increase in fluorescence is attributed to the loss in intramolecular quenching associated with DNA binding; intercalation of the Rh moiety into the mismatched site can lead to electrostatic repulsion of the anionic fluorophore away from the DNA phosphate backbone and Rh. Denaturing PAGE experiments with ^{32}P-labeled oligonucleotides indicate that the conjugate selectively binds the mismatched DNA with a binding affinity of 6×10^5 M^{-1} and, upon irradiation, cleaves the DNA backbone neighboring the mismatched site.