

Bifunctional Rhodium Intercalator Conjugates as Mismatch-Directing DNA Alkylating Agents

Ulrich Schatzschneider and Jacqueline K. Barton*

*Division of Chemistry and Chemical Engineering, California Institute of Technology,
Pasadena, California 91125*

jkbarton@caltech.edu

Received March 12, 2004

Abstract:

A conjugate of a DNA mismatch-specific rhodium intercalator, containing the bulky chrysenediimine ligand, and an aniline mustard has been prepared, and targeting of mismatches in DNA by this conjugate has been examined. The preferential alkylation of mismatched over fully matched DNA is found by a mobility shift assay at concentrations where untethered organic mustards show little reaction. The binding site of the Rh intercalator was determined by DNA photocleavage, and the position of covalent modification was established on the basis of the enhanced depurination associated with N-alkylation. The site-selective alkylation at mismatched DNA renders these conjugates useful tools for the covalent tagging of DNA base pair mismatches and new chemotherapeutic design.

Full Text (Subscription Might Be Required):

<http://pubs.acs.org/cgi-bin/article.cgi/jacsat/2004/126/i28/pdf/ja048543m.pdf>