Tuning the DNA Reactivity of \textit{cis}-Platinum: Conjugation to a Mismatch-Specific Metallointercalator

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Abstract:

A novel bimetallic conjugate combining a rhodium intercalator that selectively binds DNA mismatches and a reactive \textit{cis}-platinum analogue that targets DNA by coordination has been prepared. The site-selectivity of the bimetallic complex in forming coordination adducts is examined using mismatched and well-matched oligonucleotides of different sequences. The results indicate that through the bifunctional complex, the platinum center can be targeted near mismatched sites. Interestingly, with mismatched, DNA both intrastrand and the less common interstrand cross-linked adducts are formed. The recognition of a DNA mismatch by the bulky Rh intercalator appears to direct the Pt unit, depending upon steric contraints, to react preferentially with mismatched DNA at a site that may or may not be the preferred site of Pt coordination. Thus, the presence of a permanent link to a site-specific intercalator is able to tune the reactivity of the \textit{cis}-platinum analogue.

Full Text (Subscription May Be Required) :
http://pubs.acs.org/cgi-bin/abstract.cgi/jacsat/2004/126/i45/abs/ja047235l.html