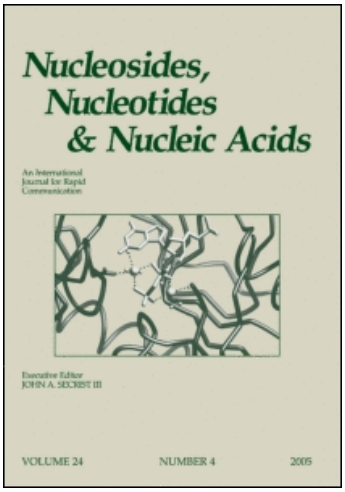

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Oligonucleotides Derivatized with Luminescent and Photoreactive RU(II) Complexes: Models for Photoelectron Transfer and Photocrosslinking

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OLIGONUCLEOTIDES DERIVATIZED WITH LUMINESCENT AND PHOTOREACTIVE RU(II) COMPLEXES : MODELS FOR PHOTOELECTRON TRANSFER AND PHOTOCROSSLINKING

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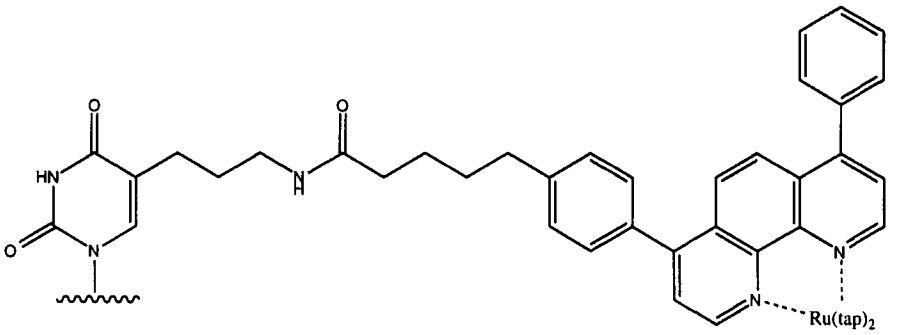
ABSTRACT: In this work we examined different aspects of the photo-reaction of $Ru(TAP)_2$ $(DIP)^{2+}$ (TAP = 1,4,5,8-tetraazaphenanthrene; DIP = 4,7 diphenylphenanthroline) with guanine by studying synthetic oligonucleotide conjugates in which the metal complex is tethered to the oligonucleotide.

It has recently been shown that Ru(II) complexes based on polyazaaromatic ligands such as TAP (1,4,5,8-tetraazaphenanthrene) and HAT (1, 4, 5, 8, 9, 12-hexaazatriphenylene) are excellent DNA photoprobes[1,2]. Depending on the number of TAP or HAT ligands in the octahedral complexes, the excited state is able to abstract an electron from a guanine base of DNA. This photo-electron transfer gives rise to luminescence quenching and leads to photo-cleavage and/or photo-adduct formation. The phororeaction of $Ru(TAP)_2$ $(DIP)^{2+}$ with guanine has been studied by using synthetic 17 mer oligonucleotide conjugates.

The metal complex was tethered to the oligonucleotide via a linker joining the DIP ligand to a central uracil residue (see below). The coupling reaction occurs beween an amino-modified oligomer containing a propylamino linker arm at the C-5 position of uracil and the carboxylic acid functionalized Ru(II) complex. The modified phosphoramidite precursor was prepared in 5 steps from 5 iodo-2'-deoxyuridine. We synthesized three different sequences: sequence **Ru 0** ($^{5'}$TTTTTTTAX**T**AAATTTA$^{3'}$ in which **X** represents the modified base) does not contain any cytosine. Sequences **Ru 1** ($^{5'}$TTTTTTCC**X**TAAATTTA$^{3'}$) and **Ru 2** ($^{5'}$TTTTTTTA**X**CCAATTTA$^{3'}$) contain two C's located in the vicinity of the attached complex towards the 3' and 5' ends respectively.



We recorded the emission spectra of the complex attached to the oligonucleotides in single and double stranded forms. Hybridization of single stranded **Ru 1** and **Ru 2** with their complementary sequences induced an important decrease in emission intensity. For the sequence **Ru 0** no luminescence quenching was observed proving that this quenching process is due to the guanines in the target sequence.

The photo-reaction products were analyzed by polyacrylamide gel electrophoresis in denaturing conditions. No direct photo-cleavage was observed. Upon increasing irradiation periods of time a retarded band appeared. This band was attributed to a cross-linking reaction between the target strand and the metalated strand through the formation of an adduct between a guanine and one of the TAP ligands.

In conclusion, the strategy we used leads to irreversible modification of a targeted guanine containing sequence. Moreover, this type of conjugates should be ideal to examine the conditions for photo-electron transfer and for the formation of photo-products with guanine residues.

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