

# Studies on the synthesis and binding with DNA of *trans*-planaraminepalladium(II) complexes of the form *trans*-PdCl<sub>2</sub>L<sub>2</sub> where L is a planaramine

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## Introduction:

In an attempt to reduce toxicity and widen the spectrum of activity, thousands of cisplatin analogues have been prepared by varying the nature of the leaving groups and the carrier ligands. However, cisplatin analogues are generally found to have a similar spectrum of activity and often develop cross-resistance with cisplatin. Thus, currently attention is also given to rule-breaker compounds with the aim of widening the spectrum of activity. One such compound is BBR3464 that have shown high activity against both cisplatin-responsive and cisplatin-resistant cancer cell lines. Recently Huq et al (2003) synthesized a number of heteronuclear tumour active multicentred metal complexes by replacing the central Pt<sup>2+</sup> ion in BBR3464 with Pd<sup>2+</sup> ion and by changing the length of the diamine chains. Other Pt-Pt-Pt and Pt-Pd-Pt complexes in which the central metal ion is bonded to a planaramine ligand were also synthesized. One such Pt-Pd-Pd complex in which the central metal ion is bonded to 2-hydroxypyridine is found to be much more active than cisplatin. This project is a natural extension of the work and aims to synthesize Pt-M-Pt complexes where M is Pt<sup>2+</sup> or Pd<sup>2+</sup> that is bonded to two planaramine ligands. This poster describes the synthesis and binding with pBR322 plasmid and salmon sperm DNAs of three *trans*-PdCl<sub>2</sub>L<sub>2</sub> complexes code named TH5, TH6 and TH7 where L = 2-hydroxypyridine, 3-hydroxypyridine and 4-hydroxypyridine respectively (Figure 1). The compounds would serve as the starting materials for the synthesis of targeted trinuclear compounds that is currently underway. Studies have also been carried on the BamH1 digestion of interacted pBR322 plasmid DNA.

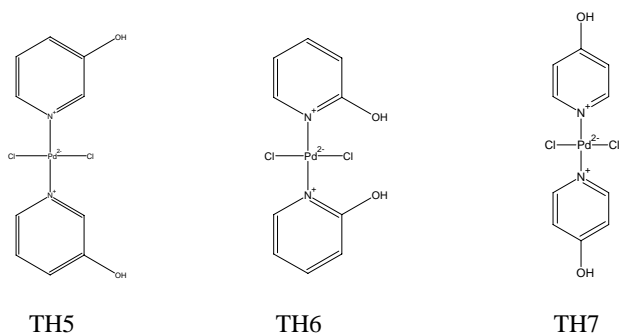


Figure 1. Structures of TH5, TH6 and TH7

It is believed that the compounds bind with DNA forming monofunctional and short-range bifunctional interstrand adducts. The compounds are found to cause conformational change in DNA and DNA damage. The variations in DNA damage and DNA conformational change illustrate structure-activity relationship.