J018 LINKAGE ISOMERIZATION IN THE REACTION OF *TRANS*-DIAMMINEDICHLOROPLATINUM(II) WITH THE DNA FRAGMENT 5'-d(TCTACGCGTTCT) Kenneth M. Comess and Stephen J. Lippard, Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA.

A novel linkage isomerization reaction between *trans*-diamminedichloroplatinum(II) and a synthetic single stranded oligonucleotide substrate, 5'-d(TCTACGCGTTCT), has been discovered in reaction chemistry designed to provide site-specifically modified genomes for biological evaluation. A *trans*-diammineplatinum(II) adduct commonly encountered on DNA, a 1,3-crosslink between two guanine bases on the same strand, was found to be unstable, rearranging to an unprecedented 1,4-crosslink between C_5 and G_8. The 1,4-diadduct is very stable. Both linkage isomers were studied by using a novel Maxam-Gilbert footprinting method, pH dependent NMR titrations, ^{195}Pt NMR spectroscopy, FAB-mass spectrometry, reverse phase HPLC, and enzymatic degradation procedures.

J019 THE USE OF METAL COMPLEXES TO COUNTER AND EXPLOIT TUMOUR TISSUE HYPOXIA IN RADIO- AND CHEMO-THERAPY RESPECTIVELY. Delwyn Evans and Michael Green, University of York, Heslington, York, YO1 5DD, U.K.

O_2 deficient tumour cells can be inert to radiotherapy which can be resolved by the use of imidazole derivatives. 1. A study has been made to assess the feasibility of using these derivatives complexed to a cis-diaqua platinum(II) species as a means to bind the radiosensitiser to DNA. 2. The more reducing environment of hypoxic tissue can be exploited to enhance the selectivity of inorganic anti-cancer complexes. In an attempt to find the mechanism of action of the $Ru(NH_3)_5Cl_3$ prodrug, the kinetics between $[Ru(NH_3)_5OH_2]^{2+}$ and various nucleobases are being studied.

J020 LINKAGE ISOMERIZATIONS OF $[(NH_3)_5Ru^{II,III}]$ ON MODIFIED NUCLEOSIDES K.J. LaChance-Galang and M.J. Clarke
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In an effort to understand metal ion movement on nucleosides and related compounds, we have undertaken an investigation of linkage isomerizations and rotamerizations of $[(NH_3)_5Ru^{II,III}]$ on modified nucleosides and heterocycles that contain an exocyclic amine and at least one endocyclic amine. Ligand systems include: 7-methylguanine, 1-methyl-2-aminoimidazole, 2-aminopyridine, 2-aminopyrimidine and 2-amino-4-oxo-6-methylpyrimidine. Changes in pH and electrochemical potential can be used to control the isomerizations and/or rotamerizations in some but not all complexes of this type. Uv-vis, NMR, cyclic and square wave voltammetry have been used to characterize the isomers and observe the conformational changes.