Synthesis and reactivity of chiral bioxazoline platininum (II) complexes: Design of potential anti-cancer drugs.

Mark H. Schofield[1], James A. Enterkin[2], Andrew L. Lee[2], Katherine S. Larabee[2], Edward A. Wydysh[2], Erwin P. L. van der Geer[2]

[1]*Department of Chemistry, Haverford College, Haverford, Pennsylvania 19041 USA.*
[2]*Department of Chemistry, Williams College, Williamstown, Massachusetts 01267 USA.*
(mschofie@haverford.edu)

Although bioxazoline ligands of palladium and copper are widely used in asymmetric catalysis, platinum complexes bearing chiral bioxazoline ligands have not been described in the literature. With this in mind, and with the dual goals of studying the interaction of chiral platinum complexes with DNA and developing new anti-cancer drugs, a series of platinum (II) complexes of the type $Pt(biox)_2I_2$ containing C_2-symmetric bioxazoline ligands (R,R- or S,S-4,4'-R2-2,2'-bioxazoline, R = -H, -Me, -iPr, -Bz) have been prepared from $PtCl_4^{2-}$ and the corresponding ligand. $Pt(biox)I_2$ complexes are not readily hydrolyzed in water, but the diaqua complexes, $[Pt(biox)(H_2O)_2]^{2+}$, are prepared by treating $Pt(biox)I_2$ with $AgNO_3$ in aqueous solution, allowing for the formation of an array of bioxazoline derivatives. The interaction of the cationic complexes, $[Pt(biox')(H_2O)_2]^{2+}$, with oligonucleotides and mononucleotides (assessed by ^1H and ^{195}Pt NMR and CD spectroscopy) is examined. Recent work on the synthesis of soluble cyclobutanedicarboxylate complexes and complexes containing related aminomethyloxazoline ligands is discussed.