Vanadyl Complexes of Phosphate Diesters

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Following the success of cis-platen as a chemotherapeutic agent, other cis-coordinated metal chlorides have been investigated for antitumor activity. The vanadium(IV) species Cp_2VCl_2 proved to be one of the most active species examined by Köpf *et.al.*[1] Studies by Marks and coworkers demonstrated that the primary interaction of Cp_2VCl_2 with DNA occurred at the oxygen atoms of the phosphate backbone rather than at the nucleobase nitrogen atoms.[2] Significant antitumor activity has also been seen for a range of vanadyl complexes of bipyridine and phenanthroline.[3] Although these complexes were shown to cause apoptosis of the tumor cells, the exact nature of the vanadium interaction is not detailed.

The trispyrazolylborate ligand is often described as a coordination chemistry mimic of the organometallic Cp^- ligand. While V^{3+}/Tp^- complexes form a variety of crystallographically characterized structural motifs with diphenylphosphate, the chemistry of VO^{2+}/Tp^- with phosphate diesters is limited to the dinuclear phosphate bridged complex $[TpVO(O_2P(OPh)_2)]_2$. The nuclearity of vanadium/phosphate ester complexes has been shown to be controlled by both the number of available coordination sites at the metal, and by the denticity of the ester.[4] We have been investigating the accessibility of other structural motifs in the vanadyl/phosphate diester reaction system through the use of mono and bidentate nitrogen ligands in place of the tridentate Tp^- ligand. A number of new bipyridine containing complexes have been synthesized and structurally characterized including the anionic complex $VO(bpy)(O_2P(OR)_2)_3^-$. The compounds are models for potential interactions of the antitumor vanadyl/bipyridine species with DNA molecules.

[1] Köpf-Maier P., Köpf H. *Z. Naturforsch. B* 1979, *34* 805.
[2] Toney, J.H., Brock, C.P., Marks, T.J. *J.Am. Chem. Soc*. 1986, *108*, 7263.
[3] US Patents # 6337348, 6432941, 6743786.
[4] Mokry L.M., Thompson, J., Bond M.R., Otieno, T., Mohan, M., Carrano, C.J. *Inorg. Chem*. 1994, *33*, 2705.