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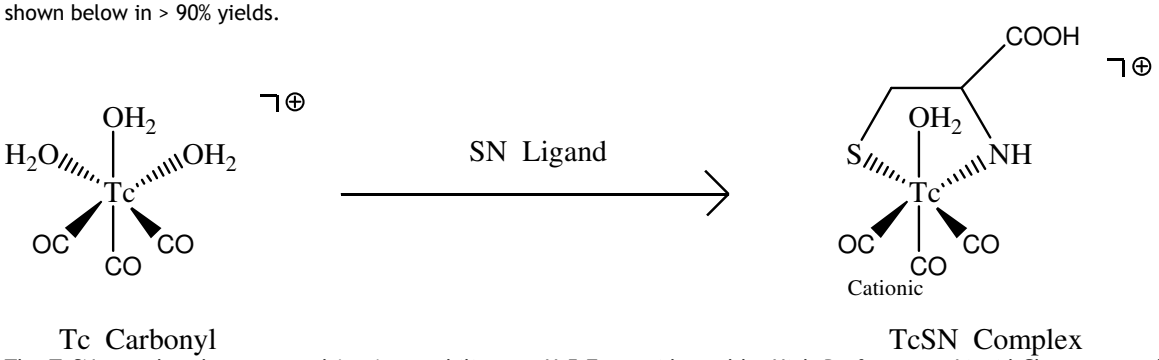
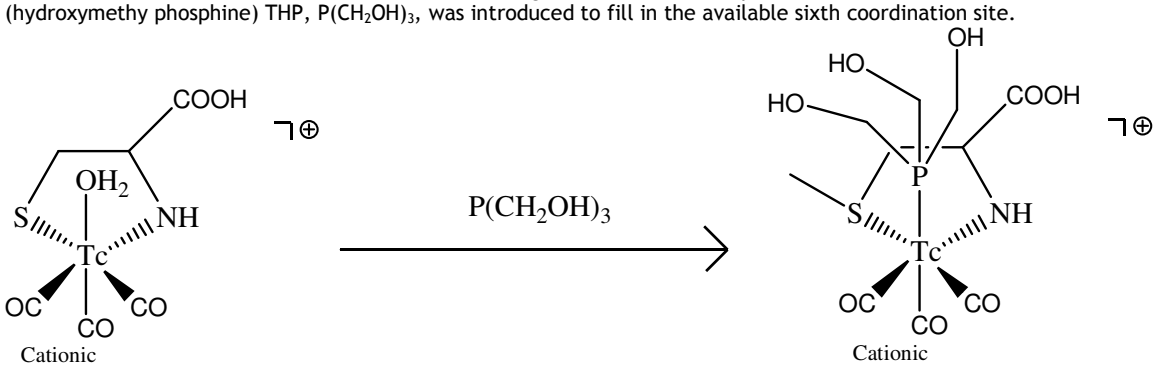
New Tc-99m carbonyl complexes of SN bifunctional ligands

Radiopharmaceuticals are drugs with two components: a radioactive element that delivers a dose of radiation to detect or kill cancer cells targeted by the radiopharmaceutical and a targeting molecule that seeks out cancer sites. Effective radiopharmaceuticals could be used for both the diagnosis and treatment of diseases such as breast cancer, prostate cancer, and various other cancers. The ideal radiochemical properties ($E\gamma$ = 140 KeV), its optimum half life ($t_{1/2}$ = 6.02 h) and ready availability make Technetium-99m one of the most attractive radioisotopes for use in imaging applications. For a radiopharmaceutical to be useful and effective for use under *in vivo* conditions, it is imperative to have high kinetic stability for the Technetium compounds and its bioconjugates. This presentation includes recent results on the design of a new chelating system towards the overall objective of the design and development of *in vivo* stable ^{99m}Tc complexes. Specifically, the new ligand system comprises two electron donors (Sulfur and Nitrogen centers – $MeSCH_2CH(COOH)NH_2$). This ligand system upon interaction with Technetium carbonyl (i.e. Tc in the +1 oxidation state) produced a well defined Tc carbonyl SN complex as shown below in > 90% yields.



Tc Carbonyl TcSN Complex

The TcSN complex demonstrated *in vitro* stability at pH 5-7 as evidenced by High Performance Liquid Chromatography (HPLC) analysis. The new TcSN complex still contained one unoccupied coordination site on the metal. This free site may result in further reactions of the Tc metal center with active ligands. In order to improve the kinetic inertness of the TcSN complex, tris (hydroxymethy phosphine) THP, $P(CH_2OH)_3$, was introduced to fill in the available sixth coordination site.



TcSN Complex TcSNP Complex

The resulting TcSNP complex demonstrated good *in vitro* stability at pH 5-7 for over 24 hours as evidenced by the HPLC analysis. Further studies to utilize the carboxylate arm in TcSNP complex for conjugations with tumor specific peptides are underway. The coordination chemistry, radiochemistry, and *in vitro* stability studies will be discussed.