Bronx STEM Scholars Program

$Re^{V}O$ FGC Tripeptide Stability Calculations:

Models to understand the structure and binding of ^{188}Re radiotherapeutic agents

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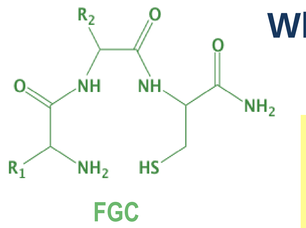
Background and the Big Picture

CHELATE: Contains radioactive metal — LINKER — **TARGETTING VECTOR:** Takes the chelate to the cancer cells i.e. an antibody

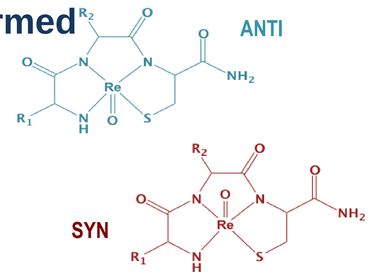
Study the energy and molecualr level dynamics of a variety of rhenium tripeptides to investigate the features that stabilize Rhenium-188 as the radioactive metal in a targetted radiotherapeutic drug for the treatment of cancer.



FGC

When Rhenium Reacts with FGC 2 Diastereomers can be formed

FGC $\xrightarrow[\text{Sodium Acetate, MeOH}]{N(C_4H_9)_4(ReOBr_4(OP(C_4H_9)_3)}$ $Re^{V}O$-FGC



Results and Data (FGC in solution)

System	Energy/h	Δ E/kcal/ mol	% of Isomers	Band Gap/ kcal/mol	Stability E /kcal/ mol
Anti-CS	-1541.528	**2.07**	82%	405.6	-844.25
Syn-CS	-1541.524		18%	429	-842.18
Anti-NP	-1541.071	**1.94**	82%	413	-278.19
Syn-NP	-1541.068		18%	413	-276.25

Results and Data (FGC Data in Vapor)

System	Energy/h	Δ E/kcal/ mol	% of Isomers	Band Gap/ kcal/mol	Stability E /kcal/ mol
Anti-CS	-1541.492	**2.98**	96%	400.4	-992.28
Syn-CS	-1541.488		4%	429	-989.30
Anti-NP	-1540.993	**2.26**	87%	369.2	-676.30
Syn-NP	-1540.99		13%	384.8	-676.04

- Anti isomers more stable (lower energy) than syn.
- Vapor systems are more stable than systems in solution
- Band gaps increase for all systems when compared to ReO.

Calculations and Formulas

$$\Delta U_{solution} = \Delta U_{gas} + \sum_{i=1}^{Nproducts} \Delta U_{i,solvation} - \sum_{j=1}^{Mreactants} \Delta U_{j,solvation}$$

$R_1\text{-CHNH2-COOH} + R_2\text{-CHNH2-COOH} + R_3\text{-CHNH2-COOH} + NH_2^- + R_eO^{+3} \xrightarrow{\Delta U_G} ReOP_1P_2P_3 + 2H_3O^+ + H_2O$

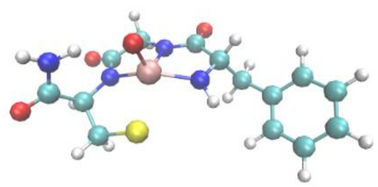
$R_1\text{-CHNH2-COOH} + R_2\text{-CHNH2-COOH} + R_3\text{-CHNH2-COOH} + NH_2^- + R_eO^{+3} \xrightarrow{\Delta U_S} ReOP_1P_2P_3 + 2H_3O^+ + H_2O$

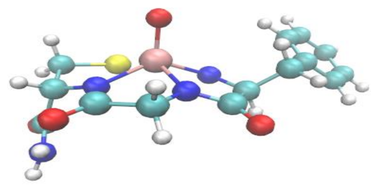
$+\Delta U_{solvation}$ reactants — (g) ➔ (aq) exothermic

$-\Delta U_{solvation}$ products — (aq) ➔ (g) endothermic

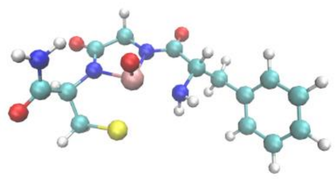
ΔE : Variation of Energy
R : Ideal gas constant (8.314)
T : Absolute Temperature (298 K)
HOMO : Higher Occupied Molecular Orbital
LUMO : Lower Unoccupied Molecular Orbital

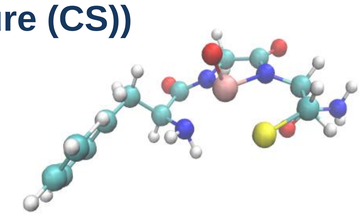
FGC ANTI & SYN Structures removing one proton (NP)





crystal structure (CS))





Oxygen, Sulfur, Nitrogen, Carbon, Hydrogen

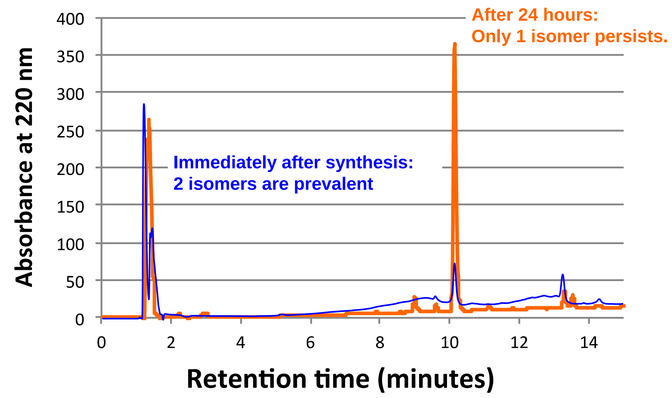
Stability Study Details

Study the energy and molecualr level dynamics of a variety of rhenium tripeptides to investigate the features that stabilize Rhenium-188 as the radioactive metal in a targetted radiotherapeutic drug for the treatment of cancer.

Computational Techniques

- Method – Density Functional Theory – B3LYP
- Basis set – metal lanl2tz(f), non-metal – 6-311+g (2p,d)
- Full geometry optimization with analytical gradients.
- Molecular Orbitals obtained for optimized structures.

HPLC Characterization



Acknowledgements

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