Final Progress Report on DOE Grant DE-FG02-01ER63192

Title: Rhodium-105 Bombesin Analogs for Prostate Cancer Radiotherapy
Project ID: 0007179
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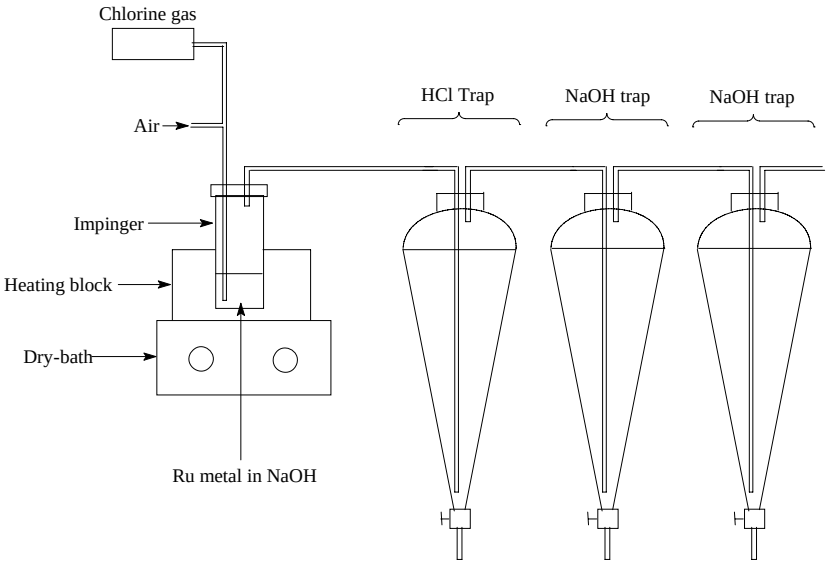
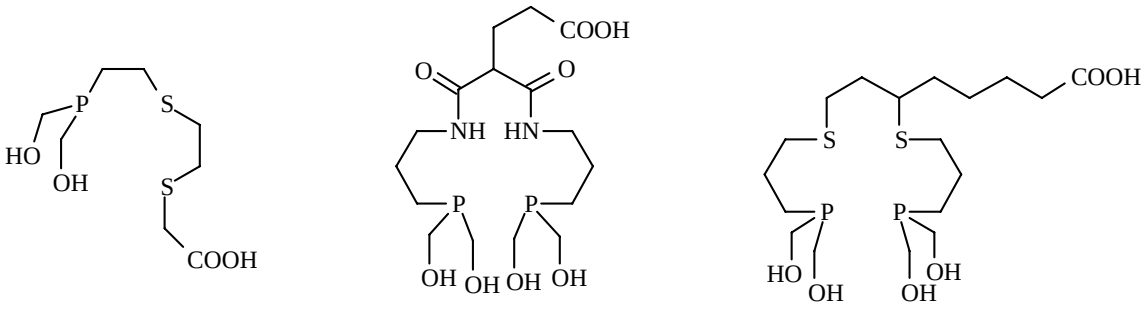
Over the period of this grant (11/01/2001 to 12/31/2005), the consistent and reproducible production of Rh-105, synthesis and evaluation of three new chelate systems based on hydroxymethyl phosphines, development of a new non-hydroxymethyl phosphine $N_2P_2$ chelate system, conjugation of two of the chelates to the bombesin peptide analog BBN[7-14]$NH_2$, evaluation of the bombesin conjugates and their Rh-105 complexes for stability, cell binding affinity, and *in vivo* biodistribution in normal mice has been developed. The BBN analogs bind to GRP receptors that are overexpressed on PC-3 prostate tumor cells.

A dedicated glove box is used for the separation and isolation of $^{105}$Rh from the target ($^{104}$Ru). All tubing/connections/valves from the point of the $Cl_2$ tank are made of Teflon to minimize/eliminate the introduction of any metal into the process (*e.g*., iron from stainless steel corrosion). The separation of $^{105}$Rh produced from the enriched $^{104}$Ru target involves oxidation of the enriched $^{104}$Ru metal target to ruthenium tetroxide with chlorine gas and sodium hydroxide solution to generate hypochlorite *in situ*. The $RuO_4$ is removed by distillation and the $^{105}$Rh remaining in the reaction vial is converted into $^{105}$Rh-chloride by acidification with hydrochloric acid and heating.

The $^{105}$Rh production process has become reproducible over the past year to consistently make 10-30 mCi of $^{105}$Rh from 1-3 mg of an enriched (99.21%) $^{104}$Ru target. The process itself involves irradiation of the enriched $^{104}$Ru target in the core of the reactor (University of Missouri Research Reactor (MURR)) for one week to yield 16-40 mCi of $^{105}$Rh. The irradiated target is processed to separate the Rh-105 in high specific activity from the $^{104}$Ru target. The irradiated target is dissolved in NaOH (2M, 3 mL) by bubbling $Cl_2$ gas through the solution (generating NaOCl *in situ*) to generate $RuO_4$ and Rh(III). The $RuO_4$ is distilled from the solution into an HCl trap to allow for recovery of the enriched Ru as $RuO_2$. The $^{105}$Rh remains in the reaction vessel, and on acidification with 0.1 M HCl, $^{105}$Rh-chloride is available for use. A schematic of the purification and Ru-104 recovery process is shown below.




A dithiaphosphine, a dithiadiphosphine and a diamidediphosphine chelate based on hydroxymethyl phosphines have been synthesized containing a pendant carboxylate group to allow for coupling to bombesin peptide analogs. In addition, a bidentate diphosphine ligand based on hydroxymethyl phosphines has been synthesized to allow

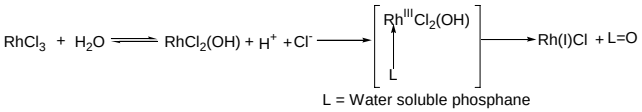



for the investigation of the chemistry of these phosphine ligands with Rh(III).

Three chelates were investigated, namely a tridentate $S_2P$, a tetradentate $N_2P_2$, and a tetradentate $S_2P_2$ chelate (shown above in their deprotected forms). Generally, the hydroxymethylphosphine moiety is protected as the tris(hydroxymethyl)phosphonium ion. These complexes are conjugated to the BBN[7-14]$NH_2$ analog through formation of an amide group by condensation of the carboxylate in the above structures and the terminal amino group of the peptide analog

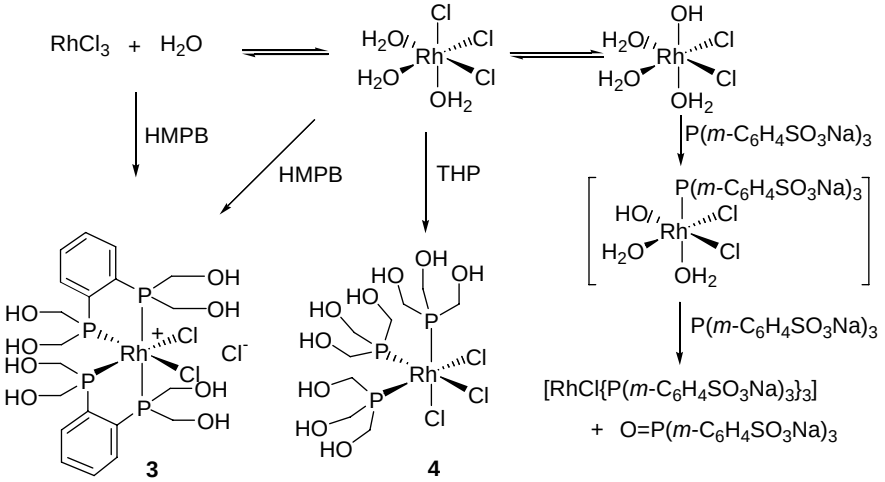
Although phosphane ligands are ubiquitous in the coordination chemistry of rhodium, their role in stabilizing $d^6$ Rh(III) centers is unknown to date. Traditionally, water-soluble phosphanes (*e.g.*, phosphatriazaadamantane (PTA) or sulfonated phosphanes) have been used to promote aqueous solubility and kinetic stability for transition metal compounds. However, the reactions of water-soluble phosphanes with $RhCl_3.xH_2O$ are seldom straightforward and often result in complex reaction mixtures. Specifically, Rh(III) in water readily oxidizes the hydrosoluble phosphanes even in the absence of oxygen. Generally, the phosphane oxidation is facilitated by the formation of rhodium hydroxo species as depicted below in equation (1). In fact, detailed redox studies by Larpent *et al.*[1] have demonstrated the formation of a transient hydroxorhodium (III) intermediate as outlined in equation (1).

Equation (1):




This means that for Rh(III) to be stabilized, it must be coordinated and stabilized with specific ligands prior to formation of the hydroxorhodium (III) intermediate (equation (1)). This can only be achieved if the coordinating ligands have extraordinary kinetics towards complexation, thereby stabilizing Rh(III) prior to the formation of the hydroxo-intermediates. Water soluble ligands such as PTA and trisodium phosphinetriyltri-*m*-benzenesulfonate (TPPTS) are not capable of stabilizing Rh(III). In this context, there is clearly a strong rationale in developing new insights to stabilize Rh(III) complexes in aqueous media.

The macroscopic Rh(III) chemistry with monodentate and bidentate hydroxymethyl phosphine ligands was investigated to insure the Rh remains in the +3 oxidation state and is not reduced to +1, the more labile oxidation state of Rh. Hydroxymethylphosphinobenzene (HMPB) and tris-hydroxymethyphosphine (THP) were reacted with $RhCl_3.xH_2O$ in water at room temperature to yield *cis*-$[RhCl_2(HMPB)_2]^+$ and *fac*-$[RhCl_3(THP)_3]$, respectively.




Both Rh(III) complexes were generated as the predominant product in high yield. Both complexes were fully characterized using standard chemical analysis techniques ($^1$H- and $^{31}$P-NMR, elemental analysis, single crystal X-ray diffraction) to confirm their identity. The relevant reactions in aqueous media are shown above, with a typical water soluble phosphine (P(*m*-$C_6H_4SO_3Na_3)_3$) shown for comparison.

The molecular structure of **3** as shown in **Figure 1** confirms the *cis* configuration of the ligand in this Rh(III) compound. The water-soluble Rh(III) compound represents the first X-ray crystal structure of a rhodium complex bearing a water soluble bisphosphane in a *cis* coordination mode. The molecular structure of **4**, showing the *fac* coordination mode, was confirmed by single crystal X-ray analysis (**Figure 2)**.

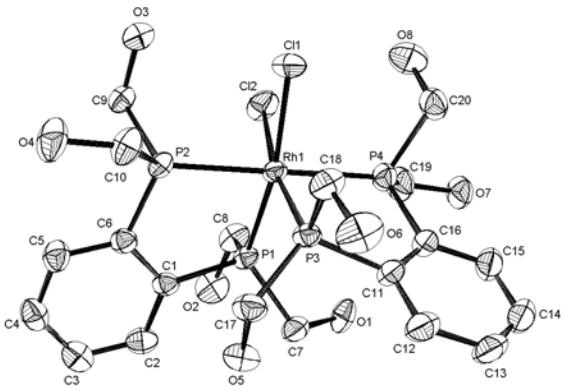



**Figure 1**: The Molecular Structure of *cis*-[Rh(HMPB)$_2$Cl$_2$]Cl (**3**). Hydrogen atoms are omitted for clarity. Pertinent bond lengths (Å) and bond angles (deg) are as follows: Rh1-P1 = 2.280(2), Rh1-P2 = 2.345(2), Rh1-P3 = 2.292(2), Rh1-P4 = 2.333(2), Rh1-Cl1 = 2.452(2), Rh1-Cl2 = 2.441(2); P1-Rh1-P2 = 83.31(6), P3-Rh1-P4 = 83.40(6), Cl1-Rh1-Cl2 = 86.02 (7), P2-Rh1-P4 = 178.62(7).

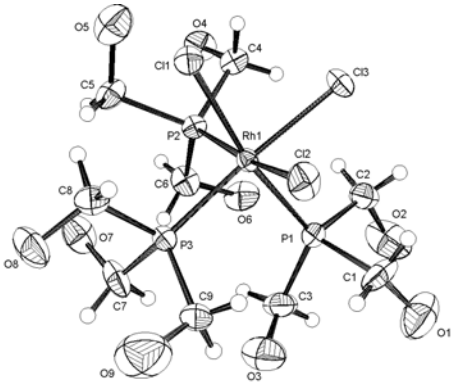


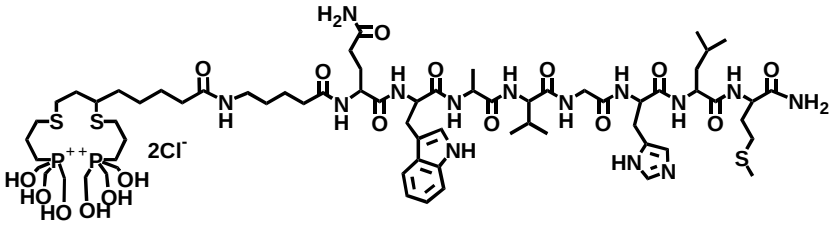

**Figure 2**: The Molecular Structure of *fac*-[Rh(THP)$_3$Cl$_3$] (**4**). Pertinent bond lengths (Å) and bond angles (deg) are as follows: Rh1-P1 = 2.295(2), Rh1-P2 = 2.286(2), Rh1-P3 = 2.2985(19), Rh1-Cl1 = 2.442(2), Rh1-Cl2 = 2.433(2); Rh1-Cl3 = 2.433 (2); P1-Rh1-P2 = 96.86(8), P2-Rh1-P3 = 95.34(7), P1-Rh1-P3 = 96.01(8).

The hydrophilic Rh(III) complexes **3** and **4** exhibit remarkable kinetic inertness in water. In particular, no Cl to $H_2O$ exchange were observed as evidenced by NMR spectroscopic experiments. The details of this work are described in our publication.[2]

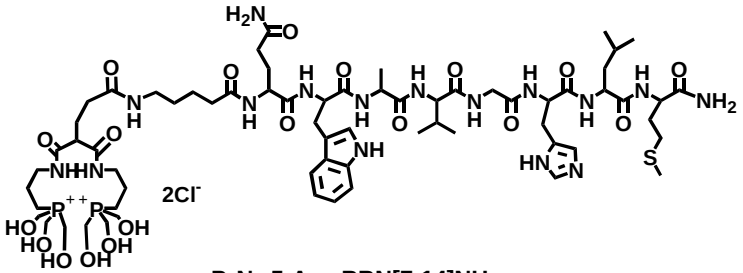
Synthesis of the macroscopic Rh(III) complexes with the $S_2P$, $N_2P_2$ and $S_2P_2$ bifunctional chelates (containing a carboxylic acid group for peptide conjugation) based on hydroxymethyl phosphines led to difficulties in that the free carboxylic acid group interfered with the synthesis, resulting in the formation of Rh oligomers/polymers. Another unexpected difficulty encountered was in the synthesis of the Rh(III) complexes as the pH requirements of the chelates resulted in the decomposition of the $RhCl_3(OH_2)_3$ starting material. The hydroxymethylphosphines are protected as their tris(hydroxymethyl)phosphonium salts. The free phosphine is generated at pH$\geq$7. This poses a problem because the $RhCl_3(OH_2)_3$ hydrolyzes to oligomeric/polymeric oxo/hydroxo species as the pH is increased above seven. A significant effort was put

forth into modifying the synthetic conditions (starting Rh(III) compound, solvent, etc.) to get around these difficulties. The Rh(III) complex [$RhCl_3(S_2P)$] has been synthesized and characterized by NMR ($^{1}H$, $^{13}C$ and $^{31}P$), HPLC, IR and UV-visible spectrophotometry. Unfortunately, X-ray quality crystals have not been obtained to allow determination of the exact structure of the complex. A tridentate chelate such as the $S_2P$ ligand can theoretically coordinate in either a facial or meridinal arrangement about the Rh(III) center. The $^{31}P$-NMR studies indicate that only one type of phosphorus environment is present, suggesting the formation of only one of the two isomers. The five membered chelate rings formed with the Rh(III) on coordination (Rh-PCCS and Rh-SCCS), however, would favor the facial arrangement of the chelate.

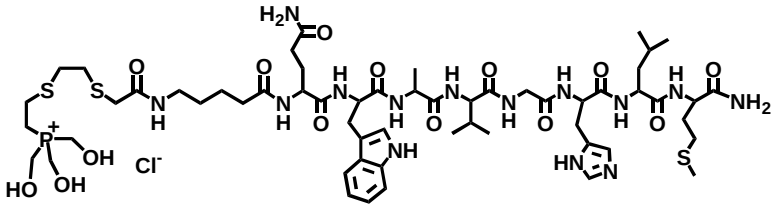
The dithiaphosphine ($S_2P$), dithiadiphosphine ($S_2P_2$) and diamidediphosphine ($N_2P_2$) chelates described above have been conjugated to BBN peptide analogs using standard solid phase peptide synthesis techniques (fmoc chemistry). The three hydroxymethylphosphine chelates were conjugated to 5-Ava-BBN[7-14]$NH_2$ through amide bond formation between the chelate carboxylic acid group and primary amine group on the 5 carbon Ava spacer of 5-Ava-BBN[7-14]$NH_2$. The free phosphine ($PH_2$) was used during the conjugation reactions since the hydroxymethylphosphine group reacts with amines. The phosphine hydrides were converted into the hydroxymethylphosphine analogs using a formylation reaction, then HPLC purified on a C18 reverse phase column, isolated as a solid (~50% yield), and characterized (ESI-MS, HPLC, $^{31}P$-NMR). The BBN-chelate conjugates were purified using reversed phase HPLC and characterized by $^{31}P$-NMR and high resolution electrospray ionization mass spectrometry (ESI-MS) to verify their structures.



**$P_2S_2$-5-Ava-BBN[7-14]$NH_2$**



**$P_2N_2$-5-Ava-BBN[7-14]$NH_2$**



**$PS_2$-5-Ava-BBN[7-14]$NH_2$**

The structures of these three BBN-conjugates are shown above. These conjugates are converted into their hydroxymethyl phosphine analogs using procedures developed in our group to generate the final products (pH≥7 generates the phosphine).

The three peptide conjugates were characterized by their $^{31}$P-NMR, ESI-MS and HPLC retention times on a reversed phase C18 HPLC gradient system. The results are shown in the table below for both the phosphine hydride and the tris(hydroxymethyl)phosphonium analogs of the three chelates.

| Peptide Conjugate | $^{31}$P-NMR | ESI-MS | | | HPLC |
|---|---|---|---|---|---|
| | ($\delta$, ppm) | Formula | Calc'd | Observed | $t_R$ (min) |
| $(PH_2)_2S_2$-5-Ava-BBN[7-14]$NH_2$ | -137.6 | $C_{62}H_{102}N_{14}O_{11}S_3P_2$ | 1376.6 | 1377.8 | 25.8 |
| $(PH_2)_2N_2$-5-Ava-BBN[7-14]$NH_2$ | -136.2 | $C_{60}H_{96}N_{16}O_{13}SP_2$ | 1342.7 | 1343.7 | 18.1 |
| $(PH_2)S_2$-5-Ava-BBN[7-14]$NH_2$ | -143.9 | $C_{54}H_{85}N_{14}O_{11}S_3P$ | 1232.5 | 1233.5 | 18.9 |
| $P_2S_2$-5-Ava-BBN[7-14]$NH_2$ | 25.6 | $C_{68}H_{116}N_{14}O_{17}S_3P_2$ | 1558.7 | 1558.0 | 14.9 |
| $P_2N_2$-5-Ava-BBN[7-14]$NH_2$ | 25.8 | $C_{66}H_{110}N_{16}O_{19}SP_2$ | 1524.7 | 1524.0 | 13.7 |
| $PS_2$-5-Ava-BBN[7-14]$NH_2$ | 24.2 | $C_{57}H_{92}N_{14}O_{14}S_3P$ | 1323.6 | 1323.0 | 14.7 |

The *in vitro* cell binding studies were carried out with the uncomplexed chelate conjugates because we were unable to successfully synthesize the macroscopic Rh(III) complexes with the hydroxymethyl phosphine chelates (see above). The BBN-chelate conjugates described above were evaluated using *in vitro* cell binding assays with PC-3 prostate cancer cells. The IC50 values were determined using standard competition studies against I-125-(Tyr$^4$)-BBN(1-14)$NH_2$. The IC50 of $S_2P$-5-Ava-BBN[7-14]$NH_2$ was determined to be 1.23 nM in PC-3 cancer cells which express the GRP receptor. IC50 values in the range 1-10 nM are deemed very good, and further *in vivo* studies are warranted.

The $^{105}$Rh chemistry has been investigated for the three hydroxymethylphosphine chelates ($S_2P$, $N_2P_2$, $S_2P_2$) to determine the best conditions for synthesis on the radiotracer level. The optimal conditions determined for the synthesis of $^{105}$Rh with the $S_2P$-5-Ava-BBN[7-14]$NH_2$ and the $S_2P_2$-5-Ava-BBN[7-14]$NH_2$ were pH ca. 5 in aqueous ethanol and heating at 80$^o$C for 1 hour to give a yield of ≥90%. The optimal conditions for the $N_2P_2$-5-Ava-BBN[7-14]$NH_2$ were pH ca. 8 in aqueous ethanol and heating at 80$^o$C for 1 hour to give a yield of ≥90%. The initial studies with the new $N_2P_2$ chelate carried out with the conditions listed for the $N_2P_2$-5-Ava-BBN[7-14]$NH_2$ and gave ≥90% yield but the radiolabeling conditions have not been optimized. The $^{105}$Rh product was separated from uncomplexed $S_2P$-5-Ava-BBN[7-14]$NH_2$ by C18 reversed phase HPLC.

The *in vitro* stability of $^{105}$Rh-$S_2P$-5-Ava-BBN[7-14]$NH_2$, $^{105}$Rh-$S_2P_2$-5-Ava-BBN[7-14]$NH_2$, and $^{105}$Rh-$N_2P_2$-5-Ava-BBN[7-14]$NH_2$ have been carried out at 37$^o$C in both serum and phosphate buffered saline (1 mM cysteine; pH 6.5). Samples were taken at various time points and analyzed by reversed phase HPLC out to 73 hours. The complex remained 100% intact in serum out to 73 hr and upon cysteine challenge remained ca. 90% intact out to 73 hr.

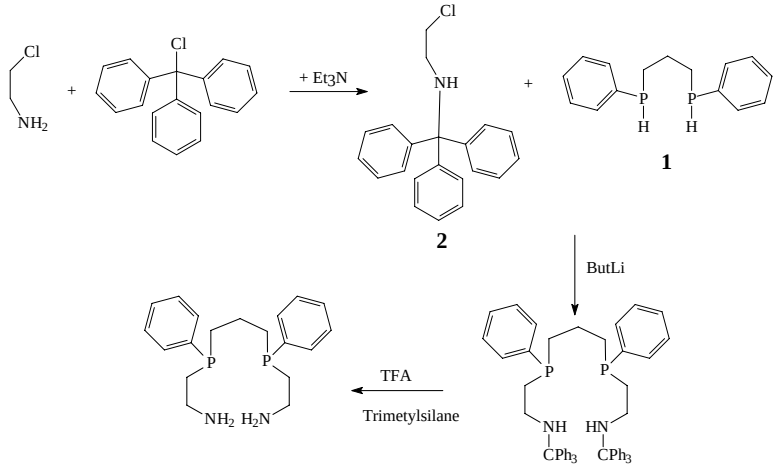
Only normal mouse biodistributions have been carried out to date, since the compounds tested ($S_2P$-5-Ava-BBN and $N_2P_2$-5-Ava-BBN) did not demonstrate sufficient uptake in the pancreas. Normal mouse pancreas expresses GRP receptors, and thus a non-tumor animal model is used as the screen for GRP receptor binding *in vivo* prior to tumor model mouse studies. The results of these studies are described below.

$^{105}$Rh-$S_2P$-5-Ava-BBN[7-14]$NH_2$ was synthesized and purified for normal mouse biodistribution studies. GRP receptors are present normally in the pancreas, so pancreatic uptake is an indicator of *in vivo* tumor uptake. Five mice were used per time

point, and the time points of 1, 4 and 24 hours post-injection were evaluated. The $^{105}$Rh-$S_2P$-5-Ava-BBN[7-14]$NH_2$ cleared very quickly with 77% urinary excretion observed at 1 hour. Very little pancreatic uptake was observed (0.45±0.13 %dose/gram). Only the kidneys showed significant uptake (13.64±1.70, 12.34±6.72, and 9.01±1.34 %dose/gram, respectively, at 1, 4 and 24 hrs), not unexpected for a radiolabeled peptide. The $S_2P$-5-Ava-BBN[7-14]$NH_2$ showed nanomolar (1.23±0.08 nM) IC50 value with PC-3 cancer cells using I-125-bombesin as the gold standard. However, the $^{105}$Rh-$S_2P$-5-Ava-BBN[7-14]$NH_2$ did not show significant pancreatic uptake. We attribute this to the very fast urinary clearance observed with this compound, suggesting that the compound is too hydrophilic. To test this hypothesis, we have synthesized $S_2P$-BBN[7-14]$NH_2$ conjugate with an 8 carbon spacer and are evaluating the $^{105}$Rh conjugate for biological activity (*i.e*., pancreatic uptake).

$^{105}$Rh-$N_2P_2$-5-Ava-BBN[7-14]$NH_2$ was synthesized and purified for normal mouse biodistribution studies. Three mice were used for obtaining a 1 h time point biodistribution. The $^{105}$Rh-$N_2P_2$-5-Ava-BBN[7-14]$NH_2$ showed 81.24±1.06%ID (51.57±11.60%ID/g) in the liver at 1 hour, with no significant clearance into the intestines, indicating a very lipophilic compound. This is interesting because the unconjugated $^{105}$Rh-$N_2P_2$-COOH showed principally urinary clearance (74.7%ID in the bladder at 2 h in Sprague-Dawley rats). We plan to reduce the lipophilicity of the BBN-chelate conjugate with the serine-glycine-serine spacer replacing the aliphatic 5-Ava spacer. This should significantly reduce the lipophilicity of the resultant BBN-chelate conjugate.

A new diaminediphosphine chelate was synthesized, in which the phosphine is not a hydroxymethyl phosphine derivative. We encountered some unexpected difficulties with the hydroxymethyl phosphine chelates (*i.e*., pH required for synthesis of Rh(III) complexes—see above), and thus a non-hydroxymethyl phosphine derivative was synthesized for comparison and evaluation. The synthetic scheme is shown below.




The new $N_2P_2$ ligand has been characterized by $^1$H-, $^{13}$C- and $^{31}$P-NMR and ESI-MS.

The Rh(III) chemistry with the new $N_2P_2$ chelate gave the product *trans*-[$RhCl_2(N_2P_2)$]$PF_6$ on reaction with $RhCl_3.xH_2O$ in an acetonitrile/ethanol solution. The complex was characterized by $^1$H- and $^{31}$P-NMR, and by single crystal X-ray diffraction (Figure 3).

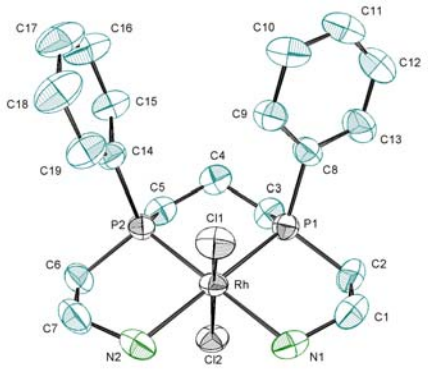
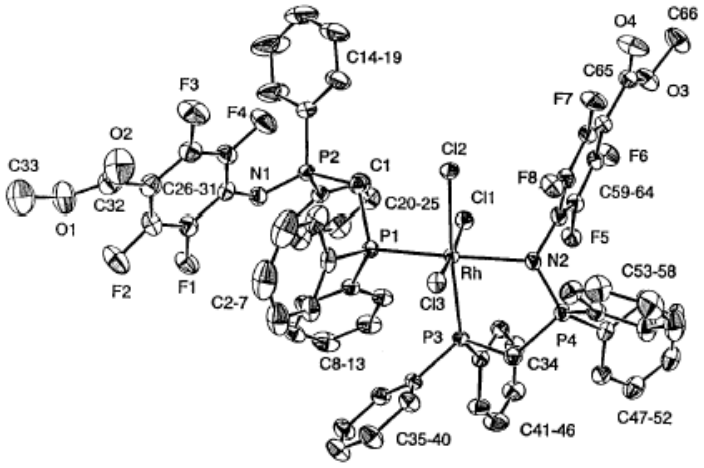


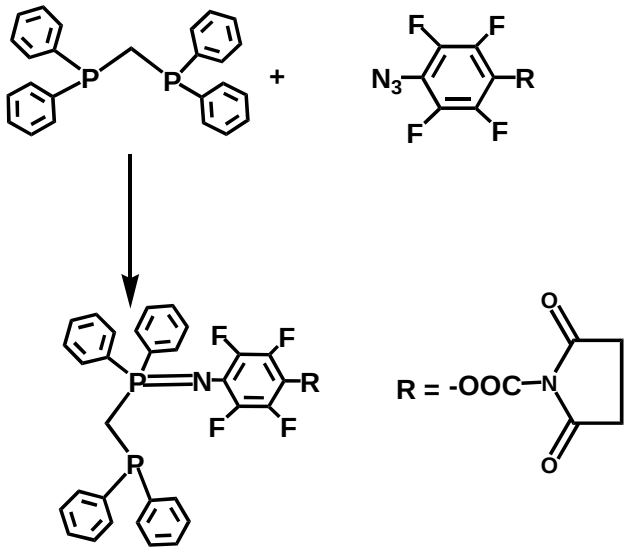

**Figure 3**: The Molecular Structure of *trans*-[$RhCl_2(N_2P_2)$]$PF_6$. Pertinent bond lengths (Å) and bond angles (deg) are as follows: Rh-P1 = 2.2468(9), Rh-P2 = 2.2527(9), Rh-N1 = 2.168(3), Rh-N2 = 2.163(3), Rh-Cl1 = 2.3378(9); Rh-Cl2 = 2.3609 (9); P1-Rh-P2 = 92.05(3), P1-Rh-N1 = 85.14(10), P2-Rh-N2 = 85.15(11), N1-Rh-N2 = 97.1(2) (unpublished results).

Preliminary mouse biodistribution studies with $^{105}$Rh-(new $N_2P_2$) in 3 animals at 1 hour showed the compound is fairly lipophilic. This is not unexpected with the phenyl substituent on each phosphine. At 1 hour, 75.56±0.29%ID (41.37±2.31%ID/g) liver uptake was observed, however, the clearance into the small intestine had already begun (4.58±0.93%ID; 2.66±0.41%ID/g). Only 6.42±0.32%ID was observed in the urine. Once conjugated to BBN[7-14]$NH_2$, the lipophilicity of the resultant compound may significantly change as we have observed with the $S_2P$-5-Ava-BBN[7-14]$NH_2$ and $N_2P_2$-5-Ava-BBN[7-14]$NH_2$. Prior to conjugation, the $^{105}$Rh-$N_2P_2$-COOH was found to be quite hydrophilic (74.72%ID in the bladder at 2 h; 2.75%ID in liver; n=2), yet the BBN conjugate is very lipophilic. To increase the hydrophilicity of the BBN conjugate a serine-glycine-serine linker will be incorporated in place of the 5-Ava group. This modification will also be used for the new $N_2P_2$ BBN conjugate, if the 5-Ava group makes the resultant $^{105}$Rh complex too lipophilic (based on biological properties).

***Phosphine-Phosphinimine BFCAs for Rh-105- Peptide Labeling***. Recently, we developed new iminophosphorane chemistry for the conjugation/metallation of bioactive molecules to specific chelating backbones. Succinimido functionalized tetrafluoroarylazide selectively oxidizes bisdiphenylphosphinomethane at one of the P(III) centers giving (iminophosphorano)phosphine in high yield (**Scheme 1**). The phosphine phosphinimine combination with Rh(III) results in bringing together two receptor-specific biomolecules across one metal center (see structure below), which has potential attractive targeting implications. The presence of two prostate cancer receptor binding bombesin units across one Rh-105 radionuclide will result in a highly efficient uptake of therapeutic radionuclide at the tumor site.



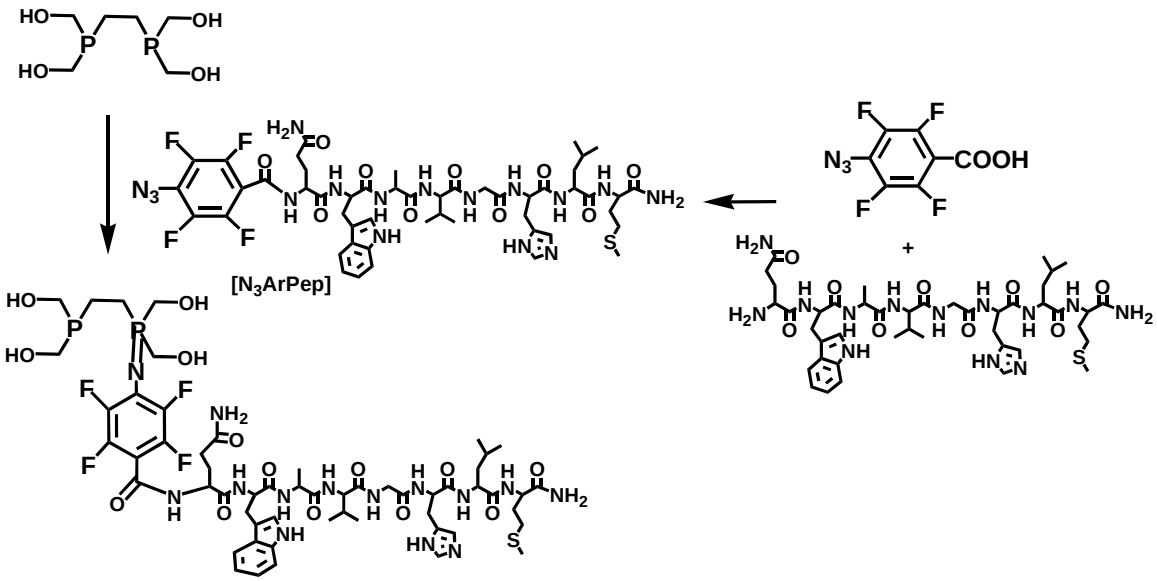

**Scheme 1**




Succinimido functionalized perfluoroarylazido (iminophosphorano)phosphine wass attached to angiotensin converting enzyme (ACE) inhibitor, lisinopril at one end, leaving the other end for chelation to Rh(III) (and Pd(II)) and radioactive analogs establishing the hetero-bifunctionality for potential *in vivo* tracking of the radiotracer. The measurement of inhibitory potency of lisinopril-metal conjugates (Rh and Pd), modified through the primary amine, reveals an increase in inhibitory potency ($IC_{50}$ for Rh complexes = 5.2 nm; for Pd complexes = 8.9 nm), retaining the targeting potential of native lisinopril toward specific biological sites.[3]

Our studies have demonstrated that functionalization of ACE inhibitors onto Rh(III) and Pd(II) metallated BFCAs opens up new possibilities for introducing other receptor avid peptides (*e.g.*, Bombesin) on iminophosphorane backbones. Specifically, we will utilize the iminophosphorane approach for the functionalization of bombesin *via* an iminato nitrogen at one arm of a hydrophilic phosphine as shown in **Scheme 2**. The bombesin functionalized phosphine-phosphinimine BFCA framework will be utilized for radiolabeling with Rh-105 as outlined in **Scheme 2**.

**Scheme 2**

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Publications and Presentations to Date Related to this Grant:

(1) “Exceptional Kinetic Propensity of Hydroxymethyl Phosphanes toward Rh(III) Stabilization in Water”, K. Raghuraman, N. Pillarsetty, W.A. Volkert, C. Barnes, S. Jurisson, K.V. Katti, *J. Am. Chem. Soc*. **2002**, *124*, 7276-7277.

(2) “Production and Supply of High Specific Activity Radioisotopes for Radiotherapy Applications”, Ketring A.R.; Ehrhardt G.J.; Embree M.F.; Bailey K.D.; Tyler T.T.; Gawenis J.A.; Jurisson S.S.; Engelbrect H.P.; Smith C.J.; and Cutler C.S.*; J. Alasbimn*, **5**(19): January 2003.

(3) “Rhodium-105 Complexes as Potential Radiopharmaceuticals”, S.S. Jurisson, presented at the Gordon Research Conference on Metals and Medicine, 22-26 July 2002, Colby-Sawyer College, NH (invited).

(4) “Unprecedented Kinetic Propensity of Hydroxymethyl Phosphanes Toward Rh(III) Stabilization in Ecofriendly Media”, K. Raghuraman, N. Pillarsetty, W.A. Volkert, C. Barnes, S. Jurisson, K.V. Katti, presented at the 224th ACS National Meeting, 18-22 August 2002, Boston, MA.

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(6) “Production of Rh-105 from Ru-104”, Engelbrecht H.P.; Cutler C.S.; Ketring A.R.; Ehrhardt G.J.; Moustapha M.E.; Higgins B.J.; Jurisson S.S.*;* 37th ACS Midwest Regional Meeting – MWRM, Lawrence, Kansas, October 23-25, 2002.

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(10) "Potential Use of $^{105}$Rh-$S_2$P-$C_x$-BBN Radiopharmaceuticals (X = 5 or 8) for Prostate Cancer Radiotherapy”, B. Ballard, H. Engelbrecht, C.S. Cutler, R. Kannan, K.V. Katti, T.J. Hoffman, S.S. Jurisson, presented at the 2005 International Symposium on Radiopharmaceutical Chemistry Meeting, Iowa City, IA, 24-28 June 2005.

Publications and Presentations following the ending date of this grant, but grant was referenced for support.

“Radiochemical labeling of $P_2N_2$ as a potential bifunctional chelating agent”, B. Ballard, H. Engelbrecht, A. Cagnolini, R. Kannan, K. Katti, C. Cutler, S. Jurisson, to be presented at the 231st ACS National Meeting, Atlanta, GA, 26-30 March 2006.

“Rhodium-105 Phosphine Complexes for Potential Applications to Radiotherapy”, B. Ballard, H. Engelbrecht, C. Cutler, R. Kannan, K. Katti, T. Hoffman, S. Jurisson, presented at the 2007 International Society of Radiopharmaceutical Science Meeting, Aachen, Germany, 24 April-4 May 2007.

**"**Radiochemical labeling of P2S2 as a potential bifunctional chelating agent”, B. D. Ballard, H.Engelbrecht, C. S. Cutler, S. S. Jurisson, presented at the 234th ACS National Meeting, Boston, MA, United States, August 19-23, 2007.

“Preparation and Use of Carrier Free $^{105}$Rh”, B. Ballard, H. Engelbrecht, C. S. Cutler, S. S. Jurisson, presented at the American Nuclear Society (ANS) Annual Meeting 2008, Anaheim, CA, 7-11 June 2008.

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