OXORHENIUM(V) AND OXOTECHNETIUM(V) COMPLEXES WITH TETRA- AND HEXADENTATE POLYAMINOPYRIDYL MOLECULES

by

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B.Sc., University of British Columbia, Canada, 1995

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE in THE FACULTY OF GRADUATE STUDIES (Department of Chemistry)

We accept this thesis as conforming to the required standard

The University of British Columbia
December 1997

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Date April 22, 1998
Abstract

Complexes with tetra- and hexadentate polyaminopyridyl ligating moieties were prepared and studied as part of a process to understand the coordination chemistry of oxorhenium and oxotechnetium metal centres as potential radiopharmaceuticals.

\[ \text{N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamineoxorhenium(V) perrhenate, } [\text{ReO(pmen))][\text{ReO}_4], \text{ N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamine\text{-}N,N'\text{-}diacetatooxorhenium(V) bromide, } [\text{ReO(bped)}]\text{Br, } \text{N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamine\text{-}N,N'\text{-}diacetatooxotechnetium(V) chloride, } [\text{TcO(bped)}]\text{Cl, were prepared and characterized. In addition, three new potential ligands: } \text{N,N'\text{-}bis(methylcarboxymethyl)\text{-}N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamine, } \text{pmen\text{-}OMe, N,N'\text{-}bis(ethylcarboxymethyl)\text{-}N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamine, pmen\text{-}OEt, and N,N'\text{-}bis(tert\text{-}butylcarboxymethyl)\text{-}N,N'\text{-}bis(2\text{-}pyridylmethyl)ethylenediamine, pmen\text{-}OBu}, \text{ were prepared for the first time and characterized. } \]

The oxorhenium and oxotechnetium complexes were characterized by mass spectrometry, elemental analyses, infrared spectroscopy, and \(^1\)H NMR spectroscopy. \(H_2\text{pmen}\) and the pmen-esters are oils and elemental analyses were not performed. Crystals suitable for X-ray diffraction studies were not obtained for any of the complexes prepared.

Characterization of the oxorhenium(V) and oxotechnetium(V) complexes revealed a number of possible geometries. \([\text{ReO(pmen)}][\text{ReO}_4]\) is proposed to be a 5-coordinate square pyramidal or trigonal bipyramidal complex. The \([\text{ReO(bped)}]\text{Br and } [\text{TcO(bped)}]\text{Cl complexes were thought to be either 5- or 7-coordinate complexes. } \text{\(^1\)H NMR of the bped}\text{- complexes showed three
AA'BB' patterns in CD$_3$OD indicative of coordinated acetate groups in a 7-coordinate monocapped trigonal prism or pentagonal bipyramidal type configuration. In D$_2$O, [ReO(bped)]$^+$ showed two AA'BB' patterns and a singlet in the $^1$H NMR characteristic of pendant acetate groups. The similarity between the bped$^2$- complexes and the pmen$^2$- complex suggests that the bped$^2$- complexes have the same possible 5-coordinate configurations as [ReO(pmen)]$^+$. Based on steric interactions and ring strain associated with the bped complexes, the monocapped trigonal prism or square pyramidal configurations were believed to be favoured. It was not possible to identify the true configuration without an X-ray diffraction study.
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<td>acetate</td>
</tr>
<tr>
<td>α</td>
<td>alpha particle</td>
</tr>
<tr>
<td>β−</td>
<td>beta particle</td>
</tr>
<tr>
<td>β+</td>
<td>positron</td>
</tr>
<tr>
<td>hbed4−</td>
<td>N,N'-bis(2-hydroxybenzyl)-ethylenediamine-N,N'-diacetate</td>
</tr>
<tr>
<td>H$_2$bped, edampda</td>
<td>N,N'-bis(2-pyridylmethyl)ethylenediamine-N,N'-diacetic acid</td>
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<td>H$_2$bbpen</td>
<td>N,N'-bis(2-hydroxybenzyl)-N,N'-bis(2-pyridylmethyl)-ethylenediamine</td>
</tr>
<tr>
<td>BFC agent</td>
<td>bifunctional chelating agent</td>
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<tr>
<td>br</td>
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</tr>
<tr>
<td>calc</td>
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</tr>
<tr>
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<tr>
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<td>deuterated methanol</td>
</tr>
<tr>
<td>CH$_3$CN</td>
<td>acetonitrile</td>
</tr>
<tr>
<td>CF$_3$SO$_3$−</td>
<td>triflate</td>
</tr>
<tr>
<td>cm$^{-1}$</td>
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<tr>
<td>COSY</td>
<td>correlated spectroscopy (NMR)</td>
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<tr>
<td>δ</td>
<td>chemical shift in parts per million (ppm) downfield from tetramethylsilane (NMR); vibrational out-of-plane bending mode (IR)</td>
</tr>
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<td>Definition</td>
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<tr>
<td>--------</td>
<td>------------</td>
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<tr>
<td>$\Delta$</td>
<td>the spread between the average chemical shift of AB patterns (ppm)</td>
</tr>
<tr>
<td>D</td>
<td>deuterium</td>
</tr>
<tr>
<td>d</td>
<td>doublet (NMR)</td>
</tr>
<tr>
<td>dd</td>
<td>doublet of doublets (NMR)</td>
</tr>
<tr>
<td>dq</td>
<td>doublet of quartets (NMR)</td>
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<tr>
<td>DMF</td>
<td>N,N'-dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>DMSO-$d_6$</td>
<td>deuterated dimethylsulfoxide</td>
</tr>
<tr>
<td>DTPA$^5-$</td>
<td>diethylenetriaminepentaacetate</td>
</tr>
<tr>
<td>$E_\gamma$</td>
<td>gamma ray or photon decay energy</td>
</tr>
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<td>$\gamma$</td>
<td>gamma ray; photon</td>
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<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>GFR</td>
<td>glomerular filtration rate</td>
</tr>
<tr>
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<td>hour(s)</td>
</tr>
<tr>
<td>HM-PAO</td>
<td>hexamethylenepropylene amine oxime</td>
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<tr>
<td>Hz</td>
<td>Hertz</td>
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IR infrared
J_{ab} NMR coupling constant between hydrogens a and b
k kilo \(10^3\)
LLD liquid-liquid diffusion
LSIMS liquid secondary ion mass spectrometry
m milli- \(10^{-3}\); medium (IR); ‘metastable’ state
M molarity; metal; mega \(10^6\)
MAG_3 mercaptoacetylglycylglycylglycine
mL millilitre
m/z mass-to-charge ratio (in mass spectrometry)
MeOH methanol
min minute(s)
mmol millimole
mol mole
MRI magnetic resonance imaging
\nu stretching vibration (IR)
NMR nuclear magnetic resonance
pD negative log of the concentration of D_3O^+
pH negative log of the concentration of H_3O^+
pled^4- N,N’-bispyridoxylethylenediamine diacetate
H_2pmen, bispicen N,N’-bis(2-pyridylmethyl)ethylenediamine
pmen-OBu^t N,N’-bis(tert-butylcarboxymethyl)-N,N’-bis
\(2\)-pyridylmethyl)ethylenediamine
pmen-OEt N,N’-bis(ethylcarboxymethyl)-N,N’-bis
\(2\)-pyridylmethyl)ethylenediamine
pmen-OMe \( \rightarrow \) N,N'-bis(methylcarboxymethyl)-N,N'-bis(2-pyridylmethyl)ethylenediamine

ppm \( \rightarrow \) parts per million (NMR)

[ReO(bped)]Br \( \rightarrow \) N,N'-bis(2-pyridylmethyl)ethylenediamine-N,N'-diacetatoxorhenium(V) bromide

[ReO(pmen)][ReO\(_4\)] \( \rightarrow \) N,N'-bis(2-pyridylmethyl)ethylenediamine-oxorhenium(V) perrhenate

Sbpen\(^4\) \( \rightarrow \) N,N'-bis(2-hydroxy-5-sulfonylbenzyl)-N,N'-bis(2-pyridylmethyl)ethylenediamine

s \( \rightarrow \) singlet (NMR); strong (IR)

t \( \rightarrow \) triplet (NMR)

td \( \rightarrow \) triplet of doublets (NMR)

tpen \( \rightarrow \) N,N,N'N'-tetra-2-picolylethylenediamine

\( T_{1/2} \) \( \rightarrow \) half-life, time for concentration to reach one-half of the initial concentration.

[TcO(bped)]Cl \( \rightarrow \) N,N'-bis(2-pyridylmethyl)ethylenediamine-N,N'-diacetatooxotechnetium(V) chloride

vs \( \rightarrow \) very strong (IR)

w \( \rightarrow \) weak (IR)

X\(^-\) \( \rightarrow \) halide ion

y \( \rightarrow \) year(s)

Y\(^-\) \( \rightarrow \) bulky counter anion
ACKNOWLEDGMENTS

I would like to thank Dr. Chris Orvig for his guidance, encouragement, and never ending patience. This appreciation; however, does not extend to Friday hockey where I was often a victim of his unorthodox, mutilative, WWF-like defensive techniques.

A special thanks to all the members of the Équipe Orvig Team, past and present: Ika Setyawati, Lenny Woo, Kathie Thompson, Li Wei Yang, Ernest Wong, Andreas Dittler-Klingemann, Peter Caravan, Mike Kovacs, “Mother” Elisabetta Gobbi, “Father” Nicolas Aebischer, Dave “Huey” Green, Barry “Duey” Liboiron, Devin “Luey” Mitchell, and Péter ”Vlad the Inserter” Buglyó. Honourable mentions go to the drunkards: Paul ”The Earl of Lard” Read, Ashley Stephens, Marco Melchior, and Leon Xu (“Warrior Princess”), who never ceased to amaze me with their eccentricities and “poetic” vocabulary.

Cheers to those outside the Orvig group: Doug and the members of the Sherman group, Rob, Olivier, the Aikidoka people, Maria, and of course my good friend Robyn.

The assistance of the departmental support staff is gratefully acknowledged, especially Ms. Liane Darge, Ms. Marietta Austria, and Mr. Borda for their patience.

The department is thanked for the T.A.ship and Dupont Merck is thanked for the contributions to the research grant.

Thanks goes out to the A.U.S., the E.U.S., The Pit Pub, The Gallery Lounge, The Fringe, and the micro-breweries for supplying the elixir necessary to survive graduate student life.
I dedicate this thesis to my parents, Robert and Sharon, to my sister Chantelle and her family, Cam, Monique, Marcus, to Uncle Lorne, and of course to my dear departed friend, Cedric.

“My brain hurts.”

– Monty Python
I. Introduction

The research and design of Tc and Re radiopharmaceuticals has greatly expanded over the past twenty years due to the ideal nuclear properties of their radionuclides and their applicability in the field of nuclear medicine. Radiopharmaceuticals are drugs containing a radionuclide that can be applied either as a diagnostic imaging agent (e.g. $^{99m}$Tc, $^{111}$In), or as a therapeutic agent (e.g. $^{186,188}$Re, $^{153}$Sm). It is possible to monitor biochemical and physiological properties in vivo by using both the nuclear properties of the radionuclide and the pharmacological properties of the radiopharmaceutical, an advantage over higher resolution magnetic resonance imaging (MRI) and ultrasound techniques. The use of metals offers a multitude of opportunities in the design of radiopharmaceuticals. The ability to modify the environment around the metal permits specific in vivo targeting to be incorporated into the molecule. The coordination chemistry of the metal determines the ultimate geometry and stability of the radiopharmaceutical. These properties will decide whether it is suitable for application in biological systems, where it will encounter a pH of ca. 7.4, a temperature of ca. 37°C, and various small molecules, proteins, enzymes, and cells, which could challenge the integrity of the complex.1,2,3

The commercial development of radiopharmaceuticals flourished in the 1970's and 80's. Prior to 1980 the focus was on renal and bone imaging, renal and hepatic function, and labelled red blood cells using $^{99m}$Tc complexes of gluconate, glucoheptonate, dimercaptosuccinic acid, phosphonates and diethylenetriaminepentaacetic acid (H$_5$DTPA).2 Little was known of the nature
of the complexes formed and the range of application was limited. To obtain a
greater understanding of technetium chemistry and to extend the range of
$^{99m}$Tc radiopharmaceuticals it was essential that new ligands be designed. In
the 1980’s the main foci of development of new radiopharmaceuticals were in
the areas of cerebral perfusion, myocardial perfusion, kidney function, and
liver function.$^{2,3}$

$^{99m}$TcO($d,l$-HM-PAO) (Ceretec™), designed by Troutner,$^{5,6}$ was the first
commercially available technetium radiopharmaceutical for imaging cerebral
blood flow (in patients who have suffered a stroke).$^{1,2,3}$ It is also claimed to be useful in
evaluating other cerebral diseases such as haematomas and Alzheimer’s disease, but it is
not approved for these uses. Despite its
initial intended use, Ceretec’s
most widespread use is in blood cell labelling.
The complex is neutral and lipophilic and its
relative ‘instability’ is thought to be the main reason why it can be
multifunctional. The exact mechanism is unknown; however, it has been
shown in plasma and in vitro that Ceretec crosses the cell membrane and
reacts with intra-cellular components which convert it to a secondary
hydrophillic form that cannot recross the membrane to exit the cell.$^{3}$ $d,l$ and
meso isomers exist, but the meso isomer is not retained in the brain as long
and is less effective than the $d$ and $l$ isomers.

$^{99m}$Tc-sestamibi (Cardiolite™) is an octahedral cationic technetium (I)
complex designed as a myocardial perfusion imaging agent for evaluating the
integrity of myocardium (abnormal vs. normal). Unsubstituted alkylisocyanides
and alkylisonitrile esters were investigated initially, but background radiation in the liver and lungs and short retention times were observed. Complexes with ether groups; however, were retained in the heart and showed better background clearance and longer retention times. Functionalization of the isonitrile groups with ether derivatives improved background clearance due to what was believed to be metabolism of the lipophilic ethers to hydrophilic hydroxyl groups in the liver which are then subject to further metabolism and elimination.

Approval for breast imaging was recently given for $^{99m}$Tc-sestamibi as Miraluma™.

$^{99m}$TcOMAG$_3^-$ (TechneScan-MAG$_3$), developed by Fritzberg and Davison, is marketed as a renal imaging agent. The anionic oxotechnetate(V) complex consists of an N$_3$S donor atom system exhibiting square pyramidal geometry with the oxo group in the apical position and the central metal slightly above the basal plane. The uncoordinated carboxylate group in the deprotonated dianion is important for efficient clearance.

$^{67}$Ga-citrate (Neoscan) has been found to be successful in the diagnosis of primary and metastatic tumours. The exact mechanism is unknown; however, it is known that $^{67}$Ga is transchelated to transferrin as soon as it is injected into the blood stream. It mimics the ferric ion in its binding to
molecules in serum and accumulates in lysosomes bound to intracellular protein.\textsuperscript{2,3,11} Gallium is not reduced \textit{in vivo} and it does not become incorporated into haemoglobin, hence it does not affect the oxygen carrying capacity of red blood cells. The exact structure is not known; however, there are presumably three waters filling the remaining coordination sites.\textsuperscript{1,2}

\textsuperscript{153}Sm(EDTMP)\textsuperscript{5-} involves a tetraphosphonate ligand and shows \textit{in vivo} localization comparable to the \textsuperscript{99m}Tc-diphosphonate bone agents.\textsuperscript{12} The primary application of \textsuperscript{153}Sm(EDTMP) is as a radiotherapeutic agent for the palliative treatment of metastatic bone cancer pain.\textsuperscript{1,2} Samarium-153 is a beta ($\beta^-$) emitting radiolanthanide with a near two day half-life, which is ideal for radiotherapeutic applications. A low energy gamma ray suitable for scintigraphic imaging is also emitted. The complex binds to the hydroxyapatite crystals of the bone and is retained on the bone while the unbound \textsuperscript{153}Sm is rapidly cleared by the blood. The added bonus of a gamma ray allows the distribution of the compound to be monitored during therapeutic application. The exact structure is not known, but using the empirical formula it is believed to contain three coordinated waters in addition to the six bound atoms of EDTMP\textsuperscript{8-}.\textsuperscript{1,2} This complex is not yet approved for clinical application.

Different applications require radionuclides with different nuclear properties. Diagnostic imaging agents must have radiation which can penetrate the body with minimal cell destruction and which can be detected by external
instrumentation. Radionuclides decaying by gamma ray (γ) or positron (β+) emission and having a relatively short half-life (less than 24 hours) are suitable for diagnostic applications. Radiotherapeutic application involves cell destruction, thus decay by particle emission (α, β−, Auger e−) and a half-life of from one to ten days are ideal properties. The half-life and mode of decay are dependent on the desired application. Imaging and therapeutic applications have opposite requirements and goals, but both share one common objective, whereby target specificity and a high target-to-background ratio are essential to the success of either directive.

The radiopharmaceutical chemist's periodic table (Figure 1.1) shows the majority of the most medically useful radionuclides, yet some chemical form of

\[ \text{Figure 1.1. Radiopharmaceutical chemist's periodic table. Split patterns indicate more than one applicable radioisotope.} \]
\(^{99m}\text{Tc}\) is used in 90% of all diagnostic scans performed in nuclear medicine departments in the North America.\(^4\) Technetium was the first of the artificially produced elements (discovered by Perrier and Segrè in 1937). Twenty-one isotopes of mass number 90 - 110 and several metastable isomers (designated with 'm') are known, and technetium metal complexes of oxidation states between -1 and +7 with coordination geometries between 4 and 9 exist. \(^{99}\text{Tc}\) is produced in gram quantities from \(^{235}\text{U}\) fusion and is the only isomer used for macroscopic chemical studies, usually as ammonium pertechnetate, \([\text{NH}_4][\text{TcO}_4]\), because of its long half-life (\(t_{1/2} = 2.11 \times 10^5\) y) and moderate \(\beta^+\) decay energy of 293 keV. \(^{99}\text{Tc}\) is also produced by means of gamma ray decay from its parent, \(^{99m}\text{Tc}\), which is easily obtained from a \(^{99}\text{Mo}/^{99m}\text{Tc}\) generator via elution through an anion exchange column with saline solution. \(^{99m}\text{Tc}\) is widely used because of its ideal nuclear properties (\(t_{1/2} = 6.02\) hr, \(E_\gamma = 140\) keV (89%)) and its ease of availability.\(^1\)\(^-\)\(^4\) There are no accompanying \(\beta^-\) emissions and the gamma ray energy is appropriate for detection by commercial gamma cameras. The half-life is long enough to prepare and administer the radiopharmaceutical, yet short enough to minimize the radiation dose to the patient. In a 1990 estimate, six to seven million administrations of \(^{99m}\text{Tc}\) radiopharmaceuticals are performed each year in the United States,\(^1\)\(^-\)\(^4\) hence the desire to develop new or improved target-specific agents is growing.

The high-energy \(\beta^-\) emitting rhenium radionuclides show promise as therapeutic agents. Rhenium is a group VII congener of technetium and the periodic relationship between the two metals enables the design of rhenium radiopharmaceuticals by analogy to already existing technetium diagnostic agents. \(^{186}\text{Re}\) has a half-life of 90 hours and emits two \(\beta^-\) particles with
energies of 1.07 MeV (77%) and 0.934 MeV (23%) as well as a gamma ray ($E\gamma = 137$ keV (9.2%)). $^{188}$Re has a half-life of 17 hours and emits a $\beta^-$ particle (2.1 MeV) and a gamma ray ($E\gamma = 155$ keV (15%)).\textsuperscript{1} These radionuclides are ideal for therapeutic and diagnostic applications because of their longer half-lives and $\beta^-$ particle emissions, combined with gamma ray emission. A 'localized' high energy radiation dose is delivered to the tissues over a longer, therapeutic period of time, while the additional gamma ray can be used along with a gamma camera as a diagnostic tool.

The use of a chelating ligand to form 5- and 6-membered rings upon complexation to a metal is of growing interest in nuclear medicine and in the design of radiopharmaceuticals. In designing a potential ligand, the type of donor atom, the size of the metal chelate ring formed upon coordination, and the overall coordination number of the metal ion must be considered.\textsuperscript{1-3} Complexes of polyaminocarboxylate ligands have been thoroughly investigated over the past thirty years, whereas complexes with polyaminopyridyl ligands have not been as extensively studied. Of particular interest are tetra- and hexadentate ligands with a single type of donor atom or containing a variety of donor atoms in various combinations (Figure 1.2).\textsuperscript{13-29}

Ethylenediamine-N,N,N',N'-tetraacetate (edta$^4^-$) is an example of a polyaminocarboxylate ligand having two nitrogen and four oxygen donor atoms that can form five 5-membered chelate rings around a single metal centre or act as a bridging ligand between two metal centres.\textsuperscript{1,4} The initial use of edta$^4^-$ was as a synthetic calcium binding additive in the manufacture of dyes in the mid 1930's in Germany.\textsuperscript{30,32} It was later discovered that its high affinity for positively charged metal ions was ideal for leeching metal ions from biological and chemical systems. From its early use in chelation therapy for the
treatment of lead poisoning, applications of edta\(^4\)- grew to encompass treatments for atherosclerosis, cardiac ailments, coronary artery disease, high blood pressure, and arthritis between the 1950's and 80's.\(^{31,32}\) Its incorporation into nuclear medicine was in the areas of labelling antibodies and measuring the glomerular filtration rate (GFR) in the kidneys.\(^1\) Edta\(^4\)- is a bifunctional chelating (BFC) agent in the labelling of antibodies because it has the ability to covalently bind to the antibody. Radionuclides of indium and other trivalent metals such as gallium and yttrium form the most stable chelates with edta\(^4\)-. A \(^{51}\)Cr—edta complex is used to measure the degree of renal impairment in patients with renal disease.\(^1\) The GFR is measured by
monitoring the clearance rate of the radiopharmaceutical from the blood. The use of edta$^{4-}$ in nuclear medicine decreased due to its lack of metal ion specificity and depletion of essential minerals during application. Hypocalcaemia, acute lead poisoning, insulin shock and nephrotoxic side reactions were common occurrences during treatment.\textsuperscript{30,32} Newer compounds, such as DTPA, that formed more stable complexes and had a greater degree of specificity were developed and these eventually replaced edta$^{4-}$.

The ethylenediamine (en) moiety is an ideal unit for constructing a multidentate ligand because the amino group is easily functionalized to incorporate other donor atoms. The most favourable donor atoms for technetium are N, P, S, and O in amine, amide, phosphine, thiol, oxime, and isonitrile functional groups.\textsuperscript{2} The N atom is an ideal donor atom for planar chelate ring-forming molecules. If the donor atoms are kept in close proximity to each other, a maximum number of 5- and 6-membered chelate rings can form upon metal ion complexation.\textsuperscript{33} Hancock notes that larger metal ions coordinate to smaller chelate rings with less ligand strain compared to smaller metal ions.\textsuperscript{34} Hexadentate ligands which contain five 5-membered chelate rings upon coordination, such as edta$^{4-}$, may result in larger metal ions adopting a coordination number of seven by coordinating an additional unidentate ligand.\textsuperscript{35} The longer M—O and M—N bond lengths in a seven coordinated complex impart less strain in the ligand. Smaller metal ions, which cannot adopt a higher coordination number of seven, may reduce strain by substituting solvent for one of the donor atoms.\textsuperscript{34}

In this research, the ethylenediamine (en) moiety was used in conjunction with 2-pyridylmethyl units to form N,N'-bis(2-pyridylmethyl) ethylenediamine (H$_2$pmen, bispicen). In H$_2$pmen, the picolyl arms provide two
heterocyclic nitrogen atoms in addition to the two basic aliphatic N atoms
provided on the en backbone to produce a N₄ tetradeutate system. H₂pmen is
a linear type molecule with the N atoms linked by 2-carbon chains (a, b, and c)
(Scheme 1.1A). When complexed to a metal, the molecule is capable of
forming an open-chain tetradeutate ligand with three 5-membered chelate rings
(x, y, and z) around the central metal ion (Scheme 1.1B). The localized lone
pair of electrons on the ethylenediamine and pyridine nitrogens should

\[
\text{N}_{\text{py}} \quad \overset{a}{\text{N}}_{\text{en}} \quad \overset{b}{\text{N}}_{\text{en}} \quad \overset{c}{\text{N}}_{\text{py}}
\]

\[
\text{A}
\]

\[
\text{N}_{\text{en}} \quad \overset{a}{\text{N}}_{\text{en}} \quad \overset{b}{\text{N}}_{\text{en}} \quad \overset{c}{\text{N}}_{\text{en}}
\]

\[
\text{B}
\]

\[
\text{N}_{\text{py}} \quad \overset{a}{\text{N}}_{\text{py}} \quad \overset{b}{\text{N}}_{\text{py}} \quad \overset{c}{\text{N}}_{\text{py}}
\]

\[
\text{C}
\]

\[
\text{Scheme 1.1. Linear tetradeutate ligand orientation around a metal centre}
\]

coordinate easily to the metal centres. In linear type molecules the terminal
donor atoms (Nₚₚ) and the metal atom lie in the coordination plane; however, it
is not essential that the penultimate donor atoms (Nₑₑ) lie in the plane also.²⁹ A
combination of short chain lengths, planarity of the chelate rings, and the Nₑₑ
donor atom's ability to bond to at least three other atoms (including the metal
ion) necessitate that the Nₑₑ atoms and the three attached atoms lie in the
plane of coordination containing the metal ion and the terminal Nₚₚ donor
atoms. Buckling may result across the line of centres of the Nₑₑ donor atoms
in order to maintain the planarity of the chelate rings (x and z) and to reduce
ring strain due to the short chain lengths between the donor atoms (Scheme 1.1C). The neutrality of the compound and the lipophilic pyridyl units may offer potential applications for crossing the blood-brain barrier. The addition of an acetate group to each amine group in the en backbone unit produced a potential N₄O₂ system in N,N'-bis[2-pyridylmethyl]ethylenediamine-N,N'-diacetate (bped²⁻, edampda). The bped²⁻ molecule should follow the same N₄ coordination as pmen²⁻ with the acetate groups pendant or coordinated.

H₂pmen¹,²,⁶,¹³,¹⁵,¹⁹,²⁰,²⁶,²⁷,⁴⁷,⁴⁸,³⁶-³⁹ and H₂bpедин⁰,⁰,²⁸,⁴⁰,⁴¹ (Figure 1.3) have been extensively investigated over the past 30 years with di- and trivalent metal ions and have been shown to have planar N₄ configurations. H₂Pmen has also shown configurations with the Nen donor atoms out of the Npy-M-Npy plane of coordination.⁴⁸ No study has been undertaken for group VII metals. This work focuses on forming complexes with oxorhenium(V) and oxotechnetium(V) involving pmen²⁻ and bpedin²⁻ molecules in attempts to investigate potential applications in nuclear medicine. The oxo form of the metals are used because of their ease of availability and predominance. Mono- and dioxo metals centres are possible from the reduction of the [NH₄][M(VII)O₄] centre in the presence of the potential ligand using a reducing agent such as sodium dithionite or stannous chloride in a one-pot synthesis. Reduced monooxo precursor units, such as [Bu₄N][ReOBr₄] or [ReO(PPh₂)Cl₃] can also be prepared via a variety of synthetic pathways. The [TcO]³⁺ and [ReO]³⁺ metal centres tend to prefer square pyramidal and octahedral geometries. Complexation of bpedin²⁻ with the [TcO]³⁺ and [ReO]³⁺ metal centres should give rise to a tetra-, penta-, or hexadentate ligand depending on whether none, one, or both of the carboxylates on the acetate arms coordinate to the metal centre.
Distortion may occur in the presence of the hexadentate bped\textsuperscript{2-} if the ligand is fully coordinated producing a seven coordinate complex. The possible combinations in which the donor atoms may coordinate will influence the overall charge on the complex and its applicability as a potential radiopharmaceutical.

Attempts to develop an alternative synthetic route for H\textsubscript{2}bped led to the first time synthesis of methyl, ethyl, and tert-butyl ester derivatives of H\textsubscript{2}pmen (pmen-OMe, pmen-OEt, and pmen-OBu\textsuperscript{t}) (Figure 1.3). In attempting to complex the pmen-esters with [TcO]\textsuperscript{3+} and [ReO]\textsuperscript{3+} metal centres it was hoped that the esters would maintain the same N\textsubscript{4} system coordination characteristics as pmen\textsuperscript{2-}, with the ester arms remaining free from coordination. The pendant ester arms in turn could be hydrolysed to produce carboxylate functional groups which might coordinate with the metal centre. The respective pH at which the complex will dissociate and the number of oxo groups on the metal centre are two important considerations that must be taken into account before this occurs. Too low a pH will dissociate the ligand from the metal and a dioxo metal centre may not allow an additional two coordination sites around the metal centre. However, if this idea proves successful, there would be an alternative pathway to the formation of the metal-bped complex. These tetradentate pmen-ester derivatives' abilities to form complexes with [TcO]\textsuperscript{3+} and [ReO]\textsuperscript{3+} metal centres were also investigated.

Three new complexes were synthesized in this work: [ReO(pmen)][ReO\textsubscript{4}], [ReO(bped)]Br, and [TcO(bped)]Cl. The complexes were difficult to make and no pure samples or x-ray quality crystals were obtained. The elemental analyses were not unambiguous; however, positive LSIMS mass spectroscopy,
infrared spectroscopy, and $^1$H NMR spectroscopy showed strong evidence of the presence of the desired complexed metal centre. Structures of the three complexes were proposed using the spectroscopic results.

A considerable amount of effort and time was expended synthesizing the pmen$^{2-}$ and bped$^{2-}$ complexes. It is hoped that future investigations will succeed at improving the purity and determining the structures of the complexes. Once the pure complexes are isolated, the potential of these complexes as radiopharmaceuticals can be investigated.
II. Experimental

II.1 Materials and Instrumentation

Materials.

Ethylenediamine-N,N'-diacetic acid, ethylenediamine, 2-pyridine carboxaldehyde, 2-(chloromethyl)pyridine hydrochloride, bromoacetic acid, methylbromoacetate, ethylbromoacetate, tert-butylbromoacetate, tetrabutylammonium bromide, sodium tetraphenylborate, sodium tetrafluoroborate, tetra(n-propyl)ammonium hexafluorophosphate, sodium triflate, sodium perchlorate, and sodium hexafluorophosphate were obtained from Aldrich. Cetyltrimethylammonium bromide and sodium acetate were obtained from BDH and triethylamine was from Fisher. Deuterium oxide ($D_2O$) and deuterated chloroform ($CDCl_3$) were purchased from Cambridge Isotope Laboratory (C.I.L.). Ammonium perrhenate and ammonium pertechnetate were gifts from Johnson-Matthey Pharmaceuticals and Dupont Merck Pharmaceuticals, respectively. All were used without further purification. All solvents were distilled from their appropriate drying agents.41

$[\text{Bu}_4\text{N}][\text{ReOBr}_4]^{43}$, $[\text{Bu}_4\text{N}][\text{ReOBr}_4(\text{H}_2\text{O})]^{44}$, $\text{PBu}_3^{44}$, $[\text{Bu}_4\text{N}][\text{TcOCl}_4]^{45}$, and $\text{N},\text{N}'$-bis(2-pyridylmethyl)ethylenediamine-N,N'-diacetic acid dihydrochloride ($H_2\text{bpéd}\cdot 2\text{HCl}$)40 were all synthesized by published procedures.

Caution! Technetium-99 is a weak $\beta$-emitter ($0.292$ MeV, $T_{1/2} = 2.12 \times 10^5$ years). All manipulations of solutions and solids were carried out in a laboratory approved for the handling of low-level radioisotopes, and normal safety procedures were followed at all times to prevent contamination.
Instrumentation.

$^1$H NMR (200 MHz and 300 MHz) and $^{13}$C NMR (50.3 MHz) spectra were referenced to TMS and recorded on Bruker AC-200E and Varian XL300 spectrometers. $^1$H COSY spectra were recorded on a Bruker AC-200E spectrometer. Mass spectra were obtained with a Kratos Concept II H32Q (Cs$^+$, LSIMS) instrument. Infrared spectra were obtained as KBr discs (solids) or using NaCl plates (oils) in the range 4000-400 cm$^{-1}$ on a Galaxy Series FTIR 5000 spectrophotometer and referenced to polystyrene. Analyses of C, H, and N were performed by Peter Borda in this department.

II.2 Syntheses of Ligands

$\textit{N,N'}$-Bis(2-pyridylmethyl)ethylenediamine ($\textit{H}_2\textit{pmen}$). This was prepared by a variation on a literature method.$^{14}$ Methanol solutions (30 mL) of ethylenediamine (5.39 g, 89.8 mmol) and 2-pyridine carboxaldehyde (20.27 g, 189 mmol) were combined to give a clear dark amber solution at room temperature. Sodium borohydride (8.49 g, 224 mmol) was added slowly giving rise to a vigorous exothermic effervescence. After two hours, the solvent was removed under reduced pressure and the resultant yellow solid was dissolved in 10% ammonium chloride (90 mL). The crude product was extracted with chloroform (3 x 75 mL) and the combined fractions dried (MgSO$_4$). The solvent was removed and the yellow-orange oil was dissolved in ethanol and 12 N HCl was added to produce the HCl salt. The resulting white precipitate was collected by suction filtration (Anal. Calc (found) for $\text{C}_{14}\text{H}_{18}\text{N}_4\cdot\text{HCl}$: C, 43.42 (43.50); H, 5.80 (6.00); N, 14.26 (14.09)), dissolved in water (150 mL), and raised to pH 12 with 5 N NaOH. The product was extracted with chloroform.
(3 x 75 mL) and dried. The solvent was removed under reduced pressure and the pale yellow oil was dried under vacuum. Yield: 14.6 g (67%). MS (+LSIMS): \(^{m/z}\) 243 ([M+H]+, \([C_{14}H_{19}N_4]^+\)). \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.85 (s, 2H), 2.34 (s, 4H), 3.48 (s, 4H), 6.65 (t, 2H), 6.89 (d, 2H), 7.13 (t, 2H), 8.05 (d, 2H). Exposure to light turns the oil a darker yellow colour and decomposes the molecule. The oil should be stored in a cool location away from any light source.

Esters

The 'pmen' ester derivatives were all prepared by a similar procedure analogous to one in the literature\(^{46}\); the preparation is given in detail only for the methyl ester.

**N,N'-Bis(methylcarboxymethyl)-N,N'-bis(2-pyridylmethyl) ethylenediamine (pmen-O\(_\text{Me}\)).** To a 30 mL methylene chloride solution of N,N'-bis(2-pyridylmethyl)ethylenediamine (0.988 g, 4.08 mmol) and diisopropylethylamine (1.51 g, 11.7 mmol) was added dropwise methylbromoacetate (1.58 g, 10.4 mmol) in 15 mL methylene chloride. After stirring the reaction for 24 h, the solvent was removed under reduced pressure and placed under vacuum for 3 h to remove any excess diisopropylethylamine. The crude oil was dissolved in 50 mL methylene chloride, washed with 0.2 N NaOH (50 mL), water (2 x 15 mL), brine (12 mL), and dried over MgSO\(_4\). The solvent was removed and 10 mL of ethylacetate was added to the red-brown oil to give a clear crimson red solution, which was passed through 5 g of silica gel in a glass frit and eluted with ethylacetate. The
pure clear yellow fractions (TLC: MeOH/CH₂Cl₂: 3/7) were combined and the solvent removed under reduced pressure, with several washings with methylene chloride to remove any residual ethylacetate to give 0.60 g (41%) of a dark brown-red oil. Elemental analysis of the oil was not done. MS (+LSIMS): m/z 387 ([M+1]+, [C₂₀H₂₇N₄O₄]+). ¹H NMR (CDCl₃): δ 2.10 (s, 2H), 2.75 (s, 2H), 3.40 (s, 2H), 3.62 (s, 3H), 3.85 (s, 2H), 7.06 (t, 2H), 7.39 (d, 2H), 7.62 (t, 2H), 8.45 (d, 2H). The oil should be stored in a cool place because the colour of the oil darkens to a brown-black colour and the molecule decomposes over a few weeks.

N,N'-Bis(ethylcarboxymethyl)-N,N'-bis(2-pyridylmethyl) ethylenediamine (pmen-OEt). Substituting ethylbromoacetate for methylbromoacetate produced a red-brown oil. Yield: 47%. MS (+LSIMS): m/z 415 ([M+1]+, [C₂₂H₃₁N₄O₄]+). ¹H NMR (CDCl₃): δ 1.16 (t, 6H), 2.78 (s, 4H), 3.37 (s, 4H), 3.86 (s, 4H), 4.08 (q, 4H), 7.08 (t, 2H), 7.39 (d, 2H), 7.55 (t, 2H), 8.43 (d, 2H).

N,N'-Bis(tert-butylcarboxymethyl)-N,N'-bis(2-pyridylmethyl) ethylenediamine (pmen-OBut). Substitution of methylbromoacetate with tert-butylbromoacetate gave a red-brown oil. Yield: 48%. MS (+LSIMS): m/z 471 ([M+1]+, [C₂₆H₃₉N₄O₄]+). ¹H NMR (CDCl₃): δ 1.36 (t, 9H), 2.75 (s, 4H), 3.25 (s, 4H), 3.87 (s, 4H), 7.05 (t, 2H), 7.40 (d, 2H), 7.53 (t, 2H), 8.42 (d, 2H).

II.3 Syntheses of Metal Complexes

[ReO(bped)]Br. To a refluxing solution of H₂bped•2HCl (60.5 mg, 0.140 mmol) in 10 mL of a methanol/ethanol mixture (MeOH/EtOH: 2/3) was added
sodium acetate (77.1 mg, 0.567 mmol) to produce a clear pale yellow solution. The solution was refluxed for ten minutes and a red acetonitrile solution (3 mL) of [Bu₄N][ReOBr₄] (100 mg, 0.131 mmol) was added dropwise to give a clear green solution. Refluxing was continued for 30 minutes and the solution was then left to stir for 2 days at room temperature. A grey solid was filtered off and the solvent of the filtrate was removed under reduced pressure. The resulting dark green solid was washed with acetone and the insoluble product was collected, dissolved in a minimum amount of methanol, passed through 150 mL of Sephadex LH20, and eluted with methanol. The fractions were collected and the solvent removed. All attempts to crystallize the product failed. Yield: 21 mg (43 %) based on the metal. MS (+LSIMS): m/z 559 ([M]+, [ReO(C₁₈H₂₀N₄O₄)]⁺). Anal. Calc (found) was fitted for ReO(C₁₈H₂₀N₄O₄)Br •[Bu₄NBr]₀.₄₅ •(NaOAc)₀.₇: C, 37.99 (37.90); H, 4.59 (4.51); N, 7.41 (7.47).

[TcO(bped)]Cl. To a clear, pale yellow methanol solution (4 mL) of H₂bped•2HCl (77.8 mg, 0.182 mmol) and sodium acetate (98.8 mg, 0.726 mmol) was added dropwise [Bu₄N][TcOCl₄] (87.6 mg, 0.176 mmol) in MeOH (2 mL). The solution was stirred for 2 days and left to stand for 2 days. A grey precipitate was then filtered out leaving a clear, dark orange-brown filtrate. The solvent was removed under reduced pressure, the crude product was filtered and washed with acetone. The product was dissolved in methanol; the solution was loaded onto 150 mL Sephadex LH20, and eluted with methanol. The brown layer was collected and the solvent removed to produce a brown solid, which was dried under vacuum for 24 hours. All attempts to
crystallize with various anions were unsuccessful. Yield: 35 mg (39 %) based on the metal. MS (+LSIMS): $m/z$ 471 ([M]$^+$, [TcO(C$_{18}$H$_{20}$N$_4$O$_4$)$^+$]. No elemental analysis of the radioactive sample was performed. $^1$H NMR: (CD$_3$OD): $\delta$ 3.72 (AB, 4H), 3.74 (AB, 4H), 4.82 (AB, 4H), 7.72 (m, 2H), 8.21 (t, 2H), 9.28 (d, 2H).

[ReO(pmen)][ReO$_4$]. To a stirring acetonitrile solution (3 mL) of bis(2-pyridylmethyl)ethylenediamine (205 mg, 0.846 mmol) was added sodium acetate (145 mg, 1.76 mmol) in methanol (3 mL) to give a clear yellow solution. The solution was degassed with nitrogen for 20 minutes before the dropwise addition of [Bu$_4$N][ReOBr$_4$] (430 mg, 0.563 mmol) in acetonitrile (5 mL), which produced a dark purple-black solution. The solution was allowed to stir 24 h at room temperature which yielded a violet precipitate. The violet powder was soluble only in DMSO and DMF, in which it changed from a cloudy violet solution to a clear yellow-orange solution. Yield: 151 mg (41%) based on metal. MS (+LSIMS): $m/z$ 443 ([M]$^+$, [ReO(C$_{14}$H$_{16}$N$_4$)]$^+$). Anal. Calc (found) was fitted for [ReO(C$_{14}$H$_{16}$N$_4$)][ReO$_4$]$\cdot$HCl: C, 23.61 (23.06); H, 2.36 (2.35); N, 7.77 (7.68). $^1$H NMR (DMSO-$d_6$): $\delta$ 4.18 (AB, 4H), 5.16 (AB, 4H), 7.68 (td, 2H), 7.90 (d, 2H), 8.15 (t, 2H), 9.62 (d, 2H).
III. Results and Discussion

III.1 Ligands: Design and Syntheses

H₂bped was originally synthesized by Martell as a mono sodium salt by means of a multi-step process and later as a dihydrochloride salt by Caravan using a one-pot synthesis with a considerably higher yield. The Caravan synthesis is shown in Scheme 3.1. Douglas formed a Co(III) complex using a one pot synthesis by assembling the ligand around the central metal. The potential of bped²⁻ as a ligand for applications in nuclear medicine is high given its tendencies to form five 5-membered chelate rings with di- and trivalent transition metals and the lanthanides. This study attempted to synthesize and investigate bped²⁻ complexes of [ReO³⁺] and [TcO³⁺] metal centres as potential radiopharmaceuticals.

There was also interest with the potential N₄ system associated with H₂pmen. In this study, only H₂pmen and H₂pmen·4HCl were synthesized.
(Scheme 3.2) and investigated. Earlier studies on H₂pmen conducted with various transition metals have shown both planar and non-planar coordination around the metal centre. The neutral H₂pmen molecule was ideal in organic solvents for metathesis reactions. H₂pmen·4HCl was useful in aqueous conditions where the reduction of [TcO₄]⁻ and complexation can be done in a one-pot synthesis.

![Scheme 3.2: Synthesis of H₂pmen and H₂pmen·4HCl.](image)

The preparation of H₂bped by means of the Caravan method gave reproducibly low yields and the consistent appearance of a contaminant that transformed the product into a yellow hygroscopic oil. These problems led to the search for alternative means of synthesizing H₂bped. The Caravan one-pot H₂bped synthesis had a small degree of sodium ions present in the final product. Some different approaches were tried to improve the yield and increase the purity of the product.
Sodium hydroxide (NaOH) was the principal base in the reaction and contamination in the final product was due to the presence of sodium ions as NaCl. H₂bped was a beige powder when slowly precipitated out of solution. Rapid precipitation of H₂bped produced a white powder with an increased level of sodium ions in the product. The white H₂bped gave greater yields, but generally formed a yellow hygroscopic oil when exposed to the atmosphere, due to an additional unknown contaminant. Potassium hydroxide (KOH) was tried in an attempt to eliminate sodium from the product, but the KOH had no affect on the overall yield and purity of the product. The yellow hygroscopic oily product was again present upon recrystallization and exposure to the atmosphere.

A second approach (Scheme 3.3) was to add the acetate groups separately to the N,N'-bis(2-pyridylmethyl)ethylenediamine (H₂pmen) unit using bromoacetic acid and follow the exact same procedure as the one-pot Caravan synthesis. Similar results were obtained from this synthesis with the appearance of the hygroscopic yellow oil. The yields were low and the small amount of product obtained showed evidence of sodium ion contamination. Different solvents of recrystallization were tried; however, there was no change in the overall appearance of the final product.
The formation and hydrolysis of an ester was tried. Acetate ester derivatives were attached to H₂pmen in place of the acetate groups. Methyl-, ethyl-, and t-butyl-ester derivatives of H₂pmen were prepared for the first time. All three pmen-ester products existed as red-brown oils (Scheme 3.4).
Base hydrolysis of the esters was tried using KOH or barium hydroxide, \( \text{Ba(OH)}_2 \), in a warm methanol solution. Within five minutes the KOH hydrolysis produced a salt which precipitated out of solution. \( \text{Ba(OH)}_2 \) did not give a salt immediately, but the \( \text{Ba}^{2+} \) was eliminated as a white \( \text{BaSO}_4 \) salt with the addition of concentrated \( \text{H}_2\text{SO}_4 \). \(^1\text{H}\) NMR spectroscopy confirmed that \( \text{H}_2\text{bped} \) was not produced via either of the base hydrolysis techniques.

Acid hydrolysis using 6M HCl was mildly successful. A flaky brown solid was obtained after the solvent was removed and the product was dried under vacuum. The pmen-\text{OBu}^\text{t} ester was the most successful of the three pmen-ester derivatives. \(^1\text{H}\) NMR spectroscopy confirmed the ester was hydrolysed to \( \text{H}_2\text{bped} \); however, there were unknown impurities present. Recrystallizing from methanol-acetone or ethanol-acetone solvent combinations produced a white precipitate, but the solid rapidly turned yellow and transformed into a yellow oily residue when exposed to air. The hygroscopic residue was recoverable by dissolving it in methanol, ethanol, or water, but numerous attempts at recrystallization routinely resulted in the reproduction of the hygroscopic oily product. The use of anionic and cationic exchange columns before attempting to recrystallize the product were unsuccessful in removing the unknown impurity that caused the product's moisture sensitivity.

### III.2 Ligands: Characterization

A characterization profile, consisting of mass spectroscopy, elemental analysis, infrared spectroscopy, and \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectroscopies, was performed on all the potential ligands.
III.2.1 Mass Spectroscopy and Elemental Analysis. Positive(+) LSIMS mass spectral studies showed strong parent peaks for [M+1]+ with the expected isotope patterns. No distinctive impurities or molecular fragments were visible with any significant intensity in any of the spectra.

Elemental analyses were conducted only on H$_2$bped and H$_2$pmen•4HCl. H$_2$pmen and the pmen-ester derivatives were oils so C,H,N analyses were not performed. The H$_2$bped analysis showed the presence of three hydrochlorides present due to a protonated carboxylate as a result of excess HCl used during the protonation process. H$_2$pmen•4HCl showed an elemental analysis within an experimental error of ± 0.3%.

III.2.2 Infrared Spectroscopy. Studies were performed with KBr discs for the salts (H$_2$bped•2HCl, H$_2$pmen•4HCl) and with NaCl plates for the oils (H$_2$pmen, pmen-OMe, pmen-OEt, pmen-OBu†). Table 3.1 lists the infrared resonances and the appropriate assignments for the spectra shown in Figure 3.1 and Figure 3.2. Given the similarities among all the potential ligands, consistent absorption frequencies were observed in all the product spectra. All molecules showed strong absorptions for the (N—H) and (C—H) stretching modes in the 3200–2400 cm$^{-1}$ region. H$_2$bped•2HCl and H$_2$pmen•4HCl showed a pronounced broadening of the (N—H) and (C—H) signal characteristic of strong intramolecular hydrogen bonding of the protonated N atoms. Strong carbonyl (C=O) stretching frequencies were evident in H$_2$bped•2HCl and the pmen-ester derivatives within the expected region of 1750–1730 cm$^{-1}$.

Pyridine (C=N) and (C=C) ring deformations were consistently observed within 1626–1434 cm$^{-1}$ for all the molecules. H$_2$pmen and its ester derivatives
**Table 3.1.** IR stretching frequencies\(^a\) (cm\(^{-1}\)) of potential ligands.

<table>
<thead>
<tr>
<th>Assignment</th>
<th>(\text{H}_2\text{bped} \cdot 2\text{HCl})(^b)</th>
<th>(\text{H}_2\text{pmen} \cdot 4\text{HCl})(^b)</th>
<th>(\text{H}_2\text{pmen})(^c)</th>
<th>pmen-OMe(^c)</th>
<th>pmen-OEt(^c)</th>
<th>pmen-OBu(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\nu(\text{N—H}))</td>
<td>3500-3200 s, br</td>
<td>3255 s, br</td>
<td>3301 s, br</td>
<td>3386 w</td>
<td>3396 m, br</td>
<td>3395 w, br</td>
</tr>
<tr>
<td>(\nu(\text{C—H}))</td>
<td>3000-2500 s, br</td>
<td>3100-2300 s, br</td>
<td>3100-2800 m, br</td>
<td>3100-2800 m, br</td>
<td>3000-2800 m, br</td>
<td></td>
</tr>
<tr>
<td>(\nu(\text{C=O}))</td>
<td>1728 vs</td>
<td>—</td>
<td>—</td>
<td>1740 vs</td>
<td>1738 vs</td>
<td>1735 vs</td>
</tr>
<tr>
<td>(\nu(\text{C=N}))(_{\text{ring}})</td>
<td>1612 s</td>
<td>1616 s</td>
<td>1591 s</td>
<td>1675 s</td>
<td>1659 s</td>
<td>1660 s</td>
</tr>
<tr>
<td>(\nu(\text{C=C}))(_{\text{ring}})</td>
<td>1548 m</td>
<td>1545 s</td>
<td>1568 s</td>
<td>1591 s</td>
<td>1591 s</td>
<td>1591 s</td>
</tr>
<tr>
<td></td>
<td>1521 m</td>
<td>1514 s</td>
<td>1474 s</td>
<td>1574 s</td>
<td>1574 s</td>
<td>1574 s</td>
</tr>
<tr>
<td></td>
<td>1463 m</td>
<td>1468 s</td>
<td>1434 s</td>
<td>1474 s</td>
<td>1474 s</td>
<td>1474 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1434 s</td>
<td>1434 s</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1203 vs</td>
<td>1194 vs</td>
<td>1154 vs</td>
</tr>
<tr>
<td>(\delta(\text{C—H}))(_{\text{out-of-plane}})</td>
<td>765 m</td>
<td>778 m</td>
<td>758 m</td>
<td>762 m</td>
<td>761 m</td>
<td>759 m</td>
</tr>
</tbody>
</table>

\(a\) Abbrev.: s= strong, m= medium, w= weak, br= broad, vs= very strong.  
\(b\) Sample analyzed as KBr disc.  
\(c\) Samples analyzed as liquid smear on NaCl disc.
Figure 3.1. IR spectra of H$_2$bped•2HCl (KBr disc), H$_2$pmen•4HCl (KBr disc), and H$_2$pmen (liquid smear on NaCl plate).
Figure 3.2. IR spectra of $\text{H}_2\text{pmen}$ and pmen-esters. All samples analyzed as a liquid smear on a NaCl plate.
showed very strong correlation among themselves and with previous studies of $H_2pmen$. $^{14,38}$ A number of common absorptions were visible in the 1387–757 cm$^{-1}$ region$^{52}$ for all of the products. Out-of-plane C–H bending of the methylene on the picolyl group occurred in the 781–740 cm$^{-1}$ region$^{52}$ for all the samples.

**III.2.3 NMR Spectroscopy.** $^1H$ NMR studies were done in two solvents: deuterium oxide (D$_2$O) for $H_2bp$ed and $H_2pmen•4HCl$, and deuterated chloroform (CDCl$_3$) for $H_2pmen$ and the pmen-ester derivatives. $H_2pmen$ and $H_2pmen•4HCl$ were used as references for the chemical shifts between $H_2bp$ed•2HCl and the pmen-esters in different solvents. CD$_3$OD dissolved all the samples, but the solvent peaks masked some of the backbone signals. The $^1H$ NMR assignments are listed in Table 3.3 and referenced to Figure 1.3. The $^1H$ NMR spectra are shown in Figures 3.3 and 3.4. The $^1H$ NMR spectrum is divided into two sections: the backbone region, (0.0 - 6.0 ppm) and the pyridine region (6.5 - 9.0 ppm). The number of signal resonances and splitting patterns for each species in the backbone region were as expected. Singlets were observed for the methylene hydrogens on the ethylenediamine ($H_7$) and the methylene hydrogens on the picolyl ($H_6$) and methylene hydrogens on the acetate ($H_8$) arms.

The four pyridine hydrogen signals represent two symmetry-equivalent sets of four pyridine hydrogens. Two doublets and two triplets were expected from the splitting of each pyridine hydrogen by its adjacent hydrogen(s). $H_1$ was split into a doublet by $H_2$, and $H_4$ was split into a doublet by $H_3$. The more downfield doublet was assigned to $H_1$ based on increased shielding in the space between the two pyridine rings$^{27}$ and previous assignments of pyridine.
### Table 3.2. $^1$H NMR (200 MHz) spectral data\(^a\) for the potential ligands (solvent is CDCl\(_3\) unless specified)\(^b\)

<table>
<thead>
<tr>
<th></th>
<th>H(_2)bped・2HCl</th>
<th>H(_2)pmen・4HCl</th>
<th>H(_2)pmen</th>
<th>pmen-OMe</th>
<th>pmen-OEt</th>
<th>pmen-OBu(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(1)(^c)</td>
<td>8.65 dd</td>
<td>8.76 dd</td>
<td>8.08 dd</td>
<td>8.43 d</td>
<td>8.44 dq</td>
<td>8.47 d, sh 4.8</td>
</tr>
<tr>
<td>3(J_{12},3J_{13}) &amp; 5.8, 0.92</td>
<td>5.3, 0.76</td>
<td>4.5, 0.49</td>
<td>4.2</td>
<td>4.9, 0.70,(0.90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H(2)(^d)</td>
<td>7.89 td(^d)</td>
<td>7.97 td(^d)</td>
<td>6.66 td(^d)</td>
<td>7.06 td(^d)</td>
<td>7.07 td(^d)</td>
<td>7.09 td(^d)</td>
</tr>
<tr>
<td>3(J_{21},3J_{23}) &amp; 6.7, 1.0</td>
<td>7.1, 1.0</td>
<td>6.5, 1.3</td>
<td>6.2, 1.0</td>
<td>6.1, 1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H(3)(^c)</td>
<td>8.43 td</td>
<td>8.51 td</td>
<td>7.15 td</td>
<td>7.54 td</td>
<td>7.55 td</td>
<td>7.58 td 7.5, 1.8</td>
</tr>
<tr>
<td>3(J_{32},3J_{34}) &amp; 7.9, 1.6</td>
<td>7.3, 1.5</td>
<td>7.6, 1.6</td>
<td>7.6, 1.8</td>
<td>7.0, 1.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H(4)(^c)</td>
<td>7.99 d</td>
<td>8.09 d</td>
<td>6.87 d</td>
<td>7.37 d</td>
<td>7.42 d</td>
<td>7.45 d 7.8</td>
</tr>
<tr>
<td>3(J_{43}) &amp; 8.0</td>
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<td>7.8</td>
<td>7.8</td>
<td>7.7</td>
<td></td>
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<tr>
<td>H(6)</td>
<td>4.49 s</td>
<td>4.68 s</td>
<td>3.46 s</td>
<td>3.84 s</td>
<td>3.86 s</td>
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<td>H(7)</td>
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<td>2.36 s</td>
<td>3.58 s</td>
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<td>H(8)</td>
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<td></td>
<td>3.37 s</td>
<td>3.36 s</td>
<td>3.29 s</td>
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<tr>
<td>H(10)(^c)</td>
<td></td>
<td></td>
<td></td>
<td>2.77 s</td>
<td>4.06 q 7.1</td>
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<tr>
<td>3(J_{10-11}) &amp;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H(11)(^c)</td>
<td></td>
<td></td>
<td></td>
<td>1.17 t</td>
<td>7.1</td>
<td>1.40 s</td>
</tr>
<tr>
<td>3(J_{11-10}) &amp;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N —H</td>
<td></td>
<td></td>
<td></td>
<td>1.83 s</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) For labelling, see Figure 1.3; \(^b\) D\(_2\)O solvent; \(^c\) coupling constants (J) in Hz. \(^d\) Resonance appears to be a pair of overlapping dd that gives rise to shoulders in the central peak; Abbrev.: s= singlet, d= doublet, dd= doublet of doublets, t= triplet, td= triplet of doublets, q= quartet, dq= doublet of quartets, sh= shoulders.
Figure 3.3. $^1$H NMR (200 MHz) spectra of $\text{H}_2\text{bped} \cdot 2\text{HCl}$ (in $\text{D}_2\text{O}$), $\text{H}_2\text{pmen} \cdot 4\text{HCl}$ (in $\text{D}_2\text{O}$), and $\text{H}_2\text{pmen}$ (in $\text{CDCl}_3$). For labelling, refer to Figure 1.3.
Figure 3.4. $^1$H NMR (200 MHz) spectra of the pmen-esters in CD$_3$OD. For labelling refer to Figure 1.3.
hydrogens in [(NH$_3$)$_5$Ru(py)]$^{2+}$ and [(NH$_3$)$_5$Co(py)]$^{3+}$. H$_2$ was split by H$_1$ and H$_3$ to form a triplet, and H$_3$ was split by H$_2$ and H$_4$ to form a triplet. H$_3$ was assigned as the downfield triplet based on a greater stabilization of electron withdrawal in a para position, compared to a meta position, and previous assignments of pyridine hydrogens in [(NH$_3$)$_5$Ru(py)]$^{2+}$ and [(NH$_3$)$_5$Co(py)]$^{3+}$. The methylene hydrogen singlets and ester group resonances were assigned using standard $^1$H NMR chemical shift charts and comparison of the H$_2$bped and the pmen-ester spectra with those of the H$_2$pmen and H$_2$pmen•4HCl.

$^{13}$C NMR spectra of the potential ligands showed half (7–11) of the expected (14–22) resonances. The observed number of peaks was indicative of the molecules possessing two-fold symmetry and equivalent pairs of carbon atoms. The assignments are listed in Table 3.3.

III.3 Metal Complexes: Design and Syntheses

Three reaction pathways were followed in attempting to complex the metals and the potential ligands: metathesis, liquid-liquid diffusion crystallization (a variation of metathesis), and reduction. All three pathways were conducted under a variety of conditions and performed both in the presence and absence of a base.

III.3.1 H$_2$bped Complexes

In past experiments, H$_2$bped complexation reactions were conducted under aqueous conditions. The use of [ReO]$^{3+}$ and [TcO]$^{3+}$ precursor reactants such as [Bu$_4$N][ReOBr$_4$], [Bu$_4$N][ReOBr$_4$(H$_2$O)]•PBu$_3$, and
Table 3.3. $^{13}$C NMR (50.3 MHz) spectral data$^a$ for the potential ligands (solvent is CDCl$_3$ unless specified).$^b$

<table>
<thead>
<tr>
<th></th>
<th>H$_2$bp$^a$ed•2HCl</th>
<th>H$_2$pmen•4HCl</th>
<th>H$_2$pmen</th>
<th>pmen–OMe</th>
<th>pmen–OEt</th>
<th>pmen–OBu$^t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(1)</td>
<td>147.3</td>
<td>145.3</td>
<td>149.2</td>
<td>148.8</td>
<td>148.7</td>
<td>148.9</td>
</tr>
<tr>
<td>C(2)</td>
<td>128.7</td>
<td>128.8</td>
<td>122.2</td>
<td>122.9</td>
<td>122.9</td>
<td>122.9</td>
</tr>
<tr>
<td>C(3)</td>
<td>143.6</td>
<td>144.3</td>
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<td>136.3</td>
<td>136.4</td>
<td>136.4</td>
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<tr>
<td>C(4)</td>
<td>127.8</td>
<td>128.6</td>
<td>121.8</td>
<td>121.8</td>
<td>121.9</td>
<td>121.8</td>
</tr>
<tr>
<td>C(5)</td>
<td>149.5</td>
<td>147.9</td>
<td>159.9</td>
<td>159.2</td>
<td>159.1</td>
<td>159.8</td>
</tr>
<tr>
<td>C(6)</td>
<td>56.2</td>
<td>48.6</td>
<td>55.1</td>
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<td>60.5</td>
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<td>51.2</td>
<td>49.6</td>
<td>52.3</td>
</tr>
<tr>
<td>C(8)</td>
<td>55.1</td>
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<td>—</td>
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<td>52.0</td>
<td>56.2</td>
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<tr>
<td>C(9)</td>
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<td>—</td>
<td>171.6</td>
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<td>170.7</td>
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<td>80.8</td>
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<tr>
<td>C(11)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>14.0</td>
<td>28.1</td>
</tr>
</tbody>
</table>

$^a$ For labelling, see Figure 1.3; $^b$ D$_2$O solvent.
[Bu₄N][TcOCl₄] require non-aqueous conditions due to their hygroscopic nature and relative ease of hydrolysis to the unreactive and insoluble ReO₂ or TcO₂. The choice of suitable solvents was limited given the sensitivity of the metal precursor reactants. Methanol was the only solvent that could be used for H₂bped, but the metal precursors could use methanol, acetone, acetonitrile, chloroform, and methylene chloride. Water can only be used during the reduction of [ReO₄]⁻ and [TcO₄]⁻ because they are not moisture sensitive.

Metathesis. The precursor reactants were employed in basic and non-basic conditions (Scheme 3.5). The most successful reactions were with the metal-acetonitrile (CH₃CN) and the ligand-methanol (MeOH) solutions.

![Scheme 3.5](image)

In the absence of base, a precipitate formed rapidly upon the combination of the two reactants. A blue-green powder was produced with Re and an olive green powder was produced with Tc. The powders were only sparingly soluble in DMSO and no crystals of these products were produced. The presence of sodium acetate or triethylamine as a base gave a clear solution. The addition of a bulky counter anion (Y⁻), such as hexafluorophosphate, perchlorate, triflate, tetrafluoroborate, and tetraphenylborate, to the reaction mixture produced a
powder that was a mixture of $[\text{Bu}_4\text{N}][\text{Y}]$ and $[\text{MO(bped)}][\text{Y}]$.

Removal of most of the tetrabutylammonium (TBA$^+$) from solution was done using Sephadex LH-20 resin. $[\text{MO(bped)}]^+\text{X}^-$ was collected and dried to give a green solid for Re ($\text{X}=\text{Br}$) and a light brown powder for Tc ($\text{X}=\text{Cl}$).

Crystallization of the $[\text{MO(bped)}][\text{Y}]$ salt was attempted with several bulky anions, but all attempts produced a fine white precipitate which consisted mainly of a TBA$^+$Y$^-$ salt. Different solvent combinations were tried, but there was no success in obtaining any of the desired $[\text{MO(bped)}][\text{Y}]$ product.

The $[\text{ReO(bped)}]\text{Br}$ metathesis reaction employed either $[\text{Bu}_4\text{N}][\text{ReOBr}_4]$ or $[\text{Bu}_4\text{N}][\text{ReOBr}_4(\text{H}_2\text{O})]\text{PBu}_3$ as a starting material. The products from either starting material gave spectroscopically identical compounds, however, the solubility of the $[\text{Bu}_4\text{N}][\text{ReOBr}_4(\text{H}_2\text{O})]\text{PBu}_3$ product was much less than that of the $[\text{Bu}_4\text{N}][\text{ReOBr}_4]$ product once the solvent of the reaction mixture was removed. The $[\text{Bu}_4\text{N}][\text{ReOBr}_4]$ product was readily solvable in MeOH and water, but the $[\text{Bu}_4\text{N}][\text{ReOBr}_4(\text{H}_2\text{O})]\text{PBu}_3$ was only soluable when heated and formed an agglomerated white precipitate when the solution cooled to room temperature. The $[\text{Bu}_4\text{N}][\text{ReOBr}_4]$ product was preferred due to the poor solubility of the $[\text{Bu}_4\text{N}][\text{ReOBr}_4(\text{H}_2\text{O})]\text{PBu}_3$ product and difficulty in removing [TBA]$^+$ from the crude product.

Since the metathesis reactions occurred very rapidly at room temperature, the same reactions were performed ca. 4°C in an ice water bath. The mixtures were slowly warmed to room temperature after the reactants were combined. There was no change in the overall outcome of the reactions and the same products were obtained.
**Liquid-liquid Diffusion Crystallization (LLD).** The process of diffusion was thought to be slow enough to bring the reactants together at a rate that would induce crystal formation (Scheme 3.6). The experiments were performed at room temperature and at 4°C. A variety of solvent combinations were tried in either two or three phase LLD systems. Methanol and acetonitrile were the most successful at generating products by layering a clear, yellow H$_2$bped-methanol solution on top of a clear, red [Bu$_4$N][ReOBr$_4$]-acetonitrile solution. In the absence of base, a green intersolvent meniscus formed within 15 minutes of layering the two solvents. The solution turned a clear blue and produced a royal blue microcrystalline powder in 24 hours. The Tc analogue gave a green solution and a green microcrystalline powder. Small rectangular prisms were visible when viewed under the microscope for both complexes, but the crystals formed in clusters and were unsuitable for X-ray analysis. The crystals were only sparingly soluble in DMSO. The presence of base gave a green solution for Re and a clear brown solution for Tc. No crystals were formed at room temperature or at 4°C. The addition of bulky counter anions (Y-) produced a fine white TBA-Y- precipitate.

**Reduction.** The reduction reactions of perrhenate ([ReO$_4$]$^-$) and pertechnetate ([TcO$_4$]$^-$) were performed in the presence of the potential ligand under aqueous conditions with sodium dithionite (Na$_2$S$_2$O$_4$) or stannous...
chloride dihydrate (SnCl\(_2\)•2H\(_2\)O) as the reducing agent. The pH of the solution was adjusted with NaOH and the reactions were carried out in either an acidic or alkaline environment. Changing the temperature, the reducing agent, or the base had no affect in producing any complexes. The reduction of Re is very difficult. Tc is much easier to reduce than Re, but tends to form an insoluble black powder, TcO\(_2\). The basicity of the pyridine groups was believed to promote the hydrolysis of the Tc to TcO\(_2\).

### III.3.2 H\(_2\)pmen and H\(_2\)pmen•4HCl Complexes

**Metathesis** The same three precursor metals were used for H\(_2\)pmen and H\(_2\)pmen•4HCl and the same conditions used in the H\(_2\)bped metathesis reactions were followed. The solubility of H\(_2\)pmen in organic solvents allowed CHCl\(_3\) and CH\(_2\)Cl\(_2\) to be used in addition to those used in the H\(_2\)bped reactions. In the absence of base, no reaction between pmen\(^2\)- and the [MO\(^3\)]\(^+\) species occurred. When two equivalents of base were added to H\(_2\)pmen, only the reaction with [ReO\(^3\)]\(^+\) was successful, producing a violet powder (Scheme 3.7). There was no reaction with the [TcO\(^3\)]\(^+\) analogue. The two Re precursors, [Bu\(_4\)N][ReOBr\(_4\)] and [Bu\(_4\)N][ReOBr\(_4\)(H\(_2\)O)]•PBu\(_3\) gave products with identical \(^1\)H NMR which were only soluble in DMSO and DMF.

![Scheme 3.7. [ReO(pmen)][ReO\(_4\)] synthesis.](image)

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**Liquid-liquid Diffusion Crystallization.** Two and three phase LLD systems were set up with MeOH, CH₃CN, CHCl₃, and CH₂Cl₂ as solvents. In all cases, the Re reaction with base succeeded in producing a violet powder. The product was identical to that of the metathesis reaction and there was no TBA⁺ contamination visible in the ¹H NMR spectrum. No crystals formed in any of the LLD systems.

**Reduction.** Reactions of H₂pmen•4HCl with [NH₄][ReO₄] and [NH₄][TcO₄] were unsuccessful. Changing the reducing agents and the pH of the solution had no effect on the reaction system. The same results were observed as in the reduction reactions with H₂bped.

**III.3.3 Ester Complexes**

The three pmen-ester derivatives (pmen-OMe, pmen-OEt, and pmen-OBu₁) were reacted with Re and Tc in the three proposed synthetic pathways, but did not yield any of the desired products. Changes in the reaction conditions, such as temperature and the equivalents of base, had no effect on the outcome. A brown oil similar in appearance to the ester starting material was obtained in all cases. A black powder was isolated in some cases when the oil was washed with chloroform or acetone. It was believed to be ReO₂ or TcO₂ because of its lack of solubility and it showed no signal in the ¹H NMR. Infrared and ¹H NMR spectra showed only the presence of the starting materials and no formation of new products. It appeared that the pmen-ester derivatives easily hydrolyse the metals and are too basic to complex under the experimental conditions.
III.4 Metal Complexes: Characterization

A total of three complexes were successfully made and characterized in this thesis: [ReO(bped)]Br, [TcO(bped)]Cl, and [ReO(pmen)][ReO₄]. No crystal structures were obtained for any of the complexes. Characterization was based on mass spectrometry, elemental analysis, infrared spectroscopy, and ¹H NMR spectroscopy.

III.4.1 Mass Spectrometry and Elemental Analysis. The reaction of H₂bped with four equivalents of sodium acetate and Re and Tc showed strong parent peaks of m/z 559 and 471 in the positive LSIMS spectra, corresponding to [ReO(bped)]⁺ and [TcO(bped)]⁺, respectively. There were no other peaks showing the corresponding metal isotope ratios, but TBA⁺ was present in both of the spectra at m/z 242. Elemental analysis of the Re complex showed evidence of TBA⁺ and sodium acetate contamination. The calculated C,H,N analysis was not unambiguous, but one possible formulation was for [ReO(bped)]Br • [TBA⁺Br⁻]₀.₄₅(NaOAc)₀.₇ (found): C, 37.99 (37.90); H, 4.59 (4.51); N, 7.41 (7.47). No elemental analysis was obtained for the Tc complex. Positive(+) LSIMS for the Re reaction without base gave three strong patterns at m/z 623, 659, and 703. A less intense pattern at m/z 559 corresponding to [ReO(bped)]⁺ was observed, but the more intense peaks, even though they showed Re isotope ratios did not represent any plausible formulation. The reaction without NaOAc was not pursued any further in favour of the reaction with four equivalents of NaOAc.

Pmen²⁻ only complexed with Re to form [ReO(pmen)][ReO₄]. Positive LSIMS spectra showed a strong parent peak at m/z 443 corresponding to
[ReO(pmen)]+. Negative LSIMS was also performed and showed the presence of [ReO₄]⁻ at m/z 252 and its presence was further confirmed by elemental analysis. Again the elemental analysis was not unambiguous, but one possible analysis was calculated for [ReO(C₁₄H₁₆N₄)][ReO₄]•HCl: C, 23.06; H, 2.35; N, 7.68 and the found values were: C, 26.61; H, 2.36; N, 7.77. A trace amount of CH₃CN (0.2 eq) may also be present if solvent was retained from the reaction mixture. Calculated: C, 23.46; H, 2.41; N, 7.99.

III.4.2 Infrared Spectroscopy. The infrared spectrum of [ReO(pmen)][ReO₄] is shown in Figure 3.5 and the assignments are listed in Table 3.4. The degree of hydrogen bonding within the ligand was greatly reduced upon complexation. The characteristic resonances between 1610–1000 cm⁻¹ were still present in the complex, but they were dwarfed in comparison to the two large signals at 908 and 785 cm⁻¹. The absorption at 785 cm⁻¹ was characteristic of trans dioxo Re complexes and of perrhenate, [ReO₄]⁻. 4,56,57 Since the possibility of a trans dioxo complex was eliminated by elemental analysis and mass spectrometry, the absorbance was assigned to the O=Re=O stretch of the of perrhenate. The large absorption at 908 cm⁻¹ was assigned to the Re=O stretch of [ReO(pmen)]+. The absorption was 40–50 cm⁻¹ lower than some characteristic complex Re=O stretch absorbances. 56,57
Figure 3.5. IR spectrum of [ReO(pmen)][ReO₄] (KBr disc).
Table 3.4. IR stretching frequencies (cm\(^{-1}\)) for [ReO(pmen)][ReO\(_4\)]\(^a\) and [Co(H\(_2\)pmen)Cl\(_2\)]ClO\(_4\)\(^b,d\) and [Pd(H\(_2\)pmen)](PF\(_6\))\(_2\)\(^b\) complexes.

<table>
<thead>
<tr>
<th>Assign.</th>
<th>H(_2)pmenc</th>
<th>[Co(H(_2)pmen)Cl(_2)](^+) (^b,d)</th>
<th>[Pd(H(_2)pmen)](^+) (^b)</th>
<th>ReO(pmen)][ReO(_4)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\nu(\text{N—H}))</td>
<td>3315 s</td>
<td>3260 s</td>
<td>3250 s</td>
<td>3435 s, br</td>
</tr>
<tr>
<td>(\nu(\text{C—H}))</td>
<td>3100-2800 s, br</td>
<td>—</td>
<td>—</td>
<td>3100-2800 w, br</td>
</tr>
<tr>
<td>(\nu(\text{C=O}))</td>
<td>1612 m</td>
<td>1610 s</td>
<td>1612 s, br</td>
<td>1608 m</td>
</tr>
<tr>
<td>(\delta(\text{CH}_2))</td>
<td>1299 w</td>
<td>—</td>
<td>—</td>
<td>1281 w</td>
</tr>
<tr>
<td>(\nu(M=O))</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>908 vs</td>
</tr>
<tr>
<td>(\nu(O=M=O))</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>785 vs</td>
</tr>
</tbody>
</table>

\(^a\) KBr disc. \(^b\) Complex data taken from ref. 48 and spectra refer to hexachlorobutadiene and parafin oil mulls. \(^c\) Sample analysed as liquid smear on NaCl disc. \(^d\) cis-\(\alpha\)-[Co(H\(_2\)pmen)Cl\(_2\)]ClO\(_4\). \(^e\) Abbr. s = strong, m = medium, w = weak, br = broad, vs = very strong.

The IR spectra from the bped\(^2\)- complexes are shown in Figure 3.6 and the assignments are listed in Table 3.5. Complexation decreased the N—H, C=O, and M=O stretching frequencies by 5–25 cm\(^{-1}\). The bands in the Tc complex were also lower that the corresponding frequencies in the Re complex, which was expected.\(^4\) The C=O stretch decreased in frequency by 20–25 cm\(^{-1}\) and the broad N—H and C—H stretching region narrowed and decreased in intensity, due to the reduction of the intermolecular hydrogen bonding. The M=O stretching frequency was decreased by 100 cm\(^{-1}\) to 925 cm\(^{-1}\) with
Figure 3.6. IR spectra of [ReO(bped)]Br and [TcO(bped)]Cl complexes (KBr disc).
Table 3.5. IR stretching frequencies\(^c\) (cm\(^{-1}\)) of bped complexes.\(^a\)

<table>
<thead>
<tr>
<th>Assign.</th>
<th>(\nu(\text{N—H}))</th>
<th>(\nu(\text{C—H}))</th>
<th>(\nu(\text{C=O}))</th>
<th>(\delta(\text{CH}_2))</th>
<th>(\nu(\text{M=O}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{H}_2\text{bped})</td>
<td>3500–3200 s, br</td>
<td>3000–2500 s, br</td>
<td>1728 vs</td>
<td>1387 m</td>
<td>—</td>
</tr>
<tr>
<td>([\text{Co(bped)}]\text{PF}_6)</td>
<td>—</td>
<td>—</td>
<td>1675 s</td>
<td>1303</td>
<td>—</td>
</tr>
<tr>
<td>([\text{ReO(bped)}]\text{Br})</td>
<td>—</td>
<td>—</td>
<td>3100-2800 w</td>
<td>1241 s</td>
<td>925 m</td>
</tr>
<tr>
<td>([\text{TcO(bped)}]\text{Cl})</td>
<td>—</td>
<td>—</td>
<td>3100-2800 w</td>
<td>1244 w</td>
<td>925 m</td>
</tr>
</tbody>
</table>

\(^a\) All samples analysed as KBr discs. \(^b\) \([\text{Co(bped)}]\text{PF}_6\) analyzed as KBr disc from ref. 39. \(^c\) Abbrev.

s=strong, m= medium, w= weak, vs= very strong, br= broad.
complexation and the addition of NaOAc. The Re- and Tc-bped complexes showed a weak signal between 770-780 cm\(^{-1}\) which is characteristic of trans dioxo stretching (O=M=O).\(^{4,56,57}\) This may be due to a small amount of trans dioxo complex, or to the presence of [MO\(_4\)\(^-\)], one of the hydrolysis products of [Bu\(_4\)N][MOX\(_4\)]\(^-\) (where M=Re, Tc, and X= Br, Cl).

**III.4.3 \(^1\)H NMR Spectroscopy.** The \(^1\)H NMR spectrum of [ReO(pmen)][ReO\(_4\)] at pD=5.5 is shown in Figure 3.7 and the data are reported in Table 3.6 along with those for some other pmen-metal complexes.\(^{48}\) A splitting pattern similar to that demonstrated by [Co(H\(_2\)pmen)Cl\(_2\)]ClO\(_4\) was observed with the [ReO(pmen)][ReO\(_4\)]. The methylene hydrogens, H\(_6\) and H\(_7\), were split into AA'BB' patterns that overlap in the 6.2 - 3.8 ppm region. A \(^1\)H COSY experiment was used to correlate the AB signals. The more downfield AB pattern was assigned to H\(_6\) and the upfield AB pattern was assigned to H\(_7\) in agreement with the [Co(H\(_2\)pmen)Cl\(_2\)]ClO\(_4\). The pyridine hydrogen splitting patterns remained as two doublets, a triplet, and a triplet of doublets (H\(_3\)). The pyridine hydrogens follow the same splitting pattern as the free H\(_2\)pmen. One noticeable difference was the large downfield shift of H\(_1\) to 9.71 ppm. This large shift may be a result of the solvent coordination and the proximity of H\(_1\) to the lower axial coordinating position occupied by the solvent molecule. The pyridine hydrogen assignments were referenced and assigned in accordance with those for [Co(bped)]PF\(_6\) by Douglas\(^{27}\) and Caravan\(^{40}\) and [Co(H\(_2\)pmen)Cl\(_2\)]ClO\(_4\) by Goodwin and Lions,\(^{29}\) and Gibson and McKenzie\(^{48}\).
Figure 3.7. $^1$H NMR (200 MHz) spectrum of [ReO(pmen)][ReO$_4$] in DMSO–d$_6$ at pD=5.3.
Table 3.6. $^1$H NMR (200 MHz) spectral data$^a,b$ of [ReO(pmen)])[ReO$_4$$^c$ and associated [Co(H$_2$pmen)Cl$_2$]ClO$_4$ complexes$^d,e$ (see Figure 4.1) (in DMSO-d$_6$).

<table>
<thead>
<tr>
<th></th>
<th>cis-α-[Co(H$_2$pmen)Cl$_2$]$^*$$^d,f$</th>
<th>cis-β-[Co(H$_2$pmen)Cl$_2$]$^+$$^e,f$</th>
<th>[ReO(pmen)][ReO$_4$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(1) ($^3$J$_{12}$)</td>
<td>9.33 d (5.5)</td>
<td>9.35 d ; 9.14 d (6)</td>
<td>9.71 d (5.0)</td>
</tr>
<tr>
<td>H(2) ($^3$J$<em>{21}$,$^3$J$</em>{23}$)</td>
<td>7.4 - 7.6 br</td>
<td>6.92</td>
<td>7.78 td (6.0, 0.79)</td>
</tr>
<tr>
<td>H(3) ($^3$J$<em>{32}$,$^3$J$</em>{34}$)</td>
<td>8.2 t</td>
<td>7.6 - 8.4</td>
<td>8.24 td (8.3, 1.3)</td>
</tr>
<tr>
<td>H(4) ($^3$J$_{43}$)</td>
<td>7.6 d</td>
<td>8.03 d (7.8)</td>
<td></td>
</tr>
<tr>
<td>H(6) ($^2$J$_{ab}$) $\Delta$ (ppm)</td>
<td>2.4 br</td>
<td>2.2 - 5.2</td>
<td>5.30 AB (20.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\Delta$ = 1.53ppm</td>
</tr>
<tr>
<td>H(7) ($^2$J$_{ab}$) $\Delta$ (ppm)</td>
<td>4.47 AB (17, 7)</td>
<td>4.28 AB (8.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\Delta$ = 0.58ppm</td>
</tr>
</tbody>
</table>

$^a$ $\Delta$ is the spread between the average chemical shifts of the AB patterns.

$^b$ Numbers in parentheses refer to coupling (J) in Hz. $^c$ [ReO(pmen)][ReO$_4$] at pD=5.5. $^d$ cis-α-[Co(H$_2$pmen)Cl$_2$]ClO$_4$. $^e$ cis-β-[Co(pmen)Cl$_2$]ClO$_4$. $^f$ Reference 48. Abbrev.: d= doublet, t= triplet, td= triplet of doublets, br= broad.

$^1$H NMR measurements were done in CD$_3$OD and D$_2$O for [ReO(bped)]Br, but only with CD$_3$OD for the [TcO(bped)]Cl complex. The spectra are shown in Figure 3.8 and the assignments are listed in Table 3.7. The [ReO(bped)]Br and [TcO(bped)]Cl splitting patterns in CD$_3$OD were identical with minor differences in chemical shifts. The pyridine hydrogen splitting
Figure 3.8. $^1$H NMR (300 MHz) spectra of $[\text{ReO(bped)}]\text{Br}$ in CD$_3$OD (top) at pD=5.5 and in D$_2$O (bottom) at pD=3.3.
Table 3.7. $^1$H NMR (300 MHz) spectral data$^{a,b}$ for bped$^{2-}$ complexes of ReO(V)$^{c,d}$, TcO(V)$^{e}$, and Co(III)$^{f,g}$. Solvents are given in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>[Co(bped)]PF$_6$ (D$_2$O)</th>
<th>[ReO(bped)]Br (D$_2$O)</th>
<th>[ReO(bped)]Br (MeOD)</th>
<th>[TcO(bped)]Cl (MeOH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(1)</td>
<td>8.95 d</td>
<td>9.12 d</td>
<td>9.13 d</td>
<td>9.27 d</td>
</tr>
<tr>
<td>$^3$J$_{12}$</td>
<td>5.9</td>
<td>5.9</td>
<td>4.9</td>
<td>6.9</td>
</tr>
<tr>
<td>H(2)</td>
<td>7.84 t</td>
<td>7.73 t</td>
<td>7.68 t</td>
<td>7.71 c</td>
</tr>
<tr>
<td>$^3$J$<em>{21}$, $^3$J$</em>{23}$</td>
<td>5.4, 7.5</td>
<td>7.4, 7.4</td>
<td>6.0, 6.0</td>
<td>6.9, 6.9</td>
</tr>
<tr>
<td>H(3)</td>
<td>8.30 t</td>
<td>8.03 td</td>
<td>8.06 t</td>
<td>8.20 t</td>
</tr>
<tr>
<td>$^3$J$<em>{32}$, $^3$J$</em>{34}$</td>
<td>7.5, 8.0</td>
<td>7.18, 1.4</td>
<td>6.0, 6.0</td>
<td>6.9, 6.9</td>
</tr>
<tr>
<td>H(4)</td>
<td>7.80 d</td>
<td>7.73 d</td>
<td>7.75 d</td>
<td>7.71 h</td>
</tr>
<tr>
<td>$^3$J$_{43}$</td>
<td>8.0</td>
<td>8.0</td>
<td>9.3</td>
<td>16.2</td>
</tr>
<tr>
<td>H(6)</td>
<td>4.53 AB</td>
<td>4.87 AB</td>
<td>4.85 AB</td>
<td>4.66 AB</td>
</tr>
<tr>
<td>$\Delta$ (ppm)</td>
<td>0.36</td>
<td>0.65</td>
<td>0.73</td>
<td>0.51</td>
</tr>
<tr>
<td>$^2$J$_{ab}$</td>
<td>15.0</td>
<td>16.2</td>
<td>10.3</td>
<td>16.2</td>
</tr>
<tr>
<td>H(7)</td>
<td>3.73 AB</td>
<td>3.99 AB</td>
<td>3.92 AB</td>
<td>3.76 AB</td>
</tr>
<tr>
<td>$\Delta$ (ppm)</td>
<td>0.38</td>
<td>0.49</td>
<td>0.53</td>
<td>0.43</td>
</tr>
<tr>
<td>$^2$J$_{ab}$</td>
<td>9.4</td>
<td>17.4</td>
<td>11.8</td>
<td>17.3</td>
</tr>
<tr>
<td>H(8)</td>
<td>3.76 AB</td>
<td>3.71 s</td>
<td>3.71 AB</td>
<td>3.75 AB</td>
</tr>
<tr>
<td>$\Delta$ (ppm)</td>
<td>0.45</td>
<td>-</td>
<td>0.12</td>
<td>0.21</td>
</tr>
<tr>
<td>$^2$J$_{ab}$</td>
<td>17.9</td>
<td>-</td>
<td>7.6</td>
<td>9.9</td>
</tr>
</tbody>
</table>

$^a$ $\Delta$ is the spread between the average chemical shifts of the AB patterns.

$^b$ Coupling constants (J) are in Hz. $^c$ [ReO(bped)]Br in D$_2$O at pD=3.3.

$^d$ ReO(bped)]Br in CD$_3$OD at pD=5.3. $^e$ [TcO(bped)]Cl in CD$_3$OD at pD=5.3.

$^f$ [Co(bped)]PF$_6$ (at 500 MHz) in D$_2$O at pD=3.2. $^g$ Reference 40.

$^h$ Resonances were overlapping and undefined. Abbrev.: s= singlet, d= doublet, t= triplet, td= triplet of doublets.

Patterns remained as two doublets, a triplet, and a triplet of doublets (H$_3$) in D$_2$O and CD$_3$OD. The backbone region splits the H$_2$bped H$_6$, H$_7$, and H$_8$.
singlets into three AA'BB' patterns in CD$_3$OD. An expansion of the backbone region is shown in Figure 3.9. The complex is rigid on the NMR time scale. Low temperature $^1$H NMR experiment in CD$_3$OD on the [ReO(bped)]Br complex showed no change in the shape of the signals in the backbone region indicative of the existence of only one species. The [ReO(bped)]Br and [TcO(bped)]Cl complexes appear to be symmetric with the plane of symmetry or a C$_2$ axis of rotation bisecting the en ring and the central metal atom. $^1$H COSY NMR was used to correlate the AB patterns.

A $^1$H NMR spectrum was also run on the [ReO(bped)]$^+$ complex in D$_2$O. The pyridine region remained unchanged; however, the backbone region showed two AA'BB' patterns for H$_6$ and H$_7$, and a singlet for H$_8$. The chemical shifts between the CD$_3$OD and D$_2$O experiments were similar, yet the difference in signal patterns between the D$_2$O and CD$_3$OD spectra indicate two different configurations. The pD difference between the D$_2$O and CD$_3$OD solutions may play a role in the different signal patterns; however, there was not enough time to investigate this possibility. The assignments made by Douglas$^{27}$ and Caravan$^{40}$ on [Co(bped)]PF$_6$ cannot be applied directly to the Re and Tc complexes. The problem lies with the unrestricted ligand orientation around the binary cobalt system versus the ternary ReO and TcO systems containing an oxo atom that restricts the ligand's orientation about the metal atom. The $^1$H NMR and proposed structures will be discussed in Chapter 4.
Figure 3.9. $^{1}H$ NMR (300 MHz) spectrum (expansion) of [ReO(bped)]Br in CD$_3$OD at pH=5.5.
IV. Proposed Structures of [ReO(bped)]Br, [TcO(bped)]Cl, and [ReO(pmen)][ReO₄] Complexes

The infrared spectra and ¹H NMR spectra of the bped²⁻ and pmen²⁻ complexes had multitudes of similarities. The absorptions in the IR spectra showed strong shifts of the M=O stretching signals to lower frequencies upon complexation. The ¹H NMR spectra of the [ReO(bped)]Br and [TcO(bped)]Cl complexes in CD₃OD showed nearly identical splitting patterns for the pyridine and backbone regions. The assignments of the pyridyl hydrogens for the bped²⁻ and pmen²⁻ complexes were in agreement with earlier studies.²⁷,⁴⁰,⁴⁷,⁴⁸ Despite having almost superposable ¹H NMR spectra, a discrepancy with the assignments proposed by Douglas and Caravan arose for the backbone region among the [Co(bped)Cl₂]ClO₄, [ReO(bped)]Br, and [TcO(bped)]Cl complexes. The assignments made for the binary [Co(bped)Cl₂]⁺ system could not be applied to the ternary [ReO(bped)]⁺ and [TcO(bped)]⁺ systems. The presence of the oxo group on the [ReO(bped)]Br and [TcO(bped)]Cl complexes reduced the freedom of orientation of bped²⁻ around the [ReO]³⁺ and [TcO]³⁺ metal centres and eliminated the probability of a [Co(bped)Cl₂]⁺ configuration.

In attempting to determine the structure from the ¹H NMR spectra, it is easier to begin with the [ReO(pmen)][ReO₄] complex and correlate the spectrum with the [ReO(bped)]Br spectra in D₂O and CD₃OD when assigning the backbone resonances. Gibson and McKenzie⁴⁸ identified four likely orientations of some H₂pmen and pmen²⁻ transition metal complexes, which are shown in Figure 4.1. Both cis-α⁻ and cis-β⁻ configurations of [Co(H₂pmen)Cl₂]ClO₄⁴⁸ and [Fe(H₂pmen)Cl₂]Cl•H₂O¹⁴ complexes have been
firmly established by earlier studies. $^1$H NMR on the cis-α- and cis-β-
[Co(H$_2$pmen)Cl$_2$]ClO$_4$ configurations showed discrete differences in splitting
patterns. The cis-α-configuration showed four signals in the pyridine region,
characteristic of equivalent pyridyl units, and two AA'BB' patterns in the
backbone region. The cis-β configurations had eight signals in the pyridine
region, indicative of two inequivalent pyridyl units, and a complex series of
signals in the backbone region. A third possibility is a square planar pmen$^2$- or
octahedral H$_2$pmen configuration of the complex. Pd(II)$^{48}$ and Fe(III)$^{14}$ have
been shown to maintain these configurations at the expense of significant steric
effects in the ligand. $^1$H NMR studies of the square planar and octahedral
configurations contained equivalent pyridyls, showing four signals, and the
methylene hydrogens produced two singlets in the backbone region due to the
$C_{2v}$ symmetry of the complexes. The IR data of the square planar
[Pd(H$_2$pmen)][PF$_6$]$_2$ complex was similar to those of the [Co(H$_2$pmen)Cl$_2$]ClO$_4$

\[ \text{Figure 4.1. } \text{H}_2\text{pmen ligand orientation around Co(III)$^{48}$,}
\text{Fe(III)$^{14}$ and Pd(II)$^{48}$ metal centres.} \]
and [ReO(pmen)][ReO₄] complexes.

Goodwin and Lions²⁹ note that the coordination covalency of N atoms of pyridine rings in open-chain planar quadridentate molecules is directed along the axes of the pyridine rings. The resultant pyridyl chelate rings are directed to a planar orientation around the metal centre with the two methylene units of the en both above (or below) the plane of coordination. A buckling of the en chelate ring across the line of centres of the Nₐₐ atoms is likely to occur in reducing strain within the ring.

The ¹H NMR of the [ReO(pmen)][ReO₄] complex showed a spectrum identical to the cis-α-[Co(H₂pmen)Cl₂]ClO₄ configuration with four pyridine signals and two AA'BB' patterns in the backbone region. The presence of the oxo group creates a five coordinate complex. Using a combination of the above results, two possible deviations of the octahedral [Co(H₂pmen)Cl₂]ClO₄ geometries that could produce the observed ¹H NMR spectra for [ReO(pmen)][ReO₄] are the square pyramidal (spy) and trigonal bipyramidal (tbp) configurations (Figure 4.2).

[Diagram of proposed structures]
The $spy$ configuration has the four N atoms occupying the basal plane and the oxo group in the apical position in accord with Goodwin and Lions.\textsuperscript{29} It is impossible to determine whether the metal centre is in or slightly above the basal plane without a crystal structure. A $C_3$ plane of symmetry bisects the en ring and the metal-oxo centre. The presence of the apical oxo group creates two different environments for the methylene hydrogens and accounts for the observation of two AA'BB' patterns in the $^1$H NMR.

The en and oxo group are in the equatorial plane of the $tbp$, while the pyridyls occupy the trans axial positions in a similar fashion to the cis-$\alpha$-[Co(H$_2$pmen)Cl$_2$]ClO$_4$ complex. A $C_2$ axis of rotation bisects the en ring and the metal centre producing four pairs of symmetry-equivalent pyridyl hydrogens and three pairs of symmetry-equivalent methylene hydrogens. Two enantiomers are possible with this structure, unlike the $spy$ structure.

A two-fold symmetry is observed in both the $spy$ and $tbp$ configurations of [ReO(pmen)][ReO$_4$]. Interconversion between $spy$ and $tbp$ geometries has been demonstrated for some complexes,\textsuperscript{60} but the orientations of the pmen$^2$-ligand in the proposed $spy$ and $tbp$ geometries for [ReO(pmen)][ReO$_4$] cannot produce the interconversions with the necessary symmetry. Figure 4.3 shows

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure4.3.png}
\caption{The ligand displacements needed to change a square pyramid into a trigonal bipyramid.}
\end{figure}
that interconversion from spy to tbp produces an unsymmetrical tbp with cis
oriented pyridyl groups. Distortion from one or the other of the two prototype
structures is likely to occur and it is uncertain which is taken as the idealized
group. The strong similarities with the IR and $^1$H NMR data between
[Co(H$_2$pmen)Cl$_2$]ClO$_4$ and [ReO(pmen)][ReO$_4$] assigned the more downfield
AA'BB' pattern to the methylene protons on the picolyl group ($H_6$) and the
upfield AA'BB' pattern was assigned to the methylene protons on the en ($H_7$) in
agreement with Gibson and McKenzie.$^{48}$

[ReO(bped)]Br showed the two AA'BB' patterns already seen in the
[ReO(pmen)][ReO$_4$] (Figure 3.9) complex and an additional singlet in D$_2$O or
AA'BB' pattern in CD$_3$OD solvents (Figure 3.10) for the methylene hydrogens
($H_8$) when the acetate arms are present. Douglas based the assignments made
for the AA'BB' patterns of [Co(bped)]ClO$_4$ on the coupling constants of AA'BB'
patterns from referenced symmetry-equivalent sets of methylene hydrogen
atoms. If these assignments are followed in the [ReO(bped)]Br complex, the
third signal would be assigned to $H_6$, the methylene hydrogens on the picolyl
group. In this case, the $N_{en}$ atoms are not coordinated in D$_2$O solvent and the
[ReO(bped)]Br complex is a N$_2$O$_2$ system of coordinated $N_{py}$ atoms and acetate
O atoms. In the CD$_3$OD spectrum, the $N_{en}$ atoms were coordinated trans to
the apical oxo group below the coordination plane via very long M—N bonds.
The structures are shown in Figure 4.4. Neither of these configurations
correlate with the observed [ReO(pmen)][ReO$_4$] $^1$H NMR spectrum and are
unlikely to occur.
The \textsuperscript{1}H NMR splitting patterns of H\textsubscript{6} and H\textsubscript{7} in the [ReO(bped)]Br and [ReO(pmen)][ReO\textsubscript{4}] spectra were near identical. The third signal in the [ReO(bped)]Br spectra, a singlet in D\textsubscript{2}O and an AA'BB' pattern in CD\textsubscript{3}OD, was assigned to the methylenes on the acetate arms (H\textsubscript{8}) on the basis that its absence in [ReO(pmen)][ReO\textsubscript{4}] generated no signal (Figure 3.9) and its presence in the [ReO(bped)]Br complex produced a signal (Figure 3.10). The strong similarity of the [ReO(bped)]Br and [Co(bped)][PF\textsubscript{6}] \textsuperscript{1}H NMR spectra showing three AA'BB' patterns strongly suggested that a N\textsubscript{4} coordination plane also exists in the [ReO(bped)]Br complex. The H\textsubscript{8} signal, AA'BB' pattern in CD\textsubscript{3}OD or singlet in D\textsubscript{2}O, suggests that the acetate arms are coordinated in methanol and pendant in water. Pendant acetate arms will give rise to a \textit{spy} or \textit{tbp} geometry. The apical oxo group above the basal plane in the \textit{spy} may force the acetate arms to reside below the coordination plane to minimize steric interactions. Free rotation of the acetate arms would create symmetry-equivalent methylene hydrogens on the acetate arms to give rise to a singlet in

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure4.4.png}
\caption{Proposed structure for [ReO(bped)]Br using assignments for [Co(bped)][PF\textsubscript{6}] from Douglas\textsuperscript{27} and Caravan\textsuperscript{40}.}
\end{figure}
D$_2$O. Free rotation of the acetate arms in the *tbp* geometry would also possible, but may be restricted due to steric interactions with the pyridyl H$_1$ protons.

The coordination of the acetate O atoms produces an N$_4$O$_2$ system and adds two additional five-membered chelate rings giving rise to a seven coordinate pentagonal bipyramid (*pbp*) or a monocapped trigonal prism (*mtp*) configuration. A monocapped octahedron is a third seven-coordinate geometry; however, it does not give the necessary symmetry required. Figure 4.5 shows the proposed bped$^2^-$ complexes with pendant and coordinated acetate arms.

**Figure 4.5.** Proposed [ReO(bped)]$^+$ structures using $^1$H NMR in D$_2$O and CD$_3$OD.
A *pbp* orients the pyridyl groups in the trans axial positions, while the en ring and acetate groups are in the equatorial plane. The structure exhibits $C_2$ symmetry with an axis of rotation bisecting the en ring and metal centre. The *mtp* contains the en and pyridyl N atoms in the equatorial plane and coordinated O atoms of the acetate groups underneath the plane in close proximity to the central metal ion. To accommodate the acetate arms oriented below the plane, the methylene groups in the en ring are elevated above the coordination plane. The configuration contains $C_s$ symmetry with a plane of symmetry bisecting the en ring and the metal centre. The *pbp* and *mtp* both give rise to equivalent pyridyl groups and three sets of symmetry-equivalent methylene hydrogen pairs in the $^1H$ NMR spectrum. The analogous [TcO(bped)]Cl complex takes the same configurations as its Re congener given the similarities in the $^1H$ NMR between the [ReO(bped)]Br and [TcO(bped)]Cl spectra.

The methylene groups in the ligands were oriented either above, below, or in the coordination plane in the proposed structures of the bped$^{2-}$ and pmen$^{2-}$ complexes. Axial and equatorial orientations of the methylene hydrogens were present in all the structures. Each methylene unit had two symmetry–inequivalent protons (i.e. a,b). Complementary methylenes gave rise to two pairs of symmetry–equivalent protons (i.e. 6a,6a'), which produced the AA'BB' patterns observed in the backbone region. Figure 4.6 shows the orientations of the methylene hydrogens in the proposed complex structures.
The proposed bped\textsuperscript{2-} and pmen\textsuperscript{2-} complex structures all contain elements of strain in ball-and-stick models. Conformational strain is experienced in all the structures because of the shorter bond lengths and bond angles of the heterocyclic N atoms.

Steric repulsion between the two pyridyl rings' substituents is pronounced in the \textit{spy} conformation of the bped\textsuperscript{2-} and pmen\textsuperscript{2-} complexes. The H\textsubscript{1} protons interact when the pyridyl rings are within the coordination plane of the \textit{spy} and \textit{mtp}. To accommodate this interaction, a twist in the pyridyl rings to orient the H\textsubscript{1} protons by placing them either above or below the plane.\textsuperscript{48} As a result of
the twist, the corresponding methylenes in the picolyl groups are oriented above and below the basal plane opposite to the pyridyl. In other words, if the $H_1$ is twisted below the plane, the corresponding methylene in the picolyl group is oriented above the plane, and visa versa. The $tbp$ and $pbp$ avoid the $H_1$ interactions between the pyridyl groups by orienting them trans to one another in the axial positions. However, there are $H_1$ interactions with the methylene hydrogens ($H_6$) and the carboxylates of the pendant and coordinated acetate arms in the bped complex. The free rotation of the pendant acetate arms is hindered and an increase in ring strain with the coordinated acetate arms is a result of their close proximity to the $H_1$ protons. This strong steric interaction makes the $tbp$ and $pbp$ configurations for the bped$^{2-}$ complexes unfavourable compared to the $spy$ and $mcp$ configurations. The $H_1$ interactions are shown in Figure 4.7.

Cumulative ring strain is common in planar polypyridyl ligands that give rise to systems of linked consecutive five-membered rings. Crystal structures of some aliphatic systems show the $N_{en}$—$M$—$N_{en}$ bond angle within an en chelate ring on the order of 87° compared to the favourable angle of 90° for octahedral and $spy$ geometries.$^{59,60}$ The en ring shows evidence of strain in all the modelled complexes. The $spy$ and $mtp$ geometries appear to have bond angles slightly less than the ideal 90° in the en ring. The $tbp$ has an en ring in the equatorial plane less than the expected 120°, and the $N_{py}$—$M$—$N_{py}$ bond angle appears to be slightly greater than 180°.

The size of the central metal ion and the donor atom may affect the stability of the structure. Hoard notes that the size of the metal will affect the conformation and cumulative ring strain in ligands involving five-membered
Hancock has also noted that hexadentate ligands that form five-membered rings tend to coordinate to larger metal ions with an additional unidentate ligand. The increase in coordination number results in longer M—N bond lengths which decreases the strain on the N—M—N bond angle. No evidence was found for the coordination of additional ligands to the metal centres, but the ligands should coordinate with less strain to the larger Re metal centre according to arguments proposed by Hoard and Hancock. The larger metal ion will increase the separation between the H$_1$ pyridyl groups and decrease the degree of steric interaction. An increase in the size of the donor
atom has the same effect as metal size and also enhances steric constraints in multidentate chelate complexes.

A six coordinate octahedral configuration of [ReO(bped)]Br and [TcO(bped)]Cl may also be possible. The carboxylate groups on the acetate arms could alternate in coordination to the [ReO]^3+ centre in a fashion similar to that shown in Figure 4.8. At room temperature the picolyl methylenes produce two pairs of symmetry-equivalent sets of methylene hydrogens. If the swinging action of the acetate arms is faster than the NMR time scale, the methylene hydrogens of the picolyl group would be equivalent and a singlet would be observed in the ^1H NMR spectrum. Low temperature ^1H NMR studies of the [ReO(bped)]Br complex were performed in CD$_3$OD in attempting to slow down any rate of exchange that may be taking place. No change in the third AA'BB' pattern associated with the picolyl methylene protons (H$_8$) was observed, thus
eliminating the possibility of a six coordinate octahedral configuration.

These proposed structures are all possibilities; however, the \( \textit{tbp} \) and \( \textit{pbp} \) configurations are not strongly favoured \( \text{bped}^{2-} \) complex configurations due to the proposed steric interactions and the tendency of oxorhenium(V) and oxotechnetium(V) to form square planar and octahedral complex. No evidence in the form of an X-ray diffraction study was available at this time to confirm a definite configuration of the \( \text{bped}^{2-} \) and \( \text{pmen}^{2-} \) complexes. All the proposed structures were based on evidence derived from mass spectrometry, elemental analysis, IR spectroscopy, and \( ^1\text{H} \) NMR spectroscopy.
References


