

the system then affords the sparingly soluble dichlorodinitrosyltungsten polymer. On the other hand, to synthesize this complex by the reaction of ClNO with $W(CO)_6$ in CH_2Cl_2 (eq 1), traces of an oxidant are first required to initiate the reaction, which probably proceeds via a catalytic, radical chain mechanism (Scheme II). The addition of the remaining ClNO must then be effected in a controlled manner with concomitant monitoring of the progress of the conversion by IR spectroscopy so that an excess of this reagent is avoided. Such an excess simply converts some of the desired $[W(NO)_2Cl_2]_n$ to $W(NO)_3Cl_3$ and $W(NO)_2Cl_4$ contaminants, a conversion that may be reversed (eq 3) by refluxing the final reaction mixture for a short time under a purge of N_2 . Of the two preparative methods, reaction 1 affords $[W(NO)_2Cl_2]_n$ in the greatest yield and purity and is most convenient for the synthesis of the

polymeric complex on a large scale.

Acknowledgment. We are grateful to the Natural Science and Engineering Research Council of Canada for support of this work in the form of grants (A5885 and E5706) to P.L. and a graduate scholarship to A.D.H. We also thank David J. Tannar and Frank N. Arcadi for experimental assistance.

Registry No. $W(NO)_2Cl_4$, 92473-06-8; $W(NO)_3Cl_3$, 92542-39-7; $W(NO)Cl_3(CH_3CN)_2$, 82983-81-1; $[W(NO)_2Cl_2]_n$, 42912-10-7; $W(CO)_6$, 14040-11-0; $W(CO)_4(NO)Cl$, 39899-80-4; $W(NO)_2Cl_2(PMePh)_2$, 92473-07-9; $W(NO)_2Cl_2(P(OMe)_3)_2$, 92473-08-0; $W(NO)_2Cl_2(PPh_3)_2$, 92542-40-0; $W(NO)_2Cl_2[OP(Me)(OMe)_2]_2$, 92473-09-1; $W(NO)_2Cl_2(dppm)_2$, 92473-10-4; $W(NO)_2Cl_2(dppm)$, 92473-11-5; $W(NO)_2Cl_2(CH_3CN)_2$, 92473-12-6; $W(NO)_2Cl_2(THF)_2$, 92473-13-7; $W(NO)_2Cl_2(Et_2O)_2$, 92473-14-8; $(\eta^5-C_5H_5)W(NO)_2Cl$, 53419-14-0; $n-Bu_3Sn(C_5H_5)$, 3912-86-5.

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Stereochemical Studies in the Development of Technetium Radiopharmaceuticals. 1. Fluxional Racemization of Technetium and Rhenium Penicillamine Complexes

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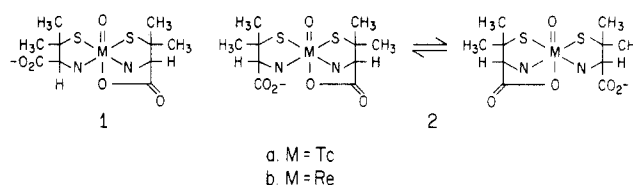
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The complexes $[(D-pen)_2MO]^-$, $[(L-pen)_2MO]^-$, and $[(D-pen)(L-pen)MO]^-$ [$M = Re, Tc$; $pen = penicillaminato, (CH_3)_2C(S^-)CH(NH_2)(CO_2^-)$] have been synthesized by $SnCl_2$ reduction of MO_4^- in the presence of optically pure or racemic penicillamine. The complexes are characterized by their chromatographic behavior, electronic spectra, fast atom bombardment mass spectra, and variable-temperature 1H NMR spectra. All complexes are six-coordinate in solution, with one tridentate penicillamine, one bidentate penicillamine, and one oxo ligand. The mixed complexes $[(D-pen)(L-pen)MO]^-$ are fluxional, racemizing by exchange of carboxylates at the site trans to the oxo ligand. Kinetics of this process were measured by complete line-shape analysis of the NMR spectra. The technetium complex racemizes with $k_1 = 940 s^{-1}$ at 25 °C and $E_a = 13.4 \pm 2.0$ kcal/mol, while the rhenium complex racemizes more slowly with $k_1 = 16.5 \pm 0.4 s^{-1}$ at 25 °C and $E_a = 18.5 \pm 1.0$ kcal/mol.

Introduction

Technetium in its +5 oxidation state has recently gained considerable attention in the development of new radiopharmaceuticals for diagnostic imaging.² Of particular interest are ^{99m}Tc complexes with tetradentate S_2N_2 chelates, which have shown promise as agents for dynamic imaging of the renal system.³ To better understand the chemistry of such complexes, we chose to investigate the penicillamine complexes of technetium, which have been reported as imaging agents for both the renal and hepatobiliary systems.⁴ Unfortunately, some reports in the medical literature have neglected to mention the enantiomeric state of the penicillamine used in

Scheme I



the pharmaceutical preparation.

Lock has recently reported the structure of a complex formed from $OTcCl_4^-$ and D-penicillamine (**1a**).⁵ In this complex one penicillamine is tridentate, coordinating through thiolate, amine, and carboxylate groups. The second penicillamine is bidentate with sulfur and nitrogen coordination. The sulfur and nitrogen atoms of the two ligands are mutually cis in this structure. The carboxylate of the second penicillamine is unable to coordinate since the oxo ligand is in the sixth position of the octahedron.

We have found that when racemic penicillamine is employed in this synthesis, a second, chromatographically separable complex is obtained in yield approximately equal to that of

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the enantiomeric pair **1a**. This complex **2a** is diastereomeric with **1a**, containing one D-penicillamine and one L-penicillamine per metal. The rhenium congeners **1b** and **2b** were similarly synthesized. Complexes **2a** and **2b** are fluxional on the NMR time scale, racemizing by exchanging carboxylate ligands at the site trans to the oxo ligand (Scheme I).

Experimental Section

General Techniques. Procedures for the safe handling and transportation of ^{99}Tc have been described elsewhere and were carefully followed at all times in this work.^{5,12}

Materials. D-Penicillamine, L-penicillamine, and D,L-penicillamine were purchased from Aldrich Chemical Co. and Sigma Chemical Co. Ammonium pertechnetate was purchased as an aqueous solution from New England Nuclear, and its concentration was confirmed by its UV spectrum. Ammonium perrhenate was purchased from Aldrich Chemical Co. Stannous chloride was purchased from Mallinckrodt. Sodium 2,2,3,3-tetradeuterio(trimethylsilyl)propionate was purchased from Wilmad Glass.

Equipment. High-performance liquid chromatography was performed on Beckman Models 330, 341, 332, and 342 equipped with Models 153 and 155-40 detectors. Columns were Ultrasphere-ODS (4.6 mm $\times$ 25 cm and 10.0 mm $\times$ 25 cm), Ultrasil-CX, and Ultrasil-AX (4.6 mm $\times$ 25 cm). Radiochemical detectors were sodium iodide scintillation crystals and spectroscopy amplifiers purchased from Ortec and Canberra. All detectors were equipped with Hewlett-Packard 3390A integrating recorders. UV-vis spectra were obtained on a Beckman DU-8 spectrometer. NMR spectra were obtained on a Nicolet NT-360 spectrometer. Liquid scintillation counting was performed on a Packard Model 3375. Mass spectra were obtained on a Varian MAT 731. Elemental analysis was performed by Galbraith Laboratories.

Syntheses. $[(\text{D-pen})_2\text{TcO}]$ (**1a**). The literature method for ^{99m}Tc complexes was scaled up as follows: A solution of D-penicillamine (15 mg, 0.10 mmol) in 10 mL of 0.1 M acetate buffer (pH 5.0) was prepared. Ammonium pertechnetate solution (0.120 mL, 10.0 mg, 0.049 mmol) was added. A solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (22.5 mg, 0.10 mmol) in 2.0 mL of 0.1 N HCl was added with stirring over 5 min. A 20- μL aliquot of this reaction was chromatographed on a 4.6 mm $\times$ 25 cm Ultrasphere-ODS column (see below). The product was collected, and the yield was determined by liquid scintillation counting. The yield of **1a** was 70%.

$[(\text{D-pen})(\text{L-pen})\text{TcO}]$ (**2a**). An identical procedure was followed except that D,L-penicillamine was used. The yields, determined as described above were 49% for **1a** and 36% for **2a**.

HPLC Separation of 1a and 2a. The above reaction mixture was chromatographed in 15% ethanol/0.01 M phosphate (pH 7.0) at 1.0 mL/min on a 4.6 mm $\times$ 25 cm Ultrasphere-ODS column or at 3.0 mL/min on a 10.0 mm $\times$ 25 cm Ultrasphere-ODS column. Detectors were set at 423 or 436 nm. Complex **2a** eluted first (ca. 4.1 min on the 4.6-mm column), followed by **1a** (ca. 6.1 min). Yields were measured by liquid scintillation counting of the collected fractions using a literature method⁶ and compared to a standard prepared from $\text{NH}_4^{99}\text{TcO}_4^-$. UV-vis spectra were recorded from the same solutions.

Syntheses. $[(\text{D-pen})_2\text{ReO}]$ (**1b**). Ammonium perrhenate (134 mg, 0.50 mmol) and D-penicillamine (200 mg, 1.34 mmol) were dissolved in 10 mL of 1 N HCl. The solution was cooled to 0 $^\circ\text{C}$. A solution of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (125 mg, 0.55 mmol) in 1.0 mL of 1 N HCl was added dropwise with stirring over 10 min. After an additional 10 min of stirring at room temperature, the reaction was neutralized by addition of 2.2 mL of 5 N NaOH.

A 20- μL aliquot of the reaction was chromatographed on a 4.6 mm $\times$ 25 cm Ultrasphere-ODS column (see below). The product was collected, and the spectroscopic yield was determined by visible spectrophotometry. The product **1b** had formed in 94% yield.

The remainder of the reaction was chromatographed on a 10 mm $\times$ 25 cm Ultrasphere-ODS column. Each injection contained 500- μL (ca. 10 mg of **1b**). The collected fractions were combined, acidified with phosphoric acid, and concentrated under aspirator vacuum to about 20 mL. The product **1b** precipitated as the free acid on cooling to 0 $^\circ\text{C}$ and was collected by filtration; yield 161 mg (0.325 mmol, 65%). Anal. Calcd for $\text{C}_{10}\text{H}_{19}\text{N}_2\text{O}_5\text{ReS}_2$: C, 24.14; H, 3.85; N, 5.63. Found: C, 24.06; H, 3.92, N, 5.62.

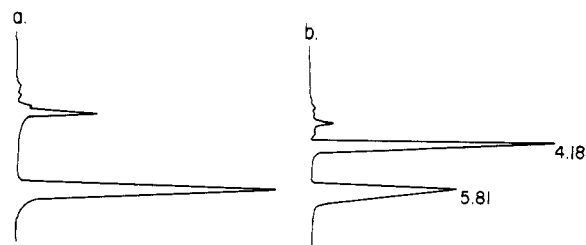


Figure 1. Reversed-phase HPLC traces of the products formed when $^{99}\text{TcO}_4^-$ was reduced in the presence of (a) D-penicillamine and (b) racemic penicillamine. Complex **1a** is at 5.81 min and **2a** is at 4.18 min. See Experimental Section for chromatographic conditions.

$[(\text{D-pen})(\text{L-pen})\text{ReO}]$ (**2b**). An identical procedure was followed except that D,L-penicillamine was used. The spectroscopic yield, determined as described above, was 43% for racemic **1b** and 45% for **2b**.

HPLC Separation of 1b and 2b. Separations were performed with 12% ethanol/0.01 M phosphate (pH 7.0) at 1.0 mL/min on a 4.6 mm $\times$ 25 cm Ultrasphere-ODS column or at 3.0 mL/min on a 10.0 mm $\times$ 25 cm Ultrasphere-ODS column. Detectors were set at 340 nm. Retention times were ca. 5.8 min for **2b** and 7.2 min for **1b**. Mixtures containing up to 0.5 mg of **1b** and **2b** combined could be separated on the 10.0-mm column. Approximately 5 mg of **2b** was isolated as described above for **1b** and was used for mass spectral and UV-vis studies.

Cation-Exchange Chromatography. Complexes were chromatographed on an Ultrasil-CX column using 0.20 M KNO_3 and 0.10 M HNO_3 /0.20 M KNO_3 as the mobile phase. Flow rate was 1.5 mL/min. Under these conditions the retention time of $(\text{en})_2\text{O}_2\text{Re}^+$ was 6.39 min in the absence of nitric acid and 5.33 min in the presence of nitric acid. Complexes **1a**, **2a**, **1b**, and **2b** eluted at the solvent front (2.35 min) in both systems.

Anion-Exchange Chromatography. An Ultrasil-AX column was used. A buffer was prepared from glycine (0.10 mol) and nitric acid (0.15 mol) in 1 L of water. The pH was adjusted by addition of aliquots of 5 N sodium hydroxide. Complexes **1a**, **2a**, **1b**, and **2b** were chromatographed at pH values from 1.06 to 8.23. Retention times ranged from 2 min (solvent front) for all complexes at pH 1.06 to 5.17 min for **1a**, 4.73 min for **2a**, and 5.58 min for **1b** and 4.80 min for **2b** at pH 8.23.

Preparation of Samples for NMR Studies. Samples of ca. 5 mg of each compound were prepared by evaporating chromatographic fractions to dryness under aspirator vacuum. The samples were redissolved in D_2O (5 mL), evaporated to dryness twice, and then dissolved in 0.5 mL of D_2O containing 0.5 mg of sodium 2,2,3,3-tetradeuterio(trimethylsilyl)propionate. The purity of each sample was confirmed by HPLC. The pH of the solution was confirmed to be 7.0 ± 0.5 on pH paper. All spectra were run in 5-mm NMR tubes. Spectra of **1a** and **1b** were obtained from racemic samples. Teflon inner tubes were employed for the technetium samples.

Results

Figure 1 shows reversed-phase HPLC traces of the products from the reduction of $\text{NH}_4^{99}\text{TcO}_4^-$ in the presence of D-penicillamine and racemic penicillamine. When L-penicillamine was substituted for D-penicillamine, a trace essentially identical with **a** was obtained. A chromatographically identical product was obtained when D-penicillamine was reacted with $\text{Cl}_4^{99}\text{TcO}_4^-$, the synthesis employed by Lock for the structural characterization of **1a**.⁵ When racemic penicillamine is employed in the synthesis, the mixed complex **2a** is also formed and is eluted earlier than **1a** in reversed-phase chromatography.

In anion-exchange chromatography, both complexes were retained significantly at neutral pH but their retention times approached the solvent front as the pH was lowered between 3.0 and 1.7. No retention on a cation-exchange column was observed as low as pH 0.7.

The rhenium complexes **1b** and **2b** were similarly synthesized except that reduction of ReO_4^- by SnCl_2 required 1 N HCl as solvent. Both rhenium complexes were retained somewhat less than their technetium congeners in reversed-

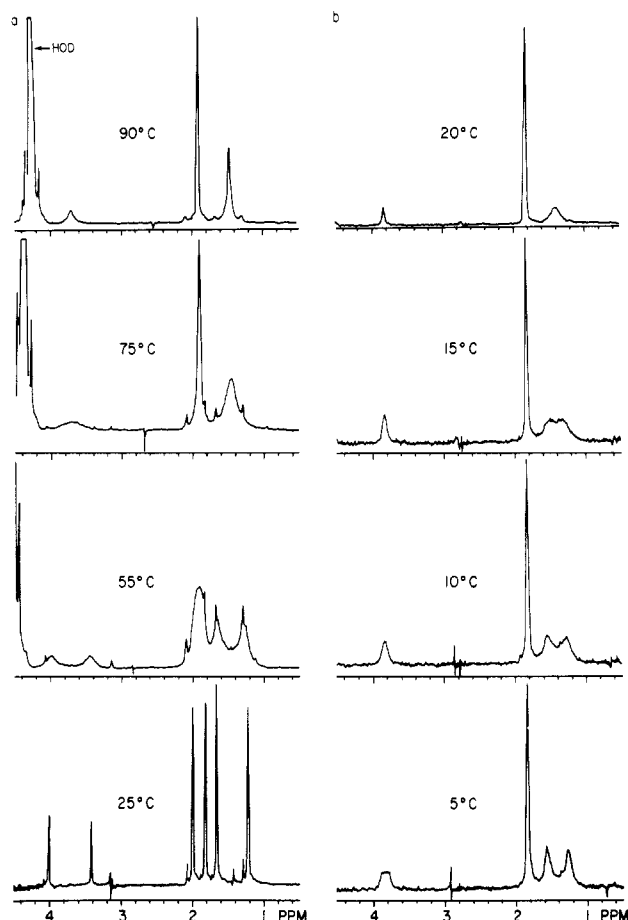


Figure 2. Variable-temperature ^1H NMR spectra of (a) $[(\text{D-pen})-(\text{L-pen})\text{ReO}]^-$ (**2b**) and (b) $[(\text{D-pen})-(\text{L-pen})\text{TcO}]^-$ (**2a**) in D_2O . Sharp resonances in the rhenium spectra are due to small amounts of **1b**, which form slowly at elevated temperatures in solutions of **2b**.⁸

phase HPLC but otherwise showed very similar chromatographic behavior.

Fast atom bombardment positive ion mass spectra of **1a** and **2a** showed ions at m/e 411 and 395. The first is assigned as the protonated parent complex and the latter as the parent ion minus its oxo ligand.⁷ The rhenium complexes **1b** and **2b** showed similarly assigned ions at m/e 497 and 481. No significant differences were found between the mass spectra of either pair of diastereomers, and no evidence for tin-containing impurities was observed.

The 360-MHz ^1H NMR spectra (Figure 2) of racemic **1b** at 25 °C in neutral D_2O showed four distinct resonances due to methyl groups and two resonances from the α protons of the amino acid ligands. The mixed complex of rhenium **2b** showed a similar spectrum at 25 °C, but increasing the temperature to 95 °C simplified the spectrum to two methyl resonances and one α -proton resonance. The technetium congener **2a** gave a similar high-temperature spectrum at 40 °C, but a low-temperature limiting spectrum was not obtained at 0 °C. No temperature dependence was observed in the spectra of racemic **1a** and **1b**. Free penicillamine was not observed in the spectrum of any complex at any temperature. Table I lists the chemical shifts of all complexes.

The rates of this fluxional process were measured by complete line-shape analysis of the spectra. For the rhenium complex three pairs of coalescing resonances were simulated, allowing three independent measurements of the rate constant at each temperature. Since we were unable to obtain a low-

Table I. Chemical Shift Data for the Penicillamine Complexes Studied^a

complex	T , °C	resonances	
		methyl	methine
$[(\text{D-pen})_2\text{TcO}]^-$ (1a)	20	1.36, 1.57, 1.83, 1.92	3.25, 3.95
$[(\text{D-pen})(\text{L-pen})\text{TcO}]^-$ (2a)	0	1.26, 1.58, 1.83	3.76, 3.88
	40	1.26, 1.83	3.82
$[(\text{D-pen})_2\text{ReO}]^-$ (1b)	20	1.28, 1.66, 1.83, 2.07	3.12, 4.08
$[(\text{D-pen})(\text{L-pen})\text{ReO}]^-$ (2b)	25	1.22, 1.66, 1.81, 1.99	3.41, 4.01
	95	1.44, 1.90	3.71
penicillamine	20	1.78, 1.88	3.98

^a Shifts were measured in D_2O at 360 MHz and are reported in ppm downfield from sodium 2,3,3,3-tetradeuterio(trimethylsilyl)propionate.

temperature limiting spectrum for **2a**, the frequencies of the limiting resonances were estimated from the line-shape analysis. One pair of methyl groups in the technetium complex **2a** gave a single sharp resonance at all temperatures and was not useful for kinetic measurements. Representative rate constants for this process are $k = 180 \pm 10 \text{ s}^{-1}$ at 5 °C and $k = 940 \pm 40 \text{ s}^{-1}$ at 25 °C for **2a**. The Arrhenius activation energy is $13.4 \pm 2.0 \text{ kcal mol}^{-1}$. The rhenium complex racemizes more slowly with $k = 16.5 \pm 0.4 \text{ s}^{-1}$ at 25 °C and $k = 610 \pm 15 \text{ s}^{-1}$ at 65 °C, giving $E_a = 18.4 \pm 1.1 \text{ kcal mol}^{-1}$. The activation entropy for racemization of **2a** is -2 eu and for **2b** is 7 eu. The uncertainty in these values could be as high as ± 5 eu so we do not consider this difference to be significant. Lack of solubility in acid solutions prevented us from studying the process at lower pH values.

Discussion

Neither technetium nor rhenium in their +5 oxidation states shows stereoselectivity in their reactions with penicillamine. Preliminary kinetic experiments on ligand-exchange reactions interconverting the diastereomers suggest that this is an equilibrium distribution of products.⁸ In comparison, Ni(II) prefers stereochemically pure complexes when reacted with racemic penicillamine, while Zn(II) favors a mixed complex.⁹

The chromatographic behavior of all penicillamine complexes studied on anion-exchange and cation-exchange HPLC columns suggests that all are monoanionic at pH 3.0 and above and uncharged at pH 1.5 and below. This is consistent with the published structure of **1a**;⁵ the free carboxylate is the only ionizable group in this pH range. The bound carboxylate and the oxo ligand remain unprotonated at pH 0.7.

The mixed complexes **2a** and **2b** exist as rapidly interconverting pairs of enantiomers. This interconversion generates an effective plane of symmetry in the complexes and results in the simplified NMR spectra. The simplified spectra require that an effective plane of symmetry be present and cannot be accounted for by different oxidation states, head-to-tail isomerism, or ligand exchange. The observation of fluxionality in the mixed-ligand complexes **2a** and **2b** but not in racemic mixtures of **1a** and **1b** argues against the complete dissociation of penicillamine as a step in this reaction. Interestingly, the molecule as a whole is racemized without inversion of its asymmetric carbon centers. The fluxionality of the mixed

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(8) (a) At neutral pH, this reaction occurs very slowly at 100 °C. It occurs much faster in the presence of base and excess ligand. A conjugate-base mechanism such as that reported for substitution of ethylenediamine in basic solutions of $(\text{en})_2\text{ReO}_2^+$ is suggested. We have no evidence to suggest that this process is related to the reaction we report in this paper. (b) Beard, J. H.; Calhoun, C.; Casey, J.; Murmann, R. K. *J. Am. Chem. Soc.* **1968**, *90*, 3389-3394.

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complexes and the similarity of the electronic spectra^{10,11} between diastereomers provide firm evidence for a head-to-head orientation of ligands in all the complexes studied.

We are aware of only one other study that compares rate data for technetium and rhenium complexes. The Tc(IV) complex TcCl_6^{2-} exchanges chloride 50 times faster than its rhenium congener, and TcBr_6^{2-} exchanges bromide 20 times faster than ReBr_6^{2-} .¹² Our data show the technetium complex

- (10) The UV-vis spectrum of **1a** is in good qualitative agreement with the previously published spectrum; however, the extinction coefficient we calculate is substantially less. For **1a**, $\lambda_{\text{max}} = 424 \text{ nm}$ ($\epsilon = 4890 \text{ M}^{-1} \text{ L}^{-1}$); for **2a**, $\lambda_{\text{max}} = 421 \text{ nm}$ ($\epsilon = 5050 \text{ M}^{-1} \text{ L}^{-1}$). For **1b**, $\lambda_{\text{max}} = 345 \text{ nm}$ ($\epsilon = 5020 \text{ M}^{-1} \text{ L}^{-1}$); for **2b**, $\lambda_{\text{max}} = 342 \text{ nm}$ ($\epsilon = 4390 \text{ M}^{-1} \text{ L}^{-1}$). The reaction of TcCl_6^{2-} with penicillamine has been reported to give a product with $\lambda_{\text{max}} = 420 \text{ nm}$ ($\epsilon = 4800 \text{ M}^{-1} \text{ L}^{-1}$), assigned as Tc(IV) because of its precursor.^{4a} The stereochemistry of the penicillamine was not reported, but this product is almost certainly **1a** or a mixture of **1a** and **2a**.
- (11) A reviewer has suggested the possibility that the relative stereochemistry of penicillamine ligands could be mutually trans rather than mutually cis. If this were the case, the mixed complexes would show static NMR spectra and the stereochemically pure complexes would show fluxional behavior. Since **1a** is chromatographically identical with the complex characterized crystallographically as mutually cis by Lock, the mixed complex **2a** must also be mutually cis to account for its fluxional behavior. The same argument rigorously proves the rhenium complexes to also be mutually cis. An alternative structure for the mixed complexes would have neither carboxylate coordinated, but this structure would not be expected to be fluxional and would not fit our chromatographic data.

2a racemizing 50 times faster than **2b** at 25 °C. Very few direct comparisons exist between the chemistry of technetium and rhenium,¹³ and our data demonstrate structural similarities and kinetic differences between the two metals. The ability to make such comparisons should prove helpful in the development of new ^{99m}Tc imaging agents as well as in the design of radiotherapeutic agents based on ¹⁸⁶Re or ¹⁸⁸Re. In addition, pharmacokinetic studies on the ^{99m}Tc penicillamine complexes show that stereoisomerism can be a significant concern in the development of new radiopharmaceuticals.¹⁴

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Registry No. **1a**, 92844-14-9; **1b**, 92998-63-5; **2a**, 92998-49-7; **2b**, 92844-15-0; $\text{NH}_4^+\text{TcO}_4^-$, 13598-66-8; $\text{NH}_4^+\text{ReO}_4^-$, 13598-65-7.

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- (14) Fritzberg, A. R.; Eshima, D.; Johnson, D. L.; Kasina, S., to be submitted for publication.

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Molecular A-Frames. Identification and Characterization of the Rhodium A-Frame Precursor Complex

Bis(μ -hydrido)dicarbonylbis(bis(diphenylphosphino)methane)dirhodium, $\text{Rh}_2(\mu\text{-H})_2(\text{CO})_2(\text{dppm})_2$

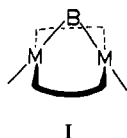
CARRIE WOODCOCK and RICHARD EISENBERG*

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The product of the borohydride reduction of $\text{Rh}_2\text{Cl}_2(\text{CO})_2(\text{dppm})_2$ has been reinvestigated and characterized as the dihydrido species $\text{Rh}_2(\mu\text{-H})_2(\text{CO})_2(\text{dppm})_2$. Under vacuum or N_2 , the complex rapidly loses H_2 as it undergoes a first-order decomposition. The decomposition is inhibited by H_2 , and solutions of the complex under H_2 are somewhat stabilized. Under D_2 the rapid formation of HD is observed. Solutions of the complex under H_2 react cleanly with various substrates. With HCl, the quantitative conversion to $\text{Rh}_2\text{Cl}_2(\text{CO})_2(\text{dppm})_2$ is observed. The complex reacts with HBr to form $\text{Rh}_2\text{Br}_2(\text{CO})_2(\text{dppm})_2$ and the new complex $[\text{Rh}_2(\mu\text{-H})(\mu\text{-CO})\text{Br}_2(\text{dppm})_2]\text{Br}$. Methyl iodide reacts with the complex to form 1 equiv of CH_4 and the new complex $\text{Rh}_2(\mu\text{-H})(\mu\text{-I})(\text{CO})_2(\text{dppm})_2$.

Introduction

Molecular A-frames are binuclear complexes of general structure I in which two d⁸ metal ions are maintained in close, fixed proximity for the binding and activation of simple substrate molecules.^{1,2} The structural integrity of A-frame



complexes is maintained through the use of difunctional

bridging ligands such as bis(diphenylphosphino)methane (dppm) and a bridgehead ligand, B, which generally consists of a small molecule or ion such as CO , H^+ , CNR , SO_2 , Cl^- , S^{2-} , and CH_2 .¹⁻⁹ Adducts of A-frame complexes have been reported in which the addend molecule is bound in the "pocket" or endo site of the A-frame structure,¹⁰⁻¹² and examples of

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