Development of Novel Water-Soluble, Organometallic Compounds for Potential Use in Nuclear Medicine: Synthesis, Characterization, and ^{1}H and ^{31}P NMR Investigations of the Complexes *fac*-[$ReBr(CO)_3L$] (L = Bis(bis(hydroxymethyl)phosphino)ethane, Bis(bis(hydroxymethyl)phosphino)benzene)

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The bidentate, water-soluble phosphine ligands, bis(bis(hydroxymethyl)phosphino)benzene (HMPB, **1**) and bis-(bis(hydroxymethyl)phosphino)ethane (HMPE, **2**) were reacted with the organometallic precursor *fac*-[$ReBr_3(CO)_3]^{2-}$, **3**, to produce the complexes *fac*-[$Re(OH_2)(CO)_3L]^{+}$ and *fac*-[$ReBr(CO)_3L$] (L = HMPE, HMPB), respectively, in good yields. The rhenium complexes *fac*-[$ReBr(CO)_3$HMPB], **5**, and *fac*-[$ReBr(CO)_3$HMPE], **8**, were characterized using ^{1}H and ^{31}P NMR spectroscopy. The structure of *fac*-[$ReBr(CO)_3$HMPB] was confirmed by single-crystal X-ray spectroscopy. The substitution reactions of HMPE/HMPB with the rhenium precursor **3** in aqueous solution were monitored using time-dependent ^{31}P NMR techniques. A significant discrepancy in the reaction kinetics and the substitution mechanism between the two bidentate ligands could be observed presumably due to the different chemical backbones.

Introduction

Phosphines occupy a unique role in the design and development of catalysts[1−3] and radiopharmaceuticals[4−7] because of their versatile bonding capability with transition metals and radiometals. The synergistic σ-donor characteristics coupled with the M → P π-back-bonding interactions (M = transition metal) of phosphine ligands result in strong phosphine−metal bonds. These complexes often exhibit optimum stability even under challenging in vivo conditions.[5,8,9] In fact, the pioneering efforts by Deutsch et al. and others have demonstrated stable technetium-99m complexes for application in nuclear medicine as myocardial perfusion agents in humans.[10] The findings that phosphine ligands produce in vivo stable complexes with radiometals (e.g., Tc-99m or Re-186/188) may be advantageously used in the design and development of radiopharmaceuticals that can be directed site-specifically to cancer tissues.

Despite superior ligating characteristics, the utility of phosphine ligands toward radiometals has been limited to a selection of alkyl-substituted mono- and bisphosphines (e.g., $((CH_3)_2PCH_2)_2$ commonly referred as dmpe).[10,11] While alkyl substituents on the P^{III} centers impart high nucleophilicity and thereby promote strong M−P bonds, their extreme oxidative instability poses severe restriction in their applications under routine laboratory and clinical settings. To achieve optimum oxidative stability in aqueous media, we have recently demonstrated that the introduction of hydroxymethyl substituents on the P^{III} centers produce phosphines that are hydrophilic and oxidatively stable in water. Prototypes of hydroxymethyl functionalized phosphines (**1** and **2**) and their coordination chemistry with Re(V) precursors are outlined in Scheme 1.[12] The corresponding $^{99m}Tc(V)$ complexes of **1** and **2** have demonstrated excellent bio clearance characteristics in rat (and mouse) models because of their high hydrophilicity.[13,14]

For a potential nuclear medical application of a transition metal compound, a high thermodynamic stability as well as a pronounced kinetic inertness is required. Since the kinetic inertness of transition metal complexes is generally dictated by

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|| H.S. Truman Memorial Veterans Hospital.

(1) Herrmann, W. A.; Kohlpaintner, C.; Manetsberger, R.; Bahrmann, H.; Kottmann, H. *J. Mol. Catal.* **1995**, *97*, 65.
(2) Herrmann, W. A.; Kohlpainter, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524.
(3) Herrmann, W. A.; Cornils, B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1048.
(4) Barrett, J. A.; Crocker, A. C.; Damphousse, D. J.; Heminway, S. J.; Liu, S.; Edwards, D.; Scott; Lazewatsky, J. L.; Kagan, M.; Mazaika, T. J.; Carroll, T. R. *Bioconjugate Chem.* **1997**, *8*, 155.
(5) Deutsch, E. *Radiochim. Acta* **1993**, *63*, 195.
(6) Dilworth, J. R.; Hutson, A.; Morton, S.; Harman, M.; Hursthouse, M.; Zubieta, J.; Archer, C.; Kelly, D. *Polyhedron* **1992**, *11*, 2151.
(7) Edwards, D. S.; Liu, S.; Barrett, J. A.; Harris, A. R.; Looby, R. J.; Ziegler, M. C.; Heminway, S. J.; Carroll, T. R. *Bioconjugate Chem.* **1997**, *8*, 146.
(8) Refosco, F.; Bolzati, C.; F.; T.; Bandoli, G. *J. Chem. Soc., Dalton Trans.* **1998**, 923.
(9) Bolzati, C.; Refosco, F.; Tisato, F.; Bandoli, G.; Dolmella, A. *Inorg. Chim. Acta* **1992**, *201*, 7.
(10) Vanderheyden, J.-L.; Ketring, A. R.; Libson, K.; Heeg, M. J.; Roecker, L.; Motz, P.; Whittle, R.; Elder, R. C.; Deutsch, E. *Inorg. Chem.* **1984**, *23*, 3184.
(11) Konno, T.; Kirchhoff, J. R.; Heeg, M. J.; Heineman, W. R.; Deutsch, E. *J. Chem. Soc., Dalton Trans.* **1992**, 3069.
(12) Reddy, V. S.; Berning, D. E.; Katti, K. V.; Barnes, C. L.; Volkert, W. A.; Ketring, A. R. *Inorg. Chem.* **1996**, *35*, 1753.
(13) Berning, D. E.; Reddy, S. V.; Katti, K. V.; Singh, P. R.; Hoffman, T. J.; Volkert, W. A.; Ketring, A. R. *J. Labelled Comp. Radiopharm.* **1995**, *37*, 459.
(14) Berning, D. E.; Katti, K. V.; Barnes, C. L.; Volkert, W. A. *J. Am. Chem. Soc.* **1999**, *121*, 1, 1658.

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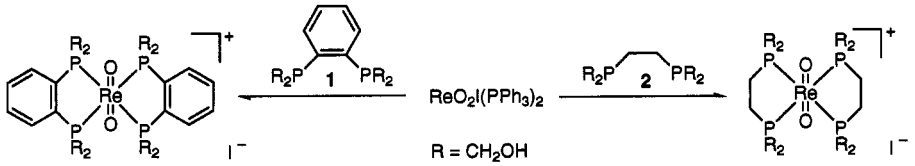
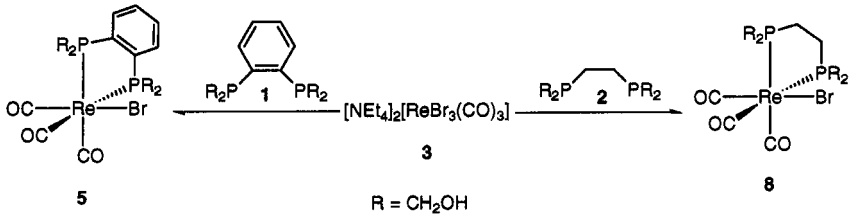
Scheme 1



Scheme 2



the oxidation state of the coordinated metal center, we decided to investigate the general coordination chemistry of **1** and **2** with low-valent rhenium(I) precursors. The results should partially answer the question of how the coordination chemistry of water-soluble bisphosphines can be translated in the development of aqueous-soluble and in vivo stable ^{188}Re(I) (or ^{99m}Tc-(I)) complexes for radiopharmaceutical applications. For the current investigations, the Re(I) precursor $[NEt_4]_2[ReBr_3(CO)_3]$, **3**, was chosen because Alberto et al. recently demonstrated its elegant synthesis, also for the corresponding ^{99}Tc analogues (i.e., $[NEt_4]_2[TcCl_3(CO)_3]$,).[15,16] The three halides are prone to substitution by water molecules in aqueous media. On the other hand, the three carbonyls are very inert against substitution. Therefore, coordination chemistry of the water-soluble bisphosphine ligands **1** and **2** with **3** would be expected to aid the development of the corresponding Re-186/188 (or Tc-99m) radiolabeled biomolecules for use in cancer therapy and diagnosis.

We report herein design and development of the novel compounds *fac*-[ReBr(CO)$_3$L] (L = bis(bis(hydroxymethyl)-phosphino)benzene (HMPB), bis(bis(hydroxymethyl)phosphino)ethane (HMPE)). The X-ray crystal structure of the representative compound *fac*-[ReBr(CO)$_3$HMPB], **5**, reported herein is the first one of its kind and has allowed comparison of the bonding parameters with its corresponding Re(V) analogues.[17] Solution properties and substitution profiles for the compounds *fac*-[ReBr(CO)$_3$HMPB] and *fac*-[ReBr(CO)$_3$HMPE] are discussed in terms of their relevance to understanding in vitro/in vivo properties of its corresponding ^{99m}Tc analogues.

Results and Discussion

Synthesis and Characterization of Complexes *fac*-[ReBr(CO)$_3$HMPB] (5) and *fac*-[ReBr(CO)$_3$HMPE] (8). We recently reported elegant synthetic strategies for the preparation of water-soluble rhenium(V)−oxo complexes with the bisphosphines HMPE (**1**) and HMPB (**2**) (Scheme 1). When reacted with $[NEt_4]_2[ReBr_3(CO)_3]$, these bisphosphines produced in water well-defined complexes of the general formula (*fac*-[ReBr(CO)$_3$L]; L = HMPB, HMPE) in good yields (Scheme 2).

The complexes **5** and **8** revealed a high kinetic inertness at various pHs, ranging from 3 to 10 at 37 °C. No decomposition or reoxidation of the metal core or ligand could be detected after a period of several weeks as verified by NMR and IR spectroscopy. This redox stability of Re(I)/Tc(I) compounds is a significant advantage compared to that of rhenium complexes in higher oxidation states +3 and +5, which often tend to reoxidize or disproportion under alkaline conditions.

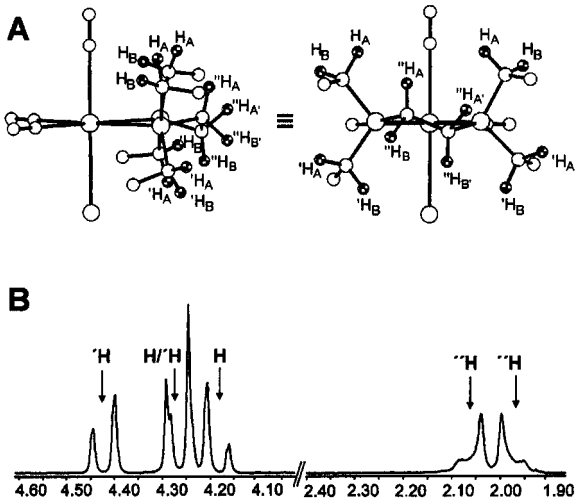


Figure 1. (A) Structure model (view along the P···P axis and the P−Re−P plane) and NMR proton assignment of complex **8**. Only C−H protons are shown. (B) ^{1}H NMR spectrum of complex **8** (DMSO-d_6).

Evidence for the molecular composition of **5** and **8** has resulted from ^{1}H and ^{31}P NMR spectroscopic investigations. Interestingly, the 1D and 2D (COSY) proton NMR spectra of compound **5** as well as of **8** revealed different AB spin systems with coupling constants of 12.9 Hz/9.3 Hz (**5**) and 13.8 Hz (**8**) for the protons of the four hydroxymethyl groups. The eight protons are nonequivalent not only by virtue of the different groups above and below the P−Re−P plane but also due to the orientation in respect to the metal center (Figure 1A). This results in the formation of two partially overlapping AB spin systems. Variable-temperature ^{1}H NMR experiments (10−90 °C) performed in D_2O revealed a low-field shift of all signals with increasing temperature (see Supporting Information). However, the doublets of the AB systems did not completely coalesce at high temperature. Obviously, the hydroxymethyl groups are significantly hindered in their free rotation around the P−C bond and retain their orientation as found in the X-ray structure of complex **5** (Figure 2). The protons signals of the ethylene backbone in complex **8** are poorly resolved (Figure 1B). It is apparent from the three-dimensional model of the

(15) Alberto, R.; Schibli, R.; Schubiger, P. A.; Abram, U.; Kaden, T. A. *Polyhedron* **1996**, *15*, 1079.
(16) Alberto, R.; Schibli, R.; Egli, A.; Schubiger, P. A.; Abram, U.; Kaden, T. A. *J. Am. Chem. Soc.* **1998**, *120*, 7987.
(17) Reddy, V. S.; Berning, D. E.; Katti, K. V.; Barnes, C. L.; Volkert, W. A.; Ketring, A. R. *Inorg. Chem.* **1996**, *35*, 1753.

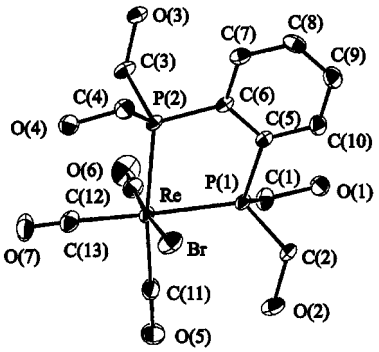


Figure 2. ORTEP presentation of the complex **5**. Ellipsoids are drawn on the 30% probability level. Protons are omitted for clarity.

Table 1. Crystal Data and Details of Data Collection for Complexes **5**

formula	$C_{13}H_{16}O_7P_2BrRe$
space group	$P2_1/n$
crystal system	monoclinic
fw	612.32
color	colorless
a [Å]	6.7036(3)
b [Å]	14.8591(7)
c [Å]	18.0338(9)
β [deg]	91.3441(10)
Z	4
temp [K]	173
R_w/R_1[a]	0.034/0.025
GOF	0.89

[a] $R_w = [\Sigma w(|F_o| - |F_c|)^2|)/\Sigma(w(|F_o|^2)]^{1/2}$; $R = \Sigma(||F_o| - |F_c||)/\Sigma(|F_o|)$.

complex and the general appearance of the spectrum that an XAA′BB′X spin system is present as reported for the complex [ReBr(dppe)(CO)$_3$] (dppe = 1,2-bis(diphenylphosphino)ethane).[18] ^{31}P coupling, relaxation, and dynamic effects result in a considerable line broadening and overlap of the ν_A and ν_B portions. Thus, only the center of the absorption is listed in the Experimental Section. At higher temperature (50−70 °C) additional splitting presumably due to P−H coupling of the ethylene signals could be observed. The CO stretch frequencies in the IR spectra were consistent with the *fac*-[M(CO)$_3$] geometry of compounds **5** and **8**. The corresponding absorptions of the carbonyl groups were observed at 2029, 1954, and 1894 cm^{-1} for **5** and 2031, 1958, and 1902 cm^{-1} for **8**, respectively. The final confirmation of the structure of **5** was provided by X-ray diffraction analysis.

X-ray Crystal Structure of 5. The ORTEP of compound **5** is shown in Figure 2. Selected bond distances and angles are summarized in Table 2. The three CO ligands are *facially* arranged with an average C−Re−C bond angle of 92.0(4)° which is very close to the ideal 90° for an octahedral geometry. The phosphine ligand is coordinated in a bidentate fashion, forming an almost planar five-membered ring with the metal center (average deviation from the P(1)−C(5)−C(6)−P(2)−Re plane, 0.064 Å). The ligand is slightly tilted toward the coordinated bromide, causing a narrowing of the Br−Re−P angles (83.56(3)° for Br(1)−Re−P(1) and 83.32(3)° for Br(1)−Re−P(2)). The angle P(1)−Re−P(2) of 80.93(4)° deviates significantly from the expected 90°. One of the oxygens of the hydroxymethyl groups at each phosphorus points toward the bromide ligand, whereas the second oxygen points toward the benzene ring. The Re−P bond distances are 2.4178(11) and 2.4264(11) Å, respectively. This is only slightly shorter than

(18) Edwards, D. A.; Marshalesa, J. *J. Organomet. Chem.* **1977**, *131*, 73.

Table 2. Selected Bond Length [Å] and Angles [deg] for Compound **5**

Re−Br(1)	2.6145(5)	P(1)−C(2)	1.853(4)
Re−P(1)	2.4179(11)	P(1)−C(1)	1.845(4)
Re−P(2)	2.4264(11)	O(7)−C(13)	1.143(6)
Re−C(11)	1.943(5)	O(5)−C(11)	1.167(6)
Re−C(12)	1.927(5)	O(6)−C(12)	1.120(6)
Re−C(13)	1.967(5)		
Br(1)−Re−P(1)	83.56(3)	P(1)−Re−C(13)	172.73(13)
Br(1)−Re−P(2)	83.32(3)	C(11)−Re−C(12)	91.6(2)
Br(1)−Re−C(11)	92.4(2)	C(11)−Re−C(13)	92.1(2)
Br(1)−Re−C(12)	175.1(2)	C(12)−Re−C(13)	92.3(2)
Br(1)−Re−C(13)	90.42(14)	C(1)−P(1)−C(2)	104.1(2)
P(2)−Re−P(1)	80.93(4)	C(1)−P(1)−C(5)	107.8(2)
P(1)−Re−C(12)	93.47(14)	C(2)−P(1)−C(5)	101.7(2)
P(1)−Re−C(11)	92.21(14)		

that in the Re(V) complex [ReO$_2$(HMPB)$_2$]I (2.461(1) Å and 2.456(1) Å, respectively).[17] The Re−Br bond length is 2.6145(5) Å. Because of a stronger π-back-bonding (enhanced by the electron rich bromine in trans position), the Re−C(12) bond length (1.927(5) Å) is shorter than the other two Re−C bond distances (Re−C(11) 1.943(5) Å and Re−C(13) 1.967(5) Å), a feature which is frequently observed in octahedral complexes of the general formula *fac*-[ReXL(CO)$_3$] (X = Cl, Br, I; L = bidentate ligand).[19]

Reaction Profiles of HMPB and HMPE with [NEt$_4$]$_2$[ReBr$_3$(CO)$_3$] using ^{31}P NMR Spectroscopy. The time-dependent, qualitative ^{31}P NMR experiments in aqueous media have unveiled interesting differences in the reaction kinetics and product distribution between the two bidentate phosphine ligands (**1** and **2**) when they were reacted with **3**.

Addition of 1 equiv of HMPB to a solution of **3** in water/DMSO (5:1) revealed, after 5 min, a strong signal of the free ligand at −29.5 ppm and a relatively weak signal of the product **5** at +30.5 ppm (Figure 3). The third peak at +38.1 ppm could be unambiguously assigned by mass spectroscopy to the cationic, monosolvated intermediate *fac*-[Re(OH$_2$)(CO)$_3$HMPB]$^+$ (**4**) (M^++1 = 551.0). After 30 min, the signals of both complexes **4** and **5** grow in intensity. Ninety minutes after the addition of ligand **1**, the signal of the final product **5** dominated the spectrum. After 5 h the free ligand was completely consumed and the intermediate **4** converted into the final product **5**.

Reaction with HMPE revealed a significantly different picture. Five minutes after the addition of HMPE to the solution of the metal precursor **3** hardly any free ligand was detectable (Figure 4). However, only small traces of product **8** could be found. The dominant peak originated from the cationic, intermediate *fac*-[Re(OH$_2$)(CO)$_3$ HMPE]$^+$, (**7**, $M^+ + 1 = 502.7$). Additionally, two doublets at +30.6 and −18.9 ppm were detected. These doublet signals are caused conceivably by the intermediate complex **6** (Figure 4) consisting of a monodentate coordination of ligand **2**. It may be noted that the two P^{III} centers in the intermediate complex **6** are unsymmetrical as evidenced by the observation of phosphorus−phosphorus coupling in its ^{31}P NMR spectrum (J = 36 Hz). The two doublets disappeared after approximately 2.5 h. At this time, the peak of the final product **8** was already dominant. However, it took again more than 5 h until completion of the reaction.

The different skeletons of ligand **1** compared to ligand **2** and the steric hindrance of the hydroxymethyl groups are presumably the reason for the contrasting reaction mechanism. In ligand **1**, which contains a benzene bridge, the phosphine functionalities

(19) Winter, M. *Gmelin: Organorhenium Compounds*, 8th ed.: Berlin, Heidelberg, New York, London, Paris, Tokyo, 1989; Vol. 1 and referenced therein.

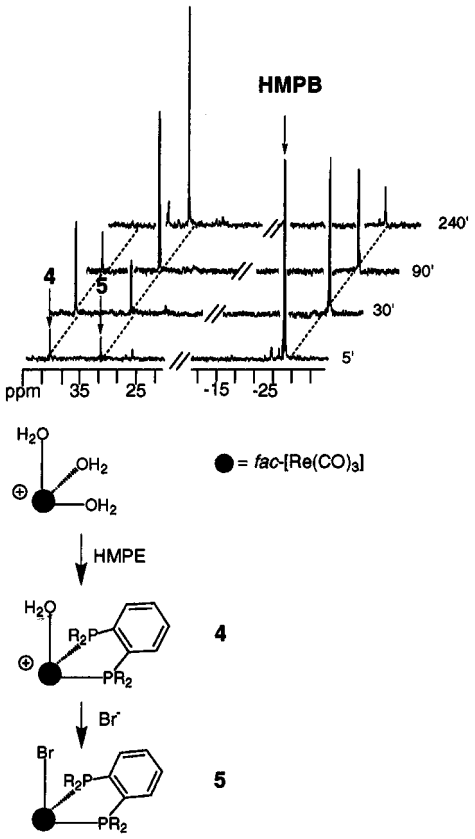


Figure 3. Time-dependent ^{31}P NMR spectra and the proposed substitution mechanism of the reaction between **3** and HMPB.

adopt an eclipsed (or syn periplanar) conformation. It is reasonable to imagine that this type of predisposition makes the monodentate coordination unlikely. Furthermore, steric hindrance due to the hydroxymethyl groups may explain why considerable amounts of free ligand remain in the reaction solution for an extended period of time. On the other hand, the flexible backbone of ligand **2** allows an anti conformation of the two phosphine groups. Thus, a coordination of the ligand to the metal center in two steps (first step, monodentate; second step, bidentate) can be expected. Obviously, the possibility of an initially monodentate coordination enhances the consumption of free ligand drastically.

Conclusion

The solution chemistry of the Re(I) complexes **5** and **8** described might provide important insights into the utility and design of such water-soluble phosphine-based organometallic complexes in general and for the development of Re(I) or Tc(I) compounds for nuclear medical applications in particular. Because of the good water-solubility and low tendency of hydroxymethyl phosphines to oxidize, these ligand systems display superior features for biomedical applications compared to those of alkyl- or arylphosphines. In fact, as a direct application of the fundamental chemistry reported herein, the in vivo studies of the corresponding ^{99m}Tc(I) carbonyl complexes of HMPB and HMPE (i.e., *fac*-[^{99m}Tc(OH$_2$)(CO)$_3$L]$^+$, L = HMPB, HMPE) have been recently investigated in our laboratory. These studies clearly demonstrated that the water-soluble ligands **1** and **2** exert strong hydrophilic characteristics on the ^{99m}Tc(I)−carbonyl complexes. It is important to recognize that the complexes *fac*-[^{99m}Tc(OH$_2$)(CO)$_3$L]$^+$ (L = HMPB, HMPE) have shown excellent pharmacokinetic properties.[20] In the context of the different approaches currently available for the

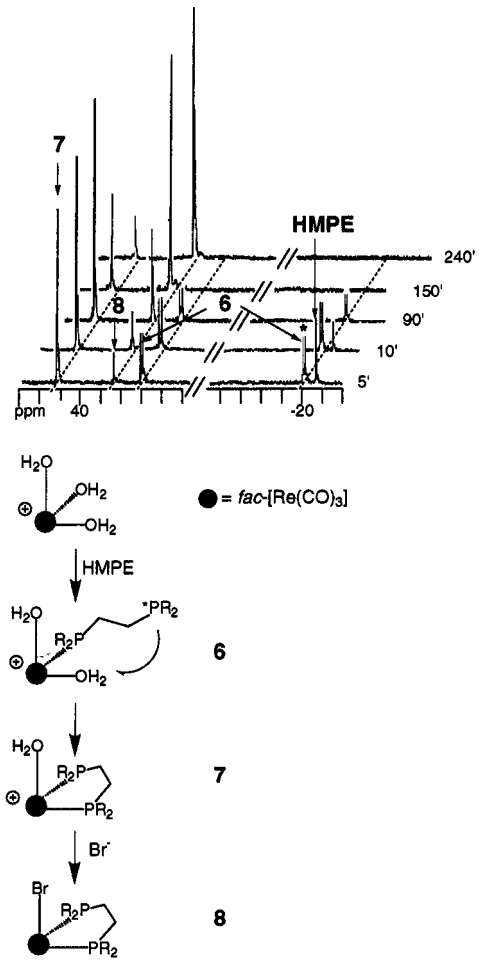


Figure 4. Time-dependent ^{31}P NMR spectra and the proposed substitution mechanism of the reaction between **3** and HMPE.

generation of technetium and rhenium carbonyls,[21−23] the results reported in this paper will also provide practically useful strategies on the application of hydroxymethyl phosphine ligands to generate in vivo stable ^{99m}Tc(I) and (^{188}Re) carbonyl compounds for their ultimate use in the design and development of site-specific (and tumor binding) radiopharmaceuticals.

Experimental Section

General. All chemicals and solvents were purchased from Fisher Scientific or Aldrich Co. and used without further purification. HMPE and HMPB were synthesized according to a literature procedure.[24,25] The metal precursor [NEt$_4$]$_2$[ReBr$_3$(CO)$_3$] (**3**) was synthesized according to a previously reported method.[15,26] Nuclear magnetic resonance spectra were recorded on a Bruker ARX-300 and a Varian Gemini 2000 spectrometer. The ^{1}H and ^{13}C chemical shifts are reported relative to residual solvent protons as a reference, while the ^{31}P shifts are reported

(20) Schibli, R.; Katti, K. V.; Higinbotham, C.; Volkert, W. A.; Alberto, R. *J. Nucl. Biol. Med.* **1999**, *26*, 711.
(21) Top, S.; Hafa, E. H.; Vessières, A.; Quivy, J.; Vaissermann, J.; Hughes, D. W.; McGlinchey, M. J.; Mornon, J.-P.; Thoreau, E.; Jaouen, G. R. *J. Am. Chem. Soc.* **1995**, *117*, 8372.
(22) Minutolo, F.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 4514.
(23) Bennouna, A.; Mousser, A.; Gorfti, A.; Salmain, M.; Cabestaing, C.; Jaouen, G. R. *Acta Cristallogr.* **1997**, *Sect. C*, 447.
(24) Reddy, V. S.; Katti, K. V.; Barnes, C. L. *Inorg. Chim. Acta* **1995**, *240*, 367.
(25) Klötzer, D.; Mading, P.; Münze, R. Z. *Chem.* **1984**, *24*, 224.
(26) Alberto, R.; Schibli, R.; Egli, A.; Schubiger, P. A.; Herrmann, W. A.; Artus, G.; Abram, U.; Kaden, T. A. *J. Organomet. Chem.* **1995**, *493*, 119.

relative to an external reference of 85% H_3PO_4 (0 ppm). IR spectra were recorded on a Galaxy Series FTIR 3000 using KBr pellets. Mass spectra were recorded on a Fisons VG Trio 2000 Quadrupole instrument.

X-ray Crystal Structure Determination. Details of the data collection and structure solution and refinement for complex **5** are summarized in Table 1. The intensity data were collected on a Simens SMART CCD system using the omega scan mode. Data were corrected for decay and absorption using the program SADABS based on the method of Blessing.[27] The structure was solved using the program SHELX S86[28] and refined on the NRCVAX system.[29−31] All hydrogen atoms were placed at the idealized positions. Atomic coordinates and their equivalent isotropic displacement coefficients are included in the Supporting Information.

Preparation of [ReBr(CO)$_3$HMPB] (5). The precursor **3** (115 mg, 0.15 mmol) was dissolved in 5 mL of H_2O. HMPB (38 mg, 0.15 mmol) was added and the reaction stirred for 3 h at room temperature. The solvent was removed under reduced pressure. Then 5 mL of dichloromethane was added to the waxy residue to extract NEt_4Br formed during the substitution reaction. Diethyl ether (20 mL) was added to the residue to convert the wax into a white powder. The powder was filtered and dried in a vacuum. Yield: 75 mg (82%). Colorless crystals of X-ray quality were obtained by slow diffusion of diethyl ether into a saturated methanolic solution of the product. Anal. ($C_{13}H_{16}O_7ReBr$). Calcd: C, 25.50; H, 2.63. Found: C, 25.32; H, 2.54. IR (cm^{-1}, KBr): 3327 (s), 2915 (w), 2029 (vs), 1954 (vs), 1894 (vs), 1430 (m), 1128 (m), 1040 (m), 885 (w), 760 (m), 613 (w), 518 (m). ^{1}H (δ, DMSO-d_6): 8.02 (m, 2 H, aromatic), 7.61 (m, 2 H, aromatic), 4.65 (d, 2 H, J = 12.9 Hz), 4.11 (d, 2 H, J = 12.9 Hz), 4.23 (d, 2 H, J = 9.3 Hz), 4.13 (d, 2 H, J = 9.3 Hz). ^{13}C (δ, DMSO-d_6): 193.1 (s, CO), 191.8 (s, CO), 188.1 (s, CO), 134.8 (s, aromatic), 132.1 (s, aromatic), 60.2 (d, CH_2OH, J_{PC} = 41 Hz), 56.3 (d, CH_2OH, J_{PC} = 40 Hz). ^{31}P (δ, DMSO-d_6): 29.7 (s).

Preparation of [ReBr(CO)$_3$HMPE] (8). Complex **8** was prepared according to the procedure used for compound **5**. Yield: 85%. No crystals suitable for X-ray analysis could be obtained from compound **8**. Anal. ($C_9H_{16}O_7ReBr$). Calcd: C, 19.16; H, 2.86. Found: C, 19.27; H, 2.66. IR (cm^{-1}, KBr): 3414 (s), 3256 (s), 2031 (vs), 1958 (vs), 1902 (vs), 1435 (m), 1358 (m), 1057 (m), 1030 (s), 610 (w), 511 (w). ^{1}H (δ, DMSO-d_6): 4.42 (d, 2 H, J = 13.8 Hz), 4.27 (d, 2 H, J = 13.8 Hz) 4.26 (d, 2 H, J = 13.8 Hz) 4.18 (d, 2 H, J = 13.8 Hz), 2.01 (broad, 4 H). ^{13}C (δ, DMSO-d_6): 193.3 (s, CO), 192.6 (s, CO), 188.7 (s, CO), 57.5 (d, CH_2OH, J_{PC} = 38 Hz), 54.6 (d, CH_2OH, J_{PC} = 35 Hz) 17.7 (d, CH_2, J_{PC} = 39 Hz). ^{31}P (δ, DMSO-d_6): 35.3 (s).

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Supporting Information Available: Additional 1D, variable-temperature, and 2D proton NMR spectra of **5** and **8**; tables of crystal data, structure solution and refinement, atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(27) Blessing *Acta Cristallogr.* **1995**, *A51*, 33.
(28) Sheldrick, G. M. *SHELXS86 -A program for the resolution of X-ray structures*, Universitiy of Göttingen, 1986.
(29) Gabe, E. J.; Le Page, Y.; Charland, J.-P.; Lee, F. L.; White, P. S. *J. Appl. Crystallogr.* **1989**, *22*, 384.
(30) Le Page, Y. *J. Appl. Crystallogr.* **1988**, *21*, 983.
(31) Le Page, Y.; Gabe, E. J. *J. Appl. Crystallogr.* **1979**, *12*, 464.