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Article

Reactions of the $Re(CO)_3(H_2O)_3^+$ Synthon with Monodentate Ligands under Aqueous Conditions

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The reactions of ammonia, pyridine (py), *N*-methyl imidazole (N-MeIm), tetrahydrothiophene (tht), and piperidine (pip) with $Re(CO)_3(H_2O)_3^+$, $\mathbf{1}^+$, were investigated employing aqueous conditions under atmospheric dioxygen. The reaction of [**1**]Br in aqueous ammonia led to $[Re(CO)_3(NH_3)_3]Br$ ([**2**]Br) as the only product isolated. For the aqueous reactions of [**1**]Br with py, N-MeIm, and tht, mixtures of products are formed because of competition between the bromide and added ligand, even when the ligand is present in excess. Substitution of the PF_6^- anion for Br^- leads to the clean formation of $[Re(CO)_3L_3][PF_6]$ ([**3**][PF_6]−[**5**][PF_6]) for py, N-MeIm, and tht, respectively, as the only products observed. Reaction of [**1**][PF_6] with pip produces the dimeric species, $(pip)(CO)_3Re(\mu\text{-}OH)_2Re(CO)_3(pip)$, **6**. Reactions of [**1**]Br were also performed in methanol for comparison purposes. The reaction with pip in this solvent led to the analogous dimer, $(pip)(CO)_3Re(\mu\text{-}OMe)_2Re(CO)_3(pip)$, **7**; however, reactions with py, N-MeIm, and tht gave $Re(CO)_3L_2Br$, **8**−**10**, respectively, as the only products. The crystal structures of compounds [**2**]Br−**10** are reported.

Introduction

Radiopharmaceuticals are modern, powerful tools for the diagnosis and treatment of many common diseases including heart disease and cancer. The most widely used nuclide for diagnostic imaging is ^{99m}Tc with over 7 million scans performed each year.[1] Now that $^{99m}Tc(CO)_3(H_2O)_3^+$ can be readily prepared in aqueous solution from $^{99m}TcO_4^-$,[2] designing syntheses of target-specific $^{99m}Tc(CO)_3L$ complexes forms a compelling research objective.[1] Practical uses of these complexes arise from their production by the facile replacement of water ligands, their *in vitro* and *in vivo* physiological stability to biomolecules, and from the ability to synthesize these compounds using an aqueous synthetic methodology, a requirement for use in biomedical applications.

The aqueous organometallic cation $Re(CO)_3(H_2O)_3^+$ $\mathbf{1}^+$ sees service as a cold model for the chemistry of $^{99m}Tc(CO)_3(H_2O)_3^+$. There has also been a recent surge in interest in this cation because of the possibility of developing compounds that contain the $^{186/188}Re(CO)_3^+$ core for radiotherapeutic purposes. While γ-emitting ^{99m}Tc has been employed for diagnostic imaging for a number of years, both ^{186}Re and ^{188}Re have only recently been considered for possible medical use as β^--emitters.[3–5] The combinations of energies and half-lives, along with their improved availability, suggest these isotopes, most notably ^{188}Re, could be adopted in pharmaceuticals for tumor radiation therapy in compromised patients with inoperable tumors or in patients ineligible for external beam radiation therapy or other common radiative practices.[4]

To guide efforts to develop new radiopharmaceuticals based on the $M(CO)_3^+$ (M = Tc, Re) cores, the fundamental aqueous chemistry of $\mathbf{1}^+$, including the kinetic, thermody-

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namic, and acid−base properties as well as clinically appropriate syntheses must be fully elucidated. Over the past 15 years, some progress has been reported. The synthesis of $[NEt_4]_2[Re(CO)_3Br_3]$ was developed since it generates **1**$^+$ in water.[6] More recently, researchers have promoted [**1**]Br[7] and $[Re(CO)_3(DMSO\text{-}O)_3][CF_3SO_3]$[8] as useful sources of the $Re(CO)_3^+$ moiety. While the latter compound will likely prove useful in the preparation of compounds for supramolecular syntheses or catalytic studies,[8,9] it is probable that [**1**]Br will prove to be the more appropriate synthon for reactions that have possible clinical relevance since it releases water instead of DMSO.

Others have examined the kinetic details of water exchange and ligand substitution to **1**$^+$ and found that the exchange of water ligands is relatively slow (6.3×10^{-3} s^{-1}) and that the rate of substitution of water with a heterocyclic amine or thioether occurs at approximately the same rate.[10,11] Acid−base studies have established the pK_a of **1**$^+$ as 7.5.[12] Using X-ray crystallography, we recently found that the solid obtained from the synthesis of **1**$^+$ is not [**1**]Br. Instead, under a variety of pH conditions both the previously known cubane compound, $[Re(CO)_3\text{-}\mu_3\text{-}(OH)]_4 \cdot 4\,H_2O$,[7] and [**1**]$[Re_2(CO)_6(\mu\text{-}Br)_3] \cdot 6\,H_2O$ were observed to crystallize.[13] When the bromide anion was exchanged for the PF_6^- anion, the formation of [**1**]$[Re(CO)_3(OH)(H_2O)_2][PF_6] \cdot H_2O$, containing both the triaquo cation and its conjugate base, was observed to crystallize at pH values between 1.5 and 5.6.[13]

Several groups, including ours, have examined $M(CO)_3^+$ compounds containing various tridentate ligands with amine, heterocyclic amine, carboxylate, and thioether groups.[5,14–21] Stability experiments have shown that the resultant compounds are often resistant to physiological decomposition in the presence of nucleophilic biological precursor molecules over several days or even months and may provide leads in the search for potential radiopharmaceuticals.[22] To understand the reactivity of larger polydentate molecules built from monodentate ligands, it is important to obtain a detailed understanding of all aspects of the chemistry including (1) the fundamental reactivity of monodentate ligands with **1**$^+$, (2) the types of conditions, for example, reactivity in water or sensitivity to atmospheric O_2, that may pertain to the preparation of compounds for clinical use, and (3) the effects different anions have on the outcome of reactions of $M(CO)_3^+$.

Herein, we report the results of the interaction of ammonia, three heterocyclic amines, and a thioether with **1**$^+$ under aqueous conditions. We discovered that the synthesis of $[Re(CO)_3(NH_3)_3]Br$ ([**2**]Br) can be accomplished using more moderate conditions than previously employed.[23–25] Application of [**1**]Br in water with other monodentate ligands led to mixtures of products resulting from complications with the bromide competing for space in the coordination sphere, and therefore, solutions of [**1**]$[PF_6]$ were utilized instead. The development of an aqueous solution of [**1**]$[PF_6]$ and its quantitative application as a synthetic reagent are discussed. Syntheses of $[Re(CO)_3L_3][PF_6]$, L = pyridine (py), *N*-methyl imidazole (N-MeIm), and tetrahydrothiophene (tht) are reported, [**3**]$[PF_6]$−[**5**]$[PF_6]$, respectively. When piperidine (pip) was employed under aqueous conditions, the dimeric compound $Re_2(CO)_6(\mu\text{-}OH)_2(pip)_2$ (**6**), was generated as the unexpected product. Reactions of monodentate ligands with [**1**]Br were also conducted in methanol to gauge the effect of the solvent on the reaction products. The reaction of [**1**]Br with piperidine produced the analogous dimer, $Re_2(CO)_6(\mu\text{-}OMe)_2(pip)_2$ (**7**). Similarly, reactions of [**1**]Br in methanol led to the neutral products, $Re(CO)_3L_2Br$, L = py **8**, N-MeIm **9**, and tht **10**, as the only products observed. Crystal structures of [**2**]Br−**10** are reported and discussed.

Results and Discussion

Syntheses. The aqueous synthesis of [**2**]Br greatly improves on previously reported preparations of [**2**]X ($X = Cl^-$, $O_2PR_2^-$; R = Me, Ph),[23–25] which required multiple steps, or the treatment of $Re(CO)_6^+$ with liquid ammonia in a sealed tube at 120 °C; Scheme 1 shows the reaction pathways explored in this Article. Simply heating an aqueous ammonia solution of [**1**]Br at 60 °C for a few hours produces [**2**]Br in high yield. Cooling the reaction tube slowly to room temperature creates crystals that are suitable for crystallography and are sufficiently pure for physical and chemical analysis.

When the reaction of [**1**]Br with excess pyridine or *N*-methyl imidazole was attempted in aqueous solution, mixtures were obtained that contained both $[Re(CO)_3L_3]Br$

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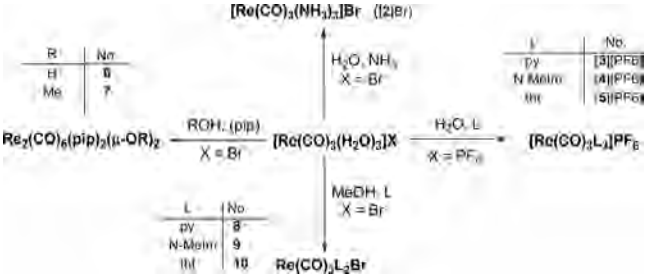
Scheme 1. Reactions Reported in This Article[a]



[a] Abbreviations: py = pyridine; N-Melm = *N*-methyl imidazole; tht = tetrahydrothiophene; pip = piperidine.

and $Re(CO)_3L_2Br$. This problem has been previously reported.[8] We eliminated competition of the bromide by employing [**1**][PF_6]. Solutions of [**1**][CF_3SO_3] have been employed for similar purposes.[15] We chose PF_6^- as the noncoordinating anion in these studies to facilitate crystallization. Aqueous solutions of [**1**][PF_6] are readily prepared by first creating aqueous solutions of [**1**]Br[7] and then exchanging Br^- for PF_6^- by careful addition of $AgPF_6$. This generates [**1**][PF_6] solutions that are essentially free of $AgPF_6$. The concentration of the solution was determined by quantitative UV−visible absorption measurements of $Re(CO)_3(bipy)H_2O^+$ prepared from these solutions and compared to spectra from independent preparations of this cation.[26] Use of [**1**][PF_6] solved the problem of multiple products being obtained because of competition from the nucleophilic bromide ion. Clean formation of **3**$^+$, **4**$^+$, and **5**$^+$ as the PF_6^- salts were observed when an excess of the appropriate ligand was employed. The synthesis of **3**$^+$ has been reported briefly in prior literature, but it was not crystallographically characterized.[8,27] Neither **4**$^+$ nor **5**$^+$ have been reported previously, although there have been two references to the corresponding tris(imidazole) complex in the literature.[28,29]

We also explored the use of aliphatic amines as ligands. As reported previously,[29] they typically bind the $Re(CO)_3^+$ moiety weakly and do not generate isolable products. We confirmed this general behavior using ethylamine. Attempts to react ethylamine with [**1**]Br led to a tricarbonyl-containing product that decomposed before purification or analysis could be completed. However, when a stoichiometric amount of piperidine was added to an aqueous solution of [**1**][PF_6], a white solid rapidly formed. While this compound and the corresponding methanol adduct described below could be prepared repeatedly, they are not as stable as other compounds reported here and decompose over a period of weeks. X-ray crystallographic analysis (see below) of crystals grown from the product of this reaction demonstrated the compound to be the bis-hydroxy-bridged dimeric species, $(pip)(CO)_3Re(\mu\text{-}OH)_2Re(CO)_3(pip)$, **6**. This structure is reminiscent of the tetranuclear cluster, $[(CO)_3(\mu\text{-}CN)Re(\mu\text{-}OH)_2Re(\mu\text{-}CN)(CO)_3]_2$,[2,30] obtained by the aqueous reaction of **1**$^+$ with KCN at pH 10. A solution of [**1**][PF_6] and piperidine at pH 9 presumably minimizes the presence of the piperidinium cation and assists in the deprotonation of the water needed to drive this reaction.

When the reaction of [**1**]Br with piperidine was performed in methanol, the analogous methoxy-bridged dimer **7** was obtained. This differs from the finding that reaction of **1**$^+$ with KCN in methanol produces $Re(CO)_3(CN)_3^{2-}$,[30] but is similar to the findings observed when $Re_2(CO)_{10}$ and pyrazine or related ditopic ligands were heated in various alcohols generating molecular squares built around the $(CO)_3Re(\mu\text{-}OH)_2Re(CO)_3$ unit.[31] Our attempts to create similar rhenium rectangles using piperazine produced white, insoluble materials that could not be identified.

Since reactions of [**1**]Br in water with py, N-MeIm, and tht give a mixture of products, methanol was employed. The syntheses of **8**[32] and **10**[33] have been reported previously using nonaqueous conditions but were not crystallographically characterized. Compounds **8**−**10** were prepared in good yield as the only product in each reaction, even in the presence of excess ligand. This strongly suggests that in solvents with lower dielectric constants, the separated charge of an ionic salt is disfavored relative to a neutral compound. Thus, the compounds $[Re(CO)_3L_3]Br$ were never observed to form as the major product using methanol. The reaction with ammonia under these conditions was not tested because $Re(CO)_3(NH_3)_2Br$ has been prepared and structurally analyzed by heating $Re(CO)_5Br$ with ammonia under pressure in benzene.[28]

Description of Structures. Crystal data and experimental details for the nine structures presented in this Article are listed in Table 1. The common characteristics of each structure include the facial arrangement of three carbonyls and the nearly octahedral orientation of six ligand donor atoms around each rhenium atom.

The structure of [**2**]Br contains four discrete compounds in the asymmetric unit. Structural data for the four cations are essentially identical, and each varies only in its relative orientations within the unit cell. Data is presented for only one cation; data for the other structures can be found in the crystallographic information file (cif file) provided as Supporting Information. The molecular structure of one cation of **2**$^+$ is shown in Figure 1. The average Re−N distance for the four structures is 2.226(15) Å, which is comparable to the Re−N distance of 2.240(6) Å in $Re(CO)_3(NH_3)_2Br$.[28]

The structures of cations **3**$^+$−**5**$^+$ are shown in Figure 2. Each of the structures is subtly different. The structure of **5**$^+$ is the most symmetric, having a C_3 axis as evidenced from the cation being built from a Re(CO)(tht) fragment.

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Table 1. Crystal Data and Structure Refinement for [**2**]Br-**10**[a]

	[**2**]Br	[**3**]PF_6	[**4**]PF_6	[**5**]PF_6	**6**	**7**	**8**	**9**	**10**
formula	$C_3H_9N_3O_3Br$ Re	$C_{18}H_{15}F_6N_3O_3PRe$	$C_{15}H_{18}F_6N_6O_3PRe$	$C_{15}H_{24}F_6O_3S_3PRe$	$C_{16}H_{20}N_2O_8$ Re_2	$C_9H_{13}NO_4Re$	$C_{13}H_{10}BrN_2O_3Re$	$C_{11}H_{12}Br$ N_4O_3 Re	$C_{11}H_{16}BrO_3$ ReS_2
FW	401.24	652.50	661.52	679.69	740.74	385.40	508.34	514.36	526.47
cryst syst	triclinic	triclinic	monoclinic	hexagonal	triclinic	triclinic	monoclinic	monoclinic	monoclinic
space group	$P\bar{1}$	$P\bar{1}$	$P2(1)$	$R3m$	$P\bar{1}$	$P\bar{1}$	$C2/c$	$P2(1)/c$	$P2(1)/c$
a (Å)	6.9409(11)	8.1881(13)	8.2618(10)	11.1729(19)	9.7445(19)	7.1308(9)	7.4888(14)	13.1022(12)	13.307(5)
b (Å)	15.361(2)	8.2792(13)	12.8134(16)	11.1729(19)	9.7953(19)	8.7059(11)	14.433(3)	7.6299(7)	9.063(3)
c (Å)	17.280(3)	16.024(2)	10.2229(12)	14.705(3)	11.264(2)	9.6359(13)	13.070(2)	15.0189(13)	12.777(4)
α (Å)	87.936(3)	101.673(2)	90	90	87.212(3)	77.992(2)	90	90	90
β (Å)	88.417(3)	97.169(2)	96.113(2)	90	75.075(3)	78.810(2)	90.540(3)	92.231(2)	97.217(6)
γ (Å)	88.849(5)	99.325(2)	90	120	86.341(3)	83.014(2)	90	90	90
V (Å^3)	1840.1(5)	1035.7(3)	1076.1(2)	1589.7(5)	1036.1(3)	571.92(13)	1412.6(4)	1500.3(2)	1528.6(9)
Z	8	2	2	3	2	2	4	4	4
ρ_{calc} (mg/m^3)	2.897	2.092	2.042	2.130	2.374	2.238	2.390	2.277	2.288
abs coeff (mm^{-1})	17.519	6.023	5.802	6.171	11.716	10.617	11.438	10.774	10.833
$2\theta_{max}$ (deg)	52.00	55.00	52.00	56.24	56.70	54.00	56.30	52.96	54.00
R indicies[a]	0.0352	0.0298	0.0250	0.0169	0.0475	0.0313	0.0291	0.0276	0.0280
$wR2 = [I > 2\sigma(I)]^b$	0.0823	0.0695	0.0519	0.0397	0.1085	0.0730	0.0693	0.0591	0.0574
data/ params	6728/409	4586/292	4135/292	969/70	4684/254	2571/137	1663/105	3097/211	3313/163

[a] All structures collected at 100(2) K.

Figure 1. Molecular structure of one cation of four structurally similar cations of [**2**]Br showing 35% thermal ellipsoids. Selected bond lengths [Å] and angles [deg]: Re(1)−N(1) 2.221(7), Re(1)−C(1) 1.918(9); N(1)−Re(1)−N(2) 83.1(3), C(1)−Re(1)−C(2) 88.1(4).

The tht ligands are folded-away from the molecular C_3 axis as a consequence of a side-on coordination mode exhibited by the sulfur-containing ligands. A few examples of metal−carbonyl compounds with S-bound tht ligands are known.[34–40] Each shows the typical folded-away orientation of the ligand. The crystal structures of [**5**][PF_6] and **10** (discussed below) are the first metal−carbonyl compounds with more than one bound tht. Cation $\mathbf{3}^+$ displays pseudo-C_s symmetry. One of the three pyridine ligands has a different orientation of the aromatic ring relative to the remaining rings. It is oriented such that the ligand plane bisects the N−Re−N angle spanned by the rhenium and the nitrogens in the other two pyridine ligands. Each of the other two ligands lies so that its ligand planes bisect the N−Re−C angle of the other pyridine nitrogen and a carbonyl carbon. Cation $\mathbf{4}^+$ has no symmetry due to the random arrangement of the three *N*-methyl imidazole ligands. Notably, the arrangement of the ligands in $\mathbf{3}^+$ and $\mathbf{4}^+$ differs from the arrangement of the pyridine and *N*-methyl imidazole donor ligands in the tripodal compounds [$Re(CO)_3(py_3COR)$]Br, R = H, Me, and [$Re(CO)_3$(N-$MeIm_3$COMe)][PF_6].[21] The structures of each of these molecules approach C_{3v} symmetry due to the enforced steric requirements of each tripodal ligand. The average Re−N distances for $\mathbf{3}^+$ and $\mathbf{4}^+$ are 2.210(20) and 2.195(4) Å, respectively. Each of these distances is longer than the comparable average Re−N distance of 2.178(15) Å measured for [$Re(CO)_3(py_3COR)$]Br, R = H, Me, and the average distance of 2.179(31) Å measured for [$Re(CO)_3$(N-$MeIm_3$COMe)][PF_6].[27] The average Re−S distance for $\mathbf{5}^+$ is 2.502(2) Å.

The structures of **6** and **7** are shown in Figure 3. Each adopts a conlateral bioctahedral geometry with a pair of bridging hydroxy or methoxy anions, and each is located around an inversion center present in the unit cell. One piperidine is on each rhenium; the piperidines are located in an *anti* conformation with respect to the $(CO)_2Re(\mu\text{-}OR)_2Re(CO)_2$ (R = H, CH_3) face. Compound **6** has two molecules in the asymmetric unit. The structural data concerning orientation and separation of atoms around the central metal are similar for each structure with the exception that both piperidine ligands in one molecule are each rotated slightly about the Re−N bond. Data is presented for only one structure; data for the other structure can be found in the cif file in Supporting Information. Hydrogen bonding is observed between the bridging hydroxides of the molecule that does not have the piperidine ligands rotated and the oxygen of a CO on the adjacent molecule (2.854 Å). The center of the $(CO)_2Re(\mu\text{-}OMe)_2Re(CO)_2$ face of **7** lies on an

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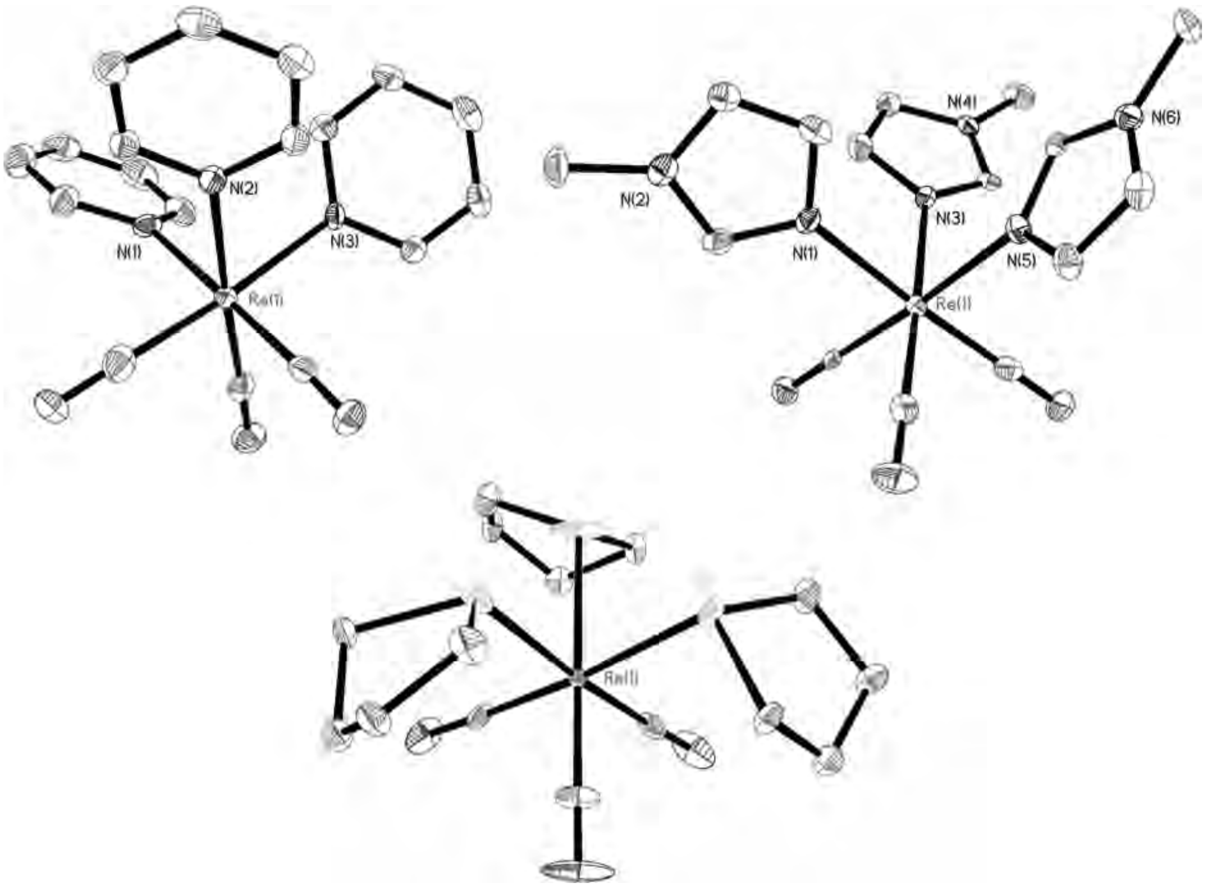

Figure 2. Molecular structures of [**3**][PF_6] (left), [**4**][PF_6] (right), and [**5**][PF_6] (bottom), each with cations only, showing 35% thermal ellipsoids. Hydrogen atoms have been omitted for clarity. A crystallographic C_3 axis was used to generate $\mathbf{5}^+$ from a Re(CO)(tht) fragment. Selected bond lengths [Å] and angles [deg] for $\mathbf{3}^+$: Re(1)−N(1) 2.216(4), Re(1)−C(1) 1.902(6); N(1)−Re(1)−N(2) 92.3(1), C(1)−Re(1)−C(2) 88.8(2). Selected bond lengths [Å] and angles [deg] for $\mathbf{4}^+$: Re(1)−N(1) 2.197(4), Re(1)−C(1) 1.918(5); N(1)−Re(1)−N(3) 84.7(2), C(1)−Re(1)−C(2) 89.6(2). Selected bond lengths [Å] and angles [deg] for $\mathbf{5}^+$: Re(1)−S(1) 2.502(2), Re(1)−C(1) 1.927(7); S(1)−Re(1)−S(1)#4 82.71(6), C(1)−Re(1)−C(1)#4 88.8(3).

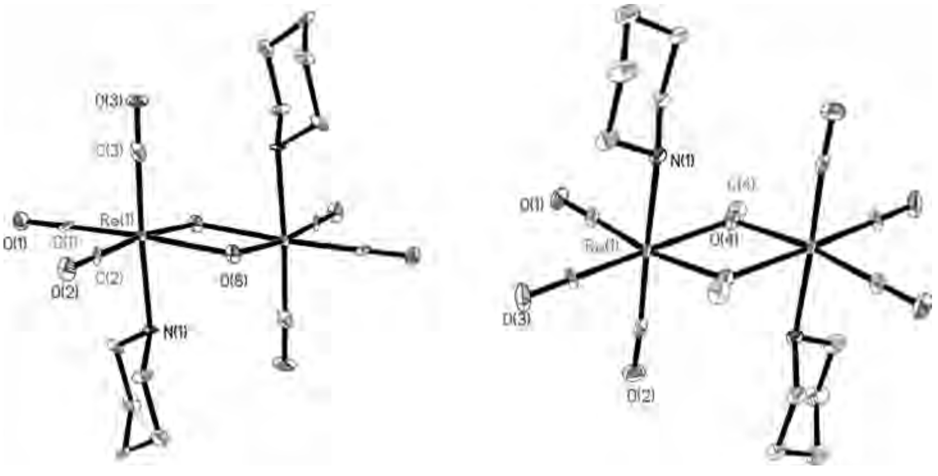

Figure 3. Molecular structures of **6** (left) and **7** (right), showing 35% thermal ellipsoids. Only one of two molecules of **6** in the asymmetric unit are shown. Hydrogen atoms have been omitted for clarity. Structures of **6** and **7** are constructed from fragments located around a crystallographic inversion center. Selected bond lengths [Å] and angles [deg] for **6**: Re(1)−N(1) 2.230(7), Re(1)−C(1) 1.909(8), Re(1)−O(8) 2.146(6); C(1)−Re(1)−C(2) 86.3(4), N(1)−Re(1)−O(8) 79.0(2), C(1)−Re(1)−N(1) 94.9(3), O(8)−Re(1)−O(8)#1 71.5(3), Re(1)−O(8)−Re(1)#1 108.5(3), C(1)−Re(1)−O(8) 170.7(3). Selected bond lengths [Å] and angles [deg] for **7**: Re(1)−N(1) 2.250(5), Re(1)−C(6) 1.900(6), Re(1)−O(1) 2.135(4); C(6)−Re(7)−C(2) 87.4(3), N(1)−Re(1)−O(4) 81.0(2), C(6)−Re(1)−N(1) 95.0(2), O(4)−Re(1)−O(4) 71.7(2), Re(1)−O(1)−Re(1)#1 108.3(2), C(7)−Re(1)−O(1) 99.4(2).

inversion center. The average Re−N distances for **6** and **7** are 2.252(8) and 2.250(5) Å, respectively.

The molecular structures of **8**−**10** are shown in Figure 4. As observed for cations $\mathbf{3}^+$−$\mathbf{5}^+$, there are subtle differences in the observed structures related to the arrangement of the ligands. Both **8** and **9** are asymmetric because of the random arrangement of the ligands in the coordination sphere. The structure of **8** is analogous to the previously reported structure of $Re(CO)_3(py)_2Cl$.[41] Compound **10** again has the tht ligands leaning away from the 3-fold axis of the three carbonyls

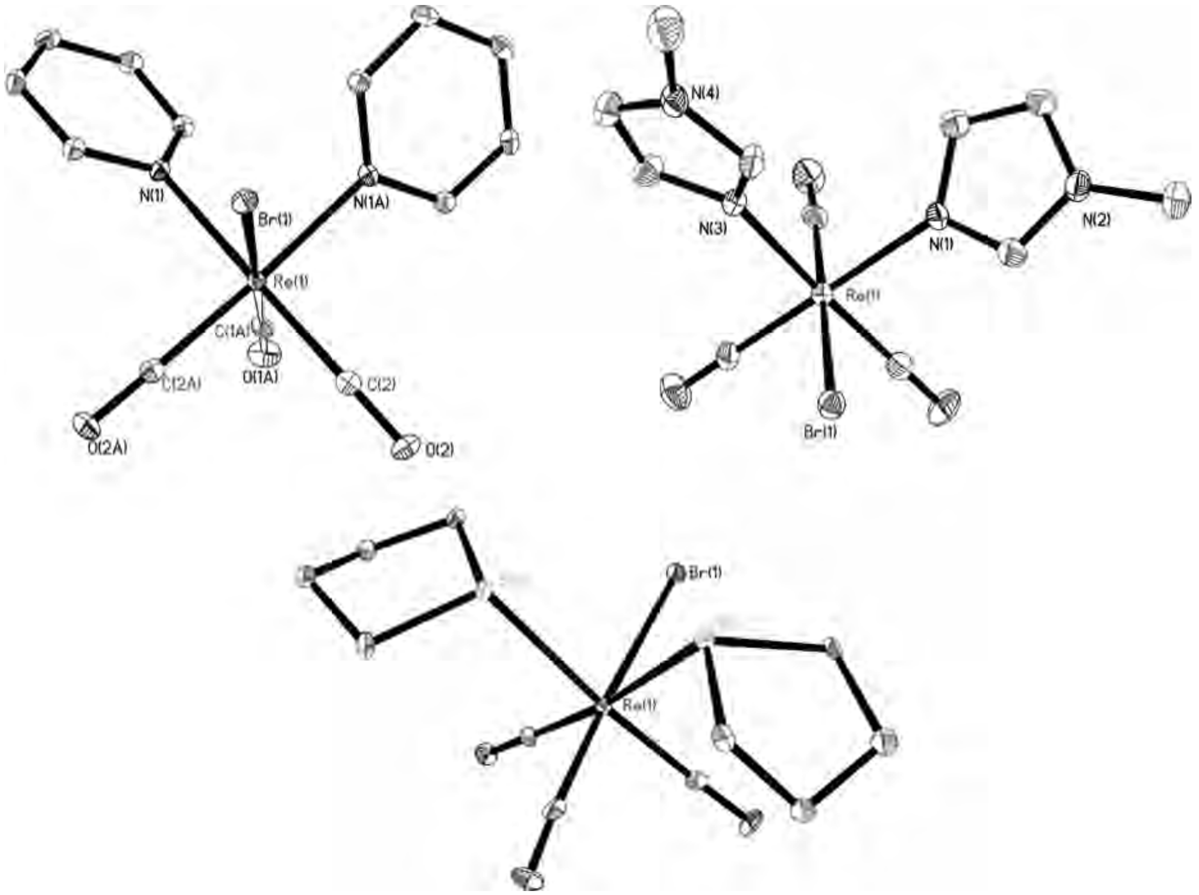

Figure 4. Molecular structures of **8**−**10** (left, right, and bottom) showing 35% thermal ellipsoids. Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [deg] for **8**: Re(1)−N(1) 2.223(4), Re(1)−C(1) 1.940(2), Re(1)−Br(1) 2.560(2); N(1)−Re(1)−N(1)#1 84.6(2), C(1)−Re(1)−C(2) 91.3(5), N(1)−Re(1)−Br(1) 88.91(13), C(1)−Re(1)−Br(1) 94.67(17), N(1)−Re(1)−C(1) 92.3(5). Selected bond lengths [Å] and angles [deg] for **9**: Re(1)−N(1) 2.192(4), Re(1)−C(1) 1.920(6), Re(1)−Br(2) 2.5606(18); N(1)−Re(1)−N(3) 85.04(16), C(1)−Re(1)−C(2) 88.5(2), N(1)−Re(1)−Br(2) 89.3(1), C(1)−Re(1)−Br(2) 98.0(2), N(1)−Re(1)−C(1) 91.1(2). Selected bond lengths [Å] and angles [deg] for **10**: Re(1)−S(1) 2.515(1), Re(1)−C(1) 1.933(6), Re(1)−Br(1) 2.6226(8); S(1)−Re(1)−S(2) 82.73(4), C(1)−Re(1)−C(2) 91.70(2), S(1)−Re(1)−Br(1) 81.43(4), C(1)−Re(1)−Br(1) 95.6(2), S(1)−Re(1)−C(2) 94.4(2).

providing apparent pseudo-C_s symmetry. However, the axial and equatorial orientations of the methylenes of the two nonplanar ligands remove the C_s symmetry. The average Re−N distances for **8** and **9** are 2.230(4) and 2.187(4) Å, respectively. The average Re−S distance for **10** is 2.510(5) Å.

Spectroscopic Characterization. Infrared spectra for [**3**][PF_6]−**10** in the solid state showed typical tricarbonyl band patterns in the region of 2030−1840 cm^{-1}, consistent with a facial tricarbonyl geometry. The exception was [**2**]Br, which showed a complex spectrum in this region when examined in the solid state. However, the infrared spectrum of a methanol solution of [**2**]Br showed the expected tricarbonyl pattern. The complexity is explained by solid state symmetry effects:[42] there are four independent molecules of [**2**]Br per asymmetric unit as determined by crystallography.

Most of the ^1H and ^{13}C NMR spectra reported are consistent with the observed structures and require no further explanation. The ^1H NMR spectrum of **10** shows two sets of resonances for the α tht protons and one set of peaks for the β tht protons. This is ascribed to the orientation of the α protons relative to the coordinated bromine. One pair of α tht protons occupies a distal position, while the other pair of α tht protons occupies a proximal position with respect to the bromine. The two pairs of β tht protons show a single set of resonances because of the larger spatial separation of these protons from the bromine and the *trans*-CO.

Conclusions

In this study, we have demonstrated that reactions involving the $Re(CO)_3^+$ core can frequently be performed to produce trisubstituted products in distilled water under an aerobic atmosphere, suggesting that [**1**]X may be useful in the syntheses of radiopharmaceuticals. A variety of trisubstituted compounds with monodentate ligands were prepared including [**2**]Br whose synthesis was greatly improved. Whereas primary amines have not previously been observed to generate stable products, reactions with the secondary amine piperidine gave dimeric compounds, which is a consequence of the ligand's basicity. Surprisingly, only stoichiometric amounts of piperidine were required for reaction, while significant excesses of the other monodentate ligands were typically employed to ensure trisubstitution. Furthermore, aqueous reactions of [**1**]Br with pyridine, *N*-methyl imidazole, and tetrahydrothiophene gave mixtures of products. To avoid this problem, we found it convenient

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(41) Belanger, S.; Hupp, J. T.; Stern, C. L. *Acta Crystallogr., Sect. C* **1998**, *54*, 1596–1600.

(42) Drago, R. S. *Physical Methods in Chemistry*; W.B. Saunders Co., 1977; p 660.

to use a noncoordinating anion, PF_6^-, for the syntheses. The reagent [**1**][PF_6] proved easy to prepare at known concentrations and was stable for months. In contrast to the compounds prepared in aqueous solution, employing [**1**]Br with monodentate ligands in methanol produced $Re(CO)_3L_2Br$ as the sole product. These results demonstrate that reactions of the $Re(CO)_3^+$ core can be conducted in aqueous solutions under an atmosphere containing oxygen and that different products may be created under these conditions. We also note that the noncoordinating anion, PF_6^-, was used in these studies to prevent its inclusion in the coordination sphere and to facilitate crystallization. Further studies are in progress to develop this chemistry.

Experimental Section

Materials and Methods. NMR spectra were recorded on a Varian 400 MHz spectrometer. IR spectra were recorded on a Nicolet Series II Magna-IR 750 spectrometer. UV−visible spectra were recorded on a Hitachi U-2800A Spectrophotometer. Elemental analyses were performed by Atlantic Microlab of Norcross, GA 30091. Starting materials were obtained from commercial sources and were used without further purification. Distilled water was used in all aqueous reactions. $[Re(CO)_3(H_2O)_3]Br$ was prepared and isolated according to the literature procedure.[7] $[Re(CO)_3(bipy)(H_2O)][CF_3SO_3]$ was prepared and purified following the literature procedure;[26] least-squares analyses of Beers Law plots determined the molar absorptivity to be $4.21(3) \times 10^3$ M^{-1} cm^{-1} at 350 nm.

X-ray Data Collection and Structure Determination. X-ray intensity data were measured at 100 K (Bruker KYRO-FLEX) on a Bruker SMART APEX CCD-based X-ray diffractometer system equipped with a Mo-target X-ray tube ($\lambda = 0.71073$ Å) operated at 2000 W power. The crystals were mounted on a cryoloop using Paratone N-Exxon oil and placed under a stream of nitrogen at 100 K. The detector was placed at a distance of 5.009 cm from the crystals. The data were corrected for absorption with the SADABS program. The structures were refined using the Bruker SHELXTL Software Package (version 6.1) and were solved using direct methods until the final anisotropic full-matrix, least-squares refinement of F^2 converged.[43] Additional experimental details are provided in Table 1.

Preparation of $[Re(CO)_3(H_2O)_3][PF_6]$ ([1][PF$_6$]). An aqueous solution of $\mathbf{1}^+$ was prepared from 5.00 g (12.3 mmol) of $Re(CO)_5Br$ in 75 mL of distilled water using the literature procedure.[7] $AgPF_6$ (2.50 g, 9.93 mmol) was added to the solution, producing a copious white precipitate that was removed by centrifugation. Smaller amounts were then added with subsequent centrifugation until no further precipitation was observed. The concentration of [**1**][PF_6] was determined by adding a slight excess of 2,2′-bipyridine to an aqueous solution of a 1.00 mL aliquot of [**1**][PF_6] and stirring it in the dark for 24 h. Comparison of the UV−visible data obtained for [**1**][PF_6] with the calibration curve obtained for a known sample of $[Re(CO)_3(bipy)(H_2O)][CF_3SO_3]$ allowed the calculation of a concentration of 0.159(1) M for the prepared solution of [**1**][PF_6]. The solution was capped and kept in the dark and showed no sign of decomposition after a year of storage.

Synthesis of $[Re(CO)_3(NH_3)_3]Br$ ([2]Br). [**1**]Br (0.200 g, 0.493 mmol) and NH_4OH (2.00 mL, 14.8 M) were added to an Ace pressure tube. The cap was tightened, and the tube was heated to 60 °C and stirred for three or more hours, producing a clear homogeneous solution. The flask was very slowly cooled to room temperature, leading to the generation of large, colorless crystals suitable for X-ray diffraction and characterization purposes. The crystalline solid was filtered, dried under high vacuum, and collected. Yield: 94%. IR: 2013(s), 1914(m), 1884(vs), 1874(vs), 1840(vs) cm^{-1}. IR (CH_3OH): 2026(s), 1906(vs) cm^{-1}. Anal. Calc. for $C_3H_9N_3O_3ReBr$; C, 9.14; H, 2.26; N, 10.48%. Found: C, 8.98; H, 2.25; N, 10.39%. Mp = 265 °C (d). ^1H NMR (d_6-DMSO): δ 3.26 (s, 9H, N*H*$_3$).

Syntheses of Rhenium Complexes ([3][PF$_6$]−[5][PF$_6$]). The procedure for the synthesis of [**3**][PF_6] is representative of each of these syntheses.

$[Re(CO)_3(py)_3][PF_6]$ ([3][PF$_6$]). [**1**][PF_6] (2.00 mL, 0.318 mmol) and pyridine (1.00 mL, 12.4 mmol) were added to 5.0 mL of distilled water in a round-bottom flask. The cloudy solution was refluxed for 1 h, resulting in a clear, colorless solution. The solvent and excess ligand were then both removed by rotary evaporation. The product was washed with ether, dried under high vacuum, and collected as a white solid. Crystals suitable for X-ray diffraction were obtained by vapor diffusion of pentane into a $CHCl_3$ solution of the complex. Yield: 98%. IR: 2026(s), 1899(vs, b) cm^{-1}. Anal. Calc. for $C_{18}H_{15}N_3O_3RePF_6$; C, 33.13; H, 2.32; N, 6.44%. Found: C, 32.90; H, 2.27; N, 6.32%. Mp = 151−154 °C. ^1H NMR (d_6-acetone): δ 8.80 (d, $^3J = 4.8$ Hz, 6H, *H* on py), 8.23 (m, 6H, *H* on py), 7.70 (m, 3H, *H* on py). ^{13}C NMR (d$_6$-acetone): δ 154.1 (*C* on py), 140.8 (*C* on py), 127.6 (*C* on py).

$[Re(CO)_3(N\text{-}MeIm)_3][PF_6]$ ([4][PF$_6$]). Crystals suitable for X-ray diffraction were obtained by vapor diffusion of hexane into a CH_2Cl_2 solution of the complex. Yield: 59%. IR: 2012(s), 1878(vs, b) cm^{-1}. Anal. Calc. for $C_{15}H_{18}N_6O_3RePF_6$; C, 27.23; H, 2.74; N, 12.70%. Found: C, 27.52; H, 2.72; N, 12.54%. Mp = 196 °C. ^1H NMR (d_6-acetone): δ 7.94 (s, 3H, *H* on MeIm), 7.30 (s, 3H, *H* on MeIm), 6.89 (s, 3H, *H* on MeIm), 3.80 (s, 9H, *CH$_3$*). ^{13}C NMR (d_6-acetone): δ 142.2 (*C* on MeIm), 130.5 (*C* on MeIm), 123.1 (*C* on MeIm), 34.2 (CH_3).

$[Re(CO)_3(tht)_3][PF_6]$ ([5][PF$_6$]). Crystals suitable for X-ray diffraction were obtained by allowing an aqueous solution of the complex to lie undisturbed for 72 h. Yield: 26%. IR: 2026(s), 1911(vs, b) cm^{-1}. Anal. Calc. for $C_{15}H_{24}S_3O_3RePF_6$; C, 26.50; H, 3.56; S, 14.15%. Found: C, 26.23; H, 3.56; S, 13.96%. Mp = 188−191 °C. ^1H NMR ($CDCl_3$): δ 3.41 (t, $^3J = 2.4$ Hz, 12H, *H* on tht), 2.20 (t, $^3J = 2.4$ Hz, 12H, *H* on tht). ^{13}C NMR ($CDCl_3$): δ 41.4 (*C* on tht), 30.9 (*C* on tht).

Synthesis of $Re_2(CO)_6(pip)_2(\mu\text{-}OH)_2$ (6). [**1**][PF_6] (1.00 mL, 0.159 mmol) and piperidine (80 μL, 0.81 mmol) were added to 5.0 mL of distilled water in a round-bottom flask. The solution was stirred for 1 min, producing a white solid. The solid was filtered and washed sparingly with distilled water. The filtered solid was dissolved in methylene chloride and dried with anhydrous magnesium sulfate. The methylene chloride filtrate was allowed to sit undisturbed until the solvent evaporated. Crystals suitable for X-ray diffraction were obtained by vapor diffusion of pentane into a CH_2Cl_2 solution of the complex. Yield: 66%. IR: 2004(s), 1848(vs, b) cm^{-1}. Anal. Calc. for $C_{16}H_{22}N_2O_8Re_2$; C, 27.11; H, 3.26; N, 4.12%. Found: C, 26.67; H, 3.40 N, 4.04%. Mp = 192 °C (d). ^1H NMR (d_6-acetone): δ 3.12 (m, 8H, *H* on pip) 1.77 (m, 8H, *H* on pip), 1.66 (m, 4H, *H* on pip), ^{13}C NMR ($CDCl_3$): δ 53.4 (*C* on pip), 27.7 (*C* on pip), 23.9 (*C* on pip).

Synthesis of $Re_2(CO)_6(pip)_2(\mu\text{-}OMe)_2$ (7). [**1**]Br (0.200 g, 0.493 mmol) and piperidine (1.00 mL, 9.70 mmol) were added to 5.0 mL of methanol in a round-bottom flask. The solution was stirred for 1 h at room temperature, resulting in a clear, colorless solution. The solution was covered and allowed to sit undisturbed for 72 h,

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[43] Sheldrick, G. M. *SHELXTL, Crystallographic Software Package,Version 6.10*, Bruker-AXS: Madison, WI, 2000.

producing **7** as clear, colorless crystals suitable for X-ray diffraction and characterization purposes. The crystals were filtered, dried under high vacuum, and washed with ether. Yield: 57%. IR: 2003(s), 1856(vs, b) cm^{-1}. Anal. Calc. for $C_{18}H_{26}N_2O_8Re_2$; C, 27.97; H, 3.65; N, 3.62%. Found: C, 28.33; H, 3.66; N, 3.74%. Mp = 220 °C (d). ^{1}H NMR ($CDCl_3$): δ 3.87 (s, 6H, OC*H*$_3$), 3.57 (m, 4H, *H* on pip), 3.04 (m, 4H, *H* on pip), 1.90−1.70 (m, 12H, *H* on pip). ^{13}C NMR ($CDCl_3$): δ 68.7 (OCH_3), 53.9 (*C* on pip), 27.8 (*C* on pip), 23.8 (*C* on pip).

Syntheses of Rhenium Complexes 8−10. The procedure for the synthesis of **8** is representative of each of these syntheses.

$Re(CO)_3(py)_2Br$ (8). [**1**]Br (0.200 g, 0.493 mmol) and pyridine (1.00 mL, 12.4 mmol) were added to 5.0 mL of methanol in a round-bottom flask. The solution was stirred and heated gently for 30 min, producing a white precipitate. The product was filtered, dried and washed with ether, and collected as a white solid. Crystals suitable for X-ray diffraction were obtained by vapor diffusion of methanol into a DMSO solution of the complex. Yield: 90%. IR: 2010(s), 1856(vs, b) cm^{-1}. Anal. Calc. for $C_{13}H_{10}N_2O_3ReBr$; C, 30.71; H, 1.98; N, 5.51%. Found: C, 30.69; H, 1.96; N, 5.41%. Mp = 295−298 °C. ^{1}H NMR (d_6-DMSO): δ 8.66 (m, 4H, *H* on py), 8.05 (m, 4H, *H* on py), 7.54 (m, 2H, *H* on py). ^{13}C NMR (d_6-DMSO): δ 154.6 (*C* on py), 140.3 (*C* on py), 127.0 (*C* on py).

$Re(CO)_3(N\text{-}MeIm)_2Br$ (9). Crystals suitable for X-ray diffraction were obtained by vapor diffusion of water into a DMSO solution of the complex. Yield: 68%. IR: 2008(s), 1851(vs, b) cm^{-1}. Anal. Calc. for $C_{11}H_{12}N_4O_3ReBr$; C, 25.69; H, 2.35; N, 10.89%. Found: C, 25.76; H, 2.30; N, 10.71% Mp = 163−166 °C. ^{1}H NMR ($CDCl_3$): δ 8.00 (s, 2H, *H* on MeIm), 7.10 (d, ^3J = 1.2 Hz, 2H, *H* on MeIm), 6.81 (d, ^3J = 1.2 Hz, 2H, *H* on MeIm), 3.67 (s, 6H, *CH$_3$*). ^{13}C NMR ($CDCl_3$): δ 141.6 (*C* on MeIm), 132.1 (*C* on MeIm), 121.2 (*C* on MeIm), 34.7 (*C*H$_3$).

$Re(CO)_3(tht)_2Br$ (10). Crystals suitable for X-ray diffraction were obtained by placing a methanol solution of the complex in a freezer for 48 h. Yield: 53%. IR: 2018(s), 1879(vs, b) cm^{-1}. Anal. Calc. for $C_{11}H_{16}S_2O_3ReBr$; C, 25.09; H, 3.06; S, 12.18%. Found: C, 24.94; H, 3.14; S, 12.13%. Mp = 180 °C (d). ^{1}H NMR ($CDCl_3$): δ 3.48 (m, 4H, *H* on tht), 3.29 (m, 4H, *H* on tht), 2.12 (m, 8H, *H* on tht). ^{13}C NMR ($CDCl_3$): δ 40.0 (*C* on tht), 30.7 (*C* on tht).

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Supporting Information Available: Crystallographic information file for other structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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