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Water-soluble carbonyl complexes of ^{99}Tc(I) and Re(I) with adamantane-cage aminophosphines PTA and CAP

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ABSTRACT

Pentacarbonyl complexes of ^{99}Tc and Re [M(CAP)(CO)$_5$]X and [M(PTA)(CO)$_5$]X (M = ^{99}Tc or Re and X = ClO_4^- or OTf$^-$) with aminophosphine ligands 1,4,7-triaza-9-phosphatricyclo[5.3.2^{14,9}]tridecane (CAP) and 1,3,5-triaza-7-phosphaadamantane (PTA) were prepared for the first time by the reaction of [MX(CO)$_5$] (M = ^{99}Tc or Re, X = ClO_4^- or OTf$^-$) with CAP and PTA in CH_2Cl_2 at room temperature. The reaction of [TcCl(CO)$_5$] with CAP in refluxing CH_2Cl_2 yields the tricarbonyl complex [^{99}TcCl(CAP)$_2$(CO)$_3$]. Treatment of [Re(H$_2$O)$_3$(CO)$_3$]Cl with CAP in aqueous solution at 40–50 °C gives the rhenium analog [ReCl(CAP)$_2$(CO)$_3$]. Both penta- and tricarbonyl phosphine complexes were characterized by spectroscopic methods (IR, NMR, MS) and single crystal X-ray diffraction. The [M(PTA)(CO)$_5$]X complexes are soluble in aqueous solutions, whereas their CAP analogs are not. The CAP complexes become water-soluble after acidification with dilute acids. As the pH of their aqueous solutions increases, they start to slowly degrade at pH 8 and completely decompose at pH 14. In acidic media, the pentacarbonyl complexes undergo stepwise protonation and are stable indefinitely.

1. Introduction

Coordination chemistry of the small adamantane-cage aminophosphines, 1,3,5-triaza-7-phosphaadamantane (PTA) and its recently synthesized analog 1,4,7-triaza-9-phosphatricyclo [5.3.2^{14,9}]tridecane (CAP), is extensively developed [1–6]. These ligands combine two kinds of donor atoms, P and N, which is of interest itself from the viewpoint of hard/soft acid–base coordination preferences. In the case of P-coordination, the uncoordinated N atoms remain available for acid–base interactions in aqueous solution (protonation), making the complexes hydrophilic. The pH-dependent hydrophilicity of the complexes opens interesting prospects for the development of new pharmaceuticals, because the degree of protonation at the nitrogen atoms can influence the biodistribution of the complexes. In particular, it is known that the pH of cancer cells is lower than that of normal cells; therefore, the uptake of the complexes in normal and cancer cells may be different due to different degrees of protonation and hence different charges of the complexes [4–8]. Technetium-99 m is the most widely used radionuclide for diagnostic purposes in nuclear medicine. Rhenium-188/186 radionuclides, in turn, show promise for radiotherapy. One of common ways to bind these nuclides to various organic molecules is the use of the [M(CO)$_3$(H$_2$O)$_3$]$^+$ (M = ^{99}Tc and Re) precursor species [9]. These complexes are robust and water-soluble and can be readily linked to biomolecules by substitution of aqua ligands with tridentate or bidentate + monodentate ligands. On the other hand, when using the pentacarbonyl core, it is possible to bind a single phosphine molecule directly to the [^{99m}Tc(CO)$_5$]$^+$ core to obtain a 1 : 1 complex with no additional ligands [10]. The aim of this study was to prepare and characterize technetium and rhenium carbonyl complexes with small adamantane-cage aminophosphines (PTA and CAP), to

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examine their acid–base behavior in aqueous solutions, and to estimate their stability under conditions simulating a biological medium. Both tri- and pentacarbonyl complexes were studied, with a focus on the pentacarbonyl species.

2. Experimental

2.1. Material and methods

All experiments were performed in air. All chemicals were of reagent grade and were purchased from Fluka (St. Petersburg, Russia). Dichloromethane and acetonitrile were distilled from P_2O_5. Silver perchlorate was prepared by precipitation of silver carbonate from silver nitrate aqueous solution with sodium carbonate, followed by dissolution of the precipitate in concentrated perchloric acid. Prior to use, $AgClO_4$ was dehydrated by heating in a vacuum at 50–60 °C. [^{99}TcI(CO)$_5$] was prepared by high-pressure carbonylation of potassium pertechnetate in a mixture of formic and hydroiodic acids at 170 °C for 2 h [10]. $K_2^{99}TcX_6$ ($X = Cl$ and Br) were prepared by reduction of $NH_4^{99}TcO_4$ with concentrated HX in the presence of excess KX [11]. [^{99}TcX(CO)$_5$] ($X = Cl$ and Br) can be prepared similarly to [^{99}TcI(CO)$_5$], but these complexes can also be prepared at ambient pressure by carbonylation of $K_2^{99}TcX_6$ with a mixture of formic and concentrated sulfuric acid at 175–180 °C for 1–2 h [12]; in this study, we used the latter procedure. [ReCl(CO)$_5$] was prepared by high-pressure carbonylation of K_2ReCl_6 with a mixture of formic and hydrochloric acids at 210 °C for 4 h [10]. Care should be taken in handling compounds of radioactive technetium. Perchlorate salts are potentially explosive and should also be handled with care. The ^{99}Tc NMR spectra were recorded from CH_2Cl_2 solutions on a Bruker AV-400 spectrometer. The ^{99}Tc shifts are given relative to aqueous $K^{99}TcO_4$ as an external reference. The IR spectra were recorded on a Shimadzu FT-IR 8700 spectrometer in the 1800–2200 cm^{-1} range using CaF_2 cells. Single crystal X-ray diffraction experiments for the compounds studied were performed at $T = 100$ K. The crystal structures were solved and refined using *SHELXL*-2014 program via Olex2 v.1.2-ac2 program interface [13,14]. Details of data collection, structure solution, and refinement are given in the Supporting Information. Molecular graphics has been created using Mercury CSD 2.0 software [15].

2.2. Synthesis

[^{99}Tc(OTf)(CO)$_5$], ***1(OTf)****.* [^{99}TcBr(CO)$_5$] (13 mg, 0.04 mmol) was dissolved in CH_2Cl_2 (3 ml), solid AgOTf (20 mg, 0.077 mmol) was added, and the mixture was stirred in the dark for 30 min. AgBr and unchanged AgOTf were filtered off. The filtrate was evaporated under reduced pressure to give a white solid (14.5 mg, 0.037 mmol). Yield 93%. Elemental analysis, %: calculated C 18.56; found: C 18.09, H 0.06, N 0.14. ^{99}Tc NMR spectrum (CH_2Cl_2, ppm): −1375. IR spectrum (CH_2Cl_2, cm^{-1}): 2165.9 vw, 2073.3 vs, 2013.5 m.

[Re(OTf)(CO)$_5$], ***2(OTf)****.* [ReBr(CO)$_5$] (0.467 g, 1.15 mmol) was dissolved in CH_2Cl_2 (20 ml), solid AgOTf (0.823 g, 3.2 mmol) was added, and the mixture was stirred in the dark overnight. On the next day, AgBr and unchanged AgOTf were filtered off. The filtrate was evaporated to dryness under reduced pressure to give a white solid (0.530 g, 1.115 mmol). Yield 97%. Elemental analysis, %: calculated C 15.15; found C 14.8, H 0.23, N 0.02. IR spectrum (CH_2Cl_2, cm^{-1}): 2165.9 vw, 2057.9 s, 2003.9 m.

[^{99}Tc(CAP)(CO)$_5$]ClO$_4$, ***3(ClO$_4$)****.* Weighed portions of [^{99}TcI(CO)$_5$] (23 mg, 0.0628 mmol) and $AgClO_4$ (39 mg, 0.188 mmol) were placed in a 10-ml vial, and dichloromethane (5 ml) was added. The vial was closed, and the reaction mixture stirred in the dark for 1 h and filtered through a paper filter to remove AgI and unchanged $AgClO_4$. The IR spectrum of the solution in the range of carbonyl stretching vibrations contained only bands of [^{99}TcClO$_4$(CO)$_5$] (2167.8 vw, 2073.3 vs, 2017.4 m cm^{-1}) [16]. No bands of the starting [^{99}TcI(CO)$_5$] (2148.6 vw, 2054.0 vs, and 2003.9 m cm^{-1}) were observed. A solution of CAP (14 mg, 0.070 mmol) in CH_2Cl_2 (1 ml) was added. The reaction mixture was stirred at room temperature for 1 h. Greenish oil was obtained after solvent evaporation. All attempts to crystallize the product failed. Elemental analysis, %: calculated C 31.26, H 3.35, N 7.81; found C 30.03, H 3.17, N 7.41. IR spectrum (CH_2Cl_2, cm^{-1}): 2146.6 m, 2094.6 w, 2054 sh, 2046.3 vs, 2007.8 vw. The oil was dissolved in 0.2 M HCl (2 ml), and concentrated perchloric acid (1 ml) was added. Large colorless crystals were grown after slow evaporation of the solution at room temperature. Single crystal X-ray diffraction analysis showed that this was [^{99}Tc(CAP-H$_2$)(CO)$_5$] Cl(ClO$_4$)$_2$·1.11H$_2$O, **[3-H$_2$](ClO$_4$)$_2$Cl·1.11H$_2$O**.

[^{99}Tc(CAP)(CO)$_5$]OTf, ***3(OTf)****.* 3.1 mg, 0.0097 mmol of [^{99}TcBr(CO)$_5$] was dissolved in dichloromethane (1 ml). Solid AgOTf (23 mg, 0.089 mmol) was added, and the mixture was stirred on a magnetic stirrer in the dark at room temperature for 1 h. The reaction mixture was filtered through a paper filter to remove AgBr and unchanged AgOTf. A solution of CAP (2.1 mg, 0.010 mmol) in CH_2Cl_2 (1 ml) was added, and the mixture was stirred at room temperature for 1 h. After the solvent evaporation in a nitrogen stream, [^{99}Tc(CAP)(CO)$_5$]OTf was obtained as a white solid. Elemental analysis, %: calculated C 30.7, H 3.07, N 7.15; found C 31.3, H 3.05, N 6.91. IR spectrum (CH_2Cl_2, cm^{-1}): 2146.6 m, 2096.5 w, 2057.9 sh, 2046.3 s ^{99}Tc NMR (CH_2Cl_2, ppm): −1744.4. ^{31}P NMR (CD_3CN, ppm): −48.75.

[Re(CAP)(CO)$_5$]ClO$_4$, ***4(ClO$_4$)****.* Weighed portions of [ReCl(CO)$_5$] (69.5 mg, 0.192 mmol) and $AgClO_4$ (176 mg, 0.848 mmol) were placed in a 10-ml vial, and dichloromethane (5 ml) was added. The vial was closed, and the reaction mixture was stirred in the dark with a stir bar for 2 h and filtered through a paper filter to remove AgCl and unchanged $AgClO_4$. The IR spectrum of the solution in the range of carbonyl stretching vibrations contained only bands of [Re(ClO$_4$)(CO)$_5$] (2165.9 w, 2059.8 s, 2005.8 m) [16]. No bands of the starting [ReCl(CO)$_5$] (2156.3 vw, 2046.3 vs, and 1984.6 m cm^{-1}) were observed. A solution of CAP (38.8 mg, 0.195 mmol) in CH_2Cl_2 (1 ml) was added. The reaction mixture was stirred at room temperature for 3 h. A yellowish powder was obtained after the solvent evaporation. Elemental analysis, %: calculated C 26.89.15, H 2.88, N 6.72; found C 27.21, H 3.31, N 6.27. The compound is spontaneously flammable on grinding in air. IR spectrum (CH_2Cl_2, cm^{-1}): 2146.6 m, 2088.8 w, 2046.3 vs, 1988.5 w. The product thus obtained was dissolved in 0.2 M HCl (2 ml), and concentrated perchloric acid (0.5 ml) was added. The mixture was allowed to slowly evaporate at room temperature. In 3 days, yellowish transparent crystals were obtained. Single crystal X-ray diffraction analysis showed that the crystals had the composition [Re(CAP-H$_2$)(CO)$_5$](ClO$_4$)Cl$_2$·0.5H$_2$O, **[4-H$_2$](ClO$_4$)Cl$_2$·0.5H$_2$O**.

[Re(CAP)(CO)$_5$]OTf, ***4(OTf)****.* [Re(OTf)(CO)$_5$] (36.1 mg, 0.076 mmol) was dissolved in dichloromethane (5 ml). Solid CAP (16.6 mg, 0.083 mmol) was added. The reaction mixture was stirred at room temperature for 3 h, after which the solvent was removed in a nitrogen stream. A white powder was obtained (33.3 mg, 0.0494 mmol). Yield 65%. MS (ESI, positive mode): calculated for [Re(CAP)(CO)$_5$]$^+$ 526.0, found 526.0. ^{31}P NMR (CD_3CN, ppm): −0.40. IR spectrum (CH_2Cl_2, cm^{-1}): 2146.6 m, 2088.8 w, 2048.3 sh, 2036.7 s, 1988.5 w.

[^{99}Tc(PTA)(CO)$_5$]ClO$_4$, ***5(ClO$_4$)****.* 51.8 mg, 0.1415 mmol of [^{99}TcI(CO)$_5$] and $AgClO_4$ (213 mg, 1.029 mmol) were placed in a 10-ml vial, and dichloromethane (6 ml) was added. The vial was closed, and the reaction mixture was stirred in the dark with a stir bar for 1 h and filtered through a paper filter to remove AgI and unchanged $AgClO_4$. Solid PTA (23 mg, 0.146 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. White crystalline precipitate was formed (24.5 mg, 0.049 mmol). Yield 35%.

Elemental analysis, %: calculated C 26.6, H 2.4, N 8.5; found, C 27.1, H 2.6, N 8.6. IR spectrum (MeCN, cm^{-1}): 2158.2 w and 2061.8 s. The crystal quality was insufficient for single crystal X-ray diffraction (SCXRD) analysis. To obtain better crystals, the precipitate was dissolved in 1 M HCl (2 ml) and the solution was slowly evaporated under ambient conditions to give single crystals of $[^{99}Tc(PTA\text{-}H)(CO)_5]ClO_4Cl$, **[5-H](ClO$_4$)Cl** of X-ray quality.

[^{99}Tc(PTA)(CO)$_5$]OTf, ***5(OTf)***. Weighed portions of $[^{99}TcBr(CO)_5]$ (13 mg, 0.0407 mmol) and AgOTf (25 mg, 0.1 mmol) were placed in a 10-ml vial, and dichloromethane (4 ml) was added. The vial was closed, and the reaction mixture was stirred in the dark with a stir bar for 1 h and filtered through a paper filter to remove AgBr and unchanged AgOTf. Solid PTA (7 mg, 0.044 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. White crystalline precipitate was formed (6.5 mg, 0.012 mmol). Yield 30%. Elemental analysis (after recrystallization from isopropanol), %: calculated for $[^{99}Tc(PTA)(CO)_5]OTf \cdot C_3H_7OH$ C 29.7.7, H 3.3, N 6.9; found C 28.8, H 3.1, N 7.1. %. IR spectrum (MeCN, cm^{-1}): 2158.2 w and 2061.8 s ^{99}Tc NMR (CD_3CN, ppm): −1762. ^{31}P NMR (CD_3CN, ppm): −58.48.

[Re(PTA)(CO)$_5$]OTf, ***6(OTf)***. $[Re(OTf)(CO)_5]$ (27 mg, 0.0568 mmol) was dissolved in dichloromethane (5 ml). Solid PTA (9.3 mg, 0.0592 mmol) was added. The reaction mixture was stirred at room temperature for 3 h. A white finely crystalline precipitate was gradually formed. The precipitate was filtered off, washed with two 1-ml portions of dichloromethane, and dried in a vacuum. White transparent crystals were obtained (16.9 mg, 0.0266 mmol). Yield 47%. MS (ESI, positive mode): calculated for $[Re(PTA)(CO)_5]^+$ 484.0; found 484.0. ^{31}P NMR (CD_3CN, ppm): −81.34. IR spectrum (MeCN, cm^{-1}): 2158.2 w and 2052.1 s.

[Re(PTA)(CO)$_5$]ClO$_4$, ***6(ClO$_4$)***. Weighed portions of $[ReCl(CO)_5]$ (73.2 mg, 0.202 mmol) and $AgClO_4$ (220 mg, 1.06 mmol) were placed in a 10-ml vial, and dichloromethane (7 ml) was added. The vial was closed, and the reaction mixture was stirred for 2 h in the dark with a stir bar and then filtered through a paper filter to remove AgCl and unchanged $AgClO_4$. Solid PTA (34 mg, 0.216 mmol) was added, and the reaction mixture was stirred at room temperature for 3 h. A white finely crystalline precipitate was gradually formed. The precipitate was filtered off, washed with two 1-ml portions of dichloromethane, and dried in a vacuum. White transparent crystals were obtained (47 mg, 0.0808 mmol). Yield 40%. Elemental analysis, %: calculated C 22.65, H 2.06, N 7.21; found C 22.03, H 2.27, N 7.45. IR spectrum (MeCN, cm^{-1}): 2158.2 m and 2052.1 s. The crystal quality was insufficient for SCXRD. Single crystals of the protonated complex $[Re(PTA\text{-}H)(CO)_5]ClO_4Cl$, **[6-H](ClO$_4$)Cl** were obtained by slow evaporation of a $[Re(PTA)(CO)_5]ClO_4$ solution in 1 M HCl under ambient conditions. The crystals thus obtained were suitable for SCXRD.

[^{99}TcCl(CAP)$_2$(CO)$_3$], ***7***. A weighed portion of $[^{99}TcCl(CO)_5]$ (45 mg, 0.164 mmol) was dissolved in CH_2Cl_2 (6 ml). Solid CAP (67 mg, 0.336 mmol) was added, and the reaction mixture was refluxed for 2 h. Slow evaporation of the solution of $[^{99}TcCl(CAP)_2(CO)_3]$ in dichloromethane yielded white crystals suitable for SCXRD. Elemental analysis, %: calculated C 45.45, H 6.49, N 15.15; found C 43.5, H 5.90, N 14.2. IR spectrum (CH_2Cl_2, cm^{-1}): 2027.0 s, 1949.9 m, and 1901.7 m.

[ReCl(CAP)$_2$(CO)$_3$], ***8***. A weighed portion of $[ReCl(CO)_5]$ (63.9 mg, 0.1767 mmol) was mixed with distilled water (5 ml). The mixture was refluxed for 1 day. To a solution of $[Re(H_2O)_3(CO)_3]Cl$ thus obtained, a solution of CAP (70 mg, 0.352 mmol) in water (3 ml) was added. A white precipitate was formed. The mixture was stirred at 40–50 °C for 3 h. The precipitate was separated by filtration, washed with distilled water, and dried in a vacuum. A white amorphous solid was obtained. Yield 65% (80.1 mg, 0.1148 mmol). Elemental analysis, %: calculated C 39.27, H 5.61, N 13.09; found C 36.87, H 5.04, N 12.02. The product was poorly soluble in methanol and acetonitrile and readily soluble in dichloromethane. Slow evaporation of the solution of $[ReCl(CAP)_2(CO)_3]$ in dichloromethane yielded white crystals suitable for SCXRD. IR spectrum (CH_2Cl_2, cm^{-1}): 2017.4 s, 1934.5 s, 1888.2 s.

3. Results and discussion

3.1. Synthesis

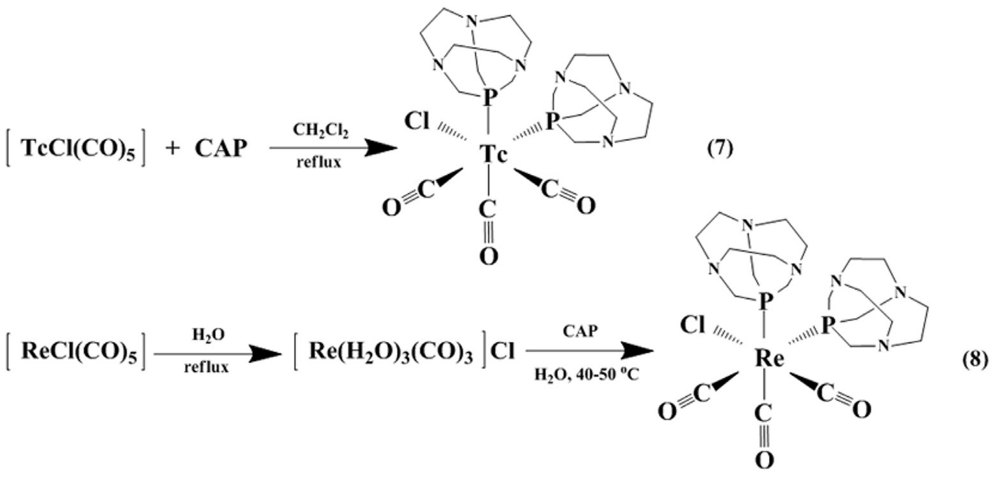
As starting compounds for preparing $[M(CAP)(CO)_5]X$ and $[M(PTA)(CO)_5]X$ ($M = {}^{99}Tc$ or Re; $X = ClO_4^-$ or OTf^-) complexes we took the corresponding $[MHal(CO)_5]$ (Hal = Br, Cl). Halide anions in $[MHal(CO)_5]$ are strongly bound to the central metal and cannot be directly substituted with σ-donor ligands without concomitant decarbonylation. Indeed, $[MHal(CO)_5]$ do not react with CAP and PTA at room temperature. In refluxing CH_2Cl_2, CAP and PTA substitute two carbonyl groups to form the tricarbonyl complexes **7** and **8**. $[ReCl(CO)_5]$ was preliminary decarbonylated in boiling water to $[Re(H_2O)_3(CO)_3]Cl$, to promote the reaction with phosphines (Scheme 1).

To ensure facile anion substitution with the pentacarbonyl core remaining intact, we substituted the halide ligand by a good leaving group by precipitation with Ag^+. For this purpose, we used perchlorate and triflate anions as the readily leaving ligands. Technetium and rhenium pentacarbonyl perchlorates were obtained as described in our previous work [16]. Their analogs $[^{99}Tc(OTf)(CO)_5]$ **1(OTf)** and $[Re(OTf)(CO)_5]$ **2(OTf)** were prepared similarly by treatment of $[^{99}TcBr(CO)_5]$ and $[ReCl(CO)_5]$ with solid AgOTf in dichloromethane. These complexes were isolated as white solids in good yields. Their IR spectra in CH_2Cl_2 in the carbonyl range (1800–2200 cm^{-1}) have the typical pentacarbonyl pattern (Figs. S1 and S6). The ^{99}Tc NMR spectrum of $[^{99}Tc(OTf)(CO)_5]$ in DCM contains one broad signal at −1375 ppm, which is close to that of $[^{99}Tc(ClO_4)(CO)_5]$ (−1353 ppm, CH_2Cl_2) as reported previously [16]. The ^{99}Tc NMR signals of the starting $[MX(CO)_5]$ (X = Cl, Br, I) are observed at −1745, −1802, and −2034 ppm, respectively [12]. $[MX(CO)_5]$ ($M = {}^{99}Tc$ or Re, $X = ClO_4^-$ or OTf^-) react in CH_2Cl_2 at room temperature with PTA and CAP to form $[M(CAP)(CO)_5]X$ (**3(X)**, $M = {}^{99}Tc$; **4(X)**, M = Re) and $[M(PTA)(CO)_5]X$ (**5(X)**, $M = {}^{99}Tc$, **6(X)**, M = Re) (Scheme 2).

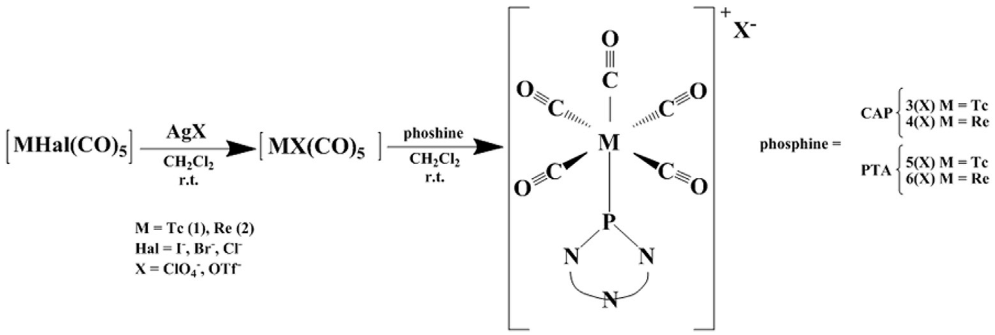
The pentacarbonyl complexes with PTA precipitated from the reaction mixture as white crystals, whereas their CAP analogs remained dissolved. $[M(PTA)(CO)_5]X$ and $[M(CAP)(CO)_5]X$ are soluble in polar organic solvents (e.g., acetonitrile). Their IR spectra in the carbonyl range (1800–2200 cm^{-1}) show typical pentacarbonyl pattern (Figs. S2, S4, S5, S7, S10, S12, S13, S16 and S17). The ^{99}Tc NMR spectra of $[^{99}Tc(CAP)(CO)_5]OTf$ in CD_2Cl_2 and in CD_3CN contains one signal at −1744.4 and −1762 ppm, respectively. For comparison, the ^{99}Tc chemical shift of $[^{99}Tc(PPh_3)(CO)_5]OTf$ in CD_2Cl_2 is −1958 ppm [10]. The ^{31}P NMR chemical shifts for the Tc and Re pentacarbonyl complexes with CAP and PTA significantly differ from those of the free ligands [3], which is consistent with the ligand coordination mode via P atom. Causes of significant differences between the chemical shifts for the Tc and Re complexes with the same ligand and for the complexes of the same metal with CAP and PTA are not fully clear; they may be associated with specific conformational and bonding features of the complexes, requiring more detailed analysis.

3.2. Single crystal X-ray diffraction

Our attempts to crystallize $[M(CAP)(CO)_5]X$ and $[M(PTA)(CO)_5]X$ complexes from organic solvents were not successful. To obtain single crystals of these compounds, we dissolved **3(ClO$_4$), 4(ClO$_4$),**



Scheme 1. Synthesis of [^{99}TcCl(CAP)$_2$(CO)$_3$] and [ReCl(CAP)$_2$(CO)$_3$] complexes.



Scheme 2. Synthesis of [M(CAP)(CO)$_5$]X and [M(PTA)(CO)$_5$]X complexes.

5(ClO$_4$), and 6(ClO$_4$) in 0.5–1 M HCl containing a few drops of concentrated perchloric acid. Slow evaporation of the solutions thus obtained gave single crystals of the protonated species **[3-H$_2$](ClO$_4$)$_2$Cl·1.11H$_2$O, [4-H$_2$](ClO$_4$)Cl$_2$·0.5H$_2$O, [5-H](ClO$_4$)Cl,** and **[6-H](ClO$_4$)Cl**. Single crystals of tricarbonyl complexes [^{99}Tc(CAP)$_2$Cl(CO)$_3$] **7** and [Re(CAP)$_2$Cl(CO)$_3$] **8** were obtained by simple evaporation of dichloromethane solutions. All the complexes crystallize in the monoclinic system except for **3(ClO$_4$)** which has an orthorhombic structure. Unfortunately, the structures of **[3-H$_2$](ClO$_4$)$_2$Cl·1.11H$_2$O** and **[4-H$_2$](ClO$_4$)Cl$_2$·0.5H$_2$O** appeared to be strongly disordered, which prevented good refinement. However, the coordination mode of the CAP ligand can be determined clearly. The unit cell parameters are summarized in Table S1. The interatomic distances and bond angles given in Tables S2–S4. The CSD nos. for **[5-H](ClO$_4$)Cl, [6-H](ClO$_4$)Cl**, **7** and **8** are 1897403, 1897396, 1897404, 1897397, respectively. In all complexes, the cage ligands are coordinated via P atoms, which agrees with the soft acid properties of the ^{99}Tc(I) and Re(I) atoms. The molecular structures of all pentacarbonyl complexes are similar and will be described exemplary with **5(ClO$_4$)**.

The crystal structure of [^{99}Tc(PTA-H)(CO)$_5$]ClO$_4$Cl contains one symmetrically independent [^{99}Tc(PTA-H)(CO)$_5$]$^+$ cation and perchlorate and chloride anions (Fig. 1). The coordination polyhedron of technetium in [^{99}Tc(PTA-H)(CO)$_5$]$^+$ is an almost ideal octahedron. The carbonyl–carbonyl and the carbonyl–PTA bond angles vary in the range from 86.33(4) to 94.58(6)°. The ^{99}Tc–C≡O fragments are linear within 2.5°. The ^{99}Tc–C bonds in the equatorial plane (2.0124(17)–2.0303(16) Å) are longer than the ^{99}Tc–C bond *trans* to the PTA ligand (2.0095(15) Å). The ^{99}Tc–P bond length is 2.4179(4) Å.

The [^{99}Tc(H-PTA)(CO)$_5$]$^+$ cations are packed in the crystal structure to form layers. Within the layer, the carbonyl and phosphine fragments are located alternatively up and down. The perchlorate and chloride anions are between the technetium cations.

Although the crystal structures of **[3-H$_2$](ClO$_4$)$_2$Cl·1.11H$_2$O** and **[4-H$_2$](ClO$_4$)Cl$_2$·0.5H$_2$O** are strongly disordered, it is clearly seen that the CAP ligand is coordinated *via* the phosphorus atom to the pentacarbonyl fragment (Fig. 1 and Fig. S39, respectively).

The crystal structure of **[6-H](ClO$_4$)Cl** is characterized by short (2.752(3) Å) contact between the oxygen atom of the perchlorate anion and oxygen atom of the carbonyl group *trans* to the PTA ligand (Fig. 2).

The structure of **7** consists of [^{99}Tc(CAP)$_2$Cl(CO)$_3$] molecules (Fig. 3). The coordination polyhedron of technetium is an almost ideal octahedron composed of three carbon atoms for the *fac*-[^{99}Tc(CO)$_3$]$^+$ moiety, two P atoms of the CAP ligands, and one Cl$^-$. The positions of the chloride ligand and C1O1 groups are strongly disordered: The chloride ligand occupies 50% positions of the carbonyl groups and *vice versa*. The ^{99}Tc–C distances range from 1.87(2) to 1.947(5) Å. The ^{99}Tc–Cl and ^{99}Tc–P distances are 2.562(7) and 2.4575(9) Å, respectively. The phosphine ligands are *cis* relative to each other, in contrast to the related triphenylphosphine derivative, in which the phosphine ligands are mutually *trans* [17,18]. This difference is probably associated with weaker steric demands of the CAP ligand as compared to triphenylphosphine. Two CAP ligands can thus be accommodated in the coordination sphere in the *cis* position, which is favorable from the viewpoint of the *trans* effect.

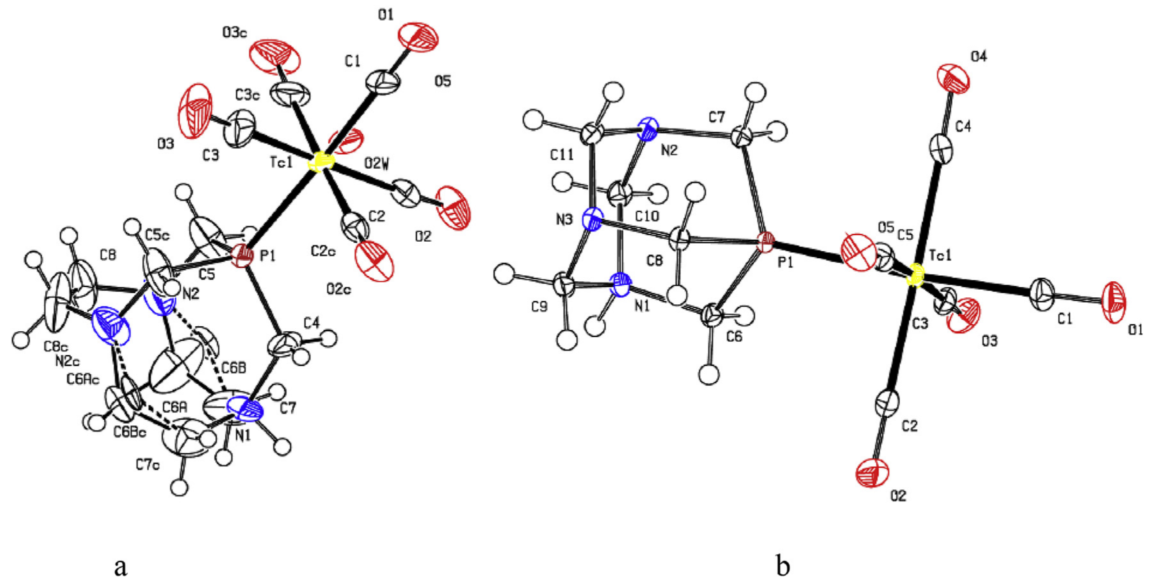


Fig. 1. Molecular structure of technetium pentacarbonyl complexes (a) **[3-H$_2$](ClO$_4$)$_2$Cl·1.11 H$_2$O** and (b) **[5-H](ClO$_4$)Cl** (chloride anions and water molecules have been omitted for clarity). Thermal ellipsoids are drawn on the 50% probability level.

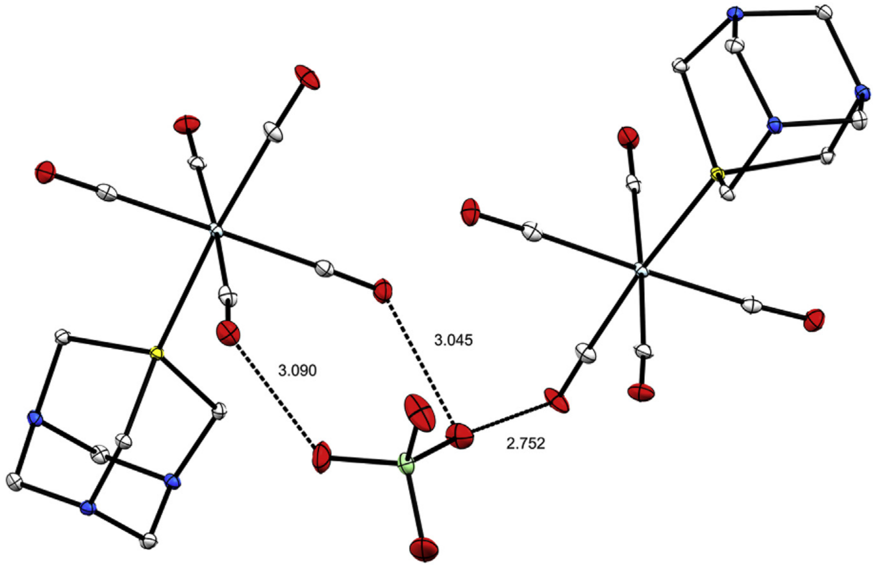


Fig. 2. Packing of pentacarbonyl cations in the crystal structure of **[6-H](ClO$_4$)Cl.**

The molecular structures of the rhenium pentacarbonyl and tricarbonyl analogs are shown in Figs. S39–S41, respectively.

3.3. *Behavior of the pentacarbonyl phosphine complexes in aqueous solutions*

The ^{99}Tc and Re pentacarbonyl complexes with PTA are soluble in water at neutral pH. The IR spectra of [M(PTA)(CO)$_5$]ClO$_4$ in aqueous solution display two bands in the carbonyl range at 2158.2 (w), 2065.6 (s) and 2160.1 (w), 2056.0 (s) cm^{-1} for Tc and Re, respectively (Figs. S18 and S24). Monitoring of the IR pattern in time shows that the complexes are stable in aqueous solutions for at least 24 h. The more hydrophobic technetium and rhenium pentacarbonyl complexes with CAP are water-insoluble at pH 7 but readily dissolve after slight acidification (pH 3). The IR spectra of these solutions contain two bands in the carbonyl range at 2156.3 (w), 2063.7 (s) and 2156.3 (w), 2054.0 (s) cm^{-1} for ^{99}Tc and Re, respectively (Figs. S21 and S26) and do not change with time for at least 24 h.

The structural data in combination with the IR, NMR, and analytical data show that the pentacarbonyl complexes with PTA and CAP ligands are protonated (apparently, via N atoms) without alteration of the coordination core. We also studied the acid–base transformations of the complexes in acid solutions by IR spectroscopy. The phosphine complexes (**3(ClO$_4$)**, **4(ClO$_4$), 5(ClO$_4$),** and **6(ClO$_4$))** were dissolved in acetonitrile and treated with increasing amounts of aqueous hydrochloric acid. When the number of moles of acid per mole of the complex ($N^{+}_{\text{equiv.H}}$) was gradually increased from 1 to 3 mol/mol in 1 mol/mol steps, the carbonyl bands in the range 2042.5–2061.8 cm^{-1} shifted to higher frequencies (Fig. 4). This shift is attributable to protonation of the nitrogen atoms in PTA and CAP. Concomitantly, the donor strength of the P atom decreases

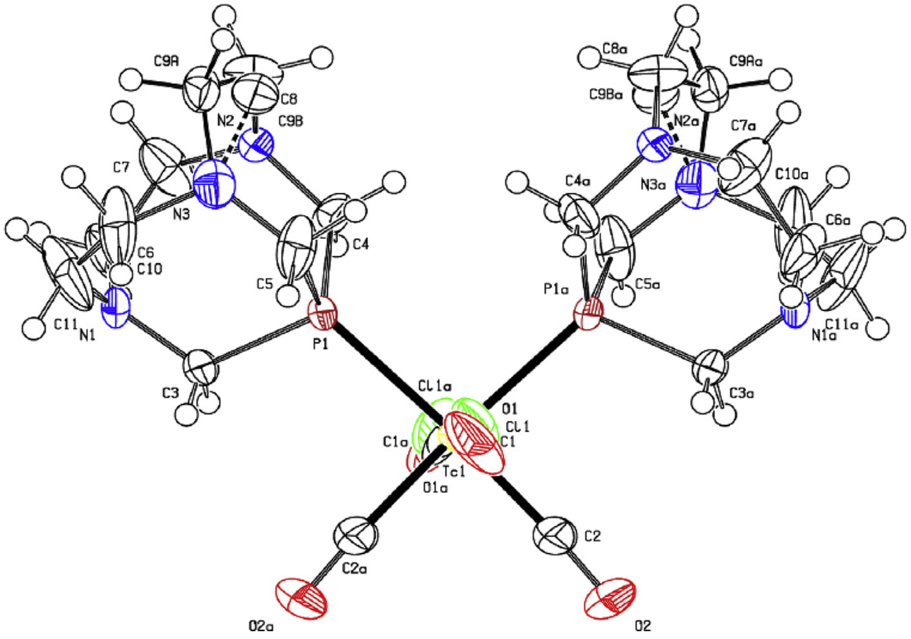


Fig. 3. Molecular structure of technetium tricarbonyl complex **[^{99}TcCl(CAP)$_2$(CO)$_3$] (7)**. Thermal ellipsoids are drawn on the 50% probability level.

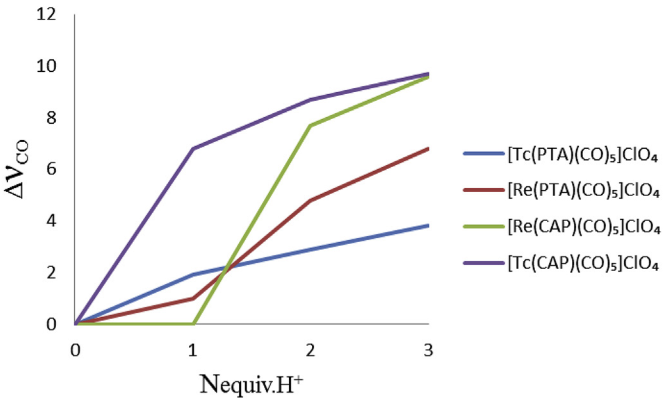


Fig. 4. Shifts ($\Delta\nu_{CO} = \nu_{starting} - \nu_{HCl}$) of the IR bands of [M(PTA)(CO)$_5$]ClO$_4$ at M = Re 2052.1 and M = ^{99}Tc 2061.8 cm^{-1} and [M(CAP)(CO)$_5$]ClO$_4$ at M = Re 2042.5 and M = ^{99}Tc 2052.1 cm^{-1} in acetonitrile as a function of the number of moles of hydrochloric acid per 1 mol of the complex ($N^{+}_{equiv.H}$).

due to inductive effects, which, in turn, leads to an increase in the CO vibration frequencies (*cf.* frequencies of the corresponding bands in the spectra of technetium pentacarbonyl complexes with anionic ligands) [12,16]. At acid concentrations above 3 mol/mol, no further shift of the carbonyl band was observed. The processes are reversible, and neutralization by the addition of a base returns the frequencies to their initial values.

The stability of the higher carbonyl complexes of technetium and rhenium in neutral and alkaline solutions is restricted by the susceptibility of the coordinated CO carbon atoms to nucleophilic attack. For example, upon alkalization [^{99}Tc(CO)$_6$]ClO$_4$ in aqueous solution immediately forms an unidentified yellow precipitate [19]; two previously known products of its thermal transformations, ^{99}Tc$_2$(CO)$_{10}$ [20] and ^{99}Tc$_3$H$_3$(CO)$_{12}$ [21], were identified, and their formation was attributed to the nucleophilic attack of the OH$^-$ anion on the carbonyl carbon atom, followed by decarboxylation of the intermediate organometallic carboxylic acid and secondary transformations of ^{99}Tc(CO)$_5^-$ and/or ^{99}TcH(CO)$_5$ [19,22]. We found that [^{99}Tc(PTA)(CO)$_5$]ClO$_4$ is stable in phosphate buffer at pH 7 (Figs. S30 and S31) for at least 24 h. At pH 8, no decomposition is observed either (Figs. S32 and S33). Thus, the complex is sufficiently stable in aqueous solutions in a typical biological pH range as found, e.g., in blood (pH 7.4). The complex almost completely decomposes at pH 10 or higher within 0.5 h (Fig. S34). At pH 14, decomposition is instantaneous and a yellow solution forms; its identification is a matter of further studies.

Along with the stability at different pH values, competition with potentially coordinating biological ligands was a further issue. To estimate the stability of these complexes in a simulated biological medium, we added excess histidine to an aqueous solution of [^{99}Tc(PTA)(CO)$_5$]ClO$_4$. The IR spectra showed that the complex is resistant to “histidine challenge” for at least 24 h. It should be noted that [^{99}Tc(NCR)(CO)$_5$]ClO$_4$ are less stable under these conditions [23]. The CAP complexes are also stable with respect to histidine challenge reaction (Figs. S22–23 and S27–29), and no ligand-to-histidine exchange was found.

4. Conclusion

Pentacarbonyl complexes of ^{99}Tc and Re with phosphine ligands CAP and PTA ([M(CAP)(CO)$_5$]X and [M(PTA)(CO)$_5$]X) were prepared for the first time and characterized by spectroscopic methods (IR, NMR, MS) and single crystal X-ray diffraction. The PTA complexes are soluble in aqueous solutions, whereas the CAP complexes are not at neutral pH. At the same time, after acidification with dilute acids the CAP complexes become water-soluble. Both CAP and PTA complexes are stable with respect to histidine challenge reaction. In phosphate buffer at pH 7 they are also stable for at least 24 h. Taking into account the protonation features of these complexes, their potential as radiopharmaceutical for tumor diagnostic will be the purpose of our future work.

We also found that [MHal(CO)$_5$] do not react with CAP and PTA at room temperature to form the corresponding pentacarbonyl complexes, because the halide anions in [MHal(CO)$_5$] are strongly bound to the central metal and cannot be directly substituted by σ-donor ligands without concomitant decarbonylation. On heating, phosphines substitute two carbonyl groups to form novel tricarbonyl complexes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jorganchem.2019.05.029.

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