Some new cationic di- and tricarbonyl complexes of technetium(I)

H. H. Knight Castro*, C. E. Hissink, J. H. Teuben and W. Vaalburg

Groningen Centre for Catalysis and Synthesis, Department of Chemistry, University of Groningen, Nijenborgh 16, 9747 AC Groningen, The Netherlands

and

K. Panek

Mallinkrodt Diagnostica (Holland) B.V., P.O. Box 3, 1755 ZG Petten, The Netherlands

(Received September 20th, 1991)

Abstract. Some new low-valent, cationic complexes of technetium-99 have been prepared. Oxidation of $\text{Tc}(_2\text{CO})_{10}$ (1) with NOPF$_6$ in acetonitrile gave $\text{Tc}([\text{CH}_2\text{CN})_2\text{CO})_2][\text{PF}_6]$ (2) quantitatively. This complex constitutes a useful precursor for cationic carbonyl complexes, as exemplified by a variety of reactions with bi- and tridentate ligands from which air-stable, water-soluble complexes of type $[\text{LTc(CO)}_3]^{n+}$ ($L = \text{1,4,7-triazacyclononane}, \text{1,4,7-trimethyl-1,4,7-triazacyclononane and 1,4,7-trithiacyclonononone}$) have been isolated and characterized. A series of mixed complexes of technetium(I) of general formula $\text{[Tc(N,N)[P(OR)_{3}]}_{n}$ (N,N = 2,2′-bipyridine, 4,4′-dimethyl-2,2′-bipyridine and R = methyl, isopropyl) has also been prepared.

Introduction

The intensive use of $^{99m}$Tc in diagnostic nuclear medicine has prompted several inorganic chemists to study the basic chemistry of technetium. Excellent reviews covering this subject have been published$^{1-3}$, and these clearly present the role of technetium in radiopharmaceuticals. $^{\text{Deutsch et al.}}^{\text{4}}$, reported, in 1981, the significant myocardial uptake of the cationic Tc(III) complexes of formula $[\text{Tc}($DIARS$)_2X_2]$ ($X = \text{Cl, Br}$). Since then, several other unipositive technetium complexes have been synthesized and tested in animals$^{3,5}$. However, human heart delineation of the most promising candidates has been less convincing than expected, except in the case of $[\text{Tc}($TBIN$)_3]^+$ ($\text{TBIN} = \text{tert-butyl isonitrile}$), the only cationic $^{99m}$Tc complex for which animal data has been usefully predictive of human biodistribution$^{10}$. A systematic comparison covering the results obtained up to 1984 together with some interesting observations on this subject have been presented by Münze$^{11}$. All Tc(I) and Tc(III) unipositive complexes have, more or less, effect on the heart, depending on their lipophilicity and reactivity rather than on their stereochemical properties. Despite the fact that Tc(I) complexes are relatively easy to prepare, especially when compared to the metastable Tc(III) intermediates, only a few cationic carbonyl complexes of Tc(I) are known, probably due to the lack of effective preparative methods for the starting materials.$^{12}$

$^{\text{Hieber et al.}}^{13}$ reported the synthesis of $[\text{Tc}($CO)$_{n}$L$_n][\text{AlCl}_4]$ complexes [$n = 0, 1, 2; L = \text{P(C}_3\text{H}_2_5)$, $\text{Biagiini Cingi}^{14}$] prepared cis- and trans-$[\text{Tc}($CO)$_3][\text{P(OR)}_3\text{P}][\text{ClO}_4]$ while studying the change of reactivity as a function of halogen in complexes $[\text{Tc}X_3][\text{P(OR)}_3\text{P}][\text{ClO}_4]$ ($X = \text{Cl, Br, I}$). An interesting starting material for cationic carbonyl complexes, $[\text{Tc}($CH$_2$CN)$_2($CO)$_2][\text{PF}_6]$, has been reported by $^{\text{Kaden et al.}}^{15}$, as well as four other derivatives from its reactions with different phenylphosphines $\text{PhPL}_2$ ($L = \text{Me, Ph, NaO,SC}_2\text{H}_4$).

Experimental

Technetium-99 was supplied by Mallinkrodt Diagnostica (Holland) laboratories in the form of dry NH$_4$$^{99m}$TcO$_4$. This isotope is a low energy (0.3 MeV) $\beta$ particle emitter with a half-life of 2.12 · 10$^5$ years, which does not present a serious health hazard when handled in milligram amounts, since the $\beta$ rays are absorbed by the glassware and there is no associated $\gamma$ radiation. When larger quantities are used (> 250 mg), a distance of 30 cm must be maintained from the working area to avoid the effect of very soft X-rays produced by the action of the $\beta$ particles on the glass. $\text{Tc}(_2\text{CO})_{10}$ was prepared according to a procedure previously reported$^{13}$. The ligands 1,4,7-triazacyclononane ([9]aneN$_3$), 1,4,7-trimethyl-1,4,7-triazacyclononane (Me$_3$[9]aneN$_3$) and 1,4,7-trithiacyclonon-4-ene ([9]aneS$_4$) were obtained from Aldrich. Reactions were carried out under nitrogen in Schlenk glassware. Solvents were dried by conventional methods, distilled under nitrogen and used immediately.

Infrared spectra were measured by using a Pye Unicam model SP3-300 spectrophotometer in NaCl cells ($\text{CH}_2\text{CN}$). $^1$H NMR spectra were recorded on a Bruker WH-90. Chemical shifts are reported in parts per million (ppm) and are referenced to residual protons in deuterated solvents [acetonitrile-$d_3$ (1.93), acetone-$d_6$ (2.05)].

$[\text{Tc}($CH$_2$CN)$_2($CO)$_2][\text{PF}_6]$ (2)

227 mg (1.3 mmol) NOPF$_6$ were added to a solution of 300 mg (0.63 mmol) $\text{Tc}(_2\text{CO})_{10}$ in 10 ml acetonitrile. A vigorous reaction took place with evolution of NO gas. After stirring of the reaction mixture for an additional 5 min, the solution was concentrated
vacuum and the product precipitated by addition of 70 ml of diethyl ether. After washing three times with small portions of ether and acetone, 0.51 g (96% yield) of white [Tc(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)PF\(_6\)] was obtained. IR (CH\(_3\)CN); ν(CO) 2169 w, 2069 vs, 2040 s, ν(PF\(_6\)) 840 vs cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 2.62 (s, CH\(_3\)).

[Tc(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)PF\(_6\)]

Following the procedure described above, 200 mg (0.47 mmol) [Tc(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)PF\(_6\)] and 235 mg (0.47 mmol) of 1,4,7-trimethyl-1,4,7-triazacyclononane. The reaction solution was stirred for 4 h at 60°C. After concentration and precipitation of the product with diethyl ether, 134 mg (57% yield) of pale yellow microcrystalline product were obtained. IR (CH\(_3\)CN); ν(CO) 2040 m, 1923 s; 2.17 (s, 3 H, CH\(_3\)).

[(9)aneN\(_3\)]\(_2\)Tc(CO)\(_5\)PF\(_6\) (3)

To 200 mg (0.47 mmol) [Tc(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)PF\(_6\)] dissolved in 15 ml acetonitrile were added. The reaction mixture was stirred at 60°C for 2 h and, by that time, some of the product had precipitated. The solution was allowed to cool until precipitation was complete and the solids were then collected by filtration, washed with ether and dried under reduced pressure. Addition of ether to the mother liquor improved the yield to 73% (174.3 mg). IR (CH\(_3\)CN); ν(CO) 2045 m, 1965 s; ν(PF\(_6\)) 840 s cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 3.05 (broad, s, CH\(_3\)).

[Tc(CO)\(_5\)](bipy)(CH\(_3\)CN)]PF\(_6\) (4)

Following the procedure described above, 200 mg (0.36 mmol) [Tc(CO)\(_5\)](bipy)(CH\(_3\)CN)]PF\(_6\) were treated with excess of P(OMe\(_3\)) and refluxed for 2 h. 5 mg (20% yield) of product crystallized from acetone/diethyl-ether (1:1). Anal. calcd. for C\(_22\)H\(_{25}\)N\(_5\)O\(_9\)P\(_4\)Tc: C 42.70, H 6.04; found: C 42.79, H 5.97%. IR (CH\(_3\)CN): ν(CO) 2060 s, 1950 vs br; 2.06 (s, 3 CH\(_3\)).

[Tc(CO)\(_5\)](bipy)(P(OMe\(_3\)))PF\(_6\) (5)

Supercations were studied by Connelly and Dahl in 1970. We found that the decacarbonyls of rhenium and manganese react with NOPF\(_6\) in acetonitrile to form [Te(CO)\(_5\)](bipy)(CH\(_3\)CN)]PF\(_6\) (6) in almost quantitative yield in a few minutes under the same reaction conditions. Further solvolysis of 2 takes place in refluxing acetonitrile without the aid of other reagent to give fac-[Te(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)]PF\(_6\). The fac configuration of the compound was prepared as described above using, in this case, a two-molar excess of P(OMe\(_3\)). The reaction mixture was refluxed for 24 h; the yield was 70%. Anal. calcd. for C\(_{60}\)H\(_{70}\)N\(_{30}\)O\(_{60}\)P\(_{10}\)F\(_{60}\)Tc: C 41.29, H 5.77; found: C 41.30, H 5.68%. IR (CH\(_3\)CN); ν(CO) 1955 s, 1875 s; ν(PF\(_6\)) 840 s cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 0.96-1.02 (d, 36 H, 12 CH\(_3\)).

[Tc(CO)\(_5\)](Me\(_3\)bipy)(CH\(_3\)CN)]PF\(_6\) (7)

This compound was prepared according to the procedure described above using, in this case, a two-molar excess of P(OMe\(_3\)). The reaction mixture was refluxed for 24 h; the yield was 70%. Anal. calcd. for C\(_{60}\)H\(_{70}\)N\(_{30}\)O\(_{60}\)P\(_{10}\)F\(_{60}\)Tc: C 41.29, H 5.77; found: C 41.30, H 5.68%. IR (CH\(_3\)CN); ν(CO) 1955 s, 1875 s; ν(PF\(_6\)) 840 s cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 0.96-1.02 (d, 36 H, 12 CH\(_3\)).

[Tc(CO)\(_5\)](Me\(_3\)bipy)(O)(P(OMe\(_3\)))PF\(_6\) (8)

[Tc(CO)\(_5\)](Me\(_3\)bipy)(CH\(_3\)CN)]PF\(_6\) in 10 ml acetonitrile were treated with 92 mg (0.5 mmol) of 4,4'-dimethyl-2,2'-bipyridine. The reaction solution was stirred at 60°C for 4 h. The solvent was removed under reduced pressure and the residue washed three times with small portions of ether to give 185 mg (71.15% yield) of a light-brown product. IR (CH\(_3\)CN); ν(CO) 2045 m, 1943 s; ν(PF\(_6\)) 840 s cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 2.07 (s, 3 H, CH\(_3\)).

[Tc(CO)\(_5\)](Me\(_3\)bipy)(O)(P(OMe\(_3\)))PF\(_6\) (9)

Results and discussion

We have reported elsewhere a novel, high-field synthetic route to Tc\(_2\)(CO)\(_{10}\) (1), based on the reductive character of sodium amalgam in THF. This procedure starts from NH\(_2\)TcO\(_2\) and gives the decacarbonyl dimer in 70-80% yields when working at 100 atm of carbon monoxide and 120°C for three days. The scope and potential diversity of NOPF\(_6\) in acetonitrile for the preparation of new metal-acetonitrile complexes was first studied by Connelly and Dahl in 1970. We found that the decacarbonyls of rhenium and manganese react with NOPF\(_6\) in acetonitrile to form [MC(CO)\(_5\)](CH\(_3\)CN)]\(_n\) species. These white crystalline complexes are air-stable, diamagnetic and soluble in polar solvents to give solutions unstable in air. We found that Tc\(_2\)(CO)\(_{10}\) was able to react in the same way giving the Tc(I) pentacarbonyl cation [Tc(CO)\(_5\)](CH\(_3\)CN)]PF\(_6\) (2) in almost quantitative yield in a few minutes under the same reaction conditions. Further solvolysis of 2 takes place in refluxing acetonitrile without the aid of other reagent to give fac-[Tc(CH\(_3\)C\(_6\)N\(_3\))\(_2\)C\(_6\)N\(_3\)]PF\(_6\). The fac configuration of the complex was prepared as described above using, in this case, a two-molar excess of P(OMe\(_3\)). The reaction mixture was refluxed for 24 h; the yield was 70%. Anal. calcd. for C\(_{60}\)H\(_{70}\)N\(_{30}\)O\(_{60}\)P\(_{10}\)F\(_{60}\)Tc: C 41.29, H 5.77; found: C 41.30, H 5.68%. IR (CH\(_3\)CN); ν(CO) 1955 s, 1875 s; ν(PF\(_6\)) 840 s cm\(^{-1}\). ¹H NMR (acetone-\(d_2\)); δ 0.96-1.02 (d, 36 H, 12 CH\(_3\)).
carbonyl ligands has been inferred from the ν(CO) bands in the infrared spectra\(^1\). The facility with which the labile nitrite groups can be replaced by other types of ligands makes the pentacarbonyl 2 an excellent starting material for the preparation of cationic technetium complexes.

During the preparation of the same type of unipositive carboxyl groups observed in every case, we conclude that the dicarboxyl modes (known two-pattern of carbonyl stretching modes (2\(v_1\)) as a reflection of the metal-CO interaction. At least one absorption maximum in the 2000-cm\(^{-1}\) region is characteristic of most compounds. In general, they all show the three-band spectral pattern of carbonyl stretching 3-5.

The spectrum of the pentacarbonyl technetium (Tc) shows the three-band pattern of carbonyl stretching modes (2\(v_1\) + \(E\)) characteristic of \(C_2\)-symmetry. Complexes 3-5 show the well-known two-band spectral pattern of carboxyl stretching modes (\(A_1\) + \(E\)) characteristic of \(C_4\) symmetry for these simple tricarbonyls cations. From the two intense ν(CO) bands observed in every case, we conclude that the dicarboxyl derivatives 6-9 must have a cis configuration. This is in agreement with the assumption that the reaction takes place via initial formation of \(\text{[ac-Tc(CH$_3$CN)$_2$(CO)$_3$]}^+\) followed by replacement of two acetonitrile ligands by the bipyridine. We also found that, in fact, no reaction would take place between the bipyridine complexes and phosphine as long as excess of acetonitrile was present, even at reflux temperature. It was necessary to use another solvent, e.g., acetone, in order to achieve conversion to the mixed complexes \(\text{[Tc(N,N)(CO)$_2$]}^+\) (6-9).

Reactions between 2 and bipyridines also take place in acetonitrile when kept at 60-65°C for 4 hours, probably via initial formation of \(\text{[ac-Tc(CH$_3$CN)$_2$(CO)$_3$]}^+\) followed by replacement of two acetonitrile ligands by the bipyridine. We also found that, in fact, no reaction would take place between the bipyridine complexes and phosphine as long as excess of acetonitrile was present, even at reflux temperature. It was necessary to use another solvent, e.g., acetone, in order to achieve conversion to the mixed complexes \(\text{[Tc(N,N)(CO)$_2$]}^+\) (6-9).

**Scheme 1**

\[
\begin{align*}
\text{TC}_2(\text{CO})_{10} & \xrightarrow{\text{NOPF}_6} \text{CH}_3\text{CN} \\
\Rightarrow \hspace{1cm} I \hspace{1cm} \Rightarrow \hspace{1cm} \text{[TC(\text{CH}_3\text{CN})(\text{CO})$_2$]}^+\text{PF}_6
\end{align*}
\]


**Scheme 2**

A widely used method of identification for metal carbonyls involves IR spectroscopy. The C-O stretching mode is sufficiently affected by the kind of metal present and the symmetry properties of the molecule, which permits rather easy identification of most compounds. In general, they all show at least one absorption maximum in the 2000-cm\(^{-1}\) region as a reflection of the metal-CO interaction.

The spectrum of the pentacarbonyl Tc shows the three-band pattern of carbonyl stretching modes (2\(A_1\) + \(E\)) characteristic of \(C_2\)-symmetry. Complexes 3-5 show the well-known two-band spectral pattern of carboxyl stretching modes (\(A_1\) + \(E\)) characteristic of \(C_4\) symmetry for these simple tricarbonyls cations. From the two intense ν(CO) bands observed in every case, we conclude that the dicarboxyl derivatives 6-9 must have a cis configuration. This is in agreement with the assumption that the reaction takes place via initial formation of \(\text{[ac-Tc(CH$_3$CN)$_2$(CO)$_3$]}^+\) because, in that case, the cis strong labilizing effect of both N atoms of bipyridine would cause the second entering phosphate ligand to replace the CO trans to the first phosphate. This means that from the two possible isomers: cis,trans and cis,cis (Figure 2), only the first one is formed. Unfortunately, due to the same local symmetry (\(C_2\)) of the carbonyl groups in these two isomers it is not possible to corroborate this assumption on basis of their ν(CO) absorptions.

\[
\begin{align*}
\text{[TC(CH$_3$CN)(CO)$_3$]}^+\text{PF}_6 & \xrightarrow{\text{CH}_3\text{CN}} \text{[TC(L)(CO)$_3$]}^+\text{PF}_6 \\
\Rightarrow \hspace{1cm} \text{2} \hspace{1cm} \Rightarrow \hspace{1cm} \text{3-5}
\end{align*}
\]

**Figure 1.** cis,trans and cis,cis isomers of complexes 6-9.

**Acknowledgement**

We thank Mallinckrodt Diagnostica (Holland) B.V. for the financial and technical support of this project.

**References**

19a. L. T. Taylor and D. H. Busch, J. Am. Chem. Soc. 89, 5372 (1967);