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LETTER

Preparation and characterization of the complexes $[Tc(CN^tBu)_x(PPh_3)_{6-x}]PF_6$ ($x=4$, 5)

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Due to the radioactive nature of the element, technetium is most readily available only in the form of pertechnetate, both in the case of the long-lived β^--emitter ^{99}Tc, as well as the metastable ^{99m}Tc used in diagnostic imaging [1]. Syntheses of compounds which utilize the pertechnetate anion as the starting material are thus valuable not only for their relative ease of preparation, but also for their potential use in nuclear medicine. We have recently become interested in the potential of mixed-ligand technetium compounds as radiopharmaceutical agents, and the success of the technetium(I) hexakis(isonitrile) compounds as myocardial imaging agents [2] has prompted our investigations of low oxidation state complexes which specifically contain isonitriles. Previous reports of such compounds include a series of complexes of the type $[Tc(CNR)_4bpy]^+$ (R = t-butyl, methyl, xylyl; NN = bidentate aromatic amine) [3] as well as the compound $[Tc(dppe)_2(CNR)_2]^+$ (R = t-butyl, cyclohexyl; dppe = 1,2-bis(diphenylphosphino)ethane) which was synthesized by Abram *et al.* from $Tc(N_2)H(dppe)_2$ [4]. Herein, we describe the direct preparation from pertechnetate of mixed-ligand technetium compounds which contain t-butyl isonitrile and triphenylphosphine ligands.

Experimental

Caution. Technetium-99 is a weak β^--emitter ($E = 0.292$ MeV, $t_{1/2} = 2.12 \times 10^5$ years). All work has been done in laboratories approved for the use of low levels of radioactive materials. Precautions have been detailed elsewhere [5].

Materials

Ammonium pertechnetate was supplied as a gift by DuPont/Biomedical Products. Triphenylphosphine was obtained from Aldrich Chemicals and t-butyl isonitrile was obtained from Fluka Chemicals. The solvents and reagents were used as received.

Measurements

The ^1H, $^{31}P\{^1H\}$ and ^{99}Tc NMR spectra were recorded on a Varian XL-300 spectrometer. The residual proton signal from the solvent was used as a reference for the ^1H spectra. The $^{31}P\{^1H\}$ chemical shifts are reported with respect to 85% H_3PO_4 and were referenced to PPh_3 which was present as a secondary, internal standard. The ^{99}Tc signals are reported with respect to $(NH_4)[TcO_4]$ and were referenced to $[Tc(CNtBu)_6]PF_6$, also present as a secondary, internal standard. Fourier transform infrared spectra were measured from 4000–400 cm^{-1} on a Mattson Cygnus 100 spectrometer using a 2 cm^{-1} bandwidth. UV–Vis spectra were recorded using a Hewlett Packard 8451A photodiode array spectrophotometer. Fast atom bombardment mass spectra (FAB-MS) of samples dissolved in a 3-nitrobenzyl alcohol matrix were recorded with a MAT 731 mass spectrometer equipped with an Ion Tech B11N FAB gun and operating at an accelerating voltage of 8 kV. The FAB gun produced a beam of 6–8 keV xenon neutrals. Electrochemical measurements were performed on N_2-purged acetonitrile solutions of the metal complexes with 0.1 M tetrabutylammonium perchlorate (TBAP, GFS Chemicals) as supporting electrolyte. The acetonitrile was of spectrophotometric grade and was kept over 3 Å molecular sieves to remove water. Experiments were conducted using a one-compartment cell with a Pt disk as the working electrode, a Pt wire as the auxiliary electrode and a SCE (Fisher) as the reference electrode. The $E_{1/2}$ values were calculated as the average of the E_{peak} values for the anodic and cathodic waves from cyclic voltammetry. $E_{1/2}$ values are measured relative to SCE and are uncorrected for junction potentials; however, the potential of the ferrocenium/ferrocene couple occurs at 0.39 V for this set-up and can be used as a secondary reference [6]. The potentiostat employed was a PAR model 174 polarographic analyzer and the data were plotted with a Hewlett Packard 7044A XY recorder. Elemental analyses were performed by Atlantic Microlab, Norcross, GA.

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Preparation of $[Tc(CN^tBu)_5(PPh_3)]PF_6$

A 0.39 ml aliquot of a 0.384 M aqueous solution of $(NH_4)[TcO_4]$ was evaporated to dryness under reduced pressure. The white solid was dissolved in 15 ml of ethanol and 0.12 g of triphenylphosphine and 70 μl of t-butyl isonitrile were added. The solution was refluxed with stirring for 1 h 15 min at which point the color was pale yellow. The solution was transferred to a beaker and the volume was reduced on a hot plate to ~10 ml. A solution of 0.15 g of $[NH_4]PF_6$ in 5 ml of water was then added followed by dropwise addition of water until the solution was cloudy with a white precipitate. The solid was collected and washed with water followed by toluene and diethyl ether. The product was recrystallized from acetone and water and dried *in vacuo*.

Yield: 0.01342 g, 0.0146 mmol, 10%. *Anal.* Calc. for $C_{43}H_{60}F_6N_5P_2Tc$: C, 56.02; H, 6.56; N, 7.60. Found: C, 55.89; H, 6.45; N, 7.58%. UV–Vis (CH_2Cl_2): λ_{max} (ϵ) 238 nm (67100 l mol^{-1} cm^{-1}). IR (KBr): ν(CN) 2170w, 2094s, 2059sh cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.34 (s, 36H, $C(CH_3)_3$); 1.58 (s, 9H, $C(CH_3)_3$); 7.5 m, 7.6 m (15H, $P(C_6H_5)_3$). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −40 (br, 200 Hz). ^{99}Tc NMR ($CDCl_3$): δ −1827 (br, 3000 Hz). FAB-MS(+): *m/z* 776 $(M)^+$; 719 $(M-tBu)^+$; 693 $(M-CNtBu)^+$; 610 $(M-2CNtBu)^+$; 514 $(M-PPh_3)^+$. $E_{1/2}$ (CH_3CN): +0.81 V versus SCE ($1e^-$, rev).

Preparation of $[Tc(CN^tBu)_4(PPh_3)_2]PF_6$

This product was prepared by a method analogous to that of $[Tc(CN^tBu)_5(PPh_3)]PF_6$ using only 50 μl of t-butyl isonitrile for a 0.43 ml aliquot of a 0.345 M solution of $(NH_4)[TcO_4]$ along with 0.4 g of triphenylphosphine. The solution turned a deeper yellow in this case. The white product was washed with water followed by benzene and diethyl ether. The product was recrystallized from acetone and water and dried *in vacuo*.

Yield: 0.0185 g, 0.0168 mmol, 11%. *Anal.* Calc. for $C_{56}H_{66}F_6N_4P_3Tc$: C, 61.12; H, 6.04; N, 5.09. Found: C, 61.41; H, 6.12; N, 5.02%. UV–Vis (CH_2Cl_2): λ_{max} (ϵ) 236 nm (43400 l mol^{-1} cm^{-1}). IR (KBr): ν(CN) 2154w, 2090s, 2059sh cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.02 (s, 36H, $C(CH_3)_3$); 7.45 m, 7.75 m (30H, $P(C_6H_5)_6$). ^{31}P NMR ($CDCl_3$): δ +50.5 (br, ~900 Hz). ^{99}Tc NMR ($CDCl_3$): δ −1760 (br, 6000 Hz). FAB-MS(+): *m/z* 955 $(M)^+$; 898 $(M-tBu)^+$; 872 $(M-CNtBu)^+$; 693 $(M-PPh_3)^+$. $E_{1/2}$ (CH_3CN): +0.79 V versus SCE ($1e^-$, rev).

Results and discussion

The compounds $[Tc(CN^tBu)_5(PPh_3)]PF_6$ and $[Tc(CN^tBu)_4(PPh_3)_2]PF_6$ are prepared by a modification of the synthesis of $[Tc(CN^tBu)_6]PF_6$, where pertechnetate is reduced by sodium dithionite in the presence of a large excess of isonitrile [2a]. In this case, the dithionite reducing agent is replaced by the phosphine itself, and the exact product obtained is determined by the stoichiometry of the isonitrile. In fact, it is necessary that slightly less than the required amount of isonitrile is used, for example, four moles in the preparation of $Tc(CN^tBu)_5(PPh_3)^+$, in order to ensure that the product is free from contamination by $Tc(CN^tBu)_6^+$, although such a procedure does reduce the yield. Attempts to synthesize the tris(isonitrile)tris(phosphine) complex failed, presumably due to the steric requirements of the phosphine ligand.

The spectral characteristics of the compounds corroborate their identities as mono- and bis(triphenylphosphine) complexes with isonitrile ligands. The ^1H NMR spectra exhibit the expected alkyl and aryl resonances with the appropriate integral areas. The presence of a single resonance in the alkyl region for $Tc(CN^tBu)_4(PPh_3)_2^+$ implies that the compound is in the *trans* configuration; however, the possibilities that the molecule is fluxional or that the alkyl resonances of the *cis* configuration may be degenerate cannot be ruled out.

The $^{31}P\{^1H\}$ NMR resonance of the mono(phosphine) complex appears upfield from free triphenylphosphine and that of the bis(phosphine) compound appears downfield from this reference. The addition of a second aryl-phosphine ligand delocalizes the backbonding in the molecule which accounts for the downfield shift of this latter signal. Both peaks are broadened due to unresolved coupling with the ^{99}Tc nucleus as seen in the spectrum of $Tc(CNtBu)_5(PPh_3)^+$ shown in Fig. 1. This coupling is not obviously apparent in the ^{99}Tc NMR spectra, although the resonance for $Tc(CNtBu)_5(PPh_3)^+$ does exhibit a slight splitting at the top of the peak (see Fig. 2).

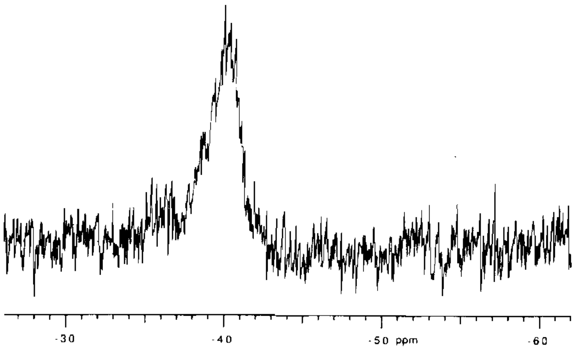

Fig. 1. The $^{31}P\{^1H\}$ NMR spectrum of $[Tc(CN^tBu)_5(PPh_3)]PF_6$ which is broadened due to ^{99}Tc–^{31}P coupling effects.

Fig. 2. The ^{99}Tc NMR spectrum of [Tc(CN^{t}Bu)$_5$(PPh$_3$)]PF$_6$ which shows slight splitting due to ^{99}Tc–^{31}P coupling effects.

In the Tc(CNR)$_4$(NN)$^+$ series, it was found from crystallographic studies that one of the isonitrile ligands is significantly bent at the nitrogen atom [3]. The result of this bend is a pseudo-internal oxidation which causes the ^{99}Tc NMR signal to appear in the Tc(III) region and also causes a lowering in frequency of the ν(CN) infrared bands. The ^{99}Tc NMR signals of the phosphine complexes fall within what has been established as the Tc(I) region [7] which implies that internal oxidation is not occurring. The infrared spectra also suggest that the isonitriles are linear since the C≡N stretches are in the same range as that of Tc(CN^{t}Bu)$_6$$^+$ (ν(CN) 2090s cm^{-1}) [2a] and not of Tc(CN^{t}Bu)$_4$bpy$^+$ (ν(CN) 1917m, 2052s cm^{-1}) [3]. Presumably, the triphenylphosphine ligand, which is a better π-acceptor and a poorer σ-donor than the aromatic amine ligands, does not sufficiently increase the electron density on the technetium center in order to allow the internal oxidation to occur. The mixed ligand compound *trans*-Tc(CNR)$_2$(dppe)$_2$$^+$ also contains what appear, from the ν(CN) values, to be linear isonitriles [4].

The mass spectra of the compounds display losses of both isonitrile and phosphine ligands as well as fragments resulting from dealkylation of the isonitrile ligands as is usually seen for technetium alkyl isonitrile complexes [8].

Both compounds have reversible one electron oxidation waves at potentials slightly less positive than that of Tc(CN^{t}Bu)$_6$$^+$ ($E_{1/2}$ +0.83 V versus SCE) [2a] but considerably more positive than the Tc(CNR)$_4$(NN)$^+$ compounds ($E_{1/2}$ +0.40 to +0.44 V versus SCE) [3]. These potentials reflect the intermediate electron donating capability of the phosphine ligand as compared with either the isonitrile or aromatic amine ligands.

While the low yields of these compounds preclude their preparation at the tracer level, this synthetic route may point the way to other mixed-ligand technetium compounds which offer the opportunity to vary the properties of the complex in a multitude of ways.

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