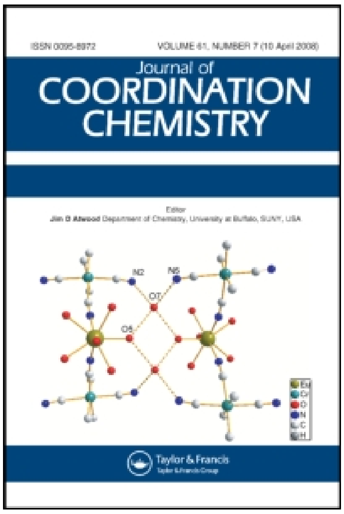

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NOTE

THE REDUCTION OF AMMONIUM PERTECHNETATE AND CHELATION OF OXOTECHNETIUM(V) BY 2-BENZIMIDAZOLE-2′-YLETHANETHIOL

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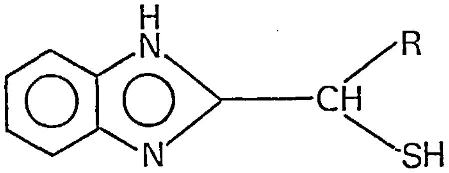
The main interest in the chemistry of technetium centres around its applications in nuclear medicine.[1] Technetium-99m, as a result of its availability and suitable nuclear properties, has emerged as the radionuclide of choice in diagnostic imaging studies, and its compounds are routinely used to image a wide variety of organ systems in the human body.[2]

The synthesis of these technetium radiopharmaceuticals often requires a prereduction of pertechnetate with sodium dithionite or stannous chloride prior to complex formation. Products of such reduction reactions generally lead to the formation of technetium(III) or oxotechnetium(V) complexes, although the production of mixtures of products is a major problem.[2] We now describe the product of the reaction between pertechnetate and 2-benzimidazole-2′-ylethanethiol (Hbls) (Figure 1). In this reaction, the ligand Hbls serves as an acid to hydrolyze oxo ligands of the pertechnetate ion, as a reducing agent for technetium(VII), and as a chelating agent for technetium(V). The product of this reaction is the cationic complex $Tc^{V}O(bls)_2^+$, which was isolated as $[TcO(bls)_2][TcO_4]$ and as $[TcO(bls)_2]BPh_4$.



R	*Abbvn*
CH_3	Hbls
H	Hbms

FIGURE 1 Benzimidazolylthiols.

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EXPERIMENTAL

Ammonium pertechnetate was obtained commercially. The ligands Hbls and benzimidazole-2-ylmethanethiol (Hbms) were prepared without difficulty according to literature procedures.[3] Scientific instrumentation used in the study is the same as was reported elsewhere.[4]

Preparation of the Complexes

$[TcO(bls)_2][TcO_4]$

To a solution of 0.2424 g of the ligand Hbls (1360 μmol) in 5 cm^3 methanol was added 1 cm^3 of a 0.34 mol dm^{-3} aqueous NH_4TcO_4 solution. The colour of the mixture solution turned green immediately, and stirring of the solution was continued for 2 h at room temperature (22°C), with the continuous precipitation of a dark green crystalline powder. This precipitate was collected by filtration, washed with ethanol, and dried *in vacuo*. It was recrystallized from acetone/ethanol. The yield was 84 mg, 78% based on Tc. The compound is soluble in acetone, acetonitrile and DMF, slightly soluble in chloroform and insoluble in dichloromethane, benzene and alcohols. Anal.: Calcd. for $C_{18}H_{18}N_4O_5S_2Tc_2$: C, 34.18; H, 2.87; N, 8.86%. Found: C, 34.08; H, 3.05; N, 8.96%. Electronic spectrum, (CH_3CN, nm, (ε/M^{-1} cm^{-1})): 590(400), 408(3000), 328 sh(3100), 290 sh(6700), 269(16800). IR spectrum (KBr): ν(Tc=O), 972(s); ν(TcO_4^-), 916(s), 874(s, br). Conductivity: Λ_M (DMF, 10^{-3} M) = 56 cm^2 mol^{-1} ohm^{-1}.

$[TcO(bls)_2]BPh_4$

To a solution of 0.2424 g of the ligand Hbls in 10 cm^3 methanol was added 1 cm^3 of a 0.34 mol dm^{-3} aqueous NH_4TcO_4 solution. This green solution was heated under reflux for 1 h, and the solution was filtered hot to give a small yield of green powder, which was found to be $[TcO(bls)_2]$ $[TcO_4]$. The filtered methanolic solution was brought to boiling and 1 cm^3 of a concentrated methanolic $NaBPh_4$ solution was added to give a fine brown precipitate, which was removed by filtration, and washed with ethanol. On cooling the filtrate and standing overnight, large brown crystals formed, which were removed and dried *in vacuo*. Elemental analyses indicated that the brown powder and the brown crystals were the same compound, *i.e.* $[TcO(bls)_2]BPh_4$. This compound is soluble in acetone, acetonitrile, THF and DMF, and is insoluble in chloroform, dichloromethane, hydrocarbons and alcohols. Anal.: Calcd. for $C_{42}H_{38}N_4BOS_2Tc$: C, 63.96; H, 4.86; N, 7.10%. Found: C, 64.01; H, 4.77; N, 7.18%. Electronic spectrum: (CH_3CN, nm, (ε/M^{-1} cm^{-1})): 592(370), 408(3100), 330 sh(3200), 290 sh(5700), 268(18900). IR spectrum (KBr): ν(Tc=O), 966(s). Conductivity: Λ_M (DMF, 10^{-3} M) = 64.6 cm^2 mol^{-1} ohm^{-1}.

RESULTS AND DISCUSSION

A general method for the preparation of technetium complexes in solution is by the reduction of the $Tc^{VII}O_4^-$ ion in the presence of coordinating ligands. These reductions require the use of reducing agents other than the coordinating ligands, and usually result in the formation of a mixture of products,[5] which is one of the

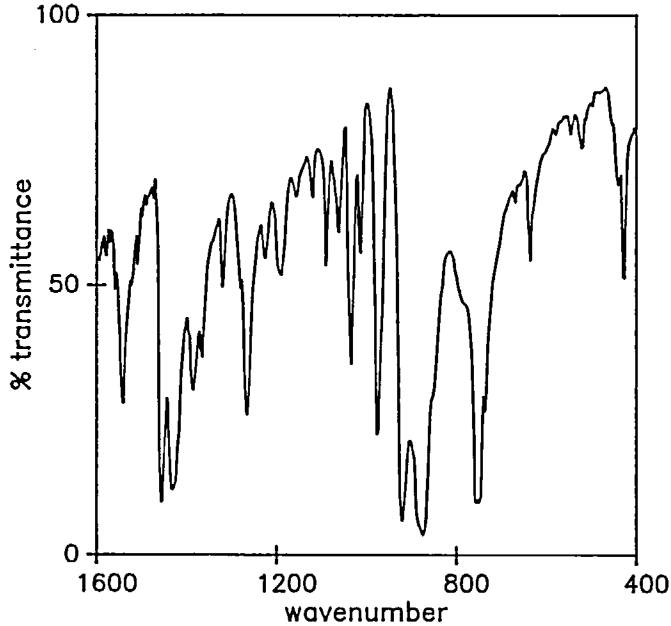

FIGURE 2(a)

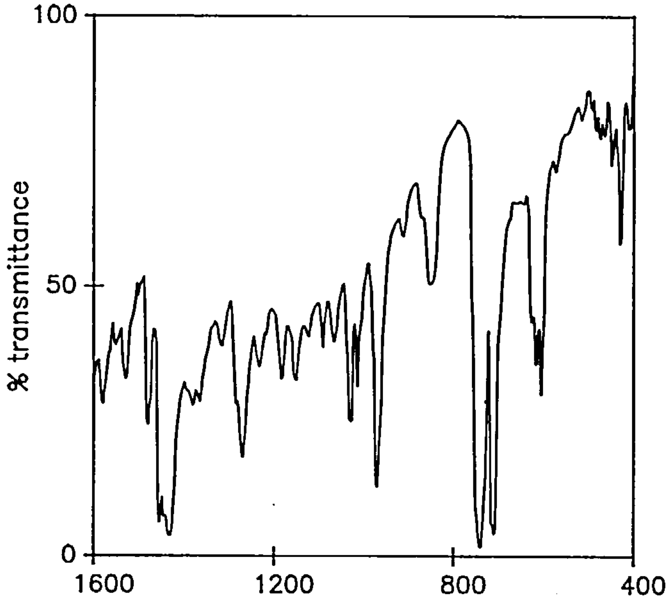

FIGURE 2(b)

GURE 2 Infrared spectra of (a) $[TcO(bls)_2][TcO_4]$ and (b) $[TcO(bls)_2]BPh_4$ in the range 400–00 cm^{-1}.

major problems in imaging procedures. We have found that the simple reaction between NH_4TcO_4 and 2-benzimidazole-2′-ylethanethiol (Hbls) in methanol produces the diamagnetic cationic technetium(V) complex $TcO(bls)_2^+$ in high yield. This complex was isolated as $[TcO(bls)_2][TcO_4]$, which precipitated out of the reaction solution, or as $[TcO(bls)_2]BPh_4$ by the addition of $NaBPh_4$. Both these compounds precipitated out of the solution analytically pure, and no problems were encountered with the formation of any byproducts.

The two products isolated in this study are indefinitely stable in air, and are soluble in polar organic solvents. They are 1:1 conductors in DMF solution, and no decomposition was observed in CH_3CN and DMF solution over a period of two days. The infrared spectra of the two compounds are given in Figure 2. $[TcO(bls)_2][TcO_4]$ exhibits a single strong absorption band at 972 cm^{-1}, which we ascribe to the Tc^{v}=O stretching vibration of $TcO(bls)_2^+$. Two strong broad bands at 916 and 874 cm^{-1} are typical of the Tc^{VII}=O stretching vibrations of the TcO_4^- anion (Figure 2a). In the salt $[TcO(bls)_2]BPh_4$, the Tc=O stretching vibration appears at 966 cm^{-1}, with only ligand bands present in the 840–910 cm^{-1} region (Figure 2b).

Both compounds are highly coloured due to intense absorptions in the visible spectrum. The green $[TcO(bls)_2][TcO_4]$ salt has bands at 590 and 408 nm in the visible region, with a strong band of maximum intensity at 269 nm, in addition to shoulders at 328 and 290 nm. The brown $[TcO(bls)_2]BPh_4$ solid gives rise to green solutions in a variety of solvents and exhibits bands at 591, 408, with shoulders at 330 and 290, and 268 nm in the electronic spectrum. (The TcO_4^- and BPh_4^- anions give absorptions around 290 nm and 274 nm respectively.) The peak at 268 nm is ascribed to the overlapping of an intraligand $\pi \rightarrow \pi^*$ transition with the oxo oxygen-to-technetium(V) charge transfer transition. The magnitude of the extinction coefficient of the peak at 590 suggests that it is due to a spin-forbidden d–d transition, with possible "stealing" from the adjacent charge transfer band at 408 nm. The intensities of all the other peaks indicate that they may be due to ligand-to-metal charge transfer.

Ligands serving as both reducing and chelating agents for technetium are rare in the literature. Classes of reducing agents that have been employed in this type of reactions include phosphines[6] and thiols,[7] and generally yield mixtures of products which require considerable manipulation in order to isolate pure complexes.

The reaction of NH_4TcO_4 with a fourfold excess of benzimidazole-2-ylmethanethiol (Hbms) under the same experimental conditions as for the preparation of $[TcO(bls)_2][TcO_4]$ did not give $[TcO(bms)_2][TcO_4]$ as product. Instead, a compound was precipitated in which TcO_4^- was absent, and that did not contain a peak in the infrared spectrum that could be ascribed to a Tc^{v}=O stretching vibration. However, this compound exhibits two strong bands at 897 and 885 cm^{-1} and a medium intensity band at 865 cm^{-1}, which is indicative of a TcO_3^+ moiety, and is a non-electrolyte in DMF. This product, obtained by the reaction of NH_4TcO_4 with Hbms, is still under investigation, and will be reported on at a later stage. What is certain, however, is that the ligands Hbls and Hbms react differently towards the pertechnetate ion. The corresponding benzimidazolylalcoholate ligands, which act as N,O donors towards technetium(V),[8] do not react with pertechnetate.

Although comments on a possible mechanism for the reduction of TcO_4^- by Hbls would be speculative, it does appear that the positive inductive effect of the methyl group on the carbon atom next to the thiol group plays a decisive role in making the ligand Hbls a stronger reducing agent than Hbms. Replacement of this methyl group by groups such as ethyl, secondary and tertiary butyl, with larger positive inductive effects, should give similar reactions with pertechnetate, and may reveal a new class of compounds that may be of significance in imaging procedures.

These simple procedures for synthesizing cationic technetium(V) complexes by reaction of substituted benzimidazolylthiols with pertechnetate could prove useful as a practical route to the preparation of a large variety of technetium(V) radiopharmaceuticals, which may be of interest in nuclear medicine.

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