

The Oxidation of Sn(II) Diphosphonates by Pertechnetate followed with Differential Pulse Polarography and Mössbauer Spectroscopy

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Abstract

The polarographic reduction and oxidation behaviour of tin(II) sulphate solutions (0.033 M $((\text{CH}_3)_4\text{N})_2\text{SO}_4$) was studied in the presence of various diphosphonates (MDP, EHDP, DCMDP, pCPMDP and DPD) in the pH range 2.5–8.5 at a dropping mercury electrode. Several tin species are present in these solutions and their concentrations vary with pH. Titration of these tin-diphosphonate solutions with pertechnetate in an argon atmosphere, followed by differential pulse polarography, revealed that four electrons are transferred and Tc(III) is formed. A three electron transfer was found for tin-pCPMDP solutions only. Sn-Mössbauer spectroscopic measurements made on EHDP-tin samples oxidized with various quantities of TcO_4^- confirmed the four electron transfer.

Introduction

The preparation of technetium labeled radiopharmaceuticals with bone seeking properties requires the reduction of pertechnetate [1]. Stannous tin is the agent which is usually used for this purpose. The reduction is carried out at pH values between 5 and 8 by adding a solution of pertechnetate to a (lyophilized) solution of stannous diphosphonate. The oxidation state of the reduced technetium and the stoichiometry of the reaction are still points of discussion and also of great interest [2].*

In studies concerning the reduction of pertechnetate with Sn(II) a variety of endpoint detection methods was used: potentiometry [3], polarography [4], amperometry [5] and iodometric backtitration of excess tin(II) [3, 4]. As pointed out by Steigman

[4] the last method is open to criticism because of potential side reactions.

In the preparation of bone seeking $^{99\text{m}}\text{Tc}$ labeled diphosphonates it is common practice in nuclear medicine to add a pertechnetate solution to a large excess of tin(II) diphosphonate. So we decided to titrate tin(II) diphosphonate solutions with pertechnetate instead of titrating in the opposite direction [3–5] because then in the initial stage of the titration Sn(II) is also in excess. A complete differential pulse polarogram between +0.05 V and –1.5 V vs. SCE was recorded after the addition of various quantities of titrant, to trace the changes in concentrations of the several tin diphosphonate species. Such a method requires some knowledge of the redox behaviour of tin(II) in the presence of diphosphonate and this will also be presented in this paper.

Polarographic data for aqueous tin(II) diphosphonate solutions were reported in a few cases only. Steigman [4] reported oxidation waves for tin(II) in 1 M sodium orthophosphate (pH = 7) at –0.29 V, in 0.2 M sodium pyrophosphate at –0.24 V and in 0.01 M sodium polyphosphate at +0.02 V. Furthermore, he noted for 0.2 M EHDP (pH = 5) ill-defined waves at +0.08 V and at –0.12 V. In a review on the role of inorganic tin in nuclear medicine Francis [6] described the use of polarographic methods for the determination of tin(II) in radiopharmaceuticals and for the tin(II) diphosphonate complex stabilities. No details were given however.

Because the electrochemical reduction behaviour of pertechnetate has been the subject of many papers [8–14] only the possible influence of diphosphonates on this reduction was examined.

Experimental

Materials

Tc-99- NH_4TcO_4 was purchased from the radiochemical centre at Amersham, U.K. (36 mg Tc/ml,

*A recent issue of *Int. J. Appl. Radiat. Isot.* is completely devoted to production, chemistry, redox reactions and properties of pertechnetate and technetium derivatives and their medical applications.

TABLE I. Abbreviations for Diphosphonic Acids.

MDP	= Methanediphosphonic acid, $\text{CH}_2(\text{PO}_3\text{H}_2)_2$
DCMDP	= Dichloromethane diphosphonic acid, $\text{CCl}_2(\text{PO}_3\text{H}_2)_2$
pCPMDP	= p-Chlorophenylmethane diphosphonic acid, $\text{CH}(\text{p-ClC}_6\text{H}_4)(\text{PO}_3\text{H}_2)_2$
EHDP	= 1-Hydroxyethane-1,1-diphosphonic acid, $\text{CH}_3\text{CHOH}(\text{PO}_3\text{H}_2)_2$
DPD	= 2,3-Dicarboxypropane-1,1-diphosphonic acid, $\text{CH}_2(\text{CO}_2\text{H})\text{CH}(\text{CO}_2\text{H})\text{CH}(\text{PO}_3\text{H}_2)_2$

5mCi Tc-99 dissolved in 8.2 ml 0.1 N NH_4OH). Five different diphosphonates were used: MDP, DCMDP, DPD, EHDP and pCPMDP (for abbreviations see Table I). MDP was purchased from Sigma Chemical Co, St. Louis, USA (M 9508). The other diphosphonates were kindly supplied by Henkel and Cie, Düsseldorf, GFR. The diphosphonates were turned into the acid form by means of a strong acid cation exchanger (Biorad, 50 W-X4, 200–400 mesh). Stannous tin sulphate (Merck, Darmstadt, GFR) was preferred over stannous tin chloride because the first salt is non hygroscopic and chloride ions might interfere with the tin diphosphonate complex formation. Stannous sulphate contained about 5% stannic tin as determined by iodometric titration. Tetramethylammonium sulphate (Fluka, Buchs, Switzerland) was used as the supporting electrolyte. As only minor differences are seen for the polarographic redox behaviour of Sn(II) in 0.033 M and in 0.1 M $(\text{CH}_3)_4\text{N})_2\text{SO}_4$, 0.033 M $(\text{CH}_3)_4\text{N})_2\text{SO}_4$ was used in all further experiments.

Measurements

Electrochemical measurements were made with a three electrode PAR model 264 polarographic analyzer equipped with a model 175 dropping mercury electrode and with a model 9002 A X-Y recorder. (EG and G; Princeton Applied Research).

All potentials are referred to a SCE. A platinum plate was used as the auxiliary electrode. The drop time of the mercury dropping electrode in all the experiments was 0.2 s. The temperature was kept at $20^\circ \pm 2^\circ$. Pulse and differential pulse polarograms were recorded at a scan rate of 5 mV/s. The differential pulse amplitude was 25 mV. For each experiment using a pulse technique the starting potential was chosen at the point of zero current in the DC polarogram. All measurements were performed under an argon atmosphere and special care was taken to remove oxygen from the different solutions before mixing them. pH adjustments were made either by addition of a $(\text{CH}_3)_4\text{NOH}$ solution (Merck, Darmstadt, GFR) or with 0.1 N sulphuric acid using a

Methrohm model E 604 pH meter equipped with a Methrohm EA 162/2 pH electrode.

Titrations

Stannous diphosphonate solutions (40 ml 0.033 M $(\text{CH}_3)_4\text{N})_2\text{SO}_4$; tin/diphosphonate molar ratio 1:4; stannous tin: 1×10^{-3} M) were titrated with a 29.8×10^{-3} M solution of Tc-99-ammonium pertechnetate at pH = 2.5 and at pH = 6.5. Special care was taken to remove oxygen from the diphosphonate solution before addition of tin sulphate by passing a humidified stream of argon for 15 min. The pertechnetate solution (kept under argon) was added to the stannous diphosphonate solutions by means of an Eppendorf pipette. In the first part of the titration portions of 100 μl pertechnetate were added. By the approach of the calculated equivalence point however (750 μl 29.8×10^{-3} M pertechnetate for 10 mg stannous sulphate, molar ratio Tc:Sn = 1:2) 25 μl portions were added. In most cases the titration was continued beyond the equivalence point until a distinct excess of pertechnetate was detected. After each addition of pertechnetate the solution was purged for two minutes with argon and a differential pulse polarogram was recorded between +0.05 V and -1.5 V. Where peaks were broad, the peak area seemed better suited as a measure of concentrations than peak heights. This procedure was used in the construction of the titration curves where absolute concentrations are irrelevant. At the equivalence point the differential pulse polarogram showed only the base line without either tin or pertechnetate peaks (see Fig. 1).

Sn-119-Mössbauer Spectroscopy

A solution was prepared containing 0.632 mM Sn(II) and 2.52 mM EHDP in 14 ml water, pH = 4.7. Care was taken to prevent stannous tin oxidation before addition of pertechnetate. In five penicillin vials two ml of this solution were mixed together with 0, 0.3, 0.9, 1.5 and 1.9 ml pertechnetate (29.8×10^{-3} M). The contents of the vials were carefully mixed and were then immediately frozen in liquid nitrogen. Next, the vials were decapsulated and the contents were lyophilized overnight. The lyophilized samples were well suited for Mössbauer spectroscopy. To establish that the presence of reduced pertechnetate does not influence the tin peaks in the Mössbauer spectrum to an important extent, one stannous EHDP sample was completely oxidized by means of hydrogen peroxide before it was lyophilized; no pertechnetate was added. The relative amount of stannic tin present in the samples was plotted against the amount of pertechnetate added. The Mössbauer spectroscopic measurements were performed at the Nuclear Solid State Physical Department of the State University of Groningen, The Netherlands.

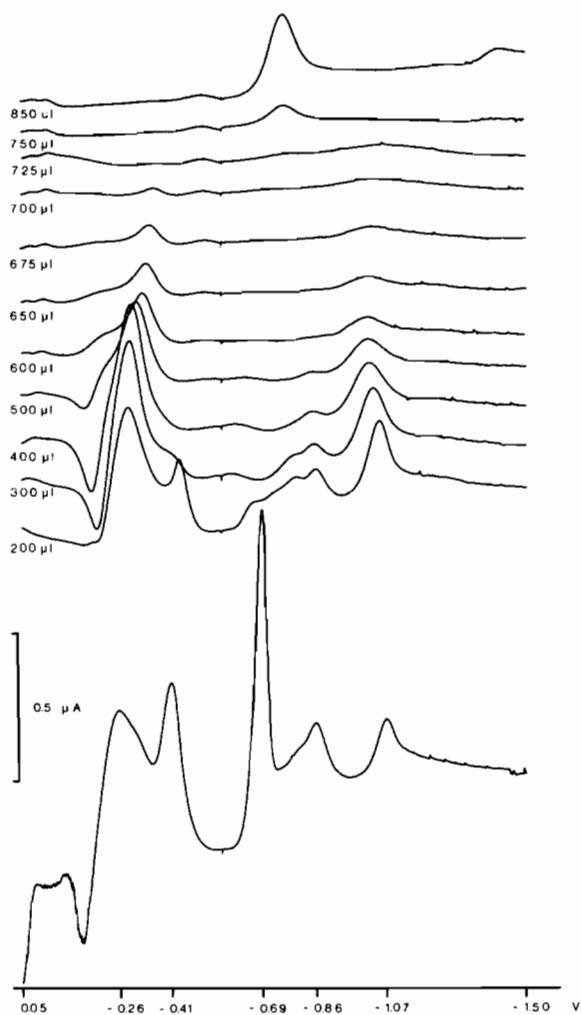


Fig. 1. Differential pulse polarograms of MDP-tin (4:1), Sn(II): 1.12×10^{-3} M, pH = 6.48, 0.033 M $((CH_3)_4N)_2SO_4$ after addition of increasing volumes of Tc-99-pertechnetate (29.8×10^{-3} M).

Results

Polarography of Sn(II) Solutions

Tin(II) solutions can be oxidized and reduced electrochemically at a dropping mercury electrode [7]. In both reactions two electrons are transferred. Polarographic waves have been reported between +0.1 V and -1.2 V (vs. SCE) depending on the pH and the presence of complexing agents (Table II).

For comparative reasons differential pulse polarograms were made of 10^{-3} M tin(II) sulphate solutions in the pH range 0.8–3.0 (Table III). Supporting electrolyte concentration was 0.033 M $((CH_3)_4N)_2SO_4$. At pH values higher than 3 precipitation of tin(II) hydroxide occurs. The potential shift of the tin(II) oxidation peak with increasing pH is in agreement with the general experience, that at higher oxidation states protons are expelled from and/or hydroxyl ions are bound to the coordination sphere surrounding a metal ion. The oxidation peak width increases with increasing pH value. The width of the reduction peak remains nearly constant. For a reversible two electron transition on theoretical grounds a peak width at half height ($w_{1/2}$) of 45 mV is expected [15]. The peak width data from Table III suggest that the electron transfer rate for the oxidation of tin(II) becomes slower with increasing pH.

Polarography of Sn(II) Diphosphonate Solutions

The redox behaviour of tin(II) sulphate solutions in the presence of five different diphosphonates (Table I) was studied at pH values between 1.5 and 8.5 with molar tin:diphosphonate ratios between 1:2 and 1:8. Table IV compiles the relevant results of the polarographic measurements for two pH values, at which the titration experiments were also made (*vide infra*). Changes in the tin-diphosphonate ratios resulted in only small changes in peak potentials.

TABLE II. Half-wave Potentials (vs. SCE) for the Oxidation and Reduction of Sn(II) in Various Media^a.

Medium	Oxidation $E_{1/2}$ (V)	Reduction $E_{1/2}$ (V)
0.1 M $HClO_4$	+0.136	-0.43
1 N HCl	-0.1	-0.47
Citric acid (satd., pH 2)	-0.05	-0.40
Malonic acid (satd., pH 2)	+0.15	-0.397
0.25 N Citrate (buffer, pH 3.5)	-0.21	-0.54
2 N Ammonium acetate (pH 4.5)	-0.16	-0.62
0.1 N Ammonium citrate (pH 6)	-0.406	-0.662
0.1 N Ammonia,		
0.1 N ammonium citrate (pH = 8.5)	-0.47	-0.752
1 N NaOH	-0.73	-1.22

^aData from ref. 6.

TABLE III. Differential Pulse Polarography of Tin(II) Sulphate Solutions^a.

pH	Oxidation		Reduction	
	E _p (V) ^b	w _{1/2} (mV) ^c	E _p (V) ^b	w _{1/2} (mV) ^c
0.87	+0.04	66	-0.42	67
1.19	-0.06	104	-0.43	68
1.88	-0.07	114	-0.42	66
3.08	-0.19	130	-0.45	67

^a0.001 M Sn(II)SO₄; 0.033 M ((CH₃)₄N)₂SO₄. ^bPeak Potentials (E_p) vs. SCE. ^cw_{1/2}, peak width at half peak height.

TABLE IV. Peak Potentials^a for the Oxidation and Reduction of Tin(II) Diphosphonate Solutions^b.

Diphosphonate/tin ratio	pH	Oxidation		Reduction		
		E _p (V)	w _{1/2} (mV)	E _p (V)	w _{1/2} (mV)	E _p (V)
MDP-tin (8:1)	2.46		-0.22	-0.55		
DCMDP-tin (8:1)	2.42	-0.07	-0.21	-0.54	-0.69	
pCPMDP-tin (4:1)	2.51		-0.15	-0.52		
EHDP-tin (4:1)	2.77	-0.09	-0.19	-0.57	-0.63	-0.77
DPD-tin (4:1)	2.54	-0.11	-0.17	-0.55	-0.63	
MDP-tin (8:1)	6.23	-0.20	-0.29	-0.41	-0.76	-0.82
DCMDP-tin (4:1)	6.49	-0.21	-0.26	-0.42	-0.77	-1.04
pCPMDP-tin (4:1)	6.49	-0.22		-0.37	-0.81	-1.00
EHDP-tin (4:1)	6.46		-0.26	-0.42	-0.71	-0.88
DPD-tin (4:1)	6.49			-0.37	-0.70	-0.89

^aPeak potentials vs. SCE in Volts from differential pulse polarography. ^bApproximately 10⁻³ Sn²⁺; 0.033 M ((CH₃)₄N)₂SO₄.

As a typical example differential pulse polarograms for EHDP-tin 4:1 ratio at pH values of 2.8 and 6.5 are given in Fig. 2.

Calculations based on acidimetric titrations of solutions containing a diphosphonic acid and tin(II) revealed several tin diphosphonate complexes to be present, depending on the pH of the solution [16]. We think that the various peaks in the polarograms correspond to reductions and oxidations of these complexes, assuming their interconversion to be slow compared with the scan rate at which the polarogram was recorded. Because these interconversion rates and their pH dependence are unknown, a more detailed analysis is impossible. Direct current polarograms of MDP-tin (4:1) solutions at pH = 2.4 and pH = 8.4 show only a very small difference in the limiting currents. This supports the conclusion, obtained earlier from the acidimetric titration experiments [16], that diphosphonates are able to stabilize supersaturated solutions of tin(II) hydroxide and that the last species which remains in solution with increasing pH is tin(II) hydroxide. For this reason the reduction peaks at -1.1 to -1.2 V in the DPP at pH = 6.4-8.5 are ascribed to the reduction of tin(II) hydroxide.

TABLE V. Peak Potentials for the Reduction of Pertechnetate^a.

TcO ₄ ⁻	pH	E _p (V)	w _{1/2} (mV)	E _p (V)	w _{1/2} (mV)	Molar ratio
TcO ₄ ⁻	4.01	-0.41	-0.58	-0.83		(3:1:20) ^b
	6.7			-0.84		
	8.33			-0.84		
TcO ₄ ⁻ + MDP (1:4) ^c	2.5	-0.32	-1.03	-1.24		(4:3:i)
	6.5		-0.75	-0.84		(3:2)
	7.3		-0.75	-0.84		(1:1)
	8.5			-0.84		
TcO ₄ ⁻ + DCMDP (1:2) ^c	2.5	-0.32	-1.03	-1.24		(4:3:i)
	4.99		-0.72	-0.83		(1.7:1)
	6.5		-0.75	-0.84		(2:5)
	7.4			-0.84		
	8.5			-0.84		

^aPeak potentials vs. SCE (V) from differential pulse polarography. ^bThese values represent ratios between the limiting currents of the waves mentioned. The third wave at pH = 2.5 was ill-defined (i), because it was the catalytic hydrogen reduction wave. ^cMolar ratio.

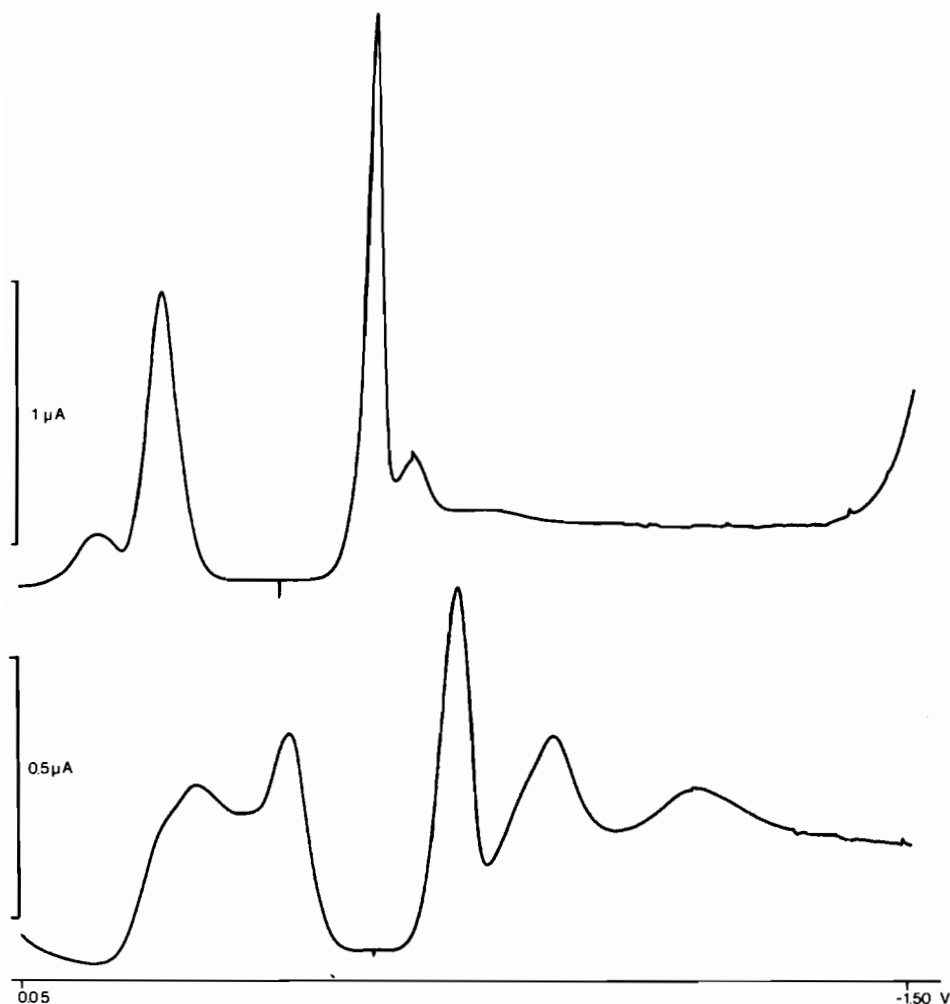


Fig. 2. Differential pulse polarogram of EHDP-tin (4:1). EHDP, 4×10^{-3} M; $SnSO_4$, 1.2×10^{-3} M; $((CH_3)_4N)_2SO_4$ 0.033 M. Oxidation peaks to the left and reduction peaks to the right of the starting points. Lower curve, pH = 2.77; upper curve, pH = 6.46. Note the difference in the current sensitivities.

Polarography of Sn(IV)-Diphosphonate Solutions

In order to find out whether Sn(IV) reduction peaks could be expected in the tin-pertechnetate titration experiments, a set of polarograms was recorded in a titration of Sn(II)-DCMDP (1:8) solutions with hydrogen peroxide at pH = 1.8. The intensity of all peaks diminished and after complete oxidation of Sn(II) no peaks were left in the differential pulse polarogram between +0.05 V and -1.5 V. This is in line with the general opinion [7] that Sn(IV) can only be reduced in strong halo acid solutions.

Pertechnetate Reduction in the Presence of Diphosphonates

The results of the polarographic reduction of pertechnetate at a dropping mercury electrode with

and without diphosphonates at various pH values are presented in Table V. The influence of diphosphonates on the half-wave potentials of the pertechnetate reduction is marginal and due to the presence of diphosphonic acid. As the results are in agreement with literature data for other buffering media only two remarks are made.

The polarographic wave at -0.84 V seen in neutral media without diphosphonates is split in the presence of diphosphonate (Table V). Such a splitting of waves is more often observed when hydrogen ions are consumed in the electrode process supplied either by a weak acid (here: diphosphonic acid) or water [17]. The peak at -0.75 V disappears at increasing pH, when a minimum is reached in the buffer capacity of the diphosphonate. For MDP ($pK_3 = 7.1$) at pH = 8.5, and for the stronger acid DCMDP ($pK_3 = 5.97$) the first wave had already disappeared at pH = 7.4.

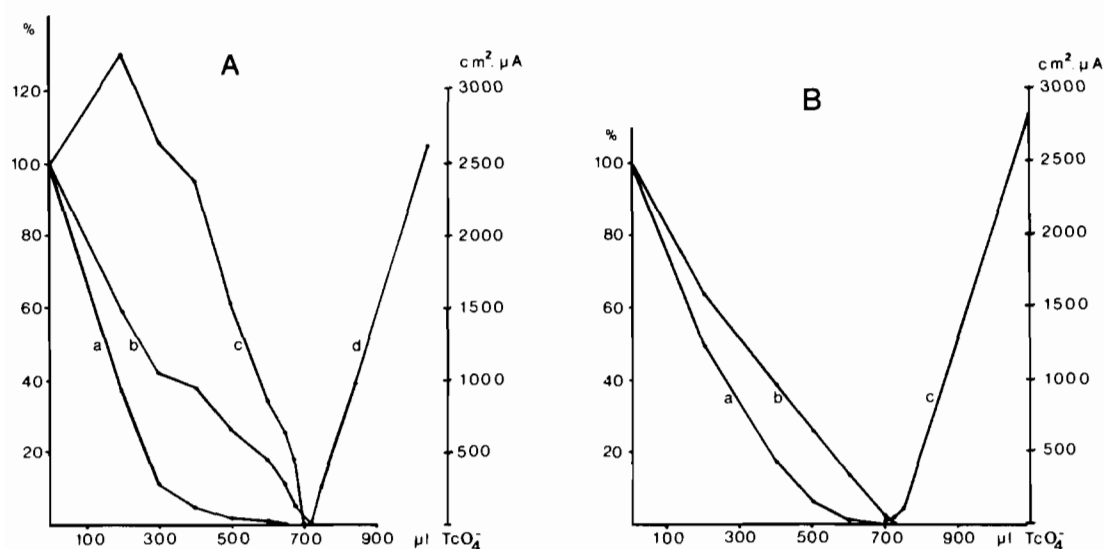


Fig. 3. Titration of 40 ml tin-diphosphonate solutions with pertechnetate (29.8×10^{-3} M). Initial tin concentration, 1.12×10^{-3} M; $((\text{CH}_3)_4\text{N})_2\text{SO}_4$ 0.033 M. The area of the tin-diphosphonate oxidation or reduction peaks are plotted as percentage of the peak surface area before the addition of pertechnetate; the pertechnetate peak area is plotted as the peak surface with a correction for the current range setting of the polarographic analyzer. A. MDP: Tin = 4.1; pH = 6.48; curve 'a' represents the stannous tin reduction peaks between -0.69 V and -0.86 V; curve 'b' represents the stannous tin oxidation peaks between -0.12 V and -0.41 V; curve 'c' represents the stannous tin reduction peak at -1.07 V and curve 'd' represents the pertechnetate reduction peak at -0.76 V. B. EHDP: Tin = 4.1; pH = 2.77; curve 'a' represents the stannous tin reduction peak at -0.57 V; curve 'b' represents the stannous tin oxidation peak at -0.20 V and curve 'c' represents the pertechnetate reduction peak at -1.03 V.

Titration of Sn(II)-Diphosphonate with TcO_4^-

These titrations were performed at two pH values, pH = 2.5 and 6.5, the last value being close to those used in medical practice. Figure 1 shows a typical example of a set of differential pulse polarograms recorded after addition of an increasing volume of a pertechnetate solution. (see Experimental section). As can be seen in this figure, the peak heights diminish on addition of pertechnetate. The equivalence point at 725 μl is characterized by the disappearance of the stannous tin peaks and the concomitant appearance of the pertechnetate peaks at -0.76 V. The calculated endpoint for a molar reaction ratio of Tc:Sn = 1:2 was 752 μl pertechnetate solution.

Figure 3 shows two typical examples of titrations of stannous diphosphonates with pertechnetate with multiple amperometric endpoint detection. Rather sharp endpoints are found at the disappearance of stannous tin peaks and the concomitant appearance of a pertechnetate peak.

When about one third of the pertechnetate has been added a colour develops resulting at the equivalence point in yellow solutions at pH = 2.5 and in pink solutions at pH = 6.5, except for EHDP which is also yellow at this pH.

No time effect was found in the amperometric titrations: no difference was seen between polarograms taken at two and twenty minutes after addition of pertechnetate. Adding the equivalent amount of

pertechnetate in one charge to the tin diphosphonate solution gave the same result as the titrations did. It seems that the consumption of stannous tin by pertechnetate occurs within two minutes. Table VI gives the results of the titrations with amperometric detection for all the diphosphonates used.

Mössbauer Spectroscopic Measurements

Samples of an EHDP-tin(II) (4:1) solution were treated with different amounts of pertechnetate and the amounts of stannous and stannic tin present in these solutions were determined by Mössbauer spectroscopy (see Experimental section for details). The tin(II) and tin(IV) peaks in these spectra are

TABLE VI. Observed Endpoints Expressed in Tin Technetium Molar Ratio.

Diphosphonate	pH	Sn/Tc Molar/Ratio
MDP	2.49	2.0
MDP	6.48	2.1
DCMDP	6.49	2.1
pCPMDP	2.51	1.6
pCPMDP	6.49	1.6
EHDP	2.77	2.1
EHDP	6.46	2.1
DPD	2.57	1.9
DPD	6.53	1.8

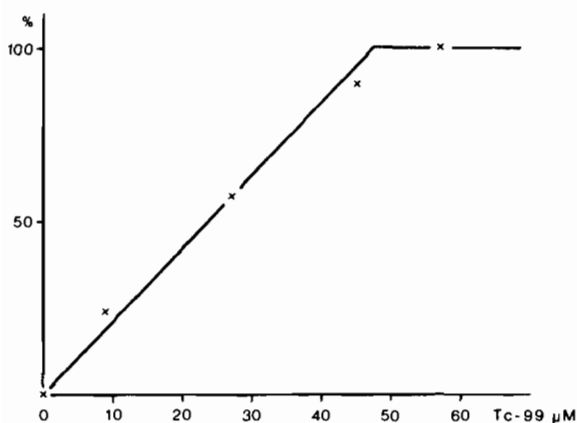


Fig. 4. Titration curve of EHDP-tin (4:1) Sn(II) (45.1×10^{-3} M; pH = 4.7; 2 ml) with pertechnetate (29.8×10^{-3} M). Detection with Mössbauer spectroscopy. The percentage of tin(IV) is plotted against the amount of pertechnetate (in μM) added. Endpoint 47.5 μM (1.59 ml) pertechnetate.

easily assigned and the peak areas of the curves gave directly a tin(II)/tin(IV) ratio. The titration curve (Fig. 4) shows an equivalence point at a Sn:Tc molar ratio of 1.9. So four electrons are involved in the reduction of pertechnetate by tin(II).

Discussion

Based on the results given above we conclude that four electrons are involved in the reduction of pertechnetate by tin(II) in the presence of MDP, DCMDP, EHDP and DPD. This means that in our experiments with these diphosphonates Tc(III) is formed. In the presence of pCPMDP only three electrons seem to be involved in the reduction of pertechnetate by tin(II). This might be related to the exceptionally high stability of the tin(II)-pCPMDP complex, giving an incomplete reduction to an average oxidation state of IV for the Tc species formed.

In all our experiments air was excluded. In clinical practice the exclusion of air is certainly less effective. The Tc(III) formed may be reoxidized to Tc(IV) by reaction with water, as Steigmann [4] suggested, or by oxygen from the air as Grassi [11] stated. However, as long as an excess of Sn(II) is available Tc(IV) can be reduced to Tc(III). When all of the tin(II) is consumed by this process Tc(IV) will no longer be reduced, but will instead be slowly oxidized to pertechnetate as is well known from common experience with technetium labeled radiopharmaceuticals.

The solutions used in this study contained 0.033 M $((\text{CH}_3)_4\text{N})_2\text{SO}_4$ as supporting electrolyte. The choice of this electrolyte was made to exclude alkali metal and chloride ions because these are supposed to interfere with complex formation more than the

tetramethyl ammonium and sulphate ions. The influence of the supporting electrolyte on our results seems only marginal, since in the Mössbauer experiments no electrolyte was added and Tc(III) was still found.

In several reports [3-5] the reduction of pertechnetate by tin(II) in various media has been described as a three electron transition. In these reports pertechnetate solutions were titrated with tin(II). Steigman [4] pointed out that an excess of tin(II) is able to reduce Tc(IV) to Tc(III). As in the initial stage of our titrations Sn(II) is in excess, this might be the reason that in our experiments a four electron transition is found. Russell and Cash [5] found, however, identical results (three electrons) in acid and neutral pyrophosphate containing solutions for the TcO_4^- with Sn(II) as well as the Sn(II) with TcO_4^- titrations. They used a high excess of pyrophosphate over tin(II) and added no supporting electrolyte. In our experiments a relatively small excess of diphosphonate was used.

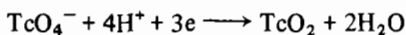
These divergent results might be due to differences in the tin-diphosphonate bonding. Figure 3 shows that the various tin(II) complexes react with pertechnetate at different rates. This was also found for the reaction of stannous diphosphonates with hydrogen peroxide. It is supposed that less firmly complexed tin(II) is more easily oxidized than tin(II) in a stable diphosphonate complex.

The three electron transition found in the titration of stannous-pCPMDP with pertechnetate also supports the idea of the importance of the binding of tin(II) for ease of oxidation.

As radiopharmaceuticals differ in some major points from the solutions used in this and other studies, conclusions can not be transposed to the radiopharmaceutical practice without care. However, we believe that there are good reasons to assume that in bone seeking radiopharmaceuticals technetium is present as Tc(III) as long as excess tin(II) is available.

Standard Redox Potential and Observed Half-Wave Potentials

Cobble determined in 1953 the standard redox potential for the TcO_4^-/TcO_2 couple using a technetium dioxide pertechnetate electrode [18]. The redox potential of this electrode has been measured in both acid and basic solutions to prove that the electrodes are reversible. The result was revised in 1955 and is now supposed to be 0.738 V (NHE) [19]. For an irreversible reduction in which protons are involved



the following expression [20] (at a dme) holds:

$$E_{1/2} = E_0 + \frac{RT}{\alpha nF} \ln \left[0.886k_e^0 \left(\frac{t}{D} \right)^{3/4} \right] + \frac{pRT}{\alpha nF} \ln (H^+)$$

where α is the transfer coefficient, k_e^0 is the heterogeneous rate constant of the electrode process at E_0 , t is the drop time of the mercury electrode, D is the diffusion coefficient of the reacting species and p represents the number of protons involved.

For this three electron reduction, at pH = 8 with $t = 0.2$ s, estimating k_e^0 to be 10^{-4} cm/s [20], D to be 10^{-5} cm²/s and α to be 0.5 and expressing the result relative to the saturated calomel electrode, we obtain $E_{1/2} = -0.83$ V. This is in reasonable agreement with the results of Table V. The difference in equilibrium potentials between the technetium and tin redox couples indicates that the equilibrium for this homogeneous reaction is completely shifted to the side of the reduced Tc species. However, the low value of $E_{1/2}$ indicates that the rate of TcO_4^- reduction (at a dme) is slow. According to contemporary theories for electron transfer processes, a low rate for the homogeneous redox reaction is also expected. However, in titration experiments as well as in medical practice this low rate is fast enough that no practical problems arise.

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