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A New Class of Oxotechnetium(5+) Chelate Complexes Containing a $TcON_2S_2$ Core

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The benzoyl-protected dimercaptodiamides $(PhCOS(CH_2)_nCONH)_2X$ (n = 1, X = $(CH_2)_2$, $(CH_2)_3$, and o-C_6H_4; n = 2, X = $(CH_2)_2$ and $(CH_2)_3$) have been synthesized. From these, via the sodium dithionite reduction of TcO_4^- in base, the technetium complexes $[TcO(S(CH_2)_nCONXNCO(CH_2)_nS)]^-$ (n = 1, X = $(CH_2)_2$, $(CH_2)_3$, and o-C_6H_4; n = 2, X = $(CH_2)_2$) have been prepared. The synthesis and characterization of the complexes, and their precursors, are presented, and the radiopharmaceutical applicability is discussed.

Introduction

The widespread use of the metastable isomer of technetium (^{99m}Tc, γ = 140 keV, $t_{1/2}$ = 6 h) in diagnostic nuclear medicine procedures is well documented.[2,3] We[4-7] and others[8-10] have previously shown, using the long-lived radionuclide ^{99}Tc, a β^- emitter ($t_{1/2} = 2.12 \times 10^5$ years), that kinetically stable oxotechnetium(5+) compounds can be readily prepared.

The work with bidentate thiols[4,5,7-9] showed that the five-coordinate $TcOS_4$ core was readily accessible either by reduction[11] of pertechnetate or by metathesis from $TcOCl_4^-$[4,12] and was kinetically stable with respect to substitution. The present study was undertaken in order to find a tetradentate ligand that would bind the oxotechnetium core, giving a complex that would be stable in vivo. This required the synthesis of a new class of ligands that would occupy the basal positions in a square pyramid and would impart kinetic stability by virtue of the chelate effect.

The amide thiolate ligands described here meet these criteria. This communication describes the syntheses of these ligands and their oxotechnetium(5+) complexes. Preliminary data on the synthesis and in vivo distribution of oxo[*N*,*N*′-ethylenebis(2-mercaptoacetimido)]technetate (VI) have been presented.[13]

Experimental Section

Technetium as $NH_4^{99}TcO_4$ was obtained as a gift from New England Nuclear, Billerica, MA. All manipulations were carried out in laboratories approved for low-level radioactivity (^{99}Tc is a weak β emitter with a half-life of 2.12×10^5 years and a particle energy of 0.292 MeV). All precautions followed were as detailed previously.[4,12] Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY, and Galbraith Laboratories, Knoxville, TN.

Melting points were obtained with a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded in the range 4000–200 cm^{-1} on a Perkin-Elmer PE180 grating infrared spectrophotometer as KBr pellets, and optical spectra were measured with a Cary 17 spectrophotometer. High-field proton NMR spectra were recorded on Bruker instruments (270, 250, and 200 MHz) while routine spectra were obtained with either a Varian T-60 or a Perkin-Elmer R-24B. The carbon-13 NMR spectrum was measured with a Jeol FX-60Q spectrometer at 15 MHz. Routine mass spectra were recorded with a Varian MAT 44 instrument, and the field desorption mass spectrum (FDMS) was measured with a Varian MAT 731 instrument described elsewhere.[14] The high-resolution electron-impact mass spectra (EIMS) were obtained with a CEC 110B (Du Pont Instruments, Monrovia, CA).

Prior to use, distilled water was passed through a Barnstead Ultrapure D8902 cartridge, followed by redistillation in a Corning AG-1 water still. All other chemicals were of reagent grade, used without further purification, and obtained from the indicated sources.

Preparation of the Ligands. The compounds *N*,*N*′-ethylenebis(2-mercaptoacetamide) and *N*,*N*′-ethylenebis(3-mercaptopropionamide) were prepared by the method of Atkinson, et al.[15] The amides *N*,*N*′-propylenebis(2-mercaptoacetamide) and *N*,*N*′-propylenebis(3-mercaptopropionamide) were prepared in analogous manner from 1,3-diaminopropane (Aldrich) and methyl thioglycolate (Aldrich),

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or methyl 3-mercaptopropionate (Aldrich). The ethylenediamine was from Baker. These dithioamides were converted to the benzoyl esters by the reaction of the corresponding disodium salt with benzoyl chloride (Baker) as described below.

Preparation of *N,N'*-Ethylenebis(benzoyl-2-mercaptoacetamide) (I). To a degassed suspension of 0.85 g (4 mmol) of *N,N'*-ethylenebis(2-mercaptoacetamide) in 50 mL of water was added 0.35 g (9 mmol) of sodium hydroxide. The mixture was stirred under N_2 for 30 min at room temperature. The resulting solution was filtered, and degassed benzoyl chloride (Baker) (1.15 g, 8.2 mmol) was added to the clear aqueous solution. A white precipitate appeared after 5 min, and this mixture was stirred at room temperature for an additional 90 min. The precipitate was filtered and twice recrystallized from absolute ethanol, giving 1.42 g (85% yield) of long white needles, mp 190–191 °C. Anal. Calcd. for $C_{20}H_{20}N_2O_4S_2$: C, 57.67; H, 4.84; N, 6.73; S, 15.40. Found: C, 57.53; H, 4.76; N, 6.81; S, 15.46. ^{1}H NMR 270 MHz (pyridine-d_5/acetone-d_6, 3:1 v/v): δ 8.98 (br s, 2 H, NH), 8.06–7.44 (mult, 10 H, phenyl), 4.14 (s, 4 H, CH_2S), 3.69 (m, 4 H, NCH_2). IR: 3275 (ν(NH)); 1670, 1650 (ν(CO)); 1550 (δ(NH)). High-resolution EIMS for $C_{20}H_{20}N_2O_4S_2$: calcd, 416.08646 (difference +1.35 mmu); found, 416.08781 (M^+).

***N,N'*-Propylenebis(benzoyl-2-mercaptoacetamide) (II).** Yield 64%; mp 179–180 °C. Anal. Calcd for $C_{21}H_{22}N_2O_4S_2$: C, 58.58; H, 5.15; N, 6.51; S, 14.89. Found: C, 58.28; H, 5.35; N, 6.67; S, 15.09. ^{1}H NMR 270 MHz (pyridine-d_5/acetone-d_6, 3:1 v/v): δ 8.80 (br s, 2 H, NH), 8.07–7.43 (m, 10 H, phenyl)), 4.15 (s, 4 H, CH_2S), 3.55 (m, 4 H, CH_2NH), 1.89 (m, 2 H, CH_2CH_2NH). IR: 3280 (ν(NH)); 1660, 1640 (ν(CO)); 1550 (δ(NH)). High-resolution EIMS for $C_{21}H_{22}N_2O_4S_2$: calcd, 430.10211 (difference −0.77 mmu); found, 430.10134 (M^+).

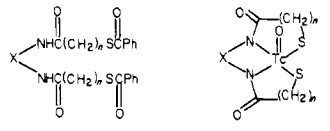
***N,N'*-Ethylenebis(benzoyl-3-mercaptopropionamide) (III).** Yield 78%; mp 201–202.5 °C. Anal. Calcd for $C_{22}H_{24}N_2O_4S_2$: C, 59.44; H, 5.44; N, 6.30; S, 14.40. Found: C, 59.21; H, 5.58; N, 6.41; S, 14.21. ^{1}H NMR 270 MHz (pyridine-d_5/acetone-d_6, 3:1 v/v): δ 8.75 (br s, 2 H, NH), 8.06–7.45 (m, 10 H, phenyl), 3.68 (m, 4 H, CH_2NH), 3.59 (t, 4 H, J = 7.0 Hz), 2.82 (t, 4 H, J = 7.0 Hz, CH_2CO and CH_2S). IR: 3285 (ν(NH)); 1660, 1630 (ν(CO)); 1540 (δ(NH)). High-resolution EIMS for $C_{22}H_{24}N_2O_4S_2$: calcd, 444.11776 (difference +0.59 mmu); found, 444.11835 (M^+).

***N,N'*-Propylenebis(benzoyl-3-mercaptopropionamide) (IV).** Yield 83%; mp 151–152 °C. Anal. Calcd for $C_{23}H_{26}N_2O_4S_2$: C, 60.24; H, 5.72; N, 6.11; S, 13.98. Found: C, 60.44; H, 5.82; N, 6.13; S, 14.04. ^{1}H NMR 270 MHz (pyridine-d_5/acetone-d_6, 3:1 v/v): δ 8.29 (br s, 2 H, NH), 8.00–7.43 (m, 10 H, phenyl), 3.41 (m, 4 H, CH_2NH), δ 3.46 (t, 4 H, J = 7.0 Hz), 2.71 (t, 4 H, J = 7.0 Hz, CH_2CO and CH_2S), 1.77 (m, 2 H, CH_2CH_2NH). IR: 3290 (ν(NH)); 1660, 1635 (ν(CO)); 1545 (δ(NH)).

Preparation of *N,N'*-*o*-Phenylenebis(benzoyl-2-mercaptoacetamide) (V). (a) To a refluxing solution of 10.8 g (0.1 mmol) of freshly sublimed *o*-phenylenediamine (Baker) in 500 mL of anhydrous THF was added dropwise 22.4 g (0.2 mmol) of chloroacetyl chloride (Baker) in 100 mL of THF. A thick white precipitate formed, and the mixture was refluxed for 2 h. The volume of the mixture was reduced to ca. 150 mL by rotary evaporation. The precipitate was collected and washed with 100 mL of chilled water. It was air-dried and recrystallized from absolute ethanol to give 14.3 g (55% yield) of white needles of *N,N'*-*o*-phenylenebis(2-chloroacetamide) (mp 195–196 °C). (b) An oxygen free solution of 3.5 g (25.5 mmol) of thiobenzoic acid (Aldrich) and 0.9 g (22.5 mmol) of sodium hydroxide in 50 mL of water was added to a solution of 3.0 g (11.5 mmol) of *N,N'*-*o*-phenylenebis(2-chloroacetamide) dissolved in a mixture of 200 mL of ethanol (95%) and 300 mL of benzene under a nitrogen atmosphere. The solution was stirred for 1 h at room temperature, and when the solvent was removed under reduced pressure, the product separated as a white precipitate. This was recovered by filtration, air-dried, and recrystallized from absolute ethanol to give 4.1 g of fluffy white needles (77% yield, mp 164–165 °C). Anal. Calcd for $C_{24}H_{20}N_2O_4S_2$: C, 62.05; H, 4.34; N, 6.02; S, 13.38. Found: C, 61.87; H, 4.48; N, 5.96; S, 13.62. IR: 3230 (ν(NH)); 1660, 1605 (ν(CO)); 1540 (δ(NH)). ^{1}H NMR 250 MHz (acetone-d_6): δ 9.21 (br s, 2 H, NH), 8.01 (d, 4 H, ortho phenyl), 7.69 (t, 2 H, para phenyl), 7.64 (m, 2 H, half of AA'BB' for *o*-phenylene), 7.56 (t, 4 H, meta phenyl), 7.20 (m, 2 H, other half of AA'BB' for *o*-phenylene), 4.04 (s, 4 H, SCH_2).

Preparation of the Technetium Complexes. Complexation of the benzoyl-protected thiols I–III and V was accomplished via the sodium dithionite (MCB) reduction of pertechnetate in a basic aqueous ethanol solution of excess compound. All attempts with IV lead to quantitative formation of $TcO_2 \cdot xH_2O$. Abbreviations for the ligands and complexes are given in Table I.

Table I. Abbreviations for the Ligands and Complexes



X	*n*		
$(CH_2)_2$	1	I = ebma	VI = $[TcO(ema)]^-$
$(CH_2)_3$	1	II = pbma	VII = $[TcO(pma)]^-$
$(CH_2)_2$	2	III = ebmp	VIII = $[TcO(emp)]^-$
$(CH_2)_3$	2	IV = pbmp	
o-C_6H_4	1	V = opbma	IX = $[TcO(opma)]^-$

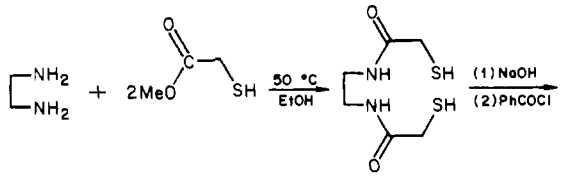
Preparation of Tetraphenylarsonium oxo[*N,N'*-ethylenebis(2-mercaptoacetimido)]technetate(5+) ($Ph_4As[TcO(ema)]$). A suspension of 0.12 g (0.29 mmol) of I was made in a mixture of 50 mL of water and 75 mL of ethanol. This was heated to 70 °C to dissolve the solid, and the pH was adjusted to 13 with 10 N NaOH. To the resulting clear solution was added 0.66 mL of a 0.331 M NH_4TcO_4 solution (0.22 mmol). Sodium dithionite (0.5 g, 2.8 mmol) was dissolved in 5 mL of water and immediately added dropwise to the reaction mixture. The solution became yellow and was stirred over heat to reduce the volume to 25 mL. After the deep yellow solution was cooled to ambient temperature and filtered, a solution of tetraphenylarsonium chloride monohydrate (Eastern Chemical) (0.25 g, 0.57 mmol) was added. A fine yellow suspension was formed, which upon standing for 12 h, deposited a yellow microcrystalline solid. This was separated and recrystallized from acetone/water by slow evaporation. The yield of yellow plates was 0.153 g (99% on the basis of Tc, mp 219–222 °C dec). Anal. Calcd for $C_{30}H_{28}AsN_2O_3S_2Tc$: C, 51.29; H, 4.02; N, 3.99; S, 9.13. Found: C, 51.65; H, 4.33; N, 3.68; S, 9.60. Optical spectrum in CH_3CN, nm (ε in l mol^{-1} cm^{-1}): 434 (sh), 363 (4300), 290 (sh). ^{1}H NMR 200 MHz (CD_2Cl_2): δ 7.92–7.63 (m, 20 H, phenyl), 3.98–3.58 (m, 4 H, ABCD system, CH_2N), 3.85, 3.79, 3.66, 3.61 (q, 4 H, AB system, J_{AB} = 11.4 Hz, SCH_2). Carbon-13 NMR 15 MHz (CD_2Cl_2): 187.2 (CO), 134.9, 133.2, 131.4, 120.5 (phenyl), 53.3 (NCH_2), 39.2 ppm (SCH_2). IR: 1615, 1600 (ν(CO)); 945 (ν(TcO)).

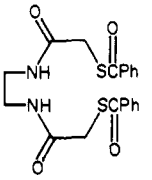
Tetraphenylarsonium oxo[*N,N'*-propylenebis(2-mercaptoacetimido)]technetate(5+) ($Ph_4As[TcO(pma)]$) was prepared with use of a 3-fold excess of compound II. The yield was 99% on the basis of Tc (mp 153.5–155 °C). Recrystallization from ethanol/water via slow evaporation afforded yellow-orange plates. Anal. Calcd for $C_{31}H_{30}AsN_2O_3S_2Tc$: C, 51.96; H, 4.22; N, 3.91; S, 8.95. Found: C, 51.33; H, 4.46; N, 4.08; S, 9.36. Optical spectrum in CH_3CN, nm (ε): 390 (3380), 290 (sh). ^{1}H NMR 250 MHz (CD_2Cl_2): δ 7.82–7.56 (m, 20 H, phenyl), 3.65 (q, 4 H, AB pair, SCH_2), 3.88 (d), 2.80 (t, 4 H, NCH_2), 2.21–1.88 (m, 2 H, NCH_2CH_2). IR: 1590, 1570 (ν(CO)); 960 (ν(TcO)).

Tetraphenylarsonium oxo[*N,N'*-ethylenebis(3-mercaptopropionimide)]technetate(5+) ($Ph_4As[TcO(emp)]$) was prepared with use of a 10-fold excess of compound III. After three recrystallizations from acetone/water by slow evaporation the yield of orange crystals was 55% on the basis of Tc (mp 187.5–189 °C). Anal. Calcd for $C_{32}H_{32}AsN_2O_3S_2Tc$: C, 52.61; H, 4.41; N, 3.83; S, 8.78. Found: C, 52.21; H, 4.64; N, 3.87; S, 8.91. Optical spectrum in CH_3CN, nm (ε): 405 (3230). ^{1}H NMR 250 MHz (CD_2Cl_2): δ 7.86–7.55 (m, 20 H, phenyl), 3.79–3.71 (m, 2 H, ABCD system, NCH_2CH_2N), 3.10–2.84 (m, 10 H, ABCD system, SCH_2CH_2 overlayed with the other half of ABCD for NCH_2CH_2N). IR: 1583, 1565 (ν(CO)); 940 (ν(TcO)).

Tetraphenylarsonium oxo[*N,N'*-*o*-phenylenebis(2-mercaptoacetimido)]technetate(5+) ($Ph_4As[TcO(opma)]$) was prepared with use of 3-fold excess of compound V. After recrystallization from hot ethanol/water the yield of yellow-gold plates was 74% on the basis of Tc (mp 221–225 °C dec). Anal. Calcd for $C_{34}H_{28}AsN_2O_3S_2Tc$: C, 54.40; H, 3.76; N, 3.73; S, 8.54. Found: C, 54.00; H, 4.03; N, 3.75; S, 8.66. Optical spectrum in CH_3CN, nm (ε): 450 (sh), 363 (3900), 285 (sh). ^{1}H NMR 60 MHz (CD_2Cl_2): δ 8.46 (m, 2 H, half of AA'BB' phenylene), 7.64 (m, 20 H, phenyl), 6.82 (m, 2 H, half of AA'BB' phenylene), 4.06 (q, 4 H, SCH_2). IR: 1635, 1620 (ν(CO)); 945 (ν(TcO)).

Scheme I





I

Results

The amide thiols were readily synthesized from the corresponding neutral diamines and thiol methyl esters. The thiol functionalities were protected as benzoyl esters to prevent the oxidation of the ligands and for convenience in isolation and characterization. They are insoluble in water, but readily soluble in hot ethanol (see Scheme I).

The reduction of pertechnetate in basic ethanol solution by sodium dithionite in the presence of an excess of the benzoyl esters gave good yields of the oxotechnetate(5+) anions VI–IX. They were isolated as their tetraphenyl arsonium salts and fully characterized. The complexes are air-stable, yellow or gold crystalline solids that are readily soluble in polar nonaqueous solvents. The infrared spectra show the characteristic absorption due to the TcO stretch in the range 940–960 cm^{-1}. The anion $TcO(ema)^-$ can be isolated with a variety of bulky cations. The FDMS of $[n\text{-}Bu_4N][TcO(ema)]$ is shown in Figure 1. The compounds are diamagnetic and show NMR spectra that are consistent with their formulations.

Discussion

The amide thiol ligands were chosen to span the basal positions of an expected square-pyramidal structure (see Figure 1). This was deemed necessary to increase the kinetic stability of the low-spin d^2 TcO core and to maximize in vivo stability. The chelate, or modifications of the basic backbone, should allow facile substitution of noncoordinating functional groups which would direct the radionuclide in vivo and make possible the study of structure–activity relationships.

The conditions of the synthesis of this series of chelates is dictated by kinetic rather than equilibrium control. It was necessary to evaluate the optimum chelate ring sizes in order to maximize the yield prior to engaging in the functionalization of the ligand backbone. Complex VI, which contains three five-membered rings, was repeatedly obtained in quantitative yields. The chelate with three six-membered rings was not obtained by the reduction of pertechnetate in the presence of *N,N'*-propylenebis(benzoyl-3-mercaptopropionamide). The result was formation of $TcO_2 \cdot xH_2O$. Unlike VI, the chelates VII and VIII could not be obtained without some $TcO_2 \cdot xH_2O$ production. This suggests, in the absence of thermodynamic stability data, that the configuration with three five-membered rings is the most favored. Chelate IX was never obtained in yields greater than 74%, which we attribute to steric constraints of the *o*-phenylene backbone.

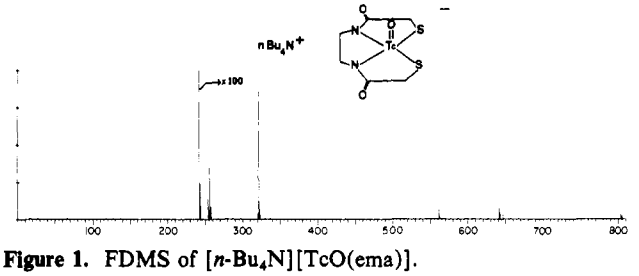


Figure 1. FDMS of $[n\text{-}Bu_4N][TcO(ema)]$.

Table II. Assignment of FDMS of $[n\text{-}Bu_4N][TcO(ema)]$

m/e	assignt[a]	m/e	assignt[a]
242	C^+	641	$H_3A_2^+$
321	H_2A^+	803	C_2A^+
561	$CA^+ = M^+$		

[a] $C^+ = [n\text{-}Bu_4N]^+$, $A^- = [TcO(ema)]^-$.

The basic reaction medium serves both to remove the benzoyl blocking group and to maximize the reaction yield by dithionite reduction. In previous studies,[11] sodium dithionite in basic solution was the optimum reductant for the formation of $[TcO(SCH_2CH_2S)_2]^-$ from pertechnetate, and this has proven true in the present study also. (Other agents tested were sodium bisulfite, sodium hypophosphite, formamidinesulfinic acid, and 1,4-dimercapto-2,3-butanediol.)

A preparation of VI using a 100-fold excess of I with no reductant gave a yield of 80%. This is consistent with previous observations[5] that the reduction can take place with use of excess dithiol with no added reducing agent.

The synthesis of VI can be accomplished in 97% yield with use of stannous chloride dihydrate in basic solution. Stannous ion is the most common reducing agent in commercially available technetium radiopharmaceutical kits;[3] however, many anomalies have been reported[16] in the images obtained with preparations involving this reductant. All attempts to synthesize VI at physiological pH (7.4) resulted in formation of $TcO_2 \cdot xH_2O$.

We have previously shown[14] that field desorption mass spectrometry (FDMS) can be used to characterize Werner-type coordination compounds that are involatile salts. The mass spectra are simple and readily interpretable. The FDMS of the tetra-*n*-butylammonium salt of VI is presented in Figure 1, and the assignments are given in Table II. The observations of cluster formation and cationization by cation attachment are consistent with those found in our previous work and serve to characterize the anion. This technique is not restricted to coordination compounds of technetium and should prove generally applicable to a wide range of coordination complexes whose mass spectra are unobtainable by conventional electron impact (EI) mass spectrometry.

There is a close similarity between these $TcON_2S_2$ complexes and the $TcOS_4$ complexes that have been previously reported.[4,5,7-9] The new complexes are five-coordinate and do not undergo substitution reactions with other thiol ligands such as ethanedithiol. None of the complexes are readily oxidized or reduced electrochemically or chemically. There is a slight variation in the TcO stretching frequencies, but they are in the same region (900–1000 cm^{-1}) as those previously found for the oxobis(dithiolato) chelates. This suggests that the new imido–thiolato chelates are electronically similar to the oxobis(dithiolato) complexes. This is further substantiated by comparing the optical spectra of these two series of five-coordinate low-spin d^2 oxotechnetium complexes (b_2^2-$^1A_1$ ground state for idealized C_{4v} symmetry).

The significant feature of VI is that it undergoes rapid renal excretion. Details of the animal distribution studies on this series of complexes will be reported elsewhere.

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spectra. We would also like to express our gratitude to Steven Carr and Dr. Catherine Costello for their aid in obtaining the mass spectra. Financial support from the Natural Sciences and Engineering Research Council of Canada (C.O.) and New England Nuclear (M.S.) is gratefully acknowledged.

Registry No. I, 75948-92-4; II, 75948-93-5; III, 75948-94-6; IV, 75948-95-7; V, 75948-96-8; VI (Ph_4As salt), 75949-45-0; VI (*n*-Bu_4N salt), 75949-46-1; VII (Ph_4As salt), 75949-48-3; VIII (Ph_4As salt), 75951-54-5; IX (Ph_4As salt), 75949-50-7; *N,N'*-ethylenebis(3-mercaptopropionamide), 818-41-7; *N,N'*-propylenebis(2-mercaptoacetamide), 75948-97-9; *N,N'*-propylenebis(3-mercaptopropionamide), 75948-98-0; *N,N'*-*o*-phenylenebis(2-chloroacetamide), 2810-42-6; *o*-phenylenediamine, 95-54-5; benzoyl chloride, 98-88-4; chloroacetyl chloride, 79-04-9; thiobenzoic acid, 98-91-9; NH_4TcO_4, 13598-66-8; *N,N'*-ethylenebis(2-mercaptoacetamide), 692-93-3.

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The Platinum Phthalimide Blues: Synthesis and Physical Characterization. Hush Model Interpretation of Optical Spectra

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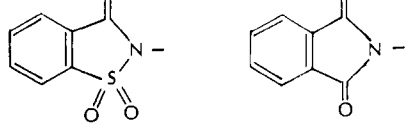
A new class of mixed-valent platinum blue compounds, prepared by using *cis*-dichlorodiammineplatinum(II) (*cis*-DDP) and potassium phthalimide, are characterized by UV-visible spectral measurements, Ce(IV) oxidative titrations, and other techniques. The formation of insoluble polymeric blue species is favored at higher temperatures and concentrations. By varying the mole ratio of starting materials, it is possible to obtain blue precipitates with different average platinum oxidation states. Semiquantitative calculations for the mixed-valence absorption profiles using Hush's formulas for class II weakly interacting MV systems indicate that this model fails to predict the half-bandwidth and the temperature dependence of at least the three platinum blues we have examined, i.e., platinum phthalimide blue, platinum α-pyridone blue, and Platinblau. All these blues with strongly interacting Pt-Pt centers are best described as class II-class III borderline or as delocalized class III mixed-valent compounds according to Robin and Day's classification.

Interest in blue platinum compounds started in 1908 when Hofmann and Bugge reported that "Platinblau" was formed in a reaction between dichlorobis(acetonitrile)platinum(II) and silver salts.[2] The compound was formulated as a monomeric platinum(II) complex, $[(CH_3CONH_2)_2Pt]\cdot H_2O$, and it was reexamined and proposed by Gillard and Wilkinson in 1964 to be polymeric with bridging amidate linkages.[3] In 1968, Brown et al. prepared a blue material by reacting trimethylacetamide with $[(CH_3CN)_2PtCl_2]$.[4,5] The blue material was formulated as the monomeric platinum(IV) complex, $[(t\text{-}C_4H_9CONH)_2PtCl_2]$. The "Platinblau" was also studied by Brown et al., and an analogous formula $[(CH_3CONH)_2Pt(OH)_2]$ was given. Since then, more blue platinum compounds have been synthesized and among them are the platinum pyrimidine blues[6] which show a high index of antitumor activity with a lower associated nephrotoxicity than *cis*-dichlorodiammineplatinum(II) or *cis*-DDP. The platinum pyrimidine blues have been obtained by incubation of various pyrimidines with the hydrolysis product of *cis*-DDP, and they were found to be polymeric and paramagnetic.[7,8] Like other blues, the platinum pyrimidine blues were isolated as amorphous solids and detailed structural information of platinum blues remained elusive until single crystals of *cis*-diammineplatinum α-pyridone blue or PPB were prepared.[9] Extensive studies on PPB were performed to determine the solid-state structure,[10] magnetic properties,[10] X-ray photoelectron spectroscopic properties,[11] and chemical and spectroscopic properties in aqueous solution.[12] All of these studies suggest that at least three properties are shared by most platinum blues in solution and in the solid state: mixed valency, oligomerization, and multidentate ligand bridging (e.g., amidate bridging). The blue color may arise from a mixed-valence or intervalence electronic transition, but no detailed absorption studies have been reported.

In order to make a comparative study about new platinum blues and to understand the origin of the blue color, we have carried out the reactions of *cis*-DDP with saccharate (I) and phthalimide (II). Both ligands are capable of amidate



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bridging with similar structures. Reactions with *cis*-DDP and saccharate did not give a blue solution nor a blue precipitate. However, the colorless product isolated seems to be an interesting 5-coordinated square-pyramidal platinum species which we will report on later.[13] On the other hand, reactions with *cis*-DDP with the use of phthalimide yielded very intense blue solutions, and blue precipitates were isolated. This paper

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