mL of Et_2O over a period of 3 h. To the residue, after stripping of the solvents, was added 150 mL of CH_2Cl_2. This mixture was extracted with H_2O to remove the salts, and then the solvents were removed again by rotary evaporation. Addition of 100 mL of EtOH to the resulting oil, stirring, and cooling furnished 14.6 g (43% yield) of colorless crystals, mp 159–161 °C. Anal. Calcd for $C_{21}H_{30}P_2S$: C, 67.00; H, 8.03; P, 16.45. Found: C, 67.41; H, 8.13; P, 16.70. Proton NMR: δ(Ph) 7.2–8.2 (m); $\delta(CH_2)$ 2.55 (dd, $^2J_{P(S)CH}$ = 12.5 Hz, $^2J_{PCH}$ = 2 Hz); $\delta(CH_3)$ 1.04 (d, $^3J_{PCCH}$ = 11.0 Hz).

$(C_6H_5)_2PCH_2P(t\text{-}C_4H_9)_2$. Reduction of $Ph_2P(S)CH_2P(t\text{-}Bu)_2$ (3.2 g, 8.5 mmol) with excess Si_2Cl_6 (4.5 g) in 20 mL of refluxing C_6H_6 for 5 h produced, after slow hydrolysis at 0 °C with 27 mL of 30% aqueous NaOH and subsequent washing of the benzene layer and removal of the solvents, a colorless oily product in 75% yield. Proton NMR: δ(Ph) 7.0–7.6 (m); $\delta(CH_2)$ 1.99 (d, $^2J_{P(t\text{-}Bu_2)CH}$ = 2.0 Hz); $\delta(CH_3)$ 1.02 (d, $^3J_{PCCH}$ = 11.0 Hz).

$(C_6H_5)_2P(S)CH_2P(S)(t\text{-}C_4H_9)_2$. Addition of elemental S_8 (0.086 g) to 1.0 g of $Ph_2P(S)CH_2P(t\text{-}Bu)_2$ in 30 mL of refluxing benzene for 4 h produced the disulfide product, which was obtained as colorless crystals (mp 162–164 °C) in 62% yield after removal of the solvent, addition of 25 ml of EtOH, and cooling. Anal. Calcd for $C_{21}H_{30}P_2S_2$: C, 61.74; H, 7.40; P, 15.16. Found: C, 61.48; H, 7.55; P, 15.40. Proton NMR: δ(Ph) 7.2–8.3 (m); $\delta(CH_2)$ 3.22 (dd, $^2J_{Ph_2P(S)CH}$ = 15.2 Hz, $^2J_{t\text{-}Bu_2P(S)CH}$ = 9.8 Hz); $\delta(CH_3)$ 1.32 (d, $^3J_{P(S)CCH}$ = 14.5 Hz).

$[(C_6H_5)_2P(S)CH_2P(t\text{-}C_4H_9)_2CH_3]Br$. Quaternization of $Ph_2P(S)CH_2P(t\text{-}Bu)_2$ (1.0 g) was carried out with 5 mL of MeBr in 50 mL of C_6H_6 in a pressure bottle at room temperature for 12 h. The white precipitate (73% yield) was removed by filtration and washed with pentane. The salt (mp 230–231 °C) retains benzene of recrystallization quite tenaciously. Drying at refluxing toluene temperature for 24 h at 10^{-3} mmHg produced the solvent-free compound. Anal. Calcd for $C_{22}H_{33}P_2S$: C, 56.05; H, 7.06; P, 13.14; Br, 16.95. Found: C, 55.96; H, 7.14; P, 13.09; Br, 16.74. Proton NMR: δ(Ph) 7.2–7.6, 8.1–8.6 (m); $\delta(CH_2)$ 3.94 (t, $^2J_{P(S)CH} \approx {}^2J_{P(+)CH}$ = 12.5 Hz); δ(P–CH_3) 2.18 (d, $^2J_{PCH}$ = 11.5 Hz); δ(C–CH_3) 1.44 (d, $^3J_{PCCH}$ = 16 Hz).

$[(C_6H_5)_2PCH_2P(t\text{-}C_4H_9)_2]Cr(CO)_4$. Direct reaction of the ligand (5.0 g, 14.5 mmol) with 3.5 g (16.0 mmol) of $Cr(CO)_6$ in 30 mL of diethylene glycol dimethyl ether (diglyme) under N_2 at a temperature of 110–125 °C proceeded until CO evolution ceased. Cooling to room temperature, addition of several milliliters of hexane, and further cooling at −10 °C overnight produced yellow crystals which were collected by filtration and washed with EtOH. Excess $Cr(CO)_6$ was removed by sublimation. The product (dec pt 175 °C) was produced in 76% yield. Anal. Calcd for $C_{25}H_{30}CrO_4P_2$: C, 59.06; H, 5.95; P, 12.18. Found: C, 58.86; H, 6.04; P, 12.17. Proton NMR: δ(Ph) 7.2–7.8 (m); $\delta(CH_2)$ 3.61 (dd, $^2J_{Ph_2PCH}$ = 9.6 Hz, $^2J_{t\text{-}Bu_2PCH}$ = 7.6 Hz); $\delta(CH_3)$ 1.27 (d, $^3J_{PCCH}$ = 13.3 Hz).

$[(C_6H_5)_2PCH_2P(t\text{-}C_4H_9)_2]Mo(CO)_4$, a yellow crystalline compound (dec pt 165 °C), was prepared in an analogous fashion at a temperature of 75–95 °C in 85% yield. Anal. Calcd for $C_{25}H_{30}MoO_4P_2$: C, 54.36; H, 5.47; P, 11.21. Found: C, 54.48; H, 5.55; P, 11.10. Proton NMR: δ(Ph) 7.2–7.8 (m); $\delta(CH_2)$ 3.66 (dd, $^2J_{Ph_2PCH}$ = 9.6 Hz, $^2J_{t\text{-}Bu_2PCH}$ = 7.1 Hz); $\delta(CH_3)$ 1.23 (d, $^3J_{PCCH}$ = 13.5 Hz).

$[(C_6H_5)_2PCH_2P(t\text{-}C_4H_9)_2]W(CO)_4$, a yellow compound (dec pt 170 °C), was prepared in the same manner at a temperature of 100–120 °C in 71% yield. Anal. Calcd for $C_{25}H_{30}O_4P_2W$: C, 46.90; H, 4.72; P, 9.67. Found: C, 46.97; H, 4.75; P, 9.48. Proton NMR: δ(Ph) 7.2–7.9 (m); $\delta(CH_2)$ 3.74 (dd, $^2J_{Ph_2PCH}$ = 9.0 Hz, $^2J_{t\text{-}Bu_2PCH}$ = 7.0 Hz); $\delta(CH_3)$ 1.21 (d, $^3J_{PCCH}$ = 14 Hz).

$[(C_6H_5)_2P(S)CH_2P(t\text{-}C_4H_9)_2]Cr(CO)_4$. The compound was prepared by the reaction of $Ph_2P(S)CH_2P(t\text{-}Bu)_2$ (0.50 g, 1.3 mmol) and 0.32 g (1.4 mmol) of $Cr(CO)_6$ in 10 mL of diglyme and 4 mL of methylcyclohexane at 100 °C for several hours. Addition of 3 mL of hexane and cooling at −10 °C for 24 h produced crystals, which were dissolved in 25 mL of CH_2Cl_2 eluted through a short neutral alumina column. After concentration of the solution, addition of hexane produced yellow crystals (dec pt 120 °C) in 51% yield. Anal. Calcd for $C_{25}H_{30}CrO_4P_2S$: C, 55.55; H, 5.59; P, 11.46. Found: C, 55.49; H, 5.59; P, 11.27. Proton NMR: δ(Ph) 7.1–8.0 (m); $\delta(CH_2)$ 2.85 (dd, $^2J_{P(S)CH}$ = 10.4 Hz, $^2J_{PCH}$ = 6 Hz); $\delta(CH_3)$ 1.34 (d, $^3J_{PCCH}$ = 13.0 Hz).

$[(C_6H_5)_2P(S)CH_2P(t\text{-}C_4H_9)_2]Mo(CO)_4$, a yellow solid (dec pt 125 °C), was prepared in 60% yield in a similar fashion. Anal. Calcd for $C_{25}H_{30}MoO_4P_2S$: C, 51.38; H, 5.17; P, 10.60. Found: C, 51.45; H, 5.15; P, 10.81. Proton NMR: δ(Ph) 7.2–8.0 (m); $\delta(CH_2)$ 2.81 (dd, $^2J_{P(S)CH}$ = 10.5 Hz, $^2J_{PCH}$ = 5.8 Hz); $\delta(CH_3)$ 1.32 (d, $^3J_{PCCH}$ = 13.0 Hz).

$[(C_6H_5)_2P(S)CH_2P(t\text{-}C_4H_9)_2]W(CO)_4$, a yellow crystalline substance (dec pt 145 °C), was prepared analogously in 83% yield. Anal. Calcd for $C_{25}H_{30}O_4P_2SW$: C, 44.66; H, 4.50; P, 9.20. Found: C, 44.63; H, 4.42; P, 9.11. Proton NMR: δ(Ph) 7.3–7.9 (m); $\delta(CH_2)$ 2.87 (dd, $^2J_{P(S)CH}$ = 10.3 Hz, $^2J_{PCH}$ = 6.4 Hz); $\delta(CH_3)$ 1.34 (d, $^3J_{PCCH}$ = 13.3 Hz).

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Registry No. $Ph_2PCH_2PMe_2$, 62263-64-3; $Ph_2PCH_2P(i\text{-}Pr)_2$, 62263-67-6; $Ph_2PCH_2P(t\text{-}Bu)_2$, 74512-04-2; $Ph_2P(S)CH_2PMe_2$, 23176-51-4; $Ph_2P(S)CH_2P(i\text{-}Pr)_2$, 54006-31-4; $Ph_2P(S)CH_2P(s\text{-}Bu)_2$ (isomer A), 74512-05-3; $Ph_2P(S)CH_2P(s\text{-}Bu)_2$ (isomer B), 74559-78-7; $Ph_2P(S)CH_2P(s\text{-}Bu)_2$ (isomer C), 74559-79-8; $Ph_2P(S)CH_2P(t\text{-}Bu)_2$, 74512-06-4; $Ph_2P(S)CH_2P(S)Me_2$, 38055-42-4; $Ph_2P(S)CH_2P(S)(i\text{-}Pr)_2$, 62264-49-7; $Ph_2P(S)CH_2P(S)(t\text{-}Bu)_2$, 74512-07-5; $[Ph_2P(S)CH_2PMe_3]Br$, 62264-42-0; $[Ph_2P(S)CH_2P(i\text{-}Pr)_2Me]Br$, 62264-43-1; $[Ph_2P(S)CH_2P(t\text{-}Bu)_2Me]Br$, 74512-08-6; $[Ph_2PCH_2PMe_2]Cr(CO)_4$, 62264-03-3; $[Ph_2PCH_2P(i\text{-}Pr)_2]Cr(CO)_4$, 62264-12-4; $[Ph_2PCH_2P(t\text{-}Bu)_2]Cr(CO)_4$, 74525-14-7; $[Ph_2PCH_2PMe_2]Mo(CO)_4$, 62264-04-4; $[Ph_2PCH_2P(i\text{-}Pr)_2]Mo(CO)_4$, 62264-13-5; $[Ph_2PCH_2P(t\text{-}Bu)_2]Mo(CO)_4$, 74525-15-8; $[Ph_2PCH_2PMe_2]W(CO)_4$, 62264-05-5; $[Ph_2PCH_2P(i\text{-}Pr)_2]W(CO)_4$, 62264-14-6; $[Ph_2PCH_2P(t\text{-}Bu)_2]W(CO)_4$, 74525-16-9; $[Ph_2P(S)CH_2PMe_2]Cr(CO)_4$, 62264-20-4; $[Ph_2P(S)CH_2P(i\text{-}Pr)_2]Cr(CO)_4$, 62264-23-7; $[Ph_2P(S)CH_2P(t\text{-}Bu)_2]Cr(CO)_4$, 74525-17-0; $[Ph_2P(S)CH_2PMe_2]Mo(CO)_4$, 62264-19-1; $[Ph_2P(S)CH_2P(i\text{-}Pr)_2]Mo(CO)_4$, 62264-22-6; $[Ph_2P(S)CH_2P(t\text{-}Bu)_2]Mo(CO)_4$, 74525-18-1; $[Ph_2P(S)CH_2PMe_2]W(CO)_4$, 62264-18-0; $[Ph_2P(S)CH_2P(i\text{-}Pr)_2]W(CO)_4$, 62264-21-5; $[Ph_2P(S)CH_2P(t\text{-}Bu)_2]W(CO)_4$, 74525-19-2; $(C_6H_5)_2P(S)CH_2Li$, 52101-86-7; $t\text{-}Bu_2PCl$, 13716-10-4; $Cr(CO)_6$, 13007-92-6; $Mo(CO)_6$, 13939-06-5; $W(CO)_6$, 14040-11-0; S_8, 10544-50-0; MeBr, 74-83-9.

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Gold(III) Oxidation of Disulfides in Aqueous Solution

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Although the use of gold-based drugs, chrysotherapy, has been an important form of treatment for rheumatoid arthritis for over half a century, our knowledge of the reactions of gold(I) and gold(III) with biologically important ligands and compounds is very limited. The current state of the art has been recently reviewed, and gold–sulfur interactions are found to be a major factor in gold biochemistry.[1] Gold is administered as thiolates such as gold(I) thioglucose and gold sodium thiomalate, because gold(III) complexes are too toxic for medicinal use.[2,3] The oxidation of thiols to disulfides[2] and methionine to methionine *S*-oxide[4,5] are cited as sources of

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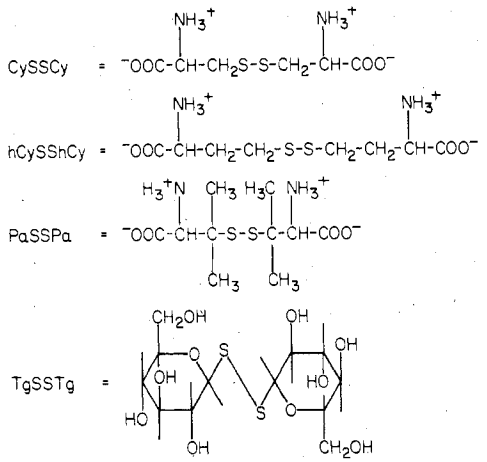
gold(III) toxicity. $AuBr_4^-$ and $AuCl_4^-$ are more potent enzyme inhibitors than the gold(I) drugs.[1] Recently Brown et al.[6] reported the oxidation of gold(I) and colloidal gold in the presence of O_2 and penicillamine and suggested that redox reactions may be important in therapeutic processes.

The redox chemistry of organic sulfur compounds is very complex, ranging from the sulfhydryl (−2 oxidation state) through the disufide (−1), sulfenic acid (+2), and various mixed disulfide oxides (e.g., RSO_2SOR) to the sulfonic acid (+4) which is the highest oxidation state that can be obtained without C–S bond cleavage. Savige and McLaren[8] have documented three pathways for the oxidation of organic disulfides: path A involves sequential oxidation of the intact disulfide to RSO_2SO_2R which is oxidatively cleaved to the sulfonic acid RSO_3H; path B involves immediate S–S bond scission to form the sulfenic acid which is further oxidized; path C entails C–S bond scission to form the alcohol ROH and RSSOH which is further oxidized to $RSSO_3H$. Paths B and C are favored in aqueous systems as employed in this study.[8]

In the course of preparing (L-cysteinato)gold(I) by the reduction of $KAuBr_4$ with L-cysteine[7] it was observed that the oxidation product, cystine, was itself capable of reducing gold(III) to metallic gold. Two aspects of this reaction, the greater reducing ability toward gold(III) of the oxidized ligand, cystine, compared to the reduced form, cysteine, and the implications of this reaction as a mechanism for the toxicity of gold(III), warranted detailed investigation. We report here the first examples of the oxidation of disulfides by gold(III) in aqueous media.

The structures of the disulfides employed are



Experimental Section[9]

From Aldrich Chemical Co. were purchased D-penicillamine disulfide, cystine, and cysteic acid monohydrate. From Sigma Chemical Co. were purchased homocystine, sodium thioglucose, cysteic acid, and homocysteic acid. $KAuBr_4 \cdot 2H_2O$ was synthesized by the method of Block.[10]

The ^{13}C NMR spectra were obtained on a Varian CFT-20 spectrometer at natural abundance in D_2O solutions which provided the lock signal. ^1H NMR spectra were obtained on a Varian T-60 spectrometer. D_2O, sometimes containing phosphate buffer, was degassed before the solutions were prepared. Dioxane and 3-(trimethylsilyl)propionic-*2,2,3,3-d*$_4$ acid, sodium salt, TSP, were employed as internal standards. ^{13}C chemical shifts are reported relative to dioxane and ^1H shifts relative to TSP. Infrared spectra were measured on a Beckman IR-12 spectrometer as Nujol and hexachlorobutadiene mulls. Gold analyses were performed on a Perkin-Elmer 360 atomic absorption spectrometer using serial dilutions of a commercial standard. CHN analyses were performed by Mr. Frank Laib of the University of Wisconsin—Milwaukee Chemistry Department staff.

Table I. ^{13}C NMR Chemical Shifts (ppm)[a]

	pH	C_1	C_2	C_3	C_4	C_5	C_6
(hCy)SS-(hCy)	≤1	104.62	−14.96	−37.36	−33.99		
(hCy)-SO_3H	≤1	104.09	−14.70	−41.34	−19.77		
PaSSPa	7.4	104.86	−4.60	−16.37	−39.80	−43.79	
$PaSO_3H$	7.4	102.62	−8.65	−9.38	−44.80	−48.01	
TgSH	7.4	17.32	10.44	13.28	3.86	11.84	5.21
TgSSTg	7.4	22.68	4.57	13.57	2.58	10.34	5.73

[a] COOH is carbon 1 in hCySH and PaSH derivatives; the methyl groups of PaSSPa and $PaSO_3H$ are listed as C_4 and C_5; the standard numbering system is employed for 1-β-D-thioglucose. All values are relative to dioxane δ(CH_2) 0.00 and are reproducible to ±0.20 ppm.

CySSCy Oxidation. $KAuBr_4$ (0.3333 g, 0.60 mmol) was added to a solution of cystine (0.0432 g, 0.18 mmol) in distilled H_2O (5 mL) and concentrated HBr (15 drops) with stirring. The reaction mixture was decolorized, and gold had deposited within 15 min. After standing for 48 h, the solution was filtered, and the gold on the frit was dissolved in aqua regia and quantitated by atomic absorption spectroscopy (0.52 mmol, 87%). The filtrate was concentrated in vacuo, and 10 volumes of absolute EtOH were added to precipitate a fine white powder, which contained K^+ and Br^- ions and had no infrared spectrum in the region 650–2000 cm^{-1}. The filtrate was again concentrated in vacuo, and 10 volumes of Et_2O were added to precipitate a white powder which an IR spectrum identical with that of cysteic acid hydrobromide (prepared from cysteic acid and HBr) and analyzed as $C_3H_8BrNO_5S$. A second reaction of $KAuBr_4$ (1.06 mmol) and cystine (0.300 mmol) in 1:1 D_2O/H_2O was used to obtain a ^{13}C NMR spectrum after filtration to remove the gold. The observed shifts δ(COO^-) 102.59, δ(CN) −16.76, and δ(CS) −17.52 were identical with those for an authentic sample, and only one set of peaks was observed with authentic cysteic acid as internal standard.

(hCy)SS(hCy) Oxidation. A solution of $KAuBr_4 \cdot 2H_2O$ (0.5514 g, 0.931 mmol) in a minimum volume of H_2O was added to *dl*-homocystine (0.0750 g, 0.279 mmol) in 5 mL of distilled H_2O and 1.0 mL of concentrated HBr. The solution was substantially decolorized within 10 min, and metallic gold began to deposit. After 12 h, the metallic gold (0.925 mmol, 99.4%) was filtered off, and the filtrate was evaporated to dryness in vacuo. The resulting solid (95% yield on the basis of KBr + $(hCy)SO_3H$) was extracted with EtOH which was evaporated to dryness and reextracted. The EtOH insoluble material was KBr. The final EtOH solution was treated with anhydrous Et_2O to yield homocysteic acid, identified by elemental analysis and its ^{13}C NMR and infrared spectra.

PaSSPa Oxidation. The reaction was carried out as above using $KAuBr_4 \cdot 2H_2O$ (0.987 g, 1.67 mmol) and penicillamine disulfide (0.149 g, 0.503 mmol) in 7.0 mL of D_2O. After several hours, an orange precipitate but no gold had deposited. Overnight the precipitate was replaced by a deposit of metallic gold (0.503 mmol, 100%). The gold was recovered and quantitated as $HAuCl_4$ by AAS. KBr and a white solid (mp 225–240 °C, 47% yield being analyzed as $(PASO_3H)_4 \cdot KBr \cdot 2H_2O$) were isolated after repeated recrystallizations as in the homocysteine reaction. A strong IR band at 1190 cm^{-1} confirmed the presence of the sulfonic acid group. The protons released were titrated with standardized NaOH by using bromocresol purple (pK_a = 6.3) as the indicator and unoxidized PaSSPa as a blank. The ^{13}C NMR spectrum of the product showed a single set of peaks: ^{13}C NMR (COOH) δ 102.62; (CN) δ −8.65; (CS) δ −9.38; (CH_3) δ −44.80, −48.01. Anal. Calcd for $4C_5H_{10}NO_5S \cdot KBr \cdot H_2O$: C, 25.45; N, 5.94; H, 5.09; K, 4.14. Found: C, 24.95; N, 5.82; H, 4.95; K, 4.24.

Partial Oxidation of PaSSPa. ^1H NMR spectra were recorded on reaction mixtures containing penicillamine disulfide (0.20 M) in D_2O and $KAuBr_4$ (1.0, 2.0, and 3.33 Au/SS mole ratios) immediately

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(9) Abbreviations: PaSSPa, CySSCy, (hCy)SS(hCy), and TgSSTg for the disulfides of penicillamine, cysteine, homocysteine, and 1-β-D-thioglucose, respectively. The reduced form and sulfonic acid derivatives are PaSH, $PaSO_3H$, etc.
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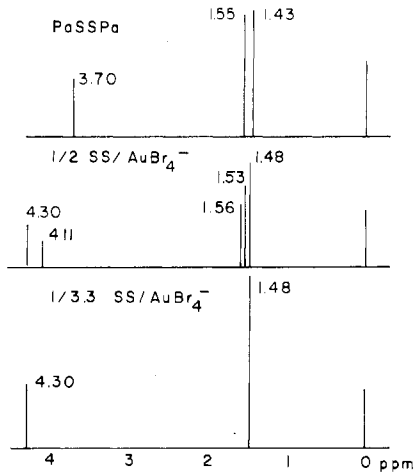

Figure 1. ^1H NMR spectra of PaSSPa and the oxidation products of $KAuBr_4$ and PaSSPa (2.0 and 3.33 mole ratios) at pH 7.4 in D_2O with TSP as an internal standard.

upon mixing and at 10 min, 30 min, and 18 h after mixing, with TSP as the internal standard. An orange precipitate formed in the 1.0 Au/SS system and was filtered off before spectra were recorded but did not form in the other systems.

TgSSTg. Samples were prepared in situ by adding a stoichiometric amount of $KI \cdot I_2$ solution to a D_2O solution of sodium thioglucose. ^{13}C NMR data revealed that complete oxidation had occurred, yielding a single product with six resonances (Table I).

TgSSTg Oxidation. TgSSTg (0.315 mmol) prepared from NaSTg (0.137 g, 0.629 mmol) was treated with $KAuBr_4 \cdot 2H_2O$ (0.581 g, 1.05 mmol). After 2 h, accumulation of the ^{13}C spectrum was begun. The spectrum consisted of 12 peaks corresponding to the published values for glucose.[11] Metallic gold (86%, 0.903 mmol) was recovered and quantitated. By fractional crystallization of the reaction mixture, a white solid, K_2SO_4, was recovered and identified by $BaSO_4$ precipitation and its IR spectrum.

Results

When a 3.33 mole ratio of $KAuBr_4$ was allowed to react with the disulfides of cysteine, homocysteine, or penicillamine in aqueous solution, metallic gold was rapidly deposited and the corresponding sulfonic acid derivative was formed (eq 1).

$$3RSSR + 10KAuBr_4 + 18H_2O \rightarrow 6RSO_3^- + 10Au^0 + 40Br^- + 10K^+ + 36H^+ \quad (1)$$

$$R = Cy, hCy, Pa$$

For cysteic and homocysteic acids the ^{13}C and ^1H NMR and infrared spectra were identical with those of authentic samples. The spectra of the penicillamine derivative showed the characteristic infrared absorption at 1160–90 cm^{-1} for a sulfonic acid derivative,[12] and the ^{13}C and ^1H chemical shifts are consistent with formation of the sulfonic acid derivative. The elemental analysis, however, indicated the consistent isolation of a KBr-containing hydrate, approximating the composition $4RSO_3H \cdot KBr \cdot 2H_2O$ in 47% yield. The low recovery is due to the repeated recrystallizations necessary to remove KBr. The CHN analysis given is the average of four individual analyses of two batches of product. Recrystallization from aqueous hydrobromic acid did not alter the analysis. Titration of the protons released in the PaSSPa reaction produced a value of 12.6 H^+/PaSSPa, in close agreement with the expected stoichiometry of 12.

The simplicity of the ^1H NMR spectrum of D-penicillamine disulfide (δ(H) 3.67, $\delta(CH_3)$ 1.47, 1.57) and the rapidity with which spectra can be obtained prompted further study by this method to seek possible intermediates in the reaction (Figure 1). When the stoichiometric amount of gold was used (3.33 Au:SS), a new pair of signals (δ(H) 4.30, $\delta(CH_3)$ 1.48) in a 1:6 intensity ratio was observed immediately after the reagents were mixed and did not change on standing. These signals can be assigned to the sulfonic acid derivative. When a 2:1 Au:SS ratio was employed, the sulfonic acid and a new set of signals at δ(H) 4.06 and $\delta(CH_3)$ 1.57 and 1.52 were observed. Overlap with the δ 1.48 signal precluded integration of the high-field signals, but the intensities are consistent with a 1:3:3 ratio. These peaks are assigned to the sulfinic acid derivative of penicillamine. Upon standing, the sulfonic acid signals grew with the concomitant loss of the sulfinic acid resonances, probably due to autoxidation of the latter.

The observation of only the sulfonic and sulfinic acids rather than six signals expected for unsymmetrical oxidation products such as RSO_2SOR etc. indicates that the reaction proceeds via path B as defined by Savige and McLaren.[8] Path C can be unambiguously eliminated by failure to detect the alcohol derivatives, ROH, which would result from S–C bond scission.

When a 1:1 Au:SS ratio was employed, an orange precipitate formed, which, after being filtered out of solution rapidly, decomposed to elemental gold. However, the supernatant contained a new species with NMR signals at δ(H) 3.90 and δ(CH) 1.47, 1.55. Although the orange solid is reminiscent of the gold(III) penicillamine complex reported by Brown[6] and the positions of the shifts for the colorless soluble product are consistent with a sulfenic acid derivative, perhaps stabilized by coordination to gold(I), further research is necessary and is in progress to explain these interesting results.

1-β-D-Thioglucose disulfide was prepared in situ from sodium thioglucose and identified by its ^{13}C NMR spectrum (Table I). The spectrum of sodium thioglucose consists of only six signals, unlike glucose, because it exists only in the β isomer. Ring opening would proceed through the energetically unfavorable thioketal form and does not occur. The ^{13}C assignments follow straightforwardly from those of glucose, except that C_3 and C_5 assignments could be reversed. C_1 which is bound to both the sulfur and ring oxygen is furthest downfield but has shifted substantially from the position of the C_1 in α- and β-glucose (92.8 and 96.7 ppm). Upon oxidation to the disulfide, C_1 shifts downfield to 91.88 ppm as expected.

The reaction of $KAuBr_4$ with 1-β-D-thioglucose disulfide follows a different course than the cysteine derivatives (eq 2).

$$TgSSTg \xrightarrow[H_2O]{KAuBr_4} 2TgOH + 2SO_4^{2-} \quad (2)$$

The ^{13}C spectrum shows glucose as one product, and potassium sulfate can be isolated. Metallic gold is deposited quantitatively. Glucose is also formed by oxidation with Br_2 demonstrating that the gold does not alter the course of the reaction. A survey of Chemical Abstracts failed to produce evidence for formation of the sulfinic or sulfonic acid derivatives of thioglucose. While the possibility of homolytic bond scission as delineated by Savige and Maclaren[8] cannot be disproven at this time, we believe that the more probable course of reaction is formation of the sulfonic acid, which then undergoes hydrolysis by a nucleophilic attack at carbon 4 to release glucose and SO_3^{2-} which is consequently autoxidized to sulfate ion during the workup of the products.[13]

Discussion

The oxidation of cystine and other disulfides by gold(III) reported here demonstrates that they are in fact effective

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(13) Roy, A. B.; Trudinger, P. A., "The Biochemistry of Inorganic Compounds of Sulfur"; Cambridge University Press: Cambridge, 1970; p 17.

reducing agents capable of reducing up to 3.33 mol of gold(III) to the elemental state. This is in striking contrast to the previously reported reduction of gold(III) to gold(I) by 3 mol of cysteine.[7] The apparent thermodynamic discrepancy that cystine is a better reducing agent results from the ability of cysteine to stabilize the resulting gold(I) complex and remove it from solution. The oxidation of colloidal gold and $KAu(CN)_2$ to gold(III) by oxygen in the presence of penicillamine was recently demonstrated by Brown et al.[6] However, the reactions reported here are thermodynamically favorable and kinetically facile in the reverse direction. It is becoming clear that the redox reactions of gold compounds containing sulfur ligands comprise a rich chemistry and that careful monitoring of the oxidation states of sulfur as well as gold is necessary to define such systems.

Although the oxidation of disulfides by $KAuBr_4$ is not unexpected from a thermodynamic standpoint, given the strong oxidizing ability of gold(III) halides,[1,14] the possibility has surprisingly not been considered in the context of the biological chemistry of gold.[1] Ironically, purple deposits of colloidal gold on the skin, a keratinous tissue rich in disulfides, are quite common among gold chemists and probably result from the reaction described here. More significantly, this reaction may play an important role in the toxicity of gold(III) which precludes its use as in chrysotherapy.[2,3] The oxidation of protein disulfides by gold(III) will disrupt the secondary and tertiary structure of a protein, altering and probably preventing its normal biological function. In fact, a recent survey of enzyme inhibition by gold complexes show gold(III) to be a much more potent inhibitor than gold(I) at equimolar concentrations.[1] Oxidized glutathione, a hexapeptide containing a disulfide moiety and insulin, and a protein with three disulfides but no methionine or free sulfhydryl groups both rapidly reduce $AuCl_4^-$ and $AuBr_4^-$. The structural consequences of these reactions are being investigated and will be reported elsewhere.

Registry No. CySSCy, 56-89-3; (hCy)SS(hCy), 870-93-9; PaSSPa, 20902-45-8; TgSSTg, 54495-24-8; $KAuBr_4$, 14323-32-1; Au, 7440-57-5; $CySO_3H$·HBr, 74562-84-8; $(hCy)SO_3H$, 504-33-6; $PaSO_3H$, 23400-34-2; TgOH, 492-61-5; NaSTg, 10593-29-0; TgSH, 7534-35-2.

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Mobility of the μ_3:η^2-CO Ligand in $Cp_3Nb_3(CO)_7$

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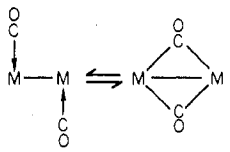
Migration of carbonyl ligands about the periphery of a metal cluster is a common phenomenon and one which may be relevant to the migration of chemisorbed CO to sites of active chain growth in certain heterogeneous Fischer–Tropsch reactions. To date, migration within molecules has been observed for carbonyls which are bound in terminal μ_2:η^1 or μ_3:η^1 modes,[1] and the low activation energies observed may be due to the compensatory nature of the physical mechanism: concerted processes (eq 1) maintain an invariant valence-electron count at each metal. Some of the more reactive sites on clean metal surfaces are the nonplanar irregularities termed



(1)

"steps" and "kinks".[2] Here, η^2 binding of CO (via both carbon and oxygen) to an angular array of metal atoms is likely; this represents a potential precursor state both to CO dissociation and to hydrogenation of the CO bond. Since the spectroscopic and structural tools available to the molecular chemist are more definitive of structure and dynamics than those currently employed by surface chemists,[2] compounds containing η^2 carbonyls are a potentially rich source of information concerning chemisorbed CO. Our earlier attempt[3] to observe migration of the μ_2:η^2-CO ligand in $Mn_2(CO)_5(Ph_2PCH_2PPh_2)_2$ yielded a lower limit (15.6 kcal/mol) on $\Delta G^{\ddagger}$ for such a process; this relatively high barrier to migration can be attributed to the 18 e → 16 e transformation associated with attaining the transition state. We report here the first observation of mobility of a six-electron-donor carbonyl ligand.

Experimental Section

All operations were carried out under a nitrogen atmosphere in solvents dried with NaK alloy. NMR spectra (^1H and ^{13}C) were recorded on Varian XL-100 (FT) and HR-220 spectrometers. Rate constants were determined by line-shape analysis using the program DNMR;[4] activation parameters were derived from a least-squares fit of the resulting rate constants.

$(C_5H_4R)Nb(CO)_4$ (R = H, Me). This procedure is a modification of an earlier report.[5] $NbCl_5$ (4 g, 0.015 mol) was dissolved in 30 mL of 1,2-dimethoxyethane (dme) and placed in the 400-mL glass liner of a high-pressure bomb. To this was added Na/K alloy (3.5 mL, 0.09 mol) and a stir bar. The liner was placed in the bomb, and the reaction was stirred under CO (100 atm, 1.2 mol) at 25 °C for 24 h. The resulting solution of $Nb(CO)_6^-$ [ν(CO) at 1853 cm^{-1}] was reacted *slowly* with a THF solution of $Hg(C_5H_4R)Cl$ (R = H, Me) (0.02 mol), made from the reaction of $HgCl_2$ (5.44 g, 0.02 mol) and $Na(C_5H_4R)$·dme (0.02 mol) in THF; this reaction was marked by gas evolution and precipitation of Hg. The reaction solution was filtered and the filtrate taken to dryness. The solid residues were placed in a sublimer. Red crystals of $(C_5H_4R)Nb(CO)_4$ sublimed at 65 °C (0.001 torr); yield 30% based on $NbCl_5$.

$(C_5H_4R)_3Nb_3(CO)_7$ (R = H, Me). $C_5H_5Nb(CO)_4$ (0.12 g, 0.4 mmol) was dissolved in 40 mL of hexane (saturated solution) and placed in a toroidal reactor.[6] The solution was photolyzed (550-W medium-pressure Hg lamp) for 20 min with a N_2 flow passing through the solution. After photolysis the solution was taken to dryness and the solid residue placed in a sublimer. Unreacted $(C_5H_5)Nb(CO)_4$ was sublimed away at room temperature (1 mm). $(C_5H_5)_3Nb_3(CO)_7$ was left unsublimed in 95% yield at 70% conversion. A similar procedure was employed for synthesis of $(C_5H_4Me)_3Nb_3(CO)_7$.

Results and Discussion

We have examined the photochemistry of $(C_5H_4R)Nb(CO)_4$ (R = H, CH_3) as an extension of our earlier work with $CpV(CO)_4$.[6] In hexane, irradiation of $CpNb(CO)_4$ yields $Cp_3Nb_3(CO)_7$, an asymmetric trimer whose structure (I) has been established independently by Herrmann, Ziegler, Weidenhammer, and Biersack;[7] the molecule contains no elements of symmetry. The ^1H NMR spectrum of $(C_5H_5)_3$-

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