Kinetics and mechanism of reduction of gold(III) complexes by dimethyl sulfide †

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The reactions between *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) and Me_2S have been studied by conventional and high-pressure stopped-flow spectrophotometry in acidic aqueous solution containing 10% (w/w) methanol. The overall stoichiometry $Au^{III}:Me_2S$ is 1:(1.0 ± 0.1) in agreement with the reaction: *trans*-$[Au(CN)_2X_2]^- + Me_2S + H_2O \longrightarrow [Au(CN)_2]^- + Me_2SO + 2H^+ + 2X^-$. Initial rapid substitution processes result in the formation of a pre-equilibrium between transient gold(III) complexes, which are reduced to $[Au(CN)_2]^-$ in a subsequent slower redox process. Complexes *trans*-$[Au(CN)_2X(Me_2S)]$ with an asymmetric electron distribution along the X–Au–S axis are reduced rapidly *via* an intermolecular process, in which Me_2S attacks a co-ordinated halide. The complex *trans*-$[Au(CN)_2(Me_2S)_2]^+$, on the other hand, undergoes slow reduction to gold(I) involving a water molecule. The rapid halide-mediated oxidation of thioethers implies that reduction of metal ions in biological systems by such moieties should be favoured in extracellular environments, where the chloride concentrations are high.

Reactions of soft nucleophiles with complexes of gold(III) often result in reduction to gold(I).[1] Redox can either take place as a direct two-electron transfer without observable intermediates,[2,3] or may involve rapid and/or consecutive substitutions followed by reductive elimination through attack on the complex by the reductant.[3–15] In some cases, the overall process can be described as a rapid formation of a transient pre-equilibrium between various mixed-ligand complexes of gold(III) followed by slower reduction of these complexes to gold(I).[11–15] Relations between the structure, stability and reactivity of complexes that undergo parallel substitution and reductive elimination through attack by a particular nucleophile have been evaluated.[15] Although both types of reaction involve an interaction between the nucleophile and the metal complex, the transition states are expected to be different.

Previous studies of mechanistic differences between the substitution and reductive-elimination reactions have focused on the metal complexes *trans*-$[Au(NH_3)_2X_2]^+$ and *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) and their reactions with thiocyanate.[14,15] In these systems the pre-equilibrium can be observed prior to reduction and the observed rate constants for the reduction can be resolved into individual ones for reduction of each of the gold(III) complexes present in the pre-equilibrium mixture. Reduction is fast for complexes having an asymmetric electron distribution along the axis X–Au–SCN, for instance *trans*-$[Au(CN)_2Cl(SCN)]^-$, reflecting a large difference in ground-state *trans* influence between the ligands X^- and SCN^-.[15] Solvational changes due to charge formation or neutralisation in the activation process influence both the sign and values of $\Delta S^\ddagger$ and $\Delta V^\ddagger$ and an analysis of the activation parameters indicates a more tightly bound transition state for the substitutions than for the reductive eliminations.[15] With thiocyanate as a nucleophile, electron transfer is suggested to occur mainly *via* an interaction between co-ordinated and attacking thiocyanate, whereas electron transfer mediated by co-ordinated halide seems to be of minor importance.[14,15]

Dimethyl sulfide can be used as a simple model for methionine, a plausible target for metal complexes *in vivo*. The large difference in chloride concentration between the intra- and extra-cellular environment makes the effect of the chloride concentration on the rate and mechanism of reactions between gold(III) complexes and sulfide moieties interesting. Reduction of $[AuCl_4]^-$ with dimethyl sulfide has been studied previously.[12] In the present investigation dimethyl sulfide has been used as the nucleophile in reactions with the dicyano complexes *trans*-$[Au(CN)_2X_2]^-$, X = Cl or Br, in order further to investigate the influence of charge and electronic properties of the reductant as well as the metal centre on the mechanism and reactivity. The nucleophilicity of dimethyl sulfide is lower than that of thiocyanate,[12,16] and the difference in ground-state *trans* influence between the halide and Me_2S is smaller than between the halide and SCN^-, favouring formation of complexes with an X–Au–S donor *trans* axis. That has enabled a direct determination of activation parameters for reduction of the metastable mixed-ligand complex *trans*-$[Au(CN)_2Br(Me_2S)]$. In addition, a slow water-assisted reduction of *trans*-$[Au(CN)_2(Me_2S)_2]^+$ has been studied.

Experimental

Chemicals and solutions

The salts $K[Au(CN)_2Cl_2]\cdot H_2O$ and $K[Au(CN)_2Br_2]\cdot 3H_2O$ were synthesized by oxidation of $K[Au(CN)_2]$ (Degussa) according to the literature.[17] Stock solutions of *ca.* 2 mmol dm^{-3} *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) were prepared by dissolving weighed amounts of the salts in an acidic aqueous ionic medium. The latter contained 10 mmol dm^{-3} perchloric acid and extra halide (10 mmol dm^{-3} NaCl or 1 mmol dm^{-3} NaBr, respectively) to suppress formation of aqua and hydroxo complexes. Stock solutions of dimethyl sulfide, $\leqslant 30$ mmol dm^{-3} Me_2S (Merck, zur Synthese), were prepared by dissolving weighed amounts in the ionic medium, containing 20% (w/w) of methanol to enhance the solubility. They were used within a few days from preparation.

The compounds NaCl (Merck, p.a.), NaBr (Merck, p.a. or Mallinckrodt, AR), $HClO_4$ (Merck, p.a.) and $NaClO_4$ (Merck, p.a.) were kept as 1.00–4.00 mol dm^{-3} aqueous stock solutions. After mixing the ionic strength was 1.00 mol dm^{-3}, with (H, Na)ClO_4 as supporting electrolyte and the solvent was water containing 10% (w/w) methanol (Merck, p.a.). Water was doubly distilled from quartz.

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† *Supplementary data available* (No. SUP 57219, 11 pp.): pseudo-first-order and second-order rate constants. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1997, Issue 1.

Apparatus

Spectra were recorded by use of a Milton Roy 3000 diode-array spectrophotometer. The kinetics was monitored at ambient pressure between 2 and 45 °C by use of the Milton Roy instrument or a Hi-Tech SF-3L stopped-flow spectrophotometer. The pressure dependence was studied at 25.0 °C by use of a Hi-Tech HPSF-56 high-pressure stopped-flow spectrophotometer.[18] Proton NMR spectra were recorded on a Varian 300 spectrometer in D_2O–MeOH using a 5 mm probe at 299.973 MHz.

Kinetics

Second-order reactions were studied under pseudo-first-order conditions with at least a ten-fold excess of Me_2S. They were started by mixing equal volumes of solutions containing a gold(III) complex and Me_2S directly in the spectrophotometer cells or stopped-flow instruments. Substitution of chloride in *trans*-$[Au(CN)_2Cl_2]^-$ by Me_2S was monitored by the increase in absorbance at 290 nm, subsequent reduction of the gold(III) complexes by the decrease in absorbance between 250 and 290 nm. Reactions at ambient pressure were studied with the stopped-flow instrument, except the slow reduction of *trans*-$[Au(CN)_2Cl(Me_2S)]$ at $1.0 < Q < 68$ [defined by equation (6) below] which was monitored by use of the Milton Roy spectrophotometer. The slow water-assisted reduction of *trans*-$[Au(CN)_2(Me_2S)_2]^+$ was studied at ambient pressure between 13 and 52 °C at 290 nm by use of the Milton Roy instrument. Reduction of *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) by Me_2S was monitored as a function of pressure between 0.1 and 175 MPa by the decrease in absorbance at 270 and 290 nm, respectively.

All kinetic runs were evaluated by use of the OLIS model 4000 data system stopped-flow version 9.04 software.[19] Observed rate constants were determined by a fit of a single exponential to the experimental kinetic traces. The pseudo-first-order rate constants given in Tables and Figures were calculated as an average of at least five independent kinetic runs. Second-order rate constants were obtained by a least-squares fit of a straight line to the pseudo-first-order rate constants *vs.* the concentration of free Me_2S. Enthalpies and entropies of activation were derived from a fit of the Eyring equation to $\ln(k/T)$ *vs.* $1/T$, volumes of activation by a fit of equation (1) to the

$$\ln k = \ln k_0 - \Delta V^{\ddagger}P/RT \qquad (1)$$

variable-pressure data, where k_0 denotes the rate constant at zero pressure and 25.0 °C.

Results and Discussion

Spectra and stoichiometry

The UV/VIS spectra of equilibrated reaction mixtures of *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) and Me_2S recorded between 200 and 300 nm indicated that the gold(III) complexes are reduced quantitatively to $[Au(CN)_2]^-$. Dimethyl sulfoxide is formed as the final oxidation product of dimethyl sulfide, as confirmed by ^1H NMR spectroscopy. Spectral data for *trans*-$[Au(CN)_2X_2]^-$ (X = Cl or Br) agreed with the literature.[20] The molar absorption coefficient of $[Au(CN)_2]^-$ at 241 nm was determined separately to be $(2.42 \pm 0.03) \times 10^3$ dm^3 mol^{-1} cm^{-1}. The stoichiometry was derived from the absorbances at 241 nm for a series of equilibrated solutions with a constant concentration of *trans*-$[Au(CN)_2Br_2]^-$ and increasing concentrations of Me_2S. The equivalence point was determined from a plot of absorptivity *vs.* concentration of Me_2S (SUP 57219): 4.2×10^{-5} mol dm^{-3} of Me_2S was consumed to produce 4.1×10^{-5} mol dm^{-3} $[Au(CN)_2]^-$, indicating a stoichiometric ratio Au : Me_2S of 1 : (1.0 ± 0.1) and an overall reaction according to (2). Spectrophotometric determination of the stoichiometry for the reaction of *trans*-$[Au(CN)_2Cl_2]^-$ with Me_2S is not possible due to complex formation between *trans*-$[Au(CN)_2Cl_2]^-$ and the dimethyl sulfoxide formed as a product in this process.

$$trans\text{-}[Au(CN)_2Br_2]^- + Me_2S + H_2O \longrightarrow [Au(CN)_2]^- + Me_2SO + 2H^+ + 2Br^- \qquad (2)$$

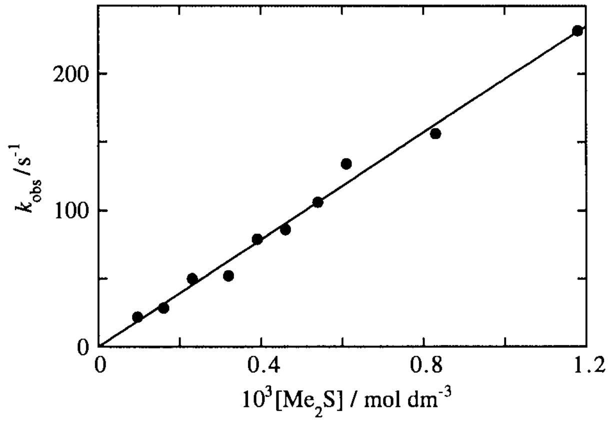


Fig. 1 Observed pseudo-first-order rate constants for substitution of one chloride by dimethyl sulfide in *trans*-$[Au(CN)_2Cl_2]^-$ as a function of the concentration of dimethyl sulfide at 5.0 °C; $c_{Au} = 5.5 \times 10^{-6}$, $[Cl^-] = 5.0 \times 10^{-3}$, $[H^+] = 5.0 \times 10^{-3}$ mol dm^{-3}, $4.2 < Q = [Cl^-]/[Me_2S] < 52.6$

Substitution

Addition of an excess of Me_2S to a solution of *trans*-$[Au(CN)_2Cl_2]^-$ results in rapid appearance of an absorbance peak at 290 nm, due to quantitative formation of *trans*-$[Au(CN)_2(Me_2S)_2]^+$. Replacement of the first chloride ligand is rate determining for this process, since the second substitution step is fast due to the *trans* effect of Me_2S. The observed rate constant is directly proportional to the excess concentration of Me_2S without any significant intercept as shown by the plot in Fig. 1. Thus, substitution takes place without any observable solvent path.

The second-order rate constant was determined to be $k_1 = (2.0 \pm 0.1) \times 10^5$ dm^3 mol^{-1} s^{-1} at 5.0 °C. Dimethyl sulfide is thus a much less efficient nucleophile towards gold(III) than is thiocyanate; substitution of chloride on *trans*-$[Au(CN)_2Cl_2]^-$ by SCN^- is too rapid to be followed by the stopped-flow technique.[15] This difference in rate is in agreement with the $n°_{Pt}$ values, 4.87 for Me_2S and 5.75 for SCN^-;[16] the reactivity ratio of about one order of magnitude for platinum(II) centres is likely to be even more pronounced for the softer gold(III) complexes.

The observed pseudo-first-order rate constant for the substitution process was determined as a function of temperature at 290 nm, giving $\Delta H^{\ddagger} = 25 \pm 3$ kJ mol^{-1} and $\Delta S^{\ddagger} = -54 \pm 3$ J K^{-1} mol^{-1} (SUP 57219). Substitution reactions on square-planar gold(III) complexes are usually characterised by negative entropies of activation,[14,20,21] see Table 1. Solvational changes seem to have a large influence on the $\Delta S^{\ddagger}$ values only when the reactions involve either highly charged and hydrated cations, such as $[Au(NH_3)_4]^{3+}$ and/or strongly bound leaving groups, *e.g.* NH_3.[22–25] The negative $\Delta S^{\ddagger}$ value obtained for the non-charged Me_2S as entering and chloride as a leaving ligand is in agreement with the classification of the gold(III) centres as soft and strongly interacting with entering ligands in an I_a process.

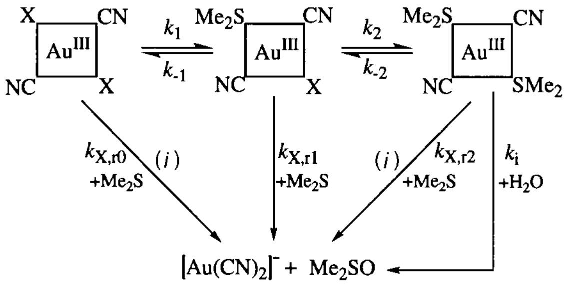
Reaction mechanism and equilibrium constants

A stoichiometric mechanism for the reaction of *trans*-$[Au(CN)_2X_2]^-$ with Me_2S is shown in Scheme 1, including all possible reaction pathways. As described elsewhere,[15] formation of transient gold(III) complexes in a pre-equilibrium gives rise to a general expression for the observed pseudo-first-order rate constant for the rate-determining redox step according to the first term in equation (3), where $k_{X,rn}$ denotes rate constants for

Table 1 Rate constants and activation parameters at 25.0 °C for the reaction of gold(III) complexes

Reaction	k/dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}	$\Delta V^{\ddagger}$/cm^3 mol^{-1}	Ref.
Substitution reactions					
$[Au(NH_3)_4]^{3+} + Cl^-$	0.36 ± 0.02	81 ± 2	20 ± 4	—	23
trans-$[Au(NH_3)_2Br_2]^+ + Cl^-$	164 ± 4	35 ± 2	-84 ± 8	—	24
trans-$[Au(NH_3)_2Cl_2]^+ + Cl^-$	$(1.9 \pm 0.3) \times 10^{-6}$	105 ± 4	-4 ± 10	—	24
trans-$[Au(CN)_2Br_2]^- + Cl^-$	1670	38.5 ± 0.4	-54 ± 5	—	20
trans-$[Au(CN)_2BrCl]^- + Cl^-$	143	45 ± 3	-50 ± 10	—	20
trans-$[Au(NH_3)Cl_3] + Cl^-$	$(3.33 \pm 0.01) \times 10^{-5}$	97 ± 2	-7 ± 4	—	23
$[Au(NH_3)_4]^{3+} + Br^-$	0.85 ± 0.02	73 ± 3	-3 ± 3	—	26
trans-$[Au(NH_3)_2Cl_2]^+ + Br^-$	1075 ± 15	28.0 ± 1.2	-93 ± 4	—	24
trans-$[Au(NH_3)_2Br_2]^+ + Br^-$	$(4.7 \pm 0.2) \times 10^{-5}$	88 ± 3	-32 ± 8	—	26
trans-$[Au(NH_3)Br_3] + Br^-$	$(2.68 \pm 0.09) \times 10^{-2}$	84 ± 4	7 ± 9	—	25
$[AuCl_4]^- + Br^-$	0.140	51	-92	—	22
trans-$[Au(CN)_2Cl_2]^- + Me_2S$	$(2.0 \pm 0.1) \times 10^{5}$[a,b] $(4 \times 10^{5}$[c]$)$	25 ± 3	-54 ± 3	—	This work
trans-$[Au(NH_3)_2Cl_2]^+ + SCN^-$	$(3.3 \pm 0.2) \times 10^{4}$[a]	33 ± 7	-48 ± 21	-4.5 ± 0.5	14, 15
$[AuCl_4]^- + SCN^-$	7.4	50	-59	—	22
$[AuCl_4]^- + I^-$	84	50	-38	—	22
$[AuCl_4]^- + N_3^-$	0.35	27	-163	—	22
$[AuCl_4]^-$ + pyridine	1.6	44	-92	—	22
Reductive eliminations					
trans-$[Au(NH_3)_2Cl(SCN)]^+ + SCN^-$	$(2.7 \pm 0.5) \times 10^3$	—	—	—	14
trans-$[Au(NH_3)_2Br(SCN)]^+ + SCN^-$	$(3.0 \pm 0.5) \times 10^2$	—	—	—	14
trans-$[Au(NH_3)_2(SCN)_2]^+ + SCN^-$	$(2.2 \pm 0.4) \times 10^2$	66 ± 4	21 ± 12	4.6 ± 0.9	14
trans-$[Au(CN)_2Cl(SCN)]^- + SCN^-$	$(7.0 \pm 1.1) \times 10^4$	—	—	—	15
trans-$[Au(CN)_2Br(SCN)]^- + SCN^-$	$(3.0 \pm 0.7) \times 10^3$	—	—	—	15
trans-$[Au(CN)_2(SCN)_2]^- + SCN^-$	$(3.1 \pm 0.1) \times 10^2$	55 ± 3	-17.8 ± 0.8	-4.6 ± 0.5	15
trans-$[Au(CN)_2Cl(Me_2S)] + Me_2S$	$(3.0 \pm 0.1) \times 10^{2}$[d]	33 ± 4	-100 ± 10[e]	-20 ± 2[e]	This work
trans-$[Au(CN)_2Br(Me_2S)] + Me_2S$	$(1.2 \pm 0.1) \times 10^{3}$[f]	44 ± 2	-38 ± 2	-10 ± 1	This work

[a] Substitution of the first chloride ligand for a thiocyanate or dimethyl sulfide. [b] At 5.0 °C. [c] Rate constant at 25.0 °C calculated from the activation parameters. [d] $k_{Cl,r1}$. [e] These values might be influenced by the temperature and pressure dependence of the equilibrium constant $K_{Cl,2}$. [f] $k_{Br,r1}$.



Scheme 1 (*i*) Not observed

$$k_{obs} = [Me_2S]\,\frac{k_{X,r0} + k_{X,r1}K_{X,1}Q^{-1} + k_{X,r2}K_{X,1}K_{X,2}Q^{-2}}{1 + K_{X,1}Q^{-1} + K_{X,1}K_{X,2}Q^{-2}} + \frac{k_iK_{X,1}K_{X,2}Q^{-2}}{1 + K_{X,1}Q^{-1} + K_{X,1}K_{X,2}Q^{-2}} \quad (3)$$

the parallel intermolecular reduction of the complexes *trans*-$[Au(CN)_2X_{2-n}(Me_2S)_n]^{n-1}$ ($n = 0$–2). The second term represents the contribution to k_{obs} from the water-assisted reduction of *trans*-$[Au(CN)_2(Me_2S)_2]^+$, with a first-order rate constant k_i, as described below. The corresponding stepwise equilibrium constants, $K_{X,1}$, $K_{X,2}$ and the ratio Q are defined by equations (4)–(6). The rate constant for reduction of the asymmetric complex

$$K_{X,1} = Q[Au(CN)_2X(Me_2S)]/[Au(CN)_2Cl_2^-] \quad (4)$$

$$K_{X,2} = Q[Au(CN)_2(Me_2S)_2^+]/[Au(CN)_2X(Me_2S)] \quad (5)$$

$$Q = [X^-]/[Me_2S] \quad (6)$$

trans-$[Au(CN)_2Br(Me_2S)]$, $k_{Br,r1}$ and the equilibrium constant $K_{Br,1}$ were obtained by a fit of equation (3) to the experimental values of k_{red} (obtained from plots of k_{obs} *vs.* total concentration of Me_2S) as a function of Q, see Fig. 2(*a*). The rate constant $k_{Br,r1}$, equilibrium constant $K_{Br,2}$ and ratio $K_{Br,1}:K_{Br,2}$ were determined as 1200 ± 100 dm^3 mol^{-1} s^{-1}, 0.50 ± 0.18 and $(8800 \pm 4500):1$. In this calculation the rate constants for reduction of *trans*-$[Au(CN)_2Br_2]^-$, $k_{Br,r0}$ and *trans*-$[Au(CN)_2(Me_2S)_2]^+$, $k_{Br,r2}$ and k_i, were assumed to be negligibly small in comparison with $k_{Br,r1}$.

For the reaction between Me_2S and *trans*-$[Au(CN)_2Cl_2]^-$ a simplified mechanism could be used, taking into account only the rapid equilibrium between *trans*-$[Au(CN)_2Cl(Me_2S)]$ and *trans*-$[Au(CN)_2(Me_2S)_2]^+$. The expression for the observed pseudo-first-order rate constant is then reduced to (7). For

$$k_{obs} = [Me_2S]\,\frac{k_{Cl,r1} + k_{Cl,r2}K_{Cl,2}Q^{-1}}{1 + K_{Cl,2}Q^{-1}} + \frac{k_iK_{Cl,2}Q^{-1}}{1 + K_{Cl,2}Q^{-1}} \quad (7)$$

$Q \geqslant 1.0$ the k_i term of equation (7) can be neglected. A least-squares fit of equation (7) to the experimental data in Fig. 2(*b*) then gives $k_{Cl,r1} = 300 \pm 10$ dm^3 mol^{-1} s^{-1} and $K_{Cl,2} = 3000 \pm 300$. In addition, a value of $K_{Cl,1} \approx 9.7 \times 10^4$ can be estimated by a combination of the overall equilibrium constants for the reactions *trans*-$[Au(CN)_2Cl_2]^- + 2\ Br^-$ from ref. 20 and *trans*-$[Au(CN)_2Br_2]^- + 2\ Me_2S$ given in Table 2. The resulting distributions of gold between the complexes *trans*-$[Au(CN)_2X_{2-n}(Me_2S)_n]^{n-1}$ as a function of log Q are shown in Fig. 2(*c*) and 2(*d*). Equilibrium data for this and related systems are summarised in Table 2.[12,14,15,20,23,26]

The presence of cyanide ligands in the inner co-ordination sphere of gold(III) increases the soft and discriminating properties of the metal centre.[15] The equilibrium constants derived for the successive replacement of halide by Me_2S given in Table 2 follow this trend. Thus, in the present systems, the overall equilibrium constants β_2, defined by equation (8), are determined to

$$\beta_2 = K_{X,1}K_{X,2} \quad (8)$$

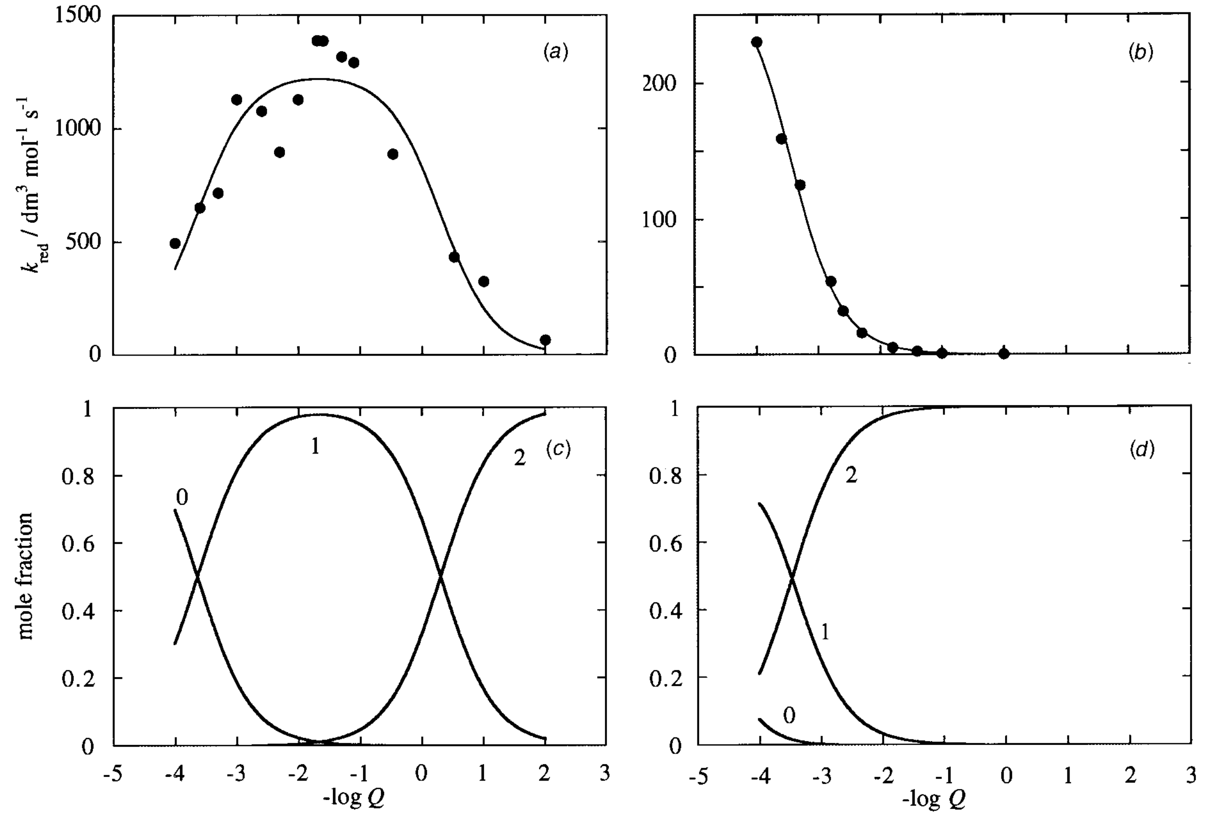


Fig. 2 Second-order rate constants for reduction of the complexes *trans*-[Au(CN)$_2$X$_{2-n}$(Me$_2$S)$_n$]$^{n-1}$ (X = Cl or Br, n = 0–2) by dimethyl sulfide, $k_{red} = k_{obs}$/[Me$_2$S], as a function of Q = [X$^-$]/[Me$_2$S] and the equilibrium distribution between the complexes in the pre-equilibrium. (*a*) Observed rate constant for X = Br$^-$; solid line calculated by a least-squares fit of equation (3) with $k_{Br,r0} \approx k_{Br,r2} \approx 0$ and $K_1/K_2 = 8800$; $c_{Au} = (0.45–2.6) \times 10^{-5}$, [H$^+$] = 5.0 × 10^{-3}, [Me$_2$S] = (0.34–18.1) × 10^{-3} mol dm^{-3}. (*b*) Observed rate constant for X = Cl; solid line represents a least-squares fit of equation (7) with $k_{Cl,r2} \approx 0$ and $K_1/K_2 = 32$; $c_{Au} = (0.25–3.2) \times 10^{-5}$, [H$^+$] = 5.0 × 10^{-3}, [Me$_2$S] = (0.11–16.5) × 10^{-3} mol dm^{-3}. (*c*) Distribution of *trans*-[Au(CN)$_2$Br$_{2-n}$(Me$_2$S)$_n$]$^{n-1}$ (n = 0–2) calculated from the equilibrium constants $K_{Br,1} = 4.4 \times 10^3$ and $K_{Br,2} = 0.50$. (*d*) Distribution of *trans*-[Au(CN)$_2$Cl$_{2-n}$(Me$_2$S)$_n$]$^{n-1}$ (n = 0–2) calculated from the equilibrium constants $K_{Cl,1} = 9.7 \times 10^4$ (estimated from the equilibrium constants in Table 2) and $K_{Cl,2} = 3.0 \times 10^3$

Table 2 Stepwise and overall equilibrium constants for the formation of gold(III) complexes with bromide, thiocyanate and dimethyl sulfide at 25.0 °C, defined by equations (4)–(6)

				$K_1:K_2$		
Reaction	K_1	K_2	β_2	Exptl.	Statistical	Ref.
[AuCl$_4$]$^-$ + Br$^-$	243	98	2.4×10^4	2.5	2.67	27
[AuCl$_4$]$^-$ + Me$_2$S	27 ± 5	0.08 ± 0.02	2.16	338	2.67	12
trans-[Au(NH$_3$)$_2$Cl$_2$]$^+$ + Br$^-$	122 ± 2[a]	29.9 ± 0.5[a]	$(3.65 \pm 0.12) \times 10^3$	4	4	24
trans-[Au(NH$_3$)$_2$Cl$_2$]$^+$ + SCN$^-$	$(1.5 \pm 0.5) \times 10^4$[b]	$(4.6 \pm 0.5) \times 10^2$[b]	$(6.9 \pm 3) \times 10^6$	33	4	14
trans-[Au(NH$_3$)$_2$Br$_2$]$^+$ + SCN$^-$	67 ± 12[a]	12 ± 3[a]	$(8.0 \pm 4) \times 10^2$	6	4	14
trans-[Au(CN)$_2$Cl$_2$]$^-$ + Br$^-$	1.1×10^3[c]	1.2×10^2[c]	1.3×10^5	9	4	20
trans-[Au(CN)$_2$Cl$_2$]$^-$ + SCN$^-$	$(4.1 \pm 0.7) \times 10^5$[b,c]	$(3.8 \pm 0.7) \times 10^4$[d]	$\geqslant 1.6 \times 10^{10}$	$\geqslant$11	4	15
trans-[Au(CN)$_2$Br$_2$]$^-$ + SCN$^-$	$\geqslant (1.0 \pm 0.3) \times 10^3$[e]	$(1.15 \pm 0.35) \times 10^2$[d]	$\geqslant 1.2 \times 10^5$	$\geqslant$9	4	15
trans-[Au(CN)$_2$Cl$_2$]$^-$ + Me$_2$S	$\approx 9.7 \times 10^4$[f]	$(3.0 \pm 0.3) \times 10^3$[d]	$\geqslant 2.9 \times 10^8$	$\geqslant$32	4	This work
trans-[Au(CN)$_2$Br$_2$]$^-$ + Me$_2$S	$(4.4 \pm 2.2) \times 10^3$[d]	0.50 ± 0.18[d]	2.2×10^3	8800	4	This work

[a] $K_n = k_n/k_{-n}$. [b] Calculated from thermodynamic data. [c] Equilibrium measurements. [d] Calculated from redox data, equation (3). [e] Estimated by assuming a statistical distribution between gold(III) complexes at equilibrium. [f] Estimated from equilibrium constants in ref. 20 and this work.

$\beta_2 \geqslant 2 \times 10^3$ for X = Br and $\approx 3 \times 10^8$ for X = Cl, whereas Cattalini and co-workers[12] have reported a β_2 value of only *ca.* 2 for the successive replacement of Cl$^-$ for Me$_2$S at [AuCl$_4$]$^-$. A switch in the affinity sequence of the metal centres is also observed; exchange of Br$^-$ for Me$_2$S takes place at *trans*-[Au(CN)$_2$Br$_2$]$^-$, but is thermodynamically unfavourable at [AuBr$_4$]$^-$.[12,27] The ratios $K_1:K_2$ for reactions with Me$_2$S as an entering ligand deviate significantly from the statistically predicted values, observed for instance for Cl$^-$/Br$^-$ exchange at gold(III),[23,26] *cf.* Table 2. Thus, the maximum fraction of the mixed-ligand complexes *trans*-[Au(CN)$_2$X(Me$_2$S)] significantly exceeds that of 50% predicted for a statistically distributed system. This feature is even more pronounced in the present systems than for the corresponding thiocyanato complexes.[15]

Reduction of bromide complexes

The rate of the reaction following the substitution process is directly proportional to the concentration of free Me$_2$S for constant Q = [Br$^-$]/[Me$_2$S] in the concentration range studied (SUP 57219). No distinct maxima in the UV/VIS spectrum of the resulting product mixture are observed between 200 and 400 nm. This reaction can be interpreted as a reduction to Au^I. Second-order rate constants k_{red} were determined from plots of k_{obs} *vs.* total concentration of Me$_2$S in the interval

$0.01 \leqslant Q \leqslant 10\,000$; values are given in Fig. 2(*a*). Addition of sodium bromide to the reaction mixture increases the rate of reduction to a maximum for $Q \approx 50$, but for further bromide addition the rate decreases again. The observed pseudo-first-order rate constant for the reduction, $k_{\mathbf{obs}}$, was studied as a function of temperature and pressure at the maximum value of $Q = 50$, where *trans*-[Au(CN)$_2$Br(Me$_2$S)] predominates completely in solution and equation (3) can be reduced to $k_{\mathbf{obs}} = [\mathrm{Me_2S}]k_{\mathbf{Br,r1}}$ (SUP 57219). The activation parameters $\Delta H^{\ddagger} = 44 \pm 2$ kJ mol^{-1}, $\Delta S^{\ddagger} = -38 \pm 2$ J K^{-1} mol^{-1} and $\Delta V^{\ddagger} = -10 \pm 1$ cm^3 mol^{-1} can be related to reduction of *trans*-[Au(CN)$_2$Br(Me$_2$S)]. The less negative entropy of activation obtained for the redox process, compared to that for substitution, is in agreement with a less tightly bound transition state of the redox reaction as would be expected if reduction takes place *via* an attack by dimethyl sulfide on co-ordinated halide, *cf.* ref. 15. It is noteworthy that the activation entropy remains negative, although contributions due to electrostriction have been minimised by the use of the non-charged Me$_2$S. However, it is difficult to draw any definite conclusions concerning differences between transition states for substitution and redox reactions based on these values. The negative values of $\Delta S^{\ddagger}$ and $\Delta V^{\ddagger}$ obtained for the redox reaction may simply reflect the bimolecular process.

Reduction of chloride complexes

As for the bromide complexes, the observed rate constant for the reaction following the substitution process is a linear function of the concentration of free Me$_2$S for constant $Q \geqslant 1.0$ (SUP 57219). The second-order rate constants for reduction, $k_{\mathbf{red}}$, increase with increasing Q in the interval $1.0 \leqslant Q \leqslant 10\,000$; values are given in Fig. 2(*b*).

The observed pseudo-first-order rate constant of equation (7) was studied as a function of temperature and pressure for constant Q under conditions where the second term is negligible (SUP 57219). The apparent activation parameters were determined to be $\Delta H^{\ddagger} = 33 \pm 4$ kJ mol^{-1} and $\Delta S^{\ddagger} = -100 \pm 11$ J K^{-1} mol^{-1} from measurements at $Q = 400$, 700 and 2000 and $\Delta V^{\ddagger} = -20 \pm 2$ cm^3 mol^{-1} was derived from measurements at $Q = 400$. These data refer to the predominant reduction of *trans*-[Au(CN)$_2$Cl(Me$_2$S)], but since this complex is present in rapid equilibrium with *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ a contribution to the activation parameters from the temperature and pressure dependence of the equilibrium constant $K_{\mathbf{Cl,2}}$ cannot be excluded. However, these results agree qualitatively with those found for reduction of the mixed-ligand bromide complex.

A decrease of Q below 1.0 for the chloride system results in a further decrease of the reduction rate together with a loss of the [Me$_2$S] dependence, indicating a change to a water-assisted mechanism for reduction of *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ (SUP 57219). Thus, for $Q = 0.1$ and $2.2 < [\mathrm{Me_2S}] < 8.6$ mmol dm^{-3}, the observed first-order rate constant, $k_{\mathbf{obs}}$, of equation (7) is reduced to k_{i} and at 25.0 °C a value of $(1.2 \pm 0.2) \times 10^{-4}$ s^{-1} is obtained, independent of [Me$_2$S]. This first-order rate constant for reduction, k_{i}, at $Q = 0.1$ was found to be independent of the temperature in the interval investigated, resulting in $\Delta H^{\ddagger} = 0 \pm 20$ kJ mol^{-1} and $\Delta S^{\ddagger} = -300 \pm 50$ J K^{-1} mol^{-1}. The reaction is too slow to be followed by high-pressure stopped flow. Reaction *via* the second-order pathway described by $k_{\mathbf{Cl,r2}}$ in Scheme 1 is not observed.

Dimethyl sulfide as a reductant

The redox reactions between Me$_2$S and *trans*-[Au(CN)$_2$X$_{2-n}$(Me$_2$S)$_n$]$^{n-1}$ seem to take place by an overall stoichiometric mechanism resembling that described earlier for similar systems.[12–15] However, in Scheme 1, the pathways described by the rate constants $k_{\mathbf{X,r0}}$ and $k_{\mathbf{X,r2}}$ are not observed for dimethyl sulfide as a reductant, whereas there is an additional reaction described by k_{i}. Ligands with different ground-state *trans* influence co-ordinated in *trans* position to each other facilitate electron transfer induced by an attack of Me$_2$S on the complex. Thus, the observed second-order rate constant for reduction of the bromide complexes reaches a maximum when the mixed-ligand complex *trans*-[Au(CN)$_2$Br(Me$_2$S)] predominates in solution. For the chloride complexes no such maximum is observed, since the equilibrium constants favour formation of *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$, allowing only a small fraction of the mixed-ligand reactive complex *trans*-[Au(CN)$_2$Cl(Me$_2$S)] to be present under the experimental conditions accessible. The same trend in reactivity is observed, however, with a sharp increase in redox rate as a function of increasing concentrations of *trans*-[Au(CN)$_2$Cl(Me$_2$S)].

Dimethyl sulfide is a less efficient nucleophile than thiocyanate, as exemplified by the smaller values of the substitution rate constants and equilibrium constants. It is also a less efficient reductant. The mixed-ligand complexes *trans*-[Au(CN)$_2$X(Me$_2$S)] are reduced more slowly than their thiocyanato analogues and *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ is not reduced at all *via* attack by Me$_2$S. Moreover, an intermolecular reduction where the two-electron transfer is initiated by an attack of dimethyl sulfide directly on the gold(III) centre or on an already co-ordinated Me$_2$S is not observed. Thus, formation of a [Me$_2$S–SMe$_2$]$^{2+}$ moiety seems unlikely even in the presence of the strongly oxidising gold(III) complexes. This observation is in agreement with other studies of the mechanism of oxidation of Me$_2$S. It has been suggested that Me$_2$S acts as a one-electron reductant producing the radical cation [Me$_2$S–SMe]$^{\bullet +}$ when Me$_2$S is used in excess.[27–30] Such a reaction mechanism is in contrast to the one observed for reduction of *trans*-[Au(CN)$_2$(SCN)$_2$]$^-$ by thiocyanate, giving rise to a reduction rate constant which depends on the concentration of free SCN$^-$; (SCN)$_2$ has been suggested as an intermediate in this process.[15] We therefore conclude that reduction of *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ is assisted by a water molecule from the solvent cage according to equation (9). This reaction mechanism implies a consumption of one molecule of Me$_2$S per reduced gold(III) moiety, consistent with the experimental stoichiometry of 1:1. The almost negligible temperature dependence observed for this slow process results in a large and negative $\Delta S^{\ddagger}$ value of -300 J K^{-1} mol^{-1} suggesting a highly organised transition state, for example a rate-determining step including not only incorporation of the water molecule in the transition state but also orientation of all reactants in such a way that the formation of products, including Me$_2$SO, would follow momentarily after electron transfer.

$$\textit{trans}\text{-}[\mathrm{Au(CN)_2(Me_2S)_2}]^+ + \mathrm{H_2O} \xrightarrow{k_{\mathrm{i}}} [\mathrm{Au(CN)_2}]^- + \mathrm{Me_2SO} + 2\mathrm{H}^+ + \mathrm{Me_2S} \quad (9)$$

By exchanging one of the co-ordinated Me$_2$S molecules in *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ for a halide (Cl$^-$ or Br$^-$) a sharp increase in the reduction rate is observed. The linear dependence of the rate on the concentration of free Me$_2$S suggests an intermolecular reaction involving attack by dimethyl sulfide on the complex. Attack on co-ordinated dimethyl sulfide seems unlikely, as discussed above. Instead, we favour a mechanism involving participation of co-ordinated halide, resulting in formation of Me$_2$SX as an intermediate after consecutive two-electron transfer, equation (10). Rapid hydrolysis of this intermediate results in formation of Me$_2$SO as the final oxidation product, equation (11). A similar reaction mechanism

$$\textit{trans}\text{-}[\mathrm{Au(CN)_2X(Me_2S)}] + \mathrm{Me_2S} \longrightarrow [\mathrm{Au(CN)_2}]^- + \mathrm{Me_2SX}^+ + \mathrm{Me_2S} \quad (10)$$

$$\mathrm{Me_2SX^+} + \mathrm{H_2O} \xrightarrow{\text{fast}} \mathrm{Me_2SO} + 2\mathrm{H}^+ + \mathrm{X}^- \quad (11)$$

has been suggested by Cattalini and co-workers[12] and was also found for reduction of platinum(IV) complexes by methionine.[31] It is further supported by the reactivity sequence *trans*-[Au(CN)$_2$Br(Me$_2$S)] > *trans*-[Au(CN)$_2$Cl(Me$_2$S)] ⩾ *trans*-[Au(CN)$_2$(Me$_2$S)$_2$]$^+$ observed in the present study.

Conclusion

The rate and mechanism for reduction of gold(III) complexes by soft nucleophiles is strongly dependent on the co-ordinative environment of the metal centre and on the nature of the reductant. For a given combination of metal complex and reducing agent the observed reactivity may vary by as much as two orders of magnitude between related complexes in the series [ML$_2$X$_{2-n}$(reductant)$_{2-n}$] (n = 0–2) as exemplified by thiocyanate and dimethyl sulfide as reductants. In both cases an asymmetric electron distribution in the mixed-ligand gold(III) complexes decreases the free energy of activation for their reduction. The intimate mechanism for reduction by those two nucleophiles is markedly different, however. Reduction with SCN$^-$ takes place mainly *via* bimolecular attack on co-ordinated SCN$^-$,[14,15] whereas reduction with Me$_2$S takes place preferably *via* attack on co-ordinated halide or, in the absence of co-ordinated halides, *via* a water-assisted reduction process. Intermolecular as well as the water-assisted reaction with dimethyl sulfide involves two-electron transfers with formation of gold(I) and Me$_2$SO as final products. The favoured halide-mediated oxidation of the thioethers has implications for redox reactions *in vivo*, suggesting that reduction of metal ions by thioether moieties in biological systems should be favoured in extracellular environments, where chloride concentrations are high.

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