

Articles

Contribution from the Chemistry Department and Department of Physics,
Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Denmark

Ammine Ligand Exchange in Tetraamminegold(III) in Aqueous Solution. Composition of Transition States and Relative Reactivity of Tetraamminegold(III) and Its Conjugated Base, Amidotriamminegold(III)

Birthe Brønnum,¹ H. Saaby Johansen,² and L. H. Skibsted*¹

Received February 9, 1988

Temperature dependence of the rate of exchange of ammonia between tetraamminegold(III) and solution ammonia in aqueous ammonium perchlorate of unit ionic strength in the pH range 5-10 has been determined by using nitrogen-15 labeling. At fixed pH, the exchange follows second-order kinetics (first order in both complex and ammonia/ammonium), and the pH dependence of the second-order constant can be accounted for in terms of reactions between the two acids NH_4^+ and $\text{Au}(\text{NH}_3)_4^{3+}$ and their conjugated bases NH_3 and $\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$, respectively. The direct exchange between NH_4^+ and $\text{Au}(\text{NH}_3)_4^{3+}$ is significant but slow (statistically corrected second-order rate constant $k = 6.0 (3) \times 10^{-5} \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$, $\Delta H^\ddagger = 84 (2) \text{ kJ}\cdot\text{mol}^{-1}$, $\Delta S^\ddagger = -42 (5) \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ at 25 °C) compared to the exchange between NH_3 and $\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$ ($k = 3.9 (2) \times 10^{-2} \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$, $\Delta H^\ddagger = 68 (2) \text{ kJ}\cdot\text{mol}^{-1}$, $\Delta S^\ddagger = -44 (8) \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$). Exchange via a transition state of the composition $[\text{Au}(\text{NH}_3)_3\text{NH}_2\cdots\text{H}\cdots\text{NH}_3]^{3+}$ is significant at intermediate pH, most likely as a result of reaction between NH_3 and $\text{Au}(\text{NH}_3)_4^{3+}$ ($k = 1.69 (6) \times 10^{-1} \text{ L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$, $\Delta H^\ddagger = 61 (2) \text{ kJ}\cdot\text{mol}^{-1}$, $\Delta S^\ddagger = -55 (6) \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$).

Introduction

Recent interest in the biochemistry of gold has arisen from the well-established use of gold(I) compounds in the treatment of rheumatoid arthritis and from the exploration of antitumor activity of both gold(I) and gold(III) compounds.³⁻⁶ In cells, gold is mainly bonded to sulfur and nitrogen donors, as has been directly shown by X-ray absorption spectroscopy for the alga *Chlorella vulgaris*.⁷ The distribution between gold(I) and gold(III) depends on the available ligands, and sulfur donors favor gold(I) over gold(III). In contrast, nitrogen donors, such as those present in the nucleic acids, favor the higher of the two common oxidation states of gold.^{8,9}

The tetraamminegold(III) ion, also previously used as a model for nitrogen-bonded gold in cells,⁷ was chosen for an exploration of the kinetics of the exchange of coordinated ammonia with aqueous solution ammonia over a wide pH range by using nitrogen-15 labeling. The results of this exchange study are reported here, yielding the time scale relevant for the exchange of gold(III) between nitrogen coordination sites. This is part of the information required to determine whether the binding of gold(III) through nitrogen to biomolecules is kinetically or thermodynamically controlled.

Gold(III) is a strongly polarizing metal center, and ammonia and amines coordinated to gold(III) are Brønsted acids even in aqueous solution.¹⁰ For tetraamminegold(III), ammine and amido complexes coexist in neutral solution ($\text{p}K_a = 7.5$),¹¹ and since both forms are sufficiently robust toward hydrolysis, the tetraamminegold(III) ion provides us with a rare example of a metal ammine/amido system for which exchange with solution ammonia can be directly studied and for which the relative reactivity of the

Table I. Acid Dissociation of Ammonium^a and Tetraamminegold(III)^b Ions in Aqueous 1.0 M Ammonium Perchlorate

$t/^\circ\text{C}$	$\text{p}K_a(\text{NH}_4^+)^c$	$\text{p}K_a(\text{Au}(\text{NH}_3)_4^{3+})^c$
25.0	9.43	7.48
17.0	9.70	7.84
8.8	9.98	8.20
0.0	10.29	8.60
$\Delta H^\ddagger/\text{kJ}\cdot\text{mol}^{-1}$	52.1	67
$\Delta S^\ddagger/\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$	-6	82

^a Calculated from data in ref 10. ^b Interpolated from data in Figure 1. ^c $\text{p}K_a = -\log (K_a/\text{mol}\cdot\text{L}^{-1})$.

two forms can be compared. This is of particular interest, since metal amides in general are believed to be highly reactive intermediates in base hydrolysis processes of metal amines in aqueous solution.^{12,13}

Experimental Section

Materials. $^{15}\text{NH}_4\text{NO}_3$ (5.8 and 98% nitrogen-15 in the ammonium moiety) was supplied by Amersham Int. $[\text{Au}(\text{NH}_3)_4](\text{NO}_3)_3$ was prepared and purified as described previously.¹¹ Other chemicals were of analytical grade.

pH Measurement. The kinetic studies were all made in a 1.0 M perchlorate medium, and the definition $\text{pH} = -\log [\text{H}^+]$ was employed throughout, with solutions of standardized perchloric acid in 1.0 M NH_4ClO_4 used as pH standards. The $\text{p}K_a$ value of $\text{Au}(\text{NH}_3)_4^{3+}$ in 1.0 M NH_4ClO_4 at different temperatures was determined spectrophotometrically¹¹ (Zeiss DMR 21 spectrophotometer) at 300 nm ($\epsilon(\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}) = 1467 \text{ cm}^{-1}\cdot\text{L}\cdot\text{mol}^{-1}$); cf. Figure 1. The $\text{p}K_a$ value of NH_4^+ in 1.0 M NH_4ClO_4 at the required temperatures was interpolated from available thermodynamic data¹⁴ and is given in Table I together with the $\text{p}K_a$ values for $\text{Au}(\text{NH}_3)_4^{3+}$ at the same temperatures.

Labeling Procedure. Nitrogen-15 labeled $[\text{Au}(\text{NH}_3)_4](\text{NO}_3)_3$ was prepared from $\text{K}[\text{AuCl}_4]$ (H. Drijfhout & Zoon's) dissolved in a super-saturated NH_4NO_3 solution according to the procedure published for the unlabeled compound, with the ammonium nitrate partly replaced by ^{15}N -enriched NH_4NO_3 . Products from two syntheses, with 11.2% and 13.3% ^{15}N ammine ligand enrichment, respectively, were used for the exchange experiments.

- Chemistry Department.
- Department of Physics.
- Lippard, S. J., Ed. *Platinum, Gold, and Other Metal Chemotherapeutic Agents*; ACS Symposium Series 209; American Chemical Society: Washington, DC, 1983.
- Mirabelli, C. K.; Johnson, R. K.; Hill, D. T.; Faucette, L. F.; Girard, G. R.; Kuo, G. Y.; Sung, C. M.; Crooke, S. T. *J. Med. Chem.* **1986**, *29*, 218.
- Ward, B.; Dabrowiak, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 3810.
- Mizuno, Y.; Komiya, S. *Inorg. Chim. Acta* **1986**, *125*, L13.
- Watkins, J. W., II; Elder, R. C.; Greene, B.; Darnall, D. W. *Inorg. Chem.* **1987**, *26*, 1147.
- Skibsted, L. H. *Adv. Inorg. Bioinorg. Mech.* **1986**, *4*, 137.
- Skibsted, L. H.; Bjerrum, J. *Acta Chem. Scand., Ser. A* **1977**, *A31*, 155.
- Block, B. P.; Bailar, J. C. *J. Am. Chem. Soc.* **1951**, *73*, 4722.
- Skibsted, L. H.; Bjerrum, J. *Acta Chem. Scand., Ser. A* **1974**, *A28*, 740.

- Basolo, F.; Pearson, R. G. *Mechanisms of Inorganic Reactions*, 2nd Ed.; Wiley: New York, 1967.
- Wilkins, R. G. *The Study of Kinetics and Mechanism of Reactions of Transition Metal Complexes*; Allyn & Bacon: Boston, MA, 1974.
- Skibsted, L. H. *Acta Chem. Scand., Ser. A* **1981**, *A35*, 229.

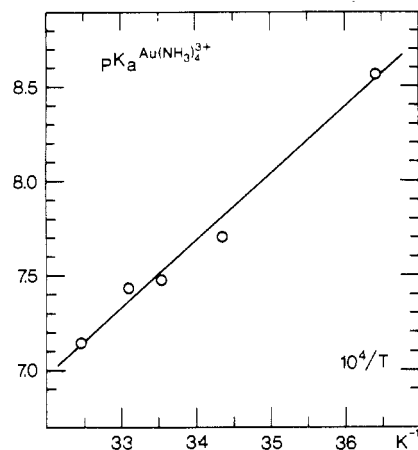


Figure 1. Temperature dependence of pK_a for $\text{Au}(\text{NH}_3)_4^{3+}$ in 1.0 NH_4ClO_4 . Experimental values were determined spectrophotometrically, and the solid line computed from $pK_a = (\Delta H^\circ/T - \Delta S^\circ)/2.30R$ is the basis for the parameters ΔH° and ΔS° for the acid dissociation (Table I).

Isotopic Analysis. The ^{15}N isotopic abundance in the labeled compounds and in the $[\text{Au}(\text{NH}_3)_4]\text{PO}_4$ samples precipitated in the exchange experiments was determined by optical emission analysis. The analytical procedure (a detailed description may be found in ref 15) involved a Dumas destruction at 400 °C of the material (copper plus copper(II) oxide).

Exchange Experiments. An aqueous 1.0 M $(\text{Na},\text{NH}_4)\text{ClO}_4$ reaction medium was employed throughout. In the acidic and neutral regions, acetate and 3-morpholinopropanesulfonate, respectively, were used to buffer the medium (0.050 M buffer concentration in most experiments), whereas standardized sodium hydroxide was used to adjust pH in the alkaline region (formation of $\text{NH}_4^+/\text{NH}_3$ buffers). pH was measured in each of the reaction media after the addition of $[\text{Au}(\text{NH}_3)_4](\text{NO}_3)_3$ at the temperature of the experiment. Weighed amounts of the labeled compound (corresponding to a complex concentration between 0.022 and 0.045 M) were dissolved in the actual reaction medium (thermostated to within 0.1 °C) to initiate the exchange reaction. Dissolution was virtually instantaneous in all experiments. Then 300 μL aliquots were removed at known times and poured into 100 μL of an ice-cold, aqueous 0.10 M phosphate precipitation reagent in which the $\text{H}_2\text{PO}_4^-/\text{HPO}_4^{2-}$ ratio was adjusted to give a final pH of around 8 in the mixture of reaction medium and precipitation reagent. A white precipitate of $[\text{Au}(\text{NH}_3)_4]\text{PO}_4$ was immediately formed.¹⁶ The mixture was cooled in ice for 2 min, and the precipitate was filtered off on a fine-porosity sintered-glass funnel, washed twice with 0.5 mL of ice-cold water, and air-dried on the filter. The precipitate was subsequently dissolved in 0.2 mL of 1 M HCl, and $\sim 10 \mu\text{L}$ of the resulting yellow solution was transferred to a 1 cm long glass capillary by capillary attraction. The solution was evaporated to dryness in the capillary ($\sim 50 \text{ }^\circ\text{C}$ in vacuum), and the residue was subjected to Dumas destruction and subsequent isotopic analysis.¹⁵

Results

Nitrogen-15 labeled $\text{Au}(\text{NH}_3)_4^{3+}$ dissolved in aqueous 1.0 M ammonium perchlorate with natural ^{15}N enrichment was found to lose ^{15}N enrichment in an exchange process that was strongly dependent on solution pH and temperature. The almost quantitative precipitation of $[\text{Au}(\text{NH}_3)_4]\text{PO}_4$ (solubility product at 25 °C is $\sim 10^{-11} \text{ mol}^2\cdot\text{L}^{-2}$)¹⁷ formed the basis for the analytical procedure, and HPO_4^{2-} was found to remove $\text{Au}(\text{NH}_3)_4^{3+}$ in a precipitation reaction that was very fast compared to the exchange reactions studied.

At fixed temperature and pH and with a large excess of ammonium ($c_{\text{NH}_4^+} \gg c_{\text{Au}}$), the exchange was found to follow first-order kinetics

$$\ln \left[\frac{\% ^{15}\text{N}(t) - \% ^{15}\text{N}(t = \infty)}{\% ^{15}\text{N}(t = 0) - \% ^{15}\text{N}(t = \infty)} \right] = -k'_{\text{obs}}t \quad (1)$$

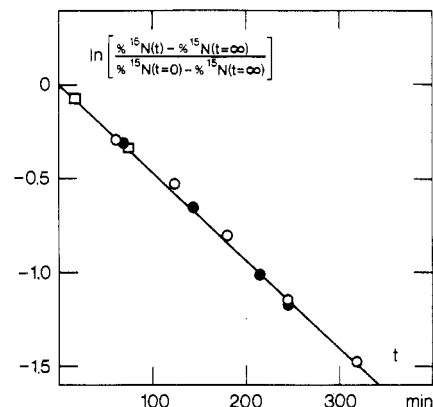


Figure 2. Plot showing that ammine ligand exchange in tetraammine-gold(III) in aqueous solution follows first-order kinetics. The initial enrichment of $\text{Au}(\text{NH}_3)_4^{3+}$, $\% ^{15}\text{N}(t = 0) = 13.3$, decreases during exchange to $\% ^{15}\text{N}(t = \infty) = 1.4$. The three different symbols refer to three independent experiments, all at 0.0 °C with $c_{\text{Au}} = 0.022 \text{ M}$ in 1.0 M NH_4ClO_4 at pH 8.08. The exchange has a half-life of 150 min under these experimental conditions.

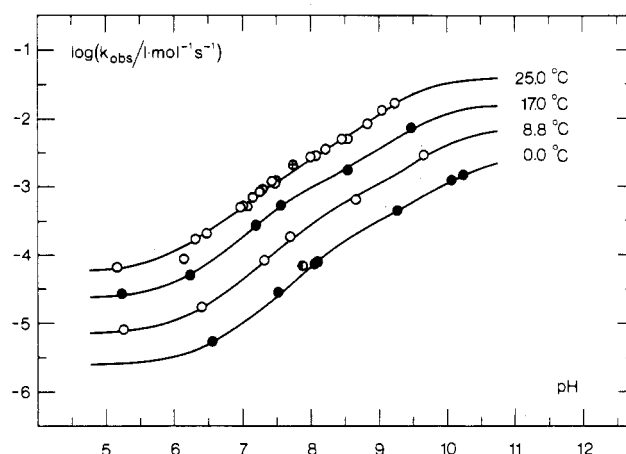
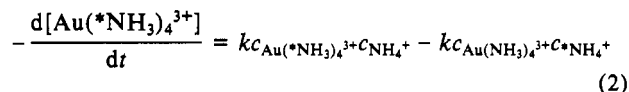


Figure 3. Plot showing that the second-order rate constant for ammine ligand exchange of $\text{Au}(\text{NH}_3)_4^{3+}$ increases with increasing pH conditions: 1.0 M NH_4ClO_4 (except 0.50 M NH_4ClO_4 plus 0.50 M NaClO_4 for \ominus), $c_{\text{Au}} = 0.022$, (except $c_{\text{Au}} = 0.044 \text{ M}$ for \bullet). Experimental points were determined as outlined in Figure 2, and the solid lines were calculated by nonlinear regression analysis (χ^2 goodness-of-fit test) according to (4) for each temperature, incorporating the pK_a values of Table I.

where $\% ^{15}\text{N}$ values denote the decreasing ^{15}N enrichment in the precipitated $[\text{Au}(\text{NH}_3)_4]\text{PO}_4$, as illustrated in Figure 2. The observed first-order rate constant was independent of buffer concentration ($0.05 < c_{\text{buffer}} < 0.10 \text{ M}$) but proportional to total ammonium concentration when in excess ($0.50 < c_{\text{NH}_4^+} < 1.0 \text{ M}$). The latter observation shows that the exchange is a second-order reaction



for which the McKay equation¹³ yields

$$\ln \left[\frac{\% ^{15}\text{N}(t) - \% ^{15}\text{N}(t = \infty)}{\% ^{15}\text{N}(t = 0) - \% ^{15}\text{N}(t = \infty)} \right] = -\left(\frac{k}{4}\right)(c_{\text{Au}}^{\text{tot}} + c_{\text{NH}_4^+}^{\text{tot}})t = -k_{\text{obs}}(c_{\text{Au}}^{\text{tot}} + c_{\text{NH}_4^+}^{\text{tot}})t = -k'_{\text{obs}}t \quad (3)$$

(tot = total.) The second-order rate constant for ammine exchange, calculated from $k_{\text{obs}} = k'_{\text{obs}}/(c_{\text{Au}}^{\text{tot}} + c_{\text{NH}_4^+}^{\text{tot}})$ is inherently statistically corrected ($\text{L}\cdot(\text{mol ligand})^{-1}\cdot\text{s}^{-1}$).¹⁸ The pH

(15) Johansen, H. S.; Middelboe, V. *Appl. Spectrosc.* **1982**, *36*, 221.

(16) Weitz, E. *Justus Liebigs Ann. Chem.* **1915**, *410*, 117.

(17) Skibsted, L. H., to be submitted for publication.

(18) Swaddle, T. W. *Adv. Inorg. Bioinorg. Mech.* **1983**, *2*, 95.

Scheme I

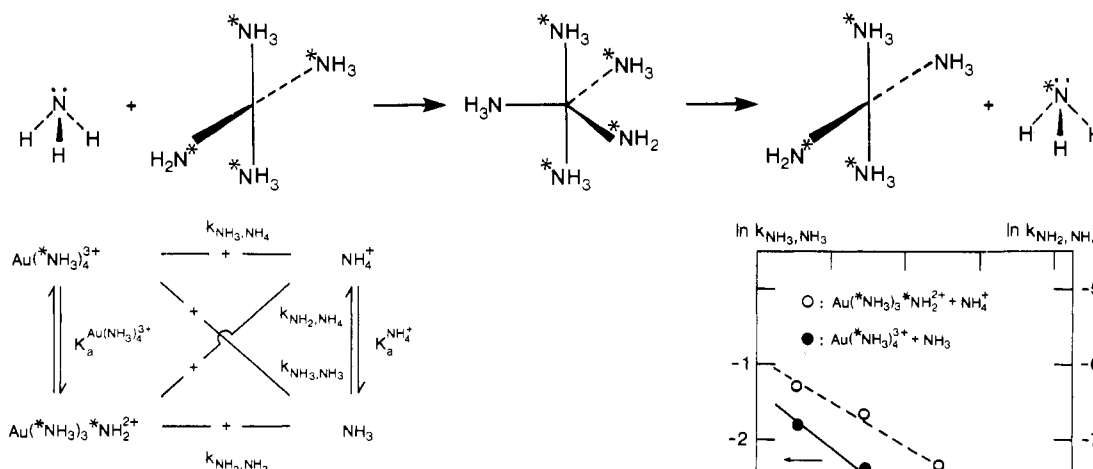


Figure 4. Four different bimolecular reactions leading to ammine ligand exchange in tetraamminegold(III) in aqueous ammonium solution.

dependence of k_{obsd} shown in Figure 3 for four different temperatures could be accounted for in terms of reaction between two conjugated acid/base pairs, i.e. $\text{NH}_4^+/\text{NH}_3$ and $\text{Au}(\text{NH}_3)_4^{3+}/\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$, according to¹³

$$k_{\text{obsd}} = \frac{1}{([\text{H}^+] + K_a^{\text{NH}_4^+})([\text{H}^+] + K_a^{\text{Au}(\text{NH}_3)_4^{3+}})} [k_{\text{NH}_3, \text{NH}_4} [\text{H}^+]^2 + (k_{\text{NH}_3, \text{NH}_3} K_a^{\text{NH}_4^+} + k_{\text{NH}_2, \text{NH}_4} K_a^{\text{Au}(\text{NH}_3)_4^{3+}}) [\text{H}^+] + k_{\text{NH}_2, \text{NH}_3} K_a^{\text{NH}_4^+} K_a^{\text{Au}(\text{NH}_3)_4^{3+}}] \quad (4)$$

The four reaction paths of Figure 4 correspond, however, to only three different transition states, since the reactants $\text{Au}(\text{NH}_3)_4^{3+}$ and NH_3 give a transition state of the same composition as the reactants $\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$ and NH_4^+ . This leads to a so-called proton ambiguity, and only the three quantities $k_{\text{NH}_3, \text{NH}_4}$, $(k_{\text{NH}_3, \text{NH}_3} K_a^{\text{NH}_4^+} + k_{\text{NH}_2, \text{NH}_4} K_a^{\text{Au}(\text{NH}_3)_4^{3+}})$, and $k_{\text{NH}_2, \text{NH}_3} K_a^{\text{NH}_4^+} K_a^{\text{Au}(\text{NH}_3)_4^{3+}}$ can be determined from the pH dependence of k_{obsd} . This was done by nonlinear regression analysis for the observed rate constants at each of the four temperatures, including values for $K_a^{\text{Au}(\text{NH}_3)_4^{3+}}$ and $K_a^{\text{NH}_4^+}$ determined in independent experiments (cf. Table I), and the results are presented in Table II. The reaction via a transition state of the composition $[\text{Au}(\text{NH}_3)_4 \cdots \text{NH}_4]^{4+}$ is slow compared to the reaction via the transition state $[\text{Au}(\text{NH}_3)_3\text{NH}_2 \cdots \text{NH}_3]^{2+}$. For both the slow and the fast latter exchange reactions, the temperature dependence is well described by the Arrhenius equation, leading to the activation parameters given in Table III. For the reaction via the transition state $[\text{Au}(\text{NH}_3)_3\text{NH}_2 \cdots \text{H} \cdots \text{NH}_3]^{3+}$, the second-order rate constants for the reaction between $\text{Au}(\text{NH}_3)_4^{3+}$ and NH_3 and for the reaction between $\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$ and NH_4^+ were calculated and are given in Table II. The Arrhenius plots for both of these two alternatives are included in Figure 5, and the slight curvature noted could indicate that both of the reaction paths contribute to the exchange reaction. The two sets of activation parameters (Table III) are, however, rather different (reflecting the significant difference in ΔH^\ddagger for the acid dissociation of NH_4^+ and $\text{Au}(\text{NH}_3)_4^{3+}$; Table I), inviting further speculation.

Discussion

Water and hydroxide are relatively ineffective as entering ligands in Au(III) complexes,⁸ and ammine ligand exchange in tetraamminegold(III) in aqueous ammonium solution becomes fast compared to hydrolysis, at least under moderate conditions of pH and temperature.¹⁹ This high discriminating power of gold(III) substrates toward nucleophiles is related to the extreme

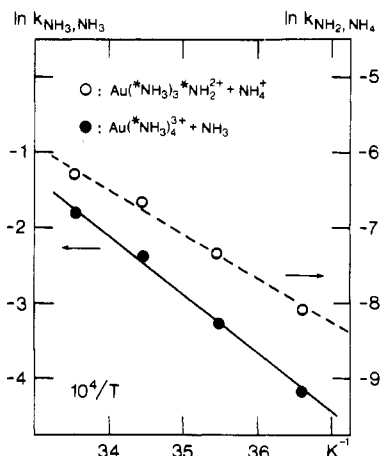
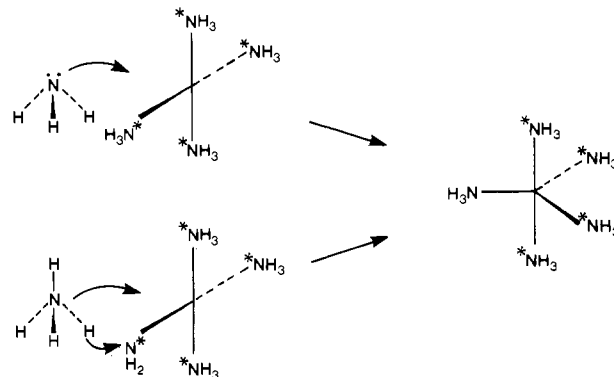


Figure 5. Temperature dependence for ammine exchange in tetraamminegold(III) via a transition state of the composition $[\text{Au}(\text{NH}_3)_3\text{NH}_2 \cdots \text{H} \cdots \text{NH}_3]^{3+}$. The second-order rate constants (in $\text{L} \cdot \text{mol}^{-1} \cdot \text{s}^{-1}$) for the two alternative pairs of reactants (see Figure 4) both give a slightly curved Arrhenius plot.

Scheme II



softness of the Au(III) metal center,^{8,9} and Au(III) has provided us with this rare opportunity to study ammine ligand exchange for a transition metal complex in aqueous solution over a wide pH range undisturbed by hydrolysis reactions.

Tetraamminegold(III) has a low-spin d^8 electronic configuration and is square-planar (D_{4h} symmetry) with a rather normal Au-N band length of 2.02 Å.²⁰ The dissociation of a proton transforms the simple σ -donor NH_3 into a ligand with π -bonding capabilities, as evidenced by the change in the UV absorption spectrum. $\text{Au}(\text{NH}_3)_4^{3+}$ is colorless (lowest energy transition is a spin-allowed $d-d$ ($^1A_{1g} \rightarrow ^1A_{2g}, ^1E_g$) transition below 250 nm²¹), whereas $\text{Au}(\text{NH}_3)_3\text{NH}_2^{2+}$ is yellow due to a lower energy ($\lambda_{\text{max}} \sim 300$ nm⁹) transition from an amido $2p_x$ orbital to a $\sigma^*(x^2 - y^2)$ molecular orbital.²² For octahedral metal complexes, amido π donation is believed to stabilize pentacoordinate intermediates in base-catalyzed ligand-substitution reactions (conjugate base mechanism),^{12,13} whereas the effect on the rate of ligand substitution in square-planar complexes is less evident. For the

(19) In moderately acidic aqueous ammonium solution, $\text{Au}(\text{NH}_3)_4^{3+}$ forms $\text{Au}(\text{NH}_3)_3\text{OH}^{2+}$ in a slow, pH-independent, reversible hydrolysis, for which the forward reaction has a (pseudo) first-order rate constant of $3 \times 10^{-6} \text{ s}^{-1}$ at 25 °C.^{8,11}

(20) Weishaupt, M.; Strähle, J. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1976**, *B31*, 554.

(21) Mason, W. R.; Gray, H. B. *J. Am. Chem. Soc.* **1968**, *90*, 5721.

(22) Baddley, W. H.; Basolo, F.; Gray, H. B.; Nöling, C.; Poë, A. *J. Inorg. Chem.* **1963**, *2*, 921.

Table II. Second-Order Rate Constants^a for Exchange of Ammonia Coordinated in Tetraamminegold(III) with Ammonia/Ammonium in Aqueous 1.0 M Ammonium Perchlorate^b

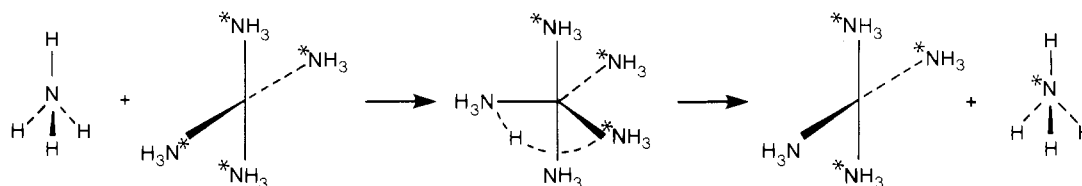
	transition state			
	[Au(NH ₃) ₄ ...NH ₄] ⁴⁺	[Au(NH ₃) ₃ NH ₂ ...H...NH ₃] ³⁺		[Au(NH ₃) ₃ NH ₂ ...NH ₃] ²⁺
reactants	Au(NH ₃) ₄ ³⁺ + NH ₄ ⁺	Au(NH ₃) ₄ ³⁺ + NH ₃ ^c	Au(NH ₃) ₃ NH ₂ ²⁺ + NH ₄ ⁺ ^c	Au(NH ₃) ₃ NH ₂ ²⁺ + NH ₃
<i>k</i> /L·mol ⁻¹ ·s ⁻¹				
25.0 °C	5.8 (5) × 10 ⁻⁵	1.64 (5) × 10 ⁻¹	1.84 (6) × 10 ⁻³	3.9 (2) × 10 ⁻²
17.0 °C	3.3 (2) × 10 ⁻⁵	9.3 (5) × 10 ⁻²	1.29 (6) × 10 ⁻³	1.65 (13) × 10 ⁻²
8.8 °C	7.4 (2) × 10 ⁻⁶	3.8 (3) × 10 ⁻²	6.4 (6) × 10 ⁻⁴	7.3 (9) × 10 ⁻³
0.0 °C	2.5 (5) × 10 ⁻⁶	1.54 (10) × 10 ⁻²	3.1 (2) × 10 ⁻⁴	2.9 (2) × 10 ⁻³

^a All rate constants are statistically corrected, i.e. based on ligand concentration. ^b Calculated by nonlinear regression analysis from the observed rate constants presented in Figure 3, including the acid dissociation constants of Table I; see text. ^c Two alternatives leading to a transition state of identical composition; cf. Figure 4.

Table III. Rate Constants and Activation Parameters at 25.0 °C for Exchange of Ammonia Coordinated in Tetraamminegold(III) with Ammonia/Ammonium in Aqueous 1.0 M Ammonium Perchlorate Solution^a

	transition state			
	[Au(NH ₃) ₄ ...NH ₄] ⁴⁺	[Au(NH ₃) ₃ NH ₂ ...H...NH ₃] ³⁺		[Au(NH ₃) ₃ NH ₂ ...NH ₃] ²⁺
reactants	Au(NH ₃) ₄ ³⁺ + NH ₄ ⁺	Au(NH ₃) ₄ ³⁺ + NH ₃ ^b	Au(NH ₃) ₃ NH ₂ ²⁺ + NH ₄ ⁺ ^b	Au(NH ₃) ₃ NH ₂ ²⁺ + NH ₃
Δ <i>H</i> [‡] /kJ·mol ⁻¹	84 (2)	61 (2)	45 (2)	68 (2)
Δ <i>S</i> [‡] /J·mol ⁻¹ ·K ⁻¹ ^c	-42 (5)	-55 (6)	-146 (6)	-44 (8)
<i>k</i> /L·mol ⁻¹ ·s ⁻¹ ^c	6.0 (3) × 10 ⁻⁵	1.69 (6) × 10 ⁻¹	1.91 (7) × 10 ⁻³	3.9 (2) × 10 ⁻²

^a Calculated from rate constants of Table II. ^b Two alternatives leading to a transition state of identical composition; cf. Figure 4. ^c Statistically corrected, i.e. based on ligand concentration.

Scheme III

diethylenediamine complex Au(dien)Cl²⁺, chloride/bromide substitution was originally found to be faster in the conjugate base Au(dien-H)Cl⁺,²³ but a reinvestigation has shown that the rates for the two substrates are comparable.²⁴

The bimolecular exchange reaction between NH₃ and Au(NH₃)₃NH₂²⁺ has a negative entropy of activation (Table III), which is typical for ligand substitution reactions in gold(III) complexes involving transition states of increased coordination number (Scheme I).⁸ The exchange via the transition state [Au(NH₃)₃NH₂...H...NH₃]³⁺ can originate from the encounter of two different pairs of reactants (Scheme II). The net increase in bonding in the transition states along the reaction coordinate for both of these pairs of reactants is also expected to result in a negative entropy of activation.²⁵ The reaction between Au(NH₃)₃NH₂²⁺ and NH₄⁺ should involve synchronous proton transfer in the transition state to create the lone pair necessary for a nucleophilic attack (donation into vacant metal p_z orbital), but despite the fact that this transfer could give large entropy effects, Δ*S*[‡] = -146 J·mol⁻¹·K⁻¹ calculated for this combination of reactants seems unrealistically negative. In contrast, the combination of NH₃ and Au(NH₃)₄³⁺ yields Δ*S*[‡] = -55 J·mol⁻¹·K⁻¹, which is not significantly different from the value for NH₃ plus Au(NH₃)₃NH₂²⁺, and we find it more likely that the exchange via the transition state in Scheme II is the result of a reaction between NH₃ and Au(NH₃)₄³⁺. Simple electrostatic arguments also suggest that the reaction of NH₄⁺ with a divalent cation would be less likely to occur than the reaction of NH₃ with a trivalent cation. Notably, this implies that solution ammonia exchanges faster with Au(NH₃)₄³⁺ than with Au(NH₃)₃NH₂²⁺ and that this difference in reactivity is an enthalpy effect. The

metal p_z orbital normally believed to accommodate the pair of electrons donated by the entering ligand¹² apparently is involved in π-bonding in Au(NH₃)₃NH₂²⁺, rendering this latter complex less subject to nucleophilic attack than the parent acid.

Also remarkable is the evidence obtained for a direct exchange of ammonia between the two cations NH₄⁺ and Au(NH₃)₄³⁺ (Scheme III). The structure of the transition state for this exchange reaction is less obvious, although it seems likely that the proton is handed from the entering to the leaving ammine ligand concomitant with the exchange at the gold(III) center. Δ*S*[‡] for this exchange is very similar to Δ*S*[‡] for the two other exchange reactions, and again, the difference in reactivity can be traced to differences in the ease with which a fifth ligand binds to form the transition state.

The exchange behavior for the square-planar tetraamminegold(III) is different from that for the octahedral hexaamminecobalt(III) complex.^{26,27} The introduction of a π-donor at the cobalt(III) center, as in hydroxopentaamminecobalt(III),²⁸ accelerates the exchange considerably; i.e., a π-donor has the opposite effect to that seen for tetraamminegold(III) (relative to amidotriamminegold(III)).

In conclusion, gold(III) exchanges ammine ligands as a result of at least two reaction paths at physiological pH and above. The activation barriers are only moderate (ca. 65 kJ·mol⁻¹), and the binding of gold(III) to nitrogen donors under physiological conditions is a result of a thermodynamic preference⁸ rather than a result of slow exchange.

Acknowledgment. This research was supported by a grant from the Carlsberg Foundation.

Registry No. Au(NH₃)₄³⁺, 43739-93-1; NH₃, 7664-41-7.

(23) Baddley, W. H.; Basolo, F. *Inorg. Chem.* **1964**, *3*, 1087.

(24) Nardin, G.; Randiaccio, L.; Annibale, G.; Pitteri, B. *J. Chem. Soc., Dalton Trans.* **1980**, 220.

(25) Kaas, K.; Skibsted, L. H. *Acta Chem. Scand., Ser. A* **1985**, *A39*, 1.

(26) Rutenberg, A. C.; Drury, J. S. *Inorg. Chem.* **1963**, *2*, 219.

(27) Llewellyn, D. R.; O'Connor, C. J.; Odell, A. L. *J. Chem. Soc.* **1964**, 196.

(28) Williams, T. J.; Hunt, J. P. *J. Am. Chem. Soc.* **1968**, *90*, 7210.