

(CF₃)₂⁺ or SF₃C₂⁺, 79.44; 131, C₂O₂CHC₂F₄⁺, 6.67; 89, SF₃⁺, 100; 79, CFSO⁺, 5.53; 78 OC₂F₂⁺, 5.59; 70, SF₂⁺, 10.30; 69, CF₃⁺, 100; 67, SOF⁺, 87.85; 65, SO₂H⁺, 7.25; 64, SO₂⁺, 9.18; 51, SF⁺, 29.41; 50, CF₂⁺, 9.67; 48, SO⁺, 13.75.

Anal. Calcd for C₃H₂F₄O₂S₂: C, 13.70; H, 0.23; F, 56.6; S, 17.42. Found: C, 13.90; H, 0.34; F, 57.2; S, 17.14.

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(University of Idaho) obtained the mass spectra, and Roger Kohnert (Oregon State University) obtained the ¹³C spectra.

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Coordination Chemistry of Gold(I) with Cyanide and 1-Methylpyridine-2-thione. Kinetics and Thermodynamics of Ligand Exchange at Gold(I) in Aqueous Solution

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The equilibrium constants for the stepwise cyanide substitution at Au(CN)₂⁻ by 1-methylpyridine-2-thione (mpt) were determined in acidic solution by UV spectroscopy. The kinetics of the forward and reverse reaction of Au(CN)₂⁻ with mpt were studied by means of the stopped-flow method. Surprisingly, the rate constant in the exergonic direction is significantly below the diffusion-controlled limit. This reveals a lower reactivity of the Au(I) center compared with the metal center of similar Hg(II) and Ag(I) complexes. The reactivity of CN⁻ toward Au(CN)(mpt) is at least 7 orders of magnitude greater than that of HCN. This is indicative of an associative mechanism.

Introduction

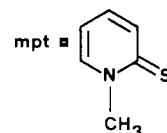
The importance of gold(I) compounds in the treatment of rheumatoid arthritis has recently increased the interest in gold(I) coordination chemistry. Although structural aspects are well documented,¹ quantitative investigations of the thermodynamics of individual ligand-exchange reactions in aqueous solution are scarce, and knowledge about their kinetics is generally limited to the observation that Au(I) complexes are labile. Isad and Sadler² have estimated the rate constants and activation parameters for thiol exchange in gold-bound thiolates in solutions that contain predominantly polynuclear Au(I) species. In a very recent study by Boles Bryan, Mikuriya, Hempel, Mellinger, Hashim, and Pasternack,³ the rate and equilibrium constants for the substitution of tetraacetylthioglucose by chloride in auranofin were measured in aqueous acid solutions. The dearth of information about the dynamics of ligand exchange is surprising in the light of the important role such processes are likely to play in the biological chemistry of Au(I).⁴

Many possibilities exist for facile reactions of Au(I)-containing antiarthritis drugs with S-containing molecules in the human body.² Indeed, some hypotheses suggest that Au(I) is the active moiety in these drugs and that sequential ligand-exchange processes alter the pharmacokinetics and intracellular distribution of the gold.⁵ Evaluation of this and other hypotheses concerning the efficacy of gold therapy will require detailed understanding of all facets of the ligand-exchange process. In this paper we report a stopped-flow kinetic study on a ligand-exchange process at a mononuclear Au(I) in aqueous solution. In addition, new equilibrium information is presented.

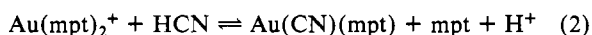
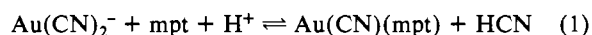
In this and several other studies, the stable linear Au(CN)₂⁻ was used as starting material. Protonation of the cyanide released

upon ligand exchange facilitates the use of ligands with very different affinities in the studies of the kinetics and equilibria of ligand substitution reactions of Au(CN)₂⁻. Cyanide can be displaced by various soft ligands without causing the disproportionation to Au(0) and Au(III). It was shown by Raman and ¹³C NMR spectroscopy that thiolates (RS⁻) form mixed-ligand complexes, RSAuCN⁻, which undergo ligand redistribution to form Au(CN)₂⁻ and Au(SR)₂⁻.⁶ The complex Au(CN)(S₂O₃)²⁻ can be formed by dissolving AuCN in aqueous thiosulfate solution.⁷ The stepwise substitution of CN⁻ on Au(CN)₂⁻ by I⁻ could be studied spectrophotometrically.⁸

The present study utilizes the S-donor ligand 1-methylpyridine-2-thione (mpt). The reactions can be monitored directly



because the UV spectrum of mpt changes upon coordination with Au(I). Some years ago we used mpt in the investigation of rate-equilibria relationships for ligand-exchange reactions at CH₃Hg^{II}.⁹ Starting with Au(CN)₂⁻, eq 1, or with Au(mpt)₂⁺,



eq 2, it was possible to investigate the stepwise substitution reactions of mpt with Au(CN)₂⁻. Similar thione complexes were shown to form linear complexes (with coordination through the S) by X-ray structure determination of chloro(1-propyl-1,3-imidazolidine-2-thione)gold(I)¹⁰ and of bis(1-propyl-1,3-

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imidazolidine-2-thione)gold(I) chloride.¹¹

The ligand-substitution reaction of eq 1 is a simple model system for the fundamental aspects of gold(I) transfer processes in which S-donor molecules are involved. Reactions of CN^- with Au(I) compounds are of therapeutic interest because the physiological distribution of Au(I) is believed to be affected by the CN^- present in the blood of smokers.¹²

Experimental Section

$\text{K}[\text{Au}(\text{CN})_2]$ was used as received from Fluka or Johnson Matthey. Electrogravimetric determination of gold showed these salts to be greater than 99% pure. The mpt was prepared by literature methods.¹³ The solid mpt was stored in the dark, and solutions containing mpt were protected from light and were used within 5 days of preparation. $\text{Au}(\text{mpt})_2\text{ClO}_4$ was prepared as follows:¹⁴ Controlled-potential electrolysis of gold wire in an acetonitrile solution of tetraethylammonium perchlorate gave solvated Au^+ ion, which was converted to $\text{Au}(\text{mpt})_2^+$ by addition of a slight excess of mpt. After some evaporation, the crude $\text{Au}(\text{mpt})_2\text{ClO}_4$ precipitated. Recrystallization from acetonitrile gave the desired product as shown by elemental analysis (Microanalytical Laboratory of the ETH Zürich). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{S}_2\text{O}_4\text{ClAu}$: C, 26.36; H, 2.58; N, 5.12; S, 11.73; Cl, 6.48; Au, 36.03. Found: C, 26.54; H, 2.66; N, 5.39; S, 11.74; Cl, 6.7; Au, 36.7. Stock solutions of NaCN (Fluka) were prepared fresh daily by dissolution of the solid in ca. 10^{-4} M NaOH. Hydroxide suppressed hydrolysis of CN^- and subsequent loss as $\text{HCN}(\text{g})$. Buffer solutions were prepared from sodium acetate or chloroacetic acid (both Fluka). Ionic strength was maintained at $I = 0.1$ M with NaClO_4 (Fluka) in studies of the first step of the ligand exchange, eq 1. Perchlorate medium is inappropriate for the study of the second step because $[\text{Au}(\text{mpt})_2]\text{ClO}_4$ was found to be only slightly soluble. The ionic strength was therefore maintained at $I = 0.1$ M with $(\text{K,H})\text{SO}_3\text{CH}_3$ in studies of eq 2. The KSO_3CH_3 was obtained by recrystallization of the crude product from the neutralization of HSO_3CH_3 (Fluka) with KOH.

Either the pH values were measured with a glass electrode, which was standardized with solutions of known $[\text{H}^+]$, or they were calculated from the quantity of standardized acid added (lower pH values).

Equilibrium Measurements. Spectra for stability constant determinations were recorded by use of a Kontron UVIKON 820 UV-visible spectrophotometer equipped with 1-cm cuvettes thermostated to 25.0 ± 0.2 °C. Digital data were transferred directly from the spectrophotometer to an HP 1000 laboratory computer system. The change in the mpt spectrum upon coordination with Au(I) permitted the calculation of stability constants by use of the SPECFIT program.¹⁵ Typically, absorbance data at 40–50 wavelengths that spanned the region 300–400 nm were used in analysis for the first equilibrium, eq 1. For the second equilibrium, eq 2, the region between 260 and 360 nm was used. Spectra were remeasured after approximately 1 h to establish that equilibrium had been reached.

Kinetic Measurements. A Durrum-Dionex D110 stopped-flow spectrophotometer was used for the kinetic measurements. Absorbance data were digitized by two transient recorders in a master-slave relationship.¹⁶ This arrangement permitted data acquisition at two data rates for each reaction mixture. Digital kinetic data were analyzed by a nonlinear least-squares fit of the first-order kinetic model.¹⁶ In most cases, kinetic data were analyzed over 4–5 half-lives. Reported k_{obs} values are the average of at least four replicates.

In strongly acidic solutions $\text{Au}(\text{CN})_2^-$ decomposed slowly to yield the yellow solid AuCN. In addition, cyanide can be lost from such solutions as $\text{HCN}(\text{g})$. For these reasons, kinetic studies were performed by mixing unbuffered, slightly basic $\text{Au}(\text{CN})_2^-$ that contained excess CN^- with buffered mpt solutions. This procedure prevents precipitation in the reactant solution, but in certain reaction mixtures below pH 2.6 turbidity arose quickly enough to interfere with the signal from the ligand-exchange process of interest. In the few cases where this problem occurred,

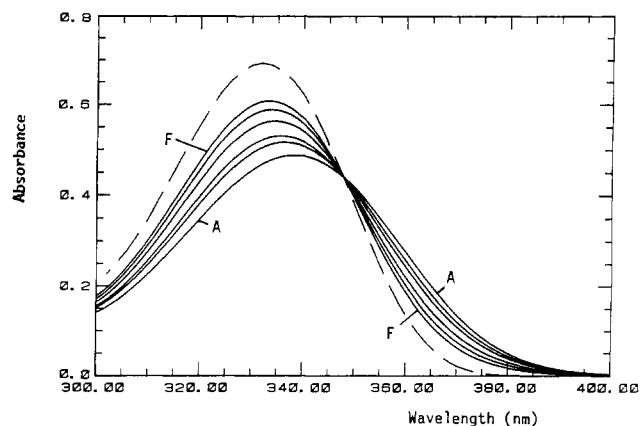


Figure 1. Equilibrium spectra of the $\text{Au}(\text{CN})_2^-/\text{mpt}$ system. Conditions: 25 °C; pH 2.66; $I = 0.1$ (NaClO_4); $[\text{mpt}]_t = 6.04 \times 10^{-5}$ M. Curves A–F (solid lines) are for $0, 0.30 \times 10^{-3}, 0.60 \times 10^{-3}, 1.50 \times 10^{-3}, 2.99 \times 10^{-3}$, and 5.98×10^{-3} M $[\text{Au}(\text{CN})_2^-]_t$. Broken line: calculated spectrum of $\text{Au}(\text{CN})(\text{mpt})$.

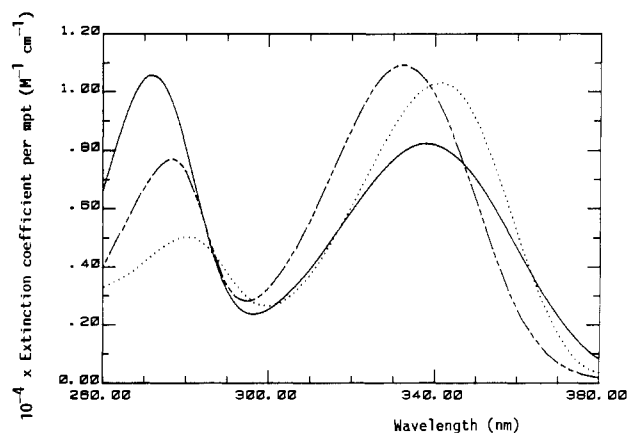


Figure 2. Spectra of mpt (—), $\text{Au}(\text{CN})(\text{mpt})$ (---), and $\text{Au}(\text{mpt})_2^+$ (···).

Table I. Equilibrium Investigation of the $\text{Au}(\text{CN})_2^-/\text{mpt}$ System (Eq 1)^a

$10^3[\text{mpt}]_t, \text{ M}$	pH	$10^3[\text{Au}(\text{I})]_t, \text{ M}$	$\log \beta_{11}^d$
3.00	2.66	0–3.00	30.93
6.00	2.66	0–6.00	30.79
6.00	1.46–4.86	3.00	31.05
			av 30.9 ± 0.2

^a 25.0 ± 0.2 °C; $I = 0.10$ M ($(\text{Na,H})\text{ClO}_4$). ^b $[\text{mpt}]_t = [\text{mpt}] + [\text{Au}(\text{CN})(\text{mpt})]$. ^c $[\text{Au}(\text{I})]_t = [\text{Au}(\text{CN})_2^-] + [\text{Au}(\text{CN})(\text{mpt})]$. ^d $\beta_{11} = [\text{Au}(\text{CN})(\text{mpt})]/[\text{Au}^+][\text{CN}^-][\text{mpt}]$.

the rate constant of the process of interest could be resolved by restricting the analysis to the first 2 or 3 half-lives of the kinetic signal. Only a small number of the kinetic experiments were analyzed in this manner, and the results were only interpreted in conjunction with experiments that showed ideal first-order behavior.

Results and Discussion

Equilibrium Studies. The equilibrium of eq 1 was studied in solutions where $[\text{Au}(\text{CN})_2^-] \gg [\text{mpt}]_t$. The extent of reaction was changed either by varying $[\text{Au}(\text{CN})_2^-]_t$ at fixed pH or by varying the pH at fixed $[\text{Au}(\text{CN})_2^-]_t$. In both studies an isosbestic point occurs near 348 nm. This is consistent with only two mpt-containing species being present. The species in addition to mpt is clearly a ligand-exchange product because the spectral difference becomes smaller at higher pH. Indeed, above pH 4 no spectral evidence of complex formation was found. Representative spectral data for the equilibrium study of eq 1 are shown in Figure 1. Conditions and results for the calculation of the overall stability of $\text{Au}(\text{CN})(\text{mpt})$ are summarized in Table I. The calculations were based on $\log \beta_2^{\text{CN}} = \log ([\text{Au}(\text{CN})_2^-]/[\text{Au}^+][\text{CN}^-]^2) = 39.0^{17}$ and $\text{p}K_a^{\text{HCN}} = 9.01^{18}$. The value obtained

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 (14) (a) Only small quantities of gold(I) perchlorate should be prepared because of possible explosion. (b) We thank K. Aeberli for the syntheses of $\text{Au}(\text{mpt})_2\text{ClO}_4$.
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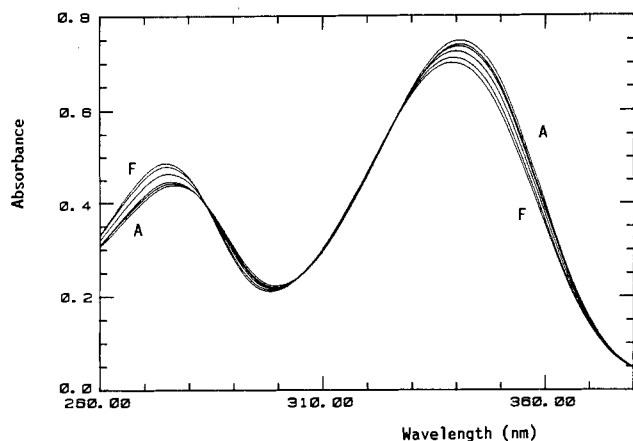


Figure 3. Equilibrium spectra of the $\text{Au(mpt)}_2^+/\text{HCN}$ system. Conditions: 25 °C; pH 2.66; $I = 0.1$ (KSO_3CH_3); $[\text{Au(I)}]_t = 5.2 \times 10^{-6}$ M; $[\text{mpt}]_t = 1.8 \times 10^{-5}$ M. Curves A–F are for $0, 0.11 \times 10^{-5}, 0.22 \times 10^{-5}, 0.54 \times 10^{-5}, 0.86 \times 10^{-5},$ and 1.08×10^{-5} M $[\text{HCN}]_t$.

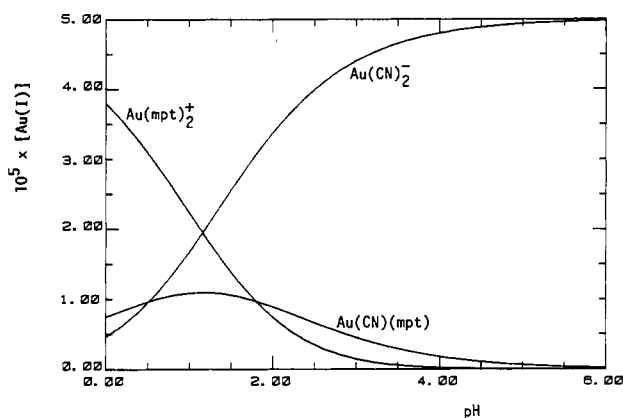


Figure 4. Distribution of Au(I) complexes in solutions where $[\text{CN}^-]_t = [\text{mpt}]_t = 2[\text{Au(I)}]_t = 1 \times 10^{-4}$ M.

Table II. Equilibrium Investigation of the $\text{Au(mpt)}_2^+/\text{HCN}$ System (Eq 2)^a

$10^5[\text{mpt}]_t,^b$ M	$10^6[\text{Au(I)}]_t,^c$ M	$10^6[\text{HCN}]_t,^d$ M	$\log \beta_2,^e$
1.80	5.15	0–10.8	23.4
7.88	35.9	0–11.2	23.2
			av 23.3 ± 0.3

^a 25.0 ± 0.2 °C; $I = 0.10$ M ($(\text{K,H})\text{SO}_3\text{CH}_3$); pH 2.66. ^b $[\text{mpt}]_t = [\text{mpt}] + [\text{Au(CN)(mpt)}] + 2[\text{Au(mpt)}_2^+]$. ^c $[\text{Au(I)}]_t = [\text{Au(CN)(mpt)}] + [\text{Au(mpt)}_2^+]$. ^d $[\text{HCN}]_t = [\text{HCN}] + [\text{CN}^-] + [\text{Au(CN)(mpt)}]$. ^e $\beta_2 = [\text{Au(mpt)}_2^+]/[\text{Au}^+][\text{mpt}]^2$.

is $\log \beta_{11} = 30.9 (\pm 0.2)$. The UV spectrum of Au(CN)(mpt) , as calculated by use of β_{11} , the spectrum of the free mpt , and experimental data, is represented by the broken line in Figure 2.

Solutions used to investigate the equilibrium of eq 2 contained an excess of mpt because this was shown to suppress the disproportionation of Au(mpt)_2^+ to metallic gold and Au(III) . The extent of reaction (eq 2) was changed by varying $[\text{HCN}]_t (= [\text{HCN}] + [\text{CN}^-] + [\text{Au(CN)(mpt)}])$ at pH 2.66. Representative data used for the calculation of $\log \beta_2^{\text{mpt}}$ are shown in Figure 3. The observed spectral changes were much smaller than those seen in the equilibrium study of eq 1. The individual precisions of the β_2 values determined were therefore smaller than those of β_{11} . Determination of $\log \beta_2$ from spectral data was based on our value of $\log \beta_{11}$ and on $\text{p}K_a^{\text{HCN}}$. Conditions and results of the experimental determination of $\log \beta_2$ are summarized in Table II. We obtained $\log \beta_2^{\text{mpt}} = 23.3 (\pm 0.3)$. The spectrum of Au(mpt)_2^+ ,

Table III. Stability^a of Au(I) Coordination Compounds in Aqueous Solution at 25 °C

X	Y	$\log \beta_{\text{XY}}^b$	$\log K_{\text{rd}}^c$	ref
CN^-	CN^-	39.0		17
mpt	mpt	23.3		d
$(\text{NH}_2)_2\text{CS}$	$(\text{NH}_2)_2\text{CS}$	22.1		e
I^-	I^-	18.5		7
SCN^-	SCN^-	17.0		f
CN^-	mpt	30.9	-0.5	d
CN^-	I^-	28.9	0.3	7
$(\text{NH}_2)_2\text{CS}$	I^-	20.4	0.2	e
I^-	SCN^-	17.9	0.3	f

^a Internally consistent values based upon $\log \beta_2^{\text{CN}^-} = \log([\text{Au(CN)}_2^-]/[\text{Au}^+][\text{CN}^-]^2) = 39.0$ and $\text{p}K_a^{\text{HCN}} = 9.01$, ignoring minor differences in ionic strength. ^b $\beta_{\text{XY}} = [\text{Au(X)(Y)}]/[\text{Au}^+][\text{X}][\text{Y}]$. ^c $K_{\text{rd}} = [\text{Au(X)(Y)}]^2/[\text{Au(X)}_2][\text{Au(Y)}_2]$. ^d This work. ^e Belevantsev, V. I.; Peshchevitskii, B. I.; Tsvlodub, L. D. *Zh. Neorg. Khim.* **1986**, *31*, 3065; *Russ. J. Inorg. Chem. (Engl. Transl.)* **1986**, *31*, 1762. ^f Belevantsev, V. I.; Peshchevitskii, B. I.; Tsvlodub, L. D. *Izv. Sib. Otd. Akad. Nauk. SSSR, Ser. Khim. Nauk* **1985**, (3), 64.

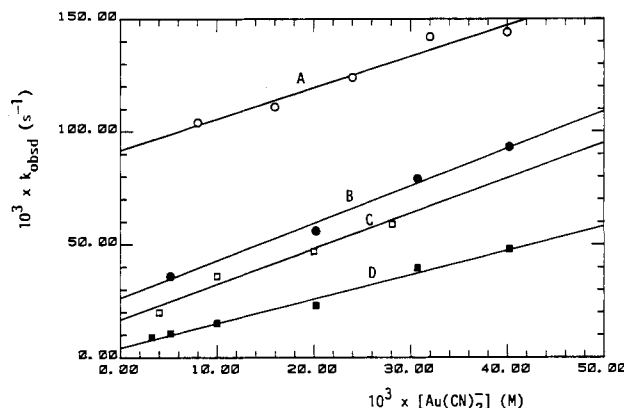
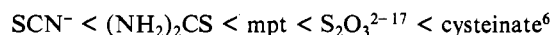


Figure 5. Resolution of k_f from k_{obsd} ($[\text{Au(CN)}_2^-]$ dependence) at 25 °C, $I = 0.1$ M ($(\text{Na,H})\text{ClO}_4$): (A) pH 3.75, $[\text{OAc}]_t = 0.01$ M, $[\text{mpt}] = 1.36 \times 10^{-5}$ M, $[\text{HCN}] = 1.05 \times 10^{-4}$ M; (B) pH 3.19, $[\text{ClCH}_2\text{COOH}]_t = 0.01$ M, $[\text{mpt}] = 1.59 \times 10^{-5}$ M, $[\text{HCN}] = 1.07 \times 10^{-4}$ M; (C) pH 2.64, $[\text{ClCH}_2\text{COOH}]_t = 0.01$ M, $[\text{mpt}] = 1.37 \times 10^{-5}$ M, $[\text{HCN}] = 1.18 \times 10^{-4}$ M; (D) pH 2.07, $[\text{mpt}] = 1.59 \times 10^{-5}$ M, $[\text{HCN}] = 1.07 \times 10^{-4}$ M.

calculated from the stability constants, the spectra of Au(CN)(mpt) and mpt , and experimental data, is represented by the dotted line in Figure 2.

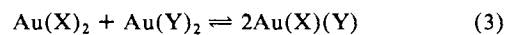
The species distribution calculated for a solution where $[\text{mpt}]_t = [\text{HCN}]_t = 2[\text{Au(I)}]_t$ is shown in Figure 4. Low pH values are required for the formation of either of the mpt -containing complexes. The formation of the mixed-ligand complex is clearly unfavorable compared to Au(CN)_2^- and Au(mpt)_2^+ .

The overall stabilities of Au(mpt)_2^+ , $\log \beta_2^{\text{mpt}} = 23.3$, and Au(CN)(mpt) , $\log \beta_{11} = 30.9$, are comparable to other known $\log \beta$ values for Au(I) complexes in aqueous solution (Table III). The order of β_2 values for a series of S-donors with Au(I) is



A very similar order is found for the stability of the corresponding complexes of the isoelectronic Hg(II) .^{19,20}

The tendency for ligand redistribution according to eq 3 is a useful measure of the stability of mixed-ligand complexes. Values



$$K_{\text{rd}} = [\text{Au(X)(Y)}]^2/[\text{Au(X)}_2][\text{Au(Y)}_2]$$

of $\log K_{\text{rd}}$ in Table III show that, in general, the tendency to redistribute is close to the statistical expectation, $\log K_{\text{rd}} = 0.6$.²¹

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Table IV. Kinetics of the Reaction of mpt with $\text{Au}(\text{CN})_2^-$ in Acidic Solution, $[\text{Au}(\text{CN})_2^-]$ Dependence^a

pH	buffer	$10^4[\text{HCN}]$, ^b M	$10^5[\text{mpt}]$, ^b M	correln ^c
2.07	$[\text{HClO}_4] = 8.51 \times 10^{-3}$ M	1.07	1.59	$10^3 k_{\text{obsd}} = 4.6 (\pm 1.4) + 1.1 (\pm 0.1) \times 10^3 [\text{Au}(\text{CN})_2^-]$
2.64	$[\text{ClCH}_2\text{COOH}]_t = 0.010$ M	1.18	1.37	$10^3 k_{\text{obsd}} = 16 (\pm 3) + 1.5 (\pm 0.2) \times 10^3 [\text{Au}(\text{CN})_2^-]$
3.19	$[\text{ClCH}_2\text{COOH}]_t = 0.010$ M	1.07	1.59	$10^3 k_{\text{obsd}} = 26 (\pm 3) + 1.7 (\pm 0.1) \times 10^3 [\text{Au}(\text{CN})_2^-]$
3.75	$[\text{CH}_3\text{COOH}]_t = 0.010$ M	1.05	1.36	$10^3 k_{\text{obsd}} = 92 (\pm 4) + 1.4 (\pm 0.2) \times 10^3 [\text{Au}(\text{CN})_2^-]$

^a 25.0 °C; $I = 0.1$ M ((Na,H)ClO₄). ^b Initial concentrations. ^c Linear least-squares regression k_{obsd} vs $[\text{Au}(\text{CN})_2^-]$; uncertainties are ± 1 standard deviation.

Table V. Kinetics of the Reaction of mpt with $\text{Au}(\text{CN})_2^-$ in Acidic Solution, $[\text{HCN}]$ Dependence^a

pH	buffer	$10^3[\text{Au}(\text{CN})_2^-]$, ^b M	$10^5[\text{mpt}]$, ^b M	correln ^c
2.80	$[\text{ClCH}_2\text{COOH}]_t = 0.010$ M	10.0	1.61	$10^3 k_{\text{obsd}} = 13 (\pm 3) + 1.07 (\pm 0.05) \times 10^5 [\text{HCN}]$ ^b
3.12	$[\text{ClCH}_2\text{COOH}]_t = 0.010$ M	15.0	1.60	$10^3 k_{\text{obsd}} = 25 (\pm 16) + 2.04 (\pm 0.08) \times 10^5 [\text{HCN}]$ ^b
3.54	$[\text{ClCH}_2\text{COOH}]_t = 0.010$ M	15.0	1.60	$10^3 k_{\text{obsd}} = 28 (\pm 14) + 5.8 (\pm 0.7) \times 10^5 [\text{HCN}]$ ^b
3.74	$[\text{CH}_3\text{COO}]_t = 0.010$ M	16.1	1.36	$10^3 k_{\text{obsd}} = 18 (\pm 11) + 9.7 (\pm 0.7) \times 10^5 [\text{HCN}]$ ^b
3.91	$[\text{CH}_3\text{COO}]_t = 0.010$ M	15.0	1.60	$10^3 k_{\text{obsd}} = 49 (\pm 30) + 15 (\pm 1) \times 10^5 [\text{HCN}]$ ^b

^a 25.0 °C; $I = 0.1$ M ((Na,H)ClO₄). ^b Initial concentrations. ^c Linear least-squares regression k_{obsd} vs $[\text{HCN}]$; uncertainties are ± 1 standard deviation.

The formation of $\text{Au}(\text{CN})(\text{mpt})$, however, is markedly disfavored ($\log K_{\text{rd}} = -0.5$), whereas $\text{Au}(\text{CN})\text{I}$ is favored ($\log K_{\text{rd}} = 0.3$). It is interesting to note that redistribution reactions that involve $\text{Hg}(\text{CN})_2$ show a similar pronounced trend of decreasing K_{rd} with decreasing $\Delta \log \beta_2$ ($= \log \beta_2^{\text{CN}^-} - \log \beta_2^{\text{X}}$).²²

Kinetic Studies. The kinetics of eq 1 were studied under pseudo-first-order reversible conditions with $[\text{Au}(\text{CN})_2^-]$ and $[\text{HCN}]$ in excess.²³ The reaction was monitored at 340 nm, where an absorbance increase was observed, or 360 nm, where a decrease was observed. These signal changes are consistent with the spectral differences between mpt and $\text{Au}(\text{CN})(\text{mpt})$; cf. Figure 2.

The kinetic data exhibited excellent first-order behavior. The pseudo-first-order rate constant, k_{obsd} , is independent of $[\text{mpt}]$ and monitoring wavelength. Thus, the kinetic data are described by eq 4. Study of the dependence of k_{obsd} on pH, $[\text{Au}(\text{CN})_2^-]$, and

$$d[\text{Au}(\text{CN})(\text{mpt})]/dt = -d[\text{mpt}]/dt = k_{\text{obsd}}[\text{mpt}] \quad (4)$$

$[\text{HCN}]$ permitted elucidation of the reaction mechanism.

At a given pH and $[\text{HCN}]$, k_{obsd} increases linearly with $[\text{Au}(\text{CN})_2^-]$ (Figure 5). Linear-least-squares regressions for these $[\text{Au}(\text{CN})_2^-]$ dependence experiments are summarized in Table IV.

The kinetics of the ligand-substitution reaction could not be studied above pH 4. Although the signal observed under such conditions appeared to be first order, the value obtained for k_{obsd} was wavelength dependent. Only a small fraction of the initial mpt is converted to $\text{Au}(\text{CN})(\text{mpt})$ at equilibrium above pH 4. Much higher $[\text{mpt}]$ was therefore needed to produce a measurable kinetic signal. On the basis of spectrophotometric measurements, we have evidence that mpt itself reacts with CN^- under such conditions. We believe the kinetics observed for reaction mixtures above pH 4 are complicated by the superposition of an unknown process on the ligand exchange of eq 1. It is likely that cyanide undergoes an addition reaction with mpt to produce a more reactive S donor. Analogous reactions are well-known for α, β -unsaturated carbonyl compounds.²⁴ Lower $[\text{mpt}]$ and lower $[\text{CN}^-]$ ($< 5 \times 10^{-8}$ M) in the experiments below pH 4 did not favor the nucleophilic addition reaction. Those experiments thus accurately measure the ligand-exchange process of interest.

The kinetic results obtained below pH 4 indicate that mixed-ligand complex formation occurs by direct reaction of $\text{Au}(\text{CN})_2^-$ with mpt. The increase of the intercept with increasing pH (cf. Figure 5) suggests that the reverse reaction is faster with CN^-

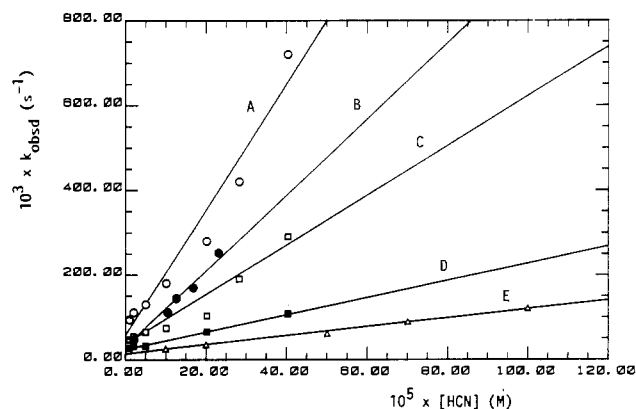


Figure 6. Resolution of the $[\text{Au}(\text{CN})_2^-]$ -independent term from k_{obsd} ($[\text{HCN}]$ dependence) at 25 °C, $I = 0.1$ M ((Na,H)ClO₄): (A) pH 3.91, $[\text{OAc}]_t = 0.01$ M, $[\text{mpt}] = 1.60 \times 10^{-5}$ M, $[\text{Au}(\text{CN})_2^-] = 1.50 \times 10^{-2}$ M; (B) pH 3.74, $[\text{OAc}]_t = 0.01$ M, $[\text{mpt}] = 1.36 \times 10^{-5}$ M, $[\text{Au}(\text{CN})_2^-] = 1.61 \times 10^{-2}$ M; (C) pH 3.54, $[\text{ClCH}_2\text{COOH}]_t = 0.01$ M, $[\text{mpt}] = 1.60 \times 10^{-5}$ M, $[\text{Au}(\text{CN})_2^-] = 10^{-2}$ M; (D) pH 3.12, $[\text{ClCH}_2\text{COOH}]_t = 0.01$ M, $[\text{mpt}] = 1.60 \times 10^{-5}$ M, $[\text{Au}(\text{CN})_2^-] = 1.50 \times 10^{-2}$ M; (E) pH 2.80, $[\text{ClCH}_2\text{COOH}]_t = 0.01$ M, $[\text{mpt}] = 1.61 \times 10^{-5}$ M, $[\text{Au}(\text{CN})_2^-] = 1.00 \times 10^{-2}$ M.

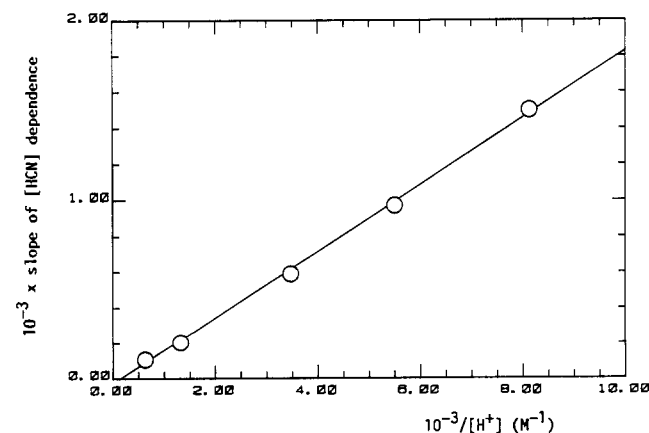


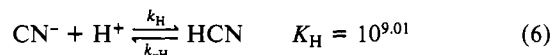
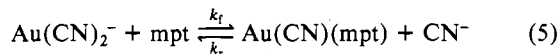
Figure 7. Resolution of k_r from the $[\text{Au}(\text{CN})_2^-]$ -independent term (slope of $[\text{HCN}]$ dependence cf. Figure 6).

than with HCN . The exact nature of the $[\text{Au}(\text{CN})_2^-]$ -independent contribution to k_{obsd} (intercepts in Figure 5) was revealed by studying k_{obsd} as a function of $[\text{HCN}]$ at various fixed pH and $[\text{Au}(\text{CN})_2^-]$ values. Results of such experiments show that k_{obsd} is linear in $[\text{HCN}]$ (Figure 6). With increasing pH and HCN excess the amplitudes of the observed signals decrease strongly for these experiments. This is in agreement with expected equilibrium positions. The error limits of the evaluated k_{obsd} values

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- (23) More precisely, $[\text{HCN}]$ was in excess compared to the change in $[\text{mpt}]$. Relatively small $[\text{HCN}]$ may be used at higher pH values because the extent of reaction is very small. E.g., at pH 3.5, $[\text{Au}(\text{CN})_2^-] = 5 \times 10^{-3}$, and $[\text{mpt}] = 1.5 \times 10^{-5}$ M, the reaction is pseudo first order in $[\text{HCN}]$ even when $[\text{HCN}] = 2[\text{mpt}]$.
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are relatively large. Thus, the upward curvature for parts A–C is statistically not significant. Parameters from linear least-squares analyses of these data are summarized in Table V. The slope of the [HCN] dependence is linear in $1/[H^+]$ (Figure 7).

In agreement with the kinetic behavior described above, the proposed mechanism for the ligand-substitution reaction of mpt with $Au(CN)_2^-$ is given by eq 5–6. The kinetics of eq 6 was



studied by Bednar and Jencks.²⁵ The reported rate constants for the proton transfers (20 °C, $I = 1.0$ M) are $k_H = 4 \times 10^{10} M^{-1} s^{-1}$ and $k_{-H} = 40 s^{-1}$. Thus, the equilibrium in eq 6 is established rapidly during the ligand-substitution reaction. The rate expression for the proposed mechanism is eq 7. In buffered solutions where

$$-d[mpt]/dt = k_f[Au(CN)_2^-][mpt] - k_r[Au(CN)(mpt)][CN^-] \quad (7)$$

$pH \ll \log K_H$, $[mpt] \ll [HCN]$, and $[mpt] \ll [Au(CN)_2^-]$, the expression for k_{obsd} is eq 8. Values for k_f and k_r were resolved from the $[Au(CN)_2^-]$ and [HCN] dependences in accord with eq 8.

$$k_{obsd} = k_f[Au(CN)_2^-] + k_r[HCN]/K_H[H^+] \quad (8)$$

The slope of the $[Au(CN)_2^-]$ dependences shown in Figure 5 is equal to k_f . We obtained $k_f = 1.4 \pm 0.2 M^{-1} s^{-1}$. The best measure of k_r is provided by the relationship between the slope of the [HCN] dependence and $1/[H^+]$. The slope ($=k_r/K_H$) of the regression in Figure 7 is $0.186 (\pm 0.004) s^{-1}$. Thus, we obtained $k_r = 1.90 (\pm 0.04) \times 10^8 M^{-1} s^{-1}$.

Actually, both k_f and k_r could be resolved from the $[Au(CN)_2^-]$ dependence alone or from the [HCN] dependence alone. Greater precision was obtained for values calculated from slopes of linear regressions, but there was also important information contained in the intercepts of both the $[Au(CN)_2^-]$ dependence and [HCN] dependence.

The intercept of the $[Au(CN)_2^-]$ dependence is equal to $k_r[HCN]/K_H[H^+]$. Thus, for each of the regressions in Table IV we could calculate k_r . The value obtained, $k_r = 2 (\pm 1) \times 10^8 M^{-1} s^{-1}$, is in excellent agreement with the more precise value resolved from the [HCN] dependence. Similarly, the intercept of the [HCN] dependence permits calculation of k_f . The intercept is equal to $k_f[Au(CN)_2^-]$. We calculated $k_f = 1.8 (\pm 0.8) M^{-1} s^{-1}$ by this method, again in agreement with the more precise determination. The agreement between alternative calculations of both k_f and k_r support the proposal that direct reaction of the incoming ligand (either mpt or CN^-) is the only significant reaction pathway in either direction. There are no measurable solvent paths in either direction and no evidence that HCN is a reactive species. The absence of a measurable HCN path for the formation of $Au(CN)_2^-$ from $Au(CN)(mpt)$ is further shown by the statistically zero intercept in Figure 7. We estimate an upper limit of $25 M^{-1} s^{-1}$ for the rate constant for the reaction of HCN with Au-

$(CN)(mpt)$. Thus, HCN is at least 8×10^6 less reactive than CN^- with $Au(CN)(mpt)$.

Direct comparison of the equilibrium and kinetic results is possible. The single-step mechanism implies that $k_f/k_r = K$. The calculated value $\log(k_f/k_r) = -8.13$ is in excellent agreement with the constant determined from equilibrium spectrophotometric measurements, $\log K = \log \beta_{11} - \log \beta_2^{CN^-} = 30.9 - 39.0 = -8.1$.

Although $Au(CN)_2^-$ decomposes to yield $AuCN(s)$ in acidic solution, the process is slow compared to the ligand exchange. We saw no indication that a proton-assisted path contributes to the reaction of interest, eq 5. Lack of acid catalysis is shown by the independence of k_f on pH (parallel lines in Figure 5). The basicity of $Au(CN)_2^-$ itself (formation of $H[Au(CN)_2]$), although possibly important at very low pH,²⁶ was shown to play no role in the present study by potentiometric experiments ($pK_a < 1$).

The rate constant $k_r = 1.9 \times 10^8 M^{-1} s^{-1}$ for the reaction of CN^- with $Au(CN)(mpt)$ is much smaller than those for similar reactions with other d^{10} complexes. Substitution of the S donor 4-nitro-2-sulfonatobenzenethiolate ($NTPS^{2-}$) by CN^- at $Ag(CN)(NTPS)^{2-}$ as well as at $CH_3Hg(NTPS)^-$ is diffusion-controlled.¹⁶ The same is the case for various ligand-substitution reactions with thione complexes of CH_3Hg^{II} .⁹ This distinct reactivity difference is even more remarkable when one considers that these reactions with Hg(II) and Ag(I) are much less exergonic than that with Au(I). The fact that k_r is appreciably smaller than expected by analogy to other d^{10} systems suggests that a fundamentally different mechanism may be in operation. However, the dramatic difference in reactivity between HCN and CN^- is strong support of an associative mechanism as commonly proposed for ligand exchange at digonal d^{10} centers. A reactivity difference between CN^- and HCN at least as large as that of the present study was observed for the formation of 2-(cyanomercurio)-4-nitrophenol from 2-((NTPS)mercurio)-4-nitrophenol.²⁷ Nucleophilicity has a very large effect on the ligand-substitution process at digonal d^{10} centers.

The reaction of mpt with $Au(CN)_2^-$ is slow ($k_f = 1.4 M^{-1} s^{-1}$), but this is expected for such an endergonic reaction. The investigation of ligand-exchange reactions of CH_3Hg^{II} complexes with a variety of ligands showed that the correlation between rate and equilibrium constants is similar to a Marcus-type relation for atom transfer.⁹ Series of similar reactions are characterized by an intrinsic barrier. Ligand-exchange rate constants approach the diffusion-controlled limit as the reactions become more exergonic. Thus it is likely that ligand-exchange reactions at $Au(CN)_2^-$ with S donors that have higher affinities than mpt are much faster.

The rate and equilibrium constants presented in this work constitute an important step toward characterizing ligand-substitution reactions on gold(I) complexes by rate-equilibria relationships that are a conducive basis for the detailed understanding of the dynamics of Au(I) in biological systems.

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Registry No. mpt, 2044-27-1; $Au(CN)_2^-$, 14950-87-9; $[Au(mpt)_2]ClO_4$, 115406-89-8.

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