for reaction 11, strongly implicates Cr^{2+} as a crucial intermediate. The effect of methanol on the overall stoichiometry requires at least one additional intermediate, which we believe to be CrO^{2+}. One plausible scheme in the absence of CH_3OH (Scheme II)

Scheme II

chain initiation

$$CrO_2^{2+} + CrCH_2OH^{2+} \rightarrow Cr^{2+} + CH_2O + H_2O \quad (11)$$

chain propagation

$$CrO_2^{2+} + Cr^{2+} \rightarrow nCrO^{2+} \quad (18)$$

$$CrO^{2+} + CrCH_2OH^{2+} \xrightarrow{H^+} Cr^{2+} + Cr^{3+} + CH_2O + H_2O \quad (20)$$

consists of reaction 11 to form Cr^{2+}, reduction of CrO_2^{2+} to CrO^{2+} (eq 18), and oxidation of $CrCH_2OH^{2+}$ (eq 20). Although we have very little information on reaction 20, we expect it to yield Cr^{2+}, irrespective of whether the reaction takes place by a one- or two-electron pathway. A complete study of the air-free reaction between CrO_2^{2+} and $CrCH_2OH^{2+}$ and of reactions 18 and 20 is in progress.[13]

Acknowledgment. This research was supported by the National Science Foundation (Grant CHE-9007283). Some of the work was carried out in the facilities of Ames Laboratory. S.L.S. acknowledges receipt of a 1967 Science and Engineering Scholarship from the Natural Sciences and Engineering Research Council of Canada.

Registry No. CrO_2^{2+}, 115185-67-6; $CrCH_2OH^{2+}$, 32108-95-5; $CrCD_2OD^{2+}$, 136358-09-3; CrO_2H^{2+}, 136358-10-6; CH_2O, 50-00-0.

Contribution from the Department of Medicinal Chemistry, Hiroshima University, School of Medicine, Kasumi, Minami-ku, Hiroshima 734, Japan, Coordination Chemistry Laboratories, Institute for Molecular Science, Myodaiji, Okazaki 444, Japan

The First Gold(III) Macrocyclic Polyamine Complexes and Application to Selective Gold(III) Uptake

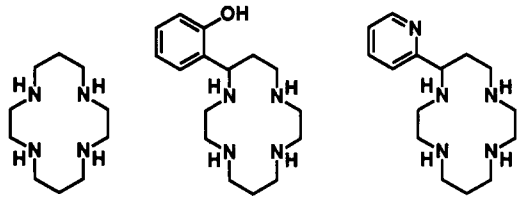
Eiichi Kimura,*[†,‡] Yasuhisa Kurogi,[†] and Toshikazu Takahashi[†]

Received July 11, 1991

The hitherto unreported gold(III) macrocyclic polyamine complexes **12**, **14**, **18**, **19**, **23**, and **24** with cyclam (1,4,8,11-tetraazacyclotetradecane, **1**), phenol-pendant cyclam **2**, pyridyl-pendant cyclam **3**, monooxocyclam **4**, phenol-pendant monooxocyclam **5**, and pyridyl-pendant monooxocyclam **6** have been synthesized and characterized. Dissociation of a proton from one of the secondary amines in the "Au^{III}-in" cyclam complexes **12**, **14**, and **18** readily occurs with pK_a values of 5.0–5.4 at 25 °C and I = 0.1 ($NaClO_4$). Although monooxocyclam **4** does not accommodate Au(III), the donor-pendant monoxocyclams **5** and **6** enclose Au(III) with concomitant dissociation of an amide proton to yield **23** and **24**, respectively. As anticipated for the diamagnetic d^8 complexes, the pendant donors only weakly interact from an axial site. The extraordinary acidity of Au(III) over other common metal ions in interaction with cyclam can be utilized for selective uptake of Au(III) with lipophilic cyclam derivatives **9** and **10**.

Introduction

Although cyclam (1,4,8,11-tetraazacyclotetradecane, **1**) has been widely used to sequester metal ions,[1] its complex with Au(III) is unknown. This is very puzzling in the light of the well-documentable Au(III) ability to form square-planar tetraamine (e.g. tetraamine, bis(ethylenediamine)) complexes.[2-4]



1 Cyclam — **2** Phenol-pendant cyclam — **3** Pyridyl-pendant cyclam

We now have isolated the Au(III)–cyclam complex **12**. Its characterization has disclosed a rigid N_4 square planarity and strong acidity of Au(III). This encouraged us to study more about the Au(III) complexation with phenol-pendant cyclam **2**,[5-11] pyridyl-pendant cyclam **3**,[12-14] and the corresponding monooxocyclams **4–6**,[15-18] which were extremely useful in defining the acidic and coordinating properties of Cu^{II},[7,10,14,16] Ni^{II},[6-10,12-14,16,17] or Zn^{II}.[7,11,18] We were also interested in how the Au(III) acidity is reflected in the smaller macrocyclic ring **7**. As the Au(III) interaction mode with macrocyclic tetraamines was disclosed, an application of cyclam derivatives **9–11** for Au(III) uptake has been investigated. The results have proved the macrocyclic polyamines

[†] Hiroshima University.
[‡] Institute for Molecular Science.

(1) (a) Bosnich, B.; Poon, C. K.; Tobe, M. L. *Inorg. Chem.* **1965**, *4*, 1102. (b) Endicott, J. F.; Lilie, J.; Kuszaj, J. M.; Ramaswamy, B. S.; Schmonsees, W. G.; Simic, M. G.; Glick, M. D.; Rillema, D. P. *J. Am. Chem. Soc.* **1977**, *99*, 429. (c) Zeigerson, E.; Ginzburg, G.; Schwartz, N.; Luz, Z.; Meyerstein, D. *J. Chem. Soc., Chem. Commun.* **1979**, 241. (d) Zuckman, S. A.; Freeman, G. M.; Troutner, D. E.; Volkert, W. A.; Holmes, R. A.; Van Derveer, D. G.; Barefield, E. K. *Inorg. Chem.* **1981**, *20*, 2386. (e) Walker, D. D.; Taube, H. *Inorg. Chem.* **1981**, *20*, 2828. (f) Ito, T.; Sugimoto, M.; Toriumi, K.; Ito, H. *Chem. Lett.* **1981**, 1477. (g) Yamashita, M.; Ito, H.; Toriumi, K.; Ito, T. *Inorg. Chem.* **1983**, *22*, 1566. (h) Beley, M.; Collin, J.-P.; Ruppert, R.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1986**, *108*, 7461. (i) Shionoya, M.; Kimura, E.; Iitaka, Y. *J. Am. Chem. Soc.* **1990**, *112*, 9237.
(2) Skibsted, L. H.; Bjerrum, J. *Acta Chem. Scand.* **1974**, *A28*, 740.
(3) Baddley, W. H.; Basolo, F.; Gray, H. B.; Nölting, C.; Pöe, A. J. *Inorg. Chem.* **1963**, *2*, 921.
(4) Kim, J.-H.; Everett, G. W., Jr. *Inorg. Chem.* **1981**, 853.
(5) Kimura, E.; Koike, T.; Takahashi, M. *J. Chem. Soc., Chem. Commun.* **1985**, 385.
(6) Iitaka, Y.; Koike, T.; Kimura, E. *Inorg. Chem.* **1986**, *25*, 402.
(7) Kimura, E.; Yamaoka, M.; Morioka, M.; Koike, T. *Inorg. Chem.* **1986**, *25*, 3883.
(8) Kimura, E.; Koike, T.; Uenishi, K.; Davidson, R. B. *J. Chem. Soc., Chem. Commun.* **1986**, 1110.
(9) Kimura, E.; Uenishi, K.; Koike, T.; Iitaka, Y. *Chem. Lett.* **1986**, 1137.
(10) Kimura, E.; Koike, T.; Uenishi, K.; Hediger, M.; Kuramoto, M.; Joko, S.; Arai, Y.; Kodama, M.; Iitaka, Y. *Inorg. Chem.* **1987**, *26*, 2975.
(11) Kimura, E.; Kurosaki, H.; Koike, T.; Toriumi, K. *J. Inclusion Phenom.*, in press.
(12) Kimura, E.; Koike, T.; Nada, H.; Iitaka, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 1322.
(13) Kimura, E. *Pure Appl. Chem.* **1989**, *61*, 823.
(14) Kimura, E.; Kotake, Y.; Koike, T.; Shionoya, M.; Shiro, M. *Inorg. Chem.* **1990**, *29*, 4991.
(15) Machida, R.; Kimura, E.; Kodama, M. *Inorg. Chem.* **1983**, *22*, 2055.

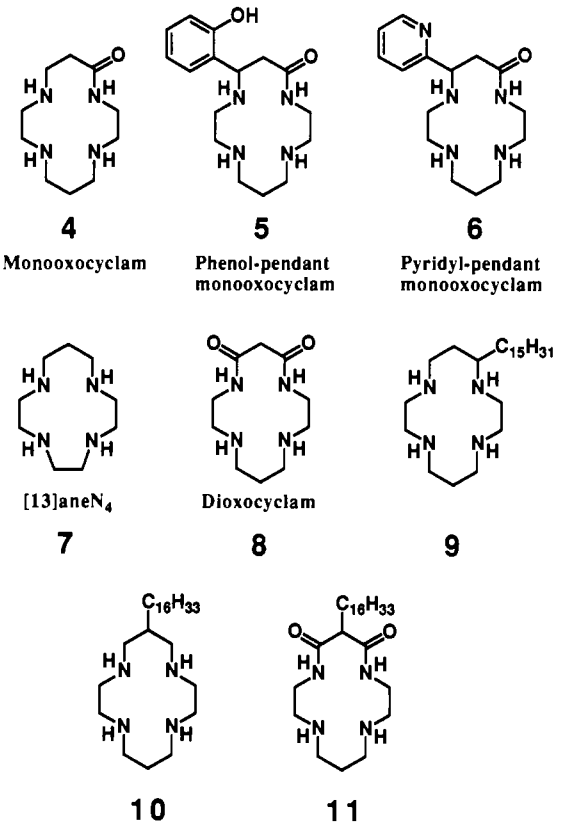
0020-1669/91/1330-4117$02.50/0

Table I. New Au^{III} Complexes of Macrocyclic Polyamines

compd	% yield of isolated salts[c]	formula[b]	IR (KBr) $\nu_{C=O}$, cm^{-1}	UV[c] λ_{max}, nm (ϵ)	^{13}C NMR[d] δ, ppm[e]
12 (yellow needles)	17	$C_{10}H_{24}N_4AuCl(ClO_4)_2$		360 (2160)	31.9, 53.2, 59.1
14 (yellow needles)	19	$C_{16}H_{28}N_4OAuCl_2(ClO_4)$		356 (2840)	31.9, 53.7, 59.0, 59.8, 119.2, 124.1, 134.0, 146.1
				268 (6000)	
18 (yellow plates)	8	$C_{15}H_{27}N_5Au(ClO_4)_3 \cdot HClO_4$		358 (2960)	31.5, 53.6, 59.1, 60.1, 128.4, 130.8, 149.2, 151.7, 164.5
19 (yellow needles)	3	$C_{10}H_{22}N_4OAuCl(ClO_4)_2$	1667	334 (2220)	32.2, 40.2, 53.1, 53.8, 54.0, 54.9, 57.8, 59.5, 61.7, 173.1
23 (yellow needles)	3	$C_{16}H_{25}N_4O_2Au(ClO_4)_2$	1588	350 (1850)	32.1, 45.5, 53.3, 53.7, 54.1, 56.0, 59.3, 62.0, 66.0, 119.2, 124.0, 134.5, 146.1, 174.8
				265 (7600)	
24 (yellow needles)	18	$C_{15}H_{24}N_5OAu(ClO_4)_2 \cdot HClO_4$	1593	336 (1850)	32.5, 47.5, 53.2, 53.7, 53.8, 54.6, 60.3, 61.5, 66.0, 127.2, 127.6, 142.0, 151.7, 154.6, 171.2
27 (yellow plates)	41	$C_9H_{22}N_4AuCl_2(AuCl_4) \cdot 2HClO_4$			49.7, 53.3, 57.6, 60.7
28 (yellow powder)	~100	$C_{10}H_{24}N_4AuCl_2(AuCl_4) \cdot 2HCl \cdot H_2O$			17.7, 21.7, 31.6, 53.1, 57.0, 58.9
29 (yellow powder)	~100	$C_{10}H_{22}N_4OAuCl_2(AuCl_4) \cdot HCl$	1638		
30 (yellow powder)	~100	$C_{10}H_{20}N_4O_2AuCl_2(AuCl_4)$	1644		

[a] Yields based on $NaAuCl_4$. [b] All these complexes gave satisfactory analyses within ±0.4%. [c] At 25 °C in H_2O (pH 8); ϵ, M^{-1} cm^{-1}. [d] At 35 °C in D_2O (pD 1). [e] Chemical shifts from internal 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (d^4).

to be the first promising prototype ligands for selective Au(III) uptake.



Results and Discussion

"Au^{III}-in" Cyclam Complex 12. Treatment of $NaAuCl_4 \cdot 2H_2O$ with equimolar cyclam **1** in refluxing CH_3CN for 1 h yielded "Au^{III}-in" complex **[12]**$Cl(ClO_4)_2$ as yellow needles, which were purified by Dowex 50X4 ion-exchange column chromatography (eluent: 3 N HCl) and recrystallization from aqueous 1 N $HClO_4$ solution. The reaction was neat and only one product, **12**, was detected on silica gel TLC (eluent: 1:1 CH_3OH–10% aqueous NaCl; R_f = 0.6). **12** is stable as a solid and in acidic aqueous solution.

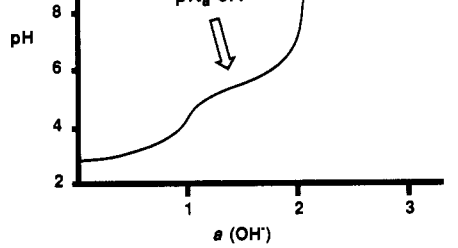
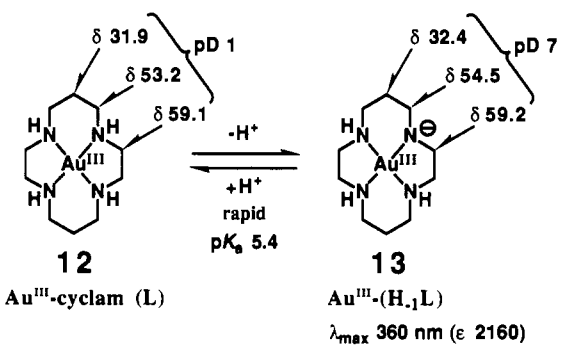


Figure 1. pH titration curves of "Au^{III}-in" cyclam complex **12** with 0.1 M NaOH at 25 °C and I = 0.1 ($NaClO_4$).



The pH titration of **12** with 0.1 M NaOH (Figure 1) showed removal of a proton with a pK_a value of 5.4 (at 25 °C, I = 0.1 M, $NaClO_4$), which is assigned to the deprotonation from one of the secondary amines of cyclam (L) to $Au^{III}(H_{-1}L)$, **13**. The deprotonated **13** has a characteristic $(N^-) \rightarrow Au^{III}$ charge-transfer (CT) absorption band[3] at λ_{max} = 360 nm (ϵ = 2160) above pH 7, which reversibly diminished upon protonation back to **12** (Figure 2). However, **13** in neutral to alkaline solution is unstable and tends slowly to decompose to precipitate gold metal. The dissociation of a proton from the cyclam NH with such a low pK_a value has never been observed with other cyclam metal complexes: very strong alkaline conditions are usually required to generate M-$(H_{-1}L)$.[19] In previous square-planar tetraamine complexes of Au(III), similar proton dissociation constants and the CT absorption bands have been reported: e.g. pK_a = 7.5 (I = 1.0 M)

(16) Kimura, E.; Koike, T.; Machida, R.; Nagai, R.; Kodama, M. *Inorg. Chem.* **1984**, *23*, 4181.
(17) Kimura, E.; Koike, T.; Nada, H.; Iitaka, Y. *Inorg. Chem.* **1988**, *27*, 1036.
(18) Kimura, E.; Koike, T.; Shiota, T.; Iitaka, Y. *Inorg. Chem.* **1990**, *29*, 4621.
(19) Barefield, E. K.; Mocella, M. T. *J. Am. Chem. Soc.* **1975**, *97*, 4238.

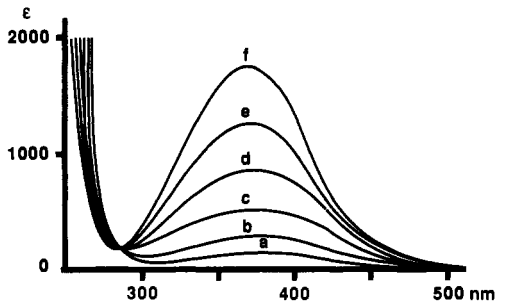
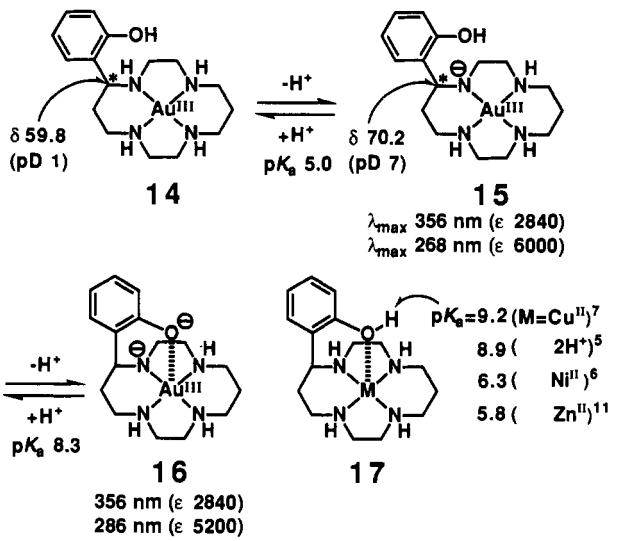


Figure 2. UV absorption spectra of **12** at 25 °C and I = 0.1 ($NaClO_4$). pH values are (a) 2.9, (b) 4.1, (c) 4.7, (d) 5.5, (e) 5.9, and (f) 7.1.

and λ_{max} = 300 nm (ϵ = 1470) for $Au^{III}(NH_3)_4$[2] and pK_a = 6.3 (I = 0.5) for $Au^{III}(en)_2$ (en = ethylenediamine).[3]

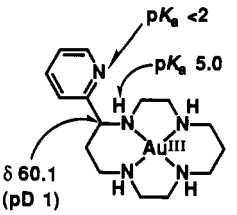
The ^{13}C NMR spectrum of **12** in D_2O at pD 1 (Table I) showed only three signals at δ 31.9, 53.2, and 59.1 ppm, while that of **13** at pD 7 displayed those at lower fields, δ 32.4, 54.5, and 59.2 ppm, which also implies rapid (on NMR scale) equilibrium for **12** ⇌ **13**, so that the four nitrogens remain equivalent. In a square-planar Zn^{II}–cyclam complex,[20] the ^{13}C NMR spectrum showed three similar signals at δ 28.7, 48.4, and 50.7 ppm in D_2O.

Gold(III) Phenol- and Pyridyl-Pendant Cyclam Complexes 14 and 18. The phenol-pendant cyclam **2** was similarly treated with $NaAuCl_4$ in CH_3CN to afford an Au(III) enclosure complex, **14**, as a major product, but prolonged reaction time made more complex reactions, resulting in formation of a few more unidentified byproducts, as shown on silica gel TLC (eluent: 1:1 CH_3OH–10% aqueous NaCl). The ^{13}C NMR spectrum of **14** in D_2O at pD 1 (Table I) defined a peak at δ 59.8 ppm as the tertiary C* bearing the phenol pendant. Reversible deprotonation with pK_a of 5.0 (pH metrically determined at 25 °C, I = 0.1 M, $NaClO_4$) occurs at the adjacent NH to **15**, as evidenced by the most dramatic low-field shift of the tertiary C* to δ 70.2 ppm at pD 7. This process is accompanied by the emergence of the CT absorption band at λ_{max} = 356 nm (ϵ = 2840) for **15**, as was seen for the pendant-less cyclam complex **13**.



The second deprotonation occurs at the phenol group with pK_a = 8.3 for **15** ⇌ **16**, which is confirmed by the UV absorption spectral change from λ_{max} = 268 nm (ϵ = 6000) to 286 nm (ϵ = 5200) due to the phenol ⇌ phenolate equilibrium with an increase in pH. It is significant that the phenolic proton dissociates only after the cyclam NH does, despite the former being far more acidic than the latter normally. This is an unambiguous illustration of the strong Au^{III} (d^8) acidity extending only to the N_4 square-planar direction. The pK_a value of 8.3 for **15** ⇌ **16** should be compared with those for phenol (pK_a = 9.8) and for the same complexes, **17**, with other cations: pK_a = 8.9 (for M = $2H^+$),[5] 9.2 (Cu^{II}),[7] 6.3 (high-spin Ni^{II}),[6] and 5.8 (Zn^{II}).[11] Apparently the axial phenolate bonding with Au^{III} (d^8) would not be as short as those with Ni^{II} (high-spin d^8; Ni^{II}–O^- bond distance of 2.02 Å)[6] and Zn^{II} (d^{10}; Zn^{II}–O^- bond distance of 1.98 Å).[11] The weaker acidity of the phenolic proton in the Au^{III} complex **15** than for the Ni^{II} and Zn^{II} complexes **17** results from the effects of an anionic (N^-) donor from cyclam and the d^8 configuration of Au^{III}. Interestingly, the phenolate absorption band (λ_{max} = 286 nm (ϵ = 5200)) for Au^{III} complex **16** is not far from those for Zn^{II} (λ_{max} = 288 nm (ϵ = 2600)),[11] $2H^+$ (λ_{max} = 292 nm (ϵ = 4000))[5] or Ni^{II} complex **17** (λ_{max} = 293 nm (ϵ = 3700)).[10] The absence of an phenol → Au^{III} CT band (coupled with the high pK_a of the phenolic proton) together indicate that the phenol interacts minimally with the Au^{III} center.

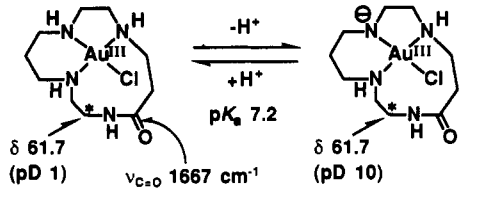
The pyridyl-pendant cyclam **3** was similarly reacted with $NaAuCl_4$ to exclusively produce an Au(III) enclosure complex, **18**, which was purified in the same manner as **14**. The pH titratiton of **18** with 0.1 M NaOH showed removal of a proton with a pK_a value of 5.0 (at 25 °C, I = 0.1 M, $NaClO_4$), which is assigned to the deprotonation from the secondary amine next to the tertiary C* bearing the pyridyl pendant. This process is accompanied by the emergence of the CT absorption at λ_{max} = 358 nm (ϵ = 2960), as was seen for the previous cyclam complexes **13** and **15**. The axial pyridyl donor does not seem to bind with Au^{III}, which evidence comes from the same chemical shifts (^{13}C NMR) of pyridyl carbons for **18** and free ligand at pD 1 (Table I). The pyridyl N is almost nonbasic, pK_a < 2. Both **14** and **18** are stable in acidic solution, but unstable in alkaline solution (pH >9).



Gold(III) Monooxocyclam Complex 19. Treatment of **4** with an equimolar of $NaAuCl_4 \cdot 2H_2O$ in CH_3CN at room temperature for 2 days yielded almost exclusively (on the same TLC column as before) a 1:1 Au^{III} complex, **19**, which was purified by Dowex 50X4 ion-exchange column chromatography (eluent: 3 N HCl) and recrystallization from aqueous 1 N $HClO_4$ solution. The "Au^{III}-out" structure of **19**, where the metal is coordinated by three NH's and one Cl^- ion, like the Au^{III}(dien)Cl complex **21** (dien = diethylenetriamine),[24] was assigned on the basis of elemental analysis, $\nu_{C=O}$ of 1667 cm^{-1} (uncoordinated amide, cf. 1663 cm^{-1} for free ligand **4**), and ^1H and ^{13}C NMR spectral data; see Table I.

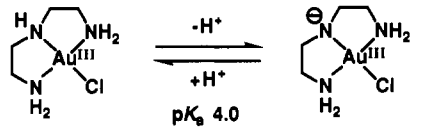
The "Au^{III}-out" monooxocyclam complex **19** showed deprotonation from the secondary amine with pK_a = 7.2, which was measured by the emergence of the CT absorption band at 334 nm (ϵ = 2220), as discussed for the former cyclam complexes. A pK_a value of 4.0 (I = 0.5 M) for the dien complex **21** ⇌ **22** reaction (λ_{max} = 369 nm (ϵ = 1900)) was reported.[3,24] **19** with an uncoordinated amide (δ 61.7 ppm at pD 1 for the C* adjacent to NHCO) was unable to go to the "Au^{III}-in" complex with amide deprotonation even under alkaline conditions (pD 10), as demonstrated by the unchanging δ 61.7 ppm for C* NHCO. However,

(20) Kato, M.; Ito, T. *Inorg. Chem.* **1985**, *24*, 504.
(21) Kimura, E.; Korenari, S.; Shionoya, M.; Shiro, M. *J. Chem. Soc., Chem. Commun.* **1988**, 1166.
(22) Kimura, E.; Dalimunte, C. A.; Yamashita, A.; Machida, R. *J. Chem. Soc., Chem. Commun.* **1985**, 1041.
(23) Kimura, E.; Lin, Y.; Machida, R.; Zenda, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1020.
(24) Nardin, G.; Randaccio, L.; Annibale, G.; Natile, G.; Pitteri, B. *J. Chem. Soc., Dalton Trans.* **1980**, 220.
(25) *Kagaku Binran*, 3rd ed.; Chemical Society of Japan: Tokyo, 1984; Vol. II.



19 **20**

λ_{max} 334 nm (ε 2220)

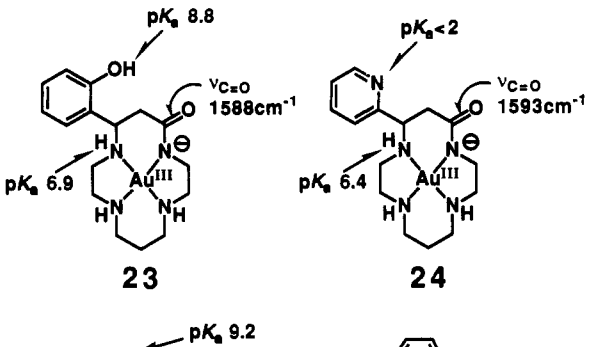


21 **22**

λ_{max} 369 nm (ε 1900)

the story is different for the following pendant-monooxocyclam complexes.

Gold(III) Phenol- and Pyridyl-Pendant Monooxocyclam Complexes 23 and 24. The phenol-pendant **5** and pyridyl-pendant monooxocyclam **6** yielded the "Au^{III}-in" products **23** (a major product) and **24** (an exclusive product, shown on silica gel TLC), respectively. Previously, we reported that Ni^{II} [16,17] and Zn^{II} [18] gave all the "M^{II}-in" complexes **25** and **26** with these ligands, which commonly showed the characteristic $\nu_{C=O}$ at ~1580 cm^{-1} indicative of the amide deprotonations and the M^{II} encapsulation. The square-pyramidal structures of **26** with Ni^{II} [17] and Zn^{II} [18] have been established by X-ray crystal analyses. The unique feature of the Au^{III} complexes, unlike those previous M^{II} complexes, is the extraordinary stability to acids with which **23** and **24** can remain in aqueous 1 N $HClO_4$ solution without protonation (to the imide anion) leading to decomplexation. Under the same conditions, **25** and **26** were readily protonated to dissociate into free ligands and divalent metal ions. In other words, the imide anions are so strongly bound to Au^{III} that there would practically be no anionic N^- electrons to share for protonation. Or, the Au^{III} ions in the cyclam cavities are stronger acids than H^+.

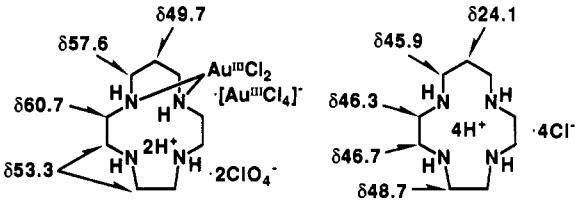


23 **24**

25 M=Cu^{II}, Zn^{II} **26** M=Ni^{II}, Zn^{II}

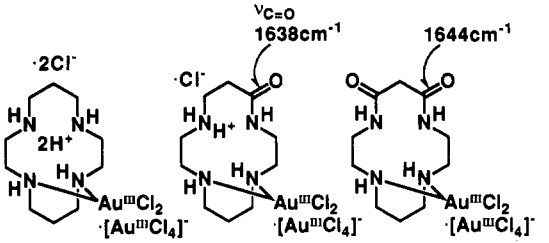
As studied in the preceding cyclam complexes, deprotonation from the phenol group in **23** (pK_a = 8.8) and deprotonation from the secondary amine (pK_a = 6.9 for **23** and 6.4 for **24**) were established. At this moment, we are not certain about the axial phenolate and pyridyl interactions with Au^{III}, but most likely they should be very weak, if any interaction is observed.

Complexation of Au^{III} with [13]aneN$_4$ 7. An identical treatment of $NaAuCl_4$ with **7** as described for cyclam **1** yielded exclusively the 1:1 "Au^{III}-out" complex **27** as yellow plates. The structure of **27** was assigned on the basis of elemental analysis and the ^{13}C NMR spectrum (D_2O at pD 1), where the most dramatic low-field shifts from the protonated free ligand **7** were seen near the proposed Au^{III} binding sites. Prolonged heating of the reaction mixture or of the isolated **27** in CH_3CN or pH 3 aqueous solution failed to produce the "Au^{III}-in" complex, unlike the larger macrocycle, cyclam **1**. Either the recovery of **27** or complex reactions with Au^0 precipitation resulted. Apparently, the 13-membered ring size is not favorable to accommodate Au^{III} in a square-planar structure.



27 **7**·4HCl

Interaction of Au(III) with Cyclam 1, Monooxocyclam 4, and Dioxocyclam 8 in Aqueous 1 N HCl Solution. We have observed that mixing cyclam **1**, monooxcyclam **4**, or dioxocyclam **8** with $NaAuCl_4$ in aqueous 1 N HCl solution immediately (within 1 min) precipitated yellow "Au^{III}-out" diamine complexes **28**, **29**, or **30** all in quantitative yields on the basis of the used $NaAuCl_4$, just as was reported for the reaction of K_2PtCl_4 with **8**.[21] The structure assignments are based on elemental analyses, ^{13}C NMR spectroscopy for **28**, and IR spectra ($\nu_{C=O}$ = 1638 cm^{-1} for **29** and 1644 cm^{-1} for **30**); see Table I.



28 **29** **30**

The isolated **28** and **29** very slowly went to the "Au^{III}-in" complex **12** (yield 3%) and the triamine complex **19**, respectively, both accompanied by dissociation of Au^{III} (major routes) and a partial gold metal precipitation, when further treated in pH 3 aqueous solution at room temperature for 30 h. In pH >7 solution, **28** did not go to **12**, but precipitated insoluble materials (Au_2O_3, Au^0, etc.). When **30** was further heated in CH_3CN or treated with a pH 3–7 solution at 60 °C, dissociation of Au^{III} (as oxides) or Au^0 from the free ligand **8** was observed. The "Au^{III}-in" complex with deprotonation from the two amides was not detected. In contrast, the "Pt^{II}-out" complex with the same structure as **30** went to the "Pt^{II}-in" complex.[21] The prospect of successful reversible Au^{III} uptake with cyclam or its derivatives has prompted us to undertake the cyclam-mediated extraction of Au^{III}.

Macrocyclic Polyamine-Mediated Extraction of Au(III). Previously, we have used a lipophilic dioxocyclam, **10** (soluble in $CHCl_3$, but insoluble in H_2O), as the solvent extraction ligand for Cu^{II} [22] and Pt^{II}.[23] For the solvent extraction of Au^{III}, we have tested **9**, **10**, and **11** as the carrier candidates. The procedure was as follows: 5 mL of 1.0 mM $NaAuCl_4$ with or without a mixture of the same amount of Cu^{II}, Fe^{III}, Co^{II}, and Pd^{II} in an aqueous 1 N HCl solution was well stirred with 5 mL of 2.0 mM ligand **9**, **10**, or **11** in $CHCl_3$ at 25 °C for 30 min. The remaining Au^{III} ion in the 1 N HCl (aqueous layer I) was measured by an atomic absorption spectrophotometer. Then, the Au^{III}-containing (as complexes) $CHCl_3$ layer was reextracted with 5 mL of distilled water (aqueous layer II) at 60 °C for 30 min, which was then assayed for Au^{III}. The results are summarized in Table II.

The best Au^{III} extraction into the $CHCl_3$ layer was achieved in 94% yield with cyclam derivative **9** (entry 3). With the second

Table II. Solvent Extraction of Au(III) with **9**, **10**, and **11** in $CHCl_3$

run	ligand in $CHCl_3$ layer	metal ions,[a] in aqueous layer I	[Au] remaining[b] in aqueous layer I, %	[Au] extracted[b] into aqueous layer II, %
1	none	Au^{III}	100	0
2	none	Au^{III}, Cu^{II}, etc.[c]	100	0
3	**9**	Au^{III}	6	81
4	**9**	Au^{III}, Cu^{II}, etc.[c]	22[d]	67
5	**10**	Au^{III}	16	65
6	**10**	Au^{III}, Cu^{II}, etc.[c]	25[e]	61
7	**11**	Au^{III}	85	9
8	**11**	Au^{III}, Cu^{II}, etc.[c]	99[f]	1
9	n-$C_{16}H_{33}NH_2$	Au^{III}	50	38
10	n-$C_{16}H_{33}NH_2$	Au^{III}, Cu^{II}, etc.[c]	42[g]	25

[a] In 1 N HCl aqueous solution. [b] All the values have errors within ±5%. [c] 1.0 mM each of Au^{III}, Cu^{II}, Fe^{III}, Co^{II}, and Pd^{II} ions were contained in 1 N HCl aqueous solution. [d] Other remaining metal ions are [Pd] = 83%, [Fe] = 99%, and [Cu] = [Co] = 100%. [e] Other remaining metal ions are [Pd] = 46%, [Fe] = 99%, and [Cu] = [Co] = 100%. [f] Other remaining metal ions are [Pd] = [Fe] = [Cu] = [Co] = 100%. [g] Other remaining metal ions are [Pd] = 51% and [Fe] = [Cu] = [Co] = 100%.

$CHCl_3$ treatment, almost all of the remaining Au^{III} was extracted (all together, >97 % yield). The second best ligand was **10** (entry 5). After the second extraction, 92% of Au^{III} was transferred with **10**. The dioxocyclam derivative **11**, which was excellent for Cu^{II} [22] and Pt^{II},[23] did not work well in this case (entry 7). For reference, we have used a lipophilic primary amine (n-$C_{16}H_{33}NH_2$, entry 9) as a carrier, which was proven not as effective as the macrocyclic tetraamines **9** and **10**.

Most interestingly, **9** and **10** showed a remarkable uptake selectivity for Au^{III} over other metal ions (Cu^{II}, Fe^{III}, Co^{II}, Pd^{II}) from aqueous 1 N HCl solution, and hence 78% (entry 4) and 75% (entry 6) of Au^{III} extraction into the $CHCl_3$ solution was respectively acheived; i.e., those other metal ions do not appreciably mask the uptake of Au^{III} by **9** and **10**. However, such Au^{III} selectivity became lower, if the mixture of these metal ions were extracted from pH ~3 aqueous solution, because Fe^{III} (70 and 96%), Co^{II} (65 and 90%), and Pd^{II} ions (95 and 97%) were also extracted into $CHCl_3$ solutions by **9** and **10**, respectively. *An important principle here is to take full advantage of the acidic properties of Au^{III} being the strongest among the competing metal ions to beat the most powerful blocking agent protons for cyclams.*

The Au^{III} ion bound to carrier **9** and **10** in the $CHCl_3$ layer was freed into distilled water (pH ~3, aqueous layer II) with 81% (of the initial Au^{III} ion in aqueous layer I) (entry 3), or 65% (entry 5) recovery yield. Thus, separation of Au^{III} from other metal ions is complete. In independent experiments, the Cu^{II} ion bound to **9** in $CHCl_3$ beforehand prepared at pH 3 could not be extracted into distilled water. Although more works are needed to find the optimum extraction conditions, the present preliminary experiments have well illustrated a promising method of the first selective Au^{III} uptake.

Conclusion

Cyclam **1**, monooxcyclam **4** and their derivatives **2**, **3**, **5**, and **6** form various types of Au^{III} complexes. The first Au^{III}-encapsulated complexes **12**, **14**, **18**, **23**, and **24** were isolated and characterized.[26] They are *stable in acidic aqueous solution, but unstable in neutral to alkaline solution.* Dissociation of a proton from one of the cyclam (equatorial) amines occurs even at neutral pH with pK_a values of 5.0–5.4 at 25 °C and I = 0.1 ($NaClO_4$). Apparently, upon deprotonation, the Au(III) ion in the cyclam complex is self-reduced to Au(0). It can be demonstrated that pH ~7 is a very basic condition for the Au(III) in cyclam. In the phenol-pendant cyclam complex **14**, the apical phenolic proton dissociates (pK_a = 8.3) only after the dissociation of the cyclam-NH finishes (pK_a = 5.0), which is a good illustration of the strong Au^{III} (d^8) acidity extending only to the square-planar N_4 direction.

In aqueous 1 N HCl solution, cyclam becomes a bidentate ligand for Au^{III} to immediately and quantitatively yield an "Au^{III}-out" complex, **28**, from which Au^{III} can be removed in pH ~3 aqueous solution in good yield. This finding was successfully applied to selective uptake of Au^{III} with lipophilic cyclams **9** and **10**.

Experimental Section

General Methods. All commercially available chemicals were of analytical reagent grade and were used without further purification. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were obtained on a JEOL GX-400 spectrometer employing D_2O as the solvent and 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (d_4) as an internal standard at 35 °C. IR and UV spectra were recorded on a Shimadzu FTIR-4200 instrument and a Hitachi U-3200 spectrophotometer, respectively. Atomic absorption (AA) spectra were recorded on a Shimadzu AA-646 spectrophotometer using a hollow cathode lamp for gold (Hamamatsu Photonics K.K.). Ion-exchange and thin-layer chromatographies were carried out on Dowex 50X4 (50–100 mesh, H^+ form) and Merck Art. 5554 TLC plates (silica gel 60 F_{254}), respectively. Syntheses of ligands **2**–**11** (except for **9**) were described earlier in detail.[5,12,15,17]

General Procedure for Preparation of Gold(III) Cyclam Complexes 12, 14, and 18. Cyclam **1** or its derivatives **2** and **3** (1.0 mmol) and $NaAuCl_4 \cdot 2H_2O$ (398 mg, 1.0 mmol) in 20 mL of CH_3CN were heated at reflux for 1 h, to which 10 mL of 0.1 N HCl aqueous solution was added, and insoluble materials (Au^0 etc.) were filtered off. After concentration of the filtrate, the residue was purified by Dowex 50X4 ion-exchange column chromatography (eluent: 3 N HCl), and recrystallization from 1 N $HClO_4$ aqueous solution afforded the pure crystalline products. Elemental analyses and UV–vis and ^{13}C NMR data are all summarized in Table I.

General Procedure for Preparation of Gold(III) Monooxocyclam Complexes 19, 23, and 24. Monooxocyclam **4** or its derivatives **5** and **6** (1.0 mmol) and $NaAuCl_4 \cdot 2H_2O$ (398 mg, 1.0 mmol) in 20 mL of CH_3CN were stirred at room temperature for 2 days. (At 60 °C, ligands were decomposed.) A 10 mL aliquot of 0.1 N HCl aqueous solution was added, and insoluble materials (Au^0 etc.) were filtered off. After concentration of the filtrate, the residue was purified by Dowex 50X4 ion-exchange column chromatography (eluent: 3 N HCl), and recrystallization from 1 N $HClO_4$ aqueous solution afforded the pure crystalline products. Elemental analyses and IR, UV–vis, and ^{13}C NMR spectral data are all summarized in Table I.

Synthesis of $C_{15}H_{31}$-cyclam 9. 1,9-Diamino-3,7-diazanonane (15 mmol) and 2-octadecenoic acid ethyl ester [$CH_3(CH_2)_{14}CH{=}CHCO_2C_2H_5$] (15 mmol) were heated at reflux in 500 mL of CH_3OH for 3 weeks. After evaporation of the solvent, the residue was purified by silica gel column chromatography, and recrystallization from n-heptane/toluene afforded the amide as colorless needles in 15% yield. Reduction of the amide with B_2H_6 in tetrahydrofuran yielded $C_{15}H_{31}$-cyclam **9** as colorless crystals in 27% yield; mp 114.0–115.0 °C. ^1H NMR ($CDCl_3$): δ 0.88 (3 H, t, J = 6.8 Hz, CH_3), 1.26 (28 H, m, $C(CH_2)_{14}C$), 1.72 (2 H, q, J = 2.6 Hz, CCH_2C), 1.74 (2H, m, CCH_2C), 1.84 (4 H, br, NH), 2.45–2.95 (15 H, m, NCH_2C).

Potentiometric Titrations. Aqueous solutions (25 mL) of Au^{III} complexes (1.00×10^{-3} M) with an equivalent of HCl were titrated with carbonate-free 0.100 M NaOH aqueous solution. pH values were read with an Orion 811 digital pH meter. The temperature was maintained at 25.00 ± 0.05 °C, and ionic strength was adjusted to 0.10 M with $NaClO_4$. $-\log [H^+]$ values were estimated with a corrections of −0.08 pH unit to the pH meter readings.[25] All the solutions were carefully protected from air by a stream of humidified Ar. The electrode system was calibrated with pH 7.00 standard buffer solutions and checked by the duplicate theoretical titration curves of 4.00×10^{-3} M HCl with a 0.100 M NaOH solution at 25 °C and I = 0.10 M ($NaClO_4$) in low- and high-pH regions.

Extraction of Au(III). In a 30 mL round-bottom flask, 5 mL of aqueous solution I containing 1.0 mM $NaAuCl_4$ in 1 N HCl with or without a mixture of the same concentration of Cu^{II}, Fe^{III}, Co^{II}, and Pd^{II} was well stirred with 5 mL of 2.0 mM ligand **9** (entry 2), **10** (entry 3), **11** (entry 4), or n-$C_{16}H_{33}NH_2$ (entry 5) in $CHCl_3$ at 25 °C for 30 min. After careful phase separation, the aqueous solution I was assayed by an atomic absorption spectrophotometer for the remaining Au^{III} ion unextracted. Then, the $CHCl_3$ layer was well stirred with 5 mL of aqueous solution II (distilled water) at 60 °C for 30 min. The aqueous solution II was assayed for the Au^{III} ion extracted; see Table II. All runs were repeated three times, and these values were within ±5%.

(26) Note Added in Proof: An X-ray crystal structure of **12** has recently proven the "Au(III)-in" structure.