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A Novel Cyclam Appended with 3-Hydroxypyridine. An Ambident Donor Ligand Comprising a Pyridyl N and a Pyridinolate O⁻ Donor

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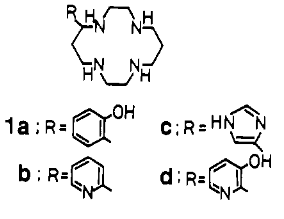
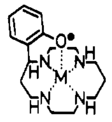
Received December 7, 1989

A new cyclam appended with ambident donor 3-hydroxypyridine (**1d**) has been synthesized to determine which adjacent donor, i.e. pyridyl N or pyridinolate O^-, apically binds with metal ions in the cyclam and how the pendant donor influences the complex structure and chemical behavior. With Ni^{II} ion, a *cis*-cyclam complex, **16**, is formed as a kinetic product, which converts to a thermodynamically more stable *trans*-cyclam complex, **18**. Crystalline Ni^{II} complex **16** was isolated from pH 9 solution and its X-ray analysis was conducted. Crystals of **16** ($C_{15}H_{26}N_5ONi(ClO_4)\cdot 3H_2O$) are monoclinic, space group *Pc*, with two molecules in the unit cell of dimensions $a = 8.127$ (1) Å, $b = 12.056$ (1) Å, $c = 11.553$ (1) Å, and $\beta = 97.53$ (1)°. The structure was solved by the heavy atom method and refined anisotropically to $R = 0.035$, $R_w = 0.048$, for 1877 independent reflections. The crystal structure of **16** reveals a folded *cis*-cyclam configuration and the pyridyl N at the fifth coordination site. The pyridyl N donor serves to enhance the rate of Ni^{II} complexation with cyclam and keeps binding with Ni^{II} without switching to the pyridinolate O^- donor in the Ni^{II}/Ni^{III} redox process. With Cu^{II} and Zn^{II}, the pyridyl N donor also is the exclusive fifth donor.

Extensive research using saturated tetradentate macrocyclic ligands has revealed a close relationship between structural features and physical and chemical properties of metal complexes.[1] Our interest in this area has been directed toward the synthesis of new macrocyclic polyamine ligands that bear additional donor groups as pendants to develop a new type of five-coordinate complexes.[2-9] Earlier, we have reported several cyclam (1,4,8,11-tetraazacyclotetradecane) ligands with a pendant arm donor such as phenol (**1a**),[3-5] pyridine (**1b**),[6] or imidazole (**1c**)[7] attached to a carbon atom in the cyclam framework. Indeed, with the introduction of these apical donors (see **2** and **3**), the existing knowledge of structures and reactivities of cyclam complexes has been greatly expanded. Furthermore, the information derived from this new class of complexes substantially helped understanding of the apical effects in biological square-planar macrocyclic tetraamine complexes (e.g. porphyrin).





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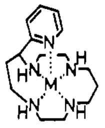

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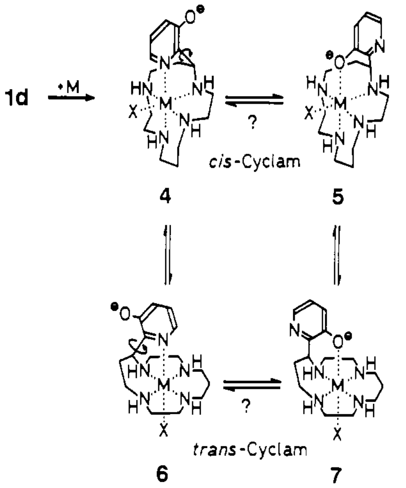
It has been determined that the phenolate O^- donor in **2** stabilizes the metal ions of higher oxidation states,[5] whereas the pyridyl N donor in **3** prefers lesser oxidized metal ions.[10] In M^{II} complexation, the phenolate O^- of **2** comes to the apex of a regular pyramidal arrangement with lesser constraint than does the pyridyl N of **3**.[4-6]

We now have turned to a new cyclam with a pendant molecule that possesses both a pyridyl N and a pyridinolate O^- (PyO^-) donor, 5-[2-(3-hydroxypyridyl)]-1,4,8,11-tetraazacyclotetradecane **1d**. Of special interest with **1d** is (i) which donor, i.e. pyridyl N in **4** and **6** or PyO^- in **5** and **7**, preferentially binds with metal ions, (ii) whether such preference varies with metal ions, metal oxidation states, or media pH, etc., and (iii) whether the kinetic coordination mode is the same as the thermodynamic one. This paper reports the results on the $Ni^{III/II}$, Cu^{II}, and Zn^{II} complexes, which have consistently display fifth binding of the pyridyl N rather than of the PyO^- donor.



Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were obtained with a JEOL GX-400 spectrometer (400 MHz, 25 °C, Me_4Si reference). IR and mass spectra were obtained with a Shimadzu FTIR-4200 and a JEOL JMS-01SG-2, respectively. UV-visible spectra (±1 nm) were

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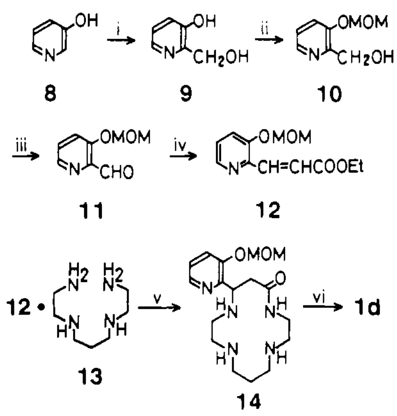
Scheme I[a]



[a](i) NaOH in H_2O, $HCHO_{aq}$; (ii) NaH in DMF, CH_3OCH_2Cl; (iii) DMSO and $(COCl)_2$ in CH_2Cl_2, Et_3N in CH_2Cl_2 at −70 °C; (iv) $Ph_3P{=}CHCOOEt$ in PhH; (v) reflux in MeOH; (vi) $BH_3{\cdot}THF$, HCl in MeOH.

recorded on a Hitachi U-3200 spectrophotometer at 25 °C. ESR spectra, both at 25 °C and 77 K, were recorded on a JES-FE1X spectrometer using Mn^{II}-doped MgO powder as reference ($g_3 = 2.034$ and $g_4 = 1.981$). For TLC analysis throughout this work, Merck precoated TLC plates (silica gel 60 F_{254}) were used. Column chromatography was carried out on silica gel (Wakogel C-300). The electrode system for the cyclic voltammetry was described earlier.[5,8]

Reagents for Ligand Synthesis. Purification of solvents was critical for successful syntheses. Tetrahydrofuran (THF) was refluxed over benzophenone/sodium and then freshly distilled in an argon atmosphere. Dichloromethane (CH_2Cl_2), dried over calcium chloride and then distilled. Dimethyl sulfoxide (DMSO) was distilled over calcium hydride and only the middle fraction was collected and stored in a dark bottle under an argon atmosphere. Triethylamine was distilled over calcium hydride and stored in the dark below 5 °C.

Ethyl 3-[2-(3-(Methoxymethoxy)pyridyl)]acrylate (12). α,β-Unsaturated ester **12** was synthesized from 3-hydroxy-2-(hydroxymethyl)-pyridine, **9**, which was prepared from 3-hydroxypyridine **8** by a previously reported method[11a] (see Scheme I). Sodium hydride, 8.99 g (55% material, 0.2 mol), was washed with two portions of dry *n*-hexane and suspended in 50 mL of DMF (dried over 4A molecular sieves). A solution of **9** (25.8 g, 0.21 mol) in 200 mL of dry DMF was added dropwise at 0 °C and the mixture was stirred at room temperature for 30 min. The resulting mixture was cooled to 0 °C and 17.4 g (0.23 mol) of chloromethyl methyl ether in 50 mL of dry DMF was added dropwise. The mixture was stirred at room temperature for 30 min, the precipitated NaCl filtered, and the solvent evaporated under reduced pressure. The residue was treated with saturated aqueous Na_2CO_3 solution and then extracted with three portions of diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered, and evaporated to give a crude oil, which was purified on a silica gel chromatographic column with *n*-hexane–AcOEt (10:1 to 1:1). The colorless oil (23.7 g, yield 68%) was shown to be 3-(methoxymethoxy)-2-(hydroxymethyl)pyridine (**10**). ^1H NMR ($CDCl_3$): δ 3.45 (3 H, s, OCH_3), 4.35 (1 H, br, CH_2OH), 4.74 (2 H, s, $PyCH_2O$), 5.18 (2 H, s, $PyOCH_2O$), 7.0–7.5 (2 H, m, PyH), 8.08–8.23 (1 H, m, PyH).

Subsequently, **10** was oxidized to 2-formyl-3-(methoxymethoxy)-pyridine (**11**) according to the Swern oxidation procedure.[11b] The formyl compound was obtained as a colorless oil in 98% yield. ^1H NMR ($CDCl_3$): δ 3.50 (3 H, s, OCH_3), 5.30 (2 H, s, OCH_2O), 7.3–7.7 (2 H, m, PyH), 8.32–8.46 (1 H, m, PyH), 10.27 (1 H, s, CHO). IR (film) 1710 cm^{-1} (C=O).

Finally, **12** was synthesized from **11** (21.8 g, 0.13 mol) with a Wittig reagent ($Ph_3P{=}CHCOOEt$, 46.0 g, 0.13 mol) in 400 mL of refluxing benzene for 4 h. After evaporation of the solvent, diethyl ether was added to the residue to precipitate triphenylphosphine oxide, which was filtered off. After the filtrate was concentrated, the residue was purified on a silica gel chromatograph with *n*-hexane–AcOEt (4:1 to 1:1), to **12** as a colorless oil (29 g, 92% yield). ^1H NMR ($CDCl_3$): δ 1.32 (3 H, t, J = 7.5 Hz, CCH_3), 3.48 (3 H, s, OCH_3), 4.25 (2 H, q, J = 7.5 Hz, CH_2C), 5.22 (2 H, s, OCH_2O), 6.99 (1 H, d, J = 16 Hz, =CHCO), 7.1–7.6 (2 H, m, PyH), 8.10 (1 H, d, J = 16 Hz, PyCH=), 8.2–8.3 (1 H, m, PyH). IR (film): 1710 cm^{-1} (C=O).

Synthesis of 1d. A solution of **12** (24.0 g, 0.01 mol) and 1,9-diamino-3,7-diazanonane (**13**) (16.3 g, 0.10 mol) in 2 L of MeOH was refluxed in a dark flask for 3 weeks. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and washed with water. The organic layer was dried over Na_2SO_4 and then concentrated. The resulting crude solid was recrystallized from CH_3CN to give monooxo macrocycle **14** as colorless prisms in 30% yield (10.6 g) (mp 134.0–135.0 °C). IR (KBr): 1660 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 1.7–1.8 (2 H, m, CCH_2C), 2.1–3.0 (15 H, m, NH, $COCH_2$, NCH_2), 3.25–3.60 (2 H, m, $CONCH_2$), 3.46 (3 H, s, OCH_3), 4.48 (1 H, t, J = 10.8 Hz, PyCH), 5.21 (2 H, m, OCH_2O), 7.12 (1 H, dd, J = 8.4, 4.7 Hz, PyH), 7.40 (1 H, dd, J = 8.4, 1.3 Hz, PyH), 8.21 (1 H, dd, J = 4.7, 1.3 Hz, PyH), 9.24 (1 H, br, CONH). Anal. Calcd for $C_{17}H_{29}N_5O_3$: C, 58.10; H, 8.31; N, 19.93. Found: C, 58.06; H, 8.37; N, 19.89.

The monooxo macrocycle **14** (5.0 g, 17 mmol) was added to a freshly distilled $BH_3{\cdot}THF$ solution, which was prepared from $NaBH_4$ (2.4 g, 64 mmol) and $BF_3{\cdot}Et_2O$ (12.3 g, 85 mmol) in 300 mL of THF. The mixture was stirred at room temperature for one day. After decomposition of the excess amount of BH_3 with MeOH, the solvent was evaporated. The resulting solid was dissolved in HCl (gas)-saturated methanol and heated at reflux for 4 h to remove the OH-protecting group. After evaporation of the solvent, the residue was neutralized with 28% NH_3 and then extracted with CH_2Cl_2. The organic layer was concentrated and then purified on a silica gel chromatograph column (eluent, CH_2Cl_2:MeOH:28% NH_3 = 20:4:1), followed by recrystallization from CH_3CN to obtain **1d** as colorless prisms (490 mg, 10% yield, mp 179.0–180.0 °C). ^1H NMR ($CDCl_3$): δ 1.73–1.76 (2 H, m, CCH_2C), 1.85–1.95 (2 H, m, $PyCCH_2C$), 2.55–2.94 (17 H, m, NCH_2 and NH), 3.08–3.13 (1 H, m, PyCNCH), 4.01 (1 H, dd, J = 11.0, 2.9 Hz, PyCH), 7.01–7.06 (2 H, m, PyH), 7.97 (1 H, dd, J = 3.7, 2.3 Hz, PyH). ^{13}C NMR ($CDCl_3$): δ 29.4, 34.5, 47.6, 49.1, 49.4, 49.8, 50.1, 51.0, 51.2, 68.8, 123.1, 123.4, 139.5, 146.9, 154.5. MS: m/z 293 (M^+). Anal. Calcd for $C_{15}H_{27}N_5O$: C, 61.40; H, 9.28; N, 23.87. Found: C, 61.43; H, 9.14; N, 23.82.

Preparation of Metal Complexes with 1d. Nickel(II) Complexes *cis*-[Ni^{II}(1d·H_{-1})]ClO_4·3H_2O (16) and *trans*-[Ni^{II}(1d·H_{-1})]ClO_4·3H_2O (18). The hydroxypyridyl pendant cyclam **1d** (150 mg) and $Ni(ClO_4)_2{\cdot}6H_2O$ (180 mg) were dissolved in 20 mL of 0.5 M $NaClO_4$ aqueous solution at room temperature, and the mixture was gradually adjusted to pH 9 with 0.1 M NaOH solution. After 3 days, purple crystals were obtained in ca. 50% yield. Anal. Calcd for $C_{15}H_{26}N_5ONi(ClO_4){\cdot}3H_2O$: C, 35.70; H, 6.39; N, 13.88. Found: C, 35.84; H, 6.43; N, 14.01. The purple solution of **16** was kept at 50 °C for 3 days, whereupon the color changed to pink. After the solution was concentrated, the trans isomer **18** was obtained in 70% yield as pink crystals. Anal. Calcd for $C_{15}H_{26}N_5ONi{\cdot}ClO_4{\cdot}3H_2O$: C, 35.70; H, 6.39; N, 13.88. Found: C, 35.57; H, 6.24; N, 13.89.

Copper(II) Complex, [Cu^{II}·1d]$(ClO_4)_2$·H_2O (21). Ligand **1d** (73 mg) and $Cu(ClO_4)_2{\cdot}6H_2O$ (92 mg) were dissolved in 5 mL of 1 M $NaClO_4$ aqueous solution heated to 40 °C. The resulting solution (pH 5) was filtered and the filtrate was allowed to stand for 1 week at room temperature. Violet crystals of **21** were obtained as the diperchlorate salt in ca. 70% yield. Anal. Calcd for $C_{15}H_{27}N_5OCu(ClO_4)_2{\cdot}H_2O$: C, 31.39; H, 5.09; N, 12.20. Found: C, 31.60; H, 5.20; N, 12.09.

Zinc(II) Complex, [Zn^{II}·1d]$(ClO_4)_2$·2H_2O (23). The ligand **1d** (73 mg) and $Zn(ClO_4)_2{\cdot}6H_2O$ (93 mg) were dissolved in 5 mL of 1 M $NaClO_4$ aqueous solution at 40 °C. The resulting solution was filtered and the filtrate was allowed to stand for 1 week at room temperature. Colorless crystals of **23** were obtained as the diperchlorate salt in ca. 50% yield. ^1H NMR (D_2O, DSS reference): δ 1.55–1.80 (2 H, m, CCH_2C), 1.90–2.20 (2 H, m, $PyCCH_2C$), 2.4–3.4 (12 H, m, NCH_2), 3.75–4.10 (2 H, m, $PyCNCH_2$), 4.89 (1 H, d, J = 4.3 Hz, PyCH), 7.3–7.5 (2 H, m, PyH), 8.12 (1 H, dd, J = 4.6, 1.2 Hz, PyH). Anal. Calcd for $C_{15}H_{27}N_5OZn{\cdot}(ClO_4)_2{\cdot}1.5H_2O$: C, 30.81; H, 5.17; N, 11.98. Found: C, 30.93; H, 5.09; N, 12.00.

Potentiometric Titrations. Aqueous solution (50 mL) of the ligand **1d** (1.00 × 10^{-3} M) with 4 equiv of $HClO_4$ in the absence or presence of M^{II} ion was titrated with 0.100 M NaOH aqueous solution at 25.0 ± 0.1 °C and I = 0.10 ($NaClO_4$) (Figure 1). The calibration of the electrode system and calculation of the protonation constants (log K_n) were described earlier.[5] The obtained log K_n values and the corresponding values of the relevant molecules[5,6,12] are listed in Table I. We have attempted to measure the complexation constants with Ni^{II}, Cu^{II}, and Zn^{II} using the potentiometric titration method. A typical result with Ni^{II} is shown in Figure 1b, which indicates that the formed complex is too stable to calculate its stability constant. Since Ni^{II} complexation equilibrium was very slow (see the next paragraph), the pH values were

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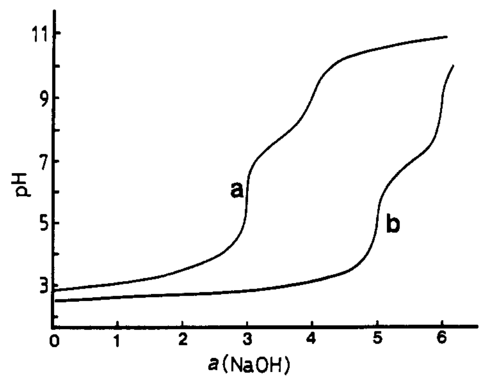

Figure 1. Titration curves for **1d** system: (a) 1.00 mM of $[\mathbf{1d}\cdot4H^+]^{4+}$; (b) part a + 1.00 mM of $Ni^{II}SO_4$.

Table I. Protonation Constants (log K_n) for Pendant Molecules and Pendant Cyclams at 25 °C[a]

cyclam	pyridine	**1b**	phenol	**1a**	3-hydroxy-pyridine	**1d**
11.5		11.47		11.75		12.04 ± 0.05
10.2		10.00		10.84		10.66 ± 0.03
			9.8[b]	8.86[b]	8.60[c]	7.80 ± 0.02[c]
	5.3[d]	<3[d]			5.10[d]	3.6 ± 0.1[d]
1.7		<2		<2		<3
<1		<2		<2		<2

[a] The first protonation constants (K_1) for phenol, **1a**, and **1d** are $[L]/[H_{-1}L^-]a_{H^+}$. For the other ligands, K_1 values are $[LH^+]/[L]a_{H^+}$. The values of relevant molecules are taken from refs 5, 6, and 12. [b] For phenol O^- donor. [c] For pyridinolate O^- donor. [d] For pyridyl N donor.

Table II. Crystal Data and Data Collection Summary for **16**

formula	$C_{15}H_{32}N_5ONi\cdot ClO_4\cdot 3H_2O$
formula wt	504.6
crystal system	monoclinic
space group	*Pc*
cell dimensions	
a, *b*, *c*, Å	8.127 (1), 12.056 (1), 11.553 (1)
β, deg	97.53 (1)
V, Å³	1122
Z	2
density calcd, g cm⁻³	1.493
crystal color	purple
crystal size, mm³	0.3 × 0.3 × 0.2
radiation	Cu Kα (graphite monochromated)
μ, cm⁻¹	27.5
2*θ* range, deg	0.2–130
scan speed, deg min⁻¹	9
phasing	heavy atom method
no. of measd reflcns	1916
no. of indep reflcns	1900 [$F_o > 3\sigma(F_o)$]
refinement	block-diagonal-matrix least-squares method
R	0.035
R_w	0.048

read after sufficient time (1 h) at each titration point.

Kinetic Measurements. The formation of Ni^{II} complex **16** with **1b** and **1d** was followed under pseudo-first-order conditions ($[Ni^{II}]$ = 11.0 mM and [ligand] = 1.0 mM, at 25.0 ± 0.1 °C and I = 0.10 $NaClO_4$) by a pH-stat method, which was identical with Kaden's procedure for measurement of the Ni^{II}/cyclam system.[13] A solution of 50.0 mM NaOH was used to keep pH constant at 6.0. The complexation reaction for the $Ni^{II}/[\mathbf{1d}\cdot2H^+]$ system was completed in ca. 15 min ($t_{1/2}$ (uncomplexed ligand) = 5.8 min). For the sake of comparison, the rate for the pyridyl-pendant cyclam $\mathbf{1b}\cdot2H^+$ with Ni^{II} was also measured under the same conditions ($t_{1/2}$ = 9.6 min).

Crystallographic Study. A purple crystal with dimensions 0.3 × 0.3 × 0.2 mm³ of **16** was used for data collection. The lattice parameters and intensity data were measured on a Rigaku AFC-5 diffractometer with graphite monochromated Cu Kα radiation. Crystal data and data collection parameters are displayed in Table II. The structure was solved by the heavy atom method and refined anisotropically by using absorption

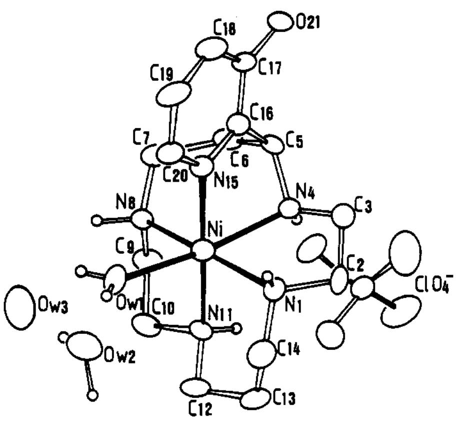

Figure 2. The X-ray crystal structure of **16**. Selected hydrogen atoms are omitted for clarity. Atoms are drawn with 30% probability ellipsoids.

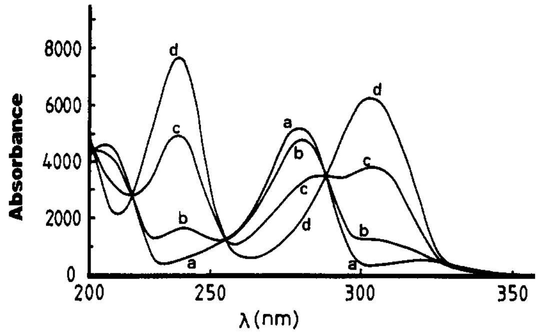

Figure 3. UV absorption spectra of **1d** at I = 0.1 M ($NaClO_4$) at 25 °C. pH values are (a) 6.5, (b) 7.1, (c) 8.0, and (d) 10.8.

Table III. Bond Distances (Å) and Bond Angles (deg) around Ni^{II} of **16** with Estimated Standard Deviations in Parentheses

Ni–N(1)	2.127 (4)	Ni–N(4)	2.088 (2)
Ni–N(8)	2.123 (3)	Ni–N(11)	2.100 (3)
Ni–N(15)	2.112 (3)	Ni–O(W1)	2.080 (4)
N(1)–Ni–N(4)	83.3 (1)	N(1)–Ni–N(11)	88.7 (1)
N(1)–Ni–O(W1)	96.9 (1)	N(4)–Ni–N(8)	90.9 (1)
N(4)–Ni–N(15)	77.9 (1)	N(4)–Ni–O(W1)	170.0 (1)
N(8)–Ni–N(11)	83.6 (1)	N(8)–Ni–N(15)	90.8 (1)
N(8)–Ni–O(W1)	90.3 (1)	N(11)–Ni–N(15)	173.7 (1)
N(15)–Ni–O(W1)	92.1 (1)	Ni–N(15)–C(16)	113.3 (3)
Ni–N(15)–C(20)	127.1 (3)		

Table IV. Selected Atomic Positional Parameters (×10⁴) for **16** with Estimated Standard Deviations in Parentheses

atom	*x*	*y*	*z*	B_{eq}, Å²
Ni	7851	2727.0 (4)	9972	3.43 (1)
N(1)	9522 (4)	1920 (3)	8976 (3)	3.23 (8)
N(4)	6792 (3)	3313 (2)	8342 (2)	2.49 (7)
N(8)	5842 (4)	3374 (2)	10765 (3)	2.73 (7)
N(11)	6549 (4)	1226 (2)	10013 (3)	2.98 (8)
N(15)	8908 (3)	4324 (2)	9929 (3)	2.72 (7)
O(21)	7573 (3)	6758 (2)	8236 (2)	3.37 (7)
O(W1)	9149 (4)	2397 (3)	11609 (3)	4.02 (9)

corrected data to give R = 0.035, R_w = 0.048, for 1877 independent observed reflections. The molecular structure is illustrated in Figure 2. Selected bond lengths and bond angles around Ni^{II}, selected atomic positional parameters, and intermolecular hydrogen bonds are presented in Table III, Table IV, and supplementary material, respectively.

Results and Discussion

A New Ligand 1d. The synthesis route of the target ligand **1d** follows our original annelation reaction between an α,β-unsaturated ester **12** and a tetraamine **13**, as shown in Scheme I.

Since 3-hydroxypyridine (pyridinol) is fairly unstable toward heat, O_2, or light, all the reactions were carried out under the mildest possible conditions. Protection of the 3-OH group was more effective with methoxymethyl (MOM) than benzyl since the former group is easier to deprotect at a later stage. The

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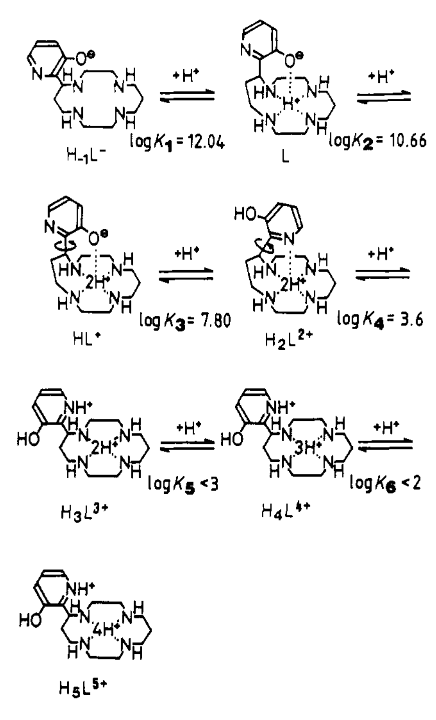
(13) Kaden, T. *Helv. Chim. Acta* **1970**, *53*, 617.

Scheme II

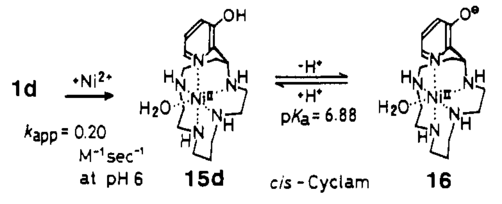


cyclization was conducted in an Ar atmosphere in a dark place, otherwise the reactants turned to a brown liquid and the desired product could not be obtained at all.

The protonation constants log K_n values for **1d** were determined by pH-metric titration (Figure 1a) and UV absorption analysis. From the UV absorption at varying pH values (see Figure 3), we have assigned the log K_3 value of 7.80 to the OH group. The structures of each protonation species are assigned as in Scheme II.

These log K_n values are compared with those of the relevant molecules in Table I. In **1d** the pyridyl N has the lower log K_4 value of 3.6 than that of 5.1 for 3-hydroxypyridine, suggesting that the former N is hydrogen-bonding with two protons in the cyclam cavity. Further, the log K_3 value of 7.80 for the PyOH group is lower than that of 8.60 for 3-hydroxypyridine. This may be interpreted to imply that upon the next deprotonation, the newly generated stronger base, PyO^- anion turns around to interact with the protons in the cyclam cavity.

Ni^{II}/1d Interaction. The pH-metric titration curve for 1:1 Ni^{II} and [**1d**·$5H^+$]$^{5+}$ with 0.1 M NaOH (Figure 1b) clearly indicates an initial five N coordinating complex, **15d**, formation below pH 4 (until a = 5) prior to the next acid–base equilibrium of the 3-hydroxyl group (pK_a = 6.88 ± 0.02) to **16**. The assignment of the PyO^- is derived from the UV absorption shifts from λ_{max} 282 nm (ϵ 5000) for **15d** at pH 5 to 238 nm (11 000) and 306 nm (6300) for **16** at pH 9 (see Figure 4). For comparison, the free ligand showed λ_{max} 285 nm (ϵ 5000) for the PyOH form at pH 6.1, and 238 nm (7900) and 303 nm (6400) for the PyO^- form (pH 10.8).



With Ni^{II} as well as with Cu^{II} and Zn^{II}/**1d** systems, the complexation buffer pH values (until a < 5) are too low to permit an accurate analysis of the complexation constants. Earlier, we reported the extremely large 1:1 complexation constants log K_{CuL} for Cu^{II}–cyclam (29.5) and –phenol pendant cyclam (**2**) (32.0) at 25 °C and I = 0.1.[5]

The apparent second-order rate constant k_{app} for the formation of the initial Ni^{II} complex **15d** determined by the pH-state method was 0.20 M^{-1} s^{-1} ($t_{1/2}$ = 5.8 min) at 25 °C, pH = 6.0, and I = 0.10 M ($NaClO_4$).

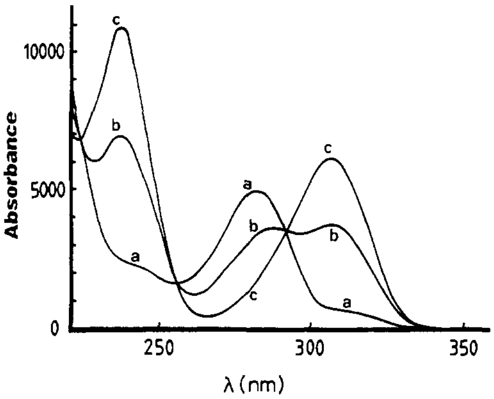
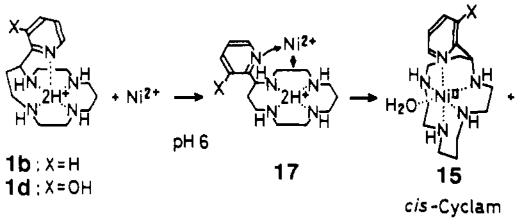


Figure 4. UV absorption spectra of **16** at I = 0.1 M ($NaClO_4$) and 25 °C. pH values are (a) 6.1, (b) 7.2, and (c) 9.0.

$$\mathrm{Ni^{II} + H_2L^{2+} \xrightarrow[k_{app}]{} Ni^{II}L + 2H^+}$$

$$d[\mathrm{Ni^{II}L}]/dt = k_{app}[\mathrm{Ni^{II}}][\mathrm{H_2L^{2+}}]$$

The initial complex structure has a *cis*-cyclam configuration and the pyridyl N coordination as characterized below. Under the



same conditions, the pyridyl-pendant cyclam **1b**,[6] which is also mostly in the disprotonated form (see Table I), interacts with Ni^{II} with the same order of k_{app} = 0.12 M^{-1} s^{-1} (or $t_{1/2}$ = 9.6 min). This kinetic product (isolable as a perchlorate salt) was found to possess a *cis*-cyclam configuration.[13] By contrast, the diprotonated pendantless cyclam (H_2L^{2+} form at pH 6, see pK_n values in Table I) reacts with Ni^{II} at a much slower rate of k_{app} = 4.2 × 10^{-3} M^{-1} s^{-1} (or $t_{1/2}$ = 4.6 h, a calculated value based on Kaden's data[13]). Thus, the pyridyl N pendant in **17** is proven to enhance the rate of Ni^{II} complexation with (diprotonated) cyclam, obviously by initially extending its free pyridyl arm to bring Ni^{II} ion to the cyclam.

Neither the potentiometric nor the spectroscopic titration clarified the structure of the initially formed nickel complexes **15d** and **16**. Hence, we undertook an x-ray crystal analysis of **16**.

X-ray Structure of Ni^{II} Complex 16. A crystalline, purple complex, **16**, was isolated as a monoperchlorate salt at pH 9. The same crystalline form was obtained by concentration of the pH titration solution at 25 °C. The X-ray structure is shown in Figure 2, *which unequivocally demonstrates a folded (cis) N_4 configuration of cyclam and the fifth coordination from the pyridyl N.* Namely, three secondary nitrogens N(1) (2.127 (4) Å), N(8) (2.123 (3) Å), and N(11) (2.100 (3) Å) of cyclam and pyridyl N(15) (2.112 (3) Å) coordinate in a square-planar fashion and a remaining N(4) (2.088(2) Å) of cyclam and water O(w1) (2.080 (4) Å) bind apically. The anionic phenolate oxygen (O(21)) strongly hydrogen bonds with O(w1) and N(8) in an adjacent Ni^{II} complex (see supplementary material). Thus, it is concluded that the interaction of Ni^{II} with **1d** proceeds to form the folded *cis*-cyclam complex **15**.

It is of interest to remark that the kinetically (i.e. initially) formed purple imidazole- (**1c**)[7] and pyridyl-pendant cyclam (**1b**) complexes of Ni^{II} [6,14] all possess *cis*-cyclam configurations (their

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(14) A bluish purple [λ_{max} 534 nm (ϵ 7) cis Ni^{II}·**1b** complex has been recently isolated as the kinetic product (Anal. Calcd for Ni^{II}·**1b**·$2(ClO_4^-)$: C, 33.67; H, 5.09; N, 13.09. Found: C, 33.90; H, 5.09; N, 13.24.).

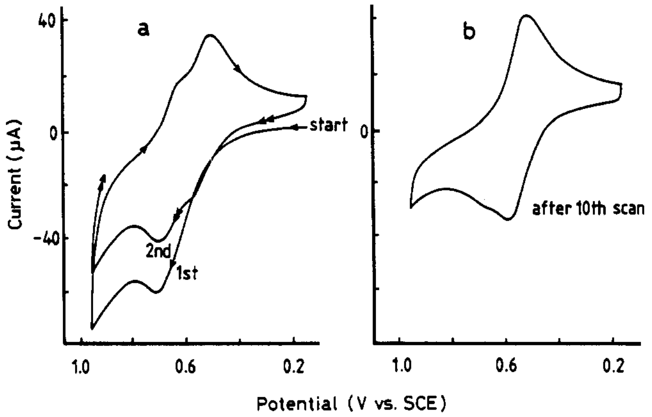
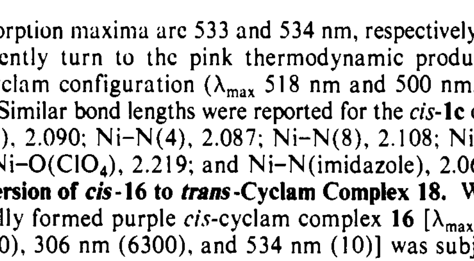


Figure 5. Cyclic voltammograms for **16** at I = 1.5 (Na_2SO_4), pH 8, scan rate = 200 mV s^{-1}, and 25 °C.

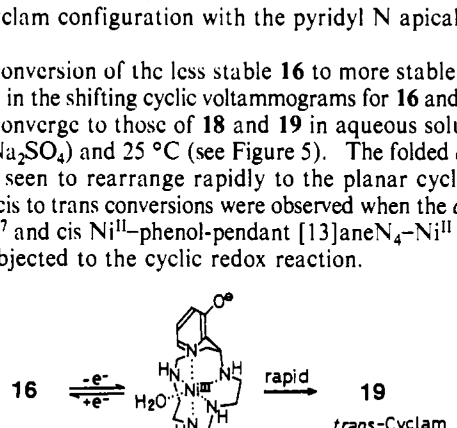
d–d absorption maxima are 533 and 534 nm, respectively), which subsequently turn to the pink thermodynamic products with *trans*-cyclam configuration (λ_{max} 518 nm and 500 nm, respectively). Similar bond lengths were reported for the *cis*-**1c** complex: Ni–N(1), 2.090; Ni–N(4), 2.087; Ni–N(8), 2.108; Ni–N(11), 2.091; Ni–O(ClO_4), 2.219; and Ni–N(imidazole), 2.067 Å.[7]

Conversion of *cis*-16 to *trans*-Cyclam Complex 18. When the kinetically formed purple *cis*-cyclam complex **16** [λ_{max} 238 nm (ϵ 11 000), 306 nm (6300), and 534 nm (10)] was subjected to heating at 50 °C for 3 days in aqueous solution, pink crystalline, trans isomer **18** [λ_{max} 238 nm (ϵ 11 000), 306 nm (6400), and 500 nm (8)] was isolated as a monoperchlorate salt in more than 70% yield.



With **18**, the reversible cyclic voltammogram (ΔE_{peak} = 60 mV) for Ni$^{III/II}$ occurs at $E_{1/2}$ = +0.53 V vs SCE at I = 1.5 (Na_2SO_4), pH 8 and 25 °C, which is near the value of +0.58 V (reversible) for the pyridyl pendant homologue **2**,[15] but far off from the value of +0.35 V (reversible) for the phenolate pendant complex **3**,[4,5] both confirmed (by X-ray studies) to be in the *trans*-cyclam configurations. Hence, we have concluded that **18** has the same *trans*-cyclam configuration with the pyridyl N apically coordination.

The conversion of the less stable **16** to more stable **18** is also observed in the shifting cyclic voltammograms for **16** and **20**, which finally converge to those of **18** and **19** in aqueous solutions at I = 1.5 (Na_2SO_4) and 25 °C (see Figure 5). The folded *cis*-cyclam of **16** is seen to rearrange rapidly to the planar cyclam of **18**. Similar cis to trans conversions were observed when the *cis*-**1c**–Ni^{II} complex[7] and cis Ni^{II}–phenol-pendant [13]aneN_4–Ni^{II} complex[16] were subjected to the cyclic redox reaction.



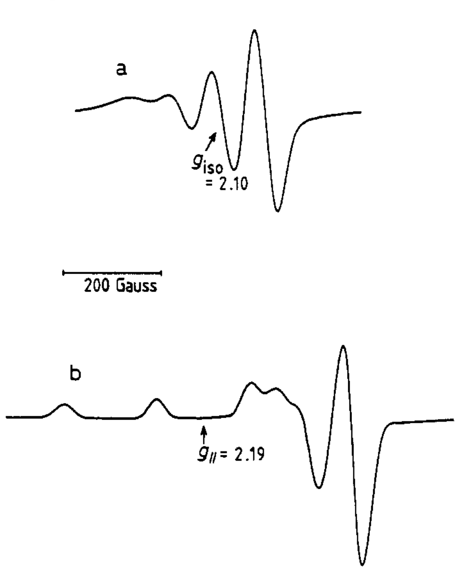
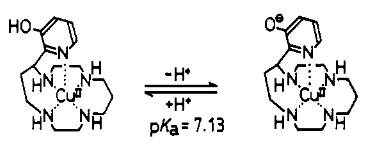


Figure 6. X-Band ESR spectra of **21** in 1:1 DMF/MeOH at (a) 25 °C and (b) 77 K.

Axial pyridyl N coordination (as in **6**) holds in aqueous solution even at elevated temperature (to 80 °C) or in the complexation initiated at higher pH (where the PyO⁻ species is present from the beginning), and no flipping to the O⁻ coordination (as in **7**) was observed. This conclusion was supported by the unchanging visible d–d absorption spectrum and cyclic voltammograms.

Ni^{III}/1d Complex. The Ni^{III} complex was prepared from the Ni^{II} complex **16** in situ by electrochemical (+0.8 V vs SCE) or chemical oxidation with $(NH_4)_2S_2O_8$ at pH 7 and 25 °C. The ESR spectrum in 1:9 ethylene glycol/H_2O at 77 K shows axial symmetry with $g_\perp$ = 2.11 > $g_\parallel$ = 2.02. Further, the absorption at $g_\parallel$ is split into a triplet with intensity ratio of 1:1:1 ($A_\parallel$(N) = 22.4 G). This observation is consistent with the existence of a low-spin, d^7, five-coordinate Ni^{III} complex in which the pyridyl N is apically coordinated. A similar ESR spectrum was reported with the pyridyl N coordinating in complex **3** (M = Ni^{III}, $g_\perp$ = 2.17, $g_\parallel$ = 2.03, $A_\parallel$(N) = 21.2 G),[6] but differs from the phenolate O⁻-bound Ni^{III} complex **2** ($g_\perp$ = 2.18, $g_\parallel$ = 2.02 with no splitting).[5]

Cu^{II}/1d Interaction. The pH-metric titration curve for [**1d**·5H$^+$]$^{5+}$ in the presence of equimolar Cu^{II} ion was quite similar to the one for the Ni^{II} complexation (Figure 1b), implying that only after Cu^{II} binds with the four N donors of cyclam and the pyridyl N, the PyOH dissociation proceeds. Indeed, we have isolated violate crystalline **21** as a diperchlorate salt [λ_{max} 274 nm (ϵ 11 000)] from pH 5 solution.



21 **22**

The ESR spectrum of **21** in 1:1 DMF/MeOH solution at 25 °C is split into four equally spaced absorptions by the interaction with the Cu^{II} nucleus (I = 3/2) (Figure 6a). The isotropic ESR parameters are g_{iso} = 2.10 and A_{iso} = 8.8 × 10^{-3} cm^{-1}. When the solution is frozen at 77 K, an ESR spectrum characteristic of axial symmetry is observed (Figure 6b), which is very similar to those of square-planar Cu^{II}–cyclam complexes.[17,18] The approximate ESR parameters of **21** are $g_\parallel$ = 2.19, $g_\perp$ = 2.06, $A_\parallel$ = 1.9 × 10^{-2} cm^{-1}, and $A_\perp$ = 3.4 × 10^{-3} cm^{-1}, where $g_\perp = (3g_{iso} - g_\parallel)/2$ and $A_\perp = (3A_{iso} - A_\parallel)/2$. These values indicate a $d_{x^2-y^2}{}^1$ ground state and a square-planar structure.[17,19,20]

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(15) From the present study, we have used an electrochemically activated (at +1.0 V vs SCE for 15 min in 0.1 M H_2SO_4) glassy carbon rod as a working electrode to get an improved *reversible* cyclic voltammogram instead of *pseudoreversible* one at +0.61 V in ref 6 for trans Ni$^{II/III}$ complex **3**.

(16) (a) Kimura, E.; Uenishi, K.; Koike, T.; Iitaka, Y. *Chem. Lett.* **1986**, 1137. (b) Kimura, E.; Koike, T.; Uenishi, K.; Davidson, R. B. *J. Chem. Soc., Chem. Commun.* **1986**, 1110.

(17) Comba, P.; Curtis, N. F.; Lawrance, G. A.; Sargeson, A. M.; Skelton, B. W.; White, A. H. *Inorg. Chem.* **1986**, *25*, 4260.

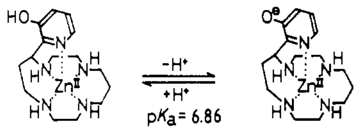
(18) Addison, A. W.; Sinn, E. *Inorg. Chem.* **1983**, *22*, 1225.

(19) Miyoshi, K.; Tanaka, H.; Kimura, E.; Tsuboyama, S.; Murata, S.; Shimizu, H.; Ishizu, K. *Inorg. Chim. Acta* **1983**, *78*, 23.

The pH-metric titration of **21**, supported by the UV spectroscopic titration, indicates PyOH dissociation with pK_a of 7.13 ± 0.02 (25 °C) to **22** [λ_{max} 242 nm (ϵ 15000), 299 nm (7900)]. The pK_a value of **21** is lower by 0.7 log unit than that of the diprotonated ligand **1d**, suggesting stronger interaction between the hydroxypyridine and the Cu^{II} ion. The d–d absorption maximum of **22** [536 nm (150)] is not significantly shifted from that of **21** [527 nm (130)], indicating that the apical coordination by the pyridyl N stays before and after PyOH deprotonation. For reference, the pyridyl-bound **3** (M = Cu^{II}) and phenolate-bound **2** (M = Cu^{II})[5,21] showed λ_{max} 518 nm (95) and 557 nm (120), respectively.

In general the 14-membered cyclam ring is well suited for square-planar coordination of Cu^{II}, resulting in strong in-plane interactions, a high-energy d–d transition, large $A_{\parallel}$ value, and small $g_{\parallel}$ value.[17,19] Our Cu^{II} complex **21** fits this pattern and therefore we assign the *trans*-cyclam configuration of **21** (and **22**). The failure to detect any other intermediate complex products led us to conclude that **21** is the thermodynamically more stable *trans*-cyclam complex.

Zn^{II}/1d Interaction. The pH-metric titration curve for [**1d**·$5H^+$]$^{5+}$ in the presence of equimolar Zn^{II} ion almost overlapped those for the Ni^{II} and Cu^{II}/**1d** systems, implying the same complexation manner with Zn^{II}, isolable as a diperchlorate salt **23**. The phenol dissociation follows with a pK_a value of 6.86 ± 0.02 to **24**. In the ^1H NMR the lower chemical shift of pyridyl group supports the pyridyl N coordination. We assign the *trans*-cyclam structure to these Zn^{II} complexes. Recently, the *trans*-cyclam configuration was established for **2** (M = Zn^{II}) by an X-ray study.[22,23]



23 **24**

Conclusion

When the newly synthesized **1d** interacts with Ni^{II}, the *cis*-cyclam–Ni^{II} complex **16** was isolated as a kinetic product, which then converted to a thermodynamically more stable trans complex **18**. The pyridyl N remains a sole fifth donor during this cis to trans isomerization and also during the oxidation of Ni^{II} to Ni^{III}. The pyridyl N pendant plays an important kinetic role in picking up Ni^{II} ion to enhance the rate of Ni^{II}–cyclam interaction. With Cu^{II} and Zn^{II} ions, the 1:1 complexes were also isolated, where the pyridyl N also is the fifth donor.

Acknowledgment. We thank for the financial support from the Ministry of Education, Science and Culture, Japan (Grant-in-Aid for Scientific Research on Priority Area of "Macromolecular Complexes", No. 63612511).

Supplementary Material Available: Tables of anisotropic temperature factors and all atomic positional parameters with standard deviations, bond lengths, bond angles, and intermolecular hydrogen bonds for **16** (6 pages); listings of observed and calculated structure factors for **16** (13 pages). Ordering information is given on any current masthead page.

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(20) Hathaway, B. J. *Coord. Chem. Rev.* **1982**, *41*, 423.

(21) The Cu^{II} complex (**2**) has a *trans*-cyclam configuration, as determined by X-ray study in ref 5.

(22) Kimura, E.; Toriumi, K.; Koike, T. Unpublished result.

(23) An attempt was made to determine Fe^{II} complexation with **1d** in H_2O. However, we failed to obtain reproducible pH titration curves due to decomposition of the complex in solution. The preparation of Fe^{III}–**1d** complex in MeOH solution also failed to yield solid products.

Contribution from Ames Laboratory and the Department of Chemistry,
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Kinetics and Mechanism of the Reactions between Alkyl Radicals and Complexes of Cobalt(III) and Ruthenium(III)

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Received November 28, 1989

The kinetics of the reactions of $^{\bullet}C_2H_5$ with cobalt(III) and ruthenium(III) complexes were studied by laser flash photolysis with $ABTS^{\bullet-}$ as a kinetic probe. Some relative rate constants were also determined by a competition method based on product ratios. The substrates included a series of $M(NH_3)_5X^{2+}$ complexes (M = Co, Ru; X = halo, aquo, thiocyanato, azido) and some bis(dimethylglyoximato)halocobalt(III) complexes. The products of these reactions are largely (>90%) the ethyl halide and ethyl thiocyanate, substantiating an inner-sphere mechanism. Minor but regular yields of C_2H_4 are also found (≤10%), suggesting a small contribution from the outer-sphere oxidation of $^{\bullet}C_2H_5$.

Introduction

The occurrence of reactions between such free radicals as $I^{\bullet}$, $HO^{\bullet}$, $SO_4^{\bullet-}$, and $^{\bullet}CH_3$ and pentaamminehalocobalt(III) complexes was first reported by Haim and Taube,[1] who found nearly quantitative formation of $Co(H_2O)_6^{2+}$. The studies with methyl radicals were of an exploratory nature; no kinetic data were sought, and the organic products were not determined. They postulated that the reaction of methyl radicals might occur by the equation

$$(NH_3)_5CoX^{2+} + {}^{\bullet}CH_3 + 5H_3O^+ \rightarrow Co_{aq}^{2+} + CH_3X + 5NH_4^+ \quad (1)$$

Our goal in this work has been to conduct kinetic measurements by means of laser flash photolysis, to determine the products formed, and to examine the mechanism of this reaction. We have done this for the ethyl radical, which gives less volatile products than methyl. The source of $C_2H_5^{\bullet}$ is the photohomolysis of ethylcobalt complexes, $C_2H_5Co(dmgH)_2OH_2$ (mostly) and $C_2H_5Co(cyclam)OH_2^{2+}$ (occasionally).[2,3] The laser flash provides the method by which the radicals are produced in a short time (<1 μs) and at concentration levels high enough to be kinetically useful.

Because the Co(III) and Ru(III) complexes to be examined in this study possess relatively small molar absorptivities in the visible region, a competing chromophore is required as a probe

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(1) Haim, A.; Taube, H. *J. Am. Chem. Soc.* **1963**, *85*, 495.

(2) Bakac, A.; Espenson, J. H. *Inorg. Chem.* **1989**, *28*, 3901.

(3) Bakac, A.; Espenson, J. H. *Inorg. Chem.* **1989**, *28*, 4319. The abbreviations are $dmgH^-$ = the monoanion of 2,3-butanedione dioxime and cyclam = 1,4,8,11-tetraazacyclotetradecane.