addition of water to the two oxocarbonium ions, **4** and the protonated aldehyde, represents a lower limit for stabilization of the protonated intermediate by a strong hydrogen bond to solvent water. This will increase the O–H distance and decrease the positive charge on the carbonyl oxygen.

We conclude that the hydrolysis of acetal derivatives does not proceed via diffusionally equilibrated oxocarbonium ions. At this point, however, it is not possible to rule out an intermediate with a lifetime of less than ca. 10^{-11} s^{-1} or the possibility that the reaction with solvent is concerted with no oxocarbonium ion intermediate.[24]

---

(23) The σ_I values for H and Me are 0 and −0.04, respectively: Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley-Interscience: New York, 1975; p 98.

(24) Kresge, A. J.; Weeks, D. P. *J. Am. Chem. Soc.* **1984**, *106*, 7140–7143.

The First Fluorinated Cyclams

Eiichi Kimura,* Mitsuhiko Shionoya, Miho Okamoto, and Hiroko Nada

Department of Medicinal Chemistry
Hiroshima University School of Medicine
Kasumi 1-2-3, Minami-ku, Hiroshima 734, Japan

Received January 28, 1988

Cyclam (1,4,8,11-tetraazacyclotetradecane) (**10**) has long been the most useful and versatile prototype in macrocyclic ligands for fundamental as well as applied coordination chemistry.[1] Recently, functionalization of its basic structure by incorporation of carbonyl group(s) adjacent to its amines, e.g., dioxocyclam (5,7-dioxo-1,4,8,11-tetraazacyclotetradecane) (**6**),[2] or by attachment of pendant donors such as phenol,[3,4] catechol,[5] pyridine,[6] and imidazole[7] to its carbon skeleton have added new dimensions to cyclam chemistry.

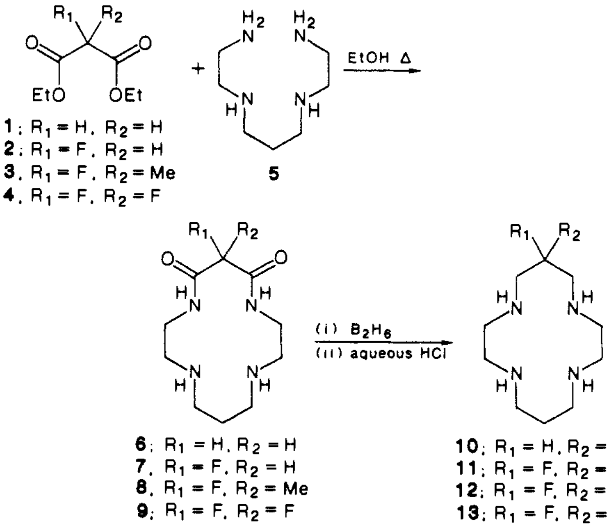
Now, for the first time, we report fluorine-containing cyclams **11**–**13** and dioxocyclams **7**–**9**. Their easy synthesis and novel properties indeed indicate the fluorination to be a new strategy for further extension of macrocyclic polyamines.

Table I. pK_a Values at I = 0.1 M ($NaClO_4$) and 25 °C and Infrared Spectra Data of Free Ligands

ligand	pK_1	pK_2	pK_3	pK_4	$\nu_{C=O}{}^a$ cm^{-1}
6	9.63	5.85			1660
7	9.37	5.65			1685
8	9.56	5.53			1680
9	9.22	5.18			1710
10	11.78	10.55	<2	<1	
11	10.96	9.41	<2	<1	
12	11.34	9.69	<2	<1	
13	10.78	7.52	<2	<1	

^{a}Nujol.

6-Fluoro-(**7**), 6-fluoro-6-methyl-(**8**), and 6,6-difluoro-5,7-dioxo-1,4,8,11-tetraazacyclotetradecane (**9**) were synthesized by condensation of **5** with each corresponding fluorine-substituted malonic ester[8] (**2**,[9] **3**, and **4**) in refluxing ethanol. The cyclization becomes faster as more F is substituted, completing within 30 min with difluorinated **4** as compared to 3 days with nonfluorinated **1**,[10] with yields of 39% (for **7**), 54% (**8**), and 33% (**9**).[11] The dioxocyclams **7**, **8**, and **9** were reduced with diborane in tetrahydrofuran to the corresponding cyclams, 6-fluoro-(**11**), 6-fluoro-6-methyl-(**12**), and 6,6-difluoro-1,4,8,11-tetraazacyclotetradecane (**13**) in yield of 45%, 34%, and 54%, respectively.[12]



1; R_1 = H, R_2 = H
2; R_1 = F, R_2 = H
3, R_1 = F, R_2 = Me
4, R_1 = F, R_2 = F

5

6; R_1 = H, R_2 = H
7, R_1 = F, R_2 = H
8, R_1 = F, R_2 = Me
9; R_1 = F, R_2 = F

10; R_1 = H, R_2 = H
11; R_1 = F, R_2 = H
12; R_1 = F, R_2 = Me
13; R_1 = F, R_2 = F

The protonation constants pK_a (Table I) for these new macrocycles (**7**–**9** and **11**–**13**) were determined by pH-metric titrations, to prove weakened amine basicities upon F substitution. The diminution in the amine basicities is most dramatic at the second stage of protonation (pK_2), in particular for cyclams series **10**–**13**. In the light of the remote location of the basic nitrogens from fluorines in dioxocyclams, the observed basicity-weakening effect by the F atoms may indirectly occur through the strengthened hydrogen bondings between the acidified (due to the electron-withdrawing effect of F) proximal amide hydrogens[13] and the distal

---

(1) For recent articles: (a) Beley, M.; Collin, J.-P.; Ruppert, R.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1984**, 1315–1316. *J. Am. Chem. Soc.* **1986**, *108*, 7461–7467, and references cited therein. Grant, J. L.; Goswami, K.; Spreer, L. O.; Otvos, J. W.; Calvin, M. *J. Chem. Soc., Dalton Trans.* **1987**, 2105–2109. (b) Tsukube, H. *J. Chem. Soc., Perkin Trans. 1* **1985**, 615–619. (c) Taniguchi, I.; Nakashima, N.; Yasukouchi, K. *J. Chem. Soc., Chem. Commun.* **1986**, 1814–1815. (d) Loncin, M. F.; Desreux, J. F.; Merciny, E. *Inorg. Chem.* **1986**, *25*, 2646–2648. (e) Kunitake, T.; Ishikawa, Y.; Shimoumura, M. *J. Am. Chem. Soc.* **1986**, *108*, 327–328. (f) Ram, M. S.; Espenson, J. M.; Bakač, A. *Inorg. Chem.* **1986**, *25*, 4115–4118. (g) Blake, A. J.; Gould, R. O.; Hyde, T. I.; Schröder, M. *J. Chem. Soc., Chem. Commun.* **1987**, 431–433. (h) Bond, A. M.; Khalita, M. A. *Inorg. Chem.* **1987**, *26*, 413–420. (i) Koora, J. D.; Kochi, J. K. *Inorg. Chem.* **1987**, *26*, 908–916. (j) Takiguchi, T.; Nonaka, T. *Chem. Lett.* **1987**, 1217–1218. (k) Collin, J.-P.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1987**, 1075–1076.

(2) (a) Kimura, E. *J. Coord. Chem.* **1986**, *15*, 1–28. (b) Ishizu, K.; Hirai, J.; Kodama, M.; Kimura, E. *Chem. Lett.* **1979**, 1045–1048. (c) Hay, R. W.; Pujari, M. P.; McLaren, F. *Inorg. Chem.* **1984**, *23*, 3033–3035. (d) Kimura, E.; Sakonaka, A.; Machida, R. *J. Am. Chem. Soc.* **1982**, *104*, 4255–4257. (e) Kimura, E.; Koike, T.; Machida, R.; Nagai, R.; Kodama, M. *Inorg. Chem.* **1984**, *23*, 4181–4188. (f) Kimura, E.; Dalimunte, C. A.; Yamashita, A.; Machida, R. *J. Chem. Soc., Chem. Commun.* **1985**, 1041–1043. (g) Fabbrizzi, L.; Kaden, T. A.; Perotti, A.; Seghi, B.; Siegfried, L. *Inorg. Chem.* **1986**, *25*, 321–327. (h) Kimura, E.; Lin, Y.; Machida, R.; Zenda, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1020–1022. (i) Kobayashi, N.; Zao, X.; Osa, T.; Kato, K.; Hanabusa, K.; Imoto, T.; Shirai, H. *J. Chem. Soc., Dalton Trans.* **1987**, 1801–1803.

(3) Kimura, E.; Koike, T.; Takahashi, M. *J. Chem. Soc., Chem. Commun.* **1985**, 385–386.

(4) Kimura, E.; Koike, T.; Uenishi, K.; Hediger, M.; Kuramoto, M.; Joko, S.; Arai, Y.; Kodama, M.; Iitaka, Y. *Inorg. Chem.* **1987**, *26*, 2975–2983.

(5) Kimura, E.; Joko, S.; Koike, T.; Kodama, M. *J. Am. Chem. Soc.* **1987**, *109*, 5528–5529.

(6) Kimura, E.; Koike, T.; Nada, H.; Iitaka, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 1322–1323.

(7) Kimura, E.; Shionoya, M.; Mita, T.; Iitaka, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 1712–1714.

(8) Umemoto, T.; Kawada, K.; Tomita, K. *Tetrahedron Lett.* **1986**, 4465–4468.

(9) This compound is a kind gift from Japan Halon Ltd.

(10) Tabushi, I.; Taniguchi, Y.; Kato, H. *Tetrahedron Lett.* **1977**, 1049–1052.

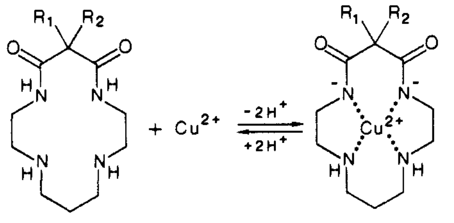
(11) **7**: mp 194.0–194.5 °C (from CH_3CN); ^1H NMR (90 MHz, $CDCl_3$) δ 1.5–1.9 (m, 2 H), 1.90 (br, 2 H), 2.4–3.0 (m, 8 H), 3.2–3.8 (m, 4 H), 5.23 (d, J = 48 Hz, 1 H), 7.45 (br, 2 H, amide NH). **8**: mp 179.5–180.0 °C (from CH_3CN); ^1H NMR (90 MHz, $CDCl_3$) δ 1.4–1.8 (m, 2 H), 1.77 (d, J = 24 Hz, 3 H), 2.4–3.0 (m, 10 H), 3.0–3.4 (m, 2 H), 3.4–3.8 (m, 2 H), 7.35 (br, 2 H, amide NH). **9**: dec 194–196 °C (from CH_3CN); ^1H NMR (90 MHz, $CDCl_3$–CD_3OD) δ 1.5–1.9 (m, 2 H), 2.5–2.9 (m, 4 H), 3.0–3.6 (m, 8 H).

(12) **11**: mp 170.0–172.0 °C (from CH_3CN); ^1H NMR (90 MHz, $CDCl_3$) δ 1.5–1.9 (m, 2 H), 2.1 (br, 4 H), 2.6–2.9 (m, 12 H), 2.9–3.2 (m, 4 H), 4.70 (d m, J = 45 Hz, 1 H). **12**: mp 112.0–113.0 °C (from CH_3CN); ^1H NMR (100 MHz, $CDCl_3$–CD_3OD) δ 1.44 (d, J = 22 Hz, 3 H), 1.8–2.1 (m, 2 H), 2.8–3.8 (m, 16 H). **13**: mp 148.5–149.0 °C (from CH_3CN); ^1H NMR (90 MHz, $CDCl_3$) δ 1.6–1.8 (m, 2 H), 2.0 (br, 4 H), 2.5–2.9 (m, 12 H), 2.8–3.3 (m, 4 H).

0002-7863/88/1510-3679$01.50/0

N lone pairs. A similar spacious effect argument may apply to explain the reduced pK_1 and pK_2 of the distal nitrogens in the fluorinated cyclams. The strong electron-withdrawing of F from the proximal nitrogens is reflected in the higher amide carbonyl stretching frequencies $\nu_{C=O}$, see Table I.[14] The fluorination to reduce amine basicities (or to increase NH^+ acidities) may become very useful for macrocyclic polyamines that form anion complexes with polyoxyanions[15] (e.g., polycarboxylates,[16] phosphates,[17] catechols[18]).

Potentiometric titration of **7**–**9** in the presence of equimolar Cu^{2+} ion showed the complexation with concomitant dissociation of the two amide protons to $[CuH_{-2}L]^0$ (see **14**) as in the case of **6**.[19] The complexation of **9** started to occur at lower pH ~3 than that of **6** (pH > ~4),[2a] with stability constant $\log K_{CuH_{-2}L}$ (= $[CuH_{-2}L][H^+]^2/[Cu][L]$) being 2.5 ± 0.2 for **9** (at $I = 0.1$ M ($NaClO_4$) and 25 °C), as compared with 1.0 for **6** (at $I = 0.2$ M ($NaClO_4$) and 25 °C).[2a] The apparently greater complex stability with **9** over **6** was supported by the ligand displacement of $CuH_{-2}L$ (L = **6**) with L = **9** (equimolar, at pH 5, 50 °C over a few days), which was monitored by each distinct $Cu^{III/II}$ potential (see the following). At present, we cannot rationalize why it is **9** with weaker bases and not **6** with stronger bases that affords a more stable $CuH_{-2}L$ complex.[20] The violet crystalline $[CuH_{-2}L]^0$ **14** was isolated, which shows $\nu_{C=O}$ at 1580, 1575, 1605, and 1620 cm^{-1} with **6**, **7**, **8**, and **9**, respectively. Electron paramagnetic resonance spectra of those complexes at 77 K (in H_2O) are similar with $g_\perp = 2.06$, $g_\parallel = 2.17$, $A_\parallel = 215$ G (G = 10^{-4} T) for **6** and $g_\perp = 2.06$, $g_\parallel = 2.18$, $A_\parallel = 217$ G for **7**–**9**. Their d–d absorptions spectra [λ_{max} nm (ϵ)] occur at 505 nm (100) with **6**, 518 nm (140) with **7**, 512 nm (70) with **8**, and 515 nm (110) with **9**, which seems to imply a little weakening of ligand fields by the fluorination.



dioxocyclams
6-9

$[CuH_{-2}L]^0$
14

Nickel (II)–cyclam (**10**–**13**) complexes were all isolated as $[NiL](ClO_4)_2$.[21] Their d–d absorptions in aqueous solution occur at 450 nm with **10**, 453 nm with **11**, 451 nm with **12**, and 492 nm with **13**, implying the dramatic LF reduction with the difluorination. Ni^{II} ions in these complexes remain mostly low-spin in aqueous solution with μ_{eff} values ranging 2.3–2.5 μ_B with **10**–**13** (by Evans method[22] at 35 °C and $I = 0.1$ M).

The effect of the F substitution is most evident in electrochemical properties of Cu and Ni complexes (Table II). The fluorinated $CuH_{-2}L$ complexes **14** showed all quasi-reversible cyclic voltammograms for $Cu^{III/II}$, as did nonfluorinated $CuH_{-2}L$.[23] The fluorinated $[NiL]^{2+}$ gave quasi-reversible voltammograms for $Ni^{III/II}$ and $Ni^{II/I}$, as did the nonfluorinated **10** complex.[24] In either system, upon fluorination, the higher oxidation states Cu^{III} and Ni^{III} become successively destabilized with respect to Cu^{II} and Ni^{II}, while the lower oxidation state Ni^I becomes successively stabilized with respect to Ni^{II}.

Table II. Half-Wave Potentials (V versus SCE)[a] for $Cu^{III/II}$ (Doubly Deprotonated **6**–**9**) and $Ni^{III/II}$ and $Ni^{II/I}$ (**10**–**13**) Complexes

	$E_{1/2}$ (V versus SCE)		
complex	for $Cu^{III/II\,b}$	for $Ni^{III/II\,c}$	for $Ni^{II/I\,d}$
$[CuH_{-2}L]^0$, L =			
6	+0.64		
7	+0.69		
8	+0.71		
9	+0.83		
$[NiL]^{2+}$, L =			
10		+0.50	−1.56
11		+0.52	−1.52
12		+0.53	−1.53
13		+0.63	−1.46

[a] All solutions were deaerated by purified Ar, and a Pt wire was used as auxiliary electrode. [b] 0.5 M (Na_2SO_4), 25 °C, pH = 7.0. Working electrode (W.E.); glassy carbon. [c] 0.5 M (Na_2SO_4), 25 °C, pH = 6–7. W.E.; glassy carbon. [d] 0.1 M ($NaClO_4$), 25 °C, pH = 7.0. W.E.; Hanging mercury drop electrode.

Fluorinated macrocyclic ligands with easy access will find great potentials in basic as well as applied studies.

---

[13] The fluctuating amide H chemical shifts in the NMR spectra prevented the quantitization of this notion.

[14] A similar $\nu_{C=O}$ (Nujol) pattern for ester is seen with fluorinated malonates: **1** (1745 and 1770 cm^{-1}), **2** (1750 cm^{-1}), and **3** (1780 cm^{-1}).

[15] For review: Kimura, E. *Topics in Current Chemistry*; Boschke, F. L., Ed.; Springer Verlag: Berlin, Heidelberg, New York, Tokyo, 1985; Vol. 128, pp 113–141.

[16] Kimura, E.; Sakonaka, A.; Yatsunami, T.; Kodama, M. *J. Am. Chem. Soc.* **1981**, *103*, 3401–3405.

[17] Kimura, E.; Kodama, M.; Yatsunami, T. *J. Am. Chem. Soc.* **1982**, *104*, 3182–3187.

[18] Kimura, E.; Watanabe, A.; Kodama, M. *J. Am. Chem. Soc.* **1983**, *105*, 2063–2066.

[19] Kodama, M.; Kimura, E. *J. Chem. Soc., Dalton Trans.* **1979**, 325–329.

[20] A referee suggested that this may be an example of reduced solvation of the fluorinated ligand **9**.

[21] The potentiometric determination of these (like unfluorinated cyclam, see: Hinz, F. P.; Margerum, D. W. *Inorg. Chem.* **1974**, *13*, 2941–2949) complexation constants were impossible due to slow kinetics. The polarographic approach for Cu^{II}-fluorinated cyclam is underway (cf. ref 4).

[22] Evans, D. F. *J. Chem. Soc.* **1959**, 2003–2005.

[23] Kodama, M.; Kimura, E. *J. Chem. Soc., Dalton Trans.* **1981**, 694–700.

[24] (a) Zeigerson, E.; Ginzburg, G.; Schwartz, N.; Luz, Z.; Meyerstein, D. *J. Chem. Soc., Chem. Commun.* **1979**, 241–243. (b) Jubran, N.; Ginzburg, G.; Cohen, H.; Meyerstein, D. *J. Chem. Soc., Chem. Commun.* **1982**, 517–519. (c) Jubran, N.; Ginzburg, G.; Cohen, H.; Koresh, Y.; Meyerstein, D. *Inorg. Chem.* **1985**, *24*, 251–258.

Oxygen Atom Transfer from an Iridium Dioxygen Complex: Oxidation of Carbon Monoxide to Carbonate

Holly J. Lawson and Jim D. Atwood*

Department of Chemistry, University at Buffalo
State University of New York
Buffalo, New York 14214

Received January 25, 1988

There has been a great deal of interest in transition-metal dioxygen complexes either as mimics of biological systems[1] or for oxidation of organic substrates.[2] A number of questions remain to be answered concerning the factors that promote reactivity and/or selectivity in oxidations by transition-metal dioxygen complexes. An understanding of the intimate mechanism of oxygen atom transfer reactions and the electronic and steric effects on reactivity is required. In this communication we present our observations concerning the oxidation of carbon monoxide by $(CH_3)Ir(P(p\text{-tolyl})_3)_2(CO)(O_2)$. The data support a rapid reversible cleavage of one iridium–oxygen bond followed by attack on free CO.

---

[1] (a) Karlin, K. D.; Cruse, R. W.; Gultneh, Y.; Farooq, A.; Hayes, J. C.; Zubieta, J. *J. Am. Chem. Soc.* **1987**, *109*, 2668. (b) Herron, N.; Tolman, C. A. *J. Am. Chem. Soc.* **1987**, *109*, 2837. (c) Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev.* **1984**, *84*, 137. (d) Collman, J. P. *Acc. Chem. Res.* **1977**, *10*, 265.

[2] (a) Khan, M. M. T.; Siddiqui, M. R. H.; Hussain, A.; Moiz, M. A. *Inorg. Chem.* **1986**, *25*, 2765. (b) Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1981**, *103*, 5832. (c) Valentine, J. S. *Chem. Rev.* **1973**, *73*, 235. (d) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981.