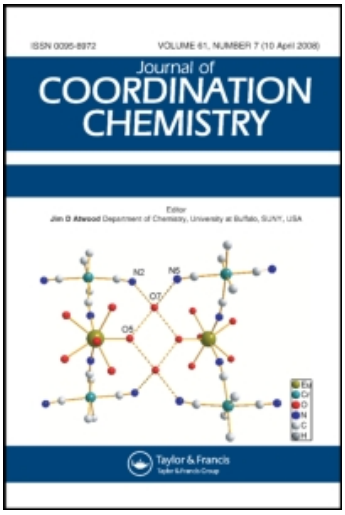


Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

Acid Dissociation Behaviour and Complexation with Nickel(II), Copper(II) and Zinc(II) for Two Conformational Isomers of Dicyclohexylcyclam

Yoshiki Moriguchi[a]; Kazunori Sakata[b]
[a] Department of Chemistry, Fukuoka University of Education, Fukuoka, Japan [b] Faculty of Engineering, Kyushu Institute of Technology, Fukuoka, Japan

To cite this Article Moriguchi, Yoshiki and Sakata, Kazunori(1991) 'Acid Dissociation Behaviour and Complexation with Nickel(II), Copper(II) and Zinc(II) for Two Conformational Isomers of Dicyclohexylcyclam', Journal of Coordination Chemistry, 23: 1, 321 — 334
To link to this Article: DOI: 10.1080/00958979109408261
URL: http://dx.doi.org/10.1080/00958979109408261

J. Coord. Chem. 1991, Vol. 23. pp. 321–334
Reprints available directly from the publisher
Photocopying permitted by license only

ACID DISSOCIATION BEHAVIOUR AND COMPLEXATION WITH NICKEL(II), COPPER(II) AND ZINC(II) FOR TWO CONFORMATIONAL ISOMERS OF DICYCLOHEXYLCYCLAM

YOSHIKI MORIGUCHI*

Department of Chemistry, Fukuoka University of Education, Munakata, Fukuoka 811-41, Japan

and KAZUNORI SAKATA

Faculty of Engineering, Kyushu Institute of Technology, Tobata, Kitakyushu, Fukuoka 804, Japan

(Received October 10, 1990)

Acid dissociation constants for two conformational isomers of dicyclohexylcyclam, *cis-anti-cis*, (*P*) and *cis-syn-cis*, (*N*) have been determined at 25, 35 and 40°C, and thermodynamic data are estimated. It was found that (*N*) shows very different behaviour from (*P*). Stability constants of (*P*) and (*N*) toward Ni(II), Cu(II) and Zn(II) have been determined by pH-titration at 25°C by using a ligand exchange reaction. It is found that the (*P*) complex is more stable for Ni(II) and the (*N*) complex is more stable for Cu(II). Contributions of the cyclohexyl group to the macrocyclic effect (*ME*) have been also estimated by considering basicity corrections. It is found that substitution of the cyclohexyl group in cyclam increases *ME* only for the Ni(II) complex of (*P*).

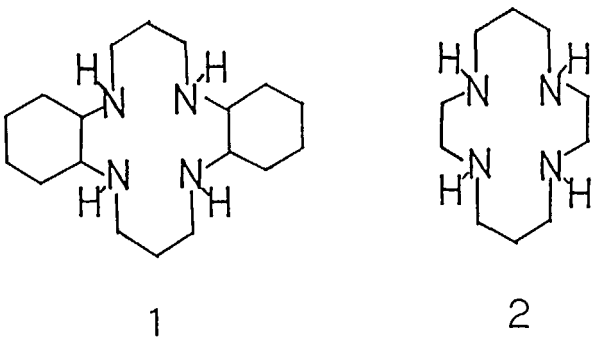
Keywords: Conformation, dicyclohexylcyclam, Ni(II), Cu(II), complex stability

INTRODUCTION

The dicyclohexylcyclam, 1 ~ 22-docosahydrodibenzo[b,i][1,4,8,11] tetraazacyclotetradecine (Cy_2cyclam, **1**) is a macrocyclic ligand which has same tetraaza ring as 1,4,8,11-tetraazacyclotetradecane (cyclam, **2**). The preparation and spectroscopic studies of (**1**) and its crystalline complexes of Co(III), Ni(II), Cu(II) and Zn(II) have been reported by one of the authors.[1] Two of five feasible conformational isomers were isolated as the free base in the crystal and their conformations have been assigned by means of ^{13}C-NMR and IR studies. One forms fine platy crystals (*P*) which melt at 194.5–196.0°C and the other is fine needles (*N*) which melt at 158.5–161.0°C. Their conformations are assigned to the *cis-anti-cis* form (**3**) and the *cis-syn-cis* form (**4**), respectively. X-ray structural studies of one of them have recently been reported by Kobiro *et al.*[2]

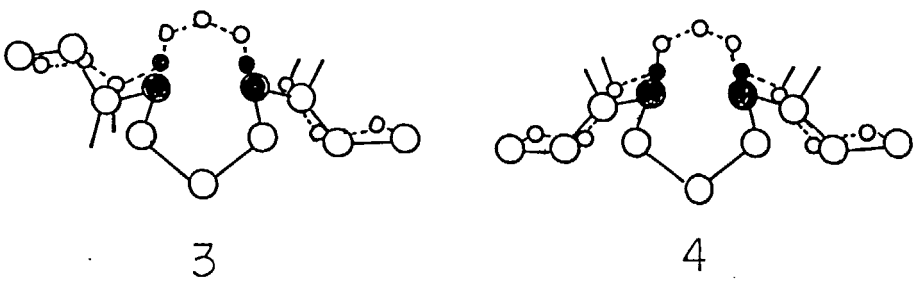
The present work has been done in order to study the physicochemical behaviour of Cy_2cyclam as a macrocyclic ligand in aqueous solution by means of pH-titration and electrophoresis. It is interesting from two points of view because there are few data on isolated conformational isomers in aqueous solutions; effect of differences in conformation on complexation selectivity toward metals based on conformational steric hindrance might be significant, and effects of two hexyl groups on the cyclam ring in relation to the Macrocyclic Effect (*ME*) may be probed.

* Author for correspondence.



1 2

FIGURE 1 Structure of Cy_2cyclam **1** and cyclam **2**.



3 4

FIGURE 2 Assigned conformational structures for free base forms of Cy_2cyclam(*P*) and (*N*).

The determination of acid dissociation and stability constants has been carried by means of the pH-titration method. The method gives a higher precision than does polarography or colorimetry. However, it is not easy to determine stability constant for complexes of macrocyclic ligands by the usual pH-titration method with continuous addition of alkaline titrant to mixed solutions of free ligand and metal because it takes a long time to attain complexation equilibrium.[3]

Here, we have tried an improved pH-titration method to determine the stability constants of Cy_2cyclam, based on a ligand exchange reaction, by dissolving the crystalline complex in large excess of dipotassium ethylenediaminetetraacetate (K_2H_2edta) solution. The stability constants for cyclam complexes were also determined in the same manner in order to compare results with published data obtained by using other methods.

EXPERIMENTAL

Materials and Reagents

Two free base ligands, Cy_2cyclam (*P*) and (*N*), and their metal complexes, [M(II)(Cy_2cyclam)] $(ClO_4)_2$, M(II) = Ni(II), Cu(II), Zn(II), were prepared by a previous method.[1] The tetrahydrogen chlorides, Cy_2cyclm (*P*).4HCl ((*P*)4HCl) and Cy_2-cyclam (*N*).4HCl ((*N*)4HCl) were prepared for each free base ligand in the following way.

(*P*)4HCl: hydrogen chloride gas was bubbled into an absolute ethanol solution of the free base (*P*) for 5 hr and the solution was stirred for 5 hr. The crystalline product was filtered, washed with absolute ethanol and dried over phosphorus pentoxide *in vacuo* at 70°C for 6 hr. *Anal*: Found: C, 47.45; H, 8.78; N, 12.24%. Calcd. for $C_{18}H_{36}N_4.4HCl$: C, 47.58; H, 8.87; N, 12.33%. The obtained material (colourless fine crystals) partially decomposed at 300°C without distinct melting.

(*N*)4HCl: the preparation of the pure tetrahydrogen chloride salt in agreement with elemental analysis is more difficult than for (*P*). The product needs additional drying *in vacuo* at 90°C for 15 hr after reaction as for (*P*). Remarkable differences between (*P*)4HCl and (*N*)4HCl are also found by DTA in the solid and ^{13}C-NMR in heavy water solutions. *Anal*: Found: C, 47.51; H, 8.90; N, 12.24%. Calcd. for $C_{18}H_{36}N_4.4HCl$: C, 47.58; H, 8.87; N, 12.33%. The obtained material (colourless fine crystals) decomposed at 270°C without distinct melting.

Cyclam.4HCl

The preparation of this ligand was carried out in the same manner as for (*P*)4HCl from commercially available free base (Aldrich Chem. Co). *Anal:* Found: C, 34.82; H, 8.14; N, 15.95%. Calcd. for $C_{10}H_{24}N_4.4HCl$: C, 34.70; H, 8.15; N, 16.18%.

[Cu(cyclam)](ClO$_4$)$_2$

The preparation used the Korbut-Daszkiewicz method.[4] *Anal:* Found: C, 25.84; H, 5.16; N, 12.11%. Calcd. for $C_{10}H_{24}N_4O_8Cl_2Cu$: C, 25.95; H, 5.23; N, 12.11%.

Commercial GR grade reagents were used for pH-titrations, electrophoresis and ^{13}C-NMR measurement without further purification. Carbonate-free potassium hydroxide solution as alkaline titrant in pH-titrations was prepared by dilution of "DILUT IT" (J.T. Baker Chem. Co.) with distilled and deionized water.

NMR and Electrophoresis Measurements

Carbon-13 NMR (15 MHz) measurements of (*P*)4HCl and (*N*)4HCl in heavy water were carried out with a JEOL JWM-60FX spectrometer operating in Fourier transform mode at room temperature and 50°C. The measurements of free bases (*P*) and (*N*) and their metal complexes cannot be carried out because of low solubility in heavy water.

The electrophoresis measurements were carried out with a Toyo filter paper PE-2 instrument and a Toyo Elepos PS-1510 stabilizer. The electrophoresis strips were Toyo filter paper No 51A (15 × 40 cm). The sample spots were detected by staining the strips with iodine vapour.

pH-Titrations

The pH-titrations for the determination of acid dissociation constants of (*P*) and (*N*) were carried out in the usual way at 25, 35 and 40°C solutions of free base (*P*) or (*N*) dissolved in a small excess of nitric, hydrochloric or hydrobromic acid with 0.1 M potassium salt of that mineral acid. The pH-titrations for the determination of stability constants of (*P*), (*N*) and cyclam with divalent metal were carried out by addition of a crystalline complex of (*P*), (*N*) or cyclam to a solution containing a large excess of K_2H_2edta, together with 0.1 M potassium nitrate. Measurements

were carried out in sealed, double-jacket glass cell (100 cm^3) equipped with glass and calomel electrodes using a Beckman Research pH meter (model 1019) with an accuracy of 0.001 pH units under an atmosphere of purified nitrogen. The pH readings showed a constant value within 5–10 min of each addition of alkaline titrant. The constant pH value within experimental error was also checked by allowing a test solution with the same composition to equilibrate for a week at neutral and high pH. The pH readings are calibrated to give $-\log[H^+]$ values directly, by titrations of standard mineral and acetic acid solutions with 0.1 M potassium hydroxide under the same experimental condition.[5]

Calculations

By addition of a crystalline complex of the macrocyclic ligand to a K_2H_2edta solution, the following ligand exchange equilibrium by considered,

$$MA^{2+} + B^{4-} \rightleftharpoons MB^{2-} + A \qquad (1)$$

$$K' = [MB^{2-}][A]/[MA^{2+}][B^{4-}] = K_{MB}/K_{MA} \qquad (2)$$

$$K_{MA} = [MA^{2+}]/[M^{2+}][A],\ K_{MB} = [MB^{2-}]/[M^{2+}][B^{4-}] \qquad (3), (4)$$

where [A], $[B^{4-}]$, $[MA^{2+}]$ and $[MB^{2-}]$ are the concentrations of free ligand, free edta anion, 1:1 macrocyclic ligand complex and edta complex, respectively.

Mass conservation leads to the set of equations (*5*)–(*8*) by assuming the presence of the normal 1:1 complexes MA^{2+} and MB^{2-} in solution. This assumption is reasonable because the pure crystalline complex with a 1:1 metal to ligand ratio is dissolved as metal species in the solution and edta exclusively forms a 1 : 1 complex.

$$T_M = [M^{2+}] + [MA^{2+}] + [MB^{2-}] \qquad (5)$$

$$T_A = \alpha_A[A] + [MA^{2+}] \qquad (6)$$

$$T_B = \alpha_B[B^{4-}] + [MB^{2-}] \qquad (7)$$

$$T_{OH} = \gamma_A[A] + \gamma_B[B^{4-}] + 4[MB^{2-}] + [OH^-] + [H^+] \qquad (8)$$

T_M, T_A, T_B and T_{OH} are the initial total concentrations of divalent metal, macrocyclic ligand, edta and added alkaline titrant. These concentrations can be obtained from experimental data. In this work, both T_M and T_A are equal to the concentration of dissolved crystalline complex MA in the solution. In (*5*)-(*8*), α_A, α_B, γ_A, and γ_B, are distribution factors for free ligand species, which depend on pH and the acid dissociation constant. These values for the macrocyclic ligand and edta can be calculated as for tetrabasic acids with equations (*9*) and (*10*),

$$\alpha_{A,B} = 1 + \frac{[H^+]}{Ka_4}\left\{1 + \frac{[H^+]}{Ka_3}\left[1 + \frac{[H^+]}{Ka_2}\left(1 + \frac{[H^+]}{Ka_1}\right)\right]\right\} \qquad (9)$$

$$\gamma_{A,B} = 4 + \frac{[H^+]}{Ka_4}\left[3 + \frac{[H^+]}{Ka_3}\left(2 + \frac{[H^+]}{Ka_2}\right)\right] \qquad (10)$$

where Ka_1, Ka_2, Ka_3 and Ka_4 are the stepwise acid dissociation constants for the macrocyclic ligand, H_4A^{4+}, or edta, H_4B. The values for Cy_2cyclam (*P*) and (*N*) were computed by using a modified program given by Motekaitis–Martell,[5] and those were used for edta 2.10, 2.78, 6.18 and 10.26, in the p*Ka* scale, at 25°C for ionic strength 0.1, respectively.[6] Arrangement and substitution of (*5*)-(*8*) by using (*3*), (*4*), (*9*) and (*10*) leads to a quadratic equation for $[B^{4-}]$, (*11*),

$$P[B^{4-}]^2 + Q[B^{4-}] + R = 0 \qquad (11)$$

where

$$P = (\alpha_A\gamma_B - \alpha_B\gamma_{A=} 4\alpha_A\alpha_B)K_{MB} \qquad (12)$$

$$Q = (T_1\gamma_A - T_2\alpha_A)K_{MB} - \alpha_B\gamma_A \qquad (13)$$

$$R = T_B\gamma_A \qquad (14)$$

$$T_1 = T_A + T_B - T_M \qquad (15)$$

$$T_2 = T_{OH} - 4T_B + [H^+] - [OH^-] \qquad (16)$$

The other species concentrations, [A], $[MA^{2+}]$ and $[MB^{2-}]$ can be calculated from (*5*)-(*8*) by substitution of $[B^{4-}]$. The ligand exchange equilibrium constant, *K'*, in (*2*), can be determined by using these values, and the stability constant, K_{MA}, for Cy_2cyclam (*P*) and (*N*) or cyclam in (*3*) can be also determined by using *K'* and the known K_{MB} value (18.52, 19.00 and 16.4 for Ni(II), Cu(II) and Zn(II) on the log scale, respectively).[6] Representative results are shown in Table I, with the experimental data.

TABLE I

Representative pH titration data for solutions of crystalline $[Cu(Cy_2cyclam\ (P)](ClO_4)_2$ in K_2H_2edta at 25°C, 0.1 M KNO_3.*

Titre V_{OH}, ml	$-\log[H^+]$	$10^{17}[M^{2+}]$ M	$10^{14}[A]^a$ M	$10^7[B^{4-}]^b$ M	$10^4[MA^{2+}]^c$ M	$10^5[MB^{2-}]^d$ M	$10^{18}K'^e$	$10^{-26}K_{MA}{}^f$ (dm^3mol^{-1})
1.500	6.2719	1.5905	3.9851	1.3865	2.2818	2.2052	2.7777	3.6001
1.550	6.3063	1.4226	4.6796	1.1533	2.2801	1.6435	2.9197	3.4250
1.600	6.3393	1.3248	5.6440	1.7283	2.2708	2.2896	3.2927	3.0730
1.650	6.3747	1.1827	6.6467	1.9365	2.2695	2.2903	3.4637	2.8871
1.700	6.4132	1.0055	7.6207	2.1877	2.2722	2.1997	3.3648	2.9719
1.750	6.4521	0.85976	8.8038	2.4707	2.2830	2.1234	3.3142	3.0173
1.800	6.4906	0.75771	10.422	2.7802	2.2843	2.1066	3.4570	2.8927
1.850	6.5295	0.67603	12.512	3.1276	2.2807	2.1143	3.7070	2.6976
1.900	6.5730	0.56529	14.554	3.5610	2.2917	2.0130	3.5908	2.7849
1.950	6.6169	0.48336	17.338	4.0513	2.2961	1.9582	3.6499	2.7398

* Initial total volume, $T_V = 100\,cm^3$; concentration of titrant (KOH), $N_{OH} = 0.09724$ M, initial total concentration of Cy_2cyclam (*P*), T_A, and metal, T_M, $T_A = 2.500 \times 10^{-4}$ M (0.0145 g crystalline complex/100 cm^3); initial concentration of K_2H_2edta, $T_B = 2.500 \times 10^{-3}$ M; [a] [A], $[Cy_2cyclam(P)]$; [b] $[B^{4-}]$, $[edta^{4-}]$; [c] $[MA^{2+}]$, $[Cu(Cy_2cyclam(P))^{2+}]$; [d] $[MB^{2-}]$, $[Cuedta^{2-}]$; [e] $K' = [MB^{2-}][A]/[MA^{2+}][B^{4-}] = K_{MB}/K_{MA}$; $K_{MB} = 1.00 \times 10^{19}$ for Cuedta; [f] $K_{MA}(av.) = (2.86 \pm 0.11) \times 10^{26}(dm^3\,mol^{-1})$, $\log K_{MA} = 26.46 \pm 0.02$.

TABLE II

Temperature dependence of acid dissociation constants for two conformational isomers of dicyclohexylcyclam and thermodynamic data[a] in aqueous solution (μ = 0.1 M KNO_3).

	pKa_2			pKa_3			pKa_4		
	25	35	40	25	35	40	25	35	40°C
Cy_2cyclam(*P*)	1.7	2.2	3.0	10.41 ±0.01	10.25 ±0.01	10.12 ±0.01	10.95 ±0.06	10.67 ±0.02	10.52 ±0.01
				$\Delta H = -8.2, \Delta S = 20.1$			$\Delta H = -12.1, \Delta S = 9.5$		
Cy_2cyclam(*N*)	1.5	2.1	2.9	10.37 ±0.04	10.22 ±0.01	9.98 ±0.01	11.31 ±0.1	11.25 ±0.06	11.27 ±0.1
				$\Delta H = -10.4, \Delta S = 12.5$			$(\Delta H \sim -2.5, \Delta S \sim 40)$[b]		
Cyclam[c]	1.5	1.4		10.5	10.18		11.49	11.11	
	$\Delta H = -3,$	$\Delta S = -3$		$\Delta H = -12.8,$	$\Delta S = 6$		$\Delta H = -12.3, \Delta S = 12$		

[a] Obtained data from a slope of logK *vs* 1/T plot, ΔH kcal mol^{-1}, ΔS cal deg^{-1} mol^{-1}. [b] Uncertain data. [c] Quoted data from Ref. 15 at 25°C, μ = 0.5.

RESULTS AND DISCUSSION

Acid Dissociation Behaviour

As shown in Table II, it is found that there is a distinct difference in acid dissociation behaviour between the two conformational isomers of Cy_2cyclam; pKa_3 is slightly greater for (*P*) than for (*N*) but the difference is almost within experimental error. The value for pKa_4, however, is somewhat greater for (*N*) than for (*P*). The difference between pKa_3 and pKa_4 is an order of magnitude, and the difference is much greater for (*N*). Both pKa_3 and pKa_4 values for (*N*) are nearer to those of cyclam than (*P*). These results suggest that the structural differences between (*P*) and (*N*) gives a gap in the third to fourth deprotonation step or the first to second protonation step. From the fact that two of four hydrogens in the free base form of cyclam are fixed inside of ring by hydrogen bonds,[7] and that its rigid ring structure gives rise to effects on deprotonation or protonation, it is assumed that the stereochemistries of hydrogens and lone pairs of electrons on nitrogens are different for (*P*) and (*N*) and this too effects acid dissociation behaviour. As shown in Figure 2, it is expected that a *cis-syn-cis* conformation, assigned for (*N*), is closely packed on one side of the ring as compared with a *cis-anti-cis* conformation, as assigned for (*P*). This conformational assignment is in agreement with the observed differences in acid dissociation behaviour between (*P*) and (*N*). Deprotonation for (*N*) occurs on one side with a large interaction; on the other hand, for (*P*), dissociation is possible on both sides of the ring with a smaller interaction. The specific structure of (*N*) may bring about the temperature dependence of pKa_4 with uncertainty and large entropy and structure changes may occur in the last deprotonation or first protonation step with rising temperature.

From the fact that the basicity of *n*-alkylamines increases with the number of carbon atoms as shown in Figure 3, it is expected that the substitution of two hexyl groups in cyclam brings about increasing basicity of nitrogen in the [14]aneN_4 ring. The value of pKa_4 for the first protonation of Cy_2cyclam, however, is smaller than for cyclam. Solubility parameters for cyclohexylamine are not available. We assume that the cyclohexyl group has a decreasing protonation on nitrogen atom in interaction with water because the ratio of solubility parameter to water increases with decreasing basicity. This is reasonable in that the solubility parameter is closely related to intermolecular interactions such as solvation and hydrogen bonding in the dissolution process.[8]

Effects of the cyclohexyl group on the acid dissociation of Cy_2cyclam may also be discussed in terms of entropy changes between Cy_2cyclam and cyclam. The entropy change for pKa_3 is greater for both (*P*) and (*N*) than for cyclam. Cyclam undergoes drastic ring deformation in the second to third deprotonation or second to third protonation step; the difference in entropy changes between Cy_2cyclam and cyclam may be related to differences in ring deformations or in their solvation interactions upon substitution of cyclohexyl groups.

Differences between (*P*) and (*N*) are also observed in acid dissociation constants and electrophoretic mobility in different supporting electrolyte solutions, as shown in Tables III and IV. From these results, it is expected that differences of counter anion would effect the behaviour of dissolved species with different conformational structures. The absolute values of p*Ka* should not be directly compared in different ionic medium. The difference between pKa_3 and pKa_4 may, however, be compared. All of p*Ka* differences are greater for (*N*) than for (*P*) and the differences decrease with

increasing anion size, in the order Cl^-, Br^-, NO_3^-. Mobility of the free base form is slightly greater for (*N*) than for (*P*). The positive charge is the same for (*P*) and (*N*) at low pH because both pKa_1 (~ 1) and pKa_2 are almost the same. It is assumed that the conformational difference brings about differences in interactions with counter anions.

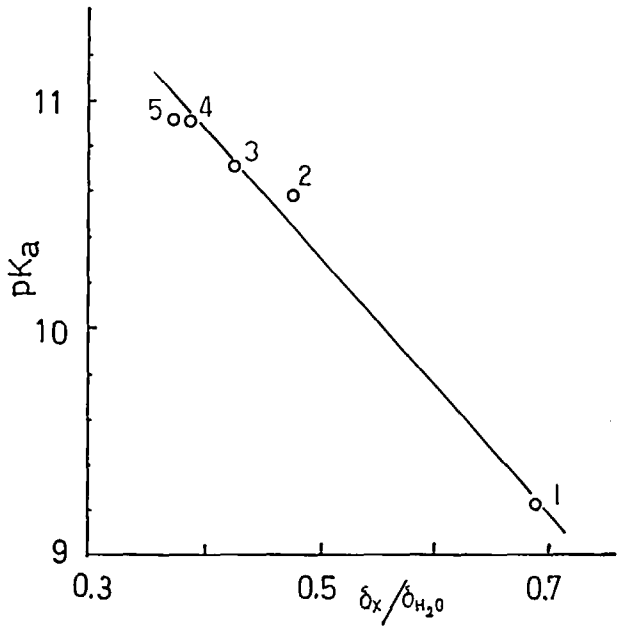


FIGURE 3 Relationship between basicity of *n*-alkyl amines and ratio of solubility parameter[8] of alkyl amines to that of water; δ_x, solubility parameter of alkyl amine; δ_{H_2O}, solubility parameter of water (23.4); 1, ammonia (16.3); 2, methylamine (11.2); 3, ethylamine (10.0); 4, *n*-propylamine (9.1); 5, *n*-pentylamine (8.7).

TABLE III
Acid dissociation constants for two conformational isomers of dicyclohexylcyclam in different supporting electrolyte solutions (0.1 M KX) at 25°C.

	KCl		KBr		KNO_3	
	(*P*)	(*N*)	(*P*)	(*N*)	(*P*)	(*N*)
pKa_3	9.99	10.07	10.43	10.29	10.41	10.37
pKa_4	10.70	11.44	11.05	11.48	10.95	11.37
pKa_4-pKa_3	0.71	1.37	0.62	1.19	0.54	1.00

The difference between (*P*) and (*N*) is also observed for their tetrahydrogen chlorides in heavy water by carbon 13-NMR measurements, as shown in Figure 4. The NMR spectrum of (*P*)4HCl is very simple and its spectrum is same at room temperature and 50°C. On the other hand, that of (*N*)4HCl is very complicated, with much fine structure; the signal for the 1-position of cyclohexyl becomes a single peak at 50°C. From these results, the molecular structure for (*N*) is expected to be of lower

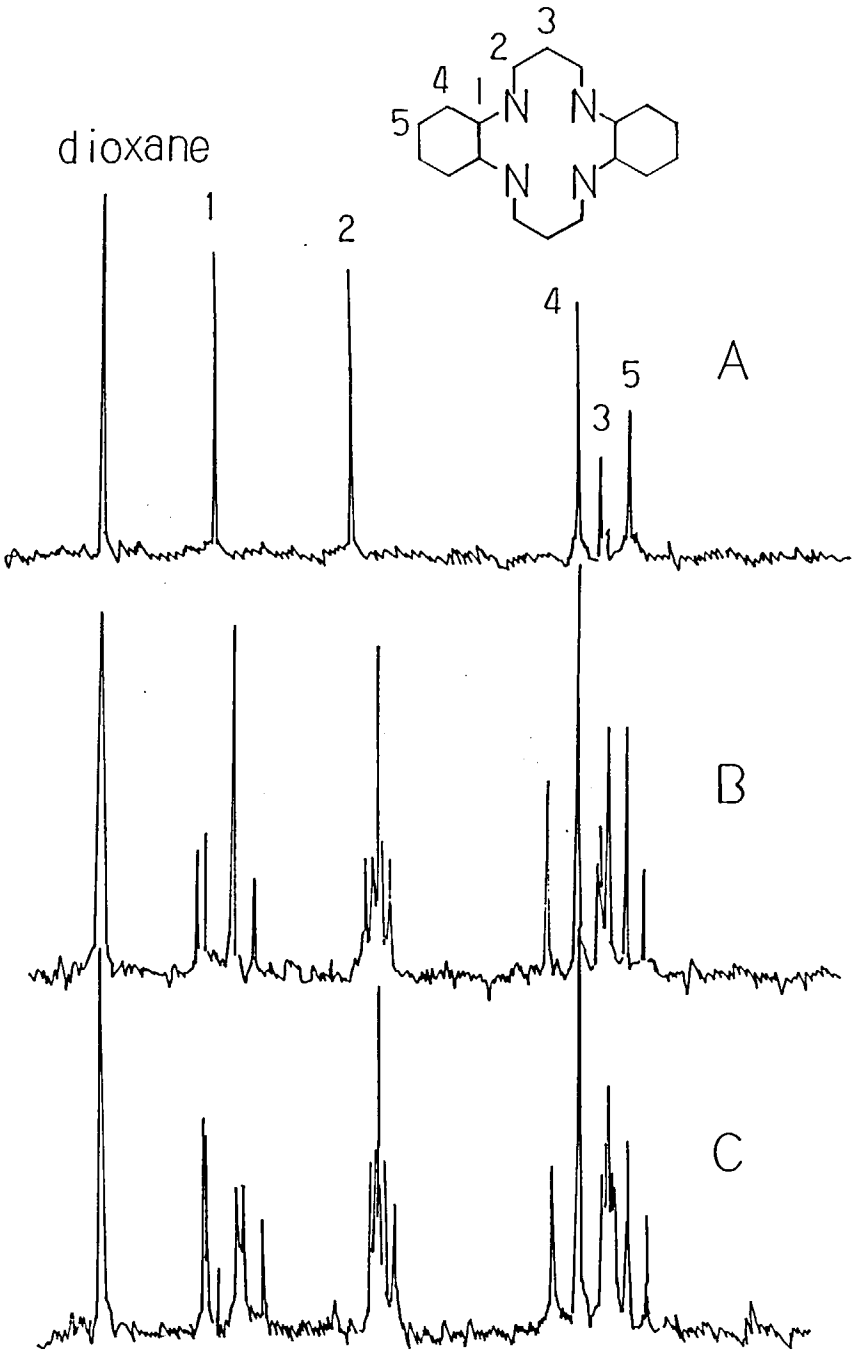


FIGURE 4 Carbon-13 NMR spectra of tetrahydrogen chlorides of Cy_2cyclam(*P*) and (*N*) in heavy water; A, (*P*)4HCl at room temperature; 1, 57.56; 2, 45.45; 3, 23.63; 4, 25.65; 5, 21.17 ppm; B, (*N*)4HCl at 50°C; C, (*N*)4HCl at room temperature.

symmetry than (*P*). The low symmetry structure fixed on the rigid ring is altered by thermal motion with rising temperature and large structural changes occur for (*N*)4HCl. This behaviour is assumed to be related to the abnormal temperature dependence of pKa_4 for (*N*) as shown in Table II. These distinct differences are also observed by DTA measurements of their solids. The DTA for (*N*)4HCl shows a more complicated curve, with a number of small endothermic transitions as compared with (*P*)4HCl.

TABLE IV

Electrophoretic mobilities[a] of two conformational isomers of dicyclohexylcyclam in different supporting electrolyte solutions.

	4HCl salt		Free base		Supporting electrolyte
	(*P*)	(*N*)	(*P*)	(*N*)	
HF–KF	0.69	0.71	0.69	0.76	0.01 M KHF_2, pH = 3
HCl–KCl	0.74	0.73	0.74	0.76	0.01 M HCl + 0.01 M KCl 1 : 1 soln., pH = 2.22
HBr–KBr	0.69	0.70	0.72	0.73	0.01 M HBr + 0.01 M KBr 1 : 1 soln., pH = 2.23
HNO_3–KNO_3	0.69	0.70	0.71	0.73	0.01 M HNO_3 + 0.01 M KNO 1 : 1 soln., pH = 2.07

[a] Relative value to mobility of Cyclam.4HCl salt at 300 volts for 30 min.

From the results described above, it is assumed that all four nitrogen protons in (*N*)4HCl are fixed on the same side of the [14]aneN$_4$ ring. We expect that the structural changes caused by elimination of a proton with increasing temperature or pH gives rise to the various effects.

TABLE V

Stability constants for two conformational isomers of dicyclohexylcyclam and related ligands at 25°C.[a]

	log K_1, log β_2[b]			
	Ni(II)	Cu(II)	Zn(II)	
Cy_2cyclam(*P*)	23.10 ± 0.1	26.46 ± 0.02	19.44 ± 0.07	This work, μ = 0.1 M KNO_3
Cy_2cyclam(*N*)	22.53 ± 0.06	27.08 ± 0.01	19.85 ± 0.06	
Cyclam		26.51 ± 0.07		
	22.2	27.2	15.5	μ = 0.2 M KCl[c]
	20.1			μ = 0.5 M NaCl, $4 \sim 8 \times 10^{-3}$ M HCl[d]
	21.2			μ = 0.1 M NaOH at 40°C[e]
en[f]	13.44	19.60	10.6	μ = 0.1
pn[g]	10.50	16.81		
cn (*cis*)[h]	13.83	19.97		
cn (*trans*)	14.66	20.35	14.27	

[a] Quoted data from Ref. [15] unless otherwise noted. [b] K_1 = [MA]/[M][A] for Cy_2cyclam(*P*), (*N*) and cyclam, β_2 = [MA_2]/[M][A]^2 for en, pn and cn. [c] Polarography, Ref. [16]. [d] Potentiometry and spectrometry, Ref. [3] [e] Colorimetry, Ref. [13]. [f] Ethylenediamine. [g] 1,3-Diaminopropane. [h] 1,2-Diaminocyclohexane.

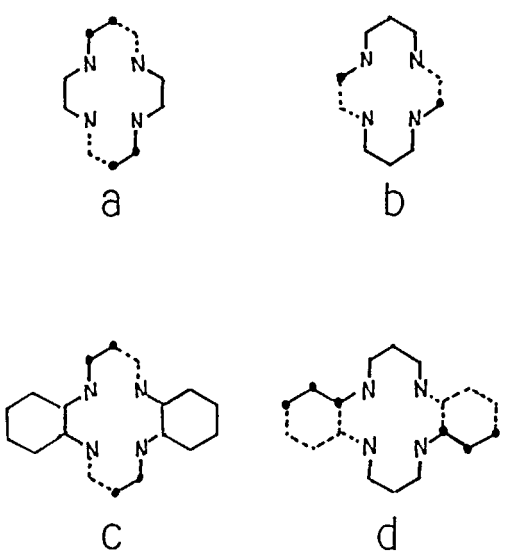
Complexation Behaviour

As shown in Table V, the differences in the stability constants for Ni(II) and Cu(II) with (*P*) and (*N*) show that (*P*) is more strongly bound for Ni(II), and (*N*) for Cu(II) and like cyclam for both metals. The stability constants for Zn(II) show little difference between (*P*) and (*N*) and are much greater than that of cyclam.

From measurements of electronic spectra in *N*,*N*-dimethylformamide and carbon 13-NMR in trifluoroacetic acid, the crystalline of Cu(II) and Ni(II) complexes are assigned as having square planar (D_{4h}), except for the Ni(II) complex of (*P*) (square-planar since the distorted octahedral equilibrium).[1] Since the Ni(II) complex of (*P*) is more stable than that of (*N*), it is suggested that the *cis-anti-cis* conformation of (*P*) is more favourable for the coordination of axial ligands as compared with the *cis-syn-cis* conformation, which is closed on one side of the ring.

Since the structures of the crystalline Zn(II) complexes of (*P*) and (*N*) prepared in this study are not assigned tetrahedral or octahedral, it is not clear whether the large differences for these (*vis-à-vis* Cu, Ni) depend on a particular property of the Zn(II) complex or different measurements of stability constants.

Conformational hindrance has been reported in two isomers of dicyclo-(18)-crown-6.[9] One, with a *cis-syn-cis* conformation, forms more stable complexes toward Na^+, K^+, Ag^+ *etc.*, than the other, with a *cis-anti-cis* conformation. This is explained by differences in solvation for a metal fixed to the polyether ring. It should be noted however that complexation of cyclic polyamines such as cyclam depends not only on metal ion size and solvation effects, but also on the coordination symmetry of the metal.



SCHEME 1 Basicity correction for nitrogen of Cy_2cyclam and cyclam. a: basicity correction of en for substituted ethyl group, $f_1 = pKa(EtNH_2)/pKa(en) = 1.08$; b: basicity correction of pn for substituted methyl group, $f_2 = pKa(MeNH_2)/pKa(pn) = 1.00$; c: basicity correction of cn for substituted ethyl group, $f_3 = pKa(EtNH_2)/pKa(cis\text{-}cn) = 1.12$, $f_3 = pKa(EtNH_2)/pKa(trans\text{-}cn) = 1.10$; d: basicity correction of pn for substituted propyl group, $f_4 = pKa(PrNH_2)/pKa(pn) = 1.03$.

The effect which increases the stability of a macrocyclic ligand complex compar with its open-chain analogue is called the "macrocyclic effect (*ME*)". Three ma effects which contribute to the *ME* are proposed;[10] 1) preorganization[11] or mul juxtapositional fixedness (MJF);[12] 2) solvation-desolvation of donor atoms in t confined space;[13] 3) inductive effects (intrinsic basicity effects).[14] Here, 1) is expect to be related to contribution of the cyclohexyl group to ring strain and conform tional hindrance, 2) is expected to be related to the influence of the two bulky a hydrophobic cyclohexyl groups on solvation–desolvation and 3) is expected to related to the covalence of the M–N bond produced by the inductive effect of t *N*-alkyl group. For the macrocyclic effect of Cy_2cyclam, it would be interesting discern which effect is the major one.

The macrocyclic effect for cyclam is estimated by comparison with its open-cha analogue, 2,3,2-tet. The effect for Cy_2cyclam, however, cannot be estimated in su a way because the cyclohexyl derivative 2,3,2-tet is not to hand. In order to estima the macrocyclic effect of Cy_2cyclam in comparison to that of cyclam, we assume imaginary open-chain analogue on the basis that cyclam and Cy_2cyclam consist ea of two pairs of symmetric segments (*a*), (*b*) and (*c*), (*d*) as shown in the Scheme; th is, cyclam consists of two *N*-alkyl substituents, ethylenediamine (en) and 1, diaminopropane (pn), and Cy_2cyclam consists of two *N*-alkyl substituents, *cis,tra* 1,2-cyclohexanediamine (*cis,trans*-cn) and 1,3-propanediamine (pn). These imagina open-chain analogues should be composed of the *N,N'*-dialkyl substituents of en, and cn. The data for mono *N*-alkyl substituents, however, are used in this wo because data for the series of *N,N'*-disubstituents with various alkyl groups are n published. Basicity correction factors based on inductive effects of substituted alk groups for the segments are assumed as shown in the Scheme. The stability constan for the imaginary open-chain analogues for cyclam and Cy_2cyclam are estimated eqations (*17*)–(*18*) with basicity correction factors as follows.

$$F_i = 1/2[f_1 \log \beta_2(\text{en}) + f_2 \log \beta_2(\text{pn})] \quad (1$$

$$F_j = 1/2[f_3 \log \beta_2(cis,trans\text{-cn}) + f_4 \log \beta_2(\text{pn})] \quad (1$$

The difference between F_i and F_j may be a measure of the basicity differen between cyclam and Cy_2cyclam, caused by only inductive effects. It amounts about 0.6 (for Ni(II)) and 0.8 (for Cu(II)) log units, corresponding to about 1 kca mol^{-1}. This value is near to that estimated for the Cu(II) complex of cyclam,[1] 2.2 kcal mol^{-1}.

We assume that the differences between the observed stability constant for cycla and F_i (KME(cyc)) and between that for Cy_2cyclam and F_j (KME(*P*), KME(*N*)) a a measure of the macrocyclic effect for each ligand. Therefore, the effect of t cyclohexyl group on the macrocyclic effect may be indicated by the differenc between KME(cyc) and KME(*P*) and KME(*N*)

These results are shown in Table VI. Since the KME differences are all negati except for the Ni(II) complex of (*P*), the cyclohexyl group decreases the macrocyc effect of cyclam ring with square-planar coordination irrespective of the conform tion of Cy_2cyclam. On the other hand, it enhances complexation for the distort octahedral Ni(II) complex of (*P*).

* 1 cal = 4.184 J.

TABLE VI
Estimations of macrocyclic effect for cyclam and dicyclohexylcyclam using equations (*17*) and (*18*).[a]

	F_i	KME(cyc)	F_j	KME(*P*)	KME(*N*)	KME(*P*) -KME(cyc)	KME(*N*) -KME(cyc)	
	12.51	9.69	13.16	9.94	9.37	0.25	−0.32	*cis*-cn
Ni(II)			13.20	9.90	9.33	0.21	−0.36	*trans*-cn
	18.99	7.51	19.84	6.36	7.26	−1.15	−0.25	*cis*-cn
Cu(II)			19.85	6.65	7.25	−0.86	−0.26	*trans*-cn

[a] Refer to Scheme in text.

TABLE VII
Thermodynamic data for related ligands and predicted values for dicyclohexylcyclam.

	Ni(II)			Cu(II)		
	log K_1	ΔH	ΔS	log K_1	ΔH	ΔS
2,3,2-tet[a]	15.9	−18.6	10	23.2	−27.7	13
Cyclam[a]	22.2	−24.1	21	26.5	−32.4	13
Cy_2cyclam(*P*)[b]	23.10	(−24.1)	(24.8)	24.46	(−32.4)	(12.3)
Cy_2cyclam(*N*)$_b$	22.53	(−24.1)	(22.2)	27.08	(−32.4)	(15.2)

[a] Quoted data from Refs [10] and [15] at 25°C; ΔH, kcal mol^{-1}; ΔS, cal deg^{-1} $mol.^{-1}$ [b] Calculated values from observed stability constants for dicyclohexylcyclams with the assumption that the enthalpy is same as for cyclam and using $\Delta S = 3.36(1.363 \log K + \Delta H)$, at 25°C.

Thermodynamic data for cyclam and Cy_2cyclam are given in Table VII. Values of ΔS for the Cy_2cyclam complexes are roughly estimated on the assumption that ΔH values for Cy_2cyclam complexes are nearly the same as for the cyclam complexes. So long as differences for ΔH between cyclam and Cy_2cyclam depend only on basicity differences, this estimation is reasonable because of the small differences between F_i and F_j. The values of ΔS for Ni(II) complexes are greater than for Cu(II) and the quantity is greatest for the Ni(II) complex of (*P*). Complexation of (*P*) toward Ni(II) causes a large entropy increase and this may be related to ring deformation associated with the distorted octahedral square planar equilibrium.

From the results described above, we suggest that the major contribution of the cyclohexyl group to the stability of the macrocyclic ligand concerns ring fit upon metal coordination or ring flexibility for complexation, involving preorganization and MJF.

ACKNOWLEDGEMENTS

We thank Mr M. Hashimoto for measurements of NMR and DTA, and Mr Y. Takeuchi and M. Yamaguchi for help with the experiments.

REFERENCES

1. K. Sakata, S. Wada, N. Sato, M. Kurisu, M. Hashimoto and Y. Kato, *Inorg. Chim. Acta*, **119**, 111 (1986).

2. K. Kobiro, A. Nakayama, T. Hino, M. Suwa, K. Kakiuchi, Y. Tobe and Y. Odaira, *Chem. Lett.*, 1979 (1990).
3. A. Evers and R.D. Hancock, *Inorg. Chim. Acta*, **160**, 245 (1989).
4. B. Korybut-Daszikiewicz, J. Mrozinski and W. Wojciechowsky, *Bull. Acad. Pol. Sci., Ser. Chim.*, **17**, 411 (1969).
5. A.E. Martell and R.J. Motekaitis, "Determination of Use of Stability Constants", (VCH Publ. Inc., New York, 1988).
6. G. Anderegg, "IUPAC Chemical Data Ser., No 14, Critical Survey of Stability Constants of EDTA Complexes", (Pergamon Press, Oxford, 1977).
7. C. Nave and M.R. Truter, *J. Chem. Soc., Dalton Trans.*, 2351 (1974).
8. J.H. Hildebrand and R.L. Scott, "The Solubility of Non-electrolytes", 3rd. ed., (Reinhold Publ. Co., New York, 1950).
9. H.K. Frensdorff, *J. Am. Chem. Soc.*, **93**, 600 (1971).
10. a) R.D. Hancock and A.E. Martell, *Comments Inorg. Chem.*, **6**, 237 (1988); b) R.D. Hancock and A.E. Martell, *Chem. Rev.*, **89**, 1875 (1989).
11. a) A. Anicini, L. Fablirizzi, P. Paoletti and P.M. Clay, *J. Chem. Soc., Dalton Trans.* 577 (1978); b) J. Cram, T. Kaneda, R.C. Helgeson, S.B. Brown, C.B. Knobler, E. Maverick and K.N. Trueblood, *J. Am. Chem. Soc.*, **107**, 3645 (1985).
12. D.H. Bush, K. Farmery, V. Goedken, V. Katovic, A.C. Melnyk, C.R. Sperati and N. Tokel. *Adv. Chem. Ser.*, **100**, 52 (1971).
13. D. Hinz and D.W. Margerum, *Inorg. Chem.*, **13**, 2941 (1974).
14. a) R.D. Hancock and G.J. McDougall, *J. Am. Chem. Soc.*, **102**, 6551 (1980); b) V.J. Tom, J.C.A. Boeyens, G.J. McDougall and R.D. Hancock, *J. Am. Chem. Soc.*, **106**, 3198 (1984).
15. R.M. Smith and A.E. Martell, "Critical Stability Constants", Vols. 1–6, (Plenum Press, New York, 1974, 1975, 1976, 1982, 1988).
16. M. Kodama and E. Kimura, *J. Chem. Soc., Dalton Trans.*, 1473 (1977).