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Synthesis of Sterically Congested Cyclam Derivatives and Their Nickel(II) Complexes

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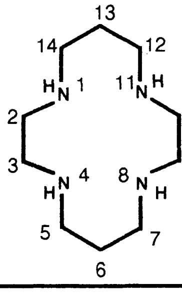
A new class of cyclam, octamethylcyclam, and its related compounds bearing tetramethylethane, *cis*- cyclohexane, or *trans*- cyclohexane subunit(s) have been synthesized. Nickel(II) complexes with sterically congested ligands have been shown to be low-spin complexes in water, while those with less congested ligands to be mixtures of low-spin and high-spin ones. Nickel(II) complexes with sterically congested ligands have been also exhibited to have higher half-wave potentials ($E_{1/2}(\mathrm{Ni}^{\mathrm{II,III}})$) than those of the complexes with less congested ligands.

Although the six-coordinate octahedral geometry of nickel(II) ion is common feature for 1,4,8,11-tetraazacyclotetradecane (cyclam) (**1**)-nickel(II) complexes especially for those with the small axial ligands such as chloride anions,[1] there is growing recognition in controlling the coordination geometry of nickel(II) ion by changing the steric environment of the coordination axis by substituents on cyclam.[2] In this context, the cyclams with methyl group(s) on 1, 4, 5, 7, 8, 11, 12, and/or 14 position(s) have been synthesized and they have been shown to control the accessibility of the axial ligands to the coordinated nickel(II) ion due to the steric barrier of the methyl group(s).[1]

In this connection, we have designed a new type of sterically congested cyclams, octamethylcyclam (**2**) and tetramethylcyclam (**3**), with eight or four methyl groups on 2, 3, 9, and 10 or 2 and 3 positions, respectively. HGS and CPK molecular model examinations of $\mathrm{Ni(2)}^{2+}$ complex suggest that two pseudo axial methyl groups on 2 and 10 (or 3 and 9) positions are facing each other and the axial coordination sites are put closely between them.[3] Therefore, it is expected that the geminal methyl groups on 2, 3, 9, and/or 10 positions would prevent axial ligand(s) from accessing to the coordinated Ni(II) ion more effectively than the methyl groups on 5, 6, 7, 12, 13, and/or 14 positions. In this paper, we wish to report on (i) the synthesis of sterically congested cyclam derivatives **2** and **3** and their related compounds, *cis*- syn-*cis*- dicyclohexanocyclam (**4s**),[4] *cis*- anti-*cis*-



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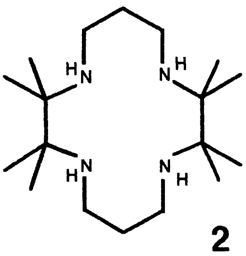

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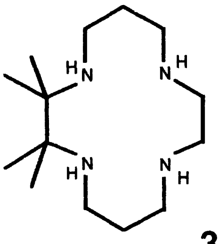

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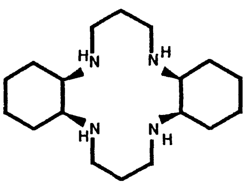
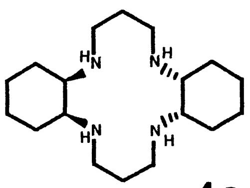
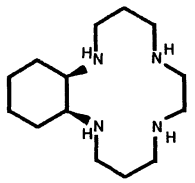


4s



4a



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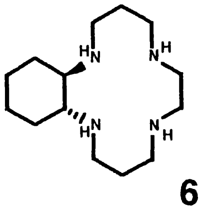

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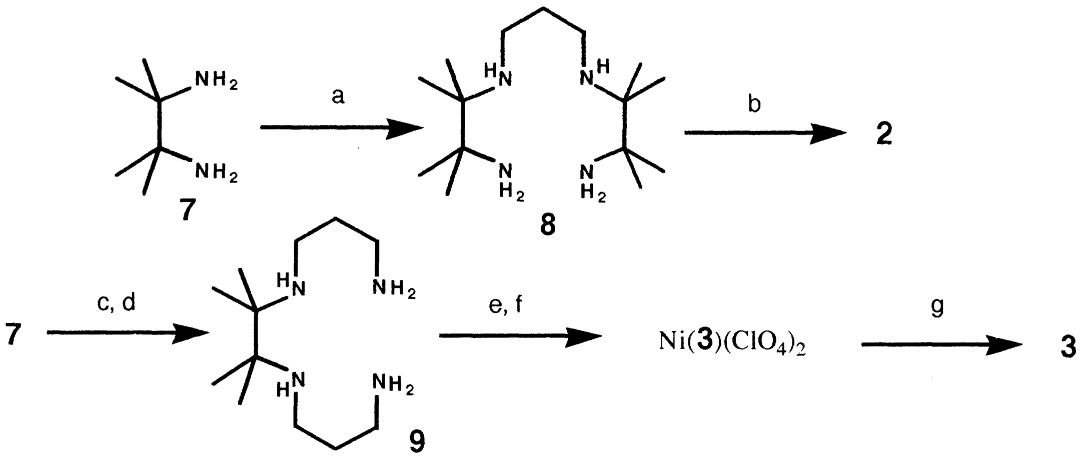
dicyclohexanocyclam (**4a**),[4] *cis*- cyclohexanocyclam (**5**), and *trans*- cyclohexanocyclam (**6**), (ii) the effect of the substituent(s) on the ethano bridge of cyclam on the spin state of coordinated Ni(II) ion in the complexes, and (iii) the effect of the substituent(s) on the redox potential for the Ni^{II}/Ni^{III} change in the complexes.

Cyclam derivatives **2** and **3** were synthesized according to Scheme 1. Reaction of an excess 2,3-dimethyl-2,3-butanediamine (**7**)[6] with 1,3-dibromopropane in the presence of Na_2CO_3 gave tetraamine **8** in 67% yield as an oil. Reaction of **8** with 1,3-dibromopropane produced octamethylcyclam (**2**) in 19% yield as crystals (mp 131-132 °C recrystallized from acetonitrile). According to the similar procedure, **4s** and **4a** were synthesized from *cis*-1,2-cyclohexanediamine.[7-9] On the other hand, reaction of diamine **7** with acrylonitrile followed by hydrogenation gave two-armed tetramethyltetraamine **9** in 54% yield as an oil. Ni(II)-templated cyclization of tetraamine **9** with glyoxal at 45-55 °C followed by hydride reduction gave $Ni(\mathbf{3})(ClO_4)_2$ complex in 40% yield as red crystals (mp >285 °C (dec.) recrystallized from water). Tetramethylcyclam (**3**) was liberated by treatment of the complex with NaCN[10] (70%, 109-110 °C from acetonitrile). Similarly, **5** and **6** were also synthesized.[8]

In order to obtain complexes of cyclams with Ni(II) ion, reactions of cyclams **1**, **2**, **3**, **4s**, **4a**, **5**, and **6** with $Ni(NO_3)_2$ were performed. Unsubstituted cyclam (**1**) gave purple complex easily by reaction of equimolar amounts of **1** and $Ni(NO_3)_2 \cdot 6H_2O$ in methanol at room temperature. Similarly, **3**, **5**, and **6** formed the corresponding complexes under similar conditions except for **5** for which ethanol was used as the solvent, while **2**, **4s**, and **4a** having sterically bulky groups on both sides gave only greenish powdery products. However, when dimethylsulfoxide was used instead of methanol, the crystalline complexes of the latters were obtained as shown in Table 1. According to the similar procedure, complexes of cyclams **1**-**6** with $NiCl_2$ and $Ni(ClO_4)_2$ were also prepared.[11]

Next, to know the effect of the substituent(s) on the ethano bridge of cyclam on spin state of coordinated



a: $BrCH_2CH_2CH_2Br$, Na_2CO_3; b: $BrCH_2CH_2CH_2Br$; c: H_2CCHCN;
d: H_2, Raney-Ni; e: OHCCHO, $Ni(ClO_4)_2$; f: $NaBH_4$; g: NaCN

Scheme 1.

Table 1. Melting points and magnetic susceptibilities of $Ni(L)(NO_3)_2$, visible absorption maxima of $Ni(L)(ClO_4)_2$, and half-wave potentials for the Ni^{II}/Ni^{III} redox change of $Ni(L)X_2$ ($X=NO_3$, Cl, and ClO_4).

L	Mp/°C	μ_{eff}/BM	$\lambda_{max}(\varepsilon)$		$E_{1/2}(Ni^{II,III})$ *vs.* SCE/V		
			in H_2O	in 5 M $NaClO_4$	$Ni(NO_3)_2$	$NiCl_2$	$Ni(ClO_4)_2$
1	265-270 (dec.)	1.65	455(40)	455(50)	0.791	0.418	0.989
5	205-210 (dec.)	0.90	446(70)	446(70)	0.818	0.429	1.019
6	250-260 (dec.)	1.94	455(40)	455(70)	0.782	0.439	0.980
3	275-285 (dec.)	<0.3	452(80)	452(80)	0.885	0.510	1.096
4 s	255-265 (dec.)	<0.3	440(80)	440(80)a)	1.079	—c)	1.078
4a	295-305 (dec.)	<0.3	455(60)	—b)	0.845	0.520	1.106
2	270-280 (dec.)	<0.3	452(70)	452(70)a)	—c)	0.895	1.413

a) In 1 M solution. Complex was salted-out in 5 M solution. b) Complex was salted-out in 1 M solution.
c) Irreversible.

Ni(II) ions, magnetic susceptibilities (Evans' method12)) and electronic spectra of complexes were measured in water (Table 1). As results, in the case of the flat complexes $Ni(\mathbf{1})^{2+}$ and $Ni(\mathbf{6})^{2+}$ and the less congested complex $Ni(\mathbf{5})^{2+}$, the values of μ_{eff} were 0.90-1.94 and the values of ε at about 450 nm (low-spin square planar species) increased in $NaClO_4$ solution as compared with in water except for $Ni(\mathbf{5})^{2+}$, suggesting they were mixtures of low-spin square planar and high-spin octahedral species. On the other hand, in the case of the complexes $Ni(\mathbf{2})^{2+}$, $Ni(\mathbf{4s})^{2+}$, and $Ni(\mathbf{4a})^{2+}$ bearing two bulky groups on both sides, the values of μ_{eff} were less than 0.3 and the values of ε did not increase in $NaClO_4$ solution except for $Ni(\mathbf{4a})^{2+}$, indicating that they were all low-spin square planar complexes.13) These results suggest that the access of anions or water molecules to the coordinated Ni(II) ion is suppressed completely by two bulky subunits whether they are *cis*-cyclohexane or tetramethylethane subunit. Interestingly, the complex with tetramethylcyclam (**3**) having only one tetramethylethane subunit turned out to be a low-spin complex, suggesting that one tetramethylethane subunit could prevent the anions or water molecules from accessing to the coordinated Ni(II) ion effectively.

Moreover, half-wave potentials of the complexes for Ni^{II}/Ni^{III} redox change ($E_{1/2}(Ni^{II,III})$) were measured by cyclicvoltammetry (acetonitrile, *n* -Bu_4NClO_4), in order to know the steric environment of axial coordination sites in the complexes (Table 1).14) As results, the flat complexes with unsubstituted cyclam $Ni(\mathbf{1})X_2$ ($X=NO_3$, Cl, and ClO_4) and *trans*- cyclohexanocyclam $Ni(\mathbf{6})X_2$ showed similar half-wave potentials, respectively. On the other hand, $Ni(\mathbf{3})X_2$ bearing one tetrametylethane subunit and $Ni(\mathbf{2})X_2$, $Ni(\mathbf{4s})X_2$, and $Ni(\mathbf{4a})X_2$ having two bulky groups on both sides showed higher values than those of flat complexes $Ni(\mathbf{1})X_2$ and $Ni(\mathbf{6})X_2$. Especially, $Ni(\mathbf{2})Cl_2$ and $Ni(\mathbf{2})(ClO_4)_2$ bearing eight methyl groups showed very high values, 0.895 and 1.413 V, respectively, indicating that the axial coordination sites of the complexes were tightly regulated by introduced alkyl groups on cyclam complexes.

Thus, it has turned out that the introduced tetramethylethane subunit(s) in cyclam complexes results in the significant change of the accessibility of axial ligands toward cyclam-nickel(II) complexes.

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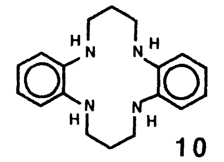
1) "Coordination Chemistry of Macrocyclic Compounds," ed by G. A. Melson, Plenum Press, New York (1979).

2) For example, see; E. Kimura, T. Koike, H. Nada, and Y. Iitaka, *Inorg. Chem.,* **27**, 1036 (1988).

3) On the other hand, while pseudo axial methyl groups on 5 and 7 positions, for example, are also close to the axial coordination sites, they leave enough space on the other part of the trimethylene bridge of the ligand.

4) Sakata *et al.* synthesized two isomers of dicyclohexanocyclams (*cis*- syn-*cis*- dicyclohexanocyclam: mp 158.5-161.0 °C recrystallized from petroleum ether and *cis*- anti-*cis*- or *trans*- anti-*trans*- dicyclohexanocyclam: 194.5-196.0 °C from petroleum ether) by hydrogenation of dibenzocyclam (**10**).$^{5)}$



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

6) R. Sayre, *J. Am. Chem. Soc.,* **77**, 6689 (1955).

7) R. Saito and Y. Kidani, *Chem. Lett.,* **1976**, 123.

8) Melting points are as follows: **4s**: 156-157 °C (recrystallized from acetonitrile),$^{4)}$ **4a**: 189-190 °C (dichloromethane),$^{4)}$ **5**: 137.5-138 °C (acetonitrile), and **6**: 218-219 °C (mixture of chloroform and ether).

9) Stereochemical assignment of syn isomer (**4s**) was done by X-ray molecular structure analysis of Ni(**4s**)-Cl$_2$. Crystal data: $C_{18}H_{36}Cl_2N_4Ni$, M =438.12, monoclinic, $P2_1/n$, a =13.757(3), b =12.780(2), c =11.751(3) Å, β =102.01(3) °, V=2020.8(7) Å^3, Z =4, D_c =1.440 g/cm^3. Intensity data ($2\theta<55°$) were collected on Rigaku four-circle diffractometer using graphite monochromatized Mo-Kα radiation and a θ-2θ scan technique was used. No absorption collection was done. Full matrix least-squares refinement based on 3335 independent reflection with $|Fo|<3\sigma(F)$ yielded an R factor of 0.057 (non-hydrogen atoms anisortropically). XRAY SYSTEM program (M. Stewart, XRAY-76, Technical Report TR-445, Computing Science Center, University of Maryland, Maryland (1976)) was used throughout the analysis. All the crystallographic computations were performed at the Crystallographic Research Center of Osaka University. As a result, the other isomer was ascribed to be anti one (**4a**).

10) E. K. Barefield, F. Wanger, A. W. Herlinger, and A. R. Dahl, *Inorg. Synth.,* **16**, 220 (1986).

11) Melting points are as follows: Ni(**2**)(ClO$_4$)$_2$: 286-303 °C (dec.), Ni(**3**)(ClO$_4$)$_2$: >285 (dec.), Ni(**4s**)-(ClO$_4$)$_2$: >300 °C,$^{5)}$ Ni(**4a**)(ClO$_4$)$_2$: >300 °C, Ni(**5**)(ClO$_4$)$_2$: >270 °C (dec.), Ni(**6**)(ClO$_4$)$_2$: >275 °C (dec.), Ni(**4s**)Cl$_2$: >295 °C (dec.), and Ni(**4a**)Cl$_2$: >300 °C. Complexes Ni(**2**)Cl$_2$, Ni(**3**)Cl$_2$, Ni(**5**)Cl$_2$, and Ni(**6**)Cl$_2$ are hygroscopic.

12) D. F. Evans, *J. Chem. Soc.,* **1959**, 2003.

13) Ni(**4s**)(ClO$_4$)$_2$ (*cis* -syn-*cis* isomer) was reported to have the square-planar geometry in *N,N*-dimethylformamide.$^{5)}$

14) Busch *et al.* reported that the positive shifts of the $E_{1/2}(Ni^{II,III})$ in the nickel complexes with methyl substituted cyclam derivatives were ascribed to the nonbonding interaction between the extraplanar ligands (solvent) coordinated to the Ni(III) ion and the axially oriented methyl groups on the six-membered chelate ring (F. V. Lovecchio, E. S. Gore, and D. H. Busch, *J. Am. Chem. Soc.,* **96**, 3109 (1974)).

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