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9. The comparison of ^{1}H-NMR spectra was done with the common intermediate, **13b**, derived from the synthetic compound, **12b**, and from the natural α-kainic acid as shown below.

12b   **13b**   α-kainic acid
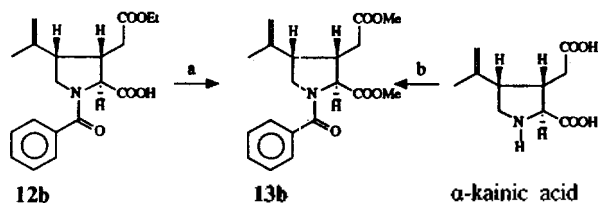
a) i) NaOH, MeOH-H$_2$O, rt, 2 hr.
   ii) CH$_2$N$_2$, Et$_2$O
b) i) PhCOCl, NaOH, H$_2$O, 0℃
   ii) CH$_2$N$_2$, Et$_2$O

Direct Template Synthesis of Iron(III) Polyaza Macrotricyclic Complex

Myunghyun Paik Suh*, Sang-Hee Park, and Do-Uk Kim

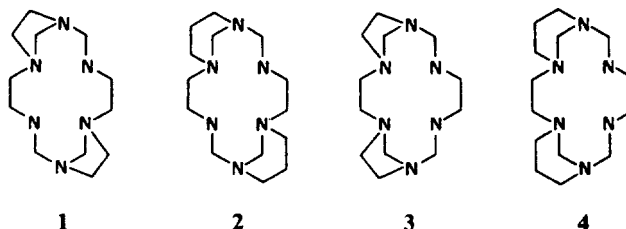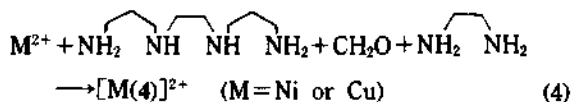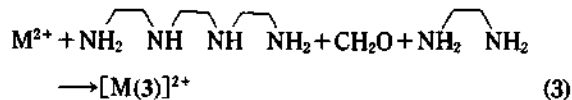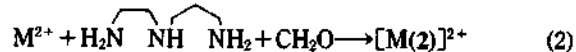*Department of Chemistry Education, Seoul National University, Seoul 151-742*
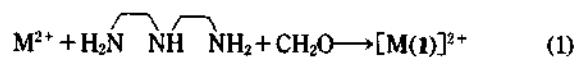
Metal template syntheses often provide selective routes toward the products that are not obtainable in the absence of metal ions. Especially, template reactions involving formaldehyde and amines facilitate the preparation of saturated polyaza multidentate, macrocyclic and macropolycyclic complexes.[1-8] The reactions are simple ("one-pot reactions"),

cheap, and high yielding.

However, iron macrocyclic complexes are not able to be synthesized by the direct template condensation reactions unless the macrocycle to be produced is highly conjugated. The direct template reactions usually lead to iron oxide instead of the desired macrocyclic complexes because Fe(II) intermediate complexes have strong tendency to react with water and a trace of oxygen. Therefore, Fe(II) macrocyclic complexes are generally synthesized by the insertion of Fe(II) ion to the free macrocycle, that is prepared separately, under an oxygen and moisture free condition.
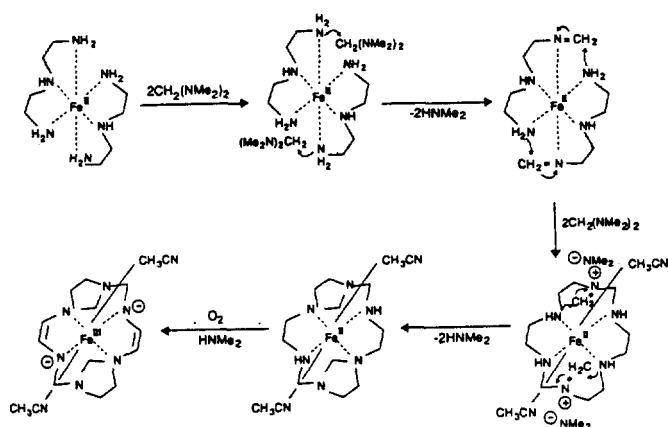
Ni(II) and Cu(II) complexes of macrotricyclic ligands 1-4 have been prepared in our laboratory by the template condensation reactions of amines and aqueous formaldehyde in the presence of Ni(II) or Cu(II) ion as described in eqs 1-4.[6-8] In these cyclization reactions, formaldehyde links two *cis* amine moieties to form methylenediamine (N-C-N) linkages. The complexes contain five-membered or six-membered sub-ring moieties that are located anti and almost perpendicular to the square coordination plane.

$$M^{2+} + H_2N \quad NH \quad NH_2 + CH_2O \longrightarrow [M(1)]^{2+} \qquad (1)$$

$$M^{2+} + H_2N \quad NH \quad NH_2 + CH_2O \longrightarrow [M(2)]^{2+} \qquad (2)$$

$$M^{2+} + NH_2 \quad NH \quad NH \quad NH_2 + CH_2O + NH_2 \quad NH_2$$
$$\longrightarrow [M(3)]^{2+} \qquad (3)$$

$$M^{2+} + NH_2 \quad NH \quad NH \quad NH_2 + CH_2O + NH_2 \quad NH_2$$
$$\longrightarrow [M(4)]^{2+} \quad (M = Ni \text{ or } Cu) \qquad (4)$$

1   **2**   **3**   **4**

In order to synthesize Fe(II) complexes of the macrotricyclic ligands 1-4, we have to obtain the free ligand from the Ni(II) or Cu(II) macrocyclic complexes. However, the free ligands are not able to be isolated because of the instability of N-C-N linkages contained in the macrocyclic ligands. It has been known that N-C-N linkages are unstable when they contain primary or secondary amines.[9] In addition, it has been revealed that N-C-N groups containing secondary nitrogens are stable as long as their nitrogens are coordinated to the metal ion.[2-8]

Therefore, the only way to obtain the Fe(II) complexes of macrocyclic ligands 1-4 is the direct template synthesis that is conducted in the absence of water and oxygen. Formaldehyde or paraformaldehyde cannot be employed in this reaction because water is produced during the Schiff base condensation reactions.

We have attempted to synthesize the Fe(II) complex of macrotricyclic ligand 1 by the direct template condensation re-

Scheme 1.

actions of [Fe(dien)$_2$]$^{2+}$ with CH$_2$(NMe$_2$)$_2$ instead of formaldehyde, and obtained Fe(III) complex of macrotricyclic ligand A. In this report, we present the synthesis and properties of the Fe(III) complex of macrotricyclic ligand A, 1,3,6,9,11,14-hexaazatricyclo[12.2.1.1^{6,9}]octadeca-4,12-dienato(2-).

A
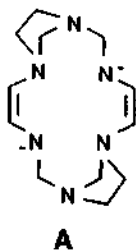
Experimental Section

Measurement. Infrared spectra were recorded with a JASCO IR-810 spectrophotometer. Conductance measurements were performed by using a Metrohm Herisau E518 conductometer and RC-216B$_2$ conductivity bridge. Electronic absorption spectra were obtained on a Shimadzu UV-260 spectrophotometer. Elemental analyses were performed by Galbraith Laboratories Inc., Knoxville, TN. U.S.A.

Synthesis. All solvents and reagents were purified according to the literature[10], and were deaerated thoroughly prior to use. CH$_2$(NMe$_2$)$_2$ were prepared according to the literature[11], fractionally distilled at 85°C, and stored with 4 Å molecular sieves.

Safety note. *Caution* ! Perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of material should be prepared and these should be handled with great caution.

[Fe(A)(CH$_3$CN)$_2$]ClO$_4$. The complexes should be prepared and handled under an atmosphere of nitrogen that is purified by passing through a BASF column and a CaCl$_2$ column. Fe(ClO$_4$)$_2 \cdot$ 6H$_2$O (4 g) is dissolved in degassed MeOH (50 m*l*) in a schlenk tube. To a stirred solution, was added diethylenetriamine (3.6 m*l*) through a syringe. White precipitates of [Fe(dien)$_2$](ClO$_4$)$_2$ were formed, which were filtered, washed with MeOH, and dried *in vacuo*. [Fe(dien)$_2$](ClO$_4$)$_2$ (2 g) was dissolved in degassed MeCN (40 m*l*) and CH$_2$(NMe$_2$)$_2$ (20 m*l*) was added. The solutions were heated at reflux under nitrogen atmosphere for 24 h. The color of

the solution turned to red and the red precipitates formed. The precipitates were filtered, washed with MeCN, and dried *in vacuo*. Yield. ~20%. Anal. Calcd for FeC$_{16}$H$_{26}$N$_8$ClO$_4$: C, 39.56; H, 5.39; N, 23.07. Found: C, 38.91, H, 5.41, N, 22.26.

Results and Discussion

Template condensation reaction of [Fe(dien)$_2$](ClO$_4$)$_2$ with CH$_2$(NMe$_2$)$_2$ in MeCN solutions under nitrogen atmosphere resulted in the six-coordinate Fe(III) complex of macrocyclic ligand A, [Fe(A)(CH$_3$CN)$_2$]ClO$_4$. The red colored complexes are stable in the air both in solid state and in MeCN solutions. The value of molar conductance of the complex is 159 Ω^{-1}M^{-1}cm^{-1} at 20°C in MeCN solutions, indicating that the complex is a 1:1 electrolyte. The infrared spectrum of the complex shows no N-H stretching around 3100-3400 cm^{-1}. It shows $v_{C=C}$ at 1600 and 1660 cm^{-1}, v_{CN} of coordinated acetonitrile at 2222 cm^{-1},[12] and ClO$_4^-$ band around 1100 cm^{-1}. UV/vis spectrum of the complex (MeCN solution) shows intense charge transfer band at $\lambda_{max} = 495$ nm with the extinction coefficient of 5800.

The proposed synthetic routes for the complex is shown in Scheme 1. CH$_2$(NMe$_2$)$_2$ links two *cis* amine nitrogens of [Fe(dien)$_2$]$^{2+}$ to form methylenediamine linkages, and produces Fe(II) macrocyclic complex of 1. Raymond also employed CH$_2$(NMe$_2$)$_2$ previously to link amine moieties in the template synthesis of some lanthanide macrocyclic complexes.[13] The Fe(II) macrocyclic complex of 1 reacts with a trace of oxygen and is oxidized to Fe(III) complex. In addition, HNMe$_2$ that is produced from CH$_2$(NMe$_2$)$_2$ during the condensation reaction deprotonates the secondary amines of the complex of 1 to give the negatively charged ligand. The secondary amine protons of the macrocycle should be much more acidic in Fe(III) complex than in Fe(II) complex and are easily deprotonated by HNMe$_2$. Oxidation of Fe(II) to Fe(III) and the introduction of double bonds in the macrocyclic ligand by the reaction with molecular oxygen have been known in other cases.[14-16] Conjugation in C=C-N$^-$ group in the macrocycle A causes M→L charge transfer in the visible region. The Fe(III) complex of A reacts with water or HClO$_4$ in MeCN to give yellow solution, whose spectra shows maximum absorption at 370 nm. This is characteristic spectra of the low spin octahedral Fe(III) macrocyclic complex that does not contain conjugated double bonds in the ligand.[16,17] This supports that the Fe(III) complex with negatively charged ligand A can be easily protonated to give the complex of neutral ligand B

$$[Fe(A)(CH_3CN)_2]^+ + 2H^+ \longrightarrow [Fe(B)(CH_3CN)_2]^{3+} \qquad (5)$$

B
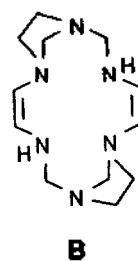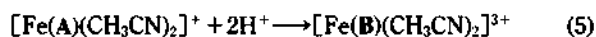
This study shows that CH$_2$(NMe$_2$)$_2$ can be utilized to link two amine moieties in the direct template synthesis of ma-

crocyclic complexes by using Fe(II) ion as a metal template. In addition, this study also shows that oxidation of Fe(II) to Fe(III) as well as the oxidative dehydrogenation of the macrocyclic ligand occur during the template reactions in the presence of base and a trace of oxygen.

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A Synthesis of the Pheromone of Mouse Mus Musculus

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The mouse pheromone, exo-7-ethyl-5-methyl-6,8-dioxabicy-

clo[3.2.1]oct-3-ene (3), has been isolated from urine of the male mouse of the species Mus musculus[1] and synthesized in a low yield.[2]

In the course of our continuing study on bicyclic ketal compounds,[3] we developed the stereoselective synthesis of exo and endo bicyclic ketal and utilized this method to the brevicomin synthesis.[4] We now report a synthesis of the pheromone 3 from exo brevicomin 1 which is synthesized from methyl vinyl ketone dimer in higy yield.
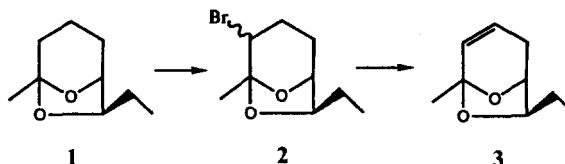
Bromination of acyclic acetals is known to occur on the carbon atom α to the functional group.[5] Accordingly, 1 was brominated with one equiv. of bromine in carbon tetrachloride for 7 hrs stirring at room temperature to obtain mono-brominated ketal 2 in 88% yield. With the addition of Na_2CO_3, the reaction was completed within 1 hr in quantitative yield. In our bicyclic ketal system, there are two carbon atoms α to the ketal and regiospecific bromination has been achieved *via* enolate **2a** without any evidence of **4** as a product. But the product showed two peaks on the capillary gas-liquid chromatogram, indicative of the presence of 1 : 1 mixture of axial and equatorial isomers, however, dibromination was occurred with excess bromine.
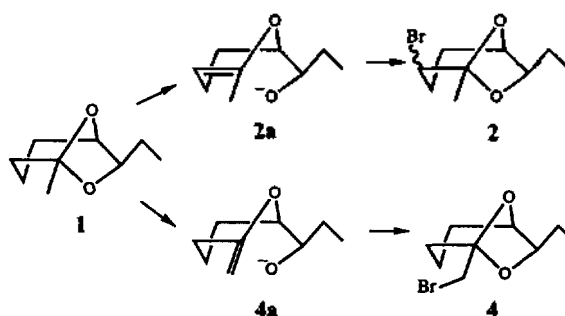
The mono-brominated ketal 2 was subjected to dehydro-bromination with various basic conditions using methoxide, *t*-butoxide, LDA, NaH and *n*-BuLi etc. Best result was achieved with *t*-butoxide at reflux in 71% yield.

Experimental

Exo-4-bromo-7-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane (2). To a 0.18 g of exo-brevicomin 1 in 8 ml of anhydrous carbon tetrachloride was added 0.39 g of Na_2CO_3 and 0.058 ml of Br_2. The reaction mixture was stirred for 1 hr at room temperature and filtered, followed by extraction with methylene dichloride (20 ml×4). The organic layer was dried ($MgSO_4$), filtered and evaporated to give 0.27 g of oilish products (quantitative yield) which are 1 : 1 mixture of axial and equatorial isomers.

^{1}H-NMR (CDCl$_3$): δ 4.23 (m, 1H), 4.08-3.96 (m, 1H), 3.90 (t, 1H), 2.40-1.60 (m, 6H), 1.59 (s, 3H), 0.91 (t, 3H); IR (neat): 2958, 1459, 1381, 1330, 1235, 790 cm^{-1}.