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# Notes

## Copper(II) Template Synthesis of a 20-Membered [1+1] Schiff Base Macrocycle and Nickel(II) Template Synthesis of a 40-Membered [2+2] Schiff Base Macrocycle from 2,6-Pyridinedicarboxaldehyde and 1,13-Diamino-4,7,10-trioxatridecane

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### Introduction

Macrocyclic ligands prepared via the metal ion templated Schiff base condensation of 2,6-dicarbonylpyridines with α,ω-diamino ethers have been shown to give diimine [1+1] macrocycles (one dicarbonyl to one diamine) and tetraimine [2+2] macrocycles (two dicarbonyls to two diamines).[1] A variety of metal ions were found to be effective templating ions, as indicated in Scheme 1.[1,2] Surprisingly absent from this list are copper(II) and nickel(II), both of which have been utilized in the preparation of $N_4$ aza-crowns.[1] For these systems, it has been found that the larger alkaline earth, lead(II), and lanthanide(III) ions seemed more effective at producing the penta- and hexadentate macrocycles, while alkali and first row transition metal ions were found to be ineffective as templates.[2] It has been suggested, especially in the cases of the 18-membered ring, L$^1$, and the 30-membered ring, L$^3$, that the ionic size of the templating ion is a major factor in the success of these reactions.[1−3] We have found a closely related system in which copper(II) can serve as the templating ion in the production of a 20-membered [1+1] macrocyclic ligand, while nickel(II) acts as the template to give a 40-membered [2+2] macrocyclic ligand.

### Results and Discussion

The [1+1] condensation of 2,6-pyridinedicarboxaldehyde with 1,13-diamino-4,7,10-trioxatridecane was achieved by the slow addition of 1 equiv of diamine to a solution containing 1 equiv each of the dialdehyde and copper(II) chloride (Scheme 2). After precipitation of the product as the hexafluorophosphate salt followed by recrystallization, emerald green crystals of the complex were obtained in 25% overall yield. An x-ray crystal structure of this complex has already been reported.[4] The 20-membered macrocycle, L$^4$, was found to be coordinated to the copper(II) only through the three nitrogen atoms. As can be seen in the structural representation (Figure 1), the copper(II) center has a nearly square pyramidal geometry, with a water molecule occupying an axial site. It is interesting to note the hairpin turn of the polyether bridge in which the first and third oxygens are hydrogen-bonded to the water molecule. The copper(II) binding site cooperates with these well-positioned ether oxygens to make an excellent $H_2O$ receptor. In the related 18-membered [1+1] macrocycle, L$^1$, reported by Fenton and coworkers the hexadentate macrocycle was approximately planar.[5] The difference between the structures, and indeed the

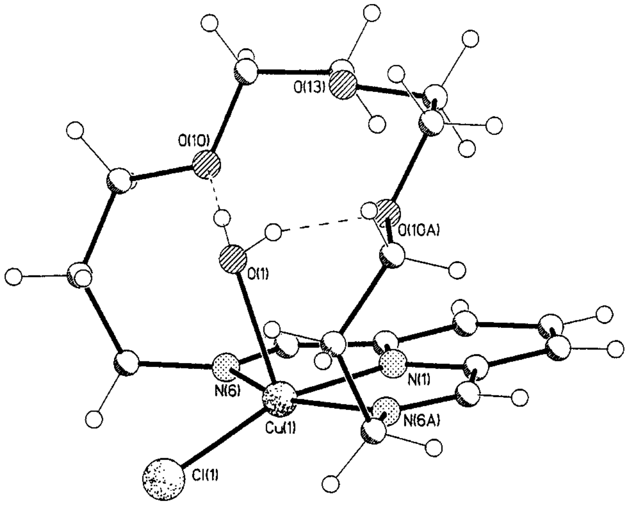
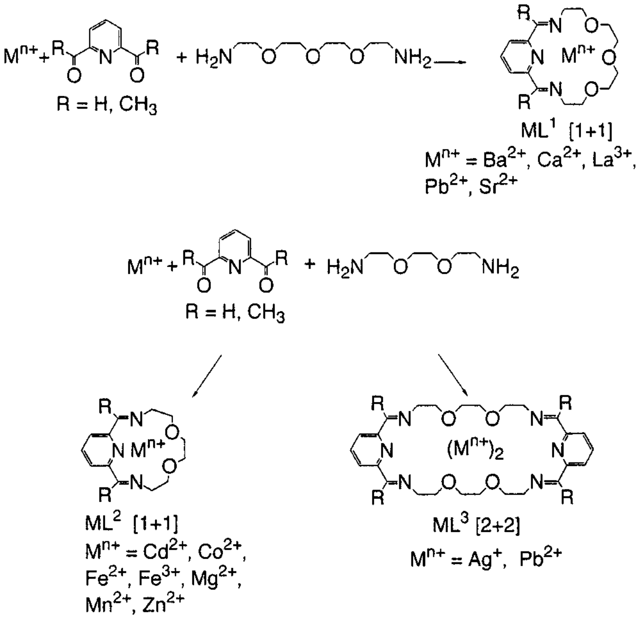
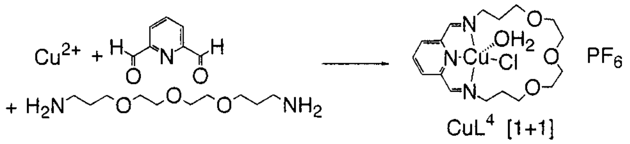


**Figure 1.** Side view of the CuL$^4$ Cl·$H_2O$ complex, showing the Cu(II) coordination geometry and the hairpin conformation of the complex.

**Scheme 1**



**Scheme 2**



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(1) Nelson, S. M. *Pure Appl. Chem.* **1980**, *52*, 2461.

(2) Fenton, D. E.; Vigato, P. A. *Chem. Soc. Rev.* **1988**, *17*, 69.

(3) Collinson, S. R.; Fenton, D. E. *Coord. Chem. Rev.* **1996**, *148*, 19.

(4) Alcock, N. W.; Busch, D. H.; Vance, A. L. *Acta Crystallogr.* **1996**, *C52*, 1134.

(5) Fenton, D. E.; Cook, D. H.; Nowell, I. W.; Walker, P. E. *J. Chem. Soc., Chem. Commun.* **1978**, 279.

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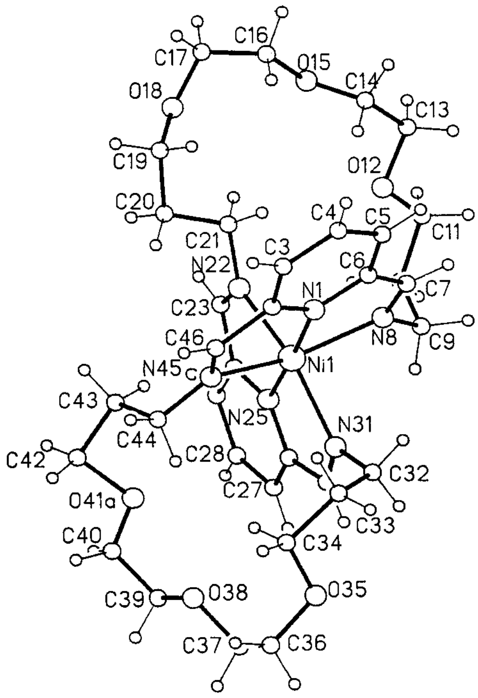
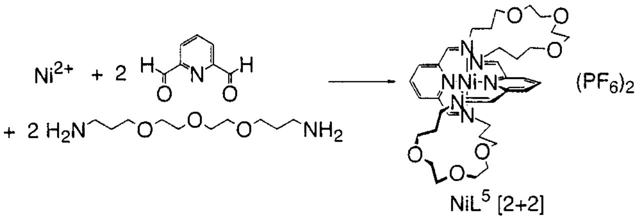


**Figure 2.** View of the NiL$^5$ complex, showing the Ni(II) coordination geometry and the overall conformation of the complex.

**Scheme 3**



effectiveness of copper(II) in the case of our 20-membered ring, may be attributable to the additional methylene groups attached to the imine nitrogens which allow the polyether bridge to fold away from the metal ion coordination sphere. With the chain out of the way, other ligands ($H_2O$ and $Cl^-$) can coordinate to the copper(II) ion, resulting in a preferred coordination mode for copper(II).

The mononuclear nickel(II) complex was synthesized by adding 2 equiv of the diamine to a solution containing 2 equiv of the dialdehyde with 1 equiv of nickel(II) chloride (Scheme 3). Precipitation of the complex as the hexafluorophosphate salt followed by recrystallization gave brown crystals of marginal x-ray quality in an overall yield of 31%. As seen in the crystal structure (Figure 2), the 40-membered ring, L$^5$, is hexadentate, coordinating only through the nitrogens to the octahedral nickel(II) center. This geometry is similar to that reported by Nelson and coworkers for mononuclear iron, cobalt, and nickel complexes of L$^3$;[6] however, those complexes had to be prepared indirectly by transmetalation of the original dilead complex. Since the 30-membered ring can coordinate to a single nickel(II) ion, the longer diamine chain of our macrocycle does not appear to provide an obvious advantage for the template synthesis. Consideration can also be given to the reaction conditions employed. In our synthesis, the diamine was added slowly to the dialdehyde/metal ion solution under high-dilution conditions at room temperature, while Nelson and coworkers mixed all the reagents at once and refluxed in methanol for 30 min.[7] Using Nelson's conditions with our reagents still gives the nickel(II) complex of L$^5$ in approximately 30% yield.

We have demonstrated the effectiveness of copper(II) and nickel(II) ions in the preparation of large di- and tetraimine macrocycles, L$^4$ and L$^5$, via the metal ion template effect. While the yield of macrocycle L$^4$ on the copper ion template was about half that reported by Fenton and coworkers for the 18-membered ring, L$^1$, using alkaline earth metal ions as templates,[8] the yield of the larger macrocycle L$^5$ on the nickel(II) template is approximately equal to yields reported by Nelson and coworkers for the dinuclear complex of the 30-membered [2+2] macrocycle, L$^3$.[7] Our results seem to indicate that as long as the resultant macrocycle can accommodate the preferred coordination mode of the templating metal ion, the size of the metal ion may not be the ultimate factor determining the success of the cyclization reaction. Similar findings regarding the roles of ring flexibility and template ion size in the synthesis of other large Schiff base macrocycles have been reported.[9,10]

## Experimental Section

Solvents were bulk or reagent grade and used as received unless otherwise noted. 1,13-Diamino-4,7,10-trioxatridecane, 2,6-pyridinedimethanol, and ammonium hexafluorophosphate were purchased from Aldrich and used as received.

**Synthesis of 2,6-Pyridinedicarboxaldehyde.** The dialdehyde was prepared by the following modified literature procedure.[11] Activated manganese(IV) dioxide (purchased from Fluka) was heated overnight at 110 °C. $MnO_2$ (100 g) and 10.0 g of 2,6-pyridinedimethanol were refluxed with stirring for 5 h in 500 mL of chloroform (Aldrich spectroscopic grade, used as received). The oxide residue was separated from the solution by vacuum filtration on a fritted glass funnel, and the black residue was rinsed with 4 × 100 mL of chloroform. Solvent was removed from the solution by rotary evaporation, and then the crude product was dissolved in a minimum amount of chloroform and passed through a short (ca. 15 cm long, ca. 4 cm diameter) silica gel column (isocratic elution with chloroform). The pure dialdehyde elutes easily and can be seen as an opaque white band in the clear silica gel while impurities remain at the top of the column. Removal of the solvent by rotary evaporation gives the product in 60−65% yield. Proton nmr resonances in ppm: 10.17 (s), 8.18 (d), 8.08 (t).

**Synthesis of 3,17,23-Triaza-7,10,13-trioxabicyclo[17.3.1]tricosa-1(23), 2,17,19,21-pentaene]copper(II) Hexafluorophosphate, [CuL$^4$(Cl)(H$_2$O)]PF$_6$.** $CuCl_2 \cdot 2H_2O$ (0.514 g, 3.02 mmol) and 2,6-pyridinedicarboxaldehyde (0.407 g, 3.01 mmol) were dissolved in 200 mL of methanol with stirring to give a light green solution. A few drops of concentrated HCl were added followed by slow addition of 1,13-diamino-4,7,10-trioxatridecane (0.665 g, 3.02 mmol) in 30 mL of methanol at a rate of ca. 15 mL/h. After 2 h, the solution was an emerald green in color, and solvent volume was reduced to ca. 50 mL by rotary evaporation. Excess $NH_4PF_6$ in 20 mL of methanol was added, and further solvent evaporation gave a precipitate. The light green powder was collected, rinsed with ethanol and diethyl ether, and recrystallized from 1:1 acetonitrile/ethanol by slow evaporation of the solvents. Two crops of emerald green crystals were collected for a yield of 25%. Anal. Calcd for $C_{17}H_{25}ClCuF_6N_3O_3P \cdot H_2O \cdot CH_3CN$: C, 36.66; H, 4.86; N, 9.00. Found: C, 36.59; H, 4.50; N, 8.81. Positive ion FAB mass spectrometry: *m/z* 417, $(CuL^4Cl)^+$. Infrared C=N stretching frequency: 1635.1 cm$^{-1}$.

**Synthesis of 3,17,25,39,45,46-Hexaaza-7,10,13,29,32,35-hexaoxatricyclo[39.3.1$^{1,45}$.1$^{19,46}$]-hexatetraconta-1 (45),2,17,19(46),20,22,24,39,41,43-decaene]nickel(II) Hexafluorophosphate, NiL$^5$(PF$_6$)$_2$.**

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(6) Nelson, S. M.; McCann, M.; Stevenson, C.; Drew, M. G. B. *J. Chem. Soc., Dalton Trans.* **1979**, 1477.

(7) Nelson, S. M.; Knox, C. V.; McCann, M.; Drew, M. G. B. *J. Chem. Soc., Dalton Trans.* **1981**, 1669.

(8) Cook, D. H.; Fenton, D. E. *J. Chem. Soc., Dalton Trans.* **1979**, 266.

(9) Constable, E. C.; Sacht, C.; Palo, G.; Tocher, D. A.; Truter, M. R. *J. Chem. Soc., Dalton Trans.* **1993**, 1307.

(10) Fenton, D. E.; Matthews, R. W.; McPartlin, M.; Murphy, B. P.; Scowen, I. J.; Tasker, P. A. *J. Chem. Soc., Dalton Trans.* **1996**, 3421.

(11) Papadopolous, E. P.; Jarrar, A.; Issadorides, C. H. *J. Org. Chem.* **1966**, *31*, 615.

**Table 1.** Crystal Data

| | |
|---|---|
| formula | $C_{34}H_{50}F_{12}N_6NiO_6P_2$ |
| fw | 987.45 |
| temp | 220(2) K |
| wavelength | 0.710 73 Å |
| cryst system | monoclinic |
| space group | $P2_1/c$ |
| unit cell dimens | $a = 11.974(6)$ Å<br>$b = 18.615(8)$ Å<br>$c = 19.408(8)$ Å<br>$\beta = 98.67(4)°$ |
| $V$ | 4276(3) $Å^3$ |
| $Z$ | 4 |
| $D$(calcd) | 1.534 $Mg/m^3$ |
| abs coeff | 0.631 $mm^{-1}$ |
| final $R$ indices [$I > 2\sigma(I)$][a] | $R1$ (on $F$) = 0.0685,<br>w$R2$ (on $F^2$) = 0.1501 |
| $R$ indices (all data)[a] | $R1$ (on $F$) = 0.1338,<br>w$R2$(on $F^2$) = 0.1801 |

[a] $R$ indices based on $F$ are denoted $R1$, and those based on $F^2$ are denoted w$R2$, e.g., $R1 = \sum||F_o| - |F_c||/\sum|F_o|$, and w$R2 = [\sum w(F_o^2 - F_c^2)^2]/\sum w(F_o)^2)^2]]^{1/2}$.

$NiCl_2 \cdot 6H_2O$ (0.366 g, 1.54 mmol) and 2,6-pyridinedicarboxaldehyde (0.416 g, 3.08 mmol) were dissolved in 1 L of 100% ethanol with stirring. 1,13-Diamino-4,7,10-trioxatridecane (0.678 g, 3.08 mmol) was dissolved in 200 mL of ethanol and added to the reaction vessel at a rate of ca. 30 mL/h. After complete addition of the diamine, solvent volume was reduced by rotary evaporation to ca. 100 mL and excess $NH_4PF_6$ in $H_2O$ was added. Removal of solvent by rotary evaporation followed by purification of the rust-brown residue on a neutral alumina column (isocratic elution using acetonitrile) with collection of the large brown band and removal of the solvent gave a powder which was recrystallized from 1:1 acetonitrile/ethanol by slow evaporation to give brown crystals in 31% overall yield. Anal. Calcd for $C_{34}H_{50}F_{12}N_6NiO_6P_2$: C, 41.36; H, 5.10; N, 8.51. Found: C, 41.17; H, 5.01; N, 8.40. Positive ion FAB mass spectrometry: *m/z* 841, $(NiL^5PF_6)^+$. Infrared C=N stretching frequency: 1634.9 $cm^{-1}$.

**Table 2.** Selected Bond Lengths (Å) and Angles (deg) for $NiL^5$

| | | | |
|---|---|---|---|
| Ni(1)-N(1) | 1.972(6) | Ni(1)-N(8) | 2.122(6) |
| Ni(1)-N(25) | 1.977(6) | Ni(1)-N(31) | 2.131(6) |
| Ni(1)-N(22) | 2.114(6) | Ni(1)-N(45) | 2.168(6) |

| | | | |
|---|---|---|---|
| N(1)-Ni(1)-N(25) | 175.1(3) | N(22)-Ni(1)-N(31) | 154.7(3) |
| N(1)-Ni(1)-N(22) | 98.2(3) | N(8)-Ni(1)-N(31) | 91.7(2) |
| N(25)-Ni(1)-N(22) | 77.1(3) | N(1)-Ni(1)-N(45) | 76.1(3) |
| N(1)-Ni(1)-N(8) | 77.4(3) | N(25)-Ni(1)-N(45) | 105.7(3) |
| N(25)-Ni(1)-N(8) | 100.9(3) | N(22)-Ni(1)-N(45) | 93.8(2) |
| N(22)-Ni(1)-N(8) | 91.5(2) | N(8)-Ni(1)-N(45) | 153.4(3) |
| N(1)-Ni(1)-N(31) | 107.0(3) | N(31)-Ni(1)-N(45) | 94.4(2) |
| N(25)-Ni(1)-N(31) | 77.6(3) | | |

**X-ray Structural Analysis.** Crystal character: large red-brown blocks, from which an irregular cleavage fragment was selected. Crystal data are given in Table 1. Data were collected with a Siemens R3m four-circle diffractometer in $\theta-2\theta$ mode. In one $PF_6$ group, four equatorial fluorine atoms were split into two 0.5 occupancy sets (after preliminary refinement of the occupancy). Analysis of the anisotropic displacement parameters suggested that more complex modeling might also have been used, but various attempted strategies were unstable in refinement. The P−F and F−F distances were constrained to give regular octahedra with P−F refined to 1.544(2) Å. Atom O(41) was disordered between two positions (0.68(2) and 0.32(2) occupancies for positions A and B).

Anisotropic temperature factors were used for all non-H atoms apart from O(41b). Hydrogen atoms were given fixed isotropic temperature factors 1.2× that of the corresponding carbon atom, inserted at calculated positions and not refined. Final refinement was on $F^2$ by least squares methods. Weighting scheme: $W = 1/(\sigma^2(F_o^2) + (0.086P)^2)$, where $P = (\max(0,F_o^2) + 2F_o^2)/3$.

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**Supporting Information Available:** Text describing the full x-ray structural analysis and tables containing final atomic coordinates, H-atom coordinates, thermal parameters, and bond lengths and angles (18 pages). Ordering information is given on any current masthead page.

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