# The Template Synthesis of the New Macrocyclic and Acyclic Metal Ion Complexes Derived from Putrescine

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## Abstract

The template reaction of 2,6-diacetylpyridine with biogenic diamine–putrescine in the presence of cadmium(II), mercury(II) or lead(II) ions produces the complexes of 22-membered macrocyclic ligand $L^1$ with an $N_6$ set of donor atoms as a result of [2 + 2] Schiff base cyclocondensation. The lead(II) complex containing Schiff base acyclic ligand $L^2$ terminated by one carbonyl and one amine group as product of the partial [2 + 2] condensation has been also isolated and might be regarded as possible intermediate in the formation of the macrocyclic $L^1$ complex. Analogous reaction involving the uranyl nitrate generates the complex containing the same Schiff base acyclic ligand $L^2$ as a final product of template reaction. The complexes were characterized by spectral data (IR, $^1H$ NMR, FAB-MS), thermogravimetric and elemental analyses. A notable feature of the FAB mass spectrum of the uranyl complex is the appearance of the clusters of the form $[(UO_2)_nO]^+$ ($n = 1$–7) along with the peak corresponding to molecular ion.

## Introduction

Recent studies have emphasized the development damage which results from accumulation of environmental pollutants: cadmium, mercury, lead, uranium in the organisms. The toxity of these metals on a biological system is connected with the displacing the essential metal ions in biomolecules, blocking the functional groups and inhibiting or enhancing their enzymatic activities. The synthesis of potential chelating agents for effective sequestering and removing toxic metal ions from the human body is a field of growing interest [1–8]. The molecular design of strong ligands specific for a given metal ion has been generally achieved considering the size fitting, the nature of the ligand–metal interaction and the orientation in the ligation. In seeking of the new stable complexes of environmentally important metal ions in view of the potential biomedical applications and expanding our studies on the coordination template effect in generating of the new supramolecular mono- and homo- or heterodinuclear polyaza and polyoxaaza macrocyclic and acyclic Schiff bases [9, 10] we wish to present the template action of metal ions of biological interest: cadmium(II), mercury(II), lead(II) and uranyl ions in the synthesis of the new complexes containing the macrocyclic ($L^1$) and open-chain ($L^2$)

ligands as results of the Schiff base condensation reactions between 2,6-diacetylpyridine and biogenic amine–putrescine.

## Experimental

### Chemicals

Putrescine (1,4-diaminobutane) (Fluka), 2,6-diacetylpyridine (Aldrich Chemical Company), lead(II) nitrate anhydrous (Merck), cadmium chloride dihydrate (POCh Gliwice), cadmium perchlorate hexahydrate (Aldrich Chemical Company), mercury(II) perchlorate trihydrate (Aldrich Chemical Company) and uranyl nitrate hexahydrate (Merck) were used as received.

### Preparation of the $L^1$ complexes – general procedure

All complexes were obtained under similar conditions. To a mixture of metal salt (0.1 mmol) in methanol (10 cm$^3$) and 2,6-diacetylpyridine (0.2 mmol) in methanol (10 cm$^3$), putrescine (0.2 mmol) in methanol (10 cm$^3$) was added dropwise with stirring. The reactions were carried out for 24–72 h. The solution volume was then reduced to 10 cm$^3$ by roto-evaporation and a yellow precipitate formed on addition of a small amount

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of diethyl ether. This was filtered off, washed with ether, and dried *in vacuo*. Yields: 70–80%.

[PbL$^1$(H$_2$O)][Pb(NO$_3$)$_4$]·H$_2$O: Anal. Calcd for C$_{26}$H$_{38}$N$_{10}$O$_{14}$Pb: C, 27.66; H, 3.39; N, 12.41. Found: C, 28.65; H, 3.42; N, 12.69.

[CdL$^1$(H$_2$O)$_4$][CdCl$_4$]·2H$_2$O: Anal. Calcd for C$_{26}$H$_{46}$N$_6$O$_6$Cl$_4$Cd$_2$: C, 34.49; H, 5.13; N, 9.28. Found: C, 34.60; H, 5.33; N, 9.37.

[CdL$^1$(H$_2$O)][Cd(ClO$_4$)$_4$]·H$_2$O: Anal. Calcd for C$_{26}$H$_{38}$N$_6$O$_{18}$Cl$_4$Cd$_2$: C, 28.67; H, 3.52; N, 7.71. Found: C, 29.12; H, 3.51; N, 7.85.

[HgL$^1$(ClO$_4$)$_2$(H$_2$O)$_2$]·H$_2$O: Anal. Calcd for C$_{26}$H$_{40}$N$_6$O$_{11}$Cl$_2$Hg: C, 35.32; H, 4.55; N, 9.50. Found: C, 35.02; H, 4.62; N, 9.69.

### Preparation of the L$^2$ Complexes

[UO$_2$L$^2$][UO$_2$(NO$_3$)$_4$(H$_2$O)$_2$]·5H$_2$O. To the mixture of UO$_2$(NO$_3$)$_2$·6H$_2$O (0.1 mmol) in methanol (10 cm$^3$) and 2,6-diacetylpyridine (0.2 mmol) in methanol (10 cm$^3$), putrescine (0.2 mmol) in methanol (10 cm$^3$) was added dropwise with stirring. The reaction was carried out for 4 h. The resulting yellow precipitate was filtered off, washed with ether, and dried *in vacuo*. Yield: 76%.

Anal. Calcd for C$_{26}$H$_{50}$N$_{10}$O$_{24}$U$_2$: C, 22.84; H, 3.96; N, 10.25. Found: C, 22.55; H, 4.11; N, 10.38.

[PbL$^2$(NO$_3$)$_2$(H$_2$O)$_2$]·2H$_2$O: To the mixture of Pb(NO$_3$)$_2$ (0.1 mmol) in methanol (10 cm$^3$) and 2,6-diacetylpyridine (0.2 mmol) in methanol (10 cm$^3$), putrescine (0.2 mmol) in methanol (10 cm$^3$) was added dropwise with stirring. The reaction was carried out for 2 h. The solution volume was then reduced to 10 cm$^3$ by roto-evaporation and a yellow precipitate formed on addition of a small amount of diethyl ether. This was filtered off, washed with ether, and dried *in vacuo*. Yield: 78%.

Anal. Calcd for C$_{26}$H$_{44}$N$_8$O$_{11}$Pb: C, 37.45, H, 5.07; N, 13.43. Found: C, 37.41; H, 4.92; N, 12.86.

### Measurements

IR spectra were recorded using CsI pellets in the range 4000–200 cm$^{-1}$ on a Perkin-Elmer 580 spectrophotometer. $^1$H NMR spectra were run on a Varian Gemini 300 spectrometer using TMS as an internal reference. FAB-mass spectra were obtained on an AMD-604 mass spectrometer with the nitrobenzyl/acetic acid or glycerine/acetic acid as matrix. Thermogravimetric measurements were performed using Shimadzu TGA-50 derivatograph (up to 250 °C, heating rate 10 °C min$^{-1}$, air atmosphere). Elemental analysis was carried out on Elementar Vario EL III microanalyzer. All data reported refer to isolated materials judged to be homogenous by thin layer chromatography performed on precoated silica gel plates (0.2 mm 60 F-254 E. Merck) and visualized by UV light.

## Results and discussion

The cadmium(II), mercury(II) and lead(II) complexes of the 22-membered macrocyclic ligand L$^1$, where L$^1$ is the product of a Schiff base cyclocondensation of two molecules of 2, 6-diacetylpyridine with two molecules of biogenic diamine–putrescine were prepared by the reaction of appropriate metal ions acting as template agents with diketone and diamine in the 1:2:2 molar ratio of the metal ion to linear precursors. However, in the reaction in which 2, 6-diacetylpyridine is allowed to react with putrescine in the presence of uranyl nitrate under the same experimental conditions, the ring closure does not occur. Instead, the uranyl complex containing acyclic ligand L$^2$ terminated by one carbonyl and one amine group as product of the partial [2 + 2] Schiff base condensation is formed. Similar acyclic complex of L$^2$ was isolated when the lead(II)-promoted condensation reaction of 2,6-diacetylpyridine with putrescine was allowed to proceed for 2 h.
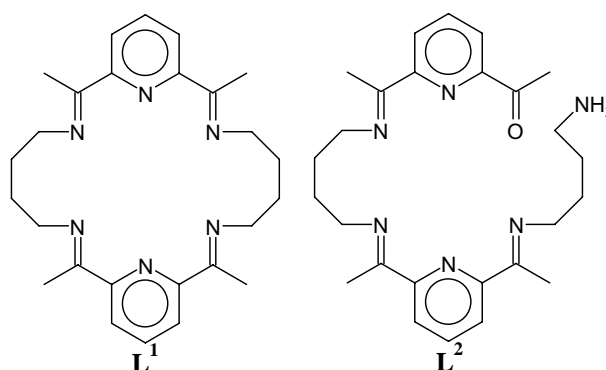


The formulations of these complexes as [PbL$^1$(H$_2$O)][Pb(NO$_3$)$_4$]·H$_2$O, [CdL$^1$(H$_2$O)$_4$][CdCl$_4$]·2H$_2$O, [CdL$^1$(H$_2$O)][Cd(ClO$_4$)$_4$]·H$_2$O, [HgL$^1$(ClO$_4$)$_2$(H$_2$O)$_2$]·H$_2$O, [UO$_2$L$^2$][UO$_2$(NO$_3$)$_4$(H$_2$O)$_2$]·5H$_2$O and [PbL$^2$(NO$_3$)$_2$(H$_2$O)$_2$]·2H$_2$O follow from spectral, thermogravimetric and elemental analyses. The complexes are yellow air stable solids, moderately soluble in DMSO.

The infrared spectra of cadmium(II), mercury(II) and lead(II) complexes of L$^1$ (Table 1) confirm the formation of the macrocyclic compound by the absence of bands characteristic of carbonyl and amine groups of the starting materials. In contrast, the IR spectra of uranyl and lead(II) complexes of L$^2$ exhibit strong absorption band at ca. 1700 cm$^{-1}$ and doublets at 3264–3012 cm$^{-1}$ attributable to the C=O stretching vibration and to the asymmetric and symmetric −NH$_2$ stretching vibrations, respectively, indicating the formation of the open-chain products containing terminal acetylpyridyl and primary amine groups. All the spectra confirm the Schiff base condensation by the presence of a strong band at 1630–1625 cm$^{-1}$ characteristic of C=N stretching modes. The spectra exhibit medium to strong bands at 1585–1437 cm$^{-1}$ as expected for the high energy ring vibrations of the coordinated pyridine. The bonding of

*Table 1.* Selected infrared and FAB mass spectral data for complexes of $L^1$ and $L^2$

| Complex | IR (cm$^{-1}$) | | | | | FAB | |
|---|---|---|---|---|---|---|---|
| | NH$_2$ | C=O | C=N | Py | X$^-$ | m/z | Assignment |
| [PbL$^1$(H$_2$O)][Pb(NO$_3$)$_4$]·H$_2$O | – | – | 1639 | 1570, 1020, 1000, 670 | 1765, 1743, 1430–1307, 815 | 656 430 | [PbL$^1$·H$_2$O]$^+$ [L$^1$]$^+$ |
| [CdL$^1$(H$_2$O)$_4$][CdCl$_4$]·2H$_2$O | – | – | 1641 | 1584, 1052, 1018, 966, 741, 546 | 250 | 562 430 | [CdL$^1$·H$_2$O]$^+$ [L$^1$]$^+$ |
| [CdL$^1$(H$_2$O)][Cd(ClO$_4$)$_4$]·H$_2$O | – | – | 1645 | 1585, 1465, 935 | 1103, 1090, 625 | 562 | [CdL$^1$·H$_2$O]$^+$ |
| [HgL$^1$(ClO$_4$)$_2$(H$_2$O)$_2$]·H$_2$O | – | – | 1635 | 1564, 1437, 940 | 1123, 1102, 1089, 635, 626 | 767 | [HgL$^1$(ClO$_4$)·2H$_2$O]$^+$ |
| [PbL$^2$(NO$_3$)$_2$(H$_2$O)$_2$]·2H$_2$O | 3264, 3078 | 1699 | 1634 | 1576, 1066, 1011, 992, 748, 539 | 1760, 1450–1354, 820 | 852 | [PbL$^2$(NO$_3$)$_2$·4H$_2$O]$^+$ |
| [UO$_2$L$^2$][UO$_2$(NO$_3$)$_4$(H$_2$O)$_2$]·5H$_2$O | 3067, 3012 | 1700 | 1635 | 1558, 1100, 1024, 984, 748, 666 | 1763, 1751 1448–1280 820 | 1906 1636 1366 1096 826 557 270 754 | [(UO$_2$)$_7$O]$^+$ [(UO$_2$)$_6$O]$^+$ [(UO$_2$)$_5$O]$^+$ [(UO$_2$)$_4$O]$^+$ [(UO$_2$)$_3$O]$^+$ [(UO$_2$)$_2$O]$^+$ [UO$_2$]$^+$ [UO$_2$L$^2$·2H$_2$O]$^+$ |

the pyridine nitrogen atom is also shown by the presence of the band at 1100–935 and 748–539 cm$^{-1}$ attributable to the ring breathing frequency and the low energy pyridine ring vibrations, respectively. All the complexes show the broad diffuse band centered at ca 3452–3420 cm$^{-1}$ due to the stretching and bending modes of lattice and coordinated water. In addition, weak bands occur at 870–860 cm$^{-1}$ region which may be assigned to rocking or wagging modes of water molecules interacting with the metal ion. The presence of water molecules bound in two different ways is supported by the results of thermogravimetric analysis. All these complexes lose their water molecules in two steps: below 100 °C and above 150 °C corresponding to the lattice and coordinated water molecules, respectively. The number of water molecules per mol of metal ion was calculated from the weight loss observed for the complexes at the respective temperature ranges.

The strong absorption at 912 cm$^{-1}$ in the IR spectra of the uranyl complexes is assigned to the asymmetric stretching vibration of the linear uranyl group. The search of the Cambridge Structural Database reveals that the U—O bond distance equal to 1.71 Å calculated [11] from this frequency is quite typical for uranyl complexes.

Information about the bonding mode of the counterions in these complexes may also be obtained from IR spectra. In the spectra of the PbL$^1$, PbL$^2$ and UO$_2$L$^2$

nitrate complexes $v$(N—O) stretching frequency is observed as splitted bands at 1765–1743 and 1450–1280 cm$^{-1}$ ranges and as a medium band at 820–815 cm$^{-1}$. The magnitude of the separation provides evidence for the coordinating (bidentate and/or monodentate) behaviour of the nitrate groups (PbL$^1$ complex: $\Delta v = 21$ and 123 cm$^{-1}$, PbL$^2$ complex: $\Delta v = 96$ cm$^{-1}$, UO$_2$L$^2$ complex, $\Delta v = 12$ and 168 cm$^{-1}$). The involvement of the perchlorates in the coordination sphere of the metal ion normally manifests itself by a splitting of the antisymmetric Cl—O stretching mode due to the reduced symmetry of the coordinated species. In the CdL$^1$ and HgL$^1$ perchlorate complexes the bands observed at 1123–1089 cm$^{-1}$ region along with band at ca. 625 cm$^{-1}$ indicate the interaction of these anions with the metal ions. The spectrum of the chloride CdL$^1$ complex shows medium absorption band at 250 cm$^{-1}$ attributable to the M—Cl frequency.

The $^1$H NMR spectra of DMSO-d$_6$ solutions of the L$^1$ complexes exhibit the expected splitting patterns and chemical shifts for pyridine ring protons at $\delta$ 8.50–8.20 (2H, t, $J = 7.9$–7.4) and $\delta$ 7.8–8.0 (4H, d, $J = 7.9$–7.4). The methylene protons adjacent to nitrogen occur at $\delta$ 3.60–3.20 (8H), the remaining methylene protons at $\delta$ 1.55–1.53 (8H, m) and the methyl protons of CH$_3$C=N groups at $\delta$ 2.80–2.50 (12H, s). The L$^2$ complexes give very similar $^1$H NMR spectra. The pyridine protons are observed at $\delta$ 8.58 (2H, t, $J = 8.7$) and $\delta$ 8.49 (4H, d,

$J = 8.7$). The proton signals of the methylene groups appear at $\delta$ 3.78 (6H, t, $J = 5.8$), $\delta$ 2.70 (2H, t, $J = 5.8$) and $\delta$ 1.72 (8H, q, $J = 5.8$). The methyl protons of the $CH_3C{=}O$ and $CH_3C{=}N$ groups occur at $\delta$ 2.56 (3H, s) and $\delta$ 2.50 (9H, s), respectively. The signal at $\delta$ 1.58 (2H, s) may be assigned to the protons of primary amine group. The integrated relative intensities of the observed signals in all the complexes are in good agreement with the required ratios consistent with the proposed formulation of these compounds.

Despite repeated attempts we have so far been unsuccesful in isolating single crystals suitable for X-ray diffraction analysis. In the absence of crystallografic information we have used the fast atom bombardment spectrometry to characterize the complexes. All the FAB mass spectra (Table 1) exhibit the peaks assigned to the species containing one metal ion coordinated to the Schiff base ligand. However, elemental analysis data for the lead(II) and cadmium(II) complexes of $L^1$ and uranyl complex of $L^2$ complexes correspond to a ratio of two metal cations to one ligand molecule. The IR spectra of these three complexes (*vide supra*) reveal the presence of coordinated counterions. These results along with the known tendency of these metal ions to form stable polyanionic species of $[MX_4]^{2-}$ type [12–16] allow us to assume that these complexes contain the cation with Schiff base ligand coordinated to the metal ion in the 1:1 ratio and tetra-anionic species with inorganic counterions coordinated to the divalent metal ion. The spectrum of the $UO_2L^2$ complex displays additional prominent features, namely the major peaks at masses higher than those of the parent ions. They form the series attributable to the uranyl-oxygen clusters of the general formula of $[(UO_2)_nO]^+$, where $n = 1{-}7$. The mass differences between adjacent clusters correspond to $UO_2$ units (separation by 270 Da). Thereafter, the general fragmentation pattern involves the sequential elimination of $UO_2$ units between the successive daughter clusters. It is worthy to note that very similar sequence of clusters species was detected in our laboratory during the FAB experiments for the other uranyl nitrate and acetate Schiff base complexes derived from various diketones and primary diamines [17, 18]. This is consistent with recent reports of uranium-oxygen cluster formation [19]. Thus, this behaviour appears to be the general trend to occur in the uranyl complexes under the conditions of FAB-MS experiments irrespective of the nature of ligands.

On the basis of the available evidence it can be concluded that lead(II), cadmium(II) and mercury(II) ions are effective templates for the synthesis of 22-membered Schiff base macrocycle derived from diacetylpyridine and biogenic diamine–putrescine. Analogous reaction involving the uranyl nitrate as template agent generates the complex containing the open-chain Schiff base ligand with uncondensed carbonyl and amino groups. The failure of this system to undergo complete condensation and cyclization may be attributed to the strong coordination of the $-NH_2$ group to the uranium ion which decreases the probability of the nucleophilic attack of the coordinated amine nitrogen on carbon atom of the carbonyl group and stabilizes the open-chain product once formed. Reduction of the time of metal-promoted reaction allowed us to isolate the open-chain lead(II) complex with the same acyclic Schiff base ligand. Comparison of the interaction strength between the nitrogen atoms of the amino groups and the metal ion in the $UO_2L^2$ and $PbL^2$ complexes inferred from IR spectra reveals the weaker coordination in the latter species. Therefore, this podate might be regarded as possible intermediate in the [2 + 2] cyclocondensation reaction leading to the formation of the $PbL^1$ macrocyclic complex, whereas in the case of uranyl complex the potential intermediate occurs to be the final product [20–22]. The results discussed in this paper demonstrate that the coordination mode of potential intermediates is one of the factors which prove to be of importance in determining the preferred pathway of the metal-ion-templated condensation in the Schiff base systems and must be taken into account in the design and synthesis of the desired products.

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