

## Synthesis of Asymmetrical Macrocyclic Ligands and their Metal Complexes

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### Abstract

Our motive behind the synthesis of this type of asymmetrical macrocyclic ligands was to examine their possible applications in cation recognition processes, as homo or heteronuclear complexes can be synthesized from alkali and transition metal cations and these complexes may also serve as models of relevance to bioinorganic chemistry such as metalloenzymes. Even though the enormous number of Schiff base macrocycles and their complexes have already been described, many more interesting systems of this type surely await discovery. These structures are found to be powerful tools used to define interesting features relating to general chemistry and application. In this study, we present the preparation of the asymmetrical acyclic and cyclic compartmental Schiff bases containing two adjacent chambers to obtain the mono and dinuclear complexes with the appropriate alkaline earth and transition metal center and their related soft and hard complexes. We used 2,3-dihydroxy benzaldehyde as a starting material and obtained the macrocyclic ligands by the reaction of 2,3-dihydroxy benzaldehyde and bis(2-aminopropyl) amine in the presence of Ba(ClO<sub>4</sub>)<sub>2</sub> as template agent, then its appropriate transition metal complex as with Ni<sup>+2</sup> in CH<sub>3</sub>OH was prepared. All of the compounds were characterized by elemental analysis, IR, <sup>1</sup>H NMR and MS spectrophotometer techniques.

### Introduction

The importance of the macrocyclic ligands have been recognized for a long time owing to their ability to form hetero-dinuclear complexes with suitable metal salts [1] and their role in studies of molecular processes taking place in biological processes, catalysis, material science transport and separation phenomena [2-6]. The symmetric and asymmetric cyclic ligands have been obtained by [2 + 2] self-condensation of appropriate keto or formyl and amine precursors or by means of template reaction in the presence of a suitable metal ion [7-14]. The acyclic ligands are asymmetric ligands, whereas the cyclic ligands both are symmetric and asymmetric. These molecular structures especially their complexity have been identified by X-ray diffraction, and mass spectroscopy [15]. Asymmetric compartmental ligands have a chamber; and different compartments [16] and form complex with metal salts or lanthanides [17]. These systems can incorporate suitable *d*- or *f*- metal ions

into the Schiff base and non-transition ions, anions or organic substrates into the crown-ether sites. The complex of the metal ions into the crown-ether cavity can change the physico-chemical properties of the metal ion bound to the Schiff base system, one chamber of the these ligands can recognize a metal ion while the other chamber can give rise to a selective recognition by formation of hydrogen bonding or complexation with anions [18]. Moreover, these Schiff bases can be reduced to the corresponding amine derivatives to investigate the difference between the imine and amine groups as recognition sites. In the present work, we report the synthesis and characterization of new compartmental Schiff base and related alkaline earth and transition metal complexes. First of all it was thought that a suitable diamine derivative of the transition metal and crown-ether moiety for the alkaline earth metal ion. We used 2,3-dihydroxy benzaldehyde as formyl precursor and bis(2-aminopropyl)amine to obtain asymmetric compartmental macrocyclic ligand, then it was found that this ligand coordinated with transition metal into the N<sub>3</sub>O<sub>2</sub> Schiff base chamber, on the other hand, the other alkaline earth metal coordinated into the crown ether moiety, this situation was clarified through <sup>1</sup>H-NMR

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and infrared spectroscopy data. Thus both transition metal and alkaline earth metal were coordinated into the asymmetrical ligand and showed oneself as hetero dinuclear structure.

## Experimental

### Materials

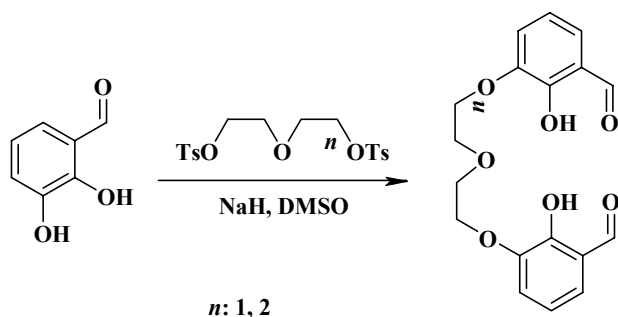
All solvents, reagents and the metal perchlorates were purchased from Aldrich, Fluka and used without further purification. Dimethylsulphoxide was purified by standard methods described in [19]. Di, triethylene glycol ditosylate derivatives were prepared according to the procedure described in [12]. The diformyl precursors 3,3'-(3,6,9-trioxaoctane-1,8-diyl-dioxy)bis(2-hydroxybenzaldehyde) and 3,3'-(3-oxapentane-1,5-diyl-dioxy)bis(2-hydroxybenzaldehyde) and their mono and hetero dinuclear complexes were prepared according to the method described in literature [17,20] as shown in Schemes 1-3.

### Methods

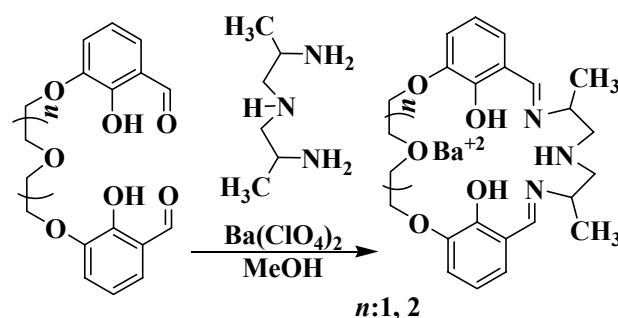
#### Acyclic Ligands and Related Complexes

##### $H_2L^1$

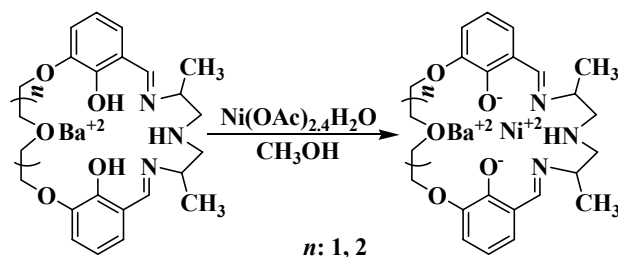
The diformyl precursor 3,3'-(3-oxapentane-1,5-diyl-dioxy)bis(2-hydroxybenzaldehyde) was prepared ( $H_2L^1$ ) by a modification of the technique reported in [17]. Firstly, the solution of 2,3-dihydroxybenzaldehyde (0.05 mmol) in dry DMSO (25 mL) was added over 2 hours to mineral oil suspension of NaH (0.10 mL) in 25 mL of dry DMSO under  $N_2$  atmosphere and maintained the temperature below  $25^\circ C$ , then it was stirred for 2 hours again after the gradual addition of solid diethylene glycol ditosylate (0.025 mmol), for additional 30 hours. The addition of 300 mL of water resulted in a yellow precipitate. This precipitate was filtered, washed with water and methanol, stirred with chloroform (50 mL) for 30 min. The solid was filtered and the chloroform phase was dried over  $MgSO_4$ , then evaporated to dryness and yellow product was purified by chromatography on silica with  $CHCl_3$  as eluent (48%), m.p.  $62^\circ C$ ;  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  10.93 (s, 2H, OH), 9.96 (s, 2H, CHO), 7.21-6.85 (m, 6H, ArH), 4.23-4.12 (m, 4H, Ar- $OCH_2$ ), 4.0-3.90 (m, 4H,  $OCH_2$ ). IR (KBr)  $1659\text{ cm}^{-1}$  (C=O); mass spec, m/e 346. Anal. Calc. C 62.38; H 5.32, Found: C 62.18; H 5.27%.



Scheme 1



Scheme 2



Scheme 3

##### $H_2L^2$

3,3'-(3,6-dioxaoctane-1,8-diyl-dioxy)bis(2-hydroxybenzaldehyde) was obtained according to the method reported in [20] by reaction of 2,3-dihydroxybenzaldehyde (0.05 mmol) in dry DMSO in the presence of mineral oil suspension of NaH (0.10 mL) with solid triethylene glycol ditosylate (0.025 mmol) that was added gradually under  $N_2$  atmosphere. The temperature was kept below  $25^\circ C$  and the mixture was refluxed for 30 hours. Then, 300 mL water was added, which resulted in brown mixture that was extracted with  $CHCl_3$  for removal of the unreacted ditosylate. Aqueous layer acidified with HCl and extracted with  $CHCl_3$ , was dried over  $MgSO_4$ . After the removal of the solvents, yellow product was purified by chromatography on silica with  $CHCl_3$  as eluent (57%), m.p.  $86-87^\circ C$ ;  $^1H$  NMR ( $CDCl_3$ , 300

MHz):  $\delta$  10.85 (s, 2H, OH), 9.88 (s, 2H, CHO), 7.30-6.60 (m, 6H, ArH), 4.31-4.12 (m, 4H, Ar-OCH<sub>2</sub>), 4.0-3.80 (m, 4H, OCH<sub>2</sub>). IR (KBr) 1650 cm<sup>-1</sup> (C=O); mass spec, m/e 390. Anal. Calc. C 61.51; H 5.63. Found: C 61.44; H 5.57%.

### Macrocyclic Ligands and Mononuclear Complexes

#### *H<sub>2</sub>L<sup>1a</sup>*

A solution of Ba(ClO<sub>4</sub>) as template agent in CH<sub>3</sub>OH (25 mL) was added to equivalent amount of diformyl precursor 3,3'-(3-oxapentane-1,5-diylidioxo)bis(2-hydroxy benzaldehyde) in CH<sub>3</sub>OH (25 mL) and the mixture was refluxed for 2 hours at room temperature. Then the appropriate diamine derivative in CH<sub>3</sub>OH (25 mL) was added to the mixture and refluxed again for 0.5 hours. After the removal of the solution the residue was treated with CHCl<sub>3</sub>. The resulting yellow solution was filtered and treated with diethyl ether. Then the collected solid product was crystallized with petroleum ether yield (66%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  8.98 (s, 2H, N=CH), 7.30-7.10 (m, 6H, ArH), 4.38-4.15 (m, 4H, Ar-OCH<sub>2</sub>), 4.10-3.80 (m, 4H, OCH<sub>2</sub>), 3.65 (s, 4H, CH<sub>2</sub>CN), 2.34 (m, 6H, -CH<sub>3</sub>). IR (KBr) 1637 cm<sup>-1</sup> (C=N); mass spec, m/e 441. Anal. Calc. C 65.33; H 7.10; N 9.51 Found: C 65.27; H 7.16; N 9.42%.

#### *H<sub>2</sub>L<sup>2a</sup>*

The compound H<sub>2</sub>L<sup>2a</sup> was synthesized by using the same procedure and scale as for H<sub>2</sub>L<sup>1a</sup>, from 3,3'-(3,6-dioxaoctane-1,8-diylidioxo)bis(2-hydroxybenzaldehyde), Ba(ClO<sub>4</sub>) and appropriate diamine derivative Bis-(2-aminopropyl)-amine yield (61%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  13.17 (s, 2H, OH) 8.92 (s, 2H, N=CH), 6.87-6.60 (m, 6H, ArH), 4.3-4.1 (m, 4H, Ar-OCH<sub>2</sub>), 3.9-3.7 (m, 4H, OCH<sub>2</sub>), 3.5 (s, 4H, CH<sub>2</sub>CN), 2.29 (m, 6H, -CH<sub>3</sub>). IR (KBr) 1625 cm<sup>-1</sup> (C=N); mass spec, m/e 485. Anal. Calc. C 64.33; H 7.19; N 8.58 Found: C 64.36; H 7.27; N 8.65%.

### Hetero-dinuclear Macrocyclic Complexes

#### *Ni Complex of the H<sub>2</sub>L<sup>1a</sup>*

Complex H<sub>2</sub>L<sup>1a</sup> was dissolved in 50 mL of CH<sub>3</sub>OH, and a solution of Ni(OAc)<sub>2</sub>·4H<sub>2</sub>O in 50 mL of CH<sub>3</sub>OH was added. The mixture was refluxed for 0.5 hours, filtered while hot, and concentrated to 50 mL. After the addition of petroleum ether the product was crystallized and filtered off, yield (53%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>

300 MHz):  $\delta$  8.09 (s, 2H, N=CH), 7.5-7.3 (m, 6H, ArH), 4.38-4.15 (m, 4H, Ar-OCH<sub>2</sub>), 3.9-3.7 (m, 4H, OCH<sub>2</sub>), 3.52 (s, 4H, CH<sub>2</sub>CN), 2.2 (m, 6H, -CH<sub>3</sub>). IR (KBr) 1630 cm<sup>-1</sup> (C=N), 540 cm<sup>-1</sup> (Ni-N), 430 cm<sup>-1</sup> (Ni-O); Anal. Calc. C 45.33; H 4.87; N 6.51 Found: C 45.24; H 4.93; N 6.59%.

#### *Ni Complex of the H<sub>2</sub>L<sup>2a</sup>*

<sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  13.09 (s, 2H, OH) 8.03 (s, 2H, N=CH), 6.8-6.6 (m, 6H, ArH), 4.36-4.14 (m, 4H, Ar-OCH<sub>2</sub>), 3.9-3.6 (m, 4H, OCH<sub>2</sub>), 3.57 (s, 4H, CH<sub>2</sub>CN), 2.3 (m, 6H, -CH<sub>3</sub>). IR (KBr) 1633 cm<sup>-1</sup> (C=N), 544 cm<sup>-1</sup> (Ni-N), 431 cm<sup>-1</sup> (Ni-O); Anal. Calc. C 45.78; H 5.26; N 6.08. Found: C 45.82; H 5.18; N 6.27%.

### Preparation of the Tosylate Derivatives

All the tosylate derivatives were prepared according to the literature [21]. 10.6 g (0.1 mol) of diethylene glycol was added to 80 mL of pyridine which was distilled freshly and was stirred continuously by mechanical stirrer at -12°C. Then, 38.2 g (0.2 mol) of *p*-toluene sulfonyl chloride was added gradually to diethylene glycol solution for 4 hours, the temperature was kept below -7°C. After the addition of the diethylene glycol solution was completed, the mixture was stirred for additional 10 hours. The crude product was washed with ice-water, water-methanol and crystallized from ethanol resulting in white crystals (59%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  4.45 (s, 6H, -CH<sub>3</sub>); 3.65 (t, 4H, -CH<sub>2</sub>-O-CH<sub>2</sub>-); 4.20 (t, 4H, CH<sub>2</sub>OTs); 7.30-7.75 (dd, 8H, ArH). IR (KBr): 3040 cm<sup>-1</sup> (C-H Aryl); 2980-2930 cm<sup>-1</sup> (-CH<sub>2</sub>-CH<sub>2</sub>-); 1550 cm<sup>-1</sup> (C=C Aryl); 1150 cm<sup>-1</sup> (C-O Alkyl). For C<sub>18</sub>H<sub>22</sub>O<sub>7</sub>S<sub>2</sub> Anal. Calc. C 52.11; H 5.30 Found: C 51.85; H 5.54%.

Triethylene glycol ditosylate yields (71%). <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  2.40 (s, 6H, -CH<sub>3</sub>); 3.40 (s, 4H, OCH<sub>2</sub>O); 3.60 (t, 4H, OCH<sub>2</sub>); 4.15 (t, 4H, CH<sub>2</sub>OTs); 7.30-7.80 (8H, ArH). IR (KBr): 3040 cm<sup>-1</sup> (C-H Aryl); 2970-2930 cm<sup>-1</sup> (-CH<sub>2</sub>-CH<sub>2</sub>-); 1550 cm<sup>-1</sup> (C=C Aryl); 1110 cm<sup>-1</sup> (C-O Alkyl). For C<sub>20</sub>H<sub>26</sub>O<sub>8</sub>S<sub>2</sub> Anal. Calc. C 52.34; H 5.67; Found: C 52.08; H 5.44.

### Physicochemical Measurements

<sup>1</sup>H-NMR spectroscopic studies and MS analyses were performed in the TÜBITAK Research Laboratories (Center of Science and Technology Research of

Turkey). The carbon, hydrogen and nitrogen analyses were carried out using Carlo Erba 1106 auto elemental analyzer. IR spectra were recorded on a Pye- Unicam SP 1025 spectrophotometer, in KBr pellets, (University of Selçuk Faculty of Sciences and Art Department of Chemistry). Melting points were determined in a capillary tube on a Buchi SPM-20 instrument.

## Results and Discussion

Our motive behind the synthesis of this type of the ligands was to examine their possible applications in cation recognition processes, as homo or heteronuclear complexes can be synthesized from alkali and transition metal cations and these complexes may also serve as models of relevance to bioinorganic chemistry such as metalloenzymes. Even though the enormous number of Schiff base macrocycles and their complexes have already been described, many more interesting systems of this type surely await discovery. These structures are found to be powerful tools used to define interesting features relating to general chemistry and application. Heterodinuclear asymmetrical macrocyclic ligands and their Ni<sup>+2</sup> complexes H<sub>2</sub>L<sup>1a</sup> and H<sub>2</sub>L<sup>2a</sup> have been prepared according to the appropriate protocols described in literature [17-20]. These compounds were characterized by elemental analysis, MS, IR and <sup>1</sup>H NMR spectroscopy. The pale yellow products H<sub>2</sub>L<sup>1a</sup>, H<sub>2</sub>L<sup>2a</sup> were stable in air and soluble in common organic solvents.

### The Diformyl Precursors

The dialdehydes H<sub>2</sub>L<sup>1</sup>, 3,3'-(3-oxapentane-1,5-diyldioxy)bis(2-hydroxybenzaldehyde) and H<sub>2</sub>L<sup>2</sup>, 3,3'-(3,6-dioxaoctane-1,8-diyldioxy)bis(2-hydroxybenzaldehyde) were synthesized in 48-57% by the reaction of 2,3-dihydroxy benzaldehyde and related di- and tri-tosylate derivatives in DMSO and purified by chromatography. Their IR spectra show a strong pick at 1659-1650 cm<sup>-1</sup> due to the C=O, the NMR spectra in CDCl<sub>3</sub> for H<sub>2</sub>L<sup>1</sup> and H<sub>2</sub>L<sup>2</sup> show chemical shifts at 9.96-9.88 ppm due to the CHO formyl protons. Acyclic ligands have different chamber O<sub>2</sub>O<sub>2</sub> as diformyl and aromatic OH and O<sub>2</sub>O<sub>n</sub> as crown-like site (*n*: 1, 2, 3). This chamber may be filled with different metal cations due to their ability to form complexes, so the reaction of the appropriate diformyl precursors with Ba(ClO<sub>4</sub>) leads to the acyclic complexes [Ba(H<sub>2</sub>L<sup>1</sup>)](ClO<sub>4</sub>)<sub>2</sub>, [Ba(H<sub>2</sub>L<sup>2</sup>)](ClO<sub>4</sub>)<sub>2</sub>, where the barium (II) ion is in the O<sub>2</sub>O<sub>n</sub> crown-like site and

the perchlorate ions are not coordinated. The IR spectra show a strong band at 1106-1083 cm<sup>-1</sup>, due to almost ionic ClO<sub>4</sub><sup>-</sup>.

### Asymmetrical Schiff Bases and their Complexes

Asymmetrical Schiff bases H<sub>2</sub>L<sup>1a</sup> and H<sub>2</sub>L<sup>2a</sup> containing a N<sub>3</sub>O<sub>2</sub> and O<sub>2</sub>O<sub>3</sub>, O<sub>2</sub>O<sub>4</sub> chamber for the complexation of the appropriate metal were synthesized according to Scheme 3. Heterodinuclear complexes were synthesized by template condensation of the appropriate precursor in the presence of M(CH<sub>3</sub>COO)<sub>2</sub>·H<sub>2</sub>O and Ba(ClO<sub>4</sub>)<sub>2</sub>. The prepared Schiff bases are stable in air and soluble in common organic solvents. The IR spectra of the asymmetrical cyclic ligands show a strong signal at 1637-1625 cm<sup>-1</sup>, no signal was detected at 1650 cm<sup>-1</sup> attributable to C=O or NH<sub>2</sub>, due to the imine protons CH=N. Furthermore due to the electron-withdrawing ability of Ba<sup>+2</sup> in the crown-ether chamber, it was observed that the stretching etheric groups at 1200-1231 cm<sup>-1</sup> and C-C stretching of the aliphatic carbon bonds at 1085-1095 cm<sup>-1</sup> is taking place. These data suggest that barium (II) ions settle into the crown-ether chamber. On the other hand, the IR spectra show a strong band at 1106-1083 cm<sup>-1</sup> due to ClO<sub>4</sub><sup>-</sup> ions that are not coordinated. It was observed that the presence of IR spectral picks at 540-430 cm<sup>-1</sup> in the Ni<sup>+2</sup> complexes. These values may be due to Ni-O or Ni-N. In the NMR spectra of the CH=N group we observed at 8.92-8.98 ppm, while the peak at 9.96-9.88 ppm due to the CHO formyl protons, which also indicates the occurrence of the condensation reaction. This situation is corroborated by the presence of the peaks due to other groups such as OCH<sub>2</sub>CH<sub>2</sub>O and NCHCH<sub>2</sub>N. These values may be shifted to a lower field, in addition, the barium complexation may affect the aromatic protons and protons of the polyethylene ring. Mono nuclear complex causes significant change for the CH<sub>2</sub>CH<sub>2</sub> protons from 4.38 and 4.10 ppm to 4.12 and 3.90 ppm respectively. The structure of the synthesized macrocyclic ligands is also confirmed by MS spectral data. The mass spectrum exhibits the highest *m/e* peaks which are in agreement with the estimated values for these compounds. All these data confirm that the self-condensation reaction gives rise to the cyclic products and proposed their molecular structure an O<sub>2</sub>O<sub>n</sub> moiety for the Ba<sup>+2</sup> an O<sub>2</sub>N<sub>3</sub> for the Ni<sup>+2</sup>. According to the above physico-chemical data reported, these molecules containing free and adjustable crown-like chamber can be used as ligands towards appropriate hard and soft metal ions.

## Conclusions

In this study, we reported the preparation of the asymmetrical acyclic and cyclic compartmental Schiff bases containing two adjacent chambers to obtain the mono and dinuclear complexes with the appropriate alkaline earth and transition metal center and their related soft and hard complexes. These systems are not very soluble and stable in water, but the complexes can be functionalized to increase their solubility in suitable solvents. Furthermore the addition of additional groups at the coordination system may enlarge the possibility of specific hetero-nuclear complexation with the consequent formation of ordered poly nuclear complexation.

## Caution

Although these experiments did not resulted in any accidents and extreme care should be taken when perchlorates are handled, because they may explode spontaneously and may be sensitive to shock. The perchlorates should only be prepared in small quantities.

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