

Complexation of 1,4-Bis-[(5-H/methyl/chloro)-2-1H-benzimidazolyl]-1,2,3,4-butanetetraols with ZnCl_2

Aydin Tavman

Istanbul University, Department of Chemistry, 34850, Avcilar, Istanbul, Turkey.

atavman@istanbul.edu.tr

ABSTRACT

1,4-Bis-[(5-H/methyl/chloro)-2-1H-benzimidazolyl]-1,2,3,4-butanetetraols (**L1–L3**) with ZnCl_2 were synthesized and characterized using elemental analysis, molar conductivity, IR, ^1H and ^{13}C -NMR spectroscopy. The complexes are bimetallic and coordination occurs through the four hydroxyl oxygen atoms.

INTRODUCTION

Some bis-benzimidazole derivatives show biological activity. For example, 1,2-bis-(2-benzimidazolyl)-ethane has *antipoliavirus* /1/, *antifungal* effects /2/. 1,3-Bis-(2-benzimidazolyl)-propane shows *antiviral* effect; and nitro and hydroxyl derivatives of it show *antifungal* character and considerable activity towards *poliovirus* formation /3/. 1,2-Bis-(2-benzimidazolyl)-1,2-ethanediol shows anti-fungal and anti-poliovirus character, and 1,4-bis-(2-benzimidazolyl)-1,2,3,4-butanetetraol (**L1**) has a negative effect on intracellular viruses /2-5. Also bis-1H-benzimidazoles are strong coordinating agents and form stable complexes with various transition metals. It is believed that bis-benzimidazole metal complexes may also be biologically active.

Bis-benzimidazoles, e.g. 2,2'-dithiobis-benzimidazole, 1,2-benzoylene-bis-benzimidazole, were used in some polymers and polyamide fibers to improve the heat resistance /6-8/. Some bis-benzimidazoles also formed stable polymers. For example, 2,2'-(1,3-phenylene)-5,5'-bisbenzimidazole resin was obtained /9/, and a bis-benzimidazole resin including phosphorus was synthesized that has high thermal stability and resistance to ignition /10/.

In this study, 1,4-bis-[(5-H/methyl/chloro)-2-1H-benzimidazolyl]-1,2,3,4-butanetetraols (**L1–L3**) with ZnCl_2 were synthesized and characterized, and the effect of the substituents on complexation was studied.

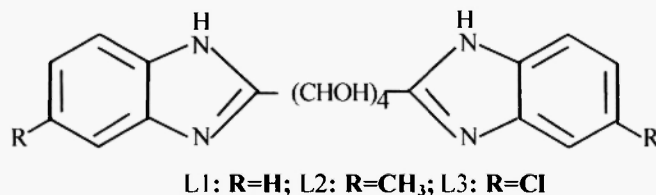


Figure 1. Formula of the ligands

MATERIALS AND METHODS

Chemicals and solvents were reagent grade. IR spectra were recorded (KBr pellets) on a Mattson 1000 Fourier Transform spectrometer. ^1H and ^{13}C -NMR spectra were run on a Bruker Ac-200 NMR spectrometer (TUBITAK-Turkey). Chemical shifts are expressed in ppm relative to TMS. The residual DMSO-d_6 signal was also used as an internal reference. Analytical data were obtained with a Carlo Erba 1106 analyser and Varian SpectraAA 220/SS atomic absorption spectrometer. The molar conductance of the compounds was measured in DMSO on a WPA CMD750 conductivity meter.

Synthesis of the Ligands

In the synthesis of **L1–L3**, 4-R-1,2-phenylenediamines ($\text{R} = \text{H}, \text{CH}_3, \text{Cl}$) and mucic acid were used according to the literature [11].

Synthesis of the Complexes

$\text{Zn}_2[\text{L1}]\text{Cl}_4$:

137 mg $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.56 mmol) was added to a suspension of **L1** (100 mg, 0.28 mmol) in EtOH (25 ml). The mixture was refluxed with constant stirring for 4 h, and then allowed to stand at room temperature overnight. After filtration the product was stirred in EtOH (20 ml) for 10 minutes to render it pure. The mixture was filtered, washed with 10 ml Et_2O and dried under vacuum.

$\text{Zn}_2[\text{L2}]\text{Cl}_4$:

122 mg $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.50 mmol) was added to a suspension of **L2** (90 mg, 0.25 mmol) in EtOH (40 ml). Synthesis procedure is the same as that of $\text{Zn}[\text{L1}]\text{Cl}_2$.

$\text{Zn}_2[\text{L3}]\text{Cl}_4$:

99 mg $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.40 mmol) was added to a suspension of **L3** (85 mg, 0.20 mmol) in EtOH (25 ml). Synthesis procedure is the same as that of $\text{Zn}[\text{L1}]\text{Cl}_2$.

RESULTS AND DISCUSSION

The analytical data and some physico-chemical properties of the compounds are given in Table 1.

General Properties

All of the complexes are colorless. The melting points of the ligands, **L1–L3**, are 282, 251 and 271°C, respectively. The benzene ring substituents decrease the melting points of the ligands.

The ligands are insoluble in polar solvents such as MeOH, EtOH, Et₂O and H₂O. However, they have low solubility in AcOH and DMSO. The complexes are moderately soluble in polar solvents. The molar conductivity of Zn₂(L1)Cl₄, Zn₂(L2)Cl₄, Zn₂(L3)Cl₄ are 16, 16 and 12 Ω⁻¹cm²mol⁻¹, respectively, in DMSO at 25±1°C. These values indicate that the complexes have non-ionic structures.

Table 1

Analytical data and some physico-chemical properties of the ligands and their ZnCl₂ complexes

Compound	El. Analysis; Found (Calcd.)				Yield %	M.p. °C	Λ ^a
	%C	%H	%N	%Zn			
C ₁₈ H ₁₈ N ₄ O ₄ ; L1	59.9 (61.0)	5.1 (5.1)	15.6 (15.8)	0	65	282	0
Zn ₂ [L1]Cl ₄ C ₁₈ H ₁₈ N ₄ Cl ₄ O ₄ Zn ₂	34.0 (34.5)	2.7 (2.9)	9.2 (8.9)	21.3 (20.9)	75	258	16
C ₂₀ H ₂₂ N ₄ O ₄ ; L2	62.9 (62.8)	5.7 (5.8)	14.5 (14.7)	0	60	251	0
Zn ₂ [L2]Cl ₄ C ₂₀ H ₂₂ N ₄ Cl ₄ O ₄ Zn ₂	36.9 (36.7)	3.6 (3.4)	8.9 (8.6)	20.5 (20.0)	55	259	16
C ₁₈ H ₁₆ N ₄ O ₄ Cl ₂ ; L3	51.3 (51.1)	3.7 (3.8)	13.0 (13.2)	0	50	271	0
Zn ₂ [L3]Cl ₄ C ₁₈ H ₁₆ N ₄ Cl ₆ O ₄ Zn ₂	31.4 (31.1)	2.3 (2.3)	8.3 (8.0)	18.7 (18.9)	60	262	12

^a Molar conductivity, measured in DMSO, Ω⁻¹cm²mol⁻¹, at 25±1°C.

IR Spectra

The IR spectral data of the ligands and the complexes are listed in Table 2.

The NH stretching vibrational frequency band in the ligands appears around 3400 cm⁻¹ as a broad band which is broadened considerably on complexation. A broad band between 3270 and 3150 cm⁻¹ belongs to OH stretching vibrational frequency in IR spectra of the ligands. ν(O–H) and ν(N–H) are in the broad band in the 2600–3600 cm⁻¹ regions due to the inter- and intra-molecular hydrogen bonding. In the complexes, hydrogen bonding weakens, probably due to hydroxyl oxygen coordination. Therefore, solubility of the complexes increases according to the ligands.

The weak or medium bands between 1586 - 1608 cm⁻¹ in the spectra of the ligands and the complexes are attributed to the ν(C=N). In the complexes they show no considerable change. In the spectra of the ligands, the aromatic C=C stretching vibrations are observed at the 1632–1620 cm⁻¹ range and the 1470–1445 cm⁻¹ range as medium or strong bands.

Table 2
The selected IR spectral data of the ligands and the complexes

Compound	Frequencies, cm ⁻¹
L1	3438 m, 3300 br, 1615 m, 1592 sh, 1439 br,s, 1276 m, 1115 s, 1053 m, 746 s
Zn ₂ [L1]Cl ₄	3438br, 3331 br, 1623 m, 1600 sh, 1461 s, 1284 s, 1108 m, 1046 m, 754 s.
L2	3461 m, 3292 br,m, 2923 m, 1631 m, 1600 sh, 1454 s, 1300 m, 1108 m, 1046 m, 808 m
Zn ₂ [L2]Cl ₄	3384 s,br, 3191 br, 2922 m, 1628 m, 1608 sh, 1416 s, 1309 m, 1104 s, 1039 s, 804 s.
L3	3439 s, 3269 m, 1632 m, 1592 w, 1454 m, 1415 m, 1285 m, 1108 m, 1054 s, 846 m, 800 m, 600 m
Zn ₂ [L3]Cl ₄	3434 s, 3268 m, 1624 w, 1586 w, 1528 m, 1447 s, 1416 m, 1274 m, 1108 m, 1047 s, 796 m, 600 m.

Characteristic medium bands at around 1040 and 1110 cm⁻¹ in the IR spectra of the free ligands are assigned to $\nu(\text{C}-\text{O})$. On complexation these bands shift to the lower frequencies. The o-substitution out-of-plane C-H bendings appear near 750 cm⁻¹ as strong bands in the **L1** and Zn₂(**L1**)Cl₄ spectra. The out-of-plane of the trisubstituted aromatic C-H bendings are at the 796-808 cm⁻¹ ranges for the compounds as strong bands for **L2**, **L3** and their ZnCl₂ complexes.

In the spectra of **L2** and Zn₂(**L2**)Cl₄, $\nu(\text{CH}_3)$ appears around 2920 cm⁻¹ as a weak band. The medium C-Cl stretching vibration frequency is observed at 600 cm⁻¹ in the spectra of **L3** and Zn₂(**L3**)Cl₄, respectively.

¹H and ¹³C-NMR Spectra

The ¹H-NMR spectral data of the ligands and the complexes are listed in Table 3 and ¹³C-NMR spectral data (APT) in Table 4.

CH¹, one of the aliphatic protons, appears at approximately 4.10 ppm as a singlet in the ligands and the complexes. CH² shows a doublet at 5.16 ppm in **L1**. However, in **L2** and **L3** it is seen at 5.16 ppm as a singlet. In the complexes CH¹ shows no shift while CH² shifts to the lower frequencies (5.29-5.32 ppm). The aliphatic carbon signals are seen at around 67 and 72 ppm in the ¹³C-NMR spectra. On complexation this signal shifts by 0.3-0.8 ppm to the higher field.

The chemical shifts of OH¹ protons are seen at 4.75, 4.72 and 4.72 ppm as broad singlets and OH² protons at 5.44 (d), 5.52 (s,br) and 5.54 ppm (s,br) for **L1**, **L2** and **L3**, respectively. The complexes show significant chemical shift differences compared to the free ligand for the OH protons. OH¹ protons disappear in the complexes, probably due to oxygen atom coordination. OH² protons shift to 5.84, 6.03 and 6.00 ppm as a broad singlet for the complexes, Zn₂(**L1-L3**)Cl₄, respectively. This shows that the coordination occurs through the hydroxyl oxygen atoms. OH¹ protons are seen as a broad peak in the ligands because of more acidic character than OH² protons. On complexation the acidic character of OH¹ protons is increased and this

proton disappears in the spectra because of its dissociation. In the literature similar complexations were observed with Fe(III), Co(II), Cu(II) /12/, Ag(I) /13/ and Hg(II) ions /14/.

The aromatic protons (H4-H7) show a complex pattern in the aromatic region in the spectra of **L1** and $\text{Zn}_2(\text{L1})\text{Cl}_4$. Protons 6 and 7 show the doublets in the spectra of **L2**, **L3** and their Zn(II) complexes. In the ^1H -NMR spectra of **L2**, the aromatic protons, H(4), H(6) and H(7), appeared at the higher field (6.99-7.40 ppm range) according to **L1** and **L3** because of the methyl group's δ^+ effect. However, in the spectra of **L3** and $\text{Zn}_2(\text{L3})\text{Cl}_4$, substituent Cl makes aromatic protons shift to the lower field. Methyl protons of **L2** and $\text{Zn}_2(\text{L2})\text{Cl}_4$ show a singlet at 2.40 and 2.45 ppm, respectively.

The ^{13}C -NMR spectra of **L1** and its complex show two different signals for the aromatic carbons. Also, **L3** only two signals were observed at the aromatic region. However, in $\text{Zn}_2(\text{L3})\text{Cl}_4$ four signals are seen for the aromatic carbons. In **L2** and $\text{Zn}_2(\text{L2})\text{Cl}_4$ three signals are observed in the aromatic region. The substituted benzimidazole carbon atom, C5, separates from C4, C6 and C7 that appear in one signal in **L2**, **L3** and their complexes. C2, C8 and C9 appear in the 155-160 ppm range in one signal in the ligands and the complexes.

Table 3
 ^1H -NMR spectral data of **L1**–**L3** and their complexes with ZnCl_2

Compound	Chemical shifts, δ_{H} , (ppm) and coupling constants, J, (Hz) (in DMSO-d_6)								
	CH ¹	OH ¹	CH ²	OH ²	H-4	H-5	H-6	H-7	N-H
L1	4.11 s,br	4.75 s,br	5.16 d J=6.5	5.44 d J=6.7	7.50 m	7.12 m	7.12 m	7.50 m	12.07 s,br
$\text{Zn}_2[\text{L1}]\text{Cl}_4$	4.10 s	---	5.31 s	5.84 s,br	7.64 m	7.27 m	7.27 m	7.64 m	---
L2	4.09 s	4.70 s,br	5.16 s	5.52 s,br	7.31 s	2.40 s*	6.99 d J=8.0	7.40 d J=8.1	12.03 s,br
$\text{Zn}_2[\text{L2}]\text{Cl}_4$	4.10 s	---	5.32 s	6.03 s,br	7.45 s	2.45 s*	7.15 d J=8.2	7.55 d J=8.2	---
L3	4.10 s	4.72 s,br	5.16 s	5.54 s,br	7.52 s	---	7.48 d J=9.0	7.14 d-d J=8.4; 2.0	12.24 s,br
$\text{Zn}_2[\text{L3}]\text{Cl}_4$	4.11 s	---	5.29 s	6.00 s,br	7.68 s	---	7.63 d J=8.9	7.30 d J=8.7	---

* 3H (CH_3)

The N–H proton exhibits a broad signal due to the fluxional behaviour near 12.10 ppm in the spectra of the ligands. In the complexes the signal of the NH protons disappears; however, in the IR spectra of the Zn(II) complexes, the broad bands around 3400 cm^{-1} assigned to $\nu(\text{NH})$ indicate that the NH hydrogen is not eliminated. This shows that the C=N nitrogen does not coordinate to the Zn(II) ion. The NH signal in the ligands appears as a broad band due to the resonance through the $\text{N}=\text{C}=\text{N}$ system in the imidazole ring. If the C=N nitrogen is coordinated to the Zn(II) ion, the $\text{N}=\text{C}=\text{N}$ system must be changed to the $\text{N}-\text{C}=\text{N}$ system and

REFERENCES

1. K. Otaki, J. Inoue, Z. Yamazaki, M. Haya, Y. Takai, M. Yasue and D. Mizuno, *Yakugaku Zasshi*, **85**, 926 (1965); CA 64:2434f.
2. B. Çakır, E. Büyükbingöl, Ü. Uçucu, U. Abbasoğlu and N. Noyanalpan, *J. Fac. Pharm. Gazi*, **5**, 71(1988).
3. S. Akihama, K. Takahashi and N. Miyajama, *Yakugaku Zasshi*, **94**, 247 (1974); CA 81:9648x.
4. D. G. O'Sullivan and A. K. Wallis, *Nature*, **198**, 1270 (1963);
5. S. Akihama and K. Takahashi, *Meiji Yakka Daigaku Kenkyu Kiyo*, **4**, 25 (1974).
6. M. Goto, S. Ito and A. Tanaka, *Can.* 944,498, **1974**. CA 81:65096c.
7. K. Sugai and S. Sato, *Japan* 73 01,427, **1973**. CA 80: 15860f.
8. V.V. Korshak, E.S. Krongauz, A.V. Travnikova and A.L. Rusanov, *Macromolecules*, **7**, 589 (1974).
9. Matsushita Electric Works, Ltd. *Jpn. Tokkyo Koho* 80 28,438, **1980**. CA 94:P23967a.
10. H. Sivriev and G. Borissov, *Eur. Polym. J.*, **13**, 25 (1977).
11. A. Tavman, B. Ülküseven and N. M. Agh-Atabay, *Trans. Met. Chem.*, **25**, 324 (2000).
12. A. Tavman, *Rev. Inorg. Chem.*, **22**, 41 (2002).
13. A. Tavman, *Rev. Inorg. Chem.*, **22**, 113 (2002).
14. A. Tavman, *Main Group Met. Chem.*, **26**, 229 (2003).

