

Binuclear Complexes Containing Barbituric Derivatives as Ligands- Precursors for Supramolecular Structures.

I. Synthesis and Spectral Properties of N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP) and its Copper(II) Complex.

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Abstract: The new Mannich base VEP (N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine), has been synthesized by condensation of veronal with formaldehyde and piperazine following a Mannich procedure. The new binuclear complex $\text{Cu}_2\text{VEP}(\text{X})_4 \cdot 4\text{H}_2\text{O}$, $\text{X}=\text{ClO}_4^-$ where VEP stands for N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine, were obtained by metal - ligand direct synthesis. Tetrahedral geometry of the metal ion was preserved in solution as well in solid state. The binuclear complex contain VEP in a chair conformation.

Keywords: copper(II) complex; Mannich base ligand; barbituric acid derivative.

1. Introduction

Barbituric acid and some of its derivatives are well known anticonvulsive, sedative and hypnotic drugs [1]. Their activity might be influenced by complex formation. In order to develop the variety of the compounds of this class, N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP) has been obtained by a Mannich type reaction [2] from (veronal) 5,5'-diethyl-barbituric acid (Hdebarb; 1H,3H,5H-5,5'-diethylpyrimidine-2,4,6-trione), piperazine and formaldehyde.

Over the years there has been a continuous interest in the chemistry of metal complexes of biologically important ligands. The study of such complexes may lead to a greater understanding of the role of the ligand in biological systems, and may also contribute to the development of new metal-based chemotherapeutic agents. Most studies have concentrated on the first-row transition metals [11],[14], and relatively few studies have concerned barbituric acid complexes of the platinum-group metals [12] or silver and gold [13].

The structural aspect of the Mannich N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP) suggests its ability to act as ligand to yield either a binuclear complex, when piperazine adopts a *chair* conformation or, mononuclear complexes when piperazine adopts a *boat* conformation. Beside this, a diversity of the complexes may be formed as a consequence of the different possibility of ligation of the barbituric moiety. The formula of the N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP) is shown in Fig. 1.

Here, we report on the synthesis of ligand N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)piperazine (VEP) and Cu (II) complex .

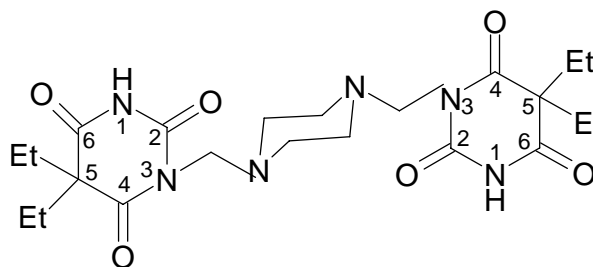


Figure 1. N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP)

2. Experimental

2.1. Materials

All chemicals were purchased from commercial sources and used without further purification. N,N'-bis-(5,5'-diethyl-barbituryl-1-methyl)-piperazine (VEP) was obtained according to the literature [2].

2.2. Physical Measurements

Electronic absorption spectrum of the complex, recorded on freshly EtOH, or dioxane solutions and dispersed in nuyol, were measured with a Lambda 12 Perkin-Elmer spectrophotometer

IR spectroscopy: IR spectra in range 600 - 4000 cm^{-1} were recorded on KBr-pellets with a Perkin - Elmer 16PC FT - IR Spectrometer

Electric conductivities were measured in EtOH, DMSO or dioxane solutions with a WTW LF 340 - A conductometer.

2.3. Syntheses

2.3.1. N,N'-bis-(5,5'-diethyl-barbituril-1-methyl)-piperazine (VEP) : 1.104 g (6mmol) veronal dissolved in ethanol (10ml) was treated with 1,436 g piperazine hexahydrate (3mmol) dissolved in ethanol (4ml); the clear solution was treated then with soluția 0,47 ml formaldehyde 35 % (6mmol). The reaction was developed in a balloon flask (50 ml) at room temperature, stirred for 5 hours, to complete the reaction. The resulting white-opalescent suspension was allowed to slow evaporation until next day. The white precipitate was collected by filtration and washed with ethanol. The compound was purified by recrystallisation from EtOH. Yield: (47%)

Anal. Calc. for $C_{22}H_{34}N_6O_6$ (M.W = 478.55g/mol):
% C 55.22, H 7.16, N 17.56; Found: % C 55.35, H 7.22, N 17.60. Results of $^1\text{HRMN}$ determination for VEP are following:
3,52(s, 2H); 2,70(s, 2H); 1,90(q, 3H); 0,81(t, 2H)
IR(KBr) ν/cm^{-1} : 2959m, 2797s, 1736m, 1698s, 1464s, 1362m, 1347s, 1013s, 834s ;

2.3.2. $\text{Cu}_2\text{VEP}(\text{ClO}_4)_4 \cdot 4\text{H}_2\text{O}$: 0,956g (2mmol) VEP dissolved in 75 cm^3 EtOH at 50°C was treated with 0,682 g $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (4mmol) dissolved in 10 cm^3 EtOH; after few minutes 0,596 g $\text{NaClO}_4 \cdot \text{H}_2\text{O}$ (4,25mmol) add when mustard solution appeared .

The reaction mixture was then stirred and heated for 3 hours and then kept in dark, for 24 hours. The mustard precipitate was separated by filtration and washed with EtOH . The compound was purified by recrystallisation from EtOH. Yield: 39% .

Anal. Calc. for $\text{C}_{22}\text{H}_{42}\text{N}_6\text{O}_{26}\text{Cl}_4\text{Cu}_2$
(M.W.=1075.50g/mol) % C 24.57; H 3.94; N 7.81; Cl 13.19; Cu 11.82; Found % C 24.60, H 3.98, N 7.85, Cl 13.16, Cu 11.86;
IR(KBr) ν/cm^{-1} : 3510s, 3420s, 2887m, 2815m, 1605s, 1453m, 1423m, 1383m, 1318m, 1121s, 1012m, 956m, 635s, 533m, 418m.

3. Results and Discussion

In analogy with N,N'-bis-(4-antipyril-methyl)-piperazine (BAMP) for which antipyrine acts as a substrate[3-6], the Mannich base N,N'-bis-(5,5'-diethyl-barbituril-1-methyl)-piperazine (VEP) can act also as bridging ligand through atoms situated on each side of the piperazine cycle. VEP contains three types of the donor atoms: one type of oxygen – carbonylic oxygen, and two types of nitrogen atoms – piperazine and barbituric nitrogen. [4]. The molecular mechanics and quantum chemical calculations show that the barbituric nitrogen atoms are more negative than that of the piperazine nitrogen atoms. However, stereochemical factors show that the piperazine nitrogen atoms are more convenient for coordination, especially when the differences between the charge density are not significant. The oxygen atom situated in the position 2 of barbituric cycle present the

most negative charge density. Each donor group consists of barbituric oxygen and the piperazine nitrogen.[5] Sterically, all these atoms are able enough to close a chelate ring with a metal ion. VEP can thus act as a potential tetradentate ligand using N_2O_2 donor atoms set, to give mononuclear or dinuclear complexes, depending on *boat* or *chair* conformation of the piperazine cycle.[7]

The synthesis of the complex was realized by direct metal – ligand procedure. In order to obtain this compound, the metal to ligand ratio was varied and the best results lead to the method presented in the previous section.

The complex is sparingly soluble in water, ethanol, carbon tetrachloride, chloroform and benzene, but soluble in DMSO and dioxane to give stable solutions at room temperature.

The molar conductivities of the freshly prepared EtOH, or dioxane solutions of the complex demonstrate its behavior as 1 : 2 electrolyte, revealing its ability to dissociate in this solvents [8] .The information regarding the geometry of the metal ion and the nature of the metal-ligand bond have been obtained from the UV-VIS and IR spectra.

3.1. Electronic spectrum:

The metal perchlorat contains the metal ion in the tetrahedral environment either the spectra were recorded on freshly solution, or on nujol mull.

The assignments of the bands for this complex are presented in Table 2 [9c].

TABLE 1. Properties of the complex containing VEP as ligand
Electronic spectrum of the complex

Complex	EtOH		Assignments
	λ (nm)	ϵ ($\text{L M}^{-1}\text{cm}^{-1}$)	
$\text{Cu}_2\text{VEP}(\text{ClO}_4)_4 \cdot 4\text{H}_2\text{O}$	755*	122*	Tetrahedral

*Dioxane;

3.2. Infrared spectra

The selected bands in the infrared spectra of the ligand VEP as well as copper (II) complex are shown in Table 2. Examination of the IR data suggests that the bands characteristic of the VEP ligand can be noticed. Some of them are shifted as a result of the coordination:

- the carbonyl bands from $1698\text{-}1713 \text{ cm}^{-1}$ are shifted to $1560\text{-}1657 \text{ cm}^{-1}$.
- bands, which can be assigned to the metal-oxygen VEP, appear in the region $533\text{-}582 \text{ cm}^{-1}$.
- the new medium intensity bands appear in the region $417\text{-}469 \text{ cm}^{-1}$; they can be assigned to the metal – piperazine nitrogen bonds.

The ν_{ClO_4} from the regions 1121 cm^{-1} and 635 cm^{-1} , respectively, are due to the ionic perchlorate .

TABLE 2. Selected bands in the IR spectra of the complex and VEP

VEP	Complex	Assignments
-	3510s 3420s	ν_{OH}
2959m 2797s	2887m 2815m	ν_{asNH}
1736m 1698s	-	$\nu_{C=O(4,6+2)}$ backbone
-	1605s	ν_{C-O}
1464s	1453m 1423m	piperazinebackbone
1362m 1347s	1383m	δCH_2
1347s	1318m	$CH_{bending}$
-	1121s	ν_{ClO_4}
1013s 834s	1012m 956m	Piperazine CH_{2LW}
-	-	$\nu_{M-O(ClO_4)}$
-	635s	ν_{ClO_4}
-	533m	ν_{M-O}
-	-	ν_{M-NCS}
-	418m	ν_{M-N}

4. Conclusions

The new binuclear $Cu_2VEP(ClO_4)_4 \cdot 4H_2O$, complex containing VEP as ligand was obtained by direct metal – ligand synthesis.

The binuclear complex contains VEP in a *chair* conformation. Tetrahedral geometry of the metal ion is preserved in solution as well in solid state.

The coordination sphere is designed by the N_2O_2 donor set of the big binucleating ligand VEP.

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