

Design, Synthesis and Structural Study of a Schiff Base Ligand Precursor of Metallosupramolecular Architectures [†]

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Abstract: The spontaneous association of organic ligands and metal ions has given rise to what is known as Metallosupramolecular Chemistry. This emerging field of Chemistry has gathered significant attention due to the numerous supramolecular structures that can be obtained, which have applications in diverse areas such as materials chemistry, biomedical chemistry and catalysis among others. In this context, Schiff Base ligands are among the most used ligands for the synthesis of helicates and mesocates. In this work, the Schiff Base ligand H₂L was designed, synthesized, and characterized. This ligand is potentially dianionic and tetradentate [N₂O₂], with a long and semi-flexible spacer, making it a bicompartamental ligand that promotes the formation of dinuclear helicate compounds. Additionally, the presence of bulky tert-butyl and ethyl groups at specific positions of the skeleton is crucial for enhancing the formation of such structures instead of mesocates. The synthesis was carried out through an imine condensation reaction between two equivalents of 4-(tert-butyl)-2-hydroxybenzaldehyde and one equivalent of 4,4'-methylenebis(2,6-diethylamine) in the presence of *p*-toluenesulfonic acid monohydrate as a catalyst. The ligand was characterized using standard techniques, and suitable crystals were obtained for study by X-ray diffraction.

Keywords: ligand; Schiff base; Metallosupramolecular Chemistry; helicate

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1. Introduction

A Schiff base is obtained through a condensation reaction between a carbonyl group and an amine, leading to the formation of an imine bond. This active group in the ligand play an important role in its applications [1]. Since Hugo Schiff introduced them in 1864 as a new class of organic compounds [2], Schiff bases and their complexes have attracted interest due to their broad properties and applications. They have applications in industry, pharmacology, biological activities, antimicrobial, antibacterial and anticancer activities [1,3–9].

In the field of Coordination Chemistry, they are one of the most versatile ligands and therefore widely used for obtaining helicate and mesocate-type metal-supramolecular architectures [10–13].

Our research group has broad experience in obtaining complexes derived from Schiff Base ligands. In 2024 we have published a study in which a family of Schiff Base ligands, with bulky groups on the branches and the spacer, was coordinatively exploited to determine whether it could favor the formation of a helicate-type architecture over a mesocate-type one [14]. To continue this study, a tetradentate Schiff Base ligand (H₂L) derived from a bisphenylmethane spacer functionalized with bulky tert-butyl groups on the branches and an ethyl group on the spacer has been studied.

2. Experimental Section

2.1. Reactants and Solvents

In the synthesis of the H₂L ligand, 4-(tert-butyl)-2-hydroxybenzaldehyde and 4,4'-methylenebis(2,6-diethylamine) were used as reagents, with absolute ethanol as solvent. Both the starting reagents and the solvent are commercially available and were used without any additional purification process.

2.2. Synthesis and Characterization of the Schiff Base Ligand H₂L

The synthesis of the ligand H₂L was carried out through an imine condensation reaction between two equivalents of 4-(tert-butyl)-2-hydroxybenzaldehyde and one equivalent of 4,4'-methylenebis(2,6-diethylamine) in the presence of the monohydrated *p*-toluenesulfonic acid catalyst. (Figure 1).

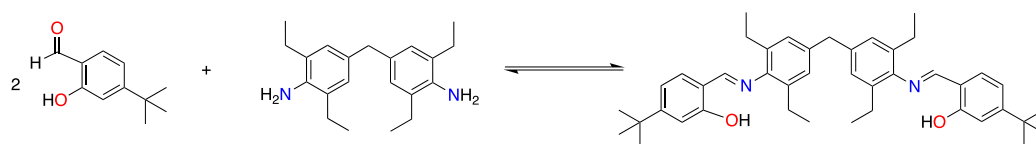


Figure 1. Scheme of the imine condensation reaction.

Specifically, 0.28 g of 4-(tert-butyl)-2-hydroxybenzaldehyde (1.60 mmol) is dissolved in absolute ethanol (50 mL). Then, 10 mg of *p*-toluenesulfonic acid, acting as a catalyst, is added. Once dissolved, 0.248 g of the spacer 4,4'-methylenebis(2,6-diethylaniline) (0.80 mmol) is then incorporated. The mixture is left under reflux and stirring for 4 h. During the synthesis, a Dean-Stark condenser was used to remove the ethanol/water azeotropic mixture formed in the reaction, thereby promoting the formation of the ligand. After the reaction time elapsed, the mixture was allowed to reach room temperature, resulting in the formation of a white precipitate, which was vacuum filtered. Slow evaporation of the mother liquors allowed to obtain crystals of the ligand that could be analyzed by single-crystal X-ray diffraction. White solid. Yield: 0.3415 g (68%); Mp = 203–210 °C; Elemental analysis, theoretical % (C₄₃H₅₄N₂O₂): C, 81.9; N, 4.4; H, 8.6; experimental %: C, 81.5; N, 4.5; H, 8.6; IR (KBr, cm⁻¹): νO-H 3421.64 (md), νC-H 2964.52 (f), νC=N 1622.1 (mf), νC-O 1286.49 (m), νCH₂ 815.87 (d); Mass spectrometry (ESI⁺): *m/z*, 653.6 [H₂L³ + Na⁺]⁺; ¹H NMR (400 MHz, acetone) δ 12.90 (s, 2H5), 8.49 (s, 2H6), 7.49 (d, J = 8.2 Hz, 2H4), 7.11–6.99 (m, 8Haromatic), 3.93 (s, 2H13), 2.53 (q, J = 7.5 Hz, 4H7, 4H9), 1.35 (s, 18H1), 1.11 (t, J = 7.5 Hz, 12H8); ¹³C NMR (75 MHz, CDCl₃) δ (2xCH) 166.31, (2xC) 161.21, (2xC) 157.60, (2xC) 145.80, (2xC) 138.09, (4xC) 134.60, (2xCH) 131.88, (4xCH) 127.19, (2xCH) 116.66, (2xC) 116.59, (2xCH) 114.46, (1xCH₂) 41.41, (2xC) 35.34, (6xCH₃) 31.19, (4xCH₂) 25.04, (4xCH₃) 15.08.

2.3. Crystallographic Data of H₂L

H₂L: C₄₃H₅₄N₂O₂; MW: 630.88 g·mol⁻¹; crystal dimensions 0.22 × 0.14 × 0.09 mm; Monoclinic, C2/c; a = 43.929 (3), b = 8.9555 (5), c = 18.5724 (11) Å; β = 97.977 (2); V = 7235.9 (7) Å³; z = 8; μ = 0.07 mm⁻¹; measured reflections = 62938; independent reflections = 7121; [R_{int}] = [0.070]; R = 0.041; wR = 0.100.

The main bond distances and angles (Table 1) are within the expected ranges for the Schiff Base ligands.

Table 1. Selected bond length and angles for ligand H₂L.

Main Bond Distances (Å)			
O1–C1	1.3502 (16)	O2–C23	1.3550 (17)
N1–C7	1.2791 (17)	N2–C21	1.279 (2)
N1–C8	1.4292 (17)	N2–C18	1.4377 (19)
C1–C6	1.4045 (19)	C21–C22	1.456 (2)

C6–C7	1.4513 (19)	C22–C23	1.403 (2)
Angles (°)			
C1–N1–C8	119.69 (11)	C17–C18–N2	199.99 (14)
N1–C7–C6	122.37 (12)	C21–N2–C18	117.59 (15)
C9–C8–N1	117.38 (12)	N2–C18–C19	116.97 (15)
C13–C8–N1	121.13 (12)	N2–C21–C22	122.90 (16)
O2–C23–C24	118.23 (14)	O2–C23–C22	121.32 (13)

3. Results and Discussion

The H₂L ligand is a Schiff base characterized primarily by the presence of an imino group. This ligand has two imino groups and two hydroxyl groups, making it potentially dianionic and tetradentate [N₂O₂]. Each [NO] binding domain is separated by a long and semi-flexible spacer, classifying it as a bicompartamental ligand (Figure 2).

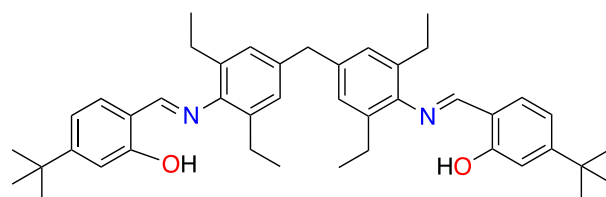


Figure 2. Structure of H₂L ligand.

The ligand was characterized using the standard techniques used for the characterization of organic compounds, both in solid state and in solution: elemental analysis, infrared spectroscopy, mass spectrometry, ¹H NMR spectroscopy, ¹³C NMR spectroscopy, and single-crystal X-ray diffraction.

Regarding the latter, the slow evaporation of the mother liquors from the synthesis of ligand H₂L, optimal crystals were obtained for study using single-crystal X-ray diffraction. This allowed for a detailed analysis of its three-dimensional structure.

As shown in Figure 3, the ligand features two binding domains oriented in opposite directions in space, which favors the formation of helical architectures upon metal coordination. Additionally, it exhibits an E conformation with respect to the imino bonds and a syn conformation of the two ligand branches relative to the spacer, as both are oriented in the same direction.

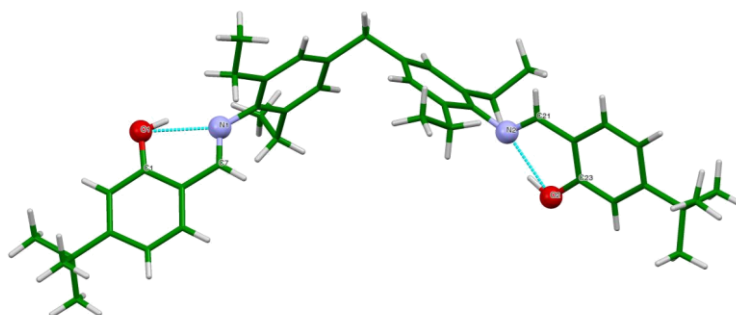


Figure 3. X-ray structure of the H₂L ligand.

On the other hand, the imino groups on the different branches have different orientations: in one branch, the hydroxyl group of the phenol is oriented towards the interior cavity of the ligand, while the other hydroxyl group is oriented towards the exterior. This conformation is explained by the presence of hydrogen bonds between the iminic nitrogen and the phenolic oxygen of the branches.

4. Conclusions

All the characterization techniques used indicate that the H₂L ligand, Schiff base, was successfully synthesized with a high degree of purity and yield. The study of its crystal structure through single-crystal X-ray diffraction allows us to confirm its successful synthesis.

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