

DFT/B3LYP and BP86 examination of mononuclear half-sandwich Nd^7 metallo anticancer drug complexes based on N,O dendritic scaffolds.

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INTRODUCTION

Research in most fields has always had as its main interest the improvement of human living conditions. The development of new therapeutic molecules depends on this, as in the case of the discovery of the activity of one of the most successful anti-cancer compounds cis-diaminedicloroplatinium (II) ($\text{cis-}[\text{PtCl}_2(\text{NH}_3)_2]$), clinically referred to as cisplatin, which has enabled the pharmaceutical industry to achieve considerable success in the field of chemotherapy. However, this first generation compound had important limitations such as: limited selectivity towards tumour tissue and high toxicity. In order to overcome the various side effects pronounced by cisplatin, several experimental and theoretical studies have been directed towards the design and development of new anti-cancer drugs complementary to cisplatin. The recent development of platinum-based anticancer drugs has used many strategies to design new agents. Most of these are based on modification of the amino ligand responsible for the adduct structure formed upon interaction with DNA. The overall objective of this work is to understand the interactions of these new bridging drugs. A better understanding of these interactions should allow the design of more potent compounds with reduced side effects. For this, the necessary geometric, electronic and thermodynamic information has been provided. The present work is mainly centered around the following four points: **(i)** Evaluate the geometric parameters; **(ii)** Evaluate topological descriptors; **(iii)** Evaluate stability; **(iv)** Evaluate the properties of the different bonds of our complexes.

I MATERIALS AND METHODS

I.A-METHODS

DFT (Density Functional Theory) It is based on the electron density, also called charge density, noted $\rho(r)$.

a-Choice of basis set

A tailoring basis set denoted GEN (LanL2DZ for $[\text{Nd}^7]$ transition metals (Co, Ir and Rh) and for halogen atoms (Br and Cl)] and 6-311+G(d,p) for other atoms has been adopted.

b-Choice of functionals

B3LYP: Becke, three-parameter, Lee-Yang-Parr

BP86: Becke and Perdew exchange functional

I.B-MATERIALS

I.B.1-HARDWARE

A desktop (Philips) dual core with **2.6*2 GoRAM /processor 160GHz** as characteristic;

A personal computer ((**LENOVO**) i 3 with **4Go RAM/ processor 2.40GHz** as characteristic;

A Calculator (CEPAMOQ).

I.B.2-SOFTWARE

Gaussian 09, Gaussian 16;

Gauss View 5.08 Gauss View 6.016 program;

Chemdraw ultra 12;

Origin 6.0;

Multiwfn.

II. RESULTS

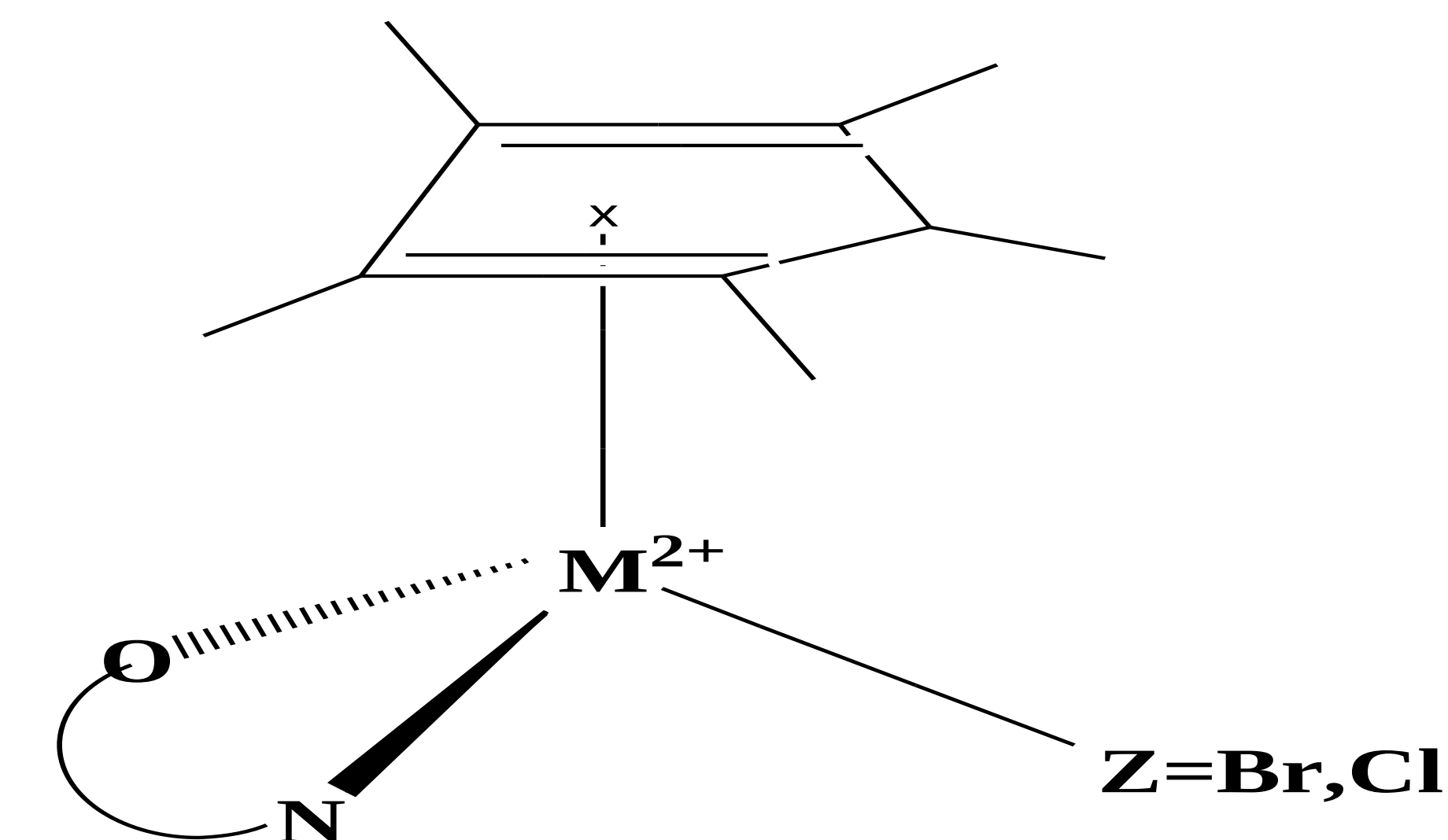


Figure 1 : Schematic representation of molecular system used.

CONCLUSION

This work consisted in presenting the anticancer molecules of the first generations with their limits, to present the motivation of this research whose main goal is the study of the interactions of these new complexes. Such a study allowing the design of new compounds more powerful, less toxic with less side effects than those of the first generations, for which we have already built a chimo library. In this work, the Nd^7 metal atoms are bonded to three ligands: the pentamethylcyclopentadienyl (CP^*), a halogen atom (Cl or Br) and the chelating ligands NnO (L). The collectively optimized structures preferred the piano-stool environment. The structures optimized collectively preferred the piano-stool environment. The intermolecular hydrogen bonds ($\text{CH}\dots\text{halogen atom}$ (2.619-2.954) and $\text{CH}\dots\text{O}$ (2.266-2.973 Å) stabilize the complexes obtained. Majority of geometric parameters estimated using B3LYP functional have been found close to experimental data. The B3LYP functional underestimates the complexation energies by about 10.57 kJ/mol (chloride cobalt complexes) and 31.05 kJ/mol (bromide complexes). Negligible **BP86** HOMO-LUMO gaps obtained are in accordance with experimental findings on the hexaminoferrous cation $[\text{Fe}(\text{NH}_3)_6]^{2+}$. This fact is attributed to the over stabilization the high spin state resulting from the presence of too much Hartree-Fock exchange by the B3LYP functional. In chloride complexes, stronger interactions are found between salicylaldimine ligand and two divalent cations: Co (-3097.15 kJ/mol) and Ir (-3436.78 kJ/mol). Except for salicylaldimine-rhodium complexes (98.51%), the contribution of the electrostatic interaction is dominating over the covalent interaction (4.06-20.45%) in the chloride rhodium complexes. But, contrary facts have been obtained for Rh bromide ones (98.52-98.6%) with exception of **3Bb** (18.63%).