An Unprecedented Zinc(2+) complex with a biologically relevant *bis*-indolyl intercalating moiety: From ligand design to Preliminary Docking Studies towards ssDNA

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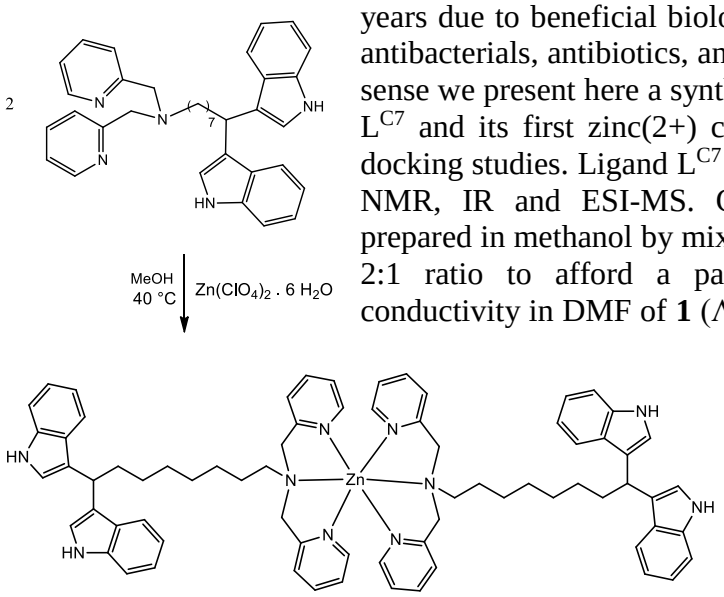
The advancement of metal complex mediated chemo-therapeutic design has been spurred largely due to the success of the cornerstone anticancer agent cisplatin.[1] Zinc containing drugs can be considered outstanding candidates to improve the efficacy in medical treatment once it is an essential trace element for growth and development in all forms of life.[2] Parallel to this, *bis*(indolyl)methanes (BIMs), have attracted considerable interest in recent years due to beneficial biological activities, including anticancer, antibacterials, antibiotics, antifungal, anti-inflammatory.[3] In this sense we present here a synthetic pathway for a bioinspired ligand L^{C7} and its first zinc(2+) complex as a viable option for DNA docking studies. Ligand L^{C7} was synthesized and characterized by NMR, IR and ESI-MS. Complex $[Zn(L^{C7})_2](ClO_4)_2$ (**1**) was prepared in methanol by mixing L^{C7} ligand and $ZnClO_4{\cdot}6H_2O$ in a 2:1 ratio to afford a pale yellowish powder (left). Molar conductivity in DMF of **1** (Λ_M= 120 μS cm^{-1}) has confirmed a 2:1 electrolyte ratio[4]. The presence of the perchlorate counterions was probed by IR spectroscopy (KBr) where a strong absorption in 1095 cm^{-1} ($\nu_{Cl\text{-}O}$) was observed. The organic moiety regarding L^{C7} was confirmed as well by direct comparison between L^{C7} and **1**. ESI(+)-MS was performed in acetonitrile and two major peak cluster at 573,23 Da ($C_{72}H_{78}N_{10}Zn$) and 542,29 Da ($C_{36}H_{39}N_5$) with a suitable isotopic pattern were found. These clusters were ascribed to the $\mathbf{1}^{2+}$ and the ligand $[L^{C7}+H^+]$ species, respectively. Preliminary docking studies of **1** towards salmon sperm DNA (ssDNA) were carried out spectrophometrically at pH 7,2 (HEPES/ACN 50% v/v) and the intrinsic binding constant K_b was determined (4.22×10^4). Upon the incremental addition of ssDNA, the CT-bands (π-π*) of **1** exhibited significant hypochromism (46%) suggesting **1** could bind to DNA *via* partial intercalation by strong stacking between an aromatic chromophore and the base pairs of ssDNA.[5] *In vitro* cytotoxicity and antimicrobial activity of **1** are object of study at the present moment and, preliminary results will be reported soon.



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