Synthesis and Theoretical Study of Gadolinium(III) Complex of Heptadentate (N₄O₃) Tripodal Schiff Base Ligand

Vida Izadkhah*, Sadegh Salehzadeh†, Reza Golbedaghi†,
Mehdi Bayat† and Leila Davoodi†
*Department of Chemistry, Islamic Azad University Hamedan Branch, Hamedan, Iran
Fax: (98)(811)4290836; E-mail: izadkhah20002000@yahoo.com*

A new potentially heptadentate (N₄O₃) Schiff base ligand {N[(CH₂)₂N = CH(2-OH-5-BrC₆H₃)]₂[(CH₂)₃N = CH(2-OH-5-BrC₆H₃)]} (H₃L) was synthesized and characterized by elemental analysis and various spectroscopic methods. This ligand was derived from the condensation reaction of a tripodal tetraamine ligand, *bis*(2-aminoethyl)(3-aminopropyl) amine (pee) with 3 equiv. of 5-bromosalicylaldehyde. The neutral gadolinium(III) complex of this bulky ligand was also synthesized. The complex was characterized by microanalysis and IR spectra. The capability of H₃L as well as its unsubstituted analogs to encapsulate a lanthanide ion, herein La(III), has been theoretically studied by *ab initio* restricted Hartree-Fock (RHF) and density functional B3LYP methods.

Key Words: Gadolinium(III), Heptadentate ligand, Schiff base complexes.

INTRODUCTION

Schiff base condensation reactions are extensively used in the preparation of an enormous range of macrocyclic, macroacyclic and open chain pedant compounds in high yields[1-7]. In coordination chemistry, Schiff bases can be coordinate to a metal center from N atom of imine or a substituted group in the aromatic ring (*e.g.*, O, S,) and form a stable complex. It has been realized recently that lanthanide complexes with macrocyclic and macroacyclic ligands are fascinating areas of research because of their importance in basic and applied chemistry[8]. These ligands able to recognize lanthanide metal ions will make them valuable for the development of applications in medicine, catalysis and material science. For instance macrocyclic and macrocyclic Schiff bases are currently under intense scrutiny as the use of gadolinium complexes as magnetic resonance imaging (MRI) contrast agents require thermodynamically stable and/or kinetically inert complexes to avoid toxicity[9-12], as cleaving agents of RNA[13],

as components in molecular devices based on photochemical processes[14] or magnetic interactions[15]. Among the large number of ligand frameworks studies, potentially heptadentate tripodal Schiff base ligands, derived from the condensation of *tris*(2-aminoethyl)amine (tren) and various ring substituted salicylaldehydes or hydroxyacetophenones, diketones, pyridine or pyrrole carboxaldehydes, have been synthesized and their coordination chemistry with trivalent transition and lanthanide metals has provoked a lot of attention[16-26]. In complexes which have driven from the condensation of tren and salicylaldehyde or substituted salicylaldehyde with formula of [LnL] (Ln = La-Lu), each tripodal heptadentate Schiff base ligand (L) effectively encapsulate the lanthanide ion and enforces a seven-coordinate geometry[27-36]. In contrast to tren Schiff bases, there has been less attention to potentially heptadentate Schiff base ligands from condensation reactions of other tripodal tetraamines such as *tris*(3-aminopropyl)amine (tpt or trpn) and corresponding asymmetrical tetraamines with appropriate aldehydes or ketones. In past, the synthesis and characterization of some complexes of fully condensed potentially heptadentate (N_7) and heptadentate (N_4O_3) tripodal Schiff base ligands have been reported[37,38]. We have also reported synthesis and characterization of two asymmetrical potentially heptadentate (N_4O_3) tripodal Schiff base ligands[39]. In this paper, the synthesis and characterization of a new asymmetrical tripodal Schiff base ligand and its gadolinium(III) complexes have been reported. We also studied the capability of this ligand for encapsulation of a lanthanide ion, herein, La(III) by *ab initio* restricted Hartree-Fock (RHF) and density functional B3LYP methods.

EXPERIMENTAL

The solvents and 5-bromosalicylaldehyde were obtained from Aldrich and were used without further purification. The tripodal tetraamine ligand, *bis*(2-aminoethyl)(3-aminopropyl)amine (pee) was prepared according to the literature methods[40,41]. IR, ^{1}H and ^{13}C{^{1}H} NMR spectra were measured on FT-IR Bomem MB 100 and NMR 90 spectrometers, respectively.

Computational method: The geometry of [La(L)] complex at gas phase were fully optimized at both the restricted Hartree-Fock and DFT (B3LYP)[42] levels of theory using Gaussian 98 set of programs[43]. The standard lanL2MB basis set was used for both calculations[44]. This basis set includes effective core potential (ECP) for lanthanide ion. Vibrational frequency analyses, calculated at the same level of theory, indicate that optimized structures are at the stationary points corresponding to local minima without any imaginary frequency. Calculations were performed on a Pentium-PC computer with 3000 MHz processor. A starting molecular mechanics structure for the *ab initio* calculations was obtained using the HyperChem 5.02 program[45].

Synthesis of ligands

Preparation of $\{N[(CH_2)_2N = CH(2\text{-}OH\text{-}5\text{-}BrC_6H_3)]_2[(CH_2)_3N = CH(2\text{-}OH\text{-}5\ BrC_6H_3)]\}$ (H_3L) (Fig. 1): To a solution of 5-bromosalicy-laldehyde (0.60 g, 3 mmol) in absolute ethanol (20 mL) was added pee (0.15 g, 1 mmol). The resulting yellow solution was stirred for 45 min at room temperature. The bright yellow microcrystals were filtered off, washed with diethyl ether and dried in air. Yield: 0.645 g (91 %). mp 116-119ºC. % Anal Calcd. (Found) for $C_{28}H_{29}N_4O_3Br_3$: C, 47.43 (46.73); H, 4.10 (4.19); N, 7.90 (7.75). IR (KBr, cm^{-1}): 3200-2400 (broad weak band, ν(O-H)), 1634, 1607, 1571 and 1478 ν(C=N) and ν(C=C)). ^1H NMR δ_H (CDCl$_3$) 1.7 (m, 2H, 2-H), 2.5 and 2.7 (m, 6H, 1-H and 4-H), 3.5 (m, 6H, 3-H and 5-H)), 6.6, 6.7 and 7.2 (m, 9H, H-Ar), 8.0 (s, 1H, 6-H), 8.1 (s, 2H, 7-H), 13.3 (b, 3H, OH). ^{13}C NMR δ_C (CDCl$_3$) 28.7 (C-2), 52.0 (C-1), 55.1 (C-4), 56.7 (C-3), 57.7 (C-5), 110.0, 119.1, 120.1, 133.4, 135.0 (C-8 to C-12), 160.4 (C-13), 164.0 (C-6), 164.6 (C-7).
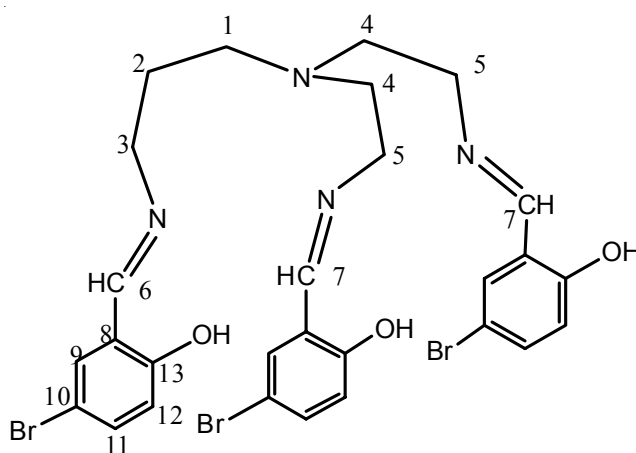

Fig. 1. Proposed Chemical structure of ligand H_3L along with NMR numbering

Preparation of [Gd(L)] complex: To a solution of pee (0.04 g, 0.25 mmol) in absolute ethanol (10 mL) was added 5-bromosalicylaldehyde (0.15 g, 0.75 mmol) in 10 mL absolute ethanol under nitrogen and $Gd(NO_3)_3 \cdot 6H_2O$ (0.25 mmol, 0.11 g) in ethanol (10 mL) and NaOH (0.12 g, 3 mmol) was added and allowed to reflux under nitrogen at low temperate for 12 h. The yellow precipitate was washed with ethanol and diethyl ether and dried in vacuum. Yield: 0.088 (41%). m.p. >200ºC. % Anal Calcd. (Found) for $C_{28}H_{26}N_4O_3Br_3Gd$: C, 38.80 (38.17); H, 3.35 (3.12); N, 6.46 (5.91). IR (cm^{-1}, Nujol): 1632, 1587 (sh), 1527, 1462 [ν(C=N) and ν(C=C)].

RESULTS AND DISCUSSION

The new potentially heptadentate (N_4O_3) tripodal Schiff base ligand, H_3L, was synthesized from the condensation reaction of tripodal tetramine ligand pee with 3 equiv. of 5-bromosalicylaldehyde in ethanol solution. The ligand is readily soluble in chloroform and is insoluble in water. The analytical and spectral data are completely consistent with the proposed formulation. Complete condensation of all primary amino groups of the pee is confirmed by the lack of $\nu(N-H)$ stretching bands in the IR 3450-3150 cm^{-1} region and presence of strong $\nu(C=N)$ bands at about 1634 and 1607 cm^{-1}. The existence of strong intramolecular hydrogen bonding inter-action between the imine nitrogen and the phenolic proton is confirmed with the observation of a weak broad band in IR 2200-3100 cm^{-1} region. The ^{1}H NMR and ^{13}C NMR spectra of these products also clearly confirm their formation and purification. The ^{1}H NMR spectrum of this ligand not only shows the absence of N-H hydrogen resonances but also the presence of two CH=N hydrogen resonances at about 8.0 and 8.1 ppm. The existence of latter two hydrogen resonances in ^{1}H NMR and two carbon resonances at about 164.0 and 164.6 ppm in the ^{13}C NMR for CH=N moiety of this ligand is due to its asymmetrical nature.

Although the ligand H_3L was successfully prepared and characterized but we found that the better method, with more yield, for preparation of its gadolinium complex is template condensation of amine and aldehyde in the presence of gadolinium salt. The IR spectrum of resulting complex contains a strong band at about 1632 cm^{-1} characteristic of imine C=N bands, confirming the formation of gadolinium complex and absence of ligand hydrolysis. Upon coordination to the metal center, the C=N and C=C stretchs in the IR spectra changed from 1634, 1607, 1571 and 1478 cm^{-1} in the free ligand, H_3L, to 1632, 1587 (sh), 1527, 1462 cm^{-1} in the related gadolinium(III) complex, GdL. Deprotonation of all phenolic func-tions is confirmed by the lack of O-H stretching bands in the IR region 3500-2500 cm^{-1} for this complex.

***Ab initio* and DFT studies:** We wish to study the relative capability of potentially heptadentate (N_4O_3) ligand, described here to encapsulate lanthanide ions. Unfortunately due to SCF convergence problems, we were not able to optimized the gadolinium(III). This was due to inherent com-plications first, resulting from partially filled *f*-orbitals and second, to the size of this bulky molecule. Thus we decided to choose La(III) complex of H_3L for *ab initio* studies. La(III) is an ion with a closed shell configuration and its stereochemistry is similar to Gd(III) metal ion. On the other hand it is well known that calculations on closed shell configurations are less

expensive than that of open shell configurations. Therefore, considering La(III) as the central lanthanide ion, the comparison of the capability of this ligand to encapsulate the lanthanide ion will make less expensive calculations. Selected bond lengths and bond angels of this complex, calculated with the LanL2MB basis set, at HF and B3LYP levels of theory are compared in Table-1 The calculations show that the imine and tertiary nitrogen donor atom as well as the three phenolat oxygen donor atoms arranged at apices of a distorted capped octahedral (Fig. 2). The considerable difference between the parameters obtained from RHF/LanL2MB calculations relative to those from B3LYP/LanL2MB is in La-N and La-O bond lengths, where La-N bond lengths are slightly longer and La-O bond lengths are slightly shorter in the former calculation. Similar structures have been determined for lanthanide complexes of heptadentate N_4O_3 tripodal Schiff base ligands[37]. As can be seen the La-tertiary nitrogen distance, La-N(20), is slightly longer than other bonds, but still it can be considered as a real bonding interaction. It is clear that upon coordination of tertiary nitrogen atom to the metal ion the triangle face defined by the other coordinated nitrogen atoms is expanded. The expansion of this triangle can be readily understand by the comparison of the sum of the calculated lengths of the sides of the triangle defined by the imine nitrogen atoms, T_N and that of oxygen atoms, T_O. The comparison of O-La-O bond angles with N_{imine}-La-N_{imine} bond angles also indicates the expansion of latter triangle due to coordination of tertiary nitrgen atom.
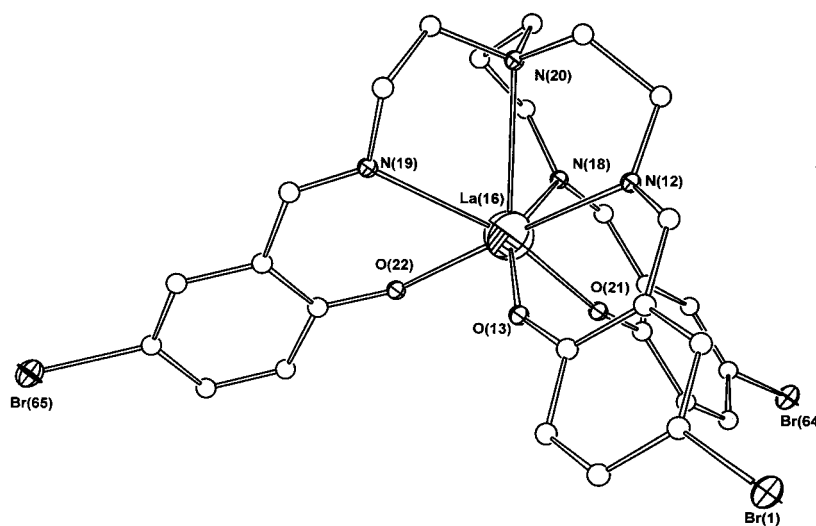

Fig. 2. Calculated molecular structure of [La(L)] complex at HF level of theory

TABLE-1
SELECTED CALCULATED BOND LENGTH (Å) AND
BOND ANGELS (°) FOR [La(L)] COMPLEX

	HF/LanL2MB	B3LYP/LanL2MB
Bond lengths		
La(16)-N(12)	2.684	2.664
La(16)-N(18)	2.808	2.783
La(16)-N(19)	2.710	2.691
La(16)-N(20)	2.888	2.856
La(16)-O(13)	2.197	2.234
La(16)-O(21)	2.201	2.236
La(16)-O(22)	2.204	2.241
T_N	13.213	13.167
T_O	9.711	9.753
Bond angles		
N(12)-La(16)-N(18)	103.5	103.0
N(12)-La(16)-N(19)	101.0	102.2
N(18)-La(16)-N(19)	118.2	119.8
N(12)-La(16)-N(20)	64.0	65.0
N(18)-La(16)-N(20)	78.0	78.4
N(19)-La(16)-N(20)	63.9	64.9
N(12)-La(16)-O(13)	67.2	68.1
N(12)-La(16)-O(21)	89.7	88.7
N(12)-La(16)-O(22)	159.6	160.4
O(13)-La(16)-N(18)	154.2	153.9
O(13)-La(16)-N(19)	87.6	86.3
O(13)-La(16)-N(20)	115.4	116.2
O(13)-La(16)-O(21)	89.2	87.6
O(13)-La(16)-O(22)	94.9	93.8
O(21)-La(16)-O(22)	100.3	98.5
N(18)-La(16)-O(21)	66.2	67.2
N(18)-La(16)-O(22)	96.8	96.6
N(19)-La(16)-O(21)	166.5	164.5
N(19)-La(16)-O(22)	67.0	67.7
N(20)-La(16)-O(21)	128.9	130.4
N(20)-La(16)-O(22)	119.6	120.6

T_N and T_O are the sum of the calculated lengths of the sides of the triangle defined by imine nitrogen atoms and oxygen atoms, respectively.

Conclusions

A new potentially heptadentate (N_4O_3) tripodal Schiff base ligand was synthesized, purified and characterized. The neutral gadolinium(III) complex of latter ligand was also synthesized. The theoretical studies show that the ligands is capable to completely encapsulate the lanthanide ions producing the neutral seven coordinated complexes.

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