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Synthesis and Characterization of Two New Asymmetrical Potentially Heptadentate (N_4O_3) Tripodal Schiff Base Ligands and a Theoretical Study

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Two new asymmetrical potentially heptadentate N_4O_3 Schiff-base ligands {[$NCH_2CH_2CH_2N{=}CH(2\text{-}OH\text{-}3,5\text{-}t\text{-}Bu_2C_6H_2)$][$CH_2CH_2CH_2N{=}CH(2\text{-}OH\text{-}C_6H_4)$]$_2$} ($H_3L^1$) and {$N[CH_2CH_2CH_2N{=}CH(2\text{-}OH\text{-}C_6H_4)][CH_2CH_2CH_2N{=}CH(2\text{-}OH\text{-}3,5\text{-}t\text{-}Bu_2\text{-}C_6H_2)]_2$} ($H_3L^2$) were synthesized and characterized by microanalysis and various spectroscopic methods (IR, ^1H NMR and ^{13}C NMR). The heptadentate N_4O_3 Schiff-base ligand H_3L^1 was derived from the condensation reaction of tripodal tetraamine ligand tris(3-aminopropyl)amine with 2 equiv. of salicylaldehyde and 1 equiv. of 3,5-di-*t*-butyl salicylaldehyde and the ligand H_3L^2 was derived from the condensation reaction of tris(3-aminopropyl)amine with 1 equiv. of salicylaldehyde and 2 equiv. of 3,5-di-*t*-butyl salicylaldehyde. The relative capability of these ligands to encapsulation of a lanthanide ion, herein La(III), has been theoretically studied by *ab initio* restricted Hartree-Fock (RHF) and DFT (B3LYP) methods. The calculation confirmed that these ligands can effectively encapsulate a lanthanide ion and enforce a seven-coordinate geometry.

Key Words: ***Ab initio*, Heptadentate, Tripodal ligands, Schiff base, Asymmetrical.**

INTRODUCTION

Macrocyclic and macro-acyclic Schiff-base ligands are currently under investigation as contrast media in magnetic resonance imaging[1-5] and as encapsulating ligands for radiopharmaceuticals[6, 7]. These ligands have gained favour due to both their relatively straight forward synthesis and their multidentate nature which results in very high binding constants for many *d*- and *f*-block metals. Among the large number of ligand frameworks studied, Schiff-base derivatives of the tren moiety [$N(CH_2CH_2NH_2)_3$] have proved to be very effective, especially those derived from the reaction of salicylaldehyde derivatives with tren. Thus, a range of symmetrical potentially heptadentate (N_4O_3) Schiff base ligands of the type $N[CH_2CH_2N{=}CH(2\text{-}OH\text{-}3\text{-}R^1\text{-}5\text{-}R^2C_6H_2)]_3$ (H_3L), derived from condensation reactions of tren with salicylaldehyde or various ring substituted salicylaldehydes, have been prepared and their coordination chemistry with a number of lanthanide ions has been extensively investigated[8-14]. In these complexes [ML] (M = La-Lu), each tripodal heptadentate Schiff base ligand (L) effectively encapsulates the lanthanide ion and enforces a seven-coordinate geometry (Fig. 1). The existence of complexes of lanthanides with larger coordination numbers is a natural consequence of their large size and of the predominantly ionic character of their bonding.

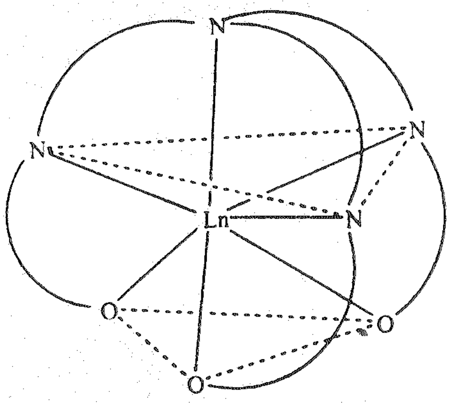

Fig. 1. The simplified structure around the lanthanide ion in neutral complexes of heptadentate (N_4O_3) tripodal Schiff base ligands derived from tren

In contrast to tren Schiff bases, there has been less attention to potentially heptadentate Schiff base ligands derived from condensation reactions of other tripodal tetraamines such as tris(3-aminopropyl)amine (tpt or trpn) with appropriate aldehydes or ketones. The synthesis and characterization of some complexes of fully condensed potentially heptadentate (N_7) and heptadentate (N_4O_3) tripodal Schiff base ligands, derived from template and/or direct condensation reactions of tpt with acetylpyridine and salicylaldehyde, respectively[15-17] is reported. The improved synthesis of asymmetrical tripodal tetraamines[15-17] is also devised. However, herein, the synthesis and characterization of two new potentially heptadentate (N_4O_3) tripodal Schiff base ligands, H_3L^1 and H_3L^2 is reported (Fig. 2). An *ab initio* RHF and DFT (B3LYP) calculation on La(III) complexes of these ligands is also reported.

EXPERIMENTAL

The solvents, hydrated metal salts and salicylaldehyde (SA) were obtained from Aldrich and were used without further purification. Tris(3-aminopropyl)amine (tpt)[20] and 3,5-di-*t*-butyl salicylaldehyde (SATBU)[21] were prepared as previously described. IR, ^1H and $^{13}C\{^1H\}$ NMR spectra were measured on FT-IR Bomem MB 100, and Bruker 500 FT-NMR spectrometers, respectively.

Computational methods: The geometries of both Lanthanum complexes were fully optimized at both the restricted Hartree-Fock (RHF) and DFT (B3LYP) levels of theory using GAUSSIAN 98 program[22] on a Pentium-PC computer with 2400 MHz processor. The standard LanL2MB basis set was used for both complexes[23]. This basis set includes effective core potential (ECP) for lanthanum atom. 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. A starting molecular mechanics structure for the *ab initio* calculations was obtained using the HyperChem 5.02 program[24].

Preparation of {[NCH$_2$CH$_2$CH$_2$N=CH(2-OH-3,5-*t*-Bu$_2$C$_6$H$_2$)][CH$_2$CH$_2$CH$_2$N=CH(2-OH-C$_6$H$_4$)]$_2$} (H$_3$L^1): To a mixture of tpt. 4HCl·H$_2$O (0.5 g, 1.42 mmol) in methanol (25 mL) was added NaOCH$_3$ (0.153 g, 2.84 mmol). The resulting mixture was refluxed for about 15 min. Then SATBU (0.33 g, 1.42 mmol) was added to the resulting solution and reflux was continued for another 20 min followed by the addition of another portion of NaOCH$_3$ (0.153 g, 2.84 mmol). After 20 min of refluxing, NaOCH$_3$ (0.23 g, 4.26 mmol) and SA (0.346 g, 2.84 mmol) was added and the mixture was refluxed for about 35 min. Slow evaporation of the solvent afforded a yellow crude product. After addition of CHCl$_3$ (20 mL), the mixture was filtered to remove insoluble NaCl. An oily product was obtained after evaporation of solvent under vacuum. Yield: 0.52 g (60%). Anal. % Calcd. (found) for $C_{38}H_{52}O_3N_4 \cdot 0.5CHCl_3$: C, 68.5 (67.9), H, 7.9 (7.8), N, 8.3 (8.4). IR (KBr, cm^{-1}): 1633 s, ν(C=N), 1468–1441 s, ν(C=C).

Preparation of {N[CH$_2$CH$_2$CH$_2$N=CH(2-OH-C$_6$H$_4$)][CH$_2$CH$_2$CH$_2$N=CH(2-OH-3,5-*t*-Bu$_2$C$_6$H$_2$)]$_2$} (H$_3$L$_2$): A procedure similar to that described for H$_3$L^1 was followed using tpt. HCl·H$_2$O (0.376 g, 1.068 mmol), SA (0.1302 g, 1.068 mmol) and SATBU (0.5 g, 2.13 mmol). Yield: 0.48 g (62%). Anal. % Calcd. (found) for $C_{46}H_{68}O_3N_4 \cdot 0.5CHCl_3$: C, 71.2 (70.5), H, 8.8 (8.5), N, 7.1 (6.8). IR (KBr, cm^{-1}): 1633 s, ν(C=N), 1444 s, ν(C=C).

RESULTS AND DISCUSSION

Two new asymmetrical heptadentate (N$_4$O$_3$) tripodal Schiff base ligands H$_3$L^1 and H$_3$L^2 were synthesized through step by step condensation of the symmetrical tripodal tetraamine tpt and two different aldehydes (Fig. 2). As shown in equation (1) the salt of polyamines will be neutralized step by step through the slow addition of appropriate base[25–27]. Thus, each neutral primary amine, formed in each step, can be condensed with appropriate aldehyde.

$$H_nL^{n+} \rightleftharpoons H_{n-1}L^{(n-1)+} + H^+ \qquad (1)$$

New potentially heptadentate tripodal Schiff-base ligand H$_3$L^1 has been prepared from the condensation reaction of tripodal tetraamine ligand tpt with 2 equiv. of SA and 1 equiv. of SATBU and ligand H$_3$L^2 has been prepared from the condensation reaction of tripodal tetraamine ligand tpt with 1 equiv. of SA and 2 equiv. of SATBU. Both the ligands are soluble in chloroform and methanol and are insoluble in water. The analytical and spectral data are completely consistent with the proposed formulations. Complete condensation of all primary amino groups of the tpt is confirmed by the lack of ν(N—H) stretching bands in the IR 3450–3150 cm^{-1} region and the presence of strong ν(C=N) stretching bands at about 1633 cm^{-1} for both H$_3$L^1 and H$_3$L^2 ligands. This conclusion is also supported by the ^{1}H NMR data which shows not only the absence of N—H hydrogen resonances but also the presence of two CH=N hydrogen resonances at about 8.3 ppm. The existence of two hydrogen resonances and two carbon resonances for CH=N moiety of each ligand as well as existence of twelve carbon resonances for aromatic rings indicating that both the SATBU and SA are condensed with tpt. ^{1}H NMR and ^{13}C{^{1}H} NMR spectral assignments for H_3L^1 and H_3L^2 are given in Table-1. The NMR numbering of atoms are shown in Fig. 2. It should be noted that these ligands are rare examples of an asymmetrical tripodal heptadentate (N_4O_3) tripodal Schiff base ligand, which are derived from the symmetrical tripodal tetraamine.

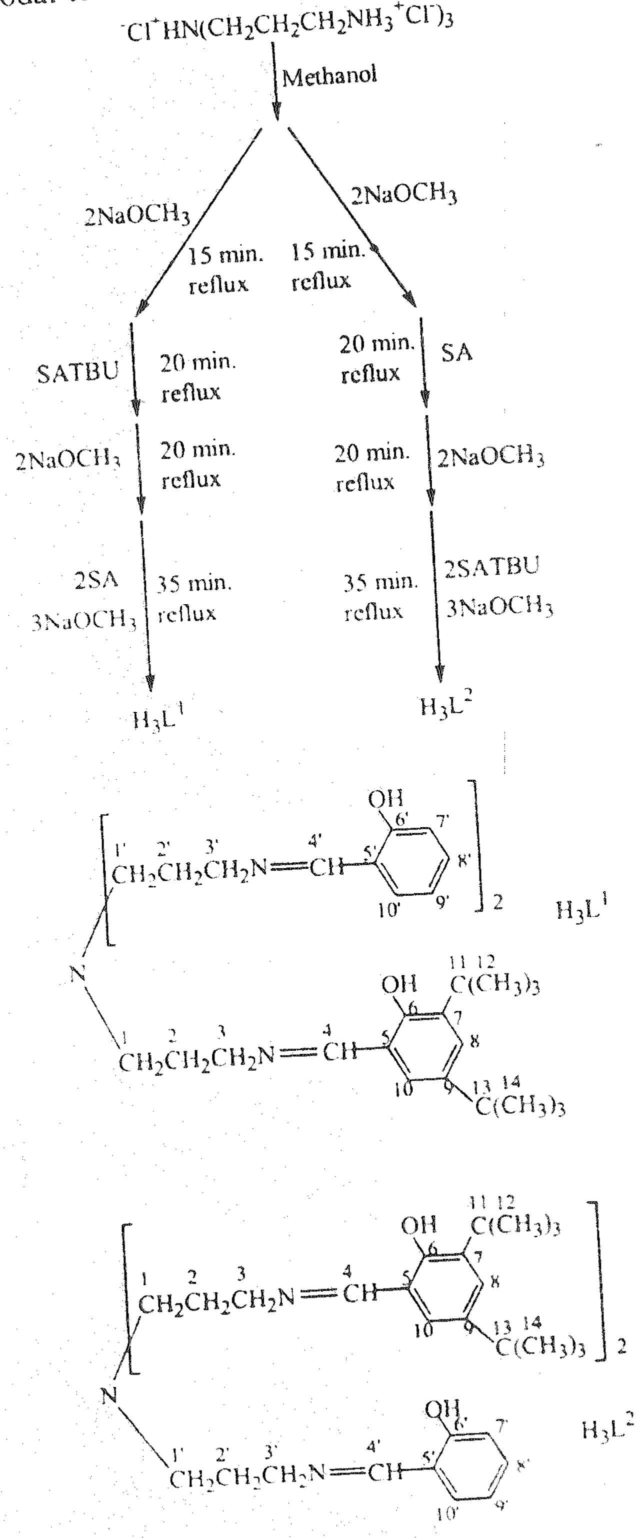

Fig. 2. The procedure of ligand synthesis along with NMR numbering for H_3L^1 and H_3L^2

TABLE-1
^{1}H NMR AND ^{13}C NMR SPECTRAL ASSIGNMENTS FOR H_3L^1 AND H_3L^2 RECORDED AT 90 MHz IN $CDCl_3$

Hydrogen atoms	δ_H (ppm)	Carbon atoms	δ_C (ppm)
H_3L^1			
H_1(2H), $H_{1'}$(4H)	2.611 (m)	C_1 $C_{1'}$	51.873 51.783
H_2(2H), $H_{2'}$(4H)	1.898 (bm)	C_2 $C_{2'}$	28.907 28.797
H_3(2H), $H_{3'}$(4H)	3.674 (m)	C_3 $C_{3'}$	57.848 57.760
H_4(1H)	8.408 (s)	C_4	166.483
$H_{4'}$(2H)	8.368 (s)	$C_{4'}$	165.489
		C_5, $C_{5'}$	118.315, 119.208
		C_6, $C_{6'}$	158.636, 161.744
		C_7, C_9	137.056, 140.358
H_8(1H), H_{10}(1H)	7.144 (s), 7.449 (s)	C_8, C_{10}	126.250, 127.199
$H_{7'}$(2H), $H_{8'}$(2H),	6.877 (d), 6.976 (m),	$C_{7'}$, $C_{8'}$, $C_{9'}$, $C_{10'}$	117.440, 118.948,
$H_{9'}$(2H), $H_{10'}$(2H)	7.245 (m), 7.330 (d)		131.668, 132.576
H_{12}(9H), H_{14}(9H)	1.374 (s), 1.518 (s)	C_{11}, C_{13}, C_{12}, C_{14}	34.595, 35.498 29.917, 32.018
OH(1H)	13.996 (bs)		
OH′(2H)	13.633 (bs)		
H_3L^2			
H_1(4H), $H_{1'}$(2H)	2.531 (bt)	C_1 $C_{1'}$	51.016 51.096
H_2(4H), $H_{2'}$(2H)	1.751 (m)	C_2 $C_{2'}$	27.896 27.976
H_3(4H), $H_{3'}$(2H)	3.550 (t)	C_3 $C_{3'}$	56.791 56.881
H_4(2H)	8.299 (s)	C_4	164.724
$H_{4'}$(1H)	8.270 (s)	$C_{4'}$	165.724
		C_5, $C_{5'}$	117.552, 118.413
		C_6, $C_{6'}$	161.005, 157.825
		C_7, C_9	136.214, 139.533
H_8(2H), H_{10}(2H)	7.133 (s), 7.432 (s)	C_8, C_{10}	125.431, 126.291
$H_{7'}$(1H), $H_{8'}$(1H),	6.866 (d), 6.965 (m),	$C_{7'}$, $C_{8'}$, $C_{9'}$ $C_{10'}$	116.592, 118.064,
$H_{9'}$(1H), $H_{10'}$(1H)	7.233 (m), 7.319 (d)		130.867, 131.729
H_{12}(18H), H_{14}(18H)	1.219 (s), 1.357 (s)	C_{11}, C_{13} C_{12}, C_{14}	33.730, 34.634 29.126, 31.182
OH(2H), OH′(1H)	13.723 (bs)		

Ab initio calculations

It is interesting to study the capability of potentially heptadentate (N_4O_3) ligands described here for encapsulation of lanthanide ions. To avoid SCF convergence problems La(III) was chosen for these calculations . La(III) is an ion with closed shell configuration and its stereochemistry is similar to other lanthanide ions. On the other hand, it is well known that calculations on closed shell configurations are less expensive than those on open shell configurations. Therefore, with considering La(III) as central lanthanide ion the capability of these ligands for encapsulation of the lanthanide with less expensive calculations can be studied.

Although the parameters obtained for the [La(L^1)] and [La(L^2)] complexes at different levels of theory described here are not identical, yet all calculations show that the three imine and the unique tertiary nitrogen donor atoms as well as the three phenolate oxygen donor are atoms arranged at apices of a distorted capped octahedral (Fig. 3 (a) and (b)). Selected bond lengths and bond angles of both

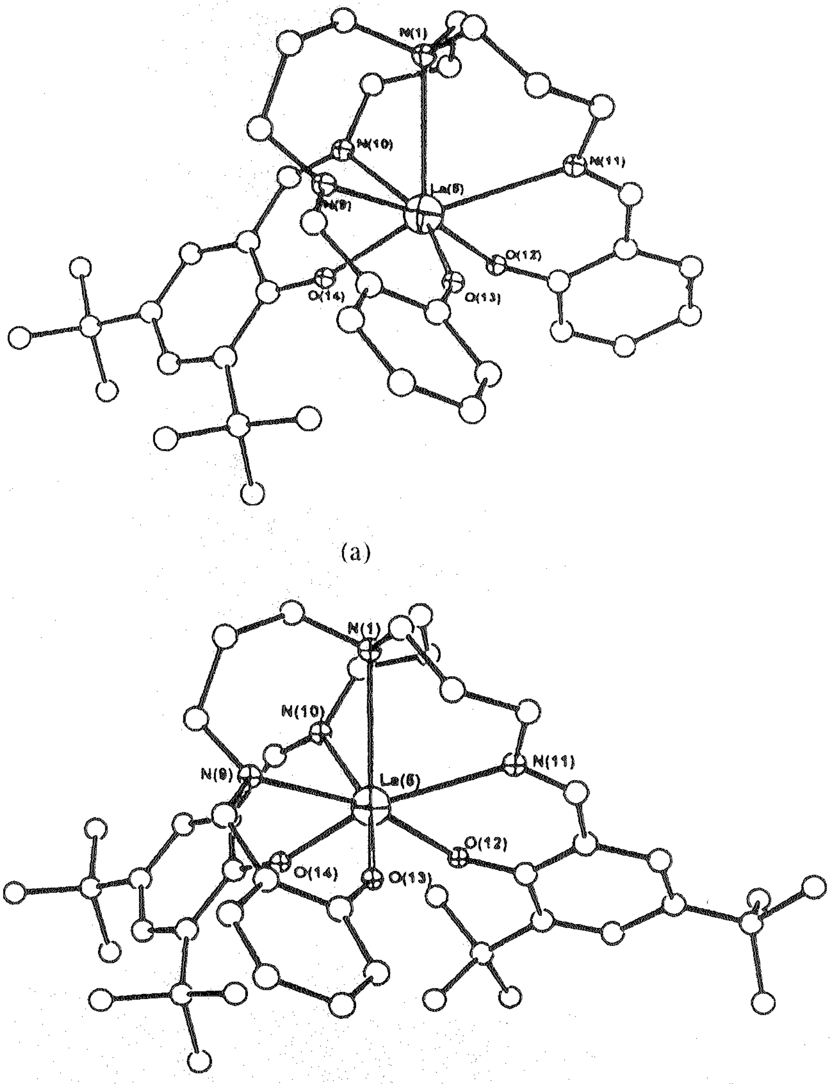

Fig. 3. Calculated molecular structure of (a) [La(L^1)] and (b) [La(L^2)] complexes, at the B3LYP/LanL2MB level of theory; hydrogen atoms are omitted for clarity

complexes are compared in Table-2. The considerable difference between the parameters obtained from RHF calculations relative to those from B3LYP is in La-N and La-O bond lengths, where La-N bond lengths are slightly longer and La-O bond lengths are always slightly shorter in former calculation. The means of bond lengths and bond angles about the metal centre for both derivatives are almost similar and thus the introduction of bulky *t*-butyl substituents seems to have essentially no significant effect upon the geometry of the LaN_4O_3 core. As can be expected, due to coordination of tertiary nitrogen atom to metal atom, the N(imine)-La-N(imine) bond angles are significantly greater than O-La-O bond angles. In both complexes, the La-tertiary nitrogen distance La-N(1), is usually slightly longer than other bonds. A similar observation was reported for all seven-coordinate complexes of corresponding tren Schiff bases[10–14].

TABLE-2
SELECTED THEORETICAL BOND LENGTHS (Å) AND BOND ANGLES (°) OF THE CALCULATED STRUCTURES

	$[La(L^1)]$		$[La(L^2)]$	
Bond lengths				
La-N (1)	2.87	**2.80**	2.87	**2.81**
La-N (9)	2.72	**2.69**	2.72	**2.68**
La-N (10)	2.74	**2.70**	2.74	**2.70**
La-N (11)	2.81	**2.77**	2.76	**2.73**
La-O (12)	2.19	**2.24**	2.21	**2.25**
La-O (13)	2.19	**2.24**	2.19	**2.24**
La-O (14)	2.20	**2.24**	2.21	**2.25**
Bond angles				
N(1)-La-N (9)	72.0	**72.5**	71.5	**72.1**
N(1)-La-N (10)	72.3	72.9	71.9	**72.7**
N(1)-La-N (11)	71.2	**71.8**	70.9	**71.8**
N(1)-La-O (12)	122.6	**123.2**	122.5	**123.1**
N(1)-La-O (13)	113.0	**113.6**	113.4	**113.9**
N(1)-La-O (14)	125.8	**126.5**	124.6	**125.5**
N(9)-La-N (10)	98.4	**99.0**	98.5	**99.0**
N(9)-La-N (11)	119/0	**119.7**	118.2	**118.9**
N(10)-La-N (11)	114.0	**114.7**	113.7	**114.5**
O(12)-La-O (13)	100.1	**99.1**	100.6	**100.0**
O(12)-La-O (14)	93.1	**91.9**	93.9	**93.0**
O(13)-La-O (14)	96.7	**95.2**	96.5	**65.1**

The parameters obtained at the RHF level are given as plain text; those for the B3LYP level are in bold.

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