

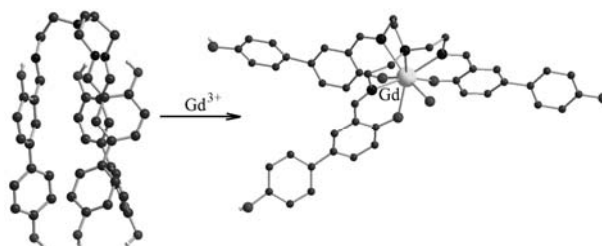
SYNTHESIS AND CRYSTAL STRUCTURES OF A TRIPODAL LIGAND DERIVED FROM 4,4'-DIHYDROXYBIPHENYL AND ITS GADOLINIUM(III) MONONUCLEAR COMPLEX

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A new tripodal Schiff-base ligand has been synthesized by reacting tris(2-aminoethyl)-amine with 3-formyl-4,4'-dihydroxybiphenyl and structurally characterized by X-ray diffraction on single crystal together with its neutral mononuclear Gd(III) complex. In this complex the Gd(III) ion is eight-coordinated by three imino nitrogen atoms, one amino nitrogen atom, three phenoxo oxygen atoms (all belonging to the tripodal ligand) and one water molecule.



INTRODUCTION

In supramolecular chemistry, the thermodynamic stability of a host-guest complex may be enhanced by chelate effect giving rise to positive cooperativity. The chelate effect is observed in the binding of metal cations by podands – chain-like hosts with a number of donor atoms situated at intervals along their length.¹ The metal ions play a structural role (organising the ligand – the podands are not pre-organised ligands), and a functional one (carrying magnetic, optical, redox or catalytic properties).

The tripodal ligands, as an extension of the podand concept to three dimensions, represent a category of molecules able to encapsulate more fully their guest. The tripodal ligands can act as receptors for different chemical species: transition metal ions,² lanthanide ions,³ actinide ions,⁴ anions,⁵ or cations and anions in the same time.⁶ The thermodynamic stability of the host-guest complexes makes from the tripodal ligands good candidates for biomedical

applications as sequestering agents for iron, aluminium or actinide ions.^{4a,7}

Of particular interest for the biomedical applications are the lanthanide complexes. Current applications range from the use of gadolinium complexes as contrast agents in magnetic resonance imaging (MRI)⁸ to the use of luminescent lanthanides emitting in the VIS (Eu^{III} or Tb^{III}) as sensors⁹ or bio-probes in fluoro-immunoassays.¹⁰ An exciting frontier for MRI is the development of responsive contrast agents sensitive to local changes of different chemical species (pH, pO₂, the concentration of Ca^{II}, Mg^{II}, Zn^{II} or K^I ions), or to reactions (a specific enzymatic activity) of interest in living biological systems.^{8a,e} For this purpose the chelating ligands must have a high affinity for lanthanide ions, in order to avoid their toxicity, and to possess functional groups which can determine changes in relaxivity (the efficiency with which a contrast agent enhances the relaxation rate) as a response to the metabolic parameter one wishes to monitor by MRI.

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In this paper we report on synthesis and structural characterization of a new tripodal Schiff-base ligand derived from 4,4'-dihydroxybiphenyl together with structural characterization of a neutral mononuclear Gd(III) complex obtained using this tripodal ligand. The tripodal ligand possesses additional functional groups (three phenoxo groups) besides the coordination site and we intended to study the conformational changes of the ligand induced by the coordination of a lanthanide ion.

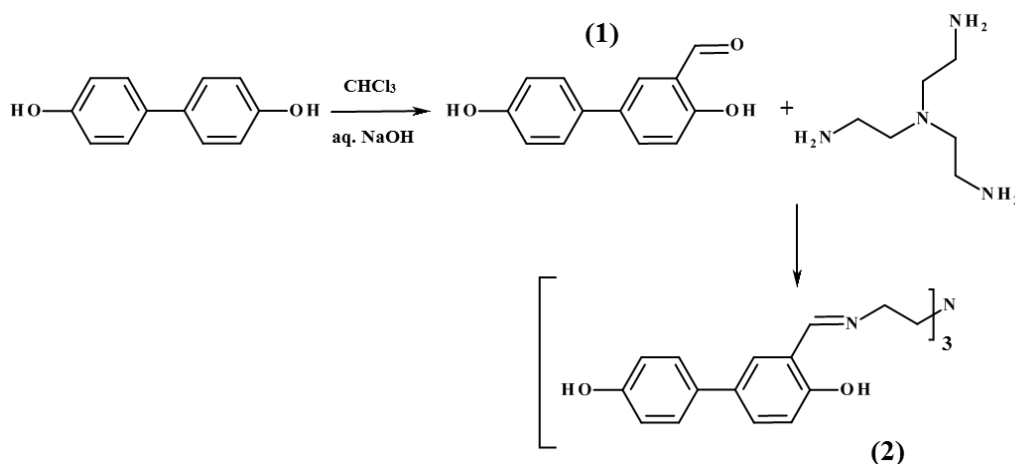
RESULTS AND DISCUSSION

The tripodal Schiff-base ligand (**2**) results by condensation reaction between tris(2-aminoethyl)-amine and 3-formyl-4,4'-dihydroxybiphenyl (**1**). The 3-formyl-4,4'-dihydroxybiphenyl was synthesised

following reported experimental procedures by a Reimer-Tiemann reaction (Scheme 1).¹¹

The organic compounds **1** and **2** were structurally characterized by X-ray diffraction on single crystal. The 3-formyl-4,4'-dihydroxybiphenyl crystallizes in the triclinic *P*-1 space group with two independent molecules in the asymmetric unit (Fig. 1). The oxygen atoms of the formyl groups are involved in intramolecular hydrogen interactions with the neighbouring hydroxo groups ($H2 \cdots O4 = 1.96 \text{ \AA}$, $H6 \cdots O5 = 1.99 \text{ \AA}$, $O2-H2 \cdots O4 = 144.7^\circ$, $O6-H6 \cdots O5 = 143.3^\circ$).

The formyl groups act also as hydrogen bond acceptor for the hydroxo groups belonging to other 3-formyl-4,4'-dihydroxybiphenyl molecules ($H1 \cdots O4' = 2.03 \text{ \AA}$, $H3 \cdots O5'' = 1.94 \text{ \AA}$, $' = -1+x, y, 1+z$; $'' = x, y, -1+z$) generating supramolecular chains with two different orientations in crystal (Fig. 2).



Scheme 1

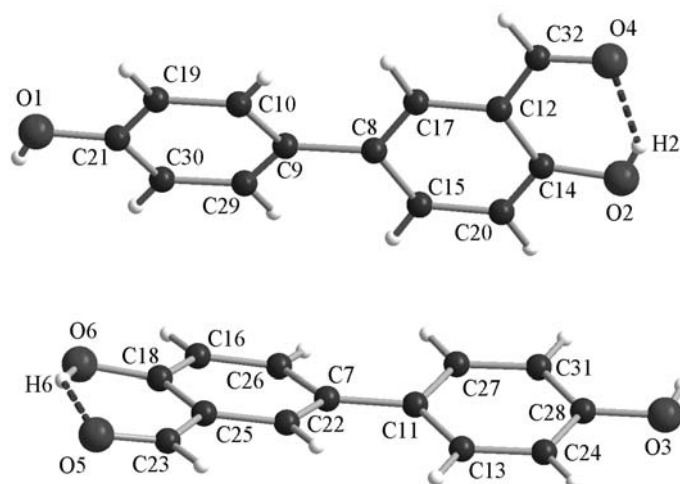


Fig. 1 – Perspective view of the asymmetric unit along with the atoms labelling scheme in crystal **1**.

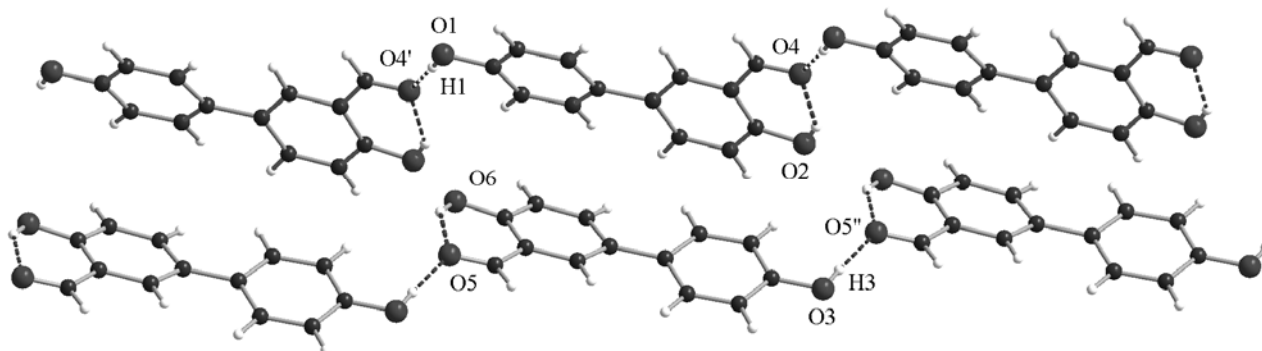


Fig. 2 – View of the supramolecular chains generated by hydrogen bonding in crystal **1** (symmetry code: ' = -1+x, y, 1+z; '' = x, y, -1+z).

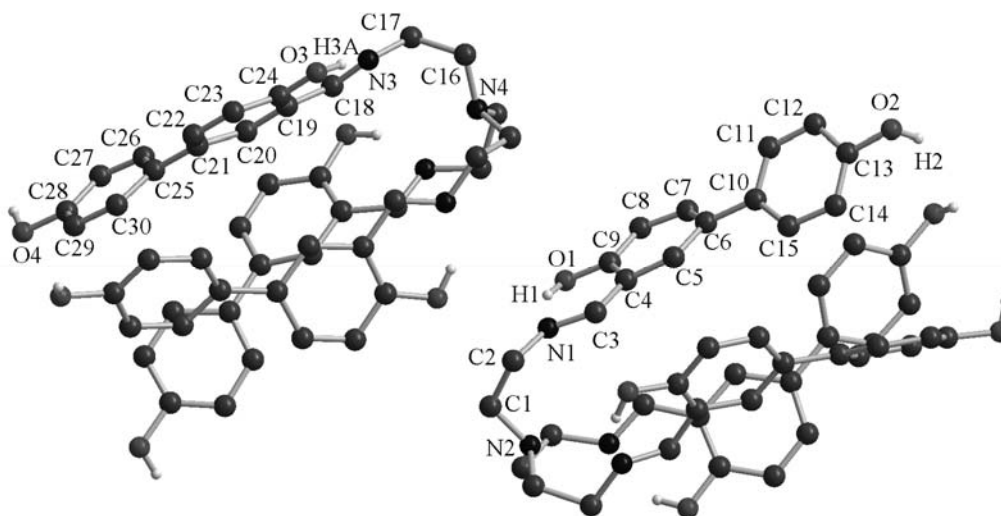


Fig. 3 – Perspective view of the tripodal ligands along with the atoms labelling scheme in crystal **2·0.75CH₃OH** (part of the hydrogen atoms were omitted for clarity).

The tripodal ligand **2** obtained by condensation reaction between tris(2-aminoethyl)-amine and the monoaldehyde **1** crystallizes in the trigonal $R\bar{3}2$ space group with two crystallographic independent molecules. Both crystallographic types of the tripodal molecules possess C_3 symmetry and adopt a jellyfish-like conformation (Fig. 3). The crystals contain also 0.75 disordered methanol molecules per tripodal ligand. The imino nitrogen atoms are involved in intramolecular hydrogen interactions with the neighbouring hydroxo groups (H1...N1 = 1.88 Å, H3A...N3 = 1.82 Å, O1-H1...N1 = 145.7°, O3-H3A...N3 = 149.2°).

The analysis of the packing diagrams in crystal **2·0.75CH₃OH** shows that each of crystallographic types of the tripodal molecules are displaced in honeycomb-like arrangements alternating along the crystallographic c axis. This supramolecular architecture is sustained by the π - π stacking interactions established between the aromatic fragments with the shortest contacts of 3.42 Å in

the **A** layers and 3.33 Å in the **B** layers (Fig. 4). The disordered methanol molecules were found only in the voids of the **A** type of the supramolecular layers containing the tripodal ligand with N1, N2, O1 and O2 atoms (Fig. 4 bottom left).

By reacting the tripodal ligand **2** with GdCl₃·6H₂O in a mixture of CH₃OH and CHCl₃ (1:1) in the presence of triethylamine as base was obtained a neutral mononuclear complex [Gd(L)(H₂O)]·2H₂O (**3**), where L is the trideprotonated form of the ligand **2**. In this complex the Gd(III) ion is eight-coordinated by three imino nitrogen atoms [Gd1-N1 = 2.414(17), Gd1-N2 = 2.545(14), Gd1-N3 = 2.587(12) Å], one amino nitrogen atom [Gd1-N4 = 2.735(15) Å], three phenoxo oxygen atoms [Gd1-O1 = 2.295(9), Gd1-O2 = 2.199(12), Gd1-O3 = 2.320(11) Å] and one water molecule [Gd1-O7W = 2.491(9) Å – Fig. 5].

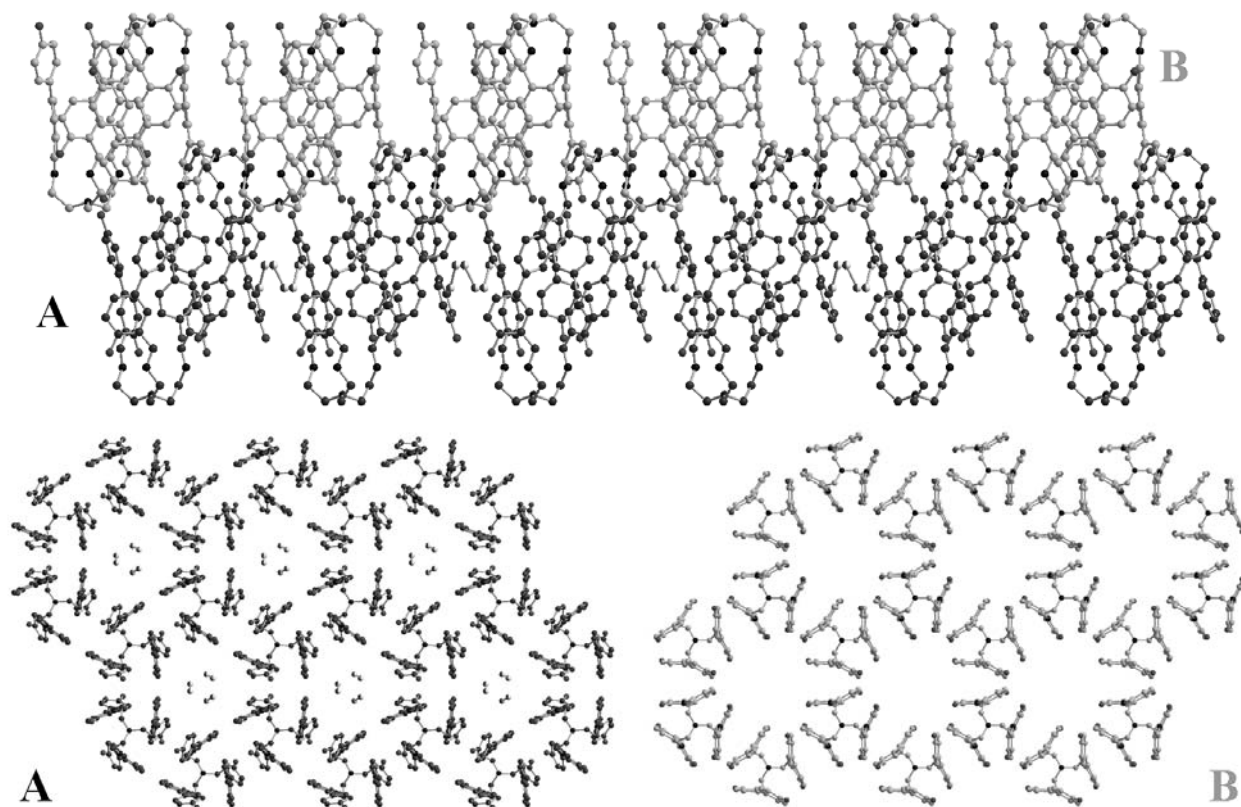


Fig. 4 – Views of the packing diagrams in crystal **2**·0.75CH₃OH along the crystallographic *b* axis (top) and along the crystallographic *c* axis with details of the two types of the honeycomb-like supramolecular layers (bottom); the hydrogen atoms were omitted for clarity.

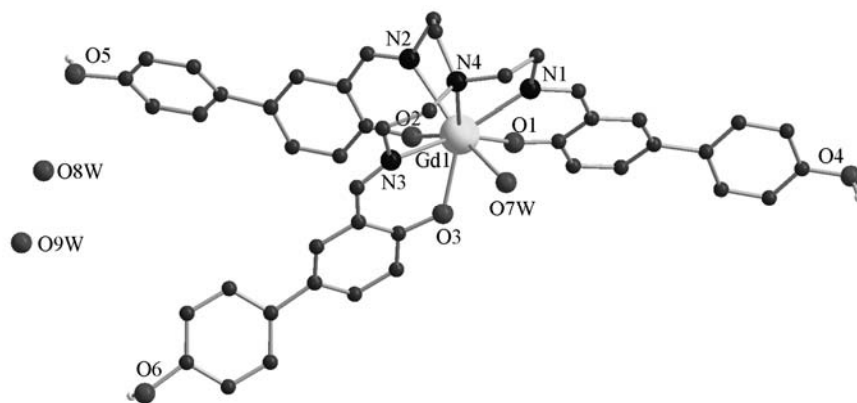


Fig. 5 – Perspective view of the asymmetric unit along with the atoms labelling scheme in crystal **3** (part of the hydrogen atoms were omitted for clarity).

The coordination to the Gd(III) ion induces a significant change of the tripodal ligand from the jellyfish-like conformation to a more flat structure. The process can be compared with the movement folding-opening of an umbrella. Through coordination of the water molecule to the metal ion, the complex loses the C_3 symmetry of the tripodal ligand.

The water molecule coordinated to the lanthanide ion is very important for the use of gadolinium complexes as contrast agents in

magnetic resonance imaging but is limiting the luminescent applications of complexes with lanthanides emitting in the VIS (Eu^{III} or Tb^{III}) by quenching of the luminescence.

EXPERIMENTAL

Materials and methods

All the chemicals used as well as all the solvents were purchased from commercial sources. All manipulations were performed under aerobic conditions.

The 3-formyl-4,4'-dihydroxybiphenyl (**1**) was synthesised following reported experimental procedures by a Reimer-Tiemann reaction.¹¹ Suitable crystals for X-ray diffraction were obtained by slow evaporation of a CH₃OH/CHCl₃ (1:1) solution.

In order to obtain the tripodal ligand **2**, 0.3 mmol of tris(2-aminoethyl)-amine and 0.9 mmol of 3-formyl-4,4'-dihydroxybiphenyl were stirred at room temperature for three hours in 120 mL mixture of CH₃OH and CHCl₃ (1:3). The yellow crystals of **2·0.75CH₃OH** resulted by slow evaporation of the resulted solution after 2-3 days. The crystals were filtered and washed with methanol and diethyl ether. Yield: 85%. IR data (KBr, cm⁻¹): 3260m, 3031w, 2931w, 2821m, 1637vs, 1587m, 1519m, 1488vs, 1450s, 1362m, 1328w, 1264s, 1244s, 1171s, 1068m, 1021m, 926w, 885w, 839w, 820m, 780w, 760w, 652w, 588w, 536w, 515w, 459w. ¹H NMR (DMSO-*d*₆), δ (ppm): 8.44 (s, 3H), 7.42-7.39 (overlapped peaks, 6H), 7.28 (d, *J* = 9, 6H), 6.85 (d, *J* = 6, 3H), 6.78 (d, *J* = 6, 6H), 3.65 (t, *J* = 6, 6H), 2.89 (t, *J* = 6, 6H).

The complex [Gd(L)(H₂O)]·2H₂O (**3**) was obtained as yellow crystals by slow evaporation at room temperature of the solution resulted by stirring 0.1 mmol of **2·0.75CH₃OH** with 0.1 mmol of GdCl₃·6H₂O in 150 mL mixture of CH₃OH and CHCl₃ (1:1) in the presence of triethylamine (0.5 mmol)

as base. Yield: 70 %. IR data (KBr, cm⁻¹): 3350 broad, 1626vs, 1515m, 1471s, 1385m, 1313m, 1264s, 1174m, 1078w, 1031w, 910w, 827m, 715w, 659w, 551w.

The IR spectra (KBr pellets) were collected on a Bruker Tensor 37 spectrophotometer in the 4000–400 cm⁻¹ range.

The ¹H NMR spectra were recorded on a Bruker Fourier 300 spectrometer at 300 MHz.

X-ray crystallography and solution of structures

Single crystals suitable for X-ray diffraction studies were obtained by slow evaporation of the solvent, as described above. Data were collected at 173 K on a Nonius Kappa CCD diffractometer for compound **1** and at 293 K on a STOE IPDS II diffractometer for compounds **2** and **3**, both using graphite-monochromated Mo K α radiation (λ = 0.71073Å). The structures were solved by direct methods and refined by full-matrix least squares techniques based on *F*². The non-H atoms were refined with anisotropic displacement parameters. A summary of the crystallographic data and the structure refinement is given in Table 1. CCDC reference numbers: 961286-961288.

Table 1

Crystallographic data, details of data collection, and structure refinement parameters for **1** and **2**

Compound	1	2·0.75CH₃OH	3
Chemical formula	C ₁₃ H ₁₀ O ₃	C _{45.75} H ₄₅ N ₄ O _{6.75}	C ₄₅ H ₄₅ GdN ₄ O ₉
<i>M</i> (g mol ⁻¹)	214.21	758.83	943.05
Temperature, (K)	173(2)	293(2)	293(2)
Wavelength, (Å)	0.71073	0.71073	0.71073
Crystal system	<i>Triclinic</i>	<i>Trigonal</i>	<i>Monoclinic</i>
Space group	<i>P</i> -1	<i>R</i> 32	<i>P</i> 21/ <i>n</i>
<i>a</i> (Å)	10.4890(5)	14.4601(9)	16.161(4)
<i>b</i> (Å)	10.6010(9)	14.4601(9)	13.7808(16)
<i>c</i> (Å)	11.8800(9)	64.485(8)	20.912(4)
α (°)	66.284(4)	90	90
β (°)	64.410(5)	90	103.825(16)
γ (°)	61.970(3)	120	90
<i>V</i> (Å ³)	1018.19(13)	11677.0(17)	4522.4(15)
<i>Z</i>	4	12	4
<i>D</i> _c (g cm ⁻³)	1.397	1.290	1.376
μ (mm ⁻¹)	0.099	0.087	1.522
<i>F</i> (000)	448	4782	1892
Goodness-of-fit on <i>F</i> ²	0.898	0.780	0.810
Final <i>R</i> 1, <i>wR</i> ₂ [<i>I</i> > 2 σ (<i>I</i>)]	0.0602, 0.1200	0.0631, 0.0423	0.0670, 0.0864
<i>R</i> 1, <i>wR</i> ₂ (all data)	0.2176, 0.1750	0.2350, 0.0685	0.2833, 0.1352
Largest diff. peak and hole (eÅ ⁻³)	0.203, -0.211	0.155, -0.215	0.770, -0.425

CONCLUSIONS

The structural characterization of the tripodal Schiff-base ligand derived from 4,4'-dihydroxybiphenyl and its neutral mononuclear Gd(III) complex allows us to study the conformational changes of the ligand induced by the coordination of the lanthanide ion. The complexes of the trivalent lanthanide ions with anionic tripodal ligands can exhibit interesting magnetic (e.g. Single-Molecule Magnet behaviour) or photophysical properties and the presence of the additional functional groups besides the coordination site makes them attractive for various application.

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