

Proceedings

# Synthesis of a new azamacrocyclic receptor with pendant-arms methylpyridine. †

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**Abstract:** In this work we report the synthesis of an azamacrocyclic ligand with methylpyridine and methyl groups in *trans* positions and their characterization by crystallographic, NMR and ESI-MS techniques and the subsequent synthesis of their complexes with the lanthanide ions.

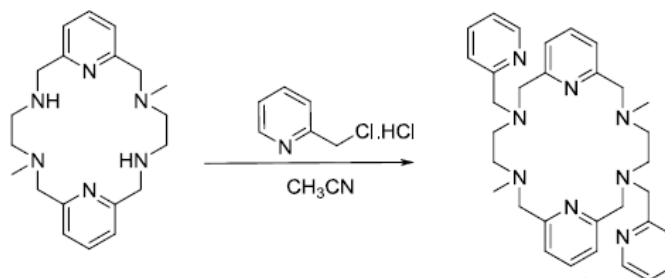
**Keywords:** Macrocyclic, Methylpyridine, lanthanide.

## 1. Introduction

Macrocyclic compounds with pendant-arms are designed with two principal aims: modification of the coordinating properties of the parent ligand, and introduction of the ancillary groups in order to provide a specific application in a particular area of scientific research such as bioinorganic chemistry [1], anionic receptors [2], contrast agents in medicine [3], and so forth. The synthesis of a new *trans*-substituted organic ligand with methylpyridine groups stemming from a precursor with secondary amines, allows optimizing its ability to coordinate to transition metals and lanthanide ions [4].

## 2. Materials and Methods

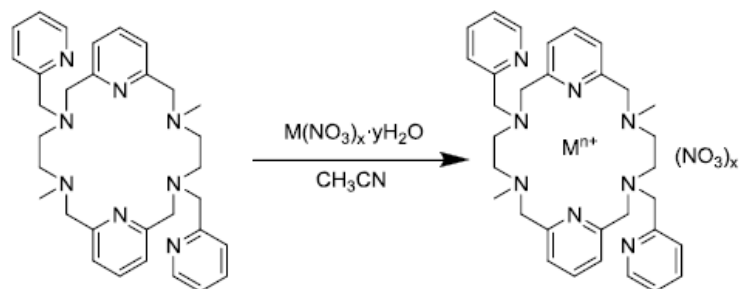
A solution of 2-(chloromethyl) pyridine hydrochloride in acetonitrile was added over a solution of the precursor ligand [5]. The mixture was refluxed for 24h, after which it was reduced and the residue was extracted with CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O. The organic phase was dried and the solvent was removed to give the ligand with pendant-arms methylpyridine (**Scheme1**).



**Scheme 1:** Synthesis of the macrocyclic ligand with pendant-arms methylpyridine.

To obtain the metal complexes, a solution of Ln(NO<sub>3</sub>)<sub>3</sub>·xH<sub>2</sub>O in acetonitrile was added over a solution of the receptor ligand in acetonitrile. The mixture was stirred for 4h at room temperature,

after which ethyl ether was added and the precipitate formed was separated and characterized as the corresponding metal complex (**Scheme2**).

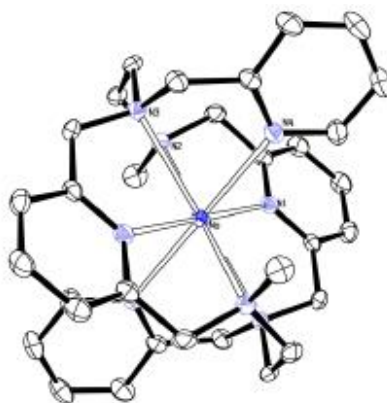


**Scheme 2:** Synthesis of their metallic complex

### 3. Results

A new macrocyclic ligand characterized by ESI-MS, NMR techniques and x-ray diffraction was obtained. Recrystallization of the ligand gave crystals valid for the resolution of its structure by X-ray diffraction (Figure 1). This structure corresponds to that of compound [NaL]I.

As shown in Table1, after the functionalization of the ligand with the pendant-arm groups, a ligand interacting with the lanthanide ions was obtained in high yields.



**Figure 1:** Crystalline structure of the cation [NaL]<sup>+</sup>

**Table 1:** Complexes of lanthanide ions.

Complex	% yield
[LaL](NO <sub>3</sub> ) <sub>3</sub> ·5H <sub>2</sub> O	72
[CeL](NO <sub>3</sub> ) <sub>3</sub> ·6H <sub>2</sub> O	76
[PrL](NO <sub>3</sub> ) <sub>3</sub> ·4H <sub>2</sub> O	46
[NdL](NO <sub>3</sub> ) <sub>3</sub> ·4H <sub>2</sub> O	45
[SmL](NO <sub>3</sub> ) <sub>3</sub> ·5H <sub>2</sub> O	74
[EuL](NO <sub>3</sub> ) <sub>3</sub> ·8H <sub>2</sub> O	81
[GdL](NO <sub>3</sub> ) <sub>3</sub> ·10H <sub>2</sub> O	82
[TbL](NO <sub>3</sub> ) <sub>3</sub> ·8H <sub>2</sub> O	85
[DyL](NO <sub>3</sub> ) <sub>3</sub> ·6H <sub>2</sub> O	89
[HoL7](NO <sub>3</sub> ) <sub>3</sub> ·5H <sub>2</sub> O	70
[ErL](NO <sub>3</sub> ) <sub>3</sub> ·5H <sub>2</sub> O	69
[TmL](NO <sub>3</sub> ) <sub>3</sub> ·3H <sub>2</sub> O	75
[YbL](NO <sub>3</sub> ) <sub>3</sub> ·3H <sub>2</sub> O	89

#### 4. Discussion

The <sup>1</sup>H-NMR spectra show the existence of two conformers in equilibrium in solution. The performance of high and low temperature <sup>1</sup>H-NMR experiments allowed the observation of the variation of the rate of this equilibrium. These results of <sup>1</sup>H-NMR, ESI-MS and X-ray diffraction are in agreement with the expected results.

The functionalization of the receptor with two methylpyridinic groups allows to prepare the complexes with the lanthanide ions accordingly.

#### 5. Conclusions

1. A synthetic route for the production of ligands with pendant-arms methylpyridine in trans positions was successfully developed.
2. The metal complexes with **L** were obtained with the series of lanthanide ions.

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**Author Contributions:** E. L. and A. M. conceived and designed the experiments; R.L. performed the experiments and wrote the paper; P. P. and F. L. analyzed the data; J. M. V. contributed reagents/materials/analysis tools.

**Conflicts of Interest:** The authors declare no conflict of interest

#### Appendix data for the Ligand

ESI (m/z): 537 [L+H]<sup>+</sup>. NMR-<sup>1</sup>H (250 MHz, CDCl<sub>3</sub>; δ (ppm): 1.64 (s, 6H); 2.24 (s, 4H); 2.58 (s, 4H); 3.02 (s, 4H); 3.53 (s, 4H); 4.63 (s, 4H); 6.92 (t, 2H); 6.96 (d, 2H); 7.17 (d, 2H); 7.34 (d, 2H); 7.57 (t, 2H); 7.70 (t, 2H); 7.75 (s, 2H).

#### References

3. Fenton, D. E. "Biocoordination Chemistry", Oxford University Press. 1993.
4. Lee, J. K.; Na, J.; Kim, T. H.; Kim, Y.-S.; Won, H.; Lee, T. S.; "Synthesis of polyhydroxybenzoxazole-based colorimetric chemosensor for anionic species", *Materials Science and Engineering*, **2004**, *24*, 261-264. DOI: 10.1016/j.msec.2003.09.020
5. M. Botta, Second Coordination Sphere Water Molecules and Relaxivity of Gadolinium(III) Complexes: Implications for MRI Contrast Agents; *Eur. J. Inorg. Chem.*, **2000**, 399-407. DOI: 10.1002/(SICI)1099-0682(200003)2000:3<399::AID-EJIC399>3.0.CO;2-B
6. K. P. Wainwright, Applications for polyaza macrocycles with nitrogen-attached pendant arms; *Adv. Inorg. Chem.*, **2001**, *52*, 293-334. DOI: 10.1016/S0898-8838(05)52006-3
7. R. Lamelas, V. García, A. Liñares, R. Bastida, E. Labisbal, A. Fernández-Lodeiro, C. Lodeiro, C. Núñez, L. Valencia; Novel trans-disubstituted hexaaza-macrocyclic ligands containing pyridine head units: Synthesis, disubstitution and colorimetric properties; *Sensors and Actuators B*, **2015**, *225*, 481-491. DOI: 10.1016/j.snb.2015.11.090



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