

Review of the Ph. D. Thesis entitled „Bone-seeking Lanthanide(III) Complexes of Macrocyclic Ligands Bearing Bis(phosphonate) Pendant Arm“

by Mgr. Tomáš Vitha

The Thesis is structured in one of the acceptable ways, containing the Introduction, Aims of the Thesis, Results and Discussion, Conclusions, References and Appendixes where papers with the participation of the candidate are included.

The work described in the Thesis was focused on the preparation and properties of two ligands and their complexes with lanthanides. Mainly the magnetic and other properties pointed to potential medicinal applications were studied. Thus, I have no doubts that the topic chosen is of high interest to wide chemical and medical community.

As regards the formal aspects of the Thesis, it is relatively clearly and logically written with very low number of typing errors etc. As an example, differences in names of ligands (sometimes written in Capital letters, sometimes not) can be mentioned.

However, for the broader discussions is the whole concept of Thesis which is written as the commented number of papers. Here I found it rather infelicitous because the papers were obviously written by corresponding authors and not by candidate himself (if yes, I apologize), so the candidate could not show his qualities completely because the similarities in style of paper and thesis are clearly visible, and by the way must be visible. If the candidate carried out unsuccessful experiments, they should have been included in the Thesis as well, since unsuccessful attempts usually serve for supervisor as a database of bad results which are not published. Secondly, their description demonstrates the thinking of the candidate when dealing with problems. This paragraph brings the opinion of reviewer, and if this matter will be discussed and explained during the defense, this will probably cause a consensus for the future work and Thesis.

Problems to be discussed during the defense:

1. the applicant should comment on quantity of work done and techniques and operated by himself

2. what is the statement of applicant to the fact that only the pure compounds are used as drugs in clinical use and the complexes synthesized contain up to ten percent of free ligand; on the other hand the presence of pairs of diastereomers are present
3. could the applicant show a model of the isomers? could be separated by crystallization and the structure in the solid state determined? could be the energetic barrier of isomerization determined or calculated?
4. could ESR spectra of paramagnetic complexes give an information about the structure of metal coordination vicinity? could the Yb NMR techniques be used?

In summary, even though I have different general opinions to the Thesis style, it describes interesting new results. Thus, **I recommend allowing the Thesis to be defended** as well as further proceedings to the degree provided that appropriate answers are given to the questions and problems raised in this review.

As a very last and highly positive recommendation for the jury members is the fact that the applicant presented a part of his work as a lecture during the seminar of Ph.D. students in 2006 (where the reviewer was present) and this was elected as the best one of ca. 50 lectures of students coming from 10 european countries and also the papers included as Appendixes of the Thesis where the applicant is the first author are printed or submitted to high quality journals such as J. Med. Chem., Langmuir and Dalton Transactions all with IF over 3.

In Sázava 10th January 2008

doc. Ing. Aleš Růžička, Ph.D.