

大環配位子結構與質子化系統及鑰系金屬離子錯合物結構之分子模擬

學生：林玉淳

指導教授：張正 博士

國立交通大學生物科技學系（研究所）碩士班

摘要

為研發應用在人造 DNA/RNA 切割試劑，我們實驗室致力於設計三價鑰系金屬離子試劑。

在此篇論文中，我們利用分子模擬軟體 CHARMM 對多胺基多酸基大環配位子系統建立一套結構最佳化的方法。利用此模擬方法，我們針對不同環境下之九員環以及十二員環系列的大環配位子進行結構最佳化之預測，進而可分析 protonation sites、配位子是否會發生 preorganization 與結構的變化，以及能量的計算。我們利用 CHARMM 計算出來的能量來判斷配位子質子化位置的穩定性，能量越低表示越穩定。並可觀察到大多數的配位子會有 preorganization 情形，對於 NO2A、DO2A 及 DO3A 而言，質子化位置的預測則是以質子化在一個二級氮和一個三級氮上為較可能的位置，而對於 12N32A 則是會質子化在兩個三級氮上；更可於 ODO2A 觀察到第一個質子會接在二級氮上，但當三級氮接上第二個質子時，二級氮上的質子便會轉移到另一個三級氮上。而由模擬的結果，我們可猜測九員環系統與鑰系金屬離子錯合的能力由大到小排列應為：NOTA > NO2A > BzNO2A > PhNO2A，此預測結果可與 NOTA > NO2A > PhNO2A 的實驗數據相印證。

另外，我們也利用量子化學軟體 Gaussian 03 計算出鑰系金屬與多胺基多酸基大環配位子錯合後有配位水的最佳化結構。

Molecular Simulation of Structures and Protonation Schemes of Macrocyclic Ligands and Structures of Lanthanide Complexes

Student : Yu-Chuen Lin

Adviser : Dr. C. Allen Chang

Department (Institute) of Biological Science and Technology

National Chiao Tung University

ABSTRACT

We make efforts in the design of trivalent lanthanide agents to investigate and develop the artificial DNA/RNA cleavage agents.

In this thesis, we report the study of the structures and protonation schemes of polyamino polycarboxylate macrocyclic ligands by use of molecular modeling software, CHARMM. We predict the optimized structures of macrocyclic ligands of cyclononane and cyclododecane systems in different environments; furthermore, we analyze the protonated sites, preorganization, conformational changes and calculated energies. We determined the stability of protonated sites of macrocyclic ligands by calculating the potential energies from CHARMM. The lower energy as well as protonated sites have predicted and indicated the stable conformations. The results reveal that most macrocyclic ligands are preorganized. As for NO₂A, DO₂A and DO₃A, protonation in secondary nitrogen and tertiary nitrogen are the preferred protonated sites; for 12N₃2A, tertiary nitrogen sites are more likely to be protonated. We also observed the proton transfer on ODO₂A between single protonated site and double protonated sites. We suppose the ability of coordination of cyclononane and lanthanide ions as following: NOTA > NO₂A > BzNO₂A > PhNO₂A, and this order can be demonstrated by experiments.

In addition, geometry optimization of the lanthanide complexes is performed by using quantum mechanics software Gaussian 03.