

Quantum chemical analysis of the coordination stability between flexible tripeptides and nickel ions using the GRRM program

Dapeng Zhang,¹ Naoki Kishimoto,¹ and Ryosuke Miyake.²

¹Graduate School of Science, Tohoku University, ²Ochanomizu University

The macrocyclic supramolecules reported by Miyake *et al.*¹, $[M_{14}L_{14}]^{28+}$ and $[M_{12}L_{12}]^{24+}$, and the catenane structure $[M_{28}L_{28}]^{56+}$ generated by the interlock of two $[M_{14}L_{14}]^{28+}$, can be formed by the self-assembly of octahedral coordination between Nickel atoms (M) and flexible tripeptide molecules (L). The amino and carboxyl groups in tripeptides play the roles of monodentate, bidentate, and tridentate sites, respectively, forming the octahedral coordination with nickel atoms. A thorough theoretical study for such giant metal complexes seems to be fraught with unprecedented challenges due to the structural flexibility of the tripeptide and the complexity of the weak interactions that can arise at many sites. To this end, we propose an indirect and feasible approach to effectively investigate the causes of supramolecular self-assembly from the perspective of coordination stability by means of quantum chemical calculations on simple models.

The calculations were performed using the B3LYP method and applying the polarizable continuum model (PCM, in water) to describe solvent effects. First, the anharmonic downward distortion following algorithm (ADDF)² coded in the global reaction route mapping program³ (GRRM) was used to search for stable conformations of the tripeptide in water, which allows us to better understand the way in which the weak intramolecular interactions occur and their effect on the structural conformation. The ADDF calculation shows that the conformation extracted from the crystal $[M_{14}L_{14}]^{28+}$ can rotate and fold due to the intramolecular hydrogen interactions, spontaneously transforming into a more stable structure, suggesting that the crystal conformation can only remain stable under specific conditions. Hereafter, sphere contraction walk algorithm (SCW)⁴ and two-point scaled hypersphere search algorithm (2PSHS)⁵ were applied to reveal a possible reaction pathway connecting the most stable conformer by ADDF calculation (designated as the Product) and the first stable conformer (designated as the Reactant). The results show a trend of decreasing energy from the Product to the Reactant direction. However, the energy trend shifts to an increase when sufficient amounts of nickel ions and counter anions are added to the Product and Reactant, which corroborates the stability of the crystal structure when nickel ions and counter anions are present. Therefore, our theoretical result can confirm that the crystal structure of tripeptide has the advantage of formation under the influence of metal ions and counter anions.

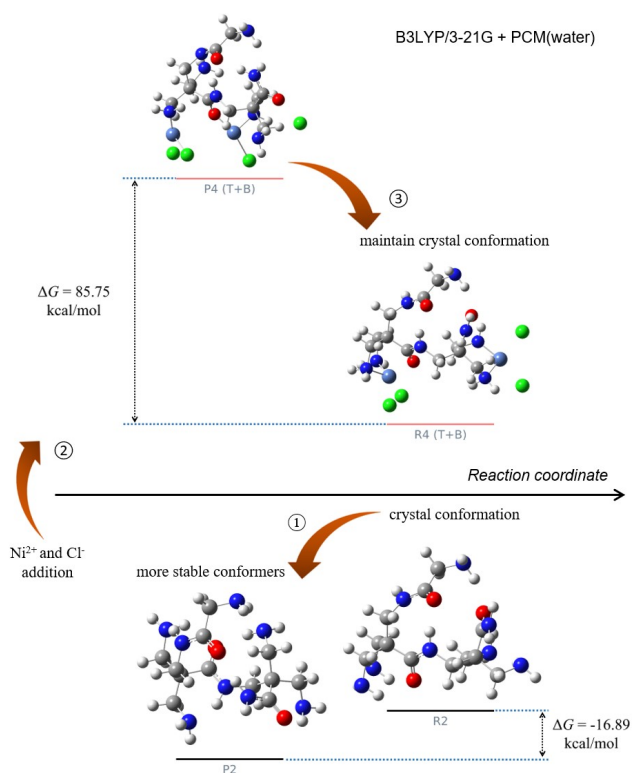


Figure 1. The schematic diagram shows the structures of nickel ions and chloride anions added to the most stable conformer **P2** and the starting point **R2** of the ADDF calculations. The structures of **P4**, **R4** (coordinated at the tridentate and bidentate sites of the flexible tripeptide) were obtained by adding two Ni^{2+} ions and four chloride anions to **P2** and **R2**, respectively. The SCW and 2PSHS calculation were applied to process **P2** to **R2** and **P4** to **R4**.

References

- [1] R. Miyake, A. Ando, et al., *J. Am. Chem. Soc.*, **2019**, 141, 22, 8675-8679.
- [2] S. Maeda, T. Taketsugu, et al., *Bull. Chem. Soc. Jpn.*, **2014**, 87, 1315-1334.
- [3] S. Maeda, Y. Harabuchi, et al., GRRM17, see http://iqce.jp/GRRM/index_e.shtml
- [4] S. Maeda, K. Ohno., *J. Chem. Phys.*, **2006**, 124, 174306.
- [5] S. Maeda, K. Ohno., *Chem. Phys. Lett.*, **2005**, 404, 95-99.