(Rh^I)$_2$錯体を用いたアルドール型反応におけるキーステップに関する理論的研究

（名古屋大学）　西本佳央，藤森嵩央，横川大輔，Irle Stephan

Theoretical investigation of the key step of an aldol-type reaction with a (Rh^I)$_2$ complex

(Nagoya University) Yoshio Nishimoto, Takahisa Fujimori, Daisuke Yokogawa, Stephan Irle

The chemical modification of a nitrile group has significant importance in the field of organic synthesis. For instance, an aldol-type reaction, which transforms a nitrile into a β-hydroxynitrile, and the hydration reaction [1] of a nitrile group attract much attention due to the industrial and pharmacological importance. Nevertheless, the difficulty of these reactions is attributed to the inertness of the nitrile group, and thus functionalization sometimes demands drastic conditions, high temperatures or high pressures, even in the presence of catalysts. Goto *et al.* reported an aldol-type reaction of organonitriles under mild conditions in 2008 [2]. In the present study we focused on the high yields of the corresponding β-hydroxynitriles and efficient catalytic activity. Because of the difficulty in functionalizing the nitrile group, it is of great importance to understand the mechanism of the efficient catalyzed reaction (Scheme 1).
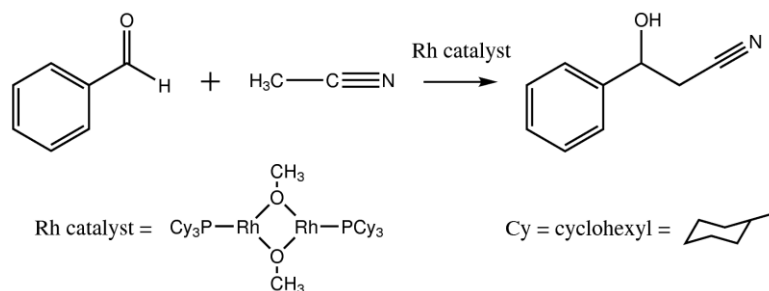
Scheme 1 Target aldol-type reaction

Our investigation was carried out using density functional theory (DFT) with the M06 functional, since we found that the inclusion of dispersion is important to reproduce the Δ*H* calculated by CCSD(T)/cc-pVTZ level of theory. We chose a moderate basis set size (6-31G(d) for non-metal elements and LanL2DZ for Rh) for geometry optimization, and energy refinement was done using a larger basis set (6-311+G(d,p) and LanL2DZ). Since the real catalyst shown in Scheme 1 has six large cyclohexyl groups, we first explored the plausible reaction mechanism using a model compound, where all cyclohexyl groups were substituted by hydrogen atoms in order to save computational cost. Solvent effect of

t-butanol was included using the polarizable continuum model (PCM).

Our model calculations for the reaction with monomer and dimer catalysts show that both catalysts are able to perform a catalytic cycle, considering the barrier heights along the chemical reaction pathway. However, because of the predicted large dimerization free energy (37.62 kcal/mol), it is highly probable that the catalyst works as a dimer. From the reaction profile of the $(Rh^I)_2$ dimer catalyst (Figure 1), the calculated highest barrier of each step is 15.15 kcal/mol (TS2), and this is reasonably consistent with the experimental reaction, which is carried out at room temperature for several hours.
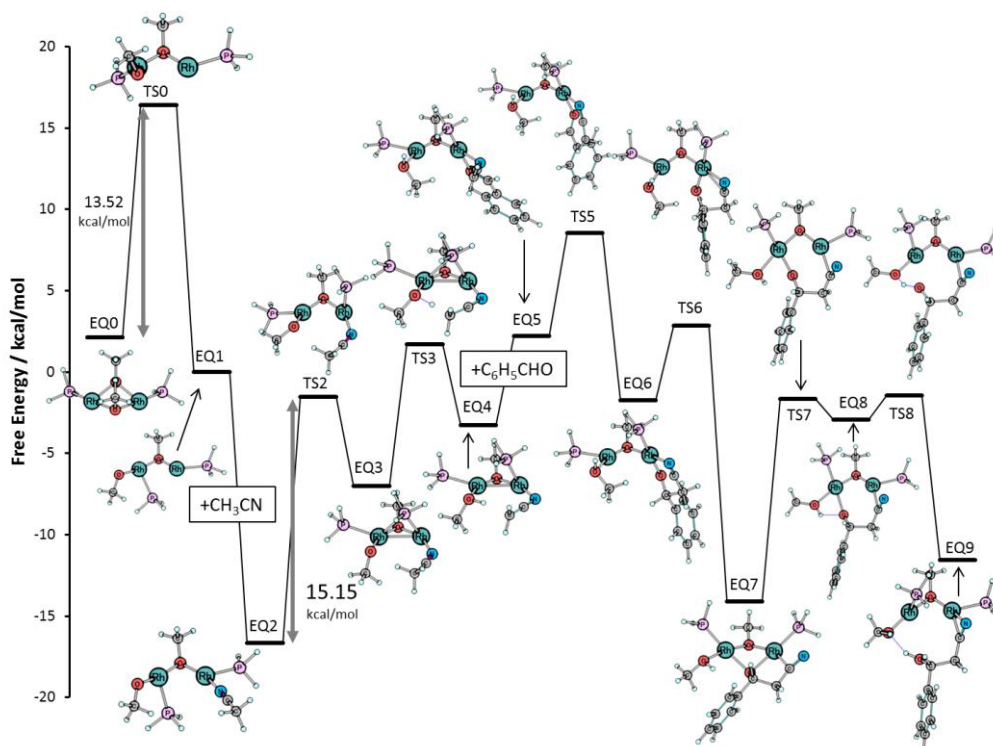

Figure 1 Reaction profile of $(Rh^I)_2$ dimer catalyst (model) at PCM-M06/6-311+G(d,p) + LanL2DZ // M06/6-31G(d) + LanL2DZ level of theory.

In the presentation, we will also discuss results of calculations for the real system.

References

[1] A. Goto, K. Endo, S. Saito, *Angew. Chem. Int. Ed.* **2008**, *47*, 3607-3609.
[2] A. Goto, K. Endo, Y. Ukai, S. Irle, S. Saito, *Chem. Commun.* **2008**, 2212-2214.