Project Title:

Computationally assisted small molecule activations

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1. Background and purpose of the project, relationship of the project with other projects

Multimetallic hydrides might serve as the true active species in the industrial hydrodenitrogenation(HDN) process on solid catalysts, examining the reactions of well-deffned multimetallic hydride complexes with aromatic N-heterocycles is of particular interest and importance.

Recently, Prof. Hou's group found that a PNP-ligated titanium hydride framework behaved differently from that bearing the C5Me4SiMe3 ligands in dinitrogen activation and functionalization. They report an unprecedented denitrogenative ring-contraction of pyridines by a dititanium tetrahydride complex bearing rigid PNP-pincer ligands, which straightforwardly afforded cyclopentadienyl and nitride units through the denitrogenation and ring contraction of a pyridine skeleton under mild conditions. The detail mechanism on the related transformations (Fig.1) remain unclear.

As we know, density functional theory (DFT) calculation plays important role in uncovering the reaction mechanisms on multimetallic hydrides medicated small molecules (such as benzene, N_2, pyridine and so on) activations. Herein, to have a better understanding about the HDN mechanism of aromatic N-heterocycles but also constitutes a novel example of skeletal editing of aromatic N-heterocycles, DFT calculations were performed.

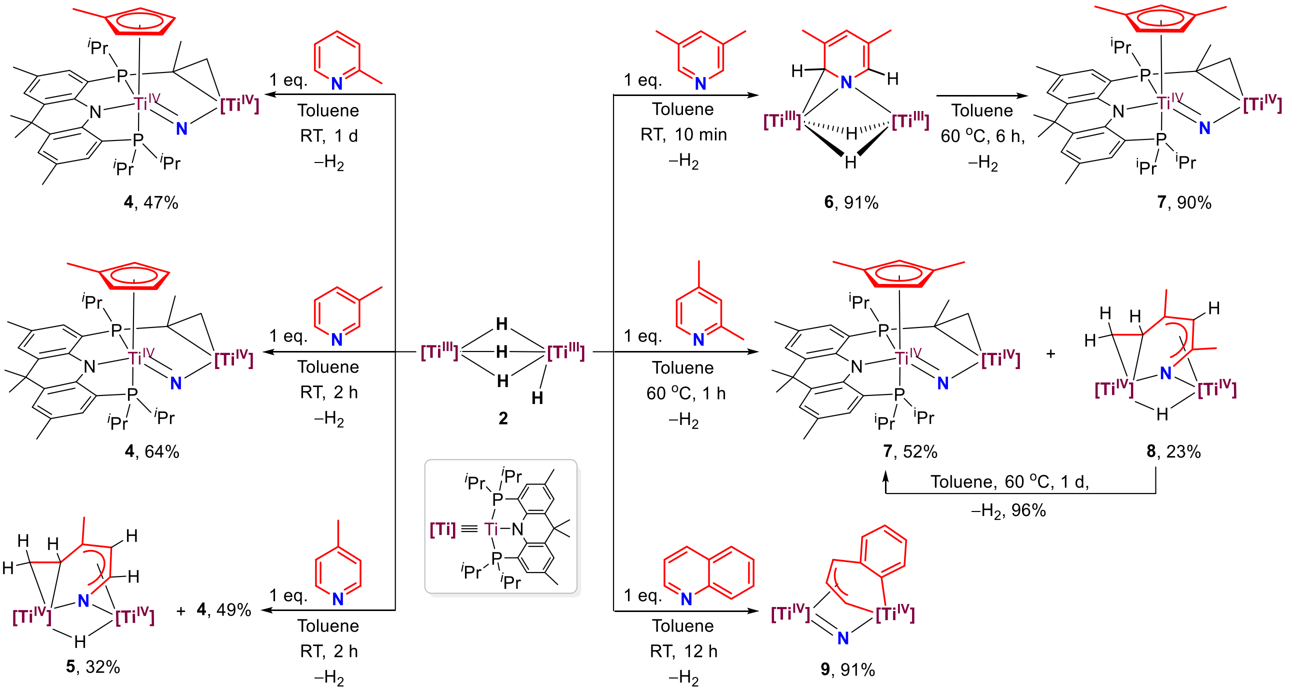

Fig. 1. Reactions of 2 with picolines, lutidines, and quinoline.

2． Specific usage status of the system and calculation method

During the fiscal year 2024, the most specified （$9.8*10^5$ core*hours） computational resources were used for my Quick User project. All calculations were performed by Gaussian 16 software together with DFT methods, such as TSPPTPSS, M062X, B3PW91, and B3LYP so on. and DFT-D3 method and SMD solvent model were used to give more accurate energy profiles.

3． Result

To better understand the mechanistic details of the reaction of **2** with pyridines, density functional theory (DFT) calculations were performed. As the reaction of **2** with 2,4-lutidine involved the most relevant transformations, including the denitrogentaion and ring contraction of 2,4-lutidine to form product **7**, ring opening of 2,4-lutidine to give product **8**, and the conversion of ring opening product **8** to denitrogenation product **7**, we herein selected this reaction as a model reaction to study the detailed reaction mechanisms. Because the molecule size is too large, simplified model complexes were used in the calculations, in which each methyl group on the acridane ring of the $^{\text{acri}}$PNP ligands was replaced by a H atom (i.e., 4,5-bis(diisopropylphosphino)-9H-acridin-10-ide). Figure 6 presents the pathways for the reaction of **2m** (a model complex of **2**) with 2,4-lutidine to yield the 1,3-dimethyl substituted Cp/nitride complex **7m** (a model complex of **7**) and the three-fused-six-membered azametallacycle **8m** (a model complex of **8**). The coordination of 2,4-lutidine to a titanium center in **2m** leads to the reductive elimination of H_2 via intermediates **A** and **B** to yield 2,4-lutidine coordinated intermediate **C**, in which the two titanium centers are reduced from Ti(III) to Ti(II). The following coordination of C=N double bond in **C** to Ti1 center readily affords species **D**, in which the C=N double is reduced to the C−N single bond. **D** has a similar core structure to the experimentally obtained 3,5-lutidine coordinated complex **6**. Subsequent C−N bond cleavage by taking two electrons from titanium centers in **D** via $\mathbf{TS_{DE}}$ yields the ring opening intermediate **E** by overcoming an energy barrier of 20.5 kcal/mol. Accordingly, the Ti(III) centers in **D** are oxidized to Ti(IV). Other possible pathways from **D** including the α-C−H bond activation to give the 2,4-dimethylpyridyl complex or hydrogenation of α-C atom by a bridging hydride were confirmed to be unfavorable (Figure S43 and S44). There are two possible pathways for the following transformation from **E**. One proceeds through nucleophilic addition of a hydride ligand (H2) to the Ti-α-C atom to give 1,4- addition intermediate **F**, which could then isomerize to thermodynamically more stable **8m** by rearranging the [$CH_2CHC(Me)CHC(Me)N$] moiety via $\mathbf{TS_{F8m}}$. The conversion of **E** to **8m** requires to overcome an energy barrier of 14.6 kcal/mol and is exergonic by 12.8 kcal/mol. In the whole process of the reaction of **2m** with 2,4-lutidine to yield **8m**, the C−N bond cleavage from **D** to give **E** ($\Delta G^{\ddagger}$ =20.5 kcal/mol) is the rate-determining step. The transformation of **2m** plus 2,4-lutidine to **8m** plus H_2 is exergonic by 19.9 kcal/mol.

Alternatively, **E** could isomerize to intermediate **I** via **G** and **H** through successively rearranging a bridging hydride ligand (H1) to a terminal one (from **E** to **G**), coordination rearrangement of [CHCHC(Me)CHC(Me)N] moiety to Ti2 (from **G** to **H**), and a flipping of the η^6-coordination [CHCHC(Me)CHC(Me)N] moiety on Ti2 to an η^3-coordination mode on Ti1 (from **H** to **I**). The reductive elimination of H_2 from **I** via **J** yields **K**, in which the titanium centers are reduced from Ti(IV) to Ti(III). Subsequent [CHCHC(Me)CHC(Me)N] unit reduction by taking two electrons from the Ti(III) centers in **K** yields **L** containing a strained three-membered azametallacycle, which readily undergoes C−N bond cleavage and Ti=N bond formation to afford dititanium nitride intermediate **M** bearing a six-membered metalacycle. Thus far, the nitrogen atom was extruded from the pyridine

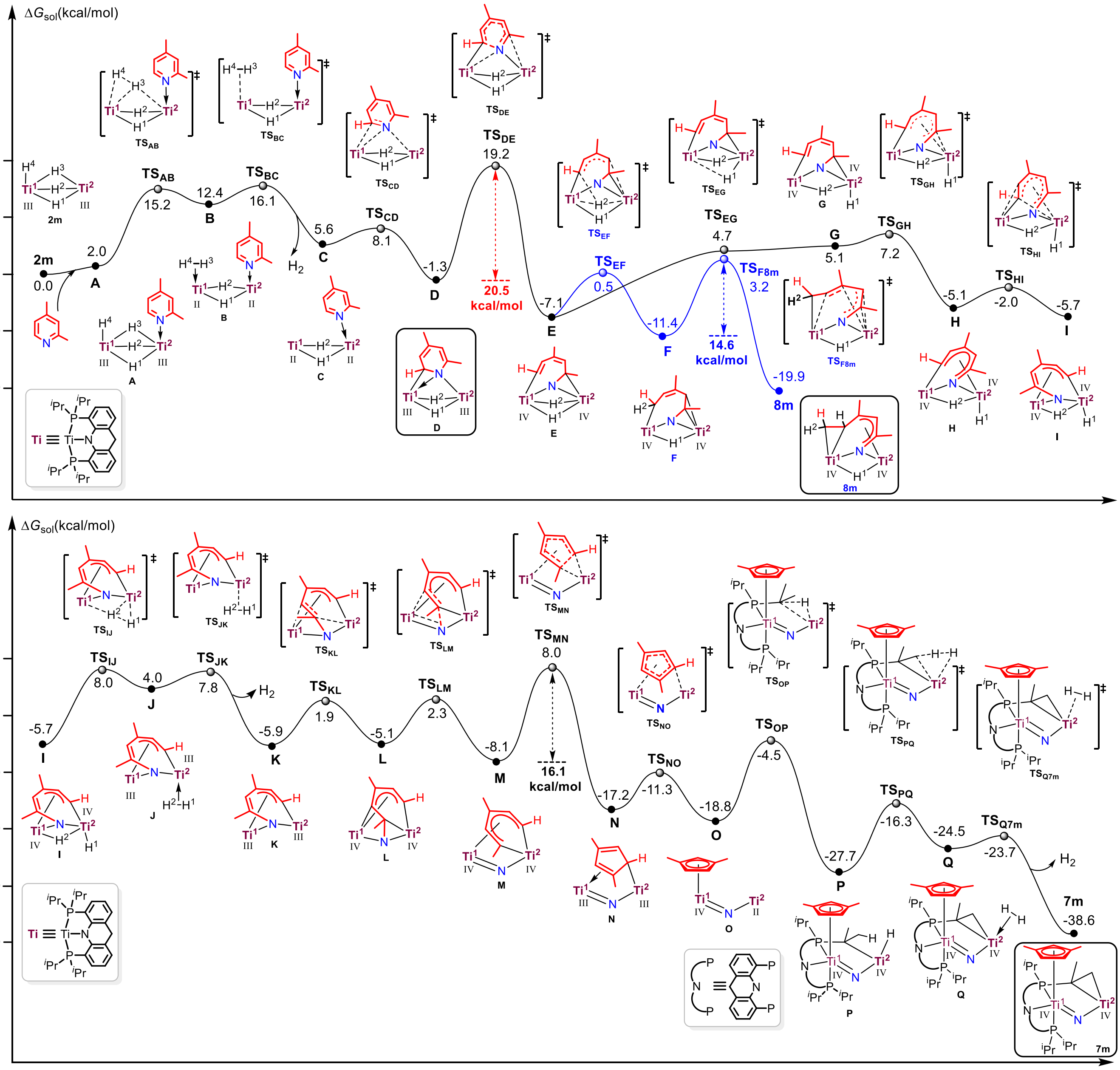

Fig. 2. Gibbs free energy profiles for the reactions of **2m** (a model complex of **2**) with 2,4-lutidine.

ring. A denitrogenated product **9** related to the structure of **M** was obtained experimentally by the reaction of **2** and quinoline. Reductive C–C bond coupling of **M** via **TS$_{MN}$** by overcoming an energy barrier of 16.1 kcal/mol yields intermediate **N** with a η^1 coordinated 1,3-dimethyl substituted Cp ligand. The subsequent η^1- to η^5- isomerization of the 1,3-dimethyl Cp unit in **N** affords intermediate **O**. **O** has a Ti(II) center, which could undergo oxidative addition reaction with the CH group at an isopropyl unit of the PNP ligand to give 1,3-dimethyl substituted cyclopentadienyl/nitride/hydride intermediate **P**.

Finally, σ-bond metathesis between the Ti–H and a methyl C–H bond via intermediate **Q** furnishes product **7m**. The whole process of the transformation of **2m** and 2,4-lutidine to **7m** and H_2 is exergonic by 38.6 kcal/mol. Notably, in the transformation of **2m** and 2,4-lutidine to **7m**, all of the four hydride ligands are released as H_2 and donating 4 electrons to reduce the pyridine unit, while no hydrogenation occurs at the pyridine ring. This is in sharp contrast to the denitrogenation mechanism of pyridine by $C_5Me_4SiMe_3$-ligated trinuclear titanium hydride complex [{(Cp')Ti}$_3$(μ_3-H)(μ-H)$_6$], in which hydrogenation of the α-carbon atom took place before the cleavage of the second C–N bond. Additionally, the C−C bond coupling reaction is easier than the denitrogenation reaction in the reaction of **2** and 2,4-lutidine, which is also in contrast with the reaction of pyridines with [{(Cp')Ti}$_3$(μ_3-H)(μ-H)$_6$].

C−N bond cleavage from **D** to give **E** ($\Delta G^{\ddagger}$ =20.5 kcal/mol) is the rate-determining step for the formation of both ring-opening product **8m** and denitrogenation product **7m** from **2m** and 2,4-lutidine. After the generation of **E**, the largest energy barriers for the formation of **7m** ($\Delta G^{\ddagger}$ =16.1 kcal/mol) and **8m** ($\Delta G^{\ddagger}$ =14.6 kcal/mol) from **E** are comparable. These results agree with the experimental results that both products **7** and **8** were obtained in the reaction of **2** with 2,4-lutidine. The reverse transformation of **8m** to **E** and then to **7m** needs to overcome a largest energy barrier of 27.9 kcal/mol (from **8m** (–19.9 kcal/mol) to $\mathbf{TS_{MN}}$ (8.0 kcal/mol)), which is accessible at heating conditions. These results also agree with the experimental observation that **8** could transform to **7** by heating at 60 °C for 1 day.

4. Conclusion

In the last year, the RICC provided enough calculation resources for our studies on the detail mechanism of ring contraction of pyridines to cyclopentadienyl units by extrusion of nitrogen at a PNP-ligated dititanium hydride cluster.

Combing with experimental data, the computational study has suggested that the ring-contraction products and ring-opening products are formed through two different pathways. The ring-opening reactions proceeded through C=N bond reduction, followed by cleavage of one C–N bond and hydrogenation, while the ring-contraction reactions proceeded through sequentially C=N bond reduction, cleavage of both C–N bonds, and C–C bond coupling, in which the second C–N bond cleavage and C–C bond coupling were easier than the first C–N bond cleavage and no hydrogenation reactions took place. These results stand in sharp contrast to the denitrogenation reactions of pyridines with the Cp'-ligated trititanium hydride complex [{(Cp')Ti}$_3$(μ_3-H)(μ-H)$_6$], which yielded linear hydrocarbon ligands and took place sequentially through reduction and deprotonation of a [HC=N] moiety, cleavage of the first C–N bond, hydrogenation, cleavage of the second C–N bond, and dehydrogenation. This work has demonstrated that the denitrogenation of an aromatic N-heterocycle can be achieved directly through C–N bond cleavage without hydrogenation of the aromatic N-heterocycle and the nuclear numbers and supporting ligands have strong influence on the reaction modes and pathways for HDN reactions. Further studies on new HDN reactions of aromatic N-heterocycles promoted by multinuclear metal hydride complexes are in progress.

5. Schedule and prospect for the future

In the following FY2025, I plan to continue collaboration with Prof. Zhaomin Hou (Organometallic Chemistry Laboratory & Advanced Catalysis Research Group, RIKEN) to investigate the related mechanisms of N-containing small molecules were activated by multimetallic hydrides. In the process of exploring the reaction mechanism, numerous DFT calculations need to be executed and computational resources is necessary. Therefore, I want to get the continuous support from RIKEN Supercomputer System in the future.

6. If no job was executed, specify the reason.

Usage Report for Fiscal Year 2024

Fiscal Year 2024 List of Publications Resulting from the Use of the supercomputer

[Paper accepted by a journal]

(1)Xiaoxi Zhou, Qingde Zhuo, Takanori Shima,* Xiaohui Kang,* and Zhaomin Hou*, Denitrogenative Ring-Contraction of Pyridines to a Cyclopentadienyl Skeleton at a Dititanium Hydride Framework, J. Am. Chem. Soc. 2024, 146, 31348−31355, October 31, 2024.