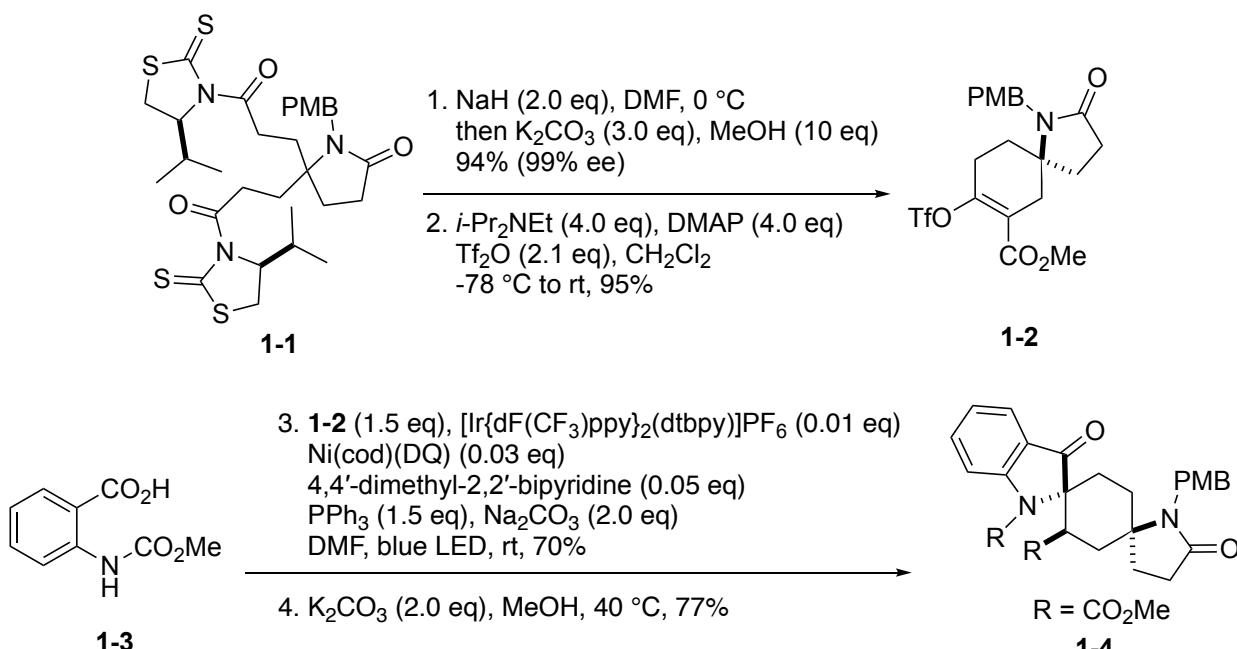


Problem Session (1)

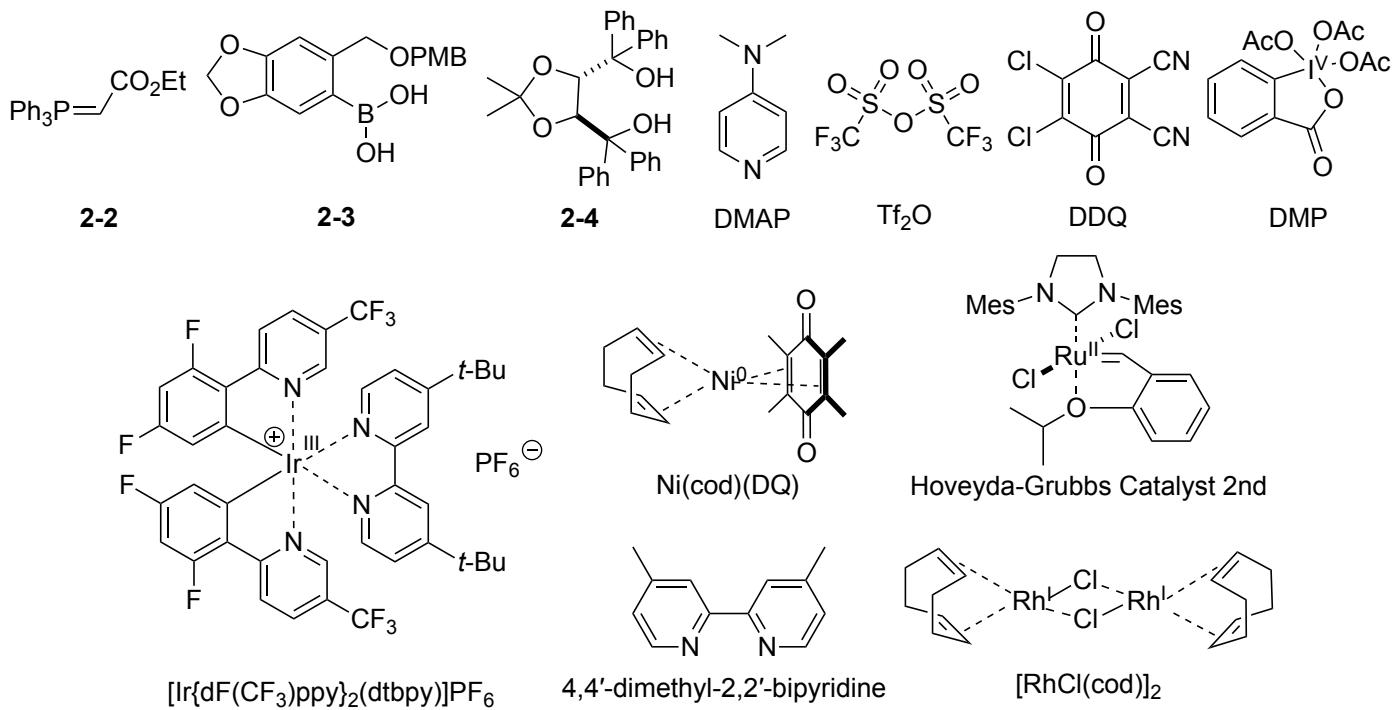
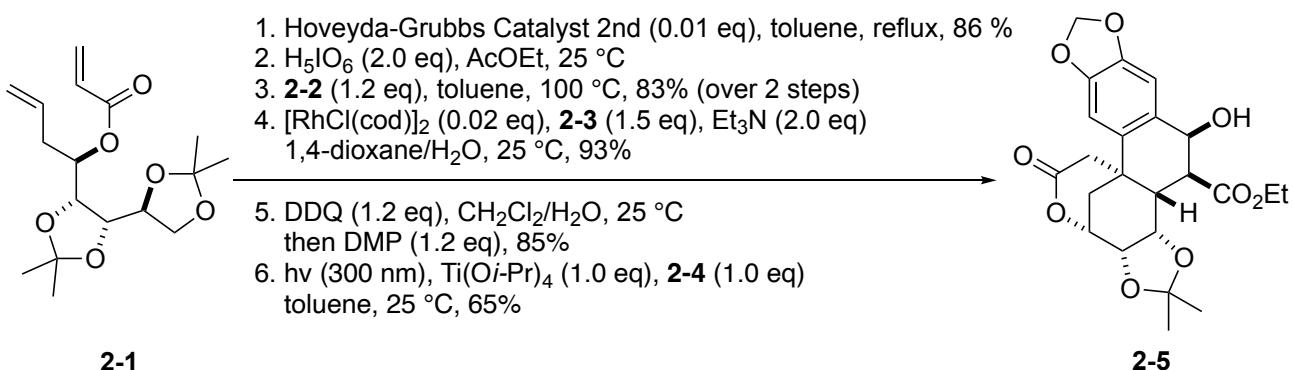
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Please provide the mechanisms for the following reactions.

Problem 1



Problem 2

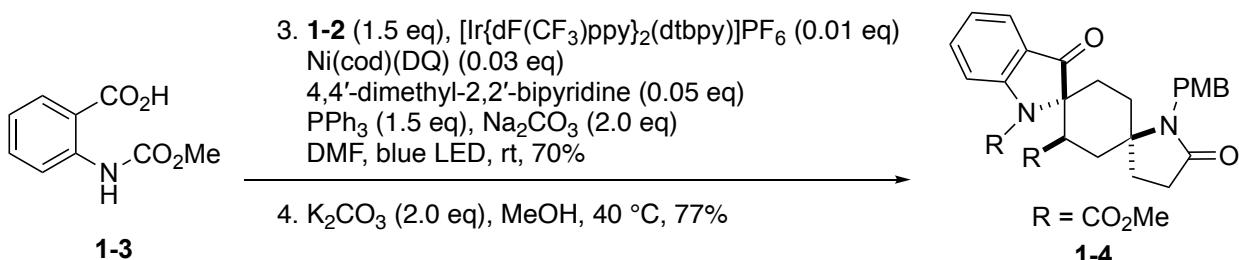
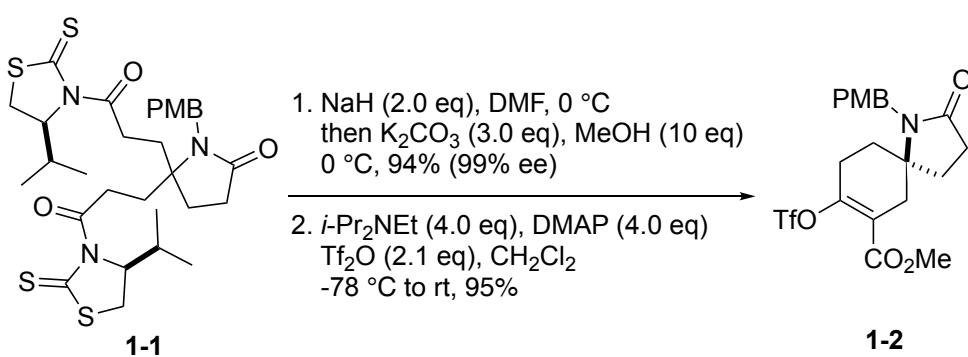


Problem Session (1) -Answer-

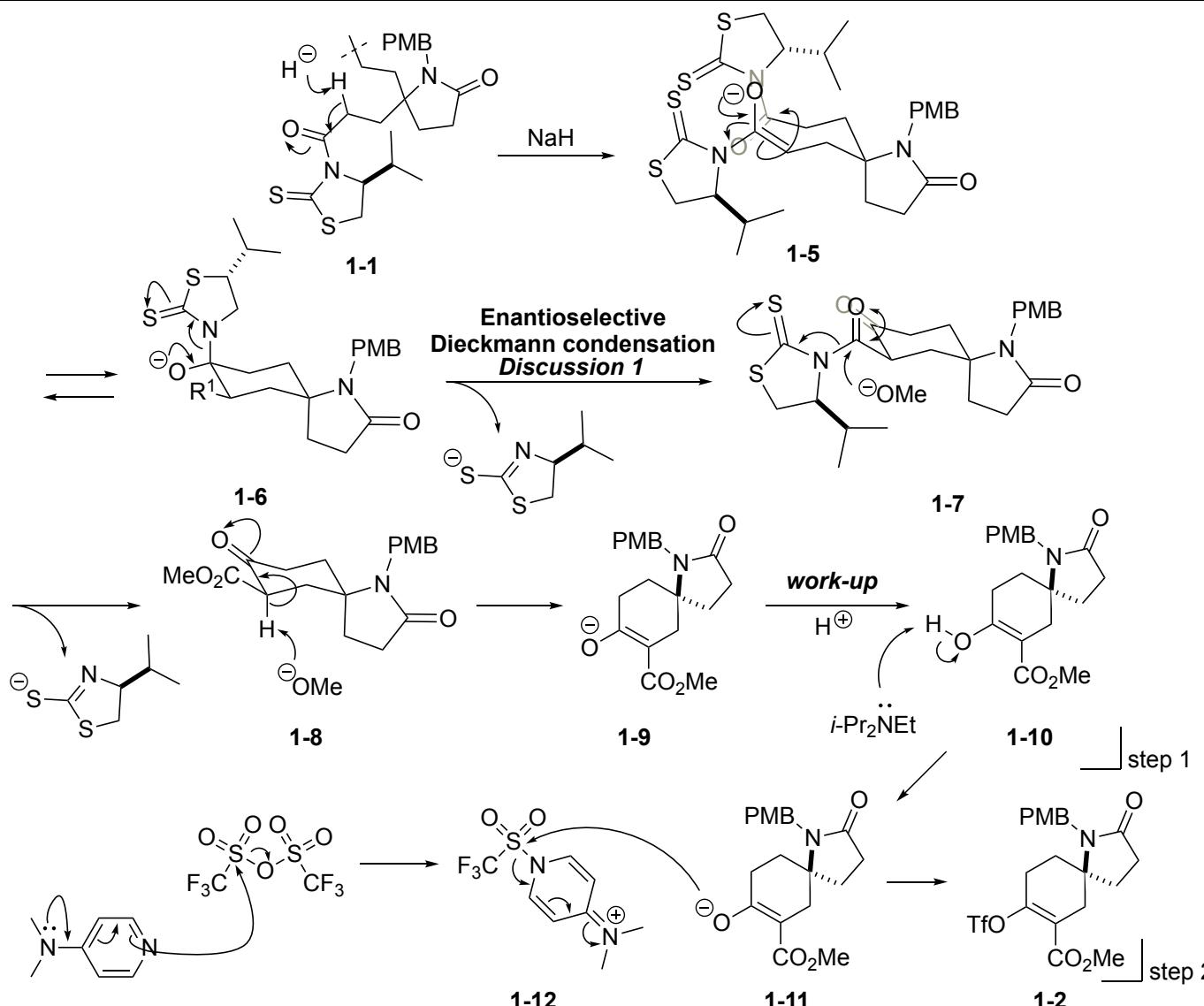
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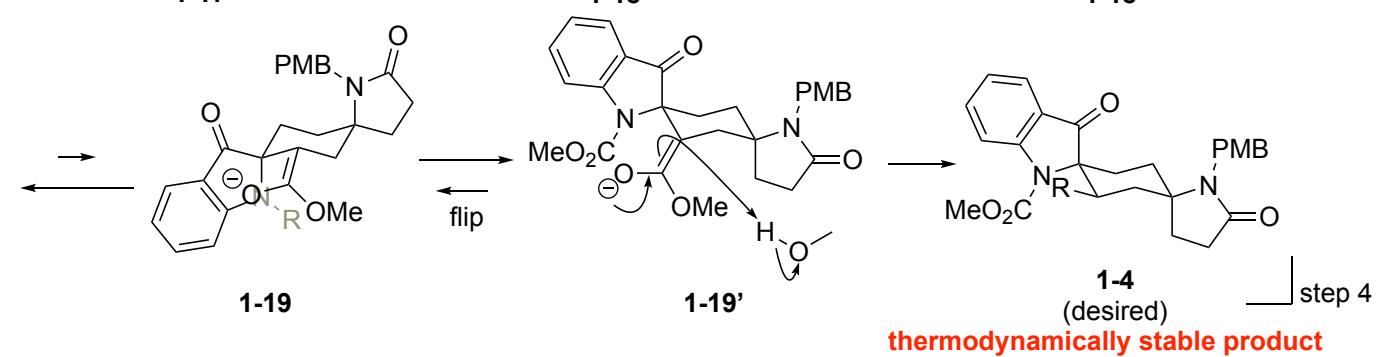
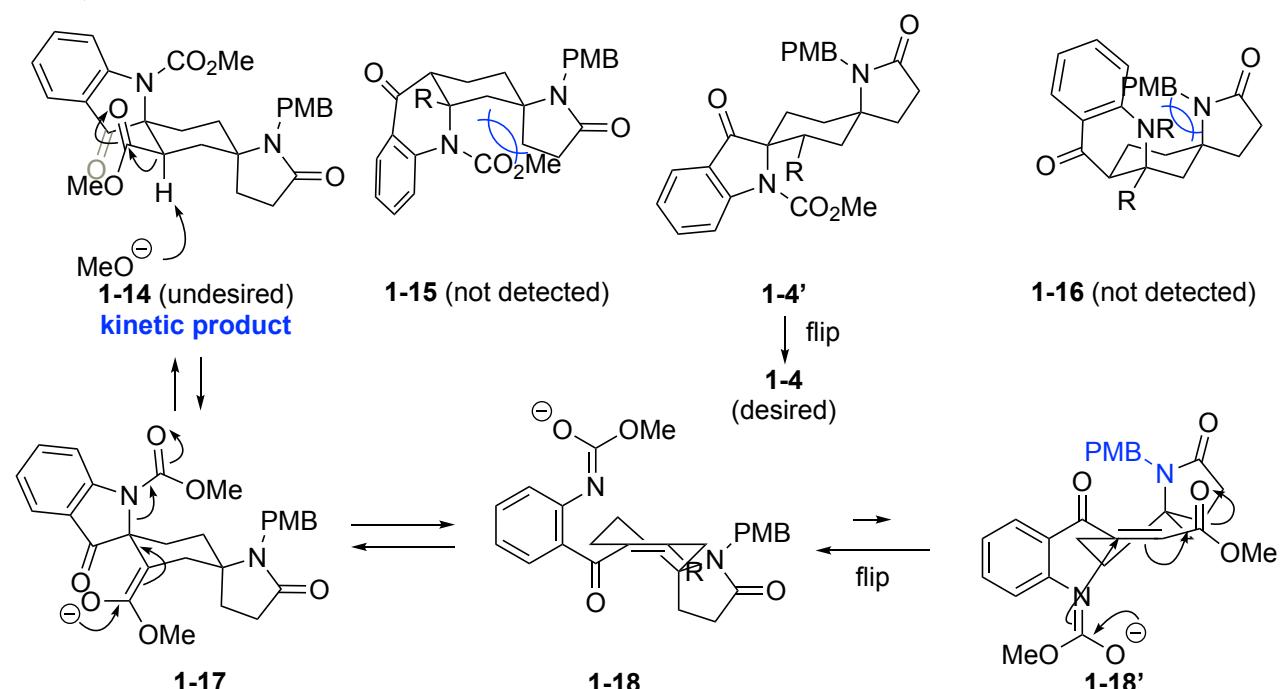
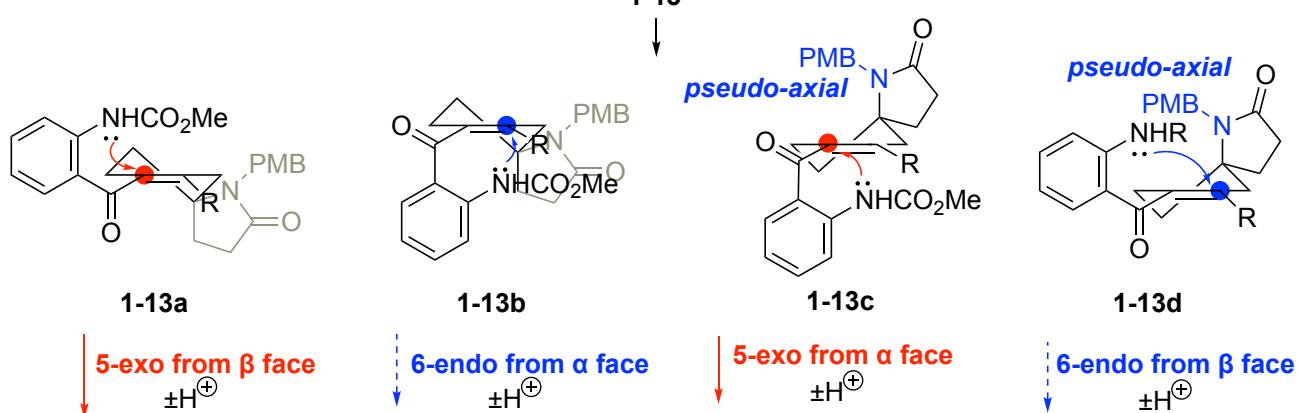
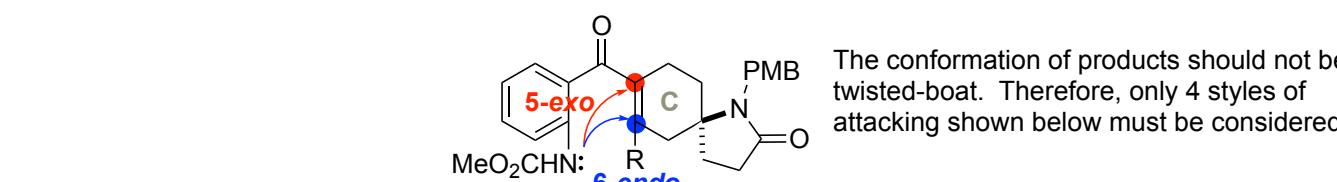
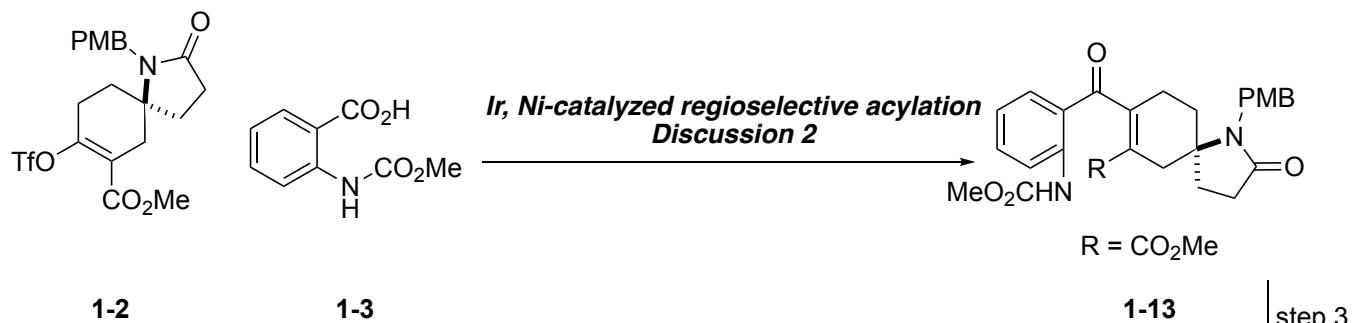
Topic: Photoreactions for Constructing Fused Multicyclic Core Skeleton

Problem 1 Total synthesis of grandilodines A, C, lapidilectine B and lundurine A

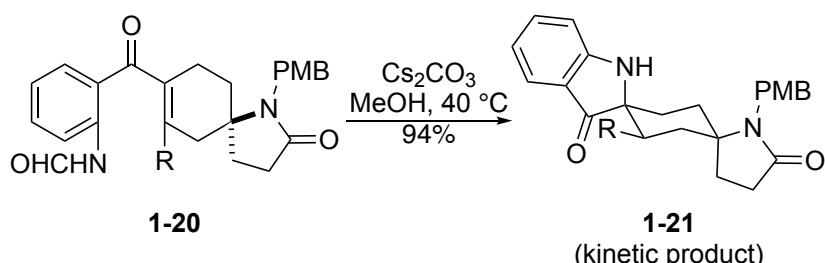


Chen, L.; Xie, K.; Zhang, J.; Zu, L. *Angew. Chem. Int. Ed.* **2022**, *61*, e202212042

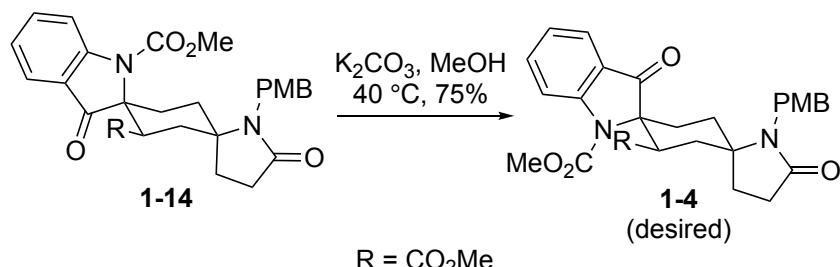




Comparative Experiment



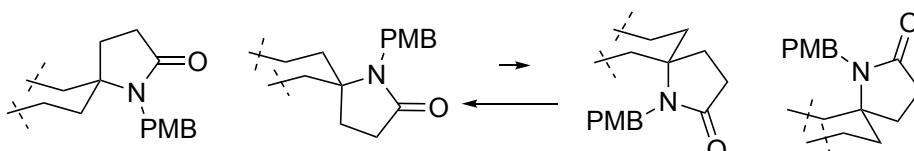
Only **1-21** is generated from less hindered substrate **1-20**. This fact suggests generating kinetic product is much faster than generating thermodynamic product.



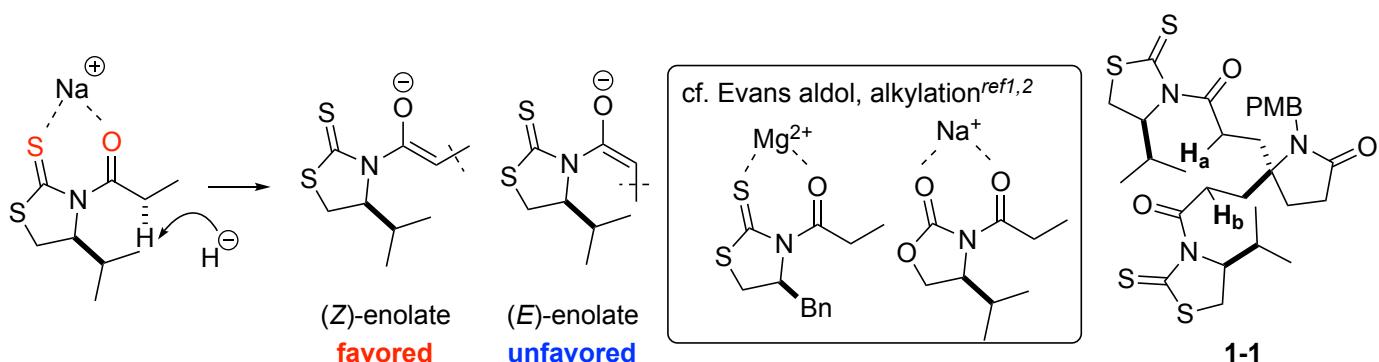
Furthermore, **1-4** was gained from **1-14** converted from **1-21** under the same condition.

Discussion 1 -Enantioselectivity of Dieckmann Condensation-

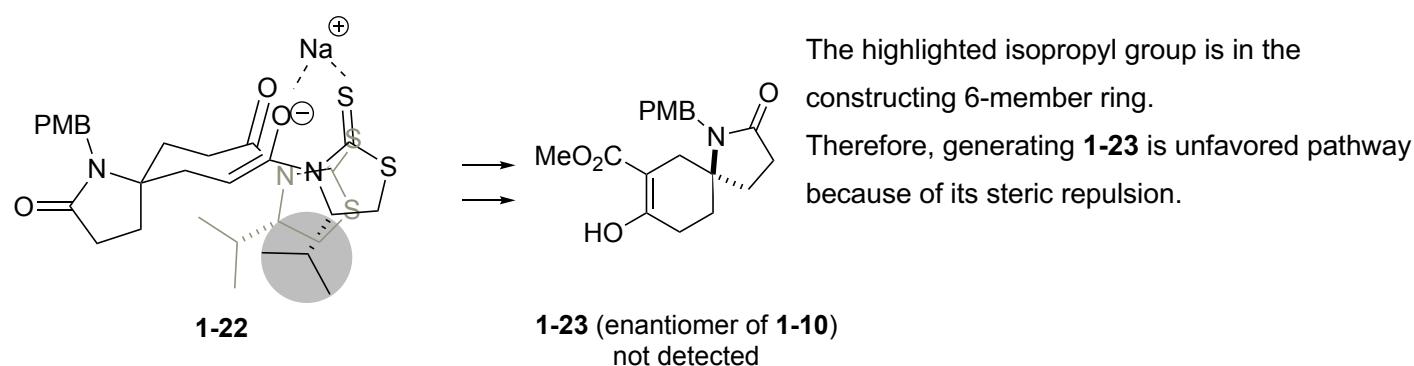
N-PMB group should be on equatorial side in order to avoid large 1,3-diaxial interaction



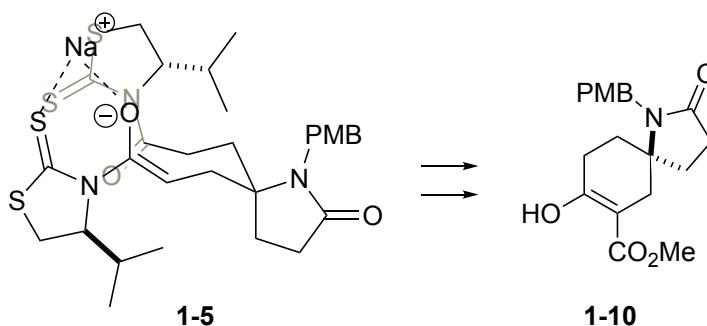
The orientation of highlighted S atom and O atom is the same due to Na^+ chelation. Also, (*Z*)-enolate will be generated preferentially to avoid repulsion. To understand the enantioselectivity, two possibilities of proton abstraction (H_a or H_b) should be discussed.



1. Deprotonation of H_a



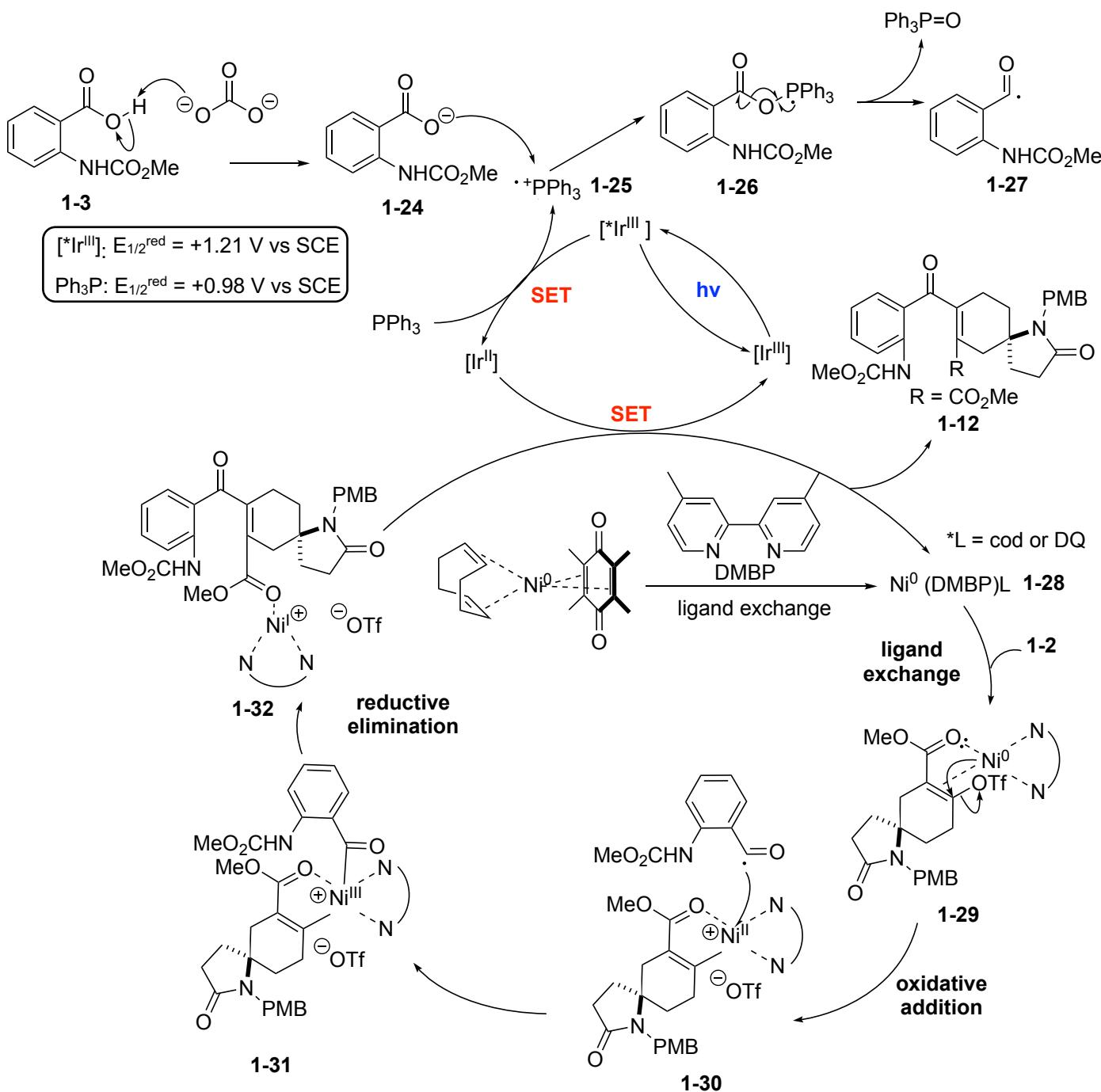
2. Deprotonation of H_b



The isopropyl groups face the opposite side of each other. Therefore, generating **1-10** is favorable.

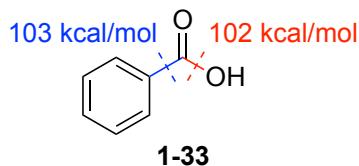
Discussion 2 -Ir, Ni-catalyzed Regioselective Acylation-

2-1 Proposed catalytic cycle ^{ref3,4}

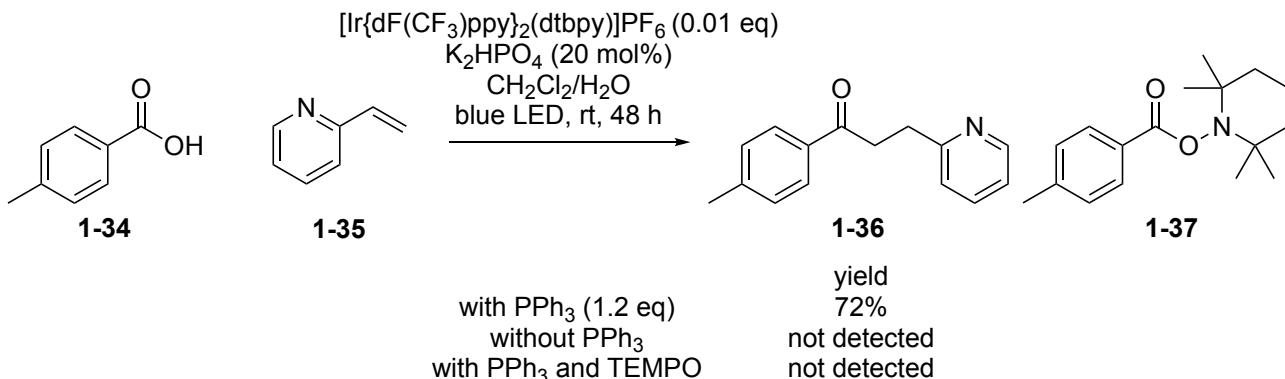


2-2 Role of PPh₃^{ref3,4}

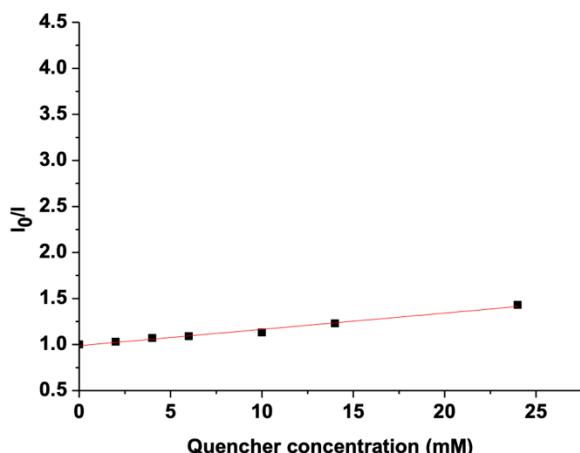
- Deoxygenation is usually difficult due to the similar bond dissociation energies of C-C and C-O bonds.



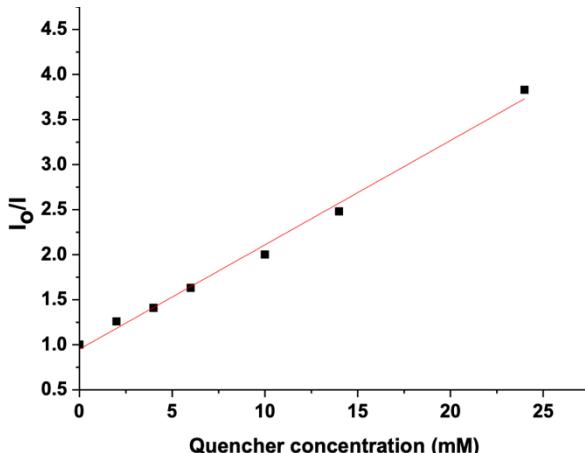
- The desired reaction did not proceed when PPh₃ was not added. Once TEMPO was added as radical quencher, **1-37** was only detected. These experiments indicate acyl radical was generated with PPh₃.



- The luminescence quenching experiment shows PPh₃ can quench [^{*}Ir^{III}] faster than **1-34**.

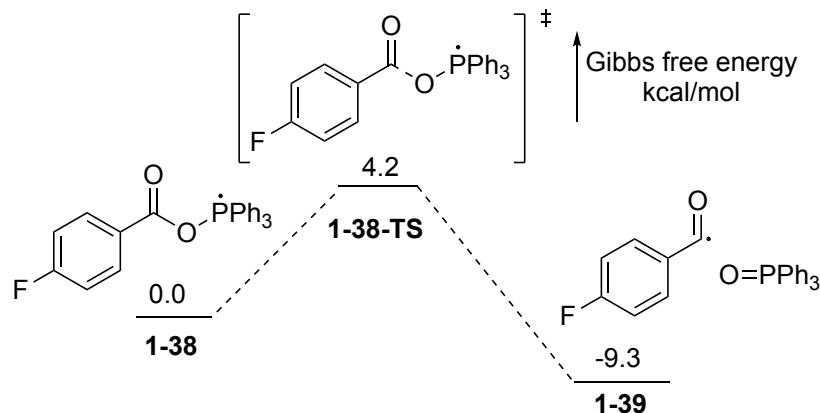


Luminescence quenching of $[{}^*\text{Ir}^{\text{III}}]$ by **1-34**



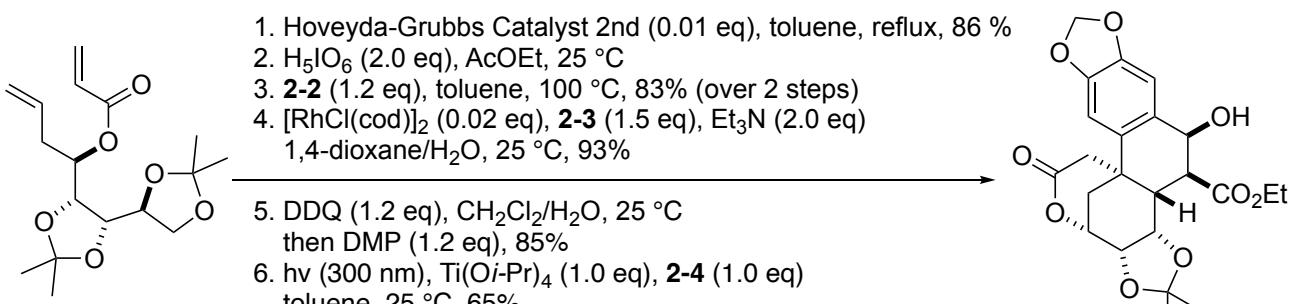
Luminescence quenching of $[{}^*\text{Ir}^{\text{III}}]$ by PPh₃

- The calculation shows the energy barrier is low and acyl radical **1-39** is more stable than intermediate **1-38**.



PBE0-D3/def2-TZVP/ SMD(DMF)//PBE0-D3/def2-SVP/SMD (DMF)

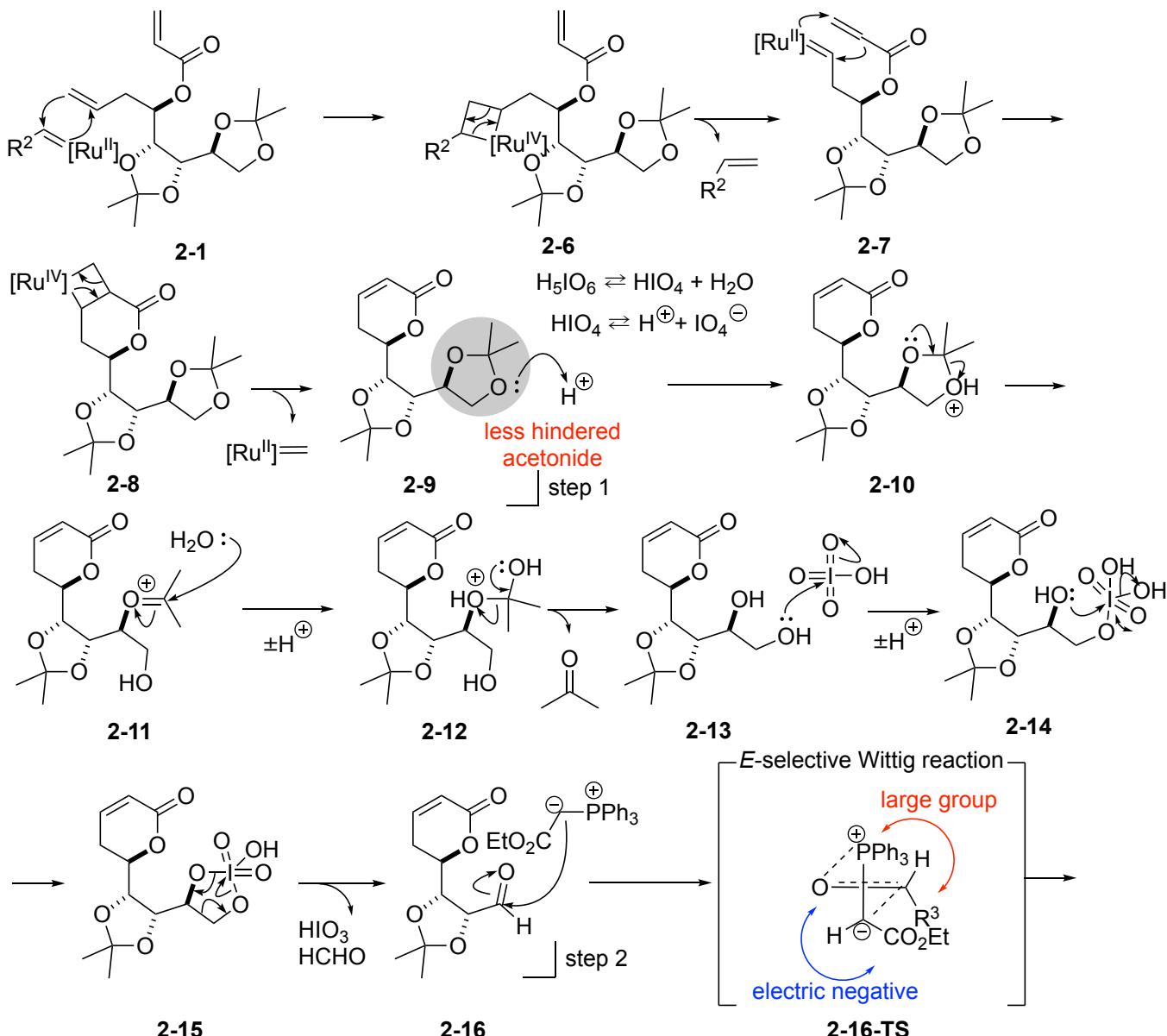
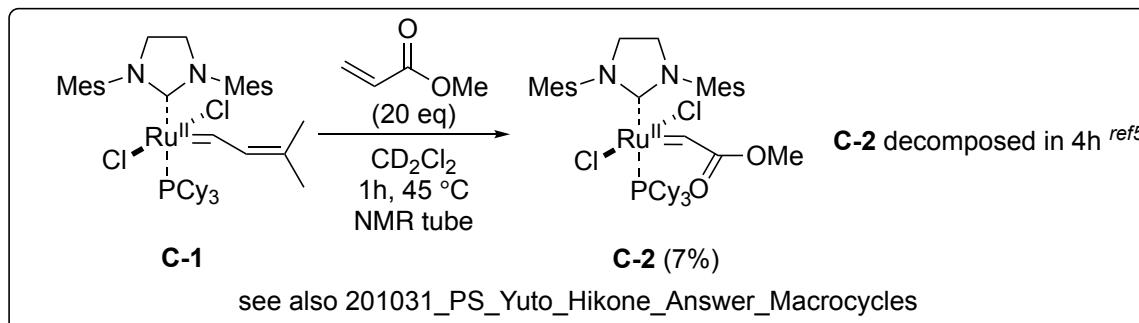
Problem 2 Total synthesis of periglaucines A–C, N,O-dimethyloxostephine and oxostephabenine

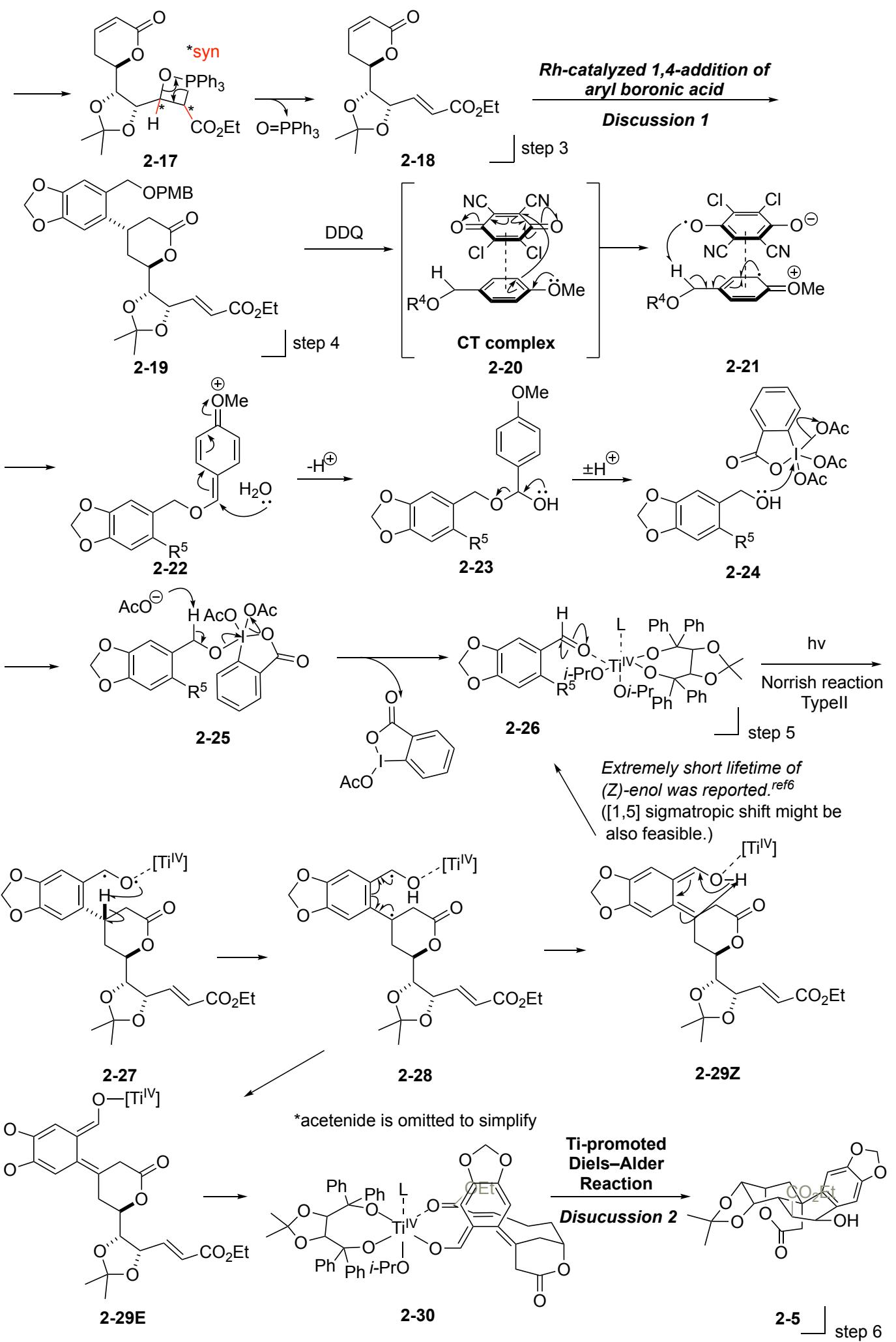


2-1

2-5

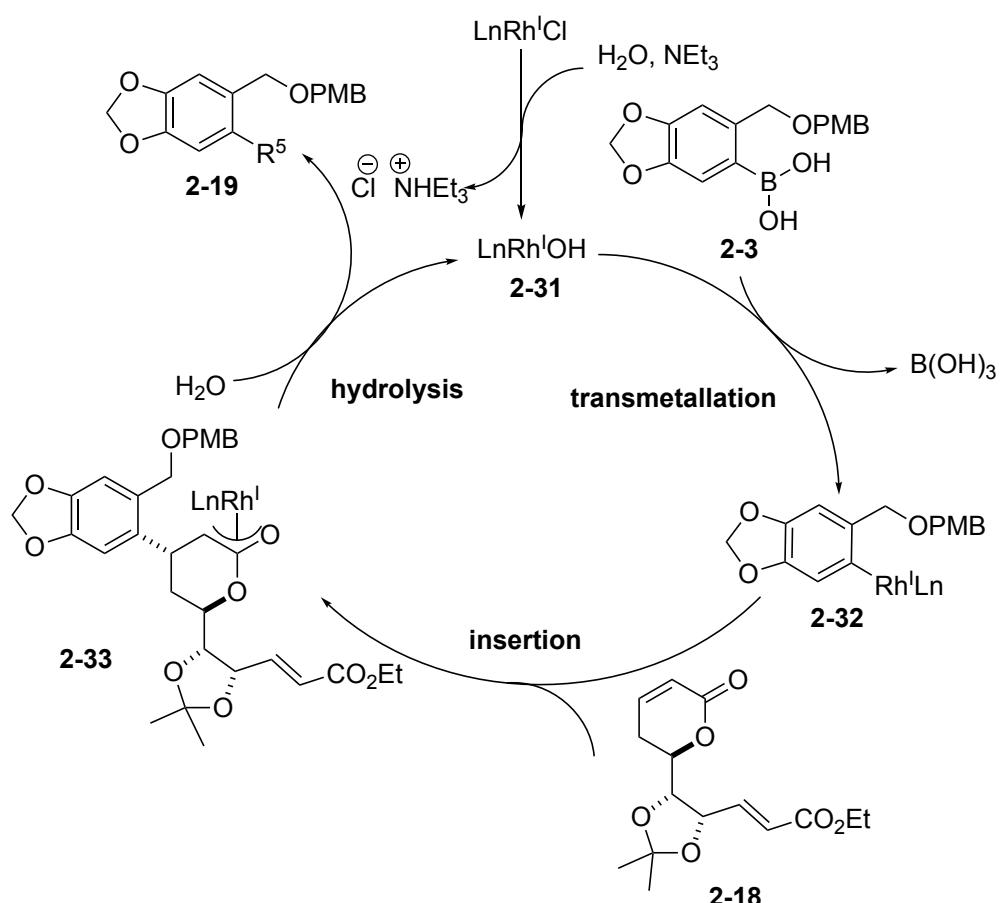
Ding, S.; Shi, Y.; Yang, B.; Hou, M.; He, H.; Gao, S. *Angew. Chem. Int. Ed.* **2023**, 62, e202214873





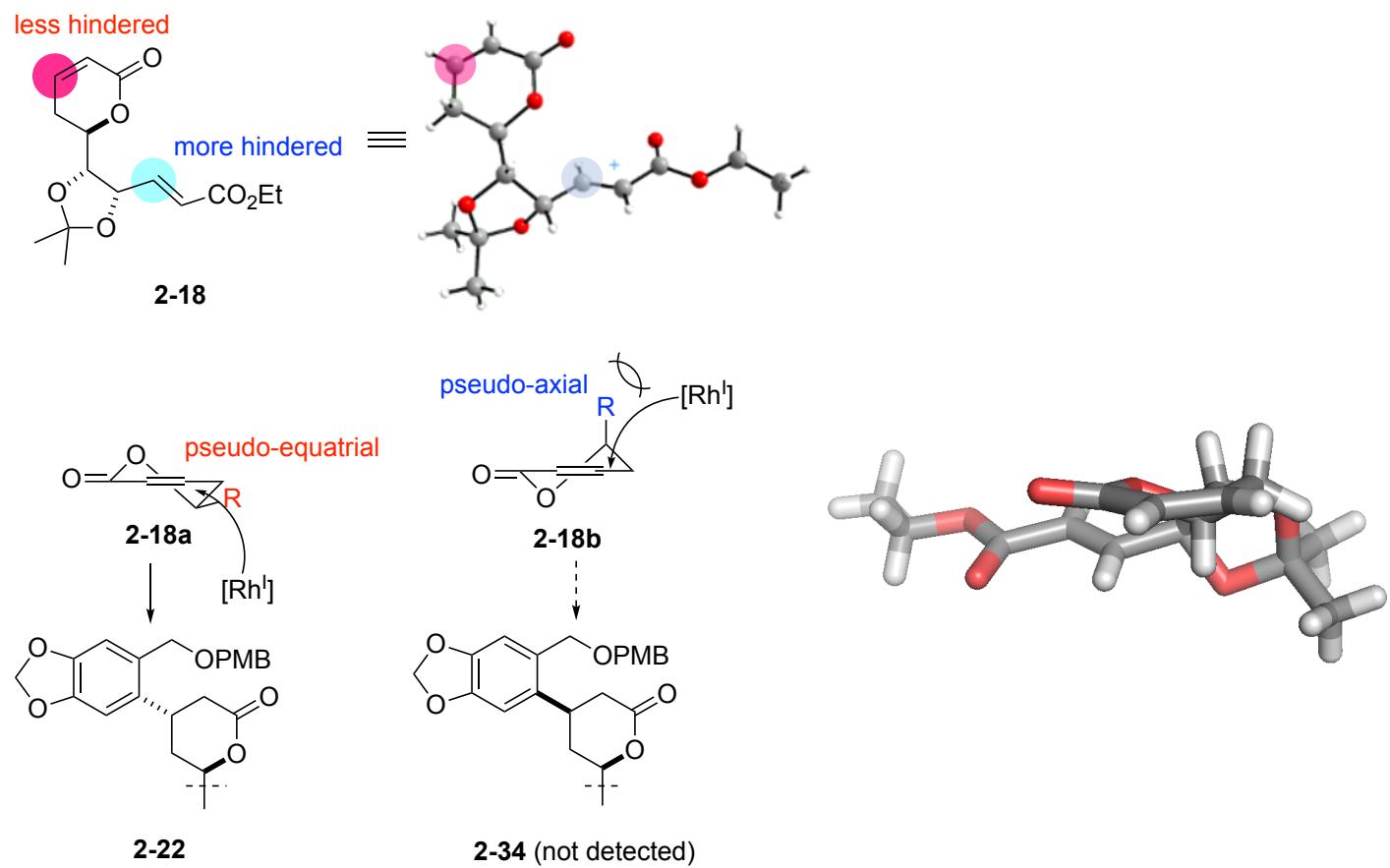
Discussion 1 -Rh-catalyzed 1,4-addition of Aryl Boronic Acid-

1-1 Proposed catalytic cycle^{ref7,8}



$\text{LnRh}^{\text{I}}\text{OH}$ complex is reported as an active intermediate for transmetalation with organoboronic acids.

1-2 Chemoselectivity and Diastereoselectivity



Discussion 2 - Ti-promoted Diels–Alder Reaction-

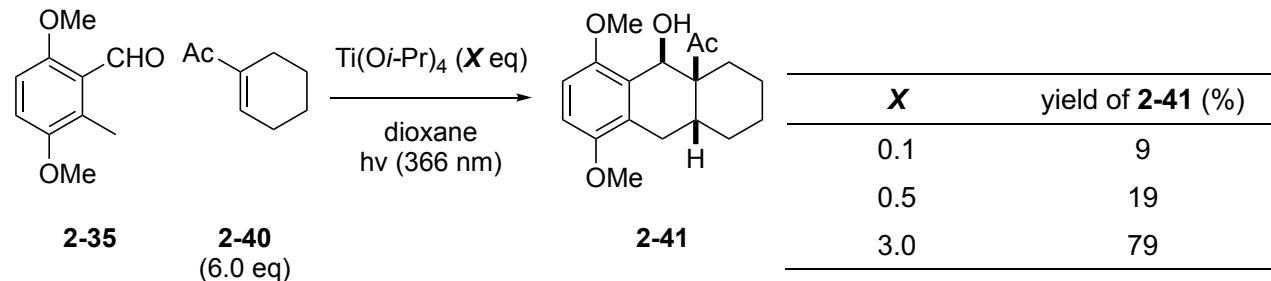
2-1 Role of $\text{Ti}(\text{O}-\text{i-Pr})_4$ ^{ref9}

- No reaction occurred without irradiation, which indicates photoenolization is crucial for the desired Diels-Alder reaction. Also, Diels-Alder reaction did not proceed without acids. This means the diene generated by photoenolization decomposed before reacting with **2-36**.

The reaction scheme shows the Diels-Alder reaction of 2,6-dimethoxybenzaldehyde (**2-35**) and cyclohexanone (**2-36**) under various conditions. Product **2-37** is formed under standard conditions, while **2-38** is formed under acidic conditions. Product **2-39** is formed when the reaction is carried out in the presence of $\text{Ti}(\text{O}-\text{i-Pr})_4$.

entry	light (nm)	acid (3.0 eq)	solvent	time (h)	yield (2-37+2-38)	yield (2-39)
1	366	none	toluene	2.0	ND	trace
2	None	$\text{Ti}(\text{O}-\text{i-Pr})_4$	dioxane	72	ND	ND
3	366	$\text{Ti}(\text{O}-\text{i-Pr})_4$	dioxane	0.5	67	3.1

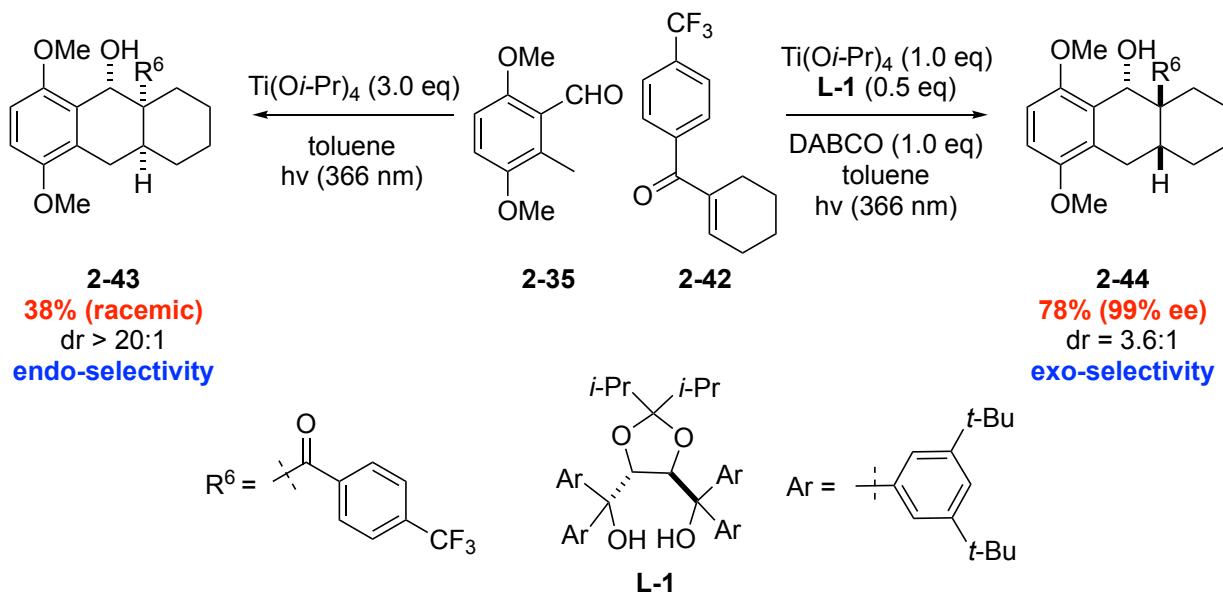
- The amount of $\text{Ti}(\text{O}-\text{i-Pr})_4$ strongly affects the yield. Stoichiometric $\text{Ti}(\text{O}-\text{i-Pr})_4$ is needed for good yields.



Considering these results, $\text{Ti}(\text{O}-\text{i-Pr})_4$ seems to form complex with dienol and dienophile and stabilizes the dienol.

2-2 Role of the chiral ligand^{ref10,11}

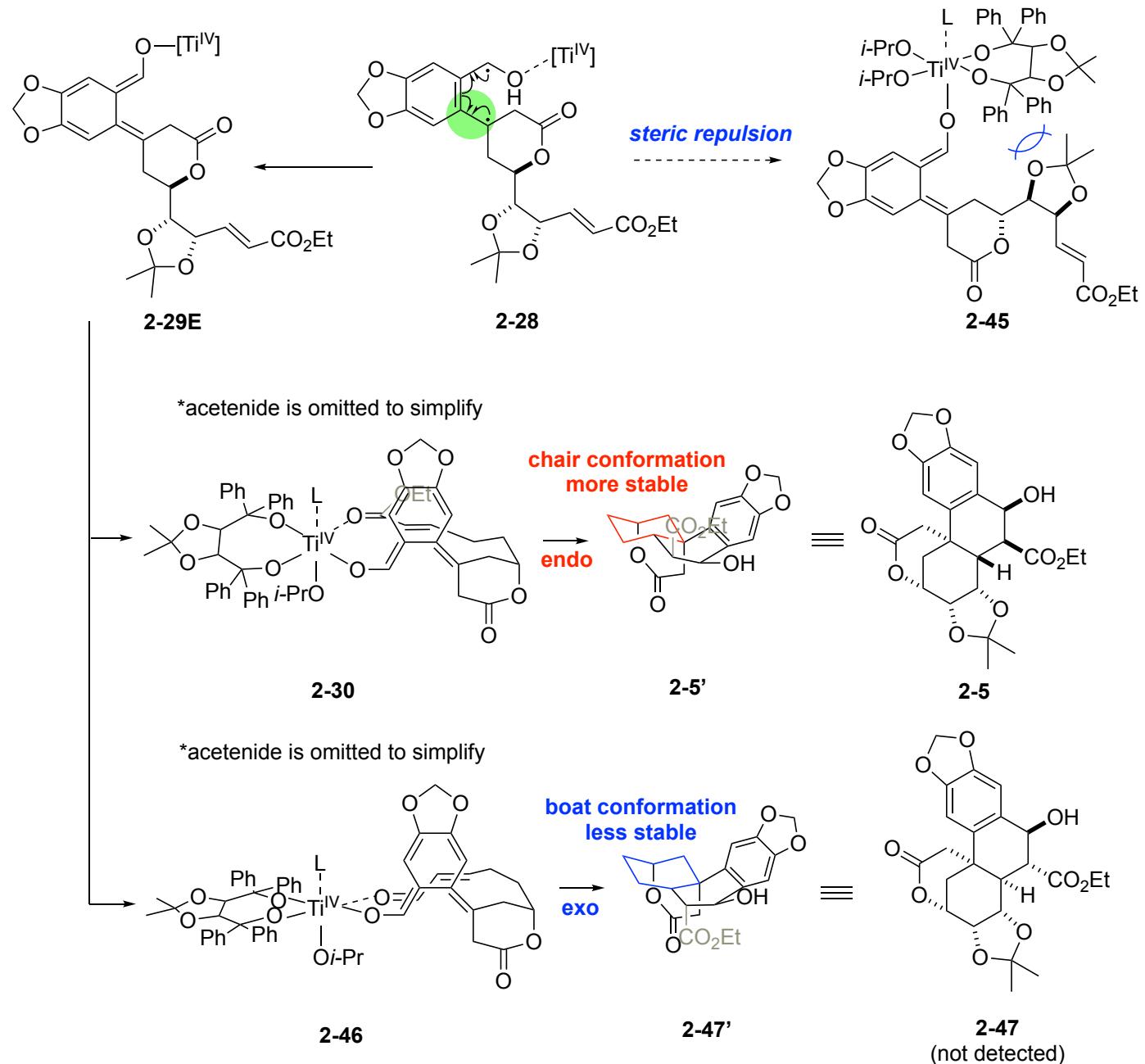
Chiral ligands can accelerate the reaction rate and control the reaction selectivity.



2-3 Selectivity on synthesis of 2-5

2-45 would not be generated due to steric repulsion between Ti complex and acetonide. This kind of limitation arising from steric repulsion is observed in other total synthesis. ^{ref12}

2 styles of dienophile approaching are possible. **2-47** should be less stable than desired **2-5** because of its boat conformation highlighted in blue, which leads **2-29E** to be converted into **2-5** only.



References: (1) Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tedrow, J. S. *Org. Lett.* **2002**, 4, 1127. (2) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, 104, 1737. (3) Li, Y.; Shao, Q.; He, H.; Zhu, C., Xue, X.; Xie, J. *Nat. Commun.*, **2022**, 13, 1 (4) Zhang, M.; Xie, J.; Zhu, C. *Nat. Commun.*, **2018**, 9, 1. (5) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, 122, 3783. (6) Haag, R.; Wirz, J.; Wagner, P. *J. Helv. Chim. Acta* **1977**, 60, 2595. (7) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, 124, 5052. (8) Sakuma, S.; Miyaura, N. *J. Org. Chem.* **2001**, 66, 8944. (9) Yang, B.; Lin, K.; Shi, Y.; Gao, S. *Nat. Commun.* **2017**, 8, 1. (10) Hou, M.; Xu, M.; Yang, B.; He, H.; Gao, S. *Chem. Sci.* **2021**, 12, 7575. (11) Hou, M.; Xu, M.; Yang, B.; He, H.; Gao, S. *Org. Lett.* **2021**, 23, 7487. (12) D. Xue.; M. Xu.; C. Zheng.; B. Yang.; M. Hou.; H. He.; S. Gao. *Chin. J. Chem.* **2019**, 37, 135.