Literature Report V

Manganese(I)-Catalyzed Enantioselective $C(sp^2)-C(sp^3)$ Bond-Forming for the Synthesis of Skipped Dienes with Synergistic Aminocatalysis

Reporter: Bao-Qian Zhao

Checker: Tong Niu

Zhao, C.; Cai, J.; Han, J.; Xie, J. *Angew. Chem. Int. Ed*. **2024**, *63*, e202400177

2024.07.01

CV of Prof. Xie Jin(谢劲)

Education & Professional Experience:

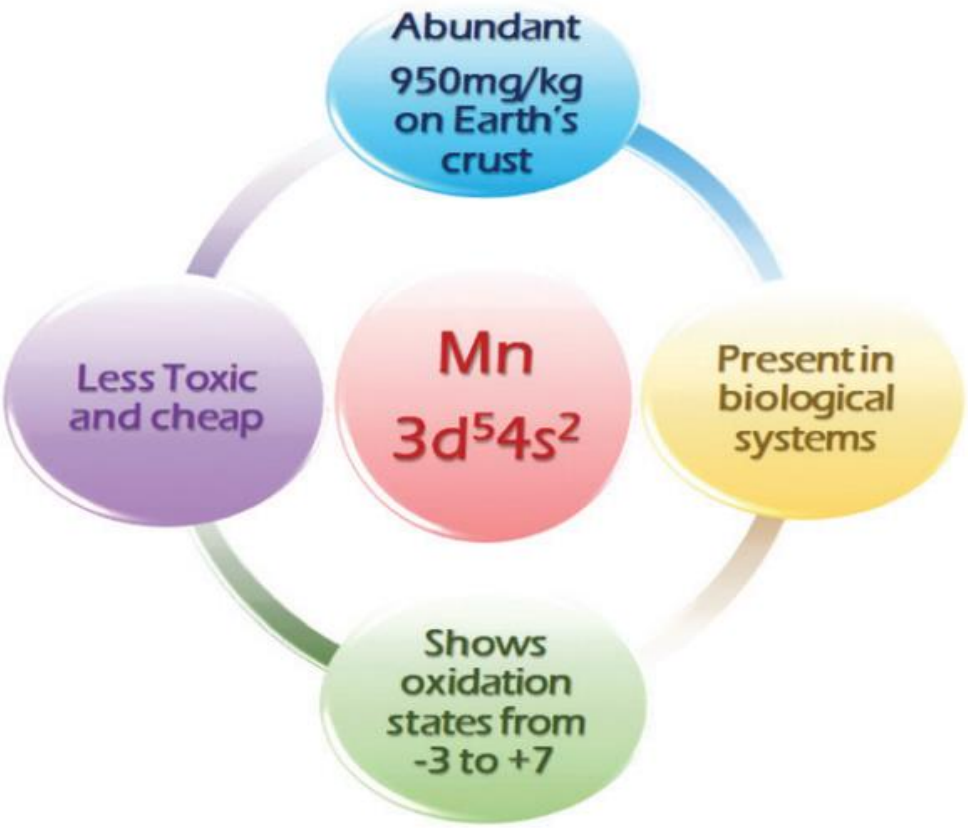
- **2004-2008** B.S., Northeast Forestry University
- **2008-2013** Ph.D., Nanjing University
- **2013-2014** Research associate, Nanjing University
- **2014-2017** Postdoc., Heidelberg University
- **2017-Present** Professor, Nanjing University

Research:

- ✓ Efficient & green synthetic methodology development
- ✓ Complex molecule synthesis and mechanistic studies
- ✓ Develop synergistic catalysis effect in organic synthesis

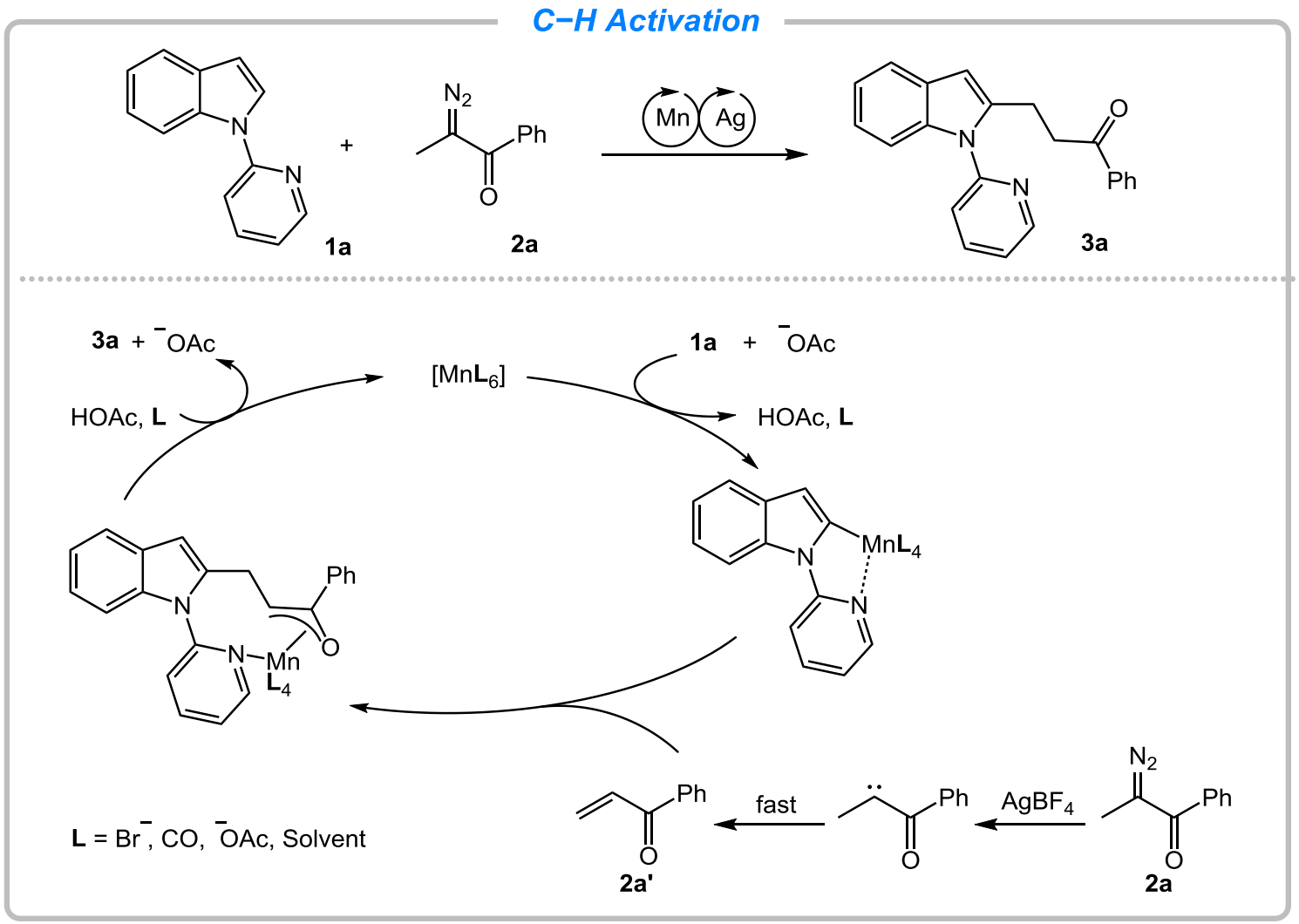
Contents

Introduction



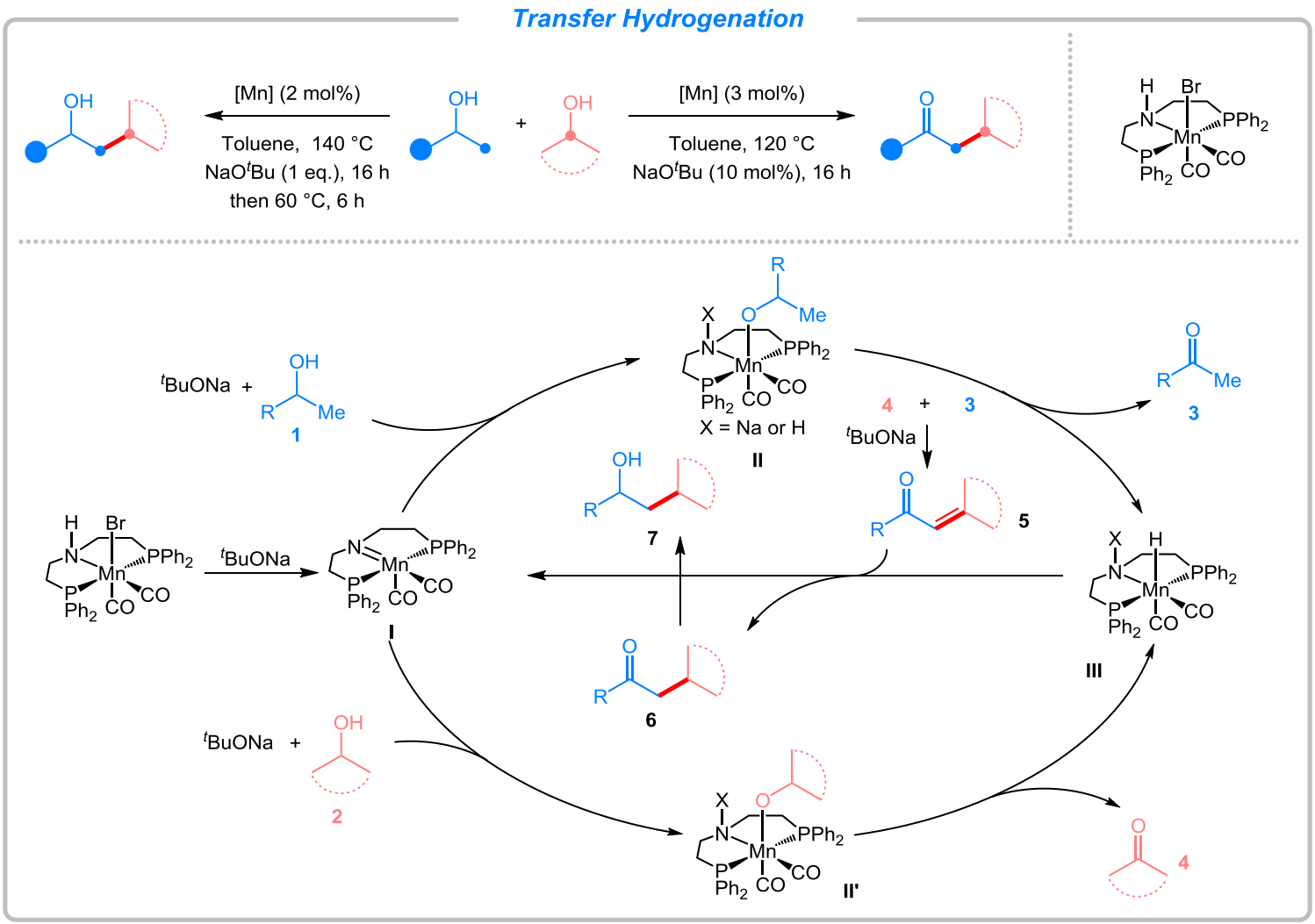
Das, K.; Waiba, S.; Jana, A.; Maji, B. *Chem. Soc. Rev*. **2022**, *51*, 4386

Introduction



Lu, Q.; Mondal, S.; Glorius, F. *Angew. Chem. Int. Ed*. **2018**, *57*, 10732

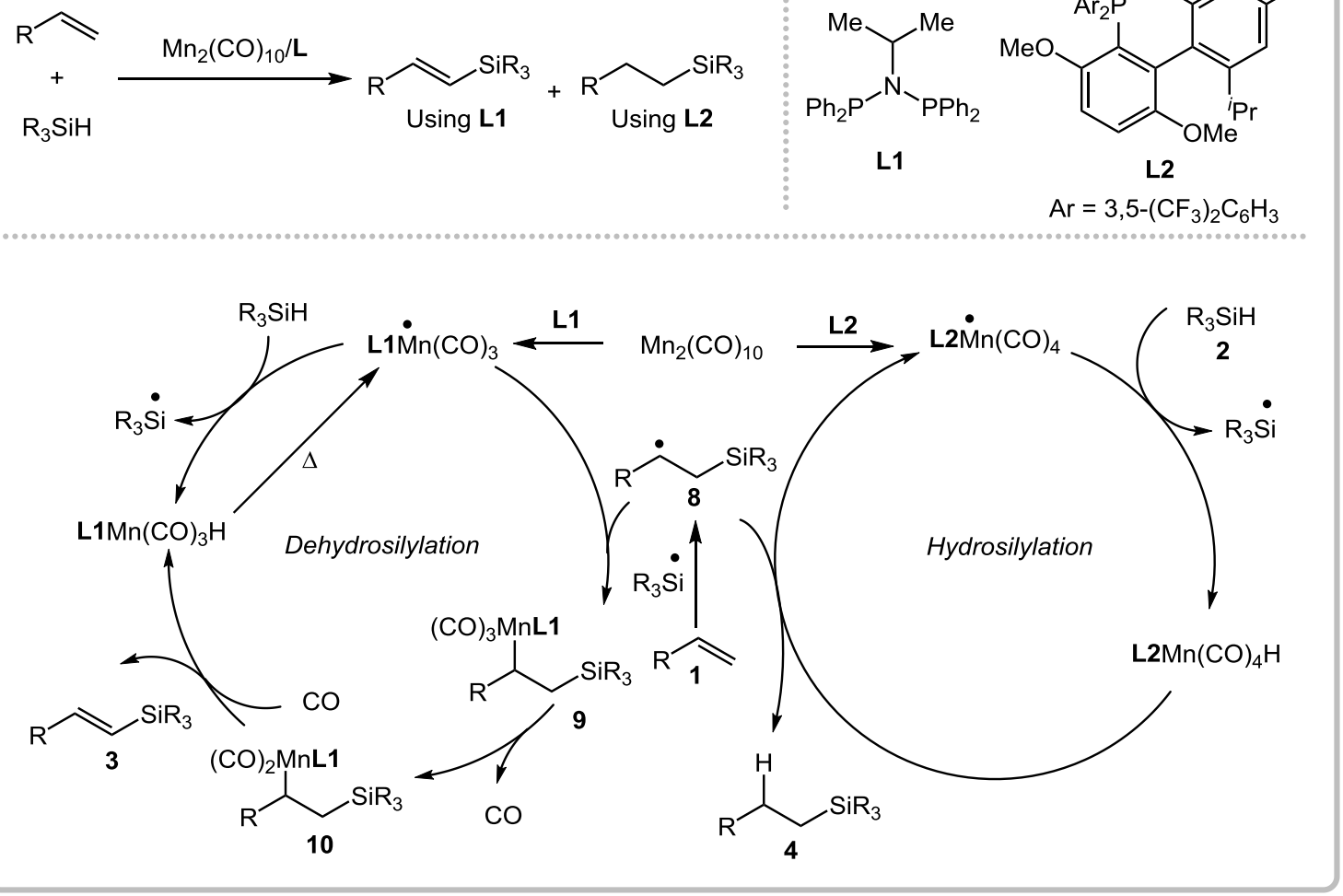
Introduction



Sun, F.; Huang, J.; Wei, Z.; Liu, W. *Angew. Chem. Int. Ed*. **2023**, *62*, e202303433

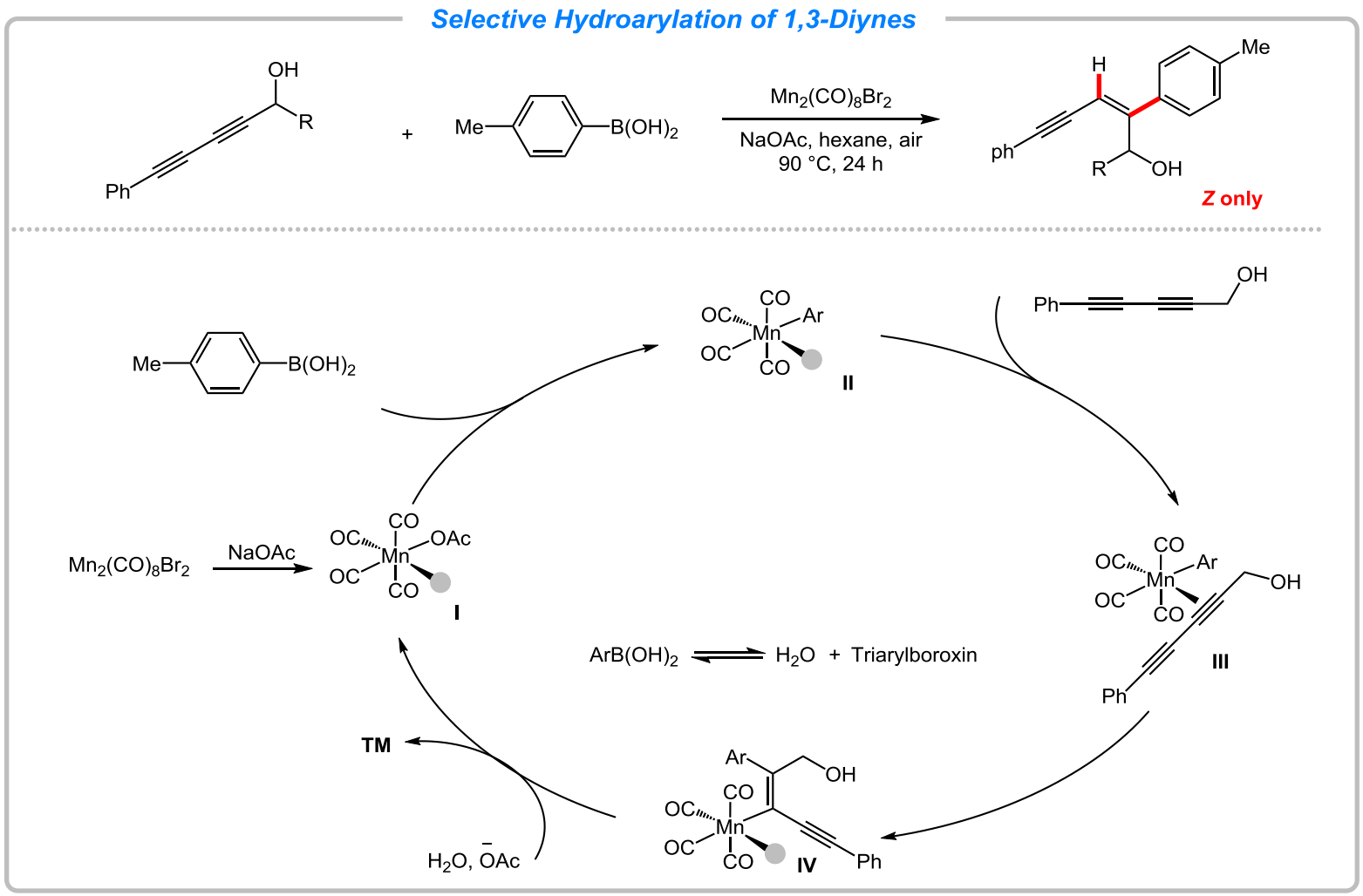
Introduction

Divergent Silylation of Alkenes



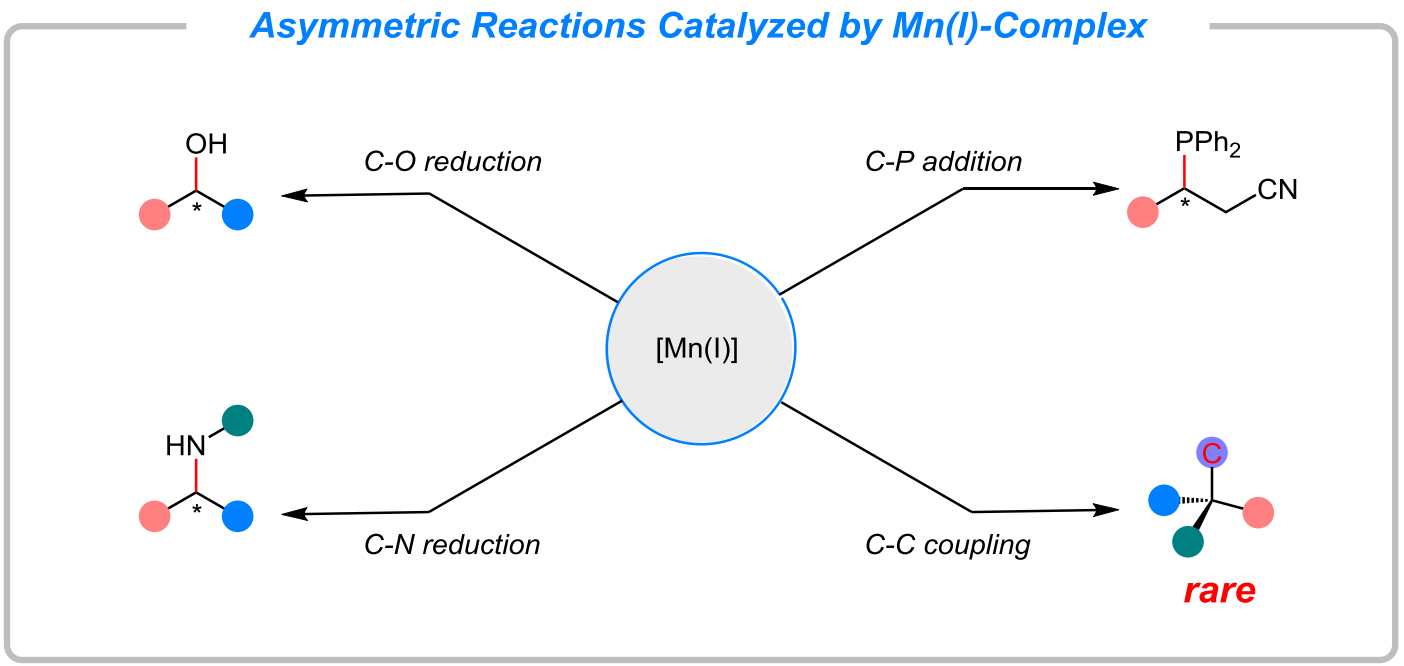
Dong, J.; Yuan, X.; Yan, Z.; Zhu, C.; Xie, J. *Nat. Chem*. **2021**, *13*, 182

Introduction



Yan, Z.; Yuan, X.; Zhao, Y.; Xie, J. *Angew. Chem. Int. Ed*. **2018**, *57*, 12906

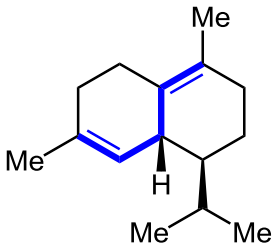
Introduction



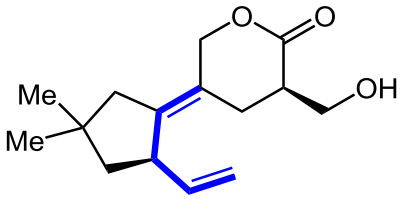
Pérez, J. M.; Ge, L.; Harutyunyan, S. R. *J. Am. Chem. Soc.* **2021**, *143*, 20071

Introduction

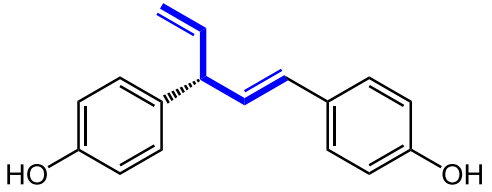
Diene Motifs in Bioactive Products



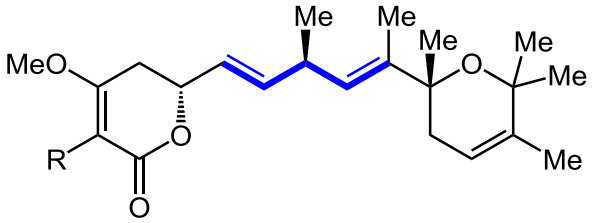
(+)-cadinene



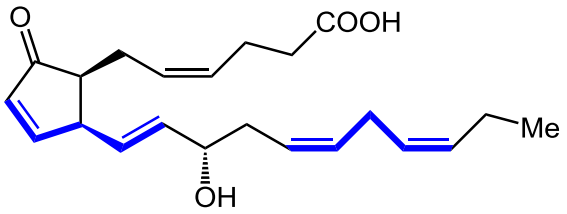
conocenolide B



(-)-Hinokiresinol



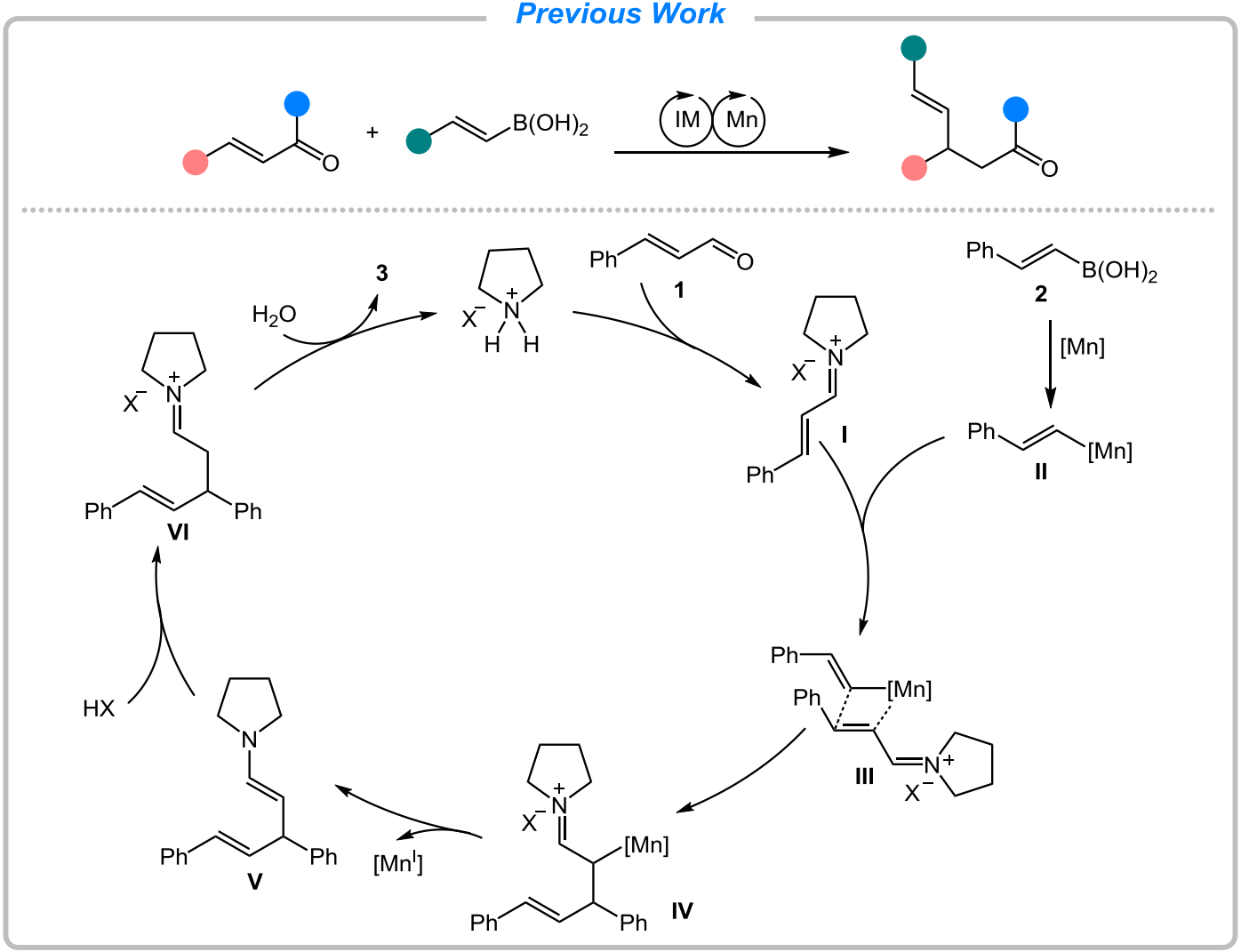
Jerangolid A



$14A_{41}$-neuroprostane

Introduction

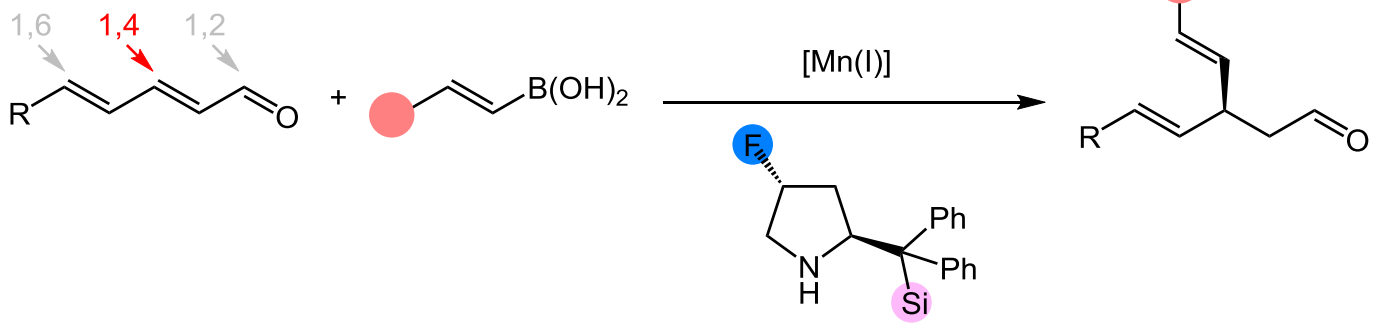
Previous Work



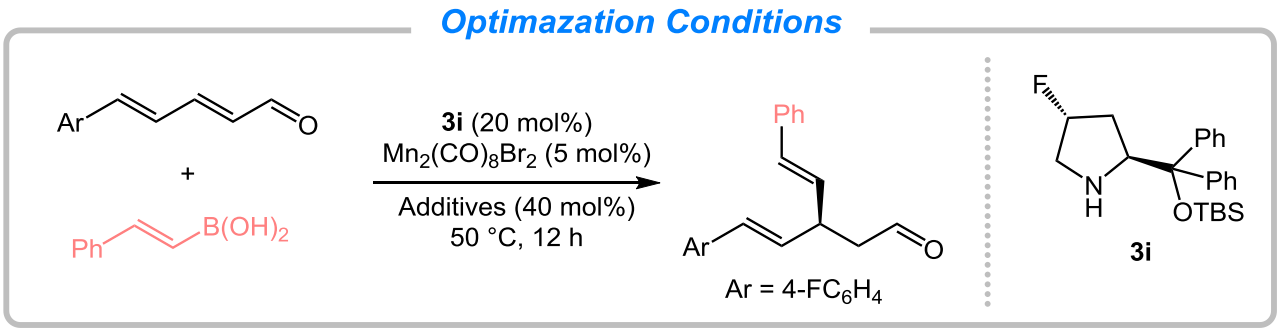
Zhao, C.; Du, C.; Guo, Z.; Xie, J. *Angew. Chem. Int. Ed*. **2023**, *62*, e202312414

Introduction

Project Synopsis



Optimazation Conditions

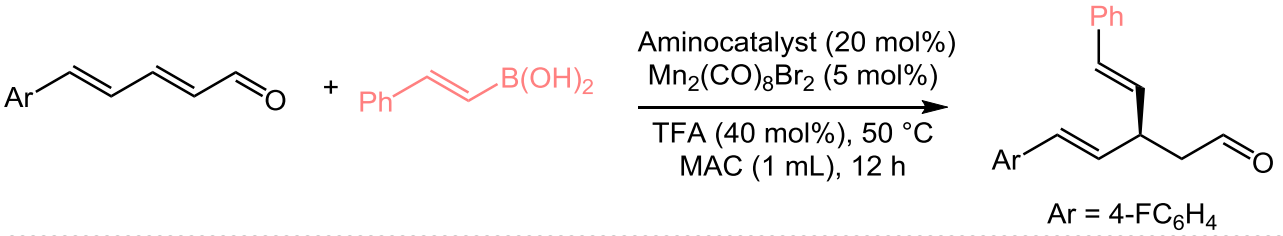


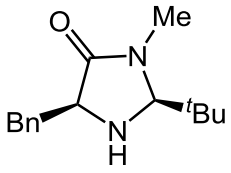
Entry	Solvent	Additives	Yield[a] (%)	*er*[b]
1	ethyl acetate	TFA	50	95:5
2	toluene	TFA	21	92:8
3	tetrahydrofuran	TFA	35	90:10
4	methyl acetate	TFA	59	95:5
5	methyl acetate	PFBA	28	94:6
6	methyl acetate	BA	33	92:8
7	methyl acetate	TSA	25	92:8
8	methyl acetate	CSA	40	91:9
9[c]	methyl acetate	TFA	ND	-
10[d]	methyl acetate	TFA	ND	-

[a] Isolated yields are shown. [b] Analyzed by HPLC on chiral columns. [c] Without **3i**. [d] Without [Mn].

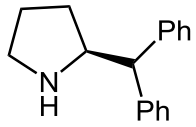
Optimazation Conditions

Optimazation Conditions



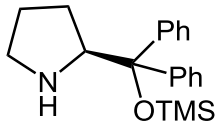


3a
yield: nd.
er: -

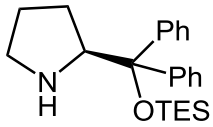


3b
yield: 65%
er: 73:27

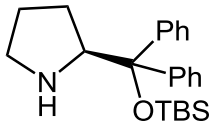
3c
yield: 59%
er: 76:24



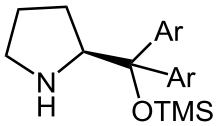
3d
yield: 49%
er: 80:20



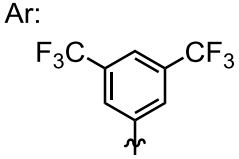
3e
yield: 55%
er: 89:11

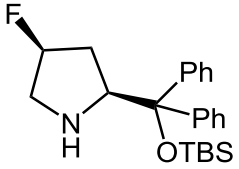


3f
yield: 51%
er: 94:6

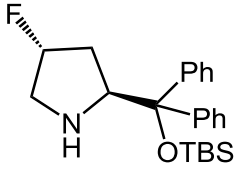


3g
yield: 53%
er: 80:20





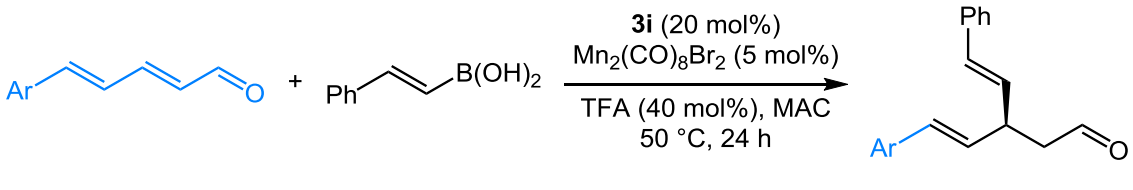
3h
yield: 48%
er: 95:5

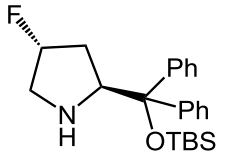


3i
yield: 59%; er: 95:5
yield: 73%; er: 95:5 (24h)

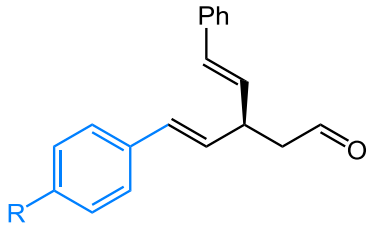
Substrate Scope

Substrate Scope of the 2,4-Dienals

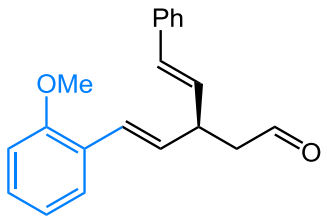




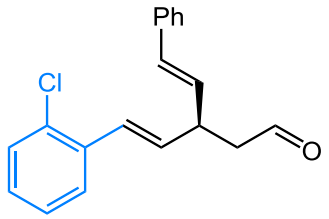
3i



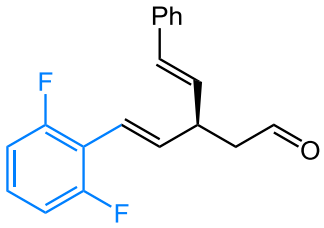
4, R = F, 73%, er: 95:5
5, R = Cl, 76%, er: 95:5
6, R = Me, 61%, er: 95:5
7, R = OMe, 58%, er: 94:6
8, R = CF_3, 65%, er: 94:6
9, R = Et, 53%, er: 95:5



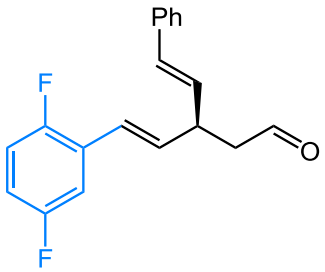
10, 65%, er: 95:5



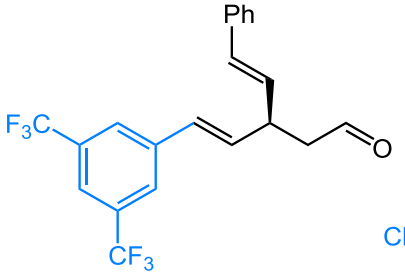
11, 53%, er: 93:7



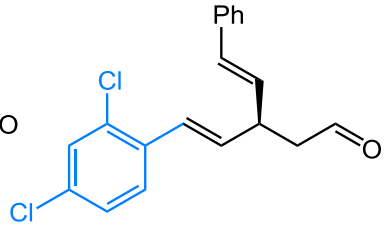
12, 56%, er: 94:6



13, 49%, er: 95:5



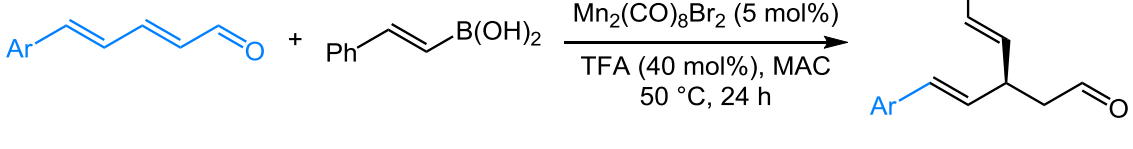
14, 51%, er: 93:7

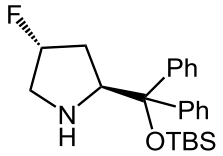


15, 63%, er: 93:7

Substrate Scope

Substrate Scope of the 2,4-Dienals





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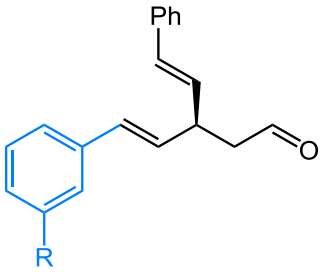
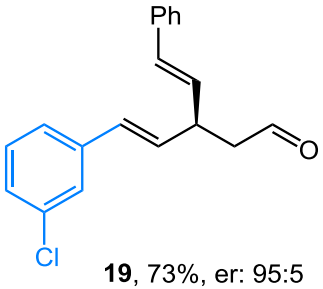
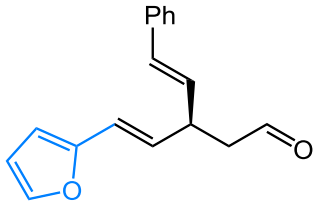


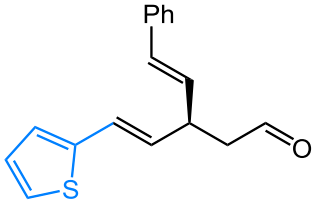
16, R = Me, 76%, er: 94:6
17, R = OMe, 68%, er: 95:5
18, R = CF_3, 52%, er: 94:6



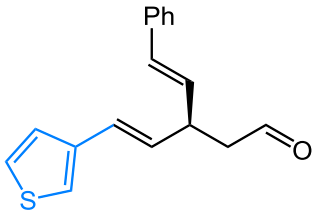
19, 73%, er: 95:5



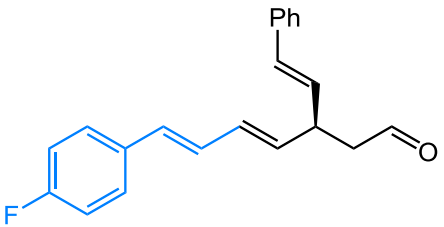
20, 59%, er: 94:6



21, 73%, er: 95:5



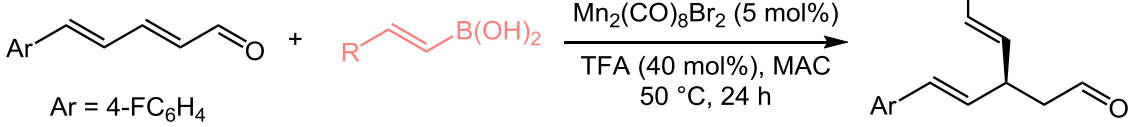
22, 78%, er: 94:6



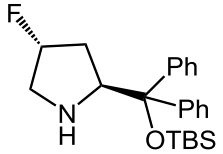
23, 58%, er: 94:6

Substrate Scope

Substrate Scope of the Alkenylboronic Acids



Ar = 4-FC_6H_4



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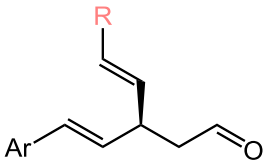
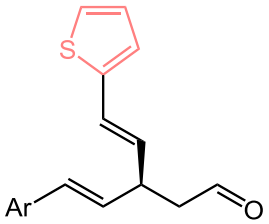
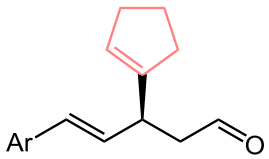


24, R = 4-BrC_6H_4, 75%, er: 92:8
25, R = 4-MeC_6H_4, 78%, er: 94:6
26, R = 4-$MeOC_6H_4$, 71%, er: 94:6
27, R = 3-ClC_6H_4, 65%, er: 95:5
28, R = 3-BrC_6H_4, 68%, er: 95:5

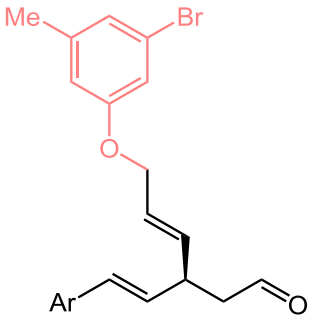
29, R =3-FC_6H_4, 58%, er: 93:7
30, R = 3-$MeOC_6H_4$, 69%, er: 95:5
31, R = 2-ClC_6H_4, 67%, er: 91:9
32, R = 2-FC_6H_4, 71%, er: 94:6
33, R = 2-MeC_6H_4, 74%, er: 95:5



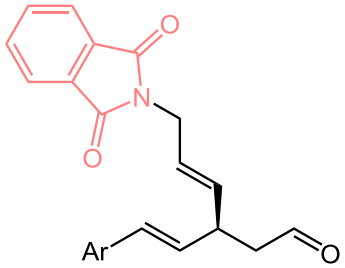
34, 72%, er: 95:5



35, 48%, er: 94:6



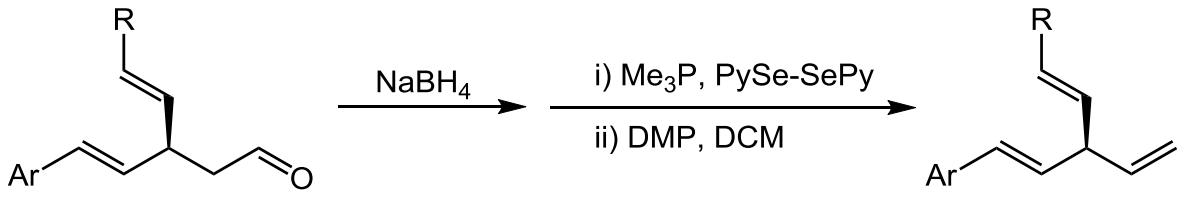
36, 58%, er: 95:5

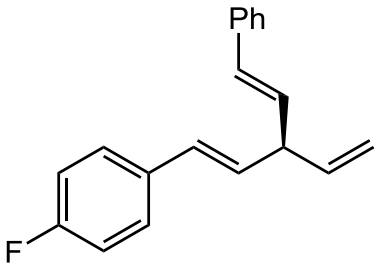


37, 58%, er: 95:5

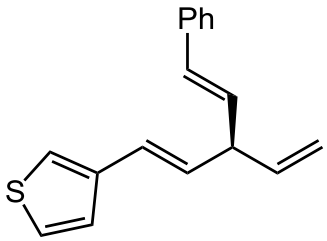
Synthetic Application

Synthetic Application

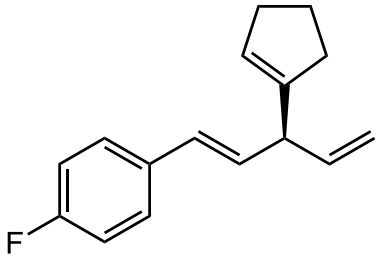




39, yield: 54%

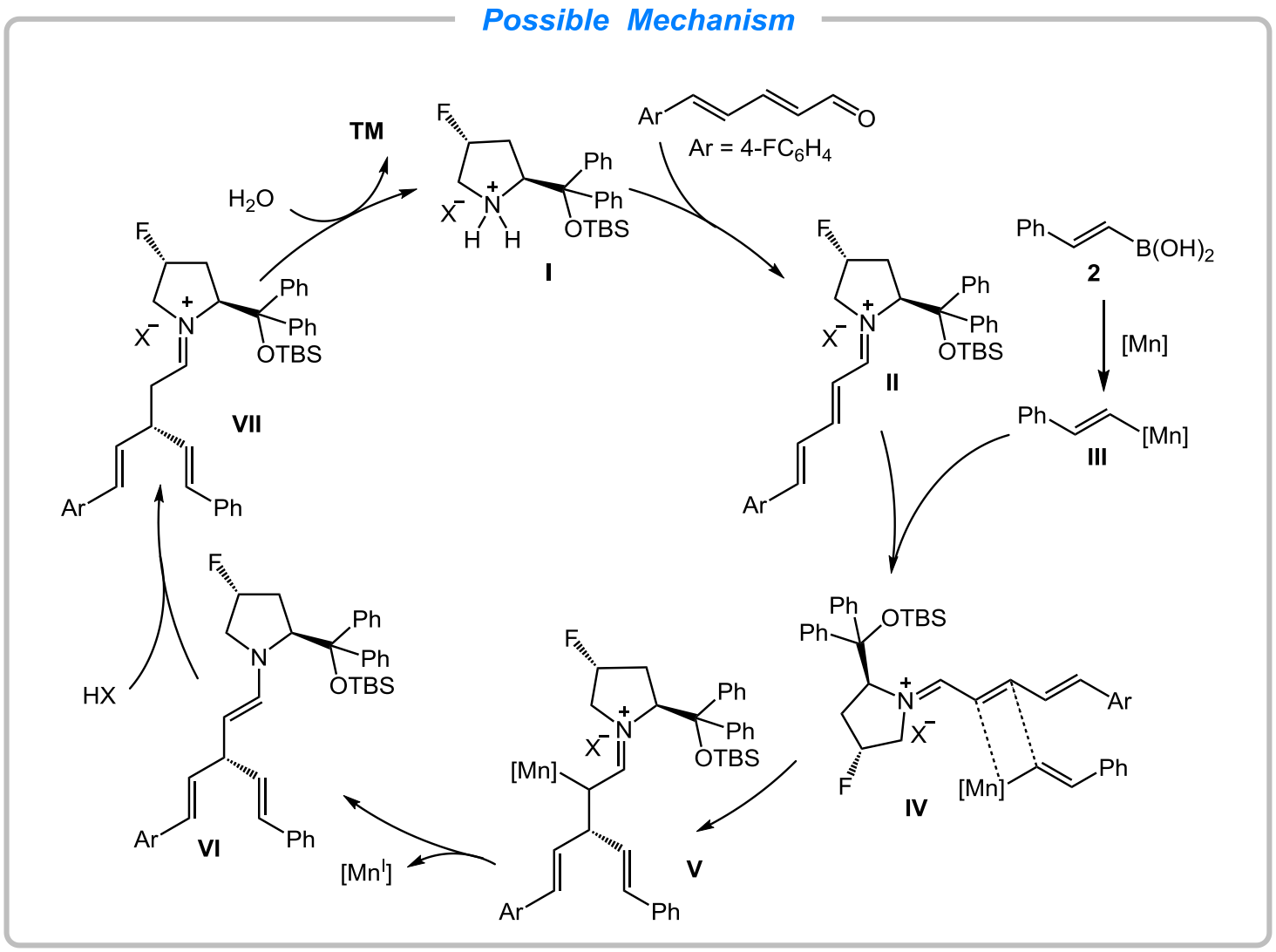


40, yield: 48%

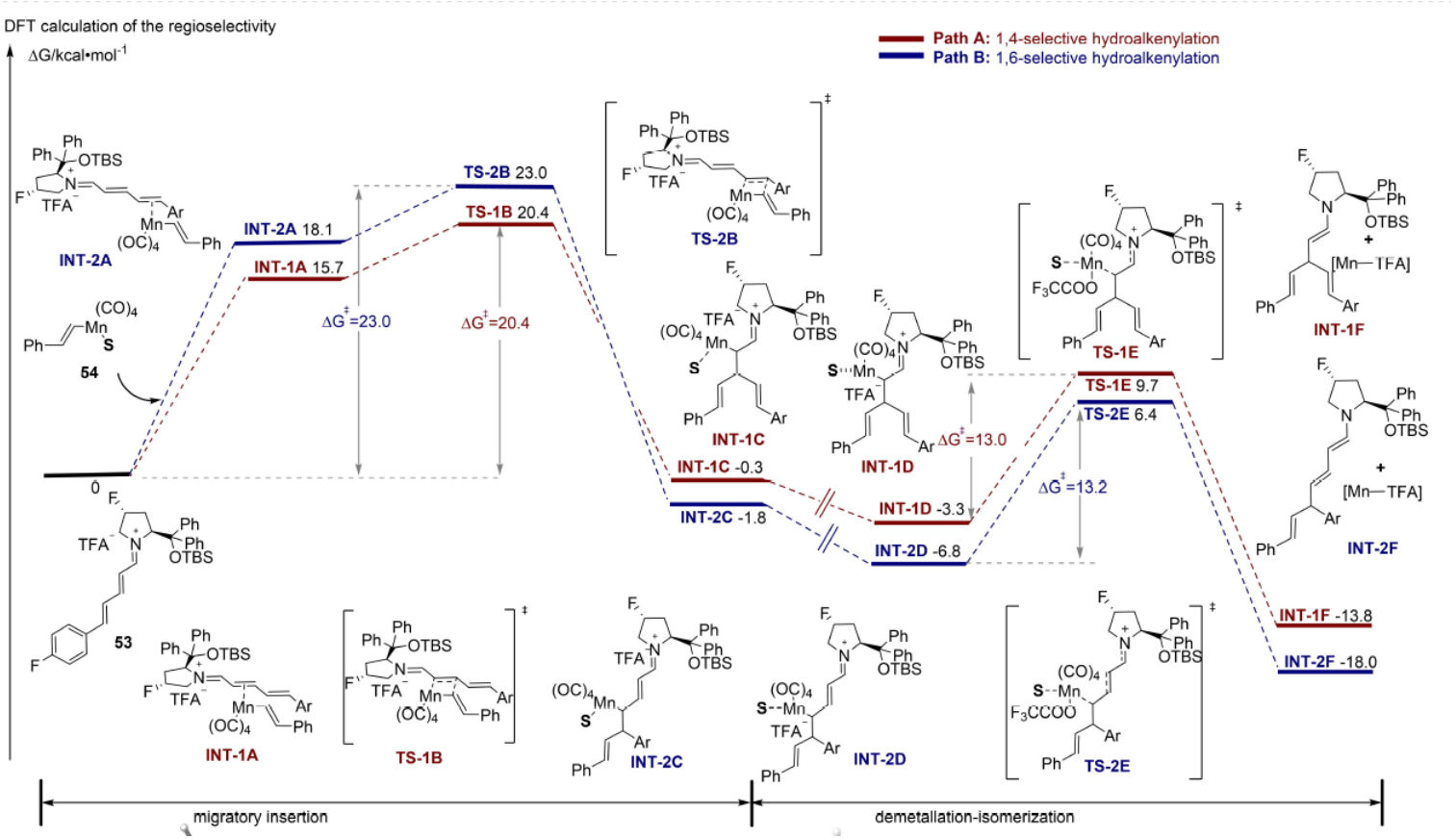


41, yield: 41%

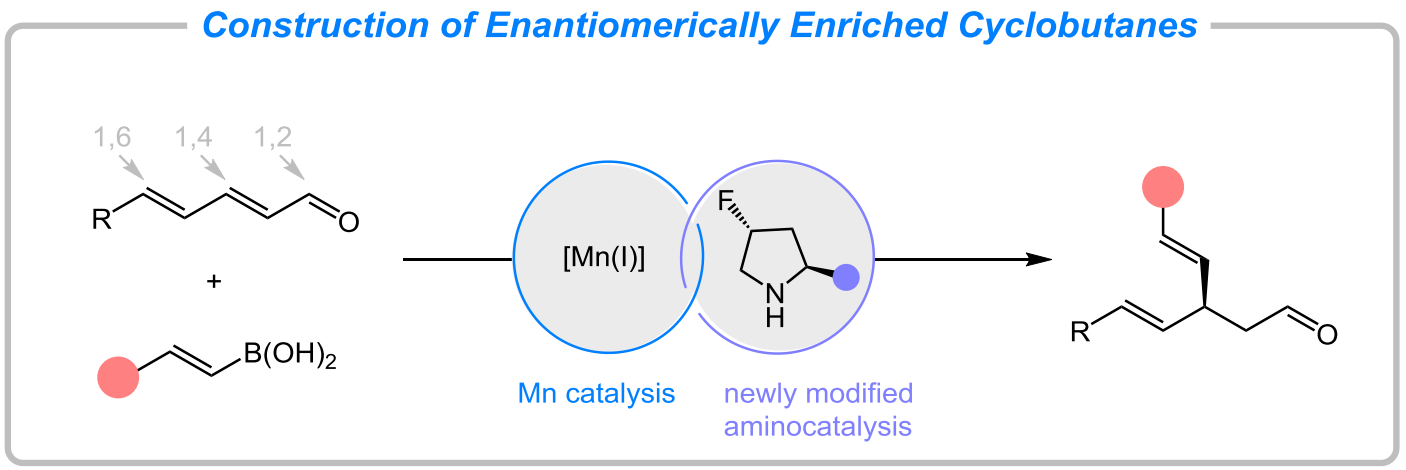
Possible Mechanism



DFT Calculation



Summary



✓ Synergistic Catalysis ✓ Exclusive Electivity ✓ Broad Substrate Scope

Writing Strategies

☐ The First Paragraph

The characteristics of manganese

✓ Manganese is constantly encountered in various living forms and plays a significant role in metabolism and antioxidant systems. It has been found to exist in multiple stable-oxidation states ranging from −3 to +7 and coordination number up to 7, making it a perfect candidate for catalysis.

Some reports about Mn(I)-catalyzed

✓ Recent explorations have extended beyond high-valent manganese catalysis to embrace manganese(I) catalysts for a plethora of valuable organic transformations. These include C−H functionalization, transfer hydrogenation and 1,2-di-functionalization of alkenes and alkynes.

Main content of this work

✓ In this paper, we have realized Mn(I)-catalyzed enantio-selective $C(sp^2)-C(sp^3)$ bond-forming with the synergistic catalysis of chiral aminocatalyst.

Writing Strategies

☐ The Last Paragraph

Summary of this work

✓ In summary, we have reported a synergistic catalytic strategy to address the great challenges in Mn(I)-catalyzed enantioselective C−C bond coupling. By merging chiral aminocatalysis and manganese(I) catalysis, highly regio- and enantio-selective 1,4-hydroalkenylation of conjugated dienals and trienals has been realized with a modified aminocatalyst.

Outlook of this work

✓ Our DFT calculations demonstrate that both 1,4- and 1,6-hydroalkenylation are thermodynamically feasible, but the former is kinetically more favorable. Furthermore, enantioselective divergent total synthesis of the analogues of (−)-Blepharocalyxin D can be achieved in four steps. The exploration of this kind of synergistic catalysis for the development of enantioselective C−C bond-forming is currently ongoing in our laboratory.

Representative Examples

- ✓ **Intriguingly** (*adv.* **有趣的是**), when the catalyst loading was decreased to 2 mol % but with an increased reaction temperature, the desired product can be obtained in a slightly decreased yield of 76 %.

- ✓ Specifically, similar yields were found for **L2** or **L3**, whereas not even traces of **4a** were found in the crude mixtures when utilizing a **L4** or /**L5** regime instead, thus showing the **subtleties** (*n*. **微妙**) of our ligand motif.

- ✓ On the other hand, the Michael-like addition process, **devoid of** (**缺乏**) the four-membered cyclic transition state as in the migratory insertion process, has a higher energy barrier of 22.3 kcal mol^{-1}.

Acknowledgement

Thanks for your attentions!