Literature Report IV

Enantioselective Inverse Electron Demand (3+2) Cycloaddition of Palladium-Oxyallyl Enabled by a Hydrogen-Bond-Donating Ligand

Reporter : Li-Xia Liu

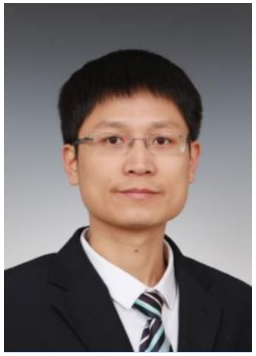
Checker : Wen-Jun Huang

Date : 2021-04-26

Zi, W. *et al. J. Am. Chem. Soc*. **2021**, *143*, 1038
Zi, W. *et al. J. Am. Chem. Soc*. **2021**, *143*, 3595

Contents

CV of Weiwei Zi



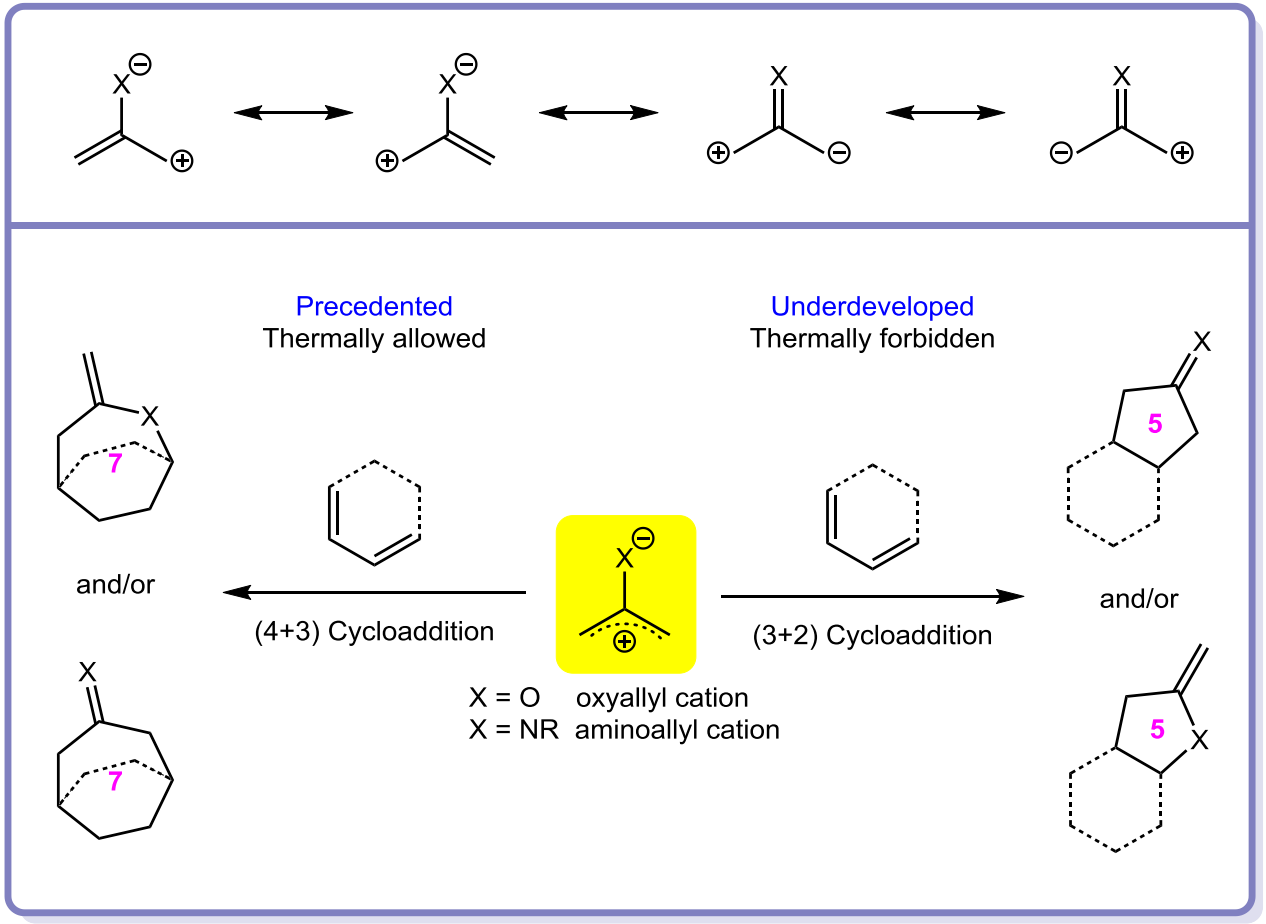
Research:

- Transition-Metal Catalysis
- Natural Products Synthesis

Education:

- **2002-2006** B.S., Lanzhou University
- **2006-2011** Ph.D., Shanghai Institute of Organic Chemistry
- **2011-2012** Assistant researcher, Shanghai Institute of Organic Chemistry
- **2012-2016** Postdoc., University of California at Berkeley
- **2016-now** Professor, Nankai University

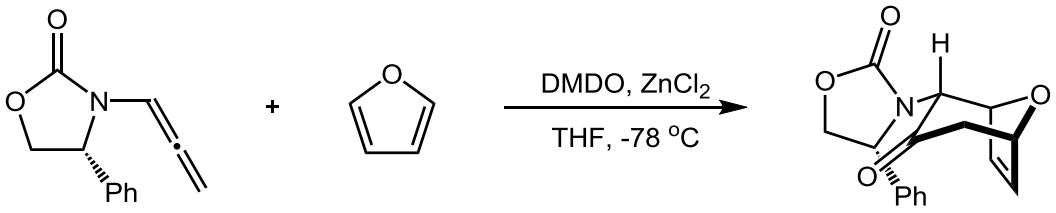
Introduction



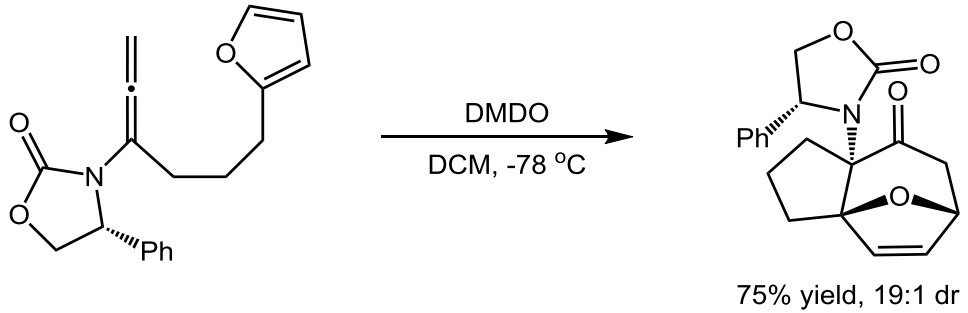
Zi, W. *et al. J. Am. Chem. Soc*. **2021**, *143*, 1038
Trost, B. M. *et al. Angew. Chem. Int. Ed.* **2019**, *58*, 6396

Introduction

◆ (4+3) cycloaddition



Hsung, R. P. *et al. J. Am. Chem. Soc.* **2001**, *123*, 7174



Hsung, R. P. *et al. Angew. Chem. Int. Ed.* **2004**, *43*, 615

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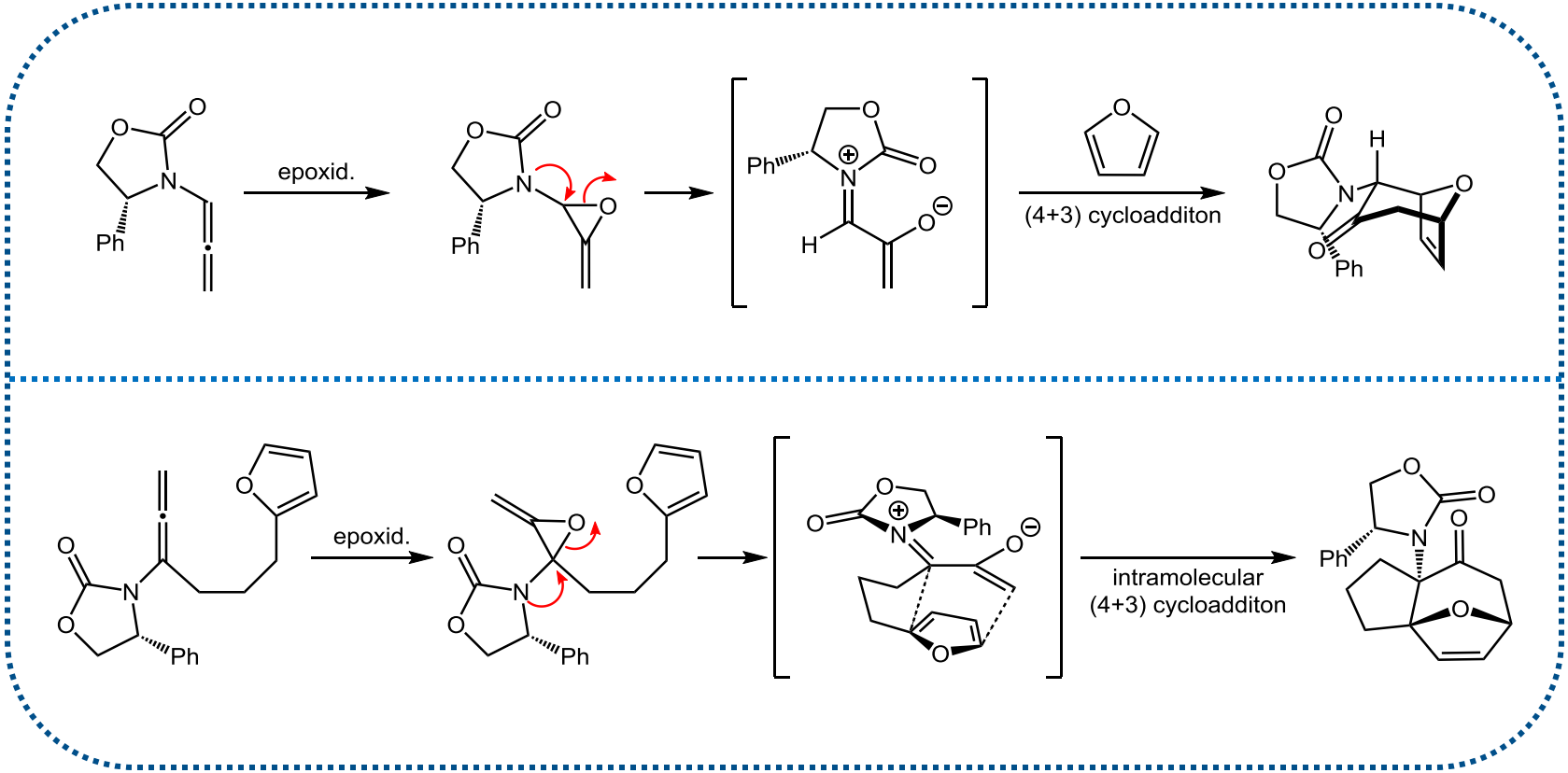
◆ Proposed mechanism



Hsung, R. P. *et al. Angew. Chem. Int. Ed.* **2004**, *43*, 615

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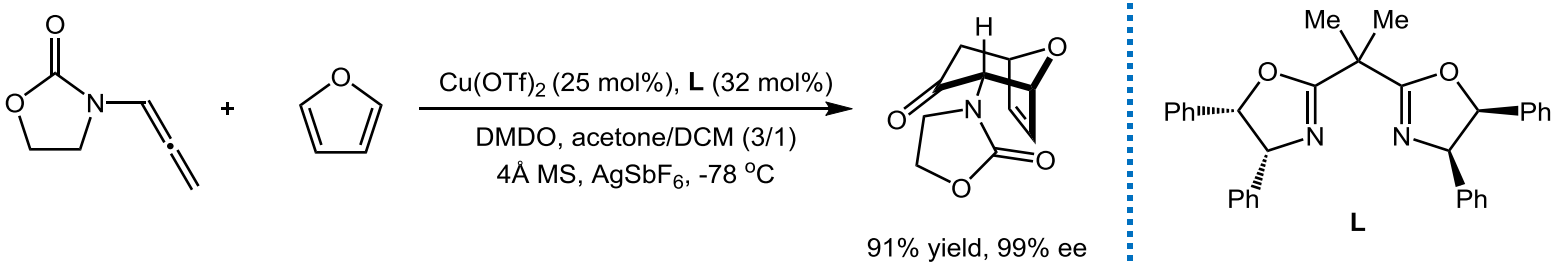
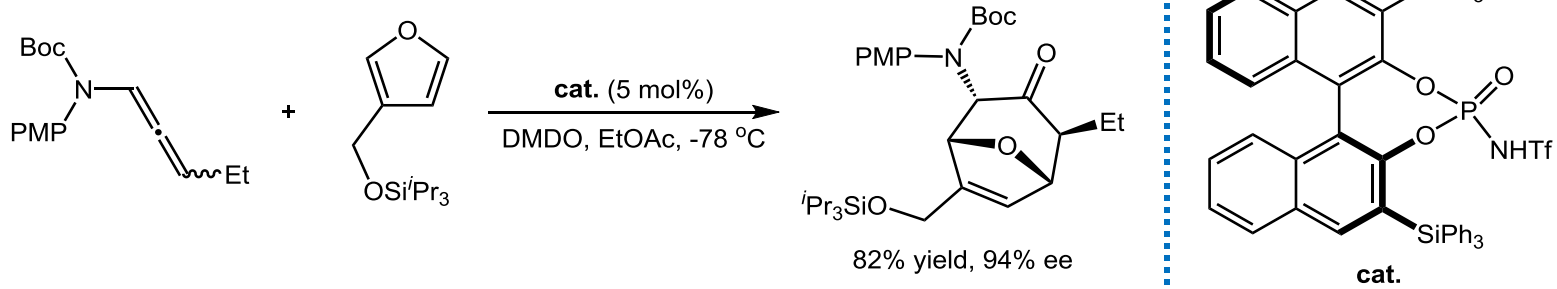
◆ (4+3) cycloaddition



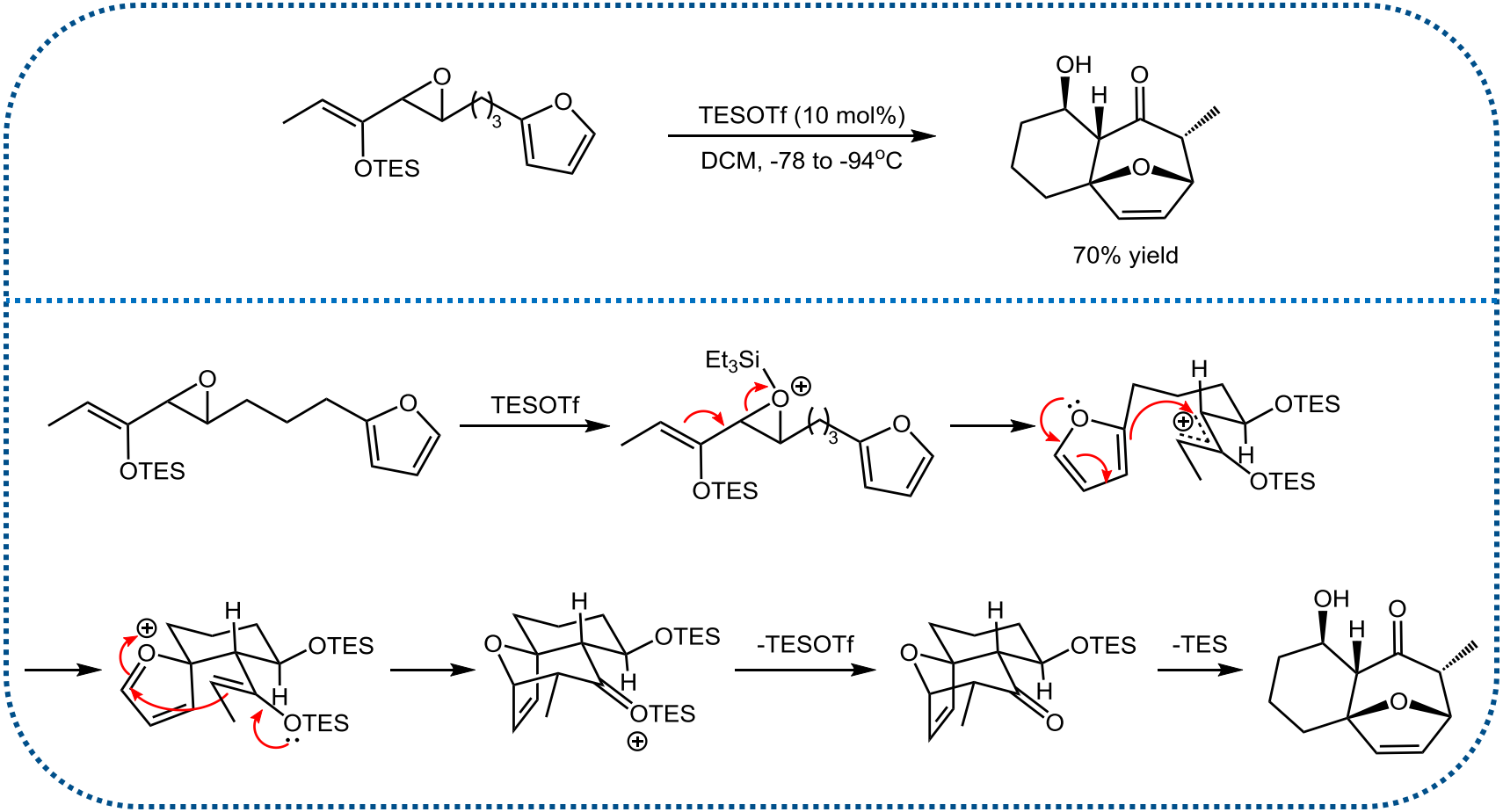
Hsung, R. P. *et al. J. Am. Chem. Soc.* **2005**, *127*, 50



Vicario, J. L. *et al. Angew. Chem. Int. Ed.* **2017**, *56*, 10535

Introduction

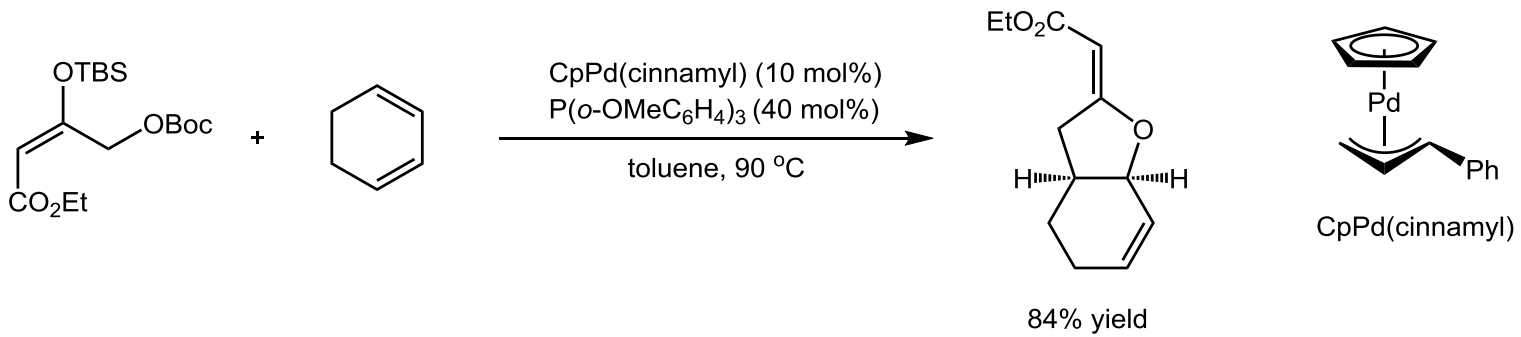
◆ (4+3) cycloaddition

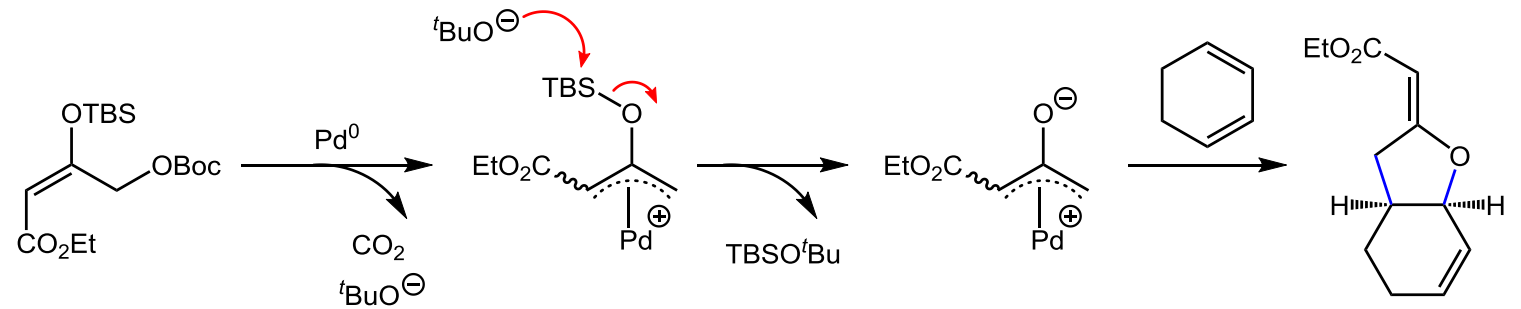


Chiu, P. *et al. J. Am. Chem. Soc.* **2009**, *131*, 4556

Introduction

◆ (3+2) Pd-oxyallyl cycloaddition





Trost, B. M. *et al. Science* **2018**, *362*, 564

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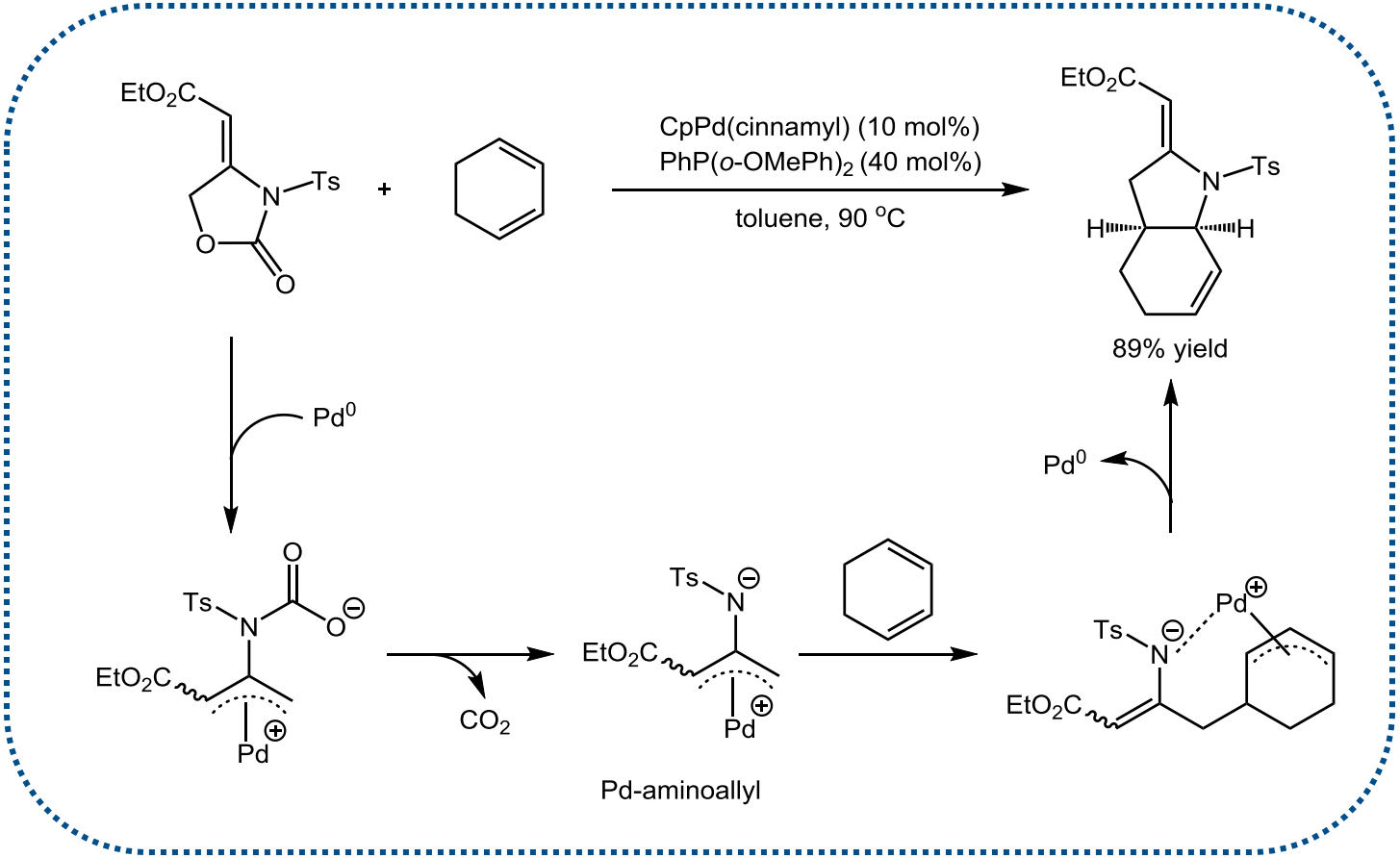
◆ (3+2) Pd-aminoallyl cycloaddition



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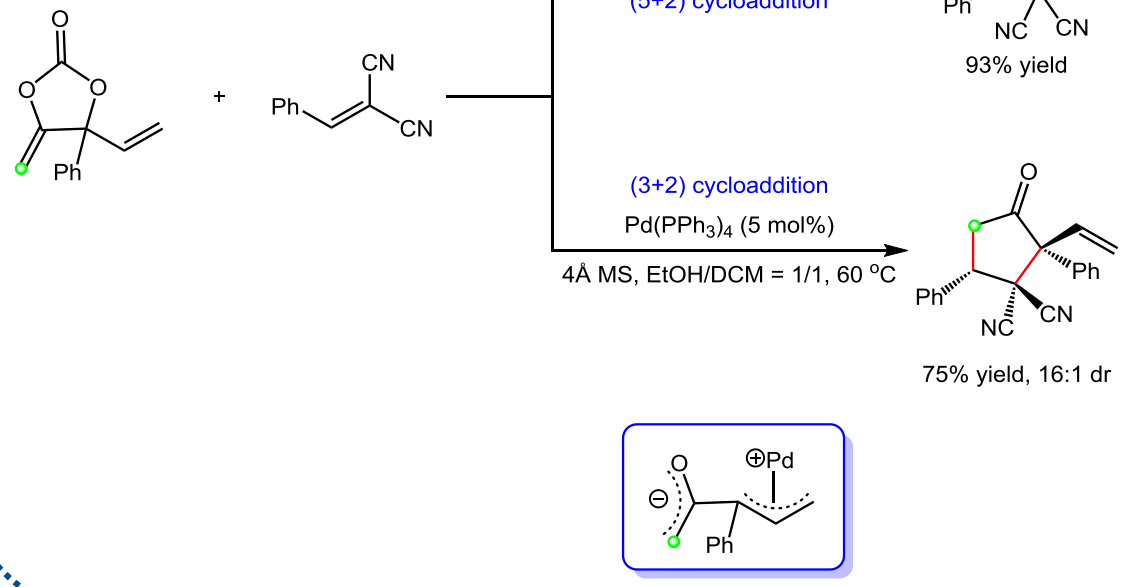
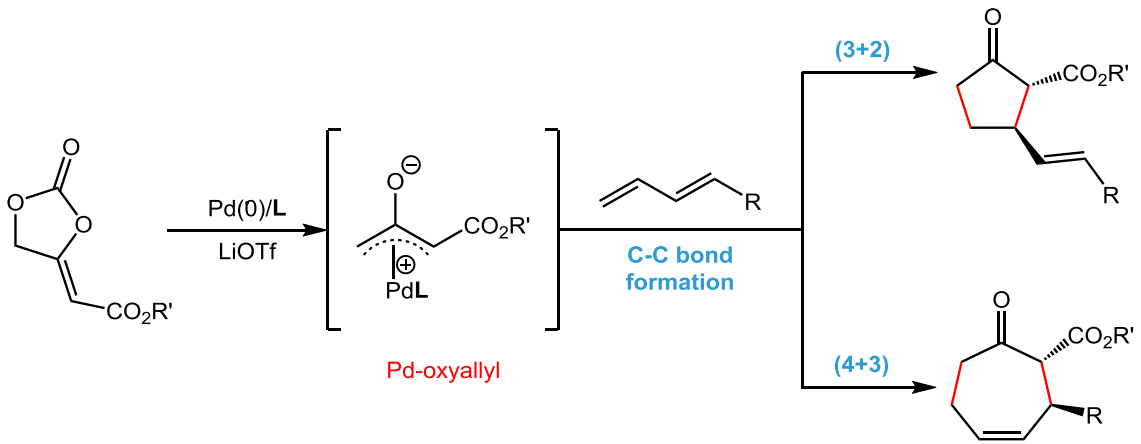


Guo, W. *et al. Org. Lett.* **2021**, *23*, 351

Regiodivergent Cycloaddition of Pd-Oxyallyl



- **Lewis acid-promoted C-C bond formation**
- **Ligand-controlled regiodivergent (3+2) and (4+3) cycloadditions**

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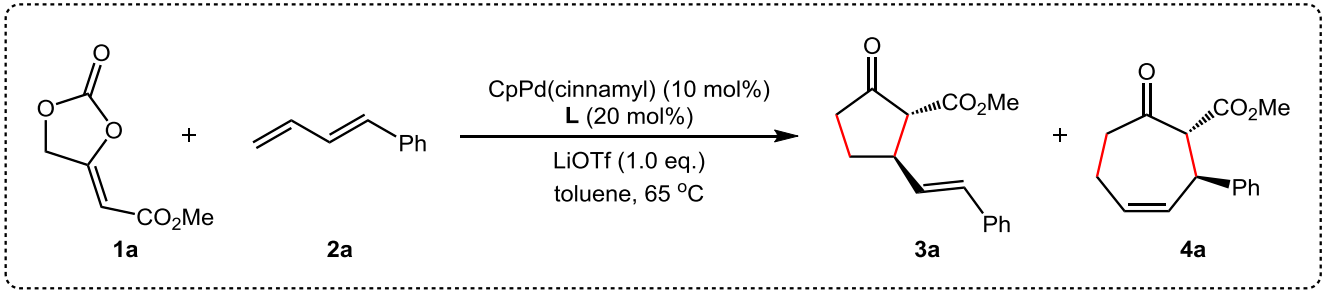
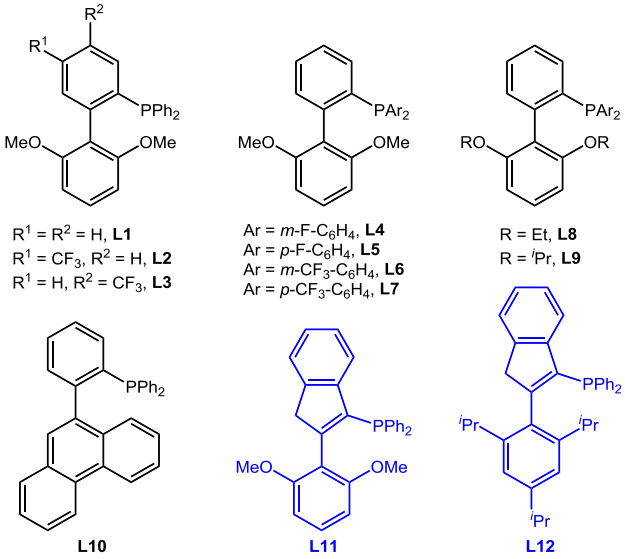
Optimization of the Reaction Conditions

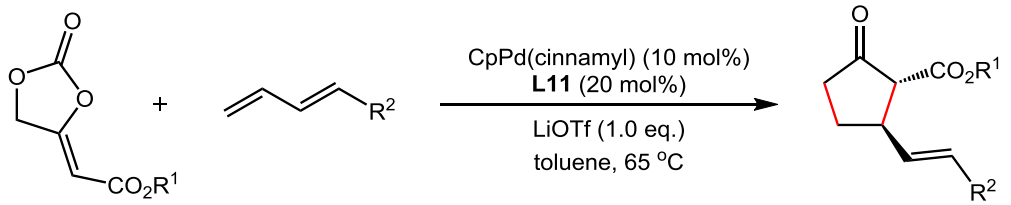


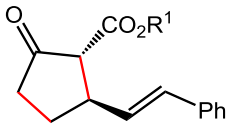
entry[a]	L	3a:4a	yield of **3a** (%)	yield of **4a** (%)
1	**L1**	5.8:1	58	10
2	**L2**	1:3.6	5	18
3	**L3**	1:4.8	5	24
4	**L4**	3.2:1	55	17
5	**L5**	>20:1	64	<5
6	**L6**	1:1.6	21	33
7	**L7**	1.1:1	39	35
8	**L8**	>20:1	60	<5
9	**L9**	1:4.3	10	43
10	**L10**	1:1.9	24	46
11	**L11**	>20:1	92	<5
12[b,c]	**L12**	1:4.3	17	73



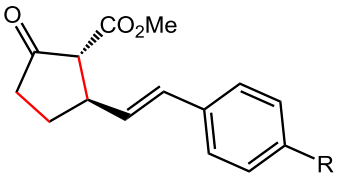
[a]Reaction conditions, unless otherwise noted: **1a** (0.1 mmol), **2a** (0.2 mmol), CpPd(cinnamyl) (10 mol %), **L** (20 mol %), toluene (3.5 mL), 65 °C, 48 h. The yield was determined by ^{1}H NMR analysis with an internal standard. [b]The amount of **L12** was 25 mol%. [c]Ph_3PO (2 mol%) was added.

Substrate Scope of (3+2) Cycloaddition

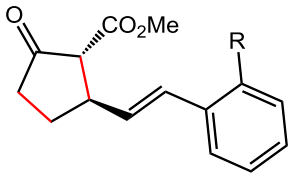




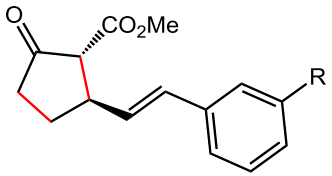
3a, R^1 = Me, 89%
3b, R^1 = Et, 69%



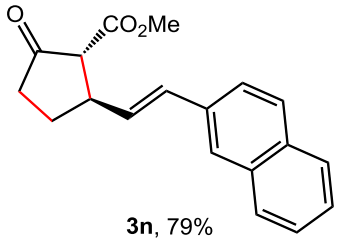
3c, R = F, 78%
3d, R = Cl, 33%
3e, R = CF_3, 56%
3f, R = CO_2Me, 59%
3g, R = NO_2, 40%
3h, R = OMe, 84%
3i, R = Me, 69%, rr = 6.4:1



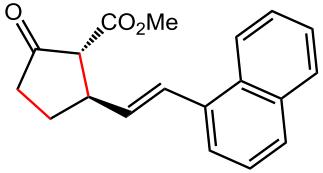
3j, R = F, 73%
3k, R = Me, 42%, rr = 4.3:1



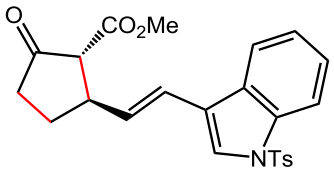
3l, R = Me, 79%
3m, R = F, 76%



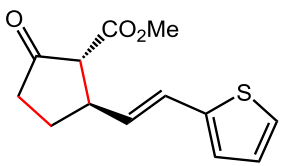
3n, 79%



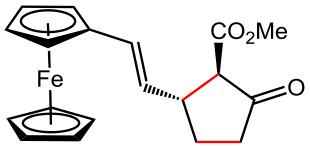
3o, 61%, rr = 6.3:1



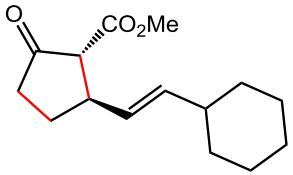
3p, 69%



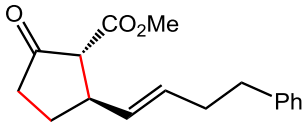
3q, 65%



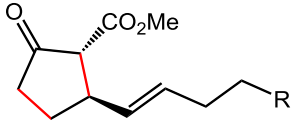
3r, 59%



3s, 54%

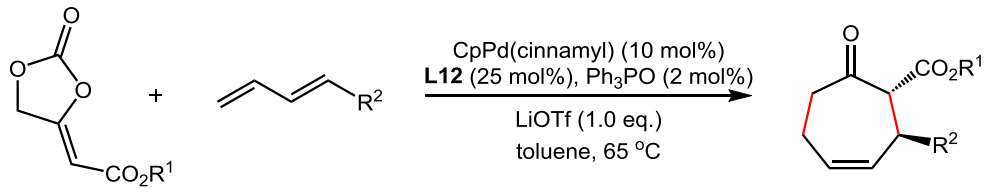


3t, 58%

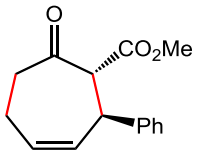


3u, R = OAc, 61%
3v, R = OTBS, 61%

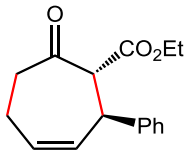
Substrate Scope of (4+3) Cycloaddition



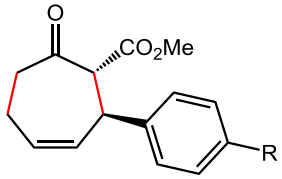
1 **2** **4**
dr >20:1



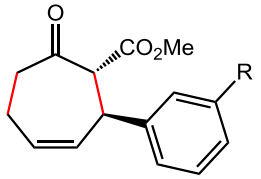
4a, 66%, rr = 4.3:1



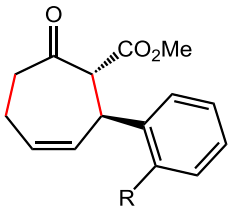
4b, 62%, rr = 3.6:1



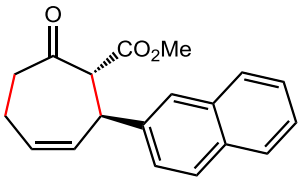
4c, R = F, 72%, rr = 5.6:1
4d, R = CF_3, 50%, rr = 4:1
4e, R = Me, 55%, rr = 3.5:1



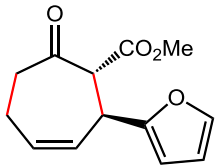
4f, R = Me, 45%, rr = 3.2:1
4g, R = F, 55%, rr = 3.5:1



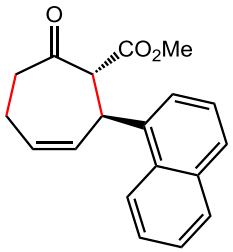
4h, R = F, 40%, rr = 3:1
4i, R = Me, 55%, rr = 9.5:1



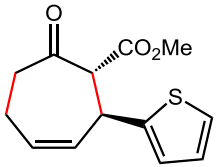
4j, 64%, rr = 3.7:1



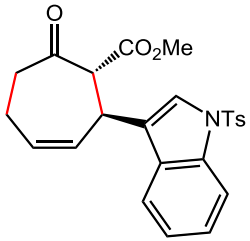
4k, 40%, rr = 5:1



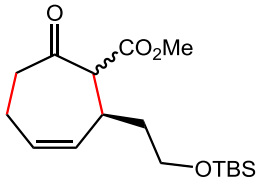
4l, 61%, rr = 6.8:1



4m, 47%, rr = 5.5:1

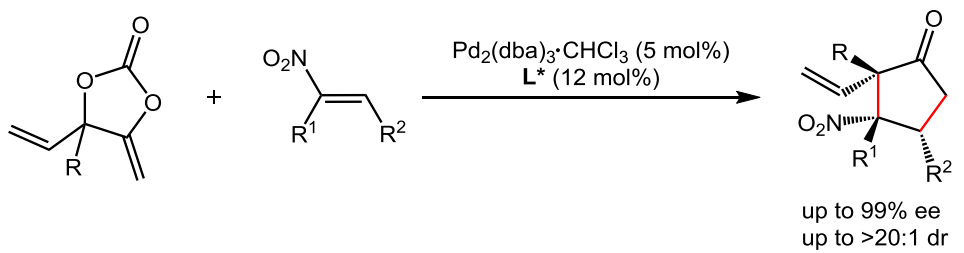


4n, 60%, rr = 4.8:1



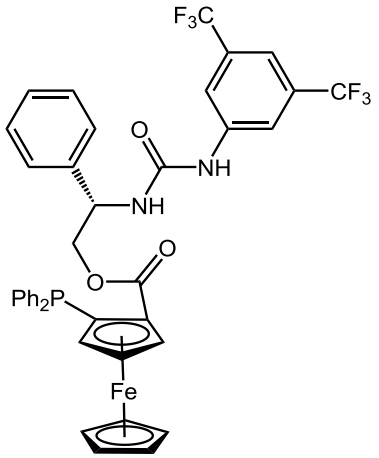
4o, 45%, dr = 2.2:1, rr = 2.7:1

(3+2) Cycloaddition of Palladium-Oxyallyl



up to 99% ee
up to >20:1 dr

- **Inverse electron demand cycloaddition reaction**
- **Enantioselective and diastereoselective**
- **Newly developed hydrogen-bond-donating ligand**



L*
(*S,Rp*)-Ph-**FeUrPhos**

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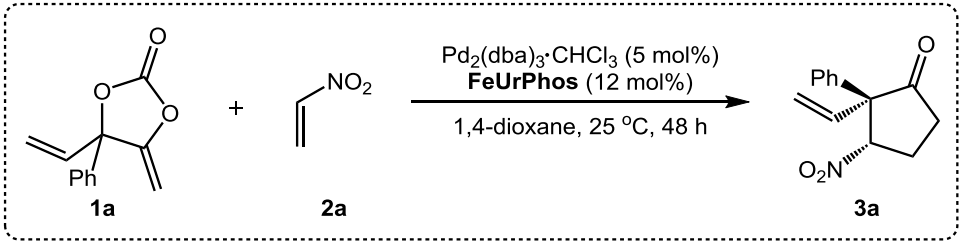
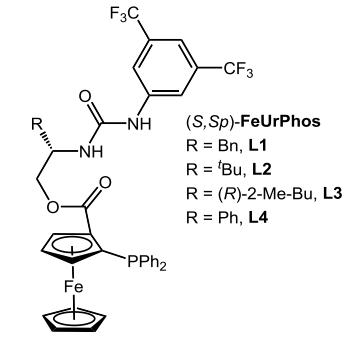
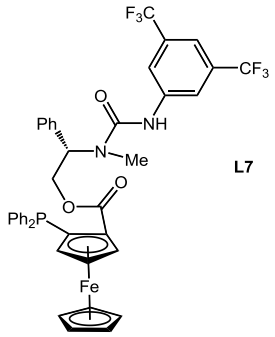
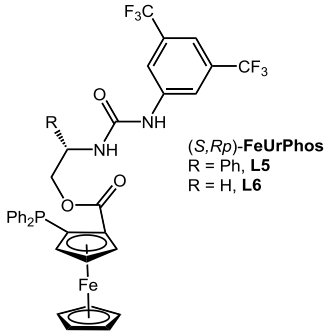
Optimization of the Reaction Conditions

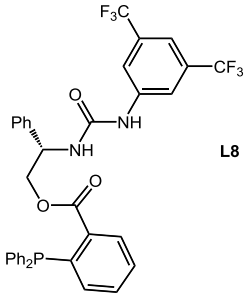


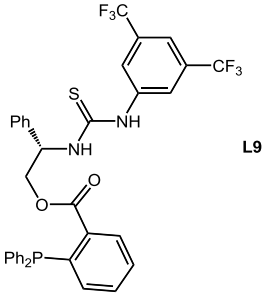
entry	Ligand	conv. (%)	yield[a] (%)	dr	ee (%)
1	**L1**	100	67	>20:1	85
2	**L2**	100	70	>20:1	94
3	**L3**	90	46	>20:1	94
4	**L4**	50	19	>20:1	85
5	**L5**	100	90	>20:1	95
6	**L6**	60	40	>20:1	25
7	**L7**	<5	<5	n.d.	n.d.
8	**L8**	100	86	>20:1	90
9	**L9**	<5	<5	n.d.	n.d.



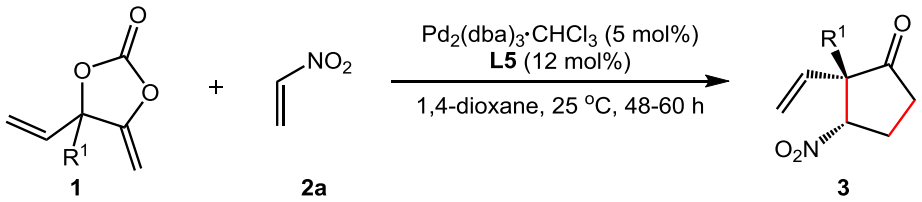




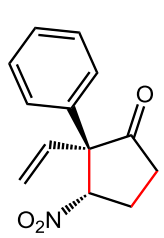




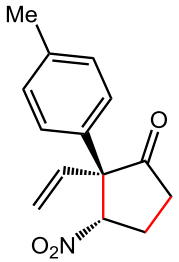
Substrate Scope with Respect to the VMCCs



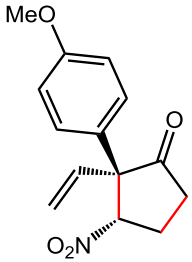
1 + **2a** → **3**



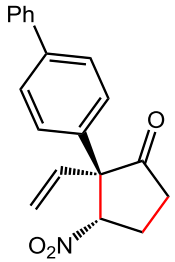
3a, 84%
>20:1 dr, 95% ee



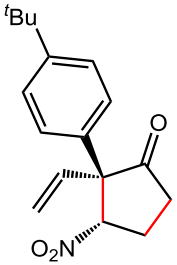
3b, 75%
>20:1 dr, 94% ee



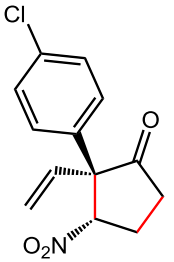
3c, 58%
>20:1 dr, 96% ee



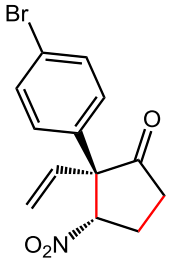
3d, 76%
>20:1 dr, 96% ee



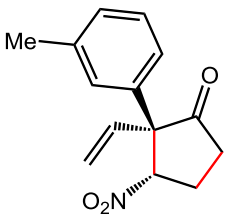
3e, 63%
16:1 dr, 90% ee



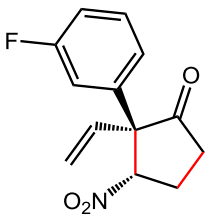
3f[a], 75%
>20:1 dr, 95% ee



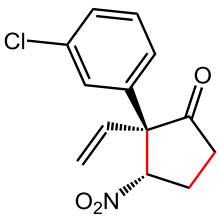
3g[a], 60%
>20:1 dr, 94% ee



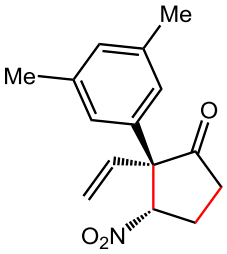
3h, 78%
>20:1 dr, 95% ee



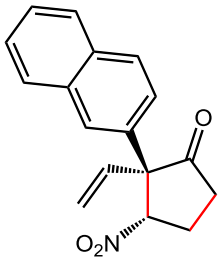
3i[a], 65%
17:1 dr, 95% ee



3j, 65%
>20:1 dr, 95% ee



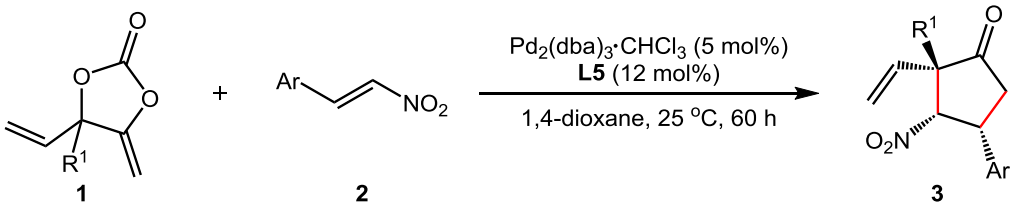
3k, 71%
>20:1 dr, 96% ee

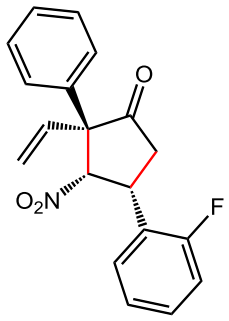


3l, 75%
>20:1 dr, 95% ee

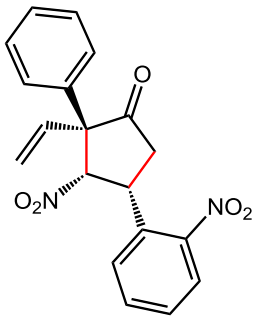
[a]**L2** was used instead of **L5**

(3+2) Cycloadditions with Nitroethylenes

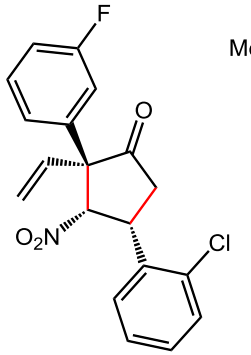




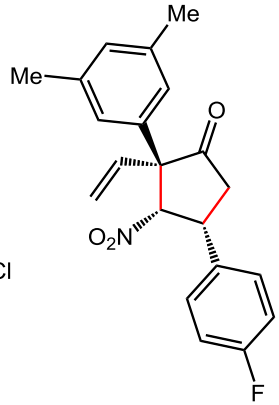
3m, 62%
7.4:1 dr, >99% ee



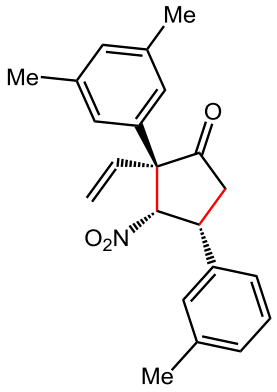
3n, 55%
6.5:1 dr, 97% ee



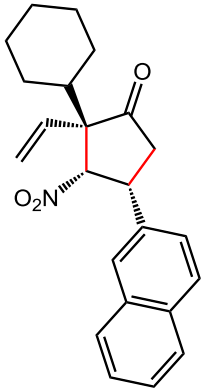
3o, 50%
5.6:1 dr, 98% ee



3p, 51%
5.4:1 dr, 98% ee

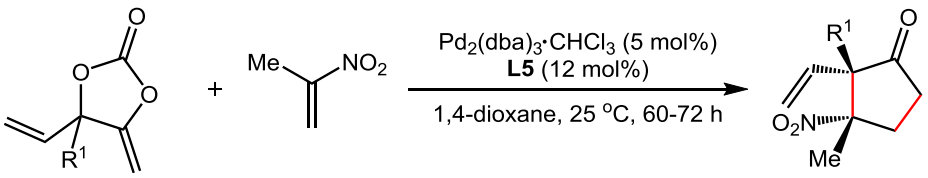


3q, 54%
6.5:1 dr, 98% ee

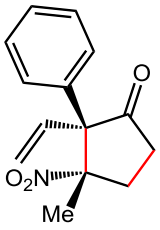


3r, 31%
1.2:1 dr, 93% ee

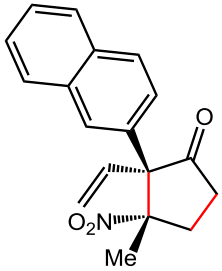
(3+2) Cycloadditions with Nitroethylene



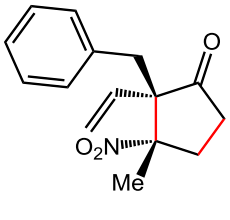
1 **2b** **3**



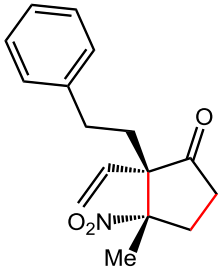
3s, 42%
>20:1 dr, 93% ee



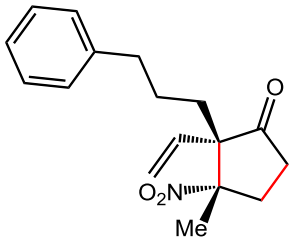
3t, 38%
>20:1 dr, 98% ee



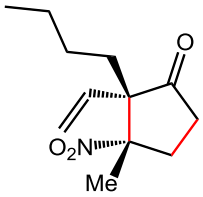
3u, 89%
>20:1 dr, 99% ee



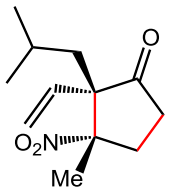
3v, 85%
>20:1 dr, 98% ee



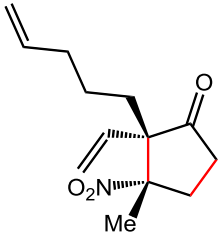
3w, 73%
>20:1 dr, 98% ee



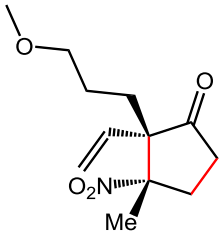
3x, 85%
>20:1 dr, 98% ee



3y, 51%
>20:1 dr, 98% ee
[60%, >20:1 dr, 97% ee (1 mmol scale)]

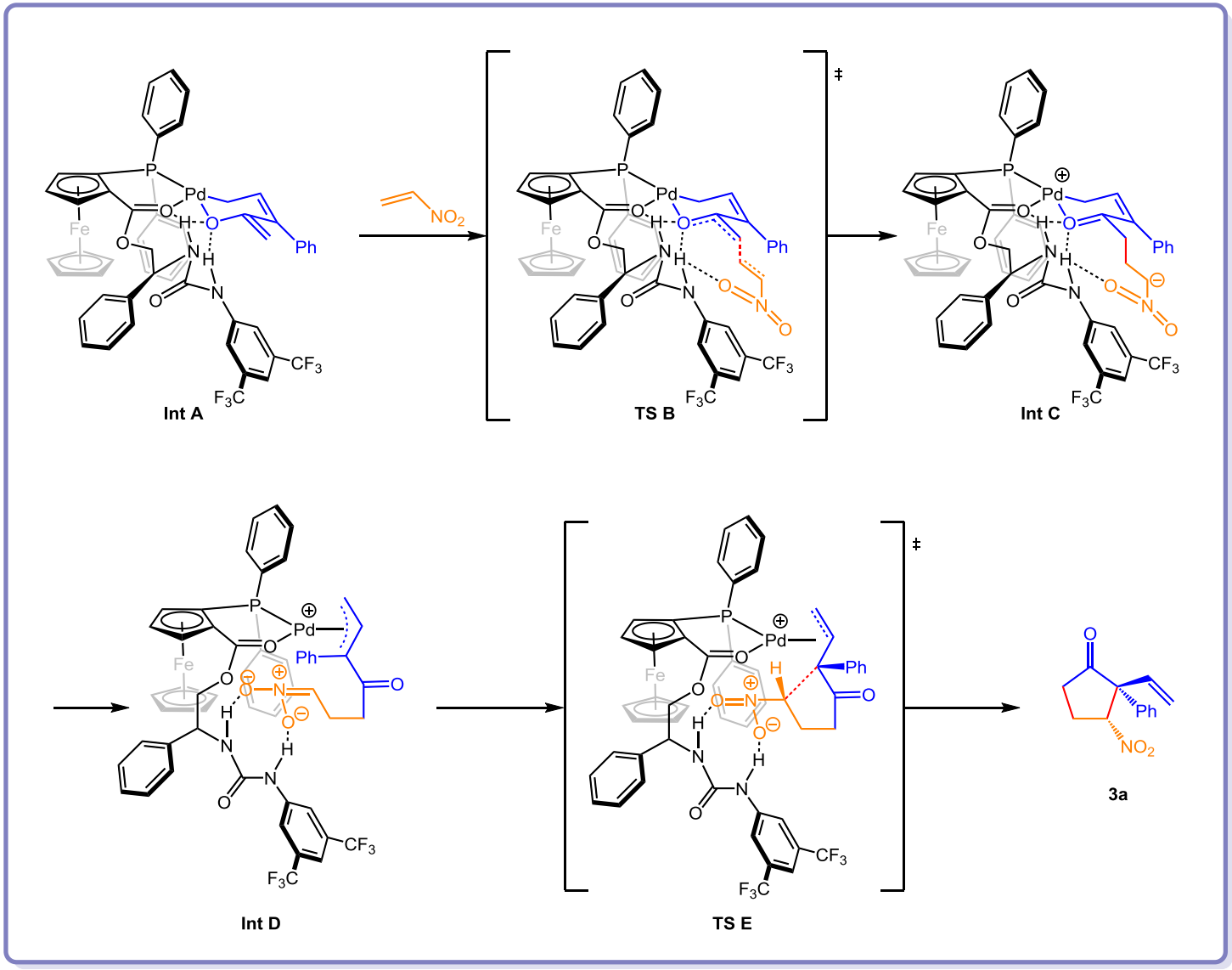


3z, 84%
>20:1 dr, 96% ee

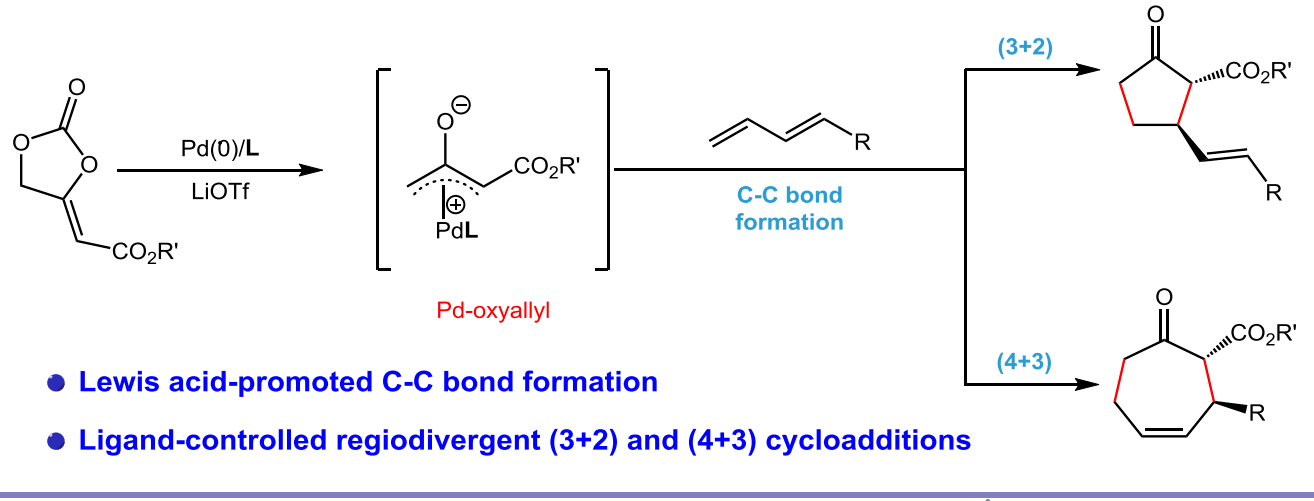


4a, 67%
>20:1 dr, 98% ee

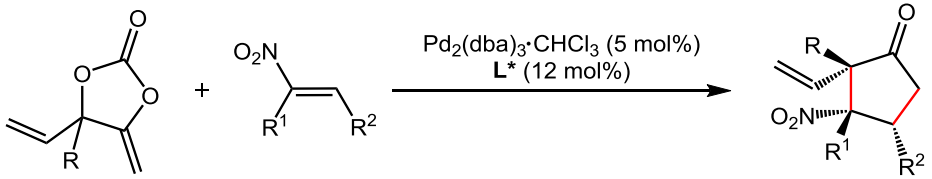
Proposed mechanism



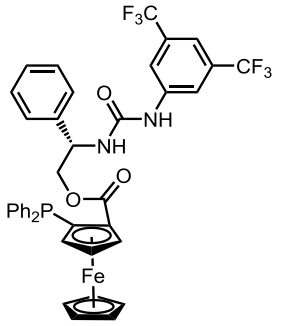
Summary



- **Lewis acid-promoted C-C bond formation**
- **Ligand-controlled regiodivergent (3+2) and (4+3) cycloadditions**



- **Inverse electron demand cycloaddition reaction**
- **Enantioselective and diastereoselective**
- **Newly developed hydrogen-bond-donating ligand**



L*
(*S,Rp*)-Ph-**FeUrPhos**

Zi, W. *et al. J. Am. Chem. Soc*. **2021**, *143*, 3595
Zi, W. *et al. J. Am. Chem. Soc*. **2021**, *143*, 1038

The First Paragraph

环加成反应的重要性

↓

氧烯丙基阳离子的(3+2)环加成反应的困难与挑战

↓

氧烯丙基阳离子的(3+2)环加成反应的一些例子及其局限性

The First Paragraph

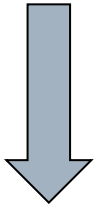
Cycloadditions are among the most powerful bond-forming reactions in organic synthesis, not only because they offer efficient access to cyclic compounds in a single step but also because they can simultaneously generate multiple stereocenters with controllable stereoselectivity. In the past several decades, oxyallyl cations related cycloaddition reactions have attracted considerable attention. These highly electrophilic species react with electron-rich 1,3-dienes (or their equivalents) exclusively via a (4+3) cycloaddition pathway to give seven-membered ring products. Because the concerted (3+2) pathway is thermally forbidden, there are few reports of cycloaddition reactions of oxyallyl cations with 2π alkene acceptors.

The First Paragraph

Rare examples include Wu's work on cycloaddition reactions of cyclic oxyallyl cations with indole derivatives and Kuwajima's work on (3+2) cycloaddition reactions of α-sulfur oxyallyl cations with enol ethers. On the other hand, due to the lack of general means for discriminating between the two faces of the planar oxyallyl cation, asymmetric variants of these cycloaddition reactions are inherently challenging. So far only a few strategies have met with success, and furan is the only successful cycloaddition partner in these works.

The Last Paragraph

工作的特点



工作的意义

The Last Paragraph

In summary, we carried out proof-of-concept studies demonstrating that inverse electron demand cycloaddition reactions of Pd-oxyallyl can be achieved by employing vinyl methylene cyclic carbonates (VMCCs) as precursors for vinyl-oxyallyl-Pd species. These reactions were accomplished with rationally designed hydrogen-bond-donating ligands, designated FeUrPhos. This method was used to realize the first enantioselective (3+2) cycloaddition reactions of Pd-oxyallyl with nitroalkenes. Cyclopentanones with up to three contiguous stereocenters were prepared with high enantioselectivity and good to excellent diastereoselectivity by means of this cycloaddition reaction. We envision that this methodology will not only open up new avenues to discover novel oxyallyl cation-related cycloaddition reactions but also inspire the utility of noncovalent interactions in asymmetric transition-metal catalysis.

Representative Examples

➢ On the other hand, due to the lack of general means for discriminating between the two faces of the planar oxyallyl cation, asymmetric variants of these cycloaddition reactions are inherently challenging.

(discriminate: v. 歧视, 区别, 辨别； inherently: adv. 内在地, 固有地, 天性地)

➢ Catalytic generation and cycloaddition of oxyallyl cations eluded synthetic chemists until a recent breakthrough by Trost et al.

(直到…最近取得了突破)

Acknowledgement

Thanks
for your attention