Literature Report III

Palladium-Based Dyotropic Rearrangement Enables A Triple Functionalization of *Gem*-Disubstituted Alkenes

Reporter: Kai Xue
Checker: Yan-Xin Sun
Date: 2024-06-21

Feng, Q.; Liu, C.-X.; Wang, Q.; Zhu, J.* *Angew. Chem. Int. Ed.* **2024**, *63*, e202316393

CV of Prof. Zhu Jieping

Background:

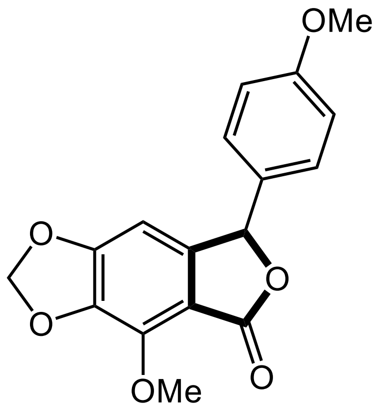
- **1984** B.S., Hangzhou Normal University
- **1984-1987** M.S., Lanzhou University
- **1987-1991** Ph.D., Université Paris XI
- **1991-1992** Associate Professor, Texas A & M University
- **1992-2010** Director of Research, ICSN CNRS, France
- **2010-now** Professor, ISIC, EPFL

Research:

- **Total synthesis of natural products**
- **Multicomponent reaction**
- **Metal-catalyzed domino process**
- **Catalytic enantioselective transformation**

Contents

Introduction



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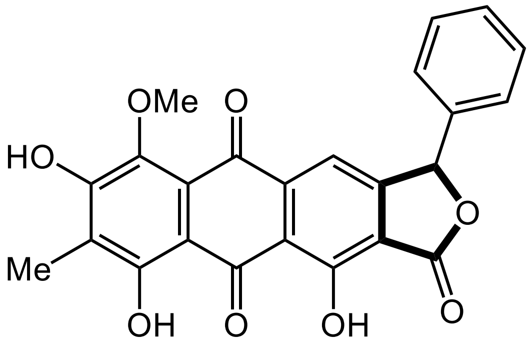

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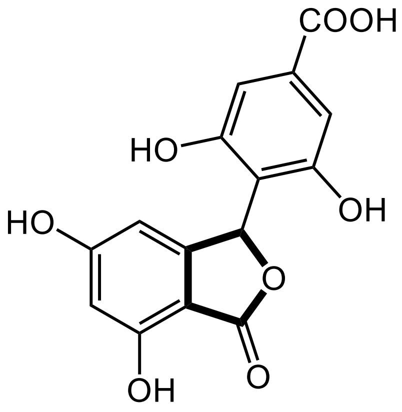
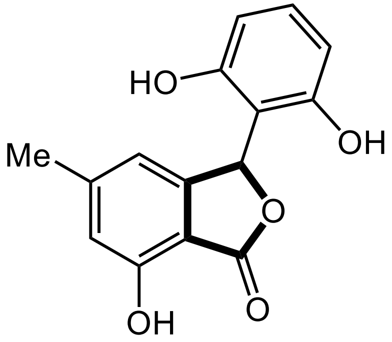


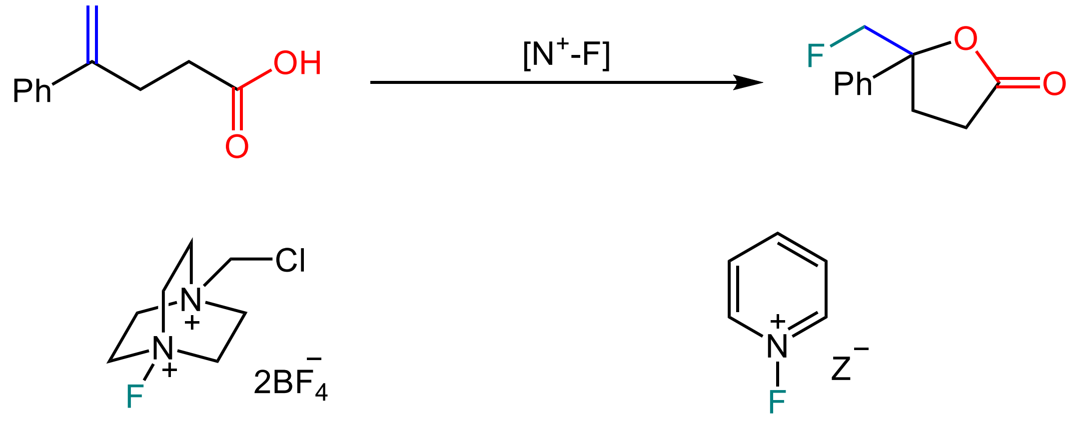
cryphonectric acid



isopestacin

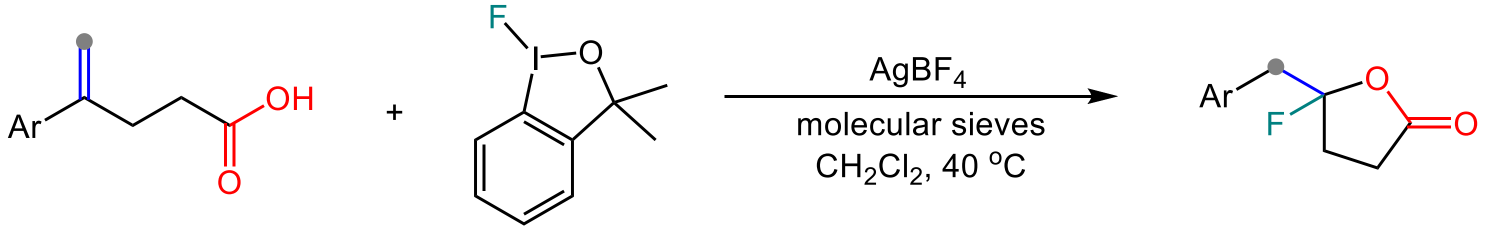
Parmar, D.; Maji, M. S.; Rueping, M;.* *Chem. Eur. J.* **2014**, *20*, 83

Introduction



Selectfluor

N-fluoropyridinium salts



Geary, G. C.; Hope, E. G.; Stuart, A. M.* *Angew. Chem. Int. Ed.* **2015**, *54*, 14911
Parmar, D.; Maji, M. S.; Rueping, M.* *Chem. Eur. J.* **2014**, *20*, 83

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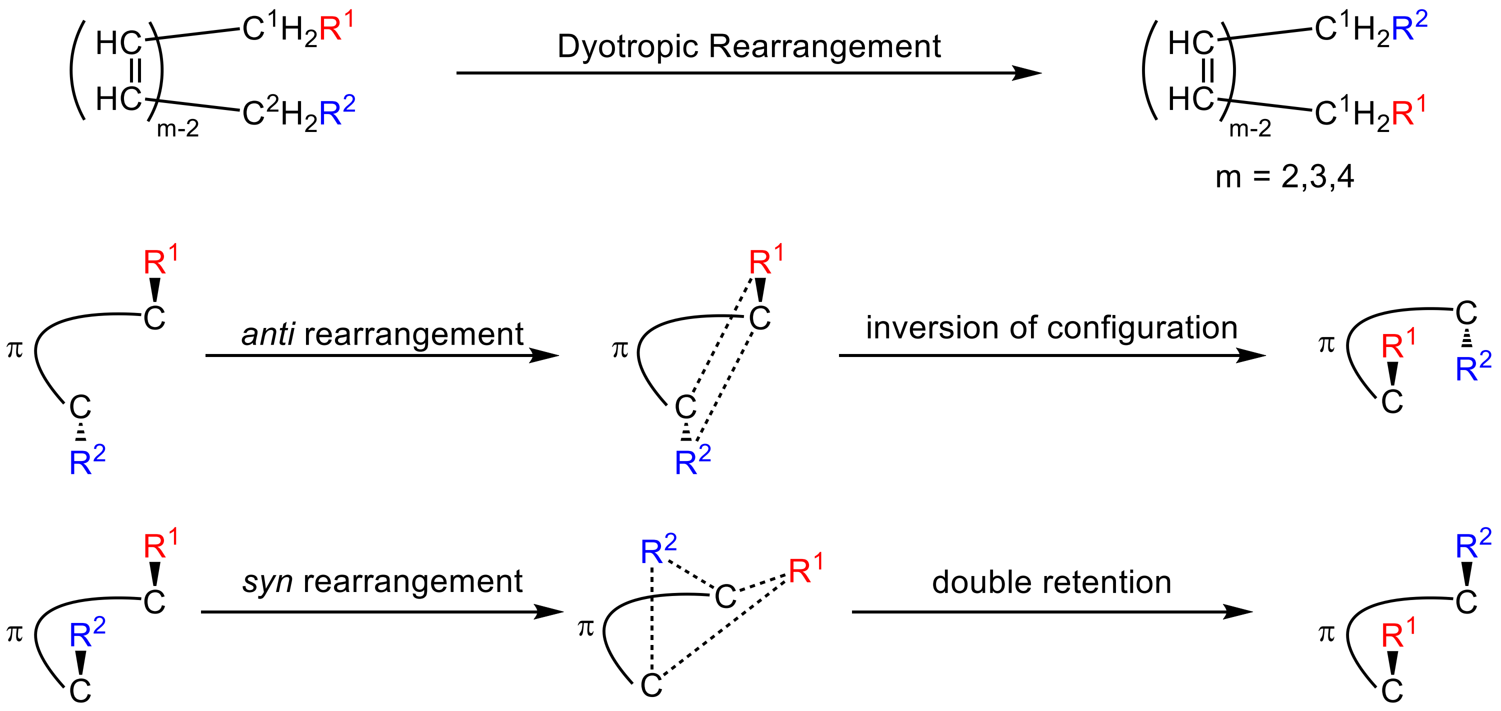

Reetz, M. T.* *Angew. Chem. Int. Ed.* **1972**, *11*, 129

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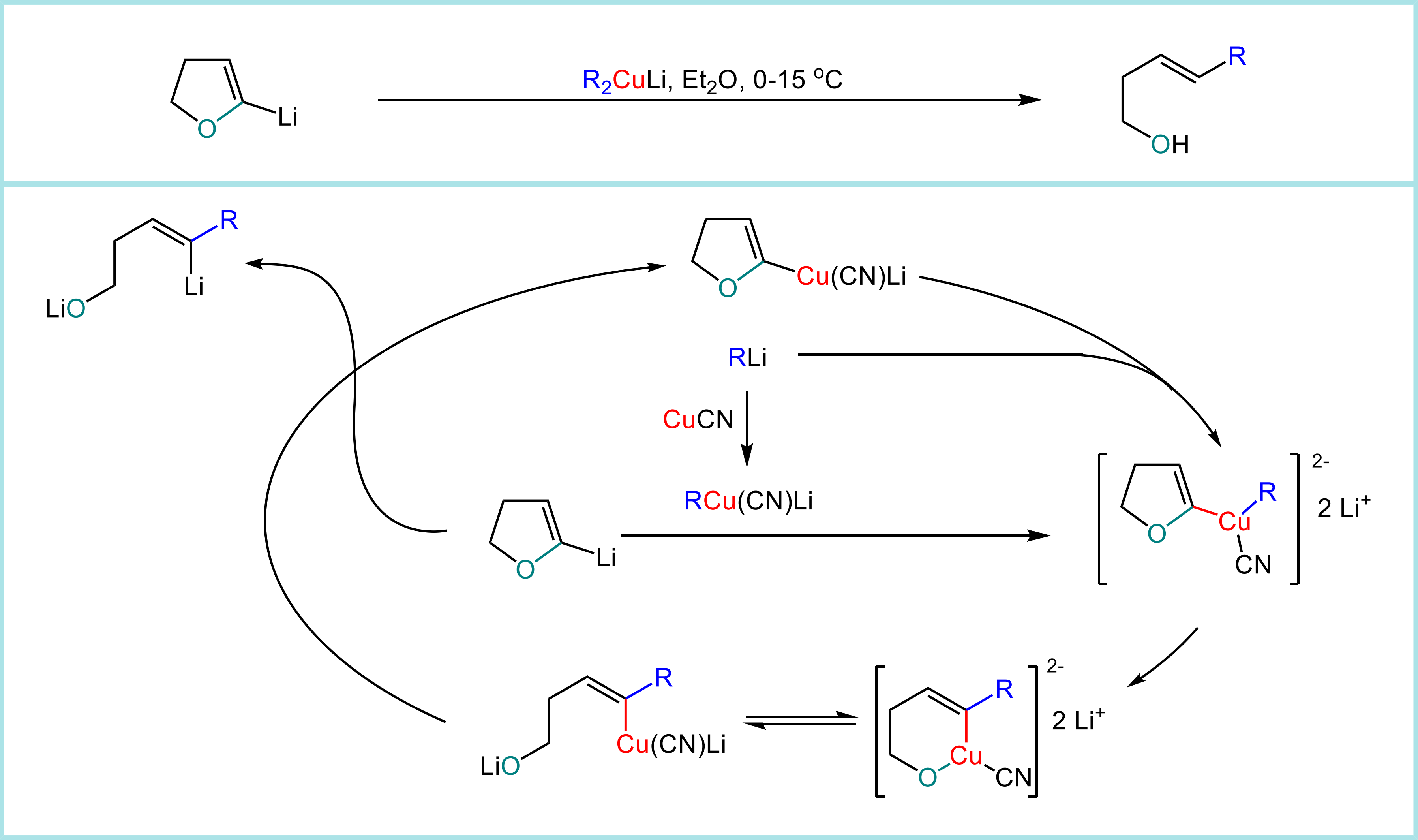
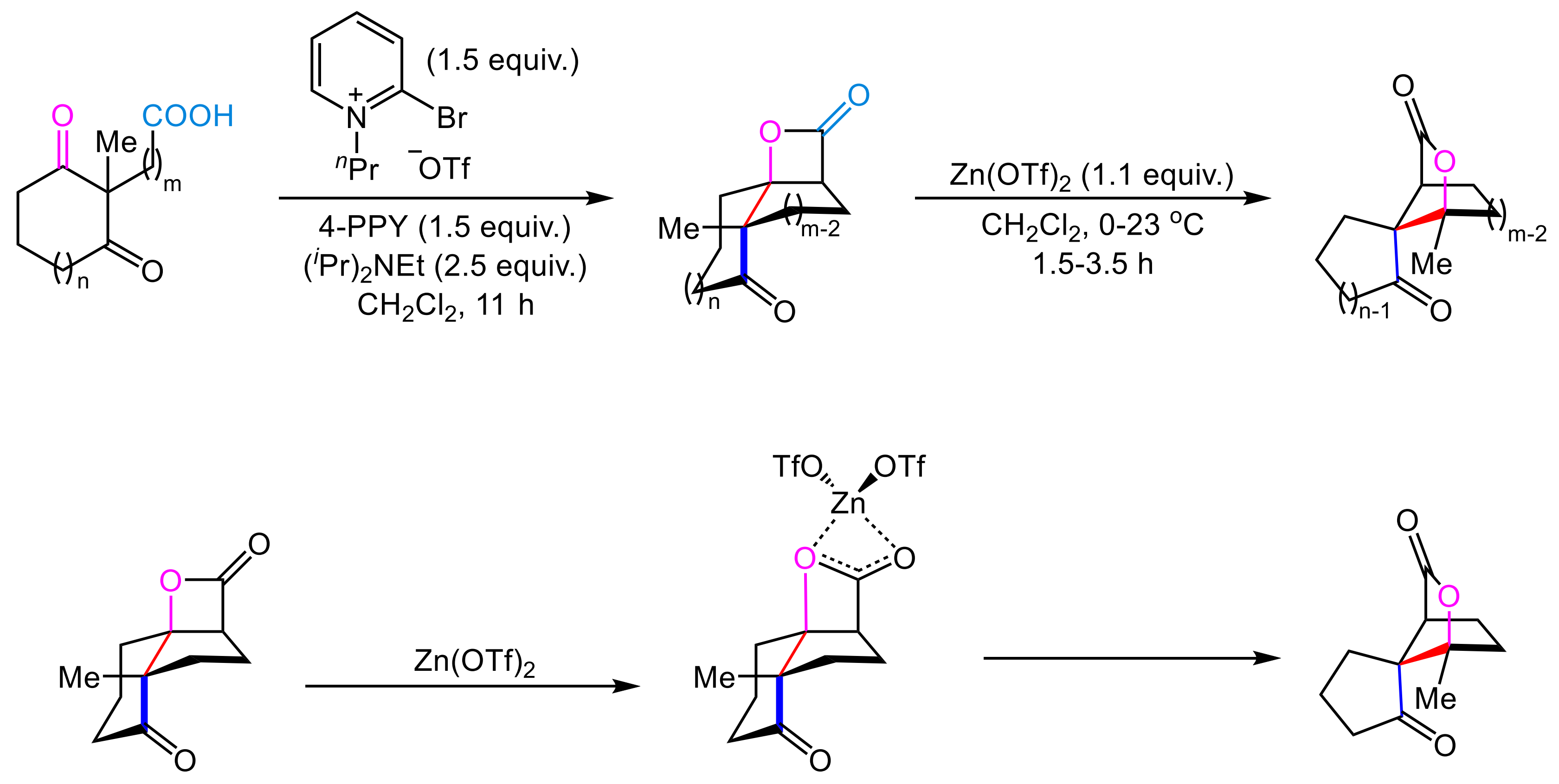


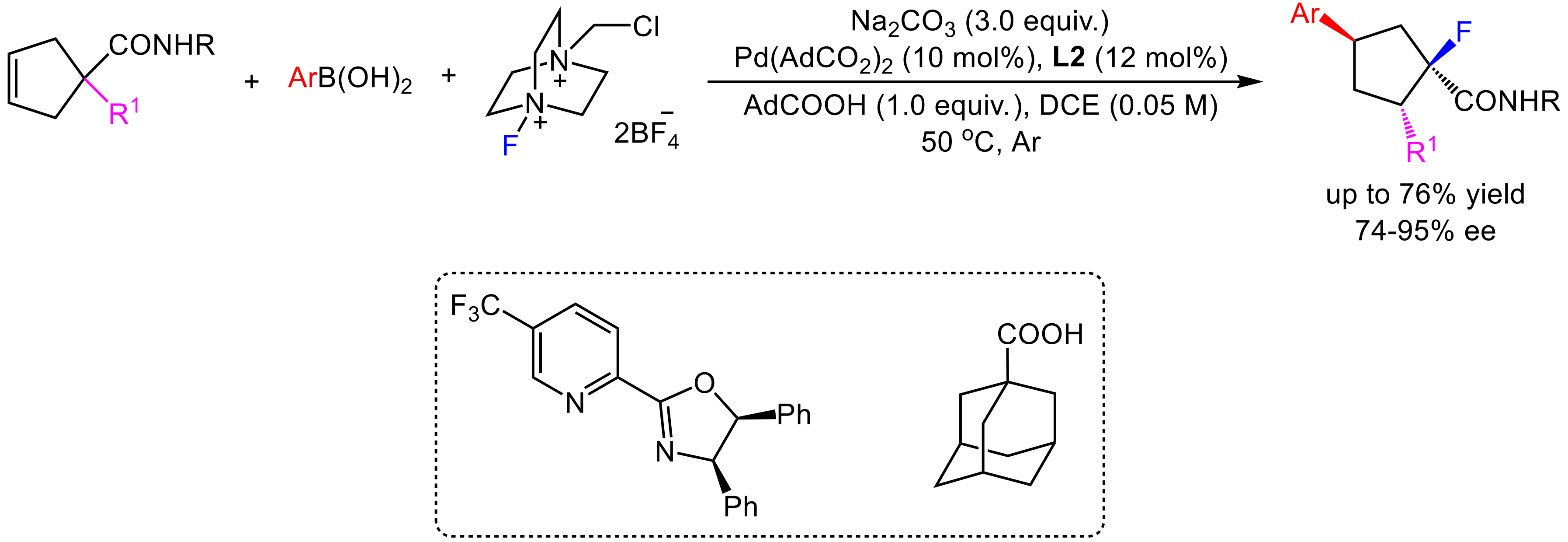
Kocieński, P.; Barber, C. *Pure Appl. Chem*. **1990**, *62*, 1933

Introduction



Purohit, V. C.; Matla, A. S.; Romo, D.* *J. Am. Chem. Soc.* **2008**, *130*, 10478

Introduction



Cao, J.; Wu, H.; Wang, Q.; Zhu, J.* *Nat. Chem.* **2021**, *13*, 671

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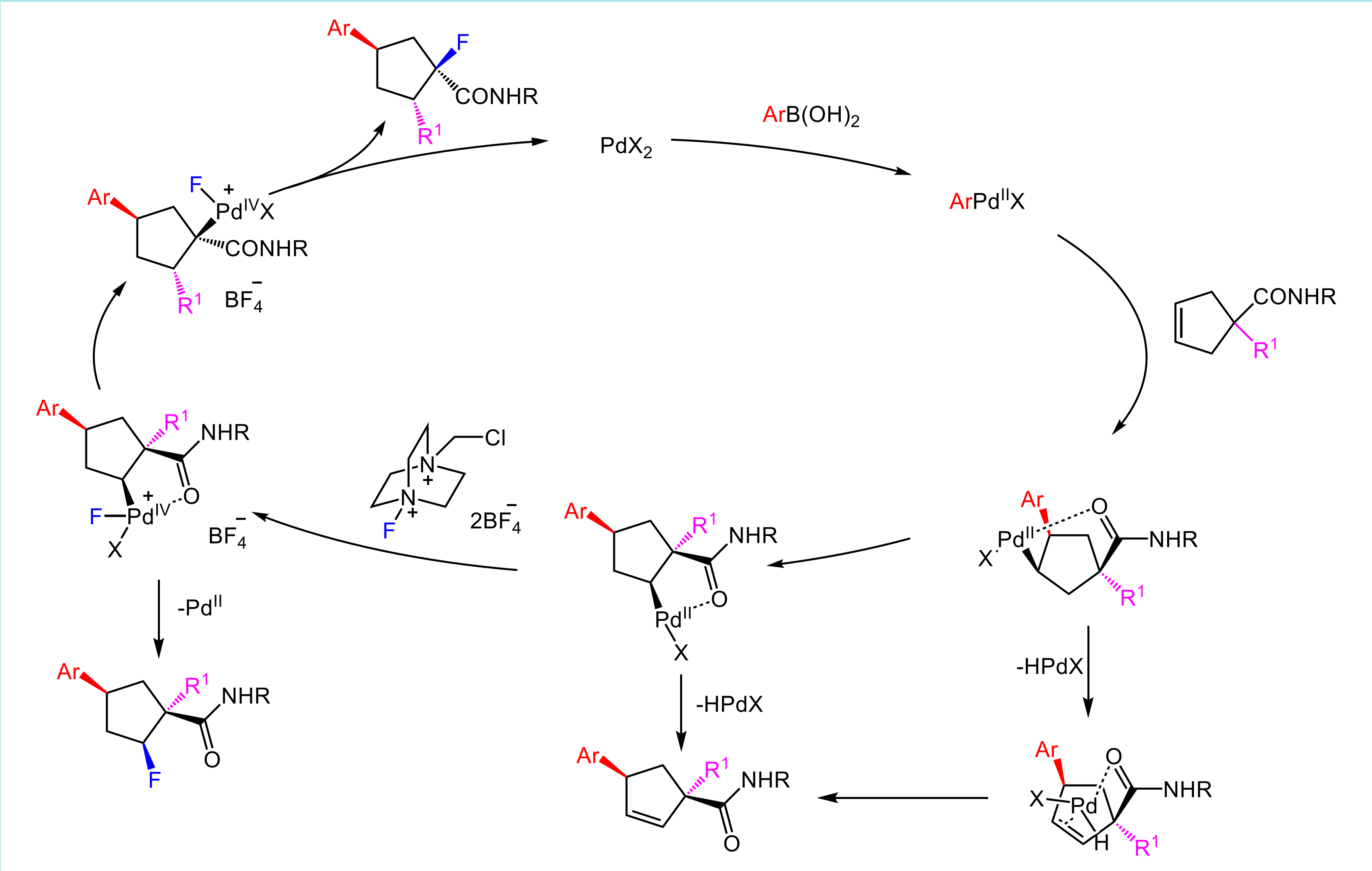

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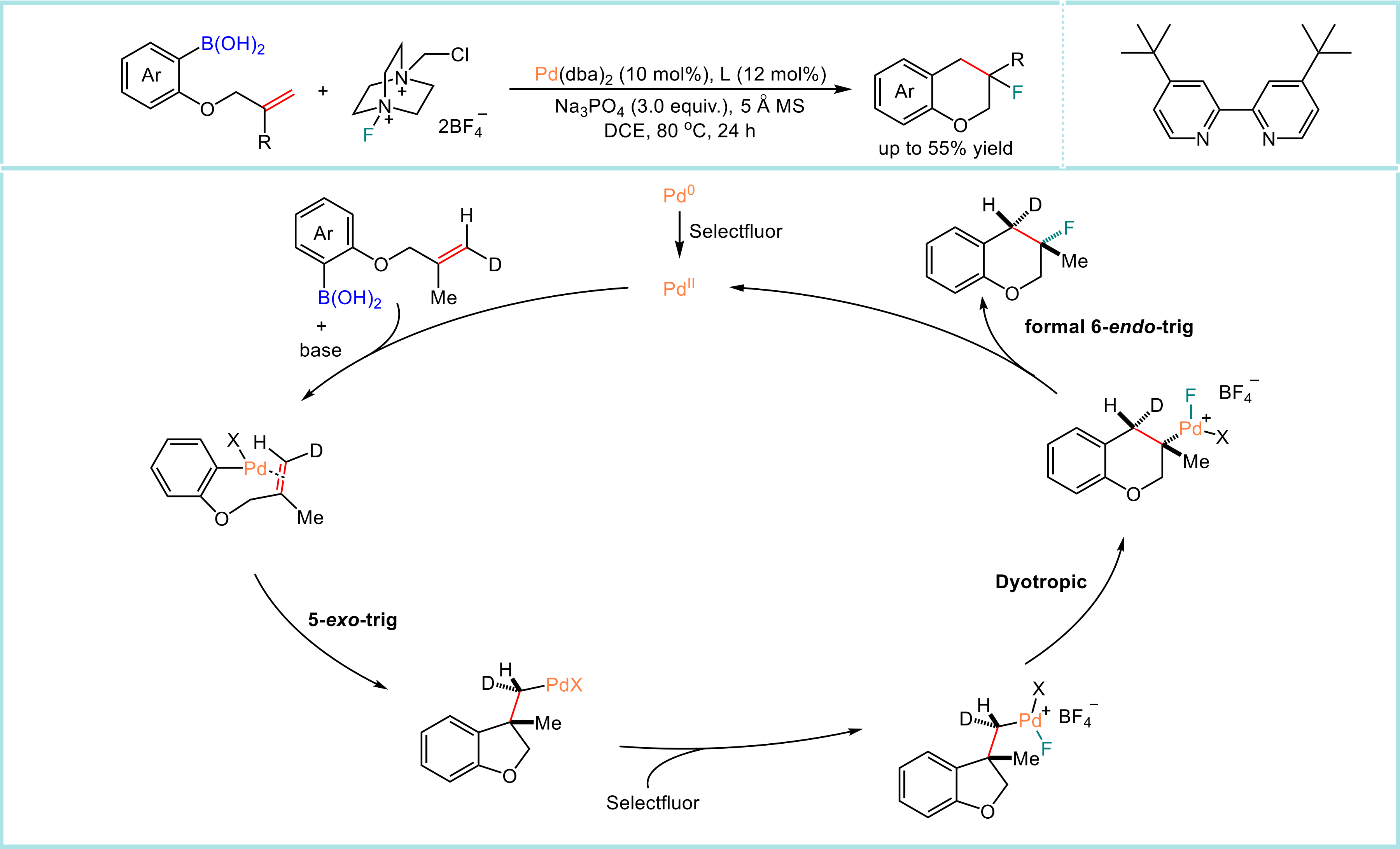
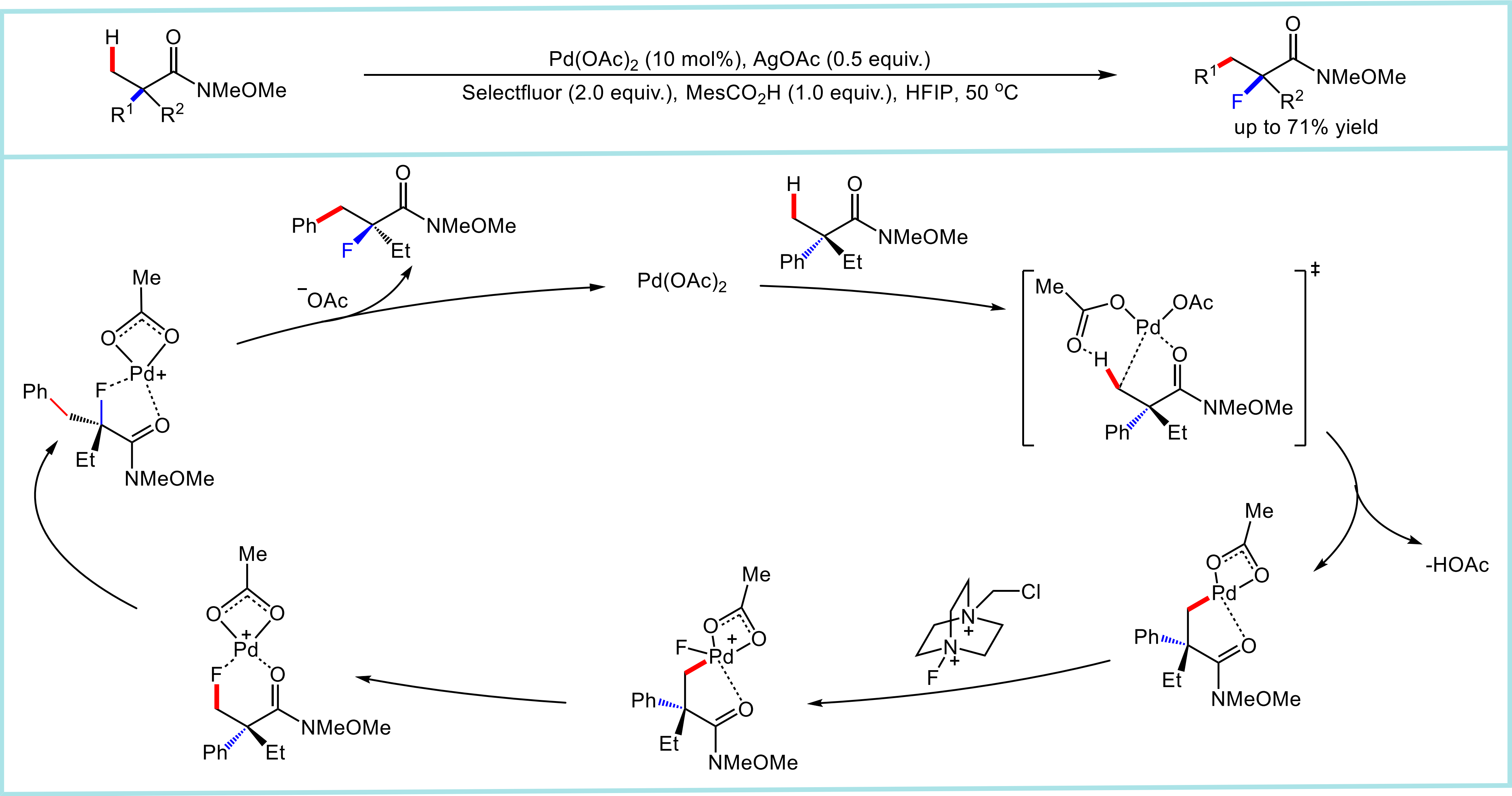


Gong, J.; Wang, Q.; Zhu, J.* *Angew. Chem. Int. Ed.* **2022**, *61*, e202211470

Introduction



Yang, G.; Wu, H.; Gallarati, S.; Corminboeuf, Clemence; Wang, Q.; Zhu, J.* *J. Am. Chem. Soc.* **2022**, *144*, 14047

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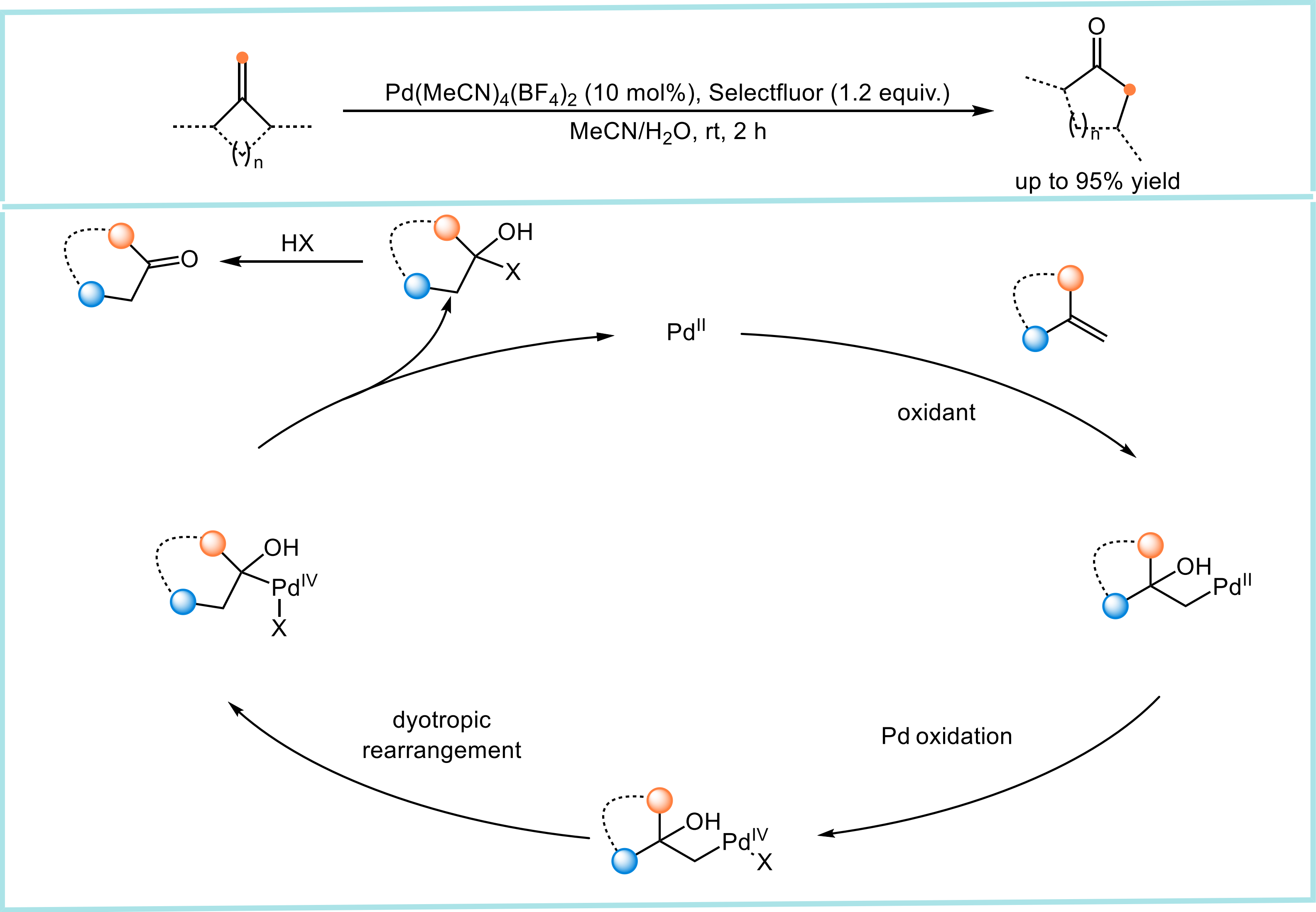
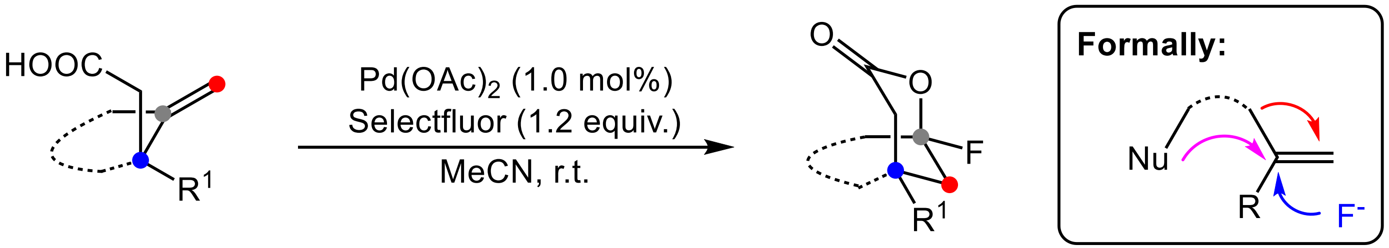


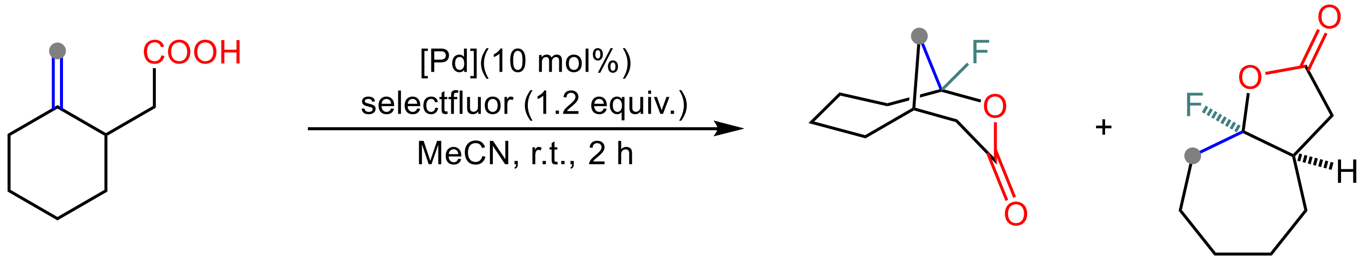
Feng, Q.; Wang, Q.; Zhu, J.* *Science* **2023**, *379*, 1363

Project Synopsis

Chemo- and Regio-selective 1,2-Alkyl/Pd(IV) Dyotropic Rearrangement



Optimization of the Reaction Conditions

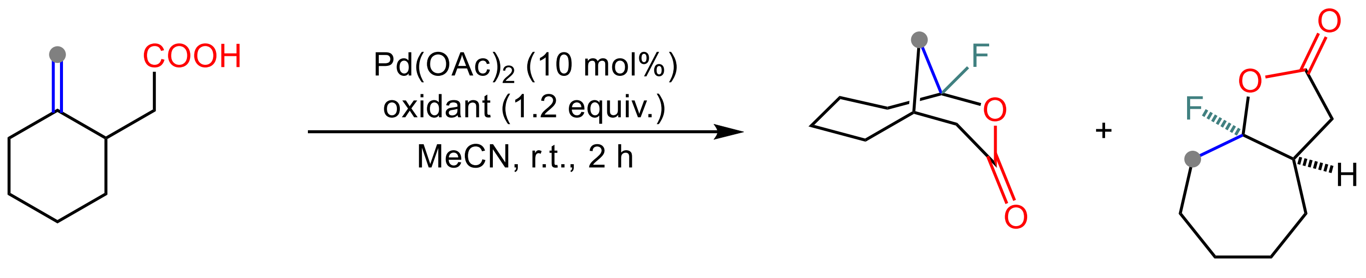


1a **2a** **3a**

entry[a]	[Pd]	con. (%)[b]	yield (**2a**, %)[b]	yield (**3a**, %)[b]
1	$Pd(MeCN)_4(BF_4)_2$	>99	48	9
2	$Pd(TFA)_2$	>99	69	19
3	**$Pd(OAc)_2$**	**>99**	**77**	**10**
4	$Pd(MeCN)_2Cl_2$	>99	46	31
5	$Pd(hfacac)_2$	>99	50	13
6	$Pd(OPiv)_2$	>99	55	11
7	$PdCl_2$	>99	53	30
8	$PdBr_2$	>99	66	17

[a] Reaction scale: **1a** (0.1 mmol), Pd-catalyst (10 mol%), selectfluor (1.2 equiv), MeCN (0.4 M). [b] Determined by analysis of the ^1H NMR spectrum of the crude mixture using mesitylene as an internal standard.

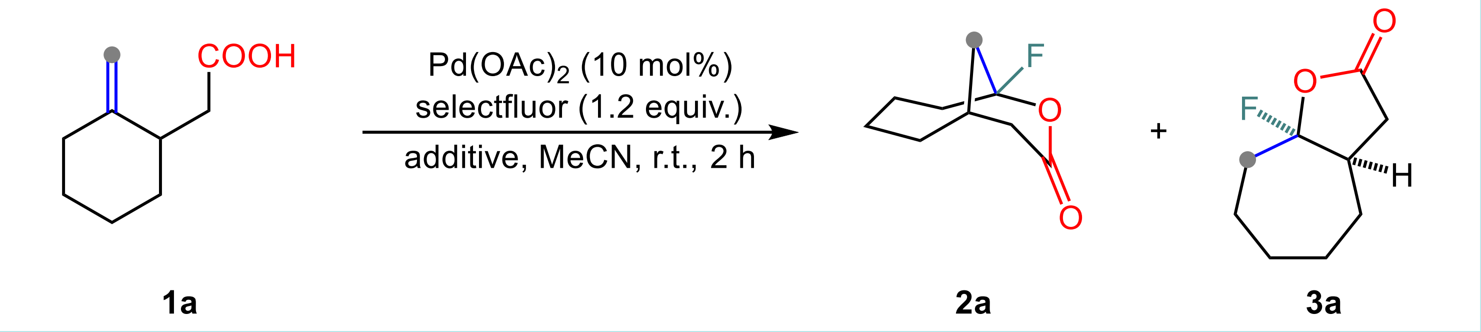
Optimization of the Reaction Conditions



entry[a]	oxidant	con. (%)[b]	yield (**2a**, %)[b]	yield (**3a**, %)[b]
1	**selectfluor**	**>99**	**76**	**10**
2	NFSI	30	0	10
3	pyridine-F-BF_4	<5	0	0
4	pyridine-F-OTf	24	0	0
5	2,6-dichloropyridine-F-BF_4	>99	<5	0
6[c]	selectfluor	>99	75	20

[a] Reaction scale: **1a** (0.1 mmol), Pd-catalyst (10 mol%), oxidant (1.2 equiv), MeCN (0.4 M). [b] Determined by analysis of the ^1H NMR spectrum of the crude mixture using mesitylene as an internal standard. [c] Reaction with selectfluor (1.5 equiv.).

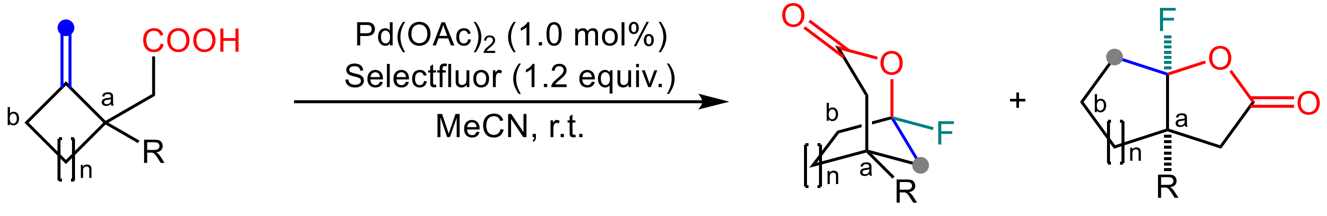
Optimization of the Reaction Conditions



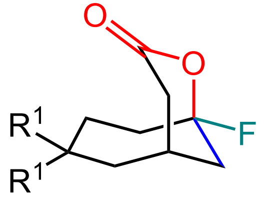
entry[a]	additive	con. (%)[b]	yield (**2a**, %)[b]	yield (**3a**, %)[b]
1	**/**	**>99**	**76**	**10**
2	bipyridine (12 mol%)	63	0	17
3	Na_2CO_3 (1 equiv.)	>99	44	10
4	Cs_2CO_3 (1 equiv.)	>99	67	16
5	NaO^{t}Bu (1 equiv.)	>99	61	16
6	NaH (1.2 equiv.)	>99	78	10
7	5 Å MS	>99	60	14

[a] Reaction scale: **1a** (0.1 mmol), Pd-catalyst (10 mol%), oxidant (1.2 equiv), MeCN (0.4 M). [b] Determined by analysis of the ^{1}H NMR spectrum of the crude mixture using mesitylene as an internal standard.

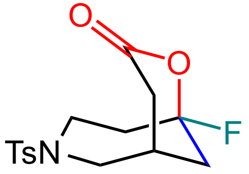
Scope of Fluorinating Lactonization



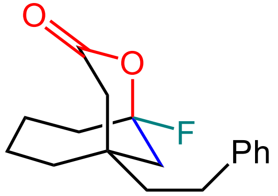
1 **2** **3**



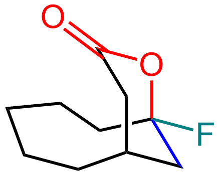
2a R^1 = H, 77%, rr = 8:1
2b R^1 = Me, 72%, rr = 17:1
2c R^1, R^1 = O, 77%, rr = 9:1



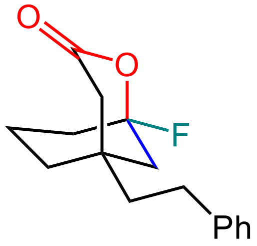
2d 59%, rr = 6:1



2e 82%, rr > 20:1

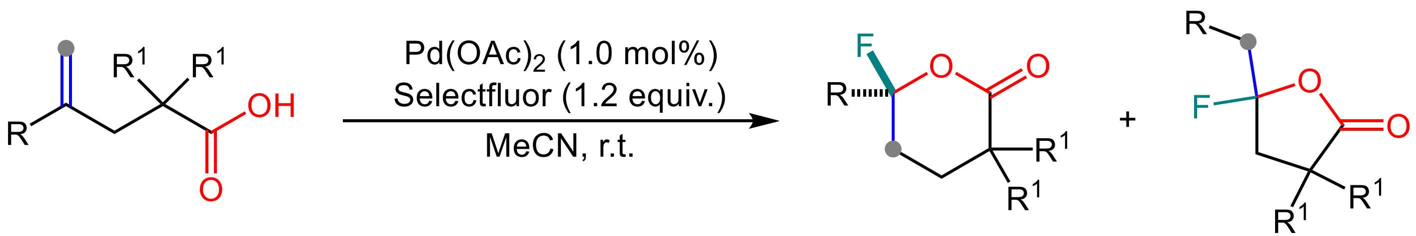


2f 61%, rr > 20:1

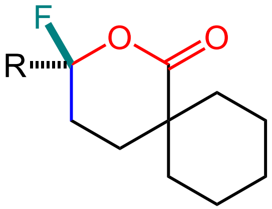


2g 79%, rr > 20:1

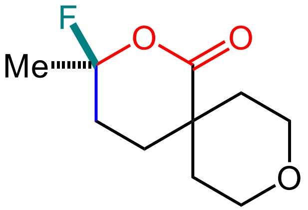
Scope of Fluorinating Lactonization



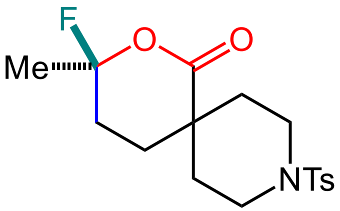
4 **5** **6**



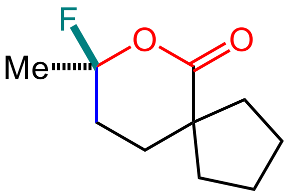
5a R = Me, 75%, rr = 10:1
5b R = $^{n}C_4H_9$, 73%, rr = 8:1
5c R = $PhCH_2CH_2CH_2$, 71%, rr = 8:1



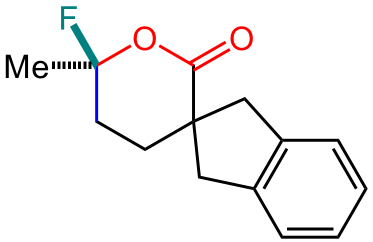
5d 58%, rr = 6:1



5e 75%, rr = 10:1

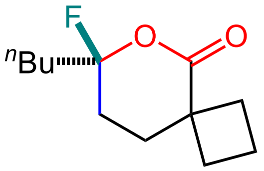


5f 79%, rr = 7.5:1

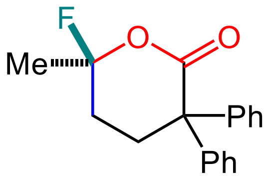


5g 61%, rr = 6:1

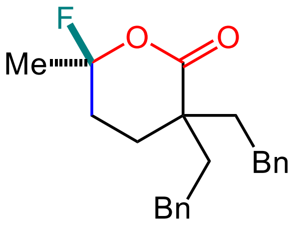
Scope of Fluorinating Lactonization



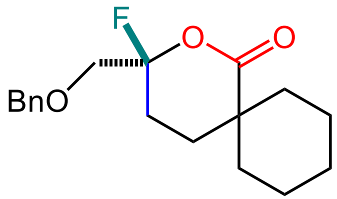
5h 65%, rr = 5.5:1



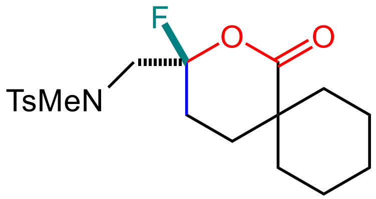
5i 49%, rr = 5:1



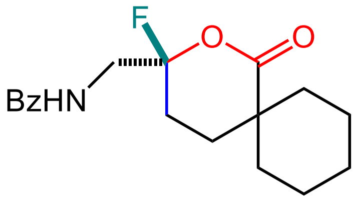
5j 68%, rr = 10:1



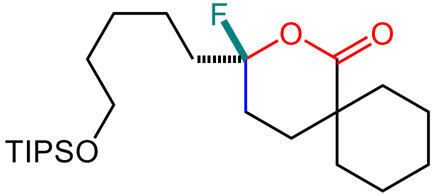
5k 39%, rr = 8:1



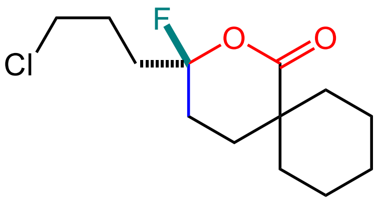
5l 47%, rr = 5.7:1



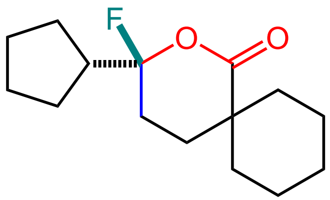
5m 43%, rr > 20:1



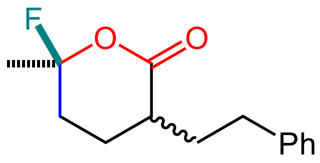
5n 59%, rr = 8:1



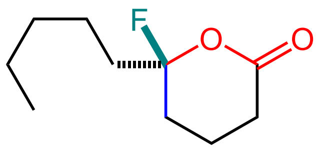
5o 86%, rr = 9:1



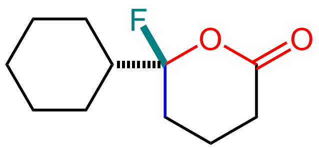
5p 71%, rr = 6:1



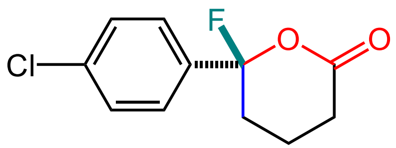
5q 45%, rr = 5:1, dr = 1.8:1



5r 59%, rr = 2.6:1

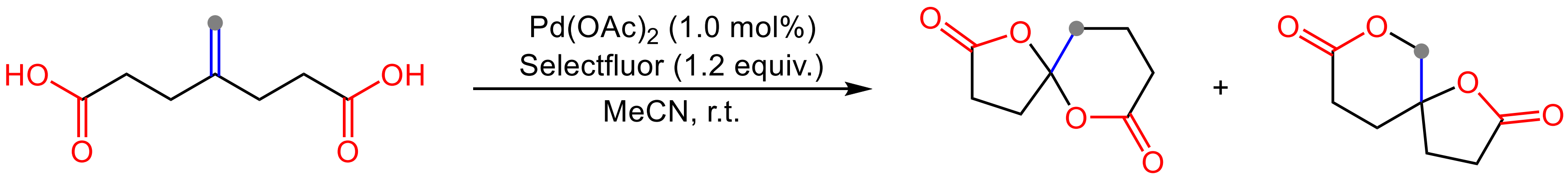


5s 62%, rr = 4:1



5t 74%, rr = 1.3:1

Scope of Fluorinating Lactonization

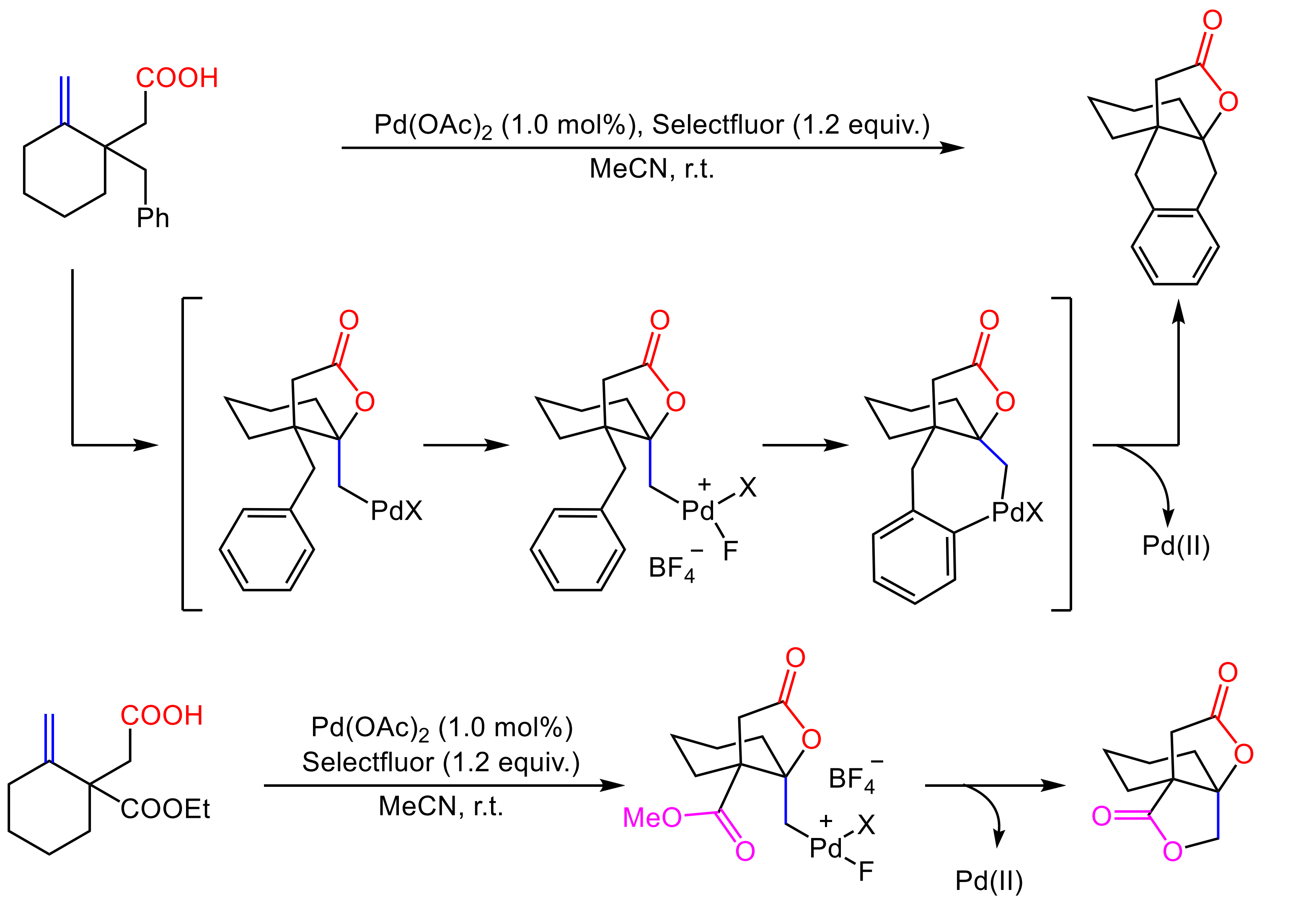


7

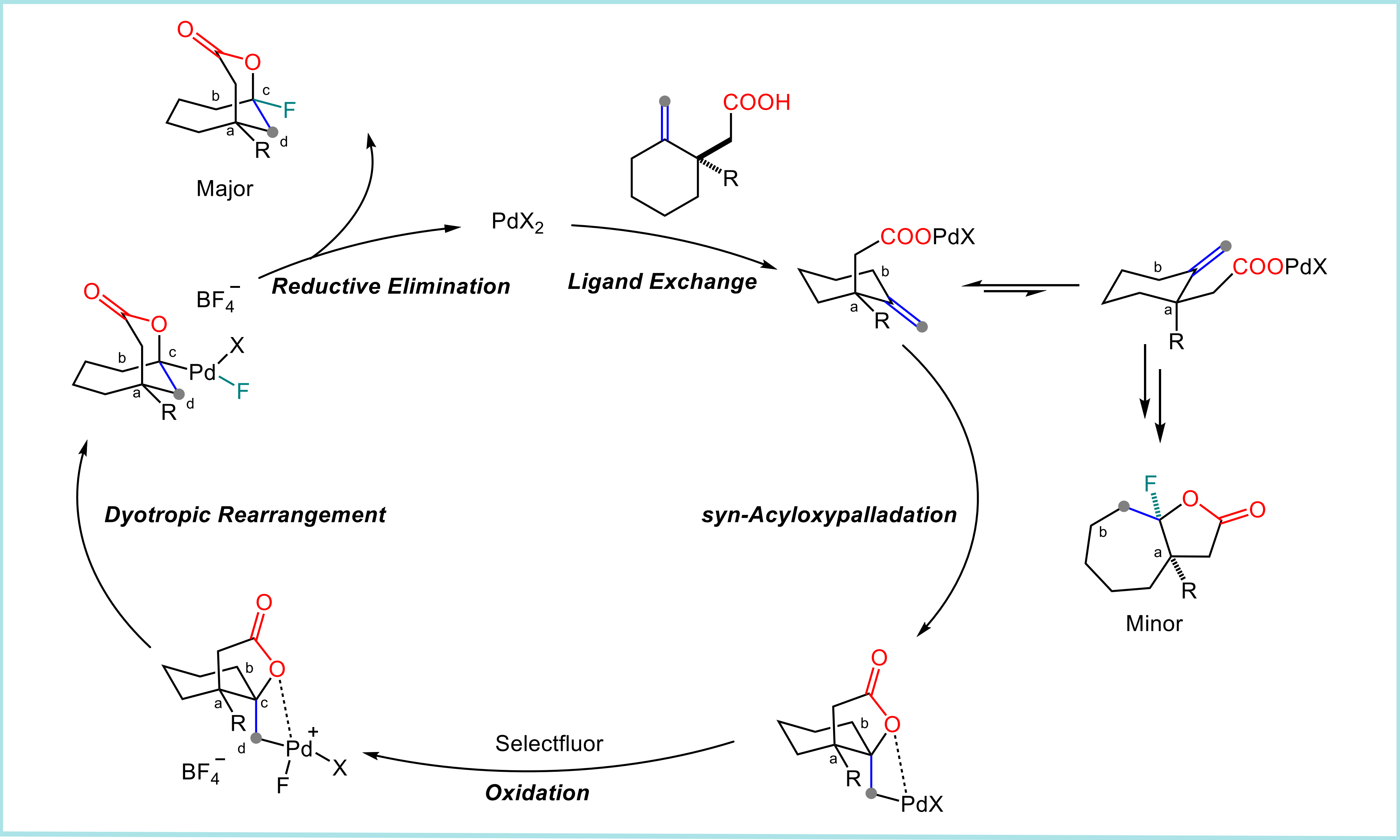
8 62%

9 0%

Mechanistic Investigation

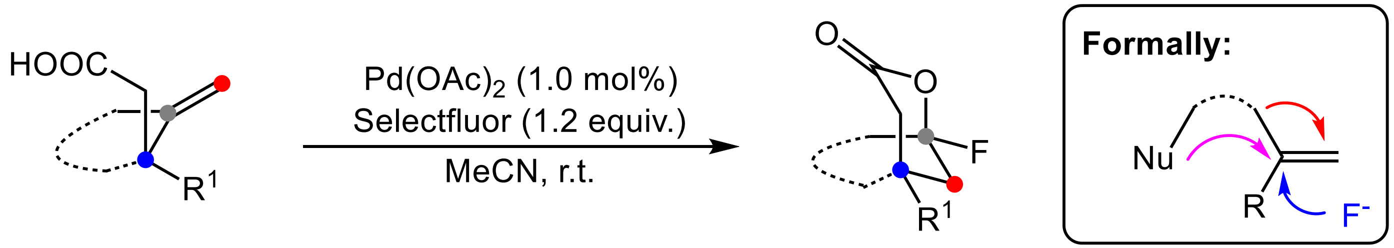


Proposed Reaction Mechanism



Summary

Chemo- and Regio-selective 1,2-Alkyl/Pd(IV) Dyotropic Rearrangement



- ☐ Formation of one C-C, one C-O and one C-F bonds
- ☐ Pd oxidation, regioselective ring-enlarging 1,2-alkyl/Pd(IV) dyotropic rearrangement and C-F bond forming reductive elimination cascade

Strategy for Writing The First Paragraph

烯羧酸的氟内酯化非常具有吸引力

- ✓ Fluorolactonization of ene-carboxylic acids is an attractive synthetic transformation that converts easily accessible starting materials to valuable fluorinated heterocycles. Using electrophilic fluorinating reagents such as Selectfluor and N-fluoropyridinium salts.

过去氟内酯的合成方法

- ✓ Nevertheless, the reaction only works with substrates bearing an aryl substituent at the C4 position in line with the proposed mechanism involving a C4 carbocation intermediate.

引出本文工作

- ✓ Of particular interest to us, Stuart and co-workers reported the formation of 5-benzyl-5-fluorodihydrofuran-2(3H)-one from the reaction of 4-arylpent-4-enoic acid with hypervalent fluoroiodane in the presence of silver tetrafluoroborate.

Strategy for Writing The Last Paragraph

总结工作

↓

强调亮点

- ✓ In summary, we have developed a palladium catalyzed migratory *gem*-fluorolactonization of *gem*-disubstituted ene-carboxylic acids. The previously unknown 6-fluoro-*γ*-lactones and its bridged analogues are readily prepared from simple starting materials via formation of one C-C, one C-O and one C-F bonds.
- ✓ Trapping experiments indicates that the reaction is initiated by 5-*exo*-trig oxypalladation followed by Pd oxidation, regioselective ring-enlarging 1,2alkyl/Pd(IV) dyotropic rearrangement and C-F bond forming reductive elimination cascade.

Representative Examples

- … domino processes to divert the conventional reaction pathways to the previously unachievable ones. (将传统的反应途径转向以前无法实现的途径)
- … allowed us to develop an unprecedented transformation (前所未有的)
- Post-transformations of these fluorolactones taking advantage of the electrophilicity of the 1-fluoroalkylcarboxylate function are also documented. (利用).

Acknowledgement

Thanks for your attention