Literature Report VIII

Enantioselective Copper-Catalyzed Sequential Hydrosilylation of Arylmethylenecyclopropanes

Reporter: Gao-Wei Wang
Checker: Qing-Xian Xie
Date: 2024-9-9

Fu, B.; Wang, L.; Chen, K.; Yuan, X.; Yin, J.; Wang, S.; Shi, D.; Zhu, B.; Guan, W.; Zhang, Q.; Xiong, T.

Angew. Chem. Int. Ed. **2024**, e202407391

CV of Prof. Tao Xiong (熊涛)

Background:

- **2001-2005** B.S., Northeast Normal University
- **2005-2008** M.S., Northeast Normal University
- **2008-2011** Ph.D., Northeast Normal University
- **2011-2014** Lecturer, Northeast Normal University
- **2012-2013** Postdoc., Colorado State University
- **2014-Now** Associate professor, Professor, Northeast Normal University

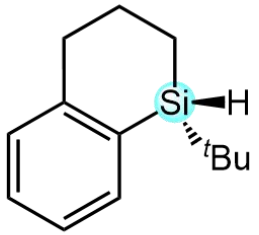
Research:

- Organic Synthetic Chemistry
- Organometallic Chemistry
- Asymmetric Catalysis

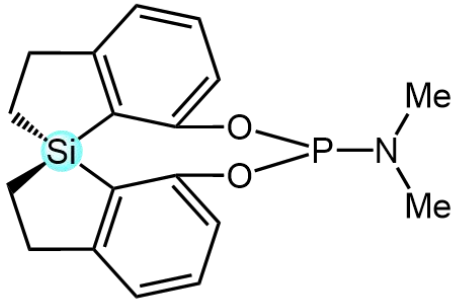
Contents

Introduction

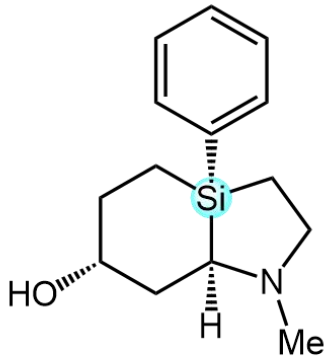
Applications of Silacarbocycles



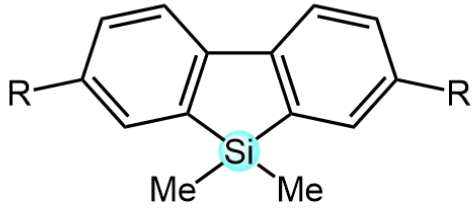
Chiral Reagent



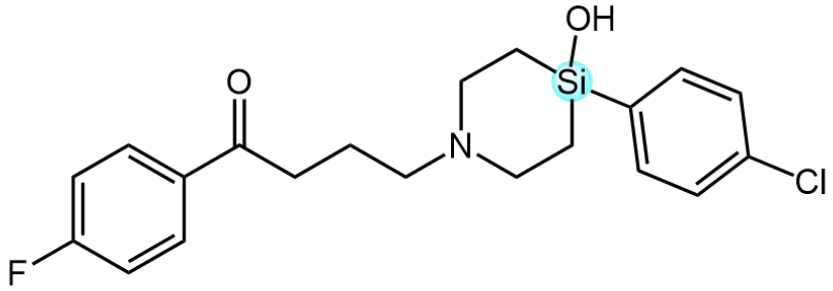
Chiral Ligand



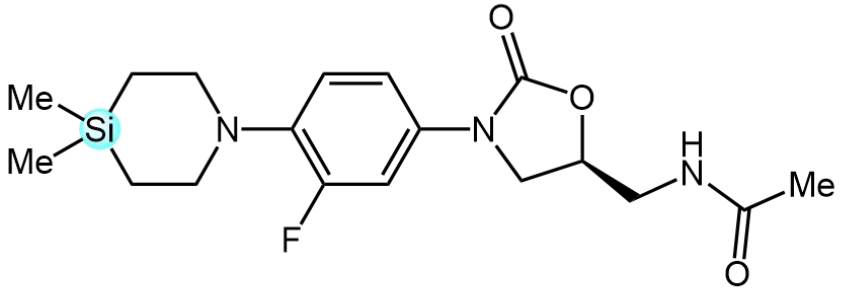
Potential Medicine
(Antidepressant Activity)



Organic Optoelectronics

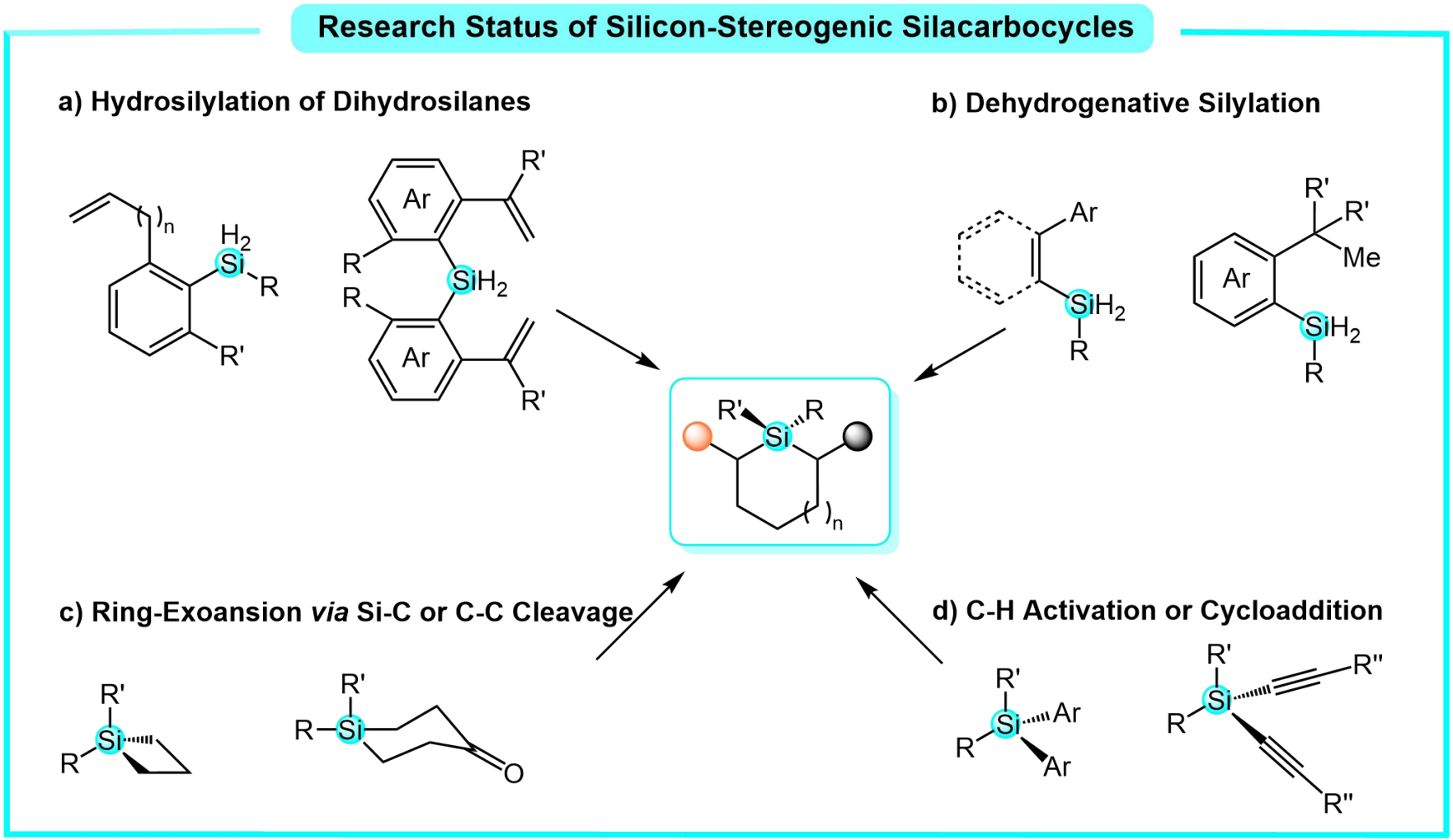


Silahaloperidol
(Modification of Metabolic Pathway)

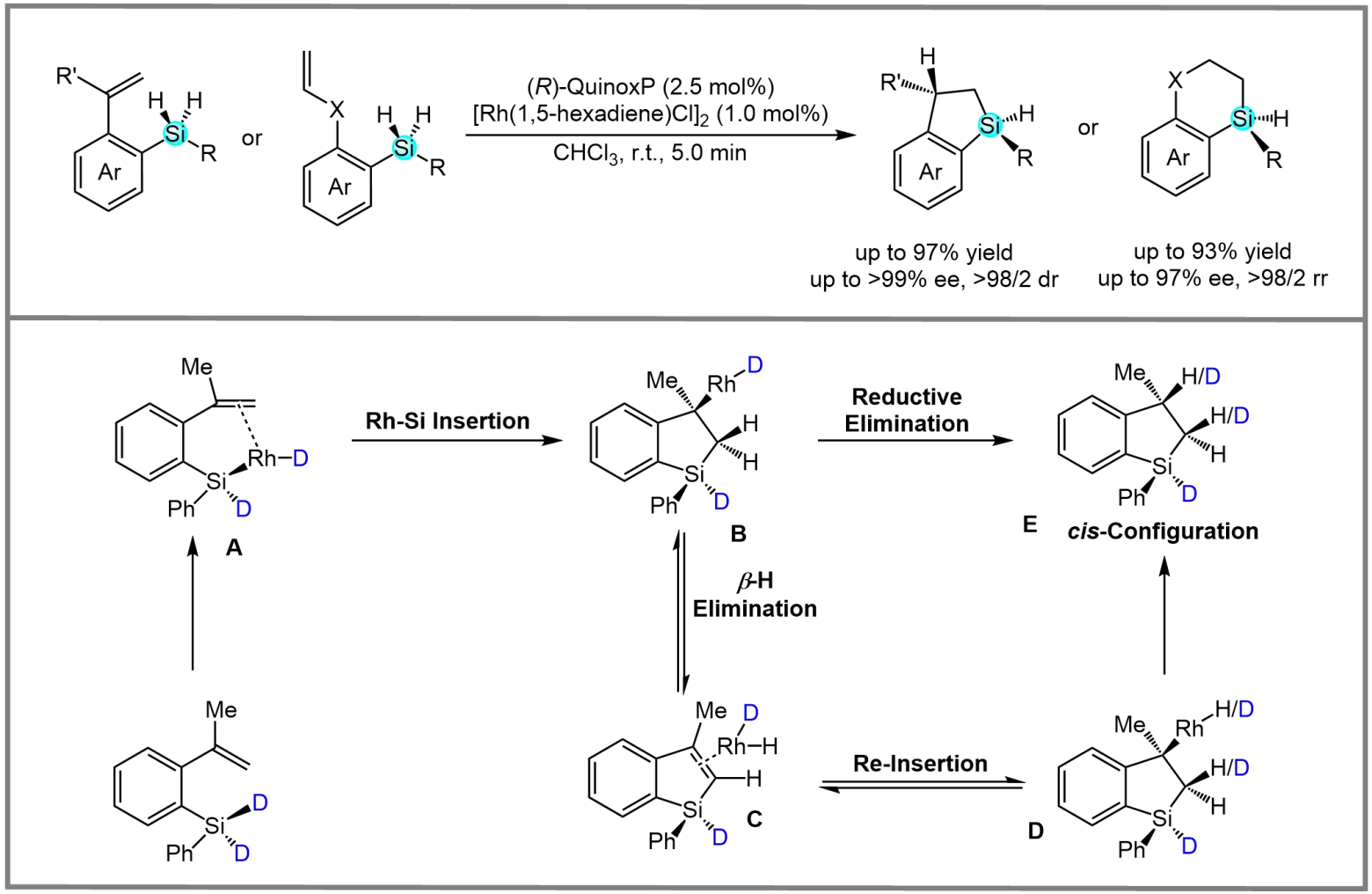


Silinezolid
(Increase in Brain/Plasma Conc.)

Introduction

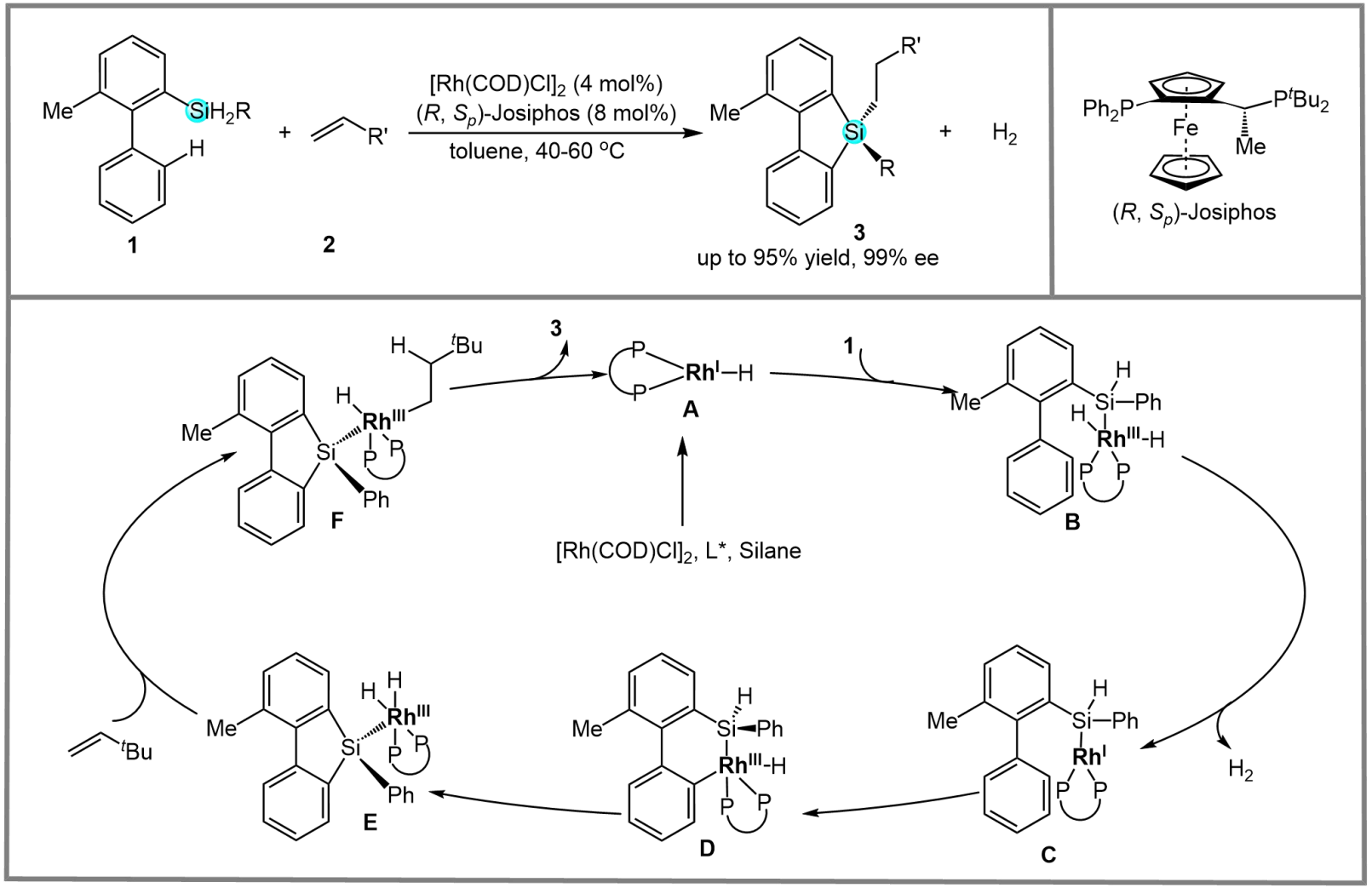


Hydrosilylation of Dihydrosilanes



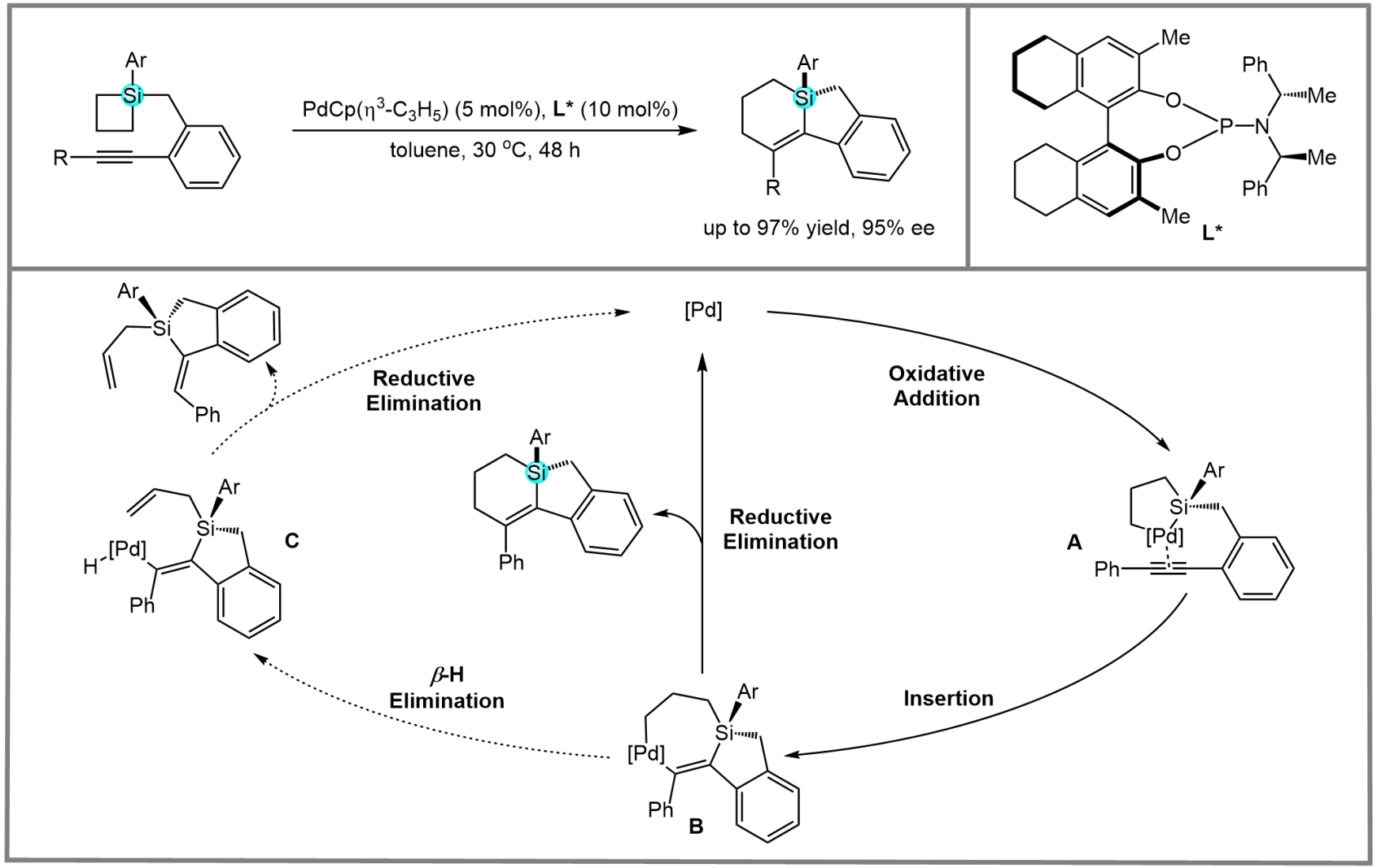
Huang, Y.-H.; Wu, Y.; Peng, Q.; Wang, P. *Angew. Chem. Int. Ed.* **2022**, *61*, e202113052

Dehydrogenative Silylation



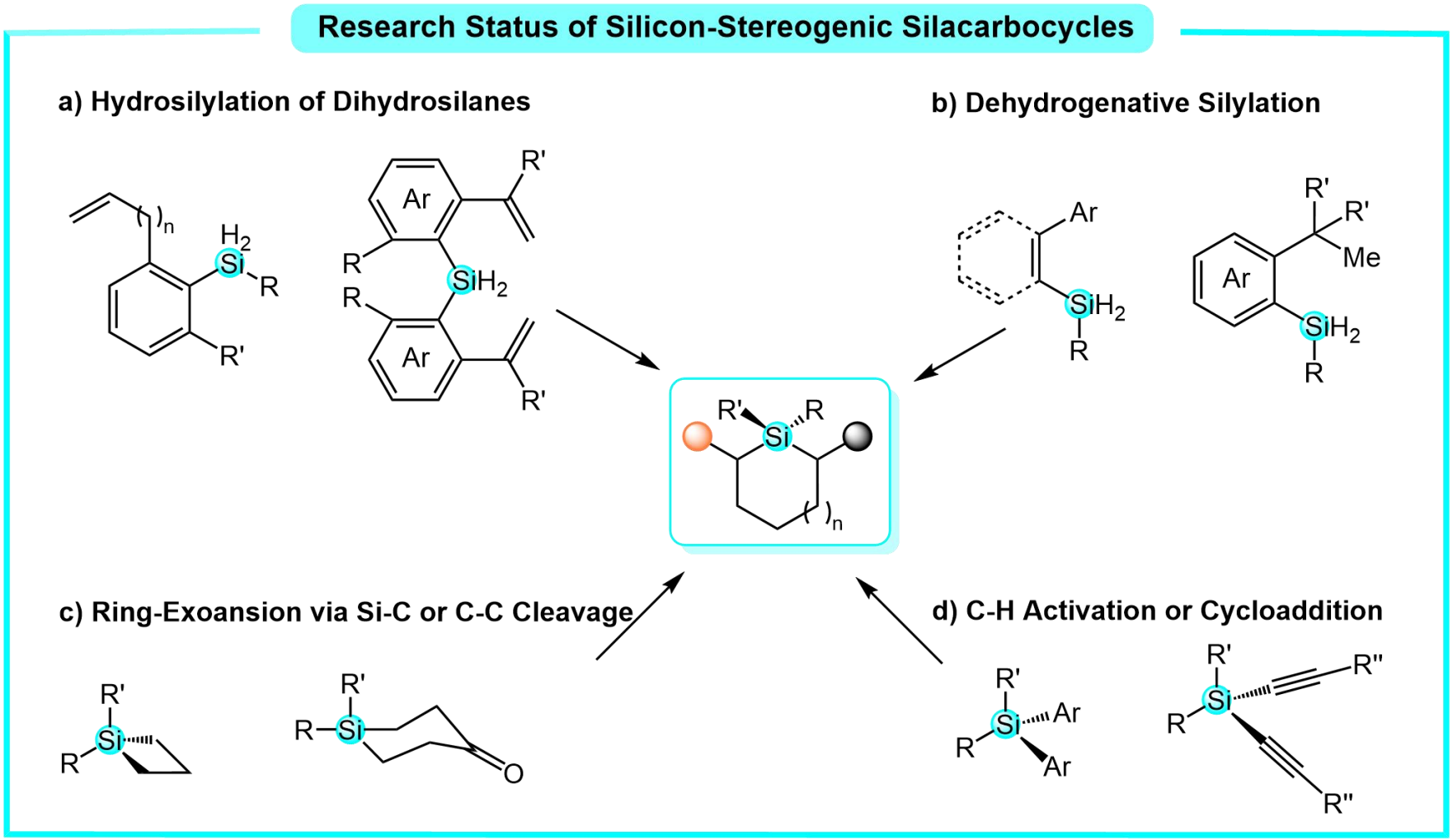
Mu, D.; Yuan, W.; He, C. *J. Am. Chem. Soc.* **2020**, *142*, 13459–13468

Ring-Expansion *via* Si-C or C-C Cleavage

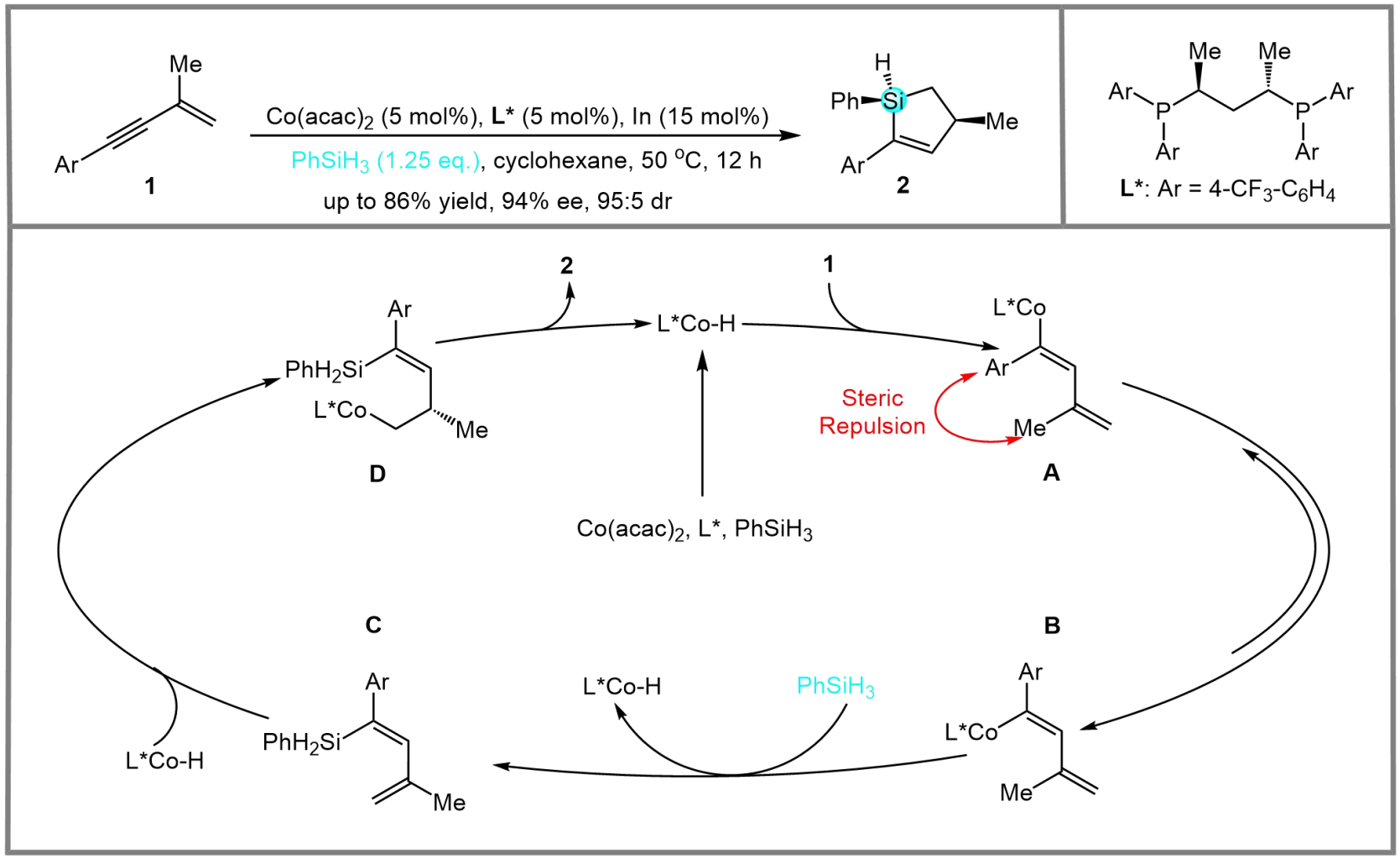


Shintani, R.; Moriya, K.; Hayashi, T. *J. Am. Chem. Soc.* **2011**, *133*, 16440–16443

Introduction

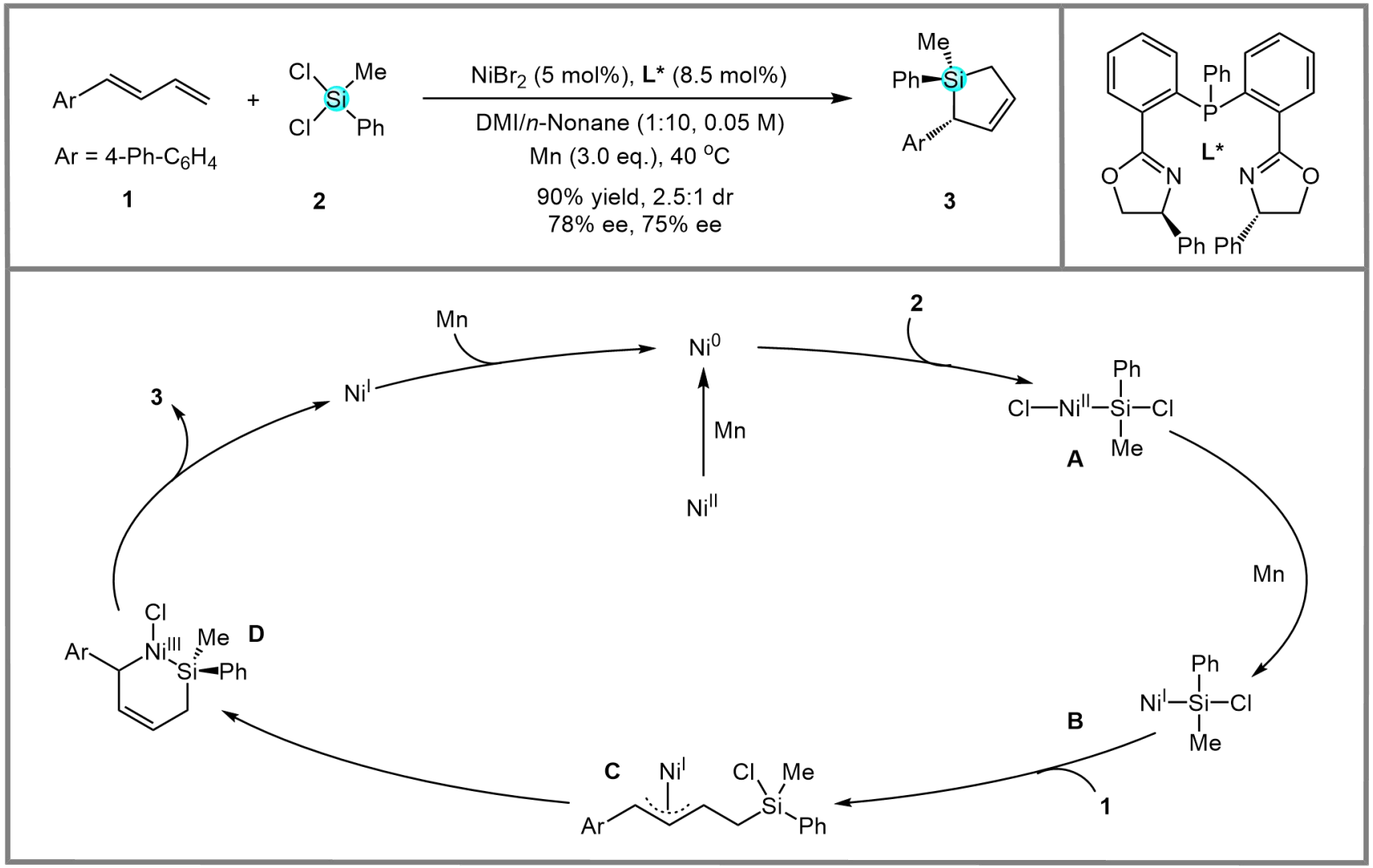


Asymmetric Synthesis of Silacarbocycles with Sila-Synthons



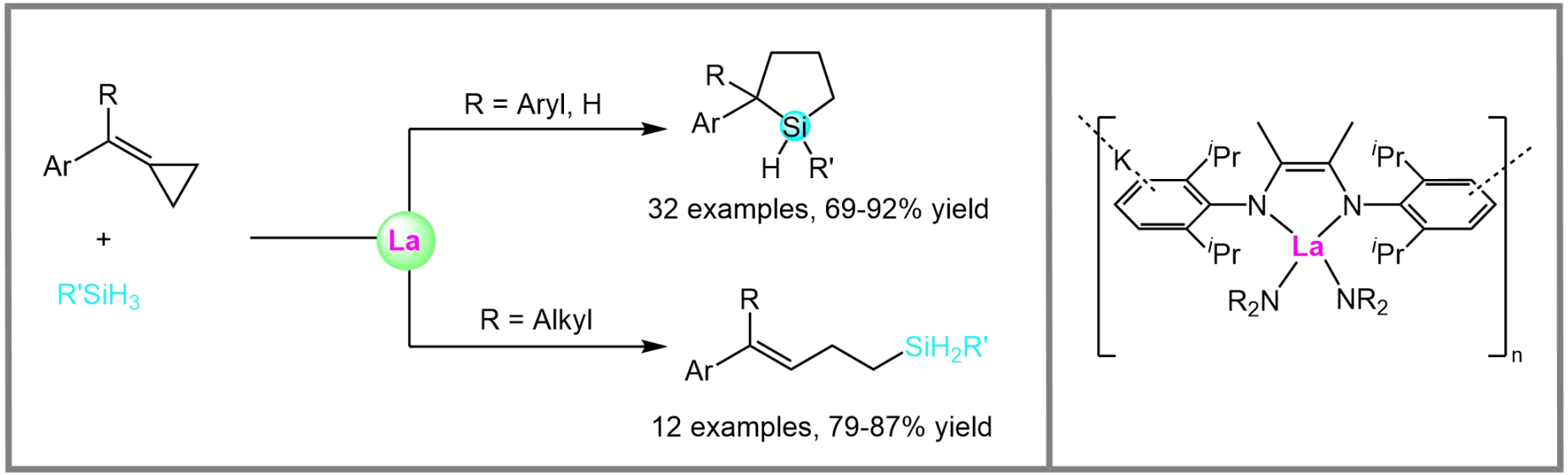
Lu, W.; Zhao, Y.; Meng, F. *J. Am. Chem. Soc.* **2022**, *144*, 5233-5240

Asymmetric Synthesis of Silacarbocycles with Sila-Synthons



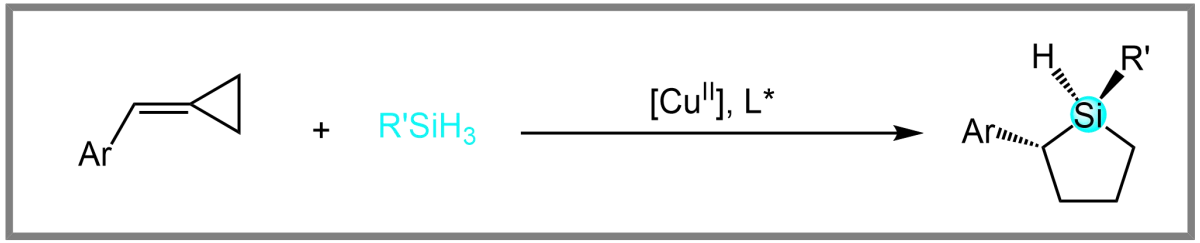
Qi, L.; Pan, Q.-Q.; Shu, X.-Z. *J. Am. Chem. Soc.* **2023**, *145*, 13008-13014

La-Catalyzed Cascade Hydrosilyations of Aryl MCPs (*racemic*)



Xu, X.; Xu, X.; Cui, C. *J. Am.Chem. Soc.* **2024**, *146*, 4060–4067

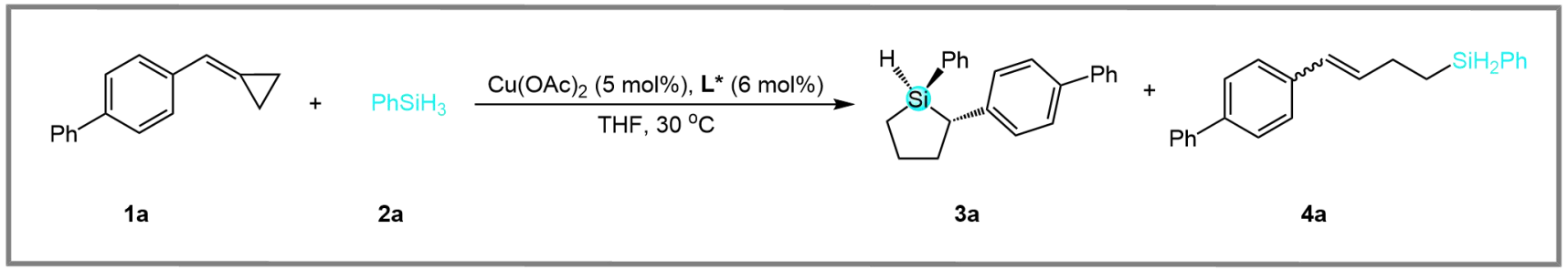
Project Synopsis



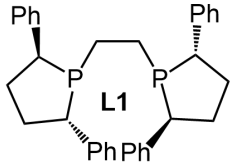
Challenges:

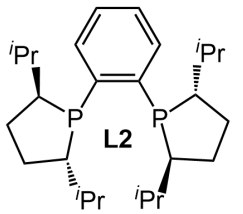
- Prematurely terminating the reaction affording either (cyclopropyl)methylsilanes or homoallylsilanes;
- The requiring a high level of enantio- and diastereoselectivity control;
- Accurately controlling the number of the Si–H bonds involved in the desired reaction when multiple Si–H bonds exist in the silanes

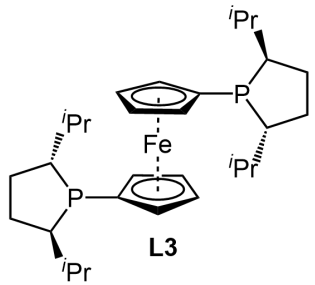
Optimization of Reaction Conditions

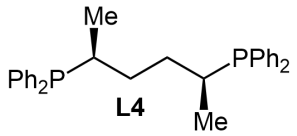


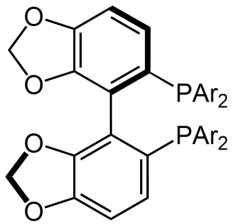
Entry	L	Solvent	3a			4a	
			Yield	ee	dr	yield	*Z* :*E*
1	L1	THF	83%	98%	5.6:1	12%	1:4.1
2	L2	THF	59%	92%	7.4:1	15%	1:1.1
3	L3	THF	trace	/	/	33%	1:3.1
4	L4	THF	trace	/	/	88%	1:9
5	L5	THF	trace	/	/	65%	1:10
6	L6	THF	95%	99%	>25:1	trace	/
7	L6	Et_2O	77%	98%	>25:1	19%	1.4:1
8	L6	2-Me-THF	16%	98%	>25:1	85%	1.:1.8
9	L6	Toluene	50%	98%	>25:1	46%	1:2.1







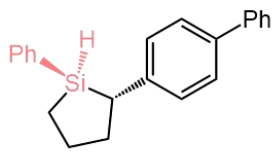




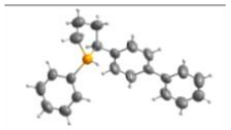
L5: Ar = Ph

L6: Ar = 3,5-^{t}Bu-4-OMe-C_6H_2

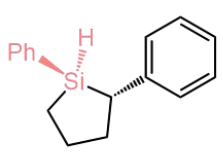
Scope of MCPs



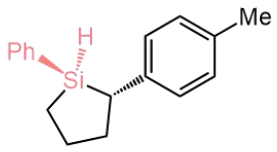
3a, 93% yield
99% ee, >25:1 dr



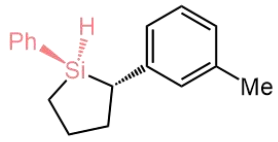
CCDC: 2299718
3a, x-ray structure



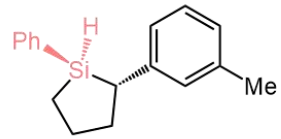
3b, 72% yield
99% ee, >25:1 dr



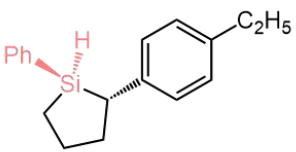
3c, 92% yield
99% ee, >25:1 dr



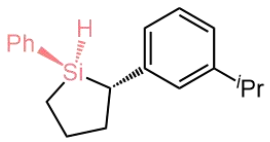
3d, 97% yield
98% ee, >25:1 dr



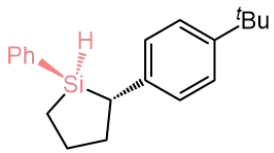
3e,[c] 33% yield
92% ee, >25:1 dr



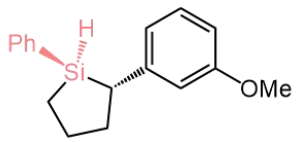
3f, 70% yield
99% ee, >25:1 dr



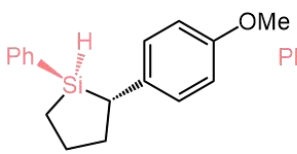
3g, 70% yield
>99% ee, >25:1 dr



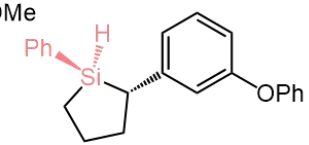
3h, 82% yield
99% ee, >25:1 dr



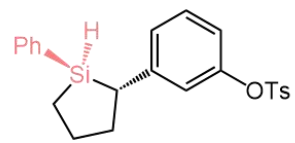
3i, 70% yield
96% ee, >25:1 dr



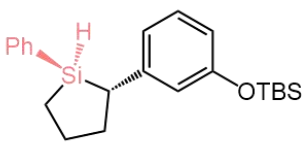
3j, 50% yield
98% ee, >25:1 dr



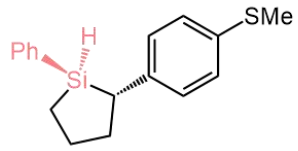
3k, 98% yield
98% ee, >25:1 dr



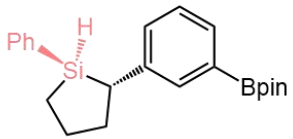
3l, 81% yield
96% ee, >25:1 dr



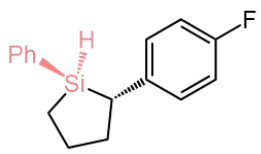
3m, 52% yield
>99% ee, >25:1 dr



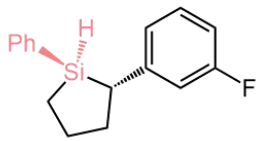
3n, 90% yield
99% ee, >25:1 dr



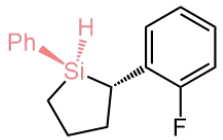
3o,[c] 52% yield
90% ee, >25:1 dr



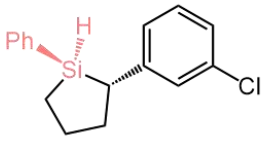
3p, 73% yield
90% ee, >25:1 dr



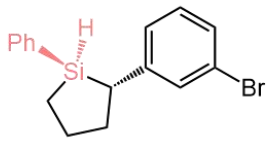
3q, 70% yield
98% ee, >25:1 dr



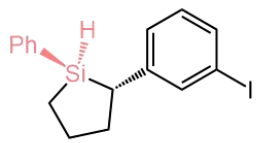
3r, 38% yield
>99% ee, >25:1 dr



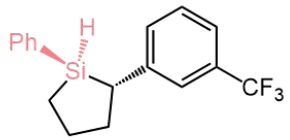
3s, 90% yield
99% ee, >25:1 dr



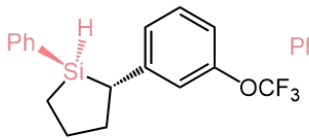
3t, 73% yield
98% ee, >25:1 dr



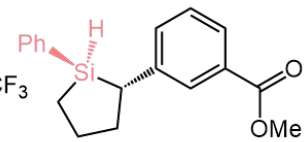
3u, 74% yield
>99% ee, 11:1 dr



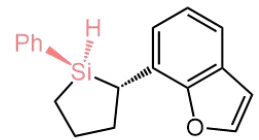
3v, 63% yield
98% ee, >25:1 dr



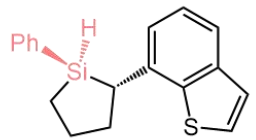
3w, 78% yield
98% ee, >25:1 dr



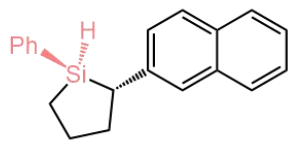
3x, 70% yield
97% ee, >25:1 dr



3y, 73% yield
98% ee, >25:1 dr



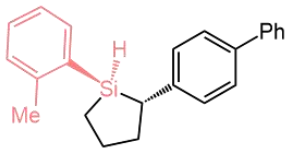
3z, 91% yield
90% ee, 20:1 dr



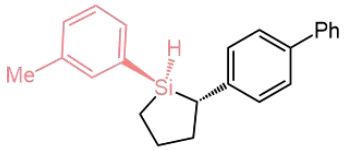
3aa, 85% yield
>99% ee, 20:1 dr

Scope of Silanes and Bioactive Molecules

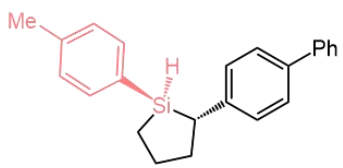
scope of silanes



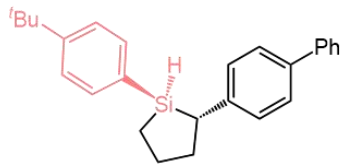
3ab, 94% yield
99% ee, >25:1 dr



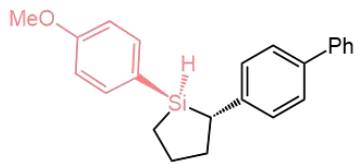
3ac, 90% yield
99% ee, >25:1 dr



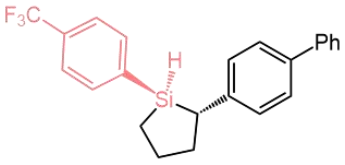
3ad, 60% yield
>99% ee, >25:1 dr



3ae, 90% yield
98% ee, >25:1 dr

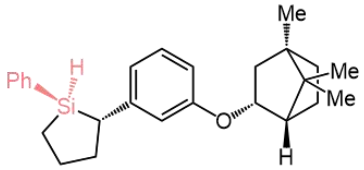


3af, 91% yield
98% ee, >25:1 dr

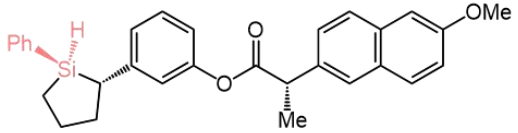


3ag, 91% yield
98% ee, >25:1 dr

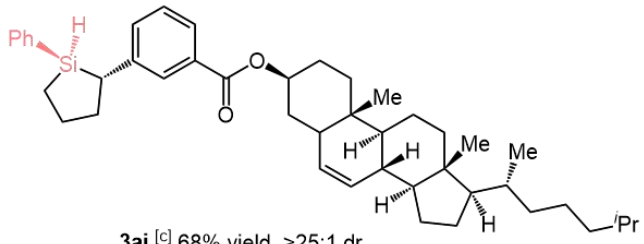
examples with core structures of bioactive molecules



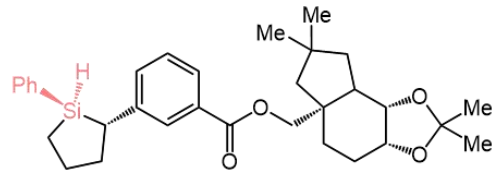
3ah,[c] 62% yield, >25:1 dr
from borneol



3ai,[c] 66% yield, >25:1 dr
from naproxen



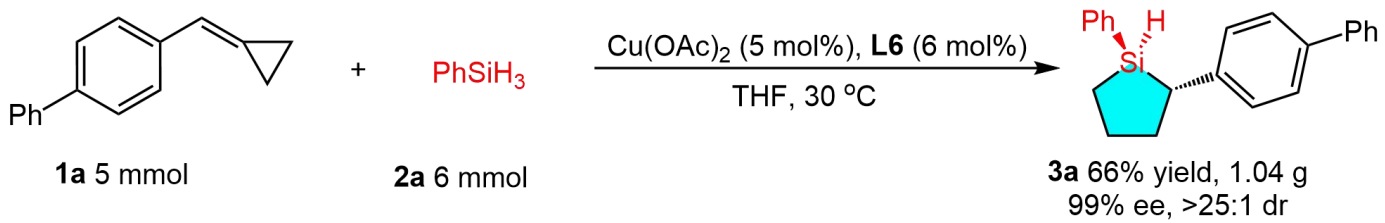
3aj,[c] 68% yield, >25:1 dr
from cholesterol



3ak,[c] 42% yield, >25:1 dr
from diacetonefructose

Scale-up Preparation and Transformations

a) Gram-scale synthesis

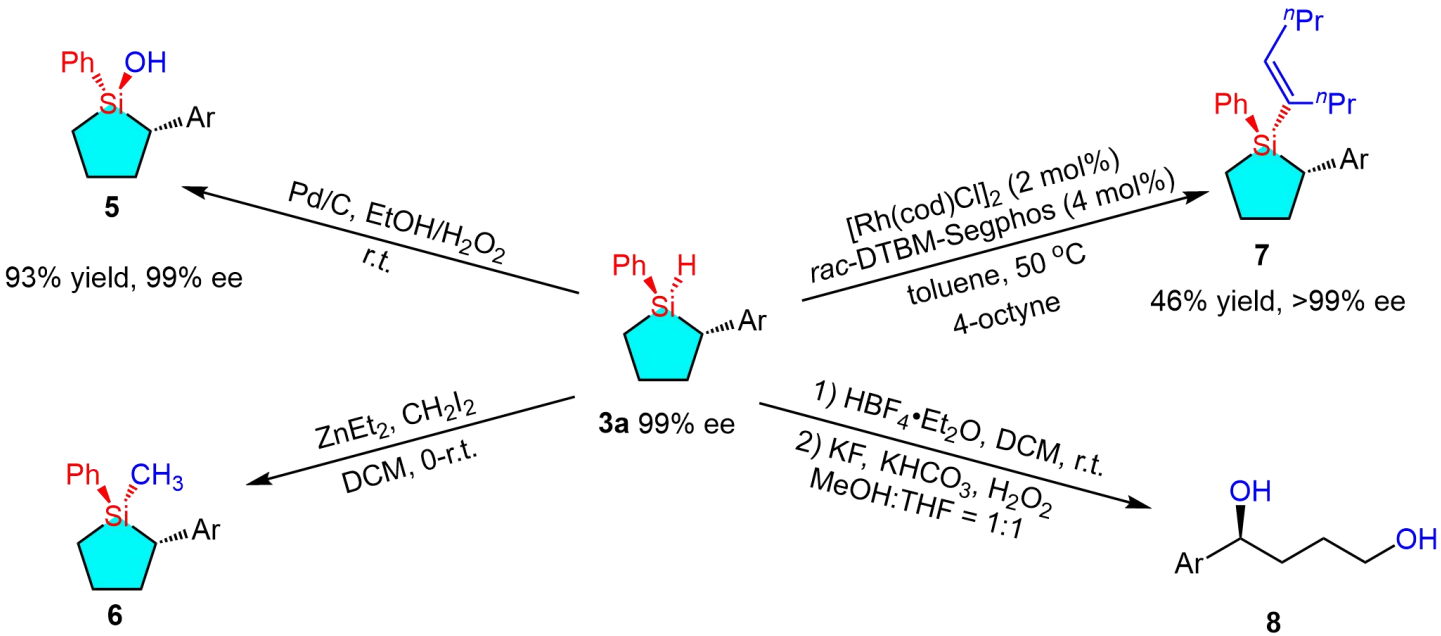


1a 5 mmol

2a 6 mmol

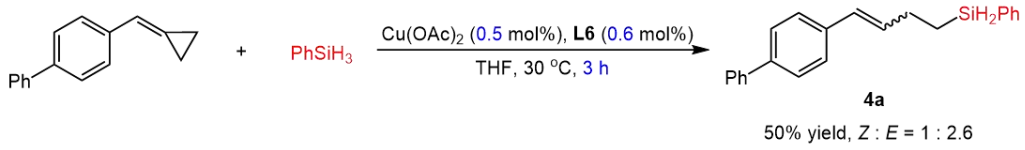
3a 66% yield, 1.04 g
99% ee, >25:1 dr

b) Stereospecific transformations of chiral silacyclopentane



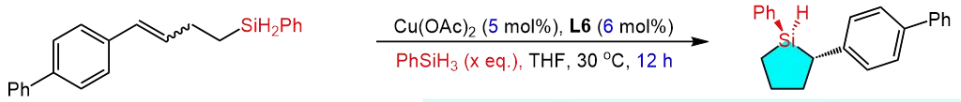
Mechanism Studies

a) Control experiments



4a

50% yield, *Z* : *E* = 1 : 2.6

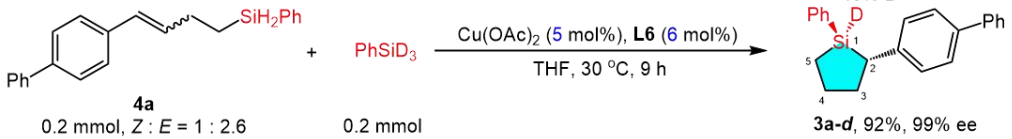


4a

0.2 mmol, *Z* : *E* = 1 : 2.6

entry	silane	**3a** (yield, ee)
1	$PhSiH_3$ (1 eq.)	93%, 99%
2	w/o $PhSiH_3$	97%, 99%

b) Deuteration-labeling experiments

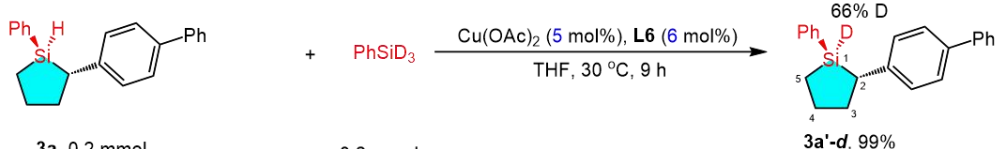


4a

0.2 mmol, *Z* : *E* = 1 : 2.6

0.2 mmol

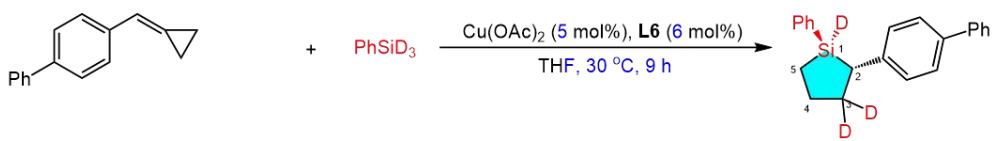
3a-*d*, 92%, 99% ee



3a, 0.2 mmol

0.2 mmol

3a'-*d*, 99%

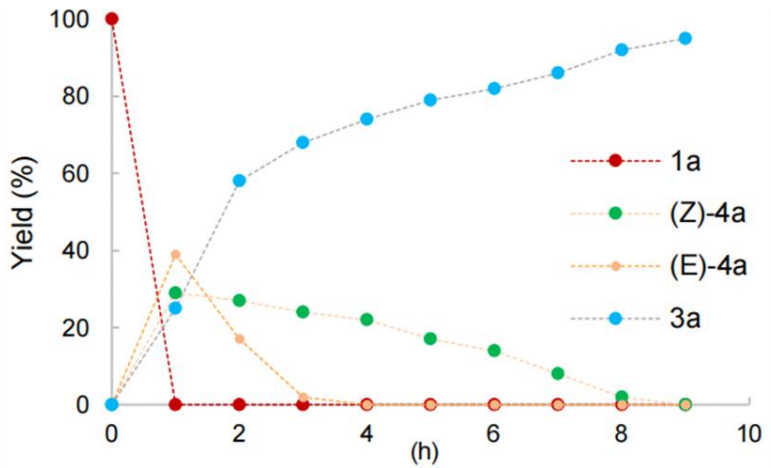


1a, 0.2 mmol

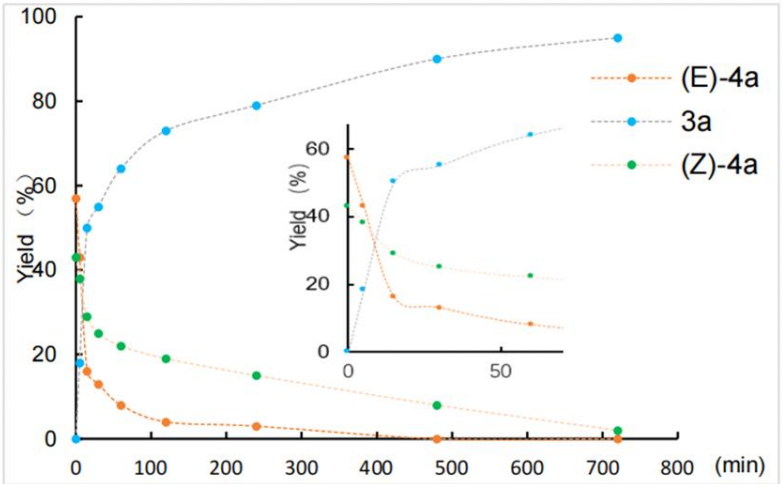
0.2 mmol

3a-*d*$_3$, 95%

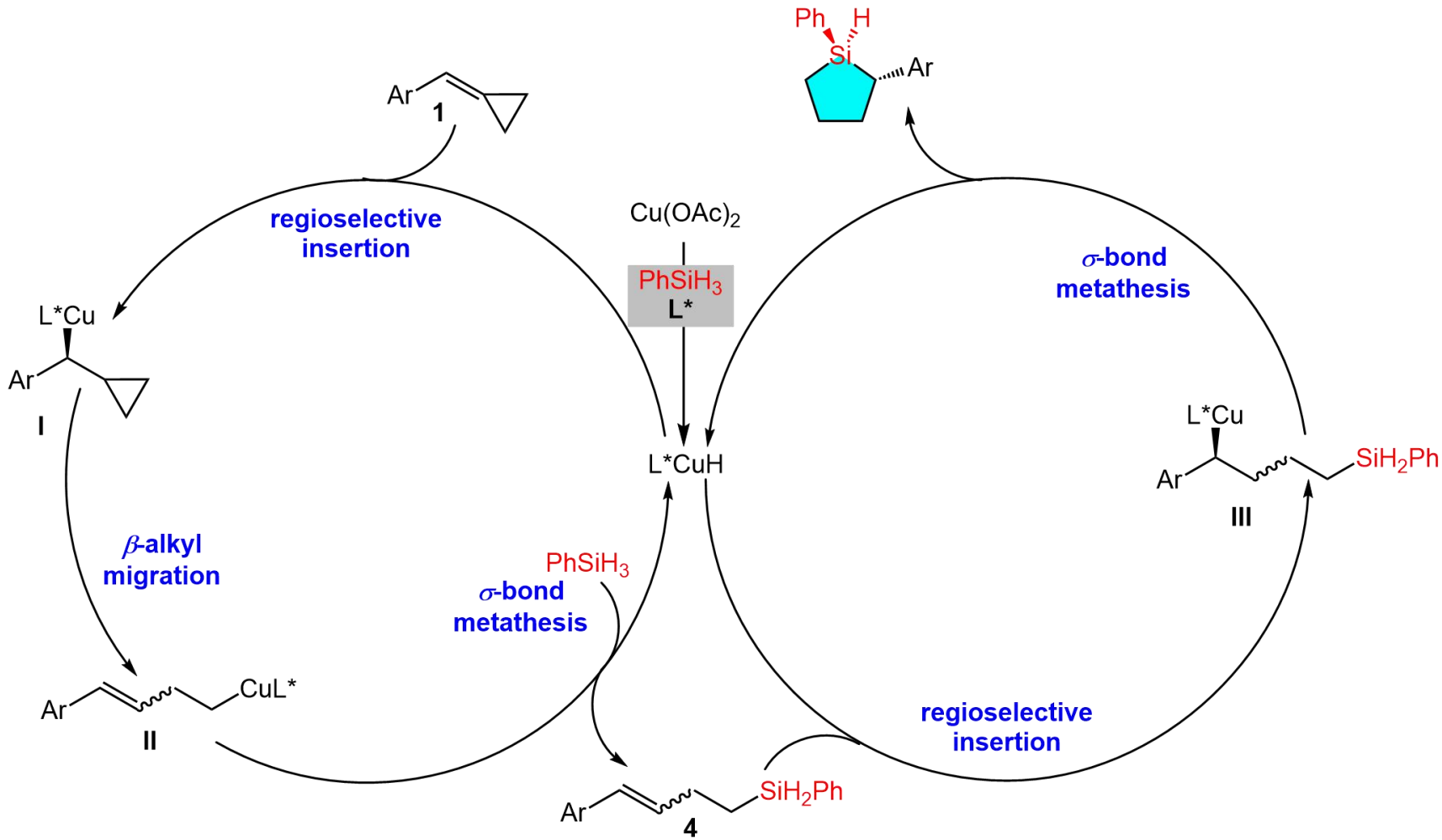
c) Time course study of the sequential hydrosilylation of **1a**



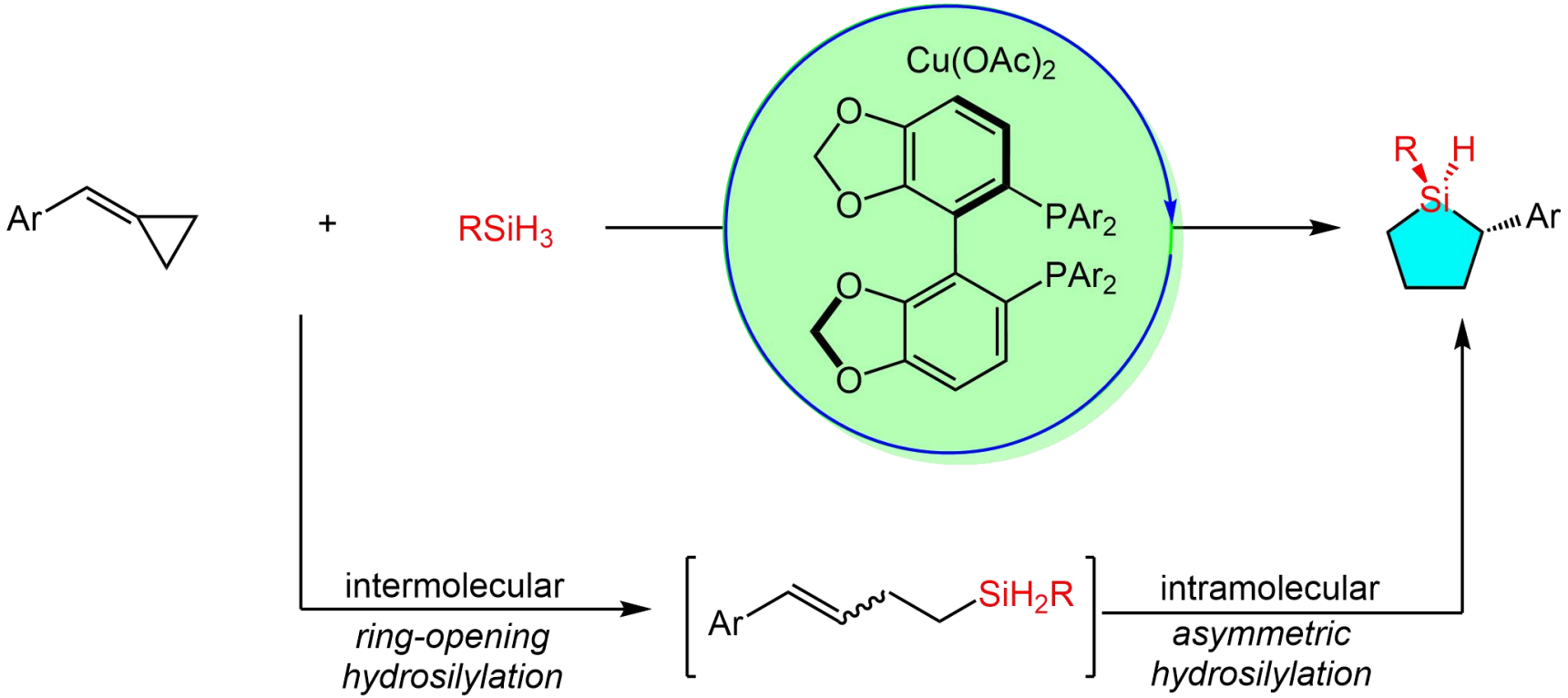
d) Time course study of the hydrosilylation toward stereoisomeric homoallylsilanes **4a**



Proposed Mechanism



Summary



- ✓ Sequential asymmetric hydrosilylation
- ✓ Consecutive Si- & C-stereogenic centers
- ✓ Generally >98% ee & > 25:1 dr
- ✓ Readily available materials

Writing Strategy

☐ The First Paragraph

硅碳环的重要性
及其应用

以往的合成方法及挑战

引出本文工作

✓ **Silacarbocycles are important and valuable compounds, which play an essential role in many areas of synthetic chemistry, such as efficient resolution reagents, mechanistic probes in transition metal-catalyzed reactions and superior performance ligands for asymmetric catalysis. In addition, these compounds have also widely utilized in the territories of material science and pharmaceuticals.**

✓ **In this regard, progress has led to various practical methods, such as cycloaddition and ring expansion reactions, that have greatly expanded the capability to produce a large number of silacarbocycles. By comparison, the access to silacarbocycles featuring silicon-stereogenic centers in an enantioselective manner have remained underdeveloped**

✓ **Herein, we report the first example of enantioselective copper-catalyzed cascade inter- and intramolecular hydrosilylations of MCPs, allowing for the expedient synthesis of chiral silacyclopentanes containing consecutive silicon- and carbon-stereogenic centers**

Writing Strategy

☐ The Last Paragraph

总结工作

✓ In summary, we have developed a copper-catalyzed asymmetric sequential hydrosilylation of aryl MCPs with various primary silanes. A wide range of silacyclopentanes featuring consecutive silicon- and carbon-stereogenic centers have been expediently prepared with readily available starting materials in high yields with excellent enantio- and diastereoselectivity

本文亮点

✓ The experimental studies disclosed that this sequential hydrosilylation reaction underwent a copper-catalyzed intermolecular ring opening hydrosilylation of aryl MCPs with silanes to produce a Z/E mixture of homoallylic silanes intermediates, followed by an intramolecular copper-catalyzed stereoselective hydrosilylation to afford chiral silacyclopentanes.

展望

✓ Further studies on the development of new methods for construction of silicon-centered chirality are underway.

Representative Examples

- ✓ Meng and collaborators developed an **intriguing** cobalt-catalyzed sequential site- and stereoselective hydrosilylation of 1,3-enynes with readily available primary aryl silanes as feedstocks. (***adj***, 有趣的，迷人的)
- ✓ Therefore, the very limited **precedents** clearly prove the need for the design and development of catalytic strategies to efficiently produce valuable silacarbocyclic compounds featuring siliconstereogenic centers from readily accessible starting materials (***n.*** 示例，范例)
- ✓ The inherent high ring strain (40 kcal mol-1) has **endowed** a number of intriguing transformations of MCPs. (***v.*** 捐赠，赋予)

Acknowledgment

Thanks
for your attention !