Literature Report 5

Catalytic Kinetic Resolution of Monohydrosilanes *via* Rhodium-Catalyzed Enantioselective Intramolecular Hydrosilylation

Reporter: Hao-Dong Chen
Checker: Yan-Jiang Yu
Date: 2024-06-24

Guo, F.-H.; Ren, F.; Wu, Y.; Wang, P. *Angew. Chem. Int. Ed.* **2024**, *63*, e202404732

CV of Prof. Peng Wang (王鹏)

Education & Experiment:

- **2003-2007** B.S., Tianjin University
- **2008-2013** Ph.D., SIOC (Prof. Yong Tang)
- **2013-2017** Research Associate, The Scripps Research Institute
- **2018-Present** Professor, SIOC

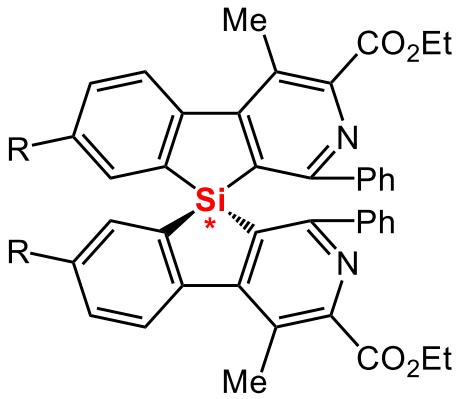
Research

- **Chiral Ligand Development**
- **Main Group Chemistry**
- **Reaction Discovery**

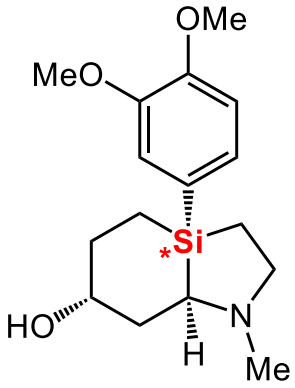
Contents

Introduction

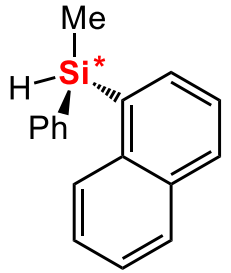
Function Organosilanes Bearing Enantioenriched Stereogenic Silicon Centers



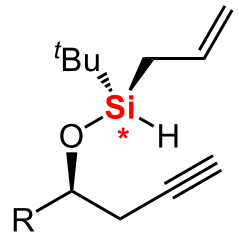
CPL-active molecule
(CPL = circularly polarized luminescence)



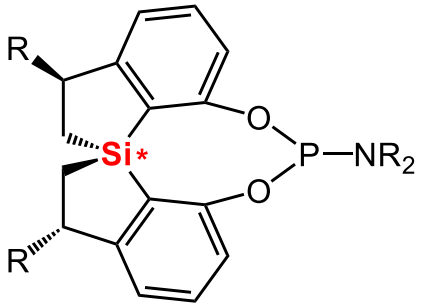
(-)-mesembranol
(antidepressant)



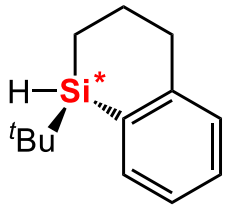
mechanistic probe



chiral auxiliaries



chiral ligand

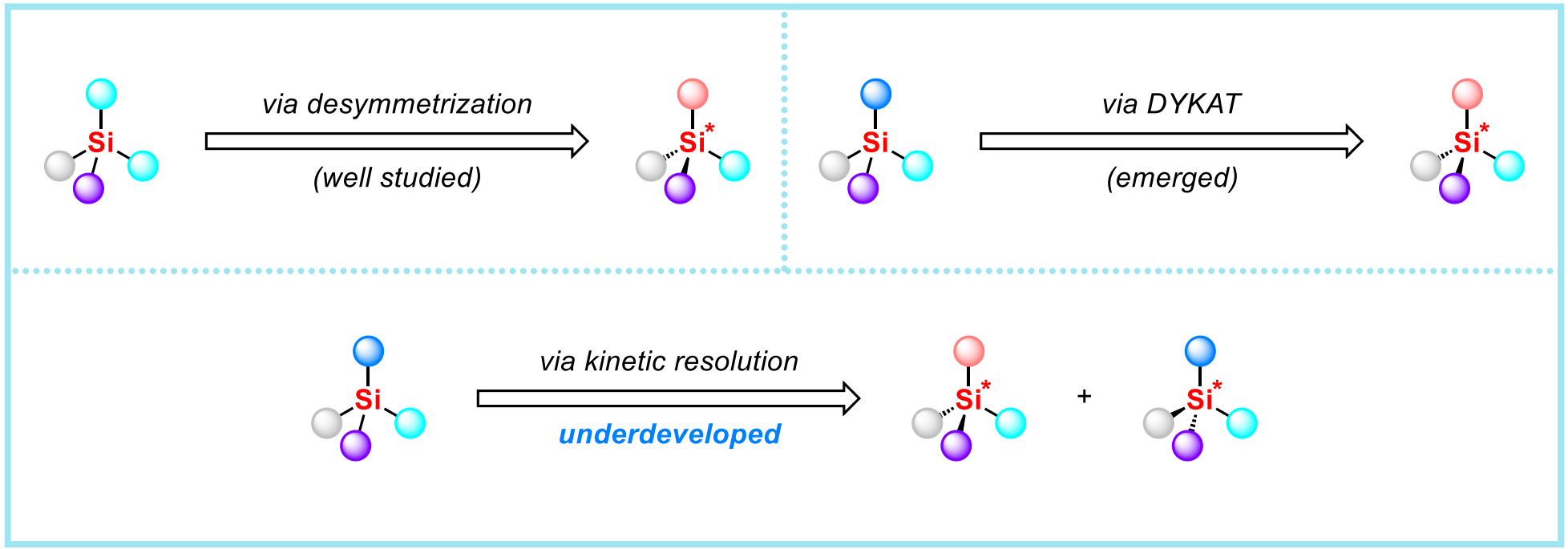


chiral reagent

Hu, T.; Zhao, C.; Zhang, Y.; Kuang, Y.; Gao, L.; Wang, W.; Su, Z.; Song, L. *Nat. Commun.* **2023**, *14*, 4900

Introduction

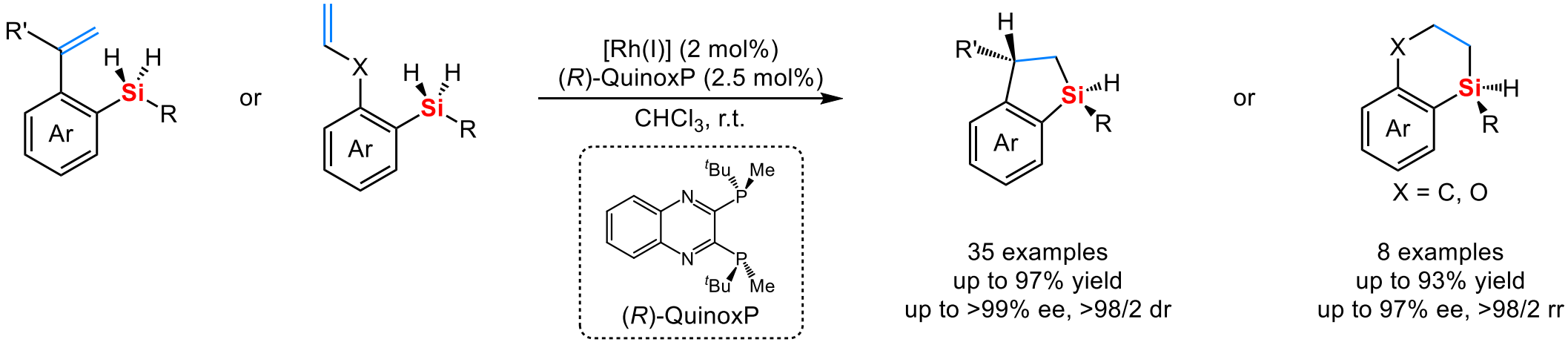
Approaches for Catalytic Construction of Si-Stereogenic Organosilanes



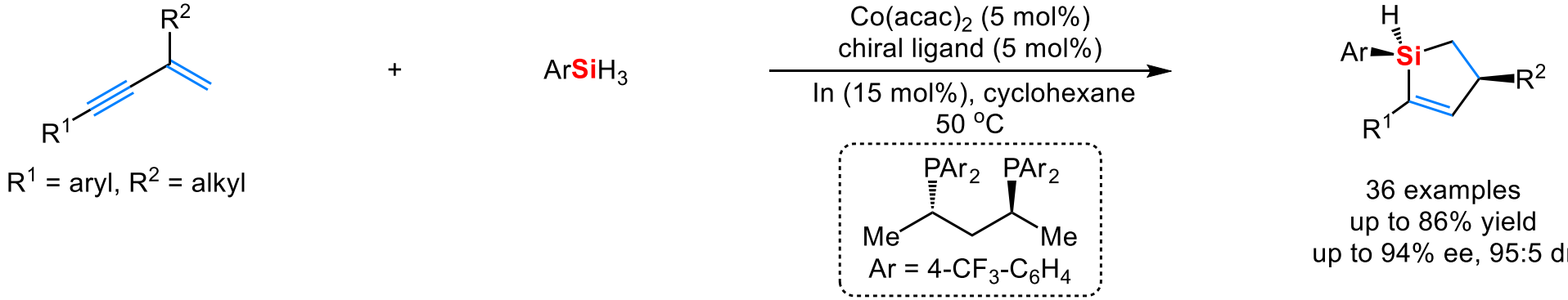
Guo, F.-H.; Ren, F.; Wu, Y.; Wang, P. *Angew. Chem. Int. Ed.* **2024**, *63*, e202404732

Introduction

Catalytic Construction of Si-Stereogenic Organosilanes via Desymmetrization



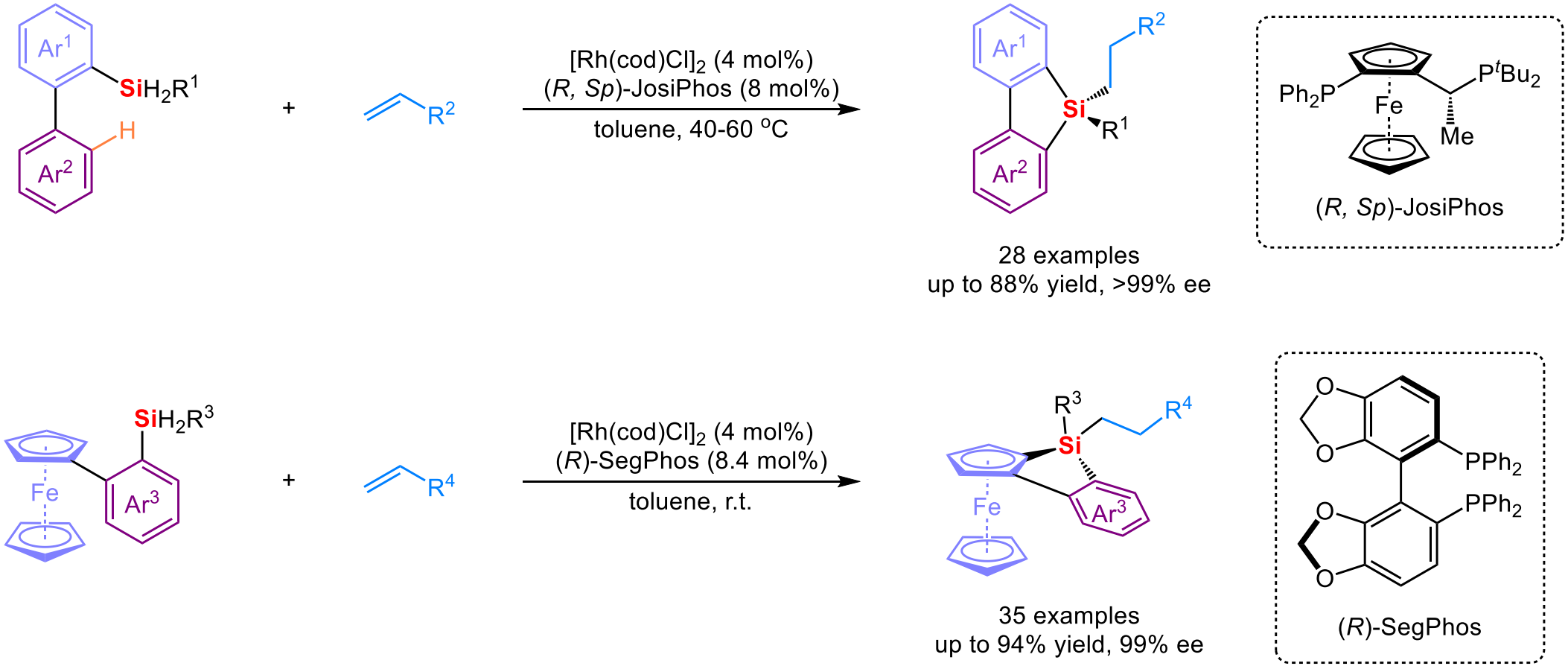
Huang, Y.-H.; Wu, Y.; Wang, P. *et al*. *Angew. Chem. Int. Ed.* **2022**, *61*, e202113052



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

Introduction

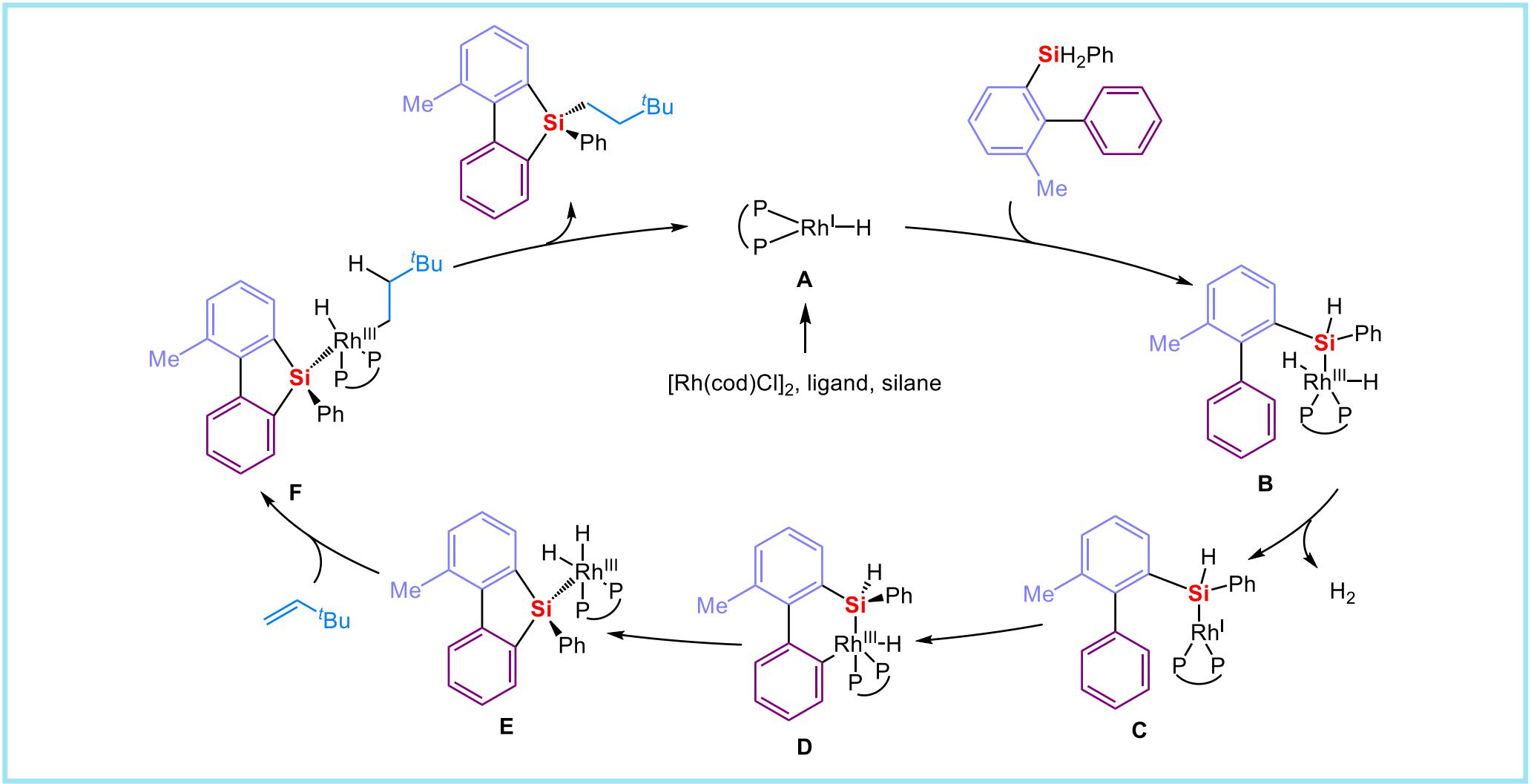
Catalytic Construction of Si-Stereogenic Organosilanes via Desymmetrization



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

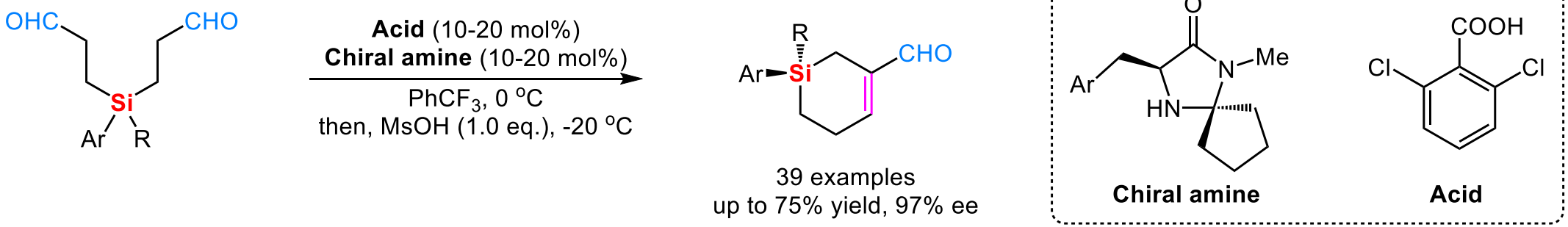
Introduction

Catalytic Construction of Si-Stereogenic Organosilanes via Desymmetrization

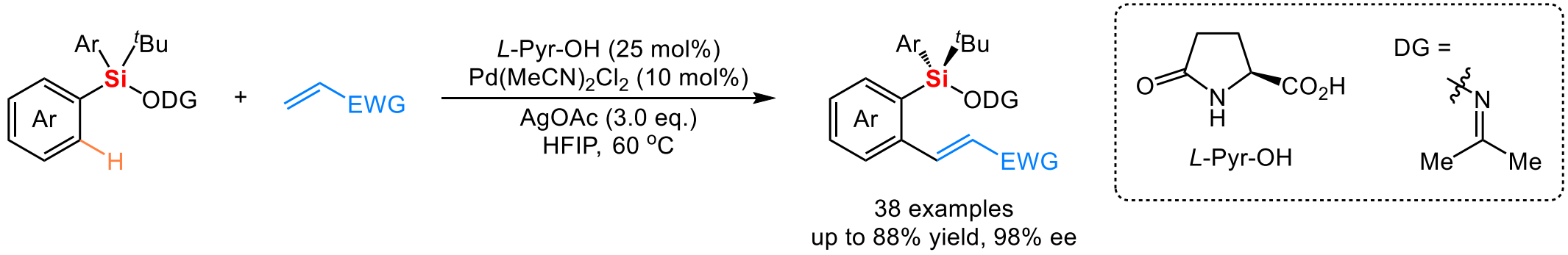


Introduction

Catalytic Construction of Si-Stereogenic Organosilanes via Desymmetrization



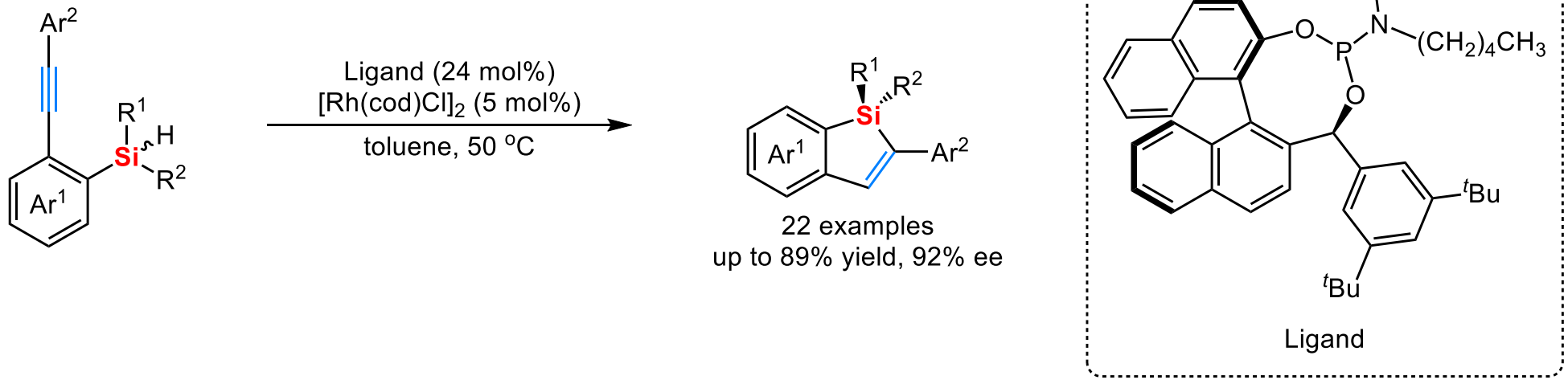
Zhang, X.-X.; Gao, Y.; Yu, J.-S. *et al. Angew. Chem. Int. Ed.* **2023**, *62*, e202217724



Zhao, J.-H.; Zheng, L.; Wang, P. *et al. Angew. Chem. Int. Ed.* **2024**, *63*, e202402612

Introduction

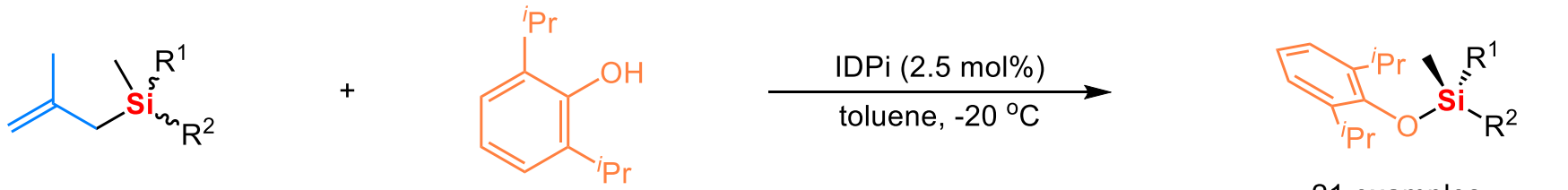
Catalytic Construction of Si-Stereogenic Organosilanes via DYKAT



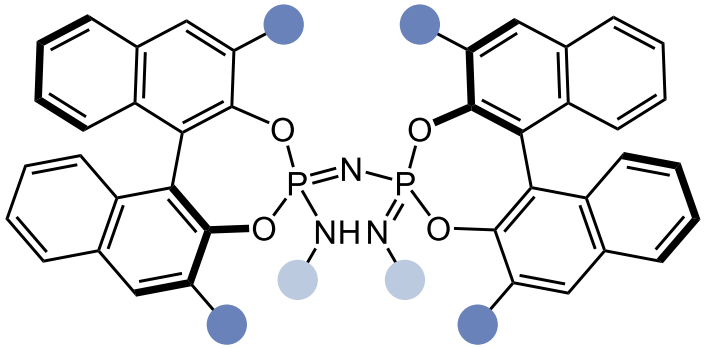
Zeng, Y.; Fang, X.-J.; Xu, L.-W. *et al. Angew. Chem. Int. Ed.* **2022**, *61*, e202214147

Introduction

Catalytic Construction of Si-Stereogenic Organosilanes via DYKAT



21 examples
up to 95% yield, 98% ee



= 4-^{t}Bu-C_6H_4

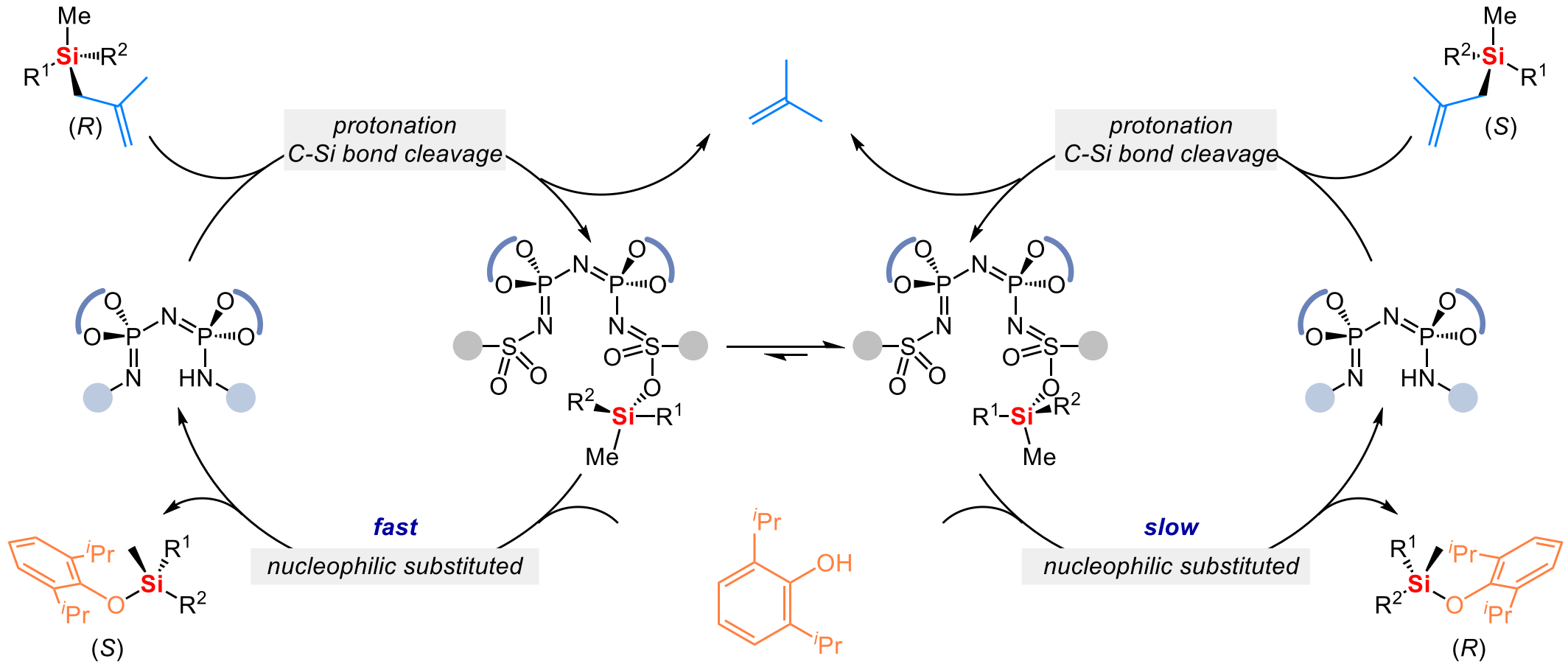
= SO_2CF_3 or SO_2-2-$C_{10}F_7$

IDPi

Zhou, H.; Properzi, R.; List, B. *et al. J. Am. Chem. Soc.* **2023**, *145*, 4994

Introduction

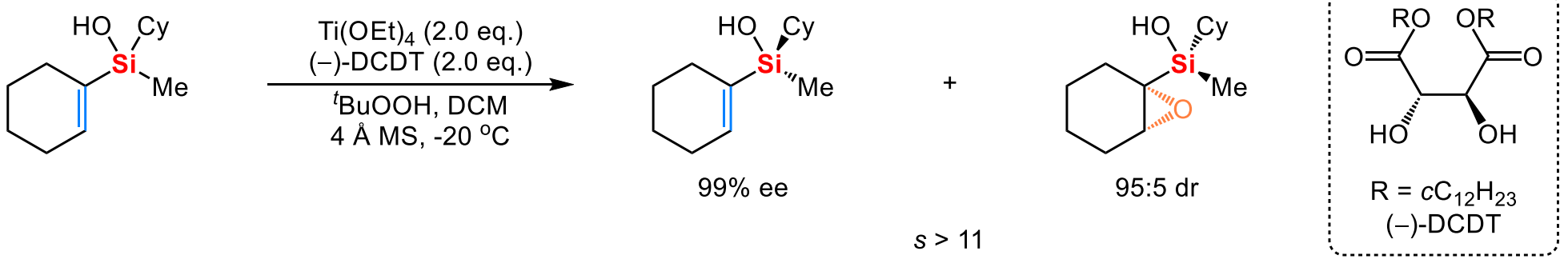
Catalytic Construction of Si-Stereogenic Organosilanes via DYKAT



Zhou, H.; Properzi, R.; List, B. *et al. J. Am. Chem. Soc.* **2023**, *145*, 4994

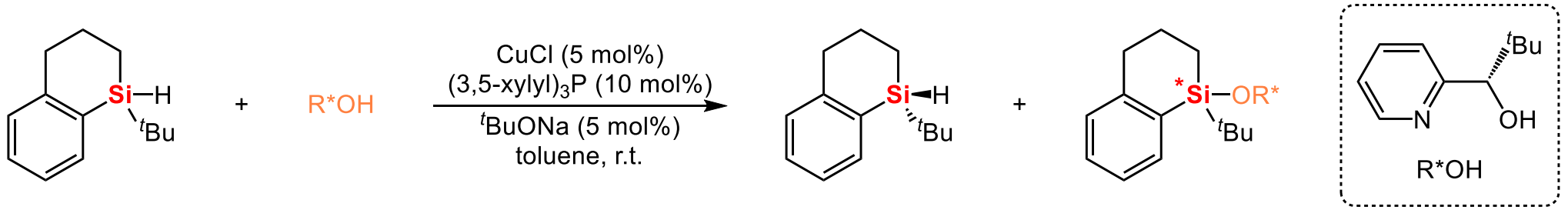
Introduction

Construction of Si-Stereogenic Organosilanes via KR



s > 11

Yamamoto, K.; Kawanami, Y.; Miyazawa, M. *J. Chem. Soc. Chem. Commun.* **1993**, 436

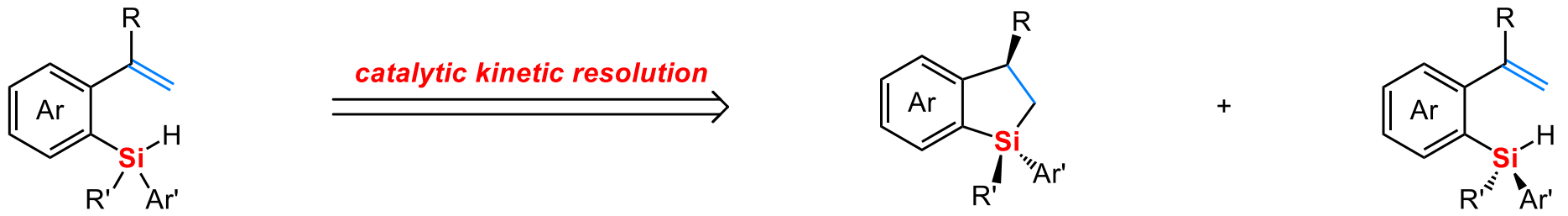


s = 4.9

Rendler, S.; Auer, G.; Oestreich, M. *et al. Adv. Synth. Catal.* **2006**, *348*, 1171

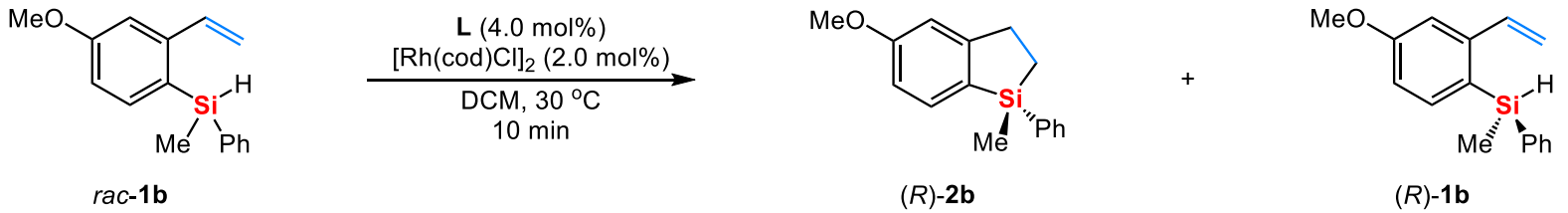
Project Synopsis

This Work: Access of Si-Stereogenic Silane via Catalytic Kinetic Resolution of Monohydrosilane

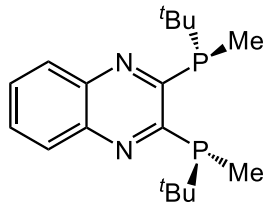


Optimization of the Reaction Conditions

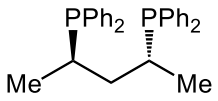
Ligand Evaluation



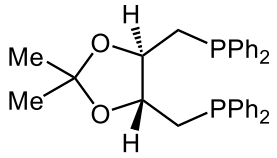
rac-**1b** (*R*)-**2b** (*R*)-**1b**



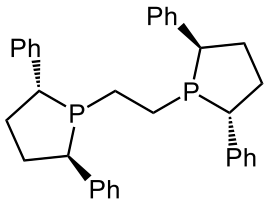
L1, (*R*)-QuinoxP
2b, 79%, 7% ee
1b, 10%, -0.4% ee
c = 89%, *s* = 1



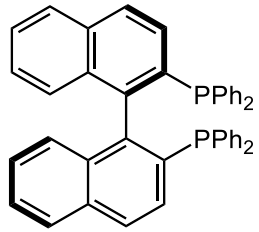
L2, (*R*)-BDPP
2b, 20%, -8% ee
1b, 63%, -5% ee
c = 24%, *s* = 2



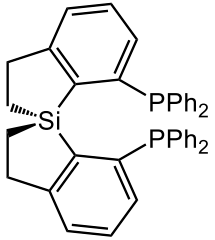
L3, (*R*)-DIOP
2b, 9%, 28% ee
1b, 74%, 4% ee
c = 11%, *s* = 2



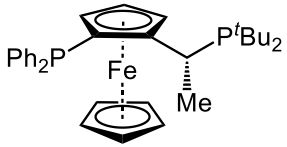
L4, (*R,R*)-Ph-BPE
2b, 5%, 45% ee
1b, 71%, -14% ee
c = 7%, *s* = 4



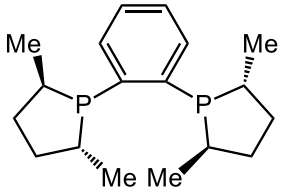
L5, (*R*)-BINAP
2b, 4%, 7% ee
1b, 79%, 4% ee
c = 5%, *s* = 8



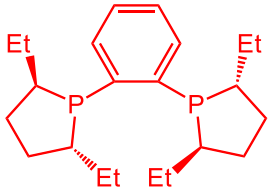
L6, (*S*)-SPSIP
2b, 16%, -5% ee
1b, 84%, 1%ee
c = 16%, *s* = 1



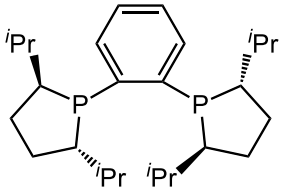
L7
2b, 5%, -5% ee
1b, 72%, 25% ee
c = 6%, *s* = 2



L8, (*R,R*)-Me-DuPhos
2b, 62%, 46% ee
1b, 27%, >99% ee
c = 70%, *s* = 11

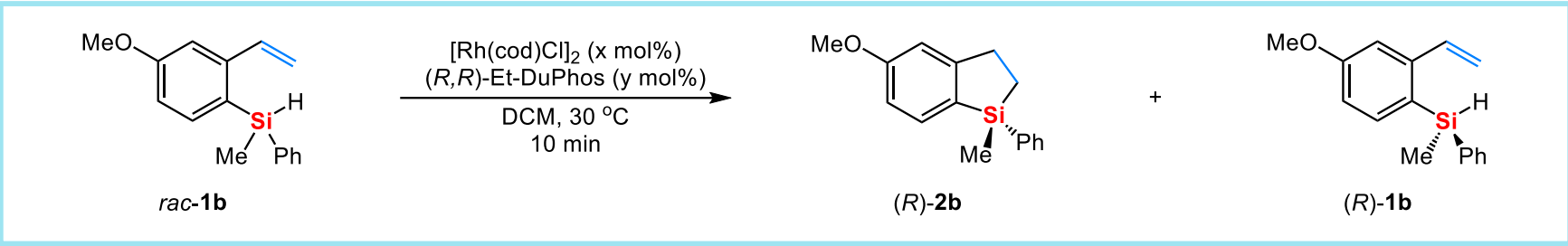


L9, (*R,R*)-Et-DuPhos
2b, 50%, 85% ee
1b, 45%, 95% ee
c = 53%, *s* = 43



L10, (*R,R*)-^{i}Pr-DuPhos
2b, 3%, 73% ee
1b, 92%, 2% ee
c = 3%, *s* = 5

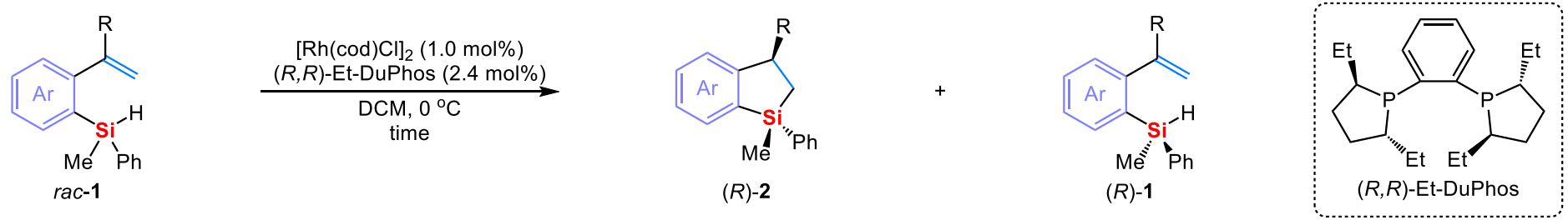
Optimization of the Reaction Conditions

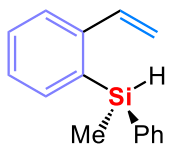


Entry	Solvent	X	Y	(*R*)-2b		(*S*)-1b		*C* (%)	*S*
				Yield (%)	Ee (%)	Yield (%)	Ee (%)		
1	DCM	2.0	4.0	50	85	45	95	53	43
2	$CHCl_3$	2.0	4.0	16	83	77	14	17	6
3	DCE	2.0	4.0	43	83	47	77	48	26
4	THF	2.0	4.0	12	74	81	10	13	6
5	PhMe	2.0	4.0	10	66	83	7	11	4
6	DCM	2.0	4.0	50	85	45	95	53	43
7	DCM	1.0	2.0	42	93	53	75	44	97
8	DCM	1.0	2.4	43	94	57	71	43	70
9[a]	DCM	1.0	2.4	40	95	60	64	40	95

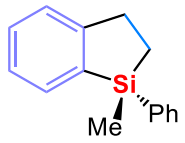
Reaction conditions: *rac*-1b (0.1 mmol), $[Rh(cod)Cl]_2$ (x mol%), (*R*,*R*)-Et-DuPhos (y mol%), DCM (1.0 mL), 30 °C, N_2, 10 min. The yield was determined by ^1H NMR using dibromomethane as the internal standard. The ee value was determined by chiral HPLC. Calculated conversion, $c = yield_{PR}/(yield_{SM} + yield_{PR})$. Selectivity, $s = Ln[(1-c)(1-ee_{SM})]/Ln[(1-c)(1+ee_{SM})]$. [a]The reaction was conducted at 0 °C, for 20 min.

Substrate Scope



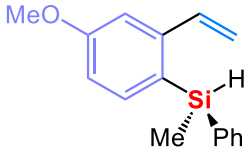


1a
44%, 96% ee

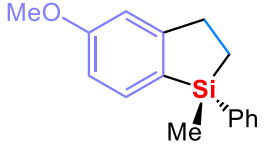


2a
49%, 84% ee

50 min, *c* = 51%, *s* = 97

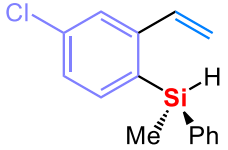


1b
45%, 98% ee

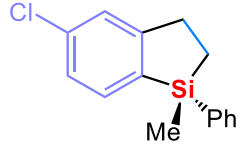


2b
49%, 88% ee

90 min, *c* = 53%, *s* = 65

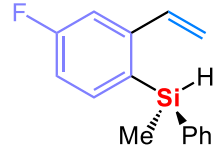


1c
48%, 94% ee

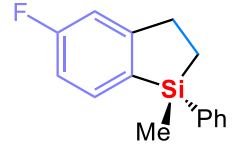


2c
46%, 77% ee

45 min, *c* = 52%, *s* = 50

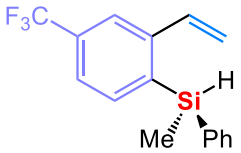


1d
51%, 90% ee

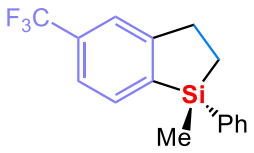


2d
46%, 89% ee

90 min, *c* = 49%, *s* = 95

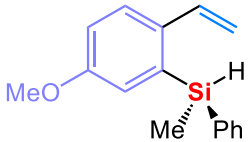


1e
45%, 81% ee

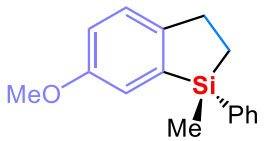


2e
52%, 76% ee

50 min, *c* = 50%, *s* = 29

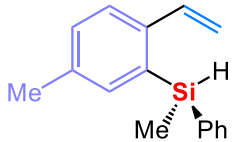


1f
50%, 89% ee

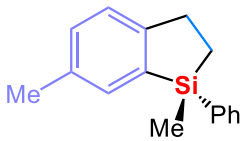


2f
50%, 92% ee

90 min, *c* = 49%, *s* = 78

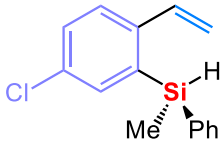


1g
48%, 94% ee

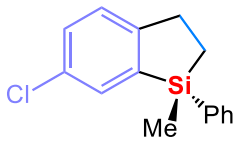


2g
46%, 92% ee

20 min, *c* = 50%, *s* = 115



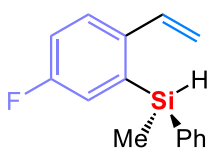
1h
50%, 91% ee



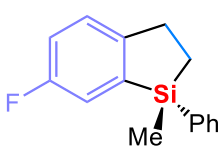
2h
46%, 85% ee

50 min, *c* = 50%, *s* = 67

Substrate Scope

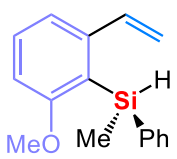


1i
49%, 84% ee

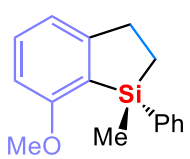


2i
47%, 87% ee

50 min, *c* = 49%, *s* = 39

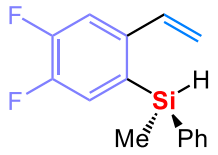


1j
47%, 73% ee

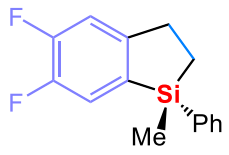


2j
47%, 79% ee

45 min, *c* = 49%, *s* = 16

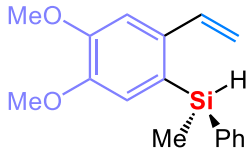


1k
47%, 87% ee

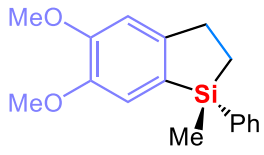


2k
49%, 80% ee

55 min, *c* = 50%, *s* = 41

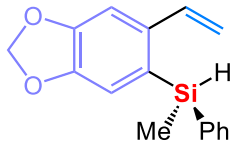


1l
48%, 88% ee

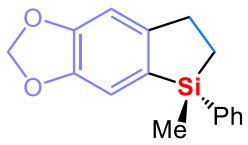


2l
43%, 91% ee

50 min, *c* = 48%, *s* = 122

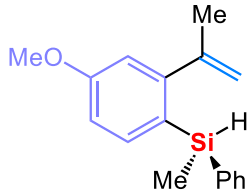


1m
48%, 92% ee

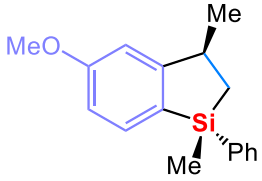


2m
52%, 91% ee

40 min, *c* = 50%, *s* = 79

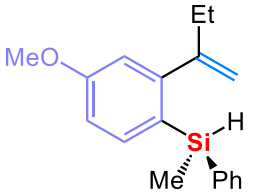


1n
51%, 84% ee

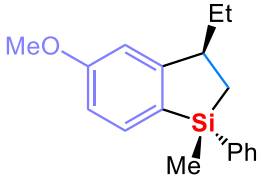


2n
44%, 90% ee, 21:1 dr

30 °C, 5 h, *c* = 50%, *s* = 30



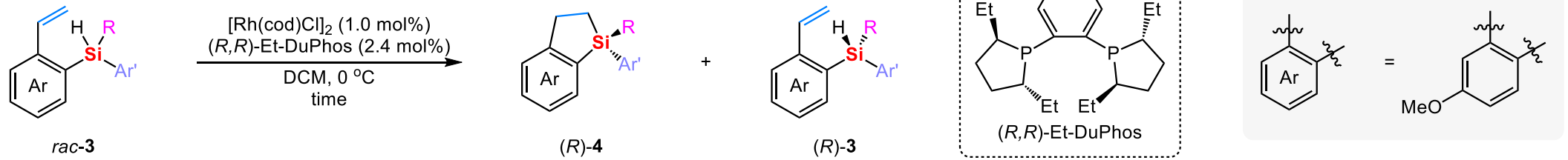
1o
49%, 68% ee

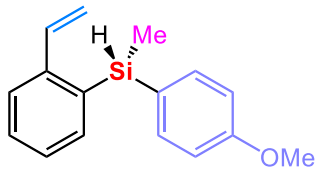


2o
51%, 86% ee, 12:1 dr

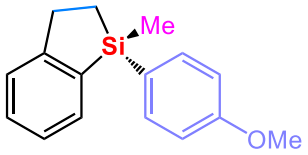
30 °C, 9 h, *c* = 47%, *s* = 15

Substrate Scope



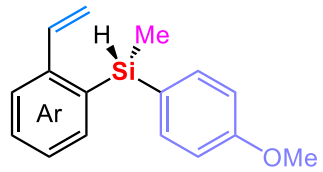


3a
49%, 92% ee

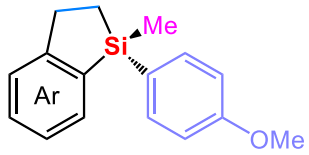


4a
51%, 88% ee

55 min, *c* = 51%, *s* = 53

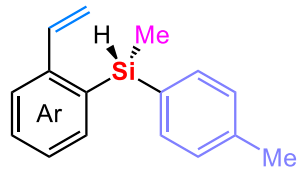


3b
49%, 80% ee

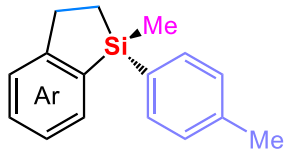


4b
45%, 91% ee

60 min, *c* = 47%, *s* = 48

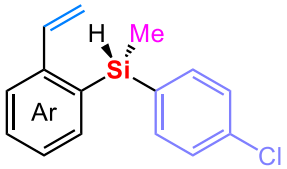


3c
51%, 88% ee

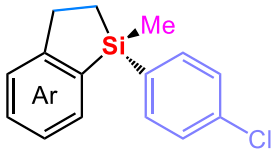


4c
49%, 93% ee

70 min, *c* = 50%, *s* = 45

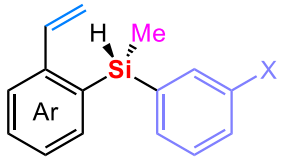


3d
47%, 96% ee

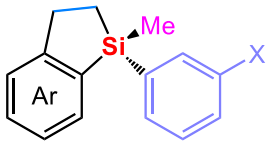


4c
49%, 89% ee

55 min, *c* = 52%, *s* = 65



X = Cl, **3e,** 52%, 83% ee



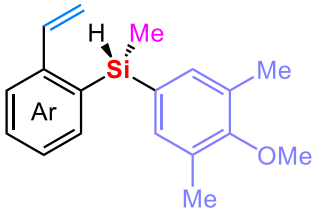
4e, 47%, 92% ee

45 min, *c* = 49%, *s* = 79

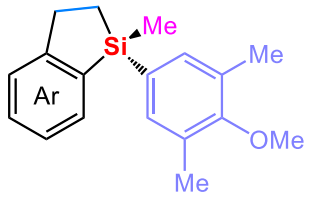
X = F, **3f,** 49%, 90% ee

4f, 51%, 92% ee

55 min, *c* = 48%, *s* = 95



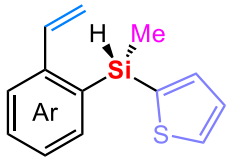
3g, 47%, 96% ee



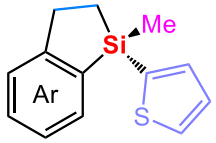
4g, 48%, 81% ee

60 min, *c* = 53%, *s* = 48

Substrate Scope

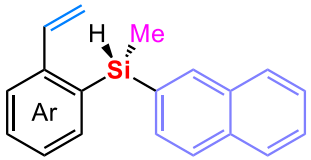


3h
46%, 87% ee

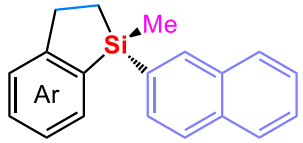


4h
50%, 87% ee

50 min, *c* = 50%, *s* = 41

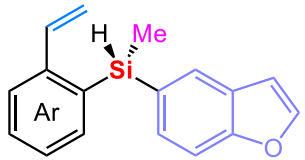


3i
52%, 81% ee

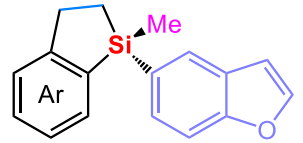


4i
47%, 83% ee

60 min, *c* = 50%, *s* = 24

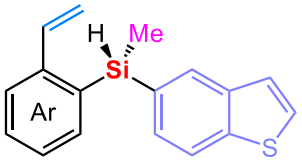


3j
49%, 93% ee

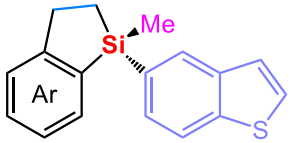


4j
50%, 89% ee

75 min, *c* = 51%, *s* = 60

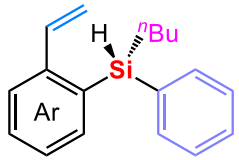


3k
49%, 91% ee

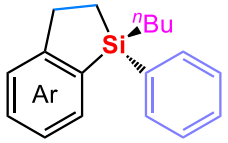


4k
49%, 88% ee

80 min, *c* = 51%, *s* = 47

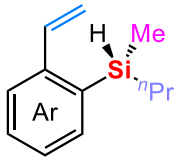


3l
48%, 74% ee

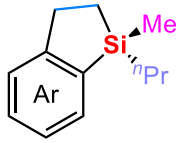


4l
45%, 75% ee

6 h, *c* = 48%, *s* = 17



3m
52%, 53% ee

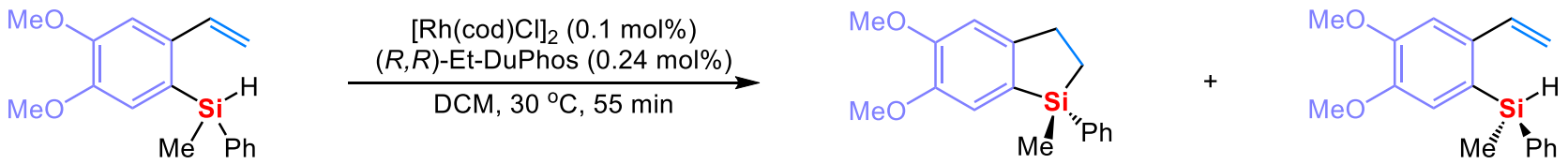


4m
46%, 56% ee

90 min, *c* = 47%, *s* = 7

Synthetic Applications

Gram-Scale Reaction

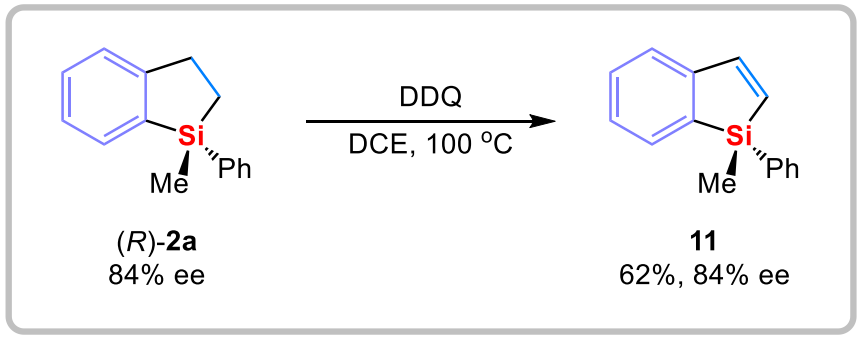


rac-**1l**
4.0 mmol, 1.1 g

(*R*)-**2l**
50%, 92% ee

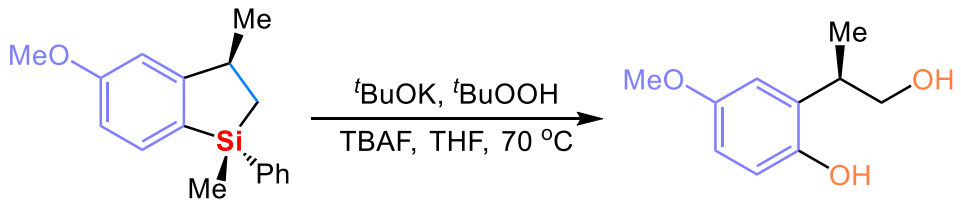
(*R*)-**1l**
50%, 92% ee

Transformation of Si-Stereogenic Dihydrobenzosilole Compounds



(*R*)-**2a**
84% ee

11
62%, 84% ee

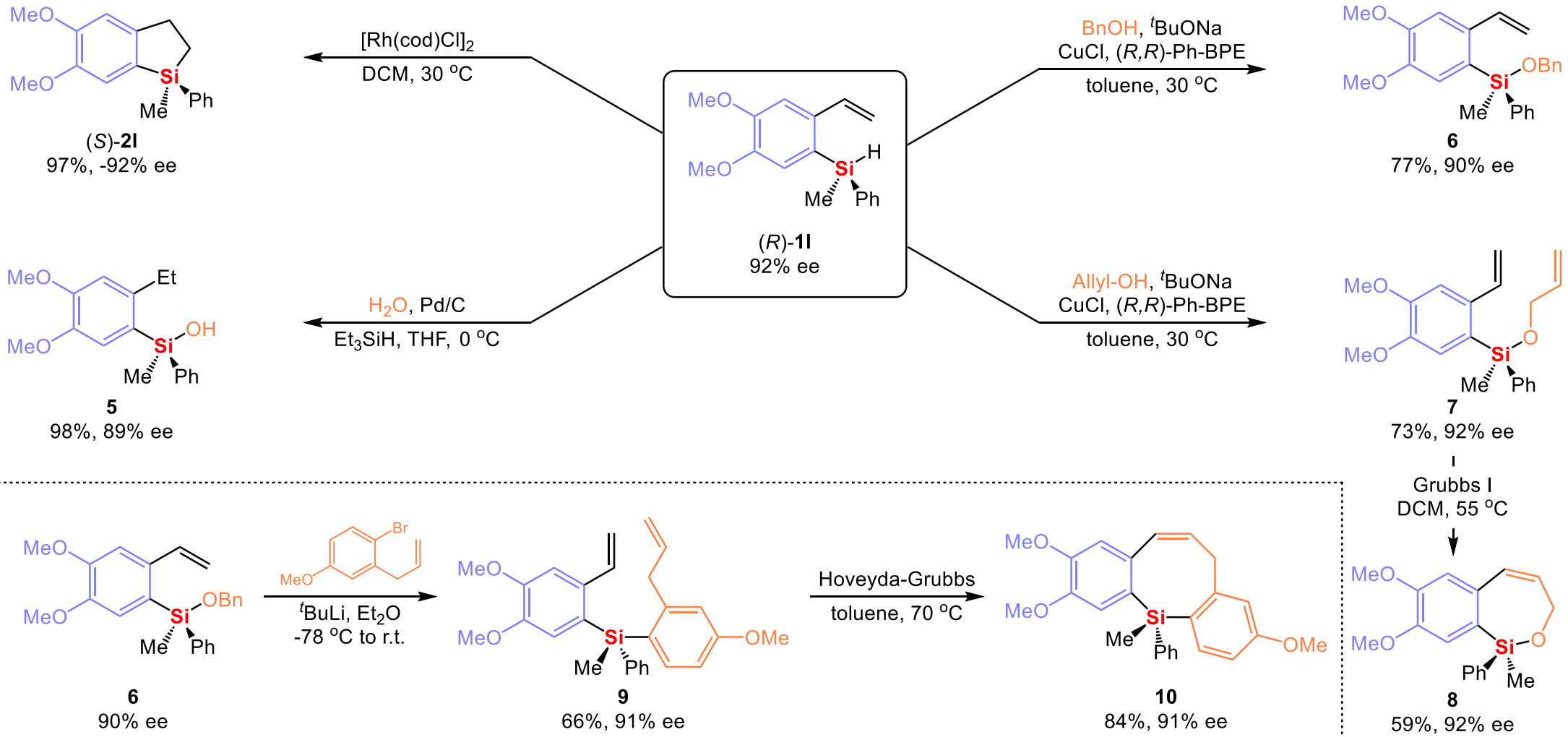


(*R*,*R*)-**2n**
90% ee, 21:1 dr

12
89%, 94% ee

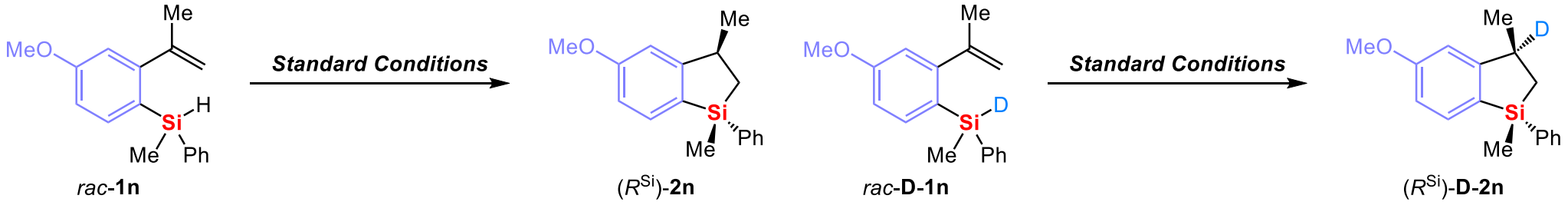
Synthetic Applications

Transformation of Monohydrosilane



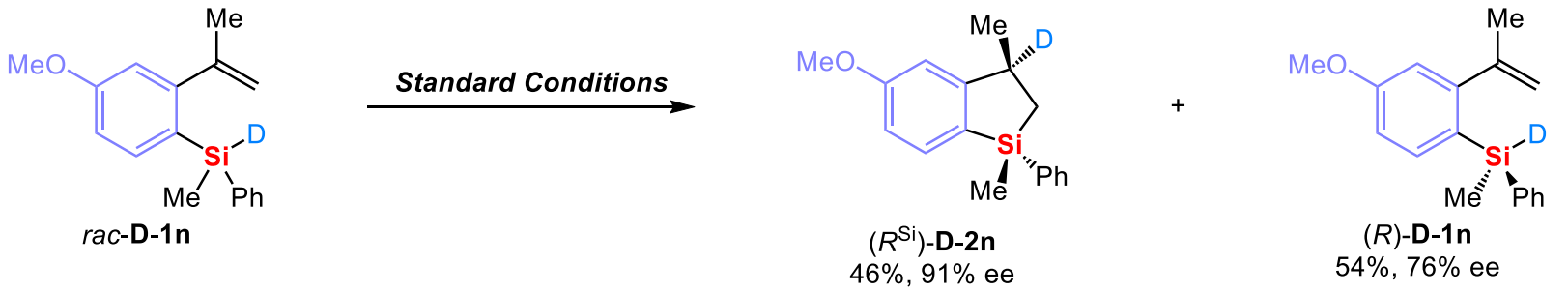
Mechanistic Investigation

Parallel KIE Experiments



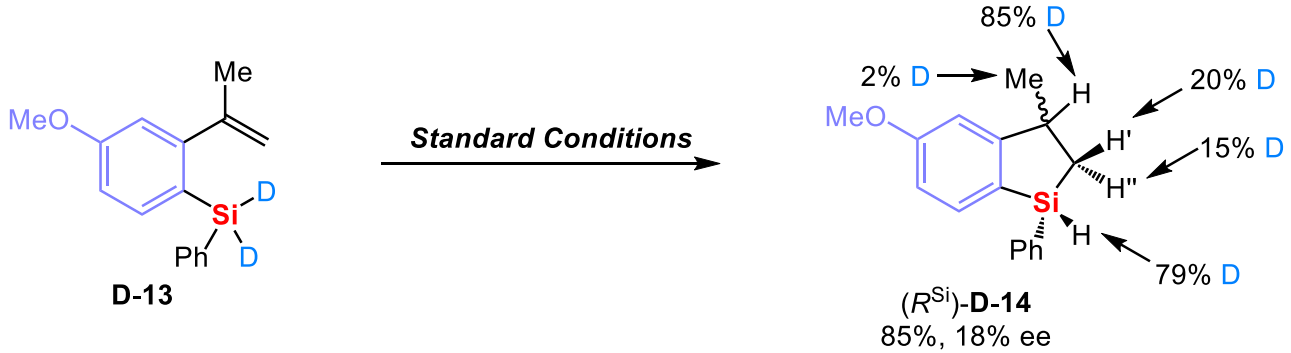
KIE = K_H/K_D = 1.02

Deuterium-Labeling Experiments

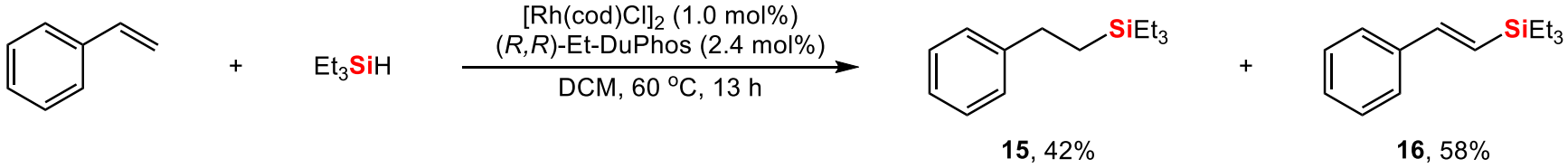


Mechanistic Investigation

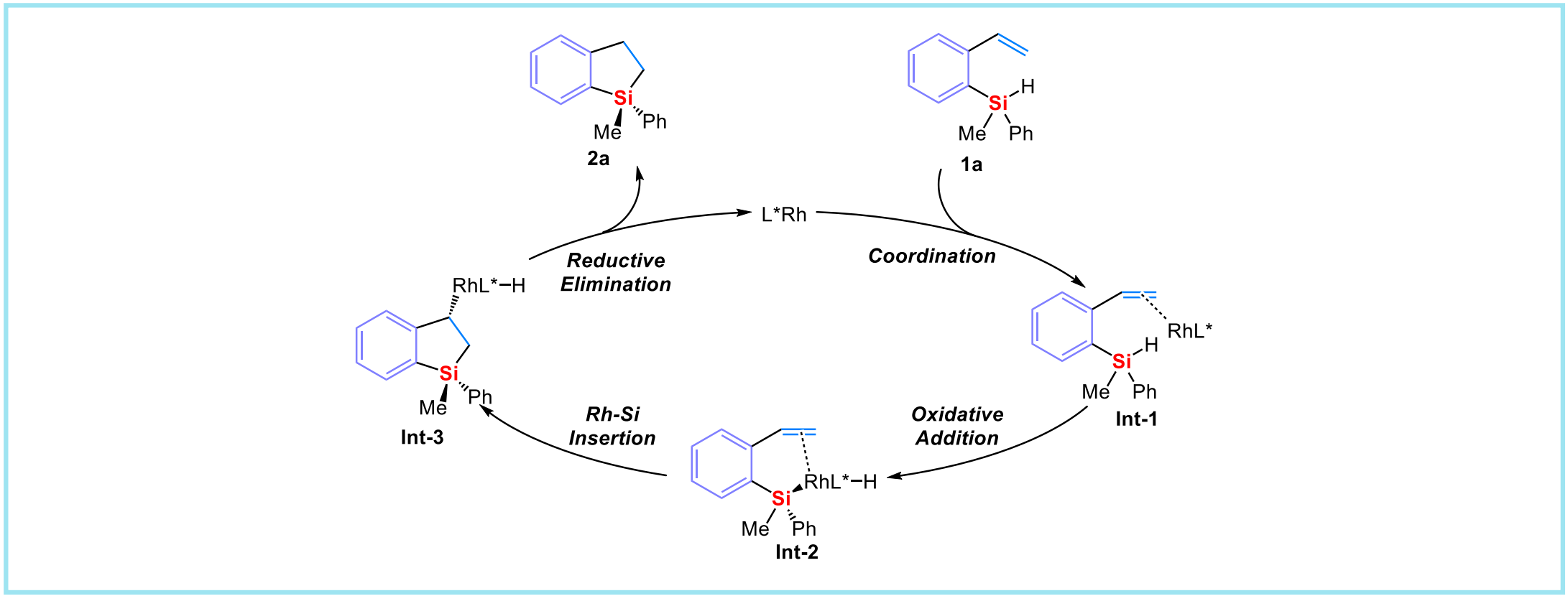
Deuterium-Labeling Experiments



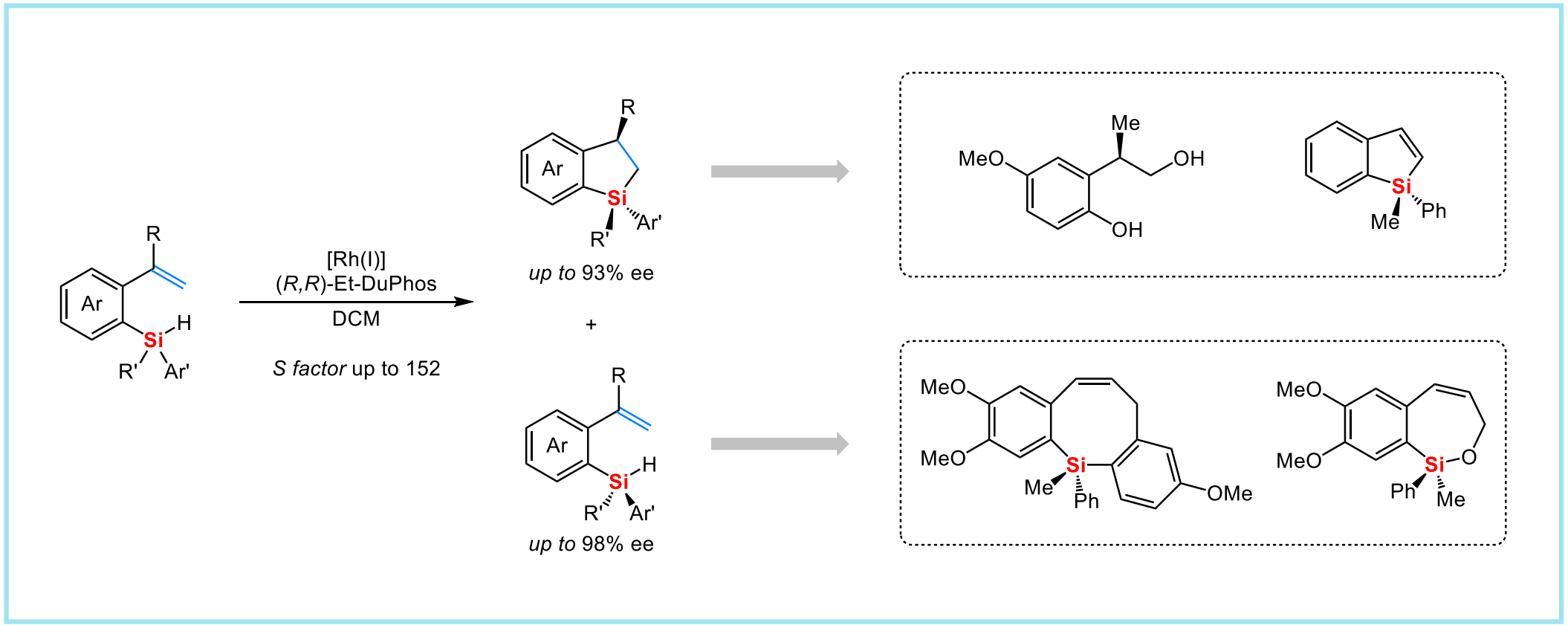
Rh-Catalyzed Hydrosilylation of Styrene with Triethylsilane



Proposed Reaction Mechanism



Summary



➢ ***Low Catalyst Loading*** ➢ ***Excellent Stereocontrol*** ➢ ***Middle-Sized Silacycle***

Strategy for Writing The First Paragraph

The Importance of Silicon-Stereogenic Organosilanes

Construction of Silicon-Stereogenic Organosilanes

The Demand to Develop New Approach

- ✓ Silicon-stereogenic organosilanes have received increasing attention in various scientific fields, including synthetic chemistry, material science and pharmaceutical chemistry…
- ✓ Currently, the majority of catalytic processes for the preparation of silicon-stereogenic organosilanes relies on enantioselective desymmetrization of prochiral precursors with two identical substitutes attached to the Si(sp^3)-atom center…
- ✓ Nevertheless, those early examples remain several limitations, including the use of stoichiometric chiral reagent or substrate, and insufficient chiral induction. To develop catalytic KR process with a chiral catalyst for the enantioselective preparation of silicon-stereogenic organosilanes is still in high demand.

Strategy for Writing The Last Paragraph

Summary of this Work

- ✓ In conclusion, the access of silicon-stereogenic organosilanes has been achieved by catalytic kinetic resolution of monohydrosilanes.

Highlights of this Work

- ✓ With this newly established protocol, both silicon-stereogenic dihydrobenzosiloles and silicon-stereogenic monohydrosilanes could be prepared with high efficiency and good to excellent enantioselectivities in one single operation. Both enantioenriched silacyclic products and monohydrosilanes are synthetically useful, which can be readily further transformed to diverse chiral compounds, including the construction of a seven-membered siloxane and an eight-membered silacycle.

Representative Examples

- Nevertheless, those early examples remain several limitations, including the use of stoichiometric chiral reagent or substrate, and insufficient chiral induction. (insufficient, adj. 不足的；不充分的)
- The replacement of the methyl group with n-butyl group led to a slight diminution in enantioselectivity, giving **4l** and **3l** in 75% ee and 74% ee, respectively. (diminution, n. 减少；降低；缩减；缩小)
- For comparison, deuterium-labeled dideuterosilane **D-13** was subjected to the same reaction conditions, delivering the corresponding product (R^{Si})-**D-14** with deuterium distribution in both *α*- and *β*-positions to the Si atom. (以作比较；为了比较)

Acknowledgement

Thanks for your attention