Literature Report IX

Visible Light-Promoted Deracemization of α-Amino Aldehyde by Synergistic Chiral Primary Amine and Hypervalent Iodine Catalysis

Reporter: Jian Chen
Checker: Kai Xue
Date: 2025-02-24

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J. Am. Chem. Soc. **2025**, *147*, 6280-6287

CV of Prof. Luo Sanzhong

Research:

- Biomimetic Catalysis
- Asymmetric Catalysis
- Organic Synthesis Methodology
- Artificial Intelligence in Chemistry

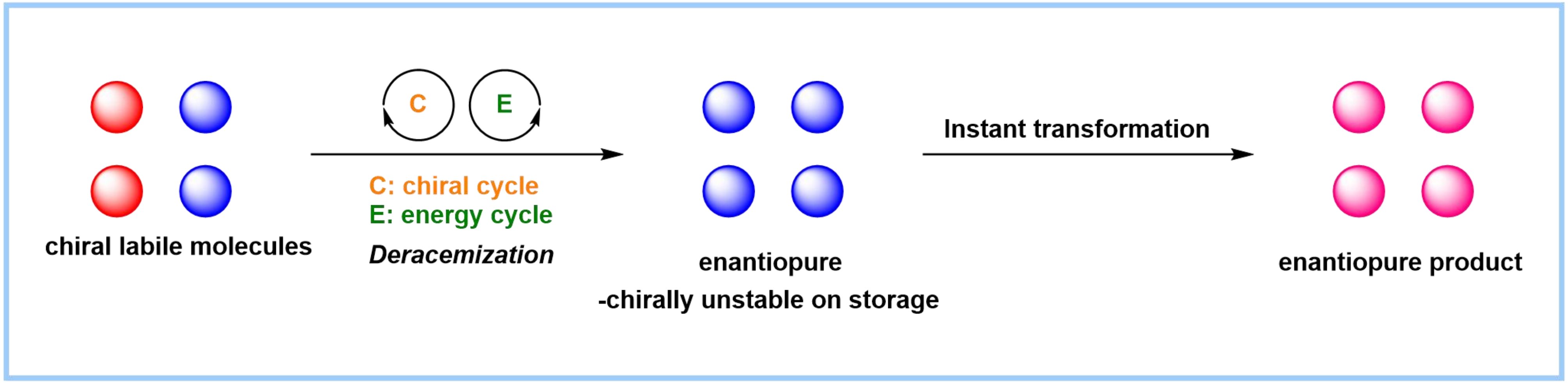
Background:

- **1995-1999** B.S., Zhengzhou University
- **1999-2002** M.S., Nankai University
- **2002-2005** Ph.D., Institute of Chemistry, Chinese Academy of Sciences
- **2005-2018** Assistant Professor, Associate Professor, Professor, ICCAS
- **2018-Now** Professor, Tsinghua University

Contents

Introduction

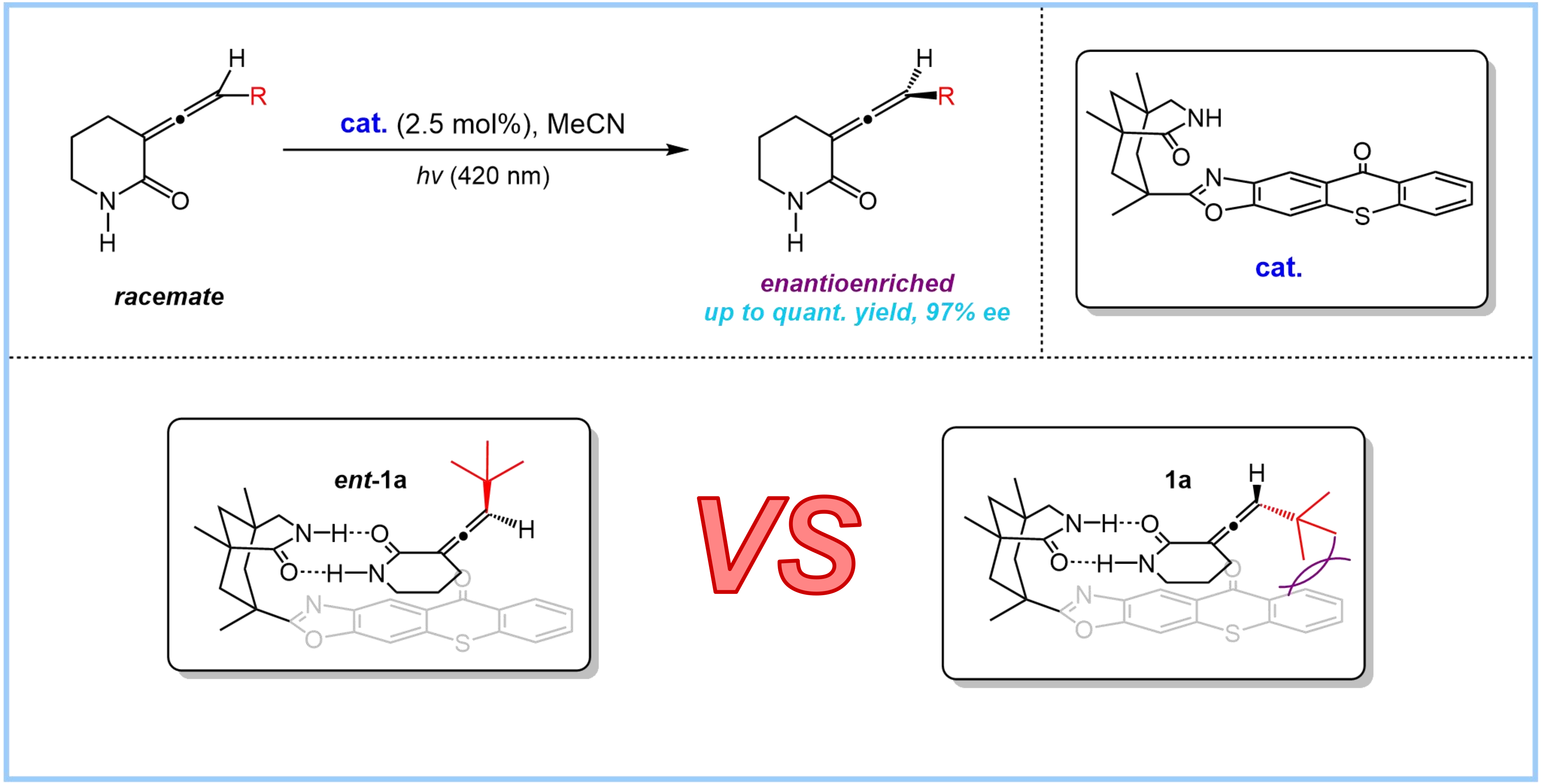
Deracemization: effective asymmetric synthesis with chiral labile molecules



- Deracemization achieves 100% yield, bypassing asymmetric synthesis bottlenecks.
- It converts accessible racemates into enantioenriched products unreachable currently.
- Structural identity avoids purification, enabling direct use for labile molecules.

Introduction

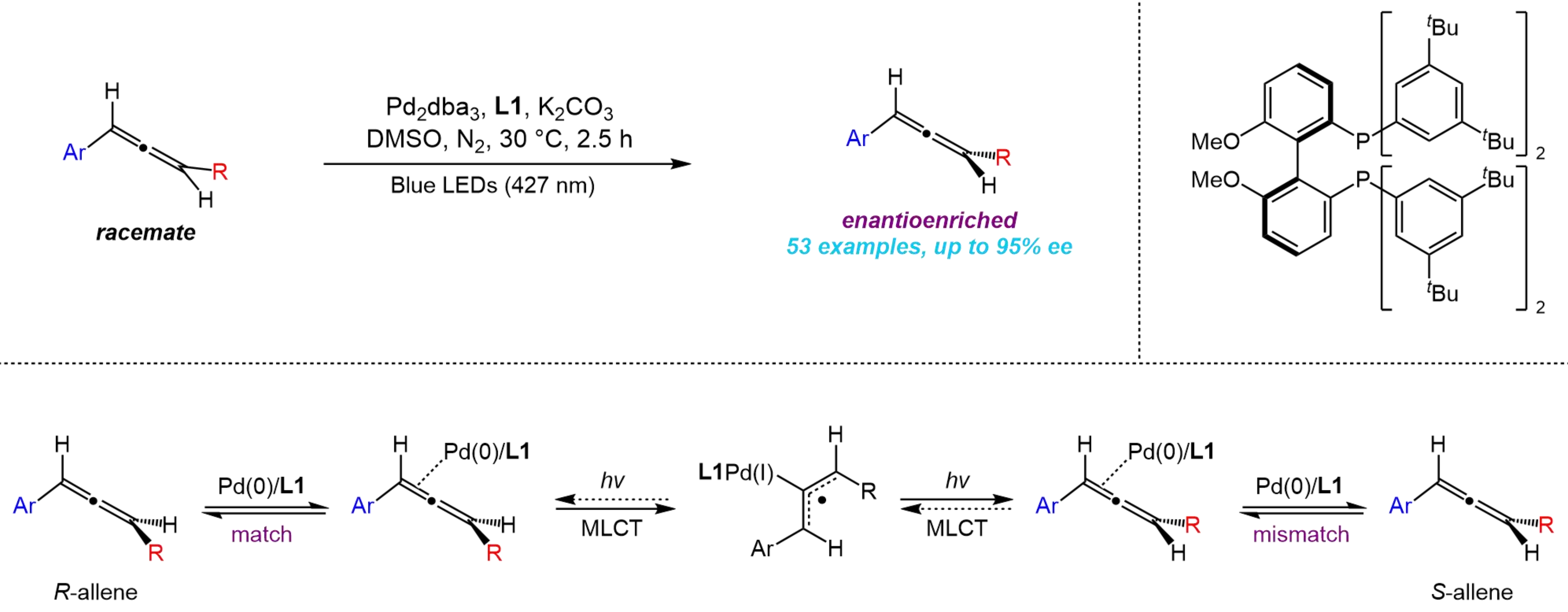
Deracemization of Allenes



Hölzl-Hobmeier, A.; Bauer, A.; Silva, A. V.; Huber, S. M.; Bannwarth, C.; Bach, T.* *Nature* **2018**, *564*, 240

Introduction

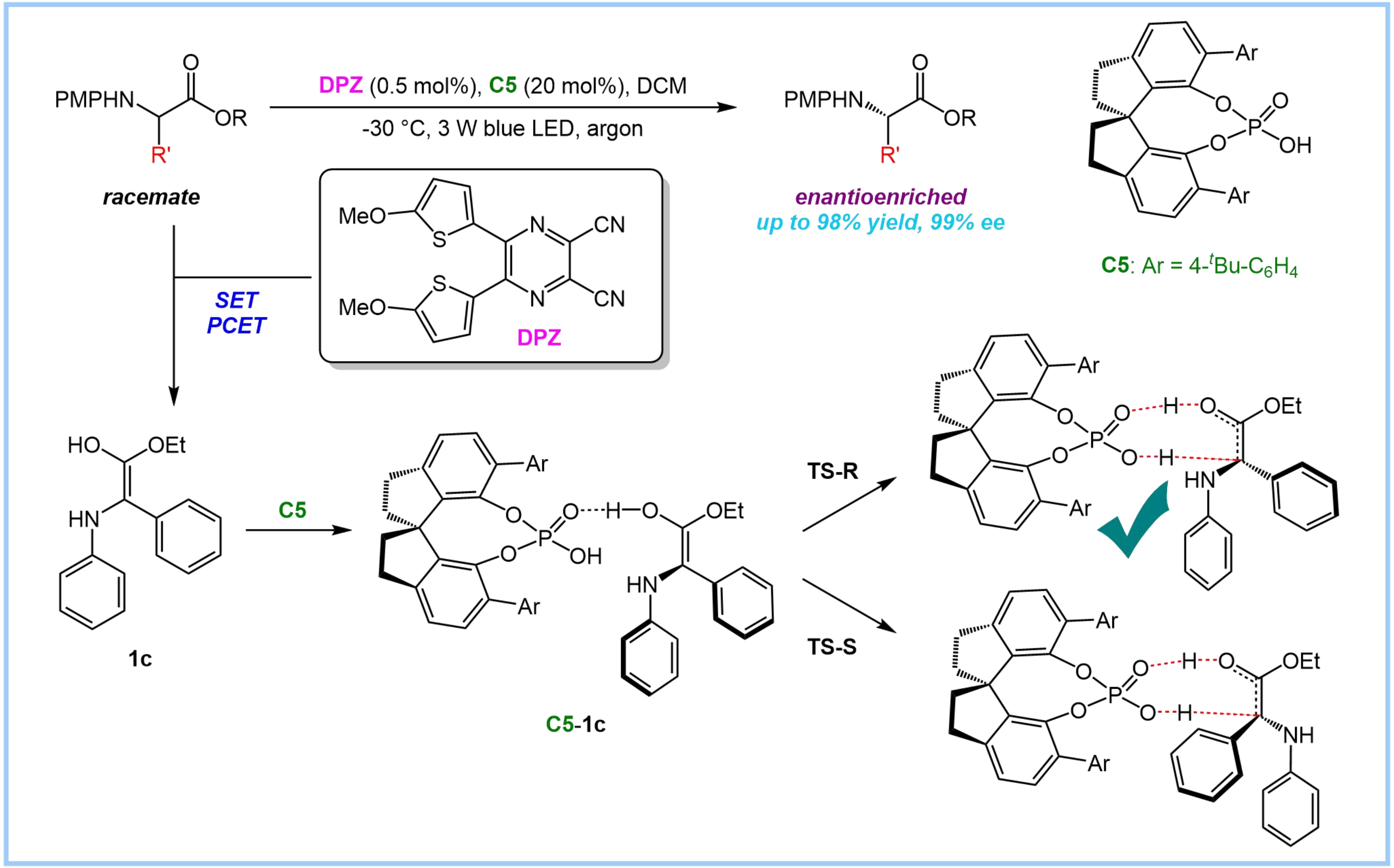
Deracemization of Allenes



Song, C.; Bai, X.; Li, B.; Dang, Y.; Yu, S.* *J. Am. Chem. Soc.* **2024**, *146*, 21137

Introduction

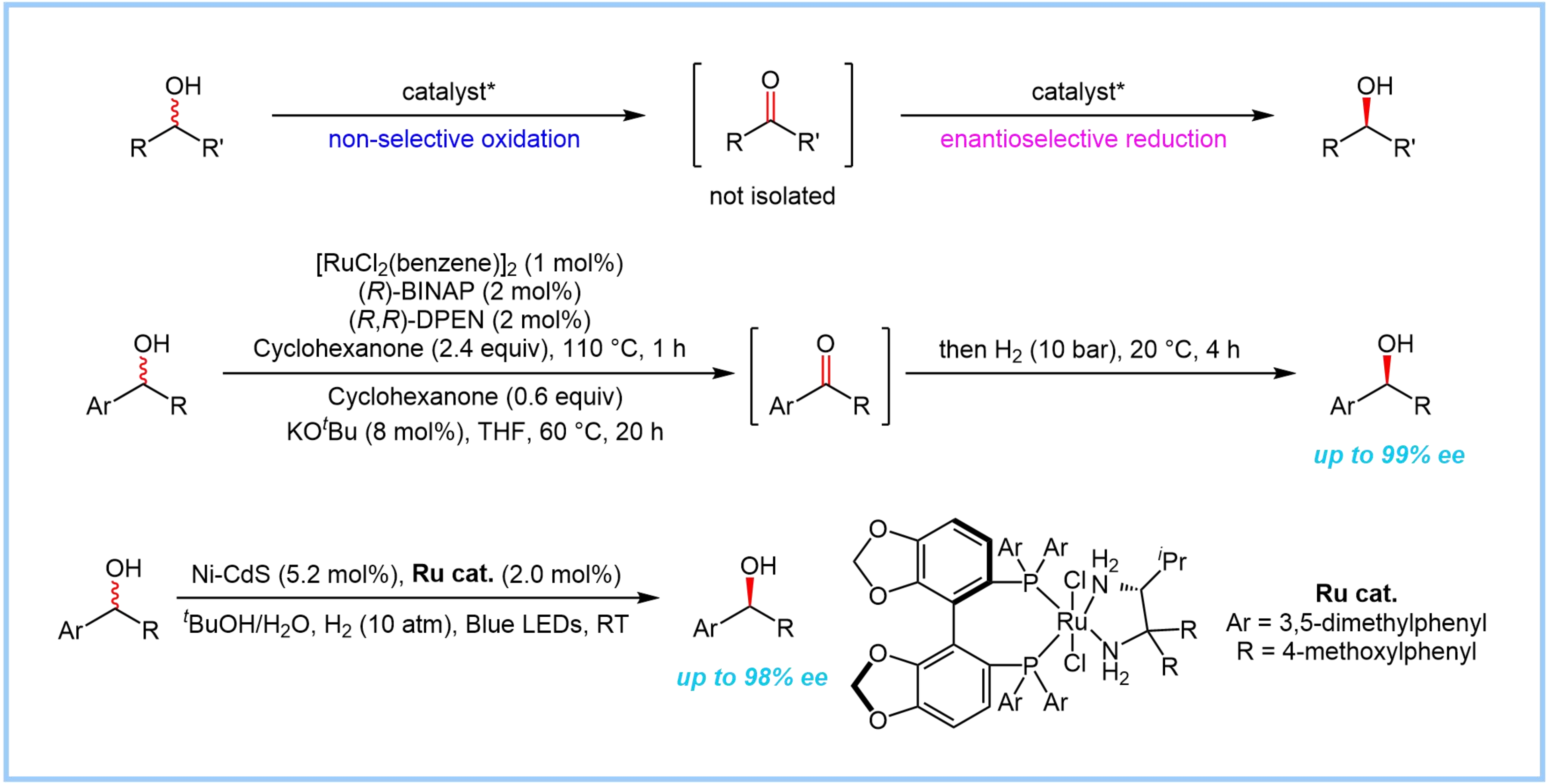
Deracemization of Amines



Gu, Z.; Zhang, L.; Li, H.; Cao, S.; Yin, Y.; Zhao, X.; Ban, X.; Jiang, Z.* *Angew. Chem. Int. Ed.* **2022**, *61*, e202211241

Introduction

Deracemization of Alcohols

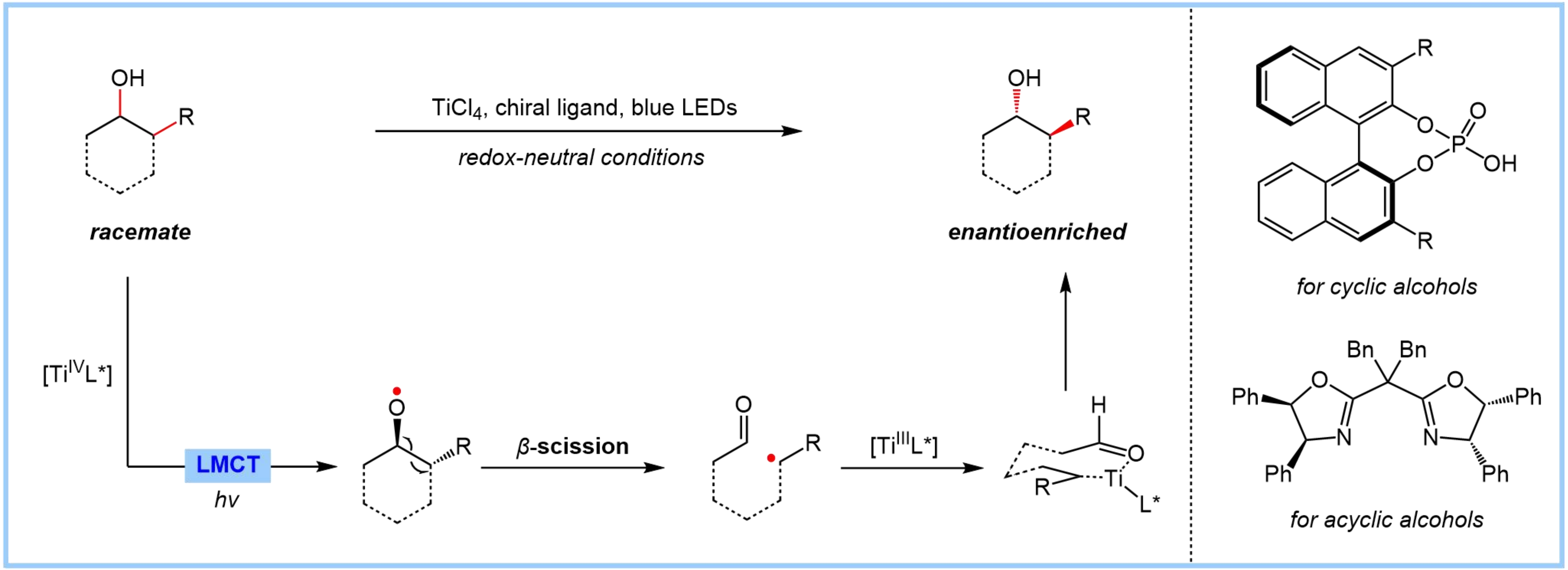


Adair, G. R. A.; Williams, J. M. J.* *Chem. Commun.* **2007**, 2608

Zhang, Z.; Hu, X.* *Angew. Chem. Int. Ed.* **2021**, *60,* 22833

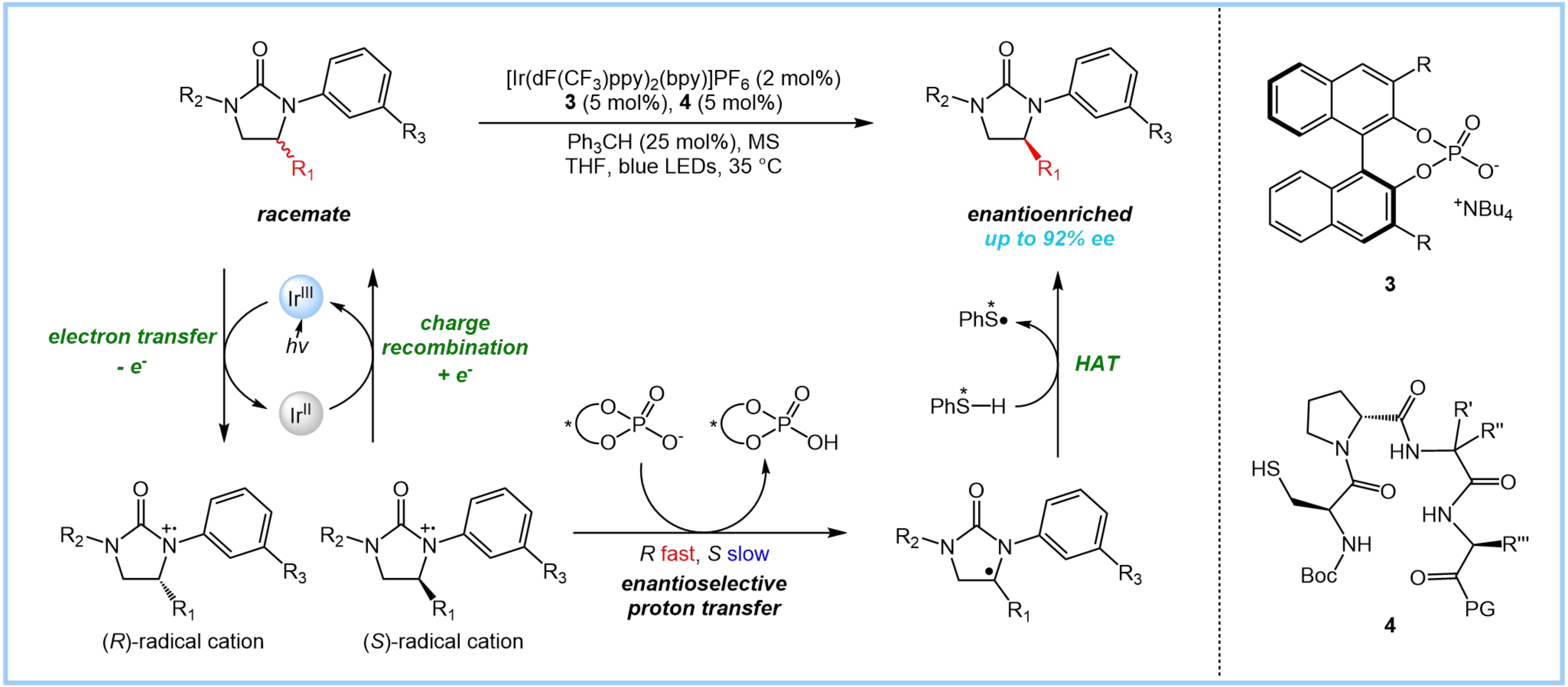
Introduction

Deracemization of Alcohols



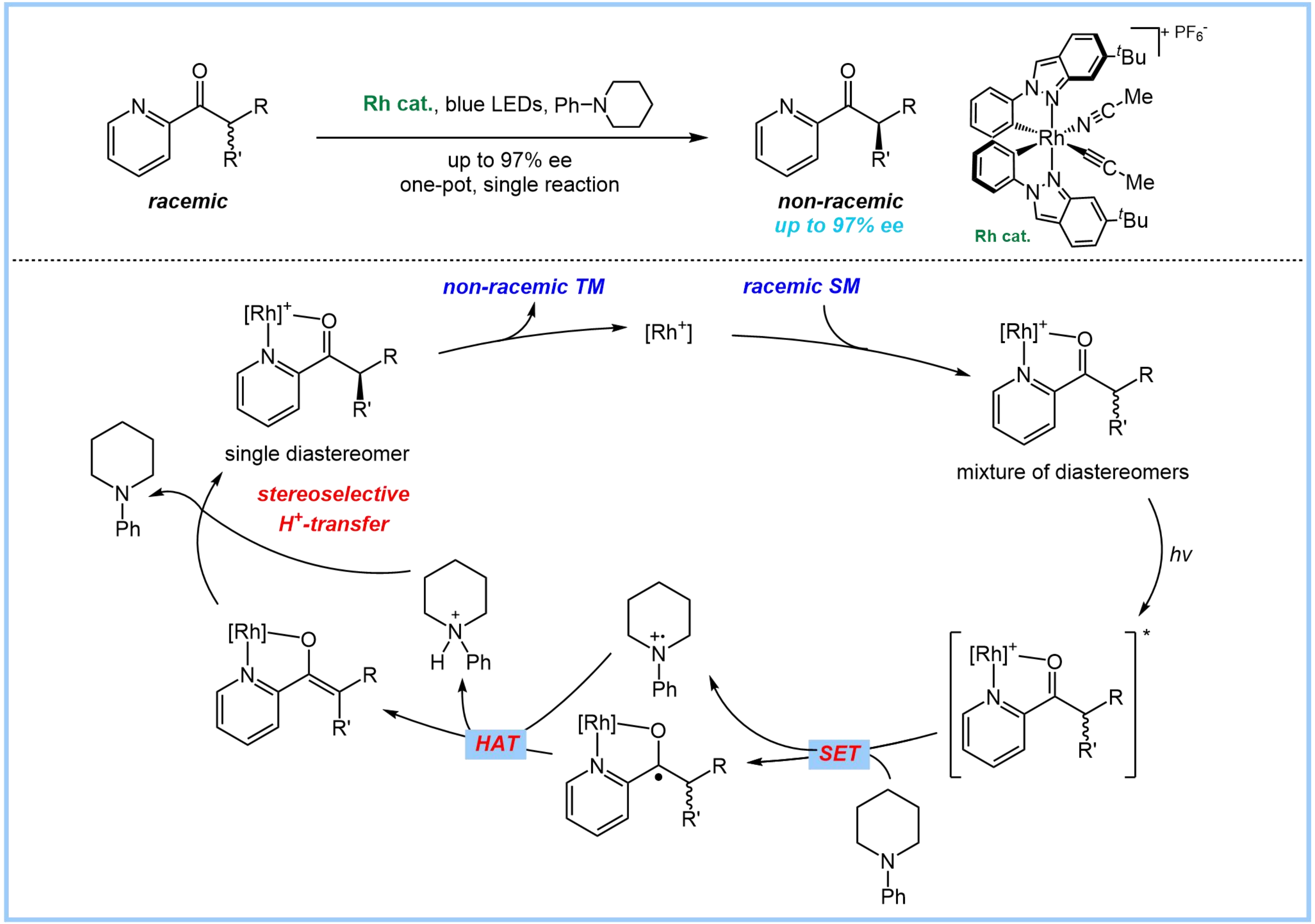
Wen, L.; Ding, J.; Duan, L.; Wang, S.; An, Q.; Wang, H.; Zuo, Z.* *Science* **2023**, *382,* 458

Introduction



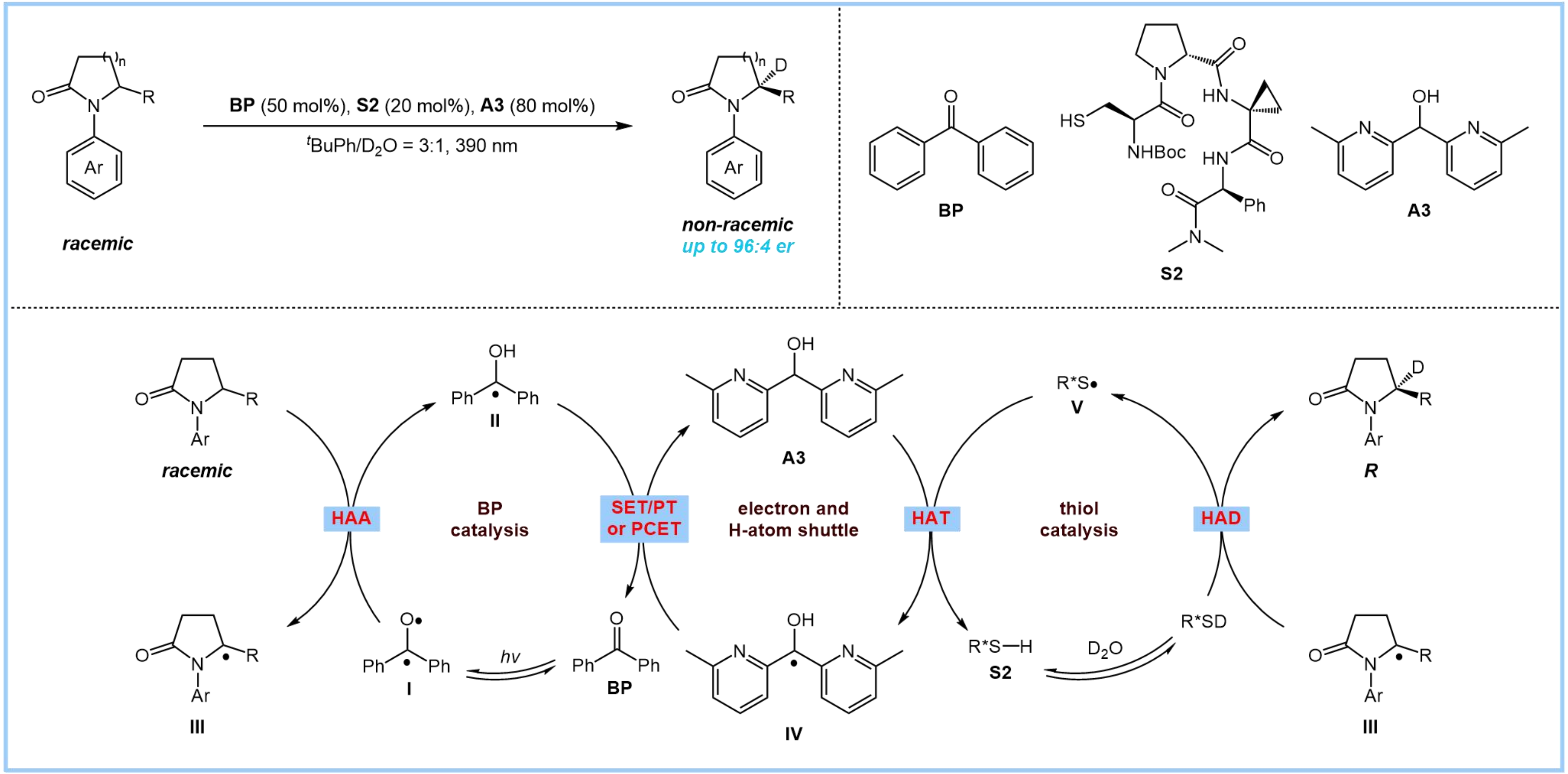
Shin, N. Y.; Ryss, J. M.; Zhang, X.; Miller, S. J.; Knowles, R. R.* *Science* **2019**, *366*, 364

Introduction



Zhang, C.; Gao, A. Z.; Nie, X.; Ye, C.-X.; Ivlev, S. I.; Chen, S.; Meggers, E.* *J. Am. Chem. Soc.* **2021**, *143*, 13393

Introduction



Yan, X.; Pang, Y.; Zhou, Y.; Chang, R.; Ye, J.* *J. Am. Chem. Soc.* **2025**, *147*, 1186

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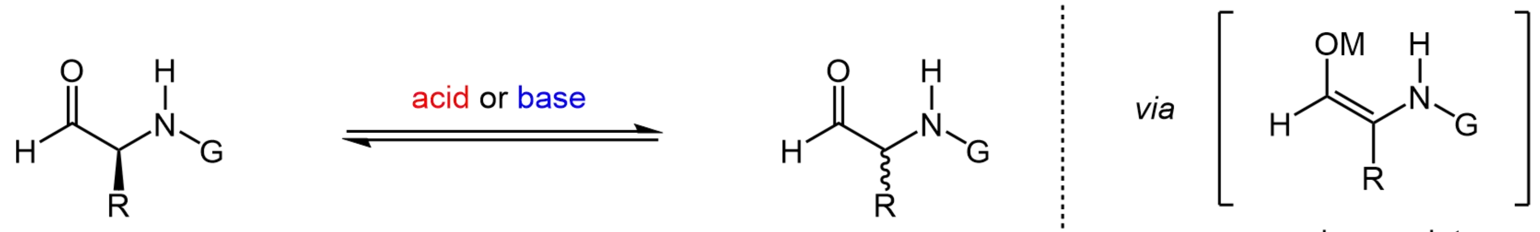
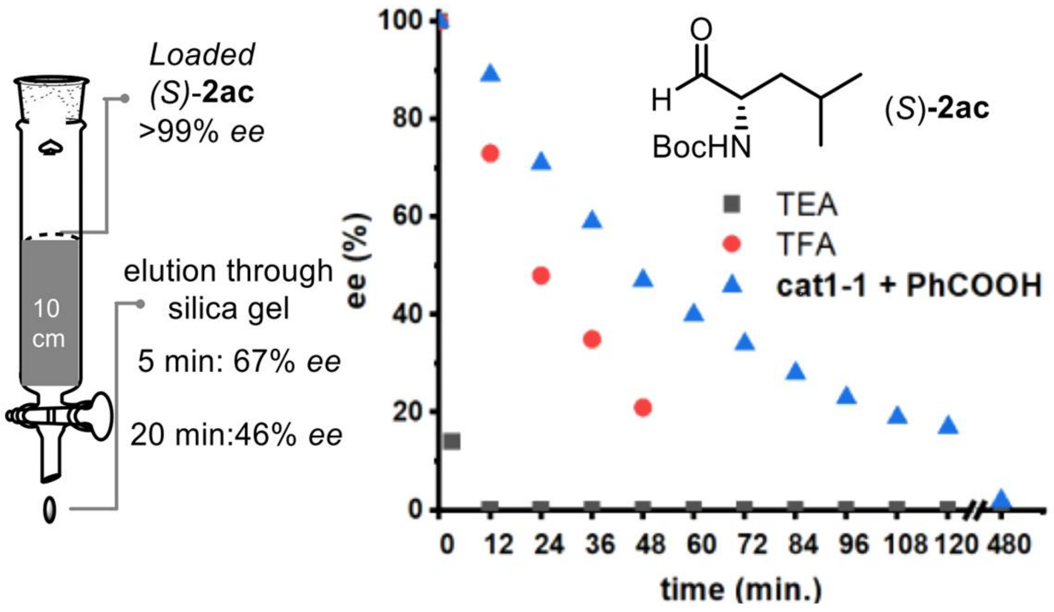
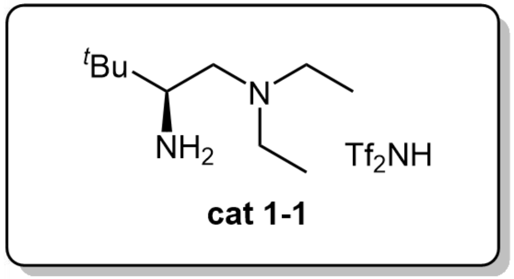


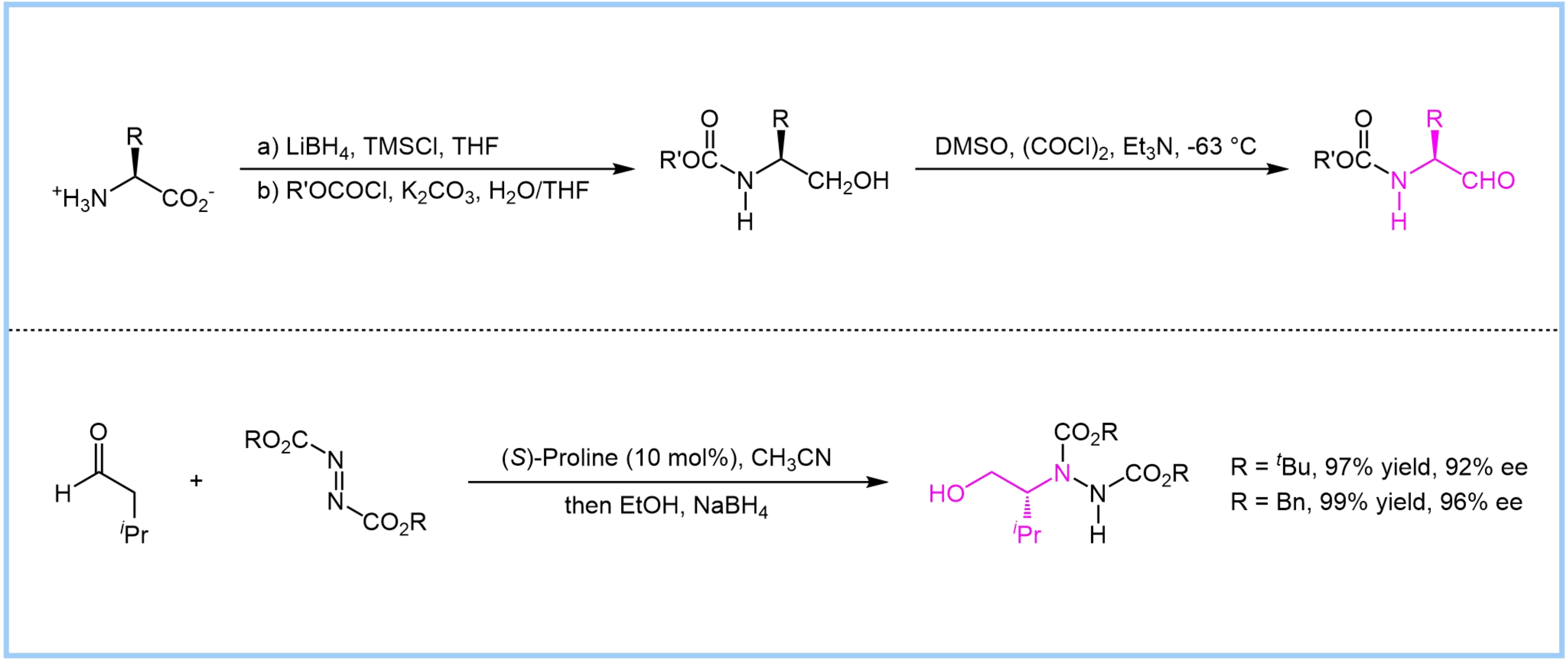
♥*versatile synthon* ♥*easy racemizable*





Introduction

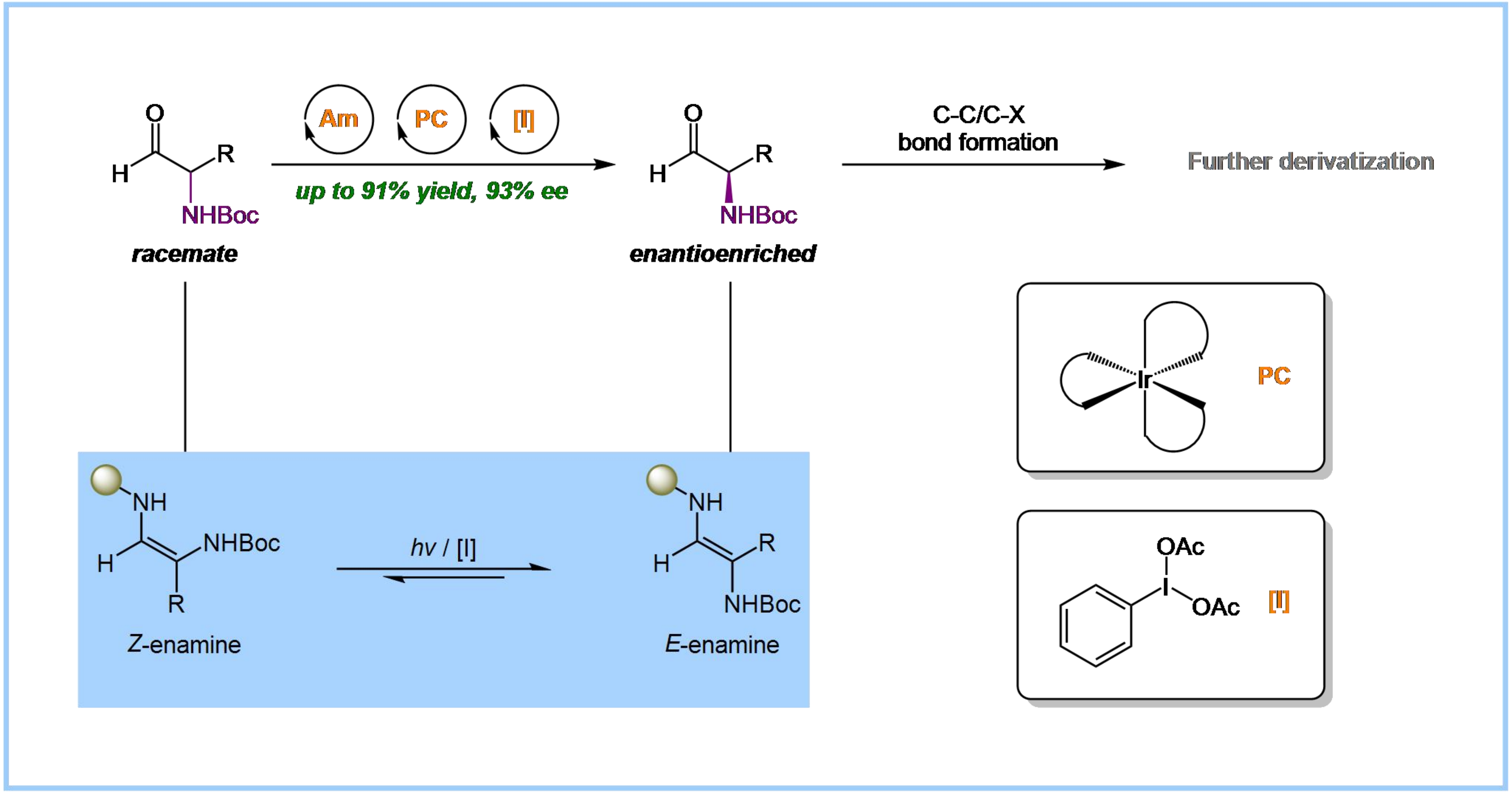
Traditional approach to preparing α-Amino Aldehyde



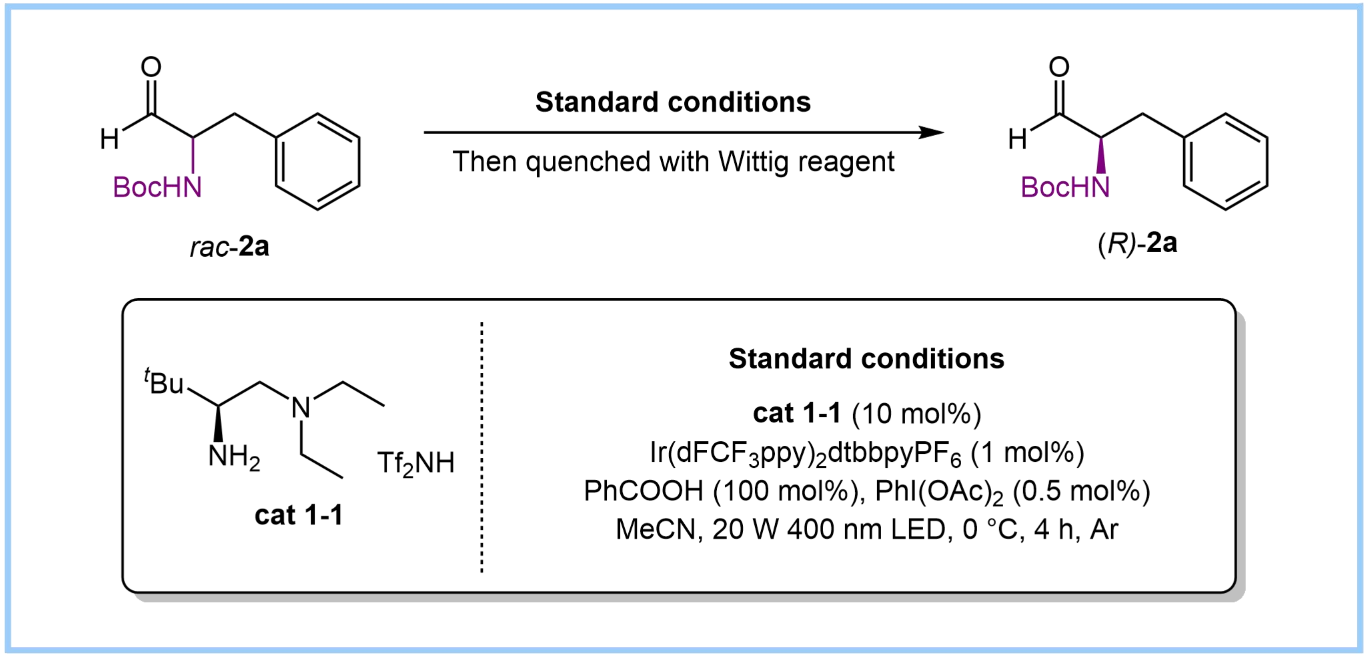
List, B.* *J. Am. Chem. Soc.* **2002**, *124*, 5656
Konradi, A. W.; Kemp, S. J.; Pedersen, S. F.* *J. Am. Chem. Soc.* **1994**, *116*, 1316

Project Synopsis

Deracemization of α-Amino Aldehyde



Optimization of Reaction Conditions

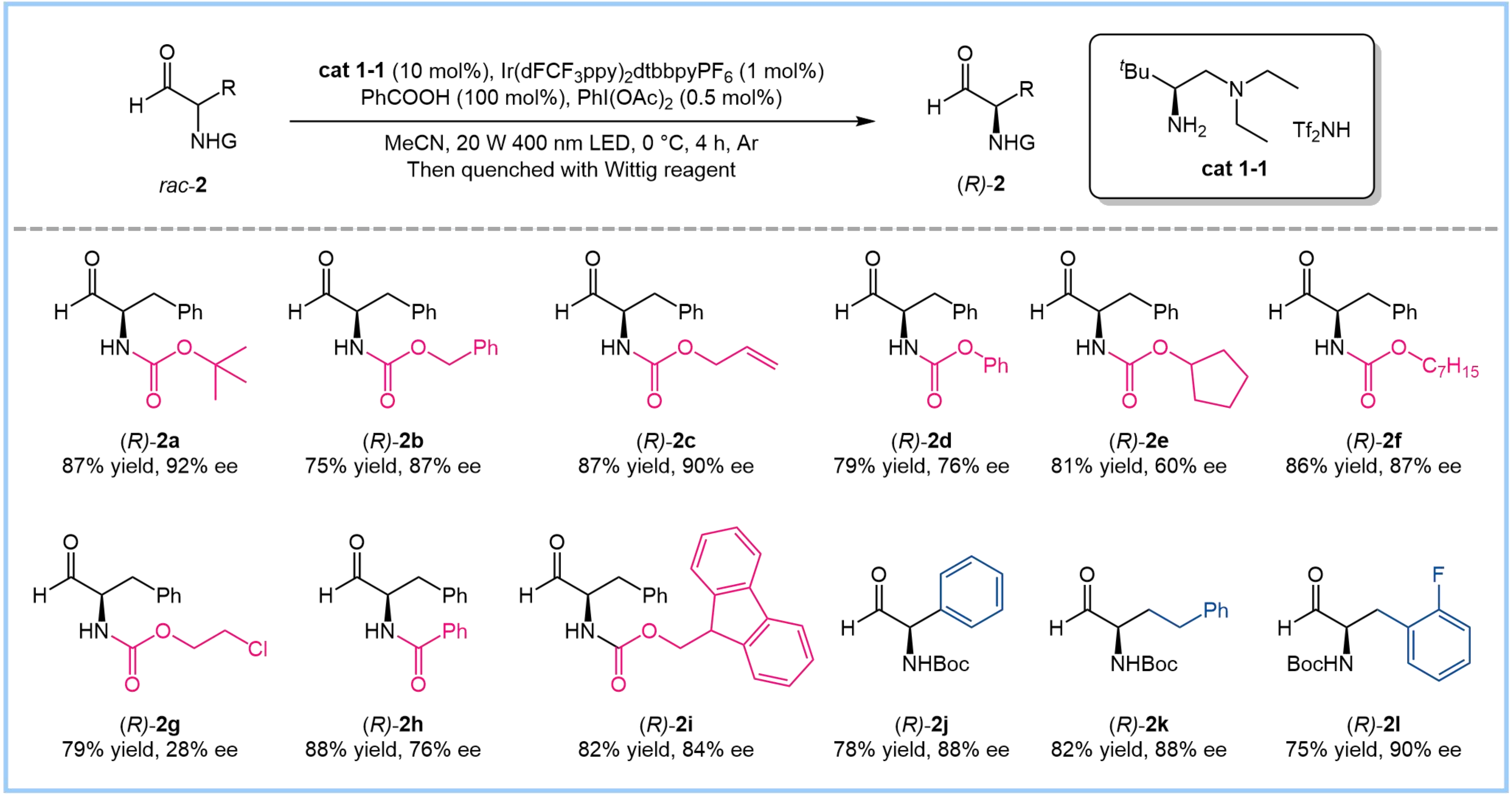


Entry	Variations from standard conditions	Yield (%)	Ee (%)
1	none	87	92
2	no $C_6H_5CO_2H$	76	11
3	$C_6H_5CO_2H$ (10 mol%)	83	83
4	without PIDA	91	71
5	PIDA (10 mol%)	79	77
6	IBX (0.5 mol%)	82	73

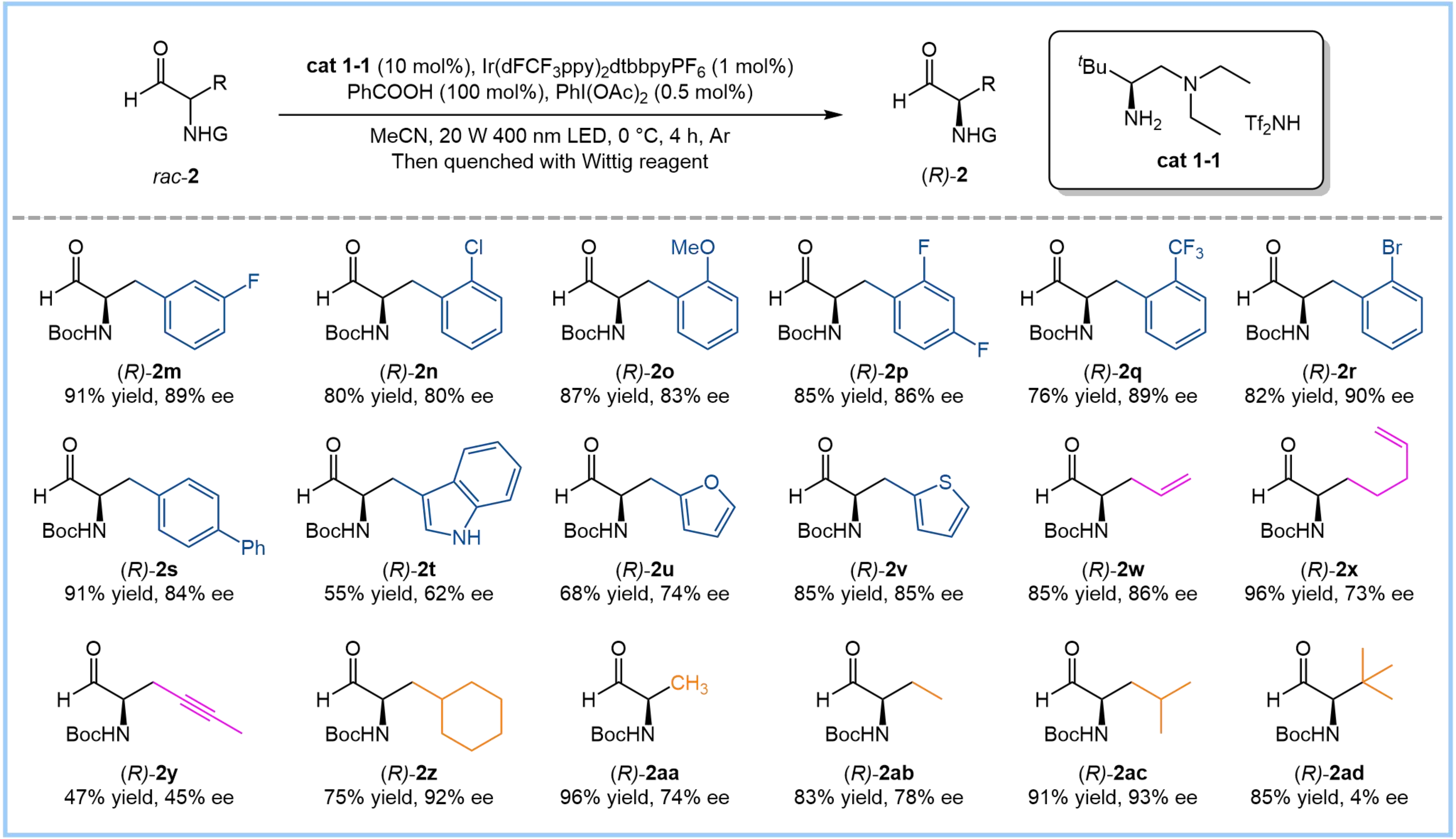
Optimization of Reaction Conditions

Entry	Variations from standard conditions	Yield (%)	Ee (%)
7	$C_6H_5I(OCOCF_3)_2$ (0.5 mol%)	87	90
8	$C_6H_5I(OH)OTs$ (0.5 mol%)	83	85
9	$Ir(ppy)_3$	78	46
10	$[Ir(dtbpy)(ppy)_2]PF_6$	79	55
11	$[Ru(bpy)_3]Cl_2$	83	rac
12	25 ^{o}C	81	49
13	no photocatalyst	80	rac
14	no amino catalyst	77	rac
15	no light	83	rac
16	stilbene (100 mol%)	82	9
17	in air	69	19

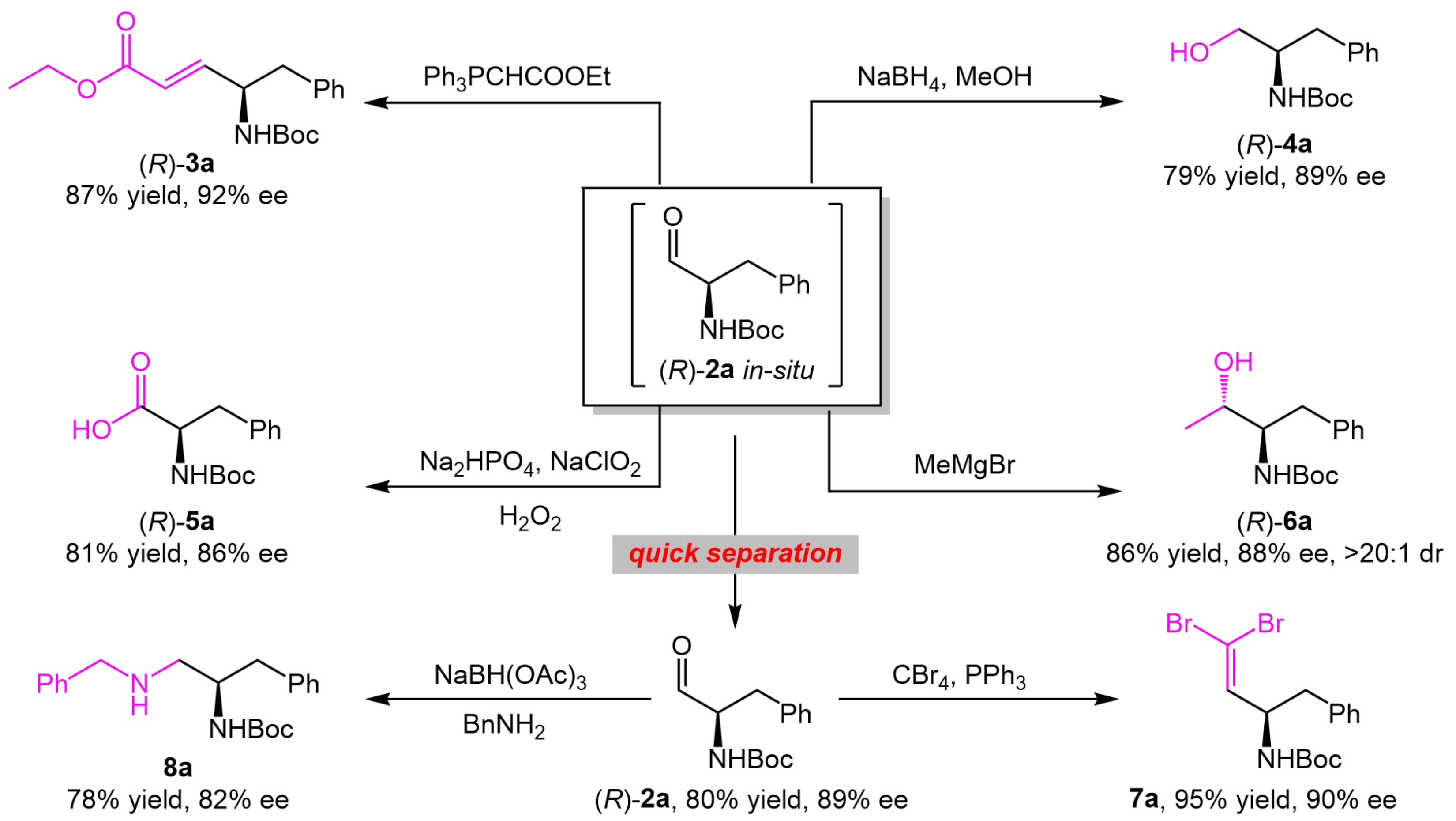
Substrate Scope



Substrate Scope

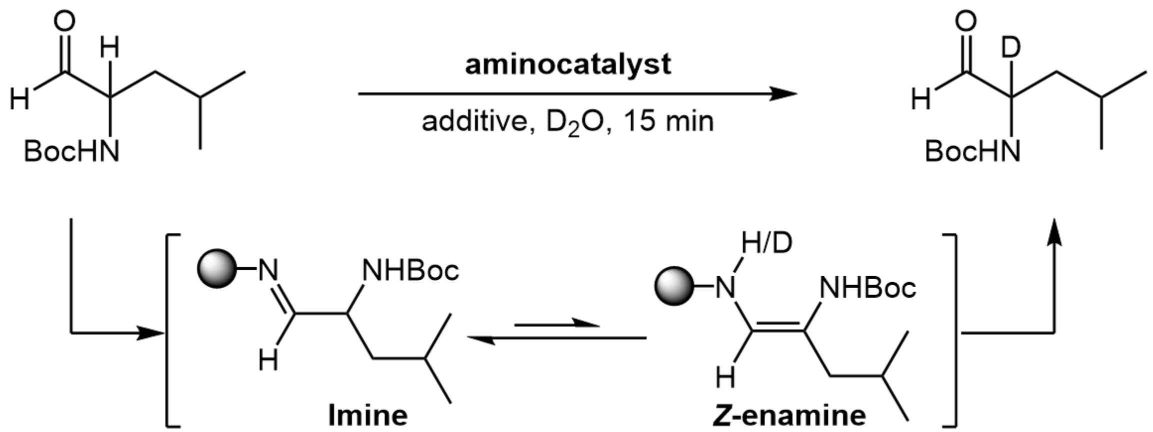


Transformations



Mechanistic Studies

A

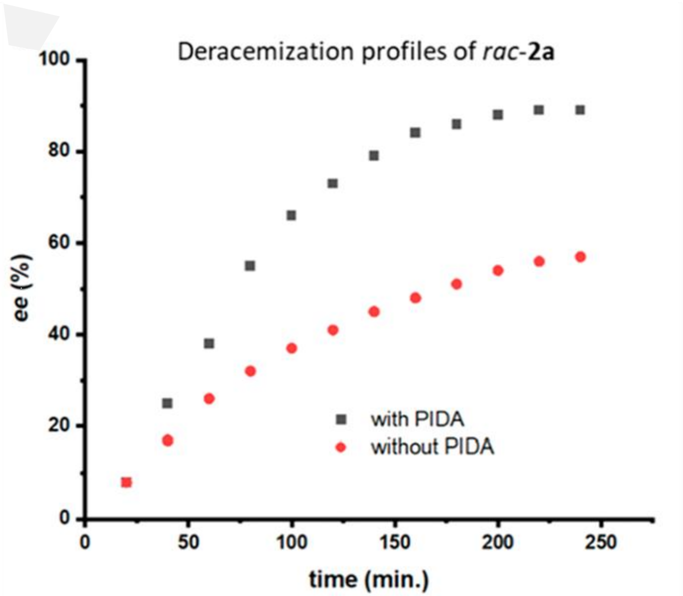


Conditions	D-ratio (%)
w/o **cat 1-1**, with $PhCO_2H$	4
with **cat 1-1**, w/o $PhCO_2H$	10
with **cat 1-1**, with $PhCO_2H$	70
N-dimethylated **cat 1-1** with $PhCO_2H$	21

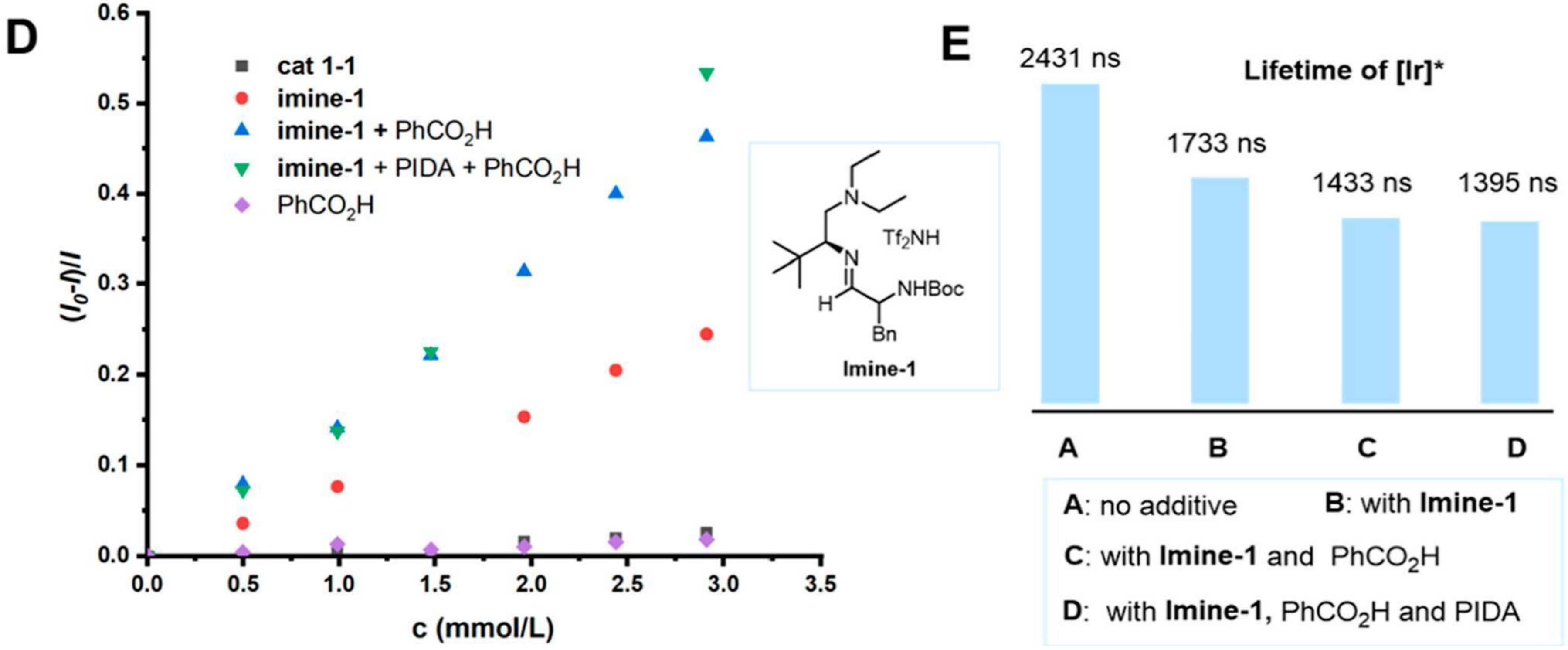
B

Photocatalyst	E_T (kcal/mol)	$E_{1/2}^{PC\_/PC^*}$ (V)	ee (%)
$[Ir(dFCF_3ppy)_2dtbbpy]PF_6$	66.9	0.89	92
$[Ir(dFCF_3ppy)_2bpy]PF_6$	62	1.32	68
$[Ru(bpy)_3]Cl_2$	48.5	0.77	rac
$Ir(ppy)_3$	59.5	0.35	46
$[Ir(dtbbpy)(ppy)_2]PF_6$	50.1	0.66	55

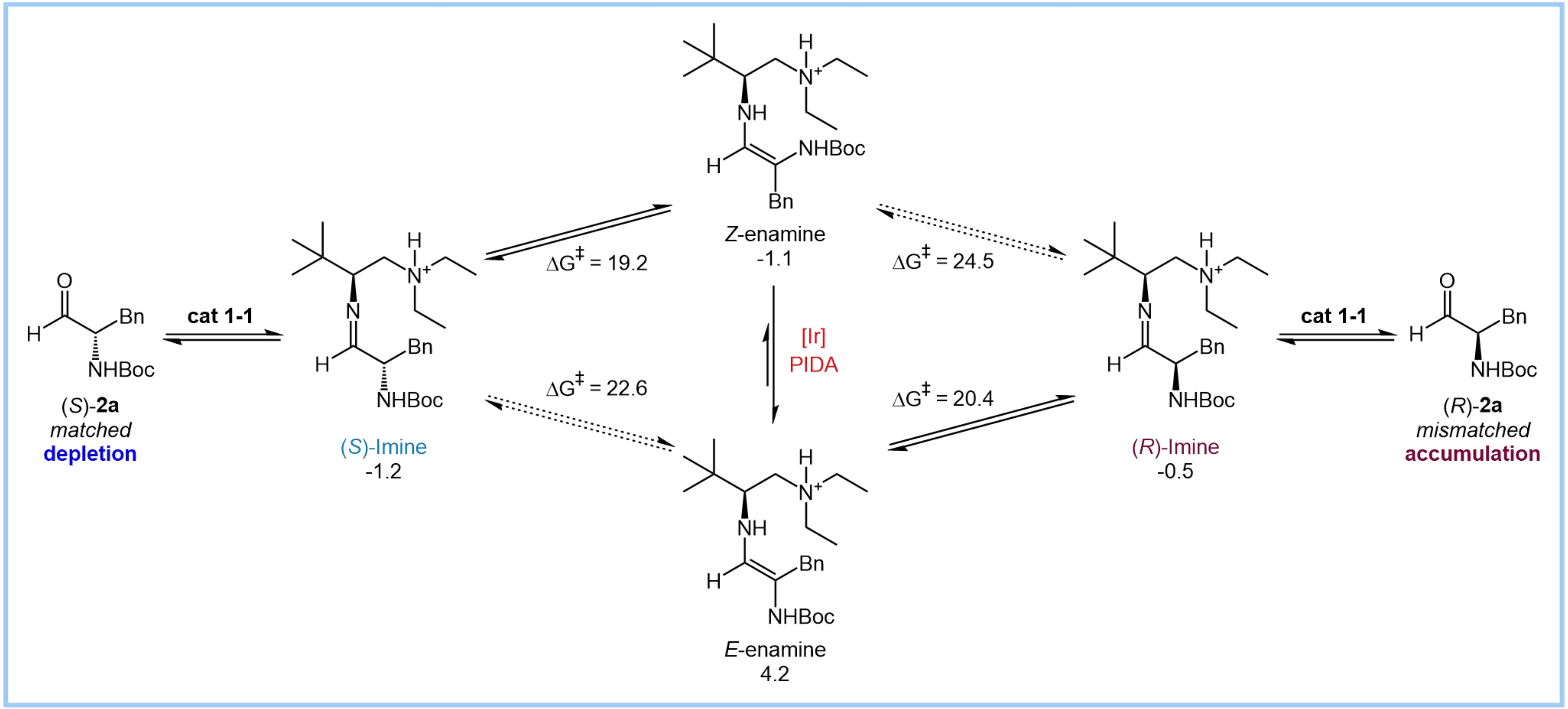
C



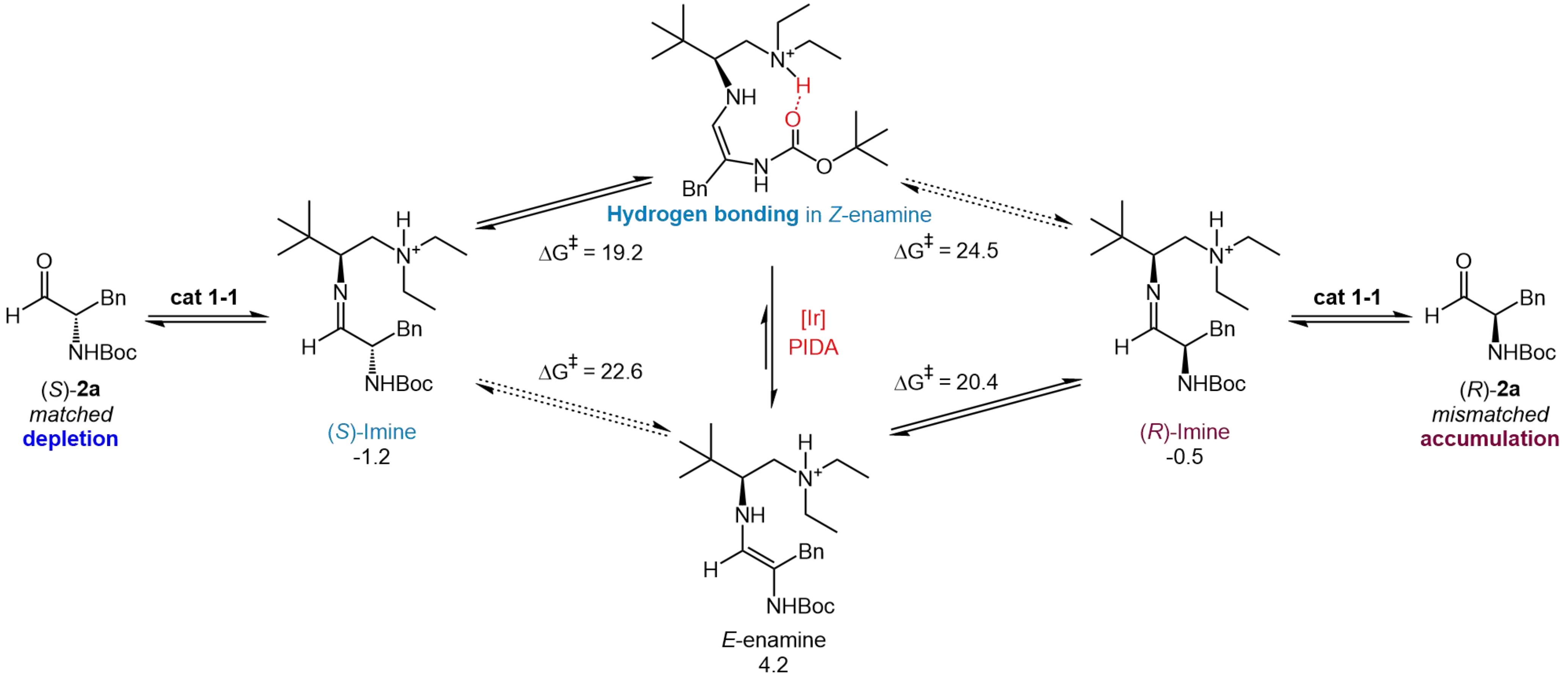
Mechanistic Studies



Proposed Mechanism

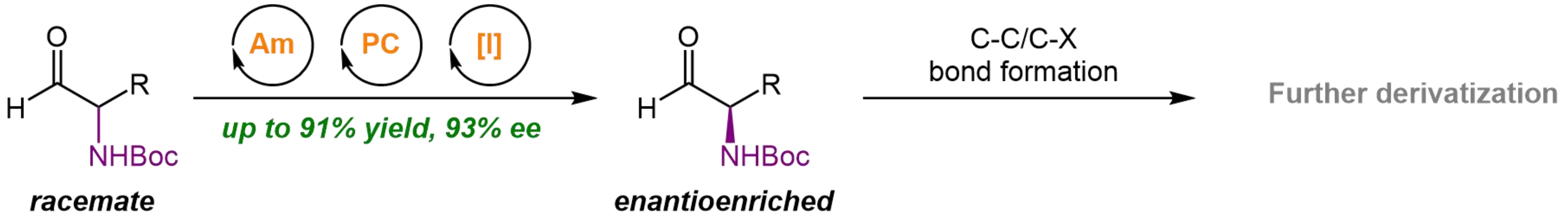


Proposed Mechanism



Summary

Deracemization of α-Amino Aldehyde



- Developing an effective deracemization of chirally labile *α*-amino aldehydes;
- Synergistic chiral primary amine and hypervalent iodine catalysis under visible light irradiation;
- Mechanistic studies verified a photochemical *Z*-*E* isomerization mediated by PIDA.

The First Paragraph

写作思路

去消旋化反应的特点

↓

去消旋化目前的应用

↓

α−氨基醛的去消旋化有待研究

The Last Paragraph

写作思路

总结工作：α-氨基醛的去消旋化

↓

强调亮点：手性胺、高价碘盐、光催化协同;机理研究

Representative Examples

- Mechanistic studies were then conducted to elucidate the possible origins of deracemization.. (elucidate : 阐明; 说明; 解释)
- Time-resolved Stern−Volmer experiments exhibited a similar pattern, where benzoic acid could shorten the lifetime of the excited photocatalyst from 1733 to 1433 ns, while PIDA showed only a marginal effect. (marginal: 边缘的; 小的; 微不足道的)
- The synergistic protocol enables the on-demand synthesis of chiral *α*-amino aldehydes with high enantioselectivity. Mechanistic studies verified a photochemical *Z*-*E* isomerization mediated by PIDA that drives the deracemization. (synergistic: 协同作用的)

Acknowledgment

Thanks for your attention !