Literature Report 3

Palladium-Catalyzed Enantioselective Carboiodination of Olefin-Tethered Aryl Iodides

Reporter: Xiang Li
Checker: Zi-Biao Zhao
Date: 2019-07-08

Zhang, Z.-M.; Zhang, J. *et al*. *J*. *Am*. *Chem*. *Soc*. **2019**, *141*, 8110.

Contents

CV of Prof. Junliang Zhang

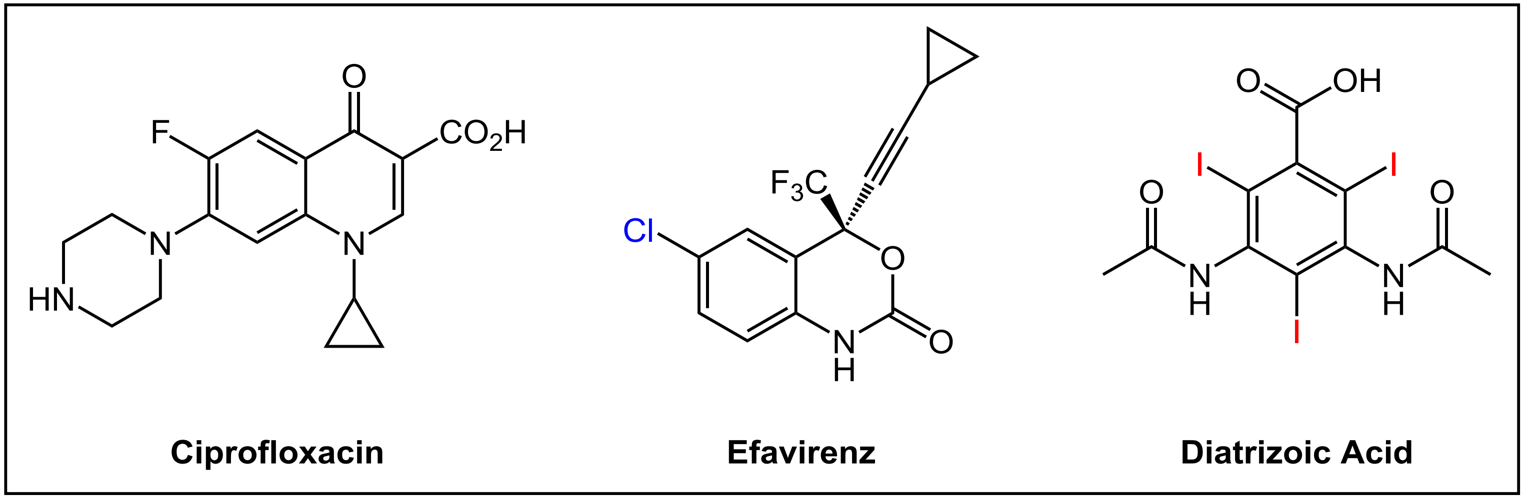
Education:

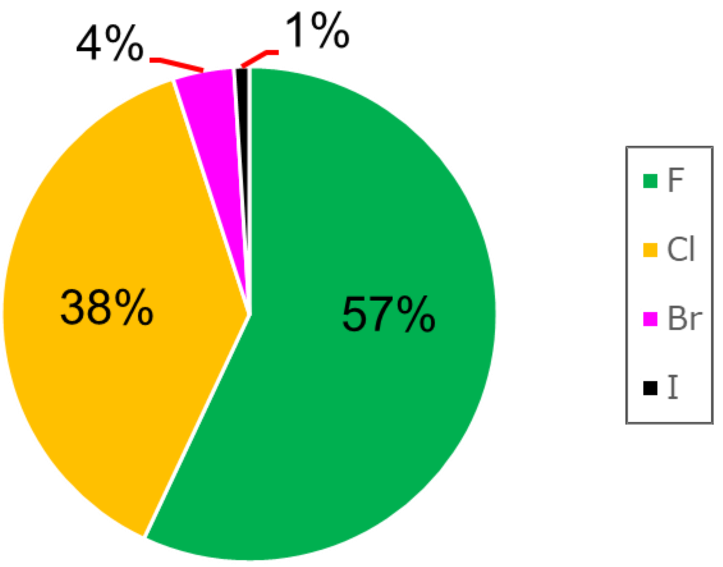
- **1993-1997** B.A., Tianjin University
- **1997-2002** Ph.D., SIOC
- **2002-2003** Research assistant, SIOC
- **2003-2005** Postdoc, University of Cologne
- **2005-2006** Postdoc, The University of Chicago
- **2006-2017** Professor, East China Normal University
- **2017-Present** Professor, Fudan University

Research:

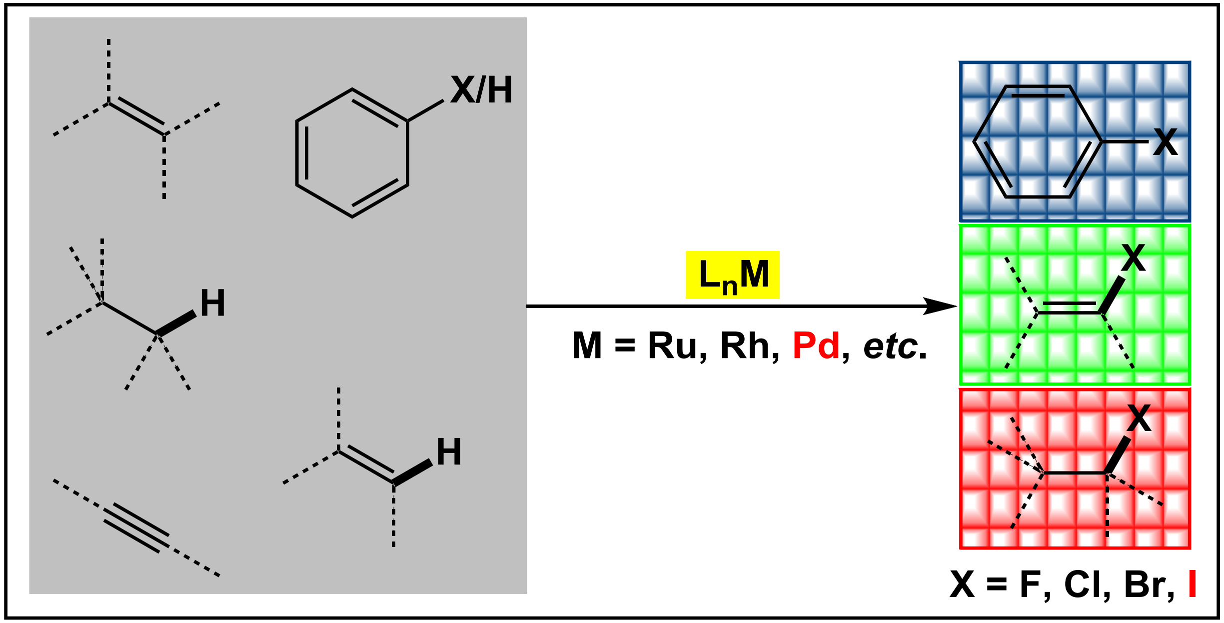
- Conjugated enynes, small ring chemistry, asymmetric catalysis

Introduction



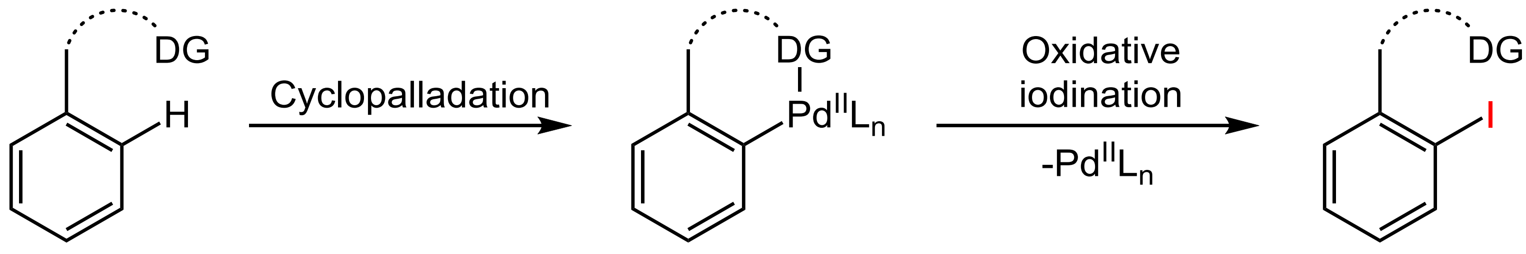


Introduction



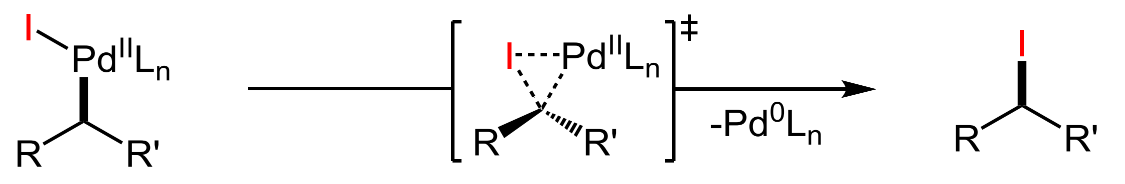
Pd-Catalyzed C-I Bond Formation

a) C(sp^2)−I Bond Formation

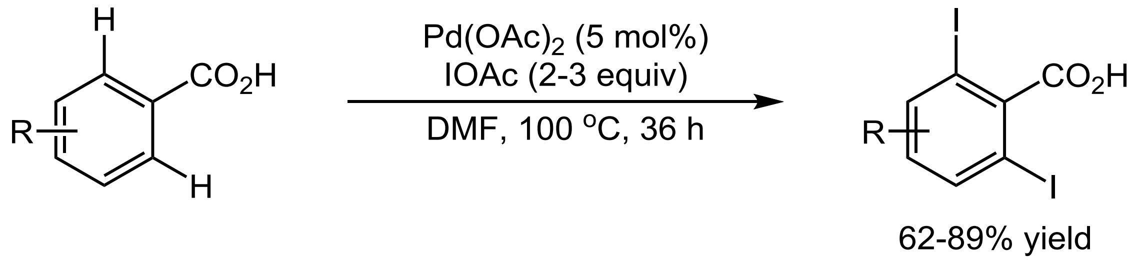


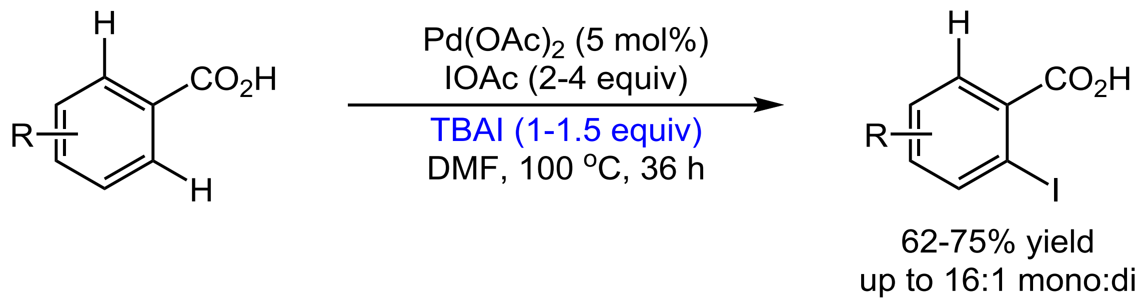
(DG = directing group)

b) C(sp^3)−I Bond Formation



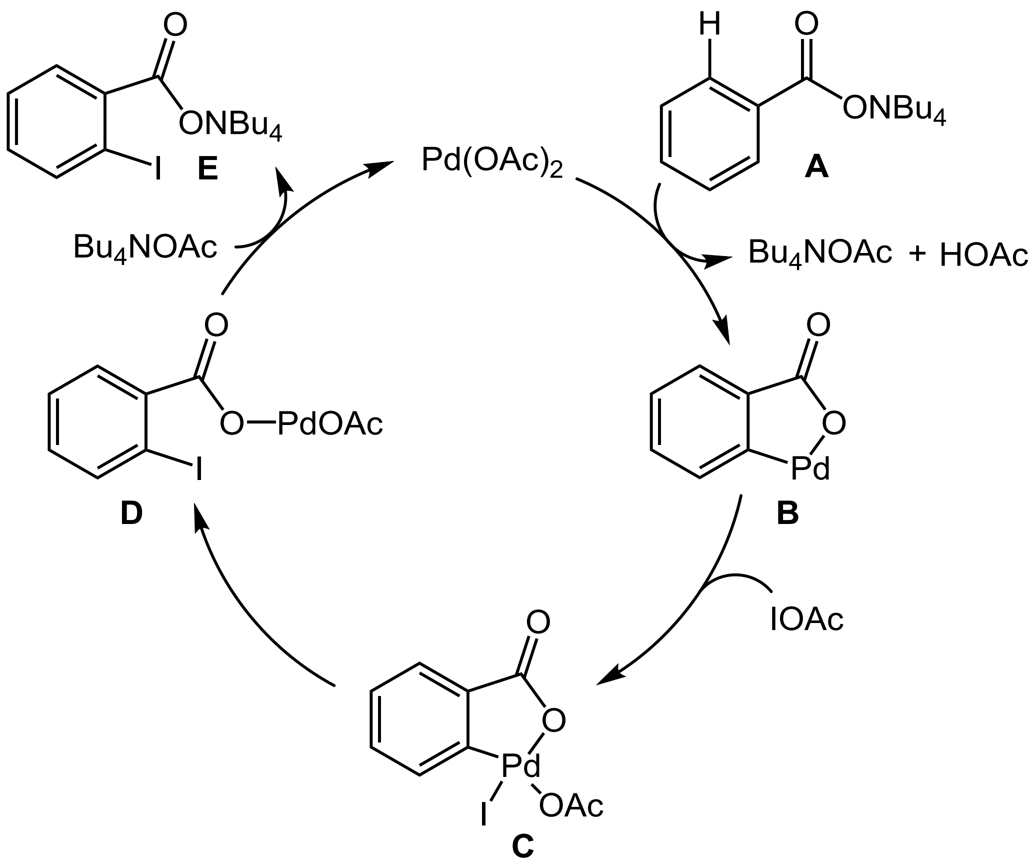
C(sp^2)–I Bond Formation





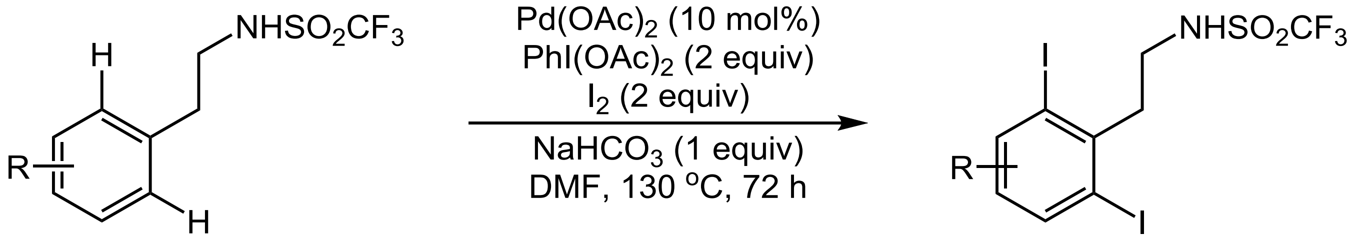
Yu, J.-Q. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2008**, *47*, 5215.

C(sp²)−I Bond Formation



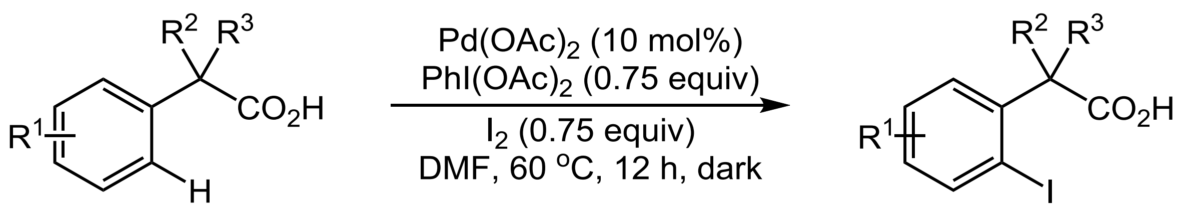
Yu, J.-Q. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2008**, *47*, 5215.

C(sp²)–I Bond Formation



56-91% yield

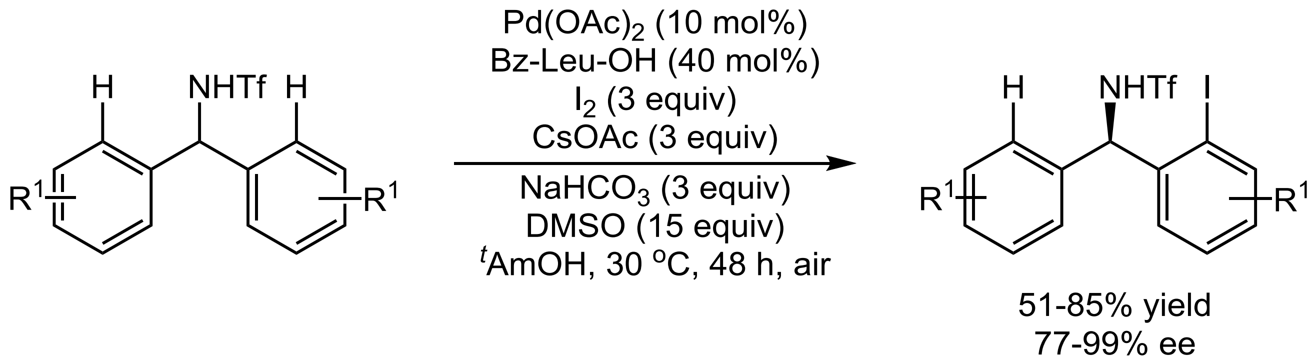
Yu, J.-Q. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2008**, *47*, 6452.

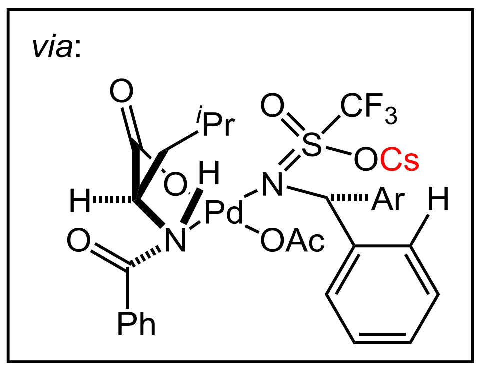


60-90% yield

Yu, J.-Q. *et al*. *Org*. *Lett*. **2010**, *12*, 3140.

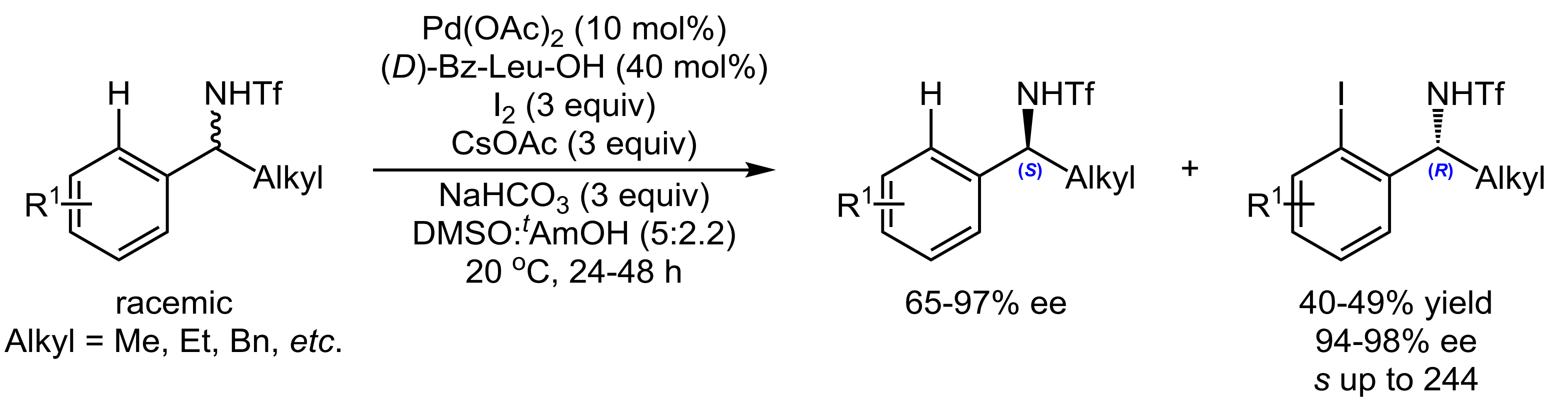
C(sp^2)−I Bond Formation



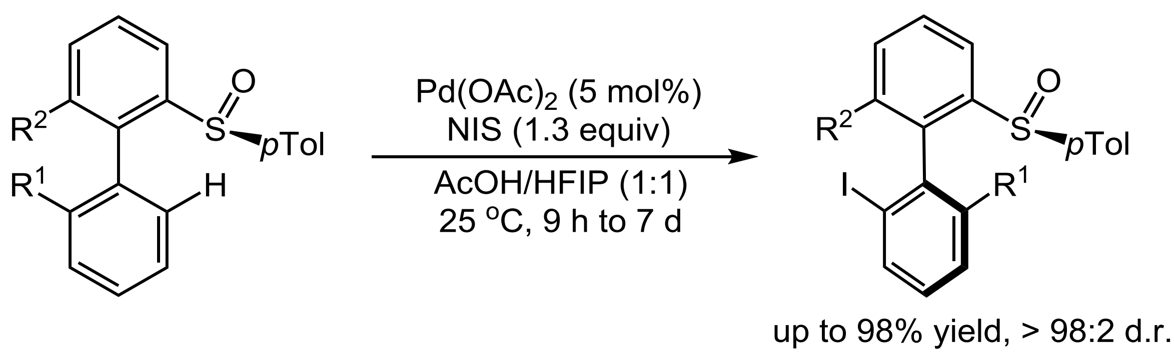


Yu, J.-Q. *et al*. *J*. *Am*. *Chem*. *Soc*. **2013**, *135*, 16344.

C(sp²)−I Bond Formation

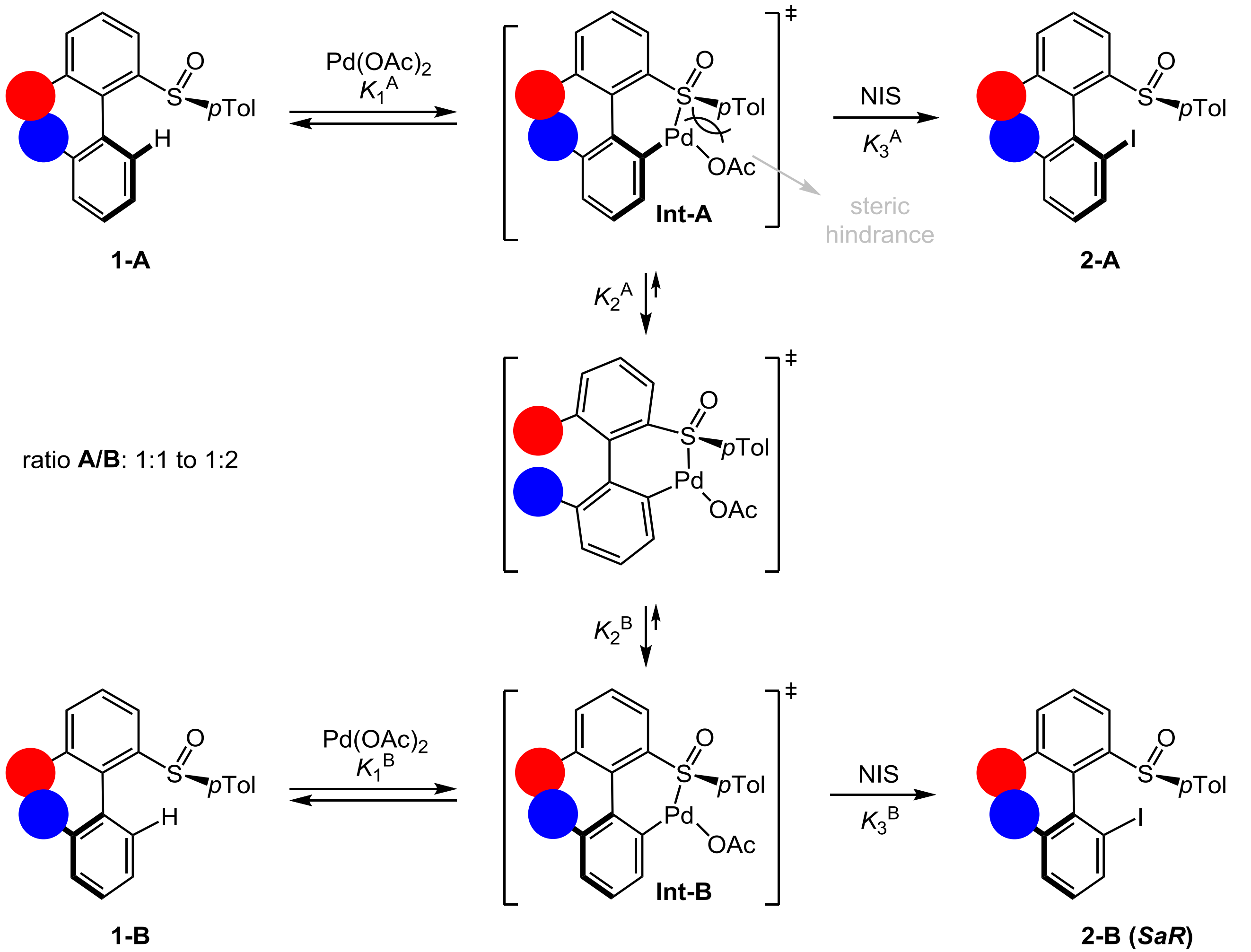


Yu, J.-Q. *et al*. *Science* **2014**, *346*, 451.



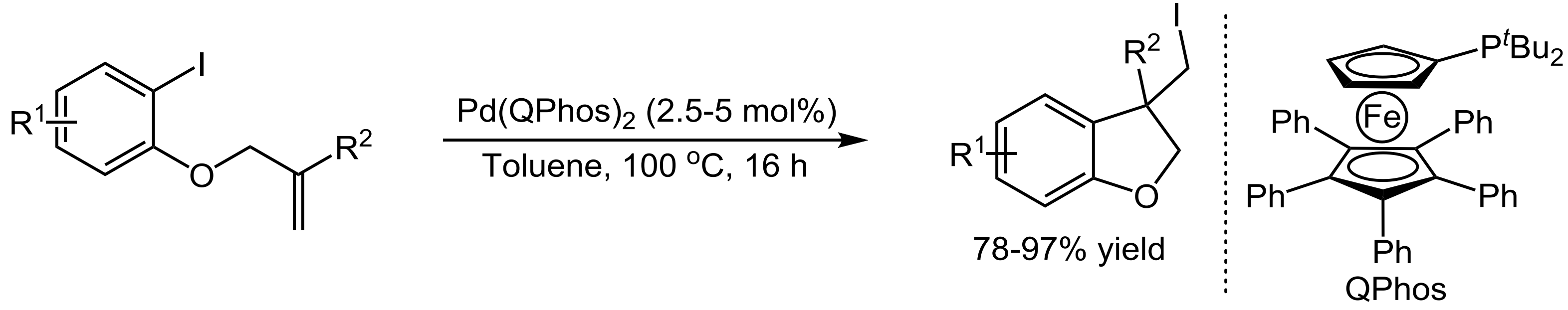
Colobert, F. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 13871.

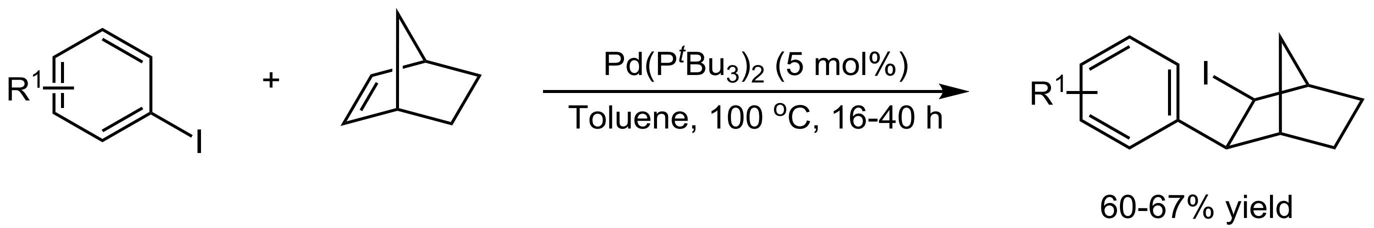
C(sp²)–I Bond Formation



Colobert, F. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 13871.

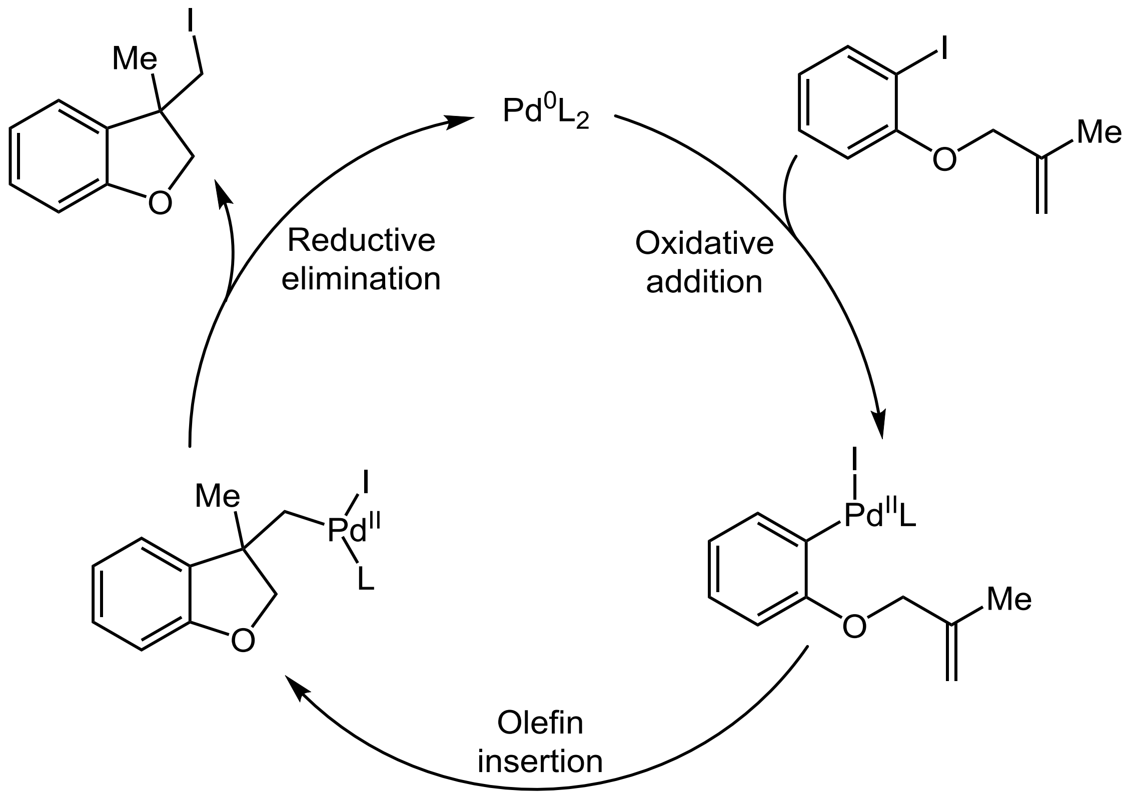
C(sp³)–I Bond Formation





Lautens, M. *et al*. *J*. *Am*. *Chem*. *Soc*. **2011**, *133*, 1778.

C(sp³)–I Bond Formation



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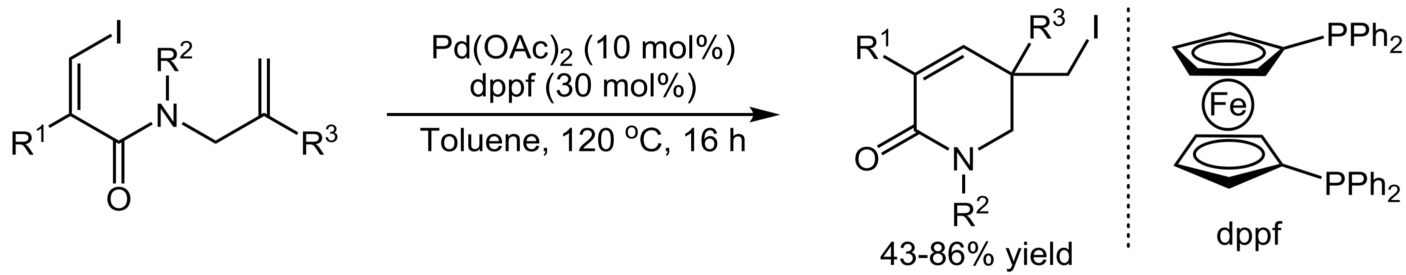
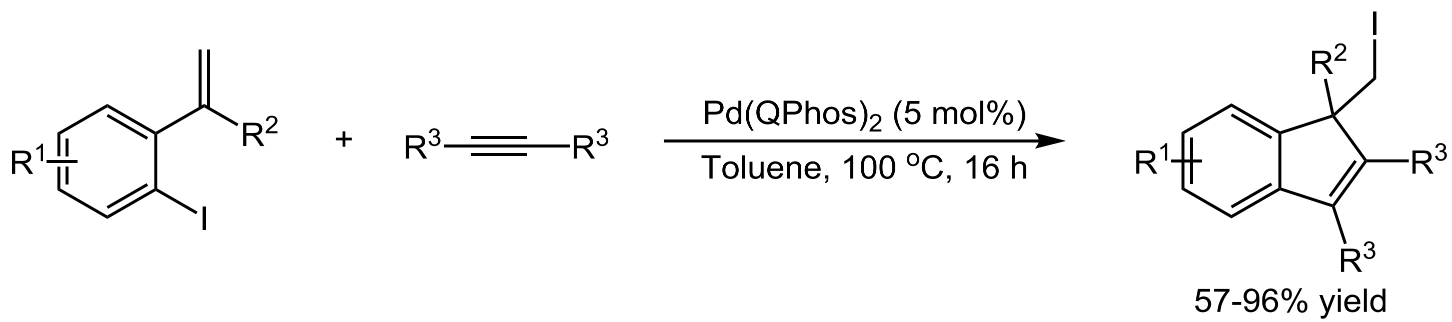
C(sp³)–I Bond Formation

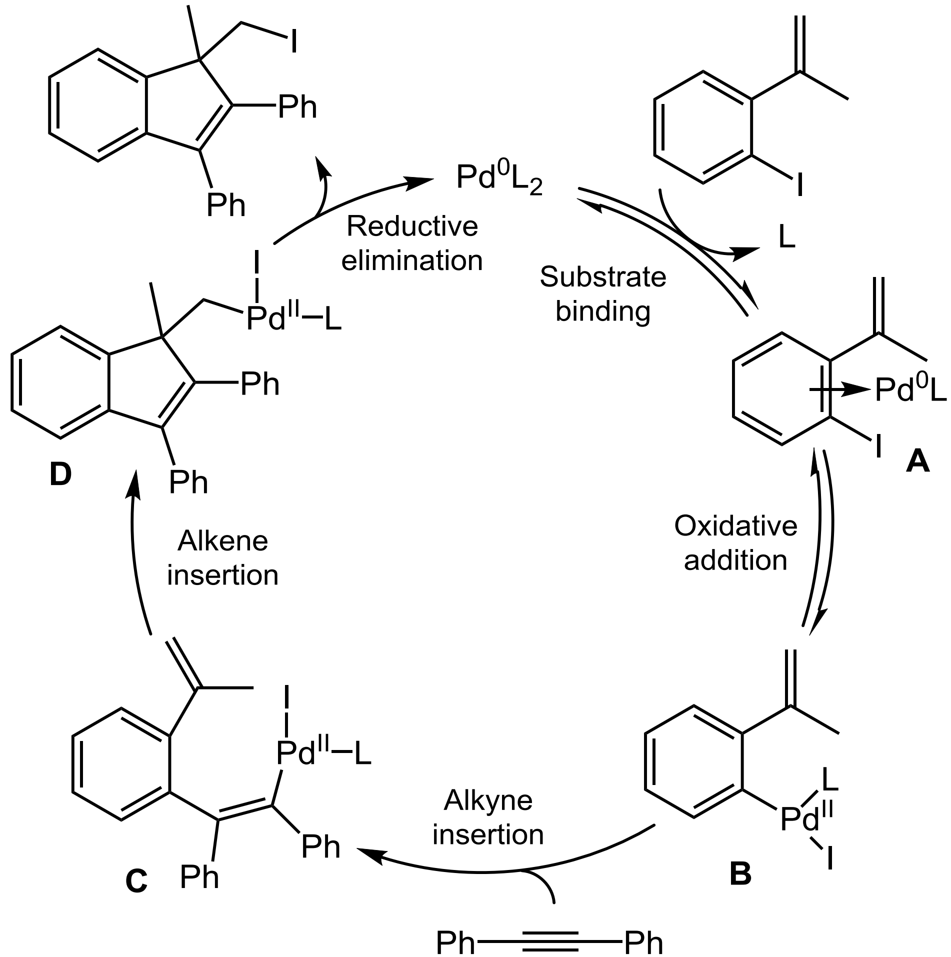


Tong, X. *et al*. *J*. *Am*. *Chem*. *Soc*. **2011**, *133*, 6187.



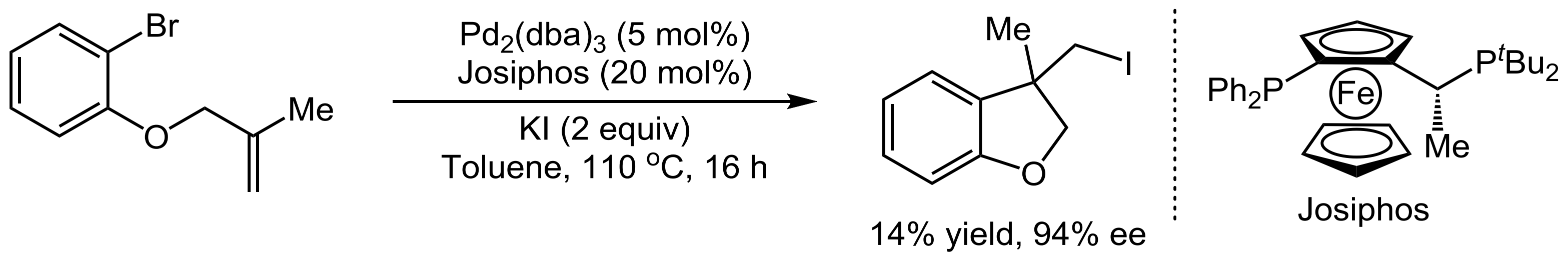
Lautens, M. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2012**, *51*, 9870.

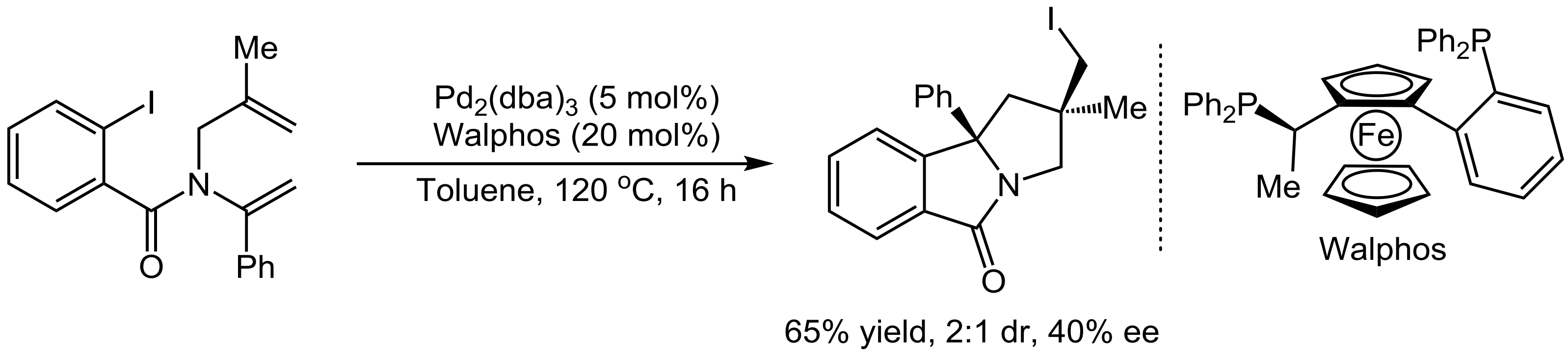
C(sp^3)–I Bond Formation



Lautens, M. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2012**, *51*, 9870.

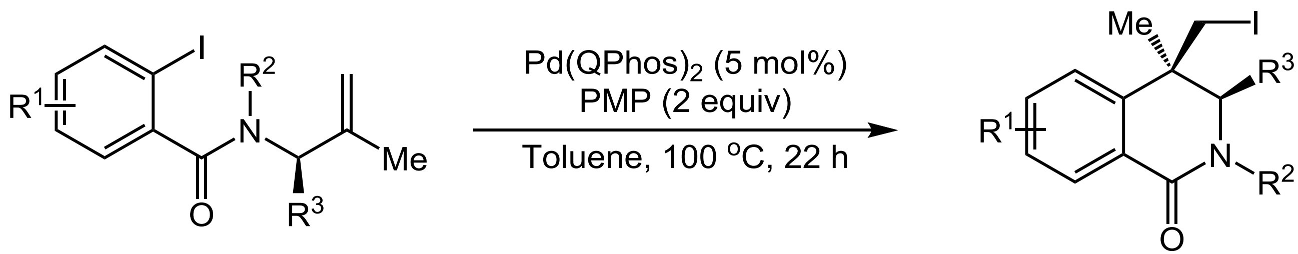
C(sp³)–I Bond Formation





Lautens, M. *et al*. *J*. *Am*. *Chem*. *Soc*. **2011**, *133*, 14916.

C(sp^3)–I Bond Formation

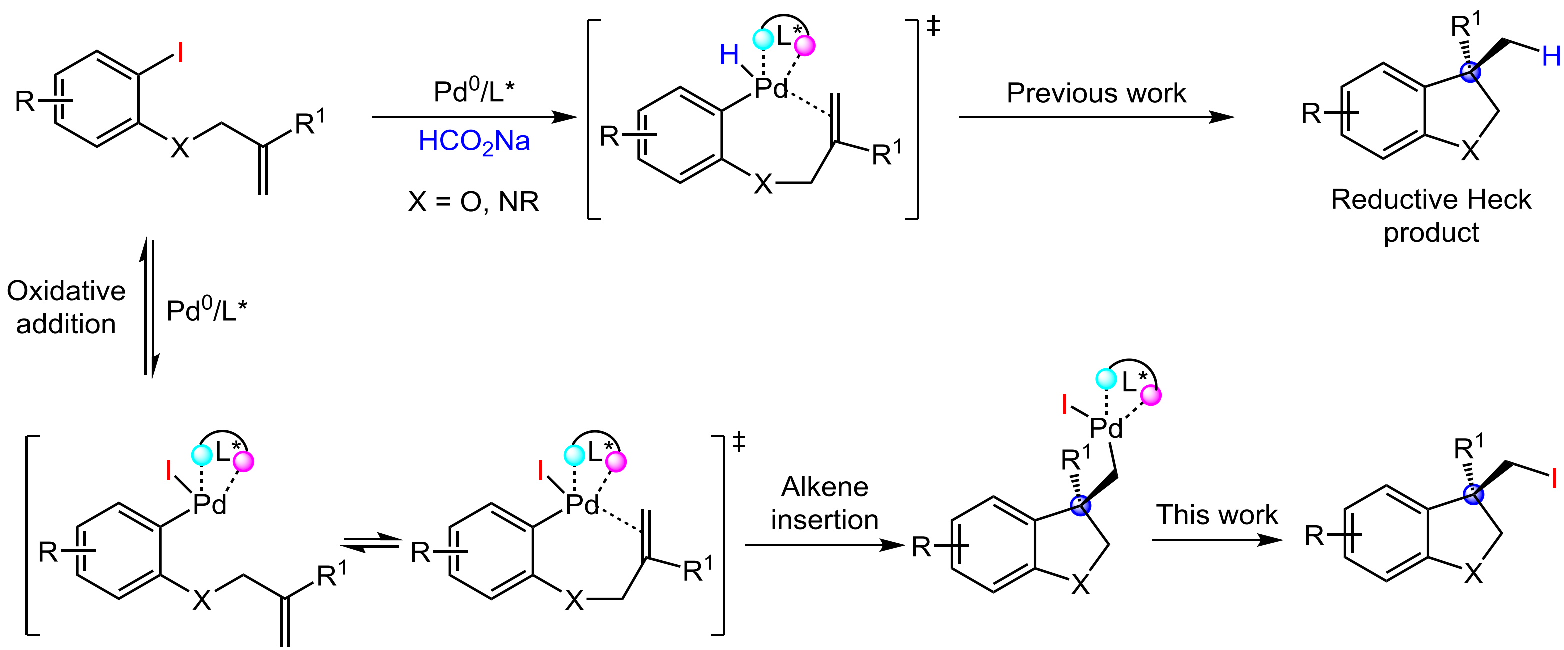


up to > 99:1 er

up to 95% yield
up to > 98:2 dr
up to > 99:1 er

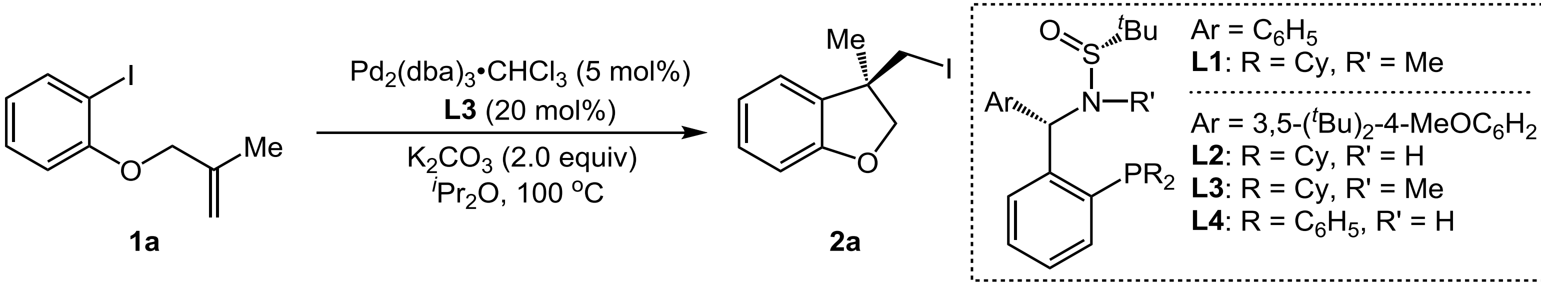
Lautens, M. *et al*. *Angew*. *Chem*. *Int*. *Ed*. **2014**, *53*, 7908.

Pd-Catalyzed Asymmetric Carboiodination



Zhang, J. *et al*. *J*. *Am*. *Chem*. *Soc*. **2019**, *141*, 8110.

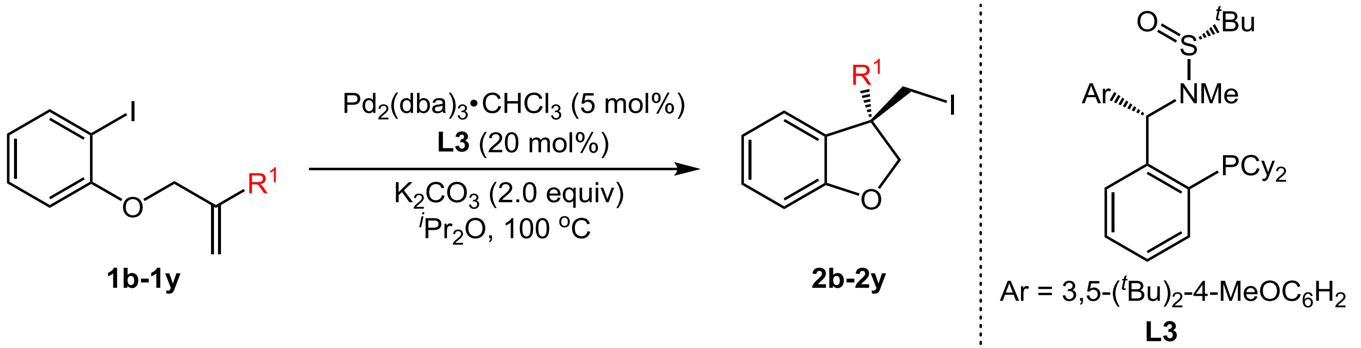
Effect of Reaction Parameters

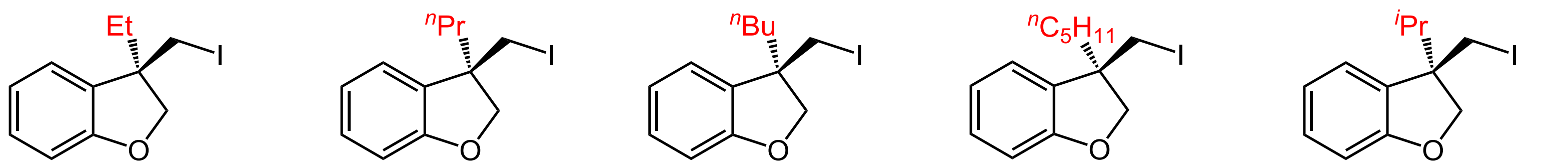


Entry	Variation from the standard conditions	*Conv.* (%)[a]	Yield (%)[b]	Er (%)[c]
1	none	100	80[d]	95.5:4.5
2	**L1** instead of **L3**	<5	trace	-
3	**L2** instead of **L3**	-	-	-
4	**L4** instead of **L3**	-	-	-
5	no K_2CO_3	73	58	95:5
6	Cs_2CO_3 instead of K_2CO_3	74	14	92.5:7.5
7	$Pd(OAc)_2$ instead of $Pd_2(dba)_3$•$CHCl_3$	82	41	91.5:8.5
8	PhMe instead of $^i Pr_2O$	100	78	94.5:5.5

Reaction conditions: **1a** (0.1 mmol), 10 mol% of catalyst ([Pd] to **L** = 1:2), solvent (2 mL), 100 °C, 14 h. [a] Determined by NMR. [b] NMR yield. [c] Determined by HPLC for product. [d] 0.3 mmol of **1a**, isolated yield.

Substrate Scope





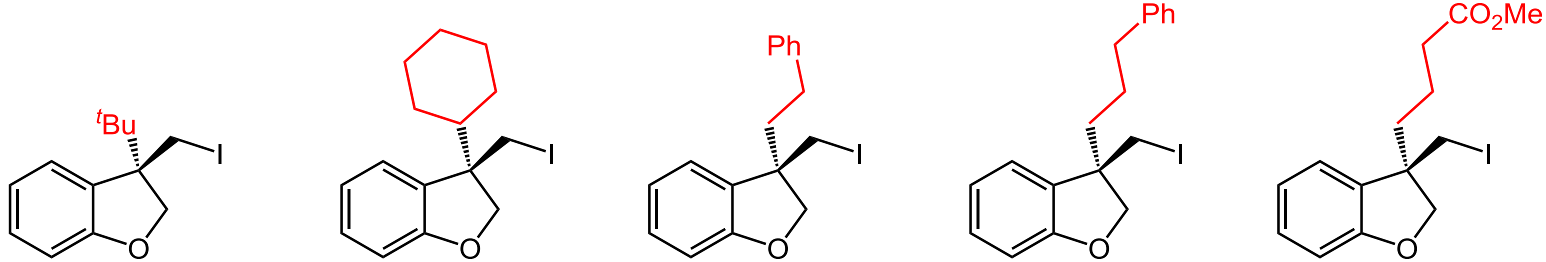
2b: 61%, 95.5:4.5 er
ent-**2b**[a]: 63%, 4.5:95.5 er

2c: 75%, 95:5 er
ent-**2c**: 76%, 5:95 er

2d: 72%, 95:5 er
ent-**2d**: 75%, 5:95 er

2e: 75%, 96:4 er
ent-**2e**: 75%, 4.5:95.5 er

2f: 74%, 96.5:3.5 er
ent-**2f**: 79%, 3.5:96.5 er



2g: 69%, 95.5:4.5 er
ent-**2g**: 67%, 4.5:95.5 er

2h: 90%, 96.5:3.5 er
ent-**2h**: 94%, 4:96 er

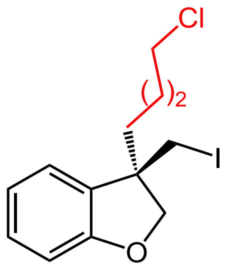
2i: 80%, 95:5 er
ent-**2i**: 78%, 5:95 er

2j: 82%, 95.5:4.5 er
ent-**2j**: 80%, 4.5:95.5 er

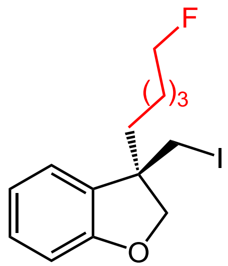
2k: 75%, 95:5 er
ent-**2k**: 73%, 5:95 er

[a] 20 mol% *ent*-**L3** was used

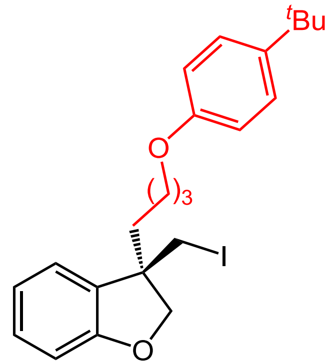
Substrate Scope



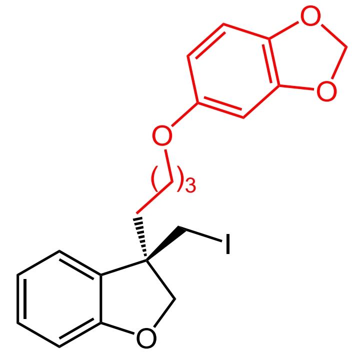
2l: 75%, 95:5 er
ent-**2l**: 76%, 5:95 er



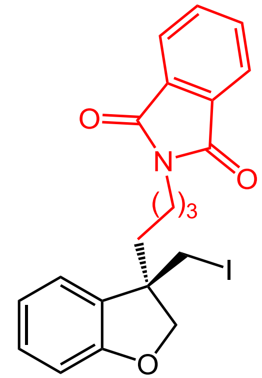
2m: 80%, 95:5 er
ent-**2m**: 82%, 5:95 er



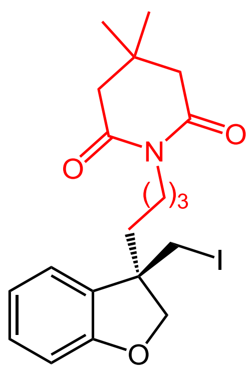
2n: 70%, 95:5 er
ent-**2n**: 72%, 5:95 er



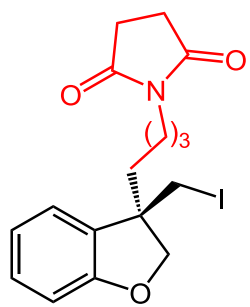
2o: 55%, 95:5 er
ent-**2o**: 53%, 5:95 er



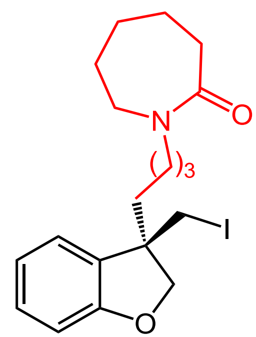
2p: 70%, 95.5:4.5 er
ent-**2p**: 72%, 4.5:95.5 er



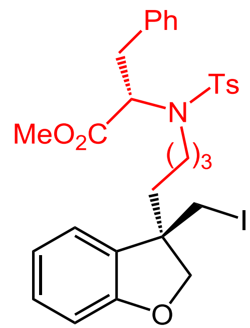
2q: 78%, 95.5:4.5 er
ent-**2q**: 75%, 4.5:95.5 er



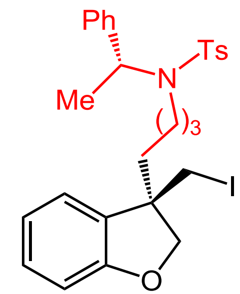
2r: 84%, 95.5:4.5 er
ent-**2r**: 81%, 5:95 er



2s: 85%, 95:5 er
ent-**2s**: 82%, 5:95 er

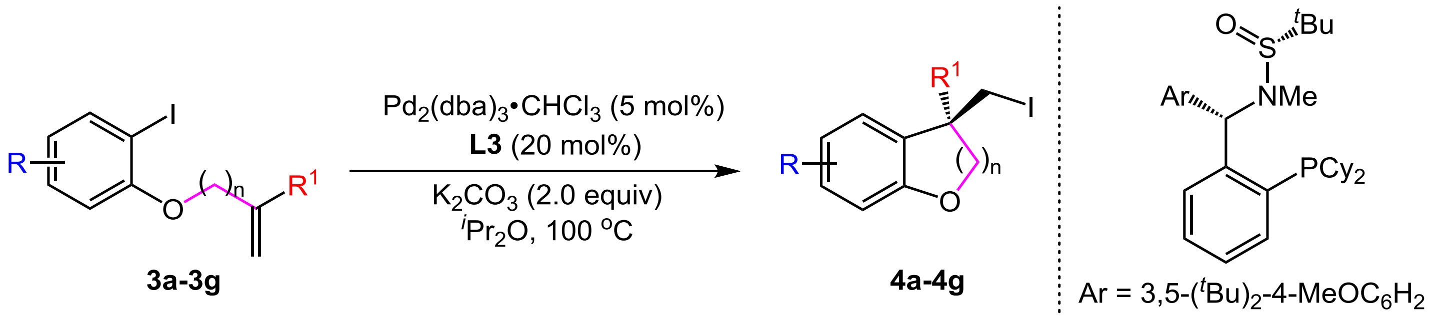


2t: 61%, > 20:1 dr

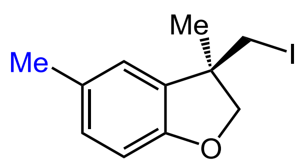


2u: 73%, > 20:1 dr

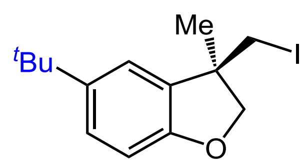
Substrate Scope



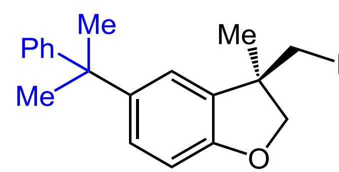
L3



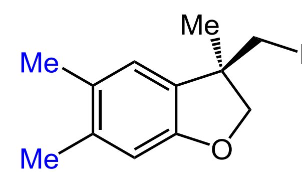
4a: 83%, 96.5:3.5 er



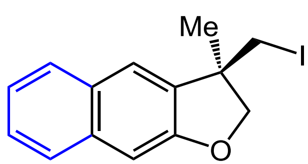
4b: 87%, 95.5:4.5 er



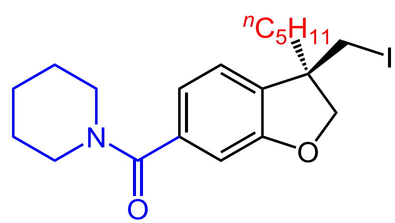
4c: 80%, 95.5:4.5 er



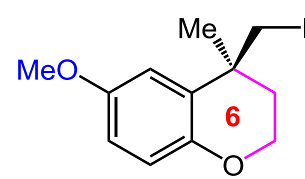
4d: 87%, 96.5:3.5 er



4e: 72%, 95.5:4.5 er



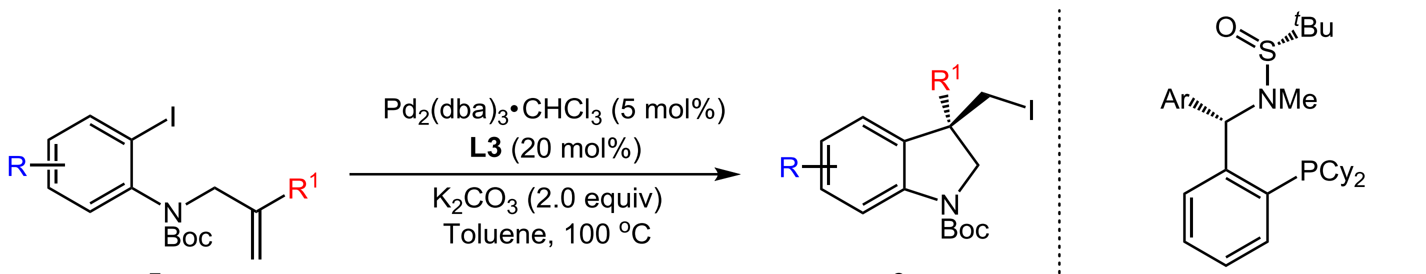
4f: 66%, 95:5 er
ent-**4f**[a]: 68%, 5:95 er



4g: 84%, 96.5:3.5 er
ent-**4g**: 82%, 3.5:96.5 er

[a] 20 mol% *ent*-**L3** was used

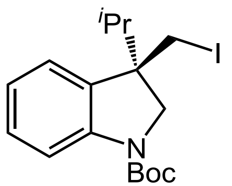
Substrate Scope



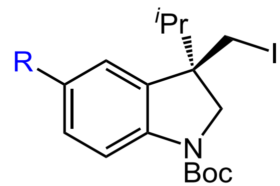
5 **6**

Ar = 3,5-(^{t}Bu)$_2$-4-MeOC$_6$H$_2$

L3

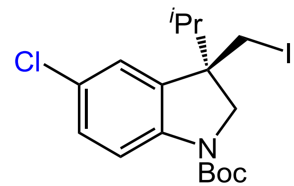


6a: 92%, 88:12 er

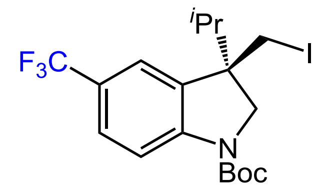


6b: R = Me 86%, 93:7 er

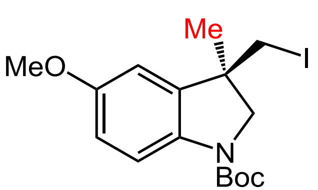
6c: R = OMe 80%, 94:6 er



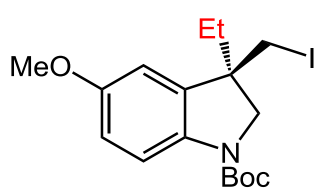
6d: 78%, 93.5:6.5 er



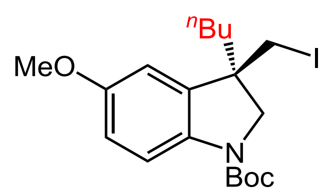
6e: 84%, 92:8 er



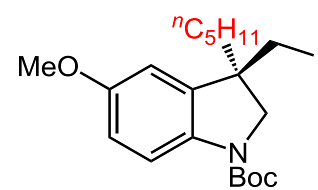
6f: 83%, 90:10 er



6g: 83%, 90:10 er



6h: 76%, 91:9 er



6i: 88%, 91:9 er

The Reaction Mechanism

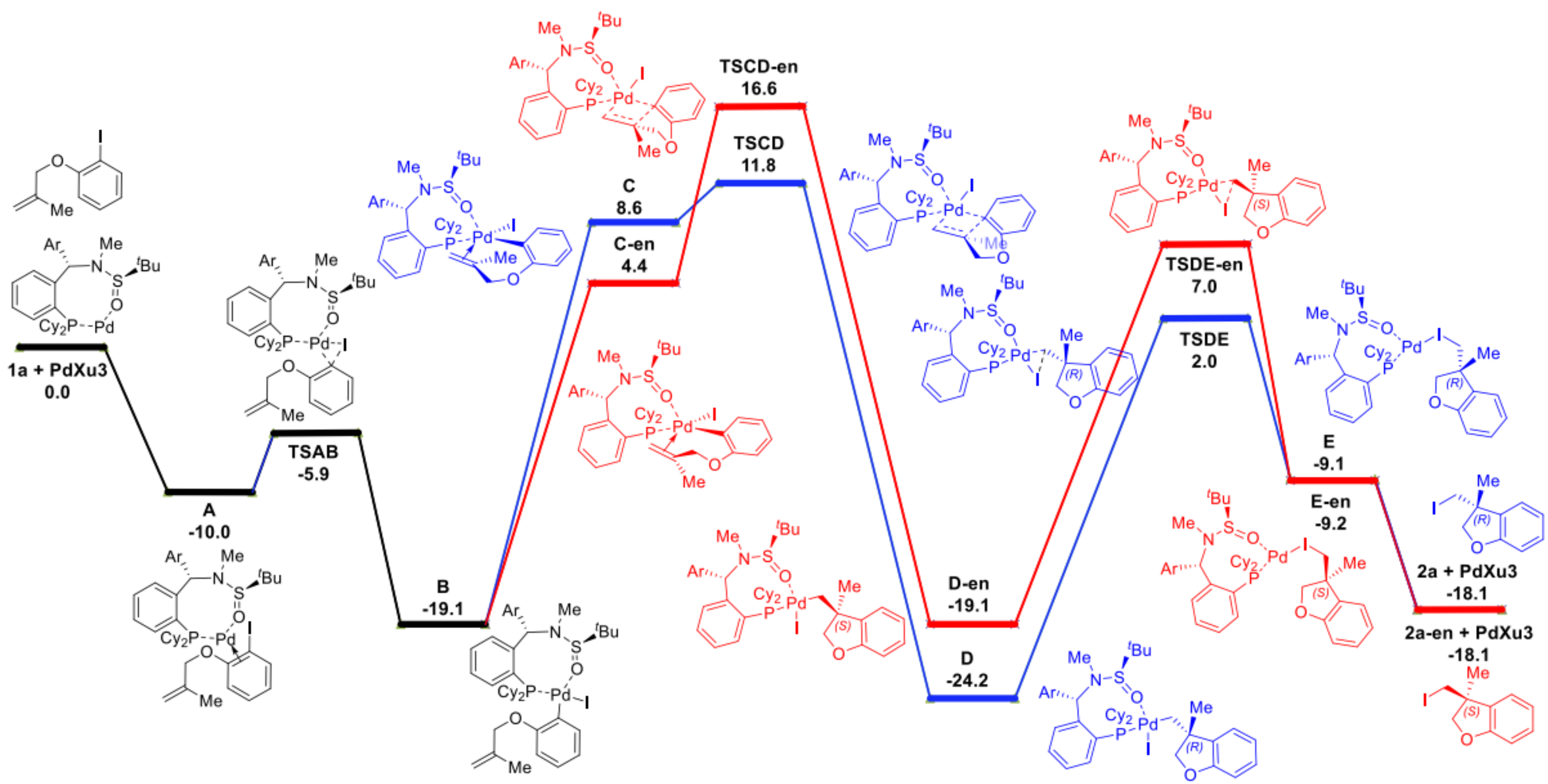
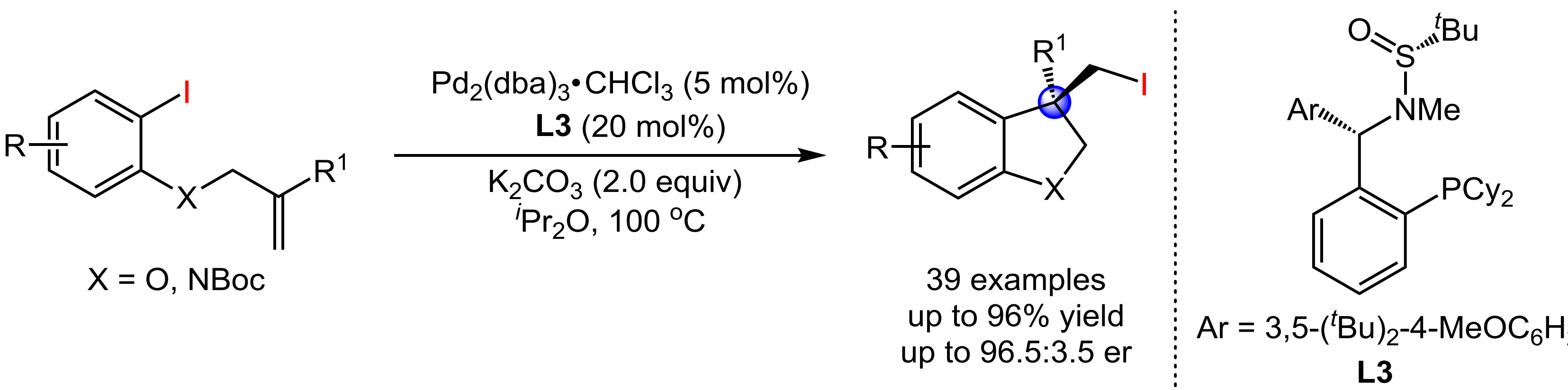


Figure 2. Free-energy reaction profiles (kcal mol^{-1}) calculated at the SMD (^{i}Pr$_2$O) B3LYP/combined basis set level at 373 K.

Summary



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The First Paragraph

From various natural product and bioactive molecules to materials, and clean energy, organic halides undoubtedly represent versatile synthetic precursors even directly as target molecules. Over past decades, transition-metal catalyzed synthesis of racemic organic halides has attracted tremendous attention. Notably, Lautens disclosed a perfect atom economical strategy to construct 2,3-dihydrobenzofuran bearing an alkyl iodide group by a domino sequence involving the oxidative addition of aryl iodide, alkene insertion and $C(sp^3)$-I reductive elimination from a Pd(II) intermediate. A particular focus was on the rate-determing reductive elimination step, which needs an exceptionally bulky and electron rich phosphine ligand such as QPhos or $P(^tBu)_3$ facilitated the $C(sp^3)$-I reductive elimination by limiting the formation of tetracoordinated intermediates.

The First Paragraph

By the employment of excess electron-rich bisphosphine ligand DPPF, Tong realized an elegant example of Pd(0)-catalyzed carboiodination reaction of (*Z*)-1-iodo-1,6-diene. The Ni-catalyzed intramolecular carboiodination reaction was also realized to generate valuable halogenated 3,3-disubstituted heterocycles and a moderately enantioselective process has also been reported. Despite much elegant progress in the racemic or diastereoselective synthesis has been made, the development of transition-metal (especially palladium-catalyzed) asymmetric carboiodination reaction with high effciency remains extremely challenging, besides the enantioselectivity, “there are few ligands known to promote the key reductive elimination” mentioned by Lautens. Thus, the development of the highly efficient and enantioselective transition-metal catalyzed carboiodination is desired.

The Last Paragraph

In summary, we have developed the first highly enantioselective palladium-catalyzed carboiodination of unactivated alkenes with the use of *N*-Me-Xu3 as the chiral ligand and K_2CO_3 as the additive, which provides an efficient synthesis of chiral 3,3-disubstituted 2,3-dihydrobenzofuran, indolines and chromane bearing an alkyl iodide and one all-carbon quaternary stereocenter. The mechanism of this Pd(0)-catalyzed asymmetric carboiodination of alkenes has been investigated with density functional theory. The DFT calculations indicated that the alkene insertion rather than the reductive elimination is the rate-determining step and accounts for the enantioselectivity and high reactivity. Moreover, further direction will focus on the development of asymmetric domino carbopalladation-initiated reactions and will be reported in the due course.

Acknowledgement

Thanks

for your attention