One-Pot Synthesis of Phenanthridinones by C-H Activation

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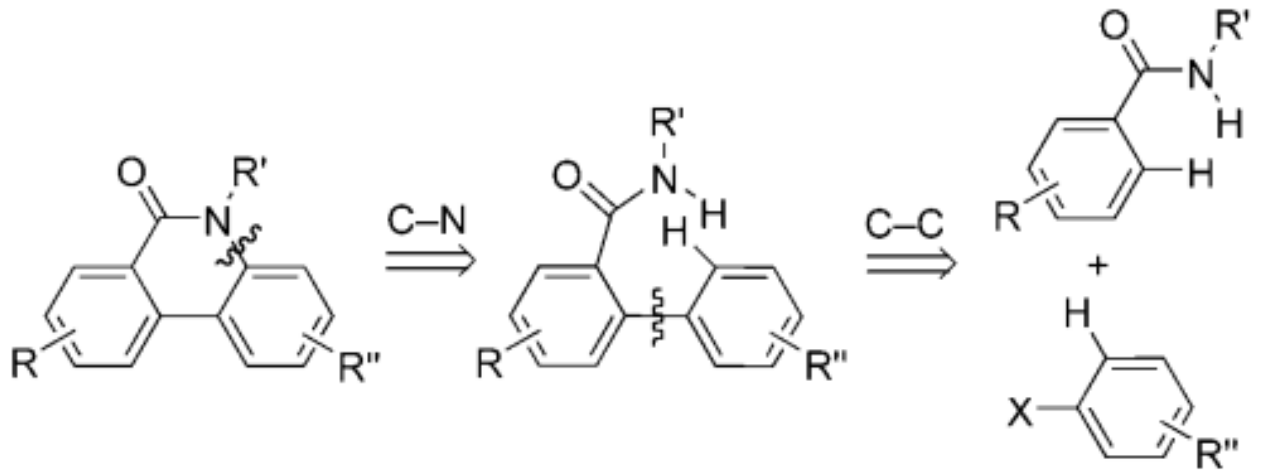
Supervisor: Prof. Zhao Jing

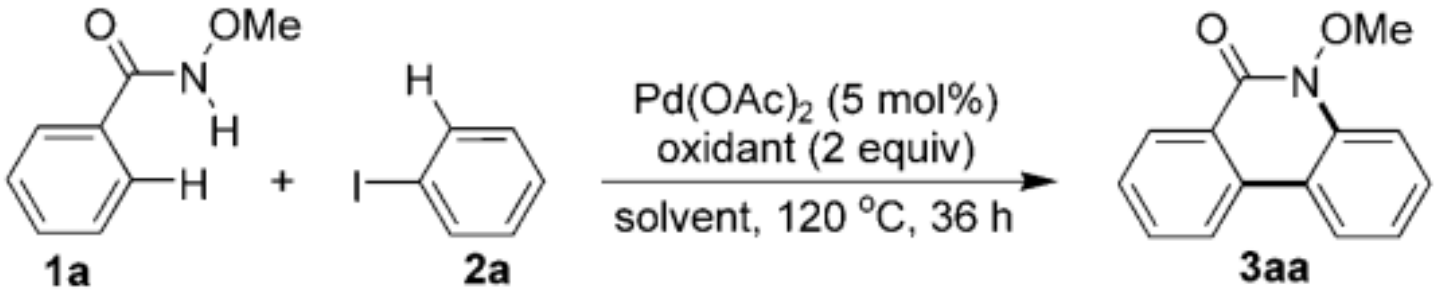
2014-02-24

Retrosynthesis of Phenanthridinones



X=I, H, $B(OH)_2$

Palladium-Catalyzed Coupling with Aryl Iodides



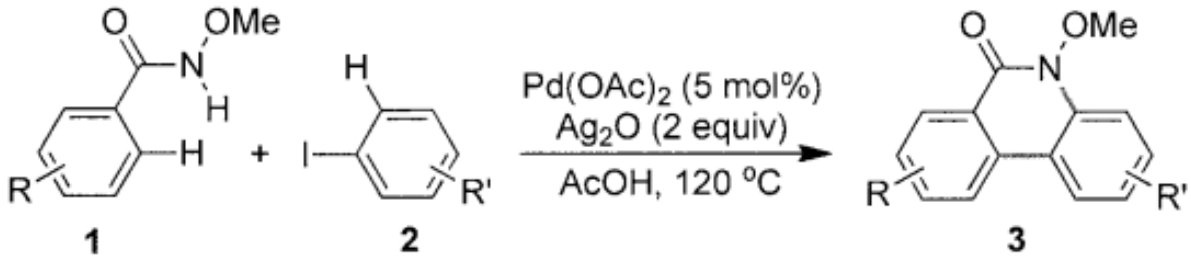
1a + 2a → 3aa

Entry	Oxidant	Yield [%]	Entry	Oxidant	Yield [%]
1[b]	AgOAc	Trace	6[c]	Ag_2O	68
2	AgOAc	61	7[d]	Ag_2O	66
3	Ag_2SO_4	29	8	$K_2S_2O_8$	13
4	AgOTf	23	9	Oxone	13
5	Ag_2O	76	10	$Cu(OAc)_2$	12

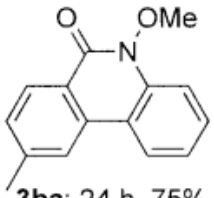
[a] Unless otherwise specified, all reactions were carried out with 1a (0.5 mmol), 2a (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), and oxidant (1.0 mmol) in AcOH (5 mL) at 120^0C for 36 h. [b] CF_3COOH was used as the solvent. [c] 0.5 mmol of 2a was used. [d] 0.5 mmol of Ag_2O was used.

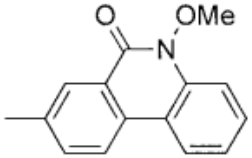
G.-W. Wang, T.-T. Yuan, D.-D. Li, *Angew. Chem. Int. Ed*. **2011**, *50*, 1380.

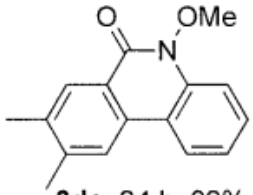
Scope of Substrates

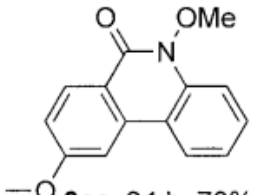


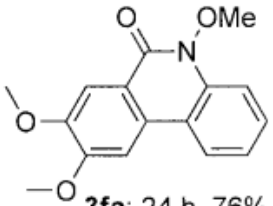
1 2 3

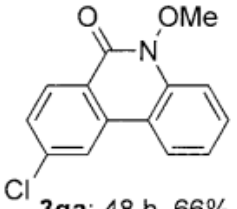

3ba; 24 h, 75%

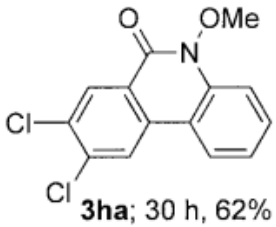

3ca; 24 h, 85%

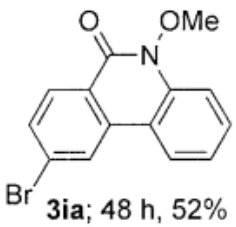

3da; 24 h, 82%

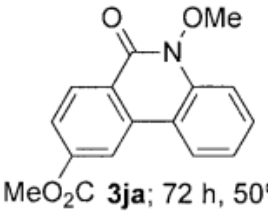

3ea; 24 h, 70%

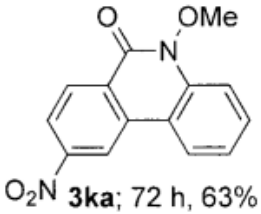

3fa; 24 h, 76%

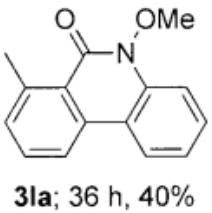

3ga; 48 h, 66%

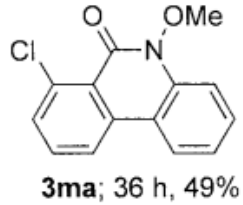

3ha; 30 h, 62%

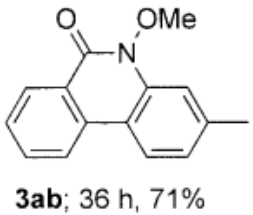

3ia; 48 h, 52%

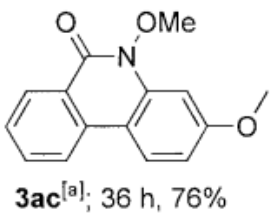

3ja; 72 h, 50%

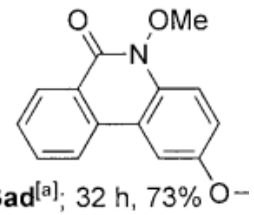

3ka; 72 h, 63%

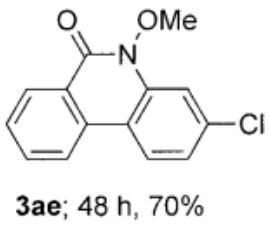

3la; 36 h, 40%

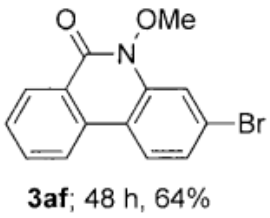

3ma; 36 h, 49%

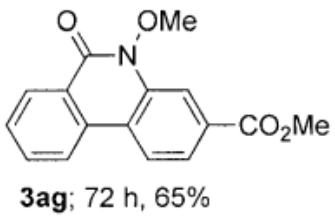

3ab; 36 h, 71%

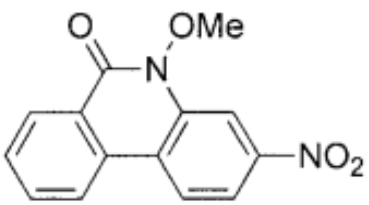

3ac[a]; 36 h, 76%

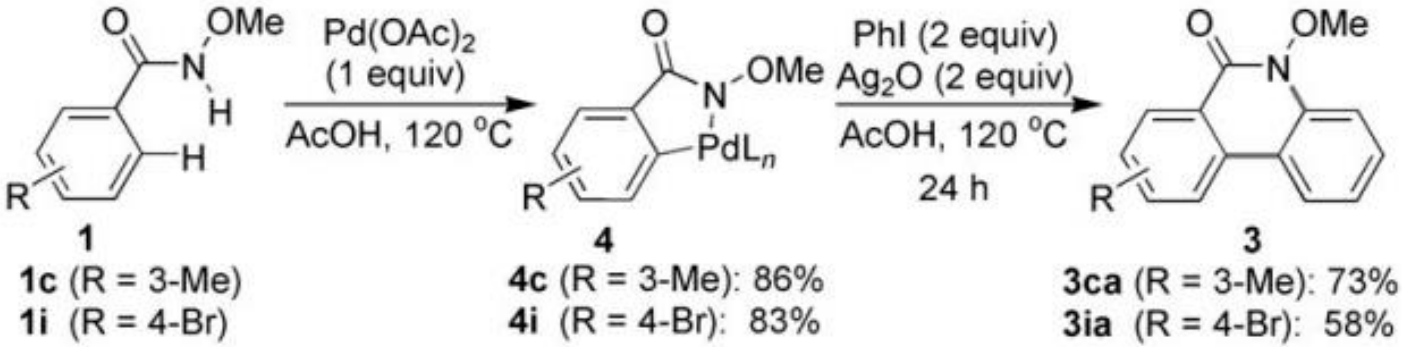

3ad[a]; 32 h, 73%


3ae; 48 h, 70%


3af; 48 h, 64%


3ag; 72 h, 65%

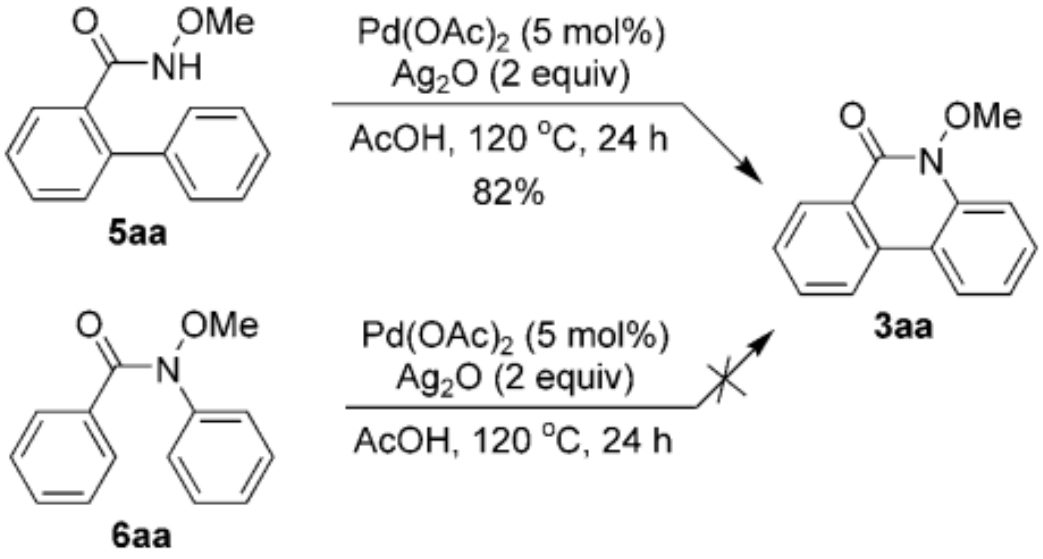

3ah; 72 h, 39%



1
1c (R = 3-Me)
1i (R = 4-Br)

4
4c (R = 3-Me): 86%
4i (R = 4-Br): 83%

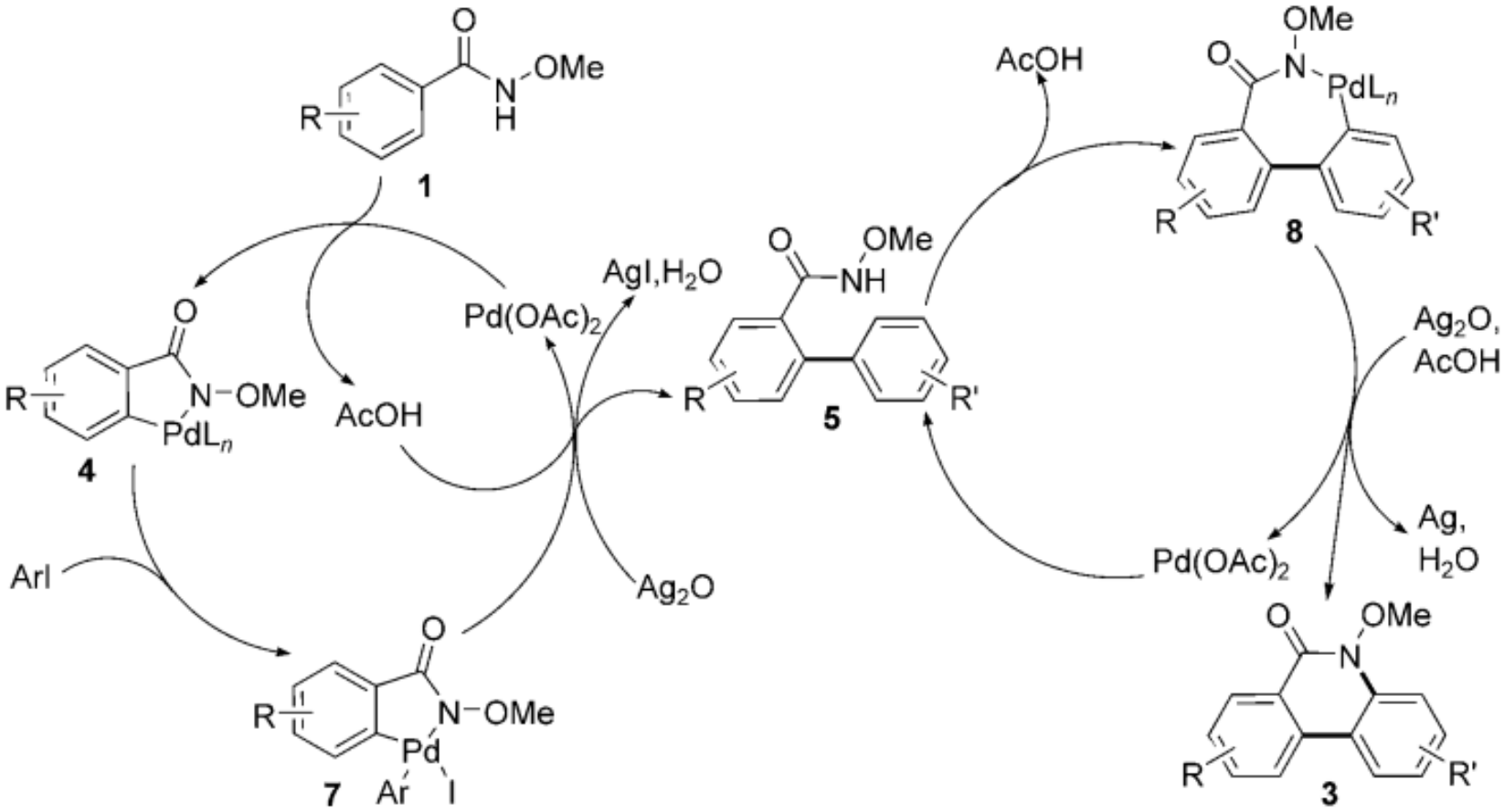
3
3ca (R = 3-Me): 73%
3ia (R = 4-Br): 58%



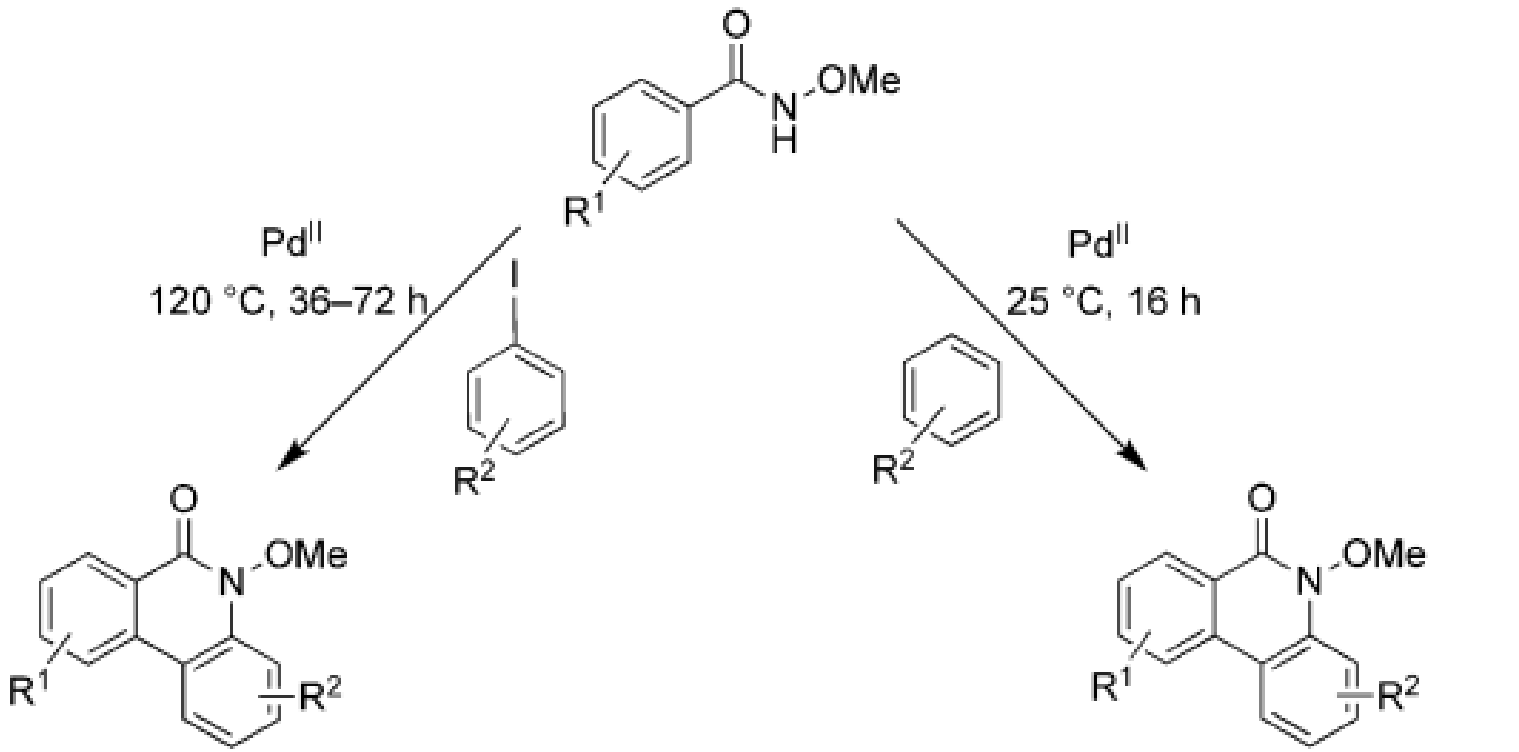
5aa

3aa

6aa


O
N
OMe
H
R
1
O
N
OMe
PdL$_n$
R
4
ArI
O
N
OMe
Pd
Ar
I
R
7
Pd(OAc)$_2$
AgI,H$_2$O
AcOH
Ag$_2$O
O
NH
OMe
R
R'
5
AcOH
OMe
O
N
PdL$_n$
R
R'
8
Ag$_2$O,
AcOH
Ag,
H$_2$O
Pd(OAc)$_2$
O
N
OMe
R
R'
3

Palladium-Catalyzed Coupling with Arenes



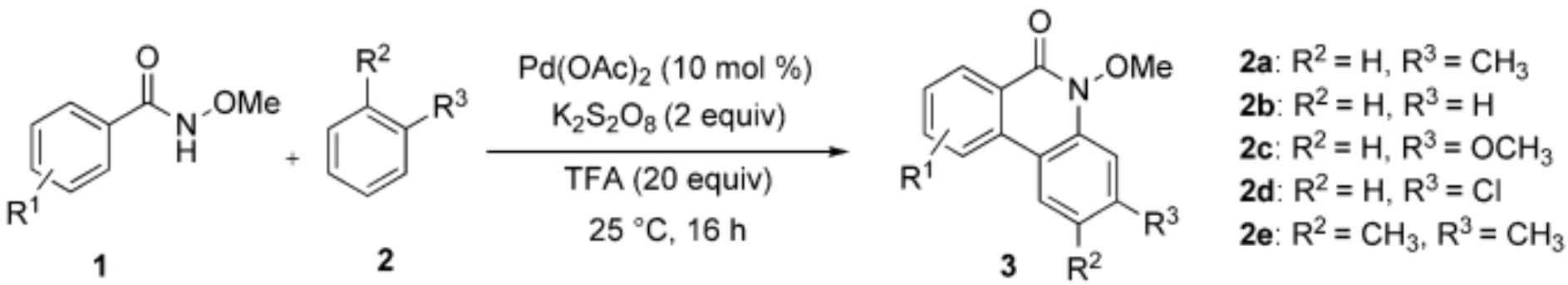
previous work

– expensive metal oxidant
– high temperature
– long reaction time

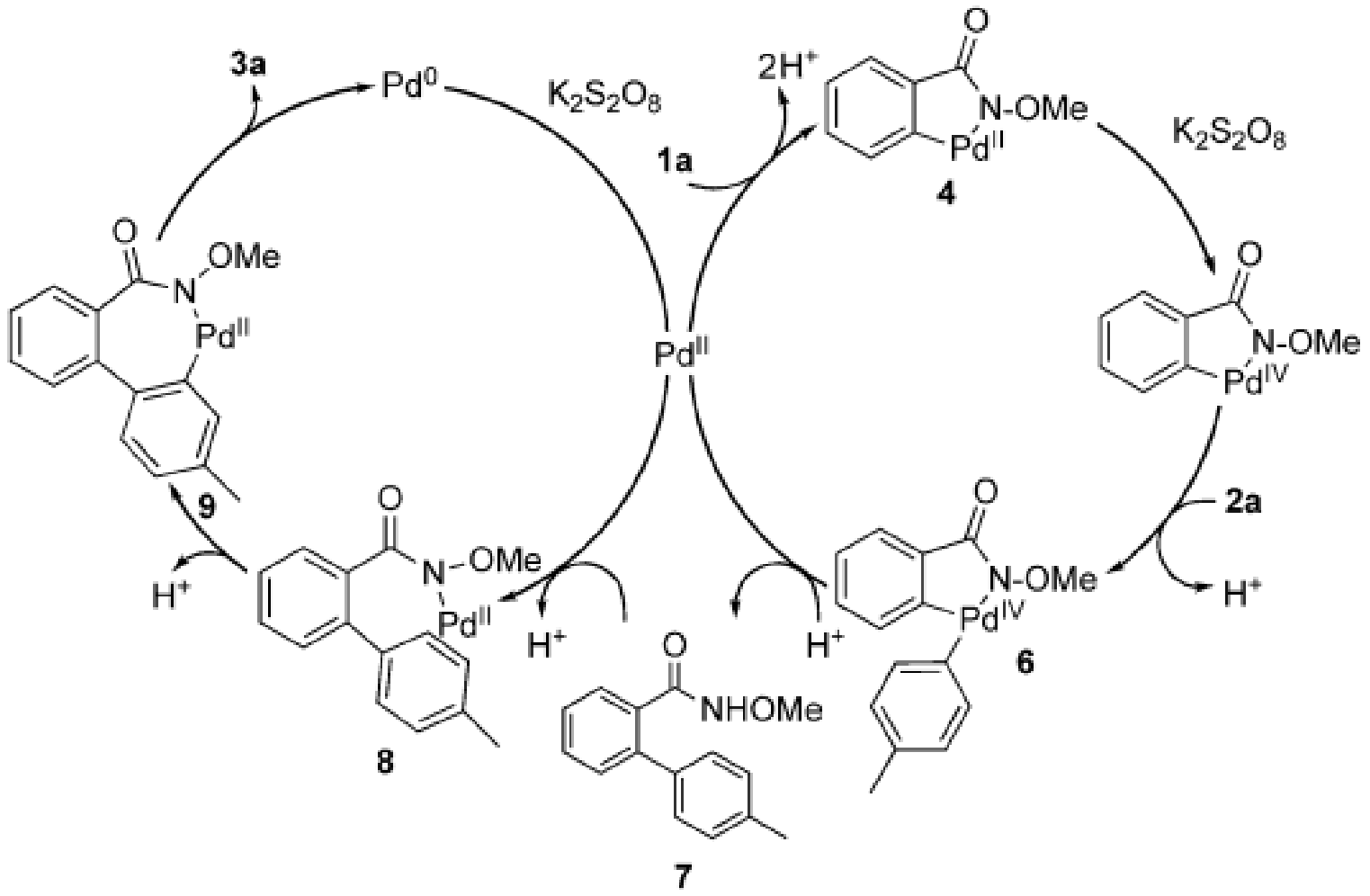
present work

– highly regioselective
– very mild conditions
– no prefunctionalization

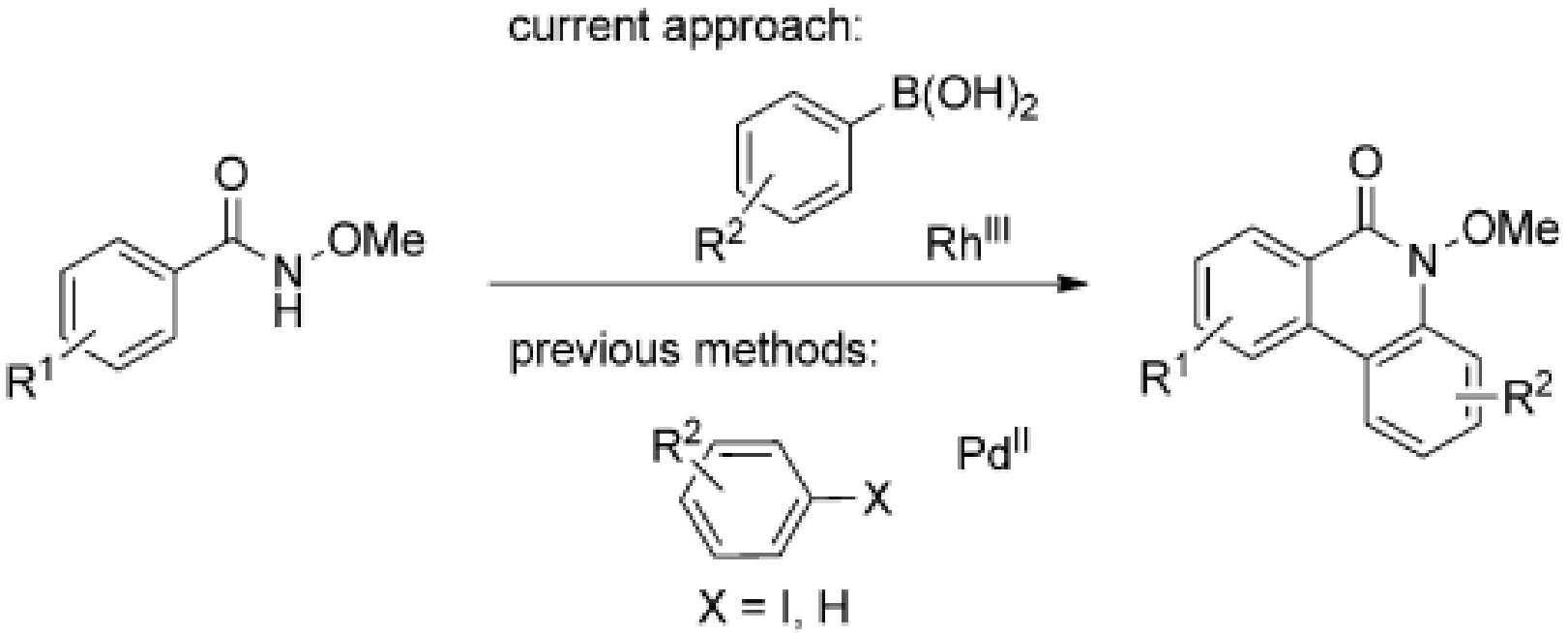
J. Karthikeyan, C.-H. Cheng, *Angew. Chem. Int. Ed*. **2011**, *50*,9880.



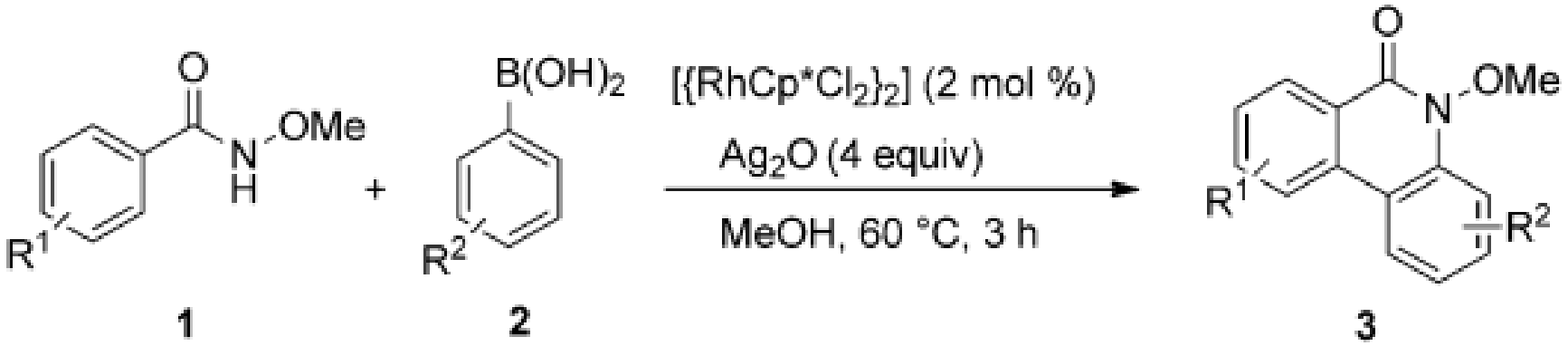
N-methoxybenzamide 1 (0.70 mmol) and an arene 2 (17.5 mmol) in the presence of $Pd(OAc)_2$ (10.0 mol%) and $K_2S_2O_8$ (1.40 mmol) in TFA (140 mmol) at 25^0C for 16 h.


3a
Pd0
K2S2O8
2H+
1a
O
N-OMe
PdII
4
K2S2O8
O
N-OMe
PdII
9
PdII
O
N-OMe
PdIV
2a
H+
H+
H+
H+
O
N-OMe
PdII
8
O
NHOMe
7
O
N-OMe
PdIV
6

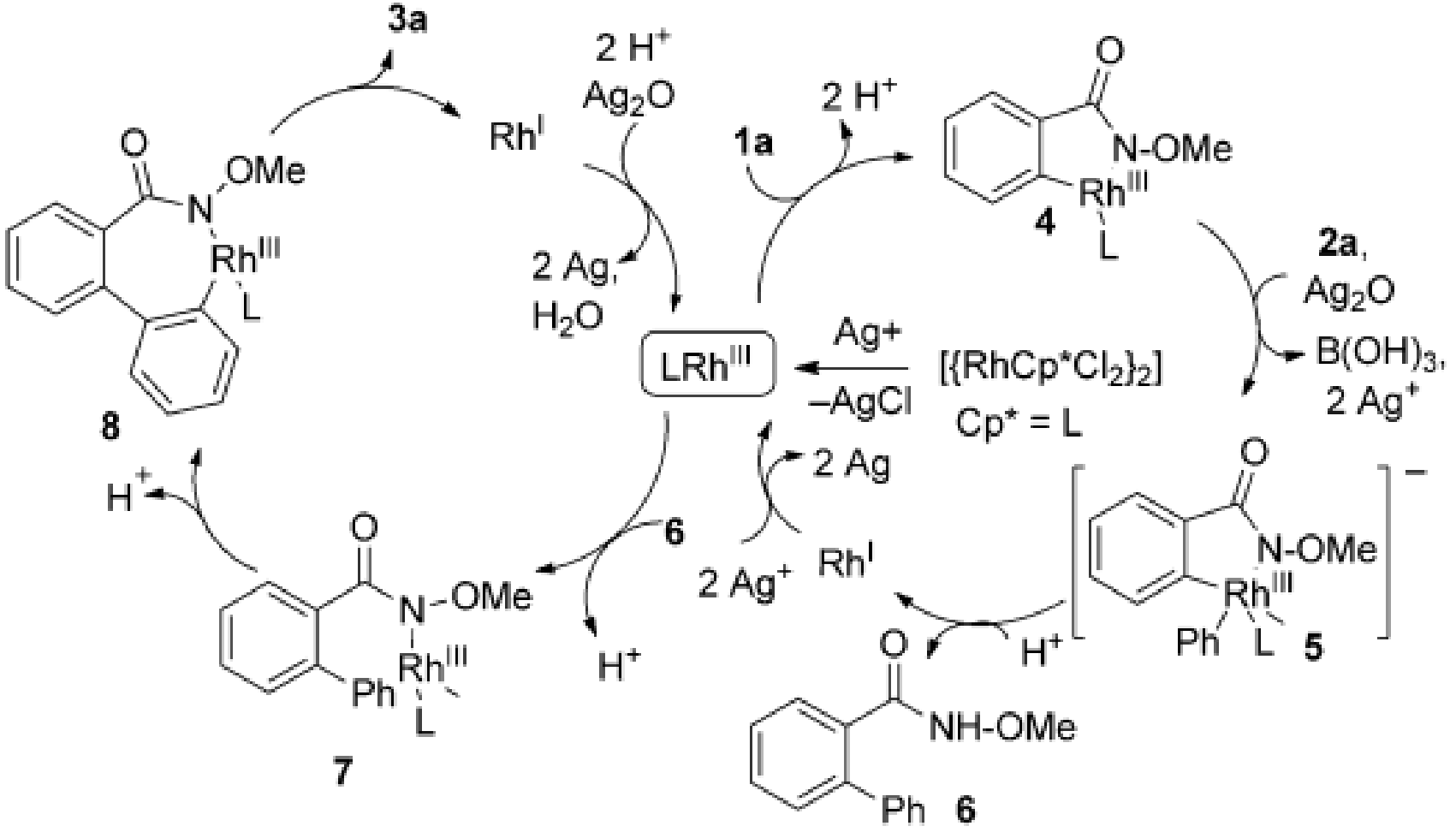
Rhodium(III)-Catalyzed Coupling with Aryl Boronic Acids



J. Karthikeyan, R. Haridharan, C.-H. Cheng, *Angew. Chem. Int. Ed*. **2012**, *51*, 12343.


O
N
H
OMe
R1
B(OH)2
R2
[{RhCp*Cl2}2] (2 mol %)
Ag2O (4 equiv)
MeOH, 60 °C, 3 h
O
N
OMe
R1
R2

1 **2** **3**


3a
2 H+
Ag2O
Rh^I
1a
2 H+
O
N-OMe
Rh^III
L
4
2a,
Ag2O
B(OH)3,
2 Ag+
2 Ag,
H2O
LRh^III
Ag+
–AgCl
[{RhCp*Cl2}2]
Cp* = L
2 Ag
2 Ag+
Rh^I
6
H+
8
H+
O
N-OMe
Rh^III
Ph
L
7
O
N-OMe
Rh^III
Ph
L
5
H+
O
NH-OMe
Ph
6