Recent Advances of Radical Oxidative Cross-Couplings

Lecturer: 胡靖宇
Supervisor: 胡金波研究员

2015.03.30

This seminar is based a recently published account paper:
Liu, C.; Liu, D.; Lei, A. *Acc. Chem. Res.*, **2014**, *47*, 3459–3470.

中国科学院上海有机化学研究所
Shanghai Institute of Organic Chemistry, CAS

Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

中国科学院上海有机化学研究所
Shanghai Institute of Organic Chemistry, CAS

Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

Background

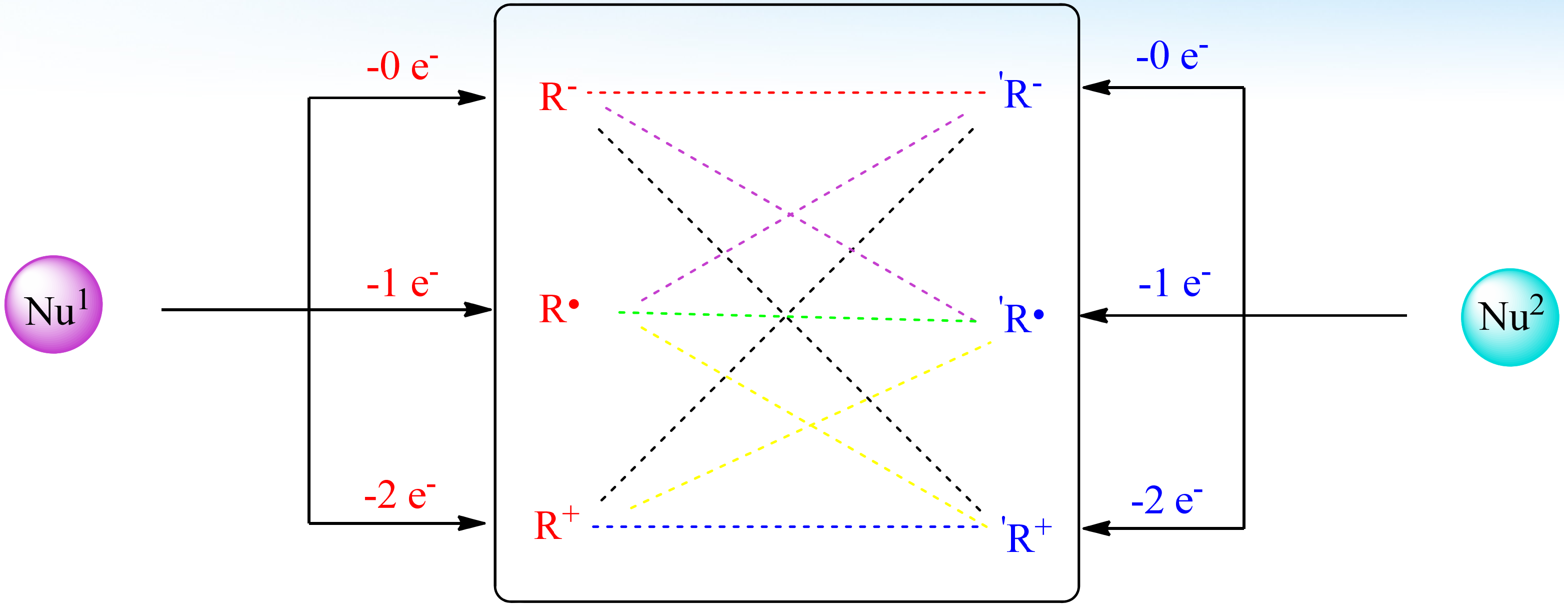
Nucleophile: In chemistry, a nucleophile is a molecule or ion with a lone pair of electrons. It donates both bonding electrons to its reaction partner (the electrophile) when forming a chemical bond.

(1) $\mathrm{Nu} + \mathrm{E} \xrightarrow{\mathrm{TM}} \mathrm{Nu\text{-}E}$ Traditional coupling

(2) $\mathrm{Nu}^1 + \mathrm{Nu}^2 \xrightarrow[\mathrm{[O]}]{\mathrm{TM}} \mathrm{Nu}^1\text{-}\mathrm{Nu}^2$ Oxidative coupling

McNaught, A. D.; Wilkinson, A. *Compendium of chemical terminology: IUPAC recommend-dations*, 2nd ed.; Blackwell Science: Oxford, England; Malden, MA, USA, **1997.**

Background



||

R^{-} + $'R^{-}$	R^{-} + $'R\cdot$	R^{-} + $'R^{+}$
$R\cdot$ + $'R^{-}$	$R\cdot$ + $'R\cdot$	$R\cdot$ + $'R^{+}$
R^{+} + $'R^{-}$	R^{+} + $'R\cdot$	R^{+} + $'R^{+}$

Background

4 models for radical oxidative cross-coupling:

$$Nu^1 + Nu^2 \xrightarrow[-2e]{\text{Oxidant}} Nu^1\text{-}Nu^2$$

Model **I**	Model **II**	Model **III**	Model **IV**
$R^- + {}'R\cdot$	$R^+ + {}'R^-$	$R\cdot + {}'R\cdot$	$R\cdot + {}'R^+$

Model **I** $\quad Nu^1 + \cdot Nu^2 \longrightarrow [Nu^1\text{-}Nu^2]^{\bullet} \xrightarrow{-e} Nu^1\text{-}Nu^2$

Model **II** $\quad Nu^1 + \cdot Nu^2 \xrightarrow{-e} Nu^1 + [Nu^2]^+ \longrightarrow Nu^1\text{-}Nu^2$

Model **III** $\quad Nu^1 + \cdot Nu^2 \xrightarrow{-e} \cdot Nu^1 + \cdot Nu^2 \longrightarrow Nu^1\text{-}Nu^2$

Model **IV** $\quad [Nu^1]^+ + \cdot Nu^2 \longrightarrow [Nu^1\text{-}Nu^2]^{\bullet +} \xrightarrow{+e} Nu^1\text{-}Nu^2$

Liu, C.; Liu, D.; Lei, A. *Acc. Chem. Res.* **2014**, *47(12)*, 3459.

Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

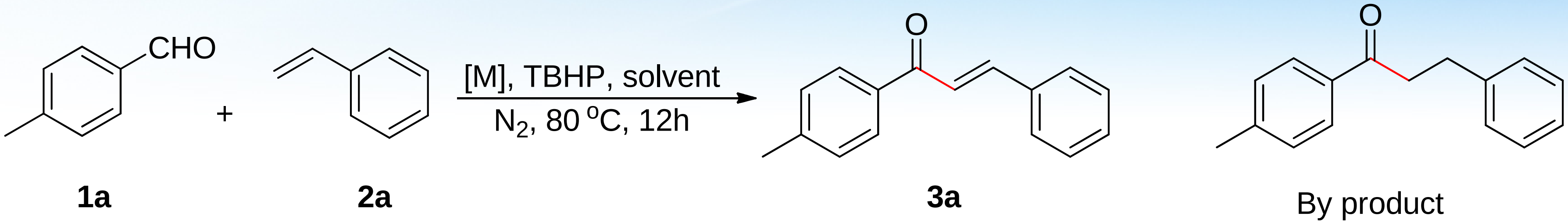
2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

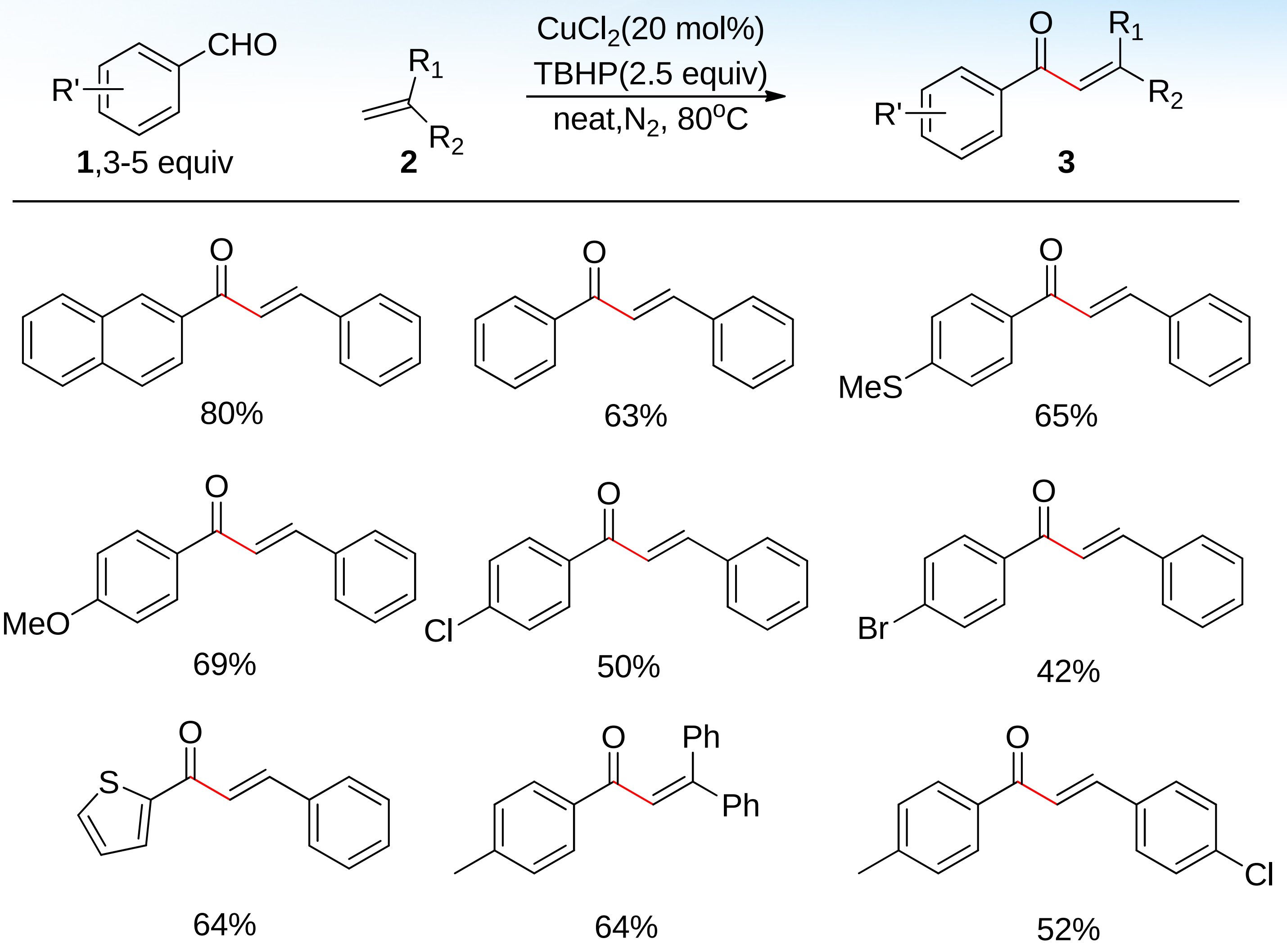
Model I in Radical Oxidative Cross-Couplings



Entry	[M]	Solvent	Yield(3a)[%][b]
1	[Ni(acac)$_2$]	benzene	--
2	[Ni(PPh$_3$)$_4$]	benzene	--
3	$CoCl_2$	benzene	--
4	$FeCl_2$	benzene	--
5	$CuCl_2$	benzene	28
6	$CuCl_2$	dioxane	--
7	$CuCl_2$	DCE	--
8	$CuCl_2$	benzene	38[c]
9	$CuCl_2$	--	76[d]

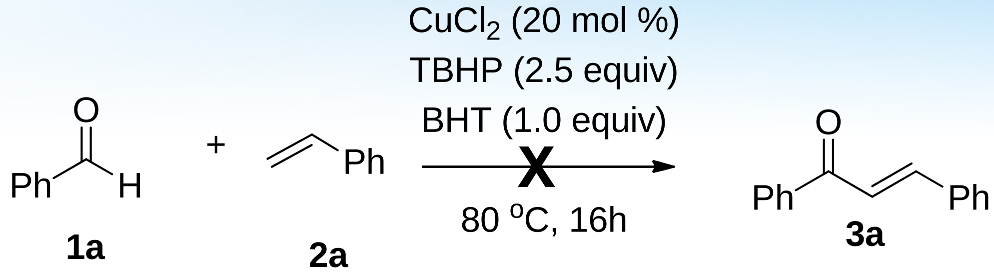
Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Angew. Chem. Int. Ed.* **2013**, *52*. 2256.

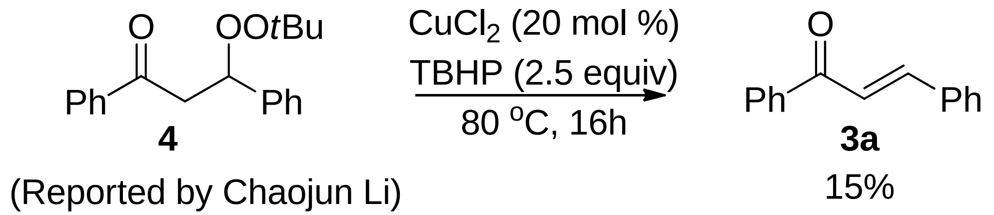
Model I in Radical Oxidative Cross-Couplings

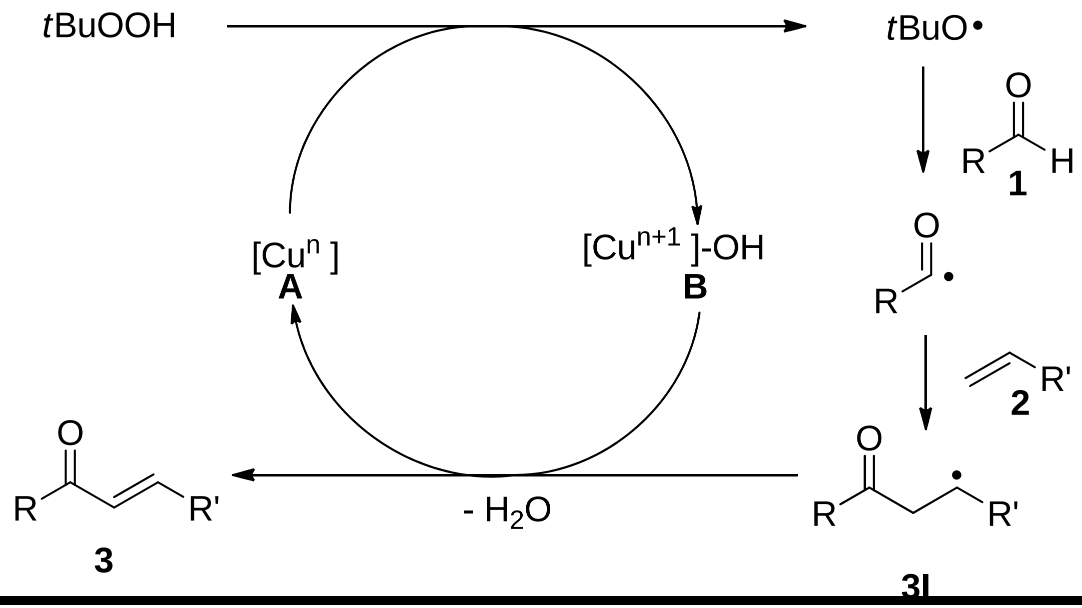


Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Angew. Chem. Int. Ed.* **2013**, *52*. 2256.

Model I in Radical Oxidative Cross-Couplings







Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

2.2 Modle II: Cation and Nucleophile

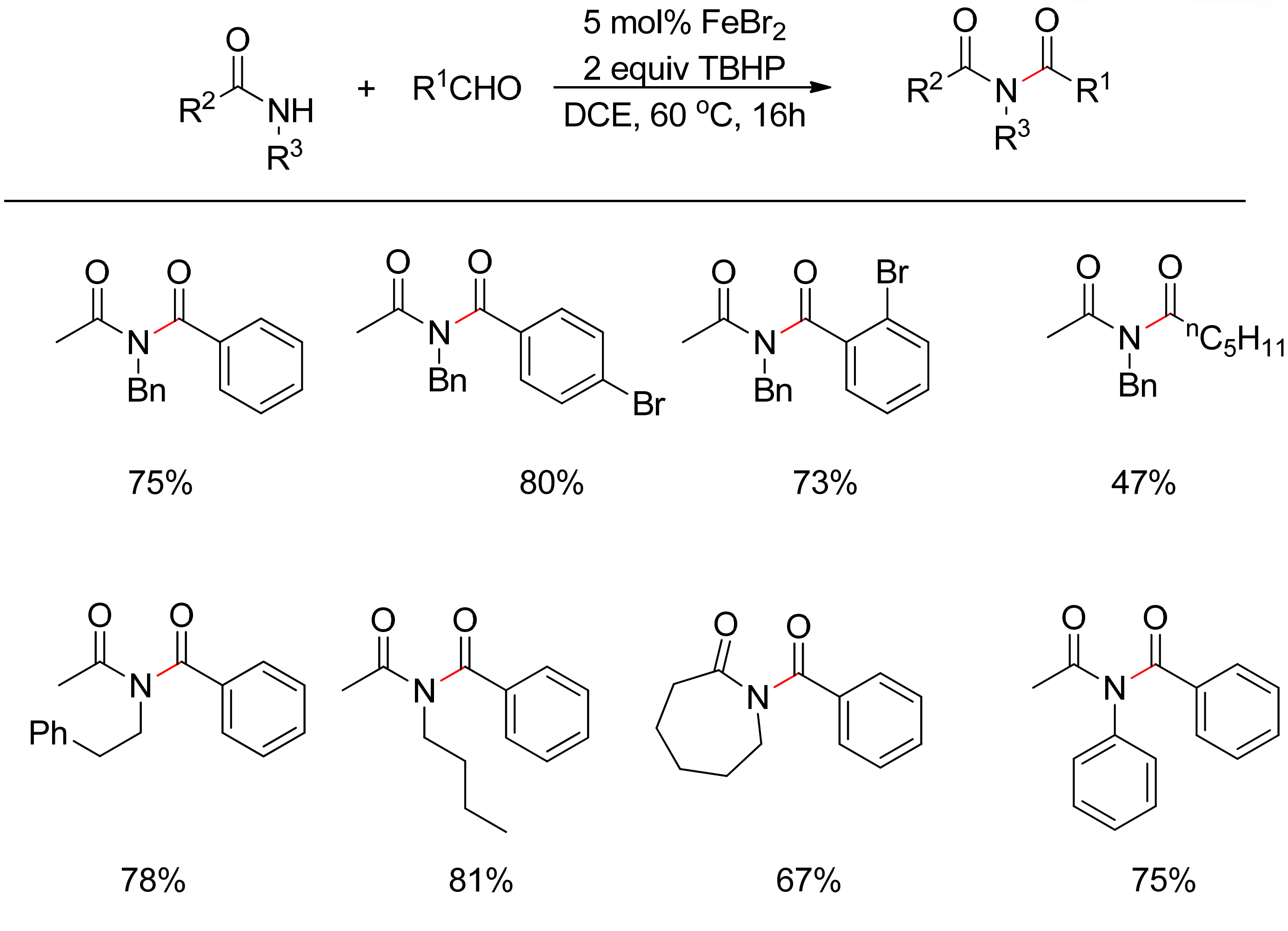
2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

中国科学院上海有机化学研究所
Shanghai Institute of Organic Chemistry, CAS

Model II in Radical Oxidative Cross-Couplings

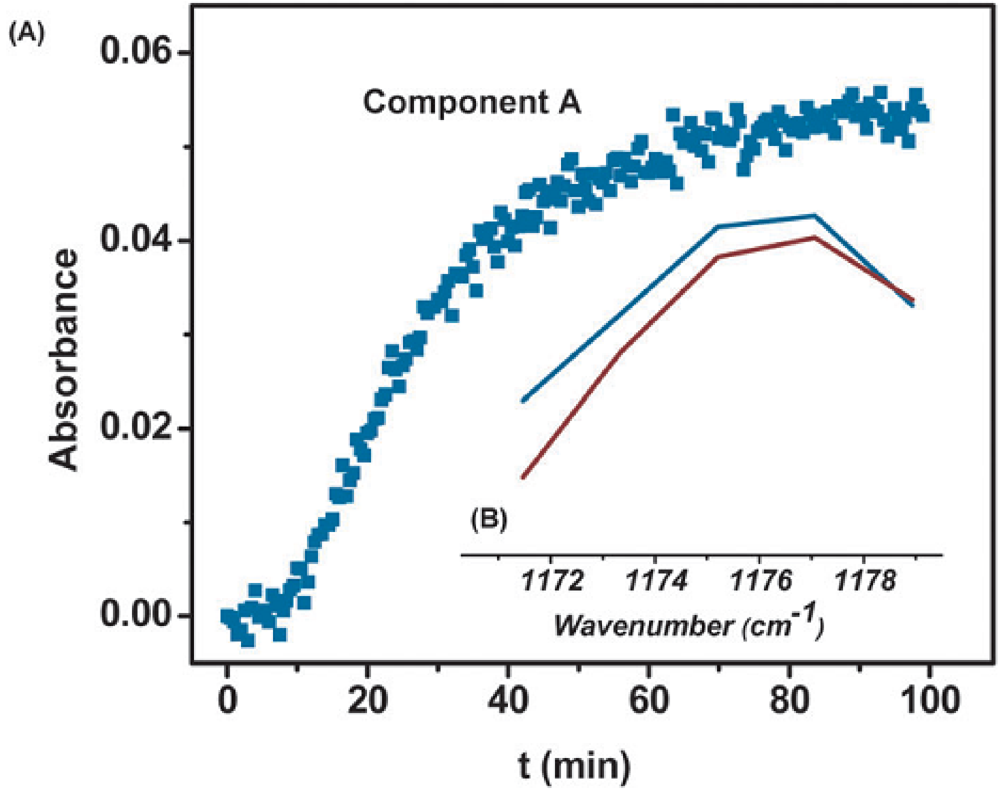


Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Chem. Commun.* **2014**, *50*, 4736.

Model II in Radical Oxidative Cross-Couplings

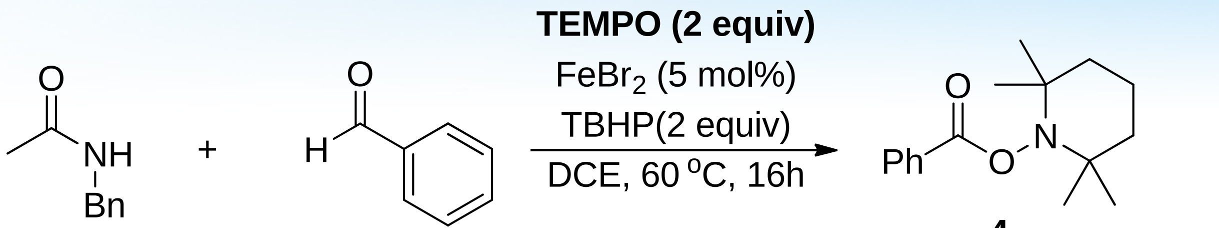
$$\underset{5}{\mathrm{PhCHO}} \;+\; \underset{1}{\mathrm{FeCl_2}} \xrightarrow[\text{DCE, 60 }^{o}\text{C}]{\text{3 equiv TBHP}} \mathrm{PhCOCl} \qquad (2)$$

5 : 1



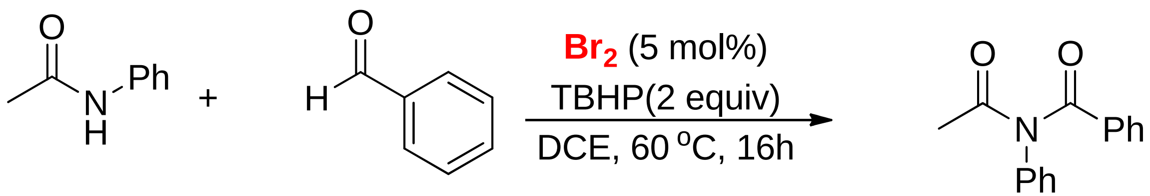
(A) Kinetic profile of the reaction. (B) IR spectra of component A (blue curve) and the authentic sample of benzoyl chloride(red curve)

Model II in Radical Oxidative Cross-Couplings



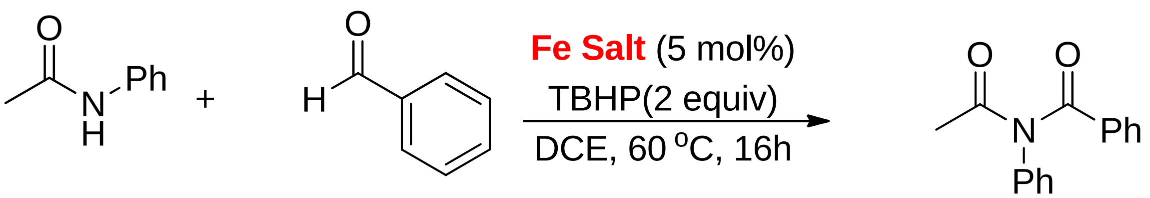
1a 2a 4 (2)

78%(base on TEMPO)



1b 2a 3ba (3)

7%



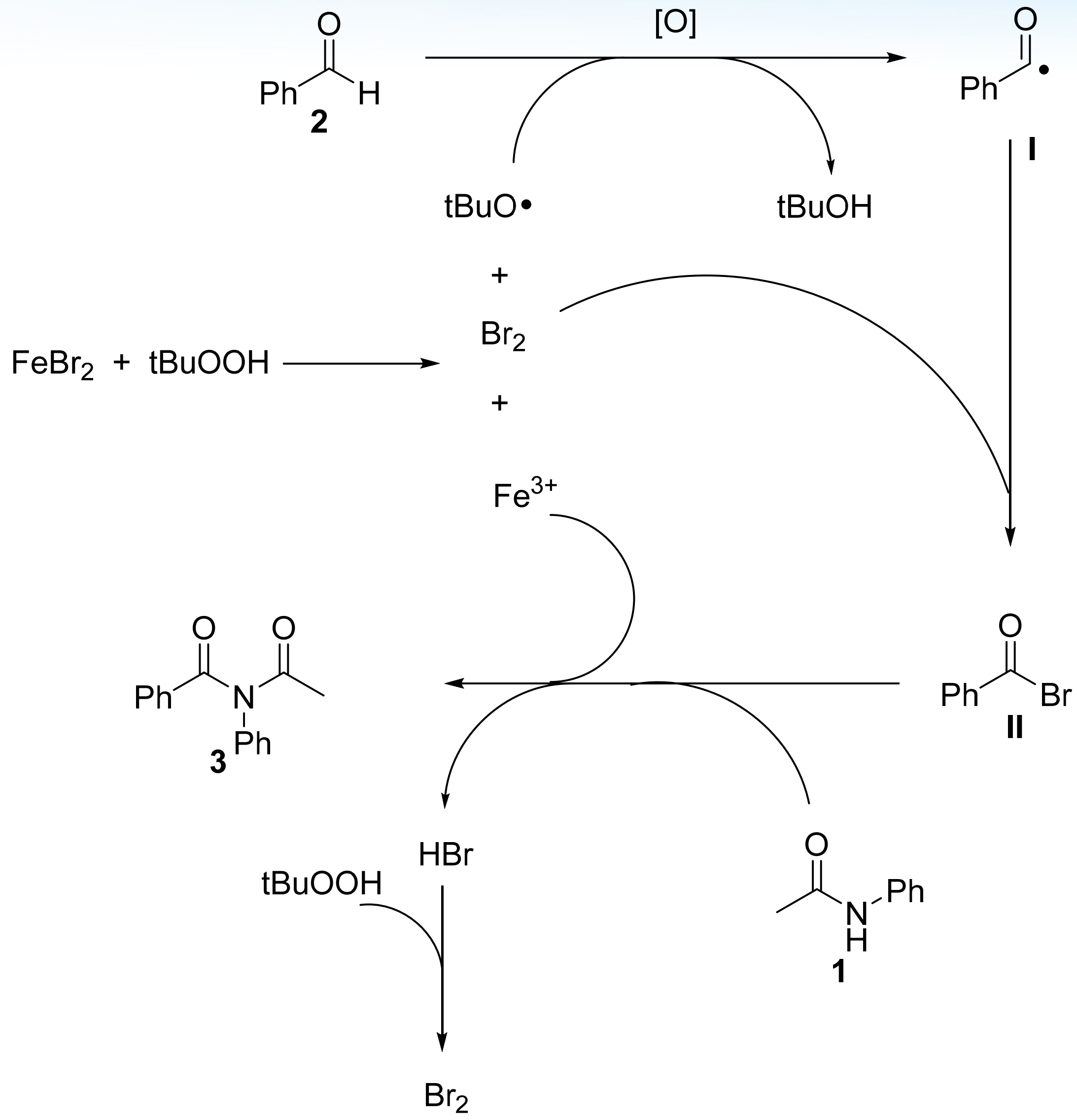
1b 2a 3ba (4)

Fe salt: $FeBr_2$, 89%

$FeBr_3$, 88%

Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Chem. Commun.* **2014**, *50*, 4736.

Model II in Radical Oxidative Cross-Couplings



Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

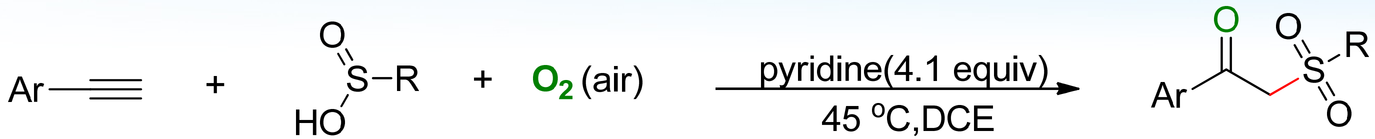
2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

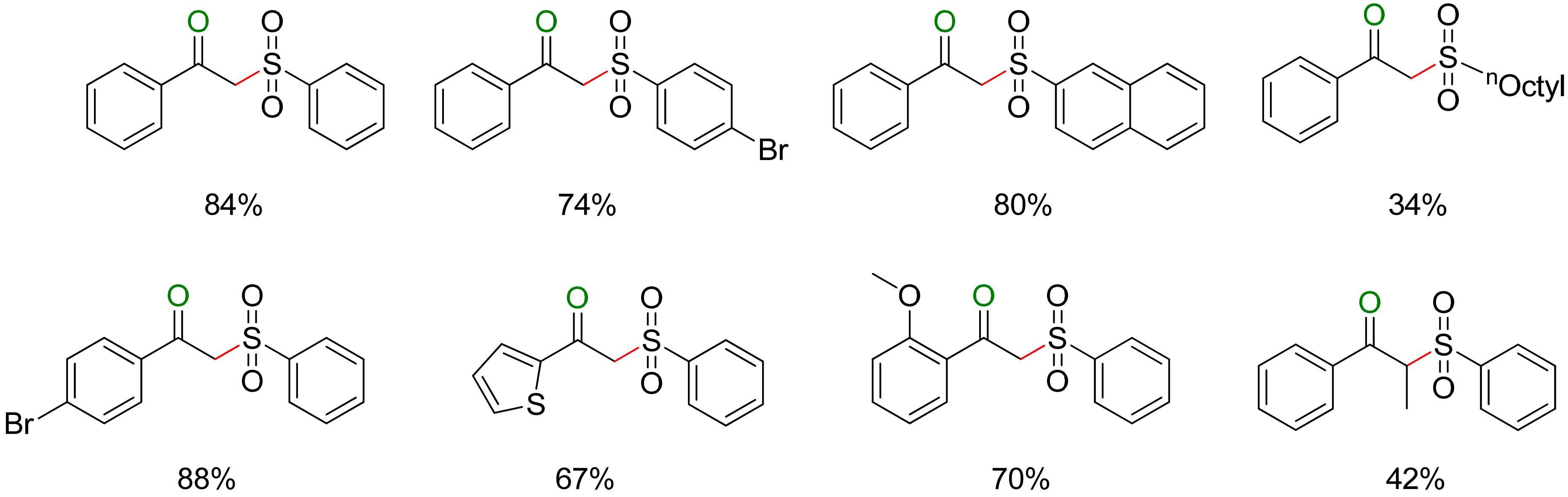
2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

Model III in Radical Oxidative Cross-Couplings

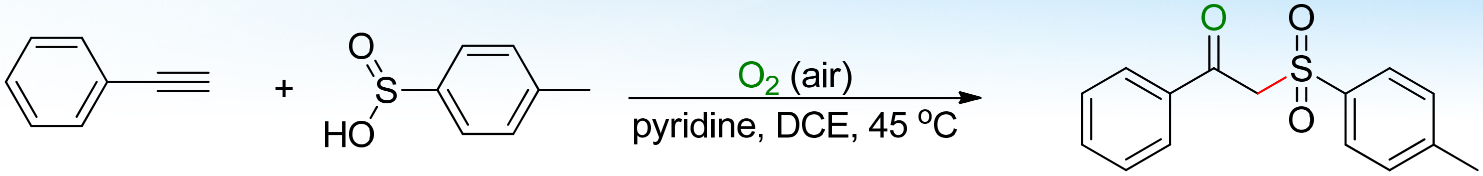


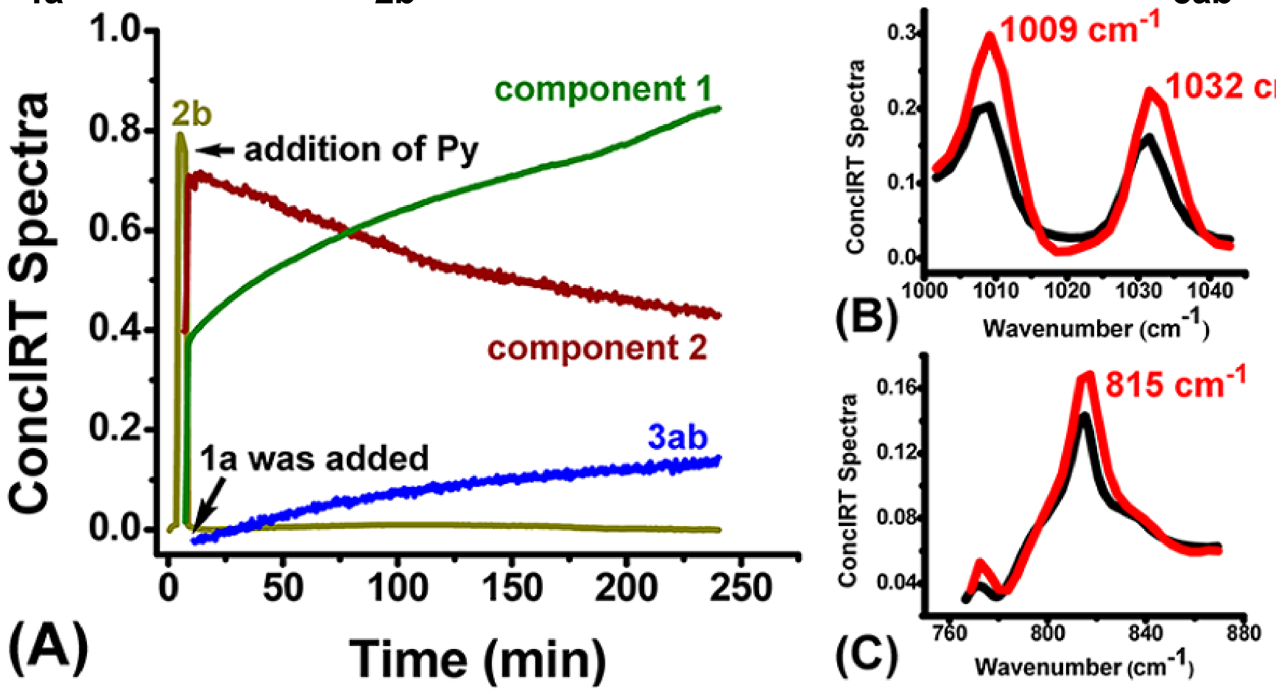
1   **2**(5 equiv)   **3**



Lu, Q.; Zhang, J.; Zhao, G.; Qi, Y.; Wang, H.; Lei, A. *J. Am. Chem. Soc.* **2013**, *135*, 11481.

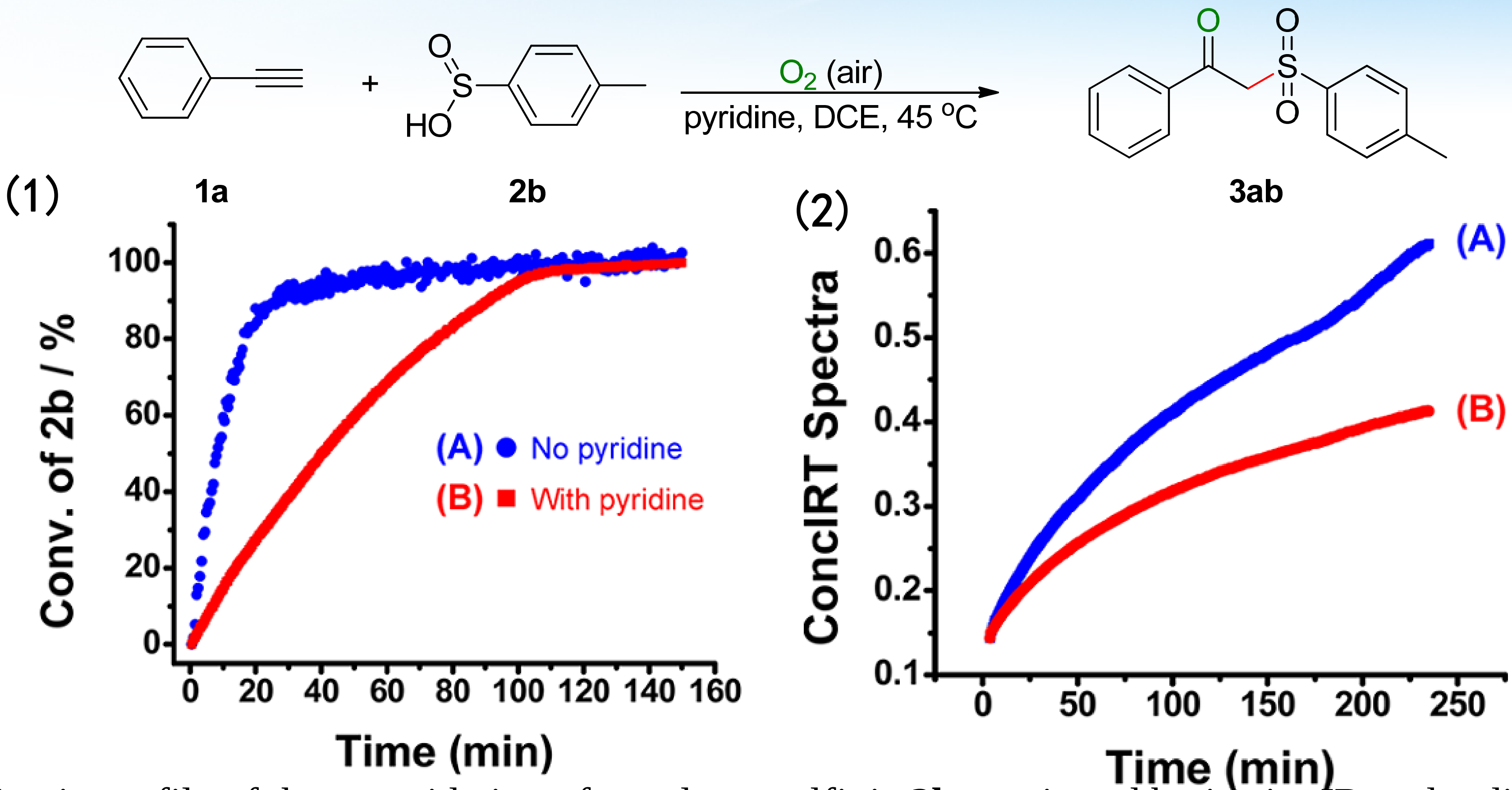
Model III in Radical Oxidative Cross-Couplings





(A) The 2D-Kinetic profile of the reaction of p-toluenesulfinic **2b** (2.0 mmol) and pyridine (1.64 mmol), and **1a** (0.4 mmol) added to $CHCl_3$ (4.0 mL) at 45 °C in succession; the reaction was monitored by operando IR. (B) ConcIRT spectra of the new component **1** (black curve) and authentic sample **(pyridinium p-toluenesulfonate**, red curve). (C) ConcIRT spectra of the new component **2** (black curve) and authentic sample (**pyridium p-toluenesulfinate**, red curve)

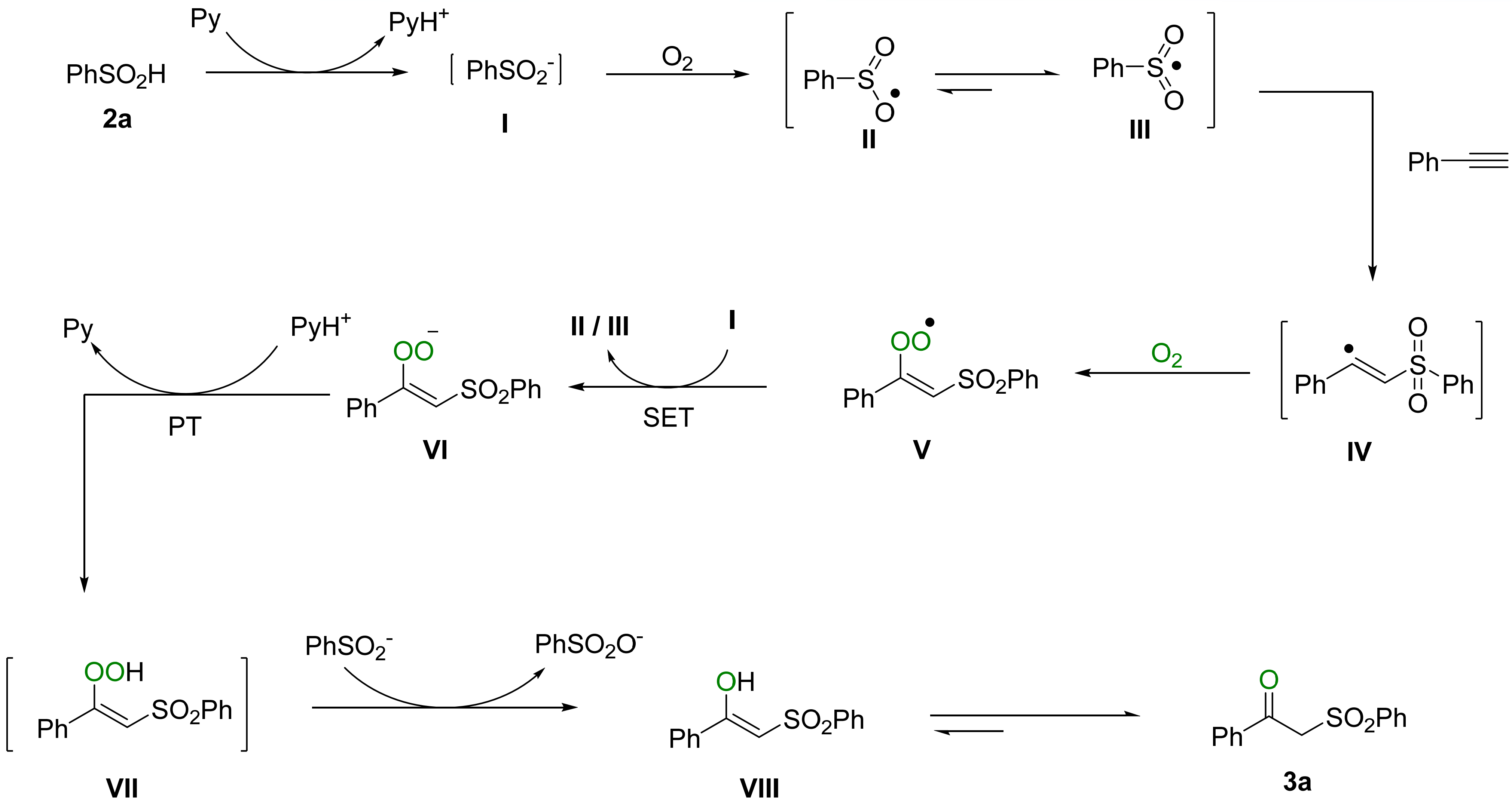
Model III in Radical Oxidative Cross-Couplings



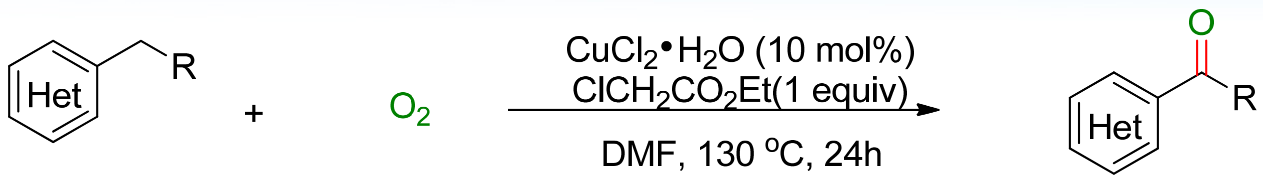
(1) Kinetic profile of the autoxidation of p-toluenesulfinic **2b** monitored by in situ IR under different conditions : (A) **2b**(2.0 mmol) in $CHCl_3$ (4.0 mL) at 45 °C, monitored by pyridinium *p*-toluene sulfonate; (B) **2b**(2.0 mmol), pyridine (0.41 mmol) in $CHCl_3$ (4.0 mL) at 45 °C, monitored by pyridinium *p*-toluenesulfonate.

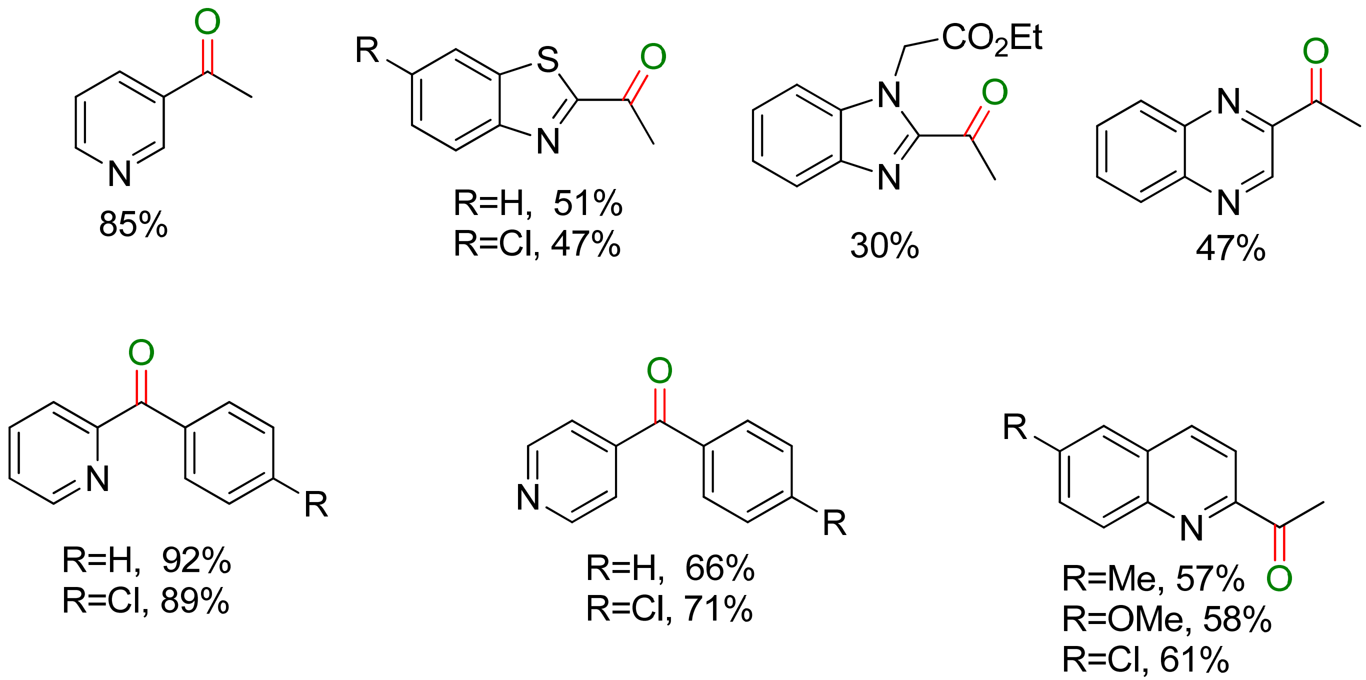
(2) Kinetic profiles of the pyridinium *p*-toluenesulfonate monitored by in situ IR under different conditions: (A) p-toluenesulfinic **2b** (2.0 mmol) and pyridine (1.64 mmol), and **1a** (0.4 mmol) in $CHCl_3$ (4.0 mL) at 45 °C; (B) autoxidation of **2b** under the same conditions without **1a**.

Model III in Radical Oxidative Cross-Couplings



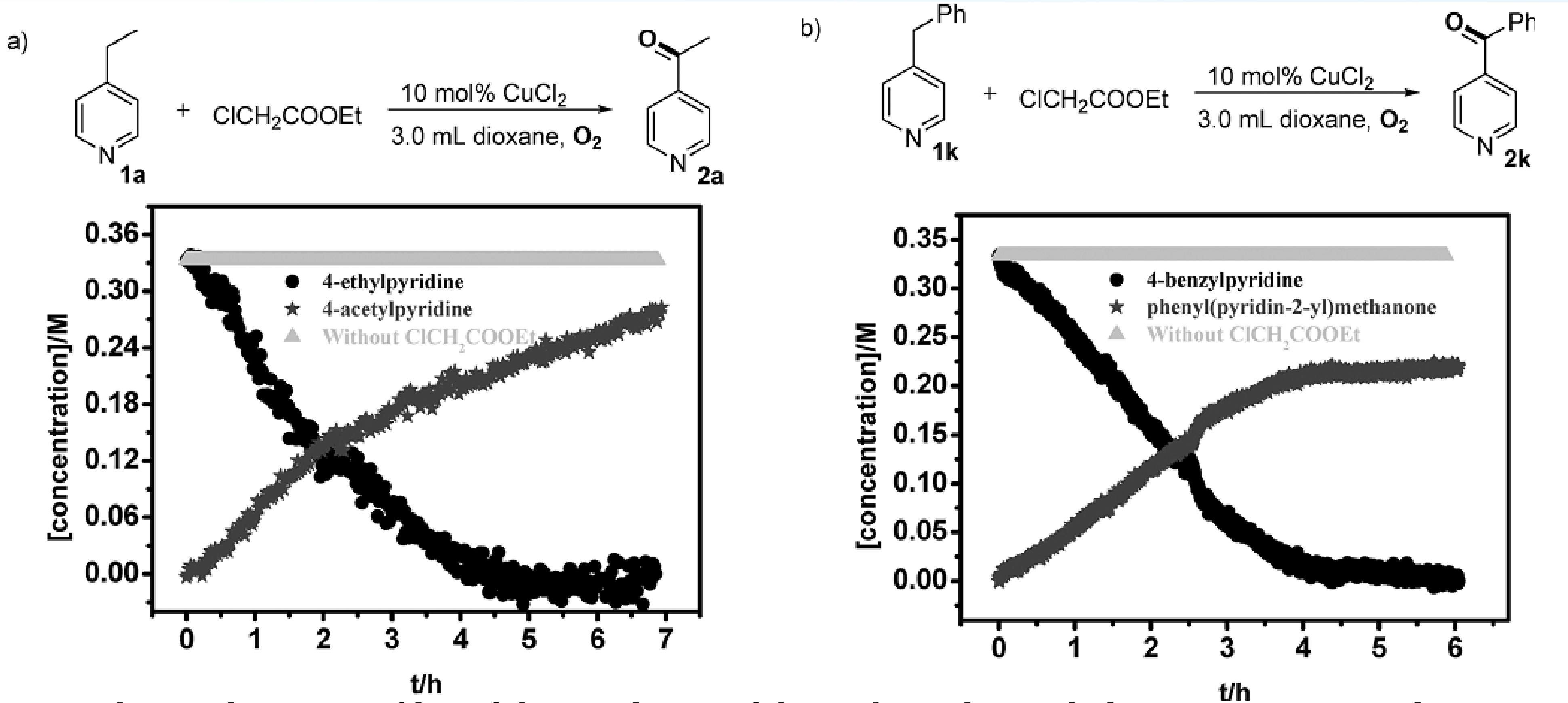
Model III in Radical Oxidative Cross-Couplings





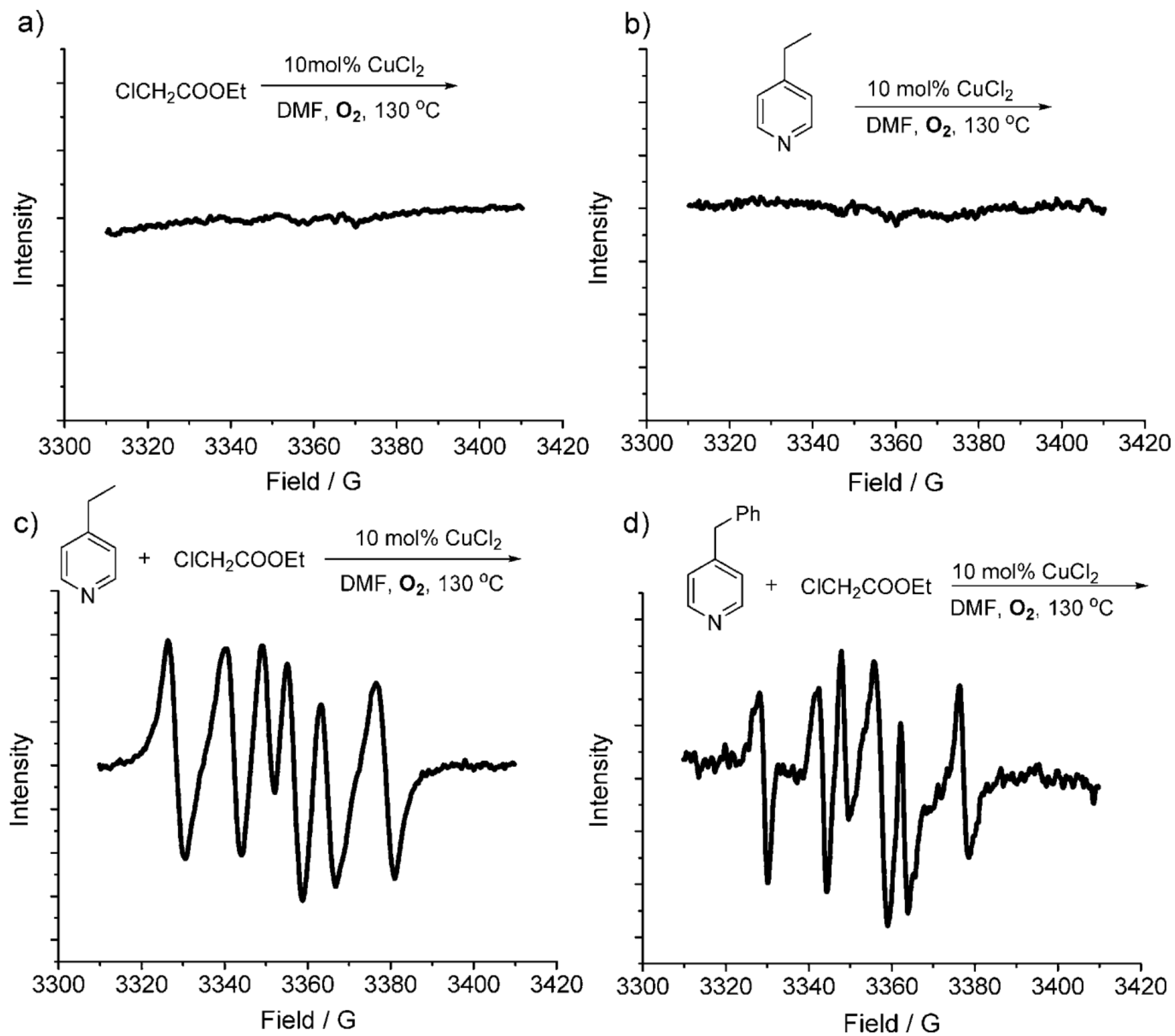
Liu, J.; Zhang, X.; Yi, Hong.; Liu, C.; Liu, R.; Zhang, H.; Zhuo, K.; Lei, A. *Angew. Chem. Int. Ed.* **2014**, ASAP.

Model III in Radical Oxidative Cross-Couplings



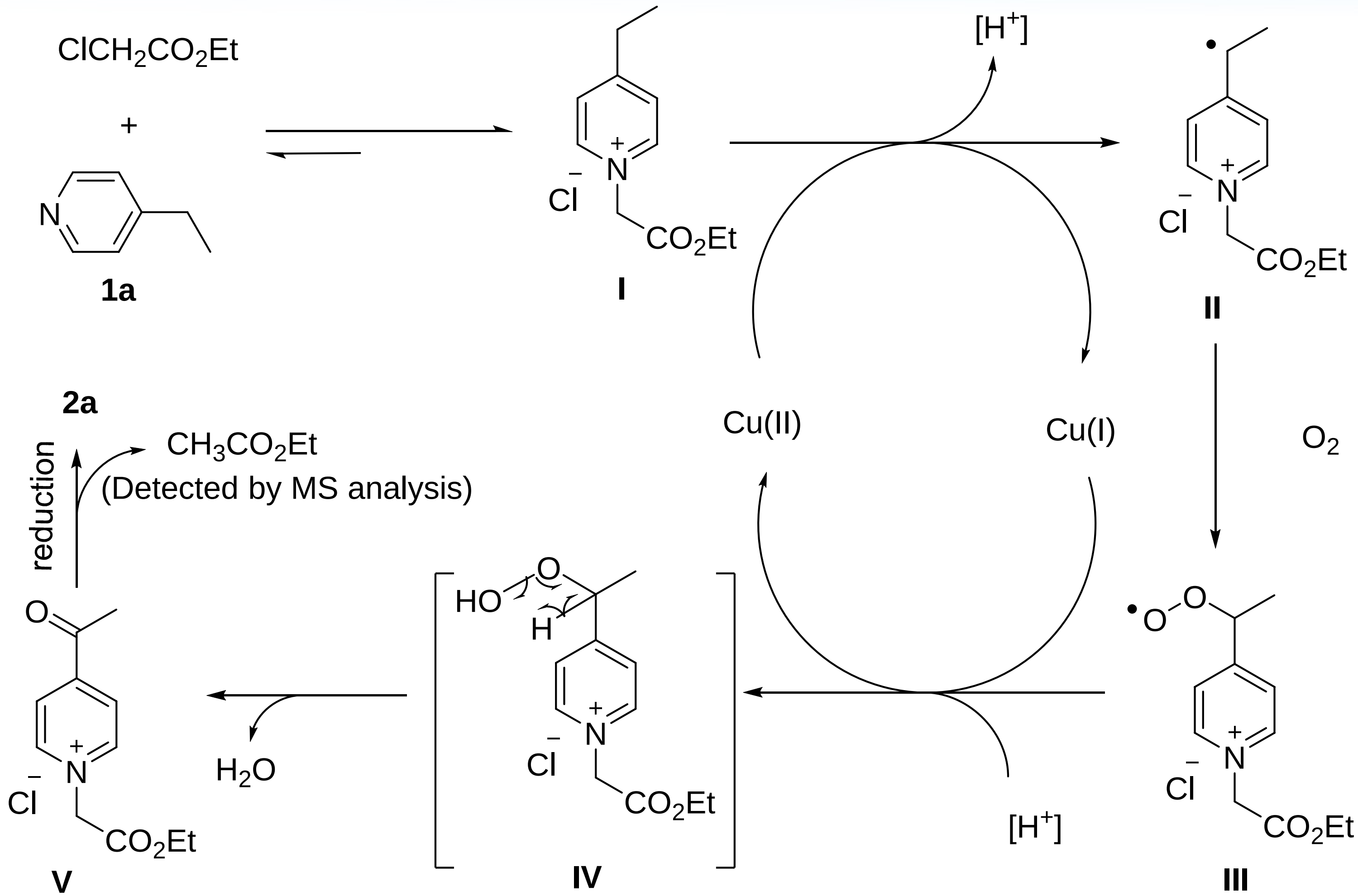
The 2D kinetic profiles of the oxidation of heterobenzylic methylenes. Reaction conditions: (a) 4-ethylpyridine (1.0 mmol), ethyl chloroacetate (1.0 mmol), and $CuCl_2$ $2H_2O$(0.10 mmol) successively added to 1,4-dioxane (3.0 mL) at 100 ^oC. b) 4-Benzylpyridine(1.0 mmol), ethyl chloroacetate(1.0 mmol) and $CuCl_2$ $2H_2O$(0.10 mmol) successively added to 1,4-dioxane (3.0 mL) at 100 ^{o}

Model III in Radical Oxidative Cross-Couplings



Electron paramagnetic resonance(EPR) spectra (X band, 9.4 GHz, room temperature)

Model III in Radical Oxidative Cross-Couplings



Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

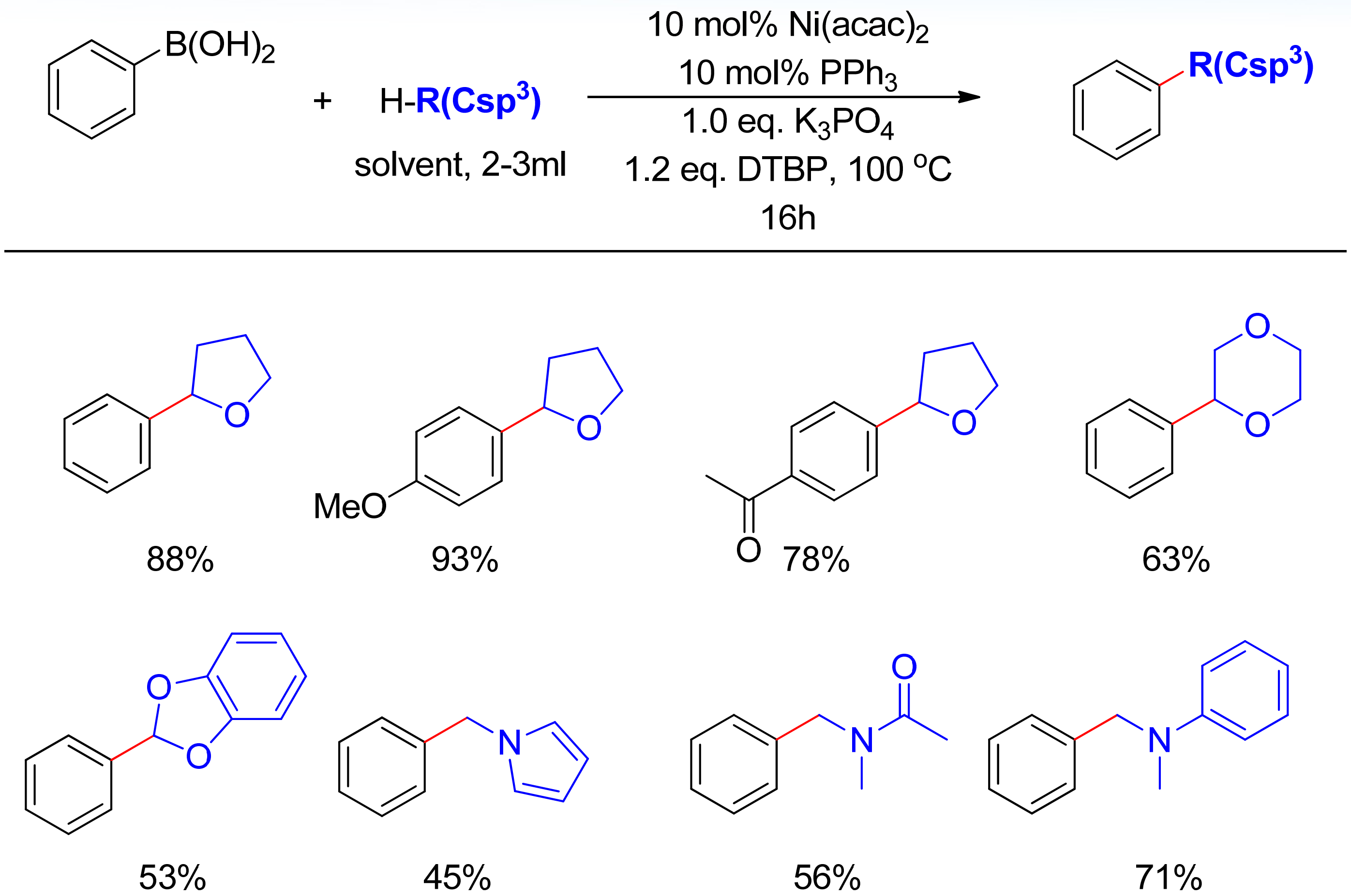
2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

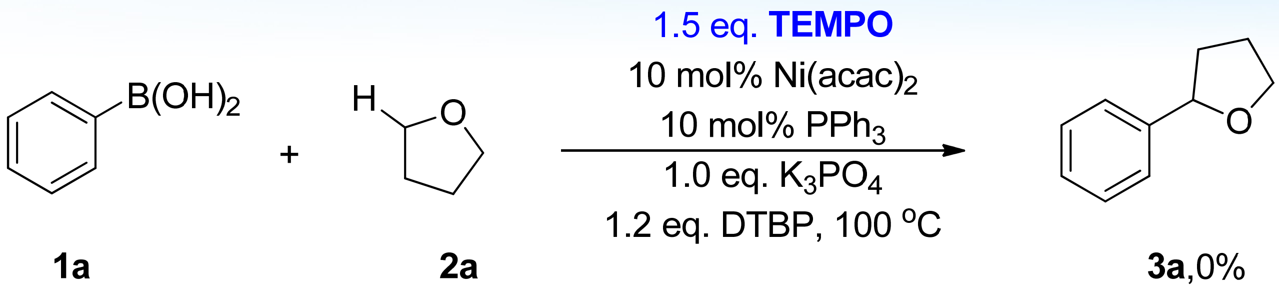
3. Summary and Outlooks

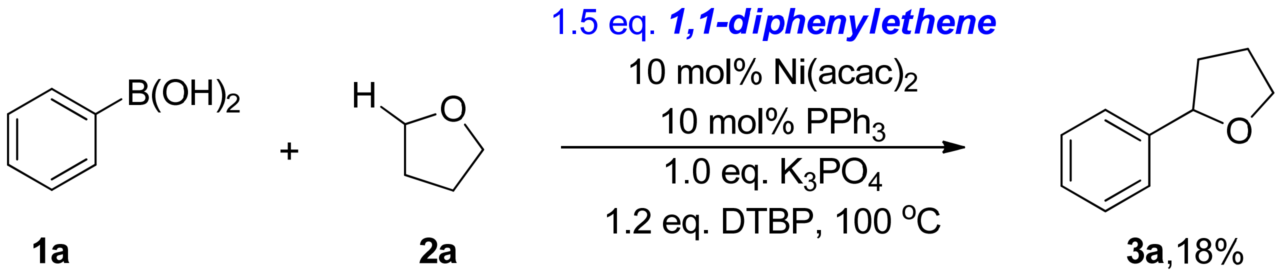
Model IV in Radical Oxidative Cross-Couplings

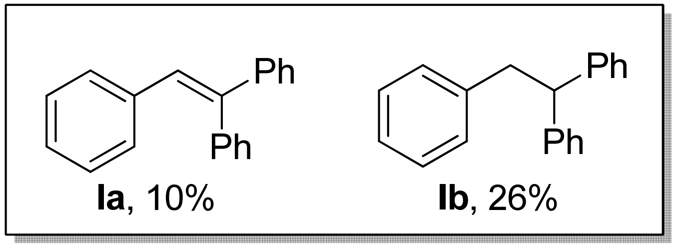


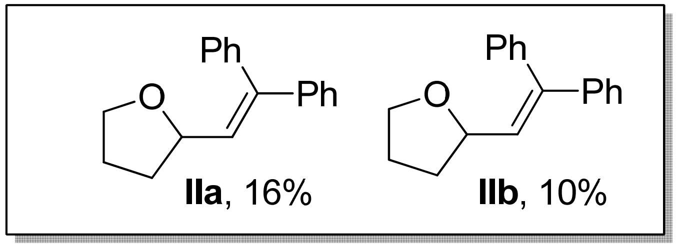
Dong L.; Li, C.; Li, H.; Lei, A. *Angew. Chem. Int. Ed.* **2013** *52*. 4453.

Model IV in Radical Oxidative Cross-Couplings



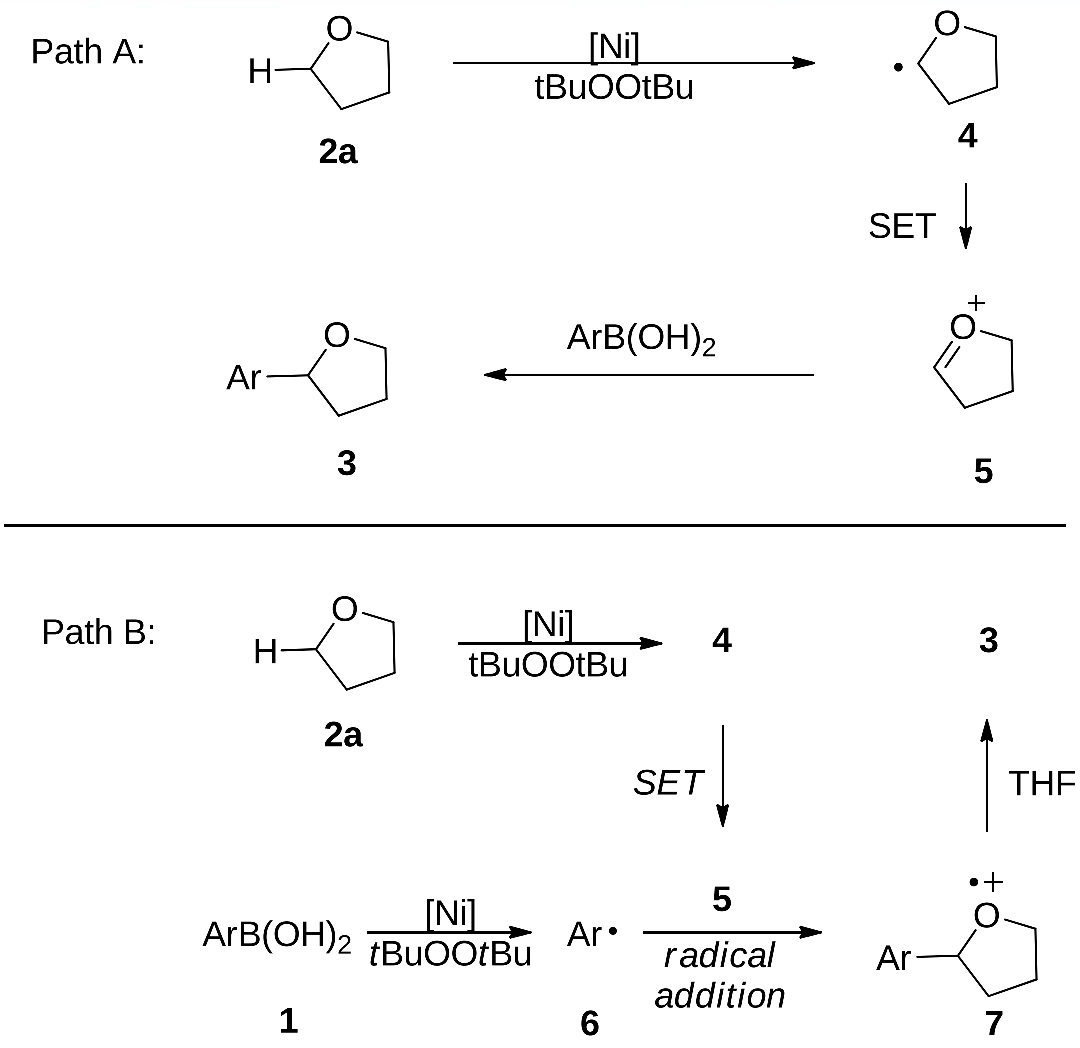






Dong L.; Li, C.; Li, H.; Lei, A. *Angew. Chem. Int. Ed.* **2013** *52*. 4453.

Model IV in Radical Oxidative Cross-Couplings



Contents

1. Background

2. Models for radical oxidative cross-coupling

2.1 Modle I: Radical and Nucleophile

2.2 Modle II: Cation and Nucleophile

2.3 Modle III: Radical and Radical

2.4 Modle IV: Radical and Cation

3. Summary and Outlooks

Summary and Outlook

Along with the development of transition metal catalyzed oxidative cross-couplings, especially of those with no noble transition metal catalysis system, the radical process becomes dominant in this re-serch area. There are still many unexplored methods and unknown insightful mechanisms left. Therefore, chances and challenges still remain, such as finding milder reaction conditions and proper ways to control the reactivity and chemoselectivity of radical species.


Thank
you