Literature Report

Gold-Catalyzed C-C Coupling Reactions

Reportor: Xin-Cheng Lin

Supervisor: Prof. Zhang-Jie Shi

2021-04-09

Background

- Background
- Gold-Catalyzed C-C Coupling Reactions
  - Oxidants-Assisted Coupling Reactions
  - Photo-Assisted Coupling Reactions
  - Dinuclear Gold-Catalyzed Coupling Reactions
- Summary

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Background

- **The source of gold**

- **The role of gold in the life**

- **The role of gold in the chemistry**

Alloy

Catalysts

Background

Relativistic Effects

79 Au
Gold
$5d^{10}6s^1$

$m = m_0/[1-(v/c)^2]^{1/2}$

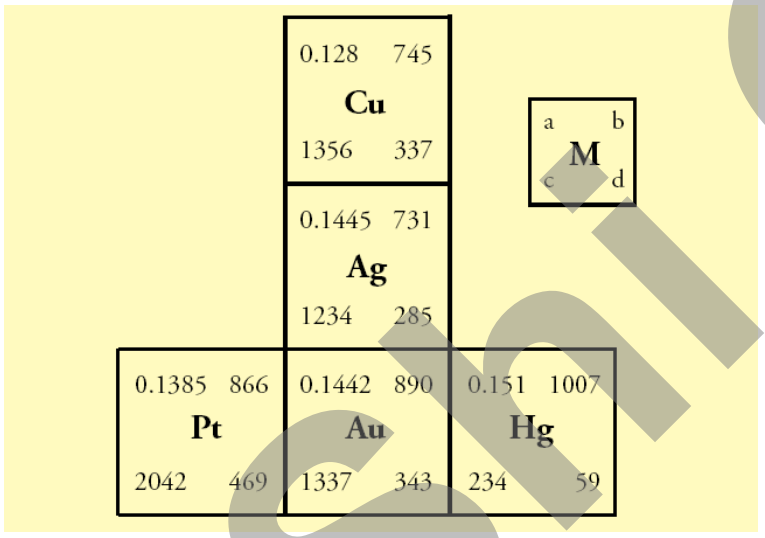
Au 1s electron as an example

$$\frac{|v|}{c} \approx \frac{79}{137} = 0.58$$

$$m = 1.23\ m_0$$

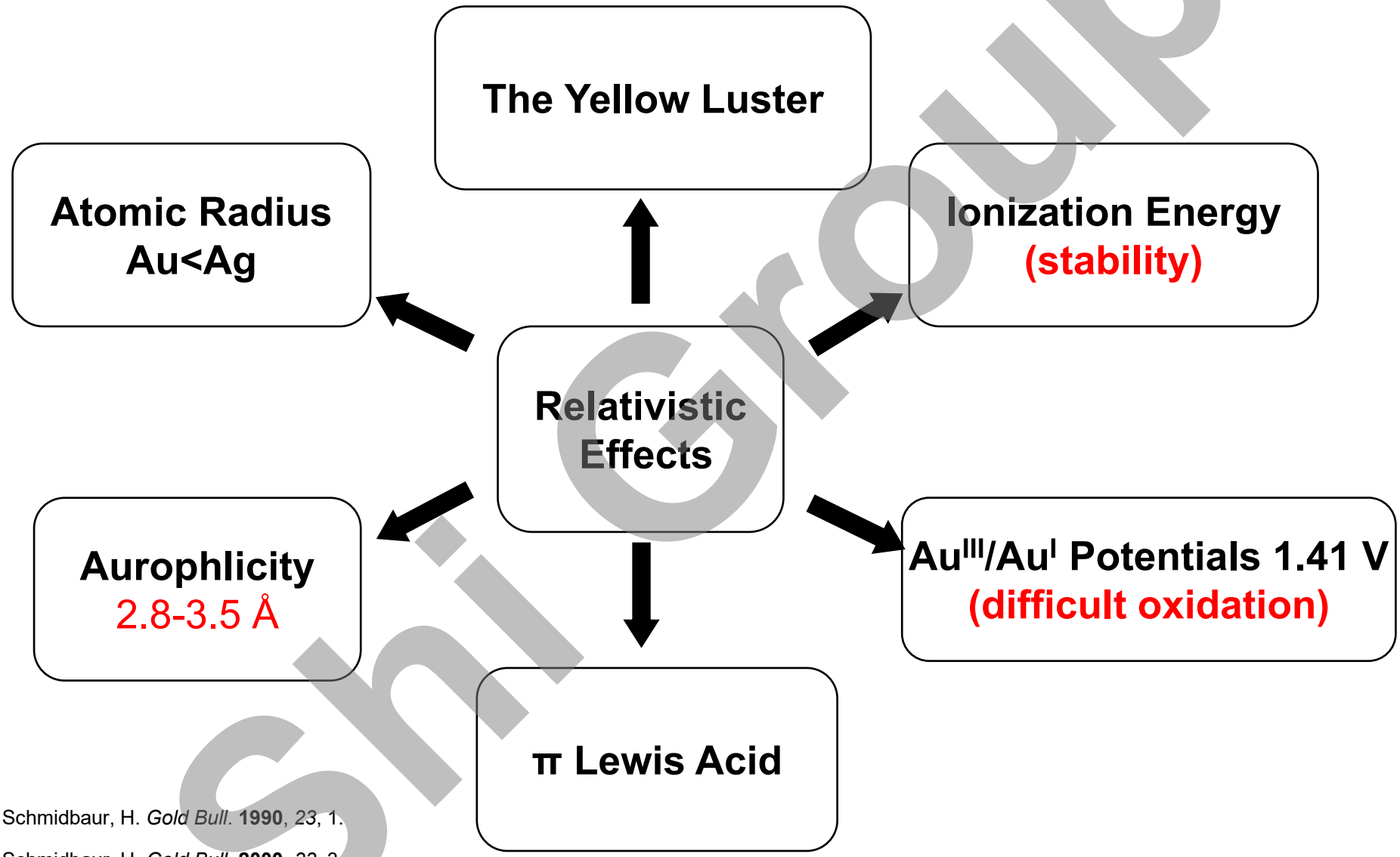
$$r_n = \alpha_0 \frac{n^2}{m_0}$$

$$\frac{r_{1s(R)}}{r_{1s(NR)}} = 0.81$$



- Contraction and stabilization of 6s and 6p orbitals
- Expansion and instability of 5d and 4f orbitals

Background



Schmidbaur, H. *Gold Bull.* **1990**, *23*, 1.

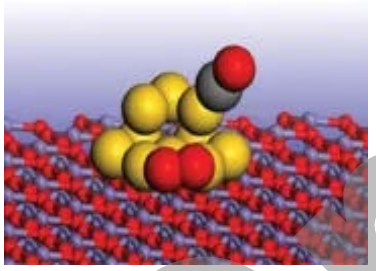
Schmidbaur, H. *Gold Bull.* **2000**, *33*, 3.

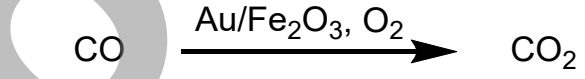
Blinder, S. M. et al. *J. Chem. Educ.* **2011**, *88,* 71.

Background

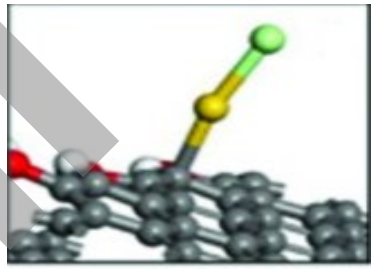
Nano Au as Catalysts

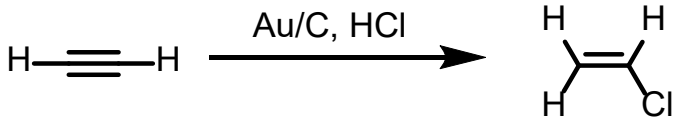
Masatake Haruta





Graham J. Hutchings



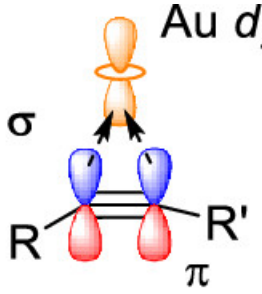


Haruta, M. et al. *J. Catal.* **1989**, *115*, 301.

Hutchings, G. J. et al. *J. Catal*. **1985**, *96*, 292.

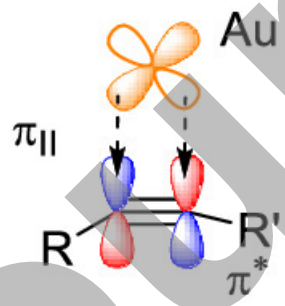
Background

Au as π Lewis Acid



237 kJ/mol

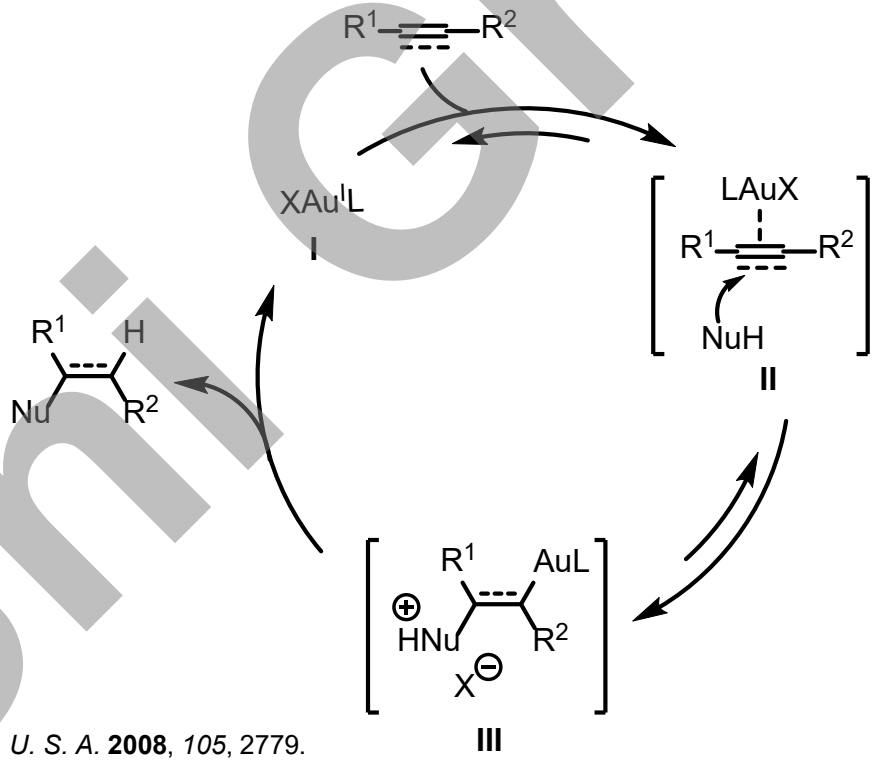
σ donor interaction



56 kJ/mol

π acceptor interaction

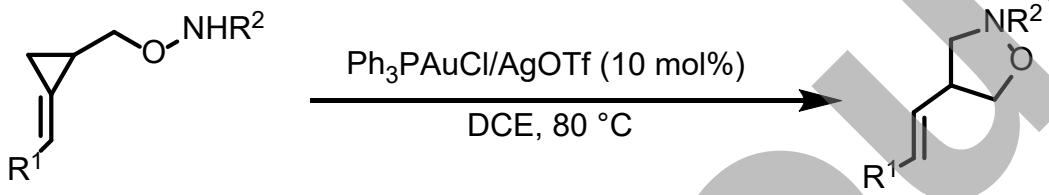
Simplified cationic gold catalytic cycle



Toste, F. D. et al. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 2779.

Background

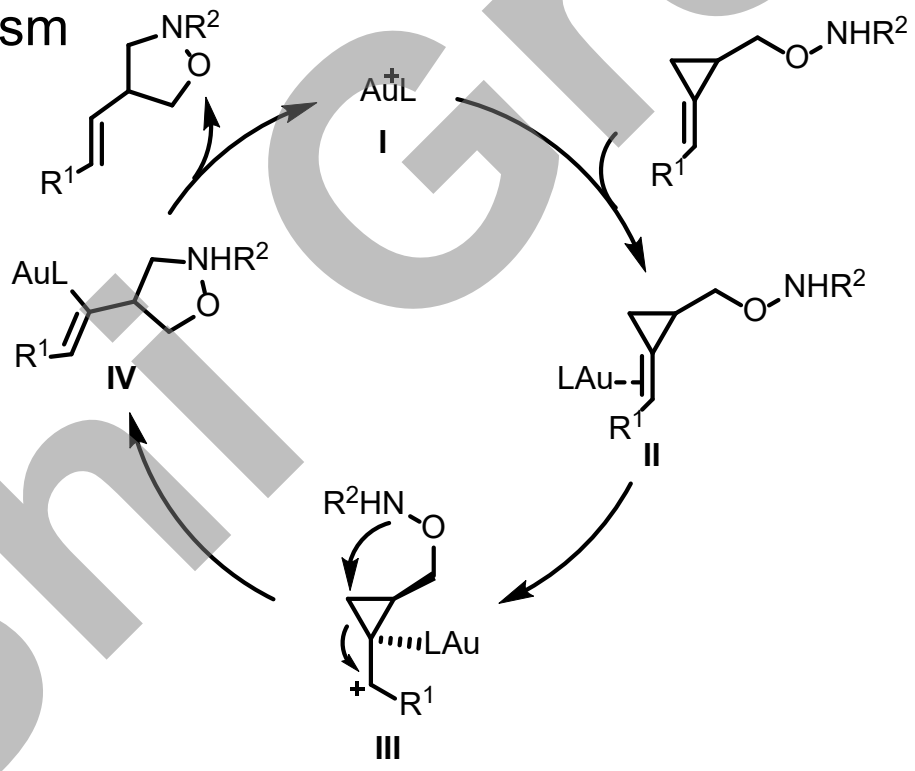
Au^{I}-Catalyzed intramolecular hydroamination



R^1 = aryl
R^2 = Ts, Ns

50-95% yield

Proposed mechanism



Shi, M. et al. *Org. Biomol. Chem.* **2012**, *10*, 3763.

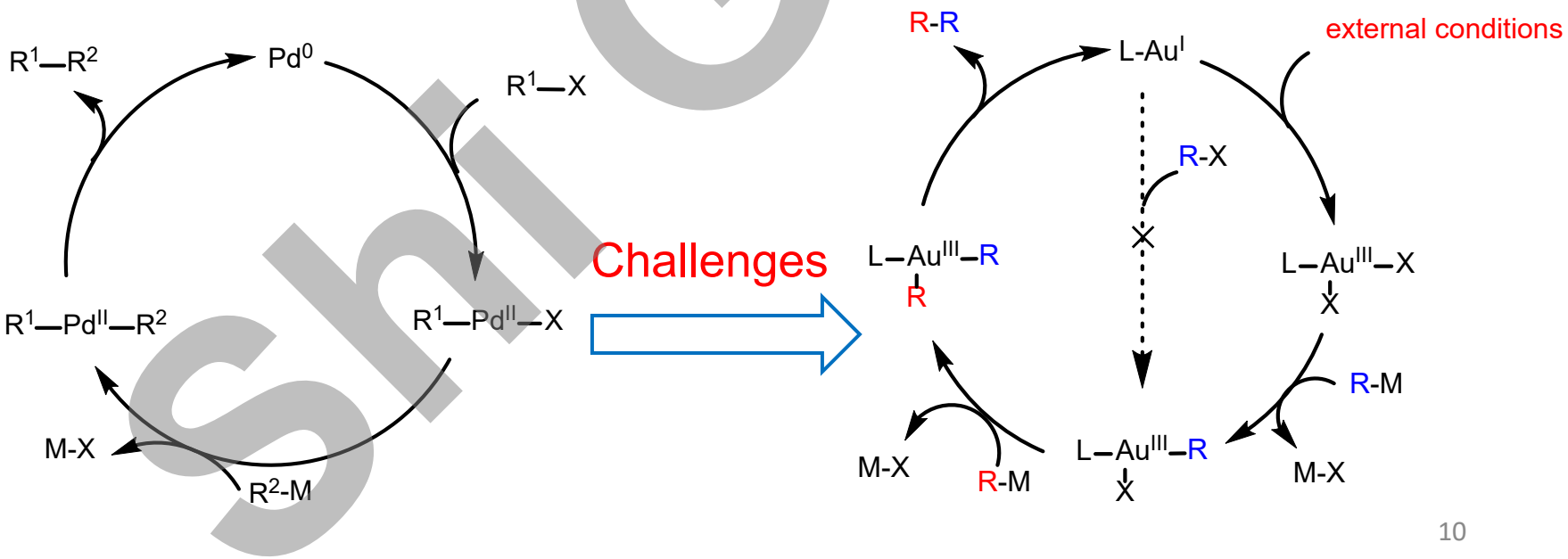
Background

The Nobel Prize in chemistry 2010 for Pd-catalyzed cross couplings

Richard F. Heck

Ei-ichi Negishi

Akira Suzuki



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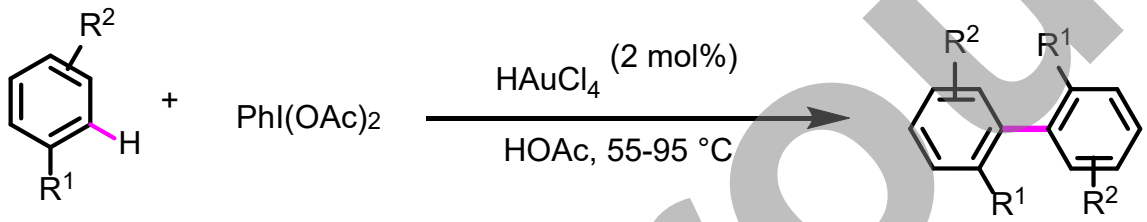
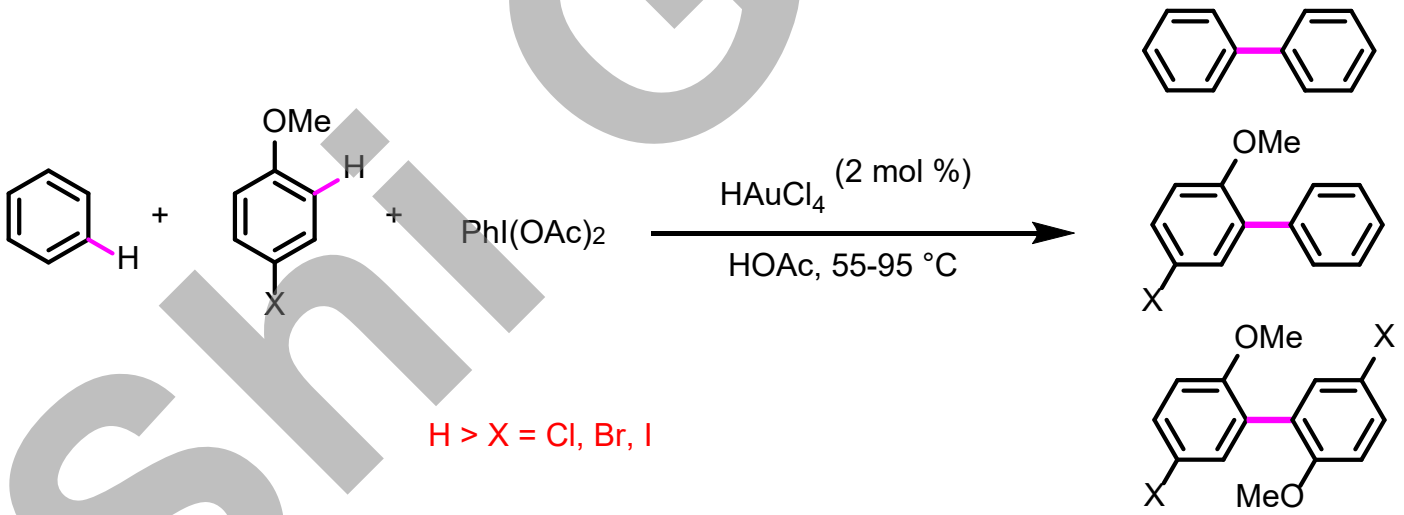
Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I} and I^{3+}-mediated coupling reactions of arenes



R^1 = H, Me, OMe, Cl; R_2 = H, Me, ^{t}Bu, F, Cl, Br, I, NO_2, COOMe

Tse, M. K. et al. *Chem. Commun*. **2008**, 386.

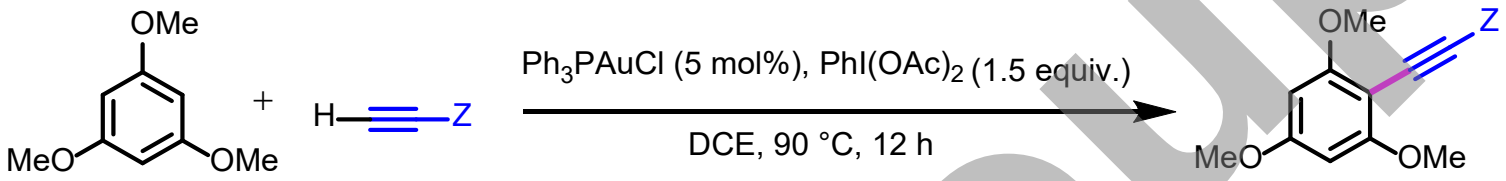


H > X = Cl, Br, I

Tse, M. K. et al. *J. Organomet. Chem.* **2009**, *694*, 524.

Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I} and I^{3+}-mediated coupling reactions of arenes and alkynes

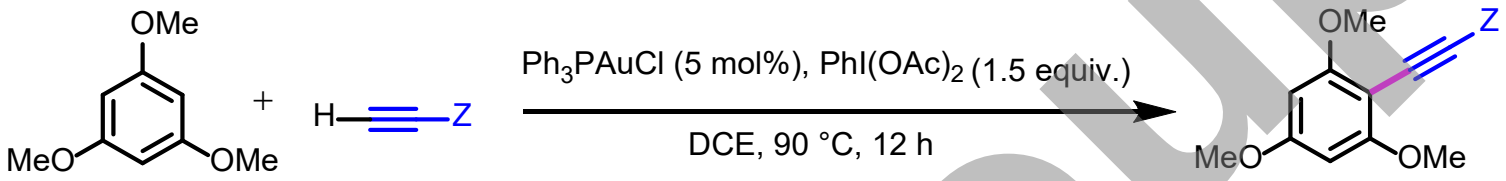


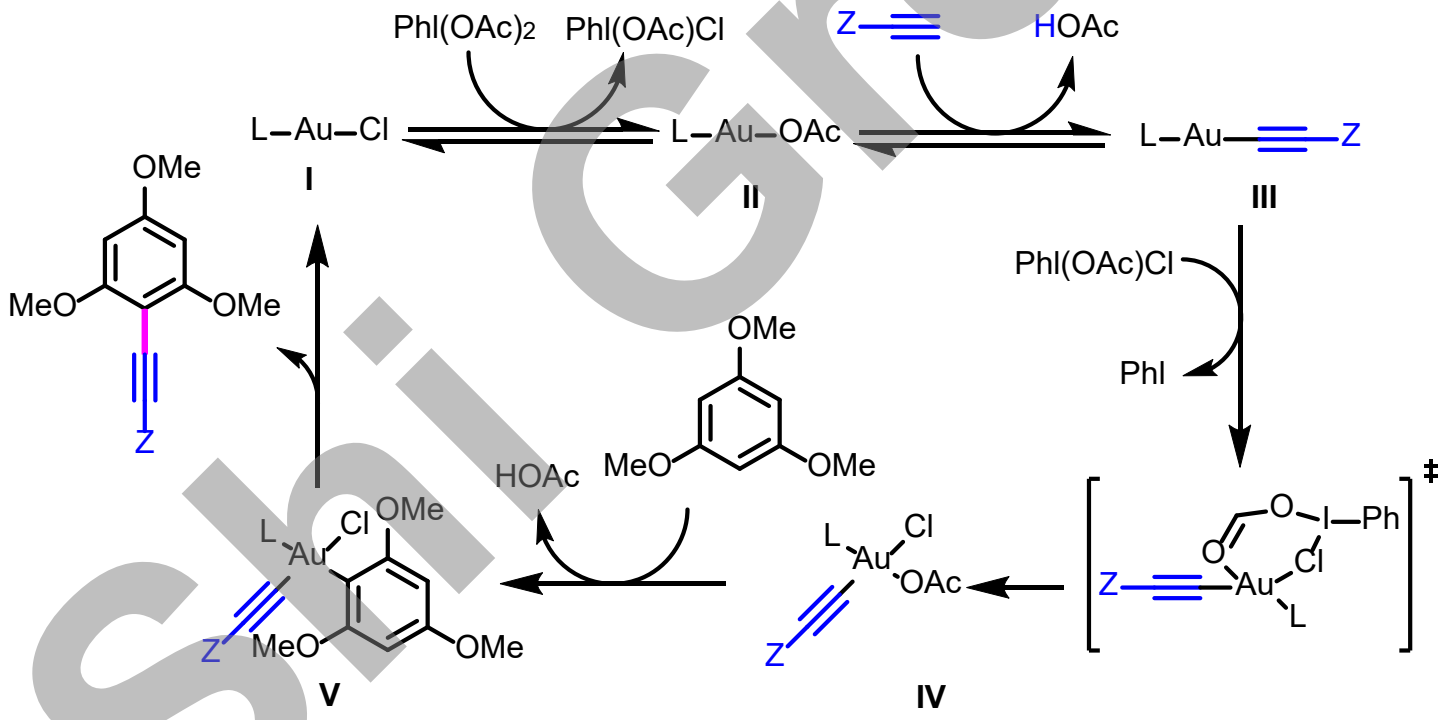
entry	substrate	yield %
1	Z = CO_2Et	75
2	Z = $CO_2{}^tBu$	60
3	Z = COPh	72
4	Z = CO(3,5-dimethoxy-phenyl)	68
5	Z = CO(*p*-$CF_3C_6H_4$)	70
6	Z = CO^tBu	31
7	Z = $CO(C_7H_{12})$	66
8	Z = $(CH_3)C{=}CH_2$	48
9	Z = Ph	25

Nevado, C. et al. *J. Am. Chem. Soc.* **2010**, *132*, 1512.

Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I} and I^{3+}-mediated coupling reactions of arenes and alkynes

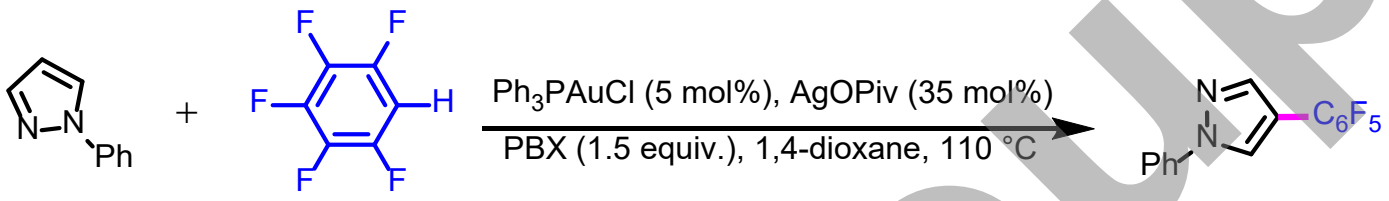




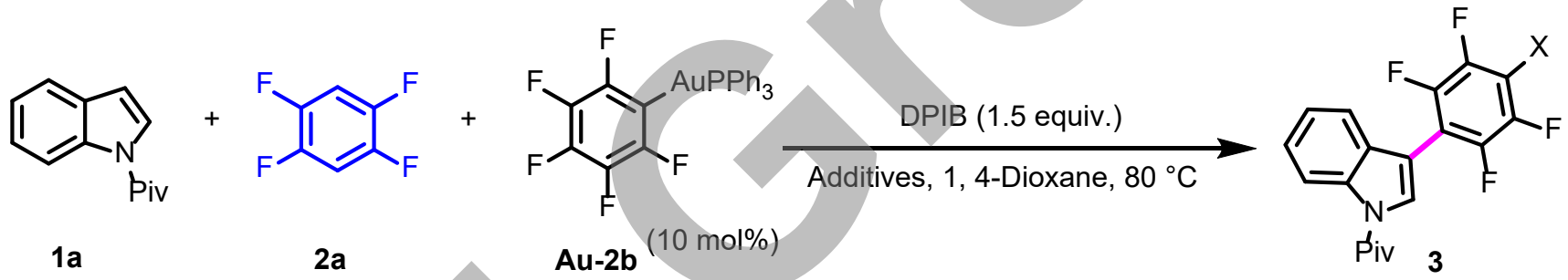
Nevado, C. et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 1021.

Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I}/Ag^{I} bimetallic and I^{3+}-mediated coupling reactions of arenes



Initial Search for Conditions



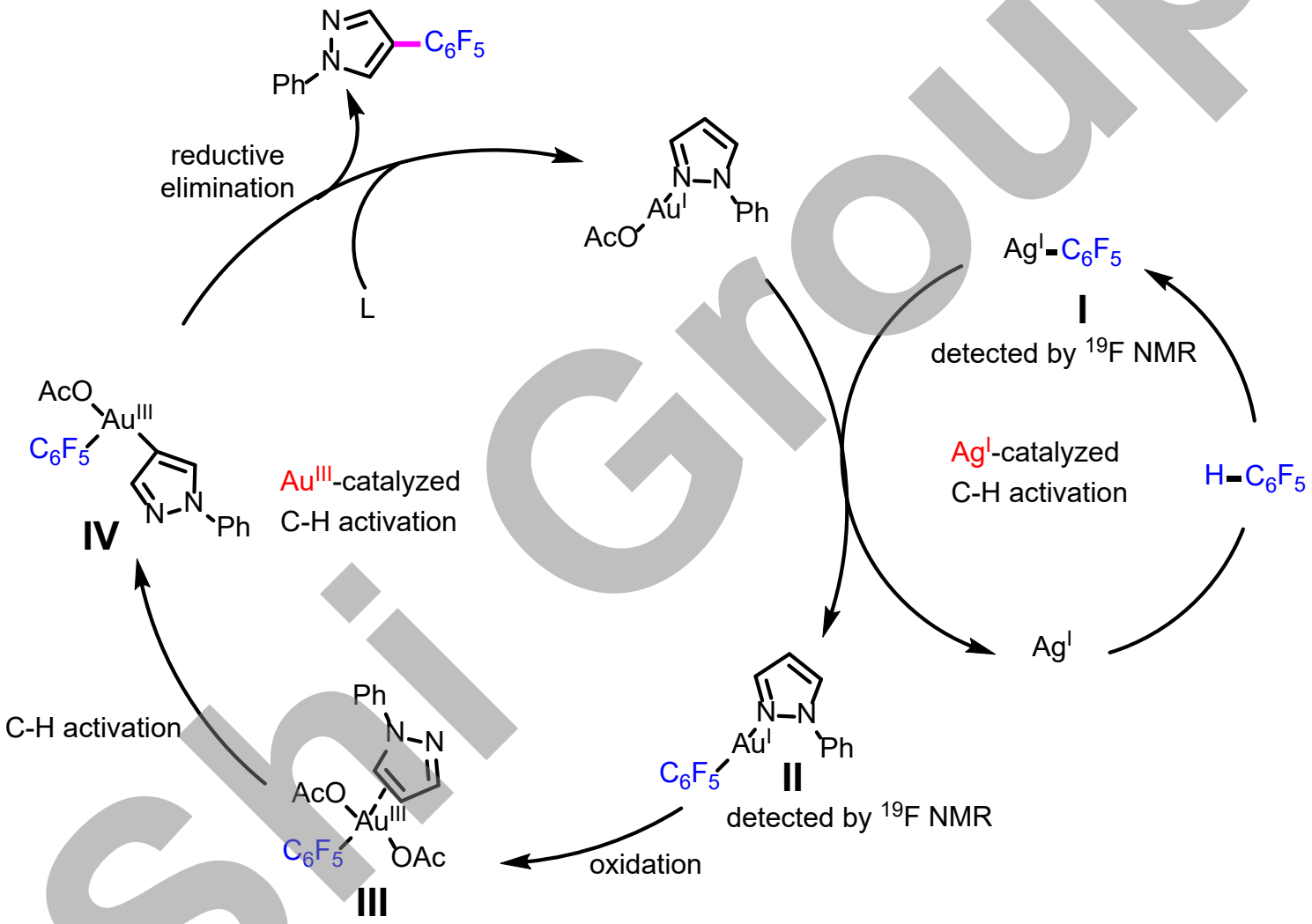
1a **2a** **Au-2b** **3**

	Additives	3a (X = F) %	3b (X = H) %
Stoichio-metric reaction of Au-2b	None	9	None
	AgOPiv (20 mol%) K_2CO_3 (2 equiv.)	None	None
Catalytic turnover	AgOPiv (20 mol%)	5	16

Larrosa, I. et al. *J. Am. Chem. Soc.* **2015**, *137*, 15636.

Oxidants-Assisted Coupling Reactions-I^{3+}

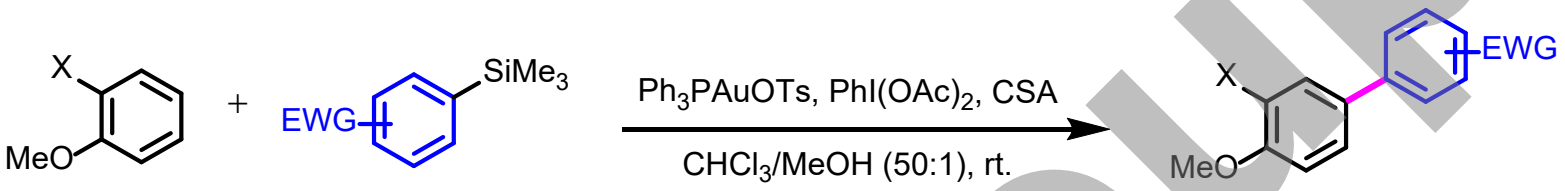
Proposed mechanism



Xie, J.; Li, S.; Zhu, C. et al. *J. Am. Chem. Soc.* **2019**, *141*, 3187.

Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I} and I^{3+}-mediated arylation of $ArSiMe_3$

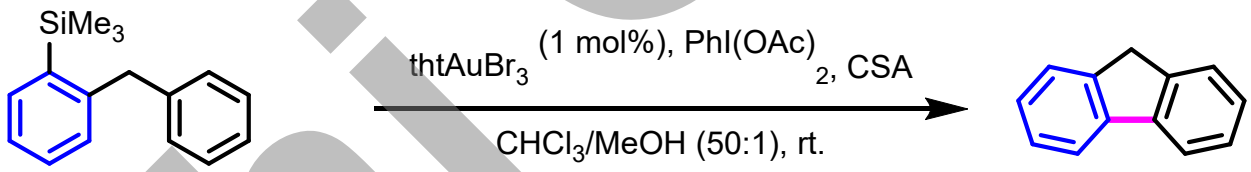


X = Cl, Br, I, OMs, CO_2Me...

CSA = camphorsulfonic acid

Mild reaction conditions; High FG tolerance; High selectivity; High yield

Lloyd-Jones, G. C. et al. *Science* **2012**, *337*, 1644.



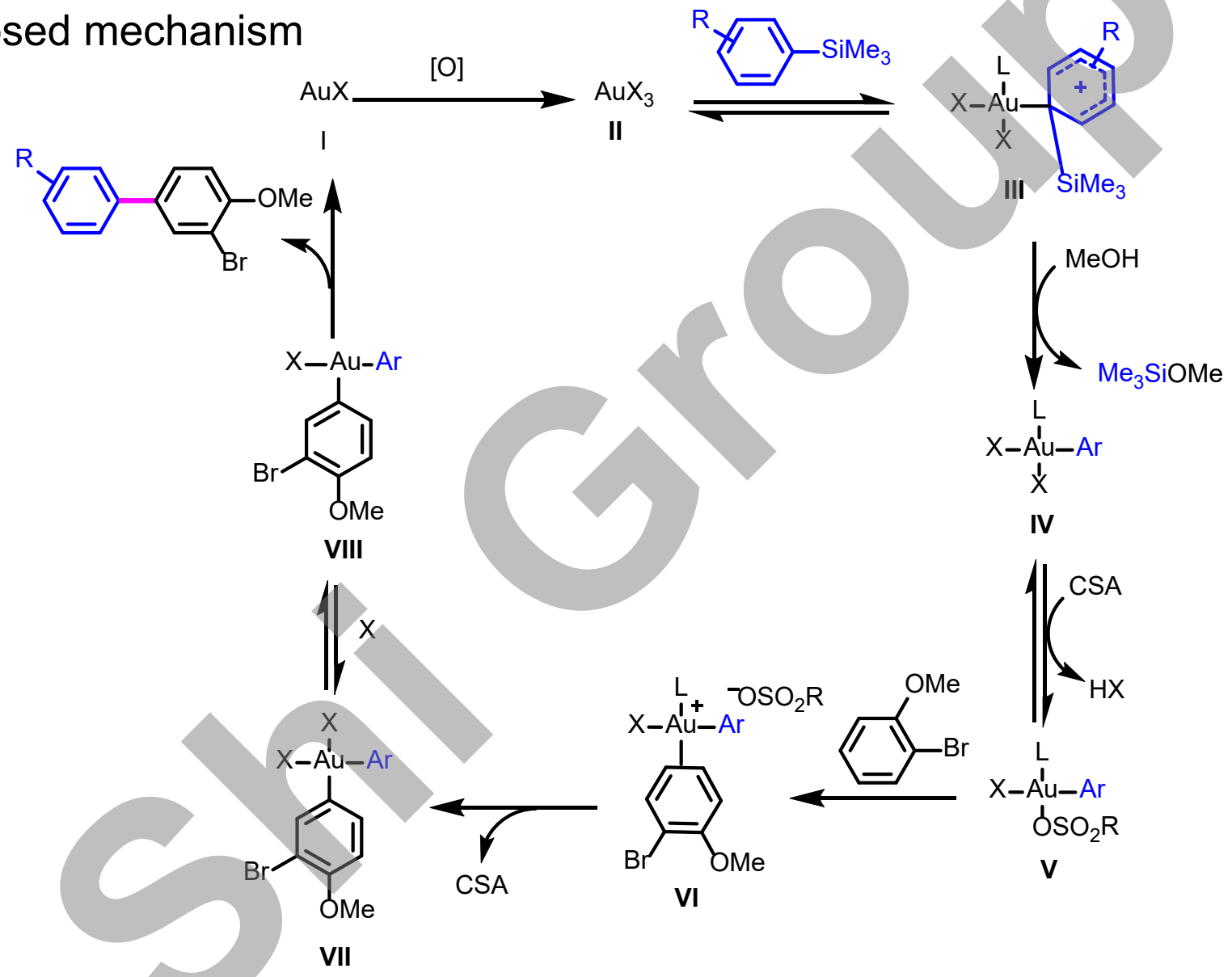
tht = tetrahydrothiophene

5 to 9-membered ring

Lloyd-Jones, G. C. et al. *J. Am. Chem. Soc.* **2017**, *139*, 245.

Oxidants-Assisted Coupling Reactions-I^{3+}

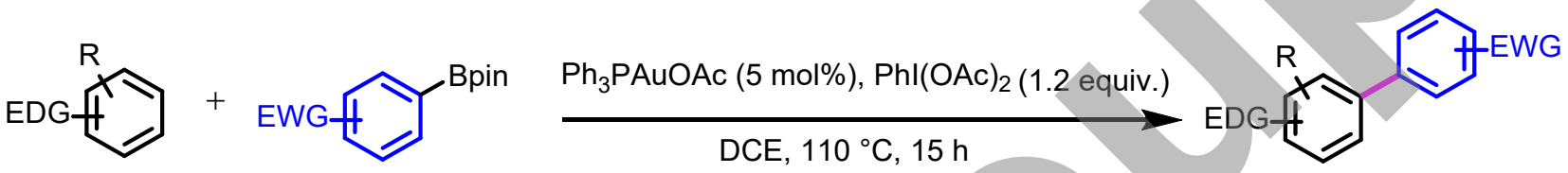
Proposed mechanism



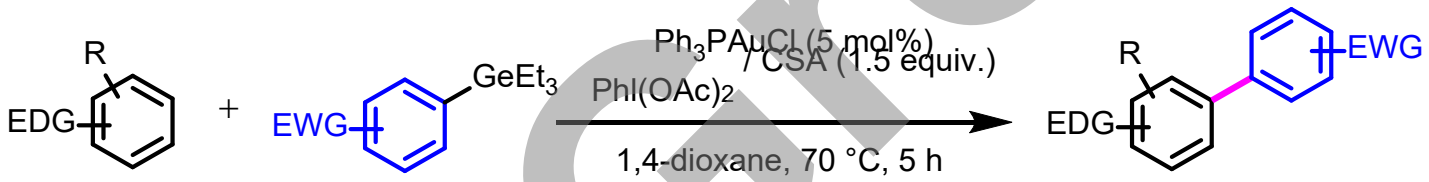
Lloyd-Jones, G. C. et al. *J. Am. Chem. Soc.* **2014**, *136*, 254.

Oxidants-Assisted Coupling Reactions-I^{3+}

Au^{I} and I^{3+}-mediated arylation of ArBpin or $ArGeEt_3$

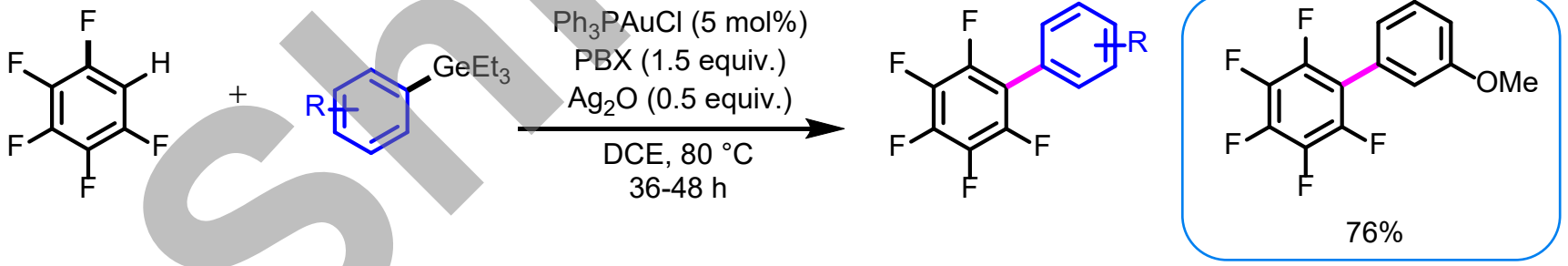


Nevado, C. et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 1021.



$GeEt_3$ > $SiMe_3$ > BR_2; R = H > I > Br > Cl High selectivity

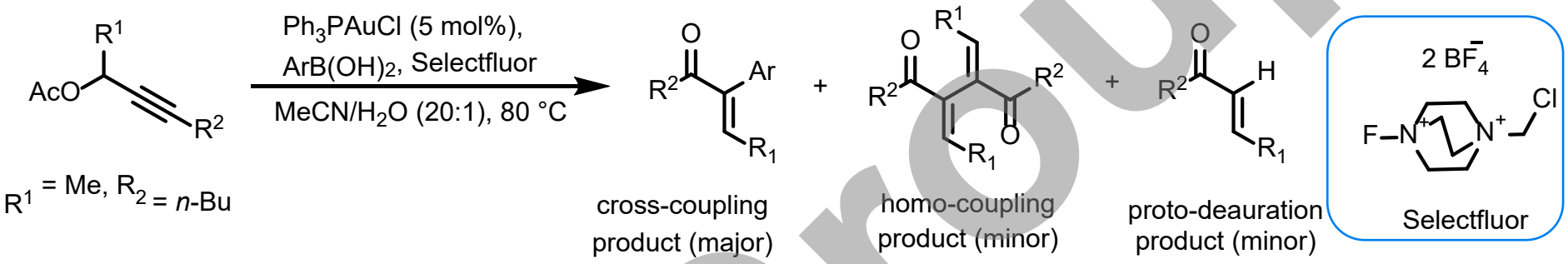
Schoenebeck, F. et al. *ACS Catal.* **2019**, *9*, 9231.



Schoenebeck, F. et al. *J. Am. Chem. Soc.* **2020**, *142*, 7754.

Oxidants-Assisted Coupling Reactions-Selectfluor

Au^{I}- and selectfluor-mediated coupling reactions of propargylic esters



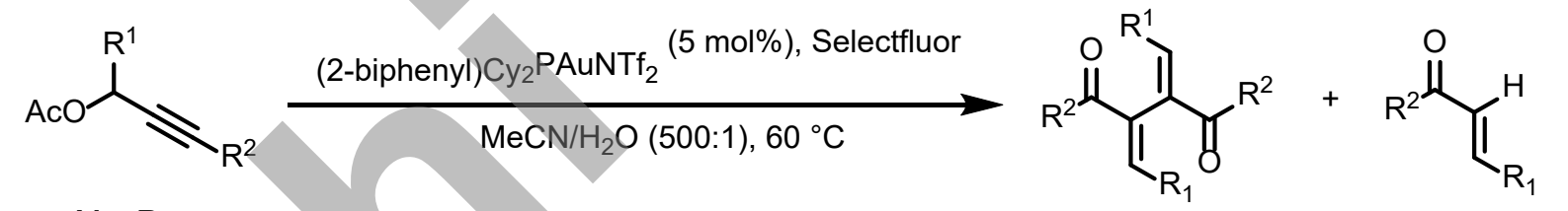
R^1 = Me, R_2 = *n*-Bu

cross-coupling product (major)

homo-coupling product (minor)

proto-deauration product (minor)

Zhang, L. et al. *Angew. Chem. Int. Ed.* **2009**, *48*, 3112.



R^1 = Me, R_2 = *n*-Bu

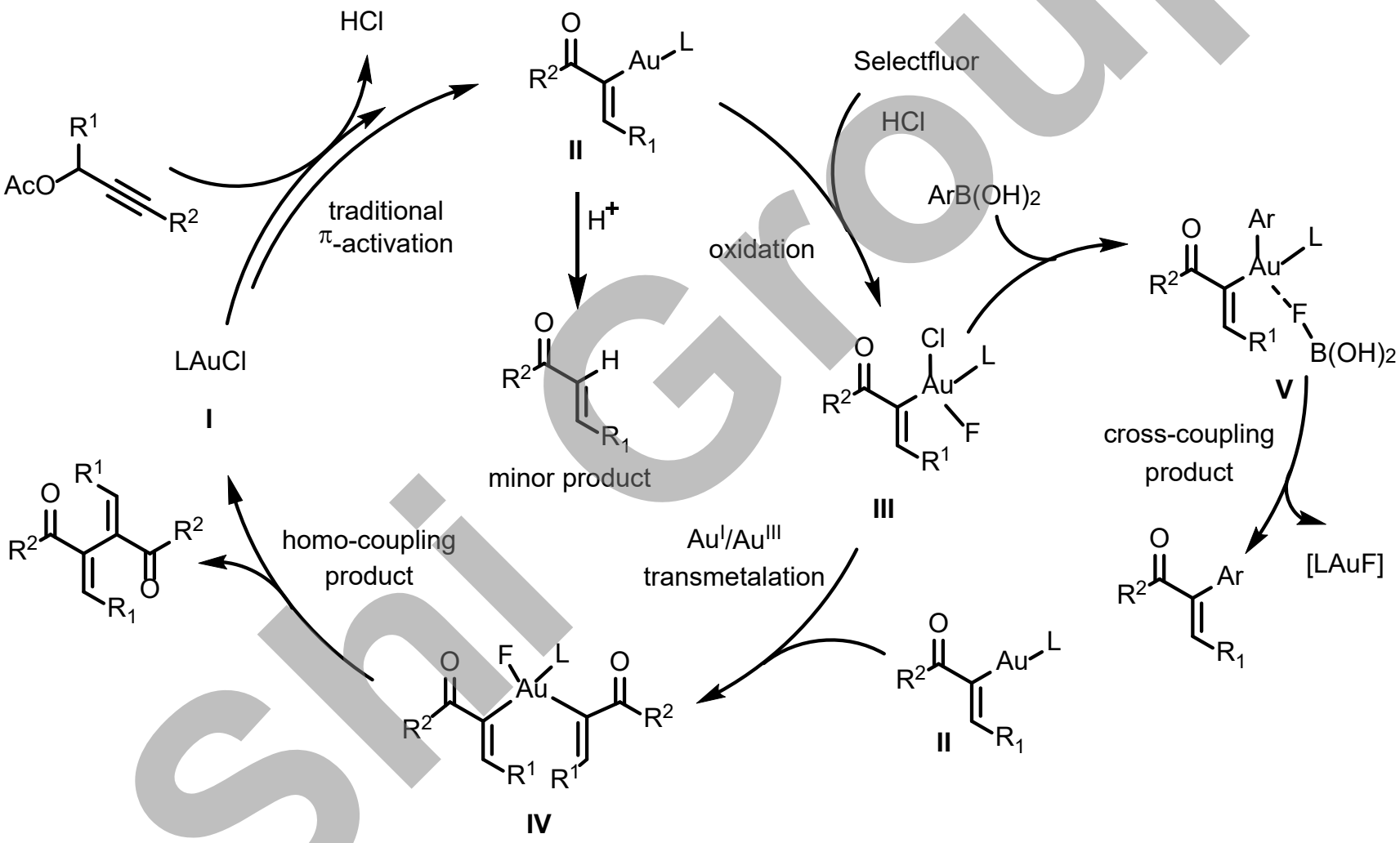
major product

minor product

Zhang, L. et al. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3884.

Oxidants-Assisted Coupling Reactions-Selectfluor

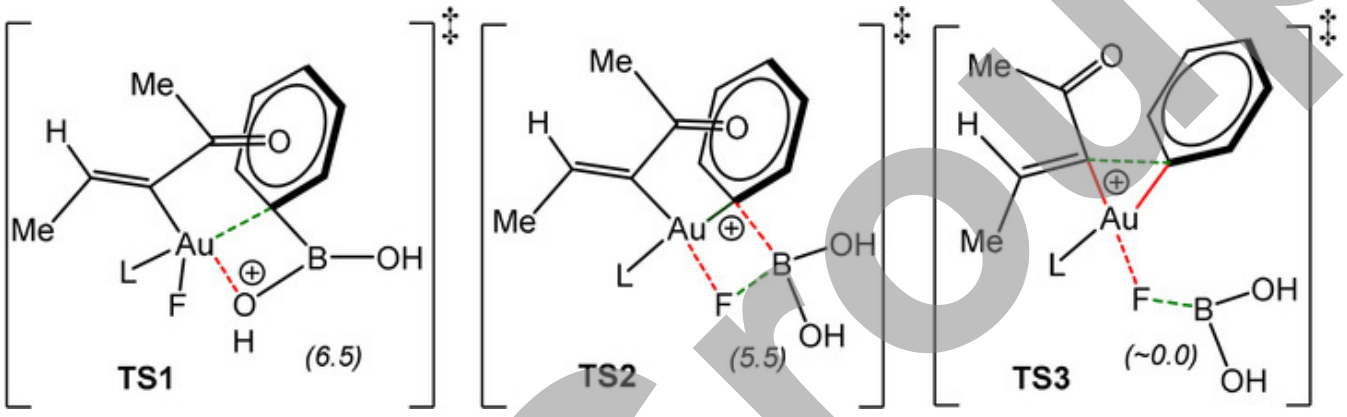
Proposed mechanism



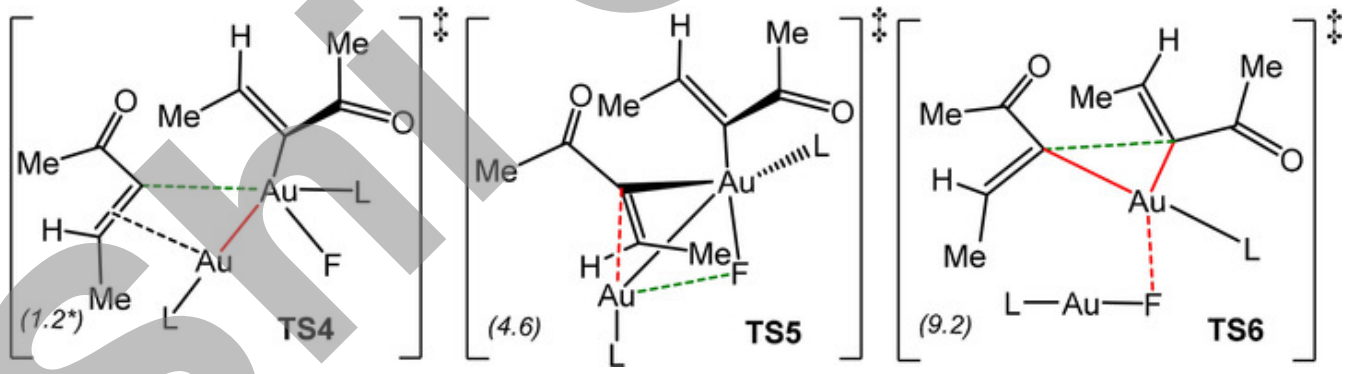
Zhang, L. et al. *Angew. Chem. Int. Ed.* **2009**, *48*, 3112.

Oxidants-Assisted Coupling Reactions-Selectfluor

DFT calculations in the presence of aryl boronic acids



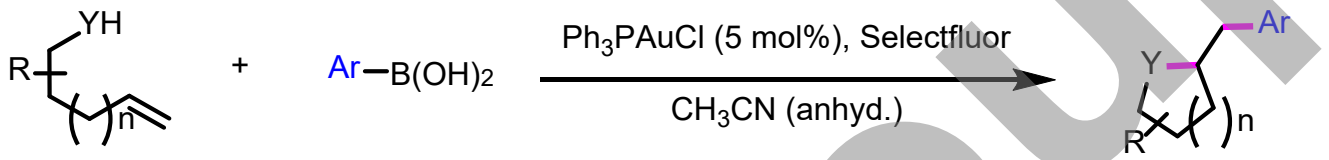
DFT calculations in the absence of aryl boronic acids



Faza, O. N.; Lopez, C. S. et al. *J. Org. Chem.* **2013**, *78*, 4929.

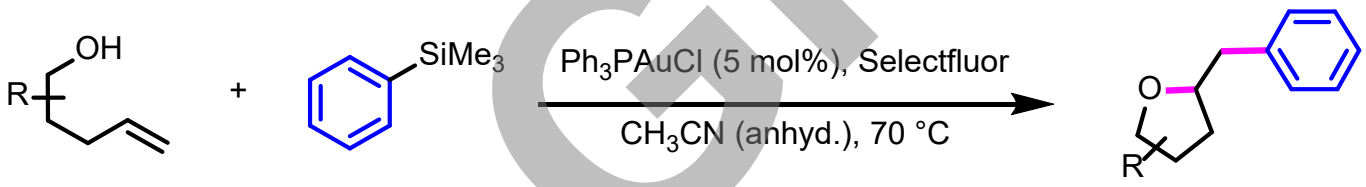
Oxidants-Assisted Coupling Reactions-Selectfluor

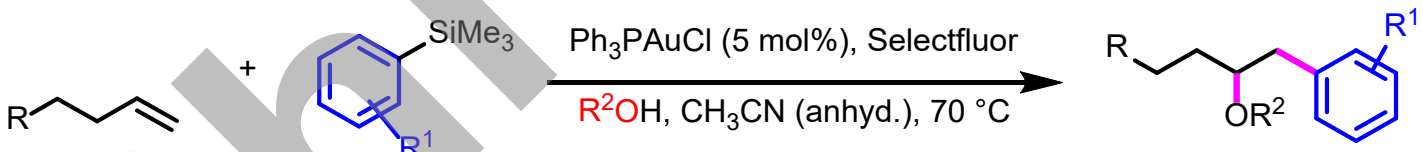
Au^{I}- and selectfluor-mediated coupling reactions of terminal alkenes



Y = O, NTs, n = 1, 2

Zhang, L. et al. *J. Am. Chem. Soc.* **2010**, *132*, 1474.

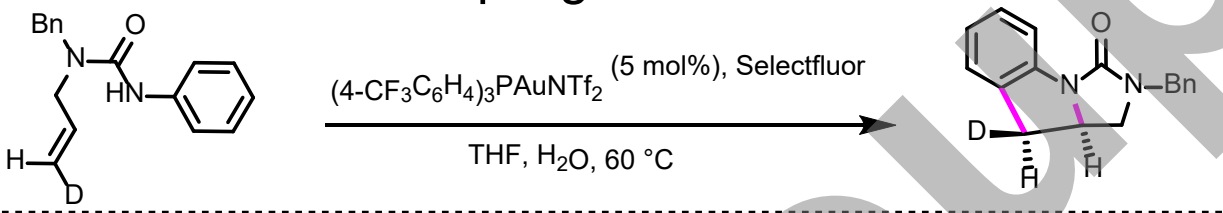




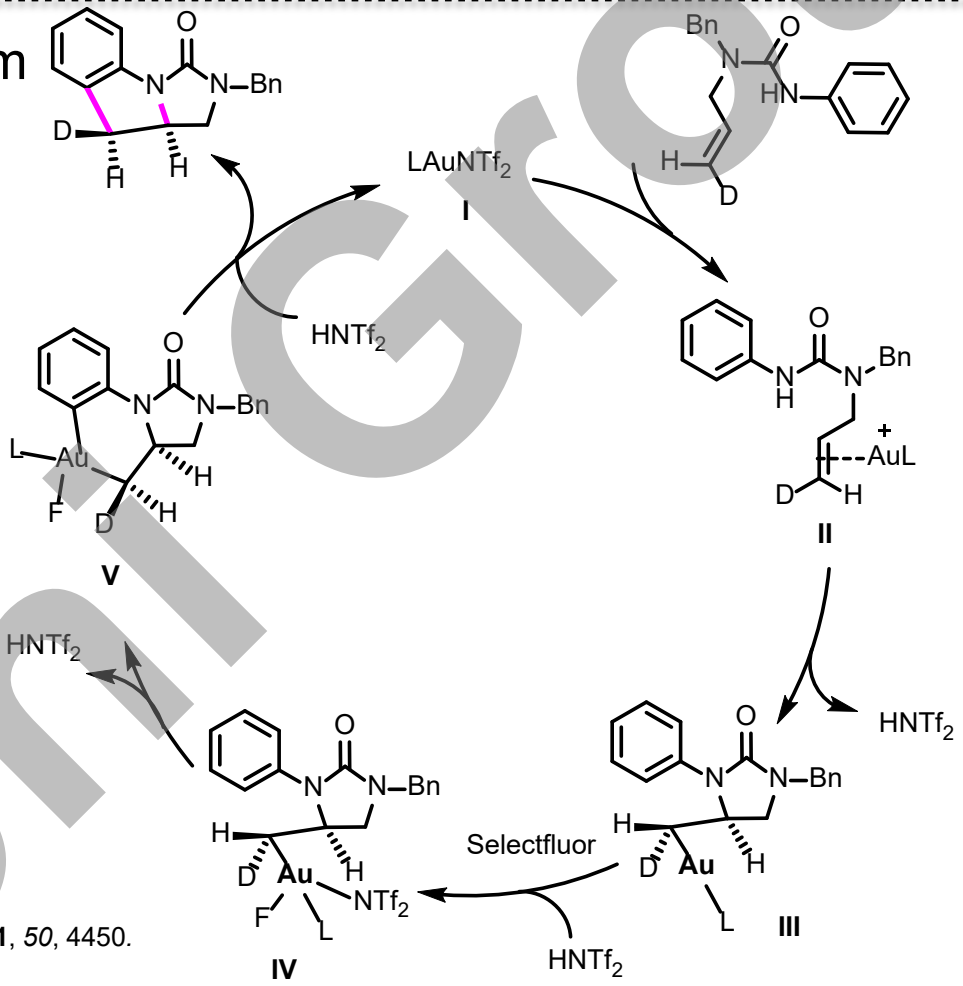
Lloyd-Jones, G. C.; Russel, C. A. et al. *Org. Lett.* **2010**, *12*, 4724.

Oxidants-Assisted Coupling Reactions-Selectfluor

Au^{I}- and selectfluor-mediated coupling reactions of unactivated arenes



Proposed mechanism



Zhang, L. et al. *Angew. Chem. Int. Ed.* **2011**, *50*, 4450.

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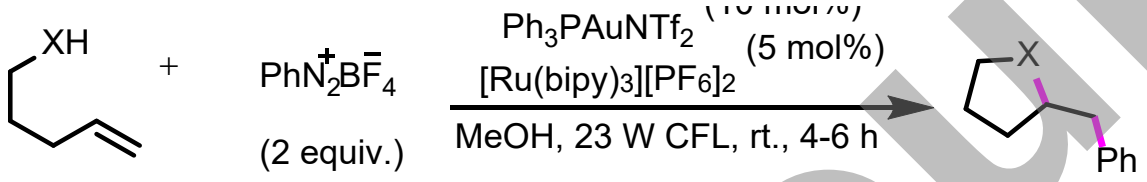
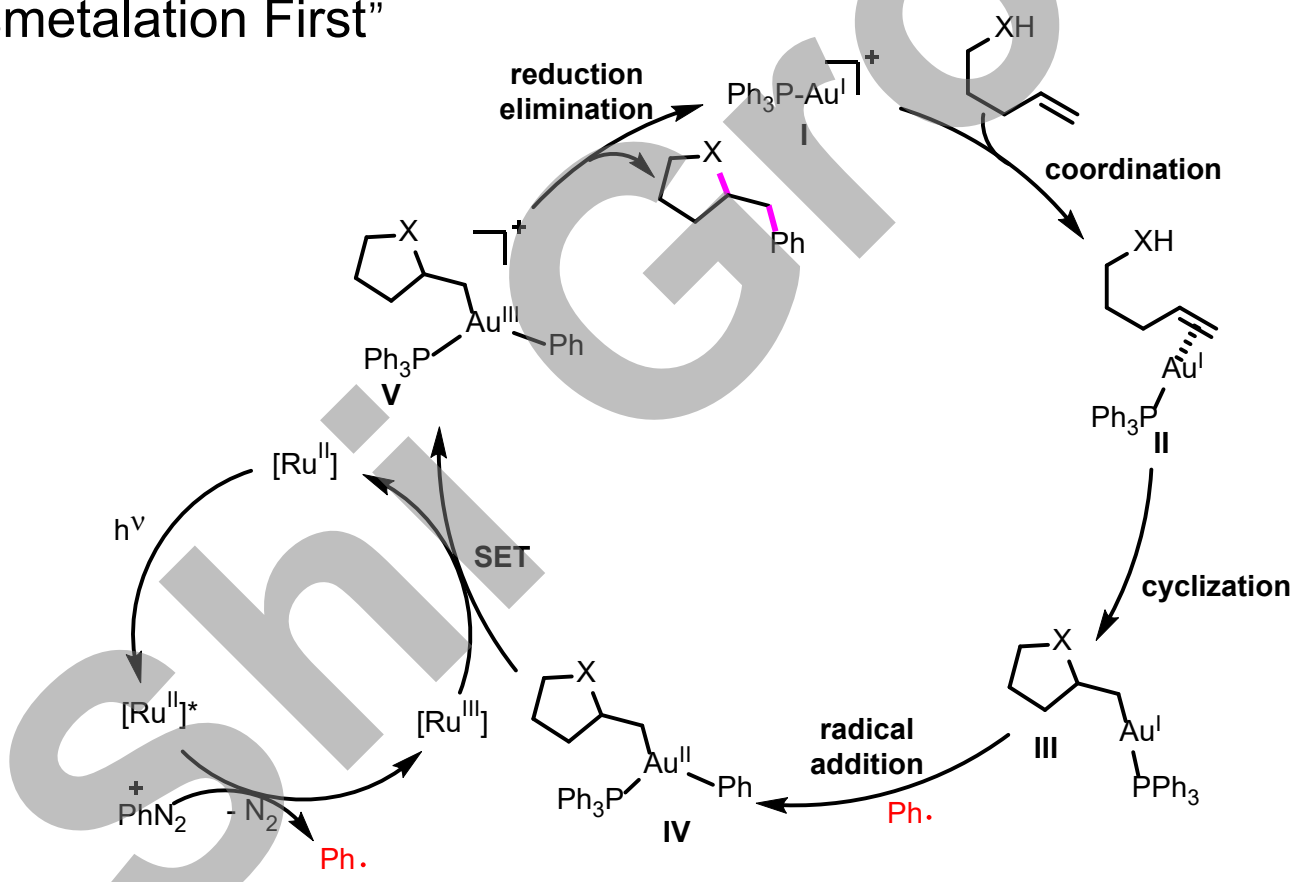
Photo-Assisted Coupling Reactions

Dual gold/photoredox mediated coupling reactions of terminal alkenes



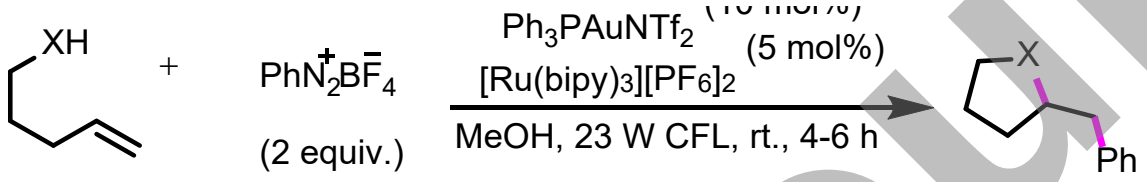
I. "Transmetalation First"



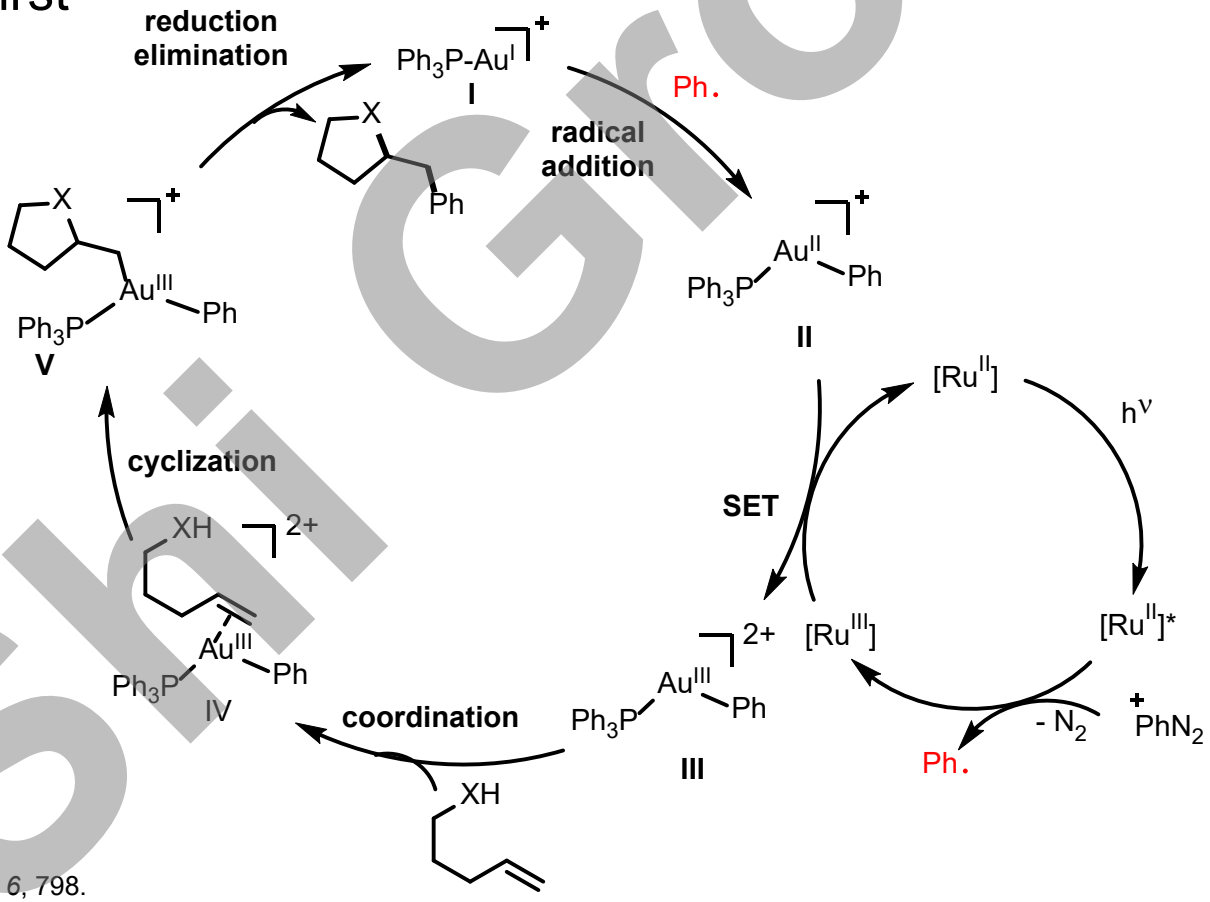
Yu, H. Z. et al. *ACS Catal*. **2016**, *6*, 798.

Photo-Assisted Coupling Reactions

Dual gold/photoredox mediated coupling reactions of terminal alkenes



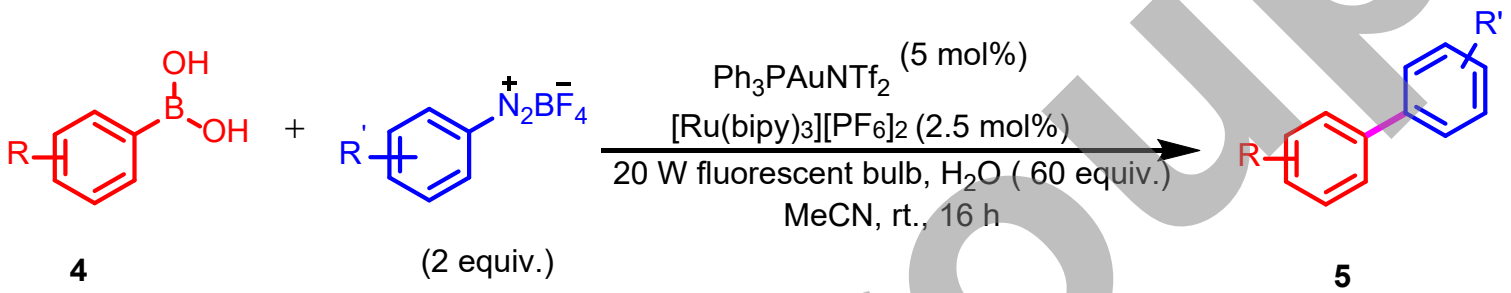
II. "Oxidation First"



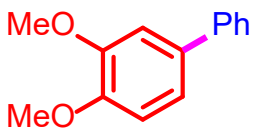
Yu, H. Z. et al. *ACS Catal*. **2016**, *6*, 798.

Photo-Assisted Coupling Reactions

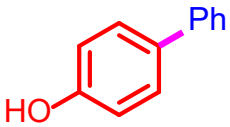
Dual gold/photoredox mediated C(sp^2)–C(sp^2) coupling reactions



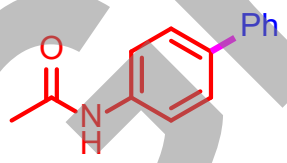
4 (2 equiv.) **5**



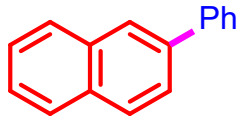
5a, 83%



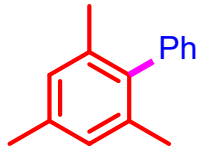
5b, 73%



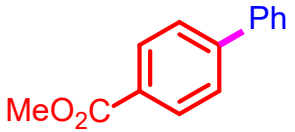
5c, 92%



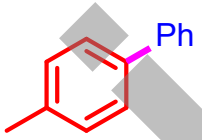
5d, 70%



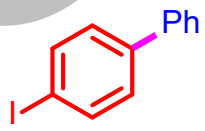
5e, 77%



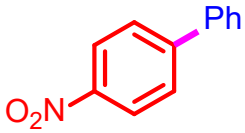
5f, 55%



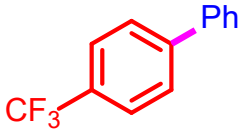
5g, 61%



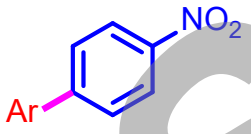
5h, 34%



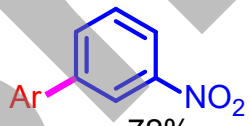
5i, 47%



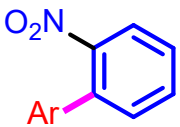
5j, 34%



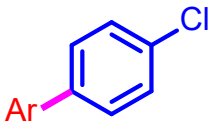
5k, 82%



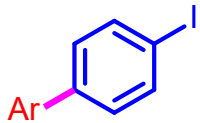
5l, 72%



5m, 39%



5n, 77%

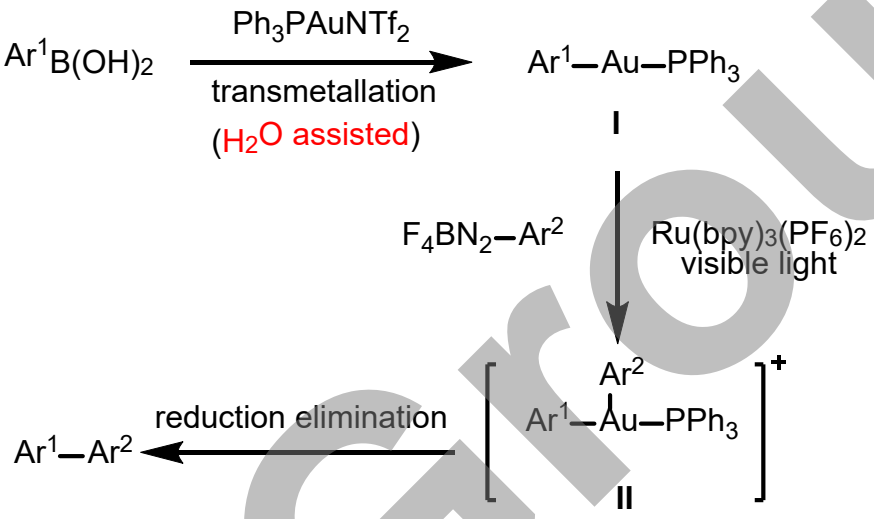


5o, 52%

Lee, A. L. et al. *Chem. Commun.* **2016**, *52*, 10163.

Photo-Assisted Coupling Reactions

Proposed mechanism

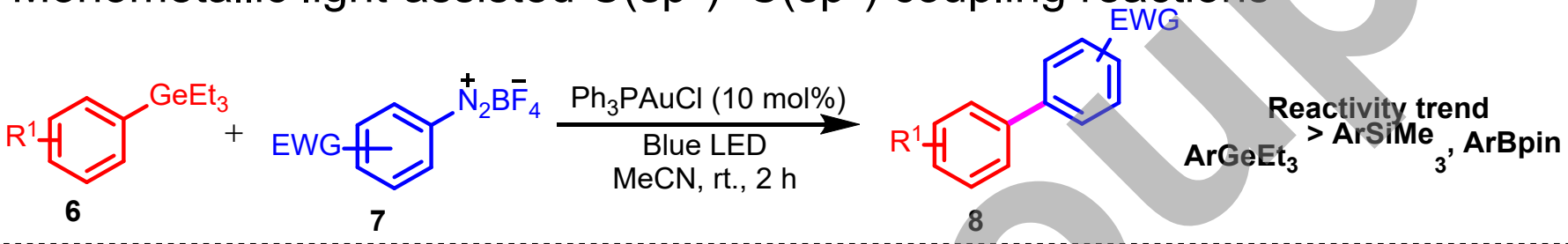


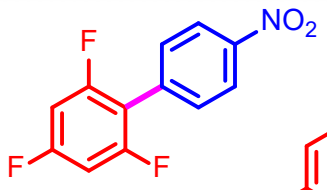
- Water is involved in aiding the transmetallation step ($Ar^1B(OH)_2 \rightarrow$ I)
- Water affects the homogeneity of the reaction mixture, and therefore the ability of light to efficiently penetrate the mixture to promote photoredox coupling

Lee, A. L. et al. *Chem. Commun.* **2016**, *52*, 10163.

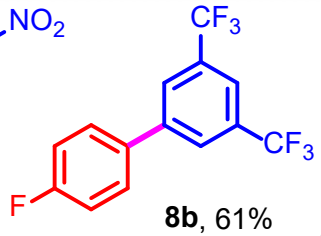
Photo-Assisted Coupling Reactions

Monometallic light-assisted $C(sp^2)$–$C(sp^2)$ coupling reactions

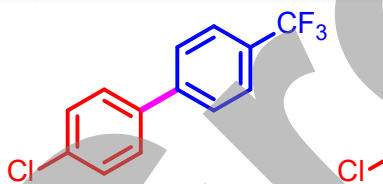




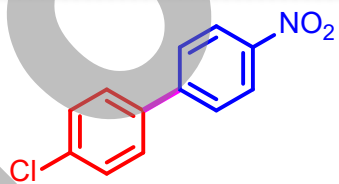
8a, 66%



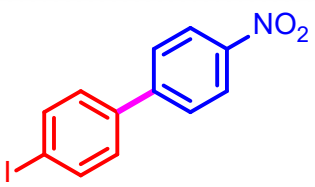
8b, 61%



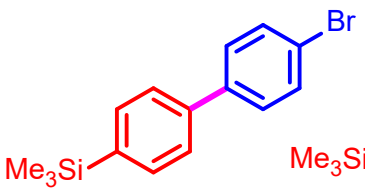
8c, 86%



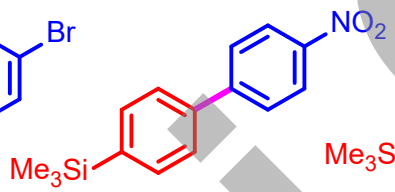
8d, 90%



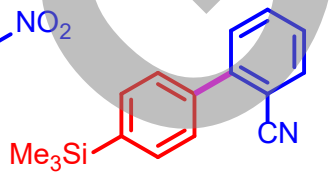
8e, 81%



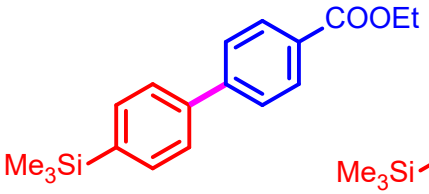
8f, 80%



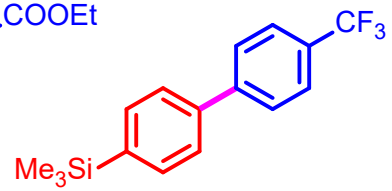
8g, 73%



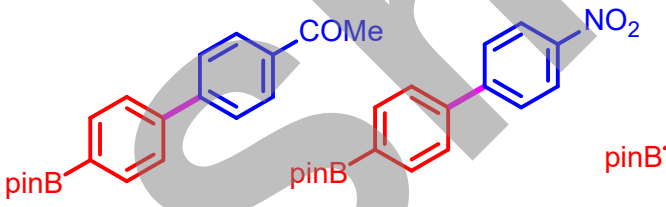
8h, 80%



8i, 66%

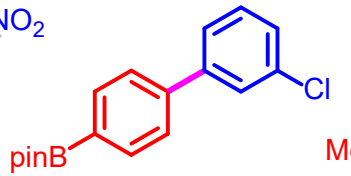


8j, 67%

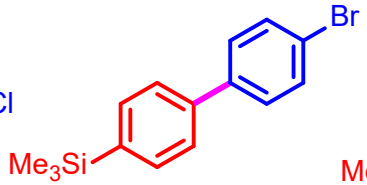


8k, 61%

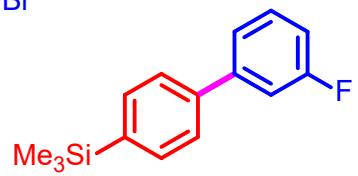
8l, 63%



8m, 80%



8n, 62%

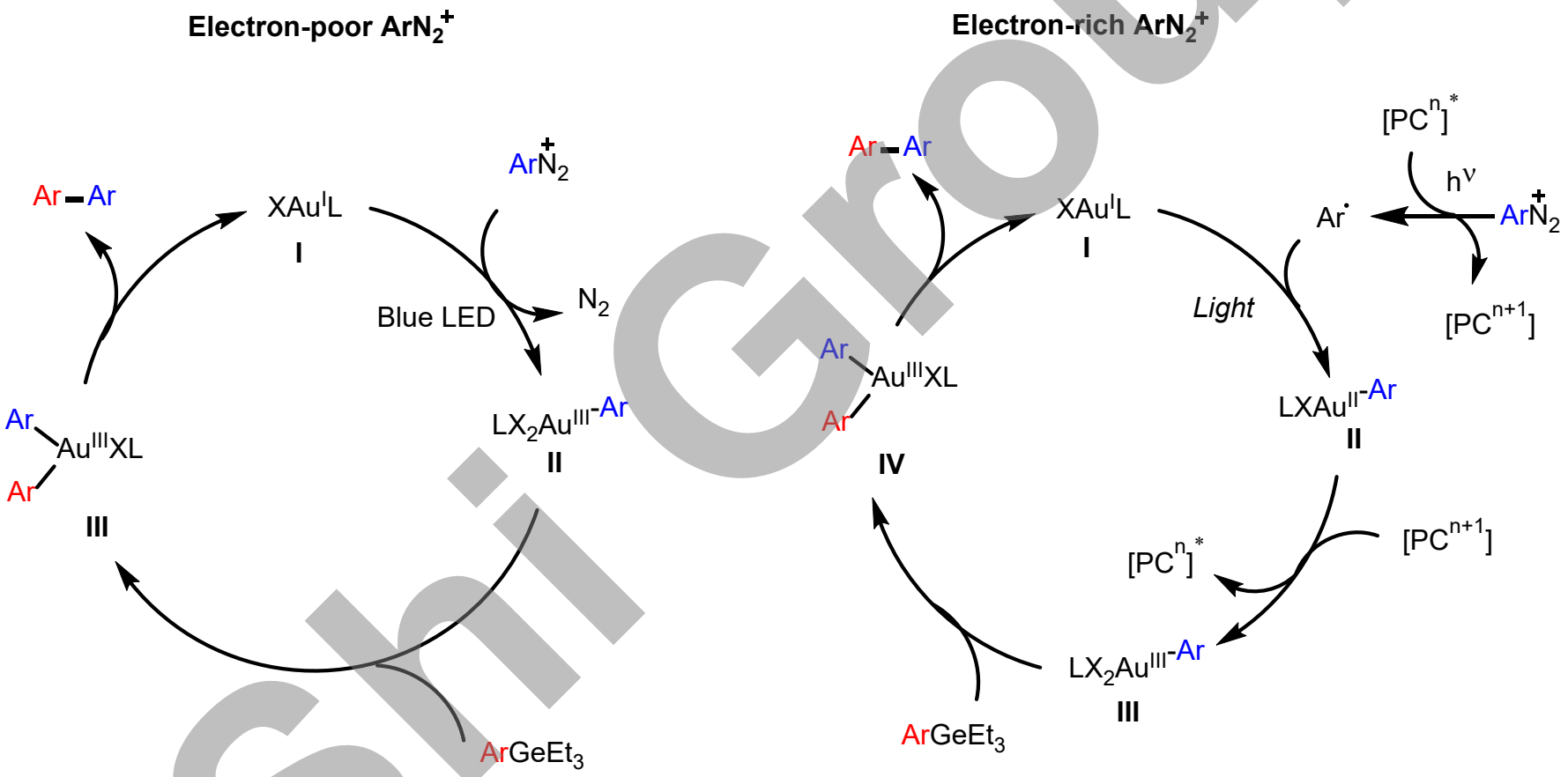


8o, 80%

Schoenebeck, F. et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 15543.

Photo-Assisted Coupling Reactions

Proposed mechanism



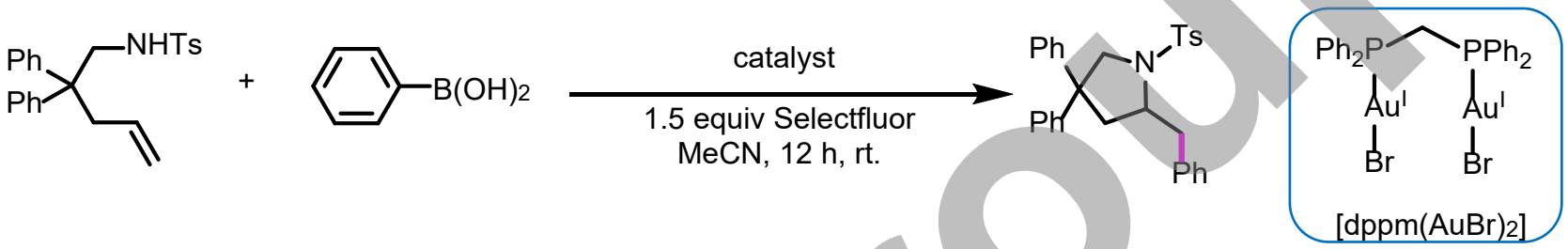
Schoenebeck, F. et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 15543.

Background

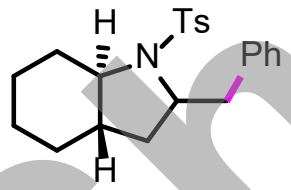
- Background
- Gold-Catalyzed C-C Coupling Reactions
  - Oxidants-Assisted Coupling Reactions
  - Photo-Assisted Coupling Reactions
  - Dinuclear Gold-Catalyzed Coupling Reactions
- Summary

Dinuclear Gold-Catalyzed Coupling Reactions

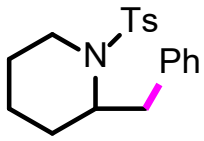
Dinuclear gold-catalyzed coupling reactions of terminal alkenes



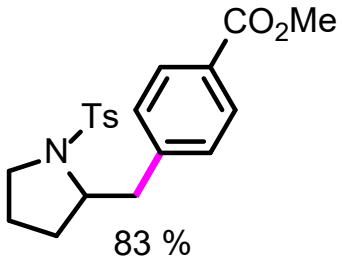
Catalyst (mol%)	Yield [%]
Ph_3PAuX (5), X = Cl, Br, I, OTf (5)	< 47
$[dppm(AuBr)_2]$ (3)	81



92 %



82 %

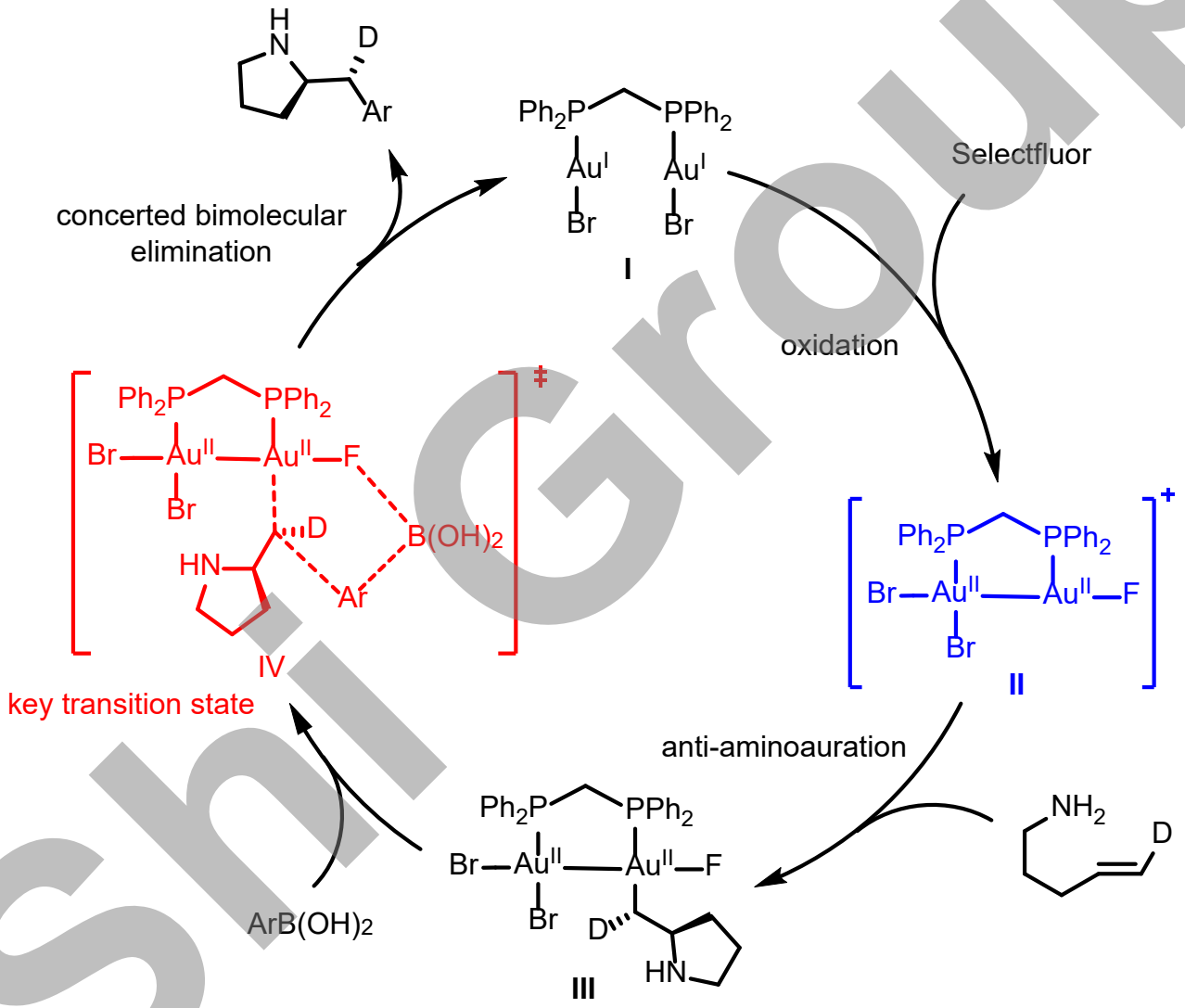


83 %

Toste, F. D. et al. *Angew. Chem. Int. Ed.* **2010**, *49,* 5519.

Dinuclear Gold-Catalyzed Coupling Reactions

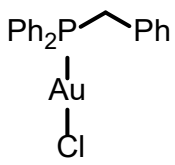
Proposed mechanism



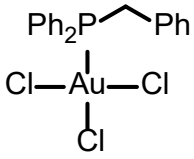
Toste, F. D. et al. *J. Am. Chem. Soc.* **2011**, *133*, 14293.

Dinuclear Gold-Catalyzed Coupling Reactions

Dinuclear gold-complexes



9



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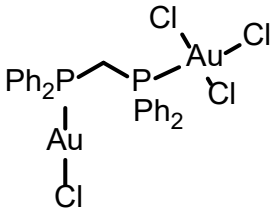
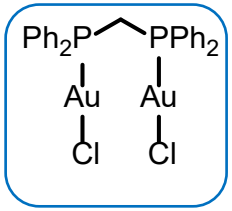
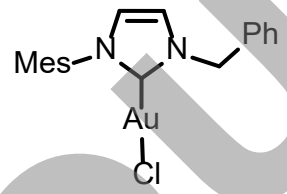


11



12



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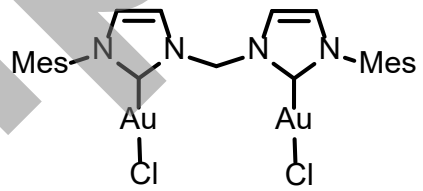


14

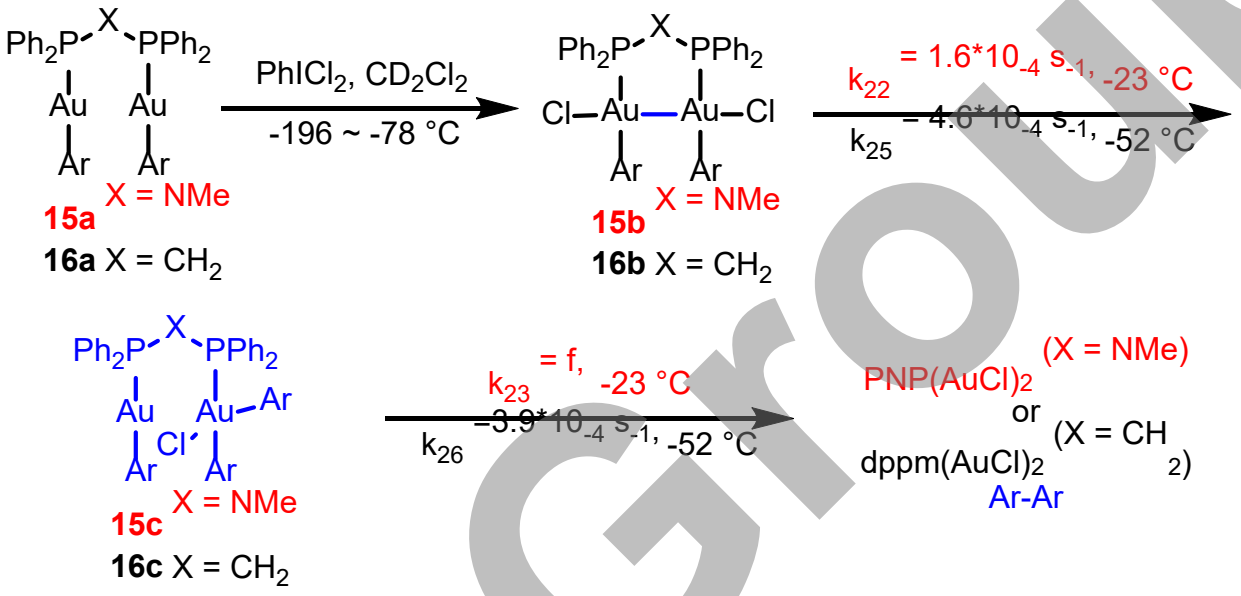
Summary of Electrochemistry Data

Complex	E_{ox} for Au(I) (V)	E_{red} for Au(III) (V)
9	1.48	/
10	/	-0.69
11	1.48	-0.53
12	1.34	/
13	1.96	/
14	1.64	/

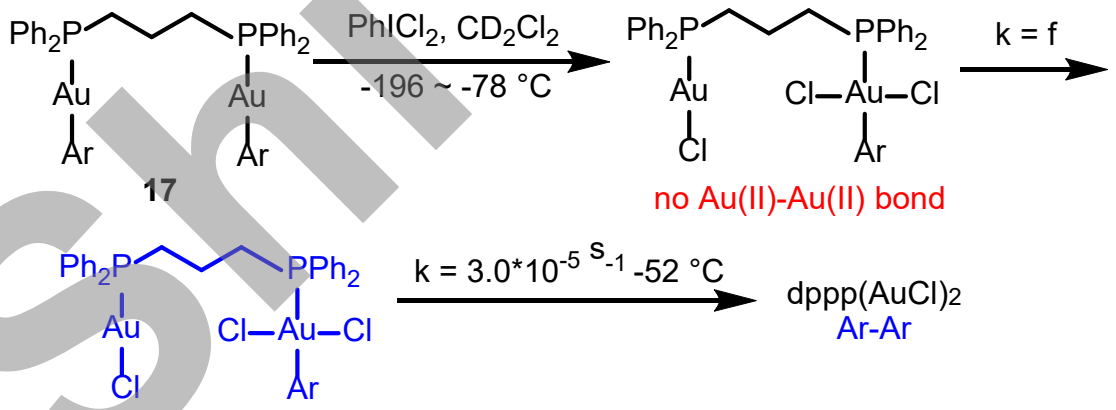
Toste, F. D. et al. *J. Am. Chem. Soc.* **2011**, *133*, 14293.

Dinuclear Gold-Catalyzed Coupling Reactions

a) Homocoupling by dinuclear gold with aurophilic interaction



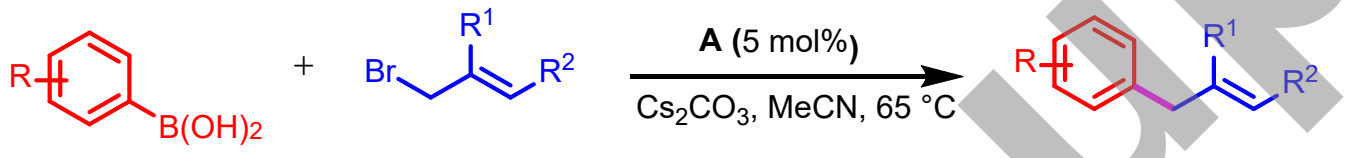
b) Homocoupling by dinuclear gold without aurophilic interaction



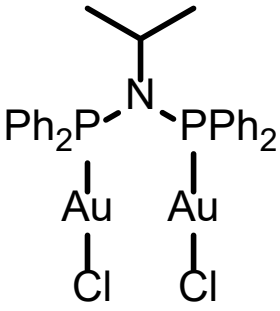
Toste, F. D. et al. *Nat. Chem.* **2014**, *6*, 159.

Dinuclear Gold-Catalyzed Coupling Reactions

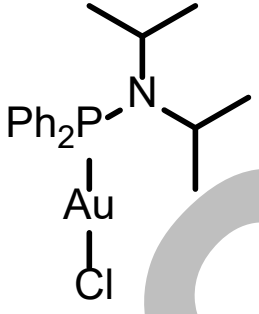
Dinuclear gold-catalyzed coupling of Ar–$B(OH)_2$ and allyl bromides



18 19 20



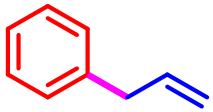
A



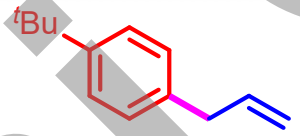
B

comparision of model reaction (product **20a**)

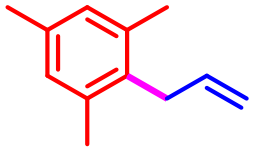
66% yield (**A** as catalyst)
vs
16% yield (**B** as catalyst)



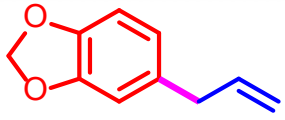
20a, 66%



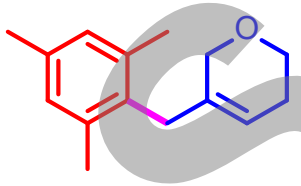
20b, 72%



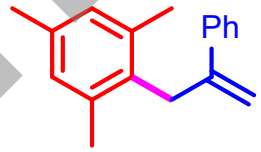
20c, 66%



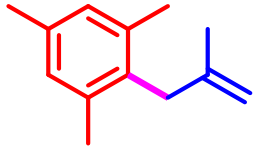
20d, 86%



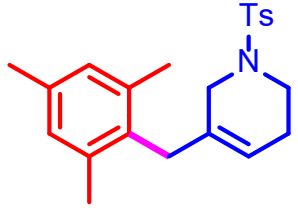
20e, 76%



20f, 57%



20g, 68%

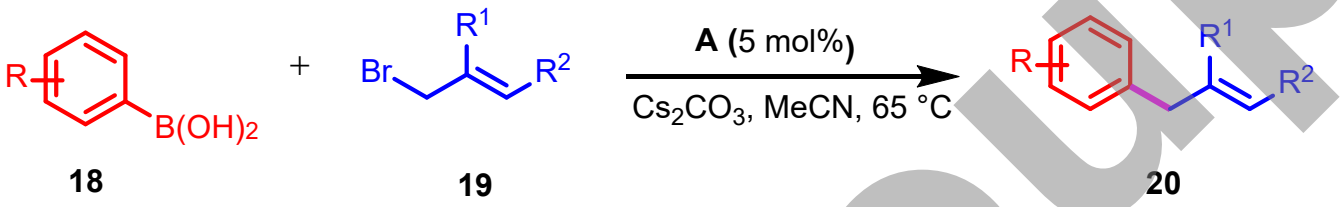


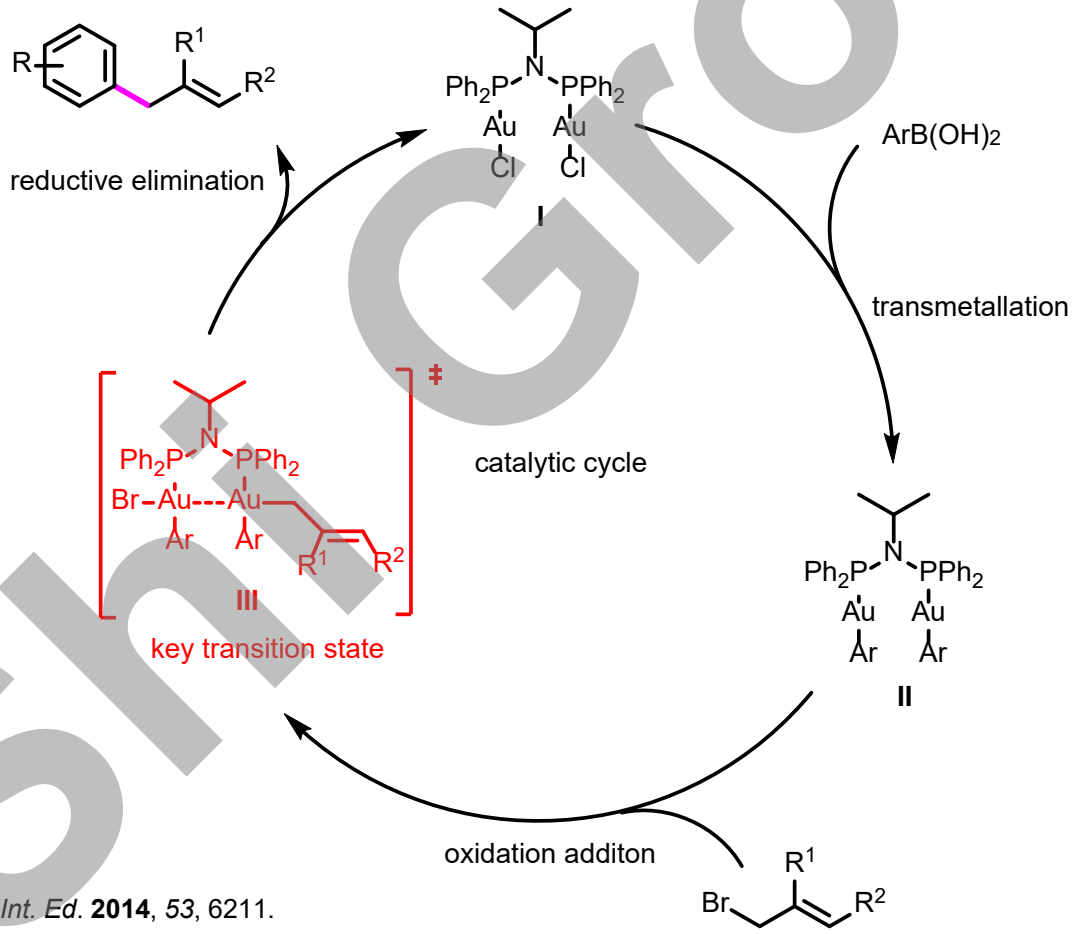
20h, 58%

Toste, F. D. et al. *Angew. Chem. Int. Ed.* **2014**, *53*, 6211.

Dinuclear Gold-Catalyzed Coupling Reactions

Dinuclear gold-catalyzed coupling of Ar–$B(OH)_2$ and allyl bromides

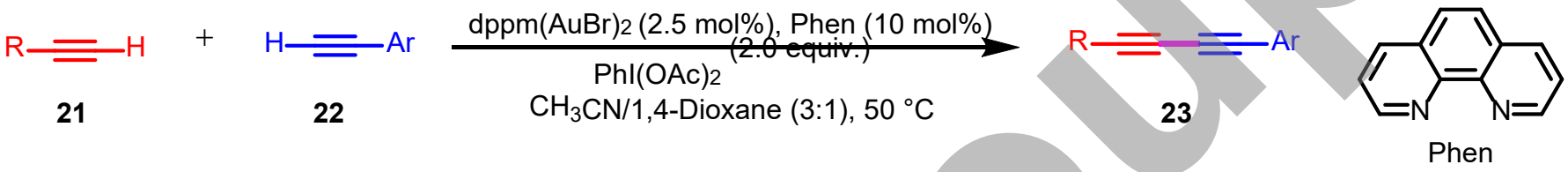


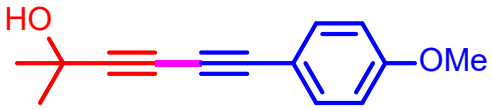


Toste, F. D. et al. *Angew. Chem. Int. Ed.* **2014**, *53*, 6211.

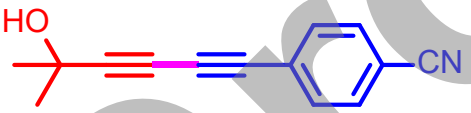
Dinuclear Gold-Catalyzed Coupling Reactions

Dinuclear gold-catalyzed coupling of aliphatic and aromatic alkynes

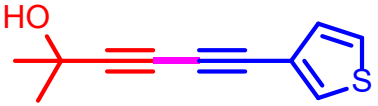




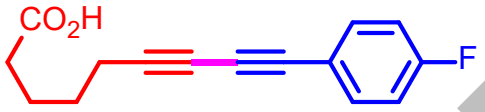
23a, 85%



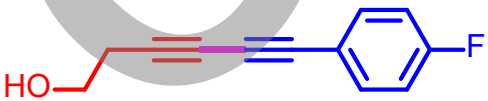
23b, 93%



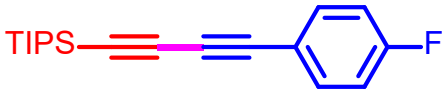
23c, 77%



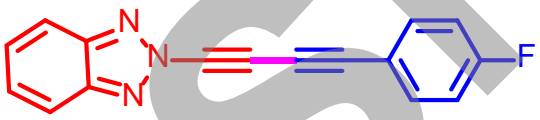
23d, 75%



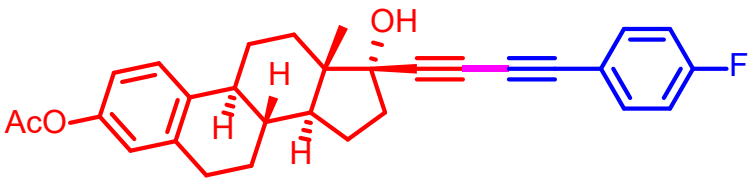
23e, 69%



23f, 90%



23g, 63%

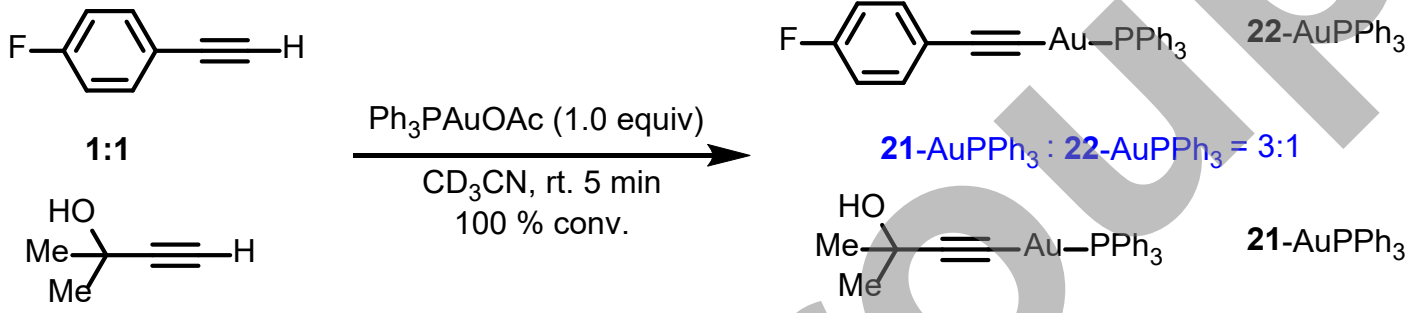


23h, 63%

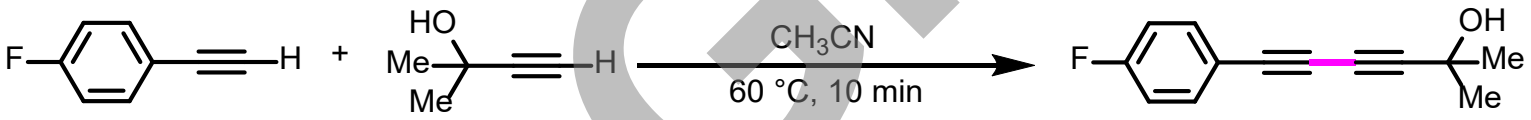
Shi, X. D. et al. *J. Am. Chem. Soc.* **2014**, *136*, 13174.

Dinuclear Gold-Catalyzed Coupling Reactions

Discrimination effect



Stoichiometric reactions

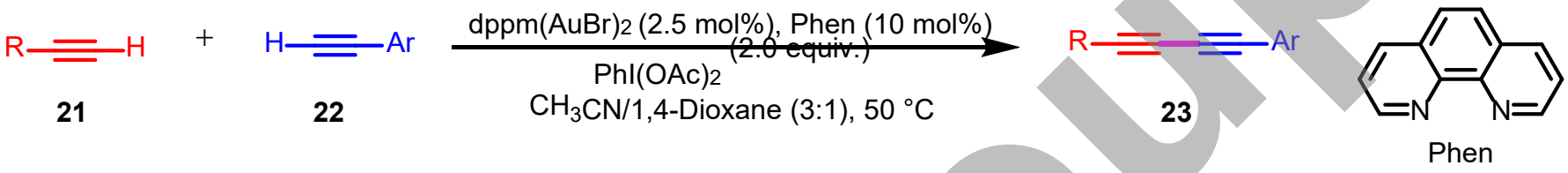


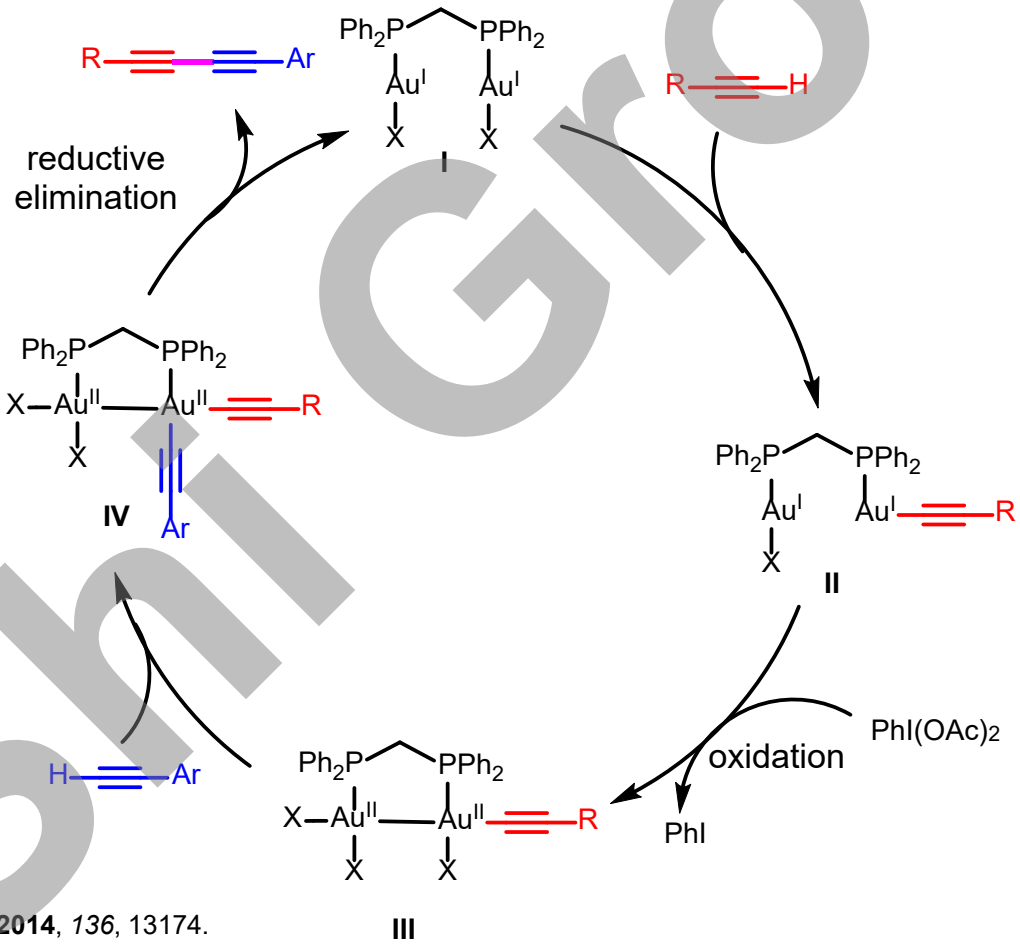
Conditions	Yield [%]	Hetero/homo
standard conditions	83	12:1
A: $AuCl_3$ (1 equiv.)	0	n.a.
B: $AuCl_3$ (1 equiv.), Phen (1 equiv.)	< 5	n.a.
C: $AuCl_3$ (1 equiv.), NaOAc (3 equiv.)	12	2:1
D: $AuCl_3$ (1 equiv.), NaOAc (3 equiv.), Phen (1 equiv.)	65	4:1

Shi, X. D. et al. *J. Am. Chem. Soc.* **2014**, *136*, 13174.

Dinuclear Gold-Catalyzed Coupling Reactions

Dinuclear gold-catalyzed coupling of aliphatic and aromatic alkynes

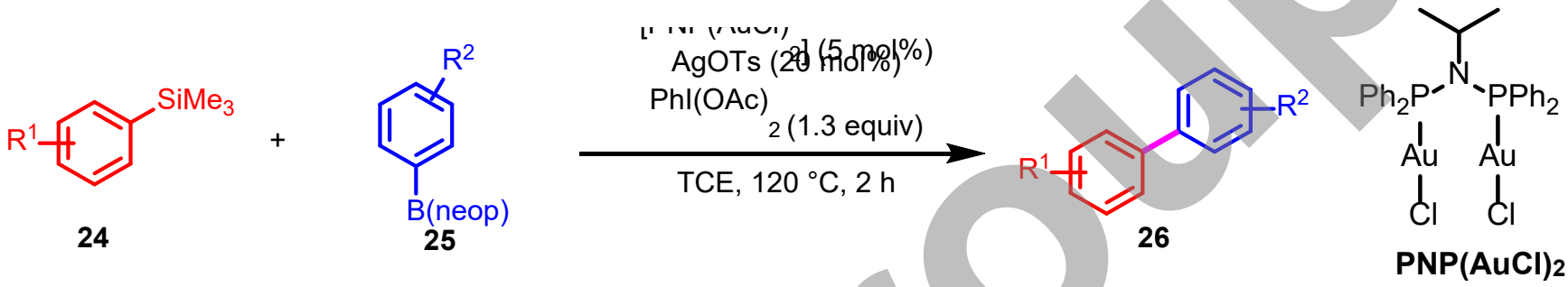


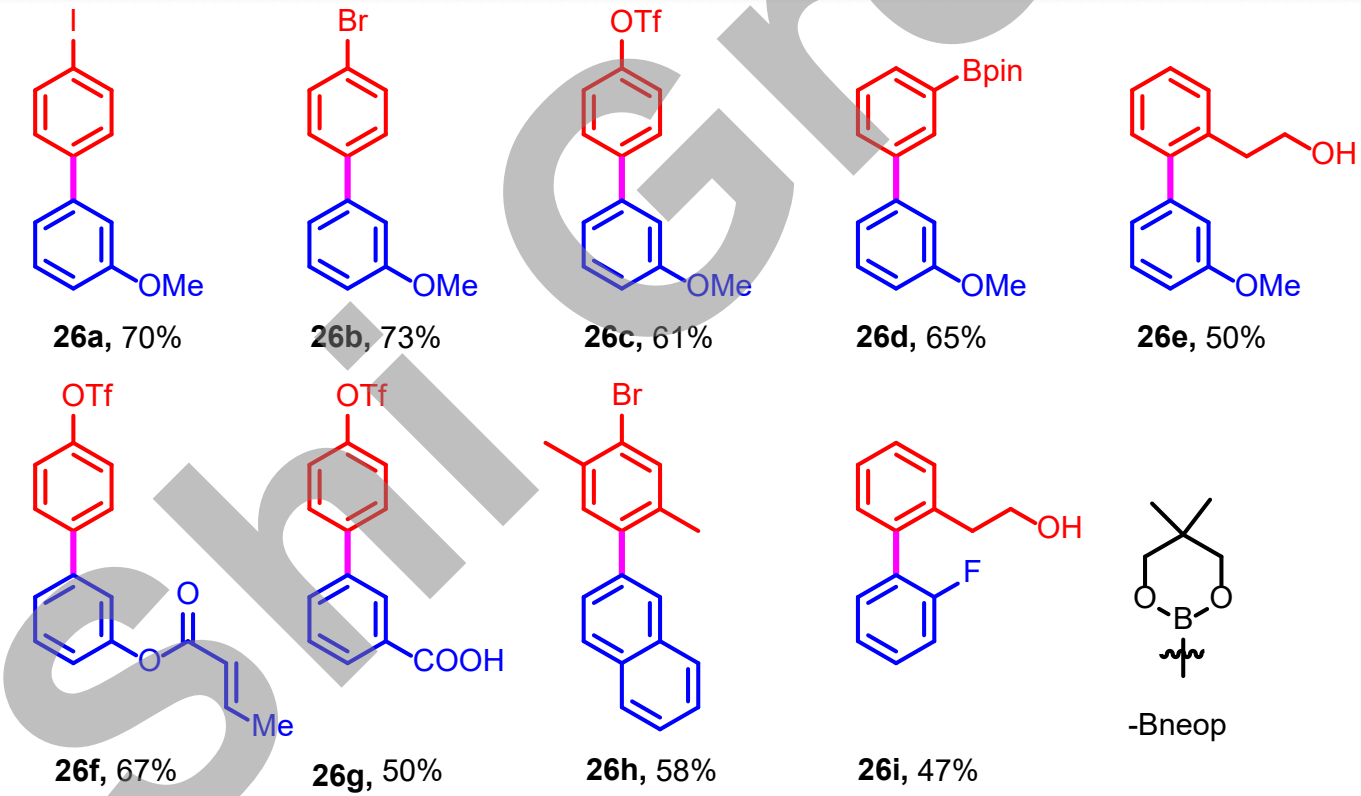


Shi, X. D. et al. *J. Am. Chem. Soc.* **2014**, *136*, 13174.

Dinuclear Gold-Catalyzed Coupling Reactions

Dinuclear gold-catalyzed coupling of arylsilanes and arylboronates

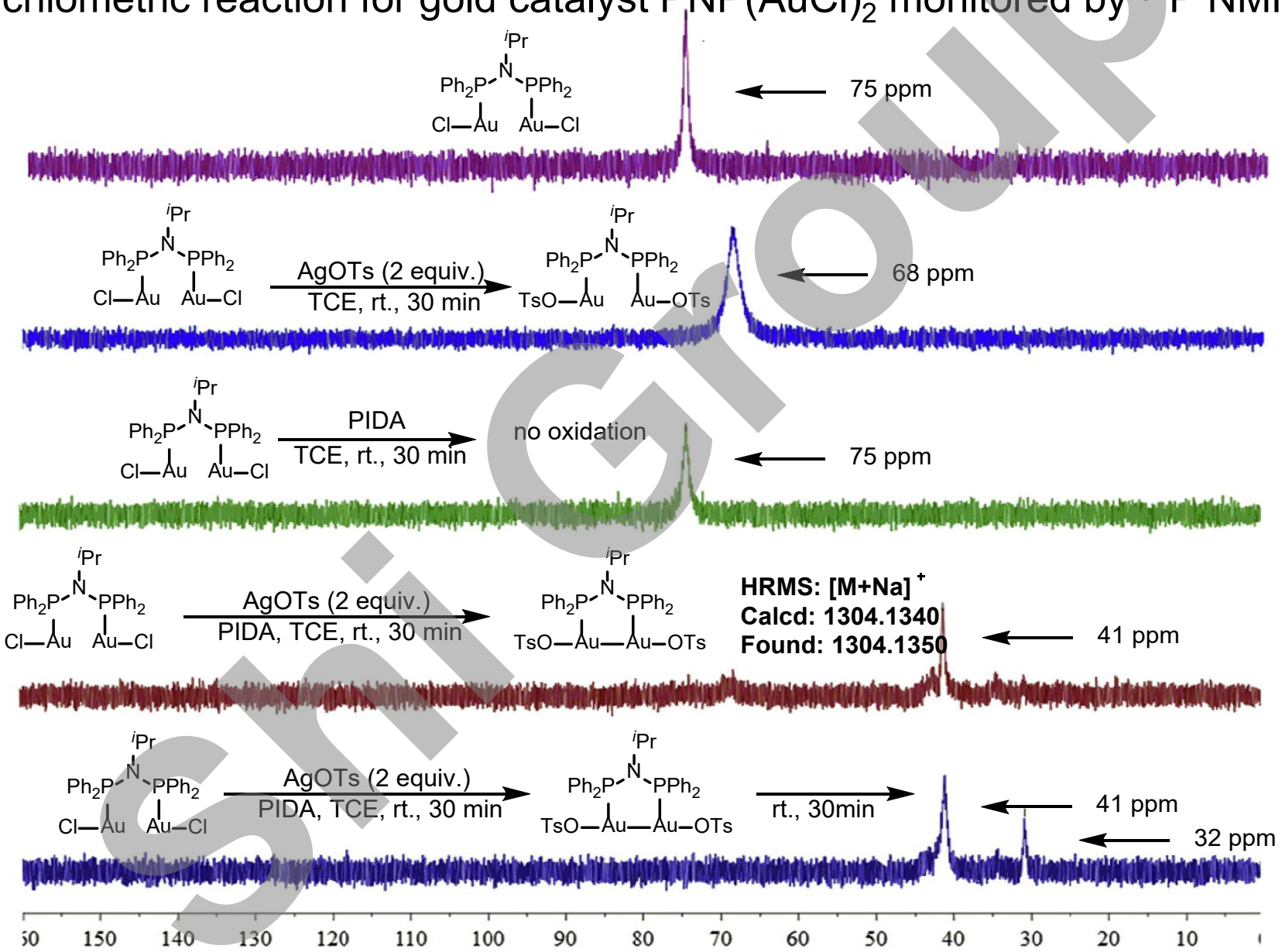




Xie, J. et al. *Chem* **2019**, *5*, 2718.

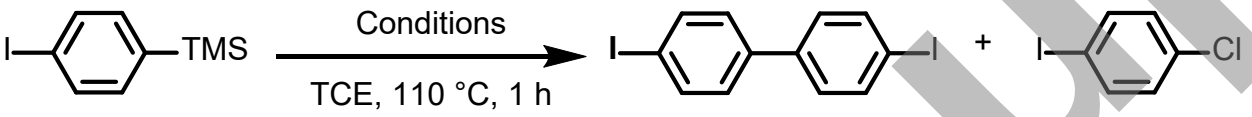
Dinuclear Gold-Catalyzed Coupling Reactions

Stoichiometric reaction for gold catalyst $PNP(AuCl)_2$ monitored by ^{31}P NMR



Dinuclear Gold-Catalyzed Coupling Reactions

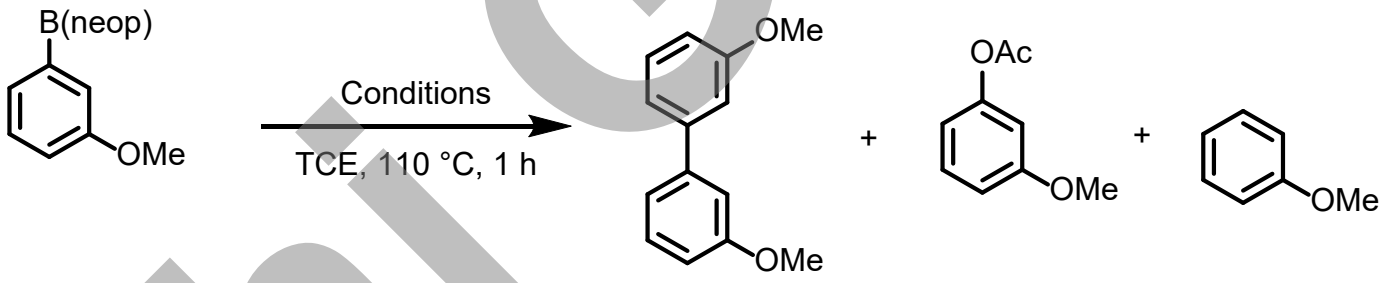
Control experiments with Ph_3PAuCl



a. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.) conversion: 0%

b. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.), $^nBu_4NOAc$ (2.6 equiv.) conversion: 0%

c. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.), PIDA (1.3 equiv.) conversion: 100%



a. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.) conversion: 0%

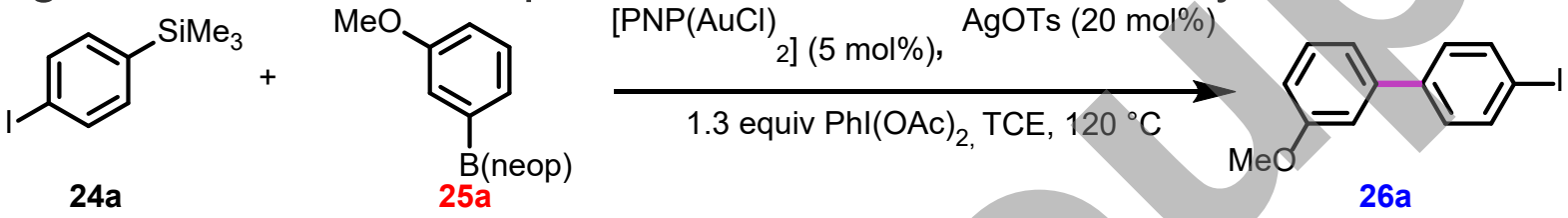
b. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.), $^nBu_4NOAc$ (2.6 equiv.) conversion: 7%

c. Ph_3PAuCl (1 equiv), AgOTs (1.2 equiv.), PIDA (1.3 equiv.) conversion: 56%

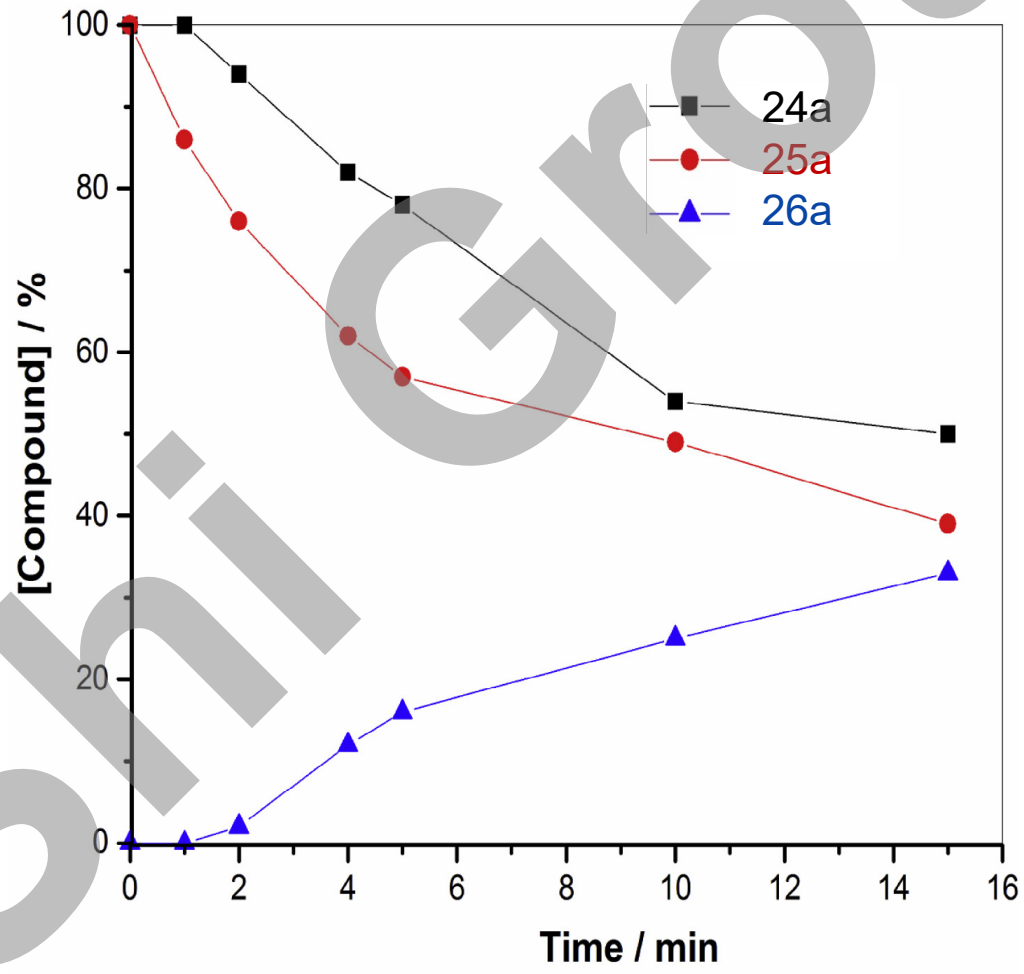
Xie, J. et al. *Chem* **2019**, *5,* 2718.

Dinuclear Gold-Catalyzed Coupling Reactions

Investigation of the consumption of **24a** and **25a** and the yield of **26a**



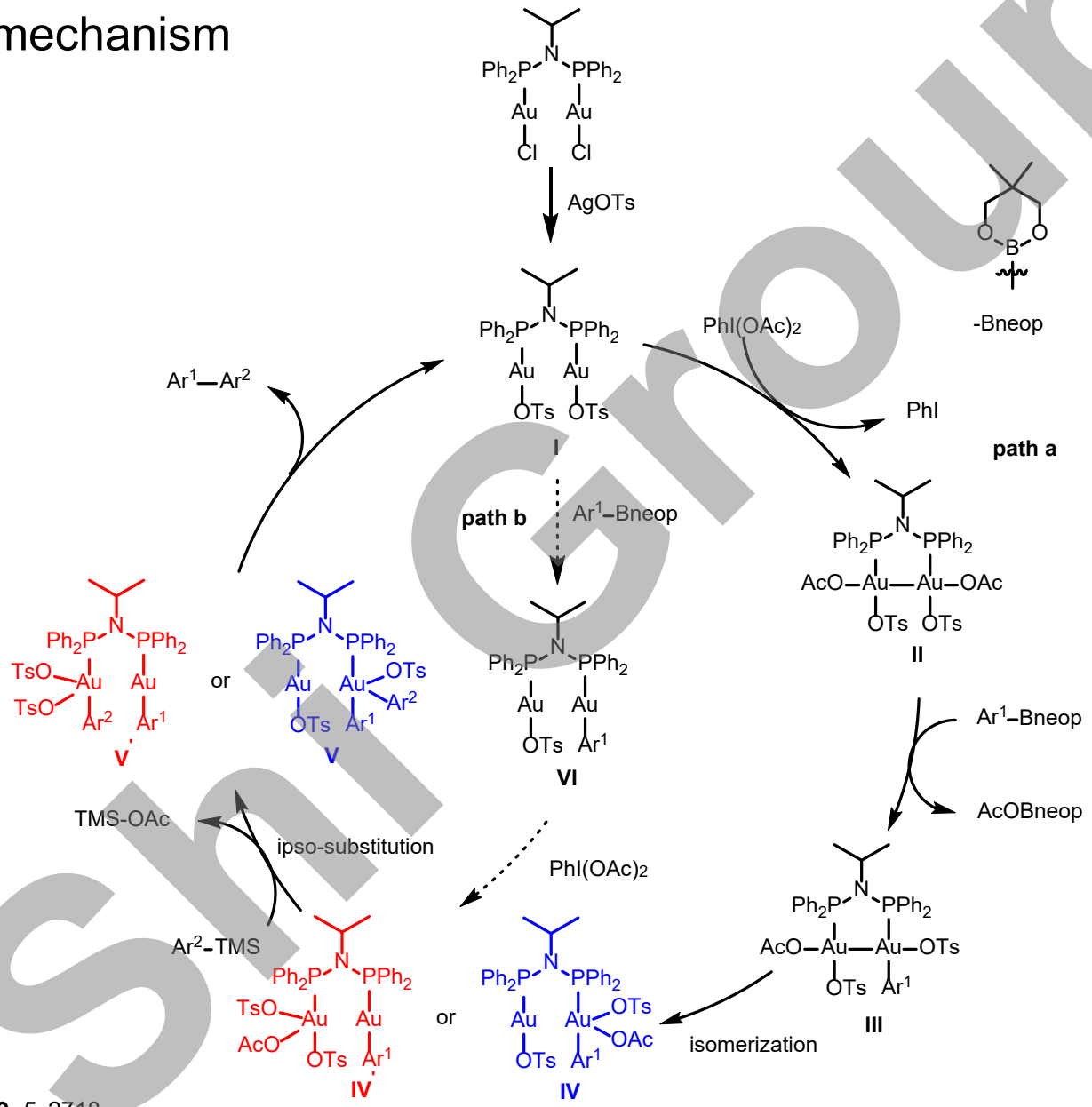
24a **25a** **26a**



Xie, J. et al. *Chem* **2019**, *5*, 2718.

Dinuclear Gold-Catalyzed Coupling Reactions

Proposed mechanism

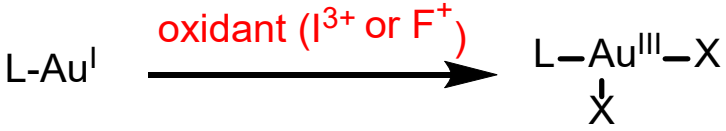


Xie, J. et al. *Chem* **2019**, *5*, 2718.

Background

- Background
- Gold-Catalyzed C-C Coupling Reactions
  - Oxidants-Assisted Coupling Reactions
  - Photo-Assisted Coupling Reactions
  - Dinuclear Gold-Catalyzed Coupling Reactions
- Summary

Summary



- Direct functionalization
- High regioselectivity
- High FG tolerance

Aryl radicals (diazonium salts)

- Dual role of oxidizing agent and substrate
- +I → +II → +III (Gold)

Dinuclear gold catalysis

Aurophilic interaction between the two gold atoms can reduce its redox potential

Thanks!