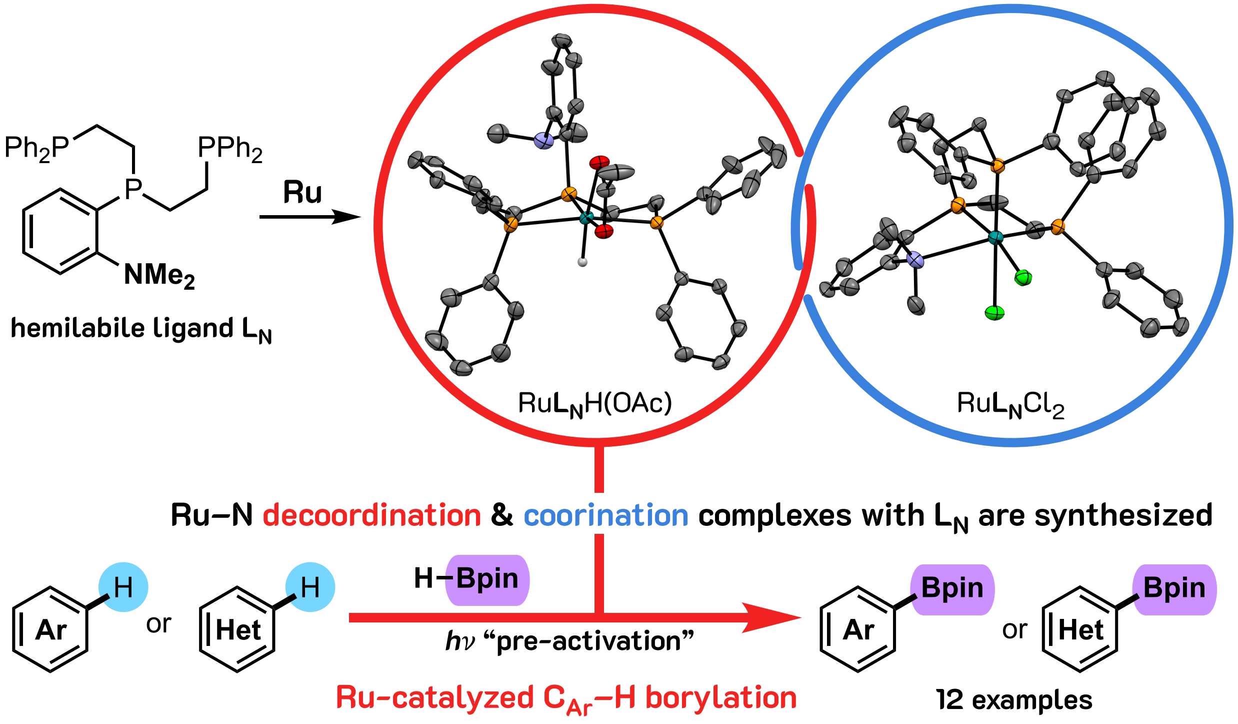
DalPhos-Au Complexes and Their Reactivities

MR May 07th 2024

Yumeng Liao, D3

Inspiration

Hemilabile ligand-supported Ru complexes (My master's work at Iwasawa lab)

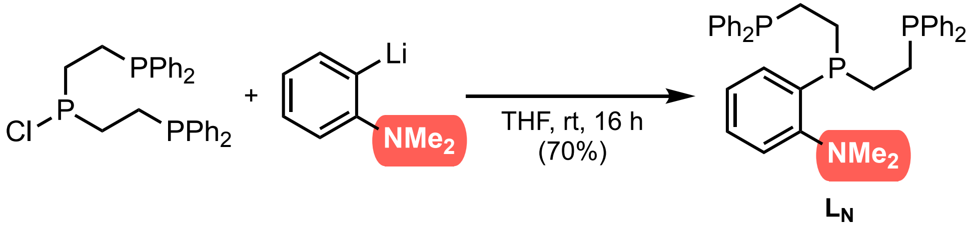


Ru–N decoordination & coorination complexes with L_N are synthesized

Ru-catalyzed C_{Ar}–H borylation

12 examples

N,N-dimethylamino group: flexible substituent in hemilabile ligand

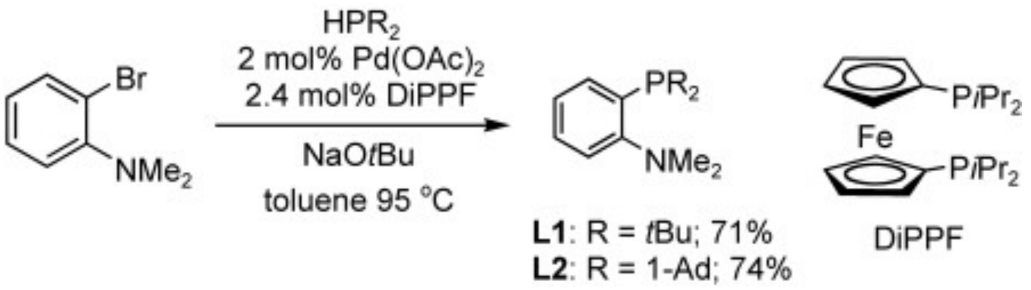


L_N

Background

Why “DalPhos”?

Chem. Eur. J. **2010**, *16,* 1983



A Highly Versatile Catalyst System for the Cross-Coupling of Aryl Chlorides and Amines

Rylan J. Lundgren, Antonia Sappong-Kumankumah, and Mark Stradiotto*[a]

DalPhos: **Phos**phine developed by chemists

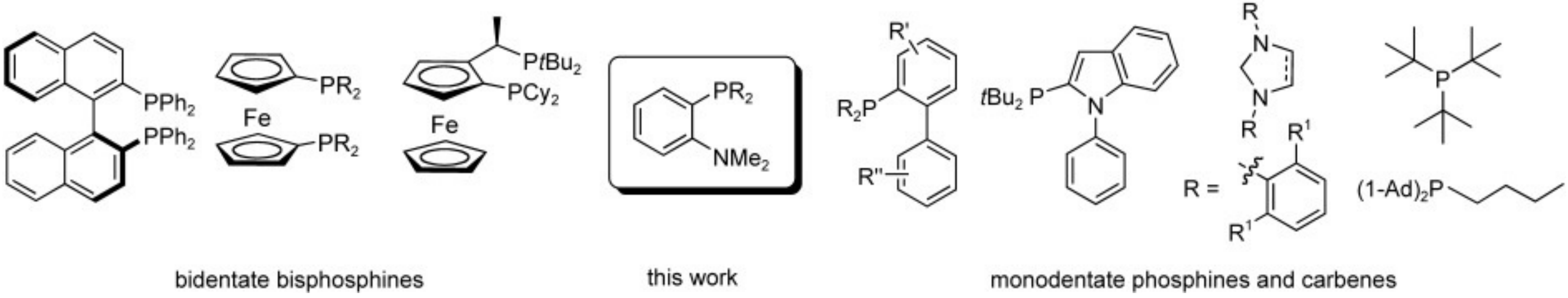
from **Dal**housie University

Prof. Mark Stradiotto

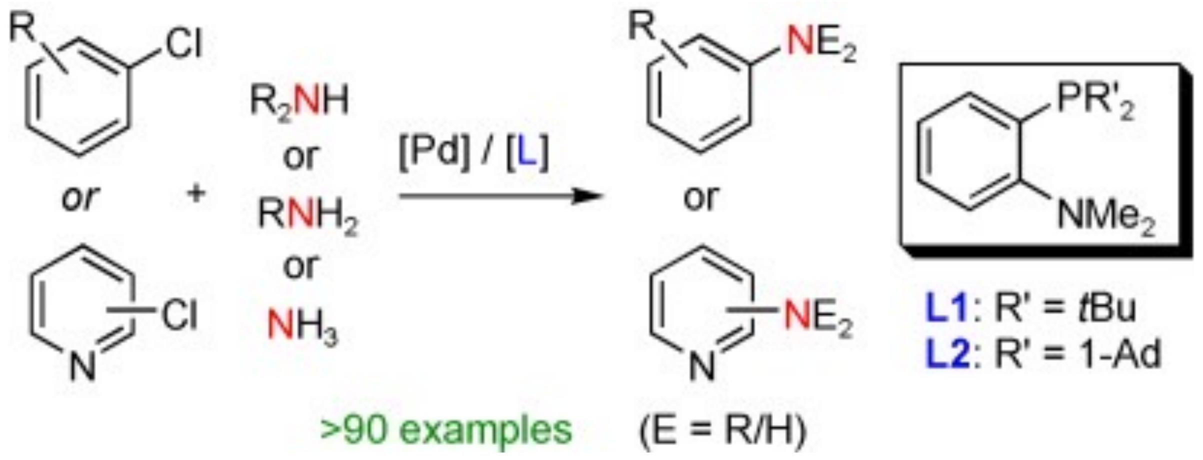
DALHOUSIE
UNIVERSITY
Inspiring Minds

1st Example Using DalPhos

Same catalytic reactivity with bidentate & monodentate ligands



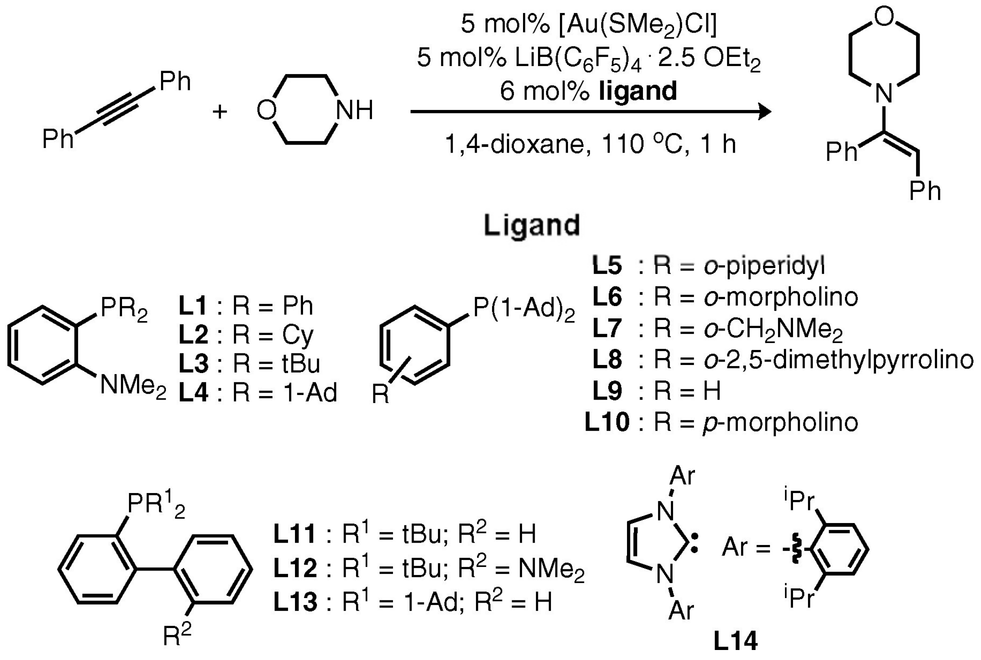
Pd-catalysed cross-coupling

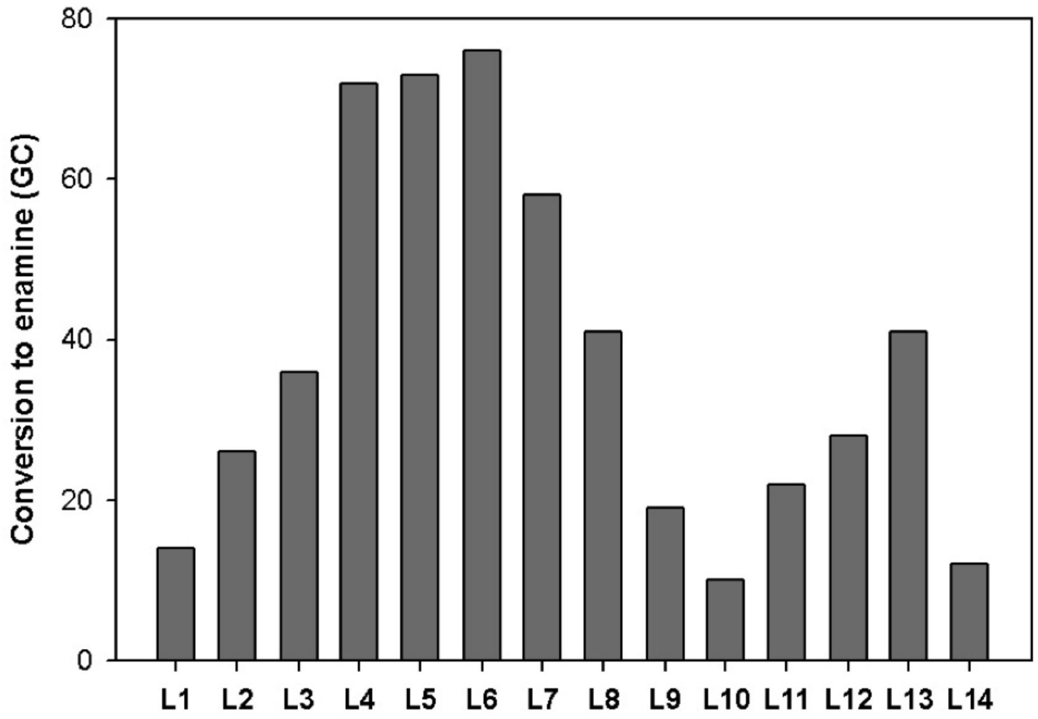


Chem. Eur. J. **2010**, *16,* 1983.

DalPhos-Au Complex Hydroamination of alkyne

Ligand screening





Substituents at phosphino group

1-Ad substituent gives best performance

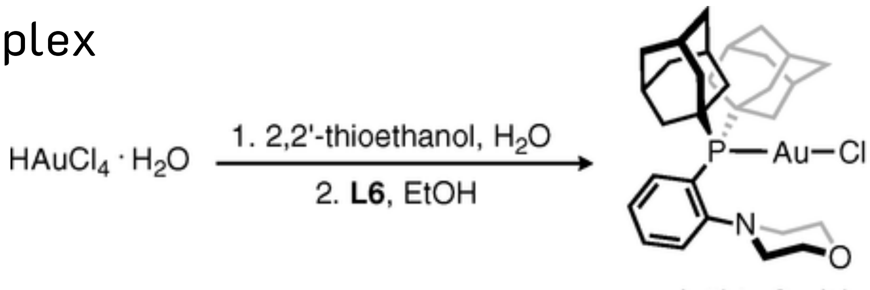
Substituents at aniline ring

o-substituent all performed well (*o*-morpholino is the best)

J. Am. Chem. Soc. **2010**, *132*, 18026.

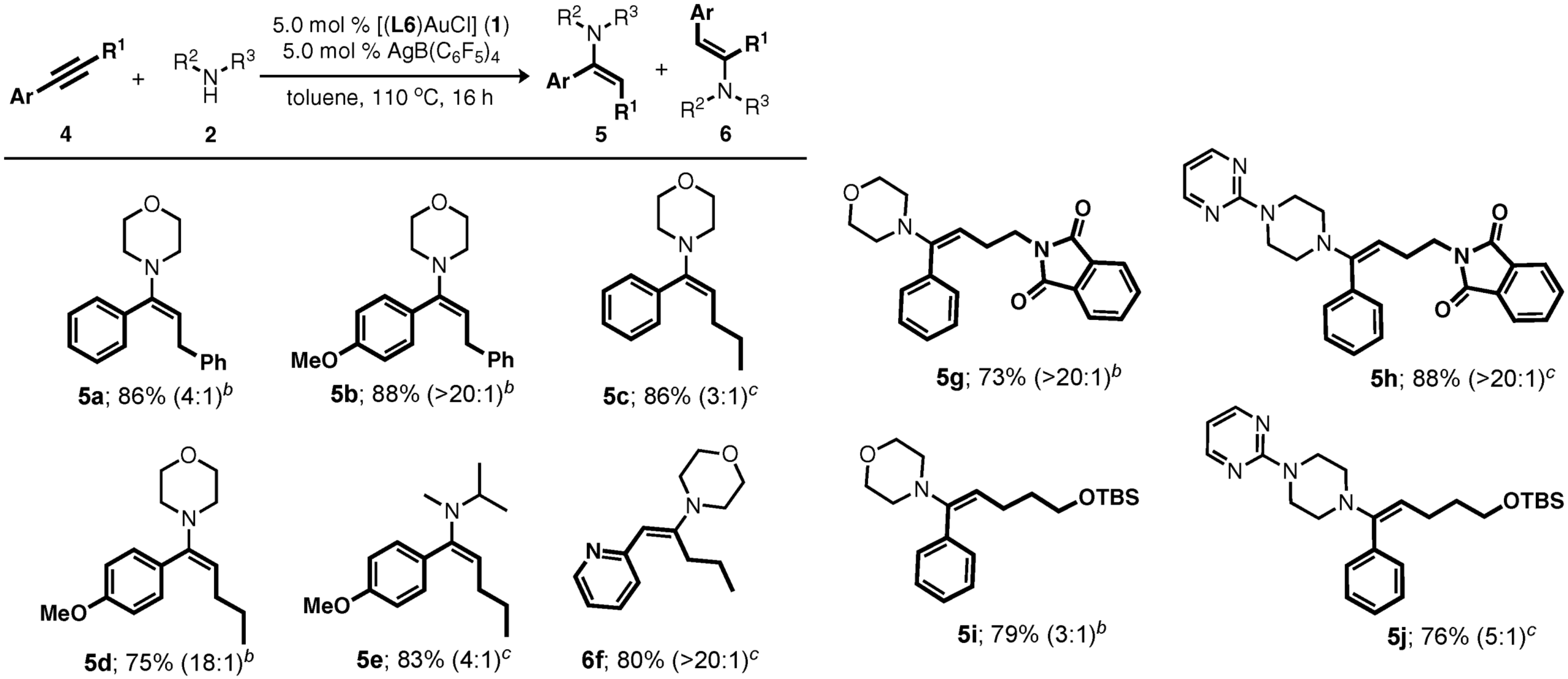
DalPhos-Au Complex | Hydroamination of alkyne

Synthesis of **L6**-Au complex



[(**L6**)AuCl] (**1**)

Same catalytic reactivity with bidentate & monodentate ligands



5a; 86% (4:1)^b

5b; 88% (>20:1)^b

5c; 86% (3:1)^c

5g; 73% (>20:1)^b

5h; 88% (>20:1)^c

5d; 75% (18:1)^b

5e; 83% (4:1)^c

6f; 80% (>20:1)^c

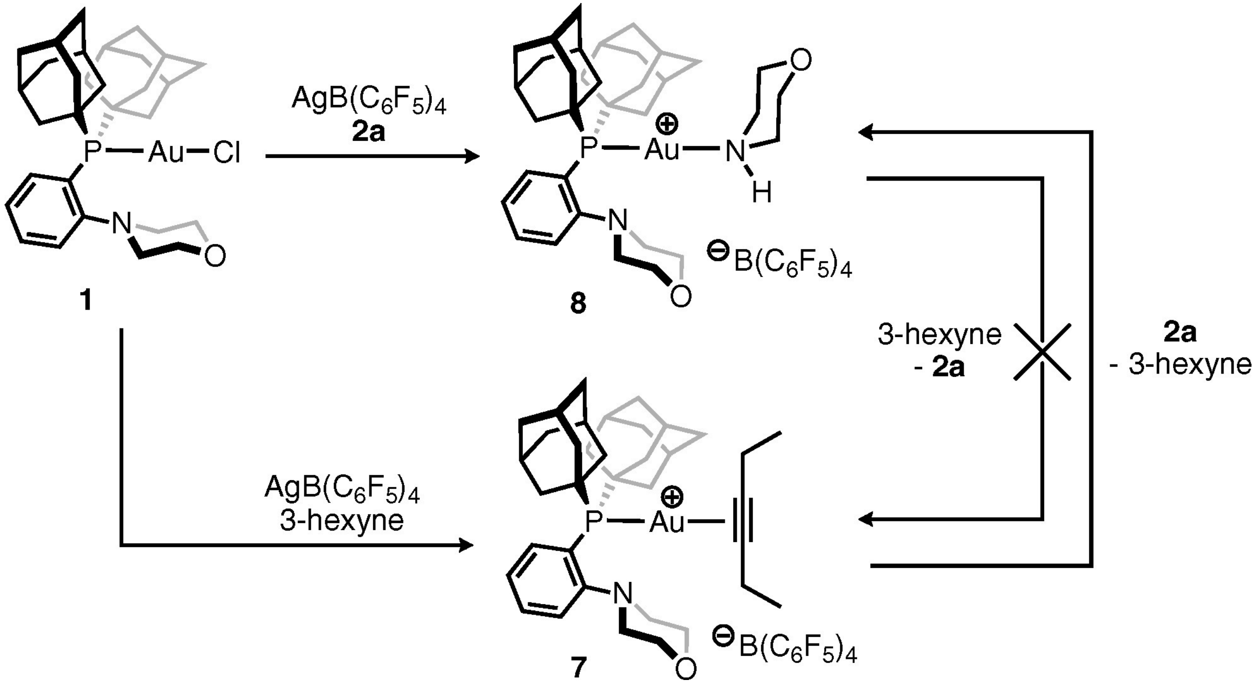
5i; 79% (3:1)^b

5j; 76% (5:1)^c

J. Am. Chem. Soc. **2010**, *132,* 18026.

Hydroamination of alkyne

Stochiometric reaction of **1** with $AgB(C_6F_5)_4$ & **2a** or 3-hexyne



***L6** is acting as a monodentate phosphine ligand*

No hemilabile feature was observed

J. Am. Chem. Soc. **2010**, *132*, 18026.

Oxidative Addition to Au(I) Background

Why OA to Au(I) is difficult?

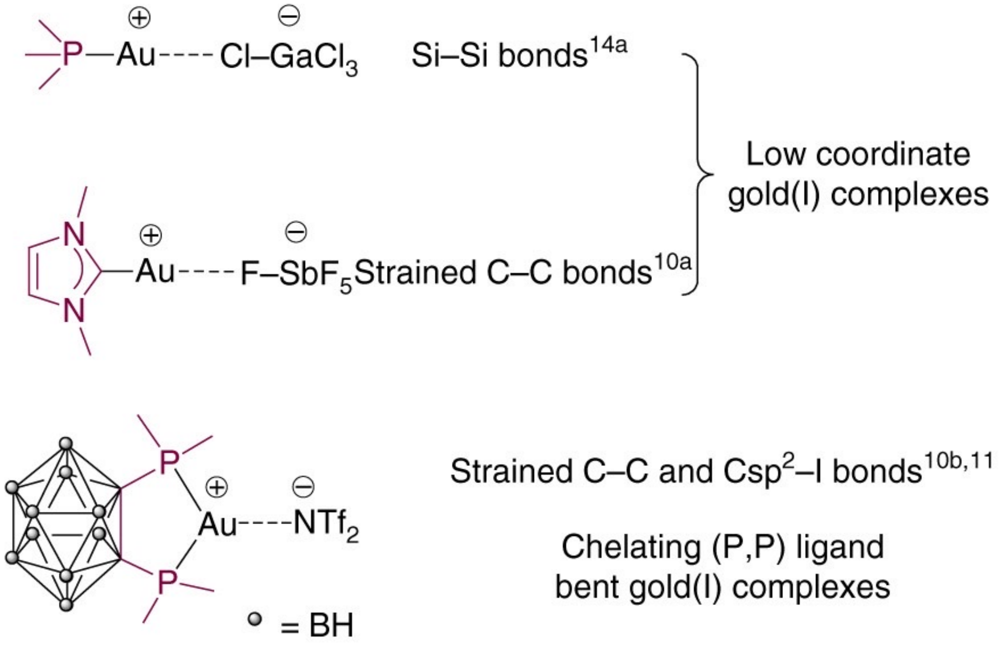
Standard Electrode Potentials and Temperature Coefficients at rt (298.15 K)

Acid solutions (pH = 0.000)	E^0 (V)
Pd^{2+}/Pd (c)	0.915
Pt^{2+}/Pt (c)	1.18
Au^{3+}/Au^{+}	1.41

High redox potential

J. Phys. Chem. Ref. Data **1989**, *18,* 1.

Intramolecular OA to cationic Au(I) complex (stoichiometric)



Si–Si bonds[14a]

Strained C–C bonds[10a]

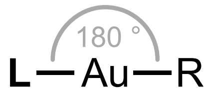
Low coordinate gold(I) complexes

Strained C–C and Csp^2–I bonds[10b,11]

Chelating (P,P) ligand
bent gold(I) complexes

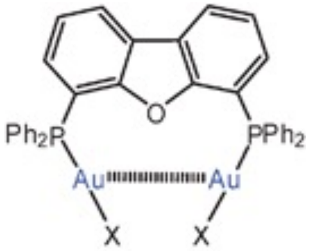
Oxidative Addition to Au(I) | Linear-Prefered Au(I)

Au(I) complex: preference in linear structure

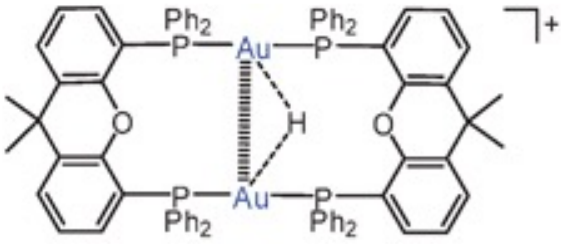


Linear structure of Au(I) complex

*If **L** is bidentate…*
Binuclear structures:



75



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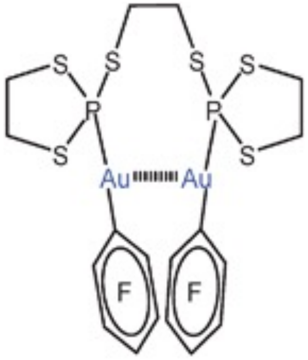

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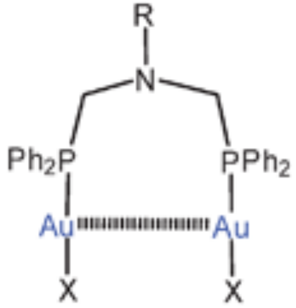

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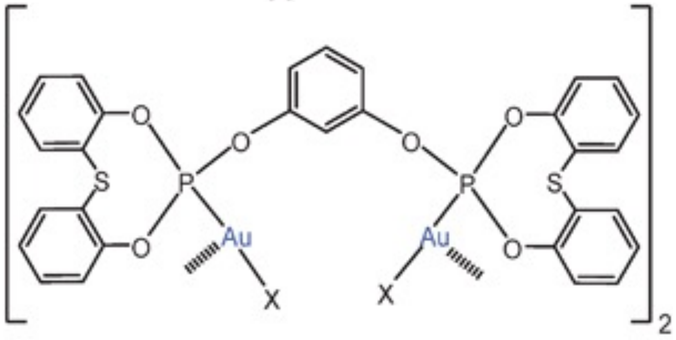

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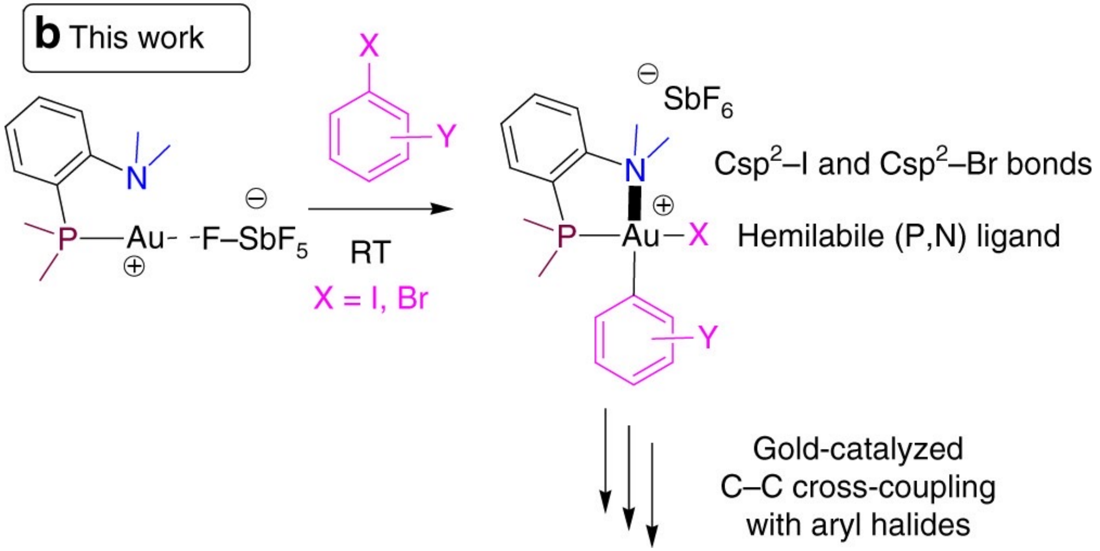
Chem. Soc. Rev. **2011**, *41*, 370.

Introduction of hemilabile DalPhos ligand



Csp^2–I and Csp^2–Br bonds

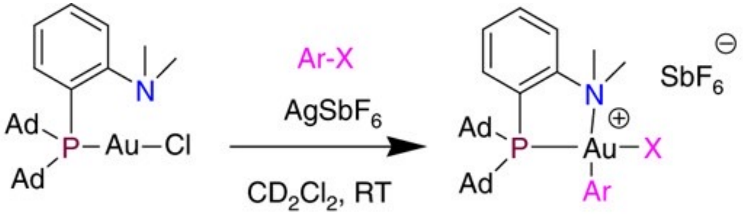
Hemilabile (P,N) ligand

Gold-catalyzed
C–C cross-coupling
with aryl halides

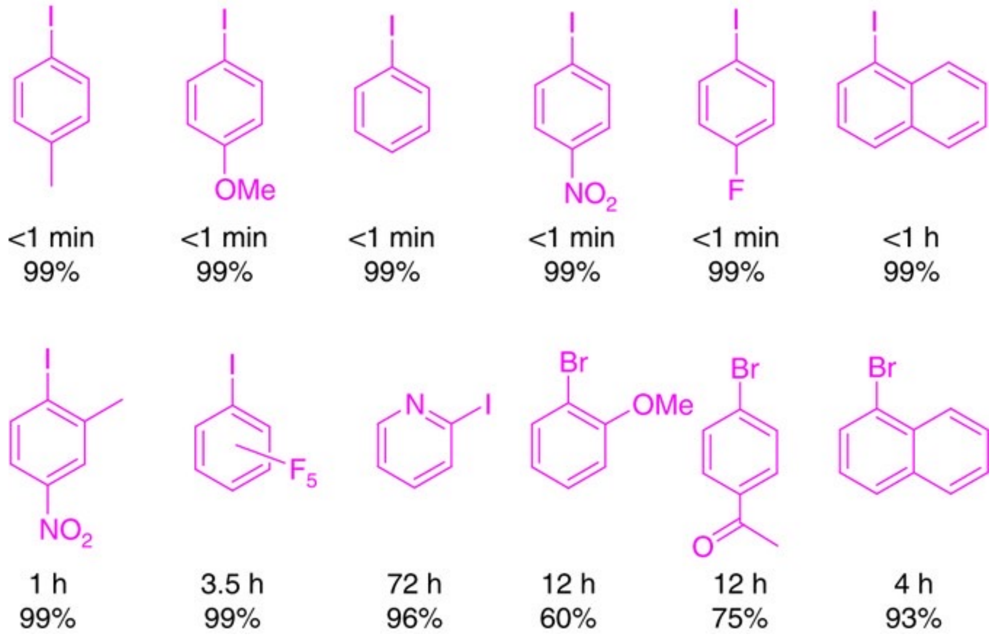
Nat. Commun. **2017**, *8*, 565.

Oxidative Addition to Au(I) | Reactivity

Oxidative addition to DalPhos-Au(I) complex



With Ar–X bond

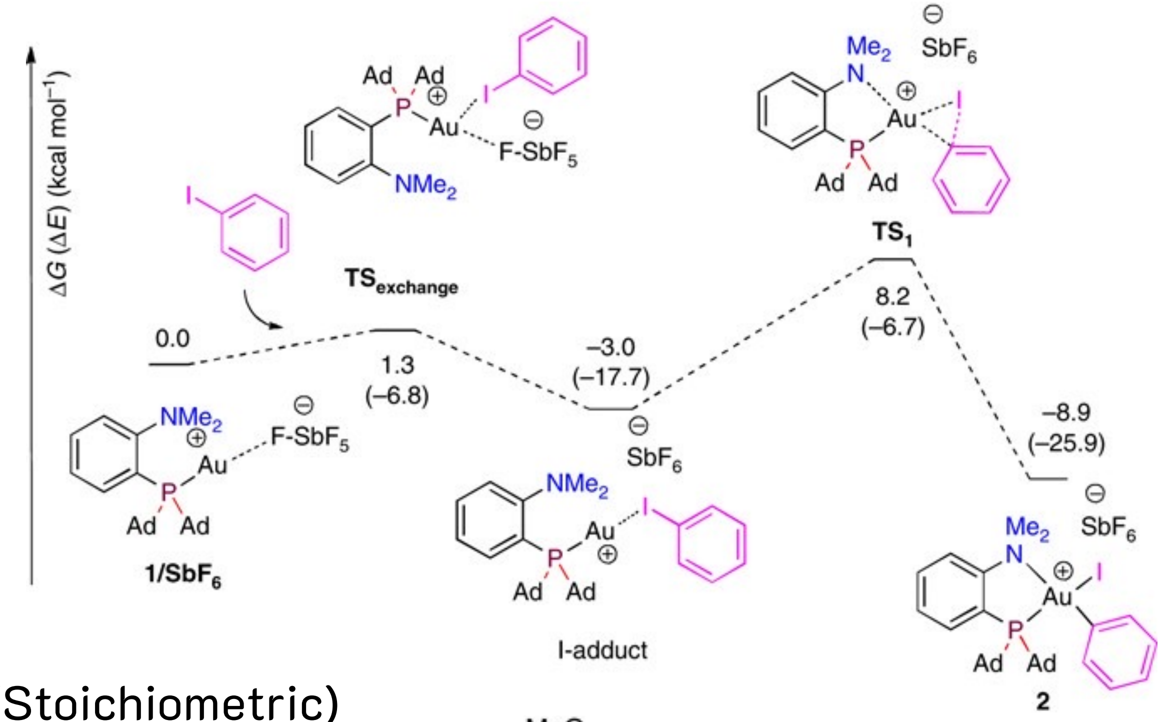


With strained C–C bond

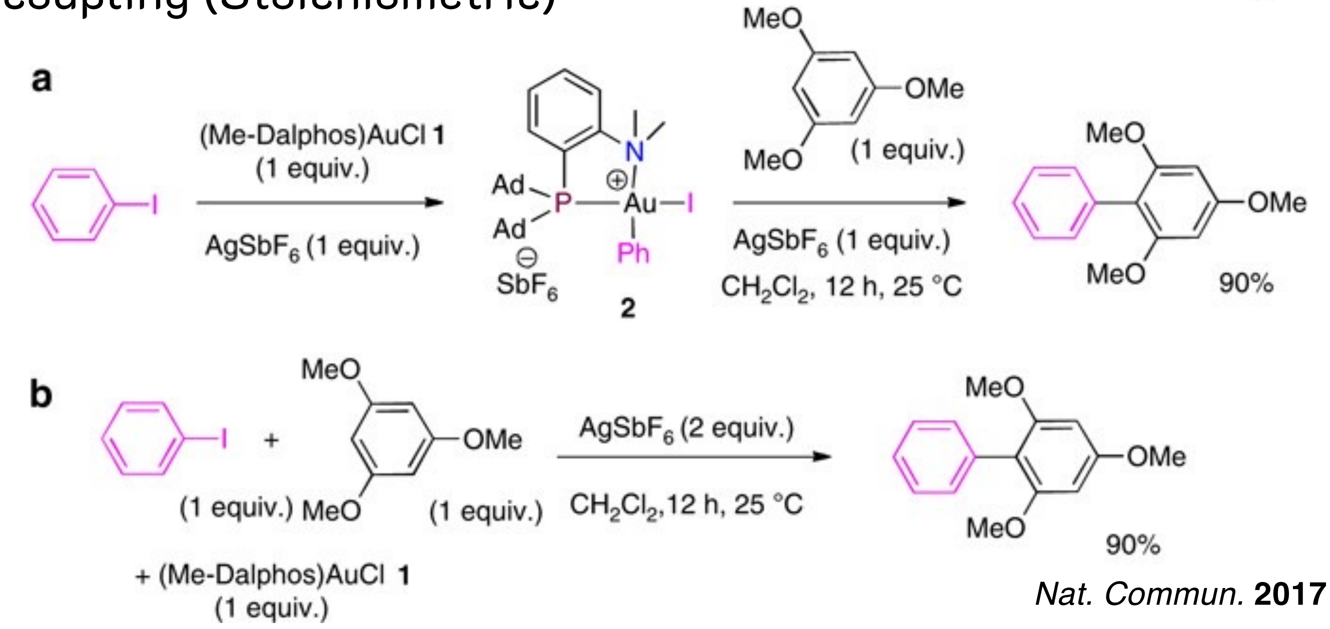
Nat. Commun. **2017**, *8*, 565.

Oxidative Addition to Au(I) Reactivity

DFT study on OA to DalPhos-Au(I)



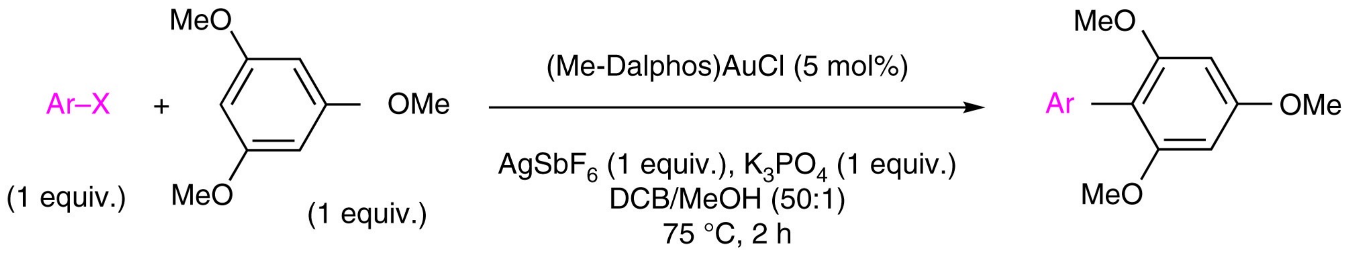
Au(III)-mediated C_{Ar}–C_{Ar} coupling (Stoichiometric)

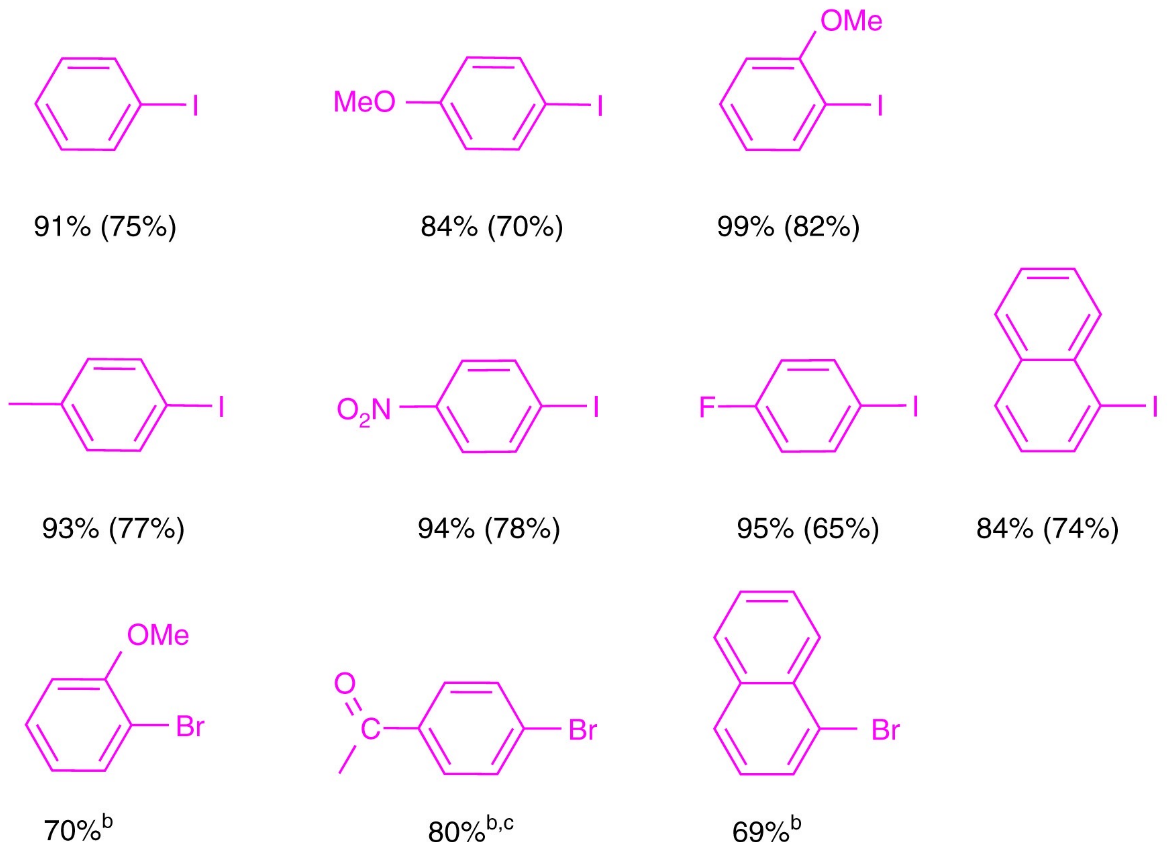


Nat. Commun. **2017**, *8*, 565.

Oxidative Addition to Au(I) | Reactivity

Au(III)-mediated C_{Ar}–C_{Ar} coupling (CATALYTIC)

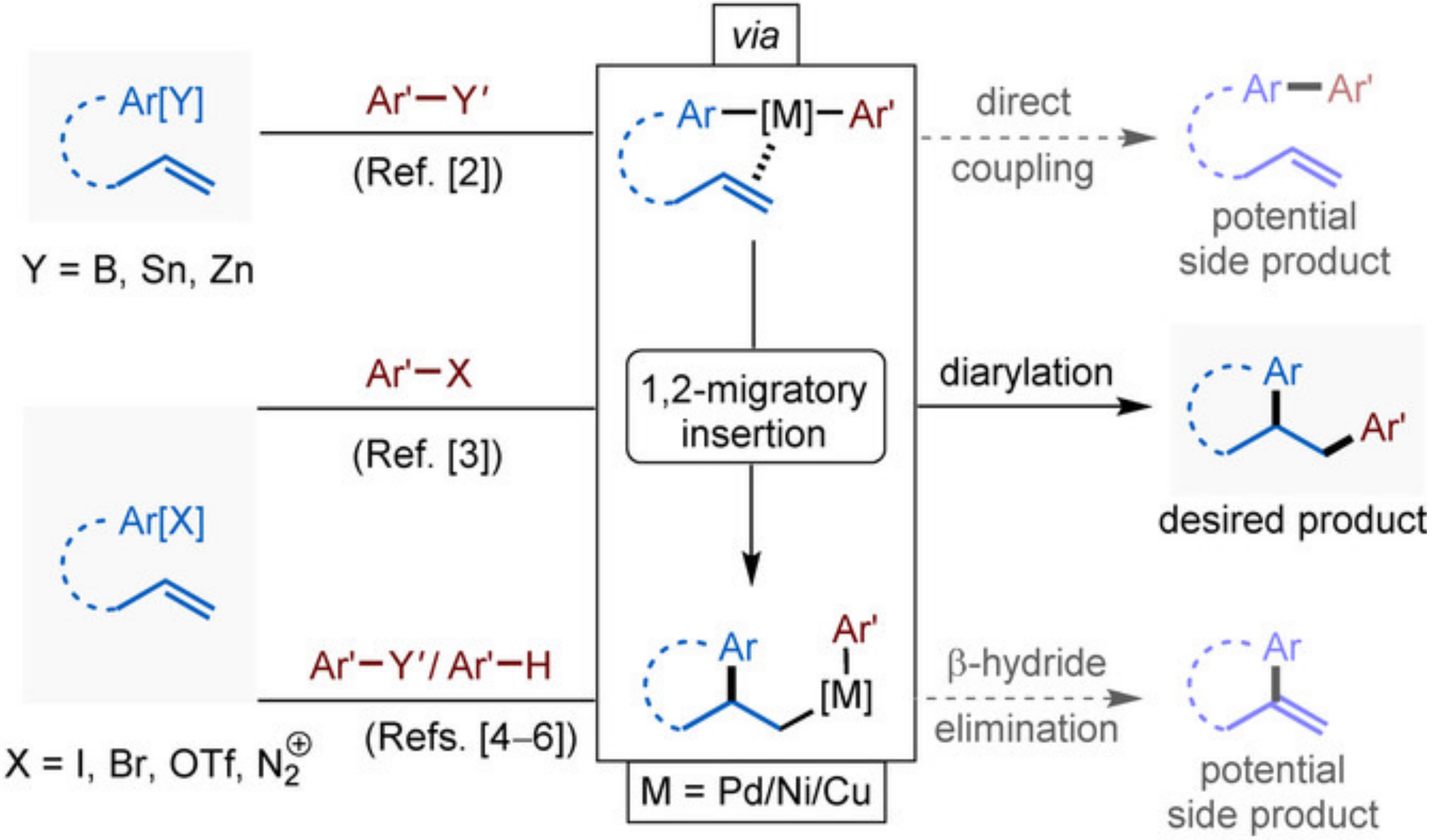




Nat. Commun. **2017**, *8*, 565.

1,2-Diarylation of Alkene | Background

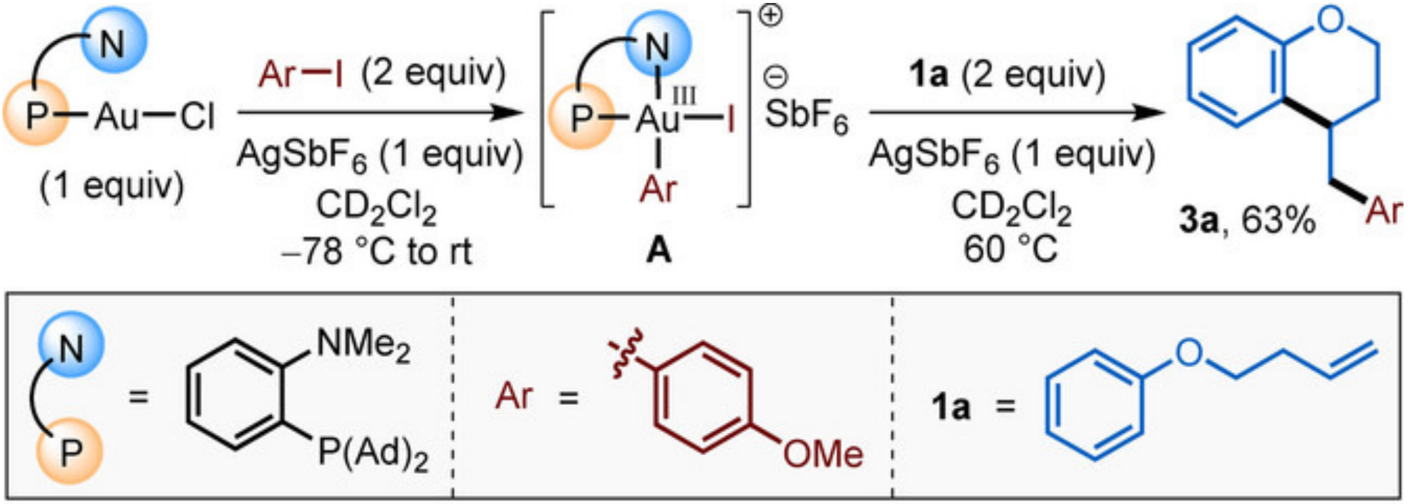
Migratory insertion approach to 1,2-diarylation of alkene (***known***)



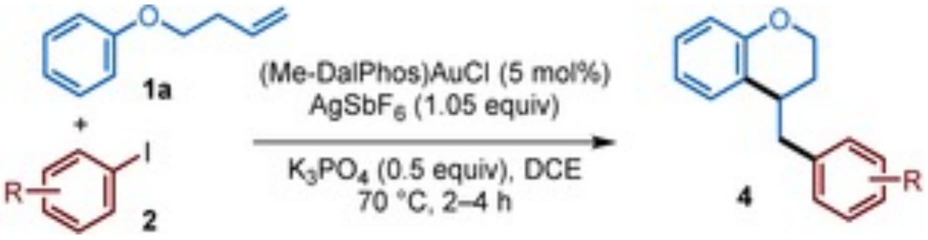
Angew. Chem. Int. Ed. **2020**, *59*, 11808.

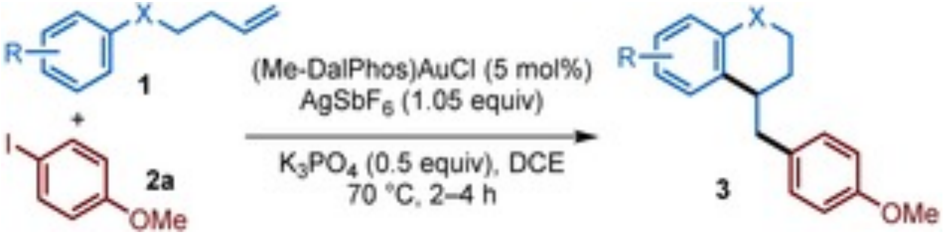
1,2-Diarylation of Alkene Reaction

Stoichiometric 1,2-diarylation of alkene



Catalytic 1,2-diarylation of alkene





Wide substrate scope of alkene and aryl halide.

EDG-, EWG-substituted arene ring, heteroarene ring, natural product derived ring etc.

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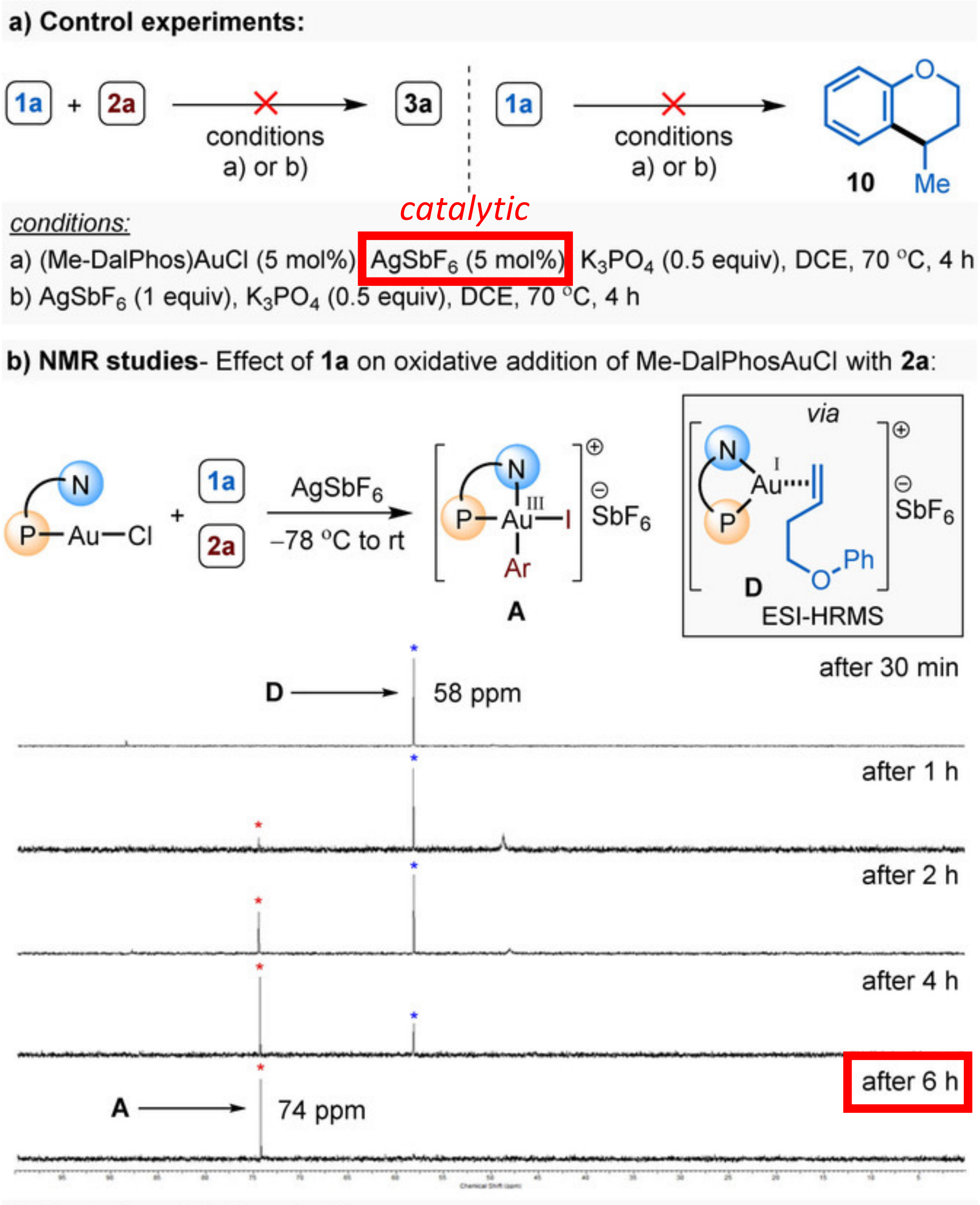
1,2-Diarylation of Alkene

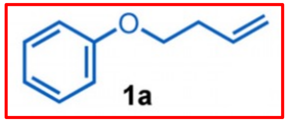
Mechanistic Study (1)

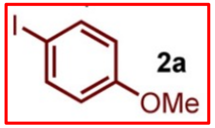


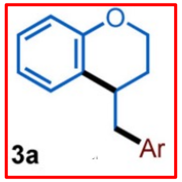
conditions:

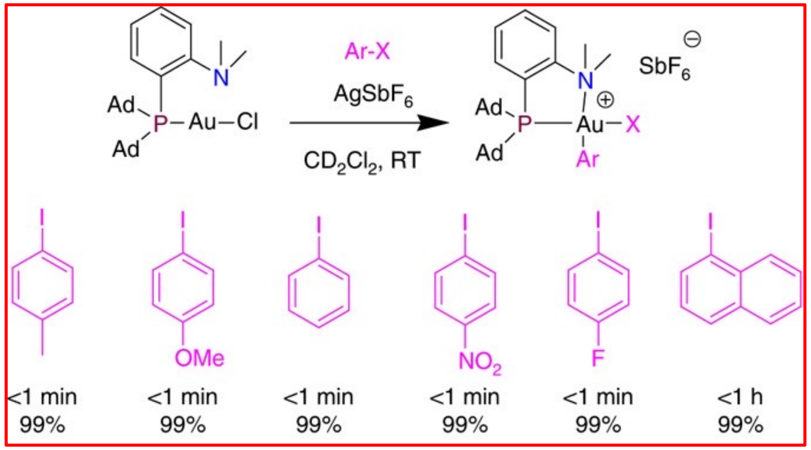
a) (Me-DalPhos)AuCl (5 mol%) AgSbF$_6$ (5 mol%) K$_3$PO$_4$ (0.5 equiv), DCE, 70 °C, 4 h

b) AgSbF$_6$ (1 equiv), K$_3$PO$_4$ (0.5 equiv), DCE, 70 °C, 4 h









*In the absence of **1a**, the OA of Ar–X (**2a**) to Au(I) is instantaneous*

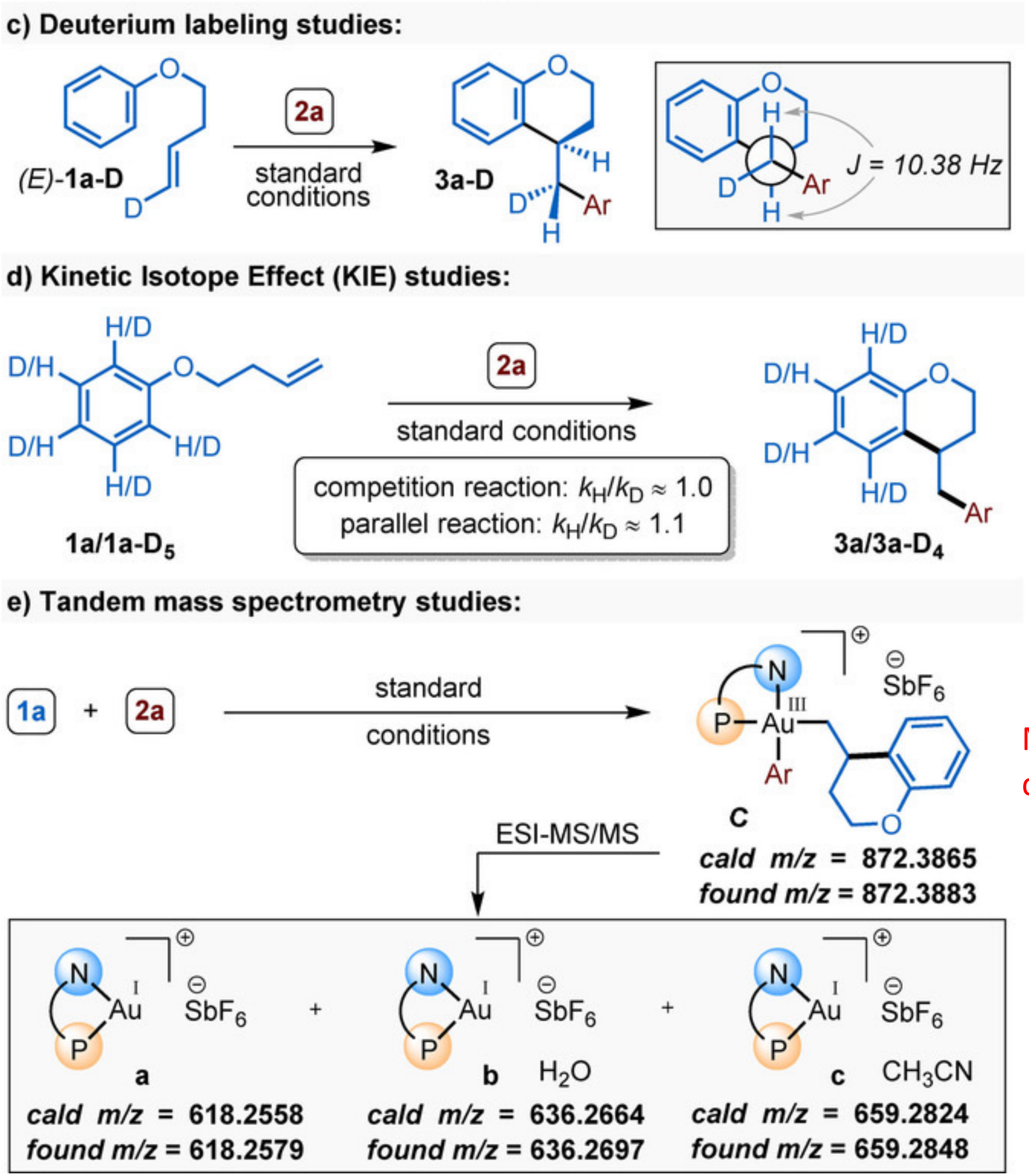
Nat. Commun. **2017**, *8*, 565.

*Full conversion to **A** (OA of **2a** to Au)requires long time in the presence of **1a***

Angew. Chem. Int. Ed. **2020**, *59*, 11808.

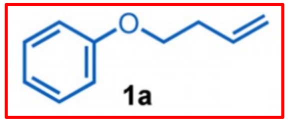
1,2-Diarylation of Alkene

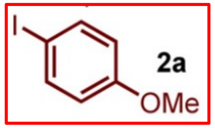
Mechanistic Study (2)

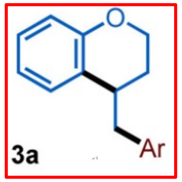


Structure of **3a-D**:
anti addition of Ar group.

Supporting a S_EAr reaction for the carboauration of alkene


1a


2a


3a

Mass-spectroscopically detectable intermediate **C**

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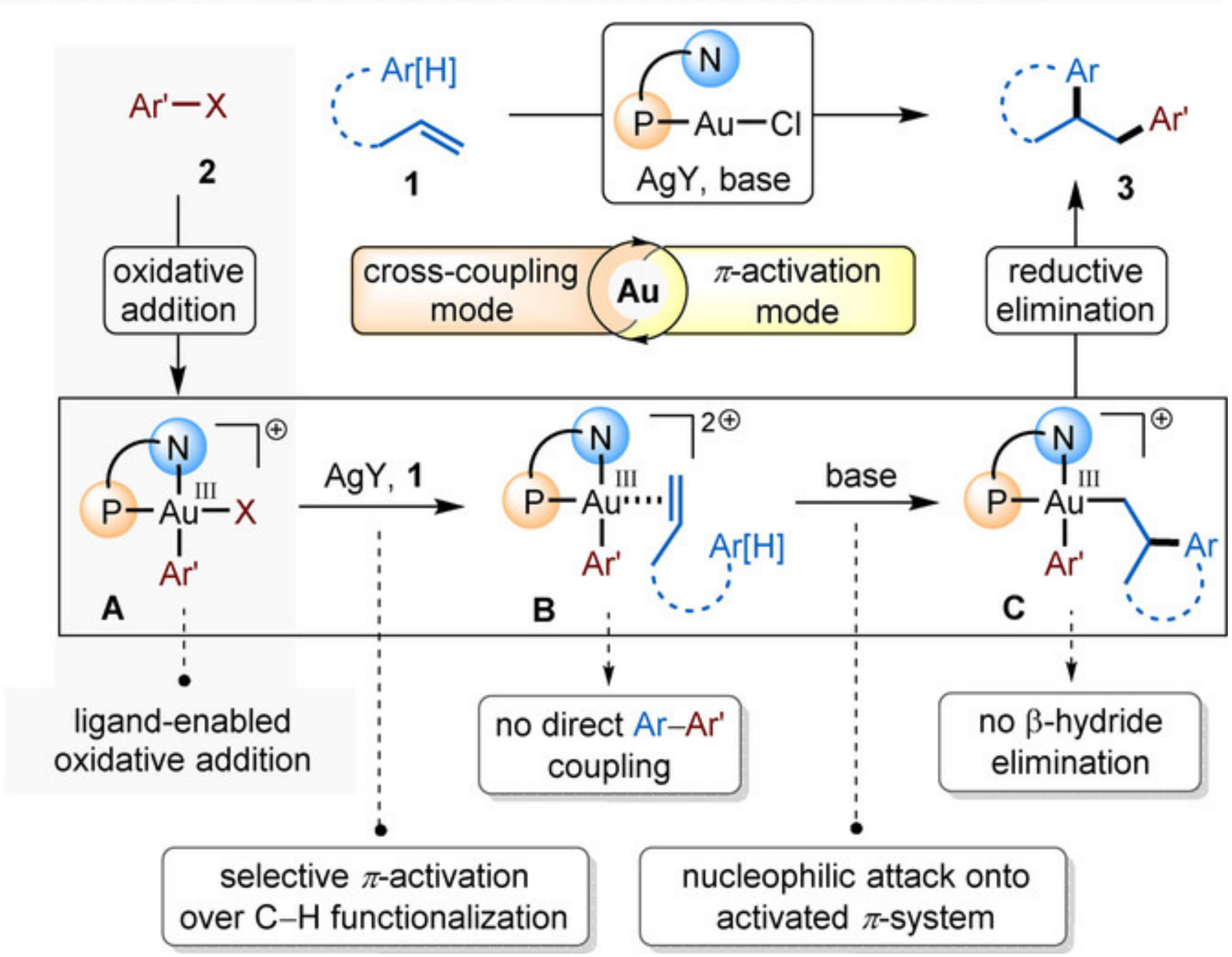
1,2-Diarylation of Alkene

Proposed mechanism



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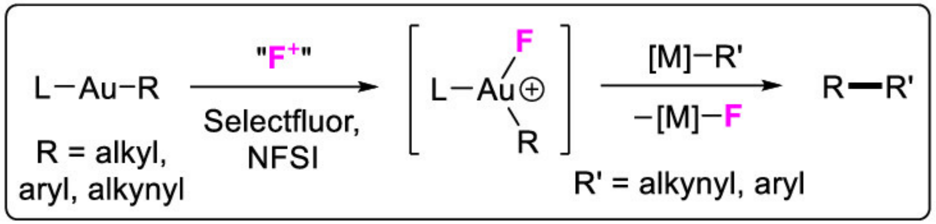
Au(III)-Mediated Aryl–F Coupling | Background

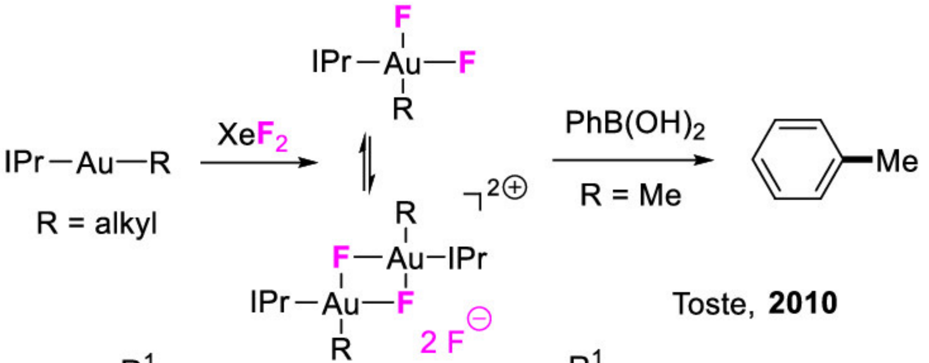
General procedure for oxidative coupling at Au with F^+



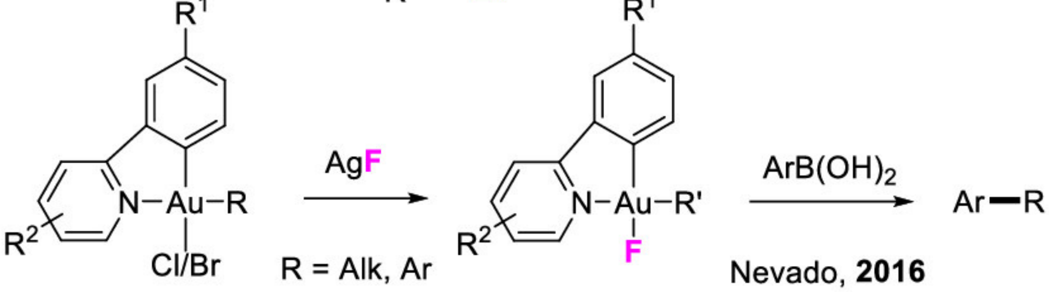
Difficulty on characterisation & isolation of Au(III)

Isolated Au(III) fluoride complexes undergoing C–C cross-coupling

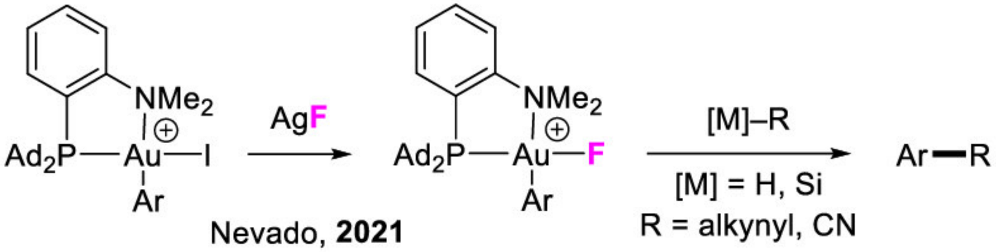
Oxidation



Halide exchange



Halide exchange

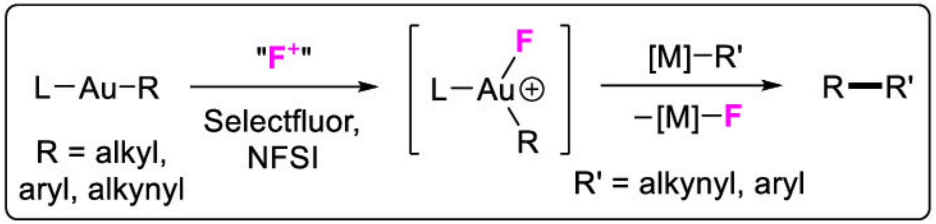


J. Am. Chem. Soc. **2024**, *146*, 11352.

Au(III)-Mediated Aryl–F Coupling

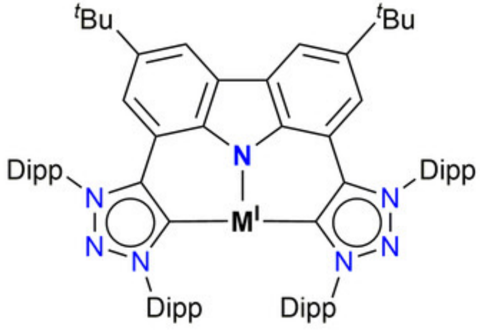
Background

Reason for the less study on oxidative fluorination of Au(I)

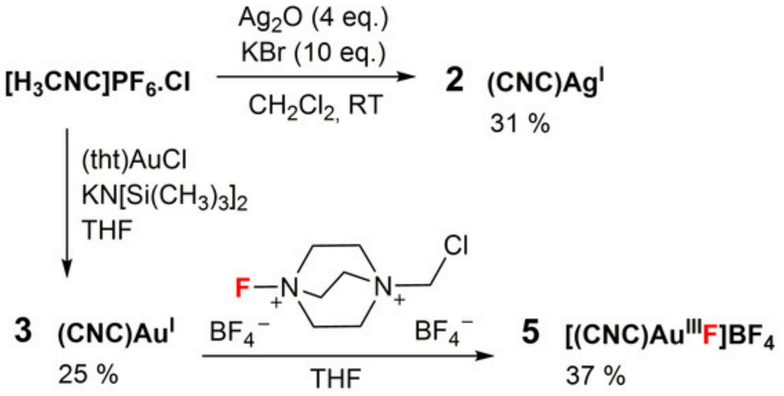


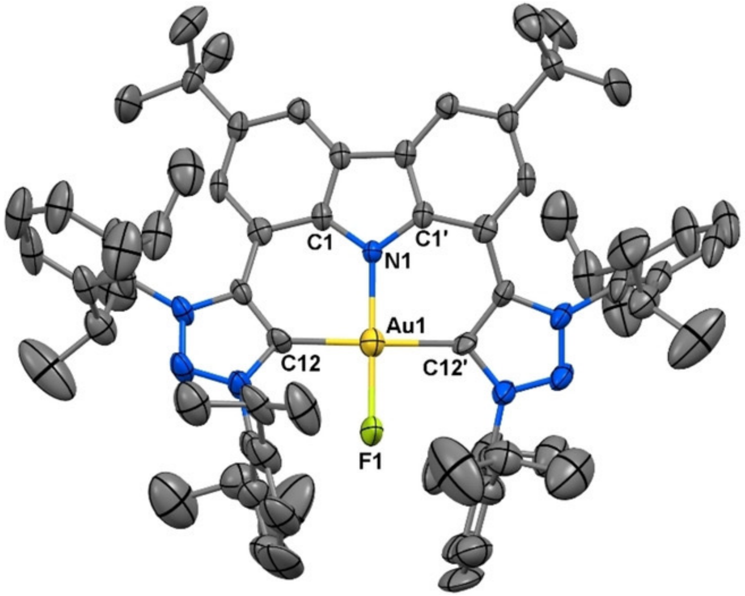
Coordinatively unsaturated

Coordinative saturation? (CNC pincer ligand)



3 (**M** = Au)



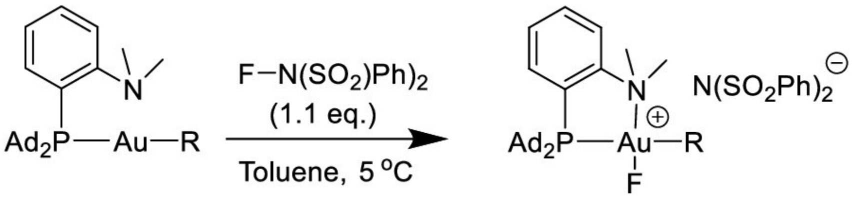


ORTEP of **5**

Chem. Eur. J. **2020**, *26,* 6993.

Au(III)-Mediated Aryl–F Coupling

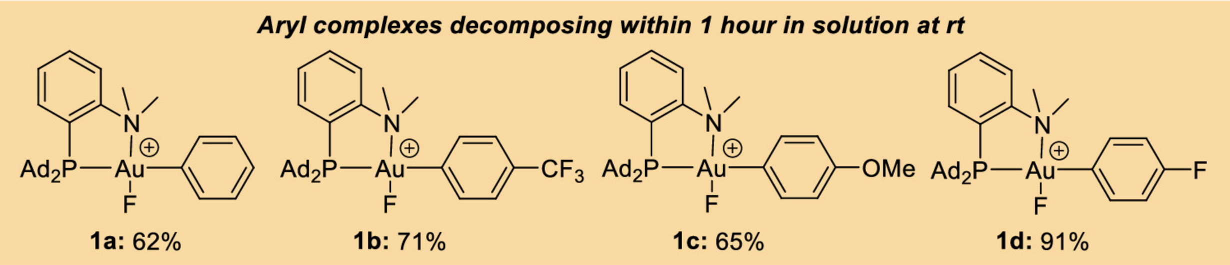
Employment of hemilabile DalPhos ligand



Hemilabile ligand-assisted saturated coordination

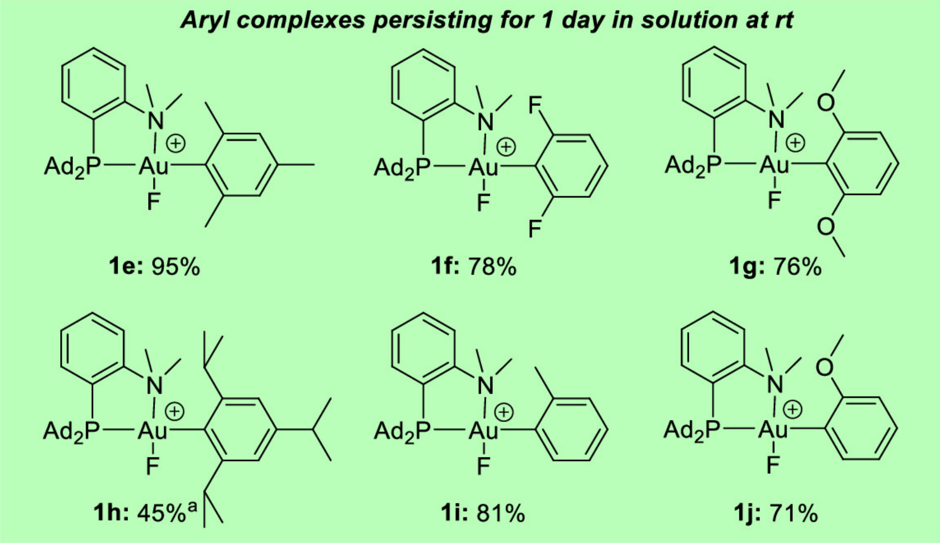
Successful isolation of F–Au(III)–R complexes,

R = aryl, alkyl



Aryl complexes decomposing within 1 hour in solution at rt

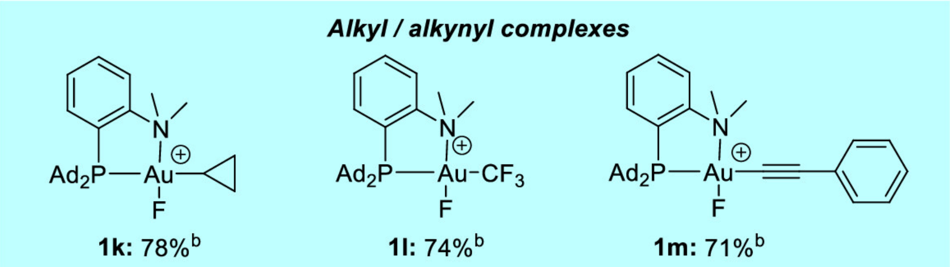
1a: 62%　**1b**: 71%　**1c**: 65%　**1d**: 91%



Aryl complexes persisting for 1 day in solution at rt

1e: 95%　**1f**: 78%　**1g**: 76%

1h: 45%[a]　**1i**: 81%　**1j**: 71%



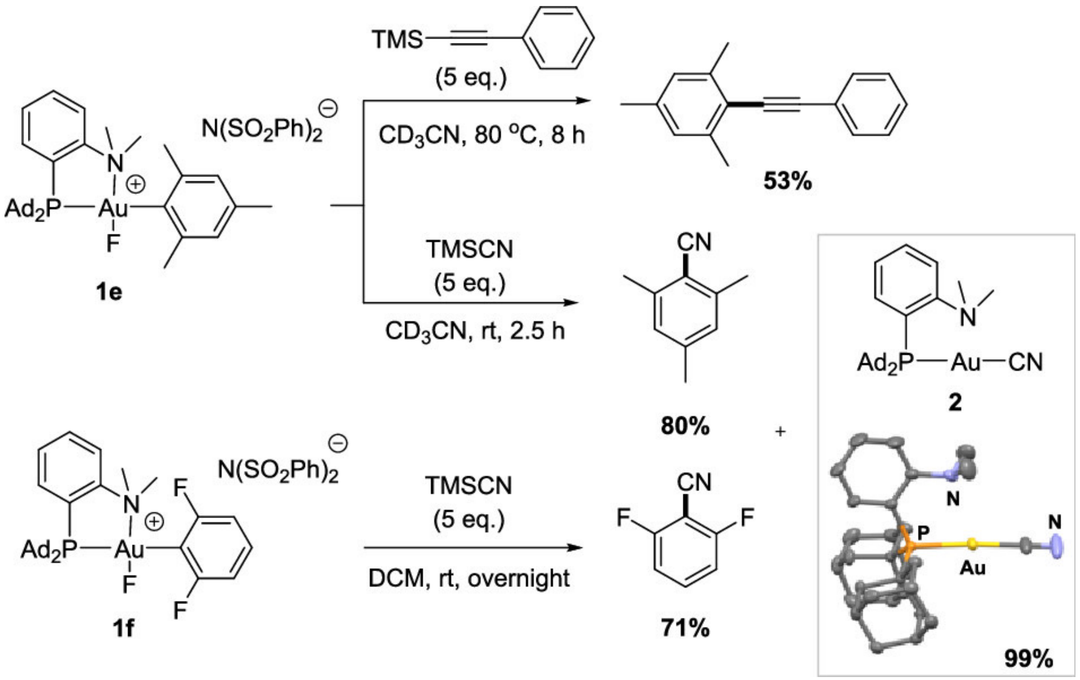
Alkyl / alkynyl complexes

1k: 78%[b]　**1l**: 74%[b]　**1m**: 71%[b]

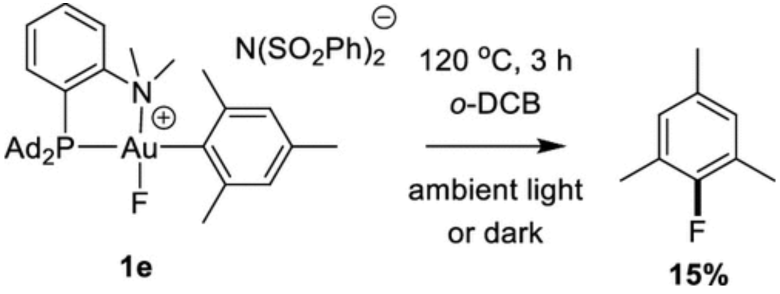
J. Am. Chem. Soc. **2024**, *146*, 11352.

Au(III)-Mediated Aryl–F Coupling | Reactivity

Transmetalation of Au(III)–F with electrophiles



Reductive elimination of Au(III)–F



J. Am. Chem. Soc. **2024**, *146*, 11352.

Au(III)-Mediated Aryl–F Coupling

Reactivity

DFT study on RE of Au(III)–F

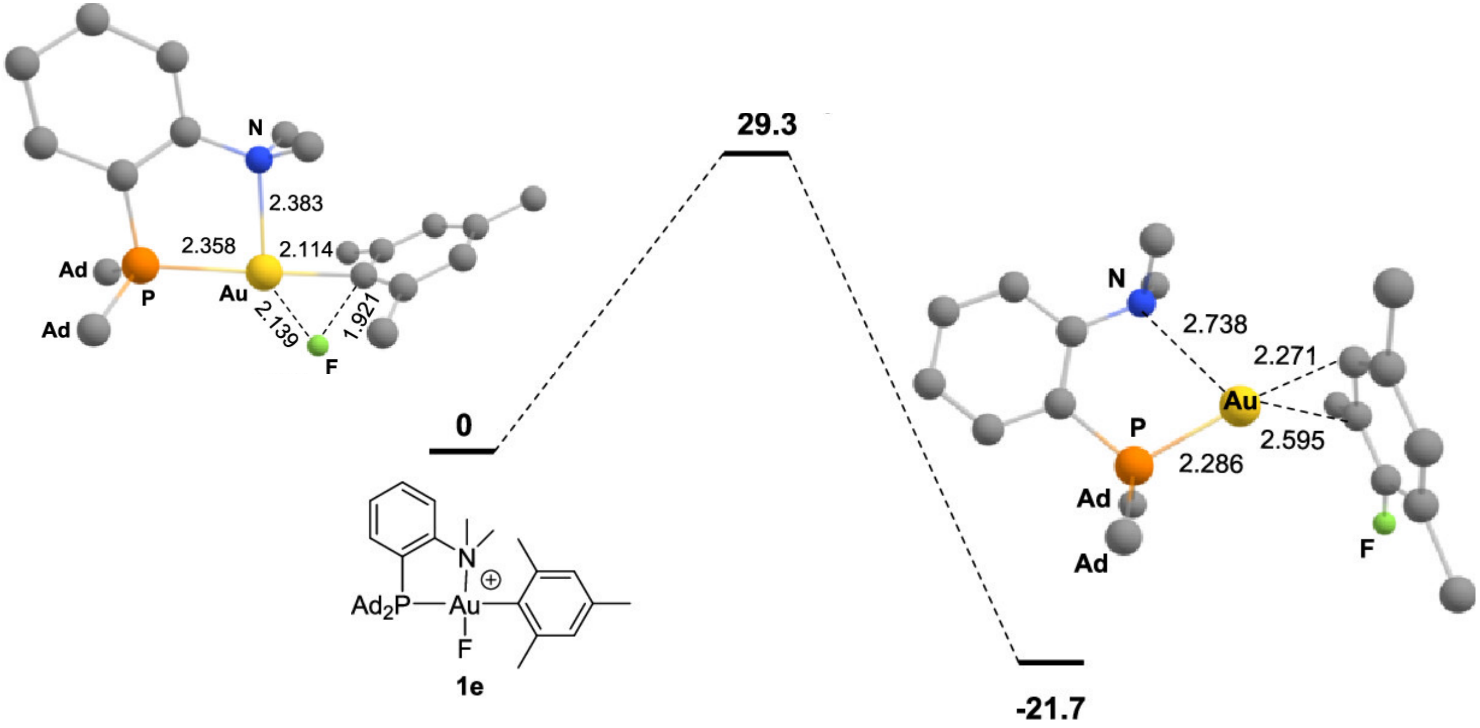
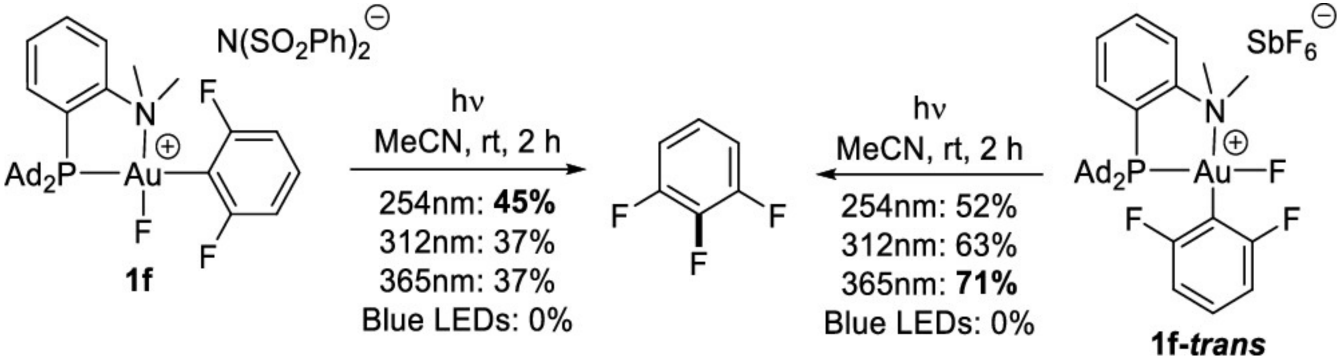


Photo-induced RE of Au(III)–F



hν
MeCN, rt, 2 h

254nm: **45%**
312nm: 37%
365nm: 37%
Blue LEDs: 0%

hν
MeCN, rt, 2 h

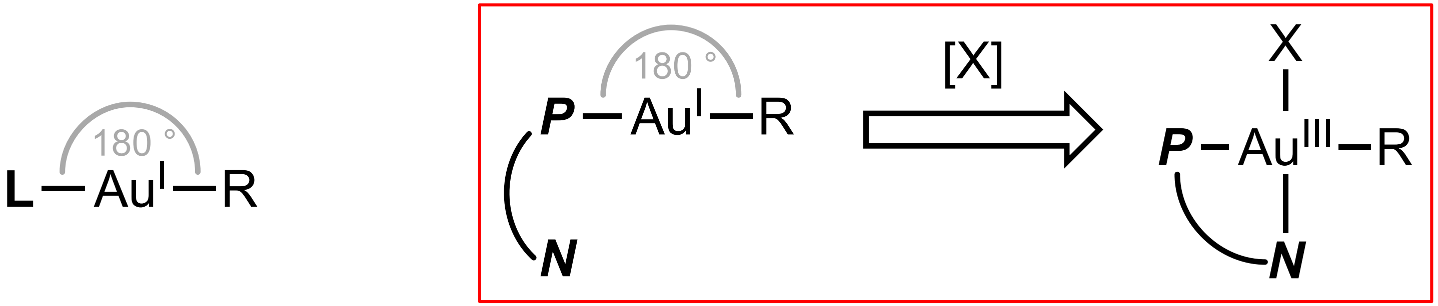
254nm: 52%
312nm: 63%
365nm: **71%**
Blue LEDs: 0%

J. Am. Chem. Soc. **2024**, *146,* 11352.

Conclusion

Hemilabile feature

The nature of Au(I) complexes that favour a linear structure limits ligand modulation. Hemilabile DalPhos ligand maintains the linear mono-coordination, while coordinates to Au(III) centre for further donation.



> Various developments of challenging reaction

> Deeper understanding on reaction mechanism (isolable intermediate)

THANK YOU FOR YOUR PATIENCE