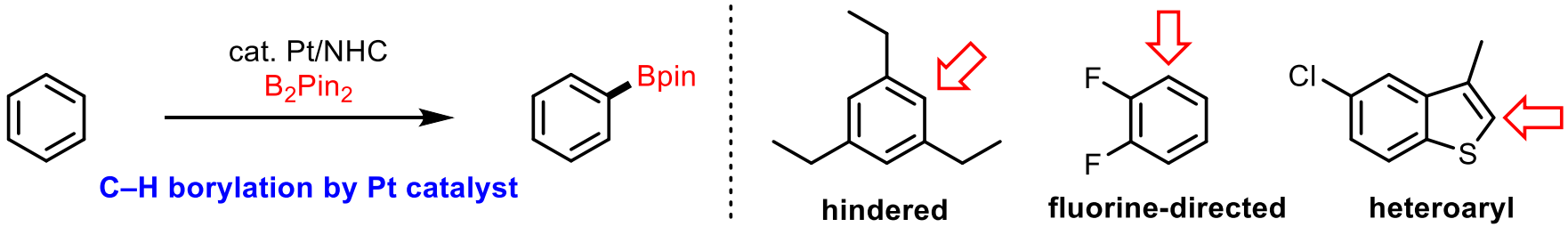
Current Literature Oct. 15 2016
Keita Takubo (Wipf group)

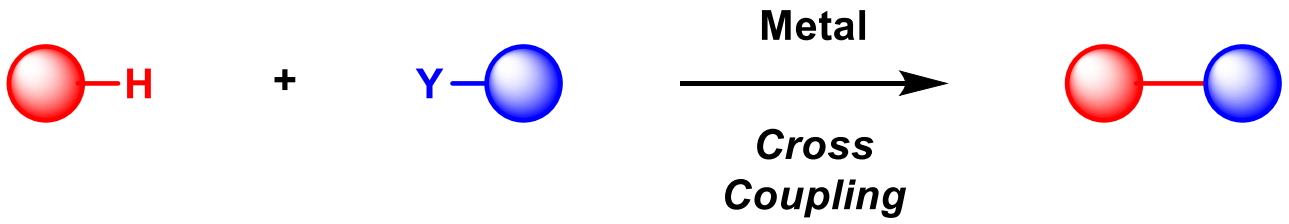
C–H Functionalization at Sterically Congested Positions by the Platinum-Catalyzed Borylation of Arenes

Takayuki Furukawa, Mamoru Tobisu,* and Naoto Chatani*

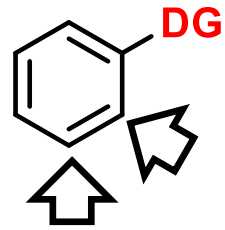
J. Am. Chem. Soc. **2015**, *137*, 12211−12214



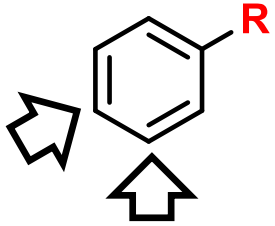
Strategies for C(sp^2)-H Functionalization



Previous work

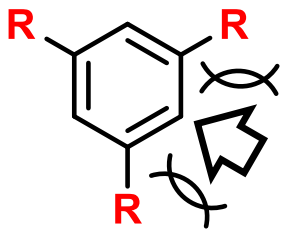


directing group

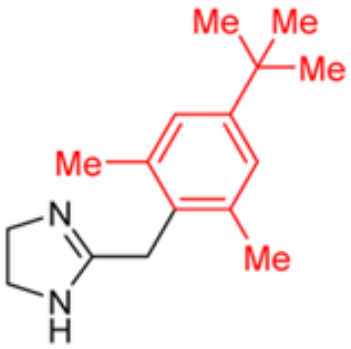


steric control

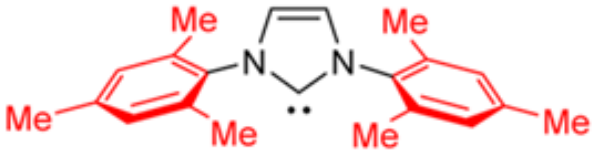
This work



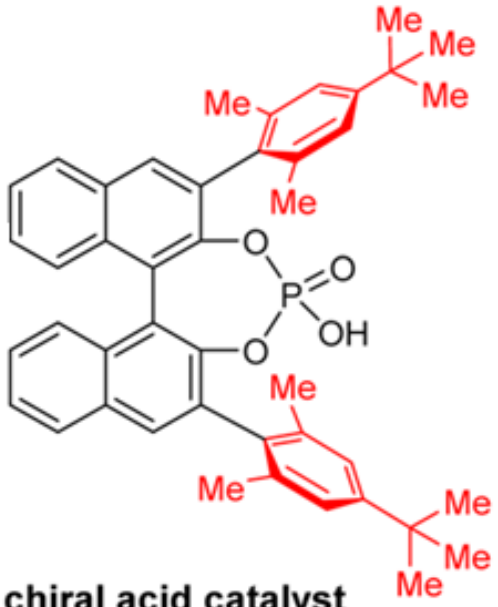
Applications of Hindered Aryl Groups



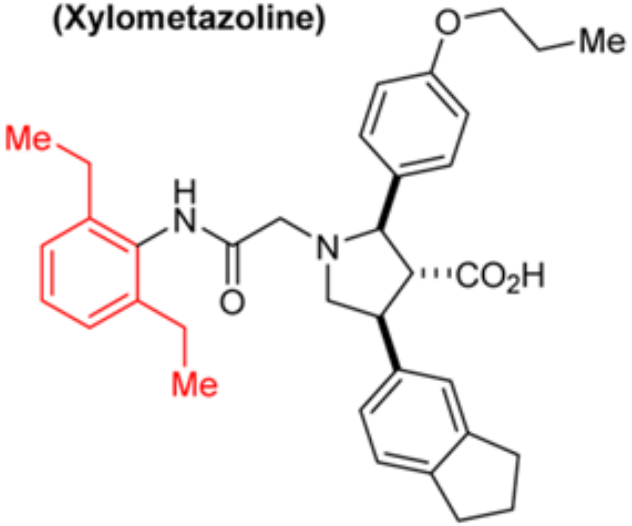
marketed drug
(Xylometazoline)



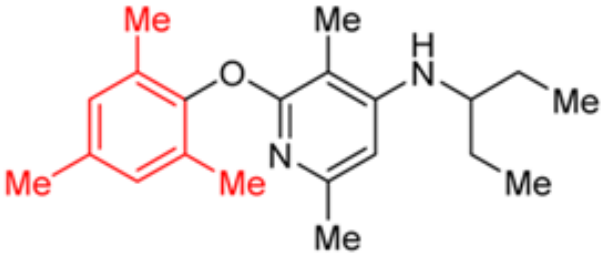
stablized carbene



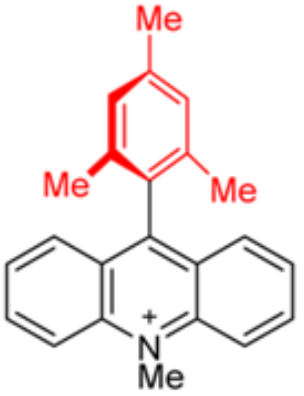
chiral acid catalyst



ET_B-selective antagonist
(A-192621)

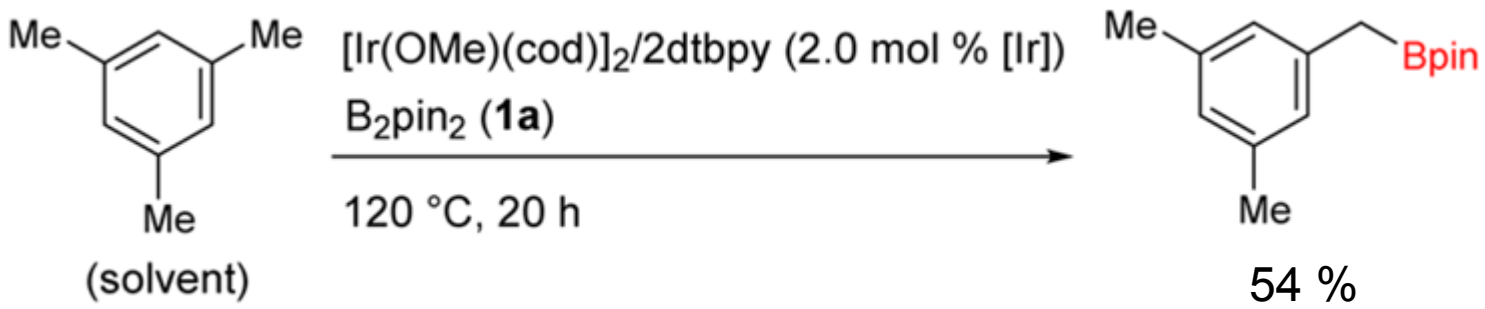


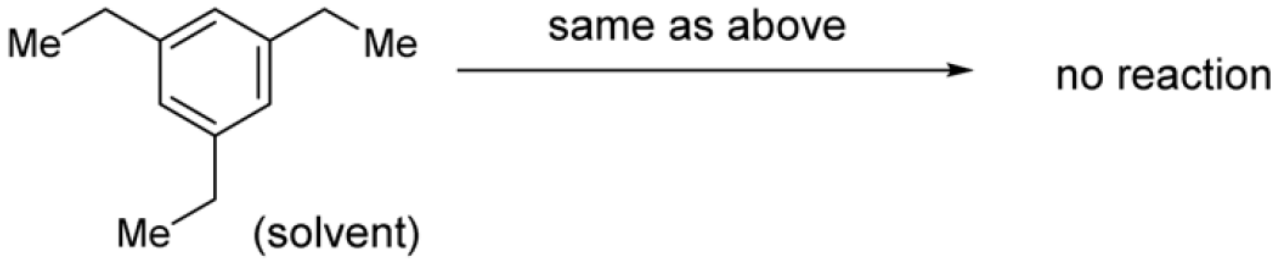
CRF_1 antagonist
(CP-376395)



photocatalyst

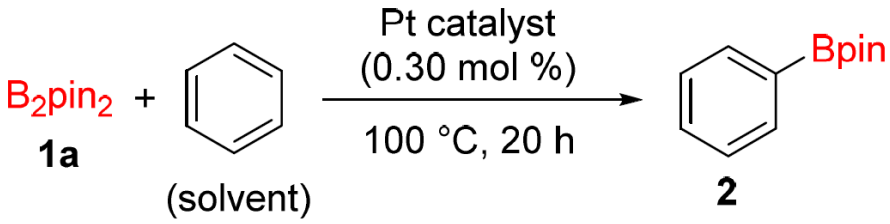
Attempted C-H Borylation of Hindered Arenes



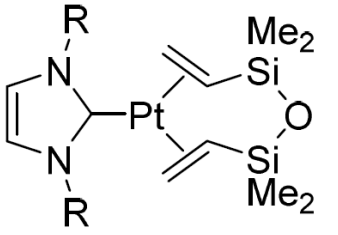


J. F. Hartwig *et al*., *J. Am. Chem. Soc*. **2015**, *137*, 8633−8643.

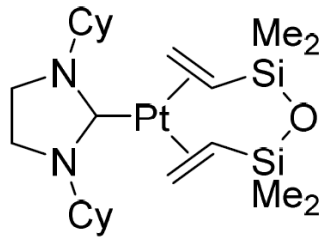
Effect of the Ligand on the Platinum-Catalyzed Borylation of Benzene



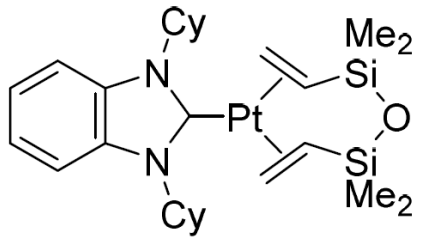
run	Pt catalyst	TON[b]
1[c]	$Pt_2(dvtms)_3$ (**3**)	5
2	Pt(IMes)(dvtms) (**4a**)	40
3	Pt(IPr)(dvtms) (**4b**)	0
4	Pt(IMe)(dvtms) (**4c**)	6
5	Pt(I^{i}Pr)(dvtms) (**4d**)	69
6	Pt(I^{t}Bu)(dvtms) (**4e**)	16
7	Pt[I(1-Ad)](dvtms) (**4f**)	58
8	Pt(ICy)(dvtms) (**4g**)	157
9	Pt(SICy)(dvtms) (**4h**)	106
10	Pt(BICy)(dvtms) (**4i**)	102
11	$Pt(PPh_3)_4$	0
12[c]	**3** + PCy_3	2
13[c]	**3** + 2,2'-bipyridine	13



4a: R = 2,4,6-$Me_3C_6H_2$
4b: R = 2,6-$^i Pr_2C_6H_3$
4c: R = Me
4d: R = ^{i}Pr
4e: R = ^{t}Bu
4f: R = 1-adamantyl
4g: R = cyclohexyl



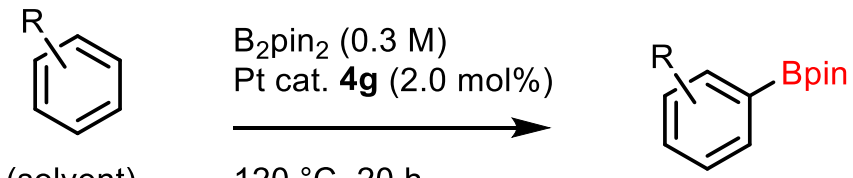
4h

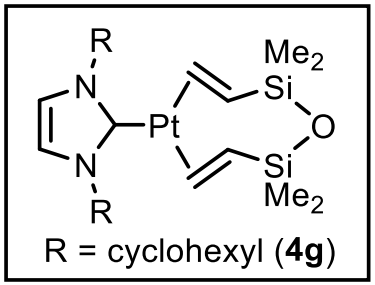


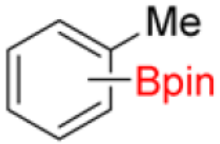
4i

a) Reaction conditions: **1a** (0.30 mmol), catalyst (0.90 μmol) in benzene (1.0 mL) at 100 °C for 20 h. b) TON: molar amount of **2** formed per molar amount of catalyst. c) **3** (6.0 μmol) and PCy_3 or 2,2'-bipyridine (6.0 μmol), if indicated, were used.

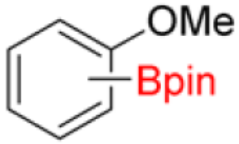
Substrate Scopes



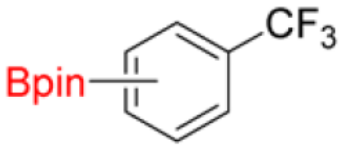




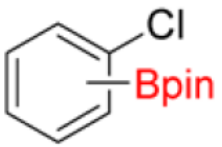
5 90%
(*o*:*m*:*p* = 30:50:20)



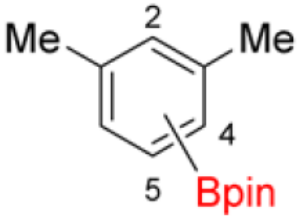
6 82%
(*o*:*m*:*p* = 22:61:17)



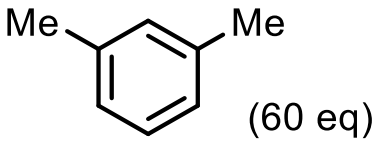
7 59%
(*o*:*m*:*p* = 0:68:32)



8 55%
(*o*:*m*:*p* = 29:53:18)
+ PhBpin (3%)



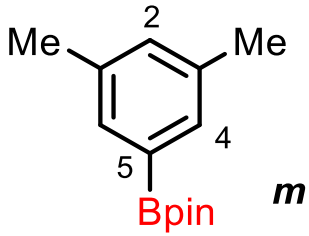
9 63%
(*2*:*4*:*5* = 10:25:65)



(60 eq)

1/2[IrCl(COD)]$_2$/bpy (3 mol %)
B_2Pin_2 (1.0 eq)

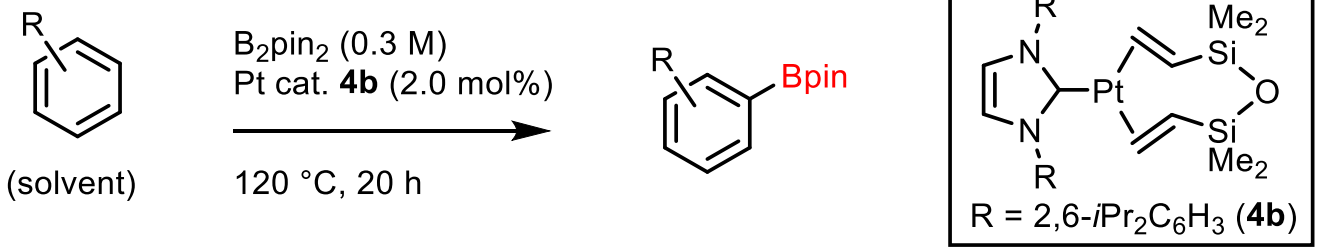
80 °C, 16 h



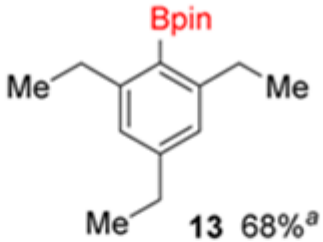
***meta* selective**

J. F. Hartwig *et al.*, *J. Am. Chem. Soc.* **2002**, *124*, 390−391.

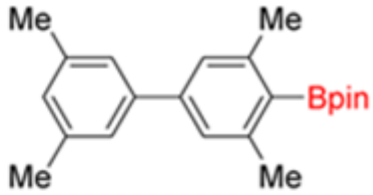
Substrate Scopes –Hindered Arenes–



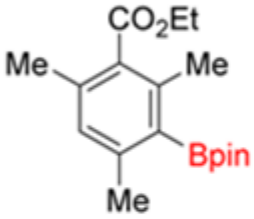
10 (R = Me) 72%
11 (R = ^{i}Pr) 59%
12 (R = ^{t}Bu) 78%



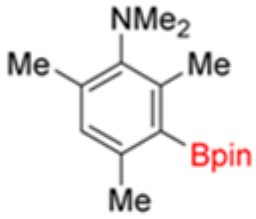
13 68%[a]



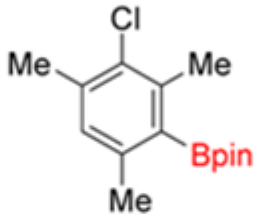
14 75%



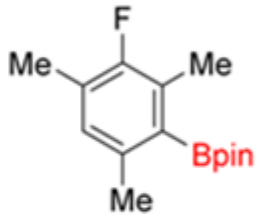
15 62%



16 58%

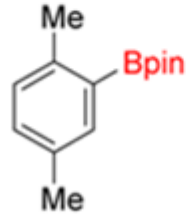


17 76%[d]

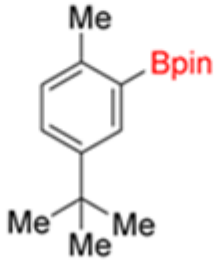


18 74%

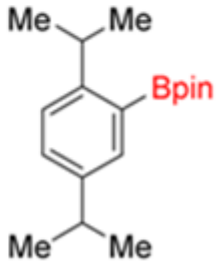
19 76%



20 82%



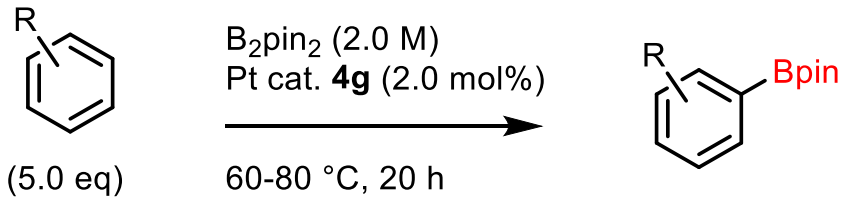
21 78%[b]

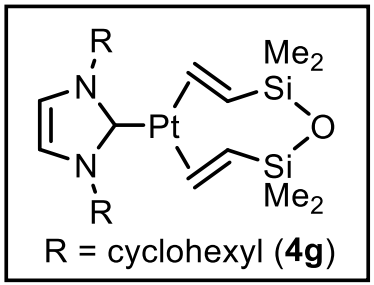


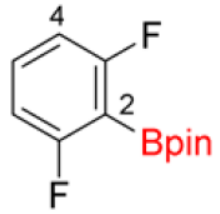
22 30%[b], 34%[a,c]

[a] At 140 ºC. [b] Compound **4f** was used as the catalyst. [c] The borylated product was isolated following its conversion to the corresponding phenol.

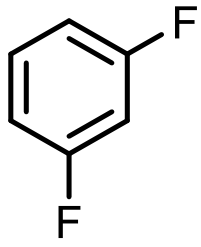
Substrate Scopes –Fluorobenzenes–





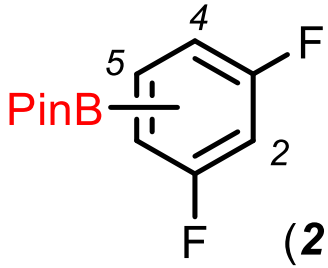


27 34% (61%)
(*2*:*4* = 82:18)
60 °C



HBPin (1.0 eq)
$[Ir(OMe)(COD)]_2$ (1.5 mol%)
dtbpy (3.0 mol%)

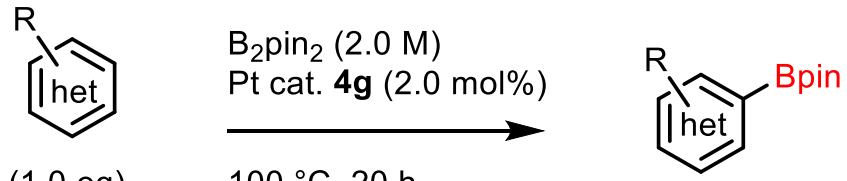
THF, 25 °C

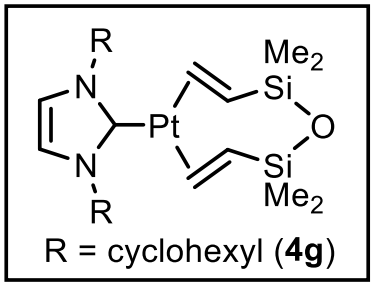


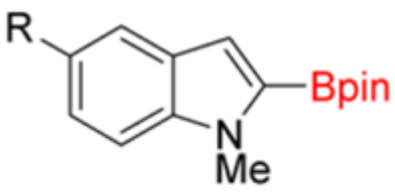
(***2*:*4*:*5* = 17:33:50**)

M. R. Smith III et al., *J. Am. Chem. Soc*. **2005**, *127*, 10539-10544

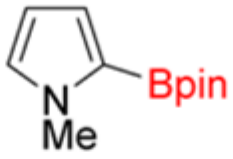
Substrate Scopes –Heteroarenes–



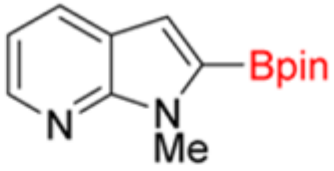




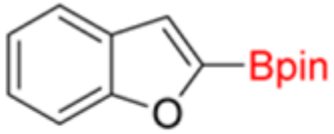
34 (R = H) 87%[e]
35 (R = CO_2Me) 63%[f]
36 (R = OMe) 79%[e]
37 (R = F) 56%[f]



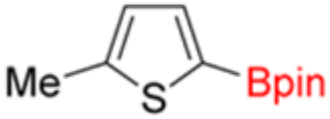
38 77%[g]



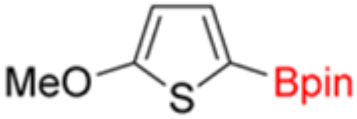
39 62%[f]



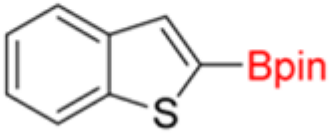
40 47% (68%)[f]
(2:3 = 75:25)



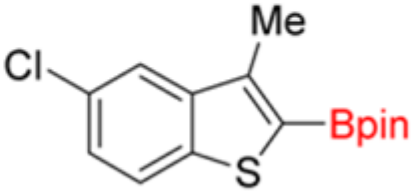
41 70%[h]



42 64%[h]



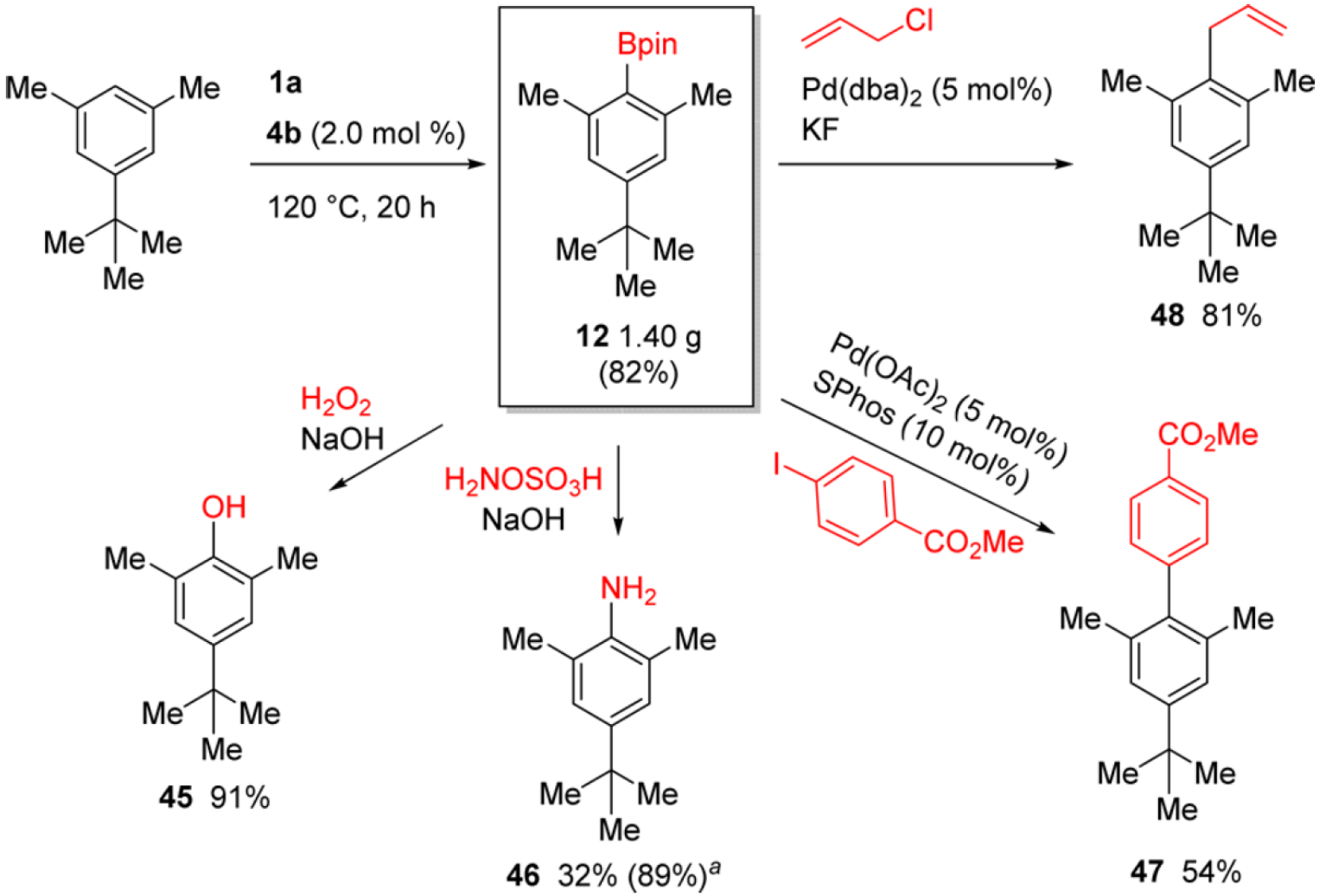
43 44%[f]
(2:3 = 92:8)



44 64%

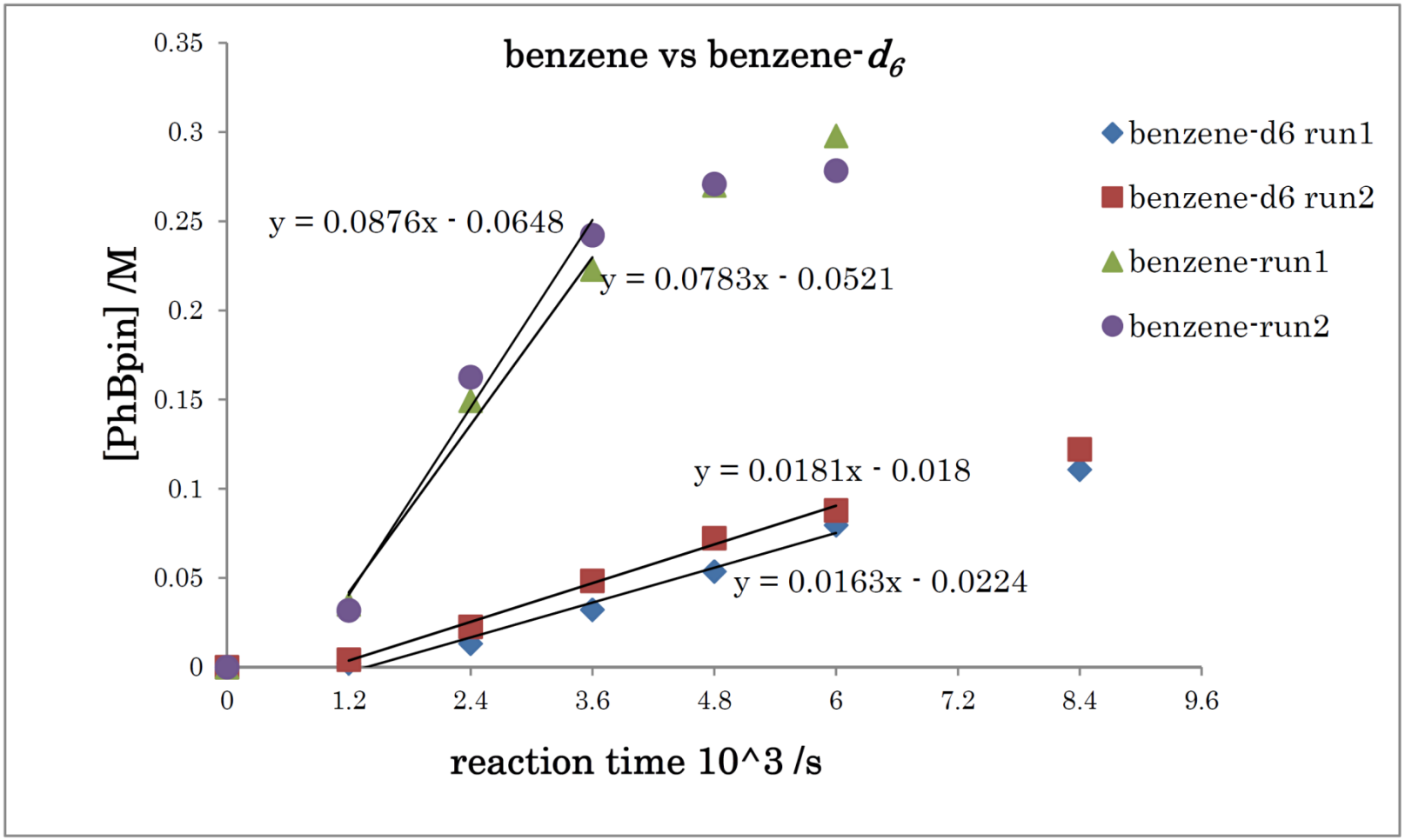
[e] Compound **1a** (2.0 equiv relative to heteroarene) was used. [f] Compound **4g** (4.0 mol %) was used. [g] *N*-Methylpyrrole (5.0 equiv to **1a**) was used. [h] Heteroarene was used as the solvent.

Synthetic Utility of the Product

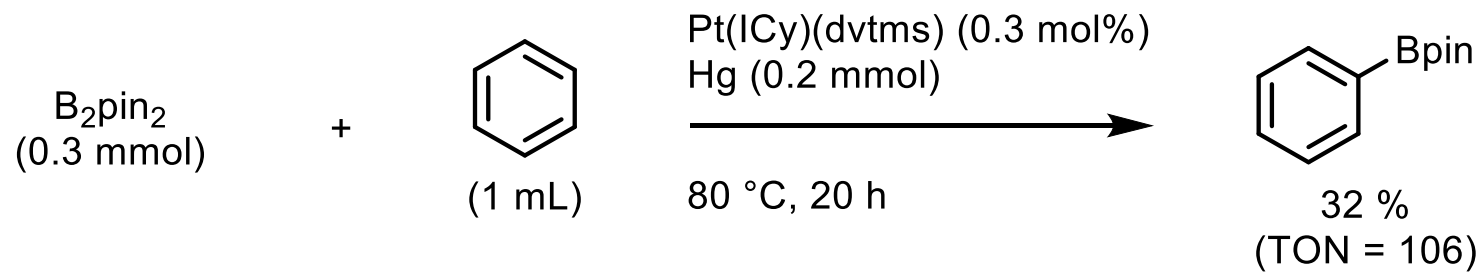


a) Yield based on the recovered starting material

Kinetic Isotope Effect



Mercury Poisoning Test



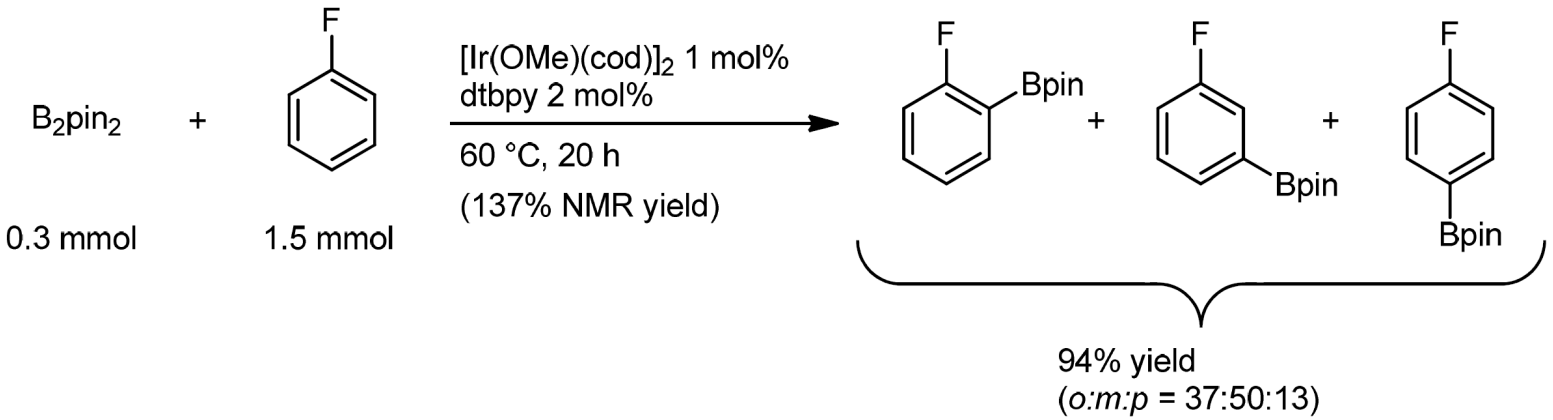
This result indicates …

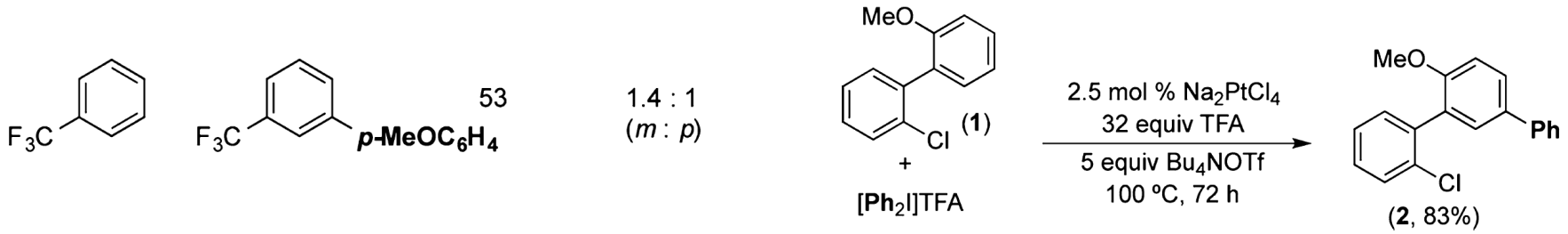
homogeneous platinum species are involved as an active catalyst.

Conclusion

- This is the first platinum catalysed C-H borylation of arenes
- High tolerance of the catalytic systems to steric hindrance
- *Ortho*-directing effect of fluorine substituents which allowed the facile synthesis of *ortho*-fluorophenylboronic ester derivatives
- C−H bond cleavage occurred during the turnover-limiting step of the catalytic cycle
- Homogeneous platinum species are involved as an active catalyst.

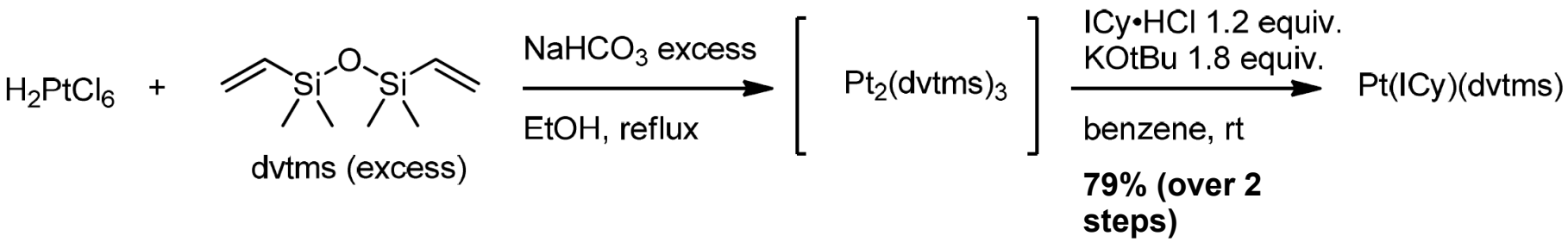
Iridium-catalyzed borylation of fluorobenzene



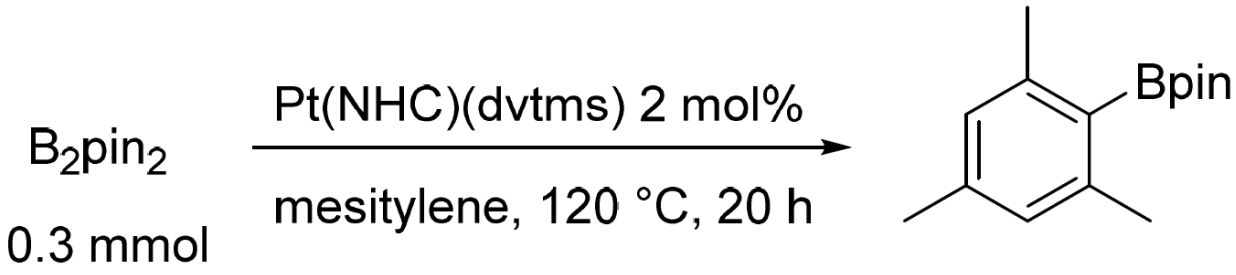


M. S. Sanford et al., *J. Am. Chem. Soc*. **2013**, *135*, 15710−15713

Synthesis of Pt(NHC)(dvtms) Complexes

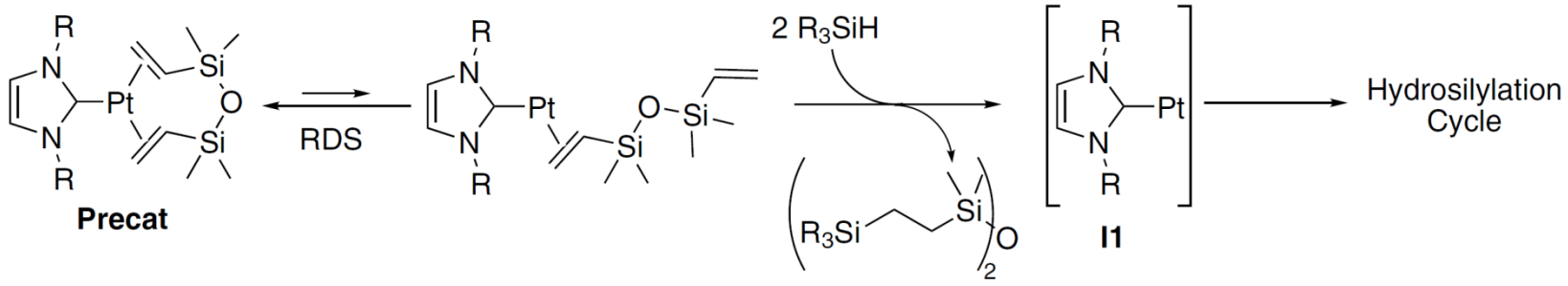


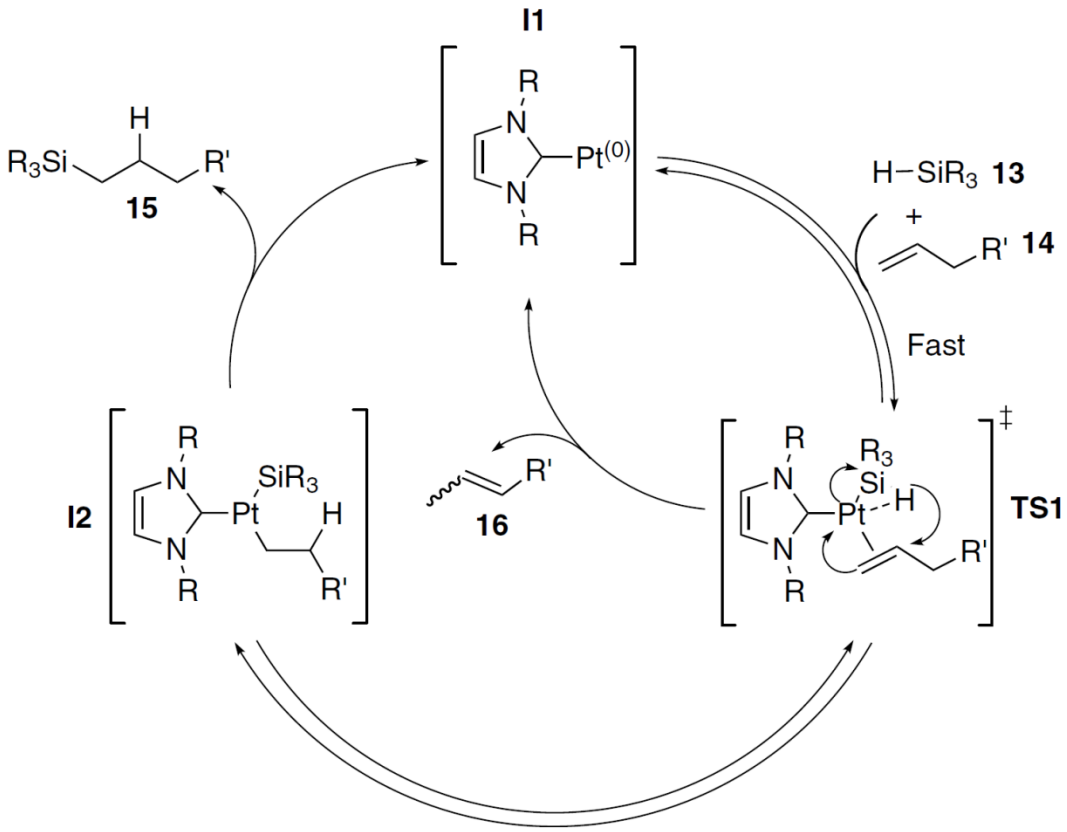
Dichlorination Substrate Scope



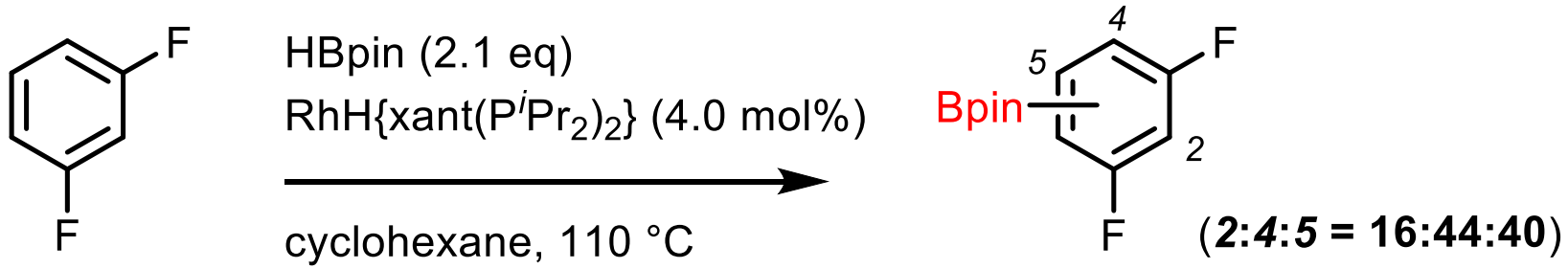
run	NHC	GC yield (%)	
		product	recovered B_2pin_2
1	IMes	46	0
2	ICy	55	5
3	SICy	18	31
4	BICy	31	28
5	IMe	0	55
6	I^{i}Pr	17	41
7	I^{t}Bu	37	0
8	IAd	66	0
9	IPr	72	0

Synthetic utility of the product

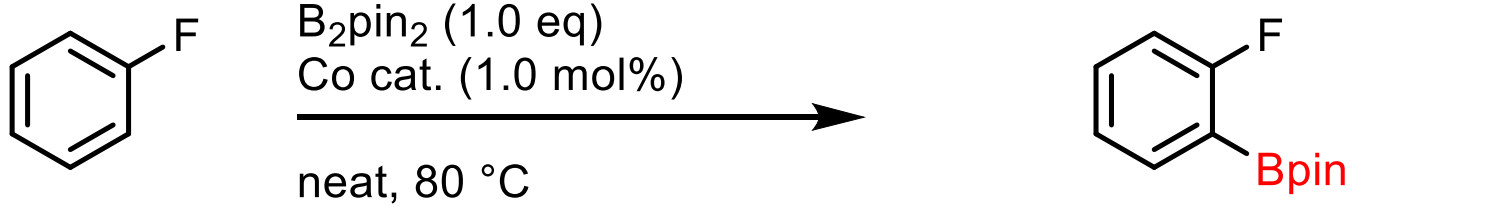




Ortho-durecting effect of fluorine



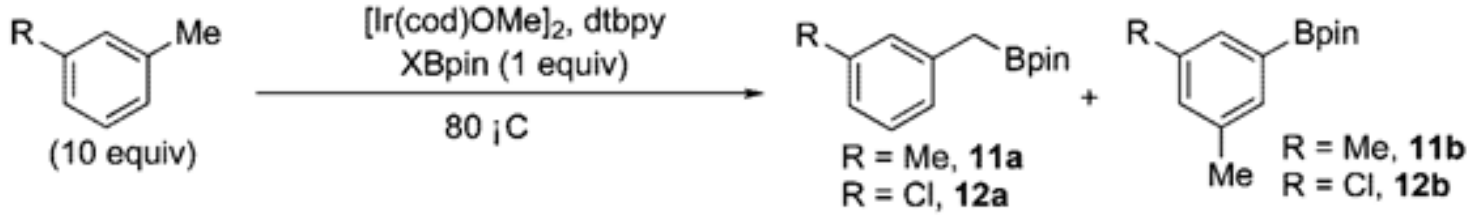
M. A. Esteruelas et al., *Organometallics* **2015**, *34,* 1911-1924



P. J. Chirik et al., *J. Am. Chem. Soc.* **2014**, *136*, 4133-4136

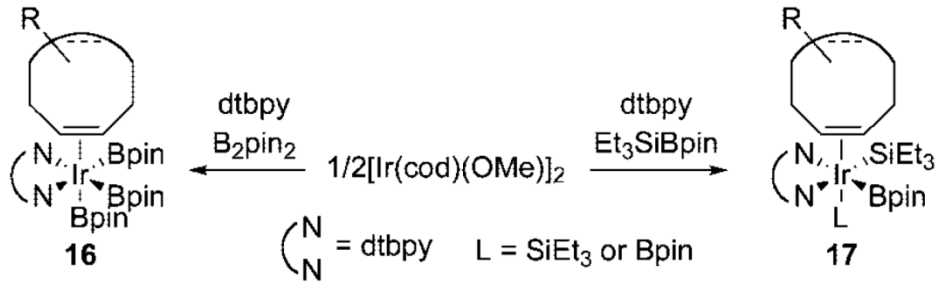
Regioselectivity Dependence of Regioselectivity on Boron Source

Table 4. Regioselectivity Dependence of Regioselectivity on Boron Source



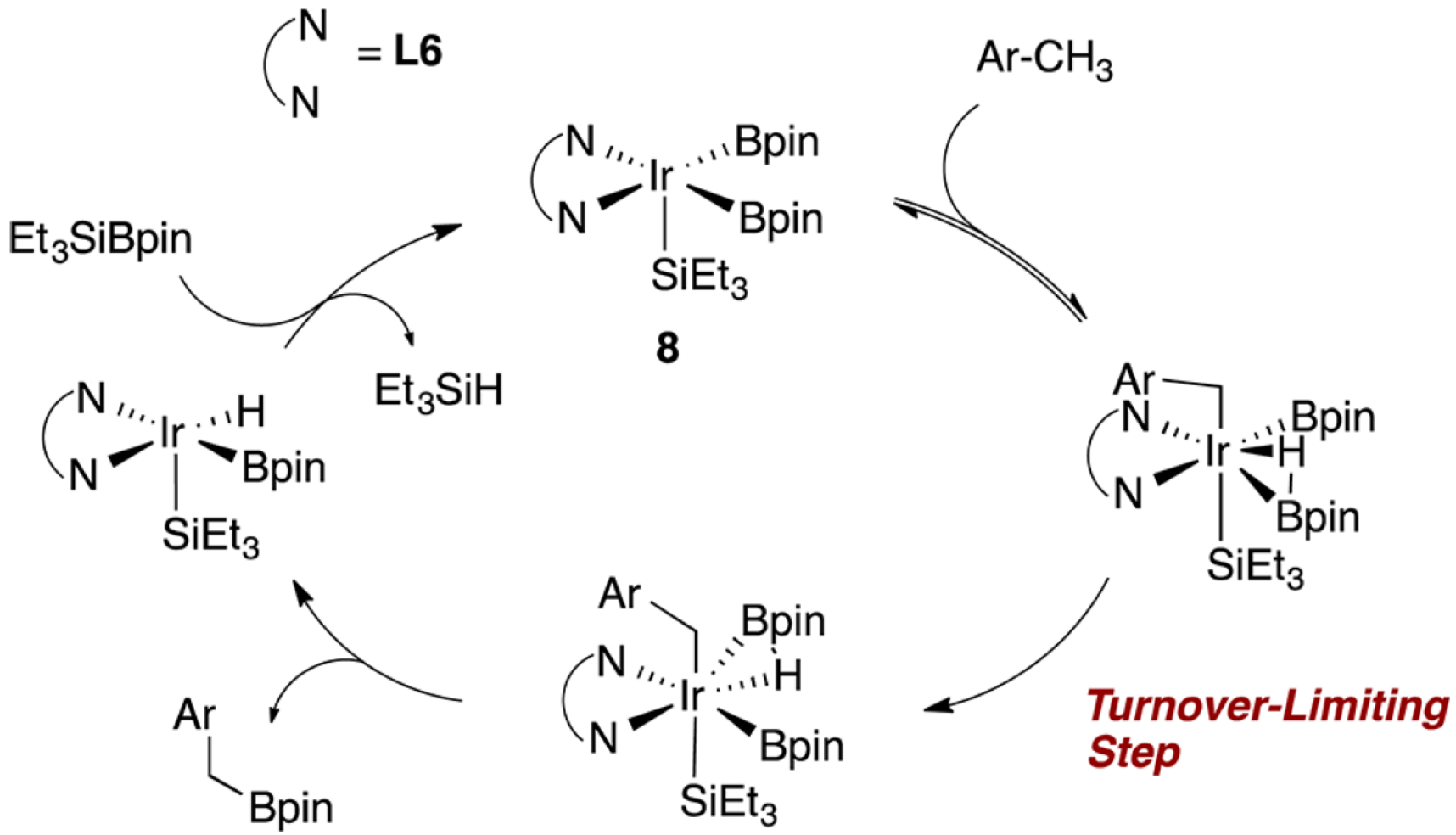
entry	R	boron reagent	$[Ir(cod)OMe]_2$, %	dtbpy, %	time, h	yield, %[a] (a:b)[b]
1	Me	B_2pin_2	1	2	12	83 (0:1)
2	Me	*t*-$BuMe_2SiBpin$	1	2	12	75 (70:30)
3	Me	$Et_3SiBpin$	1	2	12	86 (89:11)
4	Me	*n*-$Bu_3SiBpin$	1	2	12	65 (93:7)
5	Cl	B_2pin_2	0.5	1	4	102 (0:1)
6	Cl	*t*-$BuMe_2SiBpin$	0.5	1	4	98 (10:90)
7	Cl	$Et_3SiBpin$	0.5	1	4	72 (40:60)
8	Cl	*n*-$Bu_3SiBpin$	0.5	1	4	87 (60:40)

[a] Yield determined by GC. [b] **12a**:**12b** isomer ratios determined by ^1H NMR.



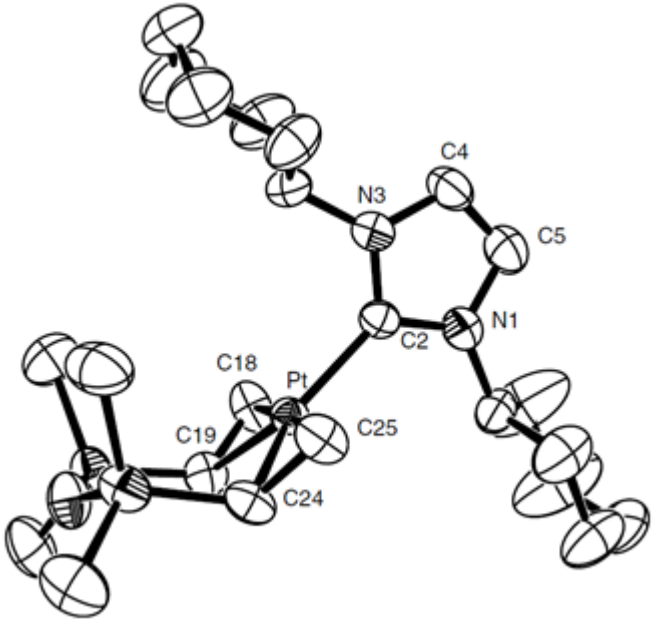
J. F. Hartwig et al.
Organometallics ***2008***, *27,* 6013–6019

Proposed mechanism of Ir catalysed borylation

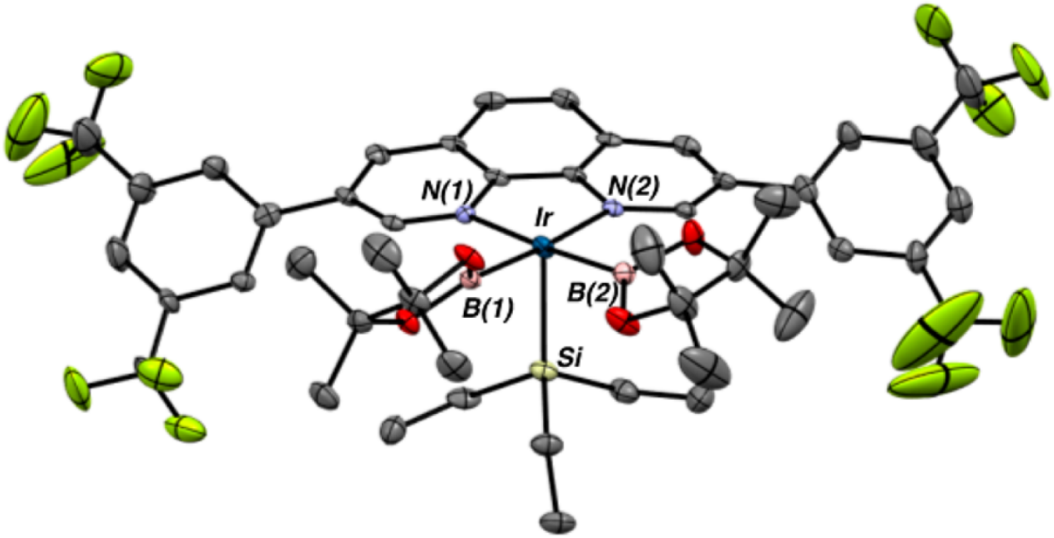


J. F. Hartwig *et al*., *J. Am. Chem. Soc*. **2015**, *137*, 8633−8643.

ORTEP structure



ORTEP of (ICy)Pt(dvtms)



Structure of Ir catalyst