STEREO GROUP MEETING: 03/31/2014

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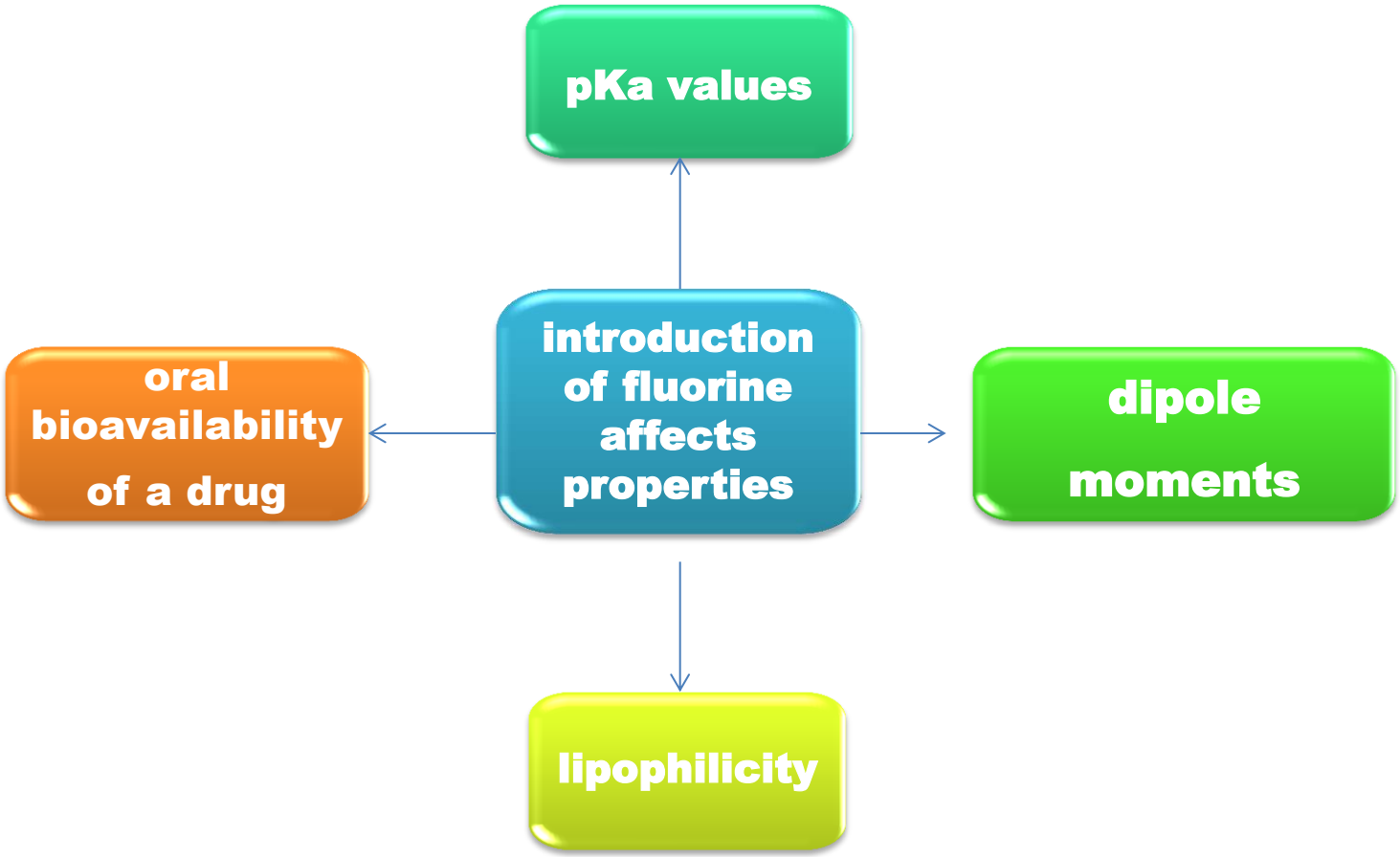
Asymmetric Palladium-Catalyzed Directed Intermolecular Fluoroarylation of Styrenes

Eric P. A. Talbot, Jeffrey M. McKenna, F. Dean Toste

J. Am. Chem. Soc. ASAP

REPORTER: Yajun REN



Jeschke, P. *ChemBioChem* **2004**, *5*, 570; Morgenthaler, M.; Kansy, M.; Müller, K. *ChemMedChem* **2007**, *2*, 1100.

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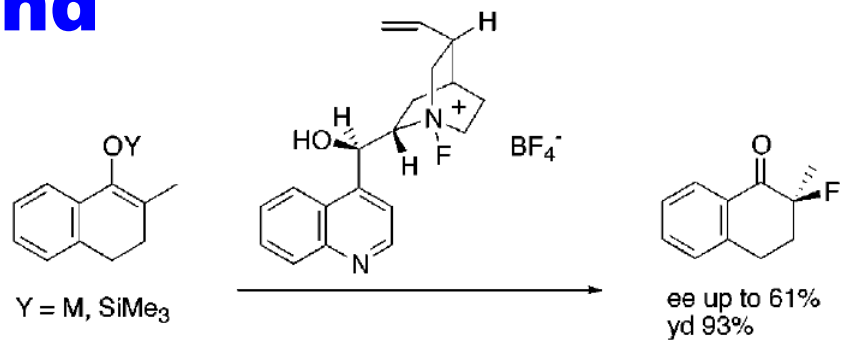
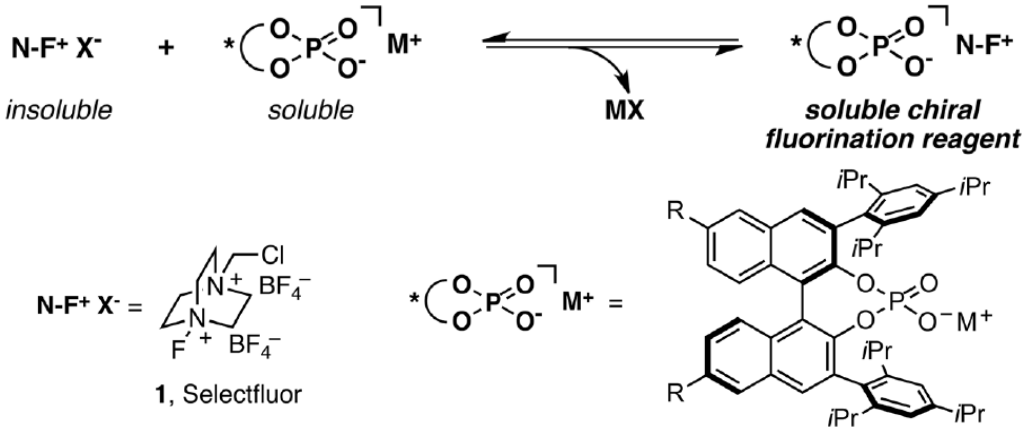


Cahard, D.; Plaquevent, J.-C.; Roques, N. *Org. Lett.* **2000**, *2*, 3699.



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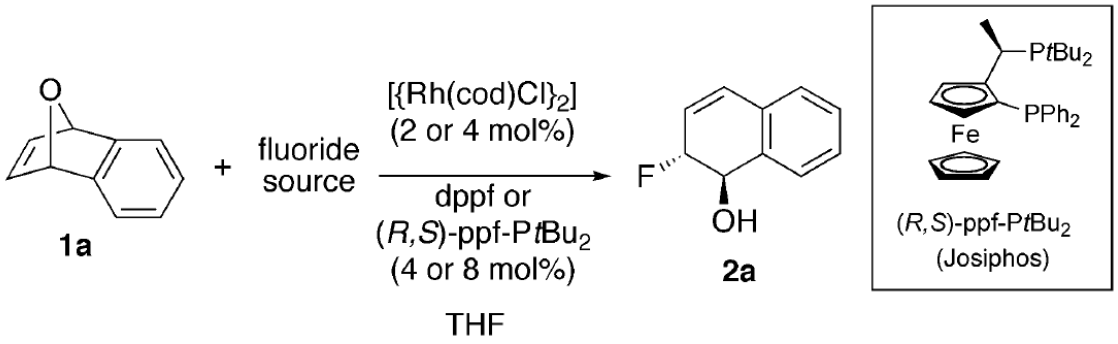
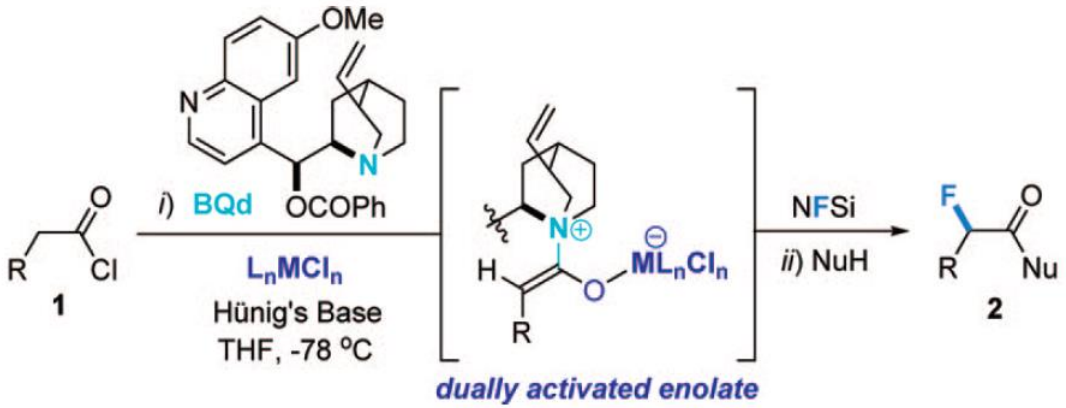


Zhu,J.; Tsui, G. C.; Lautens, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 12353.



Paull, D. H.; Widger, L. R.; Lectka, T. *J. Am. Chem. Soc*. **2008**, *130*, 17260

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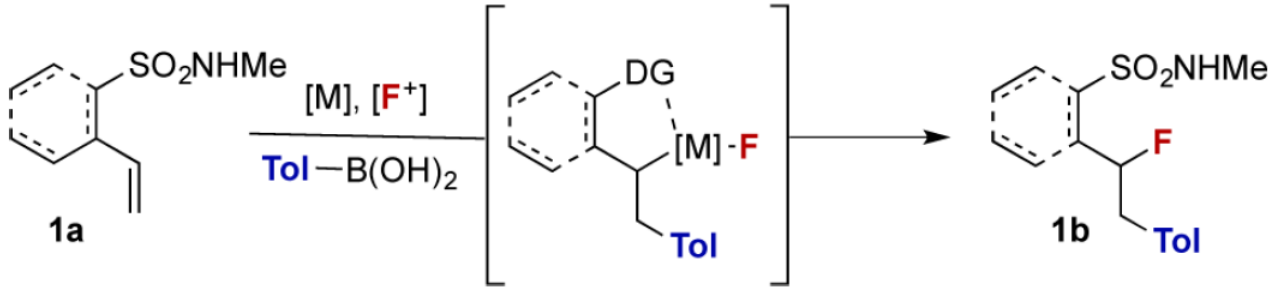
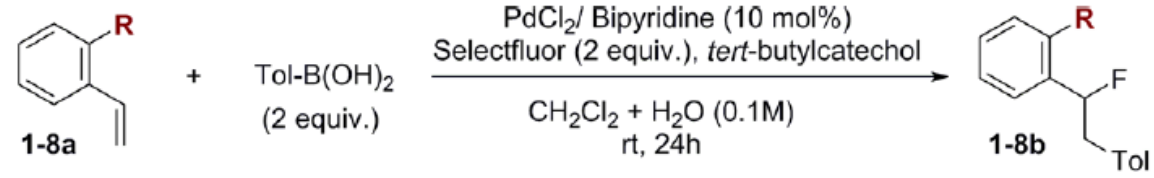
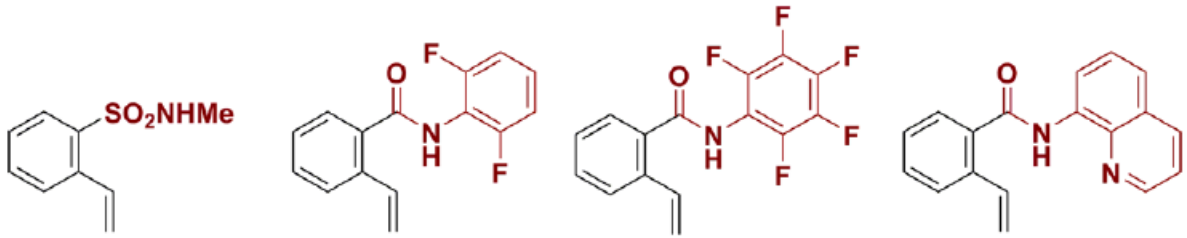


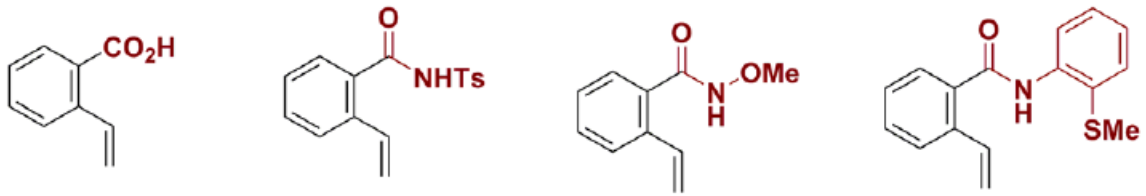
$PdCl_2$ bipyridine complex

Scheme 1. Screening of Suitable Directing Group[a]





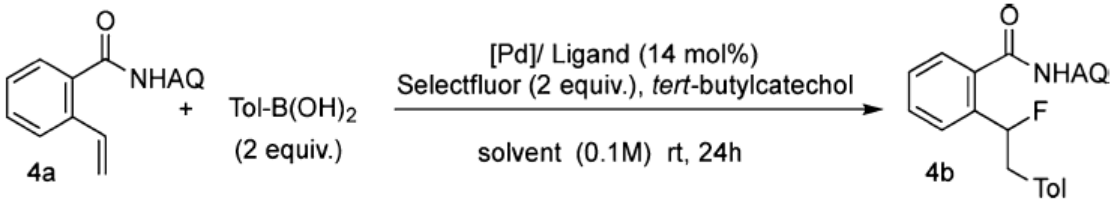
1a, 57% **2a**, 55% **3a**, 45% **4a**, 54%



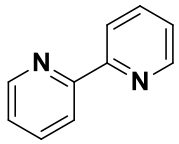
5a, 0% **6a**, 0% **7a**, 0% **8a**, 0%

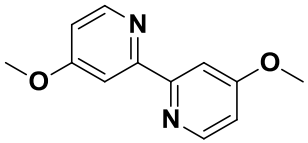
[a]Yields after chromatographic purification.

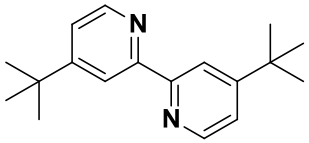
Table 1. Optimization of Fluoroarylation of Styrene 4a



entry	catalyst	ligand[c]	solvents	additive[d]	yield 4b[a]
1	$PdCl_2$	L1	CH_2Cl_2/H_2O (1/0.1)	none	54
2	$Pd(OAc)_2$	L1	CH_2Cl_2/H_2O (1/0.1)	none	67
3	$PdBr_2$	L1	CH_2Cl_2/H_2O (1/0.1)	none	54
4	$Pd(TFA)_2$	L1	CH_2Cl_2/H_2O (1/0.1)	none	61
5	$Pd(OAc)_2$	–	CH_2Cl_2/H_2O (1/0.1)	none	0
6	$Pd(OAc)_2$	L2	CH_2Cl_2/H_2O (1/0.1)	none	56
7	$Pd(OAc)_2$	L3	CH_2Cl_2/H_2O (1/0.1)	none	76
8	$Pd(OAc)_2$	L3	CH_2Cl_2	none	23
9	$Pd(OAc)_2$	L3	CH_2Cl_2/H_2O (1/0.2)	none	82
10	$Pd(OAc)_2$	L3	CH_2Cl_2/H_2O (1/0.2)	P1: 30 mol %	91 (86)[b]
11	$Pd(OAc)_2$	L5	CH_2Cl_2/H_2O (1/0.2)	P1: 50 mol %	82
12	$Pd(OAc)_2$	L3	CH_2Cl_2/H_2O (1/0.2)	P2: 30 mol %	74


L1


L2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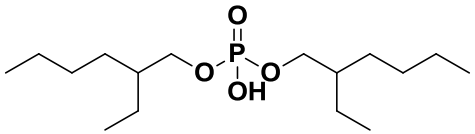
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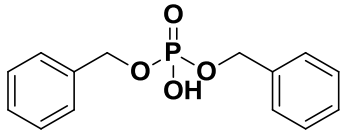
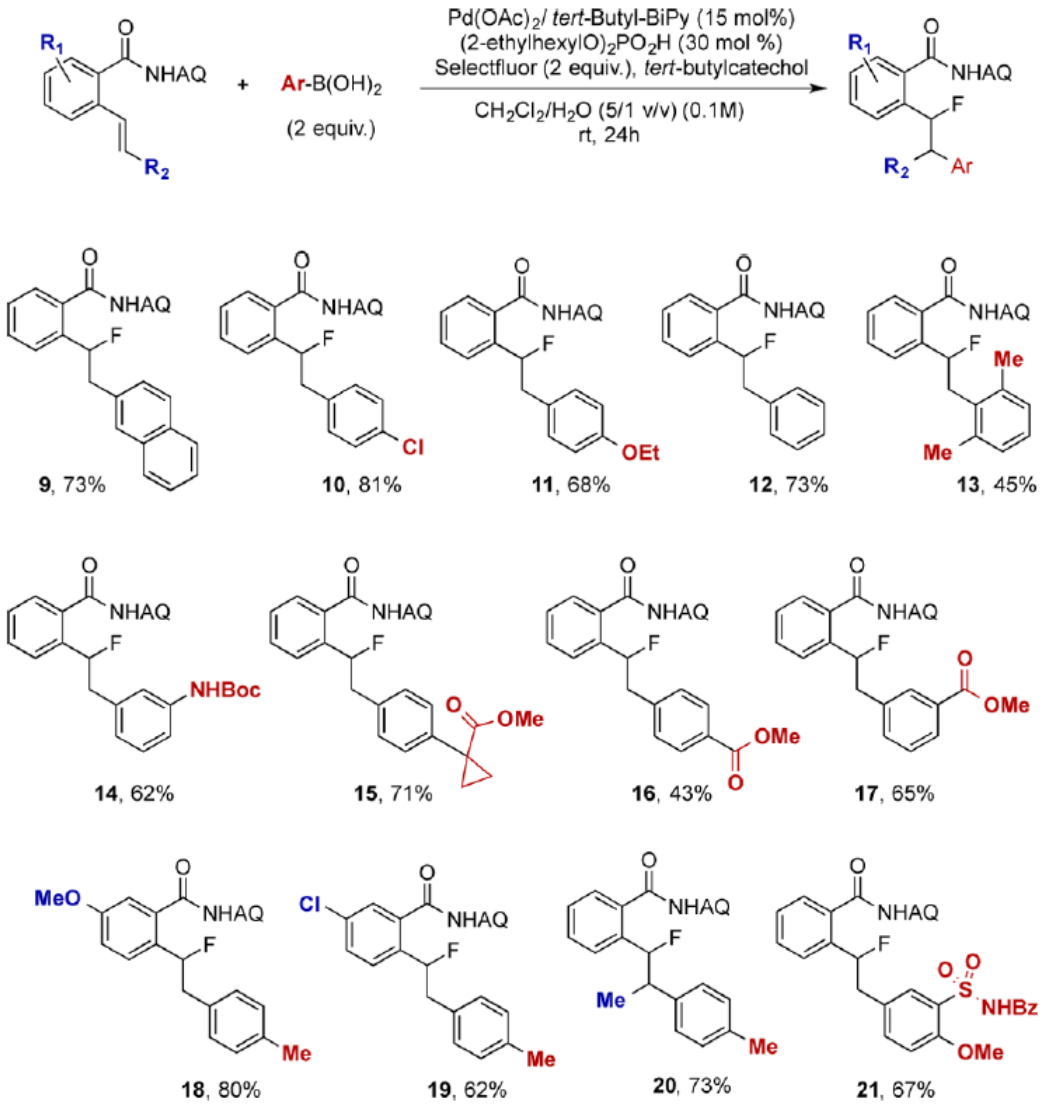
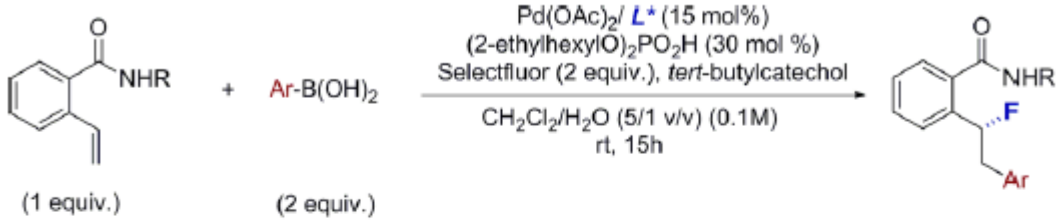

P2

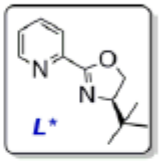
Scheme 2. Substrate Scope for AQ Directing Group[a]

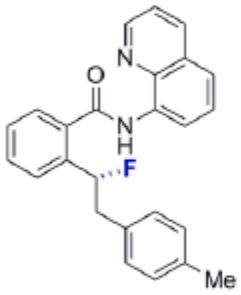


[a]Yields after chromatographic purification.

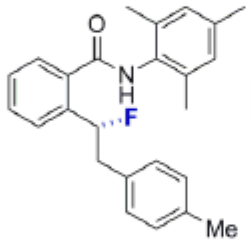
Scheme 3. Substrate Scope for Enantioselective Fluoroarylation[a]



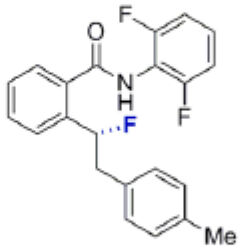




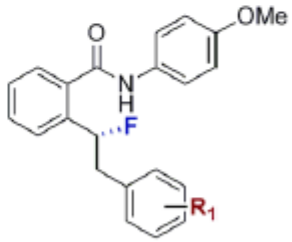
4b, 15%, 81% ee



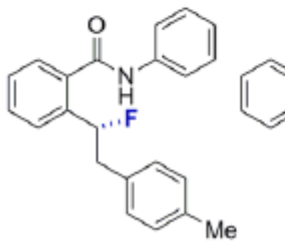
22, 72%, 76% ee



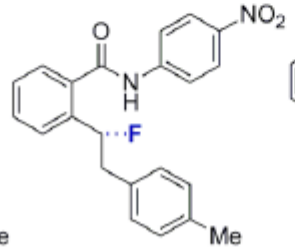
2b, 67%, 78% ee



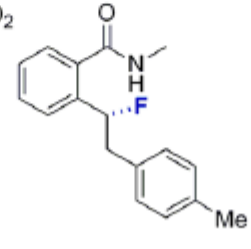
26, 74%, 96% ee, R_1= 4-Me
27, 83%, 91% ee, R_1= 4-Cl
28, 71%, 83% ee, R_1= 4-OEt
29, 71%, 87% ee, R_1= 3-F
30, 66%, 60% ee, R_1= 2,6-diMe
31, 77%, 94% ee, R_1= H
32, 60%, 90% ee, R_1=Br



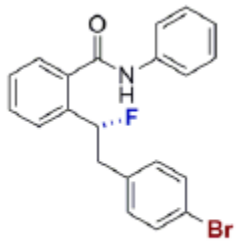
23, 76%, 96% ee



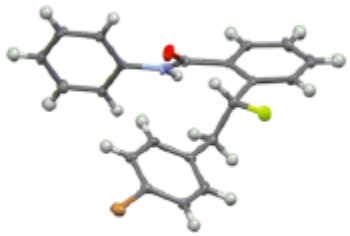
24, 73%, 93% ee



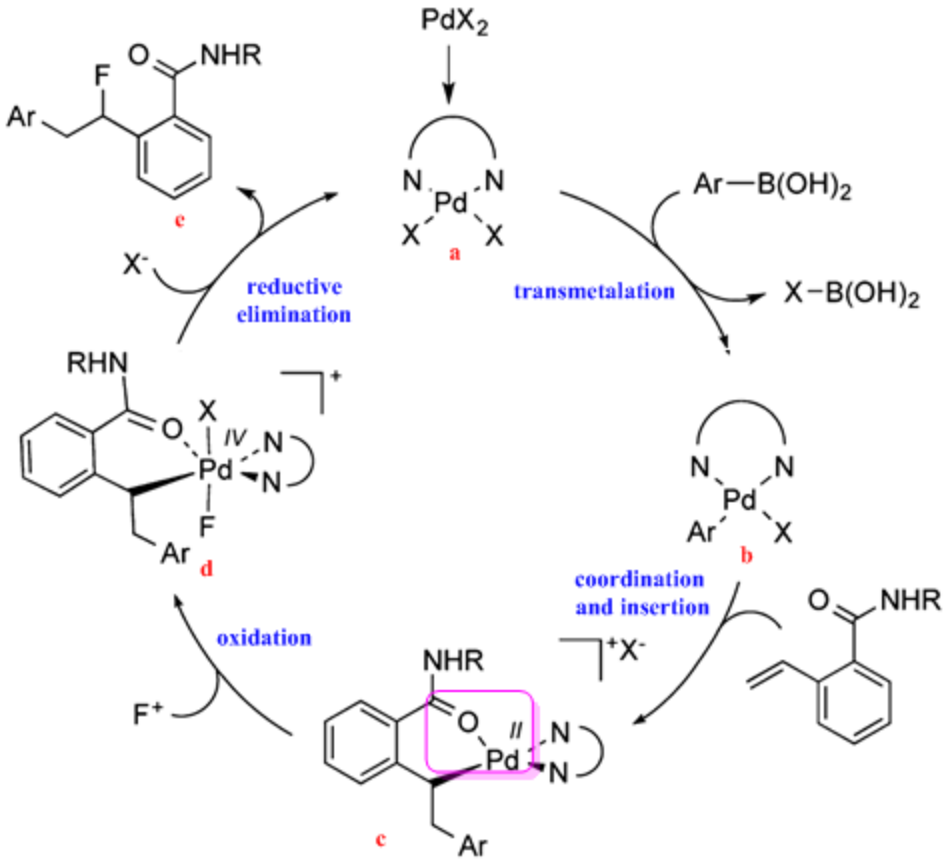
25, 47%, 92% ee



33, 37%, 81% ee



Scheme 4. Proposed Mechanism for the Directed Fluoroarylation of Styrene



conclusion

- using amide-based directing groups, they have developed a palladium-catalyzed fluoroarylation of styrenes

- The reaction allows for the synthesis of a range of enantioenirched benzylic fluorides by a three-component coupling of styrenes, Selectfluor, and boronic acids

THANK YOU FOR YOUR ATTENTION!