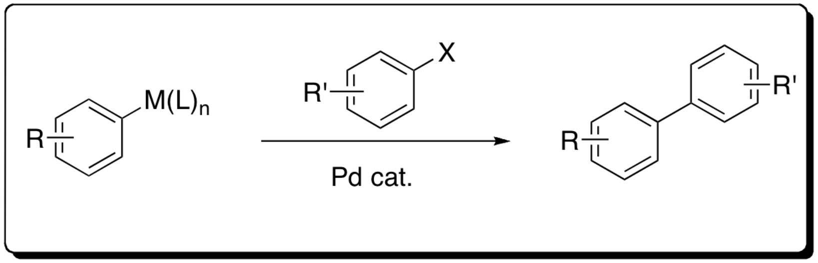
Cross-Coupling Reactions of Aromatic and Heteroaromatic Silanolates with Aromatic and Heteroaromatic Halides

Denmark, Scott E.; Smith, Russell C.; Chang,
Wen-Tau T.; Muhuhi, Joseck M.

JACS, ASAP, 2/6/2009

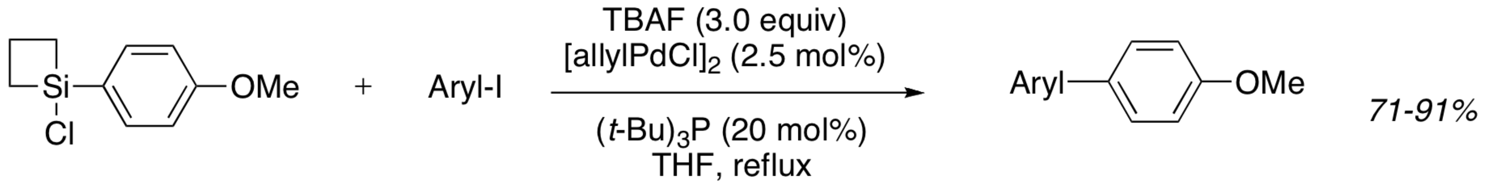
Gary Davis, Current Literature Presentation,
2/14/09

Biaryl Cross-Coupling Reactions

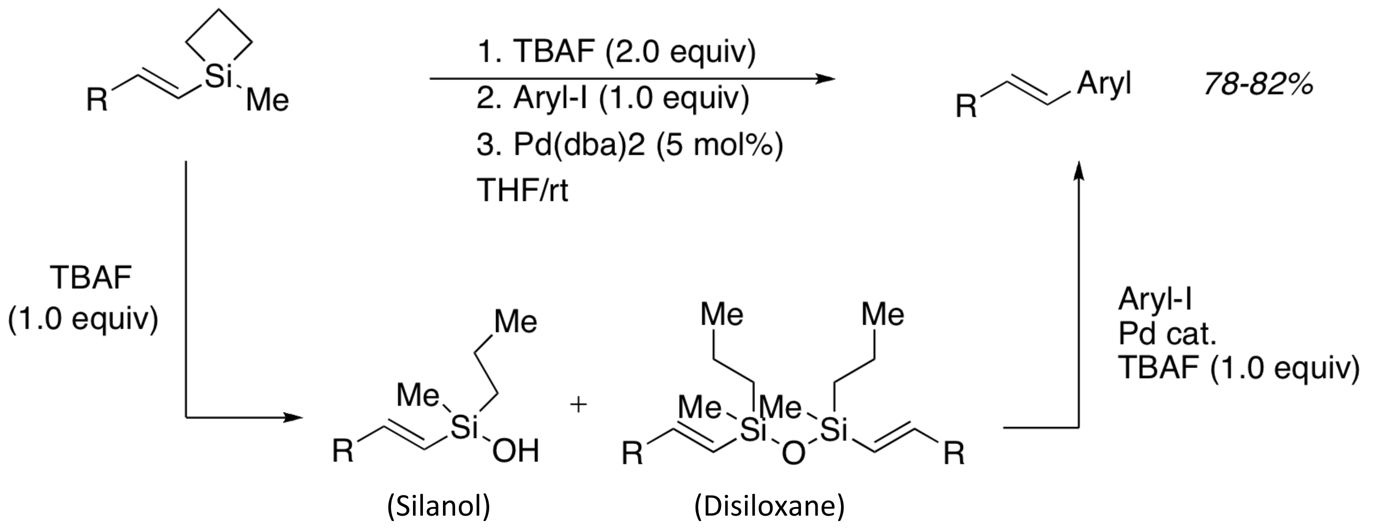


- Organomagnesium (Kumada)
- Organozinc (Negishi)
- Organotin (Stille)
- Organoboron (Suzuki)
- Organosilicon (Hiyama)

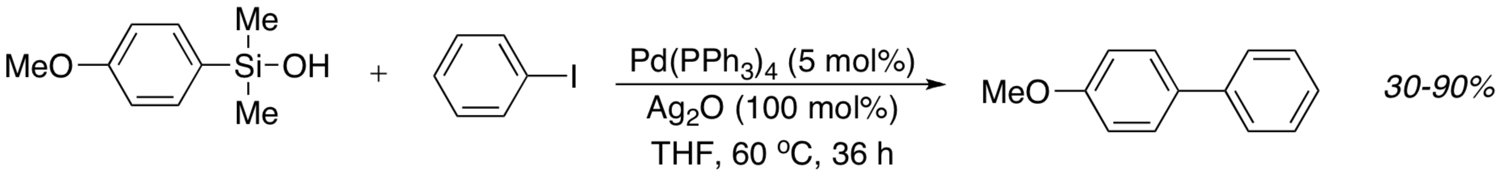
Organosilane Cross-Couplings



Denmark, S.; Wu, Z. Org. Lett. **1999**, 1, 1495-1498.

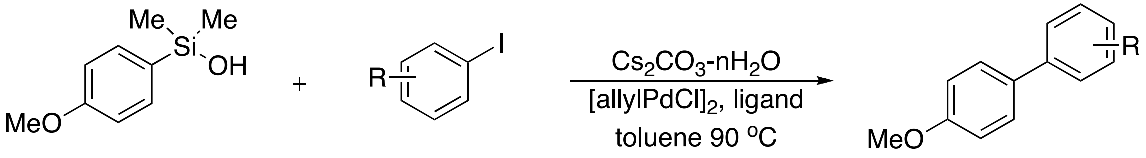


Denmark et al. Org. Lett. **2000**, 2, 2491-2494.



Hiyama et al. J. Org. Chem. **2000**, 65, 5342-5349.

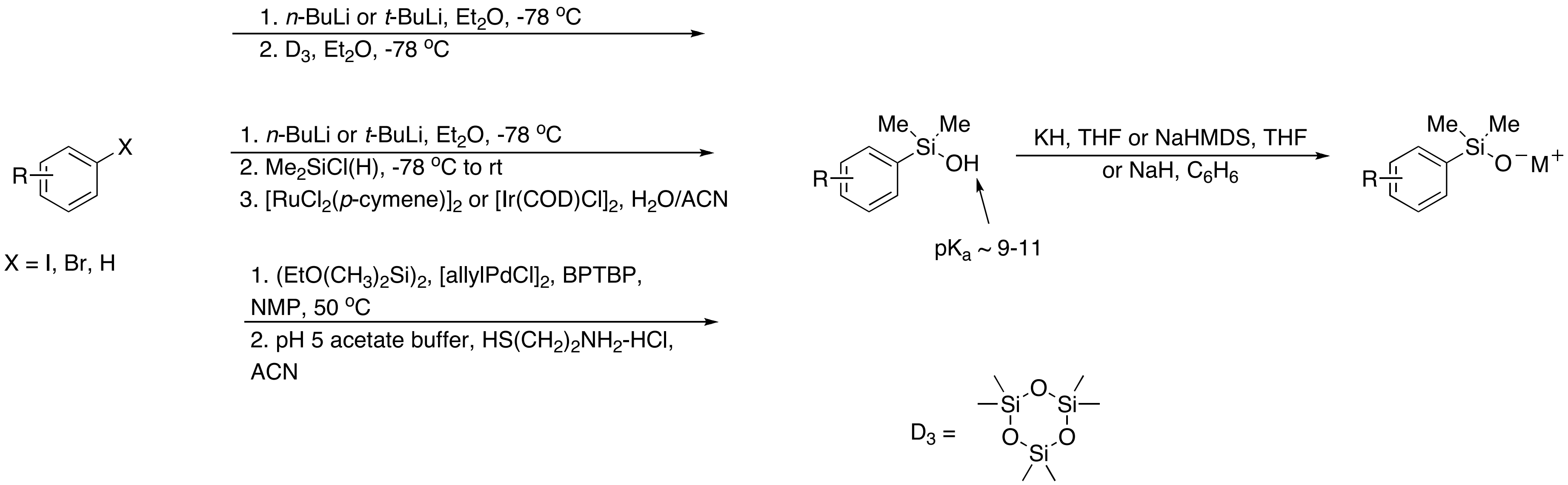
Arylsilanol Cross-Coupling



Denmark, S.; Ober, M. Org Lett. **2003**, 5, 1357-1360.

- Significant homocoupling of aryl halide was observed.
- More forcing conditions (T > 110 °C, CsOH) caused dimerization of silanol.
- Discovered dimethylsilanolate salts were stable and resistant to dimerization to disiloxanes.

Preparation of Aryl Silanolates



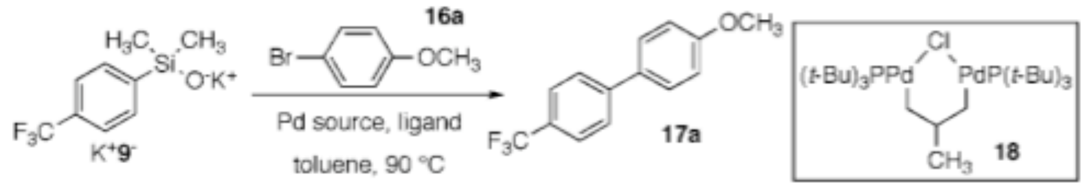
Silanol Preparation

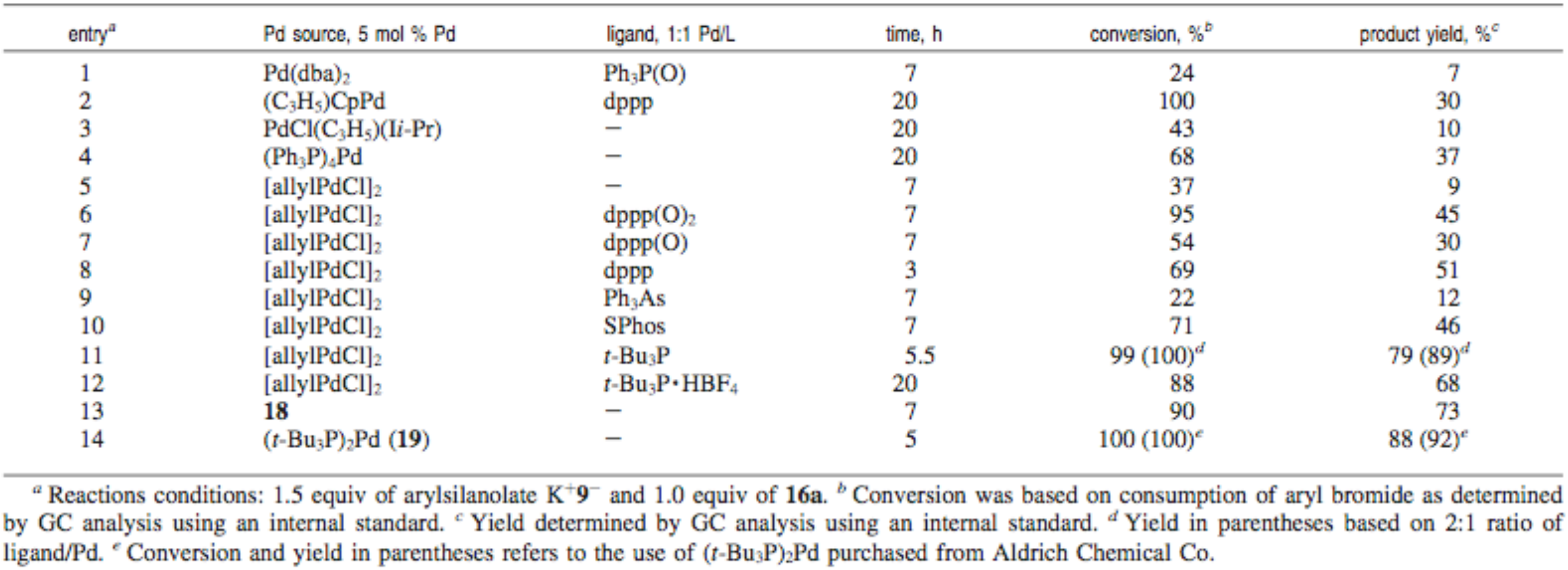
1.Halogen-Li exchange, trap with silicon electrophile

1.Catalytic oxidative hydrolysis of dimethylsilanes

1.Palladium-catalyzed silylation of aryl halides

Catalyst & Ligand Optimization





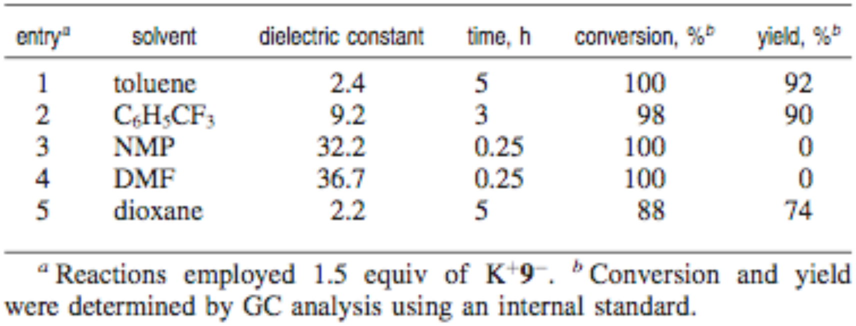
entry[a]	Pd source, 5 mol % Pd	ligand, 1:1 Pd/L	time, h	conversion, %[b]	product yield, %[c]
1	$Pd(dba)_2$	$Ph_3P(O)$	7	24	7
2	$(C_3H_5)CpPd$	dppp	20	100	30
3	$PdCl(C_3H_5)(I\textit{i}\text{-}Pr)$	–	20	43	10
4	$(Ph_3P)_4Pd$	–	20	68	37
5	$[allylPdCl]_2$	–	7	37	9
6	$[allylPdCl]_2$	$dppp(O)_2$	7	95	45
7	$[allylPdCl]_2$	dppp(O)	7	54	30
8	$[allylPdCl]_2$	dppp	3	69	51
9	$[allylPdCl]_2$	Ph_3As	7	22	12
10	$[allylPdCl]_2$	SPhos	7	71	46
11	$[allylPdCl]_2$	$t\text{-}Bu_3P$	5.5	99 (100)[d]	79 (89)[d]
12	$[allylPdCl]_2$	$t\text{-}Bu_3P\cdot HBF_4$	20	88	68
13	**18**	–	7	90	73
14	$(t\text{-}Bu_3P)_2Pd$ (**19**)	–	5	100 (100)[e]	88 (92)[e]

[a] Reactions conditions: 1.5 equiv of arylsilanolate K^+9^- and 1.0 equiv of **16a**. [b] Conversion was based on consumption of aryl bromide as determined by GC analysis using an internal standard. [c] Yield determined by GC analysis using an internal standard. [d] Yield in parentheses based on 2:1 ratio of ligand/Pd. [e] Conversion and yield in parentheses refers to the use of $(t\text{-}Bu_3P)_2Pd$ purchased from Aldrich Chemical Co.

Optimal catalyst: $(t\text{-}Bu_3P)_2Pd$ (Fu's Catalyst)

Reaction Optimization

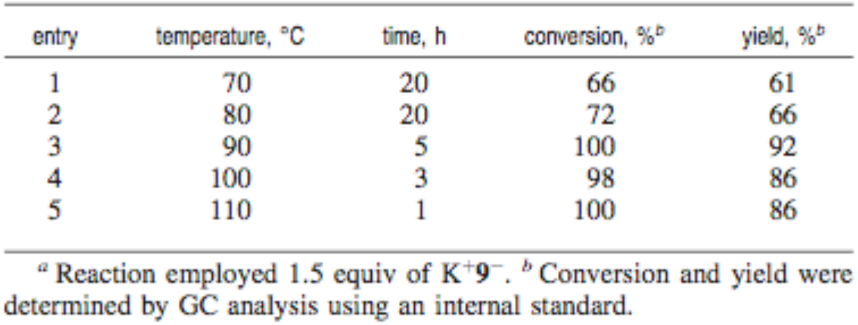
Solvent Optimization



entry[a]	solvent	dielectric constant	time, h	conversion, %[b]	yield, %[b]
1	toluene	2.4	5	100	92
2	$C_6H_5CF_3$	9.2	3	98	90
3	NMP	32.2	0.25	100	0
4	DMF	36.7	0.25	100	0
5	dioxane	2.2	5	88	74

[a] Reactions employed 1.5 equiv of K^+**9**$^-$. [b] Conversion and yield were determined by GC analysis using an internal standard.

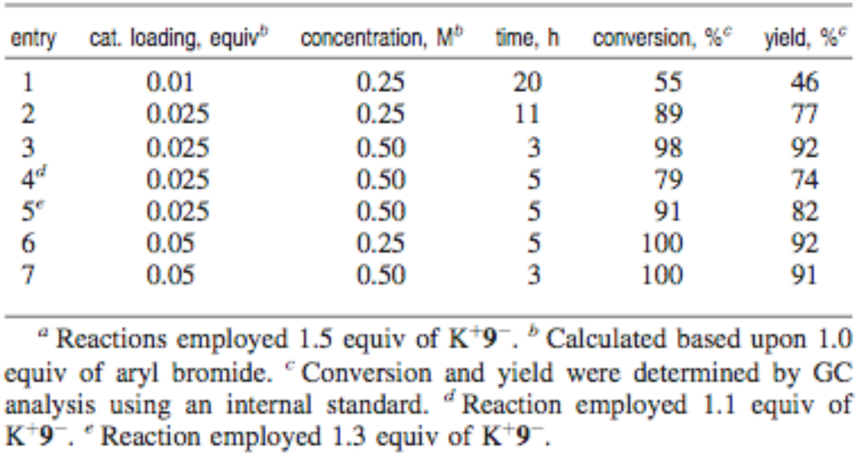
Temperature Optimization



entry	temperature, °C	time, h	conversion, %[b]	yield, %[b]
1	70	20	66	61
2	80	20	72	66
3	90	5	100	92
4	100	3	98	86
5	110	1	100	86

[a] Reaction employed 1.5 equiv of K^+**9**$^-$. [b] Conversion and yield were determined by GC analysis using an internal standard.

Catalyst Loading & Concentration Optimization

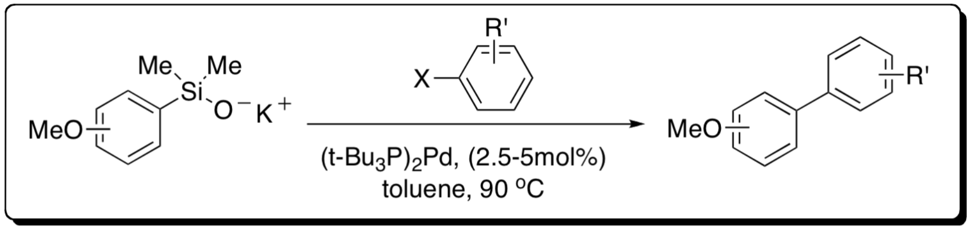


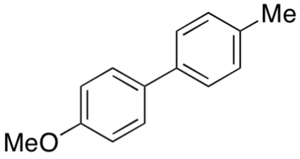
entry	cat. loading, equiv[b]	concentration, M[b]	time, h	conversion, %[c]	yield, %[c]
1	0.01	0.25	20	55	46
2	0.025	0.25	11	89	77
3	0.025	0.50	3	98	92
4[d]	0.025	0.50	5	79	74
5[e]	0.025	0.50	5	91	82
6	0.05	0.25	5	100	92
7	0.05	0.50	3	100	91

[a] Reactions employed 1.5 equiv of K^+**9**$^-$. [b] Calculated based upon 1.0 equiv of aryl bromide. [c] Conversion and yield were determined by GC analysis using an internal standard. [d] Reaction employed 1.1 equiv of K^+**9**$^-$. [e] Reaction employed 1.3 equiv of K^+**9**$^-$.

Optimal Conditions:
1.5 equiv of silanolate per aryl bromide
(t-$Bu_3P)_2Pd$ (2.5 mol%) in toluene, 90 °C.

Product Scope-Electron Donating Silanolates





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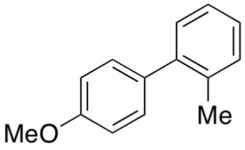

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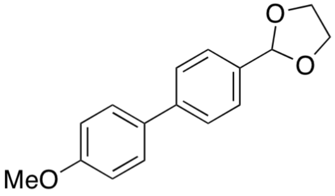

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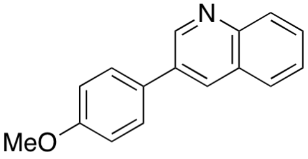

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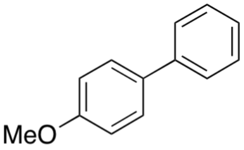
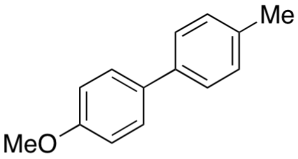
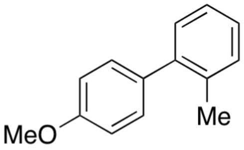


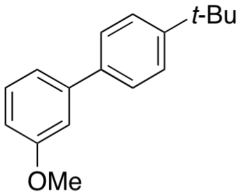
88%, (Ar-Cl)



81%, (Ar-Cl)



84%, (Ar-Cl)



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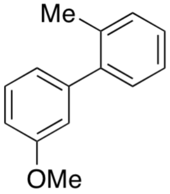

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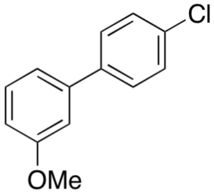

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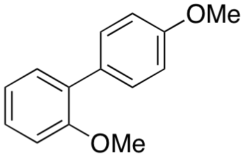

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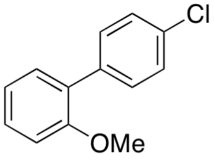

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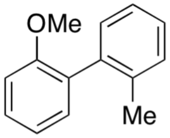
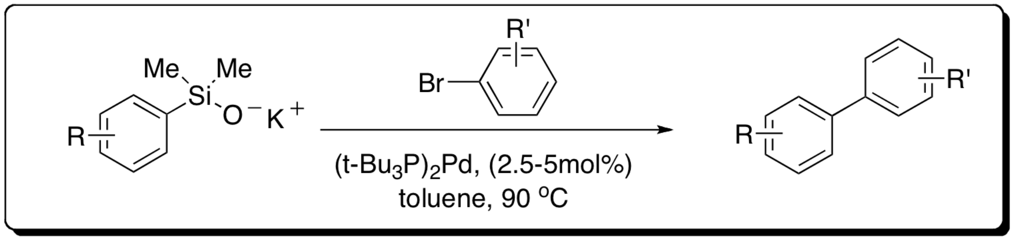
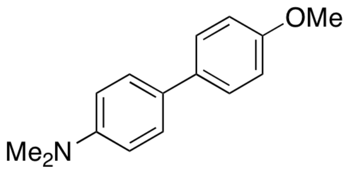


59%

Electron-Rich & Electron Neutral Silanolates



$(t\text{-}Bu_3P)_2Pd$, (2.5-5mol%)
toluene, 90 °C



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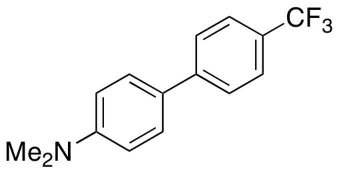

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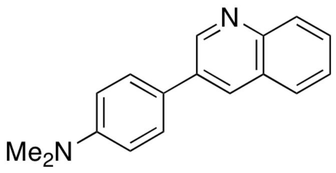

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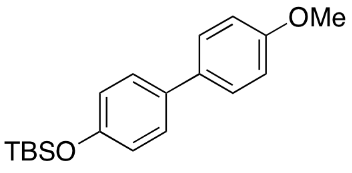

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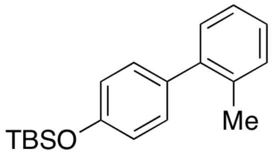

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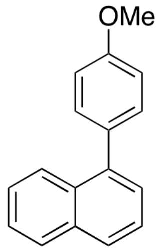

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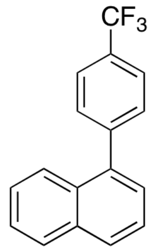

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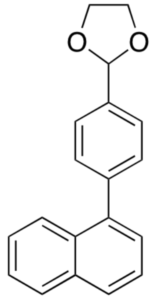

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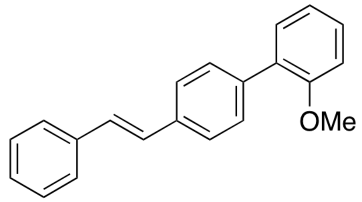

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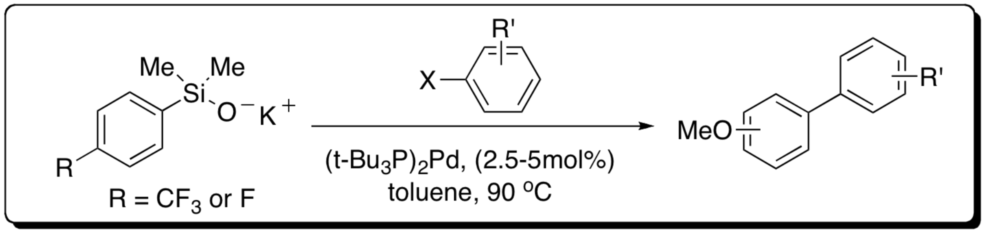
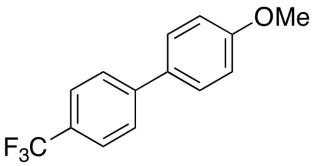
Fluorine-Containing Arylsilanolates





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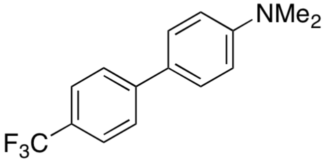

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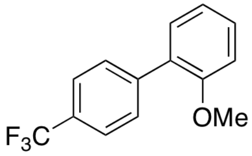

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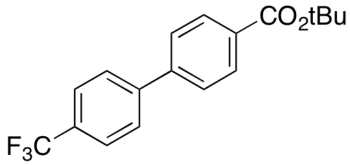

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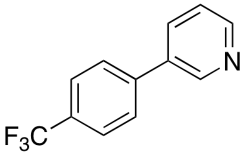

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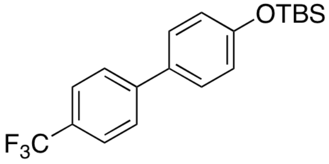
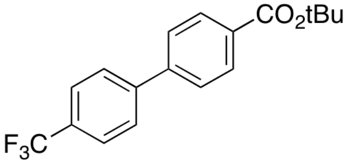
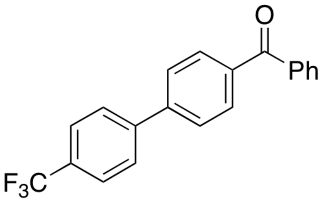


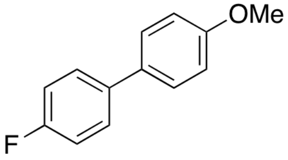
58%, (Ar-Cl)



62%, (Ar-Cl)



58%, (Ar-Cl)



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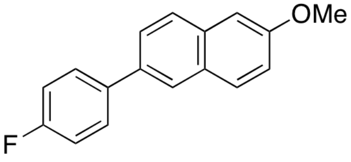

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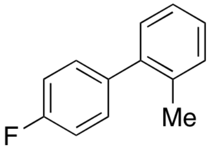

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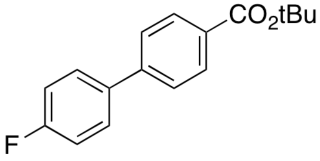

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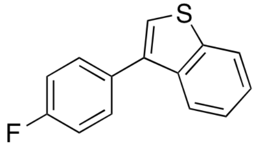

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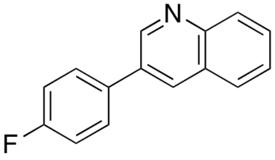

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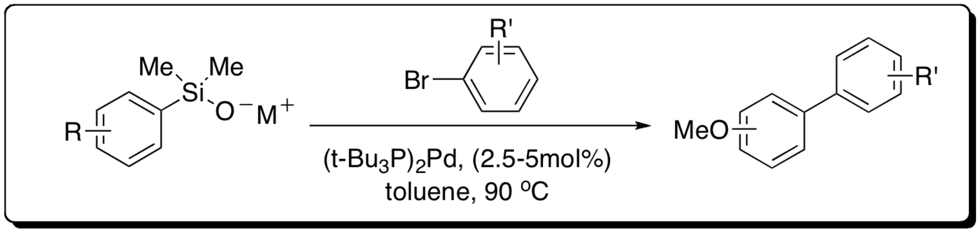
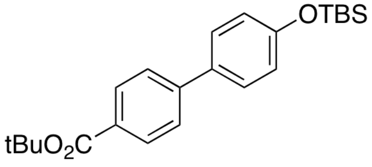
Electron-Deficient Arylsilanolates





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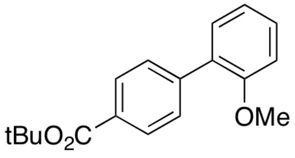

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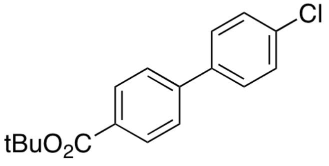

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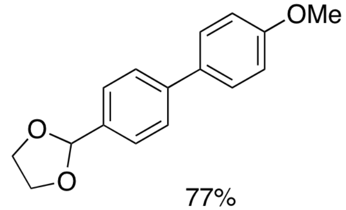

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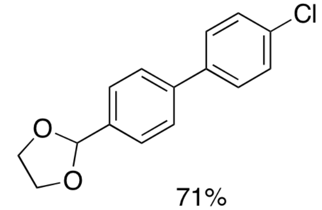

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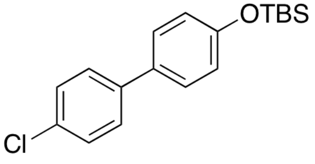

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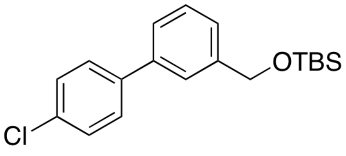

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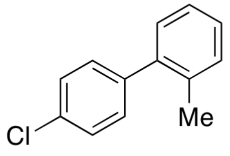

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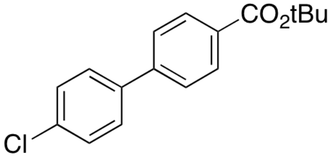

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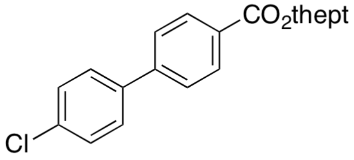

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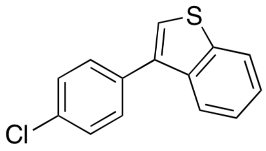

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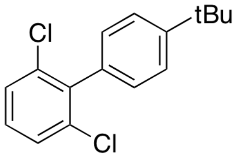

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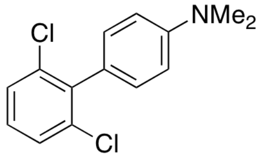

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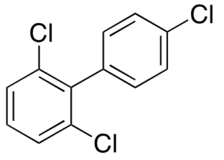

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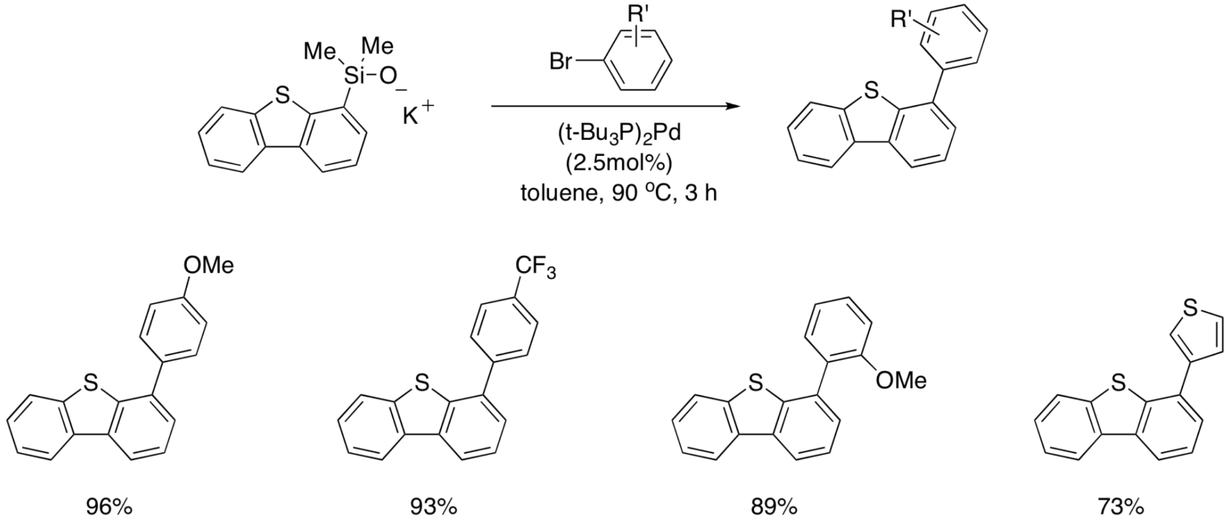
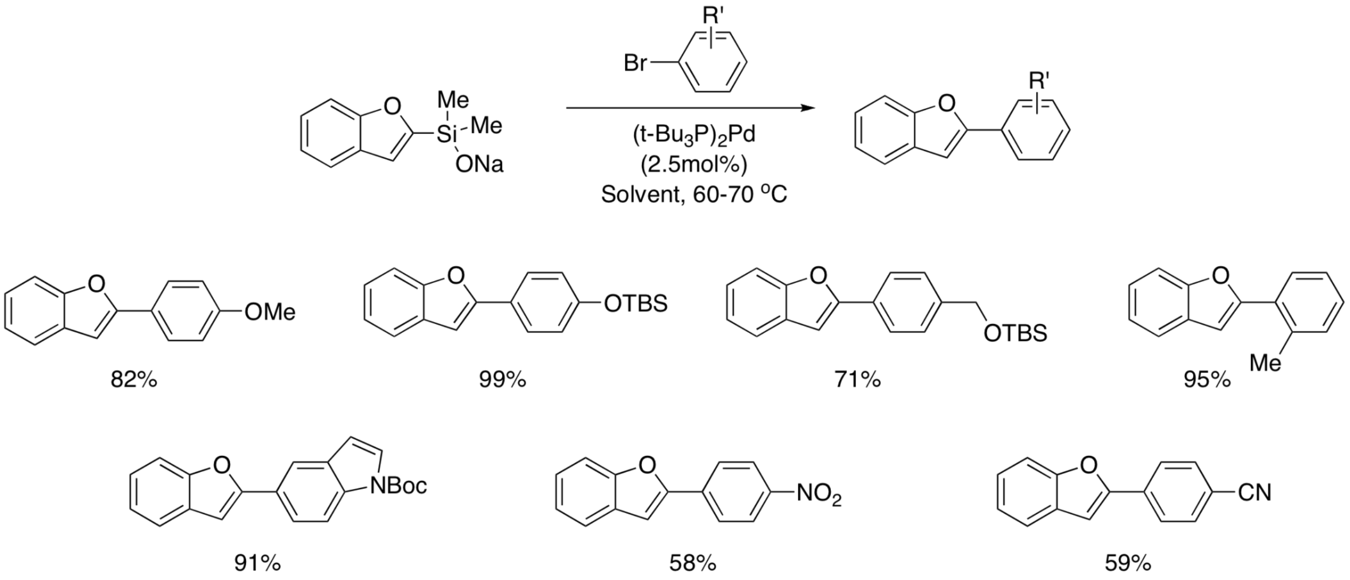
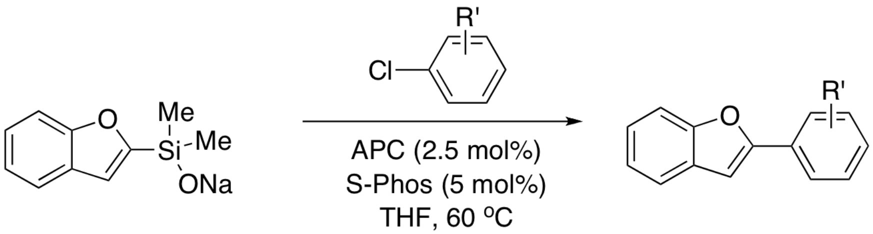
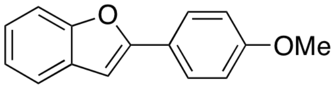
Hetetrocyclic Arylsilanolates





Heterocyclic Arylsilanolates





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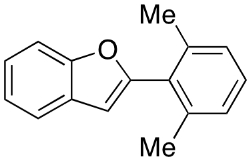

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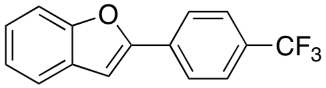

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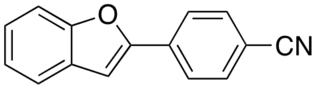

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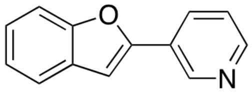

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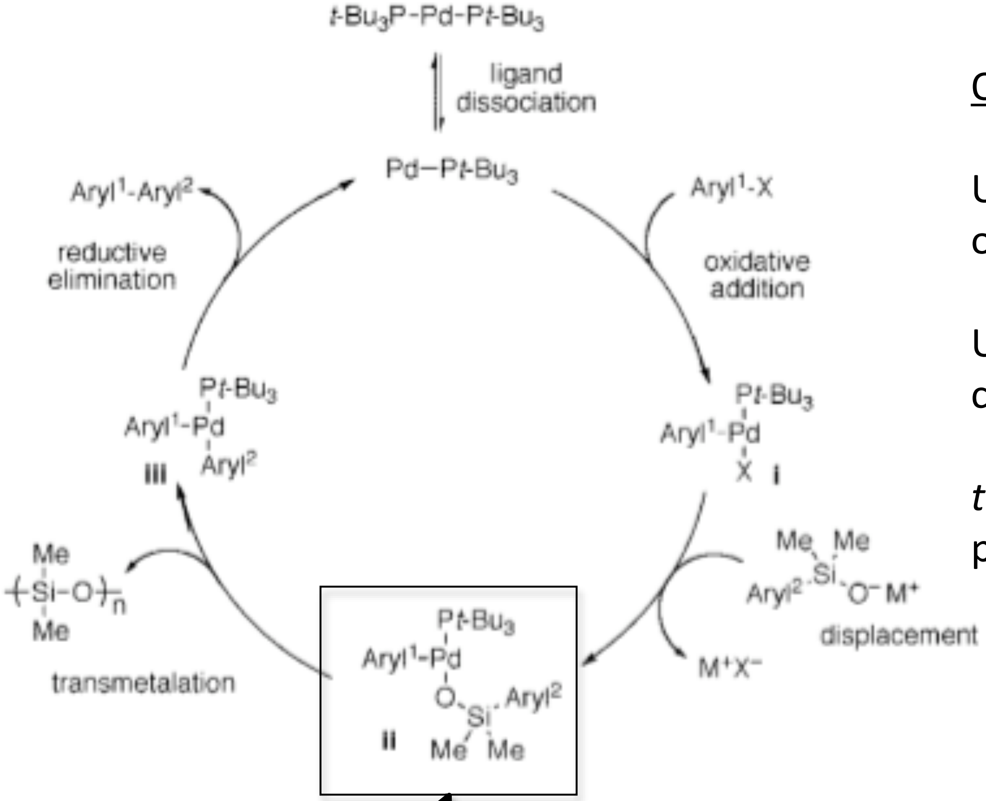
Mechanism



Based on mechanistic studies
these species undergo transmetalation.
JACS **2004**, 126, 4876-4882.

Observations:

Use of bidentate phosphine decreases opportunity for transmetalation.

Use of t-Bu$_3$P prevents second phosphine from coordination during cycle.

t-Bu$_3$P may also prevent homocoupling by preventing second oxidative insertion.

Summary

- A mild approach for assembly of a wide variety of biaryl compounds.
- Conditions are tolerable to variety of functional groups and heterocycles.
- Stability of silanolate salts makes them attractive precursors for cross-coupling reactions.
- Coupling partners have been demonstrated with aryl bromides and the more cost effective aryl chlorides.
- Provides an alternative coupling strategy to organotin and organoboron chemistries.