July 2006

LaPCat™ - Perovskite Catalysts for Organic Synthesis

- Structure and Background
- Mechanism in Organic Reactions
- Scope of Reactions and Catalysts
- Reaction Details
- Outlook

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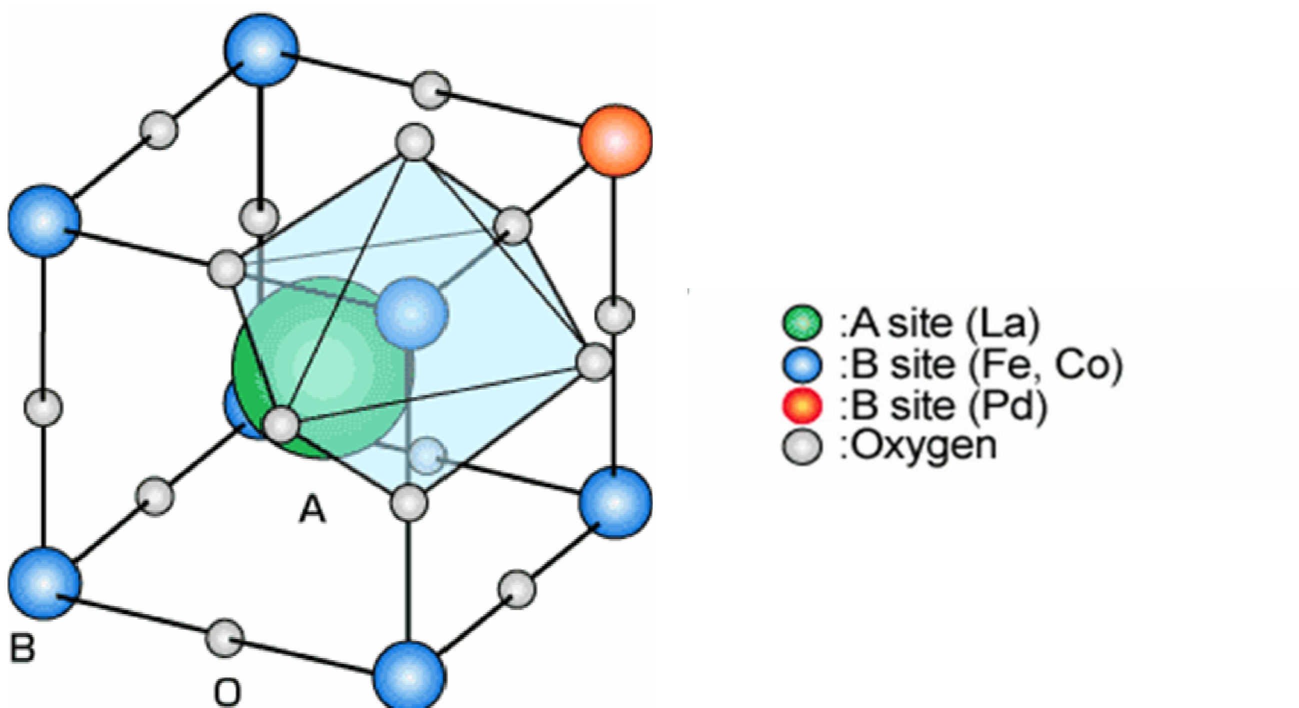
Perovskite Structure

- Perovskites have ABO_3 Structure
  - e.g. $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$



http://www.daihatsu.com/news/n2002/02091901/index2.html

Perovskite Applications

- Wide number of natural and synthetic perovskites.
- Several material applications including piezoelectricity and superconductors.
- Catalytic applications include fuel reforming and water gas shift processing.
- Palladium containing perovskites are used in high efficiency auto catalysts.

Perovskites in Organic Synthesis

- Perovskites are stable and recyclable catalysts for performing organic transformations
- They are highly active – as little as **0.01 mol % Pd** is sufficient.
- Extremely low residual **Pd levels**; filtrates of a Suzuki reaction found to contain **below 2 ppm Pd**.
- **High Turnover Numbers** (up to **400,000)** have been recorded

M. D. Smith, S. V. Ley et al.; *Chem. Commun.*, 2003, 2652-3.

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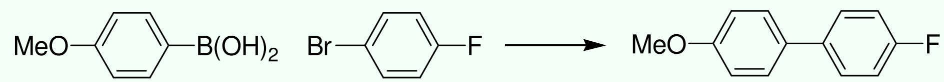
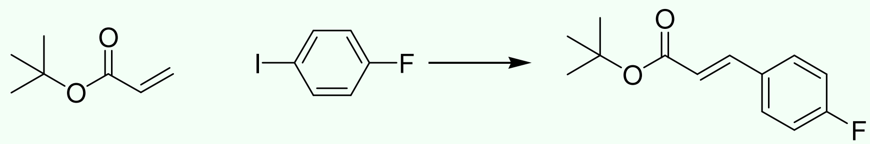
LaPCat™ Perovskite Reactions

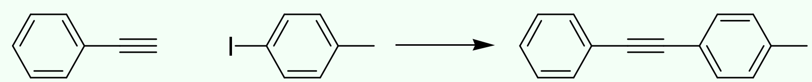
Suzuki



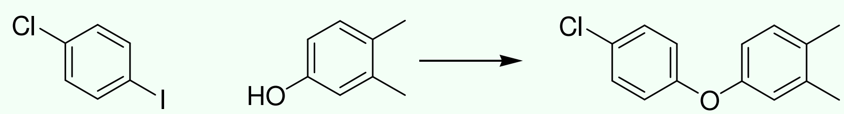
Heck



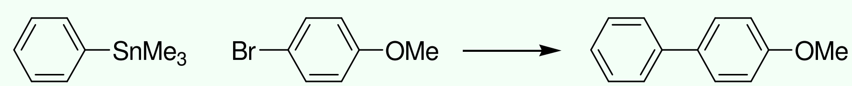
Sonogashira



Ullmann



Stille

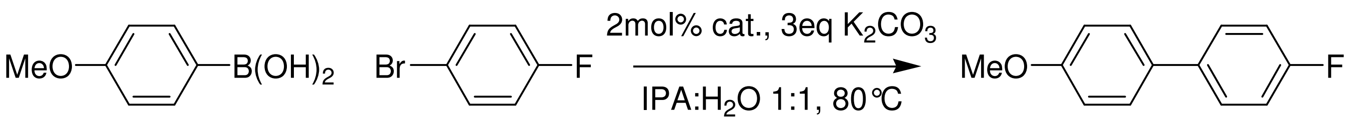


LaPCat^{TM} Perovskite Catalysts

Catalyst	*Formulation*	*Surface Area (m^2/g)*	*Particle Size (µm)*	*Reactions*
FP2	$LaFe_{0.95}Pd_{0.05}O_3$	5.5	41.1	Suzuki
FP8	$LaFe_{0.80}Pd_{0.20}O_3$	5.7	3.3	Suzuki
CoP	$LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$	3.4	4.0	Suzuki, Stille, Heck, Sonogashira
CuP	$LaFe_{0.57}Cu_{0.38}Pd_{0.05}O_3$	12	3.7	Suzuki, Sonogashira, Ullmann
CoCu	$La_{0.9}Ce_{0.1}Co_{0.60}Cu_{0.40}O_3$	7.9	5.4	Ullmann
YBCu	$YBa_2Cu_3O_7$	0.3	10.6	Ullmann

Suzuki Reactions

Different Catalysts



	Catalyst	*Loading (mol% Pd)*	*Time (h)*	*Conversion (%)*
1	FP2	0.1	1	100
2	FP8	0.4	1	100
3	CoP	0.1	1	100
4	CuP	0.1	1	100
5	CoCu	-	22	0
6	YBCu	-	22	0

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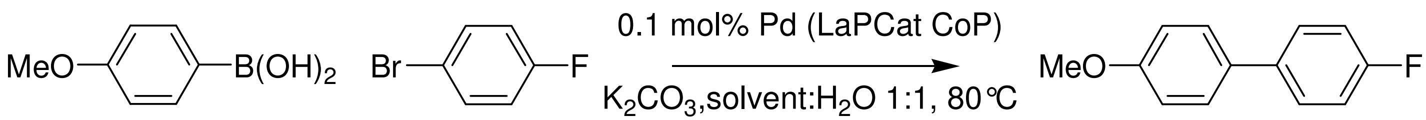
Suzuki Reactions

Solvent Compatibility



	Solvent	*Solvent:Aqueous*	*Conversion after 22h (%)*
1	IPA	1:1	100
2	Dioxane	1:1	100
3	MeCN	1:1	100
4	DME	1:1	82
5	THF	1:1	92
6	IPA	4:1	100

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Suzuki Reactions

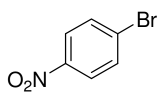
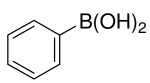
Lower Catalyst Loadings

	Catalyst	*Loading (mol% Pd)*	*Solvent*	*Conversion after 22h (%)*
1	CoP	0.10	IPA/H_2O	100
2	CoP	0.05	IPA/H_2O	100/85[a]
3	CoP	0.05	Dioxane/H_2O	100
4	CoP	0.01	IPA/H_2O	100/93[a]
5	FP2	0.005	IPA/H_2O	85[a]

[a] Isolated Yields

Suzuki Reactions

$$\underset{\textbf{1.5 eq}}{R{-}B(OH)_2} \qquad \underset{\textbf{1.0 eq}}{X{-}Ar} \quad \xrightarrow[\text{3eq } K_2CO_3\text{, IPA/}H_2O\text{ 1:1, 80°C}]{\text{0.05mol\% Pd (CoP)}} \quad R{-}Ar$$

Aryl Halide	Boronic Acid	Additive	Time (h)	Yield (%)
		TBAB	10	95
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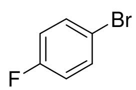
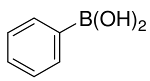
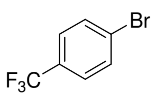
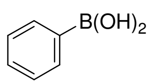
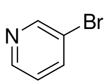
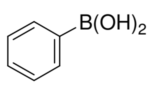
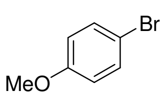
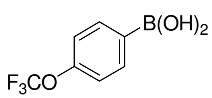
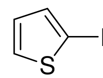
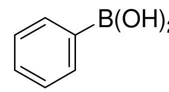
		none	3	91
		none	2	92
		none	18	85
		none	18	95

Aryl Halide	Boronic Acid	Additive	Time (h)	Yield (%)
		TBAB	18	89
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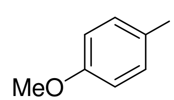
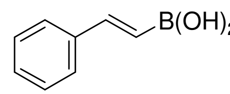
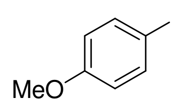
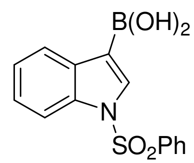
		none	18	92
		TBAB	18	70
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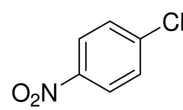
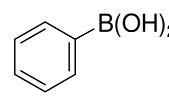
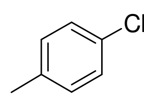
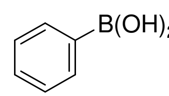
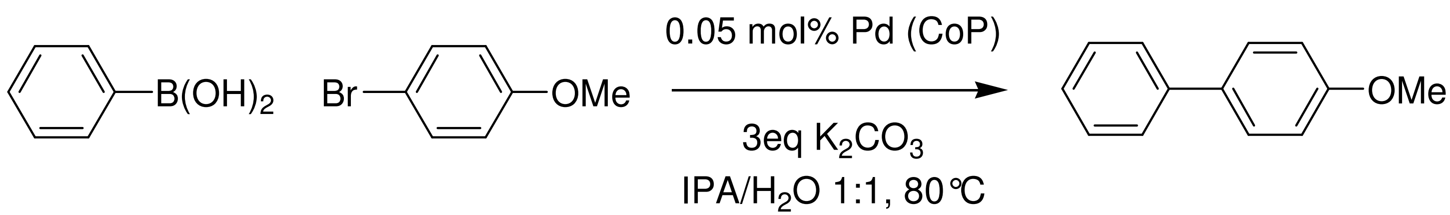
		none	1[a]	71
		none	1[a]	51

[a] Microwave conditions: IPA/H_2O 1:1, MW heating 135°C, 3eq Na_2CO_3, 0.25 mol% Pd

M. D. Smith, S. V. Ley et al.; *Chem. Commun.*, 2003, 2652-3.

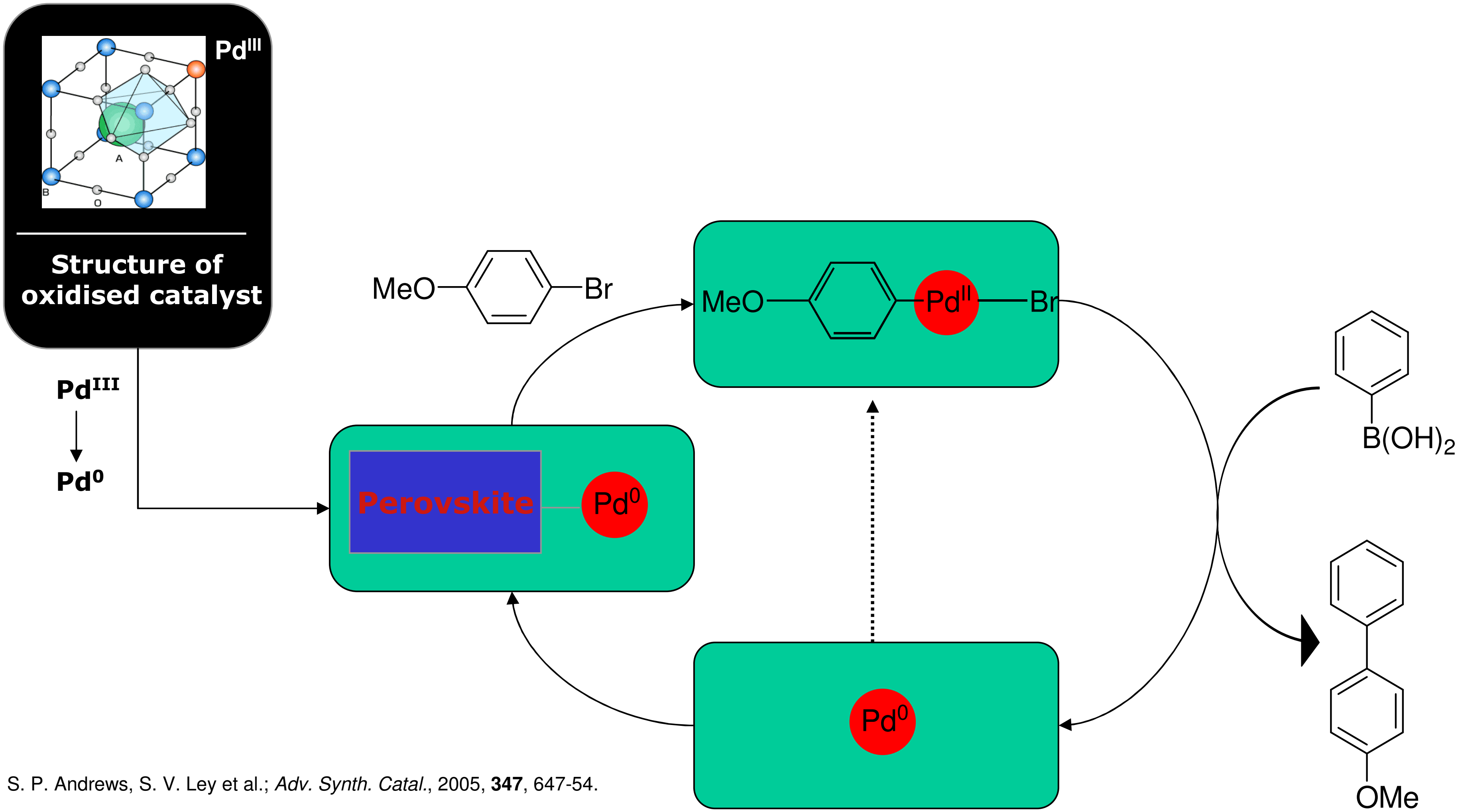
Catalyst Recovery and Recycling
Suzuki Reactions



Run	1	2	3	4	5
Yield (%)	95	93	93	95	93
Time (h)	1	0.6	2	1	1

M. D. Smith, S. V. Ley et al.; *Chem. Commun.*, 2003, 2652-3.

LaPCat™ Perovskite Mechanism in Organic Synthesis



S. P. Andrews, S. V. Ley et al.; *Adv. Synth. Catal.*, 2005, **347**, 647-54.

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Metal Leaching from LaPCat^{TM} CoP

Metal	Co	Fe	Pd
ppm	2.7	1.9	8.2
% leaching	0.29	0.14	3.63

Method: LaPCat^{TM} CoP (20mg) in DMF (2ml) heated at 120℃ for 2 days, cooled, filtered and analysed by ICP

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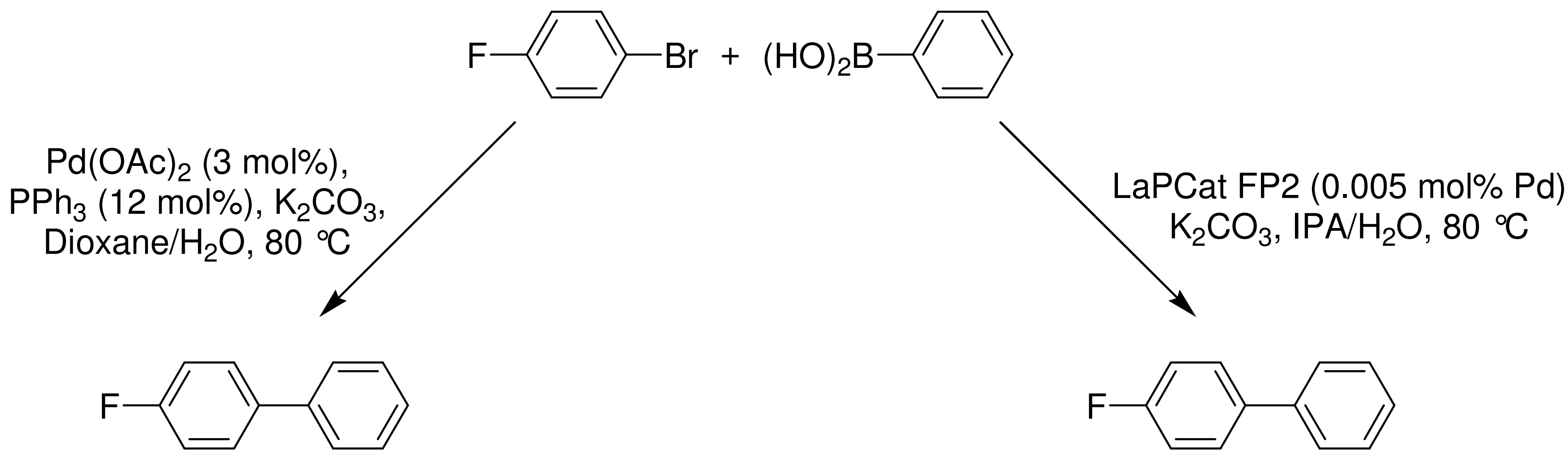
Suzuki Reactions

Heterogeneous Catalysis vs Perovskite



Procedure: Reaction heated under nitrogen for 18 h, cooled, diluted with EtOAc and filtered through celite. Aqueous layer extracted with EtOAc, dried over $MgSO_4$ and solvent removed.

Suzuki Reactions

Crude Products

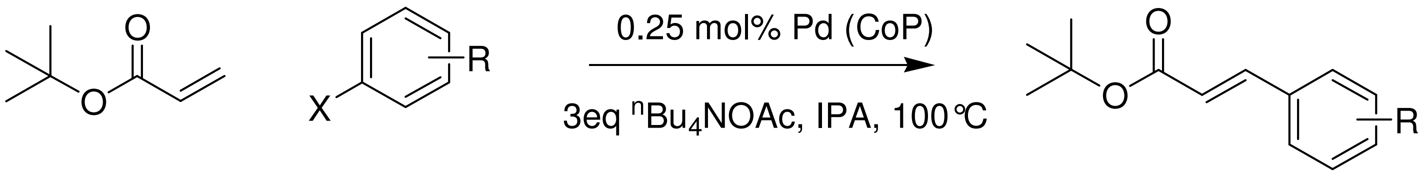
$Pd(OAc)_2/PPh_3$ LaPCat FP2

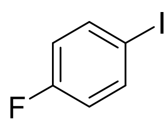
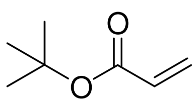
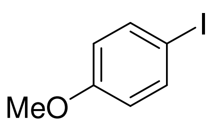
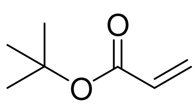
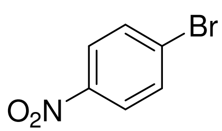
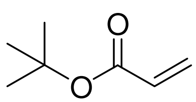
Recrystallised

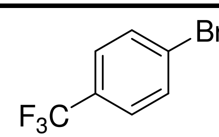
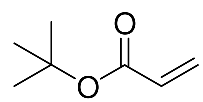
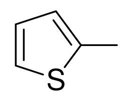
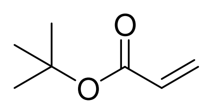
$Pd(OAc)_2/PPh_3$ LaPCat FP2

2140 ppm Pd 13 ppm Pd

Heck Reactions



Aryl Halide	Alkene	Yield (%)
		95
		99
		70

Aryl Halide	Alkene	Yield (%)
		90
		51

A. Stepan, Cambridge University, 2004, unpublished results

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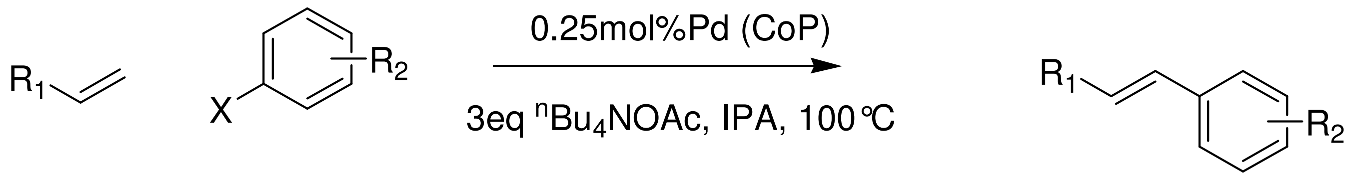
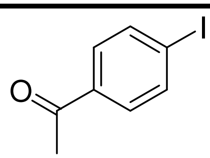
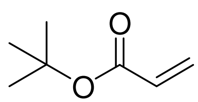
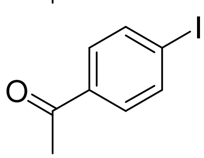
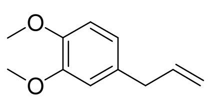
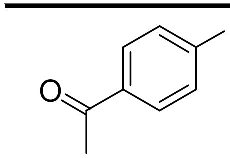
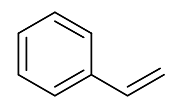
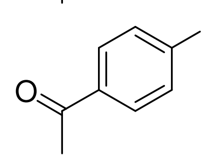
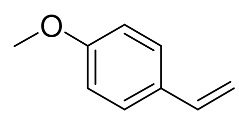
Heck Reactions



Aryl Halide	Alkene	Yield (%)
		68
		73

Aryl Halide	Alkene	Yield (%)
		59
		56

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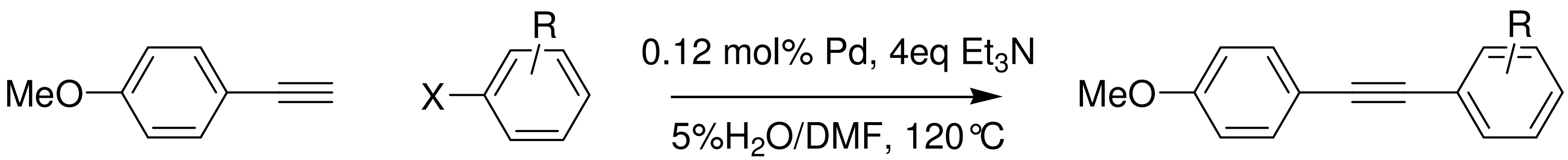
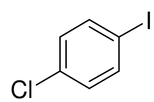
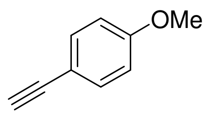
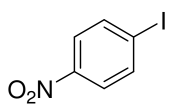
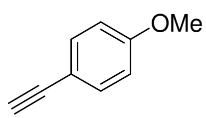
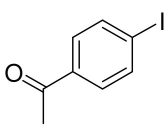
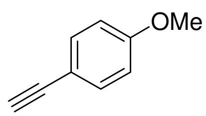
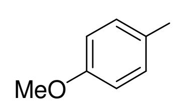
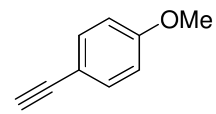
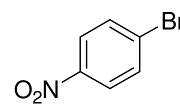
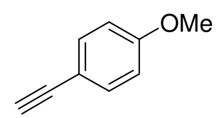
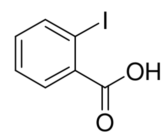
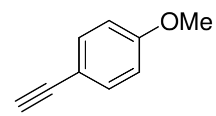
Sonogashira Reactions



Aryl Halide	Alkyne	Catalyst	Yield (%)
		CuP	71
		CuP	96
		CoP	96
		CuP	47[a]
		CuP	71[a]
		CuP	52

[a] Reaction performed in DMA

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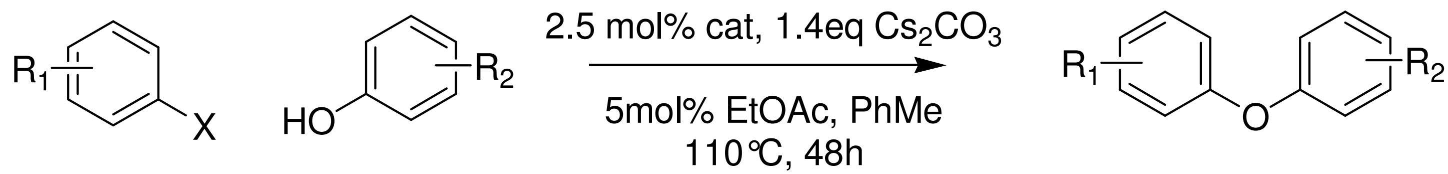
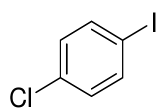
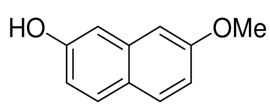
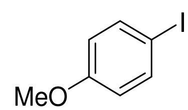
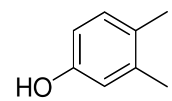
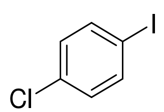
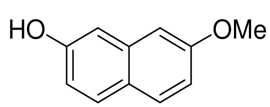
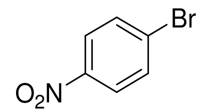
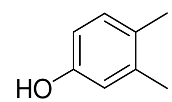
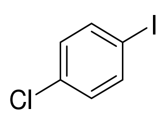
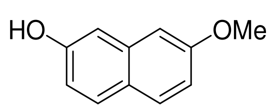
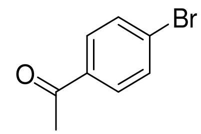
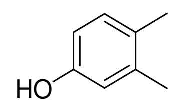
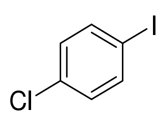
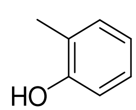
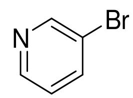
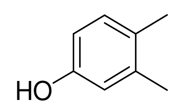
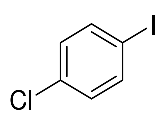
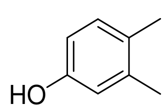
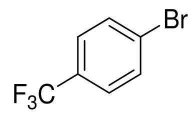
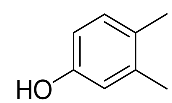


Aryl Halide	Phenol	Catalyst	Yield (%)	Aryl Halide	Phenol	Catalyst	Yield (%)
		CoCu	82			CoCu	78
		CuP	65			CoCu	89
		YBCu	73			CoCu	86
		CoCu	71			CoCu	74
		CoCu	88			CoCu	72

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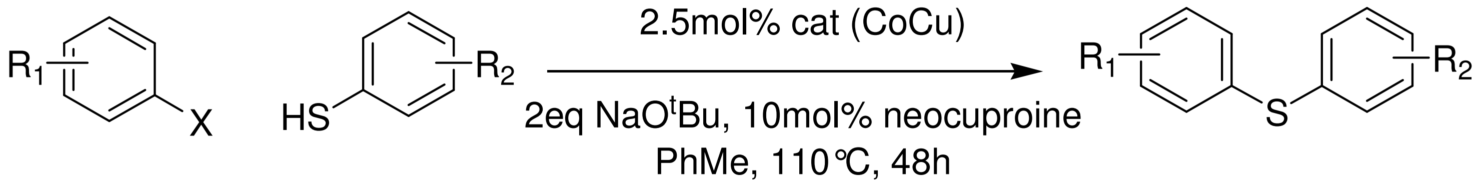
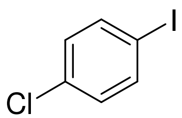
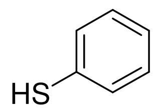
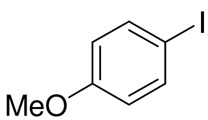
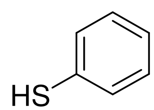
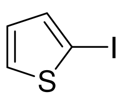
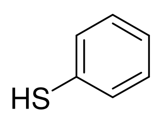
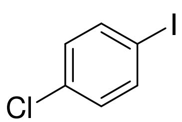
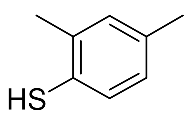
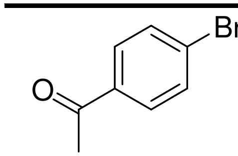
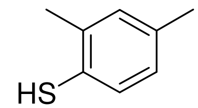
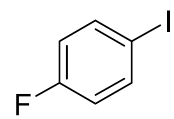
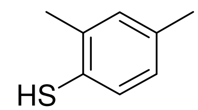
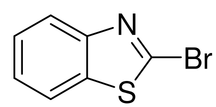
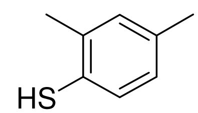
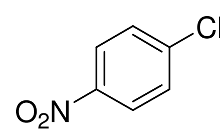
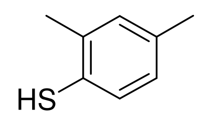


Aryl Halide	Thiophenol	Yield (%)
		91
		90
		64
		89

Aryl Halide	Thiophenol	Yield (%)
		99
		94
		78
		46

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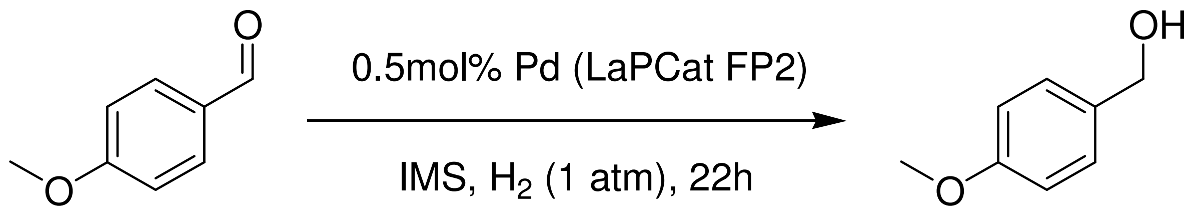
Selective Hydrogenation



Overnight reaction under H_2 balloon

98% conversion to benzyl alcohol by NMR

Conclusions

Perovskites catalyse a range of organic transformations

Work at very low catalyst loadings

Can lead to exceptionally low Pd contamination

Future work will continue to extend their applications

Reaxa’s LaPCat™ Perovskite Kit

Test Kit now available from Reaxa

Catalyst	*Formulation*	*Formula Weight*	*Quantity supplied (mg)*
FP2	$LaFe_{0.95}Pd_{0.05}O_3$	245.29	100
FP8	$LaFe_{0.80}Pd_{0.20}O_3$	252.87	100
CoP	$LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$	246.46	100
CuP	$LaFe_{0.57}Cu_{0.38}Pd_{0.05}O_3$	248.21	100
CoCu	$La_{0.9}Ce_{0.1}Co_{0.60}Cu_{0.40}O_3$	247.81	100
YBCu	$YBa_2Cu_3O_7$	666.22	100

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