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## Coupling Capabilities of Imidazole, Thiazole & Oxazole Boronic Acids & Esters

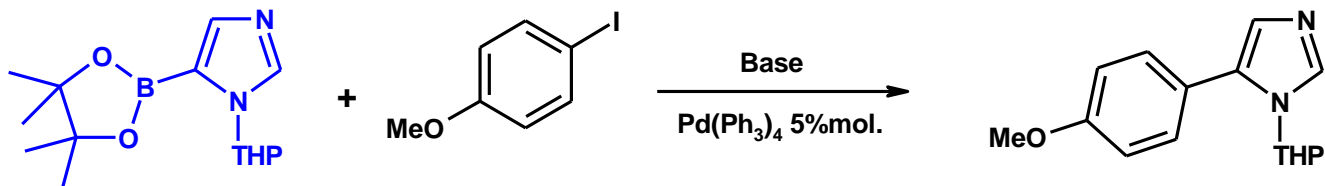


info@borochem.fr  
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- Imidazoles
- Thiazoles
- Oxazoles

# Reactivity of imidazol-5-ylboronic acids & esters

## Definition of Suzuki coupling conditions



**B12-0003**

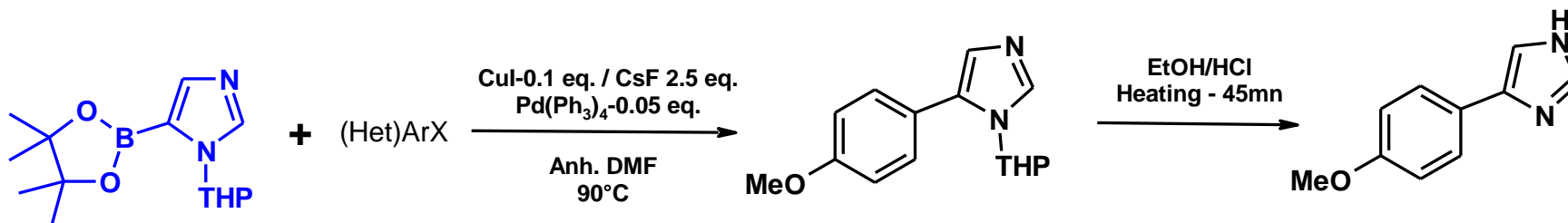
Base	Solvent	Heating	Yield (%)
$\text{K}_2\text{CO}_3$ or $\text{NaHCO}_3$	DME/water 3/2	Classic 90°C	0
$\text{K}_3\text{PO}_4$	DMF anh.	Classic 90°C	40
$\text{CsF}$ $\text{CuI}$	DMF anh.	Classic 90°C	66
$\text{CsF}$ $\text{CuI}$	dioxane	Classic 90°C	<10
$\text{CsF}$ $\text{CuI}$	DMF anh.	Microwave 130°C	31

- Imidazoles
- Thiazoles
- Oxazoles

# Reactivity of imidazol-5-ylboronic acids & esters

## Synthesis of 4(5)-arylimidazoles

Primas, N. & al.  
Tetrahedron  
2008, 64, 4596



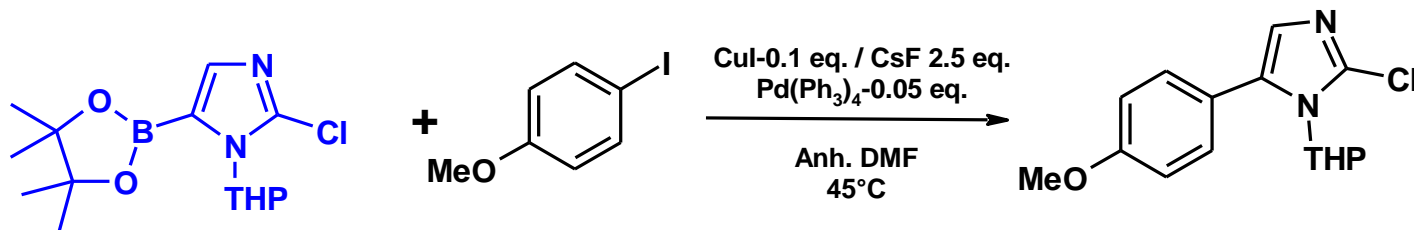
In case Ar-X contains a function sensitive to deprotection: dioxane/HCl, RT, 10-24 hours

Ar-X	Product after deprotection	Yield
		35%
		57%
		58%
		37%
		21%

- Imidazoles
- Thiazoles
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# Reactivity of imidazol-5-ylboronic acids & esters

## Reactivity in Suzuki coupling

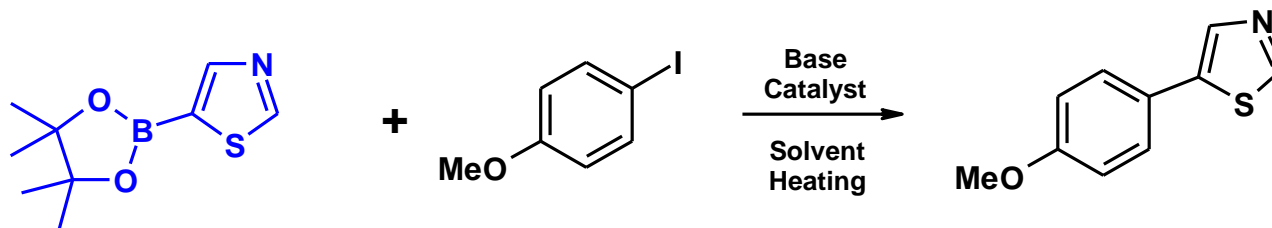


- Deboronation in aqueous conditions
- Coupling at low temperature to avoid parasitical reactions with Cl at C-2

- Imidazoles
- **Thiazoles**
- Oxazoles

# Reactivity of thiazol-5-ylboronic acids & esters

## Definition of Suzuki coupling conditions

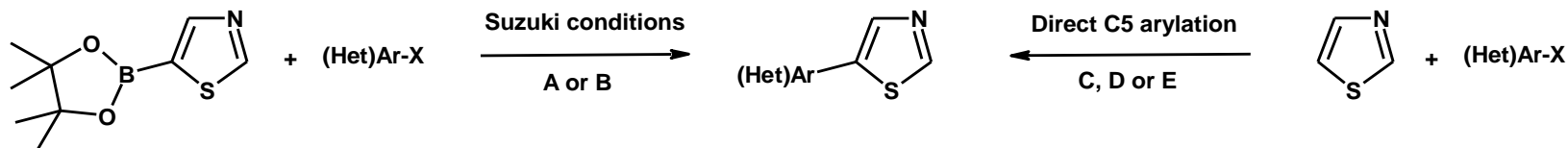


Boronic Ester	Base	Catalyst (5 mol %)	Solvent	Yield (%)
<b>B13-0001</b> (1,1 eq.)	Na <sub>2</sub> CO <sub>3</sub>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	Dioxane/water 3/1	61
<b>B13-0001</b> (2,0 eq.)	Na <sub>2</sub> CO <sub>3</sub>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	Dioxane/water 3/1	80
<b>B13-0001</b> (1,1 eq.)	Cs <sub>2</sub> CO <sub>3</sub>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	Dioxane/water 3/1	36
<b>B13-0001</b> (1,1 eq.)	Na <sub>2</sub> CO <sub>3</sub>	PdCl <sub>2</sub> (dppf)	Dioxane/water 3/1	49
<b>B13-0001</b> (1,1 eq.)	CsF CuI	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DMF anh.	54
<b>B13-0001</b> (1,1 eq.)	K <sub>3</sub> PO <sub>4</sub>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DMF anh.	54
<b>B13-0001</b> (1,1 eq.)	CsF CuI	PdCl <sub>2</sub> (dppf)	DMF anh.	68

- Imidazoles
- **Thiazoles**
- Oxazoles

# Synthesis of 5-arylthiazoles

## Comparative study Suzuki coupling/ Direct C5-H arylation



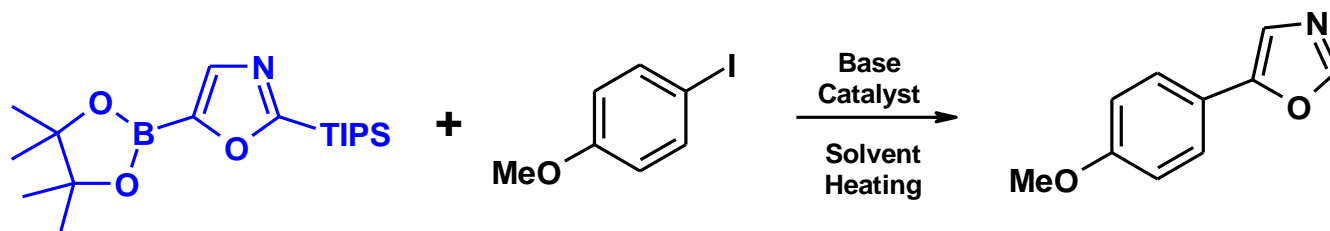
Halogenoaryl	Product	Suzuki conditions	Yield Suzuki (%)	Arylation conditions	Yield direct arylation (%)
		A	79	C	63
		A	80	C E	36 0
		B	63	C	traces
		B	67	C D	50 25
		A	67	C E	35 34
		B	74	C E	28 18

See Primas, N. & al. Tetrahedron 2009, 65, 5739 or contact us at [info@borochem.fr](mailto:info@borochem.fr) for conditions A-C

- Imidazoles
- Thiazoles
- **Oxazoles**

# Reactivity of 2-TIPS-oxazol-5-ylboronic acids & esters

## Definition of Suzuki coupling conditions

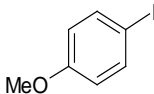
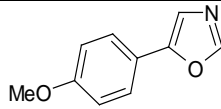
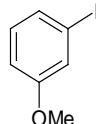
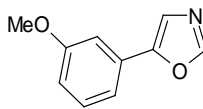
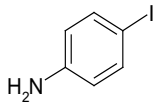
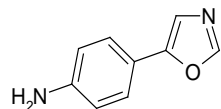
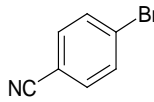
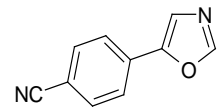
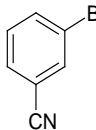
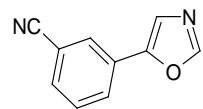
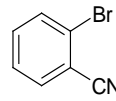
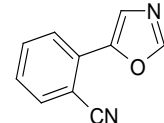


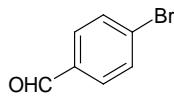
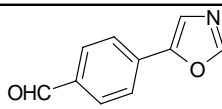
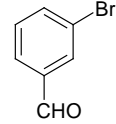
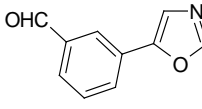
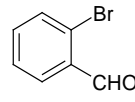
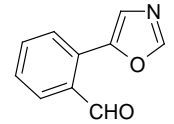
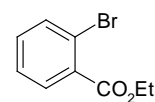
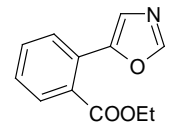
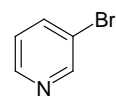
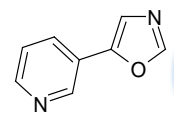
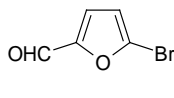
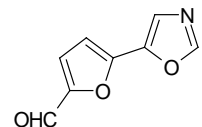
Compound (eq.)	Base	Catalyst	(% mol)	Solvent	Yield (%)
<b>B14-0001</b> (1.1 equiv)	Na <sub>2</sub> CO <sub>3</sub> (2,5 eq.)	Pd(PPh <sub>3</sub> ) <sub>4</sub>	5	Dioxane/water 3/1	79
<b>B14-0001</b> (1.1 equiv)	CsF (2,5 eq.) CuI (0,1. eq.)	Pd(PPh <sub>3</sub> ) <sub>4</sub>	5	DMF	Mixture
<b>B14-0001</b> (1.1 equiv)	Na <sub>2</sub> CO <sub>3</sub> (2,5 eq.)	Pd(OAc) <sub>2</sub>	5	Dioxane/water 3/1	31
<b>B14-0001</b> (1.1 equiv)	Na <sub>2</sub> CO <sub>3</sub> (2,5 eq.)	Pd(OAc) <sub>2</sub>	2	Dioxane/water 3/1	62

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- Imidazoles
- Thiazoles
- **Oxazoles**

# Synthesis of 5-aryloxazoles

Halogenoaryl	Coupled product	Yield (%)
		79
		90
		62
		64 <sup>a</sup>
		75
		72

Halogenoaryl	Coupled product	Yield (%)
		71
		67
		74
		53
		69
		71

Primas, N., Bouillon, A., Lancelot, J.-C., Rault, S., Tetrahedron 2009, 65, 6348