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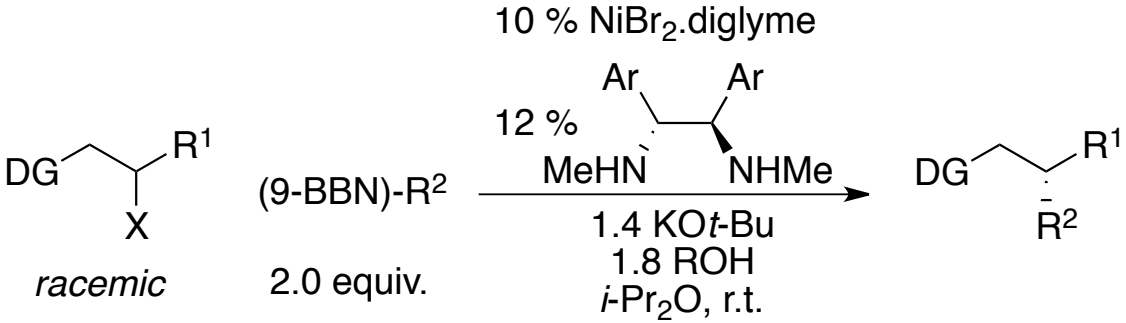
Séminaire STEREO : RCC 14.01.13

Nickel-Catalyzed Carbon-Carbon Bond-Forming Reactions of Unactivated Tertiary Alkyl Halides: Suzuki Arylations

Susan L. Zultanski and Gregory C. Fu

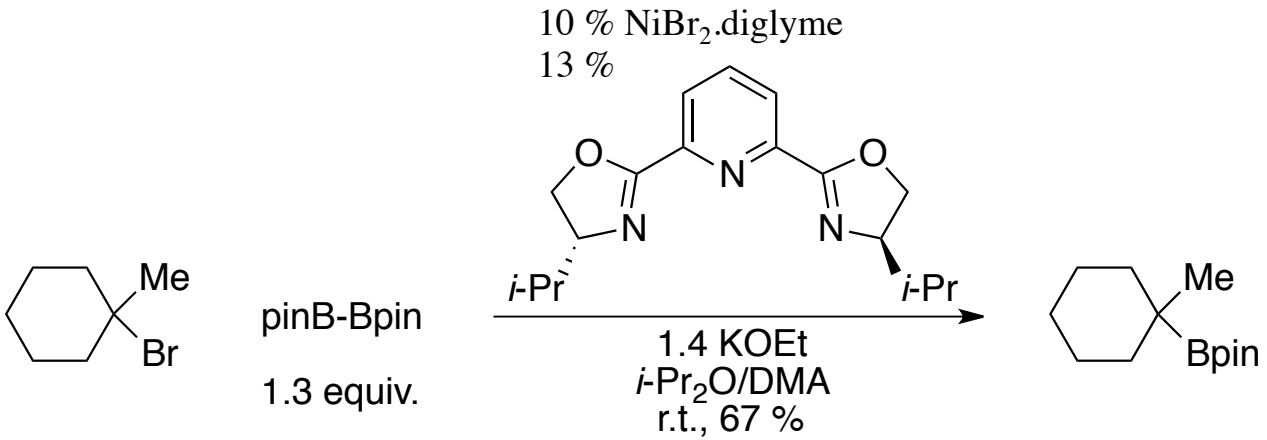
Previous work on Ni-catalyzed Cross-coupling reactions

- Unactivated primary and secondary alkyl halides:



J. Am. Chem. Soc. **2012**, 134, 5794–5797

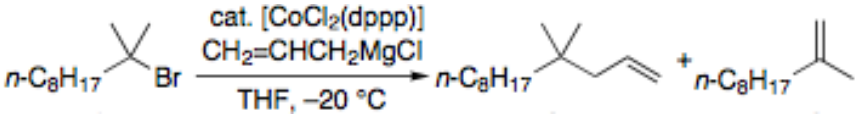
- Coupling of tertiary alkyl halides with diboron reagents:



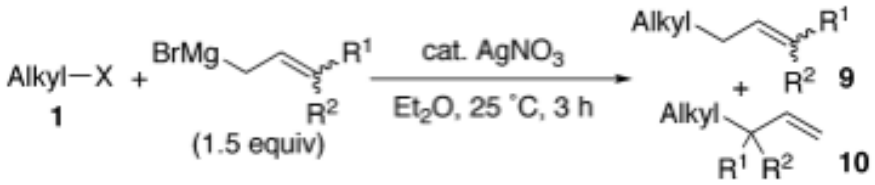
J. Am. Chem. Soc. **2012**, 134, 10693–10697

Cross-coupling of Tertiary Alkyl Halides: Oshima's work

- Allyl-grignard:

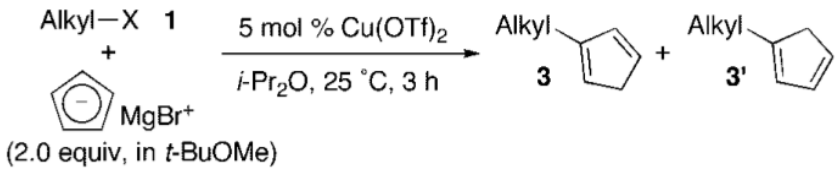


Angew. Chem. Int. Ed. **2002**, 41, 4137-4139



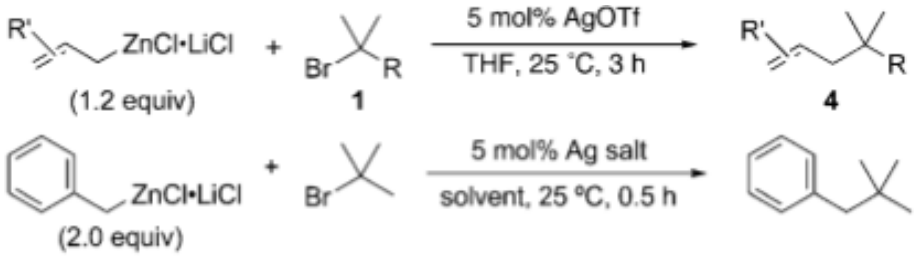
Org. Lett., **2008**, 10, 969-971

- Cyclopentadienyl-grignard:



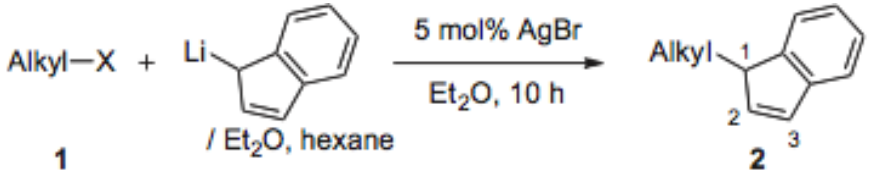
Org. Lett., **2008**, 10, 2545-2547

- Allyl- and benzyl-zinc:



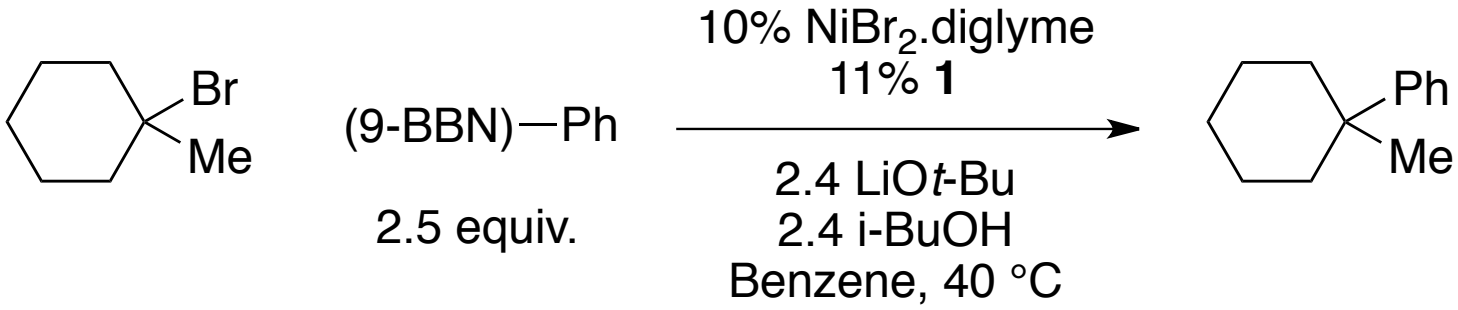
Chem. Asian J. **2010**, 5, 1487 – 1493

- Indenyllithium:

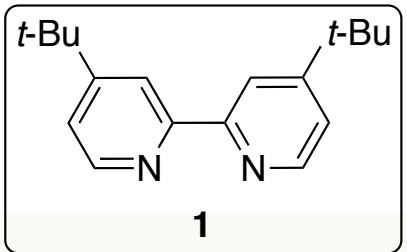


Tetrahedron, **2010**, 66, 5993-5999

Model Reaction



Variations from standard conditions	Yield (%)
-	**88**



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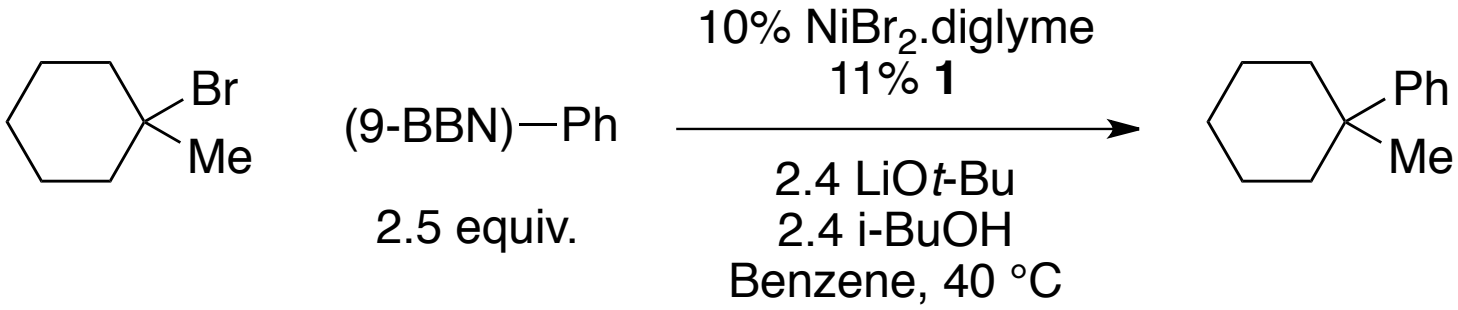
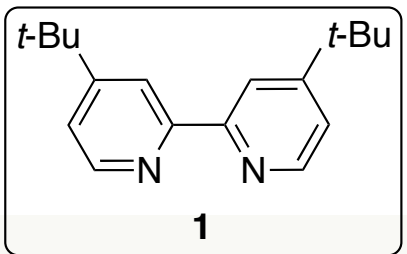
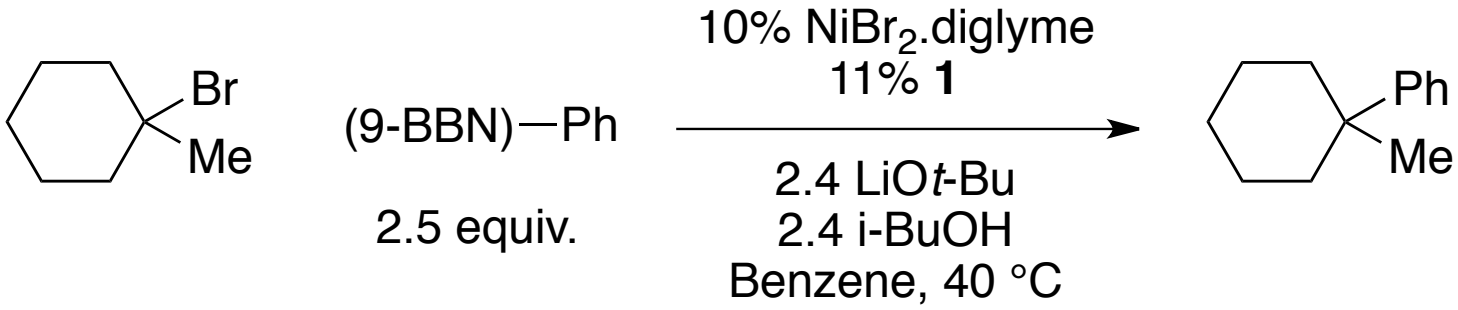


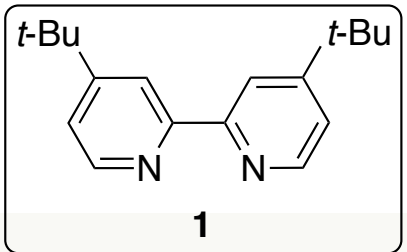
Variations from standard conditions	Yield (%)
-	**88**
No catalyst	<2
No ligand **1**	8
No LiO*t*-Bu	<2



Model Reaction

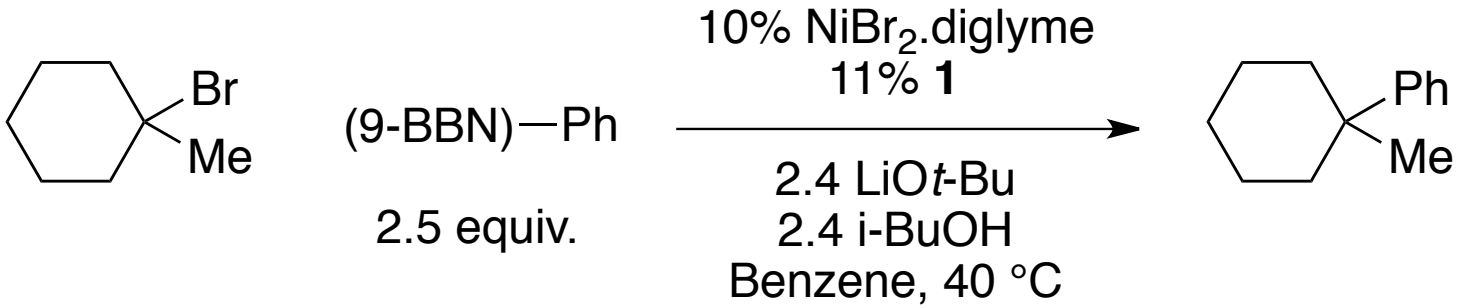


Variations from standard conditions	Yield (%)
-	**88**
No catalyst	<2
No ligand **1**	8
No LiO*t*-Bu	<2
KO*t*-Bu or NaO*t*-Bu instead of LiO*t*-Bu	<2

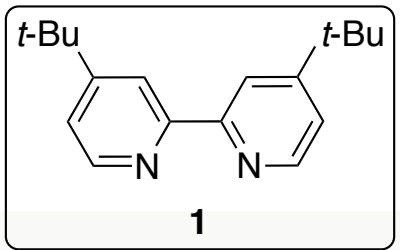


1

Model Reaction



Variations from standard conditions	Yield (%)
-	**88**
Ligand **2** instead of **1**	72
Ligand **3** instead of **1**	63
Ligand **4** instead of **1**	7



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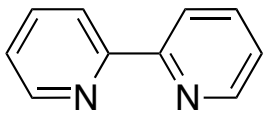

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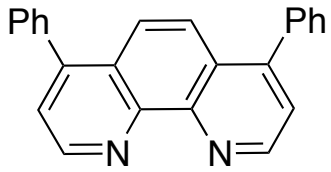

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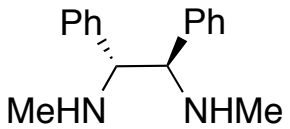

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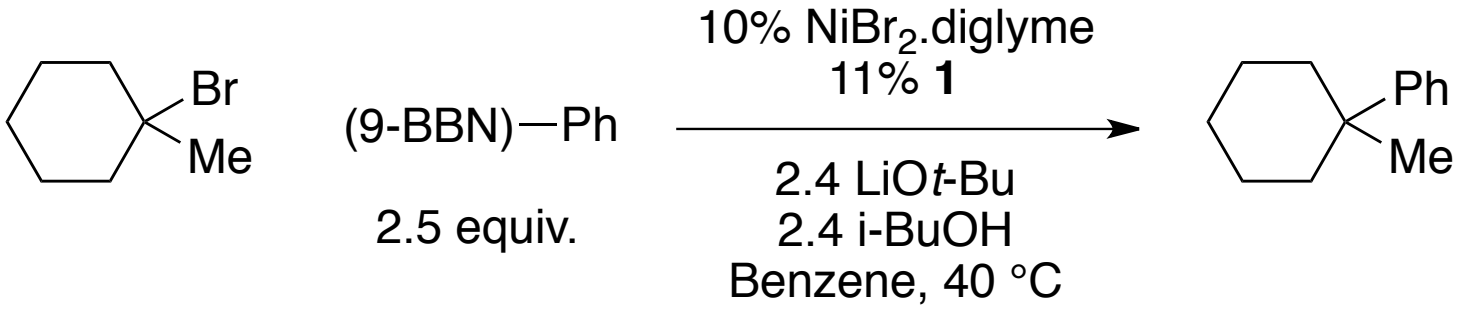
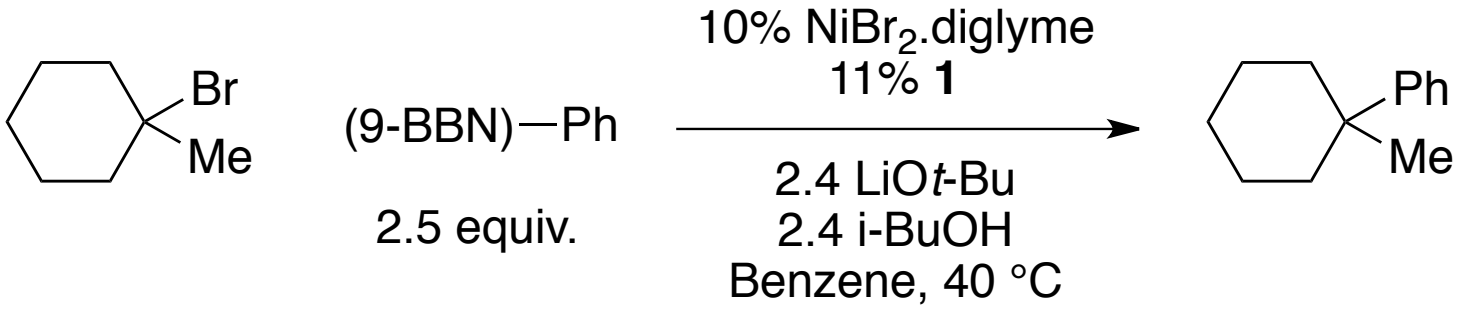
Model Reaction



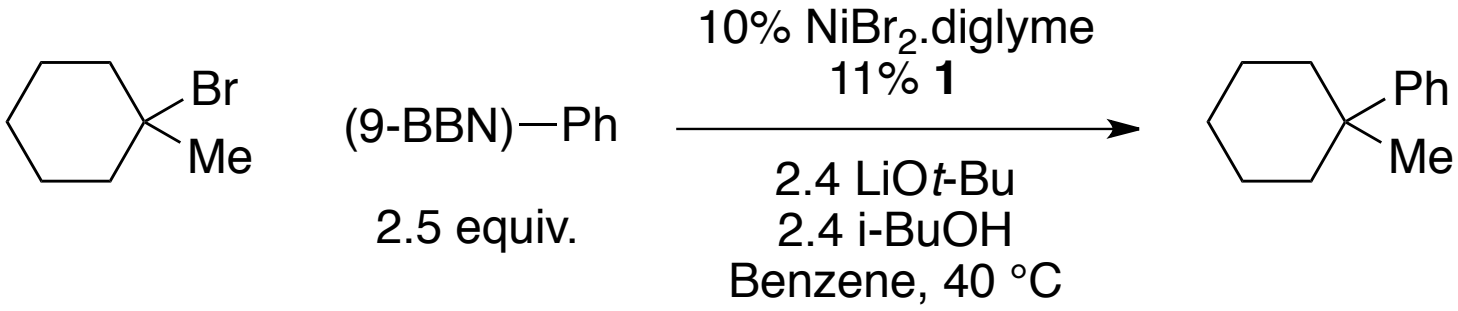
Variations from standard conditions	Yield (%)
-	**88**
Toluene instead of Benzene	45
Cyclohexane instead of Benzene	34
Et_2O instead of Benzene	13

Model Reaction



Variations from standard conditions	Yield (%)
-	**88**
Toluene instead of Benzene	45
Cyclohexane instead of Benzene	34
Et_2O instead of Benzene	13
1.8 equiv of (9-BBN)-Ph	62
5 % $NiBr_2$.diglyme, 5.5 % of **1**	53

Model Reaction



Variations from standard conditions	Yield (%)
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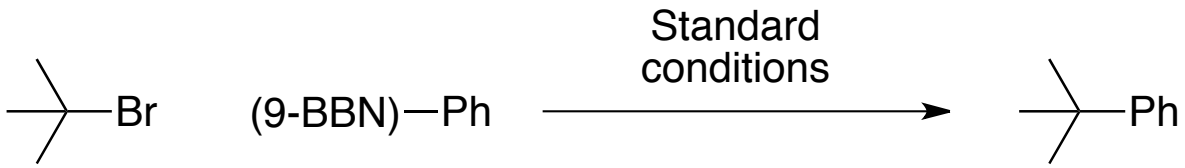
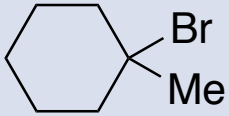
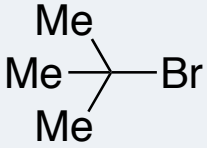
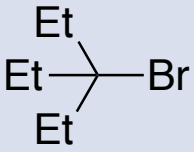
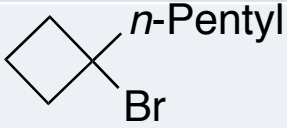
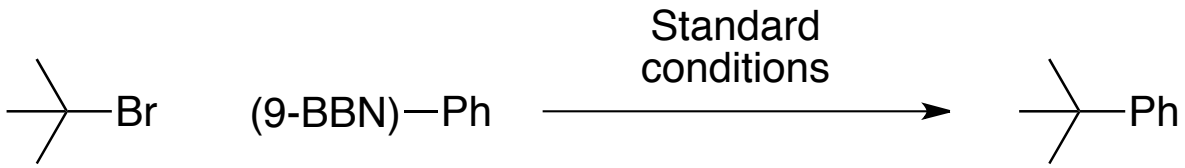
Et_2O instead of Benzene	13
1.8 equiv of (9-BBN)-Ph	62
5 % $NiBr_2$.diglyme, 5.5 % of **1**	53
0.1 equiv H_2O	89

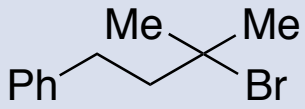
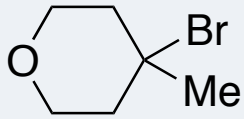
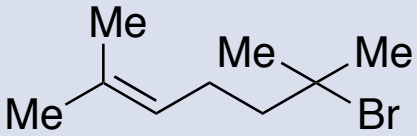
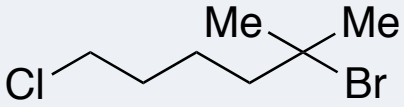
Scope of the Electrophile



Tertiary alkyl bromide	Yield (%)
	84
	71
	70
	53

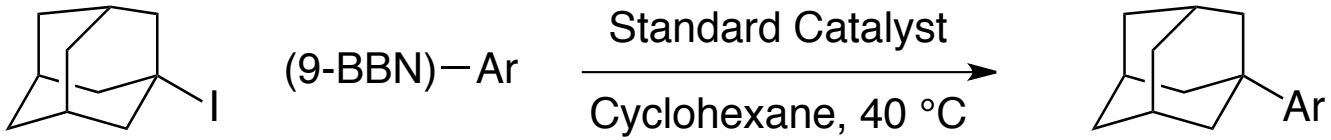
Scope of the Electrophile



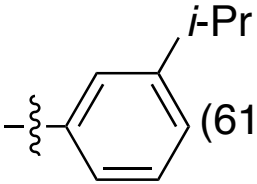
Tertiary alkyl bromide	Yield (%)
	86
	57
	76
	67

Scope of the Electrophile

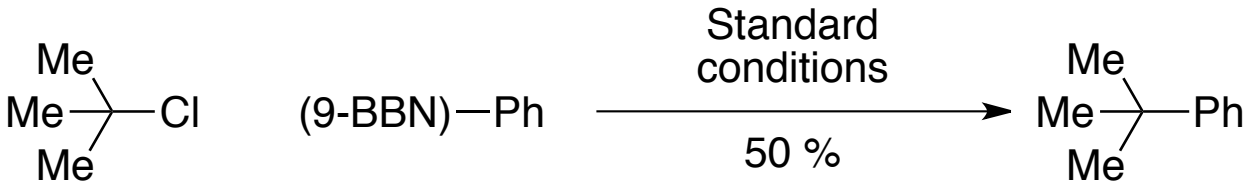
- Coupling of Iodo-adamanthane :



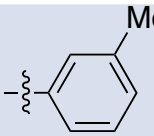
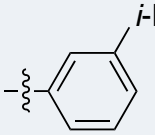
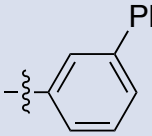
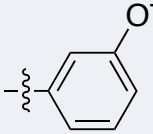
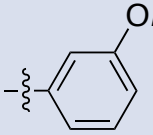
Ar = Ph (74 %)

Ar =  (61 %)

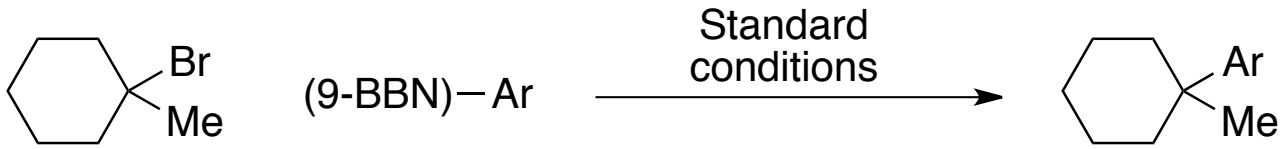
- Coupling of Trialkyl-chloride :



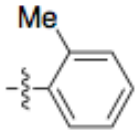
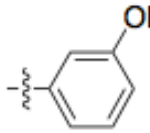
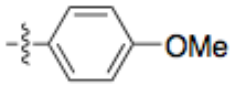
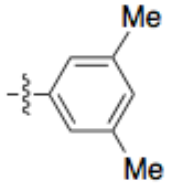
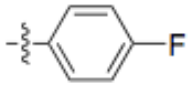
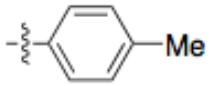
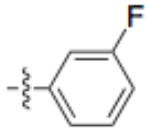
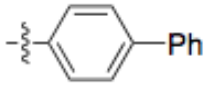
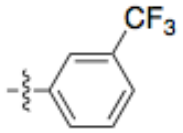
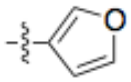
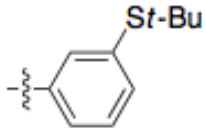
Scope of the Nucleophile

Ar	Yield (%)
	60
	61
	74
	57
	54

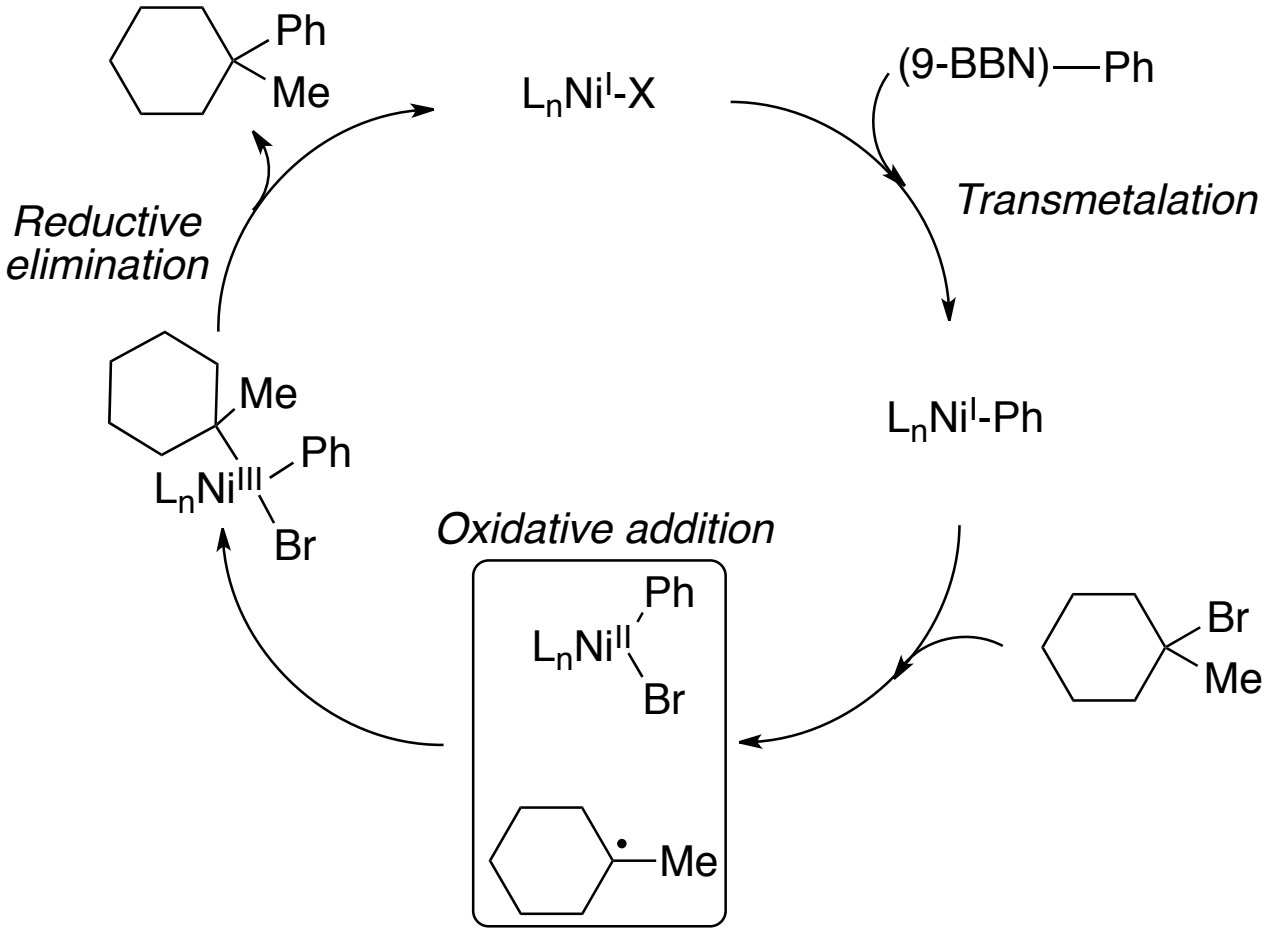
Scope of the Nucleophile



Examples of Recalcitrant Aryl-(9-BBN) Coupling Partners :

Ar	yield (%)	Ar	yield (%)
	<5		~20
	<5		<5
	15		
	<5		<5
	<5		<5
	<5		<5

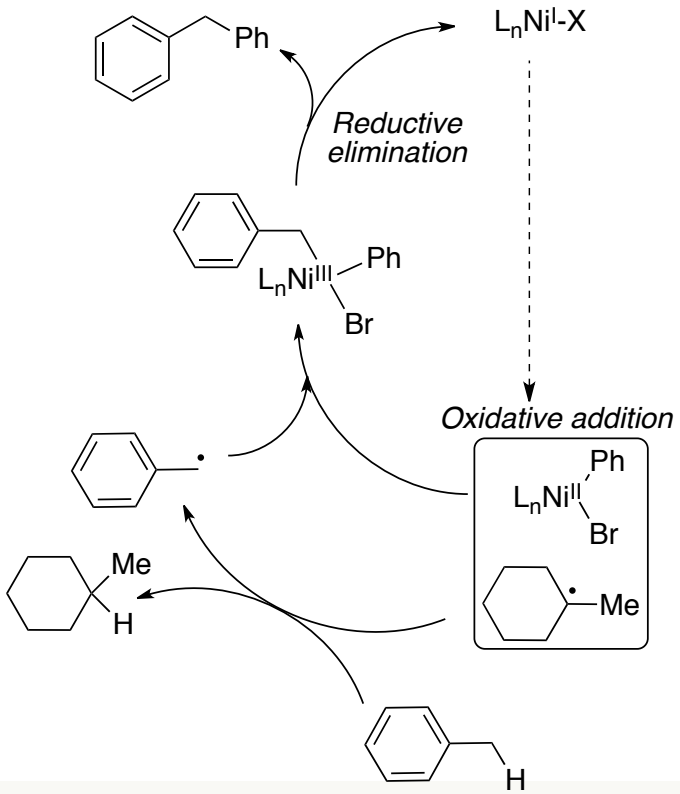
Proposed Mechanism



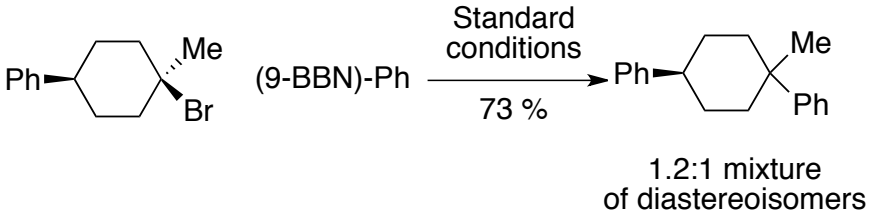
Proposed Mechanism

Reaction in Toluene:

Formation of diphenylmethane



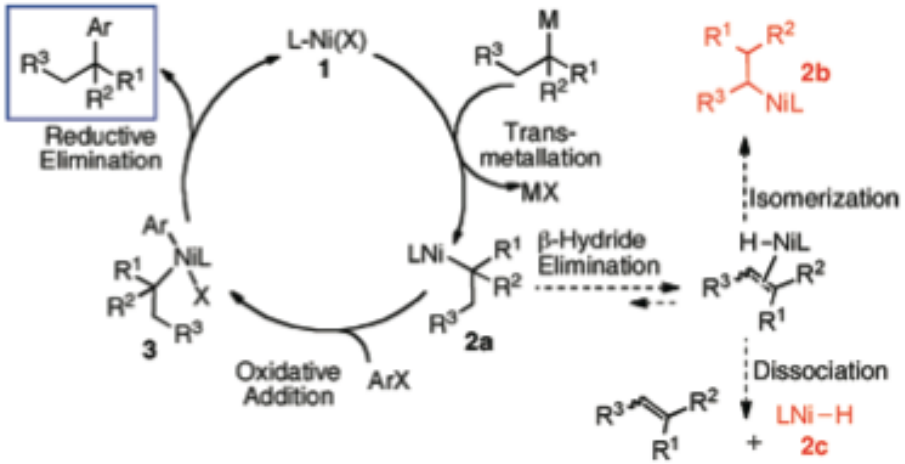
Epimerization:



1.2:1 mixture of diastereoisomers

Conclusion

- Suzuki arylation of tertiary alkyl bromides
- Use of commercially available catalyst system
- No isomerization of the alkyl group:



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