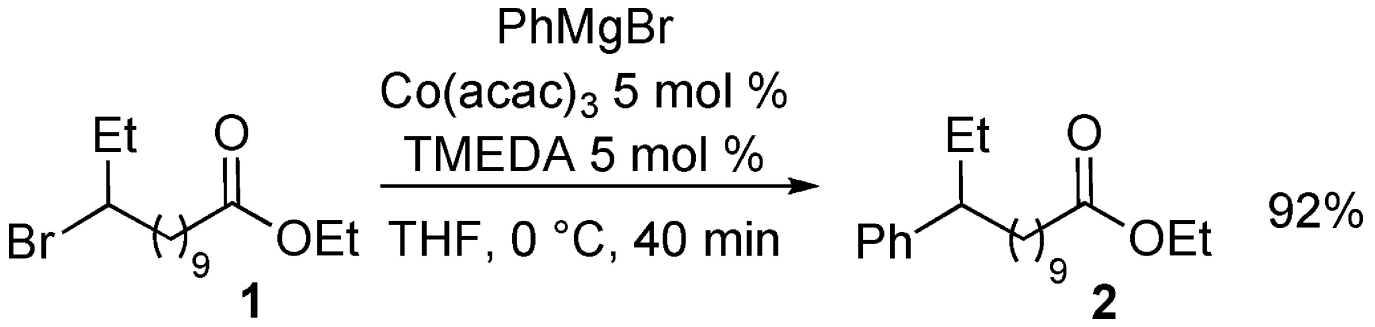
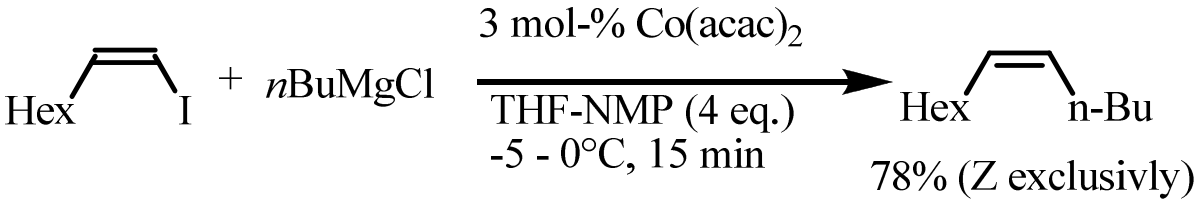
A New Efficient Catalytic System for the Chemoselective Cobalt-Catalyzed Cross-Coupling of Aryl Grignard Reagents with Primary and Secondary Alkyl Bromides

Gerard Cahiez,* Christophe Chaboche, Christophe Duplais, and Alban Moyeux

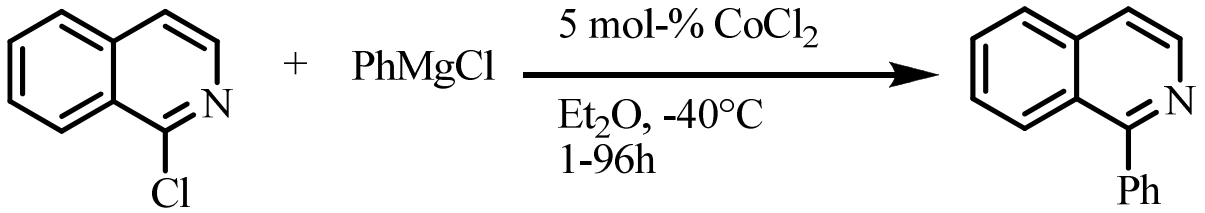


Organic Letters, **2009**, *11*, 277-280.

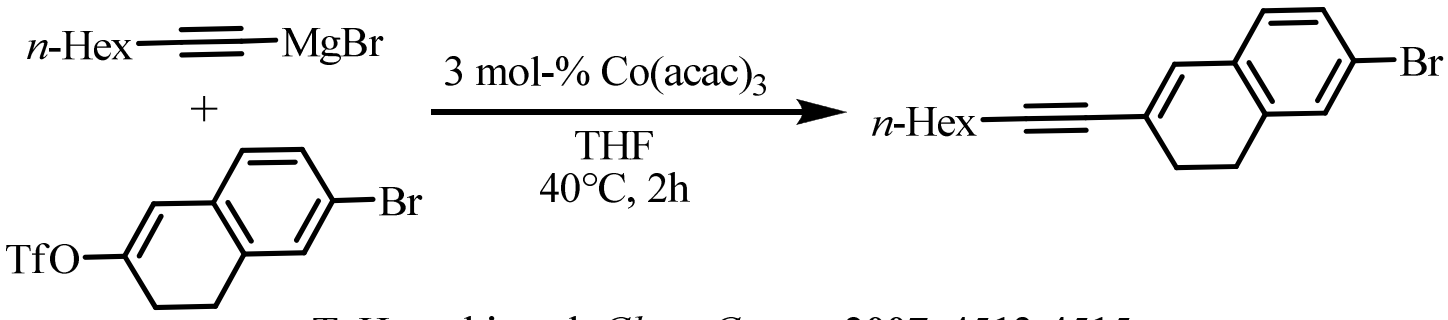
Background



G. Cahiez et al. *Tett. Letters*, **1998,** *39,* 6159-6162.



G. Cahiez, P. Knochel et al., *Synlett* **2003,** 1892-1894.



T. Hayashi et al. *Chem Comm*. **2007,** 4513-4515

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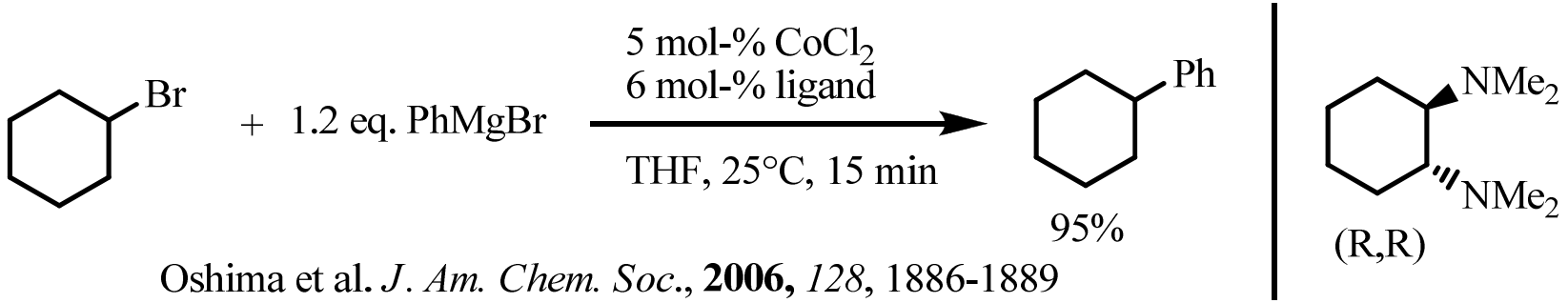
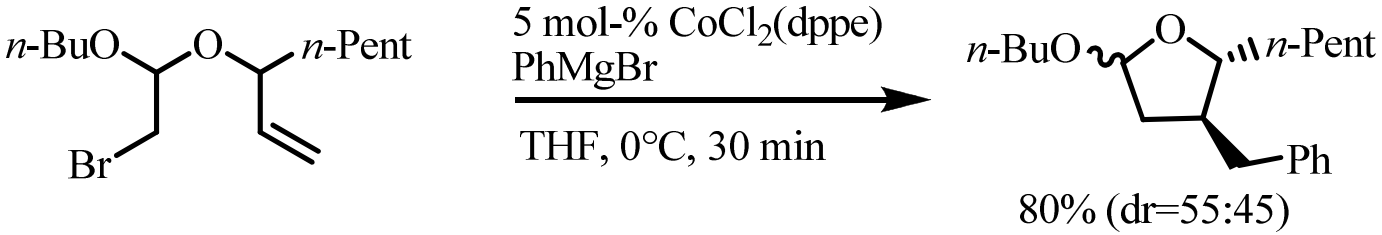
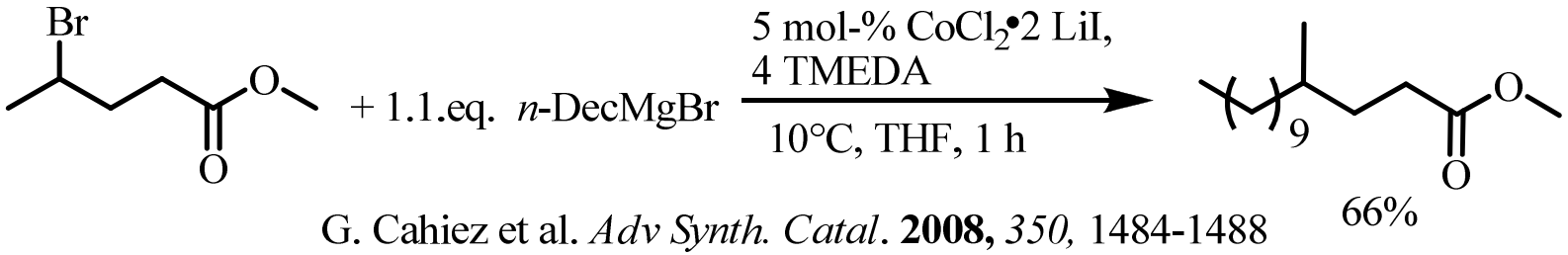


Oshima et al. *J. Am. Chem. Soc.*, **2006,** *128*, 1886-1889



K. Oshima et al. *Org. Lett.* **2007**, *9*, 1565-1567.
Review: K. Oshima et al. *Pure Appl. Chem*. **2006,** *78,* 411-446.
C. Gosmini et al. *Chem. Comm*, **2008,** 3221-3233.



G. Cahiez et al. *Adv Synth. Catal*. **2008,** *350,* 1484-1488

The Cahiez Group

Location:

Université de Cergy-Pontoise
Site de Neuville-sur-Oise
Cergy-Pontoise Cedex
North West of Paris

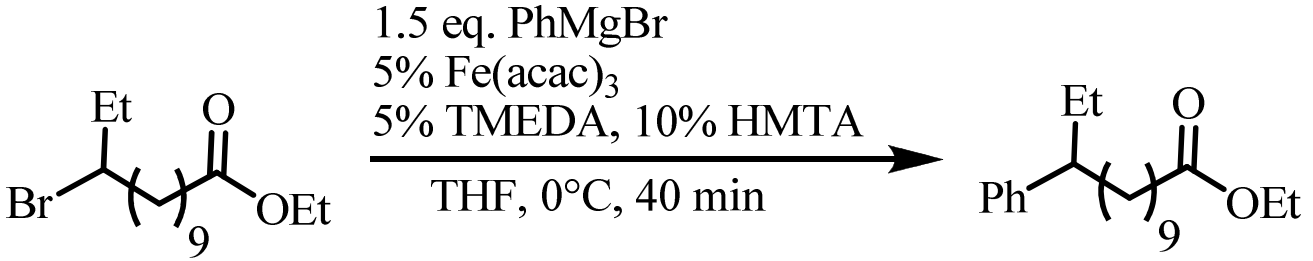
Research Interest:

Organometallic Chemistry

Iron- / Cobalt- catalyzed cross coupling reactions

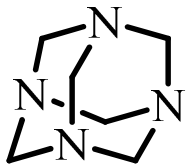
Title Paper

Initial Study



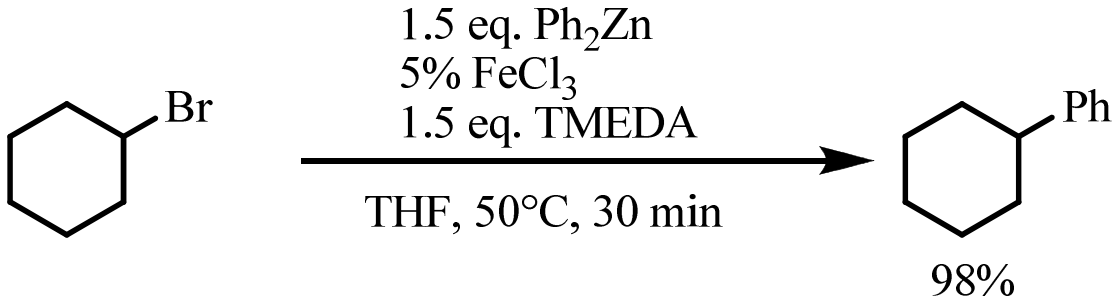
HMTA = hexamethylene tetramine 27%

G. Cahiez et al. *Org. Lett*. **2007,** *9,* 1484-1488



HMTA

Alternative



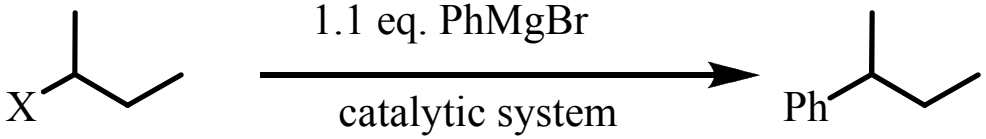
98%

N. Nakamura et al. *Synlett*. **2005,** 1794-1798

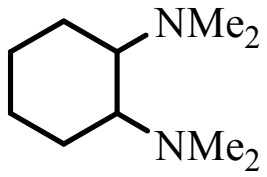
Disadvantage:
3 eq. of Grignard-reagent necessary

Modfication:
Me_3SiCH_2MgX as "dummy"
then 2 eq. of the mixed zinc reagent are necessary

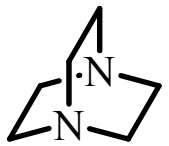
Optimization



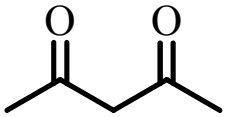
entry	X	catalytic system 5 mol-%	yield
1	I	$CoCl_2$	10
2	I	$Co(acac)_3$	14
3	I	$Co(acac)_3$/TMEDA = 1:1	94
4	I	$CoCl_2$/Ligand = 1:1	93
5	Br	$Co(acac)_3$/TMEDA = 1:1	92
6	Br	$CoCl_2$/Ligand = 1:1	73
7	Br	$Co(acac)_3/Et_3N$ = 1:5	15
8	Br	$Co(acac)_3$/DABCO = 1:1	37
9	Br	$Co(acac)_3$/dppe 1:3	traces



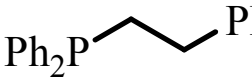
ligand



DABCO



acac



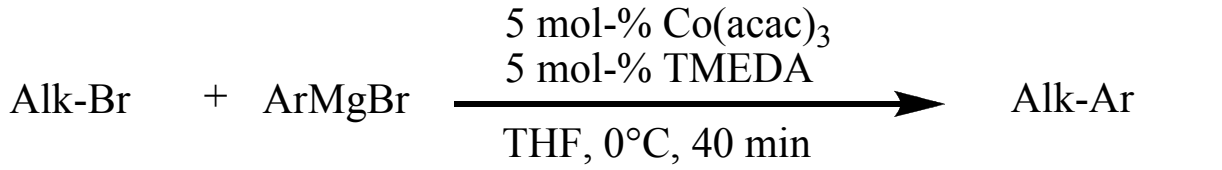
dppe

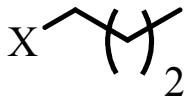
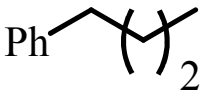
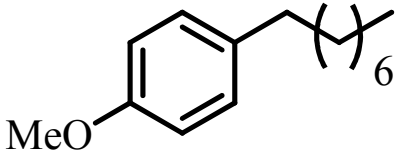
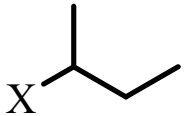
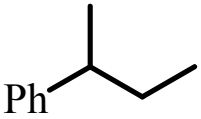
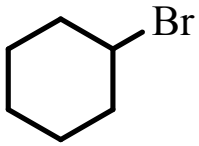
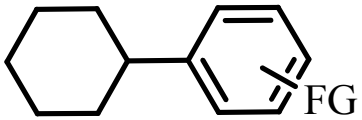
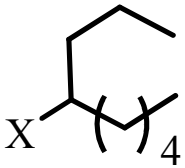
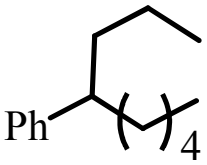
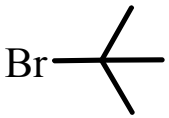
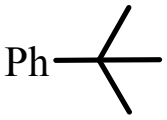
TMEDA

can be upscaled to 50 mmol
concentration: 0.5M

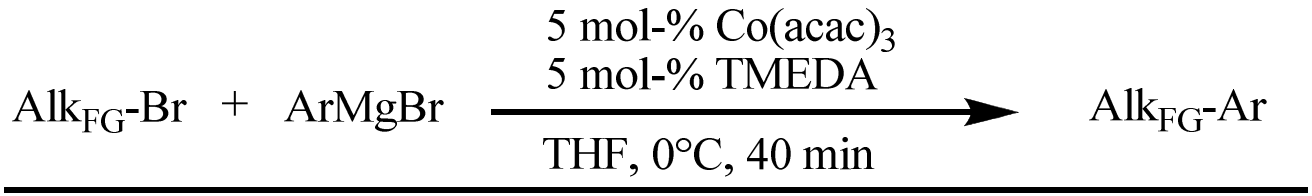
Oshima conditions give lower yields

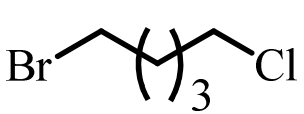
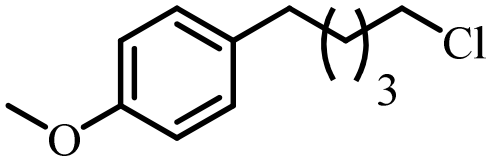
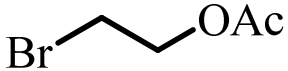
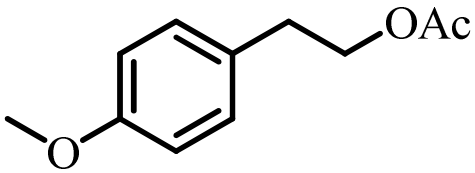
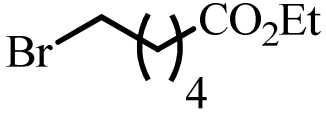
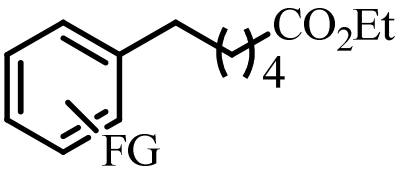
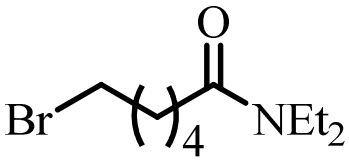
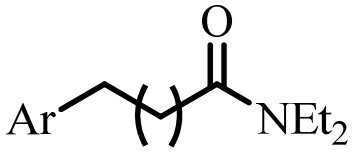
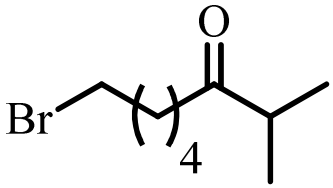
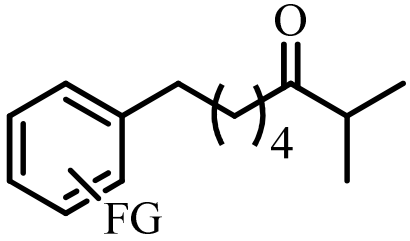
Scope and Limitations



entry	alkyl halide	product	yield
1 2 3			95% (X = I) 94% (X= Br) 10% (X = Cl)
4			96%
5 6 7			94% (X = I) 92% (X= Br) 4% (X = Cl)
8 9 10			93% 97% (FG = 4-OMe) 88% (FG = 2-OMe)
11 12			98% (X = Br) 10% (X= OTs)
13			trace

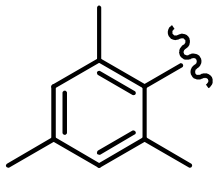
Scope and Limitations



entry	alkyl halide	product	yield
1			89
2			88
3 4			90 (FG = 4-OMe) 88 (FG = 2-OMe)
5 6			84 (Ar = Ph) 16 (Ar = Mes)
7 8			90 (FG = 4-OMe) 88 (FG = 2-OMe)

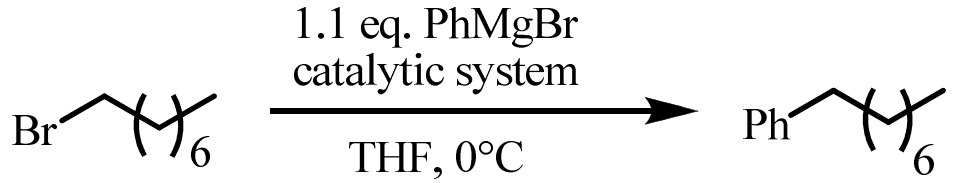
Tolerates several functionalities

Sterically hindered systems give low yields

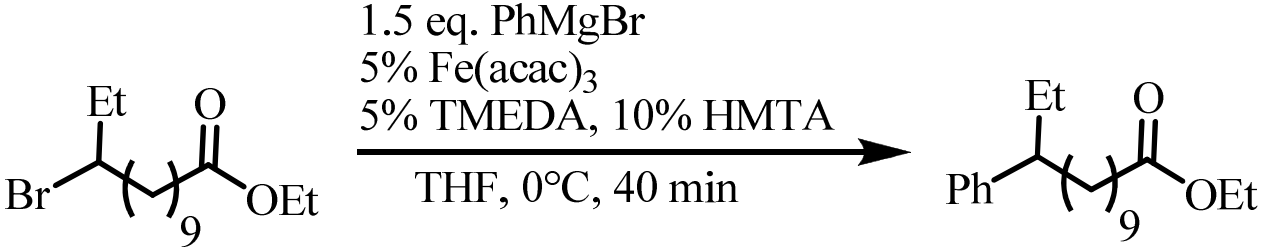


Mes

Comparison with other methods



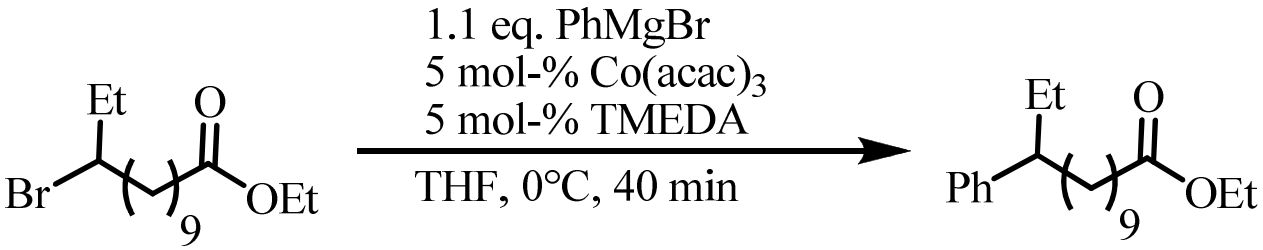
$CuCl_4Li$ 3 mol -%	70%
$Fe(acac)_3$/ 2 TMEDA/HMTA 5 mol-%	92%
$CoCl_2$/TMEDA 5 mol-%	95%



27%

HMTA = hexamethylene tetramine

G. Cahiez et al. *Org. Lett*. **2007,** *9,* 1484-1488



92%

Summary

• Development of Cobalt catalyzed cross coupling of Aryl grignard reagents with primary and secondary alkyl bromides accomplished

•Several functionalities (e.g. Ester, amides, ketones) are tolereated

•Products obtained in high yields

Major drawbacks:

Chlorines/Tosylates or tertiary alkyl bromides can not be used

Catalytic cycle is unknown and further investigations are required