

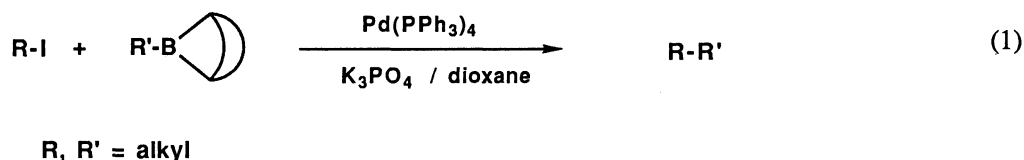
Palladium-Catalyzed Alkyl-Alkyl Cross-Coupling Reaction of 9-Alkyl-9-BBN Derivatives
with Iodoalkanes Possessing β -Hydrogens

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9-Alkyl-9-BBN derivatives undergo the cross-coupling reaction with primary iodoalkanes to give the coupling products in fairly good yields in the presence of a catalytic amount of $\text{Pd}(\text{PPh}_3)_4$ and K_3PO_4 .

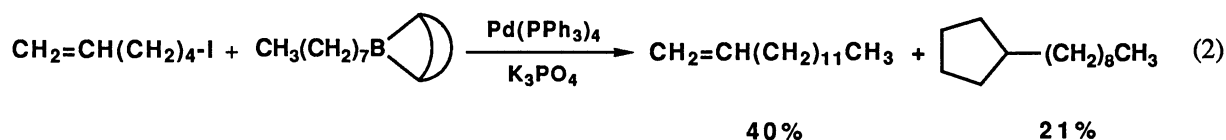
Although a wide variety of organic electrophiles, such as aryl, 1-alkenyl, benzyl, allyl, and 1-alkynyl halides, have been efficiently utilized for the palladium-catalyzed cross-coupling reactions with various organometallic reagents,¹⁾ it has been considered that such reactions can not be extended to alkyl halides with sp^3 carbon having β -hydrogens due to the slow rate of oxidative addition of alkyl halides to palladium(0) complexes and the fast β -hydride elimination from σ -alkylpalladium intermediates in the catalytic cycle. Thus, the use of alkyl halides as coupling partners is a challenging problem in several recent publications. Castle and Widdowson²⁾ have recently reported that $\text{Pd}(\text{dppf})$, formed *in situ* by the reduction of $\text{PdCl}_2(\text{dppf})$ with DIBAL, effectively catalyzes the cross-coupling reaction of iodoalkanes with Grignard reagents. Yuan and Scott³⁾ have published that the reaction reported by Widdowson²⁾ provides exclusively reduction products of alkyl halides instead of coupling products. In the course of our study⁴⁾ on the cross-coupling reaction of organoboron compounds, we have found that such reactions of usual iodoalkanes with 9-alkyl-9-BBN derivatives proceed readily in the presence of $\text{Pd}(\text{PPh}_3)_4$ and K_3PO_4 to give the corresponding coupling products in fairly good yields (Eq. 1).



A series of reactions between 9-octyl-9-BBN and 1-iodohexane (1.5 equiv.) was carried out in the presence of various catalysts and bases to establish the reaction conditions. Among the catalysts we examined, the palladium complexes with triphenylphosphine as ligand are recognized to be most effective. The best yield (64%) of tetradecane is obtained when the reaction⁵⁾ is conducted at 60 °C for 24 h by using 3 mol% of $\text{Pd}(\text{PPh}_3)_4$ and K_3PO_4 (3 equiv.) in dioxane. Although $\text{Cl}_2\text{Pd}(\text{dppf})$ is reported as a selective catalyst to avoid

β -hydride elimination, the complex does not act as an efficient catalyst in the present reaction. Other bidentate ligands such as dppe, dppp, and dppb also give lower yields of coupling products. Such bidentate ligands may retard the step of reductive elimination because it is known that the elimination only proceeds from an unsaturated, three coordinated dialkylpalladium(II) species,⁶⁾ which is markedly contrast to the coupling with aryl or vinyl derivatives which can proceed through a four coordinated saturated complex.

The detailed analysis of the reaction mixture, obtained from a molar amount of iododecane and 9-butyl-9-BBN under the above conditions, reveals the formations of butene (3%), butane (3%), decane (27%), decene (9%), and the desired tetradecane (50%). The 8% of iododecane and 30% of 9-butyl-9-BBN unreacted are recovered. Judging from the amounts of butane and butene, the β -elimination may not occur exclusively during the steps of transmetallation and reductive elimination. The results indicate that the difficulty of alkyl-alkyl coupling reaction is mainly due to the formation of decane at the step of oxidative addition of iododecane to Pd(0) complex. Previously, we reported the palladium-catalyzed carbonylative cross-coupling reaction⁷⁾ of 9-alkyl-9-BBN with iodoalkanes yielding ketones. The reaction is extremely accelerated by irradiation of light indicating to proceed through a radical process. Although the present reaction is not effected by light, it also can be presumed that a part of oxidative addition of iodoalkanes to palladium(0) takes place through such a radical process. The coupling of 9-octyl-9-BBN with 6-iodo-1-hexene under dark gives nonylcyclopentane, resulted from radical cyclization at the oxidative addition step, together with the expected product, 1-tetradecene in a ratio of 34:66 (Eq. 2).



In Table 1, the representative results of reaction between a variety of iodoalkanes and 9-alkyl-9-BBN derivatives, generated *in situ* by hydroboration of alkenes, are summarized. Primary alkyl iodides, even neopentyl iodide, smoothly couple with 9-alkyl-9-BBN to give the desired coupling products in 45-60% yields. Several functionalized compounds having cyano, ester, and acetal groups are obtained without any difficulties. The reaction can be readily extended to the coupling reaction with vinylic and aryl boron derivatives. For example, 9-[(E)-1-hexenyl]-9-BBN gives (E)-5-hexadecene in a 64% yield by the reaction with 1-iododecane. 9-Phenyl-9-BBN reacts with 1-iododecane to give decylbenzene in a 55% yield. On the other hand, alkyl bromides or secondary alkyl iodides never provide the corresponding coupling products.

To examine the effects of organometallic reagents in the coupling reaction, a molar amount of 1-iododecane is allowed to react with various butylmetal reagents under the conditions which we optimized above (Pd(PPh₃)₄ / dioxane) and the conditions established by Widdowson (Cl₂Pd(dppf) / THF).²⁾ The results are listed in Table 2. Among the reagents we examined, the 9-alkyl-9-BBN derivatives is only effective for the coupling reaction. Neither tributylborane nor lithium tetrabutylborate as a boron reagent is suitable for the present reaction. Other metal reagents, such as Mg, Zn, Al, Sn, Zr, and Hg, give no satisfactory results at all. In all of these experiments, decane and decene caused by β -hydride elimination are commonly obtained.

Table 1. Cross-Coupling Reaction of 9-Alkyl-9-BBN Derivatives with Alkyl Iodides

Halide	9-R-9-BBN	Product	Yield / % ^{a)}
$\text{CH}_3\text{-I}$		$\text{CH}_3(\text{CH}_2)_{10}\text{COOMe}$ ^{b)}	(71)
$\text{CH}_3(\text{CH}_2)_5\text{I}$		$\text{C}_{14}\text{H}_{30}$	64
			(45) ^{c)}
$\text{CH}_3(\text{CH}_2)_5\text{I}$		$\text{CH}_3(\text{CH}_2)_6\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_2\text{Ph}$	58
$\text{CH}_3(\text{CH}_2)_5\text{I}$		$\text{CH}_3(\text{CH}_2)_{15}\text{COOMe}$	54
$\text{N}\equiv\text{C}(\text{CH}_2)_3\text{I}$		$\text{NC}(\text{CH}_2)_6\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$	(61)
$\text{MeO}_2\text{C}(\text{CH}_2)_3\text{I}$			57
$\text{CH}_3(\text{CH}_2)_9\text{I}$		$\text{CH}_3(\text{CH}_2)_9\text{CH}=\text{CH}(\text{CH}_2)_3\text{CH}_3$	64
$\text{CH}_3(\text{CH}_2)_9\text{I}$		$\text{CH}_3(\text{CH}_2)_9\text{C}_6\text{H}_5$	55

a) G.L.C. yields based on 9-R-9-BBN and isolated yields are shown in the parentheses.

b) Other than methyl decanoate, two isomers, presumably methyl esters of 10-methylundecanoic acid and 9-methylundecanoic acid, were contaminated.

c) The reaction was conducted for 67 h.

Table 2. Cross-Coupling Reaction of Various Butylmetals with 1-Iododecane^{a)}

R-M	Pd(PPh ₃) ₄ / dioxane			Cl ₂ Pd(dppf) / THF		
	Conv / % ^{c)}	β-Elim / % ^{d)}	C ₁₄ H ₃₀ / %	Conv / % ^{c)}	β-Elim / % ^{d)}	C ₁₄ H ₃₀ / %
9-Bu-9-BBN ^{b)}	92	36 (3.0)	50	94	90 (3.4)	4
Bu ₃ B ^{b)}	83	67 (1.3)	7			
Bu ₄ BLi	58	47 (2.3)	2			
BuMgBr	61	28 (3.1)	5	74	45 (3.6)	2
BuZnCl	96	76 (3.7)	11	93	80	10
Et ₃ Al	38	32	0 ^{e)}	34	23 (0.9)	1 ^{e)}
Bu ₄ Sn	23	11	1	51	7	1
Cp ₂ Zr(Bu)Cl	81	62	2	52	11 (0.9)	2
BuHgCl	70	1	8			

a) All reactions were carried out by using of 1-iododecane (1.0 mmol), R-M (1.0 mmol), Pd-catalyst (0.03 mmol) and solvent (6 ml) at 60 °C for 24 h. b) The reaction was conducted in the presense of K₃PO₄ (3.0 mmol). c) Conversion of iododecane. d) Total yields of decane and decene and their ratios (decane / decene) are shown in the parentheses. e) Yield of dodecane.

References

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- 5) To a solution of 9-BBN (0.5 M solution in THF, 1 mmol) was added an alkene (1 mmol) at 0 °C. The reaction mixture was warmed up slowly to room temperature and stirred for 3-5 h to give a solution of 9-alkyl-9-BBN. Dioxane (6 ml), Pd(PPh₃)₄ (0.03 mmol), K₃PO₄ (3 mmol), and iodoalkane (1.5 mmol) were added, and then the mixture was stirred for 20-24 h at 60 °C.
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