

HIGHLY SELECTIVE SYNTHESIS OF ALLYLATED ARENES AND DIARYLMETHANES VIA
PALLADIUM-CATALYZED CROSS COUPLING INVOLVING BENZYLIC DERIVATIVES¹

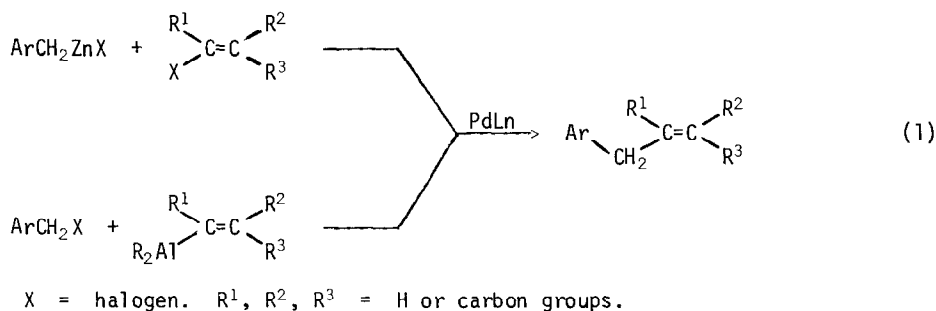
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SUMMARY: The Pd-catalyzed cross coupling of either benzylzincs with alkenyl halides or alkenylalanes with benzyl halides provides highly selective and expeditious routes to allylated arenes.

We have recently reported a highly selective Pd-catalyzed allylation of alkenyl- and arylmetals.⁴ In view of the significance of allylated arenes as part structures of various natural products including vitamins K,^{5,6} coenzymes Q,^{5,6} and maytansinoids,⁷ we undertook to develop additional selective routes to allylated arenes *via* cross coupling.

We now report that various allylated arenes can be readily synthesized in a highly stereo- and regioselective manner by the Pd-catalyzed cross coupling of either benzylzincs with alkenyl halides or alkenylalanes with benzyl halides (eq 1).

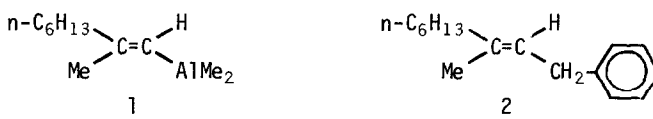


Since benzylzincs are among the most directly and cleanly obtainable benzylmetals, and since stereo- and regiodefined alkenylalanes as well as the corresponding alkenyl halides are now readily available,⁸ the methods herein described represent highly expeditious routes to allylated arenes. We further report that palladium-phosphine catalysts are also effective in promoting the reaction of arylmetals, especially arylzincs, with benzyl halides.

The experimental results of the syntheses of allylated arenes are summarized in the Table. The reaction of benzylzinc bromide, readily obtainable in essentially quantitative yield by

treating benzyl bromide with zinc powder,⁹ with alkenyl iodides or bromides in the presence of a Ni or Pd catalyst proceeds to give the cross-coupled products in a manner similar to that reported by us for the benzyl-aryl coupling.¹⁰ Although both Ni and Pd catalysts are effective, Ni catalysts, e.g., Ni(PPh₃)₄, tend to isomerize the allylated arene products into the conjugated isomers and are therefore inferior to Pd catalysts, e.g., Pd(PPh₃)₄. In the absence of a Pd or Ni catalyst, no coupling occurs under the comparable reaction conditions.

To develop a more expeditious route than that described above, an alkenylalane^{8b} (**1**), readily obtainable by the reaction of 1-octyne with Me₃Al-Cl₂ZrCp₂, was reacted with benzyl chloride and bromide in the presence of 5 mol % of Pd(PPh₃)₄. The expected product **2** was cleanly formed in 92 and 93% GLC yield, respectively. Interestingly, we note, for the first time, that ZnCl₂, which is initially added in the hope of promoting the desired reaction, only promotes the formation of undesirable homo-coupled products. Although we have previously reported that alkenylalanes react slowly with benzyl bromide and iodide to give cross coupled products in modest yields,¹¹ alkenylalanes do not appreciably react with these halides in the absence of a Pd catalyst. All isolated olefinic products obtained *via* Pd-catalyzed cross coupling are >98% pure single isomers, as judged by a combination of GLC, ¹H NMR and ¹³C NMR.¹² The following procedure for the preparation of **2** is representative. To 0.587g (0.50 mmol) of Pd(PPh₃)₄ and 1.71g (10 mmol) of benzyl bromide in 50 ml of THF is added the alkenylalane **1**, prepared from 1.10g (10 mmol) of 1-octyne, 1.44g (20 mmol) of Me₃Al and 0.584g (2 mmol) of Cl₂ZrCp₂ in 15 ml of 1,2-dichloroethane. After stirring the mixture for 3 hr at room temperature, it is sequentially treated with 3*N* HCl, pentane, water, NaHCO₃, water, and MgSO₄. Distillative workup gives 1.97g (91%) of **2**: bp 65-66° (0.05 mm); *n*^{22D} 1.4997; ¹H NMR (CDCl₃) δ 0.88 (t, J = 6Hz 3H), 1.29 (m, 8H), 1.61 (s, 3H), 2.04 (m, 2H), 3.34 (d, J = 7Hz 2H), 5.34 (t, J = 7Hz 1H), 7.17 (m, 5H); ¹³C NMR (CDCl₃) δ 14.12, 16.03, 22.77, 28.04, 29.11, 31.90, 34.33, 39.81, 123.00, 125.69, 128.33, 136.43, 141.85; High resolution MS Calcd for C₁₆H₂₄: 216.188. Found: 216.188.



The facile reaction of benzyl halides described above prompted us to develop a related Pd-catalyzed procedure for the synthesis of diarylmethanes. We have indeed found that the reaction of phenylmagnesium bromide with benzyl bromide in the presence of 5 mol % of Pd(PPh₃)₄ gives diphenylmethane in 73% yield along with biphenyl (25% yield based on phenylmagnesium bromide) and a small amount of bibenzyl. In the absence of the Pd catalyst, however, the yield of diphenylmethane is only 7%, the major products being biphenyl and bibenzyl. Beneficial effects of lowering the ionicity of the metal-carbon bond are seen in the corresponding reaction of phenylzinc chloride, which gives diphenylmethane in 92% yield along with minor amounts (< 5% each) of biphenyl and bibenzyl.

It should be pointed out here that, in some other related cross-coupling reactions, undesirable complications have been observed. Thus, although the Pd-catalyzed reaction of phenylzinc chloride with propargyl bromide proceeds cleanly, the product obtained in 92% yield is phenylallene.

Our attempts to synthesize benzylated alkynes by the Pd-catalyzed reactions of benzylzincs with 1-halo-1-alkynes have been even more disappointing, the yield of the desired products being less than 10-20%.

Despite the above-mentioned limitations, however, the benzyl-alkenyl,¹³ alkenyl-benzyl, and aryl-benzyl coupling reactions herein reported, together with the benzyl-aryl,¹⁰ alkenyl-allyl⁴ and aryl-allyl⁴ coupling reactions reported earlier by us, demonstrate the general utility of Pd catalysts in the synthesis of organic compounds containing two unsaturated hydrocarbon groups separated by the methylene group.

Table. Pd- or Ni-Catalyzed Coupling between Alkenyl and Benzyl Groups

Alkenyl derivative	Benzyl derivative	Catalyst ^a	Product ^b	Yield ^c (%)
(<i>E</i>)-1-Iodo-1-hexene	PhCH ₂ ZnBr	Ni(PPh ₃) ₄	(<i>E</i>)-1-Phenyl-2-heptene	73 (65)
(<i>E</i>)-3-Iodo-3-hexene	"	"	(<i>E</i>)-3-Benzyl-3-hexene	46 ^d
"	"	Cl ₂ Pd(PPh ₃) ₂ + <i>i</i> -Bu ₂ AlH	"	86 (79)
(<i>E</i>)-3-Bromo-3-hexene	"	"	"	78
Methyl (<i>E</i>)-3-bromo-2-methylpropenoate	"	Ni(PPh ₃) ₄	Methyl (<i>E</i>)-2-methyl-4-phenyl-2-butenolate	65
"	"	Cl ₂ Pd(PPh ₃) ₂ + <i>i</i> -Bu ₂ AlH	"	75 (62)
(<i>E</i>)-1-Iodo-2-methyl-1-octene	"	Pd(PPh ₃) ₄	2	78
(<i>E</i>)-2-Methyl-1-octenyl-dimethylalane (1)	PhCH ₂ Cl	"	"	92
"	PhCH ₂ Br	"	"	93 (91)
"	"	Pd(PPh ₃) ₄ + 10 mol % ZnCl ₂	"	70
"	"	Pd(PPh ₃) ₄ + 100 mol % ZnCl ₂	"	45

^a The amount of a Pd or Ni catalyst is 5 mol %. ^b All isolated products have been adequately characterized spectroscopically. ^c GLC yields. The numbers in parentheses are isolated yields. ^d 1-Phenyl-2-ethyl-1-pentene is formed in 15% yield.

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