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A CONVENIENT SYNTHESIS OF UNSYMMETRICAL BIBENZYLS, HOMOALLYLARENES, AND HOMOPROPARGYLARENES VIA PALLADIUM-CATALYZED CROSS COUPLING[1]

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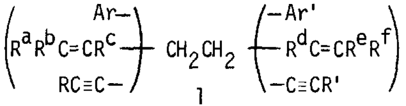
SUMMARY The palladium-catalyzed homobenzyl-aryl, homobenzyl-alkenyl, homoallyl-aryl, and homopropargyl-aryl cross coupling reactions provide the desired coupling products in high yields, whereas similar reactions involving alkynyl halides lead to low product yields

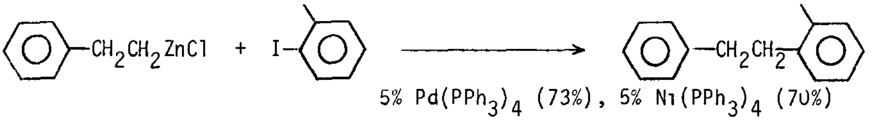
Organic compounds having two carbon-carbon double and/or triple bonds in a 1,5-relationship (1), such as 1,5-dienes and homoallylarenes, represent a wide variety of natural products Until recently, construction of such units via cross coupling had been achieved mostly by joining two allylic, propargylic, and/or benzylic groups.[2] Although satisfactory in many cases, this approach has nevertheless been limited by difficulties such as cross-homo scrambling as well as regio- and/or stereoisomerization.[3]



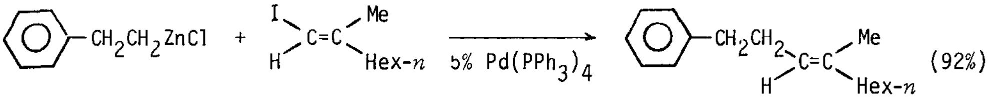
$$\left(\begin{array}{c} Ar- \\ R^aR^bC=CR^c- \\ RC\equiv C- \end{array}\right) CH_2CH_2 \left(\begin{array}{c} -Ar' \\ -R^dC=CR^eR^f \\ -C\equiv CR' \end{array}\right)$$

1

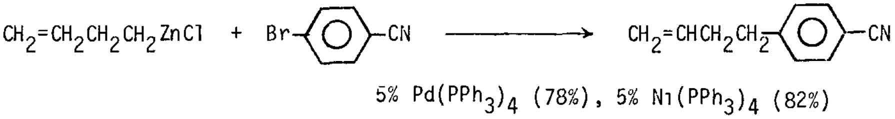
We recently reported a Pd-catalyzed cross-coupling reaction of homoallyl- or homopropargylzincs with alkenyl halides as an efficient and selective route to 1,5-dienes and 1,5-enynes.[4] We now report that the scope of this methodology may be extended to the homobenzyl-aryl (eq 1), homobenzyl-alkenyl (eq 2), homoallyl-aryl (eq 3), and homopropargyl-aryl (eq 4) cases, where the first entry in each case represents the corresponding organozinc reagent



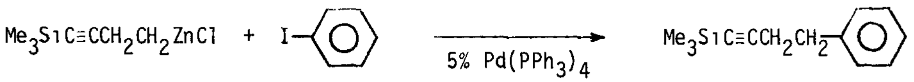
(1)



(2)



(3)



(83%) (4)

Although we previously noted that the use of $Ni(PPh_3)_4$ as a catalyst in conjunction with acetylenic reagents led to very low product yields,[4] both $Ni(PPh_3)_4$ and $Pd(PPh_3)_4$ appear to give comparable results in other instances. Except for a minor formation (<5-10%) of the dimers of aryl or alkenyl halides, these reactions are essentially free of other side reactions, such as β elimination. Unfortunately, our attempts to use alkynyl halides have resulted in disappointing results. Thus, for example, the reaction of phenylethylzinc chloride with 1-octynyl bromide or iodide in the presence of 5 mol % of $Pd(PPh_3)_4$ produced only 30-40% yields of 1-phenyl-3-decyne contaminated with significant amounts of phenylethyl halides and 1-octyne, which presumably formed via metal-halogen exchange. Use of $Cl_2Pd(Ph_2P(CH_2)_3PPh_2)$[5] did not improve the product yield.

In sharp contrast with the favorable results described above, our attempts to synthesize compounds represented by **1** via formation of the carbon-carbon bond between the two methylene groups have led to mixtures of cross- and homo-coupled products. Among them are the Pd-catalyzed reactions of benzylzinc bromide with *α*-bromo-*p*-xylene, allyl bromide, and propargyl bromide.

The following synthesis of (*E*)-1-phenyl-4-methyl-3-decene is representative. To dry ZnCl (1.36 g, 10 mmol) and Mg (0.36 g, 15 mmol) covered with THF (10 mL) under nitrogen atmosphere was added 2-phenylethyl bromide (2.78 g, 15 mmol) in 10 mL of THF. The mixture was heated for 10 h at 50°C and cooled. To this was added sequentially $Pd(PPh_3)_4$ (0.404 g, 0.35 mmol) dissolved in 4 mL of THF and (*E*)-1-iodo-2-methyl-1-octene. The mixture was stirred for 3 h at 25°C and quenched with 3N HCl. Extraction (ether), washing (aq $NaHCO_3$), drying ($MgSO_4$), and distillation gave 1.48 g (92%) of (*E*)-1-phenyl-4-methyl-3-decene: bp 101°C (0.3 mm), $n^{26}D$ 1.4928, ^1H NMR ($CDCl_3$, Me_4Si) δ 0.89 (t, 7 Hz, 3 H), 1.1-1.4 (m, 8 H), 1.53 (s, 3 H), 1.96 (t, 7 Hz, 2 H), 2.33 (t, 7 Hz, 2 H), 2.64 (t, 7 Hz), 5.18 (t, 7 Hz, 1 H), 7.22 (m, 5 H) ppm.[6]

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REFERENCES AND NOTES

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4. (a) Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* 1980, *102*, 3298. (b) Kobayashi, M.; Negishi, E. *J. Org. Chem.* 1980, *45*, 5223. (c) For a review, see Negishi, E. *Acc. Chem. Res.* 1982, *15*, 340.
5. It has been reported that the use of $Cl_2Pd(Ph_2P(CH_2)_3PPh_2)$ and other Pd-phosphine complexes containing bidentate phosphine ligands leads to higher alkylation yields [Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.*, 1979, 1871].
6. The ^{13}C NMR spectrum of this compound is available (≥98% *E*). All products were adequately characterized by ^1H NMR, IR, and high resolution mass spectrometry. For the determination of the stereochemistry of trisubstituted alkenes, see Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem.* 1981, *46*, 4093.

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