

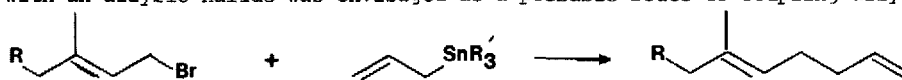
CATALYZED CROSS-COUPLING OF ALLYL BROMIDES WITH
ALLYL TIN REAGENTS

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Abstract: The reaction of allyl bromides with allyl tin reagents, catalyzed by palladium or zinc chloride gives cross-coupled products without allylic transposition in the allyl halide partner but with predominate allylic rearrangement from the tin partner.

The synthesis of compounds containing the polyisoprenoid structure by the cross-coupling reactions of allylic segments suffers from the lack of a good general procedure. The most straightforward approach, coupling reactions involving an allylic organometallic complex and an allylic electrophile, invariably results in homo-coupling products, loss of geometrical integrity at the allyl site, and lack of regioselectivity.¹

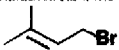

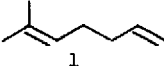
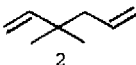




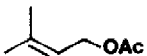



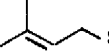



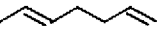
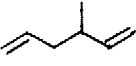
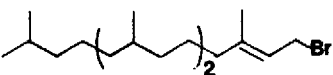



The palladium catalyzed reaction of acid chlorides or benzyl halides with tetraorganotin reagents gives coupled products in high yields.^{2,3} In the synthesis of ketones from acid chlorides, the reaction is general with respect to both reactants and a wide variety of functional groups on the acid chloride can be tolerated as a result of the exceedingly mild reaction conditions.³ The mechanism of this reaction probably involves oxidative addition of the acid chloride to the palladium(0) catalyst, metathesis of the oxidative addition product with the organotin compound to generate an acyl-organo palladium(II) complex, and reductive elimination to yield ketone and the palladium(0) catalyst. Thus, replacement of the acid chloride with an allylic halide was envisaged as a probable route to coupling allylic pieces.



The coupling reaction is catalyzed by benzylchlorobis(triphenylphosphine)palladium(II). Surprisingly, zinc chloride also was a catalyst when the tin reagent was tetraallyl tin, but was not a catalyst when this reagent was tributylcrotyl or tributylprenyl tin. The palladium complex alone was not a catalyst for the coupling of prenylacetate with tetraallyl tin; catalytic amounts of zinc chloride were also necessary. High turnovers (~ 270) were achieved when combinations of catalytic amounts of palladium alone or palladium and zinc chloride were used but molar quantities of zinc chloride did not improve the yield of coupled product.

A solution of 2.2 mmol of tin reagent,⁴ 2.2 mmole of the allyl bromide, 6.6×10^{-3} mmole of benzylchlorobis(triphenylphosphine)palladium(II), and/or 0.22 mmole zinc chloride in 1 mL solvent was heated in a capped tube at 65°C. The reaction mixture was vacuum transferred and analyzed by gas chromatography (except in the case of the phytyl bromide reaction). Prepara-

Table 1

Allyl Halide	Tin Reagent	Cat. ^a	Conditions ^b Solv. t(h)	Product(s)	Yield %		
		Pd(II)	C ₆ H ₆ 24 ^c		50-70 ^d		
					10		
		Pd(II) ZnCl ₂	THF	48		81	
					96 ^e		78
							76
ZnCl ₂		2		74			
		Pd(II) ZnCl ₂		50		17	
		Pd(II)	CHCl ₃	48		3	
						48 ^f	
		Pd(II)		48		20	
						58 ^g	
		ZnCl ₂		22		C ₁₆ H ₃₃ >95	
		Pd(II)		22		80 ^g	

a. Palladium Catalyst = benzylchlorobis(triphenylphosphine)palladium(II), (0.3 mole % based on allyl halide). ZnCl₂ (10 mole % based on allyl halide). 2.2 mmoles each of allyl halide and allyl tin with 1 mL solvent.

b. All reactions were run at 65°C unless otherwise noted.

c. T = 100°C.

d. When tetrakis(triphenylphosphine)palladium(0) was the catalyst, a 50% yield was obtained.

e. T = 25°C.

f. 40% unreacted allyl bromide was recovered.

g. 20% unreacted allyl bromide.

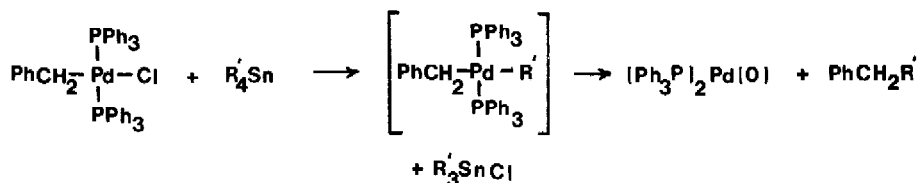
tive gas chromatography was used to obtain pure samples of the products.

The coupled products were identified by comparison of the gas chromatographic retention times with those of authentic samples⁵ and by their nmr spectra. Nmr spectra were used to establish that the 6,10,14,18-tetramethyl-1,5-nonadecadiene was the E-isomer. The ¹H 360 MHz spectrum of this compound showed chemical shifts for the vinyl methyl (δ 1.59) and the vinyl proton on the trisubstituted double bond (δ 5.50) that were consistent with the E-isomer, as was the 100 MHz ¹³C nmr spectrum.⁶ Characteristic of the E-isomer was the long range coupling between the protons of the vinyl methyl and the vinyl proton, 1.2 Hz.

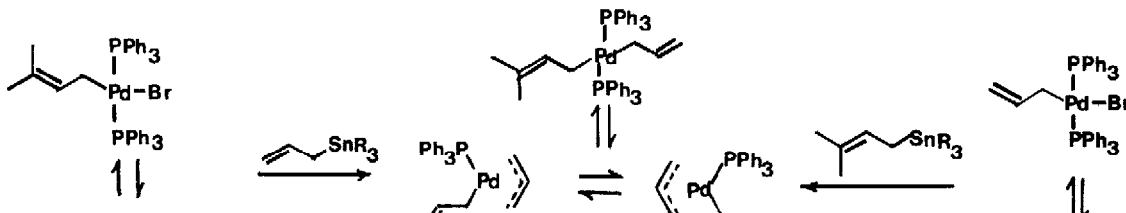
The reaction is regiospecific, at least with prenyl and phytyl bromides, but it is not clear that allylic transposition would not take place if the allylic carbons were substantially equivalent. Predominate allylic rearrangement takes place in the allyl group of the tin partner. Isomerization of the double bond in phytyl bromide to the Z-isomer does not take place. Even though the E-isomer is thermodynamically favored, modest amounts of Z-isomer would be expected from an equilibrating allylic ion.

Yields are higher when tetraallyl tin is used instead of allyltributyltin. Yields were not as high when the carbon in the allyl tin partner at which coupling occurred (by allylic transposition) was tertiary. The use of prenyl acetate in place of prenyl bromide gives lower yields of coupled product.

In the palladium catalyzed reaction, generation of a palladium(0) complex from the benzylchloropalladium(II) complex is known to take place by metathesis with tin followed by reductive elimination. The benzyl complex was used in place of tetrakis(triphenylphosphine)palladium(0), since the resulting bis(triphenylphosphine)palladium(0) complex is highly coordinatively unsaturated and as a result more reactive in an oxidative addition reaction.

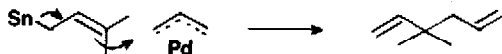


Oxidative addition of allyl halides to palladium(0) takes place rapidly,⁷ but the mechanism of the reaction of this allyl palladium complex with the allyl tin reagent is not clear. Metathesis followed by reductive elimination probably would generate a product of coupling at the least sterically hindered carbons. Thus, the coupling of prenyl bromide with allyl tin



or allyl bromide with prenyl tin should generate the same product or ratio of products.

Since allylic transposition is observed in the allylic fragment of the tin partner only, and since tetramethyl tin did not react with prenyl bromide in the presence of the palladium catalyst to give coupled product, an alternate pathway, electrophilic attack of the palladium allyl at the terminal vinyl carbon of the allyl tin reagent is a more consistent mechanism.



Initially, zinc chloride was added to aid in the metathesis reaction. Catalysis by zinc chloride alone, however, implies that its function is to serve as a Lewis acid and generate an allylic cation from the allyl bromide such that the tin reagent can serve as an electrofuge. The generation of allyl zinc by exchange with allyl tin also is possible. We are continuing to explore the scope and mechanism(s) of this coupling.

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References and Notes

1. See for example, J.A. Katzenellenbogen and R.S. Lenox, J. Org. Chem., **38**, 326 (1979) and references therein.
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