

III.2.10 Palladium-Catalyzed Cross-Coupling between Allyl-, Benzyl-, or Propargylmetals and Allyl, Benzyl, or Propargyl Electrophiles

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A. INTRODUCTION

Cross-coupling between allyl-, benzyl-, or propargylmetals and allyl, benzyl, or propargyl electrophiles is a potentially important synthetic operation. 1,5-Dienes, 1,5-enynes, and other related compounds obtainable by this process represent many natural products and related biologically important compounds. Unfortunately, this synthetic operation commonly performed with organometals containing Li and Mg has been plagued with various difficulties including regiochemical, stereochemical, and cross-homo scramblings, even though some moderately satisfactory procedures for allyl–allyl coupling^{[1],[2]} and propargyl–allyl coupling^{[3]–[5]} have been devised.

In view of some highly satisfactory Pd-catalyzed cross-coupling reactions between alkenyl-, aryl-, or alkynylmetals and allyl, benzyl, or propargyl electrophiles discussed in **Sects. III.2.8.2** and **III.2.9**, it is not unreasonable to explore related Pd-catalyzed allyl–allyl, benzyl–allyl, propargyl (or allenyl)–allyl coupling and related reactions. Most of the efforts have been focused on the Pd-catalyzed allyl–allyl coupling involving Sn.

B. Pd-CATALYZED ALLYL–ALLYL COUPLING

The Pd-catalyzed reaction of allyltins with allyl electrophiles was independently reported by Trost and Keinan^[6] and Godschalx and Stille^[7] in 1980. Some representative results are summarized in **Table 1**. Although some high product yields have been observed, they often are disappointingly low. The regio- and stereochemistry of the allylic electrophiles can be maintained in many cases. On the other hand, allyltin reagents largely undergo an allylic rearrangement, but the regiospecificity has not generally been very high. In some cases, ZnCl₂ was used as a cocatalyst.^[7] However, the reaction of allyltins and allyl bromides can proceed using just ZnCl₂ as a catalyst without resorting

TABLE 1. Pd-Catalyzed Reaction of Allyltins with Allyl Electrophiles

Allyltin	Allyl Electrophile	Pd Catalyst ^a	Product	Yield (%)	Ref.
		A		69	[6]
		A		71	[6]
		A		32	[6]
		A		4	[6]
		B	 and 	58 20	[7]
		B	 and 	50–70 10	[7]
		C	only	81	[7]
		B	 	48 3	[7]

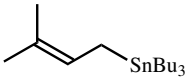
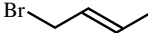
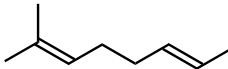
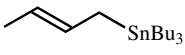
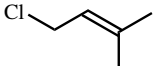
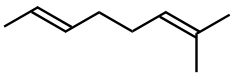
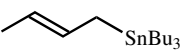
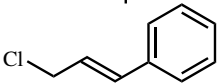
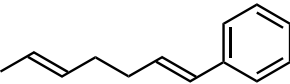
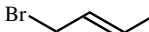
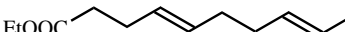
^a A = Pd(PPh₃)₄; B = Cl(PhCH₂)Pd(PPh₃)₃; C = B + ZnCl₂.

to Pd complexes.^[8] So, the roles of Pd complexes in the reactions involving both Pd and Zn are not very clear.

Along with the development of the stoichiometric reactions of preformed π -allylpalladium derivatives with allylic Grignard reagents and allylic organotin,^{[9]–[11]} a Pd-catalyzed version of the allyltin reaction was developed using maleic anhydride as an added ligand.^{[10],[11]} In contrast with the results discussed above, retention of the regio- and stereochemistry of both allyltins and allyl electrophiles to the extents of >90% was observed. However, the yields of the desired products were only poor to modest due to the formation of the two possible homocoupled products to significant extents, as indicated by the results shown in **Table 2**.

Some additional results of Pd-catalyzed allyl–allyl coupling are summarized in **Table 3**. In cases where regioisomerization, stereoisomerization, and/or cross-homo scrambling are

TABLE 2. Pd-Catalyzed Reaction of allyltins with Allyl Halides in the Presence of Maleic Anhydride^a

Allyltin	Allyl Halide	Product ^b	Yield (%)	Ref.
			40	[10]
			38	[10]
			68	[10]
^c			36	[10]

^aThe reaction is carried out in THF at 50 °C using π -allylpalladium chloride (1–2%) in the presence of maleic anhydride.

^bGreater than 90% *E,E*, where appropriate. Significant amounts (12–37%) of the two possible homocoupling products are observed.

^c EtOOC-CH₂-CH=CH-CH=CH-SnMe₂.

possible, they occur to considerable extents, and significant improvements would be necessary before these reactions can be of high value in the synthesis of stereo- and regiodefined 1,5-dienes.

Little is known about the use of allylmetals containing metals other than Sn in this reaction. There has been just one report on the Pd-catalyzed cross-coupling of allylzinc bromide with allyl acetate in 54% yield.^[16]

C. OTHER Pd-CATALYZED ALLYLATION REACTIONS USING BENZYL- AND ALLENYLMETALS AND RELATED CROSS-COUPLING REACTIONS

The current scope of other Pd-catalyzed allylation reactions using benzyl- and allenylmetals and their synthetic values are very limited. Even more limited is the scope of related benzylation and propargylation (or allenylation) with benzyl and propargyl electrophiles. Some of the results in the literature are shown in **Scheme 1**.

D. SUMMARY

The Pd-catalyzed cross-coupling reactions of allyl-, benzyl-, or propargyl (or allenyl) metals with allyl, benzyl, or propargyl electrophiles appear to be intrinsically prone to various side reactions including regio- and stereoisomerization as well as cross-homo scrambling. Although the yields of the desired compounds can be high, in some cases, they tend to be rather modest, in part, as a consequence of isomerization and scrambling processes.

TABLE 3. Additional Examples of the Pd-Catalyzed Allyl–Allyl Coupling Using Organotin

Allyl tin	Allyl Electrophile	Pd Catalyst	Product	Yield (%)	Ref
		$\text{Pd}(\text{PPh}_3)_4$		85	[12]
		$\text{Cl}_2\text{Pd}(\text{PPh}_3)_2$		89	[13]
		$\text{Pd}(\text{dba})_2$ TFP		47	[14]
				10	
		$\text{Pd}(\text{PPh}_3)_4$		70–80	[15]

(Z/E = 87:13)

(X = Br, OAc)

(I) (%)

30%

In this connection, it should be recalled that, whereas those Pd-catalyzed cross-coupling reactions involving allylic electrophiles tend to be facile and satisfactory, the use of allylmetals containing the same allyl moiety, especially those containing relatively electropositive metals, in Pd-catalyzed cross-coupling has been generally much less favorable. In Pd-catalyzed allyl-allyl coupling, the use of allylmetals is unavoidable. Consequently, it may suffer from problems associated with allylmetals.

From the viewpoint of the selective and satisfactory synthesis of stereo- and regiodefined 1,5-dienes, 1,5-enynes, and related compounds, Pd-catalyzed allyl-allyl, propargyl-allyl, and related reactions must be judged to be generally unsatisfactory, even though future developments may alleviate various difficulties associated with them. Much more satisfactory has been the use of homoallyl-, homobenzyl-, and homopropargylmetals, especially those containing Zn and Mg in their Pd- or Ni-catalyzed cross-coupling with alkenyl and aryl electrophiles, as discussed in **Sect. III.2.11.2**.

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