

Preliminary Communication

Palladium-catalyzed coupling reactions of functionalized styryl bromides with 1-propenyltributyltin

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Abstract

The palladium-catalyzed coupling reaction of 1-propenyltributyltin with functionalized styryl bromides is described. 1,3-Dienes are obtained in low to moderate yields except with β,β -dibromostyrene. The latter undergoes a novel organotin-promoted dehydrobromination-coupling sequence to give a 1,3-enyne as final product.

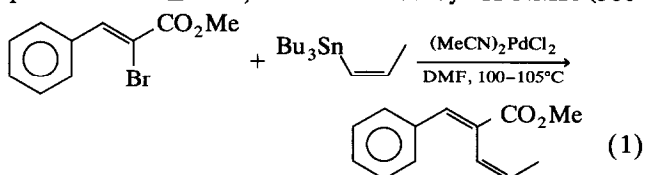
Key words: Tin; Palladium; Styryl bromide; Coupling reaction; Bromides; Catalysis

The palladium-catalyzed coupling reaction of organotin compounds with organic electrophiles has become an important synthetic method in organic chemistry [1]. This so-called Stille reaction is especially suited for the synthesis of stereodefined 1,3-dienes [2] and 1,3-enynes [3]. Vinylic iodides [3], triflates [4] and mesylates [5] have been commonly used as electrophiles in these reactions, while the more stable and readily available vinylic bromides have been rarely employed [6].

As part of a research program directed towards the synthesis of aromatic 1,3-dienes, we became interested in the Stille reaction. Consequently, a model study of the palladium-catalyzed coupling reaction of functionalized styryl bromides was undertaken, using 1-propenyltributyltin as a representative vinyltin reagent.

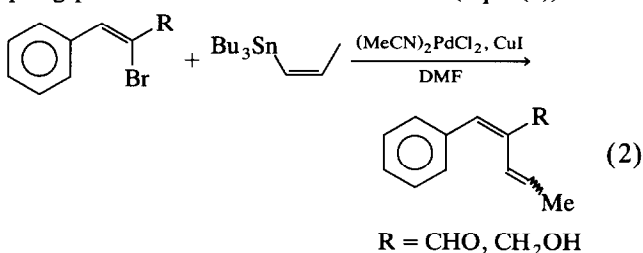
Methyl α -bromocinnamate ($\geq 95\%$ *Z*, 5.0 mmol) was treated with 1-propenyltributyltin (86% *Z*, 5.5 mmol) in the presence of *bis*(acetonitrile)dichloro-palladium(II) (7 mol%) using dry dimethylformamide (DMF, 10 mL) as solvent. The reaction mixture was heated (100–105°C) for 4 days. After work-up, the crude product was purified by column chromatography to give (1*E*,3*Z*)-1-phenyl-2-carbomethoxy-1,3-pentadi-

ene in 47% yield (eqn. (1)). The isomeric purity of this product was $\geq 95\%$, as determined by ^1H NMR (300

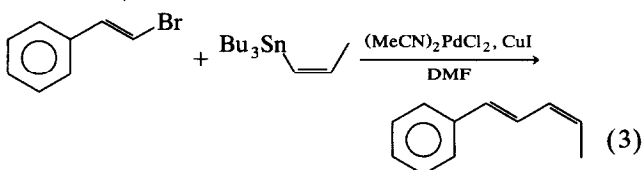


MHz) spectroscopy. Using copper iodide as co-catalyst [7] (14 mol%), the same reaction could be run at room temperature with similar results. Without catalysts [8], methyl α -bromocinnamate reacted slowly with 1-propenyltributyltin: after heating at 100–105°C for 4 days, minor amounts of the desired product could be isolated, and, after a week at room temperature, only traces of product could be detected by analytical TLC.

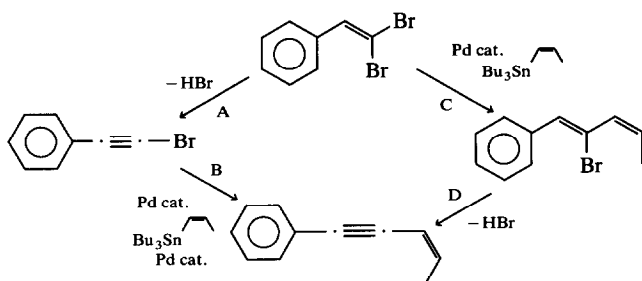
(*Z*)- α -Bromocinnamaldehyde and (*Z*)- α -bromocinnamyl alcohol gave disappointing results when reacted with 1-propenyltributyltin. The first one decomposed at room temperature under the reaction conditions and only about 2% of the corresponding diene could be isolated. The alcohol, in turn, exhibited very low reactivity. At room temperature, no reaction was observed after 4 days. However, heating at *ca.* 100°C in DMF or refluxing in toluene brought about a 19–21% of coupling product as a mixture of isomers (eqn. (2)).



β -Bromostyrene (81% *E*) was also treated with 1-propenyltributyltin, according to eqn. (3). After 3 h at *ca.* 100°C, a 85:15 *E,Z*:*E,E* mixture of 1-phenyl-1,3-pentadiene in 30% yield was obtained. By conducting the reaction at room temperature, the conjugated diene could be isolated in 39% yield after 4 days. Minor amounts of homocoupling product, 1,4-diphenyl-1,3-butadiene, were also isolated.

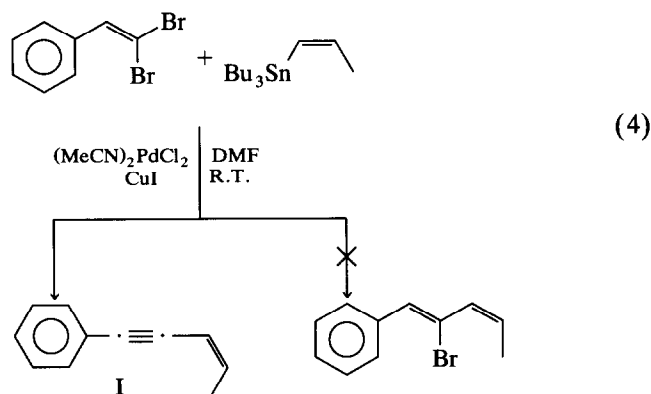


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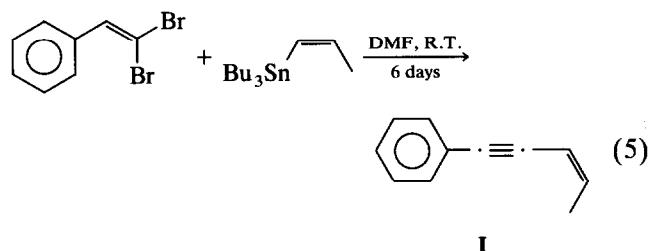
Scheme 1.

In order to obtain information about its stereochemical aspect, we decided to study the coupling process using an 1,1-dibromoalkene. Thus, the reaction of β,β -dibromostyrene with the propenyltin reagent was examined. Surprisingly, the expected 1-phenyl-2-bromo-1,3-butadiene was not produced. Instead, a 26:74 *E:Z* mixture of enyne I was obtained in 39% yield! (eqn. (4)). To explain the formation of the unexpected product I, two possible



pathways immediately come to mind (Scheme 1): first, the dibromoolefin could undergo a dehydrobromination reaction to give ω -bromophenylacetylene, which, in turn, reacts with 1-propenyltributyltin to produce the enyne I (route A–B), or, second, the initially formed 1-phenyl-2-bromo-1,3-butadiene loses HBr under the reaction conditions to give the final product I (route C–D). To test the latter possibility, an authentic sample of 1-phenyl-2-bromo-1,3-butadiene was independently synthesized and, subsequently, exposed to the reaction conditions. Careful monitoring of the reaction mixture by analytical TLC showed no evidence for the formation of compound I. On the other hand, enyne I was produced in 67% yield when ω -bromophenylacetylene was treated with 1-propenyltributyltin under palladium catalysis for 30 min. Furthermore, even in the absence of catalyst [8], 41% of compound I was isolated after 5 days. In both reactions, the isomeric

composition of enyne I was the same obtained in eqn. (4). These results implied that β,β -dibromostyrene is transformed into ω -bromophenylacetylene under the reaction conditions. Control experiments showed that this dehydrobromination reaction was not promoted by the palladium catalyst but rather by the organotin reagent. Indeed, reaction of β,β -dibromostyrene with 1-propenyltributyltin *without catalyst* [8] afforded directly enyne I in 25% yield (eqn. (5)).



The dehydrohalogenation of 1,1-dibromoolefins has been reported using alkyllithium reagents or lithium amalgam [9], and as a secondary reaction in the attempted coupling of vinylic dibromides using complex reducing agents [10]. Also, the palladium catalyzed crosscoupling of an organostannane with an iodoalkyne has been recently described [7]. However, it appears that the reaction sequence A–B (Scheme 1) represents the first examples of two chemical events: (i) a relatively slow organotin-promoted dehydrobromination of a 1,1-dibromoalkene, and (ii) a cross-coupling reaction between an alkynyl bromide and a vinyltin compound, which can occur even without palladium catalysis [8]. The mechanism and the synthetic scope of these reactions are presently under investigation and will be reported in future publications.

Acknowledgment

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References and notes

- 1 J.K. Stille, *Angew. Chem., Int. Ed. Engl.*, 25 (1986) 508.
- 2 J.K. Stille and B.L. Groh, *J. Am. Chem. Soc.*, 109 (1987) 813.
- 3 J.K. Stille and J.H. Simpson, *J. Am. Chem. Soc.*, 109 (1987) 2138.
- 4 W.J. Scott, G.T. Crisp and J.K. Stille, *J. Am. Chem. Soc.*, 106 (1984) 4630.
- 5 C.M. Hettrick, J.K. Kling and W.J. Scott, *J. Org. Chem.*, 56 (1991) 1489.
- 6 See for example: L.J. Silverberg, G. Wu, A.L. Rheingold and R.F. Heck, *J. Organomet. Chem.*, 409 (1991) 411; H.A. Dieck and R.F. Heck, *J. Org. Chem.*, 40 (1975) 1083.
- 7 L.S. Liebeskind and R.W. Fengl, *J. Org. Chem.*, 55 (1990) 5359.

8 To dismiss any possibility of catalysis by metal contamination, all glassware and stirring bars used in the non-catalyzed reactions were routinely washed with chromic acid cleaning mixture, rinsed thoroughly with demineralized water, soaked for a couple of hours with an aqueous solution containing 1% disodium ethylen-

diaminetetracetate and 2% NaOH, and finally rinsed thoroughly with demineralized water.

9 E.J. Corey and P.L. Fuchs, *Tetrahedron Lett.*, (1972) 3769.

10 R. Vanderesse, Y. Fort, S. Becker and P. Caubere, *Tetrahedron Lett.*, 27 (1986) 3517.