



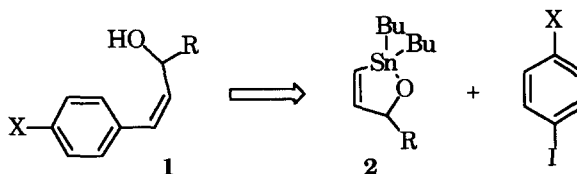
The Synthesis of Z-Allylic Alcohols via Palladium-Mediated Reactions of Stannoxanes with Aryl Halides

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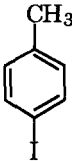
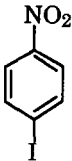
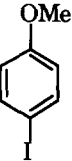
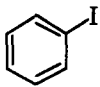
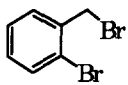
Abstract: The palladium-mediated reactions of stannoxanes with aryl halides affords Z-allylic alcohols in good to excellent yields. In many cases, the use of nitrobenzene as solvent dramatically improved the yields. Copyright © 1996 Elsevier Science Ltd

As part of a program for the synthesis of natural products that exhibited antiprotozoal activity, we required an efficient synthesis of allylic alcohols such as **1**. Typically, these compounds have been prepared by Wittig reactions, by catalytic hydrogenation of propargyl alcohols or by organometallic coupling reactions.¹⁻³ Unfortunately, many of these methods are limited by side reactions such as hydrogenolysis and by the generation of cis-trans mixtures. In the process of identifying a more reliable general procedure, we evaluated the palladium-mediated coupling of stannoxane **2** with p-iodotoluene. Although stannoxanes have been employed in synthesis for the preparation of vinyl halides, to the best of our knowledge these compounds have not been employed in organometallic coupling reactions with aryl halides.⁴



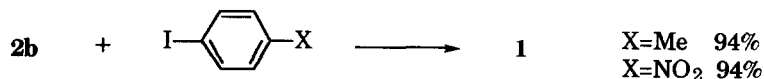
Stannoxanes **2a** (R=H) and **2b** (R=Me) were prepared from propargyl alcohol and 3-buten-2-ol in 50% and 45% yields, respectively.⁵ Stille and coworkers had studied the reactions of aryl halides and vinylstannanes to provide functionalized styrenes.⁶ Employing common palladium coupling reaction conditions with **2a** and p-iodotoluene afforded a 78% yield of **1** (X=Me, R=H). In an effort to improve the yield, we varied the catalyst, solvent, reaction temperature and the use of additives such as LiCl or BHT. Our results are collated in Table 1. Interestingly, we found that the use of nitrobenzene as solvent significantly improved the yields. As a representative procedure: to a degassed solution of 3 mL of nitrobenzene was added p-iodotoluene (87.2 mg, 0.4 mmol), Pd(Ph₃P)₄ (46 mg, 0.04 mmol), **2a** (346 mg, 1.2 mmol) and LiCl (50 mg, 1.7 mmol). The resulting solution was stirred under argon at 25 °C for 24 h. Methanol (15 mL) and 4 mL of 5% NaOH solution were added and the solution was stirred for 12 h. The MeOH was removed in vacuo and the residue was diluted with ether, filtered through Celite, washed with water, dried and concentrated in vacuo. Silica gel flash chromatography, first with hexanes to remove PhNO₂, and then with 5:1 hexanes:ethyl acetate afforded 53 mg (89% yield) of **1** (X=Me, R=H) with mp 56-57 °C.

Table 1. Formation of Cis Allylic Alcohols from **2a**

Halide	2a eq	Catalyst	Solvent	Temp °C	Time (h)	LiCl 3 eq	Inhibitor (BHT)	Yield	Z:E
	1.1	A	DMF	100	8	Y	Y	78	97:3
	0.9	A	DMF	100	5	N	Y	60	85:15
	0.9	B	Dioxane	100	12	N	N	22	
	3	A	PhNO ₂	25	24	Y	N	89	96:4
	1.1	A	PhNO ₂	70	2	N	N	66	97:3
	1	A	Toluene	80	4	N	N	60	91:9
	1.1	A	DMF	70	2	N	N	48	91:9
	3	A	PhNO ₂	25	24	Y	N	96	96:4
	1	B	PhNO ₂	25	12	Y	N	60	96:4
	1.1	A	PhNO ₂	25	12	N	N	30	
		A	Toluene	100	5	N	N	89	89:11
	1	C	PhNO ₂	50	8	Y	Y	58%	50:50

Catalyst (10 mole %): A=Pd(0). B=PdCl₂(PhCN)₂. C=Pd(0)/ZnCl₂. Yields are isolated yields based on the limiting reagent. Z:E ratios were determined by Proton NMR integration.

The use of the more soluble stannoxane **2b** led to improved yields, as illustrated below.



By virtue of its good yields and high Z:E ratios, this methodology provides an attractive alternative.

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