REACTION OF ARYL HALIDES WITH (Z)-1-ETHOXY-2-TRIBUTYLSTANNYLETHENE: A VERSATILE METHOD FOR THE INTRODUCTION OF 2-ETHOXYETHENYL GROUP INTO AROMATIC NUCLEI

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Abstract——The reaction of 4-substituted bromobenzenes, except for 4-bromophenol and 4-bromoaniline, with (Z)-1-ethoxy-2-tributylstannylethene is well prompted by the catalytic action of dichlorobis(triphenylphosphine)palladium in dimethylformamide in the presence of tetraethylammonium chloride to give (Z)-1-ethoxy-2-(4-substituted phenyl)ethene. The method is also useful for the introduction of a 2-ethoxyethenyl moiety into heteroaromatic rings such as pyridine, thiophene, indole.

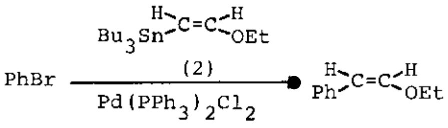
Although Heck reaction[1] has been known as one of versatile methods for introduction of olefinic side-chains into aromatic nuclei, there are few papers dealing with the synthesis of 1-aryl-2-alkoxyethenes by palladium-catalyzed reaction of aryl halides with alkoxyethene derivatives. For example, Anderson et al.[2] reported that the condensation of iodobenzene with butoxyethene was mediated by palladium-charcoal or palladium acetate to give a mixture of 1-butoxy-2-phenylethene and 1-butoxy-1-phenylethene, and Miyaura et al.[3] described that bromo- and iodobenzenes reacted with (E)-tris(2-ethoxyethenyl)borane in the presence of a palladium-phosphine complex catalyst to give (E)-1-ethoxy-2-phenylethene selectively, of which yield from iodobenzene was almost quantitatively.

The authors reports here that (Z)-1-ethoxy-2-tributylstannylethene (**2**) is an alternative reagent to convert aryl bromide (**1**) into (Z)-1-ethoxy-2-arylethenes (**3**) by the palladium-catalyzed reaction.

When bromobenzene (**1a**) was allowed to react with (Z)-1-ethoxy-2-tributylstannylethene (**2**)[4] in the presence of dichlorobis(triphenylphosphine)palladium under the conditions listed in Table I, (Z)-1-ethoxy-2-phenylethene (**3a**) was isolated in considerable yields. Based on these results, the authors used a standard procedure that is heating the substrate (**1**) and **2** in the presence of the palladium catalyst and tetraethylammonium chloride in dimethylformamide at 80°C for an appropriate time.

Then, in order to observe the electronic effect of the 4-substituents to the reaction, various 4-substituted bromobenzenes (**1b-j**) were employed to react with **2** under the standard conditions. As shown in Table II, the presence of electron-withdrawing groups in the substrates seems to be favorable for the reaction. On the other hand, 4-bromophenol (**1e**) and 4-bromoaniline (**1g**) does not undergo the palladium-catalyzed condensation, but 4-methoxy- (**1f**), 4-acetylamino- (**1i**), and 4-ethoxycarbonylaminobromobenzene (**1j**) were reacted with **2** to give the desired products (**3f,i,j**) in satisfactory yields.

Table I. Palladium-Catalyzed Cross-Coupling Reaction of Bromobenzene with **2**



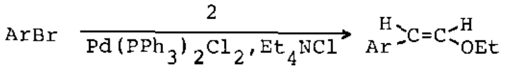
1a 3a

Solvent	Additive	Reaction temperature(°C)	Reaction time(h)	Yield (%)
THF	—	65	3	52
DMF	—	80	2	52
THF	Et_4NCl	65	3	59
DMF	Et_4NCl	80	2	78

Some heteroaromatic bromides such as 2-bromopyridine (**1k**), 3-bromopyridine (**1l**), 4-bromo-2,6-dimethylpyridine (**1m**), 2-bromothiophene (**1n**), and 3-bromo-1-mesylindole (**1o**) were treated with **2** under the same conditions. On the basis of the yields of the products, it is clear that the reaction proceeded smoothly regardless of the electronic character of the heteroaromatic rings.

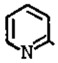
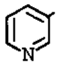
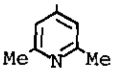
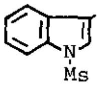
In the ^1H-nmr spectra of the products (**1a-o**), the coupling constants of two olefinic protons were observed to be 6-7 Hz, which demonstrate the Z-configuration of **2** to be entirely kept in the products.

Table II. Palladium-Catalyzed Cross-Coupling Reaction of 4-Substituted Bromobenzenes and Bromoheteroarenes with **2**



$$\mathrm{ArBr} \xrightarrow[\mathrm{DMF,\,80^\circ C}]{\mathbf{2} \atop \mathrm{Pd(PPh_3)_2Cl_2,\,Et_4NCl}} \mathrm{Ar(H)C{=}C(H)OEt}$$

1b-o 3b-d,f,h-o

	Ar	Reaction time(h)	Yield[a] (%)
1b	$4\text{-}O_2NC_6H_4$	2	86
1c	$4\text{-}EtOOCC_6H_4$	1	73
1d	$4\text{-}BrC_6H_4$	1.5	56
1e	$4\text{-}HOC_6H_4$	12	0[42]
1f	$4\text{-}MeOC_6H_4$	1	67
1g	$4\text{-}H_2NC_6H_4$	18	0[52]
1h	$4\text{-}Me_2NC_6H_4$	18	22[44]
1i	$4\text{-}AcNHC_6H_4$	18	71
1j	$4\text{-}EtOOCNHC_6H_4$	18	65
1k		3.5	62
1l		5	72
1m		12	70
1n		2.5	68
1o		9	83

a) The yields in brackets are recovery of the aryl bromide.

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Received, 16th November, 1989