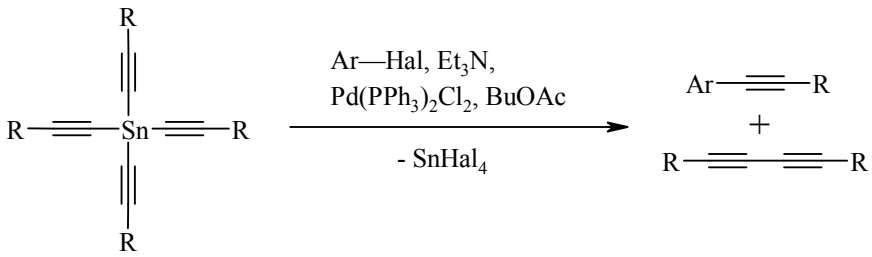
Stille-type cross coupling reactions with tetraalkynyl stannanes

Andrey S. Levashov,* Dmitriy S. Buriy, Valeriy V. Konshin and Alexey A. Andreev (deceased)

Kuban State University, 149 Stavropolskaya Str., Krasnodar 350040, Russian Federation

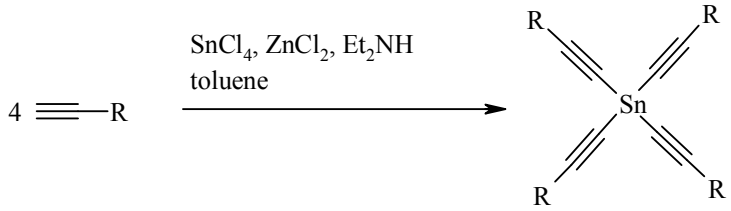
Abstract: Tetraalkynyl stannanes were reacted with aryl iodides and bromides under Stille conditions to give diaryl acetylenes and/or diaryl diacetylenes. The reaction conditions, scope and limitations of the proposed method are discussed.

Keywords: Tetraalkynyl stannanes, Stille cross coupling, acetylenes, organostannanes.



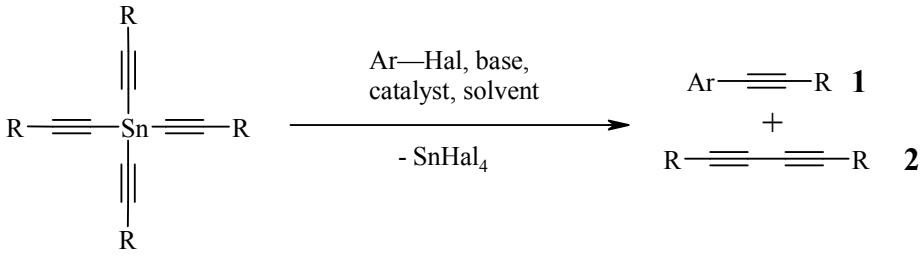
The cross coupling reaction of organic substrates with alkynyl trialkyltins discovered by John Stille in 1980-s has been widely used in the synthesis of a number of natural products and biologically active substances. This reaction is tolerant to a large number of functional groups of both the substrate and reagent. However, there are some drawbacks and limitations connected with the use of alkynyl trialkyltin compounds. First, they are highly toxic, in some cases they are more toxic than cyanides. Another disadvantage is a high molecular weight of $RC{\equiv}CSnAlk_3$ with respect to the weight of a fragment $RC{\equiv}C–$ introduced by this reagent. All these disadvantages disappear when organotin reagents containing more than one alkynyl moiety in the molecule are used. The most attractive among these reagents in terms of atom economy, low toxicity and synthetic convenience are undoubtedly tetraalkynyl stannanes $(RC{\equiv}C)_4Sn$. The aim of the present work was to study the cross coupling reactions of organyl halides with $(RC{\equiv}C)_4Sn$.

Tetraalkynyl stannanes are easily available [1,2] and could be obtained by direct alkynylation of $SnCl_4$ with phenylacetylene in the presence of equimolar amounts of zinc chloride and diethylamine in 60-80% yields [2]:



R = Ph, 4-$NO_2C_6H_4$.

To choose optimal conditions for Stille cross coupling reaction with tetraalkynyl stannanes $(RC{\equiv}C)_4Sn$, we have studied the effects of temperature, solvent and a catalyst. The reactions proceed to afford aryl acetylenes **1** along with diacetylene side products **2** according to the following scheme:



R = Ph, 4-$NO_2C_6H_4$.

Ar = 4-$NO_2C_6H_4$, 4-MeC_6H_4, Hal = I.

As a model process we selected the cross coupling reaction of 4-nitroiodobenzene with tetraphenylethynyltin, leading to the formation of 4-$NO_2C_6H_4C{\equiv}CPh$ **1a** and $PhC{\equiv}C–C{\equiv}CPh$ **2a** (as a minor by-product). The results of the experiments are shown in Tables 1,2.

Table 1. Effect of the solvent, temperture and the amine on the yields of products

Conditions \ Base		Et_2NH			Et_3N			DABCO		
solvent	t, ˚C	Yield, %		Time h	Yield, %		Time h	Yield, %		Time h
		1a	**2a**		**1a**	**2a**		**1a**	**2a**	
Et_2O	35	0	0	5	0	3	5	71	6	5
PhMe	100	55	10	7	27	14	5	87	8	0,5
MeCN	85	89	6	5	68	13	5	63	7	5
dioxane	100	84	2	3	44	6	2	78	8	5
BuOAc	100	98	2	2	85	2	5	86	5	2

As we can see from the above data, the use of PhMe and MeCN resulted in the formation of the target acetylene **1a** in good yields, but the process is accompanied by formation of essential amounts of by-product, diacetylene **2a**. The latter is due to Pd-catalyzed oxidative Glaser-type coupling of $(PhC{\equiv}C)_4Sn$ mediated by trace amounts of O_2 (all the reaction were conducted in the atmosphere of argon 99.95%). Almost quantitative yields of the desired product **1a** were obtained when ethyl acetate or butyl acetate were used as solvents. The amine is also plays an important role. We found that strong bases such as diethylamine, triethylamine, DABCO are the most effective in this reaction. Other amines such as morpholine, N-methylmorpholine or pyridine were found to be ineffective. The amine concentration is also has a significant influence on the reaction rate. Thus, in the presence of equimolar amounts of an amine the reaction proceeds quite slowly and the yield of **1a** was only 66% after 5h. Increasing the amine amounts increases the reaction rate and yields of the product **1a**. The use of a large excess of Et_2NH afforded diaryl acetylene **1a** in almost quantitative yields within only 2 hours. Next, we have studied the effect of different catalysts on the model process. It was found that $Pd(PPh_3)_2Cl_2$ gave the best results when combined with Et_2NH or Bu_3N, while $PdCl_2$ and $Pd(PhC{\equiv}N)_2Cl_2$ were much less effective. Also we studied the effect of R-substituent on the reactivity of tetraalkynyl stannanes $(RC{\equiv}C)_4Sn$ in the Stille reaction with aromatic halides. As expected, the tetraalkynyl stannanes with R = alkyl or propargyl gave lower (albeit reasonable) yields than arylethynyl stannanes.

In conclusion, we have proposed $(RC{\equiv}C)_4Sn$ as new and superior agent for Stille cross coupling, and studied the effects of different factors on the process.

Experimental

Tetraphenylethynyltin $(PhC{\equiv}C)_4Sn$

$ZnCl_2$ (1.00 g, 7.3 mmol) and Et_2NH (1.6 ml, 15.4 mmol) in dry toluene (5 ml) were placed under argon in a three-neck round-bottom flask equipped with a stirrer, dropping funnel, and a reflux condenser. The mixture was stirred at 50 °C for 15 min and then cooled to room temperature. Phenyl acetylene (6.8 mmol) was introduced followed by the slow addition of $SnCl_4$ (0.3 ml, 2.56 mmol) solution in dry toluene (4 ml). The resulting mixture was stirred for 20 min. The upper layer was separated and the lower layer extracted with toluene (3×10 ml). The combined toluene extracts were passed through a column of silanized silica and evaporated *in vacuo*. The target product was isolated as white crystalline mass and purified by recrystallization from *n*-heptane. Tetraphenylethynyltin $(PhC{\equiv}C)_4Sn$ was obtained

in 83% yield. M.p. 174 °C (heptane). FTIR spectrum, ν, cm^{-1}: 2152 (C≡C). NMR ^{1}H spectrum, δ, ppm: 7.59–7.61 (8H, m, Ph), 7.32–7.40 (12H, m, Ph). NMR ^{13}C spectrum, δ, ppm: 85.5 ($SnC^{1}\equiv$); 110.8 ($\equiv C^{2}$); 122.4 (C-Ph), 128.4 (C-Ph), 129.4 (C-Ph), 132.4 (C-Ph). NMR ^{119}Sn spectrum, δ, ppm: –322.29. GC-MS (EI, 70eV): 524 [M^{+}] (7), 404 (27), 322 (82), 202 (100), 120 (28), 102 (24).

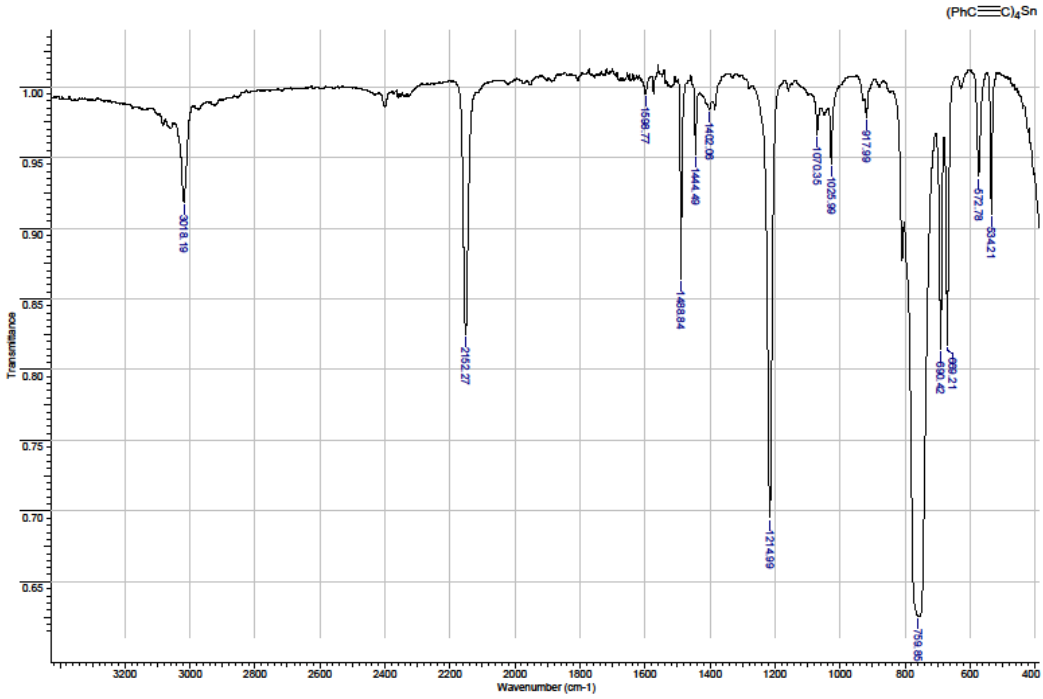


Fig. 1. IR spectrum of tetraphenylethynyltin $(PhC\equiv C)_4Sn$

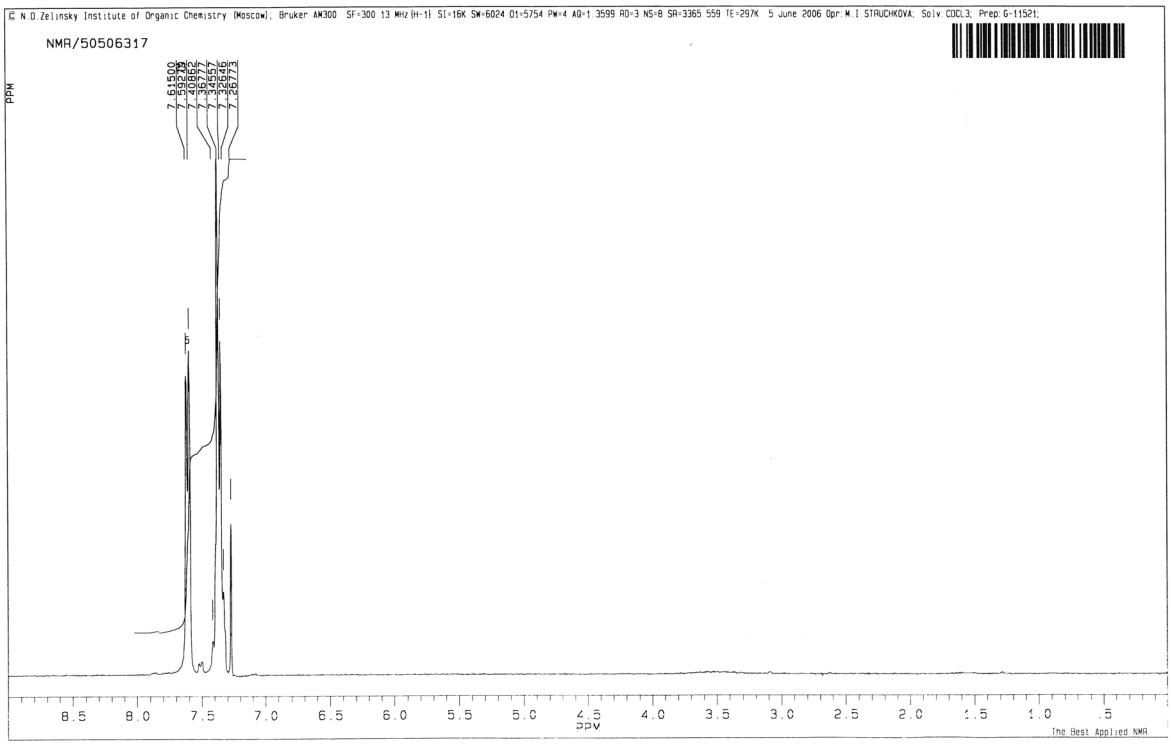


Fig. 2. ^{1}H NMR (300 MHz) spectrum of tetraphenylethynyltin $(PhC\equiv C)_4Sn$

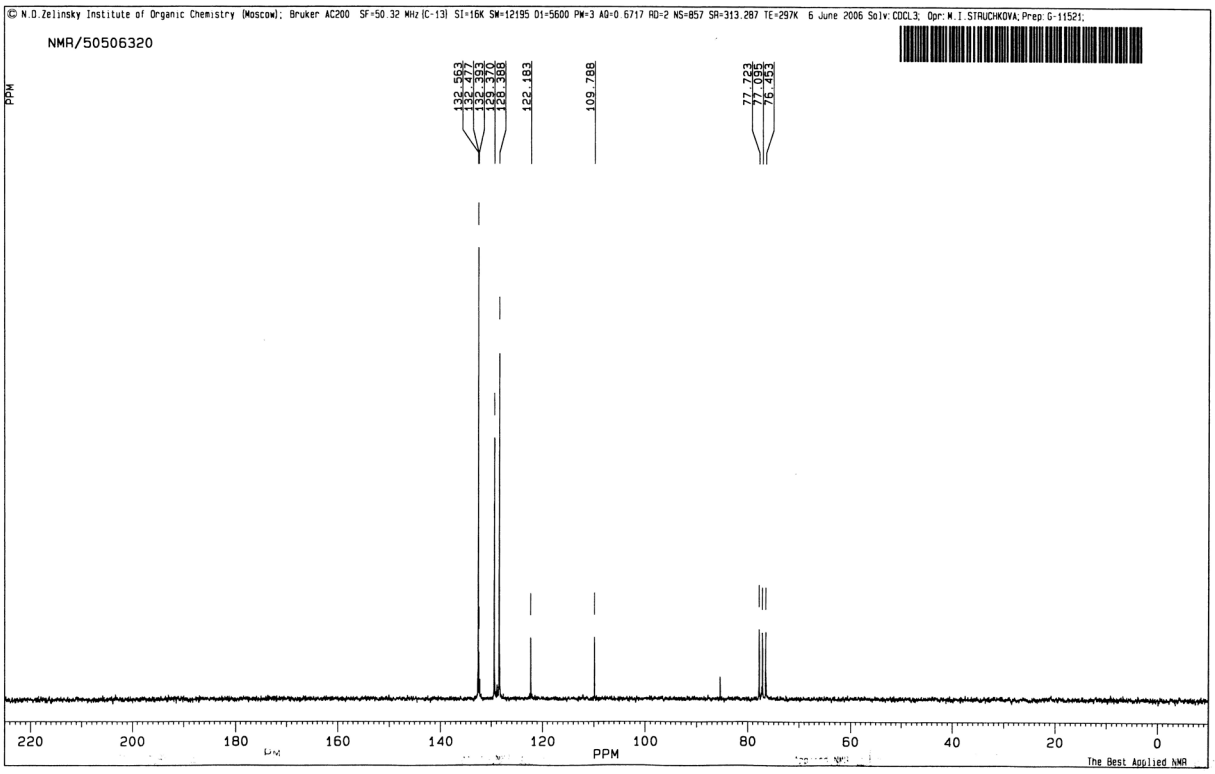


Fig. 3. ^{13}C NMR (50 MHz) spectrum of tetraphenylethynyltin $(PhC{\equiv}C)_4Sn$

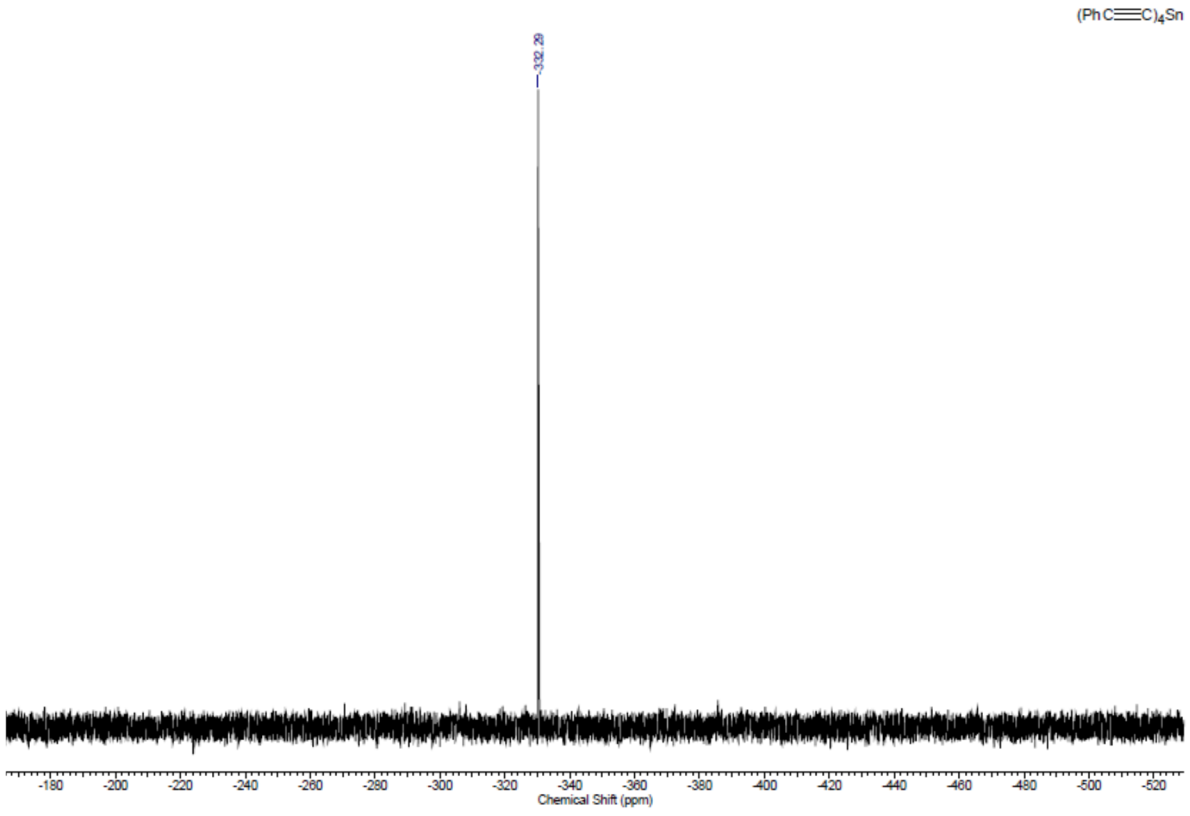


Fig. 4. ^{119}Sn NMR spectrum of tetraphenylethynyltin $(PhC{\equiv}C)_4Sn$

4-Nitrotolane 4-$NO_2C_6H_4C{\equiv}CPh$ 1a

A flask equipped with a reflux condenser, a tube for injection of inert gas and magnetic stirrer was charged with 0.1 mL of BuOAc and 0.9 mL of Et_2NH, 0.16 mmol of 4-$NO_2C_6H_4I$, 0.04 mmol $(PhC{\equiv}C)_4Sn$ and $Pd(PPh_3)_2Cl_2$ (5 mol% with respect to aryl iodide). The reaction mixture was heated for 2 h at 100 °C with stirring, after which the solvent was removed *in vacuo*, the residue was extracted with a small amount of hexane and purified by column chromatography on silica (eluent – hexane) to give pure **1a**.

References

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