Preliminary Communication

COUPLING REACTIONS BETWEEN ACETYLENIC BROMIDES AND ALKENYLTIN COMPOUNDS

Antonio J. Zapata* and Ana C. Rondón

Departamento de Química, Universidad Simón Bolívar, Apartado Postal 89000,
Caracas 1080A, Venezuela.

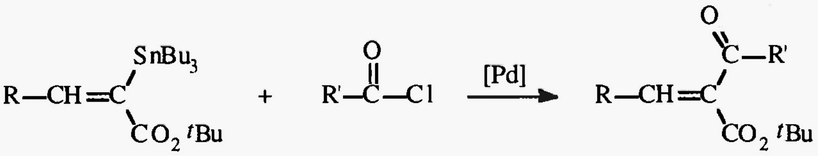
Abstract.
The coupling reaction between aromatic and aliphatic acetylenic bromides with representative alkenyltin compounds, with and without palladium catalysis, is described. Non-catalytic coupling does occur but the best yields of products are obtained under catalytic conditions.

Organotin compounds are popular reagents in organic chemistry because they can participate in a variety of synthetically useful transformations.[1] One such transformation is their palladium catalyzed coupling with unsaturated organic electrophiles, now commonly referred to as the Stille reaction (eq. 1).[2]

$$\text{R—X} + \text{R'—SnR''}_3 \xrightarrow{[\text{Pd}]} \text{R—R'} + \text{X—SnR''}_3 \qquad (1)$$

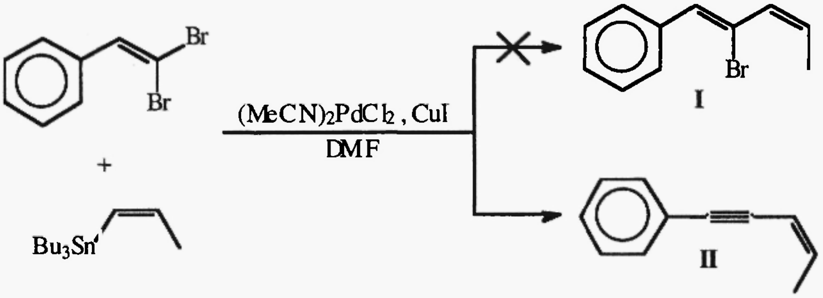
R , R' = allyl , alkenyl , alkynyl , aryl
R'' = alkyl (Me or Bu)
$X = Cl, Br, I, CF_3SO_2O$

Several years ago, in connection with our research program directed towards the development of new synthetic methodology based on organotin reagents, we became interested in applying the Stille reaction to α-stannyl-α,β-unsaturated carboxylic esters.[3] We found that these esters could react with acid chlorides, under palladium catalysis, to afford good yields of cross coupling products (eq. 2).[4]



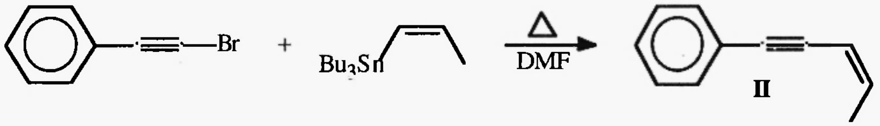
$$\text{R—CH=C}\begin{matrix}\text{SnBu}_3\\ \text{CO}_2\,t\text{Bu}\end{matrix} + \text{R'—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—Cl} \xrightarrow{[\text{Pd}]} \text{R—CH=C}\begin{matrix}\text{C(=O)—R'}\\ \text{CO}_2\,t\text{Bu}\end{matrix} \qquad (2)$$

However, the reaction failed when it wasattempted with vinylic bromides or iodides as coupling reagents. This result prompted us to explored the palladium catalyzed coupling of α–bromo-α,β-unsaturated carboxylic esters and others functionalized vinylic bromides with alkenyltin compounds.[5] Quite unexpectedly, the reaction of β,β-dibromostyrene with 1-propenyltributyltin did not afford the expected bromodiene **I** but, instead, a 39% of enyne **II** was isolated (eq. 3).



(3)

It was shown that enyne II was produced by palladium catalyzed coupling of ω-bromophenylacetylene, formed *in situ*, with 1-propenyltributyltin and, more surprisingly, that this coupling could occurred without palladium catalysis, representing the first example of such non-catalyzed coupling reaction (eq. 4).



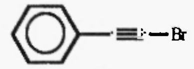
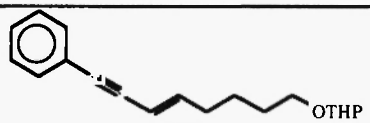
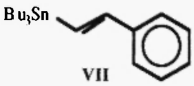
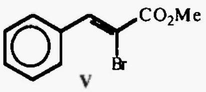
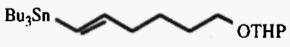
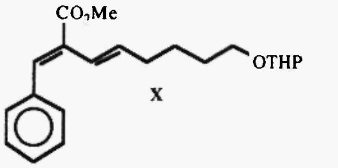
(4)

Consequently, we decided to continue our investigations by applying this reaction to others acetylenic bromides and alkenyltin compounds. Here, we report our preliminary results on the coupling reaction between aromatic and aliphatic acetylenic bromides with representative alkenyltin compounds, with and without palladium catalysis.

Non-catalyzed Coupling Reactions

The results from the non-catalyzed coupling reactions are summarized in Table I. To dismiss any possibility of catalysis by metal contamination, all glassware and stirring bars used in these 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 ethylendiaminetetraacetate and 2% sodium hydroxide, and finally rinsed thoroughly with demineralized water. The isomeric purities of organostannanes **VI** and **VII** were 88% and 86% *E*, respectively, as determined by ^{1}H NMR and HPLC analyses; bromide **V** was 95% *Z*.

Table I. Non-catalyzed Coupling Reactions[a]

bromide	organostannane	*T* (°C)	*t* (h)	product[b]	yield[c] (%)
 III	 VI	100	24	 VIII	2
 IV	 VII	90	48	 IX	14
 V	 VI	25	96	 X	58
 IV	 VI	90	120	 XI	10

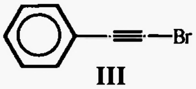
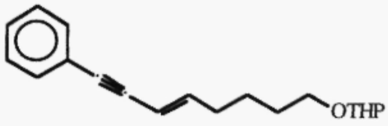
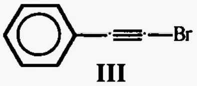
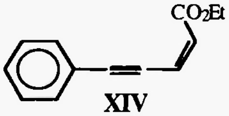
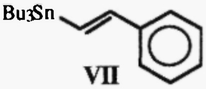
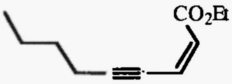
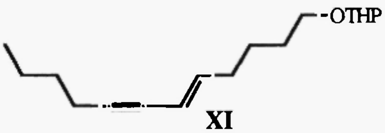
---

[a] Coupling reactions were carried out using equimolar amounts of reactants in *N,N*-dimethylformamide (DMF) as solvent.

[b] All new compounds exhibited spectral data in full accord with assigned structures and gave satisfactory combustion analyses.

[c] Isolated yields after purification by flash chromatography.

Table II. Palladium Catalyzed Coupling Reactions[a]

acetylenic bromide	organostannane	*t*(h)	product[b]	yield[c](%)
 **III**	 **VI**	8	 **VIII**	95
 **III**	 **XII**	24	 **XIV**	10
 **IV**	 **VII**	24	 **IX**	62
 **IV**	 **XIII**	24	 **XV**	75
 **IV**	 **XII**	168	 **XVI**	0
 **IV**	 **VI**	24	 **XI**	76

[a] Coupling reactions were carried out at room temperature using 2 eq. of the organostannane in *N*-methylpyrrolidinone as solvent.

[b] All new compounds exhibited spectral data in full accord with assigned structures and gave satisfactory combustion analyses.

[c] Isolated yields after purification by flash chromatography.

As it can be seen from Table I, these couplings required relatively high temperatures and long reaction periods. These could have a negative effect on the yields of enynes **VIII**, **IX** and **XI** as they were unstable under these reaction conditions. At the present time, the mechanism of these non-catalyzed coupling reactions is not clear.

Palladium Catalyzed Coupling Reactions

The palladium catalyzed coupling reactions of ω-bromophenylacetylene(**III**) and 1-bromo-1-hexyne(**IV**) were examined using a mixture of *bis*(acetonitrile)dichloropalladium(II) (5% molar) and tri-2-(furyl)phosphine (10% molar) as catalyst, *N*-methyl-pyrrolidinone as solvent, half equivalent of acetylenic bromide and slow addition (*ca.* 2 h) of organostannane. The isomeric purities of esters **XII** and **XIII** were >98% *Z* and >92% *E*, respectively, as determined by ^{1}H NMR (400 MHz) analysis. The results are summarized in Table II.[6]

This procedure afforded good yields of coupling products. Retention of geometry of the double bonds was observed. The coupling process seems to be particularly sensitive to steric hindrance as shown by the reactions of the *Z* isomer of ethyl β-tributylstannylpropenoate(**XII**) which were unsuccessful even using 1-iodo-1-hexyne as coupling partner. The utility of this procedure was illustrated by its application to the preparation of enyne **XI**, which constitutes a formal total synthesis of the sex pheromone of the pine moth, *Dendrolimus spectrobilis*, (5*E*, 7*Z*)-5,7-dodecadien-1-ol [7]. Work in this area is continuing.

Acknowledgment

This research was supported by a grant from the Decanato de Investigación y Desarrollo, Universidad Simon Bolívar.

References

(1) Pereyre, M.; Quintard, J.P; Rahm, A. *Tin in Organic Synthesis*; Butterworths, London, 1987.
(2) Stille, J.K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508.
(3) Zapata, A. ; Acuna, C. *Synthetic Comm.* **1988**, *18*, 1125.
(4) Zapata, A. ; Acuna, C. *Synthetic Comm.* **1988**, *18*, 1133.
(5) Zapata, A.; Ruiz, J. *J. Organomet. Chem.* **1994**, *479*, C6.
(6) For earlier examples of coupling reactions of haloalkynes with organotin compounds, see:
Quintard, J.; Parrain, J.; Beaudet, I. *Tetrahedron Lett.* **1992**, *33*, 3647 and
Liebeskind, L.; Fengl, R. *J. Org. Chem.* **1990**, *55*, 5359.
(7) Stille, J.K.; Simpson, J. *J. Am. Chem. Soc.* **1987**, *109*, 2138.

Received: September 20, 1996 - Accepted: September 23, 1996 -
Accepted in revised camera-ready format: October 3, 1996