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Palladium-Catalyzed Cyclization and Cross-Coupling of Acetylenic Aryl Triflates with Organotin Reagents

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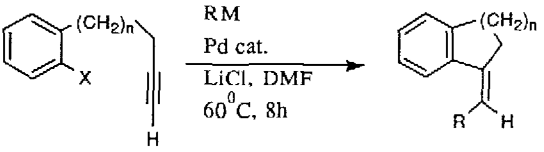
Abstract: Acetylenic aryl triflates reacted readily with vinyltributyltin, allyltributyltin, 1-(trimethylsilyl)-2-(tributylstannyl)-acetylene, and trimethylsilyltributyltin in the presence of a palladium catalyst to produce (Z)-indanylidene and (Z)-tetralinylidene substituted compounds, the stereospecificity of the reactions for the synthesis of these compounds being ≥98%.

Recently, work by Grigg[1] and ourselves[2] has shown that the Pd(II)intermediate obtained in situ from intramolecular insertion of alkynes can be further cross coupled with aryl or heteroarylzinc chloride to give stereo-defined exocyclic indan, tetralin, benzofuran, and indole derivatives in fair to good yields. However, the necessity of using vinyl or aryl halides to initiate the Heck-type reaction severely limited the application of this type of reaction in the past. Recently, the palladium-catalyzed coupling reaction of vinyl or aryl triflates with organostannanes in the presence of lithium chloride has been reported to take place in high yields under mild reaction conditions.[3] Herein, we report an alternative route along with its limitations to the synthesis of (Z)-indanylidene and (Z)-tetralinylidene substituted compounds by intramolecular cyclization and cross coupling of acetylenic aryl triflates and organotin reagents. The experimental results are summarized in Table I. Although the number of examples provided in this work is still small, the method described here also promises to provide a convenient and selective entry into stereo-defined exocyclic double bonds which are otherwise difficult to obtain.

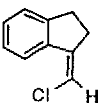
The following observations are worth noting. First, no cyclization and cross-coupling occurs in the absence of either palladium catalyst or lithium chloride indicating that the reaction of acetylenic aryl triflates and organotin is indeed catalyzed and promoted by the palladium complex and lithium chloride, respectively. Second, under otherwise comparable conditions phenyltrimethyltin, tetrabutyltin, hexamethyldistannane as well as phenylzinc chloride gave neither the cyclized and cross-coupling product nor the direct coupled product when they reacted with acetylenic aryl triflates. Third, all the stereo-defined exocyclic double bonds were obtained as isomerically ≥98% pure species, as judged by ^{1}H- and ^{13}C-NMR

Table I. The Reaction of Acetylenic Aryl Triflates or Aryl Iodide with Organo-tin or -zinc in the Presence of Pd Catalyst.



Entry	X =	R =	M =	Pd Cat.[a]	Yield (%)	Byproduct(%)
n = 1						
1	OTf	Vinyl-	$\mathrm{SnBu_3}$	A	57	--
2	OTf	Vinyl-	$\mathrm{SnBu_3}$	B	59	**1** (trace)
3	OTf	Vinyl-	$\mathrm{SnBu_3}$	C	63	--
4[b]	OTf	Vinyl-	$\mathrm{SnBu_3}$	A	36	--
5	OTf	Allyl-	$\mathrm{SnBu_3}$	A	46	**2** (39)
6	OTf	Allyl-	$\mathrm{SnBu_3}$	B	37	**3** (30)
7	OTf	Allyl-	$\mathrm{SnBu_3}$	C	39	**2** (51)
8	OTf	$\mathrm{Me_3SiC{\equiv}C}$-	$\mathrm{SnBu_3}$	A	31	--
9	OTf	$\mathrm{Me_3SiC{\equiv}C}$-	$\mathrm{SnBu_3}$	B	44	**1** (9)
10	OTf	$\mathrm{Me_3SiC{\equiv}C}$-	$\mathrm{SnBu_3}$	C	45	--
11	OTf	$\mathrm{Me_3Si}$-	$\mathrm{SnBu_3}$	A	37	--
12[c]	I	Vinyl-	ZnCl	A	53	--
13[c]	I	$\mathrm{Me_3SiC{\equiv}C}$-	ZnCl	A	69	--
14[c]	I	Allyl-	ZnCl	A	trace	**5** (46)
15[c]	I	$\mathrm{Me_3Si}$-	ZnCl	A	8	**6** (23)
16	I	Allyl-	$\mathrm{SnBu_3}$	A	43	**2** (5)
17	I	$\mathrm{Me_3Si}$-	$\mathrm{SnBu_3}$	A	54	**2** (10)
n = 2						
18	OTf	Vinyl-	$\mathrm{SnBu_3}$	B	51	--
19	OTf	Allyl-	$\mathrm{SnBu_3}$	A	51	--
20	OTf	$\mathrm{Me_3SiC{\equiv}C}$-	$\mathrm{SnBu_3}$	A	54	--
21	OTf	$\mathrm{Me_3SiC{\equiv}C}$-	$\mathrm{SnBu_3}$	B	24	**4** (25)

[a] A = 5% $\mathrm{Pd(PPh_3)_4}$, B = 5% $\mathrm{Pd(dppf)Cl_2}$, C = 5% $\mathrm{Pd(OAc)_2}$ + 10% $\mathrm{PPh_3}$ + 1 equiv $\mathrm{Et_3N}$. [b] This reaction was running in THF instead of DMF as the solvent. [c] The reaction was running in THF and in the absence of LiCl.



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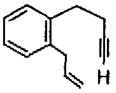

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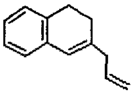

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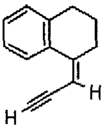

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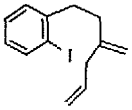

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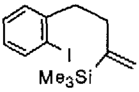

6

spectroscopy as well as by GLC. Fourth, while the formation of five- and six-membered ring can be readily achieved under the reaction conditions, the formation of four-membered ring by using 2-(2-propynyl)phenyl triflate had been unsuccessful under the similar reaction conditions. In fact, many attempts by us to promote the cyclization and cross-coupling have been uniformly unsuccessful. Fifth, the yields of the desired products can be increased to some extent by changing the solvent from THF to DMF (Entries 1, 2, 3, and 4). Probably DMF can both solubilize lithium chloride and act as good ligands to accelerate the reaction rate.[3] Sixth, in all the reactions involving acetylenic aryl triflates we have run, only allyltributyltin gave direct coupled products when $Pd(PPh_3)_4$ and $Pd(OAc)_2/PPh_3/Et_3N$[2b,2c] were used as the catalyst (Entries 5 and 7). No more than traces ($\leq$1%) of direct coupled products have been found in the other cases as we judged by their GLC as well as crude ^{1}H-NMR spectral analysis. Seventh, when $Pd(dppf)Cl_2$ was used as the catalyst, trace to 9% yield of (Z)-2,3-dihydro-1-chloromethyleneindene **1** can be detected and isolated (Entries 2 and 9). Its stereochemistry had been confirmed by its 2D-NOESY spectral analysis. We also found that low regioselectivity and desilylation may occur when $Pd(dppf)Cl_2$ was used as the catalyst (Entries 6 and 21). However, $Pd(dppf)Cl_2$ may still be satisfactory in cases where no such difficulties arise (e.g. Entries 2, 9, and 18).

While vinylzinc chloride and trimethylsilylacetylenylzinc chloride reacting with 1-(3-butynyl)-2-iodobenzene **7** in the presence of catalytic amount of $Pd(PPh_3)_4$ can give cyclized and coupled product in 53 to 69% yields (Entries 12 and 13). We found that when either allylzinc chloride or trimethylsilylzinc chloride[4] was used to react with **7** in the presence of palladium catalyst, little or no desired products had been detected either by GLC or ^{1}H-NMR spectral analysis (Entries 14 and 15). In fact, only 1-(3-methylene-5-hexenyl)-2-iodobenzene **5** can be isolated in 39 to 46% yields when allylzinc chloride was used in the above reaction. Interestingly, either allyltributyltin or trimethylsilyltributyltin can give the cyclized and coupled product in 37 to 46% isolated yield when they reacted with acetylenic aryl triflates in the presence of a pertinent palladium catalyst (e.g. Entries 5 and 11). Moreover, we also found that these organotin reagents can indeed react with acetylenic aryl iodide, e.g. **7**, in the presence of palladium catalyst, e.g. $Pd(PPh_3)_4$, to give cyclized and coupled product in 43 to 54% yields (Entries 16 and 17).[5] However, the direct coupled products are always isolated in 5 to 10% yields.

The following procedure for preparing (Z)-2,3-dihydro-1-(2-propenylene-)indene **8** is representative. To a slurry of lithium chloride (0.13 3 mmol) and $Pd(PPh_3)_4$ (0.06 g, 0.05 mmol) in 5 mL of DMF was added, under nitrogen atmosphere, 2-(3-butynyl)phenyl triflate (0.28 g, 1 mmol), prepared from 2-(3-butynyl)phenol and trifluoromethanesulfonic anhydride in carbon tetrachloride.[6] The reaction mixture was then stirred for 0.5 h. To this was added dropwise vinyltributyltin (0.41 g, 1.3 mmol). The reaction mixture was then heated at 60°C for another 8 h, quenched with water (20 mL), and extracted with ether (15 mL x 4). The organic extracts were washed with brine, dried over $MgSO_4$, concentrated, and purified by chromatography (silica gel, hexane/ethyl acetate = 4/1) to give 89 mg (57%) of **8**: ^{1}H-NMR ($CDCl_3$, TMS) δ 2.7-3.0 (m, 4 H), 5.13 (d, J = Hz, 1 H), 5.24 (d, J = 16.7 Hz, 1 H), 6.21 (d, J = 11.5 Hz, 1 H), 7.0-7.3 (m, 4 H), 7.6-7.7 (m, 1 H) ppm. ^{13}C-NMR ($CDCl_3$, TMS) δ 30.19, 34.16, 116.56, 122.55, 124.82, 125.30, 126.33, 127.84, 133.06, 140.26, 143.50, 148.53 ppm. IR (neat) ν 1630 (w), 1460 (m), 1420 (w), 1020 (w), 980 (m), 895 (m), 760 (s) cm^{-1}. MS m/z 156(M^+) 155, 141, 128, 115.

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4. These organozinc chlorides were obtained by transmetallation of the corresponding organolithium with 1 equiv of zinc chloride in THF at 0°C.

5. Under the similar reaction conditions, $Pd(dba)_2$ catalyst gave only 12 to 20% yields of the desired product.

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