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Observation of the First Heck-Type Cross-Coupling Reaction of Allenes with Aryl Halides. Synthesis of Polysubstituted 1,2-Allenyl Sulfones

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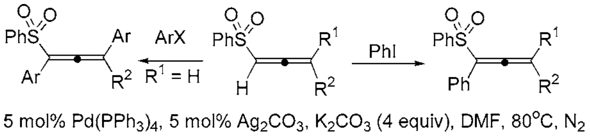
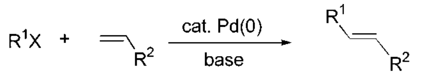
ABSTRACT

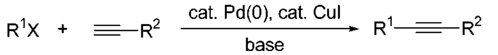


The Heck-type allenylation of aryl halides with allenes has been observed for the first time: The regioselectivity of intermolecular carbopalladation of 1,2-allenyl sulfones affording vinylic Pd intermediates is completely opposite to what was reported in the literature.

The Pd(0)-catalyzed coupling of alkenes and organic halides affording substituted alkenes (Heck reaction) has become one of the most commonly used C−C bond-forming reactions (eq 1).[1] The Pd(0)/Cu(I)-cocatalyzed reaction of terminal alkynes with organic halides (Sonogashira coupling) would afford substituted alkynes,[2] in which a carbopalladation of the C−C triple bond is not involved (eq 2).

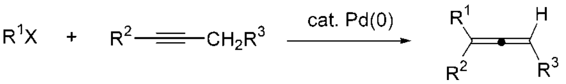


(1)



(2)

There is one report on the reaction of organic halides with nonterminal alkynes affording allenes via a sequential carboplladation and β-H elimination (eq 3).[3] However, the



(3)

carbopalladation of allenes usually afforded a π-allylic palladium intermediate **A**, which may undergo β-H elimination or allylic substitution affording nonallenic products

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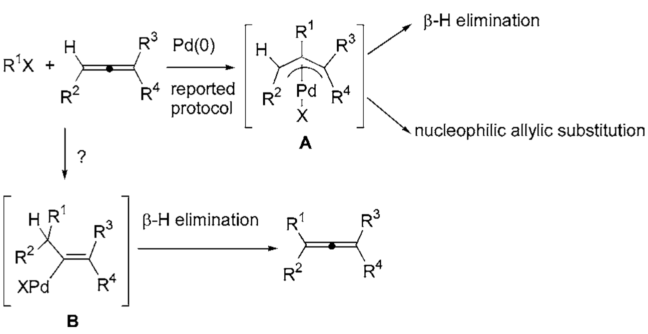
(3) Pivsa-Art, S.; Satoh, T.; Miura, M.; Nomura, M. *Chem. Lett.* **1997**, 823. In the following two reports, allenes have been proposed as intermediates formed by carbopalladation of alkynes and β-H elimination: Kadota, I.; Shibuya, A.; Gyoung, Y. S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 10262. Kadota, I.; Shibuya, A.; Lutete, L. M.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4570.

10.1021/ol050301j CCC: $30.25

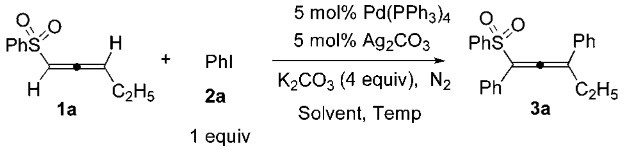
Scheme 1



(Scheme 1).[4] There is one report in which vinylic palladium intermediates were formed from the intramolecular carbopalladation of allenes. Subsequent carboxylation led to the formation of α,β-unsaturated alkenoates.[5] Thus, the regioselectivity of carbopalladation of allenes may be determined by the delocalization of the π-allylic palladium intermediate **A** and the high energy/reactivity of the allene to be formed via the β-H elimination of a vinylic Pd intermediate **B**. To the best of our knowledge, no report has been documented for the formation of substituted allenes from the Heck-type reaction of allenes with organic halides. In this paper, we wish to report the first example of allenylation of aryl halides via **B**-type intermediates.

Allenes are an important structural unit in many natural products. However, for a long period of time they were considered to be highly unstable, which retarded the development of their chemistry.[6] Recent studies show that allenes demonstrate excellent reactivities and selectivities.[7] During the course of our study on the chemistry of 1,2-allenyl sulfoxides[8,9] or sulfones,[10] we were interested to see the carbopalladation of these substrates, which may lead to the formation of synthetically useful 1,3-alkadienyl sulfones via the π-allyl palladium species-forming carbopalladadation and a subsequent β-H elimination reaction. However, to our surprise when we ran the reaction of 1,2-pentadienyl sulfone (**1a**) with PhI under the catalysis of $Pd(PPh_3)_4$ and Ag_2CO_3 in toluene 6% yield of 1,3-diphenylation product, i.e., 1,3-diphenyl-1,2-pentadienyl phenyl sulfone **3a**, was formed unexpectedly as the only product (entry 4, Table 1), indicating the exclusive unusual regioselectivity of the carbopalladation of allenes with the phenyl group connected to the 1- or 3-position (instead of the 2-position[4]) and the palladium atom connected to the center carbon atom of the 1,2-allenyl sulfones.

Table 1. Pd(0)/Ag$^+$-Catalyzed Carbopalladation Reaction of **1a** with PhI



entry	solvent	temp (°C)	time (h)	yield of **3a**[a] (%)
1	toluene	80	3	6
2	THF	80	3	4
3	dioxane	80	3	5
4	MeCN	80	3	77
5	DMF	80	3	87
6	DMF	80	3	11[b]
7	DMF	60	7	70
8	DMF	rt	12	49

[a] Isolated yield based on PhI. [b] Reaction was conducted in the absence of Ag_2CO_3.

Further screening indicated that the reaction is not good in THF or dioxane, yielding **3a** in only 4∼5% yield (entries 1−3, Table 1). MeCN is a much better solvent (entry 4, Table 1). The same reaction in DMF gave the product **3a** in the best yield (87%) (entry 5, Table 1). It is quite interesting to note that an excess amount of sulfone **1a** was required for a high-yielding reaction probably due to the fact that the formed allene **3a** may react further with PhI if PhI is in excess. Further studies showed that the yield is lower with an increased ratio of **2a/1a**. The reaction in absence of Ag_2CO_3 gave the product **3a** in only 11% yield (entry 6, Table 1). At a lower reaction temperature, the yield is lower (compare entries 7 and 8 with entry 5, Table 1). It is interesting to note that no monophenylation product was detected even when the reaction was conducted at room temperature (entry 8, Table 1).

With the standard reaction conditions in hand, the scope of the reaction was studied with the typical results summarized in Table 2. With different R^1, 1,3-diphenylation products **3** were formed in good yields. Both electron-deficient and electron-rich aryl iodides can be used (entries 4−8, Table 2).

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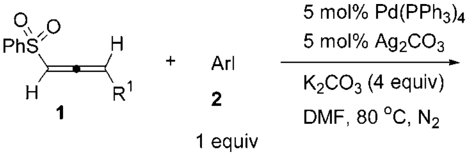
Table 2. Pd(0)/Ag$^+$-Catalyzed Reaction of 1,2-Allenic Sulfones with Organic Halides[a]

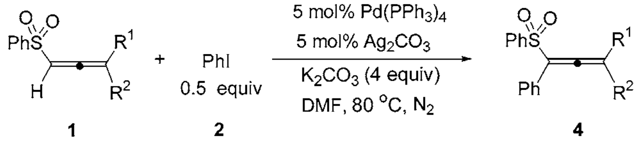


entry	R^1	ArX	time (h)	isolated yield of **3** (%)
1	Et (**1a**)	PhI (**2a**)	3	87 (**3a**)
2	Me (**1b**)	PhI (**2a**)	3	66 (**3b**)
3	*n*-pent (**1c**)	PhI (**2a**)	3	70 (**3c**)
4	Et (**1a**)	*p*-MeC_6H_4I (**2b**)	3	77 (**3d**)
5	Et (**1a**)	*p*-$MeCO_2C_6H_4I$ (**2c**)	3	74 (**3e**)
6	Et (**1a**)	*p*-$MeCOC_6H_4I$ (**2d**)	2.5	81 (**3f**)
7	Et (**1a**)	*p*-ClC_6H_4I (**2e**)	2	77 (**3g**)
8	Et (**1a**)	*p*-BrC_6H_4I (**2f**)	2	76 (**3h**)

[a] Reaction was carried out using 0.3−0.6 mmol of 1,2-allenic sulfones.

The reaction of 3,3-disubstituted 1,2-allenyl sulfones **1d−g** afforded the monoarylation products **4** in moderate to excellent yields (Scheme 2). The structures of all the products were established by the X-ray diffraction study of **4a** (Figure 1).[11]

Scheme 2



R^1	R^2	T(h)	yield of **4** (%)
Me	Et(**1d**)	16	70(**4a**)
Et	Et(**1e**)	3	62(**4b**)
Et	Ph(**1g**)	3	76(**3a**)

In conclusion, we have observed for the first time the Heck-type allenylation of aryl halides with allenes: With 3-monosubstituted 1,2-allenyl sulfones, 1,3-double arylations were observed, while the corresponding reaction of 3,3-disubstituted 1,2-allenyl sulfones afforded 1-monoarylation products.[12] The regioselectivity of intermolecular carbopalladation of 1,2-allenyl sulfones is completely opposite to what was reported in the literature.[4] Although the role of the sulfonyl group and 5 mol % Ag_2CO_3 is not clear, this reaction yielded important information for the study of carbometalation of allenes. Further studies in this area are being conducted in our laboratory.

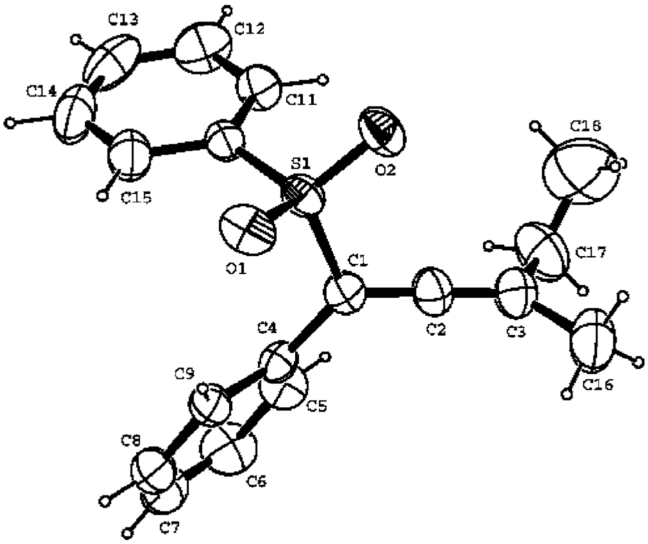


Figure 1. ORTEP drawing of **4a**.

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Supporting Information Available: Spectroscopic data and general procedure. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] Crystal data for compound **4a**: $C_{18}H_{18}O_2S$, MW 298.40, monoclinic, *Cc*(#9), MoKα, final *R* indices [$I > 2\sigma(I)$], R_1 0.046, wR_2 = 0.102, a = 14.625(2) Å, b = 8.8129(9) Å, c = 12.623(2) Å, β = 96.023(7), V = 1618.0(4) Å^3, Z = 4, number of reflections measured/unique 5850/1820 (R_{int} = 0.063), number of observations ($I > 2.00\sigma(I)$) 1108, number of variables 190, GOF indicator 1.010, CCDC 259343.

[12] For reports on the synthesis of allenes via the Pd-catalyzed coupling of 1,2-allenyl halides with organometallic reagents, see: Kleijn, R. H.; Meijer, J.; Oostveen, E. A.; Vermeer, P. *J. Organomet. Chem.* **1982**, *224*, 399. Russell, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943. For reviews, see: ref 1h and: Ma, S. *Eur. J. Org. Chem.* **2004**, 1175.