

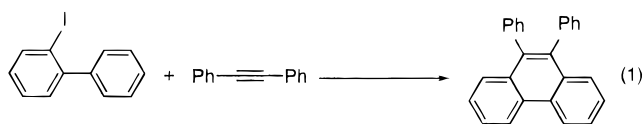
Synthesis of Polycyclic Aromatic Hydrocarbons by the Pd-Catalyzed Annulation of Alkynes

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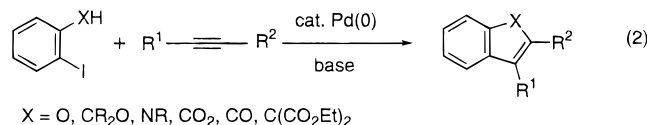
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Palladium-catalyzed annulation has recently proven useful as a means of forming polycyclic aromatic hydrocarbons. For example, Dyker¹ has synthesized disubstituted acenaphthylene derivatives from 1,8-diiodonaphthalene and alkynes in the presence of a palladium catalyst, while Grigg² has formed 7,8-diphenylacenaphthylene by the palladium-catalyzed coupling of 1-iodonaphthalene and diphenylacetylene. Substituted phenanthrenes have also been synthesized using palladium methodology.^{3,4} For example, Heck^{3b} reported in 1987 the formation of 9,10-diphenylphenanthrene in 14% yield by the reaction of 2-iodobiphenyl, diphenylacetylene, 2 mol % Pd(OAc)₂, 4 mol % PPh₃, and Et₃N in CH₃NO₂ for 2 days at 100 °C (eq 1). Our own interest in the



synthesis of hetero- and carbocycles by the Pd-catalyzed annulation of internal acetylenes (eq 2)⁵ led us to further



investigate this reaction. Herein we report improved reaction conditions, which extend the Heck process to a wide variety of internal acetylenes and 2-iodobiaryls, as well as vinylic halides and triflates bearing aryl groups in the 2-position. The resulting methodology accommodates a variety of structurally and functionally diverse aryl and vinylic substrates and affords the anticipated annulation products in moderate to excellent yields.

We initiated our studies on the reaction of 2-iodobiphenyl and diphenylacetylene (eq 1) and found that under conditions similar to those used in our palladium-catalyzed synthesis of isocoumarins,^{5b} 9,10-diphenylphenanthrene was obtained in 89% yield. Further optimization with a variety of internal alkynes has led to the development of two general procedures to affect this annulation process. **Procedure A:** 1 equiv of the

organic iodide or triflate, 1.1 or 2.0 equiv of the alkyne, 5 mol % of Pd(OAc)₂, 2 equiv of NaOAc, 1 equiv of LiCl in DMF at 100 °C. **Procedure B:** 1 equiv of the organic iodide or triflate, 1.1 or 2.0 equiv of the alkyne, 5 mol % of Pd(OAc)₂, 2 equiv of NaOAc, 3 equiv of *n*-Bu₄NCl in DMF at 100 °C. The procedure used for these reactions is strongly influenced by the structure of the alkyne. In general, procedure B works better for diarylacetylenes and silylacetylenes, while procedure A is more successful when alkyl-substituted acetylenes are used. The generality of this process has been demonstrated by the annulation of a variety of functionalized alkynes using a number of functionally substituted aryl or vinylic halides or triflates (Table 1).

As with our previous work,⁵ this annulation process works best for alkynes containing hindered groups, such as aryl, *tert*-butyl and trialkylsilyl groups. 1-Phenyl-2-(triethylsilyl)acetylene reacts with 2-iodobiaryls to give the desired 9,10-disubstituted phenanthrenes in fair yields (entries 4–6). The relatively low yields obtained in reactions employing silylacetylenes is most likely due to competing desilylation of the alkyne and subsequent palladium-catalyzed coupling of the aryl iodide to the terminal acetylene affording the corresponding diarylacetylene. Regioselectivity in the annulation of unsymmetrical acetylenes using biaryls was low and seemed to be influenced by the steric bulk of the alkyne substituents, as well as the substituents on the biaryl (entries 5 and 6).⁶ Modest regioselectivity was observed in the annulation involving 2-(2'-iodophenyl)naphthalene (entry 7).

Vinylic halides and triflates bearing aryl groups in the 2-position also serve as efficient substrates in this alkyne annulation process. A number of 9,10-disubstituted-1,2,3,4-tetrahydrophenanthrenes have been prepared in good yields by the palladium-catalyzed annulation of internal alkynes using 1-iodo-2-phenylcyclohexene or 2-phenyl-1-cyclohexenyl triflate (entries 8–13). In contrast to the annulation process using biaryls, these annulations proceed with high regioselectivity. The regiochemistry of the product shown in entries 10 and 11 of Table 1 has been confirmed by a 2D NOESY experiment.⁷ This regioselectivity is consistent with our previous acetylene annulation work in which the aryl or vinylic group adds to the less hindered end of the alkyne.⁵ Other cyclic vinylic iodides and triflates have also been employed in this annulation process. For example, 5,6-diphenyl-7*H*-benzo[*c*]fluoren-7-one was obtained in 54% yield from the reaction of 2-iodo-3-phenylindenone and diphenylacetylene (entry 14).

Acyclic vinylic iodides and triflates have also been examined. No annulation products were obtained when (*Z*)-1-iodo-2-phenylethylene was used as a substrate, perhaps due to β -hydride elimination from the presumed initial vinylic palladium intermediate. On the other hand, 2-iodo-1,1-diphenylethylene, which has no β -hydrogens, affords the expected products (entries 15 and 16), although only modest regiospecificity was observed when 3,3-dimethyl-1-phenyl-1-butyne was used as the substrate. The low regioselectivity may be due to the low steric demand of the hydrogen at the α -position of the initial vinylic palladium intermediate. A hydrogen at this position may be too small to control the regioselectivity.

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Table 1. Synthesis of Polycyclic Aromatics via Pd-Catalyzed Carboannulation of Internal Acetylenes.

entry	organic iodide/triflate	acetylene (equiv)	product(s)	procedure, ^a rxn time	% yield (isomer ratio)
1		Ph—C≡C—Ph (1.0)		X = H, A, 20h	89 ^b
2		(1.1)		X = OMe, B, 24 h	86
3		(1.1)		X = CF ₃ , A, 144 h	69
4		Ph—C≡C—SiEt ₃ (2.0)		X = H, A, 48 h	49
5		(2.0)		X = 4-OMe, A, 24 h	50 (1 : 1)
6		(2.0)		X = 2-OMe, A, 24 h	61 (3 : 1)
7		Ar—C≡C—Ar Ar = 4-MeOC ₆ H ₄ (1.1)		A, 24 h	75 (5 : 1)
8		Ph—C≡C—R (2.0)		R = Ph, X = I, B, 10 h	86
9		(2.0)		X = OTf, B, 6 h	78
10		(2.0)		X = I, B, 10 h	73
11		(2.0)		X = OTf, B, 10 h	81
12		(2.0)		X = I, B, 10 h	55
13		(2.0)		X = OTf, B, 10 h	46
14		Ph—C≡C—Ph (2.0)		A, 48 h	54
15		Ph—C≡C—t-Bu (2.0)		X = I, A, 10 h	62 (3 : 1)
16		(2.0)		X = OTf, B, 10 h	45 (2 : 1)
17		Ph—C≡C—t-Bu (2.0)		A, 48 h	46

^aProcedure A: 5 mol % of Pd(OAc)₂, 2 equiv of NaOAc, 1 equiv of LiCl in DMF at 100 °C for the specified period of time. Procedure B: 5 mol % of Pd(OAc)₂, 2 equiv of NaOAc, 3 equiv of *n*-Bu₄NCl in DMF at 100 °C for the specified period of time. ^b0.5 Equiv of LiCl were used.

tivity of the addition of the vinylic palladium to the internal alkynes. As expected, 2-iodo-1,1-diphenylpropane, having a larger methyl group as an α -substituent, reacted with 3,3-dimethyl-1-phenyl-1-butyne to afford a single regioisomer in 46% yield (entry 17).

On the basis of the profound difference in the rate of annulation onto the MeO- versus the CF₃-substituted aromatic ring (Table 1, entries 2 and 3), as well as the preference of 2-(2'-iodophenyl)naphthalene for annulation in the 1-position (Table 1, entry 7), we tentatively propose a process involving oxidative addition of the organic halide or triflate to produce an organopalladium intermediate, which rapidly inserts the acetylene to produce a vinylic palladium species. This species in turn undergoes electrophilic aromatic substitution, followed by reductive elimination of the observed product to regenerate Pd(0). An alternative mechanistic route involves oxidative addition of the neighboring aryl C–H bond to the vinylic palladium intermediate generating a Pd(IV) species, followed by reductive elimination of the product and HX, thus regenerating Pd(0) (see Supporting Information for mechanisms). No products of multiple alkyne insertion have been observed.

The palladium-catalyzed carboannulation of internal acetylenes using biaryls or styrenyl halides or triflates is a process which is quite general in scope. A fair variety of internal alkynes can be annulated using this chemistry, although the reaction is most general for aryl

acetylenes or hindered alkyl- or silylacetylenes. Functionalization of the biaryl seems to have little effect on the product yields. However, surprisingly low regioselectivity is observed in the alkyne insertion of such biaryls, while vinylic starting materials exhibit significantly enhanced regioselectivity. This methodology provides an exceptionally efficient route to a wide variety of substituted polycyclic aromatic hydrocarbons from readily available starting materials, affording the products in moderate to excellent yields. The use of readily available silyl-substituted alkynes provides silyl aromatics readily functionalized further.

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Supporting Information Available: General experimental procedure, a mechanistic representation of the Pd-catalyzed annulation, spectroscopic characterization, and copies of ¹H and ¹³C NMR spectra (36 pages).

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