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THE PALLADIUM-CATALYZED REACTION OF ARYL IODIDES WITH MONO AND DISUBSTITUTED ACETYLENES: A NEW SYNTHESIS OF TRISUBSTITUTED ALKENES.

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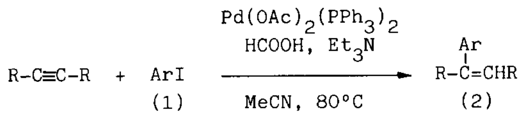
Summary: Mono and disubstituted acetylenes react with aryl iodides containing a variety of functional groups in the presence of palladium catalyst, formic acid and a tertiary amine to give trisubstituted alkenes.

We have recently reported that aryl iodides react with ∝,ß-enones and ∝,ß-enals in the presence of bis(triphenylphosphine) palladium diacetate or palladium on charcoal, formic acid and triethyl or tri-n-butylamine to give conjugate addition type products[1]. In our effort to investigate the peculiarity and the scope of this reaction, we have now discovered that in the presence of the same combination of reagents aryl iodides react with alkynes to give trisubstituted alkenes according to the following scheme:



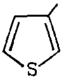
$$\text{R-C}\equiv\text{C-R} + \underset{(1)}{\text{ArI}} \xrightarrow[\text{MeCN, 80°C}]{\text{Pd(OAc)}_2(\text{PPh}_3)_2\ \ \text{HCOOH, Et}_3\text{N}} \underset{(2)}{\text{R-}\overset{\text{Ar}}{\text{C}}\text{=CHR}}$$

Scheme I

As it can be seen from the results obtained by reacting a variety of aryl iodides with diphenylacetylene (table 1), the present palladium-catalyzed reaction allows an easy and efficient synthesis of functionalyzed trisubstituted alkenes.

The following procedure, exemplified for the preparation of triphenylethene, was found satisfactory and optimization of reaction conditions was not attempted. Diphenylacetylene (2.81 mmol) was added to a mixture of phenyl iodide (6.74 mmol) and triethylamine (1.34 ml). Then, bis-(triphenylphosphine) palladium diacetate (0.014 mmol) and acetonitrile (1 ml) were added. The mixture was gently purged with argon, and formic acid (7.42 mmol) was added all at once. The mixture was stirred at 80°C under argon atmosphere for 6.5 h, diethyl ether and water were added, the organic layer was separated, washed with water, dried (magnesium sulfate), and concentrated under reduced pressure. The residue was purified through flash chromatography by eluting with n-hexane to give the addition product in 87% yield: mp 68-70° (lit[2] mp 72-73°); MS, m/e = 256 (M^+).

Table 1 - Palladium-Catalyzed Addition of Aryl Iodides to Diphenyl acetylene[a].

Aryl iodide (1) Ar	Reaction time (h)	Yield of (2) %[b,c]
Ph-	6.5	87
p-Me-C_6H_4-	6	93
p-HO-C_6H_4-	2	83
p-MeO-C_6H_4-	3	96
m-H_2N-C_6H_4-	8	85[d]
m-MeCONH-C_6H_4 -	7.5	50
p-MeCONH-C_6H_4-	3	60
p-HO-,m-EtOCO-C_6H_3-	6	71
m-OHCNHCH$_2$C$_6$H$_4$-	8	85[d]
	8	40

a) Unless otherwise noted, reactions were carried out according to the general procedure.

b) Yields are calculated on the starting diphenylacetylene and are given for pure, isolated products.

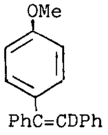
c) All of the reported compounds gave satisfactory microanalyses and 'H-NMR and MS spectra in agreement with the proposed structures.

d) The reaction was carried out by using 0.2 mol% of the palladium catalyst.

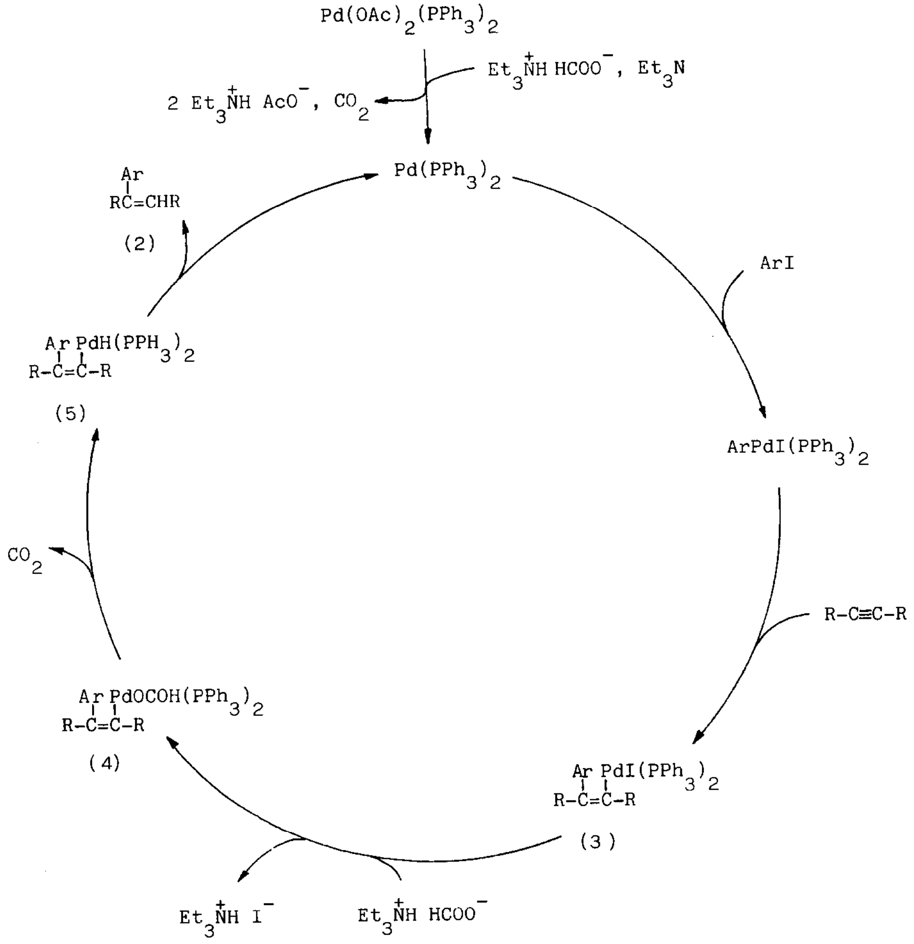
Products derived from palladium-catalyzed formation of arenes[3] and coupling of aromatic moieties[4] were also detected in variable amounts depending on the nature of the substituents in the aryl iodide together with traces of stylbene, derived from palladium-catalyzed reduction of diphenylacetylene[5] .

Although the reaction mechanism was not thoroughly studied, it seems likely that the trisubstituted alkene arises from the addition of the in situ formed arylpalladium intermediate to the alkyne, followed by the reaction with formate to give (4). Subsequent decarboxylation of (4) and reductive elimination of palladium from (5) gives raise to the olefinic derivative and regenerates the original bis(triphenylphosphine) palladium(O) catalyst (Scheme II).

The involvement of the intermediate (4) and of the decarboxylation and palladium deinsertion steps along the reaction pathway is supported by the isolation of the deutero-derivative (6) in 91% yield when 4-methoxyphenyl iodide was reacted with diphenylacetylene under our usual conditions in the presence of monodeutero formic acid (DCOOH). Furthermore, when the same reaction was carried out without formic acid (5h), no addition product was detected under usual GLC conditions.



(6)



Scheme II

Formation of the addition product through vinylic substitution on the alkene derived from palladium-catalyzed reduction of the corresponding alkyne was ruled out by the observation that, as expected, the reaction mixture was found to be free of triphenylethene when stylbene was reacted with phenyliodide in the presence of the palladium-triethylammonium formate reagent.

No attempts were made to determine the E-Z configuration of the addition products.

When the reaction was tested with asymmetrically disubstituted alkynes, a lack of regioselectivity was observed and mixtures of trisubstituted alkenes were obtained.

$$\underset{(7)}{PhC{\equiv}CAr} + PhI \longrightarrow \underset{(8)}{Ph_2C{=}CHAr} + \underset{(9)}{PhCH{=}PhAr}$$

Scheme III

A couple of representative results are reported in table 2.

An interesting feature of the described reaction is the possibility to carry out a one pot synthesis of trisubstituted alkenes from monosubstituted alkynes. The reaction was tested by reacting phenylacetylene (0.49 mmol) with phenyl iodide (3.5 mmol), triethylamine (4.9 mmol), bis(triphenylphosphine)palladium diacetate (0.049 mmol), and acetonitrile (1 ml). After 3.5 h at

Table 2 - Palladium-Catalyzed Reaction of Asimmetrically Disubstituted Alkynes with Phenyl Iodide[a,b].

Compound (7)[c] Ar	Reaction time (h)	Total yield (%) (8 + 9)[d]	Yield of (8) (%)	Yield of (9) (%)
p-MeO-C_6H_4-	8	91	42[e]	58[e]
p-MeCO-C_6H_4-	5.5	94	46[f]	35[f]

a) Reactions were carried out according to the general procedure.

b) n-Bu_3N was used instead of Et_3N.

c) Compounds (7) were prepared according to the procedure described by Sonogashira et al.[6].

d) Yields are calculated on the starting aryl,phenylacetylene (7) and are given for isolated products.

e) Relative percentages determined through GLC analysis.

f) Yields given on products isolated through preparative HPLC.

80°C the reaction was worked-up as described and triphenylethene was isolated in 96% yield.

$$PhC{\equiv}CH + PhI \longrightarrow Ph_2C{=}CHPh$$

Scheme IV

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