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An Efficient Palladium-Catalysed Reaction of Vinyl and Aryl Halides or Triflates with Terminal Alkynes

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Abstract: *In the presence of tetrakis(triphenylphosphine)palladium, vinyl and aryl halides or triflates react very rapidly in piperidine or pyrrolidine with terminal alkynes to give conjugated enynes and aryl acetylenes in high yields.*

The Stephens-Castro reaction[1] of copper acetylides with aryl and vinyl halides in boiling pyridine has been reported to be a useful route to aryl and vinyl acetylenes. Under palladium catalysis, the coupling of several metal acetylides[2-6] occurs at room temperature under mild conditions. The reaction of terminal acetylenes, in the presence of palladium complexes and copper salts, which involves the intermediate formation of a copper acetylide, is a chemoselective and efficient alternative.[7,8]. We now report that vinyl and aryl halides or triflates react very rapidly with terminal alkynes, without addition of a copper salt[9], and lead to high yields of enynes and aryl acetylenes by using Pd(PPh$_3$)$_4$ as catalyst in piperidine or pyrrolidine.

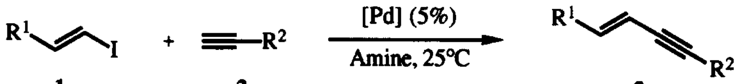
$$R^1X \quad + \quad \equiv\!\!-R^2 \quad \xrightarrow[\text{Amine}]{[Pd^0]} \quad R^1-\!\!\equiv\!\!-R^2$$

R^1 = vinyl, aryl
R^2 = n-C_5H_{11}, C_6H_5, CH_2OH, $(CH_2)_2OH$, $(CH_2)_2COOMe$
X = Br, I, OTf

The nature of the amine is critical for the success of the coupling (Table I). Thus, when (E)-1-iodo-1-heptene **1** (1 equiv.) was treated at room temperature with 3-butyn-1-ol **2** (2 equiv.) and Pd(PPh$_3$)$_4$ (5%) in Et$_3$N, *i*-Pr$_2$NH, Et$_2$NH or morpholine, low yields of cross coupling product were obtained (0-35%, entries 1, 2, 3 and 5). However by using Pd(PPh$_3$)$_4$ in pyrrolidine the enyne **3** was obtained in 93% isolated yield (entry 7); the reaction was complete within 15 min.

The coupling reaction can also be performed in piperidine in 76% yield within 1 h (entry 6). By using *n*-BuNH$_2$, an 85% yield was obtained in 23 h (entry 4).

The influence of the nature of the ligands in the palladium complex is noteworthy. Pd(PPh$_3$)$_4$, Pd(OAc)$_2$ + 2 PPh$_3$ or PdCl$_2$(PPh$_3$)$_2$ (entries 7, 8 and 9) are efficient catalysts for the coupling of vinyl iodides as opposed to vinyl chlorides which require low ligated palladium catalysts[10].



1 **2** **3**

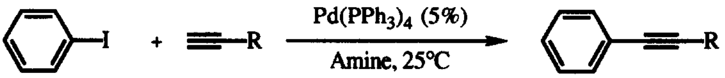
$R^1 = n\text{-}C_5H_{11}$

$R^2 = (CH_2)_2OH$

Table I

Entry	Amine	[Pd]	Time	Isolated yield (%)
1	Et_3N	$Pd(PPh_3)_4$	72 h	0
2	$i\text{-}Pr_2NH$	"	"	3
3	Et_2NH	"	26 h	33
4	$n\text{-}BuNH_2$	"	23 h	85
5	morpholine	"	8 h	35
6	piperidine	"	1 h	76
7	pyrrolidine	"	15 min	93
8	"	$Pd(OAc)_2 + 2PPh_3$	30 min	83
9	"	$PdCl_2(PPh_3)_2$	1 h	82
10	"	$PdCl_2(PhCN)_2$	22 h	57
11	"	$Pd(OAc)_2$	"	55

The influence of the nature of the amine was also observed in the reaction of iodobenzene with 1-alkynes (Table II). Thus in pyrrolidine, the coupling product **4** was obtained in 91% yield within 2.5 h at room temperature (entry 17). By using piperidine, instead of pyrrolidine, a 96% yield was obtained after 6 h (entry 16).



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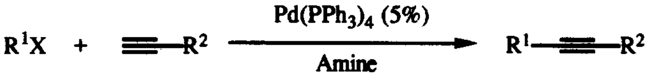
$R = (CH_2)_2OH$

Table II

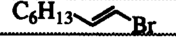
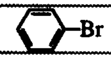
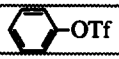
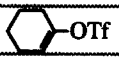
Entry	Amine	Time (h)	Isolated yield (%)
12	Et_3N	22	0
13	$i\text{-}Pr_2NH$	26	2
14	Et_2NH	24	0
15	$n\text{-}BuNH_2$	25	93
16	piperidine	6	96
17	pyrrolidine	2.5	91

The coupling of 1-alkynes with vinyl and aryl bromides or triflates[11] can also be performed in good yields in pyrrolidine or piperidine (Table III). Under these conditions, vinyl triflates react very rapidly within 5 min at room temperature (entries 27 and 28).



$R^2 = (CH_2)_2OH$
$X = Br, OSO_2CF_3$

Table III

Entry	R^1X	Amine	Time	Temperature	Isolated yield (%)
18		n-$BuNH_2$	24 h	45°C	43
19	"	piperidine	3 h	"	70
20	"	pyrrolidine	2.5 h	"	81
21		n-$BuNH_2$	3 h	80°C	92
22	"	piperidine	2 h	"	91
23	"	pyrrolidine	2 h	"	96
24		piperidine	1 h	"	96
25	"	pyrrolidine	30 min	"	93
26		Et_3N	24 h	25°C	71
27	"	piperidine	5 min	"	90
28	"	pyrrolidine	"	"	87

The reaction is chemoselective and various functional alkynes can be used (Table IV).

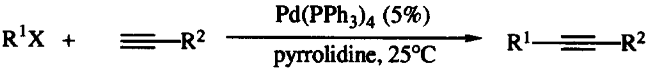
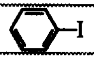


Table IV

Entry	R^1X	R^2	Isolated yield (%)
29		n-C_5H_{11}	88
30	"	CH_2OH	87
31	"	C_6H_5	95
32	"	$(CH_2)_2CO_2Me$	74
33		CH_2OH	81[a]
34		CH_2OH	93
35	"	n-C_5H_{11}	91
36		CH_2OH	88[b]
37	"	n-C_5H_{11}	96[b]

a/ Reaction was carried out at 45°C. b/ Reaction was carried out at 80°C

The influence of the nature of the amine is also noteworthy when the reaction was performed in the presence of copper iodide as a cocatalyst; very short reaction times were observed (5 to 10 minutes) by using pyrrolidine, piperidine or diisopropylamine (Table V).

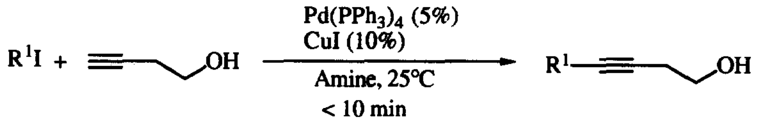
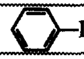
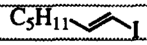


Table V

Entry	R^{1}I	Amine	Time (min)	Isolated yield (%)
38		Et$_2$NH	120	92
39	"	*i*-Pr$_2$NH	30	94
40	"	piperidine	10	95
41	"	pyrrolidine	"	93
42		Et$_2$NH	45	89
43	"	*i*-Pr$_2$NH	10	81
44	"	piperidine	"	90
45	"	pyrrolidine	"	90

In conclusion, these results show the critical importance of the nature of the amine in the palladium-catalysed reaction of vinyl and aryl halides or triflates with 1-alkynes. Further studies are in progress.

Typical procedure for the preparation of (E)-5-undecen-3-yn-1-ol (3):

To a stirred solution of (E)-1-iodo-1-heptene (224 mg, 1 mmol) and tetrakis(triphenylphosphine)-palladium (58 mg, 0.05 mmol) in pyrrolidine (1.5 ml), under an argon atmosphere, was added a solution of 3-butyn-1-ol (140 mg, 2 mmol) in pyrrolidine (1.5 ml). After stirring at room temperature for 15 min, the mixture was hydrolysed with a saturated aqueous solution of ammonium chloride and extracted with diethyl ether. The organic extract was dried over MgSO$_4$ and the solvent was removed *in vacuo*. Filtration through silica gel (elution petroleum ether : ethyl acetate, 6:4) gave 155 mg (93%) of pure alcohol **3**.[12]

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