Palladium-catalysed cross-coupling reactions of aryl-, alkenyl- and alkynyl-iodonium salts and iodanes with terminal alkynes in aqueous medium

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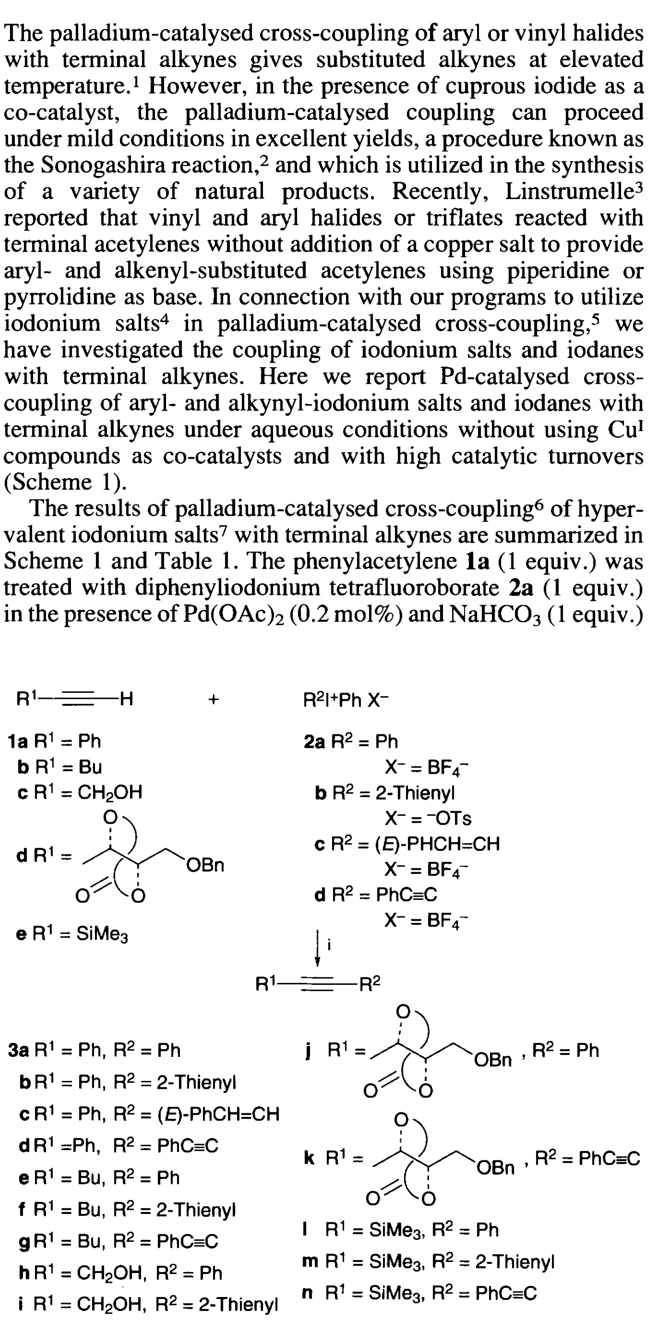
The ligand-free $Pd(OAc)_2$-catalysed coupling reaction of aryl-, alkenyl- and alkynyl-iodonium tetrafluoroborate and iodanes with terminal alkynes proceeds readily in the presence of $NaHCO_3$ in aqueous medium to afford the substituted alkynes in high yields under mild conditions.

The palladium-catalysed cross-coupling of aryl or vinyl halides with terminal alkynes gives substituted alkynes at elevated temperature.[1] However, in the presence of cuprous iodide as a co-catalyst, the palladium-catalysed coupling can proceed under mild conditions in excellent yields, a procedure known as the Sonogashira reaction,[2] and which is utilized in the synthesis of a variety of natural products. Recently, Linstrumelle[3] reported that vinyl and aryl halides or triflates reacted with terminal acetylenes without addition of a copper salt to provide aryl- and alkenyl-substituted acetylenes using piperidine or pyrrolidine as base. In connection with our programs to utilize iodonium salts[4] in palladium-catalysed cross-coupling,[5] we have investigated the coupling of iodonium salts and iodanes with terminal alkynes. Here we report Pd-catalysed cross-coupling of aryl- and alkynyl-iodonium salts and iodanes with terminal alkynes under aqueous conditions without using Cu^I compounds as co-catalysts and with high catalytic turnovers (Scheme 1).

The results of palladium-catalysed cross-coupling[6] of hypervalent iodonium salts[7] with terminal alkynes are summarized in Scheme 1 and Table 1. The phenylacetylene **1a** (1 equiv.) was treated with diphenyliodonium tetrafluoroborate **2a** (1 equiv.) in the presence of $Pd(OAc)_2$ (0.2 mol%) and $NaHCO_3$ (1 equiv.) in MeCN–H_2O (4 : 1) at room temperature for 10 minutes to afford diphenylacetylene **3a** in 96% yield. Of the four bases ($NaHCO_3$, triethylamine, Pr^i_2NEt, and pyrrolidine) tested, $NaHCO_3$ proved most effective. It is notable that even in the absence of base, comparable yields were afforded (entry 1 in Table 1). As solvent system, MeCN–H_2O (4 : 1) was better than DMF in terms of yield and reactivity. Under the same conditions, when 2-thienyl(phenyl)iodonium tosylate **2b**[8] was employed as iodonium salt, 2-thienyl-substituted acetylene **3b** was obtained as the sole product in 89% yield (entry 2). Alkenyl(phenyl)iodonium salt **2c**[7] was also coupled with the terminal alkyne **1a** to affored alkenyl-substituted alkyne **3c** in 83% yield (entry 3). This cross-coupling was applied to alkynyl(phenyl)iodonium salt **2d**[7] to provide the alkynyl-substituted acetylene **3d** in 93% yield (entry 4).[9] Treatment of hex-1-yne **1b** with diphenyliodonium salt **2a**, 2-thienyl-(phenyl)iodonium salt **2b** and alkynyliodonium salt **2d** provided the coupled products **3e–g**, respectively (entries 5–7). It is noteworthy that the coupling of prop-2-yn-1-ol **1c** with iodonium salts **2a** and **2b** afforded the substituted prop-2-yn-1-ols **3h** and **3i** without the formation of unsaturated aldehyde resulting from base-catalysed iosmerization[10] (entries 8 and 9). For the prop-2-ynylic cyclic carbonates **1d**, diphenyliodonium and alkynyliodonium tetrafluoroborates **2a** and **2d** were smoothly coupled to afford the substituted prop-2-ynylic carbonates **3j** and **3k** without any deprotection (entries 10 and 11). Finally, treatment of trimethylsilylacetylene **1e** with iodonium salts **2a–b** and **2d** afforded the substituted acetylenes **3l–n** (entries 12–14).



Scheme 1 *Reagents and conditions*: i, $Pd(OAc)_2$ (0.2 mol%), $NaHCO_3$ (1 equiv.), MeCN–H_2O (4 : 1), room temp.

In considering a plausible mechanism for the formation of the diyne **3d**, it is presumed that facile oxidative addition of the highly electrophilic alkynyliodonium salt **2d** with Pd^0 gives polar and reactive organopalladium tetrafluoroborate

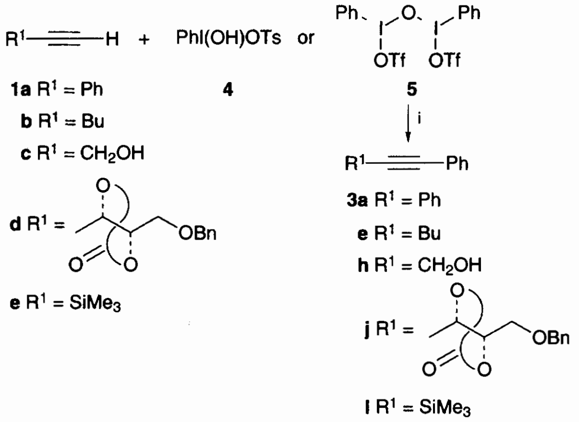
Table 1 Palladium-catalysed cross-coupling of iodonium salts with terminal alkynes[a]

Entry	Substrate	Iodonium salt	t/min	Product	Yield(%)[b]
1	**1a**	**2a**	10	**3a**	96(93)
2	**1a**	**2b**	20	**3b**	87(88)
3	**1a**	**2c**	15	**3c**	83(81)
4	**1a**	**2d**	10	**3d**	93(92)
5	**1b**	**2a**	20	**3e**	92(91)
6	**1b**	**2b**	25	**3f**	56(40)
7	**1b**	**2d**	20	**3g**	90(88)
8	**1c**	**2a**	5	**3h**	98(95)
9	**1c**	**2b**	10	**3i**	93(91)
10	**1d**	**2a**	5	**3j**	97(92)
11	**1d**	**2d**	5	**3k**	93(91)
12	**1e**	**2a**	10	**3l**	95(93)
13	**1e**	**2b**	10	**3m**	93(90)
14	**1e**	**2d**	10	**3n**	92(90)

[a] All the reactions were run with terminal alkynes (1 equiv.) and iodonium salt (1 equiv.) in the presence of $Pd(OAc)_2$ (0.2 mol%) and $NaHCO_3$ (1 equiv.) in MeCN–H_2O (4 : 1) at room temperature. [b] The yields are isolated yields. The yields in parentheses are for reactions carried out in the absence of base.

($PhC{\equiv}CPd^+ BF_4^-$). This intermediate is subjected to alkynylation with phenylacetylene **1a** to form dialkynylpalladium(II) [$(PhC{\equiv}C)_2Pd$] followed by reductive elimination to afford the coupled diyne **3d**. Alternatively, we have investigated palladium-catalysed cross-coupling of terminal alkynes with iodanes. The results are summarized in Scheme 2 and Table 2.

We coupled the terminal alkyne **1a** with readily available [hydroxy(tosyloxy)iodo]benzene (HTIB), PhI(OH)OTs **4**[11] (also known as Koser's reagent), to afford the phenyl-substituted alkyne **3a** in 78% yield (entry 1). The reaction can also be carried out in the absence of base (entry 1 in Table 2).



Scheme 2 *Reagents and conditions*: i, $Pd(OAc)_2$ (0.2 mol%), $NaHCO_3$ (1 equiv.), $MeCN-H_2O$ (4 : 1), room temp., 5 or 10 min

Table 2 Palladium-catalysed cross-coupling of iodanes with terminal alkynes[a]

Entry	Substrate	Iodonium salt	*t*/min	Product	Yield(%)[b]
1	**1a**	**4**	25	**3a**	78(75)[c]
2	**1a**	**5**	20	**3a**	80(76)
3	**1b**	**4**	30	**3e**	76(70)
4	**1b**	**5**	20	**3e**	80(74)
5	**1c**	**4**	20	**3h**	91(89)
6	**1c**	**5**	20	**3h**	95(91)
7	**1d**	**4**	30	**3j**	91(86)
8	**1d**	**5**	20	**3j**	90(88)
9	**1e**	**4**	5	**3l**	92(90)
10	**1e**	**5**	5	**3l**	96(93)

[a] All the reactions were run with terminal alkynes (1 equiv.) and iodanes (1 equiv.) in the presence of $Pd(OAc)_2$ (0.2 mol%) and $NaHCO_3$ (1 equiv.) in $MeCN-H_2O$ (4 : 1) at room temperature. [b] The yields are isolated yields. The yields in parentheses are for reactions carried out in the absence of base. [c] The yield can be improved to 93% by addition of CuI.

When the terminal alkyne **1a** was subjected to react with μ-oxobis[(trifluoromethanesulfonato)(phenyl)iodine] **5** (also known as Zefirov's reagent[12]) under the same conditions, phenyl-substituted acetylene **3a** was afforded in 80% yield (entry 2). Even without using base, a comparable yield was obtained. Treatment of hex-1-yne **1b** with **4** or **5** furnished **3e**, respectively (entries 4 and 5). It is notable that the coupling of prop-2-yn-1-ol **1c** with Koser's or Zefirov's reagent afforded **3h** without formation of any aldehyde (entries 6 and 7). For the prop-2-ynylic cyclic carbonate **1d**, coupling with **4** or **5** afforded **3j** without any deprotection (entries 8 and 9). Finally, reaction of trimethylsilylacetylene **1e** with **4** or **5** afforded the substituted alkyne **3l** (entries 10 and 11).

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