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 NaHCO₃ 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, Linstrumelle³ 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 salts⁴ in palladium-catalysed cross-coupling,⁵ we have investigated the coupling of iodonium salts and iodanes with terminal alkynes. Here we report Pd-catalysed crosscoupling 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-coupling⁶ of hypervalent iodonium salts⁷ 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 NaHCO₃ (1 equiv.)

| R ¹ | R²l+Ph X⁻ |
|--|--|
| 1a $R^1 = Ph$ b $R^1 = Bu$ c $R^1 = CH_2OH$ d $R^1 = \bigcirc $ | 2a $R^2 = Ph$ $X^- = BF_4^-$ b $R^2 = 2$ -Thienyl $X^- = -OTs$ c $R^2 = (E)$ -PHCH=CH $X^- = BF_4^-$ d $R^2 = PhC=C$ $X^- = BF_4^-$ |
| e R' = SIMe ₃ R ¹ | ↓i ===R² ♀_∖ |
| 3a $R^1 = Ph$, $R^2 = Ph$ b $R^1 = Ph$, $R^2 = 2$ -Thienyl c $R^1 = Ph$, $R^2 = (F)$ -PhCH=CH | $j R^1 = \underbrace{OBn}_{OBn}, R^2 = Ph$ |
| $dR^{1} = Ph, R^{2} = PhC \equiv C$ $eR^{1} = Bu, R^{2} = Ph$ $fR^{1} = Bu, R^{2} = 2$ Thioput | k R ¹ =OBn , R ² = PhC≡C |
| $\mathbf{g}\mathbf{R}^{1} = \mathbf{B}\mathbf{u}, \mathbf{R}^{2} = 2\text{Intertyl}$ $\mathbf{g}\mathbf{R}^{1} = \mathbf{B}\mathbf{u}, \mathbf{R}^{2} = \mathbf{P}\mathbf{h}\mathbb{C}\equiv\mathbf{C}$ $\mathbf{h}\mathbf{R}^{1} = \mathbf{C}\mathbf{H}_{2}\mathbf{O}\mathbf{H}, \mathbf{R}^{2} = \mathbf{P}\mathbf{h}$ $\mathbf{h}\mathbf{R}^{1} = \mathbf{C}\mathbf{H}_{2}\mathbf{O}\mathbf{H}, \mathbf{R}^{2} = \mathbf{R}$ | I $R^1 = SiMe_3, R^2 = Ph$ m $R^1 = SiMe_3, R^2 = 2$ -Thienyl n $R^1 = SiMe_3, R^2 = PhC \equiv C$ |
| $I \Pi = U \Pi_2 U \Pi$, $\Pi^2 = 2 I \Pi \theta V $ | |

Scheme 1 Reagents and conditions: i, $Pd(OAc)_2$ (0.2 mol%), NaHCO₃ (1 equiv.), MeCN-H₂O (4:1), room temp.

in MeCN-H₂O (4:1) at room temperature for 10 minutes to afford diphenylacetylene 3a in 96% yield. Of the four bases (NaHCO₃, triethylamine, Pri₂NEt, and pyrrolidine) tested, NaHCO₃ 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 2b8 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 2d7 to provide the alkynylsubstituted 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 iosmerization¹⁰ (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 **31–n** (entries 12–14)

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 Pd⁰ 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 | 31 | 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 NaHCO₃ (1 equiv.) in MeCN-H₂O (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.

Chem. Commun., 1996 835

(PhC=CPd+ BF₄-). This intermediate is subjected to alkynylation with phenylacetylene **1a** to form dialkynylpalladium(II) [(PhC=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%), NaHCO₃ (1 equiv.), MeCN-H₂O (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 | 31 | 92(90) | |
| 10 | 1e | 5 | 5 | 31 | 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-H₂O (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 reagent¹²) 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).

We thank generous financial support by KOSEF-OCRC and Ministry of Education (BSRI-95-3420).

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Received, 22nd November 1995; Com. 5/07639K