Copper-Catalyzed Cross-Coupling of 1-Iodoalkynes with Organostannanes

Suk-Ku Kang,* Won-Yeob Kim, Xianghua Jiao

Department of Chemistry, Sung Kyun Kwan University, Natural Science Campus, Suwon 440-746, Korea
Fax +82(331)290-7079; E-mail: skkang@chem.skku.ac.kr

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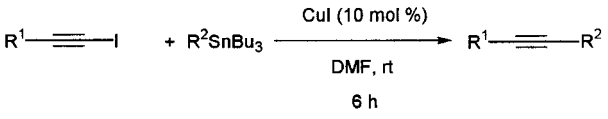
Abstract: Copper-catalyzed cross-coupling of 1-iodoalkynes with organostannanes was readily achieved in the presence of CuI (10 mol%) in DMF at room temperature for 6 hours by adding 1-iodoalkynes slowly to organostannanes.

Key words: copper-catalyzed cross-coupling, 1-iodoalkynes, organostannanes, 1-substituted acetylenes

The conjugated enyne moiety is an important structural unit in a number of natural products. The enynes have been generally prepared by the coupling reactions of terminal alkynes with aryl or vinyl halides, which is known as the Sonogashira reaction.[1] The synthesis of enynes can be also accomplished using haloalkynes with aryl and alkenyl copper compounds.[2]

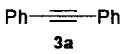
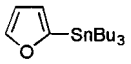
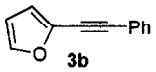
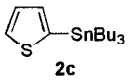
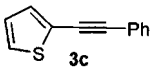
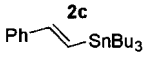
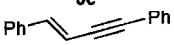
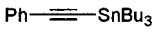
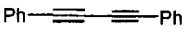
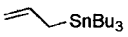
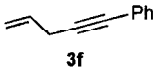
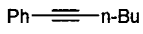
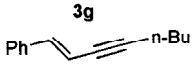
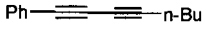
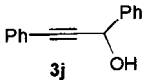
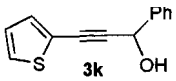
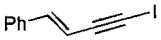
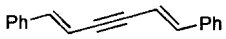
The palladium-catalyzed cross-coupling (Stille reaction)[3] of organic electrophiles such as vinyl halides or triflates with organostannanes has become an extremely powerful tool in organic synthesis. The cross-coupling of vinyl iodides or vinyl triflates with alkynylstannanes to obtain enynes in the presence of palladium catalyst has been reported.[4] However, the cross-coupling of haloalkynes with organostannanes to synthesize enynes has rarely been reported.[5] In 1990, Liebeskind et al.[6] reported the first example of the palladium-catalyzed cross-coupling of 1-iodohexyne with cyclobutenylorganostannane. Recently, palladium-catalyzed cross-coupling of 1-iodoalkynes with (*E*)-α-selanylvinylstannanes was reported by Huang et al.[7] In connection with our programs to utilize copper as a catalyst for cross-coupling,[8] we have investigated the copper iodide catalyzed cross-coupling of 1-iodoalkynes with organostannanes. Here we report copper(I) iodide catalyzed cross-coupling of 1-iodoalkynes with aryl-, alkenyl-, alkynyl-, and allylstannanes.



Initially, we examined the copper-catalyzed cross-coupling of 1-iodo-2-phenylacetylene **(1a)** and 2-furylstannane **2b** to determine the optimum reaction conditions. A series of experiments were performed. Of the catalysts tested CuI (10 mol%) was the most suitable and better than $PdCl_2$ in NMP at room temperature. As solvents among NMP, DMF, THF, THF/NMP (1: 1), and 1,4-dioxane, NMP and DMF were preferable. The addition of additives to reduce homocoupling, such as LiCl and NaCl, did not improve the yields of the cross-coupled products, even if the addition of KCl and CsCl increased the yields of the cross-coupled products with limited success. Without additives when the above reaction was conducted in the presence of CuI (10 mol%) in DMF at room temperature, the homocoupled products of bisphenylacetylene, bisfuran, and the cross-coupled product **3b** were formed in the ratio of 2:1:1. We assumed that 1-iodo-2-phenylacetylene **(1a)** is the reactive species which undergoes homocoupling. Finally, by adding **1a** slowly to organostannanes **2b** via syringe pump we could get the cross-coupled product **3b** as the major product. Thus, it is crucial to add 1-iodoalkynes slowly via a syringe pump to reduce homocoupling. The results of copper-catalyzed cross-coupling of 1-iodoalkynes with organostannanes are summarized in the Table. 1-Iodo-2-phenylacetylene **(1a)** was slowly added via a syringe pump to organostannane **2a** in DMF at room temperature for 6 hours to afford the cross-coupled product **3a**[9] in 71% yield (entry 1, Table). The reaction of **1a** with 2-furylstannane **2b** proceeded smoothly to give 2-furyl-substituted alkyne **3b** in 75% yield by adding **1a** slowly (entry 2). In considering the mechanistic explanation, it is presumed that the slow addition of 1-iodoalkynes prevents the homocoupling of 1-iodoalkynes. As indirect evidence when the same reaction was conducted by the slow addition of organostannane **2b** to **1a,** the homocoupled product of **1a** was produced in ~25% yield along with 50% yield of the cross-coupled product **3b** and bisfuran (~25%). Accordingly, the iodoalkyne **1a** was subjected to coupling with 2-thienylstannane **2c** to give the product **3c**[10] in 77% yield (entry 3). This coupling method was applied to alkenyl-, alkynyl-, and allylstannanes (entries 4–6). Thus, the iodoalkyne **1a** underwent facile cross coupling in the presence of CuI (10 mol%) with (*E*)-β-styrylstannane **2d**, 1-phenylethynylstannane **2e**, and allylstannane **2f** to afford the coupled products **3d**,[11] **3e**, and **3f** in 76, 80, and 90% yields, respectively (entries 4–6). For the alkyl-substituted 1-iodoalkyne **1b**, the reaction under the typical conditions with **2a** gave the phenyl-substituted alkyne **3g** in 88% yield (entry 7). Treatment of **1b** with alkenylstannane **2d** and alkynylstannane **2e** under the same conditions provided the coupled product **3h** and **3i** in 71 and 76% yields, respectively (entries 8 and 9). When 1-iodoalkyn-3-ol **1c** was reacted with **2a** and **2b**, the coupled products **3j** and **3k** were readily obtained (entries 10 and 11). Finally, 1-iodoalkyn-3-ene **1d** was smoothly coupled with the alkenylstannane **2d** to afford the yndiene compound **3l** in 82% yield (entry 12).

Reagent grade commercially available reagents and solvents were used. DMF was freshly distilled from CaH_2 prior to use. 1-Iodoalkynes **2a**, **2b**, and **2c** were prepared[12] from the corresponding 1-alkynes and BuLi followed by iodination with molecular iodine. The 1-iodoalkyne **2b** was prepared[13] from the corresponding 1-alkyne by treatment with NIS and $AgNO_3$.

Table 1. Copper-Catalyzed Cross-Coupling of 1-Iodoalkynes with Orgnaostannanes[a]

Entry	1-Iodoalkynes	Organostannanes	Products	Yield (%)[b]
1	PhC≡CI **1a**	$PhSnBu_3$ **2a**	 **3a**	71
2	**1a**	 **2b**	 **3b**	75
3	**1a**	 **2c**	 **3c**	77
4	**1a**	 **2d**	 **3d**	76
5	**1a**	 **2e**	 **3e**	80
6	**1a**	 **2f**	 **3f**	90
7	n-BuC≡CI **1b**	**2a**	 **3g**	88
8	**1b**	**2d**	 **3h**	71
9	**1b**	**2e**	 **3i**	76
10	Ph(HCOH)C≡CI **1c**	**2a**	 **3j**	72
11	**1c**	**2b**	 **3k**	76
12	 **1d**	**2d**	 **3l**	82

[a] Reaction conditions: 1-iodoalkynes (1 equiv), organostannanes (1 equiv), CuI (10 mol %), DMF, r.t., 6 h.
[b] The isolated yields.

Copper-Catalyzed Cross-Coupling of Organostannanes with 1-Iodoalkynes; 2-(2-Phenylethynyl)furan (3b);Typical Procedure:
To a stirred solution of 2-(tributylstannyl)furan (100 mg, 0.280 mmol), CuI (5.3 mg, 0.028 mmol) in DMF (3 mL) at r.t. was slowly added the 1-iodo-2-phenylacetylene (63.9 mg, 0.280 mmol) in DMF (3 mL) via syringe pump over 1.5 h. The mixture was stirred at r.t. for 6 h and extracted with Et_2O and washed with sat. KF (10 mL) and then brine (10 mL). The organic layer was dried (anhyd $MgSO_4$) and evaporated in vacuo. The crude product was separated by column chromatography (silica gel, hexanes, R_f 0.43) to afford **3b**; yield: 35.3 mg (75%).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44 (d, 1H), 6.67 (dd, 1H), 7.37 (m, 4H), 7.54 (m, 2H).
IR (neat): ν = 3105, 3056, 2953, 1500, 1415, 1070, 918, 690, 536 cm^{-1}.
MS (EI): *m/z* (%) = 169 (14), 168 (100), 140 (17), 139 (89), 114 (11), 70 (9), 63 (9).

Diphenylacetylene **(3a)**:[9]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (m, 6H), 7.54 (m, 4H).
IR (KBr): ν = 3036, 1560, 1500, 1070, 918, 690, 536 cm^{-1}.
MS (EI): *m/z* (%) = 178 (100), 176 (20), 152 (9), 89 (13), 76 (12).

1-Phenyl-2-(2-thienyl)acetylene **(3c)**:[10]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (m, 1H), 7.29 (m, 2H), 7.35 (m, 3H), 7.53 (m, 2H).
IR (neat): ν = 3058, 3022, 2954, 1600, 1381, 1215, 909, 735 cm^{-1}.
MS (EI): *m/z* (%) = 185 (11), 184 (100), 152 (13), 139 (30), 126 (9), 74 (11), 63 (11).

(E)-1,4-Diphenylbut-1-en-3-yne **(3d)**:[11]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.40 (d, 1H, *J* = 16 Hz), 7.06 (d, 1H, *J* = 16 Hz), 7.33 (m, 6H), 7.38 (m, 2H), 7.62 (m, 2H).
IR (KBr): ν = 3041, 3010, 1605, 1471, 843 cm^{-1}.
MS (EI): *m/z* (%) = 205 (78), 203 (100), 102 (28).

1,4-Diphenylbuta-1,3-diyne **(3e)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (m, 6H), 7.54 (m, 4H).
IR (KBr): ν = 3104, 2158, 1594, 1477, 920 cm^{-1}.
MS (EI): *m/z* (%) = 203 (16), 202 (100), 200 (23), 174 (3), 102 (22), 88 (13), 75 (6).

5-Phenylpent-1-en-4-yne **(3f)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22 (m, 2H). 5.19 (dt, 1H), 5.43 (dd, 1H), 5.92 (m, 1H), 7.31 (m, 3H), 7.45 (m, 2H).
IR (neat): ν = 3082, 3059, 3018, 2982, 2921, 2886, 1641, 1598, 1489, 916 cm^{-1}.
MS (EI): *m/z* (%) = 143 (10), 142 (90), 141 (100), 115 (55), 89 (7), 63 (8).

1-Phenylhex-1-yne **(3g)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, 3H, *J* = 7.3 Hz), 1.55 (m, 4H), 2.42 (t, 2H, *J* = 7.0 Hz), 7.34 (m, 5H).

IR (neat): ν = 3057, 1599, 1491, 1064, 909 cm^{-1}.
MS (EI): *m/z* (%) = 159 (20), 158 (30), 143 (52), 129 (30), 116 (22), 115 (100), 113 (11), 102 (9).

(E)-1-Phenyloct-1-en-3-yne **(3h)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, 3H, *J* = 7.3 Hz), 1.55 (m, 4H), 2.42 (t, 2H, *J* = 7.0 Hz), 6.17 (dt, 1H, *J* = 16 Hz), 6.88 (d, 1H, *J* = 16 Hz) 7.33 (m, 5H).
IR (neat): ν = 3062, 3010, 2932, 2872, 1486, 1463, 1404, 1104, 755, 689 cm^{-1}.
MS (EI): *m/z* (%) = 184 (34), 169 (9), 155 (20), 141 (100), 115 (59), 91 (20), 77 (10), 63 (10), 51 (7).

1-Phenylocta-1,3-diyne **(3i)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, 3H), 1.55 (m, 4H), 2.42 (t, 2H), 7.34 (m, 5H).
IR (neat): ν = 3054, 2986, 2931, 1487, 1441, 1265, 738 cm^{-1}.
MS (EI): *m/z* (%) = 182 (26), 165 (76), 152 (53), 139 (100), 126 (40), 115 (36), 91 (21), 63 (10).

1,3-Diphenylprop-2-yn-1-ol **(3j)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 1H), 5.70 (s, 1H), 7.33 (m, 4H), 7.42 (m, 2H), 7.49 (m, 2H), 7.63 (m, 2H).
IR (neat): ν = 3377, 3118, 3063, 2199, 1707, 1490, 1286, 1032, 758, 694 cm^{-1}.
MS (EI): *m/z* (%) = 209 (11), 208 (74), 207 (100), 191 (21), 179 (67), 178 (64), 165 (29), 131 (24), 130 (39), 129 (43), 102 (41), 77 (46), 51 (15).

1-Phenyl-3-(2-thienyl)prop-2-yn-1-ol **(3k)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (s, 1H), 5.71 (s, 1H), 6.99 (dd, 1H), 7.27 (m, 2H), 7.42 (m, 3H), 7.60 (m, 2H).
IR (neat): ν = 3300, 3055, 2986, 2189, 1637, 1450, 1266, 1030, 990, 737 cm^{-1}.
MS (EI): *m/z* (%) = 213 (11), 212 (82), 183 (77), 152 (14), 139 (21), 135 (100), 107 (16), 92 (19), 77 (67), 63 (37).

(E,E)-1,6-Diphenylhexa-1,5-dien-3-yne **(3l)**:
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.30 (d, 2H, *J* = 16 Hz), 7.00 (d, 2H, *J* = 16 Hz), 7.37 (m, 10H).
IR (KBr): = 3063, 1807, 1550, 1500, 1069, 915, 705, 687, 524 cm^{-1}.
MS (EI): *m/z* (%) = 230 (42), 229 (39), 228 (34), 215 (16), 115 (100), 101 (11).

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