

Cross-Coupling of Organostannanes with Organic Iodides Catalyzed by Silica-Supported Poly[3-(2-cyanoethylsulfanyl)propylsiloxane palladium] Complex Under Aqueous Medium

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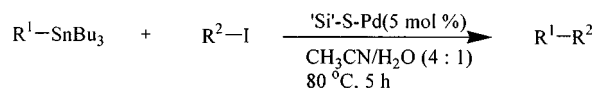
Abstract: The cross-coupling of organostannanes with organic iodides was achieved in the presence of a catalytic amount of a silica-supported sulfur palladium complex (5 mol %) in CH₃CN/H₂O (4 : 1) at 80 °C for 5 h in 71–89% yields.

Key words: silica-supported palladium, cross-coupling, organostannanes, Stille coupling, aqueous medium

The palladium-catalyzed cross-coupling of organostannanes with organic halides and triflates is known as the Stille reaction¹ and has become an extremely powerful tool for the formation of carbon-carbon bonds. This coupling reaction has been widely applied in organic synthesis due to the stability of organostannanes and its tolerance of many functional groups. However, the limitation of the Stille reaction is the forcing conditions typically at reflux in THF or dioxane and the requirement for dry environments.

In palladium-catalyzed processes, palladium catalysts are recovered by several methods including precipitation and water-soluble phosphine ligands.² As an alternative, polymer-supported palladium complexes having high activity and selectivity received much attention because they can be easily separated, recovered, and are reusable.³ Polymer-supported palladium catalysts have been used for allylic substitution,⁴ the Heck reaction,⁵ the Suzuki reaction,⁶ and telomerizations,⁷ etc. Alternatively, Jiang *et al.*,⁸ introduced the silica-supported sulfur or cyano-containing polymeric complexes in the Heck reaction. Recently, Huang *et al.*⁹ prepared some silica-supported sulfur and cyano-containing palladium complexes and utilized alkoxy-carboxylation^{9a} and amination of aryl halide,^{9b} Suzuki-type reaction,^{9c} carbonyl allylation,^{9d} Sonogashira reaction,^{9e} and the Heck reaction.^{9f} However, to the best of our knowledge no report for the Stille reaction has been known using polymer-supported or silica-supported palladium complexes. In connection with our programs to carry out the cross-coupling under aqueous conditions,¹⁰ we have investigated the silica-supported palladium complex catalyzed cross-coupling of organostannanes with organic iodides, the results are summarized in the Scheme.

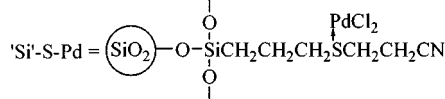
As a suitable catalyst for the Stille coupling reaction, silica-supported poly[3-(2-cyanoethylsulfanyl)propylsiloxane palladium] complex^{9a} was chosen.¹¹ Initially, to



R¹ = 4-methoxyphenyl, 2-furyl, 2-thienyl

(*E*)-PhCH=CH, PhC≡C

R² = Ph, *p*-CH₃OC₆H₄, *p*-I-C₆H₄






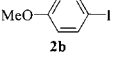
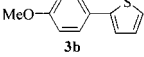

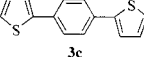


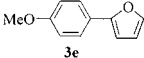
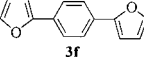
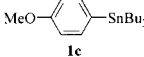
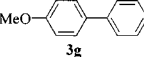
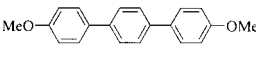
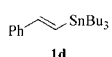

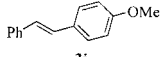
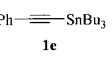

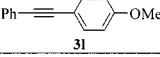
Scheme

determine the optimum conditions, the coupling of 2-thienylstannane (**1a**) with *p*-methoxyphenyl iodide (**2b**) was examined and found that CH₃CN/H₂O (4 : 1) was the best choice as solvent. The use of THF, DMF, and NMP gave lower yields (20–40%). Running the reaction in CH₃CN/H₂O (4 : 1) at 80 °C for 5 h gave the coupled product **3b** in 89% yield. For the same reaction at room temperature for 5 h gave the coupled product **3b** in 35% yield.

The results of the silica-supported palladium-catalyzed cross-coupling of organostannanes with organic iodides are summarized in Table 1.¹² The poly[3-(2-cyanoethylsulfanyl)propylsiloxane palladium] complex (Si'-S-Pd) was prepared by the procedure of Huang.^{9a} The sulfur and palladium content were 3.72 wt% and 4.63 wt%, respectively. The 2-thienylstannane **1a** was slowly added over 1 h to a solution of iodobenzene (**2a**) in the presence of Si'-S-Pd catalyst (5 mol %) in CH₃CN/H₂O (4 : 1) and stirred at 80 °C for 5 h to afford the coupled product **3a** in 80% yield (entry 1 in Table 1).¹³ Filtration and reuse of the catalyst gave the product **3a** in 72% yield. The second reuse of the catalyst gave **3a** in 67% yield with 5% decrease in yield. Under the same conditions the reaction of *p*-methoxyphenyl iodide (**2b**) with **1a** provided the coupled product **3b**¹⁴ in 89% yield (entry 2). For the 1,4-diiodobenzene **2c** with **1a**, bis-2-thienyl-substituted benzene **3c**¹⁵ was readily obtained in 78% yield (entry 3). Treatment of 2-furylstannane **1b** with iodobenzene (**2a**) gave the coupled product **3d** in 83% yield (entry 4). Coupling of **1b** with **2b** and **2c** furnished the compounds **3e**¹⁶ and **3f**¹⁷ in 83 and 83% yields, respectively (entries 5 and 6). For the *p*-methoxyphenylstannane **1c**, iodobenzene (**2a**) and 1,4-diiodo-

benzene (**2c**) was successfully coupled to give **3g** and **3h**¹⁸ in 78 and 71% yields, respectively (entries 7 and 8). This coupling was also applied to alkenyl- and alkynyl-substituted stannanes **1d** and **1e**. The alkenylstannane **1d** was reacted with iodobenzene (**2a**) and *p*-methoxyiodobenzene (**2b**) to give the substituted alkenes **3i** and **3j**¹⁹ in 73 and 75% yields (entries 9 and 10). Finally the alkynylstannane **1e** was smoothly coupled with **2a** and **2b** to afford the coupled alkynes **3k** and **3l** (entries 11 and 12).

Table 1. Silica-Supported Palladium Catalyzed Cross-Coupling of Organostannanes with Organic Iodides^a

Entry	Organo stannanes	Iodides	Time(h)	Product	Yield(%) ^b
1			6		80
2	1a		5		89
3	1a		5		78
4		2a	6		83
5	1b	2b	5		83
6	1b	2c	6		83
7		2a	5		78
8	1c	2c	5		71
9		2a	6		73
10	1d	2b	6		75
11		2a	6		77
12	1e	2b	6		79

^a The reactions were run with organostannane (1.1 equiv) and organic iodide (1 equiv) in the presence of silica-supported Pd (5 mol %) in CH₃CN/H₂O (4 : 1) at 80 °C. ^b The yields are isolated yields.

In summary, the cross-coupling of organostannanes with organic iodides in the presence of the silica-supported poly[3-(2-cyanoethylsulfanyl)propylsiloxane palladium] complex as catalyst was accomplished in aqueous medium. This polymeric catalyst can be reused without much loss of activity. This method has the advantages in separation of the product and reuse of the catalyst.

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- (10) Stille coupling of water-soluble halides with the substituted trichlorostannanes(RSnCl₃) in the presence of PdCl₂ and KOH was effected in aqueous conditions. See, (a) Rai, R.; Aubrecht, K. B.; Collum, D. B. *Tetrahedron Lett.* **1995**, 36, 3111-3114. (b) Roshchin, A. I.; Bumagin, N. A.; Beletskaya. *ibid.* **1995**, 36, 125-128.
- (11) The preparation of the catalyst is as follows. Synthesis of Si-S: To a stirred solution of fused silica (5.0 g) in toluene (120 mL) for 10 min, was added (EtO)₃SiC₃H₆SC₂H₄CN (5.0 g) and the mixture was stirred at reflux for 48 h. To the reaction mixture distilled water (30 mL) was added and stirred at reflux for another 48 h and allowed to cool, then filtered and dried at 160 °C *in vacuo*. The resulting white powder was washed with acetone (3 x 20 mL) and dried. The sulfur content was determined to be 5.95 wt% by elemental analysis. Synthesis of Si-S-Pd: A mixture of Si-S (2.0 g) and PdCl₂ (0.22 g, 1.20 mmol) in acetone (50 mL) was heated to reflux under nitrogen for 72 h. The product was allowed to cool, then filtered. The resulting gray powder was washed with distilled water (3 x 10 mL) and acetone (3 x 10 mL) and then dried *in vacuo* to afford 2.04 g of Si-S-Pd. The sulfur and palladium content were 3.72 wt% and 4.63 wt% by elemental analysis.
- (12) Satisfactory physical and spectral data were obtained in accord with the structure. Selected physical and spectral data are as follows. **3a**: TLC, SiO₂, EtOAc / hexanes 1 : 10, R_f = 0.40. ¹H NMR (400 MHz, CDCl₃), δ 7.09 (dd, 1 H, J = 5.1, 3.5 Hz), 7.27 (m, 2 H), 7.32 (dd, 1 H, J = 3.5, 1.1 Hz), 7.38 (m, 2 H), 7.62 (m, 2 H). IR (KBr) 3070, 1608, 1477, 832, 708 cm⁻¹. MS (m/e, relative intensity) = 162 (4), 161 (10), 160 (100), 128 (13), 116 (8), 115 (34). **3b**: TLC, SiO₂, hexanes, R_f = 0.21. ¹H NMR (400 MHz, CDCl₃), δ 3.84 (s, 3 H), 6.94 (m, 2 H), 7.08 (m, 1 H), 7.28 (m, 2 H), 7.57 (m, 2 H). IR (KBr) 3102, 1603, 1433, 1218, 1019

cm⁻¹. MS (m/e, relative intensity) = 191 (12), 190 (100), 175 (80), 147 (29).

3d: TLC, SiO₂, hexanes, R_f = 0.44. ¹H NMR (400 MHz, CDCl₃), δ 6.53 (m, 1 H), 6.73 (m, 1 H), 7.34 (m, 1 H), 7.45 (m, 2 H), 7.53 (m, 1 H), 7.77 (m, 2 H). IR (KBr) 3075, 1600, 1463, 1093 cm⁻¹. MS (m/e, relative intensity) = 145 (10), 144 (54), 116 (13), 115 (100), 89 (6), 63 (13), 51 (16).

3g: TLC, SiO₂, hexanes, R_f = 0.17. ¹H NMR (400 MHz, CDCl₃), δ 3.87 (s, 3 H), 7.01 (m, 1 H), 7.34 (m, 1 H), 7.45 (m, 2 H), 7.58 (m, 4 H). IR (KBr) 3055, 1265 cm⁻¹. MS (m/e, relative intensity) = 185 (13), 184 (100), 169 (43), 141 (44), 115 (34).

3i: TLC, SiO₂, hexanes, R_f = 0.45. ¹H NMR (400 MHz, CDCl₃), δ 7.12 (s, 2 H), 7.21 (m, 2 H), 7.34 (m, 4 H), 7.48 (m, 4 H). IR (KBr) 3019, 1597, 1496, 1072, 962, 909, 693 cm⁻¹. MS (m/e, relative intensity) = 180 (88), 179 (100), 178 (72), 165 (45), 89 (32), 76 (24).

3j: TLC, SiO₂, hexanes, R_f = 0.20. ¹H NMR (400 MHz, CDCl₃), δ 3.84 (s, 3 H), 6.90 (d, 2 H), 6.97 (d, 1 H), 7.07 (d, 1 H), 7.21 (s, 1 H), 7.35 (m, 2 H), 7.47 (m, 4 H). MS (m/e, relative intensity) = 210 (100), 195 (16), 167 (25), 165 (40), 152 (23).

3k: TLC, SiO₂, hexanes, R_f = 0.49. ¹H NMR (400 MHz, CDCl₃), δ 7.31 (m, 6 H), 7.53 (m, 4 H). IR (KBr) 3062, 1599, 1499, 1071, 918, 756, 689, 535, 509 cm⁻¹. MS (m/e, relative intensity) = 179 (14), 178 (100), 176 (20), 152 (10), 89 (11), 76 (12).

- (13) The typical procedure is as follows. To a stirred solution of iodobenzene (**2a**) (173 mg, 0.85 mmol) in CH₃CN/H₂O (4 : 1) (5 mL) was added silica-supported palladium (Si-S-Pd) (10.6 mg, 5 mol %) and heated to 80 °C and then 2-(tributylstannyl)thiophene (**1a**) (317 mg, 0.85 mmol) in CH₃CN/H₂O (4 : 1) (5 mL) was added slowly for an hour *via* a syringe pump. The reaction mixture was stirred at 80 °C for 5 h and cooled to room temperature and saturated NaCl solution was added. The Si-S-Pd was separated from the mixture by filtration, washed with distilled water (2 x 10 mL), ethanol (2 x 10 mL), and diethyl ether (2 x 10 mL). The reaction mixture was extracted with ether and the organic layer was dried over anhydrous MgSO₄ and evaporated *in vacuo*. The product was separated by SiO₂ column chromatography (EtOAc / hexanes 1 : 10, R_f = 0.40) to afford the coupled product **3a** (113 mg, 83%).
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