Palladium-Catalyzed Mizoroki–Heck-Type Reaction of Aryl Trimethoxysilanes

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Abstract: A palladium-catalyzed Mizoroki–Heck-type reaction of aryl trimethoxysilanes with olefins is described. A series of $ArSi(OMe)_3$ and olefins, including electron-rich and electron-deficient analogues worked well in the procedure, affording the arylation products in moderate to good yields.

Key words: palladium-catalyzed, aryltrimethoxysilanes, crosscoupling, Heck reaction, alkenes

The palladium-catalyzed arylation of olefins, also known as the Mizoroki-Heck reaction, is one of the most versatile tools available for C-C bond formation used in organic synthesis.¹ Over the past few decades, some alternative halide surrogates such as diazonium halide salts,² triflates,³ acid chlorides,⁴ and telluronium salts,⁵ have been developed for use in the Mizoroki-Heck reaction. Recently, the transition-metal catalyzed oxidative Mizoroki-Heck reaction of boronic acids with alkenes has drawn considerable attention because boronic acids are comparatively stable, nontoxic, and easily available.⁶ Compared with the organoboranes, organosilane reagents, especially aryl trialkoxysilanes, are lower-cost and easily purified by distillation or chromatography.⁷ However, much attention had been paid to transition-metal-catalyzed 1,4-conjugate addition (CA) of organosilane reagents to α , β -unsaturated conjugated compounds. The Mizoroki-Heck-type reaction (HT), which occurs as a side reaction of the 1,4-conjugated addition and results from β -H elimination of the α -metal carbonyl intermediates in the aforementioned reaction, was occasionally observed (Scheme 1).

From both organometallic and synthetic points of view, it is important to switch the reactivity of α -metal carbonyl intermediates. The reactivity of an organo-palladium species is not only determined by the intrinsic nature of palladium, but can also be tuned by the supporting ligands and reaction conditions. Zou described the tunability of a competition between β -H elimination versus hydrolysis of $\alpha\text{-rhodium}$ carbonyl intermediates in the presence of water. 6u

In 1998 and 2001, Mori and co-workers described the palladium and rhodium-catalyzed oxidative Mizoroki-Hecktype reaction of aryl silanol.⁸ However, only α , β -unsaturated conjugated compounds^{8a} or electron-deficient alkenes^{8b} were reported and the procedure was very sensitive to the electronic nature of the carbonyl substrate.^{8a} Moreover, while the synthesis of chlorosilanes, which underwent hydrolysis to form silanols, was somewhat tedious,⁹ aryl trialkoxysilanes could be readily prepared from the reaction of ArX and either tetraalkoxysilanes or trialkoxysilanes.7b,10 In 2003, Mori reported an iridiumcatalyzed Mizoroki-Heck reaction of aryl trialkoxysilanes that occurred at 120 °C.11 Herein, we wish to report a mild, palladium-catalyzed cross-coupling reaction of aryl trimethoxysilanes with alkenes, including electron-deficient, electron-rich, acyclic and cyclic conjugated alkenes.

We envisioned that the hydrolysis of the α -palladium carbonyl intermediates would be inhibited in the absence of water. Initially, we investigated the Mizoroki-Heck-type reaction of phenyl trimethoxysilane (2a) with cyclohex-2enone (1a) in the presence of $Pd(OAc)_2$ (5 mol%), bipy (10 mol%) and three equivalents of various fluoride sources in anhydrous DMF (2 mL) at 60 °C (Table 1). The results suggested that the fluoride source had a dramatic effect on the yields. Among the fluoride sources screened, only FeF₃ and AgF showed good catalytic activity (Table 1, entries 3 and 4). Remarkably, compared with other solvents, DMF proved to be the best among the array of solvents tested (Table 1, entries 4-8). The ligands were also found to be crucial for this transformation. The phosphines tested, such as tri(2-tolyl)phosphine and tris(3,5-dimethylphenyl)phosphine, which are susceptible to oxidation under air, gave moderate yields (Table 1, entries 13 and 14), whereas the phenanthroline class of



Scheme 1 Two plausible pathways for α -metal carbonyl intermediates

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| | + PhSi(OMe) ₃ – Pd, I | igand, F source solvent | → | Ph |
|-------|--|----------------------------|---------|---------------------------|
| 1a | 2a | 3aa | | |
| Entry | Ligand | F source | Solvent | Yield (%) ^b |
| 1 | bipy | TBAF-3H ₂ O | DMF | <5 |
| 2 | bipy | KF | DMF | <5 |
| 3 | bipy | FeF ₃ | DMF | 70 |
| 4 | bipy | AgF | DMF | 84 |
| 5 | bipy | AgF | THF | <5 |
| 6 | bipy | AgF | MeCN | <5 |
| 7 | bipy | AgF | toluene | <5 |
| 8 | bipy | AgF | dioxane | <5 |
| 9 | Ph ₃ P | AgF | DMF | 44 |
| 10 | 1,10-phenanthroline | AgF | DMF | 90 |
| 11 | 4,7-dimethyl- 1,10-phenanthroline | AgF | DMF | 50 |
| 12 | 2,9-dimethyl-4,7-diphenyl 1,10-phenanthroline | - AgF | DMF | 87 |
| 13 | $(2-MeC_6H_4)_3P$ | AgF | DMF | 34 |
| 14 | $(3,5-Me_2C_6H_3)_3P$ | AgF | DMF | 40 |
| 15 | | AgF | DMF | 42 |
| 16 | 1,10-phenanthroline | AgF | DMF | 88° |
| 17 | 1,10-phenanthroline | | DMF | <5 ^d |
| | | | | 1) |

^a Reaction conditions: **1a** (19 μ L, 0.2 mmol), **2a** (56 μ L, 0.3 mmol), Pd(OAc)₂ (2.2 mg, 5 mol%), ligand (10 mol%), F source (0.6 mmol), anhydrous solvent (2 mL), air, 60 °C.

^b Isolated yield.

^c Under N₂.

^d Under O₂.

ligands, which are more stable towards oxidation, provided high yields (Table 1, entries 10–12). Amongst these, 1,10-phenanthroline was found to be the most effective; using this ligand, the yield of **3aa** sharply increased to 90%.

Under our optimized reaction conditions, we explored the scope of reaction with a range of aryl trimethoxysilanes as shown in Table 2.¹² Aryl trimethoxysilane substrates worked well under the reaction conditions. Electron-rich, as well as electron-neutral aryl trimethoxysilanes coupled efficiently with cyclohex-2-enone and good yields were obtained (Table 2, entries 1 and 5). However, the steric hindrance affected the efficiency. For example, only a 22% yield of **3ad** was isolated.

 Table 2
 Mizoroki–Heck-Type Reaction of Aryl Trimethoxysilanes

 with Cyclohex-2-enone^a
 Provide Comparison of Aryl Trimethoxysilanes



^a Reaction conditions: cyclohex-2-enone (**1a**; 19 μ L, 0.2 mmol), ArSi(OMe)₃ **2** (0.3 mmol), Pd(OAc)₂ (2.2 mg, 5 mol%), 1,10-phenanthroline (3.6 mg, 10 mol%), AgF (76mg, 0.6 mmol), anhydrous DMF (2 mL), air, 60 °C.

^b Isolated yield.

In the next stage, we explored the reaction of a variety of olefins with $PhSi(OMe)_3$ as shown in Table 3. Electrondeficient olefins such as methyl acrylate **3d** reacted smoothly to afford the desired product **3da** in high yield. However, when acrylamide was subjected to the procedure, the yield dramatically decreased to 33%. The electron-rich olefin **1e** also worked well under the standard reaction conditions and provided (*E*)-stilbene (**3ea**) in 75% yield. Furthermore, styrene and 2-vinylpyridine were good reaction partners and gave 78% and 62% yields of (*E*)-stilbene (**3ba**) and (*E*)-2-styrylpyridine (**3ca**), respectively (Table 2, entries 1 and 2). However, the former compound (*E*)-2-styrylpyridine failed to undergo the arylation reaction, presumably due to steric hindrance.

Silver(I) fluoride may play a dual role in the procedure. One could be to activate the $ArSi(OMe)_3$ by forming $[ArSi(OMe)_3F]^-$, the other may be to regenerate Pd(II) from Pd(0), which is generated from the HPdX released by the β -H elimination of α -metal carbonyl intermediates (Scheme 1).

In conclusion, we have developed an efficient and mild method for a Mizoroki–Heck-type reaction of both electron-rich and electron-deficient olefins by employing readily prepared aryl trimethoxysilanes. The reaction afforded the arylation products in moderate to good yields.

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 Table 3
 Mizoroki–Heck-Type Reaction of Phenyl Trimethoxysilane with Olefins^a



^a Reaction conditions: olefin **1** (0.2 mmol), PhSi(OMe)₃ (56 μ L, 0.3 mmol), Pd(OAc)₂ (2.2 mg, 5 mol%), 1,10-phenanthroline (3.6 mg, 10 mol%), AgF (76 mg, 0.6 mmol), anhydrous DMF (2 mL), air, 60 °C. ^b Isolated yield.

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- (12) *General procedure*: Under air, a reaction tube was charged with olefin (0.2 mmol), aryl trimethoxysilane (0.3 mmol), Pd(OAc)₂ (2.2 mg, 5 mol%), 1,10-phenanthroline (3.6 mg, 10 mol%), AgF (76 mg, 0.6 mmol) and DMF (2 mL). The mixture was stirred at 60 °C. After completion of the reaction (monitored by TLC), EtOAc (20 mL) was added and the mixture was washed with water (10×3 mL). Then the organic layer was dried, concentrated in vacuo and the residue was purified by flash column chromatography on a silica gel to give the desired product.

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