

HETEROCYCLES, Vol. 95, No. 1, 2017, pp. 568-574. © 2017 The Japan Institute of Heterocyclic Chemistry
Received, 1st August, 2016, Accepted, 6th September, 2016, Published online, 20th September, 2016
DOI: 10.3987/COM-16-S(S)21

PALLADIUM-CATALYZED CROSS-COUPLING OF ARYL CHLORIDES WITH ARYLSILATRANES

**Yutaro Yamamoto, Alexandre Baralle, Anaïs Godefroy, Kei Murakami,
Hideki Yorimitsu,* and Atsuhiko Osuka**

Department of Chemistry, Graduate School of Science, Kyoto University,
Sakyo-ku, Kyoto 606-8502, Japan. E-mail: yori@kuchem.kyoto-u.ac.jp

Abstract – The cross-coupling reactions of arylsilatranes with readily available and inexpensive aryl chlorides were carried out in toluene/THF at 100 °C for 3 h in the presence of tetrabutylammonium fluoride as an activator for smooth transmetalation and catalytic amounts of palladium(II) acetate and XPhos.

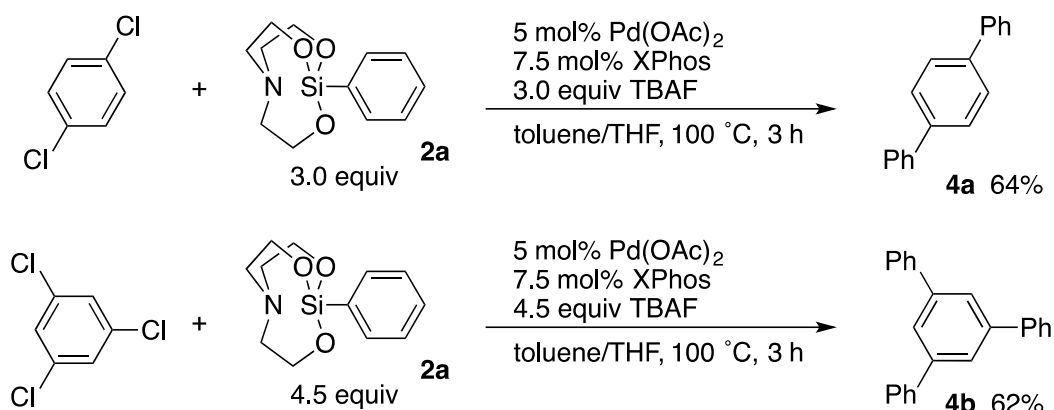
Organosilicon reagents have played a significantly important role in cross-coupling reactions and are widely used for the synthesis of various biaryls.¹ Despite the widespread use of Hiyama cross-coupling in organic synthesis, readily available, abundant, and inexpensive aryl chlorides have been employed as substrates only sporadically.² The potency of aryl chlorides in Hiyama cross-coupling should be explored.

Silatranes are an interesting class of organosilicon compounds that have a [3.3.3.0] tricyclic structure with an intramolecular interaction between the bridgehead silicon and nitrogen.³ Structurally rigid silatranes are stable under gentle hydrolysis or alcoholysis conditions and easier to handle under air compared with acyclic trialkoxysilanes.⁴ Advantageously, such stable silatranes still show reactivity for cross-coupling reactions and have been employed as reliable reagents for biaryl synthesis.^{5,6} In 2003, DeShong reported palladium-catalyzed cross-coupling of aryl bromides, iodides, and triflates with phenylsilatrane to afford the corresponding biaryls in good to excellent yields.⁶ However, these reaction conditions were not applicable to aryl chlorides. Lacking detailed survey on the scope of arylsilatranes for this cross-coupling also diminishes its synthetic utility.

Very recently, we have reported that silylsilatranes serve as silylating agents in palladium-catalyzed cross-coupling of aryl chlorides.⁷ Along this line, we envisioned that arylsilatranes would act as arylating agents for cross-coupling of aryl chlorides. This is indeed the case, and we describe herein

palladium-catalyzed cross-coupling of aryl chlorides with several arylsilatranes in the presence of TBAF (tetrabutylammonium fluoride) as an activator for smooth transmetalation.

We examined the cross-coupling of various aryl chlorides **1** with phenylsilatrane (**2a**) under palladium catalysis (Table 1). Treatment of 4-chloroanisole (**1a**) with phenylsilatrane (**2a**) in the presence of palladium(II) acetate (5 mol%), XPhos (2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl, 7.5 mol%), and TBAF (1.5 equiv, ca. 1.0 M solution in THF) in toluene at 100 °C for 3 h afforded the corresponding biaryl **3a** in 82% yield (entry 1). Interestingly, in the case of phenylation of 1-chloro-4-trimethylsilylbenzene (**1b**), not the trimethylsilyl unit of **1b** but the silatrane moiety of **2a** selectively worked as a nucleophilic partner to afford **3b** in excellent yield (entry 2). This result suggests that the silatrane moiety of **2a** was selectively activated by fluoride ion. Coupling with sterically hindered 2-chloroanisole (**1c**) proceeded but required a longer reaction time for full conversion (entry 3). Unprotected 4-chloroaniline (**1d**), 4-chlorobenzyl alcohol (**1e**), 4-chlorobenzaldehyde (**1f**), and π -extended 2-chloronaphthalene (**1g**) also successfully reacted to give **3d–3g** in good to excellent yields (entries 4–7). Electron-deficient substrates such as trifluoromethyl-, ethoxycarbonyl-, cyano-, and nitro-substituted aryl chlorides **1h–1k** also reacted smoothly (entries 8–11). The cross-coupling was efficient enough to phenylate 1,4-di- and 1,3,5-trichlorobenzene with larger amounts of **2a**, TBAF and the same amount of the palladium catalyst (Scheme 1).

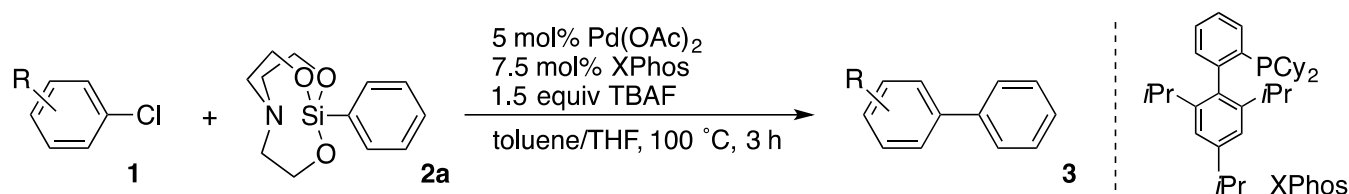


Scheme 1. Double and triple phenylation

The scope of arylsilatranes **2**⁸ was then investigated (Table 2). The cross-coupling reactions proceeded with electron-rich 4-methoxyphenylsilatrane (**2b**), 4-(*N,N*-dimethylamino)phenylsilatrane (**2c**), electron-deficient 4-trifluoromethylphenylsilatrane (**2d**), and sterically hindered 1-naphthylsilatrane (**2e**) to give **5a–5d**, in excellent to good yields (entries 1–4). Unfortunately, attempts to achieve the cross-coupling reactions of heterocyclic 2-thienylsilatrane (**2f**) and 3-thienylsilatrane (**2g**) failed (entries 5

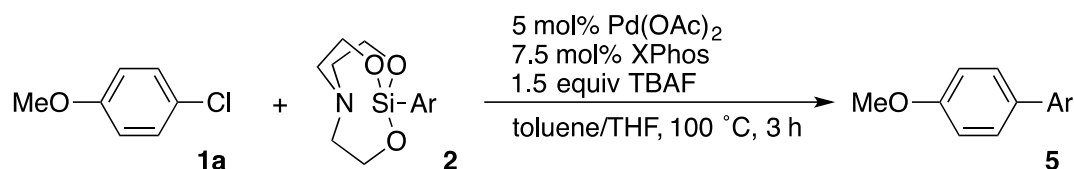
and 6) and resulted in the recovery of **1a** (41% and 77% NMR yields, respectively), probably due to the decomposition of **2f** and **2g** under the reaction conditions.⁹

Table 1. Cross-coupling of aryl chlorides **1** with phenylsilatrane (**2a**)



Entry	R	1	3	Isolated yield/%
1	4-OMe	1a	3a	82
2	4-SiMe ₃	1b	3b	90
3	2-OMe	1c	3c	78 (6 h)
4	4-NH ₂	1d	3d	72
5	4-CH ₂ OH	1e	3e	69
6	4-CHO	1f	3f	70
7	(2-chloronaphthalene)	1g	3g	92
8	4-CF ₃	1h	3h	76
9	4-CO ₂ Et	1i	3i	85
10	4-CN	1j	3j	86
11	4-NO ₂	1k	3k	74

Table 2. Scope of arylsilatrane **2**



Entry	Ar	2	5	Isolated yield/%
1	4-methoxyphenyl	2b	5a	92
2	4-(<i>N,N</i> -dimethylamino)phenyl	2c	5b	68
3	4-trifluoromethylphenyl	2d	5c	99
4	1-naphthyl	2e	5d	83
5	2-thienyl	2f	5e	<1 (NMR yield)
6	3-thienyl	2g	5f	10 (NMR yield)

In conclusion, we have shown that arylsilatranes serve as arylating agents in palladium-catalyzed cross-coupling of aryl chlorides with the aid of a fluoride activator. The reaction conditions exhibited acceptable functional group compatibility.

EXPERIMENTAL

^1H NMR (594 MHz) and ^{13}C NMR (149 MHz) spectra were taken on a JEOL ECA-600 spectrometer. Chemical shifts are reported on a delta scale in ppm relative to residual CHCl_3 ($\delta = 7.26$ ppm) for ^1H NMR and to CDCl_3 ($\delta = 77.16$ ppm) for ^{13}C NMR. Spectroscopic grade solvents were used for all spectroscopic studies without further purification. IR spectra were determined on a JASCO IR-810. High-resolution APCI-TOF mass spectra were taken on a Bruker micrOTOF. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Preparative separations were performed by silica gel chromatography.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Toluene was distilled from calcium hydride under nitrogen. Palladium(II) acetate and XPhos were purchased from Wako Pure Chemicals Industries, Ltd. and Aldrich, respectively. TBAF (ca. 1.0 M solution in THF) was purchased from Tokyo Chemical Industries Co., Ltd. and stored under nitrogen.

Procedure for Synthesis of Arylsilatranes 2a, 2b, 2e, and 2f. The synthesis of phenylsilatrane (**2a**) is representative. Phenyltrimethoxysilane (9.35 mL, 50 mmol) was added to a solution of triethanolamine (8.50 g, 57 mmol) in toluene (25 mL). The solution was stirred at 100 °C for 3 h with removing MeOH from the reaction mixture by a Dean-Stark trap. The resulting white precipitate was filtered and washed with toluene. Drying under a reduced pressure gave **2a** (9.20 g, 36.6 mmol) in 73% yield as a white solid. Phenylsilatrane (**2a**) showed the identical spectra according to the literature.⁶

Procedure for Synthesis of Arylsilatranes 2c, 2d, and 2g. The synthesis of 4-(*N,N*-dimethylamino)phenylsilatrane (**2c**) is representative. Ethoxysilatrane¹⁰ (1.32 g, 6.00 mmol) was placed in a reaction flask. The flask was purged with nitrogen, and THF (10 mL) was added. The mixture was cooled to 0 °C. 4-(*N,N*-Dimethylamino)phenyllithium¹¹ (ca. 0.69 M in 4:3 Et₂O/*n*-hexane, 8.75 mL, 6.00 mmol) was added to the solution slowly. After the addition was completed, the mixture was warmed to room temperature and stirred overnight. The reaction was quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo to afford a solid. The solid was suspended in EtOH (3 mL), and the suspension was then filtered off. The solid was washed on the filter paper with EtOH to afford **2c** (296.0 mg, 1.01 mmol) in 17% yield as a white solid.

4-Methoxyphenylsilatrane (2b): **2b** was synthesized from trimethoxy(4-methoxyphenyl)silane in 56% yield. Colorless solid. Mp 184–187 °C. IR (neat): 1593, 1274, 1238, 1123, 1084, 1016, 941, 910, 826, 796, 769, 640, and 633 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 7.65 (d, 2H, *J* = 8.6 Hz), 6.82 (d, 2H, *J* = 8.6 Hz), 3.86 (t, 6H, *J* = 5.9 Hz), 3.76 (s, 3H), and 2.91 (t, 6H, *J* = 5.9 Hz) ppm; ¹³C NMR (149 MHz, CDCl₃): δ = 159.58, 135.59, 133.38, 113.13, 57.93, 55.12, and 51.21 ppm; MS (APCI, positive): *m/z* = 281.1078. Calcd for C₁₃H₁₉NO₄Si: 281.1076 [*M*]⁺.

4-(*N,N*-Dimethylamino)phenylsilatrane (2c): Mp 218–225 °C. IR (neat): 1596, 1507, 1126, 1096, 1052, 1016, 940, 907, 812, 768, and 628 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 7.59 (d, 2H, *J* = 8.6 Hz), 6.71 (d, 2H, *J* = 8.6 Hz), 3.87 (t, 6H, *J* = 5.9 Hz), and 2.88 (t, 6H, *J* = 5.9 Hz and s, 6H; overlap) ppm; ¹³C NMR (149 MHz, CDCl₃): δ = 150.96, 135.09, 128.28, 112.79, 58.13, 51.37, and 40.96 ppm; MS (APCI, positive): *m/z* = 295.1465. Calcd for C₁₄H₂₃N₂O₃Si: 295.1472 [*M*+H]⁺.

4-Trifluoromethylphenylsilatrane (2d): **2d** was synthesized from 4-trifluoromethylphenyllithium¹¹ in 32% yield. Colorless solid. Mp 227–228 °C. IR (neat): 1323, 1154, 1123, 1098, 1057, 1017, 911, 776, 735, 696, and 595 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 7.84 (d, 2H, *J* = 7.7 Hz), 7.49 (d, 2H, *J* = 7.7 Hz), 3.91 (t, 6H, *J* = 5.9 Hz), and 2.93 (t, 6H, *J* = 5.9 Hz) ppm; ¹³C NMR (149 MHz, CDCl₃): δ = 147.55, 134.56, 129.50 (q, *J* = 31.6 Hz), 124.88 (q, *J* = 272.5 Hz), 123.77 (d, *J* = 2.9 Hz), 57.71, and 51.19 ppm; MS (APCI, positive): *m/z* = 320.0915. Calcd for C₁₃H₁₇F₃NO₃Si: 320.0924 [*M*+H]⁺.

1-Naphthylsilatrane (2e): **2e** was synthesized from 1-(trimethoxysilyl)naphthalene in 52% yield. Colorless solid. Mp 250–252 °C. IR (neat): 1118, 1085, 1016, 938, 909, 816, 771, 726, 664, 620, and 590 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 8.35 (d, 1H, *J* = 8.1 Hz), 8.13 (dd, 1H, *J* = 6.8, 1.4 Hz), 7.76 (t, 2H, *J* = 8.1 Hz), 7.46–7.36 (m, 3H), 3.94 (t, 6H, *J* = 5.9 Hz), and 2.91 (t, 6H, *J* = 5.9 Hz) ppm; ¹³C NMR (149 MHz, CDCl₃): δ = 139.46, 137.49, 134.12, 134.03, 130.14, 128.82, 128.53, 125.09, 125.00, 124.53, 58.32, and 51.56 ppm; MS (APCI, positive): *m/z* = 301.1118. Calcd for C₁₆H₁₉NO₃Si: 301.1129 [*M*]⁺.

2-Thienylsilatrane (2f): **2f** was synthesized from triethoxy(2-thienylsilane) in 65% yield. Colorless solid. Mp 218–220 °C. IR (neat): 1116, 1082, 1020, 983, 943, 916, 776, 722, 640, and 586 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 7.39 (dd, 1H, *J* = 5.0, 1.0 Hz), 7.34 (dd, 1H, *J* = 3.6, 1.0 Hz), 7.08 (dd, 1H, *J* = 5.0, 3.6 Hz), 3.90 (t, 6H, *J* = 5.9 Hz), and 2.90 (t, 6H, *J* = 5.9 Hz) ppm; ¹³C NMR (149 MHz, CDCl₃): δ = 142.13, 133.23, 128.15, 127.41, 57.66, and 51.09 ppm; MS (APCI, positive): *m/z* = 257.0535. Calcd for C₁₀H₁₅NO₃SSi: 257.0536 [*M*]⁺.

3-Thienylsilatrane (2g): **2g** was synthesized from 3-thienyllithium¹² in 11% yield. Colorless solid. Mp 166–169 °C. IR (neat): 1118, 1085, 1018, 940, 914, 769, 633, and 590 cm⁻¹. ¹H NMR (594 MHz, CDCl₃) δ = 7.58 (dd, 1H, *J* = 3.6, 1.0 Hz), 7.31–7.25 (m, 3H), 3.90 (t, 6H, *J* = 5.9 Hz), and 2.93 (t, 6H, *J* = 5.9

Hz) ppm; ^{13}C NMR (149 MHz, CDCl_3): δ = 143.03, 132.71, 131.37, 124.45, 57.79, and 51.23 ppm; MS (APCI, positive): m/z = 257.0529. Calcd for $\text{C}_{10}\text{H}_{15}\text{NO}_3\text{SSi}$: 257.0536 [M] $^+$.

Typical Procedure for Cross-Coupling of Aryl Chlorides 1 with Arylsilatrane 2. The reaction of phenylsilatrane (**2a**) with 4-chloroanisole (**1a**) (Table 1, entry 1) is representative. Palladium(II) acetate (0.025 mmol, 5.6 mg), XPhos (0.0375 mmol, 17.9 mg), and phenylsilatrane (**2a**, 0.75 mmol, 188.5 mg) were added to a Schlenk flask. The flask was then purged with nitrogen. 4-Chloroanisole (**1a**) (0.50 mmol, 71.3 mg), toluene (1.5 mL), and TBAF (0.75 mmol, 0.75 mL in ca. 1.0 M THF solution) were subsequently added. The mixture was stirred at 100 °C for 3 h, then quenched by addition of water, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (hexane) to provide **3a** (75.2 mg, 0.408 mmol) in 82% yield.

Products **3a**, [13 3b](#), [14 3c](#), [13 3d](#), [15 3e](#), [16 3f](#), [13 3g](#), [13 3h](#), [17 3i](#), [13 3j](#), [13 3k](#), [13 4a](#), [13 4b](#), [18 5a](#), [19 5b](#), [20 5c](#), [21](#) and [5d](#)²² are known compounds and showed the identical spectra according to the literature.

ACKNOWLEDGEMENTS

This work was supported by JSPS KAKENHI Grant Numbers 24685007, 26620081, JP16H01019, and JP16H04109. Y.Y. and A.B. acknowledge JSPS for a Predoctoral Fellowship and a Postdoctoral Fellowship, respectively.

REFERENCES

1. Reviews: Y. Nakao and T. Hiyama, *Chem. Soc. Rev.*, 2011, **40**, 4893; H. F. Sore, W. R. J. D. Galloway, and D. R. Spring, *Chem. Soc. Rev.*, 2012, **41**, 1845.
2. Examples of the Hiyama coupling of aryl chlorides with aryltrialkoxysilanes: M. E. Mowery and P. DeShong, *Org. Lett.*, 1999, **1**, 2137; J. H. Li, C. L. Deng, and Y. X. Xie, *Synthesis*, 2006, 969; O. Y. Yuen, C. M. So, H. W. Man, and F. Y. Kwong, *Chem. Eur. J.*, 2016, **22**, 6471. For examples of similar coupling of aryl chlorides with a broader range of arylsilanes, see the references cited therein.
3. Reviews: J. K. Puri, R. Singh, and V. K. Chahal, *Chem. Soc. Rev.*, 2011, **40**, 1791; J. G. Verkade, *Coord. Chem. Rev.*, 1994, **137**, 233; J. G. Verkade, *Acc. Chem. Res.*, 1993, **26**, 483.
4. R. J. Garant, L. M. Daniels, S. K. Das, M. N. Janakiraman, R. A. Jacobson, and J. G. Verkade, *J. Am. Chem. Soc.*, 1991, **113**, 5728; A. Yoshikawa, M. S. Gordon, V. F. Sidorkin, and V. A. Pestunovich, *Organometallics*, 2001, **20**, 927.
5. R. R. Pidaparathi, M. E. Welker, C. S. Day, and M. W. Wright, *Org. Lett.*, 2007, **9**, 1623; I. Peñafiel, I. M. Pastor, M. Yus, M. A. Esteruelas, M. Oliván, and E. Oñate, *Eur. J. Org. Chem.*, 2011, 7174; T.

- Ishiyama, T. Saiki, E. Kishida, I. Sasaki, H. Ito, and N. Miyaura, [Org. Biomol. Chem.](#), 2013, **11**, 8162.
6. S. Riggleman and P. DeShong, [J. Org. Chem.](#), 2003, **68**, 8106.
 7. Y. Yamamoto, H. Matsubara, K. Murakami, H. Yorimitsu, and A. Osuka, [Chem. Asian J.](#), 2015, **10**, 219; J.-D. Guo, T. Sasamori, Y. Yamamoto, H. Matsubara, S. Nagase, and H. Yorimitsu, [Bull. Chem. Soc. Jpn.](#), 2016, **89**, 192.
 8. The cross-coupling of **1a** with acyclic phenyltriethoxysilane under our optimized reaction conditions afforded the corresponding biaryl **3a** in 68% NMR yield along with 10% recovery of **1a**.
 9. The cleaving pathway of the 2-thienyl group on silicon by H₂O in TBAF has proposed; K. Hosoi, K. Nozaki, and T. Hiyama, [Chem. Lett.](#), 2002, **31**, 138; K. Hosoi, K. Nozaki, and T. Hiyama, [Proc. Jpn. Acad. Ser. B](#), 2002, **78**, 154.
 10. I. Iovel, L. Golomba, J. Popelis, S. Grinberga, and E. Lukevics, [Chem. Heterocycl. Compd.](#), 1999, **35**, 1059.
 11. S. Guduguntla, V. Hornillos, R. Tessier, M. Fañanás-Mastral, and B. L. Feringa, [Org. Lett.](#), 2016, **18**, 252.
 12. J. Huang, T. Wu, and Y. Qian, [Chem. Commun.](#), 2003, 2816.
 13. S.-M. Wang, X.-Y. Wang, H.-L. Qin, and C.-P. Zhang, [Chem. Eur. J.](#), 2016, **22**, 6542.
 14. A. Iijima and H. Amii, [Tetrahedron Lett.](#), 2008, **49**, 6013.
 15. M. Samarasinghureddy, G. Prabhu, T. M. Vishwanatha, and V. V. Sureshbabu, [Synthesis](#), 2013, **45**, 1201.
 16. P. C. Too, G. H. Chan, Y. L. Tnay, H. Hirao, and S. Chiba, [Angew. Chem. Int. Ed.](#), 2016, **55**, 3719.
 17. R. Bandari, T. Hçche, A. Prager, K. Dirnberger, and M. R. Buchmeiser, [Chem. Eur. J.](#), 2010, **16**, 4650.
 18. L. Baia and J.-X. Wang, [Adv. Synth. Catal.](#), 2008, **350**, 315.
 19. G. Zhang, [Synthesis](#), 2005, 537.
 20. L.-Y. Liao, K.-M. Liu, and X.-F. Duan, [J. Org. Chem.](#), 2015, **80**, 9856.
 21. L. Ackermann and A. Althammer, [Org. Lett.](#), 2006, **8**, 3457.
 22. J. Kuroda, K. Inamoto, K. Hiroya, and T. Doi, [Eur. J. Org. Chem.](#), 2009, 2251.