

Intermolecular C–H Silylation of Arenes and Heteroarenes with HSiEt₃ under Operationally Diverse Conditions: Neat/Stoichiometric and Acceptor/Acceptorless

Kang-sang Lee,* Dimitris Katsoulis, and Jongwook Choi*

Dow Corning Corporation, 2200 West Salzburg Road, Auburn, Michigan 48611, United States

Supporting Information

ABSTRACT: Efficient protocols for Rh-catalyzed intermolecular C–H silylation of unactivated arenes and heteroarenes are disclosed. The silylations are catalyzed by a Rh-complex (2 mol %) derived in situ from commercially available $Rh(nbd)_2BF_4$ and (S,S)-*i*-Pr-BPE (L3) with Et₃SiH in the presence of hydrogen acceptor under either neat (excess of arene) or stoichiometric conditions. The regioselectivity is



determined mainly by the steric bulk of the substituents and by the electronic effect as an ancillary factor. In addition, our preliminary result shows that the current protocol catalyzes the silylation of arenes in the absence of hydrogen acceptors.

KEYWORDS: C–H silylation, Rh-catalyzed silylation, intermolecular C–H silylation, silylation of unactivated arenes and heteroarenes, C–H bond activation, acceptorless C–H silylation

evelopment of efficient and practical synthetic methods for arylsilanes is an important research area in chemical synthesis due to their utility as fundamental building blocks of industrially important polymers and materials.¹ Among the methods of synthesis of arylsilanes, including reactions of haloor alkoxysilane with aryl-Grignard, or lithium reagents, the transition-metal-catalyzed C-H silvlation² of unactivated arenes is particularly attractive because it serves as a direct and atom-economical pathway with better functional group compatibility and with significantly less amount of chemical waste (magnesium- or lithium salts). Since the pioneering work by the Curtis group in 1982,³ a number of catalytic C-H silvlations have been disclosed. However, the protocols are mostly limited to intramolecular silylations⁴ or require a directing group.⁵ There are only a handful reports on intermolecular C–H silvlations of unactivated arenes without directing groups.^{3,6,7} Even in those cases, the reactions demand specialized silane agents requiring multistep synthesis (e.g., o-bissilylbenzene^{6b-d,r} or tetrafluorodialkyldisilanes^{6g,h}), or show relatively narrow substrate scopes (only arenes,⁶ or heteroarenes⁷), or suffer from low to moderate efficiency.

Recently, the seminal reports by the Hartwig group⁸ demonstrated that Rh and Ir systems can efficiently catalyze the silylation with 1,1,1,3,5,5,5-heptamethyltrisiloxane (HMTS)^{8b,c} to afford arylsiloxanes [Aryl-SiMe(OSiMe₃)₂] with a broad substrate scope of arenes including unreactive arenes as well as heteroarenes under mild conditions. However, the corresponding Rh and Ir systems have been demonstrated with a limited silane scope (only with HMTS) and are not compatible with Et₃SiH for the intermolecular C–H silylations.⁸

Several reports described the C–H silylations with Et_3SiH .^{6a,e,k,7b,i,8a} However, with our best knowledge, there is no catalytic protocol showing a broad substrate scope (both

arenes and heteroarenes) in the intermolecular C–H silylation with Et₃SiH, which has an intrinsically different reactivity compared to HMTS. For example, commonly used Ir systems are efficient in the silylation of more activated polycyclic arenes^{6k} and heteroarenes^{7b} but significantly less effective for electron-rich and -neutral benzene derivatives.^{6k}

Herein, we outline a highly efficient protocol of Rh-catalyzed intermolecular dehydrogenative C–H silylation of both unactivated arenes and heteroarenes. In the presence of commercially available Et_3SiH and cyclohexene, the reactions can be run either in excess arene or in THF with arene as the limiting reagent. Furthermore, with this protocol, certain types of arenes and heteroarenes can undergo *acceptorless* silylations to afford arylsilanes.

We began the investigation of the C–H silylation by screening a number of *in situ*-generated Rh-bisphosphine complexes to transform benzene to triethylphenylsilane (1). Initially, an excess amount of benzene (1 mL) was used with triethylsilane (1 mmol) as the limiting reagent. After screening various alkenes, cyclohexene was identified as an efficient hydrogen acceptor. As shown in Scheme 1, complexes derived from diphenyl- or dialkylphosphinoethane (L1a–d) with 1 mol % [Rh(coe)₂Cl]₂ afforded the desired product in low yield (2– 11%, entries 1–4). When *i*-Pr-DuPhos (L2) was used, the yield of the silylation was increased (17%, entry 5). Using [Rh(cod)OH]₂ and Rh(cod)₂OTf, C–H silylations afforded 1 in moderate yields (39% and 45%, respectively, entry 6 and 7). In the presence of Rh(nbd)₂BF₄, however, the yield of the desired product was significantly increased to 91% (80%

Received: December 10, 2015 Revised: January 26, 2016

	+ USiEt	2 mol % [Rh] 2.2 mol % ligand	
1 mL	1 equiv	1.5 equiv cyclohexene 80 °C, 20 h	1
entry	[Rh]	ligand	yield (%) ^b
1	[Rh(coe) ₂ Cl] ₂	R= Ph	(L1a) 5
2	[Rh(coe) ₂ Cl] ₂	R ₂ P PR ₂ R= Me	(L1b) 2
3	[Rh(coe) ₂ Cl] ₂	R= Et	(L1c) 10 ^c
4	[Rh(coe) ₂ Cl] ₂	R= <i>i</i> -Pr	(L1d) 11
5	[Rh(coe) ₂ Cl] ₂	i-Pr	17
6	[Rh(cod)OH] ₂	P [/] , <i>i</i> -Pr	3 9
7	Rh(cod) ₂ OTf	P-	45
8	$Rh(nbd)_2BF_4$	<i>i</i> -Pr'''	91 (80)
9	Rh(nbd)₂BF₄	<i>i</i> -Pr	>98 (96)
10			3 27
10			21
11	Rh(cod) ₂ OTf	<i>i</i> -Pr	<2

Scheme 1. Dehydrogenative C-H Silylations of Benzene with Et_3SiH : Screening of [Rh] and Ligand^{*a*}

"All reactions were performed with 2 mol % Rh salt based on monomer under N₂. ^bYields were determined by ¹H NMR analysis, and isolated yields are shown in parentheses. ^cHydrosilylation byproducts (79%) and desired product (12%) were obtained when 3,3-dimethyl-1-butene was used instead of cyclohexene.

isolated yield, entry 8). After further screening of a similar type of ligands, the complex derived from (S,S)-*i*-Pr-BPE (L3) and Rh(nbd)₂BF₄ was found to be an efficient catalyst for the silylation to furnish 1 quantitatively (>98% yield and 96% isolated yield, entry 9). Reactions with L3 and [Rh(cod)OH]₂ or Rh(cod)₂OTf were not efficient in this silylation (entry 10 and 11).

Under the optimal reaction conditions, various arenes were tested for the dehydrogenative C-H silvlation. As illustrated in Scheme 2, reactions with electronically variable 1,2- or 1,3disubstituted arenes furnished the desired products at the less sterically hindered *m*-positions in $81 \rightarrow 98\%$ yield (2–6) with no benzylic silylation. Reactions with monosubstituted arenes generally resulted in mixtures of meta- and para-silylation products (7–11): compared to statistical ratio (m/p = 2/1), *para*-silulation preferred with bulky *t*-butyl substituent (1/2 =m/p, 7) and less selective silulation for toluene (1.1/1 = m/p), 8). For electronically different arenes, C-H silvlations proceeded favorably at an electron-rich carbon: 1/6 = m/pfor dimethylaniline, **9** and 2.4/1 = m/p for trifluorotoluene, **10**. In the case of fluorobenzene and anisole, regioselectivity was complicated by the substituents; the silvlation of fluorobenzene afforded the *ortho*-silvlated product as major (4/1 = o/m, 11), presumably due to an inductive effect of the ortho-fluorine and relatively small steric presence of the fluorine atom.⁹ For anisole, all three regioisomers were obtained (1/3.5/1 = o/m/p)12) and resulted likely from the directing effect of the methoxy group. With heteroarenes such as 1-methylindole and benzofuran, as well as pyrrole and furan, the Rh-catalyzed silvlation delivered the desired products in high yield (76 \rightarrow 98% yield, 13–16). The reaction with thiophene was sluggish, affording 17 in 37% yield.





"All reactions were performed under N₂. Yields were determined by ¹H NMR analysis, and isolated yields are shown in parentheses. ^b2-Methoxy-4-methyl-1-triethylsilylbenzene (18%) was isolated together with 6. ^cFour mol % Rh(nbd)₂BF₄ and 4.4 mol % L₃ were used. ^dDisilylated product was obtained in 9% yield. ^e40h, Disilylated product was obtained in 6% yield.

Next, our system was further applied to the reactions where arene was used as the limiting reagent in the case that arenes are more complex and valuable. As shown in Scheme 3, aryltriethylsilane 1, 2, and 7 were isolated in 54–78% yield with use of 1 equiv of unactivated arene, 1.2 equiv of triethylsilane, and 1 mL of THF. Reactions with 1-methylpyrrole and furan furnished a mixture of mono- and bis-silylation product (75% yield, mono/bis =1/0.8, 15), but in the presence of an excess amount of Et₃SiH, only the bis-silylation product was obtained (97% yield, 18, Scheme 3). Pyridine-type heteroarenes were converted to the corresponding silylated products (68% yield for 20 and 71% yield for 21).¹⁰ Under the reaction conditions, the silylations of fused-heteroarenes were highly efficient to afford the desired products in 92–99% of isolated yield (13, 14, 22, and 23).

Furthermore, our preliminary result shows the feasibility of C-H silylation in the absence of a hydrogen acceptor, which is one step closer to a practical and cost-effective method that can be used at an industrial scale. Under the same catalytic system, but *without cyclohexene*, the C-H silylation of benzene and fluorobenzene proceeded to afford the desired products 1 and 10 in 64% and 79% yield, respectively (Scheme 4). Notably, this acceptorless protocol efficiently catalyzed the silylation of

Scheme 3. Dehydrogenative C–H Silylations of Various Arenes in THF^a



^{*a*}All reactions were performed under N₂. Yields were obtained after silica gel chromatography. ^{*b*}40h. ^{*c*}Four mol % Rh(nbd)₂BF₄ and 4.4 mol % L_3 were used. ^{*a*}2.2 equiv of Et₃SiH was used.

Scheme 4. Dehydrogenative C–H Silylations of Various Arenes without Hydrogen $\operatorname{Acceptor}^{a}$



^{*a*}All reactions were performed under N₂. Yields were determined by ¹H NMR analysis or GC-MS. ^{*b*}Reaction condition: 1 equiv of Et₃SiH, excess arene, no THF, 120 °C, 48 h. For **10**, o/m = 3.7/1. ^{*c*}Reaction condition: 1 equiv of heteroarene, 2.4 equiv of Et₃SiH, THF, 100 °C, 20 h. Corresponding 2,3-dihydrobenzofuran byproducts were obtained in 10% (with **13**) and 11% yield (with **22**).

heteroarenes to furnish the desired silylated benzofuran derivatives (13 and 22) in 90% and 89% yield, respectively.

In summary, we have developed efficient methods to synthesize various aryltriethylsilanes, which have complementary usage to arylsiloxanes^{8b,c} in silicon industry. In addition, these aryltriethylsilanes can be directly used for transition-metal-catalyzed cross-coupling reactions¹¹ and halogenation.¹² The method entails intermolecular C–H silylations of unactivated arenes and heteroarenes with three different reaction setups: (1) When arenes are structurally simple and cheaper than the silane, the reaction can be run with one equivalent of silane and excess amount of arenes without

employing solvent. (2) Only one equivalent of arene can be used in the case where arenes (especially heteroarenes) are valuable and have complex structures requiring multiple step synthesis. (3) As a preliminary result was shown, this protocol is feasible for the acceptorless C–H silylation. The regioselectivity of products is mainly affected by the steric bulk of the substituents on the arenes and by the electronic properties as a secondary factor.^{8b}

Mechanistic studies of this C–H silylation as well as further applications of the Rh-catalyzed system for various arenes and silanes are underway. Together with the silylations of HMTS, ^{8b,c} we believe, this protocol will enrich the research area of the C–H silylation by demonstrating the silylations of Et₃SiH with a broad arene scope.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b02806.

Detailed experimental procedures, compound characterization data, and NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Authors

*E-mail: kangsang.lee@dowcorning.com.

*E-mail: jongwook.choi@dowcorning.com.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank Dr. Zhanjie Li, Clark W. Swerdan, and Donald V. Eldred for helping with the NMR data collection and Alix L. Schmidt for initial catalyst screening.

REFERENCES

For reviews on the synthesis and utility of arylsilanes, see:
(a) Habich, D.; Effenberger, F. Synthesis 1979, 1979, 841–876.
(b) Jones, G. R.; Landais, Y. Tetrahedron 1996, 52, 7599–7662.
(c) Fleming, I.; Barbero, A.; Walter, D. Chem. Rev. 1997, 97, 2063–2192.
(d) Suginome, M.; Ito, Y. Chem. Rev. 2000, 100, 3221–3256.
(e) Somfai, P.; Seashore-Ludlow, B. In Comprehensive Organic Synthesis II; Knochel, P., Molander, G. A., Eds.; Elsevier B. V.: Amsterdam, The Netherlands, 2014; Vol. 1, p 27.
(f) Sun, D.; Ren, Z.; Bryce, M. R.; Yan, S. J. Mater. Chem. C 2015, 3, 9496–9508.

(2) For recent review on catalytic C-H silylations, see: (a) Hartwig, J. F. Acc. Chem. Res. 2012, 45, 864–873. (b) Cheng, C.; Hartwig, J. F. Chem. Rev. 2015, 115, 8946–8975. (c) Sharma, R.; Kumar, R.; Kumar, I.; Singh, B.; Sharma, U. Synthesis 2015, 47, 2347–2366. (d) Xu, Z.; Xu, L.-W. ChemSusChem 2015, 8, 2176–2179.

(3) Gustavson, W. A.; Epstein, P. S.; Curtis, M. D. Organometallics 1982, 1, 884–885.

(4) For examples on intramolecular C-H silylations of arenes or alkanes, see: (a) Furukawa, S.; Kobayashi, J.; Kawashima, T. J. Am. Chem. Soc. 2009, 131, 14192–14193. (b) Ureshino, T.; Yoshida, T.; Kuninobu, Y.; Takai, K. J. Am. Chem. Soc. 2010, 132, 14324–14326. (c) Simmons, E. M.; Hartwig, J. F. J. Am. Chem. Soc. 2010, 132, 17092–17095. (d) Simmons, E. M.; Hartwig, J. F. Nature 2012, 483, 70–73. (e) Kuninobu, Y.; Yamauchi, K.; Tamura, N.; Seiki, T.; Takai, K. Angew. Chem., Int. Ed. 2013, 52, 1520–1522. (f) Kuninobu, Y.; Nakahara, T.; Takeshima, H.; Takai, K. Org. Lett. 2013, 15, 426–428. (g) Kuznetsov, A.; Onishi, Y.; Inamoto, Y.; Gevorgyan, V. Org. Lett. 2013, 15, 2498–2501. (h) Murai, M.; Matsumoto, K.; Takeuchi, Y.; Takai, K. Org. Lett. 2015, 17, 3102–3105. (i) Murai, M.; Takeshima, H.; Morita, H.; Kuninobu, Y.; Takai, K. J. Org. Chem. 2015, 80, 5407– 5414. (j) Zhang, Q.-W.; An, K.; Liu, L.-C.; Yue, Y.; He, W. Angew. Chem., Int. Ed. 2015, 54, 6918-6921.

(5) For examples on intermolecular C-H silylations of arenes with directing groups, see: (a) Kakiuchi, F.; Matsumoto, M.; Tsuchiya, K.; Igi, K.; Hayamizu, T.; Chatani, N.; Murai, S. J. Organomet. Chem. 2003, 686, 134-144. (b) Ihara, H.; Suginome, M. J. Am. Chem. Soc. 2009, 131, 7502-7503. (c) Oyamada, J.; Nishiura, M.; Hou, Z. Angew. Chem., Int. Ed. 2011, 50, 10720-10723. (d) Mita, T.; Michigami, K.; Sato, Y. Org. Lett. 2012, 14, 3462-3465. (e) Choi, G.; Tsurugi, H.; Mashima, K. J. Am. Chem. Soc. 2013, 135, 13149-13161. (f) Kanyiva, K. S.; Kuninobu, Y.; Kanai, M. Org. Lett. 2014, 16, 1968-1971. (g) Takada, K.; Hanataka, T.; Namikoshi, T.; Watanabe, S.; Murata, M. Adv. Synth. Catal. 2015, 357, 2229-2232.

(6) For a report on intermolecular C-H silvlations of arenes without directing groups, see: (a) Sakakura, T.; Tokunaga, Y.; Sodeyama, T.; Tanaka, M. Chem. Lett. 1987, 16, 2375-2378. (b) Ishikawa, M.; Okazaki, S.; Naka, A.; Sakamoto, H. Organometallics 1992, 11, 4135-4139. (c) Ishikawa, M.; Sakamoto, H.; Okazaki, S.; Naka, A. J. Organomet. Chem. 1992, 439, 19-21. (d) Uchimaru, Y.; Elsayed, A. M. M.; Tanaka, M. Organometallics 1993, 12, 2065-2069. (e) Ezbiansky, K.; Djurovich, P. I.; LaForest, M.; Sinning, D. J.; Zayes, R.; Berry, D. H. Organometallics 1998, 17, 1455-1457. (f) Naka, A.; Lee, K. K.; Yoshizawa, K.; Yamabe, T.; Ishikawa, M. Organometallics 1999, 18, 4524-4529. (g) Ishiyama, T.; Sato, K.; Nishio, Y.; Miyaura, N. Angew. Chem., Int. Ed. 2003, 42, 5346-5348. (h) Saiki, T.; Nishio, Y.; Ishiyama, T.; Miyaura, N. Organometallics 2006, 25, 6068-6073. (i) Murata, M.; Fukuyama, N.; Wada, J.-i.; Watanabe, S.; Masuda, Y. Chem. Lett. 2007, 36, 910-911. (j) Ishiyama, T.; Saiki, T.; Kishida, E.; Sasaki, I.; Ito, H.; Miyaura, N. Org. Biomol. Chem. 2013, 11, 8162-8165. (k) Murai, M.; Takami, K.; Takai, K. Chem. - Eur. J. 2015, 21, 4566-4570.

(7) For examples on intermolecular silylations of C-H bonds in heteroarenes without directing groups, see: (a) Ishiyama, T.; Sato, K.; Nishio, Y.; Saiki, T.; Miyaura, N. Chem. Commun. 2005, 5065-5067. (b) Lu, B.; Falck, J. R. Angew. Chem., Int. Ed. 2008, 47, 7508-7510. (c) Sunada, Y.; Soejima, H.; Nagashima, H. Organometallics 2014, 33, 5936-5939. (d) Ref 8b and 8c. (e) Minami, Y.; Komiyama, T.; Hiyama, T. Chem. Lett. 2015, 44, 1065-1067. (f) Klare, H. F. T.; Oestreich, M.; Ito, J.-i.; Nishiyama, H.; Ohki, Y.; Tatsumi, K. J. Am. Chem. Soc. 2011, 133, 3312-3315. (g) Fedorov, A.; Toutov, A. A.; Swisher, N. A.; Grubbs, R. H. Chem. Sci. 2013, 4, 1640-1645. (h) Sasaki, M.; Kondo, Y. Org. Lett. 2015, 17, 848-851. (i) Toutov, A. A.; Liu, W.-B.; Betz, K. N.; Fedorov, A.; Stoltz, B. M.; Grubbs, R. H. Nature 2015, 518, 80-84.

(8) For Pt-catalyzed C-H silylations of Et₃SiH, see: (a) Tsukada, N.; Hartwig, J. F. J. Am. Chem. Soc. **2005**, 127, 5022–5023. For HMTSsilylations with the Rh- and Ir-catalyst system, see (b) Cheng, C.; Hartwig, J. F. Science **2014**, 343, 853–857. (c) Cheng, C.; Hartwig, J. F. J. Am. Chem. Soc. **2015**, 137, 592–595. For the mechanistic study for their Rh-catalyzed silylations, see (d) Cheng, C.; Hartwig, J. F. J. Am. Chem. Soc. **2014**, 136, 12064–12072. For the incompatibility of Ir-system with Et₃SiH, see (e) Supporting Information in ref 8c.

(9) (a) Ben-Ari, E.; Cohen, R.; Gandelman, M.; Shimon, L. J. W.; Martin, J. M. L.; Milstein, D. Organometallics **2006**, 25, 3190–3210. and references cited therein. (b) Evans, M. E.; Burke, C. L.; Yaibuathes, S.; Clot, E.; Eisenstein, O.; Jones, W. D. J. Am. Chem. Soc. **2009**, 131, 13464–13473.

(10) For the further utility of the silylation product of 2,6-lutidine in ligand synthesis, see Kuriyama, S.; Arashiba, K.; Nakajima, K.; Tanaka, H.; Kamaru, N.; Yoshizawa, K.; Nishibayashi, Y. *J. Am. Chem. Soc.* **2014**, *136*, 9719–9731.

(11) For recent reviews and examples on the cross couplings of arylsilanes, see (a) Funaki, K.; Kawai, H.; Sato, T.; Oi, S. *Chem. Lett.* **2011**, 40, 1050–1052. (b) Funaki, K.; Sato, T.; Oi, S. *Org. Lett.* **2012**, 14, 6186–6189. (c) Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. *Science* **2012**, 337, 1644–1648. For reviews, see (d) Hiyama, T. *J. Organomet. Chem.* **2002**, 653, 58–61. (e) Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, 40, 4893–4901.

(12) (a) Wilson, S. R.; Jacob, L. A. J. Org. Chem. **1986**, *51*, 4833–4836. (b) Zarate, C.; Martin, R. J. Am. Chem. Soc. **2014**, 136, 2236–2239.