Received: April 17, 2015 | Accepted: May 8, 2015 | Web Released: May 19, 2015 CL-150359

Editor's Choice

Straightforward Synthesis of HOMSi Reagents via sp^2 C–H Silylation

Yasunori Minami,*[1,2] Takeshi Komiyama,[3] and Tamejiro Hiyama*[1,2]
[1]*Research and Development Initiative, Chuo University, Kasuga, Bunkyo-ku, Tokyo 112-8551*
[2]*ACT-C, JST, Chiyoda-ku, Tokyo 102-0076*
[3]*Department of Applied Chemistry, Chuo University, Kasuga, Bunkyo-ku, Tokyo 112-8551*

(E-mail: yminami@kc.chuo-u.ac.jp, thiyama@kc.chuo-u.ac.jp)

Straightforward C–H silylation of heteroarenes and alkenes was found to provide efficient access to organo-HOMSi reagents as stable silicon reagents for cross-coupling. Various heteroarenes and terminal alkenes were silylated to show the versatility of the reaction. This method was applied in double silylation reactions to give bisHOMSi reagents. The silylation products could be used in the cross-coupling reaction with haloarenes easily.

Cross-coupling reaction for a targeted sp^{2}C–sp^{2}C bond formation has allowed us to construct a wide variety of functional π-electron-conjugated molecules. This system can be applied to cross-coupling polymerization to form π-electron-conjugated polymers for electronic devices such as conductive polymers, organic solar cells, and organic light-emitting diodes.[1] Thus, it is of great importance to readily provide user-friendly functionalized organometallic reagents with high solubility, stability, and reactivity.

Silicon-based reagents are among all useful for cross-coupling because of their stability, solubility, reactivity, and easy-handling and preparation.[2] We have already found that the tetraorganosilicon-type coupling reagents, organo-{2-(hydroxymethyl)phenyl}-dimethylsilanes (R–HOMSi) **4** are applicable to the synthesis of functionalized oligoarenes and polyarenes.[2f,2g,3] After cross-coupling, coproduced cyclic silyl ether **5** can be easily recovered and converted into **4** by treatment with organolithium or magnesium reagents.[4] Silyl ether **5** can also be transformed into hydroxy-protected H–HOMSi **1**, H–SiMe$_2${2-(PGOCH$_2$)C$_6$H$_4$} (PG: protecting group), via sequential reduction and protection.[3a] Thus, HOMSi-based coupling reaction enables us to construct π-electron-conjugated functional molecules with high performance and low waste. For achieving the straightforward and environmentally benign silicon-circulated cross-coupling protocol, it is essential to develop a simple and straightforward synthetic method for HOMSi. Thus, we focused on catalytic C–H silylation of (hetero)arenes using **1** without directing groups (Figure 1).[5,6] Herein, we report the synthesis of sp^{2}C–HOMSi reagents via straightforward silylation with an iridium catalyst.

Based on the previous findings by Murata,[6b] Falck,[6c] or Hartwig[6a,6d,6e] for C–H silylation without the assistance of directing groups, we assumed that iridium and rhodium-catalytic systems are suitable for the silylation using **1** because **1** seemed unstable in the presence of acids or cationic metal species, which might interact with the oxygen atom in **1** to cleave the C–O bond. First, we attempted a reaction of benzo[*b*]thiophene (**2a**) with 3 equiv of MOM-protected H–HOMSi **1a** under Falck's conditions: [Ir(OMe)(cod)]$_2$, dtbpy, and norbornene in THF at 80 °C,[6c] but only 9% yield of **3a** was obtained (Table 1, Run 1). The rhodium catalyst developed by Hartwig[6d] did not show any catalysis. This is probably because of the lower reactivity, steric bulkiness, and instability of **1a** derived from the pendant alkoxymethyl group. Therefore, to enhance the reactivity of **1a**, we screened various ligands, hydrogen acceptors, and solvents (see the SI, Table S1). We found that Me$_4$-phen as a more electron-donating ligand in higher concentration (2 M) of $i\mathrm{Pr}_2\mathrm{O}$ was effective for this iridium-catalyzed silylation to give **3a** in 75% isolated yield (Run 2). Moreover, the conditions allowed a low loading of both **1a** and norbornene without loss of efficiency. Other protecting groups were examined and THP (**1b**), SEM (**1c**), acetyl (**1d**), and pivaloyl (**1e**) did not interfere with the silylation of **2a** to give corresponding silanes (Runs 3–6).[7] Of note, hydrosilane-sensitive acetoxy and pivaloxy groups were used in the C–H silylation to give the corresponding 2-silylbenzothiophenes, albeit in modest yields (Runs 5 and 6). Especially, THP-protected HOMSi **3b** was obtained in the shortest reaction time in the highest (89%) yield probably owing to the stability of the THP group under the conditions (Run 3). Thus, we chose THP-protected **1b** as a silylating reagent and applied to reaction partners.

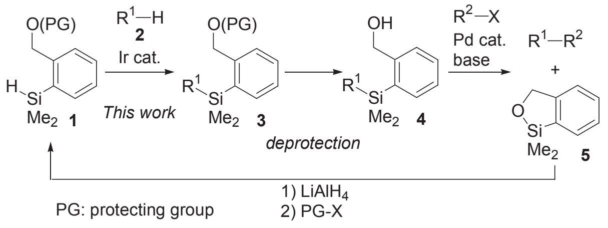
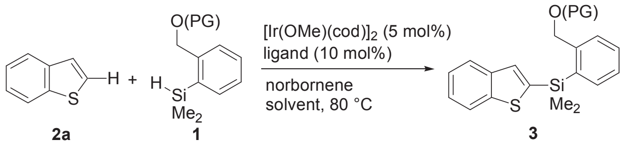


Figure 1. HOMSi-cycle for cross-coupling.

Table 1. Reaction of **2a** with **1**[a,b]

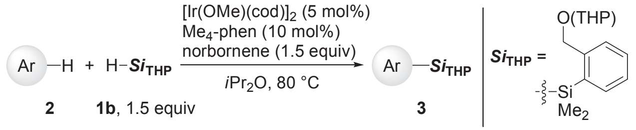


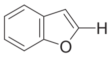
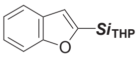
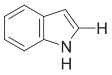
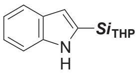
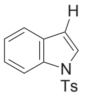
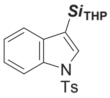
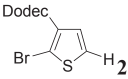
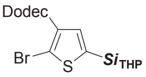
Run	**1**, PG (equiv)	Ligand	Solvent (M)	Time /h	Product, yield/%[c]
1	**1a**, MOM (3)	dtbpy	THF (0.2)	16	**3a**, 9[d]
2	**1a**, MOM (1.5)	Me$_4$-phen	$i\mathrm{Pr}_2\mathrm{O}$ (2)	48	**3a**, 75
3	**1b**, THP (1.5)	Me$_4$-phen	$i\mathrm{Pr}_2\mathrm{O}$ (2)	3	**3b**, 89
4	**1c**, SEM (1.5)	Me$_4$-phen	$i\mathrm{Pr}_2\mathrm{O}$ (2)	40	**3c**, 52
5	**1d**, Ac (1.5)	Me$_4$-phen	$i\mathrm{Pr}_2\mathrm{O}$ (2)	11	**3d**, 54
6	**1e**, Piv (1.5)	Me$_4$-phen	$i\mathrm{Pr}_2\mathrm{O}$ (2)	15	**3e**, 31

[a]Unless otherwise noted, a mixture of **1** (1.5–3 equiv), **2a** (1 equiv), [Ir(OMe)(cod)]$_2$ (0.05 equiv), ligand (0.1 equiv), and norbornene (3 equiv for Run 1, 1.5 equiv for Runs 2–6) in solvent was heated at 80 °C. [b]dtbpy: 4,4′-di-*tert*-butyl-2,2′-bipyridyl; Me$_4$-phen: 3,4,7,8-tetramethyl-1,10-phenanthroline; MOM: methoxymethyl; THP: 2-tetrahydropyranyl; SEM: 2-(trimethylsilyl)ethoxymethyl; Ac: acetyl; Piv: pivaloyl. [c]Isolated yield. [d]NMR yield.

Chem. Lett. **2015**, 44, 1065–1067 | doi:10.1246/cl.150359

Table 2. Silylation of aromatic C–H bond[a]



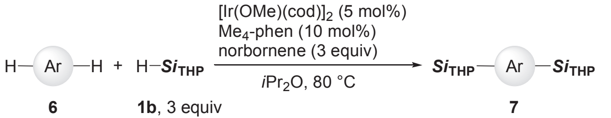
Run	2	Time/h	Product, yield/%[b]
1	 **2b**	9	 **3f**, 93
2	 **2c**	3	 **3g**, 44
3[c]	 **2d**	37	 **3h**, 29
4	 **2e**	5	 **3i**, 93

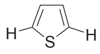
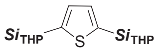
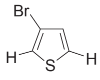
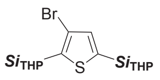
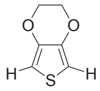
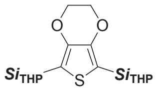
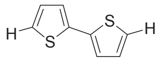
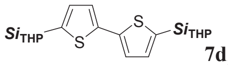
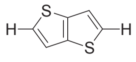
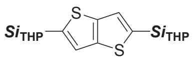
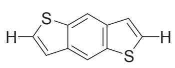
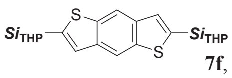
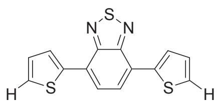
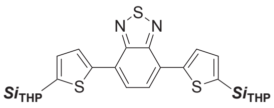
[a]Unless otherwise noted, a mixture of **2** (1 equiv), **1b** (1.5 equiv), [Ir(OMe)(cod)]$_2$ (0.05 equiv), Me$_4$-phen (0.1 equiv), norbornene (1.5 equiv), and *i*Pr$_2$O (2 M) was heated at 80 °C. [b]Isolated yield. [c]The conditions using dtbpy (0.1 equiv), *t*BuCH=CH$_2$ (1.5 equiv), and toluene (2 M) were employed.

Various arenes **2** were used in the silylation using **1b**, and the results are summarized in Table 2. Benzofuran (**2b**) was silylated at the C2 position to give **3f** in 93% yield (Run 1). Indole (**2c**) reacted to form the 2-silylated product **3g** in 44% yield (Run 2). In this case, the N–H bond did not interfere with the silylation, i.e., N–H silylation did not proceed. On the other hand, N-tosylated indole (**2d**) provided 3-silylated one **3h** in 29% yield under the conditions using dtbpy and *t*BuCH=CH$_2$ as a potent hydrogen acceptor in toluene (Run 3).[8] This C3-selectivity may be explained by the steric repulsion between the tosyl group and the silyl functionality, a metal migration from C2 to C3 after C–H activation at the C2 position, or a change in the reaction mechanism, as mentioned by Falck.[6c] 2-Brominated thiophene **2e** smoothly reacted with bromine intact to give the 5-silylated product **3i** in 93% yield, which seems to be a promising building block and a monomer for 3-alkylated thiophene (Run 4).

The successful mono C–H silylation conditions were next applied to the double silylation of thiophene-based functional pseudo-monomers, and the results are summarized in Table 3. The reaction of thiophene (**6a**) with 3 equiv of **1b** proceeded via double silylation to give 2,5-disilylthiophene **7a** in 47% yield (Run 1). To increase the yield of **7a**, we further screened ligands and hydrogen acceptors (SI, Table S2) and found that dtbpy and *t*BuCH=CH$_2$ gave **7a** in 60% yield although it took 92 h (Run 2).[9] 3-Bromothiophene (**6b**) was silylated at the 2- and 5-positions to give **7b** in 88% yield without affecting bromine (Run 3). 3,4-Ethylenedioxythiophene (**6c**) could be successfully converted to 2,5-bisHOMSi reagent **7c** in 98% yield (Run 4).[10] 2,2′-Bithiophene (**6d**), thieno[3,2-*b*]thiophene (**6e**), and benzo[1,2-*b*:4,5-*b*′]dithiophene (**6f**) provided the corresponding disilylated products **7d**, **7e**, and **7f** (Runs 5–7). In particular, gram-scale synthesis of **7f** (1.76 g) was readily achieved. 4,7-Bis(2-thienyl)benzothiadiazole (**6g**)[11] smoothly gave **7g** in 86% yield under the conditions using dtbpy and *t*BuCH=CH$_2$ (Run 8). Consequently, the double silylation approach allows easy preparation of HOMSi-based monomers, and thus the synthesis of π-conjugated polymers using the monomers and dihaloarenes will be straightforwardly carried out in due course.

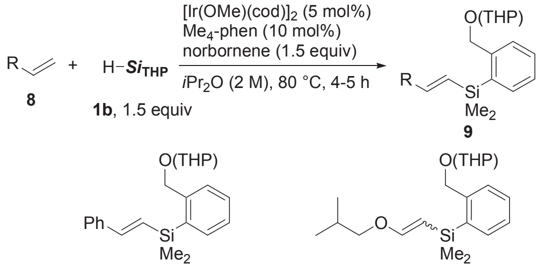
Table 3. Double silylation of aromatic C–H bonds[a]



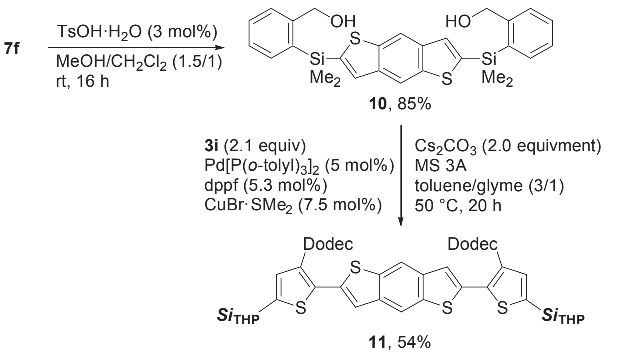
Run	1		Time /h	Product, yield/%[b]	
1		**6a**	6		**7a**, 47
2[c]		**6a**	92		**7a**, 60
3		**6b**	5		**7b**, 88
4		**6c**	5		**7c**, 98
5		**6d**	2		**7d**, 94
6		**6e**	4		**7e**, 50
7[d]		**6f**	5		**7f**, 86
8[c]		**6g**	86		**7g**, 86

[a]Unless otherwise noted, a mixture of **6** (1 equiv), **1b** (3 equiv), [Ir(OMe)(cod)]$_2$ (0.05 equiv), Me$_4$-phen (0.1 equiv), norbornene (3 equiv), and *i*Pr$_2$O (2 M) was heated at 80 °C. [b]Isolated yield. [c]The conditions using dtbpy (0.1 equiv) and *t*BuCH=CH$_2$ (3 equiv) were employed. [d]**6f** (3.0 mmol, 569 mg) and **1b** (9.0 mmol, 2.26 g) were used to give **7f** (2.57 mmol, 1.76 g).

Inspired by the direct silylation of alkenes,[12] we applied the present reaction to the synthesis of functionalized vinyl silanes (eq 1). Styrene (**8a**) was silylated to give the corresponding vinylsilane **9a** with *E*-selectivity. Next, we chose a vinyl ether as the starting material, which is a useful substrate for Lewis acid-catalyzed aldol reaction[13] and vinyl–O bond-cleaving cross-coupling.[14] We examined the silylation of isobutyl vinyl ether (**8b**) as a representative substrate and successfully obtained alkoxy vinyl HOMSi (**9b**) in 77% yield as a stereomixture ($E/Z = 16{:}1$).



9a, 98% (*E*/*Z* = >20:1) **9b**, 77% (*E*/*Z* = 16:1) (1)



Scheme 1. Deprotection/double cross-coupling.

Protected (hetero)aryl-HOMSi and alkenyl-HOMSi reagents are easily deprotected to give coupling-active HOMSi reagents. For example, treatment of THP-protected benzothienyl-HOMSi **3b** with *p*-toluenesulfonic acid in MeOH at room temperature produced active benzothienyl-HOMSi in 92% yield (see the SI, eq S1). Protected bisHOMSi **7f** could also be deprotected in MeOH and CH_2Cl_2 to give bisHOMSi **10** in 85% yield, which proceeded via double cross-coupling[3f] with bulky 2-bromo-3-dodecyl-5-silylthiophene **3i** to successfully form 2,6-dithienylbenzodithiophene bisHOMSi reagent **11** as a functionalized monomer for solar cells (Scheme 1).[15]

In conclusion, we have demonstrated that the C–H silylation of heteroarenes and terminal alkenes with hydrosilanes is the convenient and straightforward tool for the synthesis of heteroaryl- and alkenyl-HOMSi reagents. This method allows us to synthesize various bisHOMSi reagents, which are useful as building blocks toward π-conjugated functional molecules. The proper choice of ligand and hydrogen acceptor is the key to successful silylation. The produced organo-HOMSi reagents are immediately utilized in cross-coupling with haloarenes.

This work has been supported financially by a Grant-in-Aids for Scientific Research (S) (No. 21225005 to T.H.) and Young Scientists (B) (No. 25870747 to Y.M.) from JSPS and Sumitomo Chemical Foundation. Y.M. also acknowledges Asahi Glass Foundation.

Supporting Information is available electronically on J-STAGE.

References and Notes

1 For selected reviews of cross-coupling polymerization, see: a) J. Sakamoto, M. Rehahn, G. Wegner, A. D. Schlüter, *Macromol. Rapid Commun.* **2009**, *30*, 653. b) M. J. Robb, S.-Y. Ku, C. J. Hawker, *Adv. Mater.* **2013**, *25*, 5686. c) B. Carsten, F. He, H. J. Son, T. Xu, L. Yu, *Chem. Rev.* **2011**, *111*, 1493. d) Z. J. Bryan, A. J. McNeil, *Macromolecules* **2013**, *46*, 8395. e) T. Yokozawa, Y. Nanashima, Y. Ohta, *ACS Macro Lett.* **2012**, *1*, 862.

2 a) T. Hiyama, in *Metal-Catalyzed Cross-Coupling Reactions*, ed. by F. Diederich, P. J. Stang, Wiley-VCH, Weinheim, **1998**, Chap. 10, pp. 421–453. doi:10.1002/9783527612222.ch10. b) T. Hiyama, E. Shirakawa, in *Cross-Coupling Reactions* in *Topics in Current Chemistry*, ed. by N. Miyaura, Springer, **2002**, Vol. 219, pp. 61–85. doi:10.1007/3-540-45313-X_3. c) S. E. Denmark, R. F. Sweis, in *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed., ed. by A. de Meijere, F. Diederich, Wiley-VCH, Weinheim, **2004**, Chap. 4, pp. 163–216. doi:10.1002/9783527619535.ch4. d) J. Tsuji, in *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*, John Wiley & Sons, Chichester, **2004**, pp. 338–351. e) W.-T. T. Chang, R. C. Smith, C. S. Regens, A. D. Bailey, N. S. Werner, S. E. Denmark, in *Organic Reactions*, ed. by S. E. Denmark, Wiley-VCH, New Jersey, **2011**, Vol. 75, pp. 213–746. doi:10.1002/0471264180.or075.03. f) Y. Nakao, T. Hiyama, *J. Synth. Org. Chem., Jpn.* **2011**, *69*, 1221. g) Y. Nakao, T. Hiyama, *Chem. Soc. Rev.* **2011**, *40*, 4893. h) H. F. Sore, W. R. J. D. Galloway, D. R. Spring, *Chem. Soc. Rev.* **2012**, *41*, 1845.

3 a) Y. Nakao, H. Imanaka, A. K. Sahoo, A. Yada, T. Hiyama, *J. Am. Chem. Soc.* **2005**, *127*, 6952. b) Y. Nakao, A. K. Sahoo, A. Yada, J. Chen, T. Hiyama, *Sci. Technol. Adv. Mater.* **2006**, *7*, 536. c) Y. Nakao, J. Chen, M. Tanaka, T. Hiyama, *J. Am. Chem. Soc.* **2007**, *129*, 11694. d) J. Chen, M. Tanaka, A. K. Sahoo, M. Takeda, A. Yada, Y. Nakao, T. Hiyama, *Bull. Chem. Soc. Jpn.* **2010**, *83*, 554. e) S. Tang, M. Takeda, Y. Nakao, T. Hiyama, *Chem. Commun.* **2011**, *47*, 307. f) K. Shimizu, Y. Minami, Y. Nakao, K. Ohya, H. Ikehira, T. Hiyama, *Chem. Lett.* **2013**, *42*, 45.

4 R–HOMSi **4** can be alternatively prepared by metal-catalyzed silylation of haloarenes with hydrosilanes or disilanes, and rearrangement of 2-silyloxymethylbromobenzene to give protected R–HOMSi **3**, followed by deprotection. See: a) M. Iizuka, Y. Kondo, *Eur. J. Org. Chem.* **2008**, 1161. b) Y. Minami, K. Shimizu, C. Tsuruoka, T. Komiyama, T. Hiyama, *Chem. Lett.* **2014**, *43*, 201. c) P. F. Hudrlik, A. M. Hudrlik, Y. A. Jeilani, *Tetrahedron* **2011**, *67*, 10089.

5 For a review of silylation of unactivated C–H bonds, see: C. Cheng, J. F. Hartwig, *Chem. Rev.* **2015**, Article ASAP. doi:10.1021/cr5006414.

6 For examples of sp^{2}C–H silylation by hydrosilanes without directing groups, see: a) N. Tsukada, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 5022. b) M. Murata, N. Fukuyama, J. Wada, S. Watanabe, Y. Masuda, *Chem. Lett.* **2007**, *36*, 910. c) B. Lu, J. R. Falck, *Angew. Chem., Int. Ed.* **2008**, *47*, 7508. d) C. Cheng, J. F. Hartwig, *Science* **2014**, *343*, 853. e) C. Cheng, J. F. Hartwig, *J. Am. Chem. Soc.* **2015**, *137*, 592. f) M. Murai, K. Takami, K. Takai, *Chem.—Eur. J.* **2015**, *21*, 4566. g) M. Murai, K. Takami, H. Takeshima, K. Takai, *Org. Lett.* **2015**, *17*, 1798.

7 It should be mentioned that unprotected H–HOMSi is hard to isolate. For example, treatment of **1b** with TsOH in methanol always forms **5**. Attempted silylation of **2a** with H–SiMe$_2$(2-LiOCH$_2$)C$_6$H$_4$ generated from **5** and $LiAlH_4$ failed.

8 The standard conditions which employs [Ir(OMe)(cod)]$_2$, Me$_4$-phen, and norbornene in *i*Pr$_2$O reduced yield of **3h**.

9 Monosilylated thiophene could not be isolated, suggesting that the monosilylated thiophene is much more reactive than thiophene.

10 a) S. Akoudad, J. Roncali, *Chem. Commun.* **1998**, 2081. b) L. Huchet, S. Akoudad, E. Levillain, J. Roncali, A. Emge, P. Bäuerle, *J. Phys. Chem. B* **1998**, *102*, 7776. c) C. A. Thomas, K. Zong, K. A. Abboud, P. J. Steel, J. R. Reynolds, *J. Am. Chem. Soc.* **2004**, *126*, 16440. d) C. B. Nielsen, A. Angerhofer, K. A. Abboud, J. R. Reynolds, *J. Am. Chem. Soc.* **2008**, *130*, 9734. e) G. Trippé-Allard, J.-C. Lacroix, *Tetrahedron* **2013**, *69*, 861.

11 Recent reports for 4,7-dithienylbenzothiadiazole-based copolymers, see: a) P. Zhou, Z.-G. Zhang, Y. Li, X. Chen, J. Qin, *Chem. Mater.* **2014**, *26*, 3495. b) A. Saeki, S. Yoshikawa, M. Tsuji, Y. Koizumi, M. Ide, C. Vijayakumar, S. Seki, *J. Am. Chem. Soc.* **2012**, *134*, 19035.

12 a) Y. Seki, K. Takeshita, K. Kawamoto, S. Murai, N. Sonoda, *J. Org. Chem.* **1986**, *51*, 3890. b) B. Lu, J. R. Falck, *J. Org. Chem.* **2010**, *75*, 1701. c) C. Cheng, E. M. Simmons, J. F. Hartwig, *Angew. Chem., Int. Ed.* **2013**, *52*, 8984.

13 Y. Nishimoto, H. Ueda, M. Yasuda, A. Baba, *Angew. Chem., Int. Ed.* **2012**, *51*, 8073.

14 a) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346. b) L.-G. Xie, Z.-X. Wang, *Chem.—Eur. J.* **2011**, *17*, 4972. c) Y. Ogiwara, M. Tamura, T. Kochi, Y. Matsuura, N. Chatani, F. Kakiuchi, *Organometallics* **2014**, *33*, 402. d) T. Iwasaki, Y. Miyata, R. Akimoto, Y. Fujii, H. Kuniyasu, N. Kambe, *J. Am. Chem. Soc.* **2014**, *136*, 9260.

15 N. Wang, Z. Chen, W. Wei, Z. Jiang, *J. Am. Chem. Soc.* **2013**, *135*, 17060.