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Rhodium-Catalyzed Cycloisomerization of 2-Silylethynyl Phenols and Anilines via 1,2-Silicon Migration

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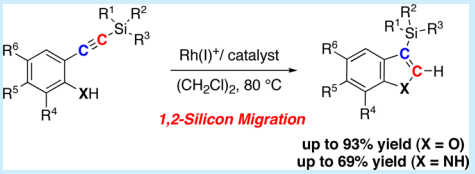
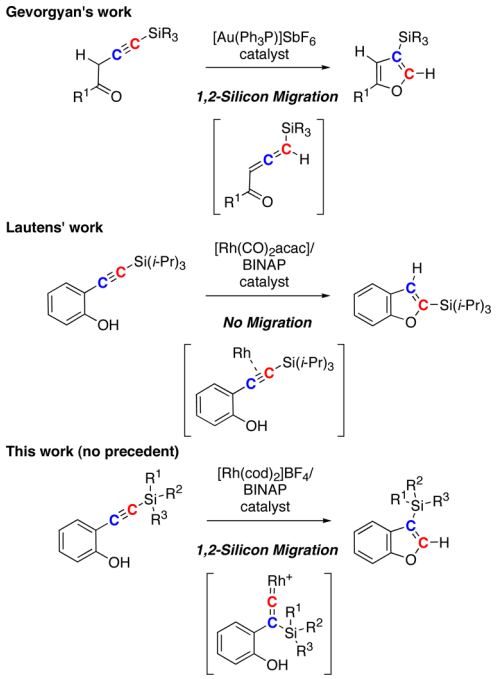
Supporting Information

ABSTRACT: It has been established that a cationic rhodium(I)/BINAP complex catalyzes the cycloisomerization of 2-silylethynylphenols, leading to 3-silylbenzofurans, via 1,2-silicon migration. Similarly, the cycloisomerization of 2-silylethynylanilines, leading to 3-silylindoles, via 1,2-silicon migration was catalyzed by a cationic rhodium(I)/H_8–BINAP complex.



The transition-metal-catalyzed cycloisomerization is a useful method for the construction of complex carbocyclic and heterocyclic frameworks.[1] For the synthesis of heterocycles, the intramolecular heterocyclization of alkynes and allenes is one of the most useful and reliable methods.[2] In order to synthesize heterocycles with unusual substitution patterns, the heterocyclization involving molecular rearrangements is attractive.[3] For example, Gevorgyan reported the gold(I)-catalyzed cycloisomerization of 4-silyl homopropargylic ketones to 3-silylfurans involving 1,2-silicon migration (Scheme 1, top).[4,5]

Scheme 1



Experimental and theoretical mechanistic studies revealed that this cycloisomerization proceeds through allenyl ketone intermediates.[4] On the other hand, Lautens reported the cycloisomerization of a 2-silylethynyl phenol via electrophilic activation of the alkyne moiety by a highly electron-deficient rhodium(I) complex as a catalyst (Scheme 1, middle).[6] Importantly, this reaction afforded not a 3-silylbenzofuran but a 2-silylbenzofuran without 1,2-silicon migration. In this paper, we disclose the unprecedented catalytic cycloiosomerization of 2-silylethynyl phenols and anilines, leading to 3-silylbenzofurans and 3-silylindoles, involving 1,2-silicon migration presumably through rhodium vinylidene intermediates (Scheme 1, bottom).[7,8]

Recently, our research group reported the modular synthesis of triphenylenes by the cationic rhodium(I)/H_8–BINAP complex-catalyzed [2 + 2 + 2] cycloaddition of bipheyl-linked diynes with alkynes.[9] In this cycloaddition, a silyl-substituted propargyl alcohol was an excellent cycloaddition partner.[9] This result prompted us to investigate the reaction of bipheyl-linked diyne and 2-silylethynyl phenol **1a**. Surprisingly, not the expected cycloaddition product but cycloisomerization product **2a** involving 1,2-silicon migration was obtained as a major product (Scheme 2).[10]

The reaction of **1a** in the absence of bipheyl-linked diyne under the above-mentioned reaction conditions afforded **2a** as a sole product, although the reaction was sluggish (Table 1, entry 1). Thus, the optimization of reaction conditions for the cycloisomerization of **1a** to **2a** was examined. In this study, active catalysts were prepared through removal of the cod ligand by hydrogenation. Screening of bisphosphine ligands (Figure 1, entries 1–6) revealed that the use of BINAP affords **2a** in the highest yield (entry 1). The yields of **2a** depend on the electron density of biaryl bisphoshine ligands (entries 1–4).

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Scheme 2

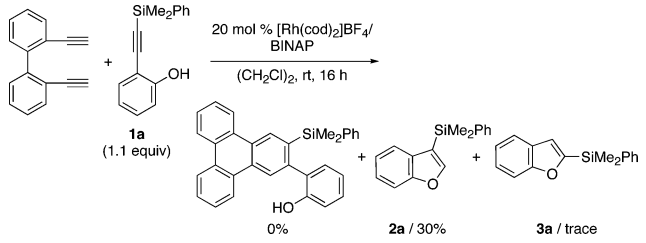
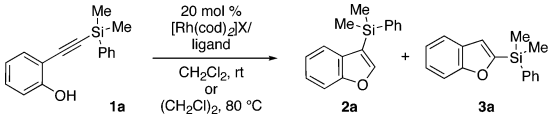


Table 1. Optimization of Reaction Conditions for Cycloisomerization of 2-Silylethynyl Phenol 1a[a]



					yield (%)[b]	
entry	ligand	X	conditions	conv (%)	2a	3a
1	BINAP	BF_4	rt, 16 h	58	54	0
2	BIPHEP	BF_4	rt, 16 h	33	25	0
3	H_8–BINAP	BF_4	rt, 16 h	23	19	0
4	Segphos	BF_4	rt, 16 h	7	0	0
5	dppf	BF_4	rt, 16 h	0	0	0
6	dppb	BF_4	rt, 16 h	14	0	0
7	BINAP	SbF_6	rt, 16 h	59	53	0
8	BINAP	OTf	rt, 16 h	21	8	0
9	BINAP	$BAr^F{}_4$[c]	rt, 16 h	73	63	0
10[d]	BINAP	BF_4	80 °C, 1 h	93	90	0
11[e,f]	BINAP	BF_4	80 °C, 16 h	94	40	42
12[e,f]	–	BF_4	80 °C, 16 h	81	7	71

[a] $[Rh(cod)_2]X$ (0.010 mmol), ligand (0.010 mmol), **1a** (0.050 mmol), and CH_2Cl_2 (1.0 mL) were used. Active catalysts were prepared through hydrogenation (1 atm, rt). [b] Isolated yield. [c] Ar^F = 3,5-$(CF_3)_2C_6H_3$. [d] $[Rh(cod)_2]BF_4$ (0.010 mmol), BINAP (0.010 mmol), **1a** (0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used. [e] $CH_2Cl)_2$ (1.0 mL) was used. [f] Without hydrogenation.

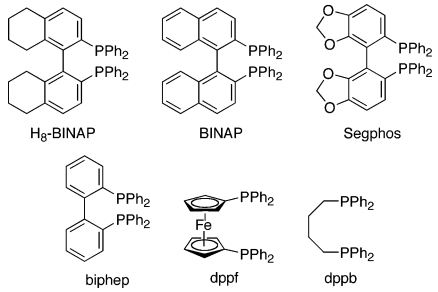


Figure 1. Structures of bisphospnine ligands.

Screening of counteranions (entries 1 and 7–9) revealed that the use of BF_4 and SbF_6 showed comparable good results (entries 1 and 7). The use of $BAr^F{}_4$ showed the highest conversion of **1a**, while the selectivity of **2a** was lower than those of BF_4 and SbF_6 (entry 9). Finally, when using BINAP as a ligand and BF_4 as a counteranion at elevated temperature (80 °C), high conversion of **1a** was reached within 1 h using 5 mol % of the catalyst to give **2a** in 90% yield (entry 10). Interestingly, when the catalyst was used without hydrogenation, a 1:1 mixture of **2a** and **3a** was obtained (entry 11). The use of $[Rh(cod)_2]BF_4$ without hydrogenation significantly increased the yield of **3a** (entry 12). Other π-electrophilic transition-metal complexes $[RhCl(PPh_3)_3/AgBF_4$, $[Ir(cod)_2]$-BF_4/BINAP, $[Pd(MeCN)_4](BF_4)_2$/BINAP, $PtCl_2/2AgBF_4$, $AgBF_4$, $AuCl(SMe_2)$/0.5BINAP, $[Au(PPh_3)]SbF_6]$ were also tested, while all of these were ineffective for this migratory cycloisomerization.

With the optimized reaction conditions in hand, we explored the scope of this cycloisomerization as shown in Figure 2. With

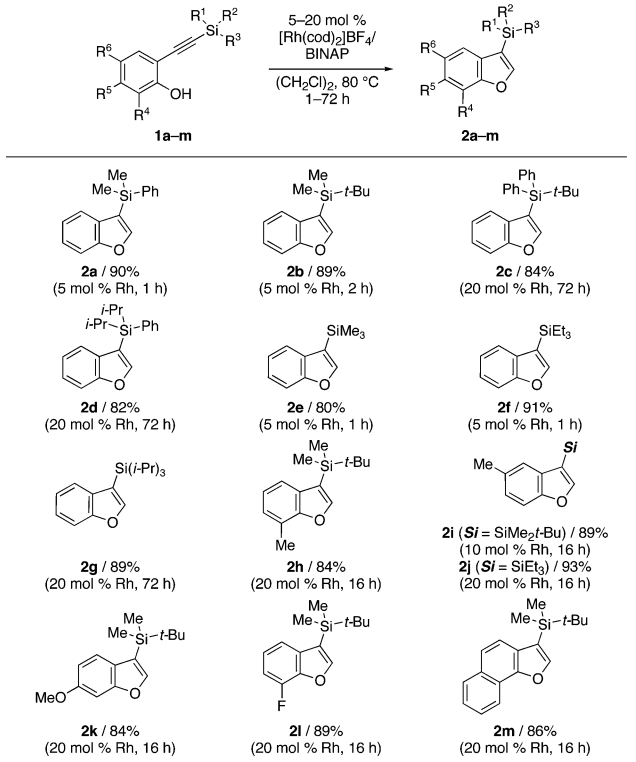
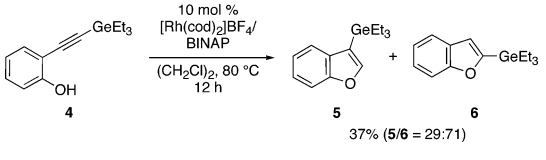


Figure 2. Rhodium-catalyzed cycloisomerization of 2-silylethynyl phenols **1a–m**. $[Rh(cod)_2]BF_4$ (0.010–0.040 mmol), BINAP (0.010–0.040 mmol), **1** (0.20 mmol), and $(CH_2Cl)_2$ (1.0 mL) were used. The cited yields are of the isolated products.

respect to the substituents at the silicon atom (R^1–R^3), not only dimethylphenyl (**1a**) but also *tert*-butyldimethyl (**1b**), *tert*-butyldiphenyl (**1c**), diisopropylphenyl (**1d**), trimethyl (**1e**), triethyl (**1f**), and triisopropyl (**1g**) groups could be employed for this reaction, although high catalyst loadings were required for sterically demanding substrates **1c** and **1d**. With respect to the substituents at the benzene ring (R^4–R^6), various substituted 3-silylbenzofurans **2h–m** were obtained in high yields, although high catalyst loadings were required.

The reaction of germyl analogue **4** was also examined as shown in Scheme 3.[11] In this case, normal cycloisomerization product **6** was obtained in higher yield than 1,2-germanium migration product **5**.

Scheme 3



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Org. Lett. XXXX, XXX, XXX–XXX

Next, we examined the rhodium-catalyzed cycloisomerization of 2-silylethynyl anilines **7** as shown in Figure 3.[12] In this case,

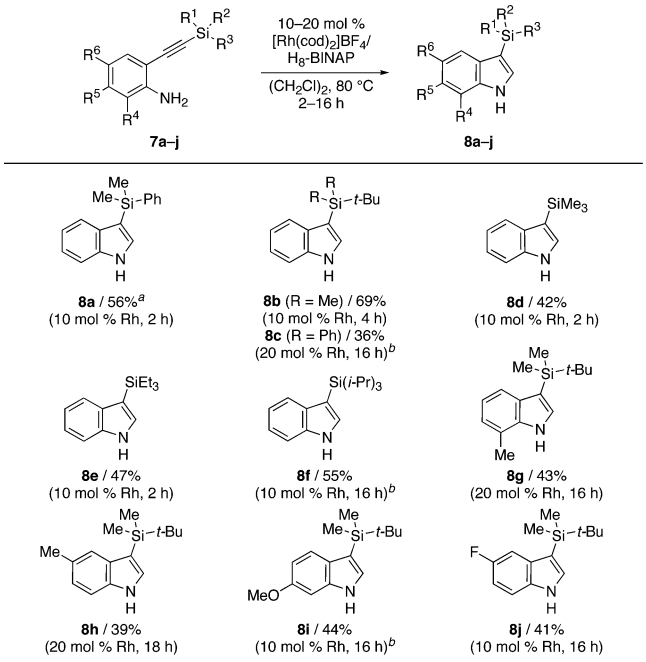
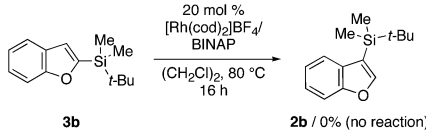


Figure 3. Rhodium-catalyzed cycloisomerization of 2-silylethynyl anilines **7a–j**. $[Rh(cod)_2]BF_4$ (0.020–0.040 mmol), H_8–BINAP (0.020–0.040 mmol), **7** (0.20 mmol), and $(CH_2Cl)_2$ (8.0 mL) were used. The cited yields are of the isolated products. [a] Isolated as a mixture of **8a** and 1H-indole. [b] $(CH_2Cl)_2$ (4.0 mL) was used.

H_8–BINAP was found to be the best ligand and diluted conditions were employed in order to suppress desilylation of 3-silylindole products **8**. Similar to the cycloisomerization of 2-silylethynyl phenols **1**, varying substitution at the silicon atom (R^1–R^3) and benzene rings (R^4–R^6) was tolerable. However, yields of 1,2-silicon migration products **8** (3-silylindoles) were moderate due to the formation of normal cycloisomerization products **9** (2-silylindoles) as byproducts.[13] Importantly, the use of H_8–BINAP in place of BINAP increased the yields of 3-silylindoles **8** and decreased the yields of 2-silylindoles **9**.[14]

In order to determine a possible reaction mechanism, the following experiments were conducted. The reaction of **3b** in the presence of the rhodium catalyst did not afford 1,2-silicon migration product **2b**, and **3b** was recovered unchanged (Scheme 4).

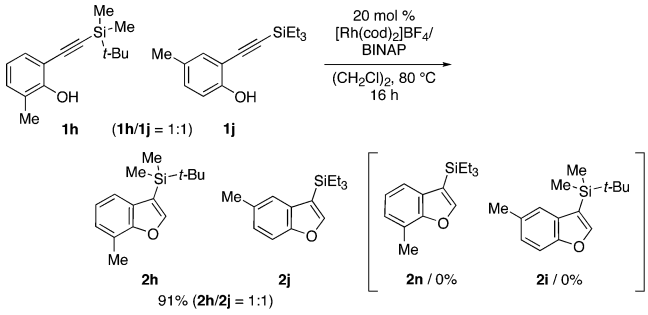
Scheme 4



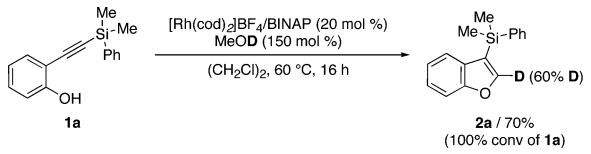
The reaction of a 1:1 mixture of **1h** and **1i** afforded a 1:1 mixture of **2h** and **2j**, and crossover products **2n** and **2i** were not generated at all (Scheme 5). This result suggests that the present cycloisomerization is an intramolecular process.

Finally, the reaction of **1a** in the presence of MeOD furnished **2a**, in which the 2-position was partially deuterated (Scheme 6).

Scheme 5

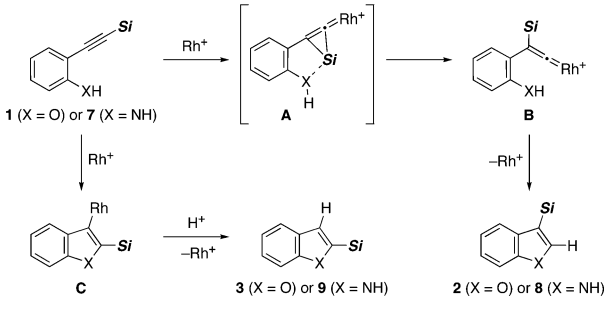


Scheme 6



Based on these observations, a possible mechanism for the rhodium-catalyzed cycloisomerization of 2-silylethynyl phenol **1** and aniline **7** is shown in Scheme 7. 2-Silylethynyl phenol **1**

Scheme 7



reacts with a cationic rhodium(I) complex to generate rhodium vinylidene **B**[15] presumably through transition state **A** which is stabilized by interaction between the phenol oxygen atom and the migrating silicon atom.[16] Subsequent oxycyclization affords **2**. On the other hand, **3** can be generated via formation of alkenyl-rhodium **C** followed by protonation. The same mechanism can be applied to the formation of **8** and **9**, while a weak interaction between the aniline nitrogen atom and the migrating silicon atom might decrease the yield of 1,2-silicon migration product **8** and increase the yield of normal cycloisomerization product **9**. In addition, the more nucleophilic nature of the amino group than the hydroxy group results in rapid cyclization to form **9** prior to the vinylidene formation. The poor ability of the electron-rich rhodium(I)/H_8–BINAP catalyst toward the electrophilic alkyne activation might account for suppression of the formation of normal cycloisomerization products **9**.

The synthetic utility of 3-silylbenzofurans is demonstrated in Scheme 8. Treatment of **2e** with ICl afforded a new compound, 3-iodobenzofuran (**10**), which cannot be obtained by iodination of benzofuran,[17] in good yield.[18]

In conclusion, we have established that a cationic rhodium(I)/BINAP complex catalyzes cycloisomerization of 2-silylethynylphenols, leading to 3-silylbenzofurans, via 1,2-silicon migration. Similarly, cycloisomerization of 2-silylethynyl-

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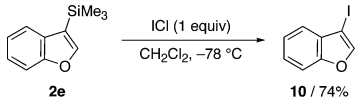
Scheme 8



anilines, leading to 3-silylindoles, via 1,2-silicon migration was catalyzed by a cationic rhodium(I)/H_8–BINAP complex. Future work will focus on further exploration of the cationic rhodium(I) complex-catalyzed cycloisomerization reactions involving molecular rearrangements.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00529.

X-ray crystallographic file (CIF)
Experimental procedures and compound characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected recent reviews of the transition-metal-catalyzed cycloisomerization, see: (a) Fang, G.; Bi, X. *Chem. Soc. Rev.* **2015**, *44*, 8124. (b) Neff, R. K.; Frantz, D. E. *Tetrahedron* **2015**, *71*, 7. (c) Michelet, V. In *Comprehensive Organic Synthesis II*; Knochel, P., Molander, G. A., Eds.; Elsevier: 2014; Vol. 5, p 1483. (d) Fürstner, A. *Acc. Chem. Res.* **2014**, *47*, 925. (e) Keilitz, J.; Malik, H. A.; Lautens, M. *Top. Heterocycl. Chem.* **2013**, *32*, 187. (f) Yamamoto, Y. *Chem. Rev.* **2012**, *112*, 4736. (g) Fehr, C. *Synlett* **2012**, *23*, 990. (h) Aubert, C.; Fensterbank, L.; Garcia, P.; Malacria, M.; Simonneau, A. *Chem. Rev.* **2011**, *111*, 1954.

(2) For reviews of the transition-metal-catalyzed intramolecular heterocyclization of alkynes and allenes, see: (a) Ayers, B. J.; Chan, P. W. H. *Synlett* **2015**, *26*, 1305. (b) Mancuso, R.; Gabriele, B. *Molecules* **2014**, *19*, 15687. (c) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084. (d) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994. (e) Alcaide, B.; Almendros, P.; Alonso, J. M. *Org. Biomol. Chem.* **2011**, *9*, 4405. (f) Weibel, J. M.; Blanc, A.; Pale, P. *Chem. Rev.* **2008**, *108*, 3149.

(3) For reviews of the transition-metal-catalyzed intramolecular heterocyclization involving molecular rearrangements, see: (a) Jana, N.; Driver, T. G. *Org. Biomol. Chem.* **2015**, *13*, 9720. (b) Egi, M.; Akai, S. *Heterocycles* **2015**, *91*, 931. (c) Tőrincsi, M.; Hornyánszky, G.; Kolonits, P.; Novák, L. *Period. Polytech., Chem. Eng.* **2015**, *59*, 16. (d) Fensterbank, L.; Malacria, M. *Acc. Chem. Res.* **2014**, *47*, 953. (e) Alcaide, B.; Almendros, P. *Acc. Chem. Res.* **2014**, *47*, 939. (f) Obradors, C.; Echavarren, A. M. *Acc. Chem. Res.* **2014**, *47*, 902. (g) Shiroodi, R. K.; Gevorgyan, V. *Chem. Soc. Rev.* **2013**, *42*, 4991. (h) Crone, B.; Kirsch, S. F. *Chem. - Eur. J.* **2008**, *14*, 3514.

(4) Dudnik, A. S.; Xia, Y.; Li, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 7645.

(5) For other examples of the transition-metal-catalyzed intramolecular heterocyclization involving 1,2-silicon migration, see: (a) Shiroodi, R. K.; Vera, C. I. R.; Dudnik, A. S.; Gevorgyan, V. *Tetrahedron Lett.* **2015**, *56*, 3251. (b) Xia, Y.; Dudnik, A. S.; Li, Y.; Gevorgyan, V. *Org. Lett.* **2010**, *12*, 5538. (c) Mochida, K.; Shimizu, M.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 8350. (d) Dankwardt, J. W. *Tetrahedron Lett.* **2001**, *42*, 5809.

(6) Boyer, A.; Isono, N.; Lackner, S.; Lautens, M. *Tetrahedron* **2010**, *66*, 6468.

(7) A single example of the rhodium-catalyzed cycloisomerization of a siloxy-linked 1,7-enyne was reported. The authors proposed that this process proceeds via the rhodium vinylidene intermediate generated through 1,2-silicon migration. See: Kim, H.; Lee, C. *J. Am. Chem. Soc.* **2005**, *127*, 10180.

(8) A single example of the rhodium-catalyzed cycloisomerization of homopropargylic alcohols to dihydrofurans was reported. The authors proposed that this process proceeds via the rhodium vinylidene intermediate generated through 1,2-hydrogen migration. See: Trost, B. M.; Rhee, Y. H. *J. Am. Chem. Soc.* **2003**, *125*, 7482.

(9) Murayama, K.; Sawada, Y.; Noguchi, K.; Tanaka, K. *J. Org. Chem.* **2013**, *78*, 6202.

(10) The gas-phase thermal cycloisomerization (750 °C) of 2-trimethylsilylethynyl phenol to 3-trimethylsilylbenzofuran involving 1,2-silicon migration was reported; see: Barton, T. J.; Groh, B. L. *J. Org. Chem.* **1985**, *50*, 158.

(11) For the transition-metal-catalyzed intramolecular heterocyclization involving 1,2-germanium migration, see: Seregin, I. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2006**, *128*, 12050.

(12) For the transition-metal-catalyzed intramolecular heterocyclization of aniline derivatives involving molecular rearrangements, see: (a) Yeung, C. F.; Chung, L. H.; Lo, H. S.; Chiu, C. H.; Cai, J.; Wong, C. Y. *Organometallics* **2015**, *34*, 1963. (b) Abbiati, G.; Marinelli, F.; Rossi, E.; Arcadi, A. *Isr. J. Chem.* **2013**, *53*, 856.

(13) The normal cycloisomerization products, 2-silylindoles **9**, were detected in ca. 10–30% yields as byproducts.

(14) See Table S1 of the Supporting Information.

(15) For the formation of rhodium vinylidenes from internal silylacetylenes, see: (a) Katayama, H.; Onitsuka, K.; Ozawa, F. *Organometallics* **1996**, *15*, 4642. (b) Werner, H.; Baum, M.; Schneider, D.; Windmueller, B. *Organometallics* **1994**, *13*, 1089. (c) Werner, H.; Schneider, D.; Schulz, M. *J. Organomet. Chem.* **1993**, *451*, 175.

(16) In the formation of rhodium vinylidene complexes from a 8-quinolinolato rhodium(I) complex and terminal alkynes, stabilization of the transition state by interaction between the oxygen atom and the migrating hydrogen atom is proposed by the DFT calculation. See: (a) Dang, Y.; Qu, S.; Wang, Z.-X.; Wang, X. *Organometallics* **2013**, *32*, 2804. For a report of the orginal reaction, see: (b) Kondo, M.; Kochi, T.; Kakiuchi, F. *J. Am. Chem. Soc.* **2011**, *133*, 32.

(17) For examples of 2-lithiation followed by iodination of benzofurans giving 2-iodobenzofurans, see: (a) Usui, S.; Hashimoto, Y.; Morey, J. V.; Wheatley, A. E. H.; Uchiyama, M. *J. Am. Chem. Soc.* **2007**, *129*, 15102. (b) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 7048.

(18) For examples of iodination of benzofurans by iodine monochloride, giving 2-iodobenzofurans, see: Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326.

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Org. Lett. XXXX, XXX, XXX–XXX