

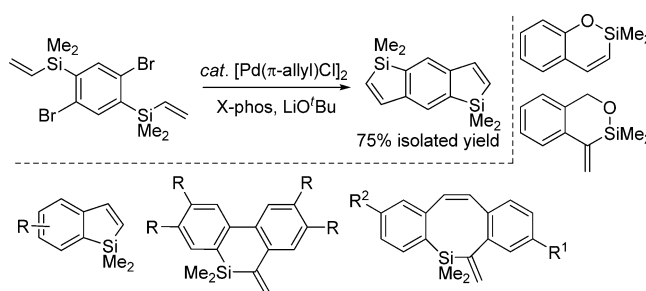
Construction of Benzosiloles, Six- and Eight-Membered Silacyclic Skeletons, via a Pd-Catalyzed Intramolecular Mizoroki–Heck Reaction of Vinylsilanes

Kunbing Ouyang,^{†,‡} Yun Liang,[§] and Zhenfeng Xi^{*,‡}

Beijing National Laboratory for Molecular Sciences (BNLMS), and Institute of Chemistry, Chinese Academy of Sciences (CAS), Beijing 100190, China, Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China, and Key Laboratory of Chemical Biology and Traditional Chinese Medicine Research, Ministry of Education, Hunan Normal University, Changsha, Hunan 410081, China
zfxi@pku.edu.cn

Received July 23, 2012

ABSTRACT



A variety of silacycles including benzosiloles, six- and eight-membered silacyclic skeletons, were efficiently synthesized via a Pd-catalyzed intramolecular Mizoroki–Heck reaction of vinylsilanes.

Silicon possesses some crucial differences from carbon (e.g., covalent radius and electronegativity). Thus, when a carbon atom is replaced by a silicon atom (the C/Si switch), the chemical and physicochemical properties of an organic compound may be changed dramatically.^{1–7} For example, silacyclopentadiene (often named silole) as organic material

of electronic and opto-electronic devices demonstrates greater superiority compared to its carbon-analogue, cyclopentadiene.^{3,4} In particular, the C/Si switch strategy has been applied successfully for odorant design^{5,6} and pharmaceutical applications.⁷ Furthermore, specific properties can be expected from totally new silicon-containing

[†] Institute of Chemistry, CAS.

[‡] Peking University.

[§] Hunan Normal University.

(1) For reviews on the synthesis and properties of silacyclic compounds, see: (a) Wang, L.; Duan, Z. *Chin. Sci. Bull.* **2012** in press. (b) Cusak, A. *Chem.—Eur. J.* **2012**, *18*, 5800–5824. (c) Bracegirdle, C.; Anderson, E. A. *Chem. Soc. Rev.* **2010**, *39*, 4114–4129. (d) Rousseau, G.; Blanco, L. *Tetrahedron* **2006**, *62*, 7951–7993. (e) Liu, J.; Zhang, S.; Zhang, W.-X.; Xi, Z. *Prog. Chem.* **2009**, *21*, 1475–1486. (f) Liu, J.; Zhang, W.-X.; Xi, Z. *Chin. J. Org. Chem.* **2009**, *29*, 491–503. (g) Fensterbank, L.; Malacria, M.; Sieburth, S. M. *Synthesis* **1997**, *8*, 813–854. (h) Dubac, J.; Laporterie, A.; Manuel, G. *Chem. Rev.* **1990**, *90*, 215–263. (i) Hermanns, J.; Schmidt, B. *J. Chem. Soc., Perkin Trans. 1* **1999**, 81–102. (j) Hermanns, J.; Schmidt, B. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2209–2230.

(2) For examples on the synthesis of silacyclic compounds, see: (a) Greene, M. A.; Prevost, M.; Tolopilo, J.; Woerpel, K. A. *J. Am. Chem. Soc.* **2012**, *134*, 12482–12484. (b) François, C.; Boddaert, T.; Durandetti, M.; Querolle, O.; van Hijfte, L.; Meerpoel, L.; Angibaud, P.; Maddaluno, J. *Org. Lett.* **2012**, *14*, 2074–2077. (c) Lazareva, N. F.; Albanov, A. I.; Shainyan, B. A.; Kleinpeter, E. *Tetrahedron* **2012**, *68*, 1097–1104. (d) Seiser, T.; Cramer, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 10163–10167. (e) Hernandez, D.; Nielsen, L.; Lindsay, K. B.; Lopez-Garcia, M. A.; Bjerlund, K.; Skrydstrup, T. *Org. Lett.* **2010**, *12*, 3528–3531. (f) Blaszykowski, C.; Brancour, C.; Dhiman, A. C.; Tensterbank, L.; Malacria, M. *Eur. J. Org. Chem.* **2009**, *11*, 1674–1678. (g) Lim, Y. M.; Lee, M. E. *Organometallics* **2008**, *27*, 1000–1004. (h) Wei, X.; Taylor, R. J. K. *Tetrahedron Lett.* **2003**, *44*, 7143–7146. (i) Mansel, S.; Rief, U.; Prosenc, M.-H.; Kirsten, R.; Brintzinger, H.-H. *J. Organomet. Chem.* **1996**, *512*, 225–236. (j) Alper, H.; Wolin, M. S. *J. Org. Chem.* **1975**, *40*, 437–438.

compounds, of which the carbon analogues cannot be synthesized or are very difficult to make. Thus, as a consequence, the development of synthetic methods for silacyclic compounds remains one of the most important frontiers in synthetic chemistry.^{1–7}

Vinyl silane is an important building block for constructing C–C bonds along with desilylation of the remaining silyl moiety.^{8–10} As shown in Scheme 1, vinylsilanes have been used in the Hiyama cross-coupling reaction to make C–C bonds using the silyl group as a leaving group.⁸

(3) For reviews on siloles, see: (a) Shimizu, M.; Hiyama, T. *Synlett* **2012**, 23, 973–989. (b) Corey, J. Y. *Adv. Organomet. Chem.* **2011**, 59, 1–180. (c) Corey, J. Y. *Adv. Organomet. Chem.* **2011**, 59, 181–328. (d) Liu, J.; Lam, J. W. Y.; Tang, B. Z. *J. Inorg. Organomet. Polym.* **2009**, 19, 249–285. (e) Chen, J.; Cao, Y. *Macromol. Rapid Commun.* **2007**, 28, 1714–1742. (f) Yamaguchi, S.; Xu, C.; Okamoto, T. *Pure Appl. Chem.* **2006**, 78, 721–730. (g) Hissler, M.; Dyer, P. W.; Réau, R. *Coord. Chem. Rev.* **2003**, 244, 1–44. (h) Yamaguchi, S.; Tamao, K. *J. Organomet. Chem.* **2002**, 653, 223–228. (i) Yamaguchi, S.; Tamao, K. *J. Chem. Soc., Dalton Trans.* **1998**, 22, 3693–3702.

(4) For selected examples on benzosiloles, see: (a) Liang, Y.; Geng, W.; Wei, J.; Xi, Z. *Angew. Chem., Int. Ed.* **2012**, 51, 1934–1937. (b) Liang, Y.; Zhang, S.; Xi, Z. *J. Am. Chem. Soc.* **2011**, 133, 9204–9207. (c) Shimizu, M.; Mochida, K.; Katoh, M.; Hiyama, T. *Sci. China Chem.* **2011**, 54, 1937–1947. (d) Shimizu, M.; Mochida, K.; Hiyama, T. *J. Phys. Chem. C* **2011**, 115, 11265–11274. (e) Liu, J.; Zhong, Y.; Lam, J. W. Y.; Lu, P.; Hong, Y.; Yu, Y.; Yue, Y.; Faisal, M.; Sung, H. H. Y.; Williams, I. D.; Wong, K. S.; Tang, B. Z. *Macromolecules* **2010**, 43, 4921–4936. (f) Mochida, K.; Shimizu, M.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, 131, 8350–8351. (g) Hudrlik, P. F.; Dai, D.; Hudrlik, A. M. *J. Organomet. Chem.* **2006**, 691, 1257–1264. (h) Wang, Z.; Fang, H.; Xi, Z. *Tetrahedron Lett.* **2005**, 46, 499–501. (i) Xu, C.; Wakamiya, A.; Yamaguchi, S. *J. Am. Chem. Soc.* **2005**, 127, 1638–1639. (j) Hoshi, T.; Nakamura, T.; Suzuki, T.; Ando, M.; Hagiwara, H. *Organometallics* **2000**, 19, 4483–4487. (k) Barton, T. J.; Groh, B. L. *Organometallics* **1985**, 4, 575–580.

(5) For reviews, see: (a) Tacke, R.; Metz, S. *Chem. Biodiversity* **2008**, 5, 920–941. (b) Doszczak, L.; Gasperi, T.; Saint-Dizier, A.; Loreto, M. A.; Enders, D. In *Perspectives in Flavor and Fragrance Research*; Kraft, P., Swift, K. A. D., Eds.; Verlag Helvetica Chimica Acta: Zurich, Wiley-VCH: Weinheim, 2005; pp 89–103. (c) Frater, G.; Bajgrowicz, J. A.; Kraft, P. *Tetrahedron* **1998**, 54, 7633–7703.

(6) For selected examples, see: (a) Ghosh, P.; Shabat, D.; Kumar, S.; Sinha, S. C.; Grynspan, F.; Li, J.; Noodleman, L.; Keinan, E. *Nature* **1996**, 382, 339–341. (b) Wannagat, U.; Munstedt, R.; Harder, U. *Liebigs Ann. Chem.* **1985**, 5, 950–958. (c) Wrobel, D.; Tacke, R.; Wannagat, U.; Harder, U. *Chem. Ber.* **1982**, 115, 1694–1704.

(7) (a) Tacke, R.; Bertermann, R.; Burschka, C.; Dörrich, S.; Fischer, M.; Müller, B.; Meyerhans, G.; Schepmann, D.; Wunsch, B.; Arnason, I.; Björnsson, R. *ChemMedChem* **2012**, 7, 523–532. (b) Meanwell, N. A. *J. Med. Chem.* **2011**, 54, 2529–2591. (c) Helder, S. A.; Luis, B. M.; Vesa-Pekka, L.; Anu, A. J.; Jarno, S.; Jouni, H. *Curr. Drug Discovery Technol.* **2011**, 8, 228–249. (d) Franz, A. K. *Curr. Opin. Drug Discovery Dev.* **2007**, 10, 654–671. (e) Bains, W.; Tacke, R. *Curr. Opin. Drug Discovery Dev.* **2003**, 6, 526–543. (f) Showell, G. A.; Mills, J. S. *Drug Discov. Today* **2003**, 8, 551–556. (g) Heinonen, P.; Sipilä, H.; Neuvonen, K.; Lönnberg, H.; Cockcroft, V. B.; Wurster, S.; Virtanen, R.; Savola, M. K. T.; Salonen, J. S.; Savola, J. M. *Eur. J. Med. Chem.* **1996**, 31, 725–729.

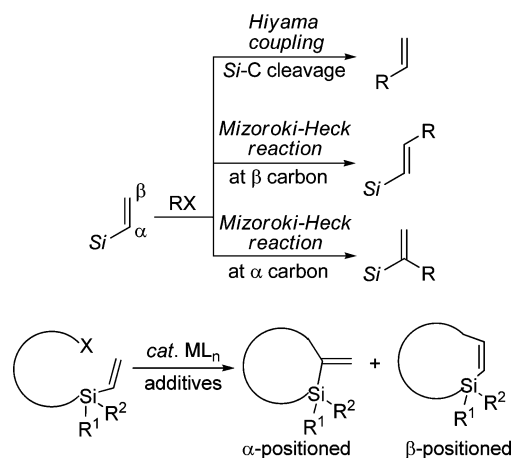
(8) (a) *The Mizoroki–Heck Reaction*; Oestrin, M., Eds.; John Wiley & Sons, Ltd.: Germany, 2009. (b) Hiyama, T. *J. Organomet. Chem.* **2002**, 653, 58–61. (c) Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Chapter 10. (d) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, 53, 920–923.

(9) Teng, Z.; Keese, R. *Helv. Chim. Acta* **1999**, 82, 515–521.

(10) (a) Czech, A.; Ganicz, T.; Noskowska, M.; Stanczyk, W. A.; Szelag, A. *J. Organomet. Chem.* **2009**, 694, 3386–3389. (b) Pawluc, P.; Hreczycho, G.; Suchecki, A.; Kubicki, M.; Marciniec, B. *Tetrahedron* **2009**, 65, 5497–5502. (c) Lo, M. Y.; Sellinger, A. *Synlett* **2006**, 18, 3009–3012. (d) Battace, A.; Zair, T.; Doucet, H.; Santelli, M. *J. Organomet. Chem.* **2005**, 690, 3790–3802. (e) Itami, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, 123, 11577–11585. (f) Itami, K.; Mitsudo, K.; Kamei, T.; Koike, T.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2000**, 122, 12013–12014. (g) Jeffery, T. *Tetrahedron Lett.* **1999**, 40, 1673–1676. (h) Yamashita, H.; Roan, B. L.; Tanaka, M. *Chem. Lett.* **1990**, 2175–2176. (i) Karabelas, K.; Hallberg, A. *Tetrahedron Lett.* **1985**, 26, 3131–3132. (j) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, 50, 3896–3900.

Conceptually, the Mizoroki–Heck reaction is a good choice to make C–C bonds while the silyl group remains in the product.^{8a,9,10} Thus, silacyclic skeletons can be constructed via an intramolecular Mizoroki–Heck reaction of vinylsilanes (Scheme 1).⁹ However, it is rarely reported that vinylsilane participates in the Mizoroki–Heck reaction.^{9,10} Among all those examples reported on intermolecular Mizoroki–Heck reactions, formation of new C–C bonds at the β -position of vinylsilane is predominate.¹⁰ To the best of our knowledge, there is only one example of the formation of a C–C bond at the α -position of vinylsilane.⁹ Meanwhile, this is also the only report of an intramolecular Mizoroki–Heck reaction leading to a five-membered silacyclic ring as a byproduct in < 30% yield.⁹

Scheme 1. Hiyama Cross-Coupling and Mizoroki–Heck Reaction of Vinylsilanes; Construction of Silacycles via a Intramolecular Mizoroki–Heck Reaction



We have recently reported the synthesis of silole derivatives via Pd-catalyzed cleavage of the Si–Me bond and the formation of six-membered silacycles via Pd-catalyzed cleavage of the silyl C(sp³)–H bond (Scheme 2).^{4a,b,11} As a continuation of our interest in this transition-metal catalyzed cleavage of the Si–C(sp³) bond and the silyl C(sp³)–H bond, we investigated silyl compounds of different substituents on the silicon center. Interestingly, as given in Scheme 2, when compound **1a** substituted with a SiMe₃ group was changed to compound **1b** substituted with a SiMe₂(CH=CH₂) group, neither product **2** nor product **4** was obtained under the same reaction conditions. Instead, a new compound **3** obviously formed via the intramolecular Mizoroki–Heck reaction, which was obtained in 28% and 50% yields, respectively. This new finding prompted us to study this intramolecular Mizoroki–Heck reaction. Here, we report our results on the synthesis of various silacycles including benzosiloles, six- and eight-membered silacyclic skeletons, via a Pd-catalyzed intramolecular Mizoroki–Heck reaction. Either the α - or β -positioned C–C bond

(11) Liang, Y.; Geng, W.; Wei, J.; Ouyang, K.; Xi, Z. *Org. Biomol. Chem.* **2012**, 10, 1537–1542.

forming reaction proceeded highly selectively depending on the structures of the products.

Scheme 2. Different Reactions around a Silyl Group

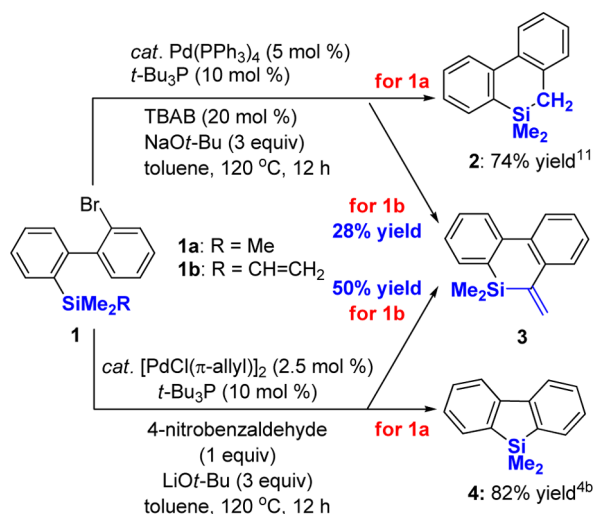


Table 1. Optimization of Reaction Conditions (see Supporting Information for details)

entry	[Pd]	ligand	base	solvent	yield of 3 (%) ^a
1	PdCl ₂	<i>t</i> -Bu ₃ P	LiOt-Bu	toluene	42
2	PdCl ₂	XPhos	LiOt-Bu	toluene	57
3	Pd ₂ (dba) ₃	<i>t</i> -Bu ₃ P	LiOt-Bu	toluene	30
4	Pd ₂ (dba) ₃	XPhos	LiOt-Bu	toluene	73
5	Pd(PPh ₃) ₄	<i>t</i> -Bu ₃ P	LiOt-Bu	toluene	28
6	Pd(PPh ₃) ₄	XPhos	LiOt-Bu	toluene	26
7	A ^b	<i>t</i> -Bu ₃ P	LiOt-Bu	toluene	(69)
8	A	XPhos	LiOt-Bu	toluene	92(90)
9	A	PCy ₃	LiOt-Bu	toluene	58
10	A	DPEPhos	LiOt-Bu	toluene	46
11	A	none	LiOt-Bu	toluene	44
12	A	XPhos	NaOt-Bu	toluene	23
13	A	XPhos	KOt-Bu	toluene	trace
14	A	XPhos	NEt ₃	toluene	trace
15	A	XPhos	LiOt-Bu	CH ₂ Cl ₂	61
16	A	XPhos	LiOt-Bu	CH ₃ CN	59
17	A	XPhos	LiOt-Bu	DMF	48

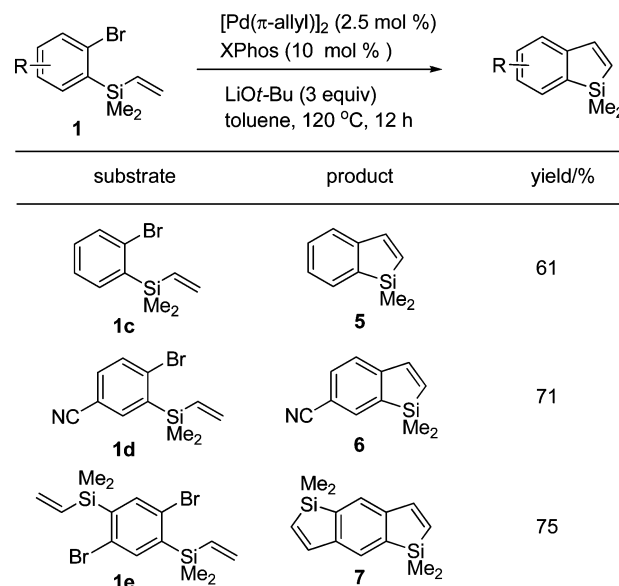
^a GC yield (C₁₂H₂₆ as internal standard), isolated yields are in parentheses. ^b A: [PdCl(π-allyl)]₂.

First, various reaction conditions were screened (see Table 1 and Supporting Information for details). Optimal reaction conditions were realized as follows: [PdCl(π-allyl)]₂

(2.5 mol %), XPhos (10 mol %), LiOt-Bu (3 equiv), toluene, 120 °C, 12 h. Under these optimized conditions, the six-membered silacyclic compound **3** was obtained in 90% isolated yield (entry 8). Obviously, this compound **3** is formed via the intramolecular Mizoroki–Heck reaction at the α-position of the vinylsilyl moiety. No β-positioned C–C coupling product was observed. This perfect α-positioned selectivity is probably due to the higher stability of the six-membered silacyclic ring.

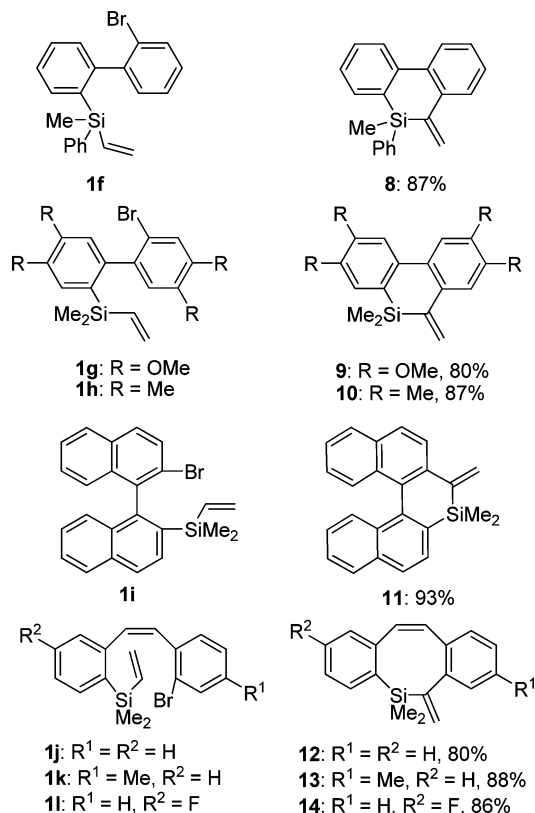
With the above optimized reaction conditions in hand, we tested various bromides containing vinylsilyl moieties, such as 2-bromo(vinylsilyl)benzenes **1c–e**. As given in Scheme 3, benzosilole derivatives **5** and **6** could be obtained in good isolated yields. A ladder-type π-conjugated molecule **7** could also be prepared in 75% isolated yield by this reaction from **1e**. Benzosiloles are important compounds in materials chemistry.^{3,4} This method provides an efficient alternative route to such compounds. It is obvious that in these cases the intramolecular Mizoroki–Heck reaction takes place at the β-position of the vinylsilyl moiety. No α-positioned C–C coupling product was obtained. This perfect β-positioned selectivity is probably due to the stable silole rings.

Scheme 3. Formation of Benzosiloles via the Intramolecular Mizoroki–Heck Reaction at the β-Position of the Vinylsilyl Moiety



In contrast to the substrates **1c–1e** which underwent the intramolecular Mizoroki–Heck reaction at the β-position of the vinylsilyl moiety, substrates **1f–1i** afforded their α-positioned C–C coupling products containing a six- or eight-membered silacyclic ring (Scheme 4), which are similar to the reaction of **1b**. As shown in Scheme 4, compound **1f**, which contains a silyl group substituted with a methyl, phenyl, and vinyl, undergoes a similar intramolecular Mizoroki–Heck reaction, affording its corresponding six-membered silacyclic product **8** in 87%

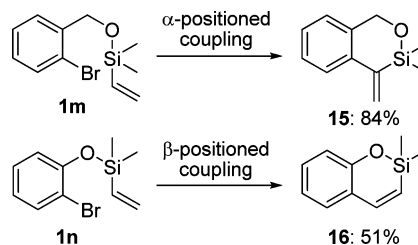
Scheme 4. Formation of Six- and Eight-Membered Silacyclic Rings via the Intramolecular Mizoroki–Heck Reaction at the α -Position of the Vinylsilane Moiety



isolated yield. The biphenyl derivatives **1g** and **1h** and the binaphthal derivative **1i** could all be used to give their corresponding six-membered silacyclic products **9–11**, respectively. Notably, the eight-membered silacyclic compounds **12–14** could be also obtained highly efficiently via the above reaction. For all these cases, the α -positioned selectivity was exclusive.

Oxasilacycles are compounds of synthetic interest.^{1b,c,2a,c,d,f} As given in Scheme 5, under the above

Scheme 5. Formation of Six-Membered Oxasilacyclic Rings via the Intramolecular Mizoroki–Heck Reaction at the α - or β -Position of the Vinylsilane Moiety



optimized reaction conditions, compound **1m** afforded the six-membered oxasilacycle **15** in 84% isolated yield as the sole product. Interestingly, compound **1n** also gave a six-membered oxasilacycle **16** as the sole product. Obviously, these two substrates **1m** and **1n** reacted at different positions of the vinylsilane moiety, which could be attributed to the stability of the six-membered rings.

In summary, we developed an efficient Pd-catalyzed intramolecular Mizoroki–Heck reaction of vinylsilanes to construct benzosiloles, six- and eight-membered silacyclic skeletons. The stability of the formed silacyclic rings controlled the reaction sites (α - or β -position) of the vinylsilane moieties. This method provides an efficient route to benzosilole derivatives, six- and eight-membered silacyclic compounds.

Acknowledgment. This work was supported by the Natural Science Foundation of China and the 973 Program (2012CB821600).

Supporting Information Available. Experimental details and scanned NMR spectra of all new products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.