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

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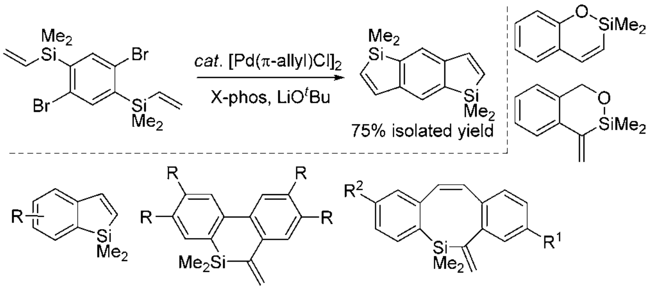
## ABSTRACT



**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

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(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.; Dhimane, 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.

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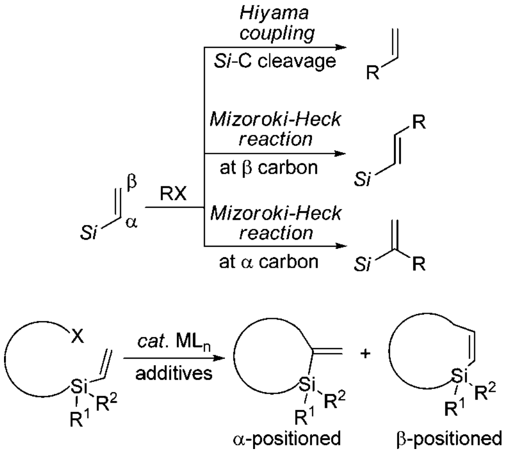
compounds, of which the carbon analogues cannot be synthesized or are very difficult to make. Thus, as a consequence, the development of synthetic methods for silacyclic compounds remains one of the most important frontiers in synthetic chemistry.[1−7]

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] 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 $\beta$-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 $C_{(sp^3)}$−H bond (Scheme 2).[4a,b,11] As a continuation of our interest in this transition-metal catalyzed cleavage of the Si−$C_{(sp^3)}$ bond and the silyl $C_{(sp^3)}$−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 $SiMe_3$ group was changed to compound **1b** substituted with a $SiMe_2(CH{=}CH_2)$ 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 $\beta$-positioned C−C bond

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(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.; Grynszpan, 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.; Wünsch, B.; Arnason, I.; Bjornsson, 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.; Cockroft, 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*; Oestrtin, 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.

(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

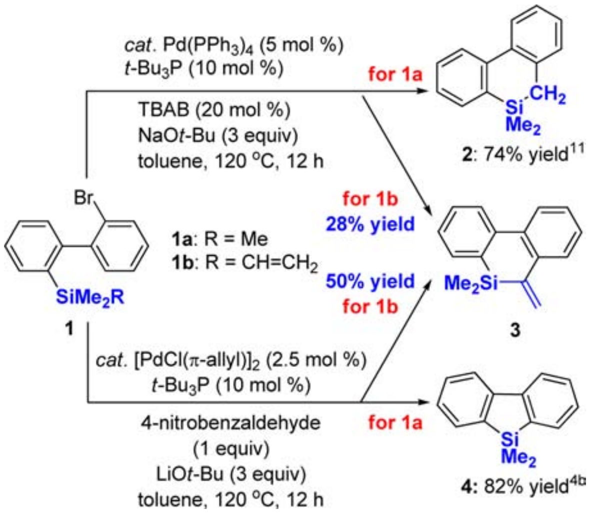
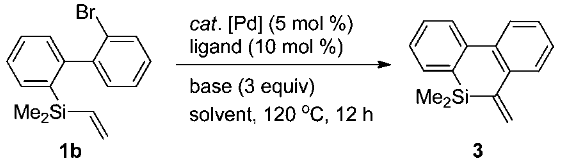


**Table 1.** Optimization of Reaction Conditions (see Supporting Information for details)



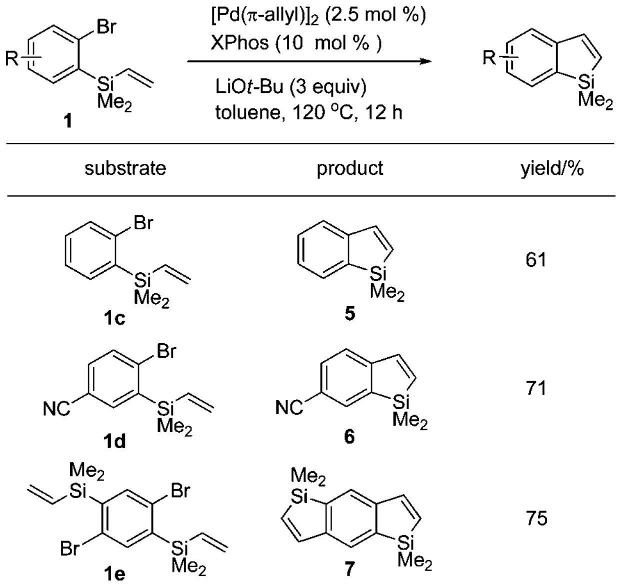
| entry | [Pd] | ligand | base | solvent | yield of **3** (%)[a] |
|---|---|---|---|---|---|
| 1 | $PdCl_2$ | *t*-$Bu_3P$ | LiO*t*-Bu | toluene | 42 |
| 2 | $PdCl_2$ | XPhos | LiO*t*-Bu | toluene | 57 |
| 3 | $Pd_2(dba)_3$ | *t*-$Bu_3P$ | LiO*t*-Bu | toluene | 30 |
| 4 | $Pd_2(dba)_3$ | XPhos | LiO*t*-Bu | toluene | 73 |
| 5 | $Pd(PPh_3)_4$ | *t*-$Bu_3P$ | LiO*t*-Bu | toluene | 28 |
| 6 | $Pd(PPh_3)_4$ | XPhos | LiO*t*-Bu | toluene | 26 |
| 7 | A[b] | *t*-$Bu_3P$ | LiO*t*-Bu | toluene | (69) |
| 8 | A | XPhos | LiO*t*-Bu | toluene | 92(90) |
| 9 | A | $PCy_3$ | LiO*t*-Bu | toluene | 58 |
| 10 | A | DPEPhos | LiO*t*-Bu | toluene | 46 |
| 11 | A | none | LiO*t*-Bu | toluene | 44 |
| 12 | A | XPhos | NaO*t*-Bu | toluene | 23 |
| 13 | A | XPhos | KO*t*-Bu | toluene | trace |
| 14 | A | XPhos | $NEt_3$ | toluene | trace |
| 15 | A | XPhos | LiO*t*-Bu | $CH_2Cl_2$ | 61 |
| 16 | A | XPhos | LiO*t*-Bu | $CH_3CN$ | 59 |
| 17 | A | XPhos | LiO*t*-Bu | DMF | 48 |

[a] GC yield ($C_{12}H_{26}$ as internal standard), isolated yields are in parentheses. [b] A: $[PdCl(\pi\text{-allyl})]_2$.

First, various reaction conditions were screened (see Table 1 and Supporting Information for details). Optimal reaction conditions were realized as follows: $[PdCl(\pi\text{-allyl})]_2$ (2.5 mol %), XPhos (10 mol %), LiO*t*-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 vinylsilane 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.

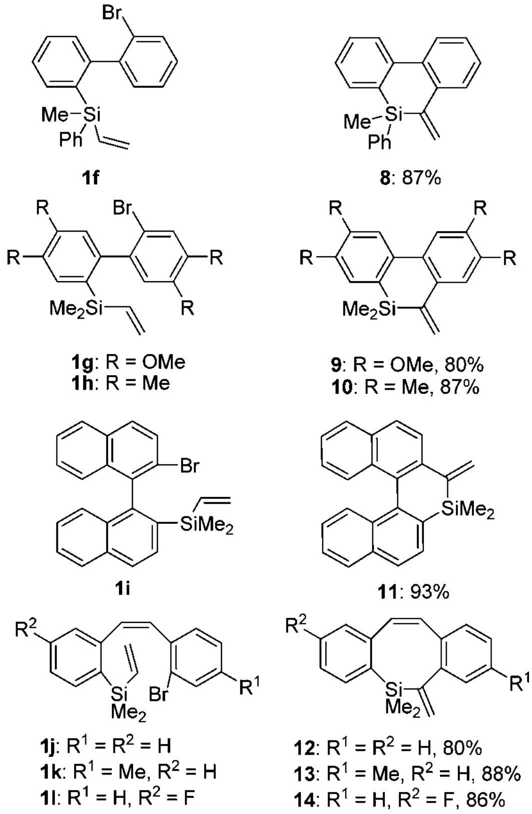
With the above optimized reaction conditions in hand, we tested various bromides containing vinylsilane moieties, such as 2-bromo(vinylsilyl)benzenes **1c**–**e**. As given in Scheme 3, benzosilole derivatives **5** and **6** could be obtained in good ioslated yields. A ladder-type $\pi$-conjugated molecule **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 vinylsilane 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 Vinylsilane Moiety



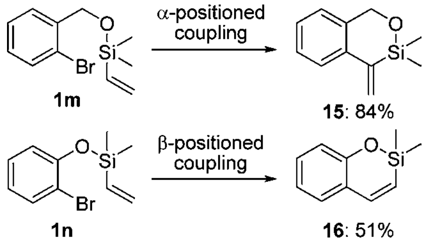
In contrast to the substrates **1c**–**1e** which underwent the intramolecular Mizoroki–Heck reaction at the *β*-position of the vinylsilane moiety, substrates **1f**–**1l** afforded their α-positioned C–C coupling products containing a six- or eight-membered silacyclic ring (Scheme 4), which are similar 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.

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



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

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**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.

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The authors declare no competing financial interest.