ORGANIC LETTERS

XXXX
Vol. XX, No. XX
000–000

Ligand-Controlled, Norbornene-Mediated, Regio- and Diastereoselective Rhodium-Catalyzed Intramolecular Alkene Hydrosilylation Reactions

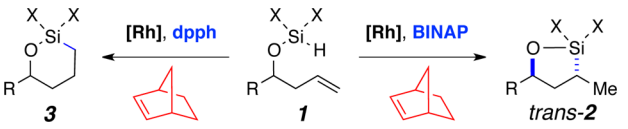
Yuanda Hua, Hiep H. Nguyen, William R. Scaggs, and Junha Jeon*

Department of Chemistry and Biochemistry, University of Texas at Arlington, Texas 76019, United States

jjeon@uta.edu

Received May 23, 2013

ABSTRACT



Ligand-controlled, norbornene-mediated, regio- and diastereoselective rhodium-catalyzed intramolecular alkene hydrosilylation of homoallyl silyl ethers (1) exploiting either BINAP or 1,6-bis(diphenylphosphino)hexane (dpph) has been developed. This method permits selective access to either *trans*-oxasilacyclopentanes (*trans*-2) or oxasilacyclohexanes (3) at will. A substoichiometric amount of norbornene markedly increased both yield and selectivity. A norbornene-mediated hydride shuttle process is discussed.

Transition-metal-catalyzed alkene hydrosilylation, a direct conversion to alkylsilanes via addition of silicon–metal hydride across a C–C double bond, is one of the most important homogeneous catalytic processes.[1] For decades, many powerful metal-catalyzed hydrosilylation strategies have been developed for the synthesis of not only biomedically significant molecules but also functional materials.[2] Research efforts have primarily focused on enhancing or altering the reactivity as well as regio- and stereoselectivity, which are facilitated through an intramolecular[3] hydrosilylation approach.[4,5] In particular, several applications of 1,3-stereocontrolled olefin hydrosilylative cyclization[6] have been demonstrated for the synthesis of a structurally complex polyketide.[7] However, most known hydrosilylation strategies utilizing Pt-, Ru-, and Rh-based catalysts to date have been limited to mainly provide thermodynamically driven 1,3-*cis*-selective hydrosilylation products regardless of olefin geometry,[4,6] leading to 1,3-*syn*-diols after oxidative desilylation[8] (Scheme 1, top). To our knowledge, a widely applicable 1,3-*trans*-selective, kinetic hydrosilylative cyclization strategy of homoallyl silyl ethers **1** accessing *trans*-oxasilacyclopentanes (*trans*-**2**) has not been accomplished,[9] which in turn hinders the selective synthesis of a 1,3-*anti*-diol scaffold[7] in biologically active complex molecules (Scheme 1, middle). In addition, the study toward the synthesis of

(1) (a) Hiyama, T.; Kusumoto, T. In *Comprehensive organic synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 8, pp 763–792. (b) Marciniec, B. In *Hydrosilylation: A Comprehensive Review on Recent Advances*; Marciniec, B., Ed.; Springer: Berlin, 2009; Vol. 1, pp 3–51.

(2) Ojima, I. In *The chemistry of organic silicon compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley: New York, 1989; Chapter 25.

(3) (a) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253. (b) Fensterbank, L.; Malacria, M.; Sieburth, S. M. *Synthesis* **1997**, 813.

(4) (a) Tamao, K.; Nakajima, T.; Sumiya, R.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6090. (b) Tamao, K.; Nakagawa, Y.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 3712. (c) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (d) Tamao, K.; Nakagawa, Y.; Ito, Y. *Organometallics* **1993**, *12*, 2291.

(5) (a) For bissilylation reaction, see: Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487. (b) For silylformylation, see: Zacuto, M. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 8587. (c) For silaboration, see: Ohmura, T.; Furukawa, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13366.

(6) (a) Denmark, S. E.; Forbes, D. C. *Tetrahedron Lett.* **1992**, *33*, 5037. (b) Hoveyda, A. H.; Hale, M. R. *J. Org. Chem.* **1992**, *57*, 1643. (c) Young, D. G. J.; Hale, M. R.; Hoveyda, A. H. *Tetrahedron Lett.* **1996**, *37*, 827. (d) Li, F.; Roush, W. R. *Org. Lett.* **2009**, *11*, 2932.

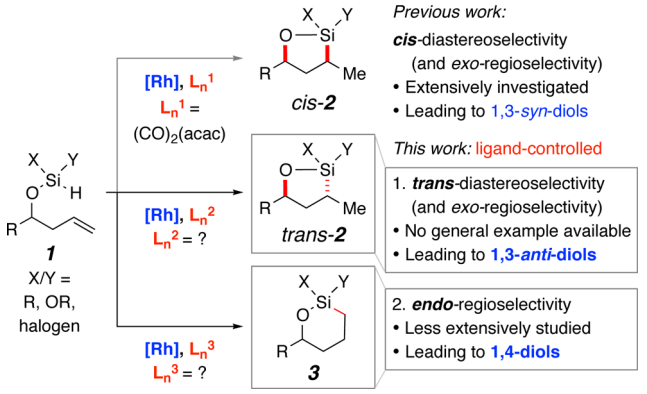
(7) (a) Bode, S. E.; Wolberg, M.; Müller, M. *Synthesis* **2006**, 557. (b) Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2021.

(8) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

(9) (a) 1,3-*trans*-Selectivity for trisubstituted allyl alcohols was reported.[4a] (b) 1,3-*trans*-Selectivity in silaboration was reported.[5c]

10.1021/ol401464n

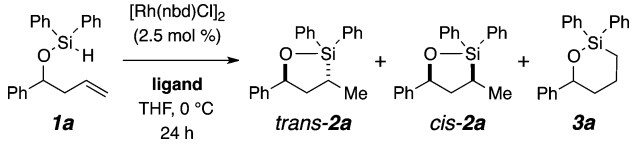
Scheme 1. Transition-Metal-Catalyzed Intramolecular Hydrosilylation: Regio- and Diastereoselectivity



oxasilacyclohexane **3** is underdeveloped,[10] which holds potential for facile synthesis of 1,4-diols (Scheme 1, bottom).[11] Here we report the first example of a regio- and *trans*-selective reaction for Rh-catalyzed, norbornene-mediated hydrosilylative cyclization of homoallyl silyl ethers and our observations that extend the understanding of this class of reactions.

Our interest in developing viable regio- and stereocontrolled Rh-catalyzed hydrosilylation reactions directly arose from the uncertainty of whether simple alteration of ligands within a catalytic system could control the reactivity and selectivity. As shown in Table 1, we first examined monodentate phosphine (entries 1−3) and phosphite (entries 4−5) ligands using **1a** as the substrate and $[Rh(nbd)Cl]_2$ as the precatalyst.[12] The monodentate ligands moderately preferred *trans*-**2a**[13] to *cis*-**2a** and **3a** [cf. Scheme 1; $Rh(CO)_2(acac)$]. We then explored bisphosphine ligands (entries 6−16). A larger ligand bite angle (from dpp-methane to dpp-propane, entries 6−8) generally increased the diastereoselectivity despite inconsequential regioselectivity.[14] However, dpp-butane and structurally modified bisphosphines (entries 9−12) did not improve selectivities. The most exciting observation occurred when *rac*-BINAP (entry 13) was employed, resulting in the formation of *trans*-**2a** with both good regio- and diastereoselectivity. It seems that a bite angle of 91°−92° is suitable to achieve the preferred diastereoselectivity. Intriguingly, the neutral $[Rh(rac\text{-BINAP})Cl]_2$ complex has been rarely utilized in alkene hydrosilylation reactions.[4,15] However, the commonly used cationic complex $[Rh(rac\text{-BINAP})]BF_4$ (entry 14) exhibited poor diastereoselectivity. This result indicated that the

Table 1. Ligand Effect for Rhodium-Catalyzed Intramolecular Hydrosilylation on Regio- and Diastereoselectivity[a]



entry	ligand (deg)[b]	conv (%)[c]	2a:3a[c]	2a (*trans*/*cis*)[c]
1	P(*o*-tol)$_3$	98	71:29	70:30
2	P(*c*-Hex)$_3$	87	77:23	51:49
3	P(*t*-Bu)$_3$	98	69:31	75:25
4	P(OEt)$_3$	100	65:35	61:39
5	P(OPh)$_3$	85	68:32	60:40
6	dpp-methane (72°)	82	74:26	54:46
7	dpp-ethane (85°)	93	85:15	57:43
8	dpp-propane (91°)	86	49:51	73:27
9	dpp-butane (98°)	87	62:38	61:39
10	dpp-benzene (83°)	100	67:33	50:50
11	dpp-ferrocene (96°)	100	62:38	68:32
12	XantPhos (107°)	97	64:36	58:42
13	***rac*-BINAP (92°)**	**85**	**79:21**	**78:22**
14	*rac*-BINAP (92°)[d]	92	74:26	58:42
15	dpp-pentane	100	5:95	52:48
16	dpp-hexane	100	4:96	66:34

[a] Conditions: silane **1a** (0.2 mmol), phosphines (10 mol % for entries 1−5, 15−16 and 7.5 mol % for entries 6−14), THF (0.25 M). *Norbornadiene (nbd) was removed after ligand exchange was completed (see* Supporting Information*).* [b] The listed bite angles are from ref 14. [c] Determined by GC/MS analysis and ^{1}H NMR spectroscopy. [d] $[Rh(cod)_2]BF_4$ was used. dpp- = 1,*n*-bis(diphenylphosphino)-, XantPhos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

coordinative halide ligand substantially impacts diastereoselectivity. On the other hand, dpp-pentane and dpp-hexane (dpph) (entries 15−16) favored 6-*endo*-*trig* cyclization to afford **3a** with excellent regioselectivity. *A simple alteration of phosphine ligands (BINAP and dpph) permits regio- and diastereocontrolled access to structurally distinct oxasilacycles (**2** and **3**) from the same precursor **1**.*

We discovered that the addition of strained bicyclic alkenes impacted both yield and selectivity (Table 2). Specifically, the reaction employing norbornadiene (nbd, entry 1) as an additive afforded *trans*-**2a** with improved regio- and diastereoselectivity (cf. Table 1, entry 13), albeit in modest yield.[16] Moreover, *a substoichiometric amount of nbe* (20 mol %, entry 2) provided a marked increase in yield (81%) as well as regio- and diastereoselectivity (**2a:3a** = 89:11, *trans*-**2a**/*cis*-**2a** = 93:7).[17] When cyclohexene was employed (entry 3), the regio- and diastereoselectivity were greatly diminished with a 33% yield. Therefore, the

(10) Corriu, R. J. P.; Kpoton, A. *J. Organomet. Chem.* **1976**, *114*, 21.
(11) Tortosa, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 3950.
(12) Petit, M.; Chouraqui, G.; Aubert, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 2037.
(13) The structure of the *trans*-**2c** was confirmed by Rychnovsky's NMR method: Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* 1993, *58*, 3511. See Supporting Information for details.
(14) Dierkes, P. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **1999**, 1519.
(15) (a) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2121. (b) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2128.
(16) Reductive dimerization of nbd by $[Rh(nbd)_2]PF_6$ has been reported. We suspect that this process may compete with the cyclization, which is responsible for the lower yield (Table 2, entry 1). (a) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 3089. (b) Roth, R. J.; Katz, T. J. *Tetrahedron Lett.* **1972**, *13*, 2503.
(17) Norbornene also impacted the Rh/dpph-catalyzed hydrosilylation, which provided a markedly increased yield [from 52% (without nbe) to 89% (with nbe)] while maintaining regioselectivity.

Table 2. Influence of Norbornene (nbe) in [Rh(*rac*-BINAP)Cl]$_2$-Catalyzed Intramolecular Hydrosilylation[a]

entry	additive (20 mol %)	conv (%)[b]	yield (%)[c]	**2a:3a**[b]	**2a** (*trans*/*cis*)[b]
1	norbornadiene	100	45	88:12	87:13
2	**norbornene**	**100**	**81**	**89:11**	**93:7**
3	cyclohexene	100	33	70:30	58:42

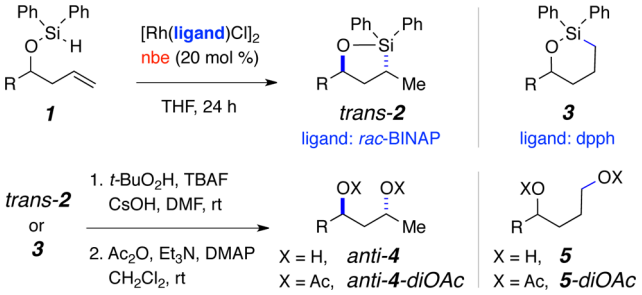
[a] Conditions: silane **1a** (0.2 mmol), [Rh(*rac*-BINAP)Cl]$_2$ (5 mol %), THF (0.25 M), 24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by ^{1}H NMR spectroscopy utilizing an internal standard (DMF).

ring-strained nature of nbe could be highly beneficial to increase the selectivities and yield.

Having recognized the optimal reaction conditions,[18] we investigated the substrate scope of ligand-controlled hydrosilylations (and subsequent oxidative desilylations/diacetylations) (Table 3). The [Rh(*rac*-BINAP)Cl]$_2$-catalyzed reactions demonstrated excellent functional group tolerance in both aromatic and aliphatic substrates. Electronic variation in the aromatic system (*trans*-**2b**, **2c**) perturbed the diastereoselectivity; **1c** provided *trans*-**2c** with diminished diastereoselectivity. The sterically hindered substrate **1d** furnished exceptional diastereoselectivity in *trans*-**2d**. Heteroaromatic substrate **1l** was also tolerated in the reaction. In a similar fashion, the Rh/dpph-catalyzed 6-*endo*-*trig* cyclization exhibited exceptional regioselectivity in both aromatic and aliphatic substrates. Electronic variation in the aromatic system (**3b**, **3c**) did not affect the regioselectivity. The cyclization tolerated the sterically hindered substrates **1d**, **1i** and heteroaromatic substrate **1l**, providing good regioselectivities. The resulting oxasilacycles *trans*-**2** and **3** were subjected to Woerpel's basic oxidation condition[19] (selected substrates were diacetylated), which furnished 1,3-*anti*-diols (*anti*-**4**) or 1,3-*anti*-diacetates (*anti*-**4**-diOAc) with stereoretention of the silicon-bearing stereogenic center[8] and 1,4-diols (**5**) or 1,4-diacetates (**5**-diOAc).

Having established a reasonably broad substrate scope, we studied the mechanistic role of nbe in the reactions. Catellani and co-worker have reported the remarkable reversible associative/dissociative metalation of nbe in Pd-catalyzed domino cross-coupling reactions.[20] In turn, Lautens et al. demonstrated the utility of this process in more complex Catellani reactions that they termed the "norbornene dance".[21] Additionally, Falck[22] and Hartwig[23] proposed that nbe serves as a stoichiometric promoter in Ir-catalyzed dehydrogenative silylation and as a H_2 acceptor in Ir-catalyzed C−H bond activation, respectively.

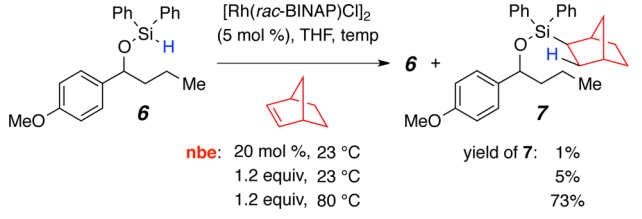
Table 3. Substrate Scope of Ligand-Controlled Hydrosilylations



		rac-**BINAP**[a]		**dpph**[b]	
entry	substrate R =	*trans*/*cis*-**2**[c]	yield (%) of *trans*-**2**[d]	**2:3**[c]	yield (%) of **3**[d]
1	**1a** Ph	93:7	81 (72)[e]	4:96	89 (74)[e]
2	**1b** *p*-MeOPh	91:9	75 (61)[e]	6:94	85 (69)[f]
3	**1c** *p*-BrPh	83:17	67 (60)[f]	7:93	88 (73)[e]
4	**1d** 2,6-di-MePh	97:3	80 (74)[e]	7:93	87 (81)[e]
5	**1e** 1-naph	79:21	62 (55)[e]	3:97	87 (84)[e]
6	**1f** allyl	93:7	76 (68)[e]	4:96	83 (65)[f]
7	**1g** *n*-pentyl	82:18	58 (50)[f]	3:97	85 (75)[e]
8	**1h** *i*-Pr	86:14	70 (62)[e]	6:94	85 (67)[e]
9	**1i** *t*-Bu	88:12	62 (45)[e]	10:90	86 (71)[e]
10	**1j** *c*-Hex	87:13	65 (55)[e]	6:94	86 (75)[f]
11	**1k** Ph(CH$_2$)$_2$	90:10	56 (50)[e]	10:90	78 (70)[f]
12	**1l** furanyl	80:20	59 (51)[f]	3:97	87 (80)[e]

[a] Conditions: silane **1** (0.2 mmol), [Rh(*rac*-BINAP)Cl]$_2$ (5 mol %), −78 to 0 °C. [b] [Rh(nbd)Cl]$_2$ (2.5 mol %), dpph (10 mol %), rt; *nbd was removed (See* Supporting Information*)*. [c] Determined by ^{1}H NMR spectroscopy. [d] Determined by ^{1}H NMR spectroscopy utilizing an internal standard (DMF). [e] Isolated yields of *anti*-**4** or **5**. [f] Isolated yields of *anti*-**4**-diOAc or **5**-diOAc.

In order to obtain mechanistic insights for the role of nbe in our system,[24] the simpler silyl ether **6**, which does not bear an alkene moiety, was subjected to identical reaction conditions (*vide infra*). We observed that the reactions of **6** with either 20 mol % or 1.2 equiv of nbe at 23 °C afforded the 2-silylnorbornane **7** (1% or 5%, respectively). However, when nbe (1.2 equiv) was employed at 80 °C, **7** was isolated in 73% yield. These results suggest that nbe likely



(18) The effect of silyl substitutions was investigated. Sterically less hindered Me$_2$HSiOR provided poor selectivity [dimethyl-*trans*-**2**/dimethyl-*cis*-**2** = 60:40 (34% NMR yield)]. We did not observe any product formation for sterically hindered substrates, (Mesityl)$_2$SiOR, *i*Pr$_2$HSiOR, and *t*Bu$_2$HSiOR under the identical conditions.

(19) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044.

(20) (a) Catellani, M.; Fagnola, M. C. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2421. (b) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119. (c) Catellani, M.; Mealli, C.; Motti, E.; Paoli, P.; Perez-Carreno, E.; Pregosin, P. S. *J. Am. Chem. Soc.* **2002**, *124*, 4336.

(21) Martins, A.; Mariampillai, B.; Lautens, M. *Top. Curr. Chem.* **2010**, *292*, 1.

(22) (a) Lu, B.; Falck, J. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 7508. (b) Lu, B.; Falck, J. R. *J. Org. Chem.* **2010**, *75*, 1701.

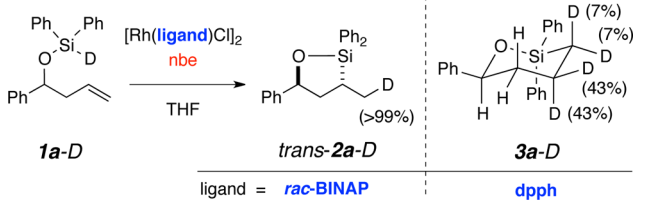
(23) Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70.

(24) The formation of norbornane (via reduction of nbe) was not observed by GC/MS analysis, which implies that nbe may not simply act as a H_2 acceptor.

resides within a coordinative sphere of a rhodium–substrate complex, and subsequent reductive elimination could produce **7** when migratory insertion is not available.

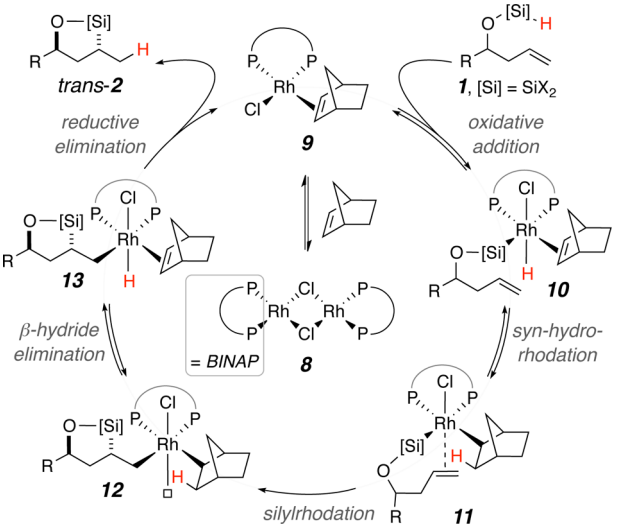
We also performed isotope-labeling experiments (Scheme 2). In sharp contrast to Bosnich[15b] and Tamao's[4d] studies, the deuterium of **1a**-D was quantitatively transferred into the terminal methyl group of *trans*-**2a**-D upon treatment with $[Rh(rac\text{-BINAP})Cl]_2$ regardless of the presence or not of nbe, indicating that reductive elimination to produce *trans*-**2a**-D is faster than β-hydride elimination when olefin silyl insertion is involved. This shows that the silylmetalation likely establishes the diastereoselection and is the turnover-limiting step. However, the Rh/dpph system resulted in multiple sites of deuteration as indicated in **3a**-D.

Scheme 2. Deuterium-Labeling Study



On the basis of these observations and related literature precedents,[20–23] a plausible mechanism of the *trans*-selective hydrosilylation is depicted in Scheme 3. We speculate that nbe acts as a catalytic vehicle (i) to facilitate the dissociation of the dimeric rhodium species **8**, thereby generating a monomeric Rh(I) complex **9**, and (ii) to activate the sequence of hydrorhodation, silylrhodation, and β-hydride elimination (**10** to **13**) involving a "hydride shuttle" process[20,21] that is regarded as the turnover-limiting step in the modified Chalk–Harrod pathway.[25] In detail, the Chalk–Harrod pathway[26] is discouraged by hydride abstraction from **10** to **11** via *syn*-hydrorhodation of the strained nbe in an *exo*-fashion, which exclusively leads to the modified Chalk–Harrod pathway[25] to provide **12** (of note, hydride is no longer present at the metal center

Scheme 3. Plausible Mechanism



in **11**). The hydride is then released via β-hydride elimination[27] (**12** to **13**), which makes reductive elimination feasible. In this scenario, nbe would accentuate inner-sphere steric hindrance within octahedral Rh(III) complex **11**, which would in turn influence the olefin migratory insertion step (**11** to **12**).[28] This consequence would be responsible for significantly enhancing regio- and diastereoselectivity.

In summary, we have developed the first method for a *trans*-selective rhodium-catalyzed intramolecular alkene hydrosilylation leading to 1,3-*anti*-diols. A substoichiometric amount of norbornene contributed to the dramatic increase of regio- and diastereoselectivity as well as yield, via a "hydride shuttle" process. In particular, either *trans*-oxasilacyclopentanes *trans*-**2** or their regioisomers oxasilacyclohexanes **3** can be formed from the same precursor **1** simply by employing either the BINAP or dpph ligand. These results underscore the importance of the steric and electronic properties of ligands in transition-metal-catalyzed processes vis-à-vis reactivity and selectivity.

Acknowledgment. We thank UT Arlington for support of our program. We acknowledge Profs. Carl Lovely, Frank Foss, and Mrs. Gabriela Trog at UTA for insightful discussions.

Supporting Information Available. Spectroscopic characterization data and procedures for preparation of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(25) (a) Randolph, C. L.; Wrighton, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 3366. (b) Brookhart, M.; Grant, B. E. *J. Am. Chem. Soc.* **1993**, *115*, 2151. (c) Sakaki, S.; Sumimoto, M.; Fukuhara, M.; Sugimoto, M.; Fujimoto, H.; Matsuzaki, S. *Organometallics* **2002**, *21*, 3788.

(26) (a) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16. (b) Sakaki, S.; Mizoe, N.; Sugimoto, M. *Organometallics* **1998**, *17*, 2510.

(27) β-Hydride elimination of a bimetallic Re/Pt-norbornene complex has been reported. Batsanov, A. D.; Howard, J. A. K.; Love, J. B.; Spencer, J. L. *Organometallics* **1995**, *14*, 5657.

(28) The regioselectivity of the Rh/dpph-catalyzed hydrosilylation is mainly dictated by dpph. In this process, nbe may simply increase the stability of a series of rhodium complexes, thereby minimizing the disilyl byproduct via oxidative coupling.[6a,15a,17]