Asymmetric Cyclization/Hydrosilylation of Functionalized 1,6-Dienes Catalyzed by Enantiomerically Pure Palladium Pyridine−Oxazoline Complexes

Nicholas S. Perch and Ross A. Widenhoefer*

Duke University
P. M. Gross Chemical Laboratory
Durham, North Carolina 27708-0346

Received February 12, 1999

The development of efficient asymmetric annulation protocols is of central importance in organic synthesis due to the wealth of biologically active and naturally occurring carbocycles.[1] Enantioselective catalysis employing transition metal complexes remains an attractive approach toward the synthesis of optically active carbocycles due to the development of numerous catalytic carbocyclization protocols[2] and due to the rapid growth of asymmetric catalysis in organic synthesis.[3] However, most efficient enantioselective transition metal-catalyzed procedures involve the addition of an H−X bond [X = H, Si, B] across a prochiral C=X bond [X = O, N, C] or oxidation of a prochiral olefin.[3] In contrast, highly enantioselective catalytic protocols which form C−C bonds are less common,[4] and efficient enantioselective carbocyclization protocols remain limited.[5]

Cyclization/hydrosilylation of dienes[6] and enynes[7] is emerging as a potential route toward the synthesis of functionalized carbocycles. However, the utility of cyclization/hydrosilylation has been limited by the absence of an asymmetric protocol. Our contribution to this growing area has been the development of Pd-catalyzed protocols for the cyclization/hydrosilylation of functionalized 1,6-[8] and 1,7-dienes.[9] For example, reaction of triethylsilane and dimethyl diallylmalonate (**1**) in the presence of (phen)PdMe(OEt_2)$^+$ $BAr'_4{}^-$ [phen = 1,10-phenanthroline; Ar′ = 3,5-$C_6H_3(CF_3)_2$] (**2**) at 0 °C for 5 min led to the isolation of the *trans*-silylated cyclopentane **3** in 93% yield (98% trans) (Scheme 1).[8] Significantly, the high activity and exceptional diastereoselectivity displayed by our Pd-catalyzed procedure pointed to the feasibility of the analogous asymmetric protocol. Here we report the first examples of asymmetric cyclization/hydrosilylation.

Scheme 1

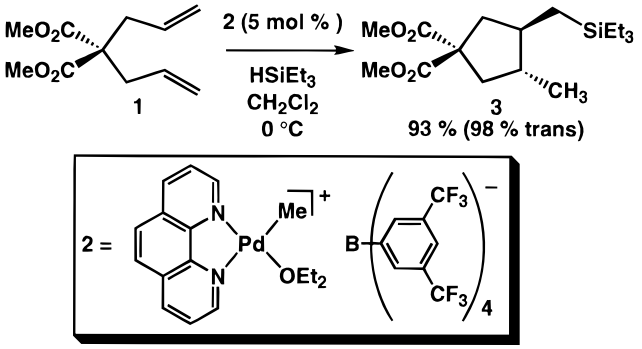
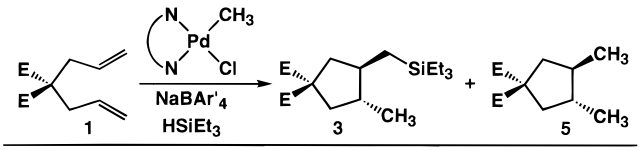
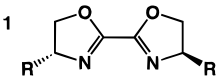
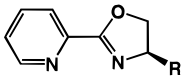


Table 1. Asymmetric Cyclization/Hydrosilylation of **1** Employing Palladium Bisoxazoline and Pyridine−Oxazoline Precatalysts (5 mol %) and $HSiEt_3$ in CH_2Cl_2



entry	N N	R	temp (°C)	time (h)	yield 3 + 5 (%)	3:5[a]	de 3 (%)[a]	ee 3 (%)[b]
1		Bn (4)	−30	24	64	8.1:1	>95	72
2		*i*-Pr (6)	−32	24	82	>50:1	>95	87
3		Me (7)	−43	48	71	>50:1	>95	79
4		*i*-Bu (8)	−45	48	84	>50:1	>95	77
5		*t*-Bu (9)	−40	48	79	8:1	91	91

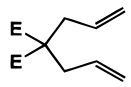
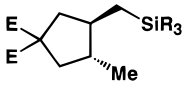
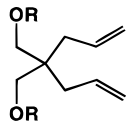
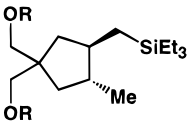
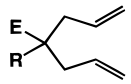
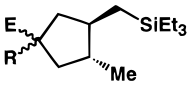
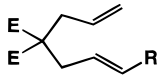
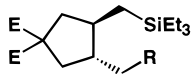
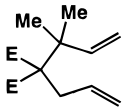
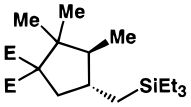
[a] Product ratio and diastereomeric excess determined by capillary GC. [b]Enantiomeric excess determined by capillary chiral GC.

Our initial approach toward the development of an asymmetric cyclization/hydrosilylation protocol employed cationic palladium bisoxazoline compounds as catalysts due to the wealth of asymmetric transformations which utilize these ligands[2] and their availability.[10] For example, reaction of **1** and $HSiEt_3$ in the presence of a 1:1 mixture of (N−N)Pd(Me)Cl [N−N = 4,4′-dibenzyl-4,5,4′,5′-tetrahydro-2,2′-bisoxazoline] (**4**) and $NaBAr'_4$[11] (5 mol %) at −30 °C for 24 h led to isolation of a 8.1:1 mixture of silylated carbocycle **3** (95% de, 72% ee) and dimethyl 3,4-dimethylcyclopentane-1,1-dicarboxylate[12] (**5**) in 64% combined yield (Table 1, entry 1). Unfortunately, this protocol led to only modest levels of stereo-induction and also suffered from sluggish reaction rates, low yield, low chemoselectivity, and lack of generality. Because none of these limitations was observed with phenanthroline catalyst **2**,[8] we reasoned that the limitations associated with precatalyst **4** stemmed from excessive steric crowding near the coordination plane. In addition, because both achiral catalyst **2** and the chiral catalyst generated from **4** converted **1** to **3** with high trans-selectivity, we reasoned that a potential chiral catalyst need set only one of the two stereocenters of the carbocycle.

(1) (a) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467. (b) Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141.
(2) (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (c) Trost, B. M. *Science* **1991**, *254*, 1471. (d) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (e) Trost, B. M.; Krische, M. J. *Synlett*, **1998**, 1.
(3) (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*: Wiley: New York, 1994. (b) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993.
(4) Notable examples include cyclopropanation and allylic substitution.[3]
(5) For key examples, see: (a) Shibisaki, M.; Boden, C. D. J.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371. (b) Overman, L. E. *Pure Appl. Chem.* **1994**, *66*, 1423. (c) Goeke, A.; Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 662. (d) McKinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145. (e) Barnhart, R. B.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821. (f) Doyle, M. P.; van Oeveren, A.; Westrum, L. J.; Protopopova, M. N.; Clayton, T. W. *J. Am. Chem. Soc.* **1991**, *113*, 8982.
(6) (a) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (b) Onozawa, S.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1994**, *35*, 8177. (c) Molander, G. A.; Nichols, P. J.; Noll, B. C. *J. Org. Chem.* **1998**, *63*, 2292. (d) Molander, G. A.; Dowdy, E. D.; Schumann, H. *J. Org. Chem.* **1998,** *63*, 3386.
(7) (a) Onozawa, S.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389. (b) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580. (c) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478. (d) Ojima, I.; Zhu, J.; Vidal, E. S.; Kass, D. F. *J. Am. Chem. Soc.* **1998**, *120*, 6690. (e) Molander, G. A.; Retsch, W. H. J. *Am. Chem. Soc.* **1997**, *119*, 8817.
(8) Widenhoefer, R. A.; DeCarli, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3805.
(9) Stengone, C. N.; Widenhoefer, R. A. *Tetrahedron Lett.* **1999**, *40*, 1451.
(10) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232.
(11) Halide abstraction forms the cationic palladium species *in situ*: Brookhart, M.; Wagner, M. I.; Balavoine, G. G. A.; Haddou, H. A. *J. Am. Chem. Soc.* **1994**, *116*, 3641.
(12) (a) Kuehne, M. E.; Damon, R. E. *J. Org. Chem.* **1977**, *42*, 1825. (b) Curran, D. P.; Shen, W. *J. Am. Chem. Soc.* **1993**, *115*, 6051.

10.1021/ja990461o CCC: $18.00
Published on Web 07/14/1999

Table 2. Asymmetric Cyclization/Hydrosilylation of 1,6-dienes Employing a 1:1 Mixture of **6** and $NaBAr'_4$ (5 mol %) in CH_2Cl_2

Entry	Diene	Silane	Temp (°C)[a]	Carbocycle Yield (%)[b]	de (%)[c]	ee (%)
						
1	E = CO_2Me	$HSiMe_2CMe_3$	–40	87	97	89[d]
2		$HSiMe_2Et$	–18	71	98	82[d]
3	E = CO_2CMe_3	$HSiMe_2Ph$	–40[f]	59[g]	≥95	87[e]
4		$HSiEt_3$	–40[f]	79[g]	≥98	90[d]
5	E = CO_2Bn		–40	83	95	86[d]
6	E = CO_2i-Pr		–40	75	98	85[d]
						
7	R = Bn		–40	91	95	79[d]
8	R = COMe		–18	89	98	86[d]
9	R = $COCMe_3$		–18	89	97	91[d]
						
	(E = CO_2Me)					
10	R = SO_2Me		–18	74	44	82[e,h]
11	R = Ph		–18	84	47	89[e,h]
						
	(E = CO_2Me)					
12	R = Me		–40	79	92	85[e]
13	R = Bu		–40	75	93	87[e]
						
14	E = CO_2Me		–18	62	95	81[e]

[a] Reaction times: −18 °C, 12 h; −40 °C, 48 h. [b]Yield refers to isolated material of >95% purity. [c]Diastereomeric excess determined by capillary GC. [d]Enantiomeric excess determined by chiral capillary GC. [e]Enantiomeric excess determined by ^1H NMR spectroscopy employing $Eu(hfc)_3$. [f]10 Mol % catalyst employed. [g]Product isolated as the corresponding dicarbomethoxy derivative. [h]Enantiomeric excess of major diastereomer.

The above hypotheses pointed to the palladium pyridine−oxazoline complexes (N−N)Pd(Me)Cl [N−N = 4-R-2-(2-pyridinyl)-2-oxazoline, R = *i*-Pr (**6**), Me (**7**), *i*-Bu (**8**), *t*-Bu (**9**)] as cyclization/hydrosilylation precatalysts.[13] Significantly, employment of complex **6** as a cyclization/hydrosilylation precatalyst led to marked improvement in yield, chemoselectivity, and stereoselectivity relative to bisoxazoline precatalyst **4** (Table 1, entries 2−5). For example, reaction of **1** and $HSiEt_3$ at −32 °C in the presence of a 1:1 mixture of valinol-derived precatalyst **6** and $NaBAr'_4$ (5 mol %) for 24 h led to the isolation of carbocycle **3** in 82% isolated yield (98% de, 87% ee), without formation of detectable quantities of **5** (Table 1, entry 2). The methyl-substituted precatalyst **7** and the leucinol-derived precatalyst **8** afforded lower stereoselectivity than did **6** (Table 1, entries 3, 4), while the *tert*-leucinol derived precatalyst **9** suffered from diminished chemo- and diastereoselectivity relative to **6** (Table 1, entry 5).

The scope of asymmetric cyclization/hydrosilylation was probed with respect to diene and silane employing precatalyst **6** (Table 2). Significantly, the protocol consistently produced high levels of diastereo- (>95%) and enantioselectivity (>85%) with a wide range of substrates and silanes. For example, the protocol tolerated a variety of silanes including dimethyl-*tert*-butylsilane, dimethylethylsilane, and dimethylphenylsilane (Table 2, entries 1−3). Similarly, a range of diesters (Table 2, entries 3−6), protected diols (Table 2, entries 7−9), and monoesters (Table 2, entries 10 and 11) underwent cyclization/hydrosilylation in good yield and with good enantioselectivity. In addition, dienes substituted at a terminal olefinic carbon atom or at an allylic carbon atom also underwent cyclization/hydrosilylation in high yield and with good regio- and stereoselectivity (Table 2, entries 12−14).

In summary, optically pure, cationic palladium pyridine−oxazoline complexes catalyze the asymmetric cyclization/hydrosilylation of functionalized 1,6-dienes. This procedure generates two adjacent stereocenters with complete (>95%) diastereoselectivity and up to 91% ee. In addition, our preliminary results indicate that palladium pyridine−oxazoline catalysts tolerate a range of silanes and dienes. We are currently working toward the development of more efficient and more stereoselective catalysts for asymmetric cyclization/hydrosilylation.

Acknowledgment. R.W. thanks the Camille and Henry Dreyfus Foundation for a New Faculty Award. Additional funding was provided by the Petroleum Research Fund. We thank Dr. B. Krzyzanowska for synthesizing 4,4-dicarbomethoxy-1,6-(*E*)-octadiene and 4,4-dicarbomethoxy-1,6-(*E*)-undecadiene.

Supporting Information Available: Experimental procedures, spectroscopic and analytical data for new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA990461O

(13) For the synthesis and applications of pyridine−oxazoline ligands, see: (a) Bolm, C.; Weickhardt, K.; Zehnder, M.; Ranff, T. *Chem. Ber.* **1991**, *124*, 1173. (b) Nishiyama, H.; Sakaguchi, H.; Nakamura, T.; Horihata, M.; Kondo, M.; Itoh, K. *Organometallics* **1989**, *8*, 846. (c) Brunner, H.; Obermann, U. *Chem. Ber.* **1989**, *122*, 499.