ORGANIC
LETTERS

2000
Vol. 2, No. 10
1469−1471

Use of Pentamethyldisiloxane in the Palladium-Catalyzed Cyclization/Hydrosilylation of Functionalized Dienes

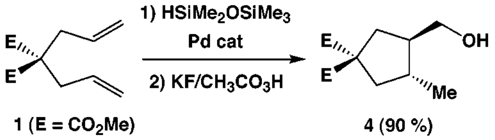
Tao Pei and Ross A. Widenhoefer*

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

rwidenho@chem.duke.edu

Received March 14, 2000

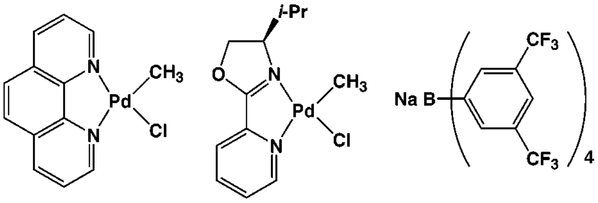
ABSTRACT



Pentamethyldisiloxane reacts with a range of functionalized dienes in the presence of a catalytic 1:1 mixture of (N–N)Pd(Me)Cl [N–N = 1,10-phenanthroline or (*R*)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline] and $NaBAr_4$ [Ar = 3,5-$C_6H_3(CF_3)_2$] to form the corresponding silylated carbocycles in good yield and with good stereoselectivity. Treatment of these silylated carbocycles with excess KF and peracetic acid at room temperature for 48 h formed the corresponding alcohols in excellent yield with retention of stereochemistry.

The use of a silyl moiety as a masked hydroxyl group has become an important strategy in the synthesis of complex alcohols and polyols.[1] The utility of this approach stems from the development of facile and high-yielding methods for both the incorporation and unmasking of the silyl group and also from the stability of organosilanes to varied reaction conditions and chromatography.[1] However, efficient unmasking of the silyl group is restricted to those silanes which possess a functional group. For example, the dimethylphenylsilyl group can be unmasked in two steps by first cleaving the phenyl group with an electrophile followed by oxidation with peracid.[2] Conversely, silanes which possess an allyl, alkoxy, amino, or chloro group undergo oxidation in the absence of an electrophile, leading to improved functional group compatibility.[3] In addition, a general procedure for the oxidation of both phenylsilanes and hindered alkoxysilanes employing *t*-BuOOH under basic conditions has recently been developed.[4]

We recently reported the cyclization/hydrosilylation of functionalized dienes catalyzed by a 1:1 mixture of (N−N)-Pd(Me)Cl [N−N = 1,10-phenanthroline (**2a**) or (*R*)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline (**2b**)] and $NaBAr_4$ [Ar = 3,5-$C_6H_3(CF_3)_2$] (**2c**) to form silylated carbocycles in good yield and with high stereoselectivity (Scheme 1).[5] Unfortunately, efficient and general cyclization/hydrosilylation was



2a **2b** **2c**

---

[1] Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

[2] Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29. (b) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229.

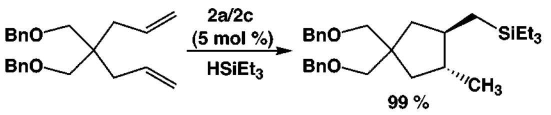
[3] Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694. (b) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37. (c) Tamao, K.; Ishida, N. *Tetrahedron Lett.* **1984**, *25*, 4249. (d) Magar, S. S.; Fuchs, P. L. *Tetrahedron Lett.* **1991**, *32*, 7513. (e) Tamao, K. Ishida, N.; Kumada, M.; *J. Org. Chem.* **1983**, *48*, 2120.

[4] Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044.

[5] (a) Widenhoefer, R. A.; DeCarli, M. A. *J. Am. Chem. Soc.* **1998**, *120*, 3805. (b) Stengone, C. N.; Widenhoefer, R. A. *Tetrahedron Lett.* **1999**, *40*, 1428. (c) Widenhoefer, R. A.; Stengone, C. N. *J. Org. Chem.* **1999**, *64*, 8681. (d) Widenhoefer, R. A.; Vadehra, A. *Tetrahedron Lett.* **1999**, *40*, 8499. (e) Perch, N. S.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 6960. (f) Perch, N. S.; Pei, T.; Widenhoefer, R. A. *J. Org. Chem.* In press.

10.1021/ol005810u CCC: $19.00

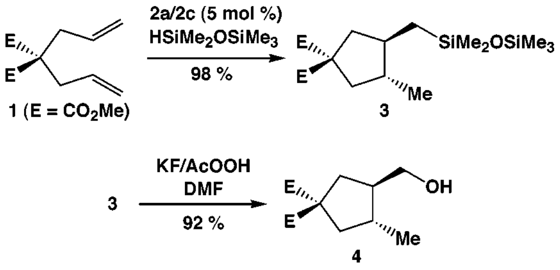
Scheme 1



achieved only with trialkylsilanes such as $HSiEt_3$; dimethylphenylsilane functioned satisfactorily in some cases but displayed poor generality, while silanes of the form $HSiMe_2X$ (X = allyl, OR, NR_2, or Cl) were completely ineffective. Therefore, we sought to identify a silane for use in palladium-catalyzed diene cyclization/hydrosilylation which would display good generality and which would cleave efficiently under mild conditions. Here we report that pentamethyldisiloxane (PMDS)[6] serves as an effective and readily oxidized silane for use in the palladium-catalyzed cyclization/hydrosilylation of functionalized dienes.[7]

Reaction of dimethyl diallylmalonate (**1**) and excess PMDS catalyzed by a 1:1 mixture of **2a** and **2c** (5 mol %) in 1,2-dichloroethane (DCE) at 0 °C for 10 min led to complete consumption of the diene. The solvent was evaporated, and the residue was extracted with hexane/EtOAc (24:1) and filtered through a plug of silica gel to give silylated carbocycle **3** in 98% yield (96% de, 95% pure) (Scheme 2).[8]

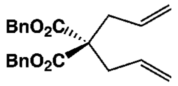
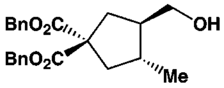
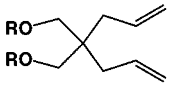
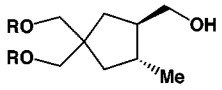
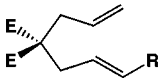
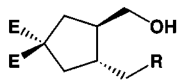
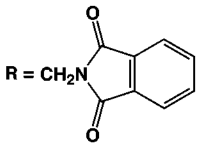
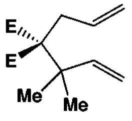
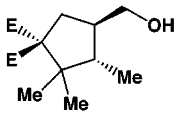
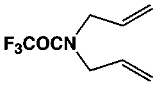
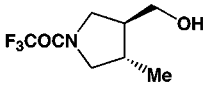
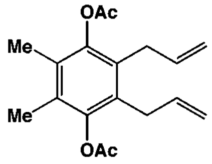
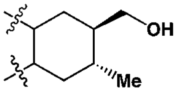
Scheme 2



Treatment of **3** with a large excess of KF and peracetic acid in DMF at room temperature for 2 days followed by workup and chromatography gave alcohol **4** in 92% yield (90% from **1**) with complete retention of stereochemistry (Scheme 2).[9]

In addition to **1**, a range of functionalized dienes reacted with PMDS in the presence of **2a/2c** and underwent subsequent oxidation to form the corresponding (hydroxymethyl)carbocycles in excellent yields and with high diastereoselectivity (Table 1). For example, diesters, diethers, and protected diols underwent facile cyclization/hydrosilylation/oxidation to form alcohols in >70% overall yield as a single diastereomer (Table 1, entries 1−5). Similarly, dienes which possessed an aliphatic, aromatic, or functional group at the terminal olefinic carbon atom also served as

Table 1. Cyclization/Hydrosilylation of Dienes Employing PMDS Catalyzed by a 1:1 Mixture of **2a** and **2c** (5 mol %) in DCE at 0 °C Followed by Oxidation with Excess KF and AcOOH in DMF at Room Temperature for 2 days

entry	diene	alcohol	yield (%)[a]	isomer ratio[b]
1			86	>50:1
				
2	R = Me		85	>50:1
3	R = Bn		76	>50:1
4	R = COMe		71	>50:1
5	R = CO*t*-Bu		79	>50:1
				
6[c]	R = Me		82	25:1
7[c]	R = Bu		76	31:1
8[c]	R = Ph		71	8.1:1
9[c]	R = CH_2OPh		84	22:1
10			70	15:1
11[c]			82	28:1
12			69	>50:1
13			57	>50:1

[a] Yields refer to the two-step conversion of diene to isolated alcohol of >95% purity. [b] Isomer ratio determined by capillary GC analysis. [c] E = CO_2Me.

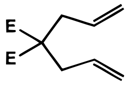
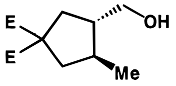
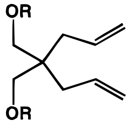
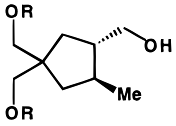
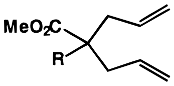
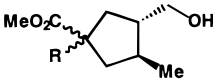
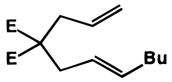
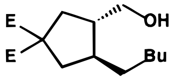
---

(6) Available from Gelest, Inc. (Tullytown, PA) for ca. $ 1/g.

(7) Tamao reported that an unspecified siloxy group ($SiMe_2OSiMe_2R$) was oxidatively cleaved in 72% yield by a two-step procedure involving acid hydrolysis followed by treament with 30% H_2O_2. No further details or development of this procedure were reported.[3b]

(8) **General procedure for cyclization/hydrosilylation:** the diene (5.0 mmol) and pentamethyldisiloxane (2.15 g, 15.0 mmol) were added sequentially to a solution of **2a** (84 mg, 0.25 mmol) and **2c** (259 mg, 0.25 mmol) in DCE (50 mL) at 0 °C. The resulting pale yellow solution was stirred for either 10 min at 0 °C (Table 1, entries 1−6, 13) or at room temperature for 1−12 h (Table 1, entries 7−12) to form a dark brown solution. Solvent and excess silane were evaporated under vacuum, and the brown residue was dissolved in hexane/EtOAc (24:1) and filtered through a plug of silica gel. Concentration under vacuum gave the corresponding silylated carbocycle as a colorless to pale yellow oil in 80−99% purity which was oxidized without further purification. Although carbocycle **3** decomposed slightly upon silica gel chromatography, all other silylated carbocycles displayed no significant sensitivity toward silica gel.

Table 2. Asymmetric Cyclization/Hydrosilylation of Dienes Employing PMDS Catalyzed by a 1:1 Mixture of **2b** and **2c** (5 mol %) at −20 °C in CH_2Cl_2 for 12 h Followed by Oxidation with Excess KF and AcOOH in DMF at Room Temperature for 2 days

entry	diene	carbocycle	yield (%)[a]	de (%)[b]	ee (%)
1	 E = CO_2Me		93	98	75[c]
2	 R = CH_2COt-Bu		85	97	82[d]
3	 R = Ph		79	71	75[e]
4	R = $CONMe_2$		83	60	79[e]
5	 E = CO_2Me		82	94	76[e]

[a] Yields refer to the isolated alcohol of >95% purity. [b] Isomer ratio determined by capillary GC. [c] ee determined by chiral GC of the silylated carbocycle. [d] ee determined by ^{19}F NMR analysis of the corresponding Mosher ester. [e] ee determined by ^1H NMR analysis of the purified silylated carbocycle employing Eu(hfc)$_3$.

effective substrates, as did dienes which possessed an allylic substituent (Table 1, entries 6−11). In addition, the cyclization/hydrosilylation/oxidation protocol was amenable to the synthesis of substituted pyrrolidines (Table 1, entry 12) and cyclohexane derivatives (Table 1, entry 13).

The reaction of PMDS with functionalized dienes was also effectively catalyzed by optically active palladium pyridine−oxazoline catalysts. For example, reaction of **1** and PMDS catalyzed by a 1:1 mixture of **2b** and **2c** (5 mol %) at −20 °C for 12 h led to the isolation of **3** in near quantitative yield. Carbocycle **3** was oxidized with KF and peracetic acid to form **4** in 93% overall yield with 98% de and 75% ee (Table 2, entry 1). Preliminary results point to the generality of asymmetric cyclization/hydrosilylation employing PMDS and precatalyst **2b** (Table 2, entries 2−5). However, the enantioselectivity of the carbocycles formed under these conditions was slightly lower than that obtained by employing $HSiEt_3$ and **2b**, which may be due to the smaller size of PMDS relative to $HSiEt_3$.[10]

In summary, the reaction of pentamethyldisiloxane (PMDS) and functionalized dienes is catalyzed by palladium phenanthroline complex **2a** and chiral palladium pyridine−oxazoline complex **2b** to form silylated carbocycles in excellent yield and with high stereoselectivity. With the exception of **3**, the silylated carbocycles are stable toward silica gel chromatography and undergo oxidation in high yield at room temperature with complete retention of stereochemistry.[9] Because of these characteristics, PMDS may have useful applications outside the scope of palladium-catalyzed cyclization/hydrosilylation. We are currently working toward the identification of disiloxane derivatives which will improve the enantioselectivity of the asymmetric procedure and/or enhance the stability of the silylated carbocycles toward hydrolysis and silica gel chromatography.

Acknowledgment is made to the National Institutes of Health (GM59830-01) and the donors of the Petroleum Research Fund (33131-G1), administered by the American Chemical Society, for support of this research. R.W. thanks the Camille and Henry Dreyfus Foundation and DuPont for new faculty awards and the Alfred P. Sloan Foundation for a research fellowship. We thank Mr. Carmine N. Stengone for performing some initial experiments.

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

OL005810U

---

(9) **General procedure for oxidation:** a suspension of the silylated carbocycle (1.75 mmol), KF (0.81 g, 14.0 mmol), and peracetic acid (32 wt % in acetic acid, 5.0 mL, 21.0 mmol) in DMF (14 mL) was stirred at room temperature for 48 h. Water (20 mL) was added, and the resulting suspension was extracted with ethyl acetate. The combined organic extracts were washed with 10% Na_2SO_3 and saturated $NaHCO_3$, dried (Na_2SO_4), concentrated, and chromatographed on silica gel to give the pure alcohol as a colorless oil.

(10) For example, under comparable conditions, the enantioselectivity of the cyclization/hydrosilylation of **1** catalyzed by a mixture of **2b** and **2c** increased in the order $HSiMe_2Et$ (82% ee) < $HSiEt_3$ (87% ee) < $HSiMe_2CMe_3$ (89% ee).