

Asymmetric Cyclization/Hydrosilylation/Oxidation of Functionalized 1,6-Dienes Employing 1,1-Dimethyl-3,3-Diphenyl-3-*tert*-Butyldisiloxane

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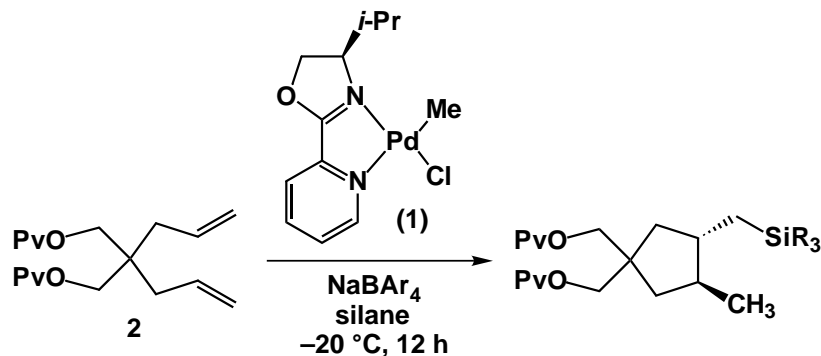
Abstract: A 1:1 mixture of (N–N)Pd(Me)Cl [N–N = (*R*)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline] (**1**) and NaBAr₄ [Ar = 3,5-C₆H₃(CF₃)₂] catalyzed the asymmetric cyclization/hydrosilylation of functionalized 1,6-dienes with 1,1-dimethyl-3,3,3-diphenyl-*tert*-butyldisiloxane at –20 °C to form silylated cyclopentanes in good yield and with up to 95% ee. These silylated carbocycles underwent oxidative cleavage of the C–Si bond at room temperature to form the corresponding alcohols with retention of stereochemistry.

Keywords: catalysis, cyclization, dienes, palladium

Introduction

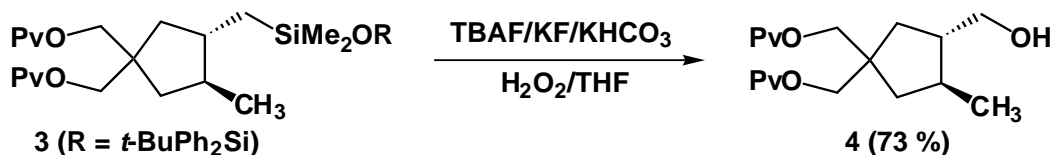
We have developed several related procedures for the cyclization/hydrosilylation of functionalized dienes catalyzed by cationic palladium complexes generated from mixtures of (N–N)Pd(Me)Cl [N–N = 1,10-phenanthroline¹ or (*R*)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline (**1**)²] and NaBAr₄ [Ar = 3,5-C₆H₃(CF₃)₂]. Our initial procedures required the use of HSiEt₃ to achieve efficient and general cyclization/hydrosilylation, and the resulting silylated carbocycles were therefore resistant to oxidative C–Si bond cleavage.³ In response to this limitation, we recently identified pentamethyldisiloxane (HSiMe₂OTMS) as an effective and readily oxidized silane for use in palladium-catalyzed cyclization/hydrosilylation.⁴ Unfortunately, the enantioselectivity of asymmetric cyclization/hydrosilylation employing HSiMe₂OTMS was significantly diminished relative to HSiEt₃ (Table 1, entries 1 and 2). Therefore, we sought to identify a silane which would give high enantioselectivity in asymmetric cyclization/hydrosilylation to form silylated carbocycles which would be reactive towards oxidative C–Si bond cleavage. Here we report that 1,1-dimethyl-3,3-diphenyl-3-*tert*-butyldisiloxane (HSiMe₂OTBDPS) serves as an effective, readily oxidized silane for the asymmetric cyclization/hydrosilylation/oxidation of 1,6-dienes, generating cyclic alcohols with up to 95% ee.

Table 1. Enantioselectivity of asymmetric cyclization/hydrosilylation of **2** catalyzed by a 1:1 mixture of **1** and NaBAR₄ as a function of silane.



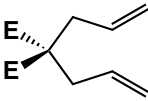
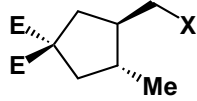
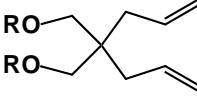
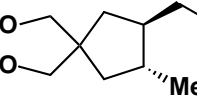
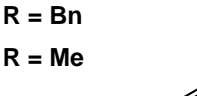

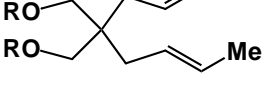
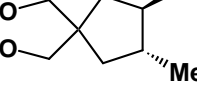
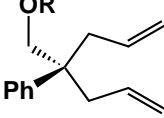
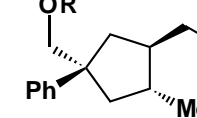
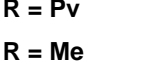

entry	silane	yield (%)	de (%)	ee (%)
1	HSiEt ₃	89	≥95	91
2	HSiMe ₂ OTMS	98	≥95	82
3	HSiMe ₂ OTBDPS	99	≥95	95

Treatment of a methylene chloride solution of 4,4-bis(trimethylacetoxymethyl)-1,6-heptadiene (**2**) and a catalytic 1:1 mixture of **1** and NaBAR₄ (5 mol %) with an excess of HSiMe₂OTBDPS⁵ at -20 °C for 12 h led to the isolation of the corresponding silylated carbocycle **3** in 99% yield with >98% de and 95% ee (Table 1, entry 3).⁶ Unfortunately, carbocycle **3** failed to oxidize under the conditions employed for oxidation of the -SiMe₂OTMS group (excess KF/AcOOH, 25 °C, 48 h)⁴ and an alternative procedure was therefore required. To this end, treatment of the **3** with a mixture of TBAF, KF, KHCO₃, and 50% H₂O₂ in THF at room temperature for 3 days led to the isolation of the corresponding alcohol **4** in 73% yield with retention of stereochemistry (Scheme 1).⁷ In addition to diene **2**, a range of functionalized 1,6-dienes underwent asymmetric cyclization/hydrosilylation with HSiMe₂OTBDPS in the presence of a catalytic 1:1 mixture of **1** and NaBAR₄ (5 mol %) to form silylated carbocycles in good yield with high enantioselectivity (Table 2). Similarly, these silylated carbocycles underwent oxidation to form the corresponding alcohols with retention of configuration (Table 2).



Scheme 1

Table 2. Asymmetric cyclization/hydrosilylation of dienes employing HSiMe₂OTBDPS catalyzed by a 1:1 mixture of **1** and NaBAR₄ (5 mol %) in CH₂Cl₂ at –20 °C for 12 h followed by oxidation with excess TBAF, KF, KHCO₃, and H₂O₂ in THF at room temperature for 3 days.

diene	carbocycle	yield (%)		de (%) ^c	ee (%)
		(X = SiR ₃) ^a	(X = OH) ^b		
 E = CO ₂ Me		99	48	>50:1	90 ^d
 R = Bn		82	76	>50:1	94 ^e
 R = Me		79	76	>50:1	85 ^f
 R = Pv		92	71	39:1	89 ^e
 R = Pv		90	69	1.3:1	92 ^e
 R = Me		85	70	1.5:1	91 ^e

^aYield of cyclization/hydrosilylation. ^bYield of oxidation. ^cIsomer ratio determined by capillary GC. ^dEnantiomeric excess determined by ¹H NMR analysis employing Eu(hfc)₃ as a chiral shift reagent. ^eEnantiomeric excess determined by ¹⁹F NMR of the corresponding Mosher ester. ^fEnantiomeric excess determined by chiral GC.

In summary, HSiMe₂OTBDPS reacts with functionalized 1,6-dienes catalyzed by **1**/NaBAR₄ to form silylated carbocycles with up to 95% ee. These silylated carbocycles undergo oxidative cleavage of the C–Si bond at room temperature with complete retention of stereochemistry. The significant enhancement in the enantioselectivity of palladium-catalyzed cyclization/hydrosilylation employing HSiMe₂OTBDPS relative to other silanes suggests the potential general utility of HSiMe₂OTBDPS in catalytic asymmetric hydrosilylation. We are currently working towards the development of more effective procedures for oxidation of the –SiMe₂OTBDPS group.

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References and Notes

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5) Synthesis of HSiMe₂OTBDPS. Saturated aqueous NaHCO₃ (120 mL) was added to a solution of TBDPSCl (13.0 mL, 50.0 mmol) and dimethylchlorosilane (16.6 mL, 150.0 mmol) in THF (120 mL) at 0 °C, warmed slowly to room temperature and stirred overnight. Work-up and chromatography gave HSiMe₂OTBDPS (12.6 g, 80%) as a colorless oil. ¹H NMR: δ 7.69-7.66 (m, 4 H), 7.42-7.36 (m, 6 H), 4.97 (septet, *J* = 2.8 Hz, 1 H), 1.06 (s, 9 H), 0.27 (s, 3 H), 0.26 (s, 3 H). ¹³C{¹H}NMR: δ 136.1, 135.2, 129.7, 127.9, 27.0, 19.7, 1.4.

6) Synthesis of **3**. Diene **2** (172 mg, 0.53 mmol) and HSiMe₂OTBDPS (0.50 g, 1.60 mmol) were added sequentially to a solution of **1** (11 mg, 0.03 mmol) and NaBAR₄ (27 mg, 0.03 mmol) in CH₂Cl₂ (6 mL) under nitrogen at -20 °C and maintained at this temperature for 12 h. Evaporation of solvent and chromatography gave **3** as a colorless oil (335 mg, 99%). ¹H NMR: 7.68-7.61 (m, 4 H), 7.40-7.30 (m, 6 H), 3.86 - 3.82 (m, 4 H), 1.78 (dd, *J* = 6.8, 13.2 Hz, 1 H), 1.69 (dd, *J* = 6.8, 13.2 Hz, 1 H), 1.43-1.26 (m, 2 H), 1.17 (s, 9 H), 1.16 (s, 9 H), 1.03 (s, 9 H), 0.99-0.93 (m, 3 H), 0.85 (d, *J* = 6.0 Hz, 3 H), 0.30 (dd, *J* = 11.0, 14.6 Hz, 1 H), 0.10 (s, 3 H), 0.09 (s, 3 H). ¹³C{¹H} NMR: 178.8, 178.7, 136.2, 135.4, 129.7, 127.8, 68.5, 44.0, 43.4, 42.4, 41.8, 41.0, 39.2, 27.5, 27.1, 22.9, 19.5, 17.7, 2.0, 1.6.

7) Synthesis of **4**.⁴ A suspension of **3** (364 mg, 0.57 mmol), TBAF (1.0 M in THF, 5.0 mL, 5 mmol), KF (410 mg, 7.0 mmol), KHCO₃ (120 mg, 1.2 mmol) and H₂O₂ (50% wt) (0.70 mL, 12.0 mmol) was stirred at room temperature for 3 days. Water/EtOAc work up followed by chromatography gave **4** (143 mg, 73%) as a colorless oil.