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Asymmetric diene cyclization/hydrosilylation/oxidation employing 1-*tert*-butyl-3,3-dimethyl-1,1-diphenyldisiloxane

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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 $NaBAr_4$ [Ar = 3,5-$C_6H_3(CF_3)_2$] catalyzed the asymmetric cyclization/hydrosilylation of functionalized 1,6-dienes with 1-*tert*-butyl-3,3-dimethyl-1,1-diphenyldisiloxane at –20°C to form silylated cyclopentanes in good yield with up to 95% ee. These silylated carbocycles underwent oxidative cleavage of the C–Si bond with H_2O_2 at room temperature to form the corresponding alcohols.

We have been investigating the cyclization/hydrosilylation of functionalized dienes catalyzed by mixtures of (N–N)Pd(Me)Cl [N–N = 1,10-phenanthroline[1] or (*R*)-(+)-4-isopropyl-2-(2-pyridinyl)-2-oxazoline (**1**)][2] and $NaBAr_4$ [Ar = 3,5-$C_6H_3(CF_3)_2$]. Our initial procedures required the use of $HSiEt_3$ 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 ($HSiMe_2OTMS$) as an effective and readily oxidized silane for use in palladium-catalyzed cyclization/hydrosilylation.[4] Unfortunately, the enantioselectivity of asymmetric cyclization/hydrosilylation employing $HSiMe_2OTMS$ was significantly diminished relative to $HSiEt_3$. For example, the reaction of 4,4-bis(trimethylacetoxymethyl)-1,6-heptadiene (**2**) with $HSiEt_3$ catalyzed by **1**/$NaBAr_4$ formed carbocycle **3** with 91% ee, while the reaction of **2** with $HSiMe_2OTMS$ in the presence of **1**/$NaBAr_4$ formed carbocycle **4** with only 82% ee (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 oxidation. Here we report that 1-*tert*-butyl-3,3-dimethyl-1,1-diphenyldisiloxane ($HSiMe_2OTBDPS$) serves as an effective silane for the asymmetric cyclization/hydrosilylation/oxidation of 1,6-dienes, generating (hydroxymethyl)cyclopentanes with up to 95% ee.

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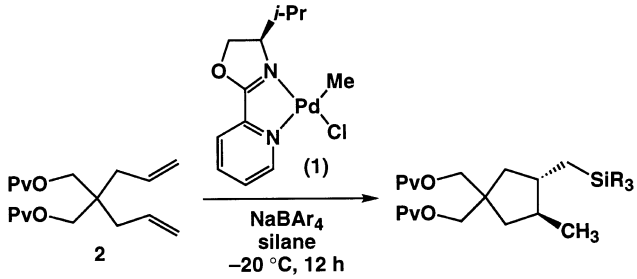
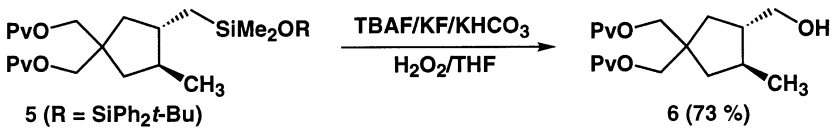
Table 1
Asymmetric cyclization/hydrosilylation of **2** catalyzed by a 1:1 mixture of **1** and $NaBAr_4$ (5 mol%) as a function of silane



Entry	Silane	Carbocycle	Yield (%)	de (%)	ee (%)
1	$HSiEt_3$	3	89	>95	91
2	$HSiMe_2OTMS$	4	98	>95	82
3	$HSiMe_2OTBDPS$	5	99	>95	95

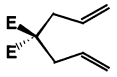
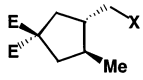
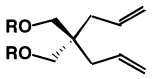
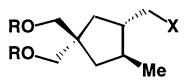
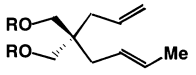
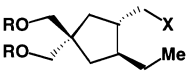
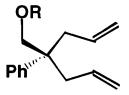
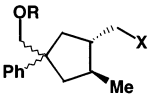
The reaction of **2** and excess of $HSiMe_2OTBDPS$[5] catalyzed by a 1:1 mixture of **1** and $NaBAr_4$ (5 mol%) in CH_2Cl_2 at –20°C for 12 h led to the isolation of silylated carbocycle **5** in 99% yield with >95% de and 95% ee (Table 1, entry 3).[6] Unfortunately, carbocycle **5** failed to oxidize under the conditions previously employed for oxidation of the $–SiMe_2OTMS$ group (KF/AcOOH, 25°C, 48 h)[4] and an alternative procedure was therefore required.[7] To this end, the reaction of **5** with a mixture of TBAF, KF, $KHCO_3$, and 50% H_2O_2 in THF at room temperature for 3 days led to the isolation of alcohol **6** in 73% yield (Scheme 1).[8] In addition to diene **2**, a range of functionalized 1,6-dienes underwent asymmetric cyclization/hydrosilylation/oxidation employing $HSiMe_2OTBDPS$ to give (hydroxymethyl)cyclopentanes in moderate to good yield with high enantioselectivity (Table 2).



Scheme 1.

In summary, $HSiMe_2OTBDPS$ reacts with functionalized 1,6-dienes in the presence of **1**/$NaBAr_4$ to form silylated carbocycles with up to 95% ee. These silylated carbocycles undergo oxidative cleavage of the C–Si bond with H_2O_2 at room temperature. The significant enhancement of the enantioselectivity of palladium-catalyzed cyclization/hydrosilylation employing $HSiMe_2OTBDPS$ relative to $HSiEt_3$ and $HSiMe_2OTMS$ suggests that $HSiMe_2OTBDPS$ may be of general use in catalytic asymmetric hydrosilylation. We are currently working towards the development of more effective procedures for oxidation of the $–SiMe_2OTBDPS$ group.

Table 2
Asymmetric cyclization/hydrosilylation of dienes employing $HSiMe_2OTBDPS$ catalyzed by a 1:1 mixture of **1** and $NaBAr_4$ (5 mol%) in CH_2Cl_2 at $-20°C$ for 12 h, followed by oxidation with excess TBAF, KF, $KHCO_3$, and 50% H_2O_2 in THF at room temperature for 3 days

diene	carbocycle	yield (%) (X = SiR_3)[a]	yield (%) (X = OH)[b]	de (%)[c]	ee (%)
					
E = CO_2Me		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,g]
R = Me		85	70	1.5:1	91[e,g]

[a]Yield of cyclization/hydrosilylation. [b]Yield of oxidation. [c]Isomer ratio determined by capillary GC. [d]Enantiomeric excess determined by ^1H NMR analysis employing $Eu(hfc)_3$ as a chiral shift reagent. [e]Enantiomeric excess determined by ^{19}F NMR of the corresponding Mosher ester. [f]Enantiomeric excess determined by chiral GC. [g]Enantiomeric excess of major diastereomer.

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4. Pei, T.; Widenhoefer, R. A. *Org. Lett.* **2000**, *2*, 1469.
5. Synthesis of $HSiMe_2OTBDPS$. Saturated aqueous $NaHCO_3$ (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, the mixture was warmed slowly to room temperature, and stirred overnight. Work-up and chromatography gave $HSiMe_2OTBDPS$ (12.6 g, 80%) as a colorless oil. ^1H NMR: δ 7.69–7.66 (m, 4H), 7.42–7.36 (m, 6H), 4.97 (septet, $J=2.8$ Hz, 1H), 1.06 (s, 9H), 0.27 (s, 3H), 0.26 (s, 3H). $^{13}C\{^1H\}$ NMR: δ 136.1, 135.2, 129.7, 127.9, 27.0, 19.7, 1.4.

6. Synthesis of **5**. Diene **2** (172 mg, 0.53 mmol) and $HSiMe_2OTBDPS$ (0.50 g, 1.60 mmol) were added sequentially to a solution of **1** (11 mg, 0.03 mmol) and $NaBAr_4$ (27 mg, 0.03 mmol) in CH_2Cl_2 (6 mL) under nitrogen at −20°C and maintained at this temperature for 12 h. Evaporation of solvent and chromatography gave **5** as a colorless oil (335 mg, 99%). ^1H NMR: δ 7.68–7.61 (m, 4H), 7.40–7.30 (m, 6H), 3.86–3.82 (m, 4H), 1.78 (dd, $J=6.8$, 13.2 Hz, 1H), 1.69 (dd, $J=6.8$, 13.2 Hz, 1H), 1.43–1.26 (m, 2H), 1.17 (s, 9H), 1.16 (s, 9H), 1.03 (s, 9H), 0.99–0.93 (m, 3H), 0.85 (d, $J=6.0$ Hz, 3H), 0.30 (dd, $J=11.0$, 14.6 Hz, 1H), 0.10 (s, 3H), 0.09 (s, 3H). $^{13}C\{^1H\}$ NMR: δ 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. The following conditions also failed to oxidize the $-SiMe_2OTBDPS$ group: (1) AcOOH/DMF/KF/25°C; (2) AcOOH/AcOH/$HgOAc_2$/25°C; (3) AcOOH/DMF/KHF_2/25°C; (4) *t*-BuOOH/CsOH/DMF/TBAF/25°C; (5) AcOOH/Py-HF/DMF/KF/25°C.
8. Synthesis of **6**.[4] A suspension of **5** (364 mg, 0.57 mmol), TBAF (1.0 M in THF, 5.0 mL, 5 mmol), KF (410 mg, 7.0 mmol), $KHCO_3$ (120 mg, 1.2 mmol) and H_2O_2 (50% wt) (0.70 mL, 12.0 mmol) was stirred at room temperature for 3 days. Water/EtOAc work-up, followed by chromatography gave **6** (143 mg, 73%) as a colorless oil.