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Organolanthanide-Catalyzed Cyclization/Boration of 1,5- and 1,6-Dienes

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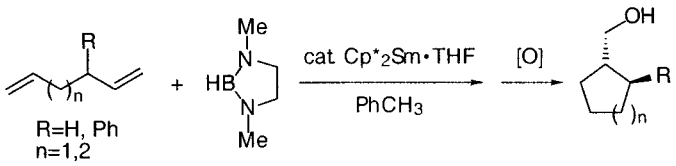
ABSTRACT



1,5- and 1,6-Dienes undergo a cyclization/boration reaction in the presence of a catalytic amount of Cp^*_2Sm·THF. The resulting organoboranes can be oxidized to the corresponding primary cyclic alcohols using standard conditions.

Group 3 and lanthanide metallocenes have been extensively investigated as catalysts promoting highly stereoselective cyclization/silylation reactions of monosubstituted and 1,1-disubstituted 1,5- and 1,6-dienes to functionalized carbocycles.[1] However, the synthetic utility of the organolanthanide-promoted cyclization/silylation reaction suffers from the fact that in some cases conversion of the organosilanes to the corresponding alcohols proved to be difficult.[2] Furthermore, synthetically useful transformations of alkylsilanes are relatively limited. Although carbon−carbon bond forming reactions via Pd(0)-catalyzed cross-coupling events have been realized, these transformations generally require activation of the organosilane by fluoride.[3] It was not obvious that the types of organosilanes generated by our cyclization/silylation protocol would be conducive to this transformation. To address these limitations, alternative reagents need to be developed to trap the cyclized organometallic intermediate leading to products that can be functionalized under mild conditions.

The use of organoboranes in organic synthesis is well established,[4] and a termination reaction involving a suitable boration reagent would create products open to the full palette of organoboron chemistry. Encouragingly, hydroboration reactions catalyzed by lanthanide metallocenes have been previously reported.[5] The resultant organoboranes were oxidized to the corresponding alcohols using basic hydrogen peroxide. However, the only reported cyclization reactions involving boranes were addition−carbocyclization protocols of enynes and diynes catalyzed by transition metals with compounds containing interheteroatom bonds such as B−Sn or B−Si.[6] In this contribution we report the first metal-catalyzed cyclization/boration reaction.

The proposed catalytic cycle of the organolanthanide-catalyzed cyclization/boration reaction is outlined in Scheme

(1) (a) Molander, G. A. *Chemtracts* **1998**, *11*, 237 and references therein. (b) Molander, G. A.; Dowdy, E. D.; Schumann, H. *J. Org. Chem.* **1998**, *63*, 3386. (c) Molander, G. A.; Nichols, P. J.; Noll, B. C. *J. Org. Chem.* **1998**, *63*, 2292. (d) Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040. (e) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (f) Onozawa, S.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1994**, *35*, 8177. (g) Molander, G. A.; Dowdy, E. D. In *Topics in Organometallic Chemistry*; Kobayashi, S., Ed.; Springer-Verlag: New York, 1999; Vol. 2, pp 120−154.

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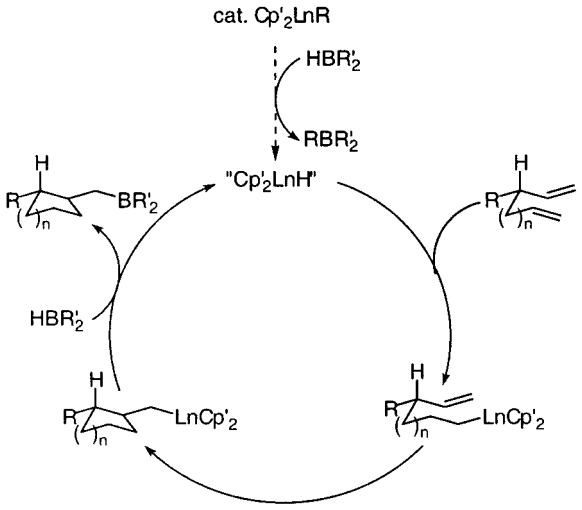
Scheme 1[a]

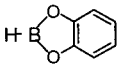
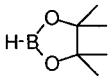
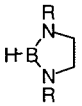


[a] Cp′ = Cp* (Pentamethylcyclopentadienyl) or Cp^{TMS} (Trimethylsilylcyclopentadienyl).

1. Most individual steps of the transformation are well precedented.[5] The precatalyst reacts with the organoborane via σ-bond metathesis to generate the catalytically active organolanthanide hydride species "Cp'_2LnH" (Cp′ = Cp* pentamethylcyclopentadienyl or Cp^{TMS} trimethylsilylcyclopentadienyl). Next, the catalyst "Cp'_2LnH" regioselectively inserts into the least hindered olefin, placing the metal with its bulky ligands at the terminus of the carbon chain. As depicted in Scheme 1, the resulting hydrocarbyl undergoes an intramolecular insertion into the second olefin through a chairlike transition structure. Finally, σ-bond metathesis produces the desired organoborane and regenerates the catalyst to complete the catalytic cycle.

In an attempt to build on the initial study by Marks and co-workers,[5] the conditions of the original lanthanide-catalyzed hydroboration reaction using catecholborane and Cp^*_2Sm·THF as the precatalyst were applied to attempt the cyclization/boration reaction of 1,5-hexadiene (**1**) (Table 1, eq 1).[7] However, examination of the reaction mixture after 18 h by ^{11}B NMR spectroscopy showed no evidence of a hydroboration reaction (entry a). An additional peak at δ 12.12 ppm in the ^{11}B NMR spectrum of the reaction mixture indicated partial decomposition of the catecholborane to different borane species.

Table 1. Optimization of the Organolanthanide Catalyzed Cyclization/Boration Reaction of 1,5-Hexadiene (**1**)[a]

	precatalyst (mol%)	borane	**6**; isolated yield (conditions)
a	Cp^*_2Sm·THF (1.6)		no reaction (rt, 18 h)
b			
	Cp^*_2YMe·THF (1.8)		42% (rt, 18 h)
	Cp^*_2Sm·THF (1.6)		50% (rt, 18 h)
	$[Cp^{TMS}{}_2YMe]_2$ (2.2)		45% (rt, 18 h)
c	Cp^*_2Sm·THF		
		R=Me	86% (rt, 18 h)
		R=Et	45% (rt, 18 h)
		R=*i*-Pr	no reaction (80 °C, 18 h)
d		R=Me	
	Cp^*_2YMe·THF (1.8)		no reaction (80°C, 18 h)
	$[Cp^{TMS}{}_2LnMe]_2$		
	Ln=Lu (1.8)		40% (80 °C, 18 h)
	Ln=Y (2.2)		62% (80 °C, 18 h)
	Ln=Sm (1.8)		74% (80 °C, 18 h)

[a] In entries a−d, all reactions were monitored by ^{11}B NMR spectroscopy. Compound **6** was isolated using the procedure in ref 7. In entry b, byproducts hex-5-ene-1-ol and 1,6-hexanediol were identified by GC-co-injection of commercial samples.

Next, pinacolborane was examined as a boration reagent in combination with different precatalysts (entry b). All of the hydroboration reactions went to completion after 18 h as evidenced by ^{11}B NMR spectroscopy. Unfortunately, the desired cyclized product cyclopentylmethanol (**6**) could only be isolated in yields up to 50%. Other byproducts, such as hex-5-ene-1-ol and 1,6-hexanediol, were identified.

Apparently, after the initial insertion of the catalyst into the olefin, σ-bond metathesis of the hydrocarbyl efficiently competes with the cyclization event to afford uncyclized organoboranes.

To slow σ-bond metathesis and hence promote the cyclization reaction, 1,3-diaza-2-boracycloalkanes were examined (entry c).[8] Only 1,3-dimethyl-1,3-diaza-2-boracyclopentane proved to be an efficient boration reagent, affording **6** in 86% yield. The cyclization/boration reaction with 1,3-diethyl-1,3-diaza-2-boracyclopentane provided **6** in only 45% yield. Examination of the reaction mixture by ^{11}B NMR spectroscopy after 18 h showed a significant amount of unreacted 1,3-diethyl-1,3-diaza-2-boracyclopentane. 1,3-

(7) **Representative Procedure for Lanthanide Catalyzed Cyclization/Boration (Table 1; Entry c, R = Me).** In a nitrogen filled glovebox, the precatalyst (0.010 g, 1.6 mol %) was dissolved in 3 mL of toluene. After the addition of 1,5-hexadiene (**1**) (0.10 g, 1.22 mmol) the resultant reaction mixture was stirred for 10 min at ambient temperature, during which time the color of the solution changed from brown/purple to red. Next, freshly distilled 1,3-dimethyl-1,3-diaza-2-boracyclopentane (0.164 g, 1.30 mmol) was added dropwise over a period of 10 min. After stirring for 18 h the reaction was found to be complete as evidenced by ^{11}B NMR spectroscopy. The solvent was removed in a vacuum. Next, 3 mL of 3M NaOH, 3 mL of THF, and 3 mL of 30% H_2O_2 were added, and the mixture was stirred for 18 h. The resulting suspension was saturated with K_2CO_3, followed by extraction with 4 × 20 mL of ether. The organic layers were combined, washed with 15 mL of saturated NH_4OH, and dried over Na_2SO_4. After removal of the solvent in a vacuum, purification by flash chromatography, followed by Kugelrohr distillation, afforded **6** (R_f 0.16 in hexane/EtOAc 10:1) in 86% yield (0.104 g, 1.04 mmol). The compound was identified by comparison of the spectral and analytical data with commercial samples (see also Supporting Information).

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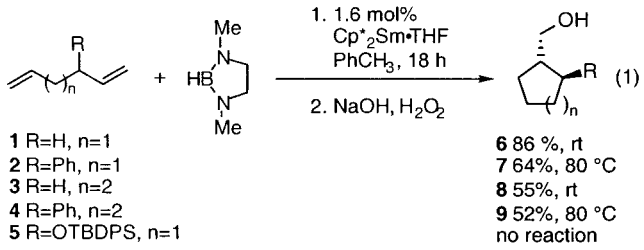
Diisopropyl-1,3-diaza-2-boracyclopentane showed no evidence of a hydroboration reaction. The increased steric bulk on the nitrogen apparently slows down the σ-bond metathesis between the hydrocarbyl and the 1,3-diaza-2-boracycloalkanes to the point where no reaction occurs.

In an attempt to optimize the cyclization/boration reaction further, different lanthanide metallocenes were tested with 1,3-dimethyl-1,3-diaza-2-boracyclopentane and substrate **1** (entry d). The cyclization/boration reaction using the divalent precatalyst Cp*$_2$Sm·THF afforded **6** after 18 h, followed by oxidative workup in 86% yield. Cp*$_2$YMe·THF did not show any activity with 1,3-dimethyl-1,3-diaza-2-boracyclopentane. The precatalysts [Cp$^{TMS}_2$LnMe]$_2$ afforded **6** after 18 h at 80 °C in yields ranging from 40% for Ln = Lu to 74% for Ln = Sm. The results illustrate that reduced substitution about the ligand and a larger metal ionic radius contribute to accelerated cyclization/boration. Considering also the ease of preparation in comparison to the other lanthanide metallocenes,[9] we decided to use Cp*$_2$Sm·THF as the precatalyst to probe the scope of the cyclization/boration with different substrates.

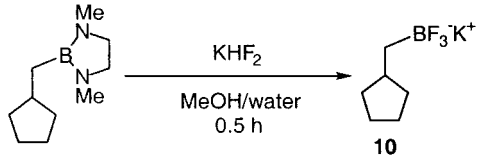
The cyclization/boration reaction with 1,3-dimethyl-1,3-diaza-2-boracyclopentane and substrates **1**−**4** catalyzed by Cp*$_2$Sm·THF afforded, after oxidative workup, the alcohols **6** and **7** containing five-membered rings in yields of 86% and 64% and the alcohols **7** and **8** containing six-membered rings in yields of 55% and 52%, respectively (eq 1). The cyclization/boration reaction is less efficient for the formation of six-membered rings, as indicated by the decreased yield of **8** and **9** relative to **6** and **7**.



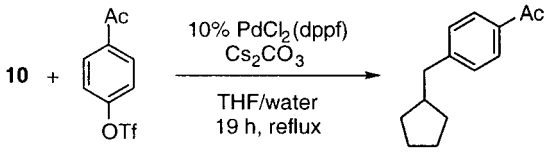
(1)

Products **6** and **8** were identified by comparison of the ^{1}H and ^{13}C NMR spectral data with commercial samples. Compounds **7** and **9** were isolated as single diastereomers. The trans stereochemistry was confirmed by comparison of the spectral data with literature data.[10] Unfortunately, we were unable to perform cyclization/boration on substrates such as compound **5** containing a protected alcohol utilizing this protocol. According to Marks, the divalent samarium precatalyst converts to a trivalent active organosamarium species by allylic C−H activation.[11] The initial allylmetallic intermediate, where R = OTBDPS, could perform irreversible reactions with the protected alcohol functional group that are perhaps responsible for this result.

The moisture sensitive borane resulting from boration/cyclization of **1** was isolated from the reaction mixture via distillation under inert atmosphere. This borane was converted to the air stable potassium trifluoroborate salt (eq 2),[12] which can undergo Suzuki cross coupling reactions (eq 3).[13]



(2)



(3)

In summary, a cyclization/boration reaction catalyzed by an organosamarium complex has been developed. This reaction produced, after oxidative workup, primary alcohols containing five- and six-membered rings. Although dienes containing protected alcohol functional groups do not undergo cyclization/boration utilizing this protocol, further studies designed to optimize and broaden the scope of this reaction are under way in our laboratory.

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Supporting Information Available: The preparation and characterization of compounds **1**−**9** and experimental procedures. This information is available free of charge via the Internet at http://pubs.acs.org.

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