Regioselective Homologation of Bis(boronate) Intermediates Derived from Rhodium-Catalyzed Diboration of Simple Alkenes

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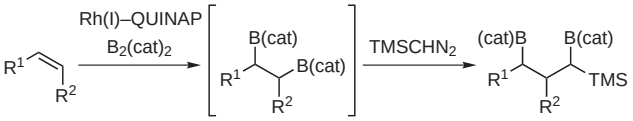
Abstract: Regioselective homologation of alkyl-1,2-bis(catecholboronates) may be accomplished by treatment of these reactive intermediates with $TMSCHN_2$. A convenient process is reported where alkene diboration and the subsequent homologation reaction are accomplished in the same reaction flask.

Key words: boron, asymmetric catalysis, silicon, regioselectivity, alkenes

By effecting the transformation of simple alkenes into alkyl 1,2-bis(boronates), the rhodium-catalyzed diboration of olefins may enable the transformation of olefins into a variety of functional substructures.[1] Whereas the domino diboration–oxidation reaction sequence effectively delivers 1,2-diols from alkenes in an asymmetric fashion, other transformations may furnish different structures.[2] In this regard, we have begun to develop alternate reaction sequences and have reported that the domino diboration–Suzuki coupling–oxidation reaction sequence is particularly effective for transforming 1-alkenes into chiral β-phenethyl alcohol derivatives.[3] This reaction sequence relies on the fact that, in Pd-catalyzed cross-coupling, less hindered C–B bonds react faster than more hindered C–B bonds thereby allowing the selective transformation of one of the two boron atoms in a diboration product.[4]

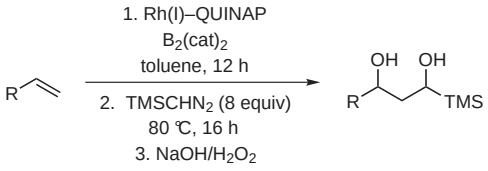
Recently, Mioskowski has described a novel homologation reaction upon treatment of catechol boronate esters with $TMSCHN_2$.[5,6] We expected that, similar to the Suzuki cross-coupling reaction mentioned above, the Mioskowski homologation might also be sensitive to substitution of the C–B bond and might therefore allow for the selective production of alkyl 1,3-bis(boronates) from alkyl 1,2-bis(boronates). In addition, since the Rh-catalyzed alkene diboration provides catechol boronate esters directly, we considered that development of a single-pot process such as that depicted in Scheme 1 would be possible and would significantly expand the range of chiral targets, which are accessible from the asymmetric diboration reaction.

Initial experiments were directed towards developing the domino diboration–homologation–oxidation sequence and towards learning about the homologation selectivity



Scheme 1

with 1-alkene substrates. Accordingly, a Rh–QUINAP-catalyzed diboration of 1-octene with bis(catecholatodiboron) was executed in THF. Subsequent to the diboration, the reaction mixture was treated with reagents for homologation as reported by Mioskowski (3 equiv of $TMSCHN_2$, refluxing THF). These experiments resulted in low product yields even with extended reaction times. It was noted that a significant amount of non-homologated material remained at the end of the reaction and therefore more forcing conditions were examined. Since the Rh–QUINAP-catalyzed diboration reaction also proceeds well in toluene, we examined the domino reaction sequence in this solvent with the homologation being conducted at higher temperature (Scheme 2). In this experiment, four equivalents of trimethylsilyldiazomethane were added to the reaction mixture subsequent to catalytic diboration. After heating at 80 °C for eight hours, an additional four equivalents of $TMSCHN_2$ were added and the reaction heated an additional 8 hours. Oxidation of the reaction mixture provided a 58% yield of 1-trimethylsilyl-1,3-nonanediol (Table 1, entry 1). Analysis of the crude ^1H NMR spectrum indicated that the primary C–B bond reacted exclusively and that the secondary C–B bond remained untouched.



Scheme 2

With experimental conditions for domino diboration–homologation developed, several terminal alkenes were explored in the tandem reaction (Table 1). Whereas styrene is a poor substrate for the domino sequence (entry 6), aliphatic alkenes appear to provide consistently higher yields (45–58%) regardless of substitution of the allylic carbon. In all cases, the 1-trimethylsilyl-1,3-diols were

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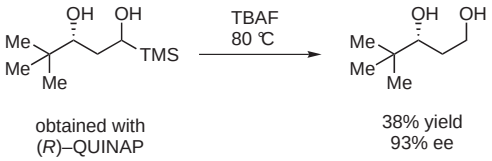
Table 1 Single-Pot Domino Diboration–Homologation–Oxidation

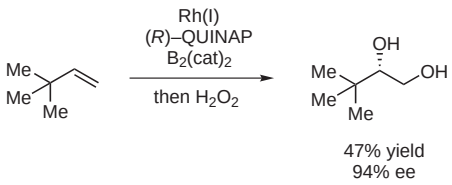
Entry	R	Yield (%)
1	hexyl	58
2	*tert*-butyl	49
3	neopentyl	51
4	cyclohexyl	55
5	isobutyl	53
6	Phenyl	15

isolated by column chromatography as a mixture of diastereomers.[7]

Because the Rh–QUINAP-catalyzed diboration is highly enantioselective when the allylic carbon of the 1-alkene is a quaternary center, the domino single-pot diboration–homologation–oxidation procedure may be used to generate optically active products with useful levels of selectivity. As depicted in Equation 1, TBAF-promoted protodesilylation of the product derived from *tert*-butylethylene provides the 1,3-diol in 93% enantiomeric excess.[8] Comparing this level of selectivity with that of the 1,2-diol obtained by diboration–oxidation (94% ee, Equation 2) suggests that the homologation reaction does not disturb the configuration of the stereogenic C–B bond in the reaction intermediate and that the level of selectivity obtained in the diboration reaction is manifest in the diboration–homologation–oxidation product.

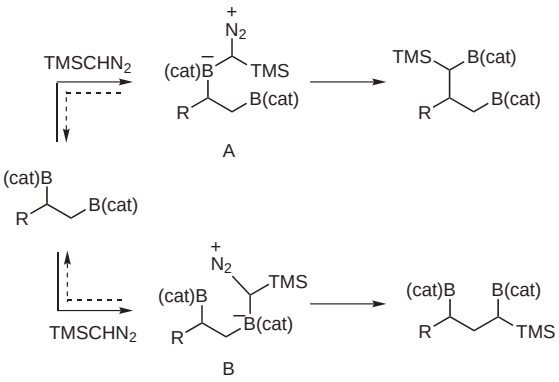


Equation 1



Equation 2

One of two explanations might account for the level and sense of regioselection in the homologation reactions described above. As depicted in Scheme 3, it is conceivable that $TMSCHN_2$ adds to the less hindered C–B bond (to give **B**) fastest and the resulting 1,2-alkyl shift provides the observed product in a selective fashion. Alternatively, it is tenable that addition of $TMSCHN_2$ to the boronate is reversible and that the rate of the subsequent rearrangement dictates the reaction outcome. The former scenario appears more plausible given that 1,2-alkyl shifts involving boronate complexes are known to favor migration of



Scheme 3

the more substituted carbon, presumably for electronic reasons.[9]

In summary, we have described the operationally simple, one-pot diboration–homologation–oxidation reaction of olefin substrates. Current efforts in our laboratory focus on developing other transformations of 1,2-bis(boronate) intermediates.

Acknowledgment

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(7) **Representative Procedure.**
A dry 16 mL vial was charged with 3.7 mg (0.013 mmol) of {bicyclo[2.2.1]hepta-2,5-diene}-(2,4-pentanedionato)-rhodium(I), 5.5 mg (0.013 mmol) of (*S*)-QUINAP, and 1.0 mL of toluene in a dry-box. The resultant solution was stirred for 3 min before 89 mg (0.37 mmol) of bis(catecholato)diboron was added. After 3 more minutes, 32 μL (0.25 mmol) of 3,3-dimethyl-1-butene was added and the solution allowed to stir for 24 h at ambient temperature. The vial was then wrapped in foil and 0.50 mL (1.0 mmol) of trimethylsilyldiazomethane (2.0 M in hexanes) was added. After stirring for 8 h at 80 °C an additional 0.50 mL (1.0 mmol) of trimethylsilyldiazomethane (2.0 M in hexanes) was added. After stirring an additional 8 h at 80 °C, the solution was cooled to 0 °C and NaOH (1.0 mL of 3 M) and H_2O_2 (1 mL of 30% solution) were added cautiously. After 6 h, the mixture was treated with 2 mL of sat. aq $Na_2S_2O_3$ and extracted with EtOAc. The crude material was purified by silica gel chromatography (3:1 hexanes–EtOAc) to provide 25 mg (49% yield) of pure 4,4-dimethyl-1-(trimethylsilyl)pentane-1,3-diol.

(8) **Procedure for Protodesilylation.**
To 38 mg of 4,4-dimethyl-1-(trimethylsilyl)pentane-1,3-diol (0.19 mmol, obtained from entry 2, Table 1) was added 2.4 mL of THF followed by 0.38 mL of TBAF (1.0 M in THF, 0.38 mmol). After stirring at 70 °C for 23 h the mixture was evaporated to dryness and the residue resuspended in EtOAc. After washing with H_2O, the solution was concentrated and the crude material purified on silica gel (2:1 hexanes–EtOAc) to give 9.4 mg (38% yield) of 4,4-dimethyl-1,3-pentanediol.

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