ORGANIC LETTERS

2003
Vol. 5, No. 14
2573−2575

Platinum-Catalyzed Tandem Diboration/Asymmetric Allylboration: Access to Nonracemic Functionalized 1,3-Diols

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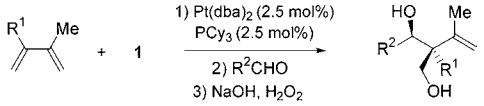
Received May 28, 2003

ABSTRACT



A single-pot tandem catalytic diene diboration/carbonyl allylation reaction is described that uses a commercially available chiral diboron reagent. The chirality of the intermediate diboration adduct is transferred to the product in the carbonyl allylation reaction, thereby providing access to enantioenriched chiral products. Notably, the reaction allows for construction of a quaternary stereocenter and furnishes a synthetically versatile C–B bond in the reaction product.

Catalytic addition of metal−metal-bonded reagents to organic substrates provides dimetallic species that are versatile intermediates in organic synthesis. Along these lines, reagents containing intermetallic bonds have been successfully added across alkenes, alkynes, dienes, enones, and imines.[1] Of the processes mentioned, bis-metalation of 1,3-dienes is particularly useful since it provides access to allyl(bis)metal species (**A**, Scheme 1),[2] and we expected that these compounds may participate in subsequent cascade reactions. As an example (Scheme 1), the allyl(bis)metallic species may engage in a carbonyl addition reaction, the product of which (**B**) may then react with a second reagent (to give **C**).[3] With appropriately substituted diene precursors, the allylmetalation reaction may allow for higher product substitution and hence allow access to quaternary stereocenters.[4,5] To develop this methodology for use in asymmetric synthesis, we have begun to examine methods for enantiocontrol in tandem dimetalation/allylation reactions. Our initial approach was to first develop mild conditions for activation of the B−B bond in chiral diboranes and subsequently to examine allylmetalation reactions of the chiral allylborane reagents.

Scheme 1

Successful development of a stereoselective tandem dimetalation/allylation reaction requires control of selectivity during each step of the multistep sequence. In this regard, we were attracted to the commercially available diboron reagent bis(diethyl-L-tartrateglycolato)diboron[6] (**1**) due to the

(1) For reviews with representative reactions, see: (a) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63. (b) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (c) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392.

(2) (a) Ishiyama, T.; Masafumi, Y.; Miyaura, N. *Chem. Commun.* **1996**, 2073. (b) Clegg, W.; Thorsten, J.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. *J. Chem. Soc., Dalton Trans.* **1998**, 1431.

(3) For diastereoselective diboration/allylboration, see: (a) Suginome, M.; Nakamura, H.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4248. (b) Suginome, M.; Matsuda, T.; Yoshimoto, T.; Ito, Y. *Org. Lett.* **1999**, *1*, 1567.

(4) For approaches to the construction of quaternary stereocenters, see: (a) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388. (b) Christoffers, J.; Mann, A. *Angew, Chem. Int. Ed.* **2001**, *40*, 4591.

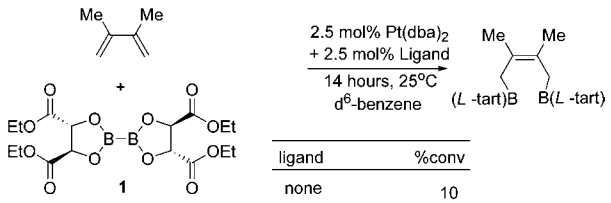
(5) For asymmetric allylmetalation reactions that generate quaternary stereocenters, see: (a) Yamamoto, Y.; Hara, S.; Suzuki, A. *Synlett* **1996**, 883. (b) Denmark, S. E.; Fu, J. *J. Am. Chem. Soc.* **2001**, *123*, 9488. (c) Kennedy, J. W.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 898.

10.1021/ol034936z CCC: $25.00
Published on Web 06/13/2003

known ability of the tartrate control element to effectively influence stereoselection in the allylmetalation reaction.[7] We have found that under appropriate conditions, (*Z*)-selective 1,4-addition across 1,3-dienes occurs. Subsequently, we surveyed the ability of the resulting bis-boronates to engage in stereoselective allylmetalation reactions. The resulting allylation product may be manipulated in situ, and the one-pot process from diene to product is the subject of this report.

The majority of diboration reactions described in the literature are catalyzed by phosphine-containing platinum-(0) metal centers. The proposed mechanism for the diboration of 1,3-dienes involves initial oxidative addition of the diborane to furnish a square-planar L_2PtB_2 intermediate.[2b,8] Since dissociation of a phosphine ligand from the L_2PtB_2 center is required for coordination of the reacting diene, we expected that a platinum catalyst with a monodentate phosphine would be most active. Addition of **1** to 2,3-dimethylbutadiene was examined with the readily available complex $Pt(dba)_2$ (Scheme 2).[9] Reactions were carried out in C_6D_6 at

Scheme 2

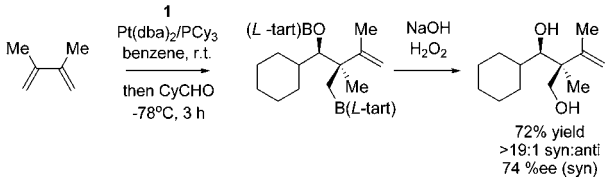


ligand	%conv
none	10
PPh_3	5
PCy_3	95

room temperature and followed by in situ ^{1}H NMR spectroscopy. While diene diboration did not proceed well at room temperature in the absence of ligand or in the presence of triphenylphosphine (<10% conversion), addition of 1 equiv of tricyclohexylphosphine relative to platinum resulted in >95% conversion to the diboration adduct after 14 h. Notably, the reaction with PCy_3 provided the required high levels of stereocontrol furnishing a >20:1 *Z*:*E* ratio of stereoisomers.[10]

Since tartrate boronate esters suffer hydrolytic cleavage in the presence of water, the diboration adducts were employed without isolation. The benzene solution obtained from the stereoselective diboration was therefore diluted with 3 parts toluene, and 4 Å powdered molecular sieves were added. Upon dropwise addition of a cyclohexane carboxaldehyde solution at −78 °C, the corresponding allylation product was obtained cleanly after oxidative workup (Scheme 3). The corresponding 1,3-diol that contains a quaternary

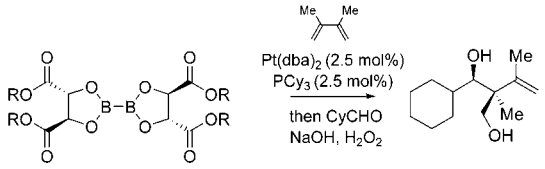
Scheme 3



carbon stereocenter was isolated in 72% yield and >19:1 syn:anti diastereoselection with the syn isomer being formed in 74% enantiomeric ratio.

In an effort to improve the reaction selectivity, the effect of tartrate structure on enantioselection was investigated (Table 1). Though a linear correlation between selectivity

Table 1. Catalytic Diboration/Allylation with Chiral Diboronates[a]



entry	tartrate (R)	% yield	% ee
1	Me	21	72
2	Et	68	74
3	*i*-Pr	38	58
4	CH(*i*-Pr)$_2$	17	60

[a] Step 1: 1 equiv of diene, 1 equiv of diboronate, benzene, rt, 12 h. Step 2: toluene, 4 Å mol sieves, 1 equiv of RCHO −78 °C, 3 h. Step 3: 50 °C, 3 h. For all reactions, syn:anti > 19:1.

and steric encumbrance is not observed, a steric component is obvious. The sterically less bulky dimethyl tartrate-derived boronate provides enantioselection on the order of that seen for diethyl tartrate. However, increasing the size of the R group to isopropyl or 2,4-dimethylpentyl (entries 3 and 4) leads to a decrease in the enantiomeric ratio and the reaction yield.[11] Reaction with tartrate amides and with amino alcohol-derived diboranes failed in the initial diboration reaction (data not shown).

Examination of a series of substrates suggests that the cis-diboration adduct leads to exclusive formation of the syn allylation adduct (>19:1 syn/anti ratio in all cases, Table 2). Yields are good to excellent for the three-step procedure regardless of substrate structure, although the enantiomeric ratio is strongly substrate dependent. Aliphatic aldehydes provide the highest enantioselectivities (entries 1−3 and 6), whereas aromatic and α,*β*-unsaturated aldehydes provide

(6) Commerically available from Aldrich Chemical Co.

(7) (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339. (c) Roush, W. R.; Hoong, L. K.; Palmer, M.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109.

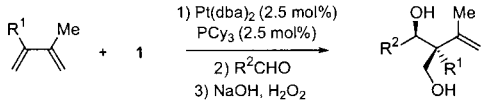
(8) For investigations on the mechanism of alkyne diboration, see: Iverson, C. N.; Smith, M. R. *Organometallics* **1996**, *15*, 5155.

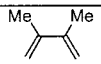
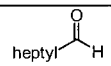
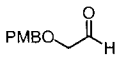
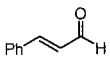
(9) Cherwinski, W. J.; Johnson B.; Lewis, J. *J. Chem. Soc., Dalton Trans.* **1974**, 1405.

(10) For the ability of basic monophosphines to promote alkyne diboration, see: Thomas, R. L.; Souza, F.; Marder, T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 1650.

(11) Beneficial effect of larger tartrate substituents in allylation reactions: Hara, S.; Yamamoto, Y.; Fujita, A.; Suzuki, A. *Synlett* **1994**, 639.

Table 2. Catalytic Diboration/Allylation of Various Aldehydes Employing Diboronate 1[a]



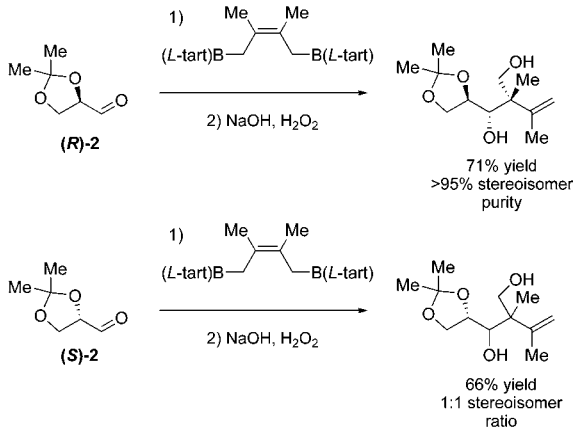
entry	diene	R_2CHO	% yield	%ee
1			68	70
2			72	74
3			58	66
4			59	40
5			65	33
6			65	74[b]

(a) Step 1: 1 equiv of diene, 1 equiv of **1**, benzene, rt, 12 h. Step 2: Add toluene, 4 Å mol sieves, 1 equiv of aldehyde, −78 °C, 3 h. Step 3: 50 °C, 3 h. All reaction >19:1 syn:anti. (b) Same procedure except that 5% $(PPh_3)_2Pt$(ethylene) was used for 24 h at 80 °C in step 1.

products with lower enantioselection. In contrast to reactions with 2,3-dimethylbutadiene, reactions with nonsymmetric isoprene face an issue involving regioselection (entry 6). Complete regiocontrol and diastereocontrol is observed in this transformation such that the resulting 1,3-diol product contains minimal substitution at the allylic stereocenter.

Given the propensity for chiral allyboronate reagents to exhibit matched and mismatched stereoselection in allylation reactions, we examined the influence of preexisting stereocenters on reaction outcome.[7] After standard diboration of 2,3-dimethylbutadiene, subsequent allyl addition proceeded smoothly with both enantiomers of aldehyde **2** (Scheme 4). The matched enantiomer is the same as that observed by

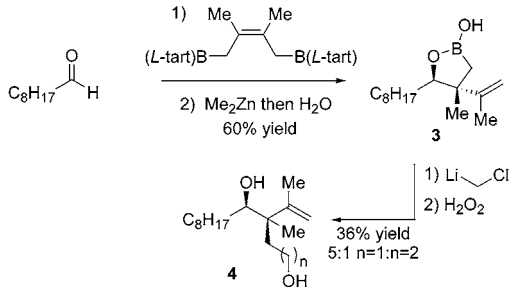
Scheme 4



Roush with simple allylboronates, and it provided the highly oxygenated product in excellent yield and as a single stereoisomer by ^1H NMR. The opposite enantiomer of substrate **2** leads to a 1:1 mixture of stereoisomers.

The reactions described above were all subjected to oxidative workup such that the remaining C−B bond in the allylation adduct was converted to the derived alcohol. The utility of C−B bonds in organic synthesis suggested that other transformations might provide access to alternate reaction products. While direct homologation of the tartrate boronate ester was unsuccessful, homologation could be accomplished if the allylation product was first converted to the derived cyclic half-ester (**3**, Scheme 5). This trans-

Scheme 5



formation occurs by direct addition of water to the allylation product, although **3** could be obtained in higher yields if it was subjected to dimethyl zinc prior to addition of water. Homologation of **3** to give **4** is accomplished by addition of chloromethyllithium according to the procedure developed by Matteson,[12] followed by oxidative workup.

In conclusion, we have developed a method that allows access to stereodefined quaternary carbon centers from commercially available starting materials. With the correct choice of aldehyde and diboronate, versatile synthetic intermediates may be accessed with a useful level of stereoisomeric purity. Efforts directed toward alternate functionalization of the intermediate alkylboronate and toward the development of catalytic asymmetric dimetalation reactions continue in our labs.

Acknowledgment. J.B.M. is appreciative of a fellowship from the Wellcome Trust. This work was supported by the NIH (GM 59417-03). J.P.M. thanks AstraZeneca, Bristol-Myers Squib, Dow, DuPont, GlaxoSmithKline, and the Packard Foundation for support.

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

OL034936Z

(12) Sadha, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687.