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Platinum-Catalyzed Diboration Using a Commercially Available Catalyst: Diboration of Aldimines to α-Aminoboronate Esters

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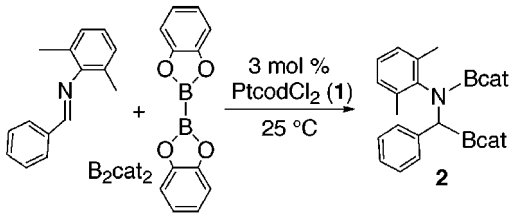
ABSTRACT



Commercially available Pt(cod)Cl_2 catalyzes the diboration of alkenes, alkynes, and aldimines using bis(catecholato)diboron (cod = 1,5-cyclooctadiene). Catalyzed aldimine diboration provides the first direct route to α-aminoboronate esters. The diboration product from *N*-benzylidene-2,6-dimethylaniline is structurally characterized.

Boronic acids and boronate esters are useful molecules in organic chemistry and biochemistry. These molecules are important intermediates in organic synthesis.[1] Boronic acids and boronate esters are used in palladium[2]- and nickel[3]-catalyzed cross-coupling reactions and, more recently, copper-catalyzed reactions to form new carbon−carbon bonds.[4] Ongoing research has led to their recent use as linkers for solid-phase synthesis,[5] in macrocyclic chemistry,[6] in organometallic synthesis,[7] and for new organic transformations.[8] Furthermore, boronic acids have been studied as fructose sensors,[9] and α-aminoboronic acids, [RR′NCHR″B$(OH)_2$], are known to bind strongly to serine proteases and related enzymes.[10]

The preparation of a wide variety of boronic acids and boronate esters with excellent control of regio-, diastereo-, and enantioselectivity has become possible with the advent of metal-catalyzed hydroboration and diboration of unsaturated organic substrates.[11] While diboration of alkynes can be catalyzed by Pt$(PPh_3)_4$[12] or Pt$(PPh_3)_2(C_2H_4)$,[13] the diboration of terminal alkenes using B_2cat_2 or B_2pin_2[14] employs

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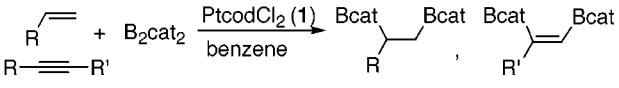
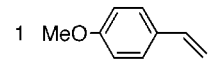
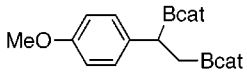
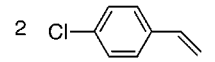
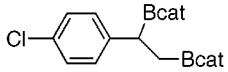
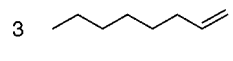
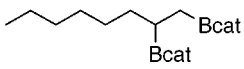
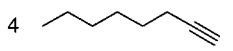
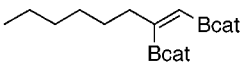
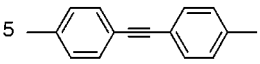
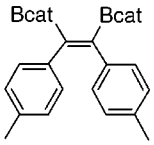
gold,[15] platinum,[16] and rhodium[17] catalysts, none of which are commercially available. The diboration of carbon−heteroatom double bonds[18] is a potentially direct route to a variety of biologically active α-functionalized boronate esters.[19] We report herein that commercially available $Pt(cod)Cl_2$, **1**, catalyzes the diboration of terminal alkenes, vinylarenes, and alkynes using B_2cat_2, as well as the first metal-catalyzed diboration of aldimines to form α-aminoboronate esters.

Excellent yields are obtained when **1** is used as a precatalyst for the diboration of terminal alkenes, vinylarenes, and alkynes (Table 1).[20] Reaction of benzene solutions of

Table 1. $Pt(cod)Cl_2$-Catalyzed Diboration[a]



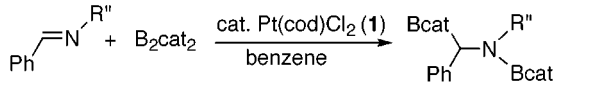
entry	substrate	product	% yield[b]
1			96 (79)[c]
2			93
3			93
4			92[d]
5			91 (56)[c,d]

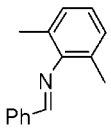
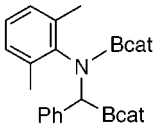
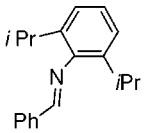
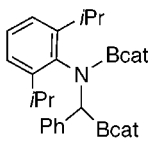
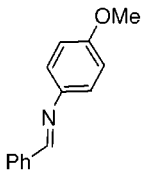
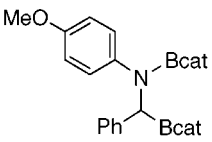
[a] Reaction conditions: 0.25 mM substrate, 1.1 equiv of B_2cat_2, 3−5 mol % of **1**, 3 h at 25 °C in benzene. [b] Yields determined by ^1H NMR spectroscopy with respect to an internal standard from an average of at least two runs. Yields in parentheses refer to isolated yields. [c] Yields of isolated product are lower due to the similarities in solubilities of the product and the degradation product of the catalyst. [d] Reaction was stirred at 55 °C for 3 h.

4-vinylanisole, 4-chlorostyrene, or 1-octene with 3−5 mol % of **1** and 1.1 equiv of B_2cat_2 at room temperature forms diboration products in greater than 90% yield (Table 1, entries 1−3).[21] Diboration of terminal alkynes, such as 1-octyne (entry 4), and internal alkynes, such as ditolylacetylene (entry 5), is accomplished in 3 h at 55 °C with use of 5 mol % of **1**.

Reaction of aldimines and B_2cat_2 in the presence of 3−5 mol % of **1** affords *rac*-α-aminoboronate esters in good yields (Table 2).[22] This catalyst precursor effects the diboration of sterically hindered aldimines, such as *N*-benzylidene-2,6-dimethylaniline (entry 1) and *N*-benzylidene-2,6-diisopropylaniline (entry 2), in 87% and 95% yield, respectively. A comparatively lower yield (66%) of α-aminoboronate ester is obtained when *N*-benzylidene-4-anisidine is used as a substrate (entry 3). The *rac*-α-aminoboronate

Table 2. $Pt(cod)Cl_2$-Catalyzed Diboration of Aldimines[a]



entry	substrate	product	% yield[b]
1			87 (78)
2			95
3			66[c]

[a] Reaction conditions: 0.25 mM substrate, 1.1 equiv of B_2cat_2, 3−5 mol % of **1**, 3 h at 25 °C in benzene. [b] Yields determined by ^1H NMR spectroscopy with respect to an internal standard from an average of at least two runs. Yield in parentheses refers to an isolated yield. [c] Reaction was stirred at 55 °C for 3 h.

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(20) **Typical procedure,** ^1H NMR yield (Table 1, entry 1): a 2 mL screw-capped vial equipped with a mini-stir bar was charged with **1** (1.7 mg, 0.005 mmol, 3 mol % of Pt), B_2cat_2 (38.0 mg, 0.16 mmol), 4-vinylanisole (18.0 mg, 0.13 mmol), and trimethoxybenzene as standard (17.6 m g, 0.10 mmol) under N_2. Benzene-d_6 (0.5 mL) was added to the vial, and the solution was stirred for 3 h, after which time the solution was transferred to a NMR tube. The yield of the diboration product was obtained with respect to trimethoxybenzene by ^1H NMR spectroscopy.

(21) Like other reported Pt catalysts, complex **1** does not mediate the diboration of acyclic internal alkenes. The only reported diboration of internal alkenes uses a Rh catalyst. See: ref 17.

(22) **Typical procedure,** isolated yield (Table 2, entry 1): a 20 mL screw-capped vial equipped with a stir bar was charged with **1** (14.4 mg, 0.038 mmol, 3 mol %), B_2cat_2 (125.3 mg, 0.53 mmol), *N*-benzylidene-2,6-dimethylaniline (101.5 mg, 0.49 mmol), and 2.0 mL of benzene under N_2. The reaction was stirred for 3 h, after which time the vial was placed in a −5 °C freezer. The benzene solvent was removed by sublimation under vacuum to yield a dark brown powder. The solid was then dissolved in 2.0 mL of ether, and the solution was placed in a −35 °C freezer overnight, after which time the product precipitated as a white solid.

ester, **2**, derived from the diboration of *N*-benzylidene-2,6-dimethylaniline was isolated by removal of benzene solvent followed by precipitation from an ether/hexanes solution. X-ray quality crystals of **2** obtained from toluene/hexanes solution contained both *R*- and *S*-isomers; the molecular structure of the *R*-isomer is shown in Figure 1,[23] confirming

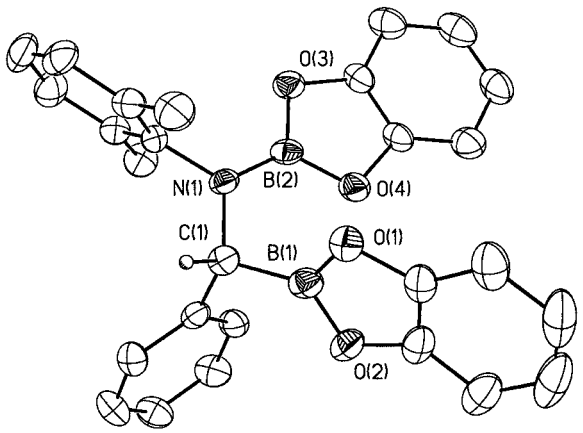

Figure 1. Molecular structure of (2,6-Me_2-Ph)N(Bcat)CHPh(Bcat), **2**. Thermal ellipsoids are drawn at 50% probability. Only the *R*-isomer is shown, and hydrogen atoms are omitted for clarity.

our ^{1}H, ^{13}C, and ^{11}B NMR spectral assignments. The only other reported crystal structures of α-aminoboronate esters are those in which the nitrogen is contained in a pyrrolidine ring.[24]

Metal-catalyzed diboration of aldimines to form α-aminoboronate esters is selective for diaryl aldimines. Mild reaction conditions are sufficient for substrates containing bulky or electron-donating substituents on the aryl group bound to the nitrogen. Thus far, significant yields of diboration products have not been observed for simple aliphatic aldimines. Initial attempts to selectively deborate the N−B bond of the product (H_2O and anhydrous HCl in ether) resulted in predominant formation of starting material. The chemical origin of this reactivity is currently being investigated, and new protocols for deboration are being explored.

Catalyst effectiveness depends on the Pt-bound halide, diene, and diboron reagent employed. Upon stirring a heterogeneous mixture of **1** and B_2cat_2 in benzene under nitrogen at room temperature for 5 h, a dark brown homogeneous solution is formed. This solution catalyzes the diboration of aldimines. A mixture of Pt(cod)Br_2 and B_2cat_2 requires stirring for over 24 h before the solution becomes homogeneous. This solution also catalyzes the diboration of aldimines, albeit in a slightly lower yield than **1**. Reaction of Pt(cod)I_2 with B_2cat_2 does not become homogeneous even upon stirring for over 1 week. Reaction of Pt(dicyclopentadiene)Cl_2 with B_2cat_2 immediately forms a brown homogeneous solution, but use of this catalyst solution results in significantly lower yields of diboration product. The effective alkene diboration catalyst, Pt(dba)$_2$ (dba = dibenzylideneacetone), also mediates the diboration of aldimines, but over 20 mol % is required for complete conversion of the starting aldimine. No reaction is observed between **1** and B_2pin_2 by ^{11}B NMR spectroscopy, and their mixtures did not catalyze diboration reactions.

Donor ligands inhibit the aldimine diboration reaction. Addition of phosphines such as triphenylphosphine or 1,1′-bis(diphenylphosphino)ferrocene deactivates the catalyst toward diboration. These results are similar to the diboration of alkynes catalyzed by Pt complexes in which the presence of added phosphines severely decreased catalyst activity.[13a] Even coordinating solvents such as THF reduce the catalyst activity; less than 5% diboration product is observed when THF is used as a solvent. This is in contrast to the excellent yields obtained using benzene or methylene chloride. Furthermore, rhodium phosphine complexes are ineffective catalysts for aldimine diboration. Wilkinson's catalyst, RhCl(PPh_3)$_3$, gives significantly more hydroboration[25] than diboration, and cationic rhodium complexes with chelating bis(phosphine) ligands are inactive.

The first step in the mechanism of platinum-catalyzed diboration is proposed to be oxidative addition of the boron−boron bond to a Pt(0) complex.[11] The reduction of air- and water-stable **1** by B_2cat_2 takes place in situ to form a catalytically active Pt(0) complex. This is evidenced by a sharp peak observed at 28 ppm in the ^{11}B NMR spectrum of the dark brown solution formed by mixing **1** and B_2cat_2, indicative of ClBcat formation. Diboration product is observed immediately by ^{1}H NMR spectroscopy when a catalytic amount of this solution is added to *N*-benzylidene-2,6-dimethylaniline and B_2cat_2. In contrast, an induction period of ca. 1 h is required before any diboration product is observed when **1** is used directly.

In conclusion, we have developed a general method for the diboration of terminal alkenes, vinylarenes, alkynes, and aldimines using a commercially available catalyst precursor. Furthermore, we have developed a direct route to α-aminoboronate esters via Pt-catalyzed diboration of aldimines. Investigations into the scope and mechanism of metal-catalyzed diboration of aldimines are currently in progress.

Acknowledgment. We thank Tom M. Cameron for preliminary aldimine diboration experiments, Professors Stephen A. Westcott and Richard D. Broene for useful

(23) Crystal data for **2**: M = 894.17, monoclinic, a = 8.4702(5) Å, b = 16.3243(11) Å, c = 32.945(2) Å, β = 90.4990(10)°, V = 4555.1(5) Å^3, T = 203(2) K, space group = $P2(1)/c$, Z = 4, Mo Kα, λ = 0.71073 Å, D_c = 1.304 g/cm^3, 14042 reflections collected, 6317 unique (R(int) = 0.0493), residuals of R1 = 0.0663 and wR2 = 0.1241 with $I > 2\sigma(I)$, 613 variable parameters used in the refinement, goodness-to-fit on F^2 = 1.038. CCDC deposition number 144949.

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(25) Hydroboration products are proposed to arise from "backwards" insertion of the aldimine into the M−B bond, followed by β-H elimination of the aldimine C−H. Details will follow in the full paper.

discussions, and the Department of Energy's Laboratory Directed Research and Development (LDRD) program for financial support of this work.

Supporting Information Available: Detailed experimental procedures and characterization and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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