Rhodium-catalyzed hydroborations of allylamine and allylimines[1]

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Abstract: The in situ rhodium-catalyzed addition of catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$) and pinacolborane (HBpin, pin = 1,2-$O_2C_2Me_4$) to allylamine, allylimine, 2- and 4-vinylpyridines, and a thienyl imine has been examined using multinuclear NMR spectroscopy. Although reactions of allylamine ($H_2NCH_2CH{=}CH_2$) and HBcat gave complex product distributions arising from competing dehydrogenative borylation pathways, addition of HBpin to allylamine using a rhodium catalyst afforded only products arising from hydroboration (RN(Bpin)$CH_2CH_2CH_2$Bpin, where R = H, Bpin) and hydrogenation (RN(Bpin)$CH_2CH_2CH_3$). Hydroboration of allylimines (RHC=N$CH_2CH{=}CH_2$, R = Ar) with HBcat occurs initially at the more reactive imine functionality to give unsaturated borylamines (RCH_2N(Bcat)$CH_2CH{=}CH_2$). Further reaction with HBcat gives varying amounts of hydroboration products RCH_2N(Bcat)$CH_2CH_2CH_2$Bcat and RCH_2N(Bcat)CH_2CH(Bcat)CH_3 as well as the diboration product RCH_2N(Bcat)CH_2CH_2CH(Bcat)$_2$, depending on the choice of catalyst. Reactions with related unsaturated pyridine derivatives are complicated by extensive degradation, which can be avoided by coordination of the pyridine nitrogen to a Lewis acid. The first examples of metal-catalyzed hydroboration of imines using HBpin are also reported.

Key words: catalysis, hydroboration, boronate esters, dehydrogenative borylation, allylimines.

Résumé : Faisant appel à la spectroscopie RMN multinucléaire, on a étudié la réaction in situ, catalysée par le rhodium, du catécholborane (HBcat, cat= 1,2-$O_2C_6H_4$) et du pinacolborane (HBpin, pin = 1,2-$O_2C_2Me_4$) avec l'allylamine, l'allylimine, les 2- et 4-vinylpyridines et une thiénylimine. Même si les réactions de l'allylamine ($H_2NCH_2CH{=}CH_2$) avec le HBcat conduisent à des distributions complexes de produits provenant de voies de borylation déshydrogénante en compétition, l'addition du HBpin à l'allylamine en présence d'un catalyseur de rhodium ne conduit qu'aux produits provenant d'une hydroboration (RN(Bpin)$CH_2CH_2CH_2$Bpin dans lequel R = H ou Bpin) ou d'une hydrogénation (RN(Bpin)$CH_2CH_2CH_3$). L'hydroboration des allylimines (RHC=N$CH_2CH{=}CH_2$, R = Ar) à l'aide de HBcat se produit initialement au niveau de la fonctionnalité imine qui est la plus réactive pour conduire à la formation de borylamines (RCH_2N(Bcat)$CH_2CH{=}CH_2$). Une réaction subséquente avec du HBcat conduit à des quantités variables de produits d'hydroboration, RCH_2N(Bcat)$CH_2CH_2CH_2$Bcat et RCH_2N(Bcat)CH_2CH(Bcat)CH_3 ainsi qu'au produit de diboration, RCH_2N(Bcat)CH_2CH_2CH(Bcat)$_2$, suivant le catalyseur choisi. Les réactions avec les dérivés insaturés de la pyridine apparentés sont compliquées par d'importantes réactions de dégradation que l'on peut éviter en procédant à une coordination de l'azote de la pyridine à l'aide d'un acide de Lewis. On rapporte aussi les premiers exemples de réactions d'hydroboration, catalysées par des métaux, d'imines à l'aide de HBpin.

Mots clés : catalyse, hydroboration, esters de l'acide boronique, borylation déshydrogénante, allylimines.

[Traduit par la Rédaction]

Introduction

The hydroboration of alkenes and alkynes, which constitutes the formal addition of a B—H bond across a carbon—carbon multiple bond, is an extremely important reaction in organic synthesis (1). Although simple boron hydride reagents such as borane ($H_3B{\cdot}X$, where X is a Lewis base) and 9-borabicyclo[3.3.1]nonane react readily with alkenes at room temperature, hydroborations with catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$) generally require elevated temperatures. The discovery that transition metals can be used to catalyze the addition of HBcat to organic substrates has become an important and well-established technique in organic synthesis (for an excellent review on hydroborations catalyzed by transition-metal complexes, see ref. 2) (3, 4). These reactions can have regio-, chemo-, or stereoselectivities, complementary, or more remarkably, opposite to those from products obtained via the uncatalyzed variant. Indeed, hydroborations of 5-hexene-2-one with HBcat proceed readily at room temperature to give exclusive formation of a borate product where the borane has added to the more reactive carbonyl double bond (4). However, when the reaction is carried out at 0°C in the pres-

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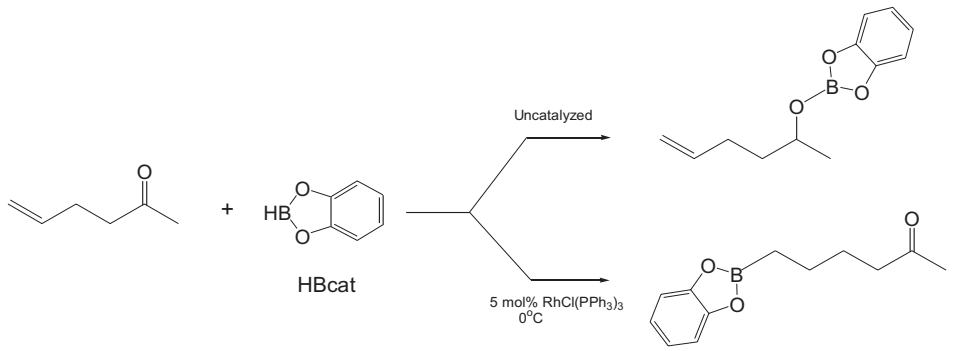
Scheme 1.



ence of a catalytic amount of Wilkinson's catalyst ($RhCl(PPh_3)_3$), addition of the B—H bond occurs primarily at the less reactive alkene moiety to give an organoboronate ester product (Scheme 1).

Organoboronate esters ($RB(OR')_2$) and boronic acids ($RB(OH)_2$) belong to a remarkable class of compounds that have been used extensively in organic (5–9), organometallic (10, 11), and solid-phase synthesis (12, 13), as well as in macrocyclic chemistry (14), molecular recognition (15), transporting molecules across biological membranes (16), redox switching (17), and as glucose sensors (18, 19). Interest in these compounds also arises from their unique biological activities (20). For instance, peptide boronic acids are among the most potent, known inhibitors of serine proteases (21). As a result, the synthesis of boron-containing amino acid derivatives has become an area of considerable interest (22, 23).

Hydroborations of tertiary allylic amines ($R_2NCH_2CH{=}CH_2$, R = alkyl, aryl) with borane ($H_3B{\cdot}X$, X = SMe_2, THF) are known to give initial formation of the expected *anti*-Markovnikov products, $R_2NCH_2CH_2CH_2BH_2$ (6, 24–26). Analogous reactions with primary and secondary amines, however, are complicated by direct interaction with the N—H bond to give a number of *N*-boryl products (27, 28). Protection of the N—H bond is usually required in these reactions to ensure chemoselective addition of the borane at the allyl group (29, 30). Unfortunately, deprotection methodologies frequently compromise the integrity of the B—C bond (31). We, therefore, decided to investigate the in situ reactions of allylamine ($H_2NCH_2CH{=}CH_2$, **1**) and related allylimine derivatives with catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$) and pinacolborane (HBpin, pin = 1,2-$O_2C_2Me_4$) to see if we could generate novel aminoboron compounds without using a protecting group.

Experimental

All reagents and solvents used were obtained from Aldrich Chemicals. Complexes $RhCl(PPh_3)_3$ (32), $[RhCl(coe)_2]_2$ (coe = *cis*-cyclooctene, (33)), and $[RhCl(cod)]_2$ (cod = *cis*-cyclooctadiene, (34)) were prepared as described elsewhere. Imines were prepared by well-established procedures (35–38). NMR spectra were recorded on a JEOL JNM-GSX270 FT NMR spectrometer. ^{1}H NMR chemical shifts are reported in ppm and referenced to residual protons in deuterated solvent at 270.1 MHz. ^{11}B NMR chemical shifts are referenced to external $F_3B{\cdot}OEt_2$ at 86.6 MHz. ^{13}C NMR chemical shifts are referenced to solvent carbon resonances as internal standards at 67.8 MHz. Multiplicities are reported as (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, (br) broad, and (ov) overlapping. Infrared spectra were obtained using a Mattson Genesis II FT IR spectrometer and are reported in cm^{-1}. Microanalyses for C, H, and N were carried out at Desert Analytics (Tucson, Arizona).

Preparation of $Rh(acac)(coe)_2$

$Rh(acac)(coe)_2$ was prepared by modification of an established procedure (39). Tl(acac) (0.42 g, 1.40 mmol) was dissolved in 10 mL of THF and added dropwise to a solution of $[RhCl(coe)_2]_2$ (0.50 g, 0.70 mmol) in 10 mL of THF. The reaction was allowed to stir for 18 h then stored for 48 h at –25°C. A greenish precipitate was filtered whereupon subsequent removal of the THF under vacuum afforded an orange solid. IR (Nujol): 2904, 1581, 1520, 1464, 1377, 1317, 1269, 1020, 897, 766, 735, 604, 550, 519. ^{1}H NMR (in C_6D_6) δ: 5.03 (s, 1H), 2.51 (br, 4H), 2.41 (br, 8H), 1.68 (br s, 12H), 1.55 (br, 4H), 1.40 (br, 6H). ^{13}C NMR δ: 185.0, 98.8 (CH), 78.0 (d, $J_{C\text{-}Rh}$ = 12 Hz, -CH=CH-), 30.3 (CH_2), 27.9 (CH_2), 27.0 (CH_2), 26.8 (CH_3).

Addition of catecholborane (HBcat) to allylamine (1)

In a typical reaction, 2 equiv of HBcat in 0.5 mL of C_6D_6 were added dropwise to a 0.5 mL C_6D_6 solution of allylamine. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. Attempts to control the selectivity of these reactions always gave minor amounts of **2**, which precipitated out of solution after ca. 1 h. **2**: IR (Nujol): 3200, 2940, 2868, 2443, 1600, 1464, 1377, 1350, 1232, 1099, 1057, 1083, 912, 808, 739, 700. ^{1}H NMR (in d_6-acetone) δ: 8.00 (br, cat), 7.09 (br ov m, cat), 6.48 (br, cat), 6.05 (br ov m, 1H, $CH{=}CH_2$), 5.40 (br ov m, 2H, $CH{=}CH_2$), 3.88 (br, 2H, -C*H*$_2$CH=CH_2). ^{11}B NMR δ: 23 (br, NBcat), 13 (s, N → HBcat). **3**: ^{1}H NMR (in C_6D_6) δ: 7.01 (d of d, *J* = 6, 3 Hz, 4H, cat), 6.73 (d of d, *J* = 6, 3 Hz, 4H, cat), 5.82 (ov d of d of t, *J* = 17, 10, 7 Hz, 1H, -C*H*=CH_2), 5.16 (d of d, *J* = 17, 2 Hz, 1H, -CH=C*H*H), 4.94 (d of d, *J* = 10, 2 Hz, 1H, -CH=CH*H*), 3.92 (d, *J* = 7 Hz, 2H, -C*H*$_2$CH=CH_2). ^{11}B NMR δ: 26 (br, NBcat). ^{13}C NMR δ: 148.6, 136.3, 122.3, 115.1, 112.1, 46.3.

Catalyzed hydroborations of allylamine (1) with HBcat

In a typical reaction, 5 equiv of HBcat in 0.5 mL of C_6D_6 were added to a 0.5 mL C_6D_6 solution of allylamine and 1 mol% $RhCl(PPh_3)_3$. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. **4**: IR

(Nujol): 3060, 2962, 2935, 2873, 1610, 1511, 1467, 1344, 1232, 1182, 1130, 1083, 1007, 941, 866, 806, 733, 680, 498. ^{1}H NMR (in d_6-acetone) δ: 7.60 (br ov m, min), 7.23 (br s, cat), 7.13 (br s, cat), 6.57 (br s, cat), 4.1–3.9 (ov m, min), 3.80 (t, J = 8 Hz, -NCH_2-), 3.58 (t, J = 8 Hz, -NCH_2-), 2.09 (ov m, -CH_2CH_2CH_2-), 1.72 (ov t of t, J = 8 Hz, -CH_2CH_2CH_2-), 1.34 (t, J = 8 Hz, -CH_2B), 0.88 (t, J = 8 Hz, -CH_2B). ^{11}B NMR δ: 35 (br, CBcat), 22 (br, NBcat), 13 (s, N → HBcat). **5**: ^{1}H NMR (in C_6D_6) δ: 7.06–6.68 (ov m, 12H, cat), 3.46 (t, J = 8 Hz, 2H, -NCH_2-), 1.90 (ov t of t, J = 8 Hz, 2H, -CH_2CH_2CH_2-), 1.07 (t, J = 8 Hz, 2H, -CH_2B). ^{11}B NMR δ: 34 (br, CBcat), 26 (br, NBcat). **6**: ^{1}H NMR δ: 7.06–6.68 (ov m, 12H, cat), 3.76 (2nd order d of d, J = 14, 8 Hz, 1H, -NCH*H*-), 3.64 (2nd order d of d, J = 14, 8 Hz, 1H, -NC*H*H-), 1.87 (ov t of q, J = 8 Hz, 1H, -C*H*(Bcat)CH_3), 1.15 (d, J = 8 Hz, 3H, -CH_3. ^{11}B NMR δ: 34 (br, CBcat), 26 (br, NBcat). **8**: ^{1}H NMR δ: 7.06–6.68 (ov m, 16H, cat), 3.62 (t, J = 8 Hz, 2H, -NCH_2-), 2.48 (ov d of t, J = 8 Hz, 2H, -CH_2CH_2CH-), 1.70 (t, J = 8 Hz, 1H, -C*H*(Bcat)$_2$). ^{11}B NMR δ: 34 (br, CBcat), 26 (br, NBcat). **9**: ^{1}H NMR δ: 7.17–6.64 (ov m, 8H, cat), 3.34 (t, J = 8 Hz, 2H, -NCH_2-), 1.57 (ov t of q, J = 8 Hz, 2H, -CH_2C$H_2$$CH_3$), 0.81 (t, J = 8 Hz, 3H, -CH_3).

Catalyzed hydroborations of $H_2NCH_2CH{\equiv}CH$ with HBcat

In a typical reaction, 5 equiv of HBcat in 0.5 mL of C_6D_6 were added to a 0.5 mL C_6D_6 solution of propargyl amine and 1 mol% $RhCl(PPh_3)_3$. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. Products were similar to those observed for reactions with **1**.

Addition of pinacolborane (HBpin) to allylamine (1)

In a typical reaction, 2 equiv of HBpin in 0.5 mL of C_6D_6 were added dropwise to a 0.5 mL C_6D_6 solution of allylamine. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. **10**: ^{1}H NMR (in C_6D_6) δ: 5.73 (ov d of d of t, J = 16, 8, 8 Hz, 1H, -CH_2C*H*=CH_2), 5.10 (d of d, J = 16, 1 Hz, 1H, -CH_2CH=C*H*H), 4.92 (d of d, J = 8, 1 Hz, 1H, -CH_2CH=CH*H*), 3.53–3.50 (br d, J = 8 Hz, 2H, -CH_2CH=CH_2), 2.21 (br s, 1H, N*H*), 1.10 (s, 12H, pin). ^{13}C NMR δ: 139.4, 112.7, 81.7, 43.7, 24.5. ^{11}B NMR δ: 24 (br, NBpin).

Catalyzed hydroborations of allylamine (1) with HBpin

In a typical reaction, 3 equiv of HBpin in 0.5 mL of C_6D_6 were added to a 0.5 mL C_6D_6 solution of allylamine and $RhCl(PPh_3)_3$ (1 mol%). The reaction mixture was allowed to stir for 12 h and then analyzed by multinuclear NMR spectroscopy. **11**: ^{1}H NMR (in C_6D_6) δ: 6.50 (ov d of d of t, J = 18, 10, 8 Hz, 1H, -CH_2C*H*=CH_2), 4.50 (d of d, J = 18, 2 Hz, 1H, -CH_2CH=C*H*H), 4.37 (d of d, J = 10, 2 Hz, 1H, -CH_2CH=C*H*H), 3.90 (d, J = 8 Hz, 2H, -CH_2CH=CH_2), 1.10 (s, 24H, pin). ^{11}B NMR δ: 26 (br, NBcat). **12**: ^{1}H NMR (in C_6D_6) δ: 3.00 (ov d of t, J = 8 Hz, 2H, -NCH_2-), 2.27 (br, 1H, N*H*), 1.60 (ov t of t, J = 8 Hz, 2H, -CH_2CH_2CH_2-), 1.07–0.99 (ov m, 26H, -CH_2B and pin). ^{11}B NMR δ: 33 (br, CBpin), 25 (br, NBpin). **13**: ^{1}H NMR δ: 3.50 (t, J = 8 Hz, 2H, -NCH_2-), 2.04 (ov t of t, J = 8 Hz, 2H, -CH_2CH_2CH_2-), 1.26–1.03 (ov m, 38H, -CH_2B and pin). ^{11}B NMR δ: 33 (br, CBpin), 25 (br, NBpin). **14**: ^{1}H NMR δ: 2.84 (ov d of t, J = 8 Hz, 2H, -NCH_2-), 2.18 (br, 1H, N*H*), 1.26 (ov t of q, J = 8 Hz, 2H, -CH_2C$H_2$$CH_3$), 1.11 (s, 12H, pin), 0.75 (t, J = 8 Hz, 3H, -CH_3). ^{11}B NMR δ: 25 (br, NBpin). **15**: ^{1}H NMR δ: 3.39 (t, J = 8 Hz, 2H, -NCH_2-), 1.74 (ov t of q, J = 8 Hz, 2H, -CH_2C$H_2$$CH_3$), 1.05 (s, 24H, pin), 0.93 (t, J = 8 Hz, 3H, -CH_3). ^{11}B NMR δ: 25 (br, NBpin).

Catalyzed hydroborations of allylimines (16a–16d) with HBcat

In a typical reaction, 3 equiv of catecholborane in 0.5 mL of C_6D_6 were added to a 0.5 mL C_6D_6 solution of allylimine **16c** in the presence of 1 mol% $RhCl(PPh_3)_3$. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. **17c**: ^{1}H NMR (in C_6D_6) δ: 7.01–6.65 (ov m, 11H, cat and Ar), 4.30 (s, 2H, -NCH_2Ar), 3.09 (t, J = 8 Hz, 2H, -NCH_2-), 1.69 (ov t of t, J = 8 Hz, 2H, -CH_2CH_2CH_2-), 0.99 (t, J = 8 Hz, 2H, -CH_2B). ^{11}B NMR δ: 35 (br, CBcat), 26 (br, NBcat). **18c**: ^{1}H NMR δ: 7.01–6.65 (ov m, 11H, cat and Ar), 4.31 (s, 2H, -NCH_2Ar), 3.46 (2nd order d of d, J = 14, 8 Hz, 1H, -NCH*H*-), 3.31 (2nd order d of d, J = 14, 8 Hz, 1H, -NC*H*H-), 1.68 (ov t of q, J = 8 Hz, 1H, -C*H*(Bcat)CH_3), 1.07 (d, J = 8 Hz, 3H, -CH_3). ^{11}B NMR δ: 35 (br, CBcat), 26 (br, NBcat). **19c**: ^{1}H NMR δ: 7.01–6.65 (ov m, 15H, cat and Ar), 4.30 (s, 2H, -NCH_2Ar), 3.25 (t, J = 8 Hz, 2H, -NCH_2-), 2.18 (ov d of t, J = 8 Hz, 2H, -CH_2CH_2CH-), 1.63 (t, J = 8 Hz, 1H, -C*H*(Bcat)$_2$). ^{11}B NMR δ: 35 (br, CBcat), 26 (br, NBcat). **20c**: ^{1}H NMR δ: 7.01–6.65 (ov m, 7H, cat and Ar), 4.30 (s, 2H, -NCH_2Ar), 3.00 (t, J = 8 Hz, 2H, -NCH_2-), 1.38 (ov t of q, J = 8 Hz, 2H, -CH_2C$H_2$$CH_3$), 0.71 (t, J = 8Hz, 3H, -CH_3). ^{11}B NMR δ: 26 (br, NBcat).

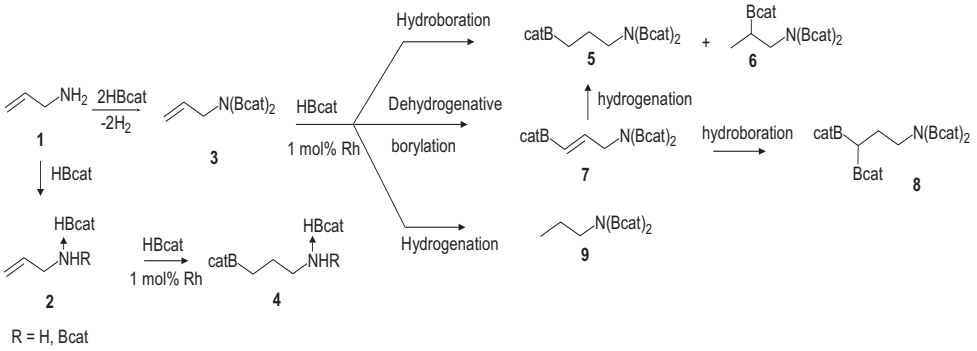
Catalyzed hydroborations of vinylpyridines-BF_3 with HBcat

In a typical reaction, 1.1 equiv of $BF_3{\cdot}OMe_2$ were added to a 0.5 mL solution of the vinylpyridine in C_6D_6. The resulting solution was allowed to stir for 2 h whereupon 1 mol% of $Rh(acac)(coe)_2$/dppb (dppb = 1,4-bis(diphenylphosphino)butane) in 0.25 mL of C_6D_6 was added to the mixture, followed by the addition of a 0.25 mL C_6D_6 solution of 1.2 equiv of HBcat. The mixture was allowed to stir for 1 h and then analyzed by multinuclear NMR spectroscopy. **22**: ^{1}H (in C_6D_6) δ: 8.55 (d, J = 5 Hz, 1H), 7.04–6.78 (ov m, 6H), 6.50 (app t, J = 5 Hz, 1H), 4.34 (q, J = 8 Hz, 1H, -C*H*(Bcat)-), 1.36 (d, J = 8 Hz, 3H, -CH_3). ^{11}B NMR δ: 34 (br, CBcat), 1 (s, NBF_3). ^{13}C NMR δ: 162.2, 148.5, 143.7, 142.5, 125.4, 123.0, 122.4, 112.7, 23.8 (br, CB), 14.9. **24**: ^{1}H NMR δ: 8.28 (d, J = 5 Hz, 2H), 7.07 (d of d, J = 3, 1 Hz, 2H), 6.88 (d of d, J = 3, 1 Hz, 2H), 6.66 (d, J = 5 Hz, 2H), 2.39 (q, J = 8 Hz, 1H, -C*H*(Bcat)-), 1.14 (d, J = 8Hz, 3H, -CH_3). ^{11}B NMR δ: 34 (br, CBcat), 1 (s, NBF_3). ^{13}C NMR δ: 161.2, 148.8, 143.3, 125.5, 124.1, 113.2, 25.6 (br, CB), 15.0.

Catalyzed hydroborations of vinylpyridines-BF_3 with HBpin

In a typical reaction, 1.1 equiv of $BF_3{\cdot}OMe_2$ were added to a 0.5 mL solution of the vinylpyridine in C_6D_6. The resulting solution was allowed to stir for 2 h whereupon $RhCl(PPh)_3$ (1 mol%) in 0.25 mL of C_6D_6 was added to the mixture, followed by the addition of a 0.25 mL C_6D_6 solution of 1.2 equiv of HBpin. The mixture was allowed to stir for 12 h and then analyzed by multinuclear NMR spectroscopy. Selected spectroscopic data for reactions with **21**: ^{1}H NMR (in C_6D_6)

Scheme 2.



δ: 3.90 (br q, *J* = 8 Hz, 1H, -C*H*(Bpin)-), 3.07 (q, *J* = 8 Hz, 2H, -CH_2CH$_3$), 1.28 (d, *J* = 8 Hz, 3H, -CH(Bpin)CH_3), 1.00 (s, Bpin), 0.94 (t, *J* = 8 Hz, 3H, -CH$_2$CH_3). ^{11}B NMR δ: 33 (br, CBpin), 23, 21, 1 (s, NBF$_3$). Selected spectroscopic data for reactions with **23**: ^{1}H NMR δ: 2.72 (d, *J* = 8 Hz), 2.30 (t, *J* = 8 Hz, -CH_2CH$_2$B), 2.14 (q, *J* = 8 Hz, 1H, C*H*(Bpin)-), 1.95 (q, *J* = 8 Hz, 2H, -CH_2CH$_3$), 1.17 (br s), 1.06 (d, *J* = 8 Hz, 3H, -CH(Bpin)CH_3), 0.98 (s, Bpin), 0.66 (t, *J* = 8 Hz, 3H, -CH$_2$CH_3). ^{11}B NMR δ: 33 (br, CBpin), 21, 1 (s, NBF$_3$).

Catalyzed hydroborations of aldimine 25 with pinacolborane (HBpin)

To a 0.5 mL C_6D_6 solution of **25** and 1 mol% RhCl(PPh$_3$)$_3$ was added 1.2 equiv of HBpin in 0.5 mL of C_6D_6. The reaction was heated at reflux for 2 h and then analyzed by multinuclear NMR spectroscopy. **26**: ^{1}H NMR (in C_6D_6) δ: 6.88–6.73 (ov m, 3H, Ar), 4.33 (s, 2H, -NCH_2Ar), 3.01 (t, *J* = 8 Hz, 2H, -NCH_2-), 1.42 (ov t of q, *J* = 8 Hz, 2H, -CH$_2$CH_2CH$_3$), 1.15 (s, 12H, pin), 0.78 (t, *J* = 8 Hz, 3H, -CH_3). ^{13}C NMR δ: 145.8, 126.4, 124.8, 124.1, 82.2, 46.8, 44.4, 24.5, 22.0, 11.1. ^{11}B NMR δ: 24 (br, NBpin).

Results and discussion

As with reactions using borane, we have found that the in situ addition of HBcat to allylamine (**1**) resulted in the initial formation of a mixture of products. Although minor amounts of Lewis acid–base adducts HBcat·HNRCH$_2$CH=CH$_2$ (**2**, R = H, Bcat) are formed (40), a competing reaction gave N(Bcat)$_2$CH$_2$CH=CH$_2$ (**3**) as the major boron-containing product in solution. No adduct formation is observed with **3**, however, as coordination of two electron-withdrawing boryl groups has either significantly reduced the nucleophilic nature of the amine or increased the steric hindrance around the nitrogen atom. Although HBcat eventually adds to the activated allyl group in these aminoboryl species, reactions take several days. However, we have found that certain rhodium complexes can be used to catalyze this addition. Rhodium-catalyzed hydroborations are believed to arise via oxidative addition of the B—H bond of the boronate ester at the metal centre, followed by coordination and subsequent insertion of the alkene into the Rh—H or Rh—B bond (41). Reductive elimination affords the desired organoboronate ester product.

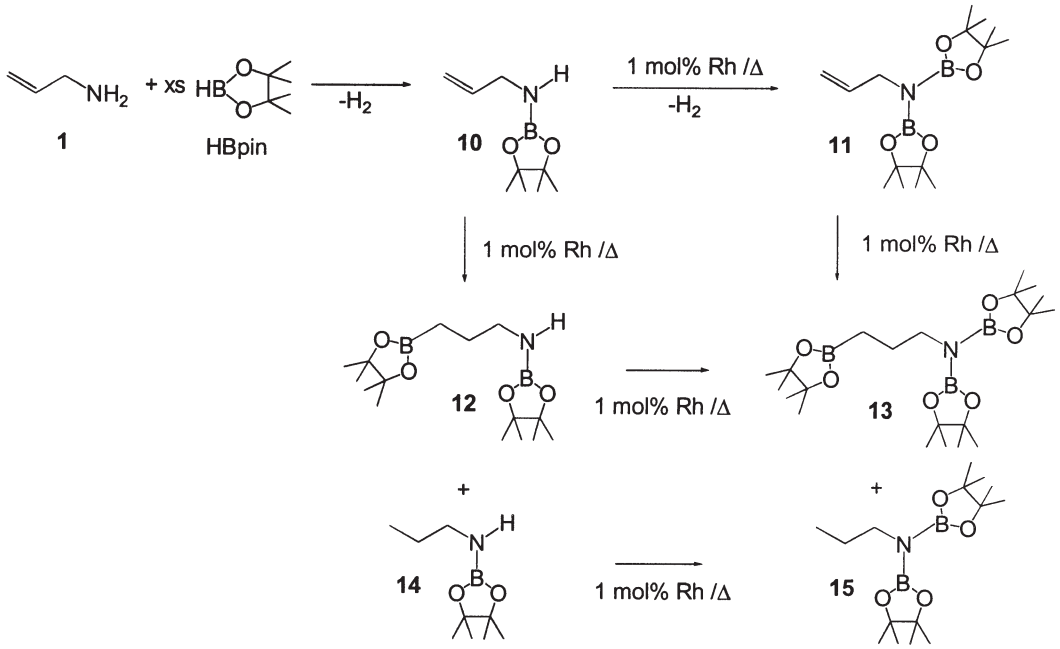
Addition of excess HBcat is required in all of these catalyzed reactions to ensure 100% conversion of the starting alkene. While hydroboration of intermediate **2** gave minor amounts of HBcat·HNRCH$_2$CH$_2$CH$_2$Bcat (**4**, R = H, Bcat), reactions with **3** gave surprisingly complex product distributions, regardless of the catalyst system used to affect this transformation (Scheme 2). Although significant amounts of the hydroboration products **5** and **6** were formed in these reactions, products (such as **8**) derived from a competing dehydrogenative borylation pathway were also observed (by NMR spectroscopy). We propose that these unique products originate from the transient alkenylboronate ester **7**, which presumably results from insertion of the activated alkene into the Rh—B bond (3, 41). Subsequent β-hydride elimination would afford the alkenylboronate ester with concomitant formation of dihydrogen (2, 41). It is possible that "hydroboration product" **5** also arises from hydrogenation of alkenylboronate ester **7**. Hydride elimination appears to be specific as products arising from abstraction of a methylene hydrogen α to the activated amine group are not observed. Alkenylboronate ester **7** can also add another equiv of HBcat to give **8**. Interestingly, we have found that compound **8** can also be generated as the major product in analogous hydroborations of H$_2$NCH$_2$C≡CH. As with most catalyzed hydroboration reactions, a small amount of hydrogenation product (**9**) is almost always observed.

The formation of these products is somewhat unusual as catalyzed hydroborations of simple alkenes, such as 1-octene, proceed smoothly to give predominant formation of the expected organoboronate ester product (2, 4). In this study, replacement of the two N—H bonds with N-Bcat groups in **3** appears to be ineffective in deactivating the amine group and catalyzed reactions proceed to give complex product distributions. The formation of multiple boronated compounds has recently been an area of considerable interest (42–44).

Metal-catalyzed hydroborations of unsaturated C—C bonds using HBpin have been reported previously (45–47).[3] In a further attempt to control selectivity we decided to examine hydroborations using HBpin (Scheme 3). Unlike reactions with HBcat, which is a stronger Lewis acid, no adduct formation was observed. Addition of excess HBpin gave the monoboryl amine HN(Bpin)CH$_2$CH$_2$=CH$_2$ (**10**), where a second equiv of the boronate ester failed to add to the amine N—H bond even at elevated temperatures. Remarkably, we have found

[3] C.M. Crudden and A. Chen. Unpublished results.

Scheme 3.



that a rhodium catalyst could be used to facilitate the addition of another equiv of HBpin to give $N(Bpin)_2CH_2CH_2{=}CH_2$ (**11**). This observation provides the first example of a metal-catalyzed hydroboration of N—H bonds.

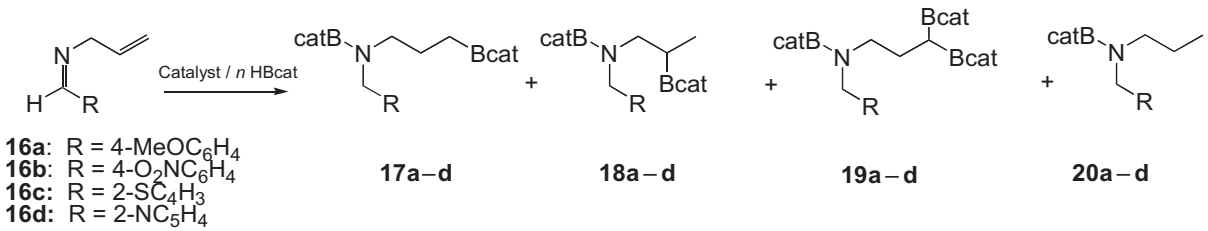
Compound **11** was observed in only minor amounts (<5% by ^{1}H NMR spectroscopy) as a competing hydroboration reaction occurred at the alkene moiety to afford a mixture of $HN(Bpin)CH_2CH_2CH_2Bpin$ (**12**) and $N(Bpin)_2CH_2CH_2CH_2Bpin$ (**13**). Not surprisingly, significant amounts of hydrogenation products $RN(Bpin)CH_2CH_2CH_3$ (where R = H or Bpin, **14** and **15**, respectively) were also observed in these reactions. The ^{1}H NMR data for the propyl group in **13** is similar to that observed for **12**, except that chemical shifts are moved to a lower field due to addition of another electron-withdrawing Bpin group. For instance, the middle CH_2 resonance in **12** is observed as an overlapping triplet of triplets at 1.60 ppm, yet for **13** this peak is found at 2.04 ppm. The ^{11}B NMR of $RN(Bpin)CH_2CH_2CH_2Bpin$ (where R = H or Bpin) shows a peak at 25 ppm corresponding to the B—N bond and a resonance at 33 ppm for the new B—C bond. No appreciable intramolecular interactions are observed in these molecules as the boron atoms appear to be three-coordinate (40, 48). This result is consistent with previous NMR data on related $NH_2CH_2CH_2CH_2B(OH)_2{\cdot}HCl$ which shows a peak in the ^{11}B NMR at 32.6 ppm (49). Interestingly, the analogous neutral compound ($NH_2CH_2CH_2CH_2B(OH)_2$) displays a resonance at 8 ppm suggesting intramolecular adduct formation between the nitrogen and the boron atom (50).

To avoid complications arising from addition of the boronate esters at the amine N—H bond, we decided to investigate hydroborations of allylimine derivatives **16a**–**d**. Addition of 1 equiv of catecholborane to allylimines **16a**–**c** proceeds cleanly to give the corresponding borylamines, where the electron-deficient boron group has added to the nitrogen atom of the imine double bond (51). A rhodium catalyst can once again be used to facilitate the addition of a second equiv of HBcat to the alkene moiety. While selectivity to 3-aminopropylboronate esters has been increased in these reactions, products arising from competing Markovnikov hydroboration, dehydrogenative borylation, and hydrogenation are all still observed to some extent (Table 1).

Reactions with **16c** were carried out with 3 equiv of HBcat to ensure complete conversion of the allyl group. Although $RhCl(PPh_3)_3$ (entry 1) gave 71% of the *anti*-Markovnikov product **17c**, use of $[RhCl(coe)_2]_2/4PPh_3$ (coe = *cis*-cyclooctene, entry 7) as a catalyst precursor gave 88% of this desired product (using ^{1}H NMR spectroscopy). Significant amounts (23%) of the hydroboration product **18c** were observed in reactions using $[RhCl(coe)_2]_2$ as a catalyst precursor (entry 6). This product arises from a Markovnikov addition of the borane to the allyl moiety. Remarkably, the diboronated ester **19c** was a major product (38%) in reactions using $Rh(acac)(coe)_2$/dppm (dppm = 1,1-bis(diphenylphosphino)methane) (entry 10). Catalyst precursors of this type are known to generate the active zwitterionic catalyst Rh(dppm)(η^6-catBcat) (52, 53). It is interesting to note that no significant change in product distributions is observed when reactions were conducted using an excess of HBcat (entry 12) or when hydroborations were carried out in $CDCl_3$ (entry 11). Although only minor differences in product distributions were observed when **16a** was used as the substrate (cf. entries 1 and 13), reactions with **16b** gave significant amounts of hydrogenation product **20b** (entry 14). Hydrogenation products are also observed in other reactions where extensive borane and (or) catalyst decomposition occurs (entries 6 and 8; (29)).

Hydroborations of the pyridine derivative **16d** gave rise to a number of different boron-containing products, also arising from the degradation of HBcat (2). Since no degradation was observed with the thiophene imine **16c** using HBcat, it is plausible that the harder nitrogen atom in the pyridine ring is responsible for this unwanted degradation pathway. To test this hypothesis, we decided to investigate the analogous hydroborations with 2- and 4-vinylpyridine (**21** and **23**, respectively). Catalyzed hydroborations of styrene proceed

Table 1. Hydroboration of allylimines with HBcat.



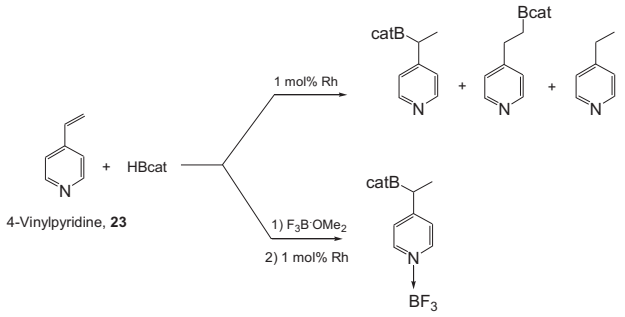
16a: R = 4-$MeOC_6H_4$
16b: R = 4-$O_2NC_6H_4$
16c: R = 2-SC_4H_3
16d: R = 2-NC_5H_4

17a–d **18a–d** **19a–d** **20a–d**

Entry	Allylimine	Catalyst system	Solvent	HBcat (*n*)	**17a–17d**	**18a–18d**	**19a–19d**	**20a–20d**
1	**16c**	$RhCl(PPh_3)_3$	C_6D_6	3	71	7	20	2
2	**16c**	$RhCl(PPh_3)_3/10PPh_3$	C_6D_6	3	78	8	13	1
3	**16c**	$[Rh(cod)Cl]_2$/dppb/$AgBF_4$	C_6D_6	3	86	5	6	3
4	**16c**	$Rh(H)(CO)(PPh_3)_3$	C_6D_6	3	80	7	10	3
5	**16c**	$Rh(H)(PPh_3)_4$	C_6D_6	3	77	14	5	4
6	**16c**	$[RhCl(coe)_2]_2$	C_6D_6	3	63	23	2	12
7	**16c**	$[RhCl(coe)_2]_2/4PPh_3$	C_6D_6	3	88	2	8	2
8	**16c**	$Rh(acac)(coe)_2$	C_6D_6	3	51	16	12	21
9	**16c**	$Rh(acac)(coe)_2/2PPh_3$	C_6D_6	3	79	18	2	1
10	**16c**	$Rh(acac)(coe)_2$/dppm	C_6D_6	3	37	20	38	5
11	**16c**	$Rh(acac)(coe)_2$/dppm	$CDCl_3$	3	59	9	15	17
12	**16c**	$RhCl(PPh_3)_3$	C_6D_6	6	75	5	19	1
13	**16a**	$RhCl(PPh_3)_3$	C_6D_6	3	88	6	5	1
14	**16b**	$RhCl(PPh_3)_3$	C_6D_6	3	51	11	1	37

Note: All reactions were conducted with 1 mol% catalyst at room temperature. Yields were calculated using ^{1}H NMR data.

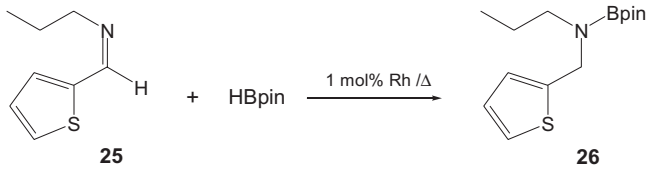
Scheme 4.



4-Vinylpyridine, **23**

24

Scheme 5.



25 **26**

smoothly to give selective formation of either the Markovnikov or *anti*-Markovnikov product, depending upon the metal catalyst employed (2). Not surprisingly, we have found that catalyzed reactions of the vinylpyridines with HBcat gave a mixture of hydroboration products, along with a significant amount of ethylpyridine. Although a number of metal complexes were examined as catalysts for this reaction, all gave mixtures of products. Oxidation of the resulting hydroborated mixtures with NaOH–H_2O_2 gave 4-ethylpyridine as the only isolable organic product (54). Similar results are also seen in reactions with HBpin. Coordination of a strong Lewis acid, such as BF_3 (55–57), to the vinylpyridines effectively eliminated these degradation pathways and the Marknovnikov hydroboration products (**22** and **24**, respectively) could be obtained in high yields (>95% by NMR spectroscopy) using $Rh(acac)(coe)_2$/dppb (dppb = 1,4-bis(diphenylphosphino)butane) as a catalyst precursor (Scheme 4) and HBcat. Reactions with HBpin gave a mixture of hydroboration products along with a significant amount of hydrogenation. Unfortunately, attempts to protect the nitrogen group with BF_3 in the hydroboration of allylamines **1** and **16d** led to polymerization of the activated alkene moiety.

We then decided to examine the rhodium-catalyzed hydroboration of allylimine **16c** using HBpin. Although no reaction was observed at room temperature, complex product distributions arising from addition at the allyl group and the imine functionality were observed when reactions were carried out at elevated temperatures (60°C). Reduction of the imine was observed by disappearance of the aldimine hydrogen at 7.89 ppm with concomitant appearance of a benzylic hydrogen at 4.36 ppm. A peak at 24 ppm in the ^{11}B NMR spectrum arises from the newly formed N—Bpin bond. This result is somewhat surprising as previous attempts to hydroborate imines using HBpin proved unsuccessful (58). To confirm that the imine was being reduced in these reactions, we decided to investigate hydroborations with saturated aldimine **25** (Scheme 5). Indeed, these reactions proceeded

to give selective formation of the desired *N*-boryl product **26** and represent the first examples of a metal-catalyzed hydroboration of an imine using HBpin (45–47).[3] Although the synthesis of chiral amines is of utmost importance in organic and medicinal chemistry, the enantioselective reduction of simple ketimine derivatives is often a synthetically challenging problem (59). As a result, future work in this area will focus on the asymmetric reduction of related ketimines using HBpin.

Conclusion

We have found that the in situ addition of HBcat to allylamine using a number of rhodium catalysts gave products derived from competing hydroboration and dehydrogenative borylation pathways.[4] The use of HBpin effectively eliminated the dehydrogenative borylation reaction and a novel rhodium-catalyzed hydroboration of N—H bonds was observed to give $N(Bpin)_2CH_2CH_2CH_2Bpin$ along with various amounts of hydrogenation product. Hydroboration of allylimines with HBcat occurs initially at the more reactive imine functionality to give unsaturated borylamines. Further reaction gives the corresponding *anti*-Markovnikov and Markovnikov hydroboration products. Reactions with related unsaturated pyridine derivatives are complicated by extensive degradation, which can be avoided by coordination of the pyridine nitrogen to a Lewis acid. We have also shown that catalyzed hydroborations of aldimines can be accomplished using HBpin. Further work will examine other catalyst systems to fine-tune product selectivities in these reactions.

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References

1. H.C. Brown, G.W. Kramer, A.B. Levy, and M.M. Midland. Organic syntheses via boranes. Wiley–Interscience, New York. 1975.
2. I. Beletskaya and A. Pelter. Tetrahedron, **53**, 4957 (1997).
3. D.E. Kadlecek, P.J. Carroll, and L.G. Sneddon. J. Am. Chem. Soc. **122**, 10 868 (2000), and refs. therein.
4. D. Männig and H. Nöth. Angew. Chem. Int. Ed. Engl. **24**, 878 (1985).
5. N. Miyaura and A. Suzuki. Chem. Rev. **95**, 2457 (1995).
6. D.S. Matteson. Tetrahedron, **45**, 1859 (1989).
7. N.A. Petasis and I.A. Zavialov. J. Am. Chem. Soc. **120**, 11 798 (1998).
8. M. Murata, T. Oyama, S. Watanabe, and Y. Masuda. J. Org. Chem. **65**, 164 (2000).
9. A.F. Littke, C. Dai, and G.C. Fu. J. Am. Chem. Soc. **122**, 4020 (2000).
10. F. Minutolo and J.A. Katzenellenbogen. Organometallics, **18**, 2519 (1999).
11. Y. Kobayashi, K. Watatani, and Y. Tokoro. Tetrahedron Lett. **39**, 7533 (1998).
12. D.G. Hall, J. Tailor, and M. Gravel. Angew. Chem. Int. Ed. Engl. **38**, 3064 (1999).
13. B. Carboni, C. Pourbaix, F. Carreaux, H. Deleuze, and B. Maillard. Tetrahedron Lett. **40**, 7979 (1999).
14. N. Farfan, H. Hopfl, V. Barba, M.E. Ochoa, R. Santillan, E. Gomez, and A. Gutierrez. J. Organomet. Chem. **581**, 70 (1999).
15. H. Kitano, M. Kuwayama, N. Kanayama, and K. Ohno. Langmuir, **14**, 165 (1998).
16. P.R. Westmark and B.D. Smith. J. Am. Chem. Soc. **116**, 9343 (1994).
17. A.N.J. Moore and D.D.M. Wayner. Can. J. Chem. **77**, 681 (1999).
18. M. Takeuchi, S. Yoda, Y. Chin, and S. Shinkai. Tetrahedron Lett. **40**, 3745 (1999).
19. H. Eggert, J. Frederiksen, C. Morin, and J. Chr. Norrild. J. Org. Chem. **64**, 3846 (1999).
20. C. Morin. Tetrahedron, **50**, 12521 (1994).
21. Z.-Q. Tian, B.B. Brown, D.P. Mack, C.A. Hutton, and P.A. Bartlett. J. Org. Chem. **62**, 514 (1997).
22. S.Y. Chen, B.S. Burnham, B.F. Spielvogel, A. Sood, S.D. Wyrick, and I.H. Hall. Appl. Organomet. Chem. **10**, 279 (1996).
23. M.C. Miller, III, A. Sood, B.F. Spielvogel, and I.H. Hall. Arch. Pharm. (Weinheim, Ger.), **331**, 153 (1998).
24. M. Ferles, J. Hauer, J. Kolar, Z. Polivka, and P. Stern. Coll. Czech. Chem. Commun. **37**, 2464 (1972).
25. M. Baboulène, J.L. Torregrosa, V. Speziale, and A. Lattes. Bull. Soc. Chim. Fr. 565 (1980).
26. J.-B. Le Toumelin and M. Baboulène. New. J. Chem. **23**, 111 (1999).
27. (*a*) A. Dicko, M. Montury, and M. Baboulène. Tetrahedron Lett. **28**, 6041 (1987); (*b*) S. Colin, L. Vaysee-Ludot, J.-P. Lecouvé, and J. Maddaluno. J. Chem. Soc. Perkin Trans. 1, 4505 (2000).
28. R. Köster. Organobor-Verbindungen II. *In* Methoden der Organischen Chemie (Houben–Weyl). Vol. XIII/3b. Thieme, Stuttgart. 1983, and refs. therein.
29. K. Burgess and M.J. Ohlmeyer. Chem. Rev. **91**, 1179 (1991).
30. M.P. Sibi and B. Li. Tetrahedron Lett. **33**, 4115 (1999).
31. K. Burgess and M.J. Ohlmeyer. J. Org. Chem. **56**, 1027 (1991).
32. J.A. Osborn and G. Wilkinson. Inorg. Synth. **28**, 77 (1990).
33. G. Giordano and R.H. Crabtree. Inorg. Synth. **28**, 88 (1990).
34. J. Chatt and L.M. Venanzi. J. Chem. Soc. 4753 (1957).
35. A.G.M. Barrett, M.A. Seefeld, A.J.P. White, and D.J. Williams. J. Org. Chem. **61**, 2677 (1996).
36. G. Wolf and E.-U. Würthwein. Chem. Ber. **124**, 655 (1991).
37. E.J. Roskamp and S.F. Pedersen. J. Am. Chem. Soc. **109**, 6551 (1987).
38. C.K. Govindan and G. Taylor. J. Org. Chem. **48**, 5348 (1983).
39. P.J. Fennis, P.H.M. Budzelaar, J.H.G. Frijns, and A.G. Orpen. J. Organomet. Chem. **393**, 287 (1990).
40. J.S. Hartman, Z. Yuan, A. Fox, and A. Nguyen. Can. J. Chem. **74**, 2131 (1996), and refs. therein.
41. C. Widauer, H. Grützmacher, and T. Ziegler. Organometallics, **19**, 2097 (2000).
42. T.B. Marder and N.C. Norman. Top. Catal. **5**, 63 (1998).

[4] Supplementary material (NMR data) may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada (http://www.nrc.ca/cisti/irm/unpub_e.shtml for information on ordering electronically).

43. F.-Y. Yang and C.-H. Cheng. J. Am. Chem. Soc. **123**, 761 (2001), and refs. therein.
44. R.T. Baker, T.M. Cameron, and S.A. Westcott. Chem. Commun. 2395 (1998).
45. S. Pereira and M. Srebnik. Tetrahedron Lett. **37**, 3283 (1996).
46. T. Ohmura, Y. Yamamoto, and N. Miyaura. J. Am. Chem. Soc. **122**, 4990 (2000), and refs. therein.
47. C.M. Vogels, P.G. Hayes, M.P. Shaver, and S.A. Westcott. Chem. Commun. 51 (2000).
48. H. Nöth and B. Wrackmeyer. *In* Nuclear magnetic resonance spectroscopy of boron compounds. Springer–Verlag, Berlin. 1978.
49. J.M. Jego, B. Carboni, and M. Vaultier. J. Organomet. Chem. **435**, 1 (1992).
50. A. Dicko, M. Montury, and M. Baboulène. Synth. Commun. **18b**, 459 (1988).
51. R.T. Baker, J.C. Calabrese, and S.A. Westcott. J. Organomet. Chem. **498**, 109 (1995).
52. C. Dai, E.G. Robins, A.J. Scott, W. Clegg, D.S. Yufit, J.A.K. Howard, and T.B. Marder. Chem. Commun. 1983 (1998).
53. S.A. Westcott, H.P. Blom, T.B. Marder, and R.T. Baker. J. Am. Chem. Soc. **114**, 8863 (1992).
54. T. Hayashi, Y. Matsumoto, and Y. Ito. Tetrahedron: Asymmetry, **111**, 601 (1991).
55. J.M. Grevy, Z. García-Hernández, A. Ramos-Organillo, and R. Contreras. *In* Contemporary boron chemistry. RSC, Cambridge. 2000. p. 422.
56. L. Weber, M. Schnieder, R. Boese, and D. Bläser. J. Chem. Soc. Dalton Trans. 378 (2001).
57. H. Höpfl. J. Organomet. Chem. **581**, 129 (1999).
58. C.M. Vogels, L.G. Nikoltcheva, H.A. Spinney, D.W. Norman, M.O. Baerlocher, F.J. Baerlocher, and S.A. Westcott. Can. J. Chem. **79**, 1115 (2001).
59. C. Bolm. Angew. Chem. Int. Ed. Engl. **32**, 232 (1993).