Hydroboration Reagents

Di(isopropylprenyl)borane: A New Hydroboration Reagent for the Synthesis of Alkyl and Alkenyl Boronic Acids

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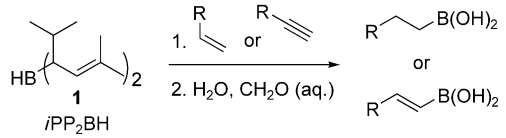
*Dedicated to Professor H. C. Brown***

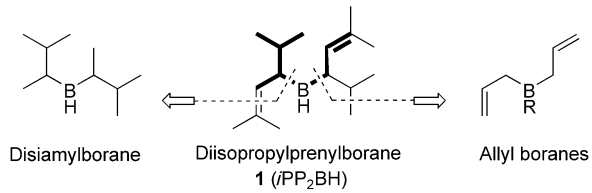
The discovery of the hydroboration reaction by Brown and Subba Rao almost 50 years ago[1] launched the era of organoborane chemistry, which today constitutes a conventional component of synthetic organic chemistry[2] sustained by the availability of organoboranes either commercially or prepared by reliable protocols.[2,3] The significance of organoboron compounds in synthesis surged when Suzuki and Miyaura discovered the transition-metal-catalyzed cross-coupling reaction,[4] which more recently has seen explosive growth, particularly in industrial practice.[5] The current high activity in this area is evidenced by the further development of cross-coupling reactions of organoboron compounds for C–C[4–6] and C–heteroatom bond formation,[7] C–H insertion,[8] allylic substitution,[9] Diels–Alder and dipolar cycloaddition,[10] and 1,2-/1,4-addition processes.[11] Consequently, the quest for new reagents and procedures for the preparation of organoboronic acids and their derivatives is a continuing necessity.

Herein we report the development and synthetic utility of di(isopropylprenyl)borane (**1**, *i*PP_2BH), a new organoborane reagent that is generated in situ and that provides rapid access to alkyl and alkenyl boronic acids and their derivatives conveniently, economically, and under mild conditions (Scheme 1).

Detailed studies by Brown and co-workers[12] and Mikhailov et al.[13] showed that although hydroboration of conjugated dienes with borane is a complex process that gives rise to mixtures of products, application of 9-BBN results in highly selective reactions in certain cases. Of particular interest, 1:1 hydroboration of 2,5-dimethylhexa-2,4-diene (**2**, Scheme 3) with 9-BBN leads to the anti-Markovnikov monohydroboration product in 90% yield.[14] Based on these studies, we postulated that the reaction of borane with slightly more than 2 equivalents of **2** would mainly lead, by double anti-Markovnikov hydroboration, to **1**, which was expected to exhibit hydroboration selectivity resembling that of disiamylborane,[2,15] reactivity towards carbonyls similar to that of allyl boranes,[3,16] and facile hydrolysis in protic media[17] (Scheme 2). Consequently, we envisaged that **1** could serve as a valuable hydroboration reagent, allowing conversion of the product boranes into the corresponding boronic acids under mild conditions similar to those used for the hydrolysis of catechol-[18] and dihaloboranes,[19] without the need for the standard strong oxidizing reagents.[2,20]

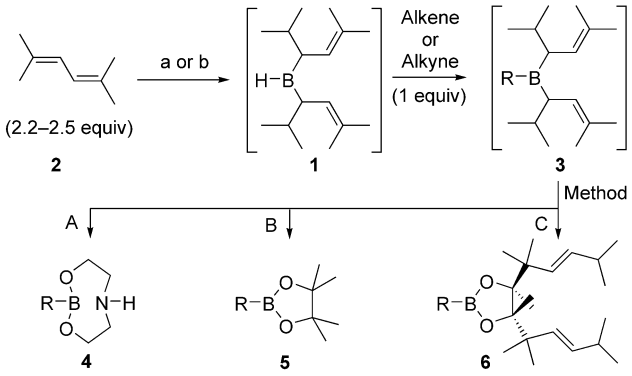


Scheme 1. General hydroboration process with **1**.



Scheme 2. Amalgamation of two classes of borane reagents in **1**. R = alkyl, alkenyl.

In pursuit of results to support this idea, we found that the addition of dimethyl sulfate to a mixture of diene **2** and $NaBH_4$ in diglyme[21] at 0–5 °C was accompanied by intensive gas evolution followed by the formation of a substantial amount of a colorless precipitate upon ageing of the mixture (3 h/0 °C). The precipitate was rapidly consumed in an exothermic reaction with phenylacetylene, leading to the presumed formation of borane **3a** (Scheme 3, R = PhCH=CH). Treatment of the reaction mixture with water and an aqueous



Scheme 3. General protocol for the hydroboration of alkenes/alkynes with **1**. Reagents and conditions: a) $NaBH_4$ (1 equiv), $(MeO)_2SO_2$ (1 equiv), diglyme, 0–5 °C, 3 h; b) BH_3·THF (1 M, 1 equiv), THF, 0–5 °C, 3 h. Method A: H_2O quench, 30 min, room temperature; then aqueous CH_2O (1 equiv), 24 h, room temperature; then $(HOCH_2CH_2)_2NH$ (1.1 equiv). Method B: H_2O quench, 30 min, room temperature; then aqueous CH_2O (1 equiv), 1 h, room temperature; then $HOCMe_2CMe_2OH$ (1.1 equiv), 24 h, room temperature. Method C: MeC(O)C(O)Me (1.1 equiv), 12 h, room temperature. R = alkyl or alkenyl; diglyme = $(MeOCH_2CH_2)_2O$.

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[**] This communication is in celebration of 91 years and with admiration and appreciation of the "from little acorns to tall trees" growth of his borane chemistry

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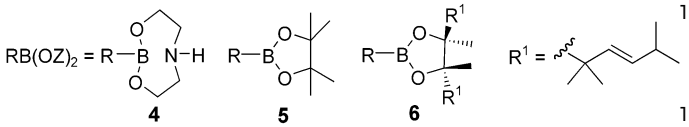
solution of formaldehyde followed by addition of diethanolamine led to the isolation of the corresponding adduct of styrylboronic acid **4a** (R = PhCH=CH) in 77% yield (method A, Scheme 3).[22]

When pinacol was added instead of diethanolamine, the corresponding borolane **5a** was isolated in 83% yield and > 99:1 anti-Markovnikov regioselectivity (GC/MS analysis of the crude mixture; method B, Scheme 3) together with the alcohol **7** (see Scheme 4).[23] Similar results were observed when commercial BH_3·THF complex in THF was used (Table 1, entry 1), but in a homogeneous reaction.

For both procedures involving $NaBH_4$ or BH_3·THF, the results may be rationalized by invoking the formation of **3**,

Table 1: Synthesis of $RB(OZ)_2$ by hydroboration of alkynes/alkenes with **1**.[a]



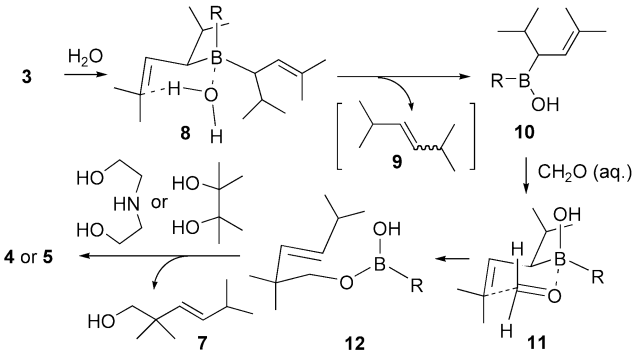
4 **5** **6**

Entry	R		NaBH$_4$ Selectivity	NaBH$_4$ Yield [%]	BH$_3$·THF Selectivity	BH$_3$·THF Yield [%]
1	Ph	**4a**		77		
		5a	99:1		99:1	83
		6a		72		
2	*p*-Tol	**4b**	99:1	74	99:1	70
3	Ph, Ph	**4c**		66		81
			100		100	
		6c				69
4	TMS	**5d**				62[b]
			96:4		84:16	
		6d		59		
5	Ph	**5e**	83			
				70	–	–
	Ph	**5f**	17			
6	EtO, EtO	**5g**	98:2	61	98:2	55
7	*n*-C$_6$H$_{13}$	**5h**	96:4	67	99:1	59
8	Ph, (CH$_2$)$_3$	**5i**	97:3	73	98:2	72
9	AcO	**5j**	93:7	55	93:7	41
10[c]	HO	**5k**	–	–	99:1	63
11	*n*Pr, *n*Pr	**4l**	> 99	68	> 99	71
12	N	**4m**		67		
		5m	> 99		> 99	74
		6m				86
13	O, O, O	**5n**	> 99	77	> 99	72
14	O	**6o**	98:2	73	–	–
15	TMS	**4p**		55		
			> 99		> 99	
		5p				68
16	Ph, Ph	**4q**	–	–	> 99	47
17	EtO, EtO	**5r**	99:1	63	99:1	59
18	Ph	**4s**				67
			98:2		97:3	
		5s		71		
19		**4t**		48		43
			91:9		96:4	
		5t				61

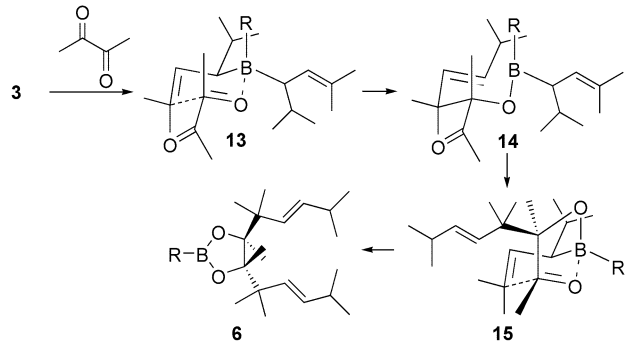
[a] Yields are for purified materials (recrystallized, distilled, or, for **6c** and **6m**, after column chromatography) and are not optimized. Selectivities were determined by GC and GC–MS analysis of the crude reaction mixtures: an aliquot of the reaction mixture was worked up according to method B by preparing the borolane derivative **5**. [b] Yield is for the mixture of α and β isomers; the yield of 98% pure (GC) **5d** (α isomer) is 42%. [c] *O*-TMS-propargyl alcohol was used as the starting material.

which as expected for allyl boranes,[17] undergoes rapid protonolysis via intermediate **8** to liberate alkene **9**[24] and yield the borinic acid **10** (Scheme 4). Reaction of **10** with formaldehyde leads to **12** via intermediate **11**. Hemiborate **12** is then esterified with diethanolamine (method A) or pinacol (method B) to afford derivatives **4** and **5**, respectively, and alcohol **7** (Scheme 4).

As chemical proof for the formation of **3** and therefore, by implication, of **1**, repetition of the model hydroboration experiment of phenylacetylene with biacetyl (1.1 equiv) as the quenching reagent gave complex borolane **6a** (R = PhCH=CH) in 72% yield as a single isomer, as judged from the ^{1}H NMR spectrum (olefinic $^3J = 18.4$ Hz, C_2 symmetry). The formation of **6** (Scheme 5) may be rationalized by the transition state **13**, which is predisposed for the formation of *trans* olefin **14**. Intramolecular boron–carbonyl coordination leads to the intermediate **15**, in which repulsion between the bulky side chains is minimized by adapting a pseudo-*trans* borolane stereochemistry. Terminal collapse of **15** affords the C_2-symmetrical *trans* borolane **6** with *trans* stereochemistry in both side chains.



Scheme 4. Proposed hydrolysis and oxidation steps of **3** to products **4** or **5** and **7** (methods A and B).



Scheme 5. Proposed mechanism for the double oxidation of **3** by biacetyl to form **6** (method C).

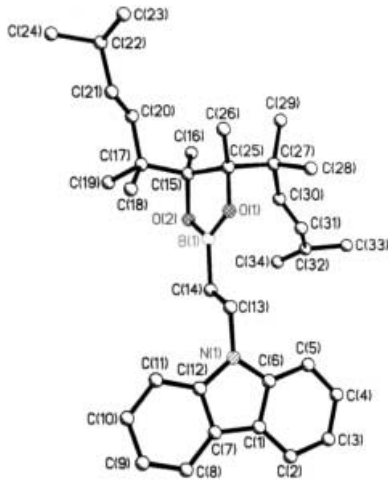


Figure 1. X-ray crystal structure of **6m** at the 50% probability level. Hydrogen atoms have been omitted for clarity.

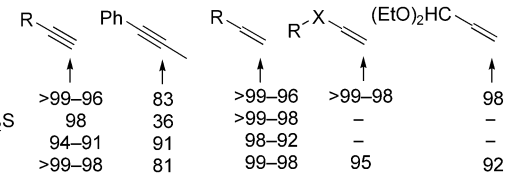


Figure 2. General trends in hydroboration with diisopropylprenylborane (iPP_2BH), dihaloborane complexes ($Hal_2BH{\cdot}Me_2S$), catecholborane (CthBH), and disiamylborane (Sia_2BH). R = *n*-alkyl, Ph; Hal = Cl, Br; X = O, Si.

In view of the C_2 symmetry of **6**, the stereochemistry of the borolane could not be confirmed by NMR spectroscopic analysis. Fortunately, suitable crystals of **6m** (see Table 1, entry 12) were obtained and X-ray crystallographic analysis established the *trans* stereochemistry of both the borolane ring and of the alkenyl chains (Figure 1).[25] This result infers its derivation from the parent **3** and strongly suggests that **1** is the main product from the reaction of diene **2** with borane.

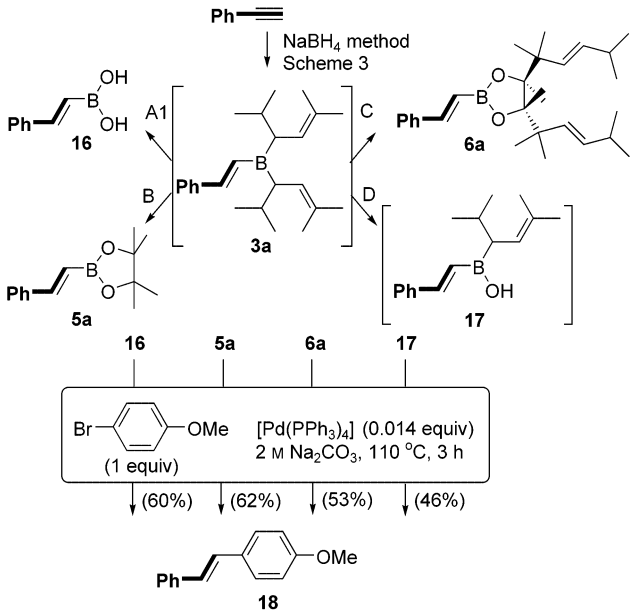
To explore the scope and limitations of the new boronic acid synthesis, representative examples of alkenes and alkynes were treated with **1** and the results are summarized in Table 1. Several pertinent conclusions may be drawn: a) hydroboration of terminal and symmetrical alkynes and alkenes proceeds in a highly selective anti-Markovnikov fashion (except Table 1, entry 5); b) both sources of borane furnish hydroborated products with comparable regioselectivity (except Table 1, entries 4 and 19); c) derivatives **4**, **5**, and **6** (Scheme 3) are obtained in modest to good yields by using conventional isolation techniques (distillation or crystallization) and in up to 86% yield by using column chromatography (Table 1, entry 12); d) sterically hindered alkenes are less reactive under the tested conditions as reflected in the modest yields of the final products (Table 1, entries 16 and 19). Although direct hydroboration of α,β-unsaturated esters (acrylates and cinnamates) was unsuccessful, these compounds were readily accessed from their protected precursors (Table 1, entries 6 and 17).[26]

The generally high hydroboration regioselectivities of iPP_2BH compare favorably with those observed for CthBH[18] and $Hal_2BH{\cdot}Me_2S$,[19] the commonly used reagents to produce the corresponding boronic acids under hydrolytic, nonoxidative conditions (Figure 2). The similar selectivities achieved with iPP_2BH (**1**) and Sia_2BH[2,15] may be attributed to their comparable steric demand (see Scheme 2).

As a logical extension of the new hydroboration procedure, the development of a sequential, "one-pot" hydroboration/Suzuki–Miyaura cross-coupling protocol was realized (Scheme 6). In all experiments, borane **3a**, generated in situ from $NaBH_4$, was coupled with 4-bromoanisole under identical conditions. However, the hydrolysis–oxidation protocol (methods A1, B, C, and D) prior to the cross-coupling step was varied for **3a**.

Thus application of methods A1 and B to **3a** led to the intermediate styrylboronic acid (**16**) and pinacolate **5a**, respectively, which upon coupling with 4-bromoanisole, afforded styrene **18** in virtually identical yields (60% and 62%). Borolane **6a** was found to be a less effective coupling partner, yielding **18** in 53% yield (method C). Interestingly, cross-coupling of the borinic acid **17**, a proposed intermediate in the hydrolysis of **3a**, also gave **18** but in a slightly lower yield (46%, method D).

In conclusion, a new and general reagent for the hydroboration of alkenes and alkynes, iPP_2BH (**1**), conveniently prepared in situ by reaction of borane with 2,5-dimethylhexa-2,4-diene (**2**), has been uncovered. Advantageous workup protocols allow rapid access to alkyl and alkenyl boronic acids and their derivatives under mild conditions. Extension to a successful "one-pot" hydroboration/Suzuki–Miyaura cross-



Scheme 6. One-pot hydroboration/Suzuki–Miyaura cross-coupling protocol. Method A1: similar to method A, but without addition of $(HOCH_2CH_2)_2NH$. Method D: H_2O quench, 1 h, room temperature. Yields are for recrystallized material and are not optimized.

coupling protocol and perusal of the current state of organoboron chemistry[2–4] hold promise for further application of these findings in organic synthesis.

Experimental Section

General procedure (**4a**): Under an argon atmosphere, a flame-dried flask was charged with $NaBH_4$ (757 mg, 20 mmol), **2** (7.1 mL, 50 mmol), and anhydrous diglyme (20 mL), and the resulting mixture was cooled in an ice bath. $(MeO)_2SO_2$ (1.9 mL, 20 mmol) was added to the stirred mixture over ~1 h while maintaining the temperature below 5 °C. The addition was accompanied by an intensive gas evolution and homogeneity of the reaction mixture. The mixture was aged, with stirring, for 3 h at 0 °C, resulting in the gradual formation of a new thick suspension, to which phenylacetylene (2.2 mL, 20 mmol) was added slowly (~20 min) while maintaining the temperature below 5 °C. The resulting mixture was stirred for 1 h at 0 °C, slowly quenched with H_2O (3 mL) (additional gas evolution), stirred for 30 min at room temperature, and treated with a solution of formaldehyde (1.5 mL, 20 mmol, aq 37 wt% solution) in a single addition. The resulting exothermic reaction was compensated by application of an ambient-temperature bath. The reaction mixture was stirred for 24 h at room temperature and diluted with EtOAc (40 mL). After separation of layers, the organic phase was dried (Na_2SO_4), transferred into a flask containing diethanolamine (2.31 g, 22 mmol), and the combined mixture was evaporated under vacuum (25 Torr, then 0.5 Torr, heating bath at 50 then 80 °C). The resulting solid residue was recrystallized from MeCN to give **4a** (3.34 g, 15.38 mmol, 77% yield) as colorless needles. M.p. 197–199 °C (MeCN); IR (KBr): $\tilde{\nu}$ = 3000 (br), 1622, 1598, 1573, 1494, 1469, 1454, 1277, 1242, 1206 cm^{-1}; ^1H NMR (400 MHz, [D_6]DMSO): $\delta = 7.36$ (d, 2H, $J = 7.8$ Hz), 7.27 (t, 2H, $J = 7.5$ Hz), 7.15 (t, 1H, $J = 7.4$ Hz), 6.84 (br s, 1H), 6.66 (d, 1H, $J = 18.1$ Hz), 6.24 (d, 1H, $J = 18.1$ Hz), 3.81–3.73 (m, 2H), 3.71–3.64 (m, 2H), 3.08–2.99 (m, 2H), 2.26–2.70 ppm (m, 2H); ^{13}C NMR (100 MHz, [D_6]DMSO): $\delta = 139.4$, 136.1, 135.1 (br), 128.4, 126.5, 125.7, 62.5, 50.4 ppm; MS (EI): *m*/*z* (%): 217 (M^+, 1), 187 (9), 186 (100), 185 (8), 130 (7), 129 (9), 114 (87), 103 (25), 77 (15); elemental analysis calcd for $C_{12}H_{16}BNO_2$: C 66.40, H 7.43, N 6.45; found: C 66.36, H 7.35, N 6.45.

General Procedure (**6m**): Under an argon atmosphere, a flame-dried flask was charged with a solution of **2** (8.10 mL, 56.92 mmol) in THF (8 mL). The solution was cooled in an ice bath, and BH_3·THF solution (1M, 26 mL) was added while maintaining the reaction temperature below 5 °C. The resulting solution was aged, with stirring, for 3 h at 0 °C, and then treated with a solution of 9-vinylcarbazole (5.00 g, 25.87 mmol) in THF (15 mL) while maintaining the temperature below 5 °C. The reaction mixture was allowed to warm to room temperature, stirred for 2 h, cooled in an ice bath, and slowly quenched with 2,3-butanedione (2.72 mL, 31.04 mmol). The reaction was stirred for 1 h, warmed to room temperature, and stirred for an additional 12 h. Concentration under vacuum and purification by flash column chromatography (silica gel, eluent: EtOAc/hexanes) gave **6m** (11.38 g, 22.16 mmol, 86%) as a colorless glass, which slowly crystallized on standing. M.p. 79–81 °C (MeCN); IR (KBr): $\tilde{\nu} = 2959$, 1630, 1598, 1485, 1464, 1453, 1380, 1347, 1325, 1237, 1081 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.12$ (d, 2H, $J = 7.7$ Hz), 7.51–7.45 (m, 4H), 7.25 (ddd, 2H, $J = 7.9$, 6.0, 2.2 Hz), 5.63 (dd, 2H, $J = 15.8$, 1.1 Hz), 5.36 (dd, 2H, $J = 15.8$, 6.6 Hz), 4.59–4.46 (m, 2H), 2.35–2.25 (m, 2H), 1.57–1.51 (m, 2H), 1.51 (s, 6H), 1.13 (s, 6H), 1.11 (s, 6H), 1.02 (d, 6H, $J = 6.8$ Hz), 1.01 ppm (d, 6H, $J = 6.8$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 139.9$, 134.3, 134.2, 125.5, 122.9, 120.3, 118.6, 108.7, 92.4, 45.7, 38.8, 31.5, 25.8, 25.5, 22.6, 22.5, 18.7, 11.5 ppm (br); MS (EI): *m*/*z* (%): 514 (M^++1, 8), 513 (M^+, 20), 293 (17), 292 (62), 291 (25), 181 (12), 180 (44), 112 (16), 111 (100); HRMS (EI): calcd for $C_{34}H_{48}BNO_2$: 513.3778; found: 513.3784.

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[1] H. C. Brown, B. C. Subba Rao, *J. Am. Chem. Soc.* **1956**, *78*, 5694–5695.

[2] H. C. Brown, *Organic Syntheses via Boranes*, Wiley, New York, **1975**; B. M. Mikhailov, Yu. N. Bubnov, *Organoboron Compounds in Organic Synthesis*, Harwood Academic Science Publishers, Amsterdam, **1984**; A. Pelter, K. Smith, H. C. Brown, *Borane Reagents*, Academic Press, New York, **1988**; D. S. Matteson, *Stereodirected Synthesis with Organoboranes*, Springer, New York, **1995**; M. Zaidlewicz, *Methods of Organic Chemistry (Houben-Weyl), 4th ed. 1952–, Vol. E21d*, **1995**, pp. 4396–4420; "Organoboranes for Syntheses": *ACS Symp. Ser.* **2001**, *783*.

[3] P. V. Ramachandran, *Aldrichimica Acta* **2002**, *35*, 23–35, and references therein.

[4] N. Miyaura, A. Suzuki, *J. Chem. Soc. Chem. Commun.* **1979**, 866–867; in an issue dedicated to 30 years of cross-coupling chemistry: N. Miyaura, *J. Organomet. Chem.* **2002**, *653*, 54–57.

[5] M. F. Lipton, M. A. Mauragis, M. T. Maloney, M. F. Veley, D. W. VanderBor, J. J. Newby, R. B. Appell, E. D. Daugs, *Org. Proc. Res. Dev.* **2003**, *7*, 385–392; N. Yasuda, *J. Organomet. Chem.* **2002**, *653*, 279–287; Y. Urawa, H. Naka, M. Miyazawa, S. Souda, K. Ogura, *J. Organomet. Chem.* **2002**, *653*, 269–278; Z. Xu, J. Singh, M. D. Schwinden, B. Zheng, T. P. Kissick, B. Patel, M. J. Humora, F. Quiroz, L. Dong, D.-M. Hsieh, J. E. Heikes, M. Pudipeddi, M. D. Lindrud, S. K. Srivastava, D. R. Kronenthal, R. H. Mueller, *Org. Process Res. Dev.* **2002**, *6*, 323–328; for a review on the use of boronic acids in protection and catalysis, see: P. Duggan, E. M. Tyndall, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1325–1339; N. Yasuda, M. A. Huffman, G.-J. Ho, L. C. Xavier, C. Yang, K. M. Emerson, F.-R. Tsay, Y. Li, M. H. Kress, D. L. Rieger, S. Karady, P. Sohar, N. L. Abramson, A. E. DeCamp,

D. J. Mathre, A. W. Douglas, U.-H. Dolling, E. J. J. Grabowski, P. J. Reider, *J. Org. Chem.* **1998**, *63,* 5438–5446.

[6] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483; A. Suzuki in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**, pp. 49–97; A. Suzuki, *J. Organomet. Chem.* **2002**, *653*, 83–90; N. Miyaura, *Top. Curr. Chem.* **2002**, *219*, 11–59; K. Fagnou, M. Lautens, *Chem. Rev.* **2003**, *103*, 169–196; G. W. Kabalka, G. Dong, B. Venkataiah, *Org. Lett.* **2003**, *5*, 893–895; G. A. Molander, M. R. Rivero, *Org. Lett.* **2002**, *4*, 107–109; J. H. Kirchhoff, C. Dai, G. C. Fu, *Angew. Chem.* **2002**, *114*, 2025–2027; *Angew. Chem. Int. Ed.* **2002**, *41*, 1945–1947; J. H. Kirchhoff, M. R. Netherton, I. D. Hills, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 13662–13663; N. Kataoka, Q. Shelby, J. P. Stambuli, J. F. Hartwig, *J. Org. Chem.* **2002**, *67*, 5553–5566; J. Yin, M. P. Rainka, X.-X. Zhang, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163; C. Bolm, J. P. Hildebrand, K. Muñiz, N. Hermanns, *Angew. Chem.* **2001**, *113*, 3382–3407; *Angew. Chem. Int. Ed.* **2001**, *40*, 3284–3308; S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angew. Chem.* **2001**, *113*, 4676–4701; *Angew. Chem. Int. Ed.* **2001**, *40*, 4544–4568.

[7] R. B. Bedford, C. S. J. Cazin, S. J. Coles, T. Gelbrich, P. N. Horton, M. B. Hursthouse, M. E. Light, *Organometallics* **2003**, *22,* 987–999; N. R. Anastasi, K. M. Waltz, W. L. Weerakoon, J. F. Hartwig, *Organometallics* **2003**, *22,* 365–369, and references therein; D. E. Portlock, R. Ostaszewski, D. Naskar, L. West, *Tetrahedron Lett.* **2003**, *44*, 603–605; P. Y. S. Lam, D. Bonne, G. Vincent, C. G. Clark, A. P. Combs, *Tetrahedron Lett.* **2003**, *44*, 1691–1694, and references therein; G. W. Kabalka, S. K. Guchhait, *Org. Lett.* **2003**, *5*, 729–731; G. W. Kabalka, B. Venkataiah, *Tetrahedron Lett.* **2002**, *43*, 3703–3705; G. K. S. Prakash, M. Mandal, S. Schweizer, N. A. Petasis, G. A. Olah, *J. Org. Chem.* **2002**, *67*, 3718–3723; D. A. Evans, J. L. Katz, G. S. Peterson, T. Hintermann, *J. Am. Chem. Soc.* **2001**, *123,* 12411–12413; C. P. Decicco, Y. Song, D. A. Evans, *Org. Lett.* **2001**, *3*, 1029–1032; J. C. Antilla, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 2077–2079; T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* **2000**, *611*, 392–402, and references therein; M. Murata, T. Oyama, S. Watanabe, Y. Masuda, *J. Org. Chem.* **2000**, *65*, 164–168.

[8] C. E. Webster, Y. Fan, M. B. Hall, D. Kunz, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 858–859; T. Ishiyama, J. Takagi, K. Ishida, N. Miyaura, N. R. Anastasi, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 390–391, and references therein; M. K. Tse, J.-Y. Cho, M. R. Smith III, *Org. Lett.* **2001**, *3*, 2831–2833.

[9] J. Ramnauth, O. Poulin, S. Rakhit, S. P. Maddaford, *Org. Lett.* **2001**, *3*, 2013–2015; T. Ishiyama, T.-a. Ahiko, N. Miyaura, *Tetrahedron Lett.* **1996**, *37*, 6889–6892.

[10] G. C. Micalizio, S. L. Schreiber, *Angew. Chem.* **2002**, *114*, 160–162; *Angew. Chem. Int. Ed.* **2002**, *41*, 152–154; A. Rastelli, R. Gandolfi, M. Sarzi-Amade, B. Carboni, *J. Org. Chem.* **2001**, *66*, 2449–2458, and references therein; S. C. Pellegrinet, M. A. Silva, J. M. Goodman, *J. Am. Chem. Soc.* **2001**, *123*, 8832–8837; R. P. Litvinovskaya, V. A. Khripach, *Russ. Chem. Rev.* **2001**, *79*, 405–424; J. Renaud, C.-D. Graf, L. Oberer, *Angew. Chem.* **2000**, *112*, 3231–3234; *Angew. Chem. Int. Ed.* **2000**, *39*, 3101–3104; C. D. Davies, S. P. Marsden, E. Stokes, *Tetrahedron Lett.* **2000**, *41*, 4229–4233; R. A. Batey, A. N. Thadani, A. J. Lough, *J. Am. Chem. Soc.* **1999**, *121*, 450–451.

[11] J.-G. Boiteau, R. Imbos, A. J. Minnaard, B. L. Feringa, *Org. Lett.* **2003**, *5*, 681–684; D. F. Cauble, J. D. Gipson, M. J. Krische, *J. Am. Chem. Soc.* **2003**, *125*, 1110–1111; C. Bolm, J. Rudolph, *J. Am. Chem. Soc.* **2002**, *124*, 14850–14851; K. Yoshida, M. Ogasawara, T. Hayashi, *J. Am. Chem. Soc.* **2002**, *124*, 10984–10985; T. Hayashi, M. Takahashi, Y. Takaya, M. Ogasawara, *J. Am. Chem. Soc.* **2002**, *124*, 5052–5058; M. Kuriyama, K. Nagai, K.-i. Yamada, Y. Miwa, T. Taga, K. Tomioka, *J. Am. Chem. Soc.* **2002**, *124*, 8932–8939; M. Pucheault, S. Darses, J.-P. Genet, *Eur. J. Org. Chem.* **2002**, 3552–3557; M. Lautens, C. Dockendorff, K. Fagnou, A. Malicki, *Org. Lett.* **2002**, *4*, 1311–1314; for recent reviews, see: G. Alvaro, D. Savoia, *Synlett* **2002**, 651–673; A. Alexakis, C. Benhaim, *Eur. J. Org. Chem.* **2002**, 3221–3226; N. Krause, Hoffmann-Röder, *Synthesis* **2001**, 171–196; T. Hayashi, *Synlett* **2001**, 879–887; M. P. Sibi, S. Manyem, *Tetrahedron* **2000**, *56*, 8033–8061; S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069–1094; R. Bloch, *Chem. Rev.* **1998**, *98*, 1407–1438; D. Enders, U. Reinhold, *Tetrahedron: Asymmetry* **1997**, *8*, 1895–1946.

[12] H. C. Brown, E. Negishi, *Pure Appl. Chem.* **1972**, *29*, 527–545, and references therein; G. W. Kramer, H. C. Brown, *J. Organomet. Chem.* **1977**, *132*, 9–27; H. C. Brown, E.-i. Negishi, *Tetrahedron* **1977**, *33*, 2331–2357.

[13] B. M. Mikhailov, A. Ya. Bezmenov, L. S. Vasil'ev, V. G. Kiselev, *Dokl. Akad. Nauk SSSR* **1964**, *155*, 141; A. Ya. Bezmenov, L. S. Vasil'ev, B. M. Mikhailov, *Izv. Akad. Nauk SSSR Ser. Khim.* **1965**, 2111; B. M. Mikhailov, *Organomet. Chem. Rev. Sect. A* **1972**, *8*, 1–65.

[14] H. C. Brown, R. Liotta, G. W. Kramer, *J. Org. Chem.* **1978**, *43*, 1058–1063; also see M. Zaidlewicz, J. Meller, *Tetrahedron Lett.* **1997**, *38*, 7279–7282.

[15] H. C. Brown, G. Zweifel, *J. Am. Chem. Soc.* **1961**, *83*, 3834–3840; G. Zweifel, G. M. Clark, N. L. Polston, *J. Am. Chem. Soc.* **1971**, *93*, 3395–3399; H. C. Brown, G. Zweifel, *J. Am. Chem. Soc.* **1961**, *83*, 1241–1246; J. A. Soderquist, A. Hassner, *J. Organomet. Chem.* **1978**, *156*, C12-C16; H. C. Brown, J. Chen, *J. Org. Chem.* **1981**, *46*, 3978–3988; *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), Wiley, Chichester, **1995**, pp. 2295–2298.

[16] B. M. Mikhailov, Yu. N. Bubnov, *Izv. Akad. Nauk SSSR Ser. Khim.* **1964**, 1874; P. Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207–2293; R. Hoffmann, J. Krüger, D. Brückner, *New J. Chem.* **2001**, *25*, 102–107; J. W. J. Kennedy, D. G. Hall, *J. Am. Chem. Soc.* **2002**, *124*, 898–899; Y. Yamamoto, M. Takahashi, N. Miyaura, *Synlett* **2002**, 128–130; M. C. Kozlowski, S. P. Waters, J. W. Skudlarek, C. A. Evans, *Org. Lett.* **2002**, *4*, 4391–4393; Y. Yamamoto, K. Kurihara, A. Yamada, M. Takahashi, Y. Takahashi, N. Miyaura, *Tetrahedron* **2003**, *59*, 537–542.

[17] The ease of hydrolysis of simple allyl boranes diminishes with increasing substitution of double bond: triallylborane reacts rapidly with alcohols at room temperature with formation of allylboronic anhydride after distillation under vacuum: B. M. Mikhailov, F. B. Tutorskaya, *Dokl. Akad. Nauk SSSR* **1958**, 479; tricrotylborane reacts with methanol at room temperature to give dicrotylmethoxyborane (hydrolysis of only one organic residue on the boron center); to cleave the second crotyl residue, heating in methanol is required: B. M. Mikhailov, V. F. Pozdnev, *Izv. Akad. Nauk SSSR Ser. Khim.* **1964**, 1477.

[18] H. C. Brown, S. K. Gupta, *J. Am. Chem. Soc.* **1975**, *97*, 5249–5255; *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), Wiley, Chichester, **1995**, pp. 1017–1020.

[19] H. C. Brown, N. G. Bhat, V. Somayaji, *Organometallics* **1983**, *2*, 1311–1316; H. C. Brown, U. S. Racherla, *J. Org. Chem.* **1986**, *51*, 895–897; H. C. Brown, J. B. Campbell, Jr., *J. Org. Chem.* **1980**, *45*, 389–395; *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), Wiley, Chichester, **1995**, pp. 1548–1552 and 1689–1690.

[20] R. Köster in *Methods of Organic Chemistry (Houben-Weyl), 4th ed. 1952–, Vol. 13/3a*, **1982**, pp. 489–853.

[21] The well-documented reduction of halides, sulfonates, and sulfates with sodium borohydride proceeds well in polar aprotic solvents such as diglyme or dimethyl sulfoxide with the generation of an equimolar amount of borane. This consideration led to the development of protocols with borane being scavenged in situ by the present alkene, thus resulting in a hydroboration reaction in situ: H. C. Brown, P. Tierney, *J. Am. Chem. Soc.* **1958**, *80*, 1552–1558; H. C. Brown, K. J. Murray, L. J.

Murray, J. A. Snover, G. Zweifel, *J. Am. Chem. Soc.* **1960**, *82*, 4233–4241; H. M. Bell, C. W. Vanderslice, A. Spehar, *J. Org. Chem.* **1969**, *34*, 3923–3926; S. Krishnamurthy, H. C. Brown, *J. Org. Chem.* **1980**, *45*, 849–856; *Encyclopedia of Reagents for Organic Synthesis* (Ed.: L. A. Paquette), Wiley, Chichester, **1995**, pp. 4522–4528.

[22] Unlike boronic acids, the corresponding diethanolamine adducts are highly stable, conveniently handled and purified compounds: K. Smith, J. B. Leach, *Organometallic Compounds of Boron*, Chapman and Hall, New York, **1985**; see also: M. Gravel, K. A. Thompson, M. Zak, C. Berube, D. G. Hall, *J. Org. Chem.* **2002**, *67*, 3–15; C. N. Farthing, S. P. Marsden, *Tetrahedron Lett.* **2000**, *41*, 4235–4238; K. A. Thompson, D. G. Hall, *Chem. Commun.* **2000**, 2379–2380.

[23] For experimental details, see Supporting Information.

[24] Experiments to isolate **9** were not conducted (see reference [17]).

[25] CCDC 193654 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[26] E. Jehanno, M. Vaultier, *Tetrahedron Lett.* **1995**, *36*, 4439–4442; J. Tailor, D. G. Hall, *Org. Lett.* **2000**, *2*, 3715–3718.

