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Catalyzed hydroboration of nitrostyrenes and 4-vinylaniline: a mild and selective route to aniline derivatives containing boronate esters

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Abstract—Transition metal catalyzed reactions of catecholborane (HBcat; cat = 1,2-$O_2C_6H_4$) with β-nitrostyrene and 3-nitrostyrene lead to products derived from competing hydrogenation and hydroboration of the alkene unit along with reduction of the nitro group. Hydroboration of 4-vinylaniline gave regioselective formation of either the branched or the linear organoboronate ester depending upon the catalyst precursors (i.e., $RhCl(PPh_3)_3$ or Rh(acac)(dppe) vs $[Cp^*IrCl_2]_2$) used to facilitate this reaction. Hydroboration products were converted to air-stable primary amines by addition of pinacol.

The hydroboration of alkenes and alkynes, which constitutes the addition of a B–H bond across a carbon–carbon multiple bond, is a remarkably 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.[2] These reactions can have regio-, chemo-, or stereoselectivities, complementary, or more remarkably, opposite to those from products obtained via the uncatalyzed variant. For example, hydroborations of vinylarenes ($ArCH{=}CH_2$) with HBcat proceed to give selectively either the expected linear product ($ArCH_2CH_2Bcat$) or the branched product ($ArCH(Bcat)CH_3$), depending upon the choice of catalyst used to affect this transformation.[3]

Although a considerable amount of research has focused on the catalyzed hydroboration of simple unsaturated hydrocarbon systems, much less is known about analogous reactions with heteroatom-containing substrates.[3,4] In an effort to expand the scope of metal catalyzed hydroborations, and generate novel aminoboron compounds, we have examined reactions of related nitrostyrene and vinylaniline derivatives with HBcat and report our results herein. We have found that addition of excess HBcat (up to 8 equiv) to β-nitrostyrene (*trans*-$C_6H_5CH{=}CHNO_2$) using a rhodium catalyst (typically $RhCl(PPh_3)_3$ or Rh(acac)(dppe); where acac = acetylacetonato and dppe = 1,2-bis(diphenylphosphino)ethane) gave only $PhCH_2CH_2NO_2$ and B_2cat_3.[5] The formation of these products arises presumably as a result of nucleophilic degradation of the starting dialkoxyborane into B_2cat_3 and dihydrogen. The liberated dihydrogen would add to the rhodium to form an active hydrogenation catalyst, which could react subsequently with the starting alkene to give $PhCH_2CH_2NO_2$.[6]

We then examined the rhodium catalyzed hydroboration of 3-nitrostyrene (3-$O_2NC_6H_4CH{=}CH_2$) to see if altering the position of the nitro group had any effect on the reaction pathway. Unfortunately, the catalyzed addition of 1 equiv of HBcat gave only hydrogenation product, 3-$O_2NC_6H_4CH_2CH_3$ and unreacted starting material, arising from degradation of the borane (Table 1, entry 1). However, in the case of 3-nitrostyrene, addition of excess HBcat (8 equiv) using the rhodium catalysts described above gave selective formation of

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Keywords: Aminoboron; Catalysis; Hydroboration; Regioselectivity.

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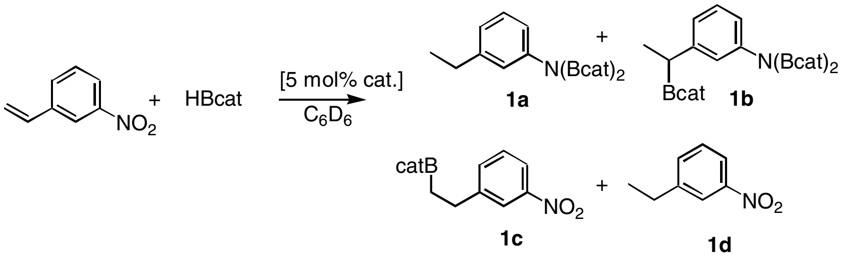
Table 1. Hydroboration of 3-nitrostyrene



Entry	Catalyst	HBcat	**1a**[a]	**1b**[a]	**1c**[a]	**1d**[a]
1	$RhCl(PPh_3)_3$	1.1	0	2	0	98
2	$RhCl(PPh_3)_3$	8	2	98	0	0
3	Rh(acac)(dppe)	8	2	98	0	0
4	$[Cp^*IrCl_2]_2$	1.1	0	0	98 (72)	2

Values in parentheses are of isolated yields.

[a] Determined by multinuclear NMR spectroscopy and confirmed by GC/MS.

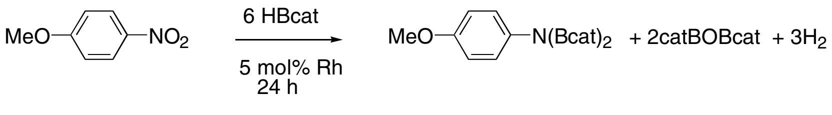
the branched hydroboration product $3\text{-}(catB)_2NC_6H_4\text{-}CH(Bcat)CH_3$ (**1b**) (>98% by ^1H NMR spectroscopy, entries 2 and 3) along with minor amounts of unwanted hydrogenation product $3\text{-}(catB)_2NC_6H_4CH_2CH_3$ (**1a**). Reactions could be carried out in a variety of solvents (benzene, toluene, THF, etc.) without significant loss of selectivity. Remarkably, concurrent reduction of the nitro group is observed in these reactions along with considerable degradation of HBcat into B_2cat_3[5] and catBOBcat.[7] It is plausible that the dihydrogen that is also formed by this degradation reaction is responsible, in conjunction with the metal catalyst, for reducing the nitro group to the corresponding amine derivative. Excess HBcat would then react rapidly with the acidic NH bonds to give products containing N(Bcat) bonds, and once again liberating H_2. To confirm that the nitro group was being reduced in these reactions, we independently converted 4-nitroanisole into 4-anisidine, and subsequently $4\text{-}(catB)_2NC_6H_4OMe$, under identical conditions (Scheme 1). In a similar study, organomagnesium reagents were used to reduce nitrosoarenes to polyfunctional diarylamines.[8]

In this study, the air-stable aniline derivative $3\text{-}H_2N\text{-}C_6H_4CH(Bpin)CH_3$ (**1e**, pin = $1,2\text{-}O_2C_2Me_4$)[9] was prepared and isolated in low yield (26%) by addition of pinacol.[10] The synthesis of amines containing boronate esters is of considerable interest owing to their use in Suzuki–Miyaura cross-coupling reactions[1b] and their potent biological activities.[11] The difficulty in preparing primary amines containing boronate esters, however, has previously limited their potential applications.[12]

Interestingly, using the iridium catalyst precursor $[Cp^*IrCl_2]_2$[13], the regioselectivities for the hydroboration reaction could be inverted in comparison to the rhodium catalyzed reactions. For instance, the linear hydroboration product $3\text{-}O_2NC_6H_4CH_2CH_2Bcat$ (**1c**) could be generated as the major product in reactions using only 1 equiv of HBcat (Table 1, entry 4). Remarkably, degradation of HBcat, and hence competing reduction of the nitro group is not observed to any significant extent in reactions using this catalyst system. This observation suggests that catalysis with this precursor may not necessarily proceed via conventional pathways that invoke initial oxidative addition of HBcat to the metal center.[14] The iridium catalyzed hydroboration of alkenes using pinacolborane (HBpin; pin = $1,2\text{-}O_2C_2Me_4$) is also known to give the corresponding primary boronate ester products.[14c,d] Attempts to catalyze this reaction with HBpin, using either the rhodium or iridium complexes, led to extensive degradation of the borane along with the formation of significant amounts of hydrogenation products (**1a** and **1d**).

The molecular structure of **1c**[15] is shown in Figure 1 and the B–O bond distances of 1.390 (1) and 1.392 (1) Å are typical for those observed in other Bcat structures where the boron is three coordinate.[16] No appreciable intermolecular interaction between the Lewis acidic boron atom and the nitro group is observed in the solid state. Addition of pinacol to compound **1c** gave $3\text{-}O_2NC_6H_4CH_2CH_2Bpin$ (**1f**), whereby subsequent hydrogenation using Pd/C gave the corresponding air-stable aniline derivative $3\text{-}H_2NC_6H_4CH_2CH_2Bpin$ (**1g**) in moderate yield (46%).

The results from reactions with nitrostyrene prompted us to investigate the catalyzed hydroboration of commercially available 4-vinylaniline. While reactions of allylamine gave complex product distributions arising from competing degradation and isomerization reac-



Scheme 1. Rhodium catalyzed reduction of 4-nitroanisole with HBcat.

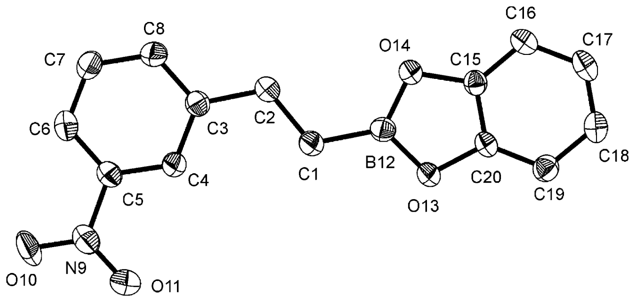


Figure 1. Molecular structure of **1c** with ellipsoids drawn at the 30% probability level. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): C(1)–B(12) 1.547(1); N(9)–O(10) 1.226(1); N(9)–O(11) 1.232(1); B(12)–O(13) 1.390(1); B(12)–O(14) 1.392(1); O(13)–B(12)–O(14) 111.15(8); O(13)–B(12)–C(1) 122.83(8); O(14)–B(12)–C(1) 126.02(8).

tions,[4b] hydroboration of 4-vinylaniline using either $RhCl(PPh_3)_3$ (Table 2, entry 2) or Rh(acac)(dppe) (entry 3) with excess HBcat gave formation of the branched product $4\text{-}(catB)_2NC_6H_4CH(Bcat)CH_3$ (**2b**) along with minor amounts of hydrogenation product $4\text{-}(catB)_2NC_6H_4CH_2CH_3$ (**2a**), as evidenced by multinuclear NMR spectroscopy. Reactions with only 1 equiv of HBcat gave a mixture of hydrogenation products, **2a**. Addition of pinacol to **2b**, however, once again gave the novel air-stable compound $4\text{-}H_2NC_6H_4CH(Bpin)CH_3$ (**2d**).

The linear isomer $4\text{-}(catB)_2NC_6H_4CH_2CH_2Bcat$ (**2c**) could be generated using the $[Cp^*IrCl_2]_2$ catalyst system, however, this reaction suffered from competing hydrogenation to give significant amounts of **2a** (entry 4). The corresponding pinacol derivative $4\text{-}H_2NC_6H_4CH_2CH_2Bpin$ (**2e**)[17] was isolated in moderate yield. Attempts to prepare **2e** directly from the catalyzed addition of pinacolborane (HBpin) using $RhCl(PPh_3)_3$ gave only $4\text{-}(pinB)NHC_6H_4CH_2CH_3$, where the corresponding hydroboration reaction again appears to be too slow to compete with the hydrogenation pathway.

In summary, we have investigated the hydroboration of nitrostyrenes and 4-vinylaniline. This methodology provides an efficient and gentle route for generating air-stable aniline derivatives containing boronate esters that are difficult to prepare by conventional techniques. Future work in this area will be to examine asymmetric variants as well as expand the scope of these reactions.

Acknowledgments

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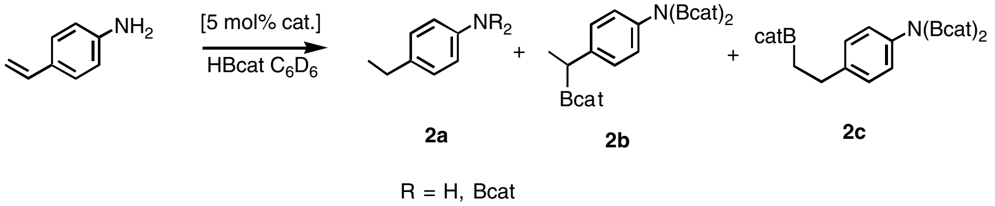
Supplementary data

Experimental details describing the synthesis, characterization, and analysis of the products are provided along with complete X-ray data for compound **1c**. Full details of the crystal structure investigation can also be obtained from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.01.144.

References and notes

1. (a) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975; (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
2. (a) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878; (b) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957; (c) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695; (d) Kadlecek, D. E.; Carroll, P. J.; Sneddon, L. G. *J. Am. Chem. Soc* **2000**, *122*, 10868; (e) Demay, S.; Volant, F.; Knochel, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1235; (f) Widauer, C.; Grützmacher, H.; Ziegler, T. *Organometallics* **2000**, *19*, 2097; (g) Hayashi, T.;

Table 2. Hydroboration of 4-vinylaniline



Entry	Catalyst	HBcat	**2a**[a]	**2b**[a]	**2c**[a]
1	$RhCl(PPh_3)_3$	1.1	98	2	0
2	$RhCl(PPh_3)_3$	4	5	95 (93)	0
3	Rh(acac)(dppe)	4	2	98 (93)	0
4	$[Cp^*IrCl_2]_2$	10	30	0	70

Values in parentheses are of isolated yields.

[a] Determined by multinuclear NMR spectroscopy and confirmed by GC/MS.

Matsumoto, Y.; Ito, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 601; (h) Segarra, A. M.; Daura-Oller, E.; Claver, C.; Poblet, J. M.; Bo, C.; Fernández, E. *Chem. Eur. J* **2004**, *10*, 6456; (i) Connolly, D. J.; Lacey, P. M.; McCarthy, M.; Saunders, C. P.; Carroll, A.-M.; Goddard, R.; Guiry, P. J. *J. Org. Chem.* **2004**, *69*, 6572; (j) Carroll, A.-M.; O'Sullivan, T. P.; Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609.

3. (a) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 8863; (b) Carroll, A.-M.; O'Sullivan, T. P.; Guiry, P. J. *Adv. Synth. Catal.* **2005**, *347*, 609; (c) Daura-Oller, E.; Segarra, A. M.; Poblet, J. M.; Claver, C.; Fernández, E.; Bo, C. *J. Org. Chem.* **2004**, *69*, 2669; (d) Segarra, A. M.; Guerrero, C.; Claver, C.; Fernández, E. *Chem. Commun.* **2001**, 1808; (e) Segarra, A. M.; Guirado, F.; Claver, C.; Fernández, E. *Tetrahedron: Asymmetry* **2003**, *14*, 1611; (f) Guiry, P. J.; McCarthy, M.; Lacey, P. M.; Saunders, C. P.; Kelly, S.; Connolly, D. J. *Curr. Org. Chem.* **2000**, *4*, 821; (g) Betley, T. A.; Peters, J. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2385; (h) Ren, L.; Chen, A. C.; Decken, A.; Crudden, C. M. *Can. J. Chem.* **2004**, *82*, 1781; (i) Ramírez, J.; Segarra, A. M.; Fernández, E. *Tetrahedron: Asymmetry* **2005**, *16*, 1289.
4. (a) Ramachandran, P. V.; Jennings, M. P.; Brown, H. C. *Org. Lett* **1999**, *1*, 1399; (b) Vogels, C. M.; O'Connor, P. E.; Phillips, T. E.; Watson, K. J.; Shaver, M. P.; Hayes, P. G.; Westcott, S. A. *Can. J. Chem.* **2001**, *79*, 1898; (c) Ramachandran, P. V.; Jennings, M. P. *Chem. Commun.* **2002**, 386; (d) Pergament, I.; Srebnik, M. *Tetrahedron Lett.* **2001**, *42*, 8059; (e) Pergament, I.; Srebnik, M. *Org. Lett.* **2001**, *3*, 217; (f) Carter, C. A. G.; Vogels, C. M.; Harrison, D. J.; Gagnon, M. K. J.; Norman, D. W.; Langler, R. F.; Baker, R. T.; Westcott, S. A. *Organometallics* **2001**, *20*, 2130; (g) Hou, X.-L.; Hong, D.-G.; Rong, G.-B.; Guo, Y.-L.; Dai, L.-X. *Tetrahedron Lett* **1993**, *34*, 8513; (h) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 5678.
5. Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *Inorg. Chem.* **1993**, *32*, 2175.
6. Harmon, R. E.; Parsons, J. L.; Cooke, D. W.; Gupta, S. K.; Schoolenberg, J. *J. Org. Chem.* **1969**, *34*, 3684.
7. (a) Harrison, D. J.; Tam, N. G.; Vogels, C. M.; Langler, R. F.; Baker, R. T.; Decken, A.; Westcott, S. A. *Tetrahedron Lett* **2004**, *45*, 8493; (b) Coombs, N. D.; Aldridge, S.; Wiltshire, G.; Kays (nee Coombs), D. L.; Bresner, C.; Ooi, L.-l. *J. Organomet. Chem.* **2005**, *690*, 2725; (c) Lang, A.; Knizek, J.; Noth, H.; Schur, S.; Thomann, M. Z. *Anorg. Allg. Chem.* **1997**, *623*, 901.
8. Kopp, F.; Sapountzis, I.; Knochel, P. *Synlett* **2003**, 885.
9. In a typical experiment, 1–8 equiv of HBcat in 0.5 mL of C_6D_6 were added dropwise to a 0.5 mL solution of the appropriate vinyl arene in C_6D_6 under an atmosphere of dinitrogen. Reactions were monitored by NMR spectroscopy. Product selectivities did not vary significantly in reactions conducted in either THF or toluene.
10. (a) Chen, A. C.; Ren, L.; Crudden, C. M. *Chem. Commun.* **1999**, 611; (b) Chen, A. C.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704; (c) Moore, A. J. N.; Wayner, D. D. M. *Can. J. Chem.* **1999**, *77*, 681.
11. (a) Smoum, R.; Rubinstein, A.; Srebnik, M. *Bioorg. Chem.* **2003**, *31*, 464; (b) Jagannathan, S.; Forsyth, T. P.; Kettner, C. A. *J. Org. Chem.* **2001**, *66*, 6375; (c) Priestly, E. S.; Decicco, C. P. *Org. Lett.* **2000**, *2*, 3095; (d) Dembitsky, V. M.; Smoum, R.; Al-Quntar, A. A.; Ali, H. A.; Pergament, I.; Srebnik, M. *Plant Sci* **2002**, *163*, 931; (e) Barranco, W. T.; Eckhert, C. D. *Cancer Lett* **2004**, *216*, 21; (f) Li, P.; Shaw, B. R. *J. Org. Chem.* **2004**, *69*, 7051; (g) Yang, W.; Gao, X.; Wang, B. *Med. Res. Rev.* **2003**, *23*, 346; (h) Yinghuai, Z.; Peng, A. T.; Carpenter, K.; Maguire, J. A.; Hosmane, N. S.; Takagaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 9875; (i) Vyakaranam, K.; Rana, G.; Hosmane, N. S.; Spielvogel, B. F. *Metal Based Drugs* **2001**, *8*, 145; (j) Vyakaranam, K.; Rana, G.; Spielvogel, B. F.; Hosmane, N. S. *Inorg. Chem. Commun.* **2001**, *4*, 629; (k) Rana, G.; Vyakaranam, K.; Ledger, S. C.; Delaney, S. L.; Maguire, J. A.; Hosmane, N. S. *Appl. Organomet. Chem.* **2003**, *17*, 361; (l) Hosmane, N. S.; Maguire, J. A. *Eur. J. Chem.* **2003**, 3989; (m) Adams, J. *Cancer Treat Rev.* **2003**, *29*, 3.
12. For leading references, see: *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005.
13. Ball, R. G.; Graham, W. A. G.; Heinekey, D. M.; Hoyano, J. K.; McMaster, A. D.; Mattson, B. M.; Michel, S. T. *Inorg. Chem.* **1990**, *29*, 2023.
14. (a) Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *Can. J. Chem.* **1993**, *71*, 930; (b) Harrison, K. N.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 9220; (c) Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 9200; (d) Yamamoto, Y.; Fujikawa, R.; Unemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695.
15. Crystallographic data for **1c**: $C_{14}H_{12}BNO_4$, $M_w = 269.06$, triclinic, P-1, $a = 6.8074(15)$ Å, $b = 7.0840(16)$ Å, $c = 13.845(3)$ Å, $\alpha = 97.244(3)°$, $\beta = 91.517(3)°$, $\gamma = 109.703°$, $V = 621.9(2)$ Å^3, $Z = 2$, $D_{\text{calcd}} = 1.437$ g cm^{-3}, $F(000) = 280$, $\mu = 0.104$ mm^{-1}, $R1 = 0.00333$ $(I > 2\sigma(I))$, $wR2 = 0.0833$ (all data), GoF = 0.949. Crystallographic information has also been deposited with the Cambridge Crystallographic Data Centre (CCDC 279656).
16. (a) Coapes, R. B.; Souza, F. E. S.; Fox, M. A.; Batsanov, A. S.; Goeta, A. E.; Yufit, D. S.; Leech, M. A.; Howard, J. A. K.; Scott, A. J.; Clegg, W.; Marder, T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 1201; (b) Clegg, W.; Elsegood, M. R. J.; Lawlor, F. J.; Norman, N. C.; Pickett, N. L.; Robbins, E. G.; Scott, A. J.; Nguyen, P.; Taylor, N. J.; Marder, T. B. *Inorg. Chem.* **1998**, *37*, 5289; (c) Nguyen, P.; Coapes, R. B.; Woodward, A. D.; Taylor, N. J.; Burke, J. M.; Howard, J. A. K.; Marder, T. B. *J. Organomet. Chem.* **2002**, *652*, 77; (d) Zheng, C.; Spielvogel, B. F.; Smith, R. Y.; Hosmane, N. S. *Z. Kristallogr. NCS* **2001**, *216*, 341.
17. Cordi, A.; Desos, P.; Atassi, G.; Pierre, A. Patent WO9831688, 1998.