Check for updates

View Article Online
View Journal

ChemComm
Chemical Communications

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: T. Hashimoto, T. Ishimaru, K. Shiota and Y. Yamaguchi, *Chem. Commun.*, 2020, DOI: 10.1039/D0CC05246A.

Volume 54
Number 1
4 January 2018
Pages 1-112

ChemComm
Chemical Communications
rsc.li/chemcomm

ISSN 1359-7345

ROYAL SOCIETY OF CHEMISTRY

COMMUNICATION
S. J. Connon, M. O. Senge *et al.*
Conformational control of nonplanar free base porphyrins: towards bifunctional catalysts of tunable basicity

This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

View Article Online
DOI: 10.1039/D0CC05246A

COMMUNICATION

Bottleable $NiCl_2$(dppe) as a catalyst for the Markovnikov-selective hydroboration of styrenes with bis(pinacolato)diboron

Toru Hashimoto,* Toshiya Ishimaru, Keisuke Shiota, and Yoshitaka Yamaguchi*

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Albeit that transition-metal-catalysed hydroboration reactions of alkenes have been extensively studied, only three examples using Ni complexes have been reported so far. In this study, we have examined hydroboration reactions of alkenes using Ni/phosphine complexes. The commercially available and bottleable complex $NiCl_2$(dppe) (dppe = 1,2-bis(diphenylphosphino)ethane) serves as a catalyst for the highly Markovnikov-selective hydroboration of styrene derivatives that affords the desired Markovnikov products in high yield.

Hydroboration reactions of alkenes are of great academic and industrial importance as a key step in the synthesis of boron-containing compounds and, accordingly, have been explored extensively.[1,2] Transition-metal-catalysed alkene hydroboration reactions have obvious advantages such as high chemo- and regioselectivity and broad functional-group compatibility. Catalysts based on precious metals such as Rh and Ir are most widely applied in hydroboration reactions due to their high activity and selectivity.[3] However, the economic and environmental concerns associated with these catalysts have led to considerable interest in replacing them with catalysts based on earth-abundant first-row transition metals.[4] Over the past decade, great progress has been made in the development of Cu-catalysed alkene hydroboration reactions.[5] The use of Fe- and Co-based catalysts has also attracted considerable attention recently owing to their unique reactivity and reaction mechanism.[6,7] The use of these metals in combination with multidentate ligands has led to tremendous advances in the Markovnikov-selective hydroboration of alkenes. Despite the excellent results achieved using Cu, Fe, and Co catalysts, the use of Ni catalysts in the Markovnikov-selective hydroboration of alkenes remains limited.[8] In 2016, Schomaker reported a heteroleptic nickel complex with both *N*-heterocyclic carbene (NHC) and tricyclohexylphosphine (PCy_3) ligands that showed high Markovnikov selectivity for the hydroboration of styrene derivatives using pinacolborane (HBPin) (Fig. 1).[8a] A nickel complex bearing a phenalenyl-based ligand (PLY) was used as an effective catalyst for alkene hydroboration.[8b] Very recently, we have reported that the β-aminoketonato-based *O,N,P*-pincer-type nickel complex **1** effectively catalyses the highly Markovnikov-selective hydroboration of styrene derivatives using bis(pinacolato)diboron (B_2pin_2).[8c,9] However, the synthesis of these nickel complexes is laborious, and their sensitivity to air and moisture requires storage under inert atmospheres. These drawbacks led us to investigate more accessible and more robust Ni complexes that effectively catalyse the hydroboration of alkenes. We focused on Ni/phosphine complexes, as many Ni/phosphine complexes are commercially available or easily synthesised, and they often show desirable stability toward air and moisture. We found that a Ni complex that bears a suitable bidentate phosphine ligand can serve as an efficient catalyst for the Markovnikov-selective hydroboration of styrene derivatives.

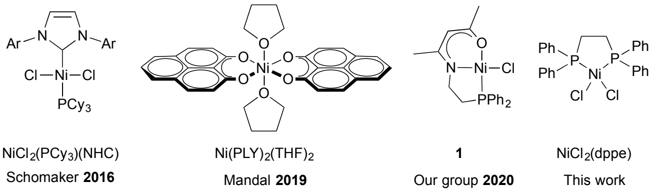


Fig. 1 Ni complexes for Markovnikov-selective hydroboration reactions.

Initially, we attempted the hydroboration of 4-methoxystyrene (**2a**) using a variety of phosphine-ligated Ni complexes under our previously reported reaction conditions (Table 1).[8c,10] Treatment of **2a** with B_2pin_2 (**3**, 2.0 equiv) in the presence of the *O,N,P*-coordinated nickel complex **1** as a catalyst (5 mol%) and KOAc as a base (2.0 equiv) in toluene/MeOH (3:1, v/v) at 25 °C afforded the corresponding

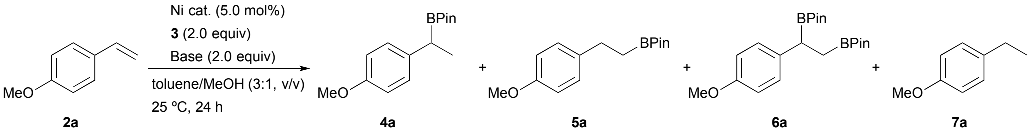
---

[a] *Department of Advanced Materials Chemistry, Graduate School of Engineering, Yokohama National University, 79-5 Tokiwadai, Hodogaya-ku, Yokohama 240-8501, Japan. E-mail: hashimoto-toru-kh@ynu.ac.jp, yamaguchi-yoshitaka-hw@ynu.ac.jp*

† Electronic Supplementary Information (ESI) available. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/D0CC05246A

Table 1 Optimisation of the reaction conditions[a]

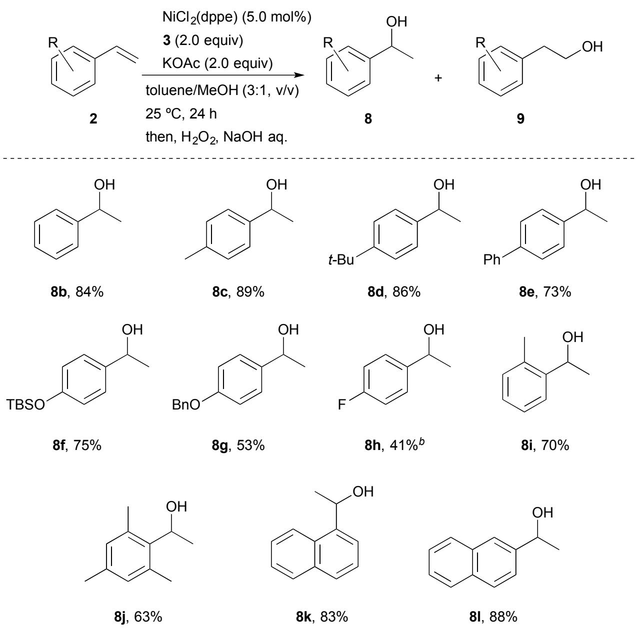


Entry	Ni cat.	Base	Yield **4a** (%)[b]	Yield **5a** (%)[b]	Yield **6a** (%)[b]	Yield **7a** (%)[c]	Recovery of **2a** (%)[c]
1	**1**	KOAc	58	<1	0	5	25
2	$NiCl_2(PPh_3)_2$	KOAc	49	6	0	6	37
3	$NiCl_2(PCy_3)_2$	KOAc	55	17	0	0	28
4	$NiCl_2$(dppe)	KOAc	97	0	0	0	0
5	$NiCl_2$(dppp)	KOAc	84	0	0	5	11
6	$NiCl_2$(dppf)	KOAc	86	0	0	0	0
7	$NiCl_2$(dppe)	NaOAc	80	0	0	10	8
8	$NiCl_2$(dppe)	KO*t*-Bu	0	11	4	76	0
9	$NiCl_2$(dppe)	NaOMe	0	0	92	0	0
10[d]	$NiCl_2$(dppe)	KOAc	0	0	0	0	97
11	$NiCl_2$(dppe)	–	0	0	0	0	85
12	–	KOAc	0	0	35	0	63

[a] Reaction conditions: **2a** (0.50 mmol), **3** (1.00 mmol), nickel catalyst (5 mol%), base (1.00 mmol), toluene (3 mL), MeOH (1 mL), 25 °C, 24 h. [b] Determined by NMR analysis using an internal standard. [c] Determined by GC analysis using an internal standard. [d] Without MeOH.

product (**4a**) in 58% yield with high Markovnikov selectivity; 25% of the **2a** could be recovered (entry 1). To improve the yield of **4a**, we examined other nickel sources (entries 2–6). Ni complexes that bear monodentate phosphine ligands, such as $NiCl_2(PPh_3)_2$ and $NiCl_2(PCy_3)_2$, were not effective for the hydroboration of **2a**, providing **4a** in merely moderate yield (entries 2 and 3). In contrast, Ni complexes that bear bidentate phosphine ligands, such as 1,2-bis(diphenylphosphino)ethane (dppe), 1,3-bis(diphenylphosphino)propane (dppp), or 1,1′-bis(diphenylphosphino)ferrocene (dppf) afforded **4a** in good-to-high yield with high Markovnikov selectivity (entries 4–6). Among these complexes, $NiCl_2$(dppe) showed the best performance, affording **4a** in 97% yield with high Markovnikov selectivity (entry 4). Using $NiCl_2$(dppe) as the catalyst, we then explored different bases. When NaOAc was used, the yield of **4a** decreased to 80% (entry 7). KO*t*-Bu did not afford **4a**, while forming **5a** in 11% yield and 4-ethylanisole (**7a**) in 76% yield (entry 8). In the case of NaOMe, **4a** was not formed (entry 9).[10] When MeOH was removed from the reaction system, **4a** was not formed, and **2a** was recovered almost quantitatively (97%) (entry 10). Reactions without KOAc or $NiCl_2$(dppe) also did not afford **4a** (entries 11 and 12).

Table 2 Hydroboration of styrene derivatives **2**[a]

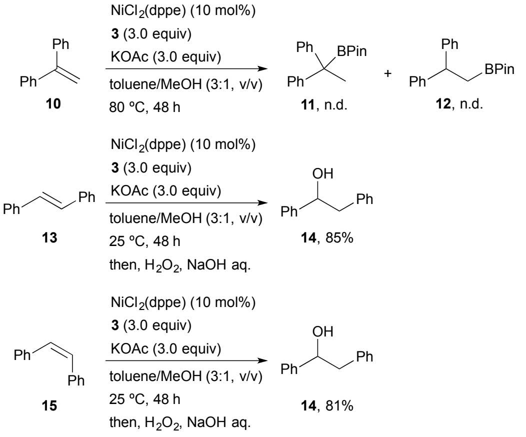


[a] Reaction conditions: **2a** (0.50 mmol), **3** (1.00 mmol), $NiCl_2$(dppe) (5 mol%), KOAc (1.00 mmol), toluene (3 mL), MeOH (1 mL), 25 °C, 24 h. Isolated yield. [b] The reaction was performed using 10 mol% of $NiCl_2$(dppe).

With the optimized reaction conditions in hand, we examined the substrate scope using various styrene derivatives (**2**), and the corresponding products (**4**) were isolated after oxidation into the respective secondary alcohols (**8**) (Table 2). The reaction using styrene (**2b**) afforded **8b** in 84% isolated yield. Styrene derivatives with a methyl (**2c**), *t*-butyl (**2d**), or phenyl (**2e**) substituent at the 4-position showed good reactivity and Markovnikov selectivity, and were converted into benzyl alcohols **8c**–**8e** in 73–89% yield. Various functionalities, such as siloxy (**2f**), benzyloxy (**2g**), and fluoro (**2h**) groups, were tolerated under the present reaction conditions, and the corresponding alcohols (**8f**–**8h**) were formed in 41–75% yield. When the sterically demanding 2-methylstyrene (**2i**) and 2,4,6-trimethylstyrene (**2j**) were used, the reactions proceeded smoothly to afford the desired products (**8i** and **8j**) in good yield.

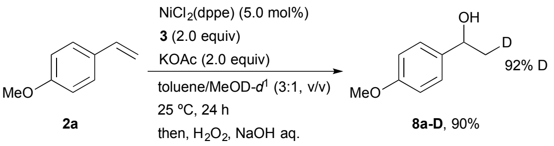
1-Vinyl- (**2k**) and 2-vinylnaphthalene (**2l**) afforded **8k** and **8l** in 83% and 88% yield, respectively. In all cases, the corresponding primary alcohols (**9**) and diborylated product (**6**) were not detected, while hydrogenated products (**7**) were formed as major by-products.

Next, we examined the hydroboration reaction of α- and β-substituted styrene derivatives (**10**, **13**, and **15**) with **3** using 10 mol% $NiCl_2$(dppe) as the catalyst (Scheme 1). The reaction with 1,1-diphenylethylene (**10**) was carried out at 80 °C for 24 h, albeit that the borylated products **11** and **12** were not formed, and **10** was recovered in 73%. In the case of *trans*-stilbene (**13**), the hydroboration reaction (48 h at 25 °C) followed by an oxidation reaction furnished **14** in 85% yield. Under the same reaction conditions, *cis*-stilbene (**15**) was also converted into **14** in 81% yield. α- or β-Alkyl-substituted styrenes and aliphatic terminal and internal alkenes did not react under the applied reaction conditions.



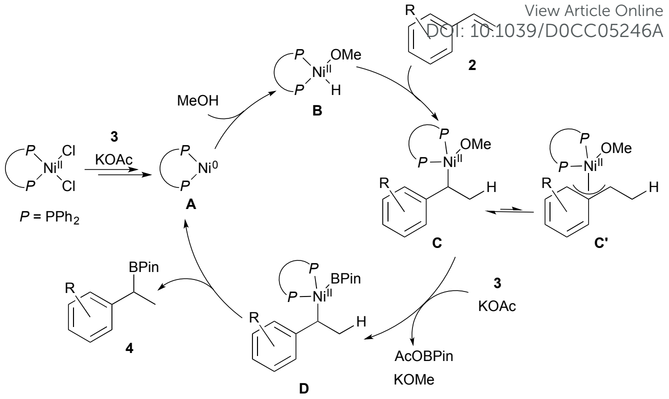
Scheme 1 Hydroboration of **10**, **13**, and **15**.

To obtain mechanistic insight into this alkene hydroboration reaction, an isotope-labelling experiment was carried out (Scheme 2). When MeOD-d^1 was used instead of MeOH, alcohol **8a-D** was formed in 90% yield with 92% deuteration of one hydrogen atom on the methyl group. On the basis of this result and of previous reports,[8a,11,12] we propose a possible reaction mechanism shown in Scheme 3. Initially, Ni(0) species **A** is generated by the reduction of **3** with $NiCl_2$(dppe) in the presence of KOAc.[8a,13] Subsequently, the oxidative addition of the O–H bond of MeOH to Ni(0) species **A** affords methoxy Ni(II) hydride **B**.[11] The hydride of **B** is transferred to the terminal carbon atom of the double bond of styrene **2** to form benzyl nickel intermediates **C** and **C'**, which might be in equilibrium. At this point, we assume that the nickel intermediate **C** would be favoured relative to **C'**.[14] Finally, **C** undergoes transmetalation with **3**, followed by a reductive elimination of **D** to generate the hydroboration product **4** under concomitant regeneration of the active nickel (0) species **A**.[15,16]



Scheme 2 Isotope-labelling experiment

View Article Online
DOI: 10.1039/D0CC05246A



Scheme 3 Proposed reaction mechanism for $NiCl_2$(dppe)-catalysed Markovnikov-selective hydroboration of styrene derivatives (**2**) with bis(pinacolato)diboron (**3**)

In summary, we have developed a $NiCl_2$(dppe)-catalysed reaction for the hydroboration of styrene derivatives with B_2pin_2 in toluene/MeOH. The air- and moisture-stable and commercially available complex $NiCl_2$(dppe) effectively catalyses the hydroboration of styrene derivatives with high Markovnikov selectivity. The reactions proceed smoothly under very mild reaction conditions to afford the products in good-to-high yield. Further experimental and computational studies on the reaction mechanism are currently in progress.

This work was financially supported by JSPS KAKENHI Grant Number JP17K05805 in Grant-in-Aid for Scientific Research (C) from MEXT (Japan), and the Collaborative Research Program of the Institute for Chemical Research, Kyoto University (2019–25). T.H. thanks the Collaborative Research Projects of the Laboratory for Materials and Structures, Institute of Innovative Research, Tokyo Institute of Technology. The authors are grateful to Prof. Masaharu Nakamura and Dr. Katsuhiro Isozaki (Kyoto Univ.) for their kind help with the HRMS measurements.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials, 2nd revised, ed., Hall, D. G., Ed., Wiley- VCH: Weinheim, **2011**.

2 (a) D. Leonori and V. K. Aggarwal, *Acc. Chem. Res.*, **2014**, *47*, 3174. (b) D. Leonori and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, **2015**, *54*, 1082. (c) K. Fagnou and M. Lautens, *Chem. Rev.*, **2003**, *103*, 169. (d) N. Miyaura and A. Suzuki, *Chem. Rev.*, **1995**, *95*, 2457. (e) R. Jana, T. P. Pathak and M. S. Sigman, *Chem. Rev.*, **2011**, *111*, 1417.

3 For reviews on precious-metal-catalysed hydroboration reactions, see: (a) K. Burgess and M. J. Ohlmeyer, *Chem. Rev.*, **1991**, *91*, 1179. (b) I. Beletskaya and A. Pelter, *Tetrahedron*, **1997**, *53*, 4957. (c) C. M. Crudden and D. Edwards, *Eur. J. Org. Chem.*, **2003**, 4695. (d) A.-M. Carroll, T. P. O'Sullivan and P. J. Guiry, *Adv. Synth. Catal.*, **2005**, *347*, 609.

4 For reviews on first-row-transition-metal-catalysed hydroboration reactions, see: (e) J. A. Schiffner, K. Müther and

View Article Online
DOI: 10.1039/D0CC05240A

M. Oestreich, *Angew. Chem.*, *Int. Ed.*, **2010**, *49*, 1194. (f) J. A. Bull, *Angew. Chem.*, *Int. Ed.*, **2012**, *51*, 8930. (g) W. Fan, L. Li and G. Zhang, *J. Org. Chem.*, **2019**, 84, 5987.

5 For hydroboration reactions using Cu catalysts, see: (a) D. Noh, H. Chea, J. Ju and J. Yun, *Angew. Chem.*, *Int. Ed.*, **2009**, *48*, 6062. (b) R. Corberán, N. W. Mszar and A. H. Hoveyda, *Angew. Chem.*, *Int. Ed.*, **2011**, *50*, 7079. (c) Y. Wen, J. Xie, C. Deng and C. Li, *J. Org. Chem.*, **2015**, *80*, 4142. (d) H. Iwamoto, K. Kubota and H. Ito, *Chem. Commun*., **2016**, *52*, 5916. (e) H. A. Kerchner and J. Montgomery, *Org. Lett.*, **2016**, *18*, 5760. (f) Y. Xi and J. F. Hartwig, *J. Am. Chem. Soc.* **2016**, *138*, 6703.

6 For hydroboration reactions using Fe catalysts, see: (a) J. V. Obligacion and P. J. Chirik, *Org. Lett*., **2013**, *15*, 2680. (b) L. Zhang, D. Peng, X. Leng and Z. Huang, *Angew. Chem., Int. Ed.*, **2013**, *52*, 3676. (c) K.-N. T. Tseng, J. W. Kampf and N. K. Szymczak, *ACS Catal.*, **2015**, *5*, 411. (d) A. J. MacNair, C. R. P. Millet, G. S. Nichol, A. Ironmonger and S. P. Thomas, *ACS Catal.*, **2016**, *6*, 7217. (e) X. Chen, Z. Cheng and Z. Lu, *Org. Lett.*, **2017**, *19*, 969.

7 For hydroboration reactions using Co catalysts, see: (a) M. L. Scheuermann, E. J. Johnson and P. J. Chirik, *Org. Lett*., **2015**, *17*, 2716. (b) W. N. Palmer, T. Diao, I. Pappas and P. J. Chirik, *ACS Catal*., **2015**, *5*, 622. (c) S. W. Reilly, C. E. Webster, T. K. Hollis and H. U. Valle, *Dalton Trans.* **2016**, *45*, 2823. (d) J. Peng, J. H. Docherty, A. P. Dominey and S. P. Thomas, *Chem. Commun*., **2017**, *53*, 4726. (e) S. R. Tamang, D. Bedi, S. Shafiei-Haghighi, C. R. Smith, C. Crawford and M. Findlater, *Org. Lett.*, **2018**, *20*, 6695. (f) P. K. Verma, A. S. Sethulekshmi and K. Geetharani, *Org. Lett*., **2018**, *20*, 7840. (g) G. Zhang, J. Wu, S. Li, S. Cass and S. Zheng, *Org. Lett*., **2018**, *20*, 7893. (h) X. Chen, Z. Cheng and Z. Lu, *ACS Catal.*, **2019**, *9*, 4025.

8 For Markovnikov-selective hydroboration reactions using Ni catalysts, see: (a) E. E. Touney, R. Van Hoveln, C. T. Buttke, M. D. Freidberg, I. A. Guzei and J. M. Schomaker, *Organometallics*, **2016**, *35*, 3436. (b) G. Vijiaykumar, M. Bhunia and S. K. Mandal, *Dalton Trans.* **2019**, *48*, 5779. (c) T. Hashimoto, K. Shiota and Y. Yamaguchi, *Org. Lett.*, **2020**, *22,* 4033.

9 (a) E. Asano, Y. Hatayama, N. Kurisu, A. Ohtani, T. Hashimoto, Y. Kurihara, K. Ueda, S. Ishihara, H. Nagao and Y. Yamaguchi, *Dalton Trans.*, **2018**, *47*, 8003. (b) N. Kurisu, E. Asano, Y. Hatayama, Y. Kurihara, T. Hashimoto, K. Funatsu, K. Ueda and Y. Yamaguchi, *Eur. J. Inorg. Chem.*, **2019**, 126. (c) T. Hashimoto, K. Funatsu, A. Ohtani, E. Asano and Y. Yamaguchi, *Molecules*, **2019**, *24*, 2296.

10 (a) A. Bonet, C. Pubill-Ulldemolins, C. Bo, H. Gulyás and E. Fernández, *Angew. Chem., Int. Ed*., **2011**, *50*, 7158. (b) N. Miralles, J. Cid, A. B. Cuenca, J. J. Carbó and E. Fernández, *Chem. Commun*., **2015**, *51*, 1693.

11 (a) L.-J. Xiao, L. Cheng, W.-M. Feng, M.-L. Li, J.-H. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed*., **2018**, *57*, 461. (b) M. Gaydou, T. Moragas and F. Juliá-Hernández, R. Martin, *J. Am. Chem. Soc.* **2017**, *139*, 12161. (c) L. González-Sebastián, M. Flores-Alamo and J. J. García, *Organometallics*, **2012**, *31*, 8200.

12 J. Huang, W. Yan, C. Tan, W. Wu and H. Jiang, *Chem. Commun*., **2018**, *54*, 1770.

13 For details, see the ESI.

14 For examples of the isolation and characterisation of benzyl nickel species, see: (a) E. Carmona, J. M. Marín, M. Paneque and M. L. Poveda, *Organometallics* **1987**, *6*, 1757. (b) E. Carmona, M. Paneque and M. L. Poveda, *Polyhedron* **1989**, *8*, 285. (c) J. R. Ascenso, M. A. A. F. de C. T. Carrondo, A. R. Dias, P. T. Gomes, M. Fátima, M. Piedade, C. C. Romao, A. Revillon and I. Tkatchenko, *Polyhedron* **1989**, *8*, 2449. (d) I. Albers, E. Álvarez, J. Cámpora, C. M. Maya, P. Palma, L. J. Sánchez and E. Passaglia, *J. Organomet. Chem.* **2004**, *689*, 833.

15 An alternative reaction mechanism could be considered: $NiCl_2$(dppe) reacts with **3** and KOAc to generate Ni-B species. The following regioselective addition of Ni-B species to a styrene derivative affords the corresponding β-borylalkylnickel species. Protonation of the Ni-C bond in the β-borylalkylnickel species then produces the desired product. For details, see ref. 8c.

16 The choice of the alcohols is critical for the present reaction. The reaction using EtOH instead of MeOH proceeded very slowly (54% conversion) to give the targeted product in 48% yield. Moreover, *i*-PrOH furnished only 15% of the desired product, while *t*-BuOH did not afforded any product. For details, see the ESI.