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Bottleable $\text{NiCl}_2(\text{dppe})$ as a catalyst for the Markovnikov-selective hydroboration of styrenes with bis(pinacolato)diboron

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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 $\text{NiCl}_2(\text{dppe})$ (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

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

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.

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

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

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)	KOt-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 NiCl₂(PPh₃)₂ and NiCl₂(PCy₃)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, NiCl₂(dppe) showed the best performance, affording **4a** in 97% yield with high Markovnikov selectivity (entry 4). Using NiCl₂(dppe) as the catalyst, we then explored different bases. When NaOAc was used, the yield of **4a** decreased to 80% (entry 7). KOt-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 NiCl₂(dppe) also did not afford **4a** (entries 11 and 12).

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

Table 2 Hydroboration of styrene derivatives ^a

8b , 84%	8c , 89%	8d , 86%	8e , 73%
8f , 75%	8g , 53%	8h , 41% ^b	8i , 70%
8j , 63%	8k , 83%	8l , 88%	

^a Reaction conditions: **2a** (0.50 mmol), **3** (1.00 mmol), NiCl₂(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 NiCl₂(dppe).

siloxyl (**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% $\text{NiCl}_2(\text{dppe})$ 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 $\text{MeOD}-d^1$ 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

Scheme 2 Isotope-labelling experiment

and of previous reports,^{8a,11,12} we propose a possible reaction mechanism shown in Scheme 3. Initially, $\text{Ni}(0)$ species **A** is generated by the reduction of **3** with $\text{NiCl}_2(\text{dppe})$ in the presence of KOAc.^{8a,13} Subsequently, the oxidative addition of the O–H bond of MeOH to $\text{Ni}(0)$ species **A** affords methoxy $\text{Ni}(\text{II})$ 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

Scheme 3 Proposed reaction mechanism for $\text{NiCl}_2(\text{dppe})$ -catalysed Markovnikov-selective hydroboration of styrene derivatives (**2**) with bis(pinacolato)diboron (**3**)

hydroboration product **4** under concomitant regeneration of the active nickel (**0**) species **A**.^{15,16}

In summary, we have developed a $\text{NiCl}_2(\text{dppe})$ -catalysed reaction for the hydroboration of styrene derivatives with B_2pin_2 in toluene/MeOH. The air- and moisture-stable and commercially available complex $\text{NiCl}_2(\text{dppe})$ 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. Katsuhiko Isozaki (Kyoto Univ.) for their kind help with the HRMS measurements.

Conflicts of interest

There are no conflicts to declare.

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- 15 An alternative reaction mechanism could be considered: NiCl₂(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 -borylalkynickel species. Protonation of the Ni-C bond in the β -borylalkynickel 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 afford any product. For details, see the ESI.