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Nickel salt-catalyzed addition reaction of arylboronic acids to aromatic aldehydes

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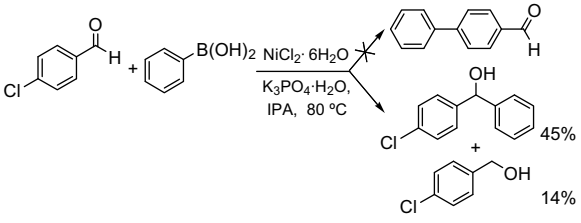
ABSTRACT

Arylation reaction of aromatic aldehydes with arylboronic acids proceeded smoothly in the presence of a base and catalytic amount of a nickel salt, $Ni(ClO_4)_2{\cdot}6H_2O$, in toluene/IPA = 5:1 or IPA to afford corresponding diarylmethanols in good to excellent yields.

Diarylmethanols are not only versatile intermediates in organic synthesis,[1] but are also important components in the construction of some molecules with biological activities.[2] Generally, diarylmethanols can be synthesized via the addition of aldehydes with organometallic reagents such as organolithium, organomagnesium, and organozinc compounds. In contrast to these frequently used organometallic reagents, organoboron reagents have been shown to be nontoxic and remarkably stable toward heat, oxygen, and moisture. Therefore, the use of organoboron reagents in the carbon–carbon bond formation reaction has recently attracted considerable attention.[3] In 1998, Miyaura and his co-workers reported the first example of a Rh(I)-catalyzed addition reaction of arylboronic acids to aldehydes.[4] Since then, several examples have been reported by other research groups.[5–7] A palladium-catalyzed addition reaction of arylboronic acids to aldehydes has also been studied.[8,9] To the best of our knowledge, the Ni-catalyzed addition reaction of arylboronic acids to aldehydes has not been reported so far even though the $Ni(cod)_2$-catalyzed addition reaction of organoboronates, trialkylboranes, and arylboroxines to aldehydes was reported by Shirakawa,[10] Yorimitsu and Oshima,[11] Kondo and Aoyama,[12] respectively. In the course of our study on the Ni-catalyzed coupling of aryl chlorides with arylboronic acids,[13] we observed that treatment of 4-chlorobenzaldehyde with phenylboronic acid in the presence of $NiCl_2{\cdot}6H_2O$ and $K_3PO_4{\cdot}H_2O$ in isopropanol (IPA) at 80 °C can bring about the addition of the phenylboron reagent to the aldehyde to produce the corresponding diarylmethanol in 45% yield along with 4-chlorobenzyl alcohol in 14% yield[14] without any cross-coupling product (Eq. 1). This observation prompted us to develop a nickel salt-catalyzed addition of arylboronic acids to aldehydes. Herein, our results are reported.



(1)

We first screened Ni sources with $K_3PO_4{\cdot}H_2O$ as a base in IPA as shown in Table 1. Among the Ni sources screened, only $Ni(ClO_4)_2{\cdot}6H_2O$ catalyzed this model addition reaction of benzaldehyde with phenylboronic acid to provide diphenylmethanol in satisfactory yield (73%, entry 3). The effect of bases and solvents on the nickel salt-catalyzed addition of arylboronic acids to aldehydes was then examined, and the results are shown in Table 2, which shows that $K_3PO_4{\cdot}H_2O$ and toluene/IPA = 5:1 were the best base and solvent, respectively (entry 12).

With $Ni(ClO_4)_2{\cdot}6H_2O$ as the catalyst, toluene/IPA = 5:1 as the solvent, and $K_3PO_4{\cdot}H_2O$ as the base, a number of aldehydes and arylboronic acids were examined, and the results are summarized in Table 3.[15] The reactions of benzaldehyde and 4-chlorobenzaldehyde with phenylboronic acid proceeded smoothly to give the corresponding diarylmethanols in high yields (89% and 90%, respectively, entries 1 and 2). Electron-rich aldehydes such as 4-methylbenzaldehyde and 4-methoxybenzaldehyde gave

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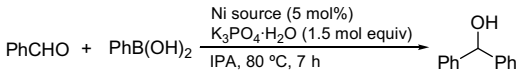
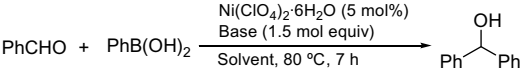
Table 1
Screening of Ni source[a]



Entry	Ni source	Yield[b] (%)
1	$NiCl_2·6H_2O$	43
2	$Ni(OAc)_2·4H_2O$	58
3	$Ni(ClO_4)_2·6H_2O$	73
4	$Ni(acac)_2·2H_2O$	0
5	$NiSO_4·6H_2O$	0

[a] The reactions were performed using benzaldehyde (0.5 mmol), 5 mol % of Ni source, and 1.5 mol equiv of $PhB(OH)_2$ and $K_3PO_4·H_2O$ in IPA (3 mL) at 80 °C for 7 h.
[b] Isolated yields.

Table 2
Effect of bases and solvents[a]



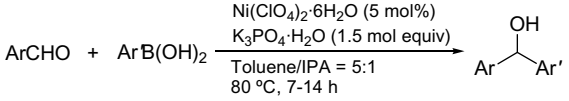
Entry	Base	Solvent	Yield[b] (%)
1	$K_3PO_4·H_2O$	IPA	73
2	KF	IPA	0
3	NaOH	IPA	0
4	K_2CO_3	IPA	8
5	K_3PO_4	IPA	5
6	$K_3PO_4·3H_2O$	IPA	7
7	$K_3PO_4·H_2O$	Toluene	54
8	$K_3PO_4·H_2O$	Dioxane	33
9	$K_3PO_4·H_2O$	CH_3CN	0
10	$K_3PO_4·H_2O$	DME	0
11	$K_3PO_4·H_2O$	EtOH	0
12[c]	$K_3PO_4·H_2O$	Toluene/IPA	89

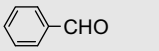
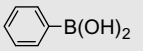
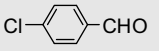
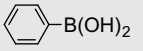
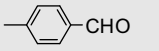
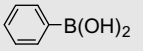
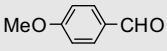
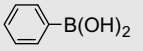
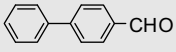
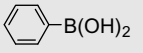
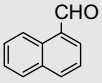
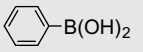
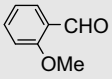
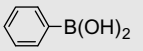
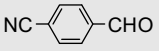
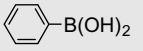
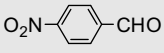
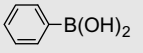
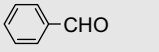
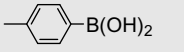
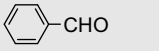
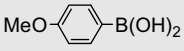
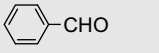
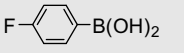
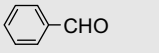
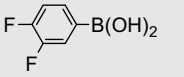
[a] The reactions were performed using benzaldehyde (0.5 mmol), 5 mol % of $Ni(ClO_4)_2·6H_2O$, and 1.5 mol equiv of $PhB(OH)_2$ and base in a solvent (3 mL) at 80 °C for 7 h.
[b] Isolated yields.
[c] The ratio of toluene to IPA is 5:1.

diarylmethanols in lower yields (35% and 62%, respectively, entries 3 and 4), but the yields were increased to 74% and 72% by using IPA as a solvent instead of the mixed solvent (toluene/IPA = 5:1). When two equivalents of phenyboronic acid were used in IPA, the addition products of 4-phenylbenzaldehyde and 1-naphthaldehyde were obtained in 89% and 75% yields (entries 5 and 6, respectively). Interestingly, the arylation of 2-methoxybenzaldehyde with phenylboronic acid proceeded smoothly in toluene/IPA = 5:1 to furnish the desired product in good yield (88%, entry 7). On the other hand, electron-deficient aldehydes such as 4-cyanobenzaldehyde and 4-nitrobenzaldehyde resulted in no reaction both in toluene/IPA = 5:1 and in IPA (entries 8 and 9). The electronic effect in arylboronic acids also showed a remarkable influence on the reaction; electron-rich arylboronic acids such as 4-methylphenylboronic acid and 4-methoxyphenylboronic acid gave moderate to good yields (80% and 72%, respectively, entries 10 and 11), but excellent yields were obtained from the reactions of electron-deficient arylboronic acids such as 4-fluorophenylboronic acid and 3,4-difluorophenylboronic acid with benzaldehyde (92% and 91%, respectively, entries 12 and 13).

In conclusion, we have found the first example of nucleophilic addition of arylboronic acids to aromatic aldehydes promoted by nickel catalyst. The reaction mechanism has not yet been clarified at present. However, it seems that the nickel salt, $Ni(ClO_4)_2·6H_2O$, plays a role of Lewis acid catalyst.

Table 3
Nickel salt-catalyzed arylation of aromatic aldehydes with arylboronic acids[a]



Entry	ArCHO	Ar′B(OH)$_2$	Yield[b] (%)
1			89
2			90
3			35 (74)[c]
4			62 (72)[c]
5			61 (89)[c,d]
6			54 (75)[c,d]
7			88
8			NR[e]
9			NR[e]
10			80
11			72
12			92
13			91

[a] The reactions were performed using aldehyde (0.5 mmol), 5 mol % of $Ni(ClO_4)_2·6H_2O$, and 1.5 mol equiv of Ar′B(OH)$_2$ and $K_3PO_4·H_2O$ in toluene/IPA (5:1, 3 mL) at 80 °C for 7–14 h.
[b] Isolated yields.
[c] The reactions were carried out in IPA.
[d] 2 Mol equiv of $PhB(OH)_2$ was used.
[e] No reaction occurred.

References and notes

1. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley and Sons: New York, 1991; (b) Kocienski, P. J. *Protective Groups*; Georg Thieme: New York, 1994.
2. (a) Meguro, K.; Aizawa, M.; Sohda, T.; Kawamatsu, Y.; Nagaoka, A. *Chem. Pharm. Bull.* **1985**, *33*, 3787; (b) Tada, F.; Tanaka, K.; Koshiro, K. *Tetrahedron: Asymmetry* **1991**, *2*, 873; (c) Botta, M.; Summa, V.; Corelli, F.; Pietro, G. D.; Lombardi, P. *Tetrahedron: Asymmetry* **1996**, *7*, 1263; (d) Artico, M.; Stefancich, G.; Silvestri, R.; Massa, S.; Apuzzo, G. *Eur. J. Med. Chem.* **1997**, *27*, 693; (e) Seto, M.; Aramaki, Y.; Imoto, H.; Akikawa, K.; Oda, T.; Kanzaki, N.; Iizawa, Y.; Baba, M.; Shiraishi, M. *Chem. Pharm. Bull.* **2004**, *52*, 819.
3. For books. See: (a) Hall, D. G. *Boronic Acid*; WILEY-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2005; (b) de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; John Wiley & Sons: Weinheim, Germany, 2004; (c) Miyaura, N. Organoboron Compounds. In *Cross-Coupling Reactions*; Miyaura, N., Ed.; Topics in Current Chemistry; Springer, 2002; Vol. 219, p 11.
4. Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279.
5. Other Rh-catalyzed arylation of aromatic aldehydes with arylboronic acids: (a) Batey, R. A.; Thadani, A. N.; Smil, D. V. *Org. Lett.* **1999**, *1*, 1683; (b) Ueda, M.;

Miyaura, N. *J. Org. Chem.* **2000**, *65*, 4450; (c) Fürstner, A.; Krause, H. *Adv. Synth. Catal.* **2001**, *343*, 343; (d) Pourbaix, C.; Carreaux, F.; Carboni, B. *Org. Lett.* **2001**, *3*, 803–805; (e) Moreau, C.; Hague, C.; Weller, A. S.; Frost, C. G. *Tetrahedron Lett.* **2001**, *42*, 6957; (f) Imlinger, N.; Mayr, M.; Wang, D.; Wurst, K.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2004**, *346*, 1836; (g) Focken, T.; Rudolph, J.; Bolm, C. *Synthesis* **2005**, 429; (h) Son, S. U.; Kim, S. B.; Reingold, J. A.; Carpenter, G. B.; Sweigart, D. A. *J. Am. Chem. Soc.* **2005**, *127*, 12238; (i) Yiğit, M.; Özdemir, İ.; Çetinkaya, E.; Çetinkaya, B. *Heteroat. Chem.* **2005**, *16*, 461; (j) Suzuki, K.; Ishii, S.; Kondo, K.; Aoyama, T. *Synlett* **2006**, 648; (k) Suzuki, K.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, *8*, 1360; (l) Jagt, R. B. C.; Toullec, P. Y.; de Vries, J. G.; Feringa, B. L.; Minnaard, A. *J. Org. Biomol. Chem.* **2006**, *4*, 773; (m) Yan, C.; Zeng, X. M.; Zhang, W. F.; Luo, M. M. *J. Organomet. Chem.* **2006**, *691*, 3391; (n) Duan, H. F.; Xie, J. H.; Shi, W. J.; Zhang, Q.; Zhou, Q. L. *Org. Lett.* **2006**, *8*, 1479; (o) Özdemir, I.; Yiğit, M.; Çetinkaya, E.; Çetinkaya, B. *Heterocylcles* **2006**, *68*, 1371; (p) Kıhnçarslan, R.; Yiğit, M.; Özdemir, İ.; Çetinkaya, E.; Çetinkaya, B. *J. Heterocycl. Chem.* **2007**, *44*, 69; (q) Gois, P. M. P.; Trindade, A. F.; Veiros, L. F.; André, V.; Duarte, M. T.; Afonso, C. A. M.; Caddick, S.; Cloke, F. G. N. *Angew. Chem., Int. Ed.* **2007**, *46*, 5750.

6. Rh-catalyzed arylation of nitriles, ketones, and imines with arylboronic acids: (a) Ueura, K.; Miyamura, S.; Satoh, T.; Miura, M. *J. Organomet. Chem.* **2006**, *691*, 2821; (b) Marelli, C.; Monti, C.; Gennari, C.; Piarulli, U. *Synlett* **2007**, 2213; (c) Duan, H.-F.; Xie, J.-H.; Qiao, X.-C.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2008**, *47*, 4351; (d) Trincado, M.; Ellman, J. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 5623.
7. Rh-catalyzed 1,4-addition to α,β-unsaturated carbonyl compounds with arylboronic acids: For reviews, see: (a) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169; (b) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829; references see: (a) Itooka, R.; Iguchi, Y.; Miyaura, N. *J. Org. Chem.* **2003**, *68*, 6000; (b) Boiteau, J.-G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2003**, *68*, 9481; (c) Gini, F. G.; Minnaard, A. J. *Org. Lett.* **2005**, *7*, 5309; (d) Martina, S. L. X.; Minnaard, A. J.; Hessen, B.; Feringa, B. L. *Tetrahedron Lett.* **2005**, *46*, 7159; (e) Paquin, J.-F.; Stephenson, C. R. J.; Defieber, C.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 3821; (f) Yuan, W.-C.; Cun, L.-F.; Gong, L.-Z.; Mi, A.-Q.; Jiang, Y.-Z. *Tetrahedron Lett.* **2006**, *47*, 4979; (g) Trenkle, W. C.; Barkin, J. L.; Son, S. U.; Sweigart, D. A. *Organometallics* **2006**, *25*, 3548; (h) Zou, G.; Guo, J.; Wang, Z.; Huang, W.; Tang, J. *Dalton Trans.* **2007**, 3055; (i) Monti, C.; Gennari, C.; Piarulli, U. *Chem.-A Eur. J.* **2007**, *13*, 1547; (j) Feng, C.-G.; Wang, Z.-Q.; Shao, C.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2008**, *10*, 4101; (k) Morgan, B. P.; Smith, R. C. *J. Organomet. Chem.* **2008**, *693*, 11.
8. The Pd-catalyzed addition reaction of phenylboronic acid to 4-chlorobenzaldehyde was found as a side reaction: Gibson, S.; Foster, D. F.; Eastham, G. R.; Tooze, R. P.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 779.
9. (a) Yamamoto, T.; Ohta, T.; Ito, Y. *Org. Lett.* **2005**, *7*, 4153; (b) Suzuki, K.; Arao, T.; Ishii, S.; Maeda, Y.; Kondo, K.; Aoyama, T. *Tetrahedron Lett.* **2006**, *47*, 5789; (c) He, P.; Lu, Y.; Dong, C.-G.; Hu, Q.-S. *Org. Lett.* **2007**, *9*, 343; (d) He, P.; Lu, Y.; Hu, Q.-S. *Tetrahedron Lett.* **2007**, *48*, 5283; (e) Lin, S.; Lu, X. *J. Org. Chem.* **2007**, *72*, 9757; (f) Qin, C.; Wu, H.; Cheng, J.; Chen, X.; Liu, M.; Zhang, W.; Su, W.; Ding, J. *J. Org. Chem.* **2007**, *72*, 4102.
10. Takahashi, G.; Shirakawa, E.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2005**, 1459.
11. (a) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2005**, *7*, 4689; (b) Hirano, K.; Yorimitsu, H.; Oshima, K. *Adv. Synth. Catal.* **2006**, *348*, 1543.
12. Arao, T.; Kondo, K.; Aoyama, T. *Tetrahedron Lett.* **2007**, *48*, 4115.
13. Zhou, L.; Miao, Q.; He, R.; Feng, X.; Bao, M. *Tetrahedron Lett.* **2007**, *48*, 7899.
14. Hydrogen transfer reaction between IPA and aldehyde can occur in the presence of $NiCl_2$: (a) Le Page, M. D.; James, B. R. *Chem. Commun.* **2000**, 1647; (b) Le Page, M. D.; Poon, D.; James, B. R. *Chem. Ind.* **2003**, *89*, 61.
15. General procedure for the arylation of aromatic aldehydes with arylboronic acids: A mixture of aldehyde (0.5 mmol), arylboronic acid (0.75 mmol), $K_3PO_4{\cdot}H_2O$ (0.75 mmol), and $Ni(ClO_4)_2{\cdot}6H_2O$ (5 mol %, relative to aldehyde) in 3 mL of toluene/IPA = 5:1 was stirred at 80 °C under a nitrogen atmosphere for 7–14 h. The reaction progress was monitored by TLC, and aldehyde disappeared after 7–14 h. When the reaction completed, the mixture was cooled to room temperature, then was quenched with water and extracted with ethyl acetate. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by silica gel column (petroleum ether/ethyl acetate = 10:1 to 5:1) to give diarylmethanols in good to excellent yields.