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Nickel-Catalyzed Cross-Electrophile aryl–allyl Coupling: An Approach to Structurally Versatile Allyl substituted arylborate

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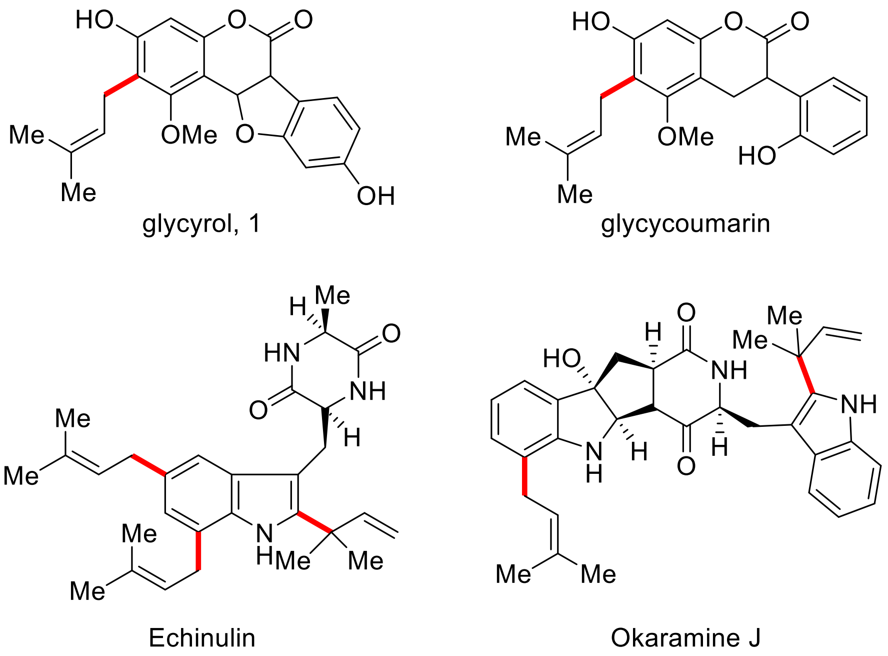
Abstract: The synthesis of allyl-substituted functional aryl compounds is one of the challenges existing in organic chemistry. Herein, we report a method for constructing allyl-substituted aryl boron compounds through nickel-catalyzed reductive allyl-aryl coupling between borylated aryl triflates and allyl alcohols. The method exhibits good substrate applicability under mild conditions. The synthetic utility of the method is highlighted by its gram-scale reaction, modification of complex molecules, and diverse transformation of the products.

Keywords: Nickel, boron, allyl alcohols, cross-coupling, reductive coupling

Introduction

Allyl aromatic hydrocarbons are widely found in natural products (**Scheme 1**), some of which are biologically and pharmacologically active[1,2].Among the active molecules, the introduction of allyl structures into the molecular structure can improve the bioactivity and bioavailability of natural product molecules, as the lipophilicity of allyl groups can increase the affinity for binding to proteins and the permeability of membranes[3,4]. Allyl groups, as active organic functional groups, contribute to the construction of structurally diverse aryl compounds[5,6]. At present, allylation of aryls is a commonly used method for the synthesis of allyl substituted aromatic compounds[7,8]. Traditional aryl-allylation reactions are accomplished through the coupling of aryl halides with allylic metals[9-11] or the allylation of aryl metals with allylic halides[12-15] (**Scheme 2a**), as well as the allylation of aryl electrophiles with allylic derivatives[16-18] (**Scheme 2b**). Although these reactions have good reactivity, the sensitivity of metal reagents to air or water limits the diversity of products.In addition, allyl derivatives need to be preactivated, which reduces the economic efficiency of the reaction. Therefore, developing a new strategy for efficiently constructing functionalised allyl-aryl molecular skeletons is an important research hotspot.


glycyrol, 1

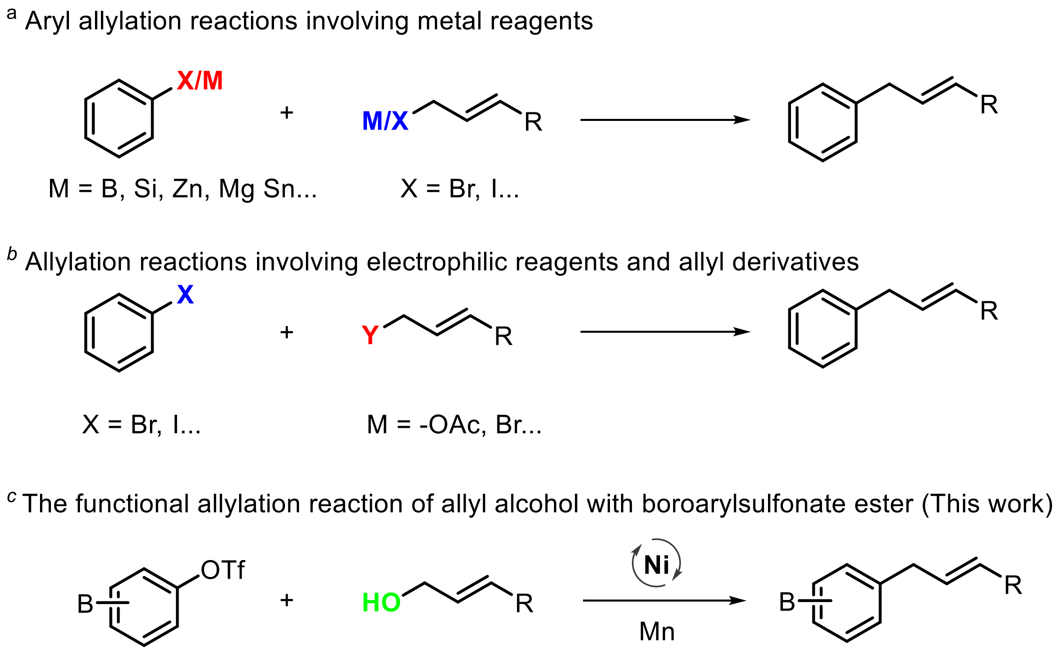
glycycoumarin

Echinulin

Okaramine J

Scheme 1 Prenylated natural products

In recent years, selective electrophilic cross-coupling has become an efficient method for constructing carbon-carbon bonds and has attracted considerable attention[19-21]. Compared with traditional nucleophilic cross-coupling reactions involving nucleophiles[22,23], electrophilic cross-coupling reactions overcome the shortcomings of traditional nucleophiles, which are sensitive to air or moisture. They feature inexpensive and abundant raw materials, simple and mild conditions, and rich product structures, and are widely used in organic synthesis[24-26]. Through a electrophilic cross-coupling strategy, chemical bonds such as C(sp3)-C(sp3)[27-31], C(sp2)-C(sp2)[32-34], and C(sp2)-C(sp3)[35-37] can be constructed, which have broad application value. In 2018, Shu's research group reported the co-catalysis of nickel and Lewis acids in the allylation of alkenols and aryl bromides[38], synthesising a series of allylated aromatic compounds with diverse molecular structures. This demonstrated the important application of the electrophilic cross-coupling strategy in allylation reactions and provided new insights into the allylation of aromatic compounds.


a Aryl allylation reactions involving metal reagents

b Allylation reactions involving electrophilic reagents and allyl derivatives

c The functional allylation reaction of allyl alcohol with boroarylsulfonate ester (This work)

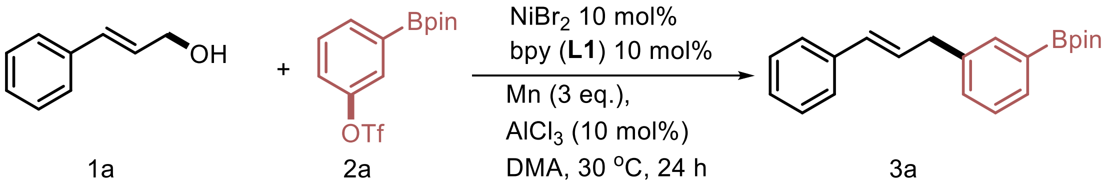
Scheme 2 Aryl allylation reaction

Arylboron reagents combine the characteristics of aromatic hydrocarbons and organoboron compounds, exhibiting broad applications in organic synthesis, materials chemistry, medicinal chemistry, and related fields[39-41]. Arylboron reagents serve as crucial precursors for the site-selective functionalization of aromatic rings and the synthesis of functionalized aryl compounds. The introduction of allyl groups at the meta-position of arylboron reagents is of significant importance for constructing structurally diverse pentenylated aromatic hydrocarbons[42,43]. We propose that the construction of allyl-substituted arylboron frameworks can be achieved through electrophilic coupling between pre-functionalized boron-containing aryl electrophiles derived from phenols and allyl alcohols (**Scheme 2c**). In this work, we demonstrate a convenient synthetic route for the one-step site-selective construction of allyl-substituted arylboron frameworks via a reductive coupling strategy, employing boron-containing aryl sulfonates as starting materials and allyl alcohols as allylating reagents, thereby enriching the structural diversity of pentenylated aromatic hydrocarbons.

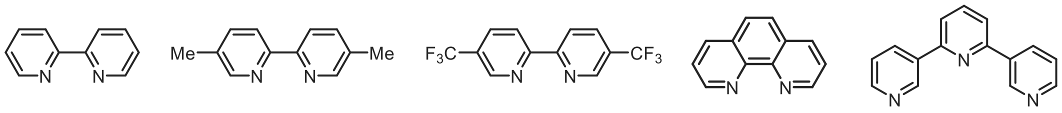
Results and discussion

The Shu group successfully achieved the cross-coupling of aryl bromides with allyl alcohols to synthesize allylated compounds via a nickel-catalyzed electrophilic cross-coupling strategy[38], demonstrating that Lewis acid-mediated activation of allyl alcohols enables the construction of allyl-substituted aromatic compounds.We recently achieved the coupling of boron-substituted bromoethylene with alkenyl sulfonates via a nickel-catalyzed double oxidative addition process, affording 1,3-conjugated alkenylboron compounds[44], thereby enabling the application of readily available sulfonate electrophiles in the synthesis of boron-containing compounds. Subsequently, we focused on a more challenging project: the cross-coupling of boron-substituted aryl sulfonates with allyl alcohols to synthesize allyl-substituted boron-containing aromatic hydrocarbons. We initiated our investigation by examining the reaction between cinnamyl alcohol (**1a**) and boron-substituted aryl sulfonate (**2a**) (Table 1). After extensive optimization, we identified the optimal reaction conditions as $NiBr_2$ (10 mol%), bpy (**L_1**, 10 mol%), Mn (3.0 equiv), $AlCl_3$ (10 mol%) in DMA solvent at 30°C, affording the target product in 82% isolated yield (Entry 1). While other nickel catalysts (Entry 2-4) also provided satisfactory yields, they proved slightly less effective than $NiBr_2$ .Bidentate ligands demonstrated high reaction yields (Entry 5-7), with electron-rich ligands exhibiting better performance than their electron-deficient counterparts.The use of terpyridine ligands resulted in diminished product yields.The reaction yield significantly decreased when Zn was employed as the reductant (Entry 10). No reaction was observed in the absence of either nickel catalyst or reducing agent.

Table 1. Optimization of the reaction conditions.[a]



Entry	Change from standard conditions	**3a** (%)
1	none	86(82)[b]
2	Ni(diglyme)Br_2 instead of $NiBr_2$	82
3	Ni(dme)Cl_2 instead of $NiBr_2$	76
4	$Ni(COD)_2$ instead of $NiBr_2$	72
5	**L2** instead of **L1**	81
6	**L3** instead of **L1**	26
7	**L4** instead of **L1**	68
8	**L5** instead of **L1**	32
10	Zn instead of Mn	21
11	no Ni or Mn	0

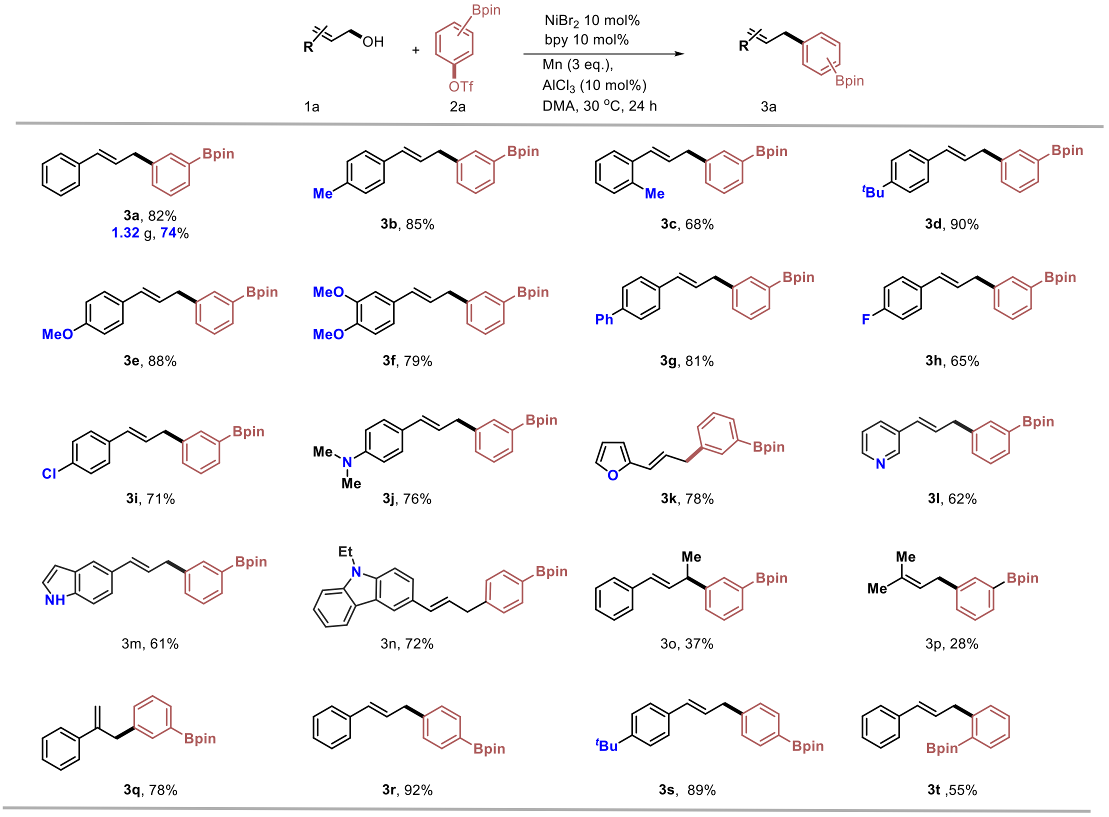


L1 **L2** **L3** **L4** **L5**

[a] **1a** (0.1mmol) and **2a** (1.5 equiv) were used.The yields were determined by GC analysis with dodecane as an internal standard.; [b] **2a** (0.2 mmol) was used, and isolated yield is given.

Aryl sulfonates exhibit superior reactivity compared to aryl bromides, along with easier accessibility, making them more suitable for constructing aryl allyl boron structural motifs. Consequently, under our optimized conditions, we expanded the structural diversity of allyl-substituted arylboron compounds. Given the widespread applications of meta-substituted aryl allyl moieties in bioactive molecules[45], we investigated the substrate scope of allyl alcohols using meta-boron-substituted aryl sulfonates. The target product was obtained in 82% isolated yield when cinnamyl alcohol was employed as the allylating reagent. We also conducted the reaction on a gram scale, achieving a yield of 74% (**3a**). Excellent yields were obtained when allyl alcohols bearing electron-donating groups on the aryl moiety were employed (**3b**-**3f**), while slightly diminished reactivity was observed with those containing electron-withdrawing substituents (**3h**-**3j**). The exclusive formation of linear products from branched allyl alcohols (**3f**, **3j**) suggests the involvement of π-allylnickel intermediates. Notably, allyl alcohols bearing extended conjugated systems afforded the product in 81% yield (**3g**). The reaction yield decreased when ortho-substituted allyl alcohols were employed (**3c**), indicating steric hindrance affects the reaction efficiency. Heterocyclic allyl alcohols, including furan (**3k**), pyridine (**3l**), indole (**3m**), and carbazole (**3n**) derivatives, also afforded good yields.Although the reaction yield with *α*-methyl substituted alcohol is relatively low, the substrate with phenyl substitution gave only the linear (*E*)-product(3o). Pentenylated aromatic hydrocarbons are present in numerous bioactive molecules, and their synthesis has been extensively investigated[46]. This structural motif could be constructed using isoprene diol, albeit with inferior reaction efficiency (**3p**). The reaction proceeded in 78% yield when β-methylenephenethyl alcohol was employed as the substrate (**3o**).Excellent yields were obtained with para-boron-substituted aryl sulfonates (**3r**, **3s**), while only moderate yields were achieved when ortho-boron-substituted aryl sulfonates were employed (**3t**).

Table 2. Scope of the reaction with allyl alcohol and borylated aryl triflates[a]

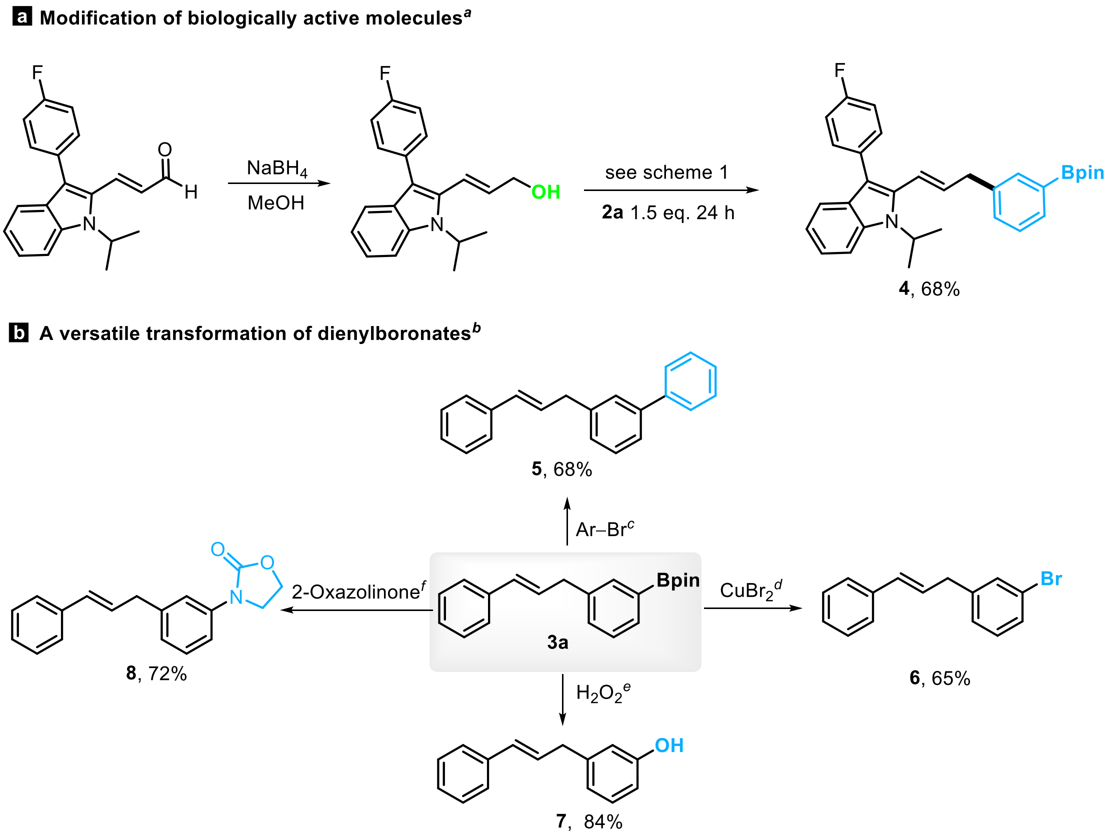


[a]Conditions as shown in Table 1, entry 1; borylated aryl triflates (0.3 mmol, 1.5 equiv) were used; isolated yields is given.

Application

The mild reaction conditions and the ubiquitous presence of allyl moieties in natural products render this method particularly suitable for the functionalization of structurally complex bioactive molecules.For instance, the allyl alcohol derived from a fluvastatin intermediate (a cholesterol-lowering drug) readily reacted with boron-substituted aryl sulfonates to afford the corresponding boron-functionalized aryl product(**4**). The diverse transformation scope of allyl-substituted arylboron compounds is illustrated in

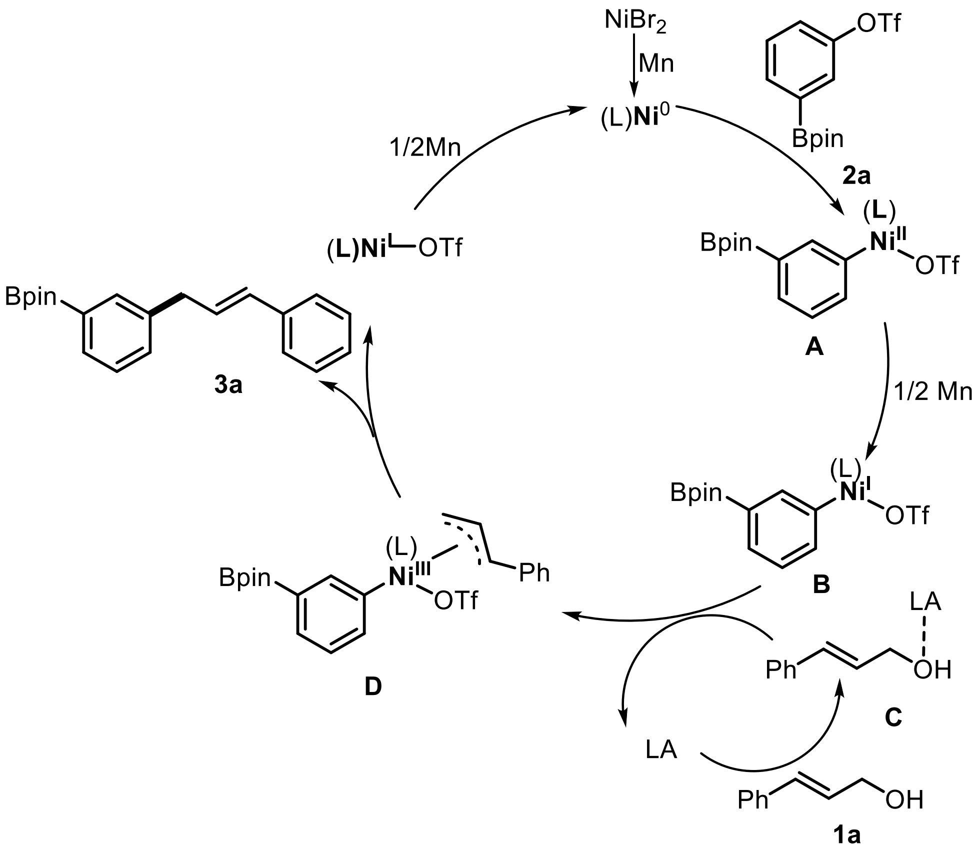
Scheme 3b. The arylboron moiety underwent Suzuki coupling with aryl bromides, as exemplified by the reaction of 3a with bromobenzene to afford allyl-substituted biphenyl compound (**5**) in 72% yield.Furthermore, the arylboronate esters could be transformed into various functional groups, including bromides (**6**) and phenols (**7**), which should significantly enhance the practical utility of this methodology in cross-coupling applications. Allyl-substituted arylboronates underwent Chan-Lam coupling with oxazoles.



Scheme 3. [a]Synthetic applications. aConditions as shown in Table 1, entry 1; isolated yields is given. [b]See Supporting Information for detailed conditions. [c]3a (0.2 mmol), ArBr (1.5 equiv), $Pd(PPh_3)_4$ (5 mol%), potassium carbonate (2 equiv, 0.4 mmol), DMF (1 mL), H_2O (50 ul), 80 °C. [d]3a (0.2 mmol), $CuBr_2$ (2

equiv), DMF/H_2O(1:1), 90 °C. [e]3a (0.2 mmol), H_2O_2 (1 equiv, 30% in H_2O), H_2O-EtOH(1:2), rt. [f]3a (0.2 mmol), 2-Oxazolinone (0.67 equiv), CuF_2 (5 mol%), DTBP(2 equiv), MeOH, rt.

Building upon previous studies[14], we propose our reaction mechanism. Manganese powder reduces Ni(II) to Ni(0). The boron-substituted aryl sulfonate first undergoes oxidative addition with Ni(0) to form the arylnickel(II) intermediate **A**, which is subsequently reduced by manganese powder to arylnickel(I) **B**. This intermediate then undergoes migratory insertion into the Lewis acid-activated allyl alcohol **C** to afford the arylnickel(III) intermediate **D**, followed by reductive elimination to yield the target product along with Ni(I)-OTf, which is reduced by manganese powder to re-enter the catalytic cycle.



Scheme 5. Proposed mechanism.

Conclusion

In summary, we have developed an efficient method for synthesizing allyl-substituted arylboron reagents through a nickel-catalyzed reductive coupling strategy between boron-substituted aryl sulfonates and allyl alcohols.This method exhibits broad substrate scope, excellent functional group tolerance, and compatibility with various heterocycles, significantly expanding the structural diversity of allyl-substituted aromatic compounds.The approach enables further transformations and derivatizations of allyl-substituted arylboron compounds, offering new possibilities for the structural modification of allylated aromatic systems.

Experimental

The procedure was conducted in an argon-filled glove box. To a reaction tube equipped with a magnetic stir bar was charged with $NiBr_2$ (4.4 mg, 10 mol%), bpy (3.1 mg, 7 mol%), $AlCl_3$ (2.7 mg, 10 mol%), Mn (33 mg, 3.0 equiv) and a solution of allyl alcohol **1** (0.2 mmol) and borylated aryl triflates **2** (0.3 mmol) in DMA (1.0 mL). and then were added solvent (0.5 mL). The reaction tube was sealed with a rubber septum, and removed from the glove box. The reaction mixture was stirred at 30 ^{o}C for 24 h. It was diluted with ethyl acetate (10 mL), washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated in vacuum. The residue was purified by flash chromatography on silica gel to afford the desired product **3**

Supporting Information

Supporting Information is available and includes parts of the detailed experimental procedures, characterization data, and copies of 1H and 13C NMR spectra for new compounds.

Conflict of Interest

There is no conflict of interest to report.

Acknowledgements

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References

1. Yang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.*, **2013**, *135*, 10642-10645. doi: 10.1021/ja405950c
2. Hu, Y.-C.; Min, X.-T.; Ji, D.-W.; Chen, Q.-A. *Trends Chem*. **2022**, 4, 658-675. doi: 10.1016/j.trechm.2022.04.004
3. Botta, B.; Monache, G. D.; Menendez, P.; Boffi, A. *Trends Pharmacol. Sci*. **2005**, *26*, 606-608. doi: 10.1016/j.tips.2005.09.012
4. Botta, B.; Vitali, A.; Menendez, P.; Misiti, D.; Monache, G. D.; *Curr. Med. Chem.* **2005**, *12*, 713-739. doi: 10.2174/0929867053202241
5. Mishra, N. K.; Sharma, S.; Park, J.; Han, S.; Kim, I. S. *ACS Catal*. **2017**, *7*, 2821-2847. doi: 10.1021/acscatal.7b00159
6. Tran, M.-K.; Ready, J. M. *Angew. Chem., Int. Ed.*, **2024**, *63*, e202407824. doi: 10.1002/anie.202407824
7. Yuan, C.; Zhang, W. *Org. Lett.* **2025**, *27*, 3877-3882. doi: 10.1021/acs.orglett.5c00584
8. Hu, A.-M.; Tu, J.-L.; Wang, K.; Yin, J.; Guo, L.; Yang C., Xia, W. *Org. Lett*. **2024**, *26*, 8572–8576. doi: 10.1021/acs.orglett.4c03188
9. Hamilton, J. Y.; Hauser, N.; Sarlah, D.; Carreira, E. M. *Angew. Chem. Int. Ed*. **2014**, *53*, 10759-10762. doi: 10.1002/anie.201406077
10. Yang, Y.; Mustard, T. J. L.; Cheong, P. H.-Y.; Buchwald, S. L. *Angew. Chem. Int. Ed*. **2013**, *52*, 14098-14102. doi: 10.1002/anie.201308585
11. Obora, Y.; Tsuji, Y.; Kobayashi, M.; Kawamura, T. *J. Org. Chem.* **1995**, *60*, 4647-4649. doi: 10.1021/jo00119a051
12. Wu, H.-B.; Ma, X.-T.; Tian, S.-K. *Chem. Commun.* **2014**, *50*, 219-221. doi: 10.1039/c3cc45772a
13. Yang, B.; Wang, Z.-X. *J. Org. Chem.*, **2017**, *82*, 4542-4549. doi: 10.1021/acs.joc.6b02564

14. Butt, N. A.; Zhang, W. *Chem. Soc. Rev.* **2015**, *44*, 7929-7967. doi: 10.1039/c5cs00144g

15. Gosmini, C.; Bégouin J.-M.; Moncomble, A. *Chem. Commun.*, **2008**, 3221-3233. doi: 10.1039/b805142a

16. Wang, S.; Qian, Q.; Gong, H. *Org. Lett.* **2012**, *14*, 3352-3355. doi: 10.1021/ol3013342

17. Anka-Lufford, L. L.; Prinsell, M. R.; Weix, D. J. *J. Org. Chem.* **2012**, *77*, 9989-10000. doi: 10.1021/jo302086g

18. Gomes, P.; Gosmini, C. Périchon, J. *J. Org. Chem.* **2003**, *68*, 1142-1145. doi: 10.1021/jo026421b

19. Everson, D. A.; Shrestha, R.; Weix, D. J. *J. Am. Chem. Soc*. **2010**, *132*, 920-921. doi: 10.1021/ja9093956

20. Han, G.-Y.; Su, P.-F.; Pan, Q.-Q.; Liu, X.-Y.; Shu, X.-Z. *Nat. Catal.* **2024**, *7*, 12-20. doi: 10.1038/s41929-023-01052-w

21. Kim, S.; Goldfogel, M. J.; Ahern, B. N.; Salgueiro, D. C.; Guzei, I. A.; Weix, D. J. *J. Am. Chem. Soc.*, **2025**, *147*, 2616–2625. doi: 10.1021/jacs.4c14769

22. Zhao, Z.-Z.; Guo, P.; Pang, X.; Shu, X.-Z. *Acc. Chem. Res.* **2024**, 57, 3356-3374. doi: 10.1021/acs.accounts.4c00614

23. Ehehalt, L. E.; Beleh, O. M.; Priest, I. C.; Mouat J. M.; Olszewski, A. K.; Ahern, B. N.; Cruz, A. R.; Chi, B. K.; Castro, A. J.; Kang, K.; Wang, J.; Weix, D. J. *Chem. Rev.* **2024**, *124*, 13397-13569. doi: 10.1021/acs.chemrev.4c00524

24. Goebel, J. F.; Löffler, J.; Zeng, Z.; Handelmann, J.; Hermann, A.; Rodstein, I.; Gensch, T.; Gessner, V. H.; Gooßen, L. J. *Angew. Chem. Int. Ed.* **2023**, *62,* e202216160. doi: 10.1002/anie.202216160

25. Chen, D.; Lepori, C.; Guillot, R.; Gil, R.; Bezzenine, S.; Hannedouche, J. *Angew. Chem. Int. Ed.* **2024**, *63*, e202408419. doi: 10.1002/anie.202408419

26. Mills, L. R. *Organometallics* **2025**, *44*, 858-865. doi: 10.1021/acs.organomet.5c00001

27. Xu, H.; Zhao, C.; Qian, Q.; Deng, W.; Gong, H. *Chem. Sci*. **2013**, *4, 4022-4029.* doi: 10.1039/c3sc51098k

28. Chen, H.; Jia, X.; Yu, Y.; Qian, Q.; Gong, H. *Angew. Chem., Chem. Int.* **2017**, 5*6, 13103–13106.* doi: 10.1002/anie.201705521

29. Yan, X.-B.; Li, C.-L.; Jin, W.-J.; Guo, P.; Shu, X.-Z. *Chem. Sci.* **2018**, *9,* 4529-4534. doi: 10.1039/c8sc00609a

30. Chen, R.; Intermaggio, N. E.; Xie, J.; Rossi-Ashton, J. A.; Gould, C. A.; Martin, R. T.; MacMillan, D. W. C. *Science*, **2024**, *383*, 1350-1357. doi: 10.1126/science.adl5890

31. Lyon, W. L.; Wang, J. Z.; Alcázar, J.; MacMillan, D.W.C. *J. Am. Chem. Soc*. **2025**, *147*, 2296−2302. doi: 10.1021/jacs.4c14965

32. Beng, T. K.; Sincavag, K.; Silaire, A. W. V.; Alwali, A.; Bassler, D. P.; Spence, L. E.; Beale, O. *Org. Biomol. Chem.* **2015**, *13*, 5349. doi: 10.1039/c5ob00517e

33. Ackerman, L. K. G.; Lovell, M. M.; Weix, D. J. *Nature*, **2015**, *524*, 454. doi: 10.1038/nature14676

34. Olivares, A. M.; Weix, D. J. *J. Am. Chem. Soc.* **2018**, *140*, 2446. doi: 10.1021/jacs.7b13601

35. He, R.-D.; Bai, Y.; Han, G.-Y.; Zhao, Z.-Z.; Pang, X.; Pan, X.; Liu, X.-Y.; and Shu, X.-Z. *Angew. Chem. Int. Ed.* **2022**, 61, e202114556. doi: 10.1002/anie.202114556

36. Dworkin, J. H.; Chen, Z. M.; Cheasty, K. C.; Rubio, A. V.; Kwon, O. *J. Am. Chem. Soc*. **2025**, 147, 13531-13544. doi: 10.1021/jacs.5c00540

37. Wu, T.; Castro, A. J.; Ganguli, K.; Rotella, M. E.; Ye, N.; Gallou, F.; Wu, B.; Weix, D. J. *J. Am. Chem. Soc.* **2025**, 147, 9449-9456. doi: 10.1021/jacs.4c16912

38. Jia, X.-G.; Guo, P.; Duan, J.; Shu, X.-Z. *Chem. Sci.* **2018**, 9, 640-645. doi: 10.1039/c7sc03140h

39. Peng, M.; Zhang, Y.; Wang, X.;Gao, H.; Tan, B. *Chem-asian J.* **2025**, 20, e202401463. doi: org/10.1002/asia.202401463

40. Gao, R.-R.; Chen, C.; Huang, Y.-B.; Wang, *X.-Y. Angew. Chem., Int. Ed.* **2025**, 64, e202500006. doi: 10.26434/chemrxiv-2024-js8z1

41. Liu, Y.; Deng, C.; Tang, L.; Qin, A; Hu, R.; Sun, J.-Z.; Tang, B.-Z. *J.Am. Chem. Soc.* **2011**, 133, 660–663. doi: 10.1021/ja107086y

42. Li, W. ; Chen, Y.; Yuan, R.; Jia, X.; Yao, Y.; Zhang, L. *Angew. Chem. Int. Ed.* **2025,** 64, e202500315. doi: 10.1002/anie.202500315

43. Liu, S.; Lu, Y.; Wang, H.; Xue, Z.; Xu, Z.; Wan, H.; Yin, Q.; Lv, T.; Liu, S.-X.; Jin, Y. *ACS Catal.* **2025**, 15, 4, 3306–3313. doi: 10.1021/acscatal.4c07252

44. Xu, G.-L.; Liu, C.-Y.; Pang, X; Liu, X.-Y.; Shu, X.-Z. *CCS. Chem.* **2022**, 4, 864-871. doi: 10.31635/ccschem.021.202100916

45. Farmer, J. L.; Hunter, H. N.; Organ M. G. *J. Am. Chem. Soc.* **2012**, *134*, 17470−17473. doi: 10.1021/ja308613b

46. Yang, Y.;Buchwald, S. L. *J. Am. Chem. Soc.* **2013**, 135, 29, 10642–10645. doi: 10.1021/ja405950c