CHEMISTRY
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Accepted Article

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To be cited as: *Chem. Eur. J.* 10.1002/chem.201904761

Link to VoR: http://dx.doi.org/10.1002/chem.201904761

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Transition Metal Free Synthesis of Heterobiaryls Through 1,2-Migration of Boronate Complex

Swagata Paul‡, Kanak Kanti Das‡, Samir Manna‡ and Santanu Panda*

Abstract: The synthesis of a diverse range of heterobiaryl has been achieved via a transition metal free sp^2-sp^2 cross coupling strategy using lithiated heterocycle, aryl or heteroaryl boronic ester and an electrophilic halogen source. The construction of heterobiaryls was carried out through electrophilic activation of the aryl-heteroaryl boronate complex which triggered 1,2-migration from boron to the carbon atom. Subsequent oxidation of the intermediate boronic ester afforded heterobiaryls in good yield. A comprehensive ^{11}B NMR study has been conducted to support the mechanism. The cross coupling between two nucleophilic cross coupling partners without transition metals reveals a reliable manifold to procure heterobiaryls in good yields. Various heterocycles like furan, thiophene, benzofuran, benzothiophene, and indole are well tolerated. Finally, we have successfully demonstrated the gram scale synthesis of the intermediates for anticancer drug and OLED material using our methodology.

The coupling of two aryl rings for the synthesis of biaryls is an important reaction and hence found applications in a myriad of syntheses and functionalization of bioactive molecules, natural products and useful materials.[1] Besides, biaryls and heterobiaryls are abundant in many marketed drugs[2] like recently approved drug for cancer rucaparib, raloxifene[3] (Scheme 1a), agrochemical products[4], and in light harvesting materials.[5] Transition metals have been extensively used for aryl-aryl cross coupling to access biaryls and heterobiaryls. One of the pioneering work is Suzuki coupling, which is a palladium catalyzed cross coupling reaction between aryl halide as an electrophilic coupling partner and organoboronate ester as a nucleophilic coupling partner (Scheme 1b).[6] Recent analysis of important methodologies applied in medicinal chemistry ranked Suzuki-Miyuara coupling after amide coupling.[7] Other well-documented cross coupling methods varying nucleophilic coupling partners are Stille coupling,[8] Negishi coupling,[9] Kumada coupling,[10] Hiyama-Denmark coupling,[11] and transition metal catalyzed C-H activation.[12] Similar to the Grignard reagents, Organolithiums are important reagents in organic synthesis.[13] Pioneering studies by Murahashi group demonstrated the palladium catalyzed cross coupling of organolithiums with vinyl halides.[14] Recently Feringa group reported cross coupling of aryl halide with organolithium reagents using palladium NHC based complex to access biaryls and heterobiaryls (Scheme 1b).[15] However, most of these current methods rely upon the cross coupling between an electrophilic and nucleophilic coupling partners. Therefore, the development of cross coupling using two nucleophilic coupling partners represent a more ideal approach.

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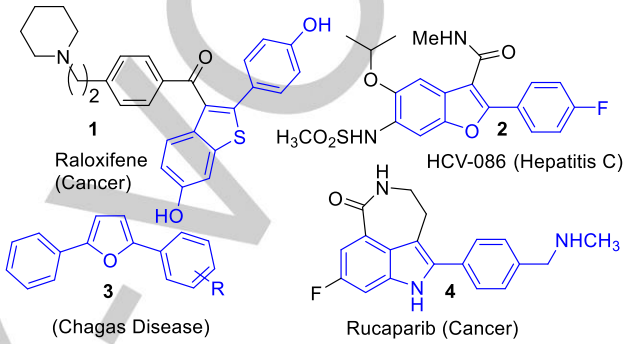
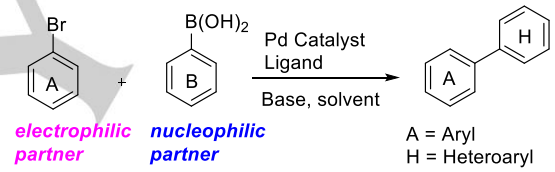
Supporting information for this article is given via a link at the end of the document.

Scheme 1. Synthesis & importance of heterobiaryls

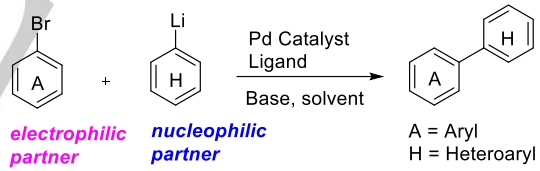
a. Heterobiaryls as a marketed drugs and bioactive compounds



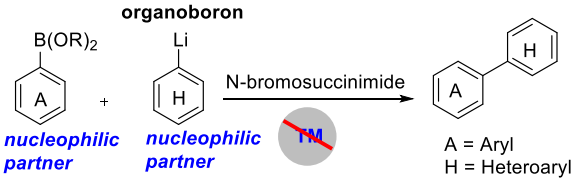
b. Suzuki coupling reaction for the synthesis of heterobiaryls



c. Murahashi-Feringa coupling using organolithium reagent



d. This work: Transition metal free coupling of organolithium and organoboron



√Coupling between two nucleophilic cross-coupling partner
√Synthesis of heterobiaryls without transition metal
√Broad scope, >40 heterobiaryls were synthesized
√Application in the gram scale synthesis of drugs intermediate

C-H arylation using aryl boron compounds was reported for the successful synthesis of biaryls.[16] However, such reactions were conducted in the presence of directing groups, transition metals and under drastic conditions[17]. In parallel with the biaryl synthesis using transition metal, there are reports without transition metals[18] for their benign toxicity, cost effectiveness, and simplicity. However, a transition metal free coupling of two nucleophilic partners for the synthesis of biaryls is rare. Hence, our group is interested to develop a novel transition metal free cross coupling between two nucleophilic

10.1002/chem.201904761

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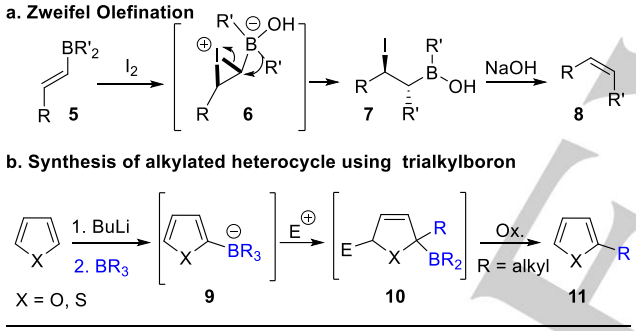
coupling partners, heteroaryl lithium and aryl boronic ester using a sacrificial electrophilic halogen source adopting the concept of 1,2-migration of boronate complex (Scheme 1c). There has been an immense interest in transition metal free C-C bond formation using 1,2-migration of boronate complexes.[19] The early example of this kind was developed by Matteson group, which is a one carbon homologation of boronic ester using lithiated dichloromethane.[20] Not only migration to the sp^3 carbon but also 1,2-migration to sp^2 carbon is equally attractive. In 1967, the Zweifel group demonstrated the 1,2-migration of vinyl boronate complex **6** in the presence of iodine (Scheme 2a).[21] In this process migration of the alkyl group from boron to carbon generates an intermediate alkyl boronic ester species **7**, which participated in an *anti*-boron-iodine elimination in presence of a base to furnish *Z*-alkene (Scheme 2a). Vinyl boronate complex can be activated by transition metal which was demonstrated by Ishikura,[22] Murakami,[23] Morken,[24] Ready[25] and others. After Zweifel's initial discovery, several groups emerged to developing C-C bond formation through 1,2-migration to the vinyl boronates.[26] Suzuki, Levy, and others applied this concept for the synthesis of C2 alkylated heterocycles using trialkylboron (Scheme 2b).[27] Recently, Aggarwal group revolutionize this approach for enantiospecefic synthesis of chiral heterocycles using chiral secondary and tertiary boronic ester.[28] However, this chemistry has never been explored using aryl boronic ester which will end up to heterobiaryls, considering its prevalence in marketed drug and bioactive compounds. An earlier approach using

Scheme 2. Previous work:Transition metal free 1,2-metalate shift

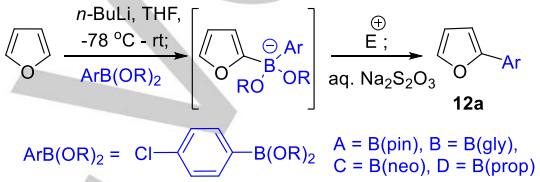


ethanolamine complexes of diorganylboron was mostly limited to dithinyl and suffered with practicality issues.[29] Herein we report a straight forward protocol for the synthesis of heterobiaryls starting from heteroaryls and aryl boronic esters. Apart from a huge substrate scope, we will demonstrate that our method can be applied for the formal synthesis of the anticancer drug Raloxifene, bioactive compound for Chagas diseases[30] and aryl thiophenes for OLED materials.[31]

We initiated our study for the synthesis of C2-aryl furan from lithiated furan, 4-chlorophenylboronic acid pinacol ester, and an electrophilic halogen source. We hypothesized that the reaction of lithiated furan (generated from the reaction of furan and *n*-BuLi) with boronic ester would generate a furan boronate complex. Mayr group recently reported that the furyl boronate complexes are much more nucleophilic compared to the parent boronate esters.[32] Electrophilic activation of furan boronate complex will either participate in aromatic electrophilic substitution (S_EAr) followed by 1,2-migration or drive towards unproductive *ipso* substitution. Among different electrophiles and oxidants tested for the activation of furan-boronate complex, NBS turns out to be ideal (Table 1, entry 3 vs 5 to 10). Also, Complete formation of boronate complex was important for optimal yield (entry 1 vs 2). Optimization of the lithiation condition using *n*-BuLi (0.7 M in hexane) improved the yield (entry 2 vs 3). For the final step, the 1,2-migration occurred at -78 °C in the presence of NBS. However, continuing the reaction with NBS at room temperature generated low yield due to undesired brominated products (entry 4). At this moment we have screened various diol protecting groups on the 4-chlorophenylboronic acid considering the difference in nucleophilicity parameters of corresponding boronatecomplexes reported by Mayr group.[33] However, we did not observe any improvement in yield using those boronic esters.

With optimized reaction conditions in hand, a broad spectrum of aromatic boronic esters were investigated. Both electron-donating and -withdrawing boronic esters were equally reactive (Scheme 3). Reactions of 4-Cl, 4-F and 4-CF_3 phenyl boronic esters afforded products (**12a**, **12d**, **12E**) in good yields. Coupling with halogen substitution provides an additional handle for Suzuki coupling with transition metals. Similarly, the aromatic boronic ester with electron donating groups (**12c, 12f**) coupled smoothly. In the case of 2-phenylfuran lower isolated yield was obtained due to the volatility of the product. In addition to the *para*-substituted aromatic boronic ester

Table 1. Optimization for the synthesis of C2-aryl furan [a]



Entry	Boronate Ester	Electrophile	Yield[b] (%)
1[c]	A	NBS	45
2[d]	A	NBS	67
3[e]	A	NBS	82
4[f]	A	NBS	75
5	A	NCS	61
6	A	NIS	< 10
7	A	Iodine	< 10
8	A	TCCA	< 10
9	A	DDQ	40
10	A	CAN	< 5
11	B	NBS	35
12	C	NBS	30
13	D	NBS	48

[a]*n*-BuLi(0.7 M in pentane,1.2 equiv) was added to Furan (1.2 equiv) in THF -78 °C, stirr -78 °C for 30 min then warm to rt for 30 min, $ArB(OR)_2$ (1 equiv) in THF was added at -78 °C and left stirring at -78 °C for 3h, electrophile or oxidant (1.2 equiv) in THF was added at -78 °C and left stirring at -78 °C for 1h, isolated yields.[c] Varrying lithiation and boron ate formation, *n*-BuLi at -78 °C then -78 °C for 10 min rt for 60 min, $ArB(OR)_2$ (1 equiv) in THF was added at -78 °C and left stirring at -78 °C for 1h, [d]*n*-BuLi at -78 °C then -78 °C for 10 min rt for 60 min, $ArB(OR)_2$ (1 equiv) in THF was added at -78 °C and left stirring at -78 °C for 3h, [e]Stirred for 3h at -78 °C after addition of NBS, [f]Stirred for 1h at -78 °C then rt for 2h after addition of NBS.

The reactivity was further extended to thiophene to access C2-arylthiophenes, which have been widely used in organic field-effect transistors, organic solar cells and organic light emitting diodes.[31a] Conducting reaction using the condition similar to furan yielded 50% of the desired 2-phenylthiophene. At this point, we decided to optimize this reaction. Out of all the electrophiles tested, NBS turned out to be optimal. Also, stirring boronate complex outside -78 °C for 10-12 minutes was hugely beneficial, considering complete conversion to the boronate complex which is essential for optimal yield. A range of aromatic and heteroaromatic boronic esters were accommodated under the optimized conditions. Substitution at *ortho*-, *meta*- and *para*-position of phenyl boronic esters were equally tolerated (Scheme 3). A diverse set of 2-aryl thiophenes were synthesized (**13a -13g**) in good yield. The moderate yield for the reaction using 4-cyanophenyl

10.1002/chem.201904761

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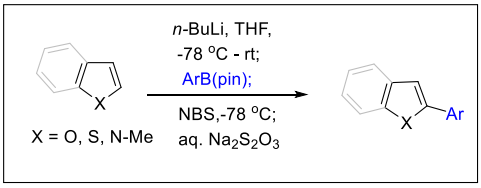
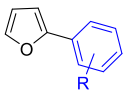
boronic ester was associated with the incomplete conversion under optimized condition. Notwithstanding, the reaction was tolerated with heteroaryl boronic ester to couple a furan with thiophene (Scheme 3, **12j**) or between two thiophene units (Scheme 3, **13j**).

In addition to furan and thiophene, we explored the reactivity with benzofuran and benzothiophene, which are prevalent in marketed drugs and bioactive compounds (Scheme 3).[33] Therefore, we examined the scope of this reaction with a variety of substituted aryl boronates under optimized reaction condition (see SI for details). Arylboronates containing electron withdrawing 4-Cl (**14b**, 89%), 4-CN (**14d**, 81%), and electron donating 4-OMe (**14c**, 86%) groups were coupled smoothly. It is noteworthy that the reaction was well tolerated

Scheme 3. Substrate scope for Heterobiaryls[a]



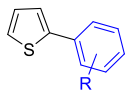
2-Aryl Furan[b]



Aryl Boronic Ester

R	Yield (%)
4-Cl (**12a**)	82
4-H (**12b**)	60
4-Me (**12c**)	77
4-F (**12d**)	68
4-CF_3 (**12e**)	62
3-OMe(**12f**)	80
3-Cl (**12g**)	65
3-Me (**12h**)	65
2-Me (**12i**)	68

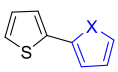
2-Aryl Thiophene[b]



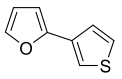
Aryl Boronic Ester

R	Yield (%)
4-Cl (**13a**)	70
H (**13b**)	76
4-Me (**13c**)	70
4-F (**13d**)	71
4-CN (**13e**)	50
4-OMe (**13f**)	56
3-Cl (**13g**)	68
3-Me (**13h**)	68
2-Me (**13i**)	62

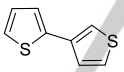
2-Heteroaryl Thiophene or furan[b]



Heteroaryl Boronic Ester

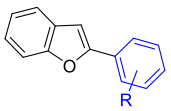


12j, 66%yield



13j, 65% yield

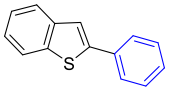
2-Aryl Benzofuran[c]



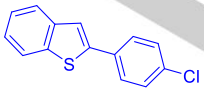
Aryl Boronic Ester

R	Yield (%)
H (**14a**)	83
4-Cl (**14b**)	89
4-OMe (**14c**)	86
4-CN (**14d**)	81
4-Me (**14e**)	92
3-Me (**14f**)	80
2-Me (**14g**)	82

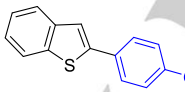
2-Aryl Benzothiophene[c]



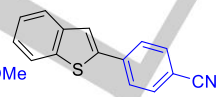
15a, 78% yield



15b, 85% yield



15c, 87% yield



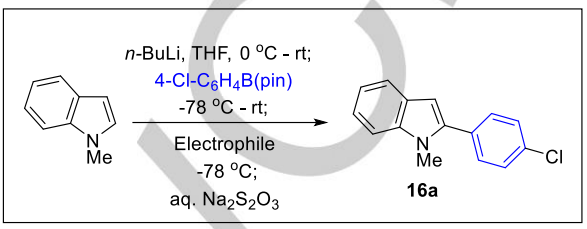
15d, 84% yield

[a]Isolated yield; [b]*n*-BuLi (1.2 equiv), Furan/Thiophene (1.2 equiv), RB(Pin) (1 equiv), NBS (1.2 equiv); [c]*n*-BuLi (1.6 equiv), Benzofuran/Benzothiophene (1.6 equiv), RB(Pin) (1 equiv), NBS (2 equiv).

with *ortho*-tolylboronic ester despite steric demand (**14g,** 82% yield). Subsequently, we examined the scope of aryl-benzothiophenes. The lithiated benzothiophenes were coupled smoothly with various aromatic boronic esters (Scheme 3, **15a**–**15d**) affording substituted 2-arylbenzothiophene over 80% isolated yield. The reaction was proved to be general for aryl boronic ester with both electron donating and electron withdrawing substituents.

The reactivity was further extended to the synthesis of C2-arylated indoles, an important skeleton present in natural products and bioactive compounds (Scheme 4).[34] Standard optimization varying the solvent and electrophiles revealed that NIS was superior compared to NBS or NCS and THF was a better solvent compared to acetonitrile or methanol (Scheme 4). We did not observe any reactivity using oxidizing agents like DDQ. With these optimized conditions in hand, we evaluated the scope of the aromatic boronic esters in conjunction with the indole. Pleasingly, several aryl boronic esters with various electronic property furnished the desired product in good yield. Variety of functional groups 4-OMe (**16c**), 4-Cl (**16a**), 4-CN (**16e**) and many others phenyl boronates (Scheme 4, **16a** – **16g**). Furthermore, various substitution at the indole nucleus was tolerated, namely 73% yield with 5-methoxylindole (**16h**), 75% yield with 4,7-dimethylindole (**16j**).

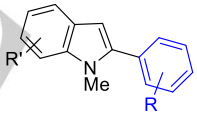
Scheme 4. Synthesis of C2-arylated indole[a]



Optimization Table

Entry	Electrophile	Solvent	Yield (%)
1	NBS	THF	< 5%
2	NBS	THF; MeOH	< 5%
3	NCS	THF	< 5%
4	NIS	THF	74
5	NIS	THF; MeOH	51
6	NIS	THF; CH_3CN	49
7	I_2	THF	< 5%
8	DDQ	THF	< 5%
9	CAN	THF	< 5%

Substrate Scope[b]



Aryl Boronic Ester

R	R'	Yield (%)
4-Cl (**16a**)	H	74
H (**16b**)	H	72
4-OMe (**16c**)	H	75[c]
4-Me (**16d**)	H	73
4-CN (**16e**)	H	80
4-F (**16f**)	H	70
3-Cl (**16g**)	H	75
3-OMe (**16h**)	H	72
3-Me (**16j**)	H	70
H (**16k**)	5-OMe	65
H (**16l**)	4,7-Me	66

[a]Isolated Yield; [b]*n*-BuLi (1.6 equiv), Indole (1.6 equiv), RB(Pin) (1 equiv), NIS (2 equiv); [e]Reaction using NCS instead of NIS.

Next, we explored the application of this methodology for the synthesis of intermediates **15e** for anticancer drug Raloxifene, bioactive compounds **12b** and light harvesting material **13h** (Scheme 5). Raloxifene, an approved drug for breast cancer constitutes a C2-arylbenzothiophene unit. Traditionally **15e** was synthesized by Suzuki coupling of 4-OMe-phenylboronic ester and 6-OMe-2-Br-benzothiophene.[35] However, we can able to synthesize the same intermediate in one pot using 6-OMe-benzothiophene and 4-OMe-phenylboronic ester using NBS (Scheme 5a). Using our method gram scale synthesis of the intermediate **15e** was achieved without transition metal over 80% yield. Next, we have applied this method for the synthesis of **12b** in 60% yield which can be further converted to the bioactive compounds for Chagas diseases (Scheme 5b).[30]

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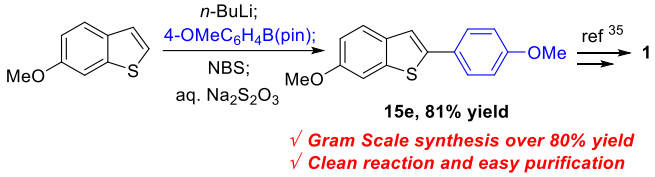
The application of this method was furthermore explored for the synthesis of **13h**, an intermediate for the synthesis of conjugated polymer for optoelectronics (Scheme 5a). Previously this compound was synthesized by Stille coupling by reacting tributyl(thiophen-2-yl) stannane with *meta*-bromotoluene.[36] However, one pot synthesis of this compound was achieved using our methodology from lithiatedthiophene and 3-methyl-phenylboronate. Organolithiums are important coupling partner which generates lithium bromide as a byproduct compared to the toxic tin reagents in Stille coupling. A number of aryl-thiophenes are present in conducting polymer to light harvesting materials,[37] which can be accessed using our methodology.

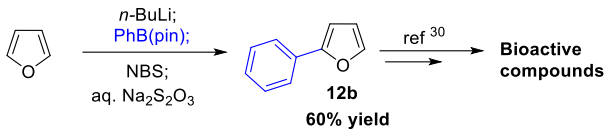
Scheme 5: Synthetic applicability

a. Synthesis of Raloxifene (breast cancer drug)

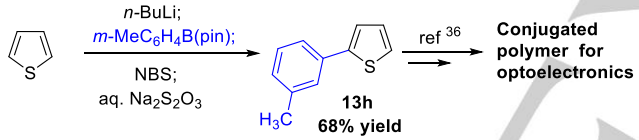


√ *Gram Scale synthesis over 80% yield*
√ *Clean reaction and easy purification*

b. Synthesis of bioactive compounds for Chagas diseases

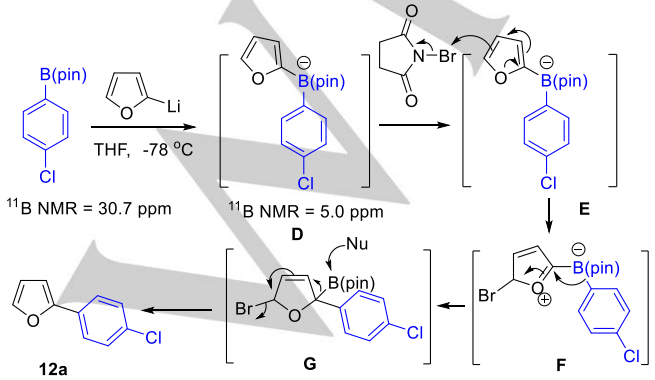


c. Synthesis of OLED materials



A tentative mechanism for this reaction is proposed based on the seminal works of Suzuki [27] and Aggarwal group.[28] We have conducted ^{11}B-NMR study to support the mechanism for this reaction (Scheme 6). The formation of boronate complex **D** after the addition of lithiated furan to the 4-chlorophenyl boronic ester was determined from the upfield shift in ^{11}B NMR (30.7 ppm to 5 ppm). The electrophilic activation of the intermediate **D** with NBS should allow 1,2-migration to generate intermediate **G**. The intermediate **G** is very unstable. After several attempt, we observed an downfiled shift in the ^{11}B NMR from 5 ppm to 30.16 ppm, which may be correspond to the intermediate **G**. In the rearomatization step, the nucleophile attacks the boronic ester in the intermediate G, followed by elimination of bromine and boronic ester from intermediate **G** afforded **12a**.

Scheme 6. Plausible Reaction Mechanism by ^{11}B NMR



In conclusion, we have developed a one pot, transition metal free cross coupling between two nucleophilic partner for the synthesis of heterobiaryls. The concept of 1,2-migration from boronate complex using cheap electrophilic halide source like NBS, reduces the cost for the synthesis of such valuable heterobiaryls. Diverse range of heterbiaryls were synthesized in good yield and applied to the gram scale synthesis of bioactive compounds, which will be immensely useful for future drug discovery. In future we will expand the scope of this reaction for the synthesis of sp^2-sp bonds.

Acknowledgements

This work was supported by DST-Ramanujan fellowship (SB/S2/RJN-171/2017) and IIT Kharagpur ISIRD grants. SP & KKD thanks IIT Kharagpur for fellowship and SM thanks CSIR India for fellowship. We extend our special thanks to MSM & AB group at IITKGP for their continuous support.

Keywords: heterobiaryl • heteroaryl • 1,2-migration • boronate ester • electrophile

Notes

The authors declare no competing financial interest

Author Contributions

‡These authors contributed equally

REFERENCES

[1] Yet, L. *Privileged structures in drug discovery*. 1st ed. Wiley, **2018**.
[2] M. Baumann, I. R. Baxendale, *Beilstein J. Org. Chem.* **2013**, *9*, 2265.
[3] P. J. Hajduk, M. Bures, Praestgaard, J.; Fesik, S. W. *J. Med. Chem.* **2000**, *43*, 3443.
[4] P. Devendar, R.-Y. Qu, W.-M. Kang, B. He, G.-F. Yang. *J. Agric. Food Chem.* **2018**, *66*, 8914.
[5] P. A. Kulkarni, J. C. Tonzola, A. Babel, A. S. Jenekhe, *Chem. Mater.* **2004**, *16*, 4556.
[6] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457.
[7] D. G. Brown, J. Boström, *J. Med. Chem.* **2016**, *59*, 4443.
[8] C. Cordovilla, C. Bartolomé, J. M. Martínez-Ilarduya, P. Espinet, *ACS Catal.* **2015**, *5*, 3040.
[9] D. Haas, J. M. Hammann, R. Greiner, P. Knochel *ACS Catal.* **2016**, *6*, 1540.
[10] T. Kohei, S. Koji, K. Makato *J. Am. Chem. Soc.* **1972**, *94*, 4374.
[11] Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc.* **2002**, *124*, 2102.
[12] M. Simonetti, D. M. Cannas, I. Larrosa, *In Advances in Organometallic Chemistry*, **2017**, *67*, 299.
[13] Z. Rappoport, I. Marek, *The chemistry of organolithium compounds part -1,* Wiley, **2004**.
[14] S.-I. Murahashi, M. Yamamura, K.-I. Yanagisawa, N. Mita, K. Kondo, *J. Org. Chem.* **1979**, *44*, 2408.
[15] (a) M. Giannerini, M. Fañ anas-Mastral, B. L. Feringa, *Nat. Chem.* **2013**, *5*, 667. (b) M. Giannerini, V. Hornillos, C. Vila, M. Fañanas-Mastral, B. L. Feringa, *Angew. Chem. Int. Ed.* **2013**, *52*, 13329.
[16] Engle, K. M.; Thuy-Boun, P. S.; Dang, M.; Yu J.-Q. *J. Am. Chem. Soc.* **2011**, *133, 18183.*
[17] Shi, Z.; Li, B.; Wan, X.; Cheng, J.; Fang, Z.; Cao, B.; Qin, C.; Wang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 5554
[18] (a) C.-L. Sun, Z.-J. Shi, *Chem. Rev.* **2014**, *114*, 9219. (b) M. C. Hilton, X. Zhang, B. T. Boyle, J. V. Alegre-Requena, R. S. Paton, A. McNally *Science* **2018**, *362*, 799.
[19] (a) S. Roscales, A. G. Csaky, *Chem. Soc. Rev.* **2014**, *43*, 8215. (b) V. K. Aggarwal, G. Y. Fang, X. Ginesta, D. M. Howells, M. Zaja, *Pure Appl. Chem.* **2006**, *78*, 215. (c) Z. He, F. Song, H. Sun, Y. Huang, *J. Am. Chem. Soc.* **2018**, *140*, 2693.
[20] D. S. Matteson, *J. Org. Chem.* **2013**, *78*, 10001.
[21] G. Zweifel, H. Arzoumanian, C. C. Whitney, *J. Am. Chem. Soc.* **1967**, *89*, 3652.

[22] (a) M. Ishikura, H. Kato, *Tetrahedron* **2002**, *58*, 9827. (b) M. Ishikura, W. Ida, K. Yanada, *Tetrahedron* **2006**, *62*, 1015.

[23] N. Ishida, Y. Shimamoto, M. Murakami, *Org. Lett.* **2010**, *12*, 3179.

[24] L. Zhang, G. J. Lovinger, E. K. Edelstein, A. A. Szymaniak, M. P. Chierchia, J. P. Morken, *Science* **2016**, *351*, 70.

[25] (a) S. Panda, J. M. Ready, *J. Am. Chem. Soc.* **2017**, *139*, 6038 (b) S. Panda, J. M. Ready, *J. Am. Chem. Soc.* **2018**, *140*, 13242.

[26] (a) D. A. Evans, R. C. Thomas, J. A. Walker, *Tetrahedron Lett.* **1976**,*17*, 1427. (b) A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, H. C. Brown, J. A. Sinclair, M. M. Midland, *J. Am. Chem. Soc.* **1973**, *95*, 3080. (c) R. J. Armstrong, V. K. Aggarwal, *Synthesis* **2017**, *49*, 3323.

[27] (a) I. Akimoto, A. Suzuki, *Synthesis* **1979**, *1979*, 146. (b) A. B. Levy, *J.*

[28] (a) A. Bonet, M. Odachowski, D. Leonori, S. Essafi, V. K. Aggarwal, *Nat Chem*. **2014**, *6*, 584. (b) M. Odachowski, A. Bonet, S. Essafi, P. Conti-Ramsden, J. N. Harvey, D. Leonori, V. K. Aggarwal, *J. Am. Chem. Soc.* **2016**, *138*, 9521.

[29] (a) G. M. Davies, P. S. Davies, W. E. Paget, J. M. Wardleworth, *Tetrahedron Lett.* **1976**, *17*, 795. (b) J. Kagan, S. K. Arora, *Tetrahedron Lett.* **1983**, *24*, 4043.

[30] A. P. Hartmann, M. R. de Carvalho, L. S. C. Bernardes, M. H. de Moraes, E. B. de Melo, C. D. Lopes, M. Steindel, J. S. da Silva, I. Carvalho, *Eur. J. Med. Chem*. **2017**, *140*, 187.

[31] (a) I. F. Perepichka, D. F. Perepichka, *Handbook of Thiophene-Based Materials: Applications in Organic Electronics and Photonics*, John Wiley & Sons, Ltd. **2009**. (b) Z. Duan, D. Hu, Ohuchi, M. Zhao, G. Zhao, Y. Nishioka, *Synthetic Metals* **2012**, *162*, 1292.

[32] G. Berionni, A. I. Leonov, P. Mayer, A. R. Ofial, H. Mayr, *Angew. Chem. Int. Ed.* **2015**, *54*, 2780.

[33] (a) A. Hiremathad, M. R. Patil, K. Chand, M. A. Santos, R. S. Keri, *RSC Adv.*, **2015**, *5*, 96809. (b) R. S. Keri, K. Chand, S. Budagampi, Somapa, S. B.; Patil, S. A.; Nagaraja, B. M. *Eur. J. Med. Chem*. **2017**, *138*, 1002.

[34] T. V. Sravanthi, S. L. Manju, *Eur. J. Pharm. Sci.* **2016**, *91*, 1.

[35] (a) T. A. Grese, S. Cho, D. R. Finley, A. G. Godfrey, C. D. Jones, C. W. Lugar, M. J. Martin, K. Matsumoto, L. D. Pennington, M. A. Winter, M. D. Adrian, H. W. Cole, D. E. Magee, D. L. Phillips, E. R. Rowley, L. L. Short, A. L. Glasebrook, H. U. Bryant, *J. Med. Chem.* **1997**, *40*, 146. (b) B. P. C. Umareddy, V. Arava, J. Chem. Pharm. Res., 2017, 9, 106.

[36] K. Amoto, T. Tominaga, *Light emitting element*. JP2008306170 (A) (**2008**).

[37] F. Zhang, D. Wu, Y. Xu, X. Feng, *J. Mater. Chem.* **2011**, *21*, 17590.

10.1002/chem.201904761

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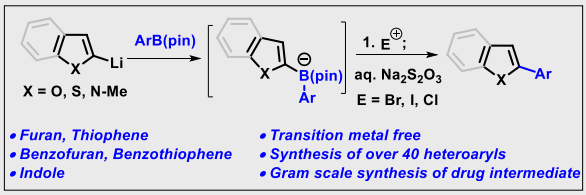

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