Tetrahedron 67 (2011) 6191–6196

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Facile synthesis of arylboronic esters by palladacycle-catalyzed bromination of 2-arylbenzoxazoles and subsequent borylation of the brominated products

Yuting Leng, Fan Yang *, Weiguo Zhu, Dapeng Zou, Yangjie Wu *, Ranran Cai

Chemistry Department, Henan Key Laboratory of Chemical Biology and Organic Chemistry, Key Laboratory of Applied Chemistry of Henan Universities, Zhengzhou University, Zhengzhou 450052, People's Republic of China

ARTICLE INFO

Article history:
Received 7 May 2011
Received in revised form 10 June 2011
Accepted 21 June 2011
Available online 25 June 2011

Keywords:
Bromination
Borylation
Palladium catalysis
HMBC spectra

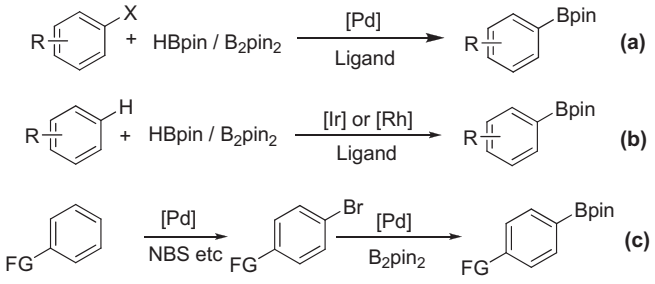
ABSTRACT

An efficient and facile synthesis of arylboronic esters bearing the benzoxazole moiety has been described using a new family of palladacycle: cyclopalladated ferrocenylimines as the catalysts. This reaction includes two concessive steps: bromination of 2-arylbenzoxazoles and subsequent borylation. The bromination of *para*-C–H bond was an electrophilic substitution process by using NBS as the brominating reagent, and the brominated products were determined by HMBC (^{1}H-detected heteronuclear multiple bond correlation) spectra. Particularly, the borylation step could be carried out successively only after removal of the solvent to afford the arylboronic esters in moderate to good yields.

1. Introduction

Transition-metal-catalyzed C–H bond functionalization has become a valuable synthetic tool for the selective oxidation of organic molecules.[1] Currently, remarkable progress has been made in the development of catalytic *C*-heteroatom bond forming reactions.[2] The halogenated arenes are extremely valuable starting materials for synthetic elaboration especially on the aspect of a variety of biologically active molecules and pharmaceutical agents.[3] Notably, Sanford and Yu developed the catalytic versions for directed C–H bond halogenation.[4,5] Wang reported a protocol for the bromination of arenes with NBS under $AuCl_3$ catalysis.[6] Very recently, Gaunt and co-workers reported a highly *para*-selective copper(II)-catalyzed direct arylation of aniline and phenol derivatives, which underwent a typically electrophilic substitution process.[7] Zhang also described palladium-catalyzed *para*-C–H aminations of anilides with *N*-fluorobenzenesulfonimide.[8] From these points of view, we consider it highly fascinating and desirable to apply this efficient *para*-C–H halogenation to the synthesis of arylboronic esters.

Arylboronic esters as a kind of versatile reagent are now widely used in organic synthesis.[9] They undergo metal-catalyzed cross-coupling reactions, 1,2- and 1,4-additions to carbonyl compounds, oxidative aminations, and additions to imines and iminiumions.[10] However, the classical preparation of arylboronic esters is often with the aid of stoichiometric organometallic reagents, such as magnesium or lithium alkyl reagents.[11] To overcome the limitation, two distinct approaches have been pursued by a number of groups. On the one hand, the pre-functionalized aryl halides could be utilized as starting materials under palladium catalysis (Scheme 1a).[12] On the other hand, several groups achieved the direct conversion of C–H bonds to C–B bonds catalyzed by Ir and Rh through selective C–H bond functionalization(Scheme 1b).[13] Our interests focused on the combined strategy of the aforementioned approaches by seeking for the possibility of developing a significant practical improvement over palladium-catalyzed C–H borylation (Scheme 1c).

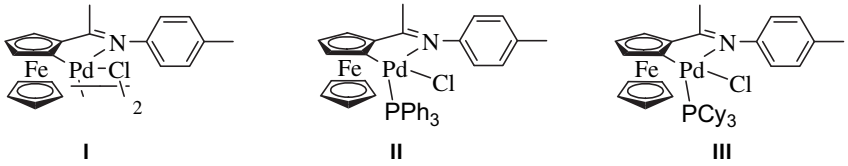


Scheme 1. Strategies for the synthesis of arylboronic esters.

* Corresponding authors. Fax: +86 371 6797 9408; e-mail addresses: yangf@zzu.edu.cn (F. Yang), wyj@zzu.edu.cn (Y. Wu).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.06.057

Cyclopalladated ferrocenylimines as a family of versatile palladacycle catalysts (Fig. 1), which were developed by our research group, have been applied to various reactions.[14] Herein we report for the first time the facile synthesis of arylboronic esters through catalytic *para*-bromination using NBS as a brominating reagent and following borylation of the new formed C–Br bond. The borylation step could be performed directly without any special treatments but removal of the solvent. It should be noted that this bromination of 2-arylbenzoxazoles was not the ligand-directed *ortho*-C–H activation process, but an electrophilic substitution at the *para*-position of the nitrogen atom in the benzene ring of benzoxazole, which could be determined by HMBC (^{1}H-detected heteronuclear multiple bond correlation) spectra.



I II III

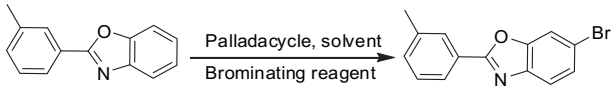
Fig. 1. Palladacycle **I**–**III**.

2. Result and discussion

In our initial study, we examined the effects on various catalysts, brominating reagents and solvents in the bromination of 2-(3-methylphenyl) benzoxazole. The results are summarized in Table 1. The reaction of 2-(3-methylphenyl) benzoxazole and NBS was carried out in the presence of $Pd(OAc)_2$ as the catalyst, and the bromination took place at the *para*-position of the nitrogen atom in the benzene ring of benzoxazole owing to its higher electronic cloud density (Table 1, entry 1). After screening the solvents, we found that the AcOH appeared to be the best choice (Table 1, entries 1–3). Then, different palladium catalysts were investigated (Table 1, entries 4–8), and palladacycle **I** as the catalyst gave the desired product in 89% yield (Table 1, entry 6). However, when the loading of catalyst or reaction temperature was reduced, low yields of products were isolated (Table 1, entries 9 and 10). Particularly, in the absence of the palladacycle catalyst, the reaction proceeded very slowly and only a low yield of 28% was observed (Table 1, entry 11). It indicated that the palladacycle indeed played an important role for the successful bromination. Finally, some other brominating reagents were also examined, but the results were not satisfactory (Table 1, entries 12–14).

Under the optimized conditions, the bromination of diverse 2-arylbenzoxazoles was examined to explore the scope of the reaction. Generally, the bromination of 2-arylbenzoxazoles is a classical electrophilic aromatic substitution at the *para*-position of the nitrogen atom in the benzene ring of benzoxazole affording the desired products in moderate to good yields, and the substituent effect has no significant influence on the reactions (Table 2). In this bromination, palladium species would act as the lewis acid catalyst. For the 2-arylbenzoxazoles bearing electron-donating groups, the desired products were isolated in high yields (Table 2, entries 1–3), and the bromination of the electron-neutral substrate also worked well at the *para*-position of nitrogen atom in benzene ring of benzoxazole with higher electronic cloud density (Table 2, entry 4). The reactions of 2-arylbenzoxazoles bearing electron-withdrawing groups also generated the products in satisfactory yields (Table 2, entries 5–11). Undoubtedly, all of the derived brominated products have at least one halogen atom and could be functionalized further to construct the complicated molecules.

Table 1
Effects of solvents, catalysts and brominating reagents on the bromination of 2-(3-methylphenyl)benzoxazole (**1a**)[a]

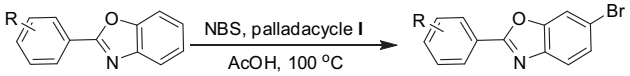


1a **2a**

Entry	Brominating reagent	Palladium source	T (°C)	Solvent	Yield (%)[b]
1	NBS	$Pd(OAc)_2$ (5 mol %)	Reflux	CH_3CN	19
2	NBS	$Pd(OAc)_2$ (5 mol %)	Reflux	DCE	22
3	NBS	$Pd(OAc)_2$ (5 mol %)	100	AcOH	67
4	NBS	$PdCl_2$ (5 mol %)	100	AcOH	36
5	NBS	$Pd_2(dba)_3$ (2.5 mol %)	100	AcOH	62
6	**NBS**	Palladacycle **I** (1 mol %)	**100**	**AcOH**	**89**
7	NBS	Palladacycle **II** (2 mol %)	100	AcOH	81
8	NBS	Palladacycle **III** (2 mol %)	100	AcOH	30
9	NBS	Palladacycle **I** (0.5 mol %)	100	AcOH	46
10	NBS	Palladacycle **I** (1 mol %)	50	AcOH	54
11	NBS	—	100	AcOH	28
12[c]	Br_2/PhI$(OAc)_2$	Palladacycle **I** (1 mol %)	100	AcOH	38
13	$CuBr_2$	Palladacycle **I** (1 mol %)	100	AcOH	20
14	Br_2	Palladacycle **I** (1 mol %)	100	AcOH	21

[a] Reaction conditions: **1a** (0.5 mmol), brominating reagent (0.75 mmol), solvent (2 mL), palladium catalyst, 8 h.
[b] Isolated yields based on **1a**.
[c] PhI$(OAc)_2$ (0.75 mmol).
Bold indicates the optimized conditions.

Table 2
Palladacycle-catalyzed the bromination of 2-arylbenzoxazoles with NBS[a]



1a-1k **2a-2k**

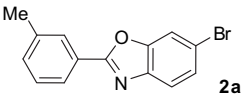
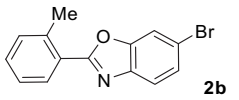
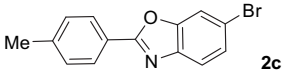
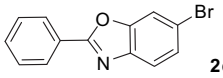
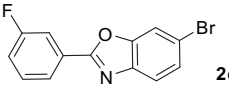
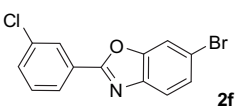
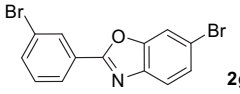
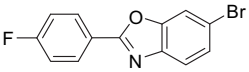
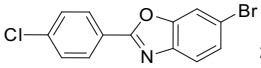
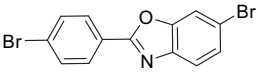
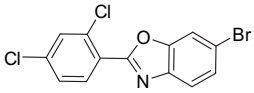
Entry	R	Product	Yield (%)[b]
1	*m*-Me	 **2a**	89
2	*o*-Me	 **2b**	86
3	*p*-Me	 **2c**	90
4	H	 **2d**	90
5	*m*-F	 **2e**	92
6	*m*-Cl	 **2f**	70

Table 2 (*continued*)

Entry	R	Product	Yield (%)[b]
7	*m*-Br	 **2g**	73
8	*p*-F	 **2h**	90
9	*p*-Cl	 **2i**	79
10	*p*-Br	 **2j**	75
11	*o*,*p*-Cl_2	 **2k**	66

[a] Reaction conditions: **1a**–**k** (0.5 mmol), NBS (0.75 mmol), palladacycle **I** (1 mol %), AcOH (2 mL), 100 °C, 8 h.
[b] Isolated yield.

The HMBC (^{1}H-detected heteronuclear multiple bond correlation) spectral data of the representative brominated product (**2a**) were utilized to confirm the assumption that the bromination took place at the *para*-position of nitrogen atom in the benzene ring of benzoxazole (Fig. 2).

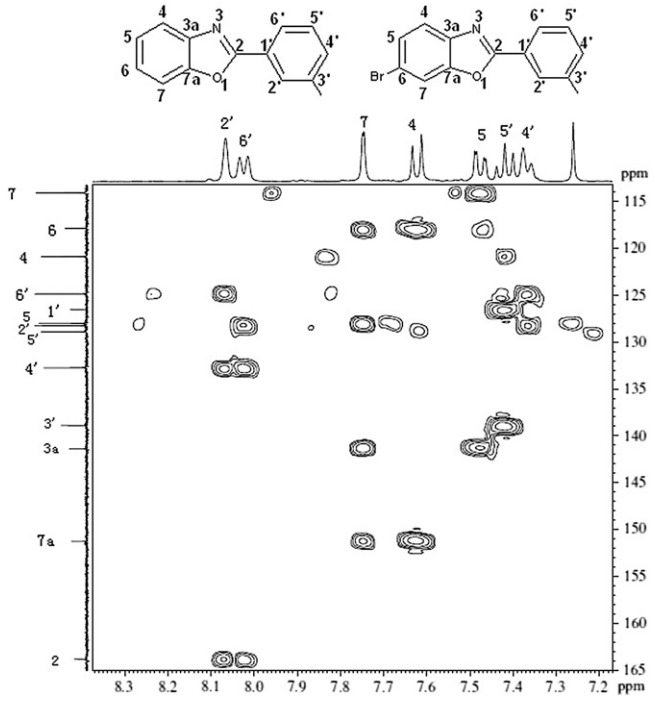


Fig. 2. HMBC spectrum of **2a**.

The HMBC spectral analysis of the 2-aryl benzoxazole containing a *meta*-substituent (**2a**) was outlined (Fig. 2). Initially, from ^{13}C NMR we could locate the position of the C**2** atom adjacent to N and O atoms with the lowest electronic cloud density, which is shifted to 163.7 ppm in the lower field. And the C**2** atom has two strong correlated H atoms (H**2′** and H**6′**), which indicates that both the H**2′** and H**6′** atoms still exist in the benzene ring and the bromination did not occur at the *ortho*-position of the directing group. Then, from ^{13}C NMR we could also assign the position of C**7a** bonded to the O atom and C**3a** adjacent to the N atom, which are located at 151.1 ppm in lower field and 141.3 ppm in a little higher field, respectively. From the HMBC spectrum, the C**7a** atom has one strong correlated H atom (H**4**) and one weak correlated atom (H**7**), and the C**3a** atom has two strong correlated H atoms (H**5** and H**7**). Given this, we could assign the position of H7 atom with the chemical shift of 7.60 ppm in the ^{1}H NMR spectrum. The coupling constant of the H**7** atom is 1.40 Hz in the ^{1}H NMR spectrum, which indicates that there is no H atom at the *ortho*-position of the C**7**–H**7** bond. Thus, the bromination should take place at the C**6**–H**6** bond.

Subsequently, we pursued the Suzuki–Miyaura/borylation of the obtained brominated products. The following borylation turned out to be compatible with the palladium-catalyzed halogenation conditions. In the typical procedure, the 2-arylbenzoxazoles were first converted into the corresponding brominated products. After the completion of bromination, the solvent was evaporated and the crude products were directly subjected to the following borylation couplings. The results of this palladacycle-catalyzed borylation of brominated 2-arylbenzoxazoles were summarized in Table 3. The reactions proceeded smoothly to afford the borylated products with moderate to good yields. The electronic effect has no influence on the borylation, and both electron-poor and electron-rich functional groups could be tolerated in these couplings. Notably, when the substrates possessed other halogen atoms, such as F, Cl, the borylation would chemoselectively occurr on the C–Br bond.

3. Conclusion

In summary, we have developed an efficient protocol for palladacycle-catalyzed direct bromination of 2-arylbenzoxazoles with NBS through an electrophilic substitution process, and the bromination took place at the *para*-position of the nitrogen atom in benzene ring of benzoxazole. Moreover, as demonstrated by Suzuki borylation, the reactions allow the combination of bromination of C–H bonds and subsequent borylation in an efficient manner. The borylated products would be applied to traditional Pd(0)/Pd(II) coupling reactions to afford the complicated π-conjugated systems with benzoxazoles moieties.

4. Experimental section

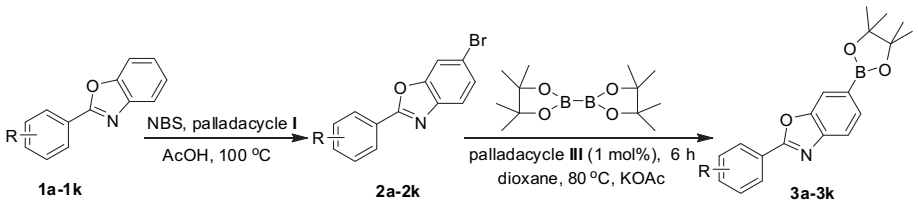
4.1. General

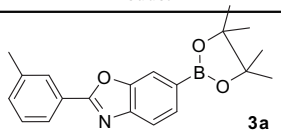
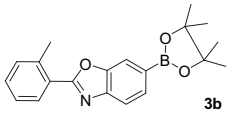
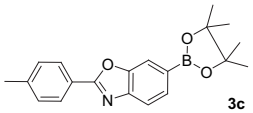
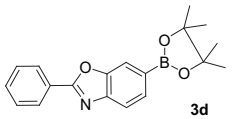
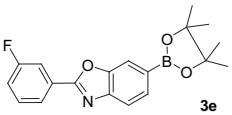
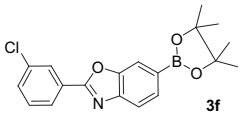
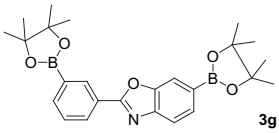
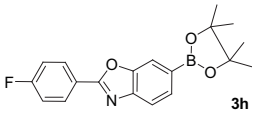
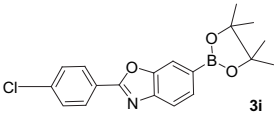
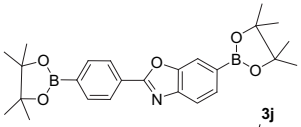
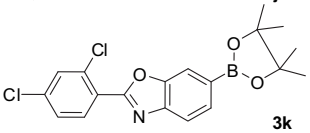
^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H COSY NMR, ^{1}H–^{13}C HSQC NMR, ^{1}H–^{13}C HMBC NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard. Melting points were measured using a WC-1 microscopic apparatus and are uncorrected. GC analysis was performed on Agilent 4890D gas chromatograph. Mass spectra were measured on an LC-MSD-Trap-XCT instrument. High-resolution mass spectra were measured on a MALDI-FTMS. Elemental analyses were determined with a Carlo Erba elemental analyzer. Dichloromethane, ethyl acetate and hexane (analytical grade) were used for column chromatography without further purification. Other solvents were purified according to the standard methods. All the 2-arylbenzoxazoles were prepared according to the previously published procedures.[15] The other chemicals were obtained from commercial sources and used as-received unless otherwise noted.

4.2. General procedure for direct bromination

Substrate (0.5 mmol), brominating reagent (0.75 mmol) and palladacycle **I** (1 mol %) were dissolved in AcOH (2 mL) in a 10 ml vial under air and heated at a specific temperature for 8 h. After the

Table 3
Palladacycle-catalyzed bromination and subsequent borylation of 2-arylbenzoxazoles[a]



Entry	R	Product	Yield (%)[b]
1	*m*-Me	 **3a**	70
2	*o*-Me	 **3b**	62
3	*p*-Me	 **3c**	56
4	H	 **3d**	73
5	*m*-F	 **3e**	81
6	*m*-Cl	 **3f**	52
7[c]	*m*-Br	 **3g**	73
8	*p*-F	 **3h**	89
9	*p*-Cl	 **3i**	77
10[c]	*p*-Br	 **3j**	70
11	*o*,*p*-Cl_2	 **3k**	68

[a] Reaction conditions: **1a**–**k** (0.5 mmol), NBS (0.75 mmol), palladacycle **I** (1 mol %), AcOH (2 mL), 100 °C; after the reaction was analyzed by TCL and GC, the solvent was evaporated in vacuo, the mixture of B_2pin_2 (0.6 mmol), KOAc (1 mmol), palladacycle **III** (1 mol %), 1,4-dioxane (2 mL) was added under N_2 and the reaction was carried out at 80 °C for 6 h.

[b] Isolated yields based on **1a**–**k**.

[c] B_2pin_2 (1.2 mmol).

reaction was complete, the mixture was diluted with CH_2Cl_2 (10 mL), filtered through a pad of Celite, and washed multiple times with CH_2Cl_2. The combined organic solutions were evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane) to give the pure product.

4.3. General procedure for bromination and borylation of the brominated products

Substrate **1** (0.5 mmol), brominating reagent (0.75 mmol) and palladacycle **I** (1 mol %) were dissolved in AcOH (2 mL) in a 10 mL vial under air and heated at a specific temperature. After the reaction was complete monitored by TCL and GC, the solvent was evaporated under reduced pressure and a mixture of B_2pin_2 (0.6 mmol), (1.2 mmol for Table 3, entries 7 and 10), KOAc (1 mmol), palladacycle **III** (1 mol %) and 1,4-dioxane (2 mL) was added under N_2. The reaction was carried out at 80 °C for 6 h, and then quenched with water. The mixture was diluted with ethyl acetate (10 mL), filtered through a pad of Celite, and followed by extraction with ethyl acetate for three times. The combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent in vacuum, the residue was purified by flash chromatography on silica gel (ethyl acetate/hexane) to give the pure product.

*4.3.1. 6-Bromo-2-(3-methylphenyl)benzoxazole (**2a**).* White solid, mp 92–93 °C, yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.45 (s, 3H), 7.34–7.47 (m, 3H), 7.61 (d, J=8.4 Hz, 1H), 7.73 (s, 1H), 8.01 (d, J=3.6 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.7, 151.2, 141.3, 138.8, 132.7, 128.9, 128.2, 128.0, 126.5, 124.8, 120.9, 117.9, 114.1, 21.4; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{11}BrNO$: 288.0024; found 288.0022.

*4.3.2. 6-Bromo-2-(2-methylphenyl)benzoxazole (**2b**).* White solid, mp 91–92 °C, yield 86%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.80 (s, 3H), 7.38 (m, 4H), 7.65 (d, J=8.4 Hz, 1H), 7.75 (s, 1H), 8.15 (d, J=1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.8, 150.7, 141.3, 139.0, 131.9, 131.2, 129.9, 127.8, 126.1, 125.6, 121.0, 117.8, 114.0, 22.3; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{11}BrNO$: 288.0024; found 288.0019.

*4.3.3. 6-Bromo-2-(4-methylphenyl)benzoxazole (**2c**).* White solid, mp 121–123 °C, yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.43 (s, 3H), 7.25–7.31 (m, 2H), 7.43 (dd, J=1.7 Hz, 8.4 Hz, 1H), 7.58 (d, J=8.4 Hz, 1H), 7.70 (s, 1H), 8.08 (d, J=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.7, 151.1, 142.4, 141.3, 129.7, 129.7, 129.6, 127.9, 127.6, 123.8, 120.7, 117.6, 114.0, 21.7; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{11}BrNO$: 288.0024; found 288.0023.

*4.3.4. 6-Bromo-2-phenylbenzoxazole (**2d**)*[16]. White solid, mp 89–91 °C, yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.27–7.54 (m, 4H), 7.60–7.62 (m, 1H), 7.72 (s, 1H), 8.21 (d, J=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.5, 151.2, 141.3, 131.8, 128.9, 128.0, 127.7, 126.6, 120.9, 117.9, 114.1.

*4.3.5. 6-Bromo-2-(3-fluorophenyl)benzoxazole (**2e**).* White solid, mp 107–108 °C, yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24–7.28 (m, 1H), 7.49–7.52 (m, 2H), 7.63–7.65 (m, 1H), 7.75–7.76 (m, 1H), 7.91–7.93 (m, 1H), 8.01–8.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.9 (d, J=245.7 Hz), 162.2 (d, J=3.2 Hz), 151.2, 141.1, 130.7 (d, J=8.0 Hz), 128.3, 123.4 (d, J=3.1 Hz), 121.1, 118.8 (d, J=21.2 Hz), 118.4, 114.6 (d, J=24.0 Hz), 114.2; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_7BrFN$: 291.9773; found 291.9773.

*4.3.6. 6-Bromo-2-(3-chlorophenyl)benzoxazole (**2f**).* White solid, mp 112–114 °C, yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.43–7.52 (m, 3H), 7.61 (d, J=8.4 Hz, 1H), 7.73 (s, 1H), 8.09 (d, J=7.6 Hz, 1H), 8.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.1, 151.2, 141.1, 135.1, 131.8, 130.3, 128.3, 128.3, 127.6, 125.7, 121.1, 118.4, 114.2; Anal. Calcd for $C_{13}H_7BrClNO$: C 50.60, H 2.29, N 4.54; found: C 50.60, H 2.33, N 4.40.

*4.3.7. 6-Bromo-2-(3-bromophenyl)benzoxazole (**2g**).* White solid, mp 129–131 °C, yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26–7.40 (m, 1H), 7.46–7.48 (m, 1H), 7.60–7.66 (m, 2H), 7.72 (s, 1H), 8.12 (d, J=7.8 Hz, 1H), 8.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=161.9, 151.1, 141.0, 134.7, 130.5, 130.4, 128.5, 128.3, 126.1, 123.0, 121.1, 118.4, 114.2; Anal. Calcd for $C_{13}H_7Br_2NO$: C 44.23, H 2.00, N 3.97; found: C 44.51, H 2.04, N 3.93.

*4.3.8. 6-Bromo-2-(4-fluorophenyl)benzoxazole (**2h**).* White solid, mp 123–124 °C, yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.17–7.27 (m, 2H), 7.44 (dd, J=1.7 Hz, 8.5 Hz, 1H), 7.58 (d, J=8.5 Hz, 1H), 7.70 (s, 1H), 8.17–8.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.9 (d, J=252.0 Hz), 162.6, 151.1, 141.2, 129.9 (d, J=8.9 Hz), 128.1, 122.9 (d, J=3.2 Hz), 120.8, 117.9, 116.1 (d, J=22.1 Hz), 116.2 (d, J=22.1 Hz), 114.0; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_7BrFNO$: 291.9773; found 291.9772.

*4.3.9. 6-Bromo-2-(4-chlorophenyl)benzoxazole (**2i**).* White solid, mp 146–148 °C, yield 79%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.45–7.49 (m, 3H), 7.59 (d, J=8.3 Hz, 1H), 7.71 (s, 1H), 8.11–8.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=114.1, 118.2, 121.0, 125.1, 128.2, 128.8, 128.9, 129.2, 129.3, 138.1, 141.2, 151.1, 162.5; Anal. Calcd for $C_{13}H_7BrClNO$: C 50.60, H 2.29, N 4.54; found: C 50.93, H 2.38, N 4.53.

*4.3.10. 6-Bromo-2-(4-bromophenyl)benzoxazole (**2j**).* White solid, mp 154–156 °C, yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26–7.48 (m, 1H), 7.60–7.66 (m, 3H), 7.72 (s, 1H), 8.05–8.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.6, 151.1, 141.2, 132.3, 129.0, 129.0, 128.2, 126.6, 125.5, 121.0, 118.3, 114.1; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_7Br_2NO$: 351.8972; found 351.8971.

*4.3.11. 6-Bromo-2-(2,4-dichlorophenyl)benzoxazole (**2k**).* White solid, mp 126–127 °C, yield 66%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38–7.51 (m, 2H), 7.58 (s, 1H), 7.67–7.70 (m, 1H), 7.77 (s, 1H), 8.08 (d, J=8.48 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=160.5, 150.9, 140.8, 137.9, 134.3, 132.5, 131.4, 128.3, 127.5, 124.2, 121.5, 118.8, 114.3; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_6BrCl_2NO$: 341.9088; found 341.9083.

*4.3.12. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(3-methylphenyl)benzoxazole (**3a**).* White solid, mp 74–75 °C, yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37 (s, 12H), 2.44 (s, 3H), 7.32–7.41 (m, 2H), 7.75–7.83 (m, 2H), 8.03–8.09 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.8, 150.3, 144.4, 138.4, 132.3, 130.7, 128.5, 128.0, 126.0, 124.6, 119.0, 116.4, 83.7, 24.7, 21.1; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{20}H_{23}BNO_3$: 336.1771; found 336.1770.

*4.3.13. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(2-methylphenyl)benzoxazole (**3b**).* White solid, mp 80–82 °C, yield 62%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.39 (s, 12H), 2.82 (s, 3H), 7.34–7.42 (m, 3H), 7.79–7.85 (m, 2H), 8.06 (s, 1H), 8.20–8.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.3, 150.2, 144.7, 139.0, 131.8, 131.1, 130.8, 130.1, 126.1, 126.1, 119.5, 116.6, 84.0, 24.9, 22.2; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{20}H_{23}BNO_3$: 336.1771; found 336.1766.

*4.3.14. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(4-methylphenyl)benzoxazole (**3c**).* White solid, mp 144–145 °C, yield 56%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.38 (s, 12H), 2.44 (s, 3H), 7.33 (d, J=8.1 Hz, 2H), 7.73–7.82 (m, 2H), 8.02 (s, 1H), 8.15–8.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.2, 150.6, 144.8, 142.2, 130.9,

129.6, 127.8, 124.3, 119.2, 116.5, 84.0, 24.9, 21.6; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{20}H_{23}BNO_3$: 336.1771; found 336.1770.

*4.3.15. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-phenylbenzoxazole (**3d**).* White solid, mp 95–96 °C, yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37 (s, 12H), 7.50–7.52 (m, 3H), 7.76–7.84 (m, 2H), 8.04 (s, 1H), 8.26–8.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.9, 150.6, 144.7, 131.7, 131.0, 128.9, 127.8, 127.1, 119.4, 116.7, 84.0, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{21}BNO_3$: 322.1614; found 322.1607.

*4.3.16. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(3-fluorophenyl)benzoxazole (**3e**).* White solid, mp 147–149 °C, yield 81%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.38 (s, 12H), 7.20–7.23 (m, 1H), 7.47–7.50 (m, 1H), 7.75–7.84 (m, 2H), 7.95 (d, 1H, J=9.3 Hz), 8.03–8.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.8 (d, J=245.5 Hz), 162.6 (d, J=3.3 Hz), 150.6, 144.4, 131.1, 130.6 (d, J=8.1 Hz), 129.0 (d, J=8.5 Hz), 123.4 (d, J=3.1 Hz), 119.5, 118.6 (d, J=21.1 Hz), 116.7, 114.6 (d, J=23.9 Hz), 114.5, 84.1, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}BFNO_3$: 340.1520; found 340.1516.

*4.3.17. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(3-chlorophenyl)benzoxazole (**3f**).* White solid, mp 122–123 °C, yield 52%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.38 (s, 12H), 7.45–7.52 (m, 2H), 7.75–7.84 (m, 2H), 8.01 (s, 1H), 8.20 (d, J=6.72 Hz, 1H), 8.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.5, 150.6, 144.4, 135.1, 131.6, 131.2, 130.2, 128.8, 127.7, 125.8, 119.5, 116.7, 84.1, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}BClNO_3$: 356.1225; found 356.1220.

*4.3.18. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl]benzoxazole (**3g**).* White solid, mp 203–204 °C, yield 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37 (s, 24H), 7.51–7.55 (m, 1H), 7.75–7.83 (m, 2H) 7.97 (d, J=7.3 Hz, 1H), 8.03 (s, 1H), 8.36 (d, J=7.9 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.0, 150.7, 144.7, 137.9, 134.1, 131.0, 130.4, 128.3, 126.5, 119.3, 116.6, 84.1, 84.0, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{25}H_{32}B_2NO_5$: 448.2466; found 448.2461.

*4.3.19. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(4-fluorophenyl)benzoxazole (**3h**).* White solid, mp 152–153 °C, yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.38 (s, 12H), 7.18–7.26 (m, 2H), 7.73–7.82 (m, 2H), 8.01 (s, 1H), 8.24–8.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=164.9 (d, J=251.5 Hz), 163.0, 150.6, 144.6, 131.1, 130.0 (d, J=8.8 Hz), 123.4 (d, J=3.1 Hz), 119.3, 116.6, 116.1 (d, J=22.0 Hz), 84.0, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}BFNO_3$: 340.1520; found 340.1523.

*4.3.20. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(4-chlorophenyl)benzoxazole (**3i**).* White solid, mp 171–172 °C, yield 77%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.38 (s, 12H), 7.47–7.50 (m, 2H), 7.73–7.83 (m, 2H), 8.01 (s, 1H), 8.17–8.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.9, 150.6, 144.5, 137.9, 131.1, 129.2, 129.0, 125.6, 119.4, 116.7, 84.1, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}BClNO_3$: 356.1225; found 356.1215.

*4.3.21. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl]benzoxazole (**3j**).* White solid, mp 248–249 °C, yield 70%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37 (s, 24H), 7.76–7.83 (m, 2H), 7.96–7.98 (m, 2H), 8.04 (s, 1H), 8.27 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.8, 150.6, 144.6, 135.2, 131.1, 129.2, 126.8, 119.4, 116.7, 84.1, 84.0, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{25}H_{32}B_2NO_5$: 448.2466; found 448.2456.

*4.3.22. 6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-yl)-2-(2,4-dichlorophenyl)benzoxazole (**3k**).* White solid, mp 126–127 °C, yield 68%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.37 (s, 12H), 7.38–7.40 (m, 1H), 7.57 (s, 1H) 7.80–7.85 (m, 2H), 8.06–8.14(m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=160.9, 150.4, 144.0, 137.6, 134.4, 132.6, 131.3, 131.1, 127.4, 124.7, 119.8, 116.9, 84.0, 24.9; HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{19}BCl_2NO_3$: 390.0840; found 390.0835.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (No. 20772114) and the Innovation Fund for Outstanding Scholar of Henan Province (No. 0621001100) for financial support of this research. We also thank Professor Jianhua Xu for his valuable comments on this paper.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.06.057.

References and notes

1. (a) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698; (b) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731; (c) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529; (d) Jun, C. H.; Lee, H.; Hong, J. B. *J. Org. Chem.* **1997**, *62*, 1200; (e) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 6616; (f) Thalji, R. K.; Ahrendt, K. A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 9692.
2. (a) Kalyani, D.; Sanford, M. S. *Top. Organomet. Chem.* **2007**, *24*, 85; (b) Kakiuchi, F.; Murai, S. *Top. Organomet. Chem.* **1999**, *3*, 47; (c) Powers, D. C.; Geibel, M. A. L.; Klein, J. E. M. N.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050; (d) Bedford, R. B.; Mitchellb, C. J.; Webster, R. L. *Chem. Commun.* **2010**, 3095; (e) Song, B. R.; Zheng, X. J.; Mo, J.; Xu, B. *Adv. Synth. Catal.* **2010**, *352*, 329; (f) Niedermann, K.; Welch, J. M.; Koller, R.; Cvengroš, J.; Santschi, N.; Battaglia, P.; Togni, A. *Tetrahedron* **2010**, *66*, 5753.
3. Butler, A.; Walker, J. V. *Chem. Rev.* **1993**, *93*, 1937.
4. (a) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523; (b) Kalyani, D. A.; Dick, R. W.; Anani, Q.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 11483.
5. Chen, X.; Hao, X. S.; Goodhue, C. E.; Yu, J. Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790.
6. Mo, F. Y.; Yan, J. M. T.; Qiu, D.; Li, F.; Zhang, Y.; Wang, J. B. *Angew. Chem., Int. Ed.* **2010**, *49*, 2028.
7. (a) Ciana, C. L.; Phipps, R. J.; Brandt, J. R.; Meyer, F. M.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 458; (b) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593.
8. Sun, K.; Li, Y.; Xiong, T.; Zhang, J. P.; Zhang, Q. *J. Am. Chem. Soc.* **2011**, *133*, 1694.
9. Hall, D. G. In *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005; p 1.
10. (a) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829; (b) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020; (c) Batey, R.; Thadani, A.; Smil, D. *Org. Lett.* **1999**, *1*, 1683; (d) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49; (e) Molander, G. A.; Katona, B.; Machrouhi, W. F. *J. Org. Chem.* **2002**, *67*, 8416; (f) Molander, G. A.; Yun, C. S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534.
11. For reviews on transition metal-catalyzed carbon-boron bond formation, see: (a) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392; (b) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2003**, *680*, 3; (c) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271; (d) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890; (e) Ishiyama, T.; Isou, H.; Kikuchi, T.; Miyaura, N. *Chem. Commun.* **2010**, 159.
12. (a) Miyarura, N. *Top. Curr. Chem.* **2002**, *219*, 11; (b) Billingsley, K. L.; Barder, T. E.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5359; (c) Billingsley, K. L.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 5589; (d) Duong, H. A.; Chua, S.; Huleatt, P. B.; Chai, C. L. L. *J. Org. Chem.* **2008**, *73*, 9177; (e) Martin, T.; Laguerre, C.; Hoarau, C.; Marsais, F. *Org. Lett.* **2009**, *11*, 3690; (f) Wang, L. H.; Li, J. Y.; Cui, X. L.; Wu, Y. S.; Zhu, Z. W.; Wu, Y. J. *Adv. Synth. Catal.* **2010**, *352*, 2002; (g) Pintaric, C.; Olivero, S.; Gimbert, Y.; Chavant, P. Y.; Duñach, E. *J. Am. Chem. Soc.* **2010**, *132*, 11825; (h) Merino, P.; Tejero, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 7164.
13. (a) Nguyen, P.; Blom, H. P.; Westcott, S. A.; Taylor, N. J.; Marder, T. B. *J. Am. Chem. Soc.* **1993**, *115*, 9329; (b) Shimada, S.; Batsanov, A. S.; Howard, J. A. K.; Marder, T. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2168; (c) Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 3056; (d) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390; (e) Whisler, M. C.; MacNeil, S.; Snieckus, V.; Beak, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2206; (f) Mertins, K.; Zapf, A.; Beller, M. *J. Mol. Catal. A: Chem.* **2004**, *207*, 21; (g) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263; (h) Murphy, J. M.; Lawrence, J. D.; Kawamura, K.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 13684; (i) Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534.
14. (a) Wu, Y. J.; Huo, S. Q.; Gong, J. F.; Cui, X. L.; Ding, L.; Ding, K. L.; Du, C. X.; Liu, Y. H.; Song, M. P. *J. Organomet. Chem.* **2001**, *637–639*, 27; (b) Xu, C.; Gong, J. F.; Yue, S. F.; Zhu, Y.; Wu, Y. J. *Dalton Trans.* **2006**, 4730; (c) Yang, F.; Wu, Y. J. *Eur. J. Org. Chem.* **2007**, 3476; (d) Yu, A. J.; Wu, Y. J.; Cheng, B. L.; Wei, K.; Li, J. Y. *Adv. Synth. Catal.* **2009**, *351*, 767; (e) Leng, Y. T.; Yang, F.; Wei, K.; Wu, Y. J. *Tetrahedron* **2010**, *66*, 1244.
15. Oshifuji, M.; Agase, R.; Namoto, N. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 873.
16. Ueda, S.; Nagasawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 641.