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Site-selective Suzuki–Miyaura reactions of 2,6-dichlorobenzoxazole

Aws M. Hamdy [a], Nadi Eleya [a], Hamid H. Mohammed [a,b], Tamás Patonay [c], Anke Spannenberg [d], Peter Langer [a,d,*]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany
[b] Department of Organic Chemistry, University of Al-Mustansiriyah, Baghdad, Iraq
[c] Department of Organic Chemistry, University of Debrecen, H-4032 Debrecen, Egyetem tér 1, Hungary
[d] Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany

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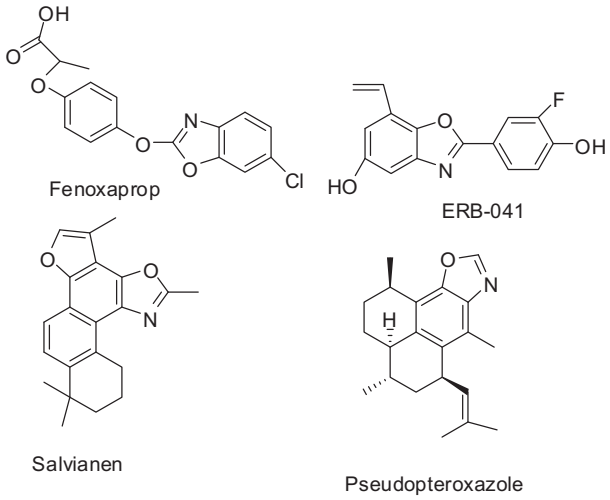
ABSTRACT

Suzuki–Miyaura reactions of 2,6-dichlorobenzoxazole provide a convenient access to arylated benzoxazoles. The reactions proceed with excellent site-selectivity in favour of position 2, due to electronic reasons.

1. Introduction

The benzoxazole moiety is an important structural motif in many biologically active natural products and pharmaceutical compounds. Examples include pseudopteroxazole and salvianen (Scheme 1).[1,2] Benzoxazoles also represent important molecules in medicinal chemistry.[3] Previous reports revealed that substituted benzoxazoles, such as the herbicide fenoxaprop, possess diverse chemotherapeutic activities, including antibiotic,[4] antimicrobial,[5–8] antiviral[9] and antitumour activities.[10,11] The 2-aryl-6-hydroxybenzoxazole ERB-041 represents an oestrogen receptor-β agonist.[12]

Traditional methods for the synthesis of substituted benzoxazoles include the oxidation of aromatic amines with persulfate and condensation of *ortho*-aminophenols with aldehydes.[13,14] Recently, general methods for the copper-catalyzed intramolecular C–O coupling reaction of 2-haloanilides were reported.[15] Nagasawa et al. reported that 2-arylbenzoxazoles and 2,6-diarylbenzoxazoles can be prepared by copper-catalyzed intramolecular oxidative C–O coupling of benzanilides.[16] Palladium catalyzed multi-component reactions of aryl halides, isocyanides and aminoalcohols have also been used for the synthesis of benzoxazoles.[17]



Scheme 1. Benzoxazoles in biologically active compounds.

In recent years, site-selective Pd catalyzed cross-coupling reactions have attracted considerable attention.[18,19] Herein, we report a new approach to arylated benzoxazoles by site-selective Suzuki–Miyaura cross-coupling reactions of commercially available 2,6-dichlorobenzoxazole (**1**) with arylboronic acids.

* Corresponding author. Fax: +49 381 4986412; e-mail address: peter.langer@uni-rostock.de (P. Langer).

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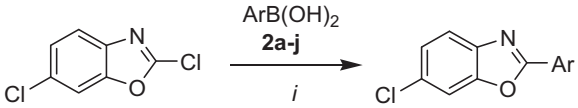
The Suzuki–Miayura reaction of commercially available 2,6-dichlorobenzoxazole (**1**) with 1.2 equiv of arylboronic acids **2a**–**j** afforded the 2-aryl-6-chlorobenzoxazoles **3a**–**j** in 72–90% yields with very good site-selectivity (Scheme 2, Table 1). The reactions



Scheme 2. Synthesis of **3a**–**j**. Reagents and conditions: i, **1** (1.0 equiv), **2a**–**j** (1.2 equiv), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (aqueous solution, 2 M), 1,4-dioxane, 80 °C, 6 h.

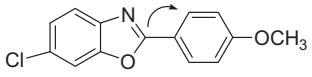
Table 1
Synthesis of **3a**–**j**

2,3	Ar	% (**3**)[a]
a	3,5-$Me_2C_6H_3$	90
b	4-EtC_6H_4	81
c	4-(MeO)C_6H_4	90
d	3-FC_6H_4	83
e	4-ClC_6H_4	88
f	Ph	90
g	2,3,4-$(MeO)_3C_6H_2$	80
h	3-MeC_6H_4	87
i	4-$^tBuC_6H_4$	72
j	4-$(F_3C)C_6H_4$	83

[a] Yields of isolated products.

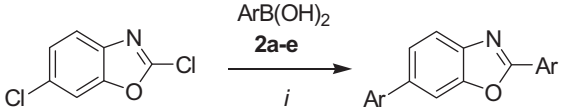
were carried out under standard conditions for Suzuki–Miyaura reactions: $Pd(PPh_3)_4$ (3.0 mol %) was employed as the catalyst and an aqueous solution of K_2CO_3 was used as the base (dioxane, 80 °C, 6 h). Very good yields were obtained for both electron rich and poor arylboronic acids. During the optimization, it proved to be important to carry out the reactions at 80 °C. A higher temperature resulted in the formation of significant amounts of diarylated products.

The structure of product **3c** was unambiguously confirmed by HMBC correlation between carbon atom C-2 of the benzoxazole moiety with the *ortho* hydrogens of the attached *p*-methoxyphenyl group (Scheme 3).



Scheme 3. Important HMBC correlation of compound **3c**.

The Suzuki–Miyaura reaction of **1** with 2.2 equiv of various arylboronic acids **2a**–**e** afforded the 2,6-diarylbenzoxazoles **4a**–**e** in 75–89% yields (Scheme 4, Table 2). The reactions had to be carried out at a higher temperature (120 °C) as compared to the synthesis of products **3**. Very good yields were obtained for products derived from both electron rich and poor arylboronic acids.



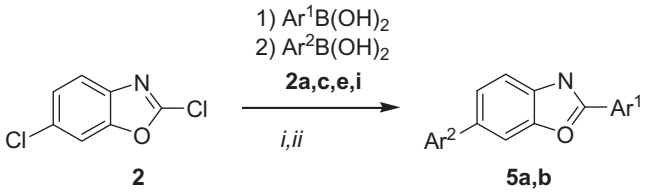
Scheme 4. Synthesis of **4a**–**e**. Reagents and conditions: i, **1** (1.0 equiv), **2a**–**e** (2.2 equiv), $Pd(PPh_3)_4$ (26 mg, 6 mol %), K_2CO_3 (aqueous solution, 2 M), 1,4-dioxane, 120 °C, 8 h.

Table 2
Synthesis of **4a**–**e**

2	4	Ar	% (**4**)[a]
a	**a**	3,5-$Me_2C_6H_3$	89
b	**b**	4-EtC_6H_4	88
c	**c**	4-(MeO)C_6H_4	88
d	**d**	3-FC_6H_4	75
e	**e**	4-ClC_6H_4	75

[a] Yields of isolated products.

The one-pot reaction of **1** with two different arylboronic acids was next studied. The reaction of **1** with 1.2 equiv of an arylboronic acid and subsequent addition of a second arylboronic acid (1.2 equiv) afforded the 2,6-diarylbenzoxazoles **5a**,**b** containing two different aryl groups in good yields (Scheme 5, Table 3). During the optimization, it proved to be important to carry out the first step at 80 °C and the second step at 120 °C. It also proved to be important to add a fresh portion of catalyst together with the second arylboronic acid. The structure of **5b** was independently confirmed by X-ray crystal structure analysis (Fig. 1).[20]



Scheme 5. Synthesis of **5a**,**b**. Reagents and conditions: i, 1) **1** (1.0 equiv), $Ar^1B(OH)_2$ 1.2 equiv), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (aqueous solution, 2 M), 1,4-dioxane, 80 °C, 6 h; 2) $Ar^2B(OH)_2$ (1.2 equiv), $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (aqueous solution, 2 M), 120 °C, 8 h.

Table 3
Synthesis of **5a**,**b**

2	5	Ar^1	Ar^2	% (**5**)[a]
e,**a**	**a**	4-ClC_6H_4	3,5-$Me_2C_6H_3$	84
i,**c**	**b**	4-$^tBuC_6H_4$	4-(MeO)C_6H_4	72

[a] Yields of isolated products.

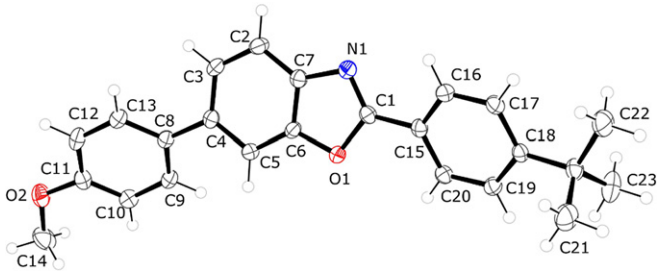
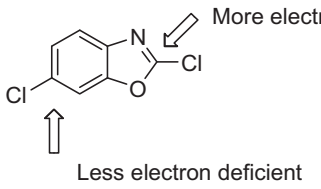


Fig. 1. Crystal structure of **5b**.

The site-selectivity in favour of position 2 can be explained by the fact that carbon C2 is more electron deficient than carbon C6 (Scheme 6). Palladium catalyzed cross-coupling reactions usually occur at the electronically more deficient position.[18,19]

We have reported a new approach to arylated benzoxazoles by site-selective Suzuki–Miyaura cross-coupling reactions of commercially available 2,6-dichlorobenzoxazole with arylboronic acids. The reactions proceed with excellent site-selectivity in favour of position C-2, which is more electron deficient than position C-6.



Scheme 6. Possible explanation for the site-selectivity of reactions of **1**.

2. Experimental section

2.1. General procedure for the synthesis of 3a–j

A 1,4-dioxane solution (3 mL) of **1**, arylboronic acid (1.2 equiv), aqueous K_2CO_3 (2.0 M, 1.0 mL) and $Pd(PPh_3)_4$ (3 mol %) was heated at 80 °C for 6 h under argon atmosphere. After cooling to 20 °C, H_2O was added and the reaction mixture was extracted with CH_2Cl_2 (3×25 mL). The organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptane/EtOAc).

*2.1.1. 6-Chloro-2-(3,5-dimethyl)benzo[d]oxazole (**3a**).* Starting with **1** (70 mg, 0.372 mmol), **2a** (66 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3a** was isolated as a white solid (86 mg, 90%), mp 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.80 (s, 6H, $2CH_3$), 7.09 (br s, 1H, ArH), 7.24 (dd, J=1.9, 8.4 Hz, 1H, ArH), 7.48 (d, J=2.0 Hz, 1H, ArH), 7.56 (d, J=8.4 Hz, 1H, ArH), 8.07 (br s, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=20.1 ($2CH_3$), 110.1, 116.6, 119.2 (C), 123.3, 124.1, 124.3 (CH), 125.3 (C), 127.3 (CH), 129.4 (C), 132.5 (CH), 139.8, 149.8 (C). IR (KBr, cm^{-1}): ν=1865.4, 1732.1, 1616.6, 1600.1 (w), 1556.0, 1451.8, 1425.8 (m), 1370.1 (w), 1331.2, 1258.8, 1227.5, 1182.4 (m), 1124.1, 1092.7, 1057.8 (w), 927.2, 915.6 (m), 864.7, 851.5, 804.8, 725.3, 702.8, 679.2 (s), 637.8 (w), 604.6, 594.8 (m), 563.6, 541.1, 509.6, 442.8 (w), 426.8 (s), 406.3 (w). GC–MS (EI, 70 eV): m/z (%)=GC–MS (EI, 70 eV): m/z (%)= 259 ($[M]^+$, ^{37}Cl, 33), 257 ($[M]^+$, ^{35}Cl, 100). sHRMS (ESI-TOF/MS): calcd for $C_{15}H_{12}{}^{37}ClNO$ ($[M+H]^+$, ^{37}Cl): 259.05724, found 259.057595, calcd for $C_{15}H_{12}{}^{35}ClNO$ ($[M+H]^+$, ^{35}Cl): 257.06019, found 257.060137.

*2.1.2. 6-Chloro-2-(4-ethylphenyl)benzo[d]oxazole (**3b**).* Starting with **1** (70 mg, 0.372 mmol), **2b** (53 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3b** was isolated as a white solid (78 mg, 81%), mp 90–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.21 (t, J=7.3 Hz, 3H, CH_3), 2.65 (q, J=7.5 Hz, 2H, CH_2), 7.25 (m, 3H, ArH), 7.49 (d, J=1.8 Hz, 1H, ArH), 7.57 (d, J=8.4 Hz, 1H, ArH), 8.05 (d, J=8.2 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=15.2 (CH_3), 29.7 (CH_2), 111.1, 120.2 (CH), 124.1 (C), 125.1, 127.7, 128.5 (CH), 130.4, 141.0, 148.6, 150.8, 163.9 (C). IR (KBr, cm^{-1}) ν=3028.5, 2961.4, 2927.7, 2869.9, 2852.8, 1939.0, 1864.3, 1741.0, 1682.9 (w), 1615.9 (s), 1602.5, 1575.1, 1555.5, 1496.9, 1487.0 (w), 1459.8, 1442.5, 1427.0, 1412.1, 1373.2, 1328.8 (m), 1310.5, 1282.7 (w), 1254.8 (s), 1231.4, 1182.2, 1169.5, 1120.6 (m), 1081.9, 1065.7 (w), 1044.1, 1010.9 (s), 964.5, 933.7 (w), 917.8, 846.1, 836.6, 829.5, 808.3 (s), 736.9, 721.2 (w), 700.9 (s), 641.9, 631.8 (w), 597.0, 576.2, 541.6 (m). GC–MS (EI, 70 eV): m/z (%)=259 ($[M]^+$, ^{37}Cl, 33), 257 ($[M]^+$, ^{35}Cl, 100), 244 (33), 243 (18). HRMS (EI, 70 eV) calcd for $C_{15}H_{12}{}^{37}ClNO$ ($[M]^+$, ^{37}Cl): 259.05724, found 259.057607; calcd for $C_{15}H_{12}{}^{35}ClNO$ ($[M]^+$, ^{35}Cl): 259.05724 found 259.057607.

*2.1.3. 6-Chloro-2-(4-methoxyphenyl)benzo[d]oxazole (**3c**).* Starting with **1** (70 mg, 0.372 mmol), **2c** (67 mg, 0.446 mmol) and $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL), and 1,4-dioxane (3 mL), **3c** was isolated as a white solid (87 mg, 90%), mp=140–142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.80 (s, 3H, OCH_3), 6.94 (d, J=9.1 Hz, 2H, ArH), 7.22 (dd, J=1.9, 8.4 Hz, 1H, ArH), 7.46 (d, J=2.0 Hz, 1H, ArH), 7.54 (d, J=8.4 Hz, 1H, ArH), 8.07 (d, J=9.0 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=55.4 (OCH_3), 111.0, 114.4 (CH), 119.1 (C), 120.0, 125.0, 129.4 (CH), 130.0, 141.0, 150.8, 162.5, 163.8 (C). IR (KBr, cm^{-1}): ν=3073.4, 3042.6, 3004.7, 2978.0, 2946.9, 2902.8, 2840.9, 2038.2, 1917.1, 1866.6 (w), 1616.8, 1601.9 (m), 1580.7 (w), 1502.1 (m), 1467.2 (w), 1452.6, 1439.5, 1428.3, 1420.4 (m), 1347.7 (w), 1332.6 (s), 1319.7, 1305.9 (m), 1283.7 (w), 1255.0, 1235.5 (m), 1283.7 (w), 1255.0 (s), 1235.5 (m), 1186.9 (w), 1174.9, 1118.4 (m), 1054.4, 1022.0 (s), 1005.9, 919.9, 864.3, 842.7 (m), 831.3, 807.7 (s), 789.4, 738.7, 698.5, 641.1, 634.4, 594.1 (m), 552.7, 531.3 (w). GC–MS (EI, 70 eV): m/z (%)=261 ($[M]^+$, ^{37}Cl, 30), 259 ($[M]^+$, ^{35}Cl, 100), 244 (32), 216 (27). HRMS (ESI-TOF/MS) calcd for $C_{14}H_{10}{}^{35}ClNO_2$ ($[M+H]^+$, ^{35}Cl): 260.4780, found 260.4600.

*2.1.4. 6-Chloro-2-(3-fluorophenyl)benzo[d]oxazole (**3d**).* Starting with **1** (70 mg, 0.372 mmol), **2d** (61 mg, 0.446 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **4d** was isolated as a white solid (77 mg, 83%), mp 122–124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.14–7.21 (m, 1H, ArH), 7.28 (dd, J=2.11, 8.23 Hz, 1H, ArH), 7.39–7.47 (m, 1H, ArH), 7.53 (d, J=2.11 Hz, 1H, ArH), 7.60 (d, J=8.45 Hz, 1H, ArH), 7.82–7.86 (m, 1H, ArH), 7.93–7.96 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=111.3 (CH), 114.55 (d, $J_{C,F}$=2.0 Hz, CH), 118.70 (d, $J_{C,F}$=21.8 Hz, CH), 120.7 (CH), 123.3 (d, $J_{C,F}$=3 Hz, CH), 125.5 (CH), 128.6 (C), 130.7 (d, $J_{C,F}$=8.0 Hz, CH), 131.1, 140.7, 150.9, 161.2 (C), 163.0 (d, $J_{C,F}$=245 Hz, CF). ^{19}F NMR (282.40 MHz, $CDCl_3$): δ=−111.52. IR (KBr, cm^{-1}): ν=3078.2, 3065.8, 3041.1, 2953.0, 2921.3, 2851.9, 1953.8, 1937.5, 1872.5, 1607.7, 1589.5 (w), 1555.8 (m), 1519.7, 1504.4 (w), 1486.2, 1469.9, 1450.9, 1435.0, 1427.7, 1327.7, 1305.7, 1294.5, 1274.3, 1261.3, 1240.3, 1209.8, 1178.0, 1154.7 (m), 1121.5, 1079.5 (w), 1057.1, 1044.9 (m), 1003.3, 969.7, 942.7, 929.6, 919.1 (w), 882.8, 862.0 (m), 808.0, 784.6 (s), 759.3, 745.9 (w), 720.8, 704.5, 673.0, 595.8 (s), 562.1, 553.1, 541.1 (w). GC–MS (EI, 70 eV): m/z (%)=249 ($[M]^+$, ^{37}Cl, 30), 247 ($[M]^+$, ^{35}Cl, 100), 219 (10), 184 (10). HRMS (ESI-TOF/MS): calcd for $C_{13}H_7{}^{37}ClFNO$ ($[M+H]^+$, ^{37}Cl): 250.02467, found 250.02516; calcd for $C_{13}H_7{}^{35}ClFNO$ ($[M+H]^+$, ^{35}Cl): 248.0273, found 248.02771.

*2.1.5. 6-Chloro-2-(4-chlorophenyl)benzo[d]oxazole (**3e**).* Starting with **1** (70 mg, 0.372 mmol), **2e** (66 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3e** was isolated as a white solid (86 mg, 88%), mp 197–200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.27 (dd, J=1.9, 8.5 Hz, 1H, ArH), 7.35–7.39 (m, 1H, ArH), 7.49–7.53 (m, 2H, ArH), 7.63 (d, J=8.5 Hz, 2H, ArH), 8.22 (d, J=8.36 Hz, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=111.2, 120.4, 125.3, 125.7, 129.1 (CH), 130.7, 134.3, 138.2, 140.9, 143.1, 150.9 (C). IR (KBr, cm^{-1}): ν=3091.3, 3065.9, 3043.6, 3027.7, 2922.6, 2851.7, 1926.0, 1909.2, 1879.0, 1615.2, 1601.6, 1579.6, 1563.6, 1550.2, 1512.7 (w), 1479.2, 1452.2, 1428.7, 1418.1, 1393.1 (m), 1356.6, 1331.3, 1318.5, 1296.1, 1280.0, 1260.0, 1233.5, 1195.3, 1178.0, 1124.1, 1105.1, 1091.2 (w), 1054.4 (m), 1017.7, 1003.8, 971.5, 962.2, 940.8, 923.7, 917.3, 866.2, 854.4 (w), 820.3, 811.4 (s), 767.2 (w), 744.3, 704.2, 697.0 (m), 666.8, 641.3, 626.7 (w), 598.3, 546.0 (m). GC–MS (EI, 70 eV): m/z (%)=267 $[M]^+$, (^{37}Cl ×2, 34), 265 (^{37}Cl ×1, ^{35}Cl ×1, 40), 263 (^{35}Cl ×2, 100), 242 (19), 63 (13). HRMS (EI, 70 eV) calcd for $C_{13}H_7{}^{37}Cl_2NO$ ($[M]^+$, ^{37}Cl ×2): 267.04159, found 267.04216; calcd for $C_{13}H_7{}^{35}Cl_2NO$ ($[M]^+$, ^{35}Cl ×2): 263.04454, found 263.04216.

*2.1.6. 6-Chloro-2-phenylbenzo[d]oxazole (**3f**).* Starting with **1** (70 mg, 0.372 mmol), **2f** (60 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3f** was isolated as a white solid (77 mg, 90%), mp 92–94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.25 (dd, J=1.1, 8.1 Hz, 1H, ArH), 7.44–7.47 (m, 3H, ArH), 7.52 (d, J=1.0 Hz, 1H, ArH), 7.59 (d, J=8.1 Hz 1H, ArH), 8.14 (dd, J=2.0, 8.6 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=110.6

(C), 111.2 (CH), 120.0 (C), 120.4, 125.0 (CH), 126.6 (C), 127.6, 128.9 (CH), 130.0, 130.6 (C), 131.8 (CH). IR (KBr, cm^{-1}): ν=3090.0, 3059.2, 3040.5, 2953.3, 2921.2, 2851.6, 1958.7, 1893.0, 1865.8, 1747.2, 1615.7, 1600.7, 1573.5, 1567.9 (w), 1551.9 (m), 1538.7, 1531.8, 1519.7, 1504.8, 1488.1, 1471.3 (w), 1447.3 (m), 1426.8, 1403.8, 1344.9 (w), 1330.1 (m), 1314.4, 1302.4, 1284.7, 1261.4, 1240.4, 1187.1, 1154.1, 1122.6, 1101.5, 1074.6 (w), 1050.3, 1021.7 (m), 974.8, 933.7 (w), 922.1, 915.5, 875.9 (m), 851.9, 825.8 (w), 806.1, 769.8 (s), 720.8 (w), 697.9, 680.2, 594.7 (s), 573.2, 540.0 (w). GC–MS (EI, 70 eV): *m/z* (%)=231 ($[M]^+$, ^{37}Cl, 44), 229 ($[M]^+$, ^{35}Cl, 100), 201 (13), 166 (26). HRMS (EI, 70 eV) calcd for $C_{13}H_8{}^{37}ClNO$ ($[M]^+$, ^{37}Cl): 231.02594, found 231.02641; calcd for $C_{13}H_8{}^{35}ClNO$ ($[M]^+$, ^{35}Cl): 229.02889, found 229.02889.

*2.1.7. 6-Chloro-2-(2,3,4-trimethoxyphenyl)benzo[d]oxazole (**3g**).* Starting with **1** (70 mg, 0.372 mmol), **2g** (80 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3g** was isolated as a white solid (95 mg, 80%), mp 76–78 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=3.86 (s, 6H, $2OCH_3$), 3.94 (s, 3H, OCH_3), 6.73 (d, *J*=8.8 Hz, 1H, ArH), 7.22 (dd, *J*=1.6, 8.0 Hz, 1H, ArH), 7.49 (d, *J*=1.8 Hz, 1H, ArH), 7.59 (d, *J*=8.8 Hz, 1H, ArH), 7.77 (d, *J*=8.8 Hz, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=56.1, 61.1, 61.7 ($3OCH_3$), 107.7, 111.0 (CH), 114.0 (C), 120.4, 124.9, 125.8 (CH), 130.2, 140.9, 143.2, 150.5, 153.6, 156.7, 161.9 (C). IR (KBr, cm^{-1}): ν=3091.4, 3068.5, 2994.6, 2962.8, 2935.6, 2874.5, 2849.4, 2838.7, 1862.9, 1609.3 (w), 1592.3 (m), 1573.9, 1555.2 (w), 1487.5, 1454.7, 1441.4, 1428.7, 1408.6 (s), 1332.5, 1310.5 (m), 1286.8, 1253.3, 1237.4, 1229.2, 1214.8 (s), 1201.7, 1174.9, 1150.0, 1126.6 (w), 1111.2, 1085.5, 1052.5, 1000.3 (s), 947.4 (w), 918.3, 906.5, 862.8, 848.7 (m), 807.0, 791.4 (s), 718.4, 705.8, 694.5 (m), 667.6, 657.5, 628.4, 614.7, 595.1, 564.3, 542.2 (w). GC–MS (EI, 70 eV): *m/z* (%)=321 ($[M]^+$, ^{37}Cl, 32), 319 ($[M]^+$, ^{35}Cl, 100), 304 (19), 290 (26), 230 (25). HRMS (EI, 70 eV) calcd for $C_{16}H_{14}{}^{35}ClNO_4$ ($[M]^+$, ^{35}Cl): 319.06059, found 319.06103.

*2.1.8. 6-Chloro-2-m-tolylbenzo[d]oxazole (**3h**).* Starting with **1** (70 mg, 0.372 mmol), **2h** (60 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3h** was isolated as a white solid (79 mg, 87%), mp 99–101 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=2.36 (s, 3H, CH_3), 7.23 (dd, *J*=2.0, 8.7 Hz, 1H, ArH), 7.27 (d, *J*=6.3 Hz, 1H, ArH), 7.32 (d, *J*=8.0 Hz, 1H, ArH), 7.47 (d, *J*=2.1 Hz, 1H, ArH), 7.56 (d, *J*=8.62 Hz, 1H, ArH), 7.91 (t, *J*=7.3 Hz, 2H, ArH), ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=21.3 (CH_3), 111.1, 120.3, 124.7, 125.2 (CH), 126.5 (C), 128.1, 128.8, 130.5 (CH), 132.6, 138.8, 140.8, 150.8, 163.8 (C). IR (KBr, cm^{-1}): ν=3085.5, 3063.2, 3040.3, 3023.2, 2953.0, 2922.0, 2855.7, 1955.8, 1865.6, 1828.0, 1789.9, 1731.3, 1619.7, 1602.9 (w), 1552.4 (m), 1504.6 (w), 1485.0 (m), 1470.1 (w), 1452.3, 1427.2 (m), 1375.0, 1345.3 (w), 1330.8 (s), 1307.7, 1282.2 (w), 930.8, 917.3 (m), 864.1, 806.5, 788.8, 716.0, 703.3, 682.5, 596.0 (s), 550.5, 529.5 (w). GC–MS (EI, 70 eV): *m/z* (%)=245 ($[M]^+$, ^{37}Cl, 34), 243 ($[M]^+$, ^{35}Cl, 100), 63 (13). HRMS (EI, 70 eV) calcd for $C_{14}H_{10}{}^{37}ClNO$ ($[M]^+$, ^{37}Cl): 245.04159, found 245.04216; calcd for $C_{14}H_{10}{}^{35}ClNO$ ($[M]^+$, ^{35}Cl): 243.04454, found 245.04216.

*2.1.9. 2-(4-tert-Butylphenyl)-6-chlorobenzo[d]oxazole (**3i**).* Starting with **1** (70 mg, 0.372 mmol), **2i** (79 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3i** was isolated as a white solid (77 mg, 72%), mp 98 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=0.5 (s, 9H, $3CH_3$), 6.47 (dd, *J*=1.9, 8.4 Hz, 1H, ArH), 6.68–6.71 (m, 3H, ArH), 6.81 (d, *J*=8.4 Hz, 1H, ArH), 7.29 (d, *J*=8.5 Hz 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=31.1 ($3CH_3$), 35.1 (C), 111.1, 120.3 (CH), 123.8 (C), 125.1, 125.9, 126.2 (CH), 130.4, 141.0, 150.8, 155.4, 163.9 (C). IR (KBr, cm^{-1}): ν=3093.0, 3062.7, 3041.4, 2956.6, 2924.6, 2902.2, 2860.4, 1916.5, 1692.8, 1673.2 (w), 1617.6 (m), 1601.1, 1573.6, 1553.2 (w), 1495.3, 1459.2 (m), 1441.8, 1430.3, 1408.6, 1359.9 (w), 1328.1 (s), 1299.0, 1286.8 (w), 1260.6 (s), 1232.3, 1202.3, 1191.6, 1121.4, 1108.0 (w), 1048.8 (s), 1022.7, 1011.0, 969.7, 955.4 (w), 918.3 (s), 874.0, 846.9 (w), 836.1, 822.1, 812.2 (s), 749.0, 733.9 (w), 702.0 (s), 637.9, 618.6, 596.7, 550.2 (w). GC–MS (EI, 70 eV): *m/z* (%)=287 ($[M]^+$, ^{37}Cl, 13), 285 ($[M]^+$, ^{35}Cl, 100), 272 (34), 271 (19), 242 (17). HRMS (EI, 70 eV); calcd for $C_{17}H_{16}{}^{37}ClNO$ ($[M]^+$, ^{37}Cl): 287.08854, found 287.08896; calcd for $C_{17}H_{16}{}^{35}ClNO$ ($[M]^+$, ^{35}Cl): 285.09149, found 285.98189.

*2.1.10. 6-Chloro-2-(4-(trifluoromethyl)phenyl)benzo[d]oxazole (**3j**).* Starting with **1** (70 mg, 0.372 mmol), **2j** (84 mg, 0.446 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **3j** was isolated as a white solid (92 mg, 83%), mp 112–115 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.29 (dd, *J*=1.72, 8.50 Hz, 1H, ArH), 7.54 (d, *J*=2.37 Hz, 1H, ArH), 7.61 (d, *J*=8.70 Hz, 1H, ArH), 7.72 (d, *J*=8.30 Hz, 2H, ArH), 8.26 (d, *J*=8.64 Hz, 2H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=111.4, 120.9 (CH), 123.4 (q, $J_{C,F}$=271 Hz, CF), 125.7, 126.0 (q, $J_{C,F}$=3.8 Hz, CH), 127.9 (CH), 130.0, 131.5 (C), 133.2 (d, $J_{C,F}$=32.0 Hz, C), 140.6, 151.0, 162.1 (C). ^{19}F NMR (282.40 MHz, $CDCl_3$): δ=−63.04. IR (KBr, cm^{-1}): ν=3100.0, 3080.7, 2954.2, 2922.8, 2852.3, 2638.4, 1931.6, 1889.7, 1804.7, 1683.3 (w), 1614.2, 1605.7 (m), 1569.6 (w), 1557.2 (m), 1512.0, 1500.5 (w), 1461.0 (s), 1426.7, 1409.5 (m), 1344.9 (w), 1320.3 (s), 1259.3 (m), 1228.9, 1208.0 (w), 1158.2, 1130.0, 1107.2, 1064.8, 1046.1, 1009.9 (s), 970.5, 964.4, 946.4, 946.8 (w), 922.2, 916.6 (m), 843.3, 833.7 (m), 825.9, 815.2 (s), 773.7, 748.4, 725.8, 715.3 (w), 696.3 (s), 660.4, 633.3, 605.8 (w), 592.4 (s), 574.7, 541.2 (w). GC–MS (EI, 70 eV): *m/z* (%)=299 ($[M]^+$, ^{37}Cl, 32), 297 ($[M]^+$, ^{35}Cl, 100), 269 (10), 63 (17) HRMS (EI): calcd for $C_{14}H_7{}^{37}ClF_3NO$ ($[M]^+$, ^{37}Cl): 299.01333, found 299.01347; calcd for $C_{14}H_7{}^{35}ClF_3NO$ ($[M]^+$, ^{35}Cl): 297.01628, found 297.01630.

2.2. General procedure for the synthesis of 4a–e

A 1,4-dioxane solution (3 mL) of **1**, arylboronic acid (2.2 equiv), aqueous K_2CO_3 (2.0 M, 1.0 mL) and $Pd(PPh_3)_4$ (6 mol %) was heated at 120 °C for 8 h under argon atmosphere. After cooling to 20 °C, H_2O was added and the reaction mixture was extracted with CH_2Cl_2 (3×25 mL). The organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (silica gel, heptane/EtAOc).

*2.2.1. 2,6-Bis(3,5-dimethylphenyl)benzo[d]oxazole (**4a**).* Starting with **1** (70 mg, 0.372 mmol), **2a** (122 mg, 0.818 mmol), $Pd(PPh_3)_4$ (26 mg, 6 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **4a** was isolated as a white solid (109 mg, 89%), mp 169–170 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=2.32 (s, 6H, $2CH_3$), 2.34 (s, 6H, $2CH_3$), 6.94 (br s, 1H, ArH), 7.09 (br s, 1H, ArH), 7.17 (br s, 2H, ArH), 7.48 (dd, *J*=1.8, 8.0 Hz, 1H, ArH), 7.67–7.70 (m, 2H, ArH), 7.82 (br s, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=21.25 ($2CH_3$), 22.70 ($2CH_3$), 109.0, 119.6, 124.1, 125.3, 125.41 (CH), 126.9 (C), 129.0, 133.3 (CH), 133.3, 138.4, 138.6, 139.1, 140.9, 141.3, 151.3, 125.3, 129.0 (C). IR (KBr, cm^{-1}): ν=3008.6, 2951.0, 2916.3, 2855.5, 2732.6, 1888.1, 1760.6, 1737.6, 1619.7 (w), 1592.9, 1551.9, 1459.6, 1410.1 (m), 1376.2, 1363.6, 1332.5, 1310.7, 1274.1 (w), 1258.7, 1230.9 (m), 1200.6, 1185.6, 1155.7, 1127.1, 1091.7, 1081.3, 1053.3, 1037.7, 993.7, 965.5, 939.5, 927.0, 919.4, 909.0, 872.1 (w), 847.1, 828.8, 815.8 (s), 776.2, 759.8, 746.7 (w), 729.3, 702.0, 682.5, 648.7 (s), 598.3, 544.0 (w). GC–MS (EI, 70 eV): *m/z* (%)=328 ($[M+H]^+$, 23), 327 ($[M]^+$, 100), 311 (10). HRMS (EI, 70 eV) calcd for $C_{23}H_{21}NO$ $[M]^+$: 327.16177; found: 327.16159.

*2.2.2. 2,6-Bis(4-ethylphenyl)benzo[d]oxazole (**4b**).* Starting with **1** (70 mg, 0.372 mmol), **2b** (97 mg, 0.818 mmol) and $Pd(PPh_3)_4$ (26 mg, 6 mol %), K_2CO_3 (2 M, 1.0 mL), and 1,4-dioxane (3 mL), **4b** was isolated as a white solid (108 mg, 88%), mp 74–77 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=1.20 (t, *J*=7.5 Hz, 6H, $2CH_3$), 2.68 (q, *J*=7.5 Hz, 4H, $2CH_2$), 7.21 (d, *J*=8.0 Hz, 2H, ArH), 7.26 (d, *J*=8.0 Hz, 2H, ArH), 7.46–7.50 (m, 3H, ArH), 7.66–7.70 (m, 2H, ArH), 8.10 (d, *J*=8.0 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=15.2, 15.5 ($2CH_3$), 28.5, 28.9 ($2CH_2$), 108.8, 119.7, 123.9 (CH), 124.6 (C), 127.3, 127.7, 128.4,

128.5 (CH), 138.3, 138.7, 141.3, 143.6, 148.2, 151.3, 163.6 (C). IR (KBr, cm^{-1}): ν=3023.5 (w), 2959.0, 2926.7, 2868.8, 1617.7 (m), 1603.3, 1577.1, 1567.4, 1551.6, 1520.0 (w), 1498.4, 1472.5, 1454.5, 1434.6, 1417.5, 1408.5 (m), 1370.8, 1335.4, 1322.7, 1289.4 (w), 1262.2 (s), 1209.2, 1180.5, 1165.1, 1135.6, 1118.1, 1081.2 (w), 1057.0, 1046.7, 1016.7 (m), 962.5, 923.1, 916.0, 874.5, 864.8 (w), 833.5, 807.9 (s), 783.6, 758.8, 738.9 (w), 701.1 (s), 648.1, 642.3, 634.0, 594.2, 553.4 (w), 529.6 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=327 ($[M]^+$, 100), 312 (60), 297 (19), 152 (10), 148 (17). HRMS (EI, 70 eV): calcd for $C_{23}H_{21}NO$ $[M]^+$: 327.16177; found: 327.161480.

*2.2.3. 2,6-Bis(4-methoxyphenyl)benzo[d]oxazole (**4c**).* Starting with **1** (70 mg, 0.372 mmol), **2c** (124 mg, 0.818 mmol), $Pd(PPh_3)_4$ (26 mg, 6 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **4c** was isolated as a white solid (108 mg, 88%), mp 180–182 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=3.79 (s, Hz, 6H, $2OCH_3$), 6.93 (t, *J*=7.4 Hz, 4H, ArH), 7.42–7.45 (m, 3H, ArH), 7.61–7.67 (m, 2H, ArH), 8.12 (d, *J*=8.5 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=55.3, 55.4 (OCH_3), 107.3, 113.3, 113.4, 118.4 (CH), 118.7 (C), 122.6, 127.3, 128.3 (CH), 132.4, 137.1, 140.1, 150.3, 158.2, 161.2, 162.3 (C). IR (KBr, cm^{-1}): ν=3071.7, 3038.4, 3012.1, 2955.7 (w), 2920.8, 2851.7 (s), 2548.6, 2478.6, 2418.7, 2402.9, 1892.2, 1730.6 (w), 1614.3, 1603.4, 1580.8, 1556.7, 1520.3, 1495.1, 1464.6, 1454.1, 1435.7, 1422.2, 1407.0 (m), 1378.2, 1364.8, 1335.0, 1319.2, 1303.7 (w), 1294.3, 1233.3, 1177.9, 1133.7, 1115.8, 1107.6, 1080.9, 1057.7, 1035.2, 1022.0, 968.6, 956.9, 922.7, 915.4, 864.5 (m), 836.7, 806.1, 787.0, 757.7, 738.2, 722.9, 698.9, 665.8, 650.9, 640.8, 627.1, 593.8, 557.8 (m), GC–MS (EI, 70 eV): *m*/*z* (%)=331 ($[M]^+$, 100), 317 (10), 316 (46), 288 (10), 165 (14). HRMS (EI, 70 eV) calcd for $C_{21}H_{17}NO_3$ $[M]^+$: 331.12029; found: 331.120195.

*2.2.4. 2,6-Bis(3-fluorophenyl)benzo[d]oxazole (**4d**).* Starting with **1** (70 mg, 0.372 mmol), **2d** (112 mg, 0.818 mmol), $Pd(PPh_3)_4$ (12 mg, 6 mol %), K_2CO_3 (2 M, 1.0 mL) and 1,4-dioxane (3 mL), **4d** was isolated as a white solid (86 mg, 75%), mp 100 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.14–7.18 (m, 2H, ArH), 7.21–7.25 (m, 1H, ArH), 7.30–7.33 (m, 1H, ArH), 7.35 (d, *J*=8.15 Hz, 1H, ArH), 7.38–7.40 (m, 1H, ArH), 7.48 (dd, *J*=2.71, 8.15 Hz, 1H, ArH), 7.67 (d, *J*=2.10 Hz, 1H, ArH), 7.72 (d, *J*=8.06 Hz, 1H, ArH), 7.84–7.88 (m, 1H, ArH), 7.95–7.98 (m, 1H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=108.1 (CH), 114.1 (d, $J_{C,F}$=21.0 Hz, CH), 114.2 (d, $J_{C,F}$=21.0 Hz, CH), 114.4 (d, $J_{C,F}$=21.8 Hz, CH), 117.5 (d, $J_{C,F}$=21.1 Hz, CH), 119.2 (CH), 121.9 (d, $J_{C,F}$=2.7 Hz, CH), 122.3 (d, $J_{C,F}$=2.7 Hz, CH), 123.2 (CH), 130.4 (d, $J_{C,F}$=8.4 Hz, CH), 130.6 (d, $J_{C,F}$=8.0 Hz, CH), 136.9 (d, $J_{C,F}$=2.3 Hz, C), 140.7, 141.8, 141.9 (C), 161.4 (d, $J_{C,F}$=3.5 Hz, C), 163.5 (d, $J_{C,F}$=247.5 Hz, CF), 163.8 (d, $J_{C,F}$=245.5 Hz, CF), 150.3 (C). ^{19}F NMR (282.40 MHz, $CDCl_3$): δ=−111.6, −112.6 ($ArCF_3$). IR (KBr, cm^{-1}): ν=3088.9, 3069.3, 2954.1, 2922.3, 2852.5, 1946.2, 1873.5, 1789.0, 1731.0, 1608.6 (w), 1577.2, 1556.6 (m), 1519.7, 1466.6 (w), 1450.5, 1413.4 (m), 1331.3, 1316.8, 1289.5, 1275.8 (w), 1262.8, 1210.6, 1182.0 (m), 1160.0, 1144.8, 1133.2, 1077.7, 1059.5, 1045.9, 1035.5, 1001.1, 974.4, 944.2 (w), 928.0, 880.1, 858.4, 815.5, 784.1, 723.2, 692.0, 678.2, 648.2 (s), 634.0, 596.6, 588.6, 573.1, 540.0 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=307 ($[M]^+$, 100), 157 (33). HRMS (EI, 70 eV): calcd for $C_{19}H_{11}F_2NO$ $[M]^+$: 307.08032; found: 307.080780.

*2.2.5. 2,6-Bis(4-chlorophenyl)benzo[d]oxazole (**4e**).* Starting with **1** (70 mg, 0.372 mmol), **2e** (122 mg, 0.818 mmol), and $Pd(PPh_3)_4$ (26 mg, 6 mol %), K_2CO_3 (2 M, 1.0 mL), and 1,4-dioxane (3 mL), **4e** was isolated as a white solid (95 mg, 75%), mp 370–372 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.37 (dd, *J*=2.2, 8.2 Hz, 1H, ArH), 7.41 (d, *J*=8.6 Hz, 2H, ArH), 7.54–7.58 (m, 3H, ArH), 7.59–7.65 (m, 3H, ArH), 8.22 (d, *J*=8.7 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=110.2, 119.4, 124.3 (CH), 124.7 (C), 126.4, 127.1, 127.3, 128.1 (CH), 129.7, 133.3, 137.2, 139.9, 142.1, 149.9, 162.3 (C). IR (KBr, cm): ν=3092.3, 3066.9, 3044.6, 3028.7, 2923.6, 2852.7, 1927.0, 1910.2, 1878.0, 1616.2, 1602.6, 1580.6, 1564.6, 1551.2, 1513.7 (w), 1480.2, 1453.2, 1429.7, 1419.1, 1394.1 (m), 1357.6, 1332.3, 1319.5, 1297.1, 1281.0, 1261.0, 1234.5, 1196.3, 1179.0, 1125.1, 1106.1, 1091.2 (w), 1054.4 (m), 1017.7, 1003.8, 971.5, 962.2, 940.8, 923.7, 917.3, 866.2, 854.4 (w), 820.3, 811.4 (s), 767.2 (w), 744.3, 704.2, 697.0 (m), 666.8, 641.3, 626.7 (w), 598.3, 546.0 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=341 ($[M]^+$, ^{37}Cl ×1, ^{35}Cl ×1, 11), 339 ($[M]^+$, ^{35}Cl ×2, 100), 305 (15), 98 (17). HRMS (EI, 70 eV) calcd for $C_{19}H_{11}{}^{35}Cl_2NO$ ($[M]^+$, ^{35}Cl ×2): 339.2013, found 339.0301.

2.3. General procedure for the synthesis of 5a,b

The reaction was carried out in a pressure tube. To a 1,4-dioxane suspension (3 mL) of **1**, arylboronic acid $Ar^1B(OH)_2$ and $Pd(PPh_3)_4$ (3 mol %) was added an aqueous solution of K_2CO_3 (2 M, 1 mL) and the resulting solution was degassed by bubbling argon through the solution for 10 min. The mixture was heated at 80 °C under an argon atmosphere for 6 h. The mixture was cooled to 20 °C. Arylboronic acid $Ar^2B(OH)_2$ and $Pd(PPh_3)_4$ (3 mol %), K_2CO_3 (2 M, 0.5 mL), and dioxane (2 mL) were added. The reaction mixture was heated under an argon atmosphere for 8 h at 120 °C. Then it was diluted with H_2O and extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, heptane/EtAOc).

*2.3.1. 2-(4-Chlorophenyl)-6-(3,5-dimethylphenyl)benzo[d]-oxazole (**5a**).* Starting with **1** (70 mg, 0.372 mmol), **2e** (66 mg, 0.446 mmol), $Pd(PPh_3)_4$ (13 mg, 3 mol %), K_2CO_3 (2 M, 1.0 mL), **2a** (66 mg, 0.446 mmol) and $Pd(PPh_3)_4$ (13 mg, 3 mol % mmol), K_2CO_3 (2 M, 0.5 mL), and 1,4-dioxane (3 mL), **5a** was isolated as a white solid (104 mg, 84%), mp 57–59 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=2.31 (s, 6H, $2CH_3$), 6.94 (d, *J*=5.2 Hz, 1H, ArH), 7.15–7.19 (m, 3H, ArH), 7.49 (dd, *J*=1.9, 8.6 Hz, 1H, ArH), 7.63–7.71 (m, 3H, ArH), 8.21 (d, *J*=8.4 Hz, 2H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=20.3 ($2CH_3$), 107.9, 118.6, 121.2 (CH), 123.2, 124.0, 124.3 (C), 124.7, 126.5, 126.9, 128.0 (CH), 128.6, 137.3, 137.4, 139.8, 140.4, 143.4 (C). IR (KBr, cm^{-1}): ν=3015.5, 2961.6, 2913.5, 2853.1, 2730.4, 1614.6, 1598.4, 1573.7, 1556.0, 1552.5, 1538.5, 1531.7, 1497.6, 1487.4, 1462.9, 1455.4, 1441.7, 1435.0, 1412.4, 1398.1, 1373.6, 1325.5 (w), 1258.3 (s), 1233.9, 1209.2, 1183.0, 1156.9, 1086.0, 1051.0, 1033.5, 1013.6, 939.6, 921.4, 896.2, 847.0 (w), 833.2, 814.7, 803.5 (s), 758.6 (w), 760.0, 694.9 (m), 666.7 (w), 647.5 (m), 647.5, 596.6, 583.0, 540.0 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=335 ($[M]^+$, ^{37}Cl, 34), 333 ($[M]^+$, ^{35}Cl, 100), 331 (17), 167 (12). HRMS (EI, 70 eV) calcd for $C_{21}H_{16}{}^{37}ClNO$ ($[M]^+$, ^{37}Cl): 335.08854, found 335.08862; calcd for $C_{21}H_{16}{}^{35}ClNO$ ($[M]^+$, ^{35}Cl): 333.09149, found 333.09147.

*2.3.2. 2-(4-tert-Butylphenyl)-6-(4-methoxyphenyl)-benzo[d]oxazole (**5b**).* Starting with **1** (70 mg, 0.372 mmol), **2i** (79 mg, 0.446 mmol) and $Pd(PPh_3)_4$ (2×13 mg, 2×3 mol %), K_2CO_3 (2 M, 1.0 mL, then 1.5 mL), **2c** (67 mg, 0.446 mmol), and 1,4-dioxane (3 mL), **5b** was isolated as a white solid (96 mg, 72%), mp=100 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=1.27 (s, 9H, $3CH_3$), 3.74 (s, 3H, OCH_3), 6.90 (d, *J*=8.0 Hz, 2H, ArH), 7.42–7.48 (m, 5H, ArH), 7.62 (d, *J*=1.3 Hz, 1H, ArH), 7.67 (d, *J*=8.4 Hz, 1H, ArH), 8.08 (d, *J*=8.4 Hz, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ=30.1 ($3CH_3$), 54.2 (OCH_3), 107.4, 113.3, 118.6, 122.6 (CH), 123.3 (C), 124.8, 126.3, 127.3 (CH), 132.3, 137.3, 140.0, 150.3, 154.0, 157.6, 158.2, 162.3 (C). IR (KBr, cm): ν=3064.0, 3032.9, 3002.4, 2961.4, 2953.5, 2927.9, 2900.6, 2865.2, 2832.5, 1617.5 (w), 1605.5 (m), 1573.1, 1552.1 (w), 1517.2, 1495.2, 1471.1, 1434.5 (m), 1408.7, 1399.1, 1363.3, 1331.0, 1302.8, 1291.9 (w), 1267.5, 1246.5, 1235.3 (s), 1194.2 (w), 1178.1 (s), 1162.7, 1131.6, 1123.1, 1110.4 (w), 1053.7, 1040.1, 1011.9 (m), 972.1, 959.1, 941.3, 923.9, 914.7, 861.3 (w), 844.8, 830.8 (m), 809.7, 797.1 (s), 755.6, 750.6, 734.4, 724.0 (w), 706.2 (s), 646.0, 629.0, 584.0 (w), 563.5, 544.0, 527.8 (m). GC–MS

(EI, 70 eV): *m*/*z* (%)=357 ([M]$^+$, 100), 342 (66), 157 (11). HRMS (EI, 70 eV): calcd for $C_{24}H_{23}NO_2$ [M]$^+$: 357.17233; found: 357.17182.

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