

Selected Paper

Substituent Effect of Imino-*O*-arenesulfonates, a Coupling Partner in Suzuki–Miyaura Reaction for Substitution of the Pyrazine Ring: A Study for the Synthesis of Coelenterazine Analogs

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Amino(aryl)pyrazines, a key intermediate in the synthesis of coelenterazine and its analogs, can be prepared in excellent yields by utilizing imino-*O*-tosylates in the Suzuki–Miyaura reaction. These imino-*O*-tosylates serve as a substitute for the corresponding imino-*O*-triflates, which are sometimes too unstable to be stored during the optimization of the reaction conditions. Aryltrifluoroborates, a coupling partner, worked well when arylboronic acids or arylboronate esters were less reactive. Aryltrifluoroborates also worked well when containing an electron-donating group attached to the aromatic ring. The study of the substituent effect of imino-*O*-arenesulfonates demonstrated a major difference in the rate of the reactions when changing from electron-donating groups to electron-withdrawing groups at the para position of arenesulfonates. Imino-*O*-arenesulfonate containing a *para*-bromo substituent only gave the desired coupling product leaving the para substituent of arenesulfonate untouched.

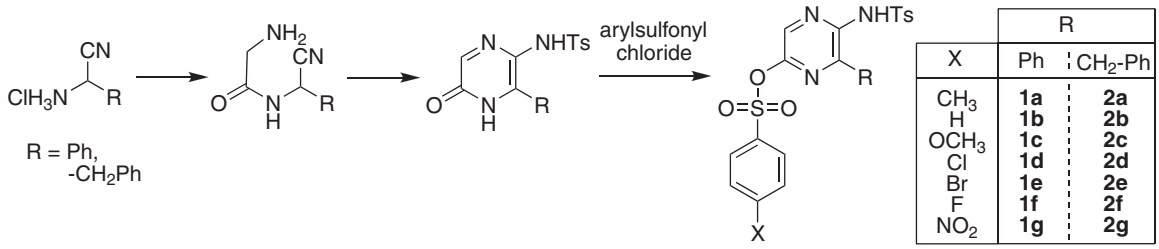
Palladium-mediated cross-coupling reactions are one of the useful methods employed to form carbon–carbon bonds in organic synthesis.[1] High functional group tolerance, easily separable and nontoxic by-products, and commercial availability of boron coupling partners have provided the Suzuki–Miyaura cross-coupling both a popular and effective tool in organic synthesis. Suzuki–Miyaura reaction involves the palladium-mediated cross-coupling between organoboron compounds and aryl/alkenyl halides/triflates in the presence of a base.[2] Using aryltrifluoroborates and arylboronate esters as alternatives to arylboronic acids have been examined to determine their usefulness in the Suzuki–Miyaura cross-coupling reaction, because of their high stability, availability of purified sample, and in order to avoid the formation of trimeric anhydride boroxime.[3] Instead of aryl, vinyl triflates, or halides, aryl tosylates were recently reported in Suzuki–Miyaura cross-coupling reaction.[4] Although these tosylates are more stable, their reactivity becomes relatively lower than the corresponding triflates or halides. Due to the lower reactivity, less expensive, more stable and easier to handle than the corresponding triflates it is therefore a challenge to develop a general protocol for the coupling between imino-*O*-tosylates and organoborons. In 1994, we reported Heck reaction of various imino-*O*-triflates with acetylenes.[5] However, there has only been incidental reporting of palladium-catalyzed Suzuki–Miyaura cross-coupling reaction of imino-*O*-tosylate with organoboron.[4c] We have found that some imino-*O*-triflates are unstable for purification or decompose during storage. In the previous report, a low yield of coupling products was obtained when the two coupling partners have the same electronic properties, such as imino-*O*-triflates[6a] or heteroaryl tosylates[4b] and organoborons containing an electron-donating group attached to the aromatic ring.[4] Herein, we demonstrate the successful utilization of imino-*O*-tosylates in the Suzuki–Miyaura cross-coupling to access various substituents into amino(aryl)pyrazines, which is the key intermediate in the synthesis of unstable coelenterazine and its derivatives,[6] together with the study of substituent effect of imino-*O*-arenesulfonates at the para position in the cross-coupling reactions.

Results and Discussion

Chemical biology studies have identified a requirement for new ways to supply new classes of analogs of these *N*-heterocycles.[7] The core skeleton of coelenterazine is aminopyrazine which has found only limited use due to unstability. The imino-*O*-tosylates **1a**–**1g** and the homologs **2a**–**2g** were prepared for this study from amino nitriles using our reported procedure as shown in Scheme 1.[6b]

The Suzuki–Miyaura reaction of imino-*O*-tosylates **1a** or **2a** and arylboronic acid **3**, arylboronate ester **4**, or aryltrifluoroborate **5** was examined in polar solvents in the presence of Pd^{II}, phosphine ligand, and base. All reactions were monitored in the same time scale as 5 h for the reaction time. The results are summarized in Table 1. Combination of $Pd(OAc)_2$ and a bulky and electron-rich phosphines **6** was found to be useful for the current coupling system. This combination was also used in the screening to optimize the cross-coupling condition. In case of imino-*O*-tosylate **1a**, the excellent yields of the coupling products were obtained when organoboron accompanied with a suitable base and solvent were used (Table 1, Entries 1, 6, and 9). However, for imino-*O*-tosylate **2a**, the coupling could only

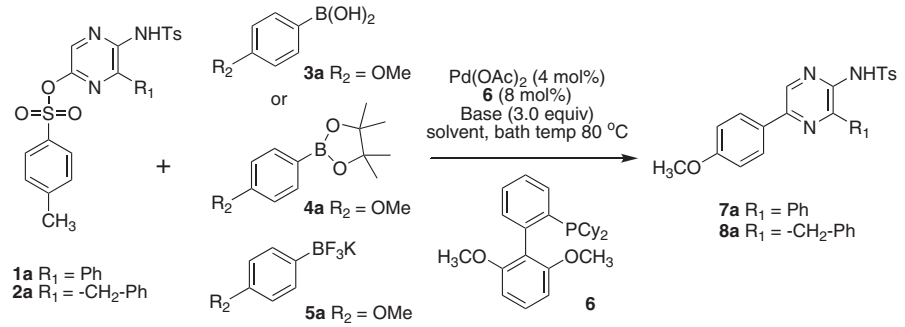
Published on the web July 10, 2009; doi:10.1246/bcsj.82.870



X	R: Ph	R: CH_2-Ph
CH_3	**1a**	**2a**
H	**1b**	**2b**
OCH_3	**1c**	**2c**
Cl	**1d**	**2d**
Br	**1e**	**2e**
F	**1f**	**2f**
NO_2	**1g**	**2g**

Scheme 1. Synthesis of imino-*O*-tosylates **1a**–**1g** and the homologs **2a**–**2g**.

Table 1. Relative Reactivity of Imino-*O*-tosylates and Organoborons[a)]



Entry	Aryl tosylate	Organoboron R_2 = OMe (equiv)	Base	Solvent	Product (% Yield)[b)]
1	**1a**	**3a** (2.0)	K_3PO_4	THF	**7a** (91)
2	**1a**	**3a** (1.1)	K_3PO_4	THF	**7a** (27)
3	**1a**	**3a** (2.0)	K_3PO_4	Dioxane	**7a** (nr)[c)]
4	**1a**	**4a** (2.0)	K_3PO_4	THF	**7a** (15)[d)]
5	**1a**	**4a** (2.0)	K_3PO_4	THF	**7a** (21)
6	**1a**	**4a** (2.0)	KOH	MeOH	**7a** (91)
7	**1a**	**4a** (1.3)	KOH	MeOH	**7a** (85)
8	**1a**	**5a** (2.0)	K_3PO_4	THF	**7a** (nr)[e)]
9	**1a**	**5a** (2.0)	KOH	MeOH	**7a** (92)
10	**1a**	**5a** (1.3)	KOH	MeOH	**7a** (28)
11	**2a**	**3a** (2.0)	K_3PO_4	THF	**8a** (11)
12	**2a**	**4a** (2.0)	KOH	MeOH	**8a** (87)
13	**2a**	**4a** (1.3)	KOH	MeOH	**8a** (73)
14	**2a**	**5a** (1.1)	KOH	MeOH	**8a** (5)
15	**2a**	**5a** (1.1)	Et_3N	Ethanol	**8a** (9)
16	**2a**	**5a** (2.0)	KOH	MeOH	**8a** (22)

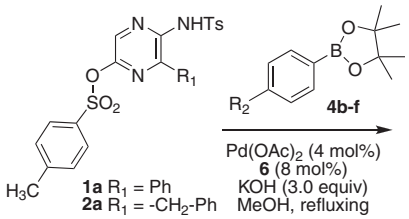
a) Reaction condition: imino-*O*-tosylate **1a** and **2a** (0.10 mmol), organoboron, $Pd(OAc)_2$ (4 mol %), ligand **6** (8 mol %), base (3.0 equiv), solvent (5.0 mL), bath temp 80 °C, 5 h. b) Isolated yield. c) PPh_3 was used as ligand in the reaction. d) [$PdCl_2$(dppf)] was used as catalyst. e) nr = no reaction.

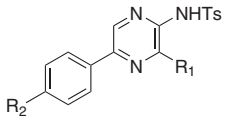
be accomplished when arylboronate ester **4a** (R = OMe) and KOH in MeOH were employed (Table 1, Entries 12 and 13). This result implied that imino-*O*-tosylate **2a** is less reactive than **1a**.

In the previous efforts to couple aryl tosylate with various organoborons in the Suzuki–Miyaura cross-coupling engendered significant stoichiometric inefficiencies as well; reported procedures required either 1.5 or 2.0[4f] equivalent of arylboronic acid or 1.0,[4b] 1.1,[4b] and 1.5[3e] equivalent of arylboronate ester or aryltrifluoroborate.[3,4] In the Table 1, we found that two equivalents of organoborons provided the best yields of the coupling products. A slightly lower yield was obtained when 1.3 equivalent of arylboronate ester was used for the reaction (Table 1, Entries 7 and 13). Less than 30% yield of product was obtained when arylboronic acid or aryltrifluoroborate was used lower than 1.3 equivalent (Table 1, Entries 2 and 10).

Under the optimum condition obtained as above, the coupling reactions of **1a** and **2a** were further examined with various arylboronate esters **4** under the condition [$Pd(OAc)_2$ (4 mol %), **6** (8 mol %), **4** (2.0 equiv), KOH (3.0 equiv), MeOH, bath temp 80 °C]. The results are shown in Table 2. We found that the coupling products between imino-*O*-tosylates **1a** or **2a** and arylboronate esters **4b**, **4c**, and **4e** were obtained in good yields. Less than 20% yield of products were observed, however, when arylboronate esters **4d** and **4f** were used having an electron-donating substituent at the para position of the aromatic ring (Table 2, Entries 3 and 5). The cross-coupling

Table 2. Reaction of Imino-*O*-tosylates **1a** or **2a** with Arylboronate Esters **4b–4f** under Optimum Condition from Table 1[a)]





R_2	R_1 = Ph	R_1 = CH_2-Ph
H	**7b**	**8b**
F	**7c**	**8c**
$N(CH_3)_2$	**7d**	**8d**
O-Ph	**7e**	**8e**
OH	**7f**	**8f**

Entry	Aryl tosylate	R_2 of arylboronate ester **4**	Product (% Yield)[b)]
1	**1a**	**4b**; H	**7b** (89)
2	**1a**	**4c**; F	**7c** (85)
3	**1a**	**4d**; $N(CH_3)_2$	**7d** (17)
4	**1a**	**4e**; *O*-Phenyl	**7e** (74)
5	**1a**	**4f**; OH (O^-)	**7f** (nr)[c)]
6	**2a**	**4b**; H	**8b** (82)
7	**2a**	**4c**; F	**8c** (79)
8	**2a**	**4e**; *O*-Phenyl	**8e** (83)

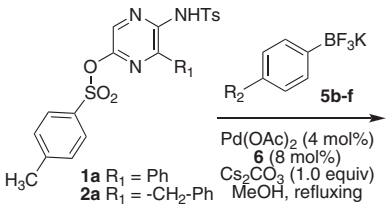
a) Reaction condition: imino-*O*-tosylate **1a** and **2a** (0.10 mmol), arylboronate ester **4b–4f** (2.0 equiv), $Pd(OAc)_2$ (4 mol %), ligand **6** (8 mol %), KOH (3.0 equiv), MeOH (5.0 mL), bath temp 80 °C, 5 h. b) Isolated yield. c) nr = no reaction.

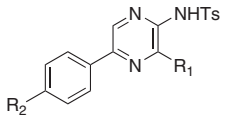
reactions between imino-*O*-tosylate **2a** and arylboronate esters **4d** and **4f** did not observe because of less reactive than **1a**.

In 2002, Miyaura has suggested that the transmetalation step is often faster with more nucleophilic/electron-rich organic fragments, and is inhibited by the steric bulk of the coupling partners.[8] Moreover, Hartwig et al. have found that reductive elimination can often be facilitated by the use of catalysts having a bulky substituent and it is believed that the reaction occurs most rapidly when the two coupling partners have opposite electronic properties, such as one electron-rich and one electron-poor.[9] This, together with the fact that cross-coupling reactions of imino-*O*-tosylate with arylboronate esters containing an electron-donating group attached to the aromatic ring under certain condition do not proceed well (Table 2, Entries 3 and 5), suggests that the reaction rate of the transmetalation step was retarded because of the same electronic property in the two coupling partners (Scheme 2; Cycle 1). Moreover, two equivalents of organoboron is necessary to use in these cross-coupling reactions in order that the rate of reaction in the transmetalation step was accelerated to accomplish the corresponded product in excellent yield within 5 h.

In addition to their air and moisture stability, the greater nucleophilicity of the potassium aryltrifluoroborates makes the organotrifluoroborates valuable coupling partner for palladium-catalyzed cross-coupling. Potassium aryltrifluoroborates can be easily prepared by various methods.

Table 3. Reaction of Imino-*O*-tosylates **1a** or **2a** with Aryltrifluoroborates **5b–5f** under Optimum Condition from Table 1[a)]





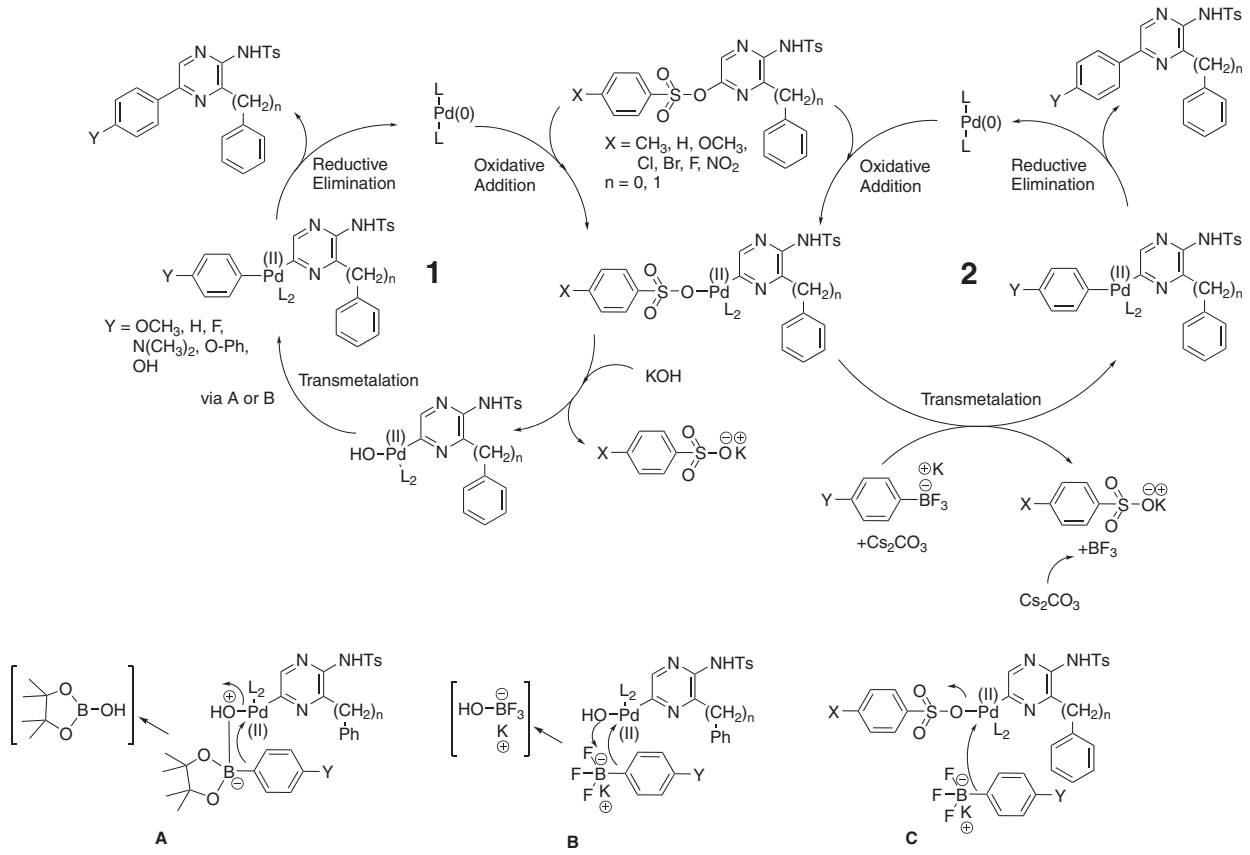
R_2	R_1 = Ph	R_1 = CH_2-Ph
H	**7b**	**8b**
F	**7c**	**8c**
$N(CH_3)_2$	**7d**	**8d**
O-Ph	**7e**	**8e**
OH	**7f**	**8f**

Entry	Aryl tosylate	R_2 of aryltrifluoroborates **5**	Product (% Yield)[b)]
1	**1a**	**5b**; H	**7b** (90)
2	**1a**	**5c**; F	**7c** (99)
3	**1a**	**5d**; $N(CH_3)_2$	**7d** (78)[c)]
4	**1a**	**5d**; $N(CH_3)_2$	**7d** (100)
5	**1a**	**5e**; *O*-Phenyl	**7e** (84)
6	**1a**	**5f**; OH	**7f** (98)[c)]
7	**1a**	**5f**; OH	**7f** (97)
8	**2a**	**5b**; H	**8b** (93)
9	**2a**	**5c**; F	**8c** (84)
10	**2a**	**5d**; $N(CH_3)_2$	**8d** (13)[c)]
11	**2a**	**5d**; $N(CH_3)_2$	**8d** (93)
12	**2a**	**5e**; *O*-Phenyl	**8e** (100)
13	**2a**	**5f**; OH	**8f** (95)[c)]
14	**2a**	**5f**; OH	**8f** (100)

a) Reaction condition: imino-*O*-tosylate **1a** and **2a** (0.10 mmol), aryltrifluoroborate **5b–5f** (2.0 equiv), $Pd(OAc)_2$ (4 mol %), ligand **6** (8 mol %), Cs_2CO_3 (1.0 equiv), MeOH (5.0 mL), bath temp 80 °C, 5 h. b) Isolated yield. c) KOH (3.0 equiv) was used as a base in the reaction.

Addition of inexpensive, aqueous KHF_2 to either an arylboronic acid or arylboronate ester will also afford the potassium organotrifluoroborate directly.[3] We examined the coupling reactions between **1a** or **2a** and various potassium aryltrifluoroborates **5b–5f** under similar optimized conditions. The results from these studies are shown in Table 3. We found that the coupling products could be obtained in excellent yields even in the cases of aryltrifluoroborates containing an electron-donating group attached at the para position of the aromatic ring. Moreover, yields of the coupling products were improved when Cs_2CO_3 was employed as a base instead of KOH. Together with our previous report,[6] this procedure can be applied to synthesize various coelenterazine analogs for chemical biology studies.

Stille et al. have reported the reactivity relationships of aryl triflates and halides such as bromide and chloride.[10a] The order of halide reactivity in oxidative addition processes is: $I > Br \approx OTf \gg Cl$.[10] The relative rate of oxidative addition of various aromatic halides is roughly proportional to the relative rate of S_NAr transformations of these substrates.[8,11] In the current report, we have focused on the relative reactivity of



Scheme 2. Mechanism of Suzuki–Miyaura cross-coupling between imino-*O*-arenesulfonates and organoborons.

imino-*O*-arenesulfonates containing various substituents at the para position **1a**–**1g** and **2a**–**2g**.

The reactivity relationships of these compounds were studied in the Suzuki–Miyaura cross-coupling reaction with 4-methoxyphenylboronate ester under the condition [$Pd(OAc)_2$ (4 mol %), **6** (8 mol %), **4a** (1.0 equiv), KOH (1.5 equiv), MeOH, bath temp 80 °C]. These competitive reaction processes were monitored by means of HPLC in terms of consumption of the starting materials and increasing of product. Due to the separation capacity in HPLC retention times, we implemented measures in the four-compound groups of imino-*O*-arenesulfonates for determining the relative rates in the cross-coupling reactions under the similar condition. However, the concentration of arylboronate esters against the concentration of imino-*O*-arenesulfonates cannot be controlled in the same amount for all groups due to small scale of the reactions (Figure 1).

After the HPLC monitoring the substituent effects at the X position in imino-*O*-arenesulfonates **1a**–**1g** and **2a**–**2g** for the cross-coupling reactions, the order of reactivity is as follows: $Br > Cl > NO_2 \approx CH_3 > OCH_3 \approx F > H$ (from Scheme 3, Figure 1). Having an electron-withdrawing group at the para position may activate the arenesulfonate so that it practically becomes a facile leaving group expected to result in the reaction proceeding faster. This implied that the oxidative addition step is the most important in the palladium-catalyzed Suzuki–Miyaura cross-coupling reaction (Scheme 2).

In the case of Br or Cl substituent on arenesulfonates **1d**, **1e** and **2d**, **2e**, the reaction might furnish possibly the corresponding **7a** or **8a**. After these experiments, the results were carefully examined. None of the cross-coupling products were resulted from any further reaction at the halide substituent attached to the arenesulfonate (such as **9** or **10** in Scheme 3). The absence of these side products was also confirmed by the mass spectrometric analysis. These results indicated that the sulfonate group of the imino-*O*-tosylate is more reactive than the Cl and Br substituents on arenesulfonate.

The catalytic cycle of the palladium-catalyzed Suzuki–Miyaura cross-coupling reaction is thought to follow a sequence involving the oxidative addition of imino-*O*-arenesulfonate to a Pd^0 complex to form heteroarylpalladium(II) arenesulfonate intermediate. The order of reactivity of imino-*O*-arenesulfonates containing various substituents at the para position was found that there is a major difference in the rates of the reactions when changing from electron-donating groups to electron-withdrawing groups at the para position of arenesulfonates. Transmetalation with arylboronic acid, arylboronate ester, or aryltrifluoroborate and reductive elimination from the resulting diarylpalladium complex affords the corresponding biaryl and regenerates the Pd^0 complex (Scheme 2).[12] At present, the selection of bases in Suzuki–Miyaura cross-coupling reaction is still empirical, and no general rule for their selection has been reported. The base in these reactions is to replace the arenesulfonate in the coordination sphere of the palladium complex and to facilitate an intramolecular transmetalation (Scheme 2; Cycle 1).[8] Alternatively, it has also been facilitated the otherwise slow transmetalation of the arylboronic acid by forming a more reactive

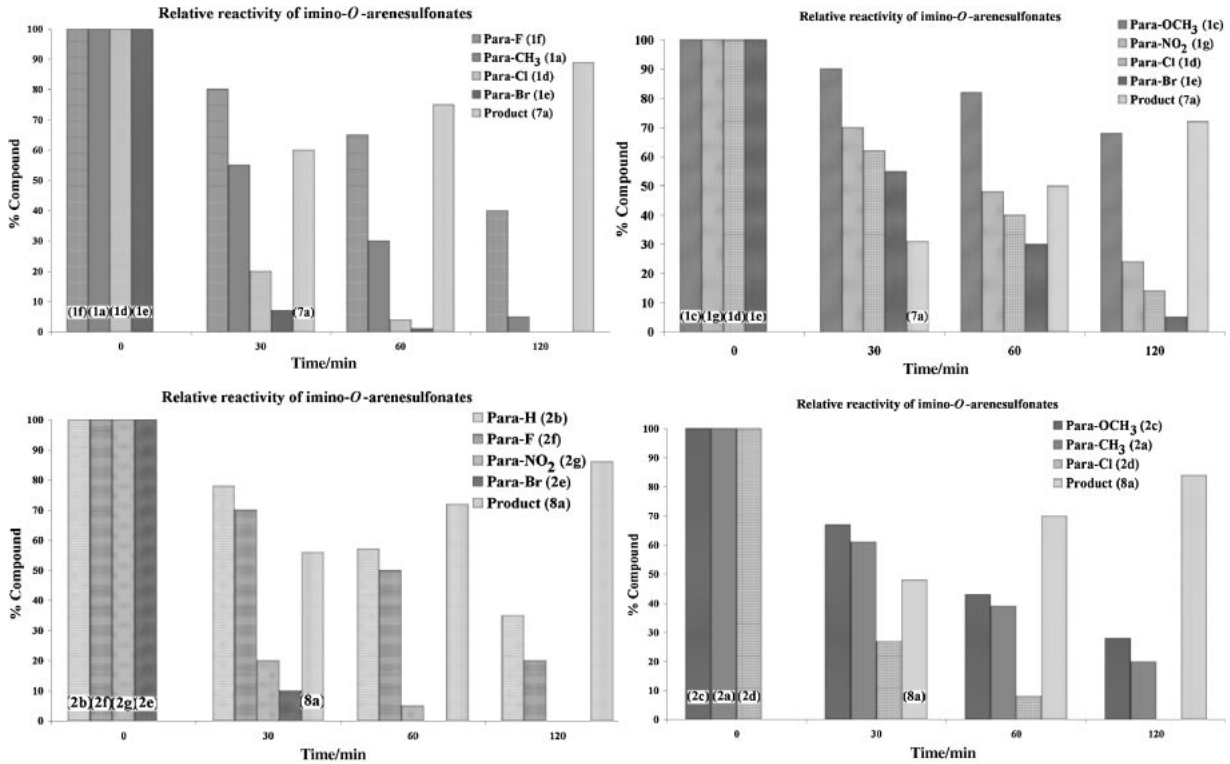
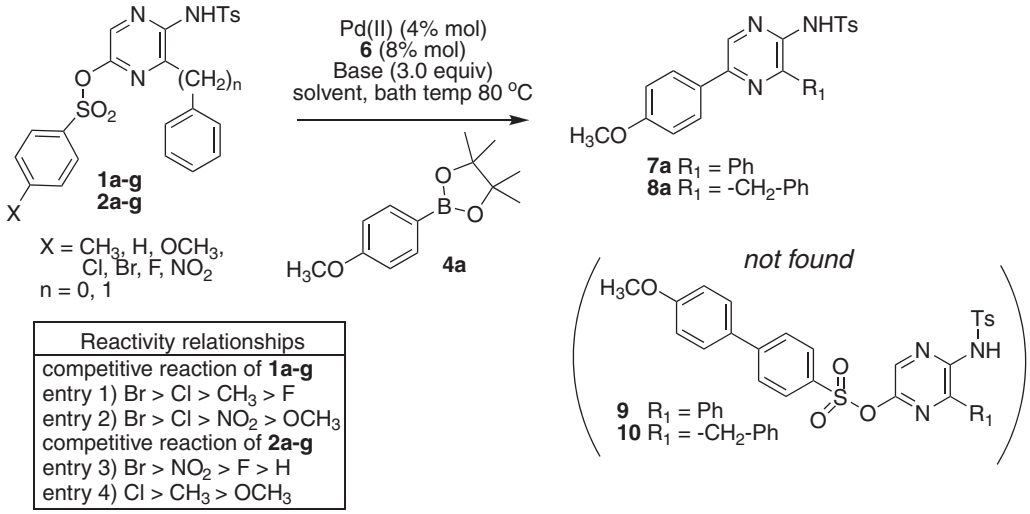


Figure 1. Relative reactivity of imino-*O*-arenesulfonates containing various substituents at the para position **1a**–**1g** and **2a**–**2g** in Suzuki–Miyaura cross-coupling reaction.



Scheme 3. Reactivity relationships of imino-*O*-arenesulfonates **1a**–**1g** and **2a**–**2g**.

arylboronate species that can react with the Pd center and transmetalate in an intramolecular reaction.[13] In the case of aryltrifluoroborate, the base is to facilitate transmetalation step that can react to form diarylpalladium complex and to neutralize the boron trifluoride, a residue from the reaction (Scheme 2; Cycle 2). The cross-coupling reactions of arylboronate ester, a coupling partner, containing an electron-donating group attached to the aromatic ring were demonstrated quite low yield because boron atom was reduced electrophilicity for interaction with OH in the transmetalation step. On the other hand, arylboronate esters containing an electron-withdrawing group Y attached to the aromatic ring were observed in good yield because of the higher electrophilicity of boron atom (Scheme 2; Part A). However, the electrophilicity of boron atom of aryltrifluoroborate is the highest when compare with arylboronate ester and arylboronic acid. A facile transmetalation in the Suzuki–Miyaura cross-coupling reaction was occurred when aryltrifluoroborate was employed in the reaction. KOH is to facilitate transmetalation step by replacing the arenesulfonate to form the active form of Pd complex which is ready to react with aryltrifluoroborate (Scheme 2; Part B). However, Cs_2CO_3 is to facilitate trans-

metalation step by activation the cleavage in B–C bond of aryltrifluoroborate and to neutralize the boron trifluoride (Scheme 2; Part C). The results indicate that there are highly dependent on organoboron reagents, bases, and presumably also electron-donating or electron-withdrawing group and the functionality therein.

Conclusion

We have accomplished the Suzuki–Miyaura cross-coupling of imino-*O*-tosylates with organoborons using electron-donating and electron-withdrawing groups attached to the aromatic ring. Aryltrifluoroborate is more reactive than arylboronate ester and arylboronic acid in these cross-coupling reactions. This study is also the first report regarding the effect of the relative reactivity of the para substituent in arenesulfonates in Suzuki–Miyaura cross-coupling.

Experimental

General Procedure. Melting points were determined by using a Yanaco MP-S3 and uncorrected. Infrared (IR) spectra were recorded in cm^{-1} and determined in NaCl cells by using a JASCO FT/IR-6100 FT-IR spectrometer. Proton NMR spectra were recorded on a Bruker AMX-400 for 400 MHz and Carbon NMR were recorded on a Bruker AMX-400 for 100 MHz. Chemical shifts (δ) were reported in parts per million (ppm) relative to tetramethylsilane (TMS). Deuterochloroform ($CDCl_3$) were used as solvent. The following abbreviations were used for multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, brt = broad triplet, dd = double of doublet, and ddd = double of double of doublet. Coupling constants (J) were reported in hertz (Hz). EI mass spectra and FAB mass spectra were performed with a JEOL JMS-700. High-resolution (HR) mass spectra were measured with JEOL JMS-700. All experiments were performed in the positive ion mode. Elemental analyses were performed by Analytical Laboratory. High-performance liquid chromatography (or High-pressure liquid chromatography, HPLC) was performed on a JASCO Gulliver system composed of two PU-980 pumps, and UV-970 UV/VIS detector and an 807-IT integrator. The system was equipped with a Devolosil ODS-5 column ($4.6 \times 250\,mm^2$). Analytical thin-layer chromatography (tlc) was conducted on precoated tlc plates: silica gel 60 F-254, layer thickness 0.25 mm. Silica gel column chromatography utilized Silica Gel 60 (spherical) 40–50 μm. The components were detected by visualization under ultraviolet light at λ of 254 and 315 nm. The organic solvents utilized in extraction, and eluent for column chromatography were of commercial grade. The organic solvents utilized for crystallization were of analytical grade.

Synthesis of the Imino-*O*-tosylates 1a–1g and the Homologs 2a–2g. The imino-*O*-tosylates **1a**–**1g** and the homologs **2a**–**2g** were synthesized by following the reference 6b. The information of the imino-*O*-tosylates **1a**–**1g** and homologs **2a**–**2g** were shown as below.

Compound 1a: Yield 80%; Melting point: 159–160 °C; IR (NaCl film): ν_{max} 3436, 1639, 1434, 1377, 1336, 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 2.44 (s, 3H), 7.27–7.37 (m, 4H), 7.39–7.60 (m, 6H), 7.83 (d, J = 7.9 Hz, 2H), 7.97 (d, J = 7.9 Hz, 2H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 21.7, 128.4, 128.5, 128.8, 129.4, 129.5, 129.7, 130.4, 133.2, 133.5, 133.6, 136.3, 140.0, 143.4, 144.7, 145.7, 148.9; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_5S_2^+$: 496.100, found: 496.102; Elemental analysis calcd for $C_{24}H_{21}N_3O_5S_2$: C, 58.17; H, 4.27; N, 8.48%. Found: C, 57.95; H, 4.26; N, 8.33%.

Compound 1b: Yield 75%; Melting point: 165–166 °C; IR (NaCl film): ν_{max} 3429, 1639, 1434, 1378, 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.44 (s, 3H), 7.32 (d, J = 8.2 Hz, 2H), 7.40–7.56 (m, 8H), 7.64–7.70 (m, 1H), 7.93–8.00 (m, 4H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 128.3, 128.6, 128.7, 129.1, 129.5, 130.4, 133.4, 133.5, 134.4, 136.3, 140.0, 143.5, 144.7, 148.8; HRMS (FAB+) calcd for $C_{23}H_{20}N_3O_5S_2^+$: 482.084, found: 482.083; Elemental analysis calcd for $C_{23}H_{19}N_3O_5S_2$: C, 57.37; H, 3.98; N, 8.73%. Found: C, 57.22; H, 3.96; N, 8.74%.

Compound 1c: Yield 74%; Melting point: 53–54 °C; IR (NaCl film): ν_{max} 3437, 1639, 1597, 1497, 1434, 1376, 1166 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 3.87 (s, 3H), 6.95 (d, J = 9.0 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.42–7.54 (m, 6H), 7.84–7.90 (m, 2H), 7.96 (d, J = 8.3 Hz, 2H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 55.8, 114.3, 127.4, 128.4, 128.5, 129.4, 129.5, 130.4, 131.1, 133.5, 133.6, 136.3, 140.0, 143.3, 144.7, 148.9, 164.3; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_6S_2^+$: 512.095, found: 512.092; Elemental analysis calcd for $C_{24}H_{21}N_3O_6S_2$: C, 56.35; H, 4.14; N, 8.21%. Found: C, 56.20; H, 3.97; N, 8.27%.

Compound 1d: Yield 76%; Melting point: 57–58 °C; IR (NaCl film): ν_{max} 3428, 1639, 1439, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.44 (s, 3H), 7.28–7.35 (m, 2H), 7.39–7.57 (m, 8H), 7.89 (d, J = 8.6 Hz, 2H), 7.97 (d, J = 8.3 Hz, 2H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 128.3, 128.6, 129.4, 129.5, 129.6, 130.3, 130.5, 133.3, 133.4, 134.8, 136.2, 140.0, 141.2, 143.6, 144.7, 148.7; HRMS (FAB+) calcd for $C_{23}H_{19}ClN_3O_5S_2^+$: 516.046, found: 516.041; Elemental analysis calcd for $C_{23}H_{18}ClN_3O_5S_2$: C, 53.54; H, 3.52; N, 8.14%. Found: C, 53.35; H, 3.72; N, 8.02%.

Compound 1e: Yield 70%; Melting point: 169–170 °C; IR (NaCl film): ν_{max} 3402, 2958, 1726, 1638, 1576, 1433, 1382, 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 7.32 (d, J = 8.2 Hz, 2H), 7.38–7.45 (m, 2H), 7.47–7.56 (m, 4H), 7.61–7.68 (m, 2H), 7.77–7.85 (m, 2H), 7.97 (d, J = 8.3 Hz, 2H), 8.07 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 128.3, 128.5, 129.4, 129.6, 129.8, 130.3, 130.5, 132.4, 133.3, 135.4, 136.2, 140.0, 143.6, 144.7, 148.7; HRMS (FAB+) calcd for $C_{23}H_{19}BrN_3O_5S_2^+$: 559.995, found: 559.993; Elemental analysis calcd for $C_{23}H_{18}BrN_3O_5S_2$: C, 49.29; H, 3.24; N, 7.50%. Found: C, 49.17; H, 3.09; N, 7.47%.

Compound 1f: Yield 81%; Melting point: 80–81 °C; IR (NaCl film): ν_{max} 3437, 1638, 1493, 1436, 1381, 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 7.13–7.23 (m, 2H), 7.28–7.35 (m, 2H), 7.39–7.59 (m, 6H), 7.92–8.03 (m, 4H), 8.07 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 116.3, 116.6, 128.3, 128.5, 129.4, 129.6, 130.5, 131.7, 131.8, 132.3, 133.3, 133.4, 136.2, 140.0, 143.5, 144.7, 148.8, 164.8, 167.4; HRMS (FAB+) calcd for $C_{23}H_{19}FN_3O_5S_2^+$: 500.075, found: 500.076; Elemental analysis calcd for $C_{23}H_{18}FN_3O_5S_2$: C, 55.30; H, 3.63; N, 8.41%. Found: C, 55.20; H, 3.74; N, 8.13%.

Compound 1g: Yield 87%; Melting point: 69–70 °C; IR (NaCl film): ν_{max} 3268, 3106, 1725, 1534, 1436, 1350, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.43 (s, 3H), 7.32 (d, J = 8.1 Hz, 2H), 7.37–7.44 (m, 2H), 7.45–7.63 (m, 4H), 7.96 (d, J = 8.2 Hz, 2H), 8.10 (s, 1H), 8.17 (d, J = 8.8 Hz, 2H), 8.31 (d, J = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 124.1, 128.2, 128.5, 129.4, 129.6, 130.2, 130.7, 133.1, 136.1, 140.0, 142.2, 143.8, 144.8, 148.6, 150.9; HRMS (FAB+) calcd for $C_{23}H_{19}N_4O_7S_2^+$: 527.070, found: 527.068; Elemental analysis calcd for $C_{23}H_{18}N_4O_7S_2$: C, 52.46; H, 3.45; N, 10.64%. Found: C, 52.46; H, 3.38;

N, 10.43%.

Compound 2a: Yield 76%; Melting point: 136–137 °C; IR (NaCl film): ν_{max} 3281, 3064, 1597, 1496, 1439, 1377, 1176 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 2.45 (s, 3H), 4.01 (s, 2H), 6.79–7.00 (m, 1H), 7.00–7.09 (m, 2H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.27–7.70 (m, 5H), 7.67 (d, $J = 8.3$ Hz, 2H), 7.79 (d, $J = 8.3$ Hz, 2H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 21.8, 39.8, 127.7, 128.3, 128.6, 128.7, 129.4, 129.8, 133.1, 133.3, 135.1, 136.0, 144.5, 145.7; HRMS (FAB+) calcd for $C_{25}H_{24}N_3O_5S_2^+$: 510.116, found: 510.114; Elemental analysis calcd for $C_{25}H_{23}N_3O_5S_2$: C, 58.92; H, 4.55; N, 8.25%. Found: C, 58.85; H, 4.41; N, 8.05%.

Compound 2b: Yield 75%; Melting point: 128–130 °C; IR (NaCl film): ν_{max} 3279, 3064, 1597, 1439, 1378, 1188 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 3.99 (s, 2H), 6.99–7.06 (m, 2H), 7.07–7.18 (m, 1H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.27–7.33 (m, 3H), 7.46–7.55 (m, 2H), 7.62–7.73 (m, 3H), 7.90 (d, $J = 7.6$ Hz, 2H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.5, 127.6, 128.2, 128.6, 128.7, 129.1, 129.3, 129.4, 134.4, 135.1, 136.0, 136.2, 144.5, 148.6; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_5S_2^+$: 496.100, found: 496.099; Elemental analysis calcd for $C_{24}H_{21}N_3O_5S_2$: C, 58.17; H, 4.27; N, 8.48%. Found: C, 58.27; H, 4.20; N, 8.65%.

Compound 2c: Yield 75%; Melting point: 134–135 °C; IR (NaCl film): ν_{max} 3437, 1638, 1596, 1578, 1497, 1439, 1376, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 3.87 (s, 3H), 4.02 (s, 2H), 6.90–6.97 (m, 2H), 7.00–7.11 (m, 3H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.28–7.35 (m, 3H), 7.69 (d, $J = 8.4$ Hz, 2H), 7.78–7.85 (m, 2H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.6, 55.7, 114.3, 127.2, 127.6, 128.2, 128.7, 129.3, 129.4, 131.0, 133.3, 135.1, 136.0, 142.5, 144.3, 144.5, 148.8, 164.3; HRMS (FAB+) calcd for $C_{25}H_{24}N_3O_6S_2^+$: 526.111, found: 526.108; Elemental analysis calcd for $C_{25}H_{23}N_3O_6S_2$: C, 57.13; H, 4.41; N, 7.99%. Found: C, 57.27; H, 4.34; N, 7.70%.

Compound 2d: Yield 75%; Melting point: 57–58 °C; IR (NaCl film): ν_{max} 3284, 3090, 1586, 1439, 1382, 1188 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 4.00 (s, 2H), 6.97–7.06 (m, 2H), 7.18–7.35 (m, 6H), 7.44 (d, $J = 8.6$ Hz, 2H), 7.69–7.76 (m, 2H), 7.79 (d, $J = 8.6$ Hz, 2H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.3, 127.6, 128.3, 128.7, 129.3, 129.4, 130.0, 133.0, 134.6, 135.0, 136.0, 141.1, 142.6, 144.5, 144.6, 148.6; HRMS (FAB+) calcd for $C_{24}H_{21}ClN_3O_5S_2^+$: 530.061, found: 530.059; Elemental analysis calcd for $C_{24}H_{20}ClN_3O_5S_2$: C, 54.39; H, 3.80; N, 7.93%. Found: C, 54.48; H, 3.66; N, 7.79%.

Compound 2e: Yield 71%; Melting point: 52–54 °C; IR (NaCl film): ν_{max} 3431, 1639, 1575, 1439, 1393, 1188 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 4.00 (s, 2H), 6.98–7.07 (m, 2H), 7.15–7.28 (m, 3H), 7.28–7.36 (m, 3H), 7.58–7.64 (m, 2H), 7.72 (d, $J = 8.5$ Hz, 4H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.4, 127.6, 128.3, 128.7, 129.3, 129.4, 129.8, 130.1, 132.5, 133.1, 135.0, 135.2, 136.0, 142.6, 144.5, 144.6, 148.7; HRMS (FAB+) calcd for $C_{24}H_{21}BrN_3O_5S_2^+$: 574.011, found: 574.010; Elemental analysis calcd for $C_{24}H_{20}BrN_3O_5S_2$: C, 50.18; H, 3.51; N, 7.31%. Found: C, 50.33; H, 3.37; N, 7.12%.

Compound 2f: Yield 76%; Melting point: 39–40 °C; IR (NaCl film): ν_{max} 3421, 1592, 1495, 1439, 1381, 1187 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H), 4.00 (s, 2H), 6.99–7.06 (m, 2H), 7.09–7.17 (m, 2H), 7.20–7.27 (m, 2H), 7.27–7.34 (m, 3H), 7.35–7.54 (m, 1H), 7.73 (d, $J = 8.3$ Hz, 2H), 7.82–7.91 (m, 2H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.2, 116.4, 116.6, 127.5, 128.2, 128.8, 129.2, 129.4, 131.5, 131.6, 132.1, 133.1, 135.1, 136.0, 144.5, 148.6, 164.7, 167.3; HRMS (FAB+) calcd for $C_{24}H_{21}FN_3O_5S_2^+$: 514.091, found: 514.091; Elemental analysis calcd for $C_{24}H_{20}FN_3O_5S_2$: C, 56.13; H, 3.93; N, 8.18%. Found: C, 56.26; H, 3.89; N, 8.08%.

Compound 2g: Yield 80%; Melting point: 64–65 °C; IR (NaCl film): ν_{max} 3402, 1638, 1609, 1534, 1439, 1387, 1187 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.41 (s, 3H), 3.98 (s, 2H), 6.96–7.04 (m, 2H), 7.22–7.45 (m, 6H), 7.76 (d, $J = 8.3$ Hz, 2H), 7.96–8.08 (m, 3H), 8.21–8.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 39.1, 124.2, 127.6, 128.3, 128.9, 129.2, 129.5, 129.9, 133.0, 134.9, 136.0, 141.9, 142.7, 144.7, 144.8, 148.6, 150.8; HRMS (FAB+) calcd for $C_{24}H_{21}N_4O_7S_2^+$: 541.085, found: 541.086; Elemental analysis calcd for $C_{24}H_{20}N_4O_7S_2$: C, 53.32; H, 3.73; N, 10.36%. Found: C, 53.48; H, 3.79; N, 10.13%.

Synthesis of Amino(aryl)pyrazines 7a–7f and 8a–8f. General Procedure for Conversion of Arylboronic Acids into Arylboronate Esters: *p*-TsOH·H_2O (7 mol %) was added to a stirred solution of arylboronic acid (1.5 mmol) and pinacol hexahydrate (5.0 mmol) in toluene (15 mL). The mixture solution was heated to reflux for 16 h in an apparatus incorporating a Dean–Stark trap. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was then dissolved with EtOAc (15 mL) before being washed with water (5 mL × 3) and brine, respectively. The organic phase was dried over anh. Na_2SO_4 and concentrated under reduced pressure to give arylboronate ester.

General Procedure for Conversion of Arylboronic Acids into Potassium Aryltrifluoroborates: Arylboronic acid (ca. 0.3 g) was dissolved in 1 mL of methanol. Excess saturated KHF_2 (ca. 1 mL) was slowly added with vigorous stirring. After 15 min, the precipitated product was obtained. The mixture was filtrated and the residue was washed with cool methanol and then dried under reduced pressure. The product was used further without any purification.

General Procedure for the Palladium-Catalyzed Cross-Coupling Reactions of Imino-*O*-tosylates with Organo Borons: Under a Argon atmosphere, imino-*O*-tosylates (0.10 mmol), organo boron (2.0 equiv), $Pd(OAc)_2$ (4 mol %), ligand **6** (8 mol %), and KOH (3.0 equiv) (or Cs_2CO_3 (1.0 equiv)) in MeOH (5.0 mL) as a solvent was refluxed at 80 °C for a period of time. After 5 h, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure. The residue was then dissolved with EtOAc (15 mL) before being washed with water (5 mL × 2) and brine, respectively. The organic phase was then dried over anh. Na_2SO_4 and concentrated to dryness under reduced pressure to give crude product, which was purified by silica gel column chromatography to provide the corresponding product.

The information of amino(aryl)pyrazines **7a–7f** and **8a–8f** were shown as below.

Compound 7a: Melting point: 181.5–182.5 °C; IR (NaCl film): ν_{max} 3429, 1638, 1609, 1515, 1456, 1435, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.38–2.45 (m, 3H), 3.82–3.86 (m, 3H), 6.93–7.00 (m, 2H), 7.31 (d, $J = 8.1$ Hz, 2H), 7.44 (bs, 1H), 7.49–7.60 (m, 3H), 7.64–7.72 (m, 2H), 7.90 (d, $J = 8.9$ Hz, 2H), 8.02 (d, $J = 8.3$ Hz, 2H), 8.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 55.3, 114.3, 127.7, 128.5, 129.3, 129.5, 129.8, 135.4, 136.8, 141.7, 142.9, 144.3, 146.8, 160.6; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_3S^+$: 432.138, found: 432.143; Elemental analysis calcd for $C_{24}H_{21}N_3O_3S$: C, 66.80; H, 4.91; N, 9.74%. Found: C, 66.81; H, 5.02; N, 9.58%.

Compound 7b: Melting point: 132–133 °C; IR (NaCl film):

ν_{max} 3250, 1595, 1451, 1437, 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.42 (s, 3H), 7.32 (d, $J = 8.2$ Hz, 2H), 7.37–7.48 (m, 4H), 7.50–7.61 (m, 3H), 7.66–7.73 (m, 2H), 7.94 (d, $J = 7.0$ Hz, 2H), 8.03 (d, $J = 8.3$ Hz, 2H), 8.61 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 126.4, 128.6, 128.9, 129.2, 129.4, 129.6, 130.0, 134.7, 135.3, 136.0, 136.7, 137.5, 141.8, 143.6, 144.4, 146.9; HRMS (FAB+) calcd for $C_{23}H_{20}N_3O_2S^+$: 402.128, found: 402.130; Elemental analysis calcd for $C_{23}H_{19}N_3O_2S$: C, 68.81; H, 4.77; N, 10.47%. Found: C, 68.79; H, 4.85; N, 10.29%.

Compound 7c: Melting point: 74–75 °C; IR (NaCl film): ν_{max} 3378, 1603, 1510, 1456, 1438, 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.42 (s, 3H), 7.08–7.17 (m, 2H), 7.32 (d, $J = 8.18$ Hz, 2H), 7.45–7.50 (m, 1H), 7.50–7.61 (m, 3H), 7.68 (d, $J = 6.9$ Hz, 2H), 7.89–7.97 (m, 2H), 8.03 (d, $J = 8.3$ Hz, 2H), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 115.8, 116.0, 128.1, 128.2, 128.5, 129.4, 129.6, 130.0, 132.1, 135.2, 136.7, 137.1, 141.8, 143.5, 144.4, 145.9, 162.4, 164.8; HRMS (FAB+) calcd for $C_{23}H_{19}FN_3O_2S^+$: 420.118, found: 420.122; Elemental analysis calcd for $C_{23}H_{18}FN_3O_2S$: C, 65.86; H, 4.33; N, 10.02%. Found: C, 65.80; H, 4.41; N, 10.21%.

Compound 7d: Melting point: 175.5–176.5 °C; IR (NaCl film): ν_{max} 3248, 1609, 1526, 1456, 1434, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.41 (s, 3H), 3.00 (s, 6H), 6.75 (d, $J = 9.0$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 7.32–7.41 (m, 1H), 7.47–7.59 (m, 3H), 7.68 (d, $J = 6.9$ Hz, 2H), 7.85 (d, $J = 8.9$ Hz, 2H), 8.00 (d, $J = 8.3$ Hz, 2H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.3, 112.2, 123.7, 127.3, 128.4, 128.6, 129.3, 129.4, 129.7, 135.8, 136.3, 137.0, 142.1, 144.1, 144.9, 151.2; HRMS (FAB+) calcd for $C_{25}H_{25}N_4O_2S^+$: 445.170, found: 445.173; Elemental analysis calcd for $C_{25}H_{24}N_4O_2S$: C, 67.54; H, 5.44; N, 12.60%. Found: C, 67.37; H, 5.47; N, 12.72%.

Compound 7e: Melting point: 177–178 °C; IR (NaCl film): ν_{max} 3274, 3255, 1588, 1489, 1455, 1438, 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.42 (s, 3H), 7.00–7.09 (m, 4H), 7.09–7.17 (m, 1H), 7.28–7.39 (m, 4H), 7.42–7.48 (m, 1H), 7.49–7.60 (m, 3H), 7.65–7.72 (m, 2H), 7.88–7.94 (m, 2H), 7.98–8.06 (m, 2H), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 116.3, 117.6, 118.8, 119.3, 121.0, 123.7, 127.9, 128.5, 129.4, 129.5, 129.8, 129.9, 135.3, 137.1, 143.3, 144.3, 156.6, 158.6; HRMS (FAB+) calcd for $C_{29}H_{24}N_3O_3S^+$: 494.154, found: 494.155.

Compound 7f: Melting point: 80–81 °C; IR (NaCl film): ν_{max} 3415, 1611, 1436, 1148 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.42 (s, 3H), 5.09–5.40 (m, 1H), 6.88 (d, $J = 8.6$ Hz, 2H), 7.31 (d, $J = 8.2$ Hz, 2H), 7.37–7.45 (m, 1H), 7.49–7.59 (m, 3H), 7.68 (d, $J = 6.8$ Hz, 2H), 7.83 (d, $J = 8.6$ Hz, 2H), 8.01 (d, $J = 8.2$ Hz, 2H), 8.51 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 115.8, 127.9, 128.5, 128.6, 129.4, 129.5, 129.9, 135.4, 136.8, 142.9, 144.3, 156.9; HRMS (FAB+) calcd for $C_{23}H_{20}N_3O_3S^+$: 418.123, found: 418.120; Elemental analysis calcd for $C_{23}H_{19}N_3O_3S$: C, 66.17; H, 4.59; N, 10.07%. Found: C, 66.18; H, 4.75; N, 9.83%.

Compound 8a: Melting point: 170–171 °C; IR (NaCl film): ν_{max} 3437, 1607, 1515, 1451, 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H), 3.86 (s, 3H), 4.25 (s, 2H), 6.85–6.91 (bs, 1H), 6.98 (d, $J = 8.8$ Hz, 2H), 7.17–7.25 (m, 4H), 7.28–7.39 (m, 3H), 7.69 (d, $J = 8.3$ Hz, 2H), 7.88 (d, $J = 8.6$ Hz, 2H), 8.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.7, 55.4, 114.4, 127.5, 127.7, 128.2, 128.7, 129.3, 129.4, 136.1, 136.5, 136.7, 143.5, 143.8, 144.1, 146.9, 160.7; HRMS (FAB+) calcd for $C_{25}H_{24}N_3O_3S^+$: 446.154, found: 446.152; Elemental analysis calcd for $C_{25}H_{23}N_3O_3S$: C, 67.40; H, 5.20; N, 9.43%. Found: C, 67.40; H, 5.12; N, 9.26%.

Compound 8b: Melting point: 163–164 °C; IR (NaCl film): ν_{max} 3236, 1589, 1496, 1451, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H), 4.26 (s, 2H), 6.99–7.15 (m, 1H), 7.16–7.50 (m, 10H), 7.71 (d, $J = 8.3$ Hz, 2H), 7.81–8.01 (m, 2H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.6, 126.3, 127.5, 128.2, 128.7, 128.9, 129.2, 129.3, 136.1, 136.4, 137.2, 143.4, 144.2, 144.5, 146.8; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_2S^+$: 416.143, found: 416.141; Elemental analysis calcd for $C_{24}H_{21}N_3O_2S$: C, 69.37; H, 5.09; N, 10.11%. Found: C, 69.35; H, 5.22; N, 9.85%.

Compound 8c: Melting point: 181–182 °C; IR (NaCl film): ν_{max} 3235, 1602, 1511, 1449, 1158 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H), 4.24 (s, 2H), 7.06–7.25 (m, 7H), 7.27–7.39 (m, 3H), 7.72 (d, $J = 8.3$ Hz, 2H), 7.81–7.97 (m, 2H), 8.33–8.61 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.5, 115.8, 116.0, 127.4, 127.5, 128.1, 128.2, 128.3, 128.7, 129.3, 129.4, 132.2, 136.0, 136.9, 144.5, 145.9, 162.4; HRMS (FAB+) calcd for $C_{24}H_{21}FN_3O_2S^+$: 434.134, found: 434.135; Elemental analysis calcd for $C_{24}H_{20}FN_3O_2S$: C, 66.50; H, 4.65; N, 9.69%. Found: C, 66.51; H, 4.80; N, 9.46%.

Compound 8d: Melting point: 193–194 °C; IR (NaCl film): ν_{max} 3248, 1609, 1525, 1440, 1363, 1325, 1164 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.37 (s, 3H), 3.01 (s, 6H), 4.23 (s, 2H), 6.76 (d, $J = 9.0$ Hz, 2H), 6.79–6.89 (m, 1H), 7.14–7.41 (m, 7H), 7.69 (d, $J = 8.3$ Hz, 2H), 7.74–7.92 (m, 2H), 8.31–8.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.3, 112.3, 127.2, 128.0, 128.1, 128.8, 129.1, 129.2, 136.1, 136.2, 136.6, 143.0, 143.8, 143.9, 151.2; HRMS (FAB+) calcd for $C_{26}H_{27}N_4O_2S^+$: 459.186, found: 459.187; Elemental analysis calcd for $C_{26}H_{26}N_4O_2S$: C, 68.10; H, 5.71; N, 12.22%. Found: C, 68.13; H, 5.60; N, 12.09%.

Compound 8e: Melting point: 155–156 °C; IR (NaCl film): ν_{max} 3227, 3061, 1589, 1490, 1449, 1400, 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.37 (s, 3H), 4.24 (s, 2H), 7.00–7.17 (m, 6H), 7.17–7.39 (m, 9H), 7.72 (d, $J = 8.3$ Hz, 2H), 7.79–7.97 (m, 2H), 8.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.55, 40.53, 118.8, 119.3, 123.7, 127.8, 128.2, 128.7, 129.3, 129.8, 136.8, 144.2, 156.6, 158.6; HRMS (FAB+) calcd for $C_{30}H_{26}N_3O_3S^+$: 508.170, found: 508.170; Elemental analysis calcd for $C_{30}H_{25}N_3O_3S$: C, 70.98; H, 4.96; N, 8.28%. Found: C, 70.99; H, 5.19; N, 7.99%.

Compound 8f: Melting point: 177–178 °C; IR (NaCl film): ν_{max} 3436, 1638, 1447, 1164 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.37 (s, 3H), 4.23 (s, 2H), 5.43–6.01 (m, 1H), 6.87 (d, $J = 8.6$ Hz, 2H), 6.93–7.11 (m, 1H), 7.14–7.41 (m, 7H), 7.62–7.87 (m, 4H), 8.23–8.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 40.6, 115.9, 127.3, 127.8, 128.7, 128.8, 129.2, 129.3, 136.3, 143.8, 143.9, 144.0, 156.9; HRMS (FAB+) calcd for $C_{24}H_{22}N_3O_3S^+$: 432.138, found: 432.137.

General Procedure for Competitive Reaction of Imino-*O*-arenesulfonates Containing Various Substituents at the Para Position 1a–1g and 2a–2g in Suzuki–Miyaura Cross-Coupling Reaction with 4-Methoxyphenylboronate Ester (4; OMe). Each of imino-*O*-arenesulfonates (ca. 1 mg) or amino(aryl)pyrazines **7a**, **8a** (ca. 1 mg) was dissolved in 95% methanol/water 0.1% TFA (200 μL) at room temperature (25 °C). Each of samples was analyzed by HPLC on a Develosil C30-UG-5 column (4.6×250 mm^2) by an isocratic elution 95% methanol/water containing 0.1% TFA for 15 min at a flow rate of 0.6 mL min^{-1}. The chromatograms were monitored at 315 nm for imino-*O*-arenesulfonates **1a**–**1g** and amino(aryl)pyrazine **7a** and at 254 nm for homologs **2a**–**2g** and amino(aryl)pyrazine **8a**, respectively. The retention time of imino-*O*-arenesulfonates **1a**–**1g** and homologs **2a**–**2g** are as follows: **1a** at 7.175 min, **1b** at 6.621 min, **1c** at

6.837 min, **1d** at 7.876 min, **1e** at 8.126 min, **1f** at 6.850 min, **1g** at 7.179 min, **7a** at 8.479 min, **2a** at 7.345 min, **2b** at 6.776 min, **2c** at 6.956 min, **2d** at 8.212 min, **2e** at 8.532 min, **2f** at 7.119 min, **2g** at 7.558 min, and **8a** at 8.684 min.

Each group of imino-*O*-arenesulfonates (0.01 mM) was mixed and dissolved with methanol (5 mL). 0.1 mL of the mixture was sampled and dried with argon air then diluted with 95% methanol/water containing 0.1% TFA (0.2 mL) and filtrated before analysis. After that, under a argon atmosphere, 4-methoxyphenylboronate ester **4a** (1 equiv of each imino-*O*-arenesulfonate), $Pd(OAc)_2$ (8 mol %), ligand **6** (16 mol %), KOH (1.5 equiv of each imino-*O*-arenesulfonate) were added to a stirred solution of mixture of imino-*O*-arenesulfonates. Due to the fact that some imino-*O*-arenesulfonates have monitored in the same retention time, the competitive reactions were done with 4 groups of starting material under the similar reaction condition. However, the concentration of arylboronate ester cannot be controlled in the same amount for all. The solution was stirred at 80 °C for a period of time. Each of aliquot 0.1 mL of this reaction mixture was sampled at 30, 60, and 120 min after refluxing, and was dried with argon air then diluted with 95% methanol/water containing 0.1% TFA (0.2 mL) and filtrated before analysis. All samples were analyzed by HPLC on a Develosil C30-UG-5 column ($4.6 \times 250\,mm^2$) by an isocratic elution 95% methanol/water containing 0.1% TFA for 25 min at a flow rate of $0.3\,mL\,min^{-1}$. The chromatogram was monitored at 315 nm for imino-*O*-arenesulfonates **1** and 254 nm for homologs **2**.

The authors are grateful for the financial supports by a Grant-in-Aid for Specially Promoted Research No. 16002007 from MEXT Japan as well as the generous scholarship to A. M. during his Ph.D. studies. We are also grateful for Dr. Magne O. Sydnes, Mr. Jurrien S. Noot and Dr. Nisachon Khunnawutmanotham to improve this manuscript. Grateful acknowledgement is also extended to Nagoya University for supports and assistance during this study.

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