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One-Pot Generation of Functionalized Benzynes from Readily Available 2-Hydroxyphenylboronic Acids

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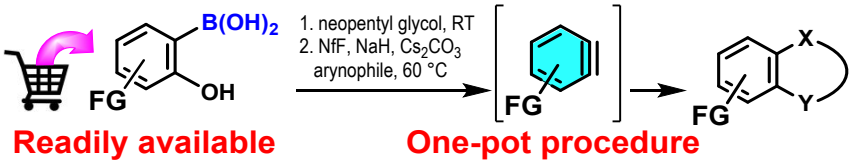
ABSTRACT: We developed a one-pot method for the generation of benzynes from a range of readily available 2-hydroxyphenylboronic acids. This method features the in-situ activation of both boronic acid and hydroxyl groups of the substrate to enhance benzyne generation at 60 °C. Such mild conditions facilitate the generation of functionalized benzynes that immediately react with diverse arynophiles to produce multi-substituted fused benzenes.

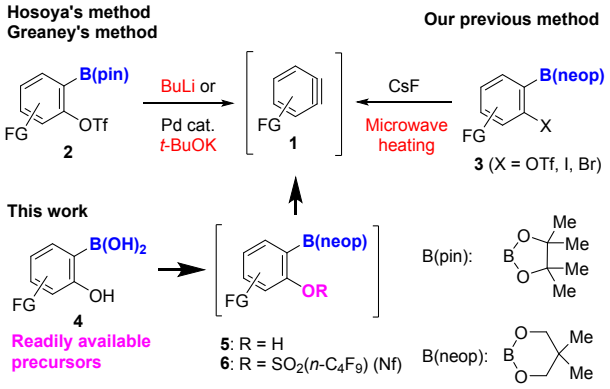


INTRODUCTION

Benzynes **1** are widely used intermediates for the preparation of many multi-substituted and/or fused-aromatic compounds through nucleophilic additions, cycloadditions, and transition-metal-catalyzed bond-forming reactions.[1] However, benzynes are too reactive to be isolated at ambient atmosphere; hence they need to be generated in-situ in the presence of arynophiles. Therefore, the selection of suitable precursors and conditions that effectively use benzynes for the synthesis of aromatic compounds is very important.[2] Currently, the most widely used benzyne precursors are 2-(trimethylsilyl)aryl trifluoromethanesulfonates (2-silylaryl triflates) owing to their abilities to efficiently generate benzynes under mild fluoride-ion-mediated conditions.[1,3] However, this method is hardly applicable to benzynes bearing reactive functional groups, such as halogens and carbonyls, as the corresponding 2-silylaryl triflates are prepared using alkyl lithium reagents during the installation of the silyl group on the benzene ring.

Based on this background, Hosoya's group,[4b] Greaney's group,[2c] and our research group[4a,c] independently discovered that 2-borylphenyl triflates **2** and **3** (Scheme 1), which are available by the borylation of aromatic rings under much milder conditions[5] than those used during silylation, serve as new precursors for the generation of functionalized benzynes. As a result, Hosoya et al.[4b] and Greaney et al.[2c] generated benzynes from pinacol boronates **2** with strong bases such as BuLi and *t*-BuOK/Pd as the catalyst. However, the difficulty in preparing functionalized benzynes remained unsolved. In contrast, our method enables the generation of a number of functionalized benzynes **1** from neopentyl glycol boronates **3** using CsF. Nevertheless, this reaction requires a relatively high temperature (120 °C) and microwave irradiation, which limits its synthetic applicability. In addition, precursors **2** and **3** are prepared through multi-step transformations from commercially available chemicals. A new method that produces a variety of functionalized benzynes directly from readily available materials under milder conditions may solve all of the above-mentioned issues.

Herein, we report the one-pot generation of benzynes **1** from readily-accessible 2-hydroxyphenylboronic acids **4** (Scheme 1). This method features the in-situ activation of both the boronic acid and hydroxyl groups of **4** to generate 2-[(neopentyl glycolato)boryl]phenyl nonaflates **6**, which are then converted into **1** at lower temperature (60 °C) than our previous method without any additional fluoride source. The generated **1** are successfully used in reactions with various arynophiles to afford substituted aromatic compounds.



Scheme 1. Previous Methods for the Generation of Benzynes from Boronic Esters (**2** or **3**) and the Method Developed in This Work.

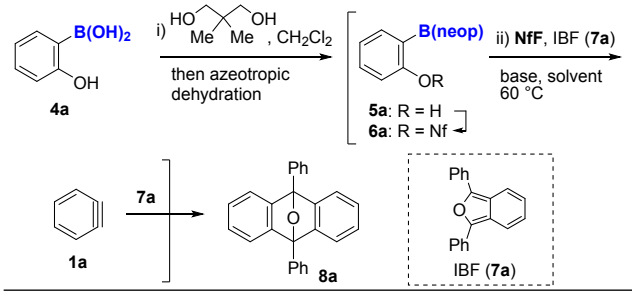
RESULTS AND DISCUSSION

Our preliminary experiments revealed that the *O*-nonaflylation of 2-[(neopentyl glycol)boryl]phenol **5a**[6] with nonafluorobutanesulfonyl fluoride (NfF)[7] gradually generated benzyne **1a** even at 60 °C.[8] We also found that the leaving ability of other sulfonyloxyl groups, such as trifluoromethanesulfonyloxyl (TfO), methanesulfonyloxyl (MsO), and *p*-toluenesulfonyloxyl (TsO), prepared by the *O*-sulfonylation of **5a**, was lower than that of the NfO group in **6a**.[8] These observations convinced us that 2-hydroxyphenylboronic acid **4a** is an ideal precursor for the one-pot generation of **1a** through the double activation of its boronic acid and hydroxyl groups. Therefore, we first searched for suitable conditions for the one-pot generation of benzyne from **4a** (Table 1). Boronic ester **5a** was prepared by the reaction

of **4a** with neopentyl glycol (1.2 equiv) in CH_2Cl_2 at RT for 3 h followed by azeotropic dehydration with toluene. Anhydrous THF was then added to crude **5a** and the resultant solution was reacted with different inorganic bases (3.0 equiv) and NfF (3.0 equiv) at 60 °C for 24 h in the presence of 1,3-diphenylisobenzofuran (IBF) (**7a**) to trap the generated **1a**. Nonaflate **6a** was produced as the major product using NaH, with only a trace amount of cycloaddition product **8a** observed (entry 1). The use of various carbonates (Li_2CO_3, Na_2CO_3, K_2CO_3, Rb_2CO_3, and Cs_2CO_3) increased the yield of **8a** (entries 2–6) in accordance with the size of the counter cation, with Cs_2CO_3 giving the best yield (96%, entry 6). However, the yield of **8a** was significantly lower (45%) when these two steps were carried out in THF in the absence of azeotropic dehydration (entry 7). Therefore, the first boronic ester should be formed in CH_2Cl_2, with the generated H_2O removed thereafter. The reactions also worked efficiently with Cs_2CO_3 in either cyclopentyl methyl ether (CPME) or MeCN to give **8a** in yields of 90–94% (entries 8 and 9). The use of a weaker or bulkier base ($CsHCO_3$ or CsOPiv, respectively) gave poor results (entries 10 and 11). K_3PO_4 was also found to be inefficient since it provided only a 17% yield of **8a** (entry 12). Therefore, Cs_2CO_3 appears to be the best choice for generating benzyne **1a** from **4a**.

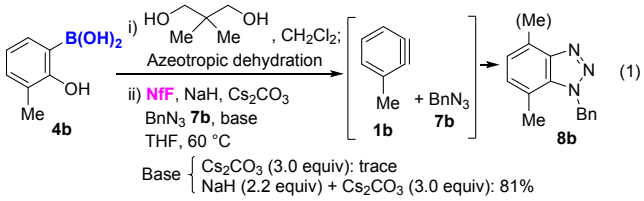
However, only a trace amount of the cycloaddition product **8b** was observed following the reaction of benzyl azide (**7b**) and 3-methylbenzyne (**1b**) generated from **4b** under the same reaction conditions using Cs_2CO_3 (Eq 1). Under that conditions, the *O*-nonaflylation of the corresponding neopentyl glycol ester **5b** seems to be extremely slow and significant amount of **5b** was observed after the reaction. After extensive studies, we found that the use of NaH as an additional base dramatically improved the yield of **8b** (81%, 1.2:1 mixture of regioisomers), which is probably due to steric hindrance associated with the methyl group that hampers *O*-nonaflylation. Hence, the optimum conditions were determined to involve the combination of NaH and Cs_2CO_3.

Table 1. One-Pot Benzyne Generation from 2-Hydroxyphenylboronic Acid 4aa



entry	base	solvent	**8a** (%)[b]
1	NaH	THF	trace
2	Li_2CO_3	THF	nd
3	Na_2CO_3	THF	12
4	K_2CO_3	THF	30
5	Rb_2CO_3	THF	53
6	Cs_2CO_3	THF	96[c]
7[d]	Cs_2CO_3	THF	45
8	Cs_2CO_3	CPME	94
9	Cs_2CO_3	MeCN	90
10	$CsHCO_3$	THF	nd
11	CsOPiv	THF	trace
12	K_3PO_4	THF	17

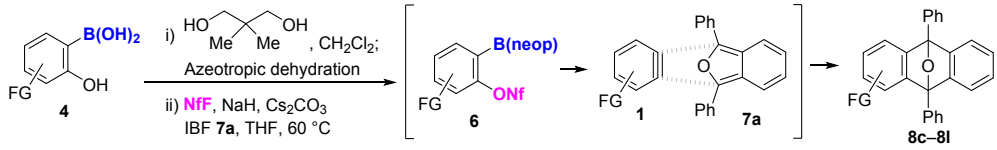
[a]Conditions: i) **4a** (1.0 equiv) and neopentyl glycol (1.2 equiv) in CH_2Cl_2 (0.10 M) at RT for 3 h, then azeotropic dehydration using toluene; ii) NfF (3.0 equiv), base (3.0 equiv), and IBF **7a** (3.0 equiv) in solvent (0.10 M) at 60 °C for 24 h. [b]GC yield. [c]Isolated yield. [d]All reagents were mixed together and stirred in THF for 24 h. NfF: nonafluorobutanesulfonyl fluoride; IBF: 1,3-diphenylisobenzofuran; nd: not detected.

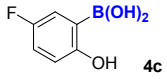
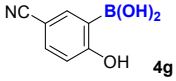
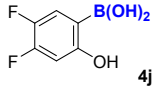
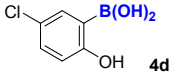
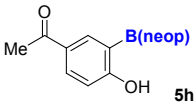
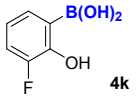
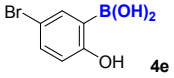
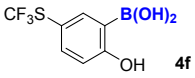
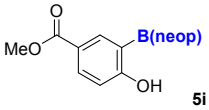


We next examined the scope of the reaction using commercially available 2-hydroxyphenylboronic acids **4b**–**4g**, **4j**, and **4k** under the optimized conditions in the presence of **7a** (Table 2, entries 1–5 and 8–10). The synthetic neopentyl glycol esters **5h** and **5i**[4c,10] were also employed to the second step of our optimized conditions because some boronic acids are expensive or commercially unavailable (entries 6 and 7). All reactions of **4c**–**4g**, **4j** provided adducts **8c**–**8g** and **8j** in yields of 62–91% (entries 1–5 and 8), whereas reactions of 3-subsituted benzynes **1b** and **1k** generated from **4b** and **4k** provided **8k** and **8l** in lower yields of 43% and 48%, respectively (entries 9 and 10). The

reaction of **5h** and **5i** bearing carbonyl groups in the absence of NaH gave much higher yields (62% and 65%) than those in the presence of NaH (entries 6 and 7). And NaH was not necessary for the reaction of **4c** and **4e** and similar yields were obtained without NaH (entries 1 and 3). Functional groups such as F, Cl, Br, CF_3S, CN, COMe and CO_2Me were tolerated under the reaction conditions, which confirmed that functionalized benzynes **1c**–**1k** were successfully generated.

Table 2. Substituent Scope of 2-Hydroxyphenylboronic Acids 4 Generating Benzynes 1[a]

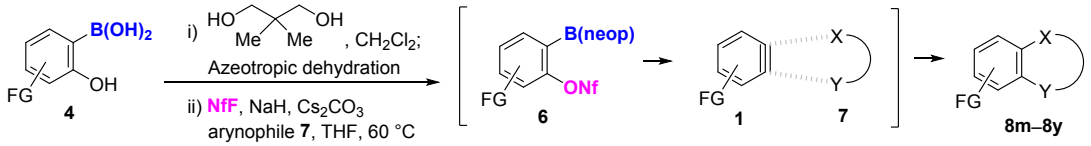


entry	precursor **4**	**1**, **8**	yield (%)[b]	entry	precursor **4**, **5**	**1**, **8**	yield (%)[b]	entry	precursor **4**	**1**, **8**	yield (%)[b]
1	 **4c**	**1c**, **8c**	90 (90)[c]	5	 **4g**	**1g**, **8g**	62	8	 **4j**	**1j**, **8j**	73
2	 **4d**	**1d**, **8d**	91	6[d]	 **5h**	**1h**, **8h**	62	9	 **4k**	**1k**, **8k**	43
3	 **4e**	**1e**, **8e**	81 (85)[c]								
4	 **4f**	**1f**, **8f**	77	7[d]	 **5i**	**1i**, **8i**	40 (65)[e]	10	**4b**	**1b**, **8l**	48

[a]Conditions: i) **4** (1.0 equiv) and neopentyl glycol (1.2 equiv) in CH_2Cl_2 (0.10 M) at RT for 3 h; ii) After azeotropic dehydration using toluene, NfF (3.0 equiv), NaH (2.2 equiv), Cs_2CO_3 (3.0 equiv), and IBF **7a** (3.0 equiv) in THF (0.10 M) at 60 °C for 24 h. [b]Isolated yield (%) of **8**. [c]Yield without NaH. [d]The reaction of **5** was started from step ii) without NaH. [e]At 80 °C.

Wider substrate scope and possible extension to other arynophiles **7** were also investigated (Table 3). Arynophiles such as alkyl azide **7b** (entry 1), furan **7c** (entry 2), nitrone **7d** (entry 3), nitrile oxide **7e** (entry 4), olefin **7f** (entry 5), cyclic urea **7g** (entry 6), amine **7h** (entry 7), sydnone **7i** (entry 8), and pyrrole **7j** (entry 9) reacted with benzyne **1a** generated from **4a** to afford the corresponding aromatic compounds **8m**–**8u** in yields of 75–96%. The combinations of substituted benzyne precursors **4c**, **4j**, **4l**, and **4m**, and other arynophiles **7b**, **7j**, and **7k** also gave cycloaddition products **8v**–**8y** in 55–83% yields (entries 10–13).

Table 3. Reaction Scope of Benzynes 1 Generated from 2-Hydroxyphenylboronic Acids 4[a]

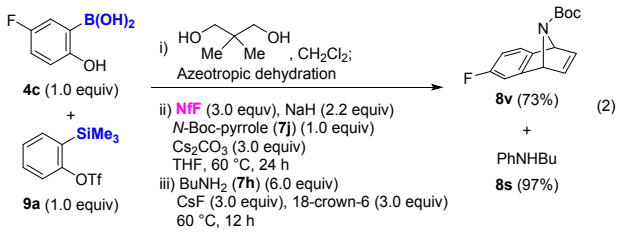


entry	precursor 4	arynophile 7	product 8	yield (%)[b]
1	4a	7b	8m	90
2	4a	7c	8n	82
3	4a	7d	8o	91
4	4a	7e	8p	76
5	4a	7f	8q	75
6	4a	7g	8r	75
7	4a	$BuNH_2$ 7h	PhNHBu 8s	87
8	4a	7i	8t	96
9	4a	7j	8u	81
10	4c	7j	8v	83
11	4l	7j	8w	73
12	4j	7b	8x	57
13	4m	7k	8y	55

[a]Conditions: i) **4** (1.0 equiv) and neopentyl glycol (1.2 equiv) in CH_2Cl_2 (0.10 M) at RT for 3 h, then azeotropic dehydration using toluene; ii) NfF (3.0 equiv), NaH (2.2 equiv), Cs_2CO_3 (3.0 equiv), and arynophile **7** (3.0 equiv) in THF (0.10 M) at 60 °C for 24 h. [b]Isolated yield (%) of **8**.

The following reaction highlights the dominant reactivity of the 2-hydroxyphenylboronic acid **4c** in the presence of 2-(trimethylsilyl)phenyl triflate (**9a**)[1,3] under the above-mentioned optimized conditions. A 1:1 mixture of the two benzyne precursors **4c** and **9a** was subjected to the optimized procedure in the presence of *N*-Boc-pyrrole (**7j**) (1.0 equiv), after which $BuNH_2$ (**7h**) (6.0 equiv), CsF (3.0 equiv), and 18-crown-6 (3.0 equiv) were added, and the resulting mixture was stirred at 60 °C for a further 12 h (Eq 2). Consequently, **8v** and **8s** were obtained in yields of 73% and 97%, respectively. It is worth noting that other cross-reaction products, such as **8u** (available from **9a** and **7j**) and 3- or 4-fluoro-*N*-butylaniline (available from **4c** and **7h**), were not obtained. These results suggest that 4-

fluorobenzyne (**1c**) was generated from **4c**, with **9a** remaining intact under the optimized conditions. In addition, benzyne (**1a**) was subsequently quantitatively formed from **9a** through the addition of CsF and 18-crown-6[2j] to the reaction mixture to give **8s** in the presence of **7h**. It is also worth noting that the use of less amount of arynophile **7j** (1.0 equiv) made the yield, 73% of adduct **8v**, which is only 10% lower than that using 3.0 equiv of **7j** (Table 3, entry 10).



Mechanistic studies

We examined the mechanism of this reaction with 2-borylphenyl nonaflate **6a**, a key intermediate involved in the generation of the benzyne from **4a** (Figure 1). A solution of **6a** and 2,5-dimethylfuran (**7c**) in THF was stirred with Cs_2CO_3 (2 equiv) at RT, and aliquots of the crude reaction mixture were removed at selected times and subjected to ^1H and ^{11}B NMR spectroscopy. The signals of **6a** almost completely disappeared within 30 min, and a set of new signals of reaction intermediate **A** was observed in both the ^1H and ^{11}B NMR spectra (Figure 1, second spectrum from the bottom, purple). These new signals gradually disappeared as another set of signals corresponding to product **8n** appearance over the next 3 h (Figure 1, third spectrum from the bottom). This third set of signals persisted for another 24 h, during which time the signals due to **A** disappeared completely; **8n** was finally obtained in 97% yield after 27 h. The same mixture was also subjected to high-resolution mass spectrometry after 0.5 h of reaction (HRMS: DART-Orbitrap MS) in negative mode. The main peak observed (m/z 567.0528) is consistent with the formula $C_{16}H_{17}BF_9O_9S$ (theoretical mass: 567.0551), which is likely to be a H_3O^+

adduct of **A** in which a carbonate ion is coordinated to the boron atom in **6a**, as shown in Figure 1. These experimental data suggest that benzyne (**1a**) is generated in a stepwise manner: the rapid coordination of a carbonate ion to the boron first forms **A** (Nu: OCO_2^-), after which gradual C-B bond fission accompanied by the elimination of the NfO^- ion yields **1a**. The stronger electron-withdrawing inductive effect of the NfO group than that of the TfO group increases the Lewis acidity of the boron atom in **6a**, which also enhances coordination to the carbonate ion (see Supporting Information).

This stepwise formation of **1a** from the 2-borylphenyl nonaflate **6a** represents a fundamental difference from the quasi-stepwise generation of benzyne from 2-silylpheyl triflate **9a**.[10,11] In addition, the higher Lewis acidity of the boron atom in **6a** compared to that of the silicon in **9a**, as well as the lower steric bulkiness of the boron, most probably facilitates the dominant attack of the relatively weak Lewis base (carbonate ion) at the boron in **6a** to form intermediate **A** in the presence of **9a**. On the other hand, reaction of the corresponding pinacol ester provided only 11% of **8n** under the same conditions, although a similar boronate intermediate was observed.[8] This result suggests that coordination of the carboxylate ion to the more hindered boron atom of the pinacol ester may not be an issue for the generation of the benzyne.

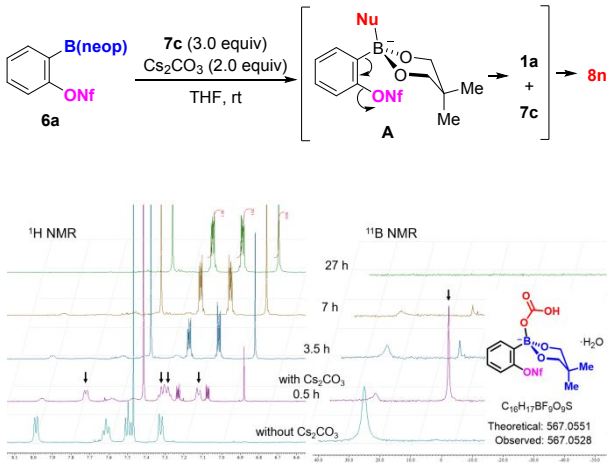


Figure 1. ^1H and ^{11}B NMR time-course study of the reaction of **6a** with **7c** in the presence of Cs_2CO_3, and HRMS data.

CONCLUSION

In summary, we developed a new one-pot method for the generation of functionalized benzynes from readily available 2-hydroxylphenylboronic acids. Currently, 137 2-hydroxylphenylboronic acids are commercially available[12] and can be used as benzyne precursors. Additionally, benzyne can be selectively generated in the presence of 2-(trimethylsilyl)phenyl triflate. Further studies regarding synthetic applications and more-detailed mechanistic investigations of this method are currently underway in our laboratory.

EXPERIMENTAL DETAILS

General considerations

Reagents. All reactions were carried out under argon atmosphere. A round-bottomed flask with a three-way stopcock or a Schlenk flask containing a magnetic stirrer was used as reactors and heated by an oil bath (Riko or Techno Sigma). Anhydrous THF and MeCN were purchased from Kanto Chemical, and purified with a Glass Contour solvent dispensing system (Nikko Hansen) using two packed columns of activated molecular sieves. Anhydrous CPME was purchased from FUJIFILM Wako Pure Chemical. 1-(3-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-4-hydroxyphenyl)ethan-1-one (**5h**),[4c] methyl 3-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-hydroxybenzoate (**5i**),[4c] *N*-*tert*-butylphenyl nitrone (**7d**),[13] 2,4,6-trimethylbenzonitrile oxide (**7e**),[14] 1,1-dimethoxyethylene (**7f**),[15] *tert*-butyl 1*H*-pyrrole-1-carboxylate (**7j**),[16] 4-(4-methoxyphenyl)-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (**7i**),[17] were prepared according to the literature. All other reagents including phenylboronic acid derivatives (**4a**–**4g** and **4j**–**4m**) were purchased from FUJIFILM Wako Pure Chemical, Tokyo Chemical Industry, Sigma-Aldrich, Nacalai tesque, Kishida Chemical, Matrix Scientific and Combi-Blocks and used without further purification. Flash chromatography[18] was performed with silica gel 60N, spherical neutral (40–50 μm), purchased from Kanto Chemical. Gel permeation chromatography (GPC) was performed with JAIGEL-2HR, purchased from Japan Analytical Industry. All reactions were monitored by thin-layer chromatography

(TLC) on glass-backed silica gel $60F_{254}$, 0.2 mm plates (Merck), and compounds were visualized under UV light (254 nm).

Analytical methods. Melting points were recorded on Yanagimoto melting point apparatus and are uncorrected. IR spectra were obtained on a SHIMADZU IRAffinity-1S. ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a JEOL JMN-ECA-500 (^{1}H: 500 MHz, $^{13}C\{^{1}H\}$: 125 MHz, $^{19}F\{^{1}H\}$: 470 MHz, ^{11}B: 160 MHz), a JEOL JMN-ECS-400 (^{1}H: 400 MHz, $^{13}C\{^{1}H\}$: 100 MHz, $^{19}F\{^{1}H\}$: 376 MHz, ^{29}Si: 79 MHz), a JEOL AL-300 (^{1}H: 300 MHz, $^{13}C\{^{1}H\}$: 75 MHz). Instrument with chemical shifts reported in ppm relative to the residual deuterated solvent. GC spectra were taken on SHIMADZU GC-2010. The mass spectra were recorded on a JEOL JMS-S3000 (MALDI, TOF), a JEOL JMS-700 (FAB), a Thermo Fisher Scientific LTQ-Orbitrap XL spectrometer equipped with DART apprication (Direct Analysis in Real Time) made by JEOL instead of using standard ESI (APCI, Orbitrap). "Yield" refers to the isolated yields of compounds showing at most only trace peaks in the ^{1}H NMR spectra that are not attributable to the assigned structure. ^{1}H NMR and melting points (where applicable) of all known compounds were taken. All new products were further characterized by high resolution mass spectrum (HRMS).

One-pot generation of benzyne from 2-borylphenol 4 (Tables 1–3, Eq 1):

General Procedure I: i) An oven-dried Schlenk tube was charged with 2-hydroxyphenylboronic acid **4** (1.0 equiv), neopentyl glycol (1.2 equiv), and a stirrer bar. The tube was capped with a rubber septum, and then evacuated and back-filled with argon. Anhydrous CH_2Cl_2 (0.10 M) was added into the tube through the septum by a syringe, after which the mixture was stirred until the mixture turned to be a clear solution. After adding ca. 2 mL of toluene to the mixture, all solvents were removed under reduced

pressure (this process was repeated three times). ii) Cs_2CO_3 (3.0 equiv) and NaH (60%, dispersion in paraffin liquid) (2.2 equiv) were added to the mixture. If arynophile **7** (3.0 equiv) was a solid, it was added at this time. The tube was evacuated and filled-back with argon (this process was repeated three times). THF (0.10 M) and NfF (3.0 equiv) were added by a syringe sequentially at room temperature. If arynophile **7** (3.0 equiv) was a liquid, it was added to the tube at this time along with THF. The mixture was stirred at 60 °C for 24 h. An aquous solution of NH_4Cl was added to the reaction mixture, after which it was extracted three times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was examined by ^1H NMR spectroscopy to determine NMR yield using 1,1,2,2-tetrachloroethane as an internal standard. This crude mixture was purified by flash column chromatography on silica gel to afford product **8**.

General Procedure II: i) An oven-dried Schlenk tube was charged with 2-hydroxyphenylboronic acid **4** (1.0 equiv), neopentyl glycol (1.2 equiv), and a stirrer bar. The tube was capped with a rubber septum, and then evacuated and back-filled with argon. CH_2Cl_2 (0.10 M) was added into the tube through the septum by a syringe, after which the mixture was stirred until the mixture turned to be a clear solution. After adding ca. 2 mL of toluene to the mixture, all solvents were removed under reduced pressure (this process was repeated three times). ii) Cs_2CO_3 (3.0 equiv) and NaH (60%, dispersion in paraffin liquid) (2.2 equiv) were added to the mixture, then evacuated and back-filled with argon (This process was repeated three times). THF (0.10 M), NfF (3.0 equiv) and arynophile **7** (3.0 equiv) were added by a syringe sequentially at room temperature. The mixture was stirred at 60 °C for 24 h. A saturated solution of NH_4Cl was added to the reaction mixture, after which it was extracted three times with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was examined by ^1H NMR spectroscopy to determine NMR yield using 1,1,2,2-tetrachloroethane as an internal standard. This crude mixture was purified by flash column chromatography on silica gel to afford product **8**.

*9,10-Diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8a**)* (Table 1, entry 6):[2b] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8a** as a colorless solid [71 mg (2% CH_2Cl_2), 96%]. Mp: 185–186 °C (187.5–180 °C, lit).[2b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (dd, *J* = 7.5, 1.5 Hz, 4 H), 7.59 (dd, *J* = 7.5, 7.5 Hz, 4 H), 7.49 (tt, *J* = 7.5, 1.5 Hz, 2 H), 7.36 (dd, *J* = 5.5, 3.0 Hz, 4 H), 7.03 (dd, *J* = 5.5, 3.0 Hz, 4 H).

Following General Procedure I, a mixture of neopentyl glycol (0.12 g, 1.2 mmol), and 2-hydroxyphenylboronic acid (**4a**) (0.14 g, 1.0 mmol) in CH_2Cl_2 (10 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with Cs_2CO_3 (1.0 g, 3.2 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.57 g, 2.1 mmol) in THF (10 mL). Then, NfF (0.55 mL, 3.0 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8a** as a colorless solid (0.27 g, 78%).

*1-Benzyl-4-methyl-1H-benzo[d][1,2,3]triazole (**8b**)* (Eq 1): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-3-methylphenylboronic acid (**4b**) (32 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), and Cs_2CO_3 (0.21 mg, 0.63 mmol) in THF (2.0 mL). Then, benzyl azide (**7b**) (0.078 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide a mixture of the titled compound **8b** (18 mg, 81 μmol) and 2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-6-methylphenol (**5b**) (4.1 mg, 19 μmol) as

a colorless oil, and a mixture of **8b** (1.8 mg, 7.9 μmol), 1-benzyl-7-methyl-1*H*-benzo[*d*][1,2,3]triazole (**8b'**) (17 mg, 78 μmol) and **5b** (4.2 mg, 19 μmol) as a colorless oil [total 81% of regioisomers, **8b** (20 mg, 89 μmol, 43%) and **8b'** (17 mg, 78 μmol, 38%)]. **8b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34–7.26 (m, 6 H), 7.16 (d, *J* = 8.5 Hz, 1 H), 7.10 (d, *J* = 7.0 Hz, 1 H), 5.84 (s, 2 H), 2.80 (s, 3 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 146.3, 134.9, 130.9, 128.9, 128.3, 127.5, 127.4, 124.3, 123.7, 107.0, 52.2, 16.7. IR: 3033 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{14}H_{14}N_3$ $[M+H]^+$: 224.1182, Found: 224.1184.

*1-Benzyl-7-methyl-1H-benzo[d][1,2,3]triazole (**8b'**)* (Eq 1) (17 mg, 78 μmol) was obtained by above-mentioned column chromatography as a mixure with **5b** (4.2 mg, 19 μmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.92 (brd, *J* = 8.5 Hz, 1 H), 7.34–7.25 (m, 3 H), 7.23 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.15–7.14 (m, 1 H), 7.06–7.04 (m, 2 H), 6.05 (s, 2 H), 2.52 (s, 3 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 146.8, 136.8, 132.7, 132.5, 129.0, 128.7, 128.0, 126.1, 120.8, 117.8, 53.1, 18.4. IR: 3035 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{14}H_{14}N_3$ $[M+H]^+$: 224.1182, Found: 224.1185.

*2-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-6-methylphenol (**5b**)* was synthesized to obtain ^{1}H and ^{13}C{^{1}H} NMR spectra data, which was used to identify products from the above mentioned crude mixture. A mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-3-methylphenylboronic acid (**4b**) (32 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. After 3 h, H_2O (ca. 5 mL) was added to the reaction and water phase was extracted with CH_2Cl_2 (ca. 5 mL) three times. Without further purification, the titled compound (**5b**) was obtained as a colorless solid (46 mg, quant). Mp: 94–96 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.50 (s, OH), 7.48 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.20 (brd, *J* = 7.5 Hz, 1 H), 6.78 (dd, *J* = 7.5, 7.5 Hz 1 H), 3.82 (s, 4 H), 2.23 (s, 3 H), 1.05 (s, 6 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 161.8, 134.2, 132.7, 124.3, 119.0, 72.3, 32.0, 21.8, 16.0 (insufficient

number of signals because of signal overlapping). IR: 3367 cm^{-1}. HRMS (MALDI, TOF): *m/z* Calcd for $C_{12}H_{17}BO_3$ $[M]^+$: 220.1265, Found: 220.1269.

*2-Fluoro-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8c**)* (Table 2, entry 1): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-fluorophenylboronic acid (**4c**) (33 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8c** as a colorless solid [71 mg (3% hexane), 90%]. Mp: 83–84 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.91 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.62–7.58 (m, 4 H), 7.52–7.48 (m, 2 H), 7.39–7.34 (m, 2 H), 7.29–7.26 (m, 1 H), 7.09–7.04 (m, 3 H), 6.69 (ddd, *J* = 9.5, 7.5, 1.5 Hz, 1 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 160.9 (d, *J* = 247.0 Hz), 153.2 (d, *J* = 8.5 Hz), 150.3, 149.8, 145.8, 134.7, 134.5, 128.9, 128.8, 128.5, 128.4, 126.6, 126.5, 126.1, 125.9, 121.3 (d, *J* = 8.5 Hz), 120.5, 120.3, 111.6 (d, *J* = 23.0 Hz), 109.2 (d, *J* = 25.0 Hz), 90.5, 90.4. ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ: –115.8. IR: 3064, 3033 cm^{-1}. HRMS (MALDI, TOF): *m/z* Calcd for $C_{26}H_{18}OF$ $[M+H]^+$: 365.1336, Found: 365.1339.

*2-Chloro-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8d**)* (Table 2, entry 2): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-chlorophenylboronic acid (**4d**) (37 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by

column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8d** as a colorless solid [75 mg (3% hexane), 91%]. Mp: 74–75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 8.5 Hz, 2 H), 7.92 (d, *J* = 8.5 Hz, 2 H), 7.62 (dd, *J* = 8.5, 8.5 Hz, 2 H), 7.61 (dd, *J* = 8.5, 8.5 Hz, 2 H), 7.54–7.49 (m, 2 H), 7.41–7.35 (m, 2 H), 7.33 (d, *J* = 1.5 Hz, 1 H), 7.27 (d, *J* = 7.5 Hz, 1 H), 7.07 (dd, *J* = 5.5, 3.0 Hz, 1 H), 7.07 (dd, *J* = 3.0, 5.5 Hz, 1 H), 7.01 (dd, *J* = 7.5, 1.5 Hz, 1 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 152.7, 149.9, 149.6, 149.0, 134.5, 134.4, 131.6, 128.9, 128.8, 128.5, 128.4, 126.6, 126.5, 126.1, 126.0, 125.6, 121.3, 121.2, 120.5, 120.4, 90.4, 90.3. IR: 3065, 3033 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{26}H_{18}O^{35}Cl$ $[M+H]^+$: 381.1041, Found: 381.1032.

*2-Bromo-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8e**)* (Table 2, entry 3):[2b] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-bromophenylboronic acid (**4e**) (45 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8e** as a colorless solid [75 mg (1% hexane, 1% CH_2Cl_2), 81%]. Mp: 170–171 °C (164–166 °C, lit).[2b] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91 (d, *J* = 7.5 Hz, 2 H), 7.91 (d, *J* = 7.5 Hz, 2 H), 7.62 (dd, *J* = 7.5, 7.5 Hz, 2 H), 7.60 (dd, *J* = 7.5, 7.5 Hz, 2 H), 7.53–7.49 (m, 2 H), 7.46 (d, *J* = 1.5 Hz, 1 H), 7.40–7.35 (m, 2 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 7.17 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.08–7.05 (m, 2H).

*9,10-Diphenyl-2-((trifluoromethyl)thio)-9,10-dihydro-9,10-epoxyanthracene (**8f**)* (Table 2, entry 4): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-((trifluoromethyl)thio)phenylboronic acid (**4f**) (50 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12

mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8f** as a colorless oil [74 mg (3% hexane), 77%]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93–7.90 (m, 4 H), 7.65–7.59 (m, 5 H), 7.55–7.50 (m, 2 H), 7.43–7.39 (m, 3 H), 7.37 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.09 (dd, *J* = 5.0, 3.5 Hz, 1 H), 7.09 (dd, *J* = 5.0, 3.5 Hz, 1 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 153.7, 152.2, 149.6, 149.3, 134.6, 134.2, 134.1, 129.1 (q, *J* = 308.0 Hz), 128.93, 128.88, 128.6, 128.5, 127.6, 126.6, 126.3, 126.2, 121.6, 121.2, 120.74, 120.72, 90.42, 90.38 (insufficient number of signals because of signal overlapping). ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ: –42.6. IR: 3066, 3034, 1602 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{27}H_{18}OF_3S$ $[M+H]^+$: 447.1025, Found: 447.1022.

*9,10-Diphenyl-9,10-dihydro-9,10-epoxyanthracene-2-carbonitrile (**8g**)* (Table 2, entry 5):[2b] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-cyanophenylboronic acid (**4g**) (34 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8g** as a colorless solid [49 mg (1% CH_2Cl_2), 62%]. Mp: 220–222 °C (216–218 °C, lit).[2b] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (d, *J* = 7.0 Hz, 2 H), 7.89 (d, *J* = 7.0 Hz, 2 H), 7.64 (t, *J* = 7.0 Hz, 2 H), 7.62 (t, *J* = 7.0 Hz, 2 H), 7.58 (brs, 1 H), 7.56–7.51 (m, 2 H), 7.44 (d, *J* = 7.0 Hz, 1 H), 7.42–7.38 (m, 3 H), 7.12–7.07 (m, 2 H).

*2-Acetyl-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8h**)* (Table 2, entry 6): Following General Procedure I [from ii)], 1-(3-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-hydroxyphenyl)ethan-1-one (**5h**) (26 mg, 0.11 mmol) was mixed with Cs_2CO_3 (0.10 g, 0.32 mmol) and 1,3-diphenylisobenzofuran (**7a**)

(60 mg, 0.22 mmol) in MeCN (1.0 mL). Then NfF (60 μL, 0.32 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) and Gel Permeation Chromatography (Chloroform) to provide the titled compound **8h** as a colorless solid (25 mg, 62%). Mp: 82–83 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.96–7.92 (m, 5 H), 7.68 (dd, *J* = 4.5, 1.5 Hz, 1 H), 7.64–7.60 (m, 4 H), 7.53–7.50 (m, 2 H), 7.43 (d, *J* = 4.5 Hz, 1 H), 7.40–7.38 (m, 2 H), 7.07–7.06 (m, 2 H), 2.52 (s, 3 H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 197.4, 155.6, 151.3, 149.9, 149.2, 135.2, 134.4, 134.3, 128.93, 128.86, 128.5, 127.6, 126.7, 126.2, 126.1, 120.74, 120.66, 120.2, 119.4, 90.5, 90.4, 26.8 (insufficient number of signals because of signal overlapping). IR: 1681 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{28}H_{21}O_2$ $[M+H]^+$: 389.1536, Found: 389.1539.

*1-Methoxycarbonyl-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene **(8i)*** (Table 2, entry 7): Following General Procedure I [from ii)], methyl 3-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-hydroxybenzoate (**5i**) (28 mg, 0.11 mmol) was mixed with Cs_2CO_3 (0.10 g, 0.32 mmol) and 1,3-diphenylisobenzofuran (**7a**) (60 mg, 0.22 mmol) in MeCN (1.0 mL). Then NfF (60 μL, 0.32 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 80 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) and (Chloroform, HP column) to provide the titled compound **8i** as a colorless solid (27 mg, 65%). Mp: 79–80 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.97–7.92 (m, 5 H), 7.79 (dd, *J* = 4.5, 1.5 Hz, 1 H), 7.64–7.59 (m, 4 H), 7.54–7.49 (m, 2 H), 7.42 (d, *J* = 4.5 Hz, 1 H), 7.40–7.38 (m, 2 H), 7.07–7.05 (m, 2 H), 3.85 (s, 3 H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 166.7, 155.5, 151.0, 149.9, 149.4, 134.4, 128.9, 128.8, 128.5, 128.0, 126.72, 126.69, 126.2, 126.1, 121.0, 120.7, 120.6, 120.1, 90.5, 52.1 (insufficient number of signals because of signal overlapping). IR: 1721 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{28}H_{21}O_3$ $[M+H]^+$: 405.1485, Found: 405.1485.

*2,3-Difluoro-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8j**)* (Table 2, entry 8): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-4,5-difluorophenylboronic acid (**4j**) (36 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8j** as a colorless solid [61 mg (3% CH_2Cl_2), 73%]. Mp: 55–57 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.88 (d, *J* = 8.0 Hz, 4 H), 7.61 (dd, *J* = 8.0, 8.0 Hz, 4 H), 7.51 (t, *J* = 8.0 Hz, 2 H), 7.37 (dd, *J* = 5.5, 3.0 Hz, 2 H), 7.17 (dd, *J* = 8.0, 8.0 Hz, 2 H), 7.07 (dd, *J* = 5.5, 3.0 Hz, 2 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 149.7, 148.0 (dd, *J* = 249.5, 14.5 Hz), 146.7 (dd, *J* = 4.0, 4.0 Hz), 134.2, 128.9, 128.6, 126.4, 126.1, 120.4, 110.8 (dd, *J* = 14.5, 7.0 Hz), 90.3. ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ: –140.2. IR: 3065, 3033 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{26}H_{17}OF_2$ $[M+H]^+$: 383.1242, Found: 383.1245.

*1-Fluoro-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8k**)* (Table 2, entry 9):[2b] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-3-fluorophenylboronic acid (**4i**) (33 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by a syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8k** as a colorless solid [34 mg (2% CH_2Cl_2), 43%]. Mp: 196–198 °C (200.5–200.7 °C, lit).[2b] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.00 (dd, *J* = 7.5, 2.0 Hz, 2 H), 7.90 (dd, *J* = 8.5, 1.0 Hz, 2 H),

7.59–7.54 (m, 4 H), 7.51–7.47 (m, 3 H), 7.39 (d, *J* = 6.5 Hz, 1 H), 7.15 (d, *J* = 7.0 Hz, 1 H), 7.13–7.02 (m, 3 H), 6.74 (dd, *J* = 8.5, 8.5 Hz, 1 H).

*1-Methyl-9,10-diphenyl-9,10-dihydro-9,10-epoxyanthracene (**8l**)* (Table 2, entry 10): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-3-methylphenylboronic acid (**4b**) (32 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 1,3-diphenylisobenzofuran (**7a**) (0.17 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8l** as a colorless solid [38 mg (2% hexane), 48%]. Mp: 81–83 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, *J* = 6.5 Hz, 2 H), 7.89 (d, *J* = 7.5 Hz, 2 H), 7.63 (d, *J* = 7.0 Hz, 1 H), 7.56–7.43 (m, 6 H), 7.35 (d, *J* = 7.0 Hz, 1 H), 7.18 (d, *J* = 7.0 Hz, 1 H), 7.12 (dd, *J* = 7.0, 7.0 Hz, 1 H), 7.04 (dd, *J* = 7.0, 7.0 Hz, 1 H), 6.94 (dd, *J* = 7.0, 7.0 Hz, 1 H), 6.79 (dd, *J* = 7.0 Hz, 1 H), 1.96 (s, 3 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 152.3, 151.0, 148.73, 148.68, 135.2, 134.8, 131.6, 129.6, 129.0, 128.8, 128.61, 128.57, 128.2, 127.2, 125.9, 125.8, 125.5, 121.6, 120.8, 118.0, 91.9, 90.1, 19.0. IR: 3060, 2955, 2924, 2854 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{27}H_{21}O$ $[M+H]^+$: 361.1587, Found: 361.1577.

*1-Benzyl-1H-benzo[d][1,2,3]triazole (**8m**)* (Table 3, entry 1):[19] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, benzyl azide (**7b**) (0.078 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **8m** as a colorless

solid (40 mg, 83%). Mp: 113–115 °C (114–115 °C, lit).[19] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 8.0 Hz, 1 H), 7.43–7.26 (m, 8 H), 5.86 (s, 2 H).

*1,4-Dimethyl-1,4-dihydro-1,4-epoxynaphthalene (**8n**)* (Table 3, entry 2):[4c] Following General Procedure II, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. NaH (20 mg, 0.46 mmol) was added to the mixture. THF (2.0 mL) and NfF (0.12 mL, 0.63 mmol) were added by syringe into the tube and the reaction mixture was stirred for 20 minutes at 60 °C. Cs_2CO_3 (0.21 g, 0.63 mmol) and 2,5-dimethylfuran (**7c**) (0.068 mL, 0.63 mmol) were then added sequentially and the reaction mixture was stirred at 60 °C for 24 h. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 8:1) to provide the titled compound **8n** as a colorless oil (30 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.13 (dd, *J* = 5.0, 3.0 Hz, 2 H), 6.98 (dd, *J* = 5.0, 3.0 Hz, 2 H), 6.78 (s, 2 H), 1.90 (s, 6 H).

*2-(tert-Butyl)-3-phenyl-2,3-dihydrobenzo[d]isoxazole (**8o**)* (Table 3, entry 3):[2n] Following General Procedure II, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (1.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by a syringe at room temperature, and the mixture was warmed to 60 °C. 1.0 mL of a THF solution of *N-tert*-butyl-α-phenylnitrone (**7d**) (0.11g, 0.63 mmol) was added to the mixture dropwise in 3 min, and the mixture was stirred at 60 °C for 24 h. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **8o** as a colorless solid (51 mg, 96%). Mp: 92–94 °C (92–94 °C, lit).[2n] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, *J* = 7.0, Hz, 2 H), 7.32 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.26–7.22 (m, 1 H), 7.14 (t, *J* = 7.0 Hz, 1 H), 6.88 (d, *J* = 7.5 Hz, 1 H), 6.81–6.77 (m, 2 H), 5.59 (s, 1 H), 1.17 (s, 9 H).

*3-Mesitylbenzo[d]isoxazole (**8p**)* (Table 3, entry 4): Following General Procedure II, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was warmed to 60 °C. After 10 minutes, 2,4,6-trimethylbenzonitrile oxide (**7e**) (0.10 g, 0.63 mmol) was added into the tube and the mixture was stirred at 60 °C for 24 h. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 10:1), followed by GPC to provide the titled compound **8p** as a colorless liquid (38 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.66 (d, *J* = 7.5 Hz, 1 H), 7.58 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.39 (d, *J* = 7.5 Hz, 1 H), 7.29 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.01 (s, 2 H), 2.37 (s, 3 H), 2.09 (s, 6 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 163.1, 157.9, 139.3, 137.7, 129.8, 128.5, 124.2, 123.6, 122.2, 121.9, 110.1, 21.2, 20.1. IR: 2920, 1613 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1226, Found: 238.1226.

*7,7-Dimethoxybicyclo[4.2.0]octa-1(6),2,4-triene (**8q**)* (Table 3, entry 5):[20] Following General Procedure II, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was warmed to 60 °C. After 10 minutes, 1,1-dimethoxyethylene (**7f**) (0.060 mL, 0.63 mmol) was added into the tube by syringe and the mixture was stirred at 60 °C for 24 h. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **8q** as a colorless oil (25 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31–7.34 (m, 1 H), 7.22–7.28 (m, 3 H), 3.45 (s, 6 H), 3.37 (s, 2 H).

*1,4-Dimethyl-1,2,3,4-tetrahydro-5H-benzo[e][1,4]diazepin-5-one (**8r**)* (Table 3, entry 6):[21] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic

acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (1.0 mL). Then, 1,3-dimethyl-2-imidazolidinone (**7g**) (1.0 mL, 9.2 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (EtOAc), followed by GPC to provide the titled compound **8r** as a colorless liquid (75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.63 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.36 (ddd, *J* = 7.0, 7.0, 2.0 Hz, 1 H), 6.98 (dd, *J* = 7.0, 7.0 Hz, 1 H), 6.86 (d, *J* = 7.0 Hz, 1 H), 3.42 (dd, *J* = 6.0, 6.0 Hz, 2 H), 3.30 (dd, *J* = 6.0, 6.0 Hz, 2 H), 3.21 (s, 3 H), 2.83 (s, 3 H).

*N-Butylaniline (**8s**)* (Table 3, entry 7):[22] Following General Procedure II, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. NaH (20 mg, 0.46 mmol) was added to the mixture. THF (2.0 mL) was added by a syringe and the mixture at 0 °C. NfF (0.12 mL, 0.63 mmol) was added to the tube and the mixture was stirred for 1 h and warmed to room temperature. Cs_2CO_3 (0.21 g, 0.63 mmol) was added at room temperature and the mixture was warmed to 60 °C. Butylamine (**7h**) (0.068 mL, 0.63 mmol) was then added by a syringe and the mixture was stirred at 60 °C for 24 h. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 10:1) to provide the titled compound **8s** as a colorless oil (28 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.17 (dd, *J* = 7.5, 7.5 Hz, 2 H), 6.68 (t, *J* = 7.5 Hz, 1 H), 6.61 (d, *J* = 7.5 Hz, 2 H), 3.59 (brs, 1 H), 3.11 (t, *J* = 7.0 Hz, 2 H), 1.66–1.55 (m, 2 H), 1.43 (tq, *J* = 7.0, 7.0 Hz, 2 H), 0.96 (t, *J* = 7.0 Hz, 3 H).

*3-(4-Methoxyphenyl)-2-phenyl-2H-indazole (**8t**)* (Table 3, entry 8):[23] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 3-phenyl-4-(4-methoxyphenyl)sydnone (**7i**) (0.17 mg, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column

chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **8t** as a colorless solid (60 mg, 96%). Mp: 120–122 °C (103–105 °C, lit).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, *J* = 9.0 Hz, 1 H), 7.70 (dd, *J* = 8.5, 1.0 Hz, 1 H), 7.46–7.34 (m, 7 H), 7.29 (d, *J* = 9.0 Hz, 2 H), 7.13 (ddd, *J* = 8.5, 6.5, 1.0 Hz, 1 H), 6.93 (d, *J* = 9.0 Hz, 2 H), 3.83 (s, 3 H).

*tert-Butyl-1,4-dihydro-1,4-epiminonaphthalene-9-carboxylate (**8u**)* (Table 3, entry 9):[2f] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxyphenylboronic acid (**4a**) (29 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, *tert*-butyl 1*H*-pyrrole-1-carboxylate (**7j**) (0.11 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 8:1) to provide the titled compound **8u** as a colorless solid (41 mg, 81%). Mp: 67–68 °C (70–72 °C, lit).[2f] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.25 (brs, 1 H), 7.00 (brs, 1 H), 6.97–6.94 (m, 4 H), 5.50 (brs, 1 H), 5.47 (brs, 1 H), 1.37 (s, 9 H).

*tert-Butyl-6-fluoro-1,4-dihydro-1,4-epiminonaphthalene-9-carboxylate (**8v**)* (Table 3, entry 10): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-fluorophenylboronic acid (**4c**) (33 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, *tert*-butyl 1*H*-pyrrole-1-carboxylate (**7j**) (0.11 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 8:1) to provide the titled compound **8v** as a colorless solid (45 mg, 83%). Mp: 49–51 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.15 (brs, 1 H), 7.06–6.90 (m, 3 H), 6.62 (ddd, *J* = 10.0, 9.0, 2.0 Hz, 1 H), 5.47 (brs, 1 H), 5.45 (brs, 1 H), 1.38 (s, 9 H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 160.3 (d, *J* = 244.5 Hz), 154.9,

151.0 (d, J = 8.5 Hz), 144.0, 143.6 (d, J = 2.0 Hz), 142.9, 142.8, 141.8, 121.6, 121.0, 110.3 (d, J = 22.0 Hz), 110.0, 109.7, 80.8, 66.8, 66.3, 66.2, 65.7, 28.1 (too much number of signals because of the existence of their amide rotamers). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ: –117.6, –117.8 (two signals because of the existence of their amide rotamers). IR: 2979, 1709 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{15}H_{16}NO_2FNa$ $[M+Na]^+$: 284.1057, found: 284.1061.

*tert-Butyl-6-(trifluoromethoxy)-1,4-dihydro-1,4-epiminonaphthalene-9-carboxylate (**8w**)* (Table 3, entry 11): Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-(trifluoromethoxy)phenylboronic acid (**4l**) (46 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63 mmol) in THF (2.0 mL). Then, *tert*-butyl 1*H*-pyrrole-1-carboxylate (**7j**) (0.11 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 8:1) to provide the titled compound **8w** as a colorless oil (50 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23 (brs, 0.5 H), 7.22 (brs, 0.5 H), 7.13 (brs, 1 H), 7.00 (brs, 1 H), 6.99 (brs, 1 H), 6.81 (dq, J = 8.0, 1.0 Hz, 1 H), 5.50 (brs, 2 H), 1.37 (s, 9 H). $^{13}C\{^{1}H\}$ NMR (400 MHz, $CDCl_3$) δ: 154.9, 150.7, 146.9, 146.3, 143.6, 143.3, 142.5, 142.1, 121.5, 120.9, 120.4 (q, J = 256.5 Hz), 117.2, 115.3, 114.8, 81.0, 66.8, 66.4, 66.8, 65.8, 28.1 (too much number of signals because of the existence of their amide rotamers). $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ: –57.9. IR: 2980, 1369 cm^{-1}. HRMS (MALDI, TOF): *m*/*z* Calcd for $C_{16}H_{16}NO_3F_3Na$ $[M+Na]^+$: 350.0974, Found: 350.0973.

*1-Benzyl-5,6-difluoro-1H-benzo[d][1,2,3]triazole (**8x**)* (Table 3, entry 12):[2f] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-4,5-difluorophenylboronic acid (**4j**) (36 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol) and Cs_2CO_3 (0.21 g, 0.63

mmol) in THF (2.0 mL). Then, benzyl azide (**7b**) (0.078 mL, 0.63 mmol) and NfF (0.12 mL, 0.63 mmol) were added by syringe sequentially. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound **8x** as a colorless solid (29 mg, 57%). Mp: 119–121 °C (120–122 °C, lit).[2f] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (dd, *J* = 9.0, 7.0 Hz, 1 H), 7.38–7.33 (m, 3 H), 7.26–7.24 (m, 2 H), 7.07 (dd, *J* = 9.0, 7.0 Hz, 1 H), 5.80 (s, 2 H).

*6-Methyl-1,2,3,4-tetraphenylnaphthalene (**8y**)* (Table 3, entry 13):[24] Following General Procedure I, a mixture of neopentyl glycol (24 mg, 0.25 mmol), and 2-hydroxy-5-methylphenylboronic acid (**4m**) (32 mg, 0.21 mmol) in CH_2Cl_2 (2.0 mL) was stirred for 3 h at room temperature. The resultant residue was mixed with NaH (20 mg, 0.46 mmol), Cs_2CO_3 (0.21 g, 0.63 mmol) and 2,3,4,5-tetraphenylcyclopenta-2,4-dien-1-one (**7k**) (0.24 g, 0.63 mmol) in THF (2.0 mL). Then, NfF (0.12 mL, 0.63 mmol) was added by syringe. The reaction mixture was stirred for 24 h at 60 °C. The crude product was purified by column chromatography on silica gel (hexane/CH_2Cl_2 = 5:2) to provide the titled compound **8y** as a colorless solid (51 mg, 55%). Mp: 217–219 °C (220.4–222.4 °C, lit).[24] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 8.5 Hz, 1 H), 7.40 (s, 1 H), 7.26–7.17 (m, 11 H), 6.87–6.80 (m, 10 H), 2.39 (s, 3 H).

Precursor selective benzyne generation (Eq 2):

An oven-dried Schlenk tube was charged with 2-hydroxy-5-fluorophenylboronic acid (**4c**) (33 mg, 0.21 mmol, 1.0 equiv), neopentyl glycol (24 mg, 0.25 mmol, 1.2 equiv), and a stirrer bar. The tube was capped with a rubber septum, and then evacuated and back-filled with argon. Anhydrous CH_2Cl_2 (2.0 mL, 0.10 M) was added into the tube through the septum by a syringe as well as 2-(trimethylsilyl)phenyl triflate (**9a**) (49 μL, 0.21 mmol, 1.0 equiv), after which the mixture was stirred until the mixture turned to be a clear solution. After adding ca. 2 mL of toluene to the mixture, all solvents were removed under reduced pressure (this process was repeated three times). Cs_2CO_3 (0.21 g, 0.63 mmol, 3.0 equiv) and NaH (20 mg, 0.46 mmol, 2.2 equiv, 60% dispersion in mineral oil) were added to the mixture, then evacuated and filled-back with argon; this process was repeated three times.

THF (2.0 mL, 0.10 M), NfF (0.12 mL, 0.63 mmol, 3.0 equiv) and *tert*-butyl 1*H*-pyrrole-1-carboxylate (**7j**) (0.11 mL, 0.63 mmol, 3.0 equiv) were added by a syringe sequentially at room temperature. The mixture was stirred at 60 °C for 24 h. After 24 h, butylamine (**7h**) (0.13 mL, 1.3 mol, 6.0 equiv) was added by syringe. CsF (95 mg, 0.63 mmol, 3.0 equiv) and 18-crown-6 (0.17 g, 0.63 mmol, 3.0 equiv) were added afterwards. Then the reaction mixture was put back into the oil bath again and stirred for 12 h. After reaction, an aquous solution of NH_4Cl was added to the reaction mixture, after which it was extracted three times with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was examined by ^1H NMR spectroscopy to determine NMR yield using tetrachloroethane as an internal standard. This crude mixture was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1) to afford product **8v** (40 mg, 0.15 mmol, 73%), another column afford **8s** (30 mg, 0.20 mmol, 97%).

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publication website at DOI: xxxxxxxxxxxxxxxxx

Preliminary experiments, additional experiments and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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