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Aryne Precursors for Selective Generation of 3-Haloarynes: Preparation and Application to Synthetic Reactions

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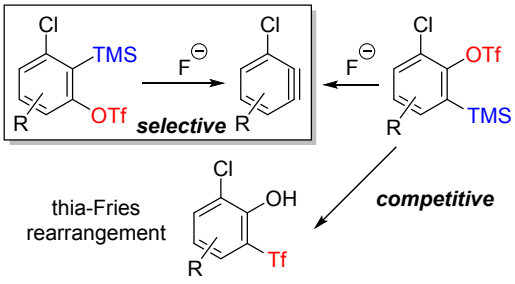
ABSTRACT: The synthesis and reaction of new 3-haloaryne precursors **2a-h** were studied. The *ortho*-(trimethylsilyl)aryl triflate precursors **2a-h** were prepared by the simple procedure involving *O*-trimethylsilylation and migration of trimethylsilyl group followed by triflation. The remarkable feature of new precursors is the selective generation of 3-haloarynes by suppressing the competitive thia-Fries rearrangement, which is the problem in the reaction using the well-known 3-haloaryne precursors. The advantage of new precursor **2a** over a typical precursor **1** was confirmed by the direct comparisons in several reactions. The application of precursors **2a-h** to the synthesis of heterocycles was also reported.



INTRODUCTION

Aryne chemistry has made great advances in organic synthesis,[1-4] particularly by the development of *ortho*-(trimethylsilyl)aryl triflates as easily activatable aryne precursors.[5,6] In recent years, various precursors bearing functional groups have been explored to increase the diversity in aryne-based products.[7-13] However, the use of unsymmetrically substituted arynes is frequency constrained by the low regioselectivity; thus, the regiocontrol using functional groups is an important task.[14,15] As a novel method controlling the regioselectivity, the introduction of silyl or boryl group at 3-position of arynes has been studied.[7,8] The inductively electron-withdrawing groups such as 3-alkoxy[9] and 3-triflyloxy[10-12] are known to direct the regioselectivity.[13]

Sufficient regiocontrol can be achieved by 3-haloarynes.[14,16] The precursor **1** is a typical precursor for generating 3-chloroaryne **C** (Figure 1). However, the generation of 3-chloroaryne **C** from **1** is plagued by the competitive thia-Fries rearrangement leading to **B**.[17] In the method using precursor **1**, we presume that the steric repulsion in anion **A** would promote thia-Fries rearrangement. We assumed that the competitive thia-Fries rearrangement could be suppressed by simply swapping the position of the triflate and trimethylsilyl (TMS) groups on the precursor. Therefore, we have started to study the viability of new precursor **2a**. Some preliminary results were reported in our patent.[18] In this paper, we report *in detail* the simple and practical method for preparing new 3-haloaryne precursors such as **2a** and the selective aryne generation from the sterically stable anions such as **D**. When a new precursor **2a** is used, thia-Fries rearrangement of anion **D** leading to the sterically unfavorable anion

E is completely suppressed. A method for synthesizing heterocycles using our new 3-haloaryne precursors is also reported.

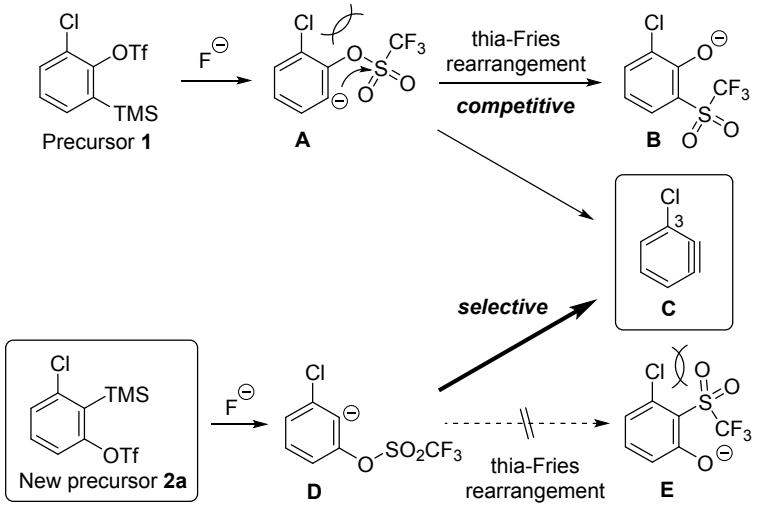
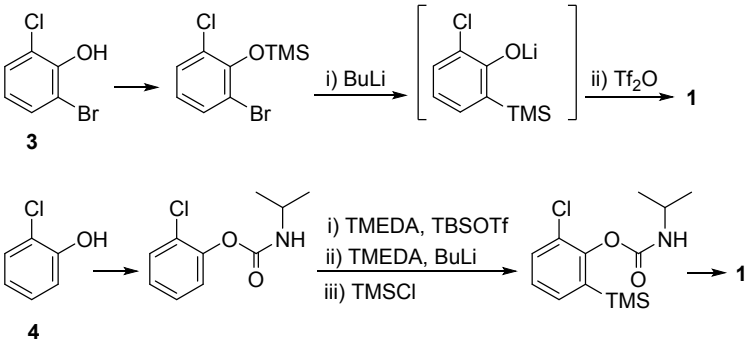


Figure 1. New precursor **2a** for selective generation of 3-chloroaryne **C**.

RESULTS AND DISCUSSION

The well-known 3-chloroaryne precursor **1** was generally prepared from the particular substrate 2-bromo-6-chlorophenol **3** *via* the bromine-lithium exchange reaction (Scheme 1).[19] Garg and Houk's group developed an alternative method starting from the readily available substrate 2-chlorophenol **4**, in which *N*-isopropylcarbamate was used as a directing group for *ortho*-metalation.[20]



Scheme 1. Two methods for preparing the known precursor **1**.

As the simple and practical approach to new precursor **2a**, we examined the direct *ortho*-metalation procedure starting from the readily available 3-chlorophenol **5a** (Figure 1). The key requirement for our method is assumed to be the selective deprotonation (metalation) of *O*-trimethylsilylated intermediate **7a** *in situ* generated by the reaction of **5a** with hexamethyldisilazane (HMDS).[21] Another problem is that the competitive elimination of chlorine atom on anion **F** giving aryne **H** might impede the expected migration of trimethylsilyl group leading to **G**.[22]

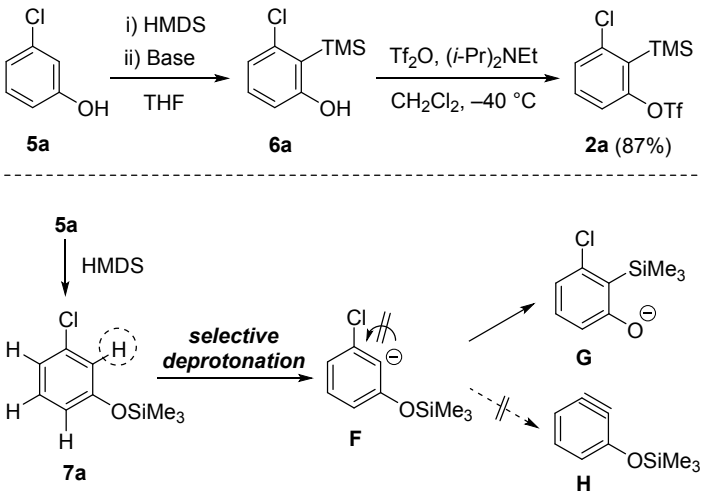


Figure 2. Synthetic approach to new precursor **2a**.

The effect of several bases on TMS-migration leading to **6a** is summarized in Table 1.[23] To prepare the *O*-trimethylsilylated intermediate **7a**, we initially allowed 3-chlorophenol **5a** to react with 1.5 equivalents of HMDS in THF at 50 °C. After being stirred at 50 °C for 5 hours, several bases were next added to this reaction mixture at –80 °C. Treatment with *t*-BuLi from –80 °C to 0 °C did not lead to the formation of the desired *C*-trimethylsilylated phenol **6a** (entry 1). *O*-Silylated intermediate **7a** and the recovered starting material **5a** were obtained in 50% and 15% yields, respectively. In contrast, the desired TMS-migration product **6a** was obtained in reasonable chemical yields when LiN(*i*-Pr)$_2$ or Li(TMP) was employed as a base (entries 2 and 3). Furthermore, the use of 2,2,6,6-tetramethylpiperidinylmagnesium chloride lithium chloride complex[24] Mg(TMP)$_2$·2LiCl led to an enhancement in chemical yield of TMS-migration product to give **6a** in 86% yield (entry 4). Mg(TMP)$_2$·2LiCl was used in the aryne generation by Tokuyama's group;[25] thus, it is important to note that Mg(TMP)$_2$·2LiCl can be used for the selective deprotonation of **7a** without the aryne generation. The conversion of *C*-silylated phenol **6a** to new precursor **2a** was achieved in 87% yield by treatment of phenol **6a** with Tf_2O in the presence of (*i*-Pr)$_2$NEt in CH_2Cl_2 at –40 °C for 5 hours (Figure 2). In fact, this procedure facilitated the gram-scale synthesis of precursor **2a**.

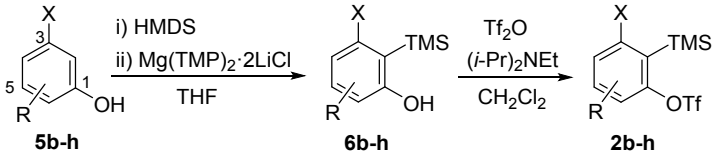
Table 1. Effect of base on TMS-migration leading to **6a**.[a]

Entry	Base (equiv.)	**6a** (% Yield)[b]
1	*t*-BuLi (1.2)	Not detected [**7a** (50), **5a** (15)]
2	LiN(*i*-Pr)$_2$ (1.2)	**6a** (57)
3	Li(TMP) (1.2)	**6a** (44)
4	Mg(TMP)$_2$·2LiCl (1.2)	**6a** (86)

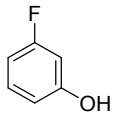
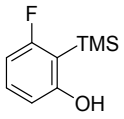
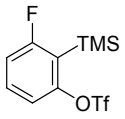
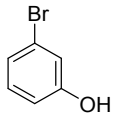
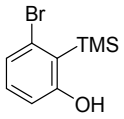
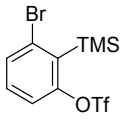
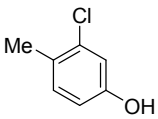
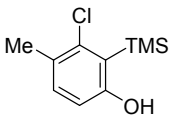
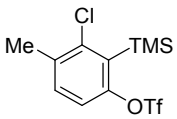
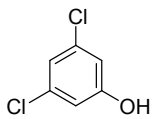
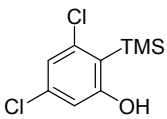
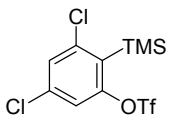
[a] After treatment of 3-chlorophenol **5a** with HMDS (1.5 equiv.) in THF at 50 °C for 5 h, base (1.2 equiv.) was added to the reaction mixture at –80 °C. The reaction mixture was stirred at –80 °C for 1 h and at –80 °C to 0 °C for 3 h. [b] Isolated yields.

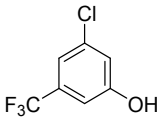
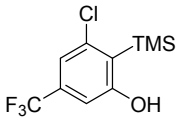
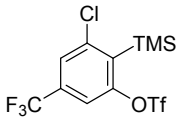
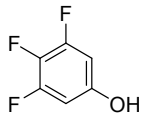
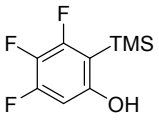
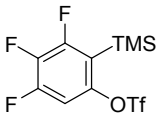
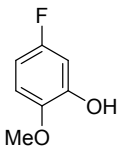
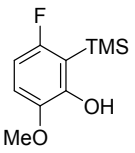
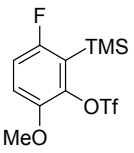
With these results in mind, we next synthesized the various precursors **2b-h** from easily available 3-halophenol derivatives **5b-h** (Table 2). In the case of 3-fluorophenol **5b**, *O*-trimethylsilylation and TMS-migration proceeded effectively to give the *C*-trimethylsilylated phenol **6b** in 81% (entry 1). 3-Fluoroaryne precursor **2b** was synthesized by the triflation of **6b** with Tf_2O. Under the similar reaction conditions using $Mg(TMP)_2{\cdot}2LiCl$, TMS-migration of 3-bromophenol **5c** did not take place effectively owing to the competitive generation of several unidentified by-products. Therefore, this transformation was re-examined by changing a base form $Mg(TMP)_2{\cdot}2LiCl$ to $LiN(i\text{-}Pr)_2$ (entry 2). The use of $LiN(i\text{-}Pr)_2$ led to the formation of *C*-silylated phenol **6c** in 34% yield, which was converted to 3-bromoaryne precursor **2c** in 75% yield. When 3-chloro-4-methylphenol **5d** was employed, the corresponding precursor **2d** was prepared with the reasonable chemical efficiency (entry 3). The use of 3,5-dichlorophenol **5e** as a substrate led to a decrease in the chemical yield of *C*-silylated phenol **6e** (entry 4). In the case of 3,5-dichlorophenol **5e**, the deprotonation at C4 position may compete with the desired deprotonation at C2 position. In contrast, *O*-trimethylsilylation and TMS-migration of 3-chloro-5-trifluorometylphenol **5f** proceeded effectively to give the *C*-silylated phenol **6f** in 69% (entry 5). 3,4,5-Trifluorophenol **5g** was converted into precursor **2g** without any problems (entry 6). Additionally, the precursor **2h** bearing a methoxy group at C6 position was synthesized with good chemical efficiencies, allowing facile incorporation of structural variety (entry 7).

Table 2. Synthesis of precursor **2b-h**.

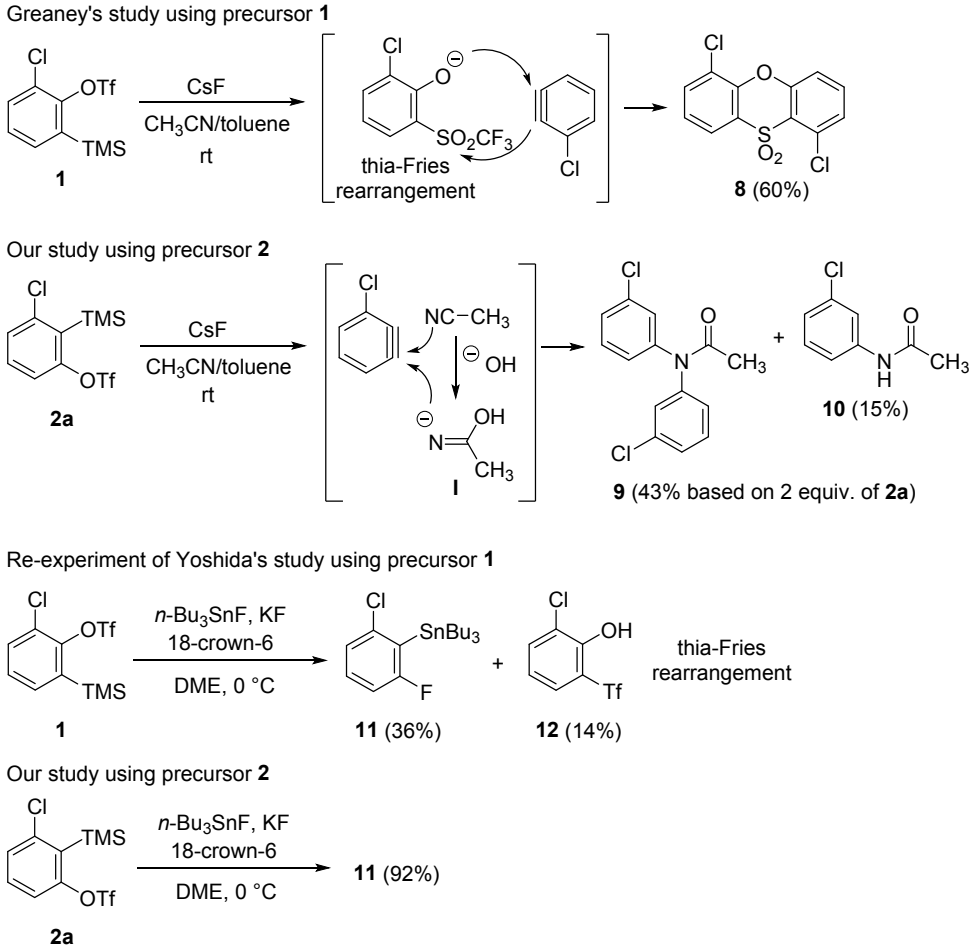


5b-h **6b-h** **2b-h**

Entry	Substrate	Phenol (% Yield)[a]	Precursor (% Yield)[a]
1[b]			
	5b	**6b** (81)	**2b** (73)
2[c]			
	5c	**6c** (34)	**2c** (75)
3[b]			
	5d	**6d** (53)	**2d** (76)
4[b]			
	5e	**6e** (30)	**2e** (60)

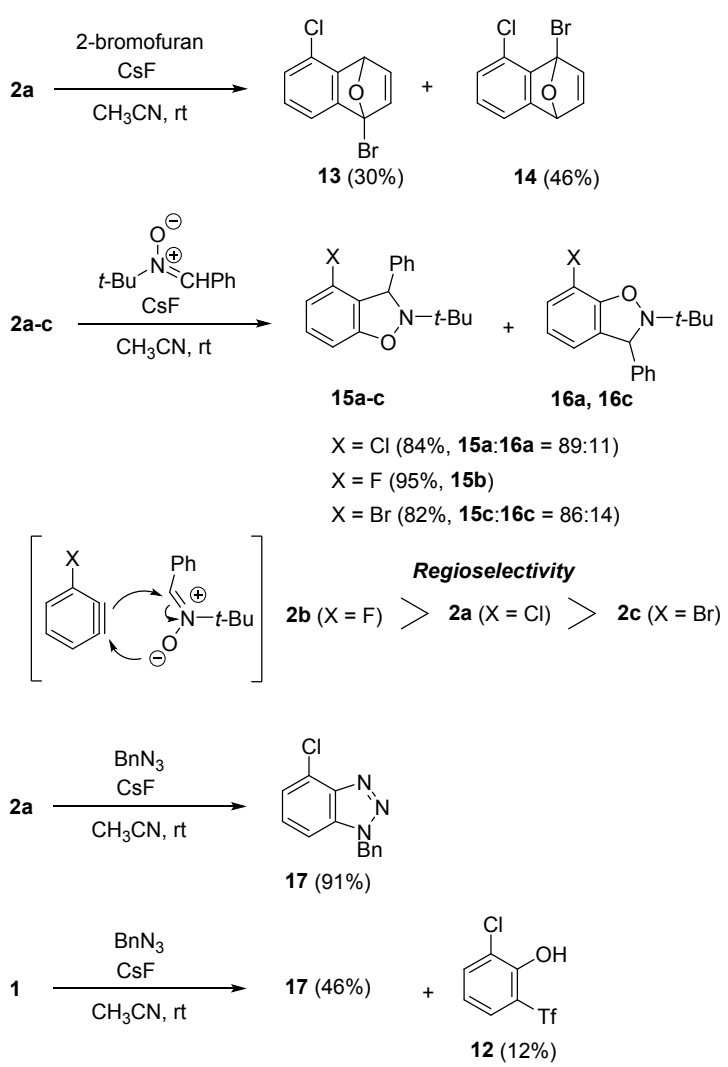
5 [b]			
	5f	**6f** (69)	**2f** (92)
6 [b]			
	5g	**6g** (69)	**2g** (76)
7 [b]			
	5h	**6h** (91)	**2h** (97)

[a] Isolated yields. [b] After treatment of 3-halophenol **5b-h** with HMDS (1.5 equiv.) in THF at 50 °C for 5 h, $Mg(TMP)_2 \cdot 2LiCl$ (1.2 equiv.) was added to the reaction mixture at –80 °C. The reaction mixture was stirred at –80 °C for 1 h and at –80 °C to 0 °C for 3 h. [c] Instead of $Mg(TMP)_2 \cdot 2LiCl$, $LiN(i\text{-}Pr)_2$ (1.2 equiv.) was used as a base under the same reaction conditions.



Scheme 2. Direct comparisons between well-known precursor **1** and new precursor **2a**.

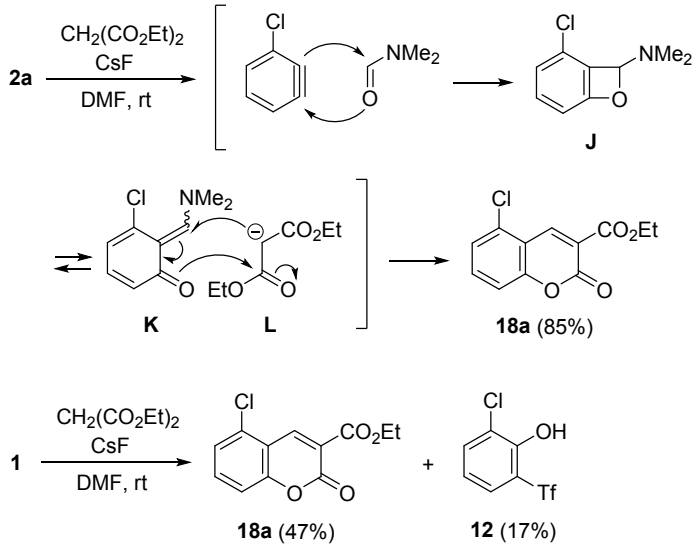
We next sought to explore the utility of our novel aryne precursor **2a** by comparing its reactivity to that of **1** (Scheme 2). Tandem thia-Fries rearrangement–cyclization of **1** giving phenoxathiindioxide **8** was reported by Greaney's group.[17b] When aryltriflate **2a** was used as an aryne precursor under the same reaction conditions, thia-Fries rearrangement was completely suppressed and the formation of the corresponding phenoxathiindioxide was not observed. In marked contrast, the *N,N*-bis(3-chlorophenyl)acetamide **9** and *N*-(3-chlorophenyl)acetamide **10** were newly obtained as a result of the selective generation of 3-chloroaryne from **2a** followed by the reaction of 3-chloroaryne with acetonitrile. Hu's group reported the reaction of aryne with acetonitrile in the diphenyliodonium-catalyzed fluorination of arynes using *ortho*-(trimethylsilyl)aryl triflates in acetonitrile. They propose that aryne reacts with anion **I** generated from acetonitrile and hydroxide.[26] Yoshida's group reported that the insertion of *n*-Bu_3SnF into 3-chloroaryne generated from **1** proceeded in 1,2-dimethoxyethane (DME) with the moderated chemical efficiency to give the insertion product **11** in 41% yield.[27] In fact, we repeated this reaction and observed the competitive formation of the desired product **11** in 36% yield and thia-Fries rearrangement product **12** in 14% yield. The dramatic improvement in the chemical efficiency of this insertion reaction was achieved by changing a precursor from **1** into **2a**. The insertion product **11** was obtained in 92% yield by using new precursor **2a**. It is also noteworthy that a chlorine atom on new precursor **2a** worked well for controlling the regioselectivities of these reactions.



Scheme 3. The utility of new precursor **2a** in cycloaddition reactions.

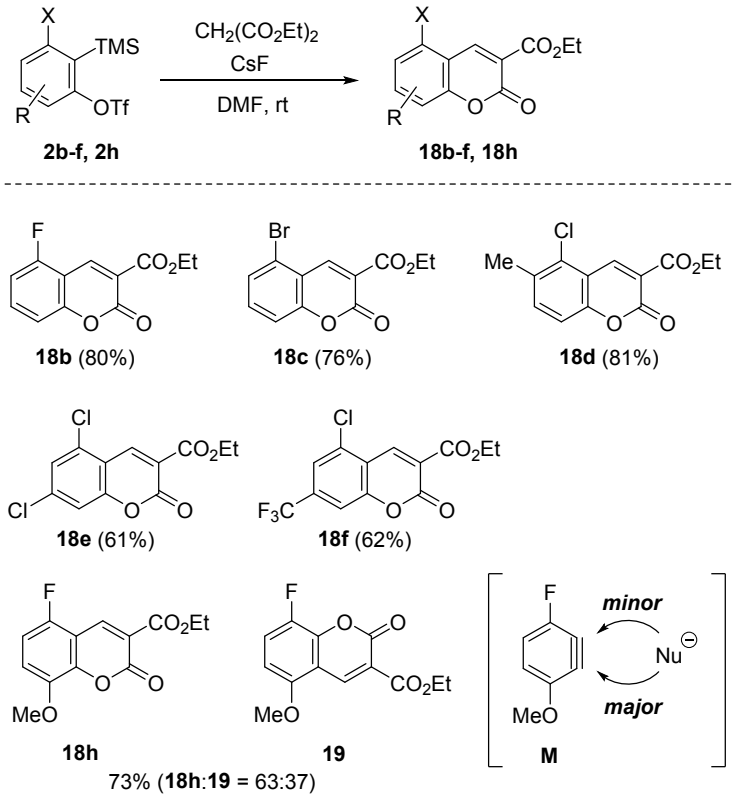
We next studied the ability of new precursor **2a** for controlling the regioselectivities in cycloaddition reactions (Scheme 3). Diels–Alder-type reaction of **2a** with 2-bromofuran proceeded effectively, although it has shown the low regioselectivity. The regioisomers **13** and **14** were obtained in about 4:6 ratio. Good regioselectivities were observed in 1,3-dipolar cycloadditions using *N*-*tert*-butyl-α-phenylnitrone. 3-Chloroaryne precursor **2a**, 3-fluoroaryne precursor **2b** and 3-bromoaryne precursor **2c** were employed. The [3+2] reaction of 3-chloroaryne, generated from **2a**, proceeded regioselectively to give the regioisomers **15a** and **16a** in 89:11 ratio. The use of precursor **2b** having a fluorine atom led to an enhancement in the regioselectivity to give the adduct **15b** in 95% yield without the formation of regioisomer, while the ratio of regioisomers **15c** and **16c** decreased to 86:14 by using 3-bromoaryne precursor **2c**. The effect of halogen atom on directing the regioselectivity (F > Cl > Br) consists with the distortion/interaction model propounded by Garg and Houk.[14] The advantage of new precursor **2a** over a typical precursor **1** was again confirmed by the [3+2] cycloaddition using benzylazide. The Huisgen-type reaction of **2a** with benzylazide proceeded regioselectively under the copper metal-free reaction conditions to give the cyclic product **17** in 91% yield. In contrast, the use of a precursor **1** led to the competitive formation of the desired product **17** and thia-Fries rearrangement product **12**.

Next, the regiocontrolling effect of new precursors **2a** on [2+2]-type reaction of aryne and *N*,*N*-dimethylformamide (DMF) was examined by using three-component coupling reaction developed by our group (Scheme 4).[28,29] In the presence of CsF, treatment of **2a** with diethyl malonate in DMF gave the coumarin derivative **18a** in 85% yield without the formation of regioisomer. This reaction proceeded *via* a route involving the highly regioselective insertion of 3-chloroaryne into C=O π-bond of DMF and the subsecent trapping of intermediate **K** with anion **L** of diethyl malonate.[30] When a precursor **1** was employed, the competitive formation of thia-Fries rearrangement product **12** was observed.



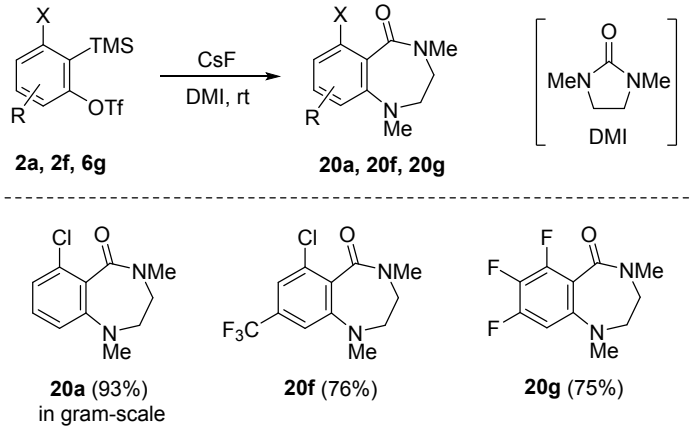
Scheme 4. Three-component coupling reaction using precursor **2a**.

The synthesis of various coumarin derivatives using new precursors is shown in Scheme 5. High regioselectivities were achieved in the reaction using 3-fluoroaryne precursor **2b** and 3-bromoaryne precursor **2c** to give the coumarin derivatives **18b** and **18c** in 80% and 76% yields, respectively. The 3-chloro-4-methylaryne precursor **2d**, 3,5-dichloroaryne precursor **2e** and 3-chloro-5-trifluoromethylaryne precursor **2f** worked well. Next, the ability of a fluorine atom on aryne for directing the regioselectivity was investigated by using the 3,6-disubstituted aryne **M** derived from precursor **2h**. The directing ability of a fluorine atom on aryne **M** decreased by the effect of methoxy group as an inductively electron-withdrawing group to give the regioisomers **18h** and **19** in 63:37 ratio.



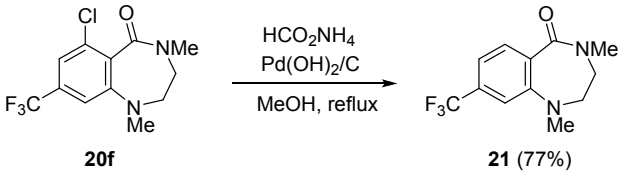
Scheme 5. The synthesis of coumarin derivatives using new precursors.

The synthesis of tetrahydrobenzodiazepine derivatives based on the insertion of arynes into C–N σ-bond is shown in Scheme 6.[31] In the presence of CsF, new precursor **2a** regioselectively reacted with 1,3-dimethyl-2-imidazolidinone (DMI) to give the benzodiazepine derivative **20a** in 93% yield. Notably, the reaction of **2a** with DMI was performed in gram scale. As expected, the use of 3-chloro-5-trifluorometylaryne precursor **2f** and 3,4,5-trifluoroaryne precursor **2g** led to the formation of the corresponding product **20f** and **20g** in good yields.



Scheme 6. The synthesis of benzodiazepine derivatives.

The chlorine atom on precursors can be used as a removable directing group. We finally show the method for reductive dechlorination (Scheme 7). In the presence of $Pd(OH)_2/C$, the hydrogenation of benzodiazepine derivative **20f** with ammonium formate gave the dechlorinated product **21** in 77% yield.



20f **21** (77%)

Scheme 7. Dechlorination of benzodiazepine derivative **20f**.

CONCLUSION

We have developed the convenient method for preparing new 3-haloaryne precursors *via* *O*-trimethylsilylation and migration of trimethylsilyl group followed by triflation. The use of new precursors suppresses the problematic thia-Fries rearrangement as a competitive side-reaction, leading to the selective generation of 3-haloarynes. New 3-haloaryne precursors were successfully applied to the regioselective synthesis of various heterocycles based on Diels-Alder-type reaction, 1,3-dipolar cycloaddition, π-bond insertion and σ-bond insertion of arynes

EXPERIMENTAL SECTION

General. Melting points were taken on a Yanaco MP-J3 and are uncorrected. Infrared spectra were measured on a JASCO FT/IR-4100. ^{1}H-NMR spectra were measured on a JEOL ECX-400 PSK (400 MHz) or Varian NMRS 600 (600 MHz) with $CDCl_3$ as an internal standard (7.26 ppm) or CD_3CN as an internal standard (1.94 ppm). ^{13}C-NMR spectra were measured on a JEOL ECX-400 PSK (100 MHz) or Varian NMRS 600 (151 MHz) with $CDCl_3$ as an internal standard (77.0 ppm) or CD_3CN as an internal standard (118.0 ppm). ^{19}F-NMR spectra were measured on a JEOL ECX-400 PSK (376 MHz) with C_6F_6 as an internal standard (–162.2 ppm). High-resolution mass spectra were recorded on a time-of-flight (TOF) mass spectrometer by use of Thermo Fisher Scientific Exactive LC/MS spectrometer. For silica gel column chromatography, SiliCycle Inc. SiliaFlash F60 was used. Preparative TLC separations were carried out on precoated silica gel plates (E. Merck $60F_{254}$). Products **6e**,[32] **7a**,[33] **10**,[34] **11**,[27] **12**[17b], **17**[14a] and **18a**[35] are known compounds.

Procedure for preparing Mg(TMP)$_2$·2LiCl: To a suspension of magnesium metal (turning, 535 mg, 22.0 mmol) in freshly distilled THF (55 mL) was added 1,2-dichloroethane (1.72 mL, 22.0 mmol) under argon atmosphere at room temperature and stirred at the same temperature for an hour. In another two neck flask, *n*-BuLi (1.6 M in hexane, 27.5 mL, 44.0 mmol) was added dropwise to a solution of 2,2,6,6-tetramethylpiperidine (TMPH, 7.43 mL, 44.0 mmol) in freshly distilled THF (22 mL) under argon atmosphere at –80 °C. After being warmed to 0 °C, this mixture was stirred at the same temperature for 30 min. To Li(TMP) solution in two neck flask was added dropwise the $MgCl_2$ solution at 0 °C and the reaction mixture was stirred at the same temperature for an hour.

General procedure for TMS-migration reaction using Mg(TMP)$_2$·2LiCl: To a solution of phenol derivatives **5a**, **5b** or **5d-h** (20.0 mmol) in freshly distilled THF (20 mL) was added 1,1,1,3,3,3-hexamethyldisilazane (HMDS, 6.26 mL, 30.0 mmol) under argon atmosphere at room temperature. After being stirred at 50 °C the same temperature for 5 hours, the reaction mixture was concentrated at reduced pressure. The obtained *O*-trimethylsilylated intermediates were used next TMS-migration reaction without purification. To a solution of *O*-trimethylsilylated intermediates (20.0 mmol) in freshly distilled THF (20 mL) was added dropwise Mg(TMP)$_2$·2LiCl solution (22.0 mmol) under argon atmosphere at –80 °C. After being stirred at the same temperature for an hour, the reaction mixture was stirred at –80 °C to 0 °C for 3 hours. The reaction mixture was diluted with iced 0.5 M sodium (+)-tartrate solution and then extracted with hexanes. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography afforded the products **6a**, **6b** or **6d-h**.

Procedure for preparing LiN(*i*-Pr)$_2$: To a solution of diisopropylamine ((*i*-Pr)$_2$NH, 3.37 mL, 24.0 mmol) in freshly distilled THF (12 mL) was added *n*-BuLi (1.6 M in hexane, 15.0 mL, 24.0 mmol) under argon atmosphere at –80 °C. After being warmed to 0 °C, this mixture was stirred at the same temperature for 30 min.

General procedure for TMS-migration reaction using LiN(*i*-Pr)$_2$: To a solution of phenol derivatives **5a** or **5c** (20.0 mmol) in freshly distilled THF (20 mL) was added 1,1,1,3,3,3-hexamethyldisilazane (HMDS, 6.26 mL, 30.0 mmol) under argon atmosphere at room temperature. After being stirred at 50 °C the same temperature for 5 hours, the reaction mixture was concentrated at reduced pressure. The obtained *O*-trimethylsilylated intermediates were used next TMS-migration reaction without purification. To a solution of *O*-trimethylsilylated intermediates (20.0 mmol) in freshly distilled THF (20 mL) was added dropwise LiN(*i*-Pr)$_2$ solution (24.0 mmol) under argon atmosphere at –80 °C. After being stirred at the same temperature for an hour, the reaction temperature was raised to 0 °C and the reaction mixture was stirred at the same temperature for 3 hours. The reaction mixture was diluted with iced water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography -afforded the products **6a** or **6c**.

3-Chloro-2-(trimethylsilyl)phenol (6a) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5a** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6a** (3.44 g, 86%) as colorless oil. Following the general procedure using LiN(*i*-Pr)$_2$, the reaction of **5a** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6a** (2.28 g, 57%) as colorless oil. IR (KBr) 3572 (br), 2954, 1582, 1423 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (1H, br t, *J* = 8.0 Hz), 6.91 (1H, d, *J* = 8.0 Hz), 6.60 (1H, d, *J* = 8.0 Hz), 5.20 (1H, br s), 0.45 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 141.6, 131.1, 123.2, 122.4, 113.7, 1.8. HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_9H_{12}{}^{35}ClOSi$ 199.0351; Found: 199.0352; Calcd for $C_9H_{12}{}^{37}ClOSi$ 201.0324; Found: 201.0310.

3-Fluoro-2-(trimethylsilyl)phenol (6b) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5b** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6b** (2.97 g, 81%) as colorless oil. IR (KBr) 3302 (br), 2924, 1605, 1441 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (1H, td, *J* = 8.2, 6.9 Hz), 6.57 (1H, td, *J* = 8.2, 1.0 Hz), 6.48 (1H, dd, *J* = 8.2, 1.0 Hz), 5.15 (1H, br s), 0.37 (9H, d, *J* = 1.8 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.0 (d, *J* = 243 Hz), 161.3 (d, *J* = 15 Hz), 131.5

(d, J = 11 Hz), 111.7 (d, J = 33 Hz), 110.7 (d, J = 3 Hz), 107.5 (d, J = 27 Hz), 0.5 (d, J = 3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −98.2 (1F, s). HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_9H_{12}FOSi$ 183.0647; Found: 183.0651.

3-Bromo-2-(trimethylsilyl)phenol (6c) Following the general procedure using LiN(*i*-Pr)$_2$, the reaction of **5c** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6c** (1.68 g, 34%) as colorless oil. IR (KBr) 3567 (br), 2954, 1583, 1564, 1418, 1251 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (1H, dd, J = 7.8, 1.0 Hz), 7.03 (1H, br t, J = 7.8 Hz), 6.64 (1H, dd, J = 7.8, 1.0 Hz), 5.30 (1H, br s), 0.48 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 131.3, 130.9, 126.1, 125.2, 114.3, 2.1. HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_9H_{12}{}^{79}BrOSi$ 242.9846; Found: 242.9841; Calcd for $C_9H_{12}{}^{81}BrOSi$ 244.9826; Found: 244.9819.

3-Chloro-4-methyl-2-(trimethylsilyl)phenol (6d) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5d** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6d** (2.29 g, 53%) as colorless oil. IR (KBr) 3584 (br), 2953, 1574, 1452, 1368, 1251 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (1H, d, J = 8.2 Hz), 6.55 (1H, d, J = 8.2 Hz), 5.19 (1H, br s), 2.27 (3H, s), 0.46 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4, 141.4, 132.4, 128.5, 123.0, 113.9, 20.3, 2.0. HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_{10}H_{14}{}^{35}ClOSi$ 213.0508; Found: 213.0509; Calcd for $C_{10}H_{14}{}^{37}ClOSi$ 215.0481; Found: 215.0470.

3,5-Dichloro-2-(trimethylsilyl)phenol (6e) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5e** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6e** (1.42 g, 30%) as colorless oil. IR (KBr) 3307 (br), 2956, 1575, 1377, 1251 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (1H, d, J = 1.8 Hz), 6.64 (1H, d, J = 1.8 Hz), 5.77 (1H, br s), 0.43 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.7, 142.1, 136.0, 122.4, 114.8, 114.2, 1.6. HRMS (ESI$^-$/TOF) m/z: [M − TMS]$^-$ Calcd for $C_6H_3{}^{35}Cl_2O$ 160.9566; Found: 160.9567; Calcd for $C_6H_3{}^{35}Cl^{37}ClO$ 162.9537; Found: 162.9535; Calcd for $C_6H_3{}^{37}Cl_2O$ 164.9509; Found: 164.9509.

3-Chloro-5-trifluoromethyl-2-(trimethylsilyl)phenol (6f) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5f** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6f** (3.70 g, 69%) as colorless oil. IR (KBr) 3601 (br), 2957, 1565, 1469, 1400, 1329 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (1H, br s), 6.84 (1H, br s), 5.78 (1H, br s), 0.46 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.6, 142.3, 133.2 (q, J = 33 Hz), 127.9, 123.0 (q, J = 274 Hz), 119.0 (q, J = 4 Hz), 110.4 (q, J = 4 Hz), 1.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.9 (3F, s). HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_{10}H_{11}{}^{35}ClF_3OSi$ 267.0225; Found: 267.0223; Calcd for $C_{10}H_{11}{}^{37}ClF_3OSi$ 269.0198; Found: 269.0192.

3,4,5-Trifluoro-2-(trimethylsilyl)phenol (6g) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5g** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:6) afforded the product **6g** (3.02 g, 69%) as colorless oil. IR (KBr) 3284 (br), 2926, 1614, 1513, 1435 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (1H, ddd, J = 11.0, 5.0, 2.3 Hz), 5.52 (1H, br s), 0.36 (9H, d, J = 1.8 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.3 (ddd, J = 243, 10, 6 Hz), 155.2 (d, J = 14 Hz), 151.7 (ddd, J = 249, 11, 6 Hz), 134.5 (ddd, J = 247, 20, 15 Hz), 109.0 (m), 99.7 (dd, J = 19, 2 Hz), 0.3 (d, J = 3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −121.8 (1F, d, J = 23 Hz), −133.9 (1F, m), −172.5 (1F, m). HRMS (ESI$^-$/TOF) m/z: [M − H]$^-$ Calcd for $C_9H_{10}F_3OSi$ 219.0459; Found: 219.0460.

3-Fluoro-6-methoxy-2-(trimethylsilyl)phenol (6h) Following the general procedure using Mg(TMP)$_2$·2LiCl, the reaction of **5h** was carried out.

Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 20:1–1:4) afforded the product **6h** (3.88 g, 91%) as colorless oil. IR (KBr) 3529 (br), 2957, 1615, 1460, 1433, 1227 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.77 (1H, dd, *J* = 8.7, 5.0 Hz), 6.47 (1H, t, *J* = 8.7 Hz), 5.97 (1H, br d, *J* = 1.4 Hz), 3.85 (3H, s), 0.35 (9H, d, *J* = 1.8 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4 (d, *J* = 235 Hz), 150.5 (d, *J* = 16 Hz), 142.3 (d, *J* = 3 Hz), 112.0 (d, *J* = 12 Hz), 111.5 (d, *J* = 36 Hz), 105.2 (d, *J* = 29 Hz), 56.4, 0.3 (d, *J* = 3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.7 (1F, s). HRMS (ESI^-/TOF) m/z: $[M - H]^-$ Calcd for $C_{10}H_{14}FO_2Si$ 213.0753; Found: 213.0750.

General procedure for the synthesis of precursor using Tf_2O: To a solution of **6a-h** (6.0 mmol) and *N*,*N*-diisopropylethylamine (1.2 mL, 6.9 mmol) in anhydrous dichloromethane (15 mL) was added dropwise trifluoromethanesulfonic anhydride (1.11 mL, 6.6 mmol) under argon atmosphere at –40 °C. After being stirred at the same temperature for 5 hours, the reaction mixture was diluted with iced water and then extracted with dichloromethane. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography afforded the products **2a-h**.

3-Chloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2a) Following the general procedure using Tf_2O, the reaction of **6a** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2a** (1.67 g, 87%) as colorless oil. IR (KBr) 2959, 1586, 1422, 1361 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.37 (1H, dd, *J* = 7.9, 1.5 Hz), 7.34 (1H, t, *J* = 7.9 Hz), 7.26 (1H, dd, *J* = 7.9, 1.5 Hz), 0.49 (9H, s). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 154.5, 142.4, 131.9, 131.2, 129.8, 118.9, 118.6 (q, *J* = 321 Hz), 1.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.1 (3F, s). HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_7H_3{}^{35}ClF_3O_3S$ 258.9449; Found: 258.9445; Calcd for $C_7H_3{}^{37}ClF_3O_3S$ 260.9420; Found: 260.9405.

3-Fluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2b) Following the general procedure using Tf_2O, the reaction of **6b** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2b** (1.38 g, 73%) as colorless oil. IR (KBr) 2960, 1606, 1440 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (1H, td, *J* = 8.2, 6.4 Hz), 7.16 (1H, br m), 7.03 (1H, dd, *J* = 8.2, 1.0 Hz), 0.42 (9H, d, *J* = 1.8 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.3 (d, *J* = 247 Hz), 154.1 (d, *J* = 15 Hz), 131.9 (d, *J* = 11 Hz), 120.3 (d, *J* = 35 Hz), 118.5 (q, *J* = 322 Hz), 116.1 (br s), 115.1 (d, *J* = 27 Hz), 0.3 (d, *J* = 4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.5 (3F, s). −94.1 (1F, m). HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_7H_3F_4O_3S$ 242.9745; Found: 242.9745.

3-Bromo-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2c) Following the general procedure using Tf_2O, the reaction of **6c** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2c** (1.70 g, 75%) as colorless oil. IR (KBr) 2960, 1583, 1552, 1421 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (1H, dd, *J* = 7.8, 1.4 Hz), 7.34−7.23 (2H, m), 0.52 (9H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ154.4, 134.0, 133.5, 131.4 (2C), 119.5 (d, *J* = 2 Hz), 118.5 (q, *J* = 323 Hz), 1.7.. ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.1 (3F, s). HRMS (ESI^-/TOF) m/z: $[M - H]^-$ Calcd for $C_{10}H_{11}{}^{79}BrF_3O_3SSi$ 374.9339; Found: 374.9343; Calcd for $C_{10}H_{11}{}^{81}BrF_3O_3SSi$ 376.9319; Found: 376.9344.

3-Chloro-4-methyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2d) Following the general procedure using Tf_2O, the reaction of **6d** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2d** (1.59 g, 76%) as colorless oil. IR (KBr) 2959, 1575, 1422 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (1H, d, *J* = 8.2 Hz), 7.15 (1H, d, *J* = 8.2 Hz), 2.38

(3H, s), 0.49 (9H, s). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.4, 142.2, 136.9, 132.5, 131.9, 118.8, 118.5 (q, *J* = 323 Hz), 20.7, 1.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.0 (3F, s). HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_8H_5{}^{35}ClF_3O_3S$ 272.9605; Found: 272.9601; Calcd for $C_8H_5{}^{37}ClF_3O_3S$ 274.9577; Found: 274.9554.

3,5-Dichloro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2e) Following the general procedure using Tf_2O, the reaction of **6e** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2e** (1.32 g, 60%) as colorless crystals. Mp ca. 20 °C (hexanes). IR (KBr) 2959, 1579, 1538, 1429, 1368 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (1H, d, *J* = 1.8 Hz), 7.28 (1H, d, *J* = 1.8 Hz), 0.48 (9H, s). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.1, 142.9, 136.4, 130.5, 129.8, 119.6, 118.5 (q, *J* = 322 Hz), 1.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.0 (3F, s). HRMS (ESI^-/TOF) m/z: $[M - H]^-$ Calcd for $C_{10}H_{10}{}^{35}Cl_2F_3O_3SSi$ 364.9455; Found: 364.9451; Calcd for $C_{10}H_{10}{}^{35}Cl^{37}ClF_3O_3SSi$ 366.9426; Found: 366.9417; Calcd for $C_{10}H_{10}{}^{37}Cl_2F_3O_3SSi$ 368.9399; Found: 368.9400. HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_7H_2{}^{35}Cl_2F_3O_3S$ 292.9055; Found: 292.9055; Calcd for $C_7H_2{}^{35}Cl^{37}ClF_3O_3S$ 294.9030; Found: 294.9026; Calcd for $C_7H_2{}^{37}Cl_2F_3O_3S$ 296.9001; Found: 296.9000.

3-Chloro-5-trifluoromethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2f) Following the general procedure using Tf_2O, the reaction of **6f** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2f** (2.22 g, 92%) as colorless oil. IR (KBr) 2961, 1554, 1449, 1431 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, br d, *J* = 1.0 Hz), 7.48 (1H, br s), 0.51 (9H, s). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.1, 143.3, 136.9, 133.6 (q, *J* = 35 Hz), 126.5 (q, *J* = 4 Hz), 122.2 (q, *J* = 273 Hz), 118.5 (q, *J* = 322 Hz), 116.1, 1.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.9 (3F, s), −72.9 (3F, s). HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_8H_2{}^{35}ClF_6O_3S$ 326.9323; Found: 326.9303; Calcd for $C_8H_2{}^{37}ClF_6O_3S$ 328.9294; Found: 328.9269.

3,4,5-Trifluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2g) Following the general procedure using Tf_2O, the reaction of **6g** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **2g** (1.61 g, 76%) as colorless oil. IR (KBr) 2963, 1626, 1496, 1430 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (1H, ddd, *J* = 9.6, 5.0, 2.3 Hz), 0.43 (9H, d, *J* = 1.8 Hz). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 155.0 (ddd, *J* = 247, 10, 5 Hz), 151.3 (ddd, *J* = 255, 12, 6 Hz), 147.1 (ddd, *J* = 16, 12, 5 Hz), 139.3 (ddd, *J* = 257, 20, 14 Hz), 118.4 (q, *J* = 322 Hz), 118.3 (dt, *J* = 31, 4 Hz), 106.5 (d, *J* = 21 Hz), 0.2 (d, *J* = 4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.4 (3F, s), −117.4 (1F, m), −129.6 (1F, m), −160.1 (1F, m). HRMS (ESI^-/TOF) m/z: $[M - H]^-$ Calcd for $C_{10}H_9F_6O_3SSi$ 350.9951; Found: 350.9949. HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_7HF_6O_3S$ 278.9556; Found: 278.9560.

3-Fluoro-6-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2h) Following the general procedure using Tf_2O, the reaction of **6h** was carried out. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:20–1:6) afforded the product **2h** (2.01 g, 97%) as colorless crystals. Mp 21−23 °C (hexanes). IR (KBr) 2960, 1578, 1464, 1417 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−6.93 (2H, m), 3.84 (3H, s), 0.43 (9H, d, *J* = 1.8 Hz). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 160.1 (d, *J* = 239 Hz), 147.3 (d, *J* = 3 Hz), 141.6 (d, *J* = 15 Hz), 122.8 (d, 35 Hz), 118.8 (q, *J* = 323 Hz), 115.2 (d, *J* = 29 Hz), 114.3 (d, *J* = 10 Hz), 56.1, 0.3 (d, *J* = 4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −71.9 (3F, m), −105.9 (1F, m). HRMS (ESI^-/TOF) m/z: $[M - H]^-$ Calcd for $C_{11}H_{13}F_4O_4SSi$ 345.0245; Found: 345.0246. HRMS (ESI^-/TOF) m/z: $[M - TMS]^-$ Calcd for $C_8H_5F_4O_4S$ 272.9850; Found: 272.9847.

Reaction of new precursor 2a with acetonitrile: To a suspension of CsF (91 mg, 0.60 mmol) in anhydrous acetonitrile-toluene (3:1, v/v, 0.40 mL) was added precursor **2a** (67 mg, 0.20 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:2) afforded the products **9** (12 mg, 43% based on 2 equiv. of **2a**) as colorless oil and **10** (5 mg, 15%) as colorless oil.

***N,N*-Bis(3-chlorophenyl)acetamide (9)** IR (KBr) 3066, 2928, 1682, 1588, 1474 cm^{-1}. ^1H NMR (400 MHz, CD_3CN at 50 °C) δ 7.41 (2H, t, J = 2.1 Hz), 7.38 (2H, d, J = 7.8 Hz), 7.33 (2H, m), 7.26 (2H, m), 1.99 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, CD_3CN at 50 °C) δ170.7, 145.2, 135.1, 131.6, 128.8, 128.1, 127.3, 23.7. HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{11}{}^{35}Cl_2NONa$ 302.0110; Found: 302.0123; Calcd for $C_{14}H_{11}{}^{35}Cl^{37}ClNONa$ 304.0082; Found: 304.0087.

***N*-(3-chlorophenyl)acetamide (10)** IR (KBr) 3303 (br), 3080, 2927, 1673, 1594, 1540, 1481, 1421 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, s), 7.34 (1H, d, J = 7.8 Hz), 7.27 (1H, br s), 7.23 (1H, t, J = 7.8 Hz), 7.08 (1H, d, J = 7.8 Hz), 2.18 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.3, 139.0, 134.6, 130.0, 124.3, 119.8, 117.7, 24.6. HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_8H_8{}^{35}ClNONa$ 192.0187; Found: 192.0191; Calcd for $C_8H_8{}^{37}ClNONa$ 194.0159; Found: 194.0169.

Reaction of precursor 1 with *n*-Bu_3SnF: To a suspension of KF (55 mg, 0.96 mmol) and 18-crown-6 (254 mg, 0.96 mmol) in anhydrous 1,2‐dimethoxyethane (DME, 4.0 mL) were added tributyltin fluoride (124 mg, 0.40 mmol) and precursor **1** (160 mg, 0.48 mg) under argon atmosphere at 0 °C. After being stirred at the same temperature for 7 hours, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **11** (60 mg, 36%) as colorless oil and **12** (15 mg, 14%) as yellow solid.

Reaction of new precursor 2a with *n*-Bu_3SnF: To a suspension of KF (55 mg, 0.96 mmol) and 18-crown-6 (254 mg, 0.96 mmol) in anhydrous 1,2‐dimethoxyethane (DME, 4.0 mL) were added tributyltin fluoride (124 mg, 0.40 mmol) and precursor **2a** (160 mg, 0.48 mg) under argon atmosphere at 0 °C. After being stirred at the same temperature for 7 hours, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1–1:10) afforded the product **11** (154 mg, 92%) as colorless oil.

Tributyl(2-chloro-6-fluorophenyl)stannane (11) IR (KBr) 2958, 1587, 1556, 1461, 1428 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (1H, m), 7.13 (1H, d, J = 7.8 Hz), 6.88 (1H, br t, J = 7.8 Hz), 1.58−1.48 (6H, m), 1.38−1.29 (6H, m), 1.28−1.12 (6H, m), 0.89 (9H, t, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.3 (d, J = 240 Hz), 142.7 (d, J = 17 Hz), 130.9 (d, J = 9 Hz), 128.6 (d, J = 50 Hz), 124.8 (d, J = 3 Hz), 112.7 (d, J = 30 Hz), 28.9 (t, J = 10 Hz), 27.2 (t, J = 33 Hz), 13.6, 12.0 (d, J = 3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −91.0 (1F, t, J = 7 Hz). HRMS (ESI^-/TOF) m/z: $[M - Bu]^-$ Calcd for $C_{14}H_{21}{}^{35}ClF^{120}Sn$ 363.0339; Found: 363.0352; Calcd for $C_{14}H_{21}{}^{35}ClF^{118}Sn$ 361.0337; Found: 361.0366.

2-Chloro-6-(trifluoromethylsulfonyl)phenol (12) IR (KBr) 3408 (br), 2926, 1666, 1591, 1685, 1204 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (1H, dd, J = 7.8, 1.4 Hz), 7.65 (1H, br d, J = 7.8 Hz), 6.87 (1H, t, J = 7.8 Hz). An exchangeable proton peak of OH group was not clearly detected. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 137.8, 131.2, 126.7, 120.0 (q, J = 326 Hz), 114.8, 113.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ

−79.1 (3F, s). HRMS (ESI⁻/TOF) m/z: [M − H]⁻ Calcd for $C_7H_3{}^{35}ClF_3O_3S$ 258.9449; Found: 258.9446; Calcd for $C_7H_3{}^{37}ClF_3O_3S$ 260.9420; Found: 260.9411.

Diels-Alder-type reaction of new precursor 2a with 2-bromofuran: To a suspension of CsF (91 mg, 0.60 mmol) in anhydrous acetonitrile (4.0 mL) were added 2-bromofuran (35 μL, 0.60 mmol) and precursor **2a** (67 mg, 0.20 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 3 hours, the reaction mixture was filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. The purification by preparative TLC (AcOEt:hexanes = 1:10, 2-fold development) afforded the isomeric products **13** (16 mg, 30%) as colorless crystals and **14** (24 mg, 46%) as colorless oil.

1-Bromo-5-chloro-1,4-dihydro-1,4-epoxynaphthalene (13) Mp 118−120 °C (CH_2Cl_2-hexanes). IR (KBr) 3019, 1587, 1448 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (1H, dd, *J* = 6.4, 1.8 Hz), 7.04−6.94 (4H, m), 5.68 (1H, d, *J* = 1.8 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5, 145.9, 144.3, 143.8, 128.4, 127.9, 118.5, 90.5, 81.9. One carbon peak was missing due to overlapping. HRMS (ESI⁺/TOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_6{}^{79}Br^{35}ClONa$ 278.9183; Found: 278.9198; Calcd for $C_{10}H_6{}^{81}Br^{37}ClONa$ 282.9135; Found: 282.9153.

1-Bromo-8-chloro-1,4-dihydro-1,4-epoxynaphthalene (14) IR (KBr) 3097, 3025, 1591, 1451 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (1H, br d, *J* = 6.9 Hz), 7.10−6.97 (4H, m), 5.86 (1H, d, *J* = 1.8 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 146.4, 145.7, 143.6, 127.5, 126.7, 126.3, 118.9, 91.9, 80.9. HRMS (ESI⁺/TOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_6{}^{79}Br^{35}ClONa$ 278.9183; Found: 278.9202; Calcd for $C_{10}H_6{}^{81}Br^{37}ClONa$ 282.9135; Found: 282.9154.

General procedure for 1,3-Dipolar cycloaddition reaction of new precursors 2a-c with nitrone: To a suspension of CsF (182 mg, 1.2 mmol) in anhydrous acetonitrile (4.0 mL) were added *N*-*tert*-butyl-α-phenylnitrone (142 mg, 0.80 mmol) and precursor **2a**, **2b** or **2c** (0.40 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 3 hours, the reaction mixture was filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. Purification by flash silica gel column chromatography afforded the products **15a-c**, **16a** and **16c**.

2-(*tert*-Butyl)-4-chloro-3-phenyl-2,3-dihydrobenzo[d]isoxazole (15a) Following the general procedure for 1,3-Dipolar cycloaddition, the reaction of **2a** was carried out. First purification by flash silica gel column chromatography (AcOEt:hexanes = 1:20) afforded the isomeric products **15a** and **16a** (97 mg, 84%) as a mixture of 89:11. The isomers **15a** and **16a** were separated by second purification by preparative TLC (AcOEt:hexanes = 1:1, 2-fold development), leading to **15a** as colorless crystals and **16a** as colorless oil. Mp 66−68 °C (hexanes). IR (KBr) 2974, 1591, 1449, 1365 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (5H, m), 7.13 (1H, br t, *J* = 8.2 Hz), 6.81 (1H, br d, *J* = 8.2 Hz), 6.75 (1H, br d, *J* = 8.2 Hz), 5.60 (1H, s), 1.18 (9H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 141.7, 130.2, 129.6, 128.5, 128.0, 127.6, 127.5, 121.4, 105.3, 66.6, 61.6, 25.3. HRMS (ESI⁺/TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}{}^{35}ClNONa$ 310.0969; Found: 310.0962; Calcd for $C_{17}H_{18}{}^{37}ClNONa$ 312.0945; Found: 312.0938.

2-(*tert*-Butyl)-7-chloro-3-phenyl-2,3-dihydrobenzo[d]isoxazole (16a) IR (KBr) 2975, 1594, 1456, 1365 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (2H, dd, *J* = 7.3, 1.6 Hz), 7.34 (2H, m), 7.26 (1H, m), 7.13 (1H, dd, *J* = 7.3, 1.8 Hz), 6.77 (1H, dd, *J* = 7.3, 1.8 Hz), 6.73 (1H, br t, *J* = 7.3 Hz), 5.64 (1H, s), 1.20 (9H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.3, 143.2, 131.7, 128.9, 128.7, 127.6, 127.2, 121.8 (2C), 112.8, 67.7, 61.3,

25.4. HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{18}{}^{35}ClNONa$ 310.0969; Found: 310.0993; Calcd for $C_{17}H_{18}{}^{37}ClNONa$ 312.0945; Found: 312.0968.

2-(*tert*-Butyl)-4-fluoro-3-phenyl-2,3-dihydrobenzo[d]isoxazole (15b) Following the general procedure for 1,3-Dipolar cycloaddition, the reaction of **2b** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:20) afforded the single product **15b** (102 mg, 95%) as white solid. IR (KBr) 2975, 1624, 1607, 1485, 1459, 1365 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (2H, br d, *J* = 7.3 Hz), 7.33 (2H, m), 7.26 (1H, m), 7.13 (1H, m), 6.61 (1H, br d, *J* = 8.2 Hz), 6.52 (1H, br t, *J* = 8.2 Hz), 5.72 (1H, s), 1.18 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4 (d, *J* = 8 Hz), 158.0 (d, *J* = 249 Hz), 142.2, 130.5 (d, *J* = 8 Hz), 128.5, 127.6, 127.2, 116.3 (d, *J* = 20 Hz), 107.8 (d, *J* = 20 Hz), 102.8 (d, *J* = 4 Hz), 64.4 (d, *J* = 3 Hz), 61.4, 25.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −118.3 (1F, dd, *J* = 9, 6 Hz). HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{18}FNONa$ 294.1265; Found: 294.1269.

4-Bromo-2-(tert-butyl)-3-phenyl-2,3-dihydrobenzo[d]isoxazole (15c) Following the general procedure for 1,3-Dipolar cycloaddition, the reaction of **2c** was carried out. First purification by flash silica gel column chromatography (AcOEt:hexanes = 1:20) afforded the isomeric products **15c** and **16c** (109 mg, 82%) as a mixture of 86:14. The isomers **15c** and **16c** were separated by second purification by preparative TLC ($CHCl_3$:hexane = 1:1, 2-fold development), leading to **15c** as white solid and **16c** as colorless oil. IR (KBr) 2974, 1585, 1444, 1365 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (5H, m), 7.07 (1H, br t, *J* = 7.8 Hz), 6.98 (1H, br d, *J* = 7.8 Hz), 6.80 (1H, br d, *J* = 7.8 Hz), 5.53 (1H, s), 1.18 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.3, 141.6, 130.4, 129.4, 128.5, 128.2, 127.6, 124.3, 117.9, 105.8, 67.8, 61.7, 25.3. HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{18}{}^{79}BrNONa$ 354.0464; Found: 354.0465; Calcd for $C_{17}H_{18}{}^{81}BrNONa$ 356.0445; Found: 356.0441.

7-Bromo-2-(tert-butyl)-3-phenyl-2,3-dihydrobenzo[d]isoxazole (16c) IR (KBr) 2974, 1589, 1452, 1365 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (2H, br d, *J* = 7.3 Hz), 7.36−7.31 (2H, m), 7.29−7.24 (2H, m), 6.82 (1H, br d, *J* = 7.3 Hz), 6.68 (1H, br t, *J* = 7.3 Hz), 5.67 (1H, s), 1.20 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.8, 143.3, 131.7, 131.2, 128.7, 127.6, 127.2, 122.5, 122.1, 99.9, 67.9, 61.4, 25.4. HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{18}{}^{79}BrNONa$ 354.0464; Found: 354.0462; Calcd for $C_{17}H_{18}{}^{81}BrNONa$ 356.0445; Found: 356.0446.

1-Benzyl-4-chloro-1,2,3-benzotriazole (17) To a suspension of CsF (182 mg, 1.2 mmol) in anhydrous acetonitrile (4.0 mL) were added benzylazide (50 μL, 0.40 mmol) and precursor **2a** (133 mg, 0.40 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 3 hours, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated at reduced pressure. Purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 0:1−1:10) afforded the product **17** (89 mg, 91%) as colorless crystals. Mp 78−80 °C (AcOEt-hexanes). IR (KBr) 3067, 3033, 1609, 1581, 1494, 1454, 1424 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.23 (8H, m), 5.86 (2H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.0, 134.2, 134.1, 129.1, 128.6, 127.9, 127.6, 125.5, 123.8, 108.5, 52.7. HRMS (ESI$^+$/TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_{11}{}^{35}ClN_3$ 244.0636; Found: 244.0637; Calcd for $C_{13}H_{11}{}^{37}ClN_3$ 246.0609; Found: 246.0610.

Procedure for three-component coupling reaction using precursor 1: To a suspension of CsF (91 mg, 0.60 mmol) and diethyl malonate (46 μL, 0.30 mmol) in anhydrous *N*,*N*-dimethylformamide (DMF, 2.0 mL) was added precursor **1** (67 mg, 0.20 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, silica gel (0.50 g) was added to the reaction mixture, which was

concentrated under reduced pressure. The purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the products **18a** (24 mg, 47%) as colorless crystals and **12** (9 mg, 17%) as yellow solid.

General procedure for three-component coupling reaction using precursor 2a-h: To a suspension of CsF (91 mg, 0.60 mmol) and diethyl malonate (46 μL, 0.30 mmol) in anhydrous *N*,*N*-dimethylformamide (DMF, 2.0 mL) was added precursors **2a-f** or **2h** (0.20 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, silica gel (0.50 g) was added to the reaction mixture, which was concentrated under reduced pressure. The purification of the residue by flash silica gel column chromatography afforded the products **18a-f**, **18h** and **19**.

5-Chloro-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18a) Following the general procedure for three-component coupling reaction, the reaction of **2a** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18a** (43 mg, 85%) as colorless crystals. Mp 140−143 °C (AcOEt-hexanes). IR (KBr) 3087, 2980, 1766, 1719, 1595, 1562, 1451 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, s), 7.55 (1H, br t, J = 8.2 Hz), 7.37 (1H, dd, J = 8.2, 1.0 Hz), 7.26 (1H, br d, J = 8.2 Hz), 4.43 (2H, q, J = 7.1 Hz), 1.41 (3H, t, J = 7.1 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 155.9, 155.8, 144.6, 134.2, 134.0, 125.4, 119.0, 116.6, 115.6, 62.2, 14.2. HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_9{}^{35}ClO_4Na$ 275.0082; Found: 275.0082; Calcd for $C_{12}H_9{}^{37}ClO_4Na$ 277.0056; Found: 277.0058.

5-Fluoro-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18b) Following the general procedure for three-component coupling reaction, the reaction of **2b** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18b** (38 mg, 80%) as colorless crystals. Mp 124−126 °C (CH_2Cl_2-hexanes). IR (KBr) 3065, 2988, 1766, 1718, 1623, 1570, 1471, 1373 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (1H, s), 7.60 (1H, br m), 7.16 (1H, br d, J = 8.4 Hz), 7.04 (1H, br t, J = 8.4 Hz), 4.43 (2H, q, J = 7.2 Hz), 1.41 (3H, t, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 159.3 (d, J = 260 Hz), 155.9, 155.4 (d, J = 5 Hz), 141.4 (d, J = 4 Hz), 134.9 (d, J = 11 Hz), 118.4, 112.6 (d, J = 4 Hz), 110.6 (d, J = 19 Hz), 108.3 (d, J = 18 Hz), 62.2, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −117.0 (1F, dd, J = 9, 6 Hz). HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_9FO_4Na$ 259.0377; Found: 259.0372.

5-Bromo-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18c) Following the general procedure for three-component coupling reaction, the reaction of **2c** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18c** (45 mg, 76%) as colorless crystals. Mp 113−114 °C (CH_2Cl_2-hexanes). IR (KBr) 3084, 2980, 1766, 1718, 1611, 1446, 1372 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (1H, s), 7.56 (1H, br d, J = 8.2 Hz), 7.48 (1H, br t, J = 8.2 Hz), 7.32 (1H, br d, J = 8.2 Hz), 4.44 (2H, q, J = 7.2 Hz), 1.42 (3H, t, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 156.0, 155.8, 147.1, 134.5, 128.9, 123.9, 119.5, 118.1, 116.3, 62.3, 14.2. HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_9{}^{79}BrO_4Na$ 318.9576; Found: 318.9597; Calcd for $C_{12}H_9{}^{81}BrO_4Na$ 320.9557; Found: 320.9584.

5-Chloro-6-methyl-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18d) Following the general procedure for three-component coupling reaction, the reaction of **2d** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18d** (43 mg, 81%) as colorless crystals. Mp 91−92 °C (CH_2Cl_2-hexanes). IR (KBr) 2985, 1766, 1714, 1615, 1572,

1471 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (1H, s), 7.49 (1H, d, *J* = 8.2 Hz), 7.18 (1H, d, *J* = 8.2 Hz), 4.43 (2H, q, *J* = 7.2 Hz), 2.45 (3H, s), 1.42 (3H, t, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.9, 156.2, 154.0, 145.3, 135.9, 133.1 (2C), 118.6, 116.5, 114.9, 62.2, 20.0, 14.2. HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{13}H_{11}{}^{35}ClO_4Na$ 289.0238; Found: 289.0236; Calcd for $C_{13}H_{11}{}^{37}ClO_4Na$ 291.0213; Found: 291.0212.

5,7-Dichloro-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18e) Following the general procedure for three-component coupling reaction, the reaction of **2e** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18e** (35 mg, 61%) as colorless crystals. Mp 72−74 °C (CH_2Cl_2-hexanes). IR (KBr) 3085, 2984, 1775, 1712, 1594, 1551, 1413 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (1H, s), 7.39 (1H, d, *J* = 1.8 Hz), 7.28 (1H, d, *J* = 1.8 Hz), 4.43 (2H, q, *J* = 7.2 Hz), 1.41 (3H, t, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 155.7, 155.3, 144.0, 140.3, 134.6, 125.9, 118.7, 116.0, 115.2, 62.4, 14.2. HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{12}H_8{}^{35}Cl_2O_4Na$ 308.9692; Found: 308.9715; Calcd for $C_{12}H_8{}^{35}Cl^{37}ClO_4Na$ 310.9664; Found: 310.9684.

5-Chloro-7-trifluoromethyl-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18f) Following the general procedure for three-component coupling reaction, the reaction of **2f** was carried out. Purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the product **18f** (40mg, 62%) as colorless crystals. Mp 77−79 °C (hexanes). IR (KBr) 3090, 2989, 1777, 1710, 1622, 1564, 1423, 1349 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (1H, s), 7.61 (1H, d, *J* = 1.0 Hz), 7.51 (1H, br s), 4.45 (2H, q, *J* = 7.2 Hz), 1.43 (3H, t, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.2, 155.4, 154.9, 143.2, 135.5 (q, *J* = 35 Hz), 135.0, 122.2 (q, *J* = 275 Hz), 122.0 (q, *J* = 4 Hz), 121.2, 119.0, 113.0 (q, *J* = 4 Hz), 62.6, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.9 (3F, s). HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{13}H_8{}^{35}ClF_3O_4Na$ 342.9955; Found: 342.9954; Calcd for $C_{13}H_8{}^{37}ClF_3O_4Na$ 344.9930; Found: 344.9929.

5-Fluoro-8-methoxy-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (18h) Following the general procedure for three-component coupling reaction, the reaction of **2h** was carried out. First purification by flash silica gel column chromatography (AcOEt:hexanes = 1:8–1:0 with 2% CH_2Cl_2) afforded the isomeric products **18h** and **19** (39 mg, 73%) as a mixture of 63:37. The isomers **18h** and **19** were separated by second purification by preparative TLC ($CHCl_3$:Et_2O = 15:1, 2-fold development), leading to **18h** as pale yellow crystals and **19** as pale yellow crystals. Mp 125−128 °C (*i*-Pr_2O-CH_2Cl_2). IR (KBr) 3089, 2981, 1765, 1711, 1624, 1580, 1494, 1442 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (1H, s), 7.10 (1H, dd, *J* = 8.7, 4.8 Hz), 6.95 (1H, t, *J* = 8.7 Hz), 4.40 (2H, q, *J* = 7.2 Hz), 3.93 (3H, s), 1.39 (3H, t, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 155.3, 152.5 (d, *J* = 253 Hz), 144.4 (d, *J* = 5 Hz), 143.4 (d, *J* = 4 Hz), 141.8 (d, *J* = 4 Hz), 118.4, 116.0 (d, *J* = 9 Hz), 109.4 (d, *J* = 21 Hz), 108.7 (d, *J* = 21 Hz), 62.1 56.7, 14.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ −128.3 (1F, m). HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{13}H_{11}FO_5Na$ 289.0483; Found: 289.0486.

8-Fluoro-5-methoxy-2-oxo-2*H*-1-benzopyran-3-carboxylic acid, ethyl ester (19) Mp 158−159 °C (hexanes). IR (KBr) 2984, 2950, 1766, 1715, 1618, 1581, 1496, 1461 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (1H, d, *J* = 1.4 Hz), 7.34 (1H, t, *J* = 9.2 Hz), 6.63 (1H, dd, *J* = 9.2, 3.2 Hz), 4.41 (2H, q, *J* = 7.2 Hz), 3.95 (3H, s), 1.41 (3H, t, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.9, 155.3, 152.9 (d, *J* = 3 Hz), 143.8 (d, *J* = 2 Hz), 143.6 (d, *J* = 13 Hz), 143.4 (d, *J* = 247 Hz), 120.8 (d, *J* = 18 Hz), 116.8, 109.9, 104.3 (d, *J* = 6 Hz), 62.0, 56.3, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −143.6 (1F, m). HRMS (ESI$^+$/TOF) m/z: [M + Na]$^+$ Calcd for $C_{13}H_{11}FO_5Na$ 289.0483; Found: 289.0482.

6-Chloro-1,2,3,4-tetrahydro-1,4-dimethyl-5*H*-1,4-benzodiazepin-5-one (20a) To a suspension of CsF (2.73 g, 18 mmol) and in distilled 1,3-dimethyl-2-imidazolidinone (DMI, 30 mL) was added precursors **2a** (2.00 g, 6.0 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, the reaction mixture was diluted with AcOEt and then filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. The purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:1–1:0) afforded the product **20a** (1.25 g, 93%) as colorless crystals. Mp 166−168 °C (CH_2Cl_2-hexanes). IR (KBr) 3074, 2943, 2815, 1652, 1587, 1480, 1450, 1397 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (1H, br t, *J* = 7.8 Hz), 7.06 (1H, dd, *J* = 7.8, 1.0 Hz), 6.81 (1H, br d, *J* = 7.8 Hz), 3.41 (2H, br m), 3.22 (3H, s), 3.18 (2H, br m), 2.79 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.1, 148.1, 132.7, 131.0, 128.8, 124.1, 116.2, 57.1, 47.8, 40.1, 33.4. HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{13}{}^{35}ClN_2ONa$ 247.0609; Found: 247.0612; Calcd for $C_{11}H_{13}{}^{37}ClN_2ONa$ 249.0582; Found: 249.0586.

6-Chloro-8-trifluoromethyl-1,2,3,4-tetrahydro-1,4-dimethyl-5*H*-1,4-benzodiazepin-5-one (20f) To a suspension of CsF (182 mg, 1.2 mmol) and in distilled 1,3-dimethyl-2-imidazolidinone (DMI, 2.0 mL) was added precursors **2f** (160 mg, 0.40 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, the reaction mixture was diluted with AcOEt and then filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. The purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:1–1:0) afforded the product **20f** (89 mg, 76%) as colorless crystals. Mp 139−140 °C (CH_2Cl_2-hexanes). IR (KBr) 2949, 1660, 1566, 1487, 1415 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (1H, d, *J* = 1.0 Hz), 7.01 (1H, s) 3.44 (2H, br m), 3.24 (2H, br m), 3.22 (3H, s), 2.84 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.9, 148.4, 133.7, 133.2 (q, *J* = 33 Hz), 131.5, 123.1 (q, *J* = 274 Hz), 120.6 (q, *J* = 4 Hz), 113.1 (q, *J* = 4 Hz), 56.9, 47.6, 40.1, 33.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.7 (3F, s). HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}{}^{35}ClF_3N_2ONa$ 315.0482; Found: 315.0502; Calcd for $C_{12}H_{12}{}^{37}ClF_3N_2ONa$ 317.0456; Found: 317.0473.

6,7,8-Trifluoro-1,2,3,4-tetrahydro-1,4-dimethyl-5*H*-1,4-benzodiazepin-5-one (20g) To a suspension of CsF (182 mg, 1.2 mmol) and in distilled 1,3-dimethyl-2-imidazolidinone (DMI, 2.0 mL) was added precursors **2g** (141 mg, 0.40 mmol) under argon atmosphere at room temperature. After being stirred at the same temperature for 12 hours, the reaction mixture was diluted with AcOEt and then filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. The purification of the residue by flash silica gel column chromatography (AcOEt:hexanes = 1:1–1:0) afforded the product **20g** (73 mg, 75%) as colorless crystals. Mp 93−94 °C (hexanes). IR (KBr) 2948, 1656, 1599, 1505, 1455 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.45 (1H, ddd, *J* = 11.9, 6.0, 2.3 Hz), 3.44 (2H, br t, *J* = 5.7 Hz), 3.23 (2H, br t, *J* = 5.7 Hz), 3.16 (3H, s), 2.74 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.0, 152.4 (ddd, *J* = 252, 10, 6 Hz), 150.0 (ddd, *J* = 256, 12, 6 Hz), 142.9 (ddd, *J* = 10, 7, 3 Hz), 135.3 (dt, *J* = 247, 16 Hz), 114.6 (dt, *J* = 12, 2 Hz), 101.6 (dd, *J* = 20, 3 Hz), 57.2, 47.5, 40.2, 33.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −131.3 (1F, m), −134.1, (1F, m), −169.2, (1F, m). HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{11}F_3N_2ONa$ 267.0716; Found: 267.0738.

8-Trifluoromethyl-1,2,3,4-tetrahydro-1,4-dimethyl-5*H*-1,4-benzodiazepin-5-one (21) To a solution of coumarin **20f** (29 mg, 0.10 mmol) in distilled MeOH (1.0 mL) were added ammonium formate (17 mg, 0.25 mmol) and $Pd(OH)_2/C$ (20%, 15 mg, 0.020 mmol) under argon atmosphere at room temperature. After being stirred for 12 hours under the reflux conditions, the reaction mixture was filtrated with folded filter paper. The filtrate was concentrated at reduced pressure. The purification of the residue by flash silica gel column chromatography

(AcOEt:hexanes = 1:2) afforded the product **21** (20 mg, 77%) as colorless oil. IR (KBr) 2941, 1647, 1488, 1329 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (1H, d, *J* = 7.8 Hz), 7.19 (1H, d, *J* = 7.8 Hz), 7.05 (1H, s), 3.44 (2H, dd, *J* = 6.4, 5.3 Hz), 3.37 (2H, dd, *J* = 6.4, 5.3 Hz), 3.20 (3H, s), 2.87 (3H, s). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.2, 147.1, 133.5 (q, *J* = 32 Hz), 131.8, 131.0, 123.8 (q, *J* = 274 Hz), 117.4 (q, *J* = 4 Hz), 114.2 (q, *J* = 4 Hz), 57.8, 47.9, 40.0, 34.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.5 (3F, s). HRMS (ESI^+/TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{13}F_3N_2ONa$ 281.0872; Found: 281.0866.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

^1H, ^{13}C and ^{19}F NMR spectra for obtained products.

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Notes

The authors declare no competing financial interest.

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