Synthesis of 2-alkyl-2-boryl-substituted-tetrahydrofurans via copper(I)-catalyzed borylative cyclization of aliphatic ketones

Koji Kubota\textsuperscript{a,b}, Minami Uesugi\textsuperscript{b}, Shun Osaki\textsuperscript{b} and Hajime Ito\textsuperscript{a,b,*}

\textsuperscript{a}Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Sapporo, Hokkaido, Japan.
\textsuperscript{b}Division of Applied Chemistry and Frontier Chemistry Center, Faculty of Engineering, Hokkaido University, Sapporo, Hokkaido, Japan.

\textit{e-mail: hajito@eng.hokudai.ac.jp, kbt@eng.hokudai.ac.jp}

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1. **Instrumentation and Chemicals**

Materials were obtained from commercial suppliers and purified by standard procedures unless otherwise noted. Solvents were also purchased from commercial suppliers, degassed via three freeze-pump-thaw cycles, and further dried over molecular sieves (MS 4A). NMR spectra were recorded on JEOL JNM-ECX400P and JNM-ECS400 spectrometers (\(^1\)H: 401 or 400 or 396 or 392 MHz, \(^{13}\)C: 99 MHz, \(^{19}\)F: 373 MHz \(^{11}\)B: 127 MHz,) Tetramethylsilane (\(^1\)H), CDCl\(_3\) (\(^{13}\)C), fluorobenzene (\(^{19}\)F), BF\(_3\)-Et\(_2\)O (\(^{11}\)B) were employed as the external standards, respectively. CuCl (ReagentPlus\(^\circledR\) grade, 224332-25G, \(\geq\)99\%) and K(O-t-Bu) / THF (1.0 M, 328650-50ML) were purchased from Sigma-Aldrich Co. and used as received. Dibromomethane was used as an internal standard to determine \(^1\)H NMR yields. Recycle preparative gel permeation chromatography (GPC) was conducted with JAI LC-9101 using CHCl\(_3\) as an eluent. GLC analyses were conducted with a Shimadzu GC-2014 or GC-2025 equipped with a ULBON HR-1 glass capillary column (Shinwa Chemical Industries) and a FID detector. High-resolution mass spectra was recorded at the Global Facility Center for Instrumental Analysis, Hokkaido University.
2. General Experimental Procedures

Procedure for the Copper(I)-Catalyzed Borylative Cyclization of 1a without MeOH (Table 1).

Copper chloride (2.5 mg, 0.025 mmol) and bis(pinacolato)diboron (139.7 mg, 0.55 mmol), 1,3-di-tert-butylimidazolium tetrafluoroborate (6.7 mg, 0.025 mmol) were placed in an oven-dried reaction vial. After the vial was sealed with a screw cap containing a Teflon-coated rubber septum, the vial was connected to a vacuum/nitrogen manifold through a needle. It was evacuated and then backfilled with nitrogen. This cycle was repeated three times. Dry THF (450 μL) and K(O-t-Bu)/THF (1.0 M, 550 μL, 0.55 mmol) were added in the vial through the rubber septum using a syringe. The dark brown color solution was formed. 1a (60.3 mg, 0.50 mmol) was then added dropwisely to the reaction mixture and the mixture was stirred for 4 h. After the reaction was complete, the reaction mixture was passed through a short silica gel eluting with EtOAc. The crude mixture was purified by flash column chromatography [SiO₂, EtOAc/hexane (dried over K₂CO₃ before used), 0:100–12:88] to give the corresponding borylation product 3a as a colorless oil. The flash column chromatography should be completed within 10 min to minimize decomposition of the product.

Procedure for the Copper(I)-Catalyzed Borylative Cyclization of 1b with MeOH (Table 2).

Copper chloride (2.5 mg, 0.025 mmol) and bis(pinacolato)diboron (139.7 mg, 0.55 mmol), 1,3-di-tert-butylimidazolium tetrafluoroborate (6.7 mg, 0.025 mmol) were placed in an oven-dried reaction vial. After the vial was sealed with a screw cap containing a Teflon-coated rubber septum, the vial was connected to a vacuum/nitrogen manifold through a needle. It was evacuated and then backfilled with nitrogen. This cycle was repeated three times. Dry THF (450 μL) and K(O-t-Bu)/THF (1.0 M, 550 μL, 0.55 mmol) were added in the vial through the rubber septum using a syringe. The dark brown color solution was formed. After 1b (105.4 mg, 0.50 mmol) was added to the mixture at 30°C, MeOH (40.5 μL, 1.0 mmol) was added dropwise. After the reaction was complete, the reaction mixture was passed through a short silica gel eluting with EtOAc. The crude mixture was purified by flash column chromatography [SiO₂, EtOAc/hexane (dried over K₂CO₃ before used), 0:100–12:88] to give the corresponding borylation product 3b as a colorless oil. The flash column chromatography should be completed within 10 min to minimize decomposition of the product.
3. Substrate Preparation

The substrate 1a was purchased from commercial suppliers and used received.

Preparation of 6-chloro-1-phenylhexan-3-one (1b).

In an oven-dried 300 mL round bottomed flask, methyl 4-chlorobutyrate (1.86 g, 13.6 mmol) was added to a suspension of N,O-dimethylhydroxylamine in THF (36 mL) at room temperature under nitrogen atmosphere and the mixture was cooled to –20°C. A THF solution of Isopropylmagnesium chloride (2.0 M, 48 mL, 96 mmol) was then added dropwise for 15 min to the reaction mixture and the mixture was stirred for 1 h. After the reaction mixture was warmed to 0°C, the mixture was stirred for 4 h. Then the reaction mixture was warmed to room temperature, the mixture was stirred for 12 h. The resulting suspension was quenched by the addition of saturated aqueous NH₄Cl. The mixture was extracted with CH₂Cl₂ three times and dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was used for the next step without purification.

In an oven-dried 100 mL round bottomed flask, the amide (993.1 mg, 6.0 mmol) was dissolved in THF (14 mL) under nitrogen atmosphere. After the reaction mixture was cooled to 0°C, a THF solution of phenethylmagnesium bromide (1.5 M, 8.0 mL, 12 mmol) was added dropwise to the reaction mixture. After stirred for 18 h at room temperature, the resulting suspension was quenched by the addition of saturated aqueous NH₄Cl. The mixture was extracted with EtOAc three times and dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO₂, EtOAc/hexane, 0:100–7:93) to afford the corresponding ketone 1b (214.0 mg, 1.0 mmol, 17%) as a colorless oil.

^1H NMR (401 MHz, CDCl₃, δ): 2.03 (quint, J = 6.5 Hz, 2H), 2.59 (t, J = 7.0 Hz, 2H), 2.76 (t, J = 7.6 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H), 3.55 (t, J = 6.4 Hz, 2H), 7.17–7.22 (m, 3H), 7.26–7.30 (m, 2H). ^13C NMR (99 MHz, CDCl₃, δ): 26.0 (CH₂), 29.5 (CH₂), 39.2 (CH₂), 44.1 (CH₂), 44.2 (CH₂), 125.9 (CH), 128.1 (CH), 128.3 (CH), 140.7 (C), 208.4 (C). HRMS–EI (m/z): [M]+ calcd for C₁₂H₁₅ClO, 210.0811; found, 210.0812.
Preparation of 1-chlorodecan-4-one (1f).

If was prepared from the corresponding alkyl halide according to the procedure for the synthesis of 1b as a colorless oil.

\[
\begin{align*}
\text{H NMR (392 MHz, CDCl}_3, \delta) & : 0.88 \text{ (t, } J = 7.0 \text{ Hz, 3H)}, 1.25–1.34 \text{ (m, 6H)}, 1.54–1.61 \text{ (m, 2H)}, 2.04 \text{ (quint, } J = 6.6 \text{ Hz, 2H)}, 2.42 \text{ (t, } J = 7.4 \text{ Hz, 2H)}, 2.61 \text{ (t, } J = 7.0 \text{ Hz, 2H)}, 3.58 \text{ (t, } J = 6.3 \text{ Hz, 2H}). \\
\text{C NMR (99 MHz, CDCl}_3, \delta) & : 14.0 \text{ (C}_H_3), 22.4 \text{ (CH}_2), 23.8 \text{ (CH}_2), 26.2 \text{ (CH}_2), 28.8 \text{ (CH}_2), 31.5 \text{ (CH}_2), 39.1 \text{ (CH}_2), 43.0 \text{ (CH}_2), 44.5 \text{ (CH}_2), 210.1 \text{ (C). HRMS–EI (m/z): } [M]^+ \text{ calcd for C}_{10}H_{19}ClO, 190.1124; \text{ found, 190.1129.}
\end{align*}
\]

Preparation of 6-chloro-1-(4-methylphenyl)hexan-3-one (1g).

The amidation was performed according to the literature procedure. In an oven-dried 100 mL round bottomed flask, 3-(p-tolyl)propionic acid (3.23 g, 20 mmol) was dissolved in CH$_2$Cl$_2$ (30 mL) and one
drop of DMF was added under nitrogen atmosphere. Then oxalyl chloride (3.79 g, 30 mmol) was added dropwised to the reaction mixture. The resulting mixture was stirred for 4 h at room temperature and then concentrated under reduced pressure to give the corresponding acid chloride. The reaction mixture was used for the next step without purification. The acid chloride was dissolved in CH$_2$Cl$_2$ (30 mL). After the reaction mixture was cooled to 0°C, N,O-dimethylylhydroxylamine (2.20 g, 22 mmol), pyridine (4.8 mL) and DMAP (472.1 mg, 4 mmol) was added to the reaction mixture and the mixture was warmed to room temperature. After stirred for 15 h, the resulting suspension was quenched by the addition of 3 M HCl. The mixture was extracted with CH$_2$Cl$_2$ three times and dried over MgSO$_4$, filtered and concentrated under reduced pressure. The crude product was used for the next step without purification.

In an oven-dried 200 mL round bottomed flask, the amide was dissolved in THF (60 mL) under nitrogen atmosphere. After the reaction mixture was cooled to 0°C, a Et$_2$O solution of allylmagnesium bromide (0.7 M, 34 mL, 24 mmol) was added dropwise to the reaction mixture and the mixture was warmed to room temperature. After stirred for 16 h, the resulting suspension was quenched by the addition of saturated aqueous NH$_4$Cl. The mixture was extracted with EtOAc three times and dried over MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO$_2$, EtOAc/hexane, 0:100–4:96) to afford the corresponding ketone S1 (3.29 g, 17 mmol, 87%) as a colorless oil.

The hydroboration was performed according to the literature procedure. In an oven-dried 200 mL round bottomed flask, S1 (1.91 g, 10 mmol) was dissolved in THF (22 mL) under nitrogen atmosphere. After the reaction mixture was cooled to 0°C, a THF solution of 9-borabicyclo[3.3.1]nonane (0.5 M, 22 mL, 11 mmol) was added dropwise to the reaction mixture and the reaction mixture heated to 60°C. After stirred for 3 h, NaBO$_3$·4H$_2$O (6.15 g, 40 mmol) and H$_2$O (44 mL) were added to the mixture at 0°C. After stirred for 2 h at room temperature, the reaction mixture was extracted with CH$_2$Cl$_2$ three times and dried over MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO$_2$, EtOAc/hexane, 0:100–40:60) to afford the corresponding alcohol S2 (1.29 g, 6.2 mmol, 62%) as a colorless oil.

The chlorination was performed according to the literature procedure. In an oven-dried 50 mL round bottomed flask, triphenylphosphine (2.41 g, 9.3 mmol), S2 (1.29 g, 6.2 mmol) and carbon tetrachloride (1.48 g, 9.3 mmol) were dissolved in acetonitrile (19 mL) under nitrogen atmosphere at 80°C. After stirred for 5 h, the resulting suspension was the extracted with CH$_2$Cl$_2$ three times and dried over MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO$_2$, EtOAc/hexane, 0:100–2:98) to afford the corresponding ketone 1g (491.6 mg, 2.2 mmol, 35%) as a yellow oil.

$^1$H NMR (392 MHz, CDCl$_3$, δ): 2.03 (quint, $J = 6.6$ Hz, 2H), 2.31 (s, 3H), 2.58 (t, $J = 7.1$ Hz, 2H), 2.73 (t, $J = 7.6$ Hz, 2H), 2.87 (t, $J = 7.3$ Hz, 2H), 3.55 (t, $J = 6.3$ Hz, 2H), 7.06–7.12 (m, 4H). $^{13}$C NMR
(99 MHz, CDCl$_3$, $\delta$): 20.9 (CH$_3$), 26.1 (CH$_2$), 29.2 (CH$_2$), 39.3 (CH$_2$), 44.3 (CH$_2$), 44.4 (CH$_2$), 128.0 (CH), 129.0 (CH), 135.5 (C), 137.6 (C), 208.7 (C). HRMS–EI ($m/z$): [M]$^+$ calcd for C$_{13}$H$_7$ClO, 224.0968; found, 224.0975.

**Preparation of 6-chloro-1-[3-(trifluoromethyl)phenyl]hexan-3-one (1h).**

![1h](image)

1h was prepared from the corresponding carboxylic acid according to the procedure for the synthesis of 1g as a colorless oil.

$^1$H NMR (392 MHz, CDCl$_3$, $\delta$): 2.04 (quint, $J = 6.6$ Hz, 2H), 2.61 (t, $J = 7.0$ Hz, 2H), 2.78 (t, $J = 7.6$ Hz, 2H), 2.97 (t, $J = 7.4$ Hz, 2H), 3.56 (t, $J = 6.3$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 7.54 (d, $J = 8.1$ Hz, 2H). $^{13}$C NMR (99 MHz, CDCl$_3$, $\delta$): 26.1 (CH$_2$), 29.3 (CH$_2$), 39.4 (CH$_2$), 43.7 (CH$_2$), 44.3 (CH$_2$), 124.2 (q, $J = 273.2$ Hz, C), 125.3 (q, $J = 3.8$ Hz, CH), 128.4 (q, $J = 32.4$ Hz, C), 128.6 (CH), 145.0 (C), 208.0 (C). HRMS–EI ($m/z$): [M]$^+$ calcd for C$_{13}$H$_{14}$ClF$_3$O, 278.0685; found, 278.0683.

**Preparation of 6-chloro-1-[4-(trifluoromethyl)phenyl]hexan-3-one (1i).**

![1i](image)

1i was prepared from the corresponding alkyl halide according to the procedure for the synthesis of 1b as a colorless oil.

$^1$H NMR (392 MHz, CDCl$_3$, $\delta$): 2.05 (quint, $J = 6.6$ Hz, 2H), 2.61 (t, $J = 7.0$ Hz, 2H), 2.79 (t, $J = 7.4$ Hz, 2H), 2.97 (t, $J = 7.4$ Hz, 2H), 3.56 (t, $J = 6.3$ Hz, 2H), 7.36–7.40 (m, 2H), 7.42–7.47 (m, 2H). $^{13}$C NMR (99 MHz, CDCl$_3$, $\delta$): 26.1 (CH$_2$), 29.2 (CH$_2$), 39.3 (CH$_2$), 43.8 (CH$_2$), 44.3 (CH$_2$), 122.9 (q, $J = 3.8$ Hz, CH), 124.1 (q, $J = 273.5$ Hz, C), 124.9 (q, $J = 3.5$ Hz, CH), 128.8 (CH), 130.6 (q, $J = 32.1$ Hz, C), 131.8 (CH), 141.8 (C), 208.0 (C). HRMS–EI ($m/z$): [M]$^+$ calcd for C$_{13}$H$_{14}$ClF$_3$O, 278.0685; found, 278.0686.
**Preparation of 6-chloro-1-(4-fluorophenyl)hexan-3-one (1j).**

![Image of molecule](image)

1j was prepared from the corresponding alkyl halide according to the procedure for the synthesis of 1b as a colorless oil.

$^1$H NMR (392 MHz, CDCl$_3$, δ): 2.03 (quint, $J = 6.6$ Hz, 2H), 2.59 (t, $J = 7.0$ Hz, 2H), 2.74 (t, $J = 7.4$ Hz, 2H), 2.88 (t, $J = 7.4$ Hz, 2H), 3.56 (t, $J = 6.1$ Hz, 2H), 6.93–6.99 (m, 2H), 7.11–7.16 (m, 2H). $^{13}$C NMR (99 MHz, CDCl$_3$, δ): 26.1 (CH$_2$), 28.7 (CH$_2$), 39.4 (CH$_2$), 44.2 (CH$_2$), 44.3 (CH$_2$), 115.0 (CH), 115.2 (CH), 129.6 (d, $J = 8.5$ Hz, CH), 136.4 (d, $J = 2.8$ Hz, C), 161.2 (d, $J = 244.5$ Hz, C), 208.4 (C).

HRMS–EI ($m/z$): [M]$^+$ caled for C$_{12}$H$_{14}$ClFO, 228.0717; found, 228.0718.
4. Borylation Product Characterization

2-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3a).

The reaction was conducted with 60.5 mg (0.50 mmol) of 1a. The product 3a was obtained in 62% yield (64.9 mg, 0.31 mmol) as a yellow oil.

$^1$H NMR (401 MHz, CDCl$_3$, $\delta$): 1.21 (s, 3H), 1.27 (s, 12H), 1.56–1.65 (m, 1H), 1.82–1.89 (m, 1H), 1.91–2.08 (m, 2H), 3.78–3.91 (m, 2H). $^{13}$C NMR (99 MHz, CDCl$_3$, $\delta$): 22.9 (CH$_3$), 24.5 (CH$_3$), 25.8 (CH$_2$), 35.0 (CH$_2$), 67.1 (CH$_2$), 83.7 (C). HRMS–EI (m/z): [M–CH$_3$]$^+$ calcd for C$_{10}$H$_{18}$BO$_3$, 197.0351; found, 197.1352.

2-phenethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3b).

The reaction was conducted with 103.0 mg (0.50 mmol) of 1b. The product 3b was obtained in 54% yield (80.6 mg, 0.27 mmol) as a colorless oil.

$^1$H NMR (392 MHz, CDCl$_3$, $\delta$): 1.29 (s, 12H), 1.65–1.72 (m, 1H), 1.76–2.03 (m, 5H), 2.52–2.62 (m, 1H), 2.76–2.84 (m, 1H), 3.87 (t, $J = 7.0$ Hz, 2H), 7.15–7.29 (m, 5H). $^{13}$C NMR (99 MHz, CDCl$_3$, $\delta$): 24.5 (CH$_3$), 24.7 (CH$_3$), 25.8 (CH$_2$), 32.3 (CH$_2$), 34.0 (CH$_2$), 39.5 (CH$_2$), 67.1 (CH$_2$), 83.8 (C), 125.5 (CH), 128.1 (CH), 128.2 (CH), 142.8 (C). HRMS–ESI (m/z): [M+Na]$^+$ calcd for C$_{18}$H$_{27}$BO$_3$Na, 325.1949; found, 325.1952.

2-hexyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3f).

The reaction was conducted with 190.7 mg (0.50 mmol) of 1f. The product 3f was obtained in 36% yield (49.9 mg, 0.18 mmol) as a colorless oil.

$^1$H NMR (392 MHz, CDCl$_3$, $\delta$): 0.85–0.89 (m, 3H), 1.27 (s, 20H), 1.40–1.55 (m, 3H), 1.77–1.85 (m, 1H), 1.87–2.00 (m, 2H), 3.82 (t, $J = 6.9$ Hz, 2H). $^{13}$C NMR (99 MHz, CDCl$_3$, $\delta$): 14.0 (CH$_3$), 22.5 (CH$_2$), 24.6 (CH$_3$), 25.9 (CH$_2$), 26.0 (CH$_2$), 29.8 (CH$_2$), 31.7 (CH$_2$), 34.1 (CH$_2$), 37.6 (CH$_2$), 67.0 (CH$_2$), 83.7 (C). HRMS–EI (m/z): [M–CH$_3$]$^+$ calcd for C$_{15}$H$_{28}$BO$_3$, 267.2134; found, 267.2133.
2-(4'-methylphenethyl)- 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3g).

The reaction was conducted with 114.3 mg (0.50 mmol) of 1g. The product 3g was obtained in 59% yield (94.0 mg, 0.30 mmol) as a colorless oil.

\[ ^1H\text{ NMR (392 MHz, CDCl}_3, \delta): 1.29 (s, 12H), 1.64–1.70 (m, 1H), 1.77–2.02 (m, 5H), 2.31 (s, 3H), 2.48–2.56 (m, 1H), 2.69–2.81 (m, 1H), 3.86 (t, \( J = 6.7\) Hz, 2H), 7.06–7.11 (m, 4H). \]

\[ ^13C\text{ NMR (99 MHz, CDCl}_3, \delta): 20.9 (CH\_3), 24.5 (CH\_3), 24.7 (CH\_3), 25.8 (CH\_2), 31.9 (CH\_2), 34.0 (CH\_2), 39.6 (CH\_2), 67.1 (CH\_2), 75.2 (brs, B–C), 83.8 (C), 128.1 (CH), 128.8 (CH), 134.8 (C), 139.7 (C). \]

HRMS – EI (m/z): [M]⁺ calcld for C\(_{19}\)H\(_{29}\)BO\(_3\), 316.2213; found, 316.2212.

2-[4'-trifluoromethylphenethyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3h).

The reaction was conducted with 138.8 mg (0.50 mmol) of 1h. The product 3h was obtained in 46% yield (84.3 mg, 0.23 mmol) as a colorless oil.

\[ ^1H\text{ NMR (400 MHz, CDCl}_3, \delta): 1.29 (s, 6H), 1.29 (s, 6H), 1.64–1.72 (m, 1H), 1.74–2.04 (m, 5H), 2.62 (dt, \( J = 5.2, 12.7\) Hz, 1H), 2.85 (dt, \( J = 5.5, 12.9\) Hz, 1H), 3.85–3.89 (m, 2H), 7.30 (d, \( J = 8.0\) Hz, 2H), 7.51 (d, \( J = 7.6\) Hz, 2H). \]

\[ ^13C\text{ NMR (99 MHz, CDCl}_3, \delta): 24.6 (CH\_3), 24.7 (CH\_3), 25.8 (CH\_2), 32.3 (CH\_2), 34.2 (CH\_2), 39.2 (CH\_2), 67.3 (CH\_2), 75.0 (brs, B–C), 84.0 (C), 124.4 (q, \( J = 272.9\) Hz, C), 125.1 (q, \( J = 3.8\) Hz, CH), 127.9 (q, \( J = 32.1\) Hz, C), 128.6 (CH), 147.0 (C). \]

HRMS – ESI (m/z): [M+Na]⁺ calcld for C\(_{19}\)H\(_{29}\)BF\(_3\)O\(_3\)Na, 393.1823; found, 393.1821.

2-[3'-trifluoromethylphenethyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3i).

The reaction was conducted with 122.7 mg (0.50 mmol) of 1i. The product 3i was obtained in 63% yield (102.4 mg, 0.28 mmol) as a colorless oil. This product contains small amount of unremovable impurities.

\[ ^1H\text{ NMR (392 MHz, CDCl}_3, \delta): 1.29 (s, 12H), 1.62–1.73 (m, 1H), 1.75–2.04 (m, 5H), 2.58–2.66 (m, 1H), 2.81–2.89 (m, 1H), 3.87 (td, \( J = 2.2, 6.8\) Hz, 2H), 7.26–7.47 (m, 4H). \]

\[ ^13C\text{ NMR (99 MHz, CDCl}_3, \delta): 20.9 (CH\_3), 24.5 (CH\_3), 24.7 (CH\_3), 25.8 (CH\_2), 31.9 (CH\_2), 34.0 (CH\_2), 39.6 (CH\_2), 67.1 (CH\_2), 75.2 (brs, B–C), 83.8 (C), 128.1 (CH), 128.8 (CH), 134.8 (C), 139.7 (C). \]

HRMS – EI (m/z): [M]⁺ calcld for C\(_{19}\)H\(_{29}\)BO\(_3\), 316.2213; found, 316.2212.
δ): 24.5 (CH₃), 24.7 (CH₃), 25.8 (CH₂), 32.2 (CH₂), 34.1 (CH₂), 39.3 (CH₂), 67.3 (CH₂), 83.9 (C), 122.4 (q, J = 6.6 Hz, CH), 124.2 (q, J = 273.5 Hz, C), 124.9 (q, J = 3.8 Hz, CH), 128.6 (CH), 130.4 (q, J = 31.8 Hz, C), 131.8 (CH), 143.7 (C). HRMS–ESI (m/z): [M+Na]⁺ calcd for C₁₇H₂₆¹¹BF₃O₃, 393.1823; found, 393.1830.

2-(4'-fluorophenethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydrofuran (3j).

The reaction was conducted with 122.9 mg (0.50 mmol) of 1j product 3j was obtained in 47% yield (75.1 mg, 0.24 mmol) as a colorless oil.

¹H NMR (392 MHz, CDCl₃, δ): 1.29 (s, 12H), 1.64–1.70 (m, 1H), 1.72–2.03 (m, 5H), 2.49–2.567 (m, 1H), 2.72–2.80 (m, 1H), 3.81–3.90 (m, 2H), 6.94 (tt, J = 5.4, 7.6 Hz, 2H), 7.11–7.16 (m, 2H). ¹³C NMR (99 MHz, CDCl₃, δ): 24.5 (CH₃), 24.7 (CH₃), 25.8 (CH₂), 31.6 (CH₂), 34.1 (CH₂), 39.7 (CH₂), 67.2 (CH₂), 75.5 (brs, B–C), 83.9 (C), 114.8 (d, J = 20.8 Hz, CH), 129.5 (d, J = 7.6 Hz, CH), 138.4 (C), 161.0 (d, J = 243.6 Hz, C). HRMS–EI (m/z): [M–CH₃]⁺ calcd for C₁₇H₂₃¹¹BF₃O₃, 305.1727; found, 305.1722.
5. Borylation Product Functionalization Procedure

Procedure for the synthesis of trifluoroborate salt 7.

\[
\begin{align*}
\text{Me} & \quad \text{(pin)B} & \quad \text{KHF}_2 \text{ (4.5 equiv)} \\
\text{3a} & \quad \text{MeOH/H}_2\text{O (2:1)} & \quad \text{rt, 2 h} \\
& \quad \text{MeF} & \quad \text{KF}_3\text{B} \\
\end{align*}
\]

KHF\(_2\) (351.5 mg, 4.5 mmol) was placed in an oven-dried reaction vial. After the vial was sealed with a screw cap containing a teflon-coated rubber septum, the vial was connected to a vacuum/nitrogen manifold through a needle. It was evacuated and then backfilled with nitrogen. This cycle was repeated three times. MeOH (2.0 mL) was added in the vial through the rubber septum using a syringe. After 3a (212.1 mg, 1.0 mmol) was added to the mixture at room temperature, H\(_2\)O (1.0 mL) was added dropwise. After 2 h, the reaction mixture was concentrated in vacuo. The resulting solid was filtered with MeOH. The filtrate was concentrated in vacuo. The resulting solid was washed with Et\(_2\)O to give 7 (132.5 mg, 0.69 mmol, 69%) as a white powder.

\(^1\)H NMR (396 MHz, CD\(_3\)CN, \(\delta\)): 0.88 (s, 3H), 1.25–1.32 (m, 1H), 1.68–1.87 (m, 3H), 3.55–3.61 (m, 1H), 3.63–3.70 (m, 1H). \(^13\)C NMR (99 MHz, DMSO-d\(_6\), \(\delta\)): 23.6 (CH\(_3\)), 26.1 (CH\(_2\)), 34.2 (CH\(_2\)), 65.4 (CH\(_2\)). \(^{11}\)B NMR (127 MHz, CD\(_3\)CN, \(\delta\)): 4.30 (q, \(J = 44.8\) Hz). \(^{19}\)F NMR (373 MHz, CD\(_3\)CN, \(\delta\)): –151.3 (q, \(J = 56.9\) Hz). HRMS–ESI (m/z): [M–K]\(^+\) calcd for C\(_5\)H\(_9\)BF\(_3\)O, 152.0740; found, 152.0741.
Procedure for the synthesis of arylated product 8 through the stereospecific cross-coupling of 3b with benzofuran.

The stereospecific cross-coupling was performed according to the literature.\textsuperscript{5} A solution of benzofuran (18.4 mg, 0.24 mmol) in THF (800 \(\mu\)L) was cooled to \(-78^\circ\text{C}\) and treated with \(n\)-BuLi in hexane (1.57 M, 153 \(\mu\)L, 0.24 mmol). The reaction mixture was warmed to room temperature and stirred for 1 h. The mixture was then cooled to \(-78^\circ\text{C}\) and the 3b (60.4 mg, 0.2 mmol) was added to the mixture as a solution in THF (400 \(\mu\)L) and the reaction stirred at the same temperature for 1 h. A solution of NBS (42.7 mg, 0.24 mmol) in THF (800 \(\mu\)L) was then added dropwise to the mixture. After 2 h at \(-78^\circ\text{C}\), aqueous Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} was added and the reaction mixture was allowed to warm to room temperature. The mixture was extracted three times with Et\textsubscript{2}O, dried over MgSO\textsubscript{4}, and filtered. The resulting crude product was purified by flash column chromatography (SiO\textsubscript{2}, Et\textsubscript{2}O/hexane, 0:100–2:98) to give the corresponding arylated product 8 (10.1 mg, 0.03 mmol, 17\% yield) as a yellow oil.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, \(\delta\)): 1.94–2.07 (m, 3H), 2.17–2.24 (m, 1H), 2.34 (td, \(J = 4.6, 12.7\) Hz, 1H), 2.38–2.43 (m, 1H), 2.48 (td, \(J = 4.7, 12.8\) Hz, 1H), 2.71 (td, \(J = 4.7, 12.7\) Hz, 1H), 4.03 (t, \(J = 6.5\) Hz, 2H), 6.65 (d, \(J = 0.8\) Hz, 1H), 7.13–7.16 (m, 3H), 7.19–7.27 (m, 4H), 7.46 (d, \(J = 7.8\) Hz, 1H), 7.56–7.55 (m, 1H). \textsuperscript{13}C NMR (99 MHz, CDCl\textsubscript{3}, \(\delta\)): 25.7 (CH\textsubscript{2}), 30.9 (CH\textsubscript{2}), 36.2 (CH\textsubscript{2}), 41.3 (CH\textsubscript{2}), 68.4 (CH\textsubscript{2}), 83.5 (C), 102.6 (CH), 111.1 (CH), 120.7 (CH), 122.6 (CH), 123.6 (CH), 125.7 (CH), 128.3 (CH), 128.4 (C), 142.1 (C), 155.0 (C), 160.7 (C). HRMS–El (m/z): [M]\textsuperscript{+} calcd for C\textsubscript{20}H\textsubscript{20}O\textsubscript{2}, 292.1463; found, 292.1464.
6. References


Filename = UBS-098-pureH_Protom-1-3
Author = element
Experiment = proton_jxp
Sample_Id = UBS-098-pureH
Solvent = CHLOROFORM-D
Creation_Time = 2-OCT-2018 14:33:18
Revision_Time = 22-APR-2019 17:22:05
Comment = single_pulse
Data_Format = 1D COMPLEX
Dim_Size = 13107
Dim_Title = Proton
Dim_Units = [ppm]
Dimensions = 1
Spectrometer = DELTA2_NMR
Field_Strength = 9.4073814[T] (400[MHz])
X_Acq_Duration = 2.18103808[s]
X_Domain = 18
X_Freq = 400.53219825[MHz]
X_Offset = 5[ppm]
X_Points = 16384
X_Prescans = 1
X_Resolution = 0.45849727[Hz]
X_Sweep = 7.51201923[kHz]
X_Sweep_Clipped = 6.00961538[kHz]
Irr_Domain = Proton
Irr_Freq = 400.53219825[MHz]
Irr_Offset = 5[ppm]
Tri_Domain = Proton
Tri_Freq = 400.53219825[MHz]
Tri_Offset = 5[ppm]
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
Recov_Gain = 40
Temp_Sol = 19.71[deg]
X_90_Width = 6.22[us]
X_Acq_Time = 2.18103808[s]
X_Angle = 45[deg]
X_Atn = 0.8[DB]
X_Pulse = 3.2[us]
Irr_Mode = Off
Tri_Mode = Off
Dante_Freeze = FALSE

Filename = UBS-098-pureH_Protom-1-1.jdf

--- PROCESSING PARAMETERS ---
dc_balance( 0, FALSE )
sweep( 0.2[Hz], 0.0[s] )
trapezoid( 0[, 0[, 80[, 100[] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm

以下に由来： UBS-098-pureH_Protom-1-1.jdf

X : parts per Million : Proton

[Diagram of chemical spectra]
以下に画像内のデータを抽出した結果です。

**Filename** = UES-039-pureC-2.jdf

**Author** = element

**Experiment** = single pulse dec

**Sample Id** = 00525013

**Solvant** = CHLOROFORM-D

**Creation Time** = 25-JAN-2019 13:07:15

**Revision Time** = 22-APR-2019 21:18:47

**Current Time** = 22-APR-2019 21:20:07

**Comment** = single pulse decoupled g

**Data Format** = 1D COMPLEX

**Dim Sizes** = 26214

**Dim Title** = 13C

**Dim Units** = ppm

**Dimensions** = X

**Site** = KES 400

**Spectrometer** = JNM-ECS400

**Field Strength** = 9.20197068[T] (390[MHz])

**X.Acq_Duration** = 1.06430464[s]

**X.Domin** = 13C

**X.Freq** = 98.5147926[MHz]

**X.Offs** = 100[ppm]

**X.Points** = 32768

**X.Prescans** = 4

**X.Rsoulation** = 0.59358061[Hz]

**X.Sweep** = 30.7817734[kHz]

**Irr_Domin** = 1H

**Irr.Freq** = 391.78655441[MHz]

**Irr.Offset** = 5[ppm]

**Clipped** = FALSE

**Scans** = 100

**Total Scans** = 100

**Relaxation Delay** = 2[s]

**Recov.Gain** = 60

**Temp.Set** = 20[°C]

**X.90.Width** = 9.11[°c]

**X.Acq.Time** = 1.06430464[s]

**X.Angle** = 30[°c]

**X.Ata** = 4.9[dB]

**X.Pulse** = 3.0366667[us]

**Irr.Ata.Dec** = 22.255[dB]

**Irr.Ata.Noe** = 22.255[°c]

**Irr.Noise** = WALTZ

**Decoupling** = TRUE

**Initial Wait** = 1[s]

**Noo** = TRUE
Filename = UES-036-pureH-4.jdf
Author = element
Experiment = single_pulse.ex2
Sample_Id = #413618
Solvent = CHLOROFORM-D
Creation_Time = 11-JUL-2018 09:47:41
Comment = single_pulse
Data_Format = 1D COMPLEX
Dim_Size = 15107
Dim_Title = 1H
Dim_Units = [ppm]
Dimensions = X
Site = ECS 400
Spectrometer = JNM-ECS400
Field_Strength = 9.20197068[T] (390[MHz])
X_Acq_Duration = 2.228224[s]
X_Domain = 1H
X_Freq = 391.78655441[MHz]
X_Offset = 5[ppm]
X_Points = 1024
X_Prescans = 1
X_Resolution = 0.401578791[Hz]
X_Sweep = 7.35294118[kHz]
Irre_Domain = 1H
Irre_Freq = 391.78655441[MHz]
Irre_Offset = 5[ppm]
Tri_Domain = 1H
Tri_Freq = 391.78655441[MHz]
Tri_Offset = 5[ppm]
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
Recvr_Gain = 40
Temp_Set = 19.4[°C]
X_90_Width = 11.04[us]
X_Acq_Time = 2.228224[s]
X_Angle = 45[deg]
X_Atn = 1.9[db]
X_Pulse = 5.52[us]
Irre_Mode = Off
Tri_Mode = Off
Danta_Preset = FALSE

X : parts per Million : 1H
----- PROCESSING PARAMETERS -----
dc_balance( 0, FALSE )
swx( 2.0[Hz], 0.0[s] )
trapezoid( 0[Hz], 80[%], 100[%] )
specfill( 1 )
fft( 1, TRUE, TRUE )
machineshift
ppm

以下由来：UES-036-pureC-2.jdf

Filename = UES-036-pureC-4.jdf
Author = element
Experiment = single_pulse_dec
Sample_id = #425824
Solvent = CHLOROFORM-D
Creation_Time = 11-JUL-2016 10:07:04
Comment = single pulse decoupled gas
Data_Format = 1D COMPLEX
Dim_Size = 26214
Dim_Title = [13C]
Dim_Units = [ppm]
Dimensions = X
Site = ECS 400
Spectrometer = JNM-ECS400

Field_strength = 9.20197068[T] 390[MHz]
X_Acq_Duration = 1.06639464[s]
X_Domain = 13C
X_Freq = 98.51479726[MHz]
X_Offset = 100[ppm]
X_Points = 32768
X_Rescans = 4
X_Resolution = 0.93958061[Hz]
X_Sweep = 30.78817734[MHz]
Irr_Domain = 1H
Irr_Freq = 391.78655441[MHz]
Irr_Offset = 5[ppm]
Clipped = FALSE
Scans = 50
Total_scans = 50

Relaxation_Delay = 2[s]
Recov_Gain = 60
Temp_Set = 19.6[°C]
X_90_Width = 9.11[μs]
X_Acq_DTime = 1.06639464[s]
X_Angle = 30[deg]
X_Atm = 4.9[dB]
X_Pulse = 3.0334477[μs]
Irr_Atm_Dec = 22.255[dB]
Irr_Atm_Hoe = 22.255[dB]
Irr_Noise = WALTZ
Decoupling = TRUE
Initial_Wait = 1[s]
Hoe = TRUE

X : parts per Million : 13C
--- PROCESSING PARAMETERS ---

dc_balance( 0, TRUE )
seap( 0.2[Hz], 0.0[s] )
trapezoid( 0[s], 80[A], 100[A] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase ppm

以下に由来: UES-052-pure8-1.jdf

Filename = UES-052-pure8-5.jdf
Author = element
Experiment = single_pulse.ex2
Sample_Id = 8#347797
Solvent = CHLOROFORM-D
Actual_Start_Time = 11-JUL-2018 16:56:36
Revision_Time = 23-APR-2019 12:35:47
Comment = single_pulse
Data_Format = 1D COMPLEX
Dim_Size = 13107
Dim_Title = 1H
Dim_Units = [ppm]
Dimensions = X
Site = ECS 400
Spectrometer = JNM-ECS400
Field_Strength = 9.201970687[T] (390[MHz])
X_Acq_Duration = 2.228224[s]
X_Domain = 1H
X_Freq = 391.78655441[MHz]
X_Offset = 5[ppm]
X_Points = 16384
X_Precs = 1
X_Resolution = 0.44878791[Hz]
X_Sweep = 7.35294118[KHz]
Irr_Domain = 1H
Irr_Freq = 391.78655441[MHz]
Irr_Offset = 5[ppm]
Tri_Domain = 1H
Tri_Freq = 391.78655441[MHz]
Tri_Offset = 5[ppm]
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
Macro_Gain = 40
Temp_Set = 19.3[°C]
X_60_Width = 11.04[us]
X_Acq_Time = 3.572224[s]
X_Angle = 45[deg]
X_Atn = 1.9[DB]
X_Pulse = 5.52[us]
Irr_Mode = Off
Tri_Mode = Off
Panta_preset = FALSE

X : parts per Million : 1H
Filename = UES-193-pureH-1.jdf
Author = element
Experiment = single_pulse.ex2
Sample_Id = 1
Solvent = ACETONITRILE-D3
Actual_Start_Time = 11-MAR-2019 22:39:16
Comment = single_pulse
Data_Format = 1D COMPLEX
Dim_Size = 13107
X_Domain = 1H
Dim_Title = 1H
Dim_Units = [ppm]
Dimensions = X
Site = ECR 400P
Spectrometer = DR122_MW
Field_Strength = 9.29821531T (400[MHz])
X_Acq_Duration = 2.20725248[s]
X_Domain = 1H
X_Offset = 5(ppm)
X_Points = 16384
X_Frequencies = 1
X_Resolution = 0.45305193[Hz]
X_Sweep = 7.42280285[kHz]
X_Domain = 1H
X_Offset = 395.88430144[MHz]
X_Offset = 5(ppm)
Clipped = FALSE
Scans = 8
Total_Scans = 8
Relaxation_Delay = 5[s]
ResovrGain = 38
Temp.Get = 20.3[dc]
X_90_Width = 13.2[us]
X_Root_Pulse_T = 2.20725248[s]
X_Sweep = 45[deg]
X_Atn = 3.5[dB]
X_Pulse = 6[us]
X_Tri_Mode = Off
Tri_Mode = Off
Dante_Freeze = FALSE

--- PROCESSING PARAMETERS ---
dc_balance( 0, FALSE )
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm

以下は例示：UES-193-pureH-1.jdf
Filename = UES-193-pureC-2.jdf
Author = element
Experiment = single_pulse_deco
Sample_Id = 1
Solvent = DMSO-D6
Actual_Start_Time = 12-MAR-2019 04:43:07
Revision_Time = 23-APR-2019 16:08:31
Comment = single pulse decoupled ga
Data_Format = 1D COMPLEX
Dim_Size = 26214
X_Domain = 13C
Dim_Title = 13C
Dim_Units = [ppm]
Dimensions = X
Site = ECS 040
Spectrometer = JNM-ECS400
Field_Strength = 9.20197068[T] (390[MHz])
X_Acq_Duration = 1.06430464[s]
X_Domain = 13C
X_Freq = 99.51479726[MHz]
X_Offset = 100[ppm]
X_Points = 32768
X Prescans = 4
X_Resolution = 0.93958061[Hz]
X_Sweep = 30.78817734[KHz]
Irr_Domain = 1H
Irr_Freq = 391.78655441[MHz]
Irr_Offset = 5[ppm]
Clipped = FALSE
Scans = 6000
Total_Scans = 6000
Relaxation_Delay = 2[s]
Recvr_Gain = 60
Temp_Get = 19.1[deg]
X_90_Width = 9.11[us]
X_Acq_Time = 1.06430464[s]
X_Angle = 30[deg]
X_Atr = 4.9[db]
X_Pulse = 3.03666667[us]
Irr_Atr_Dec = 22.255[db]
Irr_Atr_No = 22.255[db]
Irr_Noise = WALTZ
Decoupling = TRUE
Initial_Wait = 1[s]
Noe = TRUE
dc_balance(0, FALSE)
swap(2.0[Hs], 0.0[s])
trapezoid(0[%, 80[%, 100[%])
zerofill(1)
fft(1, TRUE, TRUE)
machinephase
ppm

以下に示す：UES-151-pureC-1.jdf

Filename = UES-151-pureC-2.jdf
Author = element
Experiment = single_pulse_dec
Sample_id = $#335577
Solvent = CHLOROFORM-D
Actual_Start_Time = 5-DEC-2016 16:37:36
Revision_Time = 23-APR-2019 17:15:59
Comment = single pulse decoupled ga
Data_Format = 1D COMPLEX
Dim_Size = 26214
X_Domain = 13C
Dim_Title = 13C
Dim_Units = [ppm]
Dimensions = X
Site = ECS 400
Spectrometer = JNM-ECS400
Field_Strength = 9.20170678[T] (390[MHz])
X_Acq_Duration = 1.66403464[s]
X_Domain = 13C
X_Freq = 90.51479726[MHz]
X_Offset = 100[ppm]
X_Points = 32768
X_Prescans = 4
X_Resolution = 0.93958061[Hz]
X_Sweep = 30.78917735[kHz]
X_Rate = 1
X_Offset = 391.78655441[MHz]
X_Offset = 5[ppm]
Clipped = FALSE
Scans = 800
Total_Scans = 800
Relaxation_Delay = 2[s]
Diverge_Gain = 50
Temp_Get = 20.1[dc]
X_90_Width = 9.11[us]
X_Acq_Time = 1.66403464[s]
X_Angle = 30[deg]
X_Atn = 4.9[dB]
X_Pulse = 3.03666667[us]
X_Rate = 22.255[db]
X_Rate = 22.255[db]
X_Rate = 22.255[db]
Decoupling = TRUE
Initial_Delay = 1[s]
Nse = TRUE