Rh(I)-Catalyzed Formal [2+2+2] Cycloadditions of 1,6-Diynes with Potassium (Z)-(2-bromovinyl)trifluoroborate: a New Strategy and a Facile Entry to Polysubstituented Benzene Derivatives

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I. General Information

Nuclear magnetic resonance spectra. $^1$H and $^{13}$C spectra were recorded on a Bruker AVANCE 400 spectrometer, operating at 400 MHz for $^1$H NMR, 100 MHz for $^{13}$C. NMR were reported downfield from CDCl$_3$ ($\delta$: 7.27 ppm) for $^1$H NMR. For $^{13}$C NMR, chemical shifts were reported in the scale relative to the solvent of CDCl$_3$ ($\delta$: 77.0 ppm) used as an internal reference.

Mass spectroscopy. Mass spectra were in general recorded on an AMD 402/3 or a HP 5989A mass selective detector.

Chromatography. Column chromatography was performed with silica gel (200-300 mesh ASTM).

II. Procedure for Synthesis of Compound 2

To a solution of phenylacetylene or 1-hexyne (50 mmol) in CH$_2$Cl$_2$ (100 mL) at 0°C was added BBr$_3$ (50 mmol, 4.7 mL) in CH$_2$Cl$_2$ (50 mL). The mixture was stirred at room temperature for 15 min. The resulting red-purple reaction mixture was transferred by a double-ended needle to a mixture of diethyl ether (25 mL) and aqueous NaHCO$_3$ (8.5 g of NaHCO$_3$ in 75 mL of water) at 0°C. The mixture was stirred at room temperature for 15 min. The aqueous layer was separated and extracted with CH$_2$Cl$_2$, and the combined organic phase was washed with cold water and then brine. The organic phase was subsequently dried over anhydrous sodium sulfate. Removal of solvents under vacuum followed by washing with hexanes (15 mL) yielded crude boronic acid as a pale yellow solid. Crude boronic acid was dissolved in 50 mL of methanol and aqueous KHF$_2$ (150 mmol, 11.7 g, in 75 mL of water) was added slowly with vigorous stirring. After 15 min, the precipitated product was collected and washed with cold methanol. A white solid 2 was obtained (8.5 g, 59%). [Reference: M.-L. Yao, M. S. Reddy, W. Zeng, K. Hall, I. Walfish, G. W. Kabalka, J. Org. Chem. 2009, 74, 1385–1387.]
III. General procedure for the Rh(I)-catalyzed reaction of 1,6-Diynes with Potassium (Z)-(2-bromovinyl)trifluoroborate

\[
\begin{align*}
1,6\text{-Diynes } 1 & (0.3 \text{ mmol}), \text{Potassium (Z)-(2-bromovinyl)trifluoroborate } 2 & (0.9 \text{ mmol}), \\
[\text{Rh(OH)(cod)}]_2 & (6.8 \text{ mg, 5 mol\%}), \text{PPh}_3 & (15.7 \text{ mg, 20 mol\%}) \text{ and CsF (136.8 mg, 0.9 mmol)} & \text{were added to 1,4-dioxane/H}_2\text{O (20/1, 3 mL) in Schlenk tube. The mixture was} \text{stirred at 100}^\circ\text{C and monitored by TLC. When the starting material was disappeared the reaction was cooled to room temperature. The contents were transferred to a round-bottom flask, and volatiles were removed in vacuo. Then, the mixture was purified by flash column chromatography (hexane: ethyl acetate = 30:1 to 5:1) to obtain the product 3.}
\end{align*}
\]

IV. Procedure for Synthesis of Compound 4

\[
\begin{align*}
\text{The compound 3i was obtained under the conditions for Rh(I)-catalyzed cycloaddition. To a stirring solution of LiAlH}_4 & (0.18 \text{ mmol, 6.9 mg}) \text{ in 1 mL of THF at 0}^\circ\text{C was slowly added the solution of 3i (0.15 mmol, 54.3 mg) in 3 mL THF. The mixture was brought to room temperature and heated at refluxed for another 3 hrs. Then 5 ml of 10\% aqueous NaOH and 2 mL water was cautiously added to the reaction mixture,}
\end{align*}
\]
the resulting salts were filtered, and filtrate was extracted with 3 × 10 mL portions of ethyl acetate. The ethyl acetate solutions were combined, dried over anhydrous sodium sulfate, and the solvent was removed under vacuum. Then, the mixture was purified by flash column chromatography (hexane: ethyl acetate = 2:1) to obtain the product 4 (49.5 mg, 90%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.87 (br, 1H), 3.22 (br, 1H), 4.71 (s, 2H), 4.82 (s, 2H), 7.05-7.07 (m, 2H), 7.12-7.18 (m, 5H), 7.23-7.26 (m, 3H), 7.39-7.42 (m, 2H), 7.47 (t, $J = 7.2$ Hz, 2H), 7.54 (d, $J = 6.8$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 60.62, 60.97, 126.36, 126.84, 127.35, 127.53, 127.77, 128.26, 129.54, 129.70, 130.67, 131.91, 136.64, 138.73, 139.18, 140.79, 140.86, 141.28, 141.68, 142.62; MS (m/z): 366(M$^+$); HRMS Calcd for C$_{26}$H$_{22}$O$_2$ 366.1620, Found 366.1623.

V. The Data for Products 3 and Compound 5.

![Diagram of 3aa](image)

3aa (114mg, 76%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.41 (s, 3H), 4.52 (s, 2H), 4.77 (s, 2H), 7.03-7.08 (m, 4H), 7.11-7.18 (m, 3H), 7.21-7.25 (m, 3H), 7.30 (d, $J = 8.0$ Hz, 2H), 7.36 (s, 1H), 7.39-7.48 (m, 5H), 7.71 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.48, 53.82, 53.90, 126.63, 127.12, 127.16, 127.58, 127.77, 128.03, 128.27, 128.77, 129.42, 129.74, 129.79, 130.61, 133.26, 133.56, 134.83, 136.38, 136.57, 138.15, 139.24, 140.28, 141.38, 143.62; MS (m/z): 501(M$^+$); HRMS Calcd for C$_{33}$H$_{27}$NO$_2$S 501.1762, Found 501.1757.

![Diagram of 3ba](image)

3ba (21mg, 20%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.42 (s, 3H), 4.67 (s, 2H), 4.68 (s, 2H), 7.24 (d, $J = 8.0$ Hz, 1H), 7.32-7.38 (m, 4H), 7.41-7.47 (m, 3H), 7.52 (d, $J = 7.6$ Hz, 2H), 7.80 (d, $J$
$= 7.8 \text{ Hz}, 2\text{H})$; $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$): $\delta$ 21.49, 53.53, 53.71, 121.31, 122.91, 126.90, 127.09, 127.53, 127.61, 128.83, 129.83, 133.69, 135.12, 136.83, 140.53, 141.26, 143.70; MS (m/z): 349(M$^+$); HRMS Calcd for C$_{21}$H$_{19}$NO$_2$S 349.1136, Found 349.1129.

![3ca](78mg, 75%)

$^{1}\text{H NMR}$ (400 MHz, CDCl$_3$): $\delta$ 5.14 (s, 2H), 5.40 (s, 2H), 7.17-7.33 (m, 10H), 7.43 (t, $J = 7.2 \text{ Hz}, 1\text{H})$, 7.50-7.57 (m, 5H); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$): $\delta$ 73.85, 73.90, 126.50, 126.90, 127.56, 127.77, 127.84, 128.09, 128.70, 129.45, 129.90, 130.12, 133.44, 134.97, 136.37, 138.77, 139.69, 139.84, 140.64, 140.96; MS (m/z): 348(M$^+$); HRMS Calcd for C$_{26}$H$_{20}$O 348.1514, Found 348.1515.

![3da](122mg, 83%)

$^{1}\text{H NMR}$ (400 MHz, CDCl$_3$): $\delta$ 1.28 (t, $J = 7.2 \text{ Hz}, 6\text{H})$, 3.61 (s, 2H), 3.85 (s, 2H), 4.24 (q, $J = 7.2 \text{ Hz}, 4\text{H}$), 7.20-7.23 (m, 7H), 7.29-7.34 (m, 3H), 7.43 (t, $J = 7.2 \text{ Hz}, 2\text{H}$), 7.52 (t, $J = 7.6 \text{ Hz}, 2\text{H}$), 7.62 (d, $J = 7.2 \text{ Hz}, 2\text{H}$); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$): $\delta$ 13.93, 40.35, 40.54, 60.33, 61.63, 126.19, 126.53, 127.16, 127.57, 127.92, 128.40, 128.49, 129.84, 129.98, 130.07, 135.96, 136.86, 137.28, 139.30, 140.11, 140.33, 140.47, 141.12, 171.51; MS (m/z): 490(M$^+$); HRMS Calcd for C$_{33}$H$_{30}$O$_4$ 490.2144, Found 490.2146.

![3ea](122mg, 88%)

$^{1}\text{H NMR}$ (400 MHz, CDCl$_3$): $\delta$ 1.28 (t, $J = 7.2 \text{ Hz}, 6\text{H})$, 3.61 (s, 2H), 3.85 (s, 2H), 4.24 (q, $J = 7.2 \text{ Hz}, 4\text{H}$), 7.20-7.23 (m, 7H), 7.29-7.34 (m, 3H), 7.43 (t, $J = 7.2 \text{ Hz}, 2\text{H}$), 7.52 (t, $J = 7.6 \text{ Hz}, 2\text{H}$), 7.62 (d, $J = 7.2 \text{ Hz}, 2\text{H}$); $^{13}\text{C NMR}$ (100 MHz, CDCl$_3$): $\delta$ 13.93, 40.35, 40.54, 60.33, 61.63, 126.19, 126.53, 127.16, 127.57, 127.92, 128.40, 128.49, 129.84, 129.98, 130.07, 135.96, 136.86, 137.28, 139.30, 140.11, 140.33, 140.47, 141.12, 171.51; MS (m/z): 490(M$^+$); HRMS Calcd for C$_{33}$H$_{30}$O$_4$ 490.2144, Found 490.2146.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.75 (t, $J = 7.2$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H), 1.16 (q, $J = 7.2$ Hz, 2H), 1.23-1.31 (m, 2H), 1.36 (q, $J = 7.2$ Hz, 2H), 1.49-1.57 (m, 2H), 2.38-2.49 (m, 4H), 2.44 (s, 3H), 4.66 (s, 2H), 4.68 (s, 2H), 6.93 (s, 1H), 7.24 (d, $J = 6.8$ Hz, 2H), 7.33-7.41 (m, 5H), 7.83 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 13.59, 13.89, 21.47, 22.55, 22.68, 29.90, 32.06, 32.10, 32.48, 53.03, 53.36, 126.85, 127.55, 127.97, 129.13, 129.80, 129.92, 132.54, 133.77, 133.80, 134.40, 135.20, 141.30, 141.94, 143.62; MS (m/z): 461(M$^+$); HRMS Calcd for C$_{29}$H$_{35}$NO$_2$S 461.2389, Found 461.2381.

![3fa (79mg, 60%)](image)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.42 (s, 3H), 3.28 (s, 3H), 3.36 (s, 3H), 4.23 (s, 2H), 4.39 (s, 2H), 4.68 (s, 2H), 4.76 (s, 2H), 7.15 (s, 1H), 7.29-7.41 (m, 7H), 7.82 (d, $J = 8.4$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.49, 52.55, 52.99, 58.32, 58.36, 69.82, 72.43, 127.33, 127.58, 128.12, 129.24, 129.27, 129.34, 129.81, 132.28, 133.69, 134.51, 137.66, 139.90, 142.25, 143.60; MS (m/z): 437(M$^+$); HRMS Calcd for C$_{25}$H$_{27}$NO$_4$S 437.1661, Found 437.1665.

![3ga (59mg, 40%)](image)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.03 (s, 3H), 2.10 (s, 3H), 2.44 (s, 3H), 4.71 (s, 4H), 4.90 (s, 2H), 5.03 (s, 2H), 7.21-7.24 (m, 3H), 7.35-7.41 (m, 5H), 7.82 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 20.66, 20.76, 21.50, 52.50, 52.94, 61.74, 63.54, 127.60, 127.72, 127.74, 128.34, 129.05, 129.87, 130.10, 130.66, 133.48, 134.81, 137.73, 139.13, 143.24, 143.92, 170.28, 170.44; MS (m/z): 493(M$^+$); HRMS Calcd for C$_{27}$H$_{27}$NO$_6$S 493.1559, Found 493.1565.
**3db** (120mg, 85%)  

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.82 (t, $J = 7.2$ Hz, 3H), 1.24 (t, $J = 7.2$ Hz, 3H), 1.28-1.41 (m, 2H), 1.45-1.52 (m, 2H), 2.51 (t, $J = 8.0$ Hz, 2H), 3.39 (s, 2H), 3.76 (s, 2H), 4.19 (q, $J = 7.2$ Hz, 4H), 7.23 (s, 1H), 7.32 (d, $J = 6.8$ Hz, 2H), 7.38-7.42 (m, 2H), 7.49 (t, $J = 8.4$ Hz, 4H), 7.56 (d, $J = 7.2$ Hz, 2H);  

$^{13}$C NMR (100 MHz, CDCl$_3$):  
$\delta$ 13.73, 13.90, 22.43, 32.50, 33.62, 40.28, 40.32, 60.22, 61.50, 126.81, 126.92, 128.24, 128.30, 128.44, 128.61, 129.04, 131.59, 134.64, 137.02, 137.12, 139.62, 139.67, 139.94, 140.75, 171.56; MS (m/z): 470(M$^+$); HRMS Calcd for C$_{31}$H$_{34}$O$_4$ 470.2457, Found 470.2457.

**3ab** (108mg, 75%)  

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.77 (t, $J = 7.2$ Hz, 3H), 1.15-1.24 (m, 2H), 1.38-1.45 (m, 2H), 2.42 (s, 3H), 2.46 (t, $J = 8.0$ Hz, 2H), 4.37 (s, 2H), 4.72 (s, 2H), 7.19 (d, $J = 6.8$ Hz, 2H), 7.23 (s, 1H), 7.31 (d, $J = 8.0$ Hz, 2H), 7.38-7.50 (m, 8H), 7.70 (d, $J = 8.0$ Hz, 2H);  

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 13.70, 21.44, 22.33, 32.27, 33.57, 53.72, 53.82, 127.45, 127.52, 127.55, 127.97, 128.56, 128.60, 128.67, 129.31, 129.71, 131.11, 133.65, 135.88, 136.07, 136.13, 138.32, 139.66, 141.13, 143.50; MS (m/z): 481(M$^+$); HRMS Calcd for C$_{31}$H$_{31}$NO$_2$S 481.2075, Found 481.2071.

**3cb** (69mg, 70%)  

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.82 (t, $J = 7.2$ Hz, 3H), 1.23-1.31 (m, 2H), 1.47-1.54
(m, 2H), 2.57 (t, J = 8.0 Hz, 2H), 4.92 (s, 2H), 5.30 (s, 2H), 7.29-7.34 (m, 3H), 7.39-7.51 (m, 8H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 13.78, 22.45, 32.21, 33.76, 73.73, 73.98, 127.23, 127.36, 127.84, 128.41, 128.65, 128.73, 134.24, 134.57, 134.78, 139.02, 139.35, 140.20, 140.67; MS (m/z): 328 (M\(^+\)); HRMS Calcd for C\(_{24}\)H\(_{24}\)O 328.1827, Found 328.1824.

Two isomers with the ratio of 2:1. MS (m/z): 300 (M\(^+\)); HRMS Calcd for C\(_{21}\)H\(_{16}\)O\(_2\) 300.1150, Found 300.1152

For minor isomer: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.67 (s, 1.5H), 5.39 (s, 1H), 7.07-7.09 (m, 0.67H), 7.13-7.15 (m, 0.67H), 7.22-7.24 (m, 1H), 7.25-7.27 (m, 0.33H), 7.28-7.29 (m, 0.33H), 7.35-7.38 (m, 0.33H), 7.40 (s, 0.33H), 7.42-7.51 (m, 1.67H), 7.60 (s, 0.5H). For major isomer: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.78 (s, 3H), 5.14 (s, 2H), 7.07-7.09 (m, 1.33H), 7.13-7.15 (m, 1.33H), 7.22-7.24 (m, 2H), 7.25-7.27 (m, 0.67H), 7.28-7.29 (m, 0.67H), 7.35-7.38 (m, 0.67H), 7.40 (s, 0.67H), 7.42-7.51 (m, 3.33H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 14.62, 17.13, 68.33, 68.90, 122.44, 124.19, 127.31, 127.51, 127.54, 127.71, 127.97, 128.17, 128.37, 128.52, 129.07, 129.33, 129.69, 132.70, 133.22, 133.77, 135.26, 136.33, 136.50, 137.58, 138.48, 139.58, 139.81, 143.67, 144.24, 146.14, 146.81, 171.33, 171.37.

\(3\)ja-1 (105mg, 56%)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.33 (s, 3H), 2.44 (s, 3H), 4.69 (d, J = 14.0 Hz, 1H), 4.80 (d, J = 14.0 Hz, 1H), 4.92 (s, 2H), 5.07-5.08 (m, 2H), 6.89-6.92 (m, 2H), 6.97-7.00 (m, 3H), 7.04-7.06 (m, 2H), 7.13-7.15(m, 3H), 7.19-7.20 (m, 3H), 7.30 (d, J
\[ = 8.0 \text{ Hz, 2H}, 7.40 (s, 1H), 7.70 (d, } J = 8.0 \text{ Hz, 2H)\}; ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 20.77, 21.58, 52.07, 72.94, 73.77, 125.27, 126.38, 126.87, 127.64, 127.76, 127.98, 128.00, 128.79, 129.33, 129.55, 129.80, 131.39, 131.88, 134.12, 134.46, 134.77, 136.65, 138.29, 138.68, 139.20, 140.31, 140.42, 140.49, 143.73; \text{ MS (m/z): 623 (M}^+\text{); HRMS Calcd for C}_{35}\text{H}_{30}\text{BrNO}_3\text{S 623.1130, Found 623.1128.}

\[
\begin{align*}
\text{3ja-2 (99mg, 50%)} \\
\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 2.32 (s, 3H), 2.45 (s, 3H), 4.47 (d, } J = 14.0 \text{ Hz, 1H), 4.87 (d, } J = 14.0 \text{ Hz, 2H), 4.99 (dd, } J = 12.8 \text{ Hz, } J = 21.2 \text{ Hz, 2H), 5.12 (d, } J = 12.8 \text{ Hz, 1H), 6.83-6.87 (m, 3H), 6.91 (s, 1H), 6.99-7.01 (m, 2H), 7.07-7.12 (m, 4H), 7.19-7.20 (m, 3H), 7.32 (d, } J = 8.2 \text{ Hz, 2H), 7.72 (d, } J = 8.2 \text{ Hz, 3H); ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 20.53, 21.62, 52.93, 73.11, 73.84, 102.86, 126.36, 126.89, 127.17, 127.61, 128.02, 128.26, 129.34, 129.61, 129.69, 129.80, 130.23, 131.79, 134.33, 136.24, 138.45, 138.70, 138.75, 139.29, 140.24, 140.41, 140.48, 140.98, 143.89; \text{ MS (m/z): 671 (M}^+\text{); HRMS Calcd for C}_{35}\text{H}_{30}\text{INO}_3\text{S 671.0991, Found 671.0993.}
\end{align*}
\]

\[
\begin{align*}
\text{5} \\
\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 2.26 (s, 3H), 2.42 (s, 3H), 4.71 (d, } J = 13.6 \text{ Hz, 1H), 4.99 (d, } J = 13.2 \text{ Hz, 1H), 5.23-5.30 (m, 2H), 5.39 (d, } J = 13.6 \text{ Hz, 1H), 5.70 (d, } J = 13.2 \text{ Hz, 1H), 6.18 (d, } J = 8.0 \text{ Hz, 1H), 6.63 (d, } J = 8.0 \text{ Hz, 1H), 6.68 (d, } J = 6.8 \text{ Hz, 2H), 7.00 (s, 1H), 7.14-7.18 (m, 3H), 7.22-7.24 (m, 3H), 7.37-7.43 (m, 5H), 7.51 (d, } J = 8.0 \text{ Hz, 2H); ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 20.72, 21.60, 48.52, 73.44, 73.95, 124.74, 125.91, 126.75, 127.59, 127.69, 127.81, 128.21, 128.55, 128.64, 129.41,
\end{align*}
\]
129.51, 129.71, 130.78, 133.94, 134.15, 134.30, 135.27, 135.76, 136.91, 139.53, 139.83, 142.53, 143.04, 143.69; MS (m/z): 623 (M⁺); HRMS Calcd for C₃₅H₃₀BrNO₃S 623.1130, Found 623.1133.
VI. The Spectra of Products 3, Compounds 4 and 5