Synthesis of Conjugated Tri(hetero)aryl Derivatives Based on One-Pot Double Suzuki-Miyaura Couplings using Bifunctional Dipotassium Phenylene-1,4-Bis(Trifluoroborate)

Antonio Salomone, Marilena Petrera, Donato Ivan Coppi, Filippo Maria Perna, Saverio Florio, and Vito Capriati*

Dipartimento Farmaco-Chimico, Università di Bari “A. Moro”, Consorzio Interuniversitario Nazionale “Metodologie e Processi Innovativi di Sintesi” C.I.N.M.P.I.S. Via E. Orabona 4, I-70125 Bari, Italy

Supporting Information

Table of contents

General Methods S2
Preparation of dipotassium phenylene-1,4-bis(trifluoroborate) (2) S2
Analytical data for compounds 2, 4a, 4c-f, 4h, 4l-n, 4o, 4s S3-S6
\(^1\)H NMR study of dipotassium phenylene-1,4-bis(trifluoroborate) (2) hydrolysis (Figure S1) S7
Absorption and emission spectra for compounds 4a,b, and 4p (Figures S2-S4) S8
General Methods.

$^1$H (400 or 500 or 600 MHz), $^{13}$C (125 or 150 MHz), $^{19}$F (376 MHz), and $^{11}$B (192 MHz) NMR spectra were recorded in CDCl$_3$ or DMSO-$d_6$, and chemical shifts (δ) are given in ppm relative to residual CHCl$_3$ or DMSO. $^{19}$F and $^{11}$B NMR chemical shifts were referenced to internal CFCl$_3$ (0.0 ppm) and external BF$_3$·Et$_2$O (0.0 ppm), respectively; in the latter case, a positive sign indicates a downfield shift. GC-MS spectrometry analyses were performed on a gas chromatograph (dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating at 70 eV (EI). MS-ESI and HRMS analyses were recorded on a Finnigan MAT 95Q or a Finnigan MAT90 instrument using electron impact ionization (EI). Melting points were uncorrected. Elemental analyses were performed by using a Carlo Erba CHNS-O EA1108-Elemental Analyzer. Analytical thin layer chromatography (TLC) was carried out on preloaded 0.25 mm thick plates of Kieselgel 60 F254; visualization was accomplished by UV light (254 nm). All reactions involving air-sensitive reagents were performed under argon using syringe-septum cap technique. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Compounds 4a–s were purified by flash column-chromatography on silica gel. Spectroscopic data of compounds 4b, $^1$4g, $^2$4i, $^3$4j, $^4$4k, $^5$4o, $^6$ and $^7$4r have been reported.

Preparation of phenylene-1,4-bis(potassium trifluoroborate) (2).

To a solution of benzene-1,4-diboric acid (1) (2 g, 12.1 mmol) in methanol (10 mL) was slowly added a 4.5 M solution of KHF$_2$ (79.9 mmol, 18 mL) in H$_2$O at r.t. under vigorous stirring. The resulting reaction mixture was additionally stirred for 40 min during which a solid precipitated out. The solid was then filtered on a Gooch funnel and washed with cold methanol. After drying off under high vacuum at 50 °C for 2 h, the product (2) was obtained as a white free-flowing powder (3.2 g, 92%). Recrystallization from acetone/H$_2$O solution (2/1) afforded colorless needle-shaped crystals. Analytical data: mp 342 °C dec. $^1$H-NMR (400 MHz, DMSO-$d_6$): δ =

---

7.04 (s, 4 H); $^{13}$C-NMR (150 MHz, DMSO-$d_6$): $\delta = 145.4$ (br s), 129.6; $^{19}$F-NMR (376 MHz, DMSO-$d_6$): $\delta = -137.5$ (br s); $^{11}$B-NMR (192 MHz, DMSO-$d_6$): $\delta = 4.38$ (br s); FT-IR (KBr): $\nu = 3514$, 3440, 3048, 2999, 1961, 1621, 1505, 1385, 1371, 1235, 991, 970, 939, 831, 823, 725, 579 cm$^{-1}$. Anal. Calcd. for C$_8$H$_4$B$_2$F$_6$K$_2$: C, 24.86; H, 1.39. Found: C, 24.49; H, 1.68.

(R$^*$,S$^*$)- and (R$^*$,R$^*$)-1,4-Bis(2-oxiranylnaphthyl)benzene (4a). Inseparable equimolecular mixture of diastereoisomers; column chromatography eluent: hexane/ethyl acetate 8/2; yellow solid (80%), mp 171–173 °C (ethyl acetate); $^1$H-NMR (400 MHz, CDCl$_3$): $\delta = 7.51$–7.30 (m, 12 H), 3.89 (br s, 2 H), 3.11 (br s, 2 H), 2.84 (br s, 2 H); $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta = 141.4$, 139.3, 135.1, 129.9, 129.5, 128.1, 128.0, 124.3, 51.9, 50.9; GC-MS (70 eV, EI): $m/z$ (%): 314 (M$^+$, 36), 286 (25), 281 (31), 267 (64), 265 (41), 253 (45), 252 (49) 239 (22) 207 (100), 165 (20) 73 (15); FT-IR (KBr): $\nu = 3432$, 2923, 1479, 1445, 821, 171 (s), 1693, 1595, 1468, 1392, 1250, 1194, 853, 761; cm$^{-1}$. HRMS (EI) calcd. for C$_{22}$H$_{18}$O$_2$: 314.1307. Found: 314.1296.

HPLC (OD-H, hexane/i-PrOH 9/1, 0.5 ml/min) min (% Area):13 (50) 19 (50).

1,4-Bis(2-acetylnaphthyl)benzene (4c). Column chromatography eluent: hexane/ethyl acetate 9/1; white solid (89%), mp 145 °C dec (ethyl acetate); $^1$H-NMR (600 MHz, CDCl$_3$): $\delta = 7.62$–7.58 (m, 2 H), 7.57–7.53 (m, 2 H), 7.48–7.44 (m, 4 H), 7.43 (s, 4 H), 2.11 (s, 6 H); $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta = 204.6$, 141.0, 140.6, 140.0, 131.0, 130.5, 129.6, 128.2, 127.9, 30.2; GC-MS (70 eV, EI): $m/z$ (%): 314 (M$^+$, 100), 281 (67), 252 (35), 226 (24), 195 (21), 113 (14), 43 (16); FT-IR (KBr): $\nu = 3371$; 2956, 2924, 1693, 1678, 1434, 1266, 1229, 781 cm$^{-1}$. Anal. Calcd. for C$_{22}$H$_{18}$O$_2$: C, 84.05; H, 5.77. Found: C, 83.83; H, 6.01.

1,4-Bis(2-formynylnaphthyl)benzene (4d). Column chromatography eluent: hexane/ethyl acetate 10/1; brown solid (91%), mp 156–157 °C (ethyl acetate); $^1$H-NMR (600 MHz, CDCl$_3$): $\delta = 10.04$ (s, 2 H), 8.05–8.03 (m, 2 H), 7.68–7.64 (m, 2 H), 7.54–7.49 (m, 3 H), 7.52–7.48 (m, 5 H); $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta = 192.0$, 144.9, 137.6, 133.7, 133.6, 130.7, 130.1, 128.1, 127.8; GC-MS (70 eV, EI): $m/z$ (%): 286 (M$^+$, 76), 268 (100), 228 (42), 202 (19), 181 (22), 152 (19), 113 (19), 76 (9); FT-IR (KBr): $\nu = 2841$, 2750, 1670, 1595, 1468, 1392, 1250, 1194, 853, 761; cm$^{-1}$. Anal. Calcd. for C$_{20}$H$_{14}$O$_2$: C, 83.90; H, 4.93. Found: C, 83.83; H, 5.08.

S3
1,4-Bis(3-formylphenyl)benzene (4e). Column chromatography eluent: hexane/ethyl acetate 9/1; brown solid (80%), mp 136–137 °C (ethyl acetate); ^1^H-NMR (400 MHz, CDCl\textsubscript{3}); δ = 10.08 (s, 2 H), 8.13–8.12 (m, 2 H), 7.90–7.85 (m, 4 H), 7.71 (s, 4 H), 7.63–7.59 (m, 2 H); ^13^C-NMR (125 MHz, CDCl\textsubscript{3}); δ = 192.2, 141.3, 139.3, 137.0, 132.9, 129.6, 128.9, 127.9, 127.7; GC-MS (70 eV, EI): m/z (%): 286 (M\textsuperscript{+}, 100), 258 (10), 228 (22); FT-IR (KBr): ν = 3018, 2850, 1694, 1581, 1383, 1182, 863, 788, 725, 691 cm\textsuperscript{-1}. Anal. Calcd. for C\textsubscript{20}H\textsubscript{14}O\textsubscript{2}: C, 83.90; H, 4.93. Found: C, 84.04; H, 5.10.

1,4-Bis(4-bromo-2-fluorophenyl)benzene (4f). Column chromatography eluent: hexane/ethyl acetate 98/2; yellow solid (61%), mp 153 °C dec (ethyl acetate); ^1^H-NMR (400 MHz, CDCl\textsubscript{3}): δ = 7.55–7.50 (m, 4 H), 7.37–7.30 (m, 6 H); ^13^C-NMR (150 MHz, CDCl\textsubscript{3}): δ = 159.2 (d, ^2^J\textsubscript{C-F} = 253 Hz), 134.4, 131.6, 129.0, 127.8, 127.5 (d, ^2^J\textsubscript{C-F} = 13.1 Hz), 121.6 (d, ^3^J\textsubscript{C-F} = 9.1 Hz), 119.8 (d, ^2^J\textsubscript{C-F} = 26.1 Hz); GC-MS (70 eV, EI): m/z (%): 426 [M\textsuperscript{+} + 4 (50)], 424 [M\textsuperscript{+} + 2 (100)], 422 [M\textsuperscript{+} (50)], 264 (18), 244 (10), 212 (10), 131 (10); FT-IR (KBr): ν = 2961, 1600, 1562, 1473, 1261, 871, 800, 698 cm\textsuperscript{-1}. Anal. Calcd. for C\textsubscript{18}H\textsubscript{10}Br\textsubscript{2}F\textsubscript{2}: C, 50.98; H, 2.38. Found: C, 50.69; H, 2.49.

1,4-Bis(3-chloro-4-hydroxyphenyl)benzene (4h). Column chromatography eluent: hexane/ethyl acetate 7/3; brown solid (49%), mp 153 °C dec (CH\textsubscript{2}Cl\textsubscript{2}); ^1^H-NMR (600 MHz, CDCl\textsubscript{3}); δ = 7.59 (d, J = 2.1 Hz, 2 H), 7.50 (s, 4 H), 7.45 (dd, J = 2.1, 8.5 Hz, 2 H), 7.10 (d, J = 8.5 Hz, 2 H); ^13^C-NMR (150 MHz, CDCl\textsubscript{3}); δ = 150.9, 138.4, 134.3, 127.3, 127.0, 124.7, 120.4, 116.6; ESI-MS m/z (%) 329 [M-H]\textsuperscript{-} (100); FT-IR (KBr): ν = 3496, 2918, 1602, 1577, 1528, 1488, 1359, 1285, 1056, 881, 727 cm\textsuperscript{-1}. Anal. Calcd. for C\textsubscript{18}H\textsubscript{12}O\textsubscript{2}Cl\textsubscript{2}: C, 65.28; H, 3.65. Found: C, 65.34; H, 4.04.

1,4-Bis(5-chlorothiophen-2-yl)benzene (4l). Column chromatography eluent: hexane/CH\textsubscript{2}Cl\textsubscript{2} 10/1; yellow solid (40%), mp 204–205 °C dec. (CH\textsubscript{2}Cl\textsubscript{2}); ^1^H-NMR (600 MHz, CDCl\textsubscript{3}); δ = 7.50 (s, 4 H), 7.09 (d, J = 3.8 Hz, 2 H), 6.90 (d, J = 3.8 Hz, 2 H); ^13^C-NMR (150 MHz,
CDCl₃): δ = 142.1, 133.0, 129.4, 127.2, 125.9, 122.4; GC-MS (70 eV, EI): m/z (%): 310 (M⁺, 100), 240 (15), 231 (15), 149 (30), 57 (11), 43 (21); FT-IR (KBr): ν = 2956, 2923, 2852, 1501, 1437, 827, 798 cm⁻¹. HRMS (EI) calcd. for C₁₄H₆Cl₂S₂: 309.9444. Found: 309.9437.

1,4-Bis(thiazol-2-yl)benzene (4m). Column chromatography eluent: CH₂Cl₂/methanol 10/1; brown solid (63%), mp 153 °C dec (CH₂Cl₂); ¹H-NMR (600 MHz CDCl₃): δ = 8.02 (s, 4 H), 7.87 (d, J = 2.5 Hz, 2 H), 7.33 (d, J = 2.5 Hz, 2 H); ¹³C-NMR (150 MHz, CDCl₃): δ = 167.3, 143.9, 134.7, 127.0, 119.3; GC-MS (70 eV, EI): m/z (%): 244 (M⁺, 100), 187 (18), 58 (58); FT-IR (KBr): ν = 3122, 3086, 2927, 1667, 1604, 1479, 1251, 1146, 976, 907, 732 cm⁻¹. Anal. Calcd. for C₁₂H₈N₂S₂: C, 58.99; H, 3.30; N, 11.47. Found: C, 59.34; H, 3.70; N, 11.20.

1,4-Bis(3-furan)benzene (4n): column chromatography eluent: hexane/CH₂Cl₂ 20/1; white solid (75%), mp 150 °C dec. (CH₂Cl₂); ¹H-NMR (600 MHz, CDCl₃): δ = 7.77 (br s, 2 H), 7.52 (s, 4 H), 7.51 (m, 2 H), 6.74 (m, 2 H); ¹³C-NMR (150 MHz, CDCl₃): δ = 143.7, 138.4, 131.1, 126.2, 126.1, 108.7; GC-MS (70 eV, EI): m/z (%): 210 (M⁺, 100), 181 (29), 152 (19), 105 (5); FT-IR (KBr): ν = 1524, 1161, 1055, 1012, 875, 844, 783, 595 cm⁻¹. HRMS (EI) calcd. for C₁₄H₁₀O₂: 210.0681. Found: 210.0673.

1,4-Bis(3-isoquinoline)benzene (4p). Column chromatography eluent: hexane/CH₂Cl₂ 20/1; brown solid (80%), mp 206–208 °C dec. (CH₂Cl₂); ¹H-NMR (600 MHz, CDCl₃): δ = 9.27 (s, 2 H), 8.57 (s, 2 H), 8.06–8.02 (m, 4 H), 7.73–7.69 (m, 2 H), 7.66 (s, 2 H), 7.64–7.62 (m, 2 H); ¹³C-NMR (CDCl₃, 150 MHz): δ = 152.2, 142.9, 136.6, 134.0, 132.7, 130.7, 130.3, 128.4, 127.9, 127.3, 124.6; GC-MS (70 eV, EI): m/z (%): 332 (M⁺, 100), 329 (7), 204 (6), 166 (7), 152 (4); FT-IR (KBr): ν = 3026, 1618, 1567, 1517, 1493, 1386,96, 888, 854, 838, 798, 781, 752, 596 cm⁻¹. HRMS (EI) calcd. for C₂₄H₁₆N₂: 332.1313. Found: 332.1310.

1,4-Bis[(E)-3-oxo-2-phenylprop-1-enyl]benzene (4q). Column chromatography eluent: hexane/CH₂Cl₂ 7/3; brown solid (60%), mp 153 °C dec. (CH₂Cl₂); ¹H-NMR (600 MHz, CDCl₃): δ = 9.62 (s, 2 H), 7.24–7.05 (m, 16 H); ¹³C-NMR (150 MHz, CDCl₃): δ = 193.5, 150.1, 141.3, 134.0, 133.4, 130.7, 130.3, 129.9, 128.5; ESI-MS m/z (%): 361

S5
[M-Na]$^+$ (100); FT-IR (KBr): $\nu = 3334, 2921, 2714, 1679, 1618, 1447, 1200, 1094, 762, 723, 692$ cm$^{-1}$. Anal. Calcd. for C$_{24}$H$_{18}$O$_2$: C, 85.18; H, 5.36. Found: C, 85.27; H, 5.36.

1-(2-Ethylphenyl)-4-(4-cyanophenyl)benzene (4s). Column chromatography eluent: hexane/ethyl acetate 50/1; brown solid (40%), mp 94–95 °C (ethyl acetate); $^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ = 7.77 (s, 4 H), 7.60 (d, $J = 8.0$ Hz, 2 H), 7.45 (d, $J = 8.0$ Hz, 2 H), 7.37–7.35 (m, 2 H), 7.29–7.24 (m, 2 H), 2.66 (q, $J$=7.5 Hz, 2 H), 1.15 (t, $J_1$=7.5 Hz, 3 H); $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$= 15.7, 26.1, 110.9, 118.9, 125.7, 126.8, 127.6, 127.8, 128.7, 129.8, 130.0, 132.6, 137.5, 140.7, 141.5, 142.5, 145.3; GC-MS (70 eV, EI): $m/z$ (%): 283 (M$^+$,100), 266 (83), 165(17); FT-IR (KBr): $\nu = 2966, 2926, 2221, 1604, 1480, 1384, 1109, 827$ cm$^{-1}$. Anal. calcd. for C$_{21}$H$_{17}$N: C, 89.01; H, 6.05; N, 4.94. Found: C, 88.86; H, 6.26; N, 5.13.
Figure S1. $^1$H NMR study of dipotassium phenylene-1,4-bis(trifluoroborate) (2) hydrolysis: plot of [2], [2-D$_2$] and [2-D$_4$] as a function of time. Reaction performed in a 5 mm NMR tube at 25 °C. Initial concentrations: [2] = 0.07 M, [K$_2$CO$_3$] = 0.21 M.
Figure S2. Absorption and emission spectra ($\lambda_{\text{exc}} = 260$ nm) in CHCl$_3$ (10$^{-6}$ M) for compound 4a.

Figure S3. Absorption and emission spectra ($\lambda_{\text{exc}} = 258$ nm) in CHCl$_3$ (10$^{-6}$ M) for compound 4b.

Figure S4. Absorption and emission spectra ($\lambda_{\text{exc}} = 336$ nm) in CHCl$_3$ (10$^{-6}$ M) for compound 4p.