**An Improved Method for the Bromination of Metalated Haloarenes via Lithium,
Zinc Transmetalation: A Convenient Synthesis of 1,2-Dibromoarenes.**

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Supporting Information

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General: All reagents and starting materials were obtained from commercial suppliers and used without further purification. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. For spectra recorded in CDCl_3 , chemical shifts are given relative to the solvent signal. Proton multiplicities are abbreviated as follows: d=doublet, m= multiplet, br=broad. All coupling constants (J) are reported in Hertz (Hz). Flash column chromatography was performed using silica gel 60 (230-400 mesh). Melting points are uncorrected.

A 1.0 M solution of zinc chloride was prepared according to following procedure: A 250 mL round bottom flask was charged under nitrogen with 13.63 g (0.10 mmol) zinc chloride (Fluka). The white solids were dissolved in 90 mL tetrahydrofuran. The clear solution was dried over 13.6 g 4 Å molecular sieves for 4h. The flask was occasionally shaken and the water content was determined by a Karl Fisher titration (typically below 600 ppm water).

2. General experimental procedure for the synthesis of 3-substituted-1,2-dibromoarenes:

To *n*-butyllithium in hexanes (1.95 mL, 1.55 M, 3.02 mmol) at -20°C was added a solution of 2,2,6,6-tetramethylpiperidine (0.51 mL, 3.02 mmol) in THF (4.75 mL). After aging for 30 min, the solution was cooled to -78°C and a solution of 3-substituted-1-bromobenzene (2.7 mmol) in THF (2.8 mL) was added dropwise so as to maintain the temperature at $< -70^\circ\text{C}$. After 2 hours, a 1.0 M solution of ZnCl_2 in THF (2.75 mL, 2.75 mmol) was added dropwise and allowed to stir for an additional 30 min. Bromine (0.21 mL, 4.12 mmol) was added dropwise at such rate to keep the temperature below -50°C . The reaction was monitored by HPLC (typical reaction time <30 min) and the completed reaction was allowed to warm to 25°C and quenched with H_2O . The product was extracted two times into *tert*-butyl methyl ether and the combined organic layers were washed with 1 M HCl (aq.) followed by H_2O . The organic layer was dried over Na_2SO_4 , filtered and concentrated in vacuum. The residue was purified by flash column chromatography using hexanes.

3. Compound characterization:

3-Chloro-1,2-dibromobenzene (4a): According to the general procedure, the product was obtained in 93% (0.65 g, 2.42 mmol) as white crystals after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.54 (dd, *J* = 8.00, 1.52 Hz, 1H), 7.41 (dd, *J* = 8.06 Hz, 1.52 Hz, 1H), 7.11 (t, *J* = 8.06 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 125.7, 126.6, 128.8, 129.1, 131.9, 136.2.; Melting point: 73.9 °C (Lit.: 73.5 °C).¹

1,2-Dibromo-3-fluorobenzene (4b): According to the general procedure, the product was obtained in 93% (0.67 g, 2.66 mmol) as a colorless liquid after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.40 (dt, *J* = 8.0 Hz, 1.30 Hz, 1H), 7.62 (td, *J* = 8.1 Hz, 5.60 Hz, 1H), 7.06 (td, *J* = 8.1 Hz, 2.10 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 159.7 (d, *J* = 248 Hz), 129.1, 128.9, 126.1, 114.9 (d, *J* = 23 Hz), 112.9 (d, *J* = 23 Hz); GC/MS (*m/z*): 254, 173, 143, 94, 74.

1,2,3-Tribromobenzene (4c): According to the general procedure, the product was obtained in 85% (1.10 g, 3.50 mmol) as white crystals after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.58 (d, *J* = 8.00 Hz, 2H), 7.03 (t, *J* = 8.00 Hz, 1H). ¹³C-NMR (CDCl₃, 75 MHz): 126.2, 127.7, 129.2 (2C), 132.6 (2C).² Melting point: 89.8 °C (Lit.: 87-88 °C).³

1,2-Dibromo-3-fluoro-4-iodobenzene (4d): According to the general procedure, the product was obtained in 84% (1.06 g, 2.78 mmol) as off-white crystals after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.55 (dd, *J* = 8.40 Hz, 6.30 Hz, 1H), 7.17 (dd, *J* = 8.40 Hz, 1.80 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 158.9 (d, *J* = 248 Hz), 138.3, 130.1, 126.3, 113.1 (d, *J* = 23 Hz), 79.7 (d, *J* = 30 Hz); GC/MS (*m/z*): 380, 253, 172, 93, 74.; Melting point: 63.7 °C.

3-Cyano-1,2-dibromobenzene (4e): According to the general procedure, the product was obtained in 87% (0.62 g, 2.38 mmol) as slightly yellow crystals after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.85 (dd, *J* = 8.20 Hz, 1.40 Hz, 1H), 7.62 (dd, *J* = 7.70 Hz, 1.50 Hz, 1H), 7.29 (t, *J* = 8.00 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz):

137.7, 133.0, 128.6, 128.0, 126.7, 117.9, 116.8; GC/MS (m/z): 261, 180, 100, 75.;
Melting point: 106.1 °C.

1,2-Dibromo-3-trifluoromethylbenzene (4f): The addition of 1-bromo-2-trifluoromethylbenzene and zinc chloride solution in THF was carried out at -100 °C. According to the general procedure, the product was obtained in 61% (4.10 g, 13.4 mmol) as colorless crystals after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.82 (d, *J* = 8.05 Hz, 1H), 7.64 (d, *J* = 7.67 Hz, 1H), 7.28 (t, *J* = 8.11 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 117.0, 123.0, 126.6 (q, *J* = 293 Hz, 1C), 126.7 (q, *J* = 7.5 Hz, 1C), 128.2, 132.8, 137.0.; Melting Point: 37.9 °C.

Methyl 2,3-dibromobenzoate (4g): According to the general procedure, the product was obtained in 43% (0.25g, 1.00 mmol) as a colorless liquid after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.71 (dd, *J* = 8.00 Hz, 1.50 Hz, 1H), 7.54 (dd, *J* = 7.70 Hz, 1.50 Hz, 1H), 7.20 (t, *J* = 7.80 Hz, 1H), 3.92 (s, 3H); ¹³C-NMR (CDCl₃, 75 MHz): 166.6, 135.9, 135.8, 128.9, 128.1, 127.2, 123.2, 52.7; GC/MS (m/z) 294, 263, 235, 254, 75.

1,2-dibromo-4-trifluoromethylbenzene (4h): The addition of 3-trifluoromethyl-1-bromobenzene and zinc chloride solution in THF was carried out at -100 °C. According to the general procedure, the product was obtained in 77% (5.20 g, 17.1 mmol) as a colorless liquid after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 7.90 (d, *J* = 1.64 Hz, 1H), 7.60 (d, *J* = 8.44 Hz, 1H), 7.20 (dd, *J* = 8.50, 1.82 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 121.1, 124.8, 125.5, 125.6, 129.2, 130.6, 131.3, 134.2.⁴

2,3-Dibromopyridine (4i): According to the general procedure, the product was obtained in 77% (0.59 g, 2.423 mmol) as white needles after flash column chromatography. ¹H-NMR (CDCl₃, 300 MHz): 8.31 (dd, *J* = 4.60 Hz, 1.70 Hz, 1H), 7.88 (dd, *J* = 7.90 Hz, 1.70 Hz, 1H), 7.13 (dd, *J* = 7.80 Hz, 3.20 Hz, 1H); ¹³C-NMR (CDCl₃, 75 MHz): 148.1, 143.7, 141.7, 123.8, 123.5; GC/MS (m/z): 237, 156, 76.; Melting point: 60.5 °C (Lit.: 58-59 °C)⁵.

4. Characterization of 1-metalated 2-bromo-6-fluorobenzene by NMR:

^1H and ^{13}C NMR spectra were recorded in THF- d_8 on a Bruker DRX500 spectrometer at a frequency of 500.13 MHz and 125.77 MHz, respectively. The chemical shifts (δ) are reported in ppm relative to residual THF- d_7 ; for proton ($\delta=3.58$) and THF- d_8 for carbon ($\delta=67.57$). The reaction was carried out in a NMR tube according to the general experimental procedure described above.

2-bromo-6-fluorophenyllithium (2b)

^1H -NMR (500.13 MHz, THF- d_8): 6.86 (d, $J=7.6$ Hz, 1H), 6.55-6.61 (m, 1H), 6.40 (d, $J=7.6$ Hz, 1H). ^{13}C -NMR (125.77 MHz, THF- d_8): 170.4 (d, $J=216.0$ Hz), ~170.2 (br d, $J\sim 137$ Hz), 143.1 (d, $J=41.2$ Hz), 126.5 (d, $J=5.5$ Hz), 125.8 (d, $J=3.7$ Hz), 109.8 (d, $J=42.5$ Hz).

2-bromo-6-fluorophenylzinc (3b)

^1H -NMR (500.13 MHz, THF- d_8): 6.97 (d, $J=7.6$ Hz, 1H), 6.80-6.86 (m, 1H), 6.63 (br d, $J=8.0$ Hz, 1H). ^{13}C -NMR (125.77 MHz, THF- d_8): 167.2 (d, $J=230.7$ Hz), 152.8 (d, $J=76.9$ Hz), 134.3 (d, $J=28.3$ Hz), 127.0 (d, $J=4.3$ Hz), 125.3, 110.4 (d, $J=32.6$ Hz).

5. ^1H -, ^{13}C - and ^{19}F -NMR spectra of compounds (4a-4i):

3-Chloro-1,2-dibromobenzene (4a): ^1H -NMR (CDCl_3)

3-Chloro-1,2-dibromobenzene (4a): ^{13}C -NMR (CDCl_3)

1,2-Dibromo-3-fluorobenzene (4b): ^1H -NMR (CDCl_3)

1,2-Dibromo-3-fluorobenzene (4b): ^{13}C -NMR (CDCl_3)

1,2,3-Tribromobenzene (4c): ^1H -NMR (CDCl_3)

1,2,3-Tribromobenzene (4c): ^{13}C -NMR (CDCl_3)

1,2-Dibromo-3-fluoro-4-iodobenzene (4d): ^1H -NMR (CDCl_3)

1,2-Dibromo-3-fluoro-4-iodobenzene (4d): ^{13}C -NMR (CDCl_3)

3-Cyano-1,2-dibromobenzene (4e): ^1H -NMR (CDCl_3)

3-Cyano-1,2-dibromobenzene (4e): ^{13}C -NMR (CDCl_3)

1,2-Dibromo-3-trifluoromethylbenzene (4f): ^1H -NMR (CDCl_3)

1,2-Dibromo-3-trifluoromethylbenzene (4f): ^{13}C -NMR (CDCl_3)

1,2-Dibromo-3-trifluoromethylbenzene (4f): ^{19}F -NMR (CDCl_3)

Methyl 2,3-dibromobenzoate (4g): ^1H -NMR (CDCl_3)

Methyl 2,3-dibromobenzoate (4g): ^{13}C -NMR (CDCl_3)

1,2-dibromo-4-trifluoromethylbenzene (4h): ^1H -NMR (CDCl_3)

1,2-dibromo-4-trifluoromethylbenzene (4h): ^{13}C -NMR (CDCl_3)

1,2-dibromo-4-trifluoromethylbenzene (4h): ^{19}F -NMR (CDCl_3)

2,3-Dibromopyridine (4i): ^1H -NMR (CDCl_3)

2,3-Dibromopyridine (4i): ^{13}C -NMR (CDCl_3)

2-bromo-6-fluorophenyllithium (2b): ¹H-NMR (500.13 MHz, THF-d₈)

2-bromo-6-fluorophenyllithium (2b): ¹³C-NMR (125.77 MHz, THF-d₈)

2-bromo-6-fluorophenylzinc (3b): ¹H-NMR (500.13 MHz, THF-d₈)

2-bromo-6-fluorophenylzinc (3b): ¹³C-NMR (125.77 MHz, THF-d₈)

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