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Supporting Information

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Pd(II)-Catalyzed *mono*-Selective *ortho*-Halogenation of C-H Bonds Assisted by Counter Cations: An Orthogonal Method to Directed *ortho*-Lithiation

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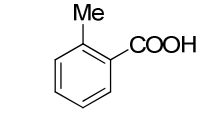
General Information: Solvents were obtained from Sigma-Aldrich and Acros and used directly without further purification. Arene carboxylic acids (Table 1) were obtained from the commercial sources. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. NMR spectra were recorded on a Varian Inova-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, b = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer Using ESI-TOF (electrospray ionization-time of flight). IR spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer.

Substrates (Table 1)



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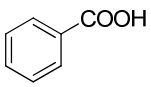

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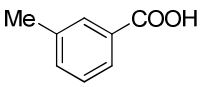

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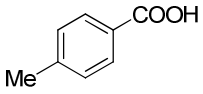

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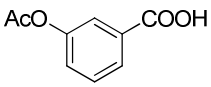

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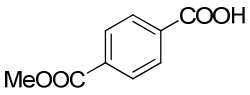

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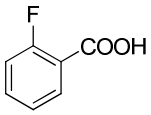

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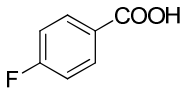

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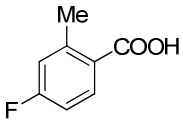

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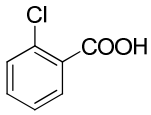

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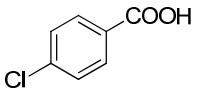

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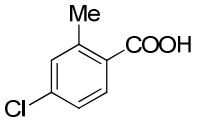

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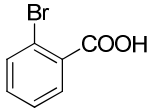

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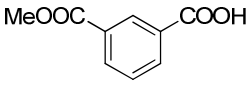

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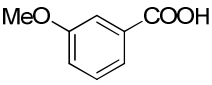

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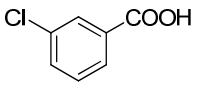

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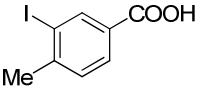

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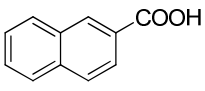

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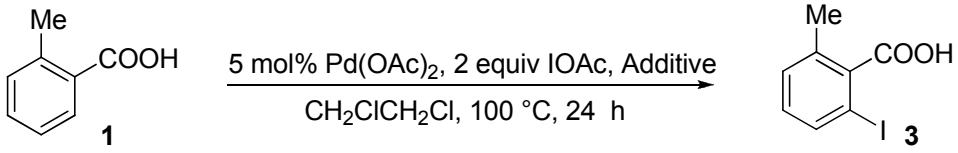
Experimental Section

The reaction was carried out under atmospheric air. Solvents were used as received without further distillation.

Effects of inorganic counter cations (Table 2)[a,b]



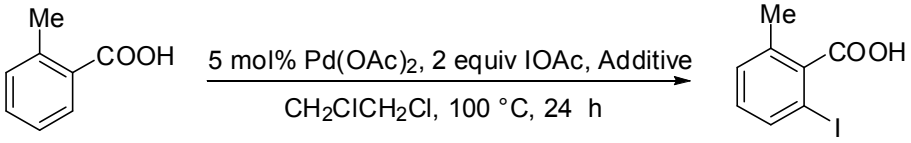
Entry	Additive	Yield [%]
1	1 equiv LiI	36
2	1 equiv $LiOAc{\cdot}H_2O$	20
3	1 equiv NaF	40
4	1 equiv NaCl	50
5	1 equiv NaI	70
6	1 equiv NaOAc	85
7	0.5 equiv Na_2CO_3	65
8	1 equiv Na_2CO_3	50
9	2 equiv Na_2CO_3	10
10	1 equiv KI	30
11	1 equiv K_2HPO_4	50
12	0.5 equiv K_2HPO_4	20
13	1 equiv CsI	30
14	1 equiv CsOAc	33
15	0.5 equiv Cs_2CO_3	77
16	1 equiv Cs_2CO_3	50
17	1 equiv $Mg(OAc)_2{\cdot}4H_2O$	10
18	1 equiv $Ba(OAc)_2$	18
19	1 equiv $Mn(OAc)_2$	41

[a] IOAc was generated *in situ* from 1 equiv I_2 and 1 equiv $PhI(OAc)_2$. [b] Isolated yield.

Procedure: In a 20 mL glass tube, substrate **1** (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) and additive (as specified in the Table 2) were dissolved in CH_2ClCH_2Cl (1 mL) under atmospheric air. The tube was sealed with a cap and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was

added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4. The solvent was removed in a rotary evaporator and the residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the white needle solid **3**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (bs, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.04 (t, *J* = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 139.0, 136.7, 136.6, 131.0, 129.8, 91.4, 20.2; IR (neat) ν 1694, 1444, 1290, 768 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_6IO_2$ $[M-H]^-$: 260.9413; found: 260.9401.

Effects of organic counter cations (Table 3)[a,b]



1 **3**

Entry	Additive	Yield [%]
1	0.5 equiv DABCO	70
2	0.5 equiv DBU	40
3	1 equiv DMF	77
4	5 equiv DMF	88
5	DMF as solvent	95 (90)
6	1 equiv DMA	14
7	DMA as solvent	10
8	1 equiv NMP	10
9	NMP as solvent	30
10	0.2 equiv Dimethylamine	2
11	1 equiv Dimethylamine	2

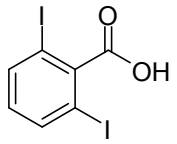
[a] Yield was determined by ^{1}H NMR. [b] Isolated yield in parenthesis.

Procedure: In a 20 mL glass tube, substrate **1** (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) and additive (as specified in the Table 3) were dissolved in a solvent (1 mL) under atmospheric air. The tube was sealed with a cap and the reaction mixture was stirred at 100 °C for 24 hours. The

reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4. The solvent was removed in a rotary evaporator and the residue was analyzed by ^{1}H NMR to determine the yield.

***ortho*-Iodination of arene carboxylic acids (4, 11-14, 16, 19)**

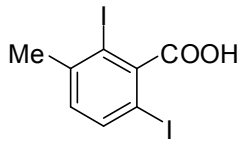
General procedure: In a 20 mL glass tube, substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (96.6 mg, 0.3 mmol) and I_2 (76.1 mg, 0.3 mmol) were dissolved in DMF (1 mL) under atmospheric air. The tube was sealed with a cap and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (50 mL) and then washed with 0.5 N HCl (10 mL × 4). The organic phase was washed with brine, dried over Na_2SO_4 and concentrated in a rotary evaporator. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the iodination product.



4a

2,6-Diiodobenzoic acid (4a)

Substrate **4** was iodinated following the general procedure. After purification by column chromatography, **4a** was obtained as a white solid (63.5 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (bs, 1H), 7.84 (d, J = 8.0 Hz, 2H), 6.82 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 144.5, 138.7 (2 C), 132.1, 90.7 (2 C); IR (neat) ν 1702, 1230, 920, 761 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_3I_2O_2$ [M-H]$^-$: 372.8223; found: 372.8238.

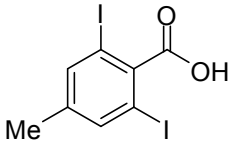


11a

2,6-Diiodo-3-methylbenzoic acid (11a)

Substrate **11** was iodinated following the general procedure. After purification by column chromatography, **11a** was obtained as a white solid (62.0 mg, 80%). ^{1}H NMR (400 MHz,

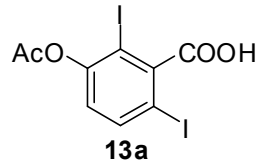
$CDCl_3$) δ 8.10 (bs, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H); 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 145.5, 142.6, 138.6, 131.4, 97.8, 86.5, 28.6; IR (neat) ν 1707, 1432, 1280, 804 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_5I_2O_2$ $[M-H]^-$: 386.8379; found: 386.8370.



12a

2,6-Diiodo-4-methylbenzoic acid (12a)

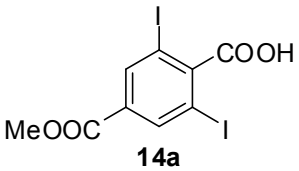
Substrate **12** was iodinated following the general procedure. After purification by column chromatography, **12a** was obtained as a white solid (67.4 mg, 87%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 142.8, 141.5, 139.4 (2 C), 90.4 (2 C), 20.3; IR (neat) ν 1583, 1287, 908 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_5I_2O_2$ $[M-H]^-$: 386.8379; found: 386.8363.



13a

3-Acetoxy-2,6-diiodobenzoic acid (13a)

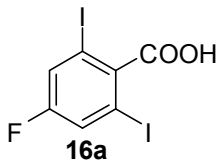
Substrate **13** was iodinated following the general procedure. After purification by column chromatography, **13a** was obtained as a white solid (56.1 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 168.2, 151.6, 146.3, 140.0, 125.1, 89.2, 86.8, 21.2; IR (neat) ν 1712, 1703, 1370, 1192, 906, 730 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_9H_5I_2O_4$ $[M-H]^-$: 430.8278; found: 430.8291.



14a

2,6-Diiodo-4-(methoxycarbonyl) benzoic acid (14a)

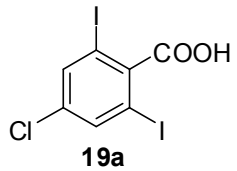
Substrate **14** was iodinated following the general procedure. After purification by column chromatography, **14a** was obtained as a white solid (63.9 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 163.5, 148.0, 139.7 (2 C), 133.2, 90.2 (2 C), 53.0; IR (neat) ν 1711, 1701, 1694, 1531, 1452, 1274, 1266, 906, 730 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_9H_5I_2O_4$ [M-H]$^-$: 430.8278; found: 430.8287.



16a

4-Fluoro-2,6-diiodobenzoic acid (16a)

Substrate 1**6** was iodinated following the general procedure. After purification by column chromatography, 1**6a** was obtained as a white solid (56.4 mg, 72%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.80 (d, J_{H-F} = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ 170.2, 162.4 (d, J_{C-F} = 128.2 Hz), 145.1, 127.7 (d, 2 C, J_{C-F} = 23.6 Hz), 91.7 (d, 2 C, J_{C-F} = 8.4 Hz); IR (neat) ν 1702, 1576, 1390, 1284, 861 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_2FI_2O_2$ [M-H]$^-$ 390.8129; found: 390.8138.



19a

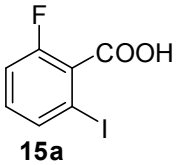
4-Chloro-2,6-diiodobenzoic acid (19a)

Substrate **19** was iodinated following the general procedure. After purification by column chromatography, **19a** was obtained as a white solid (65.3 mg, 80%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.98 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 145.7, 140.5 (2 C), 135.2, 90.8 (2 C); IR (neat) ν 1700, 1557, 1363, 1274, 866 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_2ClI_2O_2$ [M-H]$^-$: 406.7833; found: 406.7831.

***ortho*-Iodination of arene carboxylic acids (15, 17-18, 20-21)**

General procedure: In a 20 mL glass tube, substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol) and I_2 (50.8 mg, 0.2 mmol) were dissolved in DMF (1 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture cooled to room

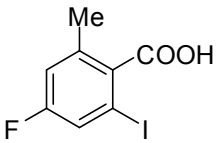
temperature and was diluted with 50 mL of ethyl acetate and then washed with HCl (0.5 N, 10 mL × 4) solution to get rid of DMF. The organic phase was washed with saturated brine, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the iodination product.



15a

2-Fluoro-6-iodobenzoic acid (15a)[1]

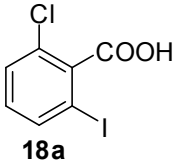
Substrate **15** was iodinated following the general procedure. After purification by column chromatography, **15a** was obtained as a white solid (42.5 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (t, J = 8.0 Hz, 1H), 7.14-7.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 159.5 (d, $J_{C\text{-}F}$ = 256 Hz), 135.8 (d, $J_{C\text{-}F}$ = 4 Hz), 133.2 (d, $J_{C\text{-}F}$ = 11 Hz), 127.2 (d, $J_{C\text{-}F}$ = 18 Hz), 116.2 (d, $J_{C\text{-}F}$ = 21 Hz), 92.7 (d, $J_{C\text{-}F}$ = 2 Hz); IR (neat) ν 1707, 1447, 1297, 864, 785 cm^{-1}.



17a

4-Fluoro-2-iodo-6-methylbenzoic acid (17a)

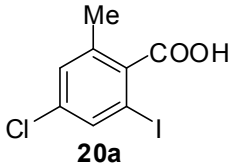
Substrate **17** was iodinated following the general procedure. After purification by column chromatography, **17a** was obtained as a white solid (49.8 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, $J_{H\text{-}F}$ = 8.0 Hz, 1H), 6.97 (d, $J_{H\text{-}F}$ = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 162.1 (d, $J_{C\text{-}F}$ = 254 Hz), 139.0 (d, $J_{C\text{-}F}$ = 8 Hz), 135.2, 124.0 (d, $J_{C\text{-}F}$ = 24 Hz), 117.2 (d, $J_{C\text{-}F}$ = 21 Hz), 91.6 (d, $J_{C\text{-}F}$ = 9 Hz), 20.5; IR (neat) ν 1702, 1571, 1283, 867 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_5FIO_2N$ [M-H]$^-$: 278.9319; found: 278.9316.



18a

2-Chloro-6-iodobenzoic acid (18a)[2]

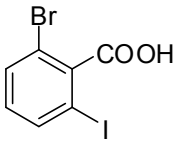
Substrate **18** was iodinated following the general procedure. After purification by column chromatography, **18a** was obtained as a white solid (49.1 mg, 87%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.89 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 168.5, 142.4, 139.3, 133.2, 131.3, 130.7, 93.0; IR (neat) ν 1706, 1388, 1280, 745 cm^{-1}.



20a

4-Chloro-2-iodo-6-methylbenzoic acid (20a)

Substrate **20** was iodinated following the general procedure. After purification by column chromatography, **20a** was obtained as a white solid (52.1 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (bs, 1H), 7.71 (s, 1H), 7.23 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 138.3, 137.7, 136.5, 136.3, 130.4, 92.1, 20.6; IR (neat) ν 1701, 1577, 1390, 1284, 863, 732 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_5ClIO_2$ $[M-H]^-$: 294.9023; found: 294.9022.



21a

2-Bromo-6-iodobenzoic acid (21a)

Substrate **21** was iodinated following the general procedure. After purification by column chromatography, **21a** was obtained as a white solid (55.4 mg, 85%). ^{1}H NMR (400 MHz, acetone-d_6) δ 10.40 (bs, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.13 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.0, 144.0, 139.7, 133.8, 133.4, 119.3, 92.8; IR (neat) ν 1706, 1576, 1291, 914, 764 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_5ClIO_2$ $[M-H]^-$: 324.8361; found: 324.8373.

***mono*-Selective iodination of *meta*-substituted arene carboxylic acids**

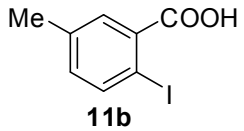
General procedure **a**: In a 20 mL glass tube, substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) and tetrabutyl

ammonium iodide (73.8 mg, 0.2 mmol) were dissolved in dichloroethane (1 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 80 °C for 2 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the iodination product.

General procedure **b**: In a 20 mL glass tube, substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) and tetrabutyl ammonium iodide (73.8 mg, 0.2 mmol) were dissolved in dichloroethane (2 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 2 hours. After the reaction mixture cooled to room temperature, iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) were added under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for another 4 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the iodination product.

General procedure **c**: In a 20 mL glass tube, substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), iodobenzene diacetate (64.4 mg, 0.2 mmol), I_2 (50.8 mg, 0.2 mmol) and tetrabutyl ammonium iodide (73.8 mg, 0.2 mmol) were dissolved in dichloroethane (1 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 60 °C for 12 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under

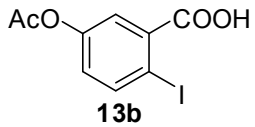
vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the iodination product.



11b

2-Iodo-5-methylbenzoic acid (11b)

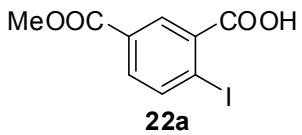
Substrate **11** was iodinated following the procedure **a**. After purification by column chromatography, **11b** was obtained as a white solid (39.3 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.85 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 141.7, 138.2, 134.6, 132.9, 132.8, 90.6, 20.8; IR (neat) ν 1737, 1698, 1560, 1216, 820 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_8IO_2$ $[M+H]^+$: 262.9564; found: 262.9558.



13b

5-Acetoxy-2-iodobenzoic acid (13b)

Substrate **13** was iodinated following the general procedure **b**. After purification by column chromatography, **13b** was obtained as a white solid (38.5 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 4.0 Hz, 1H), 6.97 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 168.8, 150.5, 142.8, 134.0, 127.2, 125.5, 90.5, 21.0; IR (neat) ν 1758, 1706, 1566, 1192, 905 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_9H_8IO_4$ $[M+H]^+$: 306.9462; found: 306.9466.

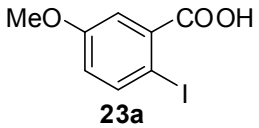


22a

2-Iodo-5-(methoxycarbonyl)benzoic acid (22a)

Substrate **22** was iodinated following the general procedure **b**. After purification by column chromatography, **22a** was obtained as a white solid (37.9 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 3.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 165.7, 142.5, 133.7, 133.5, 132.7, 130.3, 100.9,

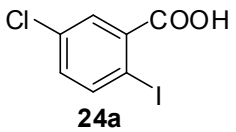
52.6; IR (neat) ν 1719, 1364, 1230, 749 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_9H_8IO_4$ $[M+H]^+$: 306.9462; found: 306.9462.



23a

2-Iodo-5-methoxybenzoic acid (23a)

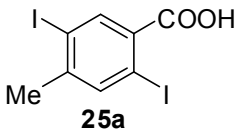
Substrate **23** was iodinated following the general procedure **c**. After purification by column chromatography, **23a** was obtained as a white solid (36.1 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 4.0 Hz, 1H), 6.77 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 159.7, 142.7, 134.0, 120.7, 117.5, 83.3, 55.8; IR (neat) ν 1694, 1566, 1260, 821 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_8IO_3$ $[M+H]^+$: 278.9513; found: 278.9514.



24a

5-Chloro-2-iodobenzoic acid (24a)

Substrate **24** was iodinated following the general procedure **b**. After purification by column chromatography, **24a** was obtained as a white solid (41.7 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 143.0, 134.7, 134.4, 133.7, 132.1, 91.9; IR (neat) ν 1700, 1297, 1251, 817 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_5ClIO_2$ $[M+H]^+$: 282.9017; found: 282.9015.



25a

2,5-Diiodo-4-methylbenzoic acid (25a)

Substrate **25** was iodinated following the general procedure **b**. After purification by column chromatography, **25a** was obtained as a white solid (55.9 mg, 72%). ^1H NMR (400 MHz, acetone-d_6) δ 8.25 (s, 1H), 7.95 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, acetone-

d_6) δ 165.2, 147.1, 142.1, 140.8, 134.5, 99.7, 93.7, 26.8; IR (neat) ν 1694, 1572, 1298, 931 cm^{-1}; HRMS (ESI-TOF) $[M+H]^+$: Calcd for $C_8H_7I_2O_2$ 388.8530; found: 388.8529.

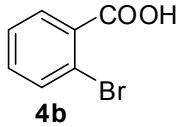
***mono*-Selective bromination of arene carboxylic acids**

General procedure **a**: In a 20 mL glass tube, iodobenzene diacetate (128.8 mg, 0.4 mmol) and I_2 (101.6 mg, 0.4 mmol) were dissolved in dichloroethane (2 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at room temperature for 1 hour to generate iodoacetate *in-situ*. Substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and tetrabutylammonium bromide (99.6 mg, 0.3 mmol) were added under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the bromination product.

General procedure **b**: In a 20 mL glass tube, iodobenzene diacetate (128.8 mg, 0.4 mmol) and I_2 (101.6 mg, 0.4 mmol) were dissolved in dichloroethane (2 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at room temperature for 1 hour to generate iodoacetate *in-situ*. Substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and tetramethylammonium bromide (46.2 mg, 0.3 mmol) were added under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the bromination product.

General procedure **c**: In a 20 mL glass tube, iodobenzene diacetate (64.4 mg, 0.2 mmol) and I_2 (50.8 mg, 0.2 mmol) were dissolved in dichloroethane (2 mL) under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at room temperature

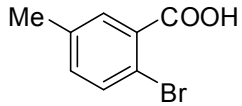
for 1 hour to generate iodoacetate *in-situ*. Substrate (0.2 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and tetrabutylammonium bromide (99.6 mg, 0.3 mmol) were added under atmospheric air. The tube was sealed with a cap, and the reaction mixture was stirred at 100 °C for 24 hours. The reaction mixture was cooled to room temperature and 10% aqueous Na_2CO_3 (5 mL) was added. The organic layer was separated and the aqueous layer was washed with diethyl ether (5 mL × 2). The aqueous layer was acidified with 2N HCl, extracted with ethyl acetate (10 mL × 3) and dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel (hexane:ether/8:1) to give the bromination product.



4b

2-Bromobenzoic acid (4b)

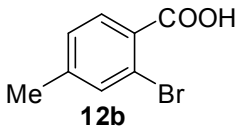
Substrate **4** was brominated following the procedure **a**. After purification by column chromatography, **4b** was obtained as a white solid (26 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 134.9, 133.6, 132.5, 130.3, 127.3, 122.6; IR (neat) ν 1676, 1590, 1309, 741 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_6BrO_2$ $[M+H]^+$: 200.9546; found: 200.9540.



11c

2-Bromo-5-methylbenzoic acid (11c)

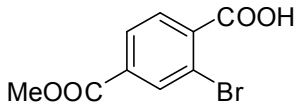
Substrate **11** was brominated following the procedure **a**. After purification by column chromatography, **11c** was obtained as a white solid (32.9 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 137.6, 134.6, 133.2, 133.1, 130.4, 119.3, 20.9; IR (neat) ν 1699, 1560, 1301, 1259, 816 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_8BrO_2$ $[M+H]^+$: 214.9702; found: 214.9707.



12b

2-Bromo-4-methylbenzoic acid (12b)

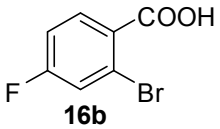
Substrate **12** was brominated following the procedure **a**. After purification by column chromatography, **12b** was obtained as a white solid (29.5 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 1H), 7.55 (s, 1H), 7.41 (d, J = 8.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 144.8, 135.5, 132.6, 128.1, 127.1, 122.7, 21.1; IR (neat) ν 1737, 1602, 1216, 766 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_8BrO_2$ $[M+H]^+$: 214.9702; found: 214.9699.



14b

2-Bromo-4-(methoxycarbonyl)benzoic acid (14b)

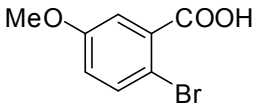
Substrate **14** was brominated following the procedure **b**. After purification by column chromatography, **14b** was obtained as a white solid (21.7 mg, 42%). ^{1}H NMR (400 MHz, methanol-d_4) δ 8.25 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (2 C), 135.7, 134.5, 131.6, 129.3, 121.4, 106.2, 53.1; IR (neat) ν 1707, 1298, 910, 744 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_9H_8BrO_4$ $[M+H]^+$: 258.9600; found: 258.9606.



16b

2-Bromo-4-fluorobenzoic acid (16b)

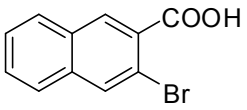
Substrate 1**6** was brominated following the general procedure **b**. After purification by column chromatography, 1**6b** was obtained as a white solid (21.4 mg, 49%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.99 (m, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.9 (d, $J_{C\text{-}F}$ = 253 Hz), 133.7 (d, $J_{C\text{-}F}$ = 10 Hz), 129.3 (d, $J_{C\text{-}F}$ = 4 Hz), 122.5 (d, $J_{C\text{-}F}$ = 10 Hz), 121.6 (d, $J_{C\text{-}F}$ = 25 Hz), 114.9 (d, $J_{C\text{-}F}$ = 21 Hz); IR (neat) ν 1697, 1591, 1261, 870 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_7H_5BrFO_2$ $[M+H]^+$: 218.9451; found: 218.9450.



23b

2-Bromo-5-methoxybenzoic acid (23b)

Substrate **23** was brominated following the general procedure **c**. After purification by column chromatography, **23b** was obtained as a white solid (33.1 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 1H), 7.39 (s, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 159.1, 135.1, 134.1, 118.7, 116.5, 111.0, 55.4; IR (neat) ν 1702, 1561, 1264, 817 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_8H_8BrO_3$ $[M+H]^+$: 230.9651; found: 230.9651.



26a

3-Bromo-2-naphthoic acid (26a)

Substrate **26** was brominated following the general procedure **b**. After purification by column chromatography, **26a** was obtained as a white solid (36.5 mg, 73%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (s, 1H), 8.22 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H); 7.57-7.65 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 169.7, 136.5, 133.9, 132.7, 132.6, 131.6, 129.9, 129.7, 128.3, 127.8, 116.5; IR (neat) ν 1696, 1457, 1296, 742 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{11}H_7BrO_2$ $[M+H]^+$: 250.9702; found: 250.9698.

References:

1. T. Rausis, M. Schlosser, *Eur. J. Org. Chem.* **2002**, 3351.
2. C. Heiss, E. Marzi, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 4625.