Supporting Information

Pd-catalyzed carbonylation of aryl C–H bonds in benzamides with CO₂

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> General Considerations

All reactions were set up using standard Schlenk techniques and carried out under a carbon dioxide (CO₂) atmosphere with dry solvents. Palladium (II) Trifluoroacetate (Pd(TFA)₂) was purchased from sinocompound and stored in glovebox. Anhydrous *N*,*N*-Dimethylformamide (DMF) was purchased from HWRK Chem Co., Ltd. Lithium tert-butoxide (LiO^tBu) was purchased from ASTATECH. Cesium carbonate (Cs₂CO₃) was purchased from Accela ChemBio. Commercially available chemicals were purchase from Admas-beta, Aldrich, Alfa, and Aesar. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2±0.03 mm using UV light as a visualizing agent and iodine in silica gel as developing agents.

¹H, ¹⁹F and ¹³C NMR spectra were recorded on a Brüker Advance 400 spectrometer (¹H: 400 MHz, ¹⁹F: 376 MHz, ¹³C: 101 MHz). Chemical shifts (δ) for ¹H and ¹³C NMR spectra are given in ppm relative to TMS, The residual solvent signals were used as references for ¹H and ¹³C NMR spectra and the chemical shifts converted to the TMS scale (CDCl₃: δ H = 7.26 ppm, δ C = 77.16 ppm, DMSO-*d*₆: δ H = 2.50 ppm, δ C = 39.52 ppm, CD₂Cl₂: δ H = 5.32 ppm, δ C = 53.44 ppm). GC data were achieved by Agilent Technologies 7890B. GC-MS was obtained using electron ionization (Agilent Technologies 7890B/GC-System and 5977A/MSD). Exact ESI mass spectra were recorded on a SHIMADZU LCMS-IT-TOF. ESI-MS were obtained on a Thermo-ITQ. TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF254), and visualization was effected at 254 nm.

Additional reaction optimization

Table S1. Screening of Pd-catalyst^a



^a As shown. ^b GC yield using *n*-dodecane as internal standard and the isolated yield was given in parentheses.

Table S2. Screening ortho-substituted benzamides^a



^a as shown. Detected by GCMS.

General synthetic methods for substrate.



Method A: To the solution of benzoyl chloride derivatives (10 mmol, 1 equiv) and Et_3N (3.5 mL, 2.5 equiv) in DCM (10 mL), an aqueous solution of methylamine (40% w/w solution, 3 mL) was add dropwise at 0 °C, then, the reaction mixture was rise to 30 °C. After 1 h, the reaction mixture quenching by 1N HCl (20 mL), and extracted by EA (20 mL) two times. The organic phase was washed with 1N HCl (20 mL), 1N NaOH (20 mL), and brine (20 mL), dried with anhydrous Na_2SO_4 , filtered and concentrated in vacuo, the residue was purified by silica gel flash column chromatography to afford the desired product.

Method B:¹ To the solution of benzoic acid derivatives (10 mmol, 1 equiv) and 1,1'-carbonyl diimidazole (1.62 g, 1 equiv) in DCM (20 mL). The reaction mixture was stirred until gas evolution was complete (20 min), an aqueous solution of methylamine (40% w/w solution, 2 mL) was added. After 1 h, the reaction mixture quenching by 1N HCl (20 mL), and extracted by EA (20 mL) two times. The organic phase was washed with 1N HCl (20 mL), 1N NaOH (20 mL), and brine (20 mL), dried with anhydrous Na₂SO₄, filtered and concentrated in vacuo, the residue was purified by silica gel flash column chromatography to afford the desired product.

Experimental procedures and characterization data

1. General produces



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **1** (0.2 mmol, 1 equiv) before moved into the glovebox. Then, Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv), $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (3 mL) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 18 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford products.

2. Gram scale synthesis



To an oven-dried Schlenk tube (500 mL) equipped with a magnetic stir bar was added **1j** (1.440 g, 6.82 mmol, 1 equiv) before moved into the glovebox. Then, Cs_2CO_3 (3.331 g, 10.2 mmol, 1.5 equiv), LiO^tBu (2.183 g, 27.3 mmol, 4 equiv), $Pd(TFA)_2$ (226.6 mg, 0.68 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (102 mL) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 24 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford white solid **2j** with 78% yields.

2-methylisoindoline-1,3-dione (2a)



23.7 mg, 74% yield, white solid; **R**_f (PE/EA 10:1): 0.33; ¹**H** NMR (400 MHz, CDCl₃) δ 7.87 - 7.82 (m, 2H), 7.73 - 7.69 (m, 2H), 3.19 (s, 3H); ¹³**C** NMR (101 MHz, CDCl₃) δ 168.46, 133.85, 132.17, 123.14, 23.92; **GCMS**: 161.0.²

2-ethylisoindoline-1,3-dione (2b)



11.9 mg, 34% yield, white solid; **R**_f(PE/EA 10:1): 0.44; ¹**H NMR** (400 MHz, CDCl₃) δ 7.87 - 7.82 (m, 2H), 7.73 - 7.69 (m 2H), 3.75 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 168.28, 133.85, 132.25, 123.14, 32.92, 13.98; **GCMS:** 175.0.²

isoindoline-1,3-dione (2d)



6.2 mg, 21% yield, white solid; **R**_f (PE/EA 5:1): 0.27; ¹**H NMR** (400 MHz, DMSO-*d*₆) δ 11.35 (s, 1H), 7.84 (s, 4H); ¹³**C NMR** (101 MHz, DMSO-*d*₆) δ 169.68, 134.76, 133.05, 123.38; **GCMS:** 147.0.³

2-phenylisoindoline-1,3-dione (2e)



9.3 mg, 21% yield, white solid; \mathbf{R}_{f} (PE/EA 10:1): 0.30; ¹H NMR (400 MHz, CDCl₃) δ 7.99 - 7.94 (m, 2H), 7.82 - 7.77 (m, 2H), 7.57 - 7.48 (m, 2H), 7.47 - 7.36 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.29, 134.41, 131.78, 131.68, 129.13, 128.12, 126.59, 123.77; **GCMS:** 223.1.⁴

5-methoxy-2-methylisoindoline-1,3-dione (2g), (2r)



25.8 mg, 67% yield, white solid (**2g**); 23.0 mg, 60% yield, white solid (**2r**); \mathbf{R}_{f} (PE/EA 10:1): 0.22; ¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 2.3 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.3 Hz, 1H), 3.93 (s, 3H), 3.16 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.32, 168.28, 164.56, 134.81, 124.85, 124.10, 119.49, 108.06,

56.06, 23.94.; **GCMS:** 191.0.²

2-methyl-5-phenoxyisoindoline-1,3-dione (2h), (2s)



42.3 mg, 84% yield, white solid **(2h)**; 39.9 mg, 79% yield, white solid **(2s)**; \mathbf{R}_{f} (PE/EA 10:1): 0.36; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, J = 8.2 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.32 (d, J = 2.2 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.13 – 7.05 (m, 2H), 3.15 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.98, 167.89, 163.35, 154.88, 134.72,

130.37, 125.67, 125.35, 125.08, 122.26, 120.42, 111.73, 24.02; **GCMS:** 253.1.



5-(*tert***-butyl)-2-methylisoindoline-1,3-dione (2i)**29.0 mg, 67% yield, white solid;

R_f (PE/EA 10:1): 0.50; ¹**H** NMR (400 MHz, CDCl₃) δ 7.88 (dd, J = 1.7, 0.7 Hz, 1H), 7.76 (dd, J = 7.9, 0.7 Hz, 1H), 7.72 (dd, J = 7.9, 1.7 Hz, 1H), 3.17 (s, 3H), 1.38 (s, 9H).; ¹³**C** NMR

(101 MHz, CDCl₃) δ 168.96, 168.55, 158.45, 132.43, 130.80, 129.53, 122.98, 120.40, 35.72, 31.15, 23.90; **GCMS:** 217.1.⁵

2-methyl-5-phenylisoindoline-1,3-dione (2j), (2t)



40.0 mg, 88% yield, white solid (2j); 35.5 mg, 75% yield, white solid (2t); \mathbf{R}_{f} (PE/EA 10:1): 0.36; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (s, 1H), 7.93 – 7.87 (m, 2H), 7.67 – 7.60 (m, 2H), 7.54 – 7.40 (m, 3H), 3.20 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.44, 168.37, 147.32, 139.05, 133.09, 132.42, 130.64, 129.19, 128.84, 127.33,

123.64, 121.80, 24.05; **GCMS:** 237.1.²

2-methyl-5-(naphthalen-2-yl)isoindoline-1,3-dione (2k), (2u)



46.9 mg, 82% yield, white solid (2k); 43.1 mg, 75% yield, white solid (2u); **R**_f(PE/EA 10:1): 0.31; ¹H NMR (400 MHz, CDCl₃) δ 8.12 (d, *J* = 1.6 Hz, 1H), 8.05 (d, *J* = 1.9 Hz, 1H), 7.98 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.90 - 7.83 (m, 3H), 7.70 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.60 - 7.47 (m, 2H),

3.18 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.39, 168.30, 147.10, 136.19, 133.45, 133.18, 133.11, 132.51, 130.57, 129.02, 128.44, 127.71, 126.87, 126.80, 126.67, 124.81, 123.63, 121.88, 24.02; **GCMS**: 287.1.

2-methyl-5-(phenylethynyl)isoindoline-1,3-dione (21)



20.7 mg, 40% yield, white solid; **R**_f (PE/EA 10:1): 0.41; ¹**H NMR** (400 MHz, CDCl₃) δ 7.96 (s, 1H), 7.82 (s, 2H), 7.60 – 7.50 (m, 2H), 7.39 (d, *J* = 5.3 Hz, 3H), 3.19 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 167.88, 167.80, 136.73, 132.51, 131.85, 130.90, 129.50, 129.21, 128.54, 126.04, 123.17, 122.13, 93.83, 87.78, 24.08; **GCMS:** 261.1.

(E)-2-methyl-5-styrylisoindoline-1,3-dione (2m)



44.1 mg, 84% yield, pale yellow solid; **R**_f (PE/EA 10:1): 0.27; ¹**H NMR** (400 MHz, CDCl₃) δ 7.88 (d, *J* = 1.5 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.47 - 7.42 (m, 2H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.27 - 7.15 (m, 2H), 7.06 (d, *J* = 16.4 Hz, 1H), 3.08 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 168.39, 168.20, 143.52, 136.14, 133.06,

132.76, 131.88, 130.39, 128.89, 128.76, 126.98, 126.59, 123.60, 120.28, 24.00; **GCMS:** 263.1.

4-(2-methyl-1,3-dioxoisoindolin-5-yl)benzonitrile (2n)



R_f(PE/EA 5:1): 0.30; ¹**H** NMR (400 MHz, CDCl₃) δ 8.09 – 8.04 (m, 1H), 7.99 – 7.89 (m, 2H), 7.81 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.6 Hz, 2H), 3.22 (s, 3H); ¹³**C** NMR (101 MHz, CDCl₃) δ 167.95, 167.90, 145.11, 143.41,

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40.1 mg, 76% yield, white solid;

133.34, 132.96, 132.71, 131.85, 128.04, 123.94, 121.93, 118.35, 112.62, 24.16; **GCMS:** 262.0.

5-(4-chlorophenyl)-2-methylisoindoline-1,3-dione (20)



38.7 mg, 71% yield, white solid; \mathbf{R}_{f} (PE/EA 10:1): 0.30; ¹H NMR (400 MHz, CDCl₃) δ 8.03 – 7.96 (m, 1H), 7.91 – 7.82 (m, 2H), 7.60 – 7.53 (m, 2H), 7.50 – 7.42 (m, 2H), 3.20 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.22, 168.16, 145.98, 137.46, 135.16, 133.20, 132.22, 130.91, 129.40, 128.55, 123.73, 121.57, 24.06; GCMS: 271.0.

5-benzoyl-2-methylisoindoline-1,3-dione (2p)



39.3 mg, 74% yield, white solid; **R**_f(PE/EA 10:1): 0.19; ¹**H NMR** (400 MHz, CDCl₃) δ 8.22 – 8.17 (m, 1H), 8.15 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.01 – 7.94 (m, 1H), 7.85 – 7.75 (m, 2H), 7.69 – 7.63 (m, 1H), 7.53 (dd, *J* = 8.4, 7.1 Hz, 2H), 3.23 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 194.71, 167.52, 142.91, 136.31, 135.39, 134.78, 133.40, 132.24,

130.03, 128.72, 124.29, 123.29, 24.24; **GCMS:** 265.1.

2-methyl-5-(trifluoromethyl)isoindoline-1,3-dione (2q)



21.1 mg, 46% yield, white solid; **R**_f (PE/EA 10:1): 0.43; ¹**H NMR** (400 MHz, CDCl₃) δ 8.11 (d, *J* = 1.3 Hz, 1H), 8.00 (t, *J* = 1.3 Hz, 2H), 3.23 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 167.06, 166.94, 136.01 (q, *J* = 3.4 Hz), 135.02, 132.88, 131.11 (q, *J* = 3.7 Hz), 123.77, 123.03 (q, *J* = 273.2 Hz), 120.44 (q, *J* = 3.8 Hz), 24.31; ¹⁹**F NMR** (376 MHz, CDCl₃) δ -62.94;

GCMS: 229.0.

2-methyl-5-phenyl-6-(trifluoromethyl)isoindoline-1,3-dione (2v)



30.7 mg, 50% yield, white solid; **R**_f (PE/EA 10:1): 0.44; ¹**H NMR** (400 MHz, CDCl₃) δ 8.23 (s, 1H), 7.83 (s, 1H), 7.49 – 7.41 (m, 3H), 7.36 – 7.29 (m, 2H), 3.24 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 167.07 , 167.03 , 148.19 (q, *J* = 1.8 Hz), 137.91 , 134.44 , 133.71 (q, *J* = 31.1 Hz), 131.00 , 128.75 , 128.50 (q, *J* = 1.8 Hz), 128.17 , 126.96 , 123.07 (q, *J* =

275.0 Hz), 121.41 (q, J = 5.5 Hz), 24.34; ¹⁹F NMR (376 MHz, CDCl₃) δ -57.11; GCMS: 305.1.

2,5-dimethyl-6-phenylisoindoline-1,3-dione (2w)



30.7 mg, 50% yield, white solid, Pd(TFA)₂ (20 mol%); **R**_f (PE/EA 10:1): 0.39; ¹**H NMR** (400 MHz, CDCl₃) δ 7.74 (s, 1H), 7.69 (s, 1H), 7.50 – 7.38 (m, 3H), 7.33 – 7.28 (m, 2H), 3.18 (s, 3H), 2.39 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 168.64, 168.55, 147.74, 142.55, 139.97, 131.03, 130.00, 128.76, 128.50, 127.96, 125.03, 124.53, 23.95, 21.34; **GCMS:** 251.1.

5,6-dimethoxy-2-methylisoindoline-1,3-dione (2x)



23.5 mg, 53% yield, white solid; \mathbf{R}_{f} (PE/EA 5:1): 0.26; ¹H NMR (400 MHz, CD₂Cl₂) δ 7.20 (s, 2H), 3.87 (s, 6H), 3.00 (s, 3H); ¹³C NMR (101 MHz, CD₂Cl₂) δ 168.50, 153.86, 125.57, 105.19, 56.46, 23.60; GCMS: 221.1.

2-methyl-1H-benzo[f]isoindole-1,3(2H)-dione (2y)



33.8 mg, 80% yield, white solid; **R**_f (PE/EA 10:1): 0.28; ¹**H NMR** (400 MHz, CDCl₃) δ 8.29 (s, 2H), 8.03 (dd, J = 6.2, 3.3 Hz, 2H), 7.68 (dd, J = 6.2, 3.2 Hz, 2H), 3.24 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 168.15, 135.34, 130.28, 129.13, 127.88, 124.55, 24.23; **GCMS:** 211.0.⁶

2-methyl-1H-benzo[e]isoindole-1,3(2H)-dione (2z)



28.7 mg, 68% yield, white solid; **R**_f (PE/EA 10:1): 0.42;

¹**H NMR** (400 MHz, CDCl₃) δ 8.88 (d, J = 9.5 Hz, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.80 (d, J = 8.3 Hz, 1H), 7.73 – 7.66 (m, 1H), 7.65 – 7.60 (m, 1H), 3.20 (s, 3H).; ¹³**C NMR** (101 MHz, CDCl₃) δ 169.71, 169.07, 136.49, 134.79, 131.41, 129.43, 128.66, 127.93, 127.47, 124.90, 118.39, 23.84; **GCMS**:

211.1.⁷

7-methyl-6H-pyrrolo[3,4-g]quinoline-6,8(7H)-dione (2aa)



24.0 mg, 57% yield, white solid; **R**_f(PE/EA 3:1): 0.14; ¹**H NMR** (400 MHz, CDCl₃) δ 9.10 (s, 1H), 8.55 (s, 1H), 8.44 – 8.31 (m, 2H), 7.61 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.28 (s, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 167.46, 167.45, 152.99, 150.53, 137.89, 131.38, 130.91, 128.44, 126.03, 124.43, 123.49, 24.43; **HRMS** (ESI+): calculated for C₁₂H₉N₂O₂⁺ [M+H]⁺

213.0659, found 213.0660.

2-methyl-1H-benzo[4,5]thieno[2,3-f]isoindole-1,3(2H)-dione (2ab)



38.2 mg, 71% yield, pale yellow solid; **R**_f(PE/EA 10:1): 0.33;

¹**H NMR** (400 MHz, CD₂Cl₂) δ 8.45 (s, 1H), 8.26 – 8.14 (m, 2H), 7.92 – 7.78 (m, 1H), 7.57 – 7.41 (m, 2H), 3.09 (s, 3H); ¹³**C NMR** (101 MHz, CD₂Cl₂) δ 168.16, 167.89, 144.74, 140.74, 139.49, 134.46, 129.89, 128.46, 128.42, 44.64 (146.24), 22.86 (2014), 23.87 (2014), 24

125.38, 123.06, 122.62, 118.10, 116.34, 23.86; **GCMS:** 267.0.

Mechanism Studies

(1) The carbonyl source experiment

1. CO instead of CO₂



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **1a** (27.0 mg, 0.2 mmol, 1 equiv) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv), $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO (shaking the tube in CO atmosphere) for 3 times, anhydrous DMF (3 mL) was added under CO and the Schlenk tube was sealed at atmospheric pressure of CO (1 atm). The resulting mixture was stirred for 18 h at 140 °C. Then, the mixture was cooled to room temperature, and the resulting was analyzed by GCMS (No desired product be detected by GCMS).

2. ¹³CO₂ instead of CO₂



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **1a** (27.0 mg, 0.2 mmol, 1 equiv) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv), Pd(TFA)₂ (6.6 mg, 0.02 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with ¹³CO₂ (shaking the tube in ¹³CO₂ atmosphere) for 3 times, anhydrous DMF (3 mL) was added under CO and the Schlenk tube was sealed at atmospheric pressure of ¹³CO₂ (1 atm). The resulting mixture was stirred for 18 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford products **2a'** (23.1 mg, 70%), and the resulting product was analyzed by MS and NMR.

2-methylisoindoline-1,3-dione-¹³C (2a')



23.1 mg, 74% yield, white solid; **R**_f (PE/EA 10:1): 0.33; ¹**H NMR** (400 MHz, CDCl₃) δ 7.89 – 7.80 (m, 2H), 7.75 – 7.67 (m, 2H), 3.19 (d, *J* = 2.6 Hz, 3H); ¹³**C NMR** (101 MHz, CDCl₃) δ 168.47, 133.86 (t, *J* = 2.3 Hz), 132.23 (dd, *J* = 33.6, 30.7 Hz), 123.16 (d, *J* = 3.2 Hz), 23.93; **GCMS:** 162.0.

(2) Kinetic isotope effect experiment

1. Intramolecular Competition Reaction



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added $[D_1]$ -**1a**⁸ (54.5 mg, 0.4 mmol, 1 equiv, D>95%) before moved into the glovebox. Cs_2CO_3 (195.5 mg, 0.6 mmol, 1.5 equiv), LiO^tBu (128.1 mg, 1.6 mmol, 4 equiv), Pd(TFA)₂ (13.3 mg, 0.04 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (6 mL) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 2 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford white solid ($[D_1]$ -**2a** + **2a**, 11.1 mg, 17%). The ratio of which was determined to be 4.26:1 by ¹H NMR.

The ratio of [D₁]-2a + 2a



2. Intramolecular Competition Reaction



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added $[D_5]$ -**1a**⁸ (28.0 mg, 0.2 mmol, 0.5 equiv) and **1a** (27.0 mg, 0.2 mmol, 0.5 equiv) before moved into the glovebox. Cs₂CO₃ (195.5 mg, 0.6 mmol, 1.5 equiv), LiO^tBu (128.1 mg, 1.6 mmol, 4 equiv), Pd(TFA)₂ (13.3 mg, 0.04 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO₂ (shaking the tube in CO₂ atmosphere) for 3 times, anhydrous DMF (6 mL) was added under CO₂ and the Schlenk tube was sealed at atmospheric pressure of CO₂ (1 atm). The resulting mixture was stirred for 2 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford white solid ([D₄]-**2a** + **2a**, 11.7 mg, 18%). The ratio of which was determined to be 2.33:1 by ¹H NMR.

¹**H NMR** of the ([D₄]-**2a** + **2a**)



(3) Intermediate capture reaction

1. Pd-catalysis (A) test⁹



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **A** (71.2 mg, 0.2 mmol, 1 equiv) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (3 mL) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 18 h at 140 °C. Then, the mixture was cooled to room temperature, the resulting was analyzed by GC (**2a**, 62%, GC yield using *n*-dodecane as internal standard)



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **1m** (47.5 mg, 0.2 mmol, 1 equiv) and **A** (7.1 mg, 0.02 mmol, 10 mol%) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (3 mL) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 18 h at 140 °C. Then, the mixture was cooled to room temperature, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to afford white solid **2m** with 79% yield. **2a** also could be detected by GCMS.

2. Control experiment of ligand



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added **1a** (27.0 mg, 0.2 mmol, 1 equiv) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv), $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the

tube in CO₂ atmosphere) for 3 times, anhydrous DMF (3 mL) and TEMDA (3 uL, 0.02 mmol, 10 mol%) was added under CO₂ and the Schlenk tube was sealed at atmospheric pressure of CO₂ (1 atm). The resulting mixture was stirred for 18 h at 140 $^{\circ}$ C. Then, the mixture was cooled to room temperature, the resulting was analyzed by GC with 74% yield.

3. Palladacycle (A) capture experiment



To an oven-dried Schlenk tube (25 mL) equipped with a magnetic stir bar was added 1a (27.0 mg, 0.2 mmol, 1 equiv) before moved into the glovebox. Cs_2CO_3 (97.7 mg, 0.3 mmol, 1.5 equiv), LiO^tBu (64.1 mg, 0.8 mmol, 4 equiv), and $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 10 mol%) was added to the tube before transferring out of the glovebox. The tube was then evacuated and back-filled with CO_2 (shaking the tube in CO_2 atmosphere) for 3 times, anhydrous DMF (3 mL) and TMEDA (3 uL, 0.02 mmol, 10 mol%) was added under CO_2 and the Schlenk tube was sealed at atmospheric pressure of CO_2 (1 atm). The resulting mixture was stirred for 2 h at 140 °C. Then, the mixture was cooled to room temperature, the resulting was analyzed by **ESI-HRMS**.

Pd-catalysis (A)



¹H NMR (400 MHz, CDCl₃) δ 7.46 (dd, 1H), 7.12 (d, J = 7.4 Hz, 1H), 7.06 – 6.94 (m, 2H), 3.00 (s, 3H), 2.89 (s, 6H), 2.69 (s, 8H), 2.56 (s, 2H).; ¹³C NMR (101 MHz, CDCl₃) δ 180.14, 146.11, 145.34, 129.16, 127.61, 126.91, 124.34, 63.67, 60.33, 51.05, 48.75, 34.76.; HRMS (ESI+): calculated for C₁₄H₂₄N₃OPd⁺ [M+H]⁺ 356.0949, found 356.0943.⁹

➢ Reference

- 1. D. L. Whitehouse, K. H. Nelson, Jr., S. N. Savinov, R. S. Löwe and D. J. Austin, *Bioorg. Med. Chem.*, 1998, **6**, 1273.
- 2. Y. Du, T., Hyster and T. Rovis, *Chem. Commun.*, 2011, **47**, 12074.
- 3. P. S. Mahajan, S. D. Tanpure, N. A. More, J. M. Gajbhiye and S. B. Mhaske, *RSC Adv.*, 2015, **5**, 101641.
- 4. F. Ji, J. Li, X. Li, W. Guo, W. Wu and H. Jiang, J. Org. Chem., 2018, 83, 104.
- 5. C. Wang, G. A. Russell and W. S. Trahanovsky, J. Org. Chem., 1998, 63, 9956.
- 6. Z. Huang, M. V. Lakshmikantham, M. Lyon and M. P. Cava, J. Org. Chem., 2000, 65, 5413.
- 7. V. Wintgens, P. Valat, J. Kossanyi, L. Biczok, A. Demeter and T. Berces, *J. Chem. Soc. Faraday Transactions*, 1994, **90**, 411.
- 8. N. S. Upadhyay, V. H. Thorat, R. Sato, P. Annamalai, S.-C. Chuang and C.-H. Cheng, *Green Chem.*, 2017, **19**, 3219.
- 9. R. Frutos-Pedreño, P. Gonzalez-Herrero and J. Vicente. *Organometallics*, 2013, **32**, 4664.

➢ ¹H NMR, ¹⁹F NMR and ¹³C NMR Spectra

2-methylisoindoline-1,3-dione (2a)



230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 fl (ppm)

17 / 41

2-ethylisoindoline-1,3-dione (2b)





2-phenylisoindoline-1,3-dione (2e)

7, 398 7, 397 7, 397 7, 397 7, 396 7, 396 7, 396 7, 398 7,



5-methoxy-2-methylisoindoline-1,3-dione (2g), (2r)







5-(tert-butyl)-2-methylisoindoline-1,3-dione (2i)















(E)-2-methyl-5-styrylisoindoline-1,3-dione (2m)









5-benzoyl-2-methylisoindoline-1,3-dione (2p)







2-methyl-5-phenyl-6-(trifluoromethyl)isoindoline-1,3-dione (2v)









5,6-dimethoxy-2-methylisoindoline-1,3-dione (2x)



2-methyl-1*H*-benzo[*f*]isoindole-1,3(2*H*)-dione (2y)









2-methylisoindoline-1,3-dione-¹³C (2a')



