Supporting Information for
Palladium-catalyzed Oxidative Activation of Arylcyclopropanes

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General: All reactions involved in the preparation of the starting materials were carried out under inert atmosphere otherwise indicated. Anhydrous diethyl ether (Et₂O) and dichloromethane (DCM) were purchased from Aldrich Chemical Co. Tetrahydrofuran (THF) was dried over sodium benzophenone ketyl. Palladium(II) chloride and bis(acetonitrile)palladium(II) chloride were purchased from Strem Chemical. Other commercial reagents of high purity were purchased and used without further purification, unless otherwise noted.

Instrumentation: Nuclear magnetic resonance (NMR) spectra were taken on Varian Mercury 400 spectrometer. ¹H NMR spectra were referenced to Me₄Si (δ 0.0 ppm), ¹³C NMR spectra were referenced to CDCl₃ (δ 77.2 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), integration.

Chromatography: Analytical thin layer chromatography (TLC) was performed on Macherey Nagel pre-coated TLC plates (silica gel 60 GF 254, 0.25 mm). Column chromatography was carried out using Silicycle 230-400 mesh silica gel.

Preparation of cyclopropyl phenol starting material 1a.

1-(2-Methoxynaphthalen-1-yl)butan-1-ol (1a-i): A solution of propylmagnesium

chloride in Et₂O (1.0 M, 20 mmol) was added into a 100 mL three-necked flask, equipped with 25 mL dropping funnel and thermometer. Additional 20 mL of anhydrous Et₂O was added, followed by cooling down to -10 °C. A solution of 2-methoxybenzaldehyde (20 mmol, in

20 mL anhydrous Et₂O) was slowly dropped into the propylmagnesium chloride solution with vigorous stirring. Temperature was maintained below 0 °C during the addition. The reaction mixture was allowed to reach room temperature and stirred for one more hour. After that, the reaction mixture was poured into finely crushed ice followed by treating with 1.0 N HCl until the solution became acidic and all the white precipitate dissolved. The solution was extracted with Et₂O (3 × 20 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (9:1 hexanes/EtOAc) afforded

the phenol **1a-i** as a white solid (3.5 g, 15.2 mmol, 76% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.8$, 1H), 7.78-7.74 (m, 2H), 7.48-7.44 (m, 1H), 7.35-7.31 (m, 1H), 7.25 (d, $J = 8.8$ Hz, 1H), 5.55 (dt, $J = 8.8$, 5.6 Hz, 1H), 3.96 (s, 3H), 3.78 (br, d, $J = 8.8$ Hz, 1H), 2.10-2.01 (m, 1H), 1.87-1.78 (m, 1H), 1.64-1.55 (m, 1H), 1.43-1.32 (m, 1H), 0.95 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 154.7, 131.9, 129.5, 129.3, 128.8, 126.7, 125.2, 123.7, 123.3, 113.5, 69.9, 56.5, 40.2, 19.8, 14.3

(E)-1-(But-1-enyl)-2-methoxynaphthalene (1a-ii): A solution of phenol **1a-i** (3.4 g,

14.8 mmol) in toluene (50 mL) was placed in a 100 mL round-bottom flask, equipped with a reflux condenser. 10 mol% of TsOH was added into the solution. The mixture was refluxed for 1 hour, then cooled to room temperature and quenched with saturated aqueous NaHCO_3 (50 mL). The organic layer was separated and aqueous layer extracted with Et_2O (2×20 mL). The combined organic layers were dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (9:1 hexanes/ EtOAc) afforded the olefin **1a-ii** as a white solid (2.4 g, 11.3 mmol, 76% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.18-8.16 (m, 1H), 7.77-7.70 (m, 2H), 7.45-7.41 (m, 1H), 7.34-7.30 (m, 1H), 7.26-7.23 (m, 1H), 6.72 (d, $J = 16$ Hz, 1H), 6.22 (dt, $J = 16$, 6.4 Hz, 1H), 3.93 (s, 3H), 2.38 (m, 2H), 1.20 (t, $J = 7.6$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 154.2, 139.3, 132.9, 129.5, 128.4, 128.3, 127.9, 126.3, 124.7, 123.6, 121.7, 113.6, 56.7, 27.2, 14.1

***trans*-1-(2-Ethylcyclopropyl)-2-methoxynaphthalene (1a-iii):** Et₂Zn (1.0 M in hexanes,

20mL, 20 mmol) was added to freshly distilled CH₂Cl₂ (20 mL) under N₂. The solution was cooled in an ice bath and a solution of trifluoroacetic acid (1.54 mL, 20 mmol) in CH₂Cl₂ (10 mL) was added dropwise into the reaction mixture via syringe. Upon stirring for 20

min, a solution of CH₂I₂ (1.61 mL, 20 mmol) in CH₂Cl₂ (10 mL) was added. After an additional 20 minutes of stirring, a solution of the olefin **1a-ii** (2.1 g, 10.0 mmol) in CH₂Cl₂ (10 mL) was added, and the ice bath was removed. After an additional 30 min of stirring, the reaction mixture was quenched with 0.1 N HCl (50 mL) and Et₂O (25 mL) and the layers were separated. The aqueous layer was extracted with hexanes. The combined organic layers were washed with saturated NaHCO₃, H₂O, and brine, and then dried over anhydrous MgSO₄, filtered, concentrated, and purified by column chromatography (9:1 hexanes/EtOAc) to yield the cyclopropane **1a-iii** as a colorless oil (1.6 g, 7.1 mmol, 71%). ¹H NMR (400 MHz, CDCl₃) δ 8.37-8.35 (m, 1H), 7.76-7.69 (m, 2H), 7.49-7.45 (m, 1H), 7.34-7.30 (m, 1H), 7.21 (d, J = 8.8, 1H), 3.93 (s, 3H), 1.86-1.80 (m, 1H), 1.66-1.62 (m, 1H), 1.48-1.37 (m, 1H), 1.13 (t, J = 7.2, 3H), 1.10-0.83 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 156.5, 135.1, 129.4, 128.4, 128.2, 126.0, 125.0, 124.0, 123.4, 114.6, 56.8, 28.0, 23.1, 15.6, 15.0, 13.6

***trans*-1-(2-Ethylcyclopropyl)naphthalen-2-ol (1a):** Ethanethiol (1.24 g, 20.0 mmol), dissolved in dry DMF (40 mL), was added to a suspension of sodium hydride (0.5 g of a 60% oil dispersion) in dry DMF (10 mL) under N₂. The mixture was stirred for 5 min before a

solution of cyclopropane **1a-iii** (2.26 g, 10.0 mmol) in dry DMF (10 mL) was added; the solution was then refluxed for 3 hours. The cooled mixture was acidified with 10 % aqueous HCl and extracted with Et₂O. The ether layer was washed with brine and dried over anhydrous MgSO₄, filtered, concentrated, and purified by column chromatography (9:1 hexanes/EtOAc) to yield phenol **1a** as a colorless oil (1.49 g, 7.0 mmol, 70%). ¹H NMR (400 MHz, CDCl₃) δ 8.24 (d, J = 8.8, 1H), 7.77 (d, J = 8 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.52-7.49 (m, 1H), 7.36-7.32 (m, 1H), 7.16 (d, J = 8.8 Hz, 1H), 6.13 (s, 1H), 1.97-1.93 (m, 1H), 1.67-1.62 (m, 1H), 1.51-1.42 (m, 1H), 1.22-1.07 (m, 4H), 1.04-1.01 (m, 1H), 0.89-0.85 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 153.3, 134.6, 129.3, 129.0, 128.7, 126.3, 124.0, 123.1, 117.5, 27.4, 22.5, 13.9, 13.7, 13.6

Preparation of cyclopropyl phenol starting material 2a.

2-(Cyclopropylmethyl)phenol (2a): Prepared from 2-allylphenol by a similar

cyclopropanation procedure used for the preparation of **1a-iii**. (74%

yield). ¹H NMR (400 MHz, CDCl₃) δ 7.23 (d, J = 8.0 Hz, 1H), 7.10-7.06

(m, 1H), 6.90-6.86 (m, 1H), 6.75 (d, J = 8.0 Hz, 1H), 5.11 (br, 1H), 2.55 (d, J = 6.8 Hz,

2H), 1.06-0.96 (m, 1H), 0.55-0.51 (m, 2H), 0.22-0.19 (m, 2H). ¹³C NMR (100 MHz,

CDCl₃) δ 153.5, 130.0, 127.7, 127.2, 120.7, 115.2, 34.3, 10.3, 4.8

Preparation of cyclopropyl benzoic acid starting material **3a.**

1-Bromo-2-cyclopropylbenzene (3a-i): Prepared from 2-bromostyrene by a similar cyclopropanation procedure used for the preparation of **1a-iii**. (93% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, $J = 8.0$ Hz, 1H), 7.24-7.18 (m, 1H), 7.03-6.99 (m, 1H), 6.92 (d, $J = 8.0$ Hz, 1H), 2.15 (m, 1H), 1.00 (m, 1H), 0.67 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.4, 132.4, 127.3, 127.0, 126.4, 126.1, 16.2, 8.2

2-Cyclopropylbenzoic acid (3a): To a solution of **3a-i** (0.99g, 5 mmol) in anhydrous

THF (20 mL) was added dropwise n-BuLi (1.6 M in hexanes, 3.75 mL, 6 mmol) at -78°C . After 30 min, anhydrous CO_2 gas was bubbled through the reaction mixture for 30 min. The mixture was allowed to warm to room temperature and stirred for an additional 30 min. The reaction was quenched with 1.0N HCl and extracted with Et_2O (3×20 mL). The combined organic layers were dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (8:2 hexanes/ EtOAc) afforded acid **3a** as a white solid (0.49 g, 3.0 mmol, 60% yield). ^1H NMR (400 MHz, CDCl_3) δ 12.22 (br, 1H), 8.03-7.93 (m, 1H), 7.46-7.42 (m, 1H), 7.26-7.24 (m, 1H), 7.23-7.22 (m, 1H), 7.05-7.03 (m, 1H), 2.85-2.78 (m, 1H), 1.07-1.02 (m, 2H), 0.75-0.71 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 174.0, 146.0, 132.8, 131.2, 129.7, 125.7, 125.3, 13.6, 9.1

Preparation of cyclopropyl benzoic acid starting material 4a.

1-(2-Bromophenyl)-2-phenylethanol (4a-i): Prepared from 2-bromobenzaldehyde and

benzylmagnesium chloride by a similar Grignard reaction procedure

used for the preparation of **1a-i**. (50% yield). ^1H NMR (400 MHz,

CDCl_3) δ 7.56-7.50 (m, 2H), 7.32-7.23 (m, 6H), 7.13-7.09 (m, 1H),

5.20 (dd, $J = 9.4, 3.2$ Hz, 1H), 3.15 (dd, $J = 13.8, 3.2$ Hz, 1H), 2.70 (dd, $J = 13.8, 9.4$ Hz,

1H), 2.14 (br, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.8, 138.1, 132.5, 129.5, 128.8,

128.5, 127.7, 127.2, 126.7, 121.7, 44.2

(E)-1-Bromo-2-styrylbenzene (4a-ii): Prepared from **4a-i** by a similar dehydration

procedure used for the preparation of **1a-ii**. (70% yield). ^1H NMR

(400 MHz, CDCl_3) δ 7.67-7.65 (m, 1H), 7.59-7.54 (m, 3H), 7.46 (d,

$J = 16$ Hz, 1H), 7.39-7.26 (m, 4H), 7.13-7.08 (m, 1H), 7.03 (d, $J =$

16 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.1, 137.0, 133.1, 131.4, 128.8, 128.7,

128.1, 127.5, 127.4, 126.8, 126.7, 124.1

***trans*-1-Bromo-2-(2-phenylcyclopropyl)benzene (4a-iii):** Prepared from **4a-ii** by a

similar cyclopropanation procedure used for the preparation of **1a-**

iii. (62% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.57-7.55 (m, 1H),

7.33-7.04 (m, 8H), 2.49-2.44 (m, 1H), 2.15-2.10 (m, 1H), 1.44 (m,

2H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.1, 141.3, 132.5, 128.3, 127.4, 127.3, 126.9,

126.8, 126.1, 125.9, 27.9, 26.8, 17.1

2-(2-Phenylcyclopropyl)benzoic acid (4a): Prepared from **4a-iv** by a similar

carboxylation procedure used for the preparation of **3a**. (85% yield).

^1H NMR (400 MHz, CDCl_3) δ 11.13 (br, 1H), 7.98-7.96 (m, 1H),

7.50-7.45 (m, 1H), 7.28-7.10 (m, 7H), 3.11-3.08 (m, 1H), 2.22-2.17

(m, 1H), 1.47-1.42 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 172.8, 144.6, 142.6, 133.1,

131.4, 128.6, 128.5, 126.4, 126.2, 125.9(5), 125.9(3), 27.7, 25.5, 18.3

Preparation of cyclopropyl benzoic amide starting materials 5a, 6a, 7a, 8a, 9a.

General procedure:

2-Cyclopropylbenzoic acid **3a** (0.32g, 2.0 mmol) was dissolved in thionyl chloride (5

mL). After stirring at 65 °C for 1 hour, the reaction mixture was concentrated under reduced pressure to remove all traces thionyl chloride. Then, the residue was diluted with CH₂Cl₂ (10 mL) and treated dropwise with Et₃N (0.28 mL, 2.0 mmol) followed by adding the corresponding amine (2.0 mmol). The reaction mixture was then stirred overnight and concentrated under reduced pressure. The residue was diluted with EtOAc (10 mL) and 1.0 N HCl (10 mL), and the layers were separated. The aqueous layer was extracted with additional EtOAc (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄, filtered, concentrated, and purified by column chromatography (7:3 hexanes/EtOAc) to yield the corresponding 2-cyclopropyl benzoic amides as white solids.

***N*-Butyl-2-cyclopropylbenzamide (5a):** 95% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.37-

7.34 (m, 1H), 7.30-7.26 (m, 1H), 7.17-7.13 (m, 1H), 6.93-6.91 (m, 1H), 6.08 (br, 1H), 3.46-3.41 (m, 2H), 2.24-2.17 (m, 1H), 1.62-1.55 (m, 2H), 1.45-1.36 (m, 2H), 0.99-0.93 (m, 5H), 0.73-0.69 (m,

2H). ¹³C NMR (100 MHz, CDCl₃) δ 170.3, 140.8, 137.8, 130.0, 127.1, 125.6, 124.9, 39.8, 31.8, 20.3, 13.9, 13.2, 9.0

***N*-(4-Chlorophenethyl)-2-cyclopropylbenzamide (6a):** 76%. ¹H NMR (400 MHz,

CDCl₃) δ 7.33-7.26 (m, 4H), 7.19-7.13 (m, 3H), 6.90 (m, 1H), 5.97 (br, 1H), 3.75-3.70 (m, 2H), 2.92 (t, J = 7.2 Hz, 2H), 2.10-2.05 (m, 1H), 0.90-0.85 (m, 2H), 0.69-0.65 (m,

2H). ¹³C NMR (100 MHz, CDCl₃) δ 170.2, 141.0, 137.5, 137.3, 132.6, 130.3, 130.3,

129.0, 127.3, 125.7, 125.0, 40.9, 35.2, 13.3, 9.1

N-tert-Butyl-2-cyclopropylbenzamide (7a): 85% yield. ^1H NMR (400 MHz, CDCl_3) δ

7.37 (m, 1H), 7.30-7.26 (m, 1H), 7.18-7.14 (m, 1H), 6.94 (m, 1H), 5.76 (br, 1H), 2.22-2.18 (m, 1H), 1.48 (s, 9H), 1.01-0.96 (m, 2H), 0.75-0.71 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 169.7, 140.5, 138.9, 129.8,

127.1, 125.7, 125.3, 51.9, 29.1, 13.4, 8.8

N-Benzyl-2-cyclopropylbenzamide (8a): 79% yield. ^1H NMR (400 MHz, CDCl_3) δ

7.44-7.42 (m, 1H), 7.38-7.26 (m, 6H), 7.19-7.15 (m, 1H), 6.24 (br, 1H), 4.65 (d, $J = 5.6$ Hz, 2H), 2.26-2.21 (m, 1H), 0.95-0.91 (m, 2H), 0.72-0.68 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.1,

141.1, 138.4, 137.3, 130.3, 129.0, 128.1, 127.3, 125.8, 125.2, 44.3, 13.4, 9.0

2-Cyclopropyl-N-phenylbenzamide (9a): 75% yield. ^1H NMR (400 MHz, CDCl_3) δ

7.77 (br, 1H), 7.70-7.60 (m, 2H), 7.53-7.52 (m, 1H), 7.39-7.34 (m, 3H), 7.25-7.21 (m, 1H), 7.17-7.13 (m, 1H), 7.01-6.99 (m, 1H), 2.30-2.27 (m, 1H), 1.05-1.00 (m, 2H), 0.81-0.77 (m, 2H). ^{13}C NMR (100

MHz, CDCl_3) δ 168.2, 141.0, 138.3, 137.5, 130.6, 129.3, 127.5, 125.9, 125.3, 124.6,

120.0, 13.5, 9.1

Preparation of cyclopropyl benzoyl sulfonamide starting material 10a.

2-Cyclopropyl-N-tosylbenzamide (10a): To a solution of 2-cyclopropylbenzoic acid **3a**

(0.32g, 2.0 mmol) in THF (10 mL) was added *p*-toluenesulfonyl isocyanate (0.46 mL, 3.0 mmol) followed by dropwise introduction of Et₃N (0.42 mL, 3.0 mmol). The mixture was then stirred at 60 °C for 1

hour. After cooling to room temperature, the solvent was removed *in vacuo*; the residue was diluted with EtOAc (30 mL) and washed with 1.0 N HCl (20 mL). The organic layer was dried over anhydrous MgSO₄, filtered, concentrated, and purified by column chromatography (6:4 hexanes/EtOAc) to yield tosyl amide **16a** as a white foam (0.54 g, 1.7 mmol, 85% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.70 (br, 1H), 8.04 (m, 2H), 7.47 (m, 1H), 7.37-7.35 (m, 3H), 7.22-7.20 (m, 1H), 7.03 (m, 1H), 2.45 (s, 3H), 2.17-2.10 (m, 1H), 0.98-0.94 (m, 2H), 0.71-0.68 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 166.3, 145.4, 141.7, 135.8, 133.8, 132.2, 129.8, 128.8, 128.3, 126.9, 126.3, 21.9, 14.0, 8.9

General procedure for the palladium-catalyzed oxidative cyclopropane activation.

To a mixture of PdCl₂ or PdCl₂(MeCN)₂ (10%) and benzoquinone (1.0 equiv) in dioxane (5 mL) was added cyclopropane substrate (0.50 mmol, 1.0 equiv). The reaction mixture

was heated at 80-100 °C until completion of the reaction as indicated by GC. After cooling to room temperature, the reaction mixture was washed with H₂O (5 mL), and extracted with Et₂O (3 × 5 mL). The organic layers were combined, dried over anhydrous MgSO₄, filtered, concentrated, and purified by column chromatography on silica gel (hexanes/EtOAc eluent) to give the products of ring-opening.

Entry 1, Table 1. 30 mol% PdCl₂, 2.0 equiv. CuCl₂, 100 °C, 24 h. Purification by column chromatography on silica gel (9:1 hexanes/EtOAc eluent) afforded **1b** (64% yield).

2-Ethyl-2-methyl-1,2-dihydronaphtho[2,1-*β*]furan (1b): ¹H NMR (400 MHz, CDCl₃)

δ 7.80 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 12.0 Hz, 1H), 7.56 (m, 1H), 7.47 (m, 1H), 7.30 (m, 1H) 7.10 (d, J = 12.0 Hz), 3.28 (dd, J = 64.4, 15.2 Hz, 2H), 1.87 (q, J = 10 Hz, 2H), 1.52 (s, 3H), 1.03 (t, J = 10 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 156.7, 131.3, 129.2, 129.1, 128.9, 126.7, 122.8, 122.7, 118.3, 112.5, 90.3, 39.6, 34.3, 26.6, 8.6

Entry 2, Table 1. 10 mol% PdCl₂, 2.0 equiv. CuCl₂, 100 °C, 24 h. Purification by column chromatography on silica gel (20:1 hexanes/EtOAc eluent) afforded **2b** (64% yield).

2-Ethylbenzofuran (2b): ¹H NMR (400 MHz, CDCl₃) δ 7.48 (m, 1H), 7.40 (m, 1H) 7.18

(m, 3H), 6.37 (d, J = 1.2 Hz, 1H), 2.80 (q, J = 7.6, 2H), 1.34 (t, J = 7.6, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 129.0, 123.0, 122.3, 120.2, 110.7,

101.0, 21.8, 11.9

Entry 3, Table 1. 10 mol% PdCl₂, 2.0 equiv. CuCl₂, 80 °C, 12 h. Purification by column chromatography on silica gel (9:1 hexanes/EtOAc eluent) afforded an inseparable mixture of **3b** and **3c** (86:14 ratio, determined by ¹H NMR, 76% total yield).

4-Methyl-1*H*-isochromen-1-one (3b): ¹H NMR (400 MHz, CDCl₃) δ 8.34 (m, 1H), 7.78

(m, 1H), 7.58-7.48 (m, 2H), 7.14 (q, *J* = 1.6 Hz, 1H) 2.17 (d, *J* = 1.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 141.3, 137.8, 134.9, 130.1, 128.5, 123.1, 121.6, 113.0, 13.1

3,3-Dimethylisobenzofuran-1(3*H*)-one (3c): ¹H NMR (400 MHz, CDCl₃) δ 7.87-7.85

(m, 1H), 7.69-7.65 (m, 1H), 7.52-7.49 (m, 1H), 7.43-7.41 (m, 1H), 1.66 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 169.9, 154.7, 134.3, 129.1, 126.0, 125.4, 120.8, 85.6, 27.6

Entry 4, Table 1. 10 mol% PdCl₂, 2.0 equiv. CuCl₂, 80 °C, 12 h. Purification by column chromatography on silica gel (9:1 hexanes/EtOAc eluent) afforded **4b** (50% yield).

4-Methyl-3-phenyl-1*H*-isochromen-1-one (4b): ¹H NMR (400 MHz, CDCl₃) δ 8.38 (m,

1H), 7.81 (m, 1H), 7.66-7.47 (m, 7H), 2.32 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 162.5, 151.2, 138.8, 134.7, 133.3, 129.7, 129.5, 129.3, 128.8, 128.2, 127.9, 123.3, 120.8, 109.1, 13.6

Entry 5, Table 1. 10 mol% PdCl₂(MeCN)₂, 2.0 equiv. benzoquinone, 80 °C, 12 h. Purification by column chromatography on silica gel afforded **5b** (65% yield), **5c** (10% yield), respectively.

2-Butyl-3-methylisoquinolin-1(2H)-one (5b): ¹H NMR (400 MHz, CDCl₃) δ 8.36 (m,

1H), 7.57 (m, 1H), 7.41-7.38 (m, 2H), 6.33 (s, 1H), 4.08 (m, 2H), 2.43 (d, J = 0.8 Hz, 3H), 1.70 (m, 2H), 1.45 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 163.2, 139.2, 136.9,

132.2, 128.0, 126.0, 125.1, 124.8, 106.1, 44.4, 31.2, 20.7, 20.5, 14.0

2-Butyl-3,3-dimethylisoindolin-1-one (5c): ¹H NMR (400 MHz, CDCl₃) δ 7.81 (m, 1H),

7.52 (m, 1H), 7.43-7.36 (m, 2H), 3.43 (m, 2H), 1.71 (m, 2H), 1.49 (s, 6H), 1.42 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 167.7, 151.8, 131.6, 131.2, 128.1, 123.7, 120.8, 62.9, 39.6,

31.7, 26.2, 20.8, 14.0

Entry 6, Table 1. 10 mol% PdCl₂(MeCN)₂, 2.0 equiv. benzoquinone, 80 °C, 12 h. Purification by column chromatography on silica gel afforded **6b** (43% yield) and **6c** (8% yield), respectively.

2-(4-Chlorophenethyl)-3-methylisoquinolin-1(2H)-one (10b): ¹H NMR (400 MHz,

CDCl₃) δ 8.39 (m, 1H), 7.59 (m, 1H), 7.44-7.39 (m, 2H), 7.27-7.25 (m, 2H), 7.18-7.16 (m, 2H), 6.30 (s, 1H), 4.24 (m,

2H), 3.00 (t, $J = 8$ Hz, 2H), 2.26 (d, $J = 1.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.1, 139.0, 137.3, 136.9, 132.6, 132.4, 130.4, 128.9, 127.9, 126.1, 125.2, 124.7, 106.3, 46.1, 34.3, 20.7

2-(4-Chlorophenethyl)-3,3-dimethylisoindolin-1-one (10c): ^1H NMR (400 MHz,

CDCl_3) δ 7.83 (m, 1H), 7.54-7.52 (m, 1H), 7.46-7.44 (m, 1H), 7.38-7.36 (m, 1H), 7.28-7.22 (m, 4H), 3.60 (m, 2H), 3.06 (m, 2H), 1.40 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ

168.0, 151.8, 138.0, 132.4, 131.8, 131.0, 130.5, 128.8, 128.2, 123.7, 120.9, 62.9, 41.7, 34.7, 26.0

Entry 7, Table 1. 10 mol% $\text{PdCl}_2(\text{MeCN})_2$, 2.0 equiv. benzoquinone, 80 °C, 12 h. Purification by column chromatography on silica gel afforded **7b** (43% yield).

***N*-tert-Butyl-2-(prop-1-en-2-yl)benzamide (7b):** ^1H NMR (400 MHz, CDCl_3) δ 7.64-

7.61 (m, 1H), 7.37-7.28 (m, 2H), 7.19-7.17 (m, 1H), 6.06 (br, 1H), 5.22 (m, 1H), 5.08 (m, 1H), 2.09 (dd, $J = 1.6, 0.8$ Hz, 3H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 168.4, 146.9, 141.7, 135.3, 130.1, 129.0,

128.7, 127.7, 115.8, 51.8, 28.7, 24.7

Entry 8, Table 1. 10 mol% $\text{PdCl}_2(\text{MeCN})_2$, 2.0 equiv. benzoquinone, 80 °C, 12 h. Purification by column chromatography on silica gel afforded **8b** (44% yield) and **8c** (6% yield), respectively.

2-Benzyl-3-methylisoquinolin-1(2H)-one (8b): ^1H NMR (400 MHz, CDCl_3) δ 8.42 (m,

1H), 7.61 (m, 1H), 7.44-7.41 (m, 2H), 7.30-7.22 (m, 3H), 7.17-7.15 (m, 2H), 6.36 (s, 1H), 5.42 (s, 1H), 2.32 (d, $J = 0.8$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 163.6, 139.7, 137.4, 137.0, 132.5,

128.9, 128.4, 127.4, 126.5, 126.1, 125.3, 124.6, 106.3, 47.3, 20.9

2-Benzyl-3,3-dimethylisoindolin-1-one (8c): ^1H NMR (400 MHz, CDCl_3) δ 7.90-7.88

(m, 1H), 7.56-7.53 (m, 2H), 7.47-7.43 (m, 2H), 7.38-7.36 (m, 1H), 7.31-7.25 (m, 3H), 4.75 (s, 2H), 1.36 (s, 6H). ^{13}C NMR (100 MHz,

CDCl_3) δ 168.1, 152.2, 138.9, 132.2, 128.6, 128.2, 127.9, 127.3,

124.0, 120.8, 63.4, 42.8, 22.9

Entry 9, Table 1. 10 mol% $\text{PdCl}_2(\text{MeCN})_2$, 2.0 equiv. benzoquinone, 80 $^\circ\text{C}$, 12 h.

Purification by column chromatography on silica gel afforded **9b** (56% yield) and **9c** (12% yield), respectively.

3-Methyl-2-phenylisoquinolin-1(2H)-one (9b): ^1H NMR (400 MHz, CDCl_3) δ 8.37 (m,

1H), 7.62 (m, 1H), 7.53-7.39 (m, 5H), 7.25-7.23 (m, 2H), 6.41 (s, 1H), 1.99 (d, $J = 0.8$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.6,

139.6, 139.3, 137.3, 132.7, 129.7, 128.7, 128.6, 128.3, 126.2, 125.3,

125.0, 105.6, 21.7

3,3-Dimethyl-2-phenylisoindolin-1-one (9c): ^1H NMR (400 MHz, CDCl_3) δ 7.92 (m,

1H), 7.61 (m, 1H), 7.51-7.42 (m, 5H), 7.23-7.26 (m, 2H), 1.52 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 152.0, 149.7, 136.1, 132.3, 130.8, 130.0, 129.6, 128.4, 124.5, 121.2, 116.4, 64.7, 27.0

Entry 10, Table 1. 10 mol% $\text{PdCl}_2(\text{MeCN})_2$, 2.0 equiv. benzoquinone, 80 $^\circ\text{C}$, 12 h. Purification by column chromatography on silica gel afforded **10b** (45% yield) and **10c** (15% yield), respectively.

4-Methyl-2-tosylisoquinolin-1(2H)-one (10b): ^1H NMR (400 MHz, CDCl_3) δ 8.29 (m,

1H), 8.02 (m, 2H), 7.75 (q, $J = 1.2$ Hz, 1H), 7.70 (m, 1H), 7.54 (m, 1H), 7.34-7.32 (m, 2H), 2.41 (s, 3H), 2.31 (d, $J = 1.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 160.6, 145.8, 137.5, 134.6, 134.0, 129.7, 129.6, 128.8,

127.7, 126.4, 123.7, 122.5, 113.5, 21.9, 16.0

3,3-Dimethyl-2-tosylisoindolin-1-one (10c): ^1H NMR (400 MHz, CDCl_3) δ 8.07-8.05

(m, 2H), 7.76-7.74 (m, 1H), 7.64 (m, 1H), 7.45-7.31 (m, 4H), 2.41 (s, 3H), 1.94 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 166.4, 153.0, 145.0, 137.0, 134.4, 129.7, 129.5, 128.8, 127.5, 125.0, 121.2

Isotopic labeling experiments

Deuterated amides **14** and **22** were obtained by stirring the corresponding protio amides in D₂O overnight, followed by extraction with anhydrous Et₂O and removal of solvents *in vacuo*. Then, the two deuterated amides were subjected to the stoichiometric PdCl₂-promoted reaction conditions.

In a typical experiment, to a solution of PdCl₂(MeCN)₂ (1.0 equiv.) in anhydrous dioxane (5 mL) was added deuterated amide **14** (0.50 mmol, 1.0 equiv). The reaction mixture was heated at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was filtered, concentrated, and purified by column chromatography on silica gel (hexanes/EtOAc eluent, 9 : 1) to give a mixture of partially deuterated products **20**, **21** and **5b**, in a 1 : 1 : 2 ratio. The partial deuterium incorporation and approximate products ratio were calculated by the proton integration in ¹H NMR (relaxation delay 1.0 sec) and confirmed by EI-MS.

¹H NMR (400 MHz, CDCl₃) δ 8.36 (m, 1H), 7.57 (m, 1H), 7.41-7.38 (m, 2H), **6.33** (s, **0.7H**), 4.08 (m, 2H), **2.43** (line broadening: **2.6H**), 1.70 (m, 2H), 1.45 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H).

EI-MS: m/z(%) 216 (M⁺ for **20** and **21**, 100%), 215 (M⁺ for **5b**, 98%)

To a solution of $\text{PdCl}_2(\text{MeCN})_2$ (1.0 equiv.) in anhydrous dioxane (5 mL) was added deuterated amide **22** (0.50 mmol, 1.0 equiv). The reaction mixture was heated at 80 °C for 12 h. After cooling to room temperature, the reaction mixture was filtered, concentrated, and purified by column chromatography on silica gel (hexanes/EtOAc eluent) to give the product **5b** with no deuterium incorporation.

PdCl_2 -promoted activation of phenylcyclopropane with H_2O and the isolation of palladium complex dimer **23.**

To a suspension of PdCl_2 (90.0 mg, 0.5 mmol, 1 equiv) in DMF- H_2O (5:2, 3.5 mL in total) was added phenylcyclopropane (0.06 mL, 0.5 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature for 24 h, then washed with H_2O (50 mL) and extracted with Et_2O (3×10 mL). The organic layers were combined, dried over anhydrous MgSO_4 , filtered, concentrated, and purified by column chromatography on silica gel (from 9:1 to 5:5 hexanes/EtOAc eluent) to give ketones **24**, **25** and palladium complex dimer **23**.

Propiophenone (24): 4.7 mg, 0.035 mmol, 8% yield. ^1H NMR (400 MHz, CDCl_3) δ

7.98-7.96 (m, 2H), 7.55-7.42 (m, 3H), 3.01 (q, $J = 7.2$ Hz, 2H), 1.23 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 201.1, 137.2, 133.1, 128.8, 128.2, 32.0, 8.5

1-Phenylpropan-2-one (25): 4.0 mg, 0.030 mmol, 6% yield. ^1H NMR (400 MHz, CDCl_3)

δ 7.34-7.20 (m, 5H), 3.70 (s, 2H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 205.8, 134.5, 129.6, 129.0, 127.3, 51.3, 29.5

di-μ-Chlorobis[(1,2,3-η)-1-phenyl-2-propenyl]di-palladium (23): 38.8 mg, 0.070

mmol, 7% yield. ^1H NMR (400 MHz, CDCl_3) δ 7.51-7.48 (m, 2H), 7.36-7.25 (m, 3H), 5.80 (m, 1H), 4.62 (d, $J = 11.2$ Hz, 1H), 3.97 (d, $J = 6.8$ Hz, 1H), 3.04 (d, $J = 12.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 137.2, 129.3, 128.7, 128.2, 106.1, 82.1, 59.7; HR-MS (EI) m/z : calculated for $\text{C}_{18}\text{H}_{18}\text{Cl}_2\text{Pd}_2$ 515.885506, found

515.888367

Support for the existence of palladium-nitrogen coordination in the activation of amides.

A low-field shift of the amide proton in ^1H -NMR was observed when amide **5a** was mixed with PdCl_2 in dioxane- d_8 within 24 h.

The amide **5a** (0.05 mmol) was mixed with 0.5 mL dioxane- d_8 in an NMR tube. This

solution was subjected to ^1H -NMR. The amide N-H chemical shift was observed at 6.93 ppm. Then PdCl_2 (0.05 mmol) was added into the solution. After 12 h and 24 h, the mixture was subjected to ^1H -NMR again. The chemical shift of amide N-H was observed at 6.99 and 7.05 ppm, respectively.

STANDARD 1H OBSERVE

Data Collected on:
nmr2-mercury400
Archive directory:

Sample directory:

File: HZ218B-P-H1

Pulse Sequence: #2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: zhe

Relax. delay 1.000 sec
Pulse 44.7 degrees
Acq. time 2.564 sec
Width 7199.4 Hz
16 repetitions
OBSERVE H1, 399.7402189 MHz
DATA PROCESSING
FT size 65536
Total time 1 min

Mixture of **20**, **21** and **5b**

File:QAZ421 Ident:80 89 Win 1000PPM Acq: 6-FEB-2006 12:37:12 +3:06 Cal:1S50750_1
70S EI+ Magnet BpM:216 BpI:1041024 TIC:8541872 Flags:HALL
File Text:HZ218B

STANDARD 1H OBSERVE

Data Collected on:
 posmpurpurin-mercury300
 Archive directory:
 /home/she/vnmrsys/data
 Sample directory:

File: P3-overnight-vaccum

Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp. 25.0 C / 298.1 K
 Operator: she

Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 2.664 sec
 Width 6006.0 Hz
 16 repetitions
 OBSERVE H1, 399.8385862 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 65536
 Total time 1 min

13C OBSERVE

Data Collected on:
 posmpurpurin-mercury300
 Archive directory:
 /home/she/vnmrsys/data
 Sample directory:

File: P3-Cl3-overnight-vaccum

Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp. 25.0 C / 298.1 K
 Operator: she

Relax. delay 1.000 sec
 Pulse 47.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 192 repetitions
 OBSERVE C13, 100.5394700 MHz
 DECOUPLE H1, 399.8405745 MHz
 Power 42 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 0 min