Pd-free Sonogashira Coupling: One pot synthesis of Phthalide via domino Sonogashira coupling and 5-exo-dig cyclization

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Supplementary Data111

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**General methods:** High quality reagents were purchased from Sigma Aldrich. Analytical grade commercial reagents and solvents were purified by standard procedures prior to use. Chromatographic purification was done with 60-120 mesh silica gel (Merck). For reaction monitoring, pre-coated silica gel 60 F254 sheets (Merck) were used. $^1$H NMR (200 MHz) spectra were recorded on a BRUCKER-AC 200 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, brs = broad singlet), coupling constant (Hz). $^{13}$C NMR (50 MHz) spectra were recorded on a BRUKER-AC 200 MHz. Spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: 77.23 ppm). HRMS (ESI) spectra were taken using Waters Xevo G2 QTof mass spectrometer. Melting points of the final compounds were recorded after recrystalization from ethanol.

**General Procedure of the preparation of 3-substituted Phthalides:**

![Chemical reaction](image)

$\text{Br}$ $\text{COOH}$ + $\text{RCOO}$ $\text{CuI, Et$_3$N}$ $\text{DMF, 80-90 °C, 3 h}$ $\text{56-90 % yields}$

Ortho-bromobenzoic acids (1mmol), terminal alkyne (0.1 mmol), Et$_3$N (3.0 mmol), CuI (10 mol %), 3mL of DMF were taken in a 25 ml round bottomed flask in argon atmosphere. The mixture was heated to 80 °C temperature for 3 h. The completion of the reaction was monitored by TLC checking. After completion of the reaction mixture was cooled to room temperature and diluted with water. It was then extracted with ethyl acetate (3×50 ml). Combined organic layer was washed with brine and evaporated to dryness under reduced
pressure. The desired phthalide was isolated by usual column chromatography with mixture ethyl acetate and petroleum ether (1:20) as eluents.

**Spectral data of Compounds:**

**3-benzylideneisobenzofuran-1(3H)-one (3a):**

White Solid; mp: 84-86 °C; Yield: 90 %; \(^1\)H NMR (200 MHz, CDCl\(_3\)) : 6.40 (1H, s), 7.29-7.44 (3H, m), 7.48-7.56 (1H, m), 7.66-7.76 (2H, m), 7.82-7.92 (3H, m); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)): 107.2, 120.0, 123.4, 125.6, 128.5, 128.9 (2C), 129.8, 130.2 (2C), 133.2, 134.6, 140.7, 144.7, 167.2; Elemental Analysis: C: 81.07 %; H: 4.54%; Found: C: 81.00%; H: 4.49%; HRMS (ESI) of C\(_{15}\)H\(_{11}\)O\(_2\)\(^+\) [M+H\(^+\)] : 223.0754; Observed : 223.0750.

**3-benzylidene-6-fluoroisobenzofuran-1(3H)-one (3b):**

White Solid; mp: 144-146 °C; Yield: 80 %; \(^1\)H NMR (400 MHz, CDCl\(_3\)) : 6.34 (1H, s), 7.29 (1H, q, \(J = 7.2\) Hz), 7.37-7.48 (3H, m), 7.53 (1H, d, \(J = 6.8\) Hz), 7.72 (1H, q, \(J = 4.0\) Hz), 7.78 (2H, t, \(J = 7.6\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 107.4, 111.9 (d, \(J = 23.9\) Hz), 122.0 (d, \(J = 8.7\) Hz), 123.1 (d, \(J = 24.5\) Hz), 125.3, 128.8, 129.0 (2C), 130.3 (2C), 133.1, 136.8, 144.0, 163.7 (d, \(J = 250.5\) Hz), 166.0 ; HRMS (ESI) of C\(_{15}\)H\(_{10}\)FO\(_2\)\(^+\) [M+H\(^+\)] : 241.0659, Observed: 241.0642; Elemental Analysis: C: 75.00%; H: 3.78%; Found: C: 74.93%; H: 3.72%;

**3-benzylidene-5,6-dimethoxyisobenzofuran-1(3H)-one (3c):**

White Solid; mp: 84-86 °C; Yield: 64 %; \(^1\)H NMR (200 MHz, CDCl\(_3\)) : 4.10 (3H, s), 4.15 (3H, s), 6.38 (1H, s), 7.21 (1H, s), 7.26 (1H, s), 7.38-7.53 (3H, m), 7.92 (2H, d, \(J = 7.6\) Hz); \(^{13}\)C NMR (50
3-(4-methoxybenzylidene)isobenzofuran-1(3H)-one (3d):

Yellow Solid; mp: 124-126 °C; Yield: 59 %; \( ^1H \) NMR (200 MHz, CDCl\(_3\)): 3.83 (3H, s), 6.35 (1H, s), 6.92 (2H, d, \( J = 8.8 \) Hz), 7.45-7.52 (1H, m), 7.64-7.73 (2H, m), 7.80 (2H, d, \( J = 8.8 \) Hz), 7.89 (1H, d, \( J = 7.6 \) Hz); \( ^{13}C \) NMR (50 MHz, CDCl\(_3\)): 55.5, 107.1, 114.4 (2C), 119.7, 123.2, 125.6, 126.0, 129.4 (2C), 131.8, 134.5, 140.9, 143.2, 159.9, 167.4; HRMS (ESI) of C\(_{17}\)H\(_{15}\)O\(_4\)\(^+\) [M+H\(^+\)]: 283.0965; Observed: 283.0943.

Elemental Analysis: C: 72.33; H: 5.00%; Found: C: 72.27; H: 4.8%;

3-(4-methylbenzylidene)isobenzofuran-1(3H)-one (3e):

White Solid; mp: 128-130 °C; Yield: 68 %; \( ^1H \) NMR (200 MHz, CDCl\(_3\)) : 2.42 (3H, s), 6.43 (1H, s), 7.23-7.35 (2H, m), 7.52-7.60 (1H, m), 7.70-7.80 (4H, m), 7.96 (1H, dd, \( J = 7.6 \) Hz); \( ^{13}C \) NMR (50 MHz, CDCl\(_3\)): 21.6, 107.4, 119.9, 123.4, 125.7, 129.7 (3C), 130.3 (2C), 130.4, 134.6, 138.8, 140.9, 144.1, 167.4; HRMS (ESI) of C\(_{16}\)H\(_{13}\)O\(_2\)\(^+\) [M+H\(^+\)]: 237.0910; Found: 237.0912; Elemental Analysis: C: 81.34; H, 5.12 %; Found: C: 81.26; H, 5.00 %;

3-(4-(tert-butyl)benzylidene)isobenzofuran-1(3H)-one (3f):

White Solid; mp: 96-98 °C; Yield: 62 %; \( ^1H \) NMR (CDCl\(_3\), 200 MHz): 1.36 (9H, s), 6.42 (1H, s), 7.42-7.57 (3H, m), 7.67-7.85 (4H, m), 7.93 (1H, d, \( J = 7.4 \) Hz); \( ^{13}C \) NMR (CDCl\(_3\), 50 MHz): 31.4 (3C), 34.9, 107.2, 119.9, 123.5, 125.7, 125.9 (2C),
129.7, 130.1 (2C), 130.5, 134.6, 140.8, 144.3, 151.9, 167.4; HRMS of C_{19}H_{19}O_{2}^{+} [M+H^{+}]: 279.1380; Observed: 279.1375; Elemental Analysis: C, 81.99; H, 6.52 %; Found : C, 81.90; H, 6.40%.

3-(2-chlorobenzylidene)isobenzofuran-1(3H)-one (3g):

White Solid; mp: 142-144 °C; Yield: 55 %; \(^1\)H NMR (CDCl\(_3\), 200 MHz): 6.35 (1H, s), 7.26-7.39 (2H, m), 7.56-7.63 (1H, m), 7.71-7.83 (4H, m), 7.95 (1H, d, \(J = 7.6\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 50 MHz): 105.6, 120.1, 123.6, 125.8, 128.3, 128.5, 129.8, 130.1, 130.4, 134.8 (2C), 135.0, 140.4, 145.6, 166.9; Elemental Analysis: C, 70.19; H, 3.53 %; Found: C, 70.10; H, 3.49%.

3-(2-hydroxyethylidene)isobenzofuran-1(3H)-one (3h):

Yellow Solid; mp: 75-77 °C; Yield: 65 %; \(^1\)H NMR (CDCl\(_3\), 200 MHz): 2.76 (1H, br), 4.59 (2H, d, \(J = 6.8\) Hz), 581 (1H, t, \(J = 6.8\) Hz), 7.48-7.59 (1H, m), 7.63-7.72 (2H, m), 7.85 (1H, d, \(J = 7.6\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 50 MHz)): 57.1, 107.2, 120.4, 124.6, 125.5, 130.4, 124.8, 139.2, 146.2, 166.8; HRMS (ESI) of C_{10}H_{9}O_{3}^{+} [M+H^{+}]: 177.0546; Found: 177.0540; Elemental Analysis: C, 68.18; H, 4.58%; Found: C, 68.10; H, 4.52%.

3-(2-phenoxyethylidene)isobenzofuran-1(3H)-one (3i):

Lihgt yellow Solid; mp: 128-130 °C; Yield: 53 %; \(^1\)H NMR (CDCl\(_3\), 200 MHz): 5.03 ( 2H, d, \(J = 6.8\) Hz), 5.89 (1H, t, \(J = 6.8\) Hz), 6.99-7.03 (3H, m), 7.30-7.38 (2H, m), 7.55-7.63 (1H, m), 7.71-7.74 (2H, m), 7.94 (1H, d, \(J = 7.6\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 50 Hz): 62.1, 103.5, 114.7 (2C), 120.5, 121.2, 124.7, 125.5, 129.7 (2C), 130.6, 134.7, 138.8,
147.1, 158.2, 166.3; HRMS (ESI) of C_{16}H_{13}O_3^{+}[M+H^+]: 253.0859; Found: 253.0848; Elemental Analysis: C, 76.18; H, 4.79 %; Found: C, 76.12; H, 4.70%

3-(2-(phenylamino)ethylidene)isobenzofuran-1(3H)-one (3j):

Yellow stickymass; Yield: 56 %; $^1$H NMR (CDCl$_3$, 200 MHz):
3.74 (1H, br), 4.25 (2H, d, $J = 6.8$ Hz), 5.74 (1H, t, $J = 6.8$ Hz),
6.69-6.79 (3H, m), 7.18-7.26 (2H, m), 7.51-7.73 (3H, m), 7.92 (1H, q, $J_1 = 7.4$ Hz, $J_2 = 1.0$ Hz); $^{13}$C NMR (CDCl$_3$, 50 MHz): 39.6, 106.4, 113.3 (2C), 118.2, 120.3, 124.7, 125.6, 129.6 (2C), 130.3, 134.7, 139.3, 146.7, 147.6, 166.8; HRMS of C_{16}H_{14}NO_2^{+}[M+H^+]: 252.1019; Observed: 252.1016; Elemental Analysis: C, 76.48; H, 5.21%; Found: C, 76.42; H, 5.15%.

3-benzylidene-5-methylisobenzofuran-1(3H)-one (3k):

White Solide; mp: 106-108 °C; Yields: 72%; $^1$H NMR (CDCl$_3$, 200 MHz): 2.53 (3H, s), 6.38 (1H, s), 7.31-7.45 (4H, m), 7.55 (1H, s), 7.76-7.86 (3H, m); $^{13}$C NMR (CDCl$_3$, 50 MHz): 22.4, 106.8, 120.1, 121.2, 125.5, 128.5, 128.9 (2C), 130.3 (2C), 131.3, 133.4, 141.3, 144.8, 146.0, 167.2; Elemental Analysis: C, 81.34; H, 5.12; Found: C, 81.25; H, 5.02 %; HRMS (ESI) of C_{16}H_{13}O_2^{+}[M+H^+]: 237.0910; Observed: 237.0908.

7-benzylidenefuro[3,4-b]pyridin-5(7H)-one (3l):

Lightyellow stickysolid; Yields: 80%; $^1$H NMR (CDCl$_3$, 200 MHz): 6.98 (1H, s), 7.37-7.51 (4H, m), 7.89-7.93 (2H, m), 8.25 (1H, dd, $J_1 = 1.6$ Hz, $J_2 = 7.8$ Hz), 8.92 (1H, dd, $J_1 = 1.6$ Hz, $J_2 = 6.8$ Hz); $^{13}$C NMR (CDCl$_3$, 50 MHz): 109.0, 117.6, 124.3, 129.1 (2C), 129.4, 131.0 (2C), 132.8, 134.0, 143.9, 156.4,
158.8, 165.0; Elemental Analysis: C, 75.33; H, 4.06; N, 6.27%; Found: C, 75.29; H, 3.98; N, 6.16%; HRMS (ESI) of $\text{C}_{14}\text{H}_{10}\text{NO}_2^+ [\text{M}+\text{H}^+]$: 224.0706; Observed: 224.0701.

3-benzylidenenaphtho[1,2-c]furan-1(3H)-one (3m):

![Structure of 3-m](image)

Yellow Solid; mp: 178-180 °C; Yields: 65%; $^1$H NMR (CDCl$_3$, 200 MHz): 6.55 (1H, s), 7.38-7.52 (5H, m), 7.80 (2H, d, $J = 8.6$ Hz), 7.93-8.01 (2H, m), 8.16 (1H, d, $J = 8.4$ Hz), 8.93 (1H, d, $J = 8.2$ Hz); $^{13}$C NMR (CDCl$_3$, 50 MHz): 108.5, 114.3, 116.6, 117.9, 124.1, 127.8, 128.8, 129.0 (2C), 129.2, 129.6, 130.6 (2C), 133.4, 134.0, 135.9, 141.5, 145.1, 167.4; Elemental Analysis: C, 83.81; H, 4.44 %; Found: C, 83.71; H, 4.30 %; HRMS (ESI) of $\text{C}_{19}\text{H}_{13}\text{O}_2^+ [\text{M}+\text{H}^+]$: 273.0910; Observed: 273.0915.

1-benzylidene-8-methoxynaphtho[1,2-c]furan-3(1H)-one (3n):

![Structure of 3n](image)

Yellowish solid; Yields: 60%; $^1$H NMR (CDCl$_3$, 200 MHz): 3.89 (3H, s), 6.78 (1H, s), 7.08-7.47 (6H, m), 7.69 (1H, s), 7.83 (2H, d, $J = 7.4$ Hz), 8.22 (1H, m); $^{13}$C NMR (CDCl$_3$, 50 MHz): 55.7, 108.5, 112.6, 120.9, 121.0, 121.2, 125.6, 125.9, 127.6, 128.0, 129.0 (2C), 130.4, 130.9 (2C), 133.9, 139.1, 146.1, 159.8, 167.5; Elemental Analysis: C, 79.46; H, 4.67%; Found: C, 79.36; H, 4.52%; HRMS (ESI) of $\text{C}_{20}\text{H}_{15}\text{O}_3^+ [\text{M}+\text{H}^+]$: 303.1016; Observed: 303.1005.
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3a):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3a):
$^1$H NMR (CDCl$_3$, 400 MHz) of Compound (3b):

$^{13}$C NMR (CDCl$_3$, 100 MHz) of Compound (3b):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3c):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3c):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3d):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3d):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3e):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3e):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3f):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3f):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3g):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3g):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3h):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3h):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3i):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3i):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3j):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3j):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3k):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3k):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3l):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3l):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3m):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3m):
$^1$H NMR (CDCl$_3$, 200 MHz) of Compound (3n):

$^{13}$C NMR (CDCl$_3$, 50 MHz) of Compound (3n):