Palladium-Catalyzed ortho-Halogen-Induced Deoxygenative Approach of Alkyl Aryl Ketones to 2-Vinylbenzoic Acids

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1. General information

All the reactions were set up under atmospheric air utilizing glassware and 25 mL Pyrex reaction tube. Commercial reagents were purchased from Sigma Aldrich, Tokyo Chemical Industry (TCI, India) pvt. Ltd., Alfa Aesar, Sd Fine-chem. Ltd. and used without further purification. Amberlite® IRA 900 Cl⁻ resin (PS) used as support (Chloride form) was purchased from Across Organics. The catalyst palladium on carbon (Pd/C) 5 wt% purchased from Sd Fine-chem. Ltd. All solvents were purchased from CDH-Central Drug House (P) Ltd., Sd Fine-chem. Ltd. and Across Organics. Reactions were monitored using thin-layer chromatography (TLC) on silica gel 60 F₂₅₄ (Merck) plates. Visualization of developed plates was performed under UV light (254 nm). Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Column chromatography was performed on 60-120 or 230-400 mesh silica. NMR characterization data were recorded at 298 K on a Bruker Advance 600 spectrometer operating at 600 MHz (¹H) and 150 MHz (¹³C) and Bruker Advance 300 spectrometer operating at 300 MHz (¹H) and 75 MHz (¹³C). ¹H NMR spectra were internally referenced to residual solvent signal (δH 7.28 ppm) or TMS. ¹³C NMR spectra were internally referenced to residual solvent signal (δC 77.00 ppm). Chemical shifts were recorded in δ (ppm) relative to the TMS, coupling constants (J) are given in Hz and multiplicities of signals are reported as follows: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; dd = doublet of doublets, td = triplets of doublets. High resolution mass spectra (HRMS) were obtained on a micro mass Q-TOF ultima spectrometer and Bruker Daltonik GmbH Impact HD model instrument. LC-MS spectra were obtained on a Waters micro mass Q-TOF Ultima Spectrometer, Germany.
Table 1S. Optimization of reaction parameters.\textsuperscript{a}

\[
\begin{array}{cccccc}
\text{Entry} & \text{Catalyst} & \text{Solvent} & \text{Temperature} & \text{Yield (\%)} \text{b} \\
\hline
1 & – & DMF & 130 ^\circ \text{C} & \text{nr} \\
2 & \text{Pd/C} & DMF & 130 ^\circ \text{C} & \text{nr} \\
3 & \text{Pd/C} & DMF & 130 ^\circ \text{C} & 76 \\
4 & \text{Pd/C} & DMA & 130 ^\circ \text{C} & 70 \\
5 & \text{Pd/C} & PEG-400 & 130 ^\circ \text{C} & \text{nd} \\
6 & \text{Pd/C} & DMSO & 130 ^\circ \text{C} & \text{nd} \\
7 & \text{Pd/C} & Xylene & 130 ^\circ \text{C} & \text{nr} \\
8 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & \text{90} \\
9 & \text{Pd@PS} & DMF & 130 ^\circ \text{C} & 60 \\
10 & \text{Pd(OAc)}_2 & DMF & 130 ^\circ \text{C} & 56 \\
11 & \text{PdCl}_2 & DMF & 130 ^\circ \text{C} & 50 \\
12 & \text{PdCl}_2(\text{PPh}_3)_2 & DMF & 130 ^\circ \text{C} & 67 \\
13 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & 73 \\
14 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 110 ^\circ \text{C} & 27 \\
15 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & 40 \\
16 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & 53 \\
17 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & 70 \\
18 & \text{Pd/C} & \text{DMF:Xylene}(3:1) & 130 ^\circ \text{C} & \text{traces} \\
\end{array}
\]

\textsuperscript{a} Standard conditions: 2-iodoacetophenone (0.20 mmol), oxalic acid (1.22 mmol) catalyst (2 mol\%), DMF:xylene (1.5:0.5) mL, 130 ^\circ \text{C}, 6 h; nd = not detectable, nr = no reaction; \textsuperscript{b} Isolated yield of 2a; \textsuperscript{c} Without oxalic acid; \textsuperscript{d} 1 mol\% of Pd/C; \textsuperscript{e} 3 equiv. of oxalic acid; \textsuperscript{f} Reaction time 3h; \textsuperscript{g} N-formylsachharin instead of oxalic acid; \textsuperscript{h} Formic acid instead of oxalic acid.
2. Preparation of starting materials and characterization data

2.1 Synthesis of 1-(2-iodo-4-methoxyphenyl)ethanone (1c).

To an oven dried round bottom flask equipped with magnetic bar were added anhydrous aluminum chloride (200 mg, 1.5 mmol), DCE (5 mL) under nitrogen at 0°C and stirred for 5 min. Then the acetyl chloride (94.2 mg, 1.2 mmol) was added drop-wise under N₂ and stirred for another 10 min. To the stirred solution, 3-iodoanisole (218 mg, 1.0 mmol) was added and the reaction mixture allows warm to room temperature and stirred at that temperature for overnight under nitrogen. The progress of reaction was monitored by TLC. After completion of reaction 5 mL of 4N HCl was added and the reaction mixture was extracted with ethyl acetate (4X5 mL). The combined organic layer was washed with brine and dried over anhydrous Na₂SO₄. The organic phase was concentrated over rotary evaporator and the crude mixture further purified by column chromatography using hexane:ethyl acetate (98:2) as eluent; gave 1c as light yellow oil (80 mg, 29%); ¹H NMR (600 MHz, CDCl₃) δ 7.60 (d, J = 8.64 Hz, 1H), 7.51 (s, 1H), 6.93 (d, J = 8.64 Hz, 1H), 3.83 (s, 3H), 2.59 (s, 3H); ¹³C NMR (600 MHz, CDCl₃) δ 198.76, 161.55, 134.25, 130.98, 127.15, 113.51, 92.96, 55.68, 28.78.

2.2 Synthesis of 1f and 1g

Methoxy substituted acetophenone(1 mmol) and I₂ (0.6 equiv.), anhydrous CH₃CN (3 mL) was added to an oven dried 25 mL round bottom flask at room temperature and stirred for 5 min. To the stirred solution bis-[(trifluoroacetoxy)iodo]benzene (BTI) (1.2 equiv.) was added at once. After a few minutes, the red-brown color of solution disappeared and the reactions were complete within 2 hours. After completion of the reaction, 5 mL of 0.1 M NaOH solution was added to the reaction mixture to quench the residual BTI and the organic part was extracted with ethyl acetate (5 x 5 mL). The combined organic layer was washed with water, brine and then dried over.
Na₂SO₄. The organic phase was concentrated over rotary evaporator and the crude mixture further purified by column chromatography using hexane and ethyl acetate as eluent.

\[
\begin{align*}
\text{H}_3\text{CO} & \text{O} \\
\text{I} & \text{CH}_3
\end{align*}
\]

**1-(2-Iodo-5-methoxyphenyl)ethanone (1f)**: Prepared as described in general procedure 2.2.

\(^1\)H NMR (600 MHz, CDCl₃) δ 2.61 (s, 3H), 3.97 (s, 3H), 7.28 (dd, \(J = 8.0\) Hz, 2.0 Hz, 1H), 7.41 (s, 1H), 7.91 (d, \(J = 8.0\) Hz, 1H).

**ESI-MS(M+H\(^+\))** calculated for C₉H₁₀IO₂\(^+\) is 277.07842 observed 277.4490.

\[
\begin{align*}
\text{H}_3\text{CO} & \text{O} \\
\text{I} & \text{CH}_3
\end{align*}
\]

**1-(2-Iodo-4,5-dimethoxyphenyl)ethanone (1g)**: Prepared as described in general procedure 2.2.

\(^1\)H NMR (600 MHz, CDCl₃) δ 2.67 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 7.12 (s, 1H), 7.37 (s, 1H); \(^{13}\)CNMR (600 MHz, CDCl₃) δ 199.72, 151.38, 148.81, 135.39, 123.44, 112.41, 81.59, 56.32, 56.09, 29.19.

**2.3 General procedure for the synthesis of 1b-1e and 1i-1n**

\[
\begin{align*}
\text{FGs} & \text{R} \quad [\text{RhCp}^*\text{Cl}_2]_2 \quad \text{AgSbF}_6 \quad \text{Cu(OAc)}_2 \\
\text{NIS} & \quad \text{1,2-DCE, 120 °C, 20 h} \quad \text{FGs} \text{R} \\
\text{R} & \text{= H, alkyl}
\end{align*}
\]

To an oven-dried screw-capped 25 mL reaction tube equipped with a magnetic stir bar were added aryl ketones (100 mg, 1.0 equiv.), [RhCp*Cl₂]₂ (3 mol%), AgSbF₆ (10 mol%), Cu(OAc)₂ (2.2 equiv.), NIS (1.4 equiv.) and 1,2-DCE (3 mL). The closed reaction tube is added to a preheated (120 °C) oil bath and stirred for 20h. The progress of reaction was monitored by TLC. After
completion of reaction, the mixture was then allowed to cool down to room temperature. 5 mL of saturated aqueous solution of sodium thiosulphate was added to remove iodine color and the organic mixture was extracted with ethyl acetate. The organic layer was washed with water, brine and then dried over Na$_2$SO$_4$. The organic phase was concentrated over rotary evaporator and the crude mixture further purified by column chromatography using hexane and ethyl acetate as eluent.

1-(2-Iodo-4-methylphenyl)ethanone (1b)$^3$: Prepared as described in general procedure 2.3.

$^1$H NMR (600 MHz, CDCl$_3$) δ 2.36 (s, 3H), 2.63 (s, 3H), 7.24 (d, $J$ = 7.8 Hz, 1H), 7.46 (d, $J$ = 7.9 Hz, 1H), 7.83 (s, 1H); $^{13}$C NMR (600 MHz, CDCl$_3$) δ 200.90, 142.83, 141.81, 140.39, 128.83, 128.78, 91.50, 29.27, 20.78.

1-(2-Iodo-6-methylphenyl)ethanone (1d)$^3$: Prepared as described in general procedure 2.3.

$^1$H NMR (600 MHz, CDCl$_3$) δ 2.30 (s, 3H), 2.58 (s, 3H), 6.99 (t, $J$ = 7.8 Hz, 1H), 7.20 (d, $J$ = 7.8 Hz, 1H), 7.67 (d, $J$ = 7.9 Hz, 1H); $^{13}$C NMR (600 MHz, CDCl$_3$) δ 206.34, 147.05, 136.43, 134.50, 130.11, 130.07, 89.30, 30.91, 19.68.

1-(2-Iodo-4,6-dimethylphenyl)ethanone (1e)$^3$: Prepared as described in general procedure 2.3.
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$2.16 (s, 3H), 2.20 (s, 3H), 2.47 (s, 3H), 6.91 (s, 1H), 7.41 (s, 1H); $^{13}$CNMR (300 MHz, CDCl$_3$) $\delta$206.47, 144.34, 140.20, 136.83, 134.20, 130.95, 89.33, 31.04, 20.56, 19.58.

$\text{Cl}$

$\text{O}$

$\text{CH}_3$

1-(4-Chloro-2-iodophenyl)ethanone (1i)$^3$: Prepared as described in general procedure 2.3.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$2.63 (m, 3H), 7.40-7.47 (m, 2H), 7.98 (d, $J=1.7$ Hz, 1H); $^{13}$C NMR (300 MHz, CDCl$_3$) $\delta$200.28, 141.86, 140.51, 137.20, 129.27, 128.31, 91.47, 29.27.

$\text{O}$

$\text{CH}_3$

1-(2-Iodophenyl)propan-1-one (1j)$^3$: Prepared as described in general procedure 2.3.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$1.25 (t, $J=7.3$ Hz, 3H), 2.93 (q, $J=14.5$, 7.2 Hz, 2H), 7.14 (t, $J=16.9$ Hz, 1H), 7.38 (d, $J=9.1$ Hz, 1H), 7.43 (t, $J=15.9$ Hz, 1H), 7.92 (d, $J=8.5$ Hz, 1H); $^{13}$CNMR (600 MHz, CDCl$_3$) $\delta$205.64, 145.01, 140.39, 131.34, 128.0, 127.47, 90.83, 35.37, 8.12.

$\text{H}_3\text{C}$

$\text{O}$

$\text{CH}_3$

1-(2-Iodo-4-methylphenyl)propan-1-one (1k)$^3$: Prepared as described in general procedure 2.3.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$1.23 (t, $J=7.2$ Hz, 3H), 2.35 (s, 3H), 2.92 (q, $J=14.5$, 7.2 Hz, 2H), 7.22 (d, $J=8.2$ Hz, 1H), 7.34 (d, $J=7.8$ Hz, 1H), 7.79 (s, 1H); $^{13}$C NMR (600 MHz, CDCl$_3$) $\delta$204.84, 142.24, 141.31, 128.74, 127.86, 91.33, 35.03, 20.77, 8.28.
1-(2-Iodophenyl)butan-1-one (1i): Prepared as described in general procedure 2.3.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$1.03 (t, 3H, $J$ = 7.40), 1.72-1.84 (m, 2H), 2.89 (t, 2H, $J$ = 7.23), 7.10-7.16 (m, 1H), 7.36-7.44 (m, 2H), 7.93 (d, 1H, $J$ = 7.89); $^{13}$CNMR (300 MHz, CDCl$_3$) $\delta$205.06, 145.00, 140.48, 131.35, 127.98, 127.58, 90.88, 43.99, 17.56, 13.76.

1-(2-Iodophenyl)pentan-1-one (1m): Prepared as described in general procedure 2.3.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$0.96 (t, $J$ = 7.3 Hz, 3H), 1.37-1.47 (m, 2H), 1.60-1.75 (m, 2H), 2.90 (t, $J$ = 7.4 Hz, 2H), 7.10-7.16 (m, 1H), 7.35-7.41 (m, 2H), 7.92 (d, $J$ = 7.8 Hz, 1H); $^{13}$CNMR (300 MHz, CDCl$_3$) $\delta$205.22, 145.07, 140.46, 131.34, 127.98, 127.57, 90.89, 41.85, 26.15, 22.33, 13.86.

1-(2-Iodophenyl)hexan-1-one (1n): Prepared as described in general procedure 2.3.

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$0.83 (t, $J$ = 6.9 Hz, 3H), 1.27-1.34 (m, 4H), 1.60-1.67 (m, 2H), 2.81 (t, $J$ = 7.4 Hz, 2H), 7.01-7.06 (m, 1H), 7.26-7.35 (m, 2H), 7.82 (d, $J$ = 7.9 Hz, 1H); $^{13}$CNMR (300 MHz, CDCl$_3$) $\delta$205.24, 145.02, 140.44, 131.33, 127.97, 127.56, 90.89, 42.08, 31.32, 23.73, 22.44, 13.91.
2.4 Synthesis of 1-(2-iodophenyl)ethanol (5).

\[
\begin{align*}
\text{C}_8\text{H}_7\text{I} \xrightarrow{\text{NaBH}_4, \text{Ethanol, 0°C - RT}} \text{C}_8\text{H}_7\text{I} - \text{OCH}_2\text{CH}_3
\end{align*}
\]

The 2-iodoacetophenone (0.81 mmol) was dissolved in ethanol and cooled to 0°C. NaBH\(_4\) (3.24 mmol) was added in one portion to this solution. The suspension was stirred for 10 min at 0°C, then allowed to warm to room temperature and stirred at that temperature for 12 h. After completion of reaction, saturated aqueous NH\(_4\)Cl was added and the organic mixture was extracted with ethyl acetate. The combined organic layer was washed with saturated aqueous NH\(_4\)Cl, brine and dried over anhydrous Na\(_2\)SO\(_4\). The organic phase was concentrated over rotary evaporator and finally yielded the desired alcohol 5 as light yellow oil (95 mg, 47%) after purification by silica gel column chromatography (using ethyl acetate and hexane as eluent); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 7.80-7.82 (m, 1H), 7.55-7.58 (m, 1H), 7.38-7.41 (m, 1H), 6.97-7.00 (m, 1H), 5.06-5.08 (m, 1H), 1.45-1.48 (m, 3H); \(^13\)C NMR (600 MHz, Chloroform-d) \(\delta\) 147.42, 139.25, 129.10, 128.69, 126.28, 97.17, 73.66, 23.71.

2.5 Synthesis of 3-methyleneisobenzofuran-1(3H)-one (6).

\[
\begin{align*}
\text{C}_8\text{H}_7\text{O} \xrightarrow{\text{SOCl}_2, \text{DMF, 60 ºC}} \text{C}_8\text{H}_7\text{O}
\end{align*}
\]

A solution of o-acetylbenzoic acid (1 mmol) in anhydrous DMF (5 mL) was placed into a round-bottomed flask equipped with a stirrer and was heated to 60°C. Thionyl chloride (1.2 equiv.) was added slowly to the stirred solution and after addition the reaction mixture was heated at 60°C for 2 hrs. The progress of reaction was monitored by TLC. After completion of reaction, the mixture allows cool down to room temperature. Then, to the reaction mixture ice cold water was added and the organic mixture was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na\(_2\)SO\(_4\). The organic phase was concentrated over rotary evaporator and the crude mixture further purified by column chromatography using hexane and
ethyl acetate as eluent, gave 6 as white solid (90 mg, 61%); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta 7.91 \ (d, \ J = 7.7 \, \text{Hz}, \ 1\text{H}), \ 7.74 \ (d, \ J = 4.4 \, \text{Hz}, \ 2\text{H}), \ 7.57-7.60 \ (m, \ 1\text{H}); \) \(^13\)C NMR (600 MHz, Chloroform-d) \(\delta 166.9, \ 151.8, \ 146.5, \ 139.0, \ 134.5, \ 130.5, \ 125.3, \ 125.1, \ 120.6, \ \text{91.3.}

**Synthesis of 2-methyl-1-phenylpropan-1-one\(^6\)**

![Chemical structure](image)

An oven dried 25ml vial charged with \([\text{RhCp}^\ast\text{Cl}]_2\) (5 mol%, 30.9 mg), \(\text{Cs}_2\text{CO}_3\) (5.0 mmol, 1629.1 mg) were added to a with a stir bar, followed by “wet” methanol and starting propiophenone (1.0 mmol, 132.9 microlitre). The vial was sealed with a microwave vial cap and a balloon of \(\text{O}_2\) was inserted via a needle through the septum. The reaction was heated to 65 °C for 24 hours. The reaction was quenched by diluting with water and extracted with \(\text{CH}_2\text{Cl}_2\). The combined organic layers were dried with anhydrous \(\text{Na}_2\text{SO}_4\), filtered, concentrated and purified by column chromatography on silica gel mess size 60-120 to give yellowish liquid product (102 mg, 69%).

**3. General procedure for the preparation of 2-vinylbenzoic acids**

2-Halophenylketones (1 equiv.), \(\text{Pd/C} \ (2 \, \text{mol} \ %)\), anhydrous oxalic acid (6 equiv.) and DMF:xylene (3:1) (1.5 mL) were added to an oven dried 25 mL screw capped reaction tube. The reaction mixture was heated at 130 °C for 6 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction it allows to cool down to room temperature. Water was added to the reaction mixture and the organic mixture was extracted with ethyl acetate (4 X 5 mL). The combined organic layer was washed with brine, dried over anhydrous \(\text{Na}_2\text{SO}_4\), and concentrated under vacuum. The resulting residue was purified by silica gel column chromatography using hexane and ethyl acetate as eluent to give the desired product.
4. Mechanistic investigations

**Synthesis of O-18 labeled 4-methylacetophenone**

\[
\text{AgOTf (10 mol%)} \quad \text{H}_2\text{O}^{18} \quad \text{EtOAc, 80 °C, 12 h}
\]

To an oven dried 5ml screw caped reaction vial equipped with stirring bar charged with EtOAc (2 ml) followed by addition of alkyne (0.5mmol, 63.4 microlitre), AgOTf (13.0mg, 10 mol %) and water (3 mmol, 27 microlitre). The reaction mixture was heated up to 80 °C for 12 hours and progress of the reaction was monitored by TLC. After completion of the reaction, the crude mixture was allowed to cool at room temperature and the solvent was removed under vacuum. The combined organic layers were dried with anhydrous Na$_2$SO$_4$, filtered, concentrated and purified by column chromatography on silica gel mess size 60-120 to give yellowish liquid product (45.0 mg, 67%). (SI, pages S70-71)

**O-18 labeled experiment for mechanistic investigation**

\[
\text{Cat. Pd/C} \quad \text{DMF:Xylene} \quad 130 °C, 6 h
\]

With the mixtures of O-16 and O-18 4-methyl-2-iodoactophenone, we set up a reaction as described in GP-3. After completion of the reaction it allows to cool down to room temperature. Water was added to the reaction mixture and the organic mixture was extracted with ethyl acetate (4 X 5 mL). The combined organic layer was washed with brine, dried over anhydrous Na$_2$SO$_4$, and concentrated under vacuum. The resulting residue was purified by silica gel column chromatography using hexane and ethyl acetate as eluent and given for UPLC/ESI-MS analysis.
On the basis of these analyses, we got both product O-16 (4-methyl-2-iodoactophenones) in major and O-18 (4-methyl-2-iodoactophenones) in minor. (SI, page S68-69)

Scheme S1: Plausible mechanism

5. Characterization data of synthesized compounds

2-Vinylbenzoic acid (Table 1, entry 2a)

Following the general procedure, 2-iodoacetophenone (50 mg, 0.20 mmol) afforded 2a (27 mg, 90%, mp: 91-93 °C) after purification by silica gel column chromatography using ethyl acetate:hexane (20:80). $^1$H NMR (600 MHz, Chloroform-d) δ 7.80-7.81 (m, 1H), 7.69 (d, $J$ = 7.8 Hz, 1H), 7.53-7.56 (m, 1H), 7.37-7.45 (m, 2H), 5.77 (dd, $J$ = 17.5, 1.1 Hz, 1H), 5.35 (dd, $J$ =
11.0, 1.1 Hz, 1H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 169.02, 138.40, 135.73, 132.27, 130.40, 130.19, 128.15, 126.98, 116.89.

**HRMS (ESI)** (M-H)$^+$ calcd. for C$_9$H$_7$O$_2$ is 147.0451 obsd. 147.0440.

### 5-Methyl-2-vinylbenzoic acid (Table 1, entry 2b)

Following the general procedure, 4-methyl-2-iodoacetophenone (50 mg, 0.19 mmol) afforded 2b (29 mg, 93%) after purification by silica gel column chromatography using ethyl acetate:hexane (20:80). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 1H NMR (600 MHz, Chloroform-d) $\delta$ 7.90 (s, 3H), 7.53-7.60 (m, 2H), 7.39 (d, $J = 8.0$ Hz, 1H), 5.68 (dd, $J = 17.4$, 1.1 Hz, 1H), 5.37 (dd, $J = 10.9$, 1.1 Hz, 1H), 2.42 (s, 3H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 172.90, 137.77, 137.43, 135.82, 133.92, 131.64, 127.44, 126.95, 115.97, 20.94.

**HRMS (ESI)** (M-H)$^+$ calcd. for C$_{10}$H$_9$O$_2$ is 161.0608 obsd. 161.0597.

### 5-Methoxy-2-vinylbenzoic acid (Table 1, entry 2c)

Following the general procedure, 4-methoxy-2-iodoacetophenone (50 mg, 0.18 mmol) afforded 2c (27 mg, 84%) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 1H NMR (300 MHz, Chloroform-d) $\delta$ 7.39-7.49 (m, 3H), 7.01-7.05 (m, 1H), 5.54 (d, $J = 17.4$ Hz, 1H), 5.24 (d, $J = 11$ Hz, 1H), 3.79 (s, 3H); $^{13}$C NMR (75 MHz, Chloroform-d) $\delta$ 172.61, 158.78, 135.38, 133.30, 128.81, 128.02, 119.86, 115.21, 115.15, 55.52.

**HRMS (ESI)** (M+Na)$^+$ calcd. for C$_{10}$H$_{10}$NaO$_3$ is 201.0522 obsd. 201.0529.
3-Methyl-2-vinylbenzoic acid (Table 1, entry 2d)

Following the general procedure, 6-methyl-2-iodoacetophenone (50 mg, 0.19 mmol) afforded **2d** (24 mg, 77%) after purification by silica gel column chromatography using ethyl acetate:hexane (20:80).\(^1\)H NMR (600 MHz, Chloroform-d) δ 7.81 (d, \(J = 7.4\) Hz, 1H), 7.42 (d, \(J = 7.20\) Hz, 1H), 7.25-7.28 (m, 1H), 7.05-7.10 (m, 1H), 5.55 (d, \(J = 11.4\) Hz, 1H), 5.28 (d, \(J = 17.8\) Hz, 1H), 2.40 (s, 3H);\(^{13}\)C NMR (150 MHz, Chloroform-d) δ 173.47, 139.81, 136.92, 135.19, 134.38, 129.41, 128.12, 126.67, 119.07, 20.88.

**HRMS (ESI)** (M-H)\(^+\) calcd. for C\(_{10}\)H\(_9\)O\(_2\)\(^+\) is 161.0608 obsd. 161.0597.

![3-Methyl-2-vinylbenzoic acid structure](image)

3,5-Dimethyl-2-vinylbenzoic acid (Table 1, entry 2e)

Following the general procedure, 4,6-dimethyl-2-iodoacetophenone (50 mg, 0.18 mmol) afforded **2e** (23 mg, 71%, mp: 102-104 °C) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70).\(^1\)H NMR (600 MHz, Chloroform-d) δ 7.61 (s, 1H), 7.24 (s, 1H), 7.01-7.06 (m, 1H), 5.51 (dd, \(J = 11.4, 1.6\) Hz, 1H) 5.26 (dd, \(J = 17.8, 1.6\) Hz, 1H), 2.37 (s, 1H), 2.36 (s, 3H);\(^{13}\)C NMR (150 MHz, Chloroform-d) δ 173.17, 136.82, 136.75, 136.38, 135.22, 135.06, 129.16, 128.56, 118.88, 20.83, 20.82.

**HRMS (ESI)** (M-H)\(^+\) calcd. for C\(_{11}\)H\(_{11}\)O\(_2\)\(^+\) is 175.0764 obsd. 175.0753

![3,5-Dimethyl-2-vinylbenzoic acid structure](image)

4-Methoxy-2-vinylbenzoic acid (Table 1, entry 2f)

Following the general procedure, 5-methoxy-2-iodoacetophenone (50 mg, 0.18 mmol) afforded **2f** (21 mg, 65%) after purification by silica gel column chromatography using ethyl acetate:hexane (20:80).\(^1\)H NMR (300 MHz, Chloroform-d) δ 8.0 (d, \(J = 8.8\) Hz, 1H), 7.51-7.60 (m, 1H), 6.99 (s, 1H), 6.776.81 (m, 1H), 5.59 (d, \(J = 17.4\) Hz, 1H), 5.32 (d, \(J = 10.9\) Hz, 1H), 3.82 (s, 3H);\(^{13}\)C NMR (75 MHz, Chloroform-d) δ 171.97, 163.25, 143.37, 136.58, 133.84, 119.57, 116.61, 112.85, 112.81, 55.44.
HRMS (ESI) (M-H)^+ calcd. for C_{10}H_{9}O_{3}^+ is 177.0557  obsd. 177.0546.

4,5-Dimethoxy-2-vinylbenzoic acid (Table 1, entry 2g)

Following the general procedure, 4,5-dimethoxy-2-iodoacetophenone (50 mg, 0.16 mmol) afforded 2g (19 mg, 56%, mp: 167-169 °C) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70).\(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 7.64-7.69 (m, 1H), 7.60 (s, 1H), 7.07 (s, 1H), 5.63 (dd, \(J=17.4, 1.1\) Hz, 1H), 5.37 (dd, \(J=11.0, 1.1\) Hz, 1H), 4.01 (s, 3H), 3.96 (s, 3H); \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 172.07, 152.87, 148.09, 136.18, 135.71, 119.00, 115.50, 113.51, 109.67, 56.06, 56.02.

HRMS (ESI) (M-H)^+ calcd. for C_{11}H_{11}O_{4}^+ is 207.0663 obsd. 207.0651.

4-Fluoro-2-vinylbenzoic acid (Table 1, entry 2h)

Following the general procedure, 5-fluoro-2-iodoacetophenone (50 mg, 0.19 mmol) afforded 2h (25 mg, 79%) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70).\(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 7.89-7.91 (m, 1H), 7.44-7.51 (m, 2H), 7.22 (td, \(J=8.46, 2.64\) Hz, 1H), 5.86 (d, \(J=17.46\) Hz, 1H), 5.41 (d, \(J=11.7\) Hz, 1H); \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 168.02, 164.47 (\(J = 247.5\) Hz), 141.84, 134.72, 133.57 (\(J = 9\) Hz), 126.43, 118.40, 115.07 (\(J = 21\) Hz), 113.46.

HRMS (ESI) (M-H)^+ calcd. for C_{9}H_{6}FO_{2}^+ is 165.0357 obsd. 165.0346.

5-Chloro-2-vinylbenzoic acid (Table 1, entry 2i)
Following the general procedure, 4-chloro-2-iodoacetophenone (50 mg, 0.18 mmol) afforded 2i (22 mg, 67%, mp: 93-95 °C) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.05 (d, $J$=2.0 Hz, 1H), 7.52-7.61 (m, 3H), 7.51 (d, $J$=17.4, 1.1 Hz, 1H), 5.45 (d, $J$=11.04, 1.1 Hz, 1H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 170.88, 139.06, 134.89, 133.41, 133.16, 131.10, 128.98, 128.28, 117.55. HRMS (ESI) (M-H)$^+$ calcd. for C$_9$H$_6$ClO$_2^+$ is 181.0061 obsd. 181.0050.

2-(Prop-1-en-1-yl)benzoic acid (Table 1, entry 2j) $E:Z = 10.8:1$

Following the general procedure, 2-iodopropiophenone (50 mg, 0.19 mmol) afforded 2j (26 mg, 83%) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.02 (d, $J$= 7.8 Hz, 1H), 7.56 (d, $J$= 7.8 Hz, 1H), 7.48 – 7.51 (m, 1H), 7.26 – 7.31 (m, 2H), 6.19 (dq, $J$ = 15.6, 6.6 Hz, 1H), 1.95 (dd, $J$ = 6.6, 1.8 Hz, 4H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 173.16, 140.68, 132.89, 131.27, 129.83, 129.05, 127.50, 126.73, 126.57, 18.81. HRMS (ESI) (M-H)$^+$ calcd. for C$_{10}$H$_9$O$_2^+$ is 161.0608 obsd. 161.0597.

5-Methyl-2-(prop-1-en-1-yl)benzoic acid (Table 1, entry 2k) $E:Z = 23.2:1$

Following the general procedure, 4-methyl-2-iodopropiophenone (50 mg, 0.18 mmol) afforded 2k (28 mg, 87%, mp: 109-111 °C) after purification by silica gel column chromatography using ethyl acetate:hexane (20:80). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 7.82 (s, 1H), 7.45 (d, $J$ = 8.4 Hz, 1H), 7.31 (dd, $J$ = 7.8, 1.8 Hz, 1H), 7.23 (dd, $J$ = 15.6, 1.8 Hz, 1H), 6.15 (dq, $J$ = 15.6, 6.6 Hz, 1H), 2.37 (s, 3H), 1.93 (dd, $J$ = 6.6, 1.8 Hz, 3H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 173.27, 137.85, 136.40, 133.82, 131.61, 129.60, 128.21, 127.45, 126.44, 20.91, 18.85. HRMS (ESI) (M-H)$^+$ calcd. for C$_{11}$H$_{11}$O$_2^+$ is 175.0764 obsd. 175.0752.
2-(But-1-en-1-yl)benzoic acid (Table 1, entry 2l) \( E:Z = 8.7:1 \)

Following the general procedure, 2-iodobutyrophenoene (50 mg, 0.18 mmol) afforded 2l (26 mg, 81%) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70).\(^1\)H NMR (600 MHz, Chloroform-d) \( \delta \) 8.02 (d, \( J = 7.8 \) Hz, 1H), 7.58 (d, \( J = 7.8 \) Hz, 1H), 7.50 (t, \( J = 7.2 \) Hz, 1H), 7.30 (t, \( J = 7.2 \) Hz, 1H), 7.26 (d, \( J = 15.6 \) Hz, 1H), 6.19 – 6.24 (m, 1H), 2.28 – 2.33 (m, 2H), 1.12 – 1.14 (m, 3H); \(^13\)C NMR (150 MHz, Chloroform-d) \( \delta \) 172.97, 140.72, 135.96, 132.90, 131.28, 127.64, 127.50, 126.77, 126.58, 26.32, 13.56.

**HRMS (ESI)** (M-H)\(^+\) calcd. for C\(_{11}\)H\(_{11}\)O\(_2\)\(^+\) is 175.0764 obsd. 175.0753.

![But-1-en-1-ylbenzoic Acid](image)

2-(Pent-1-en-1-yl)benzoic acid (Table 1, entry 2m) \( E:Z = 8.4:1 \)

Following the general procedure, 2-iodovalerophenone (50 mg, 0.17 mmol) afforded 2m (26 mg, 79%) after purification by silica gel column chromatography using ethyl acetate:hexane (30:70).\(^1\)H NMR (600 MHz, Chloroform-d) \( \delta \) 8.02 (dd, \( J = 7.8, 1.2 \) Hz, 1H), 7.58 (dd, \( J = 7.8, 1.2 \) Hz, 1H), 7.50 (td, \( J = 7.8, 1.2 \) Hz, 1H), 7.26 – 7.31 (m, 1H), 7.20 (d, \( J = 15.6 \) Hz, 1H), 6.15 – 6.20 (m, 1H), 2.26 (qd, \( J = 7.2, 1.2 \) Hz, 2H), 1.51 – 1.57 (m, 2H), 0.98 (t, \( J = 7.2 \) Hz, 3H); \(^13\)C NMR (150 MHz, Chloroform-d) \( \delta \) 173.06, 140.73, 134.32, 132.90, 131.27, 128.73, 126.78, 126.59, 126.58, 26.32, 13.77.

**HRMS (ESI)** (M-H)\(^+\) calcd. for C\(_{12}\)H\(_{13}\)O\(_2\)\(^+\) is 189.0921 obsd. 189.0910.

![Pent-1-en-1-ylbenzoic Acid](image)

2-(Hex-1-en-1-yl)benzoic acid (Table 1, entry 2n) \( E:Z = 7.1:1 \)

Following the general procedure, 2-iodohexanophenone (50 mg, 0.17 mmol) afforded 2n (25 mg, 74%) after purification by silica gel column chromatography using ethyl acetate:hexane
(30:70). $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.01 (dd, $J = 7.8$, 1.2 Hz, 1H), 7.57 (dd, $J = 7.8$, 1.2 Hz, 1H), 7.49 (td, $J = 7.8$, 1.2 Hz, 1H), 7.31 – 7.28 (td, $J = 7.8$, 1.2 Hz, 1H), 7.26 (d, $J = 15.6$ Hz, 1H), 6.14 – 6.19 (m, 1H), 2.26 – 2.30 (m, 2H), 1.47 – 1.52 (m, 2H), 1.37 – 1.43 (m, 2H), 0.93 – 0.95 (m, 3H); $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 172.93, 140.74, 134.52, 132.88, 131.27, 128.57, 127.53, 126.76, 126.57, 32.90, 31.38, 22.27, 13.98.

HRMS (ESI) (M-H)$^-$ calcd. for C$_{13}$H$_{15}$O$_2$ is 203.1077 obsd. 203.1066.

6. References

1. Friedel craft acylation reaction

Note (*): In the reference 3, Glorius et al reported [Rh(III)Cp*]-catalyzed ortho-iodination of acetophenone molecule and got 62% yield of 2-idoacetophenone. We follow the same procedure and reagent system for other acetophenones derivatives to prepare ortho iodinated acetophenones which are new and not reported in this paper.

7. Recyclability experiments:

In order to investigate the stability and recyclability of the Pd/C catalyst, we conducted a reaction of 2-idoacetophenone (1a) under standard conditions. After the reaction was completed, the Pd/C catalyst was recovered from the reaction mixture using centrifugation. It was washed with methanol and acetone and a subsequent reaction cycle was performed with the dried catalyst. To our delight, the catalyst showed excellent recyclability and could be reused up to six cycles (Figure S1).
Figure S1. Recyclability of Pd/C catalyst

8. NMR spectra of starting materials
The image contains two NMR spectra, each with labeled peaks and chemical structures.

For spectrum 1e:
- Chemical structure with peaks at 206.47, 144.34, 140.29, 136.83, 134.20, 130.95, 89.33, 77.42, 77.50, and 31.04 ppm.

For spectrum 1f:
- Chemical structure with peaks at 7.97, 2.63, 7.90, and 7.92 ppm.

The spectra are associated with compounds labeled as 1e and 1f.
UPLC SPECTRA
9. NMR spectra of final products

[Diagram showing NMR spectra of compounds 2a and 2a COOH]
$2l$, $E:Z = 8.7:1$
$^{1}$H NMR (CDCl$_3$, 600 MHz)

$^{13}$H NMR (CDCl$_3$, 150 MHz)
10. HR-MS of final products
UPLC SPECTRA