

## Supporting Information for

### Synthesis of Isocoumarins *via* Pd/C mediated Reaction of *o*-Iodobenzoic acid with Terminal alkynes

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## Experimental Section

**General methods:** Unless stated otherwise, reactions were performed under nitrogen atmosphere. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230-400 mesh) using distilled petroleum ether, ethyl acetate, dichloromethane, chloroform and methanol.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were determined in  $\text{CDCl}_3$ ,  $\text{DMSO-}d_6$  or  $\text{MeOH-}d_4$  solution on 200 and 50 MHz spectrometers, respectively. Proton chemical shifts ( $\delta$ ) are relative to tetramethylsilane (TMS,  $\delta = 0.00$ ) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants ( $J$ ) are given in hertz. Infrared spectra were recorded on a FT-IR spectrometer. Melting points were determined by using melting point apparatus and are uncorrected. Thermal analysis data [Differential Scanning Calorimetry (DSC)] was generated with the help of DSC-50 detector. MS spectra were obtained on a mass spectrometer. Chromatographic purity by HPLC was determined by using area normalization method and the condition specified in each case: column, mobile phase (range used), flow rate, detection wavelength, retention times. Microanalyses were performed using a C H N S/O analyzer.

**Preparation of 5-nitro-2-iodobenzoic acid:**<sup>1a</sup> A mixture of  $\text{HNO}_3$  (1.5 mL) and  $\text{H}_2\text{SO}_4$  (4.5 mL) was added to pre-cooled *o*-iodobenzoic acid (1.0 g, 4.03 mmol) slowly at  $0^\circ\text{C}$  and the mixture was stirred at the same temperature for 15 min. and then at  $25^\circ\text{C}$  for 30 min. The mixture was then stirred at  $130\text{-}135^\circ\text{C}$  for 1 h, cooled to room temperature and poured into ice-cold water with stirring. The light yellow solid separated was filtered and dried to afford the desired product (1.0 g, 85% yield); mp  $200\text{-}202^\circ\text{C}$  (lit<sup>1a</sup>  $197\text{-}198^\circ\text{C}$ );  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.56 (d,  $J = 3.0$  Hz, 1H), 8.29 (d,  $J = 8.6$  Hz, 1H), 8.0 (dd,  $J_1 = 8.6$  Hz,  $J_2 = 2.6$  Hz, 1H); Mass ( $m/z$ ) 293 ( $M+1$ , 100); HPLC 97%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M  $\text{KH}_2\text{PO}_4$  (pH 3.0): B,  $\text{CH}_3\text{CN}$ , gradient (T/%B): 0/20, 3/20, 16/75, 22/75, 23/20, 25/20, flow rate 1.5 mL/min, UV 220 nm, retention time 3.42 min.

**Preparation of 2-iodo-3-methoxybenzoic acid:**<sup>1b</sup> A solution of NaNO<sub>2</sub> (0.45g, 6.5 mmol) in water (3 mL) was added to a mixture of 2-amino-3-methoxybenzoic acid (1g, 5.98 mmol), 25% HCl (8 mL) and ice (10g) at 0-5 °C. The mixture was stirred at 0 °C for 20 min and then added slowly to a stirred solution of KI (15.88g, 59.32 mmol) in water (35 mL) at 0 °C. The reaction mixture was stirred for 12h at 25 °C and an aqueous solution (1M) of NaHCO<sub>3</sub> (140 mL) was added to it. The mixture was then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 mL), organic layers collected, combined and washed with water (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by column chromatography using petroleum ether/EtOAc to give the desired product (0.5 g, 30% yield); mp 144-145 °C (lit<sup>1c</sup> 148-149 °C); <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) δ 7.41 (d, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 3.91 (s, OCH<sub>3</sub>); Mass (m/z) 278 (M+1, 100%); HPLC 97.32%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.05% TFA: B, CH<sub>3</sub>CN, gradient (T/%B): 0/30, 4/30, 14/80, 18/80, 21/30, 22/30, flow rate 1.5 mL/min, UV 220 nm, retention time 7.04 min.

**2-Iodo-4,5-dimethoxybenzoic acid**<sup>1d</sup> was prepared in 70% yield via diazotization of 2-amino-4,5-dimethoxybenzoic acid using NaNO<sub>2</sub> in HCl followed by the treatment with KI according to the procedure as described above; DSC 195.5 °C (lit<sup>1e</sup> 204.5-205.5 °C); <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (s, 1H), 7.44 (s, 1H), 3.94 (s, OCH<sub>3</sub>), 3.92 (s, OCH<sub>3</sub>); Mass (m/z) 308.5 (M<sup>+</sup>, 100%); HPLC 94.56%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01M KH<sub>2</sub>PO<sub>4</sub> (pH 3.0): B, CH<sub>3</sub>CN, gradient (T/%B): 0/30, 2/30, 12/80, 18/80, 19/30, 20/30, flow rate 1.5 mL/min, UV 222 nm, retention time 5.91 min.

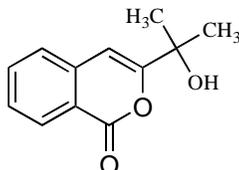
#### **Preparation of isocoumarins (IV & V):**

**A typical procedure for the preparation of IVe:** A mixture of *o*-iodobenzoic acid **I** (0.3 g, 1.21 mmol), 10% Pd/C (35 mg, 0.033 mmol), PPh<sub>3</sub> (38 mg, 0.14 mmol), CuI (14 mg, 0.07 mmol) and triethylamine (0.61g, 0.84 mL, 6.05 mmol) in EtOH (15 mL) was stirred at 25 °C for 30 min under nitrogen. The acetylenic compound **IIe** i.e. 1-hexyne (0.199g, 0.28 mL, 2.42 mmol) was added slowly to the mixture with stirring. The reaction mixture was then stirred at 80 °C for 16 h, cooled to room temperature, diluted with EtOAc (50 mL) and filtered through celite. The filtrate was collected and concentrated under

vacuum. The residue was purified by column chromatography (petroleum ether-EtOAc) to afford the desired product (0.146g, 60% yield).

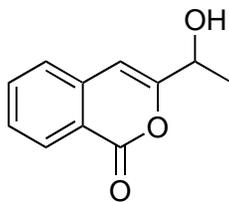
Similar reaction conditions were employed for the preparation of other isocoumarins and the yields of products for each reaction are listed in Table 2 and 3 in the main text.

### 3-(1-Hydroxy-1-methylethyl)isochromen-1-one (IVa):



White solid; mp 66-68 °C (lit<sup>2</sup> mp 70-72°C); <sup>1</sup>HNMR (200 MHz, CDCl<sub>3</sub>) δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 6.5 Hz, 1H), 7.49-7.26 (m, 2H), 6.62 (s, 1H, CH=C), 1.99 (bs, 1H, OH), 1.60 (s, 6H, 2CH<sub>3</sub>); IR (KBr, cm<sup>-1</sup>): 3381 (bs, OH), 1733 (C=O); Mass (m/z) 204 (M<sup>+</sup>, 50%), 189 (M<sup>+</sup>-15, 100%); <sup>13</sup>CNMR (50 MHz, CDCl<sub>3</sub>) 162.4 (C=O), 162.3, 137.2, 134.6, 129.2, 127.7, 125.7, 119.8, 99.7 (CH=C), 70.5 (CMe<sub>2</sub>OH), 30.9 (CH<sub>3</sub>), 28.1 (CH<sub>3</sub>); UV (MeOH, nm) 323.0, 272.0, 263.0, 239.0, 228.0; HPLC 97.3%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B, CH<sub>3</sub>CN, gradient (T/%B): 0/20, 3/20, 15/80, 20/80, 21/20, 22/20, flow rate 1.5 mL/min, UV 230 nm, retention time 8.4 min; Elemental analysis found C, 70.67; H, 5.90; C<sub>12</sub>H<sub>12</sub>O<sub>3</sub> requires C, 70.57; H, 5.92.

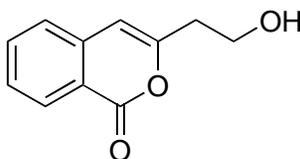
### 3-(1-Hydroxyethyl)isochromen-1-one (IVb):



colourless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.25 (d, *J* = 7.8 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 6.55 (s, 1H, CH=C), 4.60-4.55 (m, 1H, CH(OH)), 1.87 (bs, 1H, OH), 1.47 (d, *J* = 6.4 Hz, 3H, CH<sub>3</sub>), IR (neat, cm<sup>-1</sup>) 3382 (bs, OH), 1710 (C=O); M/Z (CI Mass) 190 (M<sup>+</sup>), 177 (M<sup>+</sup>-13), 149 (M<sup>+</sup>-41, 100%); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>) 161.8 (C=O), 154.8, 137.0, 135.0, 129.6, 128.2, 125.8, 120.2, 101.4

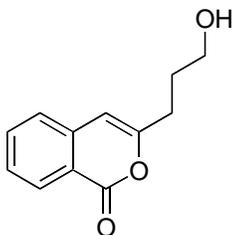
(CH=C), 58.5 (CHOH), 23.8 (CH<sub>3</sub>); UV (MeOH, nm) 322.0, 273.0, 263.0, 255.0, 239.5, 229.0; HPLC 98.1%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M KH<sub>2</sub>PO<sub>4</sub>: B, CH<sub>3</sub>CN, gradient (T/%B): 0/25, 2/25, 12/80, 18/80, 19/25, 20/25, flow rate 1.5 mL/min, UV 210 nm, retention time 5.6 min; Elemental analysis found C, 69.41; H, 5.31; C<sub>11</sub>H<sub>10</sub>O<sub>3</sub> requires C, 69.46; H, 5.30.

**3-(2-Hydroxyethyl)isochromen-1-one (IVc):**



White solid; mp: 60-62 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.25 (d, *J* = 7.8 Hz, 1H); 7.66 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.3 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 6.38 (s, 1H, CH=C), 4.00 (t, *J* = 6.2 Hz, 2H, CH<sub>2</sub>), 2.79 (t, *J* = 6.0 Hz, 2H, CH<sub>2</sub>), 1.69 (bs, -OH); IR (KBr, cm<sup>-1</sup>) 3072 (bs, OH), 1727 (C=O); M/Z (ES Mass) 191 (M+1, 100%); <sup>13</sup>CNMR (50 MHz, CDCl<sub>3</sub>) 163.0 (C=O), 154.8, 136.2, 134.8, 129.6, 127.7, 127.3, 120.0, 104.8 (CH=C), 59.4 (CH<sub>2</sub>), 36.7 (CH<sub>2</sub>); UV (MeOH, nm) 325.0, 273.0, 264.0, 240.0, 229.0; HPLC 95.9%, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M KH<sub>2</sub>PO<sub>4</sub>: B, CH<sub>3</sub>CN, Gradient (T/%B): 0/20, 3/20, 15/80, 20/80, 21/20, 22/20, flow rate 1.5 mL/min, UV 235 nm, retention time 6.96 min; Elemental analysis found C, 69.39; H, 5.33; C<sub>11</sub>H<sub>10</sub>O<sub>3</sub> requires C, 69.46; H, 5.30.

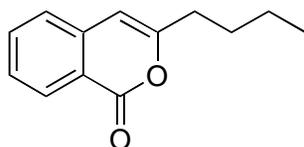
**3-(3-Hydroxypropyl)isochromen-1-one (IVd):**



White solid; mp 64-66 °C; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 8.25 (d, *J* = 8.1 Hz, 1H), 7.69-7.65 (m, 1H), 7.48-7.44 (m, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 6.30 (s, 1H, CH=C), 3.75 (t, *J* = 6.2 Hz, 2H, CH<sub>2</sub>), 2.67 (t, *J* = 7.5 Hz, 2H, CH<sub>2</sub>), 2.02-1.95 (m, 2H, CH<sub>2</sub>), 1.56 (1H, D<sub>2</sub>O exchangeable, OH); IR (KBr, cm<sup>-1</sup>): 3435 (bs, OH), 1738 (C=O), 1656; Mass (m/z)

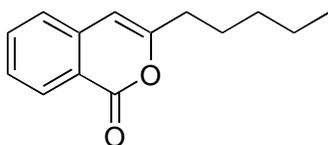
205 ( $M^{+}+1$ , 100%), 187 ( $M^{+}-18$ , 50%);  $^{13}\text{C}$ NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  162.2 (C=O), 157.4, 137.5, 134.7, 129.4, 127.6, 125.0, 120.0, 103.3 (CH=C), 61.5 ( $\text{CH}_2$ ), 29.9 ( $\text{CH}_2$ ), 15.7 ( $\text{CH}_2$ ); UV (MeOH, nm) 326.0, 273.0, 264.0, 240.0, 229.0; HPLC: 99.3%, Inertsil ODS 3V (150 x 4.6 mm) mobile phase 0.01M  $\text{KH}_2\text{PO}_4$ :  $\text{CH}_3\text{CN}$ , 0/25, 3/25, 12/80, 20/80, 21/25, 22/25; 1.5 mL / min, UV 230 nm, retention time 6.33 min; Elemental analysis found C, 70.68; H, 5.80;  $\text{C}_{12}\text{H}_{12}\text{O}_3$  requires C, 70.57; H, 5.92.

### 3-Butylisochromen-1-one (IVe):



Brown solid; mp 46-48°C (lit<sup>3</sup> mp 49.5-50.5 °C);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.26-8.24 (m, 1H), 7.68-7.64 (m, 1H), 7.46-7.42 (m, 1H), 7.34 (d,  $J = 7.8$  Hz, 1H), 6.25 (s, 1H, CH=C), 2.53 (t,  $J = 7.52$  Hz, 2H,  $\text{CH}_2$ ), 1.74-1.66 (m, 2H,  $\text{CH}_2$ ), 1.46-1.36 (m, 2H,  $\text{CH}_2$ ), 0.95 (t,  $J = 7.52$  Hz, 3H,  $\text{CH}_3$ ); IR (Neat,  $\text{cm}^{-1}$ ) 2958, 1731 (C=O), 1657; M/Z (ES Mass) 203 ( $M+1$ , 100%);  $^{13}\text{C}$ NMR (50 MHz,  $\text{CDCl}_3$ ) 158.3 (C=O), 137.7, 135.9, 134.7, 130.1, 129.5, 127.5, 123.0, 102.9 (CH=C), 37.6 ( $\text{CH}_2$ ), 28.9 ( $\text{CH}_2$ ), 22.1 ( $\text{CH}_2$ ), 13.7 ( $\text{CH}_3$ ); UV (MeOH, nm) 328.0, 273.5, 264.0, 240.0, 229.0; HPLC 99.8%, column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M  $\text{KH}_2\text{PO}_4$ : B,  $\text{CH}_3\text{CN}$ , gradient (T/%B): 0/50, 2/50, 8/80, 18/80, 19/50, 20/50, flow rate: 1.5 mL/min, UV 230 nm, retention time 10.4 min; Elemental analysis found C, 77.46; H, 6.90;  $\text{C}_{13}\text{H}_{14}\text{O}_2$  requires C, 77.20; H, 6.98.

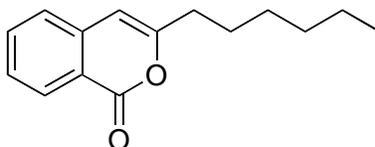
### 3-Pentylisochromen-1-one<sup>4</sup> (IVf):



Colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (dd,  $J_1 = 7.5$ ,  $J_2 = 0.5$  Hz, 1H), 7.68-7.64 (m, 1H), 7.46-7.42 (m, 1H), 7.34 (d,  $J = 7.8$  Hz, 1H), 6.25 (s, 1H, CH=C), 2.52 (t,  $J = 7.5$  Hz, 2H,  $\text{CH}_2$ ), 1.72 (t,  $J = 7.5$  Hz, 2H,  $\text{CH}_2$ ), 1.38-1.35 (m, 4H, 2 $\text{CH}_2$ ), 0.93-0.89

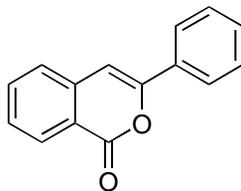
(m, 3H, CH<sub>3</sub>); IR (Neat, cm<sup>-1</sup>) 2929, 1730 (C=O), 1656, 1108; M/Z (ES Mass) 217 (M+1, 100%); <sup>13</sup>CNMR (60 MHz, CDCl<sub>3</sub>) 162.9 (C=O), 158.2, 137.5, 134.6, 129.3, 127.4, 124.9, 120.0, 102.8 (CH=C), 33.4 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>), 22.3 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>); UV (MeOH, nm) 327.0, 273.5, 264.5, 229.5; HPLC 98.4%, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile Phase: A, 0.01 M KH<sub>2</sub>PO<sub>4</sub>, B: CH<sub>3</sub>CN, Gradient (T/%B): 0/50, 2/50, 8/80, 18/80, 19/50, 20/50, flow Rate: 1.5 mL/min, UV: 228nm, retention time 9.1 min; Elemental analysis found C, 77.86; H, 7.45; C<sub>14</sub>H<sub>16</sub>O<sub>2</sub> requires C, 77.75; H, 7.46.

### 3-Hexylisochromen-1-one<sup>5</sup> (IVg):



Pale yellow oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.26-8.24 (m, 1H), 7.68-7.64 (m, 1H), 7.46-7.42 (m, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 6.25 (s, 1H, CH=C), 2.54-2.50 (m, 2H, CH<sub>2</sub>), 1.73-1.67 (m, 2H, CH<sub>2</sub>), 1.39-1.26 (m, 6H, 3CH<sub>2</sub>), 0.91-0.87 (m, 3H, CH<sub>3</sub>); IR (Neat, cm<sup>-1</sup>) 2929, 1732 (C=O), 1657, 1160; M/Z (ES Mass) 231 (M+1, 100%); <sup>13</sup>CNMR (50 MHz, CDCl<sub>3</sub>) 163.0 (C=O), 158.3, 137.6, 134.6, 129.4, 127.7, 127.4, 120.1, 102.8 (CH=C), 38.7 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 22.9 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>); UV (MeOH, nm) 328.0, 274.0, 264.5, 229.0, 204.5; HPLC 97.5%, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>, B: CH<sub>3</sub>CN, Gradient (T/%B): 0/50, 2/50, 8/80, 18/80, 19/50, 20/50, flow rate: 1.5 mL/min, UV: 228 nm, retention time 10.4 min; Elemental analysis found C, 78.32; H, 7.80; C<sub>15</sub>H<sub>18</sub>O<sub>2</sub> requires C, 78.23; H, 7.88.

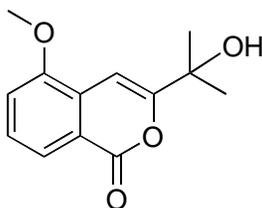
### 3-Phenylisochromen-1-one<sup>6a</sup> (IVh):



Light brown solid; mp 80-81°C (lit<sup>6b</sup> mp 86-86.5 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.29 (d, *J* = 7.8 Hz, 1H), 7.85-7.64 (m, 3H), 7.50-7.41 (m, 5H), 6.93 (s, 1H, CH=C); IR (Neat,

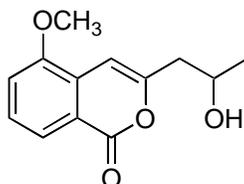
cm<sup>-1</sup>) 1738 (C=O), 1665; M/Z (ES Mass) 223 (M+1, 100%); Elemental analysis found C, 81.12; H, 4.53; C<sub>15</sub>H<sub>10</sub>O<sub>2</sub> requires C, 81.07; H, 4.54.

**3-(1-Hydroxy-1-methylethyl)-5-methoxyisochromen-1-one (Va):**



White Solid; DSC 101.86 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 (d, *J* = 6.4 Hz, 1H), 7.42 (t, *J* = 8.1 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 6.96 (s, 1H, CH=C), 3.93 (s, 3H, OCH<sub>3</sub>), 2.21 (bs, -OH), 1.60 (s, 6H, 2CH<sub>3</sub>); IR (KBr, cm<sup>-1</sup>) 3358, 1722, 1655; M/Z (ES Mass) 234 (M+1, 100%); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) 162.4 (C=O), 160.9, 154.2, 128.3, 127.7, 120.9, 120.8, 114.5, 94.3 (CH=C), 71.1 (CMe<sub>2</sub>OH), 55.8 (OCH<sub>3</sub>), 28.1 (2C, CH<sub>3</sub>); UV (MeOH, nm) 337.0, 257.0, 234.0; HPLC 98.9 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile Phase: A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B; CH<sub>3</sub>CN, Gradient (T/%B): 0/30, 2/30, 14/80, 20/80, 21/30, 22/30, flow rate: 1.5 ml/min, UV: 235 nm, retention time 6.41 min; Elemental analysis found C, 66.87; H, 6.00; C<sub>13</sub>H<sub>14</sub>O<sub>4</sub> requires C, 66.66; H, 6.02.

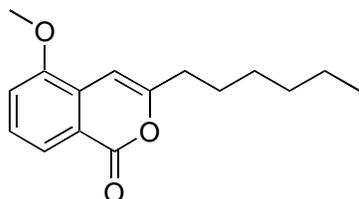
**3-(2-Hydroxypropyl)-5-methoxyisochromen-1-one (Vb):**



Gum; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.83 (d, *J* = 7.7 Hz, 1H), 7.41-7.37 (m, 1H), 7.2 (d, *J* = 7.8 Hz, 1H), 6.73 (s, 1H, CH=C), 4.33-4.30 (m, 1H, CHOH), 2.73-2.69 (m, 2H, CH<sub>2</sub>), 1.70 (bs, 1H, OH), 1.30 (d, *J* = 6.2 Hz, 3H, CH<sub>3</sub>), IR (neat, cm<sup>-1</sup>) 3408 (bs, OH), 1714 (C=O); M/Z (CI Mass) 235 (M<sup>+</sup>, 100%); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>) 162.8 (C=O), 154.2, 153.6, 127.9, 127.7, 120.7, 120.6, 114.4, 99.3 (CH=C), 66.2 (CHOH), 55.7 (OCH<sub>3</sub>), 43.33 (CH<sub>2</sub>), 22.3 (CH<sub>3</sub>); UV (MeOH, nm) 338.50, 279.50, 257.50, 235.50; HPLC 96.62%, column: inertsil ODS 3V (150 x 4.6) mm, mobile phase: A, 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B,

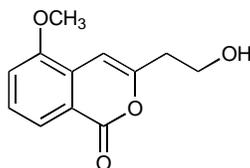
CH<sub>3</sub>CN, gradient (T/%B): 0/25, 2/25, 12/80, 18/80, 19/25, 20/25, flow rate 1.5 mL/min, UV 235 nm, retention time 6.8 min; Elemental analysis found C, 66.56; H, 6.08; C<sub>13</sub>H<sub>14</sub>O<sub>3</sub> requires C, 66.66; H, 6.02.

### 3-Hydroxy-5-methoxyisochromen-1-one (Vc):



White solid; DSC: 77.38 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84-7.82 (m, 1H), 7.37 (t, *J* = 8.1 Hz, 1H), 7.12-7.10 (m, 1H), 6.61 (s, 1H, CH=C), 3.92 (s, 3H, OCH<sub>3</sub>), 1.65 (t, *J* = 7.6 Hz, 2H, CH<sub>2</sub>), 1.72-1.58 (m, 2H, CH<sub>2</sub>) 1.37-1.29 (m, 6H), 0.90-0.87 (m, 3H); IR (KBr, cm<sup>-1</sup>) 1720 (C=O), 1654; M/Z (ES Mass) 261 (M+1, 100%); <sup>13</sup>CNMR (CDCl<sub>3</sub>, 50 MHz) 162.9 (C=O), 157.6, 153.6, 128.2, 127.6, 120.8, 120.7, 114.2, 97.1 (CH=C), 55.8 (OCH<sub>3</sub>), 33.7 (CH<sub>2</sub>), 31.4 (CH<sub>2</sub>), 28.6 (CH<sub>2</sub>), 26.9 (CH<sub>2</sub>), 22.4 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>); UV nm (MeOH) 339.5, 279.0, 257.0, 235.0; HPLC 99.5 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B; CH<sub>3</sub>CN, Gradient (T/%B): 0/60, 1/60, 5/80, 15/80, 19/60, 20/60, flow rate: 1.5 ml/min, UV 228 nm, retention time 8.0 min; Elemental analysis found C, 73.78; H, 7.72; C<sub>16</sub>H<sub>20</sub>O<sub>3</sub> requires C, 73.82; H, 7.74.

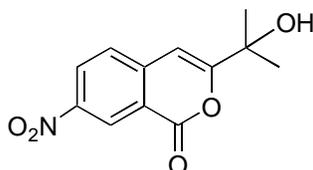
### 3-(2-Hydroxyethyl)-5-methoxyisochromen-1-one (Vc):



White solid; DSC: 112.83 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.85-7.82 (m, 1H), 7.40 (t, *J* = 8.1 Hz, 1H), 7.14-7.12 (m, 1H), 6.74 (s, 1H, CH=C), 4.01-3.98 (m, 2H, CH<sub>2</sub>), 3.92 (s, 3H, OCH<sub>3</sub>), 2.82-2.79 (m, 2H, CH<sub>2</sub>); IR (KBr, cm<sup>-1</sup>) 3383 (bs, OH), 1713 (C=O), 1652; M/Z (ES Mass) 221 (M+1, 100%); <sup>13</sup>CNMR (50 MHz, CDCl<sub>3</sub>) 162.8 (C=O), 154.0, 153.7, 128.1, 127.8, 121.04, 120.8, 114.5, 99.1 (CH=C), 59.7 (CH<sub>2</sub>), 55.8 (OCH<sub>3</sub>), 37.0 (CH<sub>2</sub>); UV nm (MeOH) 338.0, 257.5, 235.0; HPLC 99.7 %, Column: Inertsil ODS 3V

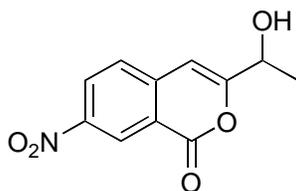
(150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>: B; CH<sub>3</sub>CN, Gradient (T/%B): 0/25, 5/25, 12/80, 18/80, 19/25, 20/25, flow rate: 1.5 ml/min, UV 235 nm, retention time 8.1 min; Elemental analysis found C, 65.31; H, 5.50; C<sub>12</sub>H<sub>12</sub>O<sub>4</sub> requires C, 65.45; H, 5.49.

**3-(1-Hydroxy-1-methylethyl)-7-nitroisochromen-1-one (Ve):**



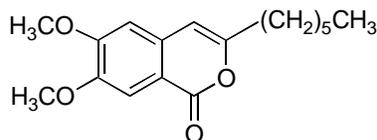
Yellow solid, mp 192-194 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.12 (s, 1H), 8.50 (d, *J* = 6.2 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 6.78 (s, 1H, CH=C), 2.17 (bs, -OH), 1.62 (s, 6H, 2CH<sub>3</sub>); IR (KBr, cm<sup>-1</sup>) 3503 (bs, OH), 1719 (C=O), 1643; M/Z (ES Mass) 249 (M+1, 100%); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 50 MHz) 165.9 (C=O), 158.9, 149.6, 142.3, 129.1, 127.3, 125.7, 120.6, 99.1 (CH=C), 71.3 (CMe<sub>2</sub>OH), 28.3 (2C, CH<sub>3</sub>); UV nm (MeOH) 330.5, 223.5; HPLC 99.40 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>: B; CH<sub>3</sub>CN, Gradient (T/%B): 0/30, 2/30, 12/80, 18/80, 19/30, 20/30 flow rate: 1.5 ml/min, UV: 223 nm, retention time 6.52 min; Elemental analysis found C, 57.66; H, 4.47; N, 5.65; C<sub>12</sub>H<sub>11</sub>NO<sub>5</sub> requires C, 57.83; H, 4.45; N, 5.62.

**3-(2-Hydroxyethyl)-7-nitroisochromen-1-one (Vf):**



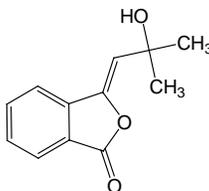
Gum; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.31 (s, 1H), 7.69 (d, *J*<sub>1</sub> = 8.1 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 6.54 (s, 1H, CH=C), 4.67-4.62 (m, 1H, CHOH), 1.85 (bs, 1H, OH), 1.48 (d, *J* = 6.9 Hz, 3H, CH<sub>3</sub>); IR (neat, cm<sup>-1</sup>) 3380 (bs, OH), 1715 (C=O); M/Z (CI Mass) 237 (M<sup>+</sup>, 100); Elemental analysis found C, 56.26; H, 3.82; N, 5.71; C<sub>11</sub>H<sub>9</sub>NO<sub>5</sub> requires C, 56.17; H, 3.86; N, 5.96.

### 3-Hexyl-6,7-dimethoxy isochromen-1-one (Vg):



White solid, mp 92-94 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.62 (s, 1H), 6.73 (s, 1H), 6.18 (s, 1H, CH=C), 3.98 (s, 3H, OCH<sub>3</sub>), 3.96 (s, 3H, OCH<sub>3</sub>), 2.51 (t, *J* = 7.5 Hz, 2H, CH<sub>2</sub>), 1.73-1.65 (m, 3H), 1.56-1.27 (m, 5H), 0.89 (t, *J* = 6.8 Hz, 3H, CH<sub>3</sub>); IR (neat, cm<sup>-1</sup>) 1719 (C=O), 1655, 1608; M/Z (CI Mass) 291 (M<sup>+</sup>, 100%); <sup>13</sup>CNMR (CDCl<sub>3</sub>, 50 MHz) 163.1 (C=O), 157.3, 155.1, 149.2, 133.4, 113.1, 109.4, 105.7, 102.5 (CH=C), 56.2 (OCH<sub>3</sub>), 56.2 (OCH<sub>3</sub>), 33.5 (CH<sub>2</sub>), 31.5 (CH<sub>2</sub>), 28.7 (CH<sub>2</sub>), 26.9 (CH<sub>2</sub>), 22.5 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>); UV nm (MeOH) 279.0, 243.5; HPLC 98.4 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B; CH<sub>3</sub>CN, Gradient (T/%B): 0/50, 2/50, 8/80, 16/80, 19/50, 20/50, flow rate: 1.5 ml/min, UV 243 nm, retention time 8.86 min; Elemental analysis found C, 70.22; H, 7.67; C<sub>17</sub>H<sub>22</sub>O<sub>4</sub> requires C, 70.32; H, 7.64.

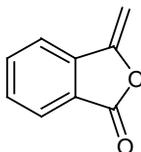
### 3-(2-Hydroxy-2-methylpropylidene)-3H-isobenzofuran-1-one<sup>6a</sup> (IIIa):



A mixture of *o*-iodobenzoic acid **I** (0.37 g, 1.49 mmol), 10% Pd/C (47 mg, 0.044 mmol), PPh<sub>3</sub> (46 mg, 0.17 mmol), CuI (17 mg, 0.09 mmol) and triethylamine (0.75g, 7.42 mmol) in 1,4-dioxane (10 mL) was stirred at 25 °C for 30 min under nitrogen. The acetylenic compound **IIa** i.e. 2-methylbut-3-yn-2-ol (0.25g, 2.97 mmol) was added slowly to the mixture with stirring. The reaction mixture was then stirred at 80 °C for 16 h, cooled to room temperature, diluted with EtOAc (40 mL) and filtered through celite. The filtrate was collected and concentrated under vacuum. The residue was purified by column chromatography (petroleum ether-EtOAc) to afford the desired product, mp 120-122 °C (lit<sup>6a</sup> 91-92 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.91 (dd, *J* = 7.8 & 0.8 Hz, 1H), 7.72-7.68 (m, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.57-7.53 (m, 1H), 5.81 (s, 1H, CH=C), 2.55 (bs, 1H, OH), 1.53 (s, 6H, 2CH<sub>3</sub>); IR (neat, cm<sup>-1</sup>) 3313 (bs, OH), 1786 (C=O), 1684; M/Z (CI Mass) 204 (M<sup>+</sup>, 10%), 189 (M<sup>+</sup>-15, 40%), 147 (100%); UV nm (MeOH) 308.5, 259.5,

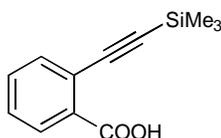
235.0; HPLC 99.36 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>: B; CH<sub>3</sub>CN, Gradient (T/%B): 0/20, 3/20, 15/80, 20/80, 21/20, 22/20 flow rate: 1.5 ml/min, UV: 235 nm, retention time 8.86 min.

**3-Methylene-3*H*-isobenzofuran-1-one<sup>6a</sup> (IIIb):**



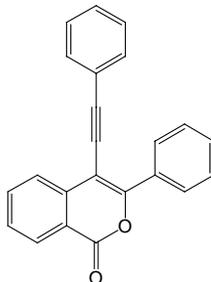
Yellow solid, mp 55-56 °C (lit<sup>6a</sup> 57-58 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 3.8 Hz, 1H), 7.64-7.54 (m, 2H), 5.24 (d, *J* = 0.9 Hz, 2H, CH<sub>2</sub>); IR (KBr, cm<sup>-1</sup>) 1780 (C=O), 1735, 1665; M/Z (CI Mass) 147 (M<sup>+</sup>, 10%), 133 (M<sup>+</sup>-14, 100%).

**2-Trimethylsilanylethynyl benzoic acid<sup>7</sup> (IIIbb):**



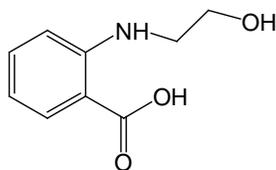
Light yellow solid; mp 95-97 °C (lit<sup>7</sup> 98-99 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.5 (bs, OH), 8.11 (t, *J* = 7.3 Hz, 1H), 7.63-7.40 (m, 3H), 0.29 (s, 9H, SiMe<sub>3</sub>); IR (neat, cm<sup>-1</sup>) 3120 (bs, OH), 2160 (w, -C≡C-), 1700 (C=O); M/Z (CI Mass) 218 (M<sup>+</sup>, 10%), 203 (M<sup>+</sup>-15, 100%).

**3-Phenyl-4-phenylethynyl isochromen-1-one<sup>8</sup> (IVhh):**



This compound was isolated as a side product in 25% yield during the synthesis of 3-phenylisochromen-1-one (**IVh**) from *o*-iodobenzoic acid and phenylacetylene; mp 141-142 °C (lit<sup>8</sup> 144-145 °C); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.34 (d, *J* = 8.1 Hz, 1H), 8.22 (d, *J* = 7.8 Hz, 2H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.86 (t, *J* = 7.2 Hz, 1H), 7.59 (t, 8.0 Hz, 1H), 7.53-7.48 (m, 5H), 7.39-7.37 (m, 3H); IR (KBr, cm<sup>-1</sup>) 1743 (C=O), 1606; M/Z (CI Mass) 322 (M<sup>+</sup>, 100%); <sup>13</sup>CNMR (CDCl<sub>3</sub>, 50 MHz) 160.8 (C=O), 156.6, 136.9, 135.0, 132.3, 131.3 (2C), 130.4, 129.4, 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 125.3, 122.7, 119.7, 99.7, 97.5, 82.7; UV nm (MeOH) 322.0, 268.0, 216.5; HPLC 97.83 %, Column: Inertsil ODS 3V (150 x 4.6) mm, mobile phase A: 0.01 M KH<sub>2</sub>PO<sub>4</sub>; B; CH<sub>3</sub>CN, Gradient (T/%B): 0/60, 1/60, 6/80, 18/80, 19/60, 20/60 flow rate: 1.5 ml/min, UV: 210 nm, retention time 10.09 min.

**2-(2-Hydroxy ethylamino)benzoic acid<sup>9</sup> (VI):**



This compound was isolated when the reaction of *o*-iodobenzoic acid (**I**) with terminal alkyne **IIa** was carried out in water instead of EtOH using 2-aminoethanol as a base maintaining the other reaction condition same as described above; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.96 (dd, *J* = 8.1 & 1.6 Hz, 1H), 7.41-7.37 (m, 1H), 6.74 (d, *J* = 8.6 Hz, 1H), 6.65-6.61 (m, 1H), 3.90-3.87 (m, 2H), 3.45-3.43 (m, 2H); IR (KBr, cm<sup>-1</sup>) 3360 (bs, NH & OH), 1673; M/Z (CI Mass) 181 (M<sup>+</sup>, 100%).

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