Supporting Information

Pd/C-mediated arylation followed by I₂-catalyzed hydration strategy: Preparation of functionalized novel indanone derivatives

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1. Experimental section	1
1.1 Chemistry	1
1.2 Pharmacology	20
1.2.1 Evaluation of PDE4B activity.....	20
1.3 Molecular Modeling Studies.....	21
1.3.1 Method.....	21

1. Experimental Section:

1.1 Chemistry

General methods

All reactions were carried out under an inert atmosphere using dry solvents, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), using UV light detection. Visualization of the spots on TLC plates was achieved either by UV light or by staining the plates in 2, 4 Di-Nitro Phenylhydrazine stain, Ninhydrin stain, KMNO₄ stain and charring on hot plate. Flash chromatography was performed on silica gel (230-400 mesh) using distilled hexane, ethyl acetate, dichloromethane. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ or acetone-*d*₆ solution by using (Wormhole-vnmrs) 400 MHz spectrometers. ¹H NMR and ¹³C NMR were recorded in CDCl₃ and DMSO-*d*₆ solvents on 400 MHz spectrometer, respectively at ambient temperature. Chemical shifts are reported as δ values relative to internal CHCl₃ δ 7.26 or TMS δ 0.0 and DMSO-*d*₆ δ 3.1 for ¹H NMR and CHCl₃ δ 77.0 and DMSO-*d*₆ δ 49.05 for ¹³C NMR. ¹H NMR data is recorded as follows: chemical shift [multiplicity, coupling constant(s) *J* (Hz), relative integral where multiplicity is defined as: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), m (multiplet), bs (broad singlet). FTIR spectra were recorded on Bruker (Alpha) spectrometer. Mass spectra were recorded on Micro Mass VG-7070H mass spectrometer for ESI and are given in mass units (*m/z*). High resolution mass spectra (HRMS) were obtained using either a TOF or a double focusing spectrometer.

Synthesis of Ethyl 5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (2):

To a stirred suspension of NaH (5.0 g, 60% in mineral oil, 125 mmol) in diethyl carbonate (20 mL) was added drop wise a solution of 5,6-dimethoxy-1-indanone (10 g, 52 mmol) in diethyl carbonate (70 mL). The mixture was then refluxed at 80 °C for 2 h, cooled to rt, and diluted with H₂O (200 mL). The aqueous phase was separated and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The oily residue was subjected to purification by column

chromatography to yield 11.68 g (85%) of **2** as a white crystalline solid. Physical characteristics are matching with literature report.

Reference: Emelen, K. V.; Wit, T. D.; Hoornaert, G. J.; Compennolle, F. *Tetrahedron* **2002**, 58, 4225-4236.

Synthesis of compound **4**

Step 1: Synthesis of Ethyl 5,6-dimethoxy-1-oxo-2-(prop-2-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (3**):** The ester **2** (10 g, 37.84 mmol) was dissolved in dry acetone (50 mL). To this was added anhydrous K_2CO_3 (6.2 g, 45.40 mmol) and the mixture was stirred at rt for 30 min. To the above stirred solution propargyl bromide (5.4 g, 45.40 mmol) was added drop wise over a period of 30 min and stirring was continued at rt for overnight. The K_2CO_3 was removed by filtration and the residue was washed with acetone. The filtrate was collected and concentrated under reduced pressure. The oily residue was purified by column chromatography to yield 10.30 g (90%) of **3** as a white crystalline solid; 1H NMR (400 MHz, $CDCl_3$): 1.3 (t, $J = 6.8$ Hz, CH_3 , 3H), 1.8 (s, CH, 1H), 2.8 (d, $J = 16.8$ Hz, CH_2 , 1H), 3.0 (d, $J = 17.2$ Hz, CH_2 , 1H), 3.3 (d, $J = 17.2$ Hz, $ArCH_2$, 1H), 3.6 (d, $J = 16.8$ Hz, $ArCH_2$, 1H), 3.9 (s, OCH_3 , 6H), 4.3-4.2 (q, OCH_2 , 2H), 6.9 (s, ArH , 1H), 7.2 (s, ArH , 1H),; mass (ES mass, m/z) 303 ($M+1$, 100%).

Step 2: Synthesis of 5,6-Dimethoxy-2-(prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (4**):** The alkyne **3** (5 g, 16.53 mmol) was dissolved in 150 mL of 30% NaOH: THF (1:1). This solution was refluxed for 12 h. THF was removed under reduced pressure, and the aqueous mixture was adjusted to pH of 7 using concentrated HCl. The aqueous phase was extracted with EtOAc (3 x 100 mL). The combined organic layer was dried over anhydrous Na_2SO_4 , filtered and concentration under reduced pressure gave the crude alkyne which was purified by column chromatography to afford 3 g (80%) of the alkyne **4** as a white crystalline solid. The physical properties are identical with literature reports. 1H NMR (400 MHz, $CDCl_3$): 1.8 (s, CH, 1H), 2.8 (dd, $J_1 = 17.2$ Hz, $J_2 = 3.8$ Hz, CH_2 , 1H), 3.0 (dd, $J_1 = 17.2$ Hz, $J_2 = 3.8$ Hz,

CH₂, 1H), 3.3 (dd, $J_1 = 16.8$ Hz, $J_2 = 4.0$ Hz, ArCH₂, 1H), 3.6 (dd, $J_1 = 16.8$ Hz, $J_2 = 4.0$ Hz ArCH₂, 1H), 3.9 (s, OCH₃, 6H), 6.9 (s, ArH, 1H), 7.2 (s, ArH, 1H); Mass (ES mass, m/z) 231 (M+1, 100%).

General Procedure for the Pd/C-mediated coupling of 2-(prop-2-ynyl)-2,3-dihydro-1H-inden-1-ones (3 and 4) with iodoarenes:

A mixture of iodo compound (0.33 mmol), 10% Pd/C (0.0022 mmol), PPh₃ (0.0086 mmol), CuI (0.022 mmol) and triethylamine (0.54 mmol) in EtOH (5 mL) was stirred for 30 min under a nitrogen atmosphere. To this mixture was added alkyne **3** or **4** (0.33 mmol) slowly and the mixture was refluxed and reaction was monitored by TLC. The mixture was then cooled to room temperature and filtered through celite; EtOH was removed under reduced pressure. The residue was diluted with water (50 mL) and extracted with EtOAc (3 x 25 mL). The organic layers were collected, combined, washed with water (2 x 25 mL), dried over anhydrous Na₂SO₄, filtered and concentrated. The residue thus obtained was purified by column chromatography using to afford the title compounds.

Spectral data of compounds synthesized

Ethyl-5,6-dimethoxy-1-oxo-2-(3-phenylprop-2-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (5a).

Off white solid; mp 118-120 °C; $R_f = 0.5$ (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 1.23 (t, $J = 6.8$ Hz, 3H), 3.12 (d, $J = 16.8$ Hz, 1H), 3.30 (d, $J = 17.2$ Hz, 1H), 3.34 (d, $J = 17.2$ Hz, 1H), 3.65 (d, $J = 16.8$ Hz, 1H), 3.91 (s, 3H), 3.98 (s, 3H), 4.19 (q, $J = 6.8$ Hz, 2H), 6.93 (s, 1H),

7.08-7.26 (m, 6H); ^{13}C NMR (CDCl_3) δ 14, 25.1, 29.6, 36.6, 56.1, 56.2, 59.7, 61.8, 82.4, 85, 105, 107.1, 123, 127.7, 127.8, 128.1 (2C), 131.4 (2C), 149.1, 149.6, 156.1, 170.3, 199.6; IR (neat, cm^{-1}) 1737, 1702; Mass (ES) m/z 379.3 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{23}\text{O}_5$ ($M+H$) $^+$ 379.1545 found 379.1534.

Ethyl 5,6-dimethoxy-1-oxo-2-(3-*o*-tolylprop-2-ynyl)-2,3-dihydro-1*H*-indene-2-carboxylate (5b).

Pale yellow Solid; mp 108-110 °C; R_f = 0.4 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.23 (t, J = 6.8 Hz, 3H), 2.07 (s, 3H), 3.15 (d, J = 16.8 Hz, 1H), 3.25 (d, J = 17.2 Hz, 1H), 3.37 (d, J = 17.2 Hz, 1H), 3.65 (d, J = 16.8 Hz, 1H), 3.91 (s, 3H), 3.97 (s, 3H), 4.19 (q, J = 6.8 Hz, 2H), 6.92 (s, 1H), 7.00-7.14 (m, 4H), 7.2 (s, 1H); ^{13}C NMR (CDCl_3) δ 14, 20.3, 25.2, 36.6, 56.1, 56.3, 59.7, 61.8, 81.1, 88.9, 105, 107.1, 122.9, 125.3, 127.8, 127.9, 129.1, 131.8, 139.8, 149.1, 149.7, 156.1, 170.4, 199.6; IR (neat, cm^{-1}) 1737, 1703; Mass (ES) m/z 393.4 ($M+1$, 90%); HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{25}\text{O}_5$ ($M+H$) $^+$ 393.1702 found 393.1707.

Ethyl 5,6-dimethoxy-1-oxo-2-(3-*p*-tolylprop-2-ynyl)-2,3-dihydro-1*H*-indene-2-carboxylate (5c).

Off white solid; mp 114-116 °C; R_f = 0.61 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.23 (t, J = 6.8 Hz, 3H), 2.23 (s, 3H), 3.05 (d, J = 16.8 Hz, 1H), 3.19 (d, J = 16.8 Hz, 1H), 3.35 (d, J = 17.2 Hz, 1H), 3.65 (d, J = 17.2 Hz, 1H), 3.92 (s, 3H), 3.98 (s, 3H), 4.19 (q, J = 6.8 Hz, 2H), 6.93 (s, 1H), 7.01-7.09 (m, 4H), 7.21 (s, 1H); ^{13}C NMR (CDCl_3) δ 14, 21, 25.1, 36.7, 56.1,

56.3, 59.8, 61.8, 82.6, 84.6, 105, 107.1, 122.9, 127.92, 127.95, 128.39, 128.67, 132.1, 137.69, 149.2, 149.7, 156.1, 170.4, 199.8; IR (neat, cm⁻¹) 1737, 1703; Mass (ES) m/z 393.5 (M+1, 95%); HRMS (ESI): calcd for C₂₄H₂₅O₅ (M+H)⁺ 393.1702 found 393.1707.

Ethyl 5,6-dimethoxy-2-(3-(2-methoxyphenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5d).

Semi solid; R_f = 0.41 (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 1.23 (t, *J* = 6.8 Hz, 3H), 3.12 (d, *J* = 16.8 Hz, 1H), 3.27 (d, *J* = 16.8 Hz, 1H), 3.41 (d, *J* = 17.2 Hz, 1H), 3.66 (d, *J* = 17.2 Hz, 1H), 3.74 (s, 3H), 3.91 (s, 3H), 3.97 (s, 3H), 4.19 (q, *J* = 6.8 Hz, 2H), 6.75-6.78 (m, 2H), 6.92 (s, 1H), 6.98 (dd, *J*₁ = 17.6 Hz, *J*₂ = 1.6 Hz, 1H), 7.16-7.21 (m, 2H); ¹³C NMR (CDCl₃) δ 14, 22.7, 25.4, 31.9, 36.6, 55.6, 56.1, 56.3, 59.9, 61.8, 89.2, 105, 107.1, 110.5, 112.4, 120.2, 127.9, 129.2, 133.5, 149.3, 149.6, 156.1, 159.9, 170.4, 199.8; IR (neat, cm⁻¹) 1736, 1701; Mass (ES) m/z 409.5 (M+1, 95%); HRMS (ESI): calcd for C₂₄H₂₅O₆ (M+H)⁺ 409.1651 found 409.1668.

Ethyl 5,6-dimethoxy-2-(3-(4-methoxyphenyl)prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5e).

Semi solid; R_f = 0.33 (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 1.23(t, *J* = 6.8 Hz, 3H), 3.03 (d, *J* = 16.4 Hz, 1H), 3.18 (d, *J* = 16.4 Hz, 1H), 3.36 (d, *J* = 16.8 Hz, 1H), 3.64 (d, *J* = 16.8 Hz, 1H), 3.75 (s, 3H), 3.91 (s, 3H), 3.98 (s, 3H), 4.19 (q, *J* = 6.8 Hz, 2H), 6.71 (d, *J* = 8.4

Hz, 2H), 6.93 (s, 1H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.21 (s, 1H); ^{13}C NMR (CDCl_3) δ 14, 25.1, 36.6, 55.2, 56.1, 56.3, 59.8, 61.8, 82.4, 83.4, 104.9, 107.1, 113.6 (2C), 115.2, 127.8, 132.7 (2C), 149.1, 149.6, 156, 159.1, 170.4, 199.7; IR (neat, cm^{-1}) 1736, 1701; Mass (ES) m/z 409.4 ($M+1$, 92%); HRMS (ESI): calcd for $\text{C}_{24}\text{H}_{25}\text{O}_6$ ($M+H$) $^+$ 409.1651 found 409.1635.

Ethyl 5,6-dimethoxy-2-(3-(2-nitrophenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5f).

Off white solid; mp 128-130 °C; $R_f = 0.3$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.24 (t, $J = 6.8$ Hz, 3H), 3.07 (d, $J = 17.2$ Hz, 1H), 3.34 (d, $J = 17.2$ Hz, 1H), 3.44 (d, $J = 17.2$ Hz, 1H), 3.69 (d, $J = 17.2$ Hz, 1H), 3.89 (s, 3H), 3.99 (s, 3H), 4.19 (q, $J = 6.8$ Hz, 2H), 6.97 (s, 1H), 7.17 (s, 1H), 7.34-7.48 (m, 3H), 7.91 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14, 25, 36.7, 56.1, 56.3, 59.4, 70.0, 80.2, 88.3, 104.9, 107.1, 122.5, 123.8, 126.7, 127.7, 129, 137.1, 147.7, 148.7, 149.8, 156.7, 170.2, 199.9; IR (neat, cm^{-1}) 1737, 1702; Mass (ES) m/z 424.3 ($M+1$, 33%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_7$ ($M+H$) $^+$ 424.1396 found 424.1419.

Ethyl 5,6-dimethoxy-2-(3-(4-nitrophenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5g).

White solid; mp 138-140 °C; $R_f = 0.37$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.23 (t, $J = 6.8$ Hz, 3H), 3.10 (d, $J = 17.2$ Hz, 1H), 3.22 (d, $J = 17.2$ Hz, 1H), 3.34 (d, $J = 17.2$ Hz, 1H), 3.67 (d, $J = 17.2$ Hz, 1H), 3.92 (s, 3H), 4.00 (s, 3H), 4.2 (q, $J = 6.8$ Hz, 2H), 6.97 (s, 1H), 7.22 (s, 1H), 7.36-7.43 (m, 2H), 7.89 (s, 1H), 8.06 (d, $J = 6.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14, 25,

36.7, 56.1, 56.3, 59.4, 61.9, 80.2, 88.3, 104.9, 107, 122.5, 124.8, 126.3, 127.7, 129.1, 137, 147.8, 148.9, 149.8, 156.3, 170.2, 199.4; IR (neat, cm^{-1}) 1737, 1703; Mass (ES) m/z 424.5 ($M+1$, 98%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_7$ ($M+H$)⁺ 424.1396 found 424.1377.

Ethyl 2-(3-(3-fluorophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5h).

Off white solid; mp 104-106 °C; R_f = 0.42 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.23 (t, J = 6.8 Hz, 3H), 3.05 (d, J = 16.8 Hz, 1H), 3.2 (d, J = 16.8 Hz, 1H), 3.34 (d, J = 17.2 Hz, 1H), 3.65 (d, J = 17.2 Hz, 1H), 3.91 (s, 3H), 3.98 (s, 3H), 4.18 (q, J = 6.8 Hz, 2H), 6.80-6.92 (m, 3H), 6.94 (s, 1H), 7.27 (s, 1H), 7.12-7.17 (m, 1H); ^{13}C NMR (CDCl_3) δ 14, 25.1, 36.7, 56.1, 56.3, 59.6, 61.9, 81.3, 86.3, 105, 107.1, 114.9, 115.4, 118, 118.4, 124.8, 125, 127.3, 127.8, 129.5, 129.7, 149, 149.8, 156.2, 159.7, 164.6, 170.2, 199.4; IR (neat, cm^{-1}) 1736, 1702; Mass (ES) m/z 397.4 ($M+1$, 65%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{22}\text{O}_5\text{F}$ ($M+H$)⁺ 397.1451 found 397.1441.

Ethyl 2-(3-(4-iodophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5i).

Semi solid; R_f = 0.5 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.24 (t, J = 6.8 Hz, 3H), 3.1 (d, J = 16.8 Hz, 1H), 3.19 (d, J = 16.8 Hz, 1H), 3.31 (d, J = 17.6 Hz, 1H), 3.64 (d, J = 17.6 Hz, 1H), 3.91 (s, 3H), 3.98 (s, 3H), 4.18 (q, J = 6.8 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 6.92 (s,

1H), 7.20 (s, 1H), 7.52 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.1, 25.2, 29.7, 36.7, 56.1, 56.3, 59.6, 61.9, 81.6, 86.7, 93.5, 105, 107.1, 122.6, 127.8, 132.9 (2C), 137.2, 149, 149.8, 156.2, 170.3, 199.5; IR (neat, cm^{-1}) 1736, 1702; Mass (ES) m/z 505.3 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{22}\text{O}_5\text{I}$ ($M+H$) $^+$ 505.0512 found 505.0513.

Ethyl 2-(3-(3,4-dichlorophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5j).

Liquid; $R_f = 0.39$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.24 (t, $J = 6.8$ Hz, 3H), 3.1 (d, $J = 17.2$ Hz, 1H), 3.18 (d, $J = 17.2$ Hz, 1H), 3.30 (d, $J = 17.2$ Hz, 1H), 3.65 (d, $J = 17.2$ Hz, 1H), 3.92 (s, 3H), 3.99 (s, 3H), 4.23 (q, $J = 6.8$ Hz, 2H), 6.91-6.94 (m, 2H), 7.09 (d, $J = 1.6$ Hz, 1H), 7.21 (s, 1H), 7.25 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14.1, 21.2, 30.6, 32.6, 40.1, 56.1, 56.2, 61.0, 63.8, 84.8, 104.4, 107.4, 109.7, 113.9, 120.4, 128.9, 129.8, 133.5, 135.2, 148.7, 155.6, 175.6, 201.1; IR (neat, cm^{-1}) 1737, 1702; Mass (ES) m/z 447.3 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{21}\text{O}_5\text{Cl}_2$ ($M+H$) $^+$ 447.0766 found 447.0786.

Ethyl-2-(3-(2,3-dioxindolin-5-yl)prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5k).

Light orange solid; mp 139-141 $^{\circ}\text{C}$; $R_f = 0.15$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.14-1.18 (t, $J = 6.8$ Hz, 3H), 3.05 (d, $J = 17.6$ Hz, 1H), 3.186 (d, $J = 17.2$ Hz, 1H), 3.318 (d, $J =$

17.6 Hz, 1H), 3.65 (d, $J = 17.2$ Hz, 1H), 3.91 (s, 3H), 3.99 (s, 3H), 4.18-4.2 (q, $J = 6.8$ Hz, 2H), 6.75 (d, $J = 7.2$ Hz, 1H), 6.95 (s, 1H), 7.42-7.7 (m, 2H), 9.3 (bs, 1H); ^{13}C NMR (CDCl_3) δ 14.1, 25, 36.6, 56.1, 56.4, 59.6, 61.9, 105, 107.1, 109.2, 112.1, 117.8, 127.7, 128.4, 128.6, 131.9, 132.1, 141.1, 148.4, 149, 149.8, 156.3, 184.3, 204.5, 205.5; Mass (ES) m/z 446.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{20}\text{NO}_7$ ($M+H$) $^+$ 446.1240 found 446.1245.

5,6-Dimethoxy-2-(3-phenylprop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6a).

Liquid; $R_f = 0.52$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.72 (dd, $J_1 = 16$ Hz, $J_2 = 7.2$ Hz, 1H), 2.93 (m, 1H), 3.11 (dd, $J_1 = 17.2$ Hz, $J_2 = 4.0$ Hz, 1H), 3.13 (dd, $J_1 = 17.2$ Hz, $J_2 = 3.6$ Hz, 1H), 3.34 (dd, $J_1 = 16$ Hz, $J_2 = 7.2$ Hz, 1H), 3.80 (s, 3H), 3.91 (s, 3H), 3.97 (s, 3H), 6.90 (s, 1H), 7.18-7.28 (m, 6H); ^{13}C NMR (CDCl_3) δ 21.4, 32, 46.3, 56.1, 56.2, 81.7, 86.9, 104.4, 107.4, 123.5, 127.7, 128.1, 129.4, 131.5, 149.1, 149.5, 155.7, 205.2; IR (neat, cm^{-1}) 1698; Mass (ES) m/z 307.3 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{19}\text{O}_3$ ($M+H$) $^+$ 307.1334 found 307.1328.

5,6-Dimethoxy-2-(3-*o*-tolylprop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6b).

Semi solid; $R_f = 0.3$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.3 (s, 3H), 2.73 (dd, $J_1 = 17.2$ Hz, $J_2 = 7.2$ Hz, 1H), 2.94-3.09 (m, 2H), 3.08 (dd, $J_1 = 17.2$ Hz, $J_2 = 3.2$ Hz, 1H), 3.37 (dd, $J_1 = 17.2$ Hz, $J_2 = 7.2$ Hz, 1H), 3.91 (s, 3H), 3.96 (s, 3H), 6.95 (s, 1H), 7.07 (m, 3H), 7.19 (s, 1H); ^{13}C NMR (CDCl_3) δ 21.09, 21.4, 31.9, 46.3, 56, 56.2, 81.8, 86.5, 104.4, 107.4, 123.2,

127.9, 128.5 (2C), 129.4, 132.1, 137.7, 149.1, 149.4, 155.7, 205.2; Mass (ES) m/z 321.3 (M+1, 100%); HRMS (ESI): calcd for $C_{21}H_{21}O_3$ (M+H)⁺ 321.1491 found 321.1479.

Ethyl-2-(3-(5,6-dimethoxy-1-oxo-2,3-dihydro-1H-inden-2-yl)prop-1-ynyl)-5,6-dihydro-4H-cyclopenta[*b*]thiophene-3-carboxylate (6c).

Off white solid; mp 148-151 °C; R_f = 0.6 (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 1.34 (t, J = 6.8 Hz, 3H), 2.40 (m, 2H), 2.74-2.98 (m, 6H), 3.11 (dd, J_1 = 16.8 Hz, J_2 = 4 Hz, 2H), 3.37 (dd, J_1 = 16.8 Hz, J_2 = 7.6 Hz, 1H), 3.91(s, 3H), 3.97 (s, 3H), 4.27 (q, J = 6.8 Hz, 2H), 6.90 (s, 1H), 7.18 (s, 1H); ¹³C NMR (CDCl₃) δ 14.3, 22.1, 22.6, 30.0, 32.0, 46.2, 56.1, 56.2, 60.2, 75.3, 96.3, 104.4, 107.4, 114.3, 129.0 (2C), 132.9, 141.9, 146.6 (2C), 149.2, 155.7, 162.6, 204.9; Mass(ES) m/z 425.1 (M+1, 100%); HRMS (ESI): calcd for $C_{21}H_{21}O_3$ (M+H)⁺ 425.1421, found 425.1434.

5,6-Dimethoxy-2-(3-(2-methoxyphenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one(6d).

Colorless liquid; R_f = 0.36 (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 2.76 (dd, J_1 = 16.8 Hz, J_2 = 8.0 Hz, 1H), 2.95 (m, 1H), 3.05 (dd, J_1 = 17.2 Hz, J_2 = 4.0 Hz, 1H), 3.13 (dd, J_1 = 17.2 Hz, J_2 = 3.6 Hz, 1H), 3.35 (dd, J_1 = 16.8 Hz, J_2 = 7.2 Hz, 1H), 3.80 (s, 3H), 3.91 (s, 3H), 3.97 (s, 3H), 6.81-6.91 (m, 3H), 7.20-7.24 (m, 3H); ¹³C NMR (CDCl₃) δ 22.7, 36.6, 55.6, 56.0, 56.3, 59.8, 61.9, 105.0, 107.1, 110.5, 112.4, 120.2, 127.2, 127.9, 129.2, 133.5, 149.3, 149.5, 156.1,

161.9, 199.9; IR (neat, cm^{-1}) 1698; Mass (ES) m/z 337.2 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{21}\text{O}_4$ ($M+H$) $^+$ 337.1440 found 337.1435.

5,6-Dimethoxy-2-(3-(4-methoxyphenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6e).

Light brown liquid; R_f = 0.52 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.72 (dd, J_1 = 17.2 Hz, J_2 = 7.2 Hz, 1H), 2.95 (m, 1H), 2.99 (dd, J_1 = 16.8 Hz, J = 4.8 Hz, 1H), 3.10 (dd, J_1 = 16.8 Hz, J_2 = 4.8 Hz, 1H), 3.33 (dd, J_1 = 17.2 Hz, J_2 = 7.2 Hz, 1H), 3.77 (s, 3H), 3.91 (s, 3H), 3.97 (s, 3H), 6.76 (d, J = 8.8 Hz, 2H), 6.9 (s, 1H), 7.18-7.20 (m, 3H); ^{13}C NMR (CDCl_3) δ 21.4, 32.0, 46.4, 55.2, 56.1, 56.2, 81.5, 85.3, 104.5, 107.5, 113.8 (2C), 115.7, 129.3, 132.9 (2C), 149.1, 149.6, 155.8, 159.2, 205.3; IR (neat, cm^{-1}) 1697; Mass (ES) m/z 337.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{21}\text{O}_4$ ($M+H$) $^+$ 337.1440 found 337.1424.

5,6-Dimethoxy-2-(3-(2-nitrophenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6f).

Yellow solid; mp 98-100 $^{\circ}\text{C}$; R_f = 0.38 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.78 (dd, J_1 = 17.6 Hz, J_2 = 7.6 Hz, 1H), 2.93-3.15 (m, 3H), 3.40 (dd, J_1 = 17.6 Hz, J_2 = 7.6 Hz, 1H), 3.90 (s, 3H), 3.98 (s, 3H), 6.93 (s, 1H), 7.19 (s, 1H), 7.33-7.51 (m, 3H) 7.95 (d, J = 8.4 Hz, 1H); ^{13}C NMR (CDCl_3) δ 21.4, 29.6, 45.9, 56.1, 56.2, 79.6, 90.0, 104.3, 107.3, 122.8, 125.2, 126.4, 129.1 (2C), 137.2, 147.9, 148.9, 149.6, 154.8, 205.4; IR (neat, cm^{-1}) 1695; Mass (ES) m/z 352.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_5$ ($M+H$) $^+$ 352.1185 found 352.1173.

5,6-Dimethoxy-2-(3-(4-nitrophenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6g).

Yellow solid; mp 108-110 °C; R_f = 0.25 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.79 (dd, J_1 = 16.8 Hz, J_2 = 6.8 Hz, 1H), 2.92-3.09 (m, 3H), 3.08 (dd, J_1 = 16.8 Hz, J_2 = 4.8 Hz, 1H), 3.37 (dd, J_1 = 16.8 Hz, J_2 = 6.8 Hz, 1H), 3.91 (s, 3H), 3.98 (s, 3H), 6.93 (s, 1H), 7.20 (s, 1H), 7.39-7.44 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 8.08 (m, 2H); ^{13}C NMR (CDCl_3) δ 21.4, 32, 45.9, 56.1, 56.2, 79.5, 90.0, 104.3, 107.3, 122.4, 125.2, 126.3, 129.0 (2C), 137.2, 147.9, 148.9, 149.5, 155.8, 204.7; IR (neat, cm^{-1}) 1698; Mass (ES) m/z 352.3 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{18}\text{NO}_5$ ($M+H$) $^+$ 352.1185 found 352.1200.

2-(3-(3-Fluorophenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6h).

Colorless liquid; R_f = 0.55 (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.59 (dd, J_1 = 17.3 Hz, J_2 = 7.5 Hz, 1H), 2.94 (m, 2H), 3.08 (dd, J_1 = 16.8 Hz, J_2 = 4.8 Hz, 1H), 3.33 (dd, J_1 = 17.2 Hz, J_2 = 7.2 Hz, 1H), 3.91 (s, 3H), 3.97 (s, 3H), 6.90-7.26 (m, 6H); ^{13}C NMR (CDCl_3) δ 21.3, 32.1, 46.1, 56.1, 56.2, 88.1, 104.4, 107.4, 114.8, 115.3, 118.1, 118.6, 127.4, 129.1, 129.5, 129.7, 149.0, 149.5, 155.8, 205.0; IR (neat, cm^{-1}) 1698; Mass (ES) m/z 325.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{18}\text{O}_3\text{F}$ ($M+H$) $^+$ 325.1240 found 325.1235.

2-(3-(4-Iodophenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6i).

Colorless liquid; $R_f = 0.4$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.71 (dd, $J_1 = 17.2\text{Hz}$, $J_2 = 7.2\text{Hz}$, 1H), 2.93 (m, 2H), 3.04 (dd, $J_1 = 16.8\text{Hz}$, $J_2 = 4.8\text{Hz}$, 1H), 3.33 (dd, $J_1 = 17.2\text{Hz}$, $J_2 = 7.2\text{Hz}$, 1H), 3.91 (s, 3H), 3.97 (s, 3H), 6.90 (s, 1H), 6.98 (d, $J = 8\text{Hz}$, 2H), 7.19 (s, 1H), 7.57 (d, $J = 8\text{Hz}$, 2H); ^{13}C NMR (CDCl_3) δ 29.7, 36.9, 56.1, 56.3, 59.6, 86.7, 93.5, 105.2, 107.3, 122.8, 127.9, 132.9 (2C), 137.2 (2C), 149.0, 149.6, 156.3, 170.3, 199.8 ; IR (neat, cm^{-1}) 1697; Mass (ES) m/z 433.2 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{18}\text{O}_3\text{I}$ ($M+H$) $^+$ 433.0290 found 433.0289.

2-(3-(2-Amino-5-methylphenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6j).

Light brown solid; mp 126-128 °C; $R_f = 0.6$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.15 (s, 3H), 2.82-3.08 (m, 4H), 3.30-3.37 (m, 1H), 3.91 (s, 3H), 3.96 (s, 3H), 6.53 (d, $J = 8\text{ Hz}$, 1H), 6.84-6.91 (m, 3H), 7.19 (s, 1H); IR (neat, cm^{-1}) 3460, 3354, 1694; ^{13}C NMR (CDCl_3) δ 17.0, 21.1, 30.6, 56.1, 56.2, 61.0, 83.3, 107.4, 109.6, 113.7, 128.9, 129.7 (2C), 133.5 (2C), 148.8 (2C), 149.5 (2C), 154.5, 201.6; Mass (ES) m/z 336.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3\text{N}$ ($M+H$) $^+$ 336.1600 found 336.1594.

5-(3-(5,6-Dimethoxy-1-oxo-2,3-dihydro-1H-inden-2-yl)prop-1-ynyl)indoline-2,3-dione (6k).

Orange solid; mp 108-110 °C; R_f = 0.33 (3:7 EtOAc : Hex); ^1H NMR (DMSO- d_6) δ 2.74-2.80 (dd, J_1 = 17.6 Hz, J_2 = 7.6 Hz, 1H), 2.93-3.15 (m, 3H), 3.37-3.43 (dd, J_1 = 17.6 Hz, J_2 = 7.6 Hz, 1H), 3.79 (s, 3H), 3.88 (s, 3H), 6.8-7.6 (m, 5H), 6.82-7.62 (m, 5H), 11.14 (bs, 1H); Mass (ES) m/z 374.3 (M-1, 100%); HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{22}\text{O}_3\text{N}$ (M+H) $^+$ 376.1185 found 376.1170.

Pd/C-mediated coupling of alkynes **3** and **4** with 1,4-diiodobenzene

A mixture of 1,4-di-iodobenzene (0.33 mmol), 10% Pd/C (0.0022 mmol), PPh₃ (0.0086 mmol), CuI (0.022 mmol) and triethylamine (0.54 mmol) in EtOH (5 mL) was stirred for 30 min under a nitrogen atmosphere. To this mixture was added alkyne **3** or **4** (0.33 mmol) slowly and the mixture was refluxed and reaction was monitored by TLC. The mixture was then cooled to room temperature and filtered through celite; EtOH was removed under reduced pressure. The residue was diluted with water (50 mL) and extracted with EtOAc (3 x 25 mL). The organic layers were collected, combined, washed with water (2 x 25 mL), dried over anhydrous Na₂SO₄, filtered and concentrated. The residue thus obtained was purified by column chromatography using to afford the title compounds.

Spectral data of compounds synthesized

Diethyl-2,2'-(3,3'-(1,4-phenylene)bis(prop-2-yne-3,1-diyl))bis(5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate) (5l).

Light yellow solid; mp 113-115 °C; $R_f = 0.15$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.18 (t, $J = 6.8$ Hz, 6H), 2.99 (d, $J = 17.2$ Hz, 2H), 3.16 (d, $J = 17.2$ Hz, 2H), 3.28 (d, $J = 16.8$ Hz, 2H), 3.61 (d, $J = 16.8$ Hz, 2H), 3.87 (s, 6H), 3.94 (s, 6H), 4.15 (q, $J = 6.8$ Hz, 4H), 6.90 (m, 6H), 7.16 (s, 2H); ^{13}C NMR (CDCl_3) δ 13.9 (2C), 25.1 (2C), 36.5 (2C), 56 (2C), 56.2 (2C), 59.6 (2C), 61.7 (2C), 81.9 (2C), 86.8 (2C), 104.9 (2C), 107 (2C), 122.4 (2C), 127.6 (2C), 131 (4C), 148.9 (2C), 149.6 (2C), 156 (2C), 170.1 (2C), 199.4 (2C); IR (neat, cm^{-1}) 1737, 1702; Mass (ES) m/z 679.7 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{40}\text{H}_{39}\text{O}_{10}$ ($M+H$) $^+$ 679.2543 found 679.2567.

2,2'-(3,3'-(1,4-Phenylene)bis(prop-2-yne-3,1-diyl))bis(5,6-dimethoxy-2,3-dihydro-1H-inden-1-one) (6l).

Colorless liquid; $R_f = 0.1$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.72 (dd, $J_1 = 19.6$ Hz, $J_2 = 7.6$ Hz, 1H), 2.94-3.07 (m, 3H), 3.33 (dd, $J_1 = 19.6$ Hz, $J_2 = 7.6$ Hz, 1H), 3.77 (s, 3H), 3.90 (s, 6H), 3.96 (s, 6H), 6.9 (s, 2H), 7.12-7.18 (m, 5H), 7.28 (s, 1H); IR (neat, cm^{-1}) 1697; Mass (ES) m/z 535.5 ($M+1$, 50%); HRMS (ESI): calcd for $\text{C}_{34}\text{H}_{31}\text{O}_6$ ($M+H$) $^+$ 535.2121 found 535.2148.

Synthesis of ketones 7 and 8 via I_2 -mediated hydration of alkynes 5 and 6.

To a solution of alkyne **5** or **6** (0.15 mmol) dissolved in DCM-H₂O (4.9 mL of DCM + 0.1 mL of H₂O) was added catalytic amount of iodine (0.015 mmol) and the mixture was stirred at rt. After completion of the reaction (monitored by TLC) the mixture was then diluted with dichloromethane (25 mL) and washed with saturated aqueous solution of Na₂S₂O₃ (25 mL). The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude product obtained was purified by column chromatography.

Spectral data of compounds synthesized

Ethyl-5,6-dimethoxy-1-oxo-2-(3-oxo-3-phenylpropyl)-2,3-dihydro-1H-indene-2-carboxylate (**7a**).

Colorless low melting solid; R_f = 0.33 (3:7 EtOAc : Hex); ¹H NMR (CDCl₃) δ 1.23 (t, J = 6.8 Hz, 3H), 2.38-2.41 (m, 2H), 3.11-3.23 (m, 3H), 3.62 (d, J = 16.8 Hz, 1H), 3.92 (s, 3H), 3.95 (s, 3H), 4.31 (q, J = 6.8 Hz, 2H), 6.89 (s, 1H), 7.19 (s, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.94 (d, J = 7.2 Hz, 2H); ¹³C NMR (CDCl₃) δ 12.3, 29.7, 32.9, 39.9, 56.1, 56.2, 60.0, 65.1, 107.4, 114.2, 128.1, 128.6 (2C), 129.4, 130.8, 133.0, 136.8, 148.7, 149.5, 155.6, 171.4, 199.8, 206.9; Mass (ES) m/z 397.4 (M+1, 80%); HRMS (ESI): calcd for C₂₃H₂₅O₆ (M+H)⁺ 397.1651 found 397.1652.

Ethyl-5,6-dimethoxy-1-oxo-2-(3-oxo-3-m-tolylpropyl)-2,3-dihydro-1H-indene-2-carboxylate (**7b**).

Colorless liquid; $R_f = 0.4$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.23 (t, $J = 6.8$ Hz, 3H), 2.3-2.45 (m, 3H), 3.13-3.2 (m, 3H), 3.63 (d, $J = 17.6$ Hz, 1H), 3.92 (s, 3H), 3.98 (s, 3H), 4.2 (q, $J = 6.8$ Hz, 2H), 6.88 (s, 1H), 7.19 (s, 1H), 7.26 (s, 1H), 7.30-7.37 (m, 2H), 7.73 (d, $J = 8$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14.4, 21.0, 25.2, 29.7, 36.7, 56.1, 56.2, 62.7, 105.0, 107.1, 122.9, 127.7, 127.9, 128.4, 128.7, 132.1, 136.1, 149.3, 149.9, 157.7, 174.0, 197.2, 201.0; Mass (ES) m/z 411.4 ($M+1$, 100%).

Ethyl-2-(3-(3-fluorophenyl)-3-oxopropyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (7c).

Yellow solid; mp 143-145 °C; $R_f = 0.4$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 1.2 (t, $J = 6.8$ Hz, 3H), 2.3-2.4 (m, 2H), 3.0-3.22 (m, 3H), 3.65 (d, $J = 8.4$ Hz, 1H), 3.92 (s, 3H), 3.98 (s, 3H), 4.41 (q, $J = 6.8$ Hz, 2H), 6.89 (s, 1H), 7.19 (s, 1H), 7.25 (m, 1H), 7.43 (m, 1H), 7.62 (d, $J = 8.8$ Hz, 1H), 7.73 (d, $J = 8$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14.1, 22.7, 33.8, 35.5, 55.2, 56.1, 56.4, 67.4, 104.5, 107.3, 113.7, 114.3, 129.3, 129.9, 130.4, 138.2, 148.5, 149.8, 156.6, 162.4, 177.6, 196.2, 204.3; Mass (ES) m/z 415.3 ($M+1$, 100%).

5,6-Dimethoxy-2-(3-oxo-3-phenylpropyl)-2,3-dihydro-1H-inden-1-one (8a).

Colorless liquid; $R_f = 0.33$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.04-2.26 (m, 2H), 2.78-2.82 (m, 2H), 3.15-3.34 (m, 3H), 3.91 (s, 3H), 3.96 (s, 3H), 6.87 (s, 1H), 7.19 (s, 1H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.98 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 26.3, 35.9, 39.9, 46.5, 56.2, 104.4, 115.1, 128.0, 128.6 (2C), 129.4, 130.8, 133.3, 136.2, 141.0, 148.5, 149.7, 153.4, 200.0, 209.1; Mass (ES) m/z 325.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{20}\text{H}_{21}\text{O}_4$ ($M+H$) $^+$ 325.1440 found 325.1448.

5,6-Dimethoxy-2-(3-(4-methoxyphenyl)-3-oxopropyl)-2,3-dihydro-1H-inden-1-one (8b).

Colorless liquid; $R_f = 0.42$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.04-2.26 (m, 2H), 2.78-2.82 (m, 2H), 3.15-3.34 (m, 3H), 3.86 (s, 3H), 3.91 (s, 3H), 3.96 (s, 3H), 6.87 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 2H), 7.18 (s, 1H), 7.97 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.7, 33.8, 35.5, 46.6, 55.4, 56.1, 56.2, 104.3, 107.3, 113.7, 114.0, 129.3, 129.9, 130.4, 139.2, 148.8, 149.5, 155.6, 163.4, 198.5, 207.1; Mass (ES) m/z 355.4 ($M+1$, 100%); HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{23}\text{O}_5$ ($M+H$) $^+$ 355.1545 found 355.1546.

2-(3-(3-Fluorophenyl)-3-oxopropyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (8c)

Colorless liquid; $R_f = 0.32$ (3:7 EtOAc : Hex); ^1H NMR (CDCl_3) δ 2.12-2.31 (m, 2H), 2.77-2.81 (m, 2H), 3.12-3.33 (m, 3H), 3.86 (s, 3H), 3.91 (s, 3H), 3.96 (s, 3H), 7.05 (s, 1H), 7.16 (d, $J = 8.6$ Hz, 2H), 7.48 (s, 1H), 7.92 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.7, 29.7, 35.9, 46.5, 56.1, 56.2, 104.4, 107.4, 110.8, 124.2 (2C), 133.3 (2C), 136.2, 141.7, 148.0, 149.5, 153.6, 200.0, 206.9; Mass (ES) m/z 355.4 ($M+1$, 100%).

1.2. Pharmacology

PDE4B protein production and purification

PDE4B cDNA was sub-cloned into pFAST Bac HTB vector (Invitrogen) and transformed into DH10Bac (Invitrogen) competent cells. Recombinant bacmids were tested for integration by PCR analysis. *Sf9* cells were transfected with bacmid using Lipofectamine 2000 (Invitrogen) according to manufacturer's instructions. Subsequently, P3 viral titer was amplified, cells were infected and 48 h post infection cells were lysed in lysis buffer (50 mM Tris-HCl pH 8.5, 10 mM 2-Mercaptoethanol, 1 % protease inhibitor cocktail (Roche), 1 % NP40). Recombinant His-tagged PDE4B protein was purified as previously described in a literature.¹ Briefly, lysate was centrifuged at 10,000 rpm for 10 min at 4 °C and supernatant was collected. Supernatant was mixed with Ni-NTA resin (GE Life Sciences) in a ratio of 4:1 (v/v) and equilibrated with binding buffer (20 mM Tris-HCl pH 8.0, 500 mM-KCl, 5 mM imidazole, 10 mM 2-mercaptoethanol and 10 % glycerol) in a ratio of 2:1 (v/v) and mixed gently on rotary shaker for 1 hour at 4 °C. After incubation, lysate-Ni-NTA mixture was centrifuged at 4,500 rpm for 5 min at 4 °C and the supernatant was collected as the flow-through fraction. Resin was washed twice with wash buffer (20 mM Tris-HCl pH 8.5, 1 M KCl, 10 mM 2-Mercaptoethanol and 10% glycerol). Protein was eluted sequentially twice using elution buffers (Buffer I: 20 mM Tris-HCl pH 8.5, 100 mM KCl, 250 mM imidazole, 10 mM 2-mercaptoethanol, 10% glycerol, Buffer II: 20 mM Tris-HCl pH 8.5, 100 mM KCl, 500 mM imidazole, 10 mM 2-mercaptoethanol, 10% glycerol). Eluates were collected in four fractions and analyzed by SDS-PAGE. Eluates containing PDE4B protein were pooled and stored at -80°C in 50% glycerol until further use.

PDE4B enzymatic assay

The inhibition of PDE4B enzyme was measured using PDElight HTS cAMP phosphodiesterase assay kit (Lonza) according to manufacturer's recommendations. Briefly, 10 ng of PDE4B enzyme was pre-incubated either with DMSO (vehicle control) or compound for 15 min before incubation with the substrate cAMP (5 µM) for 1 h. The reaction was halted with stop solution followed by incubation with detection reagent for 10 minutes in dark. Luminescence values (RLUs) were measured by a Multilabel plate reader (Perkin Elmer 1420 Multilabel counter). The percentage of inhibition was calculated using the following formula and IC50s were computed using GraphPad Prism Version 5.04 software.

$$\% \text{ inhibition} = \frac{(\text{RLU of vehicle control} - \text{RLU of inhibitor})}{\text{RLU of vehicle control}} \times 100$$

Reference:

1. Wang, P.; Myers, J. G.; Wu, P.; Cheewatrakoolpong, B.; Egan, R. W.; Billah, M. M. *Biochem. Biophys. Res. Commun.* **1997**, *19*, 320.

1.3. Molecular Modeling Studies

Method: The docking analysis of **5a** was performed using Maestro, version 9.2 [1] implemented from Schrödinger molecular modeling suite. The molecule **5a** was sketched in 3D format using build module of maestro and LigPrep module was used to produce low-energy conformers. The structural coordinates of Phosphodiesterase (PDB ID: 1XMY) [2] were obtained from the protein data bank (PDB). Row PBD protein structure was prepared by giving preliminary treatment like adding hydrogen, adding missing residues, refining the loop with prime and finally minimized by using OPLS-2005 force field. The grid for molecular docking was generated with bound co-crystallized ligand. The molecule **5a** was docked using Glide in extra-precision mode, with up to three poses saved per molecule. The ligand was kept flexible, whereas the receptor was kept rigid throughout the docking studies. The lowest energy conformations were selected and, the ligand interactions (H-Bond and Hydrophobic interactions) with target protein were determined.

Table S-1: Glide score and contributing XP parameters.

Compound code	GScore		LipophilicEvdW	PhobEn	HBond	Electro	LowMW
	R	S					
5a	-5.93	-5.48	-3.58	-0.0	-0.69	-1.43	-0.24

GScores: glide score

LipophilicEvdW: Chemscore lipophilic pair term and fraction of the total protein-ligand vdw energy

PhobEn: Hydrophobic enclosure reward

HBond: Rewards for hydrogen bonding interaction between ligand and protein

LowMW: Reward for ligands with low molecular weight

Electro: Electrostatic reward

References

- [1] Maestro, version 9.2; Schrodinger, LLC: New York, NY, 2011.

- [2] Graeme L. Card, Bruce P. England, Yoshihisa Suzuki, Daniel Fong, Ben Powell, Byunghun Lee, Catherine Luu, Maryam Tabrizizad, Sam Gillette, Prabha N. Ibrahim, Dean R. Artis, Gideon Bollag, Michael V. Milburn, Sung-Hou Kim, Joseph Schlessinger, Kam Y.J. Zhang, Structural Basis for the Activity of Drugs that Inhibit Phosphodiesterases. *Structure*, 12 (12), 2004, 2233-2247, DOI:10.1016/j.str.2004.10.004.

^1H & ^{13}C NMR Spectra

Ethyl 5,6-dimethoxy-1-oxo-2-(3-phenylprop-2-ynyl)-2,3-dihydro-1H-indene-2-carboxylate (5a).

^1H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

51 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 O: 0-10

ILS/CHU/C-41-264

UT1009_66 139 (3.205) Cm (139:142:103:110)

Minimum: -1.0
Maximum: 5.0 5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
379.1534	379.1545	-1.1	-2.9	12.5	52.7	C23 H23 O5

Elemental Composition Report

Ethyl 5,6-dimethoxy-1-oxo-2-(3-*o*-tolylprop-2-ynyl)-2,3-dihydro-1*H*-indene-2-carboxylate (5b).

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

200 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-3 O: 0-10

ILS/CHU/C-41-287

UT1009_45 142 (3.265) Cm (142:145)

Minimum: -1.0

Maximum: 5.0 5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
393.1707	393.1702	0.5	1.3	12.5	425.5	C24 H25 O5

Elemental Composition Report

Ethyl 5,6-dimethoxy-1-oxo-2-(3-*p*-tolylprop-2-ynyl)-2,3-dihydro-1*H*-indene-2-carboxylate (5c).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

50 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 O: 0-10

ILS/CHU/C-41-292

UT1009_52 146 (3.360) Cm (145:147-113:115)

Minimum:				-1.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
393.1707	393.1702	0.5	1.3	12.5	22.0	C24 H25 O5

Elemental Composition Report

Ethyl 5,6-dimethoxy-2-(3-(2-methoxyphenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5d).

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

51 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-45 H: 0-60 O: 0-10

HRMS

UT1009_329 1034 (35.756) Cm (1034:1040-291:319x5.000)

1: TOF MS ES+
6.44e+004

Minimum:				-1.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
409.1668	409.1651	1.7	4.2	12.5	44.1	C24 H25 O6

Elemental Composition Report

Ethyl 5,6-dimethoxy-2-(3-(4-methoxyphenyl)prop-2-ynyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (5e).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

154 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-2 O: 0-10

ILS/CHU/C-41-294

UT1009_49 131 (3.020) Cm (130:131-107:113)

Minimum:

Maximum:

5.0 5.0 -1.0

5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
409.1635	409.1651	-1.6	-3.9	12.5	183.0	C ₂₄ H ₂₅ O ₆

Elemental Composition Report

Ethyl 5,6-dimethoxy-2-(3-(2-nitrophenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (5f).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

208 formula(e) evaluated with 2 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-3 O: 0-10

ILS/CHU/C-41-286

UT1009_56 131 (3.021) Cm (131:132)

Minimum:				-1.0		
Maximum:		5.0	10.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
424.1419	424.1396	2.3	5.4	13.5	42.3	C23 H22 N O7
	424.1450	-3.1	-7.3	22.5	1674.4	C29 H18 N3 O

Elemental Composition Report

Ethyl 5,6-dimethoxy-2-(3-(4-nitrophenyl) prop-2-ynyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5g).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

208 formula(e) evaluated with 2 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-3 O: 0-10

ILS/CHUI/C-41-291

UT1009_59 137 (3.159) Cm (137)

Minimum:

Maximum:

5.0

5.0

-1.0

80.0

Mass

Calc. Mass

mDa

PPM

DBE

i-FIT

Formula

424.1377

424.1396

-1.9

-4.5

13.5

7.8

C23 H22 N O7

424.1356

2.1

5.0

9.5

75.7

C18 H22 N3 O9

Elemental Composition Report

Ethyl 2-(3-(3-fluorophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5h).

¹H NMR (CDCl₃)

Elemental Composition Report

Ethyl 2-(3-(4-iodophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5i).

¹H NMR (CDCl₃)

^{13}C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

415 formula(e) evaluated with 2 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-3 O: 0-10 I: 0-1

ILS/CHUI/C-41-293(1)

UT1009_46 146 (3.356) Cm (143:146-93:101)

Elemental Composition Report

Ethyl 2-(3-(3,4-dichlorophenyl) prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (5j).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

Ethyl2-(3-(2,3-dioxindolin-5-yl)prop-2-ynyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (5k).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

160 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-40 H: 0-42 N: 0-3 O: 0-10

HRMS

UT1009_329 429 (14.844) Cm (427.431-296.312x5.000)

2: TOF MS ES-
4.46e+003

Minimum: -1.0
Maximum: 5.0 5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
446.1245	446.1240	0.5	1.1	16.5	9.5	C ₂₅ H ₂₀ N O ₇

Elemental Composition Report

Diethyl 2,2'-(3,3'-(1,4-phenylene)bis(prop-2-yne-3,1-diyl))bis(5,6-dimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate) (5l).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

24 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-45 H: 0-60 O: 0-10

HRMS

UT1009_329 668 (23.117) Cm (668.670-595.611x5.000)

Elemental Composition Report

5,6-Dimethoxy-2-(3-phenylprop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6a).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

42 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 O: 0-10

ILS/CHU/C-41-295

UT1009_51 129 (2.975) Cm (129)

1: TOF MS ES+
1.77e+005

Minimum:				-1.0		
Maximum:		5.0	5.0	80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
307.1328	307.1334	-0.6	-2.0	11.5	32.2	C20 H19 O3

Elemental Composition Report

5,6-dimethoxy-2-(3-*o*-tolylprop-2-ynyl)-2,3-dihydro-1*H*-inden-1-one (6b).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

48 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-40 H: 0-42 O: 0-15

HRMS

UT1009_329 352 (12.183) Cm (351:356-(328:340+308:315)x2.000)

1: TOF MS ES+
2.27e+005

Minimum:

Maximum:

5.0

5.0

-1.0

80.0

Mass

Calc. Mass

mDa

PPM

DBE

i-FIT

Formula

321.1479

321.1491

-1.2

-3.7

11.5

68.3

C₂₁ H₂₁ O₃

Elemental Composition Report

Ethyl 2-(3-(5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-inden-2-yl)prop-1-ynyl)-5,6-dihydro-4*H*-cyclopenta[*b*]thiophene-3-carboxylate (**6c**).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

5,6-Dimethoxy-2-(3-(2-methoxyphenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6d).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

5,6-Dimethoxy-2-(3-(4-methoxyphenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6e).

^1H NMR (CDCl_3)

^{13}C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

44 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 O: 0-10

ILS/CHU/C-41-285

UT1009_62 132 (3.034) Cm (132:134-87:94)

Minimum:				-1.0		
Maximum:	5.0	10.0		80.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
337.1424	337.1440	-1.6	-4.7	11.5	42.0	C21 H21 O4

Elemental Composition Report

5,6-Dimethoxy-2-(3-(2-nitrophenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6f).

¹H NMR (CDCl₃)

^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

176 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-45 H: 0-60 N: 0-3 O: 0-10

HRMS

UT1009_329 1428 (49.394) Cm (1427:1431-1403:1409x5.000)

1: TOF MS ES+
5.63e+004

Minimum: 5.0 5.0 -1.0
Maximum: 80.0

Mass Calc. Mass mDa PPM DBE i-FIT Formula

352.1173 352.1185 -1.2 -3.4 12.5 23.3 C20 H18 N O5

Elemental Composition Report

5,6-Dimethoxy-2-(3-(4-nitrophenyl)prop-2-ynyl)-2,3-dihydro-1H-inden-1-one (6g).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

104 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-40 H: 0-42 N: 0-1 O: 0-15

HRMS

UT1009_329 55 (1.908) Cm (55:60-(38:42+75)x2.000)

1: TOF MS ES+
1.11e+004

Minimum:

Maximum:

5.0

5.0

-1.0

80.0

Mass

Calc. Mass

mDa

PPM

DBE

i-FIT

Formula

352.1200

352.1185

1.5

4.3

12.5

1.6

C20 H18 N O5

Elemental Composition Report

2-(3-(3-Fluorophenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6h).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

DEPT ^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

152 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-45 H: 0-60 O: 0-10 F: 0-3

HRMS

UT1009_329 1282 (44.350) Cm (1282.1283-1260.1269x5.000)

1: TOF MS ES+
2.85e+003

Minimum:				-1.0			
Maximum:		5.0	5.0	80.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula	
325.1235	325.1240	-0.5	-1.5	11.5	0.0	C20 H18 O3 F	
	325.1229	0.6	1.8	15.5	5.0	C23 H17 O2	

Elemental Composition Report

2-(3-(4-Iodophenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6i).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

2-(3-(2-Amino-5-methylphenyl) prop-2-ynyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (6j).

¹H NMR (CDCl₃)

^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

128 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-50 H: 0-60 N: 0-2 O: 0-10

ILS/CHU/C-41-275

UT1009_68 121 (2.790) Cm (121)

Minimum: -1.0
Maximum: 5.0 5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
336.1594	336.1600	-0.6	-1.8	11.5	80.9	C21 H22 N O3

Elemental Composition Report

**5-(3-(5,6-Dimethoxy-1-oxo-2,3-dihydro-1H-inden-2-yl)prop-1-ynyl)indoline-2,3-dione
(6k).**

¹H NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -2.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

192 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-50 N: 0-4 O: 0-8

ILS-CHU-C41-276

UT1109_227 10 (0.147) Cm (10:14-51:57x2.000)

1: TOF MS ES+
8.93e+003

Minimum:

Maximum:

5.0

5.0

-2.0

80.0

Mass

Calc. Mass

mDa

PPM

DBE

i-FIT

Formula

376.1170

376.1185

1.5

4.0

14.5

1.6

C22 H18 N O5

Elemental Composition Report

2,2'-(3,3'-(1,4-Phenylene)bis(prop-2-yne-3,1-diyl))bis(5,6-dimethoxy-2,3-dihydro-1H-inden-1-one) (6l).

¹H NMR (CDCl₃)

Elemental Composition Report

Ethyl 5,6-dimethoxy-1-oxo-2-(3-oxo-3-phenylpropyl)-2,3-dihydro-1H-indene-2-carboxylate (7a).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

50 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-45 H: 0-60 O: 0-10

HRMS

UT1009_329 1145 (39.616) Cm (1145:1147-1115:1118x5.000)

1: TOF MS ES+
7.89e+003

Elemental Composition Report

Ethyl 5,6-dimethoxy-1-oxo-2-(3-oxo-3-m-tolylpropyl)-2,3-dihydro-1H-indene-2-carboxylate (7b).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Ethyl 2-(3-(3-fluorophenyl)-3-oxopropyl)-5,6-dimethoxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (7c).

^1H NMR (CDCl_3)

^{13}C NMR (CDCl_3)

5,6-Dimethoxy-2-(3-oxo-3-phenylpropyl)-2,3-dihydro-1H-inden-1-one (8a).

^1H NMR (CDCl_3)

^{13}C NMR (CDCl_3)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -2.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

101 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-50 O: 0-8 S: 0-2

ILS-CHU-C41-309

UT1109_226 13 (0.194) Cm (13:16-48:56/2.000)

1: TOF MS ES+
3.09e+004

Minimum:

Maximum:

5.0

5.0

-2.0

80.0

Mass

Calc. Mass

mDa

PPM

DBE

i-FIT

Formula

325.1448

325.1440

0.8

2.5

10.5

101.7

C20

H21

O4

Elemental Composition Report

5,6-Dimethoxy-2-(3-(4-methoxyphenyl)-3-oxopropyl)-2,3-dihydro-1H-inden-1-one (8b).

¹H NMR (CDCl₃)

¹³C NMR (CDCl₃)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -2.0, max = 80.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

45 formula(e) evaluated with 1 results within limits (up to 4 best isotopic matches for each mass)

Elements Used:

C: 0-30 H: 0-50 O: 0-10

ILS-CHU-C41/310

UT1109_221 9 (0.137) Cm (9:10)

Minimum: 5.0 5.0 -2.0
Maximum: 5.0 5.0 80.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
355.1548	355.1545	0.23	0.8	10.5	2263.9	C21 H23 O5

Elemental Composition Report

2-(3-(3-fluorophenyl)-3-oxopropyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (8c)

¹H NMR (CDCl₃)

^{13}C NMR (CDCl₃)