

EXPERIMENTAL SECTION

General Methods. Reactions were monitored by thin-layer chromatography (TLC) carried out on Merck-silica plates using UV-light and anisaldehyde or potassium permanganate stains for visualization. Column chromatography was performed on silica gel (60–120 mesh) using hexanes and ethyl acetate as eluents. NMR data were recorded on 400 and 500 MHz spectrometers. ^{13}C and ^1H chemical shifts in NMR spectra were referenced relative to signals of CDCl_3 (δ 7.263 ppm for ^1H and 77.16 ppm for ^{13}C). Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz), respectively. HRMS were recorded by electron spray ionization (ESI) method on a Q-TOF Micro with lock spray source. Known compounds data have been compared with the reported data and references were given appropriately. Characterization data for new compounds is given below and soft copy of each ^1H , ^{13}C NMR spectra for all new compounds were given in accompanying supporting information file.

2-Iodo-5-methoxybenzaldehyde (**16**)

A solution of 3-methoxybenzaldehyde **16** (1 g, 7.35 mmol), silver nitrate (1.24 g, 7.35 mmol), and iodine (2.1 g, 8.08 mmol), in methanol (30 mL) was stirred for 14 h at room temperature under nitrogen atmosphere. The yellow precipitate of silver iodide was filtered off and washed with methanol. Excess iodine was reduced with aq. sodium thiosulphate solution and extracted with EtOAc. Removal of the solvent on a rotary evaporator and purification of the crude by column chromatography (19:1 hexane:ethyl acetate) gave the 2-iodo-5-methoxybenzaldehyde **17** (1.36 g, 5.19 mmol, 71 %) as a pale yellow solid.

^1H NMR (400 MHz, CDCl_3): δ = 10.0 (1 H, s), 7.80 (1 H, d, J = 8.7 Hz), 7.42 (1 H, d, J = 2.9 Hz), 6.91 (1 H, dd, J = 2.9 & 8.6 Hz), 3.84 (3 H, s) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 195.5, 160.4, 141.1, 135.8, 123.6, 113.6, 89.9 and 55.7 ppm.

IR (neat): 3073, 2923, 2854, 1669, 1591, 1450, 1382, 1198, 1052, 932, 865, 818, 645 and 587 cm^{-1}

TLC: R_f = 0.6 (9:1; hexane:EtOAc)

2-(4-Hydroxybut-1-yn-1-yl)-5-methoxybenzaldehyde (**18**)

To a solution of 2-iodo-5-methoxybenzaldehyde **17** (750 mg, 2.86 mmol) and 3-butyn-1-ol (260 mg, 3.71 mmol, 0.28 mL) in dry THF (10 mL) and DIPA (5 mL) were added $(\text{Ph}_3\text{P})_2\text{PdCl}_2$ (20 mg, 0.03 mmol) and CuI (81 mg, 0.43 mmol) under nitrogen. The reaction mixture was stirred at room temperature for 14 h. Reaction mixture was diluted with saturated aq. NH_4Cl (10 mL) and ethyl acetate (20 mL). Aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4 . Evaporation of the solvent and purification of the crude mixture by column chromatography (8:2, hexane: EtOAc) gave the alcohol **18** (475 mg, 1.34 mmol, 81 %) as a yellow oil.

^1H NMR (400 MHz, CDCl_3): δ = 10.4 (1 H, s), 7.44 (1 H, d, J = 8.5 Hz), 7.35 (1 H, d, J = 2.8 Hz), 7.08 (1 H, dd, J = 2.8 & 8.5 Hz), 3.84-3.87 (5 H, m), 2.74 (2 H, t, J = 6.2 Hz), 2.17 (1 H, br s) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 191.9, 159.5, 137.4, 134.8, 121.5, 119.5, 110.7, 92.4, 78.1, 61.2, 55.7 and 24.1 ppm.

IR (neat): 3429, 3056, 2982, 1690, 1607, 1495, 1424, 1266, 1161, 1039, 736 and 453 cm^{-1}

TLC: R_f = 0.4 (4:1; hexane:EtOAc)

HR ESI-MS: $[\text{C}_{12}\text{H}_{13}\text{O}_3]^+ = [\text{M}+\text{H}]^+$ requires 205.0845; found 205.0865

2-(But-3-en-1-yn-1-yl)-5-methoxybenzaldehyde (19) & 4-(2-Formyl-4-methoxyphenyl)but-3-yn-1-yl 4-methylbenzenesulfonate (20)

To an ice-cold solution of the alcohol **18** (450 mg, 2.20 mmol) in dry CH_2Cl_2 (5 mL) were added triethylamine (5 mL), 4-toluenesulfonylchloride (544 mg, 2.86 mmol) and DMAP (54 mg, 0.44 mmol). The reaction was stirred at room temperature for 36 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4 . Evaporation of the solvent and purification of the crude mixture by column chromatography (9:1, hexane: EtOAc) gave the enyne-aldehyde **19** (275 mg, 1.47 mmol, 67%) as a pale yellow solid. Further elution with (4:1, hexane:EtOAc) gave the tosylate **20** (125 mg, 0.35 mmol, 16 %) as a yellow solid.

2-(but-3-en-1-yn-1-yl)-5-methoxybenzaldehyde (10)

^1H NMR (400 MHz, CDCl_3): δ = 10.4 (1 H, s), 7.47 (1 H, d, J = 8.6 Hz), 7.39 (1 H, d, J = 2.8 Hz), 7.10 (1 H, dd, J = 2.8 & 8.6 Hz), 6.05 (1 H, dd, J = 11.2 & 17.5 Hz), 5.77 (1 H, dd, J = 2.0 & 17.5 Hz), 5.60 (1 H, dd, J = 2.0 & 11.2 Hz), 3.86 (3 H, s) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 191.7, 159.9, 137.3, 134.7, 127.8, 121.8, 119.5, 116.8, 109.9, 93.6, 85.4 and 55.7 ppm.

IR (neat): 3055, 2984, 2849, 1689, 1603, 1491, 1424, 1267, 1161, 1033, 895, 738 and 455 cm^{-1}

TLC: R_f = 0.6 (9:1; hexane:EtOAc)

HR ESI-MS: $[\text{C}_{12}\text{H}_{13}\text{O}_3]^+ = [\text{M}+\text{H}]^+$ requires 205.0845; found 205.0865

M.P: 45-48° C

4-(2-Formyl-4-methoxyphenyl)but-3-yn-1-yl 4-methylbenzenesulfonate (20)

^1H NMR (400 MHz, CDCl_3): δ = 10.3 (1 H, s), 7.81 (2 H, d, J = 8.3 Hz), 7.36 (2 H, dd, J = 8.6 & 11.3 Hz), 7.31 (2 H, d, J = 8.0 Hz), 7.06 (1 H, dd, J = 2.8 & 8.6 Hz), 4.21 (2 H, t, J = 6.8 Hz), 3.85 (3 H, s), 2.84 (2 H, t, J = 6.8 Hz), 2.41 (3 H, s) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 191.5, 159.7, 145.1, 137.5, 134.8, 132.9, 130.0, 128.0, 121.6, 119.3, 109.8, 89.8, 78.3, 67.6, 55.7, 21.7 and 20.7 ppm.

IR (neat): 3057, 2980, 2850, 2752, 1692, 1602, 1492, 1427, 1364, 1267, 1225, 1177, 1096, 1032, 981, 898, 820, 738, 557 and 488 cm^{-1}

TLC: R_f = 0.3 (9:1; hexane:EtOAc)

M.P:70-72° C

HR ESI-MS: $[\text{C}_{19}\text{H}_{19}\text{O}_5\text{SNa}]^+ = [\text{M}+\text{H}]^+$ requires 371.0773; found 371.0769

(2-(But-3-en-1-yn-1-yl)-5-methoxyphenyl)prop-2-yn-1-ol (21)

To an ice-cold solution of enyne-aldehyde **19** (270 mg, 1.45 mmol) in dry THF (5 mL) was added ethynylmagnesium bromide (5.8 mL, 2.9 mmol, 0.5 M solution in THF) and stirred the reaction at 0° C for 2 h. The reaction mixture was diluted with saturated aq. NH_4Cl and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4 . Evaporation of the

solvent and purification of the crude mixture by column chromatography (4:1, hexane: EtOAc) gave the propargylic alcohol **21** (270 mg, 1.27 mmol, 88%) as a yellow oil.

^1H NMR (400 MHz, CDCl_3): δ = 7.38 (1 H, dd, J = 2.0 & 8.5 Hz), 7.25 (1 H, d, J = 1.6 Hz), 6.81 (1 H, d, J = 8.5 Hz), 6.02 (1 H, ddd, J = 1.2, 7.6 & 11.2 Hz), 5.82 (1 H, s), 5.72 (1 H, dt, J = 1.9 & 17.5 Hz), 5.53 (1 H, dd, J = 1.8 & 11.2 Hz), 3.83 (3 H, t, J = 3.3 Hz), 3.02 (1 H, br s), 2.63 (1 H, q, J = 0.8 Hz) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 160.1, 143.5, 133.9, 126.8, 117.1, 114.3, 113.4, 112.1, 92.3, 87.0, 82.9, 74.5, 62.8 and 55.4 ppm.

IR (neat): 3425, 3301, 3055, 2982, 2845, 1605, 1493, 1427, 1266, 1159, 1031, 971, 895, 738 and 512 cm^{-1}

HR ESI-MS: $[\text{C}_{14}\text{H}_{12}\text{O}_2\text{Na}]^+ = [\text{M}+\text{Na}]^+$ requires 235.0735; found 235.0726

TLC: R_f = 0.5 (8:2; hexane:EtOAc)

1-[2-(But-3-en-1-yn-1-yl)-5-methoxyphenyl]-5-(4-methoxyphenyl)penta-2,4-diyne-1-ol (23)

To a solution of an propargylic alcohol **21** (250 mg, 1.18 mmol), and bromoalkyne^{9b} **22** (242 mg, 1.30 mmol) in 1,2-DCE (8 mL) and piperidine (0.6 mL, 5.9 mmol, freshly degassed) at 0 °C under nitrogen atmosphere, was added CuCl (12 mg, 0.12 mmol), and reaction mixture was stirred 0 °C for 30 minutes. The reaction mixture was diluted with aq. NH_4Cl (10 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layer was washed with brine (10 mL) and dried over Na_2SO_4 . Evaporation of the solvent and purification of the crude mixture by flash column chromatography (4:1, hexane:EtOAc) gave the corresponding diyne **23** (255 mg, 0.745 mmol, 63 %) as a yellow oil.

^1H NMR (400 MHz, CDCl_3): δ = 7.40 (3 H, t, J = 8.9 Hz), 7.21 (1 H, s), 6.82 (3 H, d, J = 8.6 Hz), 6.04 (1 H, dd, J = 11.2 & 17.5 Hz), 5.92 (1 H, s), 5.74 (1 H, d, J = 17.5 Hz), 5.54 (1 H, d, J = 11.2 Hz), 3.84 (3 H, s), 3.79 (3 H, s) ppm.

^{13}C NMR (100 MHz, CDCl_3): δ = 160.5, 160.2, 143.2, 134.3, 134.0, 126.9, 117.1, 114.4, 114.2, 113.4, 113.3, 112.2, 92.5, 87.0, 80.7, 79.5, 72.3, 71.2, 63.6, 55.5 and 55.4 ppm.

IR (neat): 3407, 3055, 2986, 2844, 1605, 1507, 1427, 1265, 1172, 1030, 895, 739 and 544 cm^{-1}

TLC: $R_f = 0.5$ (8:2; hexane:EtOAc)

HR ESI-MS: $[C_{23}H_{18}O_3Na]^+ = [M+H]^+$ requires 365.1154; found 365.1140

7-methoxy-1-[(4-methoxyphenyl)ethynyl]-9H-fluoren-9-one (**14**)

Reaction 1: A solution of enyne-diyne alcohol **23** (100 mg, 0.292 mmol) in dry 1,2-DCB (5 mL), was heated at 150 °C for 28 h. The reaction mixture was filtered through a short silica gel column (eluent: hexane and hexane/ethyl acetate 9:1) to give the cyclised ketone product **14** (60 mg, 0.18 mmol, 60%) as a yellow solid.

Reaction 2: To a solution of diyne **23** (100 mg, 0.292 mmol) in dry EtOAc (5 mL), was added IBX (106 mg, 0.38 mmol) and the reaction mixture was heated at 80 °C for 2 h. The reaction mixture was filtered through a short silica gel column (eluent: hexane/ethyl acetate 9:1) to give the cyclised product **14** (60 mg, 0.18 mmol, 60%) as a yellow solid.

1H NMR (400 MHz, $CDCl_3$): $\delta = 7.64$ (2 H, d, $J = 8.7$ Hz), 7.37 (2 H, d, $J = 8.2$ Hz), 7.32 (1 H, t, $J = 8.1$ Hz), 7.25 (1 H, d, $J = 7.3$ Hz), 7.19 (1 H, d, $J = 2.1$ Hz), 6.95 (1 H, dd, $J = 2.3$ & 8.1 Hz), 6.90 (2 H, d, $J = 8.7$ Hz), 3.84 (3 H, s), 3.83 (3 H, s) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 192.0, 161.1, 160.2, 145.3, 136.1, 135.6, 134.1, 133.8, 133.3, 131.6, 121.4, 120.1, 118.8, 115.2, 114.2, 114.1, 109.2, 96.2, 85.6, 55.8$ and 55.4 ppm.

IR (neat): 3055, 2985, 2937, 2839, 1712, 1582, 1510, 1488, 1468, 1438, 1421, 1265, 1172, 1103, 1027, 955, 895, 833, 801, 741, 704, 612 and 532 cm^{-1}

HR ESI-MS: $[C_{23}H_{16}O_3Na]^+ = [M+Na]^+$ requires 363.0997; found 363.0987

TLC: $R_f = 0.6$ (4:1; hexane:EtOAc)

M.P.: 128-130 °C

7-methoxy-9-(4-methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-9H-fluoren-9-ol (**28**)

To an ice-cold solution of cyclised ketone **14** (50 mg, 0.15 mmol) in dry THF (2 mL) was added *p*-anisylmagnesium bromide (2 mL in THF, 0.19 mmol, freshly prepared from *p*-bromoanisole and Mg). After 2 h, the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with ethyl acetate (2

x 10 mL). The combined organic layer was washed with brine (10 mL) and dried over Na₂SO₄. Evaporation of the solvent and purification of the crude mixture by flash column chromatography gave the corresponding tertiary alcohol **28** (55 mg, 0.12 mmol, 84 %) as yellow oil.

¹H NMR (400 MHz, CDCl₃): δ = 7.54 (2 H, dd, *J* = 4.0 & 6.8 Hz), 7.32-7.36 (3 H, m), 7.29 (1 H, d, *J* = 8.7 Hz), 7.14 (2 H, d, *J* = 8.7 Hz), 6.85 (2 H, d, *J* = 7.4 Hz), 6.81 (3 H, d, *J* = 8.7 Hz), 6.76 (1 H, d, *J* = 3.6 Hz), 3.81 (3 H, s), 3.76 (3 H, s), 3.75 (3 H, s), 3.33 (1 H, d, *J* = 3.7 Hz) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 160.6, 159.9, 158.8, 152.0, 150.4, 140.9, 135.3, 133.0, 131.1, 130.1, 129.3, 126.6, 121.2, 119.0, 116.1, 115.0, 114.9, 114.0, 113.6, 110.0, 95.5, 85.0, 83.9, 55.5, 55.4 and 55.3 ppm.

IR (neat): 3440, 3055, 2982, 2931, 2841, 1605, 1508, 1458, 1427, 1262, 1173, 1031, 895, 738, 534 and 425 cm⁻¹

HR ESI-MS: [C₃₀H₂₄O₄Na]⁺ = [M+Na]⁺ requires 471.1572; found 471.1588

TLC: R_f = 0.4 (4:1; hexane:EtOAc)

4-(7-methoxy-9-(4-methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-9H-fluoren-9-yl)phenol (29)

To an ice-cold solution *tert*-alcohol **28** (40 mg, 0.089 mmol) and phenol (17 mg, 0.18 mmol), in dry CH₂Cl₂ (2 mL) was added trifluoromethanesulfonic acid (0.2 mL, 0.18 mmol 0.1 M solution) to the reaction mixture and stirred the reaction mixture for 1 h, at same temperature. Diluted the reaction mixture with cold water (5 mL) and CH₂Cl₂ (10 mL). The aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL). The combined organic layer was washed with brine and dried over anhydrous Na₂SO₄. Evaporation of the solvent and purification of the crude material by column chromatography (eluent: hexane/ethyl acetate 4:1) afforded the phenol inserted product **29** (34 mg, 0.064 mmol, 73%) as a yellow solid.

¹H NMR (400 MHz, CDCl₃): δ = 7.63 (2 H, d, *J* = 8.3 Hz), 7.30 (2 H, s), 7.23 (2 H, dd, *J* = 8.8 Hz), 7.18 (2 H, d, *J* = 8.3 Hz), 7.00 (2 H, d, *J* = 8.6 Hz), 6.88 (1H, d, *J* = 7.9 Hz), 6.83 (1 H, s) 6.79 (2 H, d, *J* = 8.3

Hz), 6.71 (2 H, d, $J = 8.7$ Hz), 6.64 (2 H, d, $J = 8.4$ Hz), 4.64 (1 H, s), 3.80 (3 H, s), 3.75 (3 H, s), 3.73 (3 H, s) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 160.2, 159.5, 158.1, 155.6, 155.1, 151.9, 140.7, 135.1, 134.0, 132.7, 132.1, 130.8, 130.26, 130.21, 127.5, 120.7, 119.2, 115.9, 114.8, 114.5, 113.9, 113.4, 113.0, 111.0, 95.8, 87.5, 65.0, 55.5, 55.3$ and 55.2 ppm.

IR (neat): 3055, 2985, 2929, 2840, 1605, 1508, 1462, 1440, 1423, 1264, 1175, 1109, 1032, 896, 831, 738, 553, 435 and 418 cm^{-1}

TLC: $R_f = 0.4$ (8:2; hexane:EtOAc)

HR ESI-MS: $[\text{C}_{36}\text{H}_{28}\text{O}_4\text{K}]^+ = [\text{M}+\text{K}]^+$ requires 563.1625; found 563.1602

M.P:148-150 °C

















