Experiment section

Reagents and general methods

All reagents were purchased from commercial suppliers and were dried and purified when necessary, and **3a-c**, **3f**, **4b-i**, **4w-y**, **5a-h**, **5v-y**, **6a-h** and **6v-y** were prepared as previously described.

Melting points were determined in capillary tubes on an electrothermal PIF YRT-3 apparatus and without correction. ESI-MS spectra were obtained from VG ZAB-HS spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a AVANCE III 400MHz spectrometer at 400 MHz and 100 MHz and a Varian INOVA 500NB spectrometer at 500 MHz and 125 MHz, respectively, using TMS as internal standard and $CDCl_3$ or DMSO-d_6 as solvent and chemical shifts (d) were expressed in ppm. HRMS were obtained from ESI-Q-TOF maxis 4G spectrometer. Silica gel F254 were used in analytical thin-layer chromatography (TLC) and silica gel were used in column chromatography respectively.

General procedure for the preparation of 1-substituted-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (1d-e)

A mixture of L-tryptophan (40.8g, 200mmol), acetic acid (300ml) and the appropriate aldehydes (210mmol) was refluxed for 3 h, then cooled and adjusted pH to 5 with concentrated ammonium hydroxide, the precipitated product was collected by filtration and washed well with water and dried to provide the intermediates **1d-e**. Further purification was not necessary and used directly for the next steps.

General procedure for the preparation of ethyl 1-substituted-1,2,3,4-tetrahydro-β-carboline-3-carboxylate (2d-e)

1-substituted 1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid **1d-e** (100mmol), anhydrous ethanol (300ml) and $SOCl_2$ (20ml) was heated at reflux for 4 h, and then evaporated in reduced pressure. The resulting mixture was poured into H_2O (200ml) and neutralized with sodium hydrogen carbonate. The solution was extracted with ethyl acetate (3×150 ml). The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated to give intermediates **2d-e**. Further purification was not necessary and used directly for the next steps.

General procedure for the preparation of ethyl 1-substituted-β-carboline-3-carboxylate (3d-e)

Ethyl 1-substituted-1,2,3,4-tetrahydro-β-carboline-3-carboxylate **2d-e** (100mmol) and sulfur (9.6g, 300mmol) in xylene (200ml) was heated at reflux for 8 h. Completion of the reaction as indicated by TLC. The solution was cooled and stored at 4 ℃ for 3 h, and then filtered and washed generously with petroleum ether, the solid was purified by column chromatography with ethyl acetate and petroleum ether (1:1), ethyl acetate as the eluent to successfully afford the intermediates **3d-e**.

Ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate (3d)

Starting from ethyl 1-(4-methoxyphenyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylate **2d** (35.0g, 100mmol) and sulfur (9.6g, 300mmol), white solid was obtained (28.6g, 83%), mp 167.6-169.5℃. ESI-MS m/z: 347.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 9.02 (1H, s, ArH), 8.80 (1H, s, ArH), 8.21 (1H, d, *J*=7.6Hz, ArH), 7.86-7.82 (2H, m, ArH), 7.56-7.54 (2H, m, ArH), 7.38-7.34 (1H, m, ArH), 6.96-6.92 (2H, m, ArH), 4.52 (2H, q, *J*=7.2Hz, $COOC\boldsymbol{H}_2CH_3$), 3.81 (3H, s, $OC\boldsymbol{H}_3$), 1.48 (3H, t, *J*=7.2Hz, $COOCH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 159.7, 142.8, 141.0, 137.6, 135.0, 129.7, 129.4, 129.3, 128.5, 121.9, 121.5, 120.5, 116.1, 113.6, 112.3, 61.3, 55.0, 14.4.

Ethyl 1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate (3e)

Starting from 1-(3,4-dimethoxyphenyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylate **2e** (38.0g, 100mmol) and sulfur (9.6g, 300mmol), white solid was obtained (29.7g, 79%), mp 144.4-147.1℃. ESI-MS m/z: 377.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 9.06 (1H, s, ArH), 8.81 (1H, s, ArH), 8.22 (1H, d, J = 7.6Hz, ArH), 7.62-7.57 (2H, m, ArH), 7.45 (2H, d, J=8.4Hz, ArH), 7.40-7.35 (1H, m, ArH), 6.91 (1H, d, J=8.0Hz, ArH), 4.53 (2H, q, J=7.2Hz, $COOC\boldsymbol{H}_2CH_3$), 3.89 (3H, s, $OC\boldsymbol{H}_3$), 3.88 (3H, s, $OC\boldsymbol{H}_3$),1.49 (3H, t, J=7.2Hz, $COOCH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 149.3, 149.0, 142.8, 140.9, 137.5, 135.0, 130.1, 129.3, 128.5, 122.0, 121.7, 120.7, 120.6, 116.2, 112.2, 111.2, 110.3, 61.3, 55.6, 14.4.

General procedure for the preparation of ethyl 1,9-disubstituted-β-carboline-3-carboxylate (4j-m and 4o-v).

Ethyl 1-substituted-β-carboline-3-carboxylate **3c-e** (10mmol) and anhydrous DMF (50ml) was stirred at RT until clear, and then 60% NaH (0.6g, 15mmol) and halogenated alkane (20-40mmol) were added. The mixture was stirred at RT for 0.5-2 h. After completion of the reaction as indicated by TLC, the solution was poured into H_2O (150ml), and extracted with ethyl acetate. The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated. The resulting oil was crystallized from ethyl ether or ethyl ether-petroleum ether to provide compounds **4j-m** and **4o-v**.

Ethyl 9-methyl-1-phenyl-β-carboline-3-carboxylate (4j)

Starting from ethyl 1-phenyl-β-carboline-3-carboxylate **3c** (3.16g, 10mmol) and iodomethane (20mmol), white solid was obtained (2.47 g, 75%), mp 134.1-135.0℃. ESI-MS m/z: 331.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.88 (1H, s, ArH), 8.25 (1H, d, J=8.0Hz, ArH), 7.67-

7.63(3H, m, ArH), 7.56-7.44 (4H, m, ArH), 7.40-7.37 (1H, m, ArH), 4.52 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 3.48 (3H, s, NC***H***$_3$), 1.48 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 143.9, 143.0, 139.1, 137.2, 136.3, 129.8 (**2C**), 128.7, 128.6, 128.1, 121.5, 121.3, 120.6, 116.4, 110.0, 61.4, 32.9, 14.4.

Ethyl 9-ethyl-1-phenyl-β-carboline-3-carboxylate (4k)

Starting from ethyl 1-phenyl-β-carboline-3-carboxylate **3c** (3.16g, 10mmol) and bromoethane (20mmol). White solid was obtained (2.41 g, 70%), mp 127.6-129.8℃. ESI-MS m/z: 345.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89 (1H, s, ArH), 8.26 (1H, d, *J*=7.6Hz, ArH), 7.65-7.60(3H, m, ArH), 7.52-7.47 (4H, m, ArH), 7.37 (1H, t, *J*=7.2Hz, ArH), 4.52 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 4.00 (2H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 1.47 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$), 1.00 (3H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 143.9, 141.9, 139.3, 137.0, 135.3, 130.1, 129.2, 128.6, 128.5, 128.0, 121.6 (**2C**), 120.5, 116.4, 110.2, 61.3, 39.1, 14.4, 13.9.

Ethyl 9-benzyl-1-phenyl-β-carboline-3-carboxylate (4l)

Starting from ethyl 1-phenyl-β-carboline-3-carboxylate **3c** (3.16g, 10mmol) and benzyl bromide (20mmol), white solid was obtained (2.76g, 68%), mp 149.5 -152.6℃. ESI-MS m/z: 407.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.93 (s, 1H), 8.28 (1H, d, *J* = 8.0 Hz, ArH), 7.53 – 7.57 (1H , m, ArH), 7.33 – 7.41 (5H, m, ArH), 7.25-29 (2H, m, ArH), 7.06 – 7.15 (3H, m, ArH), 6.53 (2H, d, *J* = 6.8 Hz, ArH), 5.21 (s, 2H, C***H***$_2$Ph), 4.51 (2H, q, *J* = 7.2 Hz, COOC***H***$_2$CH$_3$), 1.46 (3H, t, *J* = 7.2 Hz, COOCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.17, 144.45, 142.96, 138.85, 137.70, 136.54, 136.01, 130.55, 129.60, 129.05, 128.64, 128.45, 128.07, 127.23, 125.58, 121.78, 121.75, 121.12, 116.64, 111.00, 61.58, 48.20, 14.53.

Ethyl 9-(3-phenylpropyl)-1-phenyl-β-carboline-3-carboxylate (4m)

Starting from ethyl 1-phenyl-β-carboline-3-carboxylate **3c** (3.16g, 10mmol) and 1-bromo-3-phenylpropane (30mmol), white solid was obtained (3.17g, 73%), mp 147.6-148.9℃. ESI-MS m/z: 435.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.88 (1H, s, ArH), 8.24 (1H, d, *J*=7.6Hz, ArH), 7.69-7.62 (2H, m, ArH), 7.62-7.51 (4H, m, ArH), 7.40-7.30 (2H, m, ArH), 7.23-7.13 (3H, m, ArH), 6.94 (1H, d, *J*=6.8Hz, ArH), 4.52 (2H, q, *J*=7.2Hz, $COOC\boldsymbol{H_2}CH_3$), 3.97 (2H, t, *J*=8.0Hz, $NC\boldsymbol{H}_2CH_2CH_2Ph$), 2.12 (2H, t, *J*=8.0Hz, $NCH_2CH_2C\boldsymbol{H}_2Ph$), 1.75-1.67 (2H, m, $NCH_2C\boldsymbol{H}_2CH_2Ph$), 1.47 (3H, t, *J*=7.2Hz, $COOCH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 143.9, 142.1, 140.4, 139.2, 137.1, 135.4, 130.1, 129.4, 128.6 (**2C**), 128.2, 128.1, 127.8, 125.9, 121.6, 121.5, 120.6, 116.5, 110.2, 61.3, 44.1, 32.6, 30.4, 14.4.

Ethyl 9-methyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate (4o)

Starting from ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate **3d** (3.46g, 10mmol) and iodomethane (30mmol), white solid was obtained (2.74 g, 76%), mp 161.0-162.6℃. ESI-MS m/z: 361.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.85 (1H, s, ArH), 8.25 (1H, d, *J*=8.0Hz, ArH), 7.66-7.57 (3H, m, ArH), 7.47 (1H, d, *J*=8.4Hz, ArH), 7.36 (1H, t, *J*=7.2Hz, ArH), 7.07-7.03 (2H, m, ArH), 4.52 (2H, q, *J*=7.2Hz, $COOC\boldsymbol{H_2}CH_3$), 3.90 (3H, s, $OC\boldsymbol{H}_3$), 3.52 (3H, s, $NC\boldsymbol{H}_3$), 1.48 (3H, t, *J*=7.2Hz, $COOCH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 160.0, 143.8, 143.1, 137.2, 136.4, 131.6, 131.1, 129.7, 128.7, 121.5, 121.4, 120.6, 116.2, 113.5, 110.0, 61.4, 55.3, 32.9, 14.4.

Ethyl 9-butyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate (4p)

Starting from ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate **3d** (3.46, 10mmol) and n-iodobutane (40mmol), yellow solid was obtained (3.01g, 75%), mp 114.2-115.2℃. ESI-MS m/z: 403.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.86 (1H, s, ArH), 8.25 (1H, d, *J*=7.6Hz,

ArH), 7.64-7.56 (3H, m, ArH), 7.48 (1H, d, *J*=8.4Hz, ArH), 7.36 (1H, t, *J*=7.6Hz, ArH), 7.04 (2H, d, *J*=8.8Hz, ArH), 4.51 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 4.01 (2H, t, *J*=7.6Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 3.90 (3H, s, OC***H***$_3$), 1.47 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$), 1.41-1.33 (2H, m, NCH$_2$C***H***$_2$CH$_2$CH$_3$), 0.93-0.83 (2H, m, NCH$_2$CH$_2$C***H***$_2$CH$_3$), 0.67 (3H, t, *J*=7.2Hz, NCH$_2$CH$_2$CH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.1, 159.9, 143.8, 142.2, 137.0, 135.7, 131.8, 130.7, 130.0, 128.4, 121.6, 121.5, 120.4, 116.2, 113.5, 110.4, 61.3, 55.3, 44.3, 30.9, 19.6, 14.4, 13.3.

Ethyl 9-benzyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate (4q)

Starting from ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate **3d** (3.46g, 10mmol) and benzyl bromide (20mmol), white solid was obtained (3.14 g, 72%), mp 146.5-147.8℃. ESI-MS m/z: 437.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.90 (1H, s, ArH), 8.28 (1H, d, *J*=7.6Hz, ArH), 7.58-7.54 (1H, m, ArH), 7.40-7.35 (4H, m, ArH), 7.15-7.09 (3H, m, ArH), 6.84-6.80 (2H, m, ArH), 6.61-6.58 (2H, m, ArH), 5.28 (2H, s, NC***H***$_2$Ph), 4.51 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 3.83 (3H, s, OC***H***$_3$), 1.47 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.1, 159.9, 144.2, 142.8, 137.6, 136.6, 136.1, 131.3, 130.7, 130.4, 128.8, 128.3, 127.1, 125.5, 121.7, 121.6, 120.9, 116.3, 113.4, 110.9, 61.4, 55.3, 48.1, 14.4.

Ethyl 9-(3-phenylpropyl)-1-(4-methoxyphenyl)-β-carboline-3-carboxylate (4r)

Starting from ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate **3d** (3.46g, 10mmol) and 1-bromo-3-phenylpropane (30mmol), white solid was obtained (3.2 g, 69%), mp 135.4-137.8℃. ESI-MS m/z: 465.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.85 (1H, s, ArH), 8.24 (1H, d, *J*=8.0Hz, ArH), 7.61-7.53 (3H, m, ArH), 7.37-7.34 (2H, m, ArH), 7.21 (2H, t, *J*=7.2Hz, ArH), 7.15 (1H, t, *J*=7.2Hz, ArH), 7.06 (2H, d, *J*=8.8Hz, ArH), 6.94 (2H, d, *J*=7.2Hz, ArH), 4.51 (2H, q,

J=7.2Hz, COOC***H***$_2$CH$_3$), 4.05 (2H, t, *J*=7.6Hz, NC***H***$_2$CH$_2$CH$_2$Ph), 3.92 (3H, s, OC***H***$_3$), 2.17 (2H, t, *J*=7.6Hz, NCH$_2$CH$_2$C***H***$_2$Ph), 1.74-1.65 (2H, m, NCH$_2$C***H***$_2$CH$_2$Ph), 1.47 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.1, 159.9, 143.8, 142.2, 140.4, 137.2, 135.6, 131.7, 130.7, 130.2, 128.5, 128.2, 127.9, 125.9, 121.6 (**2C**), 120.6, 116.3, 113.6, 110.3, 61.3, 55.3, 44.2, 32.7, 30.4, 14.4.

Ethyl 9-ethyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate (4s)

Starting from ethyl 1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **3e** (3.76g, 10mmol) and bromoethane (30mmol), yellow solid was obtained (3.31 g, 82%), mp 135.8-136.1℃. ESI-MS m/z: 405.1 (100) [M+H]$^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.87 (1H, s, ArH), 8.25 (1H, d, *J*=7.6Hz, ArH), 7.65-7.61 (1H, m, ArH), 7.49 (1H, d, *J*=8.4Hz, ArH), 7.37 (1H, t, *J*=7.2Hz, ArH), 7.19-7.15 (2H, m, ArH), 7.00 (1H, d, *J*=8.0Hz, ArH), 4.51 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 4.05 (2H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 3.97 (3H, s, OC***H***$_3$), 3.92 (3H, s, OC***H***$_3$), 1.47 (3H, t, *J*=7.2Hz, COOCH$_2$C***H***$_3$), 1.03 (3H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.3, 149.6, 148.8, 144.0, 142.2, 137.2, 135.6, 132.2, 130.4, 128.8, 122.2, 122.0, 121.9, 120.8, 116.6, 112.8, 110.9, 110.6, 61.5, 56.2 (2C), 39.4, 14.6, 14.4.

Ethyl 9-butyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate (4t)

Starting from ethyl 1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **3e** (3.76g, 10mmol) and n-iodobutane (30mmol), white solid was obtained (3.02 g, 70%), mp 117.2-118.3℃. ESI-MS m/z: 433.1 (100) [M+H]$^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.87 (1H, s, ArH), 8.25 (1H, d, *J*=7.6Hz, ArH), 7.65-7.61 (1H, m, ArH), 7.48 (1H, d, *J*=8.4Hz, ArH), 7.37 (1H, t, *J*=7.2Hz, ArH), 7.20-7.15 (2H, m, ArH), 7.01 (1H, d, *J*=8.0Hz, ArH), 4.52 (2H, q, *J*=7.2Hz, COOC***H***$_2$CH$_3$), 4.00 (3H, t, *J*=7.2Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 3.97 (3H, s, OC***H***$_3$), 3.93 (3H, s, OC***H***$_3$), 1.47 (3H, t, *J*=7.2Hz,

$COOCH_2C\boldsymbol{H}_3$), 1.45-1.37 (2H, m, $NCH_2C\boldsymbol{H}_2CH_2CH_3$), 0.95-0.86 (2H, m, $NCH_2CH_2C\boldsymbol{H}_2CH_3$), 0.68 (3H, t, *J*=7.2Hz, $NCH_2CH_2CH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 149.4, 148.7, 143.8, 142.3, 137.0, 135.7, 132.0, 130.2, 128.6, 122.1, 121.6 (2C), 120.5, 116.4, 112.6, 110.7, 110.5, 61.4, 56.0, 55.9, 44.3, 31.2, 19.8, 14.4, 13.4.

Ethyl 9-benzyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate (4u)

Starting from ethyl 1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **3e** (3.76g, 10mmol) and benzyl bromide (30mmol), yellow solid was obtained (3.91g, 84%), mp 158.9-161.2℃. ESI-MS m/z: 467.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (1H, s, ArH), 8.30 (1H, d, *J*=7.6Hz, ArH), 7.58-7.54 (1H, m, ArH), 7.41-7.33 (2H, m, ArH), 7.18-7.11 (3H, m, ArH), 7.00 (1H, dd, *J*=8.0, 2.0Hz, ArH), 6.84-6.81 (2H, m, ArH), 6.60-6.58 (2H, m, ArH), 5.26 (2H, s, $NC\boldsymbol{H}_2Ph$), 4.52 (2H, q, *J*=7.2Hz, $COOC\boldsymbol{H}_2CH_3$), 3.92 (3H, s, $OC\boldsymbol{H}_3$), 3.49 (3H, s, $OC\boldsymbol{H}_3$), 1.47 (3H, t, *J*=7.2Hz, $COOCH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 149.1, 148.1, 143.9, 142.5, 137.2, 136.5, 135.7, 131.2, 130.0, 128.7, 128.2, 126.8, 125.1, 121.9, 121.4, 121.3, 120.8, 116.3, 112.1, 110.6, 110.4, 61.2, 55.7, 55.1, 47.7, 14.2.

Ethyl 9-(3-phenylpropyl)-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate (4v)

Starting from ethyl 1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **3e** (3.76g, 10mmol) and 1-bromo-3-phenylpropane (30mmol), yellow solid was obtained (3.56g, 72%), mp 134.1-135.6℃. ESI-MS m/z: 495.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (1H, s, ArH), 8.24 (1H, d, *J*=8.4Hz, ArH), 7.62-7.58 (1H, m, ArH), 7.38-7.34 (2H, m, ArH), 7.23-7.13 (5H, m, ArH), 7.01 (1H,d, *J*=8.0Hz, ArH), 6.94 (2H, d, *J*=7.2Hz, ArH), 4.52 (2H, q, *J*=7.2Hz, $COOC\boldsymbol{H}_2CH_3$), 4.05 (2H, t, *J*=7.6Hz, $NC\boldsymbol{H}_2CH_2CH_2Ph$), 3.99 (3H, s, $OC\boldsymbol{H}_3$), 3.91 (3H, s, $OC\boldsymbol{H}_3$), 2.19 (2H, t, *J*=7.6Hz, $NCH_2CH_2C\boldsymbol{H}_2Ph$), 1.77-1.70 (m, 2H, $NCH_2C\boldsymbol{H}_2CH_2Ph$), 1.47 (t, *J*=7.2Hz, 3H, $COOCH_2C\boldsymbol{H}_3$);

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 149.8, 149.1, 144.1, 142.6, 140.8, 137.5, 136.0 (2C), 132.3, 130.6, 129.0, 128.6, 128.2, 126.3, 122.5, 122.0, 121.0, 116.7, 113.1, 111.0, 110.7, 61.7, 56.4, 56.3, 44.6, 33.2, 30.9, 14.8.

General procedure for the preparation of 1,9-disubstituted-3-hydroxymethyl-β-carboline (5i-u).

A fine suspension of compounds **3d** and **4j-v** (10mmol) in dry THF (100ml) was treated with $LiBH_4$ (30mmol), and the mixture was stirred at room temperature for 9 h. The reaction was cooled, treated with 10% aq. HCl (20ml), and stirred for 4 h. The reaction mixture was neutralized with 10% aq. NaOH solution and extracted with ethyl acetate. The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated. The residue obtained was purified by silica column chromatography with ethyl acetate as the eluent. Upon recrystallization, white crystals were obtained.

9-Methyl-1-phenyl-3-hydroxymethyl-β-carboline (5i)

Starting from ethyl 9-methyl-1-phenyl-β-carboline-3-carboxylate **4j** (3.30g, 10mmol), white solid was obtained (2.07 g, 72%), mp 143.6-144.3℃. ESI-MS m/z: 289.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (1H, d, *J*=7.6Hz, ArH), 7.93 (1H, s, ArH), 7.65-7.62 (2H, m, ArH), 7.61-7.57 (1H, m, ArH), 7.55-7.47 (3H, m, ArH), 7.41 (1H, d, *J*=8.4Hz, ArH), 7.30 (1H, t, *J*=7.6Hz, ArH), 4.95 (2H, s, C***H***$_2$OH), 3.45 (3H, s, NC***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.0, 143.2, 142.6, 139.4, 134.2, 131.0, 129.5, 128.4, 128.3, 128.0, 121.4, 120.9, 119.6, 110.2, 109.6, 64.7, 32.7.

9-Ethyl-1-phenyl-3-hydroxymethyl-β-carboline (5j)

Starting from ethyl 9-ethyl-1-phenyl-β-carboline-3-carboxylate **4k** (3.44g, 10mmol), yellow solid

was obtained (2.05 g, 68%), mp 173.5-174.5℃. ESI-MS m/z: 303.0 (100) $[M+H]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.15 (1H, d, *J*=8.1Hz, ArH), 7.93 (1H, s, ArH), 7.60-7.45 (6H, m, ArH), 7.41 (1H, d, *J*=8.4Hz, ArH), 7.30-7.24 (1H, m, ArH), 4.94 (2H, s, C***H***$_2$OH), 3.97 (2H, q, *J*=6.9Hz, NC***H***$_2$CH$_3$), 0.95 (3H, t, *J*=6.9Hz, NC***H***$_2$CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 142.9, 142.3, 139.7, 133.3, 131.5, 129.1, 128.5, 128.4, 128.1, 121.6, 121.4, 119.7, 110.4, 110.0, 64.8, 39.0, 13.8.

9-Benzyl-1-phenyl-3-hydroxymethyl-β-carboline (5k)

Starting from ethyl 9-benzyl-1-phenyl-β-carboline-3-carboxylate **4l** (4.06g, 10mmol), white solid was obtained (2.73g, 75%), mp 133.5-133.9℃. ESI-MS m/z: 365.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 – 8.21 (1H, m, ArH), 7.99 (1H, s, ArH), 7.52-7.56 (1H, m, ArH), 7.37 – 7.41 (3H, m, ArH), 7.27 – 7.34 (4H, m, ArH), 7.07 – 7.15 (3H, m, ArH), 6.53-6.55 (2H, m, ArH), 5.20 (2H, s, C***H***$_2$Ph), 4.96 (2H, s, C***H***$_2$OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.36, 143.30, 143.24, 139.27, 136.99, 133.86, 131.68, 129.37, 128.82, 128.44, 128.41, 128.04, 127.09, 125.66, 121.71, 121.40, 120.25, 110.62, 110.50, 64.86, 48.08.

9-(3-Phenylpropyl)-1-phenyl-3-hydroxymethyl-β-carboline (5l)

Starting from ethyl 9-(3-phenylpropyl)-1-phenyl-β-carboline-3-carboxylate **4m** (4.20g, 10mmol), yellow oil was obtained (2.70g, 69%). ESI-MS m/z: 393.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (1H, d, *J*=8.0Hz, ArH), 7.93 (1H, s, ArH), 7.62-7.60 (2H, m, ArH), 7.58-7.49 (4H, m, ArH), 7.31-7.27 (2H, m, ArH), 7.25-7.11 4H, (m, ArH), 6.93 (2H, d, *J*=7.6Hz, ArH), 4.94 (2H, s, C***H***$_2$OH), 3.94 (2H, t, *J*=8.0Hz, NC***H***$_2$CH$_2$CH$_2$Ph), 2.10 (2H, t, *J*=8.0Hz, NCH$_2$CH$_2$C***H***$_2$Ph), 1.70-1.60 (2H, m, NCH$_2$C***H***$_2$CH$_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 142.0, 141.6, 140.0 , 138.9, 132.3, 130.6, 128.6, 127.8, 127.7, 127.6, 127.5, 127.3, 125.2, 121.0, 120.5, 119.0, 110.1,

109.2, 64.2, 43.2, 32.0, 29.5.

1-(4-Methoxyphenyl)-3-hydroxymethyl-β-carboline (5m)

Starting from ethyl 1-(4-methoxyphenyl)-β-carboline-3-carboxylate **3d** (3.46g, 10mmol). White solid was obtained (2.22 g, 73%), mp 167.4-169.4℃. ESI-MS m/z: 305.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (1H, s, ArH), 8.12 (1H, d, *J*=8.0Hz, ArH), 7.92 (2H, d, *J*=8.8Hz, ArH), 7.82 (1H, s, ArH), 7.57-7.48 (2H, m, ArH), 7.34-7.27 (1H, m, ArH), 7.15-7.07 (2H, m, ArH), 4.96 (2H, s, C$\boldsymbol{H}_2$OH), 3.90 (3H, s, OC$\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.5, 150.5, 141.4, 140.7, 131.7, 130.8, 129.9, 129.6, 127.9, 121.4, 121.0, 119.2, 114.0, 112.3, 109.6, 64.7, 55.2.

9-Methyl-1-(4-methoxyphenyl)-3-hydroxymethyl-β-carboline (5n)

Starting from ethyl 9-methyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate **4o** (3.60g, 10mmol). Yellow solid was obtained (2.35g, 74%), mp 161.0-162.6℃. ESI-MS m/z: 319.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (1H, d, *J*=7.6Hz, ArH), 7.89 (1H, s, ArH), 7.63-7.56 (3H, m, ArH), 7.42 (1H, d, *J*=8.4Hz, ArH), 7.30 (1H, t, *J*=7.6Hz, ArH), 7.06 (2H, d, *J*=8.4Hz, ArH), 4.94 (2H, s, C$\boldsymbol{H}_2$OH), 3.91 (3H, s, OC$\boldsymbol{H}_3$), 3.49 (3H, s, NC$\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 147.9, 143.4, 142.6, 134.4, 131.8, 131.0, 130.8, 128.4, 121.4, 121.0, 119.6, 113.5, 109.9, 109.7, 64.7, 55.3, 32.8.

9-Butyl-1-(4-methoxyphenyl)-3-hydroxymethyl-β-carboline (5o)

Starting from ethyl 9-butyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate **4p** (4.02g, 10mmol), yellow solid was obtained (2.72g, 76%), mp 90.5-91.9℃. ESI-MS m/z: 359.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (1H, d, *J*=7.6Hz, ArH), 7.90 (1H, s, ArH), 7.56-7.48 (3H, m, ArH), 7.40 (1H, d, *J*=8.0Hz, ArH), 7.24 (1H, t, *J*=7.6Hz, ArH), 6.99 (2H, d, *J*=8.4Hz, ArH), 4.91 (2H, s, C$\boldsymbol{H}_2$OH), 3.94 (2H, t, *J*=7.6, NC$\boldsymbol{H}_2$CH$_2$CH$_2$CH$_3$), 3.84 (3H, s, OC$\boldsymbol{H}_3$), 1.34-1.26 (2H, m,

$NCH_2C\boldsymbol{H}_2CH_2CH_3$), 0.90-0.81 (2H, m, $NCH_2CH_2C\boldsymbol{H}_2CH_3$), 0.63 (3H, t, *J*=7.6Hz, $NCH_2CH_2CH_2C\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 148.1, 142.5, 142.4, 133.3, 131.8, 131.1, 130.3, 128.0, 121.4, 121.1, 119.4, 113.2, 110.1, 109.9, 64.6, 55.0, 43.9, 30.6, 19.5, 13.2.

9-Benzyl-1-(4-methoxyphenyl)-3-hydroxymethyl-β-carboline (5p)

Starting from ethyl 9-benzyl-1-(4-methoxyphenyl)-β-carboline-3-carboxylate **4q** (4.36g, 10mmol), yellow oil was obtained (3.07g, 78%). ESI-MS m/z: 395.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.13 (1H, m, ArH), 7.94 (1H, s, ArH), 7.51-7.46 (1H, m, ArH), 7.30-7.28 (4H, m, ArH), 7.09 (2H, d, *J*=7.2Hz, ArH), 6.81-6.77 (2H, m, ArH), 6.59-6.57 (2H, m, ArH), 5.20 (2H, s, $NC\boldsymbol{H}_2Ph$), 4.91 (2H, s, $C\boldsymbol{H}_2OH$), 3.79 (3H, s, $OC\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 148.2, 143.1, 143.0, 137.0, 133.9, 131.6, 131.5, 128.6, 128.3(2C), 127.7, 127.0, 125.6, 121.6, 120.1, 113.4, 110.6, 110.2, 64.7, 55.3, 48.0.

9-(3-Phenylpropyl)-1-(4-methoxyphenyl)-3-hydroxymethyl-β-carboline (5q)

Starting from ethyl 9-(3-phenylpropyl)-1-(4-methoxyphenyl)-β-carboline-3-carboxylate **4r** (4.50g, 10mmol), yellow solid was obtained (2.83g, 67%), mp 83.0-88.1℃. ESI-MS m/z: 423.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (1H, d, *J*=7.6Hz, ArH), 7.90 (1H, s, ArH), 7.57-7.52 (3H, m, ArH), 7.33-7.12 (6H, m, ArH), 7.07-7.02 (2H, m, ArH), 6.92 (2H, d, *J*=6.8Hz, ArH), 4.93 (2H, s, $C\boldsymbol{H}_2OH$), 4.02 (2H, t, *J*=7.6Hz, $NC\boldsymbol{H}_2CH_2CH_2Ph$), 3.90 (3H, s, $OC\boldsymbol{H}_3$), 2.15(2H, t, *J*=7.6Hz, $NCH_2CH_2C\boldsymbol{H}_2Ph$), 1.70-1.61 (2H, m, $NCH_2C\boldsymbol{H}_2CH_2Ph$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 148.0, 142.7, 142.5, 140.6, 133.5, 131.9, 131.4, 130.5, 128.3, 128.2, 127.9, 125.8, 121.6, 121.3, 119.7, 113.5, 110.3, 110.0, 64.7, 55.3, 44.0, 32.8, 30.2.

9-Ethyl-1-(3,4-dimethoxyphenyl)-3-hydroxymethyl-β-carboline (5r)

Starting from ethyl 9-ethyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **4s** (4.02g,

10mmol), white solid was obtained (2.97g, 82%), mp 152.8-153.8℃. ESI-MS m/z: 363.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (1H, d, *J*=7.6Hz, ArH), 7.94 (1H, s, ArH), 7.62-7.58 (1H, m, ArH), 7.45 (1H, d, *J*=8.4Hz, ArH), 7.30 (1H, t, *J*=7.6Hz, ArH), 7.18-7.16 (2H, m, ArH), 7.03-7.01 (1H, m, ArH), 4.95 (2H, s, C***H***$_2$OH), 4.05 (2H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 3.99 (3H, s, OC***H***$_3$), 3.93 (3H, s, OC***H***$_3$), 0.99 (3H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.5, 148.8, 148.1, 143.0, 142.6, 133.6, 132.6, 131.8, 128.7, 122.0, 121.9, 121.8, 120.0, 112.6, 111.0, 110.6, 110.3, 65.1, 56.2 (2C), 39.3, 14.3.

9-Butyl-1-(3,4-dimethoxyphenyl)-3-hydroxymethyl-β-carboline (5s)

Starting from ethyl 9-butyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **4t** (4.32g, 10mmol), white solid was obtained (2.81g, 72%), mp 144.2-144.9℃. ESI-MS m/z: 391.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (1H, d, *J*=7.6Hz, ArH), 7.94 (1H, s, ArH), 7.58 (1H, t, *J*=7.2 Hz, ArH), 7.43 (1H, d, *J*=8.4 Hz, ArH), 7.30 (1H, d, *J*=7.2Hz, ArH), 7.16-7.14 (1H, m, ArH), 7.01 (1H, d, *J*=8.8Hz, ArH), 4.95 (2H, s, C***H***$_2$OH), 3.98 (2H, t, *J*=7.2Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 3.96 (3H, s, OC***H***$_3$), 3.92 (3H, s, OC***H***$_3$), 1.41-1.33 (2H, m, NCH$_2$C***H***$_2$CH$_2$CH$_3$), 0.94-0.85 (2H, m, NCH$_2$CH$_2$C***H***$_2$CH$_3$), 0.67 (3H, t, *J*=7.2Hz, NCH$_2$CH$_2$CH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 148.5, 147.8, 142.6, 142.4, 133.4, 132.2, 131.2, 128.2, 121.8, 121.5, 121.2, 119.5, 112.3, 110.6, 110.2, 110.0, 64.7, 55.9, 55.8, 44.1, 30.9, 19.7, 13.4.

9-Benzyl-1-(3,4-dimethoxyphenyl)-3-hydroxymethyl-β-carboline (5t)

Starting from 9-benzyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **4u** (4.66g, 10mmol), yellow solid was obtained (3.22g, 76%), mp 166.2-167.8℃. ESI-MS m/z: 425.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (1H, d, *J*=7.6Hz, ArH), 7.98 (1H, s, ArH), 7.54-7.50 (1H, m,

ArH), 7.33-7.27 (2H, m, ArH), 7.14-7.11 (3H, m, ArH), 6.99-6.96 (1H, m, ArH), 6.84 (1H, d, *J*=8.4 Hz, ArH), 6.78 (1H, d, *J*=2.0Hz, ArH), 6.63-6.60 (2H, m, ArH), 5.23 (2H, s, NC***H***$_2$Ph), 4.95 (2H, s, C***H***$_2$OH), 3.92 (3H, s, OC***H***$_3$), 3.47 (3H, s, OC***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 148.2, 148.1, 143.0, 142.9, 137.1, 133.7, 131.8, 131.3, 128.6, 128.4, 126.9, 125.4, 121.7, 121.5, 121.2, 120.1, 112.0, 110.6, 110.4, 110.3, 64.8, 55.9, 55.3, 47.8.

9-(3-Phenylpropyl)-1-(3,4-dimethoxyphenyl)-3-hydroxymethyl-β-carboline (5u)

Starting from ethyl 9-(3-phenylpropyl)-1-(3,4-dimethoxyphenyl)-β-carboline-3-carboxylate **4v** (4.94g, 10mmol), yellow solid was obtained (3.34g, 74%), mp 98.3-103.3℃. ESI-MS m/z: 453.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (1H, d, *J*=7.6Hz, ArH), 7.93 (1H, s, ArH), 7.59-7.55 (1H, m, ArH), 7.35-7.27 (2H, m, ArH), 7.23-7.12 (5H, m, ArH), 7.03-7.01 (1H, m, ArH), 6.94-6.92 (2H, m, ArH), 4.95 (2H, s, C***H***$_2$OH), 4.04 (2H, t, *J*=8.0Hz, NC***H***$_2$CH$_2$CH$_2$Ph), 3.99 (3H, s, OC***H***$_3$), 3.91 (3H, s, OC***H***$_3$), 2.18 (2H, t, *J*=8.0 Hz, NCH$_2$CH$_2$C***H***$_2$Ph), 1.74-1.70 (2H, m, NCH$_2$C***H***$_2$CH$_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 148.6, 147.8, 142.7, 142.5, 140.6, 133.4, 132.2, 131.5, 128.4, 128.2, 127.9, 125.9, 121.8, 121.6, 121.3, 119.7, 112.4, 110.6, 110.2, 110.0, 64.8, 55.9 (2C), 44.1, 32.8, 30.4.

General procedure for the preparation of 1,9-disubstituted-β-carboline-3-carbaldehyde (6i-u).

To a solution of compounds **5i-u** (10mmol) in CH_3CN (120 ml) was added activated MnO_2 (50 mmol). The suspension was refluxed for 2 h and then cooled and filtered through Celite. The filtrate was passed through silica gel and washed with dichloromethane, and the solvent was removed under reduced pressure. The residue was crystallized from acetone or acetone-petroleum ether to afford white crystals **6i-u**.

9-Methyl-1-phenyl-β-carboline-3-carbaldehyde (6i)

Starting from 9-methyl-1-phenyl-3-hydroxymethyl-β-carboline **5i** (2.88g, 10mmol), yellow solid was obtained (2.46 g, 86%), mp 147.2-149.4℃. ESI-MS m/z: 287.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$) δ^1H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, C***H***O), 8.73 (1H, s, ArH), 8.23 (1H, d, *J*=8.0Hz, ArH), 7.70-7.61 (3H, m, ArH), 7.60-7.52 (3H, m, ArH), 7.48 (1H, d, *J*=8.4 Hz, ArH), 7.42-7.38 (1H, m, ArH), 3.50 (3H, s, NC***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 143.9, 142.9, 142.8, 138.6, 136.7, 129.6, 129.3, 128.9, 128.7, 128.2, 121.4, 121.2, 120.9, 113.0, 110.0, 32.7.

9-Ethyl-1-phenyl-3-β-carboline-3-carbaldehyde (6j)

Starting from 9-ethyl-1-phenyl-3-hydroxymethyl-β-carboline **5j** (3.02g, 10mmol), yellow solid was obtained (2.46g, 82%), mp 123.1 – 124.7℃. ESI-MS m/z: 301.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, C***H***O), 8.77 (1H, s, ArH), 8.27 (1H, d, *J*=8.0Hz, ArH), 7.68-7.63 (3H, m, ArH), 7.61-7.54 (3H, m, ArH), 7.50 (1H, d, *J*=8.4Hz, ArH), 7.41 (1H, t, *J*=7.6Hz, ArH), 4.04 (2H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 1.05 (3H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 144.0, 142.6, 141.8, 138.9, 135.9, 130.0, 128.9, 128.8, 128.7, 128.2, 121.6 (**2C**), 120.9, 113.3, 110.3, 39.1, 22.3.

9-Benzyl-1-phenyl-β-carboline-3-carbaldehyde (6k)

Starting from 9-benzyl-1-phenyl-3-hydroxymethyl-β-carboline **5k** (3.64g, 10mmol), yellow solid was obtained (2.82g, 78%), mp 140.9-142.7℃. ESI-MS m/z: 363.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, ArH), 8.80 (1H, s, ArH), 8.34-8.24 (1H, m, ArH), 7.58 (1H, ddd, *J*=8.4, 7.2, 1.2Hz, ArH), 7.46-7.28 (8H, m, ArH), 7.19-7.08 (3H, m, ArH), 6.62-6.46 (2H, m, ArH), 5.24 (2H, s, C***H***$_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 144.4, 143.2, 142.8, 138.4, 136.5, 136.0, 130.3, 129.2, 128.9, 128.6, 128.3, 128.1, 127.1, 125.2, 121.6 (**2C**), 121.3, 113.2,

110.9, 48.0, 22.4.

9-(3-Phenylpropyl)-1-phenyl-β-carboline-3-carbaldehyde (6l)

Starting from 9-(3-phenylpropyl)-1-phenyl-3-hydroxymethyl-β-carboline **5l** (3.92g, 10mmol), yellow solid was obtained (3.16g, 81%), mp 129.4-130.5℃. ESI-MS m/z: 391.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.24 (1H, s, C***H***O), 8.74 (1H, s, ArH), 8.23 (1H, d, *J*=7.6Hz, ArH), 7.66-7.58 (6H, m, ArH), 7.39-7.34 (2H, m, ArH), 7.24-7.14 (3H, m, ArH), 6.95 (2H, d, *J*=6.8Hz, ArH), 3.98 (2H, t, *J*=8.0Hz, NC***H***$_2$$CH_2CH_2Ph$), 2.15 (2H, t, *J*=7.6Hz, NCH_2CH_2C***H***$_2$Ph), 1.77-1.69 (m, 2H NCH_2C***H***$_2$$CH_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 144.1, 143.0, 142.2, 140.3, 139.1, 136.2, 130.3, 129.1, 129.0 (2C), 128.5, 128.3, 127.9, 126.0, 121.8, 121.7, 121.1, 113.4, 110.4, 44.3, 32.7, 30.5.

1-(4-Methoxyphenyl)-β-carboline-3-carbaldehyde (6m)

Starting from 1-(4-methoyphenyl)-3-hydroxymethyl-β-carboline **5m** (3.04g, 10mmol), yellow solid was obtained (2.35g, 78%), mp 236.6-238.1℃. ESI-MS m/z: 303.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.29 (s, 1H, C***H***O), 8.76 (1H, s, ArH), 8.69 (1H, s, ArH), 8.22 (1H, d, *J*=8.0Hz, ArH), 7.98-7.95 (2H, m, ArH), 7.65-7.55 (2H, m, ArH), 7.42-7.38 (1H, m, ArH), 7.18-7.13 (2H, m, ArH), 3.92 (3H, s, OC***H$_3$***); ^{13}C NMR (100 MHz, DMSO-d_6): δ 193.1, 160.0, 143.2, 142.5, 141.6, 135.2, 130.0, 129.7, 129.1, 128.8, 122.1, 121.4, 120.6, 114.2, 113.4, 112.9, 55.4.

9-Methyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde (6n)

Starting from 9-methyl-1-(4-methoyphenyl)-3-hydroxymethyl-β-carboline **5n** (3.18g, 10mmol), yellow solid was obtained (2.37g, 75%), mp 156.9-158.0℃. ESI-MS m/z: 317.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, C***H***O), 8.73 (1H, s, ArH), 8.25 (1H, d, *J*=7.6Hz, ArH), 7.69-7.65 (1H, m, ArH), 7.62-7.59 (2H, m, ArH), 7.49 (1H, d, *J*=8.4Hz, ArH), 7.12-7.08 (1H, m,

ArH), 7.12-7.08 (1H, m, ArH), 3.92 (3H, s, OC***H***$_3$), 3.56 (3H, s, NC***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 160.0, 143.9, 143.1, 143.0, 137.0, 131.2, 130.7, 129.7, 128.9, 121.5, 121.4, 120.9, 113.7, 112.7, 110.1, 55.3, 32.9.

9-Butyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde (6o)

Starting from 9-butyl-1-(4-methoyphenyl)-3-hydroxymethyl-β-carboline **5o** (3.60g, 10mmol), yellow solid was obtained (2.72g, 76%), mp 103.0-105.8℃. ESI-MS m/z: 359.1 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, C***H***O), 8.74 (1H, s, ArH), 8.25 (1H, d, *J*=8.0Hz, ArH), 7.67-7.63 (1H, m, ArH), 7.60-7.55(2H, m, ArH), 7.50 (1H, d, *J*=8.4Hz, ArH), 7.41-7.37 (1H, m, ArH), 7.11-7.08 (2H, m, ArH), 4.04 (2H, t, *J*=7.6Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 3.92 (3H, s, OC***H***$_3$), 1.45-1.38 (2H, m, NCH$_2$C***H***$_2$CH$_2$CH$_3$), 0.97-0.89 (2H, m, NCH$_2$CH$_2$C***H***$_2$CH$_3$), 0.69 (3H, t, *J*=7.2Hz, NCH$_2$CH$_2$CH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 159.9, 143.9, 142.8, 142.2, 136.3, 131.3, 130.2, 130.0, 128.8, 121.6, 121.5, 120.8, 113.6, 113.0, 110.5, 55.2, 44.2, 30.8, 19.5, 13.2.

9-Benzyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde (6p)

Starting from 9-benzyl-1-(4-methoyphenyl)-3-hydroxymethyl-β-carboline **5p** (3.94g, 10mmol), yellow solid was obtained (2.90g, 74%), mp 146.1-146.9℃. ESI-MS m/z: 393.0 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.24 (s, 1H, C***H***O), 8.78 (s, 1H, ArH), 8.29 (d, *J*=8.0Hz, 1H, ArH), 7.60-7.56 (m, 1H, ArH), 7.43-7.33 (m, 4H, ArH), 7.18-7.12 (m, 3H, ArH), 6.88-6.84 (m, 2H, ArH), 6.62 (d, *J* = 6.8 Hz, 2H, ArH), 5.31 (s, 2H, NC***H***$_2$Ph), 3.85 (s, 3H, OC***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 159.9, 144.3, 143.4, 142.8, 136.8, 136.2, 130.9, 130.4, 130.3, 129.1, 128.4, 127.2, 125.4, 121.8, 121.7, 121.2, 113.6, 112.8, 111.0, 55.3, 48.1.

9-(3-Phenylpropyl)-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde (6q)

Starting from 9-(3-phenylpropyl)-1-(4-methoyphenyl)-3-hydroxymethyl-β-carboline **5q** (4.22g, 10mmol), yellow solid was obtained (3.40g, 81%), mp 109.5-112.1℃. ESI-MS m/z: 421.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.25 (1H, s, C***H***O), 8.72 (1H, s, ArH), 8.23 (1H, d, *J*=7.6Hz, ArH), 7.63-7.57 (3H, m, ArH), 7.37 (2H, t, *J*=7.6Hz, ArH), 7.24-7.20 (2H, m, ArH), 7.18-7.15 (1H, m, ArH), 7.12-7.09 (2H, m, ArH), 6.99-6.92 (2H, m, ArH), 4.07 (2H, t, *J*=7.6Hz, NC***H***$_2$$CH_2CH_2Ph$), 3.93 (3H, s, OC***H***$_3$), 2.21 (2H, t, *J*=7.6Hz, NCH_2CH_2C***H***$_2$$Ph$), 1.74 (2H, m, NCH_2C***H***$_2$$CH_2Ph$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 160.0, 143.9, 143.1, 142.2, 140.3, 136.3, 131.3, 130.3, 130.2, 128.8, 128.2, 127.8, 125.9, 121.7 (2C), 120.9, 113.8, 112.8, 110.4, 55.3, 44.2, 32.7, 30.3.

9-Ethyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde (6r)

Starting from 9-ethyl-1-(3,4-dimethoyphenyl)-3-hydroxymethyl-β-carboline **5r** (3.62g, 10mmol), white solid was obtained (2.84g, 79%), mp 178.9-179.3℃. ESI-MS m/z: 361.0 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.26 (s, 1H, C***H***O), 8.75 (1H, s, ArH), 8.26 (1H, d, *J*=7.6Hz, ArH), 7.68-7.64 (1H, m, ArH), 7.51 (1H, d, *J*=8.4Hz, ArH), 7.42-7.38 (1H, m, ArH), 7.20-7.18 (2H, m, ArH), 7.05 (1H, d, *J*=8.8Hz, ArH), 4.10 (2H, q, *J* = 7.2 Hz, NC***H***$_2$$CH_3$), 4.00 (3H, s, OC***H***$_3$), 3.95 (3H, s, OC***H***$_3$), 1.09 (3H, t, *J*=7.2Hz, NCH_2C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 149.6, 148.8, 143.9, 143.0, 142.0, 136.2, 131.7, 130.2, 129.0, 121.9, 121.8, 121.6, 121.0, 113.1, 112.0, 110.9, 110.4, 56.0, 55.9, 39.3, 14.2.

9-Butyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde (6s)

Starting from 9-butyl-1-(3,4-dimethoyphenyl)-3-hydroxymethyl-β-carboline **5s** (3.90g, 10mmol), yellow solid was obtained (2.95g, 76%), mp 152.8-153.1℃. ESI-MS m/z: 389.1 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 10.26 (1H, s, C***H***O), 8.74 (s, 1H, ArH), 8.25 (1H, d, *J*=7.6Hz, ArH),

7.67-7.63 (1H, m, ArH), 7.50 (1H, d, *J*=8.4Hz, ArH), 7.39 (1H, t, *J*=7.6Hz, ArH), 7.19-7.16 (2H, m, ArH), 7.06 (1H, d, *J*=8.8Hz, ArH), 4.03 (2H, t, *J*=7.6Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 4.00 (3H, s, OC***H***$_3$), 3.95 (3H, s, OC***H***$_3$), 1.50-1.42 (2H, m, NCH$_2$C***H***$_2$CH$_2$CH$_3$), 1.01-0.90 (2H, m, NCH$_2$CH$_2$C***H***$_2$CH$_3$), 0.72 (3H, t, *J*=7.2Hz, NCH$_2$CH$_2$CH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 192.1, 148.9, 148.2, 143.2, 142.2, 141.6, 135.6, 131.0, 129.3, 128.2, 121.2 (2C), 121.0, 120.2, 112.2, 111.8, 110.3, 110.0, 55.4, 55.3, 43.7, 30.5, 19.1, 12.8.

9-Benzyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde (6t)

Starting from 9-benzyl-1-(3,4-dimethoyphenyl)-3-hydroxymethyl-β-carboline **5t** (4.24g, 10mmol), yellow solid was obtained (3.50g, 83%), mp 150.4-151.1℃. ESI-MS m/z: 423.1 (100) [M+H]$^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.25 (1H, s, C***H***O), 8.80 (1H, s, ArH), 8.30 (1H, d, *J*=8.0Hz, ArH), 7.61-7.56 (1H, m, ArH), 7.42 (1H, t, *J*=7.6Hz, ArH), 7.35 (1H, d, *J*=8.4Hz, ArH), 7.21-7.14 (3H, m, ArH), 7.01 (1H, dd, *J*=8.4, 2.0Hz, ArH), 6.89 (1H, d, *J*=8.0Hz, ArH), 6.79 (1H, d, *J*=2.0Hz, ArH), 6.64-6.62 (2H, m, ArH), 5.30 (2H, s, NC***H***$_2$Ph), 3.94 (3H, s, OC***H***$_3$), 3.48 (3H, s, OC***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 193.0, 149.2, 148.2, 144.1, 143.1, 142.6, 136.5, 136.2, 130.9, 130.1, 129.0, 128.3, 127.0, 125.1, 121.6, 121.5, 121.1, 112.8, 111.6, 110.8, 110.6, 55.8, 55.1, 47.8.

9-(3-Phenylpropyl)-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde (6u)

Starting from 9-(3-phenylpropyl)-1-(3,4-dimethoyphenyl)-3-hydroxymethyl-β-carboline **5u** (4.52g, 10mmol), white solid was obtained (3.73g, 83%), mp 129.5-130.7℃. ESI-MS m/z: 451.1 (100) [M+H]$^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.26 (1H, s, C***H***O), 8.73 (1H, s, ArH), 8.24 (1H, d, *J*=8.0Hz, ArH), 7.64-7.60 (1H, m, ArH), 7.40- 7.37 (2H, m, ArH), 7.24-7.14 (5H, m, ArH), 7.06 (1H, d, *J*=8.4Hz, ArH), 6.95 (2H, d, *J*=6.8Hz, ArH), 4.08 (2H, t, *J*=8.0Hz, NC***H***$_2$CH$_2$CH$_2$Ph), 4.01 (3H, s, OC***H***$_3$), 3.93 (3H, s, OC***H***$_3$), 2.23 (2H, t, *J*=7.6Hz, NCH$_2$CH$_2$C***H***$_2$Ph), 1.82-1.74 (2H, m,

$NCH_2C\boldsymbol{H}_2CH_2Ph$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.7, 149.3, 148.5, 143.6, 142.7, 141.9, 140.0, 135.9, 131.2, 129.9, 128.6, 128.0, 127.5, 125.6, 121.4 (2C), 120.6, 112.6, 112.0, 110.5, 110.2, 55.7, 55.6, 44.0, 32.5, 30.3.

General procedure for the preparation of target compounds (7a-y).

A mixture of compounds **6a-y** (2.0mmol), piperazine (3.0mmol) and anhydrous sym-dichloroethane (40ml) was stirred at 60 ℃ for 15 min. The solvent was evaporated under vacuum to give the crude schiff base, which was used directly in the next step without further purification. $NaBH_3CN$ (10mmol) was added to a solution of the crude schiff base in anhydrous sym-dichloroethane (40ml). The mixture was stirred at room temperature for 24 h, then poured into H_2O (150ml) and adjusted pH > 9 with sodium hydroxide. The mixture was extracted with dichloromethane (3×100ml). The organic phase was washed with water and brine, then dried over anhydrous sodium sulfate, filtered and evaporated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/CH_3OH= 200:1, 100:1). The target compounds were obtained.

1,4-Bis((9-ethyl-β-carboline-3-yl)methyl)piperazine (7a)

Starting from 9-ethyl-β-carboline-3-carbaldehyde **6a** (0.45g, 2.0mmol), yellow solid was obtained (0.28g, 56%), white solid was obtained (0.28g, 56%). EI-MS m/z: 502.9 $[M+H]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.81 (2H, s, ArH), 8.13 (2H, d, J=7.8Hz, ArH), 8.02 (2H, s, ArH), 7.55-7.61 (2H, m, ArH), 7.43 (2H, d, J=7.8Hz, ArH), 7.23-7.29 (2H, m, ArH), 4.42 (4H, q, J=7.2Hz, $NC\boldsymbol{H}_2CH_3$), 3.88 (4H, s, $C\boldsymbol{H}_2$), 2.68 (8H, s $N(C\boldsymbol{H}_2C\boldsymbol{H}_2)_2N$), 1.48 (6H, t, J=7.2Hz, $NCH_2C\boldsymbol{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.2, 141.2, 135.4, 131.2, 129.5, 128.4, 122.2, 121.3, 119.6, 114.5, 109.4, 65.1, 53.6, 38.3, 14.5. HRMS (ESI) calcd for $C_{32}H_{34}N_6$ $[M+H]^+$ 503.2918, found 503.2927.

1,4-Bis((9-butyl-β-carboline-3-yl)methyl)piperazine (7b)

Starting from 9-butyl-β-carboline-3-carbaldehyde **6b** (0.51g, 2.0mmol), white solid was obtained (0.24g, 43%). EI-MS m/z: 559.0 $[M+H]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.81 (2H, s, ArH), 8.13 (2H, d, *J*=7.8Hz, ArH), 8.02 (2H, s, ArH), 7.54-7.61 (2H, m, ArH), 7.43 (2H, d, *J*=8.4Hz, ArH), 7.22-7.28 (2H, m, ArH), 4.36 (4H, t, *J*=7.2Hz, NC$\boldsymbol{H}_2$$CH_2CH_2CH_3$), 3.89 (4H, s, C$\boldsymbol{H}_2$), 2.71 (8H, s, N(C$\boldsymbol{H}_2C\boldsymbol{H}_2$)$_2$N), 1.82-1.94 (4H, m, $NCH_2C\boldsymbol{H}_2CH_2CH_3$), 1.33-1.46 (4H, m, $NCH_2CH_2C\boldsymbol{H}_2CH_3$), 0.96 (6H, t, *J*=7.2Hz, $NCH_2CH_2CH_2C\boldsymbol{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.0, 141.7, 135.9, 131.3, 129.2, 128.4, 122.2, 121.4, 119.6, 114.6, 109.6, 65.1, 53.5, 43.5, 31.7, 20.9, 14.2. HRMS (ESI) calcd for $C_{36}H_{42}N_6$ $[M+H]^+$ 559.3544, found 559.3553.

1,4-Bis((9-benzyl-β-carboline-3-yl)methyl)piperazine (7c)

Starting from 9-benzyl-β-carboline-3-carbaldehyde **6c** (0.57g, 2.0mmol), yellow solid was obtained (0.32g, 51%), white solid was obtained (0.32g, 51%). EI-MS m/z: 627.3 $[M+H]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.77 (2H, s, ArH), 8.16 (2H, d, *J*=7.8Hz, ArH), 8.05 (2H, s, ArH), 7.50-7.57 (2H, m, ArH), 7.41 (2H, d, *J*=8.4Hz, ArH), 7.25-7.30 (8H, m, ArH), 7.13-7.17 (4H, m, ArH), 5.55 (4H, s, C$\boldsymbol{H}_2$Ph), 3.88 (4H, s, C$\boldsymbol{H}_2$), 2.69 (8H, s, N(C$\boldsymbol{H}_2$C$\boldsymbol{H}_2$)$_2$N); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.6, 136.4, 136.1, 131.5, 129.4, 128.9, 128.5, 127.7, 126.6, 126.5, 122.1, 121.2, 119.9, 114.7, 109.7, 64.5, 52.8, 47.1. HRMS (ESI) calcd for $C_{42}H_{38}N_6$ $[M+H]^+$ 627.3231, found 627.3237.

1,4-Bis((9-(4-fluorobenzyl)-β-carboline-3-yl)methyl)piperazine (7d)

Starting from 9-(4-fluorobenzyl)-β-carboline-3-carbaldehyde **6d** (0.61g, 2.0mmol), yellow solid was obtained (0.25g, 38%). EI-MS m/z: 662.8 $[M+H]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.75 (2H, s, ArH), 8.16 (2H, d, *J* =7.8Hz, ArH), 8.05 (2H, s, ArH), 7.52-7.58 (2H, m, ArH), 7.39 (2H, d,

J=7.8Hz, ArH), 7.30 (2H, d, *J*=7.2Hz, ArH), 7.10-7.15 (4H, m, ArH), 6.92-6.98 (4H, m, ArH), 5.52 (4H, s, C***H***$_2$Ph), 3.88 (4H, s, C***H***$_2$), 2.70 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6, 141.8, 135.9, 132.4, 131.5, 129.6, 128.8, 128.5, 122.3, 121.5, 120.2, 116.2, 115.9, 114.7, 109.8, 65.0, 53.4, 46.7. HRMS (ESI) calcd for $C_{42}H_{36}N_6F_2$ 663.3042 $[M+H]^+$, found 665.3042.

1,4-Bis((9-(3-phenylpropyl)-β-carboline-3-yl)methyl)piperazine (7e)

Starting from 9-(3-phenylpropyl)-β-carboline-3-carbaldehyde **6e** (0.63g, 2.0mmol), white solid was obtained (0.34g, 50%). EI-MS m/z: 683.0 $[M+H]^+$. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.74 (2H, s, ArH), 8.13 (2H, d, *J*=7.8Hz, ArH), 8.03 (2H, s, ArH), 7.52-7.57 (2H, m, ArH), 7.34 (2H, d, *J*=8.4Hz, ArH), 7.14-7.27 (12H, m, ArH), 4.37 (4H, t, *J*=7.8Hz, C***H***$_2$CH$_2$CH$_2$Ph), 3.89 (4H, s, C***H***$_2$), 2.70-2.74 (12H, m, N(C***H***$_2$C***H***$_2$)$_2$N, CH$_2$CH$_2$C***H***$_2$Ph), 2.21-2.31 (4H, m, CH$_2$C***H***$_2$CH$_2$Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.3, 141.6, 140.8, 135.8, 131.3, 129.3, 128.7, 128.4, 126.4, 122.2, 121.4, 119.7, 114.5, 109.6, 65.2, 53.6, 43.1, 33.5, 30.6. HRMS (ESI) calcd for $C_{46}H_{46}N_6$ $[M+H]^+$ 683.3857, found 683.3858.

1,4-Bis((1,9-dimethyl-β-carboline-3-yl)methyl)piperazine (7f)

Starting from 1,9-dimethyl-β-carboline-3-carbaldehyde **6f** (0.45g, 2.0mmol), white solid was obtained (0.16 g, 32%). EI-MS m/z: 502.9 [M+H]+. ^{1}H NMR (300 MHz, CDCl3): δ 8.10 (2H, d, *J*=7.8Hz, ArH), 7.90 (2H, s, ArH), 7.54-7.58 (2H, m, ArH), 7.39 (2H, d, *J*=8.4Hz, ArH), 7.20-7.26 (2H, m, ArH), 4.10 (6H, s, NCH_3), 3.85 (4H, s, C***H***$_2$), 3.07 (6H, s, C***H***$_3$), 2.70 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (75 MHz, CDCl3): δ 142.5, 141.0, 135.1, 129.6, 128.1, 121.6, 121.2, 119.5, 112.6, 109.4, 64.4, 53.0, 32.3, 23.6. HRMS (ESI) calcd for $C_{32}H_{34}N_6$ $[M+H]^+$ 503.2918, found 503.2926.

1,4-Bis((9-isobutyl-1-methyl-β-carboline-3-yl)methyl)piperazine (7g)

Starting from 9-isobutyl-1-methyl-β-carboline-3-carbaldehyde **6g** (0.51g, 2.0mmol), white solid was obtained (0.2g, 27%), mp 193.3-194.7℃. ESI-MS m/z: 587.4 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.12 (2H, d, *J*=8.0Hz, ArH), 7.93 (s, 2H, ArH), 7.53 (2H, t, *J*=7.6Hz, ArH), 7.44 (2H, d, *J*=8.4Hz, ArH), 7.25-7.23 (2H, m, ArH), 4.33 (4H, d, *J*=7.6Hz, $NC\boldsymbol{H}_2CH(CH_3)_2$), 3.85 (4H, s, $C\boldsymbol{H}_2N(CH_2)_2(CH_2)_2NC\boldsymbol{H}_2$), 3.01 (6H, s, $C\boldsymbol{H}_3$), 2.71 (8H, s, $N(C\boldsymbol{H}_2C\boldsymbol{H}_2)_2N$), 2.32-2.20 (2H, m, $NCH_2C\boldsymbol{H}(CH_3)_2$), 0.92 (12H, d, *J*=6.8Hz, $NCH_2CH(C\boldsymbol{H}_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 142.3, 140.3, 134.4, 129.7, 127.6, 121.4, 121.1, 119.1, 112.0, 110.2, 64.6, 53.3, 51.7, 30.5, 23.7, 20.1. HRMS (ESI) calcd for $C_{38}H_{46}N_6$ 587.3857 $[M+H]^+$, found 587.3854.

1,4-Bis((9-(3-chlorobenzyl)-1-methyl-β-carboline-3-yl)methyl)piperazine (7h)

Starting from 9-(3-chlorobenzyl)-1-methyl-β-carboline-3-carbaldehyde **6h** (0.64g, 2.0mmol), white solid was obtained (0.29g, 33%), mp 211.9-213.0℃. ESI-MS m/z: 723.3 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.19-8.17 (2H, m, ArH), 8.00 (2H, s, ArH), 7.54-7.50 (2H, m, ArH), 7.31-7.28 (4H, m, ArH), 7.24-7.17 (4H, m, ArH), 7.05 (2H, s, ArH), 6.84 (2H, d, *J*=7.2Hz, ArH), 5.74 (4H, s, $NC\boldsymbol{H}_2Ph$), 3.88 (4H, s, $C\boldsymbol{H}_2N(CH_2)_2(CH_2)_2NC\boldsymbol{H}_2$), 2.85 (6H, s, $C\boldsymbol{H}_3$), 2.76 (8H, s, $N(C\boldsymbol{H}_2C\boldsymbol{H}_2)_2N$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 142.1, 140.6, 140.3, 135.0, 134.5, 130.4, 130.0, 128.5, 127.8, 125.6, 123.6, 121.8, 121.5, 120.1, 112.5, 109.6, 64.6, 53.4, 47.7, 23.2. HRMS (ESI) calcd for $C_{44}H_{40}N_6Cl_2$ 723.2764 $[M+H]^+$, found 723.2760.

1,4-Bis((9-methyl-1-phenyl-β-carboline-3-yl)methyl)piperazine (7i)

Starting from 9-methyl-1-phenyl-β-carboline-3-carbaldehyde **6i** (0.57g, 2.0mmol), white solid was obtained (0.21g, 34%), mp > 250 ℃. ESI-MS m/z: 627.3 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, *J*=7.6Hz, 2H, ArH), 8.13 (2H, s, ArH), 7.63-7.56 (6H, m, ArH), 7.52-7.46 (6H, m, ArH), 7.39 (2H, d, *J*=8.4Hz, ArH), 7.31-7.27 (2H, m, ArH), 3.99 (4H, s,

C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.42 (6H, s, NC***H***$_3$), 2.78 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (100 MHz, CDCl$_3$): δ 143.3, 143.1, 140.0, 134.3, 130.9, 129.8, 128.3, 128.2, 128.1, 121.7, 121.2, 119.6, 112.8, 109.6, 64.5, 53.2, 32.8. HRMS (ESI) calcd for $C_{42}H_{38}N_6$ 627.3231 $[M+H]^+$, found 627.3235.

1,4-Bis((9-ethyl-1-phenyl-β-carboline-3-yl)methyl)piperazine (7j)

Starting from 9-ethyl-1-phenyl-β-carboline-3-carbaldehyde **6j** (0.60g, 2.0mmol), white solid was obtained (0.15g, 23%), mp 204.5-205.9 ℃. ESI-MS m/z: 655.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.20 (2H, d, *J*=7.6Hz, ArH), 8.13 (2H, s, ArH), 7.61-7.54 (6H, m, ArH), 7.52-7.46 (6H, m, ArH), 7.40 (2H, d, *J*=8.4Hz, ArH), 7.30-7.28 (2H, m, ArH), 3.97 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.95 (4H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 2.75 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 0.96 (6H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 146.7, 143.0, 142.0, 140.1, 133.0, 131.1, 129.1, 128.2, 128.0, 121.6, 121.5, 119.4, 112.6, 109.8, 64.4, 53.3, 38.9, 13.8. HRMS (ESI) calcd for $C_{44}H_{42}N_6$ 655.3544 $[M+H]^+$, found 655.3548.

1,4-Bis((9-benzyl-1-phenyl-β-carboline-3-yl)methyl)piperazine (7k)

Starting from 9-benzyl-1-phenyl-β-carboline-3-carbaldehyde **6k** (0.78g, 2.0mmol), white solid was obtained (0.26g, 33%), mp > 250 ℃. ESI-MS m/z: 779.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.24 (2H, d, *J*=7.6Hz, ArH), 8.17 (2H, s, ArH), 7.52-7.48 (2H, m, ArH), 7.37-7.32 (8H, m, ArH), 7.30-7.27 (6H, m, ArH), 7.16-7.08 (6H, m, ArH), 6.59 (4H, d, *J*=6.4Hz, ArH), 5.16 (4H, s, NC***H***$_2$Ph), 3.97 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 2.77 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (100 MHz, CDCl$_3$): δ 147.2, 143.4, 142.9, 139.6, 137.1, 133.6, 131.2, 129.4, 128.4, 128.3, 128.2, 128.0, 126.9, 125.6, 121.7, 121.5, 120.0, 112.8, 110.4, 64.5, 53.4, 48.0. HRMS (ESI) calcd for $C_{54}H_{46}N_6$ 779.3857 $[M+H]^+$, found 779.3866.

1,4-Bis((9-(3-phenylpropyl)-1-phenyl-β-carboline-3-yl)methyl)piperazine (7l)

Starting from 9-(3-phenylpropyl)-1-phenyl-β-carboline-3-carbaldehyde **6l** (0.78g, 2.0mmol), white solid was obtained(0.31g, 37%), mp 180.7-182.8 ℃. ESI-MS m/z: 835.4 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=7.6Hz, ArH), 8.12 (2H, s, ArH), 7.62-7.60 (4H, m, ArH), 7.54-7.49 (8H, m, ArH), 7.29-7.27 (4H, m, ArH), 7.21 (4H, t, *J*=7.6Hz, ArH), 7.14 (2H, t, *J*=6.8Hz, ArH), 6.95 (4H, d, *J*=7.6Hz, ArH), 3.97 (4H, s, C***H***$_2$N$(CH_2)_2(CH_2)_2$NC***H***$_2$), 3.91(4H, t, *J*=8.0Hz, NC***H***$_2$$CH_2CH_2$Ph), 2.75 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 2.11 (4H, t, *J*=7.6Hz, NCH_2CH_2C***H***$_2$Ph), 1.70-1.62 (4H, m, NCH_2C***H***$_2$$CH_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 143.0, 142.2, 140.7, 140.0, 133.1, 131.0, 129.3, 128.82, 128.1, 127.9, 125.8, 121.6, 121.3, 119.5, 112.7, 109.7, 64.4, 53.2, 43.9, 32.7, 30.2. HRMS (ESI) calcd for $C_{58}H_{54}N_6$ 835.4483 $[M+H]^+$, found 835.4480.

1,4-Bis((1-(4-methoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7m)

Starting from 1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde **6m** (0.60g, 2.0mmol), white solid was obtained (0.17g, 26%), mp 239.1-240.1 ℃. ESI-MS m/z: 659.3 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (2H, s, ArH), 8.15 (2H, d, *J*=8.0Hz, ArH), 8.03 (2H, s, ArH), 7.90-7.88 (4H, m, ArH), 7.54-7.46 (4H, m, ArH), 7.30-7.28 (2H, m, ArH), 7.09-7.07 (4H, m, ArH), 3.98 (4H, s, C***H***$_2$N$(CH_2)_2(CH_2)_2$NC***H***$_2$), 3.88 (6H, s, OC***H***$_3$), 2.77 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.0, 147.2, 141.9, 141.2, 132.4, 131.4, 130.4, 130.2, 128.4, 122.1, 121.4, 119.8, 114.6, 112.8, 112.7, 64.8, 55.8, 53.5. HRMS (ESI) calcd for $C_{42}H_{38}N_6O_2$ 659.3129 $[M+H]^+$, found 659.3129.

1,4-Bis((9-methyl-1-(4-methoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7n)

Starting from 9-methyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde **6n** (0.72g, 2.0mmol),

white solid was obtained (0.25g, 36%), mp >250 ℃. ESI-MS m/z: 687.3 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=7.6Hz, ArH), 8.08 (2H, s, ArH), 7.60-7.54 (6H, m, ArH), 7.39 (2H, d, *J*=8.4Hz, ArH), 7.29 (2H, d, *J*=7.6Hz, ArH), 7.03 (4H, d, *J*=8.4Hz, ArH), 3.96 (4H, s, C***H***$_2$N$(CH_2)_2(CH_2)_2$NC***H***$_2$), 3.89 (6H, s, OC***H***$_3$), 3.46 (6H, s, NC***H***$_3$), 2.74 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 146.9, 143.3, 142.9, 134.3, 132.4, 131.0, 130.8, 128.2, 121.6, 121.3, 119.6, 113.6, 112.5, 109.6, 64.6, 55.4, 53.3, 32.8. HRMS (ESI) calcd for $C_{44}H_{42}N_6O_2$ 687.3442 $[M+H]^+$, found 687.3444.

1,4-Bis((9-butyl-1-(4-methoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7o)

Starting from 9-butyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde **6o** (0.72g, 2.0mmol), white solid was obtained (0.27g, 35%), mp 141.7-143.9 ℃. ESI-MS m/z: 771.4 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=7.6Hz, ArH), 8.09 (2H, s, ArH), 7.57-7.51 (6H, m, ArH), 7.40 (2H, d, *J*=8.4Hz, ArH), 7.28 (2H, s, ArH), 7.02 (4H, d, *J*=8.8Hz, ArH), 3.96 (4H, s, C***H***$_2$N$(CH_2)_2(CH_2)_2$NC***H***$_2$), 3.94 (4H, t, *J*=7.6Hz, NC***H***$_2$$CH_2CH_2CH_3$), 3.89 (6H, s, OC***H***$_3$), 2.75 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 1.38-1.30 (4H, m, NCH_2C***H***$_2$$CH_2CH_3$), 0.94-0.84 (4H, m, NCH_2CH_2C***H***$_2$$CH_3$), 0.67 (6H, t, *J*=7.6Hz, $NCH_2CH_2CH_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 146.5, 142.9, 142.4, 133.4, 132.6, 131.0, 130.5, 128.0, 121.6, 121.4, 119.4, 113.5, 112.5, 110.0, 64.4, 55.3, 53.2, 44.1, 30.8, 19.7, 13.4. HRMS (ESI) calcd for $C_{50}H_{54}N_6O_2$ 771.4381 $[M+H]^+$, found 771.4380.

1,4-Bis((9-benzyl-1-(4-methoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7p)

Starting from 9-benzyl-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde **6p** (0.78g, 2.0mmol), white solid was obtained (0.31g, 37%), mp 230.8-231.4 ℃. ESI-MS m/z: 839.4 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.22 (2H, d, *J*=7.6Hz, ArH), 8.14 (2H, s, ArH), 7.51-7.47 (2H, m,

ArH), 7.31-7.27 (8H, m, ArH), 7.14-7.10 (6H, m, ArH), 6.79 (4H, d, *J*=8.4Hz, ArH), 6.65-6.63 (4H, m, ArH), 5.20 (4H, s, NC***H***$_2$Ph), 3.96 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.82 (6H, s, OC***H***$_3$), 2.76 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.5, 147.2, 143.2, 142.8, 137.1, 133.7, 132.1, 131.2, 130.5, 128.3, 128.2, 126.9, 125.6, 121.6, 121.5, 119.9, 113.4, 112.5, 110.4, 64.4, 55.3, 53.3, 47.9. HRMS (ESI) calcd for $C_{56}H_{50}N_6O_2$ 839.4068 $[M+H]^+$, found 839.4064.

1,4-Bis((9-(3-phenylpropyl)-1-(4-methoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7q)

Starting from 9-(3-phenylpropyl)-1-(4-methoxyphenyl)-β-carboline-3-carbaldehyde **6q** (0.84g, 2.0mmol), white solid was obtained (0.30g, 34%), mp 184.9-186.5 ℃. ESI-MS m/z: 895.5 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (2H, d, *J*=7.6Hz, ArH), 8.09 (2H, s, ArH), 7.55-7.50 (6H, m, ArH), 7.29 (2H, d, *J*=8.4Hz, ArH), 7.24-7.18 (4H, m, ArH), 7.15-7.11 (2H, m, ArH), 7.04 (4H, d, *J*=8.4Hz, ArH), 6.94 (4H, d, *J* = 6.8 Hz, ArH), 3.98 (4H, t, *J*=7.6Hz, NC***H***$_2$CH$_2$CH$_2$Ph), 3.96 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.90 (6H, s, OC***H***$_3$), 2.75 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 2.16 (4H, t, *J*=7.6Hz, NCH$_2$CH$_2$C***H***$_2$Ph), 1.71-1.63 (4H, m, NCH$_2$C***H***$_2$CH$_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 146.9, 142.9, 142.3, 140.8, 133.3, 132.6, 131.1, 130.6, 128.2, 128.0, 127.9, 125.8, 121.6, 121.5, 119.5, 113.6, 112.4, 109.9, 64.5, 55.3, 53.3, 44.0, 32.8, 30.2. HRMS (ESI) calcd for $C_{60}H_{58}N_6O_2$ 895.4694 $[M+H]^+$, found 895.4691.

1,4-Bis((9-ethyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7r)

Starting from 9-ethyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde **6r** (0.72g, 2.0mmol), white solid was obtained (0.23g, 30%), mp 231.8-233.4 ℃. ESI-MS m/z: 775.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (2H, d, *J*=7.6Hz, ArH), 8.11 (2H, s, ArH), 7.60-7.50 (2H, m, ArH), 7.42 (2H, d, *J*=8.0Hz, ArH), 7.29 (2H, d, *J*=7.6Hz, ArH), 7.16-7.14 (2H, m, ArH), 6.99 (2H, d, *J*=8.8Hz, ArH), 4.00 (4H, q, *J*=7.2Hz, NC***H***$_2$CH$_3$), 3.97 (10H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$,

OC***H***$_3$), 3.91 (6H, s, OC***H***$_3$), 2.75 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 0.99 (6H, t, *J*=7.2Hz, NCH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 148.5, 146.5, 142.9, 142.1, 133.1, 132.8, 131.1, 128.2, 121.8, 121.7, 121.6, 119.5, 112.7, 112.4, 110.8, 109.9, 64.4, 56.0, 55.9, 53.3, 39.0, 14.0. HRMS (ESI) calcd for $C_{48}H_{50}N_6O_4$ 775.3966 $[M+H]^+$, found 775.3968.

1,4-Bis((9-butyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7s)

Starting from 9-butyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde **6s** (0.78g, 2.0mmol), white solid was obtained (0.23g, 28%), mp 213.0-214.1 ℃. ESI-MS m/z: 831.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (2H, d, *J*=8.0Hz, ArH), 8.11 (2H, s, ArH), 7.56 (2H, t, *J*=7.6Hz, ArH), 7.40 (2H, d, *J*=8.0Hz, ArH), 7.28 (2H, d, *J*=7.2Hz, ArH), 7.14-7.12 (4H, m, ArH), 6.99 (2H, d, *J*=8.4Hz, ArH), 3.97 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.96 (6H, s, OC***H***$_3$), 3.93 (4H, t, *J*=7.2Hz, NC***H***$_2$CH$_2$CH$_2$CH$_3$), 3.91 (6H, s, OC***H***$_3$), 2.76 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N), 1.42-1.34 (4H, m, NCH$_2$C***H***$_2$CH$_2$CH$_3$), 0.96-0.87 (4H, m, NCH$_2$CH$_2$C***H***$_2$CH$_3$), 0.68 (6H, t, *J*=7.2Hz, NCH$_2$CH$_2$CH$_2$C***H***$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 148.5, 146.5, 142.8, 142.2, 133.2, 132.8, 130.9, 128.0, 121.9, 121.5, 121.3, 119.3, 112.5, 112.4, 110.8, 109.9, 64.4, 56.0, 55.8, 53.2, 44.1, 31.0, 19.8, 13.4. HRMS (ESI) calcd for $C_{52}H_{58}N_6O_4$ 831.4592 $[M+H]^+$, found 831.4592.

1,4-Bis((9-benzyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7t)

Starting from 9-benzyl-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde **6t** (0.85g, 2.0mmol), white solid was obtained (0.36g, 40%), mp 230.8-231.4 ℃. ESI-MS m/z: 899.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25-8.19 (2H, m, ArH), 7.52-7.48 (2H, m, ArH), 7.31 (2H, t, *J*=7.2Hz, ArH), 7.20-7.12 (8H, m, ArH), 6.97-6.94 (2H, m, ArH), 6.82 (2H, d, *J*=8.4Hz, ArH), 6.76 (2H, d, *J*=1.6Hz, ArH), 6.67-6.64 (4H, m, ArH), 5.19 (4H, s, NC***H***$_2$Ph), 4.00 (4H, s, C***H***$_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC***H***$_2$), 3.91 (6H, s, OC***H***$_3$), 3.44 (6H, s, OC***H***$_3$), 2.82 (8H, s, N(C***H***$_2$C***H***$_2$)$_2$N);

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 148.1 (**2C**), 143.1, 142.6, 137.2, 133.5, 132.1, 130.9, 128.4, 128.3, 126.8, 125.4, 121.8, 121.6, 121.2, 119.9, 112.0, 110.7, 110.3, 64.1, 55.9, 55.2, 52.9, 47.7. HRMS (ESI) calcd for $C_{58}H_{54}N_6O_4$ 899.4279 $[M+H]^+$, found 899.4269.

1,4-Bis((9-(3-phenylpropyl)-1-(3,4-dimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7u)

Starting from 9-(3-phenylpropyl)-1-(3,4-dimethoxyphenyl)-β-carboline-3-carbaldehyde **6u** (0.90g, 2.0mmol), white solid was obtained (0.20g, 21%), mp 201.3-202.0 ℃. ESI-MS m/z: 955.5 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=8.0Hz, ArH), 8.10 (2H, s, ArH), 7.54 (2H, t, *J*=7.6Hz, ArH), 7.32-7.27 (4H, m, ArH), 7.20 (4H, t, *J*=7.2Hz, ArH), 7.15-7.11 (2H, m, ArH), 7.00 (2H, d, *J*=8.4Hz, ArH), 6.94 (4H, d, *J*=7.2Hz, ArH), 3.99 (4H, t, *J*=7.2Hz, NC$\boldsymbol{H}_2$$CH_2CH_2$Ph), 3.98 (6H, s, OC$\boldsymbol{H}_3$), 3.96 (4H, s, C$\boldsymbol{H}_2N(CH_2)_2(CH_2)_2NC\boldsymbol{H}_2$), 3.89 (6H, s, OC$\boldsymbol{H}_3$), 2.75 (8H, s, N(C$\boldsymbol{H}_2C\boldsymbol{H}_2$)$_2$N), 2.18 (4H, t, *J*=7.6Hz, NCH_2CH_2C$\boldsymbol{H}_2$Ph), 1.74-1.66 (4H, m, NCH_2C$\boldsymbol{H}_2$$CH_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1, 148.6, 146.7, 142.8, 142.3, 140.7, 133.2, 132.7, 131.1, 128.2, 128.1, 127.9, 125.8, 121.9, 121.6, 121.4, 119.6, 112.6, 112.5, 110.7, 109.9, 64.4, 56.0, 55.9, 53.3, 44.0, 32.9, 30.5. HRMS (ESI) calcd for $C_{62}H_{62}N_6O_4$ 955.4905 $[M+H]^+$, found 955.4912.

1,4-Bis((1-(3,4,5-trimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7v)

Starting from 1-(3,4,5-trimethoxyphenyl)-β-carboline-3-carbaldehyde **6v** (0.72g, 2.0mmol), white solid was obtained (0.21g, 27%), mp 166.3-169.1 ℃. ESI-MS m/z: 779.4 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (2H, s, ArH), 8.17 (2H, d, *J*=7.6Hz, ArH), 8.09 (2H, s, ArH), 7.57-7.53 (2H, m, ArH), 7.49 (2H, d, *J*=8.0Hz, ArH), 7.32-7.28 (2H, m, ArH), 7.13 (4H, s, ArH), 4.00 (4H, s, C$\boldsymbol{H}_2$N$(CH_2)_2(CH_2)_2$NC$\boldsymbol{H}_2$), 3.95 (12H, s, 3,5-diOC$\boldsymbol{H}_3$), 3.92 (6H, s, 4-OC$\boldsymbol{H}_3$), 2.79 (8H, s, N(C$\boldsymbol{H}_2$C$\boldsymbol{H}_2$)$_2$N); ^{13}C NMR (100 MHz, DMSO-d_6): δ 152.9, 146.6, 141.4, 141.0, 137.7, 133.9, 132.0, 129.9, 127.9, 121.6, 120.8, 119.2, 112.36 (d, *J* = 22.9 Hz), 105.7, 64.2, 60.0, 55.8, 52.9.

HRMS (ESI) calcd for $C_{46}H_{46}N_6O_6$ 779.3552 $[M+H]^+$, found 779.3546.

1,4-Bis((9-methyl-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7w)

Starting from 9-methyl-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-carbaldehyde **6w** (0.75g, 2.0mmol), white solid was obtained (0.28 g, 35%), mp > 240 ℃. EI-MS m/z: 807.4 $[M+H]^+$. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (2H, d, J =7.8Hz, Ar***H***), 7.90 (2H, s, Ar***H***), 7.53-7.57 (2H, m, Ar***H***), 7.39 (2H, d, J =8.4Hz, Ar***H***), 7.21-7.27 (2H, m, Ar***H***), 4.10 (6H, s, NC$\boldsymbol{H}_3$), 3.85 (4H, s, C$\boldsymbol{H}_2$), 3.07 (6H, s, C$\boldsymbol{H}_3$), 2.70 (8H, s, N(C$\boldsymbol{H}_2$C$\boldsymbol{H}_2$)$_2$N); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.6, 141.0, 135.1, 129.6, 128.2, 121.6, 121.2, 119.5, 112.7, 109.4, 64.4, 53.0, 32.4, 23.6. HRMS (ESI) calcd for $C_{48}H_{50}N_6O_6$ $[M+H]^+$ 807.3865, found 807.3863.

1,4-Bis((9-butyl-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7x)

Starting from 9-butyl-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-carbaldehyde **6x** (0.84g, 2.0mmol), white solid was obtained (0.20g, 22%), mp > 240 ℃. ESI-MS m/z: 891.5 (100) $[M+H]^+$. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J=7.6Hz, 2H, ArH), 8.13 (2H, s, ArH), 7.57 (2H, t, J=7.6Hz, ArH), 7.41 (2H, d, J=8.4Hz, ArH), 7.29 (2H, d, J=7.6Hz, ArH), 6.79 (4H, s, ArH), 3.97 (4H, s, C$\boldsymbol{H}_2$N(CH$_2$)$_2$(CH$_2$)$_2$NC$\boldsymbol{H}_2$), 3.91 (4H, t, J=6.0Hz, NC$\boldsymbol{H}_2$CH$_2$CH$_2$CH$_3$), 3.89 (6H, s, 4-OC$\boldsymbol{H}_3$), 3.88 (12H, s, 3,5-diOC$\boldsymbol{H}_3$), 2.77 (8H, s, N(C$\boldsymbol{H}_2$C$\boldsymbol{H}_2$)$_2$N), 1.48-1.41 (4H, m, NCH$_2$C$\boldsymbol{H}_2$CH$_2$CH$_3$), 1.02-0.93 (4H, m, NCH$_2$CH$_2$C$\boldsymbol{H}_2$CH$_3$), 0.72 (6H, t, J=7.2Hz, NCH$_2$CH$_2$CH$_2$C$\boldsymbol{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 146.4, 142.8, 142.2, 138.0, 135.6, 133.0, 130.9, 128.2, 121.6, 121.2, 119.5, 112.8, 109.9, 106.5, 64.4, 60.8, 56.1, 53.2, 44.2, 31.3, 19.8, 13.5. HRMS (ESI) calcd for $C_{54}H_{62}N_6O_6$ 891.4804 $[M+H]^+$, found 891.4806.

1,4-Bis((9-(3-phenylpropyl)-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-yl)methyl)piperazine (7y)

Starting from 9-(phenylpropyl)-1-(3,4,5-trimethoxyphenyl)-β-carboline-3-carbaldehyde **6y** (0.96g,

2.0mmol), white solid was obtained (0.34g, 34%), mp 230.0-231.0 ℃. ESI-MS m/z: 1015.5 (100) $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=8.0Hz, ArH), 8.13 (2H, s, ArH), 7.57-7.53 (2H, m, ArH), 7.33-7.28 (4H, m, ArH), 7.23-7.19 (4H, m, ArH), 7.15-7.12 (2H, m, ArH), 6.98-6.96 (4H, m, ArH), 6.81 (4H, s, ArH), 3.98 (4H, t, *J*=7.2Hz, $NC\boldsymbol{H}_2CH_2CH_2Ph$), 3.96 (4H, s, $C\boldsymbol{H}_2N(CH_2)_2(CH_2)_2NC\boldsymbol{H}_2$), 3.93 (6H, s, 4-$OC\boldsymbol{H}_3$), 3.86 (12H, s, 3,5-di$OC\boldsymbol{H}_3$), 2.76 (8H, s, $N(C\boldsymbol{H}_2C\boldsymbol{H}_2)_2N$), 2.22 (4H, t, *J*=7.6Hz, $NCH_2CH_2C\boldsymbol{H}_2Ph$), 1.77-1.74 (4H, m, $NCH_2C\boldsymbol{H}_2CH_2Ph$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 146.4, 142.7, 142.1, 140.6, 138.0, 135.4, 133.0, 131.0, 128.2, 127.8, 125.8, 121.6, 121.2, 119.6, 112.9, 109.8, 106.6, 64.3, 60.8, 56.0, 53.2, 44.1, 32.8, 30.7. HRMS (ESI) calcd for $C_{64}H_{66}N_6O_6$ 1015.5117 $[M+H]^+$, found 1015.5115.