Electronic Supplementary Material (ESI) for RSC Advances.

Synthesis and Biological Evaluation of Peptidomimetics Containing Tryptamine Moiety as Potential Antitumor Agents

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Supporting Information

Experimental Section

Instrumentation and chemicals

All melting points (m.p.) were obtained with a digital model X-5 apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Brucker spectrometer at 400 MHz with $CDCl_3$ as the solvent and TMS as the internal standard. Chemical shifts are reported in d (parts per million) values. Coupling constants ^{n}J are reported in Hz. Mass spectra were performed on a MicroMass Quattro micro^{TMB} API instrument. Analytical thin-layer chromatography (TLC) was carried out on precoated plates, and spots were visualized with ultraviolet light. All chemicals or reagents used for syntheses were commercially available, were of AR grade, and were used as received. Anhydrous CH_2Cl_2 and CH_3CN were dried according to standard methods. All other solvents and reagents were analytical reagent and used directly without purification.

General synthetic procedure for 2a-k

A solution of di-tert-butyl pyrocarbonate (22 mmol) or benzyl carbonochloridate (22 mmol) in CH_2Cl_2 (4 mL) and NaOH (22 mmol) in H_2O (4 mL) was added dropwise to an ice-cooled solution of amino acid (**1a-k**, 20 mmol) in aqueous solution of sodium hydroxide. Then the reaction then stirred at room temperature for several hours and monitored to the completion by thin-layer chromatography. The solution was washed with CH_2Cl_2, acidized, washed with ethyl acetate, sodium chloride aqueous

solution and dried with anhydrous Na_2SO_4. The filtrate was evaporated under a reduced pressure to get N-substituted amino acids, which was used directly for the next reaction without further purification.

General synthetic procedure for Ia-k and IIa-d

N-protected amino acids (2 mmol) and dicyclohexylcarbodiimide (2.4 mmol) were located into an oven-dried round-bottomed flask equipped with a magnetic stir bar, and acetonitrile (25 mL) was then added. After 30 min, tryptamine (0.38 g, 2.4 mmol) or tryptophol (0.38 g, 2.4 mmol) and 4-dimethylaminopyridine (0.024 g, 0.2 mmol) were sequentially added and the reaction mixture was stirred at room temperature for about 48 h, and the reaction was followed by TLC. The mixture was evaporated under a reduced pressure and the residue purified by silica gel column-chromatography (ethyl acetate/petroleum ether) to give target compounds **Ia-k** and **IIa-d**. Their physicochemical properties and the spectra data are as follows:

(*S*)-tert-Butyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate **Ia**. This compound was obtained following the above method as white powder, m.p. 145-147 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (bs, 1H), 7.60 (d, J = 8 Hz, 1H), 7.37 (d, J = 8 Hz, 1H), 7.20 (t, J = 8 Hz, 1H), 7.12 (t, J = 8 Hz, 1H), 7.04 (d, J = 4 Hz, 1H), 6.14 (bs, 1H), 4.85 (bs, 1H), 4.01 (s, 1H), 3.60-3.50 (m, 2H), 2.96 (t, J = 8 Hz, 2H), 1.63-1.55 (m, 2H), 1.48-1.43 (m, 1H), 1.41 (s, 9H), 0.89 (d, J = 4 Hz, 6H); ESI-MS: calcd for $C_{21}H_{31}N_3O_3$ ($[M+H]^+$), 374.2; found, 374.6.

(*S*)-tert-Butyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate **Ib**. This compound was obtained following the above method as light yellow powder, m.p. 127-128 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (bs, 1H), 7.60（d, J = 8 Hz, 1H), 7.37 (d, J = 8 Hz, 1H), 7.20 (t, J = 8 Hz, 1H), 7.12 (t, J = 8 Hz, 1H), 7.03 (d, J = 2 Hz, 1H), 6.07 (bs,1H), 5.83 (bs, 1H), 4.18 (d, J = 8 Hz, 1H), 3.83-3.79 (m, 2H), 2.96 (t, J = 8 Hz, 2H), 2.16-2.02 (m, 1H), 1.41 (s, 9H), 0.90 (d, J = 4 Hz, 6H); ESI-MS: calcd for $C_{20}H_{29}N_3O_3$ ($[M-H]^-$), 358.2; found, 358.8.

(*S*)-tert-Butyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate **Ic**. This compound was obtained following the above method as shell powder, m.p. 115-117 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (bs, 1H), 7.49 (d, J = 8 Hz, 1H), 7.35 (d, J = 8 Hz, 1H), 7.22-7.16 (m, 5H), 7.10 (t, J = 8 Hz, 1H), 6.82 (s, 1H), 5.77 (bs, 1H), 5.06 (bs, 1H), 4.22 (s, 1H), 3.50 (d, J = 4 Hz, 2H), 3.00 (d, J = 8 Hz, 2H), 2.84-2.79 (m, 2H), 1.37 (s, 9H); ESI-MS: calcd for $C_{24}H_{29}N_3O_3$ ($[M+Na]^+$), 430.2; found, 430.6.

(*S*)-tert-Butyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-3-(1*H*-indol-3-yl)-1-oxopropan-2-yl)carbamate **Id**. This compound was obtained following the above method as light yellow powder, m.p. 154-156 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (s, 1H), 7.82 (s, 1H), 7.67 (d, J = 8 Hz, 1H), 7.42 (d, J = 8 Hz, 1H), 7.34 (t, J = 8 Hz, 2H), 7.18-7.23 (m, 2H), 7.14 (t, J = 8 Hz, 1H), 7.06 (t, J = 8 Hz, 1H), 6.85 (d, J = 4 Hz, 1H), 6.52 (s, 1H), 5.57 (bs, 1H), 5.18 (bs, 1H), 4.35 (s, 1H), 3.49-3.44 (m, 2H), 3.30 (d, J = 12 Hz, 1H), 3.06 (t, J = 8 Hz, 1H), 2.68 (d, J = 14 Hz, 2H), 1.41 (s, 9H); ESI- MS: calcd for $C_{26}H_{30}N_4O_3$ ([M+Na]$^{+}$), 469.2; found, 470.0.

(*S*)-Benzyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate **Ie**. This compound was obtained following the above method as white powder, m.p. 102-103 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (bs, 1 H), 7.59 (d, J = 8 Hz, 1 H), 7.40-7.30 (m, 6 H), 7.20 (t, J = 8 Hz, 1 H), 7.12 (t, J = 8 Hz, 1 H), 6.96 (s, 1 H), 6.04 (bs, 1 H), 5.07 (s, 2 H), 4.07 (s, 1 H), 3.58 (t, J = 8 Hz, 1 H), 2.95 (t, J = 8 Hz, 2 H), 1.65-1.60 (m, 2 H), 1.50-1.40 (m, 1 H), 0.87 (d, J = 8 Hz, 6 H); ESI-MS: calcd for $C_{24}H_{29}N_3O_3$ ([M+Na]$^{+}$), 430.2; found, 430.3.

(*S*)-Benzyl(1-(2-(1*H*-indol-3-yl)ethyl)amino)-3-methyl-1-oxobutan-2-ylcarbamate **If**. This compound was obtained following the above method as white powder, m.p. 110-112 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (bs, 1 H), 7.59 (d, J = 8 Hz, 1H), 7.35 (bs, 6H), 7.20 (t, J = 8 Hz, 1H), 7.12 (t, J = 8 Hz, 1 H), 6.96 (s, 1 H), 5.94 (s, 1H), 5.29 (s, 1H), 5.07 (s, 2H), 3.88 (t, J = 8 Hz, 1H), 3.60 (t, J = 8 Hz, 2H), 2.96 (s, 2H), 2.15-2.05 (m, 1H), 0.90 (d, J = 8 Hz, 3H), 0.85 (d, J = 8 Hz, 3H); ESI-MS: calcd for $C_{23}H_{27}N_3O_3$ ([M+Na]$^{+}$), 416.2; found, 416.2

(*S*)-Benzyl (1-((2-(1*H*-indol-3-yl)ethyl)amino)-1-oxo-3-phenylpropan-2-yl)arbamate **Ig**. This compound was obtained following the above method as white powder, m.p. 102-103 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (bs, 1 H), 7.59 (d, J = 8 Hz, 1H), 7.40-7.30 (m, 6 H), 7.20 (t, J = 8 Hz, 1 H), 7.12 (t, J = 8 Hz, 1 H), 6.96 (s, 1 H), 6.04 (bs, 1 H), 5.07 (s, 2 H), 4.07 (s, 1 H), 3.58 (t, J = 8 Hz, 1 H), 2.95 (t, J = 8 Hz, 2 H), 1.65-1.60 (m, 2 H), 1.50-1.40 (m, 1 H), 0.87 (d, J = 8 Hz, 6 H); ESI-MS: calcd for $C_{27}H_{27}N_3O_3$ ([M+Na]$^{+}$), 464.2; found, 464.3.

(*S*)-Benzyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-3-(1*H*-indol-3-yl)-1-oxopropan-2-yl)carbamate **Ih**. This compound was obtained following the above method as light brown powder, m.p. 118-119 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (bs, 2H), 7.65 (d, J = 8 Hz, 1H), 7.42 (d, J = 8 Hz, 1H), 7.35-7.29 (m, 8H), 7.19 (t, J = 8 Hz, 2 H), 7.13-7.04 (m, 3H), 6.76 (s, 1H), 6.49 (s, 1H), 5.59 (s, 1H), 5.49 (s, 1H), 4.40 (s,

N-H), 3.50-3.47 (m, 2 H), 3.30 (d, *J* = 10 Hz, 1H), 3.06 (dd, *J* = 8 Hz, 2H), 2.76-2.61 (m, 2 H); ESI-MS: calcd for $C_{29}H_{28}N_4O_3$ ([M+Na]$^+$), 503.2; found, 503.2.

(*R*)-Benzyl(1-((2-(1*H*-indol-3-yl)ethyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate **Ii**. This compound was obtained following the above method as white powder, m.p. 129-130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (bs, 1 H), 7.48 (d, *J* = 8 Hz, 1 H), 7.40-7.27 (m, 7 H), 7.24-7.08 (m, 6 H), 6.77 (s, 1 H), 5.72 (bs, 1 H), 5.29 (bs, 1 H), 5.04 (s, 2 H), 4.29 (s, 1 H), 3.49 (d, *J* = 8 Hz, 2 H), 3.00 (d, *J* = 8 Hz, 2 H), 2.85-2.77 (m, 2 H); ESI- MS: calcd for $C_{27}H_{27}N_3O_3$ ([M+Na]$^+$), 464.2; found, 464.5.

(*R*)-Benzyl (2-((2-(1*H*-indol-3-yl)ethyl)amino)-2-oxo-1-phenylethyl)carbamate **Ij**. This compound was obtained following the above method as light brown powder, m.p. 122-123 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1 H), 7.50 (d, *J* = 8 Hz, 2 H), 7.37-7.28 (m, 10 H), 7.19 (t, *J* = 8 Hz, 1 H), 7.09 (t, *J* = 8 Hz, 1 H), 6.62 (s, 1 H), 6.16 (s, 1 H), 5.68 (s, 1 H), 5.07 (s, 2 H), 3.65-3.55 (m, 1 H), 3.52-3.42 (m, 1 H), 2.98-2.88 (m, 1 H), 2.87-2.75 (m, 1 H); ESI-MS: calcd for $C_{26}H_{25}N_3O_3$ ([M+Na]$^+$), 450.2; found, 450.2.

(*S*)-Benzyl (1-((2-(1*H*-indol-3-yl)ethyl)amino)-4-(methylthio)-1-oxobutan-2-yl) carbamate **Ik**. This compound was obtained following the above method as white powder, m.p. 119-121 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (bs, 1H), 7.59 (d, *J* = 8 Hz, 1H), 7.36-7.28 (m, 6H), 7.20 (t, *J* = 8 Hz, 1H), 7.12 (t, *J* = 8 Hz, 1H), 6.98 (s, 1H), 6.13 (bs, 1H), 5.44 (bs, 1H), 5.11-5.04 (m, 2H), 4.23 (d, *J* = 12 Hz, 1H), 3.63-3.57 (m, 2H), 2.96 (t, *J* = 8 Hz, 2H), 2.53-2.37 (m, 2H), 1.95-1.84 (m, 2H); ESI- MS: calcd for $C_{23}H_{27}N_3O_3S$ ([M+Na]$^+$), 448.2; found, 448.2.

(*S*)-2-(1*H*-Indol-3-yl)ethyl-2-(((benzyloxy)carbonyl)amino)-4-methyl pentanoate **IIa**. This compound was obtained following the above method as light yellow semisolid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (bs, 1H), 7.61 (d, *J* = 12 Hz, 1H), 7.35（d, *J* = 8 Hz, 6H), 7.20 (t, *J* = 8 Hz, 1H),7.13 (t, *J* = 8 Hz, 1H), 7.03 (s, 1H), 5.13 (bs, 1H), 5.11 (d, *J* = 2 Hz, 2H), 4.38 (dt, *J* = 8 Hz, 3H), 3.11 (t, *J* = 8 Hz, 2H), 1.70-1.65 (m, 2H), 1.48-1.42 (m, 1H), 0.90 (dd, *J* = 8 Hz, 6H); ESI-MS: calcd for $C_{24}H_{28}N_2O_4$ ([M+Na]$^+$), 431.2; found, 431.8.

(*S*)-2-(1*H*-Indol-3-yl)ethyl 2-(((benzyloxy)carbonyl)amino)-3-methyl butanoate **IIb**. This compound was obtained following the above method as light yellow semisolid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (bs, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.36 (t, *J* = 4 Hz, 1H), 7.20 (t, *J* = 8Hz, 1H), 7.13 (t, *J* = 8 Hz, 1H), 7.03 (s, 1H), 5.26 (d, *J* = 8 Hz), 5.11 (s, 2H), 4.44-4.36 (m, 2H), 4.32-4.29 (m, 1H), 3.12 (t, *J* = 8 Hz, 2H),

2.14-2.11 (m, 1H), 0.97 (dd, *J* = 8 Hz, 6H); ESI-MS: calcd for $C_{23}H_{26}N_2O_4$ ([M+Na]$^+$), 417.2; found, 417.5.

(*S*)-2-(1*H*-Indol-3-yl)ethyl 2-(((benzyloxy)carbonyl)amino)-3-(1*H*-indol-3-yl)propanoate **IIc**. This compound was obtained following the above method as light brown semisolid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.87 (s, 1H), 7.56 (d, *J* = 8 Hz, 1H), 7.45 (d, *J* = 8 Hz, 1H), 7.35-7.28 (m, 7H), 7.25-7.10 (m, *J* = 8 Hz, 3H), 7.03 (t, *J* = 8 Hz, 1H), 6.85 (s, 1H), 6.66 (s, 1H), 5.32 (d, *J* = 8 Hz, 1H), 5.15-5.07 (dd, *J* = 8 Hz, 2H), 4.73 (dd, *J* = 4 Hz, 1H), 4.36-4.30 (m, 2H), 3.25 (d, *J* = 8 Hz, 2H), 3.01 (t, *J* = 8 Hz, 2H); ESI-MS: calcd for $C_{29}H_{27}N_4O_3$ ([M+Na]$^+$), 504.2; found, 504.5.

(*S*)-2-(1*H*-Indol-3-yl)ethyl 2-((tert-butoxycarbonyl)amino)-3-phenyl propanoate **IId.** This compound was obtained following the above method as shell powder, m.p. 95-97 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.61 (d, *J* = 8 Hz, 1H), 7.36 (d, *J* = 8 Hz, 1H), 7.19 (m, 5H), 7.00 (s, 3H), 4.99 (d, *J* = 12 Hz, 1H), 4.59 (d, *J* = 8 Hz, 1H), 4.37 (t, *J* = 8 Hz, 2H), 3.12-2.95 (m, 4H), 1.43 (s, 9H); ESI-MS: calcd for $C_{24}H_{28}N_2O_4$ ([M+Na]$^+$), 431.2; found, 431.7.

General synthetic procedure for IIIa-g

Thionyl chloride (3.3 mL, 45 mmol) was added dropwise to an ice-cooled solution of tryptophan (30 mmol) in methanol solution (30 mL). Then the mixtures were heated under reflux for 10 h until all the starting materials had disappeared as indicated by TLC. The reaction mixture was allowed to stand at room temperature, and the mixture was evaporated under a reduced pressure to get tryptophan methyl ester hydrochloride.

Triethylamine (0.4 mL, 3 mmol) was added dropwise to the solution of tryptophan methyl ester hydrochloride (0.38 g, 1.5 mmol) in acetonitrile solution (25 mL). The mixture was heated under reflux for 2 h to get tryptophan methyl ester. At the same time, N-protected amino acids (1.5 mmol) and dicyclohexylcarbodiimide (l.7 mmol) were added to acetonitrile solution (15 mL), stirring for 30 min at room temperature. Then the two solutions were mixed, stirring at room temperature for about 48h, and the reaction was followed by TLC. After completion of the reaction, the solvents were removed by rotary evaporation and the residual solid is purified by silica gel column- chromatography (ethyl acetate/petroleum ether) to give target compounds **IIIa-g** as white solid or crystal.

(*S*)-Methyl 2-(2-((tert-butoxycarbonyl)amino)-4-methyl pentanamido)-3-(1*H*-indol-3-yl)propanoate **IIIa**. This compound was obtained following the above method as yellow semisolid, m.p. 64-65 ^{o}C; ^{1}H

NMR (400 MHz, $CDCl_3$): δ 8.2 (s, 1H), 7.52 (d, J = 8 Hz, 1H), 7.34 (d, J = 8 Hz, 1H), 7.17 (t, J = 8 Hz, 1H), 7.10 (t, J = 8 Hz, 1H), 7.05 (s, 1H), 6.58 (d, J = 8 Hz, 1H), 4.96-4.88 (m, 1H), 4.88-4.82 (m, 1H), 4.12 (s, 1H), 3.65 (s, 3H), 3.31 (d, J = 4 Hz, 2H), 1.42 (s, 2H), 1.41 (s, 9H), 0.91 (s, 1H), 0.89 (d, J = 4 Hz, 6H); ESI-MS: calcd for $C_{23}H_{33}N_3O_5$ ($[M+Na]^+$), 454.2; found, 454.8.

(*S*)-Methyl 2-(2-((tert-butoxycarbonyl)amino)-3-methylbutanamido)-3-(1*H*-indol-3-yl)propanoate **IIIb**. This compound was obtained following the above method as light yellow powder, m.p. 137-139 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (bs, 1H), 7.52 (d, J = 8 Hz, 1H), 7.34 (d, J = 8 Hz, 1H), 7.18 (t, J = 8 Hz, 1H), 7.12 (d, J = 8 Hz, 1H), 6.41 (d, J = 8Hz, 1H), 5.07 (d, J = 8 Hz, 1H), 4.91 (d, J = 8 Hz, 1H), 3.93 (s, 1H), 3.65 (s, 3H), 3.45-3.29 (m, 2H), 2.05 (s, 1H), 1.43 (s, 9H), 0.87 (dd, J = 4 Hz, 6H); ESI-MS: calcd for $C_{22}H_{31}N_3O_5$ ($[M+H]^+$), 418.2; found, 418.7.

(*S*)-Methyl 2-(2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-(1*H*-indol-3-yl)propanoate **IIIc**. This compound was obtained following the above method as white powder, m.p. 163-165 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 (bs, 1H), 7.36-7.28 (m, 3H), 7.24-7.21 (m, 2H), 7.19-7.15 (m, 3H), 7.16 (m, 9H), 6.36 (s, 1H), 4.85 (s, 1H), 4.35 (s, 1H), 4.11 (s, 1H), 3.62 (s, 3H), 3.25 (d, J = 4 Hz, 2H), 3.01 (d, J = 8 Hz, 2H), 1.35 (s, 9H); ESI-MS: calcd for $C_{26}H_{31}N_3O_5$ ($[M+H]^+$), 466.2; found, 467.0.

(*S*)-Methyl 2-(2-(((benzyloxy)carbonyl)amino)-4-methylpentanamido)-3-(1*H*-indol-3-yl)propanoate **IIId**. This compound was obtained following the above method as light yellow powder, m.p. 195-197 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (bs, 1H), 7.50 (d, J = 8 Hz, 2H), 7.35-7.30 (m, 6H), 7.16 (t, J = 8 Hz, 1H), 7.08 (t, J = 8 Hz, 1H), 6.95 (s, 1H), 6.61 (bs, 1H), 5.17 (bs, 1H), 5.03 (d, J = 8 Hz, 2H), 4.92-4.85 (m, 1H), 4.22 (s, 1H), 3.66 (s, 3H), 3.29 (d, J = 4 Hz, 2H), 1.75-1.70 (m, 2H), 1.16-1.05 (m, 1H), 0.88 (d, J = 4 Hz, 6H); ESI-MS: calcd for $C_{26}H_{31}N_3O_5$ ($[M+H]^+$), 466.2; found, 466.6.

(*S*)-Methyl 2-(2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-(1*H*-indol-3-yl)propanoate **IIIe**. This compound was obtained following the above method as white powder, m.p. 146-147 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (bs, 1H), 7.50 (d, J = 8 Hz, 1H), 7.38-7.30 (m, 6H), 7.17 (t, J = 12 Hz, 1H), 7.09 (t, J = 8 Hz, 1H), 6.94 (s, 1H), 6.43 (s, 1H), 5.34 (d, J = 8 Hz, 1H), 5.05 (s, 2H), 4.91 (dd, J = 8 Hz, 1H), 4.03 (s, 1H), 3.67 (s, 3H), 3.35-3.25 (m, 2H), 2.08-2.03 (m, 1H), 0.99 (dd, J = 8 Hz, 6H); ESI-MS: calcd for $C_{25}H_{29}N_3O_5$ ($[M+H]^+$), 474.2; found, 474.7.

(*S*)-Methyl 2-(2-(((benzyloxy)carbonyl)amino)-3-phenylpropanamido)-3-(1*H*-indol-3-yl)propanoate **IIIf**. This compound was obtained following the above method as light yellow powder , m.p. 120-122 ^oC;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (bs, 1H), 7.45-7.14 (m, 12H), 7.05 (t, J = 8 Hz, 2H), 6.81 (s, 1H), 6.41 (s, 1H), 5.30 (m, 1H), 5.00 (d, J = 4 Hz, 2H), 4.86 (d, J = 4 Hz, 1H), 3.66-3.60 (m, 3H), 3.23 (d, J = 12 Hz, 2H), 3.02 (d, J = 8 Hz, 1H), 1.71 (s, 1H); ESI-MS: calcd for $C_{29}H_{29}N_3O_5$ ($[M+Na]^+$), 522.2; found, 522.6.

(*S*)-Methyl2-(2-(((benzyloxy)carbonyl)amino)-3-(1*H*-indol-3-yl)propanamido)-3-(1*H*-indol-3-yl)propanoate **IIIg.** This compound was obtained following the above method as shell powder, m.p. 185-187 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 2H), 7.65 (s, 1H), 7.33-7.28 (m, 1H), 7.24-7.11 (m, 4H), 6.99-6.88 (m, 2H), 6.55 (s, 1H), 6.16 (d, J = 4 Hz, 1H), 5.41(s, 1H), 5.08 (s, 2H), 4.79 (d, J = 8 Hz, 1H), 4.50 (s, 1H), 3.61 (s, 3H), 3.34 (d, J = 12 Hz, 1H), 3.36-3.06 (m, 3H); ESI-MS: calcd for $C_{31}H_{30}N_4O_5$ ($[M+H]^+$), 539.2; found, 539.8.

***In vitro* cytotoxicity assays**

The *in vitro* cytotoxicity of the synthesized compounds against different human cancer cell lines (HepG2, Huh-7, A875, and BEL-7402/5-FU) were measured with the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. All the data of the experiment were analyzed with SPSS software, and the 50% inhibitory concentrations (IC_{50}) of each compound for the different cell lines were determined. A control was run for each test, and all assays were performed in triplicate on three independent experiments, and measurement data were expressed as the mean ± S.D.