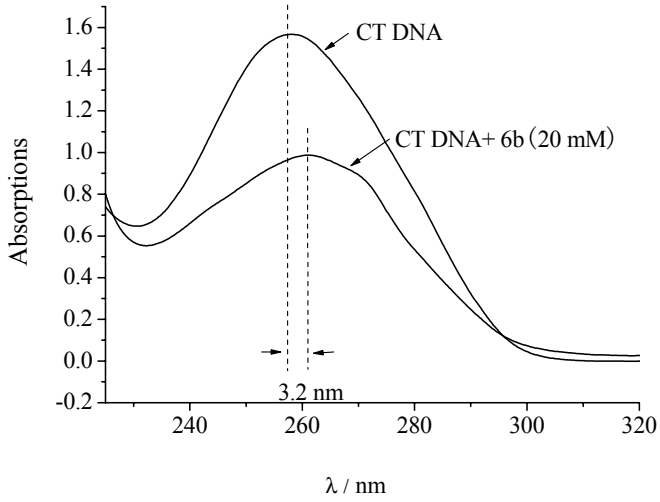

Fig 1 UV spectra of CT DNA explain **6b** induced hypochromic effect and bathochromic shift. a) Without **6b**; b) With **6b**. Final concentration of CT DNA, 240μM; final concentration of **6b**, 20μM; pH=7.4.

Experimental

General

All chemicals were purchased from commercial suppliers and were purified when necessary. The protected amino acids with L-configuration were purchased from sigma chemical Co. Chromatography was performed on Qingdao silica gel H. The purities of the intermediates and the products were measured by TLC analysis (Merck silica gel plates of type 60 F_{254}, 0.25mm layer thickness) and HPLC analysis (waters, C_{18} column, 4.6×150mm). Melting points were determined in capillary tubes on an electrothermal SM / XMP apparatus and without correction. UV spectra were measured on Shimadzu UV 2550, FT-IR spectra were run on a infrared spectrometer. ESI-MS was determined by Micromass Quattro micro TM API, waters Co. ^{1}HNMR (500 Hz) and ^{13}C NMR (125 Hz) spectra were acquired on a Bruker AVANCE Ⅱ 500 in $CDCl_3$ with TMS as internal standard, or in DMSO-d_6 and chemical shifts were expressed in ppm (d). Optical rotations were determined with a Jasco P-1020 Polarimeter. The statistical analysis of all the biological data was carried out by use of ANOVA test, $p<0.05$ is considered significant.

Methyl 1-(2,2-dimethoxyethyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylate (1)

A suspension of 5.0g (19.6 mmol) of L-tryptophan methylester, 50 ml of methanol and 6.0 ml

(23.6 mmol) of 1,1,3,3-tetramethoxypropane was adjusted pH 1-2 with hydrochloric acid (5N) and stirred at 318K for 48h. The reaction mixture was evaporated under vacuum, the residue was diluted with water and the aqueous solution was extracted with ethyl acetate (30ml×3). The organic phase was separated, washed successively with 10% sodium carbonate and saturated sodium chloride, dried over anhydrous sodium sulfate, filtered and the filtrate was evaporated under vacuum. The residue was purified by silica gel chromatography (Chloroform: Methanol, 30:1) to provide 5.4 g (88.5%) of the title compound as a pale yellow oil consisted of 60% of **(1S,3S)-1** and 29% of **(1R,3S)-1**. FAB-MS (m/e) 319 $[M+H]^+$.

Methyl 1-(2,2-dimethoxyethyl)-β-carboline-3-carboxylate (2)

A mixture of 4.3g（13.783mmol）of methyl 1-(2,2-dimethoxyethyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylate and 100 ml of DMF was stirred at 273K until a clear solution was formed, to which then 3.04 g (19.296mmol) of $KMnO_4$ was added. The reaction mixture was stirred at 273K for 1h, at room temperature for 3 h, TLC (chloroform/methanol, 15:1) indicated the complete disappearance of methyl 1-(2,2-dimethoxyethyl)-1,2,3,4-tetrahydro-β-carboline -3-carboxylate. The formed precipitates were filtered and the filtrate was evaporated under vacuum. The residue was diluted with 100ml of ethyl acetate, and the solution was washed successively with water and saturated aqueous sodium chloride, and the organic phase was separated and dried over anhydrous sodium sulfate. After filtration the filtrate was evaporated under vacuum. The residue was solidified in acetone to give 3.47g (80.3％) of the title compound as a yellow power. Mp 134.5-136℃; ESI/MS (m/e) 315$[M+H]^+$; ^{1}HNMR($CDCl_3$):δ/ppm=8.81(s, 1H), 8.37(d, J=7.5 Hz, 1H), 7.30(t, J=7.5 Hz, 1H), 7.62.(m, 1H), 7.41 (m, 1H), 5.04 (t, J=6.0 Hz, 1H), 3.92 (s, 3H), 3.47 (d, J=6.0 Hz, 2H), 3.29(s, 6H); ^{13}CNMR($CDCl_3$): δ/ppm =166.59, 142.04, 141.62, 137.29, 136.28, 128.85, 127.82, 122.48, 120.49, 116.64, 112.95, 104.12, 79.66, 53.65, 52.36, 38.23. Anal.Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. found: C, 64.80; H, 5.59; N, 8.70

Methyl 9-benzyl-1-(2,2-dimethoxyethyl)-β-carboline-3-carboxylate (3)

A mixture of 5.50g (17.54mmol) of methyl 1-(2,2-dimethoxyethyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylate, 20ml of anhydrous DMF and 20ml of anhydrous THF was stirred to form

a clear solution, and then 1.05g (26.32mmol, 60%) of NaH were added. The mixture was stirred at room temperature for 30 min, to which 2.98g (17.54mmol) of benzyl bromide was added and the reaction mixture was stirred for 4h. To the reaction mixture 200g of ice was added and the solution was extracted with ethyl acetate (100ml×3). The organic phase was separated, washed with saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. After filtration the filtrate was evaporated under vacuum. The residue was purified with silica gel chromatography (petroleum ether/acetone, 2:1). To give 4.337g (61.2%) of the title compound as a colorless power . Mp 122.7-125 ℃; ESI/MS (m/e) 405 $[M+H]^+$; ^{1}HNMR ($CDCl_3$): δ/ppm= 8.86 (s, 1H), 8.27 (d, J=8.0Hz, 1H), 7.61 (m, 1H), 7.47 (d, J=8.0Hz, 1H), 7.40 (m, 1H) ,7.33 (m, 2H) , 7.25 (m, 1H), 6.999 (m, 2H), 6.02 (s, 2H), 4.98 (t, J=5.5 Hz, 1H), 4.07 (s, 3H), 3.48 (d, J=5.5 Hz, 2H), 3.34 (s, 6H); ^{13}CNMR ($CDCl_3$): δ/ppm= 166.72, 142.67, 141.24, 137.53, 137.34, 137.06, 129.93, 129.07, 129.03, 127.56, 125.46, 121.63, 121.54, 120.95, 116.36, 110.30, 105.83, 54.78, 52.46, 48.17, 39.84. Anal.Calcd for $C_{24}H_{24}N_2O_4$: C, 71.27; H, 5.98; N, 6.93. found: C, 71.28; H, 5.80; N, 6.71.

Methyl 9-benzyl-1-carbonylmethyl-β-carboline-3-carboxylate (4)

A mixture of 1.0 g (2.475mmol) of methyl 9-benzyl-1-(2,2-dimethoxyethyl)-β-carboline-3-carboxylate, 14ml of acetic acid and 2ml of water was stirred at room temperature for 16h. To the reaction mixture 200g of ice was added. The formed precipitates were collected by filtration to provide 538mg (60.7%) of the title compound which was directly used for the next reaction without purification.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylphenylalanine methylesters (5a)

$[\alpha]_D^{20}$= -5.2 (c=0.01, $CHCl_3$); ESI/MS (m/e) 522 $[M+H]^+$; ^{1}H NMR ($CDCl_3$): δ/ppm= 8.832 (s, 1H), 8.24 (d, J=7.8 Hz, 1H), 7.60 (t, J=4.8 Hz, 1H), 7.44 (m, 1H), 7.38 (m, 1H) , 7.32 (m, 2H), 7.27 (m, 1H), 7.24 (m, 2H), 7.22 (m, 1H), 7.12 (m, 2H), 7.04 (m, 1H), 6.92(m, 1H), 5.80 (s, 2H), 4.05 (s, 3H), 3.63 (s, 3H), 3.52 (t, J=4.2 Hz, 1H), 3.33 (t, J=4.2Hz, 2H), 3.16 (m, 1H), 2.94 (m, 2H); ^{13}CNMR ($CDCl_3$): δ/ppm= 174.68, 166.70, 143.37, 142.46, 137.59, 137.28, 137.10, 136.84, 129.70, 129.09, 129.01, 128.36, 127.67, 126.10, 125.40, 121.72, 121.67, 121.06, 116.28 , 110.35, 63.09, 52.06, 51.69, 48.38, 47.40, 39.80, 35.52. Anal.Calcd for $C_{32}H_{31}N_3O_4$ C, 73.68; H, 5.99; N,

8.06. Found C, 73.89; H, 6.10; N, 8.29.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylalanine methylesters (5b)

$[\alpha]_D^{20}$= -3.6(c=0.01, $CHCl_3$); ESI/MS (m/e) 446$[M+H]^+$; ^{1}H NMR ($CDCl_3$): δ/ppm= 8.84 (s, 1H), 8.25 (d, J=7.5 Hz, 1H), 7.59 (m, 1H),7.48 (d, J=7.5 Hz, 1H), 7.41 (m, 1H), 7.31 (m, 2H), 7.26 (m, 1H), 7.02 (m, 1H), 6.98 (m, 1H), 5.89 (s, 2H), 4.06 (s, 3H), 3.70 (s, 3H), 3.09 (m, 2H), 3.04 (m, 2H), 3.00 (m, 1H), 1.31 (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ/ppm= 175.84, 166.70, 143.48, 142.44, 137.22, 137.06, 136.81, 129.69, 129.12, 129.00, 127.73, 125.41, 121.70, 121.66, 121.07, 116.26, 110.36, 56.83, 52.54, 51.77, 48.54, 47.04, 35.60, 18.93. Anal.Calcd for $C_{26}H_{27}N_3O_4$ C 70.09, H 6.11, N 9.43. Found: C, 70.30; H, 6.00; N, 9.65.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylisoleucine methylesters (5c)

$[\alpha]_D^{20}$=4.6 (c=0.01, $CHCl_3$)； ESI/MS (m/e) 488$[M+H]^+$; ^{1}H NMR ($CDCl_3$):δ/ppm= 8.83 (s, 1H), 8.24 (d, J=7.8 Hz, 1H), 7.593 (t, J=7.2Hz, 1H), 7.45 (m, 1H), 7.30 (m, 2H), 7.28 (m, 1H), 7.25 (m, 1H), 6.99 (m, 2H), 5.89 (s, 2H), 4.04 (s, 3H), 3.66 (s, 3H), 3.36 (m, 2H), 3.09 (m, 2H), 2.91 (m, 1H), 1.67 (m, 1H), 1.52 (m, 2H), 0.97 (t, J=7.2 Hz, 3H), 0.88 (d, J=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$):δ/ppm= 175.32, 166.75, 143.66, 142.46, 137.28, 137.15, 136.86, 129.69, 129.10, 128.99, 127.69, 127.54, 125.44, 121.69, 121.67, 121.05, 116.29, 110.33, 66.51, 52.58, 51.37, 48.47, 48.14, 38.13, 36.00, 25.59, 15.54, 11.43. Anal.Calcd for $C_{29}H_{33}N_3O_4$ C, 71.44; H, 6.82; N, 8.62. Found C, 71.62; H, 6.91; N, 8.40.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylglycine methylesters (5d)

ESI/MS (m/e) 432$[M+H]^+$; ^{1}HNMR ($CDCl_3$): δ/ppm= 8.83 (s, 1H), 8.31 (d, J=7.8 Hz, 1H), 7.59 (m, 1H), 7.46 (m, 1H), 7.42 (m, 1H), 7.32 (m, 2H), 7.22 (m, 1H), 7.11 (m, 1H), 6.99 (m, 1H) 5.87 (s, 2H), 4.02 (s, 3H), 3.72 (s, 3H), 3.53 (m, 2H), 3.37(m, 2H), 3.18 (m,1H).;^{13}C NMR ($CDCl_3$): δ/ppm= 171.79, 166.48, 143.77, 142.32, 137.13, 136.84, 136.68, 129.77, 129.14, 128.92, 127.76, 125.37, 121.67, 121.60, 121.15, 120.90, 116.33, 110.34, 52.55, 51.92, 50.37, 48.53, 48.26, 34.42. Anal.Calcd for $C_{25}H_{25}N_3O_4$ C, 69.59; H, 5.84; N, 9.74. Found C, 69.41; H, 5.73; N, 9.52.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylphenylalanine (6a)

Mp 226-229℃. $[\alpha]_D^{20}$=-28.9 (c=0.01, DMSO); ESI/MS (m/e) 494[M + H]$^+$; ^{1}H NMR (DMSO-d_6): δ/ppm= 8.93(s, 1H), 8.50 (d, J=8.0 Hz, 1H), 7.73 (d, J=8.5 Hz, 1H), 7.65 (m, 1H), 7.39 (t, J=8.0Hz, 1H), 7.34 (m, 2H),7.32(m, 1H), 7.29 (m, 2H), 7.21(m, 1H), 7.15 (m, 2H), 7.05 (m, 1H), 6.95 (m, 1H), 5.96 (s, 2H), 3.52 (t, J=4.2Hz, 1H), 3.33 (t, J=4.2 Hz, 2H), 3.15 (m, 1H), 2.94 (m, 3H). ^{13}C NMR (DMSO-d_6): δ/ppm= 172.49, 170.28, 166.83, 156.70, 142.66, 141.84, 138.42, 137.13, 136.17, 130.74, 129.79, 129.71, 129.37, 127.87, 126.63, 126.03, 125.93, 122.65, 121.54, 121.30, 116.66, 115.58, 111.55.62.48, 52.32, 48.78, 30.37. Anal.Calcd for $C_{30}H_{27}N_3O_4$ C, 73.01; H, 5.51; N, 8.51. Found C, 73.22 , H, 5.62 , N, 8.30.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylalanine (6b)

Mp.226-228℃. $[\alpha]_D^{20}$=11.7 (c=0.01, DMSO). ESI/MS (m/e) 432[M+H]$^+$; ^{1}H NMR (DMSO-d_6): δ/ppm= 8.95 (s, 1H), 8.50 (d, J=7.8 Hz, 1H), 7.73 (m, 1H), 7.63 (m, 1H), 7.38 (m, 1H), 7.35 (m, 2H), 7.21 (m, 1H), 7.08 (m, 1H), 6.96 (m, 1H), 5.99 (s, 2H), 3.65 (m, 1H), 3.35(m, 2H), 3.10 (m, 2H), 1.28(m, 3H). ^{13}C NMR (DMSO-d_6): δ/ppm= 170.43, 166.85, 142.63, 141.45, 138.43, 137.29, 136.23, 129.79, 129.63, 127.86, 125.98, 122.65, 121.53, 116.65, 111.52, 57.82, 48.22, 43.81, 30.27, 16.16 . Anal.Calcd for $C_{24}H_{23}N_3O_4$ C, 69.05; H, 5.55; N, 10.07. Found C, 68.86; H, 5.43; N, 10.29.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylisoleucine (6c)

Mp. 214-216℃. $[\alpha]_D^{20}$=-26.9(c=0.01, DMSO); ESI/MS (m/e) 460[M+H]$^+$; .^{1}H NMR (DMSO-d_6): δ/ppm= 8.95(s, 1H), 8.51 (d, J=7.5 Hz, 1H), 7.74 (m, 1H), 7.64 (t, J=7.0Hz, 1H), 7.39 (d, J=7.5Hz, 1H), 7.31 (m, 2H), 7.23 (m, 1H), 7.03 (m, 1H), 6.99 (m, 1H), 6.01 (s, 2H), 3.58 (m, 1H), 3.28 (m, 2H), 3.17 (m, 2H), 1.56 (m, 1H), 1.26 (m, 2H), 0.917(m, 3H) 0.88 (m, 3H); ^{13}C NMR (DMSO-d_6): δ/ppm= 167.29, 166.48, 142.72, 141.27, 138.48, 137.56, 136.62, 129.78, 129.38, 126.01, 122.67, 121.51, 121.32, 116.65, 111.43, 51.12, 48.32, 45.15, 36.54, 30.17, 25.03, 15.32, 12.48; Anal.Calcd for $C_{27}H_{29}N_3O_4$ C, 70.57; H, 6.36; N, 9.14. Found C, 70.38; H, 6.27; N, 9.33.

N-(9-Benzyl-3-carboxylcarboline-1-yl)ethylglycine (6d)

M.p.187-189℃ ; ESI/MS (m/e) 404[M+H]$^+$; ^{1}H NMR (DMSO-d_6): δ/ppm= 8.98 (s, 1H), 8.49 (d, J=7.8Hz, 1H), 7.73 (d, J=8.4Hz, 1H), 7.63 (t, J=7.2Hz, 1H), 7.38 (t, J=7.2Hz, 1H), 7.31 (m, 2H),

7.21(m, 1H), 7.08 (m, 1H), 6.96 (m, 1H), 5.99 (s, 2H), 3.59 (t, J=6Hz, 2H), 3.45 (t, J=6Hz, 2H), 3.30 (s, 2H). ^{13}C NMR (DMSO-d_6): δ/ppm=167.29, 166.84, 142.63, 141.22, 138.44, 137.35, 136.26, 129.78, 129.37, 126.00, 122.64, 121.51, 121.31, 116.65, 111.53, 50.10, 48.19, 45.15, 30.37. Anal.Calcd for $C_{23}H_{21}N_3O_4$ C, 68.47; H, 5.25; N, 10.42. Found C, 68.26; H, 5.12; N, 10.63.