Supporting Information

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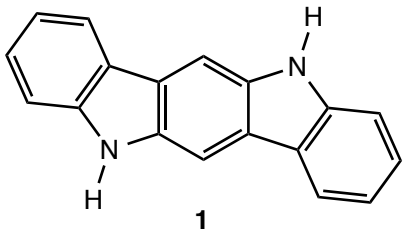
General Methods. Distilled water was used in all of the experiments. Organic extracts were dried over Na_2SO_4, filtered, and concentrated using a rotary evaporator at aspirator pressure (20-30mmHg). Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60, 230-400 mesh). 1H and 13C NMR spectra were measured at 400 MHz and 100 MHz, respectively, using Me4Si as internal standard.
Chemical shifts are reported in ppm downfield (δ) from Me4Si.



1

To a stirred solution of 3,3'-diindolylmethane (1.24 g, 5.0 mmol) in methanol (30 mL) was added trimethyl orthoformate (0.84 mL) and 6 drops of concentrated H_2SO_4. The reaction mixture was refluxed at 60 °C for 1 hour. The resulting product mixture was filtered and washed with cold methanol. **1** was used without further purification (1.06 g, 4.14 mmol, 82%).

See spectra on page S17

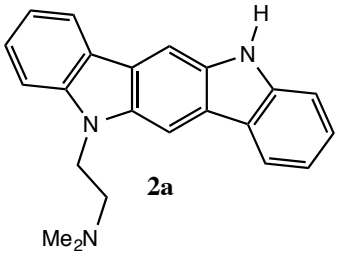
^{1}H NMR: (400 MHz, DMSO-d_6)

11.0 (s, 2H); 8.20 (d, J = 7.72 Hz, 2H); 8.11 (s, 2H); 7.46 (d, J = 8.00 Hz, 2H); 7.39 (t, J = 7.04 Hz, 2H); 7.14 (t, J = 7.88 Hz, 2H).

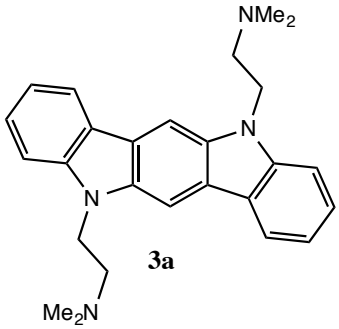
^{13}C NMR: (100 MHz, DMSO-d_6)

141.5; 135.5; 125.8; 123.1; 123.0; 120.6; 118.1; 110.9; 100.9.

HRMS (ESI): calculated for $C_{18}H_{13}N_2$: 257.1079; found $(M+Na)^+$: 257.1038



2a



3a

Indolo[3,2-*b*]carbazole (1 g, 3.9 mmol) was added to a stirring solution of NaH (390 mg, 9.8 mmol) and DMF (8 mL). The reaction mixture was allowed to stir under argon for 1 hour. Then, 2-chloro-*N,N*-dimethylethylamine hydrochloride (1.29 g, 8.9 mmol) was added slowly, and the reaction mixture was allowed to stir until completion as monitored by TLC (rf **3a**: 0.25, 3:1 EtOAc/MeOH; rf **2a**: 0.35, 3:1 EtOAc/MeOH). The crude mixture of **3a** and **2a** was poured into ice and the product was filtered. Purification by column chromatography (9:1 EtOAc/MeOH) afforded **3a** (0.9 g, 2.26 mmol, 58%) and **2a** (0.21 g, 0.64 mmol).

See spectra on page S18 and S19, respectively

3a

^{1}H NMR: (400 MHz, $CDCl_3$)

8.23 (d, *J* = 7.60 Hz, 2H); 8.07 (s, 2H); 7.54 (t, *J* = 7.00 Hz, 2H); 7.48 (d, *J* = 8.04 Hz, 2H); 7.27 (t, *J* = 7.68 Hz, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$)

141.5; 136.0; 125.8; 123.0; 122.9; 120.3; 118.3; 108.2; 98.7; 57.1; 45.9; 41.9.

HRMS (ESI): calculated for $C_{26}H_{33}N_4$: 400.2627; found $(M+2H)^+$: 400.2721

2a

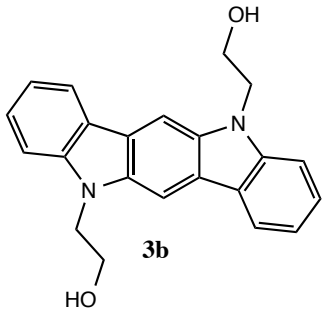
^{1}H NMR: (400 MHz, DMSO-d_6)

11.09 (s, 1H); 8.28 (s, 1H); 8.25 (d, *J* = 7.76 Hz, 1H); 8.24 (d, *J* = 7.36 Hz, 1H); 8.16 (s, 1H); 7.58 (d, *J* = 8.16 Hz, 1H); 7.49 (t, *J* = 8.12 Hz, 2H); 7.39 (m, 1H); 7.19 (m, 2H); 4.60 (t, *J* = 6.96, 2H); 2.77 (s, 2H); 2.33 (s, 6H).

^{13}C NMR: (100 MHz, DMSO-d_6)

141.6; 141.5; 135.9; 135.6; 129.3; 128.6; 126.1; 126.0; 123.1; 123.0; 122.7; 122.6; 120.7; 118.3; 118.1; 111.0; 109.1; 100.2; 99.4; 57.2; 45.8; 40.6.

HRMS (ESI): calculated for $C_{22}H_{20}N_3Na$: 349.1555; found $(M+Na)^+$: 349.1627



3b

A mixture of indolo[3,2-*b*]carbazole (1.0 g, 3.90 mmol) and NaH (390 mg, 9.75 mmol) was stirred under argon for an hour at room temperature. (Bromomethoxy)(tert-butyl)dimethylsilane (1.9 mL, 8.97 mmol) was added dropwise and the mixture was allowed to stir until the completion of the reaction monitored by TLC (10:1 Hexane/ EtOAc; rf = 0.4). The mixture was quenched with sodium bicarbonate and diluted with CH_2Cl_2. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (100:1 Hexane/EtOAc) gave corresponding the silyl ether **4a** (2.06 g, 3.60 mmol, 92%).

To the silyl ether (2.06 g, 3.60 mmol) in THF (1 mL), tetra-*n*-butylammonium fluoride (4 mL; 2M solution in THF) was added. The reaction was monitored by TLC (rf = 0.3; 1:1 Hexane/EtOAc). Purification by column chromatography (2:1 Hexane/ EtOAc) afforded **3b** (1.48 g, 3.50 mmol, 98%).

See spectra on page S20

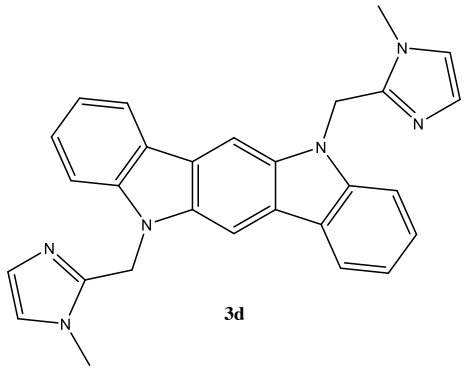
^{1}H NMR (400 MHz, DMSO-d_6)

8.31 (s, 2H), 8.23 (d, J = 7.5 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.48 – 7.39 (m, 2H), 7.17 (dd, J = 10.9, 3.9 Hz, 2H), 4.93 (s, 2H), 4.53 (t, J = 5.8 Hz, 4H), 3.86 (s, 4H).

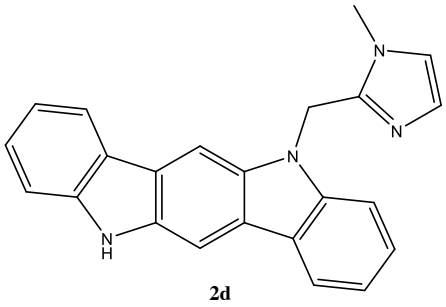
^{13}C NMR: (100 MHz, DMSO-d_6)

142.07, 136.36, 125.98, 122.71, 122.56, 120.55, 118.26, 109.56, 99.79, 59.81, 45.82.

HRMS (ESI): calculated for $C_{22}H_{21}N_2O_2$: 345.1603; found $(M+H)^+$: 345.1636



3d



2d

To 5,11-dihydroindolo[3,2-b]carbazole (0.1 g, 0.39 mmol) in DMF (0.78 ml) was slowly added sodium hydride (0.049 g, 2.03 mmol). The reaction mixture was stirred for 30 minutes. Then, 2-(chloromethyl)-1-methyl-1H-imidazole (0.12 g, 0.897 mmol) was added and the mixture was stirred at room temperature until completion (rf mono = 0.4; 1:1 Hexane/EtOAc; rf di = 0.1; Hexane/EtOAc). Purification by column chromatography afforded **3c** (0.06 g, 0.14 mmol, 35 % yield) and **2d** (0.03 g, 0.09 mmol, 22 % yield).

See spectra on pages S21 and S22, respectively

3d

^{1}H NMR (400 MHz, DMSO-d_6)

8.43 (s, 2H), 8.15 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.20 (t, J = 7.4 Hz, 2H), 7.08 (s, 2H), 6.82 (s, 2H), 5.78 (s, 4H), 3.52 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6)

143.9, 141.9, 136.4, 126.9, 126.2, 122.9, 122.7, 120.4, 118.9, 110.0, 100.3, 79.64, 33.2.

HRMS (ESI): calculated for $C_{28}H_{25}N_6$: 445.2141; found $(M+H)^+$: 445.2086

2d

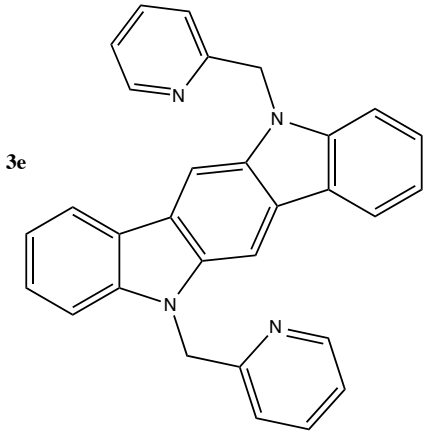
^{1}H NMR (400 MHz, DMSO-d_6)

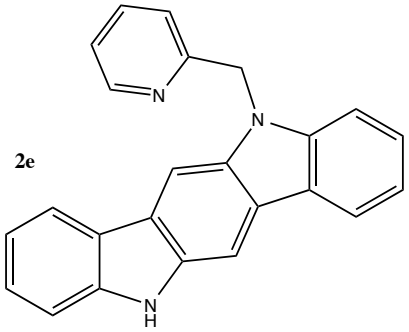
11.16 (s, 1H), 8.39 (s, 1H), 8.25 (d, J = 7.7 Hz, 1H), 8.20 (s, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 8.2 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.41 (dd, J = 13.9, 7.0 Hz, 2H), 7.17 (dd, J = 15.3, 7.7 Hz, 2H), 7.09 (s, 1H), 6.86 (s, 1H), 5.79 (s, 2H), 3.51 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6)

141.9, 141.6, 136.2, 135.7, 126.8, 126.1, 126.1, 123.0, 123.0, 122.9, 122.8, 120.7, 120.4, 118.7, 118.3, 111.1, 109.8, 100.2, 100.0, 79.6, 33.2.

HRMS (ESI): calculated for $C_{23}H_{19}N_4$: 351.1610; found $(M+H)^+$: 351.1584





To 5,11-dihydroindolo[3,2-b]carbazole (0.2 g, 0.780 mmol) stirring in DMF (1.56 ml), slowly add sodium hydride (0.097 g, 4.06 mmol). Let the reaction mixture stir for 30 minutes. Then, slowly add 2-(bromomethyl)pyridine (0.31 g, 1.79 mmol) and stir at room temperature until completion (rf mono = 0.4; 1:1 Hexane/EtOAc; rf di = 0.1; Hexane/EtOAc). Purification by column chromatography afforded **3d** (0.08 g, 0.18 mmol, 23.4 % yield) and **2e** (0.12 g, 0.35 mmol, 44.3 % yield)

See spectra on pages S23 and S24, respectively

3e

^{1}H NMR (400 MHz, DMSO-d_6)

8.53 (d, J = 4.1 Hz, 2H), 8.37 (s, 2H), 8.20 (d, J = 7.8 Hz, 2H), 7.62 (dd, J = 8.7, 6.9 Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 7.39 (t, J = 7.6 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.17 (t, J = 7.4 Hz, 2H), 6.94 (d, J = 7.9 Hz, 2H), 5.81 (s, 4H).

^{13}C NMR (100 MHz, DMSO-d_6)

157.7, 149.7, 141.7, 137.5, 136.4, 126.3, 123.0, 122.8, 122.8, 121.3, 120.7, 118.8, 109.6, 100.2, 48.4, 40.6, 40.4, 40.2, 39.9, 39.8, 39.5, 39.3, 18.3, 11.9.

HRMS (ESI): calculated for $C_{30}H_{23}N_4$: 439.1923; found $(M+H)^+$: 439.1970

2e

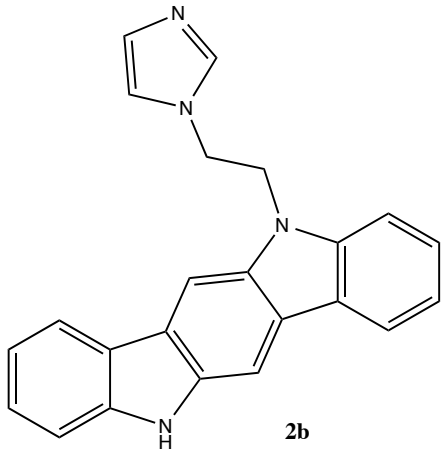
^{1}H NMR (400 MHz, acetone-d_6)

10.22 (s, 1H), 8.61 (d, J = 4.5 Hz, 1H), 8.29 (s, 1H), 8.26 – 8.20 (m, 2H), 8.19 – 8.15 (m, 1H), 7.59 (t, J = 7.7 Hz, 1H), 7.52 (dd, J = 14.8, 8.1 Hz, 2H), 7.43 (ddd, J = 8.2, 7.2, 1.2 Hz, 1H), 7.37 (ddd, J = 9.3, 5.3, 1.7 Hz, 1H), 7.27 – 7.17 (m, 2H), 7.14 (ddd, J = 8.0, 7.2, 1.0 Hz, 1H), 6.89 (d, J = 7.9 Hz, 1H), 5.82 (s, 2H).

^{13}C NMR (100 MHz, acetone-d_6)

157.8, 149.3, 141.8, 141.5, 136.8, 136.3, 135.8, 125.7, 125.6, 123.4, 123.2, 123.1, 122.9, 122.3, 120.6, 120.1, 120.0, 118.4, 118.0, 110.5, 108.7, 100.8, 99.0, 48.3.

HRMS (ESI): calculated for $C_{24}H_{18}N_3$: 348.1501; found $(M+H)^+$: 348.1465



2b

A mixture of 5,11-dihydroindolo[3,2-b]carbazole (0.2 g, 0.78 mmol) and sodium hydride (0.1 g, 2.34 mmol) in DMF (2.6 ml) was added dropwise over 60 minutes to a solution of DMF (0.5 ml) and 1-(2-chloroethyl)-1H-imidazole (0.26 g, 1.95 mmol). Upon consumption of the starting material (TLC monitoring: 1:1 Hexane/EtOAc, rf = 0.2), the reaction mixture was quenched with aqueous sodium bicarbonate and extracted with DCM. Purification by column chromatography (1:1 Hexane/EtOAc) to obtain **2b** (50 mg, 0.143 mmol, 18.3% yield)

See spectra on page S25

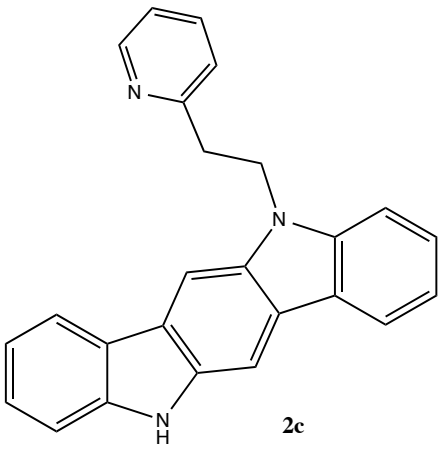
^{1}H NMR (400 MHz, Acetone-d_6)

10.29 (s, 1H), 8.25 – 8.14 (m, 4H), 7.51 (t, J = 7.3 Hz, 2H), 7.37 (dt, J = 17.4, 7.4 Hz, 4H), 7.17 (dd, J = 15.0, 7.7 Hz, 3H), 4.89 (t, J = 6.0 Hz, 2H), 4.67 (t, J = 5.9 Hz, 2H).

^{13}C NMR (100 MHz, Acetone-d_6)

141.7, 141.5, 135.9, 135.8, 125.6, 125.6, 123.4, 123.3, 122.9, 122.9, 120.1, 119.9, 118.3, 118.1, 110.5, 108.2, 100.7, 98.7, 45.3, 44.3.

HRMS (ESI): calculated for $C_{23}H_{19}N_4$: 351.1610; found $(M+H)^+$: 351.1587



2c

A mixture of 5,11-dihydroindolo[3,2-b]carbazole (0.2 g, 0.78 mmol) and sodium hydride (0.1 g, 2.34 mmol) in DMF (2.6 ml) was added dropwise over 60 minutes to a solution of DMF (0.5 ml) and 2-(2-chloroethyl)pyridine (0.276 g, 1.95 mmol). Upon consumption of the starting material (TLC monitoring: 2:1 Hexane/EtOAc, rf = 0.4), the reaction mixture was quenched with aqueous sodium bicarbonate and extracted with DCM. Purification by column chromatography (4:1 Hexane/ EtOAc) to obtain 5-(2-(pyridin-2-yl)ethyl)-5,11-dihydroindolo[3,2-b]carbazole (20mg, 0.055 mmol, 7.09 % yield).

See spectra on page S26

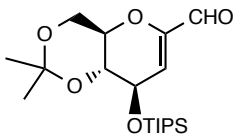
^{1}H NMR (400 MHz, Acetone-d_6)

10.21 (s, 1H), 8.66 (d, J = 3.4 Hz, 1H), 8.27 – 8.11 (m, 4H), 7.59 – 7.46 (m, 3H), 7.41 (dd, J = 8.0, 7.1 Hz, 2H), 7.17 (ddd, J = 11.4, 7.4, 3.1 Hz, 4H), 4.92 (t, J = 7.2 Hz, 2H), 3.38 (dd, J = 18.9, 11.7 Hz, 2H).

^{13}C NMR (100 MHz, Acetone-d_6)

159.1,149.3, 141.5, 141.5, 136.4, 135.9, 135.5, 125.5, 125.5, 123.7, 123.4, 123.3, 122.9, 122.8, 121.6, 120.1, 120.0, 118.1, 117.9, 110.5, 108.5, 100.7, 98.9, 42.8, 36.7.

HRMS (ESI): calculated for $C_{25}H_{20}N_3$: 362.1657; found 362.1595 $(M+H)^+$



6

To 3-O-TIPS-4,6-*O*-acetonide glucal[10] (0.5 g, 1.46 mmol) in THF (2.3 mL) was added potassium *tert*-butoxide (261 mg, 2.33 mmol, 1.6 equiv) and the solution was cooled to -78 °C. Then *n*-butyllithium (1.46 mL, 2M in hexanes, 2.92 mmol) was added dropwise and the solution was stirred at -78°C for one hour. Then DMF (0.5 mL) was added and the solution was stirred for 10 minutes. The mixture was quenched with sodium bicarbonate and diluted with EtOAc. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (5:1 hexane/EtOAc) afforded **6** (0.5 g, 1.35 mmol, 92%).

See spectra on page S27

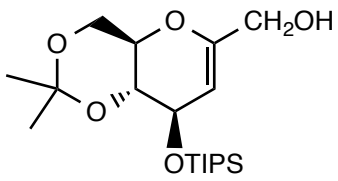
^{1}H NMR: (400 MHz, $CDCl_3$)

9.14 (s, 1H); 5.63 (d, *J*=2.0 Hz, 1H); 4.58 (dd, *J*=7.2, 2.4 Hz, 1H); 4.00 (dd, *J*=11.2, 5.2 Hz, 1H); 3.88-3.74 (m, 3H); 1.45 s, 3H); 1.35 (s, 2H); 1.10-1.00 (m, 42 H).

^{13}C NMR: (100 MHz, $CDCl_3$)

185.8; 150.8; 123.7; 99.7; 72.3; 72.2; 70.3; 70.2; 68.2; 68.1; 61.4; 28.7; 18.7; 17.9; 17.8; 12.1.

HRMS (ESI): calculated for $C_{19}H_{34}NaO_5Si$: 393.2073; found 393.2061 $(M+Na)^+$



7

To **6** (0.5 g, 1.35 mmol) in THF (1 mL) was added L-selectride (1.5 mL, 1.5 mmol) at -78 °C. After an hour of stirring at -78 °C, water was added dropwise. Then, 10% NaOH (0.3 mL) and 30 % H_2O_2 (0.3 mL) were added cautiously at 0°C. Then the reaction mixture was allowed to stir for 30 minutes. The mixture was quenched with sodium bicarbonate and diluted with EtOAc. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (4:1 Hexane/EtOAc) gave **7** (0.44 g, 1.18 mmol, 88%).

See spectra on page S28

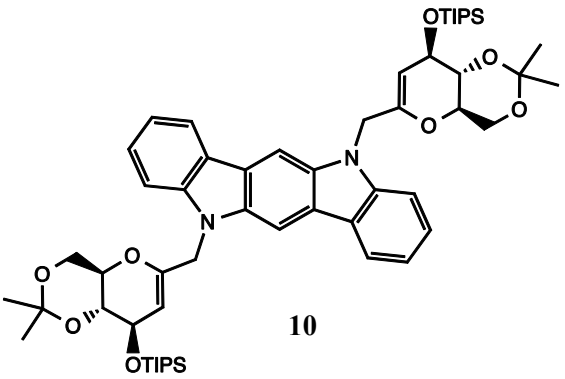
^{1}H NMR (400 MHz, $CDCl_3$)

5.32 (s, 1H), 4.79 (d, *J* = 1.9 Hz, 1H), 4.45 (d, *J* = 7.0 Hz, 1H), 4.07 – 3.94 (m, 3H), 3.91 – 3.68 (m, 3H), 1.52 (s, 3H), 1.42 (s, 3H), 1.21 – 0.87 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$)

152.8, 102.3, 99.6, 73.3, 69.8, 67.9, 61.8, 28.9, 18.9, 18.0, 17.9, 12.3.

HRMS (ESI): calculated for $C_{19}H_{36}O_5Si$: 495.2938; found $(M+Na)^+$ 495.2880



10

To **7** (0.44 g, 1.18 mmol) dissolved in THF (1 mL) is added MsCl (0.1 mL, 1.30 mmol). Then, Et_3N (0.30 ml, 2.15 mmol) is added dropwise at 0 ºC. The mixture was allowed to stir for 1 hour. The mixture was then quenched with saturated sodium bicarbonate and diluted with diethyl ether. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the product **8** as an oil. The product was used without further purification (0.52 g, 1.15 mmol, 98%).

A mixture of **1** (0.20 g, 0.78 mmol) and NaH (0.1 g, 2.34 mmol) was stirred under argon for an hour at room temperature in DMF (1.95 ml). Then **8** (0.78 g, 1.73 mmol) dissolved in DMF (1.95 ml) was added dropwise at 0 °C. The mixture was allowed to stir until the completion of the reaction monitored by TLC (10:1 Hexane/EtOAc; rf = 0.5). The mixture was quenched with sodium bicarbonate and diluted with CH_2Cl_2. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (100:1 Hexanes/EtOAc) afforded **10** (0.6 g, 0.62 mmol, 80 % yield).

See spectra on page S29

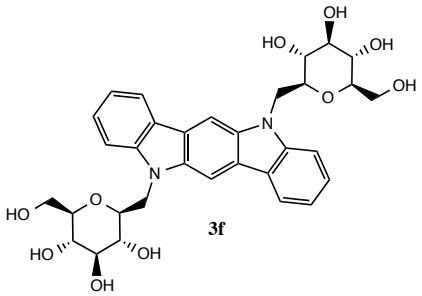
^{1}H NMR (400 MHz, Acetone-d_6)

8.18 (d, J = 8.2 Hz, 4H), 7.50 (d, J = 8.2 Hz, 2H), 7.47 – 7.41 (m, 2H), 7.25 – 7.16 (m, 2H), 5.05 – 4.90 (m, 4H), 4.72 (d, J = 1.7 Hz, 2H), 4.39 (d, J = 5.9 Hz, 2H), 3.90 – 3.77 (m, 6H), 3.77 – 3.66 (m, 2H), 1.47 (s, 6H), 1.34 (s, 6H), 0.97 (d, J = 3.6 Hz, 42H).

^{13}C NMR (100 MHz, Acetone-d_6)

149.9, 141.9, 136.4, 125.6, 123.2, 122.9, 119.9, 118.3, 109.0, 102.8, 99.2, 73.4, 70.2, 68.2, 61.4, 44.4, 18.6, 17.5, 17.5, 12.1.

HRMS (ESI): calculated for $C_{56}H_{81}N_2O_8Si_2$: 965.5531; found $(M+H)^+$: 965.5542



3f

To **10** (80 mg, 0.08 mmol) dissolved in THF (0.1 mL), borane-dimethylsulfide complex (0.08 mL, 0.17 mmol) was added dropwise at 0 ºC. The reaction mixture was stirred overnight at 0 º Then 3M NaOH (0.1 mL) and 30 % H_2O_2 (0.1 mL) were added cautiously at 0°C. The reaction mixture was allowed to stir for 30 minutes. The mixture was quenched with saturated sodium bicarbonate and diluted with EtOAc. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (8:1 Hexane/EtOAc; rf: 0.25) gave the corresponding secondary alcohol (54 mg, 0.05 mmol, 67%).

To the alcohol (54 mg, 0.05 mmol) in THF (0.1 mL) is added tetrabutylammonium fluoride solution (0.1 mL, 0.13 mmol). The reaction mixture was allowed to stir overnight at room temperature. Upon completion of the reaction, the mixture was concentrated *in vacuo*. Purification by column chromatography (1:1 Hexane/ EtOAc) afforded an intermediate diol (32.6 mg, 0.05 mmol, 96%).

The intermediate diol (32.6 mg, 0.05 mmol) was dissolved in CH_3CN/H_2O (50:1 ratio; 0.5 mL). Then bismuth (III) chloride (10 mol %) was added, and the reaction was allowed to stir overnight at room temperature. Purification by reverse phase column chromatography (water; TLC: rf = 0.2, 10:1 EtOAc/MeOH) gave **3f** (27.9 mg, 0.05 mmol, 92%)

See spectra on page S30

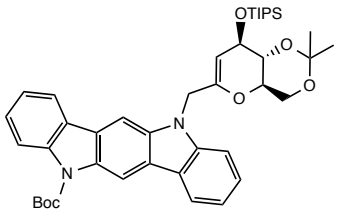
^{1}H NMR (400 MHz, DMSO-d_6)

8.37 (s, 2H), 8.19 (d, J = 7.7 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.17 (t, J = 7.4 Hz, 2H), 4.75 (d, J = 14.7 Hz, 2H), 4.50 (d, J = 6.4 Hz, 1H), 4.46 (d, J = 6.4 Hz, 1H), 3.56 (t, J = 9.0 Hz, 4H), 3.37 (dd, J = 11.4, 5.1 Hz, 8H), 3.24 (t, J = 8.5 Hz, 3H), 3.16 (t, J = 9.1 Hz, 3H), 3.11 – 2.95 (m, 4H).

^{13}C NMR (100 MHz, DMSO-d_6)

142.6, 137.1, 125.9, 122.9, 122.6, 120.4, 118.4, 110.1, 100.45, 80.7, 80.4, 78.6, 72.1, 70.6, 62.1, 46.0.

HRMS (ESI): calculated for $C_{32}H_{36}N_2O_{10}$: 631.2268; found $(M+Na)^+$: 631.2259



11

A mixture of indolo-[3,2-b] carbazole (0.5 g, 1.95 mmol) and NaH (195 mg, 4.88 mmol) was stirred under argon for an hour at room temperature in DMF (2 mL). Then, Boc_2O (936 mg, 4.29 mmol) dissolved in DMF (1 mL) was added. The mixture was allowed to stir until the completion of the reaction as monitored by TLC (10:1 Hexane:/EtOAc; rf = 0.54). The mixture was quenched with sodium bicarbonate and diluted with CH_2Cl_2. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (100:1 Hex/EtOAc) to provide the Boc-protected indolo-[3,2-b] carbazole (869 mg, 1.90 mmol, 97%).

The di-Boc protected product (869 mg, 1.90 mmol) was dissolved in THF (2 mL). *n*-BuLi (4.75 mL, 9.5 mmol) was added portionwise over a period of 2-3 hours. The reaction was monitored by TLC (rf: 0.4, 10:1 hexane/EtOAc). The mixture was quenched with saturated sodium bicarbonate and diluted with CH_2Cl_2. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (95:5 Hex/EtOAc) gave **9** (550 mg, 1.54 mmol, 81%).

To **9** (0.55 g, 1.54 mmol) dissolved in DMF (0.6 mL) was added t-BuOK (241 mg, 2.16 mmol) under ice. The reaction mixture was allowed to stir for 1 hour. Then, **8** (833 mg, 1.85 mmol) dissolved in DMF (1 mL) was added dropwise at 0 °C. The mixture was allowed to stir until the completion of the reaction monitored by TLC (10:1 Hexane: EtOAc; rf = 0.5). The mixture was quenched with sodium bicarbonate and diluted with CH_2Cl_2. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (100:1 Hex/EtOAc) gave **11** (400 mg, 0.56 mmol, 37%).

See spectra on page S31

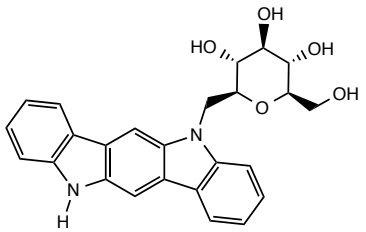
^{1}H NMR (400 MHz, Acetone-d_6)

9.00 (s, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 7.1 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 2H), 7.54 – 7.43 (m, 3H), 7.35 (td, *J* = 7.5, 1.6 Hz, 1H), 7.24 (dd, *J* = 10.6, 3.9 Hz, 1H), 4.94 (q, *J* = 16.8 Hz, 2H), 4.65 (s, 1H), 4.33 (d, *J* = 6.6 Hz, 1H), 3.84 – 3.72 (m, 3H), 3.66 (dd, *J* = 16.5, 6.9 Hz, 1H), 1.88 (t, *J* = 9.7 Hz, 9H), 1.43 (s, 3H), 1.30 (s, 3H), 0.92 (s, 21H).

^{13}C NMR (100 MHz, Acetone-d_6)

151.0, 149.6, 141.9, 139.2, 137.9, 132.9, 126.9, 126.2, 125.9, 125.1, 123.3, 123.3, 122.7, 119.9, 119.5, 119.0, 116.3, 109.3, 107.1, 102.8, 99.2, 99.2, 83.4, 73.4, 70.2, 68.2, 61.3, 44.3, 27.8, 18.5, 17.4, 17.3, 12.0.

HRMS (ESI): calculated for $C_{42}H_{54}N_2O_6Si$: 733.3649; found $(M+H)^+$: 733.3734



2f

To **11** (400 mg, 0.56 mmol) dissolved in THF (0.5 mL), borane-dimethylsulfide complex (0.6 mL, 0.6 mmol) was added dropwise at 0 ºC. The reaction mixture was stirred overnight at 0ºC. Then 3M NaOH (0.6 mL) and 30 % H_2O_2 (0.6 mL) were added cautiously at 0°C. Then the reaction mixture was allowed to stir for 30 minutes. The mixture was quenched with sodium bicarbonate and diluted with EtOAc. The organic layer was washed brine and dried over anhydrous Na_2SO_4. The solvent was concentrated *in vacuo* to give the crude product as an oil. Purification by column chromatography (1:1 Hexane/EtOAc; rf: 0.25) gave the secondary alcohol (288 mg, 0.4 mmol, 71%).

To the hydroboration product (288 mg, 0.4 mmol) in THF (0.2 mL) was added tetrabutylammonium fluoride solution (0.6 mL, 0.6 mmol). The reaction mixture was allowed to stir overnight at room temperature. Upon completion of the reaction, mixture was concentrated *in vacuo*. Purification by column chromatography (1:1 Hexane/EtOAc) afforded the intermediate diol (220 mg, 0.38 mmol, 96%).

The diol (220 mg, 0.38 mmol) was dissolved in CH_3CN/H_2O (50:1 ratio; 0.5 mL). Then, Bismuth (III) chloride (5 mol%) was added, and the reaction was allowed to stir overnight at room temperature. Purification by reverse phase column chromatography (Water; TLC: rf = 0.2 4:1 EtOAc/MeOH) provided the corresponding tetraol (190 mg, 0.36 mmol, 94%).

The Boc-protected tetraol (190 mg, 0.36 mmol) was refluxed in water (0.5 mL) overnight. The reaction mixture was purified by reverse phase column chromatography (5:1, H_2O/CH_3CN; rf: 0.2, 3:1, EtOAc/MeOH) to afford **2f** (146 mg, 0.34 mmol, 94%).

See spectra on page S32

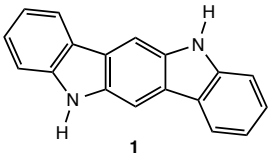
^{1}H NMR: (400 MHz, $CDCl_3$)

8.31 (s, 1H); 8.20 (d, *J* = 8.0 Hz, 1H); 8.10 (d, *J* = 8.0 Hz, 1H); 8.03 (s, 1H); 7.67 (d, *J* = 8.0 Hz, 1H); 7.42 (m, 2H); 7.30 (m, 2H); 7.15 (m, 1H); 3.67 (m, 6H); 3.33 (m, 7H).

^{13}C NMR: (100 MHz, $CDCl_3$)

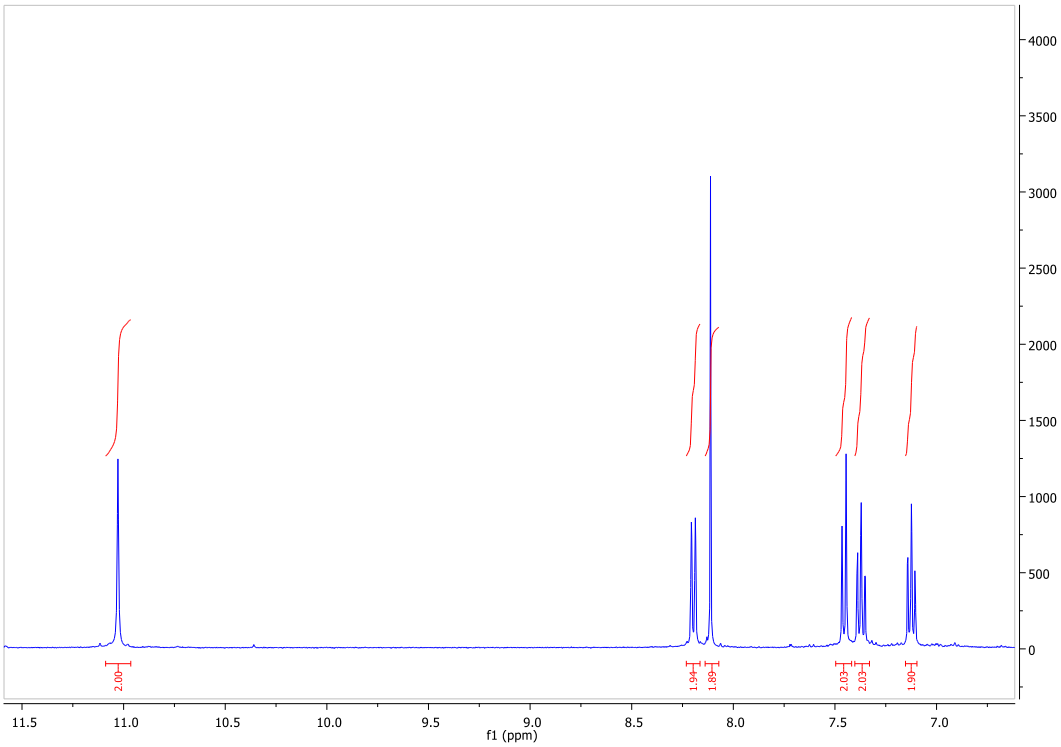
142.5; 141.5; 136.7; 135.5; 134.5; 128.0; 127.6; 127.1; 125.1; 123.2; 122.8; 119.7; 119.2; 117.7; 117.6; 109.9; 109.2; 99.7; 99.2; 79.7; 78.4; 71.9; 70.1; 61.6; 52.6.

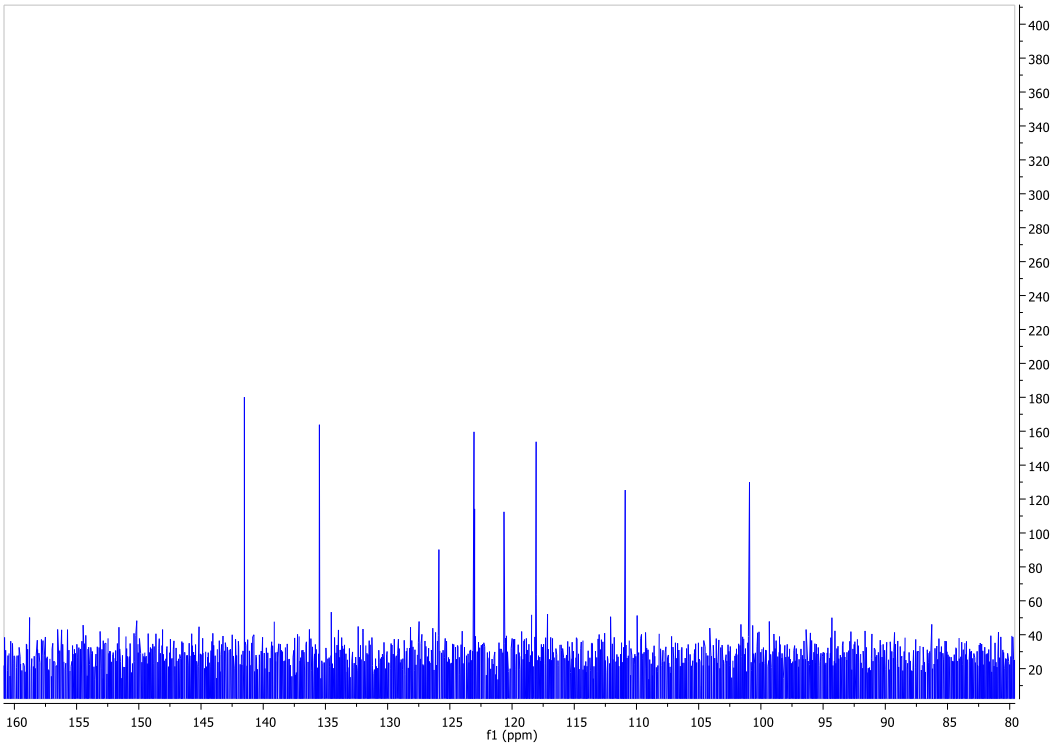
HRMS (ESI): calculated for $C_{25}H_{24}N_2O_5$: 455.1583; found $(M+Na)^+$: 455.1517

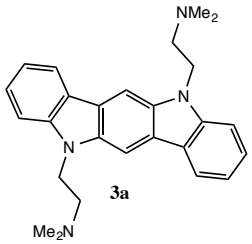


1

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

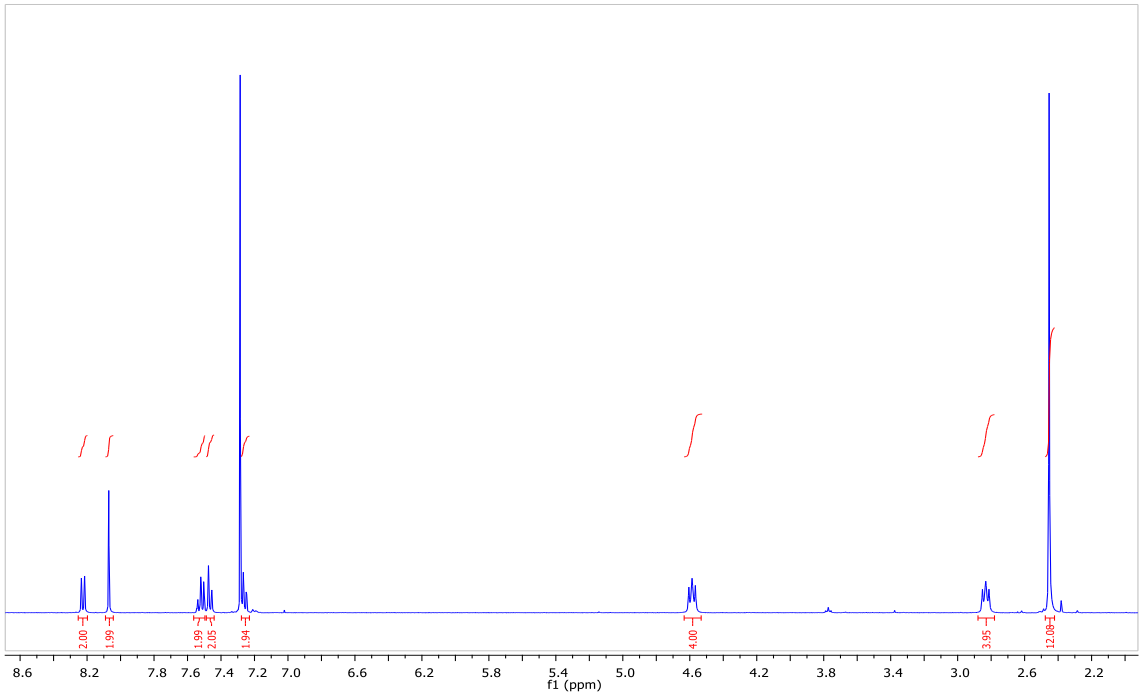


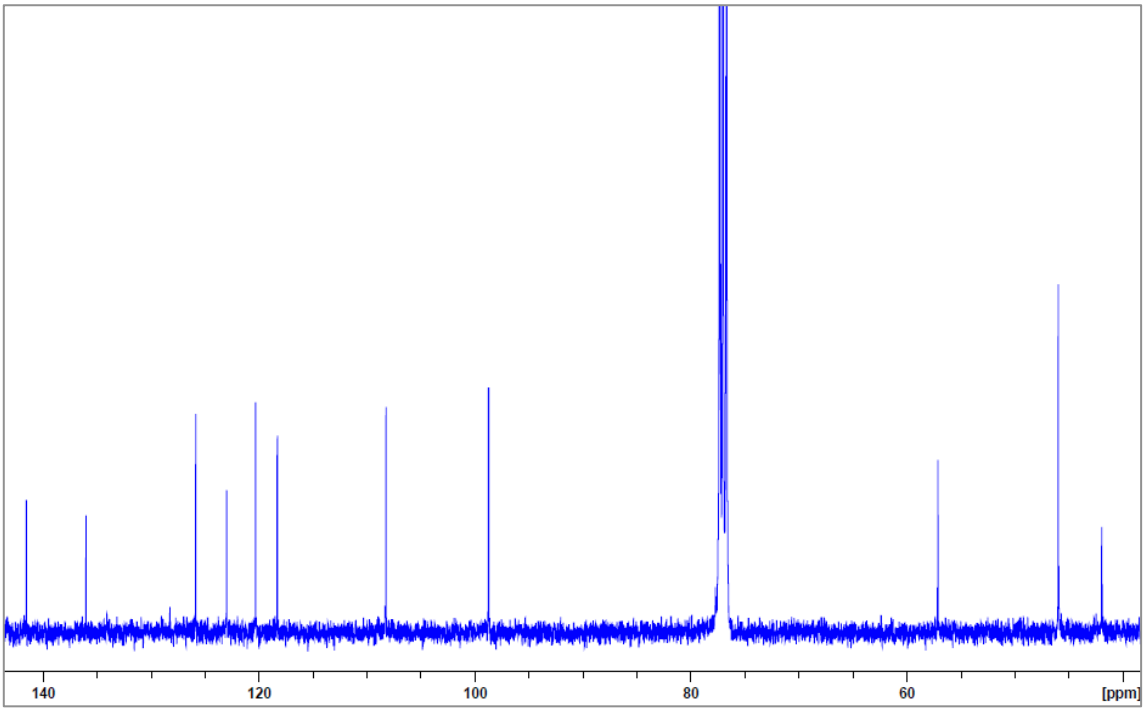


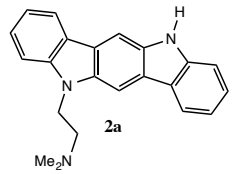


3a

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

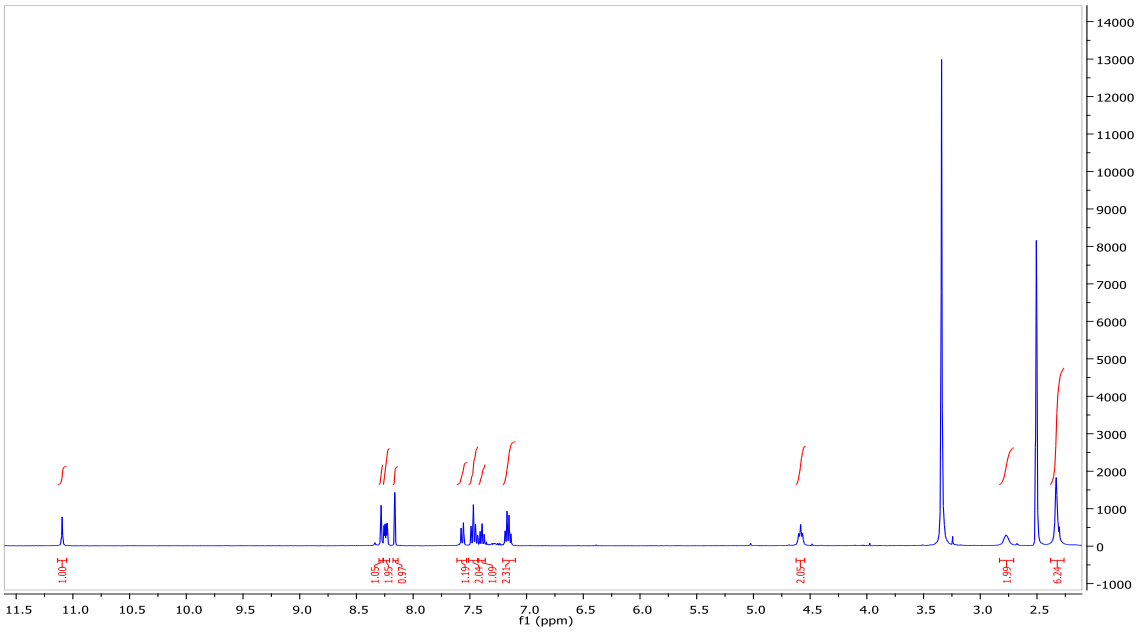


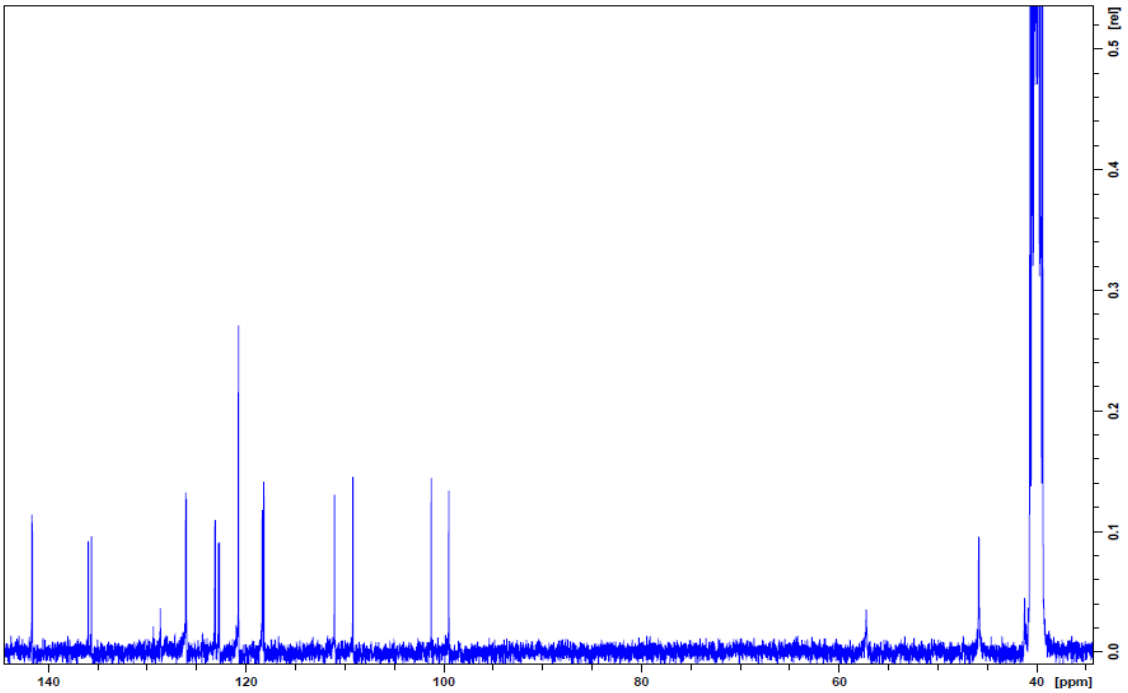


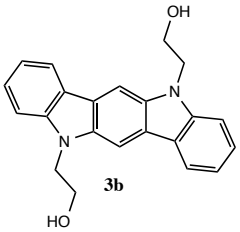


2a

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

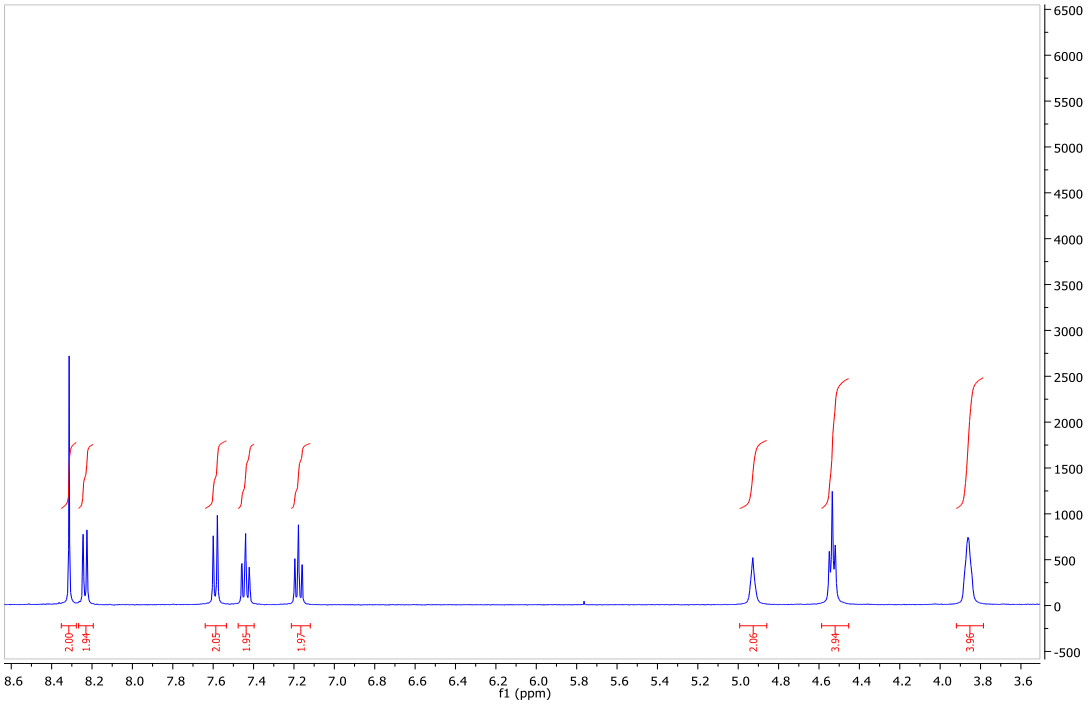


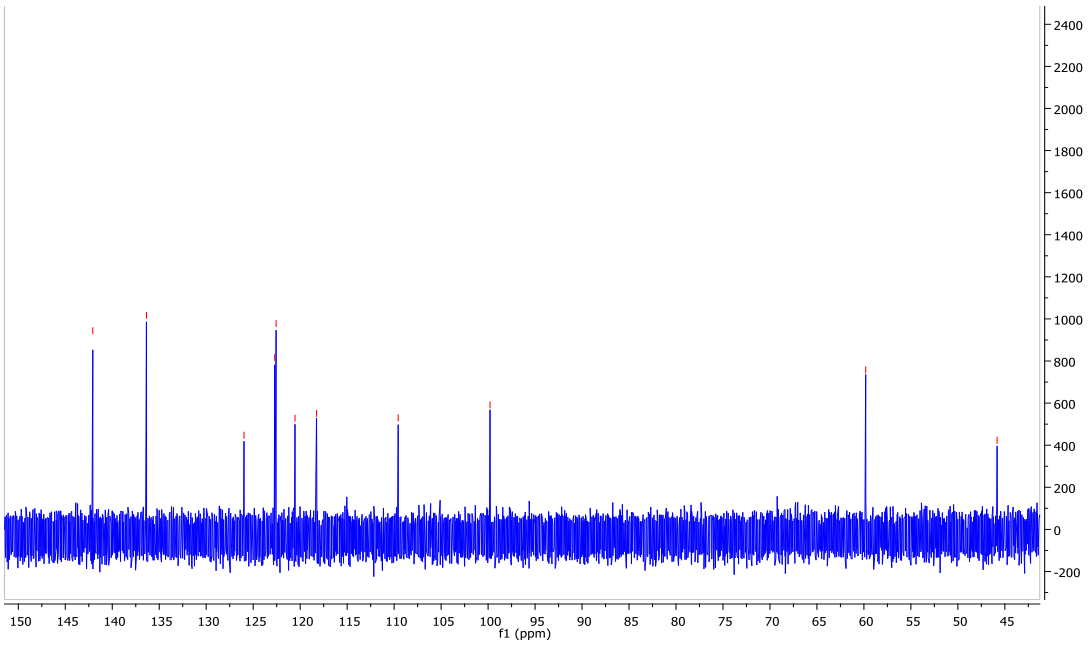


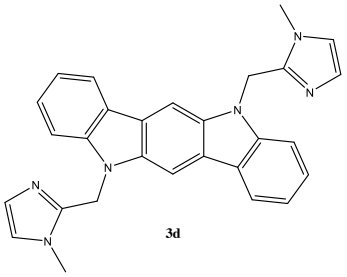


3b

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

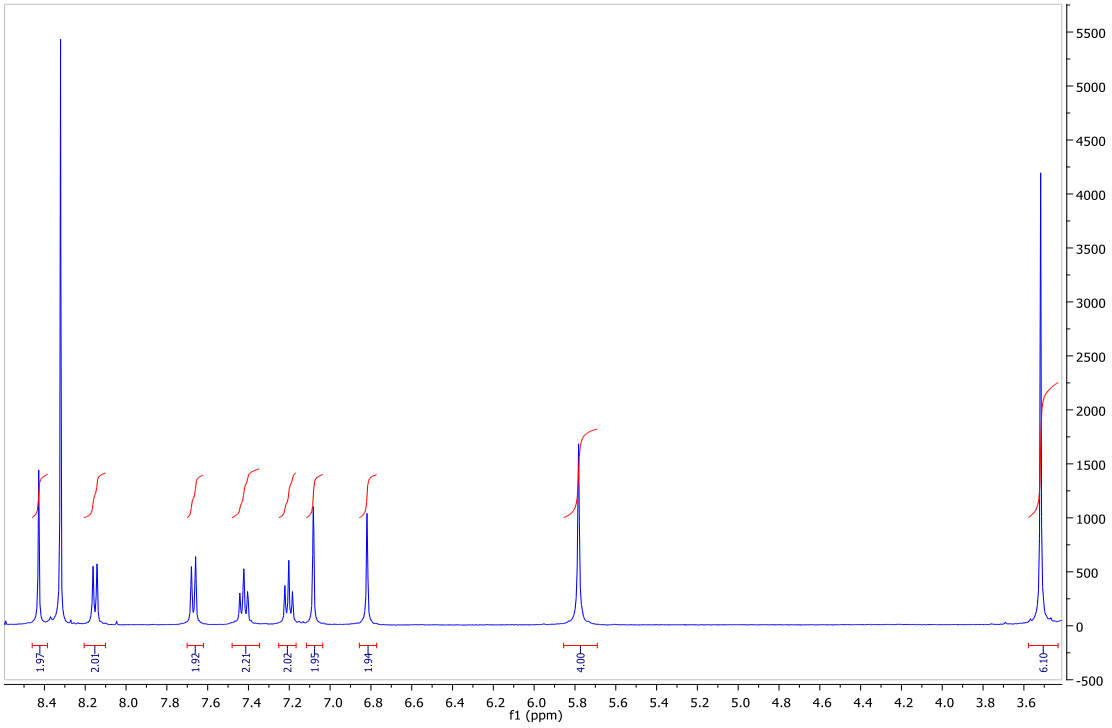


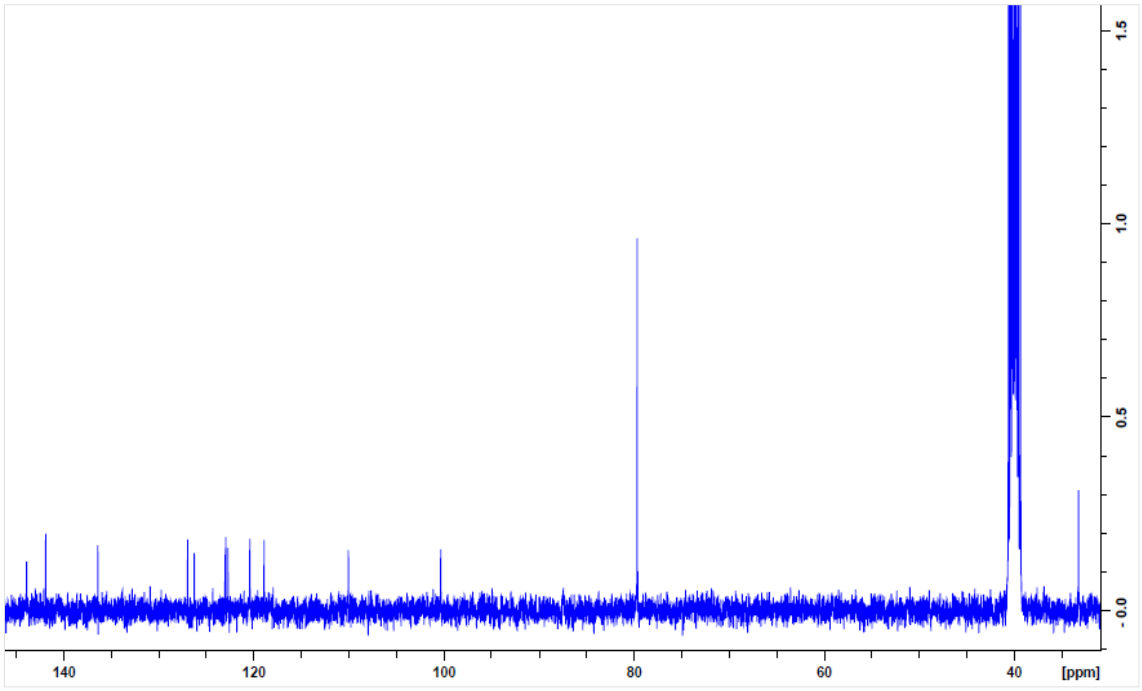


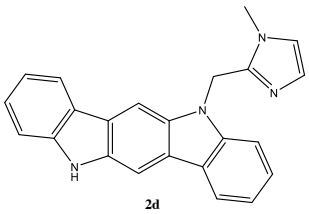


3d

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

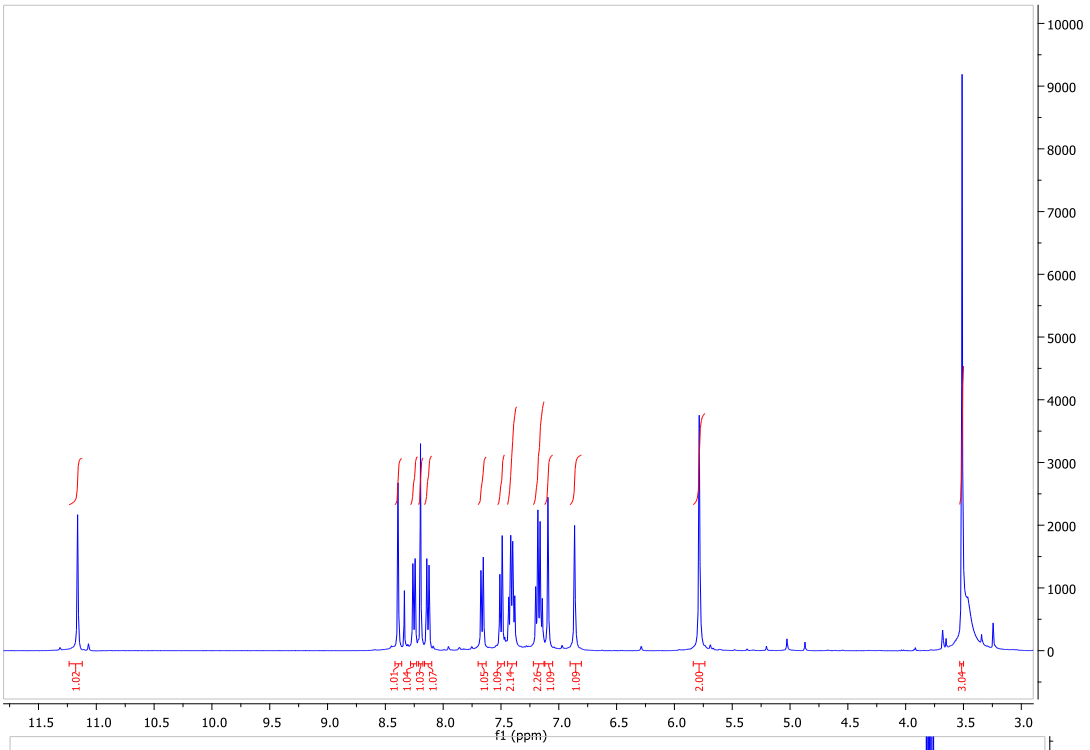


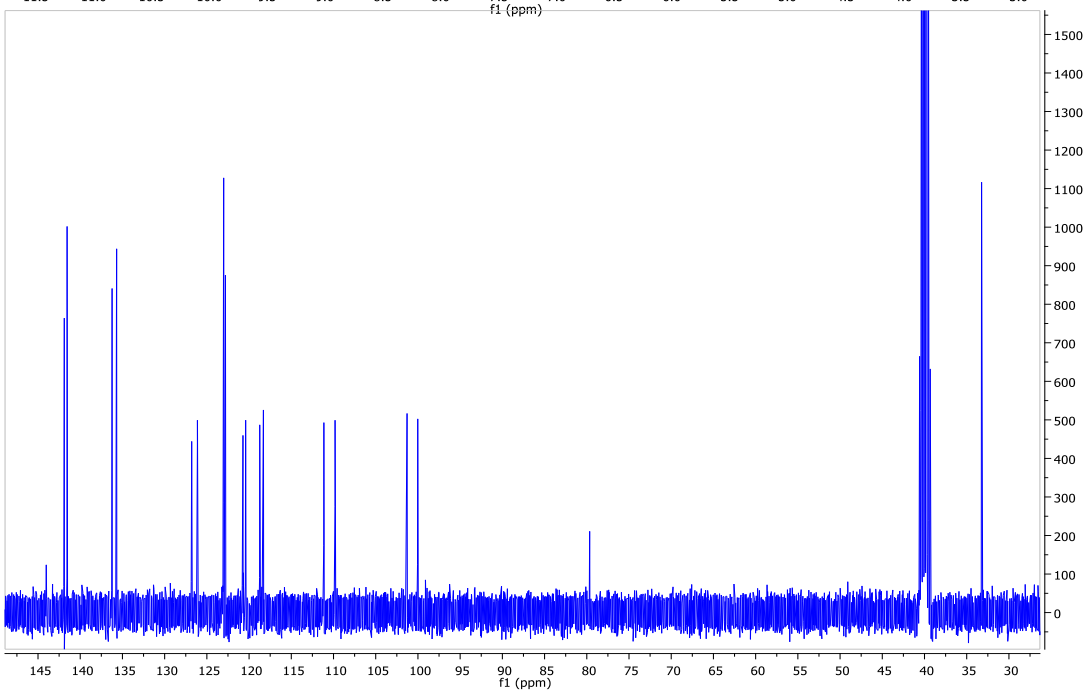


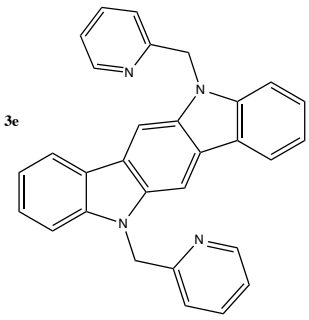


2d

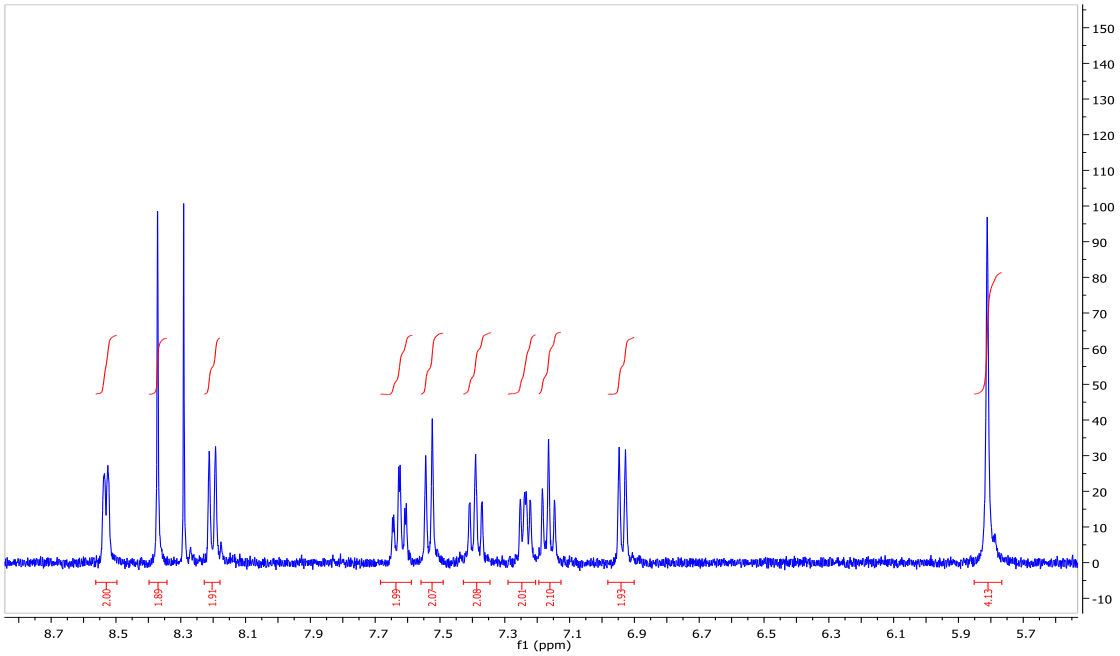
^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

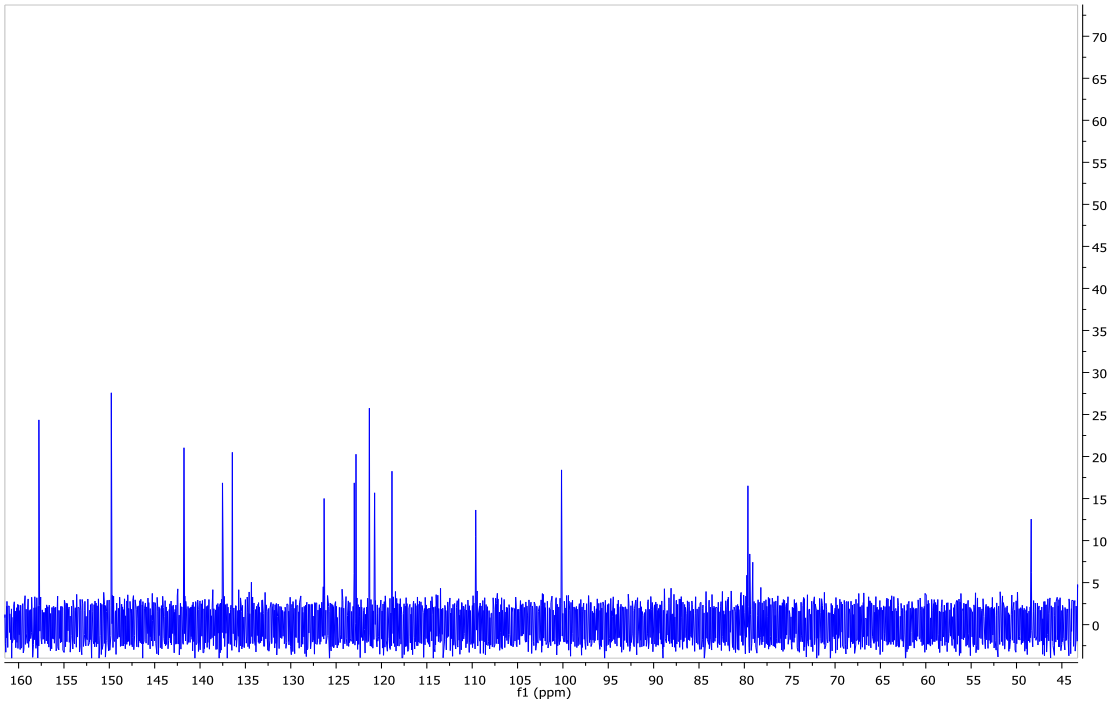


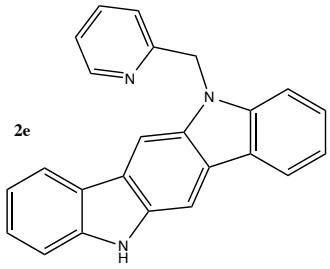




1H(400 MHz) and 13C NMR (100 MHz) spectra

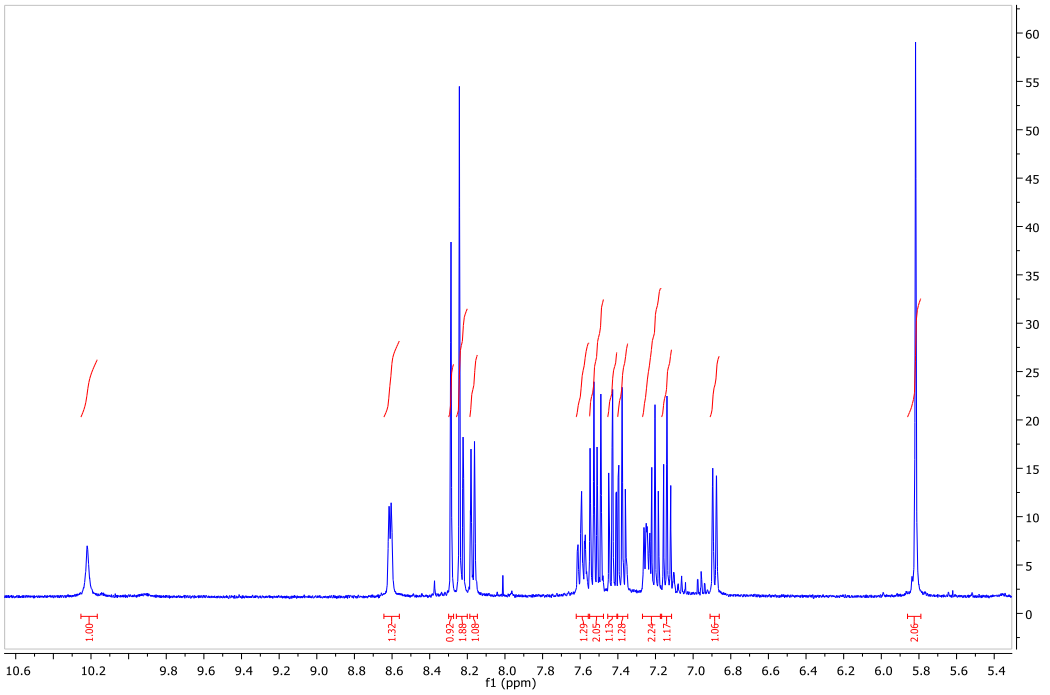


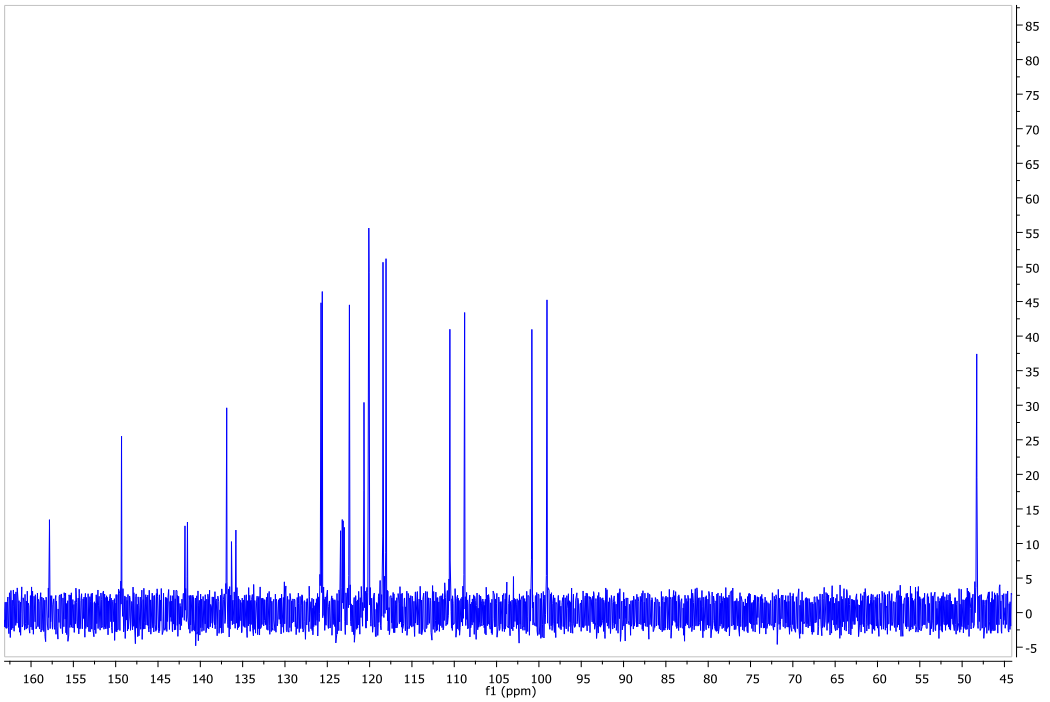


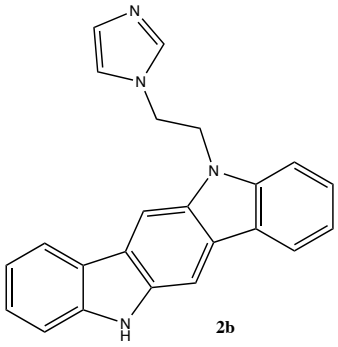


2e

1H(400 MHz) and 13C NMR (100 MHz) spectra

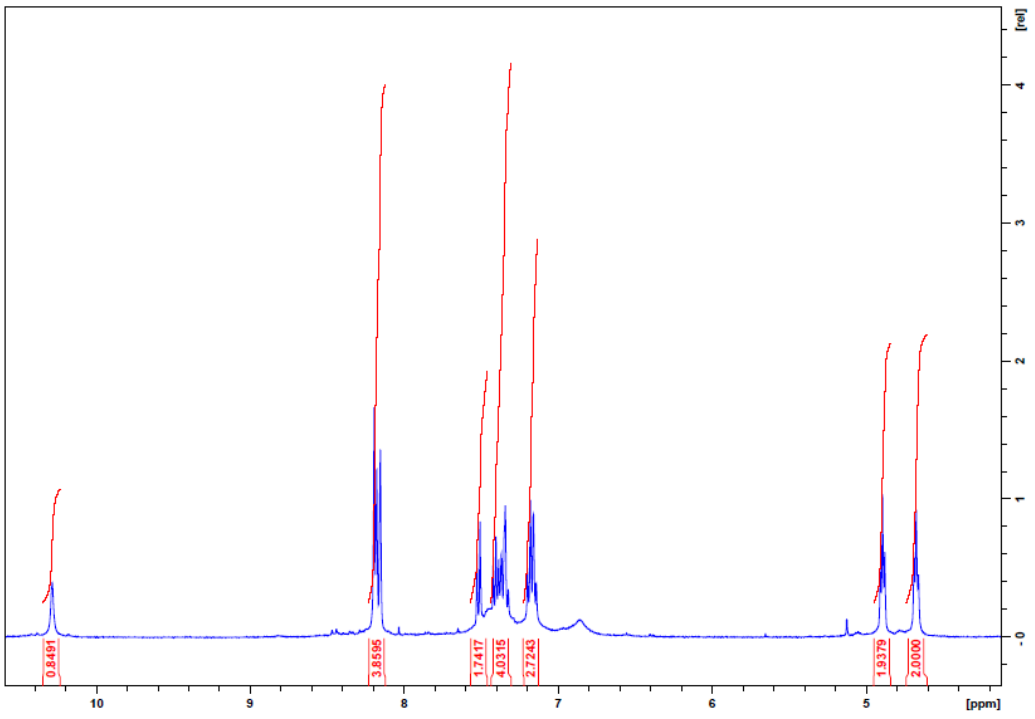


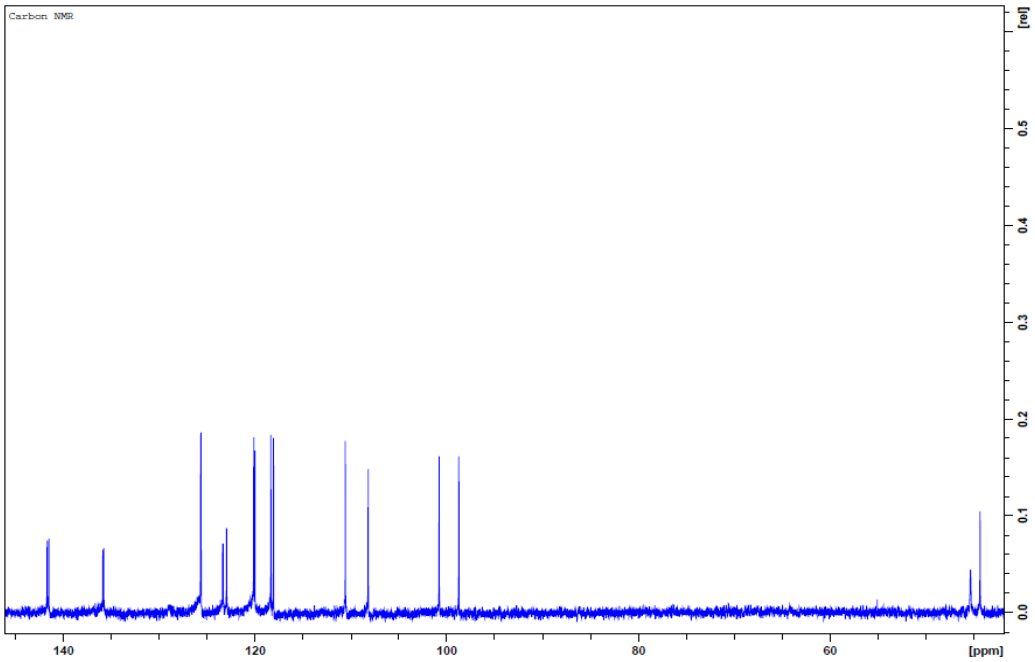


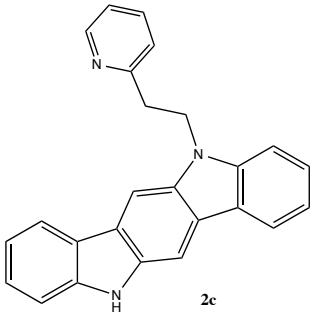


2b

1H(400 MHz) and 13C NMR (100 MHz) spectra

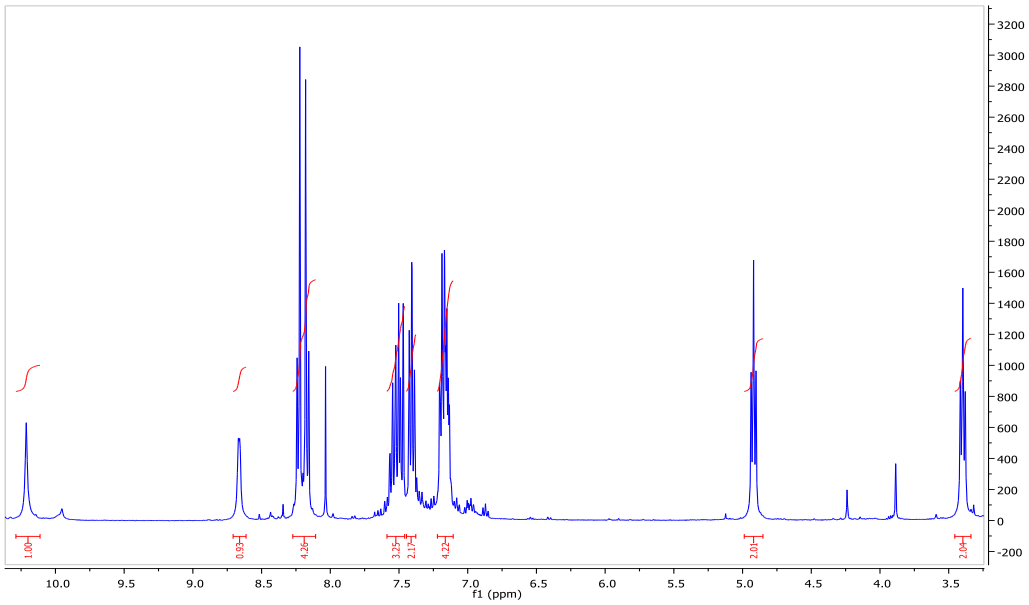


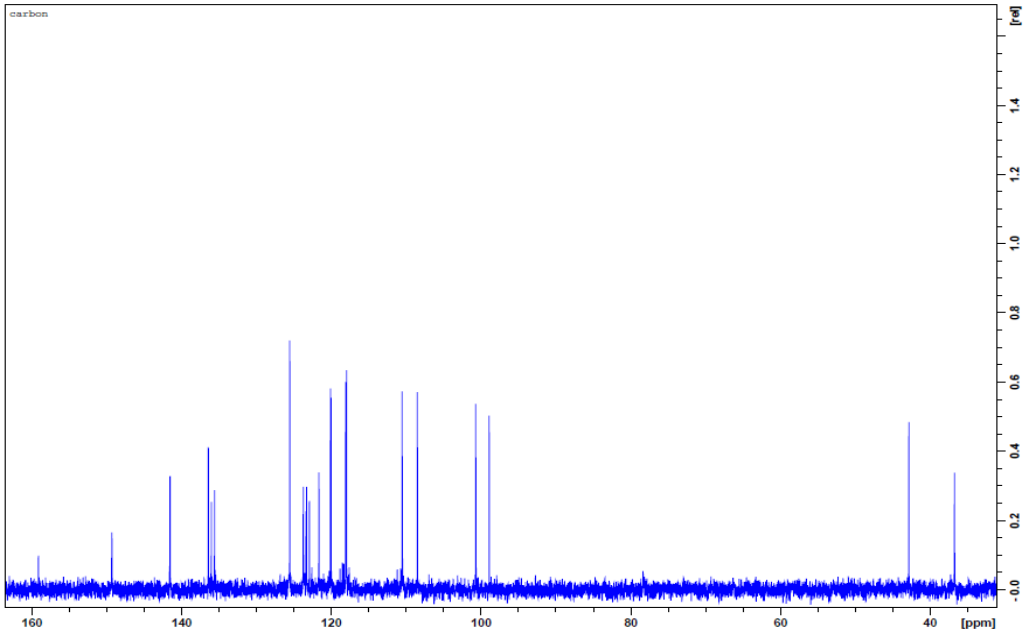


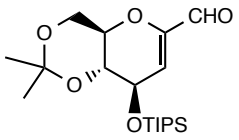


2c

1H(400 MHz) and 13C NMR (100 MHz) spectra

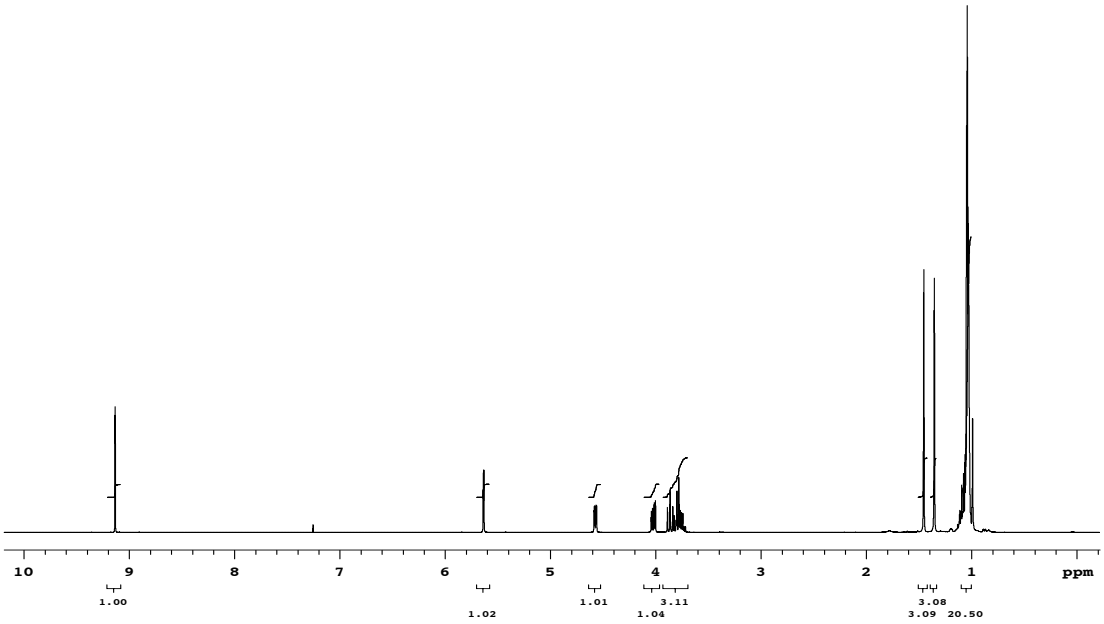


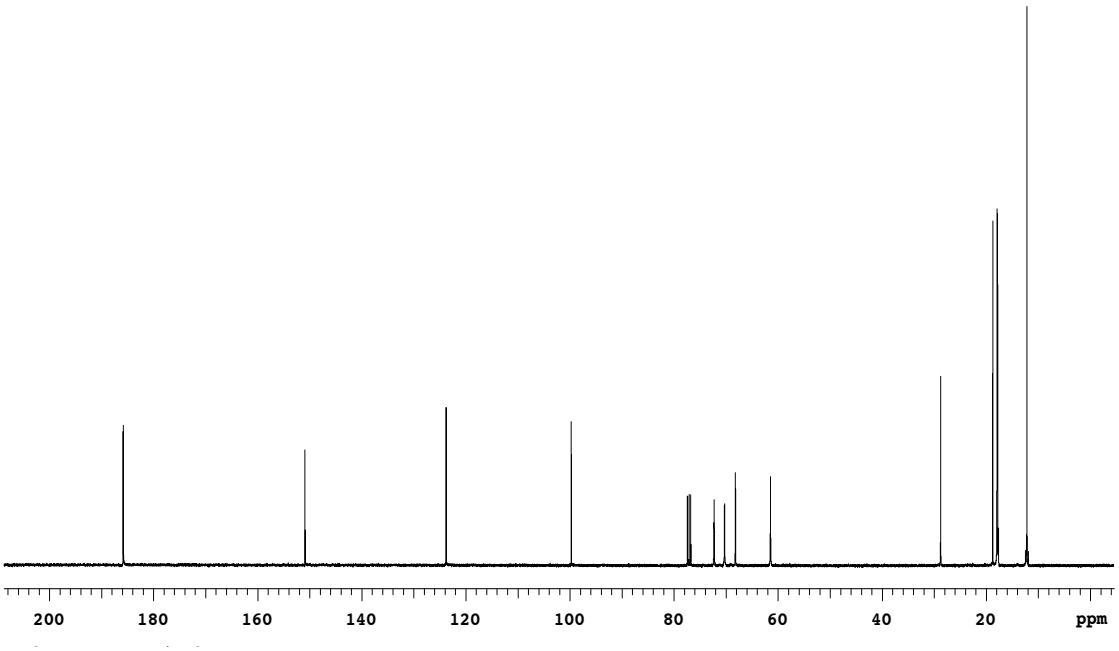


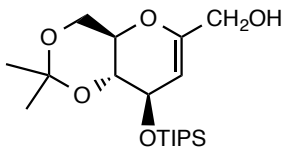


6

1H(400 MHz) and 13C NMR (100 MHz) spectra

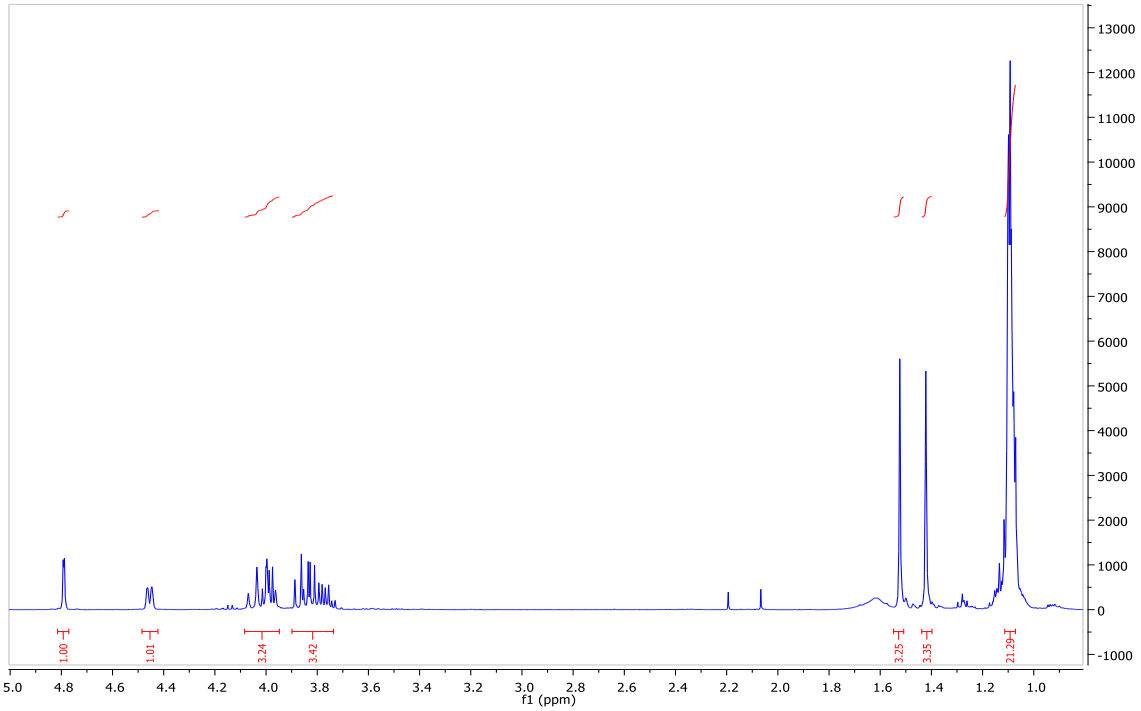


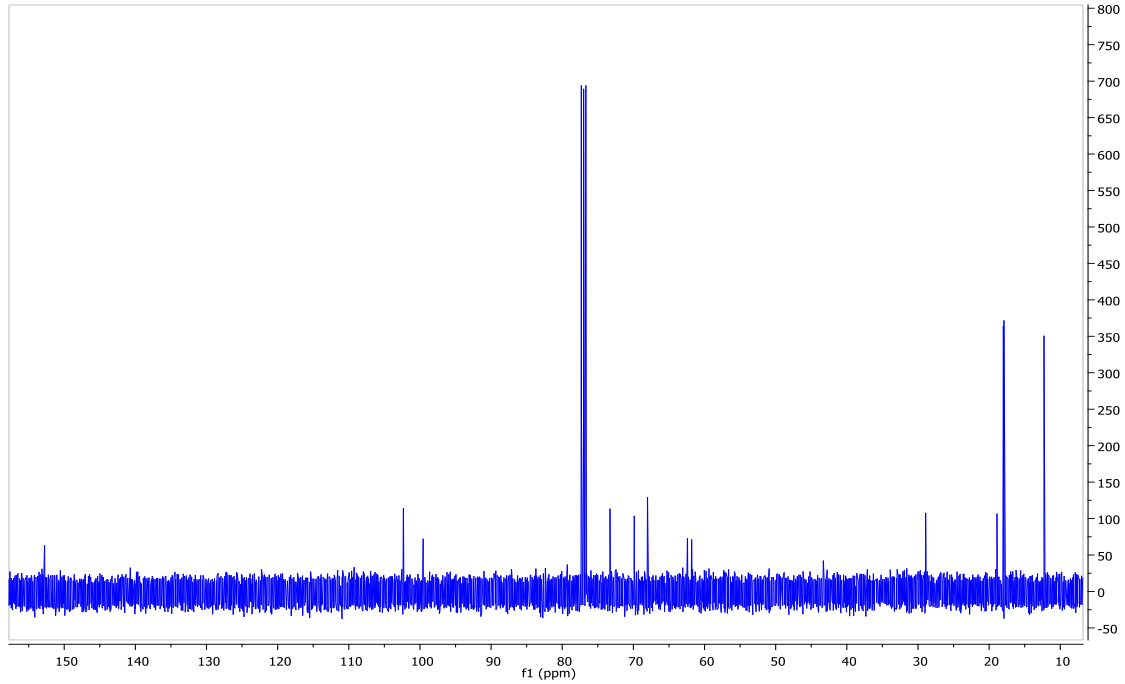


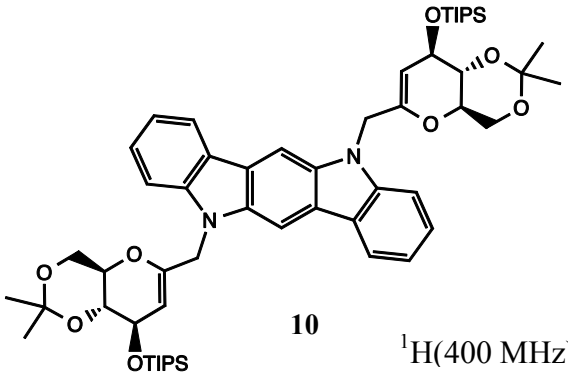


7

1H(400 MHz) and 13C NMR (100 MHz) spectra

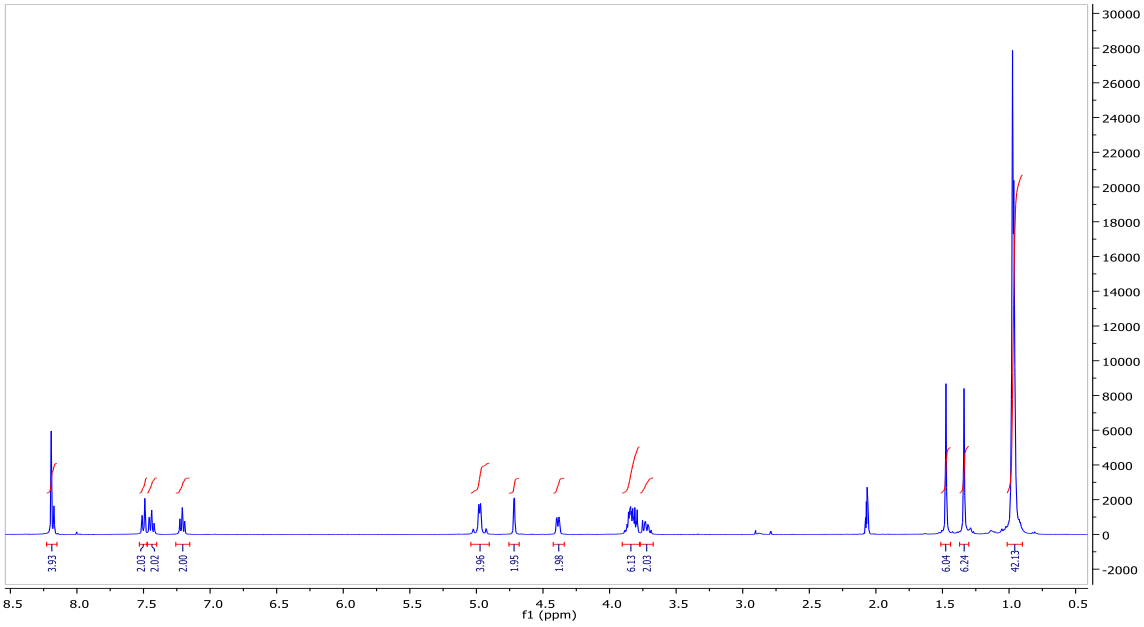


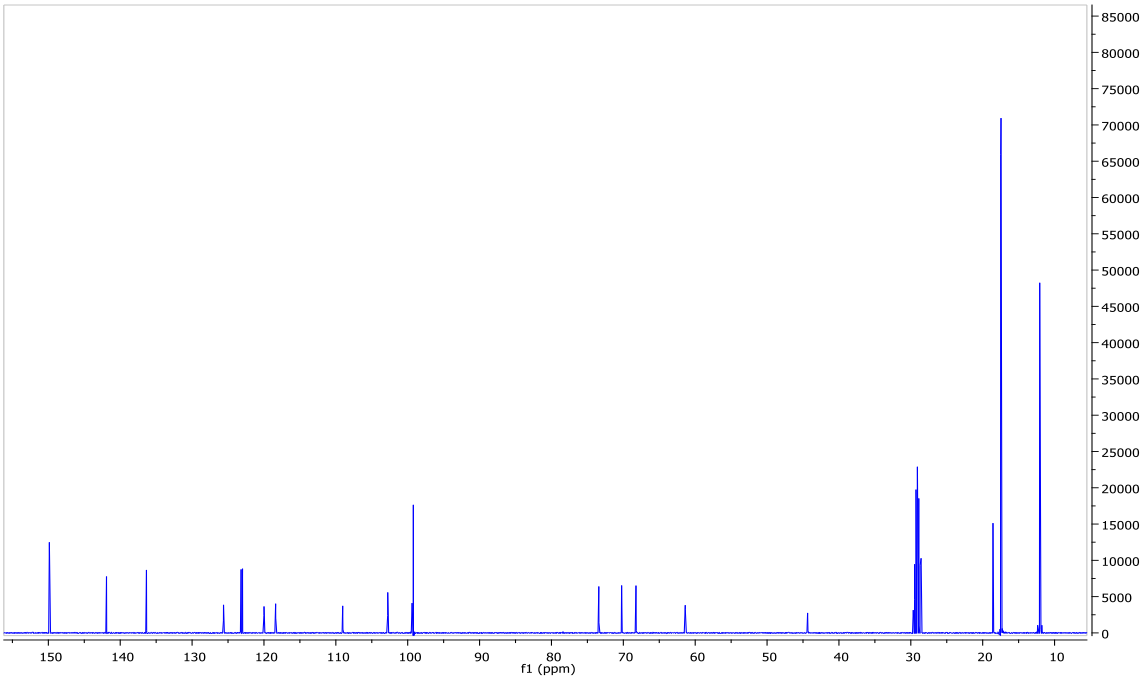


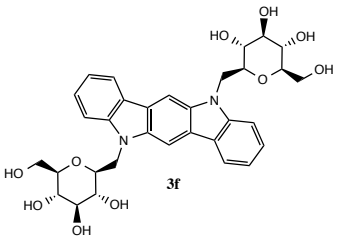


10

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

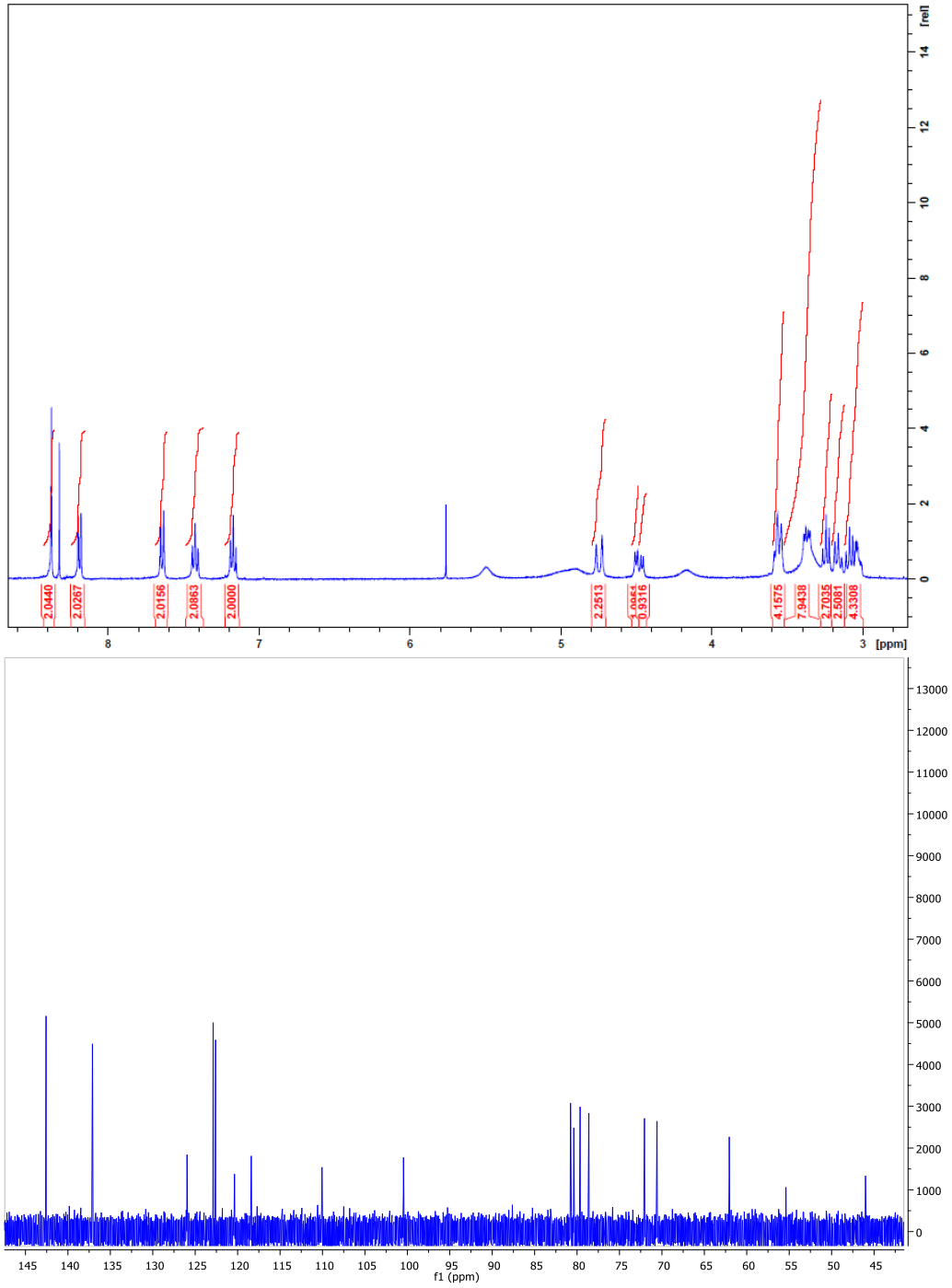


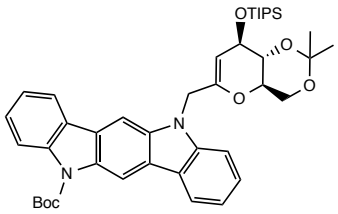




3f

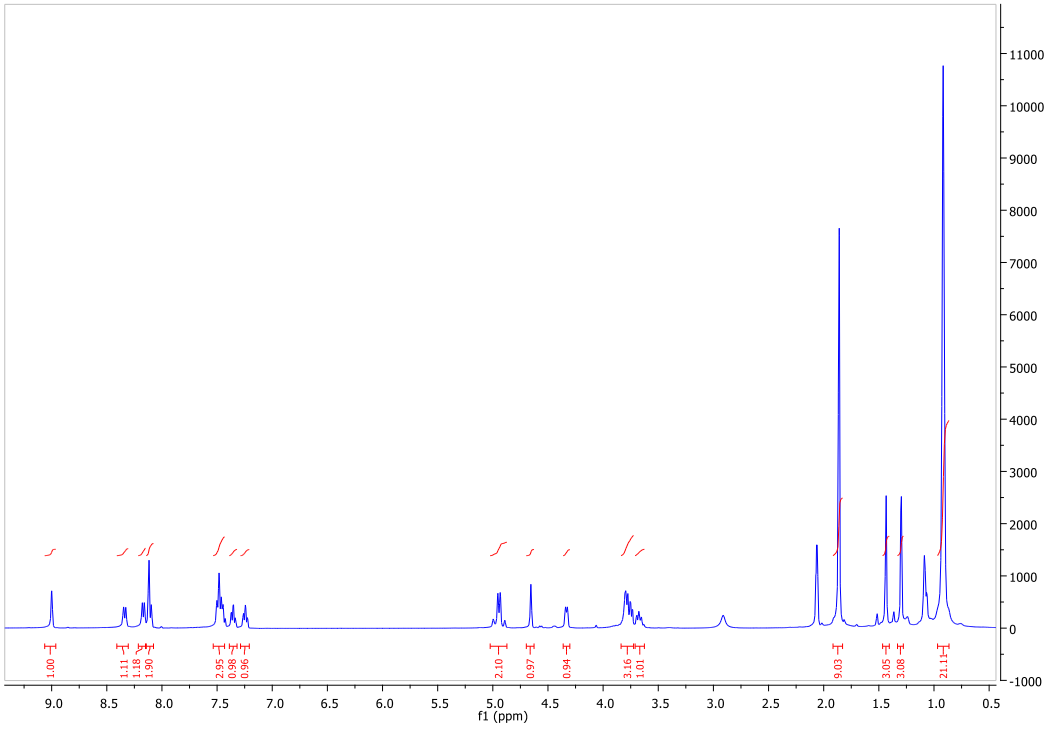
^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

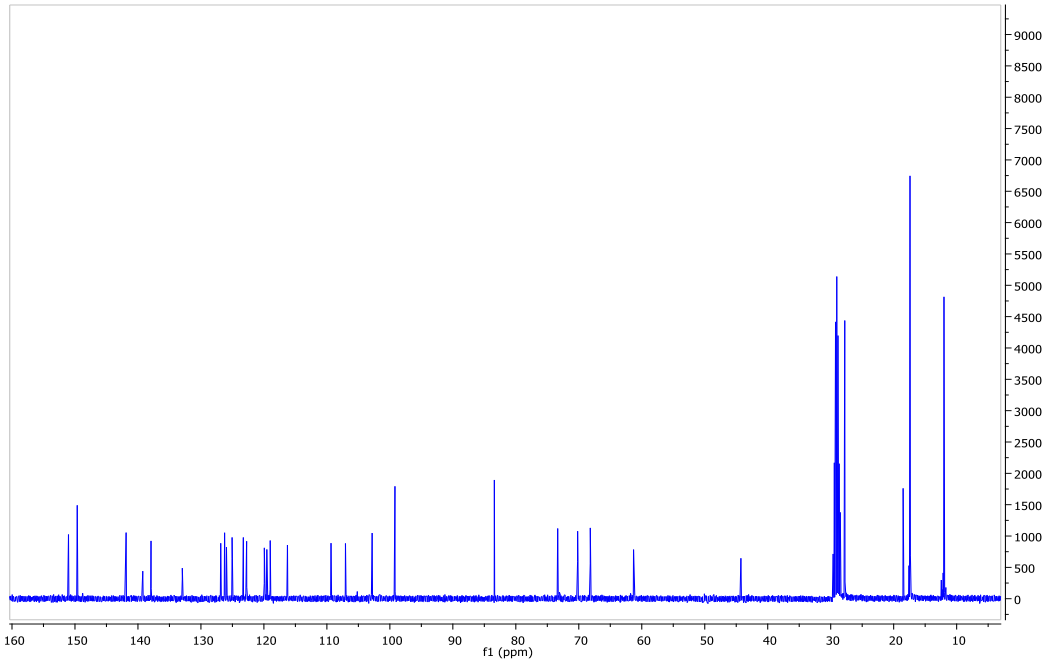




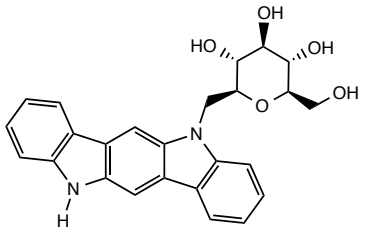
11

^{1}H(400 MHz) and ^{13}C NMR (100 MHz) spectra

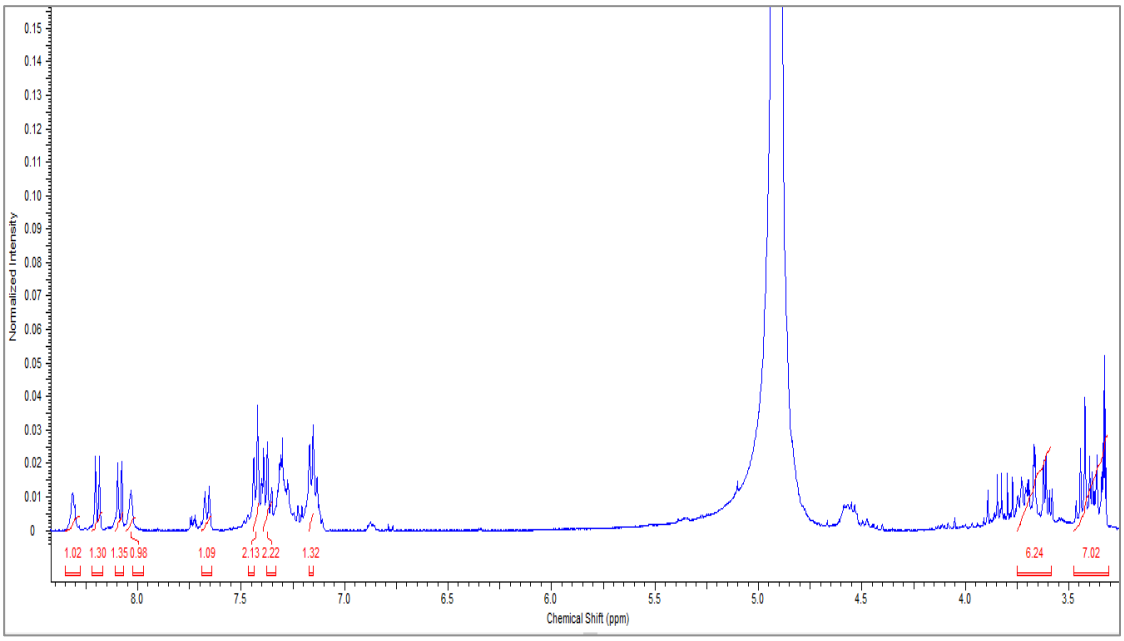


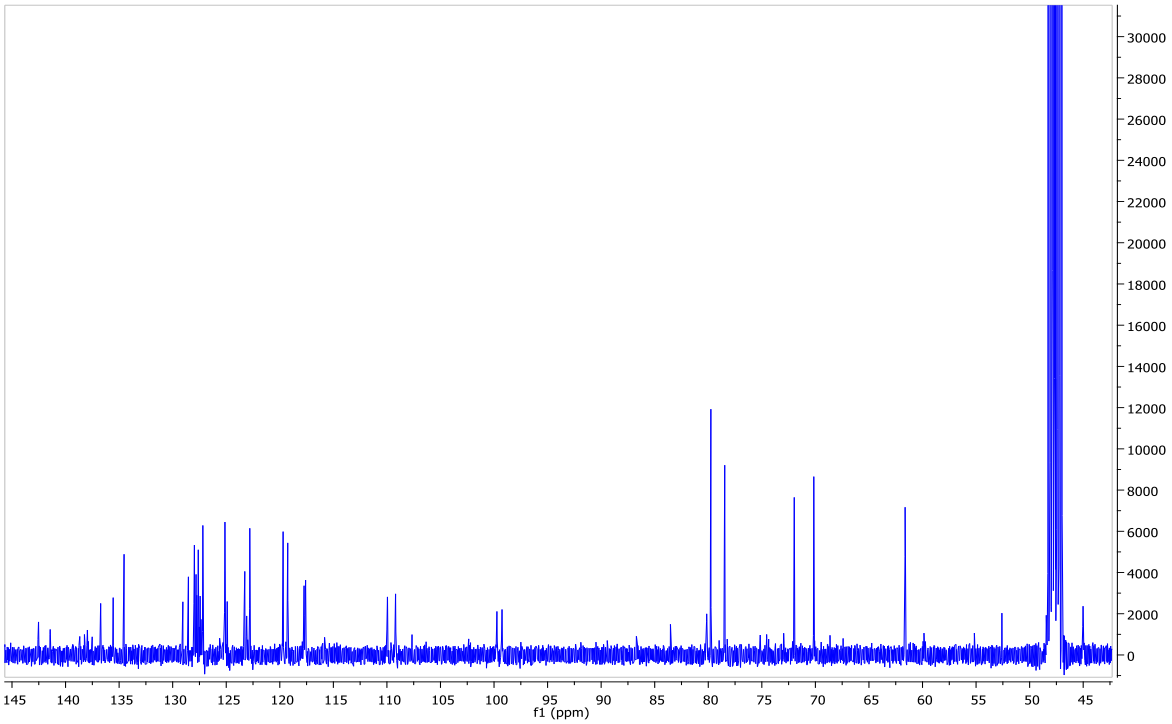


1H(400 MHz) and 13C NMR (100 MHz) spectra



2f





DNA Binding Studies

Materials: CT-DNA and Salmon Testes DNA were purchased from CALBIOCHEM. Solutions of CT-DNA and Salmon Testes DNA were prepared in 10mM Tris-EDTA buffer at pH 5.38 (as described in Jenkins: Jenkins, T.C. Optical Absorbance and Fluorescence Techniques for Measuring DNA-Drug Interactions. In *Methods in Molecular Biology, Drug-DNA Interaction Protocols;* Fox, K.R., Ed. Humana: Totowa, 1997; Vol 90, pp.195-217) and gave a 1.83:1 absorbance ratio at 260 nm and 280 nm. DNA and ligand concentrations were determined using 8452A HP Diode Array Spectrophotometer: CT-DNA, ε_{260} = 6600 M^{-1} cm^{-1}(1.82:1 absorbance ratio at 260 nm and 280 nm); Methyl Green, ε_{631} = 85, 300 M^{-1} $cm^{-}1$; Hoechst 33342, ε_{340} = 47,000 M^{-1} cm^{-1}; Ethidium Bromide, ε_{480} = 5450 M^{-1} cm^{-1}; 2a-2f & 3a-3e, ε_{336} = 24,816 M^{-1} cm^{-1}; poly (dT), ε_{265} = 9000 M^{-1} cm^{-1}per base; poly (dA) • poly (dT), ε_{260} = 6000 M^{-1} cm^{-1} per base pair; Oligo Extinction Coefficient Calculator from www.scripps.edu was used to determine the concentration of the hairpin deoxyoligonucleotides.

Fluorescence studies (Perkin Elmer Luminescence Spectrometer (LS 50B): The maximum emission wavelength of **2a-3f** was 404 nm when the excitation wavelength was 320 nm. Fluorescence titrations were recorded from 320 nm to 520 nm after an equilibration period of 3 min. Ex Slit (nm) = 10.0; Em Slit (nm) = 10.0; Scan Speed (nm/min) = 200.

EB competitive experiments

Constant concentrations of CT-DNA and EtBr were titrated with increasing concentrations of the ligands. The maximum emission wavelength was 590 nm when the excitation wavelength was 490 nm. Fluorescence titrations were recorded from 540 nm to 692 nm after an equilibration period of 3 min. Ex Slit (nm) = 10.0; Em Slit (nm) = 10.0; Scan Speed (nm/min) = 200.

Viscosity Studies

Viscosity experiments were performed with an Ostwald viscometer in a constant water bath at 23.0 ± 1°C. Solutions of constant DNA concentrations and varying ligand concentrations in Tris-EDTA buffer were incubated for 30 minutes. A digital stopwatch was used to record the flow time. The relative viscosity was calculated from the following equation:

$$\eta = \frac{t - t_0}{t_0}$$

where t_0 and t are the flow time in the absence and presence of the ligand. η is the viscosity in the presence of the ligand and η_0 is the viscosity in the absence of the ligand. The data were graphed as $(\eta/\eta_0)^{1/3}$ vs. [ligand]/[DNA].

Thermal denaturation studies

UV thermal denaturation samples (2 mL) were prepared by mixing CT-DNA in 100 mM NaCl and 10mM Tris-EDTA buffer (pH 5.38) in 1cm path length quartz cuvettes. The DNA to ligand ratio was 5:1. Thermal denaturation spectra were obtained from 8452A

HP Diode Array Spectrophotometer connected to 89090A Peltier Temperature Controller. Absorbance readings were taken for temperature ranging from 25 ˚C to 95 ˚C. Temperature was increased gradually with a speed of 1˚C/min with an absorbance reading every 1 ˚C. First derivative plots were used to determine the T_m value.

References for extinction coefficients:

Poly(dT), poly(dA).poly(dT):

Kumar, Sunil, Liang Xue, and Dev P Arya. "Neomycin-neomycin Dimer: An All-carbohydrate Scaffold with High Affinity for AT-rich DNA Duplexes." *Journal of the American Chemical Society*, 133.19 (2011): 7361-7375

EtBr:

Saucier, J.M., Festy, B. & LePecq, J.-B. (1971) *Biochimie* 53, 973-980.

Methyl Green:

Kim, S K, and B Nordén. "Methyl Green. A DNA Major-Groove Binding Drug." *FEBS Letters*, 315.1 (1993): 61-64.

Hoechst 33342:

http://www.piercenet.com/product/hoechst-33342-fluorescent-stain

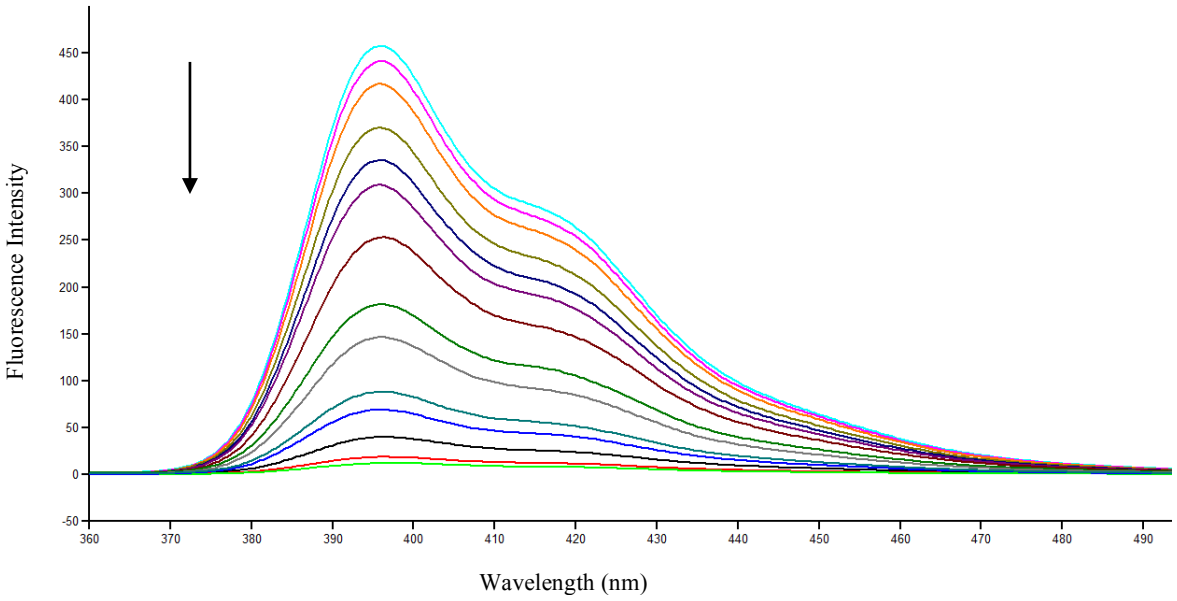


Fig.1. Fluorescence spectra of **3a** in the presence of varying concentrations of CT-DNA, **[3a]** = 6.4 x 10^{-8} mol L^{-1},[CT-DNA] = 0.02, 0.03, 0.05, 0.08, 0.13, 0.20, 0.30, 0.40, 0.60, 0.90, 1.20, 2.4, 5.4, and 8.40 x 10^{-6} mol L^{-1}, respectively; pH: 5.48

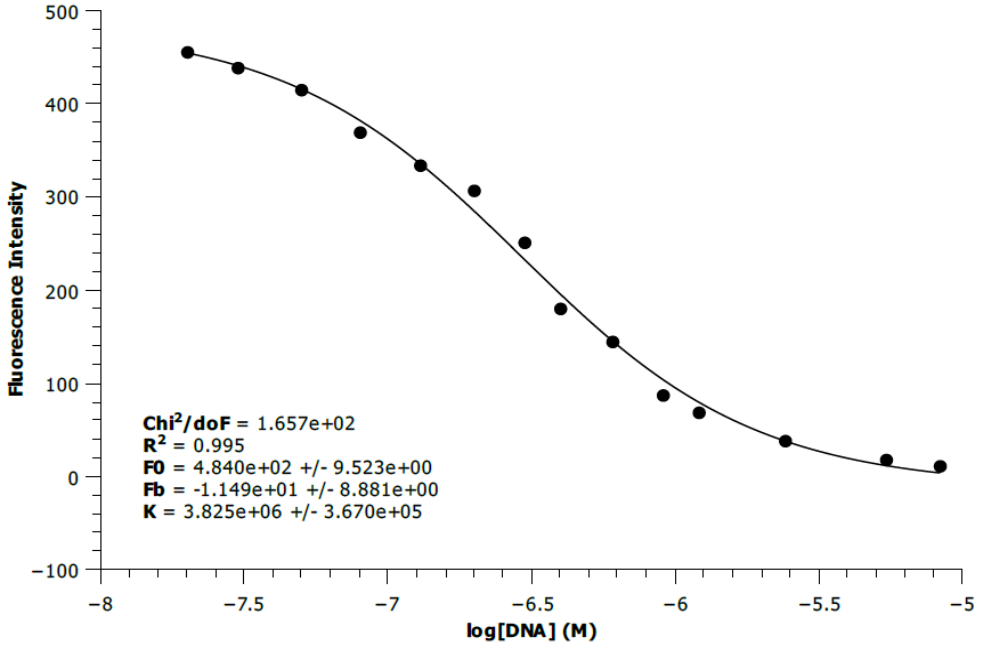


Fig. 2. Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA, **[3a]** = 6.4 x 10^{-8} mol L^{-1}, C_{DNA} = 0.02, 0.03, 0.05, 0.08, 0.13, 0.20, 0.30, 0.40, 0.60, 0.90, 1.20, 2.4, 5.4, and 8.40 x 10^{-6} mol L^{-1}; pH: 5.48

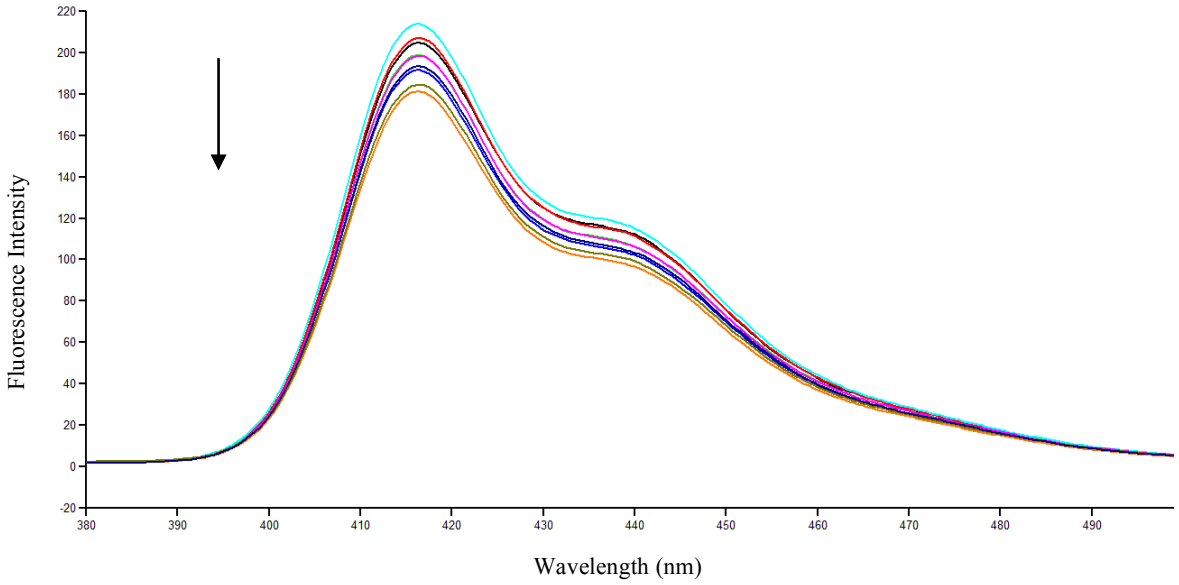


Fig.3. Fluorescence spectra of **3f** in the presence of varying concentrations of CT-DNA, **[3f]**= 3.99 x 10^{-8} mol L^{-1}, C_{DNA} = 0.10, 0.40, 0.70, 2.73, 12.13, 95.40, and 303.20 x 10^{-7} mol L^{-1}.

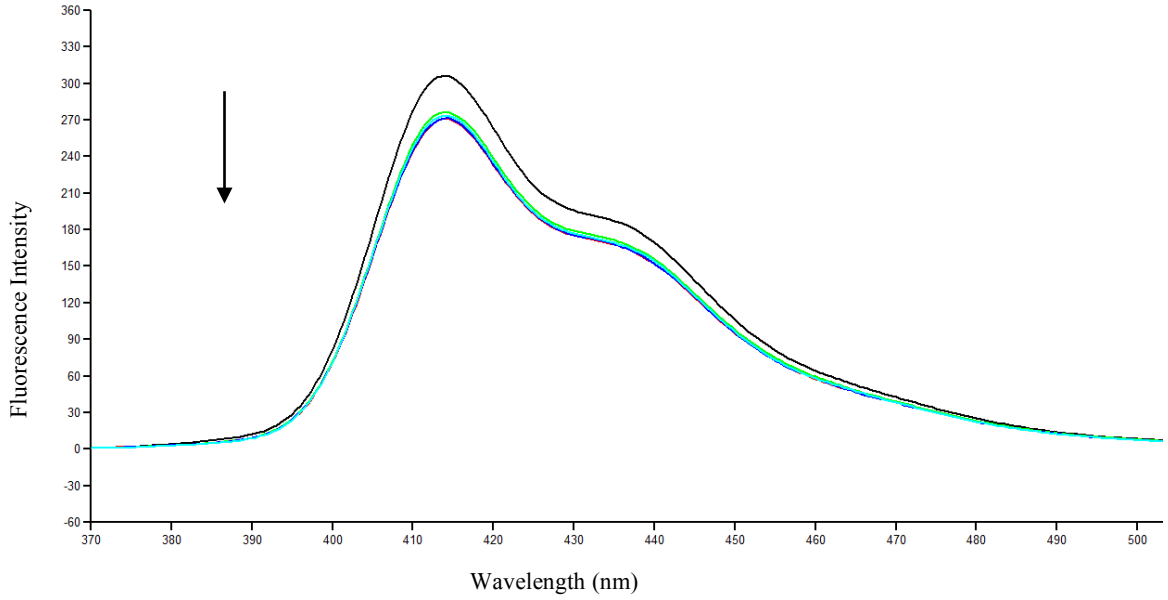


Fig. 4. Fluorescence spectra of **2f** in the presence of varying concentrations of CT-DNA, **[2f]** = 5.04 x 10^{-8} mol L^{-1}, C_{DNA} = 0.41, 0.90, 1.40, 4.24, 27.28, and 148.40 x 10^{-7} mol L^{-1}.

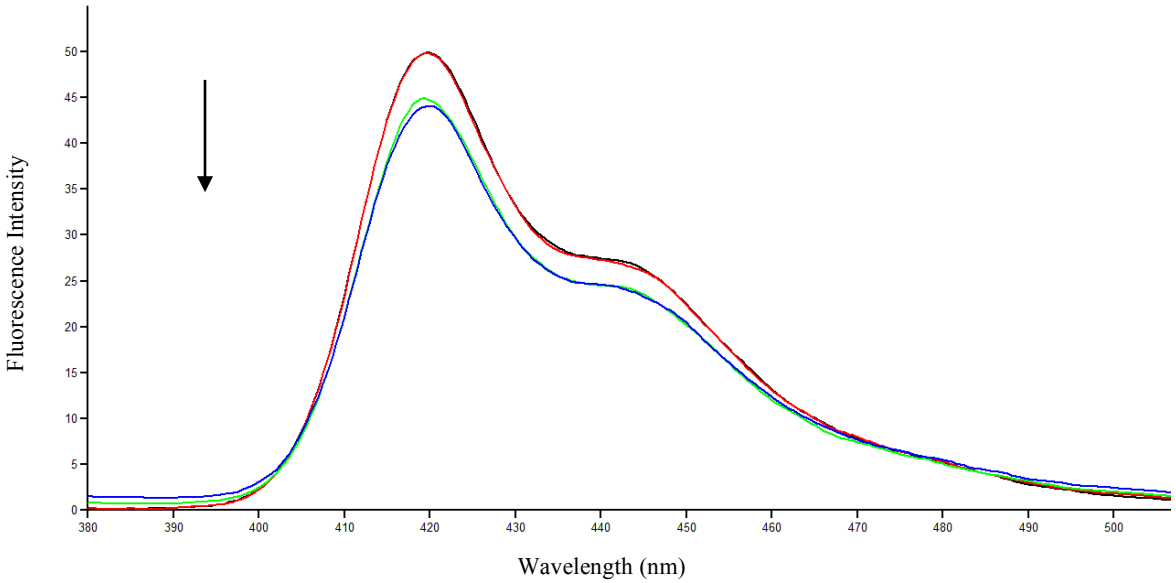


Fig.5. Fluorescence spectra of **3b** in the presence of varying concentrations of CT-DNA, **[3b]** = 2.95 x 10^{-8} mol L^{-1}, C_{DNA} = 0.30, 106.12, and 181.92 x 10^{-4} mol L^{-1}.

Ethidium Bromide displacement

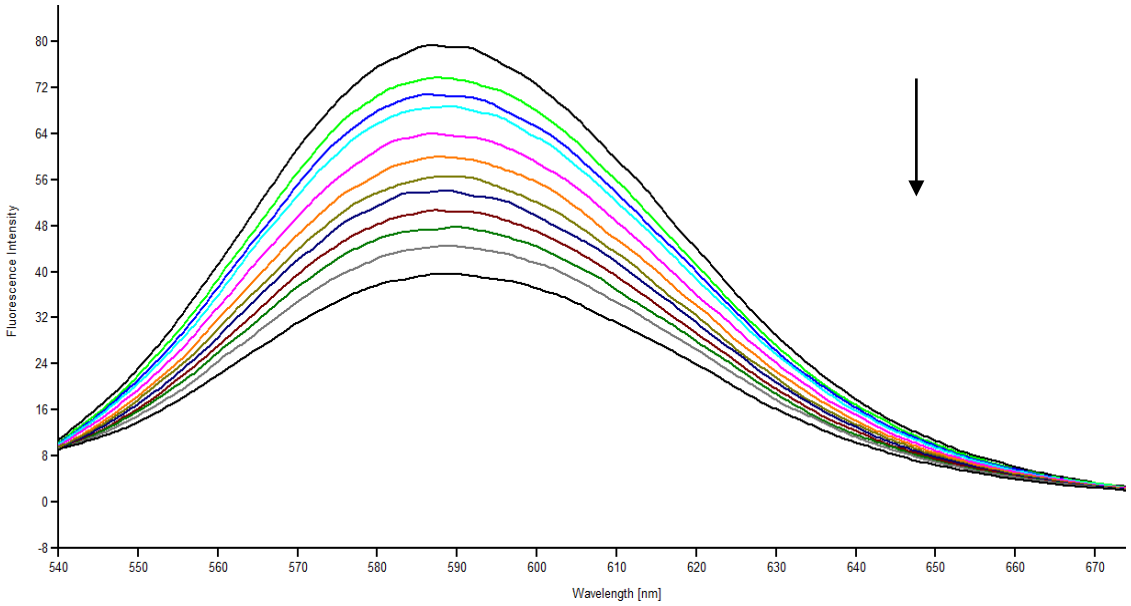


Fig.6. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2a**; [CT-DNA] = 8.27 x 10^{-6} mol L^{-1}, [EtBr] = 8.27 x 10^{-6} mol L^{-1}, **[2a]** = 0.00, 0.83, 1.25, 1.87, 2.70, 3.53, 4.36, 5.19, 6.23, 7.69, 9.35, and 11.83 x 10^{-6} mol L^{-1}.

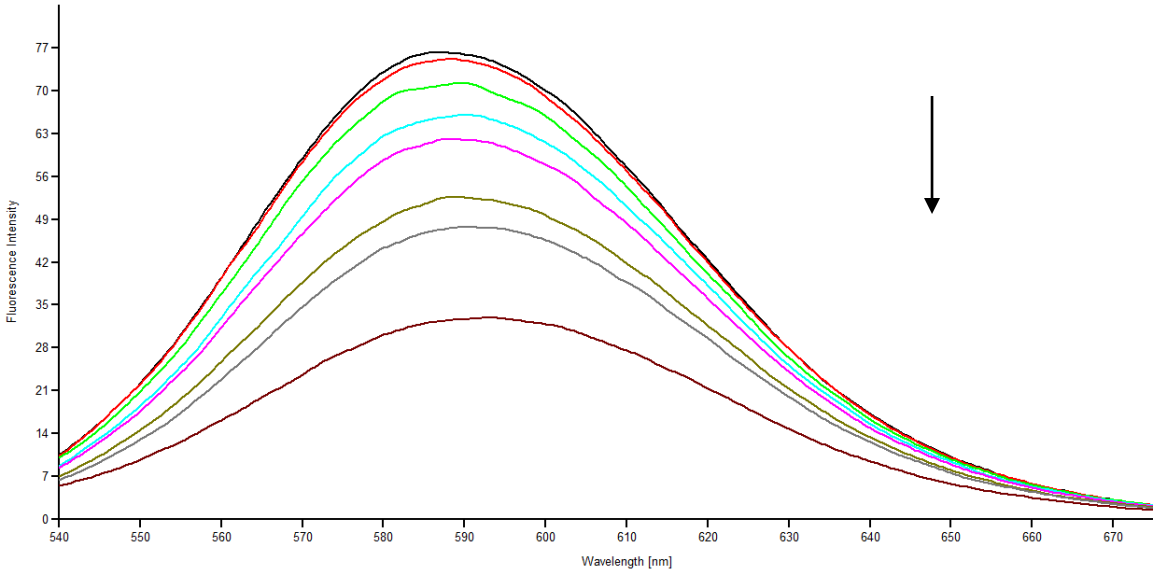


Fig.7. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2b**; [CT-DNA] = 8.27 x 10^{-6} mol L^{-1}, [EtBr] = 8.64 x 10^{-6} mol L^{-1}, **[2b]** = 0.00, 0.44, 0.77, 1.76, 2.09, 2.42, 2.64, and 2.97 x 10^{-6} mol L^{-1}.

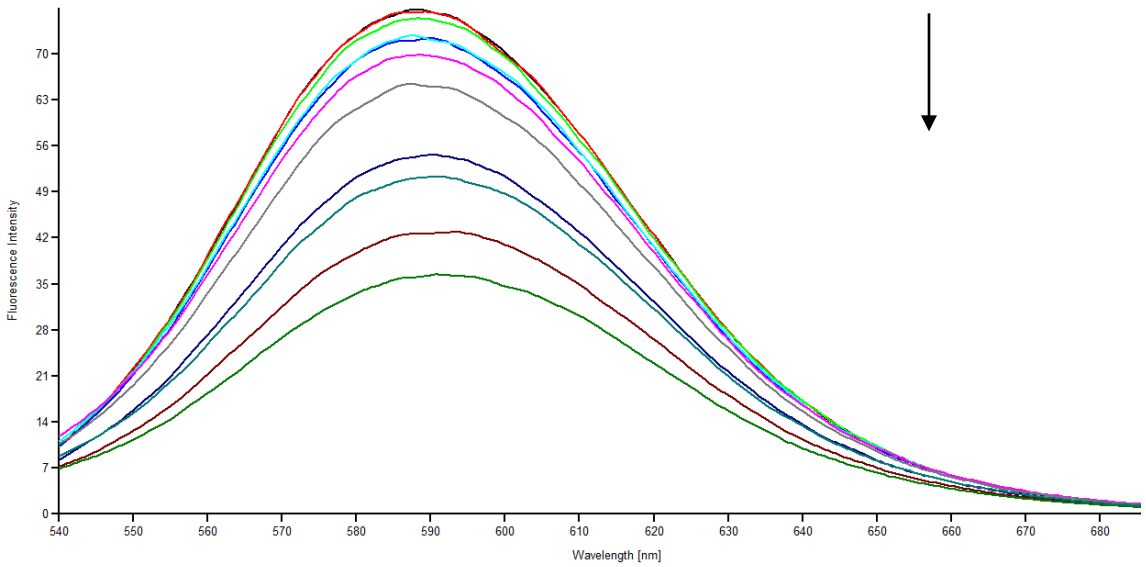


Fig.8. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2c**; [CT-DNA] = 8.27 x 10^{-6} mol L^{-1}, [EtBr] = 8.27 x 10^{-6} mol L^{-1}, **[2c]** = 0.00, 0.22, 0.77, 1.88, 2.98, 4.41, 5.52, 5.74, 6.62, 7.72, and 8.82 x 10^{-6} mol L^{-1}.

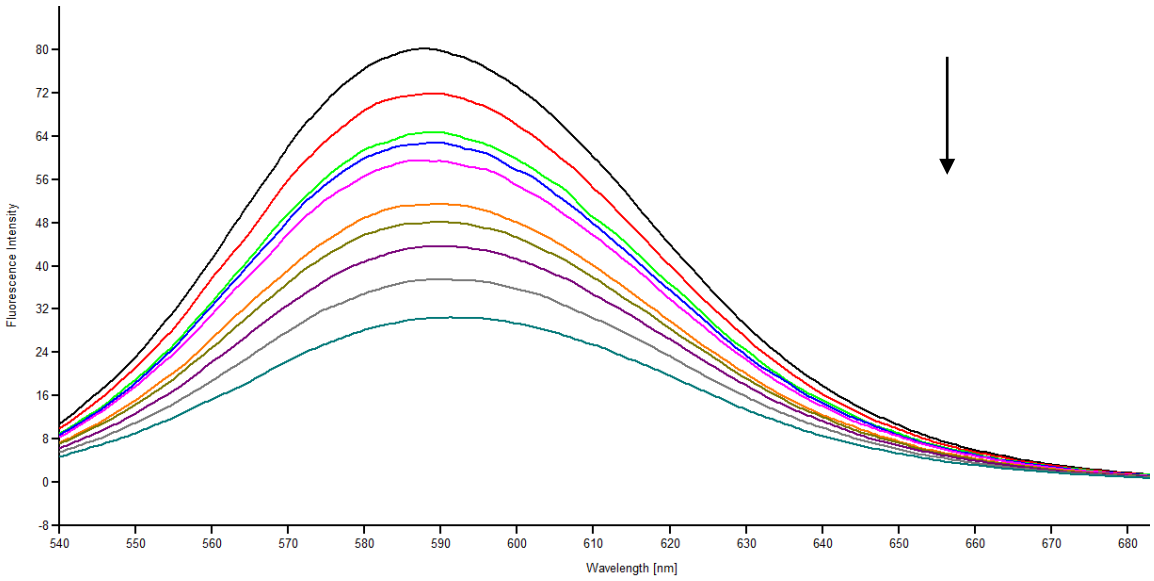


Fig.9. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2d**; [CT-DNA] = 8.20 x 10^{-6} mol L^{-1}, [EtBr] = 8.80 x 10^{-6} mol L^{-1}, **[2d]** = 0.00, 1.10, 1.54, 2.20, 2.86, 3.30, 3.63, 4.29, 5.50, and 6.60 x 10^{-6} mol L^{-1}.

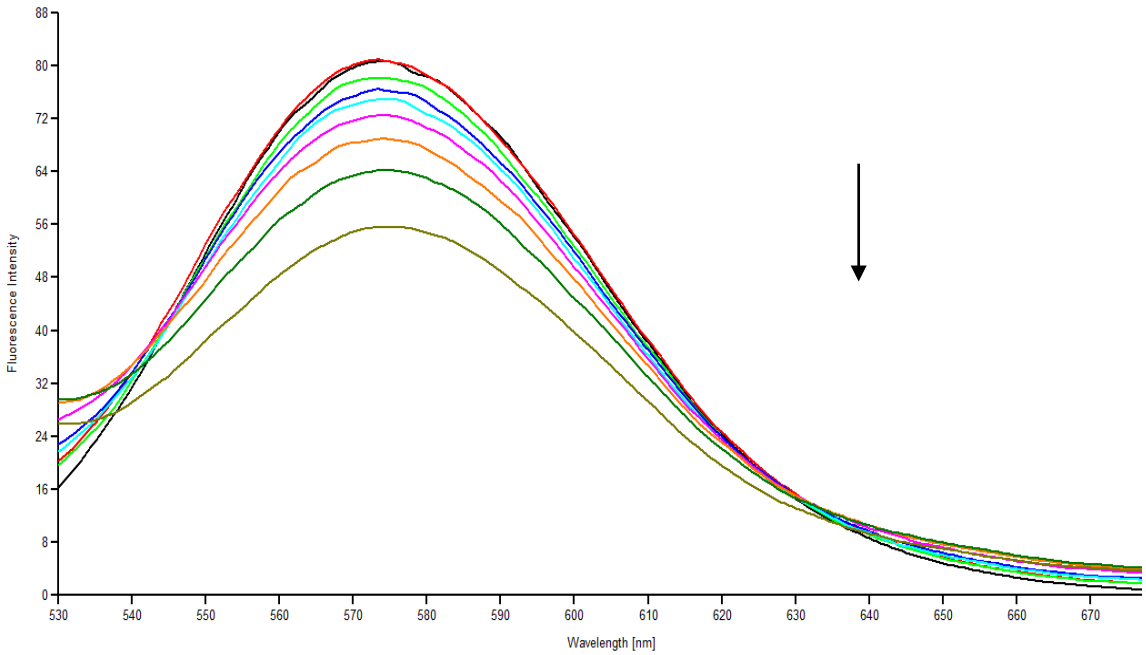


Fig.10 Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2e**; [CT-DNA] = 8.07 x 10^{-6} mol L^{-1}, [EtBr] = 8.11 x 10^{-6} mol L^{-1}, **[2e]** = 0.00, 3.13, 5.36, 7.59, 9.83, 12.06, 14.29, 16.53, and 18.76 x 10^{-6} mol L^{-1}.

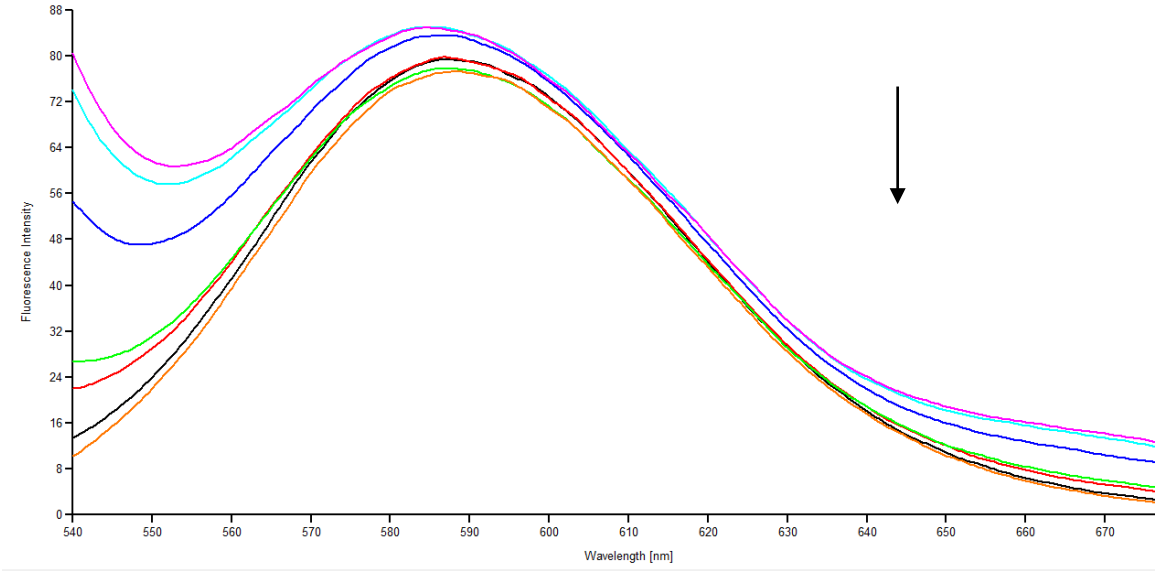


Fig.11. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **2f**; [CT-DNA] = 8.33 x 10^{-6} mol L^{-1}, [EtBr] = 8.53 x 10^{-6} mol L^{-1}, **[2f]** = 0.00, 4.24, 10.61, 14.86, 25.47, 29.71, and 36.08 x 10^{-6} mol L^{-1}.

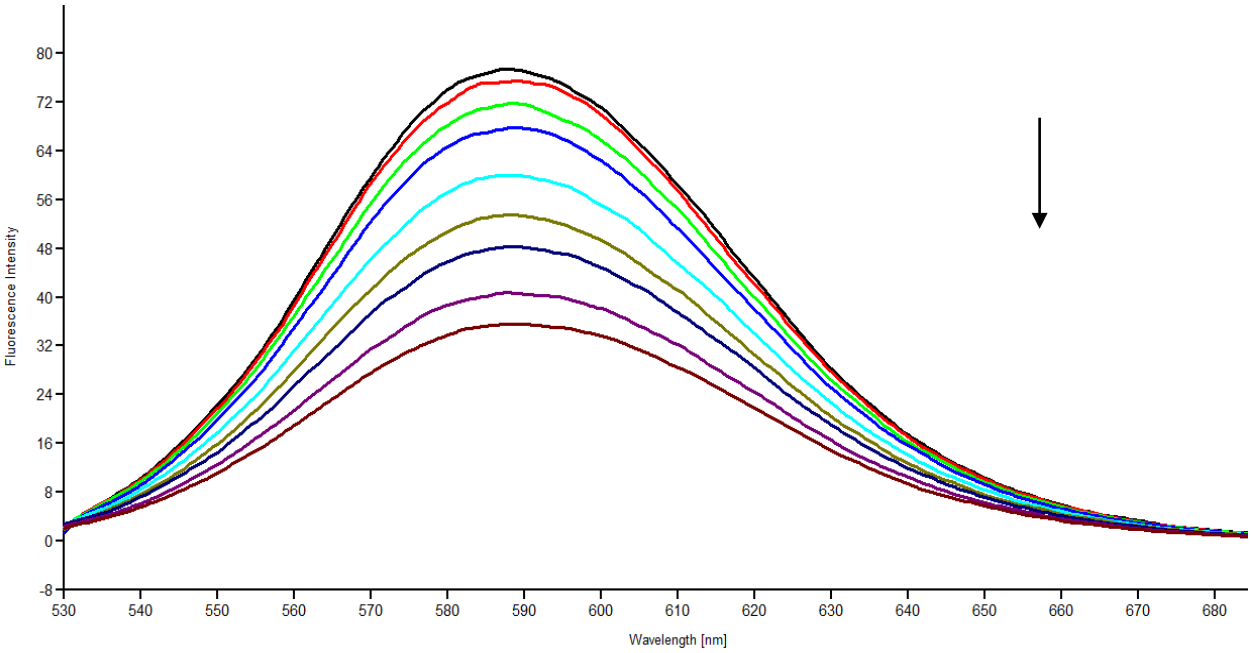


Fig.12. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **3a**; [CT-DNA] = 8.07 x 10^{-6} mol L^{-1}, [EtBr] = 8.47 x 10^{-6} mol L^{-1}, **[3a]** = 0.00, 0.10, 0.35, 0.60, 1.10, 1.76, 2.47, 3.70, and 4.93 x 10^{-6} mol L^{-1}.

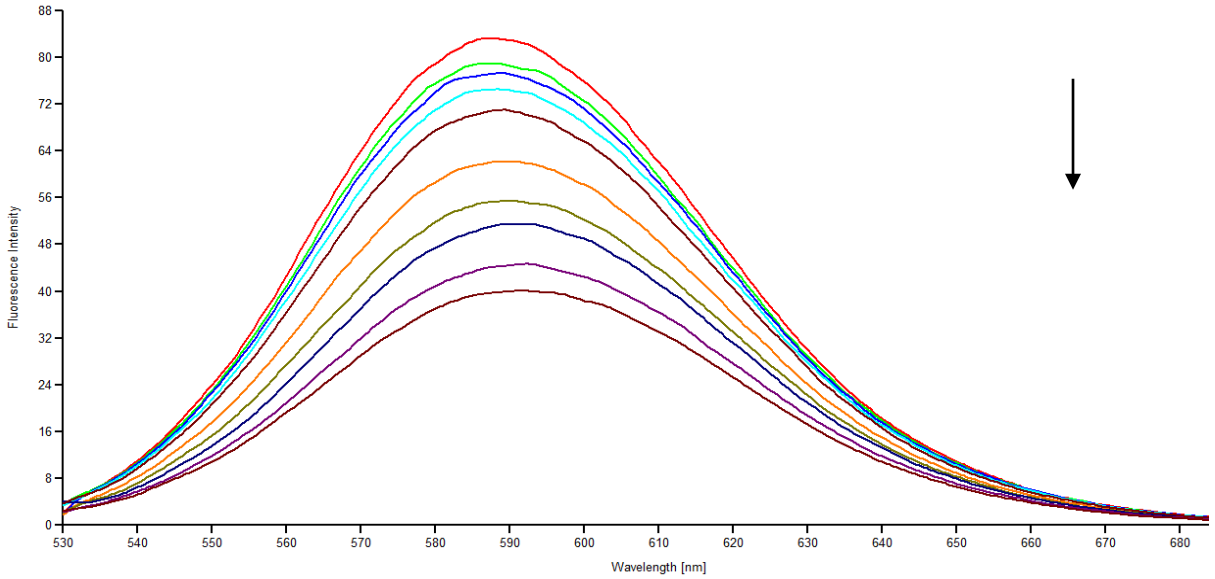


Fig.13. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **3d**; [CT-DNA] = 8.07 x 10^{-6} mol L^{-1}, [EtBr] = 8.11 x 10^{-6} mol L^{-1}, **[3d]** = 0.00, 0.22, 0.44, 0.56, 0.68, 0.78, 0.89, 1.11, 1.33, and 1.45 x 10^{-6} mol L^{-1}.

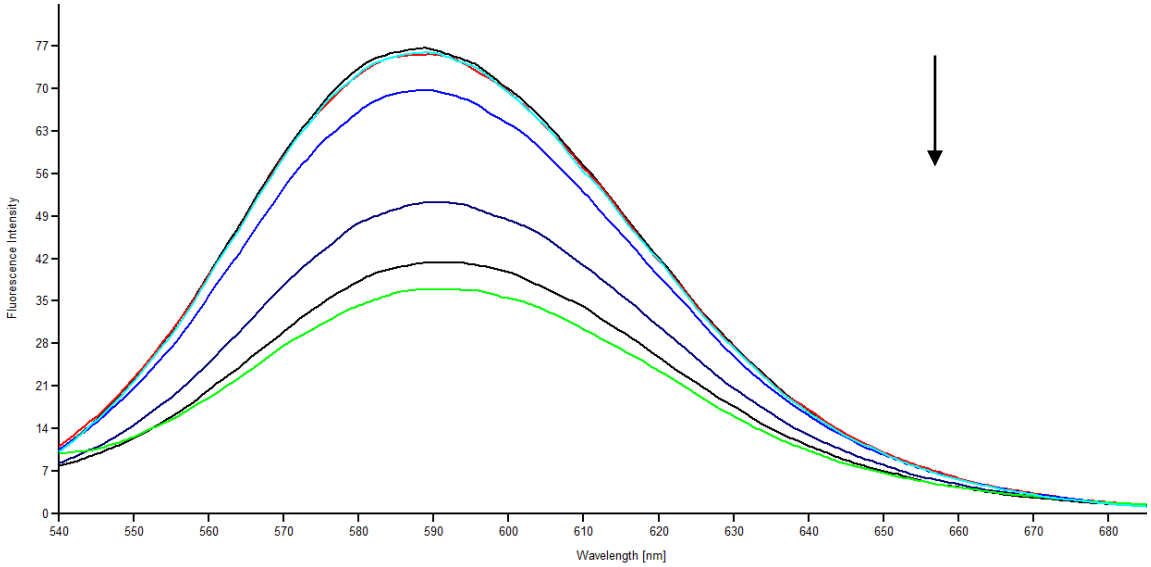


Fig.14. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **3e**; [CT-DNA] = 8.07 x 10^{-6} mol L^{-1}, [EtBr] = 8.09 x 10^{-6} mol L^{-1}, **[3e]** = 0.00, 0.28, 0.96, 1.52, 2.89, 3.72, and 4.83 x 10^{-6} mol L^{-1}.

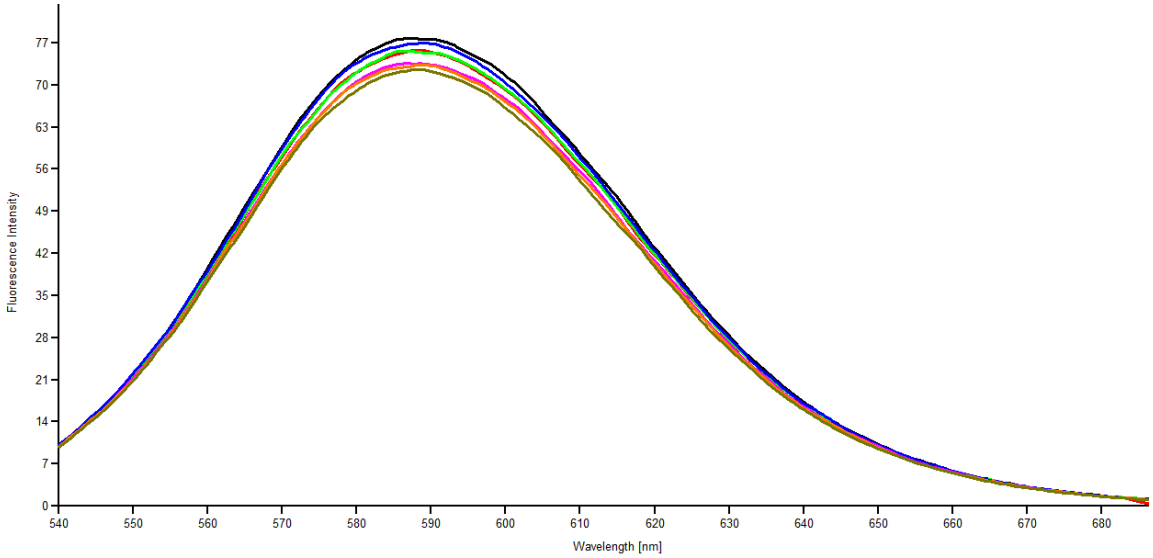


Fig.15. Fluorescence spectra of Ethidium Bromide and CT-DNA in the presence of varying concentrations of **3f**; [CT-DNA] = 8.53 x 10^{-6} mol L^{-1}, [EtBr] = 8.33 x 10^{-6} mol L^{-1}, **[3f]** = 0.00, 7.87, 27.53, 47.20, 66.87, 86.53, and 125.87 x 10^{-6} mol L^{-1}.

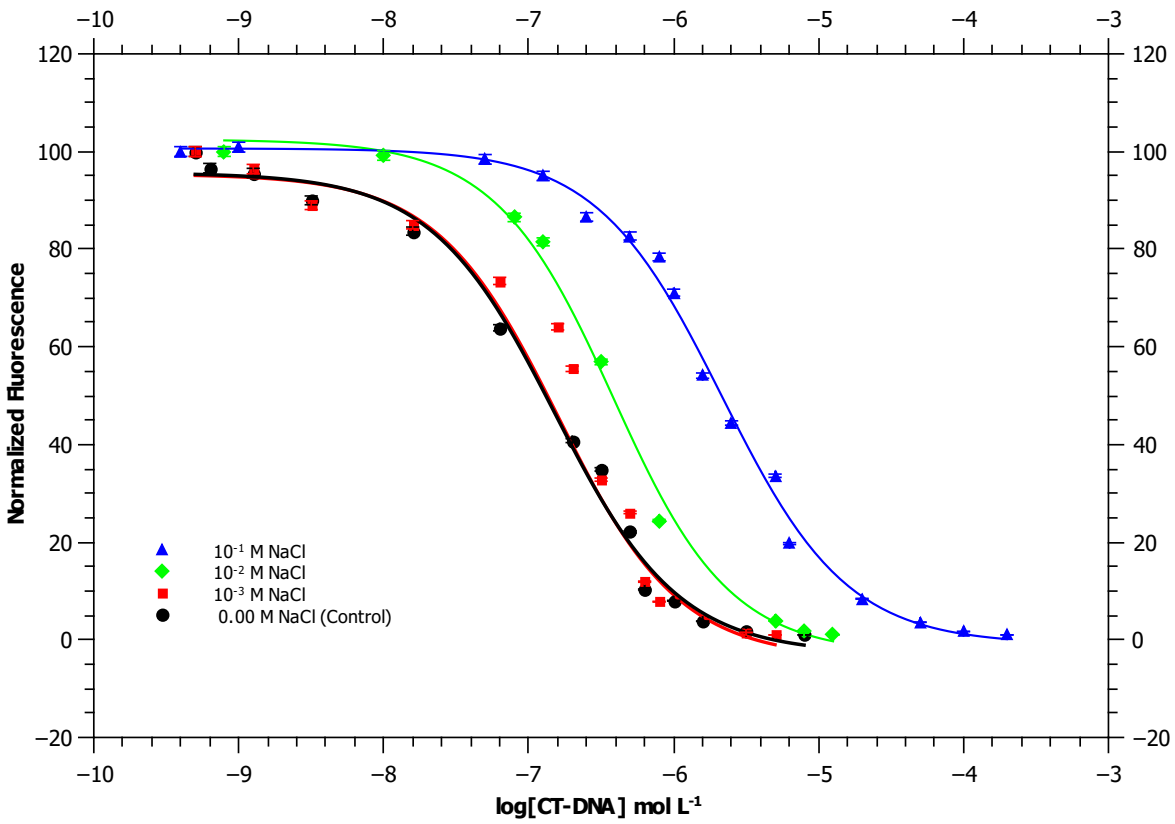
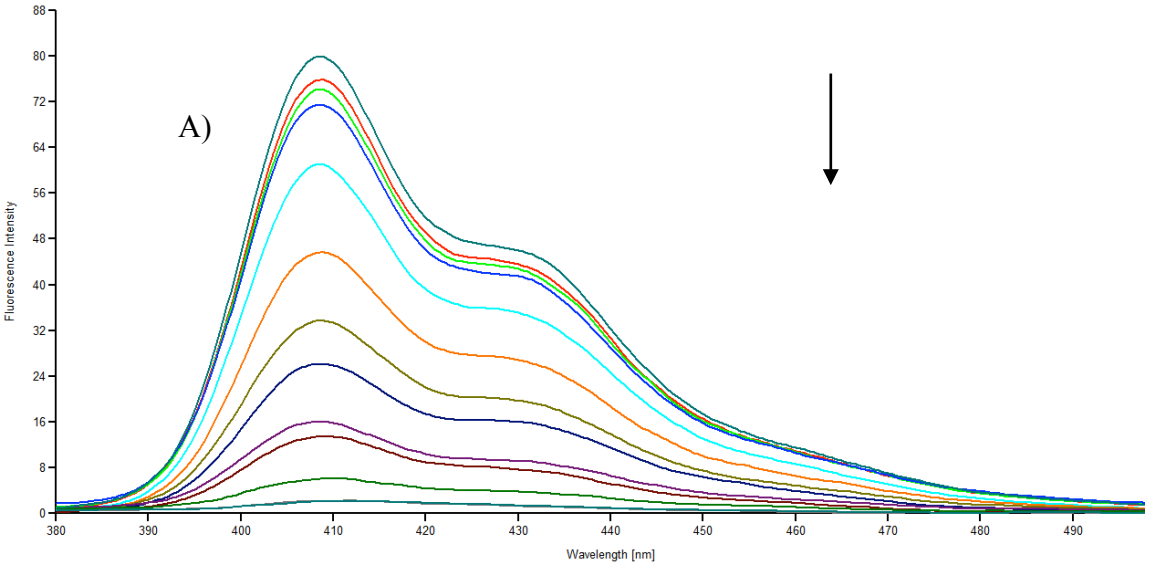
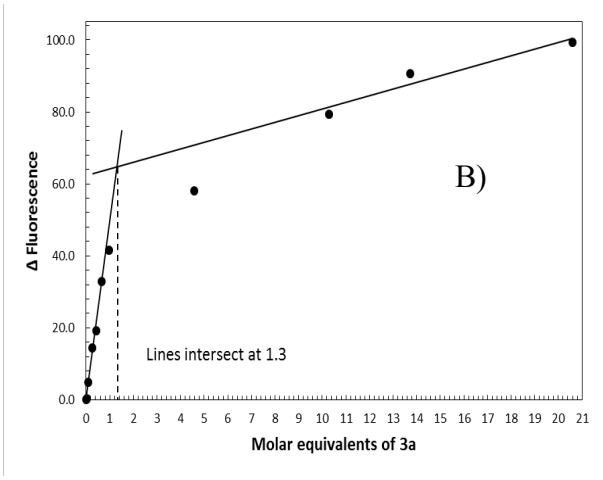


Fig.16. Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA in the presence of varying concentrations of NaCl.
0.00 M NaCl: [**3a**] = 1.00 x 10^{-8} mol L^{-1}, C_{DNA} = 0.005, 0.007, 0.012, 0.033, 0.16, 0.63, 2.20, 2.99, 4.56, 6.29, 9.43, 14.15, 29.87, and 77.03 x 10^{-7} mol L^{-1}
0.001 M NaCl: [**3a**] = 2.00 x 10^{-8} mol L^{-1}, C_{DNA} = 0.005, 0.012, 0.033, 0.16, 0.63, 1.41, 2.20, 2.99, 4.56, 6.29, 7.86, 29.87 and 53.45 x 10^{-7} mol L^{-1}
0.01 M NaCl: [**3**a] = 1.00 x 10^{-7} mol L^{-1}, C_{DNA} = 0.007, 0.093, 0.84, 1.31, 3.18, 7.48, 54.23, 74.80, and 130.90 x 10^{-7} mol L^{-1}
0.1 M NaCl: [**3a**] = 5.00 x 10^{-8} mol L^{-1}, C_{DNA} = .0004, .0011, .050, 0.13, 0.27, 0.55, 0.75, 1.12, 1.68, 2.62, 4.49, 6.36, 18.70, 46.75, 93.50, and 187.00 x 10^{-6} mol L^{-1}





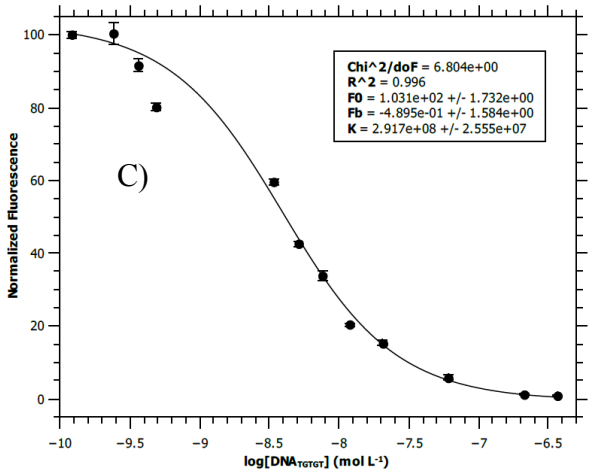


Fig.17 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of **5'-CGTGTGTCAAAAAGACACACG** hairpin sequence; [**3a**] = 8.0 x 10^{-9} mol L^{-1}, [DNA_{TGTGT}] = 0.0, 0.01, 0.02, 0.04, 0.05, 0.34, 0.51, 0.76, 1.19, 2.04, 6.07, 21.25, and 36.43 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'-CGTGTGTCAAAAAGACACACG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-CGTGTGTC AAAAAGACACACG hairpin deoxyoligonucleotide.

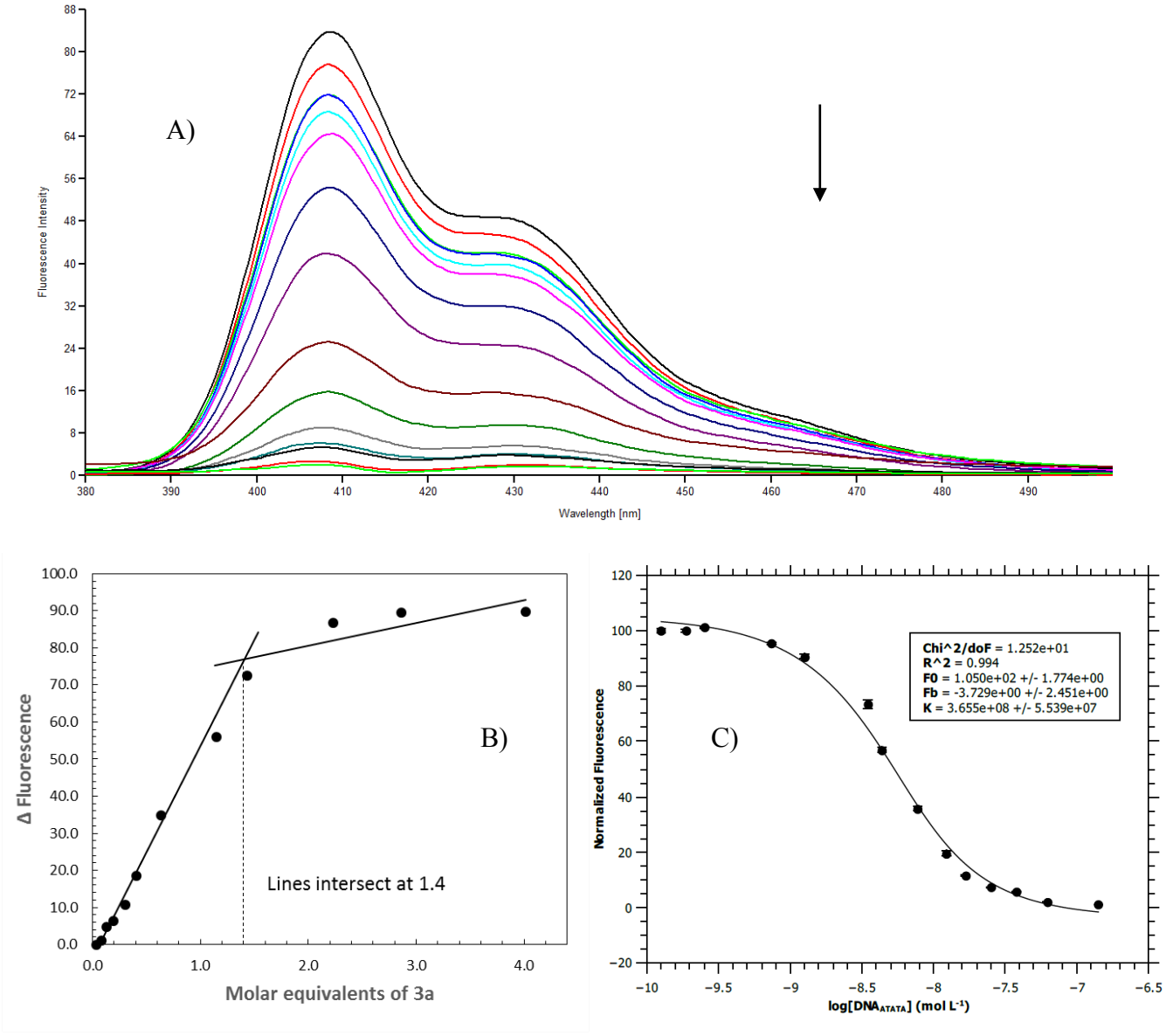


Fig.18 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGATATACAAAAAGTATATCG** hairpin sequence; [**3a**] = 8.0 x 10^{-9} mol L^{-1}, [DNA_{ATATA}] = 0.00, 0.035, 0.070, 0.11, 0.14, 0.29, 0.32, 0.39, 0.47, 0.56, 0.74, 0.91, 1.08, 1.48, 1.76, 2.46, 3.52, 5.28, 8.80, 12.31, 15.83, 22.87, 28.14, and 36.94 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'-CGATATACAAAAAGTATATCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-CGATATACAAAAAGTATATCG hairpin deoxyoligonucleotide

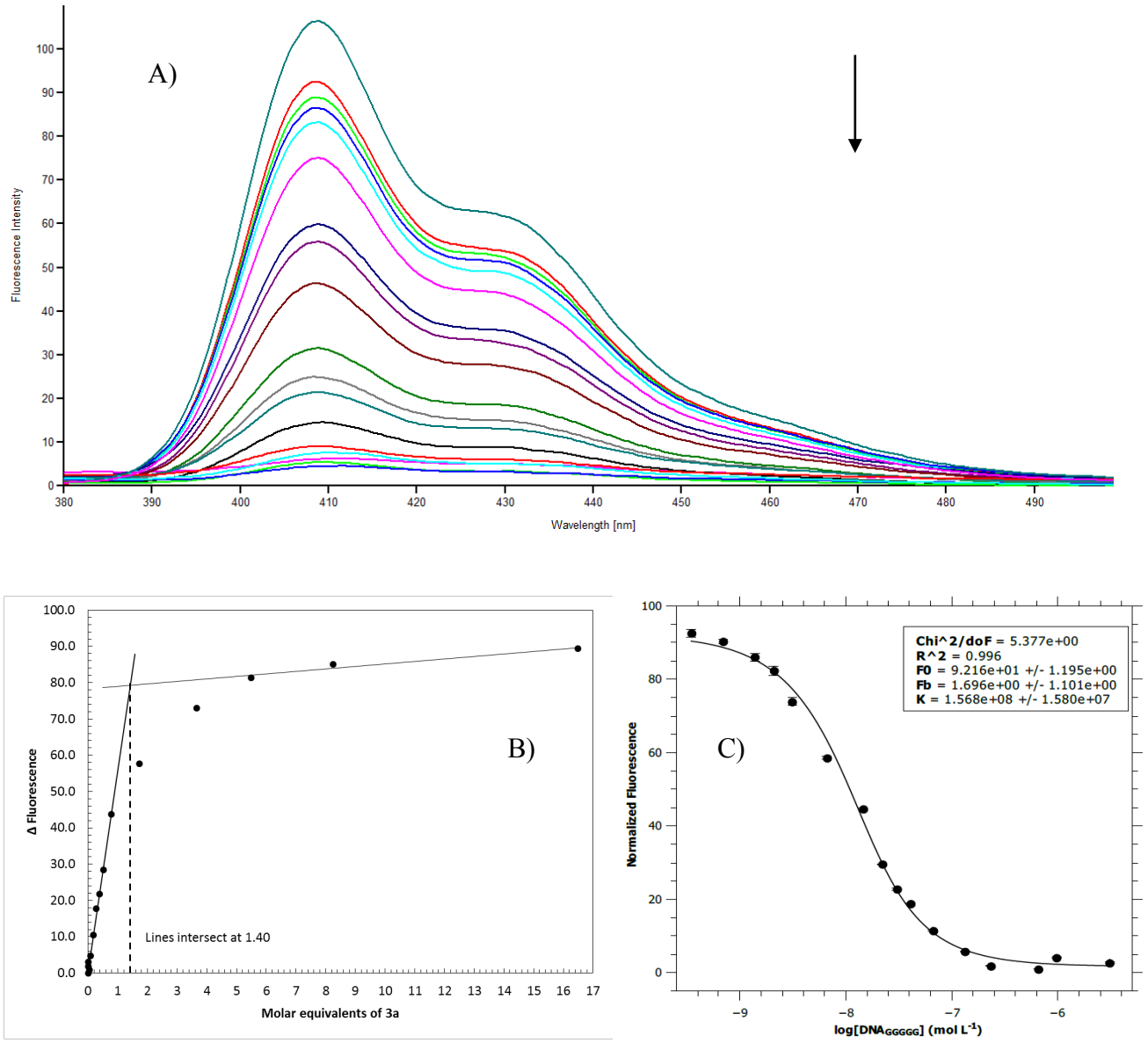


Fig.19. A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGGGGGGCAAAAAGCCCCCCG** hairpin sequence; [**3a**] = 1.14 x 10^{-8} mol L^{-1}, [DNA_{GGGGG}] = 0.0, 0.04, 0.07, 0.14, 0.21, 0.31, 0.66, 1.5, 2.2, 3.0, 4.0, 6.6, 13, 23, 65, 97, and 310 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'- CGGGGGGCAAAAAGCCCCCCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-CGGGGGGCAAAAAGCCCCCCG hairpin deoxyoligonucleotide

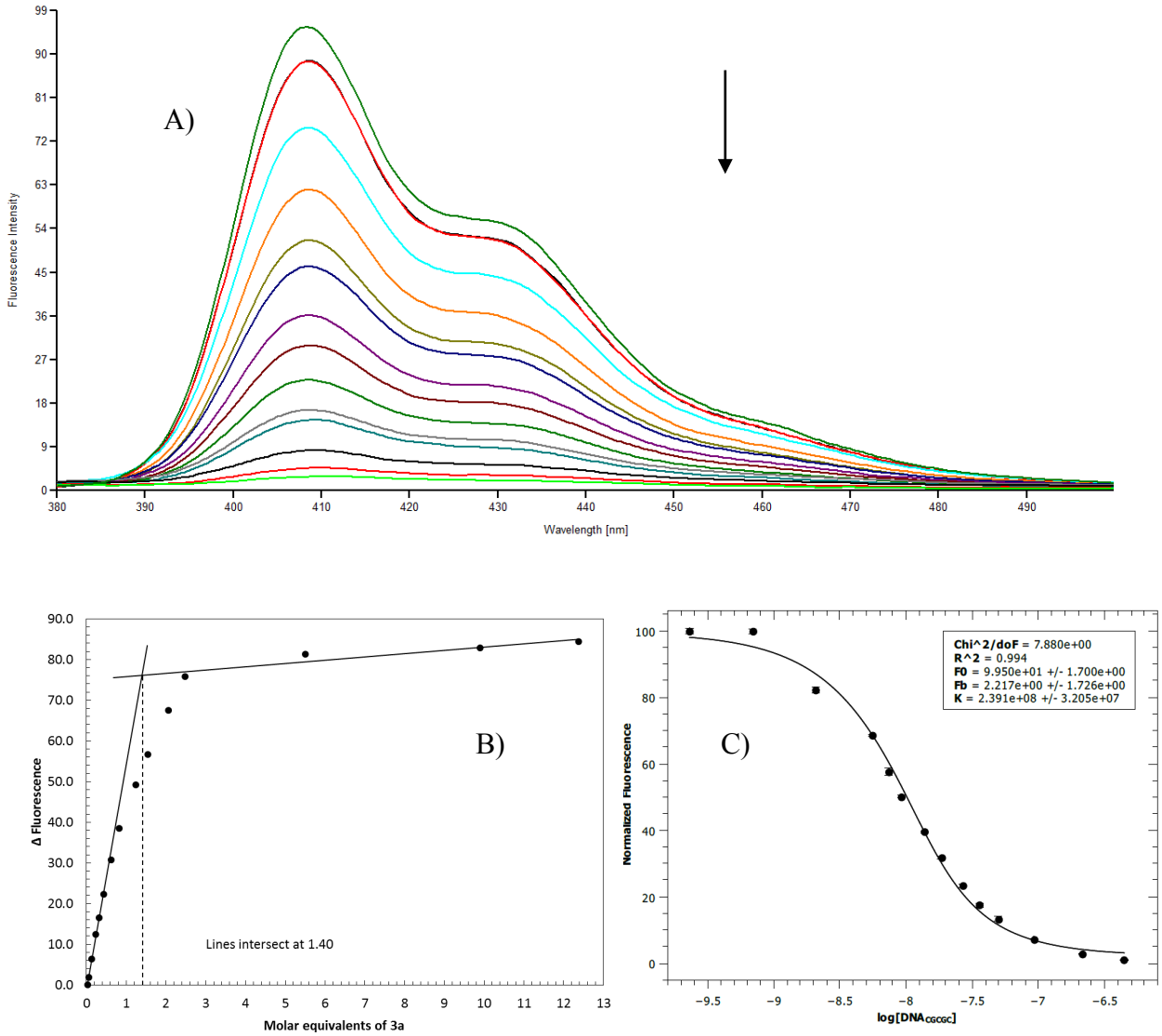


Fig.20. (A) Fluorescence spectra of **3a** in the presence of varying concentrations of **5'-CGCGCGCCAAAAAGGCGCGCG** hairpin sequence; [**3a**] = 1.14 x 10^{-8} mol L^{-1}, [DNA_{CGCGC}] = 0.0, 0.02, 0.07, 0.21, 0.55, 0.74, 0.92, 1.38, 1.84, 2.67, 3.59, 4.97, 9.21, 21.49, and 44.52 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'-CGCGCGCCAAAAAGGCGCGC hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'- CGCGCGCCAAAAAGGCGCGCG hairpin deoxyoligonucleotide

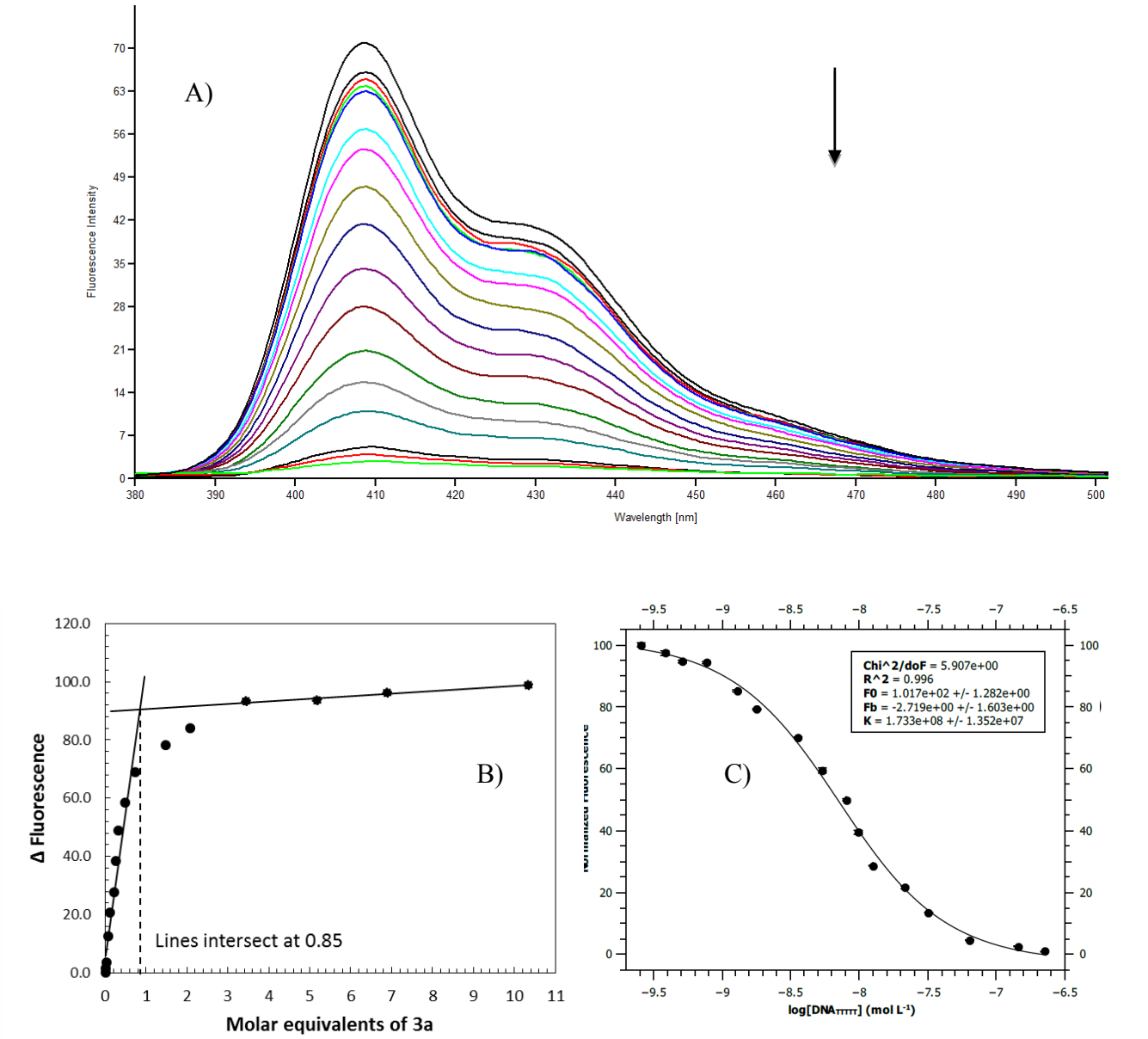


Fig.21. A) Fluorescence spectra of **3a** in the presence of varying concentrations of **5'-CGTTTTTCAAAAAGAAAAACG** hairpin sequence; [**3a**] = 2.65 x 10^{-9} mol L^{-1}, [DNA_{TTTTT}] = 0.0, 0.03, 0.04, 0.05, 0.08, 0.13, 0.18, 0.36, 0.54, 0.81, 0.99, 1.3, 2.2, 3.2, 6.4, 14, and 22 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'- **CGTTTTTCAAAAAGAAAAACG** hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-**CGTTTTTCAAAAAGAAAAACG** hairpin deoxyoligonucleotide

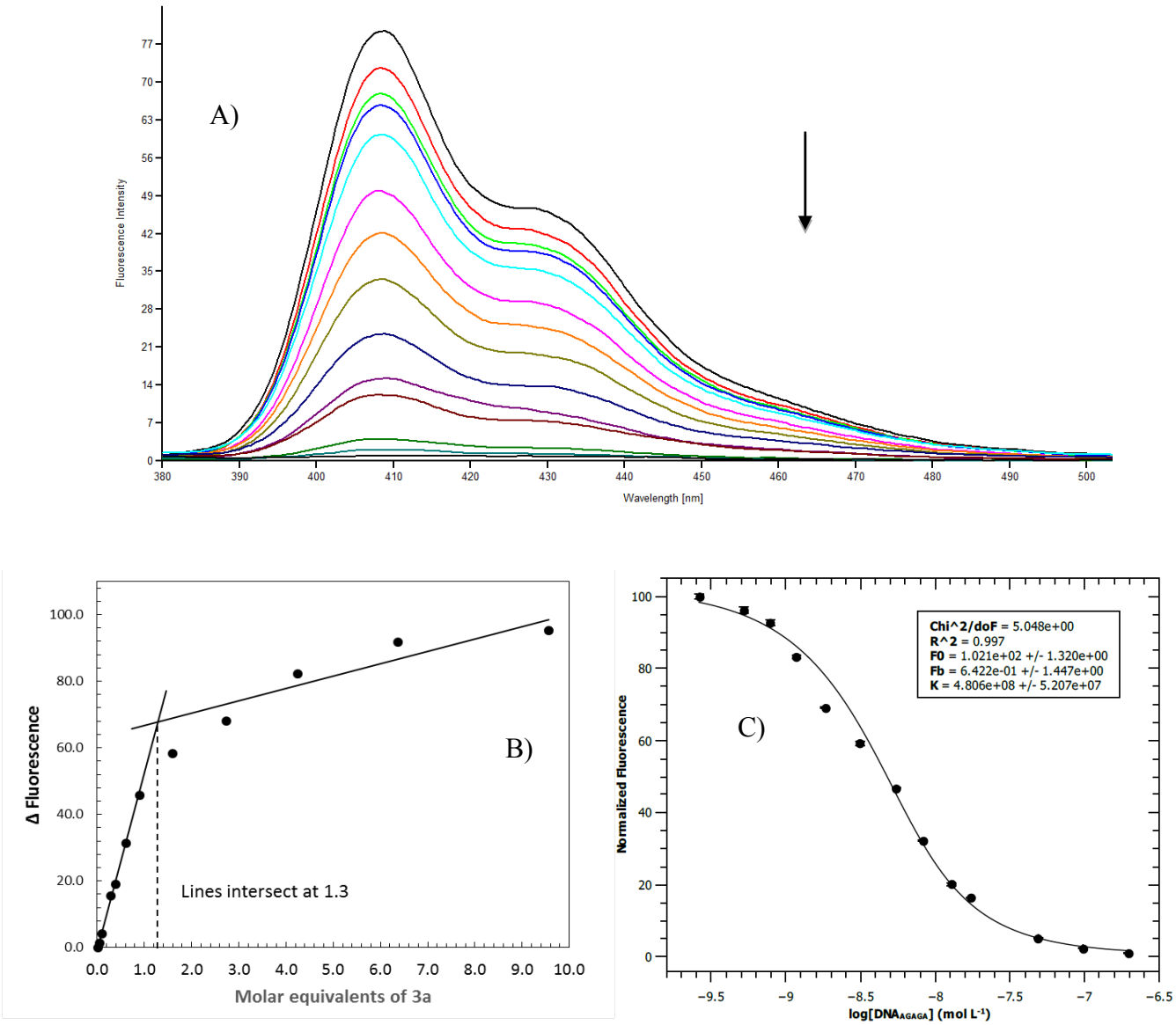


Fig.22 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of **5'-CGAGAGACAAAAAGTCTCTCG** hairpin sequence; [**3a**] = 7.0 x 10^{-9} mol L^{-1}, [DNA_{AGAGA}] =0.0, 0.03, 0.05, 0.08, 0.12, 0.18, 0.31, 0.55, 0.82, 1.3, 1.7, 4.9, 9.8, and 20 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'- CGAGAGACAAAAAGTCTCTCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'- CGAGAGACAAAAAGTCTCTCG hairpin deoxyoligonucleotide.

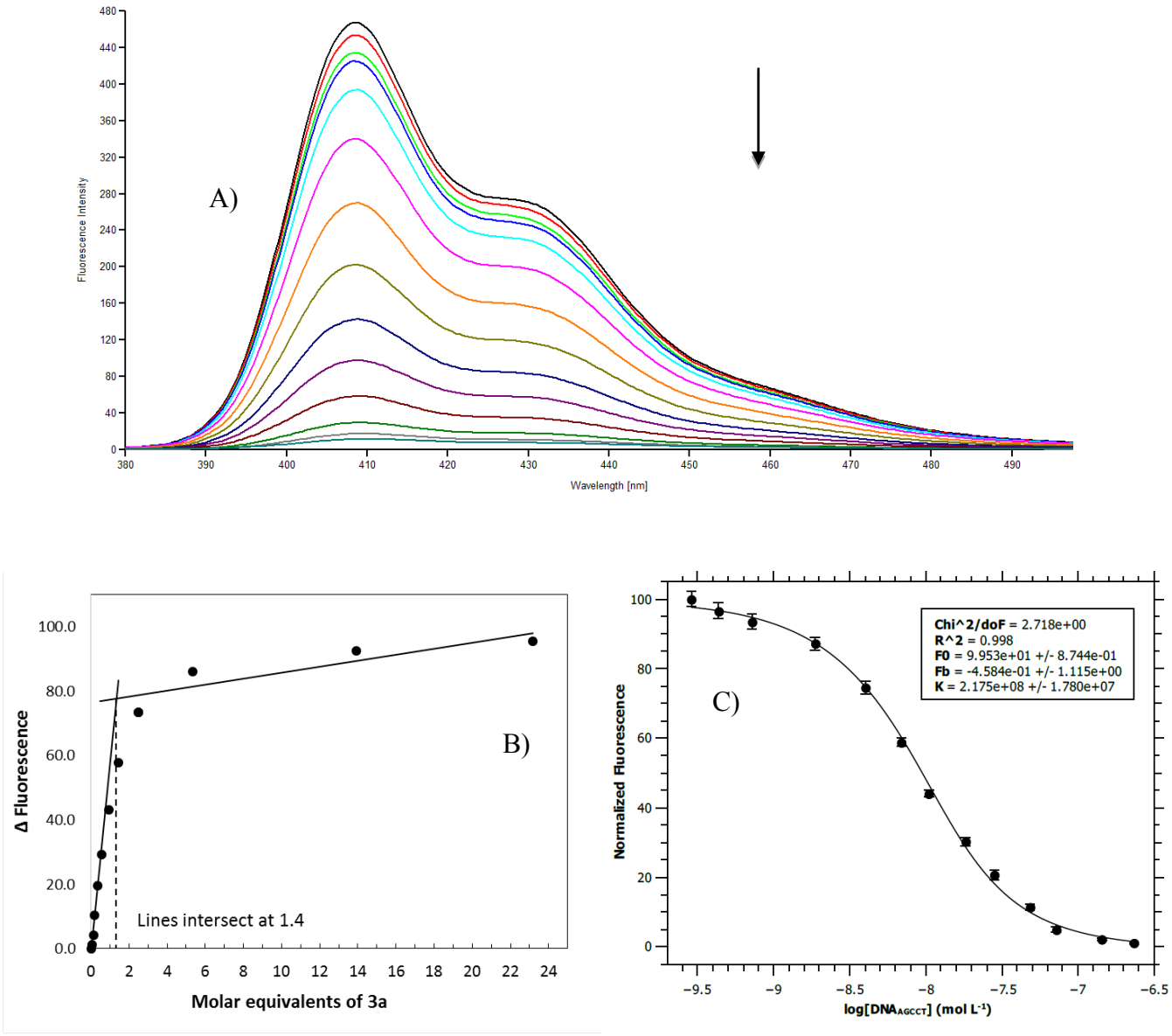


Fig.23 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGAGCCTCAAAAAGAGGCTCG** hairpin sequence; [**3a**] = 5.0 x 10^{-8} mol L^{-1}, [DNA_{AGCCT}] 0.0, 0.03, 0.04, 0.07, 0.19, 0.40, 0.69, 1.05, 1.81, 2.8, 4.8, 7.2, 14, and 23 x 10^{-8} mol $L^{-1;}$ (B) Titration curve of **3a** against a 5'-CGAGCCTCAAAAAGAGGCTCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-CGAGCCTCAAAAAGAGGCTCG hairpin deoxyoligonucleotide

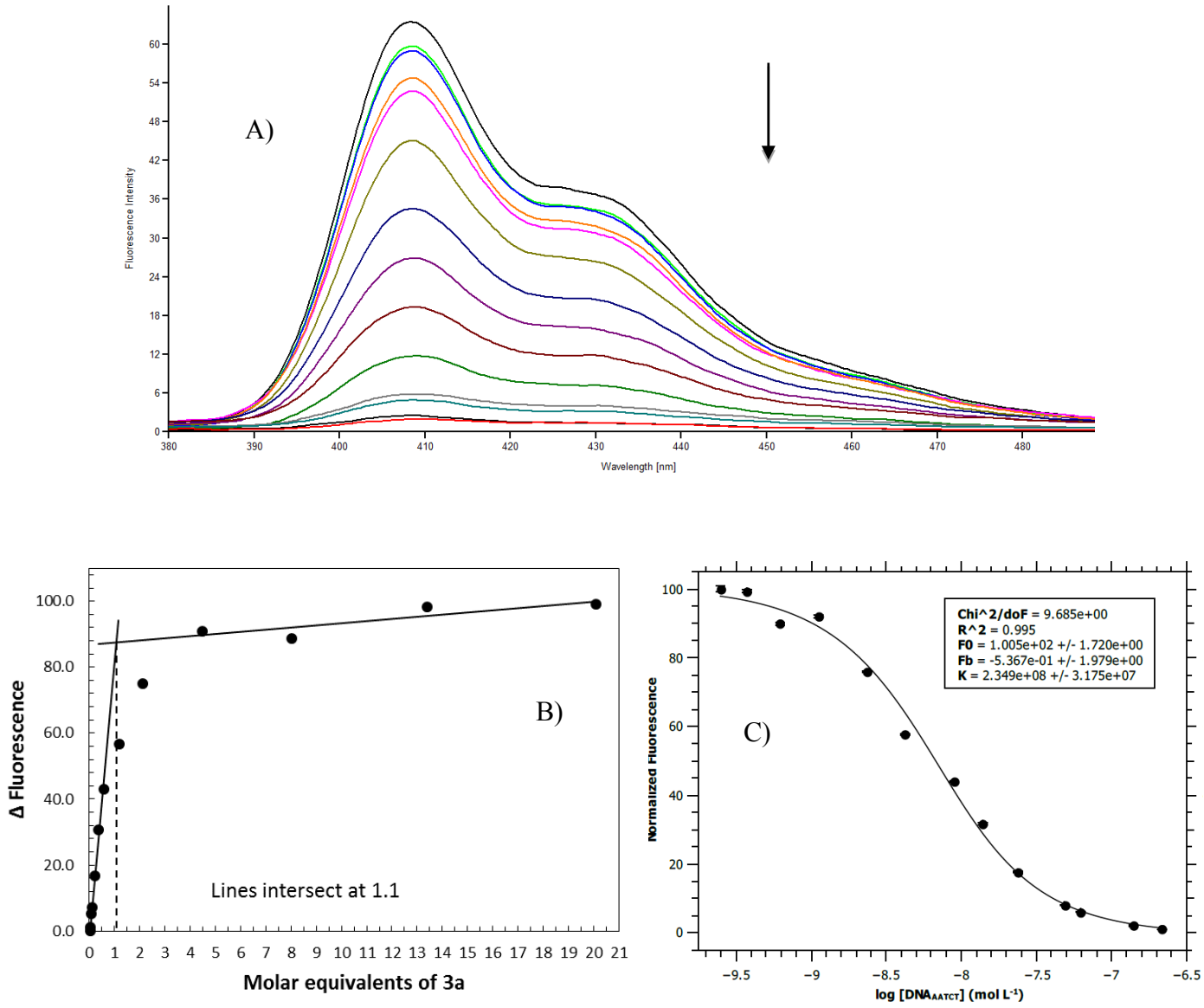


Fig.24 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGAATCTCAAAAAGAGATTCG** hairpin sequence; [**3a**] = 5.0 x 10^{-9} mol L^{-1}, [DNA_{AATCT}] 0.0, 0.02, 0.04, 0.06, 0.11, 0.24, 0.42, 0.90, 1.4, 2.4, 4.9, 6.2, 14, and 22 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'-CGAATCTCAAAAAGAGATTCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'-CGAATCTCAAAAAGAGATTCG hairpin deoxyoligonucleotide

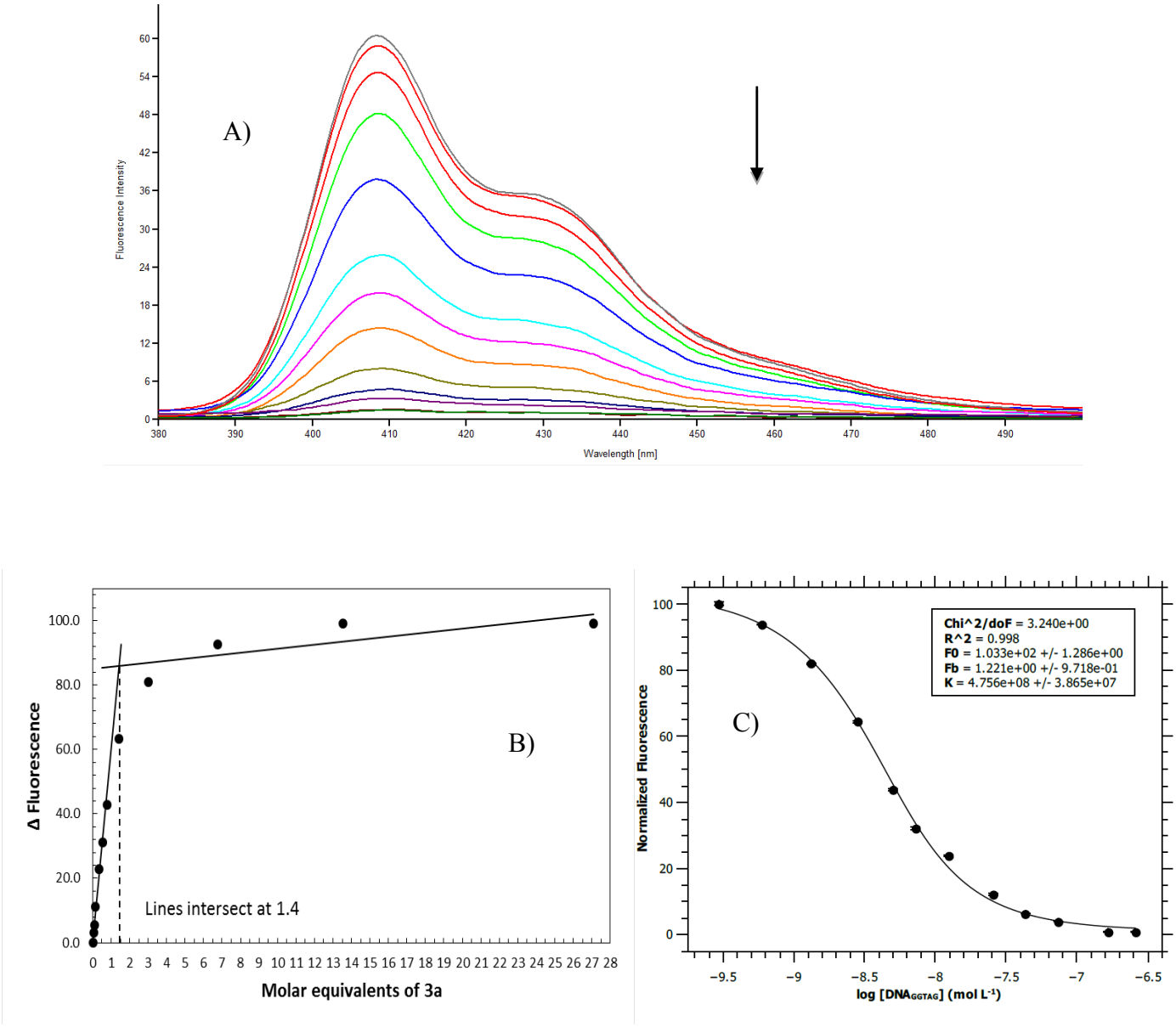


Fig.25 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGGGTAGCAAAAAGCTACCCG** hairpin sequence; [**3a**] = 5.0 x 10^{-9} mol L^{-1}, [DNA_{AATCT}] 0.0, 0.03, 0.06, 0.13, 0.28, 0.50, 0.72, 1.2, 2.6, 4.3, 7.4, 17, and 26 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'- CGGGTAGCAAAAAGCTACCCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'- CGGGTAGCAAAAAGCTACCCG hairpin deoxyoligonucleotide

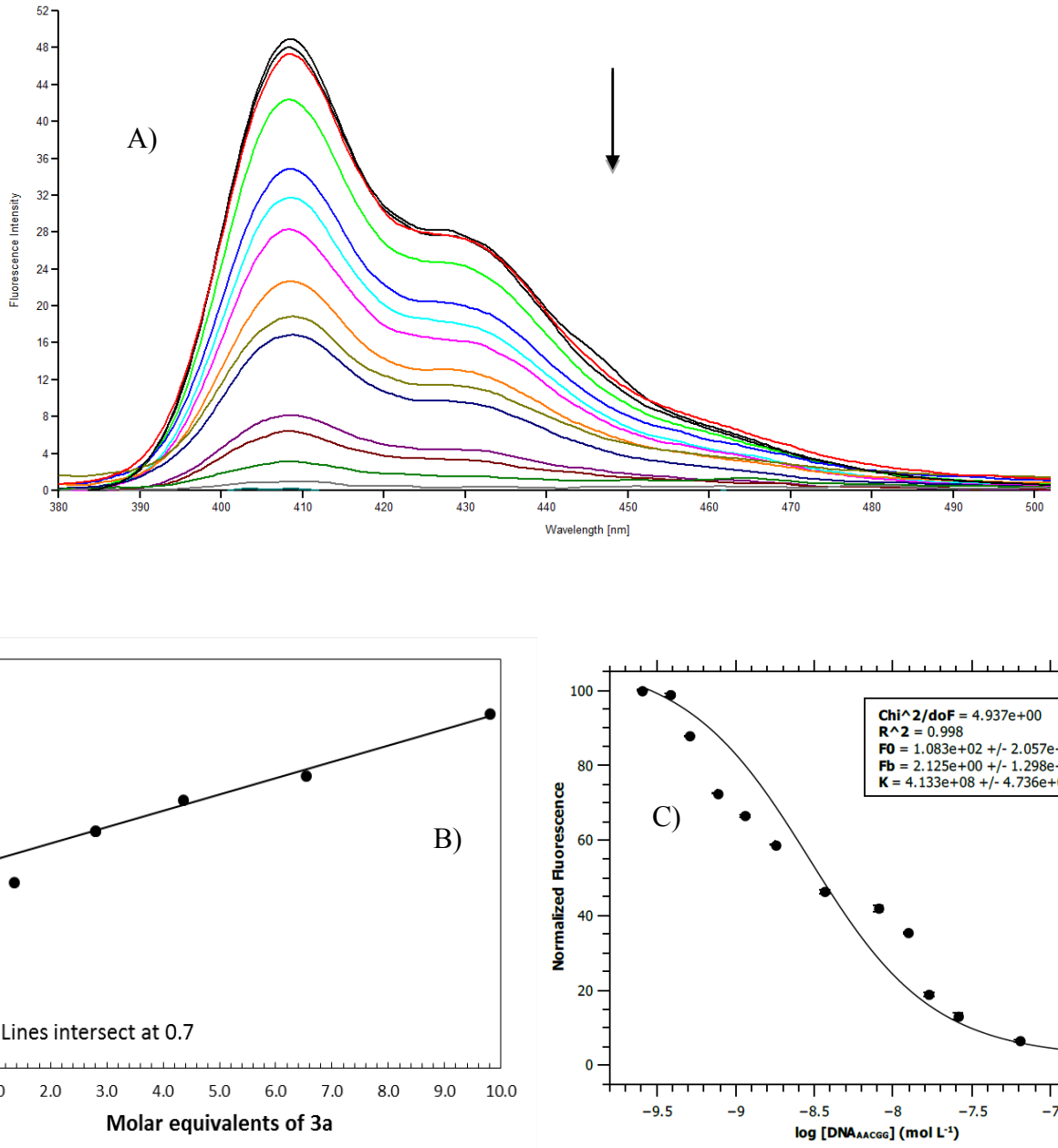


Fig.26 (A) Fluorescence spectra of **3a** in the presence of varying concentrations of 5'-**CGAACGGCAAAAAGCCGTTCG** hairpin sequence; [**3a**] = 5.0 x 10^{-9} mol L^{-1}, [DNA_{AATCT}] 0.00, 0.035, 0.070, 0.11, 0.14, 0.29, 0.32, 0.39, 0.47, 0.56, 0.74, 0.91, 1.08, 1.48, 1.76, 2.46, 3.52, 5.28, 8.80, 12.31, 15.83, 22.87, 28.14, and 36.94 x 10^{-8} mol L^{-1}; (B) Titration curve of **3a** against a 5'- CGAACGGCAAAAAGCCGTTCG hairpin sequence; (C) Least Squares Fitting analysis of fluorescence spectra of **3a** with CT-DNA 5'- CGAACGGCAAAAAGCCGTTCG hairpin deoxyoligonucleotide.

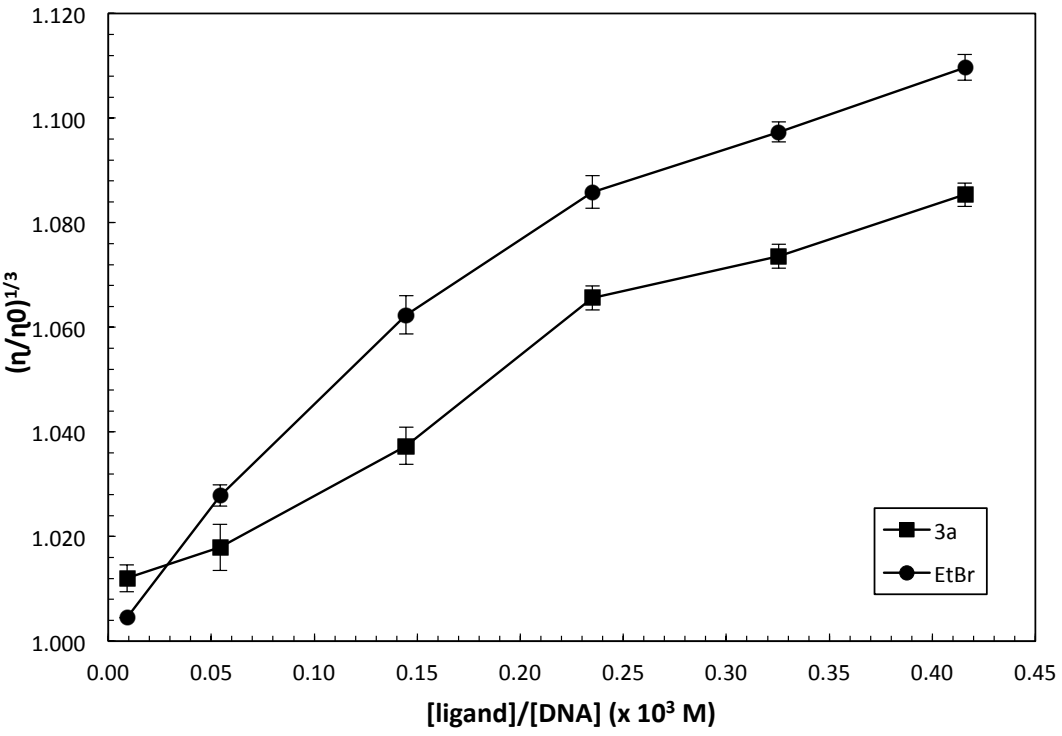


Fig. 27. Effect of increasing amount of **3a** (■) and EB (●) on the relative viscosity of CT-DNA. EB (●): [CT-DNA] = 4.81 x 10^{-4} M, [EB] = 0.435, 2.61, 6.96, 11.3, 15.7, and 20.0 x 10^{-5} M; **3a** (■): [CT-DNA] = 4.81 x 10^{-4} M, [**3a**] = 0.776, 2.72, 6.60, 10.5, 14.4, and 18.2 x 10^{-5} M.

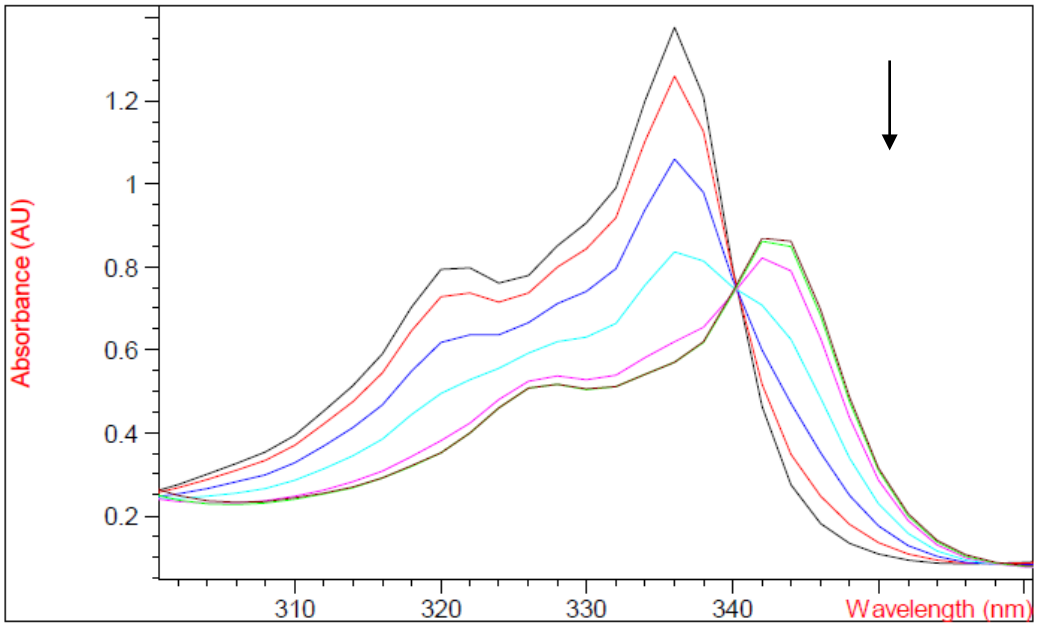


Fig.28. UV spectra of **3a** in the absence and presence of increasing amounts of CT-DNA. [**3a**] = 4.08 x 10^{-5} mol L^{-1}; [CT-DNA] = 0.00 10.44, 31.26, 62.32, 103.42, 164.42, 234.61, and 313.57 x 10^{-6} mol L^{-1}; Peak shift: 336 → 342

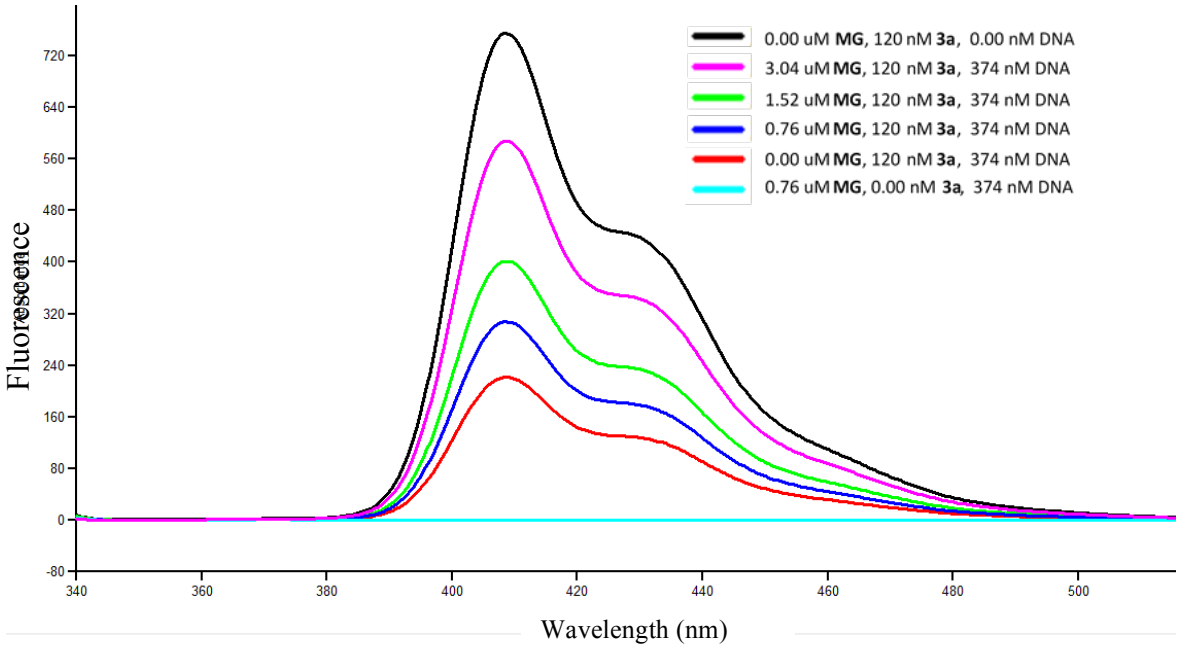


Fig.29. Fluorescence spectra of **3a** in the presence of **CT-DNA** and varying concentrations of Methyl Green (**MG**); λ_{ex} = 330 nm, and λ_{em} = 405 nm

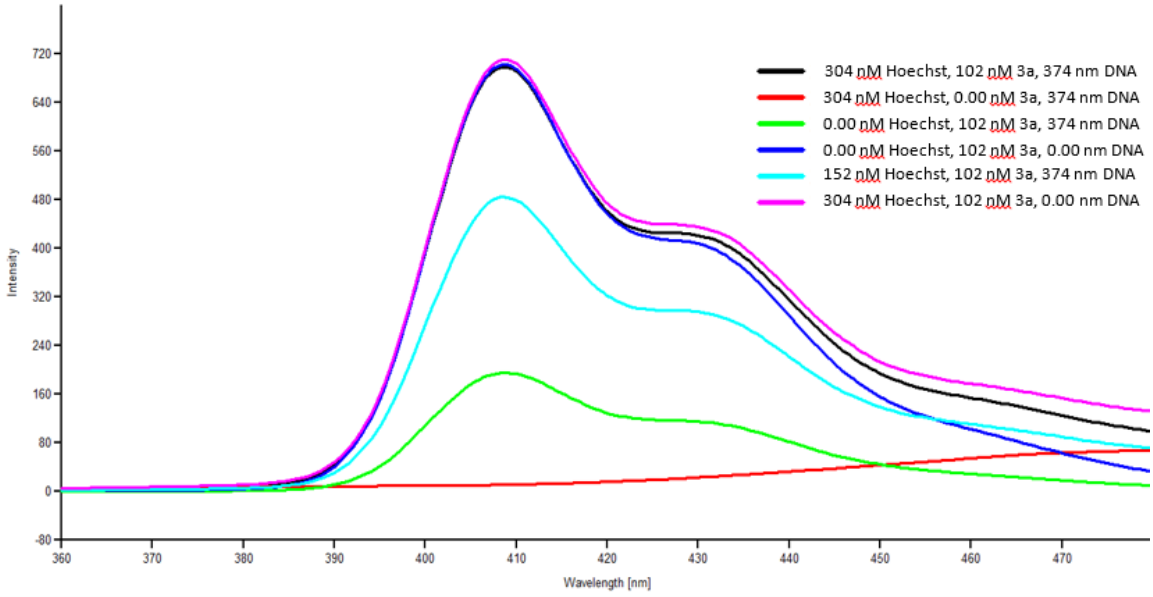


Fig. 30. Fluorescence spectra of **3a** in the presence of **CT-DNA** and varying concentrations of Hoechst 33342; λ_{ex} = 330 nm, and λ_{em} = 405 nm

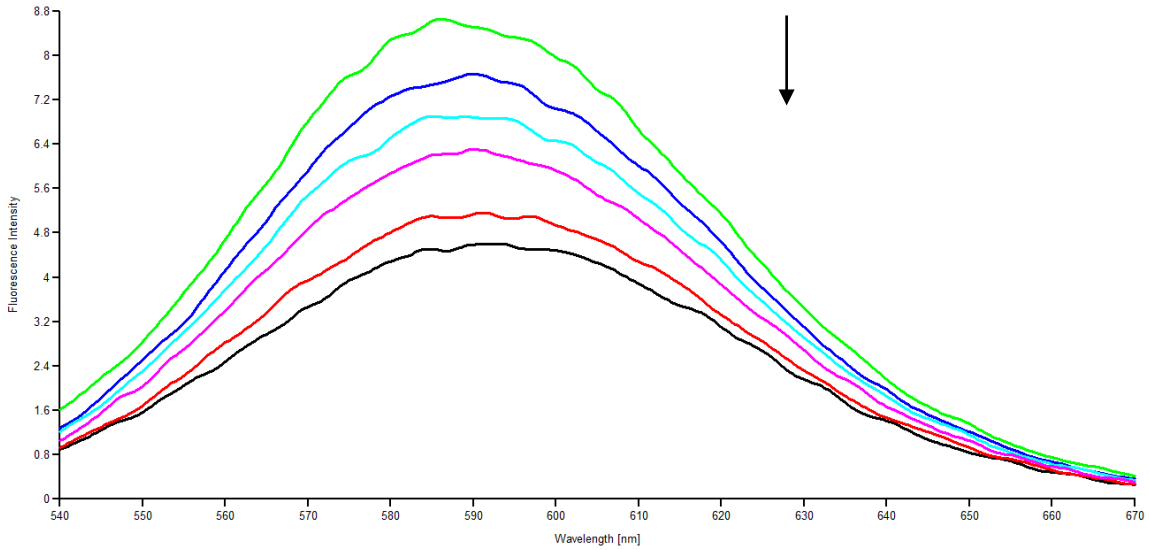


Fig.31 Fluorescence spectra of Ethidium Bromide and poly (dA) • poly (dT) in the presence of varying concentrations of **3a**; [CT-DNA] = 1.08x 10^{-6} mol L^{-1}, [EtBr] = 2.07 x 10^{-6} mol L^{-1}, **[3a]** = 0.00, 0.088, 0.18, 0.35, 0.80, and 1.42 x 10^{-6} mol L^{-1}.

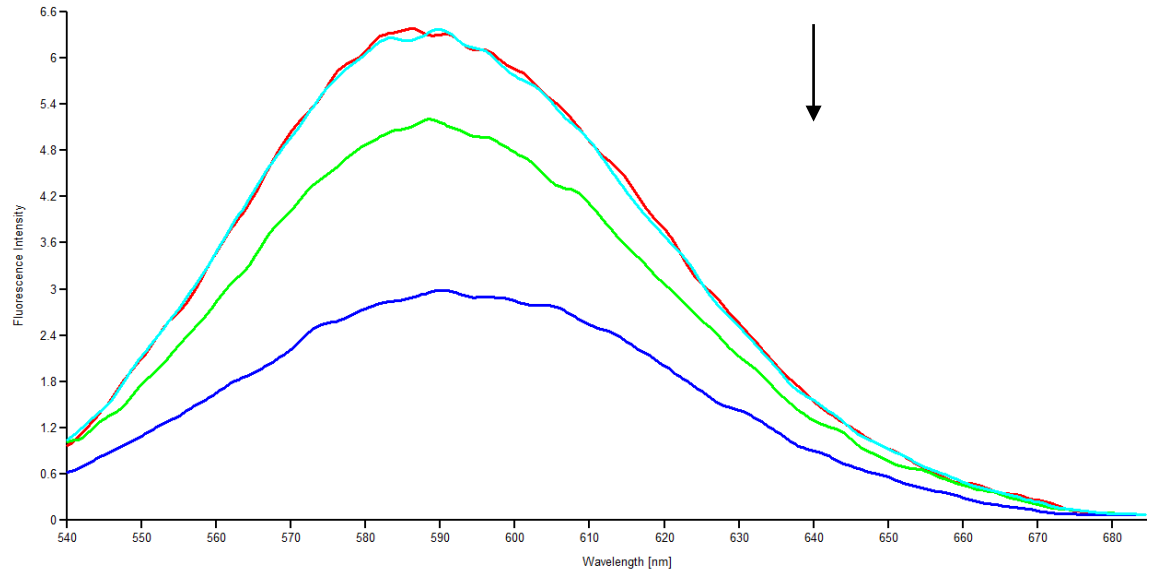


Fig.32. Fluorescence spectra of Ethidium Bromide and poly (dA)•$[poly(dT)]_2$ in the presence of varying concentrations of **3a**; [CT-DNA] = 3.24 x 10^{-9} mol L^{-1}, [EtBr] = 1.38 x 10^{-6} mol L^{-1}, **[3a]** = 0.00, 0.30, 1.50, and 4.51 x 10^{-6} mol L^{-1}.

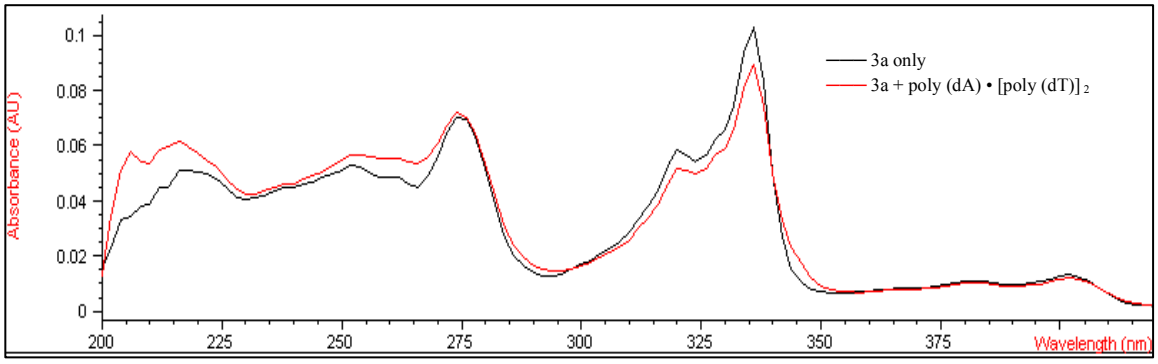


Fig.33a. UV spectra of **3a** (3.93×10^{-6} M; red line) and poly (dA) • [poly (dT)]$_2$ (1.18×10^{-6} M; black line)

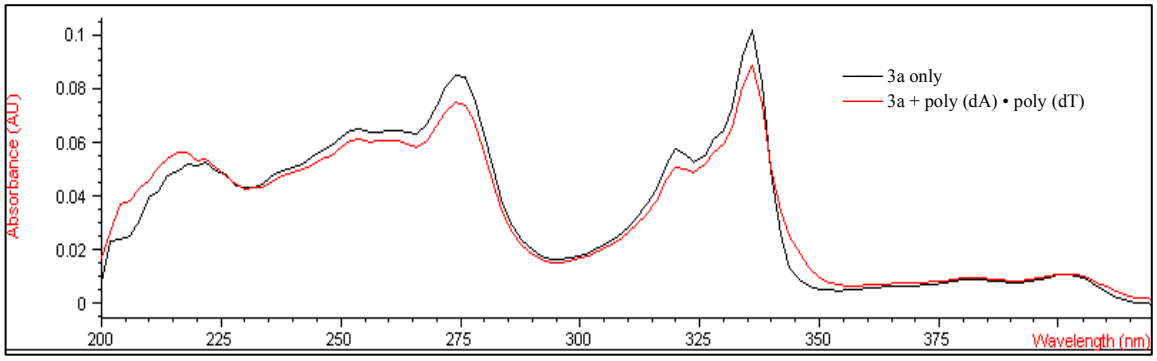


Fig.33b. UV spectra of **3a** (3.93×10^{-6} M; red line) and poly (dA) • poly (dT) (1.84×10^{-6} M; black line)

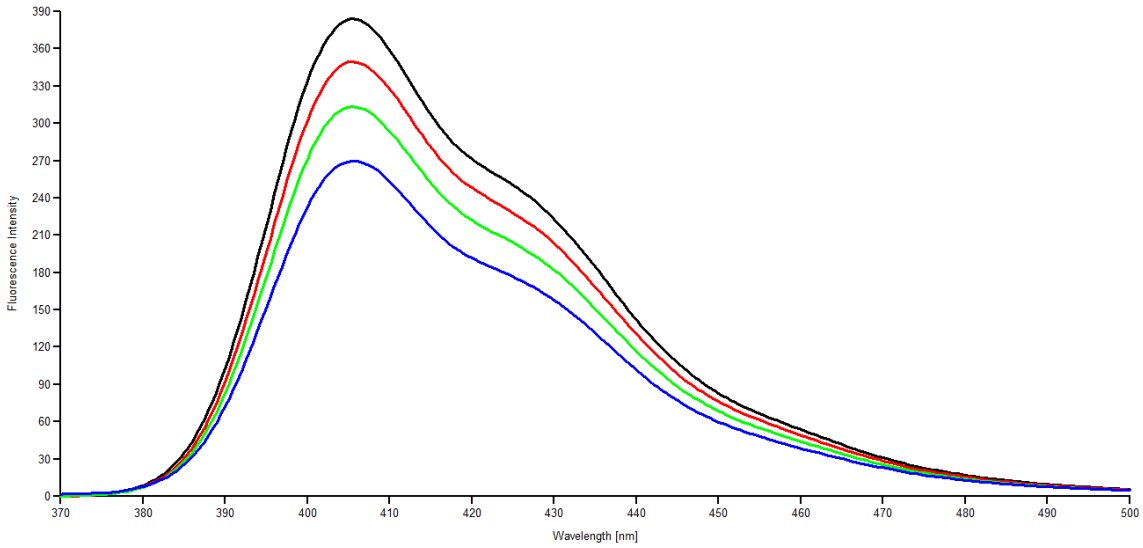


Fig.34. Fluorescence spectra of **3d** in the presence of varying concentrations of poly (dT); [**3d**] = 4.03 x 10^{-8} mol L^{-1}, [$DNA_{poly(dT)}$] = 0.00, 3.29, 11.51, and 20.56 x 10^{-6} mol L^{-1}

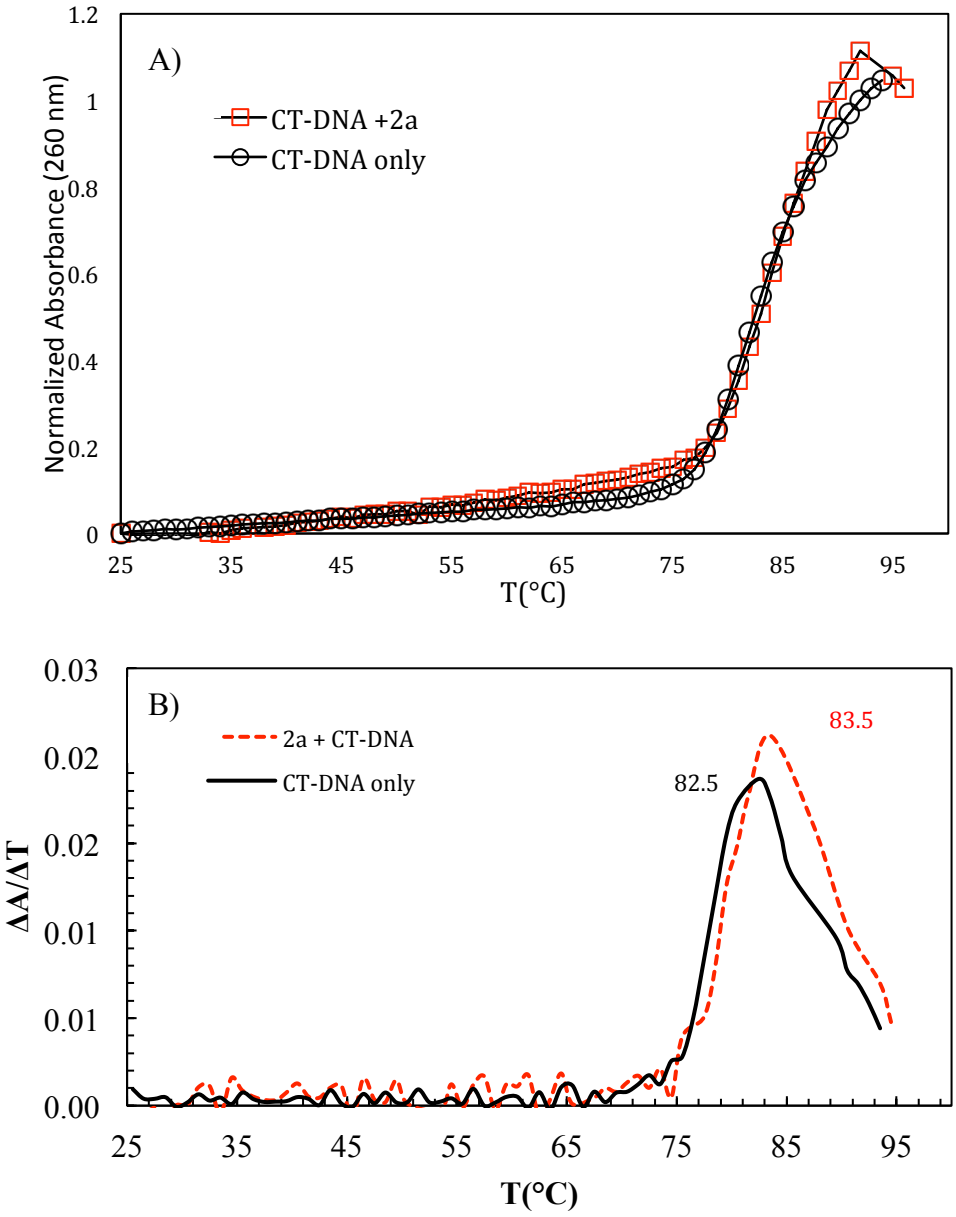


Fig. 35. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **2a** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **2a**; [CT-DNA] = 6.55 x 10^{-5} M; **[2a]** = 1.33 x 10^{-5} M.

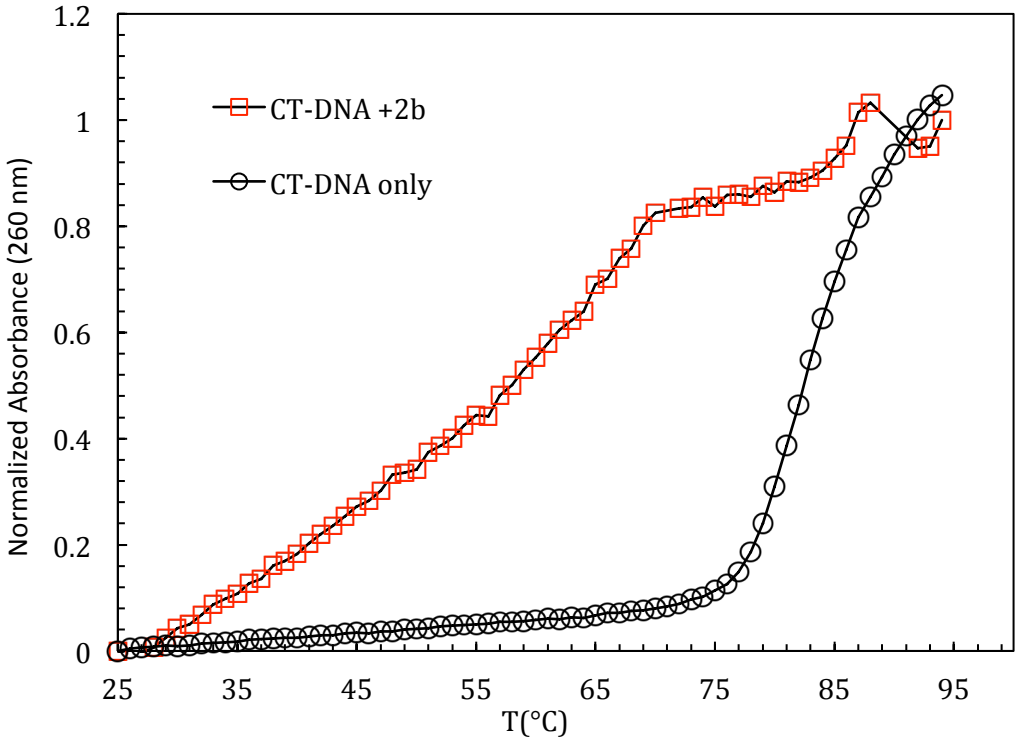


Fig. 36. UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **2b** (red square)

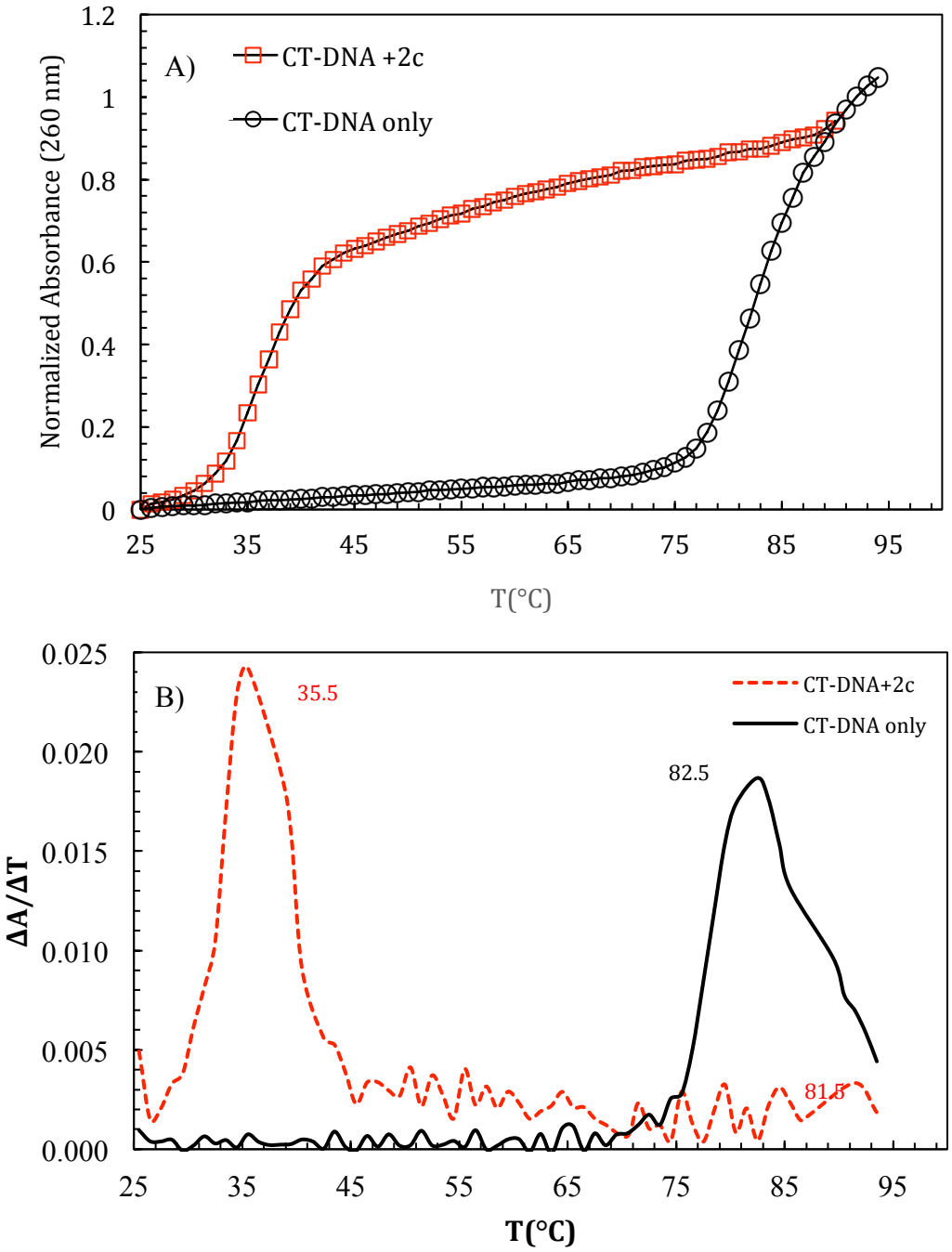


Fig.37. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **2c** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **2c**; [CT-DNA] = 6.55 x 10^{-5} M; **[2c]** = 1.33 x 10^{-5} M.

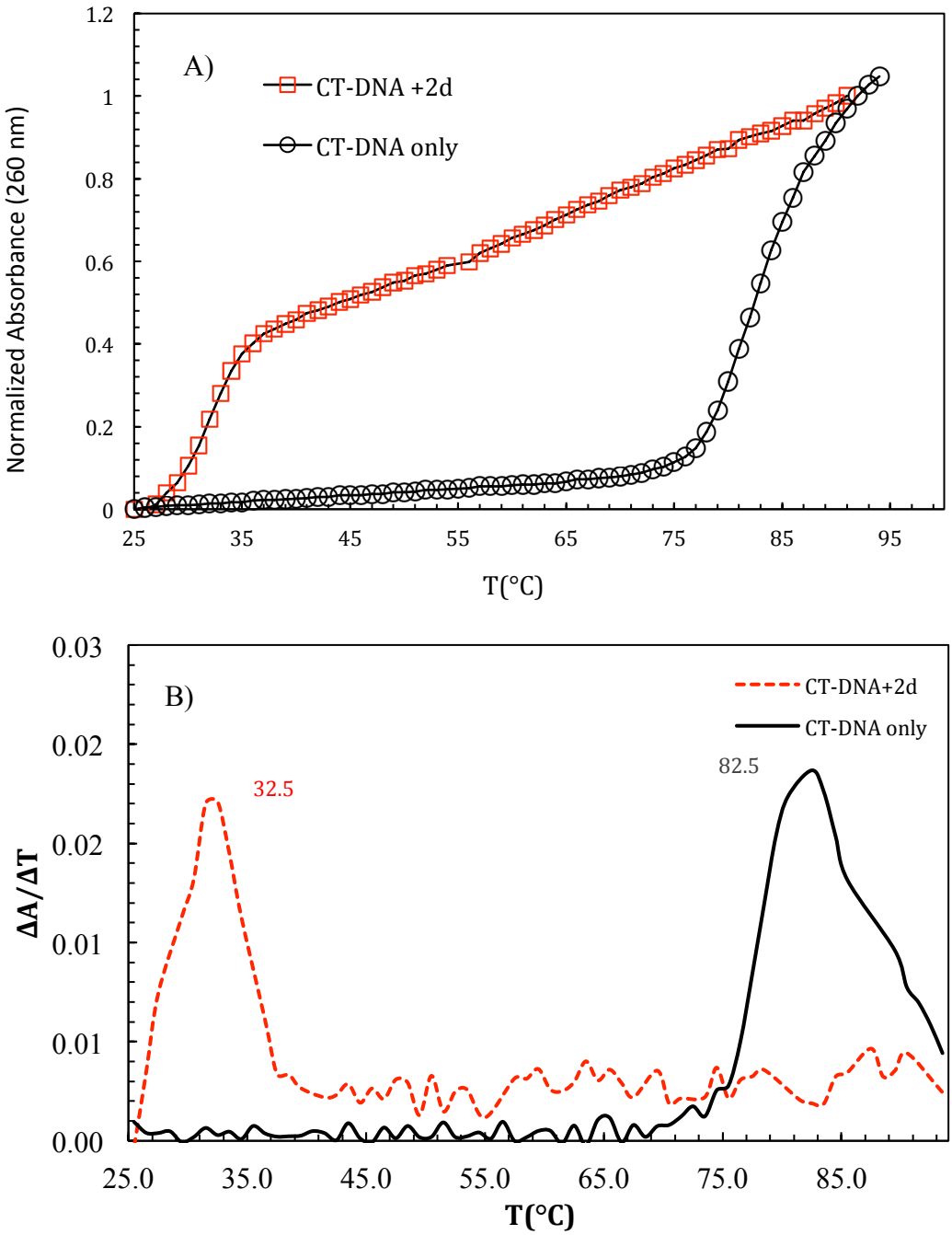


Fig.38. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **2d** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **2d**; [CT-DNA] = 6.55 x 10^{-5} M; **[2d]** = 1.32 x 10^{-5} M.

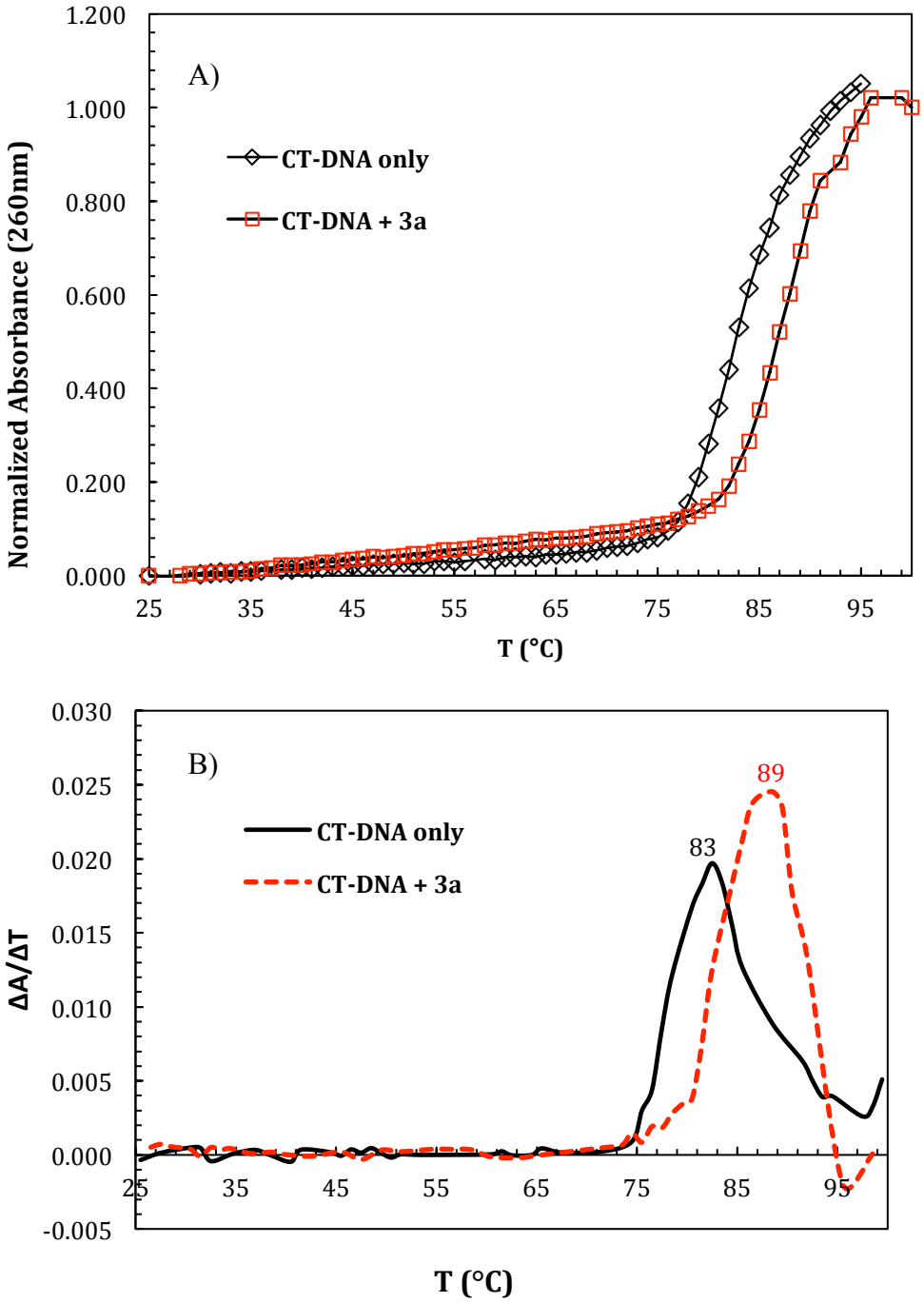


Fig.39. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **3a** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **3a**; [CT-DNA] = 7.45 x 10^{-5} M; **[3a]** = 1.42 x 10^{-5} M.

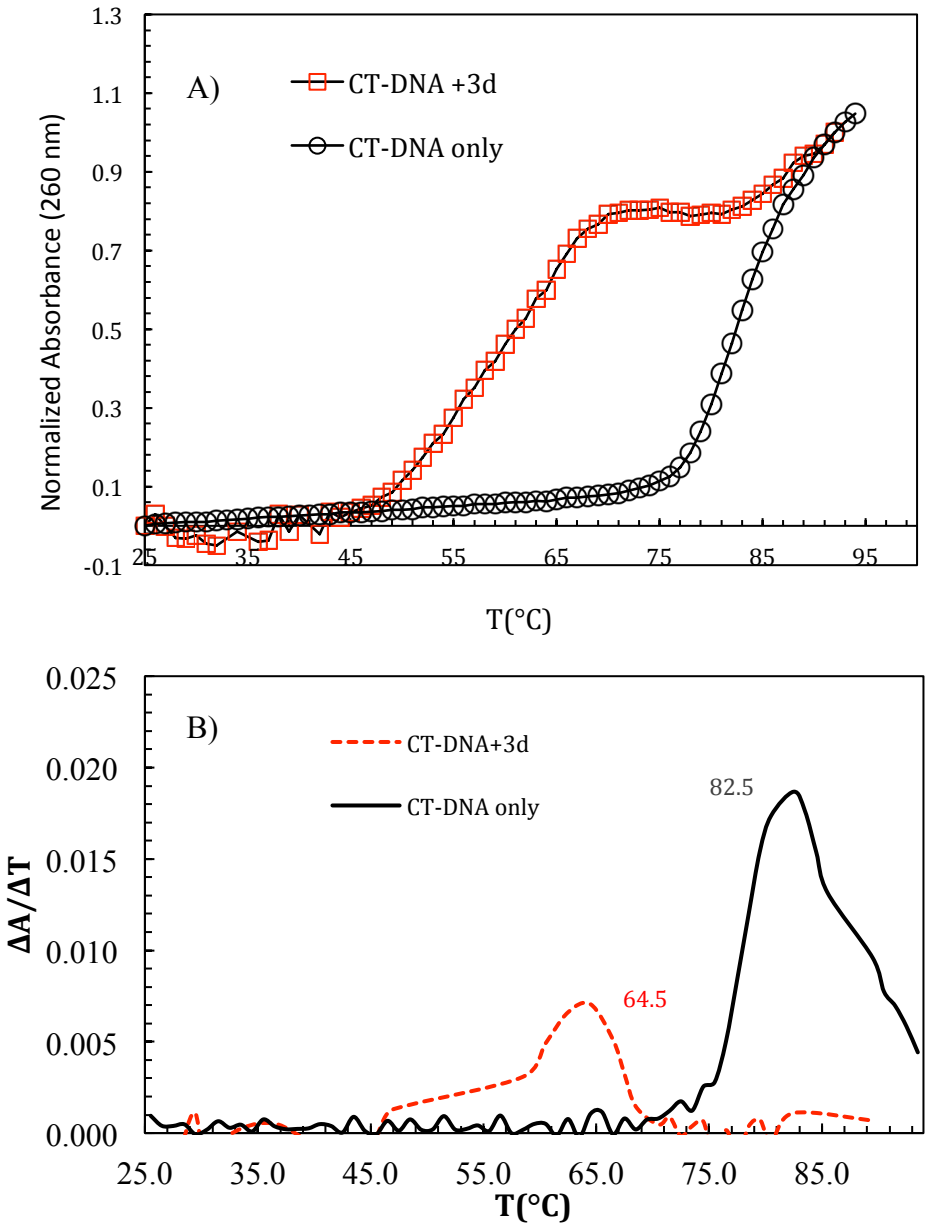


Fig.40. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **3d** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **3d**; [CT-DNA] = 6.55 x 10^{-5} M; **[3d]** = 1.32 x 10^{-5} M.

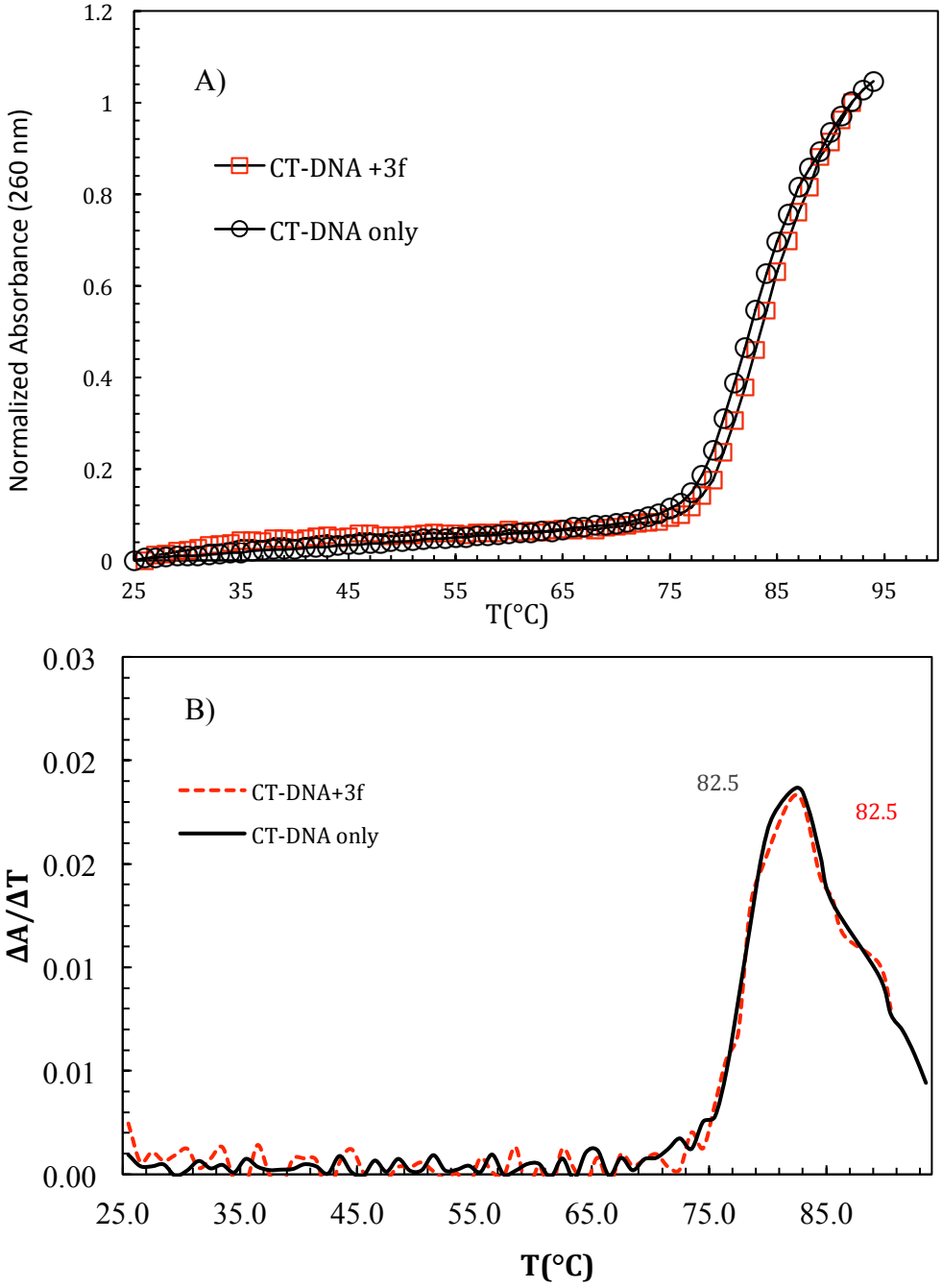


Fig.41. (A) UV thermal denaturation profile of CT-DNA in the absence (black circle) and presence of **3f** (red square); (B) First derivative plots of CT-DNA in the absence (solid line) and presence (dashed line) of **3f**; [CT-DNA] = 6.55 x 10^{-5} M; **[3f]** = 1.33 x 10^{-5} M.

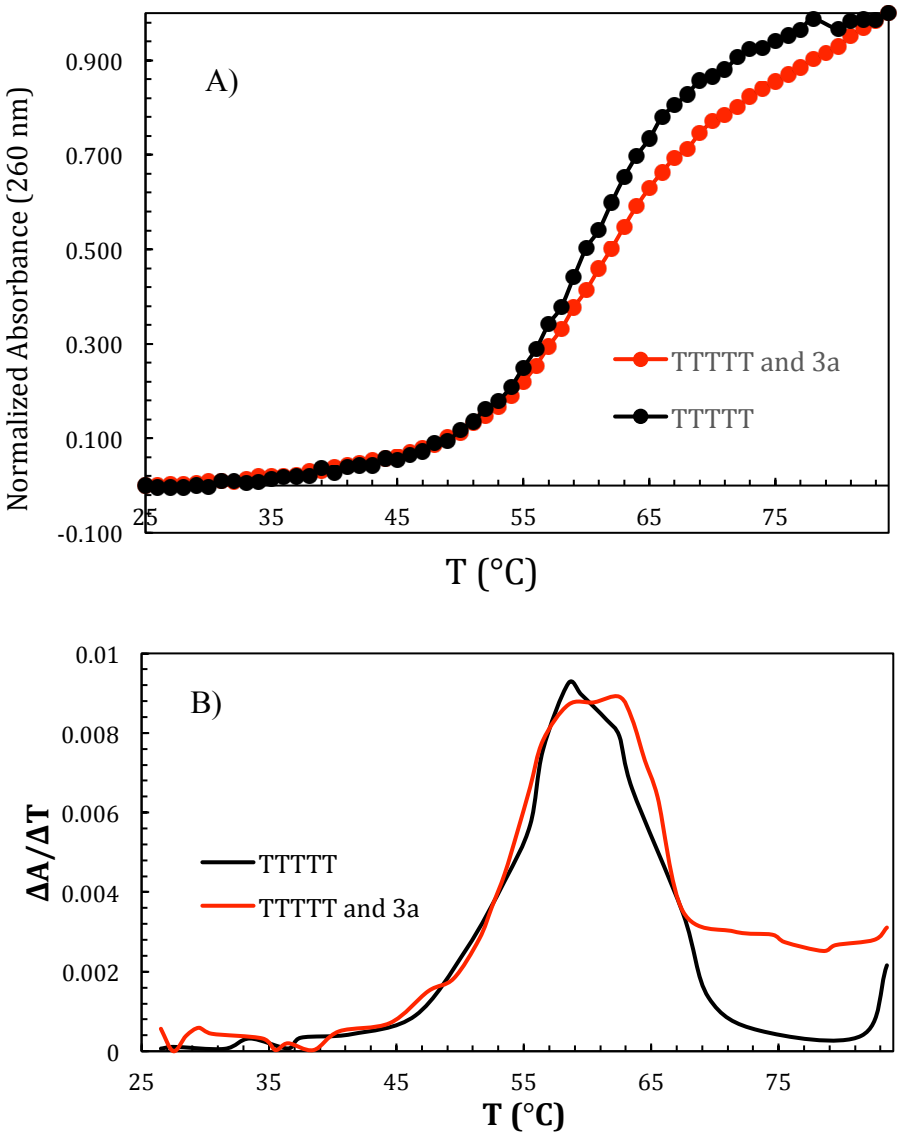


Fig. 42 (A) UV thermal denaturation profile of **5'-CGTTTTTCAA AAAGAAAAACG** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); (B) First derivative plots of CT-DNA in the absence (black line) and presence (red line) of **3a**; $[DNA_{TTTTT}] = 3.4 \times 10^{-6}$ M; $[3a] = 6.1 \times 10^{-7}$ M.

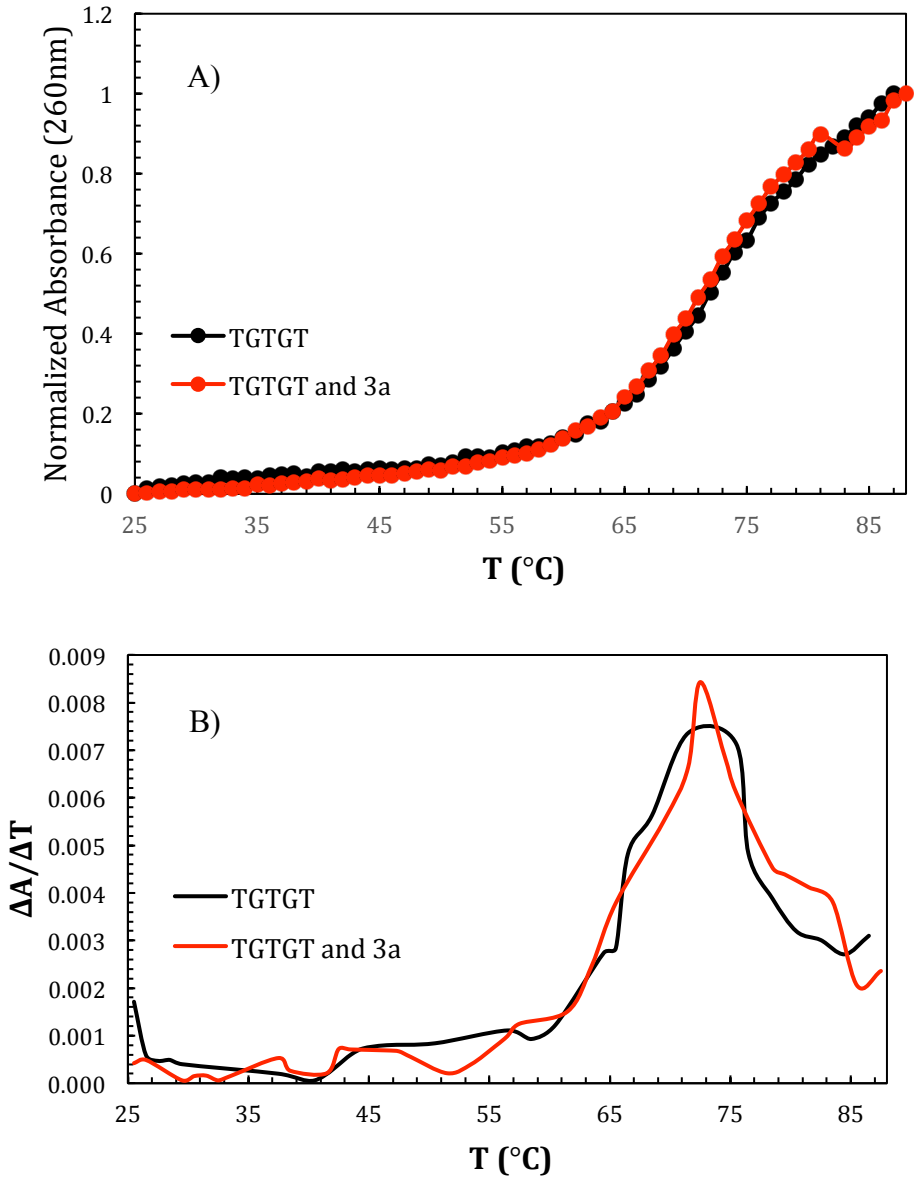
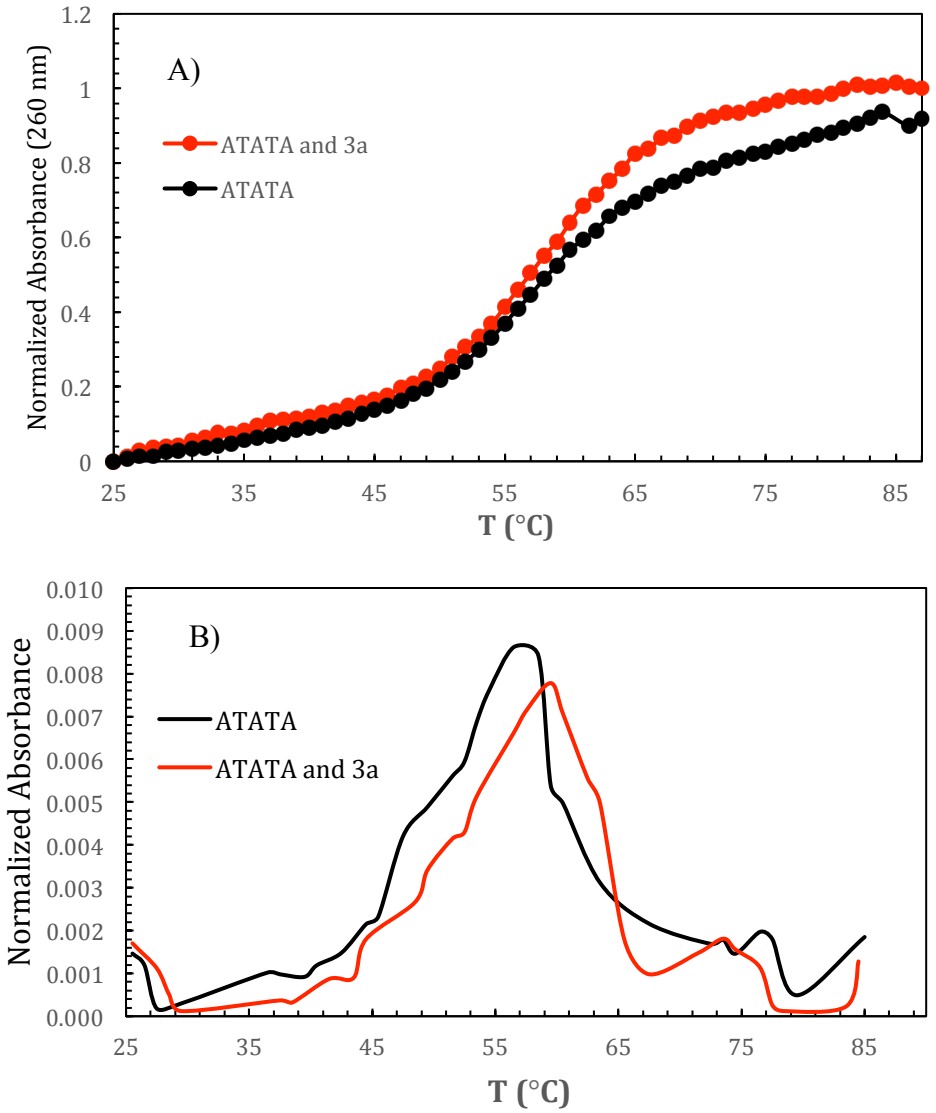


Fig. 43 (A) UV thermal denaturation profile of **5'- CGTGTGTCAAA AAGACACACG** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); (B) First derivative plots of CT-DNA in the absence (black line) and presence (red line) of **3a**; $[DNA_{TGTGT}] = 3.4 \times 10^{-6}$ M; $[3a] = 6.2 \times 10^{-7}$ M.

Fig. 44 (A) UV thermal denaturation profile of **5'- CGATATACAAAAAGTATATCG** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); (B) First derivative plots of CT-DNA in the absence (black line) and presence (red line) of **3a**; $[DNA_{ATATA}] = 3.4 \times 10^{-6}$ M; [3a] = 6.2×10^{-7} M.



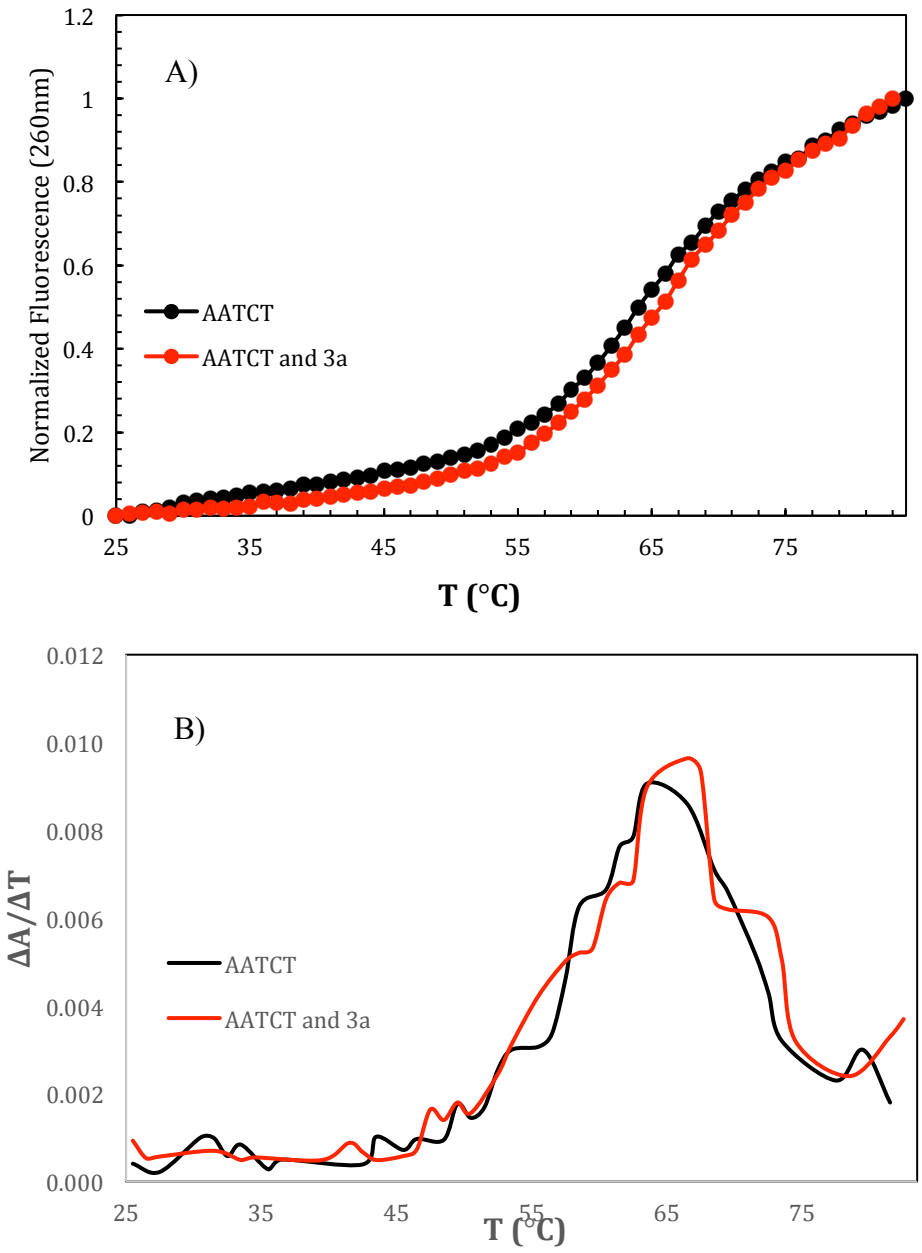


Fig. 45 (A) UV thermal denaturation profile of **5'-** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); (B) First derivative plots of CT-DNA in the absence (black line) and presence (red line) of **3a**; $[DNA_{AATCT}] = 3.4 \times 10^{-6}$ M; $[3a] = 9.0 \times 10^{-7}$ M.

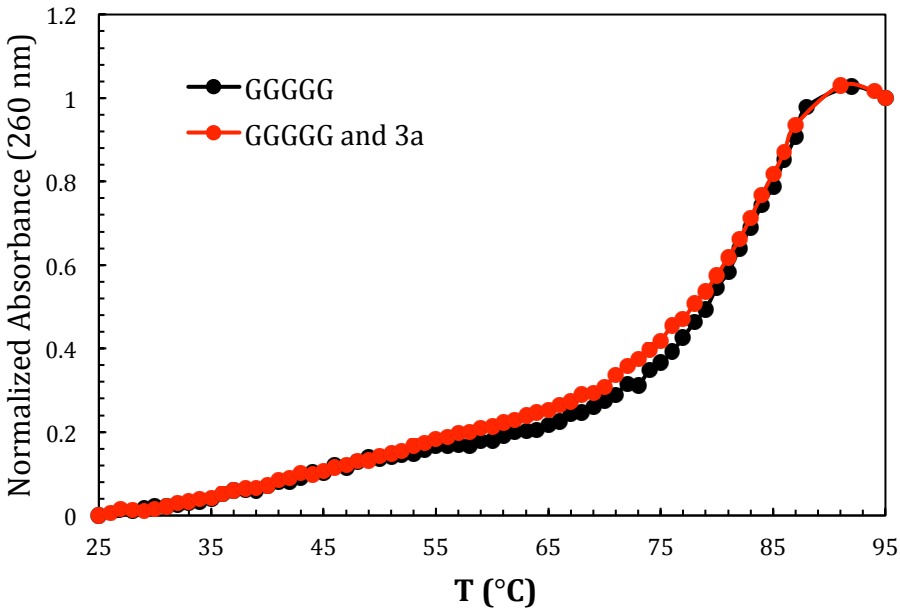


Fig. 46a. UV thermal denaturation profile of **5'-CGGGGGGCAAAAAGCCCCCCG** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); Note: A definite melting transition was difficult to obtain due to high melting temperature profile of this GGGGG hairpin sequence.

hairpin	TGTGT ACACA	TATAT ATATA	AATCT TTAGA	GGGGG CCCCC	AAAAA T TTT T
K_a (x10^{7}M^{-1})	29.2 (±2.6)	36.5 (±5.5)	23.5 (±3.2)	15.7 (±1.6)	17.3 (±1.5)
ΔT_M	-1	3	3	-1	2

hairpin	GGTAG CCATC
K_a (x10^{7}M^{-1})	47.6 (±3.9)
ΔT_M	0

Fig 47. Comparison of fluorescence and melting data for the binding of **3a** to hairpin oligodeoxynucleotides. Obtaining melting transitions for hairpins containing GC-rich sequences was difficult due to the elevated temperatures (~80°C) required for melting and errors thus introduced due to solvent evaporation/evaporative cooling.

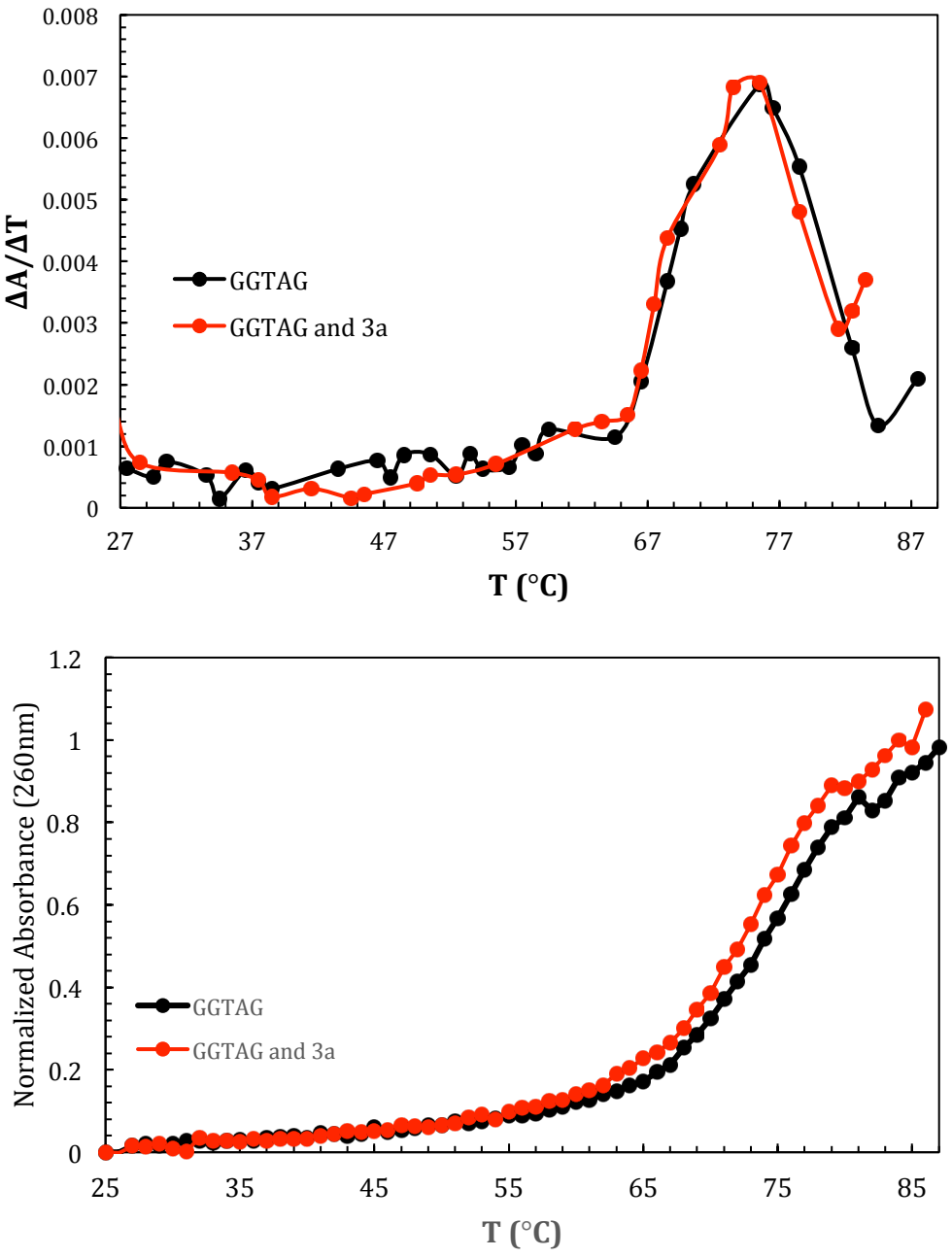


Fig. 46b (A) UV thermal denaturation profile of **5'-CGGGTAGCAAAAAGCTACCCG** hairpin sequence in the absence (black circle) and presence of **3a** (red circle); (B) First derivative plots of CT-DNA in the absence (black line) and presence (red line) of **3a**; $[DNA_{AATCT}] = 3.4 \times 10^{-6}$ M; $[3a] = 9.9 \times 10^{-7}$ M.

Cell Permeability Assay

Cell Permeability Assay details

1. Cells incubated for 3 days
2. After sufficient cell growth, the media from the cells is discarded, and the wells are washed with PBS buffer once
3. Separate solutions of the drug to be tested and the control are prepared in a separate media solution (devoid of hormone growth factors; contains bovine serum albumin)
4. The cells are incubated for an hour
5. The media from the cells is discarded
6. The wells are washed 3 times to get rid of any residual drug lingering outside the cells in the wells
7. The cells are lysed to expose the cells' contents
8. The solutions are centrifuged; supernatant is collected.
9. Perform a fluorescence detection

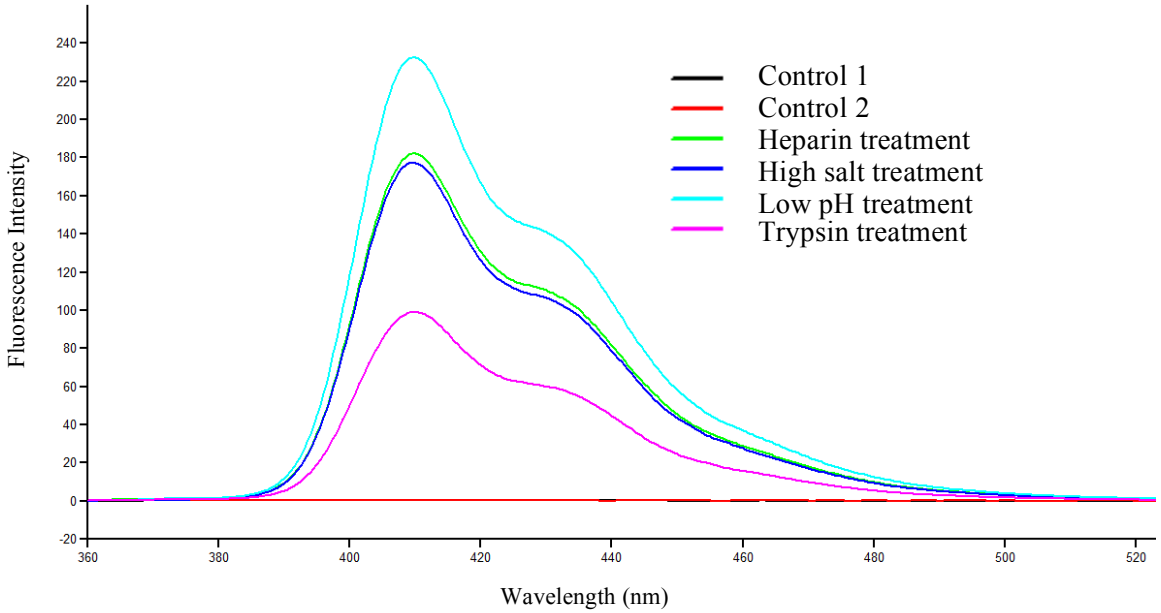


Fig.48. Fluorescence detection of **3a** in Hep2G cells incubated with **3a** for 4.5 hours.

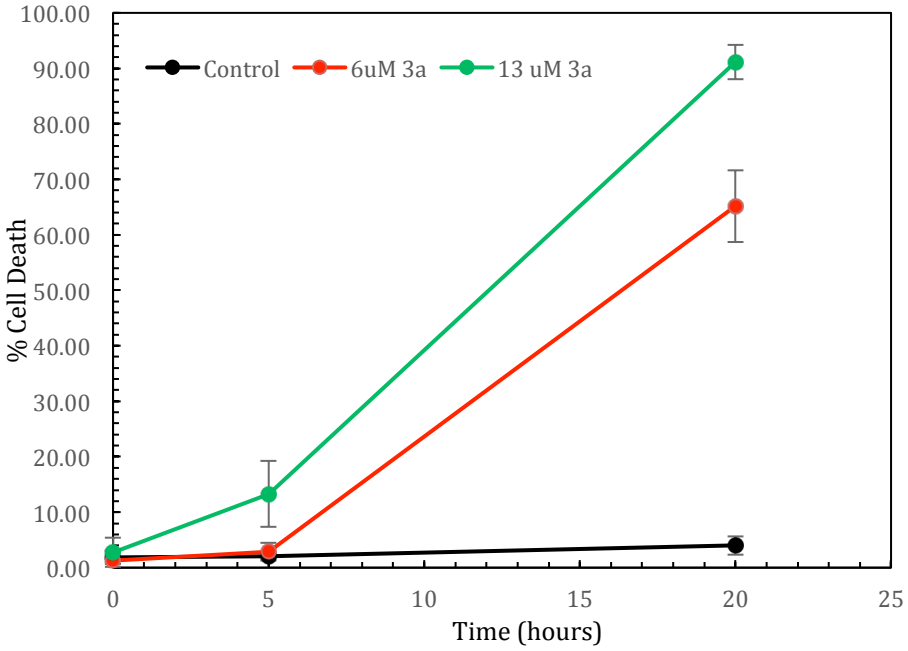


Fig.49. % cell death of 0.4% Trypan blue treated monocytes at 0, 5, and 19.5 hours. Cells were treated with no drug (control), 6uM and 13uM of **3a.**

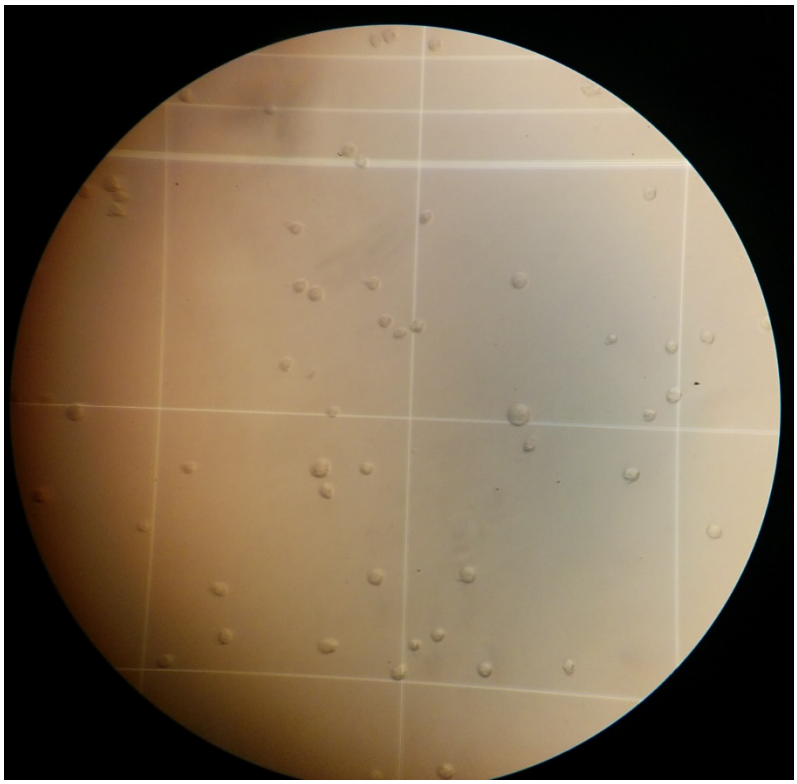


Fig.50. Monocytes after **5 hour** incubation; 0 uM dose of **3a** (0.4% Trypan blue dye treatment)

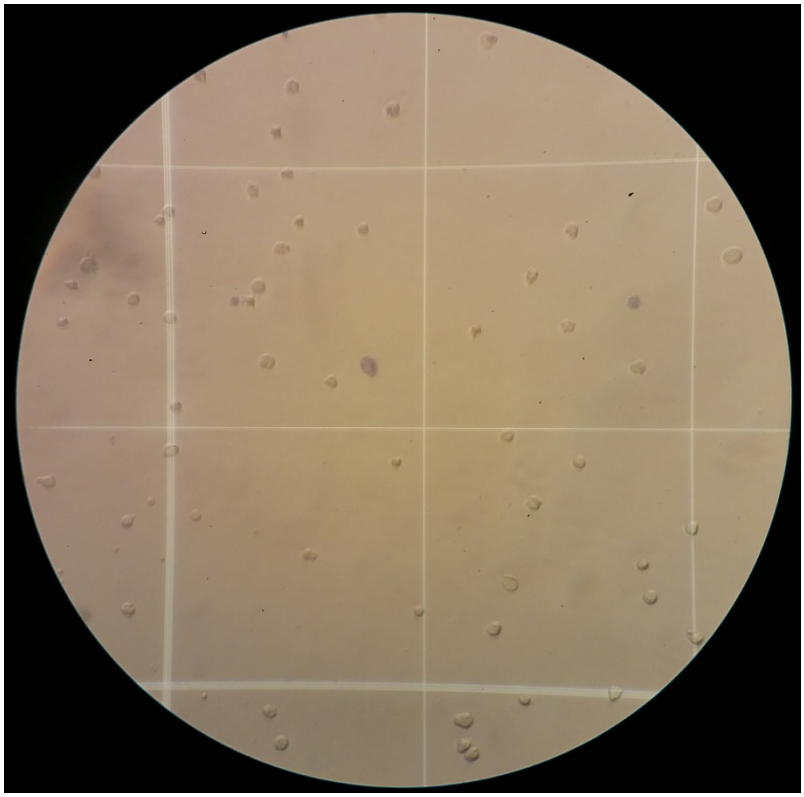


Fig.51. Monocytes after **5 hour** incubation; ~6 uM dose of **3a** (0.4% Trypan blue dye treatment)

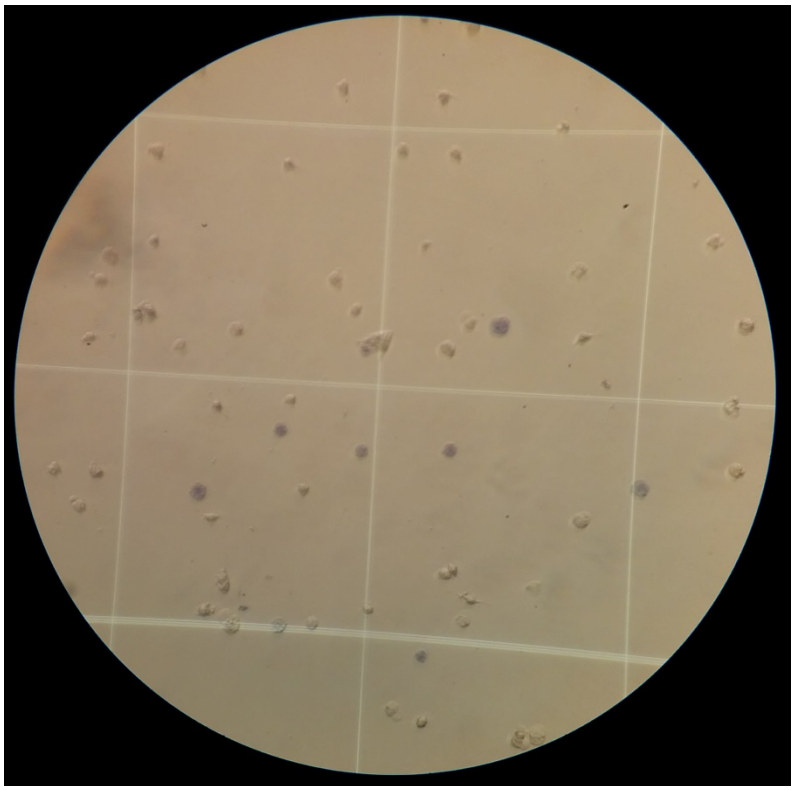


Fig. 52. Monocytes after **5 hour** incubation; ~13uM dose of **3a** (0.4% Trypan blue dye treatment)

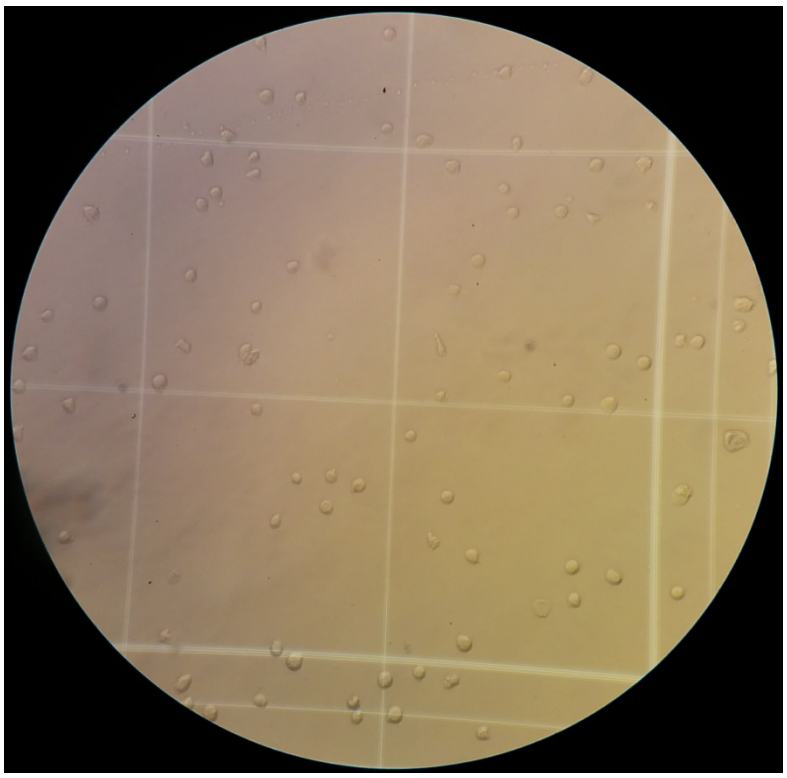


Fig. 53. Monocytes after **19.5 hours** incubation; 0 uM dose of **3a** (0.4% Trypan blue dye treatment)

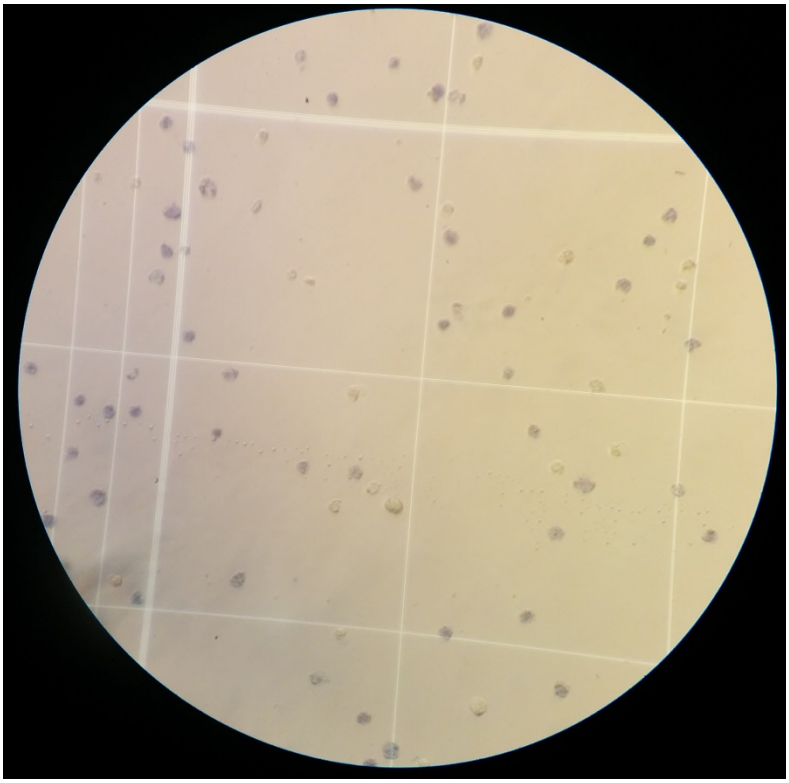


Fig.54. Monocytes after **19.5 hours** incubation; ~6 uM dose of **3a** (0.4% Trypan blue dye

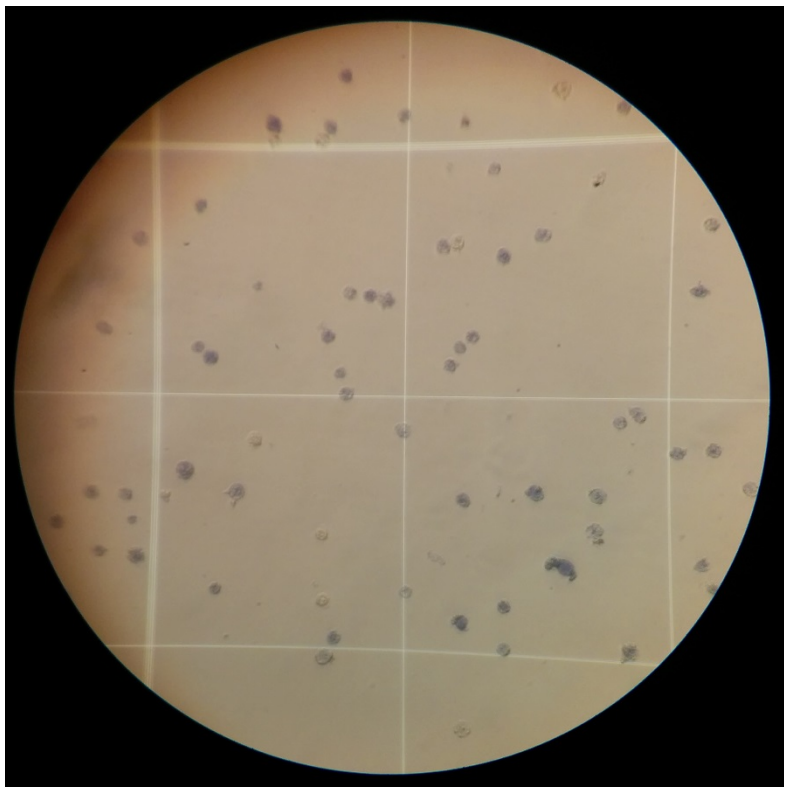


Fig.55. Monocytes after **19.5 hours** incubation; ~13uM dose of **3a** (0.4% Trypan blue dye treatment)