Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Targeting abasic site-containing DNA with Annelated Quinolizinium Derivatives: The Influence of Size, Shape and Substituents

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Electronic Supporting Information

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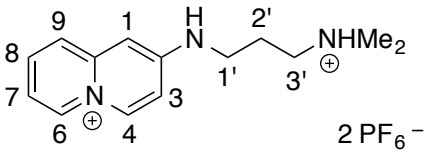
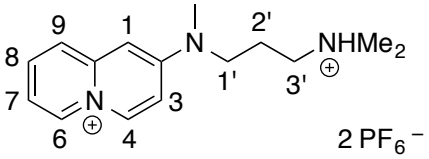
1. Synthesis

General Procedure for the synthesis of (aminoalkyl)aminoquinolizinium derivatives (GP1). A solution of the corresponding haloquinolizinium derivative (1 molar equiv.) and the diamine (3 molar equiv.) in 2-PrOH was stirred under reflux for 2 h or 3 h, respectively. After cooling the reaction mixture to room temperature the solvent was removed in vacuo. Water (2 ml) was added to the red-brown viscous residue, the suspension was filtered (and for derivatives **1e** and **1f** the filtrate was adjusted to a pH of 4 with acetic acid). An aq. solution of $NaPF_6$ (6 molar equiv.) was added while the solution was stirred at 70 °C. A solid precipitated, and the suspension was cooled to room temperature. The precipitate was separated by filtration, washed three times with ice-cold water and recrystallized from water/AcOH (**1e**, **1f**) or MeOH/H_2O (**1g**, **1h**).



1e

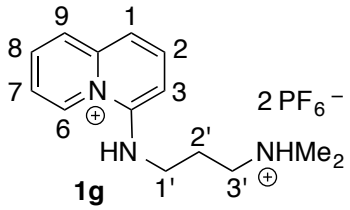
2-[(3-Dimethylammoniopropyl)amino]quinolizinium bis(hexafluorophosphate) (1e): According to GP1, 2-bromoquinolizinium tetrafluoroborate (**1b**) (177 mg, 600 µmol) and *N*,*N*-dimethyl-1,3-propanediamine (184 mg, 1.80 mmol, 225 µl) were stirred in 2-PrOH (7.5 ml) for 2 h to give orange-colored needles (108 mg, 207 µmol, 33%); m.p. = 200–202 °C (dec.). – ^{1}H-NMR (400 MHz, CD_3CN): δ = 2.00–2.07 (m, 2 H, 2'-H), 2.84 (s, 6 H, $N(CH_3)_2$), 3.15–3.19 (m, 2 H, 3'-H), 3.37–3.42 (m, 2 H, 1-H), 6.60 (br s, 1 H, N^+H), 7.01 (d, ^4J = 3 Hz, 1 H, 1-H), 7.16 (dd, ^3J = 7 Hz, ^4J = 3 Hz, 1 H, 3-H), 7.25 (dt, ^3J = 7 Hz, 1 H, 7-H), 7.72-7.74 (m, 2 H, 8-H, 9-H), 8.31 (d, ^3J = 7 Hz, 1 H, 6-H), 8.39 (d, ^3J = 7 Hz, 1 H, 4-H). – ^{13}C-NMR (100 MHz, CD_3CN): δ = 24.0 (C2'), 40.6 (C1'), 44.2 (2 × $N(CH_3)_2$), 56.6 (C3'), 100.6 (ar-CH), 115.1 (ar-CH), 118.4 (ar-CH), 125.4 (ar-CH), 135.3 (ar-CH), 135.5 (ar-CH), 137.6 (ar-CH), 145.9 (ar-C_q), 153.9 (ar-C_q). – MS (ESI^+): *m*/*z* (%) = 230 (100) $[M - H(PF_6)_2]^+$. – El. Anal. calcd (%) for $C_{14}H_{22}N_3PF_6 \times HPF_6$ (521.3 g/mol): C 32.26, H 4.06, N 8.06; found: C 32.86, H 3.67, N 8.22.



1f

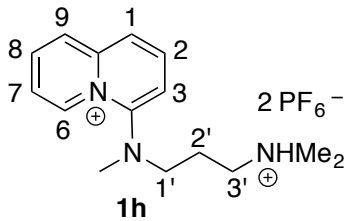
2-[(3-Dimethylammoniopropyl)(methyl)amino]quinolizinium bis(hexafluorophosphate) (1f): According to GP1, 2-bromoquinolizinium tetrafluoroborate (**1b**) (67.6 mg, 200 µmol) and *N*,*N*,*N'*-trimethyl-1,3-propanediamine (69.7 mg, 600 µmol, 87.9 µl) were stirred in 2-

PrOH (2.5 ml) for 3 h to give a light beige-colored solid (13.0 mg, 24.3 µmol, 12%); m.p. = 156–158 °C (dec.). – ^{1}H-NMR (600 MHz, [D$_6$]DMSO): δ = 1.93–1.98 (m, 2 H, 2'-H), 2.78 (s, 6 H, N(CH$_3$)$_2$), 3.10 (t, ^3J = 8 Hz, 2 H, 3'-H), 3.20 (s, 3 H, N$_{ar}$(CH$_3$)), 3.67 (t, ^3J = 7 Hz, 2 H, 1'-H), 7.33-7.35 (m, 2 H, 7-H, 9-H), 7.58-7.59 (m, 1 H, 3-H), 7.78-7.81 (m, 1 H, 8-H), 7.82-7.86 (m, 1 H, 1-H), 8.65 (d, ^3J = 7 Hz, 1 H, 6-H), 8.85 (d, ^3J = 8 Hz, 1 H, 4-H), 9.28 (br s, 1 H, N$^+$H). – ^{13}C-NMR (150 MHz, [D$_6$]DMSO): δ = 21.6 (C2'), 38.1 (N$_{ar}$(CH$_3$)), 42.4 (2 × N(CH$_3$)$_2$), 48.5 (C1'), 54.1 (C3'), 101.6 (ar-CH), 110.7 (ar-CH), 116.8 (ar-CH), 124.1 (ar-CH), 133.6 (ar-CH), 134.1 (ar-CH), 136.8 (ar-CH), 143.2 (ar-C$_q$), 151.9 (ar-C$_q$). – MS (ESI$^+$): *m/z* (%) = 244 (100) [M – H(PF$_6$)$_2$]$^+$. –El. Anal. calcd (%) for C$_{15}$H$_{24}$N$_3$PF$_6$ × HPF$_6$ (535.3 g/mol): C 33.66, H 4.33, N 7.85; found: C 33.04, H 3.87, N 8.13.



1g

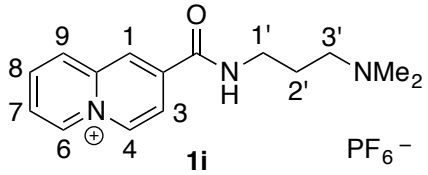
4-[(3-Dimethylammoniopropyl)amino]quinolizinium bis(hexafluorophosphate) (1g): According to GP1 4-chloroquinolizinium (500 mg, 1.99 mmol) and *N*,*N*-dimethyl-1,3-propanediamine (610 mg, 5.97 mmol, 745 µl) were stirred in 2-PrOH (25 ml) for 3 h to give a beige-colored microcrystalline solid (84.0 mg, 224 µmol, 8%); m.p. = 206-208 °C (dec.). – ^{1}H-NMR (400 MHz, CD$_3$CN): δ = 2.11–2.18 (m, 2 H, 2'-H), 2.81 (s, 6 H, N(CH$_3$)$_2$), 3.21 (t, ^3J = 8 Hz, 2 H, 3'-H), 3.58 (t, ^3J = 7 Hz, 2 H, 1'-H), 6.58 (br s, 1 H, N$^+$H), 7.22 (d, ^3J = 9 Hz, 1 H, 3-H), 7.71 (d, ^3J = 8 Hz, 1 H, 1-H), 7.76–7.79 (m, 1 H, 7-H), 7.95–7.99 (m, 1 H, 8-H), 8.16–8.20 (m, 2 H, 2-H, 9-H), 8.65 (d, ^3J = 7 Hz, 1 H, 6-H). – ^{13}C-NMR (100 MHz, CD$_3$CN): δ = 23.8 (C2'), 42.0 (C1'), 44.2 (2 × N(CH$_3$)$_2$), 56.7 (C3'), 106.3 (ar-CH), 116.1 (ar-CH), 122.8 (ar-CH), 127.8 (ar-CH), 128.8 (ar-CH), 134.0 (ar-CH), 139.2 (ar-CH), 143.7 (ar-C$_q$), 148.4 (ar-C$_q$). – MS (ESI$^+$): *m/z* (%) = 230 (100) [M – H(PF$_6$)$_2$]$^+$. – El. Anal. calcd (%) for C$_{14}$H$_{22}$N$_3$PF$_6$ × HPF$_6$ (521.3 g/mol): C 32.26, H 4.06, N 8.06; found: C 31.75, H 3.68, N 7.52.



1h

4-[3-(Dimethylammoniopropyl)(methyl)amino)]quinolizinium bis(hexafluorophosphate) (1h): According to GP1 4-chloroquinolizinium tetrafluoroborate (**1c**) (201 mg, 800 µmol) and *N*,*N*,*N'*-trimethyl-1,3-propanediamine (279 mg, 2.40 mmol, 352 µl) were stirred in 2-PrOH (10 ml) for 2 h to give a orange-colored microcrystalline solid (111 mg, 206 µmol, 26%); m.p. = 220-222 °C (dec.). – ^{1}H-NMR (400 MHz, [D$_6$]DMSO): δ = 1.93–2.00 (m, 2 H, 2'-H), 2.75

(s, 6 H, $N(CH_3)_2$), 2.88 (s, 3 H, $N_{ar}(CH_3)$), 3.07–3.11 (m, 2 H, 3'-H), 3.31-3.34 (m, 2 H, 1'-H), 7.82–7.84 (m, 1 H, 2-H), 8.02–8.06 (m, 1 H, 7-H), 8.30–8.40 (m, 3 H, 8-H, 1-H, 3-H), 8.57–8.60 (m, 1 H, 9-H), 9.15 (br s, 1 H, N^+H), 9.28–9.30 (m, 1 H, 6-H). – ^{13}C-NMR (100 MHz, [D_6]DMSO): δ = 21.3 (C2'), 39.9 ($N(CH_3)$), 42.3 (2 × $N(CH_3)_2$), 50.7 (C1'), 54.4 (C3'), 115.7 (ar-CH), 122.0 (ar-CH), 123.2 (ar-CH), 127.9 (ar-CH), 130.8 (ar-CH), 135.8 (ar-CH), 137.4 (ar-CH), 143.8 (ar-C_q), 151.7 (ar-C_q). – MS (ESI^+): *m/z* (%) = 244 (100) $[M - H(PF_6)_2]^+$. – El. Anal. calcd (%) for $C_{15}H_{24}N_3PF_6 \times HPF_6$ (535.3 g/mol): C 33.66, H 4.33, N 7.85; found: C 33.59, H 4.18, N 7.55.



1i

***N*-(3-Dimethylaminopropyl)quinolizinium-9-carboxamide hexafluorophosphate (1i)**: To a warm (50–60 °C) solution of quinolizinium-2-carboxylic acid (**1d**)[1] (290 mg, 1.13 mmol) in MeCN (12 ml), *N*-methylmorpholine (124 µl, 1.13 mmol) was added. Under argon-gas atmosphere the suspension was cooled to −20 °C and treated with isobutyl chloroformate (127 µl, 1.13 mmol). The reaction mixture was stirred at this temperature for 15 min. A solution of *N*,*N*-dimethyl-1,3-propanediamine (141 µl, 1.13 mmol) and pyridinium hydrochloride (131 mg, 1.13 mmol) in DMF (3 ml) was added dropwise. The reaction mixture was stirred at –15 °C for 2 h and subsequently at room temperature for 18 h. The precipitate was separated by filtration and dissolved in water. An aq. solution of HPF_6 was added, the precipitate was separated and crystallized from MeOH to give the product (76.5 mg, 190 µmol, 17%) as white solid; m.p. = 163–165 °C. – ^{1}H-NMR (600 MHz, CD_3CN): δ = 2.00–2.08 (m, 2 H, 2'-H), 2.86 (s, 6 H, $N(CH_3)_2$), 3.16 (t, ^3J = 7 Hz, 2 H, 3'-H), 3.52 (q, ^3J = 7 Hz, 2 H, 1'-H), 7.83 (br s, 1 H, NH), 8.09 (dd, ^3J = 7 Hz, 1 H, 7-H), 8.17 (dd, ^3J = 7 Hz, ^4J = 2 Hz, 1 H, 3-H), 8.41 (dd, ^3J = 9 Hz, ^3J = 7 Hz, ^4J = 1 Hz, 1 H, 8-H), 8.51 (d, ^3J = 9 Hz, 1 H, 9-H), 8.71 (s, 1 H, 1-H), 9.04 (d, ^3J = 7 Hz, 1 H, 4-H), 9.06 (d, ^3J = 7 Hz, 1 H, 6-H). – ^{13}C-NMR (100 MHz, CD_3CN): δ = 25.3 (C2'), 37.3 (C1'), 44.0 (2 × $N(CH_3)_2$), 56.3 (C3'), 122.2, (CH), 126.4 (CH), 126.8 (CH), 129.3 (CH), 137.9 (CH), 138.1 (CH), 139.3 (CH), 141.1 (ar-C_q), 144.0 (ar-C_q), 164.9 (ar-C_q). – MS (ESI^+): *m/z* (%) = 258 (100) $[M - PF_6]^+$. – El. Anal. calcd (%) for $C_{15}H_{20}F_6N_3OP \times HPF_6$ (549.3 g/mol): C 32.80, H 3.85, N 7.65; found: C 32.84, H 3.37, N 7.68.

[1] R. M. Acheson, D. M. Goodall, *J. Chem. Soc.,* 1964, 3225.

General procedure for the synthesis of *trans*-styrylpyridine derivatives (GP2) [2]

If not stated otherwise, a mixture of chlorobenzaldehyde (2.00 g, 11.4 mmol), acetic anhydride (1.73 ml, 18.3 mmol) and 2-methylpyridine (1.13 ml, 11.4 mmol) was stirred under reflux for 16 h. After cooling to room temperature water and $CHCl_3$ were added. The aqueous layer was extracted with $CHCl_3$ (3 x 10 ml) and the organic layer was washed with water (3 x 50 ml). The combined organic layers were dried with $MgSO_4$, filtered, and the solvent was removed in vacuo. The product was purified by crystallization or column chromatography.

***trans*-2-(2',3'-Dichloro-2-styryl)pyridine (9b)**: Column chromatography (SiO_2, $CHCl_3$/MeOH 10/0.1, R_f = 0.87) gave a yellow-brown solid (2.03 g, 8.11 mmol, 71%); m.p. = 61−63 °C. – ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.13 (d, ^3J = 16 Hz, 1 H, CH), 7.19–7.23 (m, 2 H, CH), 7.39 (dd, ^4J = 1 Hz, ^3J = 8 Hz, 1 H, CH), 7.46 (d, ^3J = 8 Hz, 1 H, CH), 7.61 (dd, ^4J = 1 Hz, ^3J = 8 Hz, 1 H, CH), 7.68 (ddd, ^4J = 1 Hz, ^3J = 8 Hz, ^3J = 8 Hz, 1 H, CH), 7.98 (d, ^3J = 16 Hz, 1 H, CH), 8.63 (d, ^3J = 5 Hz, 1 H, CH). – ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 122.7 (CH), 123.1 (CH), 125.5 (CH), 127.6 (CH), 129.5 (CH), 130.2 (CH), 132.0 (C_q), 132.5 (CH), 134.0 (C_q), 137.2 (CH), 137.6 (C_q), 150.0 (CH), 155.3 (C_q).

***trans*-2-(2',4'-Dichloro-2-styryl)pyridine (9c)**: Crystallization from MeOH gave a beige-colored solid (1.53 g, 6.12 mmol, 54%); m.p. = 73−74 °C (Lit.: 75−76 °C).[2] – ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.16 (d, ^3J = 16 Hz, 1 H, CH), 7.20–7.23 (m, 1 H, CH), 7.25–7.28 (m, 1 H, CH), 7.43 (d, ^3J = 2 Hz, 1 H, CH), 7.47 (d, ^3J = 8 Hz, 1 H, CH), 7.67 (d, ^3J = 8 Hz, 1 H, CH), 7.71 (ddd, ^4J = 2 Hz, ^3J = 5 Hz, ^3J = 8 Hz, 1 H, CH), 7.93 (d, ^3J = 16 Hz, 1 H, CH), 8.64 (d, ^3J = 5 Hz, 1 H, CH).

***trans*-2-(2',5'-Dichlor-2-styryl)pyridine (9d)**: Crystallization from MeOH/heptane gave a white solid (1.00 g, 4.00 mmol, 35%); m.p. = 63−64 °C. – ^{1}H-NMR (400 MHz, [D_6]DMSO): δ = 7.30 (dd, ^3J = 5 Hz, ^3J = 8 Hz, 1 H, CH), 7.38 (dd, ^4J = 2 Hz, ^3J = 8 Hz, 1 H, CH), 7.50–7.54 (m, 3 H, CH), 7.80 (td, ^4J = 2 Hz, ^3J = 8 Hz, 1 H, CH), 7.91 (d, ^3J = 16 Hz, 1 H, CH), 8.02 (d, ^4J = 2 Hz, 1 H, CH), 8.61 (d, ^3J = 5 Hz, 1 H, CH). – ^{13}C-NMR (100 MHz, [D_6]DMSO): δ = 123.1 (CH), 123.7 (CH), 125.4 (CH), 126.4 (CH), 129.1 (CH), 131.2 (CH), 131.2 (C_q), 132.2 (C_q), 135.8 (CH), 136.9 (CH), 149.6 (CH), 153.7 (C_q).

***trans*-2-(2'-Chloro-5'-nitro-2-styryl)pyridine (9e)**. From 2-chloro-5-nitrobenzaldehyde (10.0 g, 53.9 mmol), acetic anhydride (7.50 ml, 18.3 mmol) and 2-methylpyridine (5.30 ml, 53.9 mmol); green solid (11.8 g, 45.3 mmol, 84%); m.p. = 118−119 °C (Lit. 122−123 °C).[2] – ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.30 (dd, ^3J = 8 Hz, ^3J = 5 Hz, 1 H, CH), 7.34 (d, ^3J = 16 Hz, 1 H, CH), 7.52 (d, ^3J = 8 Hz, 1 H, CH), 7.59 (d, ^3J = 9 Hz, 1 H, CH), 7.80 (dt, ^3J = 7 Hz, 1 H, CH), 8.07–8.10 (m, 1 H, CH), 8.08 (d, ^3J = 16 Hz, 1 H, CH), 8.61 (d, ^3J = 3 Hz, 1 H, CH), 8.68 (d, ^3J = 5 Hz, 1 H, CH).

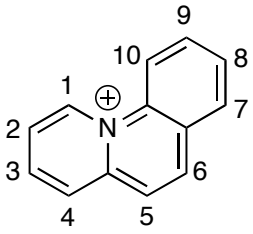
[2] A. Fozard, C. K. Bradsher, *J. Org. Chem.,* 1966, **31**, 2346.

***trans*-2-(2',6'-Dichloro-2-styryl)pyridine (9f)**: Column chromatography (SiO_2, $CHCl_3$/MeOH 98/2, R_f = 0.77) gave a viscous orange-colored oil (1.42 g, 5.66 mmol, 50%). – ^{1}H-NMR (400 MHz, CD_3OD): δ = 7.16 (d, ^3J = 16 Hz, 1 H, CH), 7.19 (d, ^3J = 8 Hz, 1 H, CH), 7.28 (ddd, ^4J = 1 Hz, ^3J = 5 Hz, ^3J = 8 Hz, 1 H, CH), 7.37 (d, ^3J = 8 Hz, 1 H, CH), 7.55 (dt, ^4J = 1 Hz, ^4J = 1 Hz, ^3J = 8 Hz, 1 H, CH), 7.60 (d, ^3J = 16 Hz, 1 H, CH), 7.78 (ddd, ^4J = 2 Hz, ^3J = 8 Hz, ^3J = 8 Hz, 1 H, CH), 8.53 (d, ^3J = 5 Hz, 1 H, CH). – ^{13}C-NMR (100 MHz, [D_6]DMSO): δ = 123.1 (CH), 123.2 (CH), 125.5 (CH), 128.8 (2 x CH), 129.4 (CH), 133.4 (C_q), 133.7 (C_q), 136.0 (CH), 136.9 (CH), 149.6 (CH), 153.7 (C_q).

General procedure for the synthesis of Chlorobenzo[*c*]quinolizinium derivates.

A stirred solution of the *trans*-2-(dichloro-2-styryl)pyridine derivative (1.00 g, 4.00 mmol) in acetone (30 ml) was irradiated with a high-pressure Hg-lamp (Heraeus TQ150; λ > 250 nm) at room temp. for 1 h. The solvent was removed in vacuo and the residue was stirred at 170 °C for 1 h. After cooling to room temperature the reaction mixture was dissolved in water (10 ml) and the solution was filtered (Mikrofilter 0.45 µm). The solvent was removed in vacuo and the product was crystallized from MeOH/ethyl acetate.

Numbering of benzo[*c*]quinolizinium:



4a

10-Chlorobenzo[*c*]quinolizinium tetrafluoroborate (4b): Brown solid (41 mg, 136 µmol, 4%); m.p. = 149−151 °C. – ^{1}H-NMR (600 MHz, [D_6]DMSO): δ = 8.03 (t, ^3J = 8 Hz, 1 H, 8-H), 8.23–8.26 (m, 1 H, 2-H), 8.25–8.32 (m, 1 H, CH), 8.27 (dd, ^4J = 2 Hz, ^3J = 8 Hz, 1 H, 9-H), 8.34 (dd, ^4J = 2 Hz, ^3J = 8 Hz, 1 H, 7-H), 8.38 (d, ^3J = 9 Hz, 1 H, 5-H), 8.67 (d, ^3J = 9 Hz, 1 H, 6-H), 8.71–8.74 (m, 2 H, 3-H, 4-H), 10.39 (dd, ^4J = 1 Hz, ^3J = 7 Hz, 1 H, 1-H). – ^{13}C-NMR (150 MHz, [D_6]DMSO): δ = 122.4 (CH), 123.9 (CH), 124.5 (C_q), 127.7 (CH), 129.3 (CH), 130.1 (C_q), 131 (CH), 131.8 (C_q), 135.4 (CH), 136 (CH), 139.8 (CH), 141.8 (CH), 144.6 (C_q). – MS (ESI$^+$): *m*/*z* (%) = 214 (100) [M – BF_4]$^+$. − El. Anal. calc (%) for $C_{13}H_9NClBF_4 \times 0.5\ H_2O$ (309.5 g/mol): C 50.29, H 3.25, N 4.51; found: C 50.65, H 3.03, N 4.45.

9-Chlorobenzo[*c*]quinolizinium chloride (4c): Pale-yellow solid (612 mg, 2.45 mmol, 61%). m.p. = 360–361 °C (Lit.: 355 °C).[2] – ^{1}H-NMR (400 MHz, CD_3OD): δ = 8.10 (dd, ^4J = 2 Hz, ^3J = 9 Hz, 1 H, CH), 8.23–8.27 (m, 1 H, CH), 8.30 (d, ^3J = 9 Hz, 1 H, CH), 8.36 (d, ^3J = 9 Hz, 1 H, CH), 8.64–8.67 (m, 3 H, CH), 9.25 (s, 1 H, CH), 10.28 (d, ^3J = 7 Hz, 1 H, CH).

8-Chlorobenzo[*c*]quinolizinium tetrafluoroborate (4d): Yellow solid (111 mg, 369 µmol, 11%); m.p. = 302–303 °C (dec.). – ^{1}H-NMR (600 MHz, [D$_6$]DMSO): δ = 8.22 (dd, ^4J = 2 Hz, ^3J = 9 Hz, 1 H, 9-H), 8.30 (t, 1 H, ^3J = 6 Hz, 2-H), 8.46 (d, ^3J = 9 Hz, 1 H, 5-H), 8.56 (d, ^4J = 2 Hz, 1 H, 7-H), 8.66–8.70 (m, 2 H, 3-H, 6-H), 8.75 (d, 1 H, ^3J = 8 Hz, 4-H), 9.25 (d, ^3J = 9 Hz, 1 H, CH), 10.48 (d, ^3J = 7 Hz, 1 H, 1-H). – ^{13}C-NMR (150 MHz, [D$_6$]DMSO): δ = 120.7 (CH), 124.3 (CH), 124.7 (CH), 128.1 (C$_q$), 128.5 (CH), 129.0 (CH), 132.4 (CH), 133.1 (C$_q$), 134.9 (C$_q$), 135.2 (CH), 135.3 (CH), 141.0 (CH), 143.2 (Cq). – MS (ESI$^+$): *m*/*z* (%) = 214 (100) [*M* – BF$_4$]$^+$. – El. Anal. cald (%) for C$_{13}$H$_9$NClBF$_4$ (301.5 g/mol): C 51.79, H 3.01, N 4.65; found: C 51.78, H 3.26, N 4.62.

8-Nitrobenzo[*c*]chinolizinium chloride (4e): From **9e** (2.00 g, 7.67 mmol) in acetone (800 ml), *t* = 48 h; brown solid (1.02 g, 3.91 mmol, 51%); m.p. = 295–296 °C (dec.; Lit. 306–307 °C).[2] – ^{1}H-NMR (400 MHz, [D$_6$]DMSO): δ = 8.38 (td, ^3J = 3 Hz, ^3J = 7 Hz, 1 H, CH), 8.58 (d, ^3J = 9 Hz, 1 H, CH), 8.78–8.82 (m, 2 H, CH), 8.88 (dd, ^3J = 3 Hz, ^3J = 9 Hz, 1 H, CH), 8.91 (d, ^3J = 9 Hz, 1 H, CH), 9.38 (d, ^3J = 3 Hz, 1 H, CH), 9.45 (d, ^3J = 9 Hz, 1 H, CH), 10.58 (d, ^3J = 7 Hz, 1 H, CH).

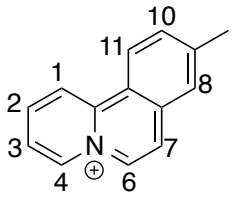
7-Chlorobenzo[*c*]quinolizinium chloride (4f): Yellow solid (72.2 mg, 289 µmol, 7%); m.p. = 280–282 °C. – ^{1}H-NMR (400 MHz, [D$_6$]DMSO): δ = 8.17 (t, ^3J = 8 Hz, 1 H, 9-H), 8.26 (d, ^3J = 8 Hz, 1 H, 8-H), 8.31 (ddd, ^4J = 2 Hz, ^3J = 7 Hz, ^3J = 8 Hz 1 H, 2-H), 8.51 (d, ^3J = 9 Hz, 1 H, 5-H), 8.73 (t, ^3J = 8 Hz, 1 H, 3-H), 8.79 (dd, ^4J = 2 Hz, ^3J = 9 Hz, 1 H, 4-H), 8.90 (d, ^3J = 9 Hz, 1 H, 6-H), 9.18 (d, ^3J = 9 Hz, 1 H, 10-H), 10.45 (d, ^3J = 7 Hz, 1 H, 1-H). – ^{13}C-NMR (100 MHz, [D$_6$]DMSO): δ = 117.8 (CH), 124.6 (C$_q$), 124.8 (CH), 128.6 (CH), 130.9 (CH), 131.7 (CH), 132.7 (CH), 132.8 (CH), 135.4 (CH), 135.8 (C$_q$), 141.4 (CH), 143.2 (C$_q$), 149.6 (C$_q$). – MS (ESI$^+$): *m*/*z* (%) = 214 (100) [M – Cl]$^+$. − El. Anal. calcd (%) for C$_{13}$H$_9$NCl$_2$ (250.1 g/mol): C 62.43, H 3.63, N 5.60; found: C 62.60, H 3.61, N 5.59.

8-Aminobenzo[*c*]quinolizinium tetrafluoroborate (4g): Under inert gas atmosphere, a suspension of 8-nitrobenzo[*c*]quinolizinium chloride (500 mg, 1.92 mmol) and SnCl$_2$(H$_2$O)$_2$ (2.60 g, 11.5 mmol) in EtOH (25 ml) was stirred at 90 °C for 3.5 h. After cooling the solution to room temp. the solvent was removed by destillation. The residue was dissolved in water and filtered. An aq. solution of NaBF$_4$ (sat.) was added and the solution was extracted with CH$_3$NO$_2$. After removal of the solvent the product was obtained as yellow solid (25.2 mg, 109 µmol, 6%); m.p. = 228–229 °C (dec.). – ^{1}H-NMR (600 MHz, [D$_6$]DMSO): δ = 6.39 (br s, 2 H, NH$_2$), 7.11 (d, ^4J = 2 Hz, 1 H, 7-H), 7.35 (dd, ^3J = 3 Hz, ^3J = 9 Hz, 1 H, 9-H), 8.06 (ddd, ^4J = 1 Hz, ^3J = 7 Hz, ^3J = 7 Hz, 1 H, 2-H), 8.09 (d, ^3J = 9 Hz, 1 H, 5-H), 8.34 (d, ^3J = 8 Hz, 1 H, 3-H), 8.36 (d, ^3J = 9 Hz, 1 H, 6-H), 8.46 (dd, ^4J = 1 Hz, ^3J = 9 Hz, 1 H, 4-H), 8.73 (d, ^3J = 9 Hz, 1 H, 10-H), 10.0 (d, ^3J = 7 Hz, 1 H, 1-H). – ^{13}C-NMR (150 MHz, [D$_6$]DMSO): δ = 108.1 (CH), 118.9 (CH), 121.3 (CH), 122.3 (CH), 124.0 (CH), 125.1 (C$_q$), 128.1 (CH), 129.0 (C$_q$), 132.5 (CH), 135.8 (CH), 137.0 (CH), 140.5 (C$_q$), 150.6 (C$_q$). – MS (ESI$^+$): *m*/*z* (%) = 195 (100) [M – NH$_2$]$^+$. − El. Anal. calcd (%) for C$_{13}$H$_{11}$N$_2$BF$_4$ x 0.5 H$_2$O (290.0 g/mol): C 53.65, H 4.05, N 9.62; found: C 53.85, H 3.67, N 9.43.

7-Methylbenzo[*c*]quinolizinium tetrafluoroborate (4h). Under inert gas atmosphere, a suspension of **4f** (250 mg, 1.00 mmol), methylboronic acid (120 mg, 2.00 mmol), Pd(dppf)Cl_2-CH_2Cl_2 (24.5 mg, 0.03 mmol) and KF (232 mg, 4.00 mmol) in DME/H_2O/MeOH (2/1/1, 12.0 ml) was stirred at 110 °C for 70 h. After cooling the reaction mixture to room temp. the precipitate was filtered off and the solvent of the filtrate was removed in vacuo. The residue was dissolved in a small amount of water and an aq. solution of $NaBF_4$ (sat.) was added. The precipitate was separated by filtration and dried in vacuo to give the product as brown solid (48.5 mg, 170 µmol, 17%); m.p. = 229–230 °C. – ^{1}H-NMR (600 MHz, [D_6]DMSO): δ = 2.83 (s, 3 H, CH_3), 7.89 (d, ^3J = 7 Hz, 1 H, 8-H), 8.06 (t, ^3J = 8 Hz, 1 H, 9-H), 8.24 (t, ^3J = 7 Hz, 1 H, 2-H), 8.38 (d, ^3J = 9 Hz, 1 H, 5-H), 8.63 (t, ^3J = 7 Hz, 1 H, 3-H), 8.69 (d, ^3J = 8 Hz, 1 H, 4-H), 8.83 (d, ^3J = 9 Hz, 1 H, 6-H), 8.95 (d, ^3J = 8 Hz, 1 H, 10-H), 10.34 (d, ^3J = 7 Hz, 1 H, 1-H). – ^{13}C-NMR (150 MHz, [D_6]DMSO): δ = 18.9 (CH_3), 115.9 (CH), 122.5 (CH), 124.3 (CH), 125.7 (C_q), 128.3 (CH), 131.2 (CH), 132.3 (CH), 133.3 (CH), 134.6 (CH), 134.6 (C_q), 138 (C_q), 140.3 (CH), 142.9 (C_q). – MS (ESI$^+$): *m*/*z* (%) = 194 (100) [M – BF_4]$^+$. – El. Anal. cald (%) for $C_{14}H_{12}NBF_4$ (281.1 g/mol): C 59.83, H 4.30, N 4.98; found: C 59.68, H 4.10, N 4.97.

General procedure for the synthesis of benzo[*a*]quinolizinium and dibenzo[*a*,*f*]quinolizinium derivates.

A solution of 2-(4-methylphenyl)pyridine or 2-(4-methylphenyl)quinoline[3] and hydroxylamine in DMSO was stirred at room temperature for 12 d. The precipitate was separated by filtration and washed with acetone (in case of no precipitation the DMSO was removed by destillation and the residue was washed with acetone). The remaining solid was dissolved in aq. HBr (48%, 15 ml) and the solution was stirred under reflux for 24 h. The solvent was removed in vacuo. The remaining residue was treated with water and the suspension was filtered. An aq. solution of $NaBF_4$ (sat.) was added to the filtrate. The precipitate was filtered, washed with a small amount of water, THF and diethylether, and recrystallized from CH_3OH/EtOAc.



9-Methylbenzo[*a*]quinolizinium tetrafluoroborate (3b): Colorless solid (580 mg, 2.53 mmol, 61%); m.p. = 237–239 °C. – ^{1}H-NMR (600 MHz, [D_6]DMSO): δ = 2.63 (s, 3 H, CH_3), 7.89 (d, ^3J = 8 Hz, 1 H, 7-H), 8.04 (s, 1 H, 8-H), 8.19 (*t*, ^3J = 7 Hz, 1 H, 3-H), 8.25 (d,

[3] V. Pandarus, D. Desplantier-Giscard, G. Gingras, F. Béland, R. Ciriminna and M. Pagliaro, *Org. Process Res. Dev.* **2013**, *17*, 1492.

^3J = 7 Hz, 1 H, 10-H), 8.61 (t, ^3J = 8 Hz, 1 H, 2-H), 8.94 (d, ^3J = 7 Hz, 1 H, 11-H), 9.00 (d, ^3J = 8 Hz, 1 H, 6-H), 9.40–9.43 (m, 2 H, 1-H, 4-H). – ^{13}C-NMR (150 MHz, [D$_6$]DMSO): δ = 21.5 (CH_3), 122.5 (C_q), 122.8 (CH), 122.8 (CH), 123.9 (CH), 125.7 (CH), 127.5 (CH), 131.3 (CH), 131.5 (C_q), 132.6 (CH), 139.3 (CH), 139.9 (CH), 142.7 (C_q), 145.1 (C_q). − MS (ESI$^+$): *m*/*z* (%) = 194 (100) [M – BF_4]$^+$; − El. Anal. cald (%) for $C_{14}H_{12}NBF_4$ x 0.5 H_2O (290.1 g/mol): C 57.97, H 4.22, N 4.83; found: C 57.61, H 3.96, N 4.82.

9-Methyldibenzo[*a*,*f*]quinolizinium tetrafluoroborate (5b): Because of significant impurities after workup according to general procedure, this product was further purified by MPLC (water/CH_3CN/CF_3COOH: 50/50/0.1) to give a yellow solid (12.0 mg, 0.03 µmol, <1%). ^{1}H-NMR (600 MHz, [D$_6$]DMSO): δ = 2.67 (s, 3 H, CH_3), 7.97 (dd, ^4J = 2 Hz, ^3J = 9 Hz, 1 H, 10-H), 8.08 (t, ^3J = 7 Hz, 1 H, 2-H), 8.18 (s, 1 H, 8-H), 8.25–8.28 (m, 1 H, 3-H), 8.46 (d, ^3J = 7 Hz, 1 H, 7-H), 8.48 (dd, ^4J = 2 Hz, ^3J = 8 Hz, 1 H, 1-H), 9.04 (d, ^3J = 9 Hz, 1 H, 13-H), 9.19 (d, ^3J = 9 Hz, 2 H, 4-H, 11-H), 9.37 (d, ^3J = 9 Hz, 1 H, 12-H), 10.0 (d, ^3J = 7 Hz, 1 H, 6-H). – ^{13}C-NMR (150 MHz, [D$_6$]DMSO): δ = 21.6 (CH_3), 118.3 (CH), 118.6 (CH), 122.5 (CH), 123.5 (C_q), 126.8 (CH), 126.9 (CH), 127.1 (CH), 127.3 (C_q), 129.9 (CH), 130.5 (CH), 132.9 (CH), 133.4 (C_q), 133.8 (CH), 135.4 (C_q), 139.6 (CH), 144.0 (C_q), 146.5 (C_q). − MS (ESI$^+$): *m*/*z* (%) = 244 (100) [M – TfAc]$^+$.

2. Spectrophotometric titrations

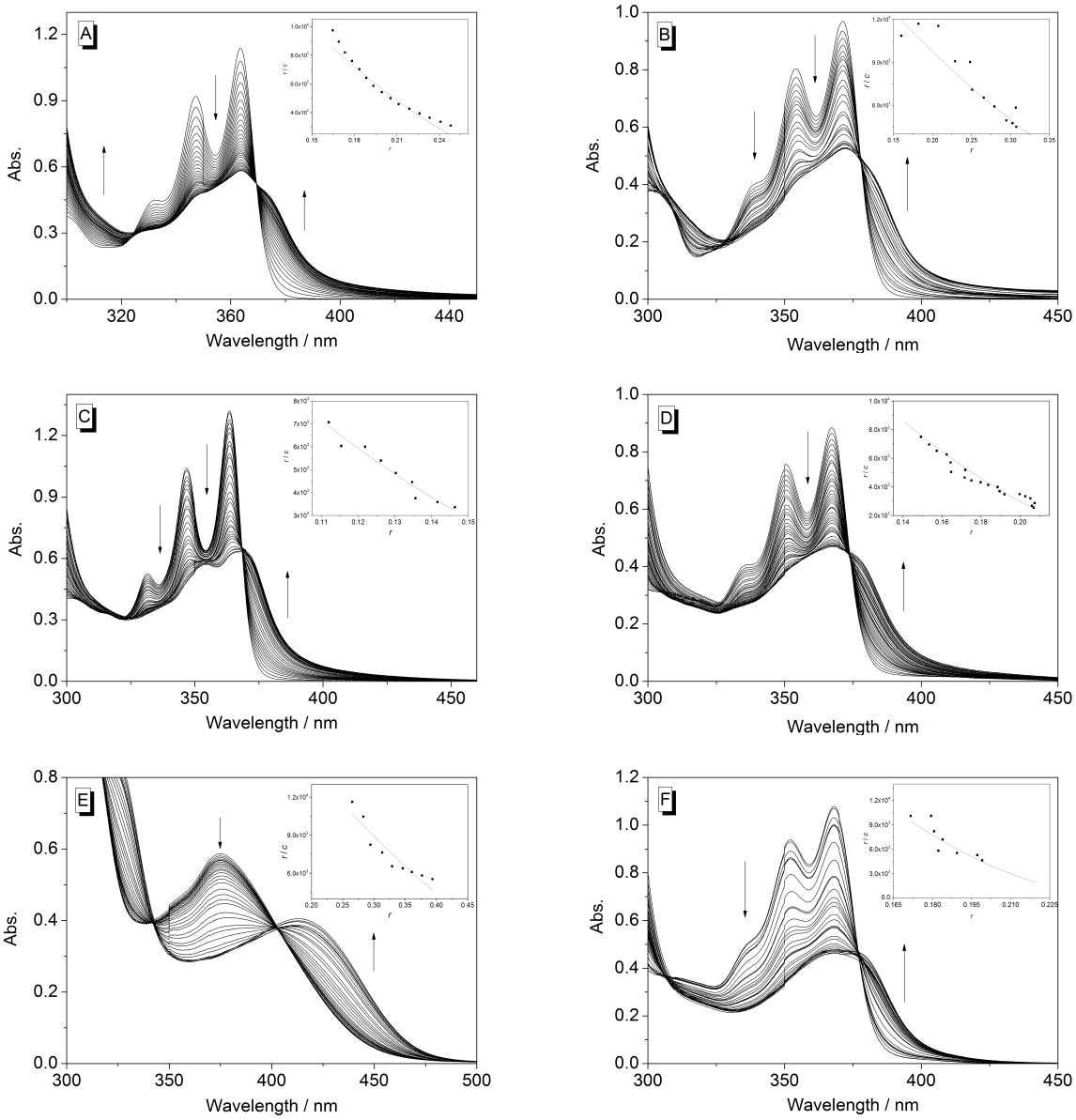


Figure S1. Spectrophotometric titrations of **4a** (A), **4c** (B), **4d** (C), **4f** (D), **4g** (E), and **4h** (F) with ct DNA in BPE buffer (c_{Ligand} = 0.10 mM). The arrows indicate the changes of the bands upon addition of ct DNA. Insets: Scatchard plot, r/c vs r; r = ligand-to-DNA ratio of bound ligand to DNA, fitted to the theoretical model.

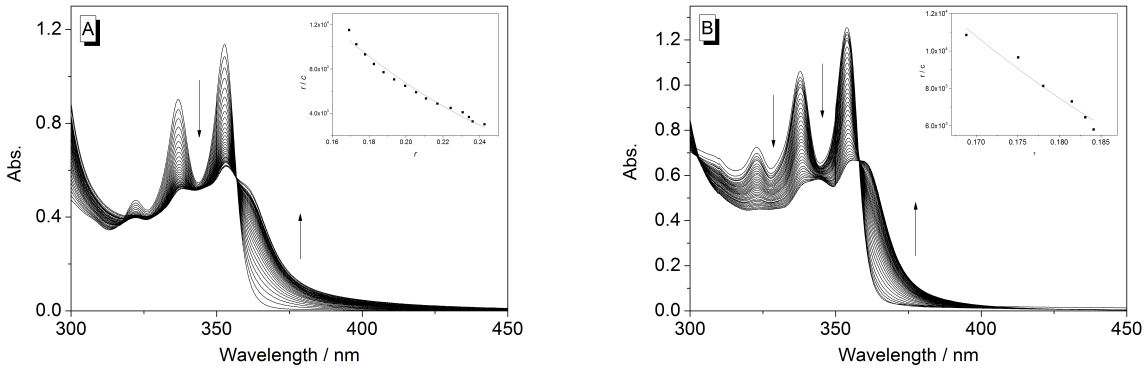


Figure S2. Spectrophotometric titrations of **3a** (A) and **3b** (B) with ct DNA in BPE buffer (c = 0.10 mM). in BPE buffer (c_{Ligand} = 0.10 mM). The arrows indicate the changes of the bands upon addition of ct DNA. Insets: Scatchard plot, r/c vs r; r = ligand-to-DNA ratio of bound ligand to DNA, fitted to the theoretical model.

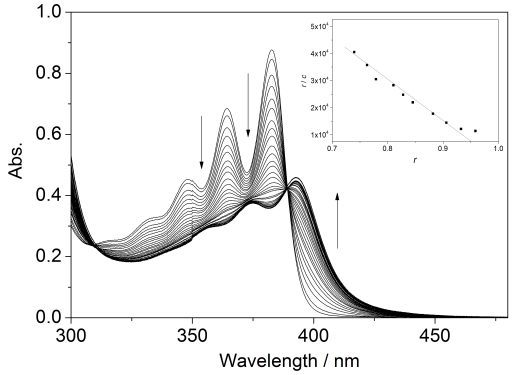


Figure S3. Spectrophotometric titrations of **5b** with ct DNA in BPE buffer (c = 0.10 mM). in BPE buffer (c_{Ligand} = 0.10 mM). The arrows indicate the changes of the bands upon addition of ct DNA. Insets: Scatchard plot, r/c vs r; r = ligand-to-DNA ratio of bound ligand to DNA, fitted to the theoretical model.

3. Spectrofluorimetric titrations

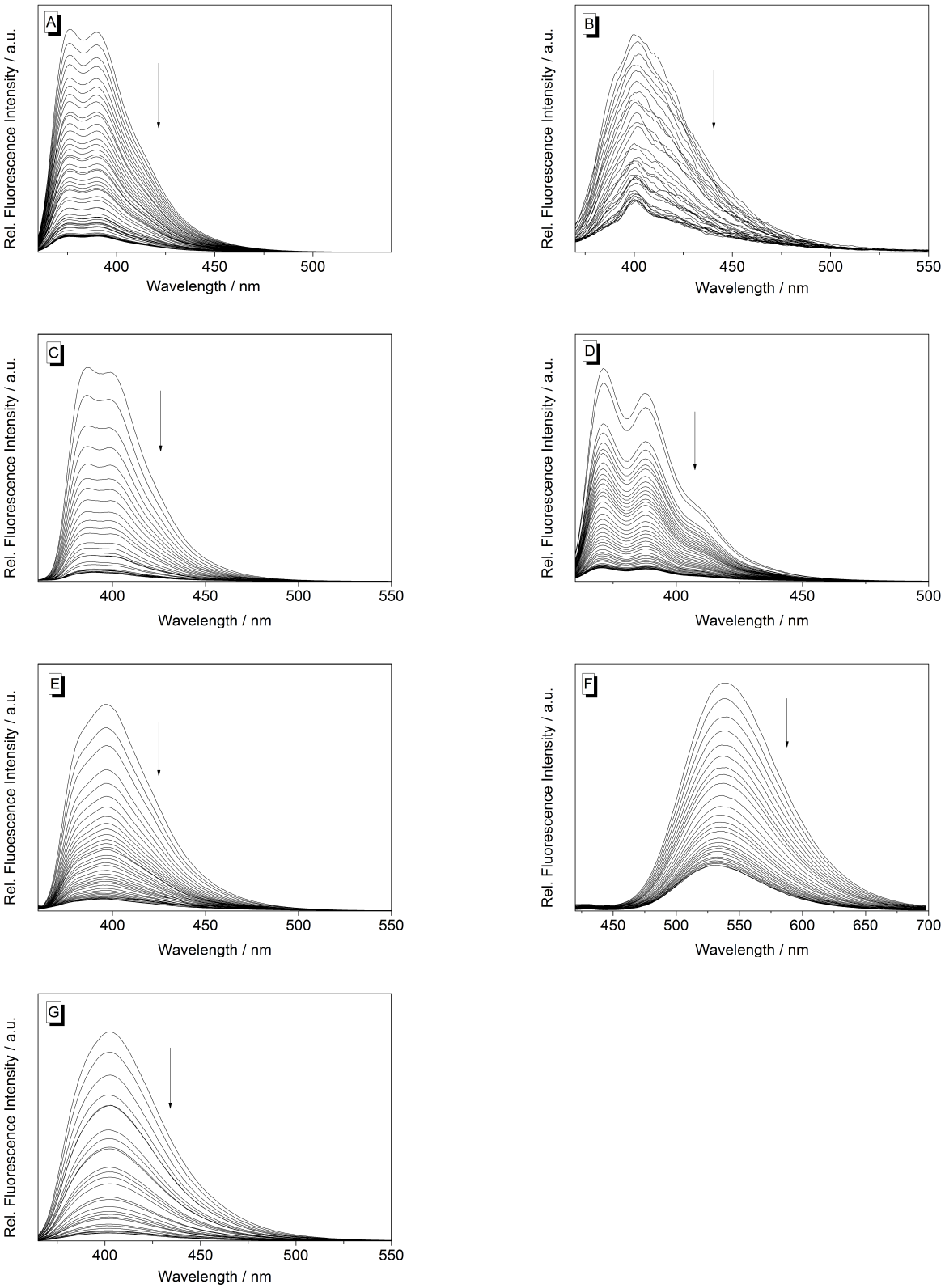


Figure S4. Spectrofluorimetric titration of **4a** (A, c = 10 μM, λ_{ex} = 324 nm), **4b** (B, c = 10 μM, λ_{ex} = 325 nm), **4c** (C, c = 10 μM, λ_{ex} = 328 nm), **4d** (D, c = 10 μM λ_{ex} = 320 nm), **4f** (E, c = 10 μM, λ_{ex} = 342 nm), **4g** (F, c = 10 μM λ_{ex} = 324 nm), and **4h** (G, c = 10 μM, λ_{ex} = 307 nm) with ct DNA in BPE buffer. The arrows indicate the changes of the bands upon addition of DNA.

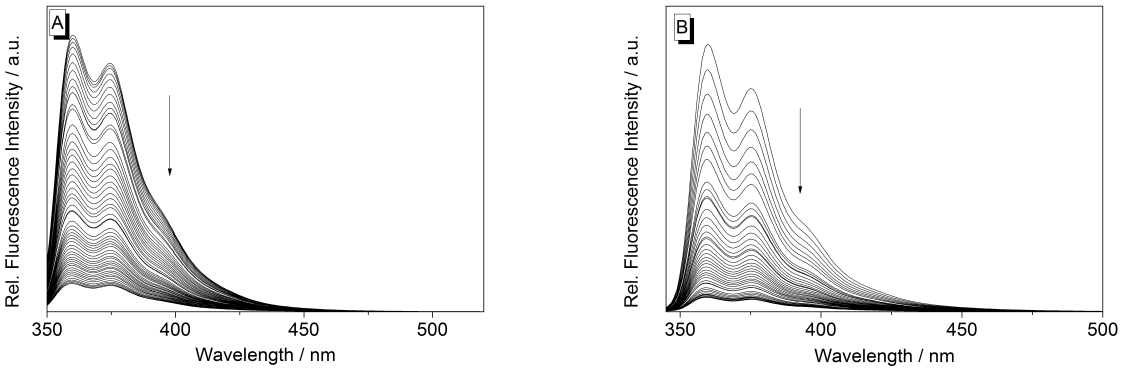


Figure S5. Spectrofluorimetric titration of **3a** (A, c = 10 µM, λ_{ex} = 318 nm) and **3b** (B, c = 10 µM, λ_{ex} = 303 nm) with ct-DNA in BPE buffer. The arrows indicate the changes of the bands upon addition of DNA.

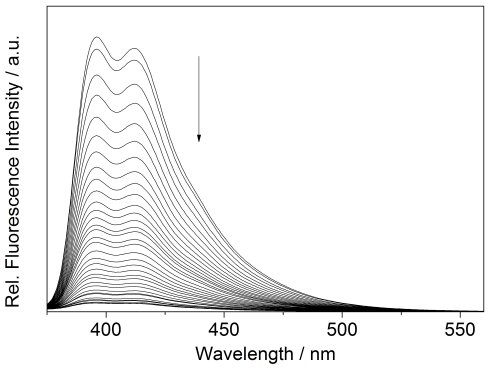


Figure S6. Spectrofluorimetric titration of **5b** (c = 10 µM, λ_{ex} = 310 nm) with ct-DNA in BPE buffer. The arrows indicate the changes of the bands upon addition of DNA.

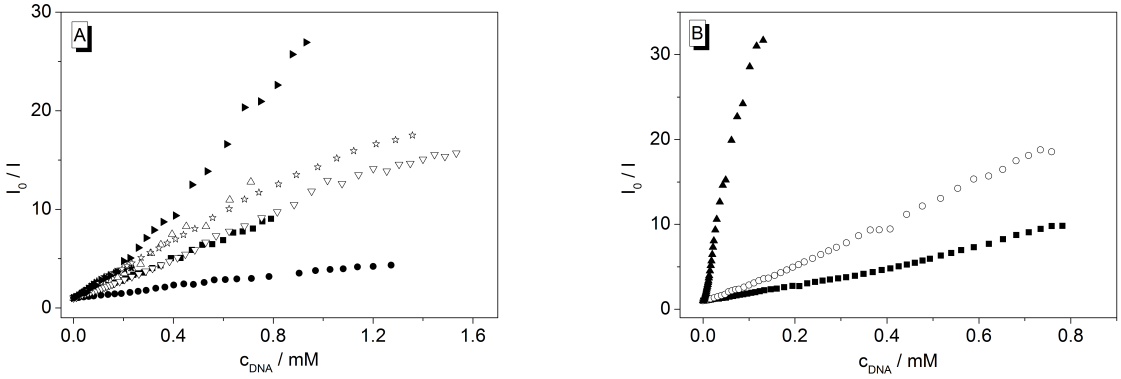


Figure S7. A: Relative fluorescence intensities of benzoquinolizinium derivatives **4a** (■), **4b** (●), **4c** (△), **4d** (▽), **4f** (☆), **4h** (◀) upon addition of ct DNA in phosphate buffer. B: Relative fluorescence intensities of benzoquinolizinium derivatives **3a** (■), **3b** (□) and **5a** (▲) upon addition of ct DNA in BPE buffer.

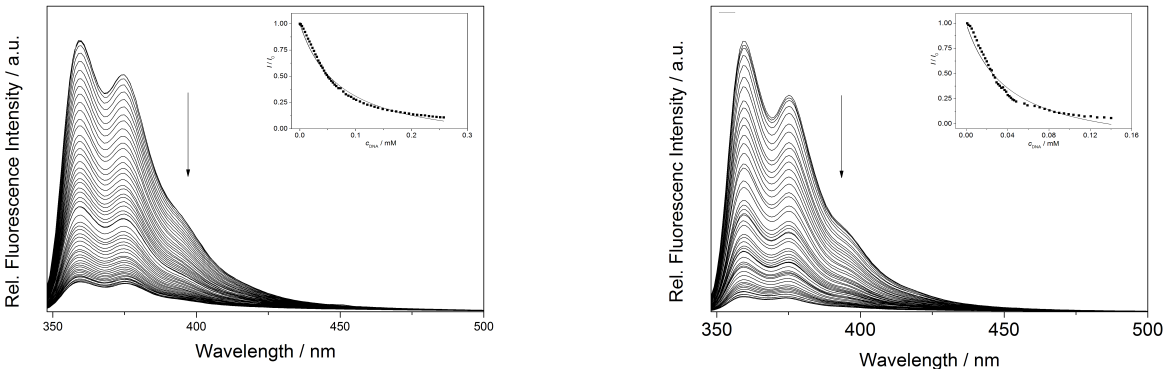


Figure S8. Fluorimetric titration of **3a** (left) and **3b** (right, 10 μM) with **TX** in ODN buffer. Inset: Plot of relative emission intensity, I / I_0, *versus* c_{DNA} fitted to the theoretical model.

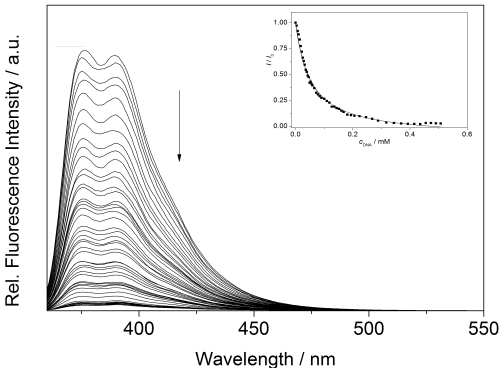


Figure S9. Fluorimetric titration of **4a** with **TX** in ODN buffer. Inset: Plot of relative emission intensity, I / I_0, *versus* c_{DNA} fitted to the theoretical model.

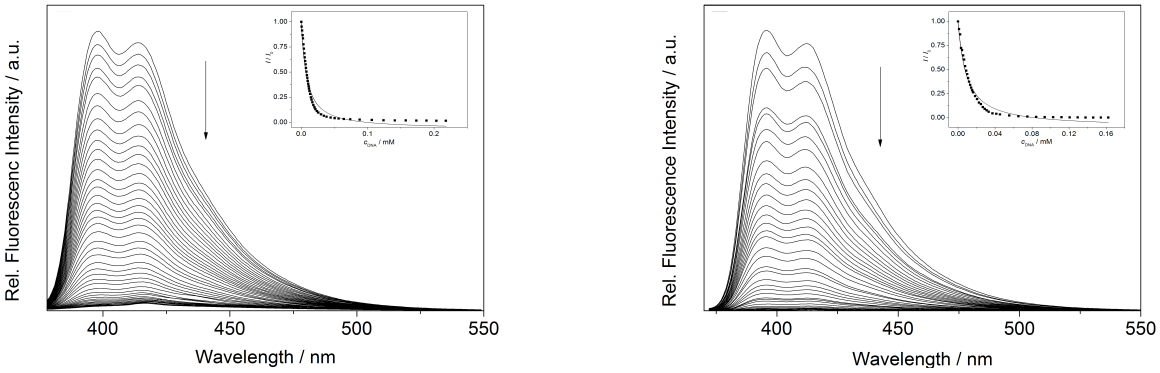


Figure S10. Fluorimetric titration of **5a** (left) and **5b** (right) with **TX** in ODN buffer. Inset: Plot of relative emission intensity, I / I_0, *versus* c_{DNA} fitted to the theoretical model.

4. Thermal DNA denaturation studies

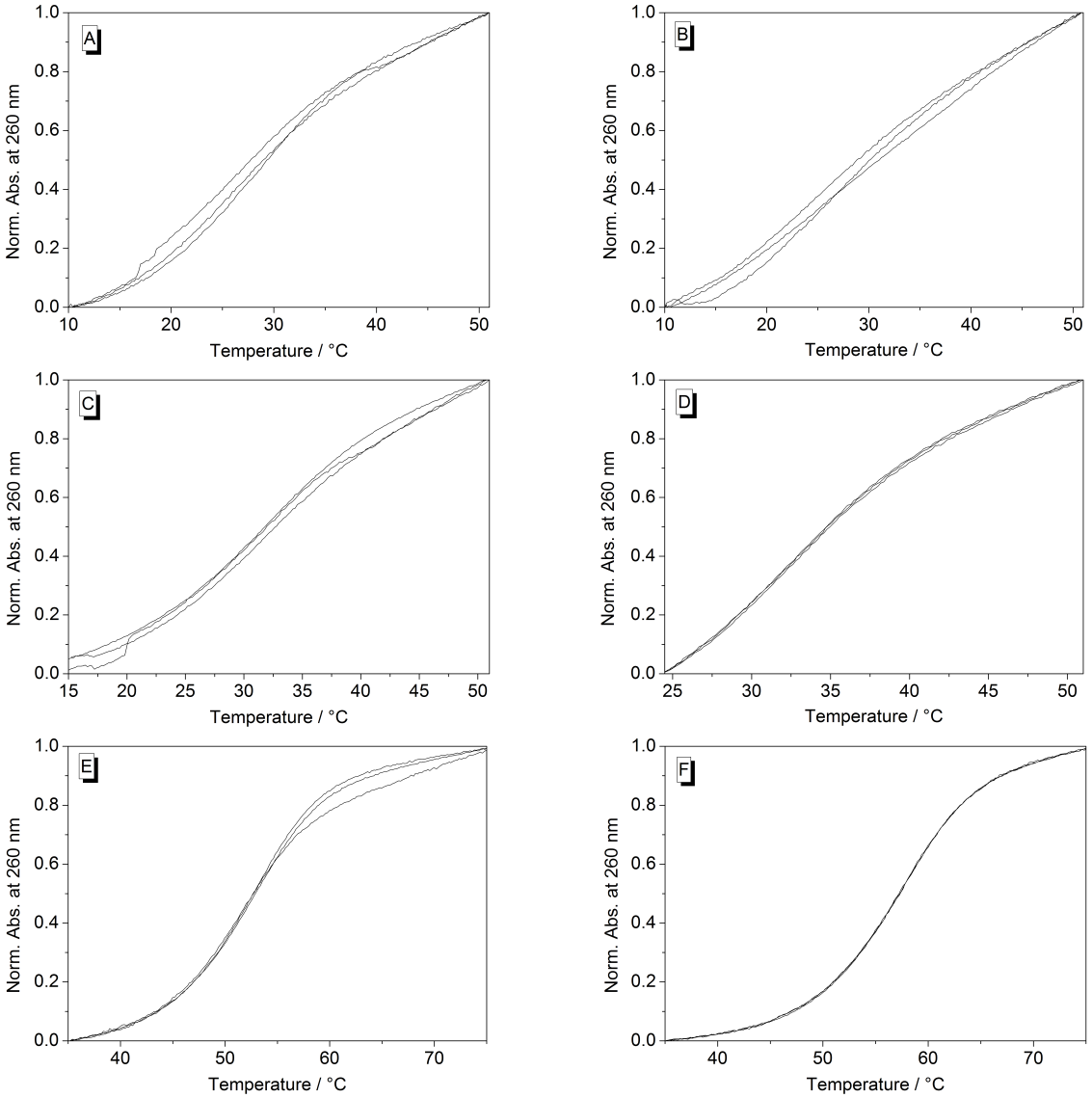


Figure S11. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1a** at *LDR* = 0, 0.5, and 2.0.

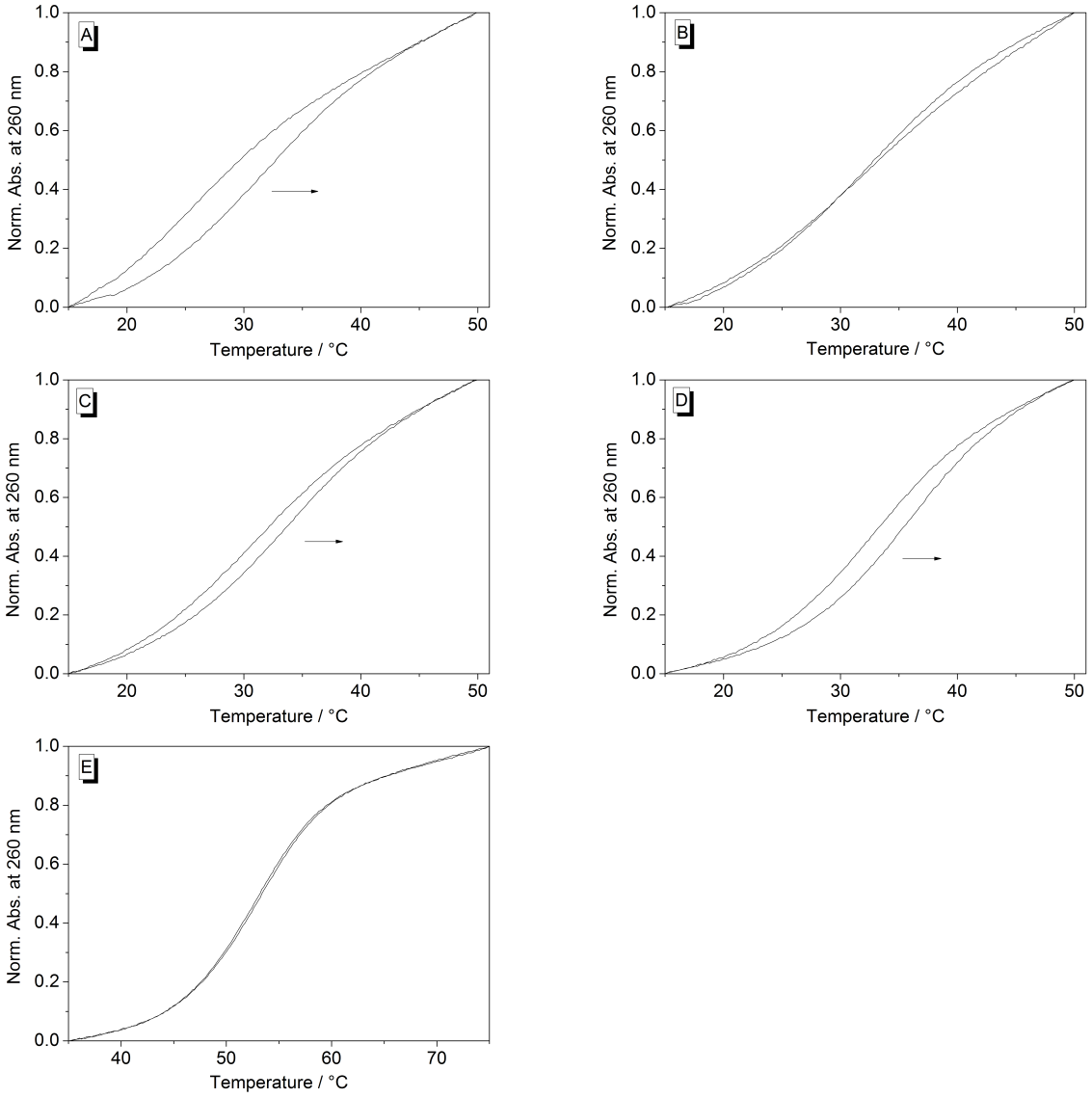


Figure S12. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1e** at *LDR* = 0 and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

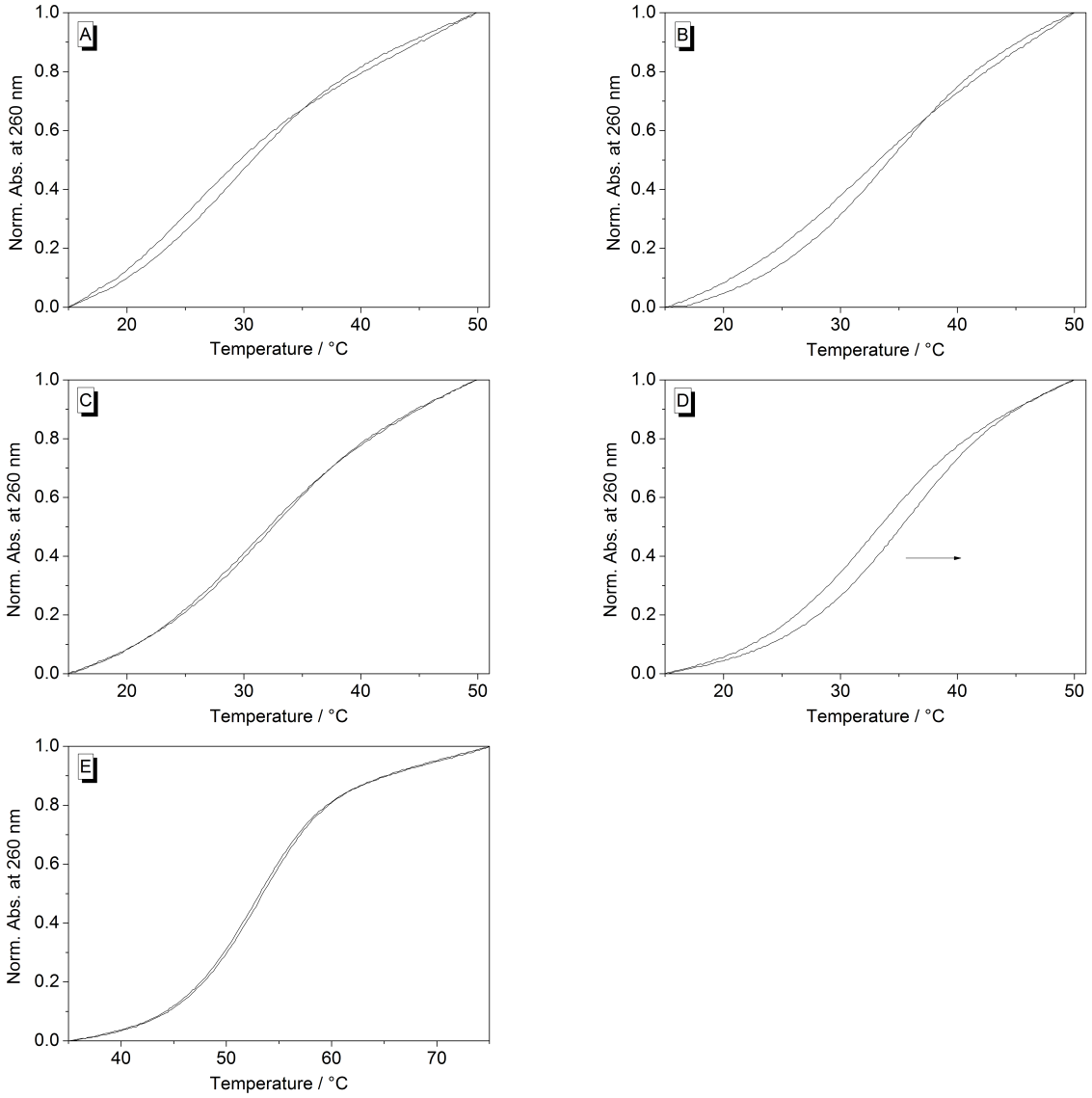


Figure S13. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1f** at *LDR* = 0 and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

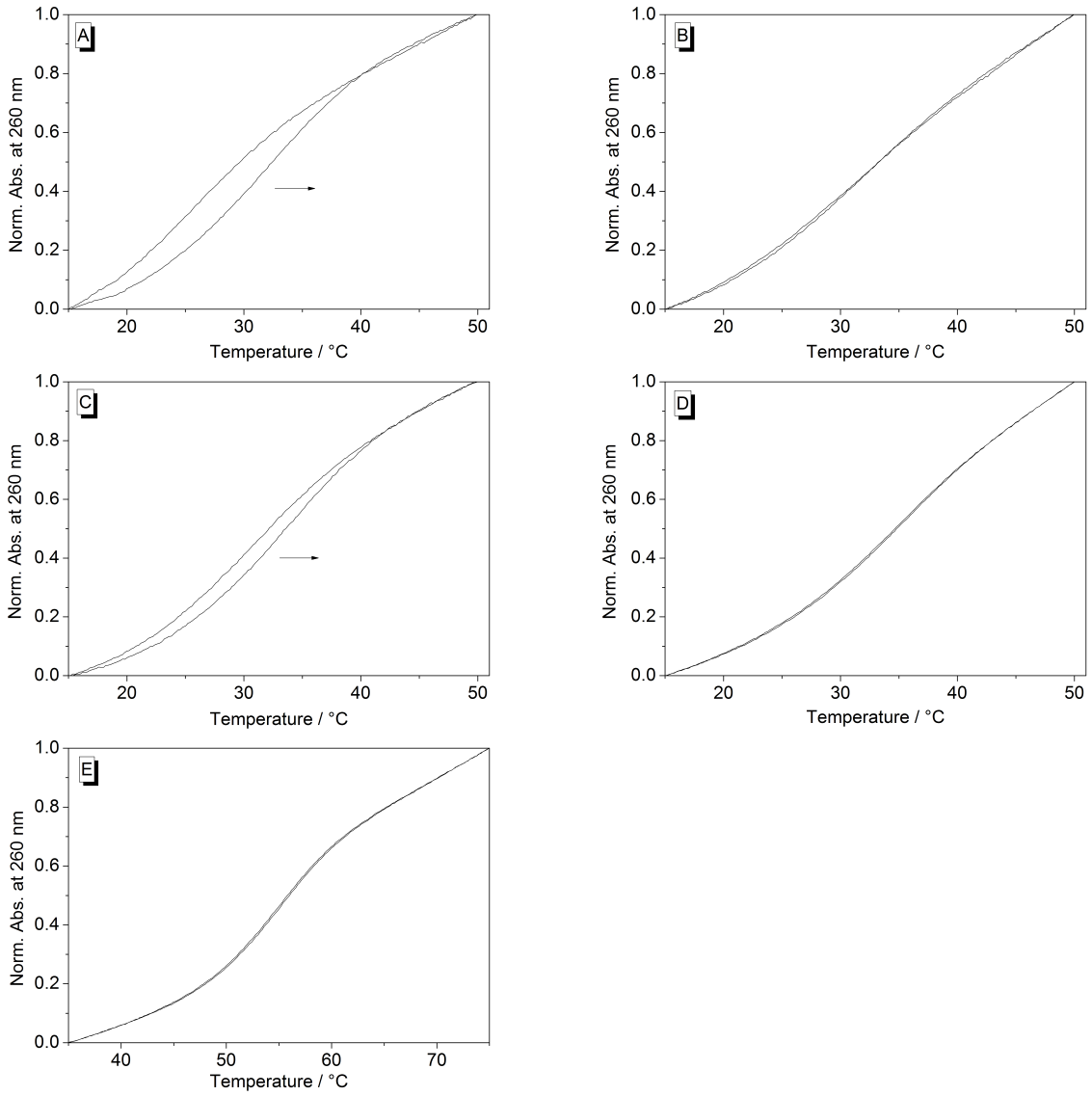


Figure S14. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1g** at *LDR* = 0 and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

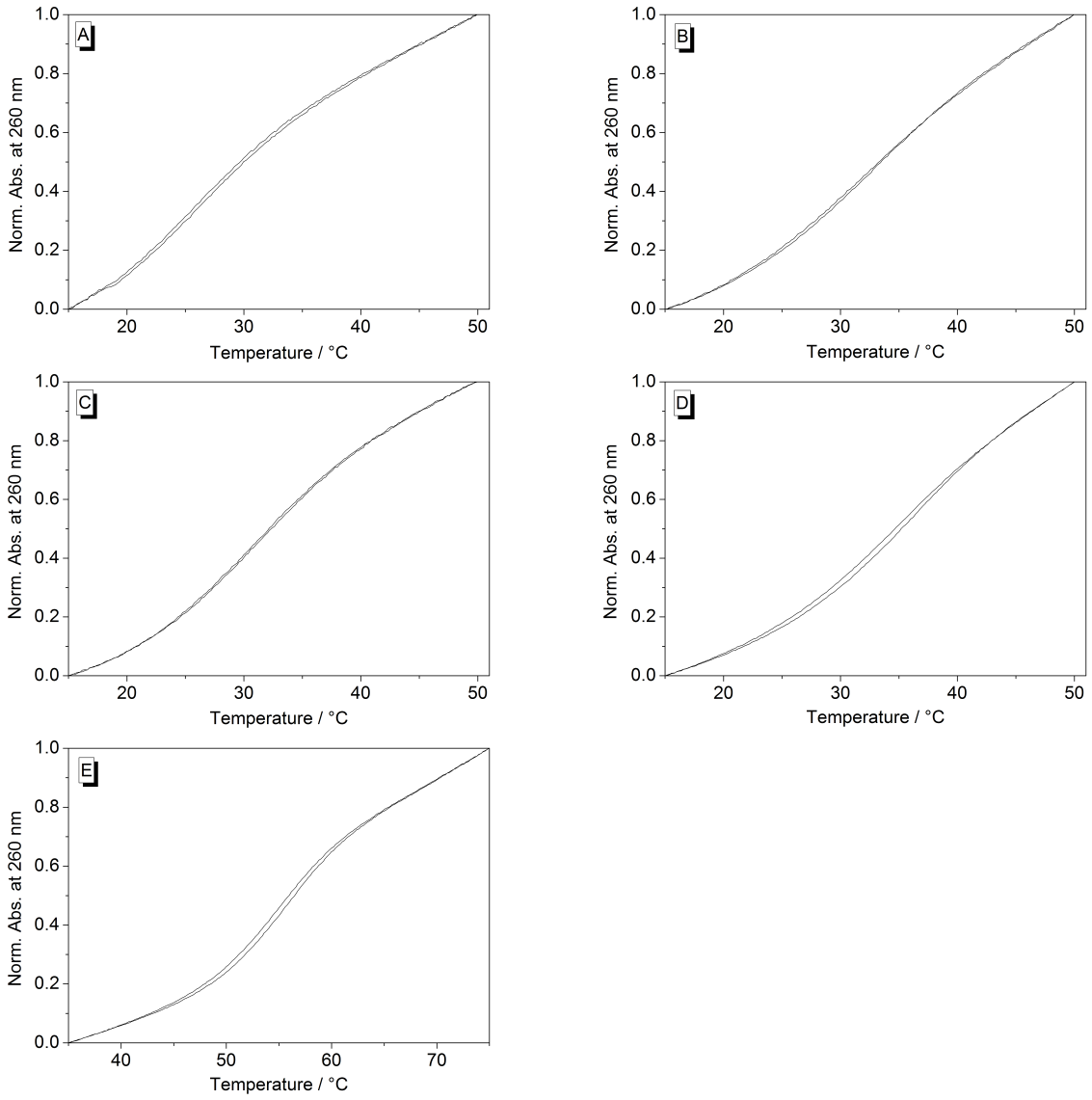


Figure S15. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1h** at *LDR* = 0 and 2.0.

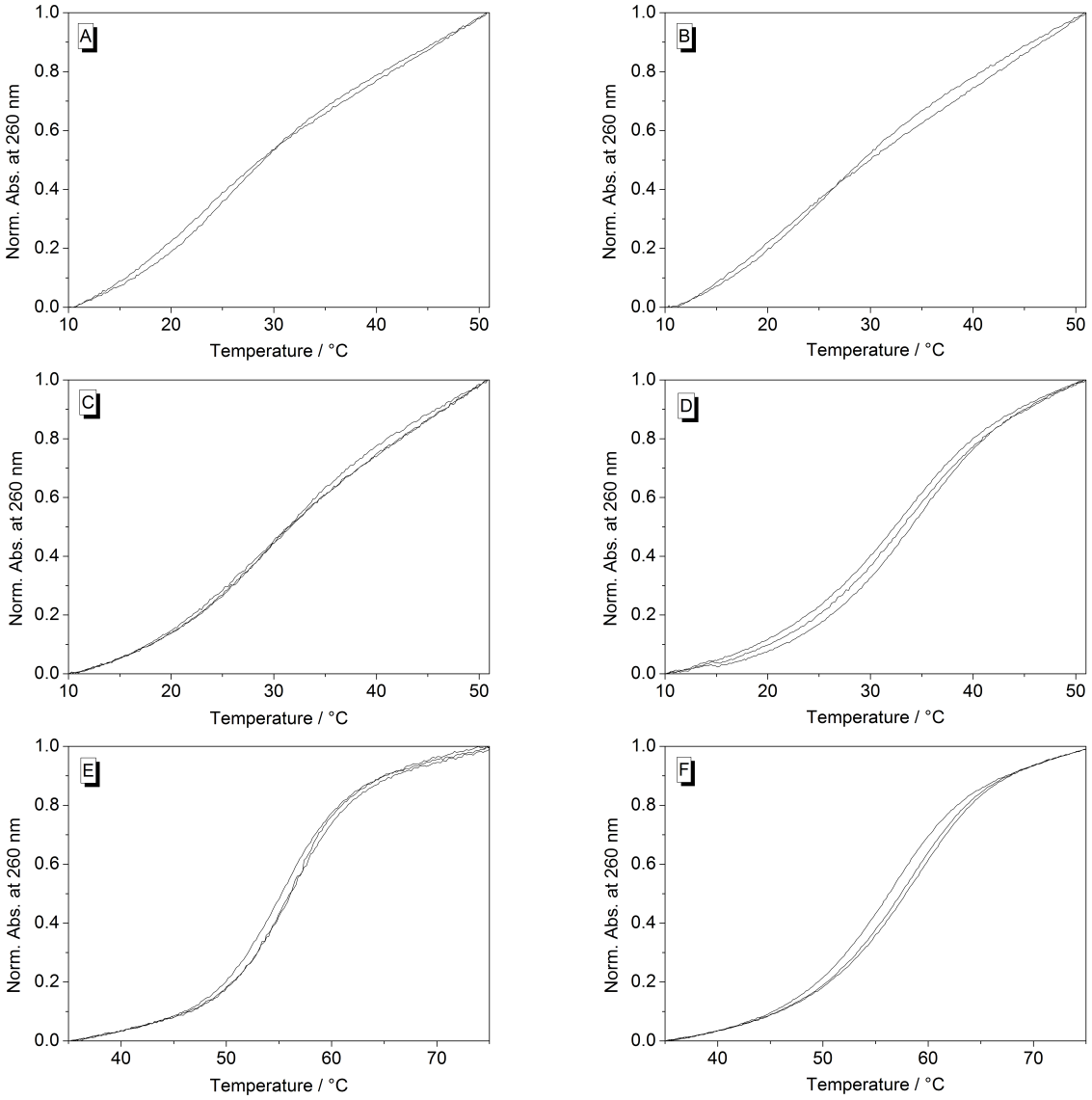


Figure S16. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **1i** at *LDR* = 0, 0.5, and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

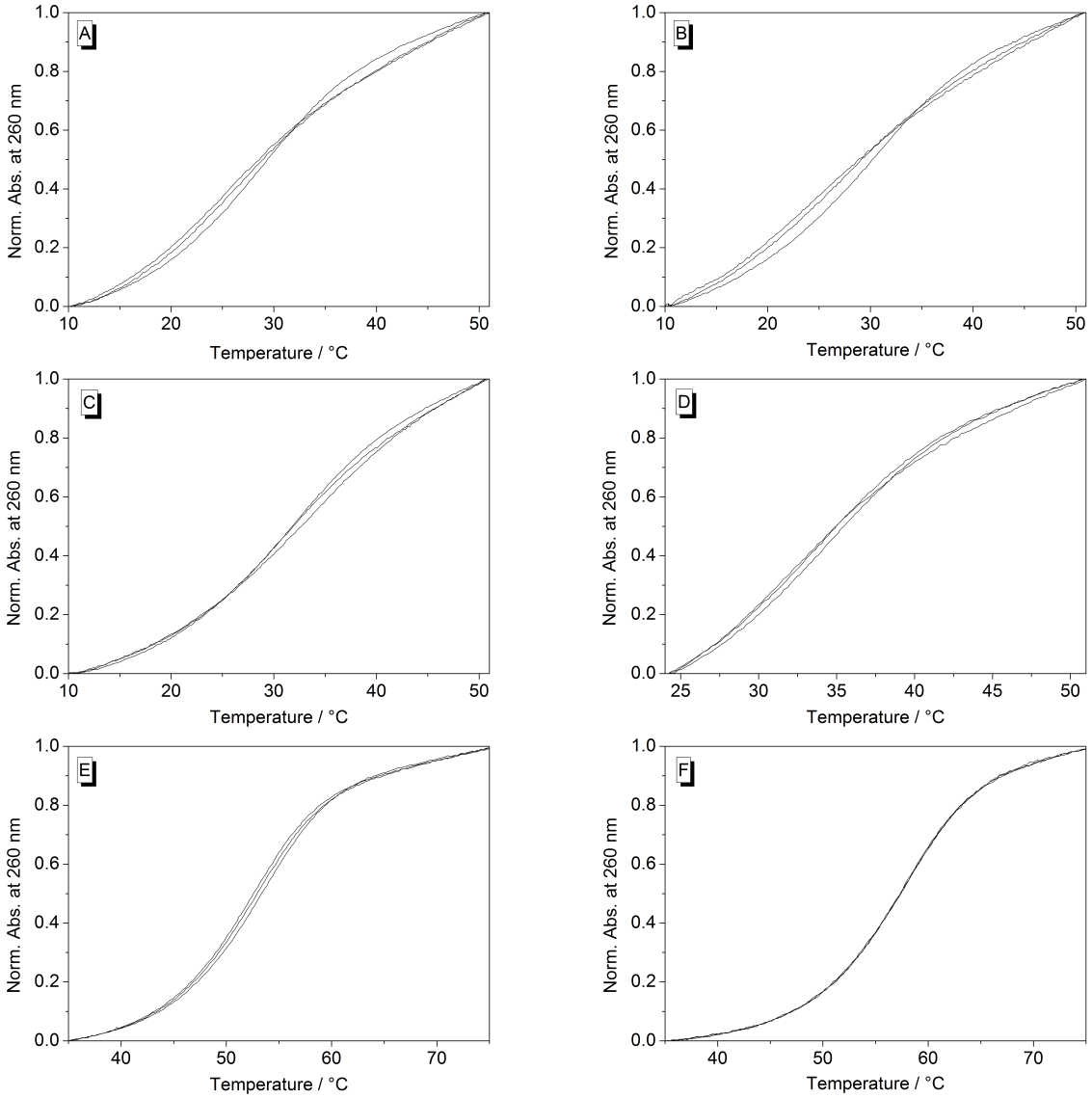


Figure S17. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **3a** at *LDR* = 0, 0.5 and 2.0.

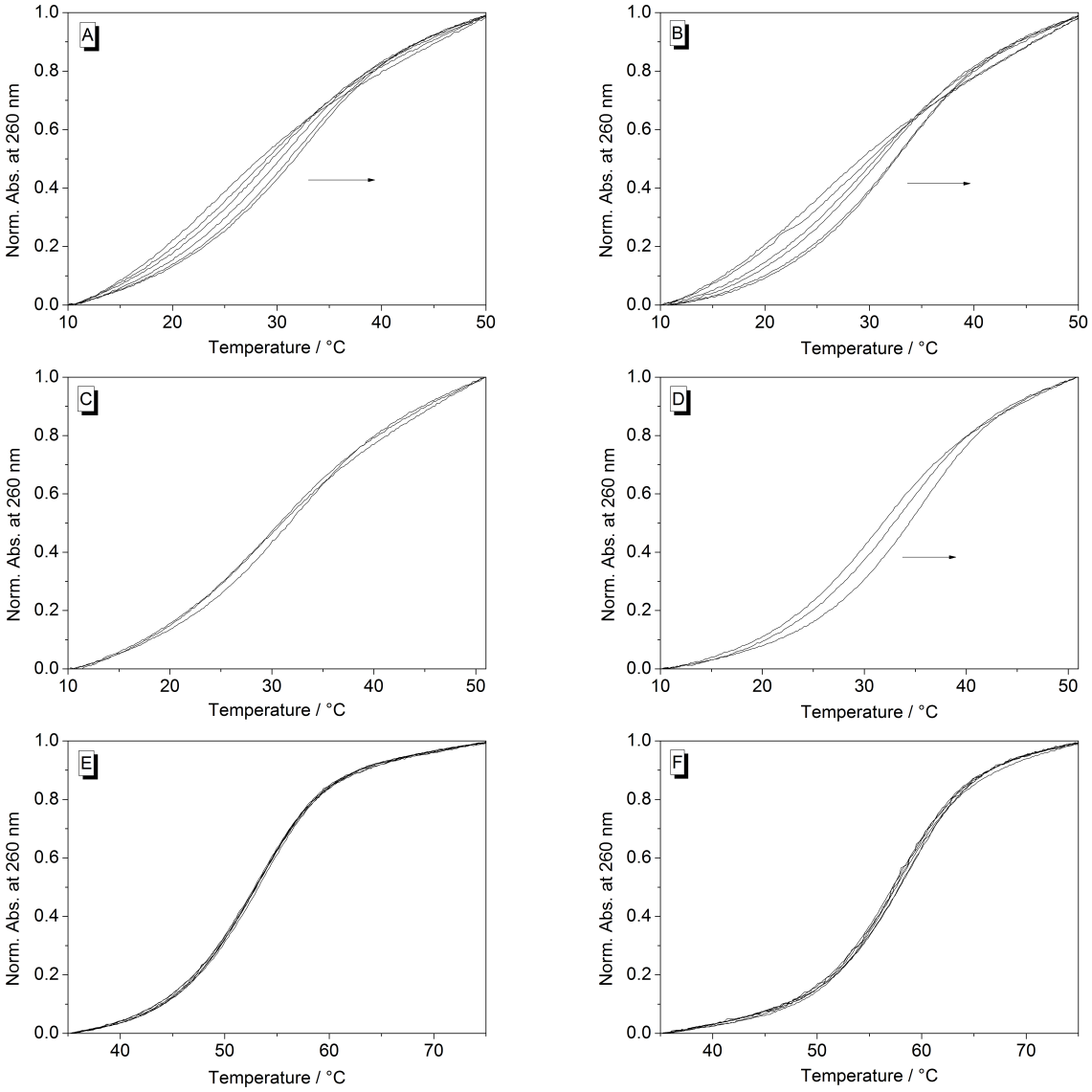


Figure S18. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 µM in ODN buffer) in the presence of ligand **3b** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

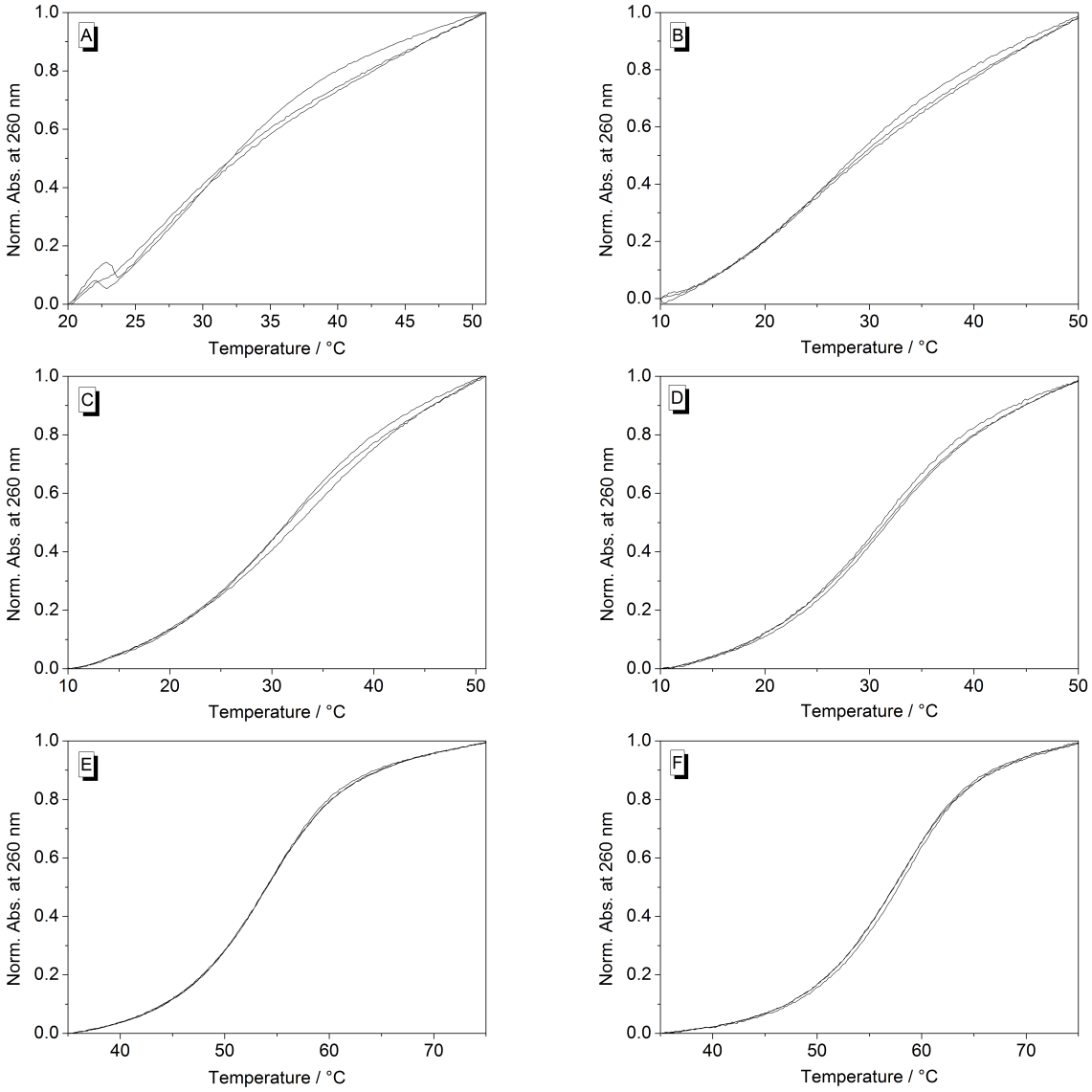


Figure S19. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5 μM in ODN buffer) in the presence of ligand **4a** at *LDR* = 0, 0.5 and 2.0.

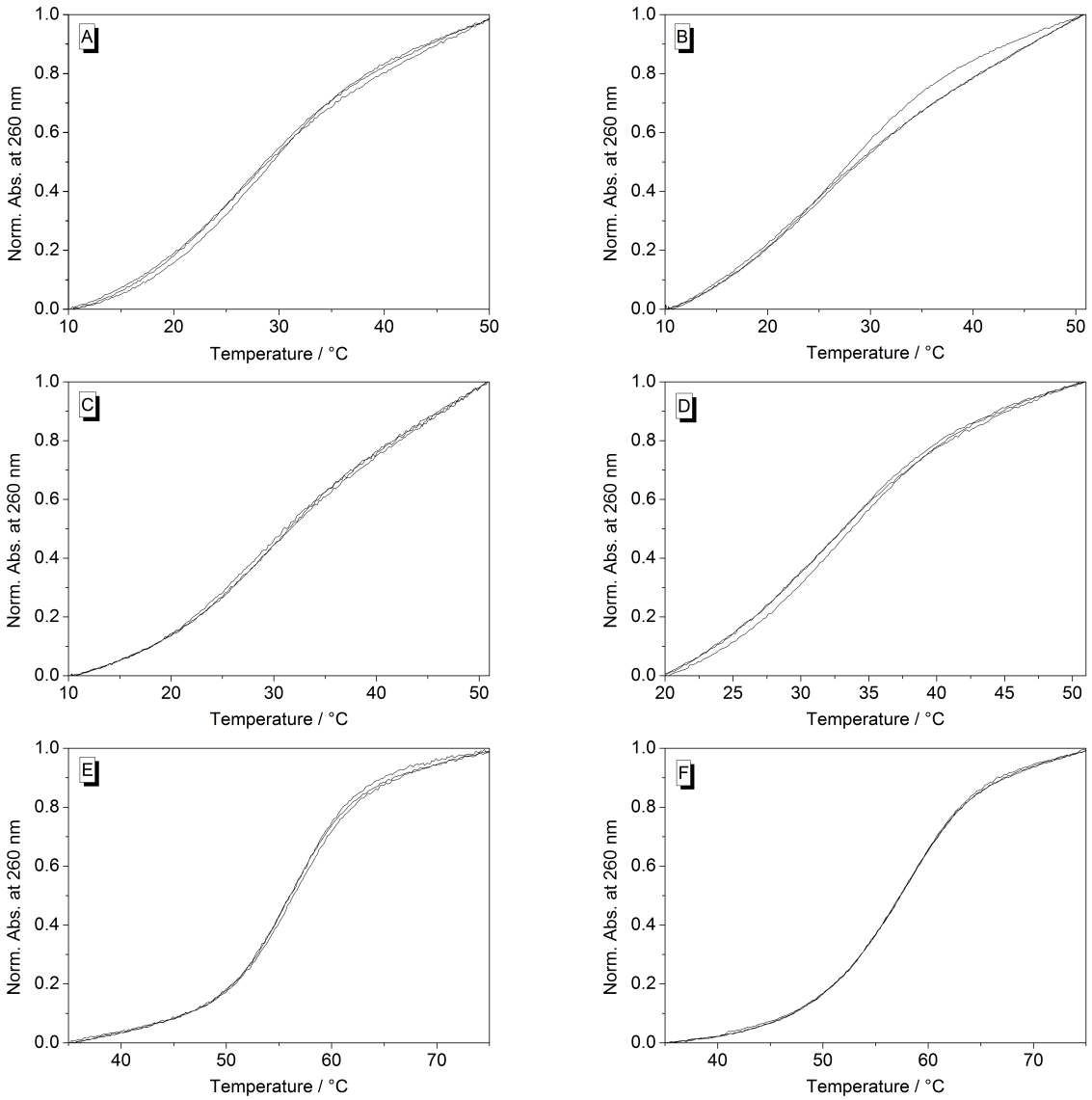


Figure S20. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **4b** at *LDR* = 0, 0.5 and 2.0.

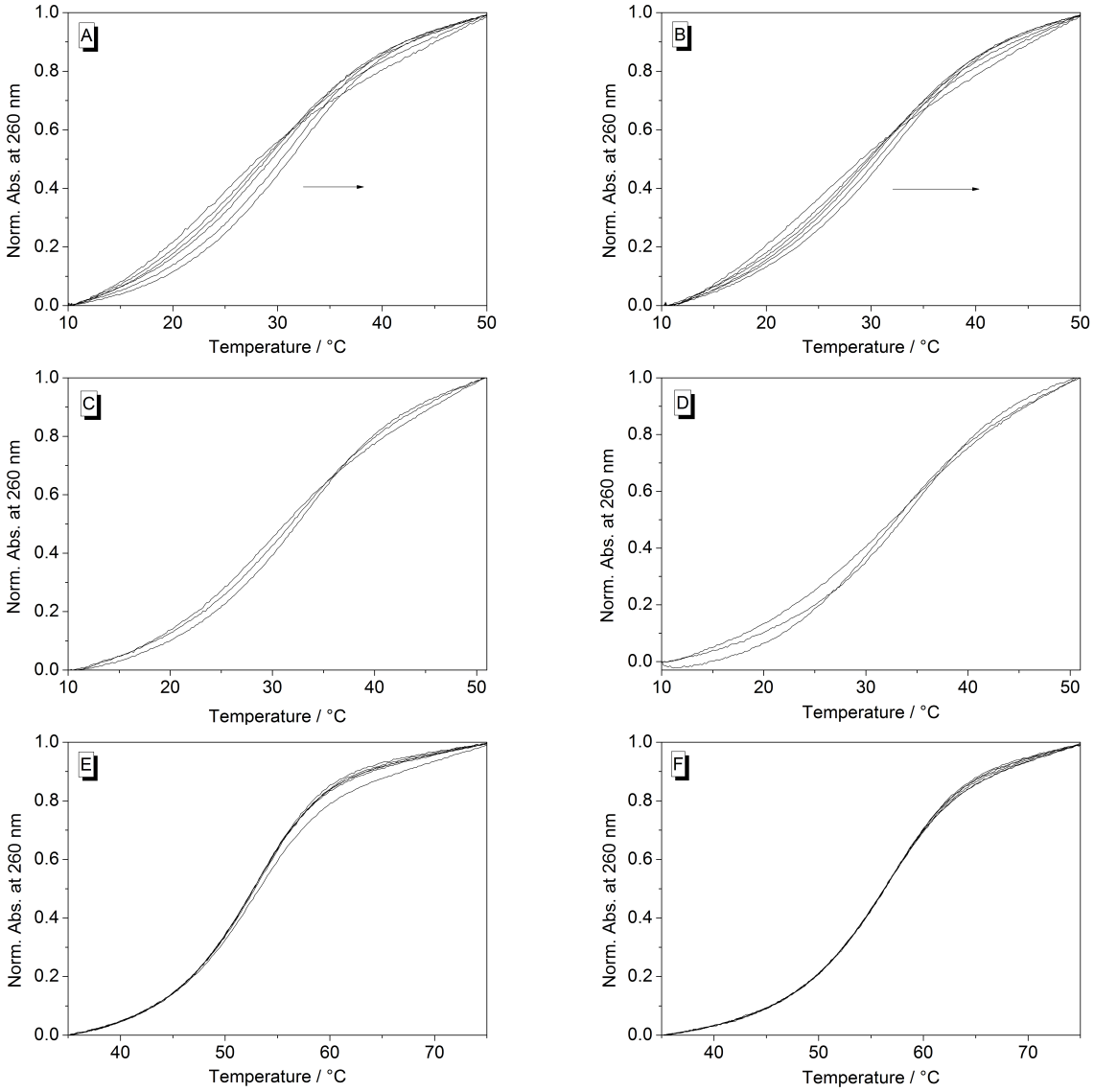


Figure S21. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **4c** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

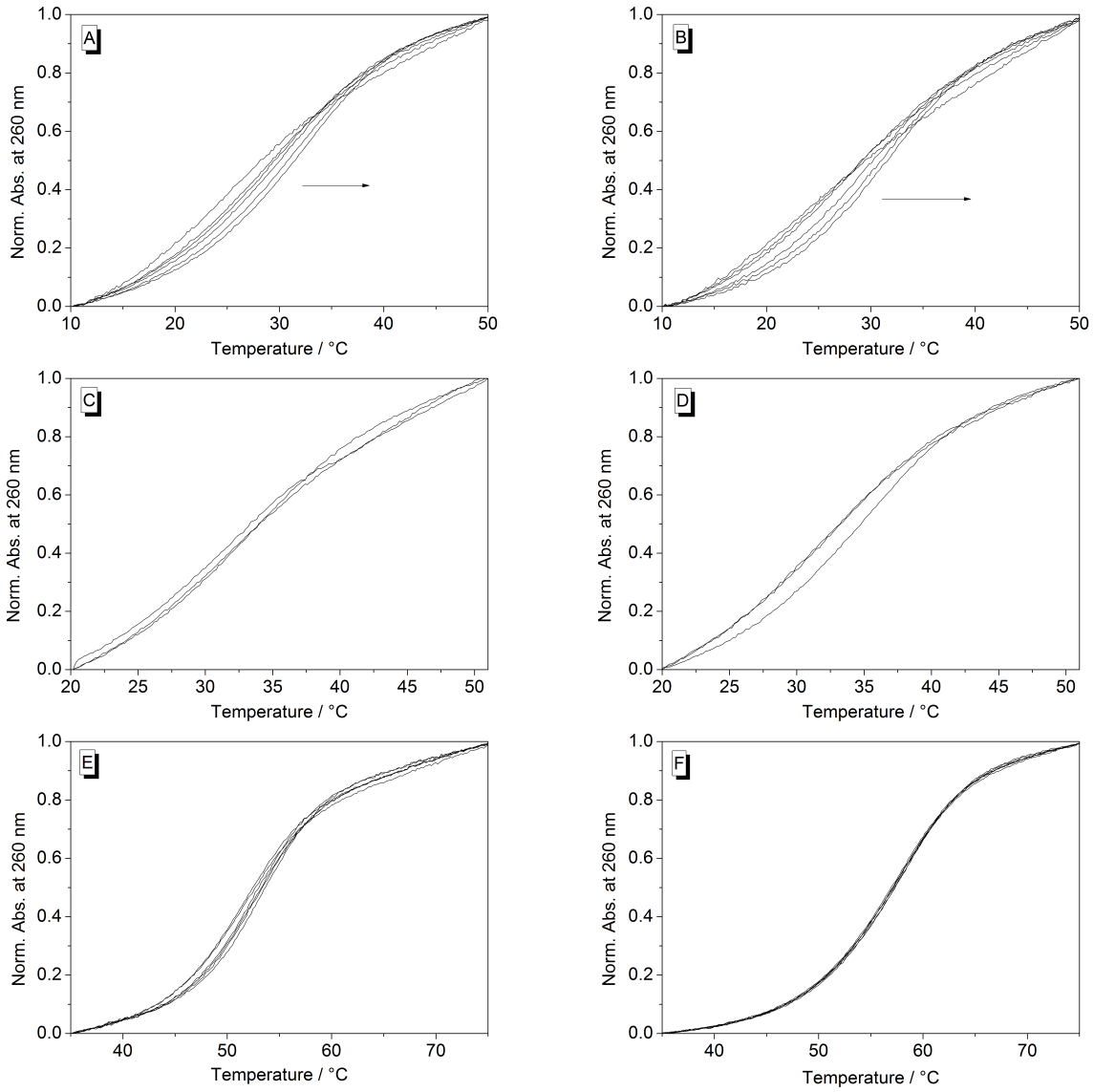


Figure S22. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 µM in ODN buffer) in the presence of ligand **4d** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

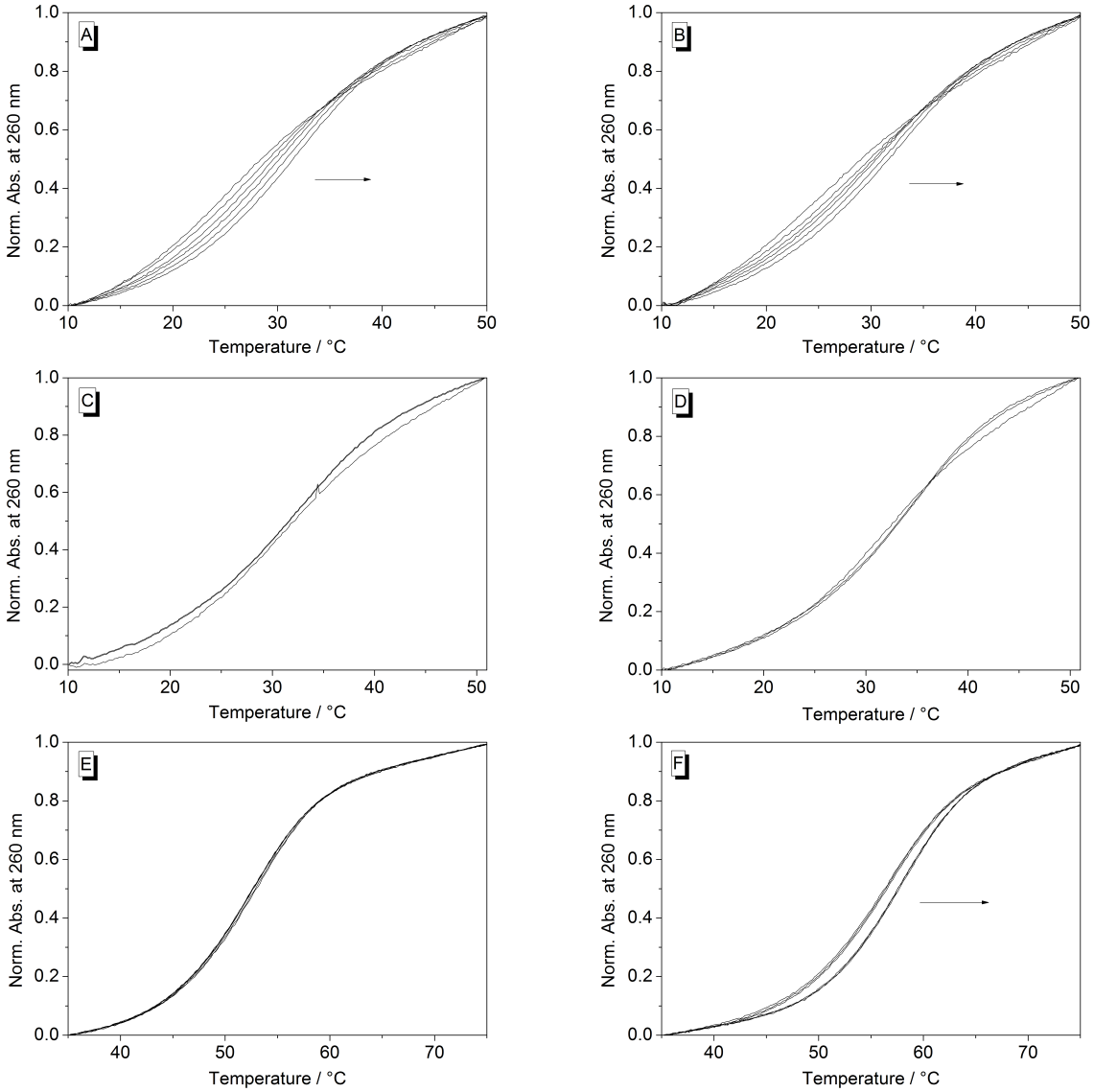


Figure S23. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5 µM in ODN buffer) in the presence of ligand **4f** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

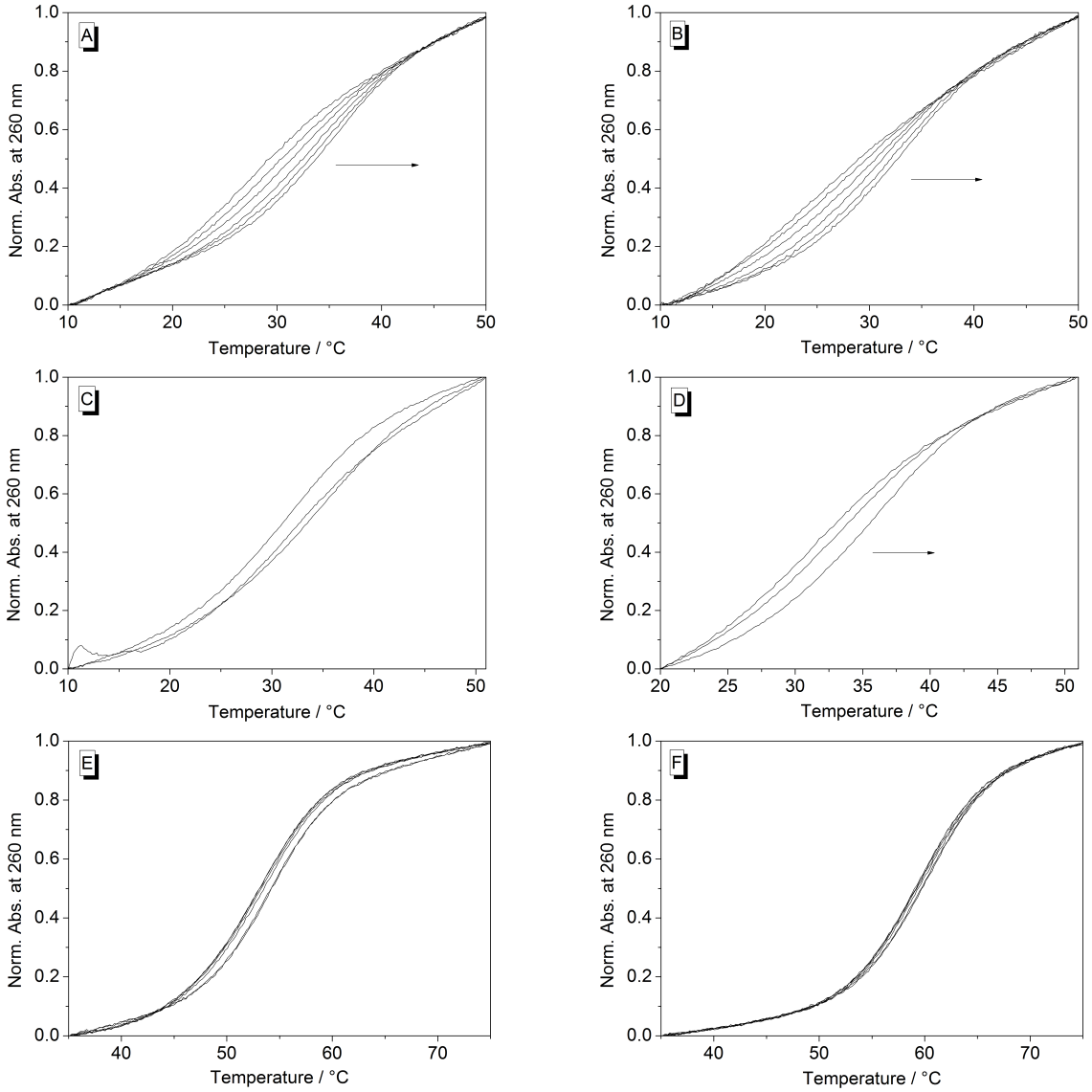


Figure S24. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 µM in ODN buffer) in the presence of ligand **4g** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

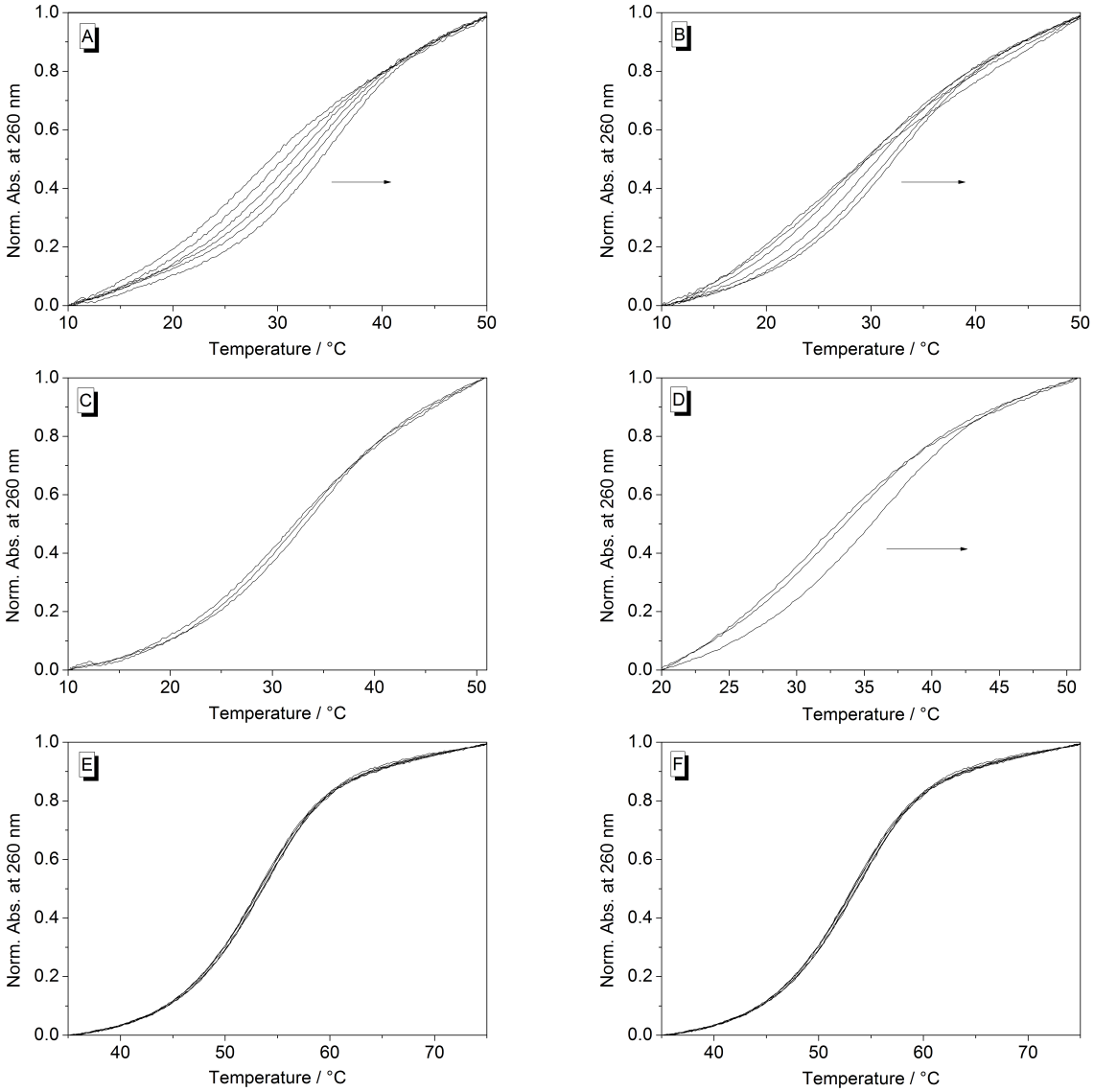


Figure S25. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 µM in ODN buffer) in the presence of ligand **4h** at *LDR* = 0, (0.2), 0.5, (1.0), (1.5), and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

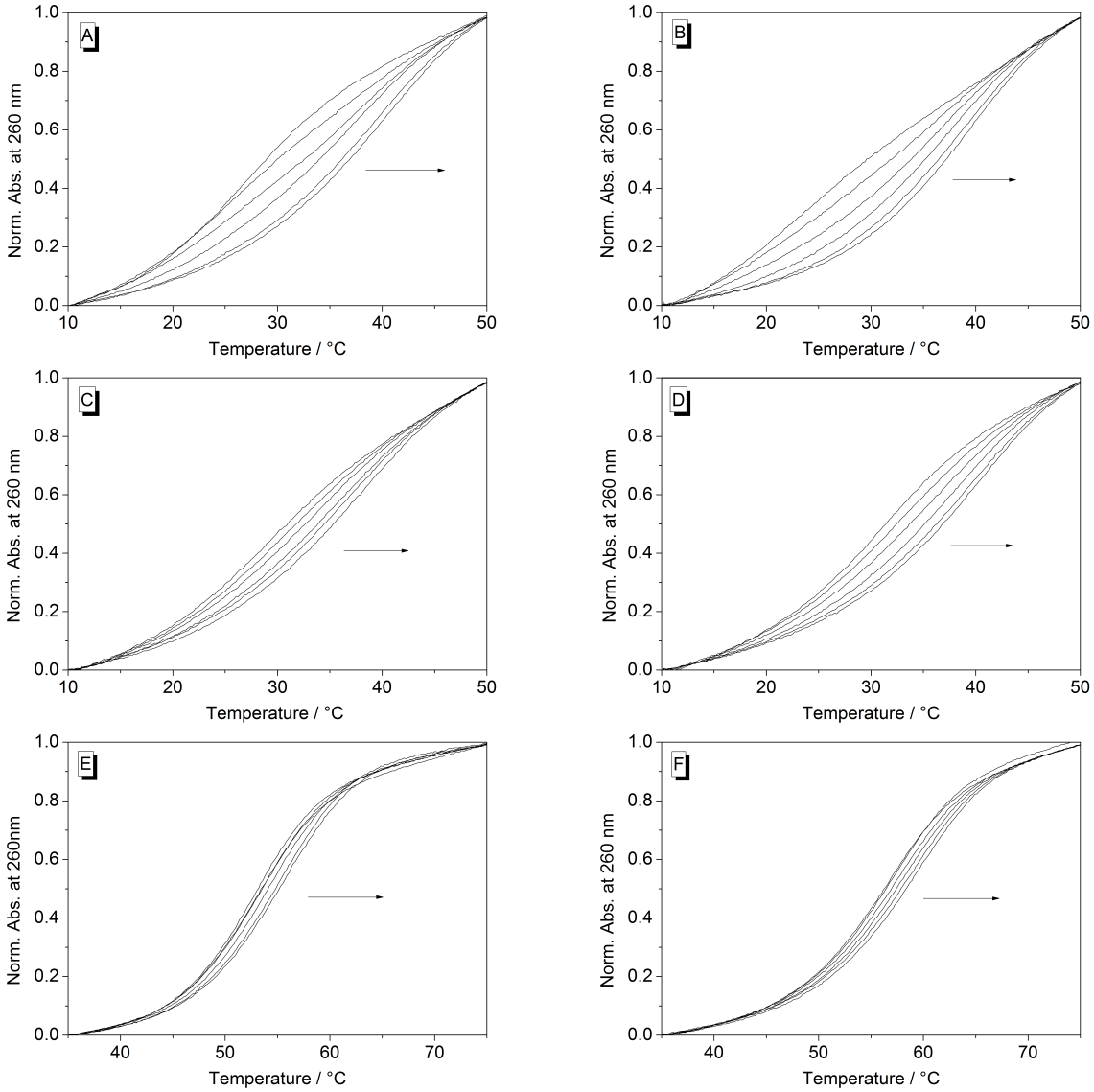


Figure S26. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **5a** at *LDR* = 0, 0.2, 0.5, 1.0, 1.5, and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.

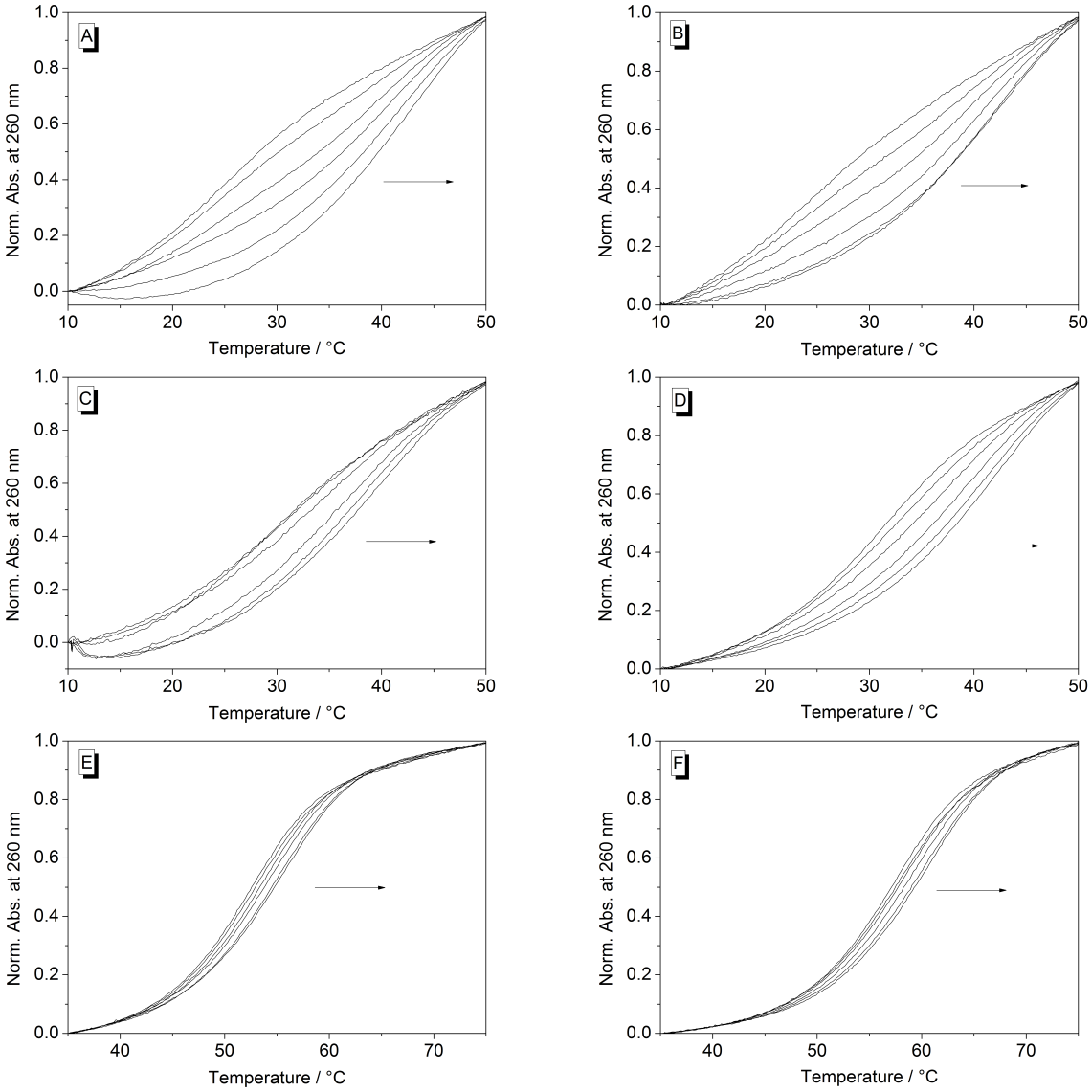


Figure S27. Thermal denaturation profiles of AP-DNA **CX** (A), **TX** (B), **AX** (C), **GX** (D) and the regular DNA **TA** (E) and **CG** (F) (c_{DNA} = 5.0 μM in ODN buffer) in the presence of ligand **5b** at *LDR* = 0, 0.2, 0.5, 1.0, 1.5, and 2.0. Arrows indicate steady and significant changes of the shift of the melting curves with increasing *LDR*.