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

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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 NaPF₆ (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/H₂O (1g, 1h).

2-[(3-Dimethylammoniopropyl)amino]quinolizinium bis(hexafluorophosphate) (1e): According to GP1, 2-bromoquinolizininium tetrafluoroborate (1b) (177 mg, 600 µmol) and N,N,N'-trimethyl-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.). – ¹H-NMR (400 MHz, CD₃CN): δ = 2.00–2.07 (m, 2 H, 2'-H), 2.84 (s, 6 H, N(CH₃)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, 3J = 7 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). – ¹³C-NMR (100 MHz, CD₃CN): δ = 24.0 (C2'), 40.6 (C1'), 44.2 (2 × N(CH₃)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-C₆), 153.9 (ar-C₆). – MS (ESI⁺): m/z (%) = 230 (100) [M – H(PF₆)₂]⁺. – El. Anal. calcd (%) for C₁₄H₂₂N₅PF₆ × HPF₆ (521.3 g/mol): C 32.26, H 4.06, N 8.06; found: C 32.86, H 3.67, N 8.22.

2-[(3-Dimethylammoniopropyl)(methyl)amino]quinolizinium bis(hexafluorophosphate) (1f): According to GP1, 2-bromoquinolizininium 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.). – 1H-NMR (600 MHz, [D₆]DMSO): δ = 1.93–1.98 (m, 2 H, 2'-H), 2.78 (s, 6 H, N(CH₃)₂), 3.10 (t, 3J = 8 Hz, 2 H, 3'-H), 3.20 (s, 3 H, N₆(CH₃)), 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). – 13C-NMR (150 MHz, [D₆]DMSO): δ = 21.6 (C2'), 38.1 (N₆(CH₃)), 42.4 (2 × N(CH₃)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-C₆), 151.9 (ar-C₆). – MS (ESI⁺): m/z (%) = 244 (100) [M – H(PF₆)₂]⁺. – El. Anal. calcd (%) for C₁₅H₂₄N₆PF₆ × HPF₆ (535.3 g/mol): C 33.66, H 4.33, N 7.85; found: C 33.04, H 3.87, N 8.13.

![Image of chemical structure](image_url)

4-[(3-Dimethylammoniopropyl)amino]quinolizinium bis(hexafluorophosphate) (1g): According to GP 1 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.). – 1H-NMR (400 MHz, CD₂CN): δ = 2.11–2.18 (m, 2 H, 2'-H), 2.81 (s, 6 H, N(CH₃)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). – 13C-NMR (100 MHz, CD₂CN): δ = 23.8 (C2'), 42.0 (C1'), 44.2 (2 × N(CH₃)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-C₆), 148.4 (ar-C₆). – MS (ESI⁺): m/z (%) = 230 (100) [M – H(PF₆)₂]⁺. – El. Anal. calcd (%) for C₁₄H₂₂N₆PF₆ × HPF₆ (521.3 g/mol): C 32.26, H 4.06, N 8.06; found: C 31.75, H 3.68, N 7.52.

![Image of chemical structure](image_url)

4-[(3-Dimethylammoniopropyl)(methyl)amino]quinolizinium bis(hexafluorophosphate) (1h): According to GP 1 4-chloroquinolizinium tetrafluoroborate (1c) (201 mg, 800 µmol) and N₆,N₆,N₆′-trimethyl-1,3-propanediamine (279 mg, 2.40 mmol, 352 µl) were stirred in 2-PrOH (10 ml) for 2 h to give an orange-colored microcrystalline solid (111 mg, 206 µmol, 26%); m.p. = 220–222 °C (dec.). – 1H-NMR (400 MHz, [D₆]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$_{q}$(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$_{13}$H$_2$N$_3$PF$_6$ × 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.

N-(3-Dimethylaminopropyl)quinolizinium-9-carboxamide hexafluorophosphate (II): 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$_3$CN): δ = 2.00–2.08 (m, 2 H, 2'-H), 2.86 (s, 6 H, N(CH$_3$)$_2$), 3.16 (t, $^3$J = 7 Hz, 2 H, 3'-H), 3.52 (q, $^3$J = 7 Hz, 2 H, 1'-H), 7.83 (br s, 1 H, NH), 8.09 (dd, $^3$J = 7 Hz, 1 H, 7-H), 8.17 (dd, $^3$J = 7 Hz, $^4$J = 2 Hz, 1 H, 3-H), 8.41 (dd, $^3$J = 9 Hz, $^3$J = 7 Hz, $^4$J = 1 Hz, 1 H, 8-H), 8.51 (d, $^3$J = 9 Hz, 1 H, 9-H), 8.71 (s, 1 H, 1-H), 9.04 (d, $^3$J = 7 Hz, 1 H, 4-H), 9.06 (d, $^3$J = 7 Hz, 1 H, 6-H). – $^{13}$C-NMR (100 MHz, CD$_3$CN): 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$_{13}$H$_2$N$_3$OP × 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.

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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 CHCl₃ were added. The aqueous layer was extracted with CHCl₃ (3 x 10 ml) and the organic layer was washed with water (3 x 50 ml). The combined organic layers were dried with MgSO₄, 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 (SiO₂, CHCl₃/MeOH 10/0.1, Rf = 0.87) gave a yellow-brown solid (2.03 g, 8.11 mmol, 71%); m.p. = 61–63 °C. - ¹H-NMR (400 MHz, CDCl₃): 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). - ¹³C-NMR (100 MHz, CDCl₃): δ = 122.7 (CH), 123.1 (CH), 125.5 (CH), 127.6 (CH), 129.5 (CH), 130.2 (C₉), 132.5 (CH), 134.0 (C₉), 137.2 (CH), 137.6 (C₉), 150.0 (CH), 155.3 (C₉).

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 – ¹H-NMR (400 MHz, CDCl₃): 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'-Dichloro-2-styryl)pyridine (9d): Crystallization from MeOH/heptane gave a white solid (1.00 g, 4.00 mmol, 35%); m.p. = 63–64 °C. – ¹H-NMR (400 MHz, [D₆]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). – ¹³C-NMR (100 MHz, [D₆]DMSO): δ = 123.1 (CH), 123.7 (CH), 125.4 (CH), 126.4 (CH), 129.1 (CH), 131.2 (CH), 131.2 (C₉), 132.2 (C₉), 135.8 (CH), 136.9 (CH), 149.6 (CH), 153.7 (C₉).

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 – ¹H-NMR (400 MHz, CDCl₃): 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).

trans-2-(2',6'-Dichloro-2-steryl)pyridine (9f): Column chromatography (SiO₂, CHCl₃/MeOH 98/2, Rᵣ = 0.77) gave a viscous orange-colored oil (1.42 g, 5.66 mmol, 50%). – ¹H-NMR (400 MHz, CD₃OD): 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, ³J = 1 Hz, ³J = 8 Hz, 1 H, CH), 7.60 (d, ³J = 16 Hz, 1 H, CH), 7.74 (ddd, ⁴J = 2 Hz, ³J = 8 Hz, ³J = 8 Hz, 1 H, CH), 8.71 (d, ³J = 5 Hz, 1 H, CH). – ¹³C-NMR (100 MHz, [D₆]DMSO): δ = 123.1 (CH), 123.2 (CH), 125.5 (CH), 128.8 (2 x CH), 129.4 (CH), 133.4 (C₉), 133.7 (C₉), 136.0 (CH), 136.9 (CH), 149.6 (CH), 153.7 (C₉).

General procedure for the synthesis of Chlorobenzo[c]quinolizinium derivates.
A stirred solution of the trans-2-(dichloro-2-steryl)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:

10-Chlorobenzo[c]quinolizinium tetrafluoroborate (4b): Brown solid (41 mg, 136 µmol, 4%); m.p. = 149–151 °C. – ¹H-NMR (600 MHz, [D₆]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). – ¹³C-NMR (150 MHz, [D₆]DMSO): δ = 122.4 (CH), 123.9 (CH), 124.5 (C₉), 127.7 (CH), 129.3 (CH), 130.1 (C₉), 131 (CH), 131.8 (C₉), 135.4 (CH), 136 (CH), 139.8 (CH), 141.8 (CH), 144.6 (C₉). – MS (ESI⁺): m/z (%) = 214 (100) [M – BF₄]⁺. – El. Anal. calc (%) for C₁₁H₉NClBF₄ × 0.5 H₂O (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). – ¹H-NMR (400 MHz, CD₃OD): 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]quinolinium tetrafluoroborate (4d): Yellow solid (111 mg, 369 μmol, 11%); m.p. = 302–303 °C (dec.). – 1H-NMR (600 MHz, [D₆]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). – 13C-NMR (150 MHz, [D₆]DMSO): δ = 120.7 (CH), 124.3 (CH), 124.7 (CH), 128.1 (C₆), 128.5 (CH), 129.0 (CH), 132.4 (CH), 133.1 (C₆), 134.9 (C₆), 135.2 (CH), 135.3 (CH), 141.0 (CH), 143.2 (C₆). – MS (ESI⁺): m/z (%) = 214 (100) [M – BF₄]⁺. – El. Anal. calcd (%) for C₁₃H₉NClBF₄ (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]chinolinium 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). – 1H-NMR (400 MHz, [D₆]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]quinolinium chloride (4f): Yellow solid (72.2 mg, 289 μmol, 7%); m.p. = 280–282 °C. – 1H-NMR (400 MHz, [D₆]DMSO): δ = 8.17 (t, 3J = 8 Hz, 1 H, 9-H), 8.26 (d, 3J = 8 Hz, 1 H, 9-H), 8.31 (ddd, 3J = 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, 3J = 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). – 13C-NMR (100 MHz, [D₆]DMSO): δ = 117.8 (CH), 124.6 (C₆), 124.8 (CH), 128.6 (CH), 130.9 (CH), 131.7 (CH), 132.7 (CH), 132.8 (CH), 135.4 (CH), 135.8 (C₆), 141.4 (CH), 143.2 (C₆), 149.6 (C₆). – MS (ESI⁺): m/z (%) = 214 (100) [M – Cl]⁺. – El. Anal. calcd (%) for C₁₃H₉NCl₂ (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]quinolinium tetrafluoroborate (4g): Under inert gas atmosphere, a suspension of 8-nitrobenzo[c]quinolinium chloride (500 mg, 1.92 mmol) and SnCl₂(H₂O)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 distillation. The residue was dissolved in water and filtered. An aq. solution of NaBF₄ (sat.) was added and the solution was extracted with CH₃NO₂. After removal of the solvent the product was obtained as yellow solid (25.2 mg, 109 μmol, 6%); m.p. = 228–229 °C (dec.). – 1H-NMR (600 MHz, [D₆]DMSO): δ = 6.39 (br s, 2 H, NH₂), 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). – 13C-NMR (150 MHz, [D₆]DMSO): δ = 108.1 (CH), 118.9 (CH), 121.3 (CH), 122.3 (CH), 124.0 (CH), 125.1 (C₆), 128.1 (CH), 129.0 (C₆), 132.5 (CH), 135.8 (CH), 137.0 (CH), 140.5 (C₆), 150.6 (C₆). – MS (ESI⁺): m/z (%) = 195 (100) [M – NH₃]⁺. – El. Anal. calcd (%) for C₁₃H₁₁N₂BF₄ x 0.5 H₂O (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)Cl₂·CH₂Cl₂ (24.5 mg, 0.03 mmol) and KF (232 mg, 4.00 mmol) in DME/H₂O/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 NaBF₄ (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.

-¹H-NMR (600 MHz, [D₆]DMSO): δ = 2.83 (s, 3 H, CH₃), 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). –¹³C-NMR (150 MHz, [D₆]DMSO): δ = 18.9 (CH₃), 115.9 (CH), 122.5 (CH), 124.3 (CH), 125.7 (C₆), 128.3 (CH), 131.2 (CH), 132.3 (CH), 133.3 (CH), 134.6 (CH), 134.6 (C₆), 138 (C₆), 140.3 (CH), 142.9 (C₆). – MS (ESI⁺): m/z (%) = 194 (100) [M – BF₄]⁺. – EL Anal. cald (%) for C₁₄H₁₂NBF₄ (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]quinolinizium and dibenzo[a,f]quinolizinium derivates.

A solution of 2-(4-methylphenyl)pyridine or 2-(4-methylphenyl)quinoline³ 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 distillation 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 NaBF₄ (sat.) was added to the filtrate. The precipitate was filtered, washed with a small amount of water, THF and diethylether, and recrystallized from CH₃OH/EtOAc.

9-Methylbenzo[a]quinolinizium tetrafluoroborate (3b): Colorless solid (580 mg, 2.53 mmol, 61%); m.p. = 237–239 °C. –¹H-NMR (600 MHz, [D₆]DMSO): δ = 2.63 (s, 3 H, CH₃), 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,

**9-Methylbenzo[a,f]quinolizinium tetrafluoroborate (5b):** Because of significant impurities after workup according to general procedure, this product was further purified by MPLC (water/CH₃CN/CF₃COOH: 50/50/0.1) to give a yellow solid (12.0 mg, 0.03 μmol, <1%). ¹H-NMR (600 MHz, [D₆]DMSO): δ = 2.67 (s, 3 H, CH₃), 7.97 (dd, ³J = 2 Hz, ²J = 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). – ¹³C-NMR (150 MHz, [D₆]DMSO): δ = 21.6 (CH₃), 118.3 (CH), 118.6 (CH), 122.5 (CH), 123.5 (C₆), 126.8 (CH), 126.9 (CH), 127.1 (CH), 127.3 (C₆), 129.9 (CH), 130.5 (CH), 132.9 (CH), 133.4 (C₆), 133.8 (CH), 135.4 (C₆), 139.6 (CH), 144.0 (C₆), 146.5 (C₆). – 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 ($c_{\text{Ligand}} = 0.10$ 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, $\lambda_{ex} = 324$ nm), 4b (B, $c = 10$ µM, $\lambda_{ex} = 325$ nm), 4c (C, $c = 10$ µM, $\lambda_{ex} = 328$ nm), 4d (D, $c = 10$ µM $\lambda_{ex} = 320$ nm), 4f (E, $c = 10$ µM, $\lambda_{ex} = 342$ nm), 4g (F, $c = 10$ µM $\lambda_{ex} = 324$ nm), and 4h (G, $c = 10$ µM, $\lambda_{ex} = 307$ 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, \(c = 10 \mu M, \lambda_{ex} = 318\) nm) and 3b (B, \(c = 10 \mu M, \lambda_{ex} = 303\) 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 (\(c = 10 \mu M, \lambda_{ex} = 310\) 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 \mu M 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 \mu M 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 \mu M 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) (cDNA = 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) ($c_{\text{DNA}} = 5.0 \mu M$ 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 \, \mu M 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) ($c_{\text{DNA}} = 5.0 \mu M$ 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 \mu M 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) (cDNA = 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 \text{ 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) \((c_{DNA} = 5.0 \mu M\) 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) ($c_{DNA} = 5 \mu M$ 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 $LDR$. 

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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) ($c_{\text{DNA}} = 5.0 \, \mu\text{M in ODN buffer}$) in the presence of ligand 4g at $LDR = 0, (0.2), 0.5, (1.0), (1.5), \text{and } 2.0$. 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 \mu M 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) \((c_{\text{DNA}} = 5.0 \text{ µM in ODN buffer})\) in the presence of ligand 5a at \(LDR = 0, 0.2, 0.5, 1.0, 1.5, \text{ and } 2.0\). 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) (cDNA = 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.