Supporting Information

Different Cytotoxicities and Cellular Localizations of Novel Quindoline Derivatives With or Without Boronic Acid Modifications in Cancer Cells

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A. Experimental Procedures:

Materials and general methods: All starting materials and solvents were obtained from commercial sources and used without further purification. Thin-layer chromatography (TLC) was performed on precoated E. Merck silica-gel 60 F254 plates. Column chromatography was performed on silica gel (200-300 mesh Qingdao China). Melting points were determined on a Mitamura-Riken micro-hot stage and were not corrected. $^1$HNMR and $^{13}$CNMR spectra were obtained on a Bruker 600 spectrometer with tetramethylsilane (Me$_4$Si) as the internal standard, and chemical shifts were recorded in δ values. Mass spectra were recorded on a Q-TOF Global mass spectrometer. The important intermediate 11-Chloroquindoline 1 was synthesized as reported [1]. Analytical data for compound 6 has been previously presented [2].

General procedure for the synthesis of 11-chloroquindoline 1:

\[ \text{Step 1.} \text{NaOH (54 g, 204 mmol) and H}_2\text{O (350 mL) placed in a sealed flask which was equipped with a}\]
\[ \text{thermometer and constant pressure dropping funnel, then cooled the flask to -7 °C, Br}_2 (34.9 g, 218 mmol) was}\]
\[ \text{slowly added so that the temperature did not rise above -5 °C. After the addition, phthalimide 1-1 (30.0 g, 204}\]
\[ \text{mmol) was added portionwise, then the solution of NaOH (28 g) and H}_2\text{O (40 mL) was added, refluxed for 2 min,}\]
\[ \text{cooled to room temperature, adjusted the pH to 4-5 with cond HCl. The resulting precipitates were collected by}\]
\[ \text{filtration and recrystallized from H}_2\text{O to give 22.0 g (78.7%) of anthranilic acid 1-2 as white crystals, m.p.: 144-146 °C.}\]

\[ \text{Step 2. Anthranilic acid 1-2 (10.6 g, 77 mmol), dimethylformamide (13 mL), and dioxane (13 mL)}\]
\[ \text{were placed in a sealed flask, which was cooled to 0 °C, and then chloroacetyl chloride (10.4 g, 92 mmol) was}\]
\[ \text{slowly added so that the temperature did not rise above 1 °C. After addition, the}\]
\[ \text{temperature was maintained at 0 °C for a further 10 min, and then the mixture was stirred overnight at}\]
\[ \text{room temperature. The contents of the flask were poured into water (200 mL), and the resulting}\]
\[ \text{precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give 15.9 g (96.4%) of}\]
\[ \text{1-3 as gray solid.}\]

\[ \text{Step 3. Aniline (16.3 g, 175 mmol), dimethylformamide (70 mL), and the crude acid 1-3 (10.7 g, 50}\]
\[ \text{mmol) were stirred and heated at 80 °C for 24 h. After the cooling process, the reaction mixture was}\]
poured into water (350 mL), and sufficient NaOH solution (20%) was added to dissolve the precipitate. The pH was checked, and if necessary, more NaOH solution was added to raise the pH to 9. The mixture was extracted with chloroform, and the aqueous phase was then acidified to pH 4-5 with acetic acid solution (30%), and the resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give 10.1 g (74.8%) of 1-4 as white solid.

**Step 4.** The crude product from above 1-4 (9.5 g, 40 mmol) and polyphosphoric acid (400 g) were stirred at 130 °C for 3 h, and then the mixture was poured into iced/water (1800 mL) and neutralized with saturated KOH solution. The mixture was then centrifuged and the precipitate washed with neutral water (3×25 mL), ethanol (25 mL), and then dried to give 9.1 g (90%) of 1-5 as deep green solid.

**Step 5.** The crude product 1-5 (8.2 g, 35 mmol) and phosphorus oxychloride (87 mL) were stirred under reflux at 100 °C for 4 h. After the reaction mixture was cooled, it was poured into iced/water (800 mL) and then neutralized with saturated KOH solution, and the resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give the crude product 1, which was chromatographed over silica gel with chloroform to give 5.3 g (60.0%) of pure 11-chloroquindoline 1 as yellow solid. m.p.: 219–221°C.

**General procedure for the synthesis of 11-animo-10H-indolo[3,2-b]quinoline (2a-2d):** A mixture of 11-Cl-10H-indolo[3,2-b]quinoline 1 (7.2 mmol), chain diamine (36 mmol) and 1 drop of concentrated HCl in 2-ethoxyethanol (18 mL) was refluxed for 17 h. Then the mixture was cooled, poured into ice/water (100 mL), made basic with KOH (10%) solution. The resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give the crude product 2a-2d, which was purified by flash chromatography on silica gel (chloroform/methanol: 5/1 then chloroform/methanol/triethylamine: 200/100/1).

**General procedure for the synthesis of 11-(benzoic acid side-chain)-10H-indolo[3,2-b]quinoline (3a-3d):** DMT-MM was synthesized as the literature procedure[3], m.p.: 115-117°C (116-117°C in ref). A mixture of 1 (1.0 mmol), benzoic acid (0.16 g, 1.3 mmol), and DMT-MM (0.36 g, 1.3 mmol) was stirred at room temperature in 2-ethoxyethanol (10 mL) for 18 h. The mixture was poured into water (60 mL), the resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give the crude product 3a-3d, which was purified by flash chromatography on silica gel (chloroform/methanol: 20/1 then 5/1).

**General procedure for the synthesis of 11-(4-carboxyphenylboronic acid side–chain)-10H-indolo[3,2-b]quinoline (4a-4d):** A mixture of 1 (1.0 mmol), 4-carboxyphenylboronic acid (0.22 g, 1.3 mmol), and DMT-MM (0.36 g, 1.3 mmol) was stirred at room temperature in 2-ethoxyethanol (10 mL) for 18 h. The mixture was poured into water (60 mL), the resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give the crude product 4a-4d, which was purified by flash chromatography on silica gel (chloroform/methanol: 2/1 then chloroform/ methanol/triethylamine: 20/10/1).

**General procedure for the synthesis of 11-(3-carboxyphenylboronic acid side-chain)-10H-indolo[3,2-b]quinoline (4e-4h):** A mixture of 1 (1.0 mmol), 3-carboxyphenylboronic acid (0.22 g, 1.3 mmol), and DMT-MM (0.36 g, 1.3 mmol) was stirred at room temperature in 2-ethoxyethanol (10 mL) for 18 h. The mixture was poured into water (60 mL), the resulting precipitate was filtered, washed with neutral water (3×15 mL), and then dried to give the crude product 4e-4h, which was purified by flash chromatography on silica gel (chloroform/methanol: 2/1 then chloroform/methanol/triethylamine: 20/10/1).

**Bioactivities study:** All synthesized quindoline derivatives 2a-2d, 3a-3d and 4a-4h were dissolved in...
DMSO at a final concentration of 0.1% initially and further diluted with cell culture medium for cellular viability assay. Both human colon cancer cells (HCT116 and HT29) and lung cancer cells (H1299 and A549) were obtained from Shanghai Cell Bank of Chinese Academy of Sciences (Shanghai, China). McCoy’s 5A medium was used for colon cancer cell culture and RPMI1640 medium was used for lung cancer cell culture, respectively. Both media were supplemented with 5% fetal bovine serum (HyClone), penicillin (100 units/mL), and streptomycin sulfate (100 μg/mL) (HyClone) under an atmosphere of 5% CO₂ and 100% relative humidity. The cells were passed aged with trypsin every 3-4 days and revived periodically from frozen stocks.

**Cellular viability assay and IC₅₀ calculation:** For cellular viability assay, a 96-wells plate was seeded with 2000 cells/well in complete cell culture medium. After 24h, the medium was removed and 200 μL complete medium containing serial concentrations of each drug was added to each well. Cells were cultured 48h, followed by adding 20 μL of resazurin (2 mg/mL dissolved in water, catalog no. R7017-5G, Sigma) to the media for 16 h. The fluorescent signal was monitored using 544nm excitation wavelength and 595 nm emission wavelength by Spectramax M5 plate reader (Molecular Devices). The relative fluorescence unit (RFU) generated from the assay was proportional to the number of living cells in each well. The IC₅₀ value of each drug was calculated by the Logit approach.

**Flow cytometry analysis:** Flow cytometry analysis was performed as previously described with some modifications. HT29 or A549 cells were harvested by trypsination and seeded in 6-well plates (5 x 10⁵ cells/well) with McCoy or RPMI1640 complete medium. The compounds 2a, 3a, 4a, or 4e was added to each well at a final concentration of 10 μM, respectively. After incubation for 24 h at 37 ºC, the cells were harvested, washed with PBS for three times, and then analyzed by FCMFCS500MPL (Beckman Coulter, USA), with a 488 nm laser excitation and a 525 nm emission filter. Data were analyzed with WinMDI2.8 software. A minimum of 10,000 events were counted for each sample. Results were expressed in mean fluorescence intensity arbitrary units (au).

**Confocal analysis:** The confocal analysis was performed according to C. Hao. For confocal imaging, HT29 or A549 cells were seeded on glass cover slips in cell culture media overnight before treated with or without the compounds 2a, 3a, 4a or 4e at the concentration of 10 μM for 24 h at 37 ºC. After that, the media were removed, and the cells were washed with PBS for three times. The fluorescence of compounds was measured at 520 ± 20 nm by Laser Scanning Confocal Microscope (Zeiss LSM 510, GER).

### B. Compound characterization

**11-(2-Aminoethyl)amino-10H-indolo[3,2-b]quinoline (2a):** yellow powder, yield: 78.8%; m.p.: 188-198°C; ¹H NMR (d-DMSO, 500 MHz) δ (ppm): 8.42 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 7.4 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.69-7.50 (m, 3H), 7.43 (t, J = 7.2 Hz, 1H), 7.21 (d, J = 7.1 Hz, 1H), 3.37 (d, J = 5.6 Hz, 2H); ¹³C NMR (d-DMSO, 126 MHz) δ (ppm): 146.17, 145.31, 143.72, 135.34, 129.24, 129.10, 126.75, 122.87, 122.54, 122.10, 121.43, 119.74, 119.40, 118.32, 112.45, 44.13, 40.91; HRMS (ESI) m/z: calcd. for C₁₇H₁₇N₄, 277.1448; found: 277.1455.

**11-(3-Aminopropyl)amino-10H-indolo[3,2-b]quinoline (2b):** yellow powder, yield: 75.7%; m.p.: 176-192°C; ¹H NMR (d-DMSO, 500 MHz) δ (ppm): 8.37 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 7.4 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.59-7.49 (m, 3H), 7.38 (t, J = 7.2 Hz, 1H), 7.18 (t, J = 7.1 Hz, 1H), 3.91 (d, J
= 5.6 Hz, 2H), 2.84 (d, J = 5.6 Hz, 2H), 1.83-1.87 (m, 2H); 13CNMR (d-DMSO, 126 MHz) δ (ppm):
146.24, 145.53, 143.60, 128.69, 126.49, 122.42, 122.34, 122.26, 121.37, 119.32, 118.95, 117.81, 112.18, 46.47, 42.37, 37.91; HRMS (ESI) m/z: calcd. for C_{19}H_{19}N_{4}, 291.1604; found: 291.1611.

**11-(3-N-Methylaminopropyl)amino-10H-indolo[3,2-b]quinoline (2c):** yellow powder, yield: 80.5%; m.p.: 182-190°C; 1HNMR (d-DMSO, 500 MHz) δ (ppm): 8.37 (d, J = 8.5 Hz, 1H), 8.23 (d, J = 7.7 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.58-7.49 (m, 3H), 7.39 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 3.89 (t, J = 6.2 Hz, 2H), 2.80 (t, J = 5.8 Hz, 2H), 2.42 (s, 3H), 1.91 (m, 2H); 13CNMR (d-DMSO, 126 MHz) δ (ppm): 146.22, 145.44, 143.68, 136.39, 129.32, 128.84, 126.53, 122.51, 122.28, 122.22, 121.39, 119.51, 118.99, 117.85, 112.26, 47.43, 46.15, 42.49, 35.29; HRMS (ESI) m/z: calcd. for C_{19}H_{21}N_{4}, 305.1761; found: 305.1764.

**11-(6-aminohexyl)amino-10H-indolo[3,2-b]quinoline (2d):** yellow powder, yield: 68.5%; m.p.: 180-190°C; 1HNMR (d-DMSO, 500 MHz) δ (ppm): 10.86 (s, NH), 8.38 (d, J = 8.3 Hz, 1H), 8.22 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.56-7.49 (m, 2H), 7.38 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.3 Hz, 1H), 2.60 (t, J = 7.1 Hz, 2H), 2.46-2.33 (m, 2H), 1.79-1.76 (m, 2H), 1.62-1.67 (m, 2H), 1.46-1.34 (m, 4H); 13CNMR (d-DMSO, 121 MHz) δ (ppm): 146.08, 145.63, 143.55, 136.00, 129.39, 126.55, 122.52, 122.27, 121.35, 119.78, 119.19, 118.22, 112.37, 46.14, 45.67, 33.75, 30.74, 26.44, 26.30; HRMS (ESI) m/z: calcd. for C_{21}H_{25}N_{4}, 333.2074; found: 333.2078.

**N-(2-((10H-indolo[3,2-b]quinolin-11-yl)amino)ethyl)benzamide (3a):** yellow powder, yield: 82.4%; m.p.: 187-190°C; 1HNMR (d-DMSO, 500 MHz) δ (ppm): 12.20 (s, 1H), 9.38 (s, 1H), 8.70 (s, 1H), 8.59-8.58 (d, J = 8.6 Hz, 1H), 8.50-8.49 (d, J = 7.9 Hz, 1H), 8.14-8.13 (d, J = 8.4 Hz, 1H), 8.00-7.99 (d, J = 7.3 Hz, 2H), 7.86-7.76 (m, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.59-7.49 (m, 4H), 7.32-7.29 (t, J = 7.5 Hz, 1H), 4.15-4.11 (dd, J = 12.8, 6.1 Hz, 2H), 3.75-3.71 (dd, J = 13.5, 6.5 Hz, 2H); 13C NMR (d-DMSO, 126 MHz) δ (ppm): 168.49 (C), 143.20 (C), 133.78 (CH), 132.23 (CH), 130.62 (CH), 128.90 (2CH), 127.87 (2CH), 123.87 (CH), 123.29 (CH), 122.39 (CH), 120.34 (CH), 116.37 (CH), 113.21 (CH), 43.94 (CH2), 41.05 (CH2); HRMS (ESI) m/z: calcd. for C_{25}H_{25}ON_{4}, 381.1710; found: 380.1715.
80.6%; m.p.: 210-214°C; ¹H NMR (d-DMSO, 500 MHz) δ (ppm): 10.97 (s, NH), 8.72-8.70 (t, J = 5.4 Hz, 1H), 8.53-8.51 (d, J = 8.5 Hz, 1H), 8.31-8.30 (d, J = 7.7 Hz, 1H), 8.06-8.04 (d, J = 8.4 Hz, 1H), 7.89-7.87 (d, J = 7.4 Hz, 2H), 7.65-7.61 (m, 2H), 7.57-7.54 (t, J = 7.5 Hz, 1H), 7.52-7.49 (t, J = 7.3 Hz, 1H), 7.45-7.42 (m, 3H), 7.24-7.18 (m, 2H), 3.97-3.95 (d, J = 5.4 Hz, 2H), 3.44-3.41 (dd, J = 12.4, 6.3 Hz, 2H), 1.96-1.93 (dd, J = 12.8, 6.3 Hz, 2H); ¹³C NMR (d-DMSO, 126 MHz) δ (ppm): 166.93 (CO), 143.47 (C), 134.94 (C), 131.55 (CH), 129.33 (CH), 128.67 (2CH), 127.69 (2CH), 123.02 (CH), 122.69 (CH), 121.64 (CH), 119.56 (CH), 118.95 (CH), 117.64 (CH), 112.67 (CH), 42.98 (CH₂), 37.11 (CH₂), 30.84 (CH₂); HRMS (ESI) m/z: calcd. for C₂₅H₂₃ON₄, 395.1866; found: 395.1863.

N-(3-((10H-indolo[3,2-b]quinolin-11-yl)amino)propyl)-N-methylbenzamide (3c): yellow powder, yield: 79.5%; m.p.: 220-222°C; ¹H NMR (d-DMSO, 500 MHz) δ (ppm): 11.64 (s, NH), 8.66-8.65 (d, J = 7.3 Hz, 1H), 8.55-8.52 (m, 1H), 8.38-8.37 (d, J = 7.3 Hz, 1H), 8.16-8.15 (d, J = 6.8 Hz, 1H), 7.85-7.82 (t, J = 7.6 Hz, 1H), 7.77-7.73 (m, 1H), 7.67-7.64 (t, J = 7.6 Hz, 1H), 7.57-7.47 (m, 1H), 7.43-7.29 (m, 3H), 7.08-6.83 (m, 2H), 4.14 (s, 2H), 3.65 (s, 2H), 2.95 (s, 3H), 2.13-2.93 (m, 2H); ¹³C NMR (d-DMSO, 126 MHz) δ (ppm): 170.95 (CO), 143.02 (C), 136.89 (C), 131.34 (C), 130.92 (CH), 129.77 (CH), 128.64 (CH), 128.14 (CH), 127.20 (2CH), 126.31 (2CH), 124.11 (CH), 123.68 (CH), 122.56 (CH), 120.67 (CH), 113.56 (CH), 49.04 (CH₂), 37.66 (CH₂), 32.86 (CH₃), 28.94 (CH₂); HRMS (ESI) m/z: calcd. for C₂₆H₂₅ON₄, 409.2023; found: 409.2025.

N-(6-((10H-indolo[3,2-b]quinolin-11-yl)amino)hexyl)benzamide (3d): yellow powder, yield: 84.2%; m.p.: 182-185°C; ¹H NMR (d-DMSO, 500 MHz) δ (ppm): 10.87 (s, NH), 8.45-8.43 (d, J = 8.4 Hz, 1H), 8.41-8.39 (t, J = 5.5 Hz, 1H), 8.29-8.27 (d, J = 7.8 Hz, 1H), 8.02-8.01 (d, J = 8.5 Hz, 1H), 7.82-7.77 (m, 2H), 7.64-7.57 (m, 2H), 7.57-7.50 (m, 1H), 7.50-7.44 (m, 1H), 7.44-7.38 (m, 3H), 7.24-7.18 (m, 1H), 6.99 (s, NH), 3.86 (s, 2H), 3.23-3.20 (dd, J = 12.9, 6.8 Hz, 2H), 1.73-1.67 (dt, J = 14.6, 7.2 Hz, 2H), 1.52-1.41 (qd, J = 14.7, 7.3 Hz, 4H), 1.35-1.29 (dt, J = 14.8, 7.2 Hz, 2H); ¹³C NMR (d-DMSO, 126 MHz) δ (ppm) 166.55 (CO), 143.38 (C), 135.18 (C), 131.40 (CH), 129.71 (CH), 129.41 (CH), 128.93 (CH), 128.65 (2CH), 127.83 (C), 127.57 (2CH), 122.95 (C), 122.84 (CH), 121.65 (CH), 119.61 (CH), 117.39 (CH), 112.70 (CH), 55.49 (CH₂), 45.65 (CH₂), 30.75 (CH₂), 29.60 (CH₂), 26.79 (CH₂), 26.57 (CH₂); HRMS (ESI) m/z: calcd. for C₂₈H₂₉ON₄, 437.2336; found: 437.2333.

4-(2-(10H-indolo[3,2-b]quinolin-11-ylamino)ethylcarbamoyl)phenyl-boronic acid (4a): yellow powder, yield: 76.4%; m.p.: 250-257°C; ¹H NMR (d-DMSO, 600 MHz) δ (ppm): 11.54 (s, NH), 8.36 (d,
$J = 8.4$ Hz, 1H), 8.27 (d, $J = 8.3$ Hz, 2H), 7.91 (d, $J = 8.5$ Hz, 2H), 7.83-7.68 (m, 1H), 7.67-7.55 (m, 2H), 7.44 (t, $J = 7.4$ Hz, 1H), 7.24 (t, $J = 7.1$ Hz, 1H), 4.02 (d, $J = 5.6$ Hz, 2H), 3.68 (d, $J = 5.5$ Hz, 2H); $^{13}$CNMR ($d$-DMSO, 151 MHz) $\delta$ (ppm): 168.61, 143.56, 137.13, 135.30, 134.54, 134.36, 132.83, 131.20, 129.39, 126.71, 122.94, 122.26, 121.55, 119.54, 119.49, 117.76, 116.89, 112.51, 44.03, 41.58; HRMS (ESI) $m/z$: calcd. for $C_{24}H_{22}BN_4O_3$, 425.1785; found: 425.1773.

4-(3-(10H-indolo[3,2-b]quinolin-11-ylamino)propylcarbamoyl)phenyl-boronic acid (4b): yellow powder, yield: 80.4%; m.p.: 232-242°C; $^1$HNMR ($d$-DMSO, 600 MHz) $\delta$ (ppm): 10.88 (s, NH), 8.48 (d, $J = 8.7$ Hz, 1H), 8.28 (d, $J = 7.6$ Hz, 1H), 8.03 (d, $J = 8.5$ Hz, 2H), 7.84 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 7.9$ Hz, 2H), 7.65-7.62 (2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.46 (t, $J = 7.2$ Hz, 1H), 7.24 (t, $J = 7.1$ Hz, 1H), 3.95 (d, $J = 5.8$ Hz, 2H), 3.43 (d, $J = 6.0$ Hz, 2H); $^{13}$CNMR ($d$-DMSO, 151 MHz) $\delta$ (ppm): 167.19, 143.46, 137.50, 129.31, 126.13, 123.07, 122.36, 121.51, 119.57, 112.51, 119.66, 118.80, 117.54, 115.20, 112.68, 49.06, 42.97, 37.20; HRMS (ESI) $m/z$: calcd. for $C_{25}H_{24}BN_4O_3$, 439.1941; found: 439.1940.

4-((3-(10H-indolo[3,2-b]quinolin-11-ylamino)propyl)(methyl)carbamoyl)phenyl-boronic acid (4c): yellow powder, yield: 82.5%; m.p.: 223-231°C; $^1$HNMR ($d$-DMSO, 600 MHz) $\delta$ (ppm): 8.47 (d, $J = 8.5$ Hz, 2H), 8.26 (d, $J = 7.7$ Hz, 1H), 7.82 (d, $J = 7.5$ Hz, 1H), 7.61 (d, $J = 8.5$ Hz, 2H), 7.45 (s, 1H), 7.35 (d, $J = 7.5$ Hz, 2H), 7.23 (d, $J = 7.5$ Hz, 2H), 3.92 (t, $J = 6.2$ Hz, 2H), 2.93 (t, $J = 5.8$ Hz, 2H), 2.88 (s, 3H), 1.91-1.90 (m, 2H); $^{13}$CNMR ($d$-DMSO, 151 MHz) $\delta$ (ppm): 117.17, 137.50, 134.20, 129.31, 126.13, 123.07, 122.36, 121.51, 119.57, 119.80, 112.57, 46.16, 44.72, 42.83, 37.51; HRMS (ESI) $m/z$: calcd. for $C_{26}H_{26}BN_4O_3$, 453.2092; found: 453.2090.

4-(6-(10H-indolo[3,2-b]quinolin-11-ylamino)hexylcarbamoyl)phenyl-boronic acid (4d): yellow powder, yield: 74.5%; m.p.: 232-237°C; $^1$HNMR ($d$-DMSO, 600 MHz) $\delta$ (ppm): 110.65 (s, NH), 8.40 (d, $J = 7.3$ Hz, 1H), 8.23 (d, $J = 7.7$ Hz, 1H), 8.00 (d, $J = 8.4$ Hz, 1H), 7.83-7.90 (m, 2H), 7.77 (d, $J = 7.5$ Hz, 2H), 7.60-7.51 (m, 3H), 7.39 (t, $J = 7.3$ Hz, 1H), 7.20 (t, $J = 6.3$ Hz, 1H), 3.85-3.77 (m, 2H), 3.24 (d, $J = 5.9$ Hz, 2H), 1.69 (d, $J = 5.9$ Hz, 2H), 1.52-1.36 (m, 6H); $^{13}$CNMR ($d$-DMSO, 151 MHz) $\delta$ (ppm): 166.67, 145.88, 145.35, 143.55, 136.42, 136.16, 134.33, 129.09, 128.93, 126.73, 126.45, 122.60, 122.48, 122.12, 122.08, 121.36, 119.47, 119.26, 118.07, 112.40, 46.14, 45.64, 30.86, 29.60, 26.82, 26.60; HRMS (ESI) $m/z$: calcd. for $C_{28}H_{30}BN_4O_3$, 481.2411; found: 481.2417.
3-(2-(10H-indolo[3,2-b]quinolin-11-ylamino)ethylcarbamoyl)phenyl-boronic acid (4e): yellow powder, yield: 82.3%; m.p.: 247-255°C; \(^1\)HNMR (\(d\)-DMSO, 600 MHz) \(\delta\) (ppm): 11.46 (s, NH), 8.48-8.28 (m, 2H), 8.21-8.28 (m, 1H), 7.99-8.02 (m, 2H), 7.68-7.71 (m, 1H), 7.48-7.62 (m, 3H), 7.38-7.43 (m, 1H), 7.13-7.24 (m, 2H), 3.99 (d, \(J = 5.7\) Hz, 2H), 3.68 (d, \(J = 5.7\) Hz, 2H); \(^13\)CNMR (\(d\)-DMSO, 151 MHz) \(\delta\) (ppm): 168.99, 146.89, 145.17, 143.64, 143.61, 137.66, 135.74, 133.34, 129.38, 129.04, 127.90, 126.85, 122.68, 122.51, 122.42, 122.09, 121.80, 121.45, 119.22, 118.03, 117.21, 112.32, 44.09, 41.70; HRMS (ESI) \(m/z\): calcd. for C\(_{24}\)H\(_{22}\)BN\(_4\)O\(_3\), 425.1785; found: 425.1775.

3-(3-(10H-indolo[3,2-b]quinolin-11-ylamino)propylcarbamoyl)phenyl-boronic acid (4f): yellow powder, yield: 76.4%; m.p.: 231-238°C; \(^1\)HNMR (\(d\)-DMSO, 600 MHz) \(\delta\) (ppm): 10.69 (s, NH), 8.59-8.38 (m, 2H), 8.29-8.20 (m, 2H), 8.04-7.97 (m, 2H), 7.93-7.85 (m, 1H), 7.62-7.47 (m, 3H), 7.44-7.39 (m, 2H), 7.23-7.18 (m, 1H), 3.89 (t, \(J = 6.36\) Hz, 2H), 3.42 (t, \(J = 6.58\) Hz, 2H), 1.92-1.87 (m, 2H); \(^13\)CNMR (\(d\)-DMSO, 151 MHz) \(\delta\) (ppm): 167.68, 146.05, 145.34, 143.59, 137.13, 135.80, 134.19, 133.54, 129.18, 128.98, 127.69, 126.72, 122.51, 122.09, 121.45, 119.48, 119.32, 119.22, 112.41, 42.84, 37.15, 31.01; HRMS (ESI) \(m/z\): calcd. for C\(_{25}\)H\(_{24}\)BN\(_4\)O\(_3\), 439.1941; found: 439.1933.

3-((3-(10H-indolo[3,2-b]quinolin-11-ylamino)propyl)(methyl)carbamoyl)phenyl-boronic acid (4g): yellow powder, yield: 80.2%; m.p.: 225-233°C; \(^1\)HNMR (\(d\)-DMSO, 600 MHz) \(\delta\) (ppm): 10.72 (s, NH), 8.20 (d, \(J = 8.4\) Hz, 2H), 8.01-7.93 (m, 2H), 7.84-7.75 (m, 2H), 7.68-7.53 (m, 4H), 7.43-7.39 (m, 2H), 7.23-7.18 (m, 2H), 3.88 (t, \(J = 6.2\) Hz, 2H), 2.87 (s, 3H), 2.79 (t, \(J = 5.8\) Hz, 2H), 1.95-1.88 (m, 2H); \(^13\)CNMR (\(d\)-DMSO, 151 MHz) \(\delta\) (ppm): 171.49, 146.01, 145.57, 143.64, 143.60, 132.79, 129.17, 126.83, 122.94, 122.25, 121.42, 119.40, 112.44, 46.19, 44.73, 42.78, 37.60; HRMS (ESI) \(m/z\): calcd. for C\(_{26}\)H\(_{26}\)BN\(_4\)O\(_3\), 453.2092; found: 453.2101.

3-(6-(10H-indolo[3,2-b]quinolin-11-ylamino)hexylcarbamoyl)phenyl-boronic acid (4h): yellow powder, yield: 76.4%; m.p.: 229-240°C; \(^1\)HNMR (\(d\)-DMSO, 600 MHz) \(\delta\) (ppm): 10.81 (s, NH), 8.43
(d, J = 8.4 Hz, 2H), 8.26-8.21 (m, 2H), 7.62-7.52 (m, 4H), 7.44-7.36 (m, 2H), 7.30-7.10 (m, 2H), 3.37 (t, J = 7.0 Hz, 2H), 3.25-3.21 (m, 2H), 1.73-1.68 (m, 2H), 1.62-1.43 (m,6H);

\(^{13}\)CNMR (d-DMSO, 151 MHz) \(\delta\) (ppm): 167.16, 143.43, 143.38, 126.96, 134.44, 133.46, 129.31, 129.24, 129.11, 127.64, 122.90, 122.87, 122.84, 122.77, 122.67, 121.47, 119.53, 119.50, 119.07, 112.58, 65.37, 45.65, 30.79, 29.64, 28.80, 25.57; HRMS (ESI) m/z: calcd. for C\(_{28}\)H\(_{30}\)BN\(_4\)O\(_3\), 481.2411; found: 481.2397.


C. Copies of \(^1\)H and \(^{13}\)C NMR spectra of compounds: 7a-7d, 8a-8d, 9a-9d
D. Copies of HRMS (ESI) spectra of compounds: 7a-7d, 8a-8d, 9a-9d
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 ppm

Monoisotopic Mass, Odd and Even Electron Ions
1349 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)

Minimum: 425.1773  Difference: 5.0  \% 50.3

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Electronic Supplementary Material (ESI) for Chemical Communications
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM  DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0  Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ion
1375 formula(s) evaluated with 1 results within limits (all results (up to 1000) for each mass)

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Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DEE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 0.01 Abundance = 10%

Microscopic Mass, Odd and Even Electron ions
630 formula(s) evaluated with 3 results within limits (all results (up to 1000) for each mass)

Y9U-C-A
20130105/7 Y9U-C-A H N O C 67.54600 (M+) M = 300.00, 493.30600-0.0001000; S = (rel. 3.000)

% 106

414.1647 481.2417

415.1528 481.2417

414.1647 481.2417

415.1528 481.2417

Minimum: -1.5 Maximum: 50.0

Mass Calc. Mass % deviation ppm Rel. DEE Score Formula

481.2417 481.9611 0.6 1.3 16.5 2 C28 H31 N O
481.2900 1.7 3.5 13.0 1 C28 H31 N O
481.2435 -0.4 -3.8 8.3 3 C29 H33 O N H

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Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0  Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron ions

1316 form ula(s) evaluated with 2 results within limits (all results up to 10000 for each mass)

Minimum: 405.3  407.1  411.3  415.3  423.3  425.3  427.1  429.1  431.7  437.1  455.0  465.0  474.0
Maximum: 230.0  5.0  -50.0
Mass  Calc. Mass  m/z  PPM  DBE  Group  Formula
425.1775  425.1774  0.1  0.2  13.0  1  C24 H23 B N O4 Br
425.1785  -1.0  -2.3  16.5  2  C24 H23 B N O4 Br

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Elemental Composition Report

Single Mass Analysis

Isolated Cluster Parameter: Separation = 0, Abundance = 1.3%

Elemental Analysis:

Calculated: C 67.08%, H 7.06%, N 4.69%

Found: C 66.82%, H 7.34%, N 4.37%

Note: Results may vary due to experimental conditions.

Chemical Structure:

[Chemical structure image]

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**Elemental Composition Report**

**Single Mass Analysis**

Tolerance = 5.0 PPM  
DBE: min = -15, max = 50.0  
Isotope cluster parameters: Separation = 1.0  
Abundance = 10%

Macrospectro Mass, Odd and Even Electron ions  
630 formuлаe evaluated with 2 results within limits (all results (up to 1000) for each mass)

![Molecular Structure Image]

**Millenium**: 481.2197  
**Retention**: 4.7  
**Calc. Mass**: 481.2200  
**m/z**: 481.2200  
**PPM**: -0.7  
**DBE**: 13.0  
**Score**: 1  
**Formula**: C28 H31 N  

**Chemical Structures and Formulas**

- C28 H31 N
- HO

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