

SUPPLEMENTAL INFORMATION

Imidazolium salts as small-molecule urinary bladder exfoliants in a murine model

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Experimental Methods

Synthesis and Characterization of Intermediates and Imidazolium Salts 3 – 9

Synthesis of 4,5-dichloro-1-(quinolin-2-ylmethyl)imidazole. 4,5-Dichloroimidazole (2.00 g, 14.6 mmol) and KOH (0.90 g, 16 mmol) were stirred in acetonitrile (25 mL) and the mixture was heated at reflux for 45 min. 2-(Chloromethyl)quinoline hydrochloride (3.13 g, 14.6 mmol), KOH (0.82 mg, 14.6 mmol), and additional acetonitrile (25 mL) were added and the mixture was heated at reflux for 5 h. The generated precipitate was removed by filtration and the volatile components were removed under reduced pressure to yield a viscous brown liquid. Upon slight physical agitation of the liquid, a crystalline solid quickly formed. Diethyl ether (5 mL) was added and the mixture was cooled using a LN₂/iPrOH bath. The solid was thoroughly triturated while in the mixture, collected by filtration, and washed with several small aliquots of cold diethyl ether. The solid was dried in air to yield the product as a light tan crystalline solid (3.33 g, 82%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.39 (d, *J* = 8.6 Hz, 1H), 8.04 (s, 1H), 7.97 (dd, *J* = 8.2 Hz, 1.1 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.75 (ddd, *J* = 8.4 Hz, 6.9 Hz, 1.3 Hz, 1H), 7.59 (ddd, *J* = 8.1 Hz, *J* = 6.8 Hz, *J* = 1.2 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 5.57 (s, 2H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) δ 155.2, 146.9, 137.4, 137.0, 130.0, 128.5, 127.9, 127.0, 126.7, 124.5, 119.1, 112.8, 50.8.

Synthesis of 1-(naphthalen-2-ylmethyl)imidazole. To a stirred suspension of 60% NaH (1.2 g, 30 mmol) in tetrahydrofuran (100 mL) was added imidazole (2.04 g, 30.0 mmol). The mixture was stirred for 20 min and a solution of 2-(bromomethyl)naphthalene (6.6 g, 30 mmol) in tetrahydrofuran (160 mL) was added. The mixture was stirred and heated at reflux for 4 h and left at ambient temperature overnight. The volatile components were removed under reduced pressure, and the residue was treated with 1 N HCl (30 mL) and ice and shaken with diethyl ether. The aqueous portion was separated and made basic with NaOH and extracted twice with diethyl ether. The combined organic portions were dried and the volatile components were removed under reduced pressure to yield an off-white powder (5.41 g, 87%). ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.89 (m, 3H), 7.81 (s, 1H), 7.76 (s, 1H), 7.51 (m, 2H), 7.40 (dd, *J* = 8.5 Hz, 1.2 Hz, 1H), 7.23 (bs, 1H), 6.94 (bs, 1H), 5.36 (s, 2H). ¹³C{¹H} NMR (100 MHz, DMSO-*d*₆) δ 137.4, 135.3, 132.8, 132.3, 128.7, 128.3, 127.6, 127.5, 126.4, 126.1, 126.0, 125.5, 119.6, 49.6.

Synthesis of 1-(quinolin-2-ylmethyl)imidazole. Imidazole (3.00 g, 44.1 mmol) and potassium hydroxide (2.47 g, 44.1 mmol) were stirred in acetonitrile (30 mL) and heated at reflux until the

base was consumed and two distinct layers were observed. 2-(Chloromethyl)quinoline hydrochloride (3.15 g, 14.7 mmol) was added and the mixture was heated at reflux for 20 h. The precipitate was removed by filtration and the volatile components were removed under reduced pressure. The residue was dissolved in chloroform (50 mL) and washed with 5% KOH *aq* (4 × 25 mL, 2 × 50 mL). The organic layer was dried (Na₂SO₄) and the volatile components were removed under reduced pressure, yielding a brown solid. The solid was recrystallized from a minimum volume of hot acetonitrile, yielding a tan, crystalline solid (1.75 g, 57%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.35 (d, *J* = 8.6 Hz, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.85 (s, 1H), 7.76 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.59 (dd, 1H), 7.27 (d, *J* = 8.6 Hz, 1H), 7.27 (d, *J* = 0.7 Hz, 1H), 6.97 (d, *J* = 0.7 Hz, 1H), 5.51 (s, 2H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) δ 157.2, 146.9, 137.9, 137.3, 129.9, 128.8, 128.5, 127.8, 126.9, 126.6, 119.9, 119.4, 51.86.

Synthesis of 1-(quinolin-2-ylmethyl)benzimidazole. A mixture of benzimidazole (1.42 g, 12.0 mmol) and KOH (733 mg, 13.1 mmol) in acetonitrile (10 mL) was stirred and heated at reflux until the base was consumed. To the reaction mixture was added 2-(chloromethyl)quinoline hydrochloride (2.14 g, 10.0 mmol). The reaction mixture was stirred and heated at reflux for 4 h. The precipitate was removed by filtration and the volatile components were removed under reduced pressure. The residue was dissolved in chloroform (25 mL) and the organic solution was washed with 5% KOH *aq* (4 × 25 mL) and water (1 × 25 mL). The organic layer was dried (MgSO₄) and the volatile components removed under reduced pressure to yield the crude product as a light yellow powder (2.30 g). The crude product was recrystallized from acetonitrile, collected by filtration, washed with several small volumes of cold acetonitrile, and dried in air to yield the product as light yellow crystals (2.05 g, 79%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.49 (s, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 7.3 Hz, 1H), 7.75 (ddd, *J* = 8.4 Hz, 7.0 Hz, 1.2 Hz, 1H), 7.70 (m, 1H), 7.57 (m, 1H), 7.50 (m, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.18 (m, 2H), 5.81 (s, 2H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) δ 156.6, 147.0, 144.6, 143.5, 137.3, 133.9, 129.9, 128.5, 127.8, 127.0, 126.6, 122.4, 121.5, 119.45, 119.43, 110.5, 50.1.

Synthesis of 2-((2-(2-methoxyethoxy)ethoxy)methyl)benzimidazole. *o*-Phenylenediamine (1.00 g, 9.25 mmol) and 2-(2-(2-methoxyethoxy)ethoxy)acetic acid (1.80 mL, 11.73 mmol) were combined, stirred, and heated at 140 °C overnight. The melt was cooled to room temperature, made basic with ammonium hydroxide, and extracted with dichloromethane (4 × 50 mL). The organic layers were combined, dried (MgSO₄), and the volatile components were removed under reduced pressure to yield the crude product as an oil. The oil was purified by column chromatography using a mobile phase of ethyl acetate/hexanes (10:90, *R_f* = 0.30) to yield the product as a brown, viscous oil. (1.80 g, 75%). ¹H NMR (500 MHz, DMSO-*d*₆) δ 12.42 (bs, 1H), 7.52 (m, 2H), 7.16 (m, 2H), 4.71 (s, 2H), 3.65 (m, 2H), 3.58 (m, 2H), 3.52 (m, 2H), 3.43 (m, 2H), 3.23 (s, 3H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) δ 151.4, 121.6, 71.3, 69.7, 69.63, 69.57, 66.2, 58.0.

Synthesis of 3. A solution of 4,5-dichloro-1-(quinolin-2-ylmethyl)imidazole (556 mg, 2.00 mmol) and 2-(bromomethyl)quinoline (493 mg, 2.22 mmol) in hot acetonitrile (2.5 mL) was stirred and heated at reflux for 4 h. After 3 h, additional acetonitrile (2 mL) was added to aid in stirring of the mixture, which had turned deep purple in color and generated a large amount of precipitate. The mixture was allowed to cool to ambient temperature and the solid was collected by filtration. The solid was washed with several small volumes of cold acetonitrile followed by two small volumes of diethyl ether, removing much of the purple color. The solid was dried in air to yield a faint purple powder (498 mg, 50%) Mp: 171-173 °C. ¹H NMR (500 MHz, DMSO-

d_6) δ 9.94 (s, 1H), 8.55 (d, J = 8.3 Hz, 2H), 8.06 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.79 (m, 2H), 7.73 (d, J = 8.6 Hz, 2H), 7.66 (m, 2H), 6.07 (s, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, DMSO- d_6) δ 152.7, 146.7, 138.5, 137.7, 130.2, 128.5, 128.0, 127.2, 127.1, 119.6, 119.5, 52.6. HRMS (ESI $^+$): Calcd for $\text{C}_{23}\text{H}_{17}\text{Cl}_2\text{N}_4$ [M-Br] $^+$: m/z 419.0825. Found: 419.0865. Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{BrCl}_2\text{N}_4$: C, 55.23; H, 3.43; N, 11.20. Found: C, 55.37; H, 3.40; N, 11.15.

Crystal data for 3. $\text{C}_{23}\text{H}_{17}\text{BrCl}_2\text{N}_4$, M = 500.21, monoclinic, a = 12.8193(9) Å, b = 5.6286(3) Å, c = 29.2571(18) Å, β = 95.960(3)°, V = 2099.6(2) Å 3 , T = 100(2) K, space group $\text{P2}_1/\text{n}$, Z = 4, 21151 reflections measured, 4180 independent reflections (R_{int} = 0.0496). The final R_I values were 0.0342 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0726 ($I > 2\sigma(I)$). The final R_I values were 0.0505 (all data). The final $wR(F^2)$ values were 0.0800 (all data).

Synthesis of 4. A solution of 1-(naphthalen-2-ylmethyl)imidazole (500 mg, 2.40 mmol) and 2-(chloromethyl)quinoline (440 mg, 2.48 mmol) in hot acetonitrile (1 mL) was stirred and heated at reflux for 15 min. A precipitate formed after ca. 3 min, and additional acetonitrile (2 mL) was added to aid in stirring. The precipitate was triturated in the hot reaction mixture, collected by filtration, washed with small portions of acetonitrile, and dried in air. A white, microcrystalline solid was collected (797 mg, 86%). Further purification was obtained by the addition of petroleum ether to a vigorously stirred solution of the product in a minimum volume of chloroform, resulting in the formation of a precipitate. The solid was collected via vacuum filtration, washed with small portions of petroleum ether, and dried in air. A white microcrystalline solid was collected and characterized. Mp: 213 – 216 °C. ^1H NMR (500 MHz, DMSO- d_6) δ 9.69 (s, 1H), 8.46 (d, J = 8.6 Hz, 1H), 8.04 – 7.92 (m, 5H), 7.79 (m, 1H), 7.74 (m, 1H), 7.64 – 7.57 (m, 4H), 5.87 (s, 2H), 5.74 (s, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, DMSO- d_6) δ 154.2, 146.7, 137.7, 137.4, 132.7, 132.7, 132.4, 130.0, 128.7, 128.4, 127.9, 127.8, 127.7, 127.5, 127.2, 126.9, 126.7, 125.6, 123.8, 122.4, 119.9, 53.4, 52.1. MS (ESI $^+$): Calcd for $\text{C}_{24}\text{H}_{20}\text{N}_3$ [M-Br] $^+$: m/z 350.2. Found: 350.0. (ESI): Calcd for Cl $^-$: m/z 35.0. Found: 35.2. Anal. Calcd for $\text{C}_{24}\text{H}_{20}\text{ClN}_3$: C, 74.70; H, 5.22; N, 10.89. Found: C, 74.29; H, 5.31; N, 10.77.

Crystal data for 4. $\text{C}_{24}\text{H}_{20}\text{ClN}_3$, M = 385.88, orthorhombic, a = 7.8984(3) Å, b = 12.6063(5) Å, c = 38.3695(17) Å, V = 3820.4(3) Å 3 , T = 100(2) K, space group Pbca , Z = 8, 17156 reflections measured, 3864 independent reflections (R_{int} = 0.0647). The final R_I values were 0.0557 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1171 ($I > 2\sigma(I)$). The final R_I values were 0.0877 (all data). The final $wR(F^2)$ values were 0.1308 (all data).

Synthesis of 5. A solution of 1-(quinolin-2-ylmethyl)imidazole (500 mg, 2.39 mmol) and 2-chloromethylquinoline (466 mg, 2.63 mmol) in hot acetonitrile (1 mL) was stirred and heated at reflux for 15 min. A precipitate formed after ca. 3 min, and additional acetonitrile (2 mL) was added to aid in stirring. The precipitate was triturated in the hot reaction mixture, collected by filtration, washed with small portions of acetonitrile, and dried in air. An off-white powder was collected (739 mg, 80%). Mp: 192 – 193 °C. ^1H NMR (500 MHz, DMSO- d_6) 9.77 (t, J = 1.4 Hz, 1H), 8.49 (d, J = 8.3 Hz, 2H), 8.03 (dd, J = 8.1 Hz, 1.2 Hz, 2H), 8.02 (d, J = 1.4 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H), 7.77 (ddd, J = 8.5 Hz, 6.9 Hz, 1.5 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.63 (ddd, J = 8.1 Hz, 6.9 Hz, 1.2 Hz, 2H), 5.96 (s, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, DMSO- d_6) δ 154.4, 146.8, 138.4, 137.5, 130.1, 128.5, 128.0, 127.2, 126.9, 123.4, 119.8, 53.5. MS (ESI $^+$): Calcd for $\text{C}_{23}\text{H}_{19}\text{N}_4$ [M-Br] $^+$: m/z 351.2. Found: 351.0. (ESI): Calcd for Cl $^-$: m/z 35.0. Found: 35.4. Anal. Calcd for $\text{C}_{23}\text{H}_{19}\text{ClN}_4$: C, 71.40; H, 4.95; N, 14.48. Found: C, 71.39; H, 4.96; N, 14.52.

Crystal data for 5. $C_{23}H_{19}ClN_4 \cdot 2H_2O$, $M = 422.90$, monoclinic, $a = 44.6860(13)$ Å, $b = 8.9727(3)$ Å, $c = 15.9304(5)$ Å, $\beta = 98.3424(15)^\circ$, $V = 6319.8(3)$ Å³, $T = 100(2)$ K, space group Cc, $Z = 12$, 42570 reflections measured, 12735 independent reflections ($R_{int} = 0.0240$). The final R_I values were 0.0296 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0724 ($I > 2\sigma(I)$). The final R_I values were 0.0317 (all data). The final $wR(F^2)$ values were 0.0740 (all data).

Synthesis of 6. A solution of 1-(quinolin-2-ylmethyl)imidazole (418 mg, 2.00 mmol) and 2-(chloromethyl)-6-methoxynaphthalene (456 mg, 2.21 mmol) in hot acetonitrile (1 mL) was stirred and heated at reflux for 1 h. A precipitate formed after ca. 3 min, and additional acetonitrile (3 mL) was added to aid in stirring. The mixture was allowed to cool to ambient temperature before diethyl ether (5 mL) was added and stirred for 10 min. The solid was collected by filtration and washed with small volumes of diethyl ether. The solid was dissolved in a minimum volume of chloroform and petroleum ether was added to the vigorously stirred solution to yield a white precipitate. The solid was collected by filtration, washed with small volumes of petroleum ether, and dried in air to yield a white powder (679 mg, 82%). Mp: 197 – 199 °C. ¹H NMR (500 MHz, DMSO-*d*₆) 9.66 (t, $J = 1.4$ Hz, 1H), 8.46 (d, $J = 8.6$ Hz, 1H), 8.01 (d, $J = 8.1$ Hz, 1H), 7.97 (m, 1H), 7.96 (m, 1H), 7.91 (m, 2H), 7.84 (d, $J = 9.0$ Hz, 1H), 7.80 (d, $J = 8.6$ Hz, 1H), 7.75 (m, 1H), 7.63 (m, 1H), 7.63 (d, $J = 8.6$ Hz, 1H), 7.56 (dd, $J = 8.3$ Hz, 1.5 Hz, 1H), 7.38 (d, $J = 2.4$ Hz, 1H), 7.23 (dd, $J = 9.0$ Hz, 2.4 Hz, 1H), 5.86 (s, 2H), 5.68 (s, 2H), 3.89 (3H, s). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) 157.8, 154.2, 146.7, 137.6, 137.5, 134.2, 130.1, 129.9, 129.3, 128.4, 128.1, 127.9, 127.6, 127.4, 127.2, 126.9, 126.2, 123.8, 122.4, 119.9, 119.2, 105.96, 55.2, 53.4, 52.1. MS (ESI⁺): Calcd for $C_{25}H_{22}N_3O$ [M-Br]⁺: m/z 380.2. Found: 380.0. (ESI): Calcd for Cl⁻: m/z 35.0. Found: 35.3. Anal. Calcd for $C_{25}H_{22}ClN_3O$: C, 72.20; H, 5.33; N, 10.10. Found: C, 72.35; H, 5.32; N, 10.08.

Crystal data for 6. $C_{25}H_{22}ClN_3O$, $M = 415.90$, monoclinic, $a = 20.9877(8)$ Å, $b = 7.8518(3)$ Å, $c = 12.5246(4)$ Å, $\beta = 98.2944(14)^\circ$, $V = 2042.35(13)$ Å³, $T = 100(2)$ K, space group P2₁/c, $Z = 4$, 22260 reflections measured, 4138 independent reflections ($R_{int} = 0.0537$). The final R_I values were 0.0461 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1059 ($I > 2\sigma(I)$). The final R_I values were 0.0700 (all data). The final $wR(F^2)$ values were 0.1195 (all data).

Synthesis of 7. A solution of 1-(naphthalen-2-ylmethyl)imidazole (250 mg, 1.20 mmol) and 6-methoxy-2-(chloromethyl)naphthalene (273 mg, 1.32 mmol) in acetonitrile (1.5 mL) was stirred and heated at reflux for 6 h. A precipitate was generated and additional acetonitrile (2.5 mL) was added to aid in stirring. The solid was homogenized by vigorous stirring and trituration of the precipitate in the hot reaction mixture and collected by filtration. The solid was washed with several small volumes of acetonitrile and once with diethyl ether. The solid was dried overnight under dynamic vacuum resulting in a white powder (453 mg, 91%). Mp: 202 – 204 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.73 (bs, 1H), 8.00 (bs, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.94 (m, 5H), 7.87 (d, $J = 8.8$ Hz, 1H), 7.83 (d, $J = 8.8$ Hz, 1H), 7.57 (m, 3H), 7.53 (dd, $J = 8.6$ Hz, 1.7 Hz, 1H), 7.36 (d, $J = 2.4$ Hz, 1H), 7.22 (dd, $J = 8.6$ Hz, 2.4 Hz, 1H), 5.65 (s, 2H), 5.60 (s, 2H), 3.88 (s, 3H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) 157.8, 136.6, 136.5, 134.1, 132.68, 132.65, 132.2, 129.7, 129.4, 128.7, 128.0, 127.8, 127.62, 127.59, 127.56, 126.68, 126.65, 126.2, 125.7, 122.89, 122.86, 119.2, 105.9, 55.2, 52.2, 52.1. HRMS (ESI⁺): Calcd for $C_{26}H_{23}N_2O$ [M-Cl]⁺: m/z 379.1805. Found: 379.1823. Anal. Calcd for $C_{26}H_{23}ClN_2O$: C, 75.26; H, 5.59; N, 6.75. Found: C, 75.11; H, 5.60; N, 6.58.

Synthesis of 8. A solution of 1-(quinolin-2-ylmethyl)benzimidazole (0.50 g, 1.9 mmol) and 2-(chloromethyl)quinoline (0.37 g, 2.1 mmol) in hot acetonitrile was stirred and heated at reflux

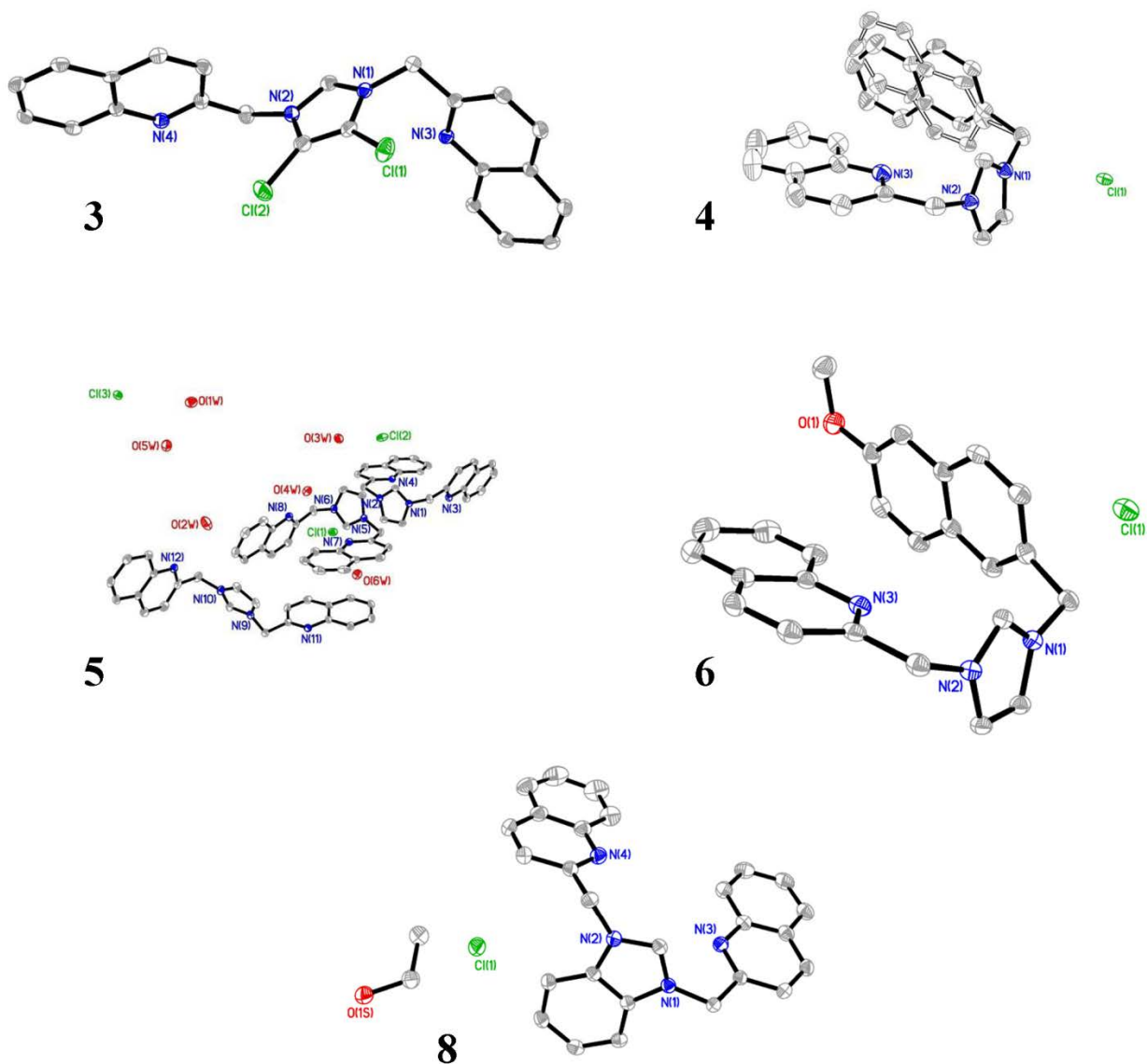
overnight. The precipitate was collected by filtration of the hot reaction mixture, washed with diethyl ether, and dried in air to yield an off-white powder (0.73 g, 86%). Mp: 216 – 219 °C. ¹H NMR (500 MHz, DMSO-*d*₆) 10.35 (s, 1H), 8.52 (d, 2H, *J* = 8.6 Hz), 8.03 (m, 4H), 7.79 (m, 4H), 7.74 (m, 2H), 7.63 (m, 4H), 6.28 (s, 4H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) 153.8, 146.8, 144.6, 137.6, 131.4, 130.1, 128.5, 128.0, 127.3, 127.0, 126.7, 120.0, 113.9, 51.4. HRMS (ESI⁺) calcd for C₂₇H₂₁N₄ [M-Cl]⁺: *m/z* = 401.1766, found *m/z* = 401.1768. Anal. Calcd for C₂₇H₂₁ClN₄•C₂H₆O: C, 72.11; H, 5.63; N, 11.60. Found: C, 71.85; H, 5.35; N, 11.71.

Crystal data for 8. C₂₇H₂₁ClN₄•C₂H₆O, *M* = 482.99, orthorhombic, *a* = 11.8063(13) Å, *b* = 16.070(2) Å, *c* = 26.419(3) Å, *V* = 5012.6(10) Å³, *T* = 100(2) K, space group Pbca, *Z* = 8, 27216 reflections measured, 5089 independent reflections (*R*_{int} = 0.0616). The final *R*_i values were 0.0512 (*I* > 2σ(*I*)). The final *wR*(*F*²) values were 0.1326 (*I* > 2σ(*I*)). The final *R*_i values were 0.0711 (all data). The final *wR*(*F*²) values were 0.1558 (all data).

Synthesis of 9. A mixture of 2-((2-(2-methoxyethoxy)ethoxy)methyl)benzimidazole (1.41 g, 5.63 mmol) and KOH (0.40 g, 7.13 mmol) in acetonitrile (2 mL) was stirred and heated at reflux for 30 min. 2-(Chloromethyl)quinoline (1.01 g, 5.69 mmol) was added and the mixture was heated at reflux overnight. The precipitate was removed by filtration of the hot reaction mixture. To the filtrate was added 2-(bromomethyl)naphthalene (1.25 g, 5.65 mmol) and the mixture was heated at reflux overnight. The precipitate was collected by filtration of the hot reaction mixture and transferred to a separate flask. The sticky brown solid was stirred in acetonitrile, and the solvent was removed by decantation. Diethyl ether was added to the sticky residue and stirred, removing the color from the solid. The solid was collected by filtration. The white solid was purified by column chromatography using a mobile phase of methanol/chloroform (10:90, *R*_f = 0.67) to yield a white powder (2.02 g, 58%). Mp: 209 – 211 °C. ¹H NMR (500 MHz, DMSO-*d*₆) 8.49 (d, 1H, *J* = 8.6 Hz), 8.14 (m, 1H), 8.08 (m, 1H), 7.98 (m, 4H), 7.89 (m, 1H), 7.79 (d, 1H, *J* = 8.6 Hz), 7.67 – 7.54 (m, 8H), 6.39 (s, 2H), 6.25 (s, 2H), 5.44 (s, 2H), 3.72 (m, 2H), 3.35 (m, 2H), 3.29 (m, 2H), 3.21 (m, 2H), 3.09 (s, 3H). ¹³C{¹H} NMR (125 MHz, DMSO-*d*₆) 153.5, 150.6, 146.5, 137.4, 132.6, 132.5, 131.8, 131.6, 131.1, 129.9, 128.7, 128.3, 127.9, 127.7, 127.6, 127.2, 127.0, 126.9, 126.7, 126.6, 126.3, 124.9, 119.9, 113.90, 113.85, 70.9, 70.4, 69.35, 69.34, 60.7, 57.87, 57.86, 50.0, 49.0. HRMS (ESI⁺) Calcd for C₃₄H₃₄N₃O₃ [M-Br]⁺: *m/z* 532.2600. Found 532.2238. Anal. Calcd for C₃₄H₃₄BrN₃O₃: C, 66.67; H, 5.59; N, 6.86. Found: C, 66.39; H, 5.66; N, 6.82.

Crystallographic Data for Imidazolium salts 3 – 6, 8

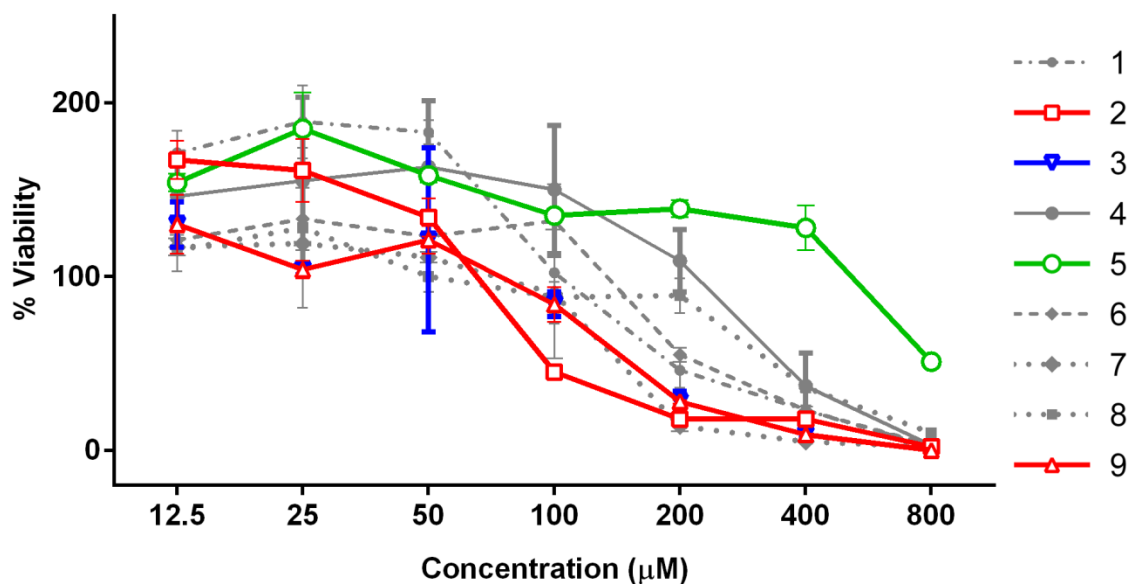
CCDC 1058089 – 1058092 and 1060094 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



Supplemental Figure 1. Thermal ellipsoid plots of **3** – **6**, **8**. All thermal ellipsoids have been drawn at the 50% probability level. Hydrogen atoms, carbon atom labels, and the anion of **3** have been removed for clarity.

Supplemental Table 1. Summary of crystal data, intensity collection, and structural refinement parameters for imidazolium salts **3** – **6**, **8**.

	Compound				
	3	4	5	6	8
empirical formula	C ₂₃ H ₁₇ BrCl ₂ N ₄	C ₂₄ H ₂₀ ClN ₃	C ₂₃ H ₁₉ ClN ₄ •2 H ₂ O	C ₂₅ H ₂₂ ClN ₃ O	C ₂₇ H ₂₁ ClN ₄ •C ₂ H ₆ O
molecular weight (Da)	500.21	385.88	422.90	415.90	482.99
cryst color, habit	colorless plate	colorless plate	colorless block	colorless plate	colorless block
crystal size (mm³)	0.21 x 0.08 x 0.05	0.30 x 0.10 x 0.04	0.24 x 0.18 x 0.17	0.20 x 0.152 x 0.02	0.33 x 0.23 x 0.21
temperature (K)	100(2)	100(2)	100(2)	100(2)	100(2)
crystal system	monoclinic	orthorhombic	monoclinic	monoclinic	orthorhombic
space group	P2 ₁ /n	Pbca	Cc	P2 ₁ /c	Pbca
<i>a</i> (Å)	12.8193(9)	7.8984(3)	44.6860(13)	20.9877(8)	11.8063(13)
<i>b</i> (Å)	5.6283(3)	12.6063(5)	8.9727(3)	7.8518(3)	16.070(2)
<i>c</i> (Å)	29.2571(18)	38.3695(17)	15.9304(5)	12.5246(4)	26.419(3)
<i>α</i> (deg)	90	90	90	90	90
<i>β</i> (deg)	95.960(3)	90	98.3424(15)	98.2944(14)	90
<i>γ</i> (deg)	90	90	90	90	90
<i>V</i> (Å³)	2099.6(2)	3820.4(3)	6319.8(3)	2042.35(13)	5012.6(10)
<i>Z</i>	4	8	12	4	8
<i>d</i>_{calcd} (g cm⁻³)	1.582	1.342	1.333	1.353	1.280
abs coeff (mm⁻¹)	2.231	0.215	0.209	0.210	0.182
GOF^a on <i>F</i>²	1.036	1.079	1.036	1.035	1.073
R1^b%	0.0342	0.0557	0.0296	0.0461	0.0512
wR2^c%	0.0726	0.1171	0.0724	0.1059	0.1326



Supplemental Figure 2. Dose-dependent effects of imidazolium salts on viability of cultured uroepithelial cells. 5637 bladder cells were treated for 15 min with the indicated concentrations of compounds **1** through **9**, and viability was measured by standard MTT assay. Relative cytotoxicity, normalized to untreated cells lysed subsequently with detergent, of each compound and dose is shown (mean \pm SD). Data are representative of 2-3 independent experiments per compound, with triplicate wells. Data from 60-min incubations are shown in **Figure 3** of the main manuscript.