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SUPPORTING INFORMATION

4-Quinolone Derivatives: High-Affinity Ligands at the Benzodiazepine Site of Brain GABA_A Receptors. Synthesis, Pharmacology and Pharmacophore Modelling.

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Contents:

Spectroscopic data (¹H, ¹³C NMR and HRMS data) for all synthesized compounds

Elemental analyses for all new target compounds.

Spectroscopic data.

^1H and ^{13}C NMR were recorded at room temperature with a Bruker AR300 or a Bruker DR400 spectrometer. The spectra were recorded in CDCl_3 , $\text{DMSO}-d_6$, and CD_3OD , and the solvent signals (7.27 and 77.0, 2.50 and 39.5 or 3.31 and 49.0 ppm, respectively) were used as reference. The raw data were transformed and the spectra were evaluated with the standard Bruker UXNMR software (rev. 941001). EI mass spectra were recorded at 70 eV with a Jeol S102 spectrometer and ESI spectra were recorded with Micromass Q-TOF Micro.

Diethyl 4-ethylanilinomethylenemalonate (2a). ^1H NMR (CDCl_3) δ 1.24 (3H, t, $J = 7.6$ Hz), 1.33 (3H, t, $J = 7.1$ Hz), 1.39 (3H, t, $J = 7.1$ Hz), 2.65 (2H, q, $J = 7.6$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 4.32 (2H, q, $J = 7.1$ Hz), 7.07 (2H, d, $J = 8.4$ Hz), 7.21 (2H, d, $J = 8.4$ Hz), 8.52 (1H, d, $J = 13.8$ Hz), 11.01 (1H, d, $J = 13.8$ Hz); ^{13}C NMR (CDCl_3) δ 14.2, 14.4, 15.5, 28.1, 59.9, 60.2, 92.8, 117.2, 117.2, 129.1, 129.1, 137.0, 141.1, 152.1, 165.7, 169.1. HRMS (EI): for $\text{C}_{16}\text{H}_{21}\text{NO}_4$ calcd: 291.1471 $[\text{M}]^+$; found: 291.1455.

3-Ethoxycarbonyl-6-ethyl-4-quinolone (2). ^1H NMR ($\text{DMSO}-d_6$) δ 1.22 (3H, t, $J = 7.6$ Hz), 1.28 (3H, t, $J = 7.1$ Hz), 2.73 (2H, q, $J = 7.6$ Hz), 4.21 (2H, q, $J = 7.1$ Hz), 7.56 (2H, m), 7.97 (1H, bs), 8.50 (1H, s), 12.26 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 14.3, 15.5, 27.9, 59.5, 109.5, 118.8, 123.7, 127.2, 132.6, 137.2, 140.4, 144.4, 164.9, 173.4. HRMS (EI): for $\text{C}_{14}\text{H}_{15}\text{NO}_3$ calcd: 245.1052 $[\text{M}]^+$; found: 245.1055.

6-Ethyl-3-propoxycarbonyl-4-quinolone (3). ^1H NMR ($\text{DMSO}-d_6$) δ 0.96 (3H, t, $J = 7.4$ Hz), 1.22 (3H, t, $J = 7.5$ Hz), 1.67 (2H, m), 2.73 (2H, q, $J = 7.5$ Hz), 4.12 (2H, t, $J = 6.6$ Hz), 7.56 (2H, m), 7.98 (1H, s), 8.50 (1H, s). ^{13}C NMR ($\text{DMSO}-d_6$) δ 10.5, 15.5, 21.7, 27.9, 65.1, 109.5, 118.8, 123.7, 127.3, 132.7, 137.2, 140.5, 144.4, 165.0, 173.4. HRMS (EI): for $\text{C}_{15}\text{H}_{17}\text{NO}_3$ calcd: 259.1208 $[\text{M}]^+$; found: 259.1210.

3-Butoxycarbonyl-6-ethyl-4-quinolone (4). ^1H NMR ($\text{DMSO}-d_6$) δ 0.93 (3H, t, $J = 7.3$ Hz), 1.22 (3H, t, $J = 7.6$ Hz), 1.43 (2H, m), 1.64 (2H, m), 2.73 (2H, q, $J = 7.6$ Hz), 4.16 (2H, t, $J = 6.5$ Hz), 7.56 (2H, m), 7.97 (1H, bs), 8.49 (1H, s), 12.24 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 13.6, 15.5, 18.7, 27.8, 30.4, 63.2, 109.5, 118.8, 123.7, 127.2, 132.6, 137.1, 140.4, 144.3, 165.0, 173.4. HRMS (EI): for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ calcd: 273.1365 $[\text{M}]^+$; found: 273.1360.

6-Ethyl-3-(3-methylbutoxycarbonyl)-4-quinolone (5). ^1H NMR ($\text{DMSO}-d_6$) δ 0.92 (6H, d, $J = 6.6$ Hz), 1.22 (3H, t, $J = 7.6$ Hz), 1.56 (2H, m), 1.76 (1H, m), 2.72 (2H, q, $J = 7.6$ Hz), 4.19 (2H, q, $J = 6.7$ Hz), 7.53 (1H, d, $J = 8.3$ Hz), 7.58 (1H, dd, $J_1 = 8.5$ Hz, $J_2 = 1.8$ Hz), 7.97 (1H, d, $J = 1.8$ Hz), 8.48 (1H, s). ^{13}C NMR ($\text{DMSO}-d_6$) δ 15.5, 22.4, 24.6, 27.9, 37.1, 62.0, 109.5, 118.9, 123.7, 127.3, 132.7, 137.2, 140.5, 144.4, 165.0, 173.4. HRMS (EI): for $\text{C}_{17}\text{H}_{21}\text{NO}_3$ calcd: 287.1521 $[\text{M}]^+$; found: 287.1523.

6-Ethyl-3-(2-methylbutoxycarbonyl)-4-quinolone (6). ^1H NMR ($\text{DMSO}-d_6$) δ 0.90 (3H, t, $J = 7.5$ Hz), 0.96 (3H, d, $J = 6.5$ Hz), 1.22 (4H, m), 1.50 (1H, m), 1.75 (1H, hex, $J = 6.6$ Hz), 2.73 (2H, q, $J = 7.6$ Hz), 3.98 (1H, dd, $J_1 = 10.7$ Hz, $J_2 = 6.5$ Hz), 4.05 (1H, dd, $J_1 = 10.7$ Hz, $J_2 = 6.5$ Hz), 7.54 (1H, d, $J = 8.4$ Hz), 7.58 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 1.9$ Hz), 7.98 (1H, d, $J = 1.9$ Hz), 8.49 (1H, s). ^{13}C NMR ($\text{DMSO}-d_6$)

δ 11.2, 15.5, 16.4, 25.6, 27.9, 33.8, 68.0, 109.5, 118.8, 123.7, 127.3, 132.7, 137.2, 140.4, 144.4, 165.2, 173.4. HRMS (EI): for $C_{17}H_{21}NO_3$ calcd: 287.1521 [M]⁺; found: 287.1525.

6-Ethyl-3-pentoxycarbonyl-4-quinolone (7). ¹H NMR (DMSO-*d*₆) δ 0.89 (3H, t, *J* = 7.1 Hz), 1.22 (3H, t, *J* = 7.6 Hz), 1.36 (4H, m), 1.66 (2H, m), 2.73 (2H, q, *J* = 7.6 Hz), 4.15 (2H, t, *J* = 6.6 Hz), 7.54 (1H, d, *J* = 8.4 Hz), 7.58 (1H, dd, *J*₁ = 8.4 Hz, *J*₂ = 1.9 Hz), 7.97 (1H, d, *J* = 1.9 Hz), 8.49 (1H, s). ¹³C NMR (DMSO-*d*₆) δ 13.9, 15.5, 21.9, 27.7, 27.9, 28.0, 63.6, 109.5, 118.8, 123.7, 127.3, 132.7, 137.2, 140.5, 144.4, 165.0, 173.4. HRMS (EI): for $C_{17}H_{21}NO_3$ calcd: 287.1521 [M]⁺; found: 287.1521.

6-Ethyl-3-(2-ethylbutoxycarbonyl)-4-quinolone (8). ¹H NMR (DMSO-*d*₆) δ 0.89 (6H, t, *J* = 7.5 Hz), 1.22 (3H, t, *J* = 7.6 Hz), 1.41 (4H, m), 1.57 (1H, m), 2.73 (2H, q, *J* = 7.6 Hz), 4.10 (2H, d, *J* = 5.7 Hz), 7.53 (1H, d, *J* = 8.4 Hz), 7.58 (1H, dd, *J*₁ = 8.4 Hz, *J*₂ = 1.9 Hz), 7.98 (1H, d, *J* = 1.9), 8.48 (1H, s). ¹³C NMR (DMSO-*d*₆) δ 11.0, 11.0, 15.5, 22.9, 22.9, 27.9, 39.7, 65.3, 109.5, 118.8, 123.7, 127.3, 132.6, 137.2, 140.4, 144.4, 165.2, 173.4. HRMS (EI): for $C_{18}H_{23}NO_3$ calcd: 301.1678 [M]⁺; found: 301.1672.

3-Cyclopentoxycarbonyl-6-ethyl-4-quinolone (9). ¹H NMR (DMSO-*d*₆) δ 1.22 (3H, t, *J* = 7.6 Hz), 1.58 (2H, m), 1.73 (4H, m), 1.88 (2H, m), 2.72 (2H, q, *J* = 7.6 Hz), 5.22 (1H, m), 7.53 (1H, d, *J* = 8.4 Hz), 7.57 (1H, dd, *J*₁ = 8.4 Hz, *J*₂ = 1.8 Hz), 7.97 (1H, d, *J* = 1.8 Hz), 8.44 (1H, s). ¹³C NMR (DMSO-*d*₆) δ 15.6, 23.4, 23.4, 27.9, 32.4, 32.4, 76.0, 109.9, 118.8, 123.7, 127.3, 132.7, 137.2, 140.4, 144.2, 164.7, 173.5. HRMS (EI): for $C_{17}H_{19}NO_3$ calcd: 285.1365 [M]⁺; found: 285.1365.

6-Ethyl-3-*i*-propoxycarbonyl-4-quinolone (10). ¹H NMR (DMSO-*d*₆) δ 1.22 (3H, t, *J* = 7.6 Hz), 1.27 (6H, d, *J* = 6.3 Hz), 2.72 (2H, q, *J* = 7.6 Hz), 5.05 (1H, hep, *J* = 6.3 Hz), 7.56 (2H, m), 7.97 (1H, s), 8.45 (1H, d, *J* = 6.4 Hz), 12.22 (1H, d, *J* = 6.4 Hz); ¹³C NMR (DMSO-*d*₆) δ 15.5, 21.8, 21.8, 27.8, 66.6, 109.8, 118.8, 123.6, 127.2, 132.6, 137.2, 140.3, 144.2, 164.2, 173.4. HRMS (EI): for $C_{15}H_{17}NO_3$ calcd: 259.1208 [M]⁺; found: 259.1208.

6-Ethyl-3-(4-methyl-2-pentoxycarbonyl)-4-quinolone (11). ¹H NMR (DMSO-*d*₆) δ 0.88 (6H, m), 1.22 (6H, m), 1.33, (1H, m), 1.67 (2H, m), 2.72 (2H, q, *J* = 7.6 Hz), 5.06 (1H, m), 7.56 (2H, m), 7.98 (1H, s), 8.48 (1H, s), 12.25 (1H, bs); ¹³C NMR (DMSO-*d*₆) δ 15.5, 20.5, 22.1, 22.9, 24.2, 27.9, 44.7, 68.2, 109.8, 118.8, 123.7, 127.3, 132.6, 137.2, 140.4, 144.2, 164.5, 173.5. HRMS (EI): for $C_{18}H_{23}NO_3$ calcd: 301.1678 [M]⁺; found: 301.1678.

6-Ethyl-3-(3-pentoxycarbonyl)-4-quinolone (12). ¹H NMR (DMSO-*d*₆) δ 0.90 (6H, t, *J* = 7.4 Hz), 1.22 (3H, t, *J* = 7.6 Hz), 1.61 (4H, m), 2.73 (2H, q, *J* = 7.6 Hz), 4.84 (1H, m), 7.54 (1H, d, *J* = 8.4 Hz), 7.58 (1H, dd, *J*₁ = 8.4 Hz, *J*₂ = 1.8 Hz), 7.98 (1H, d, *J* = 1.8 Hz), 8.47 (1H, s). ¹³C NMR (DMSO-*d*₆) δ 9.6, 9.6, 15.5, 26.1, 26.1, 27.8, 75.4, 109.9, 118.9, 123.7, 127.3, 132.6, 137.3, 140.3, 144.1, 164.9, 173.4. HRMS (EI): for $C_{17}H_{21}NO_3$ calcd: 287.1521 [M]⁺; found: 287.1519.

3-Carboxy-6-ethyl-4-quinolone (13). ¹H NMR (DMSO-*d*₆) δ 1.24 (3H, t, *J* = 7.6 Hz), 2.79 (2H, q, *J* = 7.6 Hz), 7.76 (2H, m), 8.10 (1H, s), 8.85 (1H, s); ¹³C NMR (DMSO-*d*₆) δ 15.4, 27.9, 107.4, 119.7, 122.9, 124.4, 134.4, 137.8, 142.2, 144.6, 166.6, 178.1. HRMS (EI): for $C_{12}H_{11}NO_3$ calcd: 217.0739 [M]⁺; found: 217.0753.

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Diethyl anilinomethylenemalonate (14a). ^1H NMR (CDCl_3) δ 1.33 (3H, t, $J = 7.1$ Hz), 1.38 (3H, t, $J = 7.1$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 4.31 (2H, q, $J = 7.1$ Hz), 7.15 (3H, m), 7.37 (2H, m), 8.53 (1H, d, $J = 13.6$ Hz), 11.01 (1H, d, $J = 13.6$ Hz); ^{13}C NMR (CDCl_3) δ 14.5, 14.6, 60.2, 60.5, 93.6, 117.3, 117.3, 125.0, 130.0, 130.0, 139.4, 152.1, 165.9, 169.2. HRMS (EI): for $\text{C}_{14}\text{H}_{17}\text{NO}_4$ calcd: 263.1158 $[\text{M}]^+$; found: 263.1155.

3-Ethoxycarbonyl-4-quinolone (14). ^1H NMR ($\text{DMSO}-d_6$) δ 1.28 (3H, t, $J = 7.1$ Hz), 4.21 (2H, q, $J = 7.1$ Hz), 7.41 (1H, t, $J = 7.5$ Hz), 7.62 (1H, d, $J = 8.1$ Hz), 7.71 (1H, m), 8.16 (1H, d, $J = 8.0$ Hz), 8.55 (1H, s), 12.30 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 14.3, 59.6, 109.8, 118.8, 124.7, 125.6, 127.3, 132.4, 139.0, 144.9, 164.8, 173.4. HRMS (EI): for $\text{C}_{12}\text{H}_{11}\text{NO}_3$ calcd: 217.0739 $[\text{M}]^+$; found: 217.0749.

3-Butoxycarbonyl-4-quinolone (15). ^1H NMR ($\text{DMSO}-d_6$) δ 0.92 (3H, t, $J = 7.4$ Hz), 1.42 (2H, hex, $J = 7.4$ Hz), 1.64 (2H, m), 4.17 (2H, t, $J = 6.5$ Hz), 7.42 (1H, t, $J = 8.1$ Hz), 7.63 (1H, d, $J = 8.1$ Hz), 7.71 (1H, t, $J = 8.1$ Hz), 8.16 (1H, d, $J = 8.1$ Hz), 8.54 (1H, s), 12.41 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 13.7, 18.8, 30.4, 63.4, 118.8, 124.7, 125.5, 125.6, 127.2, 132.4, 139.0, 144.9, 164.9, 173.5. HRMS (EI): for $\text{C}_{14}\text{H}_{15}\text{NO}_3$ calcd: 245.1052 $[\text{M}]^+$; found: 245.1051.

Diethyl 4-bromoanilinomethylenemalonate (16a). ^1H NMR (CDCl_3) δ 1.33 (3H, t, $J = 7.1$ Hz), 1.38 (3H, t, $J = 7.1$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 4.31 (2H, q, $J = 7.1$ Hz), 7.02 (2H, d, $J = 8.8$ Hz), 7.48 (2H, d, $J = 8.8$ Hz), 8.45 (1H, d, $J = 13.5$ Hz), 11.00 (1H, d, $J = 13.5$ Hz); ^{13}C NMR (CDCl_3) δ 14.5, 14.6, 60.4, 60.7, 94.5, 117.8, 118.8, 118.8, 133.0, 133.0, 138.6, 151.6, 165.7, 169.1. HRMS (EI): for $\text{C}_{14}\text{H}_{16}\text{NO}_4^{79}\text{Br}$ calcd: 341.0263 $[\text{M}]^+$; found: 341.0258.

6-Bromo-3-ethoxycarbonyl-4-quinolone (16). ^1H NMR ($\text{DMSO}-d_6$) δ 1.28 (3H, t, $J = 7.1$ Hz), 4.22 (2H, q, $J = 7.1$ Hz), 7.60 (1H, d, $J = 8.8$ Hz), 7.86 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 2.3$ Hz), 8.22 (1H, d, $J = 2.3$ Hz), 8.59 (1H, s), 12.41 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 14.3, 59.7, 110.1, 117.4, 121.5, 127.8, 128.7, 135.1, 138.0, 145.3, 164.6, 172.1. HRMS (EI): for $\text{C}_{12}\text{H}_{10}\text{NO}_3^{79}\text{Br}$ calcd: 294.9844 $[\text{M}]^+$; found: 294.9839.

Diethyl 4-propylanilinomethylenemalonate (17a). ^1H NMR (CDCl_3) δ 0.94 (3H, t, $J = 7.3$ Hz), 1.33 (3H, t, $J = 7.1$ Hz), 1.39 (3H, t, $J = 7.1$ Hz), 1.62 (2H, m), 2.58 (2H, t, $J = 7.5$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 4.32 (2H, q, $J = 7.1$ Hz), 7.07 (2H, d, $J = 8.5$ Hz), 7.18 (2H, d, $J = 8.5$ Hz), 8.52 (1H, d, $J = 13.8$ Hz), 11.01 (1H, d, $J = 13.8$ Hz); ^{13}C NMR (CDCl_3) δ 13.7, 14.3, 14.4, 24.5, 37.3, 60.0, 60.3, 92.9, 117.2, 117.2, 129.7, 129.7, 137.0, 139.7, 152.2, 165.8, 169.2. HRMS (EI): for $\text{C}_{17}\text{H}_{23}\text{NO}_4$ calcd: 305.1627 $[\text{M}]^+$; found: 305.1622.

3-Ethoxycarbonyl-6-propyl-4-quinolone (17). ^1H NMR ($\text{DMSO}-d_6$) δ 0.90 (3H, t, $J = 7.3$ Hz), 1.28 (3H, t, $J = 7.1$ Hz), 1.62 (2H, hex, $J = 7.3$ Hz), 2.68 (2H, t, $J = 7.3$ Hz), 4.21 (2H, q, $J = 7.1$ Hz), 7.55 (2H, m), 7.94 (1H, bs), 8.50 (1H, s), 12.25 (1H, bs); ^{13}C NMR ($\text{DMSO}-d_6$) δ 13.5, 14.3, 24.0, 36.8, 59.5, 109.5, 118.7, 124.4, 127.2, 133.0, 137.2, 138.8, 144.4, 164.9, 173.4. HRMS (EI): for $\text{C}_{15}\text{H}_{17}\text{NO}_3$ calcd: 259.1208 $[\text{M}]^+$; found: 259.1213.

Diethyl 4-*i*-propylanilinomethylenemalonate (18a). ^1H NMR (CDCl_3) δ 1.25 (6H, d, $J = 6.9$ Hz), 1.33 (3H, t, $J = 7.1$ Hz), 1.39 (3H, t, $J = 7.1$ Hz), 2.90 (1H, hep, $J = 6.9$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 4.31 (2H, $J = 7.1$ Hz), 7.08 (2H, d, $J = 8.4$ Hz), 7.23 (2H, d, $J = 8.4$ Hz), 8.52 (1H, d, $J = 13.8$ Hz), 11.01 (1H, d, $J = 13.8$ Hz); ^{13}C NMR (CDCl_3) δ 14.3, 14.4, 24.0, 24.0, 33.5, 60.0, 60.3, 92.9, 117.3, 117.3, 127.7,

127.7, 137.1, 145.9, 152.2, 165.8, 169.1. HRMS (EI): for $C_{17}H_{23}NO_4$ calcd: 305.1627 [M]⁺; found: 305.1617.

3-Ethoxycarbonyl-6-*i*-propyl-4-quinolone (18). ¹H NMR (DMSO-*d*₆) δ 1.24 (6H, d, *J* = 6.9 Hz), 1.28 (3H, t, *J* = 7.1 Hz), 3.03 (1H, hep, *J* = 6.9 Hz), 4.21 (2H, q, *J* = 7.1 Hz), 7.55 (1H, d, *J* = 8.5 Hz), 7.62 (1H, dd, *J*₁ = 8.5 Hz, *J*₂ = 2.0 Hz), 8.00 (1H, d, *J* = 2.0 Hz), 8.51 (1H, s), 12.26 (1H, bs); ¹³C NMR (DMSO-*d*₆) δ 14.3, 23.8, 23.8, 33.1, 59.5, 109.5, 118.8, 122.1, 127.2, 131.3, 137.3, 144.4, 144.9, 164.9, 173.4. HRMS (EI): for $C_{15}H_{17}NO_3$ calcd: 259.1208 [M]⁺; found: 259.1209.

Diethyl 4-benzylanilinomethylenemalonate (19a). ¹H NMR (CDCl₃) δ 1.33 (3H, t, *J* = 7.1 Hz), 1.39 (3H, t, *J* = 7.2 Hz), 3.98 (2H, s), 4.25 (2H, q, *J* = 7.2 Hz), 4.32 (2H, q, *J* = 7.1 Hz), 7.07 (2H, d, *J* = 8.5 Hz), 7.21 (5H, m), 7.31 (2H, m), 8.51 (1H, d, *J* = 13.8 Hz), 11.01 (1H, d, *J* = 13.8 Hz); ¹³C NMR (CDCl₃) δ 14.3, 14.4, 41.2, 60.0, 60.3, 93.1, 117.3, 117.3, 126.2, 128.5, 128.5, 128.8, 128.8, 130.2, 130.2, 137.4, 138.0, 140.7, 152.0, 165.7, 169.1. HRMS (ESI): for $C_{21}H_{24}NO_4$ calcd: 354.1705 [MH]⁺; found: 354.1690.

6-Benzyl-3-ethoxycarbonyl-4-quinolone (19). ¹H NMR (DMSO-*d*₆) δ 1.27 (3H, t, *J* = 7.1 Hz), 4.07 (2H, s), 4.20 (2H, q, *J* = 7.1 Hz), 7.25 (5H, m), 7.56 (2H, m), 7.97 (1H, s), 8.50 (1H, d, *J* = 6.7 Hz), 12.28 (1H, d, *J* = 6.7 Hz); ¹³C NMR (DMSO-*d*₆) δ 14.3, 40.6, 59.5, 109.6, 119.0, 124.9, 126.1, 127.2, 128.5, 128.5, 128.8, 128.8, 133.3, 137.3, 138.0, 140.9, 144.5, 164.8, 173.3. HRMS (ESI): for $C_{19}H_{17}NO_3Na$ calcd: 330.1106 [MNa]⁺; found: 330.1097.

6-Benzyl-3-propoxycarbonyl-4-quinolone (20). ¹H NMR (DMSO-*d*₆) δ 0.96 (3H, t, *J* = 7.4), 1.66 (2H, m), 4.07 (2H, s), 4.11 (2H, t, *J* = 6.6), 7.20 (1H, m), 7.28 (4H, m), 7.54 (1H, d, *J* = 8.4), 7.59 (1H, dd, *J* = 8.4, 1.8), 7.98 (1H, bs), 8.50 (1H, d, *J* = 6.6), 12.28 (1H, d, *J* = 6.6). ¹³C NMR (DMSO-*d*₆) δ 10.5, 21.7, 40.6, 65.1, 109.6, 119.0, 124.9, 126.1, 127.3, 128.5, 128.5, 128.8, 128.8, 133.3, 137.4, 138.1, 140.9, 144.5, 165.0, 173.3. HRMS (ESI): for $C_{20}H_{20}NO_3$ calcd: 322.1443 [MH]⁺; found: 322.1431.

Diethyl 4-ethylanilinoethylidenemalonate (21a). ¹H NMR (CDCl₃) δ 1.29 (9H, m), 2.08 (3H, s), 2.66 (2H, q, *J* = 7.6 Hz), 4.23 (4H, m), 7.02 (2H, d, *J* = 8.1 Hz), 7.19 (2H, d, *J* = 8.1 Hz), 11.20 (1H, s); ¹³C NMR (CDCl₃) δ 14.4, 14.6, 15.7, 18.1, 28.5, 59.9, 60.8, 94.3, 126.1, 126.1, 128.8, 128.8, 135.8, 142.8, 162.2, 169.0, 169.0. HRMS (EI): for $C_{17}H_{23}NO_4$ calcd: 305.1627 [M]⁺; found: 305.1622.

3-Ethoxycarbonyl-6-ethyl-2-methyl-4-quinolone (21). ¹H NMR (DMSO-*d*₆) δ 1.21 (3H, t, *J* = 7.5 Hz), 1.27 (3H, t, *J* = 7.1 Hz), 2.37 (3H, s), 2.71 (2H, q, *J* = 7.5 Hz), 4.21 (2H, q, *J* = 7.1 Hz), 7.46 (1H, d, *J* = 8.4 Hz), 7.54 (1H, d, *J* = 8.4 Hz), 7.87 (1H, s), 11.81 (1H, bs); ¹³C NMR (DMSO-*d*₆) δ 14.2, 15.5, 18.1, 27.8, 60.2, 114.5, 118.0, 123.0, 124.6, 132.5, 137.4, 139.3, 148.4, 166.9, 173.3. HRMS (EI): for $C_{15}H_{17}NO_3$ calcd: 259.1208 [M]⁺; found: 259.1208.

Diethyl 4-bromoanilinoethylidenemalonate (22a). ¹H NMR (CDCl₃) δ 1.31 (6H, m), 2.08 (3H, s), 4.24 (4H, m), 6.98 (2H, d, *J* = 8.6 Hz), 7.49 (2H, d, *J* = 8.6 Hz), 11.12 (1H, s); ¹³C NMR (CDCl₃) δ 14.1, 14.3, 17.7, 59.9, 60.7, 95.5, 119.6, 125.7, 125.7, 132.3, 132.3, 137.2, 160.7, 168.3, 168.6. HRMS (EI): for $C_{15}H_{18}NO_4^{79}Br$ calcd: 355.0419 [M]⁺; found: 355.0406.

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6-Bromo-3-ethoxycarbonyl-2-methyl-4-quinolone (22). ^1H NMR (DMSO- d_6) δ 1.27 (3H, t, $J = 7.1$ Hz), 2.39 (3H, s), 4.24 (2H, q, $J = 7.1$ Hz), 7.51 (1H, d, $J = 8.8$ Hz), 7.82 (1H, dd, $J_1 = 8.8$ Hz, $J_2 = 2.3$ Hz), 8.13 (1H, d, $J = 2.3$ Hz), 12.06 (1H, bs); ^{13}C NMR (DMSO- d_6) δ 14.1, 18.3, 60.5, 115.1, 116.4, 120.7, 126.0, 127.2, 135.0, 138.1, 149.5, 166.4, 172.1. HRMS (EI): for $\text{C}_{13}\text{H}_{12}\text{NO}_3^{79}\text{Br}$ calcd: 309.0001 [M] $^+$; found: 308.9995.

6-Ethyl-3-propylaminocarbonyl-4-quinolone (23). ^1H NMR (DMSO- d_6) δ 0.93 (3H, t, $J = 7.2$ Hz), 1.23 (3H, t, $J = 7.6$ Hz), 1.54 (2H, hex, $J = 7.2$ Hz), 2.75 (2H, q, $J = 7.6$ Hz), 3.29 (2H, q, $J = 7.2$ Hz), 7.62 (2H, m), 8.06 (1H, s), 8.69 (1H, s), 10.10 (1H, t, $J = 7.2$ Hz), 12.62 (1H, bs); ^{13}C NMR (DMSO- d_6) δ 11.5, 15.5, 22.6, 27.9, 40.0, 110.7, 119.0, 123.3, 126.1, 133.0, 137.4, 140.6, 142.9, 164.5, 176.0. HRMS (EI): for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2$ calcd: 258.1368 [M] $^+$; found: 258.1367.

3-Butylaminocarbonyl-6-ethyl-4-quinolone (24). ^1H NMR (CD_3OD) δ 1.00 (3H, t, $J = 7.3$ Hz), 1.32 (3H, t, $J = 7.6$ Hz), 1.48 (2H, m), 1.64 (2H, m), 2.83 (2H, q, $J = 7.6$ Hz), 3.46 (2H, t, $J = 6.9$ Hz), 7.57 (1H, d, $J = 8.5$ Hz), 7.67 (1H, dd, $J_1 = 8.5$ Hz, $J_2 = 2.0$ Hz), 8.18 (1H, d, $J = 2.0$ Hz), 8.74 (1H, s); ^{13}C NMR (DMSO- d_6) δ 13.7, 15.5, 19.7, 27.9, 31.4, 37.8, 110.7, 119.0, 123.3, 126.1, 133.0, 137.4, 140.6, 142.9, 164.4, 176.0. HRMS (EI): for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$ calcd: 272.1525 [M] $^+$; found: 272.1523.

6-Benzyl-3-propylaminocarbonyl-4-quinolone (25). ^1H NMR (DMSO- d_6) δ 0.92 (3H, t, $J = 7.3$ Hz), 1.53 (2H, hex, $J = 7.3$ Hz), 3.28 (2H, m), 4.10 (2H, s), 7.20 (1H, m), 7.29 (4H, m), 7.63 (2H, m), 8.06 (1H, s), 8.68 (1H, s), 10.05 (1H, t, $J = 5.5$ Hz); ^{13}C NMR (DMSO- d_6) δ 11.5, 22.6, 40.0, 40.6, 110.8, 119.2, 124.5, 126.1, 126.1, 128.5, 128.5, 128.8, 128.8, 133.6, 137.5, 138.2, 140.8, 143.1, 164.4, 176.0. HRMS (EI): for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2$ calcd: 320.1525 [M] $^+$; found: 320.1526.

Propyl-2-methyl-7-oxo-4,7-dihydro-pyrazolo[1,5-a]pyrimidine-6-carboxylate (27). ^1H NMR (DMSO- d_6) δ 0.95 (3H, t, $J = 7.4$ Hz), 1.66 (2H, m), 2.28 (3H, s), 4.09 (2H, t, $J = 6.6$ Hz), 6.04 (1H, s), 8.45 (1H, s); ^{13}C NMR (DMSO- d_6) δ 10.5, 14.2, 21.8, 65.0, 91.8, 97.5, 143.8, 146.9, 152.0, 153.6, 164.3. HRMS (EI): for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_3$ calcd: 235.0957 [M] $^+$; found: 235.0958.

Ethyl-7-oxo-4,7-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate (28). ^1H NMR (DMSO- d_6) δ 1.27 (3H, t, $J = 7.1$ Hz), 4.20 (2H, q, $J = 7.1$ Hz), 6.23 (1H, s), 7.84 (1H, s), 8.52 (1H, s); ^{13}C NMR (DMSO- d_6) δ 14.5, 59.1, 93.2, 96.3, 108.7, 142.7, 149.8, 155.1, 165.3. HRMS (EI): for $\text{C}_9\text{H}_9\text{N}_3\text{O}_3$ calcd: 207.0644 [M] $^+$; found: 207.0658.

Propyl-7-oxo-4,7-dihydropyrazolo[1,5-a]pyrimidine-6-carboxylate (29). ^1H NMR (DMSO- d_6) δ 0.97 (3H, t, $J = 7.4$ Hz), 1.68 (2H, m), 4.14 (2H, t, $J = 6.6$ Hz), 6.31 (1H, d, $J = 1.9$ Hz), 7.92 (1H, d, $J = 1.9$ Hz), 8.23 (1H, s); ^{13}C NMR (DMSO- d_6) δ 10.4, 21.7, 65.5, 91.3, 98.5, 140.7, 143.4, 145.4, 153.2, 160.8. HRMS (EI): for $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_3$ calcd: 221.0800 [M] $^+$; found: 221.0812.

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Elemental analysis

Compd.	Formula	Cald.			Found		
		C%	H%	N%	C%	H%	N%
1	C ₁₃ H ₁₀ NO ₃ F ₃	54.74	3.53	4.91	54.89	3.67	4.71
2	C ₁₄ H ₁₅ NO ₃	68.56	6.16	5.71	68.53	6.32	5.69
3	C ₁₅ H ₁₇ NO ₃	69.48	6.61	5.40	69.27	6.43	5.17
4	C ₁₆ H ₁₉ NO ₃	70.31	7.01	5.12	70.10	6.85	4.88
5	C ₁₇ H ₂₁ NO ₃	71.06	7.37	4.87	71.12	7.43	4.90
6	C ₁₇ H ₂₁ NO ₃	71.06	7.37	4.87	71.16	7.52	4.65
7	C ₁₇ H ₂₁ NO ₃	71.06	7.37	4.87	71.31	7.62	4.59
8	C ₁₈ H ₂₃ NO ₃	71.73	7.69	4.65	71.75	7.78	4.54
9	C ₁₇ H ₁₉ NO ₃	71.56	6.71	4.91	71.77	6.54	4.61
10	C ₁₅ H ₁₇ NO ₃	69.48	6.61	5.40	69.78	6.49	5.23
11	C ₁₈ H ₂₃ NO ₃	71.73	7.69	4.65	71.51	7.88	4.87
12	C ₁₇ H ₂₁ NO ₃	71.06	7.37	4.87	71.22	7.22	4.62
13	C ₁₂ H ₁₁ NO ₃	66.35	5.10	6.45	66.47	5.34	6.31
14	C ₁₂ H ₁₁ NO ₃	66.35	5.10	6.45	66.18	5.00	6.26
15	C ₁₄ H ₁₅ NO ₃	68.56	6.16	5.71	68.44	6.32	5.55
16	C ₁₂ H ₁₀ NO ₃ Br	48.67	3.40	4.73	48.51	3.64	4.52
17	C ₁₅ H ₁₇ NO ₃	69.48	6.61	5.40	69.69	6.48	5.27
18	C ₁₅ H ₁₇ NO ₃	69.48	6.61	5.40	69.66	6.29	5.25
19	C ₁₉ H ₁₇ NO ₃	74.25	5.57	4.56	74.13	5.80	4.31
20	C ₂₀ H ₁₉ NO ₃	74.75	5.96	4.36	74.43	6.25	4.33
21	C ₁₅ H ₁₇ NO ₃	69.48	6.61	5.40	69.32	6.87	5.26
22	C ₁₃ H ₁₂ NO ₃ Br	50.35	3.90	4.52	50.63	3.69	4.67
23	C ₁₅ H ₁₈ N ₂ O ₂	69.75	7.02	10.84	69.61	7.06	11.15
24	C ₁₆ H ₂₀ N ₂ O ₂	70.56	7.40	10.29	70.45	7.67	10.49
25	C ₂₀ H ₂₀ N ₂ O ₂	74.98	6.29	8.74	75.03	6.41	8.69
26	C ₁₀ H ₁₁ N ₃ O ₃	54.30	5.01	19.00	54.05	5.24	19.32
27	C ₁₁ H ₁₃ N ₃ O ₃	56.16	5.57	17.86	56.30	5.43	18.20
28	C ₉ H ₉ N ₃ O ₃	52.17	4.38	20.28	52.36	4.21	20.44
29	C ₁₀ H ₁₁ N ₃ O ₃	54.30	5.01	19.00	54.54	4.91	19.28