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Supplement: 2-Amino-4-arylthiazole Derivatives as Anti-giardial Agents: Synthesis, Biological Evaluation and QSAR Studies

Characterization data of the compounds 1a-g

4-Phenyl-thiazol-2-ylamine (1a): Straw color solid: mp 148°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.05 (s, 2H), 6.99 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3 (C), 149.9 (C), 134.9 (C), 128.6 (2CH), 127.3 (C), 125.6 (2CH), 101.6 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_8N_2S$ $[M]^+$: 176.0408. Found: 176.0409. Yield: 88%.

4-(4-Chloro-phenyl)-thiazol-2-ylamine (1b): Straw color solid: mp 165°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.11 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9 (C), 146.3 (C), 132.5 (C), 132.2 (C), 128.9 (2CH), 127.5 (2CH), 102.8 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_7N_2SCl$ $[M]^+$: 210.0018. Found: 210.0007. Yield: 91%.

4-(4-Bromo-phenyl)-thiazol-2-ylamine (1c): Straw color solid: mp 179°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.10 (s, 2H), 7.07 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5 (C), 148.7 (C), 134.2 (C), 131.5 (2CH), 127.7 (2CH), 120.2 (C), 102.2 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_7N_2SBr$ $[M]^+$: 255.9493. Found: 255.9476. Yield: 99%.

4-(4-Nitro-phenyl)-thiazol-2-ylamine (1d): Orange solid: mp 286°C.^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, *J* = 9.0 Hz, 2H), 8.03 (d, *J* = 9.0 Hz, 2H), 7.40 (s, 1H), 7.23 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7 (C), 147.9 (C), 146.0 (C), 140.9 (C), 126.4 (2CH), 124.2 (2CH), 106.7 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_7N_3O_2S$ $[M]^+$: 221.0259. Found: 221.0249. Yield: 99%.

4-Tolyl-thiazol-2-ylamine (1e): Yellow solid: mp 121°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.05 (s, 2H), 6.89 (s, 1H), 2.88 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3 (C), 150.0 (C), 136.5 (C), 132.4 (C), 129.2 (2CH), 125.3 (2CH), 100.7 (CH), 20.9 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{10}H_{10}N_2S$ $[M]^+$: 190.0565. Found: 190.0565. Yield: 80%.

4-(4-Methoxy-phenyl)-thiazol-2-ylamine (1f): Yellow solid: mp 197°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.95 (s, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4 (C), 159.5 (C), 144.1 (C), 127.3 (2CH), 124.5 (C), 114.3 (2CH), 100.2 (CH), 55.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{10}H_{10}N_2OS$ $[M]^+$: 206.0514. Found: 206.0520. Yield: 80%.

4-(2-Amino-thiazol-4-yl)-phenol (1g): Yellow solid: mp 179°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.54 (s, 1H), 7.59 (d, *J* = 8.6 Hz, 2H), 6.98 (s, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.71 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2 (C), 156.9 (C), 150.2 (C), 127.1 (2CH), 126.5 (C), 115.3 (2CH), 98.6 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_8N_2OS$ $[M]^+$: 192.0357. Found: 192.0370. Yield: 62%.

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Characterization data of the compounds 2a-f

***N*-(4-Phenyl-thiazol-2-yl)-acetamide (2a):** Straw color solid: mp 212°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.23 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.57 (s, 1H), 7.31 (t, *J* = 7.3Hz, 1H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9 (C), 158.1 (C), 148.9 (C), 134.4 (C), 127.9 (C), 128.9 (2CH), 125.8 (2CH), 108.0 (CH), 22.6 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_{10}N_2OS$ $[M]^+$: 218.0514. Found: 218.0503. Yield: 95%.

***N*-[4-(4-Chloro-phenyl)-thiazol-2-yl]-acetamide (2b):** Straw color solid: mp 260°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.26 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.61 (s, 1H), 2.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1 (C), 158.4 (C), 147.7 (C), 133.4 (C), 132.5 (C), 129.0 (2CH), 127.6 (2CH), 108.8 (CH), 22.7 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_9N_2OSCl$ $[M]^+$: 252.0124. Found: 252.0117. Yield: 90%.

***N*-[4-(4-Bromo-phenyl)-thiazol-2-yl]-acetamide (2c):** Straw color solid: mp 265°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.27 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.63 (s, 1H), 2.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0 (C), 158.3 (C), 147.7 (C), 133.7 (C), 131.9 (2CH), 127.9 (2CH), 121.0 (C), 108.9 (CH), 22.7 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_9N_2OSBr$ $[M]^+$: 297.9598. Found: 297.9595. Yield: 96%.

***N*-[4-(4-Nitro-phenyl)-thiazol-2-yl]-acetamide (2d):** Orange solid: mp 290°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.35 (s, 1H), 8.26 (d, *J* = 8.6 Hz, 2H), 8.10 (d, *J* = 8.6 Hz, 2H), 7.90 (s) (s, 1H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2 (C), 158.7 (C), 146.7 (C), 146.6 (C), 140.4 (C), 126.7 (2CH), 124.4 (2CH), 112.5 (CH), 22.7 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_9N_3O_3S$ $[M]^+$: 263.0365. Found: 263.0381. Yield: 82%.

***N*-(4-Tolyl-thiazol-2-yl)-acetamide (2e):** Yellow solid: mp 217°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.19 (s, 1H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.46 (s, 1H), 2.29 (s, 3H), 2.14 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0 (C), 158.1 (C), 149.1 (C), 137.4 (C), 131.9 (C), 129.6 (2CH), 125.9 (2CH), 107.2 (CH), 22.7 (CH_3), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{12}H_{12}N_2OS$ $[M]^+$: 232.0670. Found: 232.0662. Yield: 73%.

***N*-[4-(4-Methoxy-phenyl)-thiazol-2-yl]-acetamide (2f):** Yellow solid: mp 192°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.20 (s, 1H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.39 (s, 1H), 6.97 (d, *J* = 8.6 Hz, 2H), 3.76 (s, 3H), 2.14 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0 (C), 159.2 (C), 158.0 (C), 148.8 (C), 127.3 (C), 127.2 (2CH), 114.3 (2CH), 106.1 (CH), 55.4 (CH_3), 22.7 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{12}H_{12}N_2O_2S$ $[M]^+$: 248.0619. Found: 248.0623. Yield: 90%.

Characterization data of the compounds 3a-f

***N*-(4-Phenyl-thiazol-2-yl)-benzamide (3a):** Straw color solid: mp 70°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.80 (s, 1H), 8.13 (d, *J* = 7.6 Hz, 2H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.65 (s, 1H), 7.62 (t, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5 (C), 158.8 (C), 149.4 (C), 134.5 (C), 132.8 (C), 132.2 (C), 128.9 (2CH), 128.8 (2CH), 128.4 (2CH), 128 (CH), 126.0 (2CH), 108.7 (CH). HRMS (EI, 70 eV) Calcd for $C_{16}H_{12}N_2OS$ $[M]^+$: 280.0670. Found: 280.0667. Yield: 97%.

***N*-[4-(4-Chloro-phenyl)-thiazol-2-yl]-benzamide (3b):** Straw color solid: mp 173°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.80 (s, 1H), 8.10 (d, *J* = 7.4 Hz, 2H), 7.96 (d, *J* = 8.5 Hz, 2H), 7.72 (s, 1H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6 (C), 158.9 (C), 148.1 (C), 133.4 (C), 133 (CH), 132.5 (C), 132.1 (C), 129.0 (2CH), 128.9 (2CH), 128.4 (2CH), 127.7 (2CH), 109.5 (CH). HRMS (EI, 70 eV) Calcd for $C_{16}H_{11}N_2OSCl$ $[M]^+$: 314.0281. Found: 314.0277. Yield: 95%.

***N*-[4-(4-Bromo-phenyl)-thiazol-2-yl]-benzamide (3c):** Straw color solid: mp 202°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.80 (s, 1H), 8.11 (d, *J* = 7.3 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.72 (s, 1H), 7.63 (t, *J* = 7.8 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5 (C), 158.9 (C), 148.1 (C), 133.7 (C), 132.9 (CH), 132 (C), 131.9 (2CH), 128.8 (2CH), 128.3 (2CH), 128.0 (2CH), 121.1 (C), 109.5 (CH). HRMS (EI, 70 eV) Calcd for $C_{16}H_{11}N_2OSBr$ $[M]^+$: 359.9755. Found: 359.9742. Yield: 92%.

***N*-[4-(4-Nitro-phenyl)-thiazol-2-yl]-benzamide (3d):** Orange solid: mp 226°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.94 (s, 1H), 8.33 (d, *J* = 8.6 Hz, 2H), 8.22 (d, *J* = 8.6 Hz, 2H), 8.12 (d, *J* = 8.0 Hz, 2H), 8.06 (s, 1H), 7.66 (t, *J* = 7.0 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7 (C), 159.3 (C), 147.1 (C), 146.6 (C), 140.5 (C), 133.0 (C), 132.6 (CH), 128.6 (2CH), 128.1 (2CH), 126.6 (2CH), 124.4 (2CH), 113.6 (CH). HRMS (EI, 70 eV) Calcd for $C_{16}H_{11}N_3O_3S$ $[M]^+$: 325.0521. Found: 325.0524. Yield: 40%.

***N*-(4-Tolyl-thiazol-2-yl)-benzamide (3e):** Yellow solid: mp 140°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.75 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.64 (t, *J* = 7.0 Hz, 1H), 7.59 (s, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5 (C), 158.6 (C), 149.4 (C), 137.4 (C), 132.9 (C),132.2 (C), 131.8 (C), 129.5 (2CH), 128.9 (2CH), 128.4 (2CH), 125.9 (2CH), 107.9

(CH), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{17}H_{14}N_2OS$ $[M]^+$: 294.0827. Found: 294.0817. Yield: 92%

***N*-[4-(4-Methoxy-phenyl)-thiazol-2-yl]-benzamide (3f):** Yellow solid: mp 177°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.74 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 2H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.64 (t, *J* = 7.0 Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.4 (C), 159.2 (C), 158.3 (C), 132.9 (CH), 132.2 (C), 128.9 (2CH), 128.4 (2CH), 127.4 (2CH), 127.4 (C), 114.3 (2CH), 106.8 (CH), 55.3 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{17}H_{14}N_2O_2S$ $[M]^+$: 310.0776. Found: 310.0766. Yield: 85%.

Characterization data of the compounds 4a-f

Furan-2-carboxylic acid (4-phenyl-thiazol-2-yl)-amide (4a): Straw color solid: mp 130°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.74 (s, 1H), 8.01 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 3.5 Hz, 1H), 7.67 (s, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.0 Hz, 1H), 6.74 (dd, *J* = 1.8 & 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.0 (C), 156.1 (C), 149.3 (C), 147.5 (CH), 145.6 (C), 134.2 (C), 129.0 (2CH), 128.1 (CH), 125.9 (2CH), 116.8 (C), 112.6 (C), 108.7 (CH). HRMS (EI, 70 eV) Calcd for $C_{14}H_{10}N_2O_2S$ $[M]^+$: 270.0463. Found: 270.0465. Yield: 99%.

Furan-2-carboxylic acid [4-(4-chloro-phenyl)-thiazol-2-yl]-amide (4b): Straw color solid: mp 142°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.76 (s, 1H), 7.99 (s), 7.93 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.70 (s, 1H), 7.67 (d, *J* = 3.6 Hz, 1H), 6.73 (dd, *J* = 1.9 & 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.2 (C), 156.1 (C), 148.1 (C), 147.6 (CH), 145.6 (C), 133.3 (C), 132.5 (C), 129.0 (2CH), 127.7 (2CH), 117.2 (CH), 112.6 (CH), 109.5 (CH). HRMS (EI, 70 eV) Calcd for $C_{14}H_9N_2O_2SCl$ $[M]^+$: 304.0073. Found: 304.0051. Yield: 87%.

Furan-2-carboxylic acid [4-(4-bromo-phenyl)-thiazol-2-yl]-amide (4c): Straw color solid: mp 169°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.77 (sa, 1H), 8.00 (s), 7.87 (d, *J* = 8.2 Hz, 2H), 7.71 (s, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 3.5 Hz, 1H), 6.74 (dd, *J* = 1.8 & 3.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.2 (C), 156.1 (C), 148.1 (C), 147.6 (CH), 145.6 (C), 133.6 (C), 131.9 (2CH), 128.0 (2CH), 121.1 (C), 116.9 (CH), 112.6 (CH), 109.5 (CH). HRMS (EI, 70 eV) Calcd for $C_{14}H_9N_2O_2SBr$ $[M]^+$: 349.9548. Found: 349.9543. Yield: 93%.

Furan-2-carboxylic acid [4-(4-nitro-phenyl)-thiazol-2-yl]-amide (4d): Orange solid: mp 228°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.88 (s, 1H), 8.31 (d, *J* = 8.9 Hz, 2H), 8.17 (d, *J* = 8.9 Hz, 2H), 8.01 (brs, 2H), 7.69 (d, *J* = 3.4 Hz, 1H), 6.75 (dd, *J* = 1.6 & 3.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.7 (C), 156.3 (C), 147.7 (CH), 147.2 (C), 146.7 (C), 145.5 (C), 140.4 (C), 126.8 (2CH), 124.5 (2CH), 117.1 (CH), 113.2 (CH), 112.7 (2CH). HRMS (EI, 70 eV) Calcd for $C_{14}H_9N_3O_4S$ $[M]^+$: 315.0314. Found: 315.0314. Yield: 87%.

Furan-2-carboxylic acid (4-tolyl-thiazol-2-yl)-amide (4e): Yellow solid: mp 144°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.71 (brs, 1H), 8.00 (s, 1H), 7.81 (d, *J* = 7.9 Hz, 2H), 7.68 (d, *J* = 3.5 Hz, 1H), 7.57 (s, 1H), 7.24 (d, *J* = 7.9 Hz, 2H), 6.74 (dd, *J* = 1.8 & 3.6 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.9 (C), 156.1 (C), 149.4 (C), 147.5 (CH), 145.6 (C), 137.4 (C), 131.8 (C), 129.6 (2CH), 125.9 (2CH), 116.7 (CH), 112.6 (CH), 107.9 (CH), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{15}H_{12}N_2O_2S$ $[M]^+$: 284.0619. Found: 284.0627. Yield: 91%.

Furan-2-carboxylic acid [4-(4-methoxy-phenyl)-thiazol-2-yl]-amide (4f): Yellow solid: mp 133°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 12.69 (brs, 1H), 8.00 (dd, *J* = 0.7 & 1.4 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 3.6 Hz, 2H), 6.99 (t, *J* = 8.6 Hz, 2H), 7.49 (s, 1H), 6.74 (dd, *J* = 1.8 & 3.5 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.2 (C), 157.9 (C), 156.1 (C), 149.2 (C), 147.5 (CH), 145.7 (C), 127.3 (2CH), 125.2 (C), 116.7 (CH), 114.3 (2CH), 112.6 (CH), 106.7 (CH), 55.3 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{15}H_{12}N_2O_3S$ $[M]^+$: 300.0569. Found: 300.0559. Yield: 80%.

Characterization data of the compounds 5a-e

5-Bromo-4-phenyl-thiazol-2-ylamine (5a): Straw color solid: mp 96°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (dd, *J* = 8.6 & 1.2 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.35 Hz, 1H), 7.35 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.9 (C), 148.0 (C), 134.7 (C), 129.2 (2CH), 128.8 (2CH), 128.9 (C), 88.1 (C). HRMS (EI, 70 eV) Calcd for $C_9H_7N_2SBr$ $[M]^+$: 253.9513. Found: 253.9528. Yield: 50%.

5-Bromo-4-(4-chloro-phenyl)-thiazol-2-ylamine (5b): Straw color solid: mp 165°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.33 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2 (C), 147.0 (C), 133.6 (2C), 130.7 (2CH), 129.4 (2CH), 88.9 (C). HRMS (EI, 70 eV) Calcd for $C_9H_6N_2SClBr$ $[M]^+$: 287.8847. Found: 287.8830. Yield: 80%.

5-Bromo-4-(4-bromo-phenyl)-thiazol-2-ylamine (5c): Straw color solid: mp 164°C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.36 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1 (C), 146.9 (C), 133.9 (C), 130.9 (2CH), 132.2 (2CH), 122.1 (C), 88.8 (C). HRMS (EI, 70 eV) Calcd for $C_9H_6N_2SBr$ $[M]^+$: 333.8618. Found: 333.8602. Yield: 77%.

5-Bromo-4-(4-nitro-phenyl)-thiazol-2-ylamine (5d): Orange solid: mp 218°C. ^1H NMR ($CDCl_3$, 400 MHz)

δ 8.18 (brs, 4H), 7.44 (brs, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.5 (C), 146.5 (C), 145.1 (C), 140.0 (C), 129.0 (2CH), 123.8 (2CH), 91.1 (C). HRMS (EI, 70 eV) Calcd for $C_9H_6N_3O_2SBr$ $[M]^+$: 300.9344. Found: 300.9323. Yield: 63%.

5-Bromo-4-tolyl-thiazol-2-ylamine (5e): Yellow solid: mp 116°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.30 (s, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8 (C), 148.1 (C), 138.2 (C), 131.9 (C), 129.7 (2CH), 128.7 (2CH), 87.3 (C), 21.8 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{10}H_9N_2SBr$ $[M]^+$: 269.9649. Found: 269.9647. Yield: 77%.

Characterization data of the compounds 6a-f

***N*-(5-Bromo-4-phenyl-thiazol-2-yl)-acetamide (6a):** White solid: mp 238°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.53 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4 (C), 157.1 (C), 145.8 (C), 133.3 (C), 128.5 (2CH), 128.1 (3CH), 97.0 (C), 22.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_9N_2OSBr$ $[M]^+$: 297.9598. Found: 297.9595. Yield: 90%.

***N*-[5-Bromo-4-(4-chloro-phenyl)-thiazol-2-yl]-acetamide (6b):** Straw color solid: mp 260°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.54 (s, 1H), 7.86 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5 (C), 157.3 (C), 144.6 (C), 133.1 (C), 132.1 (C), 129.7 (2CH), 128.6 (2CH), 97.6 (C), 22.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_8N_2OSClBr$ $[M]^+$: 329.9229. Found: 329.9236.

Yield: 93%.

***N*-[5-Bromo-4-(4-bromo-phenyl)-thiazol-2-yl]-acetamide (6c):** Straw color solid: mp 274°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.55 (s, 1H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5 (C), 157.3 (C), 144.6 (C), 132.5 (C), 131.6 (2CH), 130.0 (2CH), 121.8 (C), 97.7 (C), 22.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_8N_2OSBr_2$ $[M]^+$: 377.8683. Found: 377.8700. Yield: 92%.

***N*-[5-Bromo-4-(4-nitro-phenyl)-thiazol-2-yl]-acetamide (6d):** Orange solid: mp 277°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.66 (s, 1H), 8.35 (d, *J* = 9.0 Hz, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 2.18 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7 (C), 157.6 (C), 146.9 (C), 143.7 (C), 139.5 (C), 129.0 (2CH), 123.9 (2CH), 100.4 (C), 22.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{11}H_8N_3O_3SBr$ $[M]^+$: 342.9449. Found: 342.9432. Yield: 78%.

***N*-(5-Bromo-4-p-tolyl-thiazol-2-yl)-acetamide (6e):** White solid: mp 231°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.51 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 2.32 (s, 3H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3 (C), 157.0 (C), 145.8 (C), 137.9 (C), 130.6 (C), 129.1 (2CH), 127.9 (2CH), 96.4 (C), 22.4 (CH_3), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{12}H_{11}N_2OSBr$ $[M]^+$: 311.9755. Found: 311.9772. Yield: 92%.

***N*-[5-Bromo-4-(4-methoxy-phenyl)-thiazol-2-yl]-acetamide (6f):** Yellow solid: mp 246°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.48 (s, 1H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3 (C), 159.2 (C), 156.9 (C), 145.6 (C), 129.4 (2CH), 125.8 (C), 113.9 (2CH), 95.4 (C), 55.3 (CH_3), 22.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{12}H_{11}N_2O_2SBr$ $[M]^+$: 325.9725. Found: 325.9709. Yield: 98%.

Characterization data of the compounds 7a-f

***N*-(5-Bromo-4-phenyl-thiazol-2-yl)-benzamide (7a):** Brown solid: mp 95°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.08 (s, 1H), 8.11 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8 (C), 157.8 (C), 146.4 (C), 133.2 (CH), 133.3 (C), 131.4 (C), 128.9 (2CH), 128.6 (2CH), 128.5 (CH), 128.4 (2CH), 128.2 (2CH), 98.0 (C). HRMS (EI, 70 eV) Calcd for $C_{16}H_{11}N_2OSBr$ $[M]^+$: 359.9755. Found: 359.9767. Yield: 81%.

***N*-[5-Bromo-4-(4-chloro-phenyl)-thiazol-2-yl]-benzamide (7b):** Straw color solid: mp 102°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.08 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.54 (brd, *J* = 8.2 Hz, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9 (C), 158.0 (C), 145.2 (C), 133.3 (2C), 132.2 (C), 131.4 (CH), 130.0 (2CH), 128.9 (2CH), 128.7 (2CH), 128.4 (2CH), 98.6 (C). HRMS (EI, 70 eV) Calcd for $C_{16}H_{10}N_2OSClBr$ $[M]^+$: 393.9365. Found: 393.9384. Yield: 92%.

***N*-[5-Bromo-4-(4-bromo-phenyl)-thiazol-2-yl]-benzamide (7c):** Straw color solid: mp 165°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.10 (brs, 1H), 8.10 (d, *J* = 7.8 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8 (C), 158.0 (C), 145.2 (C), 133.2 (CH), 132.5 (C), 131.3 (C), 131.6 (2CH), 130.2 (2CH), 128.9 (2CH), 128.4 (2CH), 121.9 (C), 98.6 (C). HRMS (EI, 70 eV) Calcd for $C_{16}H_{10}N_2OSBr$ $[M]^+$: 439.8840. Found: 439.8859. Yield: 91%.

***N*-[5-Bromo-4-(4-nitro-phenyl)-thiazol-2-yl]-benzamide (7d):** Green solid: mp 240°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.20 (s, 1H), 8.38 (d, *J* = 8.7 Hz, 2H), 8.22 (d, *J* = 8.7 Hz, 2H), 8.12 (d, *J* = 7.7 Hz, 2H), 7.66 (t, *J* = 7.3 Hz, 1H),

7.56 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7 (C), 157.7 (C), 147.4 (C), 144.6 (C), 140.1 (C), 133.6 (CH), 132.1 (CH), 129.7 (2CH), 129.3 (2CH), 128.9 (2CH), 124.5 (2CH), 101.5 (C). HRMS (EI, 70 eV) Calcd for $C_{16}H_{10}N_3O_3SBr$ $[M]^+$: 404.9606. Found: 404.9593. Yield: 85%.

***N*-(5-Bromo-4-tolyl-thiazol-2-yl)-benzamide (7e):** Yellow solid: mp 130°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.05 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.1 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8 (2C), 157.7 (C), 146.4 (C), 138.1 (2CH), 133.2 (CH), 131.2 (C), 130.6 (C), 129.2 (2CH), 128.9 (2CH), 128.4 (2CH), 97.4 (C), 21.1 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{17}H_{13}N_2OSBr$ $[M]^+$: 373.9911. Found: 373.9929. Yield: 77%.

***N*-[5-Bromo-4-(4-methoxy-phenyl)-thiazol-2-yl]-benzamide (7f):** Yellow solid: mp 150°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.04 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 2H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8 (C), 159.4 (C), 157.6 (C), 146.2 (C), 133.2 (CH), 131.5 (C), 129.6 (2CH), 128.9 (2CH), 128.4 (2CH), 125.8 (C), 114.0 (2CH), 96.4 (C), 55.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{17}H_{13}N_2O_2SBr$ $[M]^+$: 389.9365. Found: 389.9878. Yield: 76%.

Characterization data of the compounds 8a-f.

Furan-2-carboxylic acid (5-bromo-4-phenyl-thiazol-2-yl)-amide (8a): Brown solid: mp 173°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.06 (s, 1H), 8.04 (d, *J* = 1.7 Hz, 1H), 7.89 (d, *J* = 7.4 Hz, 2H), 7.70 (d, *J* = 3.6 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 6.76 (dd, *J* = 1.7 & 3.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.1 (C), 156.3 (C), 147.9 (CH), 146.3 (C), 145.1 (C), 133.2 (C), 128.6 (2CH), 128.2 (2CH), 128.6 (CH), 117.4 (CH), 112.6 (CH), 97.8 (C). HRMS (EI, 70 eV) Calcd for $C_{14}H_9N_2O_2SBr$ $[M]^+$: 349.9548. Found: 349.9553. Yield: 77%.

Furan-2-carboxylic acid [5-bromo-4-(4-chloro-phenyl)-thiazol-2-yl]-amide (8b): Straw color solid: mp 172°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.09 (s, 1H), 8.04 (t, *J* = 1.6 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 3.6 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.70 (s, 1H), 6.76 (dd, *J* = 1.6 & 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.3 (C), 156.4 (C), 148.0 (CH), 145.1 (C), 145.0 (C), 133.2 (C), 132.1 (C), 129.9 (2CH), 128.7 (2CH), 117.4 (CH), 112.7 (CH), 98.4 (C). HRMS (EI, 70 eV) Calcd for $C_{14}H_8N_2O_2SClBr$ $[M]^+$: 383.9149. Found: 383.9153. Yield: 83%.

Furan-2-carboxylic acid [5-bromo-4-(4-bromo-phenyl)-thiazol-2-yl]-amide (8c): Straw color solid: mp 174°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.10 (sa, 1H), 8.03 (d, *J* = 1.3 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 3H), 6.76 (dd, *J* = 1.6 & 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.4 (C), 156.4 (C), 147.9 (CH), 145.1 (C), 145.2 (C), 132.5 (C), 131.6 (2CH), 130.2 (2CH), 121.9 (C), 117.4 (CH), 112.7 (CH), 98.4 (C). HRMS (EI, 70 eV) Calcd for $C_{14}H_8N_2O_2SBr_2$ $[M]^+$: 427.8653. Found: 427.8630. Yield: 88%.

Furan-2-carboxylic acid [5-bromo-4-(4-nitro-phenyl)-thiazol-2-yl]-amide (8d): Green solid: mp 238°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.20 (s, 1H), 8.40 (d, *J* = 8.8 Hz, 2H), 8.20 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 1.5 Hz, 1H), 7.69 (d, *J* = 3.6 Hz, 1H), 6.76 (dd, *J* = 1.7 & 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.1 (C), 156.7 (C), 147.9 (CH), 146.9 (C), 145.5 (C), 144.1 (C), 139.5 (C), 129.2 (2CH), 124.0 (2CH), 117.4 (CH), 112.7 (CH), 100.9 (C). HRMS (EI, 70 eV) Calcd for $C_{14}H_8N_3O_4SBr$ $[M]^+$: 394.9398. Found: 394.9420. Yield: 82%.

Furan-2-carboxylic acid (5-bromo-4-tolyl-thiazol-2-yl)-amide (8e): Yellow solid: mp 159°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.10 (brs, 1H), 8.03 (d, *J* = 1.5 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 3.6 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.75 (dd, *J* = 1.6 & 3.6 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.1 (C), 156.4 (C), 145.1 (C), 147.9 (CH), 146.4 (C), 138.1 (C), 130.5 (C), 129.2 (2CH), 128.1 (2CH), 117.3 (CH), 112.7 (CH), 97.1 (C), 21.1 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{15}H_{11}N_2O_2SBr$ $[M]^+$: 363.9704. Found: 363.9707. Yield: 80%.

Furan-2-carboxylic acid [5-bromo-4-(4-methoxy-phenyl)-thiazol-2-yl]-amide (8f): Yellow solid: mp 177°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.00 (brs, 1H), 8.03 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 3.2 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.75 (t, *J* = 1.8 Hz, 1H), 3.80 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.4 (C), 157.0 (C), 156.4 (C), 147.8 (CH), 145.2 (C), 146.1 (C), 129.6 (2CH), 125.7 (C), 114.3 (CH), 114.0 (2CH), 112.7 (CH), 96.2 (C), 55.4 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{15}H_{11}N_2O_3SBr$ $[M]^+$: 379.9653. Found: 379.9654. Yield: 77%.

Characterization data of the compounds 9 and 10.

Acetic acid 4-(2-acetylamino-thiazol-4-yl)-phenyl ester (9): Yellow solid: mp 234°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.26 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.56 (s, 1H), 2.27 (s, 3H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5 (C), 169.0 (C), 158.2 (C), 150.2 (C), 148.1 (C), 132.2 (C), 126.9 (2CH), 122.4 (2CH), 108.1 (CH), 22.7 (CH_3), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{13}H_{12}N_2O_3S$ $[M]^+$: 276.0569. Found: 276.0563. Yield: 83%.

Acetic acid 4-(2-acetylamino-5-bromo-thiazol-4-yl)-phenyl ester (10): Yellow solid: mp 233°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.53 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 2.28 (s, 3H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5 (C), 169.4 (C), 157.2 (C), 150.4 (C), 145.1 (C), 131.0 (C), 129.2 (2CH), 122.0 (2CH), 97.1 (C), 22.4 (CH_3), 21.0 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{13}H_{10}N_2O_3SBr$ $[M]^+$: 354.9575. Found: 354.9543. Yield: 80%.

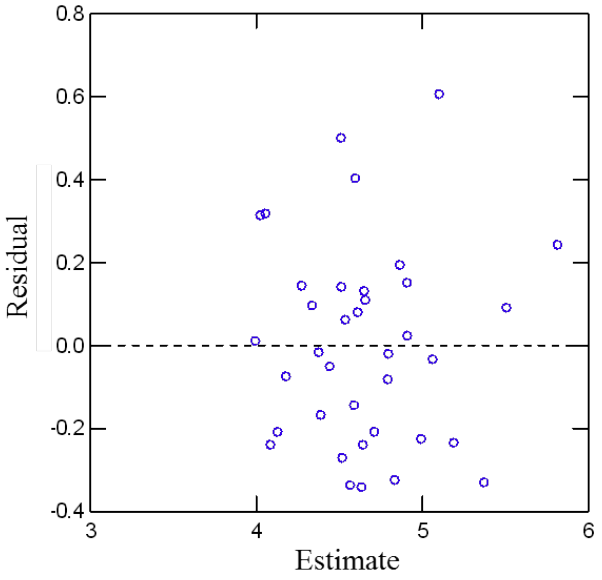
Supplementary Table 1: Values of molecular descriptors for Equation 1.

Comp.	E2M	RDF115m	MATS6v	Hypnotic_80	F10[O-O]	Comp.	E2M	RDF115m	MATS6v	Hypnotic_80	F10[O-O]
1a	0.166	0.000	-0.265	1.000	0.000	**5a**	0.230	0.000	-0.007	1.000	0.000
1b	0.114	0.000	-0.295	1.000	0.000	**5b**	0.516	0.000	-0.022	1.000	0.000
1c	0.077	0.000	-0.746	1.000	0.000	**5c**	0.565	0.000	-0.498	1.000	0.000
1d	0.153	0.000	-0.279	1.000	0.000	**5d**	0.442	0.000	-0.037	1.000	0.000
1e	0.160	0.000	-0.295	1.000	0.000	**5e**	0.280	0.000	-0.022	1.000	0.000
1f	0.149	0.000	0.308	1.000	0.000	**6a**	0.516	0.000	-0.482	1.000	0.000
1g	0.146	0.000	0.276	1.000	0.000	**6b**	1.358	0.000	-0.455	1.000	0.000
2a	0.339	0.000	-0.163	1.000	0.000	**6c**	0.901	0.000	-0.543	0.000	0.000
2b	0.160	2.398	-0.187	1.000	0.000	**6d**	1.098	0.001	-0.222	1.000	0.000
2c	0.164	0.000	-0.355	1.000	0.000	**6e**	1.952	0.013	-0.455	1.000	0.000
2d	0.261	0.311	-0.173	1.000	0.000	**6f**	0.793	0.020	-0.147	1.000	1.000
2e	0.317	0.000	-0.187	1.000	0.000	**7a**	0.297	0.000	-0.361	0.000	0.000
2f	0.297	0.002	0.093	1.000	1.000	**7b**	0.997	0.000	-0.357	0.000	0.000
3a	0.490	0.000	-0.091	1.000	0.000	**7c**	1.007	0.000	-0.422	0.000	0.000
3b	0.326	0.000	-0.116	0.000	0.000	**7d**	1.141	0.000	-0.155	0.000	0.000
3c	0.231	0.000	-0.255	0.000	0.000	**7e**	0.593	0.378	-0.357	0.000	0.000
3d	0.331	0.000	-0.044	0.000	0.000	**7f**	0.321	0.012	-0.11	0.000	1.000
3e	0.364	0.157	-0.116	0.000	0.000	**8a**	0.517	0.258	-0.315	1.000	0.000
3f	0.371	0.063	0.109	1.000	1.000	**8b**	1.356	2.708	-0.313	0.000	0.000
4a	0.331	0.06	-0.196	1.000	0.000	**8c**	1.301	6.556	-0.345	0.000	0.000
4b	0.274	1.568	-0.205	1.000	0.000	**8d**	1.367	1.905	-0.198	0.000	0.000
4c	0.232	1.785	-0.250	1.000	0.000	**8e**	0.893	1.053	-0.313	0.000	0.000
4d	0.290	0.679	-0.164	1.000	0.000	**8f**	0.993	0.416	-0.152	0.000	1.000
4e	0.337	0.118	-0.205	1.000	0.000	**9**	0.246	0.136	0.001	1.000	1.000
4f	0.312	0.958	-0.0480	1.000	1.000	**10**	0.854	0.001	-0.142	1.000	1.000

Supplementary Table 2: Experimental and predicted antigiardial activity of training and validation sets molecules.

Comp	Exp[a]	Pred[b]	Δ	Comp	Exp	Pred	Δ
1a[c]	3.97	5.03	-1.06	**5a**	4.22	5.00	-0.78
1b[c]	4.53	5.02	-0.49	**5b**[c]	4.63	5.11	-0.48
1c	4.77	5.10	-0.33	**5c**	4.96	5.22	-0.26
1d	4.45	5.03	-0.58	**5d**[c]	4.56	5.09	-0.53
1e	4.69	5.04	-0.35	**5e**	4.39	5.02	-0.63
1f	4.01	4.91	-0.90	**6a**	5.71	5.20	0.51
1g	4.34	4.92	-0.58	**6b**	6.06	5.50	0.56
2a	4.29	5.07	-0.78	**6c**	5.03	5.14	-0.11
2b	3.85	4.58	-0.73	**6d**	5.04	5.36	-0.32
2c[c]	4.02	5.05	-1.03	**6e**[c]	6.41	5.71	0.70
2d	5.01	4.99	0.02	**6f**	5.6	5.39	0.21
2e	4.4	5.07	-0.67	**7a**	4.43	4.88	-0.45
2f	4.51	5.17	-0.66	**7b**	4.94	5.14	-0.20
3a[c]	4.36	5.11	-0.75	**7c**[c]	4.54	5.15	-0.61
3b	3.92	4.85	-0.93	**7d**	4.78	5.15	-0.37
3c	4.11	4.84	-0.73	**7e**	4.6	4.92	-0.32
3d	4.66	5.05	-0.39	**7f**	5	5.00	0.00
3e[c]	4.25	4.83	-0.58	**8a**	5.06	5.12	-0.06
3f	5.06	5.18	-0.12	**8b**	4.23	4.77	-0.54
4a	4.78	5.07	-0.29	**8c**	4.37	4.06	0.31
4b	4.36	4.78	-0.42	**8d**[c]	5.14	4.89	0.25
4c	4.42	4.73	-0.31	**8e**	4.5	4.90	-0.40
4d[c]	4.37	4.93	-0.56	**8f**[c]	5.78	5.18	0.60
4e	4.77	5.06	-0.29	**9**	4.25	5.15	-0.90
4f	4.71	5.03	-0.32	**10**[c]	5.54	5.42	0.12

[a]Experimental data in Log(1/IC_{50} μM). [b]Predicted data in Log(1/IC_{50} μM)
[c]Validation set molecules.



Supplementary Figure 1: Plot of residual against measured values.