Supporting Information

In Vivo Active Aldosterone Synthase Inhibitors with Improved Selectivity: Lead Optimization Providing a Series of Pyridine Substituted 3,4-Dihydro-1*H*-quinolin-2-one Derivatives

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Contents

a) NMR spectroscopic data of compounds 1–4, 6–11, 13–26

3-(5,6,7,8-tetrahydronaphthalen-2-yl)pyridine (1). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 1.76 (m, 4H), 2.78 (m, 4H), 7.23 (d, ^{3}J = 8.5 Hz, 1H), 7.56–7.59 (m, 2H), 8.03 (dd, ^{3}J = 7.9 Hz, ^{3}J = 5.7 Hz, 1H), 8.77 (m, 1H), 8.80 (d, ^{3}J = 5.4 Hz, 1H), 9.17 (d, ^{4}J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 22.47, 22.49, 28.5, 28.8, 124.2, 126.9, 127.7, 129.9, 131.0, 137.8, 138.6, 140.0, 140.6, 141.8.

6-Pyridin-3-yl-1,2,3,4-tetrahydronaphthalen-2-ol (2). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.87 (m, 1H), 2.08 (m, 1H), 2.44 (bs, 1H), 2.73 (dd, ^{2}J = 16.4 Hz, ^{3}J = 7.6 Hz, 1H), 2.89 (dd, ^{2}J = 15.1 Hz, ^{3}J = 8.8 Hz, ^{3}J = 6.3 Hz, 1H), 3.03 (m, 1H), 3.12 (dd, ^{2}J = 16.4 Hz, ^{3}J = 4.7 Hz, 1H), 4.21 (m, 1H), 7.17 (d, ^{3}J = 7.9 Hz, 1H), 7.29–7.34 (m, 3H), 7.82 (ddd, ^{3}J = 7.9 Hz, ^{4}J = 2.2 Hz, ^{4}J = 1.6 Hz, 1H), 8.53 (dd, ^{3}J = 4.7 Hz, ^{4}J = 1.9 Hz, 1H), 8.77 (dd, ^{4}J = 2.2 Hz, ^{5}J = 0.6 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 27.0, 31.3, 38.1, 66.8, 123.5, 124.6, 127.2, 139.2, 134.2, 134.6, 135.5, 136.56, 136.59, 148.0.

3-(6-Methoxy-5,6,7,8-tetrahydronaphthalen-2-yl)pyridine (3). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.90 (m, 1H), 2.08 (m, 1H), 2.82–2.87 (m, 2H), 3.01 (dt, ^{2}J = 16.7, ^{3}J = 6.3, 1H), 3.10 (dd, ^{2}J = 16.7, ^{3}J = 5.0, 1H), 3.43 (s, 3H), 3.70 (m, 1H), 7.18 (d, ^{3}J = 7.9 Hz, 1H), 7.30–7.35 (m, 3H), 7.82 (m, 1H), 8.55 (dd, ^{3}J = 4.8, ^{4}J = 1.6, 1H), 8.80 (d, ^{4}J = 1.6 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 26.8, 27.3, 34.8, 55.9, 75.4, 123.4, 124.6, 127.3, 130.2, 134.1, 134.6, 135.5, 136.6, 139.9, 148.2, 148.3.

3-(6-Ethoxy-5,6,7,8-tetrahydronaphthalen-2-yl)pyridine (4). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.24 (t, ^{3}J = 6.9 Hz, 3H), 1.86 (m, 1H), 2.10 (m, 1H), 2.81–2.87 (m, 2H), 3.00 (dt, ^{2}J = 16.7 Hz, ^{3}J = 5.7 Hz, 1H), 3.12 (dd, ^{2}J = 16.4 Hz, ^{3}J = 4.7 Hz, 1H), 3.61 (m, 2H), 3.78 (m, 1H), 7.18 (d, ^{3}J = 7.9 Hz, 1H), 7.29 (s, 1H), 7.31–7.34 (m, 2H), 7.82 (m, 1H), 8.54 (dd, ^{3}J = 4.7 Hz, ^{4}J = 1.6 Hz, 1H), 8.81 (d, ^{4}J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 15.7, 27.3, 28.3, 35.5, 63.5, 73.9, 123.4, 124.5, 127.2, 130.2, 134.1, 135.0, 135.4, 136.6, 137.0, 148.2, 149.3.

6-Pyridin-3-yl-3,4-dihydronaphthalene-2-carbonitrile (6). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.59 (td, ^{3}J = 8.5 Hz, ^{4}J = 1.6 Hz, 2H), 2.98 (t, ^{3}J = 8.5 Hz, 2H), 7.22 (s, 1H), 7.25 (d, ^{3}J = 7.6 Hz, 1H), 7.34–7.38 (m, 2H), 7.44 (dd, ^{3}J = 7.9 Hz, ^{4}J = 1.9 Hz, 1H), 7.86 (m, 1H), 8.60 (dd, ^{3}J = 4.7 Hz, ^{4}J = 1.6 Hz, 1H), 8.82 (d, ^{3}J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 24.7, 26.9, 110.2, 119.5, 123.6, 125.8, 126.7, 128.6, 131.0, 134.2, 135.7, 136.2, 139.6, 141.0, 148.2, 149.0.

4-Methyl-7-pyridin-3-yl-3,4-dihydro-2*H*-1,4-benzoxazine (7). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.92 (s, 3H), 3.31 (t, ^{3}J = 4.4 Hz, 2H), 4.32 (t, ^{3}J = 4.4 Hz, 2H), 6.73 (d, ^{3}J = 8.2 Hz, 1H), 7.02 (d, ^{4}J = 2.2 Hz, 1H), 7.08 (dd, ^{3}J = 8.2 Hz, ^{4}J = 2.2 Hz, 1H), 7.27 (ddd, ^{3}J = 7.9 Hz, ^{3}J = 4.7 Hz, ^{5}J = 0.9 Hz, 1H), 7.78 (ddd, ^{3}J = 7.9 Hz, ^{4}J = 2.2 Hz, ^{4}J = 1.6 Hz, 1H), 8.47 (dd, ^{3}J = 5.9 Hz, ^{4}J = 1.6 Hz, 1H), 8.78

(d, ^4J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 38.6, 49.0, 64.9, 112.7, 114.3, 120.0, 123.4, 127.4, 133.4, 136.3, 136.6, 144.6, 147.4, 147.7.

3-(2,3-Dihydro-1,4-benzodioxin-6-yl)pyridine (8). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 4.29 (s, 4H), 6.95 (d, ^3J = 8.2 Hz), 7.05 (dd, ^3J = 8.2 Hz, ^4J = 2.2 Hz, 1H), 7.09 (d, ^4J = 2.2 Hz, 1H), 7.30 (ddd, ^3J = 7.8 Hz, ^3J = 4.7 Hz, ^5J = 0.9 Hz, 1H), 7.78 (ddd, ^3J = 7.9 Hz, ^4J = 2.1 Hz, ^4J = 1.6 Hz, 1H), 8.52 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1H), 8.78 (d, ^4J = 2.2 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 64.37, 64.43, 115.9, 117.9, 120.1, 123.4, 131.2, 133.9, 136.0, 143.8, 144.0, 147.98, 148.01.

6-Pyridin-3-yl-3,4-dihydronaphthalen-2(1*H*)-one (9). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.58 (t, ^3J = 6.6 Hz, 2H), 3.13 (t, ^3J = 6.6 Hz, 2H), 3.62 (s, 2H), 7.22 (d, ^3J = 7.9 Hz, 1H), 7.34 (ddd, ^3J = 7.9 Hz, ^3J = 5.1 Hz, ^5J = 0.9 Hz, 1H), 7.41–7.44 (m, 2H), 7.85 (ddd, ^3J = 7.9 Hz, ^4J = 2.2 Hz, ^4J = 1.6 Hz, 1H), 8.57 (dd, ^3J = 5.1 Hz, ^4J = 1.6 Hz, 1H), 8.83 (dd, ^4J = 2.2 Hz, ^5J = 0.7 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 28.5, 38.0, 44.7, 123.5, 125.7, 126.3, 129.0, 133.3, 134.2, 136.2, 136.5, 137.5, 148.2, 148.5, 209.9.

5-Pyridin-3-yl-2,3-dihydro-1*H*-inden-1-one (10). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.75 (t, ^3J = 6.0 Hz, 2H), 3.22 (t, ^3J = 6.0 Hz, 2H), 7.40 (ddd, ^3J = 7.9 Hz, ^3J = 4.7 Hz, ^5J = 0.9 Hz, 1H), 7.57 (m, 1H), 7.67 (m, 1H), 7.85 (d, ^3J = 7.9 Hz, 1H), 7.91 (ddd, ^3J = 7.9 Hz, ^4J = 2.5 Hz, ^4J = 1.6 Hz, 1H), 8.64 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1H), 8.81 (d, ^4J = 1.6 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 25.9, 36.5, 123.7, 124.4, 125.3, 126.7, 134.7, 135.8, 136.7, 144.2, 148.5, 149.4, 155.9, 206.3.

6-(5-Methoxypyridin-3-yl)-3,4-dihydronaphthalen-2(1*H*)-one (11). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.60 (t, ^3J = 6.9 Hz, 2H), 3.14 (t, ^3J = 6.9 Hz, 2H), 3.64 (s, 2H), 3.92 (s, 3H), 7.23 (d, ^3J = 7.6 Hz, 1H), 7.53 (dd, ^4J = 2.5 Hz, ^4J = 1.9 Hz, 1H), 7.43 (dd, ^3J = 7.6 Hz, ^4J = 1.9 Hz, 1H), 7.44 (m, 1H), 8.29 (d, ^4J = 2.5 Hz, 1H), 8.45 (d, ^4J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 28.5, 38.1, 44.8, 55.7, 119.1, 125.8, 126.5, 128.9, 133.5, 136.1, 136.4, 136.9, 137.5, 140.6, 155.8, 210.0.

5-Pyridin-3-yl-1,3-dihydro-2*H*-indol-2-one (13). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 3.53 (s, 2H), 6.91 (d, ^3J = 7.9 Hz, 1H), 7.42 (dd, ^3J = 7.9 Hz, ^3J = 4.7 Hz, 1H), 7.52 (d, ^3J = 7.9 Hz, 1H), 7.56 (s, 1H), 7.97 (m, 1H), 8.49 (dd, ^3J = 4.7 Hz, ^4J = 1.3 Hz, 1H), 8.81 (d, ^4J = 2.2 Hz, 1H), 10.50 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 35.8, 109.6, 123.0, 123.8, 126.3, 126.9, 130.2, 133.5, 135.8, 143.9, 147.2, 147.7, 176.3.

1-Methyl-6-pyridin-3-yl-3,4-dihydroquinolin-2(1*H*)-one (14). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.68 (t, ^3J = 7.3 Hz, 2H), 2.97 (t, ^3J = 7.3 Hz, 2H), 3.38 (s, 3H), 7.06 (d, ^3J = 8.2 Hz, 1H), 7.33 (ddd, ^3J = 7.9 Hz, ^3J = 4.8 Hz, ^5J = 0.6 Hz, 1H), 7.37 (d, ^4J = 2.1 Hz, 1H), 7.45 (dd, ^3J = 8.3 Hz, ^4J = 2.2 Hz, 1H), 7.82 (ddd, ^3J = 7.9 Hz, ^4J = 2.2 Hz, ^4J = 1.6 Hz, 1H), 8.55 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1H), 8.81

(d, ^4J = 2.2 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 25.5, 29.6, 31.6, 115.2, 123.5, 126.0, 126.3, 126.9, 132.2, 133.9, 135.7, 140.6, 147.9, 148.3, 170.2.

1-Ethyl-6-pyridin-3-yl-3,4-dihydroquinolin-2(1*H*)-one (15). ^{1}H-NMR (500 MHz, $CDCl_3$): δ =1.30 (t, ^3J = 7.3 Hz, 3H), 2.70 (t, ^3J = 7.6 Hz, 2H), 2.99 (t, ^3J = 7.6 Hz, 2H), 4.04 (q, ^3J = 7.3 Hz, 2H), 7.13 (d, ^3J = 8.2 Hz, 1H), 7.37 (ddd, ^3J = 7.9 Hz, ^3J = 4.7 Hz, ^5J = 0.6 Hz, 1H), 7.41 (d, ^4J = 2.2 Hz, 1H), 7.48 (dd, ^3J = 8.5 Hz, ^4J = 2.2 Hz, 1H), 7.85 (ddd, ^3J = 7.9 Hz, ^4J = 2.2 Hz, ^4J = 1.6 Hz, 1H), 8.58 (dd, ^3J = 5.0 Hz, ^4J = 1.6 Hz, 1H), 8.84 (dd, ^4J = 2.5 Hz, ^5J = 0.6 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.8, 25.7, 31.8, 37.4, 115.2, 123.6, 126.1, 126.7, 127.3, 132.2, 133.9, 135.7, 139.6, 148.0, 148.4, 169.7.

1-(1-Methylethyl)-6-pyridin-3-yl-3,4-dihydroquinolin-2(1*H*)-one (16). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.54 (d, ^3J = 6.9 Hz, 6H), 2.61 (t, ^3J = 7.3 Hz, 2H), 2.80 (t, ^3J = 7.3 Hz, 2H), 4.73 (sep, ^3J = 6.9 Hz, 1H), 7.23 (d, ^3J = 8.5 Hz, 1H), 7.35 (ddd, ^3J = 7.9 Hz, ^3J = 5.0 Hz, ^5J = 0.9 Hz, 1H), 7.38 (d, ^4J = 2.2 Hz, 1H), 7.43 (dd, ^3J = 8.5 Hz, ^4J = 2.2 Hz, 1H), 7.83 (ddd, ^3J = 7.9 Hz, ^4J = 2.2 Hz, ^4J = 1.6 Hz, 1H), 8.56 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1H), 8.84 (dd, ^4J = 2.2 Hz, ^5J = 0.6 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 20.2, 26.0, 33.4, 48.5, 117.0, 123.6, 125.7, 126.4, 129.2, 132.3, 133.9, 135.8, 140.4, 148.0, 148.4, 171.1.

8-Chloro-6-pyridin-3-yl-3,4-dihydroquinolin-2(1*H*)-one (17). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.54 (m, 2H), 3.01 (m, 2H), 7.45 (ddd, ^3J = 8.0 Hz, ^3J = 4.8 Hz, ^5J = 0.8 Hz, 1H), 7.60 (d, ^4J = 2.0 Hz, 1H), 7.69 (d, ^4J = 2.0 Hz, 1H), 8.06 (ddd, ^3J = 8.0 Hz, ^4J = 2.5 Hz, ^4J = 1.5 Hz, 1H), 8.53 (dd, ^3J = 4.8 Hz, ^4J = 1.5 Hz, 1H), 8.88 (dd, ^4J = 2.5 Hz, ^5J = 0.8 Hz, 1H), 9.64 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 25.3, 30.3, 119.7, 123.8, 125.0, 125.6, 127.4, 131.7, 133.7, 133.8, 134.8, 147.3, 152.4, 170.3.

8-Nitro-6-pyridin-3-yl-3,4-dihydroquinolin-2(1*H*)-one (18). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.64 (t, ^3J = 7.9 Hz, 2H), 3.13 (t, ^3J = 7.9 Hz, 2H), 7.50 (ddd, ^3J = 8.2 Hz, ^3J = 4.9 Hz, ^5J = 0.9 Hz, 1H), 8.09 (d, ^4J = 2.1 Hz, 1H), 8.15 (ddd, ^3J = 7.9 Hz, ^4J = 2.4 Hz, ^4J = 1.5 Hz, 1H), 8.29 (d, ^4J = 2.1 Hz, 1H), 8.59 (dd, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1H), 8.95 (dd, ^4J = 2.4 Hz, ^5J = 0.6 Hz, 1H), 9.88 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 25.0, 29.3, 121.4, 123.9, 128.5, 130.6, 132.3, 133.1, 133.2, 134.0, 135.0, 147.4, 149.0, 170.0.

6-(5-Methoxypyridin-3-yl)-3,4-dihydroquinolin-2(1*H*)-one (19). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.50 (t, ^3J = 7.6 Hz, 2H), 2.96 (t, ^3J = 7.9 Hz, 2H), 3.89 (s, 3H), 6.95 (d, ^3J = 8.2 Hz, 1H), 7.53 (dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, 1H), 7.55 (dd, ^4J = 2.8 Hz, ^4J = 1.9 Hz, 1H), 7.59 (d, ^4J = 1.6 Hz, 1H), 8.22 (d, ^4J = 2.5 Hz, 1H), 8.44 (d, ^4J = 1.6 Hz, 1H), 10.20 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 24.8, 30.3, 55.6, 115.5, 117.7, 124.3, 125.8, 126.4, 130.4, 135.8, 136.1, 138.5, 139.4, 155.6, 170.2.

6-(5-methoxypyridin-3-yl)-1-methyl-3,4-dihydroquinolin-2(1*H*)-one (20). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.69 (t, ^{3}J = 7.9 Hz, 2H), 2.98 (t, ^{3}J = 7.9 Hz, 2H), 3.39 (s, 3H), 3.91 (s, 3H), 7.06 (d, ^{3}J = 8.2 Hz, 1H), 7.33 (dd, ^{4}J = 2.8 Hz, ^{4}J = 1.9 Hz, 1H), 7.37 (d, ^{4}J = 2.2 Hz, 1H), 7.46 (dd, ^{3}J = 8.5 Hz, ^{4}J = 2.2 Hz, 1H), 8.27 (d, ^{4}J = 2.8 Hz, 1H), 8.43 (d, ^{4}J = 1.9 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 25.5, 29.6, 31.6, 55.7, 115.2, 118.7, 126.2, 126.5, 126.9, 132.1, 135.8, 136.5, 140.4, 140.7, 155.8, 170.3.

6-Isoquinolin-4-yl-3,4-dihydroquinolin-2(1*H*)-one (21). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.51 (t, ^{3}J = 7.3 Hz, 2H), 2.96 (t, ^{3}J = 7.3 Hz, 2H), 7.02 (d, ^{3}J = 8.2 Hz, 1H), 7.29 (dd, ^{4}J = 8.2 Hz, ^{4}J = 1.9, 1H), 7.34 (s, 1H) 7.70 (m, 1H), 7.76 (m, 1H) 7.88 (d, ^{3}J = 8.5 Hz, 1H), 8.17 (d, ^{3}J = 8.2 Hz, 1H), 8.39 (s, 1H), 9.29 (s, 1H), 10.26 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 24.8, 30.3, 115.2, 124.0, 124.2, 127.4, 128.0, 128.7, 129.2, 129.9, 130.9, 132.2, 133.3, 138.2, 142.3, 151.6, 170.3.

6-Isoquinolin-4-yl-1-methyl-3,4-dihydroquinolin-2(1*H*)-one (22). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.73 (t, ^{3}J = 7.6 Hz, 2H), 2.99 (t, ^{3}J = 7.7 Hz, 2H), 3.43 (s, 3H), 7.12 (d, ^{3}J = 8.2 Hz, 1H), 7.32 (d, ^{4}J = 1.9, 1H), 7.40 (dd, ^{3}J = 8.2 Hz, ^{4}J = 2.2 Hz, 1H), 7.63 (m, 1 H), 7.68 (m, 1 H), 7.91 (d, ^{3}J = 7.9 Hz, 1H), 8.03 (d, ^{3}J = 7.6 Hz, 1H), 8.46 (s, 1 H), 9.24 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 25.4, 29.6, 31.6, 114.8, 124.6, 126.5, 127.2, 128.0, 128.4, 129.1, 129.3, 130.6, 131.5, 132.4, 134.2, 140.4, 142.8, 152.0, 170.4.

6-Pyrimidin-5-yl-3,4-dihydroquinolin-2(1*H*)-one (23). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.50 (t, ^{3}J = 7.6 Hz, 2H), 2.95 (t, ^{3}J = 7.6 Hz, 2H), 6.98 (d, ^{3}J = 8.2 Hz, 1H), 7.59 (dd, ^{3}J = 8.2 Hz, 1H), 7.66 (s, 1H), 9.08 (s, 2H), 9.11 (s, 1H), 10.22 (s, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 24.8, 30.2, 115.7, 124.5, 125.6, 126.2, 127.1, 132.9, 139.1, 154.0, 156.6, 170.2.

6-Pyridin-3-yl-3,4-dihydroquinoline-2(1*H*)-thione (24). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.87 (m, 2H), 2.97 (m, 2H), 7.20 (d, ^{3}J = 8.2 Hz, 1H), 7.46 (dd, ^{3}J = 7.9 Hz, ^{3}J = 4.7 Hz, 1H), 7.59 (dd, ^{3}J = 8.5 Hz, ^{4}J = 1.9 Hz, 1H), 7.62 (s, 1H), 8.04 (m, 1H), 8.53 (dd, ^{3}J = 4.7 Hz, ^{4}J = 1.6 Hz, 1H), 8.87 (d, ^{4}J = 2.2 Hz, 1H), 12.30 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 23.9, 116.6, 123.8, 125.9, 126.1, 126.5, 132.7, 133.7, 135.0, 136.8, 147.4, 148.2, 199.6.

8-Chloro-6-pyridin-3-yl-3,4-dihydroquinoline-2(1*H*)-thione (25). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 2.91 (m, 2H), 3.00 (m, 2H), 7.46 (ddd, ^{3}J = 7.9 Hz, ^{3}J = 4.9 Hz, ^{5}J = 0.9 Hz, 1H), 7.66 (d, ^{4}J = 2.1 Hz, 1H), 7.76 (d, ^{4}J = 2.0 Hz, 1H), 8.09 (ddd, ^{3}J = 7.9 Hz, ^{4}J = 2.4 Hz, ^{4}J = 1.5 Hz, 1H), 8.56 (dd, ^{3}J = 4.9 Hz, ^{4}J = 1.5 Hz, 1H), 8.91 (dd, ^{4}J = 2.4 Hz, ^{5}J = 0.9 Hz, 1H), 11.31 (bs, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 25.6, 39.4, 120.5, 123.8, 125.2, 126.0, 129.7, 133.4, 133.6, 133.8, 133.9, 147.5, 148.8, 201.5.

7-Pyridin-3-yl-2*H*-1,4-benzothiazin-3(4*H*)-one (26). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 3.51 (s, 2H), 7.07 (d, ^{3}J = 8.5 Hz, 1H), 7.44 (ddd, ^{3}J = 7.9 Hz, ^{3}J = 4.9 Hz, ^{5}J = 0.6 Hz, 1H), 7.54 (dd, ^{3}J = 8.2

Hz, ^{4}J = 2.1 Hz, 1H), 7.70 (d, ^{4}J = 2.1 Hz, 1H), 8.03 (ddd, ^{3}J = 7.9 Hz, ^{4}J = 2.4 Hz, ^{4}J = 1.5 Hz, 1H), 8.52 (dd, ^{3}J = 4.9 Hz, ^{4}J = 1.5 Hz, 1H), 8.86 (dd, ^{4}J = 2.4 Hz, ^{5}J = 0.6 Hz, 1H), 10.68 (s, 1H). ^{13}C-NMR (125 MHz, DMSO-d_6): δ = 28.7, 117.6, 120.0, 123.8, 131.6, 132.3, 133.1, 133.7, 134.5, 137.3, 147.3, 148.3, 165.1.

b) Synthesis and spectroscopic data of compounds 1a, 5a, 5b, 6a, 14a–16a

5,6,7,8-Tetrahydronaphthalen-2-yltrifluoromethanesulfonate (1a). 5,6,7,8-Tetrahydronaphthalen-2-ol (593 mg, 4.0 mmol), *N*-Phenylbis(trifluoromethansulfonimide) (1,57 g, 4.4 mmol) and K_2CO_3 (830 mg, 6.0 mmol) in 6.0 mL THF were mixed in a microwave tube and immediately heated to 120 °C for 8 minutes using microwave irradiation (initial irradiation power 100 W). After complete conversion (TLC control) and cooling to room temperature 20 mL of distilled water were added and the reaction mixture was extracted four times with 15 mL of Et_2O. After washing the combined organic fractions with water (twice) and brine and drying over $MgSO_4$ the combined organic solvent fractions were filtered through a silica pad to remove polar impurities. After evaporation of the solvent 1.04 g (3.71 mmol, 93 %) crude **1a** was obtained as a dark yellow oil, which was used in the next step without further purification and characterization.

6-Bromo-1,2,3,4-tetrahydronaphthalene-2-carbonitrile (5a). To a solution of **5b** (468 mg, 2.00 mmol) in 5 mL dry ethanol was added sodium borohydride (283 mg, 10.0 mmol) and the mixture was heated at reflux for 10 h. After dilution with 20 ml diethyl ether, the mixture was quenched with 50 mL of water. After three times extraction with diethyl ether, the organics were washed with water and brine, dried over $MgSO_4$ and evaporated to dryness. Purification by crystallization from ethanol and flash chromatography on silica gel (petroleum ether/ethyl acetate, 7/3, R_f = 0.33) afforded **5a** as colorless needles (100 mg, 0.42 mmol, 21 %). ^{1}H-NMR (500 MHz, DMSO-d_6): δ = 1.95 (m, 1H), 2.03 (m, 1H), 2.82 (m, 2H), 2.90 (dd, ^2J = 16.7 Hz, ^3J = 7.3 Hz, 1H), 3.03 (dd, ^2J = 16.7 Hz, ^3J = 5.4 Hz, 1H), 3.27 (m, 1H), 7.07 (d, ^3J = 8.2 Hz, 1H), 7.30 (dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, 1H), 7.33 (d, ^4J = 1.8 Hz, 1H).

6-Bromo-3,4-dihydronaphthalene-2-carbonitrile (5b). A mixture of 6-bromo-2-tetralone (1.50 g, 6.66 mmol), trimethylsilyl cyanide (727 mg, 7.33 mmol) and zinc iodide (51 mg, 0.16 mmol) in 15 mL dry toluene was stirred for 8 h at room temperature. Pyridine (10 mL) was added and phosphorous oxychloride (3 mL) was then added dropwise. The mixture was refluxed for 6 h, stirred for additional 12 h at room temperature and then treated carefully with 300 mL of 10 % HCl. After three times extraction with ethyl acetate, the organics were washed with water and brine, dried over $MgSO_4$ and evaporated to dryness. Purification by flash chromatography on silica gel (petroleum ether/ethyl acetate, 7/3, R_f = 0.57) afforded **5b** as a pale yellow solid (1.09 g, 4.66 mmol, 70 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.52 (d, ^3J = 8.5 Hz, 2H), 2.88 (d, ^3J = 8.5 Hz, 2H), 7.00 (d, ^3J = 7.9 Hz, 1H), 7.12 (s, 1H), 7.31 (s, 1H), 7.35 (dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, 1H).

6-Pyridin-3-yl-3,4-dihydronaphthalen-2-yl trifluoromethanesulfonate (6a). A solution of potassium bis(trimethylsilyl)amide (7.3 mL, 3.67 mmol, 0.5 M in toluene) was added dropwise to a

solution of **9** (630 mg, 2.82 mmol) and *N*-phenyltrifluoromethanesulfonimide (1.31 g, 3.67 mmol) in 20 mL dry THF at -78 °C under an atmosphere of nitrogen. After stirring for 1 h at -78 °C the mixture was quenched with water and extracted three times with diethyl ether. The combined organic extracts were washed with water and brine, dried over $MgSO_4$ and evaporated to dryness. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, 1/1, R_f = 0.31) to afford **6a** as a pale yellow oil (562 mg, 1.58 mmol, 56 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.74 (t, ^3J = 8.5 Hz, 2H), 3.13 (t, ^3J = 8.5 Hz, 2H), 6.53 (s, 1H), 7.18 (d, ^3J = 7.6 Hz, 1H), 7.34–7.37 (m, 2H), 7.41 (dd, ^3J = 7.6 Hz, ^4J = 1.9 Hz, 1H), 7.84 (ddd, ^3J = 7.9 Hz, ^4J = 2.2 Hz, ^4J = 1.6 Hz, 1H), 8.58 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1H), 8.82 (d, ^4J = 1.9 Hz, 1H).

6-Bromo-1-methyl-3,4-dihydroquinolin-2(1*H*)-one (14a). To a solution of **12a** (339 mg, 1.50 mmol) in 10 mL dry DMF was added KO*t*Bu (336 mg, 3.0 mmol) and the mixture was stirred for 1 h at room temperature. Methyl iodide (426 mg, 3.0 mmol) in 5 mL DMF was added via canula and stirring was continued for 12 h. The reaction was quenched by addition of 100 mL of 1 N HCl and the mixture was extracted three times with ethyl acetate. The combined organic extracts were washed with water and brine, dried over $MgSO_4$ and evaporated in vacuo. The crude product was purified by flash chromatography on silica (petroleum ether/ethyl acetate, 7/3, R_f = 0.21) to afford **14a** as a colorless solid (281 mg, 1.17 mmol, 78 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.62 (t, ^3J = 7.9 Hz, 2H), 2.86 (t, ^3J = 7.5 Hz, 2H), 3.31 (s, 3H), 6.82 (d, ^3J = 8.5 Hz, 1H), 7.27 (d, ^4J = 2.2 Hz, 1H), 7.33 (dd, ^3J = 8.5 Hz, ^4J = 2.2 Hz, 1H).

6-Bromo-1-ethyl-3,4-dihydroquinolin-2(1*H*)-one (15a) was obtained as described for **14a** starting from **12a** (750 mg, 3.32 mmol), KO*t*Bu (804 mg, 6.64 mmol) and ethyl bromide (724 mg, 6.64 mmol) after flash chromatography on silica gel (petroleum ether/ethyl acetate, 4/1, R_f = 0.19) as a colorless solid (583 mg, 2.29 mmol, 59 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 6.9 Hz, 3H), 2.61 (t, ^3J = 7.6 Hz, 2H), 2.85 (t, ^3J = 7.9 Hz, 2H), 3.94 (q, ^3J = 6.9 Hz, 2H), 6.86 (d, ^3J = 8.8 Hz, 1H), 7.28 (d, ^4J = 2.5 Hz, 1H), 7.33 (dd, ^3J = 8.8 Hz, ^4J = 2.5 Hz, 1H).

6-Bromo-1-(1-methylethyl)-3,4-dihydroquinolin-2(1*H*)-one (16a) was prepared as described for **14a** starting from **12a** (750 mg, 3.32 mmol), KO*t*Bu (804 mg, 6.64 mmol) and isopropyl bromide (817 mg, 6.64 mmol) and additionally heating at 100 °C. Flash chromatography on silica gel (petroleum ether/ethyl acetate, 4/1, R_f = 0.21) afforded **16a** as a pale yellow solid (347 mg, 1.29 mmol, 33 %). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.49 (d, ^3J = 6.9 Hz, 6H), 2.53 (t, ^3J = 7.3 Hz, 2H), 2.78 (t, ^3J = 7.6 Hz, 2H), 4.64 (sep, ^3J = 6.9 Hz, 1H), 6.98 (d, ^3J = 8.8 Hz, 1H), 7.27 (d, ^4J = 2.2 Hz, 1H), 7.30 (dd, ^3J = 8.5 Hz, ^4J = 2.2 Hz, 1H).

c) Elemental analysis results of compounds 1–26

compound	CHN calcd			CHN found		
	C	H	N	C	H	N
1	73.31	6.56	5.70	73.24	6.58	5.85
2	79.38	6.74	6.17	79.50	6.38	6.28
3	67.12	6.75	4.89	66.88	6.61	4.85
4	68.40	7.08	4.69	68.18	7.05	4.76
5	81.43	6.06	11.87	81.30	6.20	11.78
6	82.73	5.21	12.06	82.61	5.31	11.74
7	74.31	6.24	12.38	74.18	6.54	12.10
8	73.23	5.20	6.57	73.15	5.45	6.54
9	67.56	5.58	5.52	67.34	5.26	5.21
10	79.72	5.34	6.64	79.82	5.67	6.74
11	75.87	5.97	5.53	75.67	6.17	5.81
12	74.42	5.43	12.40	74.45	5.81	12.26
13	72.51	4.95	13.01	72.83	4.86	12.88
14	75.08	5.96	11.68	75.04	6.16	11.60
15	75.65	6.42	11.03	75.82	6.40	10.67
16	76.66	6.81	10.52	76.48	6.88	10.15
17	64.57	4.34	10.76	64.73	4.54	10.40
18	62.45	4.12	15.61	62.48	4.11	15.46
19	70.85	5.55	11.02	70.85	5.66	10.64
20	71.17	6.04	10.37	71.41	5.89	10.23
21*	78.32	5.18	10.15	78.61	5.60	9.90
22	79.14	5.59	9.72	79.23	5.24	9.35
23	68.29	5.01	18.32	68.61	4.85	18.01
24	69.97	5.03	11.66	69.60	5.03	11.54
25	61.20	4.04	10.20	61.43	3.92	10.24
26	63.55	4.26	11.40	63.82	4.12	11.12

* HPLC/MS performed for purity: The Surveyor-LC-system consisted of a pump, an autosampler, and a PDA detector. Mass spectrometry was performed on a TSQ Quantum (Thermo Electron Corporation, Dreieich, Germany). The triple quadrupole mass spectrometer was equipped with an electrospray interface (ESI). In some cases, ionization was accomplished by APCI. The system was operated by the standard software Xcalibur. A RP18 100-3 column (Macherey-Nagel GmbH, Duehren, Germany) was used as stationary phase. All solvents were HPLC grade. The HPLC method used for the purity determination started with a 16 min gradient from 3% acetonitrile in water containing 1 ‰ TFA to 100 % acetonitrile containing 1 ‰ TFA. The injection volume was 10 µL and flow rate was set to 350 µL/min. MS analysis was carried out at a spray voltage of 3800 V, a capillary temperature of 350 °C and a source CID of 10 V. Spectra were acquired in positive ionization mode from 100 to 1000 m/z and full scan UV-mode. Data of compound **21**: R_t = 3.63 min, *m/z* = 275.04, purity > 98%.