



## Supporting Information

for

### **One-pot multicomponent green Hantzsch synthesis of 1,2-dihydropyridine derivatives with antiproliferative activity**

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## **Analytical data of the products**

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Diethyl 4,6-dimethyl-2-phenyl-1,2-dihydropyridine-3,5-dicarboxylate (**5a**) [1,2].  $C_{19}H_{23}NO_4$ . Yellow solid. M.P.: 145 °C. IR (KBr,  $cm^{-1}$ ): 3429 (m), 3327 (w), 3018 (s), 2939 (m), 2899 (m), 1685 (s), 1701 (s), 1651 (m), 1444 (m), 1371 (s), 1222 (s).  $^1H$  NMR (500 MHz, Chloroform-*d*)  $\delta$  ppm = 7.37 – 7.19 (m, 5H), 5.63 (d,  $J = 4.0$  Hz, 1H), 5.27 (s, 1H), 4.31 – 4.06 (m, 4H), 2.41 (s, 3H), 2.25 (s, 3H), 1.33 (t,  $J = 7.1$  Hz, 3H), 1.24 (t,  $J = 7.0$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ , 298 K)  $\delta$  (ppm) = 167.85, 166.88, 154.23, 146.31, 143.27, 128.59, 127.77, 126.40, 111.09, 103.91, 59.90, 59.64, 55.12, 21.31, 19.52, 14.36, 14.25. MS (ES+):  $m/z = 330.25$  (M+1), 329.23 (M), 328.21, 315.22, 314.16, 298.20, 252.14, 224.14, 196.12, 178.05, 150.09, 115.04, 77.03.

Diethyl 2-(2-hydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5b**) [3].  $C_{19}H_{23}NO_5$ . Yellow solid. M.P.: 91 °C. IR (KBr,  $cm^{-1}$ ): 3333 (w, br), 3014 (w), 2958 (w), 1634 (m), 1612 (m), 1488 (m), 1215 (s), 668 (m).  $^1H$  NMR (500 MHz, Chloroform-*d*)  $\delta$  (ppm) = 8.62 (dd,  $J = 7.9, 1.7$  Hz, 1H), 7.57 (ddd,  $J = 8.3, 7.2, 1.7$  Hz, 1H), 7.41 – 7.31 (m, 2H), 4.49 (p,  $J = 7.1$  Hz, 2H), 4.11 – 4.06 (m, 4H), 2.81 (s, 3H), 2.69 (s, 3H), 1.44 (t,  $J = 7.2$  Hz, 3H), 1.15 (t,  $J = 7.1$  Hz, 3H).  $^{13}C$  NMR (126 MHz, Acetone)  $\delta$  (ppm) = 168.41, 161.06, 160.24, 153.76, 152.96, 150.37, 133.44, 126.22, 125.39, 119.95, 117.37, 115.01, 62.76, 58.86, 53.92, 23.89, 19.47, 14.49, 14.48. MS (ES+):  $m/z = 345.23$  (M), 297.09, 268.07, 248.0, 225.13, 152.09, 139.07, 126.06, 115.07, 77.05.

Diethyl 2-(2,4-dihydroxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5c**).  $C_{19}H_{23}NO_6$ . Yellow solid. M.P.: 118 °C. IR (KBr,  $cm^{-1}$ ): 3335 (m, br), 3014 (w), 2959 (w), 1636 (m), 1614 (m), 1488 (m), 1215 (s), 669 (m).  $^1H$  NMR (500 MHz, Chloroform-*d*)  $\delta$  (ppm) = 8.49 (d,  $J = 8.7$  Hz, 1H), 6.88 (dd,  $J = 8.7, 2.4$  Hz, 2H), 6.83

(d,  $J = 2.4$  Hz, 1H), 4.50 (q,  $J = 7.1$  Hz, 4H), 4.29 – 4.18 (m, 2H), 2.80 (s, 3H), 2.68 (s, 3H), 1.46 (t,  $J = 7.1$  Hz, 6H), 1.37 – 1.27 (m, 1H), 1.30 – 1.24 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 171.63, 167.50, 166.09, 153.62, 148.74, 136.76, 134.42, 132.95, 129.54, 127.45, 107.80, 104.15, 60.05, 59.65, 51.22, 21.10, 19.21, 14.45, 14.31. MS (ES+):  $m/z = 361.46$ , (M), 359.35, 356.91.

Diethyl 2-(2,4-dichlorophenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5d**).  $\text{C}_{19}\text{H}_{21}\text{Cl}_2\text{NO}_4$ . Yellow solid. M.P.: 82-84 °C IR (KBr,  $\text{cm}^{-1}$ ): 3018 (w) 2956 (w), 2357(w), 2328 (m), 1606 (m), 1219 (m), 771 (s), 667 (m).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  (ppm) = 7.41 (d,  $J = 2.1$  Hz, 1H), 7.28 – 7.19 (m, 2H), 5.96 (d,  $J = 4.2$  Hz, 1H), 5.56 (d,  $J = 4.2$  Hz, 1H), 4.30 – 4.04 (m, 4H), 2.52 (s, 3H), 2.15 (s, 3H), 1.33 (t,  $J = 7.1$  Hz, 3H), 1.16 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 171.72, 167.48, 166.09, 153.83, 148.71, 136.71, 134.31, 132.85, 129.53, 127.45, 107.81, 104.10, 60.00, 59.75, 51.22, 21.16, 19.31, 14.36, 14.21. MS (ES+):  $m/z = 398.3$ , 397.10 (M-1), 368.03, 352.05, 252.13, 224.11, 196.07.

Diethyl 2-(3-methoxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5e**) [2].  $\text{C}_{20}\text{H}_{25}\text{NO}_5$  Yellow solid. M.P.: 119-121 °C. IR (KBr,  $\text{cm}^{-1}$ ): 3333 (w, br), 3014 (w), 2958 (w), 1633 (m), 1612 (m), 1489 (m), 1215 (s), 667 (m).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  (ppm)= 7.23 (t,  $J = 7.8$  Hz, 1H), 6.94 – 6.88 (m, 2H), 6.81 (ddd,  $J = 8.2, 2.6, 1.0$  Hz, 1H), 5.61 (d,  $J = 4.1$  Hz, 1H), 5.29 (d,  $J = 3.8$  Hz, 1H), 4.24 (dq,  $J = 10.8, 7.1$  Hz, 1H), 4.17 (dq,  $J = 7.2, 3.4$  Hz, 3H), 3.79 (s, 3H), 2.41 (s, 3H), 2.25 (s, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H), 1.25 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  (ppm) = 14.45, 14.48, 19.63, 21.33, 55.12, 55.24, 59.74, 60.05, 103.93, 110.7,

112.24, 113.2, 118.81, 129.72, 144.92, 146.26, 154.23, 159.88, 167.00, 167.95. MS (ES+):  $m/z = 359.73, 355.15, 252.17, 224.13, 196.11, 178.08$ .

Diethyl 2-(2-methoxyphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5f**) [2].  $C_{20}H_{25}NO_5$  Yellow solid. M.P.: 124 °C. IR (KBr,  $cm^{-1}$ ): 3427 (m), 3325 (w), 3018 (s), 2981(m), 1681 (s), 1648 (s), 1498 (m), 1215 (s), 750 (s).  $^1H$  NMR (500 MHz,  $CDCl_3$ , 298 K)  $\delta$  (ppm) = 7.28 - 7.23 (m, 1H), 7.18 (dd,  $J = 1.7, 7.5$  Hz, 1H), 6.94 - 6.89 (m, 2H), 5.94 (d,  $J = 3.8$  Hz, 1H), 5.73 (br s, 1H), 4.25 - 4.05 (m, 4H), 3.93 (s, 3H), 2.50 (s, 3H), 2.14 (s, 3H), 1.31 (t,  $J = 7.1$  Hz, 3H), 1.19 (t,  $J = 7.1$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  (ppm) = 167.81, 166.90, 156.68, 154.99, 143.86, 129.01, 128.77, 128.01, 120.55, 110.36, 107.8, -102.87, 59.74, 59.39, 55.45, 49.42, 21.51, 19.65, 14.37, 14.28. MS (ES+):  $m/z = 359.23, 330.16, 252.13, 224.13, 196.08, 178.07, 150.09$ .

Diethyl 2-(4-methylphenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5g**) [2].  $C_{20}H_{25}NO_4$  Yellow solid. M.P.: 108 °C. IR (KBr,  $cm^{-1}$ ): 3333 (w, br), 3014 (w), 2958 (w), 1633 (m), 1612 (m), 1489 (m), 1215 (s), 667 (m).  $^1H$  NMR (500 MHz,  $CDCl_3$ , 298 K)  $\delta$  (ppm) = 7.14-7.16 (m, 2H), 6.66-6.63, (m, 2H), 5.55 (s, 1H), 4.17-4.07 (m, 4H), 2.82 (s, 1H), 2.4 (s, 3H), 2.25 (s, 3H) 2.07 (s, 3H), 1.27 (t,  $J = 7.0$  Hz, 3H), 1.21 (t,  $J = 7.0$  Hz, 3H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  (ppm) = 167.89, 166.94, 154.18, 145.95, 140.42, 137.45, 129.25, 129.13, 126.36, 110.76, 103.46, 59.86, 59.59, 54.82, 21.33, 21.10, 19.53, 14.36, 14.30. MS (ES+):  $m/z = 343.24$  (M), 314.20, 270.20, 252.17, 224.13, 196.11, 178.08.

Diethyl 2-(4-dimethylaminophenyl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5h**).  $C_{21}H_{28}N_2O_4$  Yellow solid. M.P.: 128 °C. IR (KBr,  $cm^{-1}$ ): 3018 (w), 2954 (w), 2357(w), 2325 (m), 1603 (m), 1219 (m), 772 (s), 665 (m).  $^1H$  NMR (500 MHz,  $CDCl_3$ , 298 K)  $\delta$  (ppm) = 7.22 (d,  $J$  = 8.5 Hz, 2H), 6.67 (d,  $J$  = 7.9 Hz, 2H), 5.50 (d,  $J$  = 4.5 Hz, 1H), 5.23 (br s, 1H), 4.27 - 4.10 (m, 4H), 2.94 (s, 6H), 2.40 (s, 3H), 2.22 (s, 3H), 1.33 (t,  $J$ =7.03 Hz, 3 H), 1.23 (t,  $J$ =7.09 Hz, 3 H).  $^{13}C$  NMR (126 MHz,  $CDCl_3$ )  $\delta$  (ppm) = 168.13, 167.15, 154.27, 150.33, 145.54, 131.73, 127.57, 112.53, 111.24, 103.08, 59.87, 59.62, 54.84, 40.64, 21.55, 19.68, 14.50, 14.42. MS (ES+):  $m/z$  = 372.46 (M), 357.23, 299.22, 271.20, 253.18, 224.15, 196.11, 121.13, 105.08, 91.07.

Diethyl 4,6-dimethyl-2-(naphthalen-1-yl)-1,2-dihydropyridine-3,5-dicarboxylate (**5i**).  $C_{23}H_{25}NO_4$ . M.P.: 138-139 °C. IR (KBr  $cm^{-1}$ ): 3432, (m), 3332 (m), 3018 (s), 2872 (m), 1672 (m), 1615 (m), 1215 (s), 757 (s).  $^1H$  NMR (500 MHz, CHLOROFORM- $d$ )  $\delta$  (ppm) = 8.21 (d,  $J$ =8.4 Hz, 1 H), 7.92 (d,  $J$ =8.1 Hz, 1 H), 7.81 (d,  $J$ =8.1 Hz, 1 H), 7.45 - 7.67 (m, 4 H), 6.52 (d,  $J$ =3.5 Hz, 1 H), 5.21 (br s, 1 H), 4.14 - 4.30 (m, 2 H), 4.02 (qq,  $J$ =10.7, 7.11 Hz, 2 H), 2.52 - 2.57 (m, 3 H), 2.07 (s, 3 H), 1.35 (t,  $J$ =7.2 Hz, 3 H), 1.04 (t,  $J$ =7.1 Hz, 3 H).  $^{13}C$  NMR (126 MHz, Acetone)  $\delta$  (ppm) = 168.04, 167.93, 157.36, 155.73, 147.93, 138.66, 135.29, 132.62, 129.69, 128.96, 127.01, 126.91, 125.76, 124.27, 109.71, 103.01, 62.54, 59.77, 51.33, 23.18, 20.83, 14.82, 13.61. MS (ES+):  $m/z$ = 379.24, 350.19, 306.18, 278.17, 252.14, 196.06, 178.10, 128.11, 107.11, 77.04.

Diethyl 2-(benzo[d][1,3]dioxol-4-yl)-4,6-dimethyl-1,2-dihydropyridine-3,5-dicarboxylate (**5j**).  $C_{20}H_{23}NO_6$ . M.P.: 142 °C. IR (KBr,  $cm^{-1}$ ): 3429 (m), 3327 (w), 3018 (s), 2981(m), 2899 (m), 1683 (s), 1652 (s), 1502 (m), 1215 (s), 752 (s), 665 (m).  $^1H$  NMR (500 MHz,  $DMSO-d_6$ )  $\delta$  (ppm) = 8.58 (d,  $J$  = 4.6 Hz, 1H), 6.83 (d,  $J$  = 8.0 Hz,

1H), 6.74 (d,  $J = 1.8$  Hz, 1H), 6.69 – 6.63 (m, 1H), 5.97 (s, 2H), 5.41 (d,  $J = 4.4$  Hz, 1H), 4.15 – 3.97 (m, 4H), 2.31 (s, 3H), 2.18 (s, 3H), 1.19 (dt,  $J = 19.0, 7.1$  Hz, 3H) 1.15 (t,  $J = 19.0, 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ , 298 K)  $\delta$  (ppm) = 167.98, 167.01, 154.03, 147.95, 147.29, 146.02, 137.68, 119.83, 110.89, 108.22, 107.27, 103.49, 101.12, 60.05, 59.78, 55.07, 21.40, 19.67, 14.47, 14.43. MS (ES+):  $m/z$  373.4 (M), 358.21, 344.04, 300.3, 252.2, 224.06, 196.12.

Diethyl 4-cyclohexyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (**4b**) [4].  $\text{C}_{19}\text{H}_{29}\text{NO}_4$ . M.P: 111-114 °C. IR (KBr,  $\text{cm}^{-1}$ ): 3433 (m), 3335 (m), 2872 (m), 1674 (m), 1622 (m), 1215 (m), 1099 (w), 756 (s).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 5.53 (s, 1H), 4.26 – 4.10 (m, 4H), 3.92 (d,  $J = 5.7$  Hz, 1H), 2.32 (s, 6H), 1.60 (d,  $J = 46.9$  Hz, 2H), 1.58 (br s, 4H), 1.32 (t,  $J = 7.1$  Hz, 6H), 1.12-1.08 (m, 3H), 0.98-0.93 (m, 2H). MS (ES+):  $m/z$  = 335.4, 252.14, 224.14, 196.07, 179.16.

(*E*)-Diethyl 4-(but-1-en-1-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (**4c**).  $\text{C}_{17}\text{H}_{25}\text{NO}_4$ . Yellow solid. M.P: 125-128 °C. IR (KBr,  $\text{cm}^{-1}$ ): 3435 (m), 3342 (m), 3016 (m), 2960 (m), 1678 (m), 1465 (m), 1273 (m), 1215 (s), 1099 (w), 754 (s).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 5.41 (br s, 1H), 5.33 (t,  $J = 4.4$  Hz, 2H), 4.38 (s, 1H), 4.22 (dd,  $J = 10.8, 7.1$  Hz, 3H), 4.13 (dd,  $J = 10.8, 7.1$  Hz, 1H), 2.29 (s, 6H), 1.95 (dd,  $J = 7.4, 4.2$  Hz, 2H), 1.28 (t,  $J = 7.1$  Hz, 6H), 0.91 (t,  $J = 7.4$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 167.84, 144.25, 130.57, 102.32, 59.60, 36.12, 25.34, 19.44, 14.41, 13.82. MS (ES+):  $m/z$  = 308.23, 307.21, 306.20, 305.20.

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