Electronic Supplementary Information

HMF in multicomponent reactions: utilization of 5-hydroxymethylfurfural (HMF) in the Biginelli reaction

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1. General information

Reagents and solvents were supplied by Aldrich, Acros, Lancaster, Alfa Aesar, Fluka or TCI and purchased at the highest commercial quality to be used without further purification, unless otherwise stated in the procedure. NMR spectra were recorded on a Bruker DRX-300 (^{1}H: 300 or 400 MHz; ^{13}C: 75 or 100 MHz) spectrometer using $CDCl_3$, DMSO-d_6. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on a Thermo Finnigan LCQ Advantage mass. High-resolution mass spectra (HRMS) were recorded on Bruker MicrOTOF-Q II XL spectrometer using ESI as ionization source. Analytical thin-layer chromatography was carried out on silica gel Merck 60 D254 (0.25 mm). Flash chromatographies were performed on Merck Si 60 silica gel (40–63 μm).

2. General procedure

A mixture of HMF (2 mmol), 1,3-dicarbonyl compound (2 mmol), urea-type compound (3 mmol) and $ZnCl_2$ (20 mol%) was stirred at 80 °C in a sealed tube during 8 h to 24 h.

Depending on the substrates, two work-ups were performed after completing the reaction. For the preparation of products **4a**, **4c**, **4d**, **4j** and **4p**, after addition of water (3 mL) to the reaction vessel, the mixture was stirred and cooled down to 0 °C. The expected product precipitated and was then filtered. The cake was rinsed with cold water (3 mL) and dried overnight giving the Biginelli product. After concentration, the filtrate was purified by column chromatography on silica gel with DCM/MeOH (50:1 – 15:1) as eluent. For the preparation of products **4b**, **4e - 4i** and **4k - 4o**, the reaction mixture was transferred into a separating funnel with MeOH (3 mL). After addition of water (50 mL), the mixture was extracted with EtOAc (4 x 50 mL). The combined organic layers were washed with brine (15 mL), dried over $NaSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel with DCM/MeOH (50:1 – 15:1).

3. Characterization data of products

5-Acetyl-4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4a):

Reaction time: 8 h; Global yield: 86%; (78% yield after simple filtration + additional 8% yield after purification of the filtrate by column chromatography).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (d, 1H, J = 1.2 Hz, H_1), 7.88 (dd, 1H, J = 3.4, 1.2 Hz, H_3), 6.16 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.03 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.27 (d, 1H, J = 3.4 Hz, H_4), 5.18 (t, 1H, J = 5.6 Hz, OH), 4.33 (d, 2H, J = 5.6 Hz, CH_2), 2.25 (s, 3H, C$\underline{H}_3$-C_6), 2.17 (s, 3H, C$\underline{H}_3$CO). ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.9 ($\underline{C}OCH_3$), 155.1, 154.9 ($C_{2'}$, $C_{5'}$), 152.4 (C_2), 149.0 (C_6), 107.7 ($C_{4'}$), 107.1 (C_5), 106.3 ($C_{3'}$), 55.7 (CH_2OH), 47.9 (C_4), 30.0 ($\underline{C}H_3CO$), 19.0 ($\underline{C}H_3$-C_6). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{12}H_{14}N_2NaO_4$ 273.0846; Found 273.0850.

6-Ethyl-4-[5'-(hydroxymethyl)furan-2'-yl]-5-propionyl-3,4-dihydropyrimidin-2(1*H*)-one (4b):

Reaction time: 24 h; Global yield: 42% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (d, 1H, J = 1.8 Hz, H_1), 7.84 (dd, 1H, J = 3.6, 1.8 Hz, H_3), 6.17 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.02 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.31 (d, 1H, J = 3.6 Hz, H_4), 5.19 (t, 1H, J = 5.6 Hz, OH), 4.34 (d, 2H, J = 5.5 Hz, C$\underline{H}_2$OH), 2.79-2.50 (m, 3H, CH_2, C$\underline{H}$CO), 2.31-2.25 (m, 1H, C$\underline{H}$CO), 1.10 (t, 3H, J = 7.4 Hz, C_6-CH_2C$\underline{H}_3$), 0.88 (t, 3H, J = 7.2 Hz, $COCH_2C\underline{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.8 ($\underline{C}OCH_2CH_3$), 155.2, 155.1 ($C_{2'}$, $C_{5'}$), 153.9 (C_6), 152.8 (C_2), 107.8 ($C_{4'}$), 106.6 ($C_{3'}$), 105.4 (C_5), 55.9 ($\underline{C}H_2OH$), 48.0 (C_4), 33.1 ($CO\underline{C}H_2$), 24.6 (C_6-$\underline{C}H_2$), 13.0 (C_6-$CH_2\underline{C}H_3$), 8.4 ($COCH_2\underline{C}H_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{14}H_{18}N_2NaO_4$ 301.1159; Found 301.1164.

Methyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4c):

Reaction time: 9 h; Global yield: 85% yield after filtration.

^{1}H NMR (300 MHz, DMSO-d_6) δ 9.23 (d, 1H, J = 1.3 Hz, H_1), 7.78 (dd, 1H, J = 3.6, 1.3 Hz, H_3), 6.16 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.00 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.18-5.13 (m, 2H, H_4 and OH), 4.32 (d, 2H, J = 5.6 Hz, CH_2), 3.57 (s, 3H, OCH_3), 2.24 (s, 3H, C_6-C$\underline{H}_3$). ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.5 (CO_2), 155.0, 154.8 ($C_{2'}$, $C_{5'}$), 152.3 (C_2), 149.8 (C_6), 107.7 ($C_{4'}$), 106.0 ($C_{3'}$), 96.4 (C_5), 55.7 ($\underline{C}H_2OH$), 50.9 ($CO_2\underline{C}H_3$), 47.7 (C_4), 17.8 (C_6-$\underline{C}H_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{12}H_{14}N_2NaO_5$ 289.0795; Found 289.0791.

Ethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4d):

Reaction time: 16 h; Global yield: 82% yield after filtration.

^{1}H NMR (300 MHz, DMSO-d_6) δ 9.20 (s, 1H, H_1), 7.76 (d, 1H, J = 1.2 Hz, H_3), 6.16 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.00 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.20-5.12 (m, 2H, H_4 and OH), 4.32 (d, 2H, J = 5.6 Hz, C$\underline{H}_2$OH), 4.04 (q, 2H, J = 7.1 Hz, C$\underline{H}_2$CH$_3$), 2.23 (s, 3H, C_6-C$\underline{H}_3$), 1.14 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$). ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1 (CO_2), 155.2, 154.7 ($C_{2'}$, $C_{5'}$), 152.4 (C_2), 149.4 (C_6), 107.7 ($C_{4'}$), 105.9 ($C_{3'}$), 96.7 (C_5), 59.3 ($O\underline{C}H_2CH_3$), 55.7 ($\underline{C}H_2OH$), 47.8 (C_4), 17.8 (C_6-$\underline{C}H_3$), 14.2 ($CH_2\underline{C}H_3$).HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{13}H_{16}N_2NaO_5$ 303.0951; Found 303.0951.

Isopropyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4e):

Reaction time: 24 h; Global yield: 62% after purification by column chromatography.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (d, 1H, J = 2.0 Hz, H_1), 7.75 (dd, J = 3.4, 1.8 Hz, 1H, H_3), 6.16 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.99 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.18-5.15 (m, 2H, H_4 and OH), 4.86 (h, 1H, J = 6.3 Hz, C<u>H</u>$(CH_3)_2$), 4.31 (d, 2H, J = 5.6 Hz, C<u>H</u>$_2$OH), 2.22 (s, 3H, C_6-C<u>H</u>$_3$), 1.18 (d, 3H, J = 6.3 Hz, CH(C<u>H</u>$_3)_2$), 1.09 (d, 3H, J = 6.3 Hz, CH(C<u>H</u>$_3)_2$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6 (CO_2), 155.3 ($C_{2'}$), 154.6 ($C_{5'}$), 152.4 (C_2), 149.1 (C_6), 107.6 ($C_{4'}$), 105.9 ($C_{3'}$), 97.0 (C_5), 66.4 (<u>C</u>H$(CH_3)_2$), 55.7 (<u>C</u>H$_2$OH), 47.9 (C_4), 21.8 (CH(<u>C</u>H$_3)_2$), 21.6 (CH(<u>C</u>H$_3)_2$), 17.8 (C_6-<u>C</u>H$_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{14}H_{18}N_2NaO_5$ 317.1108; Found 317.1105.

***t*ert-Butyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4f):**

Reaction time: 24 h; Global yield: 63% after purification by column chromatography.
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.10 (d, 1H, J = 1.6 Hz, H_1), 7.70 (dd, 1H, J = 3.3 Hz, 1.6 Hz, H_3), 6.17 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.98 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.17 (t, 1H, J = 5.4 Hz, OH), 5.12 (d, 1H, J = 3.3 Hz, H_4), 4.32 (d, 2H, J = 5.4 Hz, C<u>H</u>$_2$OH), 2.19 (s, 3H, C_6-C<u>H</u>$_3$), 1.36 (s, 9H, C(C<u>H</u>$_3)_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5 (CO_2), 155.5 ($C_{2'}$), 154.6 ($C_{5'}$), 152.4 (C_2), 148.3 (C_6), 107.6 ($C_{4'}$), 105.7 ($C_{3'}$), 98.1 (C_5), 79.2 (<u>C</u>$(CH_3)_3$), 55.8 (<u>C</u>H$_2$OH), 48.2 (C_4), 27.9 (C(<u>C</u>H$_3)_3$), 17.7 (C_6-<u>C</u>H$_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{15}H_{20}N_2NaO_5$ 331.1264; Found 331.1274.

Benzyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4g):

Reaction time: 24 h; Global yield: 58% after purification by column chromatography.
^{1}H NMR (300 MHz, DMSO-d_6) δ 9.30 (d, 1H, J = 1.2 Hz, H_1), 7.81 (dd, 1H, J = 3.4, 1.2 Hz, H_3), 7.40-7.20 (m, 5H, H_{Ar}), 6.17 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.98 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.23 (d, 1H, J = 3.4 Hz, H_4), 5.18 (t, 1H, J = 5.6 Hz, OH), 5.15-5.02 (AB, 2H, PhC<u>H</u>$_2$), 4.33 (d, 2H, J = 5.6 Hz, C<u>H</u>$_2$OH), 2.27 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.8 (CO_2), 155.1, 154.8 ($C_{2'}$, $C_{5'}$), 152.3 (C_2), 150.3 (C_6), 136.7 (C_{qAr}), 128.4 (2 CH_{Ar}), 127.7 (CH_{Ar}), 127.5 (2 CH_{Ar}), 107.7 ($C_{4'}$), 106.1 ($C_{3'}$), 96.3 (C_5), 64.9 (<u>C</u>H$_2$Ph), 55.8 (<u>C</u>H$_2$OH), 47.8 (C_4), 17.9 (CH_3). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{18}H_{18}N_2NaO_5$ 365.1108; Found 365.1115.

Dibenzyl 4-[5'-(hydroxymethyl)furan-2'-yl]-2,6-dimethyl-1,4-dihydropyridine-3,5 -dicarboxylate (4g'):

5% yield of Hantzsch product **4g'** was obtained along with Biginelli Product **4g**.
^{1}H NMR (300 MHz, DMSO-d_6) δ 9.07 (s, 1H, H_1), 7.36-7.26 (m, 10H, H_{Ar}), 6.06 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.72 (dd, 1H, J = 3.1, 0.7 Hz, $H_{3'}$), 5.21-5.00 (m, 6H, H_4, 2C<u>H</u>$_2$Ph and OH), 4.26 (d, 2H, J = 5.5 Hz, C<u>H</u>$_2$OH), 2.27 (s, 6H, 2 CH_3). ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.4 (2 CO_2), 158.0 ($C_{2'}$), 153.7 ($C_{5'}$), 147.1 (C_2, C_6), 136.9 (2 $C_{q,Ar}$), 128.3 (4 CH_{Ar}), 127.6 (2 CH_{Ar}), 127.4 (4 CH_{Ar}), 107.5 ($C_{4'}$), 104.9 ($C_{3'}$), 98.4 (C_3, C_5), 64.7 (2 <u>C</u>H$_2$Ph), 55.8 (<u>C</u>H$_2$OH), 32.7 (C_4), 18.3 (2 CH_3). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{28}H_{27}NNaO_6$ 496.1731; Found 496.1709.

Allyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4h):

Reaction time: 24 h; Global yield: 60% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 (d, 1H, J = 2.0 Hz, H_1), 7.82 (dd, 1H, J = 3.8, 2.0 Hz, H_3), 6.16 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.01 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.94-5.82 (m, 1H, C<u>H</u>CH_2), 5.26-5.08 (m, 4H, OH, CHC<u>H</u>$_2$ and H_4), 4.60-4.46 (m, 2H, OC<u>H</u>$_2$CH=CH_2), 4.32 (d, 2H, J = 5.7 Hz, C<u>H</u>$_2$OH), 2.26 (s, 3H, C_6-C<u>H</u>$_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.7 (CO_2), 155.1 ($C_{2'}$), 154.8 ($C_{5'}$), 152.3 (C_2), 150.2 (C_6), 133.1 (<u>C</u>H=CH_2), 117.0 (CH=<u>C</u>H_2), 107.7 ($C_{4'}$), 106.1 ($C_{3'}$), 96.4 (C_5), 63.8 (O<u>C</u>H_2CH=CH_2), 55.8 (<u>C</u>H_2OH), 47.7 (C_4), 17.9 (C_6-<u>C</u>H_3). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{14}H_{16}N_2NaO_5$ 315.0951; Found 315.0945.

2-Methoxyethyl -4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (4i):

Reaction time: 24 h; Global yield: 47% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.26 (d, 1H, J = 2.0 Hz, H_1), 7.79 (dd, 1H, J = 3.6, 2.0 Hz, H_3), 6.17 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.03 (dd, 1H, J = 3.1, 0.6 Hz, $H_{3'}$), 5.21 (d, 1H, J = 3.6 Hz, H_4), 4.34 (s, 2H, C<u>H</u>$_2$OH), 4.14-4.10 (m, 2H, CH_2OCO), 3.72-3.39 (m, 2H, CH_3OC<u>H</u>$_2$), 3.22 (s, 3H, OCH_3), 2.25 (s, 3H, C_6-C<u>H</u>$_3$). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.2 (CO_2), 155.2, 154.9 ($C_{2'}$ and $C_{5'}$), 152.6 (C_2), 149.9 (C_6), 107.8 ($C_{4'}$), 106.2 ($C_{3'}$), 96.8 (C_5), 70.1 (CH_3O<u>C</u>H_2), 62.6 (<u>C</u>H_2OCO), 58.2 (O<u>C</u>H_3), 55.9 (<u>C</u>H_2OH), 48.0 (C_4), 18.0 (C_6-<u>C</u>H_3). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{14}H_{18}N_2NaO_6$ 333.1057; Found 333.1051.

Ethyl 4-hydroxy-6-[5'-(hydroxymethyl)furan-2'-yl]-2-oxo-4-(trifluoromethyl)hexahydro pyrimidine-5-carboxylate (4j):

Reaction time: 8 h; Global yield: 84%; (66% yield after simple filtration + additional 18% yield after purification of the filtrate by column chromatography).

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (s, 1H, H_3), 7.47 (s, 1H, C_4-OH), 7.32 (d, 1H, J = 1.2 Hz, H_1), 6.30 (d, J = 3.2 Hz, 1H, $H_{3'}$), 6.19 (d, J = 3.2 Hz, 1H, $H_{4'}$), 5.24 (t, 1H, J = 5.8 Hz, CH_2O<u>H</u>), 4.86 (d, 1H, J = 11.7 Hz, H_6), 4.33 (d, 2H, J = 5.8 Hz, C<u>H</u>$_2$OH), 3.96-3.88 (m, 2H, C<u>H</u>$_2$$CH_3$), 3.08 (d, 1H, J = 11.7 Hz, H_5), 0.98 (t, 3H, J = 7.1 Hz, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8 (CO_2), 155.6 ($C_{5'}$), 153.3 (C_2), 149.8 ($C_{2'}$), 133.1-116.2 (q, J = 286 Hz, CF_3), 109.3 ($C_{3'}$), 107.4 ($C_{4'}$), 80.3 (q, J = 31 Hz, C_4), 60.5 (<u>C</u>$H_2$$CH_3$), 55.6 (<u>C</u>$H_2$OH), 48.1 ($C_5$), 47.1 ($C_6$), 13.7 ($CH_3$). ^{19}F NMR (282 MHz, DMSO-d_6) δ -80.70. HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{13}H_{15}F_3N_2NaO_6$ 375.0774; Found 375.0771.

5-Acetyl-4-[5'-((benzyloxy)methyl)furan-2'-yl]-6-methyl-3,4-dihydropyrimidin-2(1H)-one (4k):

Reaction time: 16 h; Global yield: 66% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.27 (d, 1H, J = 1.8 Hz, H_1), 7.93 (dd, 1H, J = 3.5, 1.8 Hz, H_3), 7.40-7.25 (m, 5H, H_{Ar}), 6.34 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.08 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.31 (d, 1H, J = 3.6 Hz, H_4), 4.48 (s, 2H, PhC<u>H</u>$_2$), 4.39 (s, 2H, C<u>H</u>$_2$$OCH_2$Ph), 2.26 (s, 3H, C_6-C<u>H</u>$_3$), 2.18 (s, 3H, COC<u>H</u>$_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.8 (<u>C</u>OCH_3), 156.1 ($C_{2'}$), 152.4 (C_2), 151.1 ($C_{5'}$), 149.0 (C_6), 138.1 ($C_{q,Ar}$), 128.3 (2 CH_{Ar}), 127.7 (2 CH_{Ar}), 127.5 (C_{Ar}), 110.3 ($C_{4'}$), 107.1 (C_5), 106.3 ($C_{3'}$), 71.0 (Ph<u>C</u>H_2), 63.4 (<u>C</u>$H_2$$OCH_2$Ph), 47.9 ($C_4$), 30.0 (CO<u>C</u>$H_3$), 19.0 ($C_6$-<u>C</u>$H_3$). HRMS

(ESI) m/z: Calcd for $[M+Na]^+$ $C_{19}H_{20}N_2NaO_4$ 363.1315; Found 363.1305.

Ethyl 4-[5'-((benzyloxy)methyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4l):

Reaction time: 24 h; Global yield: 56% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (d, 1H, J = 1.6 Hz, H_1), 7.83 (dd, 1H, J = 3.1 Hz, 1. 6 Hz, H_3), 7.40-7.20 (m, 5H, H_{Ar}), 6.34 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.07 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.23 (d, 1H, J = 3.1 Hz, H_4), 4.47 (s, 2H, C$\underline{H}_2$Ph), 4.40 (s, 2H, $C_{5'}$-C$\underline{H}_2$), 4.11-3.95 (m, 2H, C$\underline{H}_2$CH$_3$), 2.26 (s, 3H, C_6-C$\underline{H}_3$), 1.13 (t, 3H, J = 7.1 Hz, CH$_2$C$\underline{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.1 (CO_2), 156.3 ($C_{2'}$), 152.4 (C_2), 150.9 ($C_{5'}$), 149.5 (C_6), 138.1 ($C_{q,\ Ar}$), 128.3 (2 CH_{Ar}), 127.7 (2 CH_{Ar}), 127.5 (CH_{Ar}), 110.3 ($C_{4'}$), 106.0 ($C_{3'}$), 96.7 (C_5), 71.0 (C$\underline{H}_2$Ph), 63.4 ($C_{5'}$-C$\underline{H}_2$), 59.3 (C$\underline{H}_2$CH$_3$), 47.9 (C_4), 17.8 (C_6-C$\underline{H}_3$), 14.2 (CH$_2$C$\underline{H}_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{20}H_{22}N_2NaO_5$ 393.1421; Found 393.1435.

Diethyl 4-[5'-((benzyloxy)methyl)furan-2'-yl]-2,6-dimethyl-1,4-dihydropyridine-3,5 -dicarboxylate (4l'):

8% yield of Hantzsch product **4l'** was obtained along with Biginelli Product **4l**.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.93 (s, 1H, H_1), 7.38-7.24 (m, 5H, H_{Ar}), 6.23 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.81 (d, 1H, J = 3.1, 1.0 Hz, $H_{3'}$), 5.06 (s, 1H, H_4), 4.43 (s, 2H, PhC$\underline{H}_2$), 4.32 (s, 2H, C$\underline{H}_2$OBn), 4.15-3.95 (m, 4H, OC$\underline{H}_2$CH$_3$), 2.26 (s, 6H, C_6-CH$_3$, C_2-CH$_3$), 1.16 (t, 6H, J = 7.1 Hz, OCH$_2$C$\underline{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7 (CO_2), 159.3 ($C_{2'}$), 149.8 ($C_{5'}$), 146.44 (C_2, C_6), 138.2 ($C_{q,\ Ar}$), 128.2 (2 CH_{Ar}), 127.6 (2 CH_{Ar}), 127.5 (CH_{Ar}), 110.2 ($C_{4'}$), 104.7 ($C_{3'}$), 98.5 (C_3, C_5), 70.8 (Ph$\underline{C}$H$_2$), 63.4 ($\underline{C}$H$_2$OBn), 59.1 (2 $\underline{C}$H$_2$CH3), 33.0 (C_4), 18.2 (C_2-$\underline{C}$H$_3$, C_6-$\underline{C}$H$_3$), 14.3 (2 OCH$_2\underline{C}$H$_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{25}H_{29}NNaO_6$ 462.1887; Found 462.1876.

5-Acetyl-4-[5'-(hydroxymethyl)furan-2'-yl]-1,6-dimethyl-3,4-dihydropyrimidin-2(1H)-one (4m):

Reaction time: 24 h; Global yield: 30% after purification by column chromatography.

^{1}H NMR (300 MHz, DMSO-d_6) δ 8.08 (d, 1H, J = 4.2 Hz, H_3), 6.17 (d, 1H, J = 3.1 Hz, $H_{4'}$), 6.05 (dd, 1H, J = 3.1, 0.5 Hz, $H_{3'}$), 5.22 (d, 1H, J = 4.1 Hz, H_4), 5.16 (t, 1H, J = 5.7 Hz, OH), 4.33 (d, 2H, J = 5.6 Hz, C$\underline{H}_2$OH), 3.07 (s, 3H, NCH$_3$), 2.42 (s, 3H, C_6-CH$_3$), 2.19 (s, 3H, COCH$_3$). ^{13}C NMR (75 MHz, DMSO-d_6) δ 195.0 ($\underline{C}$OCH$_3$), 155.2, 154.5 ($C_{2'}$ and $C_{5'}$), 153.3 (C_2), 150.5 (C_6), 110.1 (C_5), 107.6 ($C_{4'}$), 106.4 ($C_{3'}$), 55.7 ($\underline{C}$H$_2$OH), 47.0 (C_4), 30.0 (CO$\underline{C}$H$_3$), 29.8 (NCH$_3$), 16.6 (C_6-$\underline{C}$H$_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{13}H_{16}N_2NaO_4$ 287.1002; Found 287.0999.

Ethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4n):

Reaction time: 24 h; Global yield: 42% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (s, 1H, H_1), 9.65 (s, 1H, H_3), 6.18 (d, 1H, J = 3.0 Hz, $H_{4'}$), 6.05 (d, 1H, J = 3.1 Hz, $H_{3'}$), 5.24-5.17 (m, 2H, H_4 and OH), 4.33 (d, 2H, J = 5.5 Hz, C$\underline{H}_2$OH), 4.10-3.98 (m, 2H, C$\underline{H}_2$CH$_3$), 2.29 (s, 3H, C_6-C$\underline{H}_3$), 1.13 (t, 3H, J = 7.1 Hz, CH$_2$C$\underline{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.9 (C_2), 164.9 (CO_2), 155.3 ($C_{5'}$), 153.9 ($C_{2'}$), 146.2 (C_6), 107.9 ($C_{4'}$), 107.1 ($C_{3'}$), 98.3 (C_5), 59.8 ($\underline{C}$H$_2$CH$_3$), 55.8 ($\underline{C}$H$_2$OH), 47.9 (C_4), 17.3 (C_6-$\underline{C}$H$_3$), 14.2 (CH$_2\underline{C}$H$_3$). HRMS (ESI) m/z: Calcd for $[M+Na]^+$ $C_{13}H_{16}N_2NaO_4S$ 319.0723; Found 319.0729.

Ethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carboxylate (4o):

Reaction time: 8 h; Global yield: 44% after purification by column chromatography.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.81 (s, 1H, H_1), 7.46 – 7.42 (m, 1H, H_9), 7.39 – 7.34 (m, 1H, H_6), 7.11 – 7.00 (m, 2H, H_7, H_8), 6.53 (d, 1H, J = 0.8 Hz, H_4), 6.38 (d, 1H, J = 3.2 Hz, $H_{3'}$), 6.14 (d, 1H, J = 3.1 Hz, $H_{4'}$), 5.11 (t, 1H, J = 5.7 Hz, $CH_2O\underline{H}$), 4.20 (d, 2H, J = 5.7 Hz, $C\underline{H}_2OH$), 4.14-3.98 (m, 2H, $C\underline{H}_2CH_3$), 2.46 (s, 3H, C_2-$C\underline{H}_3$), 1.17 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.1 (CO_2), 155.1 ($C_{5'}$), 151.9 ($C_{2'}$), 147.7 (C_2), 145.5 (C_{10a}), 142.2 (C_{9a}), 131.6 (C_{5a}), 121.9 (C_8), 120.2 (C_7), 116.8 (C_6), 109.8 (C_9), 108.4 ($C_{3'}$), 107.6 ($C_{4'}$), 94.3 (C_3), 59.4 ($\underline{C}H_2CH_3$), 55.6 ($\underline{C}H_2OH$), 49.4 (C_4) , 18.8 (C_2-$\underline{C}H_3$), 14.1 ($CH_2\underline{C}H_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{19}H_{20}N_3O_4$ 354.1448; Found 354.1445.

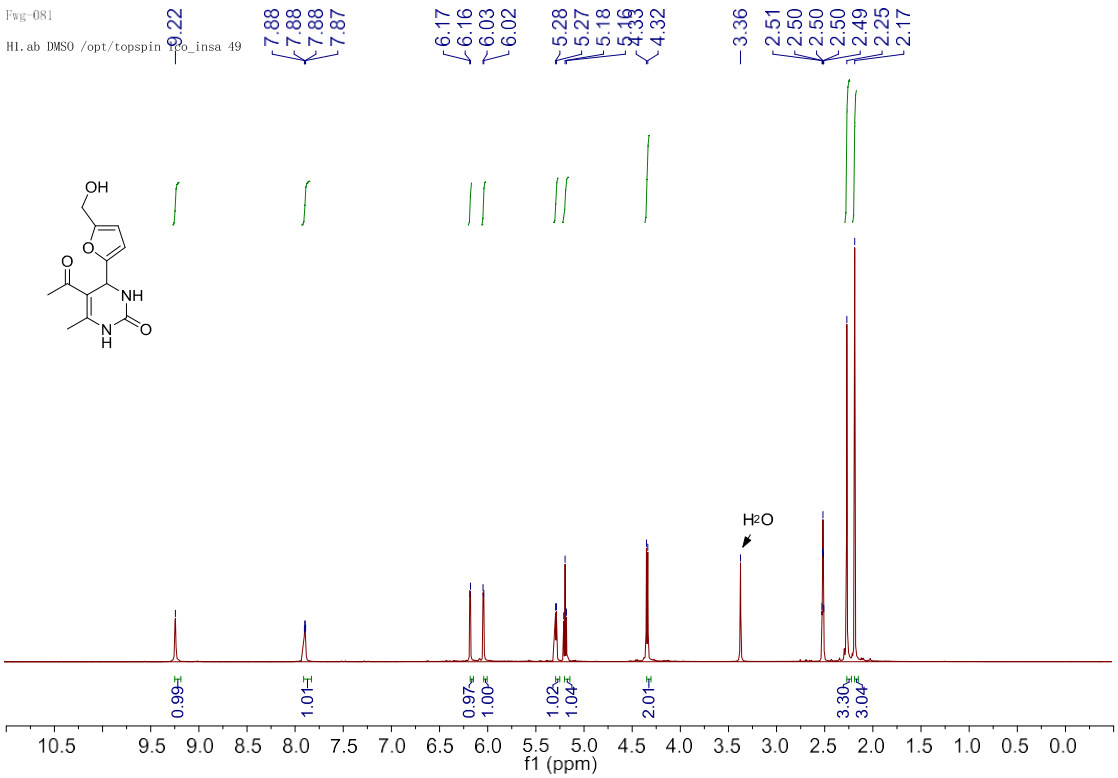
Ethyl 7-[5'-(hydroxymethyl)furan-2'-yl]-5-methyl-4,7-dihydro-[1,2,4]triazolo[1,5-a] pyrimidine-6-carboxylate (4p)

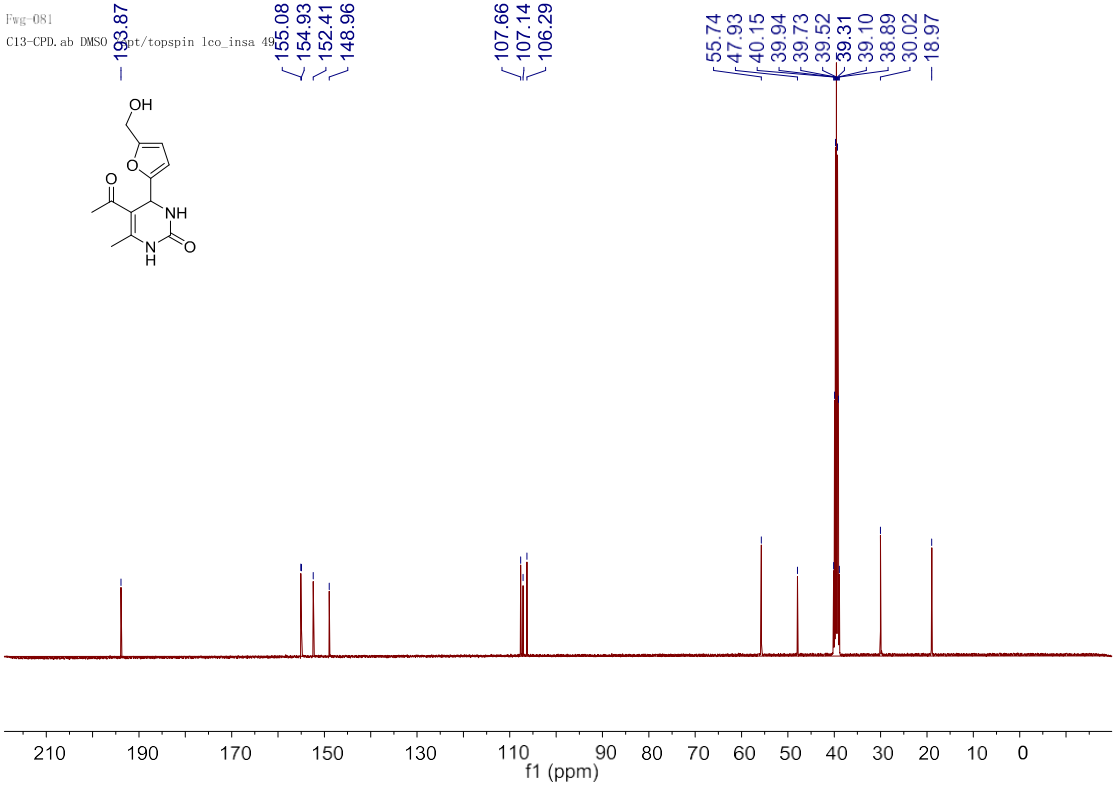
Reaction time: 8 h; Global yield: 83% after filtration.

^{1}H NMR (300 MHz, DMSO-d_6) δ 10.84 (s, 1H, H_4), 7.70 (s, 1H, H_2), 6.34 (s, 1H, H_7), 6.22 (d, 1H, J = 3.2 Hz, $H_{3'}$ or $H_{4'}$), 6.17 (d, 1H, J = 3.2 Hz, $H_{3'}$ or $H_{4'}$), 5.16 (t, 1H, J = 5.8 Hz, OH), 4.26 (d, 2H, J = 5.8 Hz, $C\underline{H}_2OH$), 4.10-3.92 (m, 2H, $C\underline{H}_2CH_3$), 2.40 (s, 3H, C_5-$C\underline{H}_3$), 1.11 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$). ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.0 (CO_2), 155.2 ($C_{5'}$), 152.6 ($C_{2'}$), 150.1 (C_2), 147.4 (C_5), 147.1 (C_{3a}), 108.1 ($C_{3'}$ or $C_{4'}$), 107.8 ($C_{3'}$ or $C_{4'}$), 94.6 (C_6), 59.5 ($\underline{C}H_2CH_3$), 55.6 ($\underline{C}H_2OH$), 53.1 (C_7), 18.5 (C_5-$\underline{C}H_3$), 14.0 ($CH_2\underline{C}H_3$). HRMS (ESI) m/z: Calcd for $[M+H]^+$ $C_{14}H_{17}N_4O_4$ 305.1244; Found 305.1244.

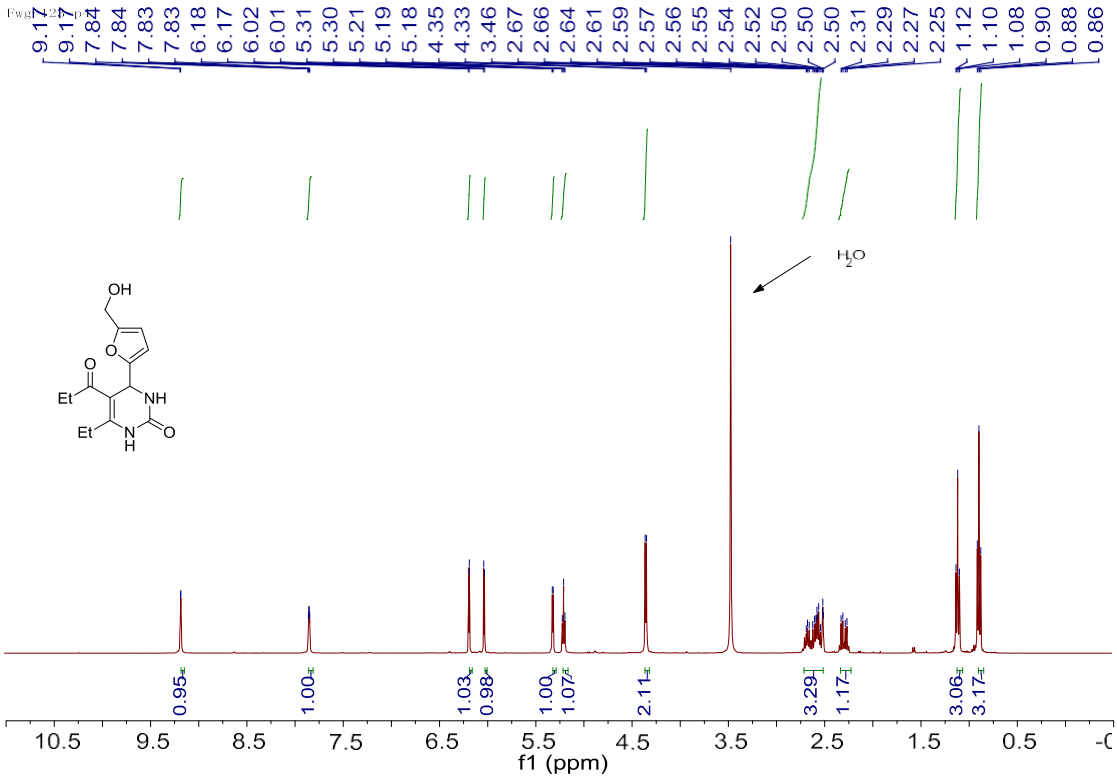
4. ^{1}H and ^{13}C NMR spectra of products

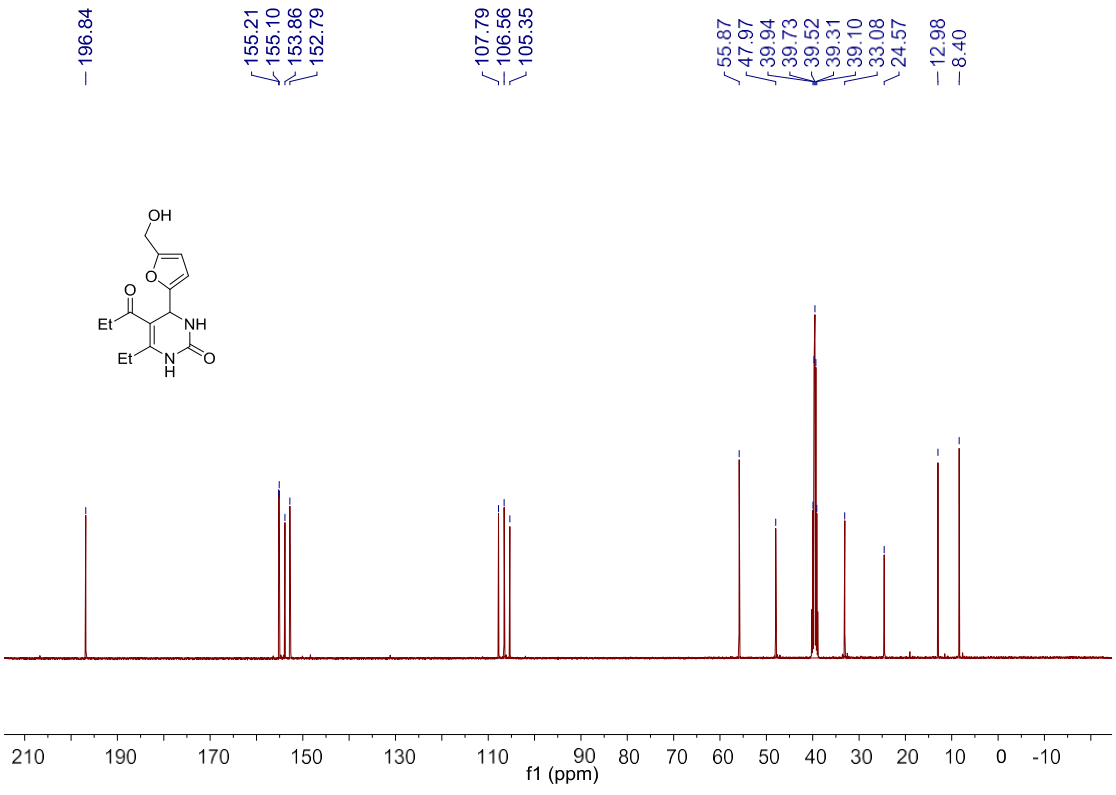
5-Acetyl-4-[5-(hydroxymethyl)furan-2-yl]-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4a)



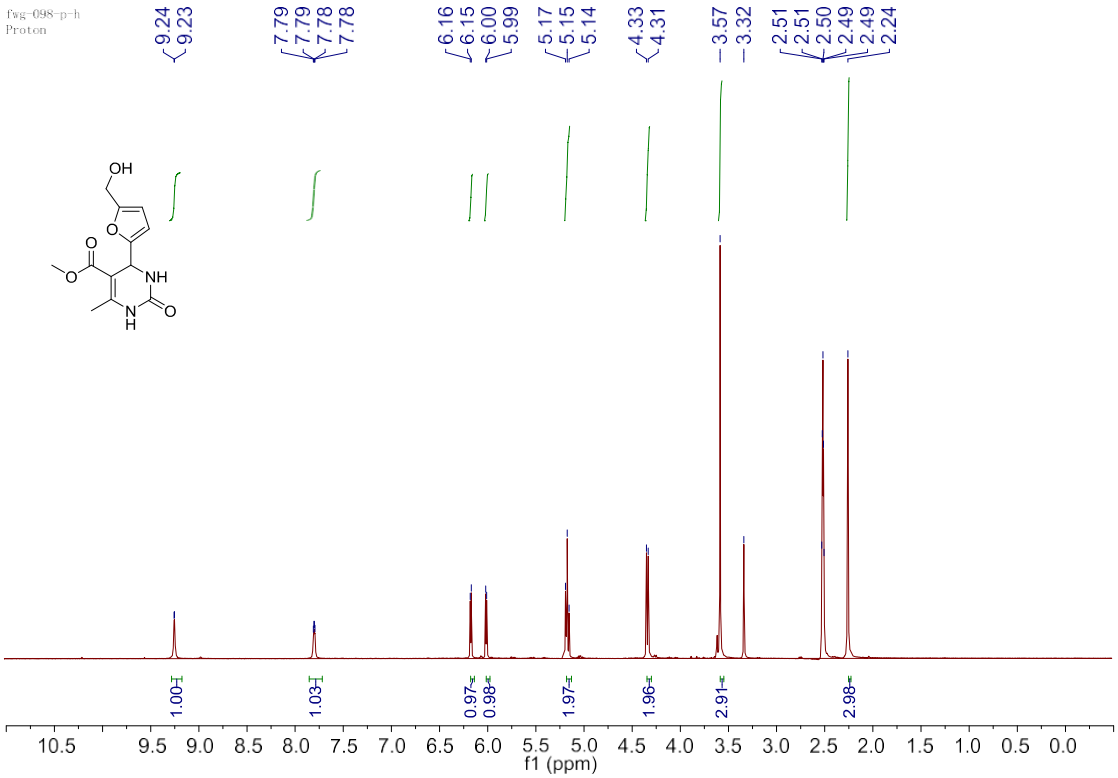


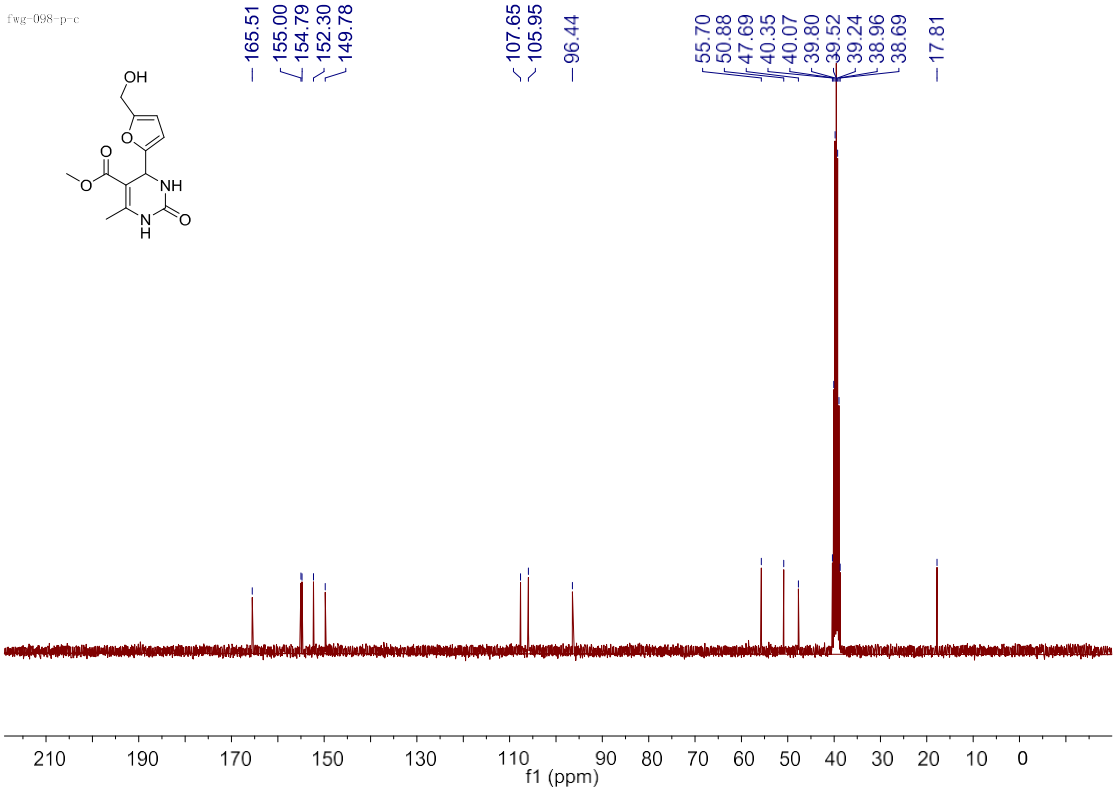
6-Ethyl-4-[5'-(hydroxymethyl)furan-2'-yl]-5-propionyl-3,4-dihydropyrimidin-2(1*H*)-one (4b)



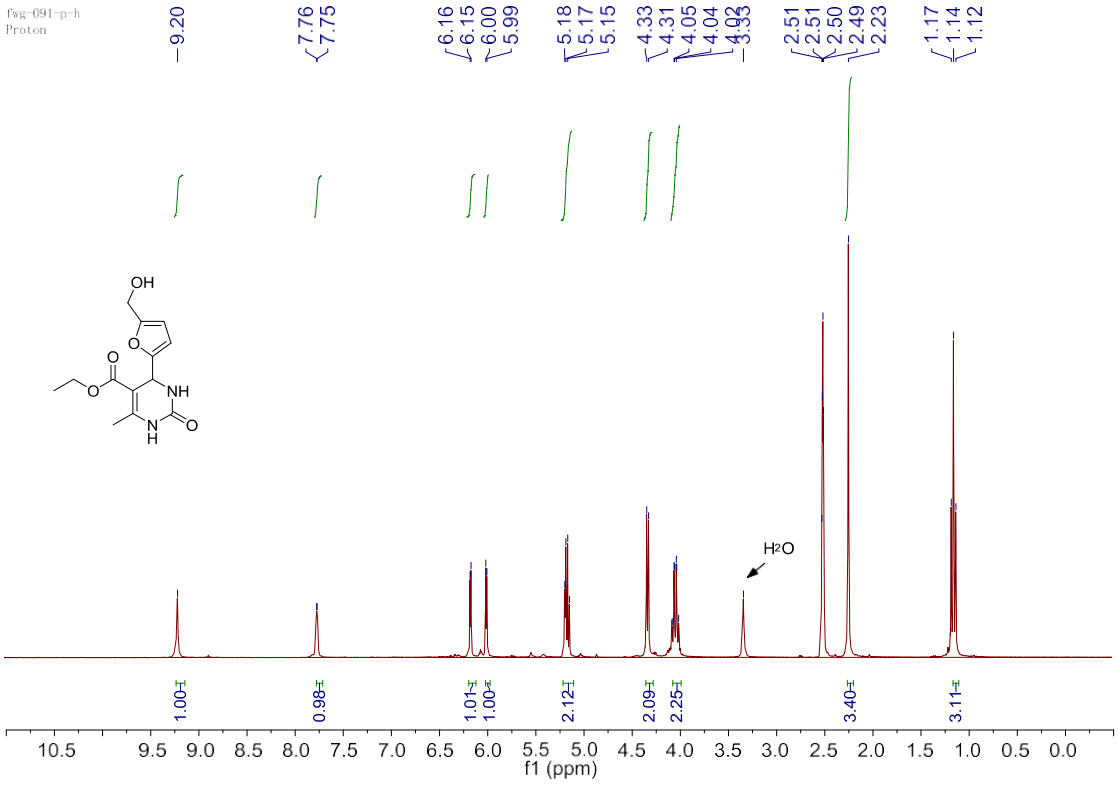


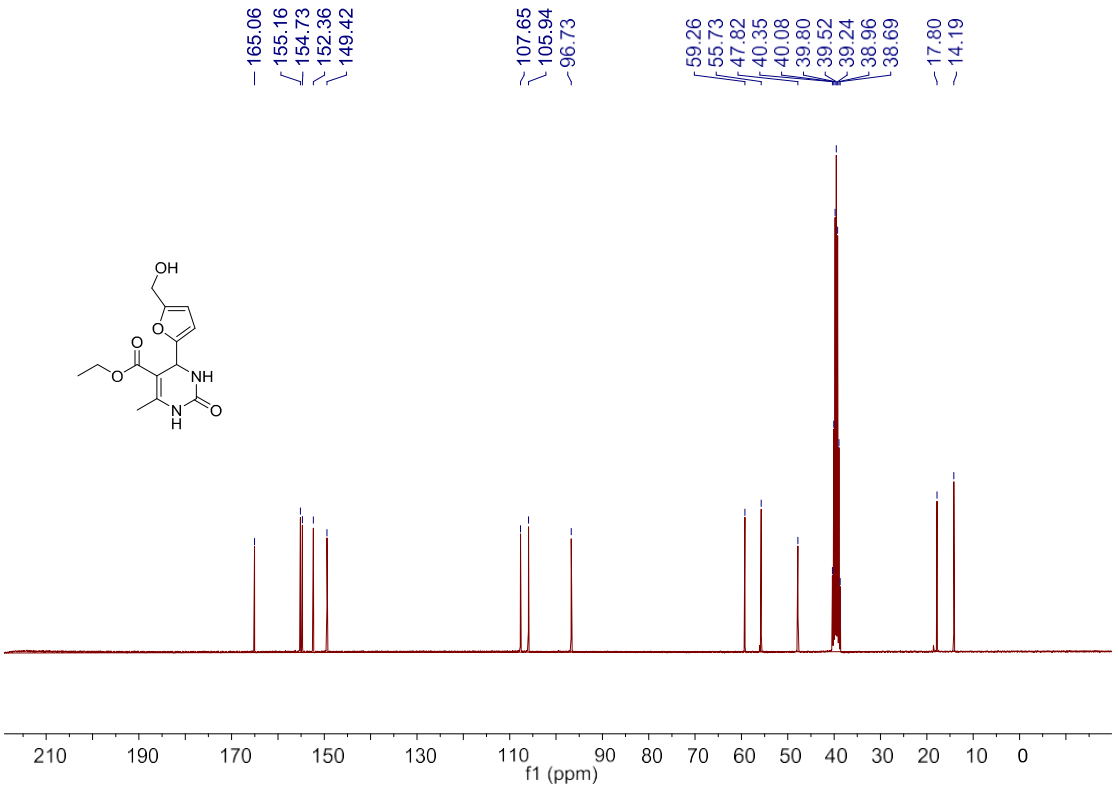
Methyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4c)



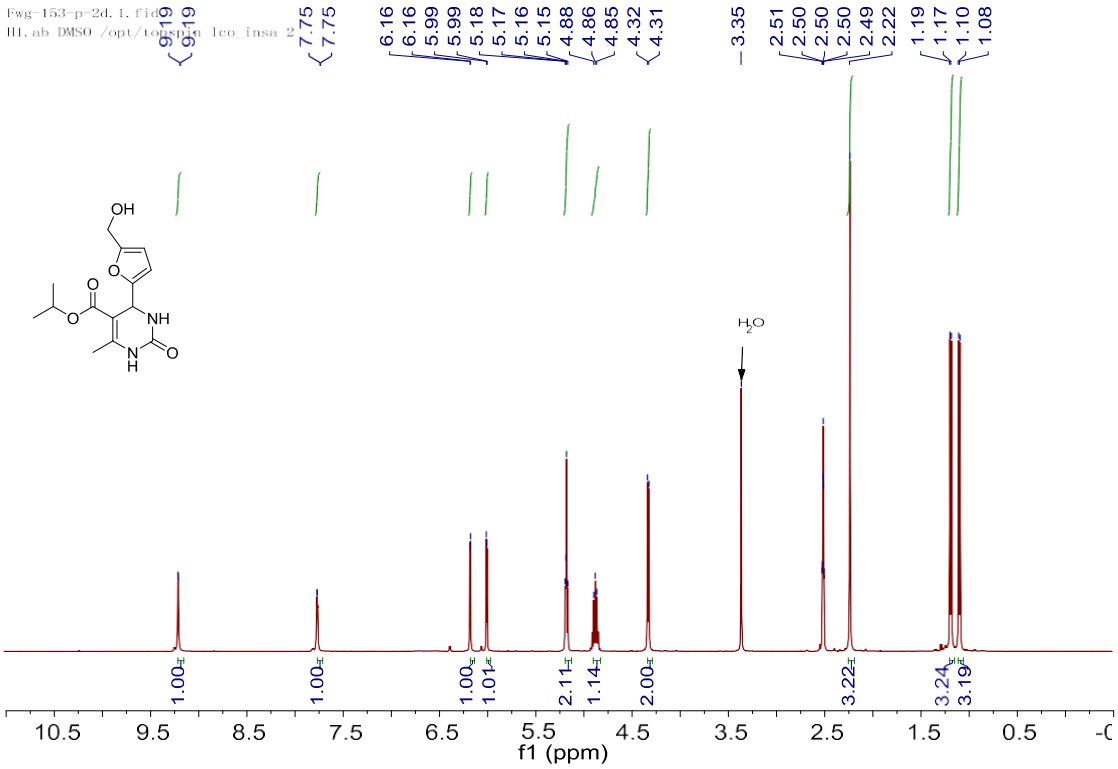


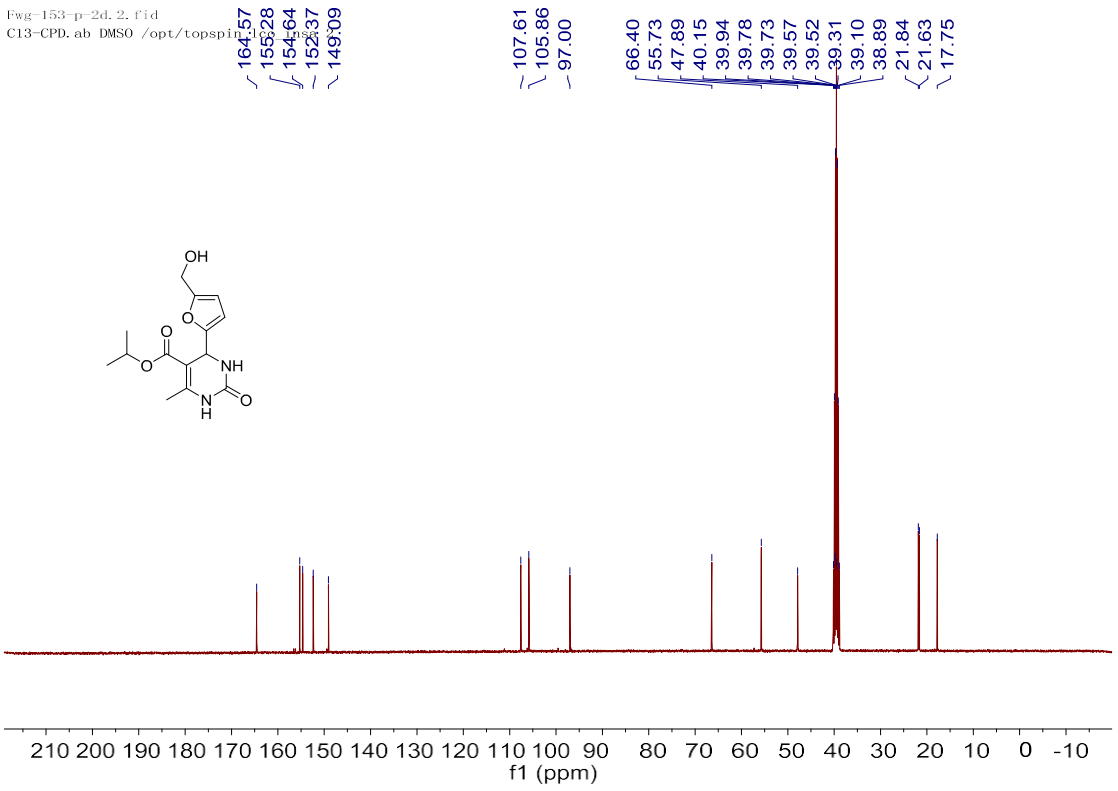
Ethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4d)



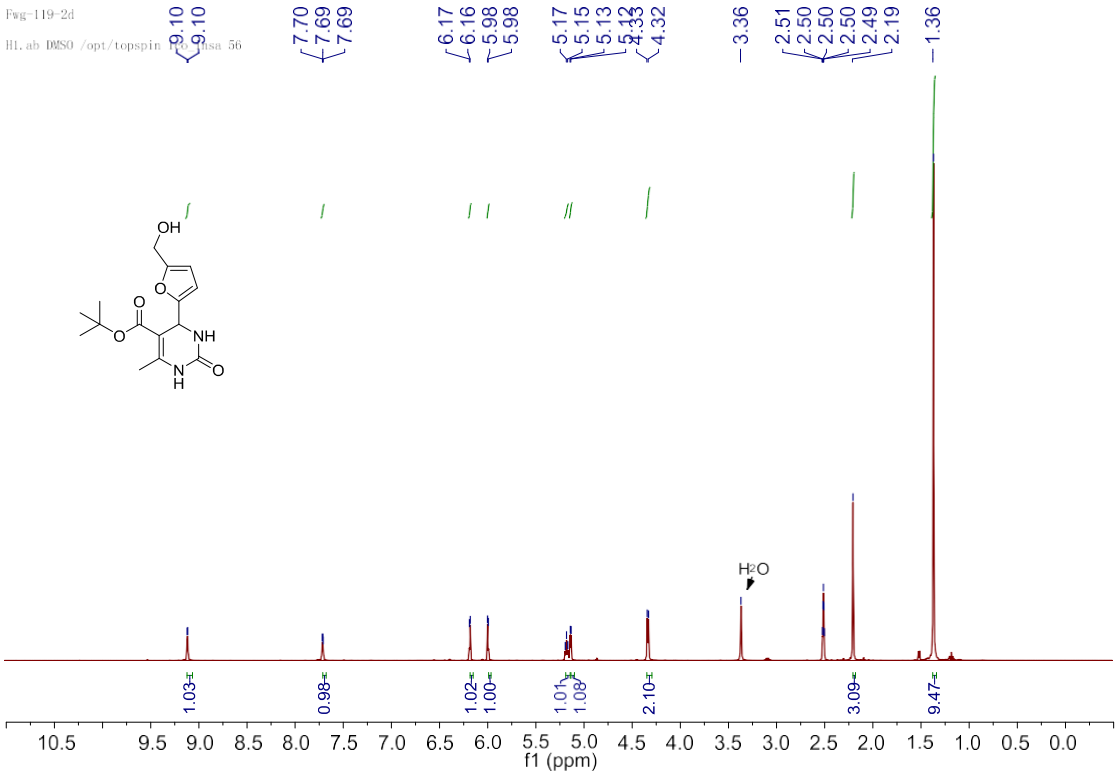


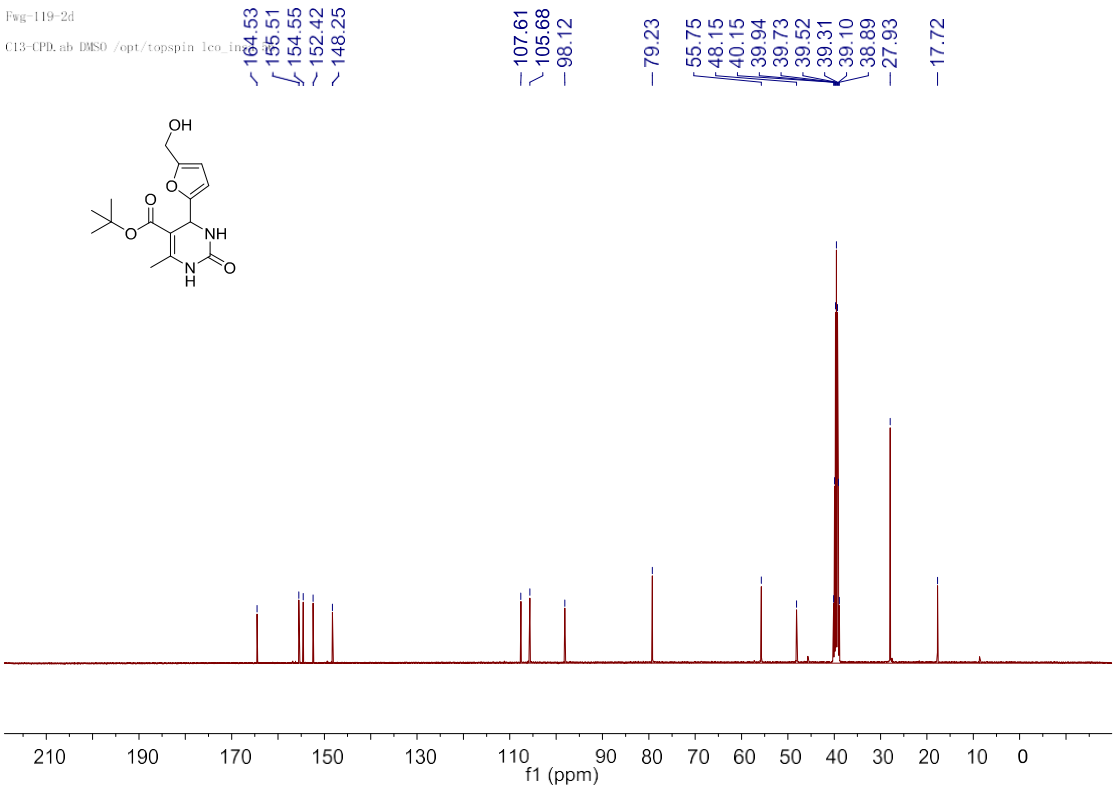
Isopropyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4e)



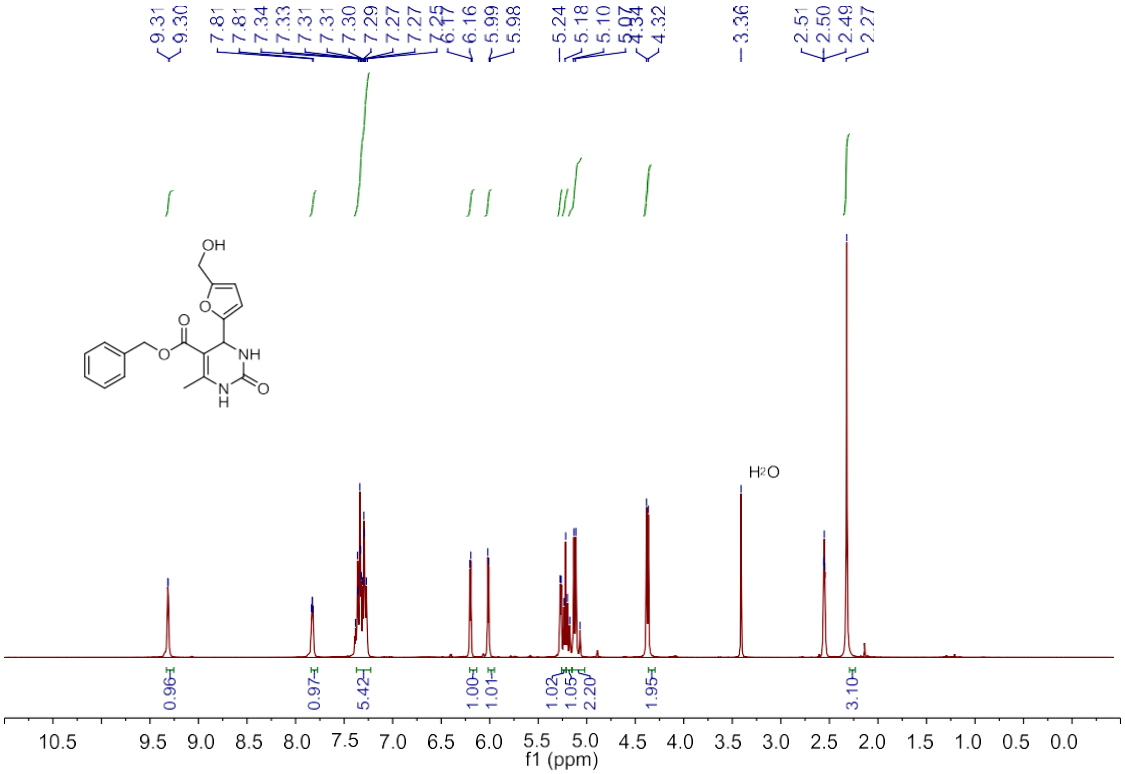


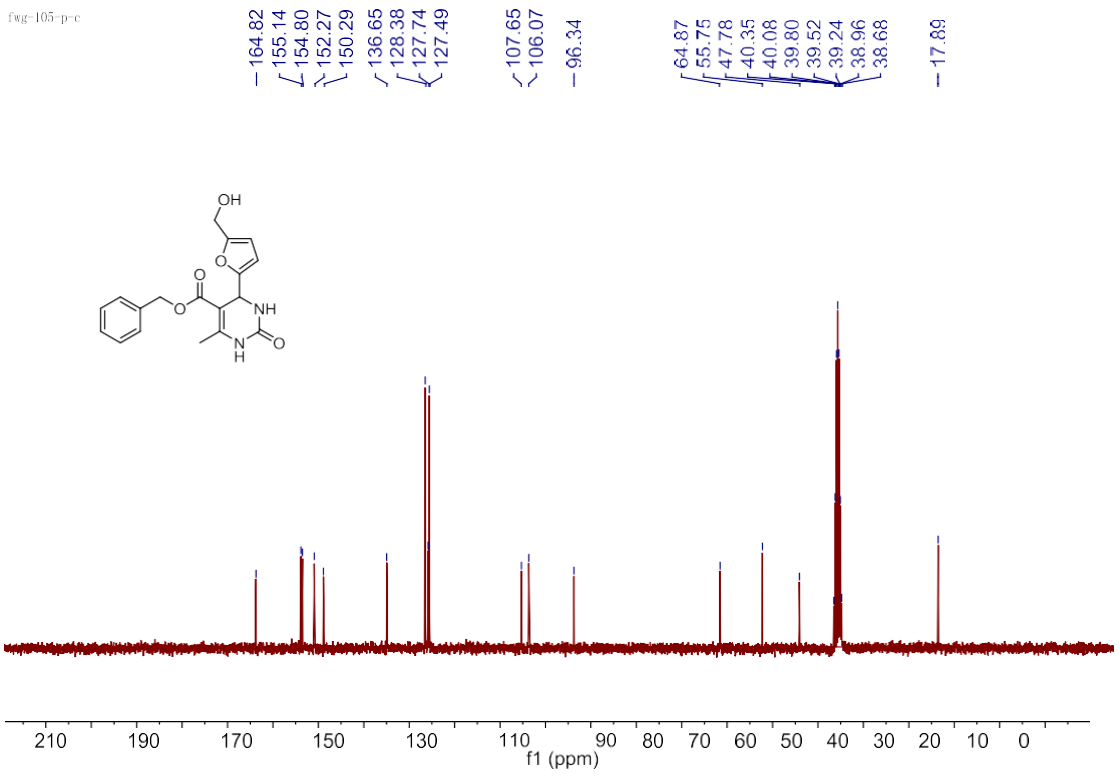
***tert*-Butyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4f)**



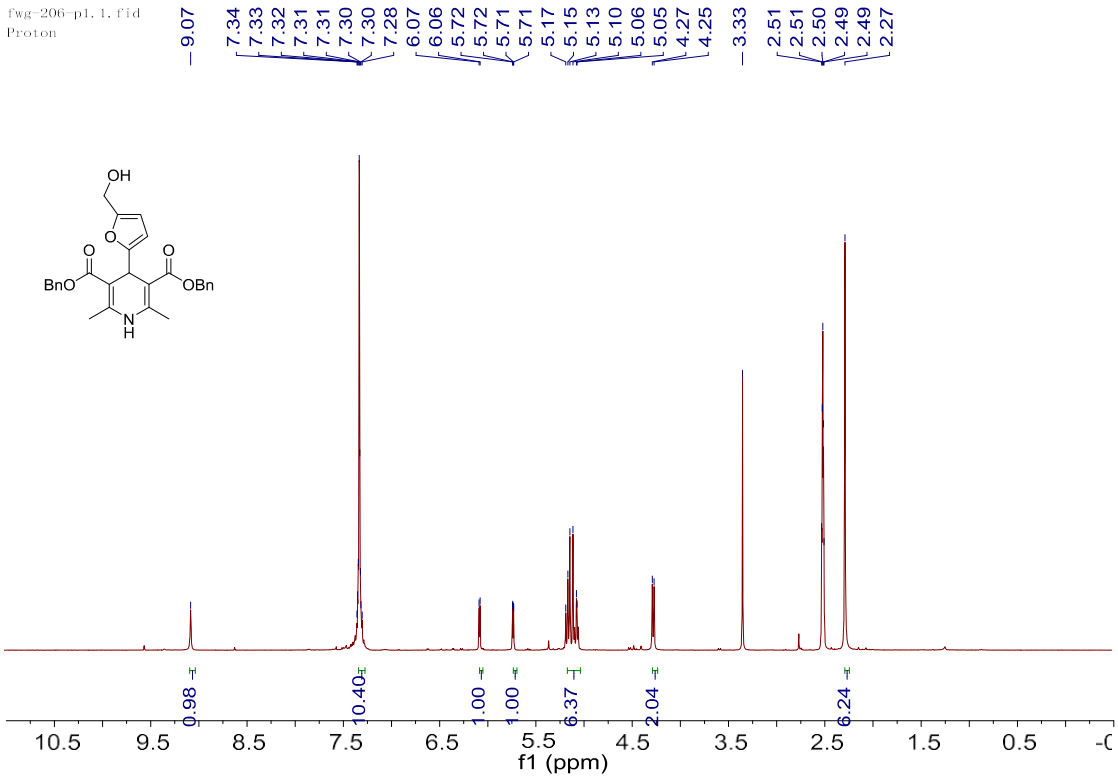


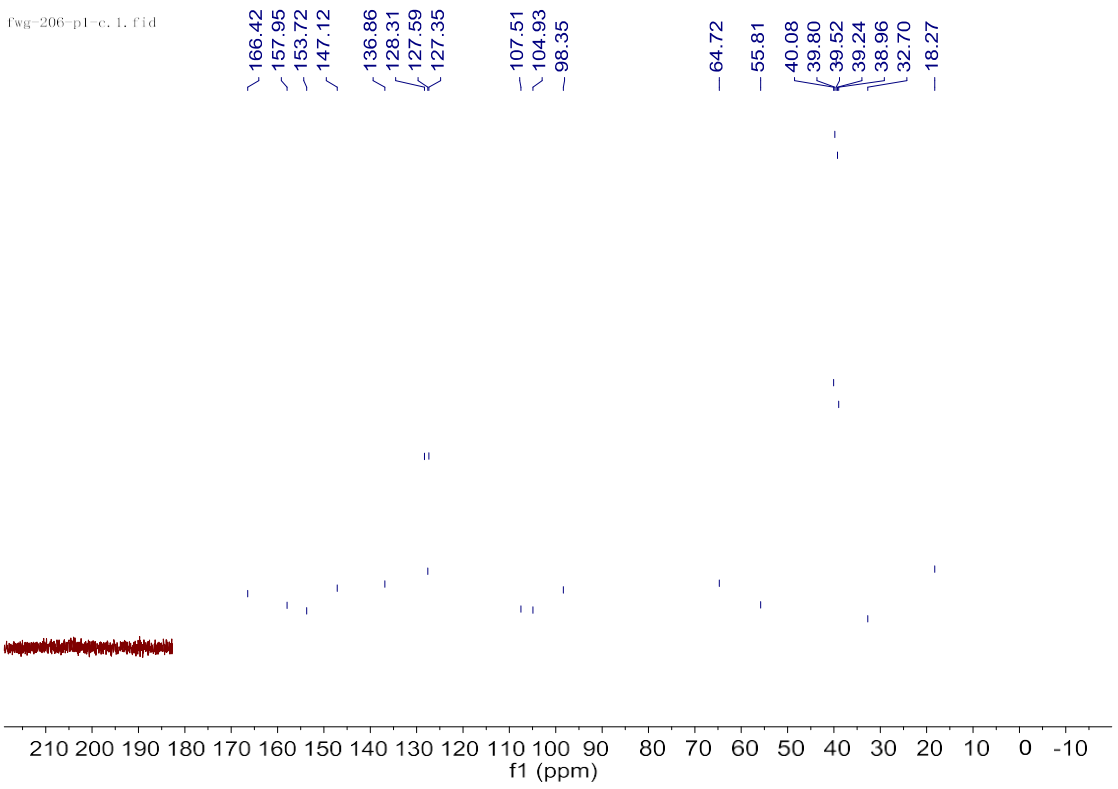
Benzyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4g)



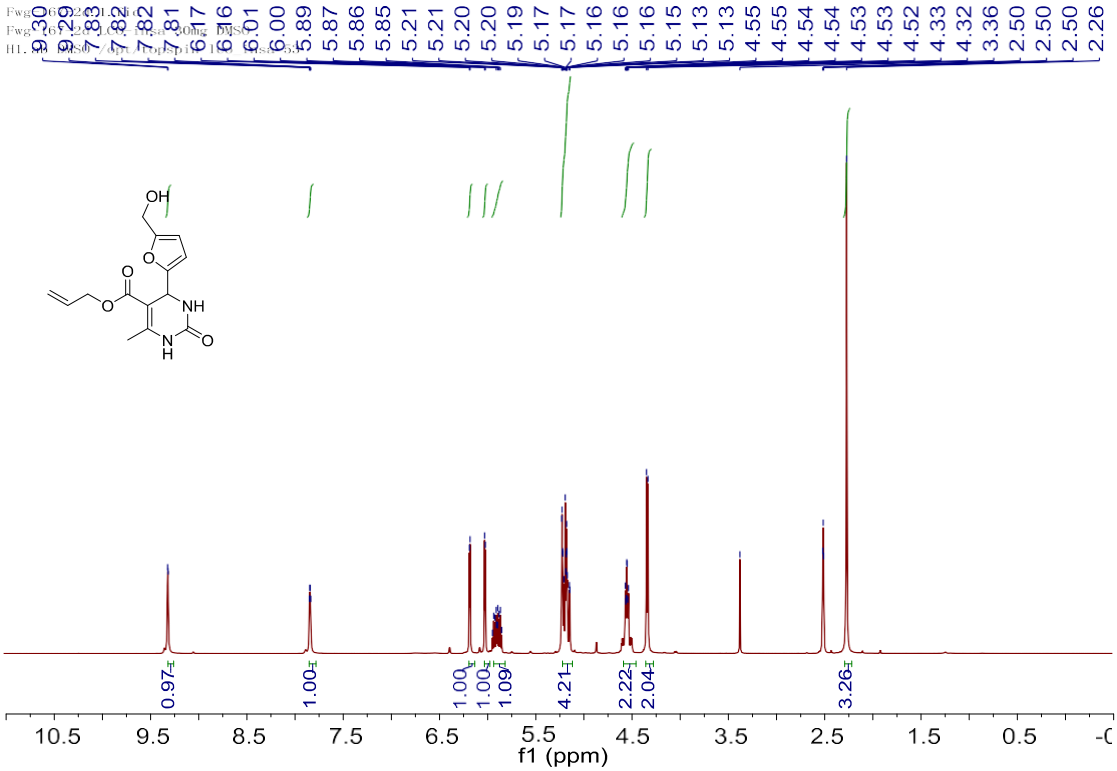


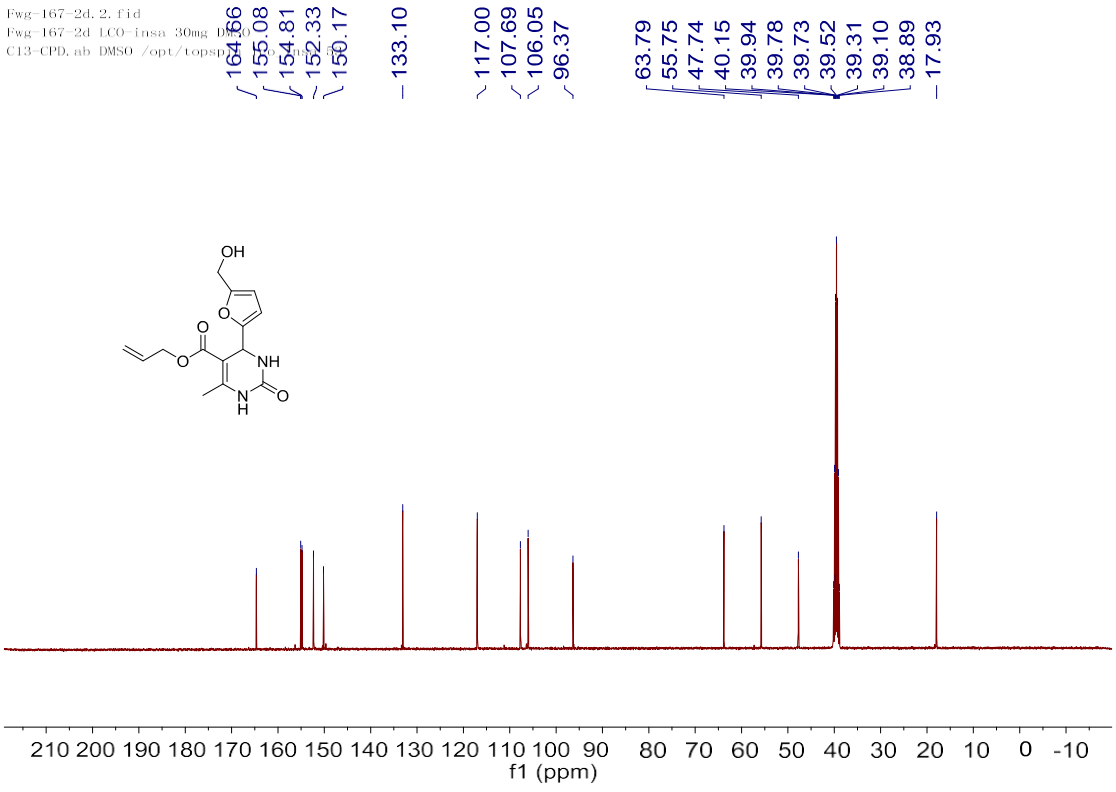
Dibenzyl
4-[5'-(hydroxymethyl)furan-2'-yl]-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (4g')



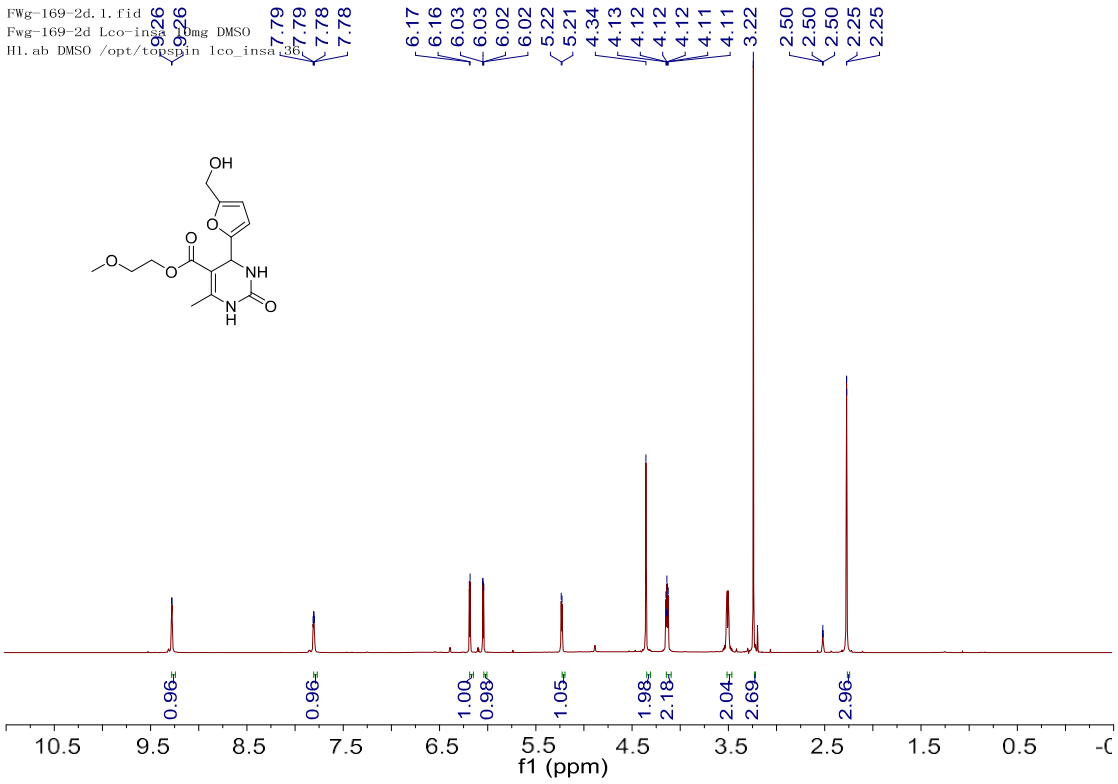


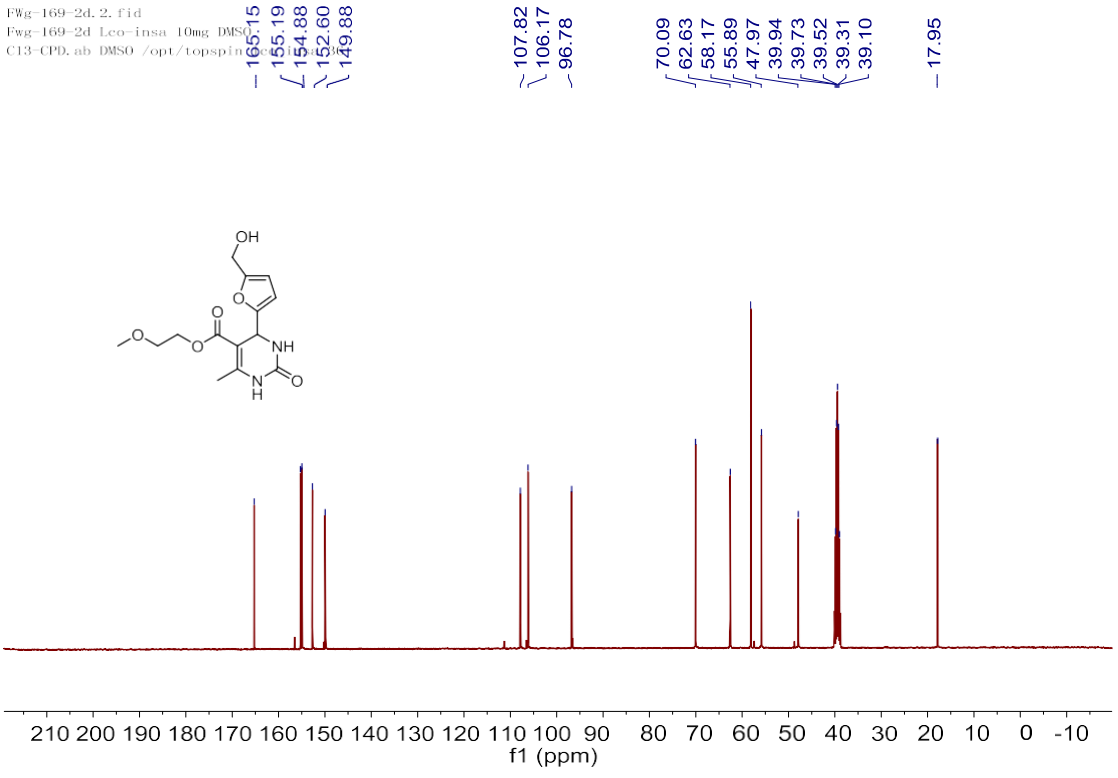
Allyl 4-(5-(hydroxymethyl)furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4h)



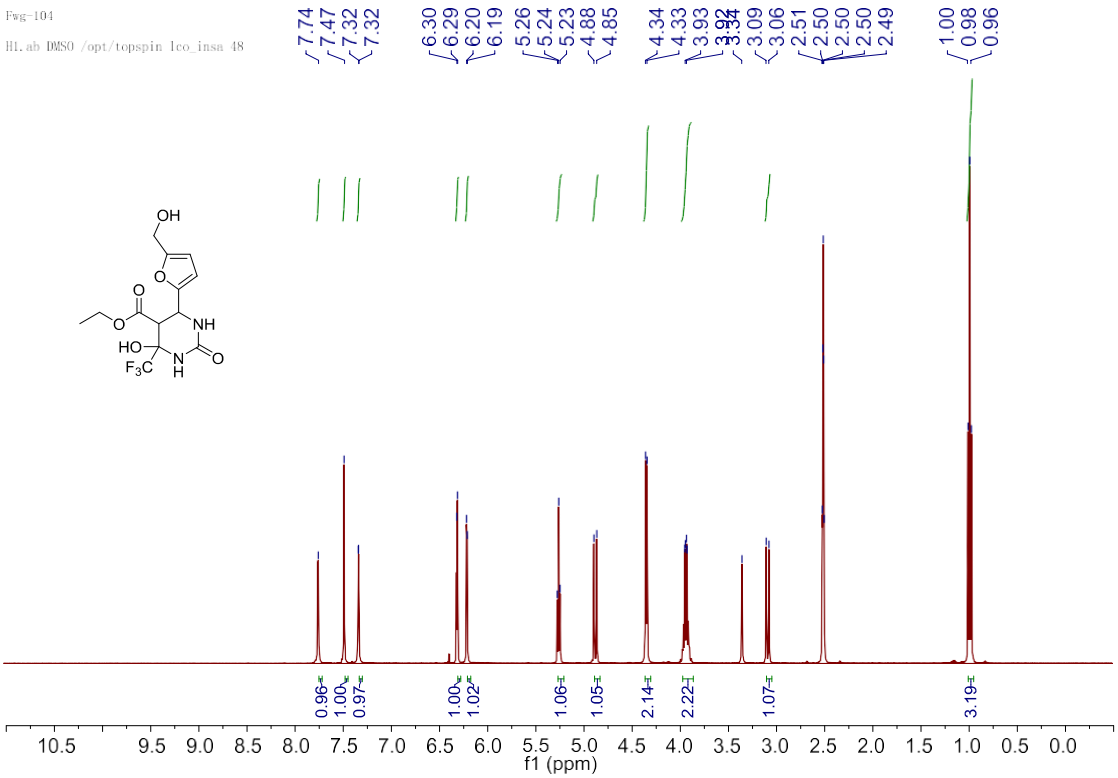


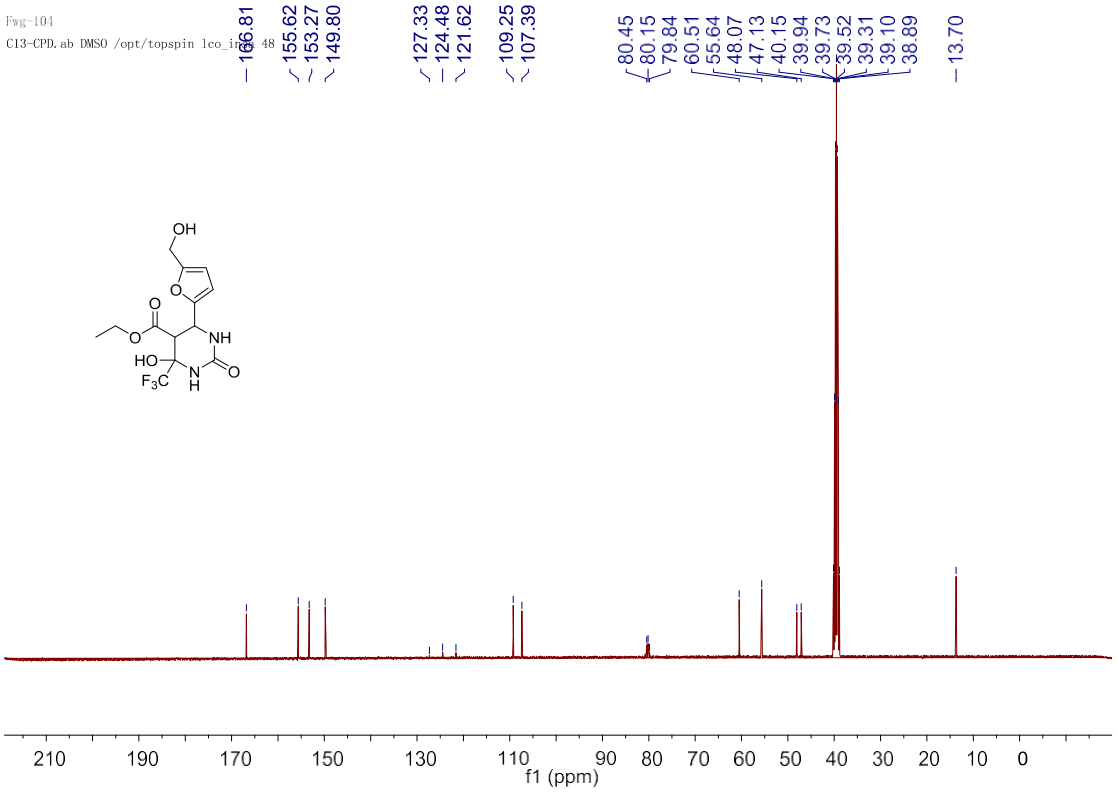
2-Methoxyethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4i)

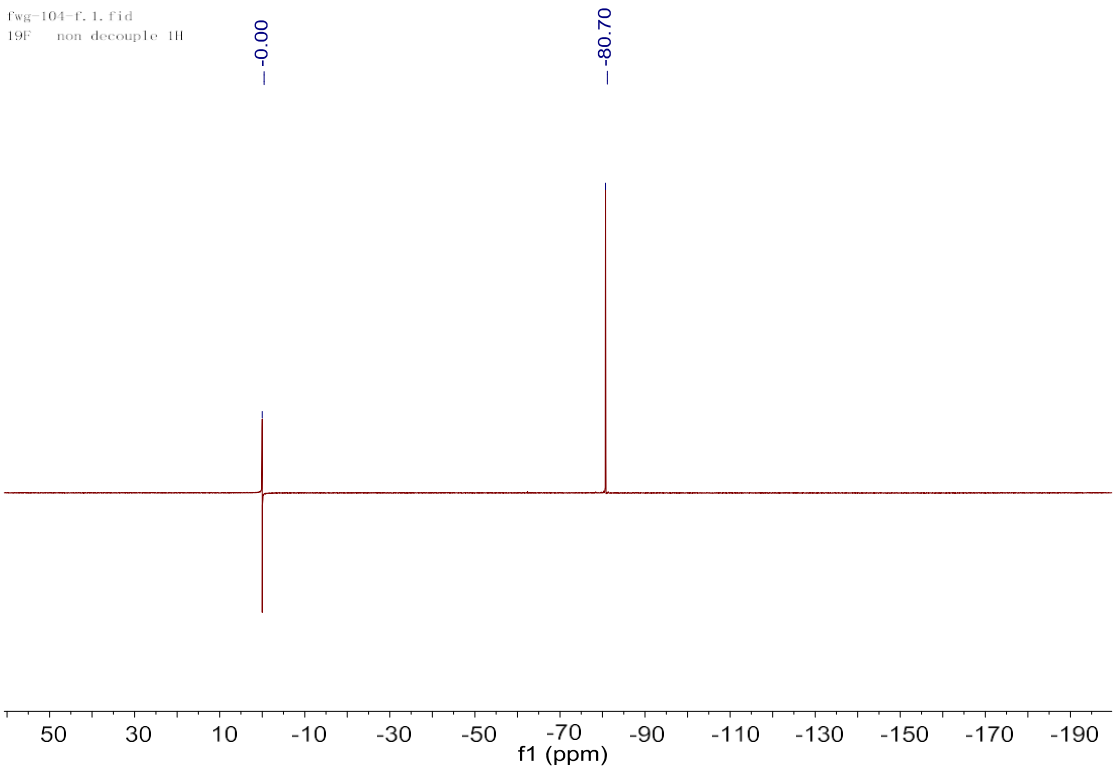




Ethyl
4-hydroxy-6-[5-(hydroxymethyl)furan-2-yl]-2-oxo-4-(trifluoromethyl)hexahydropyrimidine-5-carboxylate (4j)



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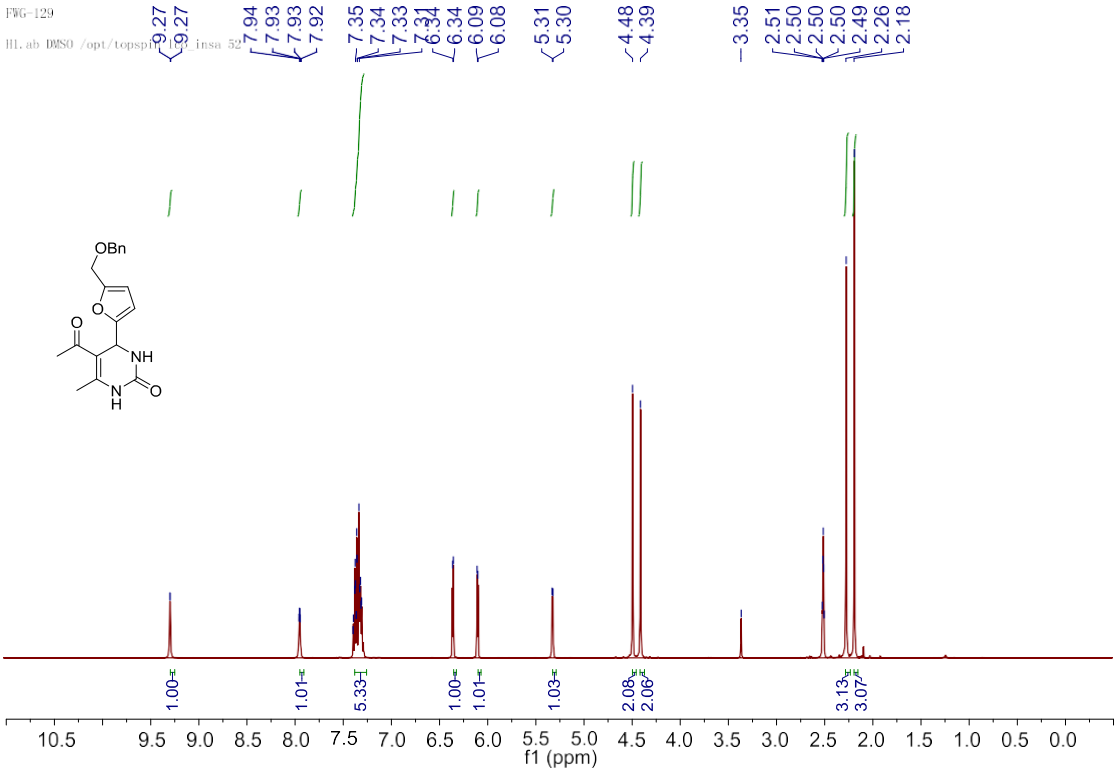
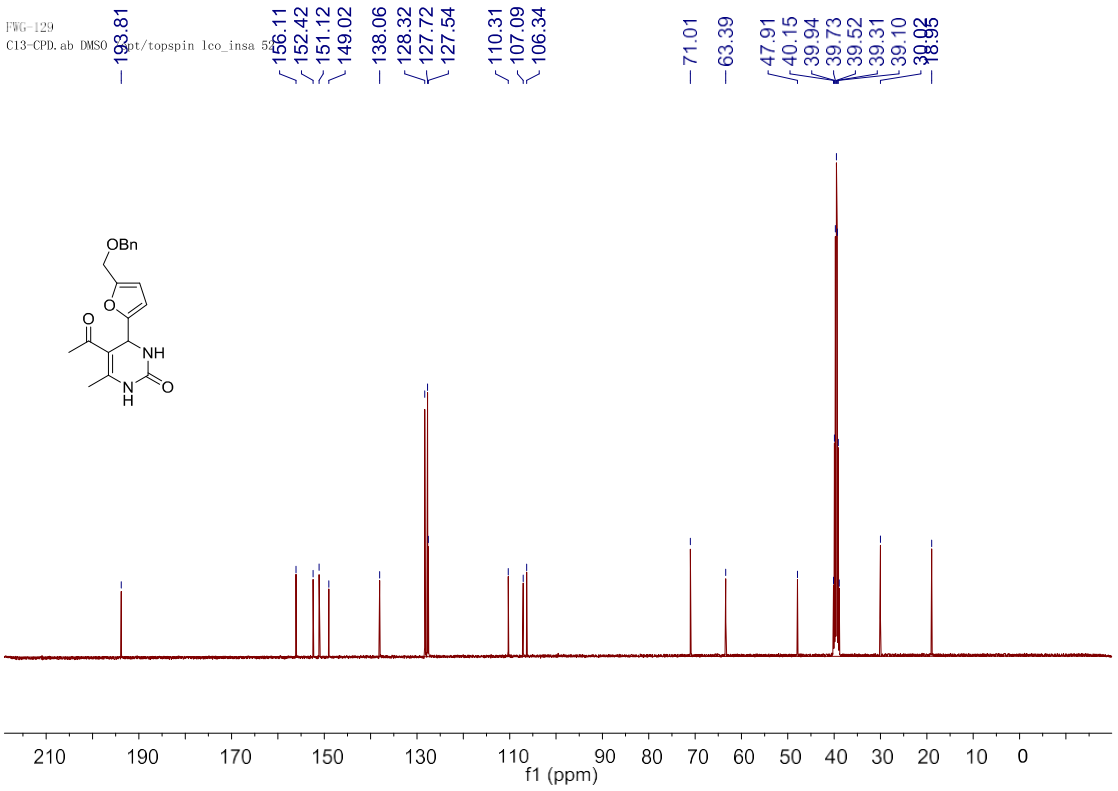
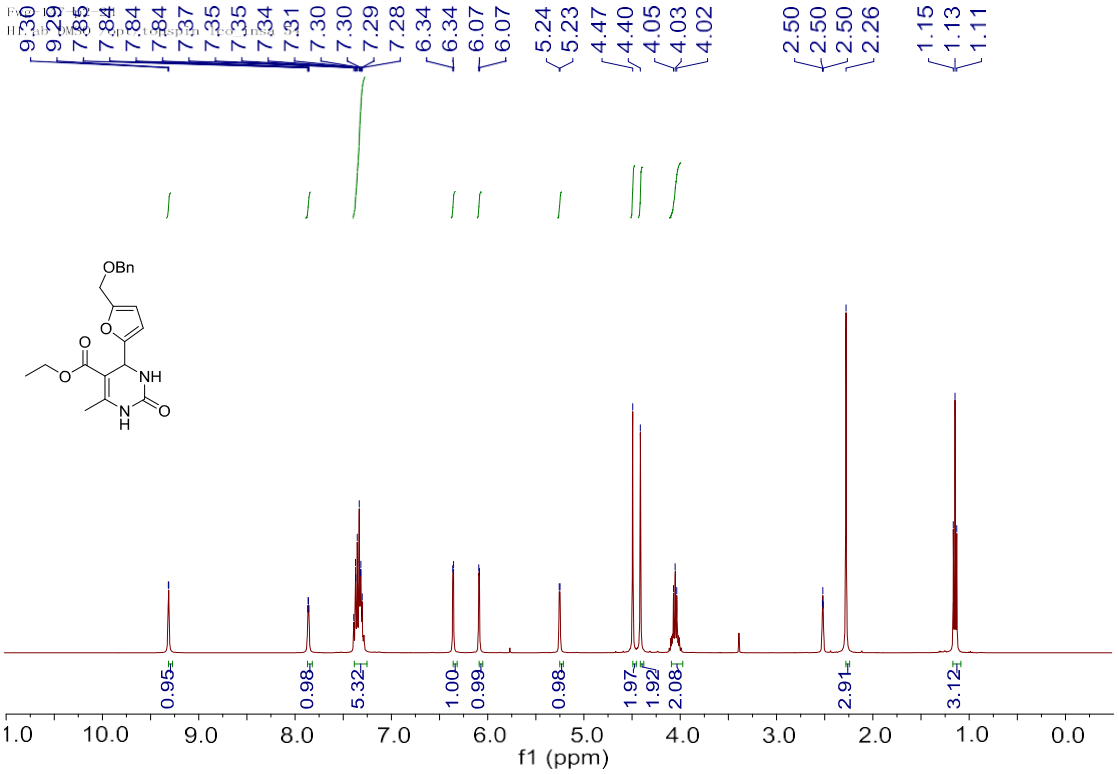
-130
-150
-170
-190
f1 (ppm)

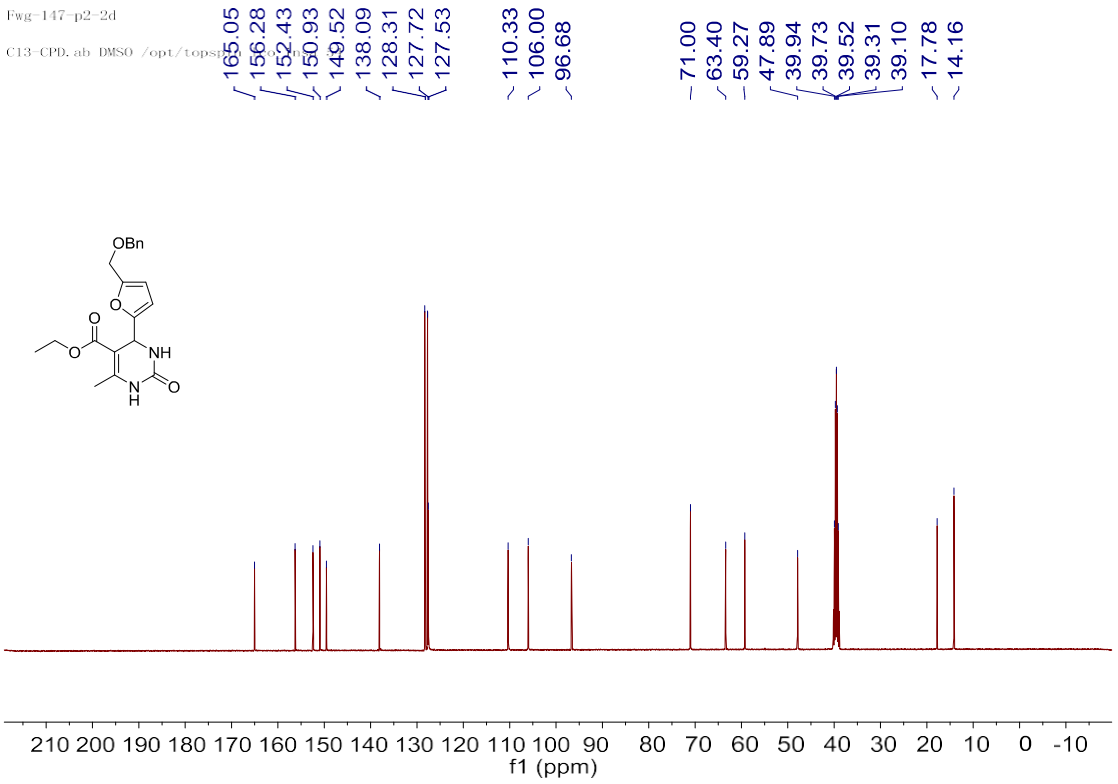
5-Acetyl-4-[5'-((benzyloxy)methyl)furan-2'-yl]-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (4k)



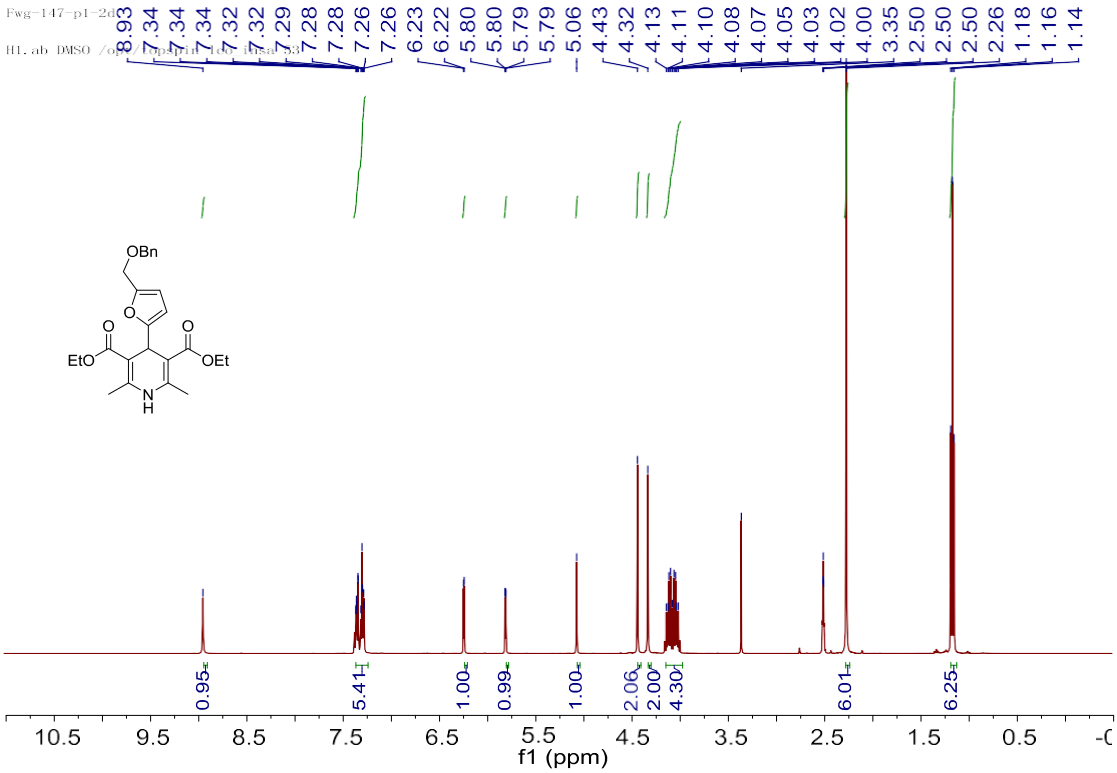


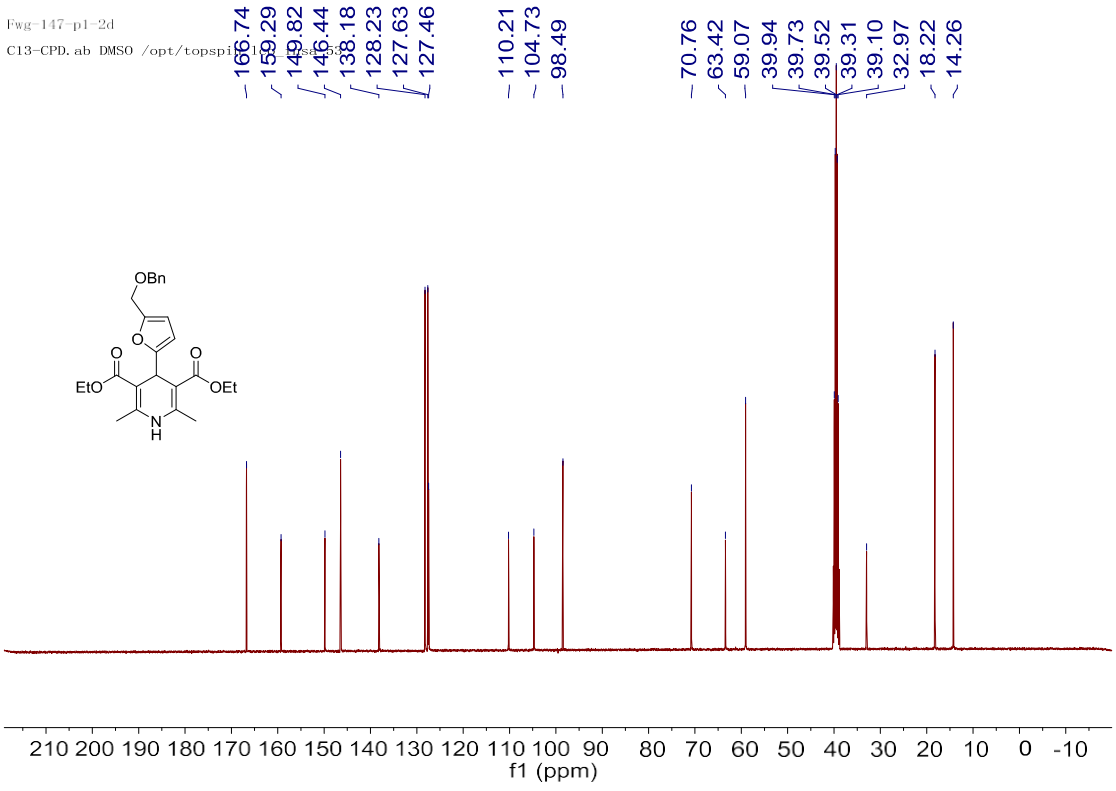
Ethyl 4-[5'-((benzyloxy)methyl)furan-2'-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4l)



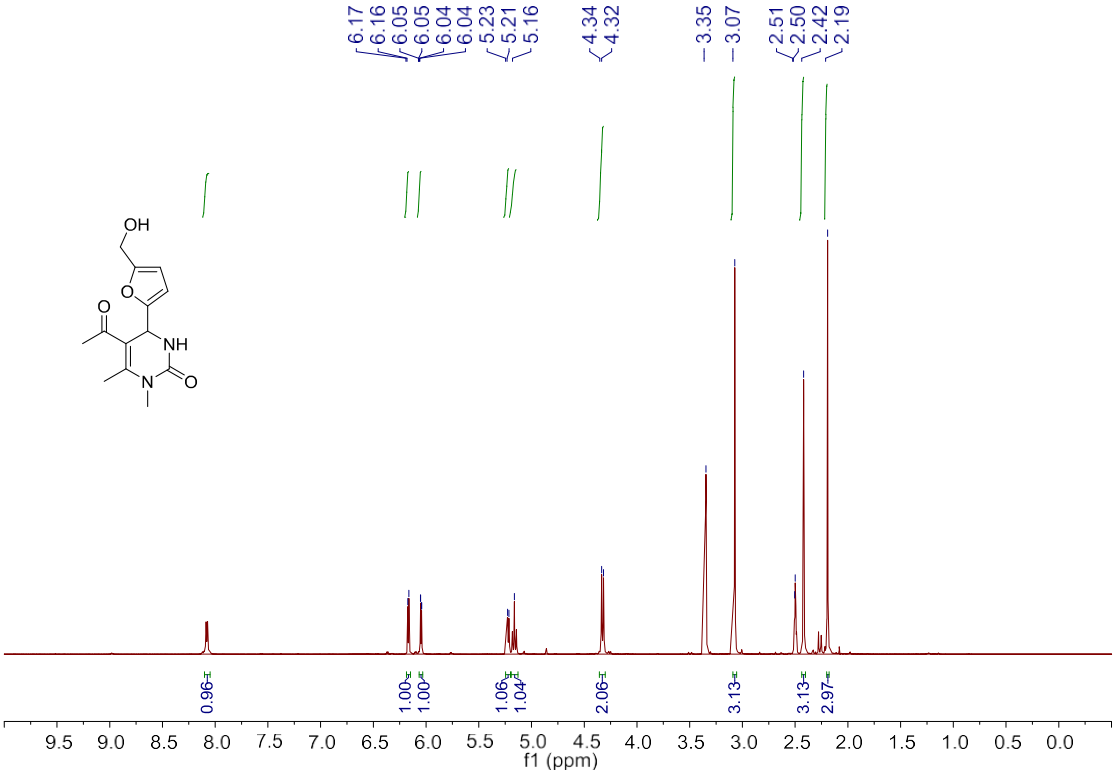


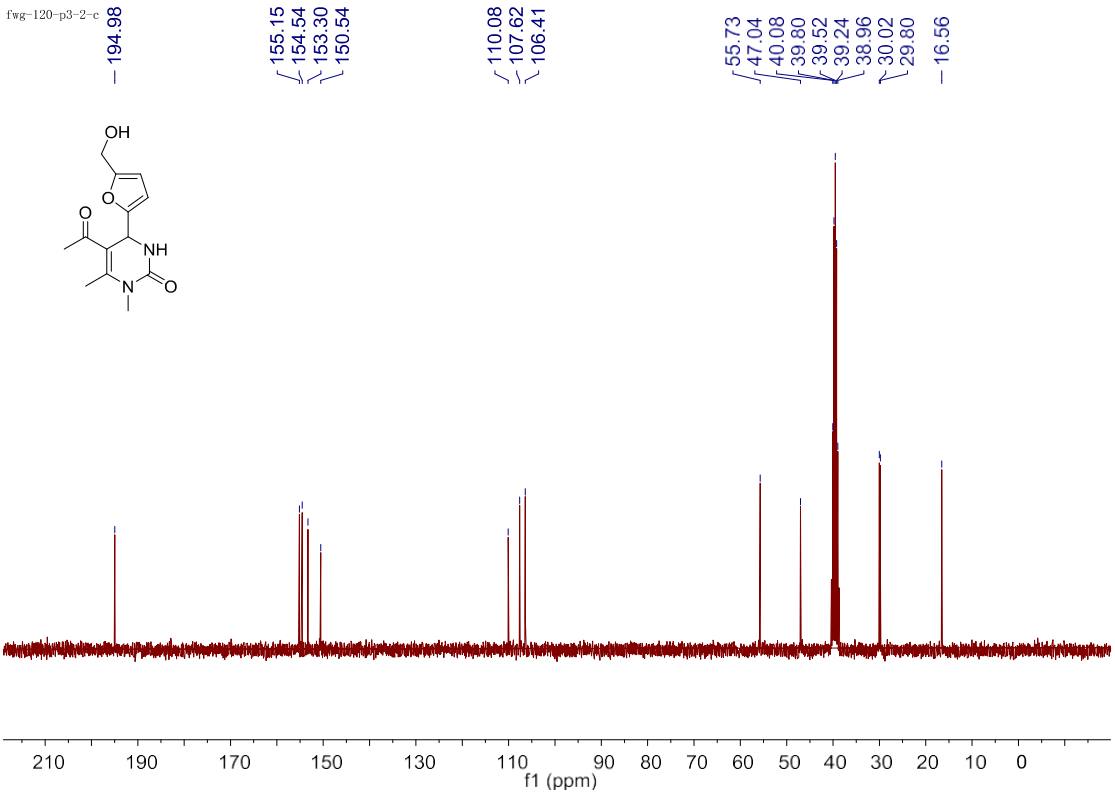
Diethyl 4-[5'-((benzyloxy)methyl)furan-2'-yl]-2,6-dimethyl-1,4-dihydropyridine-3,5 -dicarboxylate (4l')



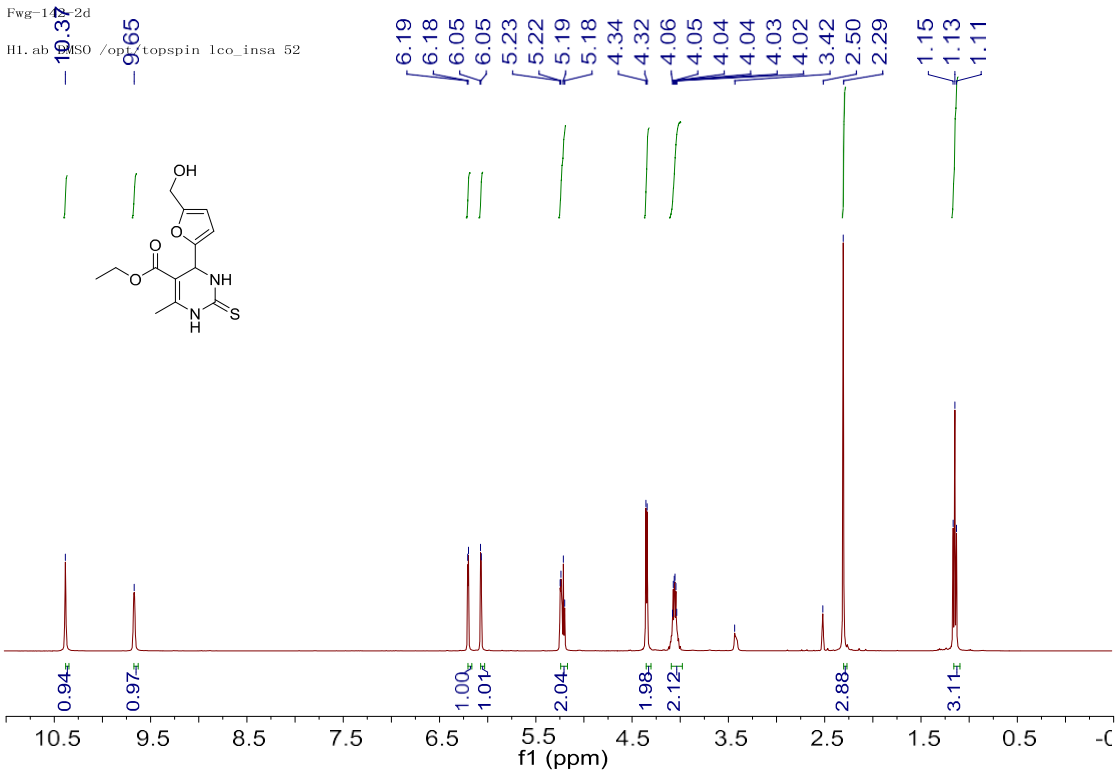


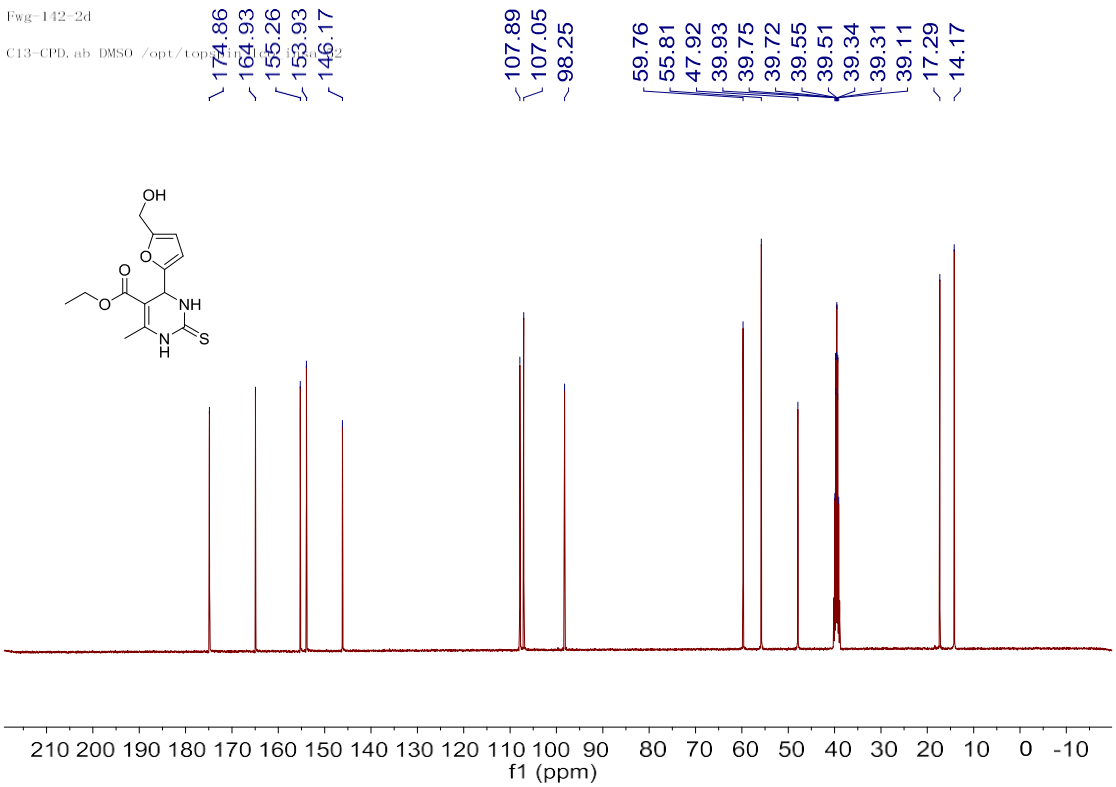
5-Acetyl-4-[5'-(hydroxymethyl)furan-2'-yl]-1,6-dimethyl-3,4-dihydropyrimidin-2(1*H*)-one (4m)



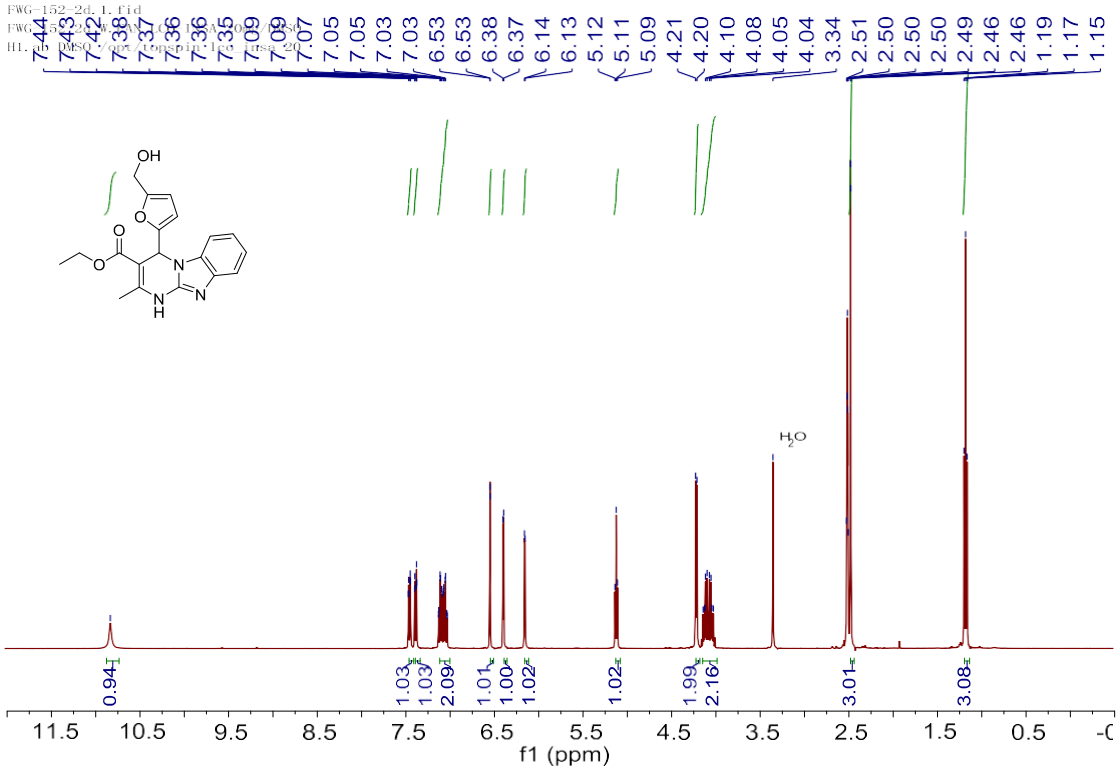


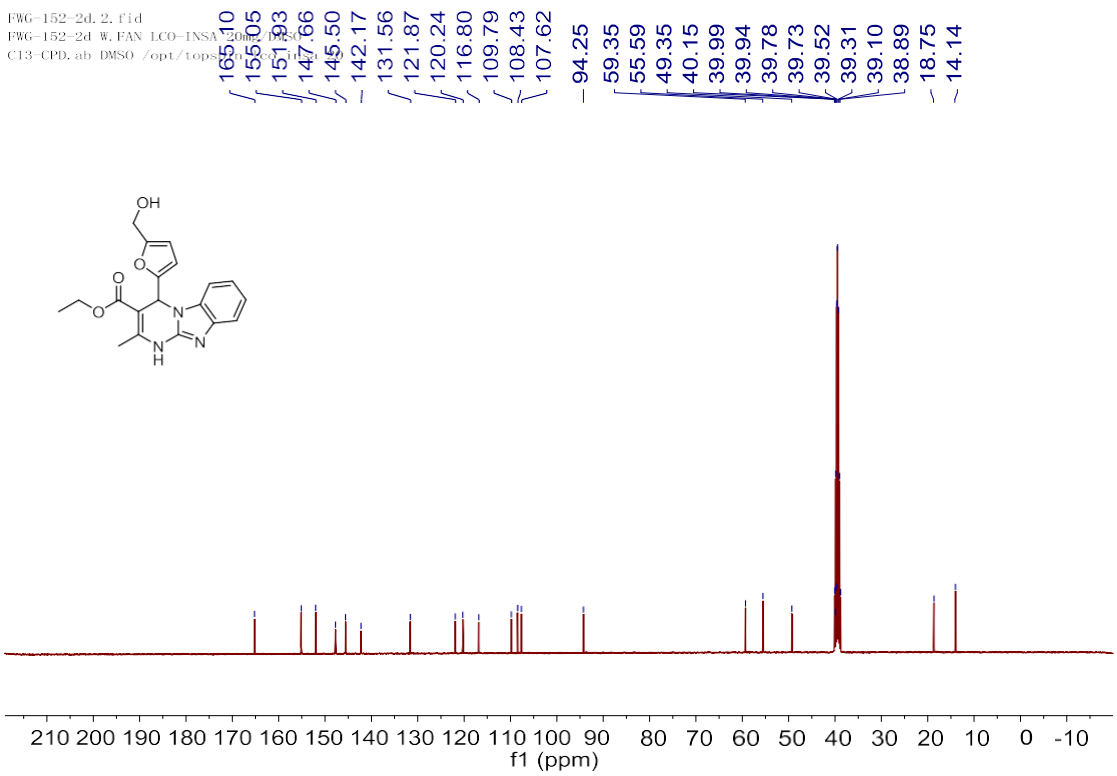
Ethyl 4-[5’-(hydroxymethyl)furan-2’-yl]-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine -5-carboxylate (4n)





Ethyl 4-[5'-(hydroxymethyl)furan-2'-yl]-2-methyl-1,4-dihydrobenzo[4,5]imidazo[1,2-*a*] pyrimidine-3-carboxylate (4o):





Ethyl 7-[5'-(hydroxymethyl)furan-2'-yl]-5-methyl-4,7-dihydro-[1,2,4]triazolo[1,5-*a*] pyrimidine-6-carboxylate (4p)