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SUPPLEMENTARY MATERIAL TO

Synthesis, antimycobacterial and antifungal evaluation of new 4-(furan-2-ylmethyl)-6-methylpyridazin-3(*2H*)-ones

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*4-(2-Furylmethyl)-6-methylpyridazin-3(2*H*)-one (**2**)*. m.p. 126–127 °C. IR; 3124 (N–H), 2960, 2842 (C–H), 1648 (C=O), 1609, 1562, 1505, 1473, 1434 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 400 MHz); δ 2.18 (3H; s; –CH_3), 3.80 (2H; s; –CH_2-), 6.20 (1H; d; furan H_3, J= 3.2 Hz), 6.39 (1H; dd; furan H_4, J_1 = 3.2 Hz, J_2 = 2 Hz), 6.98 (1H; s; pyridazinone H_5), 7.56 (1H; d; furan H_5, J = 1.6 Hz), 12.76 (1H; s; NH) ppm. ^{13}C-NMR (DMSO-d_6, 100 MHz); δ 20.21 (CH_3), 27.20 (CH_2), 107.38, 110.61 (furan C_3, C_4), 131.08 (pyridazinone C_5), 139.11 (pyridazinone C_4), 142.17 (furan C_5), 144.11 (pyridazinone C_6), 150.89 (furan C_2), 160.18 (pyridazinone CO) ppm. ESI-MS (*m/z*): 191.27 $[M+H]^+$, 213.27 $[M+Na]^+$ (100%). Anal. Calcd. For $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.96; H, 5.34; N, 14.70.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N-phenylacetamide (**5a**)*

Yield 45 %; m.p. 124–125 °C. IR; 3265 (N–H), 3088 (C–H), 1671, 1658 (C=O), 1613, 1600, 1553, 1501, 1446 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.30 (3H; s; –CH_3), 3.95 (2H; s; –CH_2–), 4.95 (2H; s; C$\underline{H}_2$CONH), 6.21 (1H; d; furan H_3, J = 3.2 Hz), 6.35–6.36 (1H; dd; furan H_4, J_1 = 3 Hz, J_2 = 2 Hz), 6.85 (1H; s; pyridazinone H_5), 7.05 (1H; t; Ar–$H_{4''}$), 7.23–7.27 (2H; m; Ar–$H_{3'',5''}$ ve $CHCl_3$), 7.38 (1H; dd; furan H_5, J_1 = 2 Hz, J_2 = 0.8 Hz), 7.48 (2H; d; Ar–$H_{2'',6''}$, J = 7.6 Hz), 8.95 (1H; s; NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.94 (CH_3), 28.34 (CH_2), 57.83 ($\underline{C}H_2CO$), 108.15, 110.63 (furan C_3, C_4), 119.83, 124.25, 128.84, 131.17, 137.70, 140.16, 142.26, 145.76 (aromatic carbons), 150.14 (furan C_2), 160.59 (pyridazinone CO), 165.19 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 324.34 $[M+H]^+$, 346.30 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{18}H_{17}N_3O_3$: C, 66.66; H, 5.30; N, 13.00. Found: C, 67.01; H, 5.43; N, 13.00.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--4-methylphenyl)acetamide (**5b**)*

Yield 39 %; m.p. 112 °C. IR; 3271 (N–H), 3072 (C–H), 1702, 1640 (C=O), 1607, 1546, 1515, 1446 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 400 MHz); δ 2.23 (3H; s; –CH_3), 2.25 (3H;

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s; –CH_3), 3.85 (2H; s; –CH_2–), 4.83 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J= 2.8 Hz), 6.40–6.42 (1H; dd; furan H_4, J_1 = 3.2 Hz, J_2 = 2 Hz), 7.05 (1H; s; pyridazinone H_5), 7.11 (2H; d; Ar–$H_{3'',5''}$, J = 8.4 Hz), 7.45 (2H; d; Ar–$H_{2'',6''}$, J = 8.8 Hz), 7.58 (1H; d; furan H_5, J = 1.2 Hz), 10.18 (1H; s; NH) ppm. ^{13}C-NMR (DMSO-d_6, 100 MHz); δ 20.27, 20.40 (CH_3), 27.59 (CH_2), 54.73 ($\underline{C}H_2$CO), 107.54, 110.64 (furan C_3, C_4), 119.00, 129.15, 130.93, 132.27, 136.22, 138.79, 142.24, 143.85 (aromatic carbons), 150.73 (furan C_2), 159.09 (pyridazinone CO), 164.90 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 338.35 $[M+H]^+$, 360.31 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 12.46. Found: C, 67.42; H, 5.74; N, 12.41.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(4-methoxyphenyl)acetamide (**5c**)*

Yield 38 %; m.p. 73 °C. IR; 3268 (N–H), 1649 (C=O), 1600, 1546, 1463, 1440, 1415 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 400 MHz); δ 2.23 (3H; s; –CH_3), 3.72 (3H; s; –OCH_3), 3.85 (2H; s; –CH_2–), 4.81 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J = 3.2 Hz), 6.41 (1H; t; furan H_4,), 6.88 (2H; d; Ar–$H_{3'',5''}$, J =9.2 Hz), 7.05 (1H; s; pyridazinone H_5), 7.48 (2H; d; Ar–$H_{2'',6''}$, J = 9.2 Hz), 7.58 (1H; m; furan H_5,), 10.12 (1H; s; NH) ppm. ^{13}C-NMR (DMSO--d_6, 100 MHz); δ 20.27 (CH_3), 27.60 (CH_2), 54.66 ($\underline{C}H_2$CO), 55.12 (OCH_3), 107.54, 110.64 (furan C_3, C_4), 113.89, 120.51, 130.91, 131.88, 138.79, 142.24, 143.83, 155.25 (aromatic carbons), 150.74 (furan C_2), 159.09 (pyridazinone CO), 164.65 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 354.29 $[M+H]^+$, 376.26 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.31; H, 5.56; N, 11.66.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(4-nitrophenyl)acetamide (**5d**)*

Yield 37 %; m.p. 165-166 °C. IR; 3227 (N–H), 1719, 1648 (C=O), 1595, 1576, 1503 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.35 (3H; s; –CH_3), 3.97 (2H; s; –CH_2–), 5.02 (2H; s; C$\underline{H}_2$CONH), 6.20 (1H; dd; furan H_3, J_1 = 3.2 Hz, J_2 = 0.8 Hz), 6.36 (1H; dd; furan H_4, J_1 = 1.6 Hz, J_2 = 0.8 Hz), 6.98 (1H; s; pyridazinone H_5), 7.37 (1H; dd; furan H_5, J_1 = 1.6 Hz, J_2 = 0.8 Hz), 7.48–7.52 (2H; m; Ar–$H_{2'',6''}$), 7.96-8.00 (2H; m; Ar–$H_{3'',5''}$), 9.95 (1H; s; NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.95 (CH_3), 28.48 (CH_2), 58.09 ($\underline{C}H_2$CO), 108.12, 110.68 (furan C_3, C_4), 119.10, 124.64, 131.95, 139.83, 142.35, 143.28, 143.62, 146.33 (aromatic carbons), 149.91 (furan C_2), 160.77 (pyridazinone CO), 165.79 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 369.27 $[M+H]^+$, 391.21 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{18}H_{16}N_4O_5$: C, 58.69; H, 4.38; N, 15.21. Found: C, 58.26; H, 4.25; N, 15.11.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(4-chlorophenyl)acetamide (**5e**)*

Yield 46 %; m.p. 131 °C. IR; 3277 (N–H), 3082 (C–H), 1708, 1649 (C=O), 1551, 1489, 1421, 1400 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 400 MHz); δ 2.24 (3H; s; –CH_3), 3.85 (2H; s; –CH_2–), 4.85 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J = 3.2 Hz), 6.40–6.41 (1H; dd; furan H_4, J_1 = 3.2 Hz, J_2 = 2 Hz), 7.06 (1H; s; pyridazinone H_5), 7.37 (2H; d; Ar–$H_{3'',5''}$, J = 8.8 Hz), 7.58–7.61 (3H; m; Ar–$H_{2'',6''}$ and furan H_5,), 10.43 (1H; s; NH) ppm. ^{13}C-NMR (DMSO-d_6, 100 MHz); δ 20.24 (CH_3), 27.59 (CH_2), 54.86 ($\underline{C}H_2$CO), 107.54, 110.64 (furan C_3, C_4), 120.57, 126.95, 128.71, 131.02, 137.66, 138.80, 142.25, 143.95 (aromatic carbons), 150.71 (furan C_2), 159.08 (pyridazinone CO), 165.37 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 358.24 $[M+H]^+$, 380.21 $[M+Na]^+$ (% 100), 382.20 $[M+Na+2]^+$. Anal. calcd. for $C_{18}H_{16}ClN_3O_3$: C, 60.42; H, 4.51; N, 11.74. Found: C, 60.12; H, 4.43; N, 11.66.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(4-fluorophenyl)acetamide (**5f**)*

Yield 55 %; m.p. 132 °C. IR; 3294 (N–H), 3095 (C–H), 1703, 1645 (C=O), 1598, 1557, 1537, 1409 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 400 MHz); δ 2.24 (3H; s; –CH_3), 3.85 (2H; s; –CH_2–), 4.85 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J = 2.8 Hz), 6.40–6.41 (1H; dd; furan H_4, J_1 = 2.6 Hz, J_2 = 1.6 Hz), 7.06 (1H; s; pyridazinone H_5), 7.13–7.18 (2H; t; Ar–$H_{3'',5''}$), 7.57–7.60 (3H; m; Ar–$H_{2'',6''}$ and furan H_5), 10.34 (1H; s; NH) ppm. ^{13}C-NMR (DMSO-d_6, 100 MHz); δ 20.26 (CH_3), 27.59 (CH_2), 54.75 ($\underline{C}H_2$CO), 107.54, 110.64 (furan C_3, C_4), 115.36, 120.76, 130.99, 135.11, 138.80, 142.24, 143.92, 156.83 (aromatic carbons), 150.72 (furan C_2), 159.14 (pyridazinone CO), 165.12 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 342.29 $[M+H]^+$, 364.26 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{18}H_{16}FN_3O_3$: C, 63.34; H, 4.72; N, 12.31. Found: C, 63.23; H, 4.79; N, 12.15.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(3-chloro-4-fluorophenyl)acetamide (**5g**)*

Yield 39 %; m.p. 140–141 °C. IR; 3280 (N–H), 3076 (C–H), 1711, 1644 (C=O), 1593, 1555, 1538, 1400 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.32 (3H; s; –CH_3), 3.95 (2H; s; –CH_2–), 4.95 (2H; s; C$\underline{H}_2$CONH), 6.19 (1H; dd; furan H_3, J_1 = 3 Hz, J_2 = 0.6 Hz), 6.35 (1H; dd; furan H_4, J_1 = 3 Hz, J_2 = 1.8 Hz), 6.92 (2H; ; pyridazinone H_5 and Ar–$H_{6''}$), 7.13–7.15 (1H; m; Ar–$H_{5''}$), 7.37 (1H; dd; furan H_5, J_1 = 2 Hz, J_2 = 0.8 Hz), 7.63 (1H; dd; Ar–$H_{2''}$, J_1 = 6.8 Hz J_2 = 2.4 Hz), 9.41 (1H; s; NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.92 (CH_3), 28.42 (CH_2), 57.84 ($\underline{C}H_2$CO), 108.09, 110.64 (furan C_3, C_4), 116.20, 119.16, 120.74, 121.64, 131.60, 134.46, 139.89, 142.27, 146.00, 153.27, 155.71 (aromatic carbons), 150.02 (furan C_2), 160.64 (pyridazinone CO), 165,24 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 398.18 $[M+Na]^+$ (% 100), 400.17 $[M+Na+2]^+$. Anal. calcd. for $C_{18}H_{15}ClFN_3O_3$: C, 57.53; H, 4.02; N, 11.18. Found: C, 57.41; H, 3.91; N, 11.06.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(naphthalen-1-yl)acetamide (**5h**)*

Yield 41 %; m.p. 165 °C. IR; 3303 (N–H), 2956 (C–H), 1671, 1651 (C=O), 1603, 1544, 1504, 1467, 1434 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.33 (3H; s; –CH_3), 4.01 (2H; s; –CH_2–), 5.10 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J = 3.2 Hz), 6.34 (1H; dd; furan H_4, J_1 = 3.4 Hz, J_2 = 2 Hz), 6.87 (1H; s; pyridazinone H_5), 7.36–7.37 (1H; dd; furan H_5, J_1 = 1.8 Hz, J_2 = 1.2 Hz), 7.43-7.56 (3H; m; Ar–H), 7.65 (1H; d; Ar–H J = 8.4 Hz), 7.84 (1H; d; Ar–H J = 7.6 Hz), 7.98 (1H; d; Ar–H J = 8.4 Hz), 8.14 (1H; d; Ar–H J = 7.2 Hz), 9.39 (1H; s; NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.96 (CH_3), 28.29 (CH_2), 58.34 ($\underline{C}H_2$CO), 108.22, 110.65 (furan C_3, C_4), 119.21, 120.73, 125.26, 125.74, 125.91, 126.12, 126.37, 128.64, 131.28, 132.47, 133.96, 140.36, 142.31, 146.10 (aromatic carbons), 150.05 (furan C_2), 160.80 (pyridazinone CO), 165,79 ($\underline{C}$ONH) ppm. ESI-MS (*m/z*): 374.29 $[M+H]^+$, 396.25 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25. Found: C, 70.47; H, 5.14; N, 11.23.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--((1,1'-biphenyl)-2-yl)acetamide (**5i**)*

Yield 45 %; m.p. 158–159 °C. IR; 3288 (N–H), 3045 (C–H), 1697, 1642 (C=O), 1522, 1475, 1449, 1437, 1418 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.14 (3H; s; –CH_3), 3.82 (2H; s; –CH_2–), 4.79 (2H; s; C$\underline{H}_2$CONH), 6.22 (1H; d; furan H_3, J = 3.2 Hz), 6.39 (1H; dd; furan H_4, J_1 = 3 Hz, J_2 = 1.8 Hz), 6.66 (1H; s; pyridazinone H_5), 7.14–7.19 (2H; m; Ar–H), 7.23–7.26 (2H; m; Ar–H), 7.34–7.38 (4H; m; Ar–H), 7.43 (1H; m; furan H_5), 7.75

(1H; s; NH), 8.36 (1H; d; Ar–H J =8.4 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.92 (CH_3), 28.15 (CH_2), 56.20 ($\underline{C}H_2CO$), 108.32, 110.70 (furan C_3, C_4), 121.30, 124.51, 127.75, 128.44, 128.84, 129.17, 130.03, 130.50, 132.38, 134.28, 137.97, 140.35, 142.29, 145.50 (aromatic carbons), 150.12 (furan C_2), 159.74 (pyridazinone CO), 165.03 ($\underline{C}ONH$) ppm. ESI-MS (*m/z*): 400.27 $[M+H]^+$, 422.25 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.08; H, 5.39; N, 10.30.

*2-[5-(Furan-2-ylmethyl)-3-methyl-6-oxopyridazin-1(6H)-yl]-N--(pyridin-2-yl)acetamide (**5j**)*

Yield 44 %; m.p. 178 °C. IR; 3264 (N–H), 3087, 2983, 2949 (C–H), 1671, 1658 (C=O), 1613, 1600, 1553, 1501, 1445 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.28 (3H; s; $-CH_3$), 3.97 (2H; s; $-CH_2-$), 4.99 (2H; s; $C\underline{H}_2CONH$), 6.21 (1H; dd; furan H_3, J_1 = 3.2 Hz, J_2 = 0.8 Hz), 6.36 (1H; dd; furan H_4, J_1 = 3 Hz, J_2 = 2 Hz), 6.79 (1H; s; pyridazinone H_5), 7.03 (1H; ddd; Ar–H J_1 = 7.4 Hz, J_2 = 5 Hz, J_3 = 0.8 Hz), 7.39 (1H; m; furan $H_{5'}$), 7.68 (1H; ddd; Ar–H J_1 = 8.6 Hz, J_2 = 7.2 Hz, J_3 = 1.4 Hz), 8.19 (1H; d; Ar–H J = 8.4 Hz), 8.28 (1H; ddd; Ar–H; J_1 = 5.1 Hz, J_2 = 2 Hz, J_3 = 0.8 Hz), 9.18 (1H; s; NH) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 21.00 (CH_3), 28.23 (CH_2), 56.51 ($\underline{C}H_2CO$), 108.25, 110.61 (furan C_3, C_4), 114.37, 120.03, 130.80, 138.42, 140.56, 142.24, 145.55, 147.77, 150.25, 151.09 (aromatic carbons), 160.32 (pyridazinone CO), 165.57 ($\underline{C}ONH$) ppm. ESI-MS (*m/z*): 325.31 $[M+H]^+$, 347.27 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{17}H_{16}N_4O_3$: C, 62.95; H, 4.97; N, 17.27. Found: C, 62.66; H, 4.92; N, 16.97.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-phenylpiperazin--1-yl)ethyl]pyridazin-3(2H)-one (**6a**)*

Yield 40 %; m.p. 124 °C. IR; 3116, 2982, 2828 (C–H), 1647 (C=O), 1605, 1535, 1493, 1443 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 500 MHz); δ 2.22 (3H; s; $-CH_3$), 3.12–3.14 (4H; m; piperazine), 3.59–3.66 (4H; m; piperazine), 3.84 (2H; s; $-CH_2-$), 4.99 (2H; s; $C\underline{H}_2CO$), 6.22 (1H; d; furan H_3, J= 3.05), 6.41 (1H; m; furan $H_{4'}$), 6.83 (1H; m; Ar–H), 6.98 (2H; d; Ar–H J = 8.25), 7.05 (1H; s; pyridazinone H_5), 7.25 (2H; m; Ar–H), 7.58 (1H; s; furan $H_{5'}$) ppm. ^{13}C-NMR (DMSO-d_6, 125 MHz); δ 20.73 (CH_3), 28.14 (CH_2), 44.43, 48.88 (piperazine carbons), 53.25 ($\underline{C}H_2CO$), 108.00, 111.13 (furan C_3, C_4), 116.42, 119.88, 129.48, 131.35, 139.19, 142.72, 144.17 (aromatic carbons), 151.26 (furan C_2), 159.57 (pyridazinone CO), 165.20 ($CH_2\underline{C}ON$) ppm. ESI-MS (*m/z*): 393.31 $[M+H]^+$, 415.30 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{22}H_{24}N_4O_3$: C, 67.33; H, 6.16; N, 14.28. Found: C, 67.24; H, 6.10; N, 14.21.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-(4-methylphenyl)piperazin -1-yl)ethyl]pyridazin-3(2H)-one (**6b**)*

Yield 47 %; m.p. 140 °C. IR; 3127, 3105, 2982, 2810 (C–H), 1679, 1649 (C=O), 1605, 1537, 1512, 1445 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.27 (6H; d; $-CH_3$), 3.11–3.19 (4H; m; piperazine), 3.64–3.67 (2H; m; piperazine), 3.78–3.80 (2H; m; piperazine), 3.93 (2H; s; $-CH_2-$), 4.99 (2H; s; $C\underline{H}_2CO$), 6.19 (1H; d; furan H_3, J = 3.2), 6.35 (1H; dd; furan H_4, J_1 = 2.8 Hz, J_2 = 1.6 Hz), 6.78 (1H; s; pyridazinone H_5), 6.83–6.86 (2H; m; Ar–$H_{2'',6''}$), 7.10 (2H; d; Ar–$H_{3'',5''}$, J = 8 Hz), 7.38 (1H; m; furan $H_{5'}$) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.46 (CH_3), 21.00 (CH_3), 28.25 (CH_2), 42.10, 44.88, 50.00 (piperazine carbons), 52.96 ($\underline{C}H_2CO$), 108.06, 110.58 (furan C_3, C_4), 117.16, 130.23, 140.08, 142.11, 144.67, 148.77 (aromatic carbons), 150.57 (furan C_2), 160.04 (pyridazinone CO), 164.71 ($CH_2\underline{C}ON$) ppm. ESI-MS (*m/z*): 429,28 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{23}H_{26}N_4O_3$: C, 67.96; H, 6.45; N, 13.78. Found: C, 67.83; H, 6.51; N, 13.68.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-(4-methoxyphenyl)piperazin--1-yl)ethyl]pyridazin-3(2H)-one (**6c**)*

Yield 47 %; m.p. 121–122 °C. IR; 3047, 2996, 2838 (C–H), 1671, 1641 (C=O), 1599, 1510, 1463, 1447 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.26 (–CH_3), 3.04–3.12 (4H; m; piperazine), 3.64–3.66 (2H; m; piperazine), 3.77–3.80 (5H; m; piperazine and –OCH_3), 3.93 (2H; s; –CH_2–), 4.99 (2H; s; CH_2CO), 6.19 (1H; d; furan H_3, J = 2.8 Hz), 6.35 (1H; dd; furan H_4, J_1 = 3 Hz, J_2 = 1.8 Hz), 6.78 (1H; s; pyridazinone H_5), 6.84–6.92 (4H; m; Ar–H), 7.37 (1H; m; furan H_5,) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.98 (CH_3), 28.24 (CH_2), 42.22, 44.99, 50.93 (piperazine carbons), 52.96 (CH_2CO), 55.54 (OCH_3), 108.04, 110.57 (furan C_3, C_4), 114.54, 119.08, 130.58, 140.08, 142.10, 144.67, 145.18, 154.50 (aromatic carbons), 150.57 (furan C_2), 160.05 (pyridazinone CO), 164.71 (CH_2CON) ppm. ESI-MS (*m/z*): 423.42 $[M+H]^+$, 445.39 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{23}H_{26}N_4O_4$: C, 65.39; H, 6.20; N, 13.26 Found: C, 65.17; H, 6.20; N, 13.16.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-(4-nitrophenyl)piperazin--1-yl)ethyl]pyridazin-3(2H)-one (**6d**)*

Yield 51 %; m.p. 153–154 °C. IR; 2879 (C–H), 1673, 1650 (C=O), 1595, 1505, 1483, 1434 (C=N ve C=C). ^{1}H-NMR (DMSO-d_6, 500 MHz); δ 2.22 (3H; s; –CH_3), 3.52-3.54 (2H; m; piperazine), 3.62 (4H; m; piperazine), 3.72 (2H; m; piperazine), 3.84 (2H; s; –CH_2–), 5.00 (2H; s; CH_2CO), 6.22 (1H; dd; furan H_3, J_1 = 3.2 Hz, J_2 = 0.7 Hz), 6.41 (1H; dd; furan H_4, J_1 = 3.1 Hz, J_2 = 1.9 Hz), 7.03–7.05 (3H; m; pyridazinone H_5 ve Ar–$H_{2'',6''}$), 7.58 (1H; dd; furan H_5, J_1 = 1.8 Hz, J_2 = 0.8 Hz), 8.09 (2H; m; Ar–$H_{3'',5''}$) ppm. ^{13}C-NMR (DMSO-d_6, 125 MHz); δ 20.72 (CH_3), 28.14 (CH_2), 43.71, 46.21, 46.42 (piperazine carbons), 53.25 (CH_2CO), 107.99, 111.13 (furan C_3, C_4), 113.06, 126.21, 131.37, 137.50, 139.20, 142.71, 144.20, 154.80 (aromatic carbons), 151.28 (furan C_2), 159.57 (pyridazinone CO), 165.52 (CH_2CON) ppm. ESI-MS (*m/z*): 460,38 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{22}H_{23}N_5O_5$: C, 60.40; H, 5.30; N, 16.01 Found: C, 60.35; H, 5.38; N, 15.79.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-(4-chlorophenyl)piperazin--1-yl)ethyl]pyridazin-3(2H)-one (**6e**)*

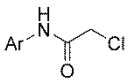
Yield 51 %; m.p. 146–147 °C. IR; 3047, 2935 (C–H), 1677, 1649 (C=O), 1537, 1497, 1467, 1451, 1432 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.25 (3H; s; –CH_3), 3.13–3.21 (4H; m; piperazine), 3.65–3.67 (2H; m; piperazine), 3.77–3.80 (2H; m; piperazine), 3.92 (2H; s; –CH_2–), 4.98 (2H; s; CH_2CO), 6.19 (1H; d; furan H_3, J = 2.8 Hz), 6.35 (1H; dd; furan H_4, J_1 = 3.2 Hz, J_2 = 2 Hz), 6.78 (1H; s; pyridazinone H_5), 6.82–6.84 (2H; m; Ar–$H_{2'',6''}$), 7.21–7.26 (2H; m; Ar–$H_{3'',5''}$), 7.37 (1H; d; furan H_5, J = 1.6 Hz) ppm. ^{13}C--NMR ($CDCl_3$, 100 MHz); δ 20.98 (CH_3), 28.23 (CH_2), 41.90, 44.71, 49.40 (piperazine carbons), 52.92 (CH_2CO), 108.06, 110.57 (furan C_3, C_4), 117.96, 125.59, 129.13, 130.61, 140.07, 142.11, 144.71, 149.46 (aromatic carbons), 150.53 (furan C_2), 160.03 (pyridazinone CO), 164.79 (CH_2CON) ppm. ESI-MS (*m/z*): 427,38 $[M+H]^+$, 449,35 $[M+Na]^+$ (% 100), 451,34 $[M+Na+2]^+$. Anal. calcd. for $C_{22}H_{23}ClN_4O_3$: C, 61.90; H, 5.43; N, 13.12 Found: C, 61.79; H, 5.57; N, 12.91.

*4-(Furan-2-ylmethyl)-6-methyl-2-[2-oxo-2-(4-(4-fluorophenyl)piperazin--1-yl)ethyl]pyridazin-3(2H)-one (**6f**)*

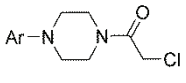
Yield 50 %; m.p. 105 °C. IR; 2921, 2855 (C-H), 1667, 1644 (C=O), 1606, 1507, 1446 (C=N ve C=C). ^{1}H-NMR ($CDCl_3$, 400 MHz); δ 2.26 (3H; s; –CH_3), 3.08–3.16 (4H; m; piperazine), 3.65–3.67 (2H; m; piperazine), 3.78–3.80 (2H; m; piperazine), 3.93 (2H; s; –CH_2–), 4.99 (2H; s; CH_2CO), 6.19 (1H; d; furan H_3, J = 3.2), 6.35 (1H; dd; furan H_4, J_1 = 3

Hz, J_2 = 1.8 Hz), 6.78 (1H; s; pyridazinone H_5), 6.87–6.90 (2H; m; Ar–$H_{2'',6''}$), 6.96–7.00 (2H; m; Ar–$H_{3'',5''}$), 7.37 (1H; dd; furan H_5, J_1 = 2 Hz, J_2 = 0.8 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz); δ 20.99 (CH_3), 28.23 (CH_2), 42.10, 44.88, 50.46 (piperazine carbons), 52.95 ($\underline{C}H_2CO$), 108.06, 110.58 (furan C_3, C_4), 115.73, 118.76, 130.62, 140.08, 142.12, 144.73, 147.53, 156.52, 158.90 (aromatic carbons), 150.53 (furan C_2), 160.06 (piridazinon CO), 164.76 ($CH_2\underline{C}ON$) ppm. ESI-MS (*m/z*): 411,46 $[M+H]^+$, 433,43 $[M+Na]^+$ (% 100). Anal. calcd. for $C_{22}H_{23}FN_4O_3$: C, 64.38; H, 5.65; N, 13.65 Found: C, 64.11; H, 5.77; N, 13.47.

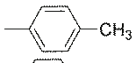
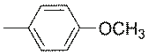
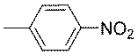
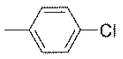
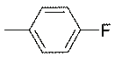
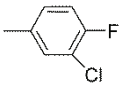
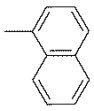
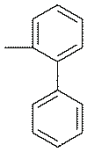
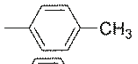
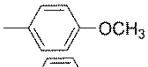
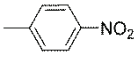
TABLE S-I. Yields, melting points and literature melting points of 2-Chloro-*N*-arylacetamides (**3a-j**) and 2-chloro-1-(4-arylpiperazin-1-yl)ethanones (**4a-f**)

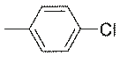
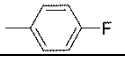


3a-j



4a-f

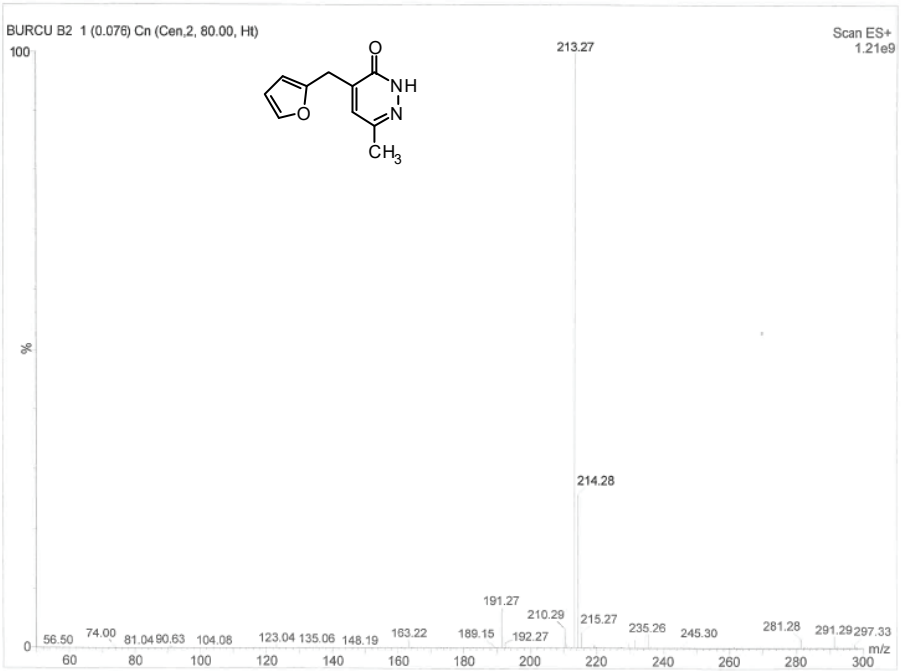
Compound	Ar	Yield (%)	M.p. [Lit M.p.] (° C)
3a		94.9	133 [132][1]
3b		96.8	119 [130][2]
3c		96.0	119 [119-120][3]
3d		92.0	118 [118][2]
3e		93.2	148 [150][2]
3f		94.2	131 [130-131][4]
3g		92.4	75 [75-77][5]
3h		90.1	150 [154][6]
3i		86.2	152 [152-153][6]
3j		83.4	175 [178-180][7]
4a		67.6	75 [77][8]
4b		83.2	75 [60-1][9]
4c		81.4	106 [109-111][10]
4d		78.28	104 [100-101][11]

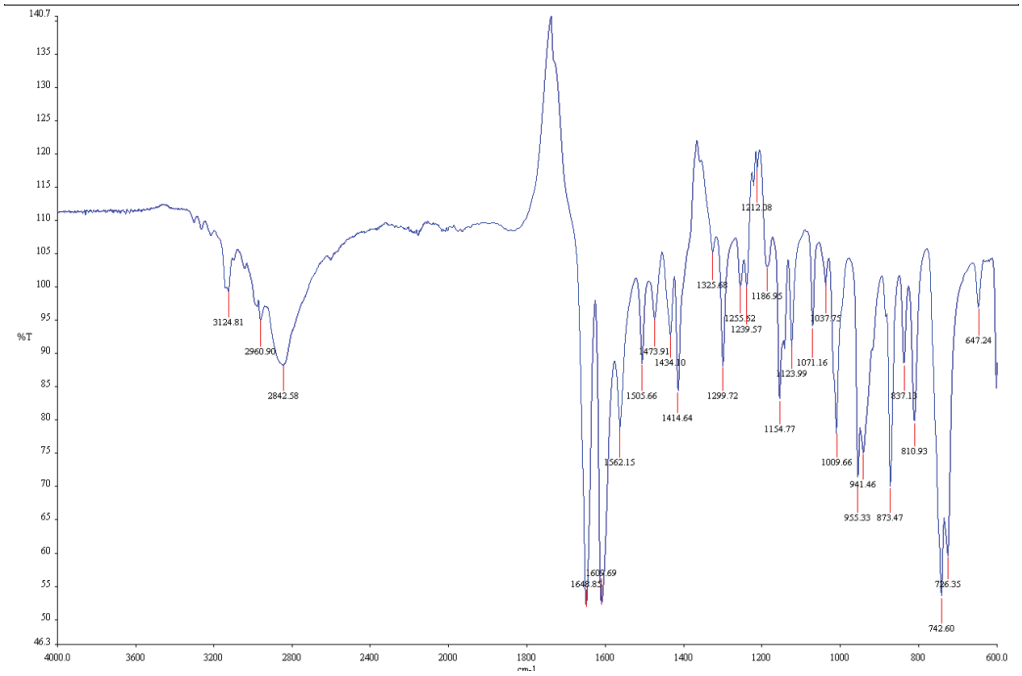
4e		77.17	81 [84-85][12]
4f		85.13	104 [95][13]

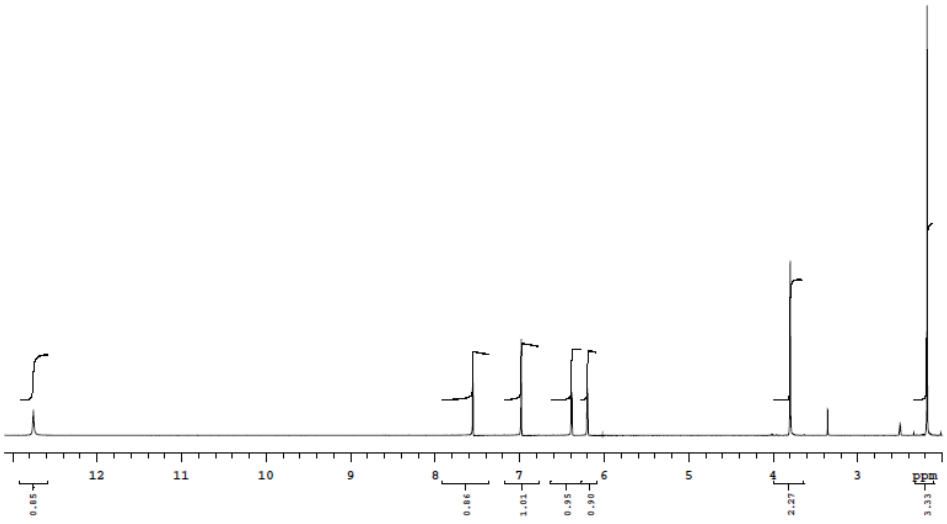
REFERENCES

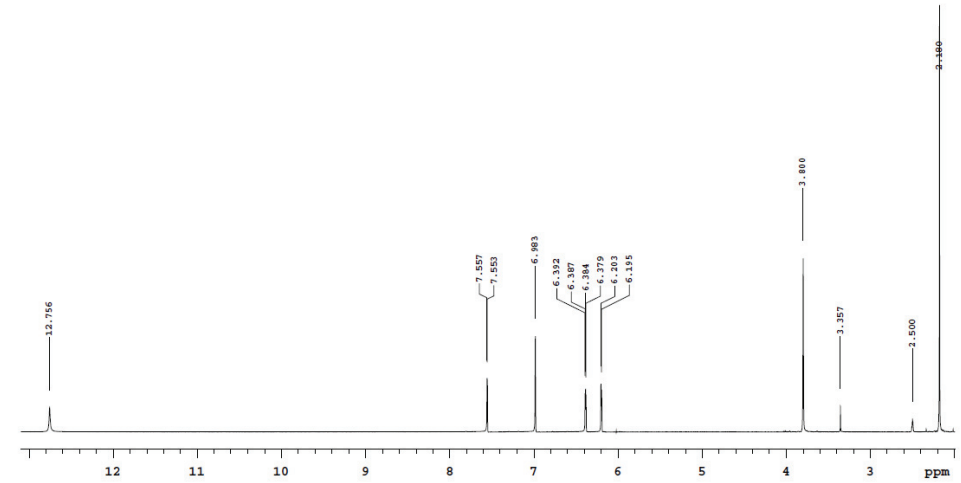
1. N. P. Sahu, C. Pal, N. B. Mandal, S. Banerjee, M. Raha, A. P. Kundu, A. Basu, M. Ghosh, K. Roy, S. Bandyopadhyay, *Bioorganic Med. Chem.* **10** (2002) 1687–1693 (https://doi.org/10.1016/S0968-0896(02)00046-9)
2. A. D. Desai, K. H. Chikhalia, *E-Journal Chem.* **2** (2005) 15–20 (https://doi.org/10.1155/2005/575290)
3. I. N. Peixoto, H. D. S. Souza, B. F. Lira, D. F. Silva, E. O. Lima, J. M. Barbosa-Filho, P. F. de Athayde-Filho, *J. Braz. Chem. Soc.* **27** (2016) S1–S19 (https://doi.org/10.5935/0103-5053.20160063)
4. P. G. Baraldi, D. Preti, M. A. Tabrizi, F. Fruttarolo, G. Saponaro, S. Baraldi, R. Romagnoli, A. R. Moorman, S. Gessi, K. Varani, P. A. Borea, *Bioorganic Med. Chem.* **15** (2007) 2514–2527 (https://doi.org/10.1016/j.bmc.2007.01.055)
5. D. C. P. Singh, S. R. Hashim, R. G. Singhal, *E-Journal Chem.* **8** (2011) 635–642 (https://doi.org/10.1155/2011/482831)
6. V. Pace, L. Castoldi, W. Holzer, *Chem. Commun.* **49** (2013) 8383–8385 (https://doi.org/10.1039/c3cc44255a)
7. V. Patil, K. Tilekar, S. Mehendale-Munj, R. Mohan, C. S. Ramaa, *Eur. J. Med. Chem.* **45** (2010) 4539–4544 (http://dx.doi.org/10.1016/j.ejmech.2010.07.014)
8. R. K. Sharma, Y. Younis, G. Mugumbate, M. Njoroge, J. Gut, P. J. Rosenthal, K. Chibale, *Eur. J. Med. Chem.* **90** (2015) 507–518 (https://doi.org/10.1016/j.ejmech.2014.11.061)
9. N. Sati, S. Kumar, S. Sati, *Int. J. Drug Design & Discovery* **2(1)** (2011) 419-424
10. D. Szkatuła, E. Krzyżak, P. Stanowska, M. Duda, B. Wiatrak, *Int. J. Mol. Sci.* 22 (**2021)** 7678 (https://doi.org/10.3390/ijms22147678)
11. S. Gupta, D. Pandey, D. Mandalapu, V. Bala, V. Sharma, M. Shukla, et al., *MedChemComm* **7**(11) (2016) 2111-2121 (http://dx.doi.org/10.1039/C6MD00426A)
12. K. Kamiński, B. Wiklik, J. Obniska, *Med. Chem. Res.* **24** (2015) 3047–3061 (https://doi.org/10.1007/s00044-015-1360-6)
13. B. Begam, K. Singh, A. Rahman, *Indian J. Heterocyclic Chem*., **26** (2016) 147.

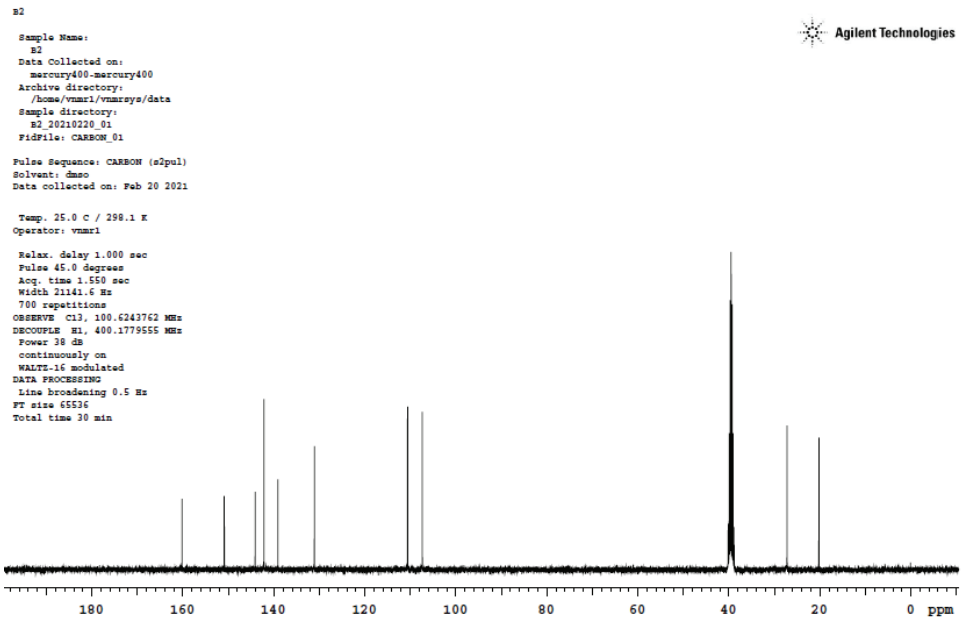
4-(2-FURYLMETHYL)-6-METHYLPYRIDAZIN-3(*2H*)-ONE (**2**)

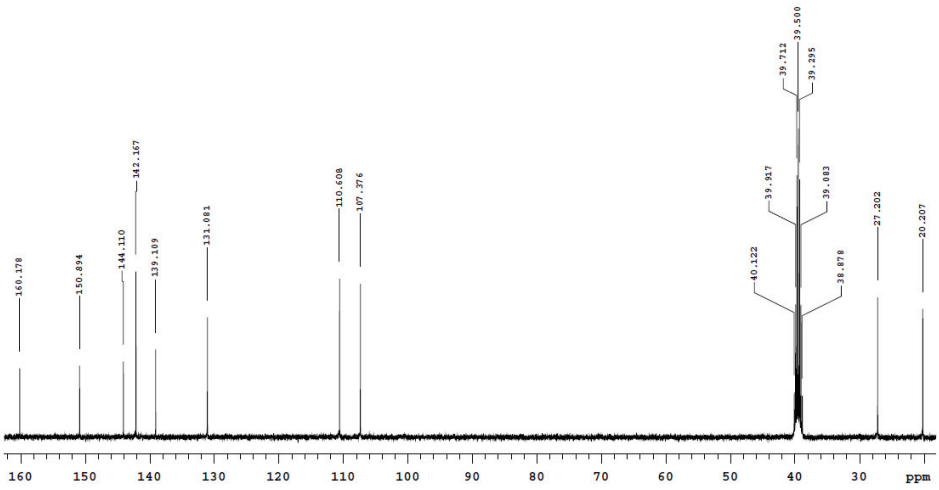




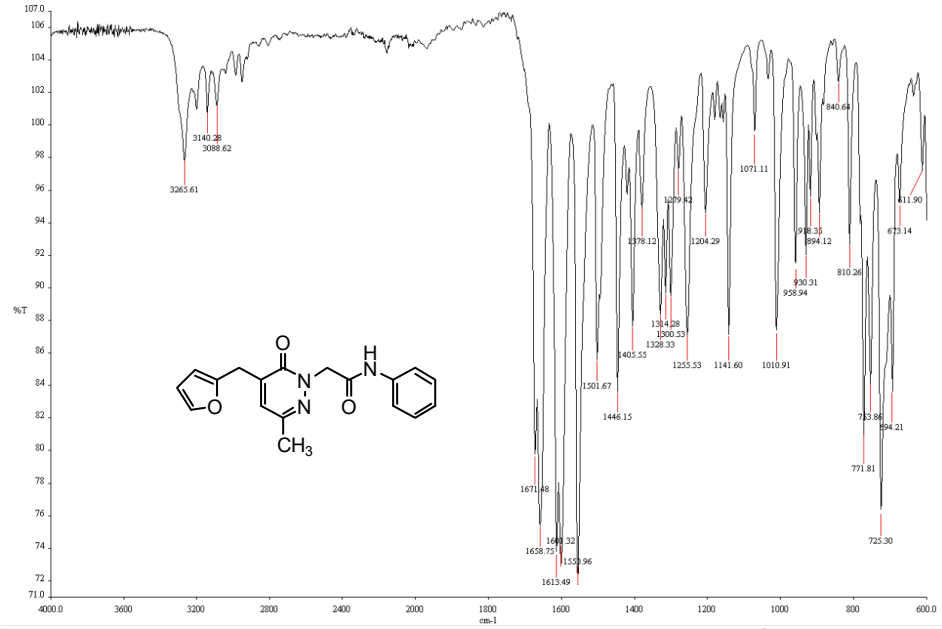


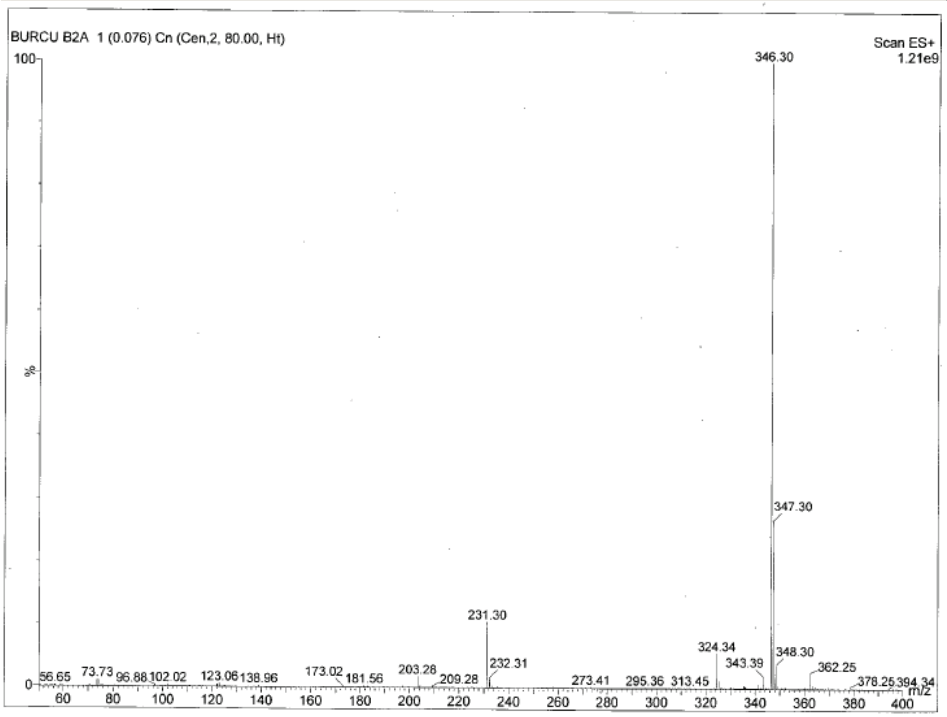


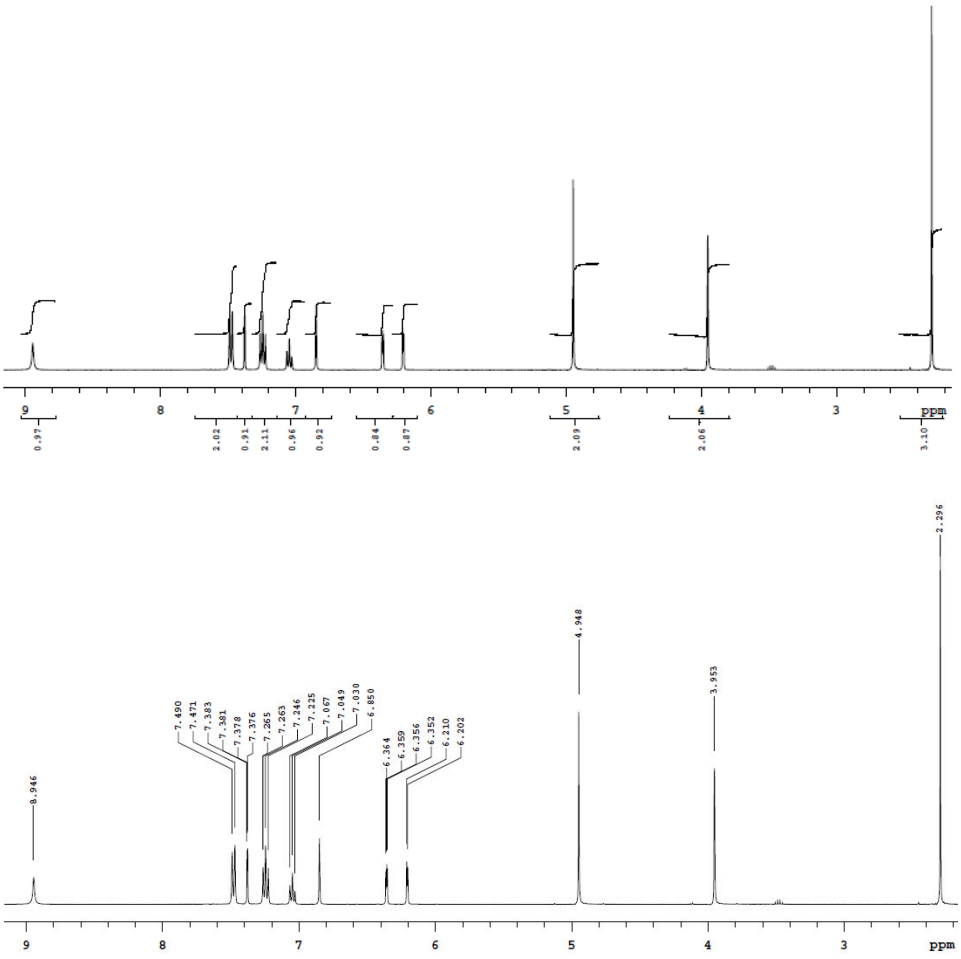


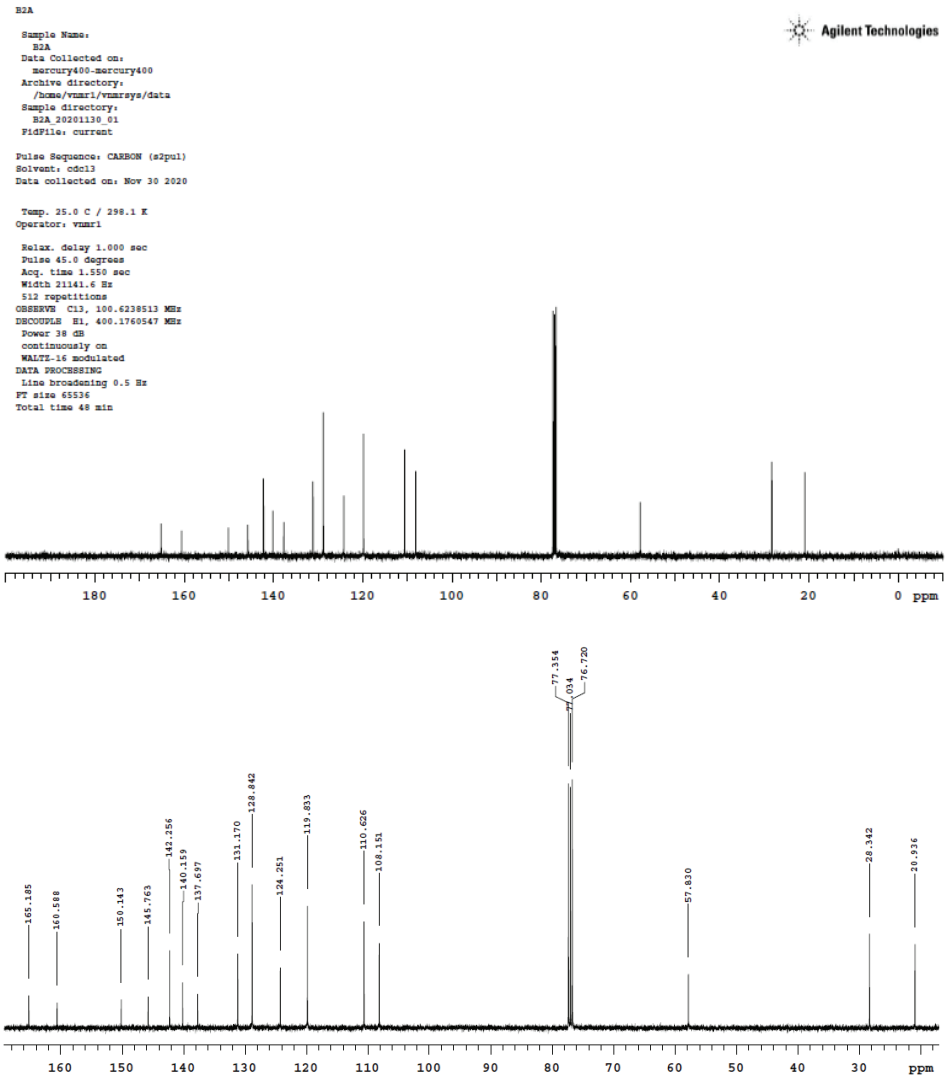


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-PHENYLACETAMIDE (**5a**)

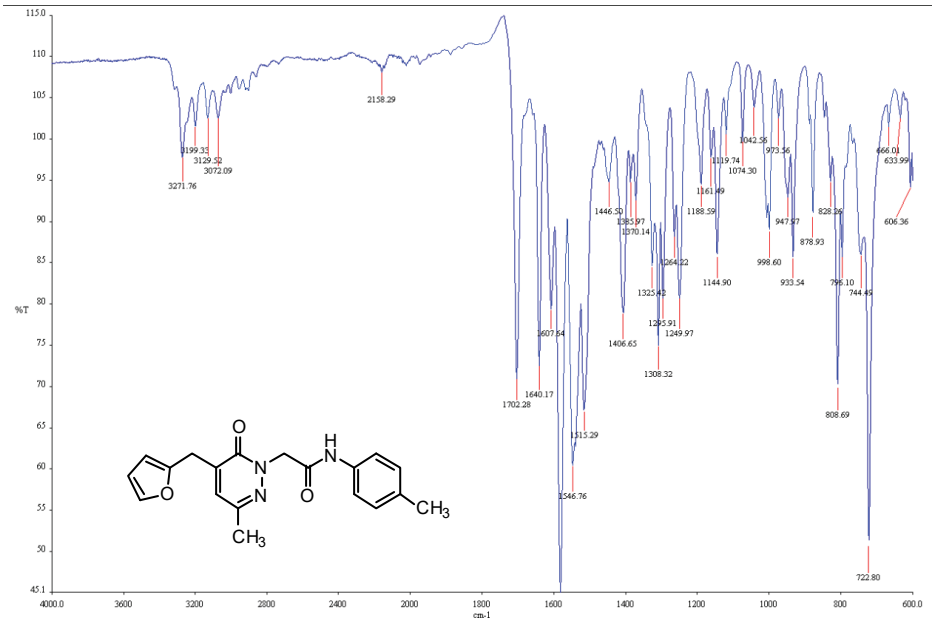


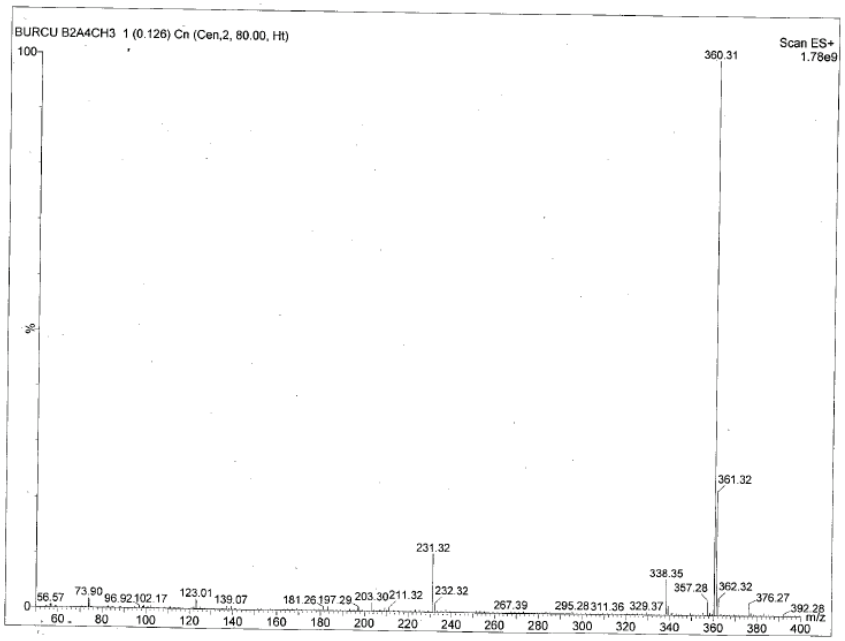


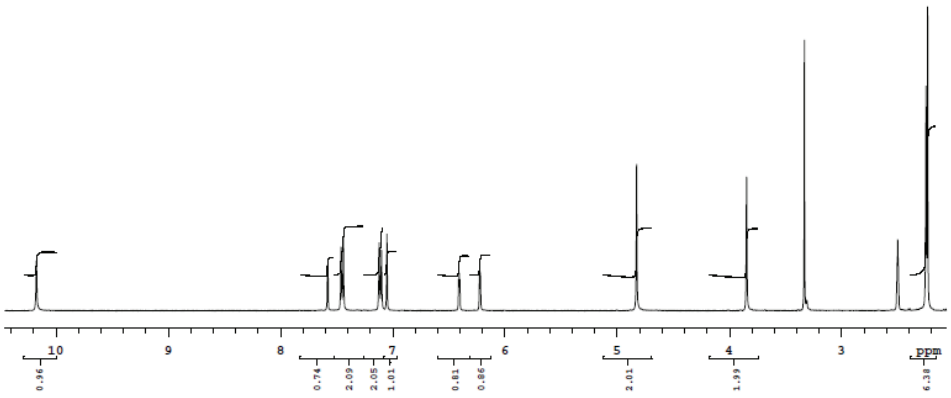


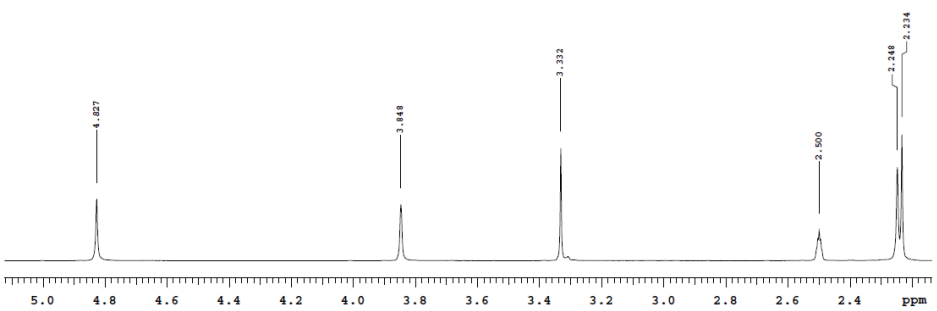


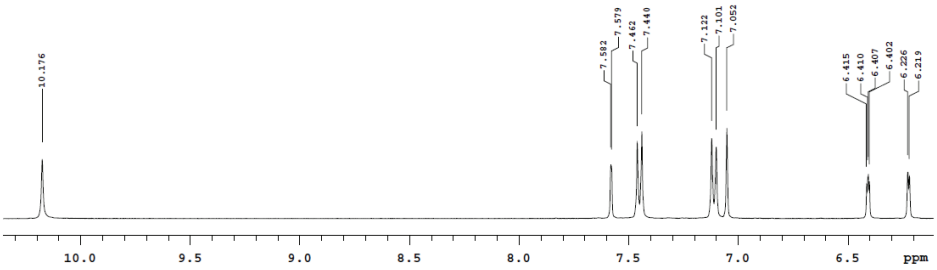
2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(4-METHYLPHENYL)ACETAMIDE (5B)

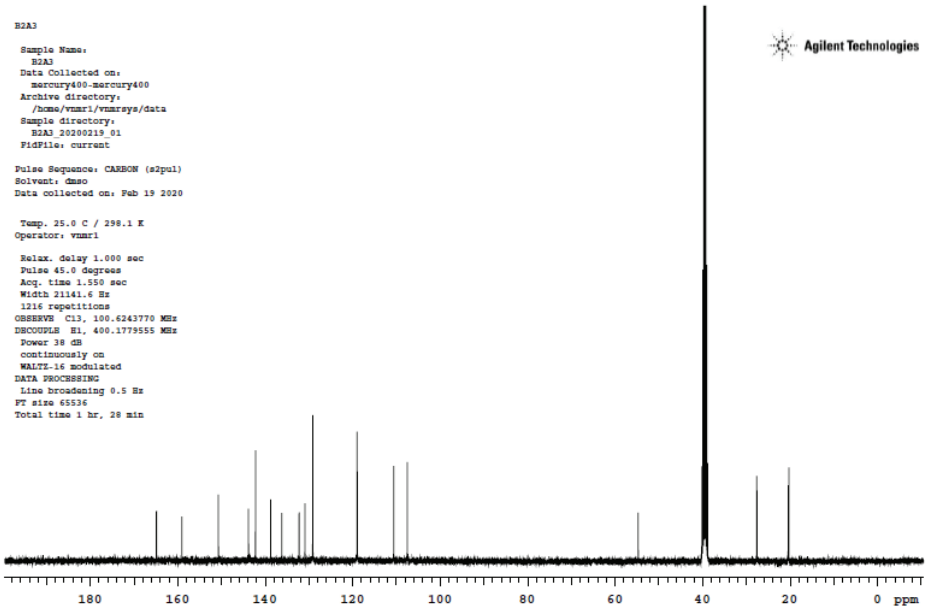


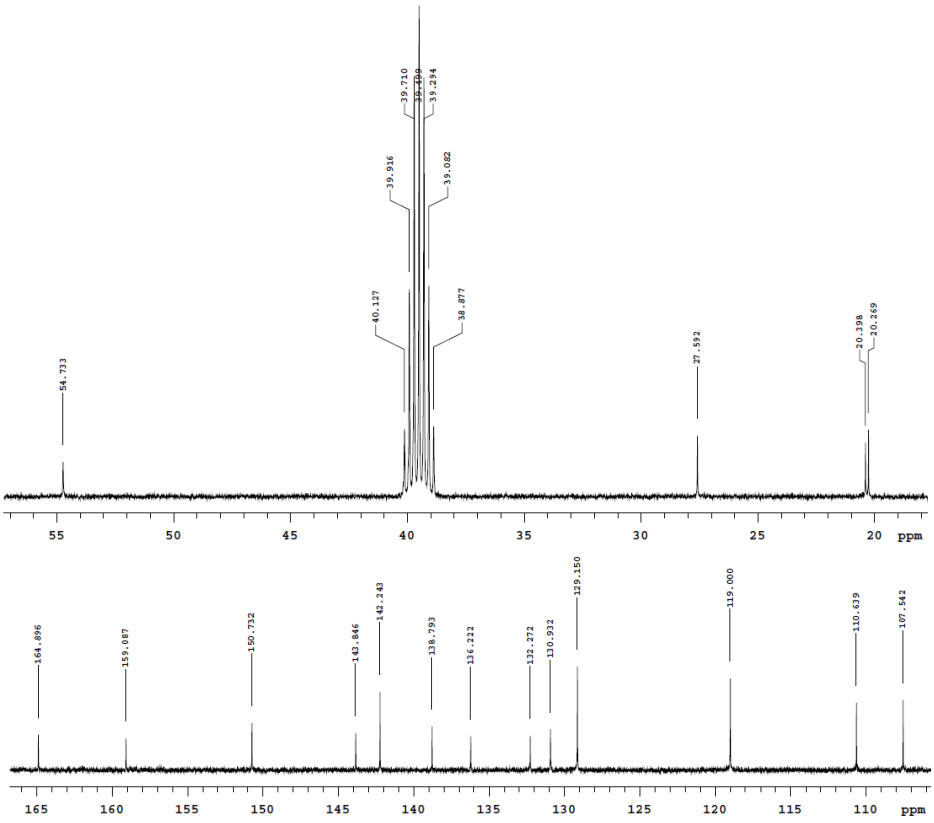




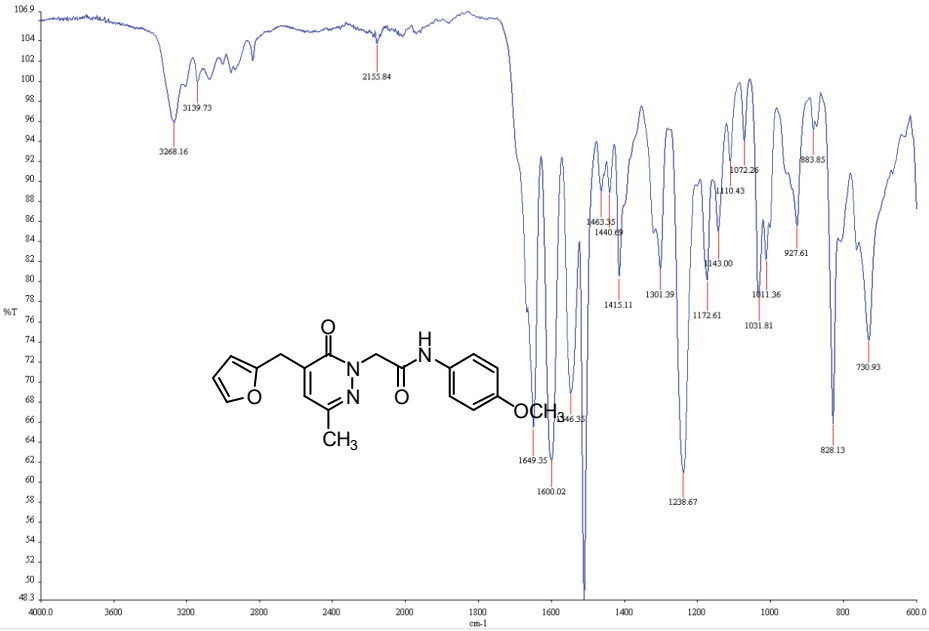


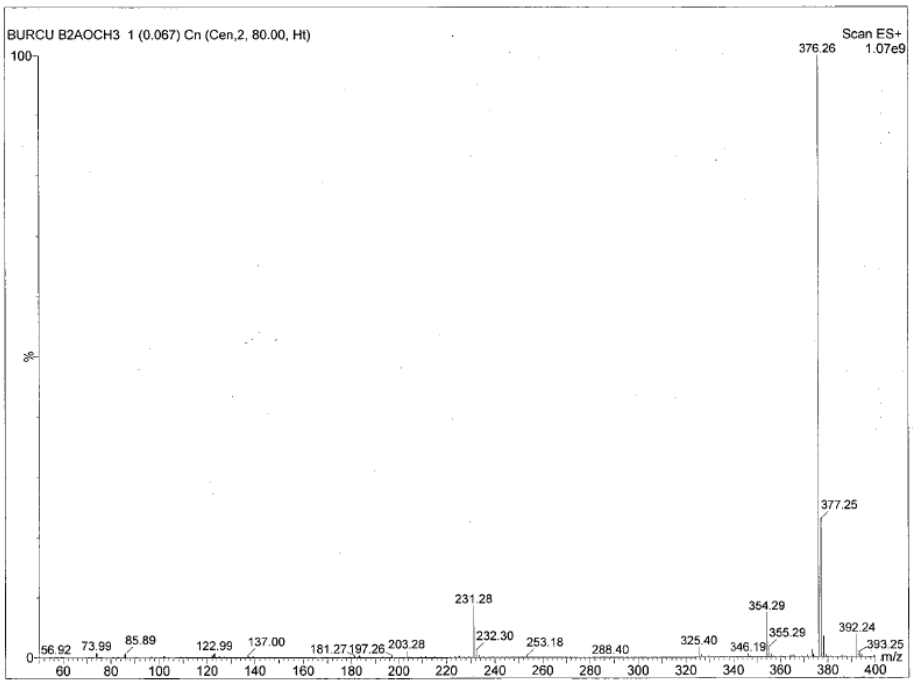


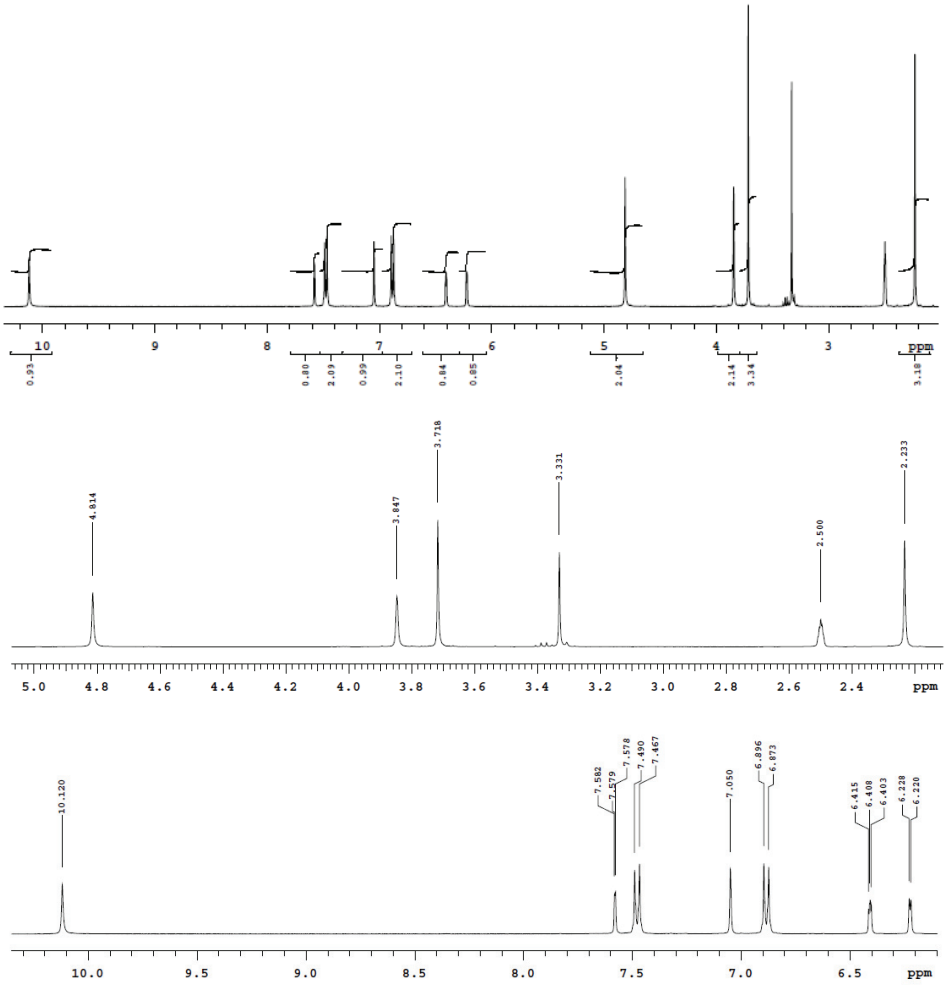


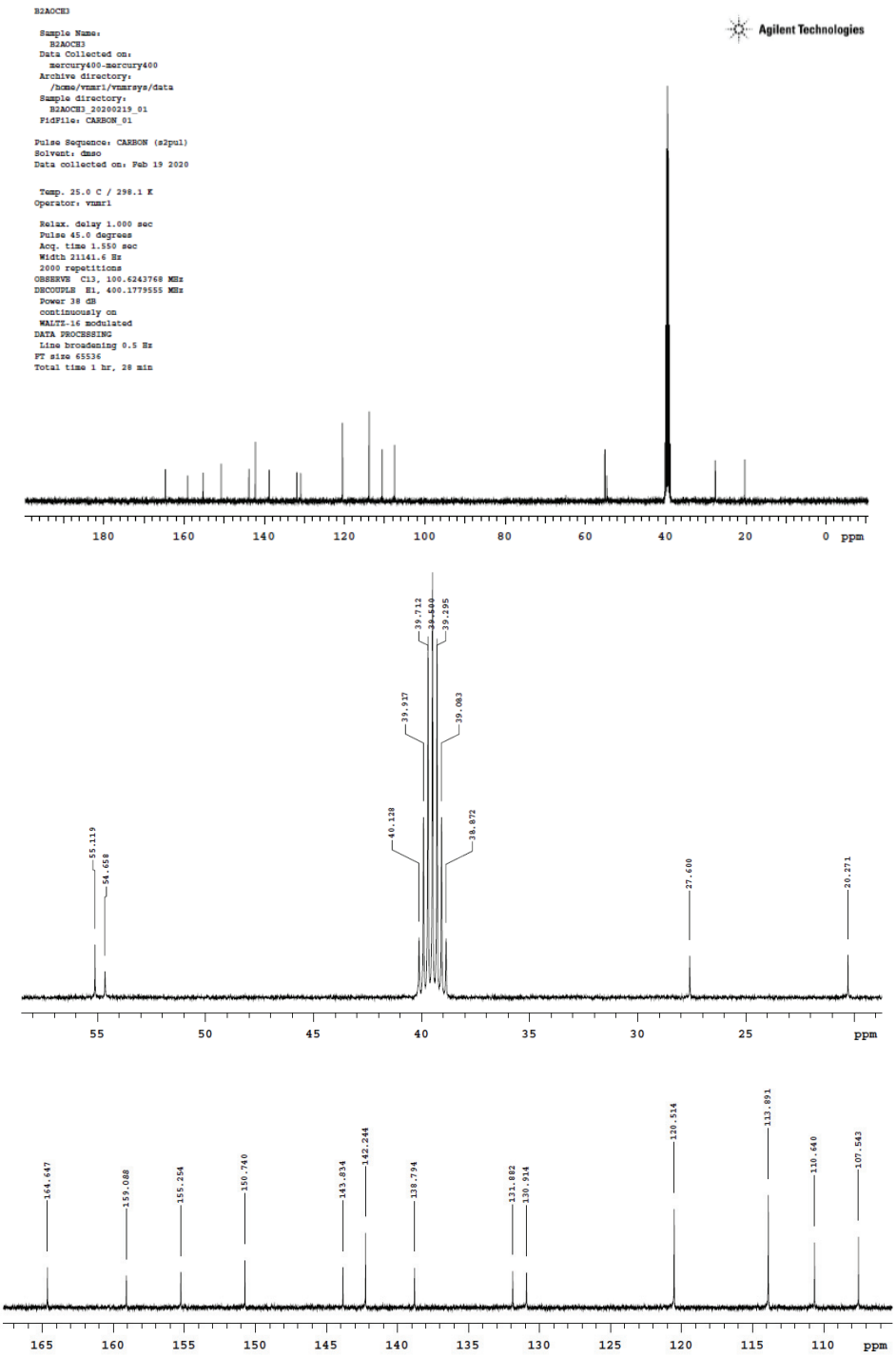


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(4-METHOXYPHENYL)ACETAMIDE (5C)

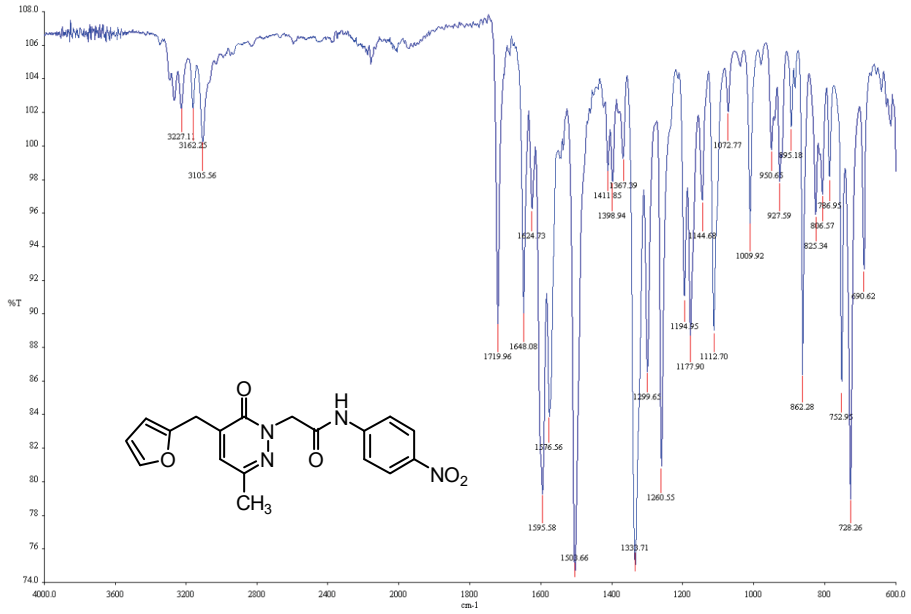


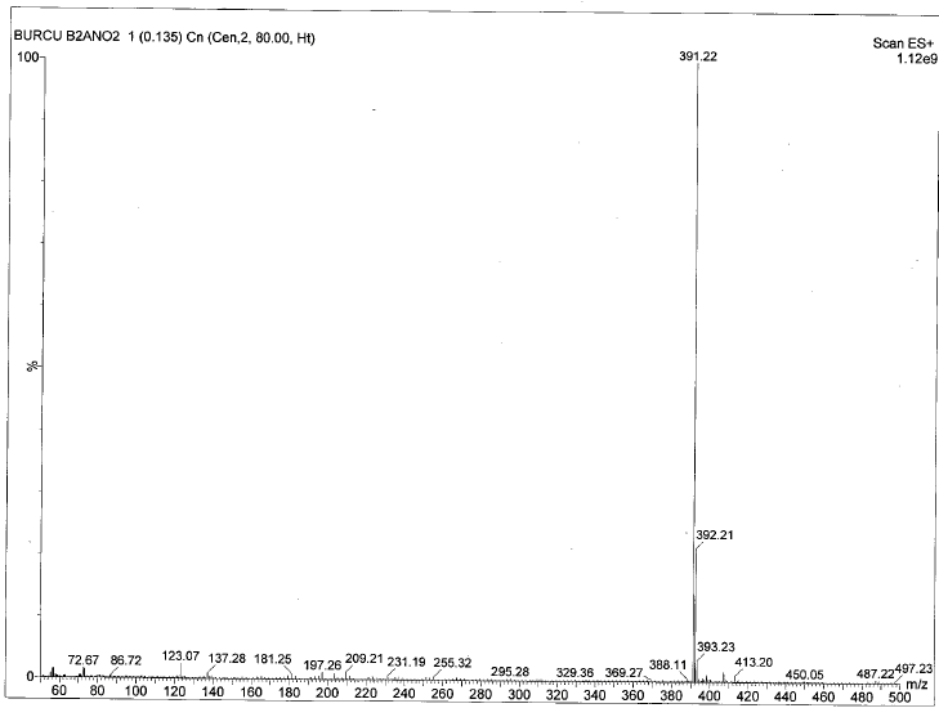


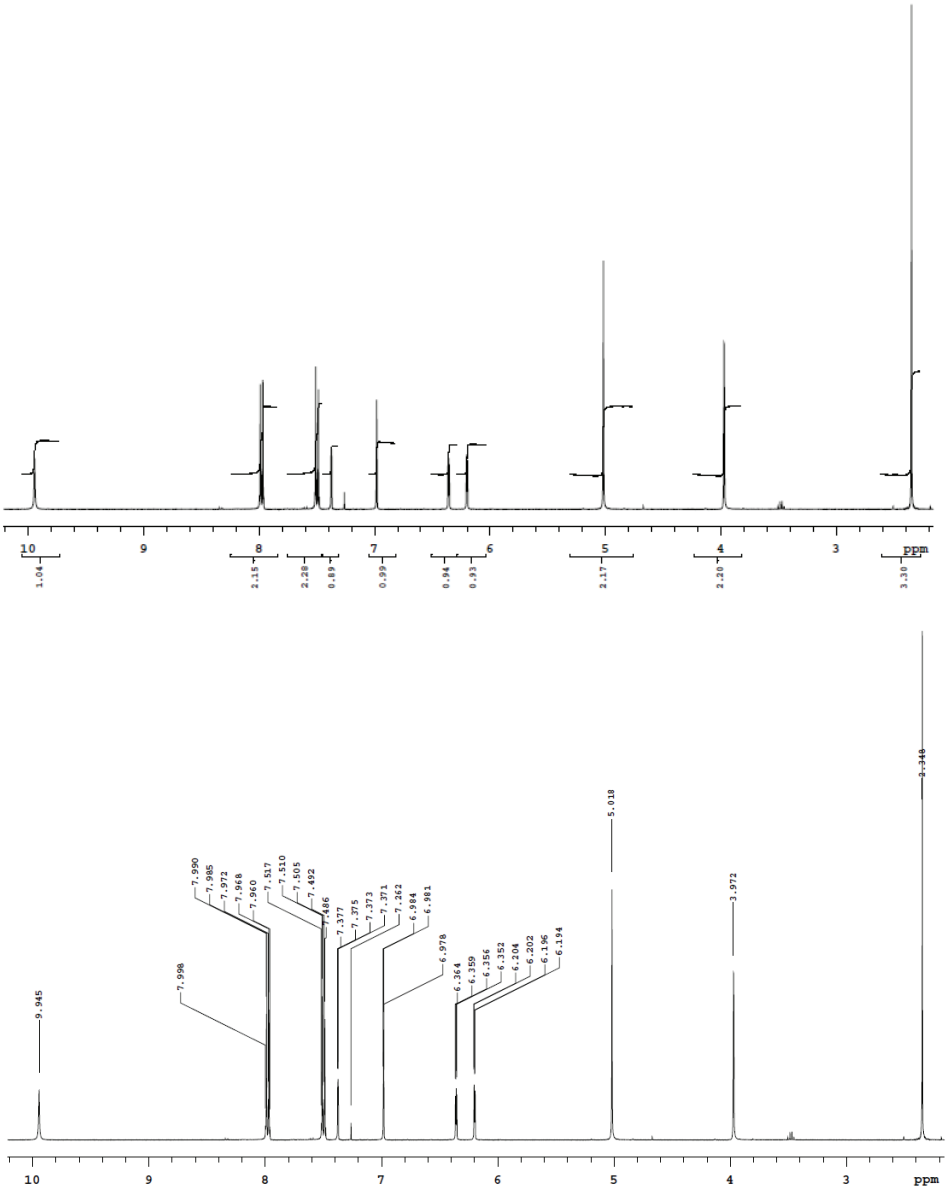


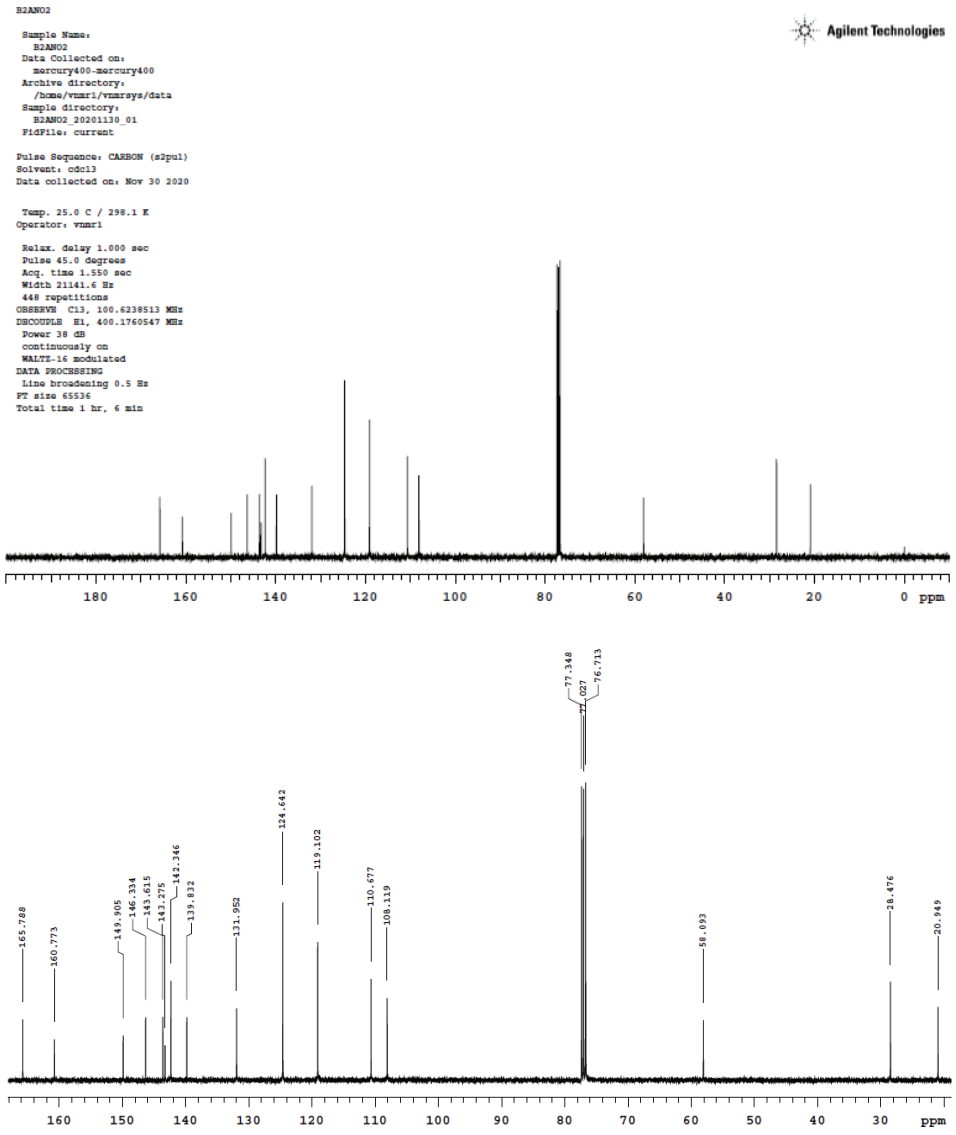


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(4-NITROPHENYL)ACETAMIDE (5D)

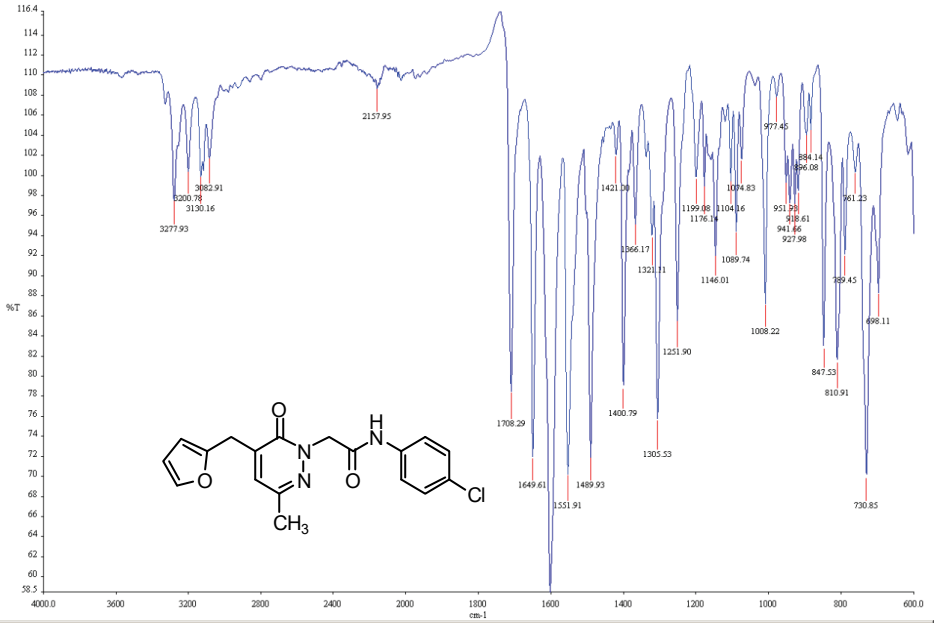


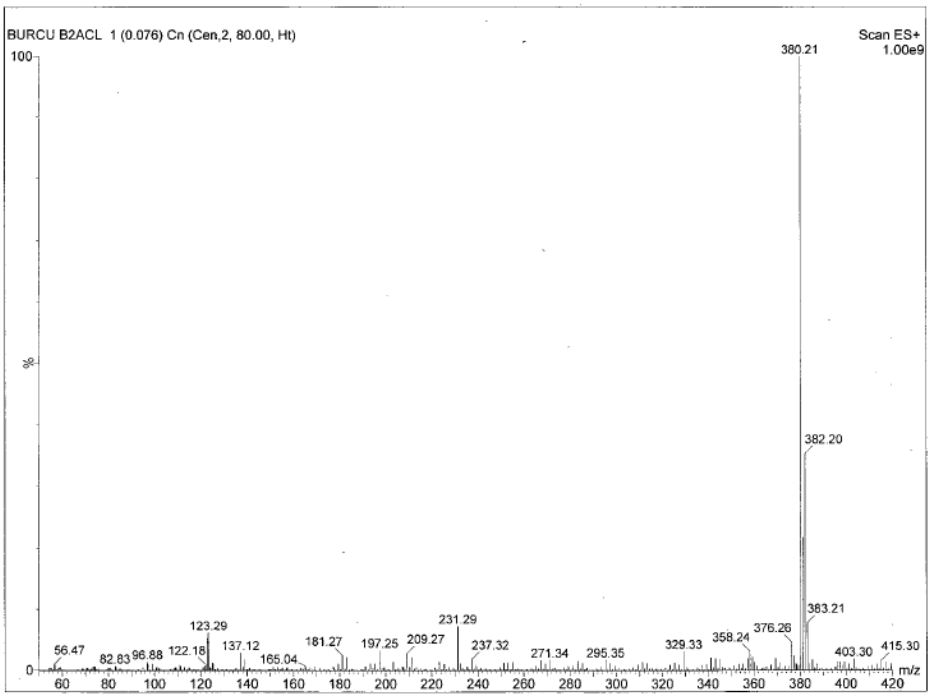


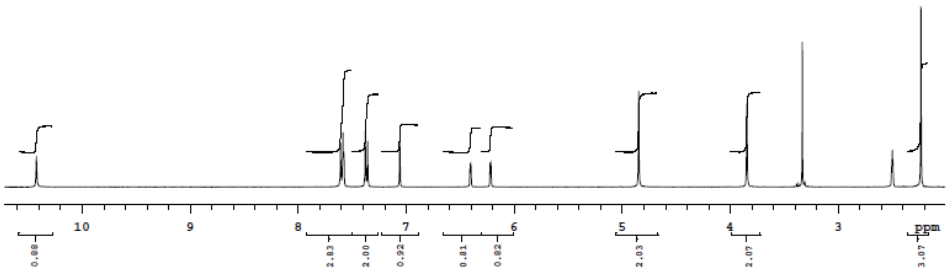


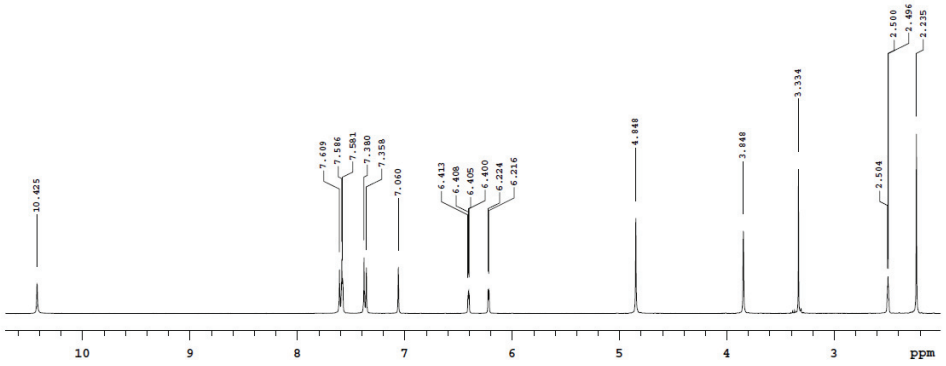


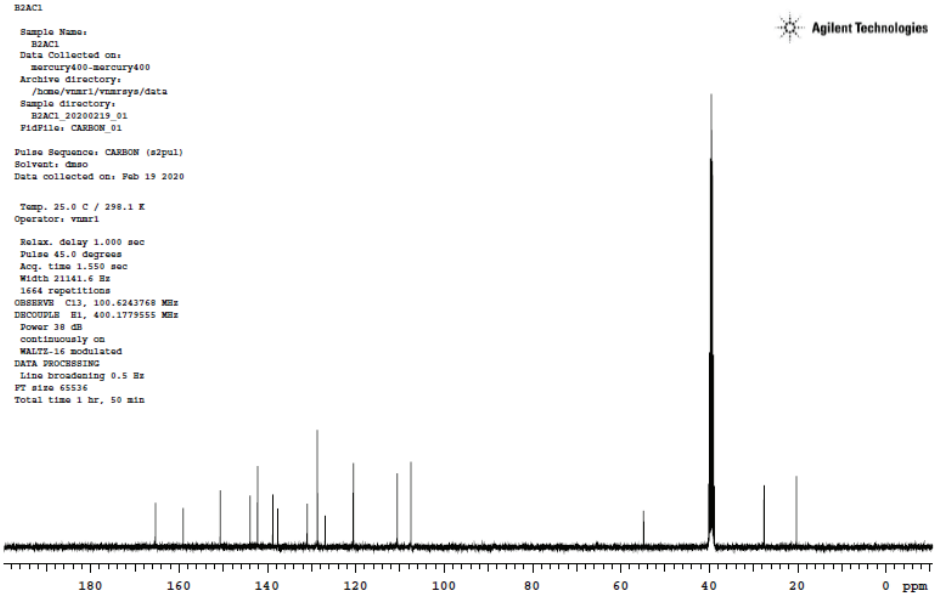
2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(4-CHLOROPHENYL)ACETAMIDE (5E)

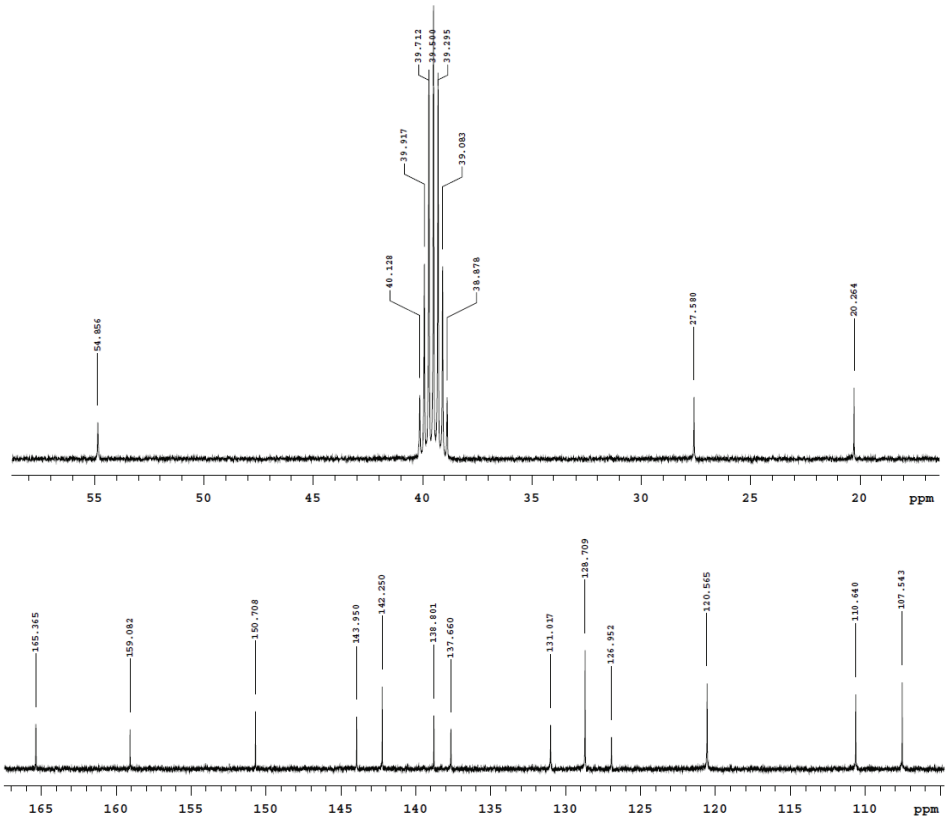




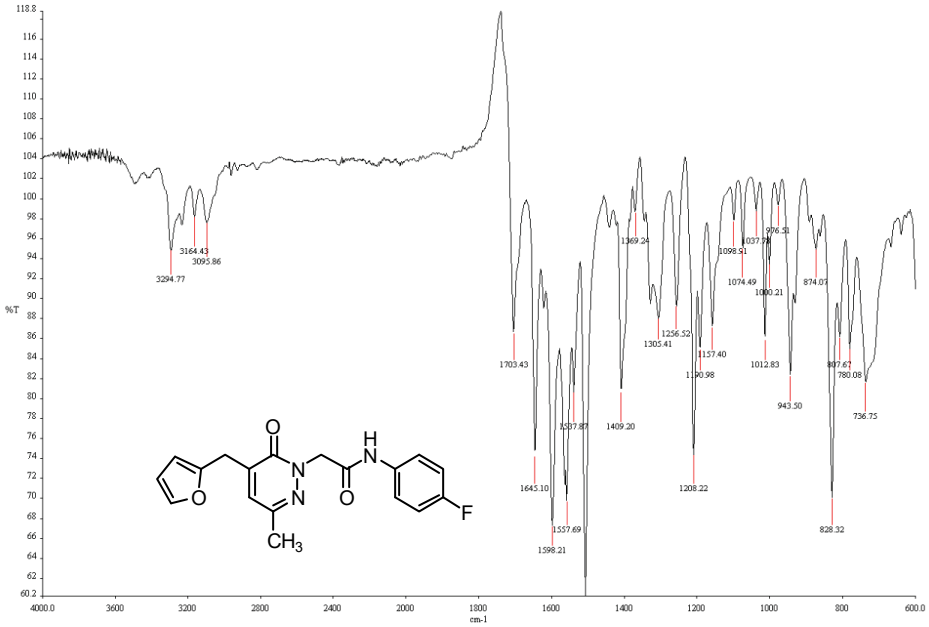


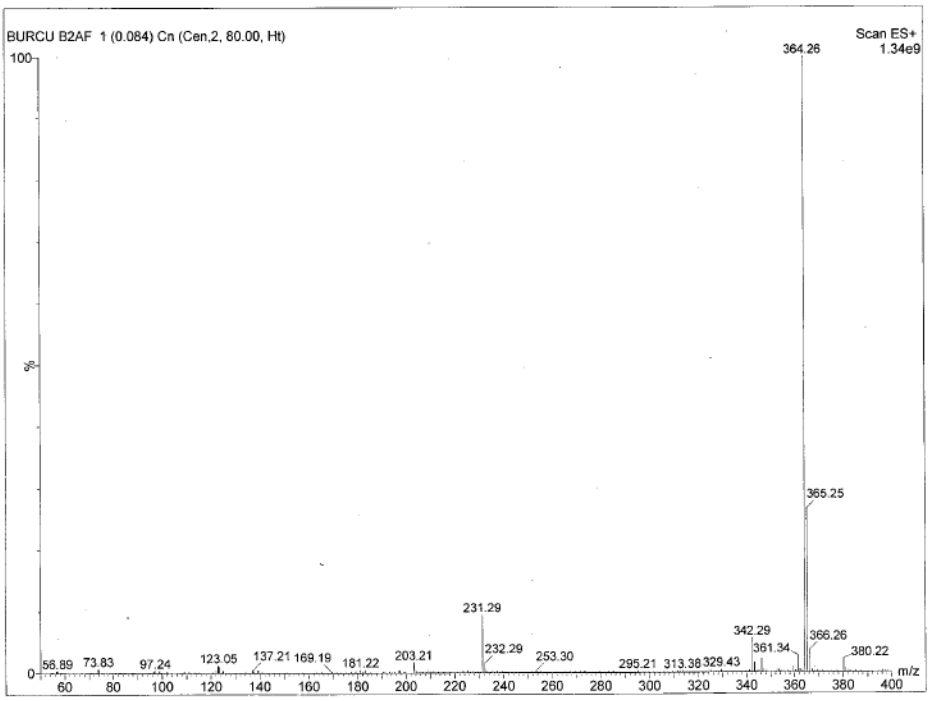


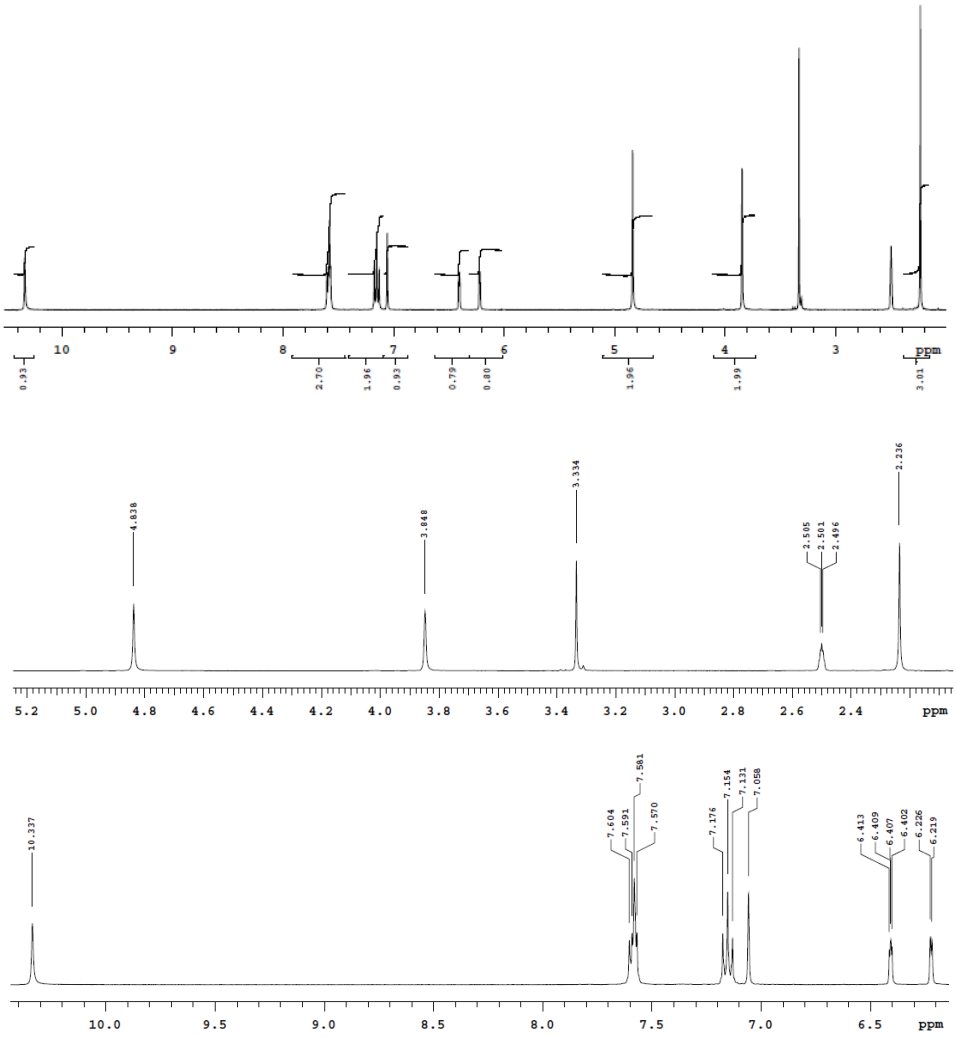


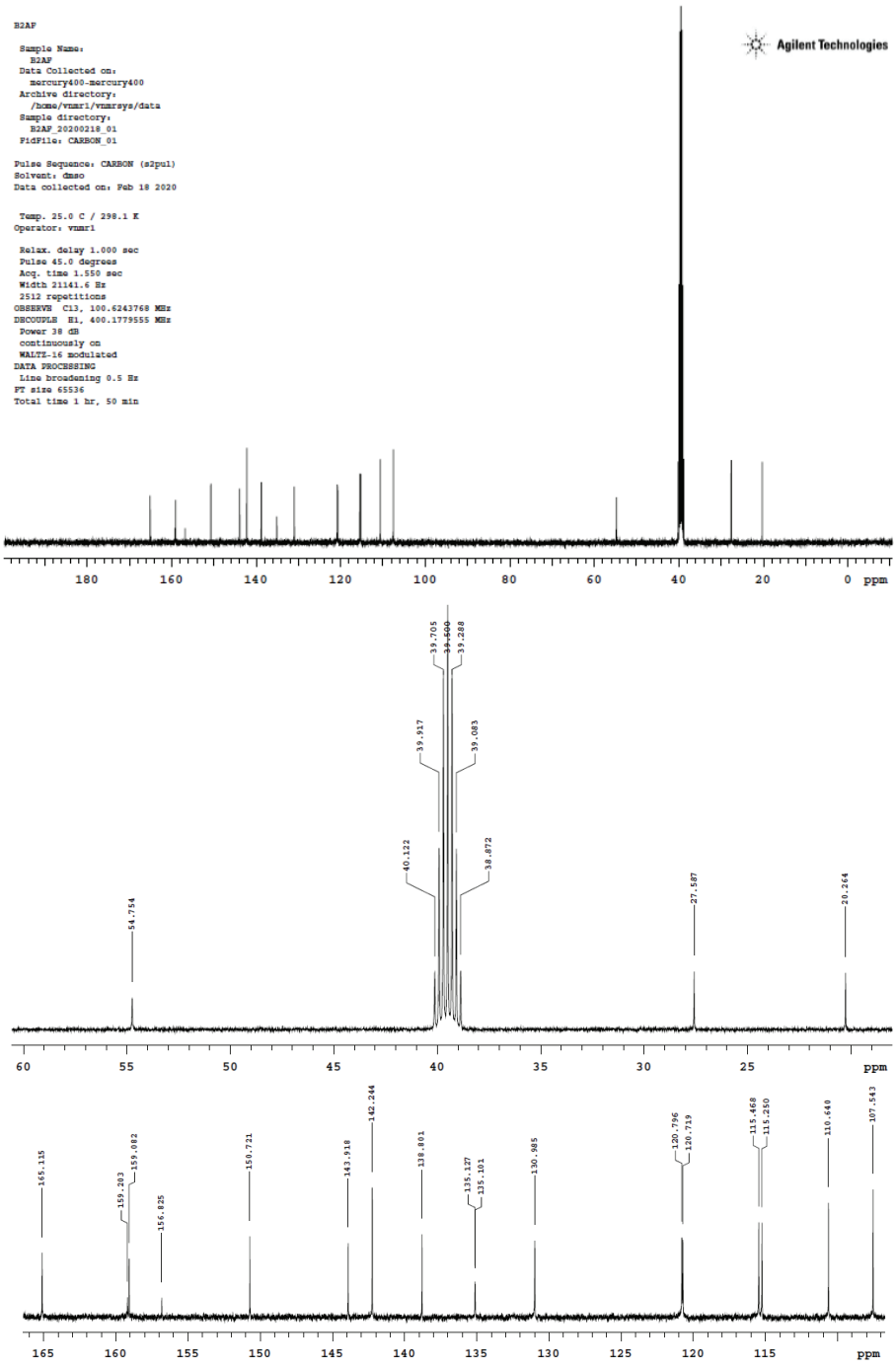


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(4-FLUOROPHENYL)ACETAMIDE (5F)

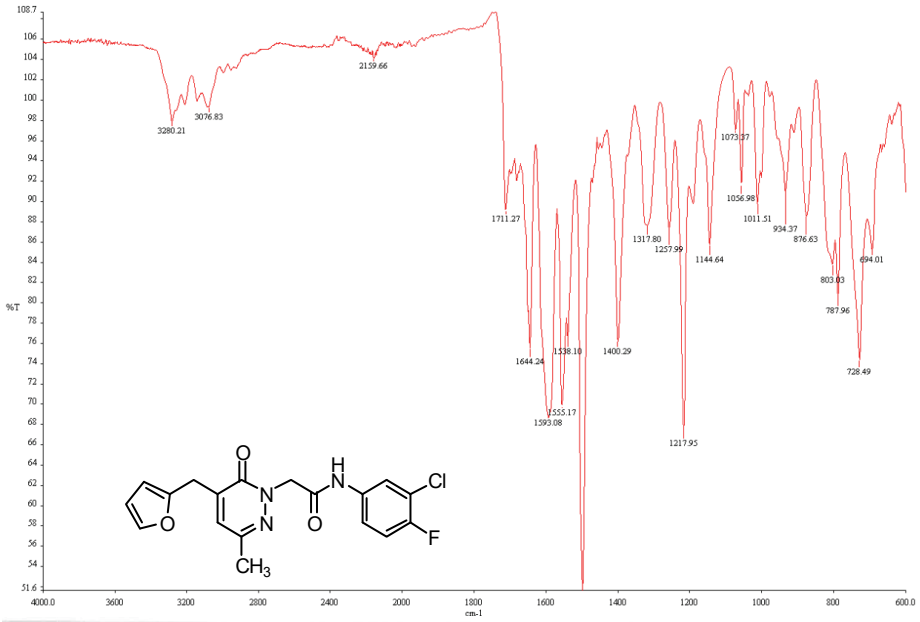


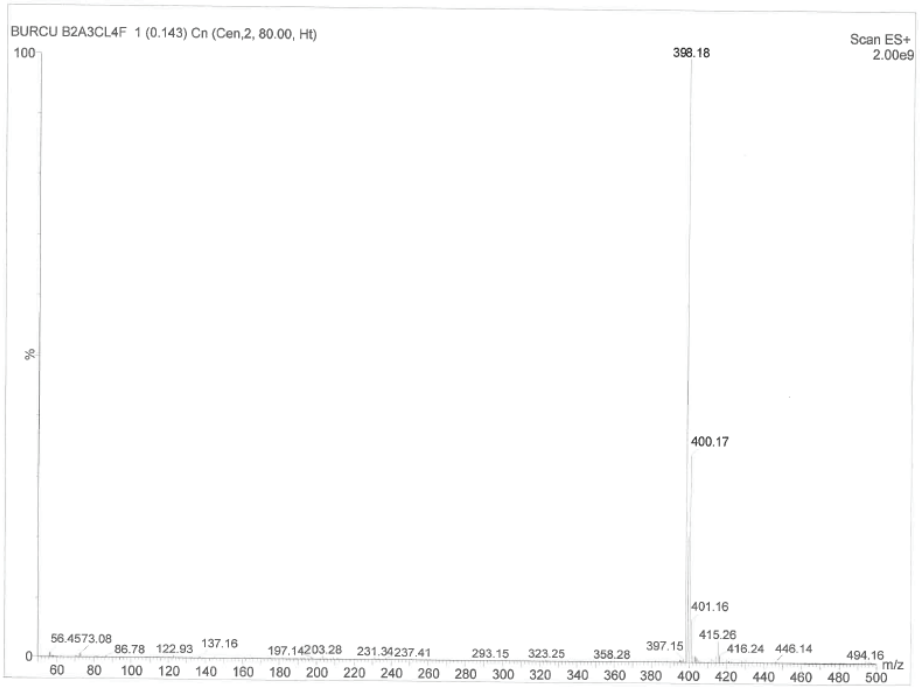


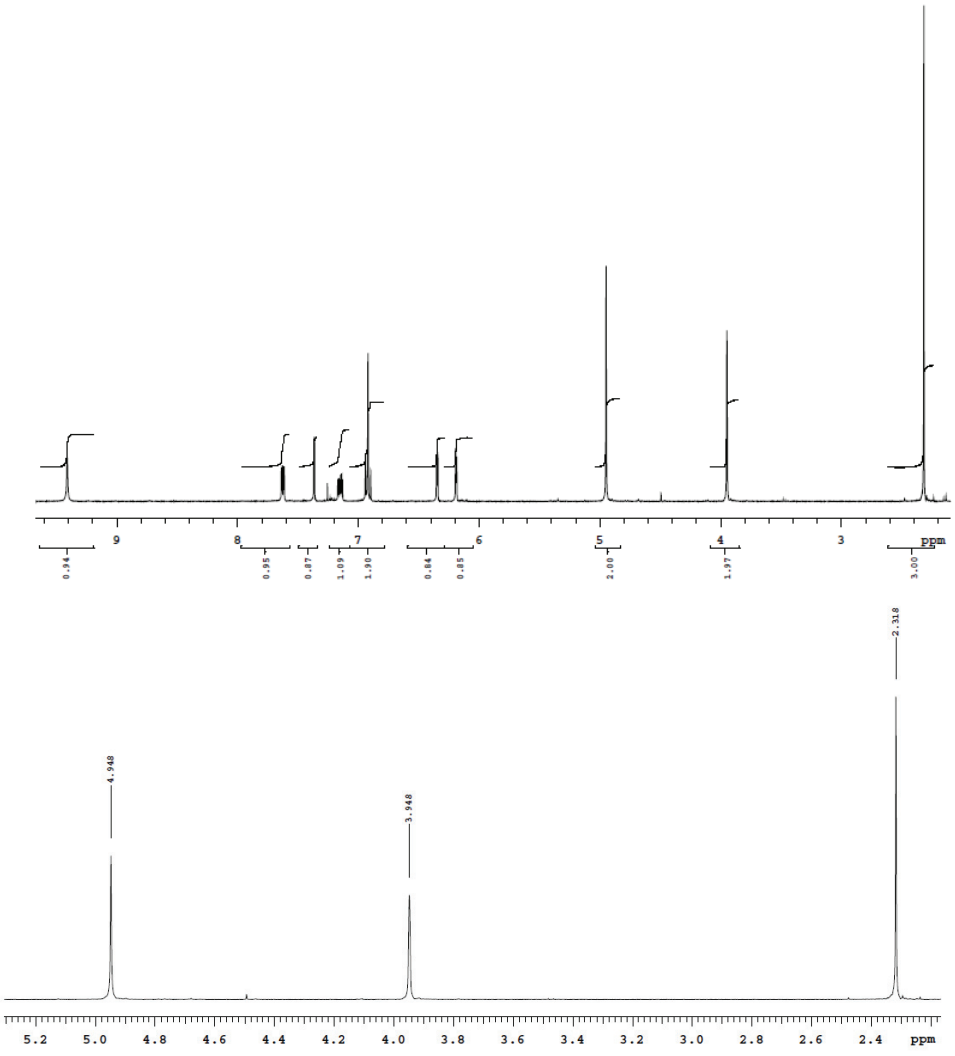


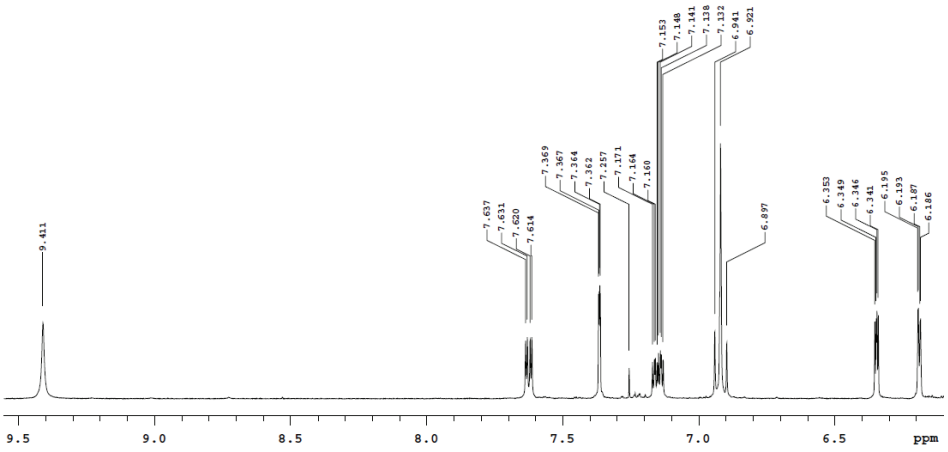


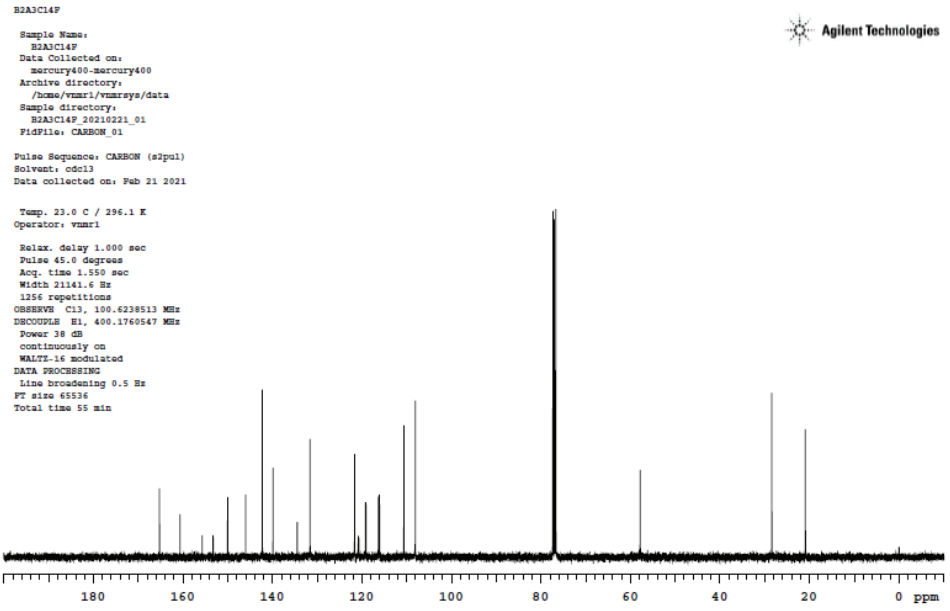
2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(3-CHLORO-4-FLUOROPHENYL)ACETAMIDE (5G)

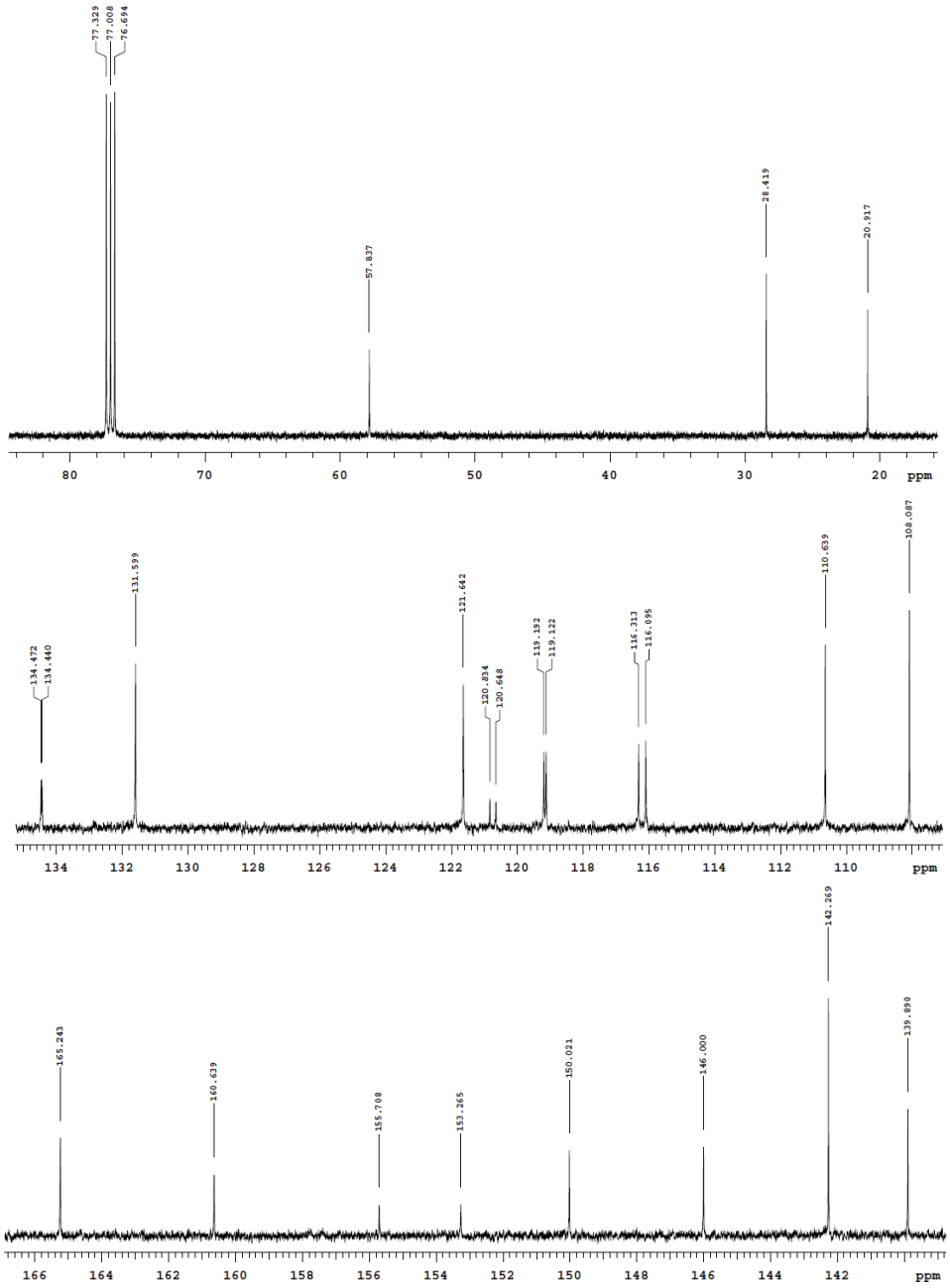




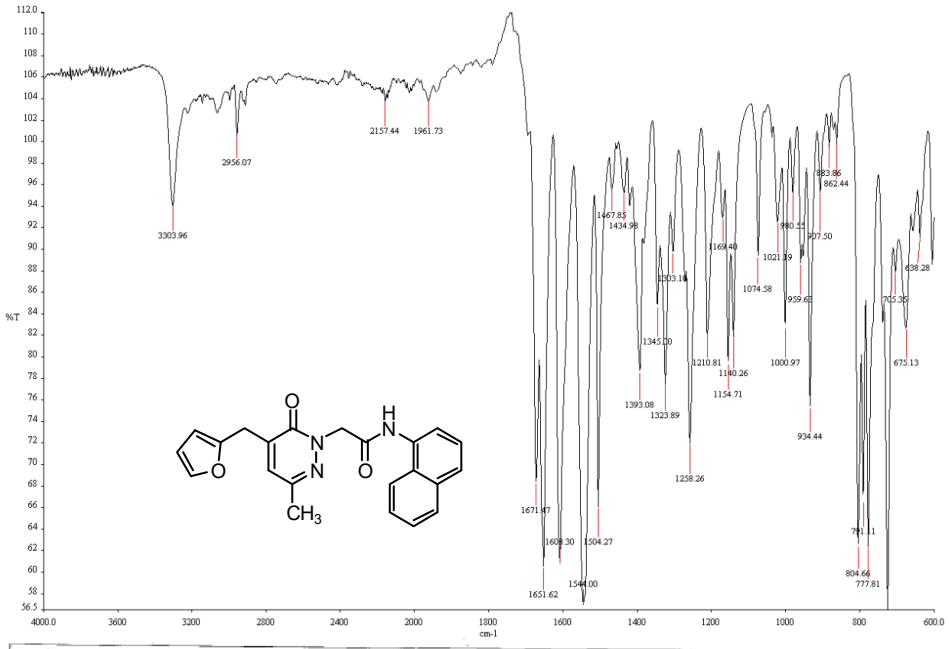


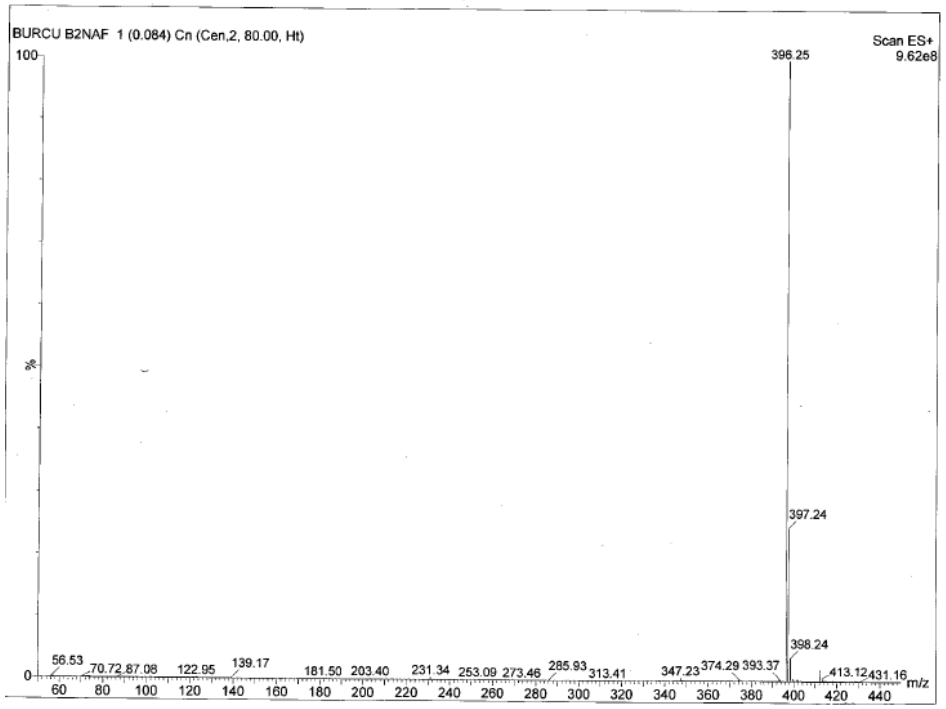


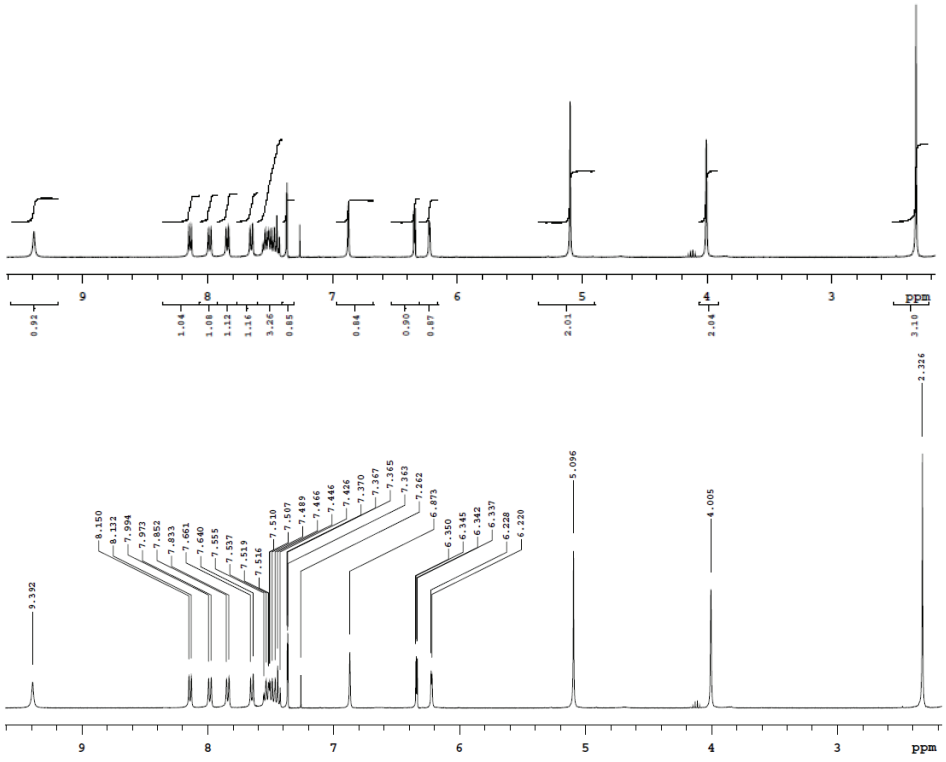


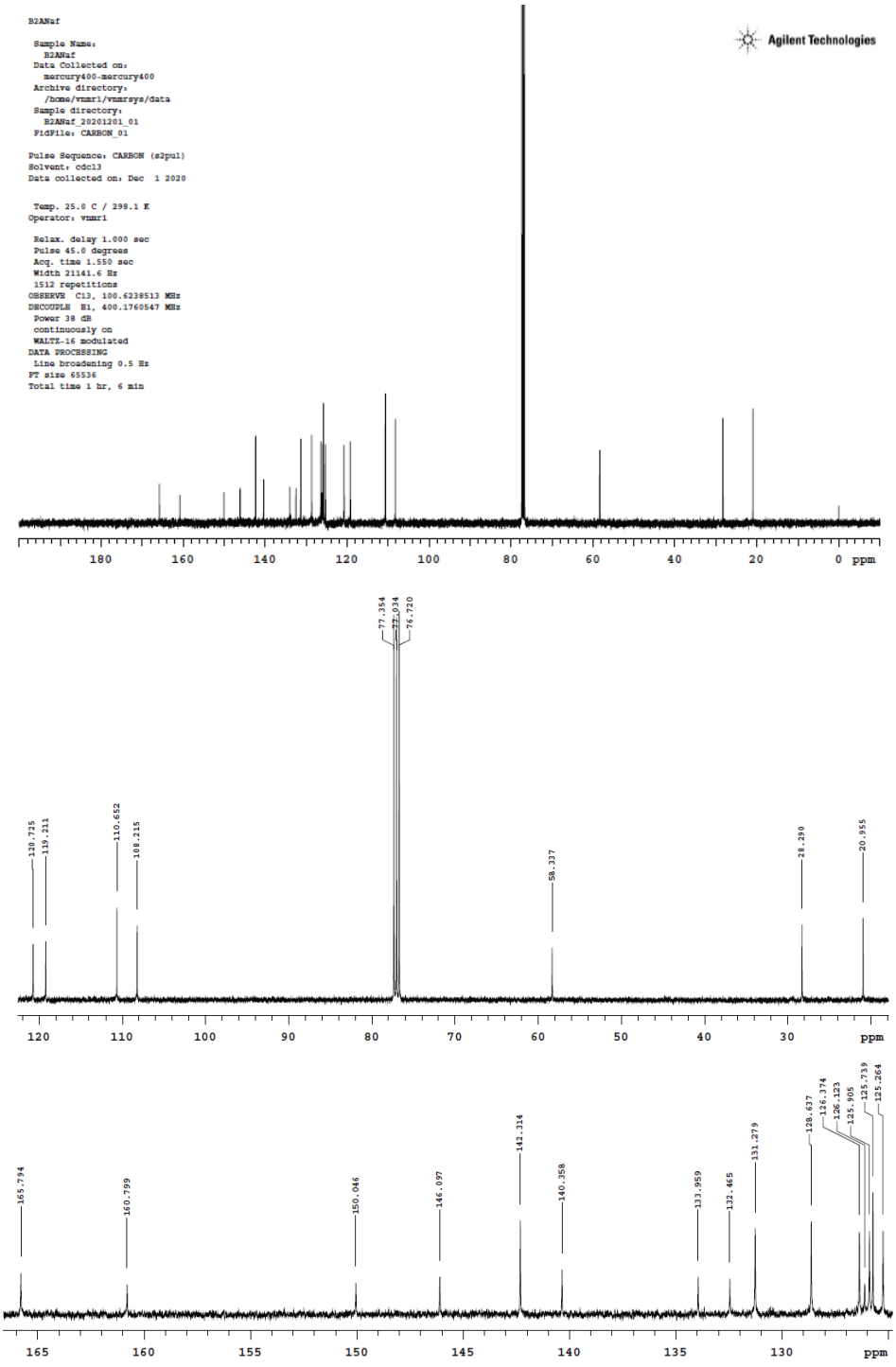


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(NAPHTHALEN-1-YL)ACETAMIDE (5H)

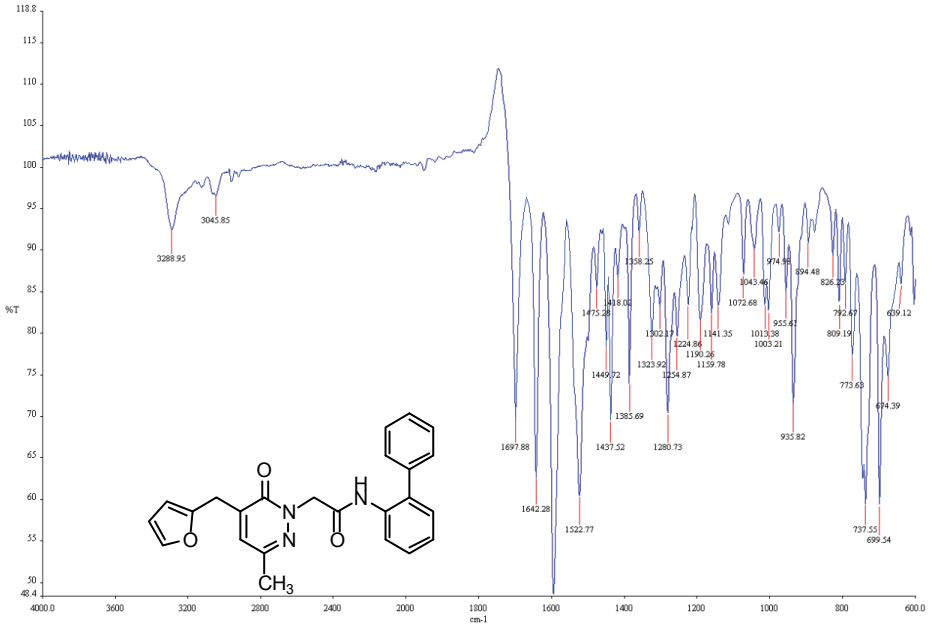


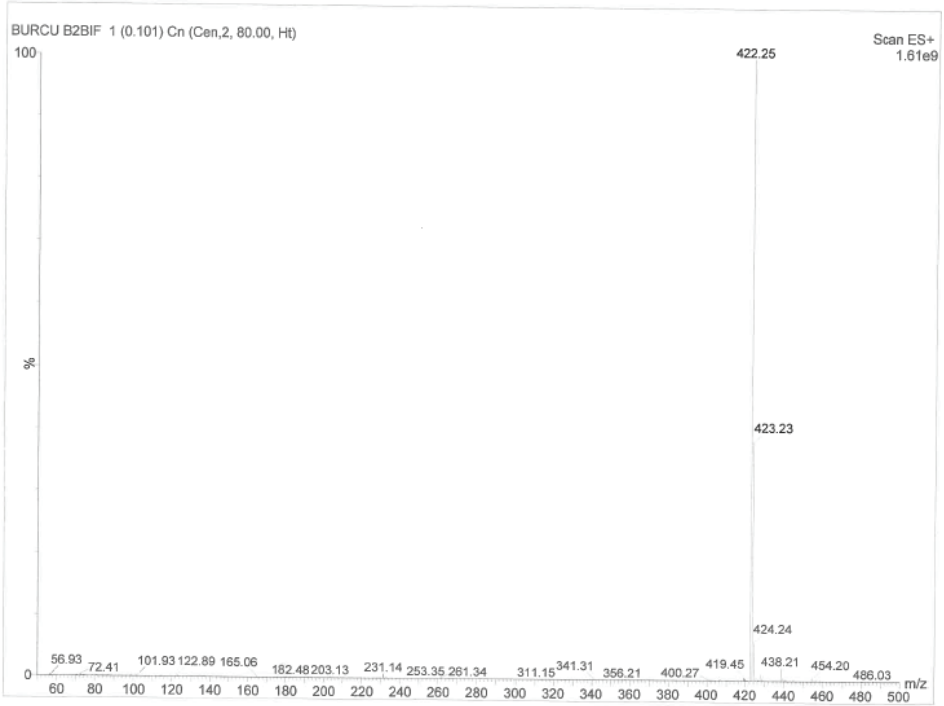


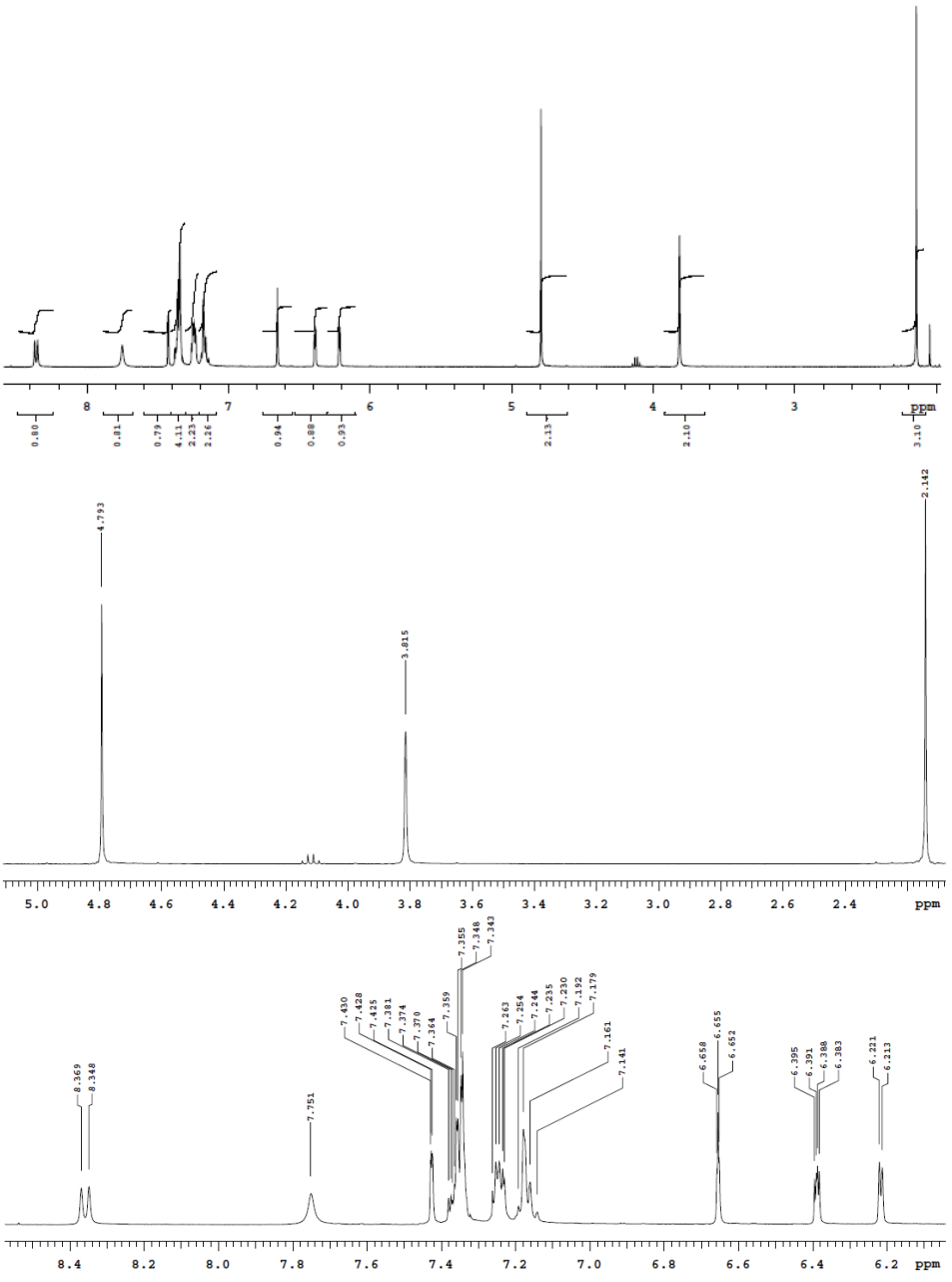


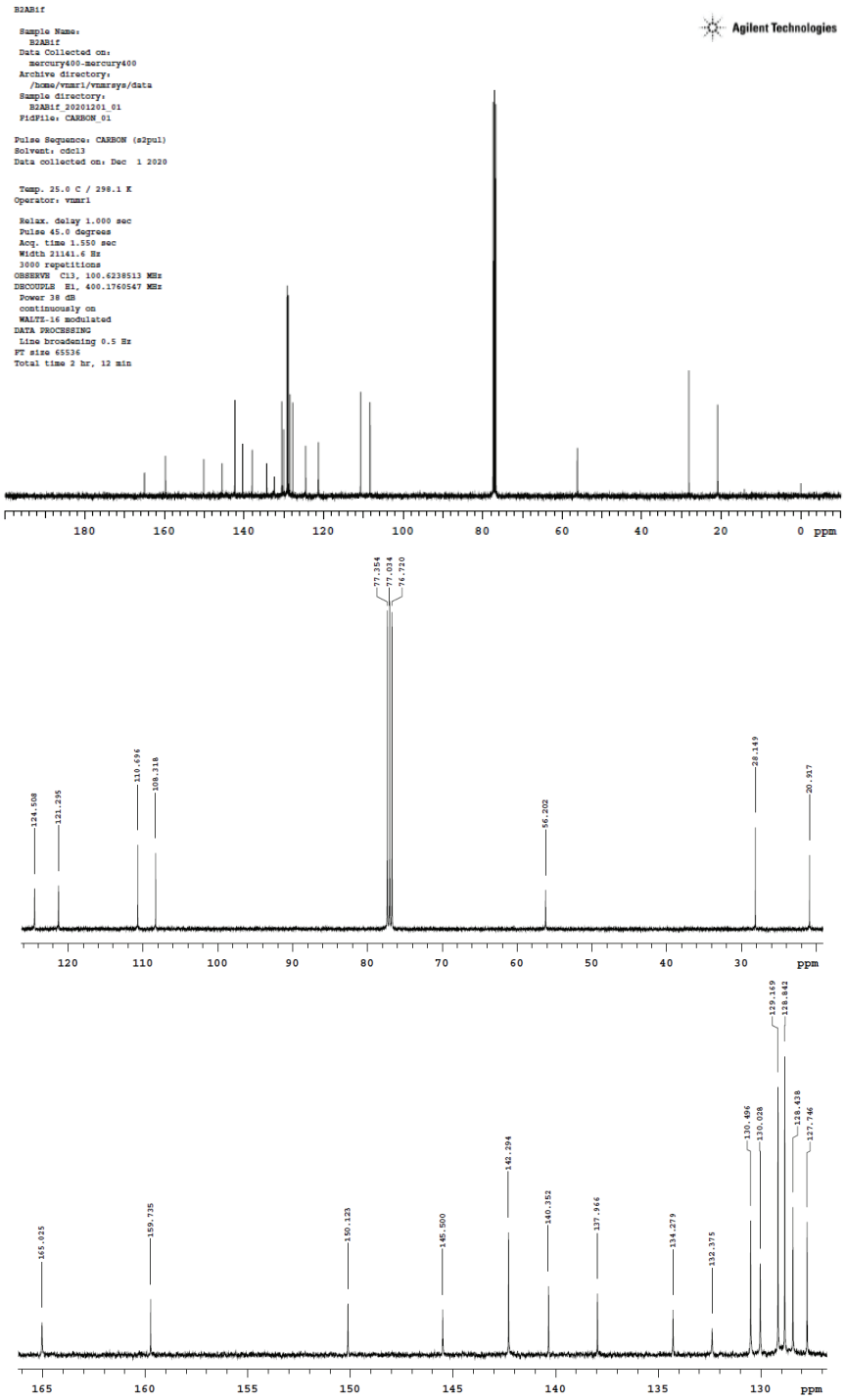


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-((1,1'-BIPHENYL)-2-YL)ACETAMIDE (5I)

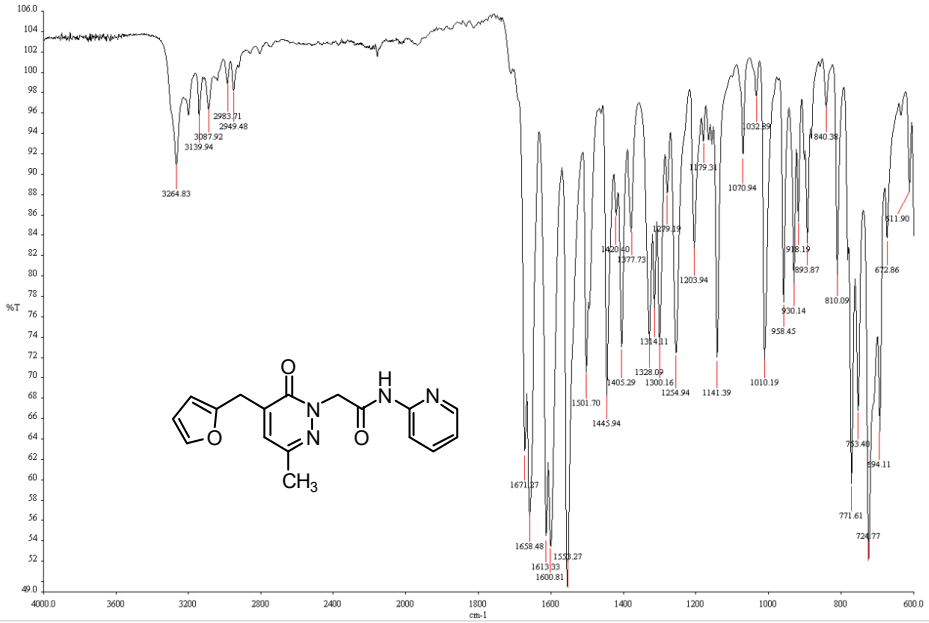


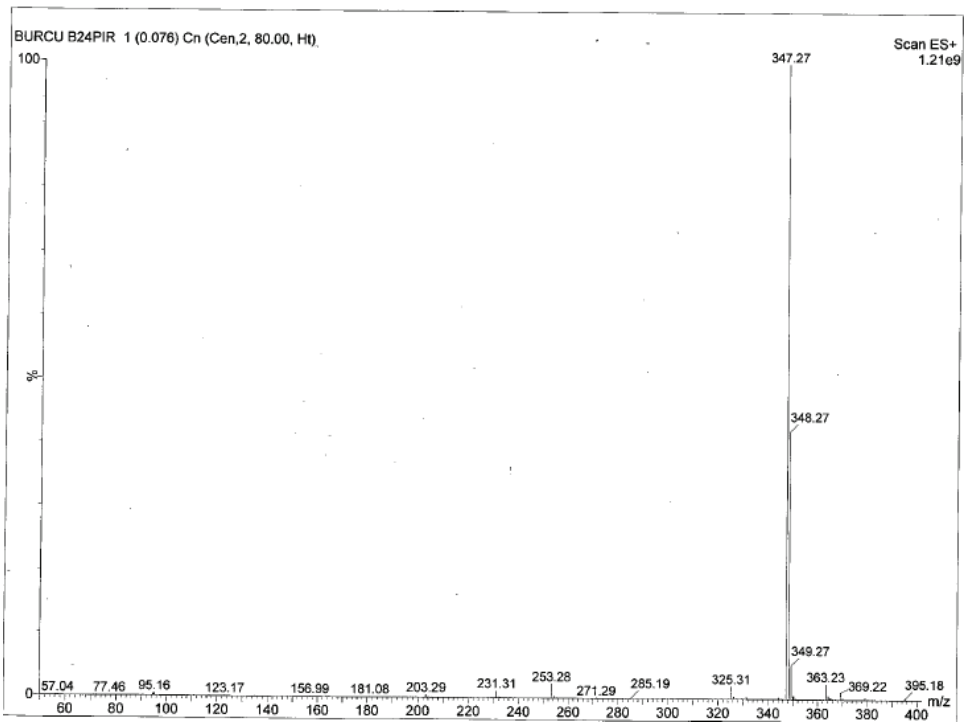


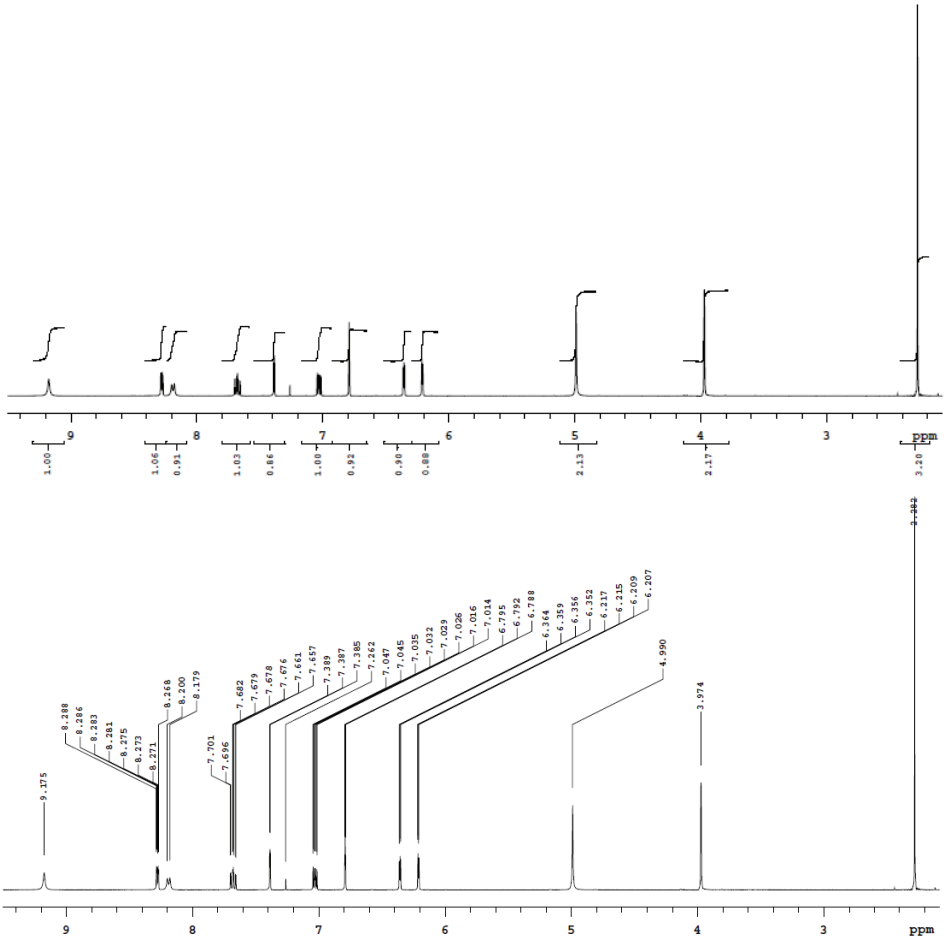


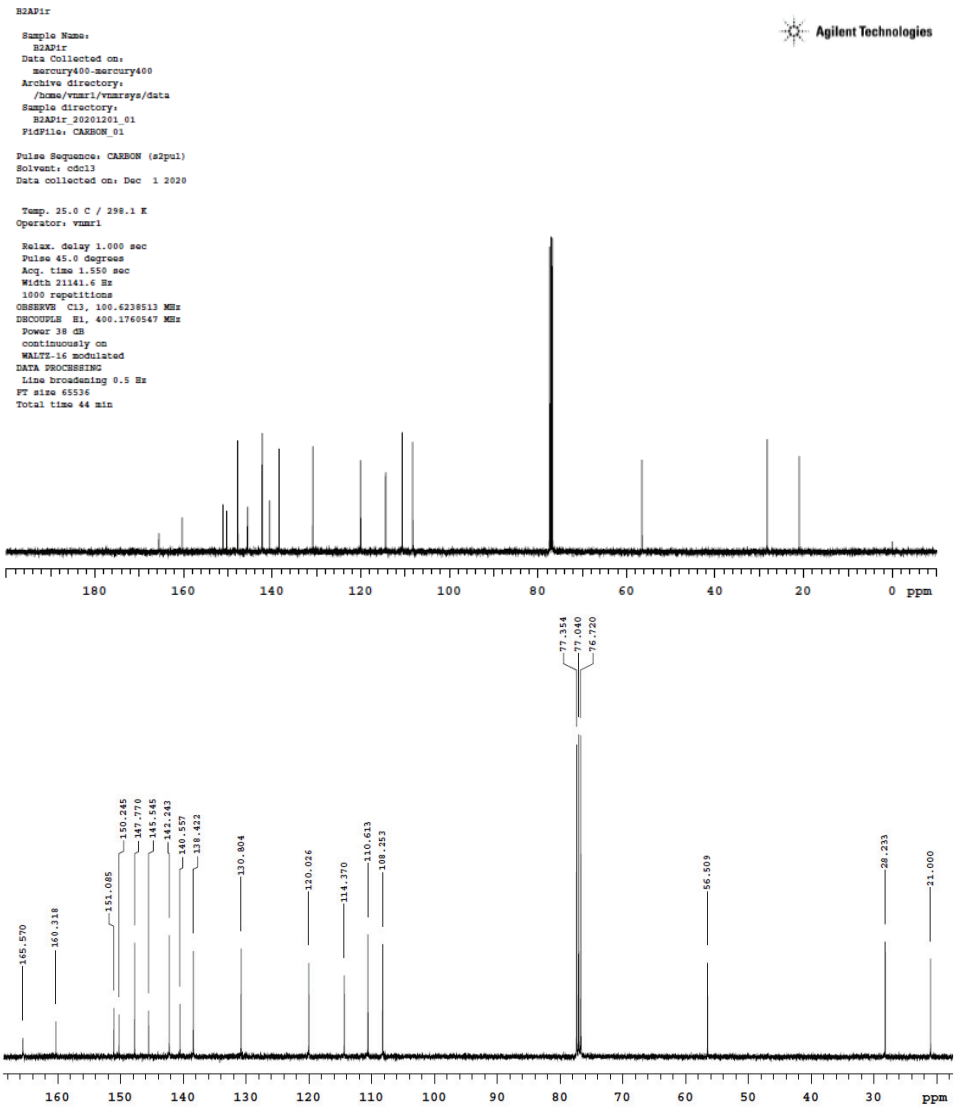


2-[5-(FURAN-2-YLMETHYL)-3-METHYL-6-OXOPYRIDAZIN-1(6*H*)-YL]-*N*-(PYRIDIN-2-YL)ACETAMIDE (5J)

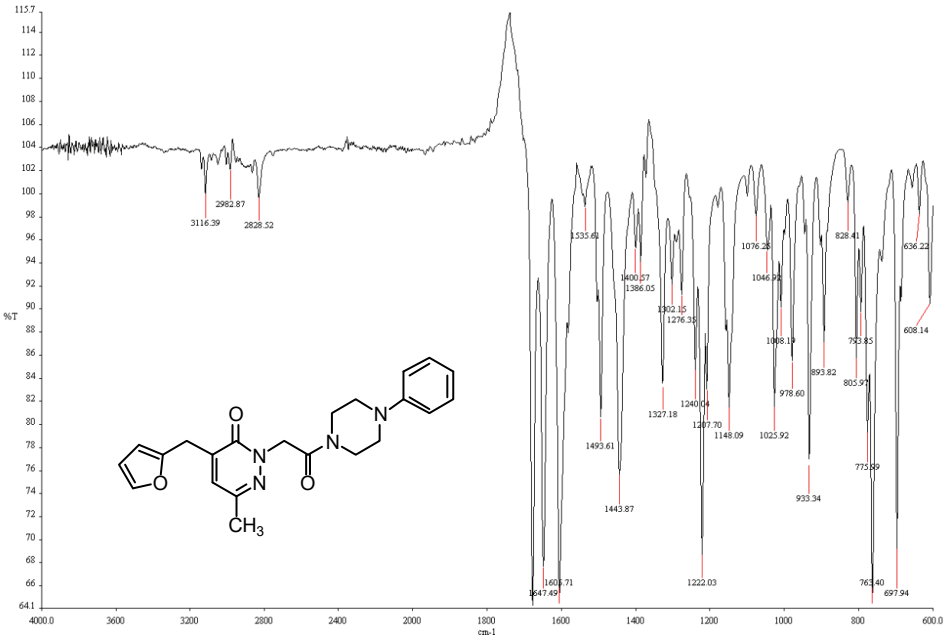


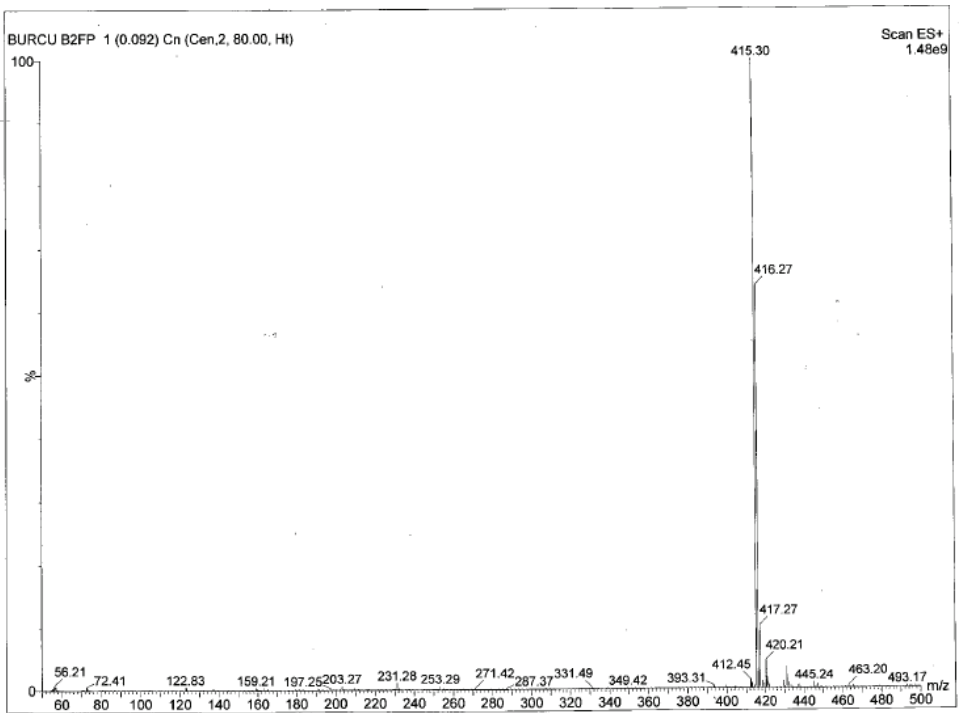


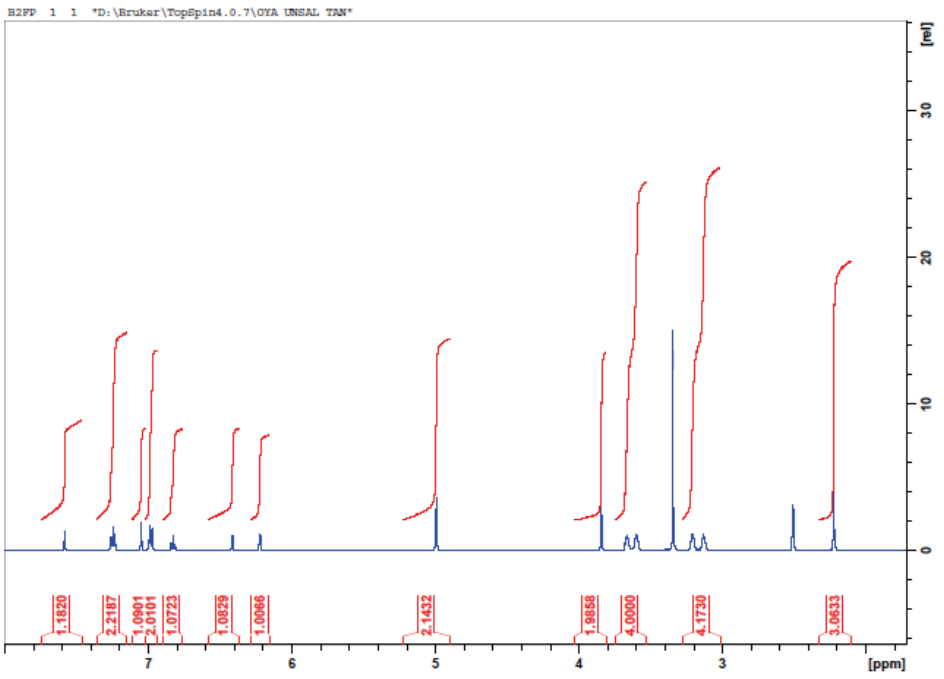


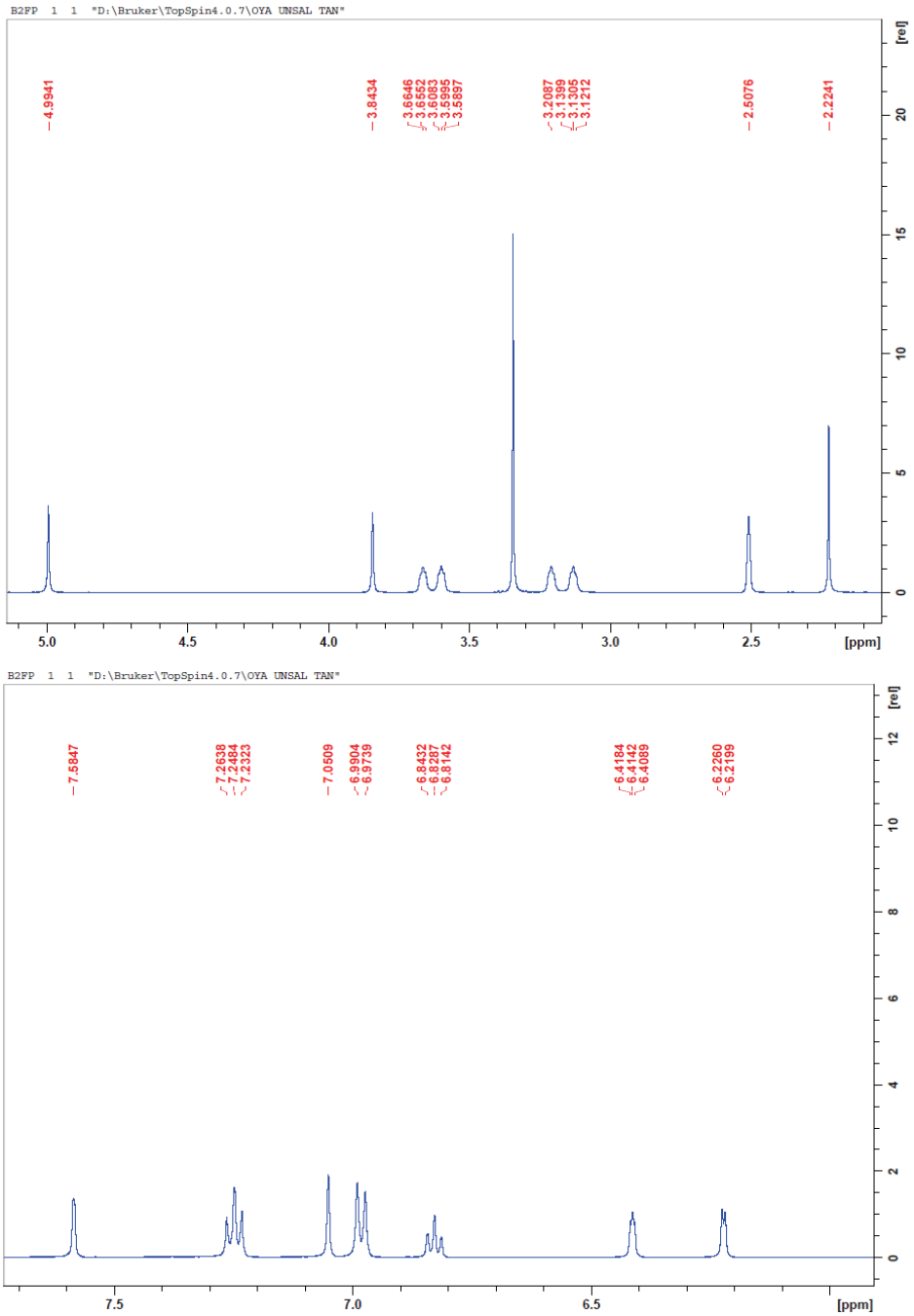


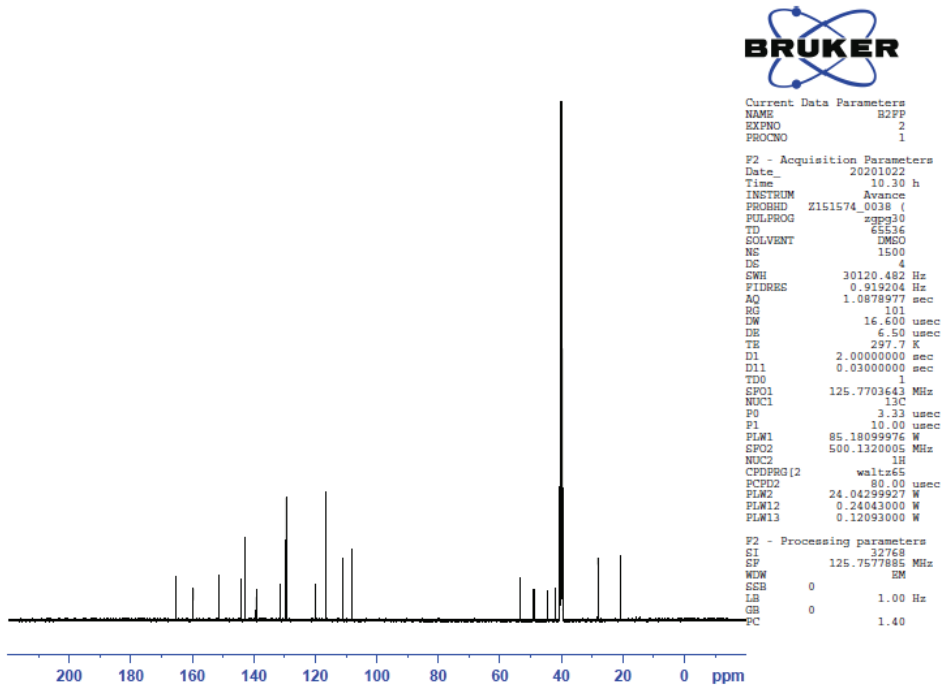
4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-PHENYLPIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6A)

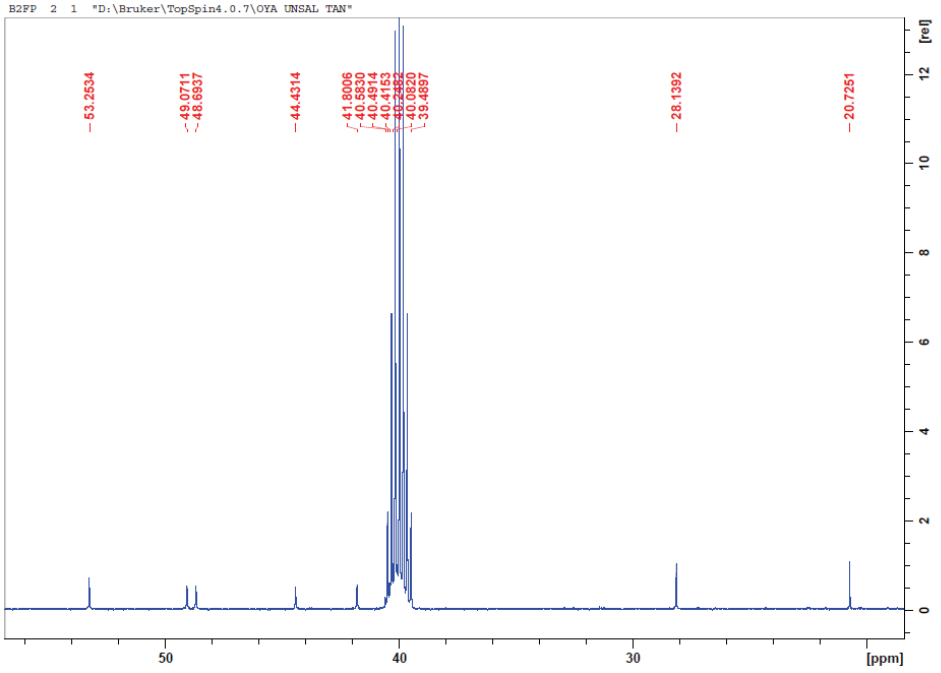


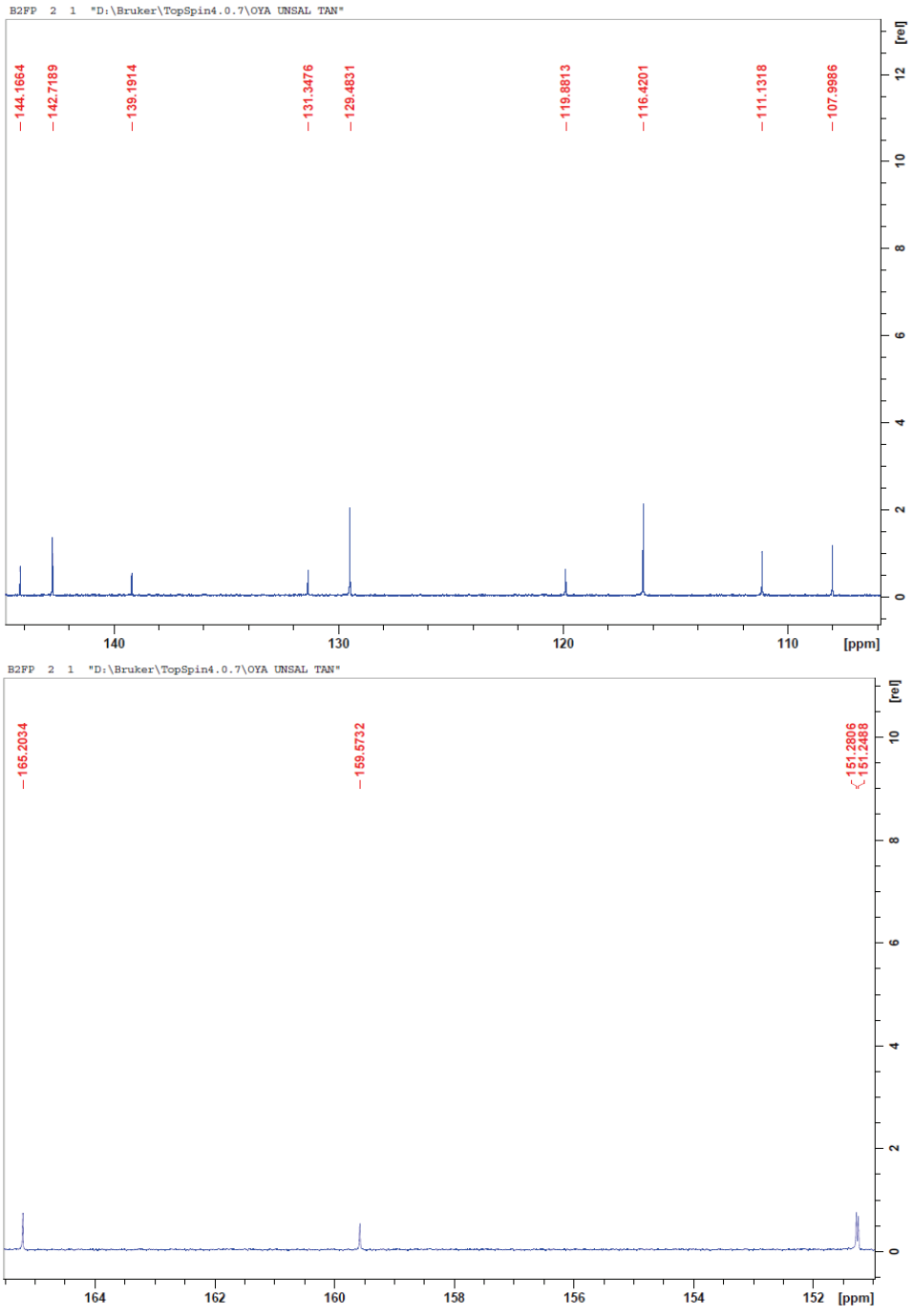




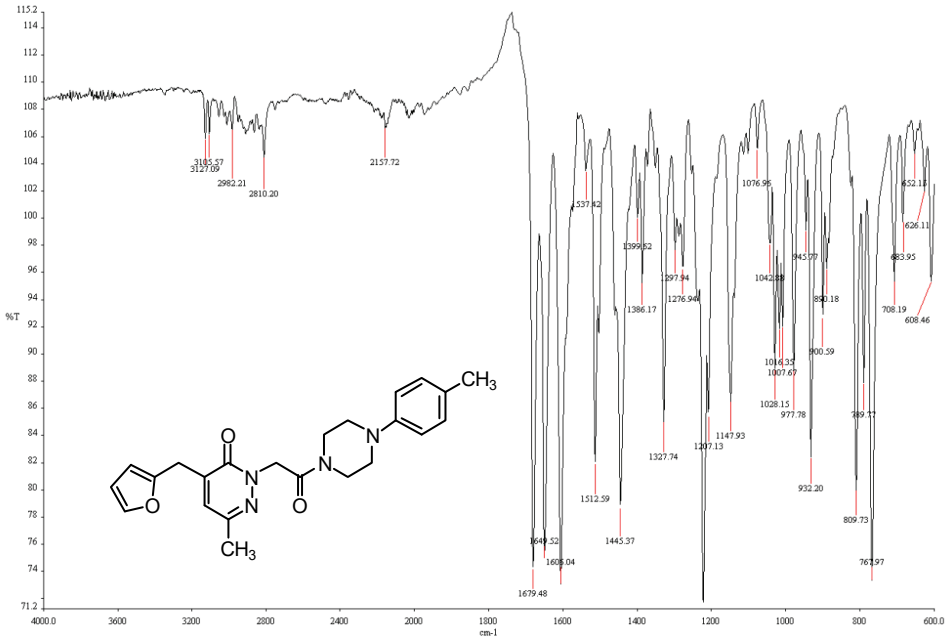


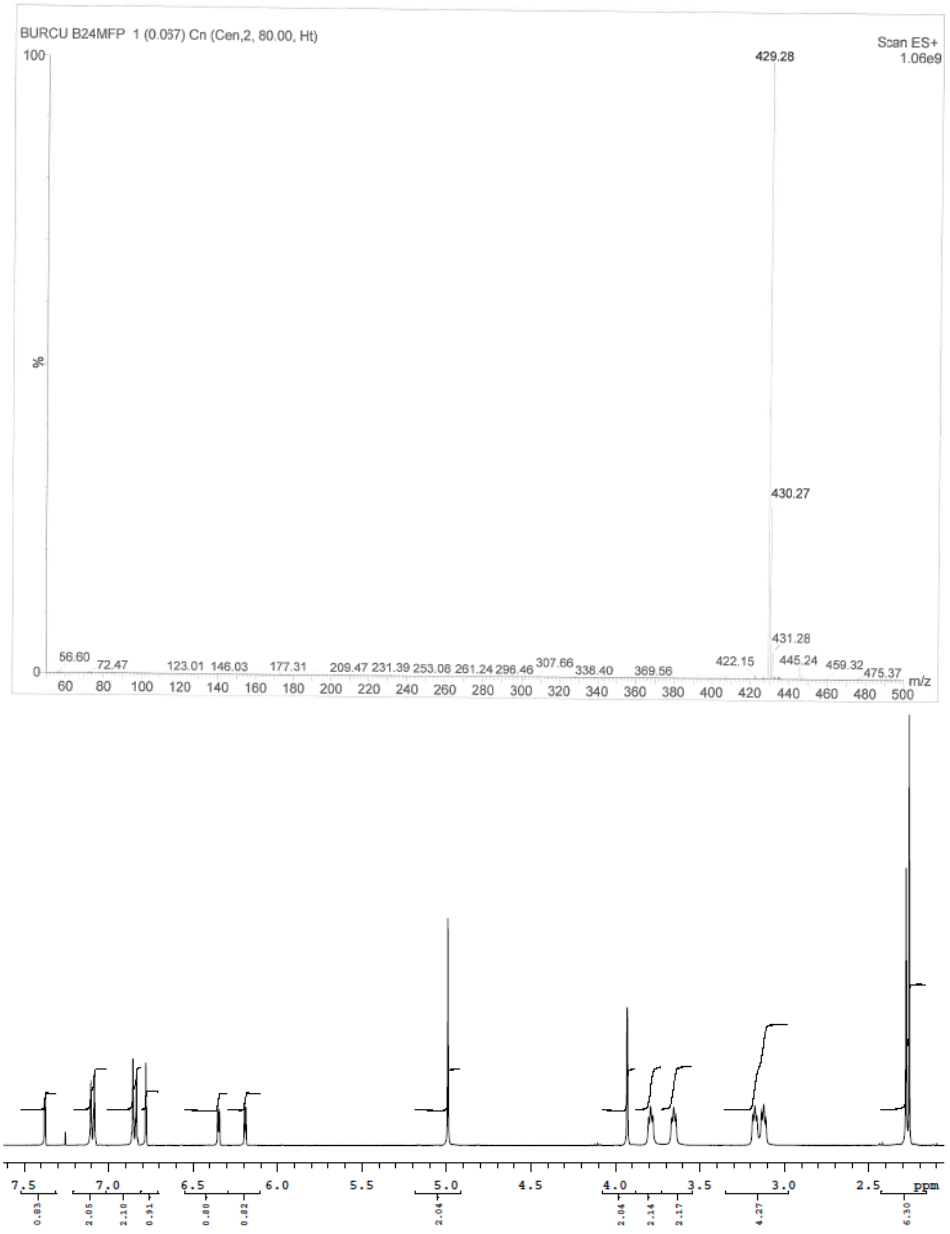


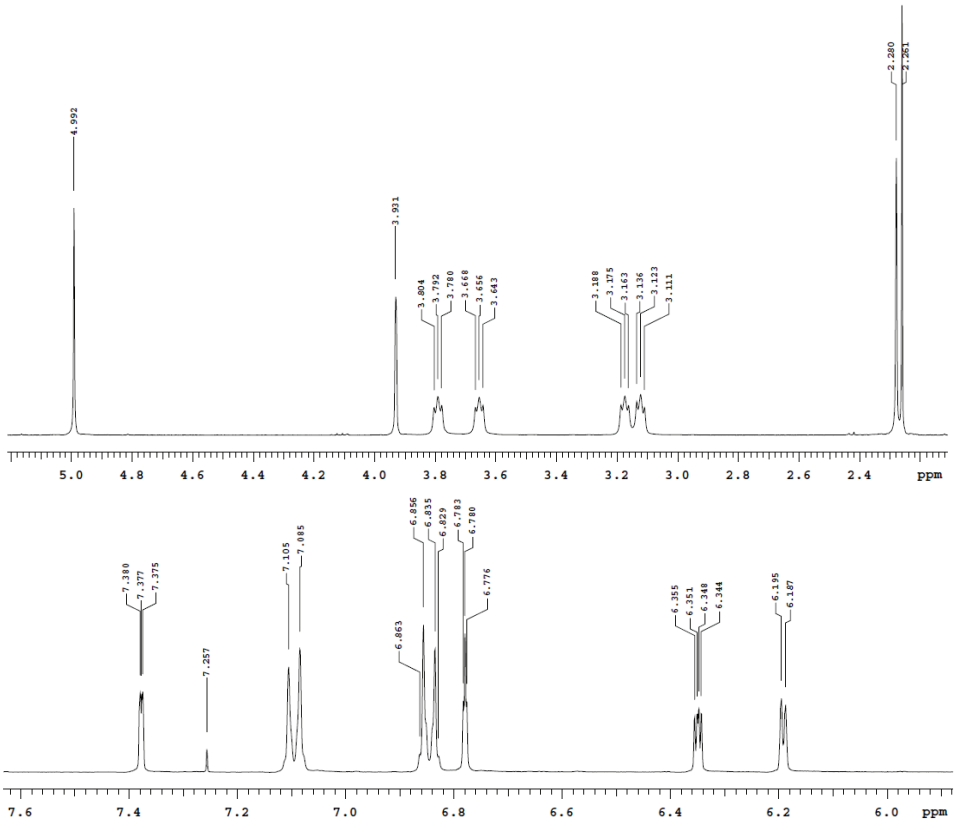


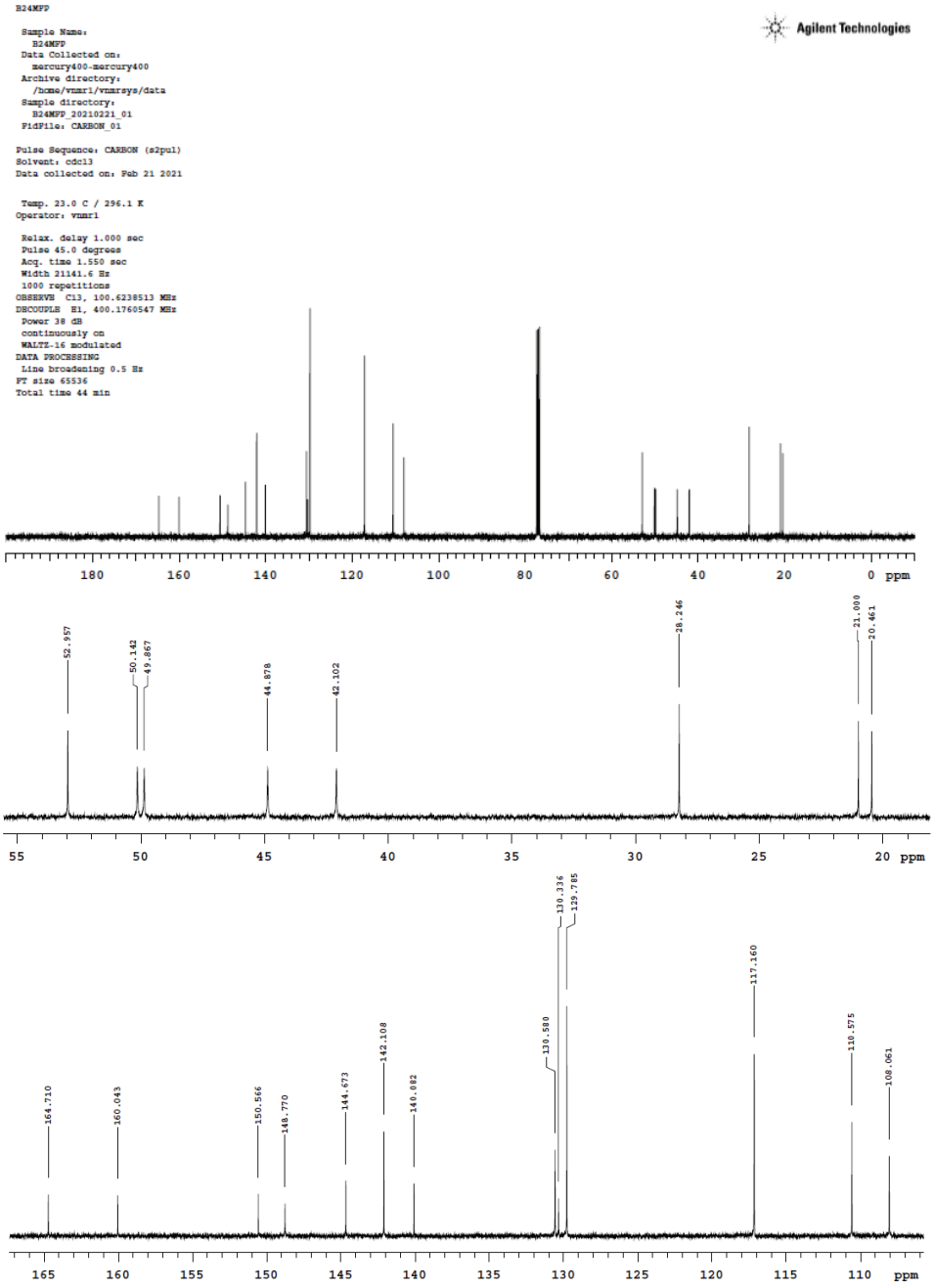


4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-(4-METHYLPHENYL)PIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6B)

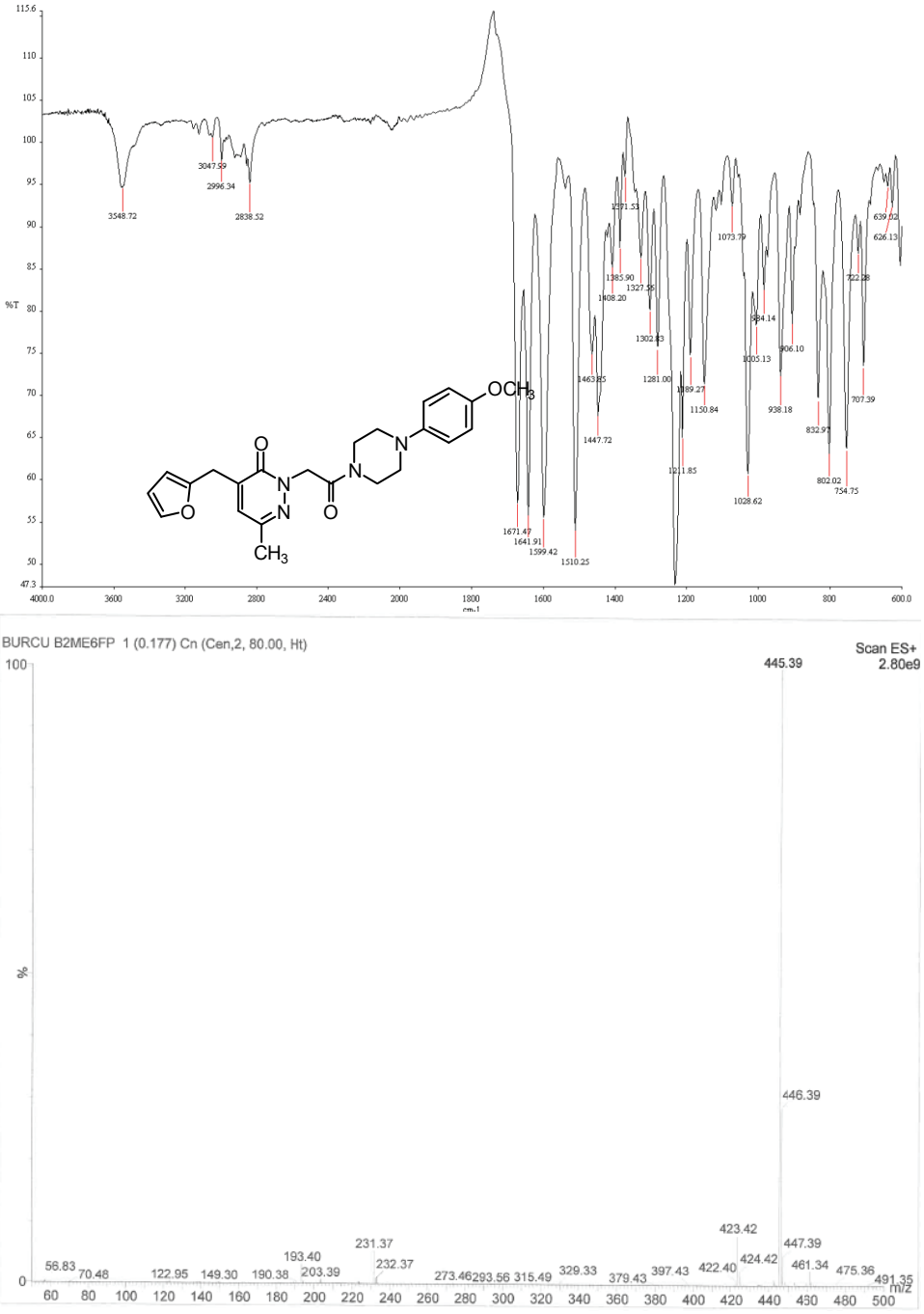


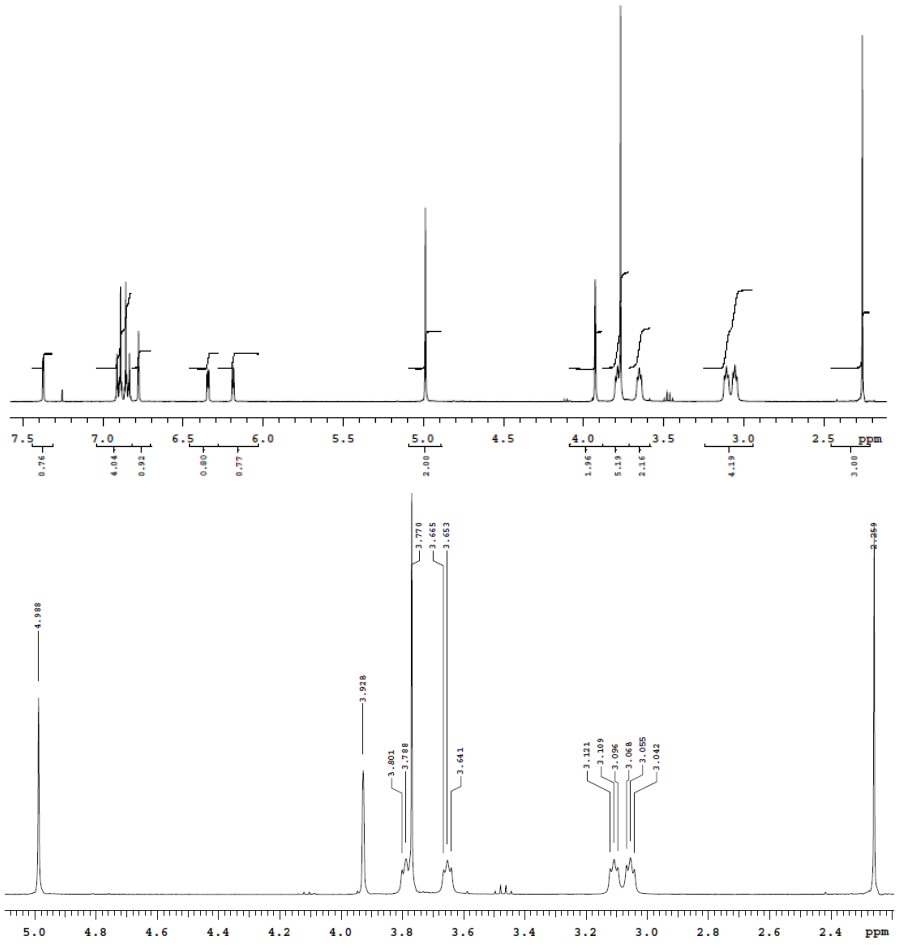


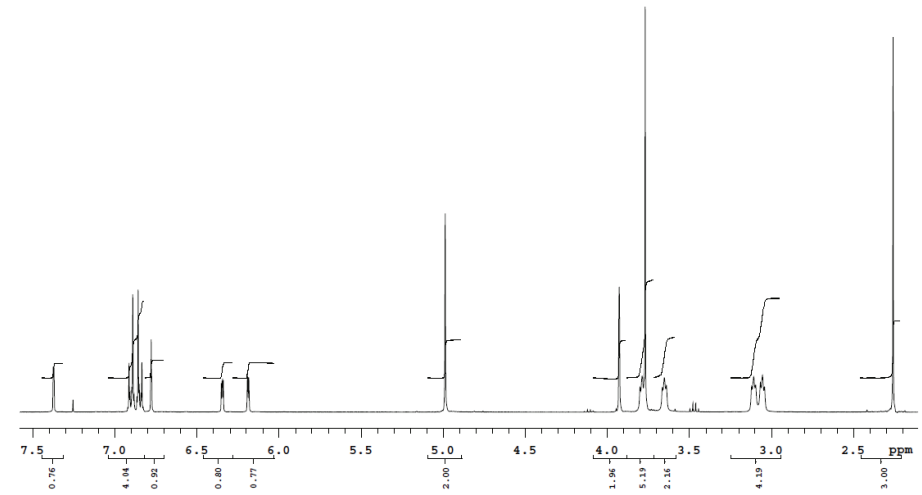


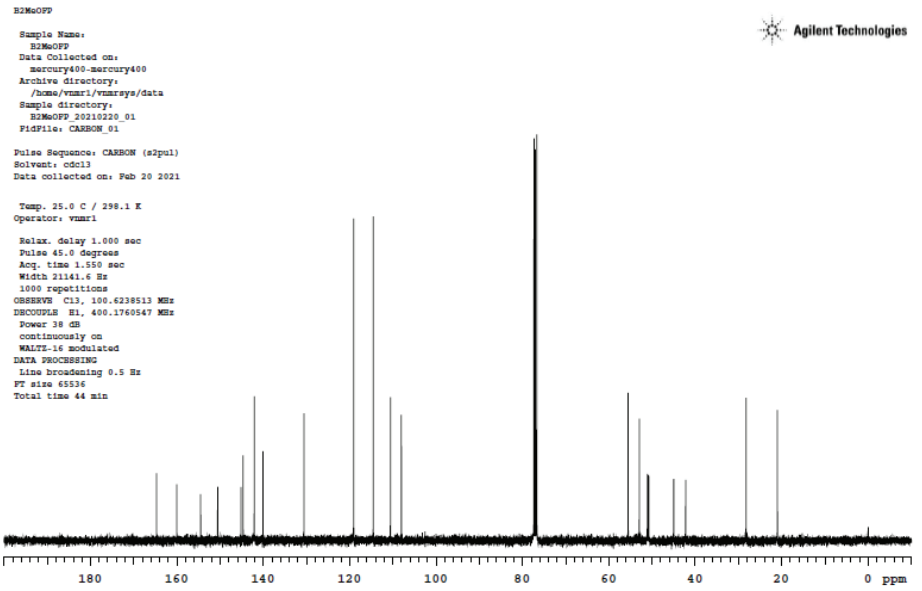


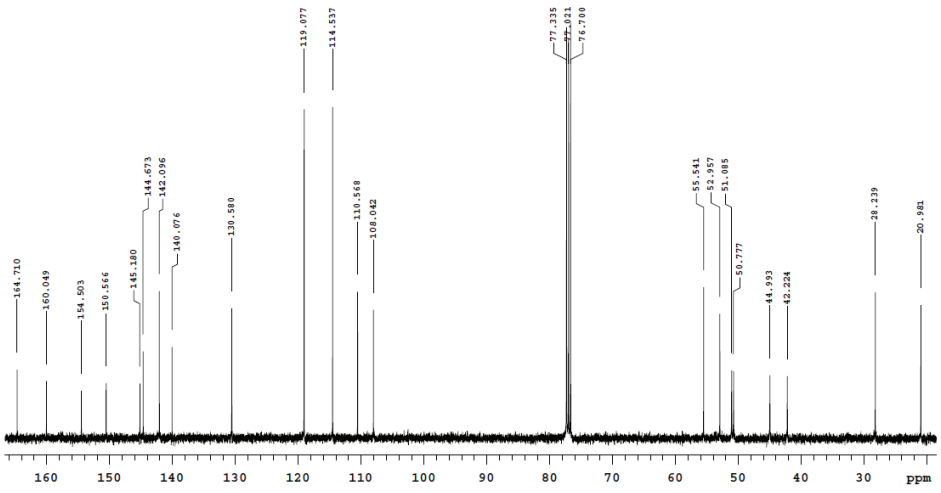
4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-(4-METHOXYPHENYL)PIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6C)



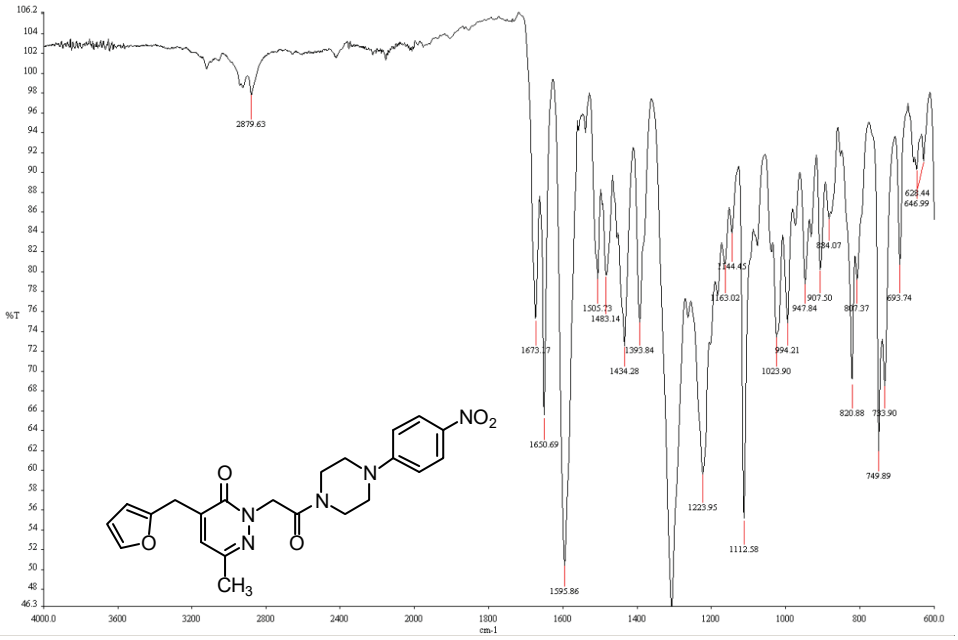


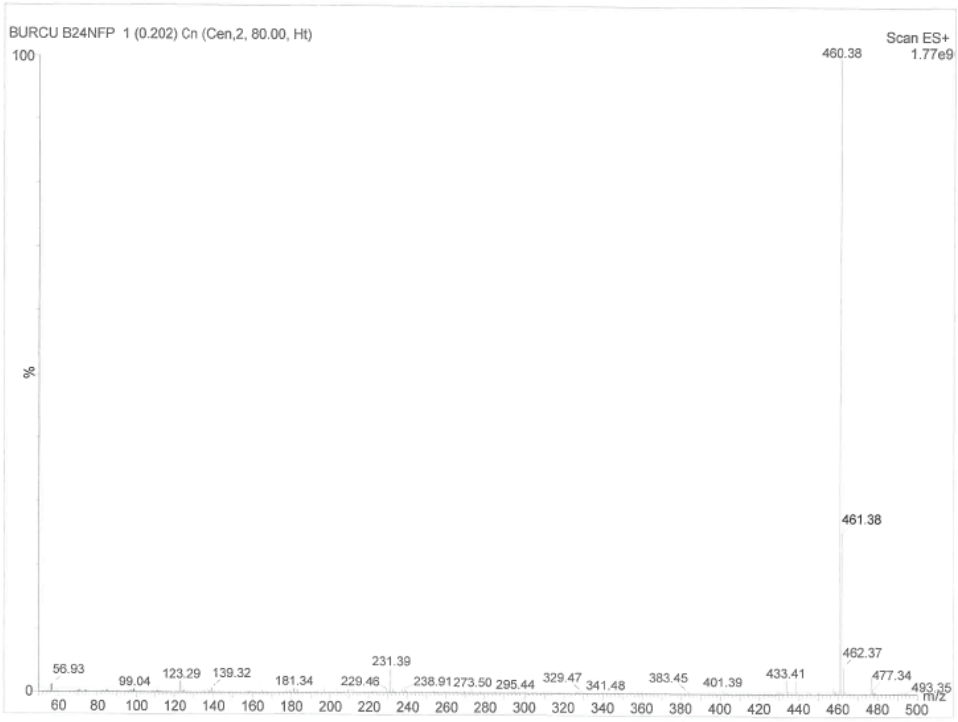


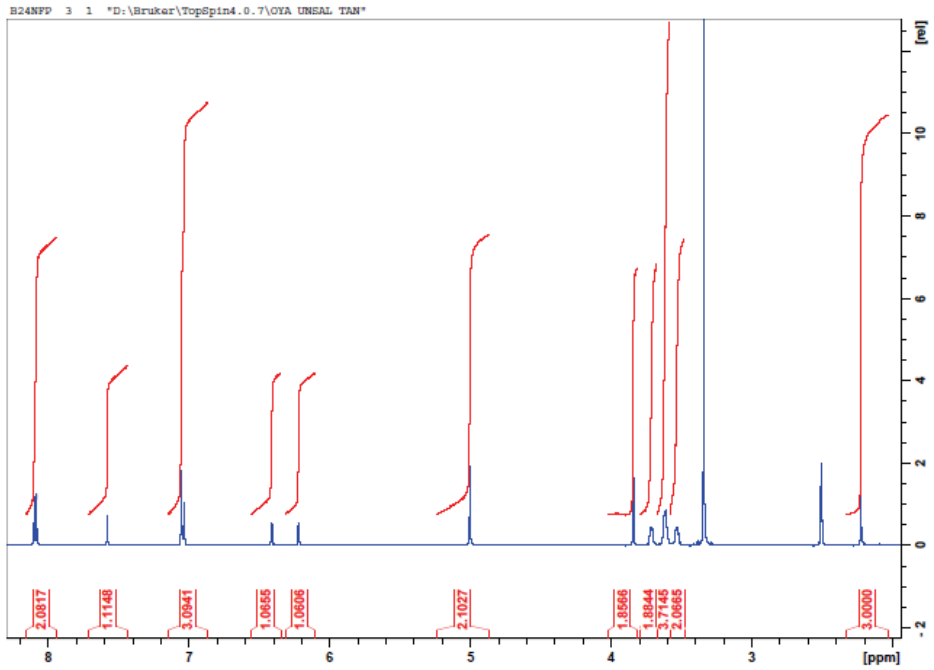


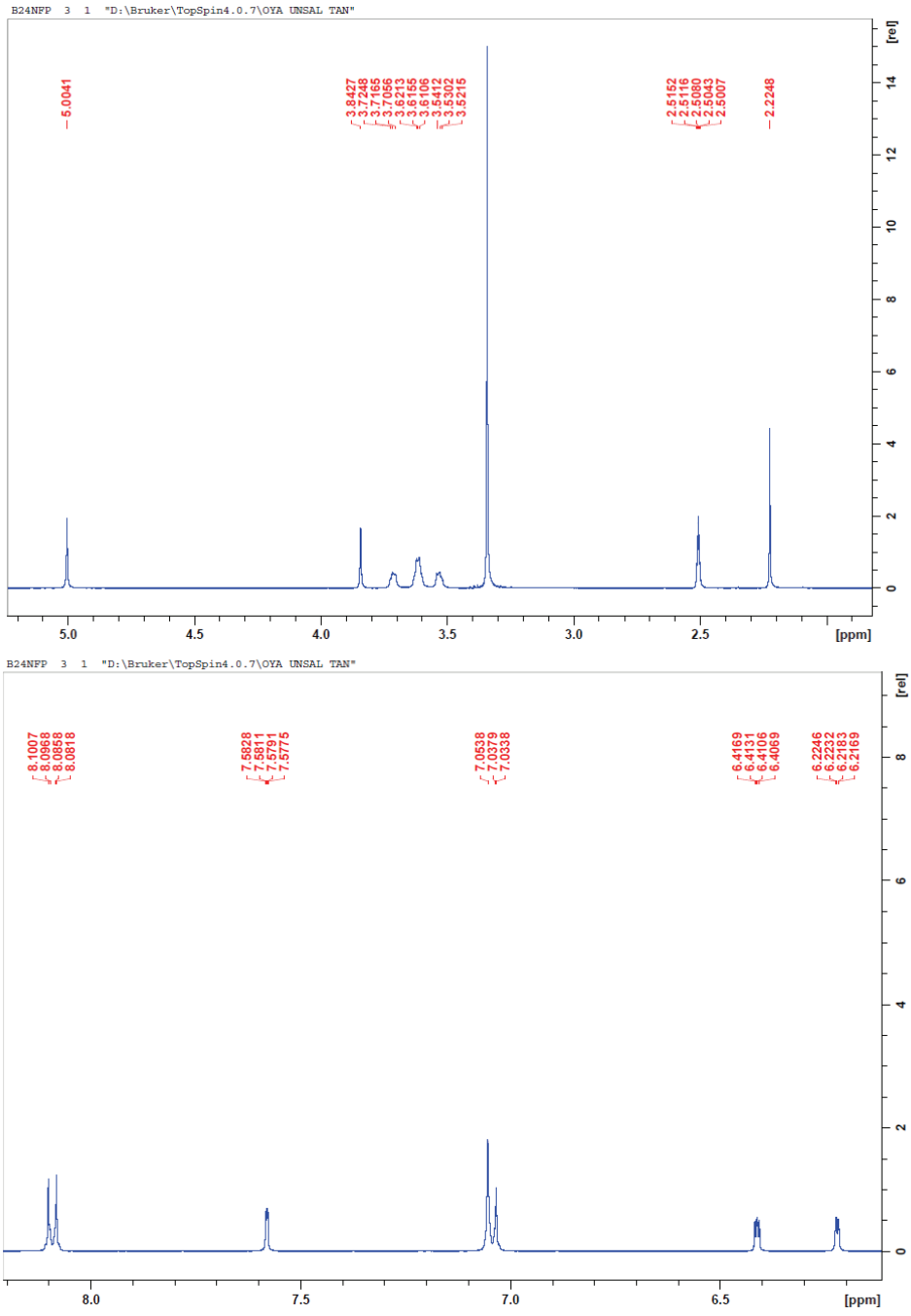


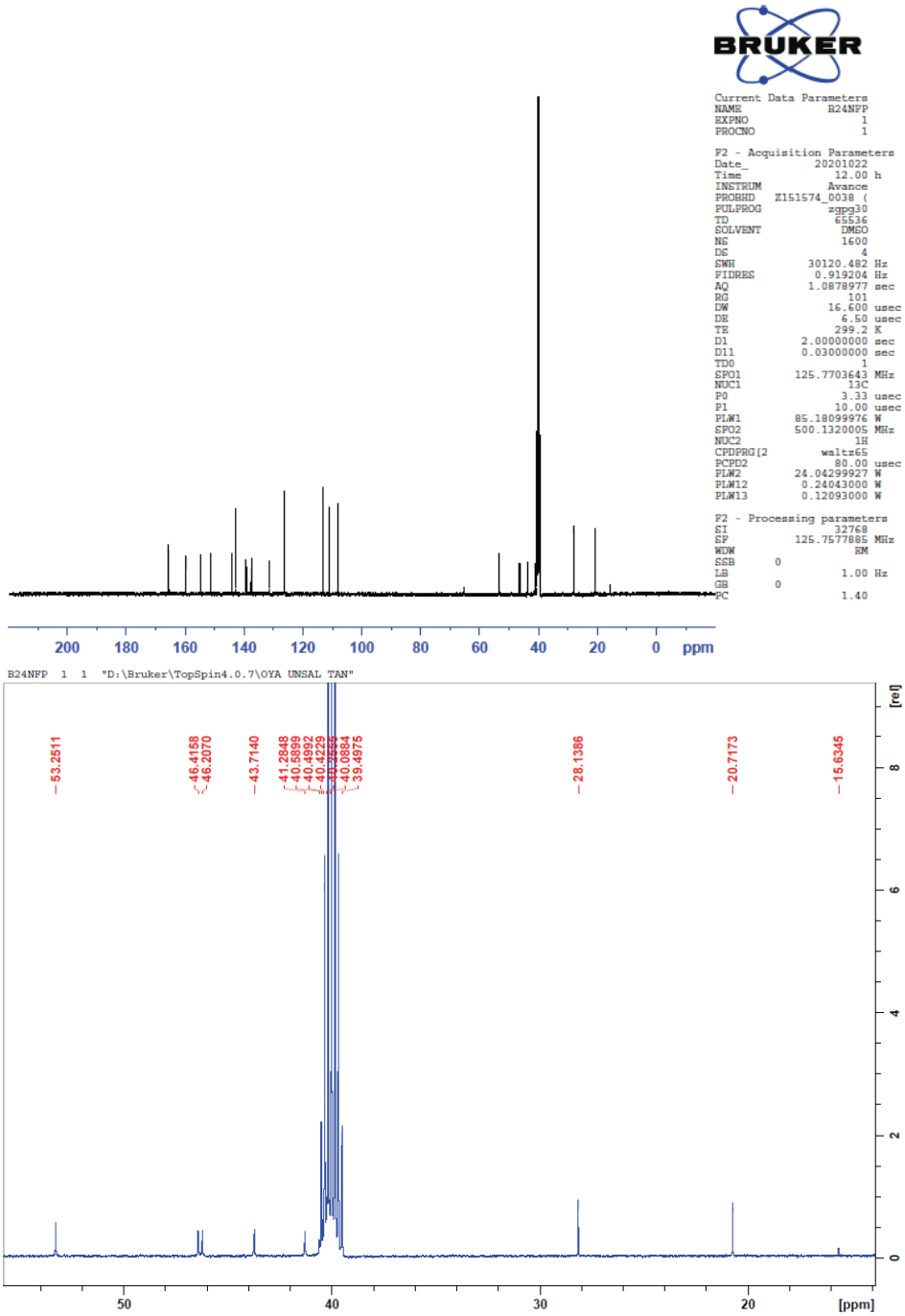
4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-(4-NITROPHENYL)PIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6D)

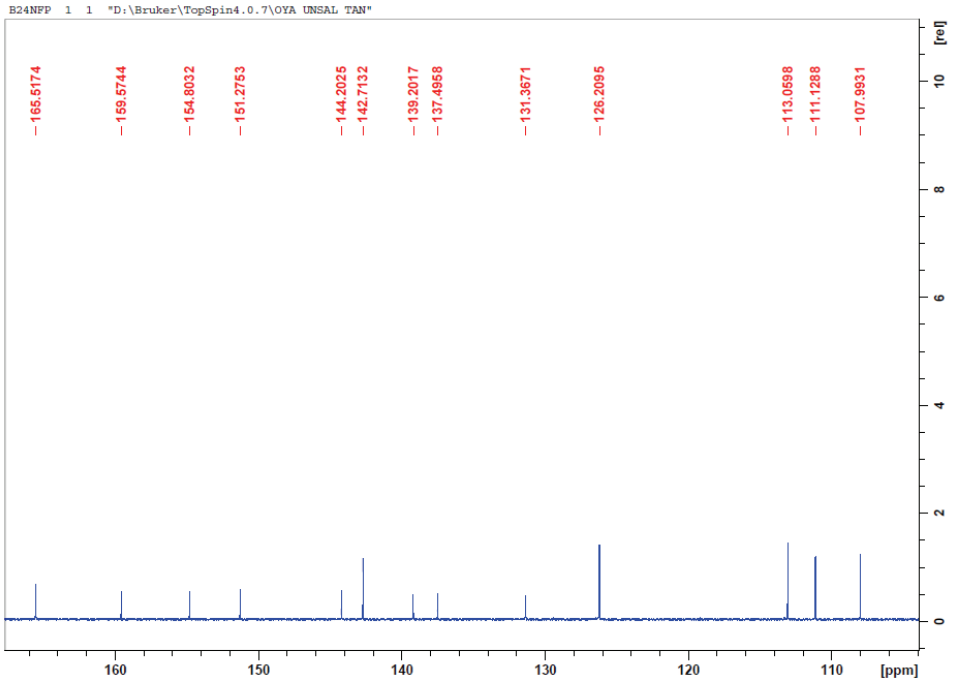




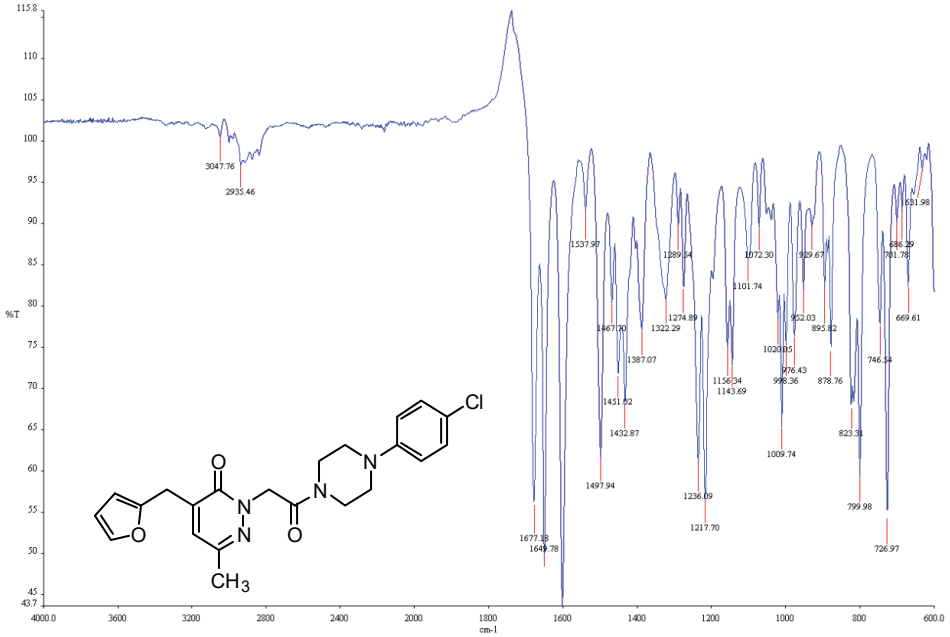


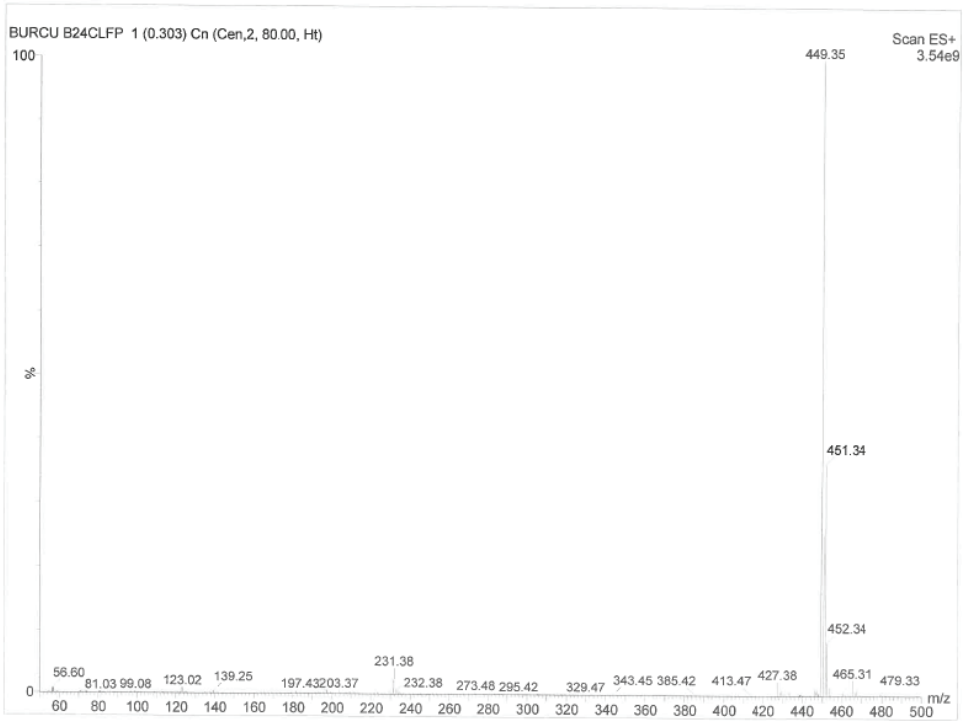


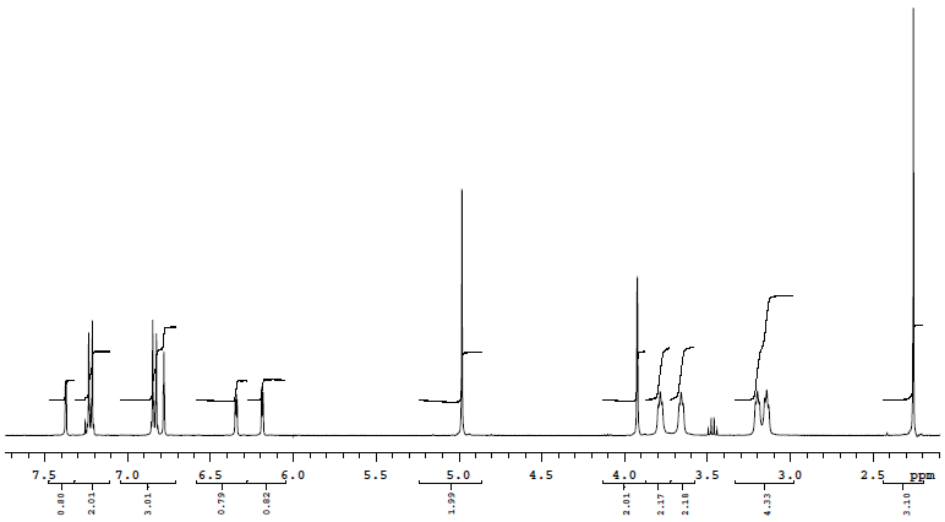


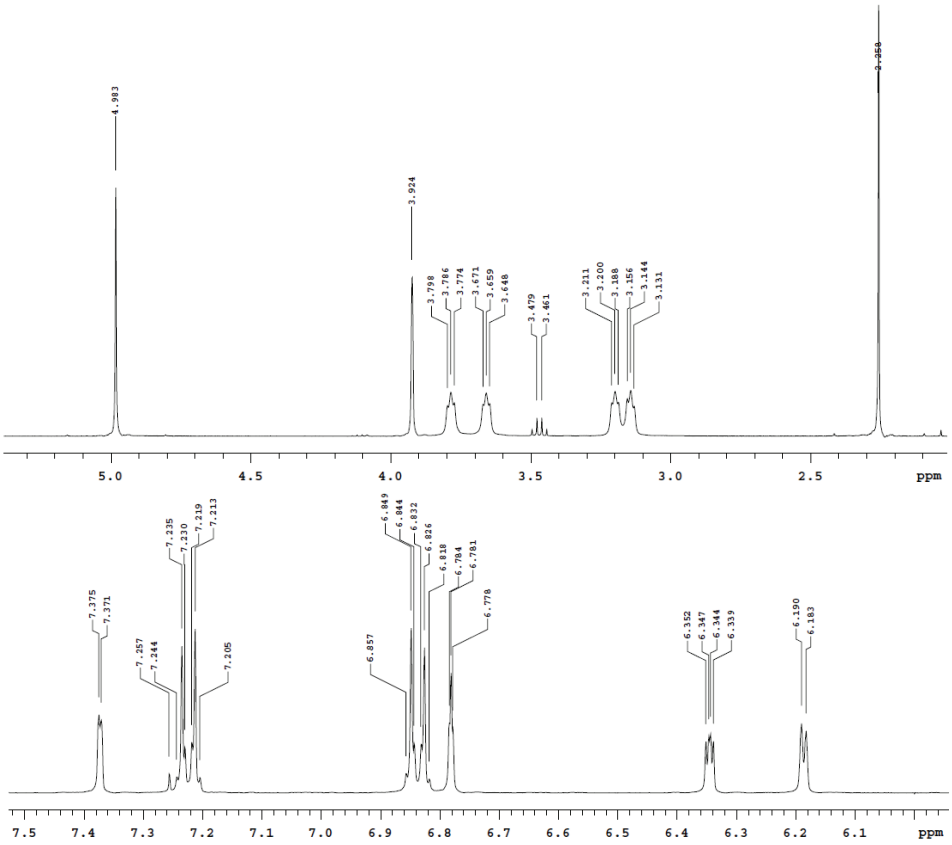


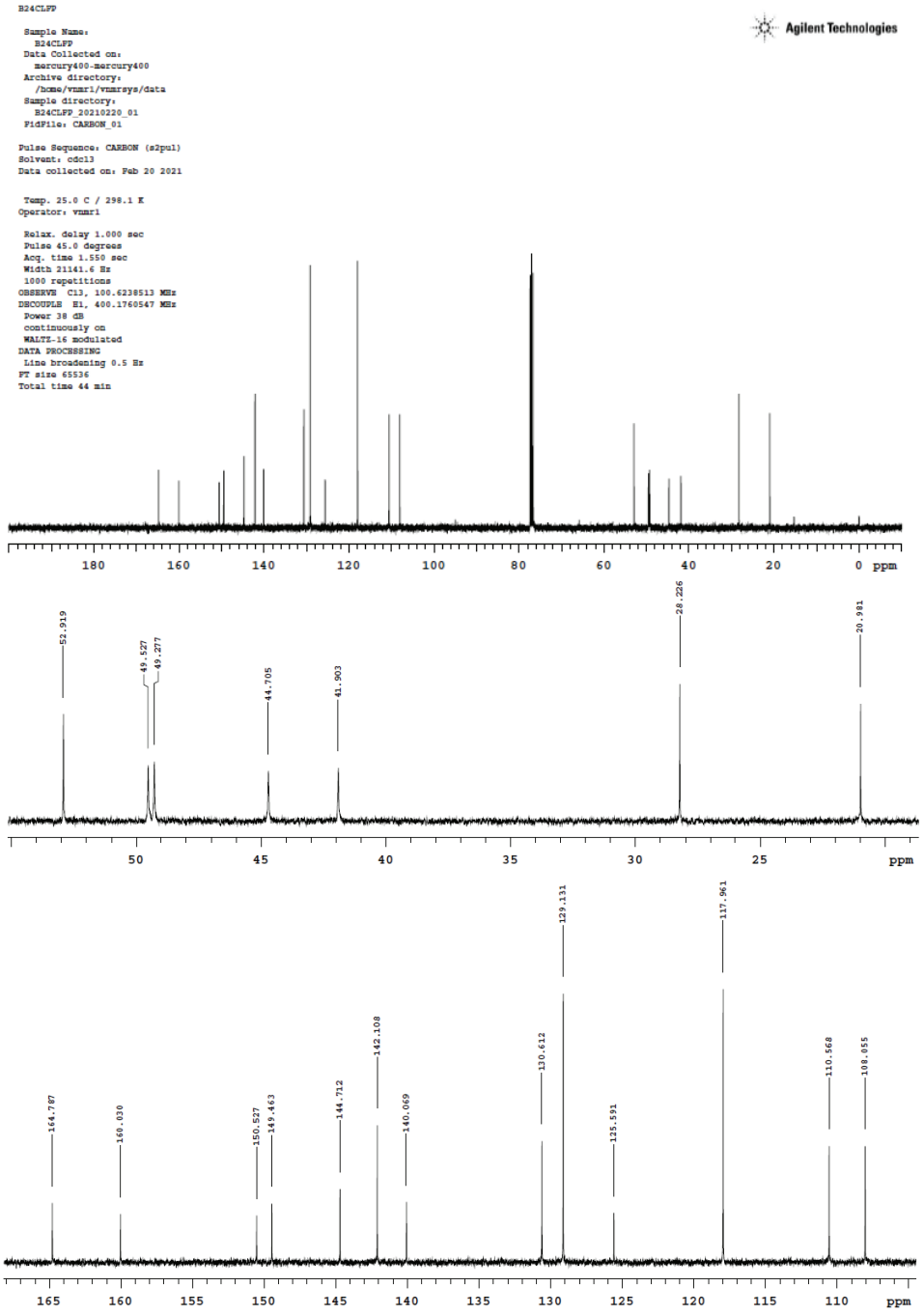
4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-(4-CHLOROPHENYL)PIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6E)











4-(FURAN-2-YLMETHYL)-6-METHYL-2-[2-OXO-2-(4-(4-FLUOROPHENYL)PIPERAZIN-1-YL)ETHYL]PYRIDAZIN-3(2*H*)-ONE (6F):