Electronic Supplementary Material (ESI) for RSC Advances

An efficient ultrasound-assisted one-pot chemoselective synthesis of pyrazolo[3,4-*b*]-pyridine-5-carbonitriles in aqueous medium using NaCl as a catalyst

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Experimental

Melting points were recorded on a Toshniwal apparatus and are uncorrected. The purity of compounds was checked on thin layers of silica gel in various non-aqueous solvent systems e.g. benzene:ethyl acetate(9:1), benzene:dichloromethane (8:2). IR spectra (KBr) were recorded on a Shimadzu FT IR–8400s spectrophotometer and ^{1}HNMR and ^{13}CNMR spectra were recorded on a Bruker DRX-300 instrument at 300 and 75, respectively, in DMSO-d_6 relative to tetramethylsilane as an internal reference. Mass spectrum of representative compound was recorded on Waters Xevo Q-Tof and API-2000 AB SCIEX spectrometer at 70 eV. Ultrasound irradiation was provided by ultrasonic processor probe (Processor SONOPROS PR-1000MP, OSCAR ULTRASONICS with power input 230V, 50 Hz, 4 Amps and power variac 0-230V and 3Amps) operating at 20 kHz, 750W with 6mm/12 mm tip diameter probes.

1.1 Conventional synthesis of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-5-carbonitrile ***(4b)****:*

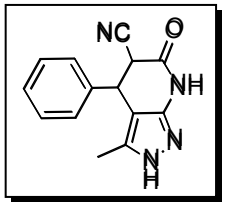
A mixture of 4-chlorobenzaldehyde **1b** (2.0 mmol), ethyl cynoacetate **2** (2.0 mmol) and 3-amino-5-methylpyrazole **3** (2.0 mmol) and 10 mol % sodium chloride was heated at reflux in water (30 ml) for 5 hr. After completion of the reaction as indicated by TLC (n-hexane: ethyl acetate, 7:3), the reaction mixture was allowed to cool. The solid product was filtered washed with water, dried and recrystallised from ethanol.

3.2 Ultrasonics synthesis of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2H-pyrazolo[3,4-b]pyridine-5-carbonitrile ***(4b)****:*

A mixture of 4-chlorobenzaldehyde **1b** (2.0 mmol), ethyl cynoacetate **2** (2.0 mmol) and 3-amino-5-methylpyrazole **3** (2.0 mmol) and 10 mol % sodium chloride in 20 ml water was introduced in a heavy walled pear-shaped two-necked flask with non-standard taper outer joint. The flask was attached to a 12mm tip diameter probe and the reaction mixture was sonicated for the 25 min at 50% power of the processor and in a 4 s pulse mode till a solid product separates out. Completion of the reaction was monitored by TLC using n-hexane: ethyl acetate (7:3) as the eluent. Upon completion, the reaction, the solid product was filtered washed with water, dried and recrystallised from ethanol.

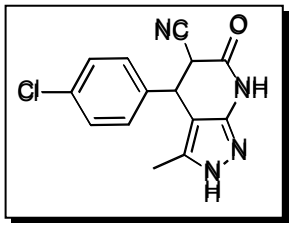
Representative data

3-methyl-6-oxo-4-phenyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4a)



White powder; IR (KBr) cm^{-1}: 3570, 3290, 2240, 1710, 1535; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.49 (s, 3H, CH_3), 4.41 (d, ^3J = 12.0 Hz, 1H, CH), 4.65 (d, ^3J = 11.7 Hz, 1H, CH), 7.12-7.56 (m, 5H, ArH), 10.96 (s, 1H, NH_{amid}), 11.99 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.95, 36.82, 43.92, 101.05, 117.58, 127.95, 128.66, 130.29, 135.77, 137.76, 147.68, 163.61 ppm.; (*cis* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 2.02 (s, 3H, CH_3), 4.51 (d, ^3J = 6.6 Hz, 1H, CH), 4.84 (d, ^3J = 6.9 Hz, 1H, CH), 7.12-7.56 (m, 5H, ArH), 10.99 (s, 1H, NH_{amid}), 12.04 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.51, 36.82, 42.84, 101.87, 117.05, 126.51, 128.10, 130.08, 137.77, 137.18, 147.59, 163.34 ppm; +ESI MS (m/z): 253 $[M+H]^+$.

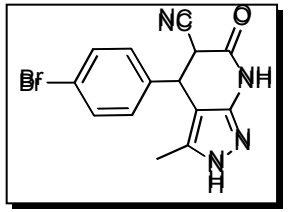
4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b)[1]



White powder; IR (KBr) cm^{-1}: 3572, 3294, 2244, 1706, 1540; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.47 (s, 3H, CH_3), 4.49 (d, ^3J = 12.0 Hz, 1H, CH), 4.68 (d, ^3J = 11.7 Hz, 1H, CH), 7.13-7.61 (m, 4H, ArH), 10.95 (s, 1H, NH_{amid}), 11.99 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 10.01, 36.67, 43.78, 100.51, 117.50, 129.27, 130.75, 132.90, 135.74, 138.56,

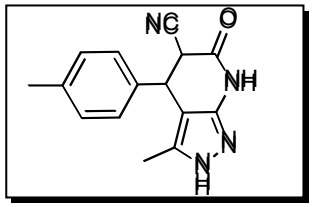
147.67, 163.33 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.06 (s, 3H, CH_3), 4.54 (d, ^{3}J = 6.6 Hz, 1H, CH), 4.89 (d, ^{3}J = 6.0 Hz, 1H, CH), 7.13-7.61 (m, 4H, ArH), 11.00 (s, 1H, NH_{amid}), 12.08 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.52, 36.67, 42.66, 101.28, 117.10, 129.61, 130.75, 132.70, 135.74, 139.50, 147.67, 163.09 ppm; +ESI MS (m/z): 287 $[M+H]^+$.

4-(4-bromophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4c)[1]



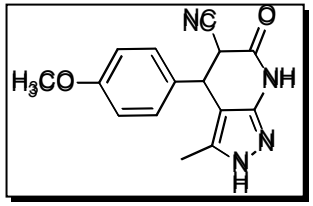
White powder; IR (KBr) cm^{-1}: 3572, 3294, 2244, 1706, 1540; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.44 (s, 3H, CH_3), 4.53 (d, ^{3}J = 12.0 Hz, 1H, CH), 4.74 (d, ^{3}J = 11.7 Hz, 1H, CH), 7.34-7.67 (m, 4H, ArH), 10.99 (s, 1H, NH_{amid}), 12.30 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 10.04, 36.26, 43.74, 100.48, 117.51, 122.02, 130.64, 132.23, 135.78, 139.08, 147.71, 163.26 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.01 (s, 3H, CH_3), 4.59 (d, ^{3}J = 6.6 Hz, 1H, CH), 4.93 (d, ^{3}J = 6.0 Hz, 1H, CH), 7.34-7.67 (m, 4H, ArH), 11.05 (s, 1H, NH_{amid}), 12.13 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.50, 36.26, 42.62, 101.25, 117.16, 121.91, 129.87, 132.21, 135.62, 139.89, 147.61, 163.03 ppm; +ESI MS (m/z): 331 $[M+H]^+$.

3-methyl-6-oxo-4-*p*-tolyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4d)[1]



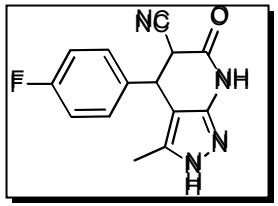
White powder; IR (KBr) cm^{-1}: 3575, 3315, 2250, 1710, 1542; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.46 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.39 (d, ^3J = 11.7 Hz, 1H, CH), 4.66 (d, ^3J = 12 Hz, 1H, CH), 7.01-7.29 (m, 4H, ArH), 10.99 (s, 1H, NH_{amid}), 12.01 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.93, 21.18, 37.13, 44.04, 100.99, 117.70, 127.56, 128.40, 129.80, 135.81, 136.41, 137.51, 147.65, 163.59 ppm. (*cis* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 2.01 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 4.46 (d, ^3J = 6.9 Hz, 1H, CH), 4.87 (d, ^3J = 6.6 Hz, 1H, CH), 7.01-7.29 (m, 4H, ArH), 11.02 (s, 1H, NH_{amid}), 12.10 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.54, 21.06, 37.13, 42.88, 101.93, 117.25, 127.56, 128.64, 129.76, 135.41, 137.22, 137.51, 147.65, 163.38 ppm; +ESI MS (m/z): 267 $[M+H]^+$.

4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)[1]



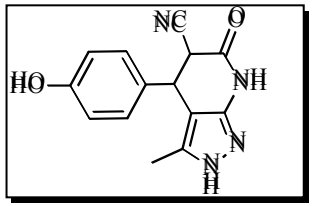
White powder; IR (KBr) cm^{-1}: 3566, 3274, 2238, 1694, 1530; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.48 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.38 (d, ^3J = 12.0 Hz, 1H, CH), 4.63 (d, ^3J = 12.0 Hz, 1H, CH), 6.87-7.32 (m, 4H, ArH), 10.93 (s, 1H, NH_{amid}), 11.96 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.92, 36.66, 44.16, 55.53, 101.24, 114.53,117.73, 129.88, 131.24, 135.76, 147.62, 159.00, 163.64 ppm. (*cis* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 2.00 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 4.45 (d, ^3J = 6.9 Hz, 1H, CH), 4.83 (d, ^3J = 6.6 Hz, 1H, CH), 6.87-7.32 (m, 4H, ArH), 10.96 (s, 1H, NH_{amid}), 12.06 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.53, 36.66, 44.16, 55.48, 102.08, 114.53, 117.29, 128.82, 132.39, 135.29, 147.62, 159.18, 163.35 ppm; +ESI MS (m/z): 283 $[M+H]^+$. HR-ESI-MS m/z: 283.0780 (Calcd for $C_{15}H_{15}N_4O_2$, 283.1195).

4-(4-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4f):



White powder; IR (KBr) cm^{-1}: 3572, 3286, 2238, 1702, 1546; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.48 (s, 3H, CH_3), 4.38 (d, ^{3}J = 12.0 Hz, 1H, CH), 4.63 (d, ^{3}J = 11.7 Hz, 1H, CH), 6.84-7.32 (m, 4H, ArH), 10.94 (s, 1H, NH_{amid}), 11.97 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.53, 37.10, 44.02, 101.00, 117.70, 128.65, 129.79, 135.75, 136.42, 137.44, 147.66, 163.58 ppm.; (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.01 (s, 3H, CH_3), 4.45 (d, ^{3}J = 6.9 Hz, 1H, CH), 4.83 (d, ^{3}J = 6.6 Hz, 1H, CH), 6.84-7.32 (m, 4H, ArH), 10.97 (s, 1H, NH_{amid}), 12.07 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.93, 37.10, 42.87, 101.93, 117.24, 127.55, 129.75, 135.35, 136.42, 137.20, 147.60, 163.36 ppm; +ESI MS (m/z): 271 $[M+H]^{+}$.

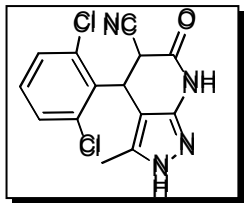
4-(4-hydroxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4g)[1]



White powder; IR (KBr) cm^{-1}: 3582, 3276, 2256, 1708, 1548; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.47 (s, 3H, CH_3), 4.75 (d, ^{3}J = 12.0 Hz, 1H, CH), 4.84 (d, ^{3}J = 12.0 Hz, 1H, CH), 7.69-8.32 (m, ArH, 4H), 11.05 (s, 1H, NH_{amid}), 12.12 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 10.11, 36.96, 44.25, 100.17, 117.35, 124.85, 130.69, 136.12, 147.88, 148.10, 148.41, 162.91 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.02 (s, 3H, CH_3), 4.79 (d, ^{3}J = 6.9 Hz, 1H, CH), 5.07 (d, ^{3}J =

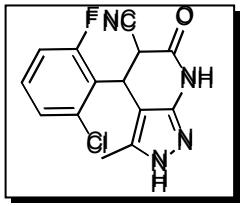
6.6 Hz, 1H, CH), 7.69-8.32 (m, ArH, 4H), 11.17 (s, 1H, NH_{amid}), 12.20 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.49, 36.96, 43.19, 100.81, 117.29, 124.92, 130.15, 136.71, 147.96, 148.10, 148.25, 162.72 ppm; +ESI MS (m/z): 269 $[M+H]^+$.

4-(2,6-dichlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4h)[1]



White powder; IR (KBr) cm^{-1}: 3604, 3336, 2262, 1714, 1530; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.51 (s, 3H, CH_3), 4.94 (d, ^3J = 12 Hz, 1H, CH), 5.53 (d, ^3J = 12.3 Hz, 1H, CH), 7.41-7.65 (m, 3H, $3CH_{arom}$), 11.05 (s, 1H, NH_{amid}), 12.06 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.34, 36.75, 38.95, 97.52, 117.03, 128.96, 131.15, 131.36, 135.54, 137.01, 147.34, 162.71 ppm. (*cis* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.91 (s, 3H, CH_3), 5.21 (d, ^3J = 9.0 Hz, 1H, CH), 5.57 (d, ^3J = 9.0 Hz, 1H, CH), 7.41-7.65 (m, 3H, $3CH_{arom}$), 10.99 (s, 1H, NH_{amid}), 12.02 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.61, 34.05, 38.07, 96.23, 116.84, 128.77, 130.75, 130.91, 135.17, 135.95, 148.26, 163.77 ppm; +ESI MS (m/z): 321 $[M+H]^+$.

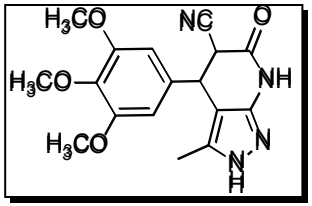
4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)



White powder; IR (KBr) cm^{-1}: 3612, 3344, 2248, 1716, 1536; (*trans* isomer) ^1H NMR (300 MHz, DMSO-d_6) δ: 1.54 (s, 3H, CH_3), 4.74 (d, ^3J = 12.6 Hz, 1H, CH), 5.17 (d, ^3J = 12.6 Hz, 1H, CH), 7.18-7.54 (m, ArH, 3H), 10.97 (s, 1H, NH_{amid}), 12.11 (brs, 1H,

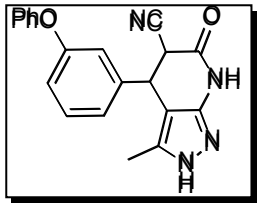
$NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.95, 37.52, 44.24, 97.54, 116.62, 123.52, 125.84, 127.43, 133.71, 136.14, 147.32, 160.37, 162.78 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.00 (s, 3H, CH_3), 5.13 (d, ^{3}J = 9.0 Hz, 1H, CH), 5.22 (d, ^{3}J = 9.0 Hz, 1H, CH), 7.18-7.54 (m, ArH, 3H), 11.02 (s, 1H, NH_{amid}), 12.05 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.55, 37.52, 42.09, 97.87, 117.17, 123.32, 126.09, 127.43, 132.11, 134.87, 147.81, 160.37, 162.69 ppm; +ESI MS (m/z): 304.9 $[M+H]^+$.

3-methyl-6-oxo-4-(3,4,5-trimethoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4j):



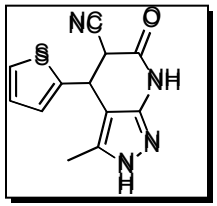
White powder; IR (KBr) cm^{-1}: 3562, 3268, 2256, 1714, 1528; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.54 (s, 3H, CH_3), 3.68 (s, 3H, OCH_3), 3.75 (s, 6H, OCH_3), 4.37 (d, ^{3}J = 12.3 Hz, 1H, CH), 4.77 (d, ^{3}J = 12.0 Hz, 1H, CH), 6.48-6.86 (m, 2H, CH_{arom}), 10.96 (s, 1H, NH_{amid}), 11.98 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.83, 37.63, 43.81, 56.44, 60.51, 100.88, 106.10, 117.69, 135.04, 136.11, 137.27, 147.54, 153.48, 163.60 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.07 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 4.47 (d, ^{3}J = 6.3 Hz, 1H, CH), 4.86 (d, ^{3}J = 6.6 Hz, 1H, CH), 6.48-6.86 (m, 2H, CH_{arom}), 10.98 (s, 1H, NH_{amid}), 12.07 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.68, 37.63, 42.73, 56.24, 60.41, 101.71, 104.99, 117.28, 135.51, 135.86, 137.27, 147.54, 153.31, 163.60 ppm; +ESI MS (m/z): 343 $[M+H]^+$.

3-methyl-6-oxo-4-(3-phenoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4k):



White powder; IR (KBr) cm^{-1}: 3568, 3284, 2238, 1705, 1542; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.48 (s, 3H, CH_3), 4.50 (d, ^{3}J = 12.0 Hz, 1H, CH), 4.69 (d, ^{3}J = 12.0 Hz, 1H, CH), 7.14-7.63 (m, ArH, 9H), 10.96 (s, 1H, NH_{amid}), 12.00 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.92, 36.61, 43.98, 100.83, 115.91, 116.19, 116.77, 117.54, 129.77, 130.87, 135.69, 135.78, 136.61, 147.62, 160.48, 163.55 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.02 (s, 3H, CH_3), 4.56 (d, ^{3}J = 6.9 Hz, 1H, CH), 4.89 (d, ^{3}J = 6.6 Hz, 1H, CH), 7.14-7.63 (m, ArH, 9H), 11.00 (s, 1H, NH_{amid}), 12.09 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.52, 36.61, 42.89, 101.61, 115.88, 116.16, 116.32, 117.12, 129.66, 131.04, 135.57, 135.73, 136.71, 147.56, 160.33, 163.40 ppm; +ESI MS (m/z): 345 $[M+H]^+$.

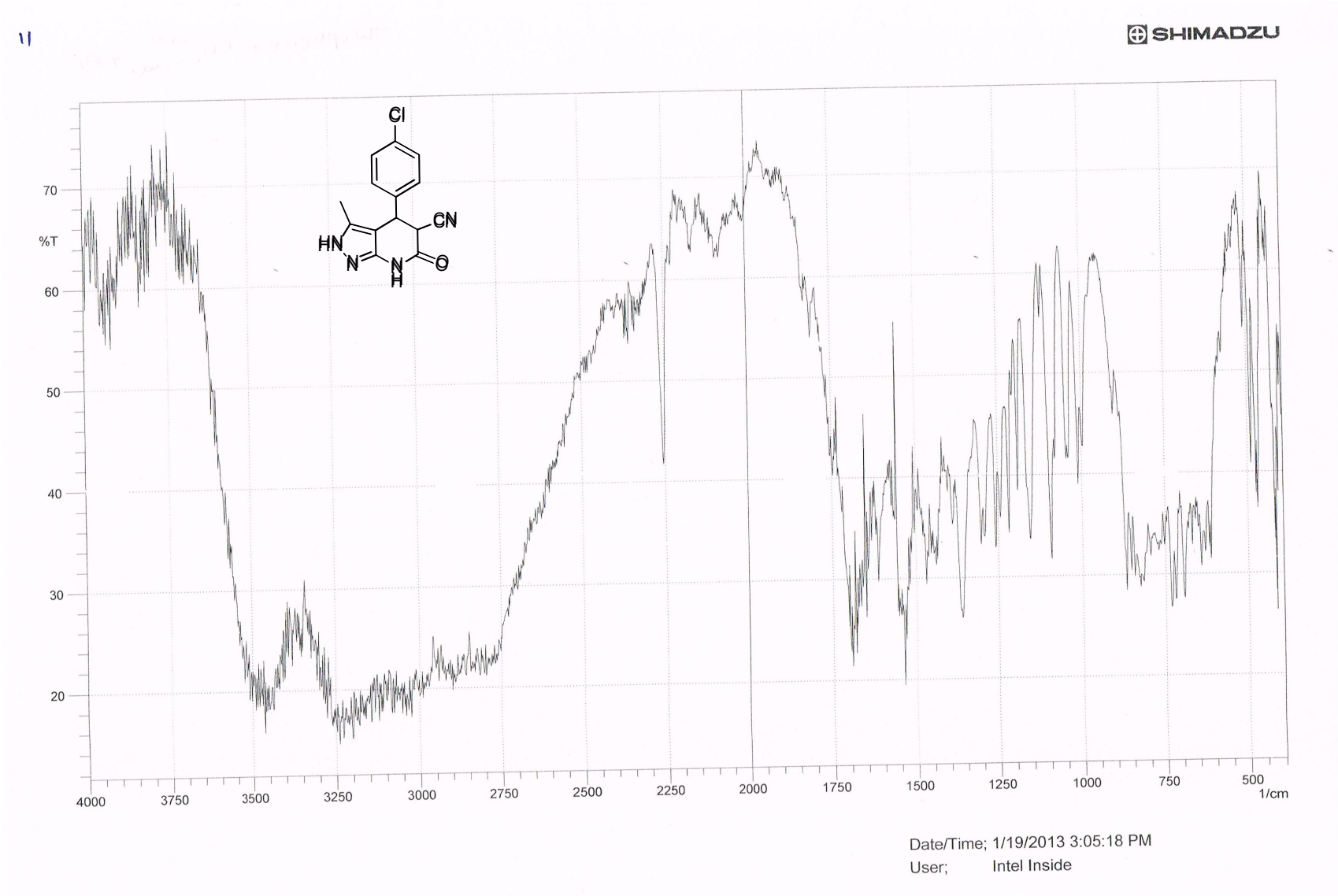
3-methyl-6-oxo-4-(thiophen-2-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4l)



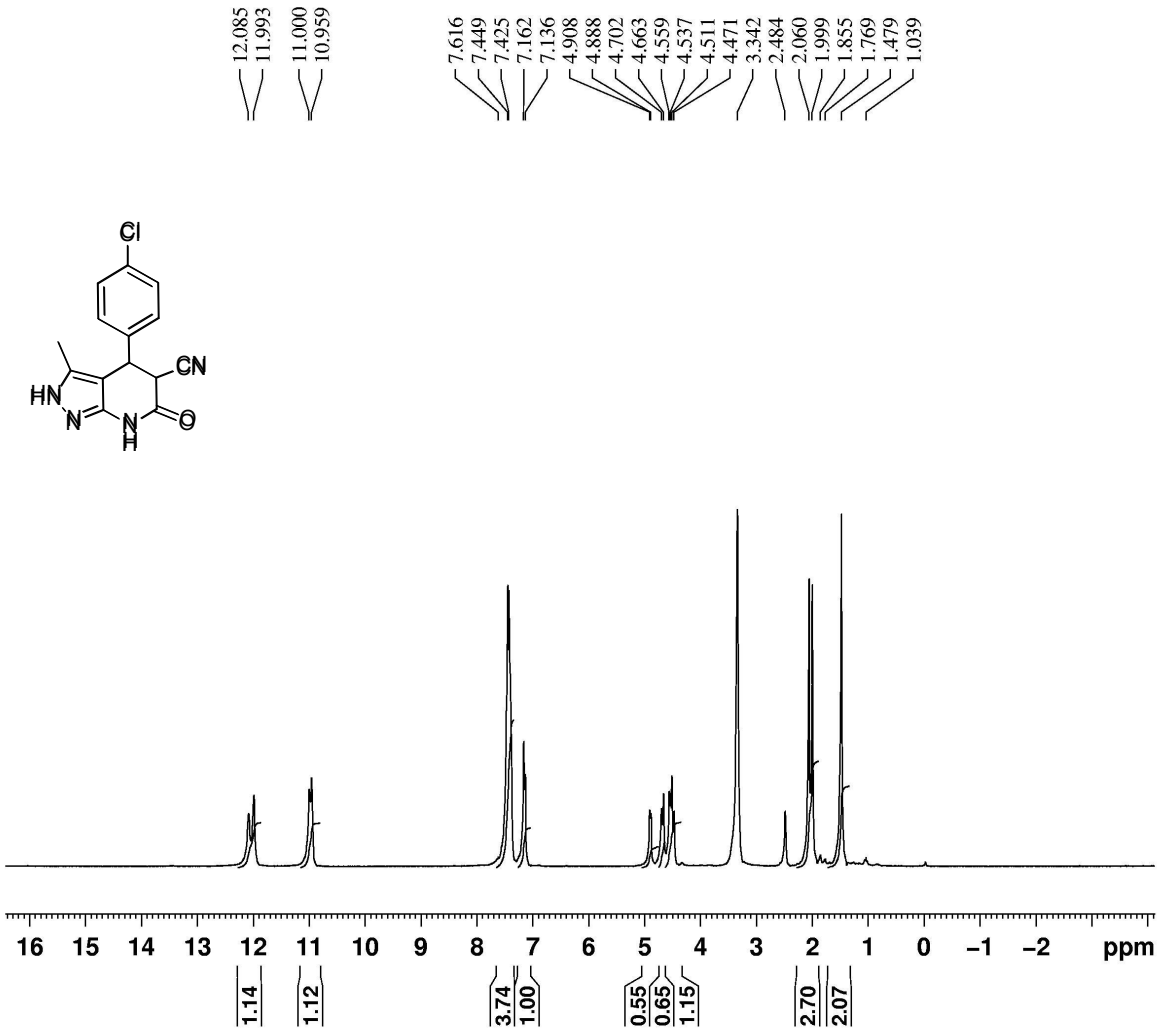
White crystalline solid; IR (KBr) cm^{-1}: 3570, 3282, 2248, 1716, 1534; (*trans* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.07 (s, 3H, CH_3), 4.38 (d, ^{3}J = 12.0 Hz, 1H, CH), 4.64 (d, ^{3}J = 11.7 Hz, 1H, CH), 6.97-7.51 (m, ArH, 3H), 10.99 (s, 1H, NH_{amid}), 12.10 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 10.01, 35.54, 42.39, 101.96, 117.07, 125.96, 126.21, 127.73, 135.07, 142.66, 146.84, 162.52 ppm. (*cis* isomer) ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.69 (s, 3H, CH_3), 4.44 (d, ^{3}J = 6.9 Hz, 1H, CH), 4.80 (d, ^{3}J = 6.6 Hz, 1H, CH), 6.97-7.51 (m, ArH, 3H), 10.99 (s, 1H, NH_{amid}), 12.06 (brs, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (75 MHz, DMSO-d_6) δ: 9.38, 35.54, 43.71, 100.64, 116.97, 125.76, 126.65, 127.34, 135.67, 143.23, 146.72, 162.41 ppm; +ESI MS (m/z): 258.9 $[M+H]^+$.

Reference

1. A. Rahmati Tetrahedron Lett. 51 (2010) 2967



IR Spectrum of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b)

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Current Data Parameters
NAME       March-09-2012
EXPNO                 61
PROCNO                 1

F2 - Acquisition Parameters
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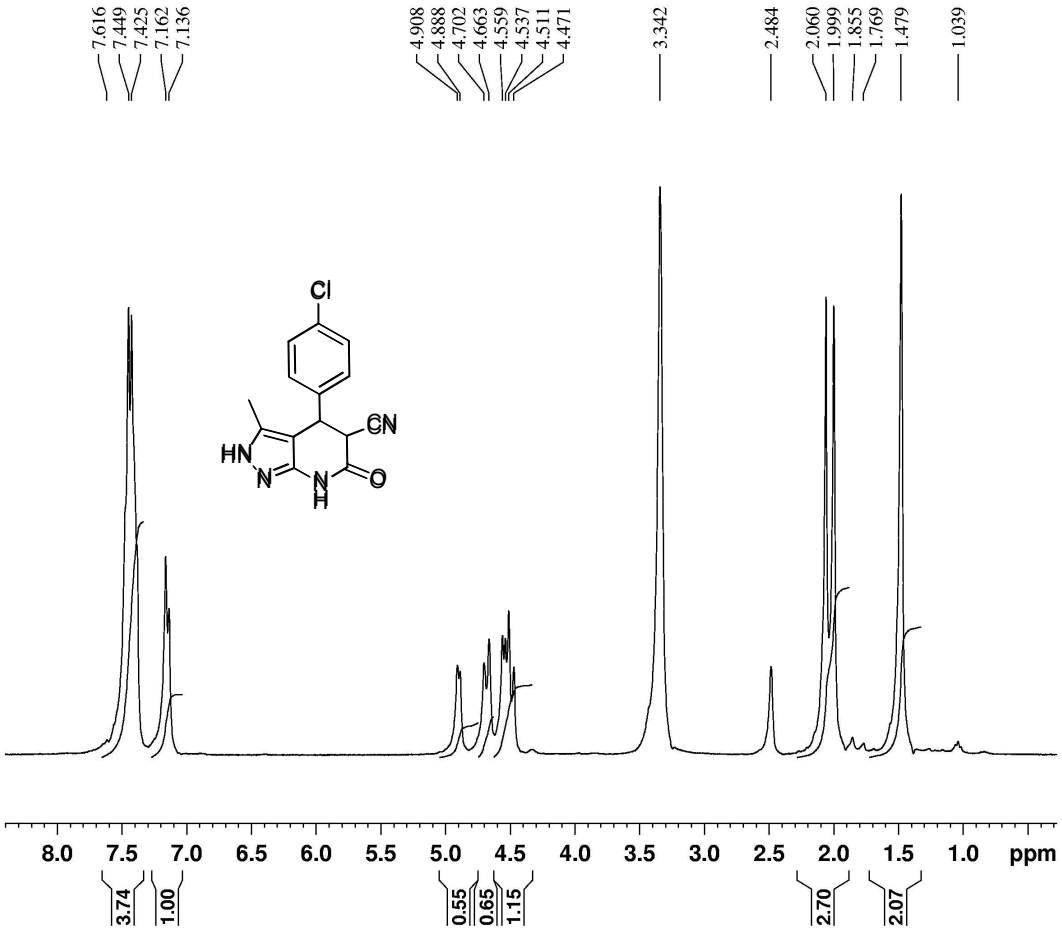
Time               17.25
INSTRUM            av300
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                 161.3
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.70 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300070 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

^{1}H NMR of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b)

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Current Data Parameters
NAME       March-09-2012
EXPNO                 61
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120309
Time               17.25
INSTRUM            av300
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                 161.3
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 10.70 usec
PL1                -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300070 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```
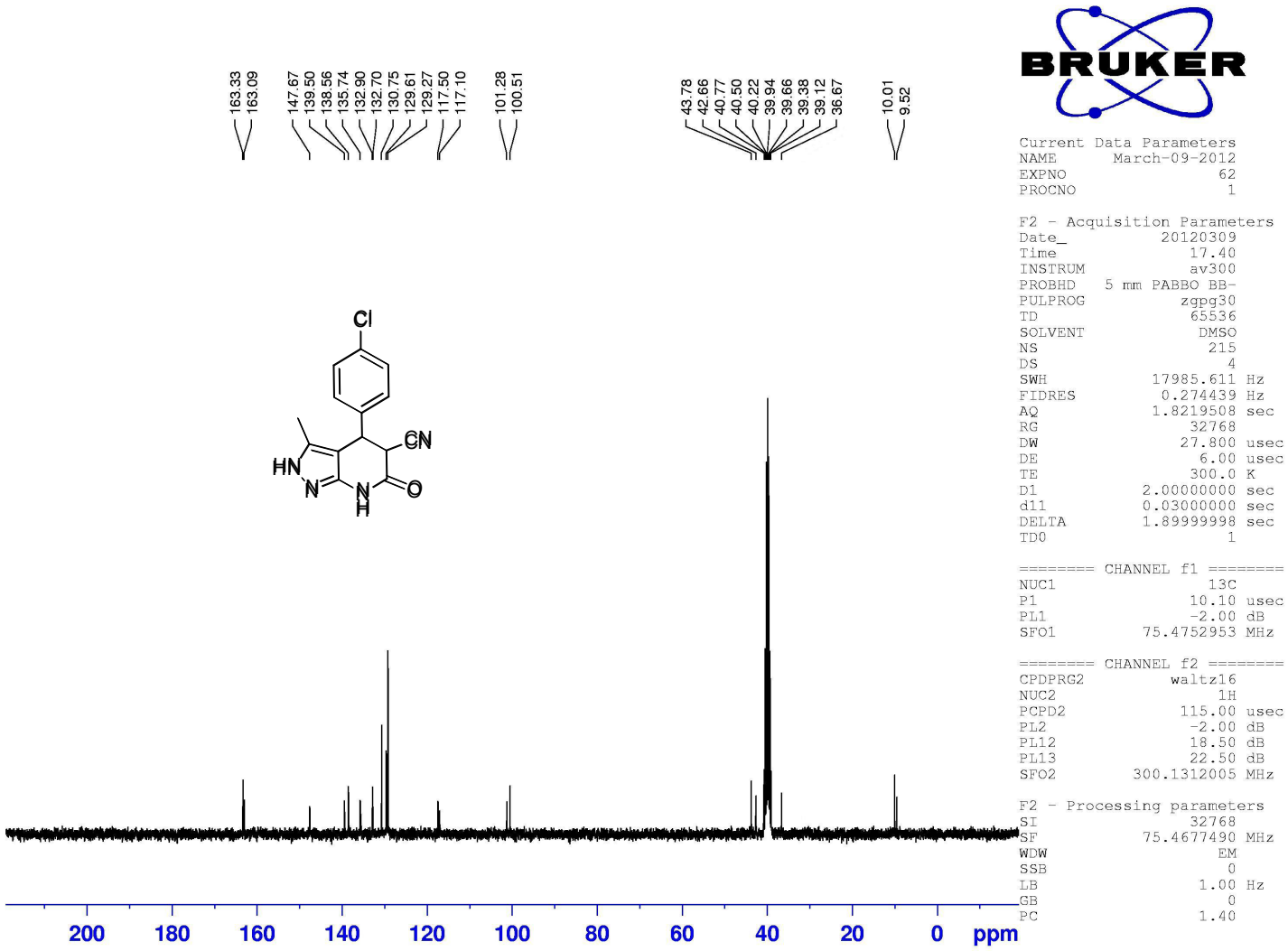
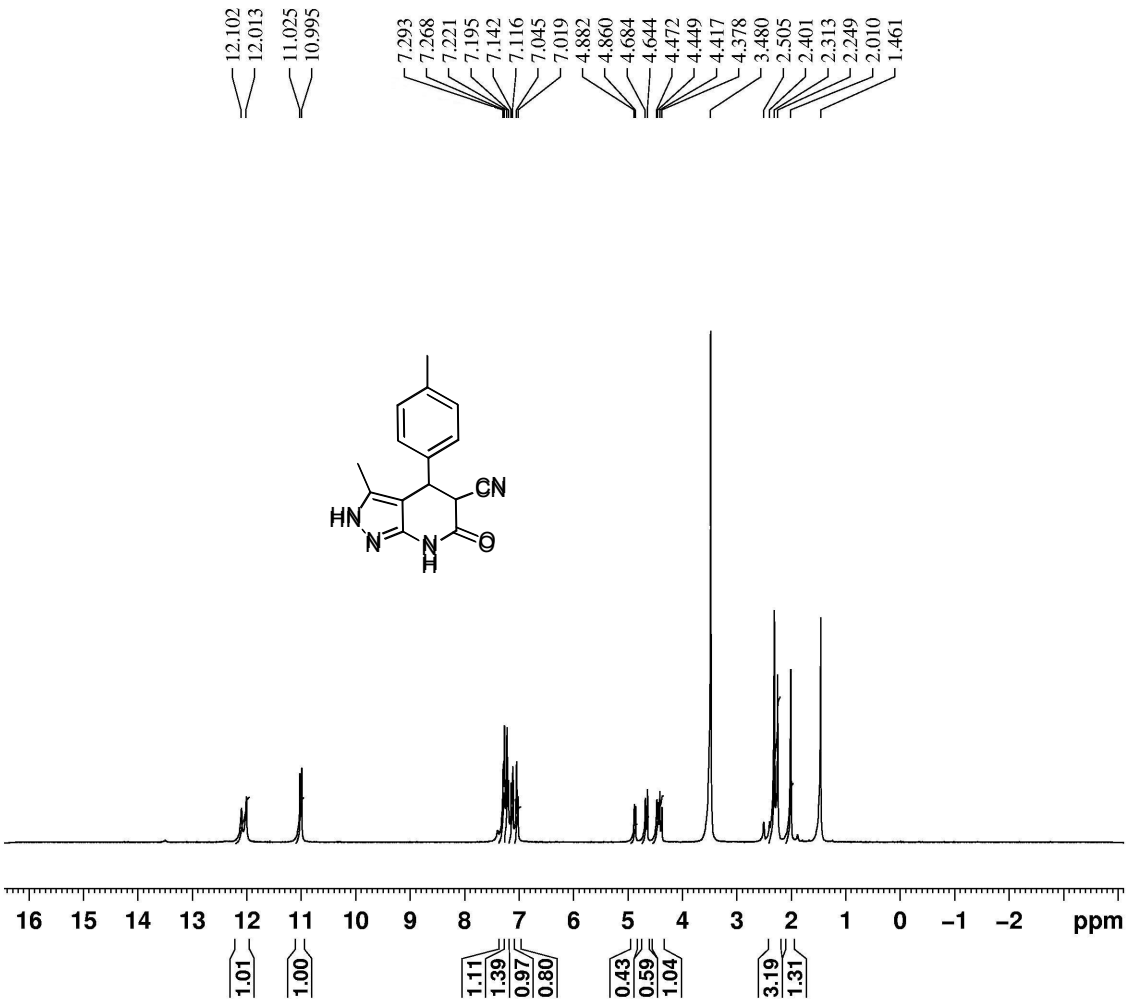

^{1}H NMR of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b)



^{13}C NMR of 4-(4-chlorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4b)

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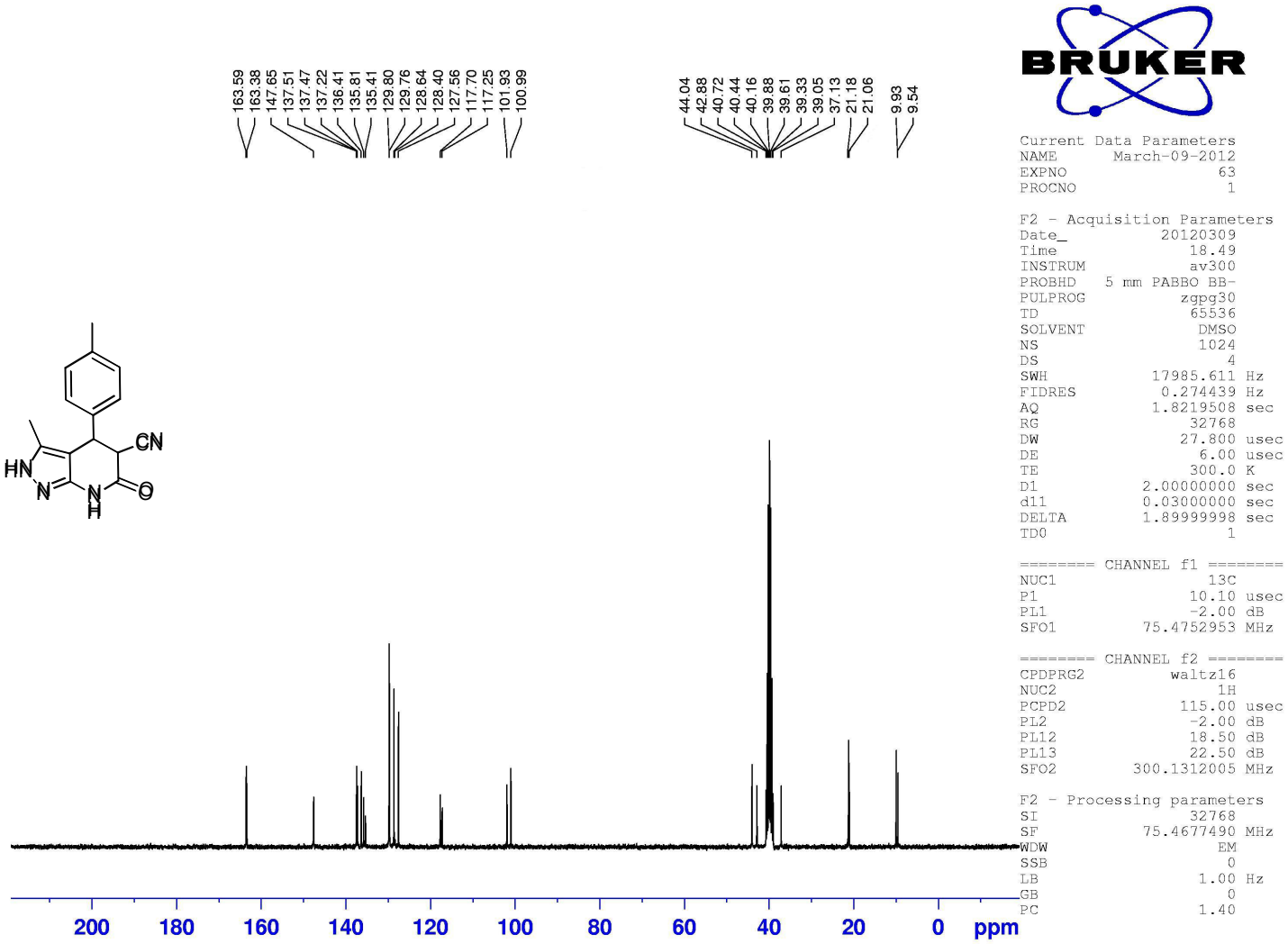
NAME       March-09-2012
EXPNO                 64
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120309
Time               21.30
INSTRUM            av300
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT              DMSO
NS                     6
DS                     2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                     4
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1

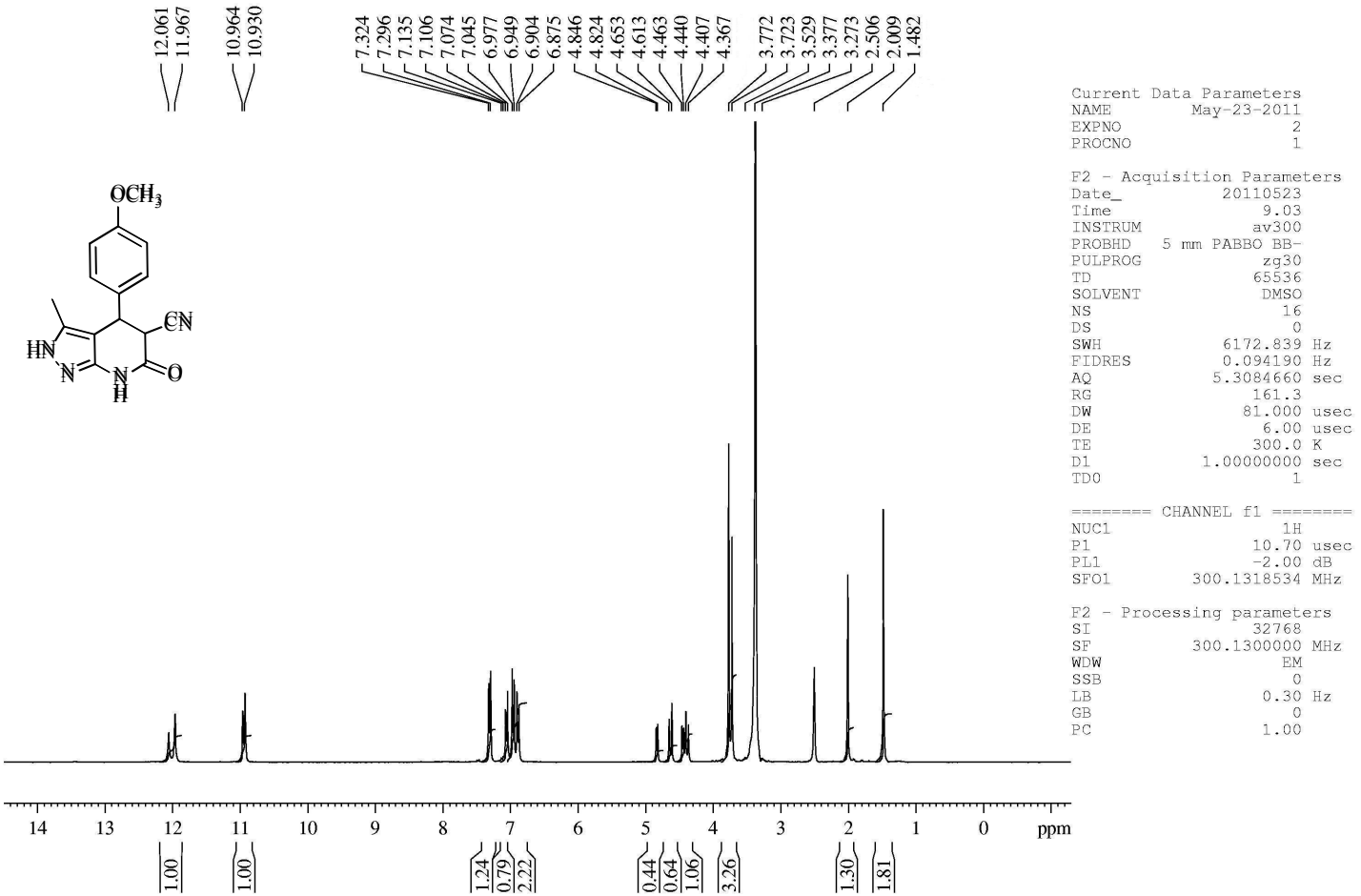
======== CHANNEL f1 ========
NUC1                  1H
P1                10.70 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

[1]H NMR of 3-methyl-6-oxo-4-*p*-tolyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4d)



^{13}C NMR of 3-methyl-6-oxo-4-*p*-tolyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4d)

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Current Data Parameters
NAME         May-23-2011
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20110523
Time                9.03
INSTRUM            av300
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     0
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                 161.3
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.70 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```
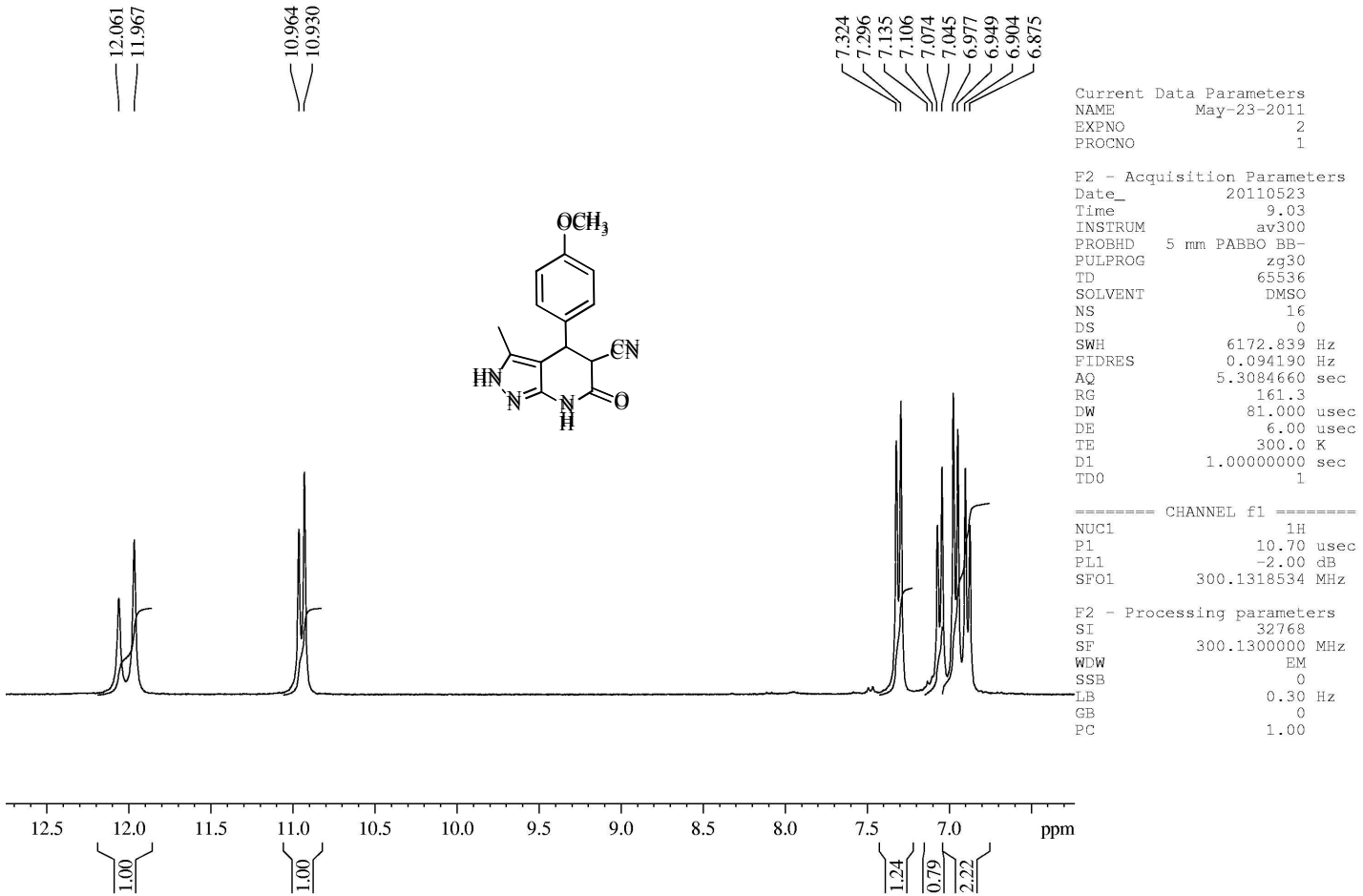
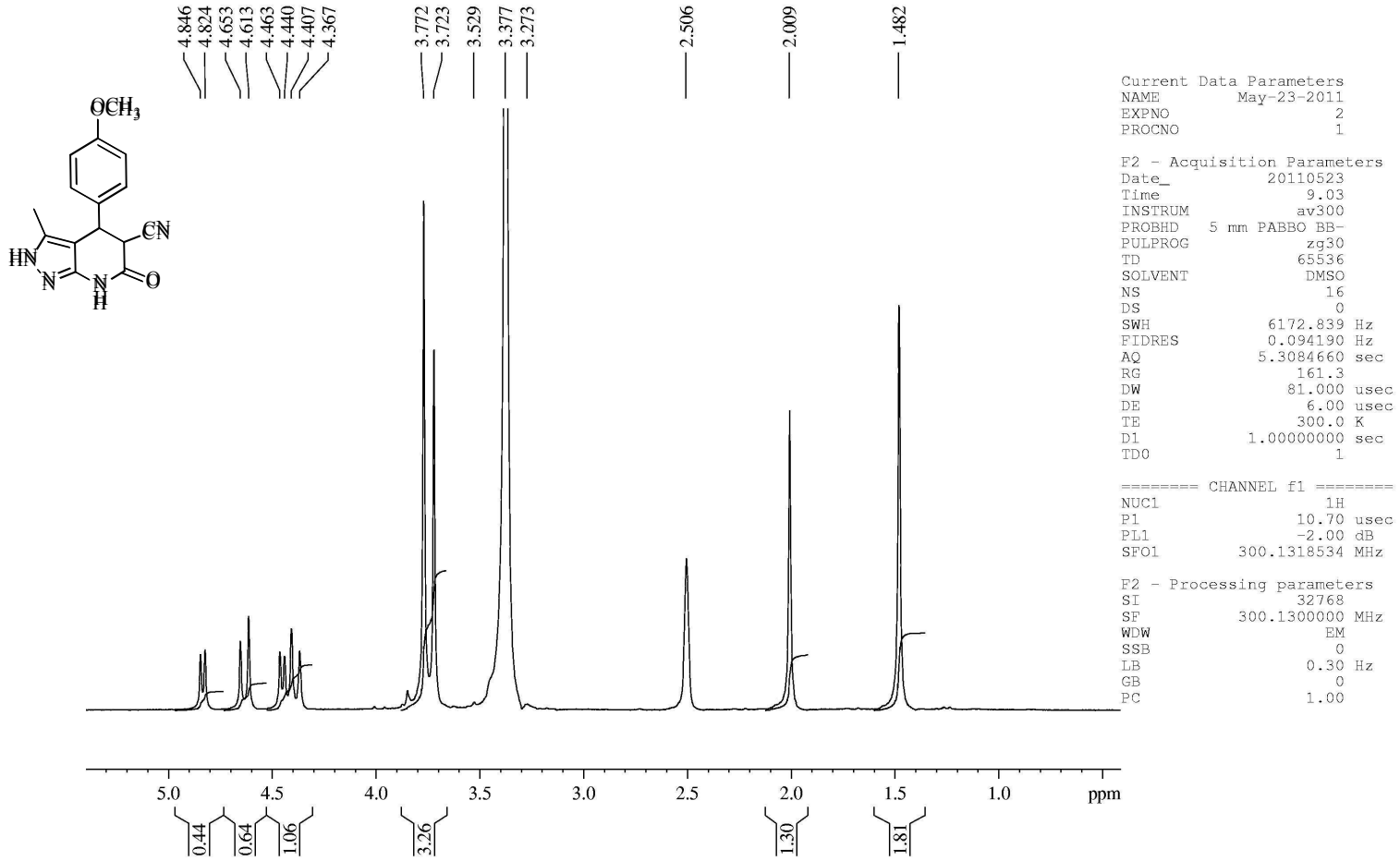
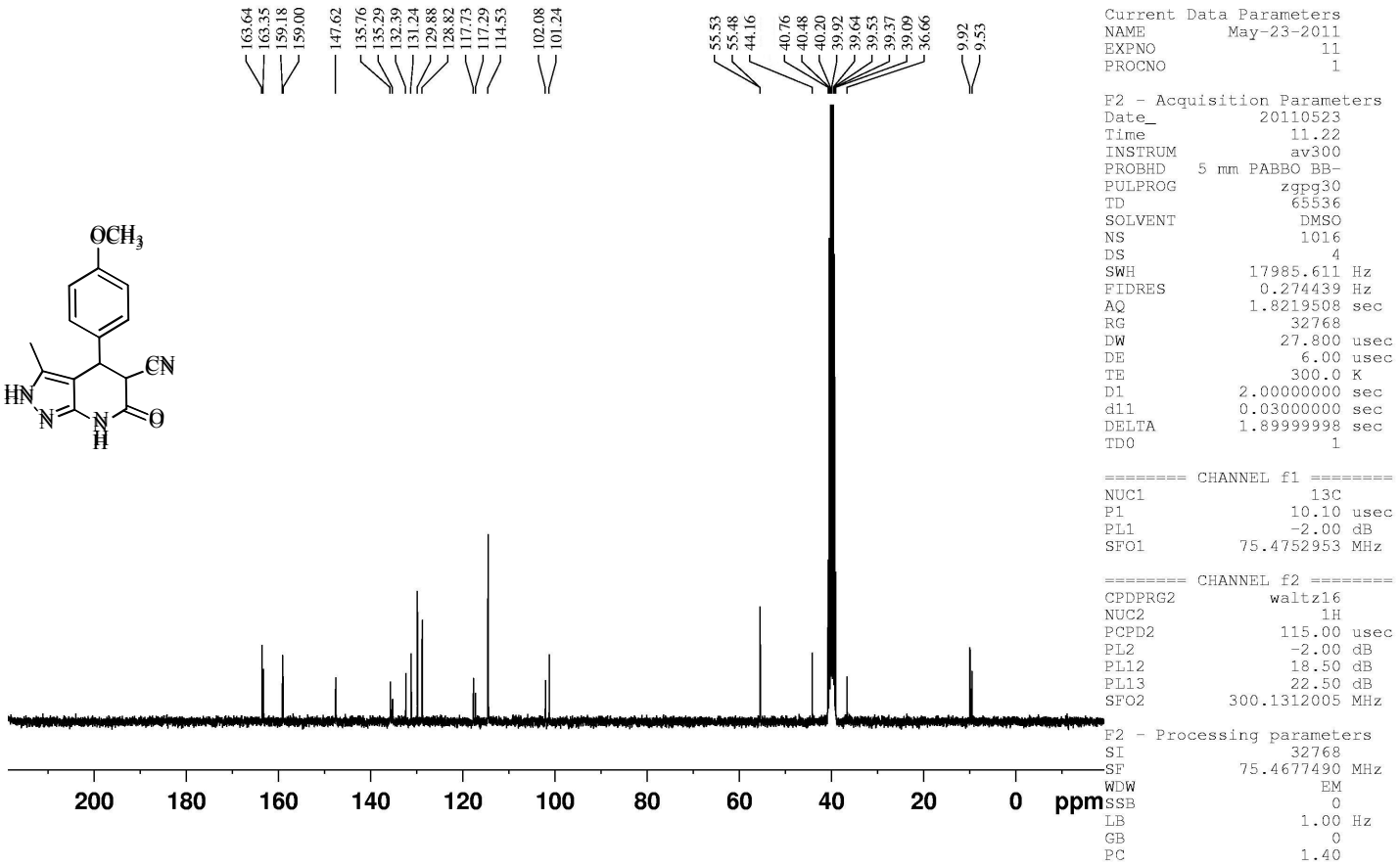

^{1}H NMR of 4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)



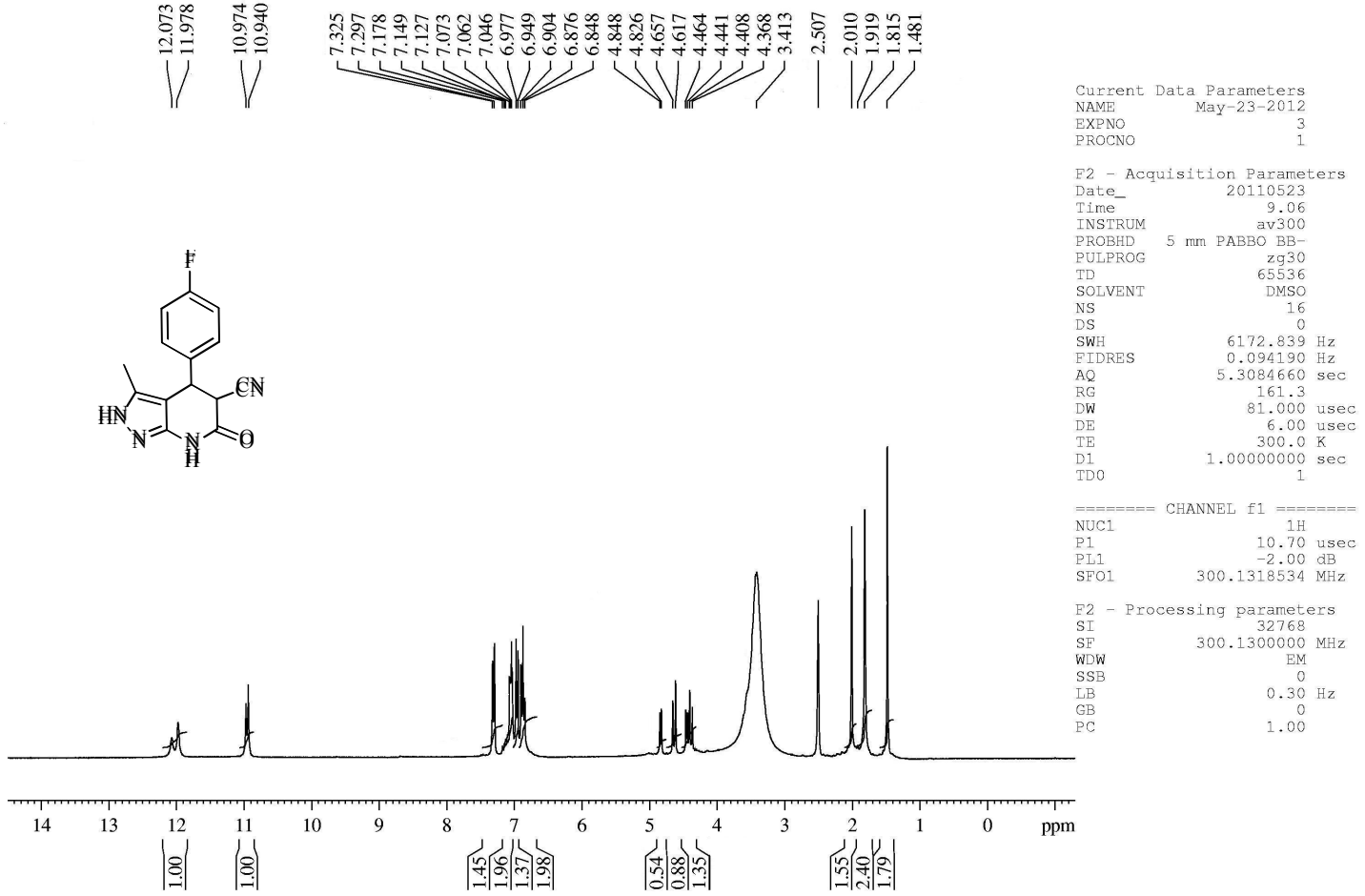
^{1}H NMR of 4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)



^{1}H NMR of 4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)



^{13}C NMR of 4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)

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Current Data Parameters
NAME         May-23-2012
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
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Time                9.06
INSTRUM           av300
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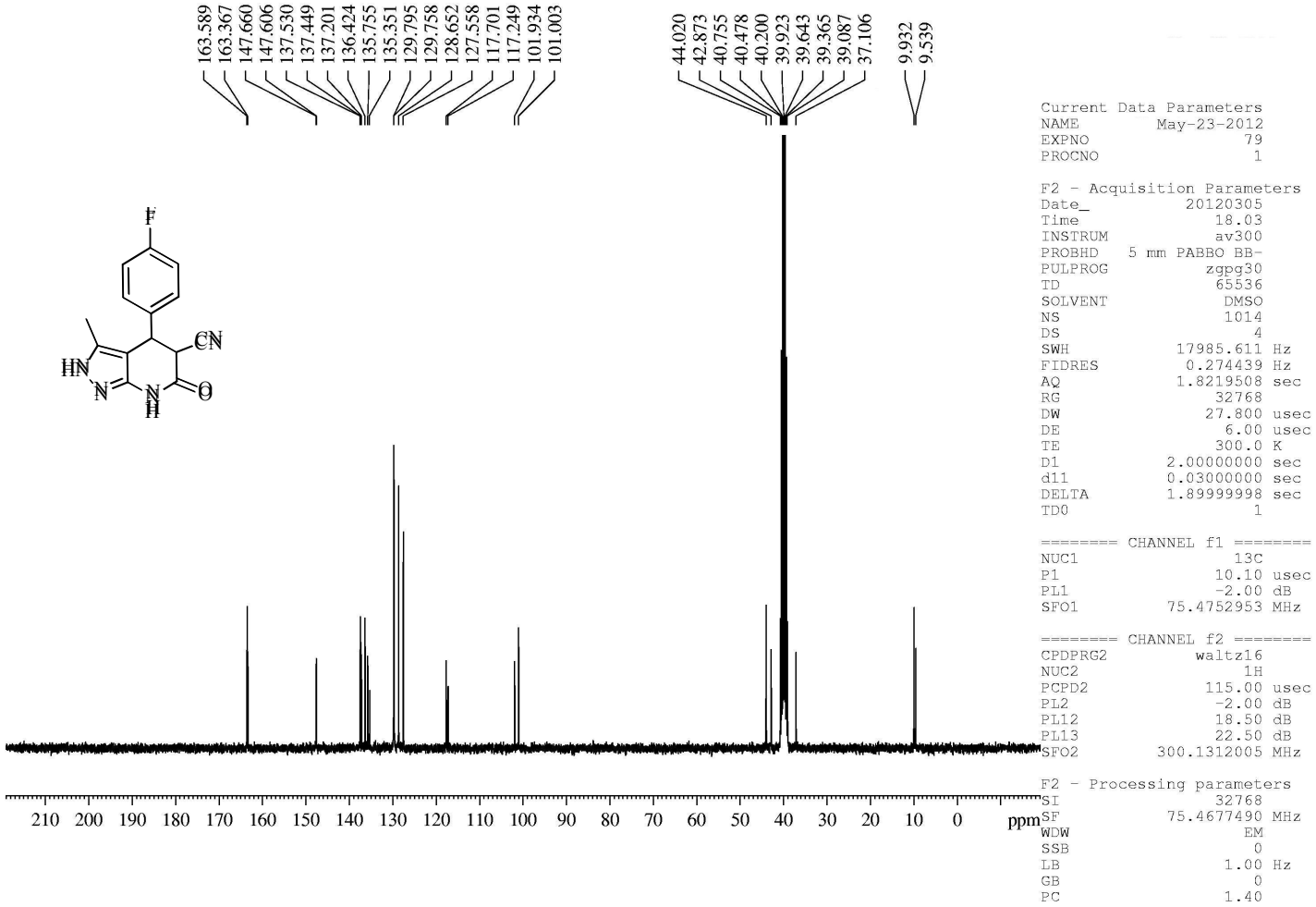
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     0
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                 161.3
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1

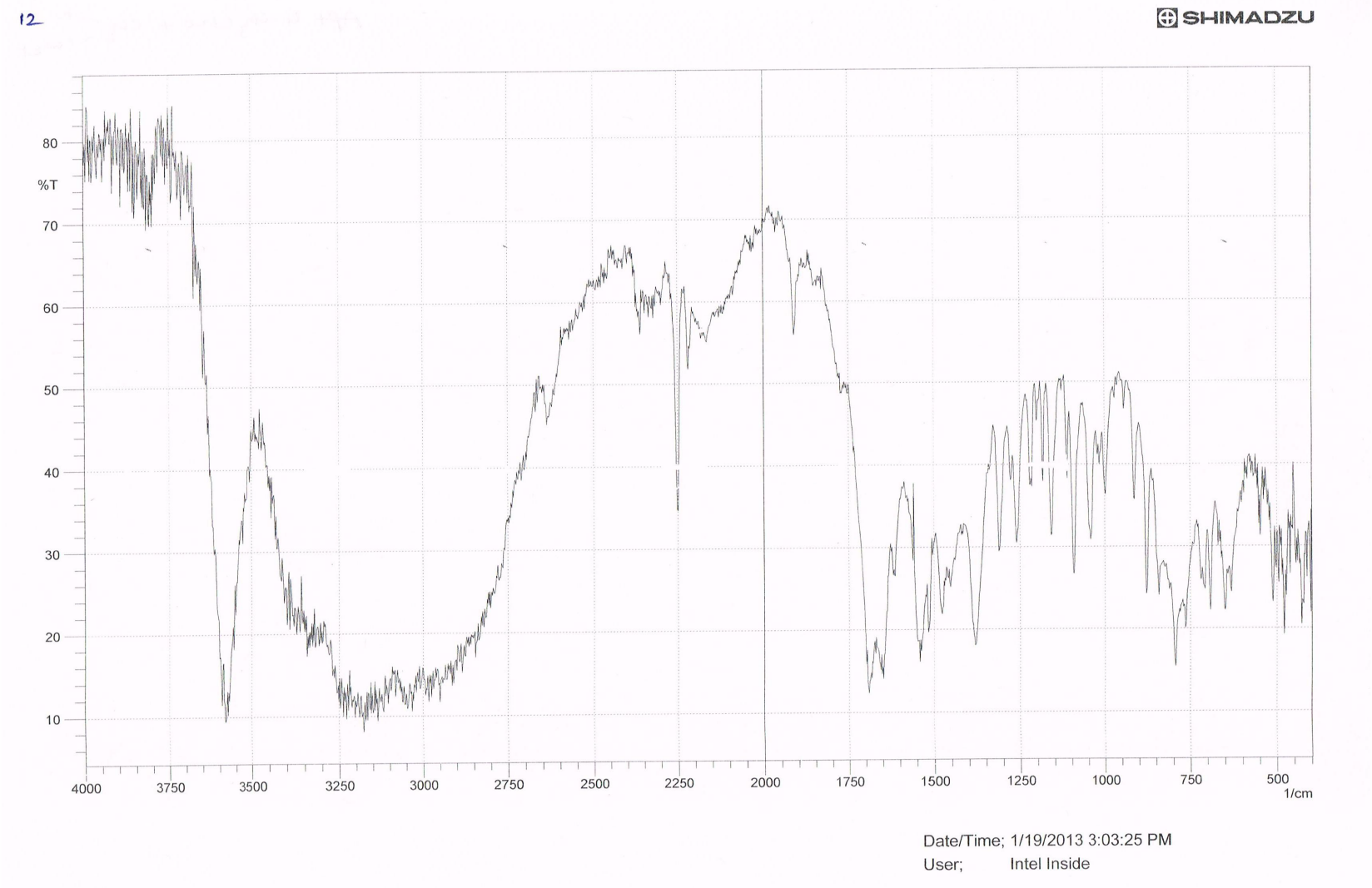
======== CHANNEL f1 ========
NUC1                  1H
P1                10.70 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

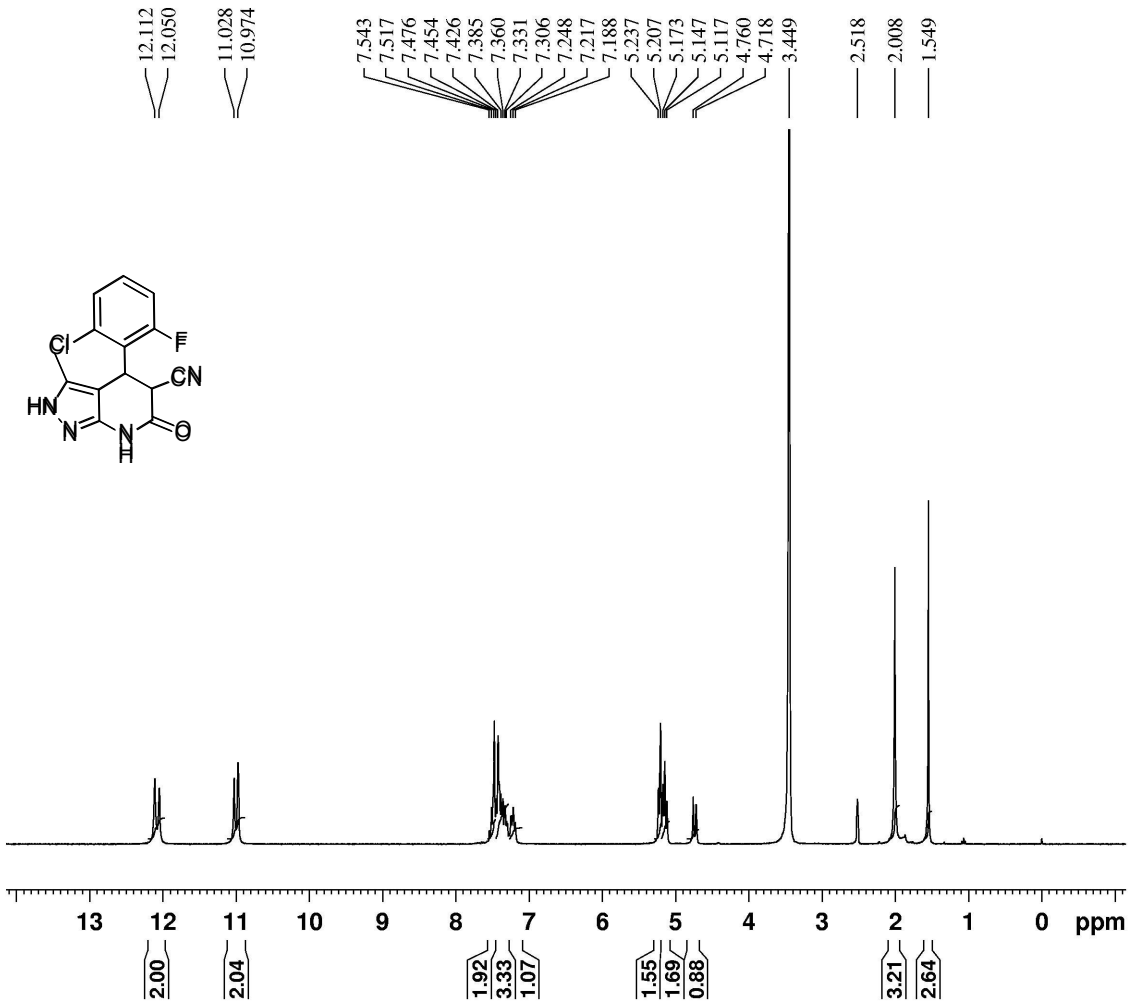
^{1}H NMR of 4-(4-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4f)



^{13}C NMR of 4-(4-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4f)



IR Spectrum of 4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)

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Current Data Parameters
NAME      AUGUST-06-2012
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120806
Time               10.06
INSTRUM            av300
PROBHD   5 mm DUL 13C-1
PULPROG             zg30
TD                 65536
SOLVENT              DMSO
NS                     32
DS                      2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                   256
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.10 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1299966 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```
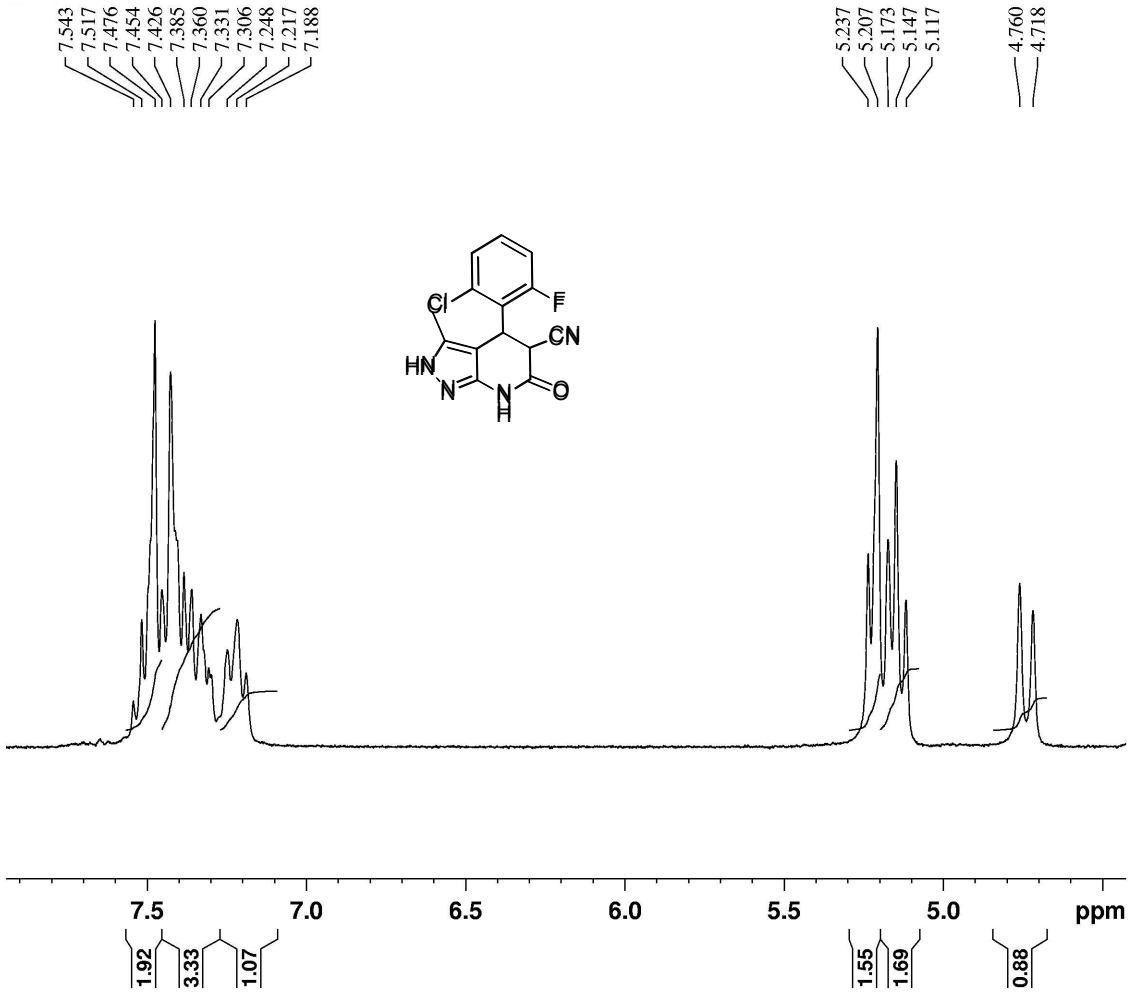

^{1}H NMR of 4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)

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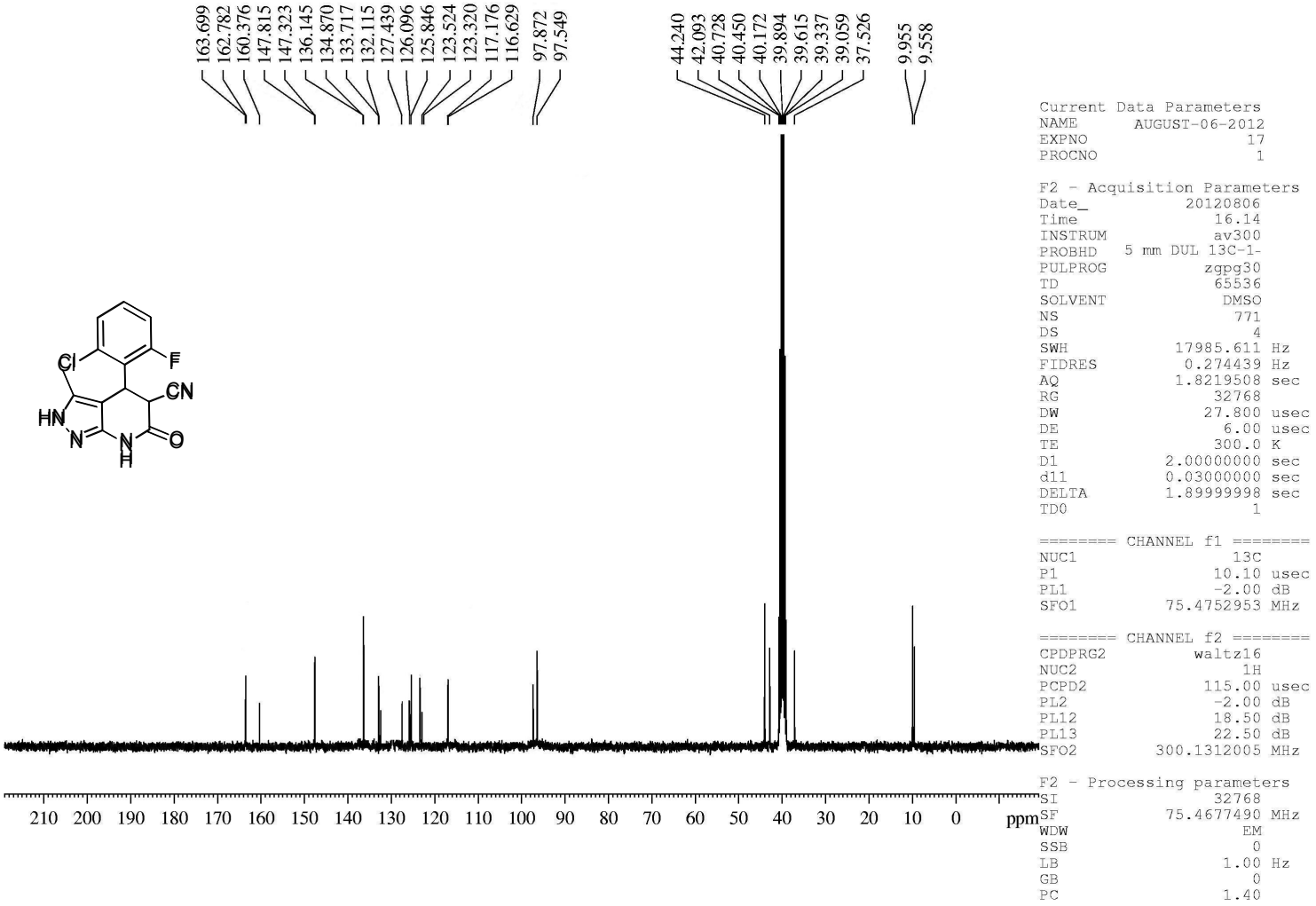
Current Data Parameters
NAME      AUGUST-06-2012
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120806
Time               10.06
INSTRUM            av300
PROBHD   5 mm DUL 13C-1
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    32
DS                     2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                   256
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1

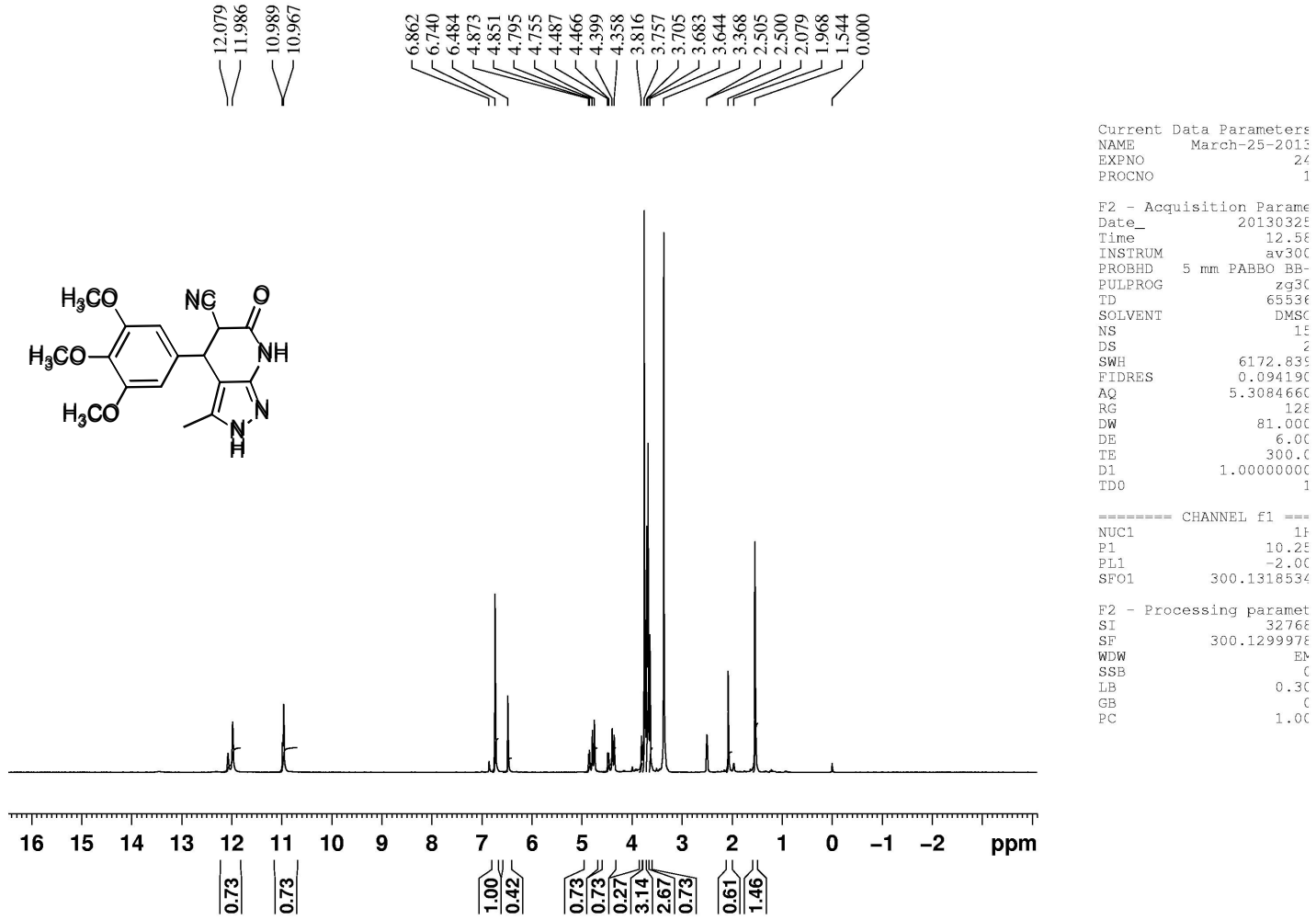
======== CHANNEL f1 ========
NUC1                  1H
P1                10.10 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1299966 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

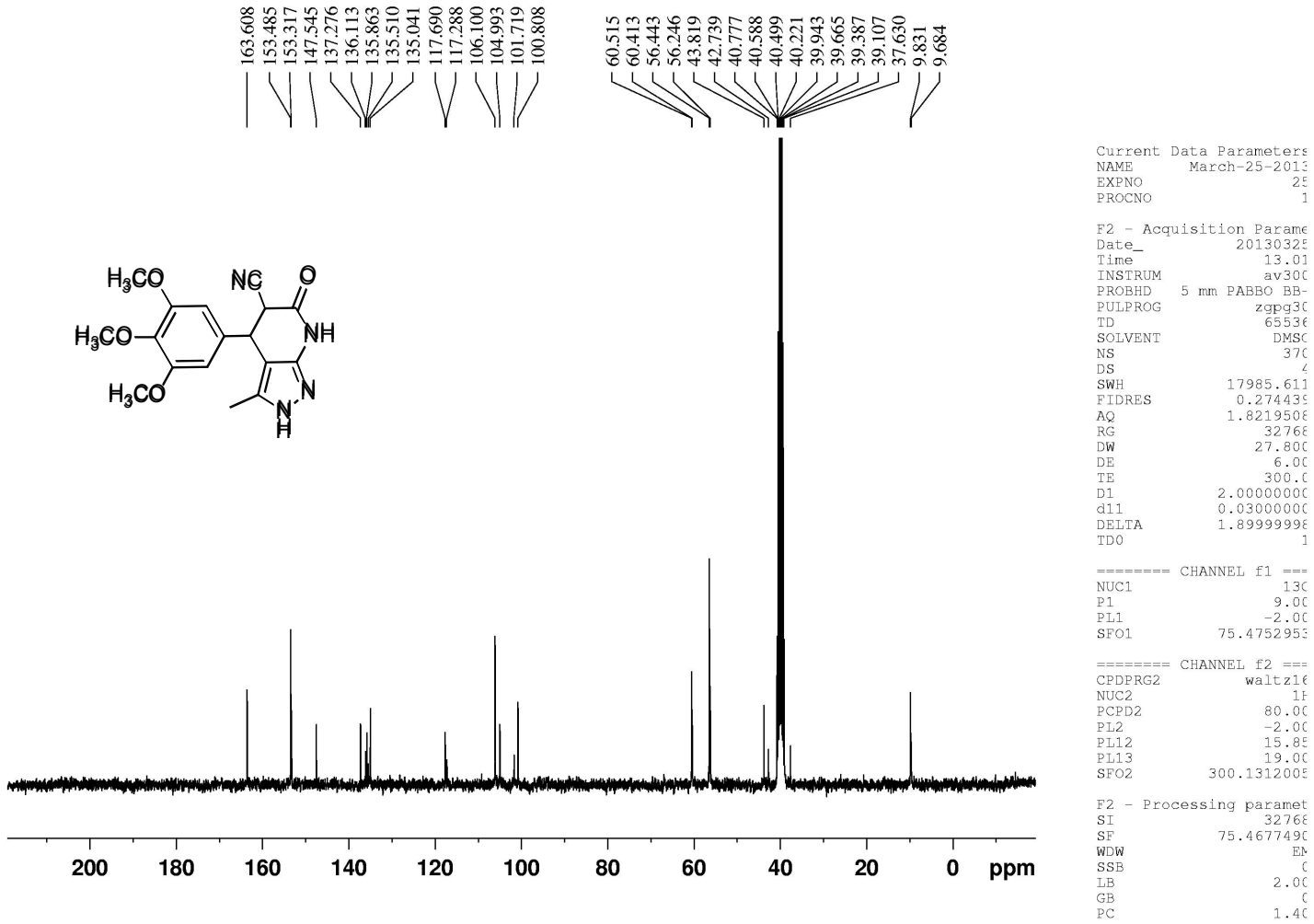
[1]H NMR of 4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)



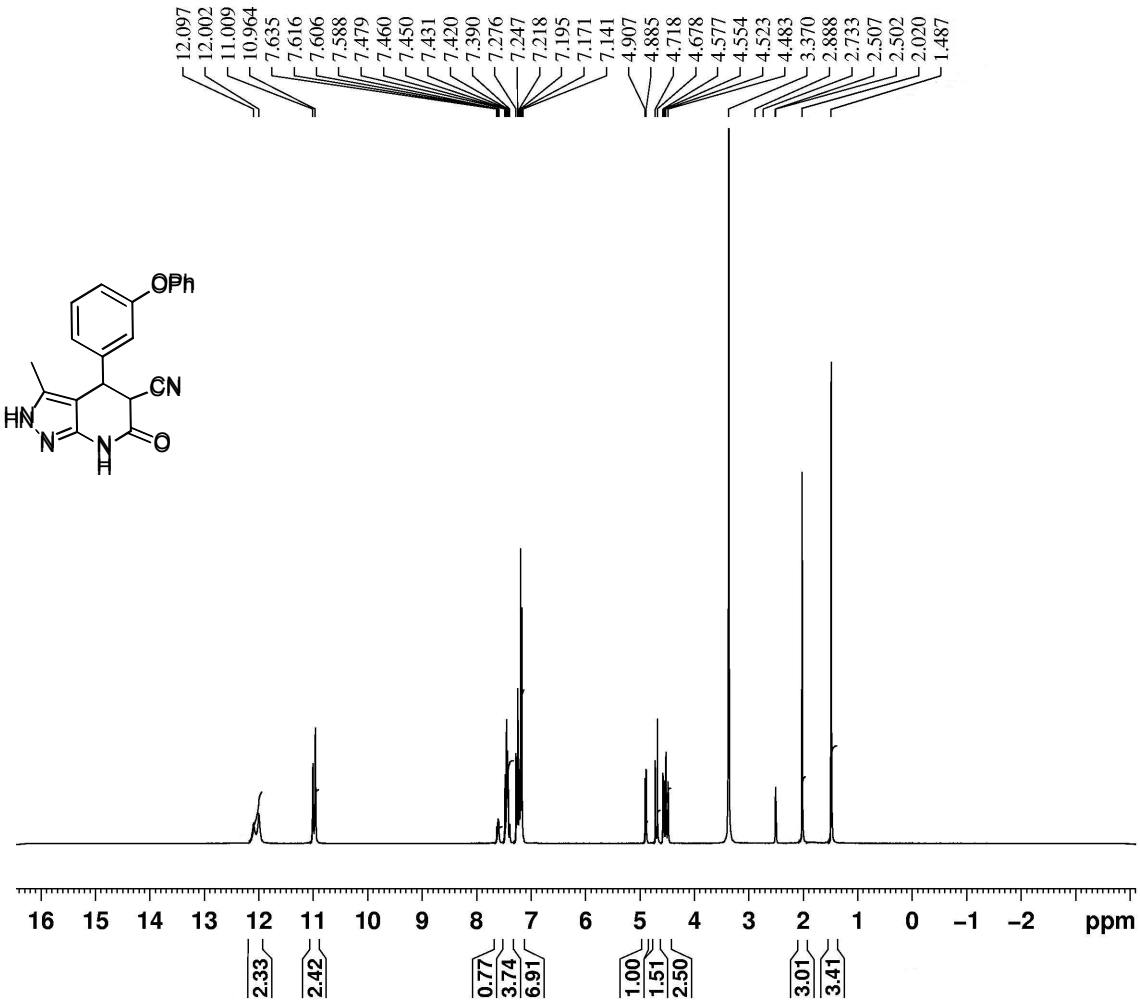
^{13}C NMR of 4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)



^{1}H NMR of 3-methyl-6-oxo-4-(3,4,5-trimethoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4j)



^{13}C NMR of 3-methyl-6-oxo-4-(3,4,5-trimethoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4j)

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PROCNO                 1

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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    12
DS                     0
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                   128
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.70 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF          300.1300000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```
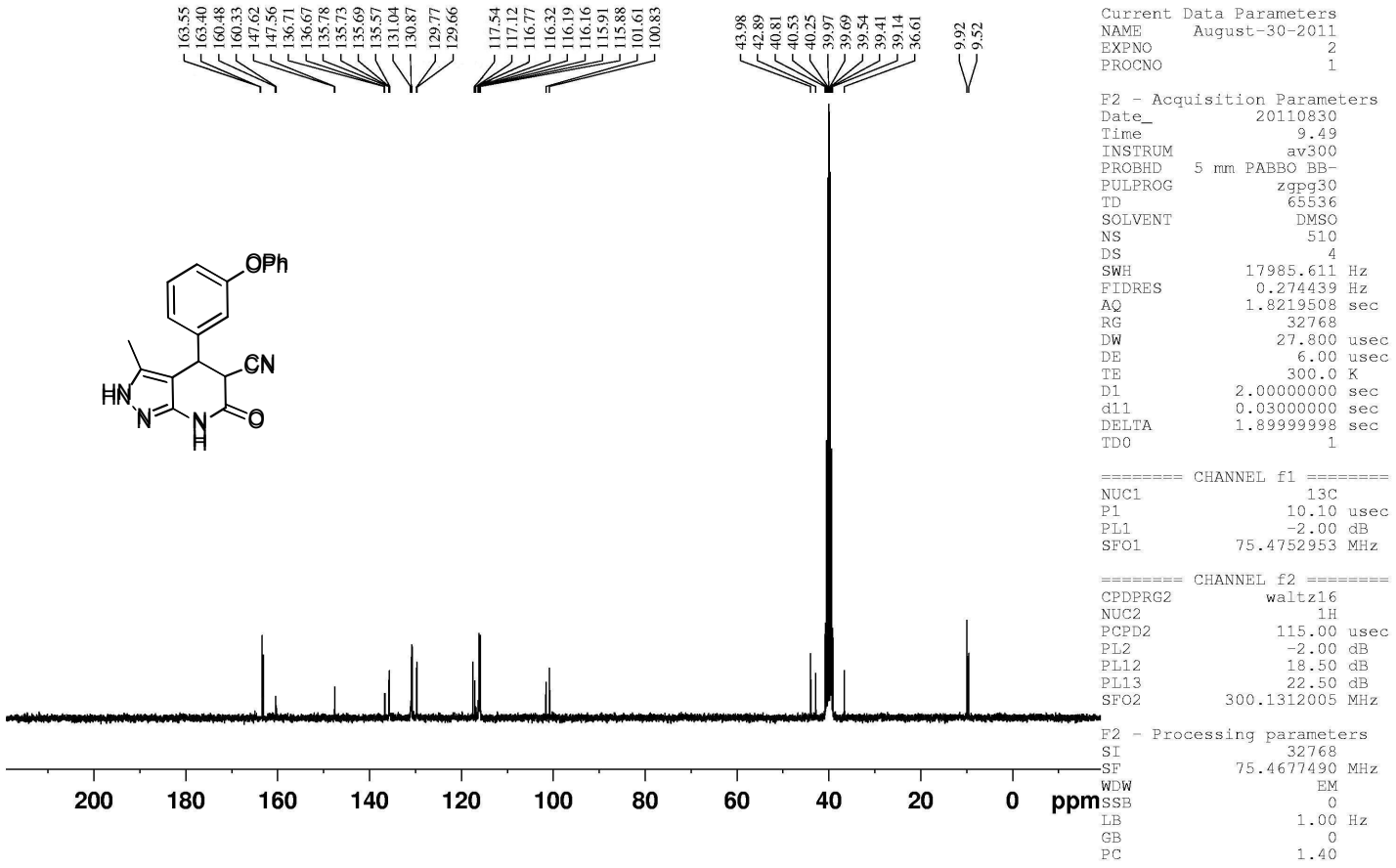
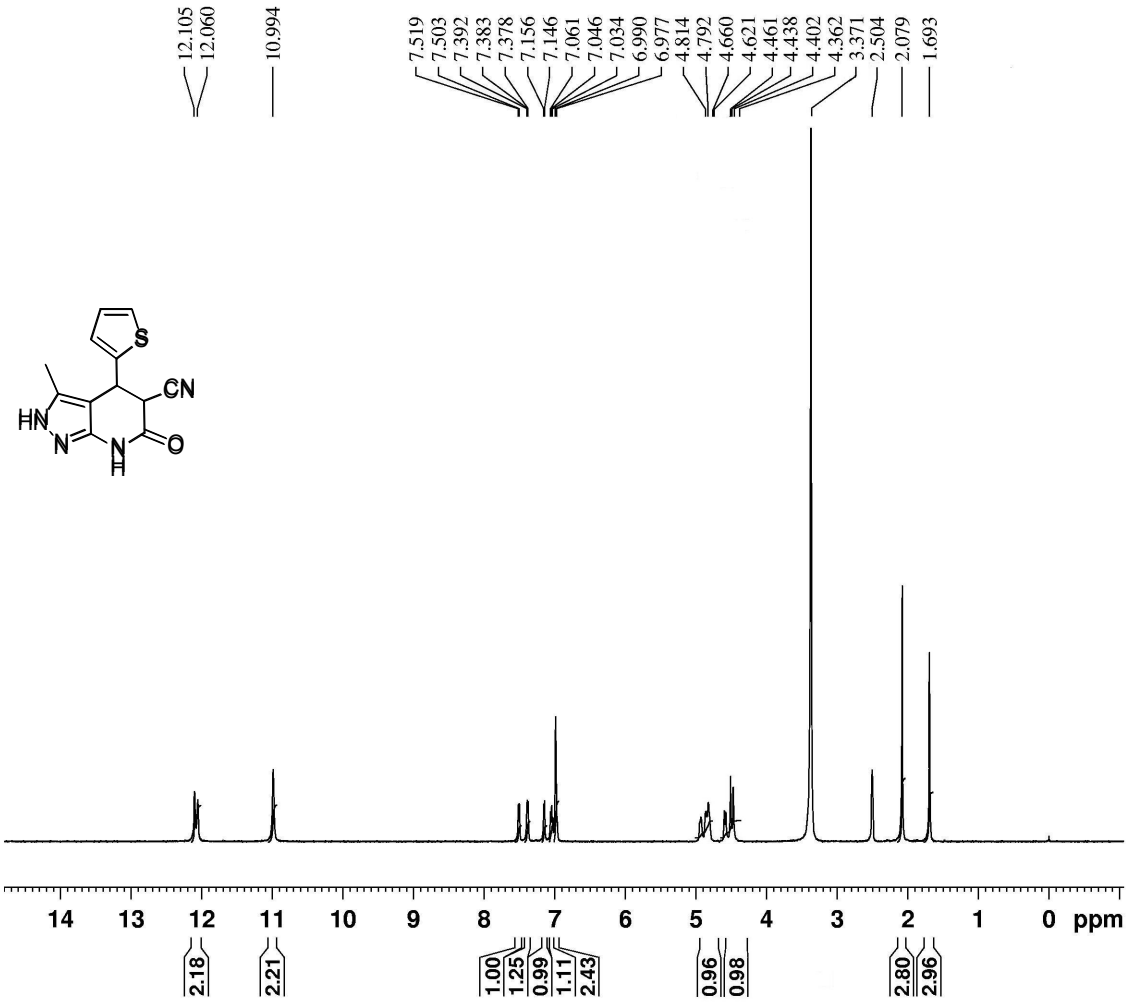

[1]H NMR of 3-methyl-6-oxo-4-(3-phenoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4k)



^{13}C NMR of 3-methyl-6-oxo-4-(3-phenoxyphenyl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4k)

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Current Data Parameters
NAME      AUGUST-06-2012
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120806
Time               10.20
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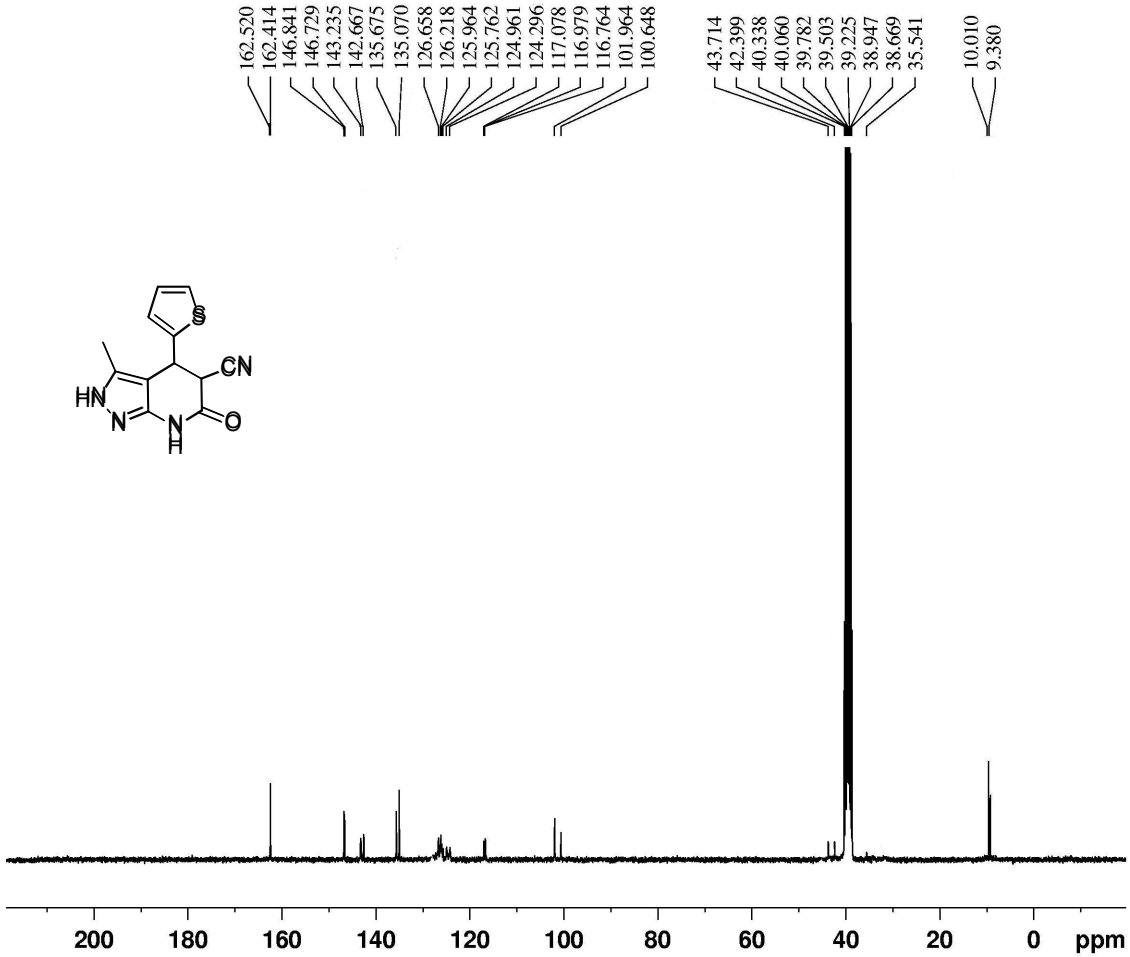
PROBHD   5 mm DUL 13C-1
PULPROG             zg30
TD                 65536
SOLVENT              DMSO
NS                     32
DS                      2
SWH             6172.839 Hz
FIDRES          0.094190 Hz
AQ              5.3084660 sec
RG                   256
DW                81.000 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.10 usec
PL1               -2.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                 32768
SF           300.1300007 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

[1]H NMR of 3-methyl-6-oxo-4-(thiophen-2-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4l)

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Current Data Parameters
NAME      AUGUST-06-2012
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120806
Time               17.07
INSTRUM            av300
PROBHD   5 mm DUL 13C-1
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                  9478
DS                     4
SWH           17985.611 Hz
FIDRES         0.274439 Hz
AQ            1.8219508 sec
RG                 32768
DW                27.800 usec
DE                 6.00 usec
TE                300.0 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   8.30 usec
PL1                 -2.00 dB
SFO1         75.4752950 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2               80.00 usec
PL2                 -2.00 dB
PL12                16.00 dB
PL13                20.00 dB
SFO2        300.1312000 MHz

F2 - Processing parameters
SI                 32768
SF           75.4677818 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```
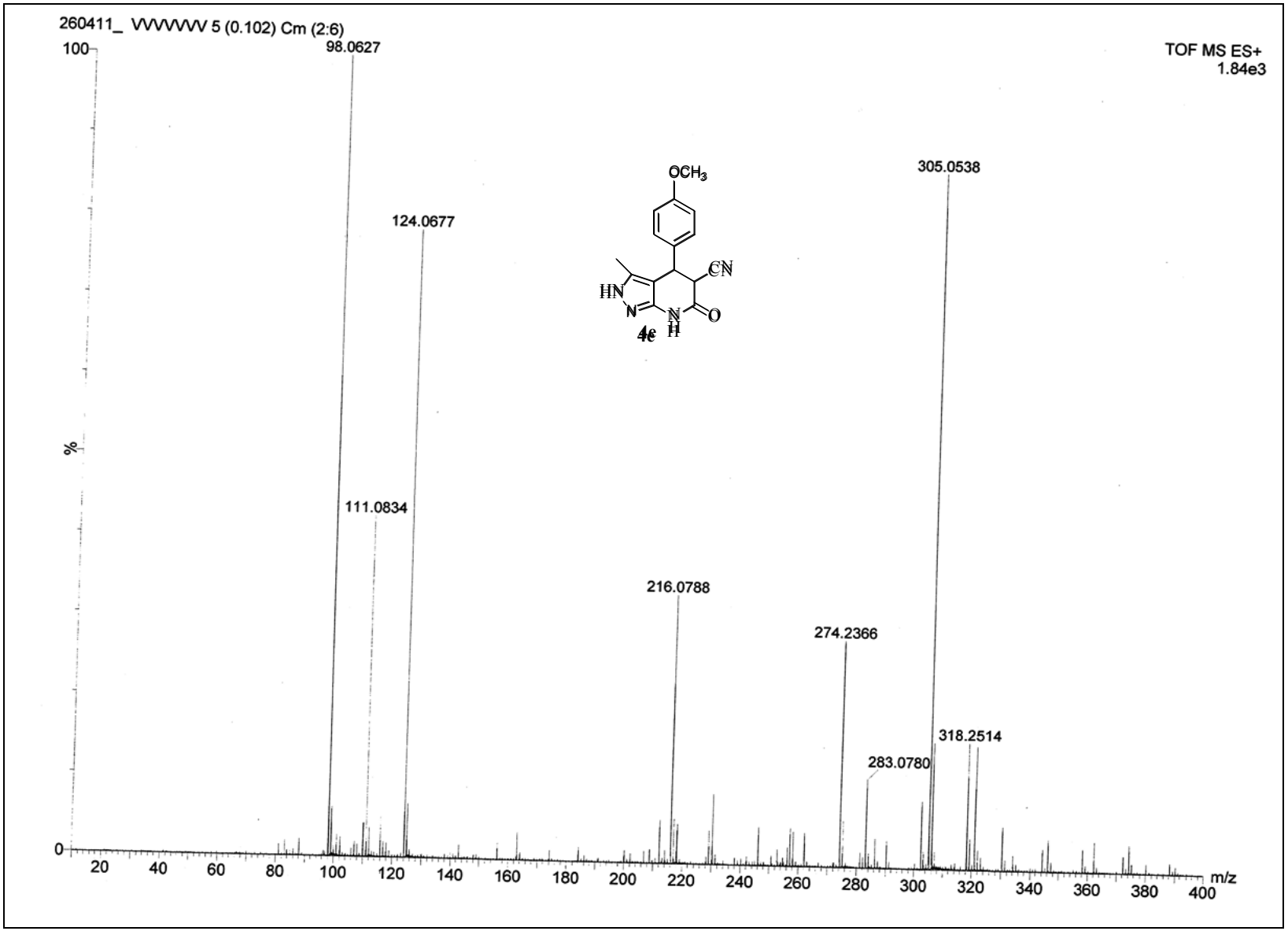
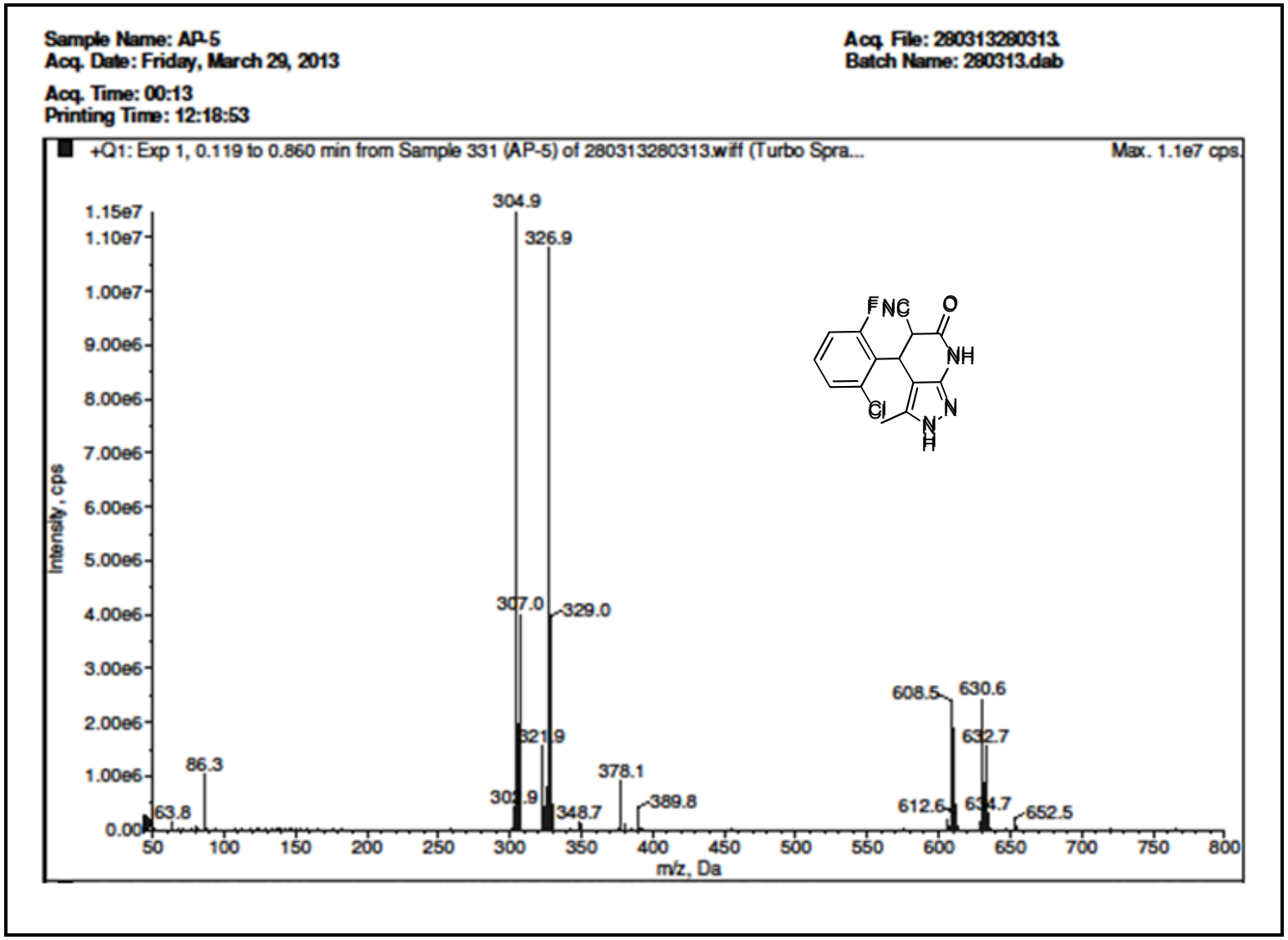
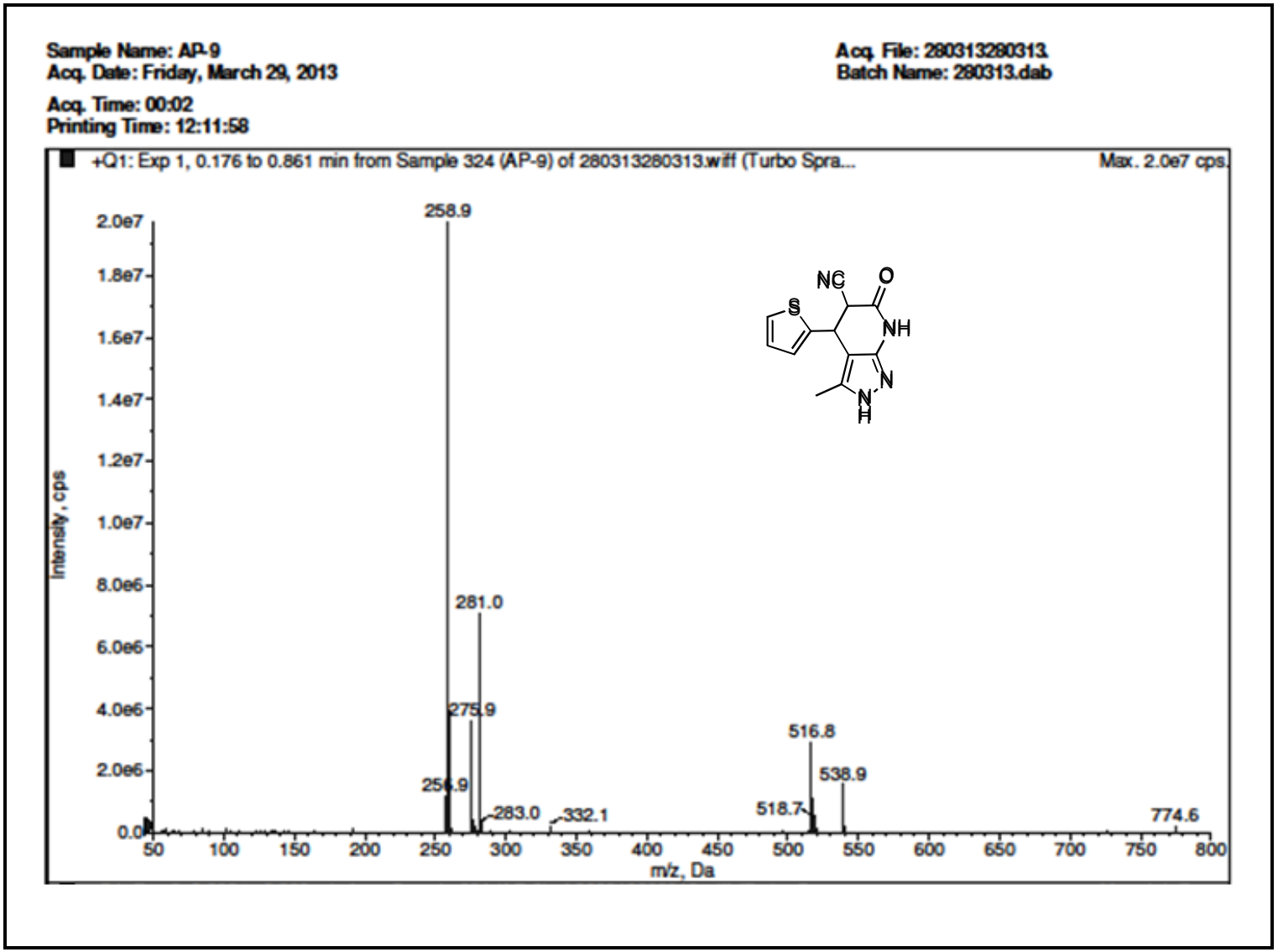

^{13}C NMR of 3-methyl-6-oxo-4-(thiophen-2-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4l)



HRMS of 4-(4-methoxyphenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4e)



Mass spectra of 4-(2-chloro-6-fluorophenyl)-3-methyl-6-oxo-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-b]pyridine-5-carbonitrile (4i)



Mass spectra of 3-methyl-6-oxo-4-(thiophen-2-yl)-4,5,6,7-tetrahydro-2*H*-pyrazolo[3,4-*b*]pyridine-5-carbonitrile (4l)