Supporting Information

Regioselective Synthesis of Spirodihydrofuran Barbiturates and Spirocyclopropane Barbiturates *via* Cascade Reaction

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1. General Information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer using $CDCl_3$ as the solvent and TMS as an internal standard. IR spectra were determined on a Thermo Nicolet IR200 unit. High resolution mass spectra (HRMS) were obtained on an Agilent Technologies 6540 UHD Accuratemass Q-TOF LC/MS using the ESI technique. X-ray crystallographic data were collected using an Agilent Xcalibur Eos Gemini diffractometer at 293(2) K. Melting points were determined using an aXT5 Apparatus and are uncorrected. All reagents were obtained from commercial suppliers without further purification. All solvents were used directly without further purification. Chromatography was performed on silica gel (100–200 mesh). Petroleum ether and ethyl acetate were used for column chromatography.

2. Preparation of Substrates

All of the barbiturate-based olefin substrates were prepared from the corresponding aldehydes and *N,N'*-dimethylbarbituric acid according to the reported procedure.[1]

3. General procedure for spirocyclopropane barbiturates 3

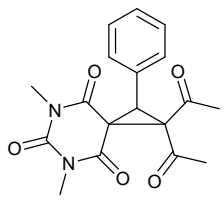
Barbiturate-based olefin **1** (1.0 mmol) was added to a stirred mixture of the acetylacetone (1.5 mmol), and K_2CO_3 (1.3 mmol) in ethyl acetate (10 mL), followed by NBS (1.5 mmol). The reaction mixture was stirred at r.t. and monitored by TLC. After the reaction was complete, the mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum: ethyl acetate (6:1, v/v) as an eluent to afford the pure product **3**.

4. General procedure for spirodihydrofuran barbiturates 4

Barbiturate-based olefin **1** (1.0 mmol) was added to a stirred solution of the acetylacetone (1.5 mmol), and DBU (1.1 mmol) in CH_2Cl_2 (10 mL), then NBS (1.5 mmol) was added after an hour. The reaction solution was stirred at r.t. and monitored by TLC. After the reaction was complete, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum: ethyl acetate (4:1, v/v) as an eluent to afford the pure product **4**.

5. Characterization Data of the Products

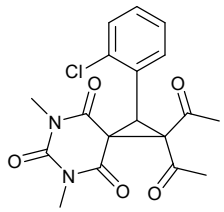
1,1-diacetyl-5,7-dimethyl-2-phenyl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3a)



3a

White solid (72% yield); mp 151-153 ^{o}C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H), 4.08 (s, 1H), 3.39 (s, 3H), 3.29 (s, 3H), 2.47 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 197.9, 195.9, 166.0, 163.2, 150.9, 130.2, 129.8, 128.2, 67.2, 49.1, 42.4, 29.9, 29.3, 28.9, 28.6； IR (KBr, cm^{-1}): 3020, 2959, 2926, 1682, 1456, 1376, 1243, 813, 754, 699, 477; HR-MS (ESI) calcd for $C_{18}H_{19}N_2O_5^+$ [$(M+H)^+$] 343.1284, Found 343.1285.

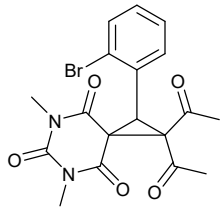
2-(2-chlorophenyl)-1,1-diacetyl-5,7-dimethyl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3b)



3b

White solid (63% yield); mp 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.0 Hz, 1H), 7.41 – 7.19 (m, 4H), 3.88 (s, 1H), 3.41 (d, *J* = 0.6 Hz, 3H), 3.24 (s, 3H), 2.53 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 196.0, 166.0, 163.3, 151.0, 134.6, 132.8, 129.6, 129.1, 128.9, 127.0, 67.3, 46.5, 42.8, 29.4, 29.3, 29.0, 28.8; IR (KBr, cm^{-1}): 3020, 2959, 2925, 1681, 1457, 1432, 1376, 1287, 1181, 758; HR-MS (ESI) calcd for $C_{18}H_{18}ClN_2O_5^+$ [$(M+H)^+$] 377.0899, Found 377.0897.

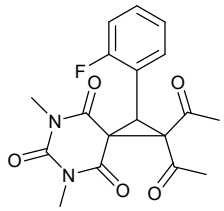
2-(2-bromophenyl)-1,1-diacetyl-5,7-dimethyl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3c)



3c

White solid (76% yield); mp 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.8 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.37 (td, *J* = 7.7, 1.1 Hz, 1H), 7.19 (td, *J* = 7.8, 0.9 Hz, 1H), 3.87 (s, 1H), 3.41 (s, 3H), 3.24 (s, 3H), 2.53 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.9, 196.3, 166.2, 163.4, 151.2, 133.2, 132.6, 130.8, 130.0, 127.8, 125.4, 77.5, 77.2, 76.9, 68.0, 48. 9, 43.3, 29.6, 29.5, 29.2, 29.0; IR(KBr, cm^{-1}): 3021, 2961, 2925, 1682, 1458, 1430, 1375, 1287, 1243, 1181, 1075, 757; HR-MS (ESI) calcd for $C_{18}H_{18}BrN_2O_5^+$ [$(M+H)^+$] 421.0394, Found 421.0393.

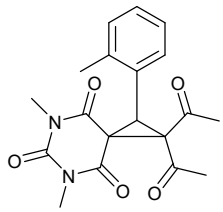
1,1-diacetyl-5,7-dimethyl-2-(2-fluorophenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3d)



3d

White solid (62% yield); mp 159-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (t, *J* = 7.7 Hz, 1H), 7.30 (td, *J* = 7.3, 1.0 Hz, 1H), 7.18 (td, *J* = 7.7, 0.8 Hz, 1H), 6.98 (ddd, *J* = 10.5, 8.3, 0.8 Hz, 1H), 3.85 (s, 1H), 3.40 (s, 3H), 3.28 (s, 3H), 2.51 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.66, 195.59, 165.84, 163.57, 161.1 (d, J_{C-F} = 245.4 Hz), 150.92, 132.5 (d, J_{C-F} = 2.5 Hz), 130.0 (d, J_{C-F} = 8.7 Hz), 124.1 (d, J_{C-F} = 3.4 Hz), 117.8 (d, J_{C-F} = 13.0 Hz), 114.9 (d, J_{C-F} = 21.8 Hz), 65.97, 41.9 (d, J_{C-F} = 1.8 Hz), 41.4 (d, J_{C-F} = 2.2 Hz), 29.50, 29.30, 28.85; IR (KBr, cm^{-1}): 3021, 2961, 2925, 2362, 1677, 1457, 1375, 1288, 1243, 1184, 761; HR-MS (ESI) calcd for $C_{18}H_{18}FN_2O_5^+$ [$(M+H)^+$] 361.1194, Found 361.1191.

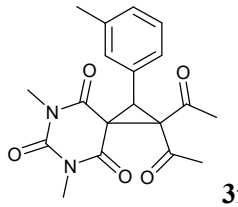
1,1-diacetyl-5,7-dimethyl-2-(2-methylphenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3e)



3e

White solid (77% yield); mp 147-149 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.3 Hz, 1H), 7.29 – 7.11 (m, 3H), 3.95 (s, 1H), 3.41 (s, 3H), 3.27 (s, 3H), 2.48 (s, 3H), 2.16 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.19, 196.25, 166.08, 163.23, 150.91, 137.19, 130.44, 130.26, 129.18, 128.44, 125.95, 67.78, 47.94, 42.47, 29.64, 29.36, 28.94, 28.87, 19.99; IR (KBr, cm^{-1}): 3021, 2957, 2924, 1682, 1455, 1371, 1285, 1240,1180, 756; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1444.

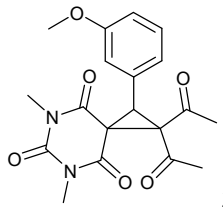
1,1-diacetyl-5,7-dimethyl-2-(3-methylphenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3f)



3f

White solid (88% yield); mp 130-132 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 2H), 7.12 (t, *J* = 7.7 Hz, 2H), 4.04 (s, 1H), 3.39 (s, 3H), 3.29 (s, 3H), 2.46 (s, 3H), 2.34 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 195.9, 166.0, 163.2, 150.9, 137.9, 130.9, 129.7, 129.0, 128.1, 127.1, 67.1, 49.3, 42.5, 30.0, 29.3, 28.9, 28.6, 21.4; IR (KBr, cm^{-1}): 3021, 2957, 2924, 1682, 1456, 1374, 1285, 1241, 1182, 755; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1444.

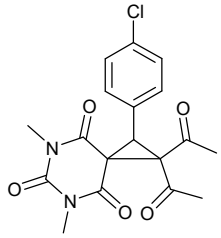
1,1-diacetyl-5,7-dimethyl-2-(3-methoxyphenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3g)



3g

White solid (53% yield); mp 137-139 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 16.3, 8.3 Hz, 1H), 7.00 (s, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.84 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.05 (s, 1H), 3.80 (s, 3H), 3.38 (s, 3H), 3.29 (s, 3H), 2.46 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197. 9, 195.9, 166.0, 163.2, 159.3, 150.9, 131.3, 129.2, 122.3, 116.3, 113.5, 67.1, 55.3, 49.0, 42.5, 30.0, 29.3, 28.9, 28.6; IR (KBr, cm^{-1}): 3021, 2961, 2926, 1682, 1458, 1429, 1376, 1286, 1246, 1174, 755; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_6^+$ [$(M+H)^+$] 373.1394, Found 373.1393.

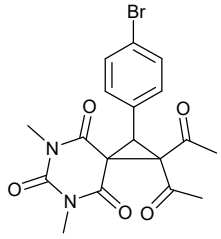
2-(4-chlorophenyl)-1,1-diacetyl-5,7-dimethyl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3h)



3h

Colourless needle (73% yield); mp 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 4.01 (s, 1H), 3.39 (s, 3H), 3.29 (s, 3H), 2.46 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 197.6, 195.7, 165.7, 163.1, 150.7, 134.2, 131.7, 128.4, 128.3, 67.1, 48.0, 42.4, 29.7, 29.4, 29.0, 28.7; IR (KBr, cm^{-1}): 3020, 2959, 2924, 1681, 1455, 1374, 1283, 1244, 841, 756; HR-MS (ESI) calcd for $C_{18}H_{18}ClN_2O_5^+$ $[(M+H)^+]$ 377.0899, Found: 377.0902.

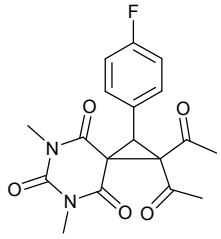
2-(4-bromophenyl)-1,1-diacetyl-5,7-dimethyl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3i)



3i

White solid (64% yield); mp 191-193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 3.99 (s, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.44 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 195.7, 165.7, 163.1, 150.7, 132.0, 131.3, 128.8, 122.4, 67.0, 47.9, 42.3, 29.7, 29.4, 29.0, 28.7; IR (KBr, cm^{-1}): 3020, 2959, 2924, 2362, 1681, 1457, 1374, 1241, 1180, 837, 755; HR-MS (ESI) calcd for $C_{18}H_{18}BrN_2O_5^+$ $[(M+H)^+]$ 421.0394, Found 421.0393.

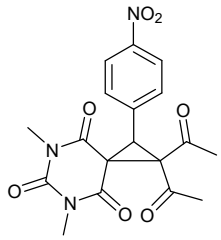
1,1-diacetyl-5,7-dimethyl-2-(4-fluorophenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3j)



3j

White solid (74% yield); mp 185-187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 2H), 7.05 – 6.96 (m, 2H), 4.02 (s, 1H), 3.38 (s, 3H), 3.28 (s, 3H), 2.46 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 195.8, 165.8, 163.1, 162.4 (d, *J* = 248.2 Hz), 150.8, 132.2 (d, *J* = 8.2 Hz), 125.5 (d, *J* = 3.4 Hz), 115.2 (d, *J* = 21.6 Hz), 67.1, 48.3, 42.6, 29.7, 29.3, 28.9, 28.6; IR(KBr, cm^{-1}): 3020, 2959, 2924, 1682, 1513, 1457, 1376, 1286, 1236, 1172, 755; HR-MS (ESI) calcd for $C_{18}H_{18}FN_2O_5^+$ $[(M+H)^+]$ 361.1194, Found 361.1192.

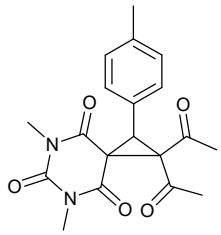
1,1-diacetyl-5,7-dimethyl-2-(4-nitrophenyl)-5,7-diazaspiro[2,5]octane-4,6,8-trione (3k)



3k

White solid (73% yield); mp 197-199 °C; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.8Hz, 2H), 7.59 (d, *J* = 8.3Hz, 2H), 4.10 (s, 1H), 3.40 (s, 3H), 3.31 (s, 3H), 2.50 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 197.1, 195.4, 165.4, 163.1, 150.5, 147.4, 137.2, 131.4, 123.2, 67.1, 46.4, 42.0, 29.7, 29.5, 29.1, 28.7; IR (KBr, cm^{-1}): 2959, 2926, 1682, 1519, 1458, 1375, 1350, 1288, 1181, 845, 756; HR-MS (ESI) calcd for $C_{18}H_{18}N_3O_7^+$ [$(M+H)^+$] 388.1139, Found 388.1138.

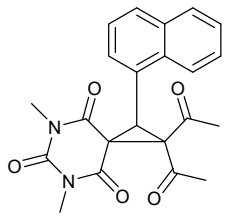
1,1-diacetyl-5,7-dimethyl-2-(4-methylphenyl)- 5,7-diazaspiro[2,5]octane-4,6,8-trione (3m)



3m

White solid (74% yield); mp 131-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 4.04 (s, 1H), 3.38 (s, 3H), 3.28 (s, 3H), 2.46 (s, 3H), 2.33 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.0, 196.0, 166.0, 163.2, 150.9, 138.1, 130.1, 128.9, 126.6, 67.2, 49.4, 42.6, 29.9, 29.3, 28.9, 28.7, 21.2; IR (KBr, cm^{-1}): 3021, 2961, 2924, 1683, 1456, 1371, 1284, 1244, 1178, 1076, 759, 473; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1447.

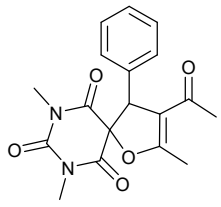
1,1-diacetyl-5,7-dimethyl-2-naphthalen-1-yl-5,7-diazaspiro[2,5]octane-4,6,8-trione (3n)



3n

White solid (66% yield); mp 171-173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 1H), 7.90 – 7.85 (m, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 7.3 Hz, 1H), 7.55 – 7.47 (m, 2H), 7.44 (t, *J* = 8.2 Hz, 1H), 4.41 (s, 1H), 3.48 (s, 3H), 3.12 (s, 3H), 2.51 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5, 196.8, 166.2, 163.3, 150.9, 133.5, 132.5, 129.3, 129.2, 128.7, 126.9, 126.0, 125.9, 125.1, 122.5, 67.2, 47.5, 42.5, 30.4, 29.5, 28.9, 28.8; IR (KBr, cm^{-1}): 3023, 2962, 1683, 1454, 1373, 1287, 1245, 1178, 1081, 755, 472; HR-MS (ESI) calcd for $C_{22}H_{21}N_2O_5^+$ [$(M+H)^+$] 393.1445, Found 393.1444.

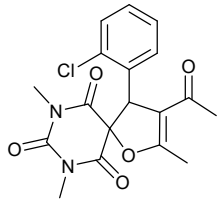
3-acetyl-4-phenyl-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4a)



4a

White solid (77% yield); mp 137-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 3H), 7.10 – 7.02 (m, 2H), 4.73 (q, *J* = 1.4 Hz, 1H), 3.41 (s, 3H), 2.56 (s, 3H), 2.55 (d, *J* = 1.4 Hz, 3H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 169.8, 166.9, 164.3, 150.1, 135.4, 129.1, 128.9, 128.3, 112.9, 88.6, 62.1, 29.6, 29.4, 28.3, 15.0; IR (KBr, cm^{-1}): 3020, 2961, 2926, 1690, 1635, 1609, 1446, 1377, 1240, 1046, 953, 753, 705; HR-MS (ESI) calcd for $C_{18}H_{19}N_2O_5^+$ [(M+H) $^+$] 343.1284, Found 343.1288.

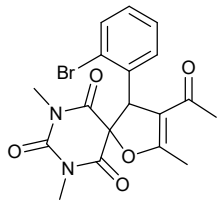
3-acetyl-4-(2-chlorophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4b)



4b

White solid (94% yield); mp 212-214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 - 7.31 (m, 1H), 7.31 - 7.20 (m, 2H), 7.18 - 7.12 (m, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 3.38 (s, 3H), 2.69 (s, 3H), 2.56 (d, *J* = 1.2 Hz, 3H), 1.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 170.1, 166.5, 164.3, 150.1, 133.6, 133.2, 130.9, 130.1, 129.4, 127.5, 113.0, 87.4, 56.7, 29.3, 29.2, 28.4, 14.9; IR(KBr, cm^{-1}): 2959, 2927, 1697, 1443, 1378, 1234, 1130, 1096, 1043, 754; HR-MS (ESI) calcd for $C_{18}H_{18}ClN_2O_5^+$ [$(M+H)^+$] 377.0899, Found 377.0895.

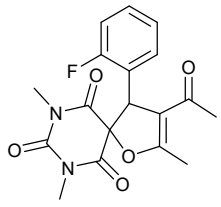
3-acetyl-4-(2-bromophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4c)



4c

White solid (78% yield); mp 263-264 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.31 (td, *J* = 7.6, 1.1 Hz, 1H), 7.21 – 7.12 (m, 2H), 5.39 (d, *J* = 1.4 Hz, 1H), 3.38 (s, 3H), 2.69 (s, 3H), 2.56 (d, *J* = 1.4 Hz, 3H), 1.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 170.0, 166.4, 164.3, 150.0, 134.8, 132.7, 131.1, 130.4, 128.1, 124.3, 113.4, 87.4, 59.4, 29.4, 29.2, 28.4, 14.9; IR (KBr, cm^{-1}): 3021, 2961, 2925, 1696, 1623, 1442, 1377, 1339, 1220, 1134, 1040, 945, 795, 750; HR-MS (ESI) calcd for $C_{18}H_{18}BrN_2O_5^+$ [$(M+H)^+$] 421.0394, Found 421.0393.

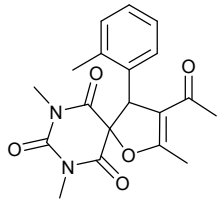
3-acetyl-4-(2-fluorophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4d)



4d

White solid (92% yield); mp 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, J = 13.0, 5.9 Hz, 1H), 7.18 – 7.00 (m, 3H), 5.17 (s, 1H), 3.40 (s, 3H), 2.69 (s, 3H), 2.55 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 170.2, 166.6, 164.3, 160.3 (d, J_{C-F} = 245.8 Hz), 150.0, 130.6 (d, J_{C-F} = 8.4 Hz), 130.2 (d, J_{C-F} = 2.5 Hz), 124.8 (d, J_{C-F} = 3.5 Hz), 122.6 (d, J_{C-F} = 13.3 Hz), 115.1 (d, J_{C-F} = 21.9 Hz), 111.8, 87.4, 53.0 (d, J_{C-F} = 4.3 Hz), 29.4, 29.3, 28.3, 15.1; IR (KBr, cm^{-1}): 3021, 2958, 2927, 1693, 1637, 1612, 1447, 1378, 1233, 1130, 1045, 950, 758; HR-MS (ESI) calcd for $C_{18}H_{18}FN_2O_5^+$ [$(M+H)^+$] 361.1194, Found 361.1195.

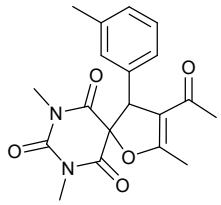
3-acetyl-4-(2-methylphenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4e)



4e

White solid (75% yield); mp 211-213 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.09 (m, 3H), 7.04 (d, J = 6.6 Hz, 1H), 5.09 (s, 1H), 3.37 (s, 3H), 2.59 (s, 3H), 2.54 (s, 3H), 2.24 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 169.1, 166.9, 164.6, 150.2, 135.5, 133.4, 130.5, 129.1, 128.6, 126.7, 114.3, 88.4, 57.0, 29.3, 29.2, 28.4, 18.9, 14.9; IR (KBr, cm^{-1}): 3021, 2957, 2925, 1690, 1636, 1611, 1445, 1376, 1233,1128, 1045, 948, 755; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1444.

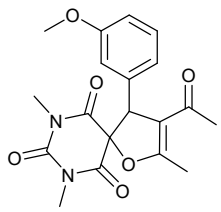
3-acetyl-4-(3-methylphenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4f)



4f

White solid (78% yield); mp 201-203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, J = 7.6 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 6.88 – 6.78 (m, 2H), 4.69 (d, J = 1.2 Hz, 1H), 3.41 (s, 3H), 2.57 (s, 3H), 2.54 (d, J = 1.3 Hz, 3H), 2.31 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 169.8, 166.9, 164.3, 150.1, 138.8, 135.2, 129.8, 128.9, 128.8, 125.4, 112.8, 88.7, 62.1, 29.6, 29.3, 28.3, 21.3, 14.9; IR (KBr, cm^{-1}): 3020, 2957, 2925, 1690, 1634, 1608, 1444, 1376, 1126, 1047, 950, 754, 706; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1443.

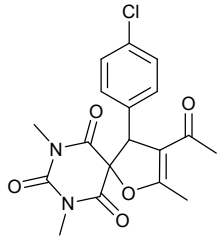
3-acetyl-4-(3-methoxyphenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4g)



4g

White solid (62% yield); mp 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.9 Hz, 1H), 6.85 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.64 (d, *J* = 7.4 Hz, 1H), 6.57 (s, 1H), 4.70 (s, 1H), 3.76 (s, 3H), 3.40 (s, 3H), 2.63 (s, 3H), 2.54 (d, *J* = 1.3 Hz, 3H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 169.9, 166.9, 164.2, 160.0, 150.1, 136.9, 130.0, 120.6, 114.7, 113.6, 112.8, 88.6, 62.1, 55.3, 29.6, 29.3, 28.4, 14.9; IR (KBr, cm^{-1}): 3019, 2957, 2926, 1690, 1635, 1606, 1444, 1377, 1279, 1045, 754; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_6^+$ $[(M+H)^+]$ 373.1394, Found 373.1393.

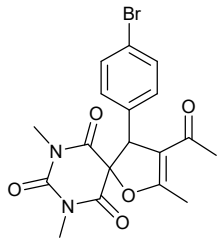
3-acetyl-4-(4-chlorophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4h)



4h

White solid (77% yield); mp 207-209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 2H), 4.68 (d, *J* = 1.4 Hz, 1H), 3.40 (s, 3H), 2.66 (s, 3H), 2.55 (d, *J* = 1.4 Hz, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 169.8, 166.6, 164.1, 150.0, 135.0, 134.0, 129.6, 129.1, 113.3, 88.2, 61.3, 29.6, 29.4, 28.4, 15.1; IR (KBr, cm^{-1}): 3021, 2960, 2923, 1706, 1625, 1444, 1379, 1342, 1221, 1041, 955, 847, 797, 752; HR-MS (ESI) calcd for $C_{18}H_{18}ClN_2O_5^+$ $[(M+H)^+]$ 377.0899, Found 377.0896.

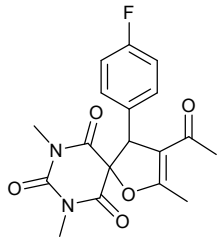
3-acetyl-4-(4-bromophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4i)



4i

White solid (78% yield); mp 178-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.1 Hz, 2H), 4.67 (s, 1H), 3.40 (s, 3H), 2.66 (s, 3H), 2.55 (d, *J* = 1.1 Hz, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.5, 169.9, 166.6, 164.1, 150.0, 134.5, 132.0, 129.9, 123.2, 113.3, 88.1, 61.4, 29.6, 29.4, 28.5, 15.1; IR (KBr, cm^{-1}): 3021, 2961, 2925, 1696, 1623, 1442, 1377, 1339, 1220, 1134, 1040, 945, 795, 750; HR-MS (ESI) calcd for $C_{18}H_{18}BrN_2O_5^+$ $[(M+H)^+]$ 421.0394, Found 421.0392.

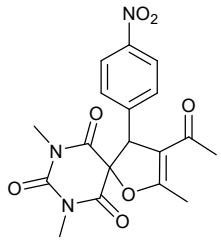
3-acetyl-4-(4-fluorophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4j)



4j

White solid (78% yield); mp 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 – 6.94 (m, 4H), 4.70 (d, *J* = 1.4 Hz, 1H), 3.40 (s, 3H), 2.66 (s, 3H), 2.55 (d, *J* = 1.4 Hz, 3H), 1.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192. 7, 169.7, 166.7, 164.2, 162.9 (d, J_{C-F} = 249.2 Hz), 150.1, 131.3 (d, J_{C-F} = 3.4 Hz), 130.1 (d, J_{C-F} = 8.1 Hz), 115.9 (d, J_{C-F} = 26.0 Hz), 113.3, 88.3, 61.3, 29.6, 29.4, 28.5, 15.1; IR (KBr, cm^{-1}): 3019, 2958, 2925, 1690, 1635, 1607, 1509, 1443, 1377, 1232, 1128, 1046, 949, 850, 755; HR-MS (ESI) calcd for $C_{18}H_{18}FN_2O_5^+$ [$(M+H)^+$] 361.1194, Found 361.1193.

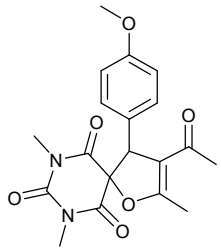
3-acetyl-4-(4-nitrophenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4k)



4k

White solid (78% yield); mp 121-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H), 4.81 (s, *J* = 1.2 Hz ,1H), 3.41 (s, 3H), 2.66 (s, 3H), 2.59 (d, *J* = 1.3 Hz, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 169.9, 166.3, 163.9, 149.9, 147.9, 142.8, 129.3, 123.8, 114.2, 87.7, 60.8, 29.7, 29.5, 28.5, 15.3; IR (KBr, cm^{-1}): 3150, 3075, 2957, 2926, 1698, 1373, 1350, 1289, 1183, 816, 637; HR-MS (ESI) calcd for $C_{18}H_{18}N_3O_7^+$ [$(M+H)^+$] 388.1139, Found 388.1140.

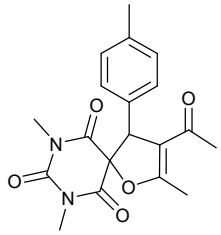
3-acetyl-4-(4-methoxyphenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4l)



4l

White solid (57% yield); mp 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (d, *J* = 7.8 Hz, 2H), 6.83 (d, *J* = 7.8 Hz, 2H), 4.68 (d, *J* = 1.3 Hz, 1H), 3.78 (s, 3H), 3.40 (s, 3H), 2.64 (s, 3H), 2.53 (d, *J* = 1.5 Hz, 3H), 1.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 169.6, 166.9, 164.4, 160.0, 150.2, 129.5, 127.2, 114.3, 113.0, 88.6, 61.5, 55.3, 29. 6, 29.3, 28.4, 14.9; IR (KBr, cm^{-1}): 3020, 2957, 2925, 1690, 1610, 1443, 1376, 1246, 1128, 1043, 755; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_6^+$ [$(M+H)^+$] 373.1394, Found 373.1395.

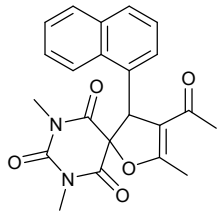
3-acetyl-4-(4-methylphenyl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4m)



4m

White solid (89% yield); mp 192-194 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 7.4 Hz, 2H), 4.69 (d, *J* = 1.2 Hz, 1H), 3.40 (s, 3H), 2.59 (s, 3H), 2.54 (d, *J* = 1.4 Hz, 3H), 2.32 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 169.7, 166.9, 164.4, 150.2, 139.0, 132.2, 129.6, 128.2, 112.9, 88.6, 61.9, 29.6, 29.4, 28.3, 21.1, 14.9; IR (KBr, cm^{-1}): 3020, 2960, 2924, 2314, 1691, 1611, 1444, 1376, 1241, 1128, 1047, 948, 755; HR-MS (ESI) calcd for $C_{19}H_{21}N_2O_5^+$ [$(M+H)^+$] 357.1445, Found 357.1444.

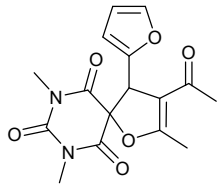
3-acetyl-4-(naphthalen-1-yl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]-2-decene-6,8,10-trione (4n)



4n

White solid (86% yield); mp 219-221 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.72 (m, 3H), 7.54 (s, 1H), 7.53 – 7.45 (m, 2H), 7.15 (s, 1H), 4.89 (d, *J* = 1.2 Hz, 1H), 3.44 (s, 3H), 2.60 (d, *J* = 1.3 Hz, 3H), 2.37 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 170.0, 166.9, 164.3, 150.1, 133.3, 133.0, 132.7, 128.8, 128.0, 127.8, 127.7, 126.9, 126.9, 125.5, 113.0, 88.6, 62.2, 29.7, 29.4, 28.3, 15.0; IR (KBr, cm^{-1}): 3019, 2958, 2924, 2387, 1691, 1629, 1439, 1376, 1232, 1125, 1046, 950, 753, 487; HR-MS (ESI) calcd for $C_{22}H_{21}N_2O_5^+$ [$(M+H)^+$] 393.1445, Found 393.1447

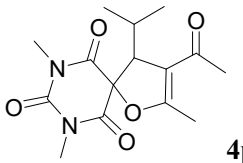
3-acetyl-4-(furan-2-yl)-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]- 2-decene-6,8,10-trione (4o)



4o

White solid (85% yield); mp 162-164 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 1.8, 0.7 Hz, 1H), 6.34 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.17 (d, *J* = 3.3 Hz, 1H), 4.86 (d, *J* = 1.5 Hz, 1H), 3.39 (s, 3H), 2.92 (s, 3H), 2.50 (d, *J* = 1.5 Hz, 3H), 2.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 170.0, 166.4, 163.9, 150.2, 149.1, 143.2, 111.2, 110.9, 110.2, 87.0, 55.0, 29.4, 29.2, 28.9, 15.0; IR (KBr, cm^{-1}): 3022, 2958, 2925, 2386, 1694, 1634, 1440, 1378, 1237, 1130, 1047, 948, 752; HR-MS (ESI) calcd for $C_{16}H_{17}N_2O_6^+$ [$(M+H)^+$] 333.1081, Found 333.1080.

3-acetyl-4-isopropyl-2,7,9-trimethyl-1-ox-7,9-diazaspiro[4,5]- 2-decene-6,8,10-trione (4p)



4p

White solid (63% yield); mp 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (s, 1H), 3.35 (s, 3H), 3.29 (s, 3H), 2.43 (s, 3H), 2.34 (d, *J* = 1.8 Hz, 3H), 1.85 (m, 1H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 167.5, 166.9, 165.1, 150.4, 115.3, 89.0, 60.2, 30.5, 29.6, 29.5, 29.2, 21.6, 18.7, 15.3; IR(KBr, cm^{-1}): 2967, 2930, 2359, 1697, 1629, 1446, 1375, 1217, 1088, 1034, 951, 749; HR-MS (ESI) calcd for $C_{15}H_{21}N_2O_5^+$ [$(M+H)^+$] 309.1445, Found 309.1447

6. References

1) H. Liu, Y. Liu, C. Yuan, G.-P. Wang, S.-F. Zhu, Y. Wu, B. Wang, Z. Sun, Y. Xiao, Q.-L. Zhou, and H. Guo, *Org. Lett.,* 2016, **18**, 1302.

2) M. Szostak, B. Sautier, M. Spain, M. Behlendorf, and D. J. Procter, *Angew. Chem. Int. Ed.* 2013, **52**, 12559.

7. The Single Crystal X-ray Diffraction Study of 3h

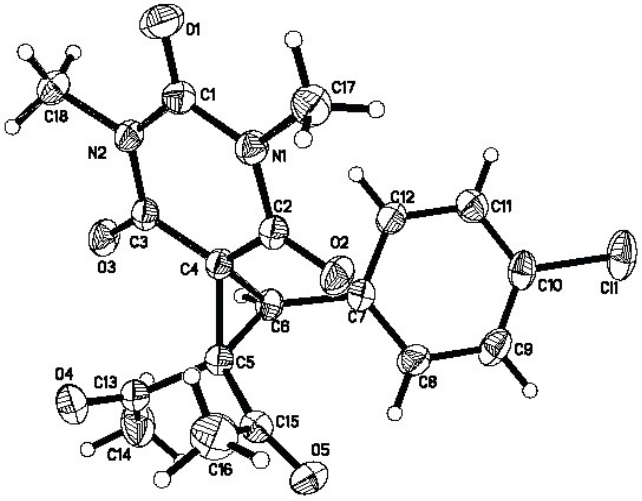
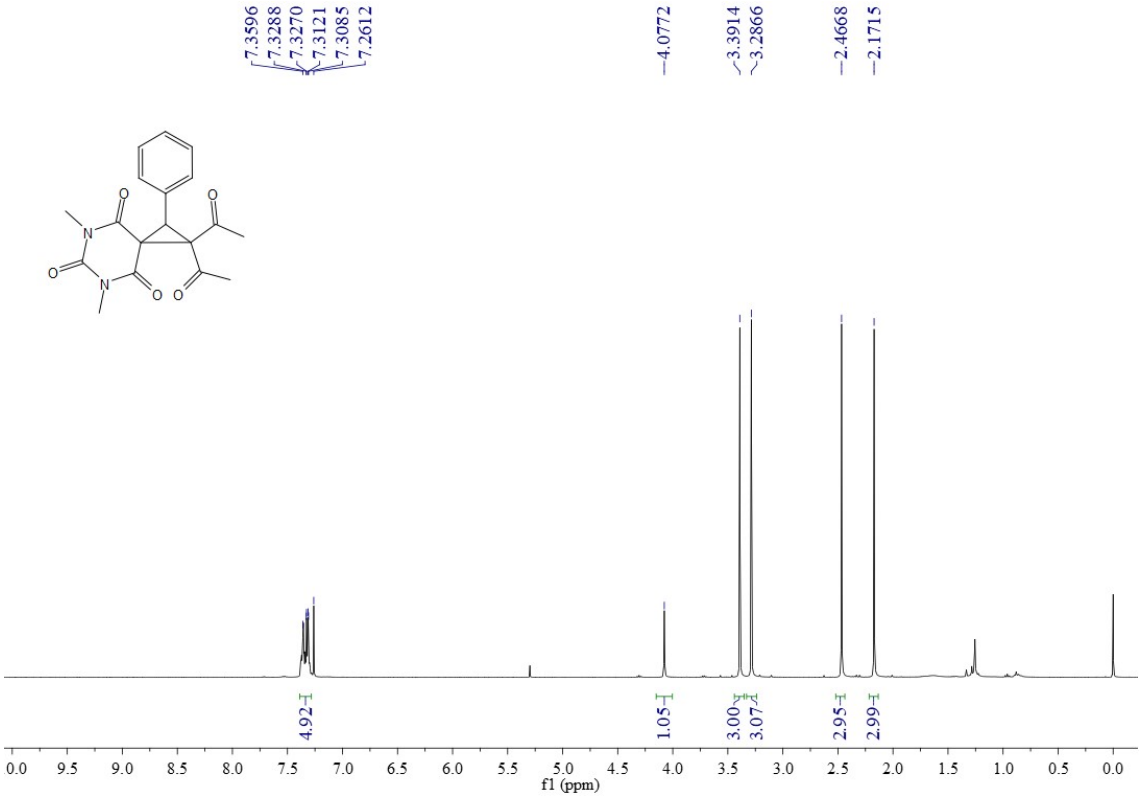


Table S1 Crystal data and structure refinement for **3h**

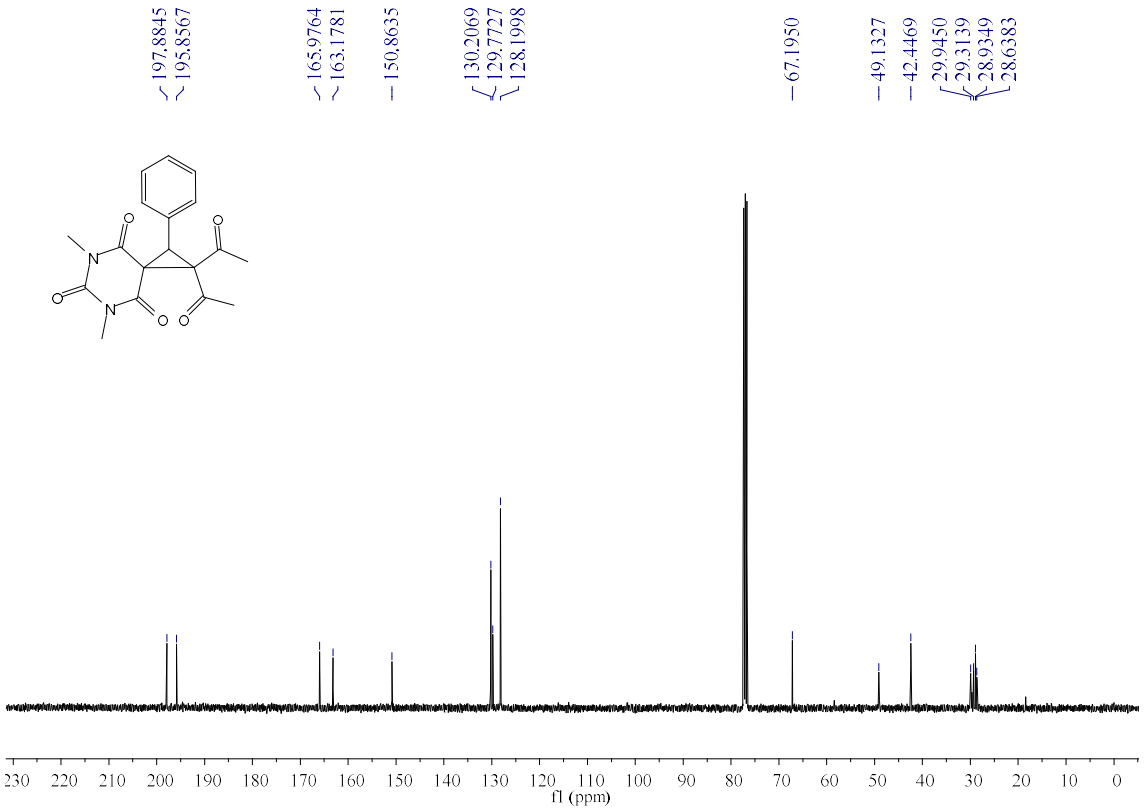
Identification code	201811442
Empirical formula	$C_{18}H_{17}ClN_2O_5$
Formula weight	376.78
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.7345(3)
b/Å	14.0642(4)
c/Å	13.0475(4)
α/°	90
β/°	91.839(3)
γ/°	90

Volume/Å^3	1785.39(10)
Z	4
ρ_{calc}g/cm^3	1.402
μ/mm^{-1}	2.181
F(000)	784.0
Crystal size/mm^3	0.19 × 0.14 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.248 to 134.13
Index ranges	-11 ≤ h ≤ 7, -16 ≤ k ≤ 16, -15 ≤ l ≤ 15
Reflections collected	12681
Independent reflections	3190 [R_{int} = 0.0334, R_{sigma} = 0.0271]
Data/restraints/parameters	3190/0/240
Goodness-of-fit on F2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0484, wR_2 = 0.1375
Final R indexes [all data]	R_1 = 0.0587, wR_2 = 0.1493
Largest diff. peak/hole / e Å^{-3}	0.34/-0.43

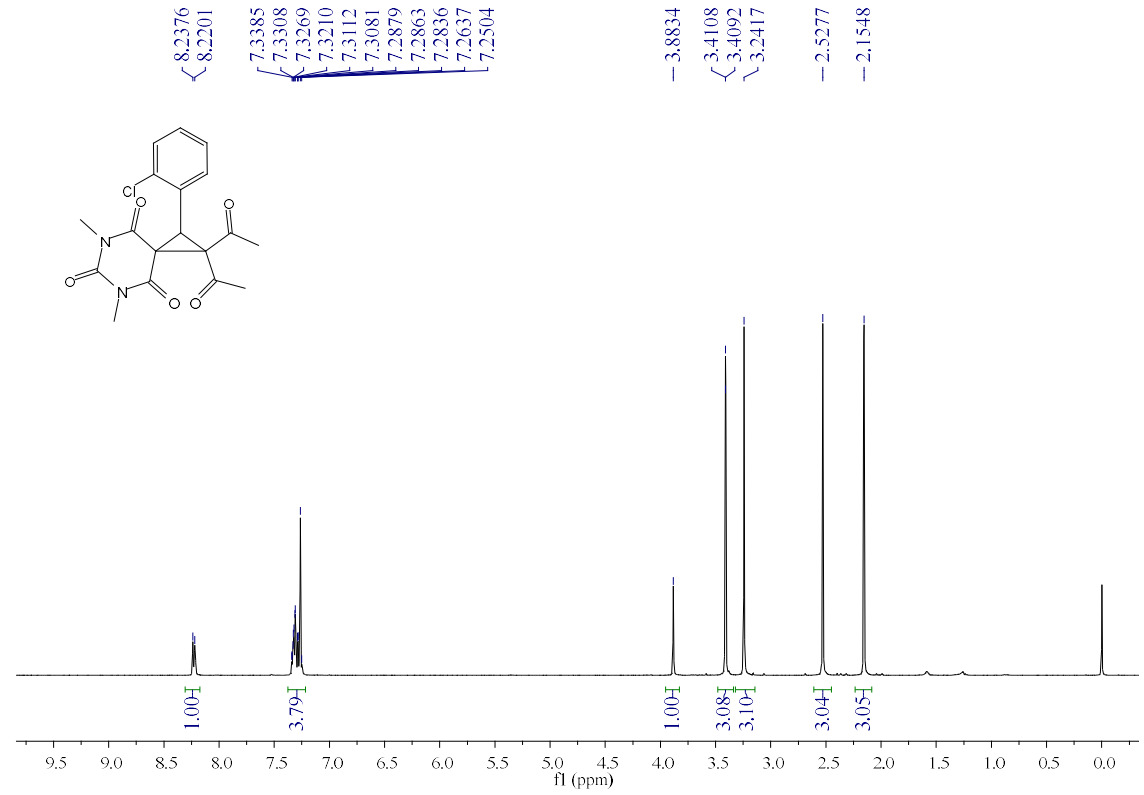
8. Copies of ^{1}H and ^{13}C NMR Spectra for the Products



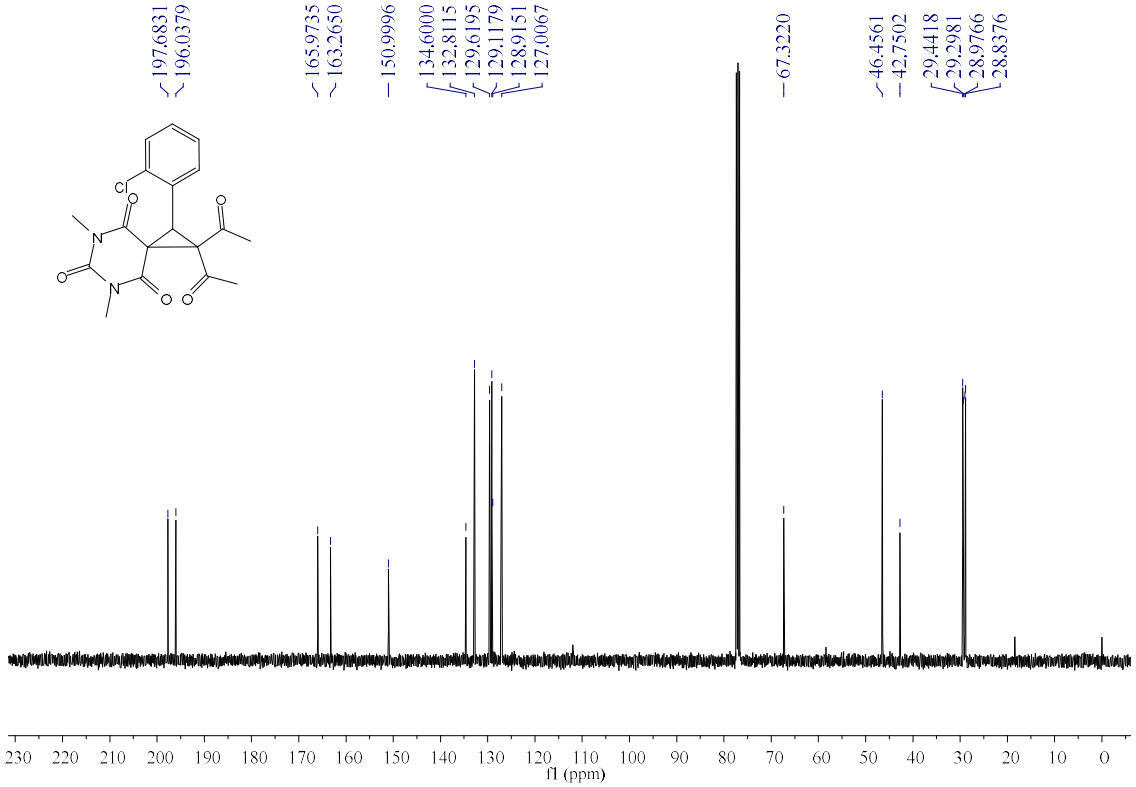
^{1}H NMR of compound **3a**



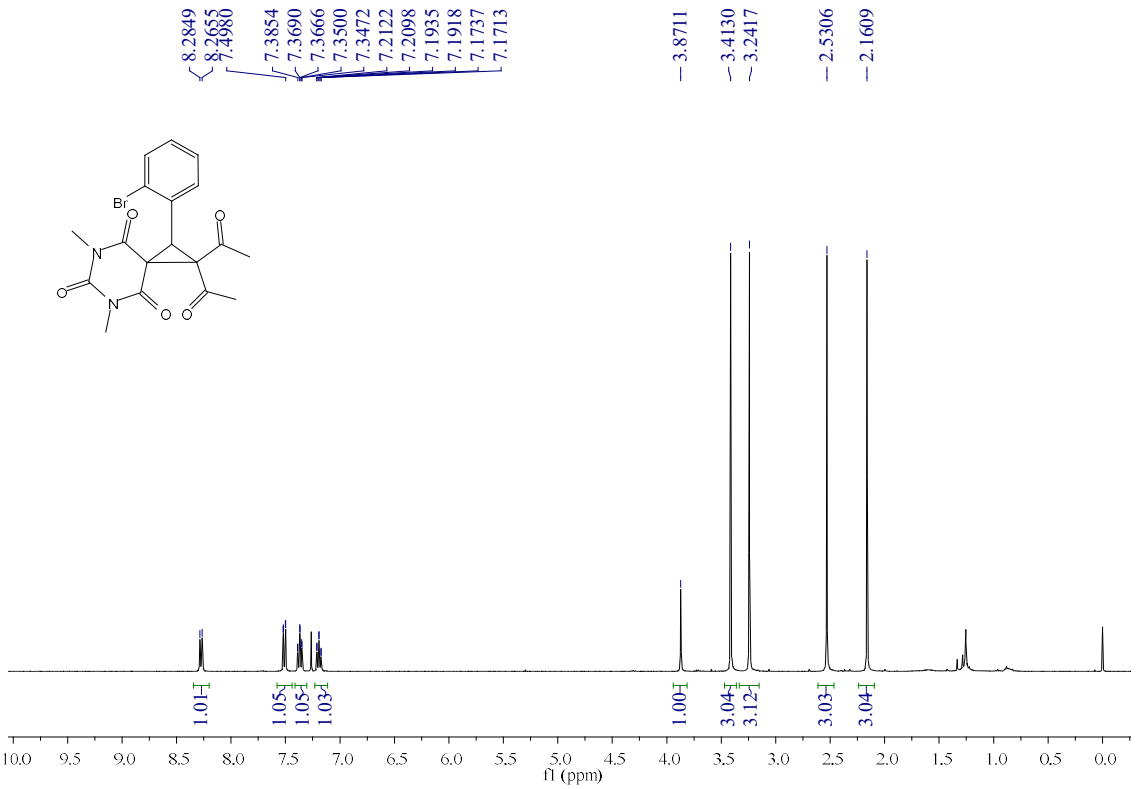
^{13}C NMR of compound **3a**



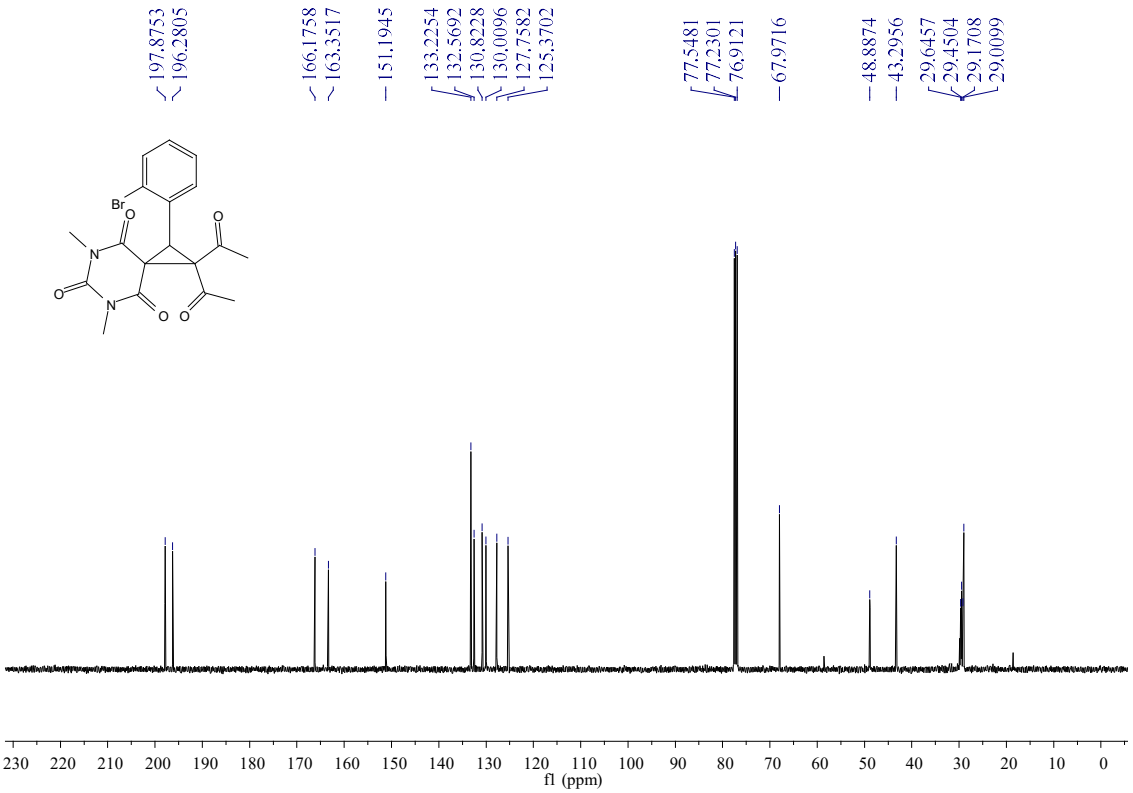
^{1}H NMR of compound **3b**



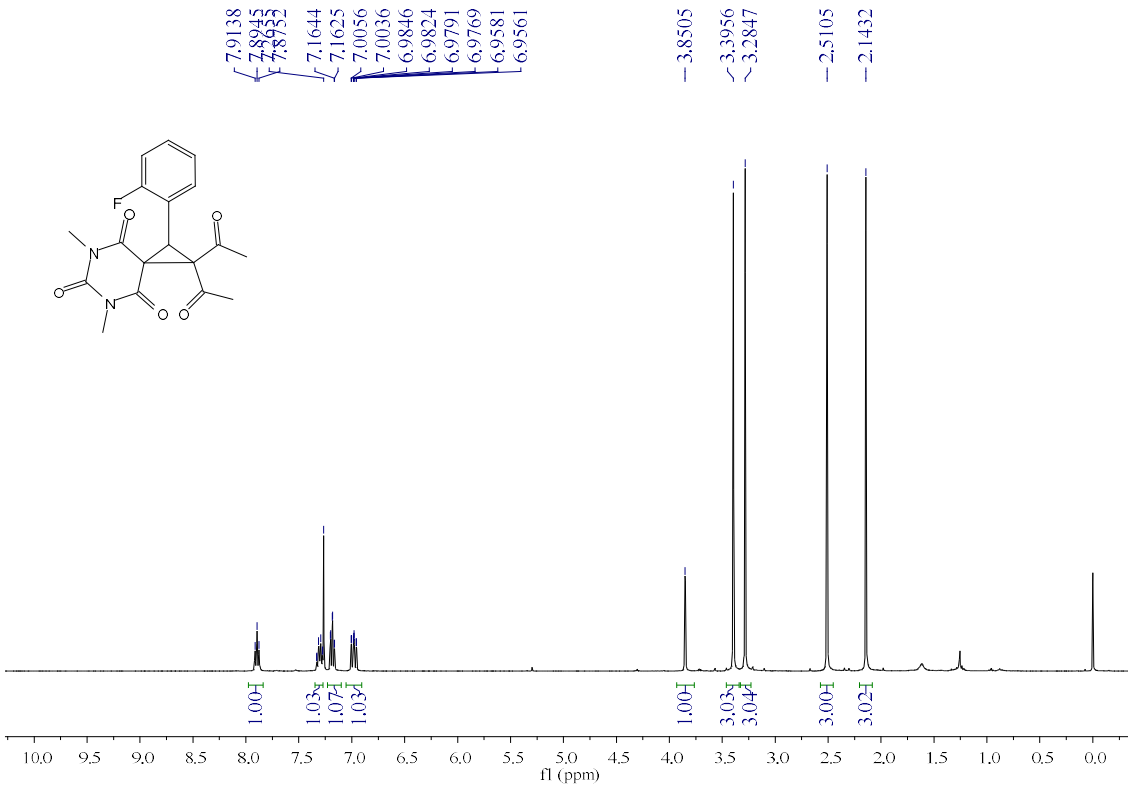
^{13}C NMR of compound **3b**



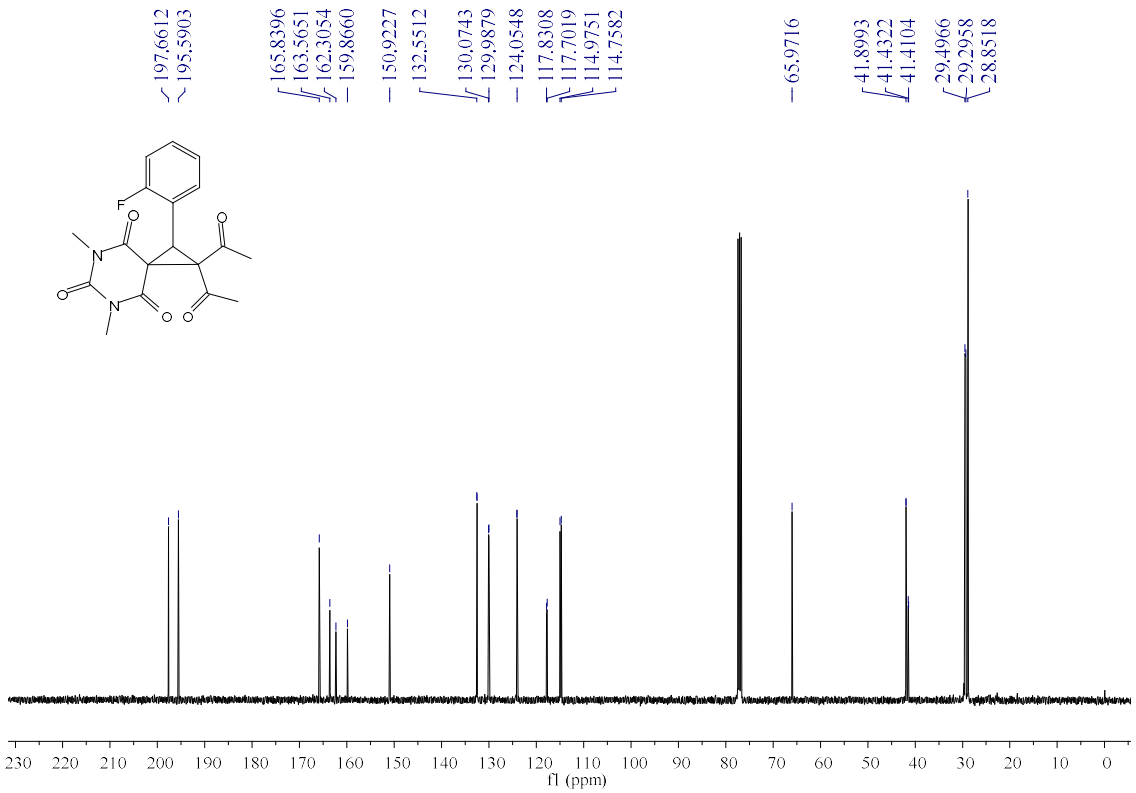
^{1}H NMR of compound **3c**



^{13}C NMR of compound **3c**



^{1}H NMR of compound **3d**



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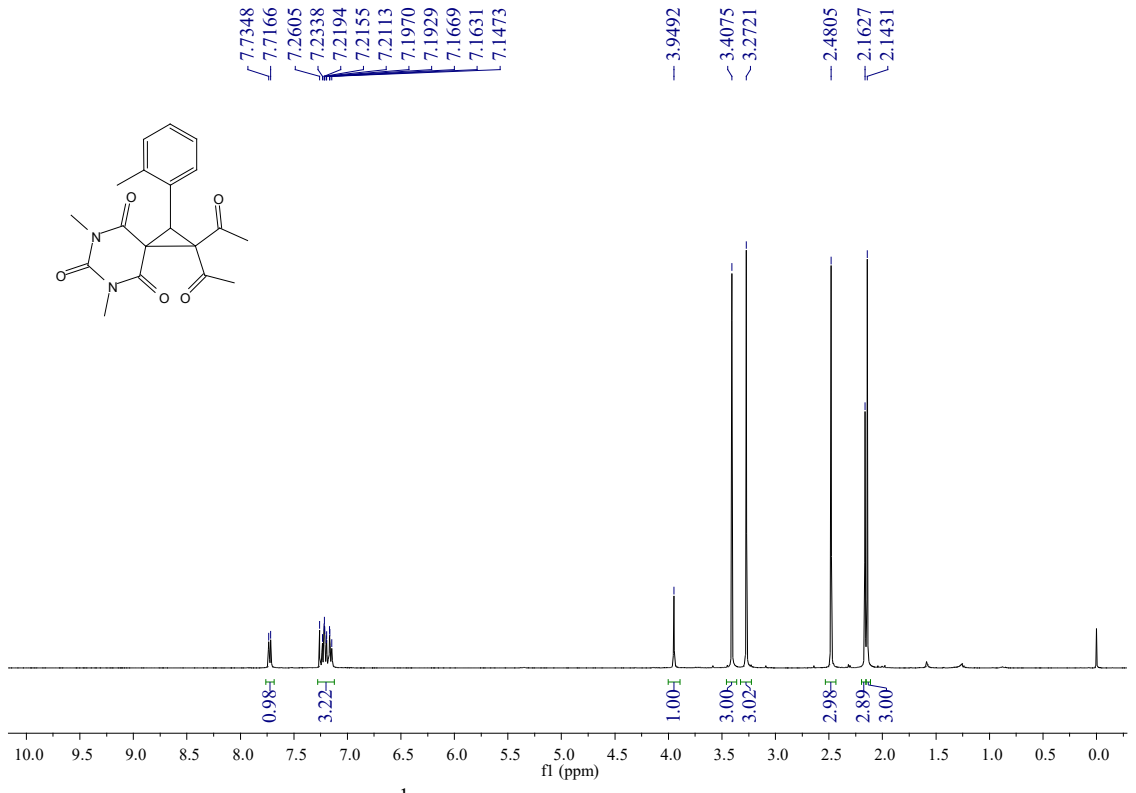
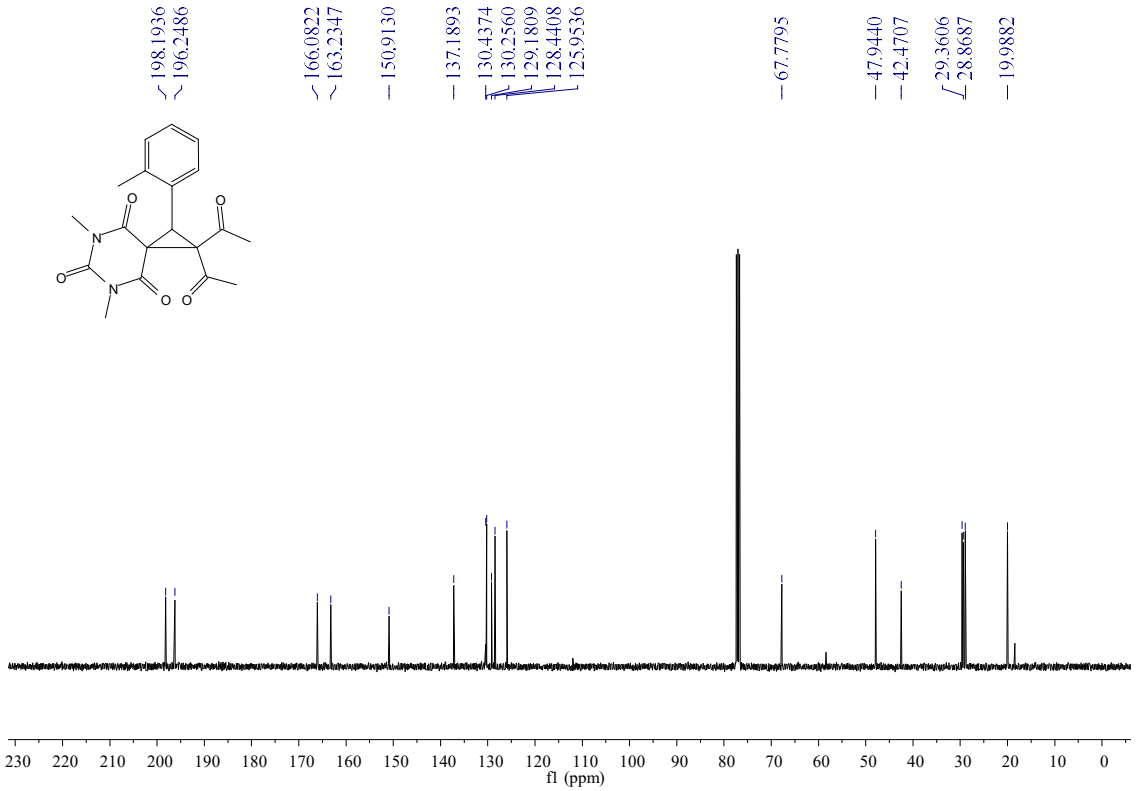
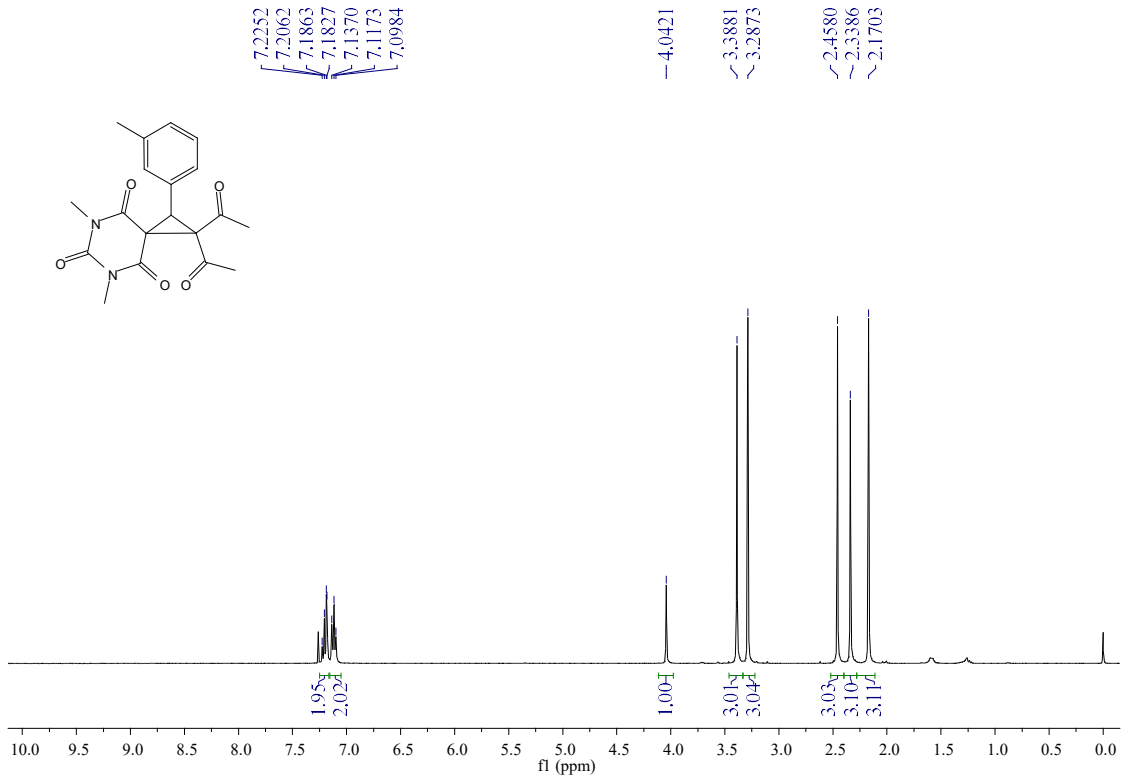


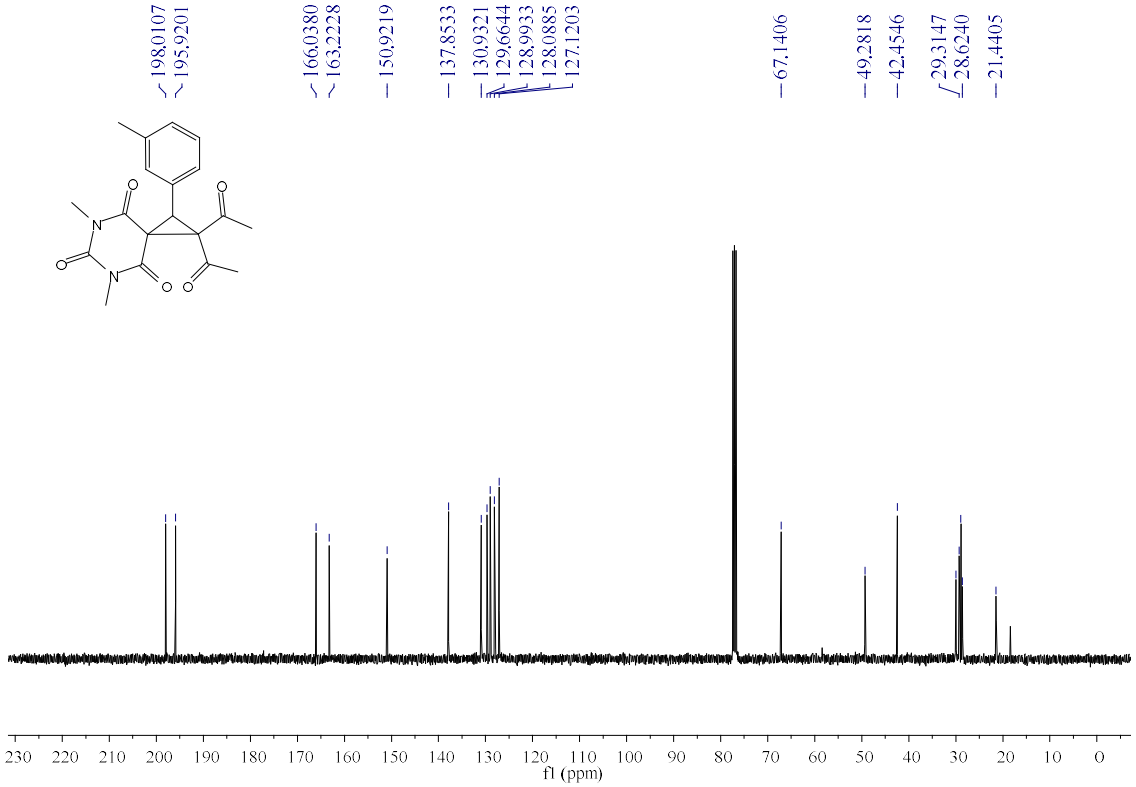
^{1}H NMR of compound **3e**



^{13}C NMR of compound **3e**



^{1}H NMR of compound **3f**



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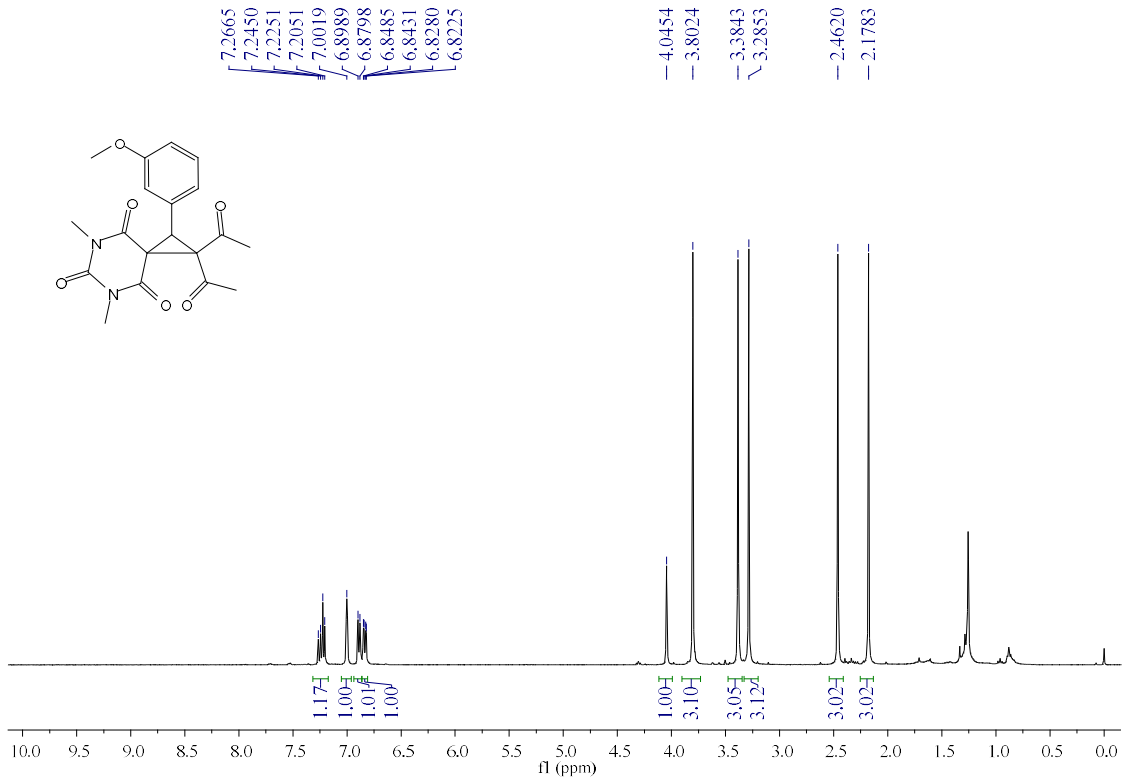
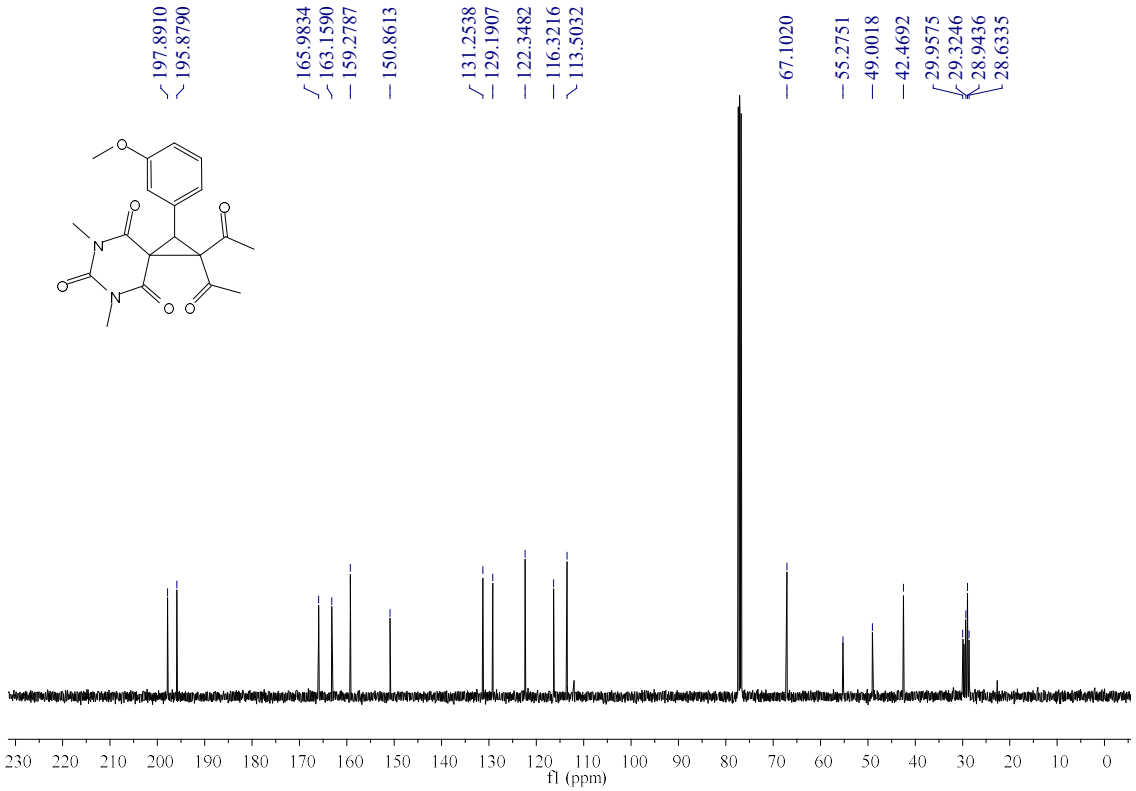


^{1}H NMR of compound **3g**



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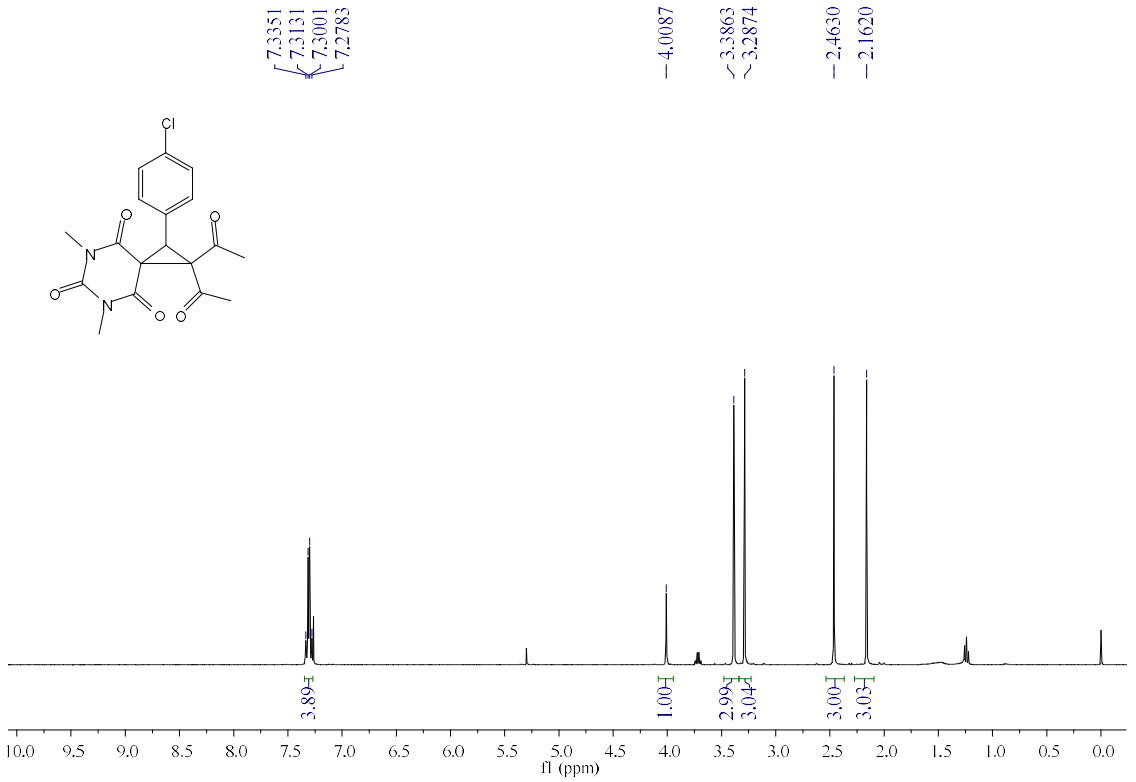
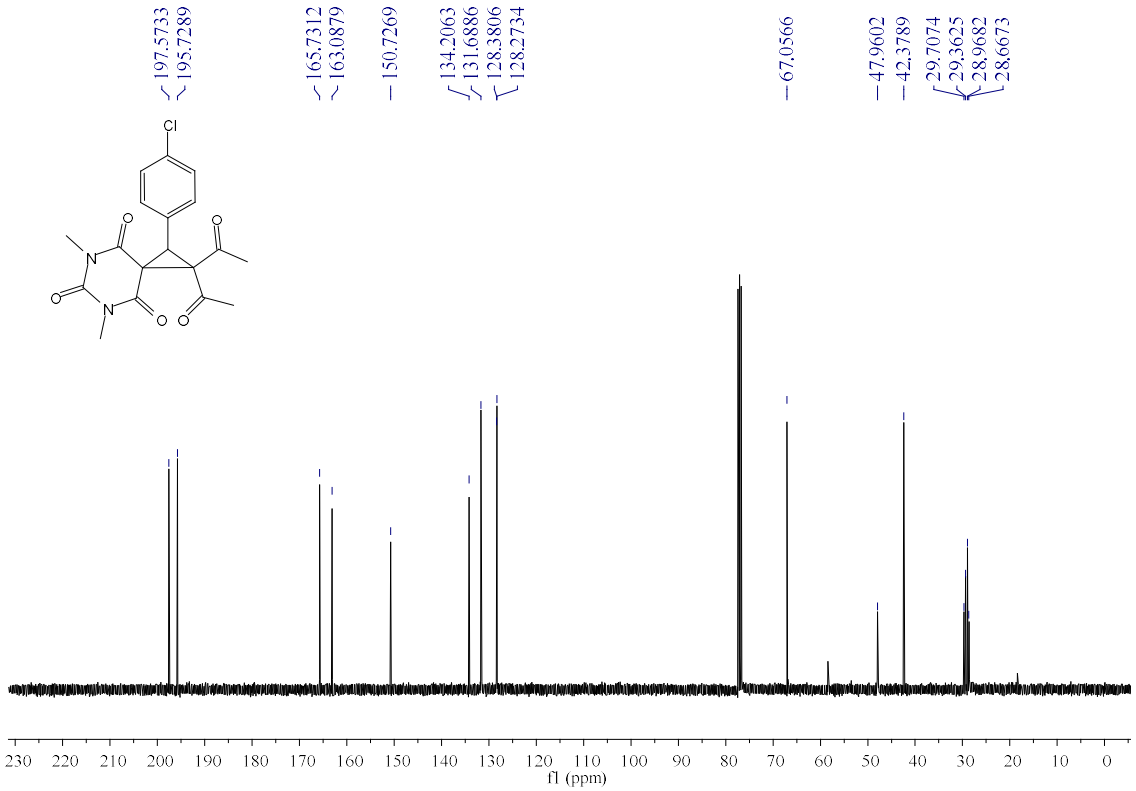


^{1}H NMR of compound **3h**



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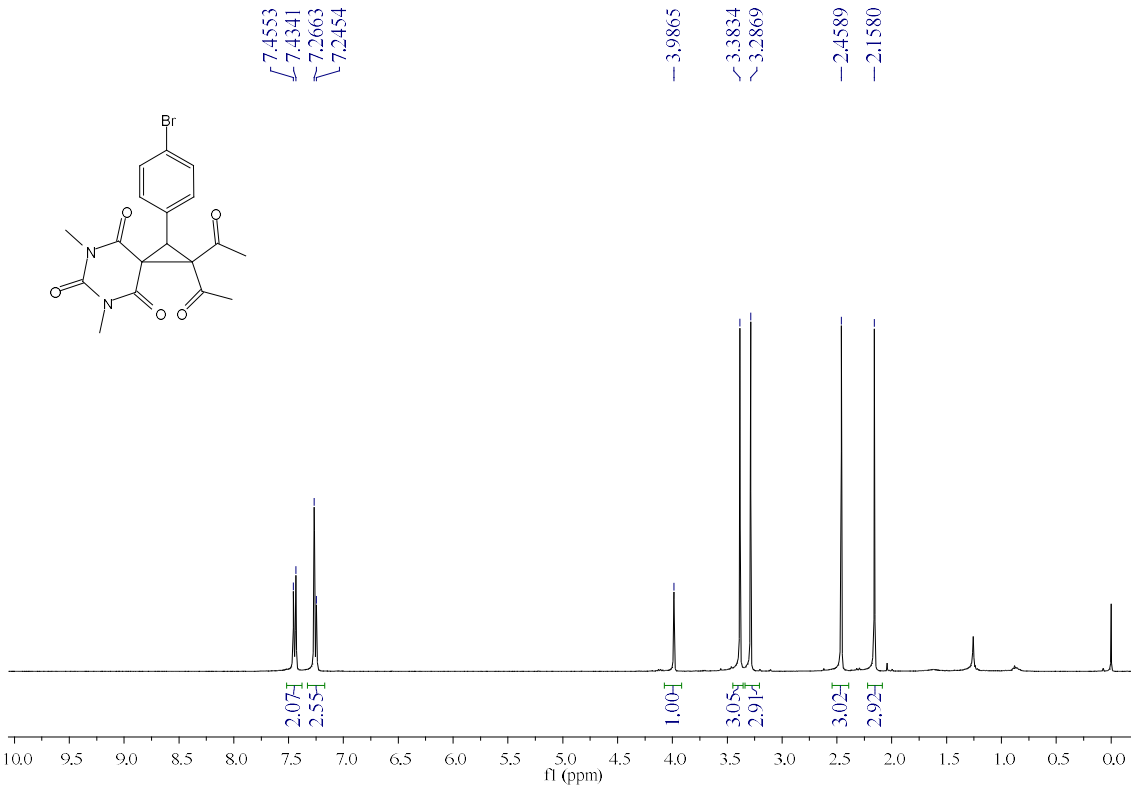
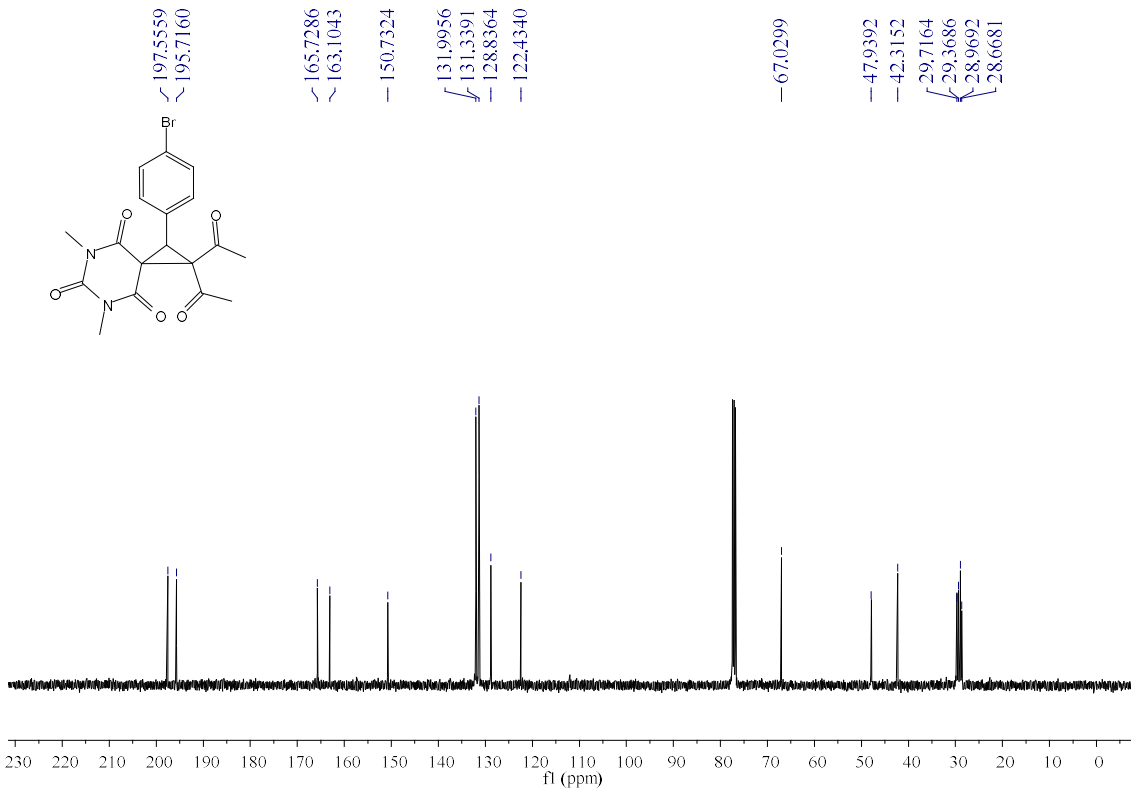
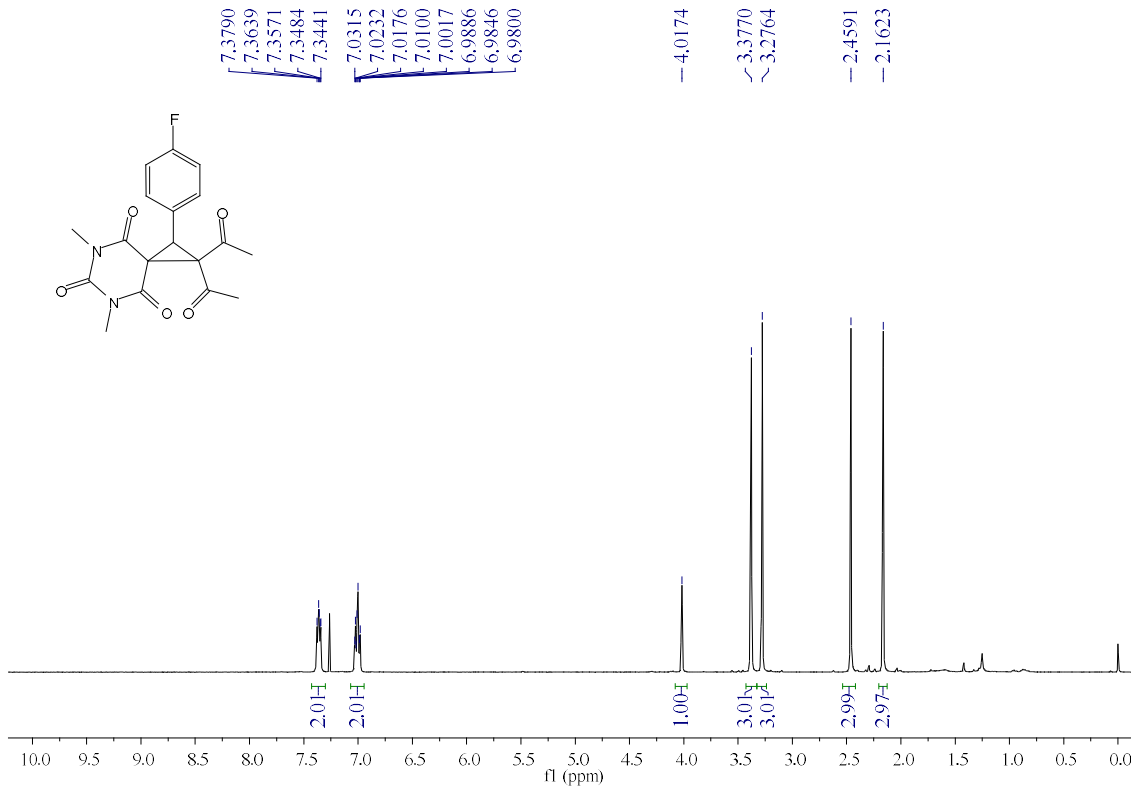


^{1}H NMR of compound **3i**



^{13}C NMR of compound **3i**



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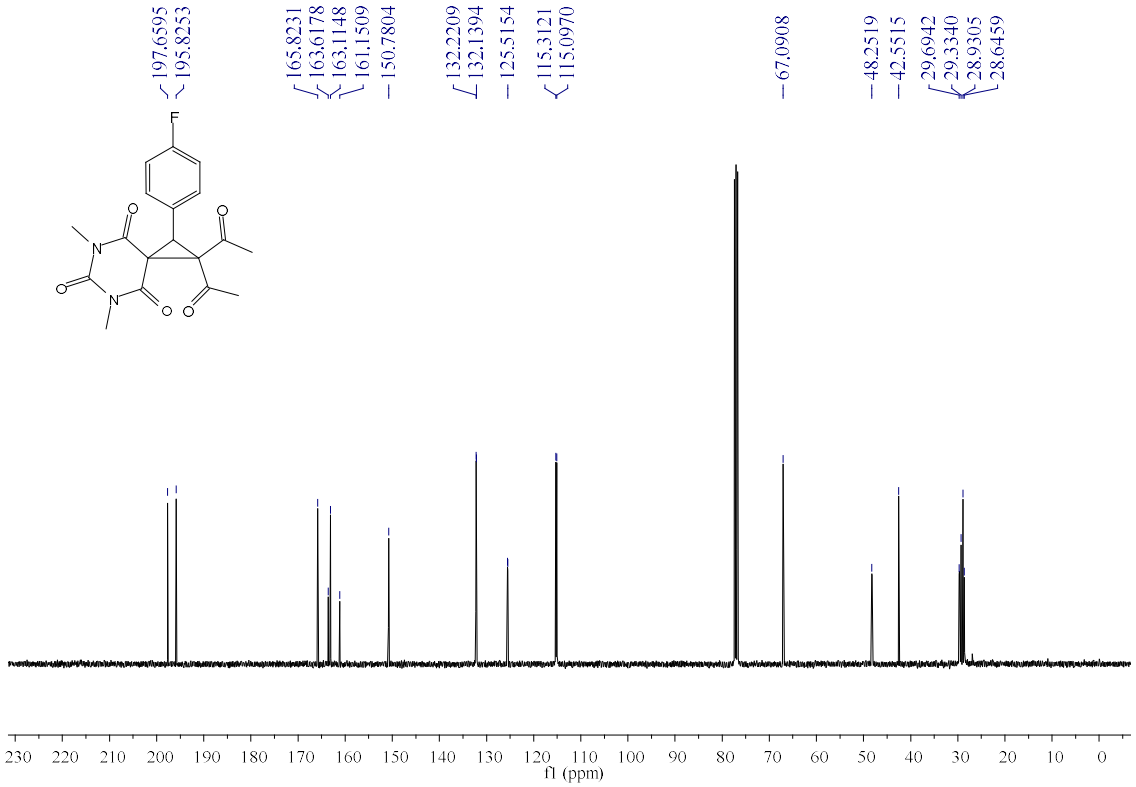

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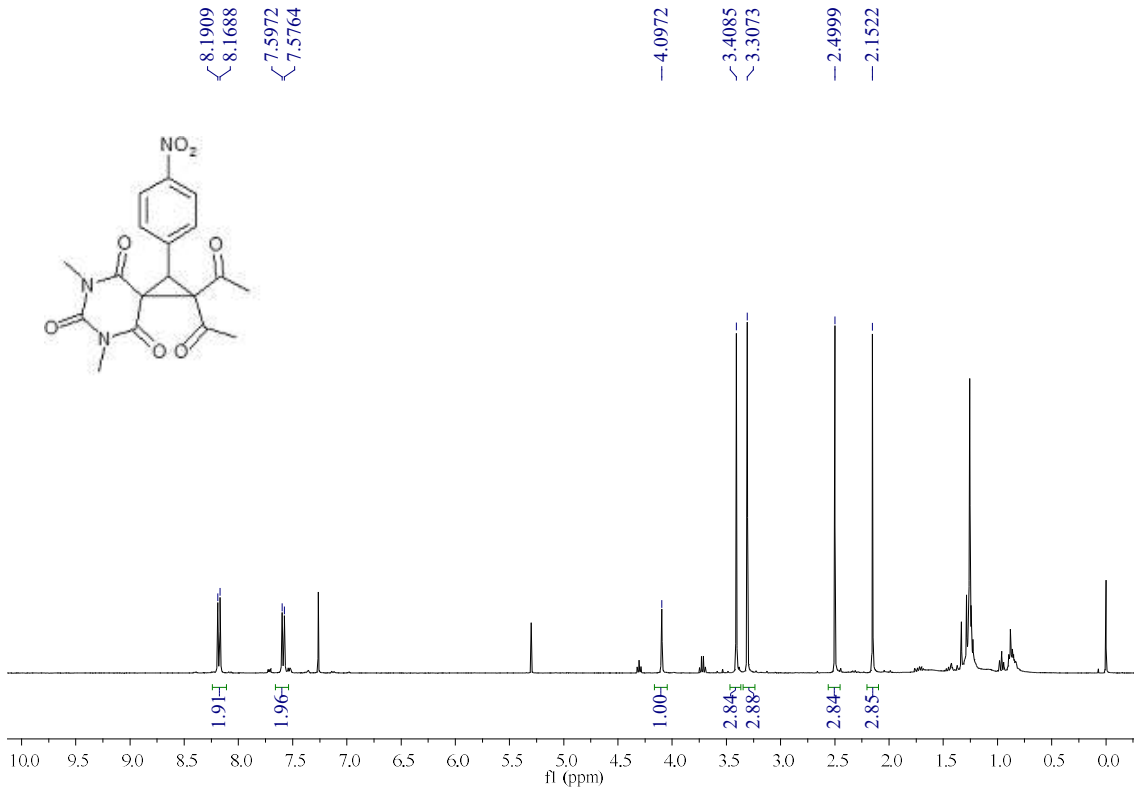

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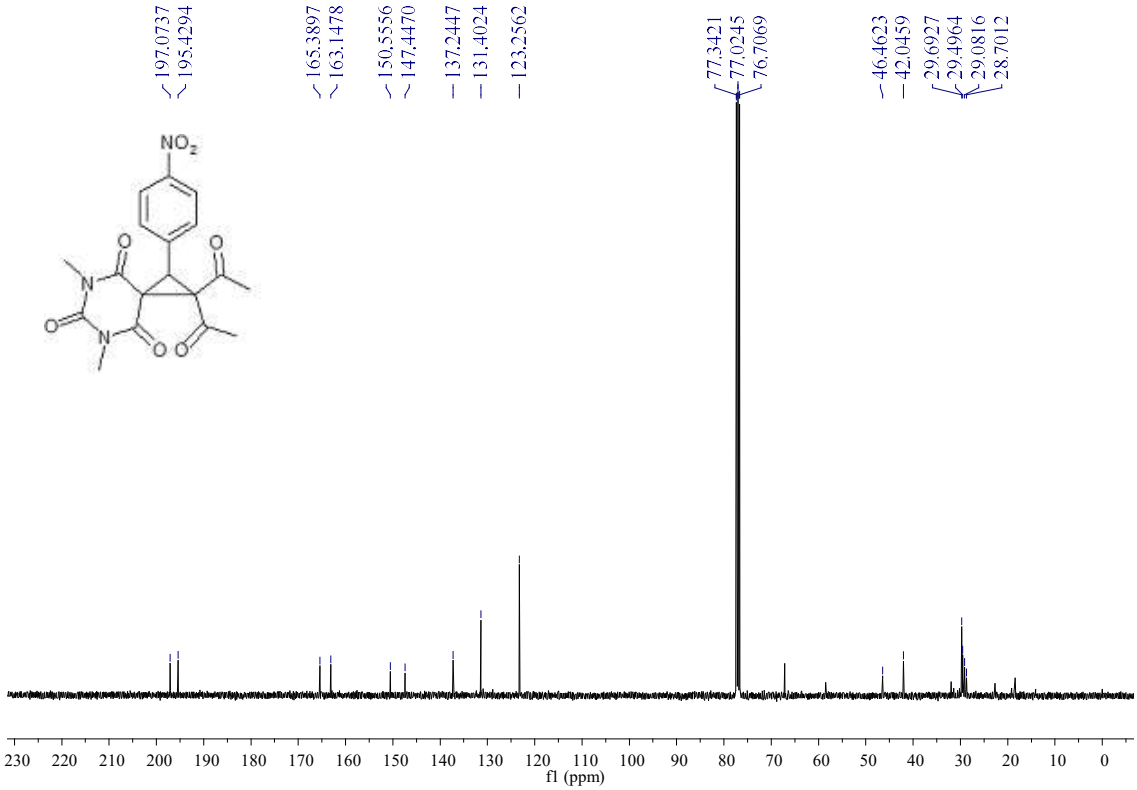

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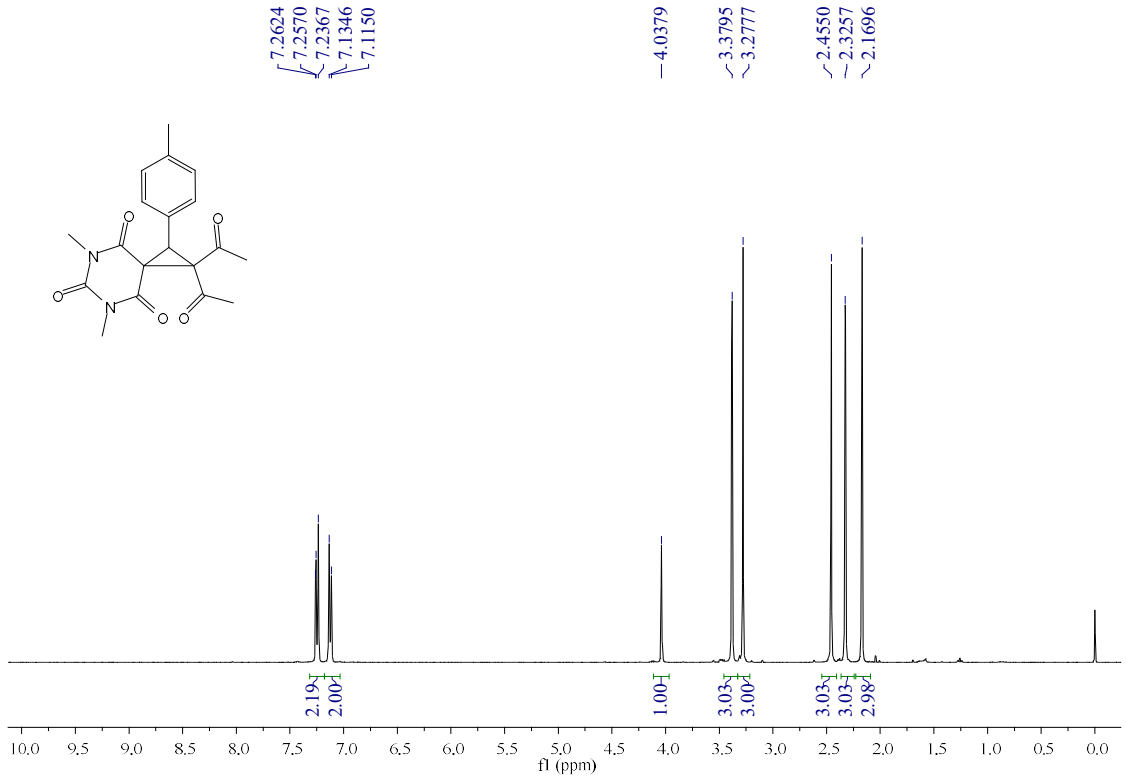

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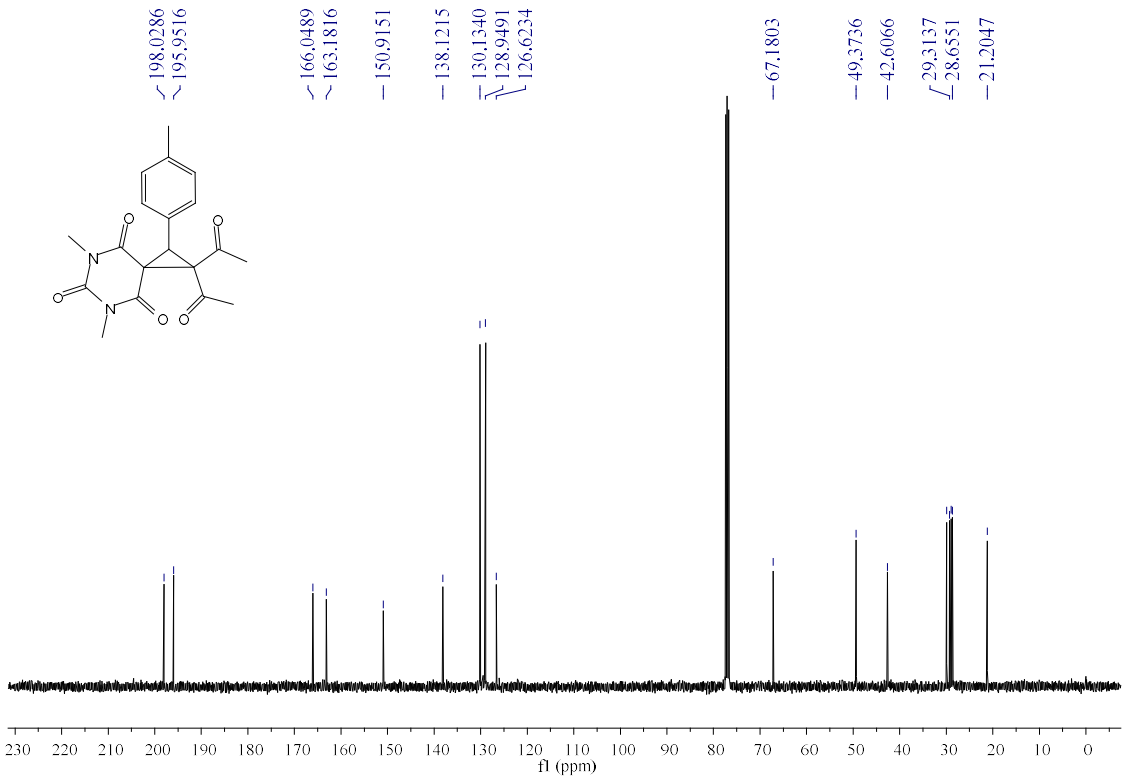

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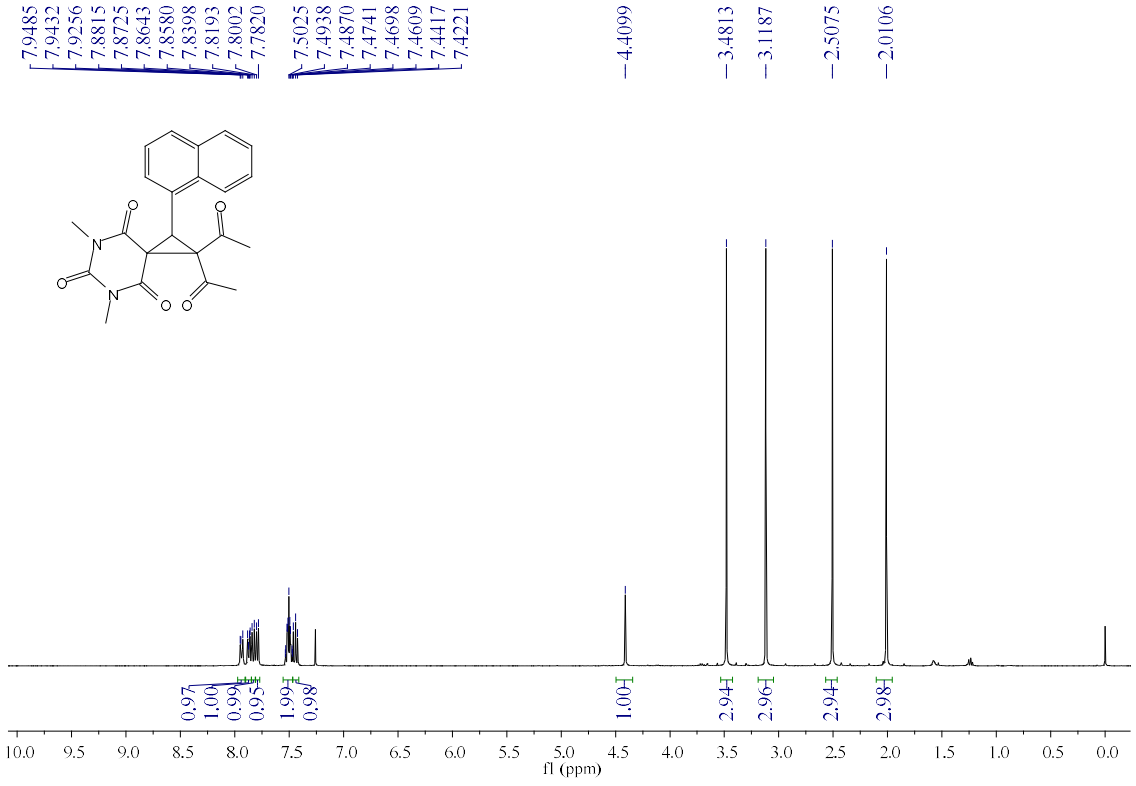

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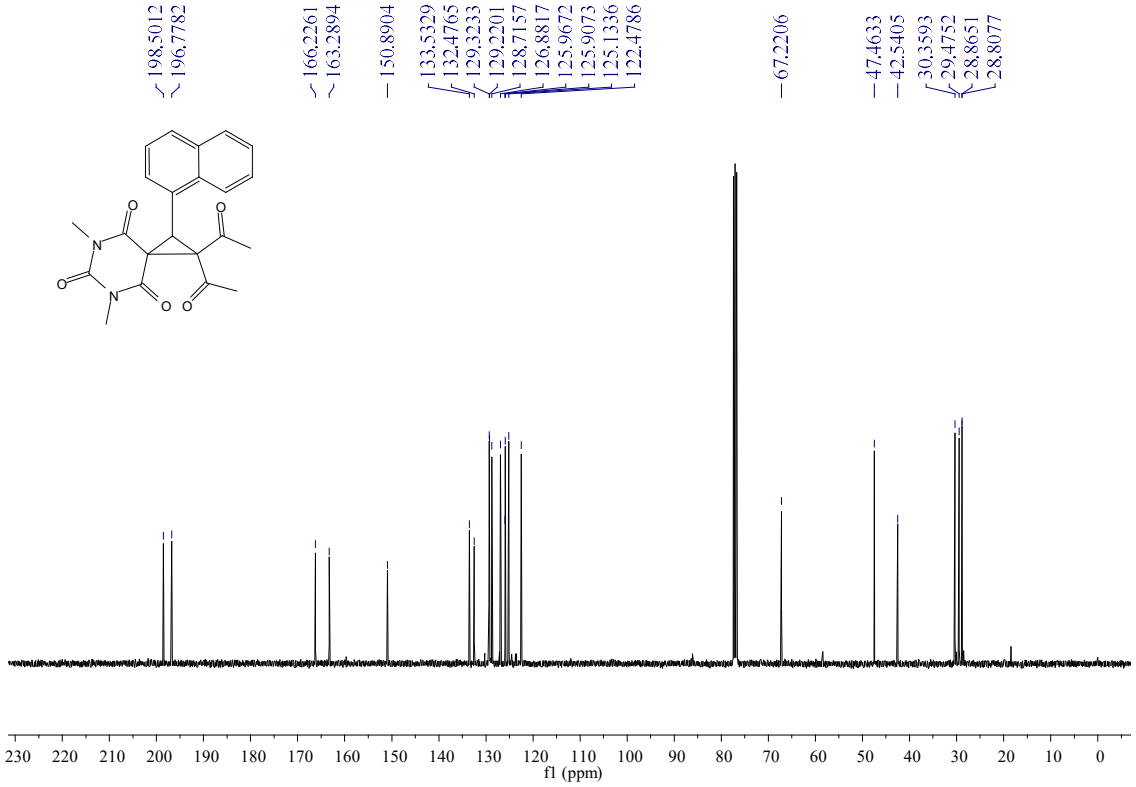

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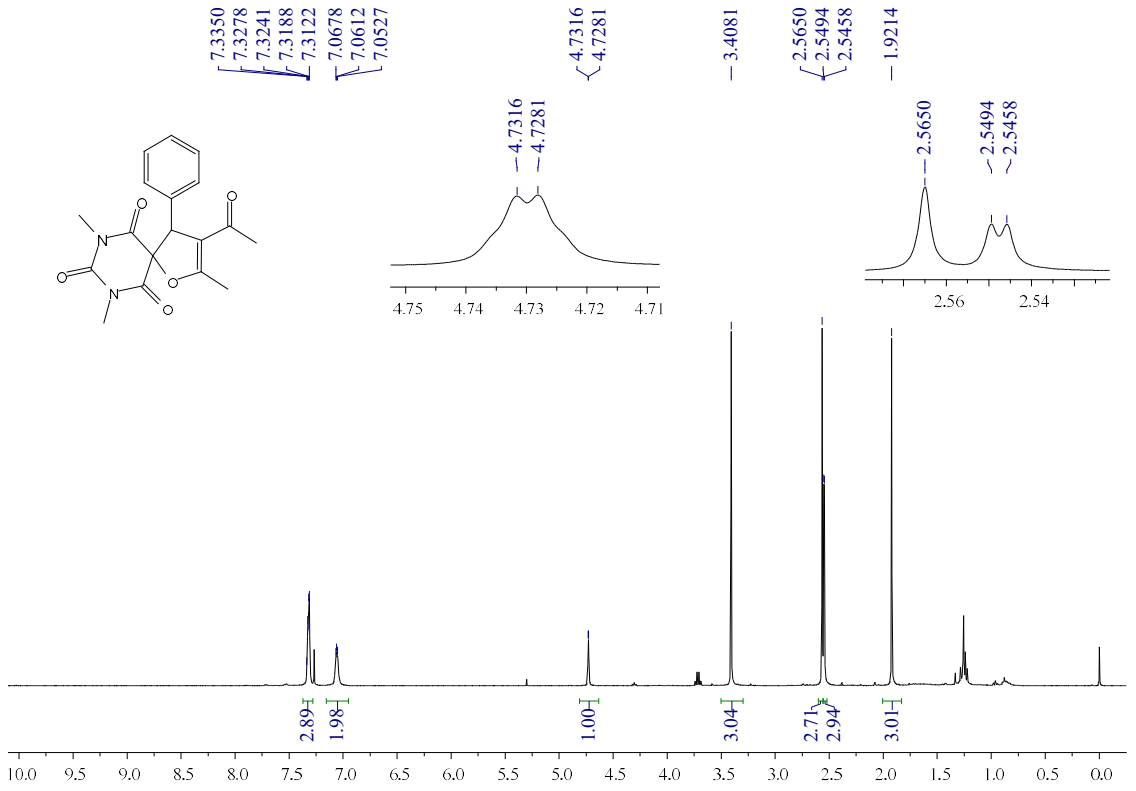
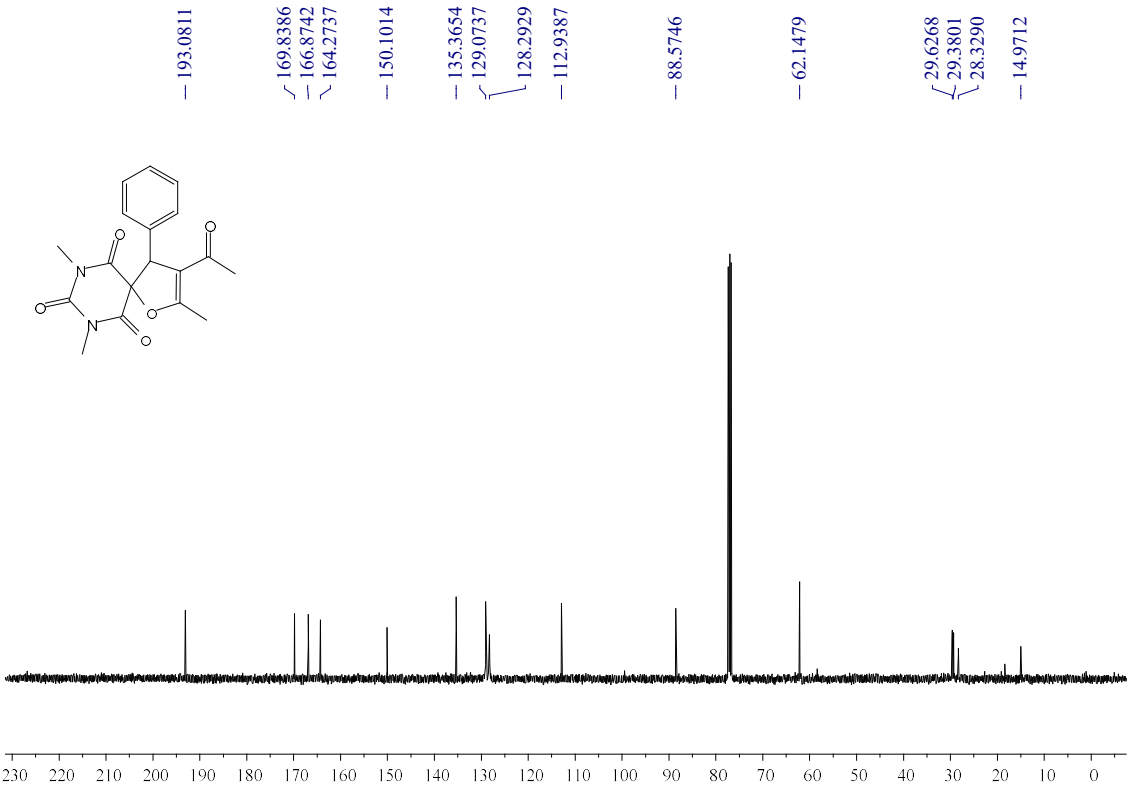
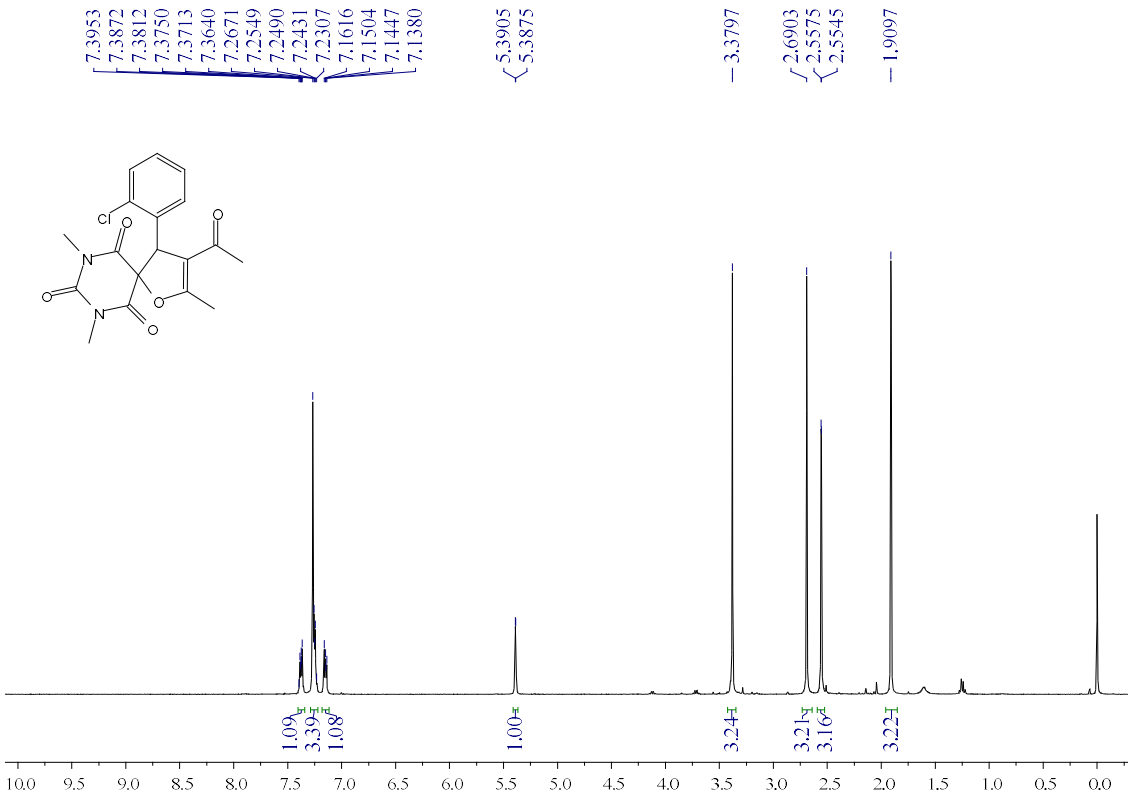


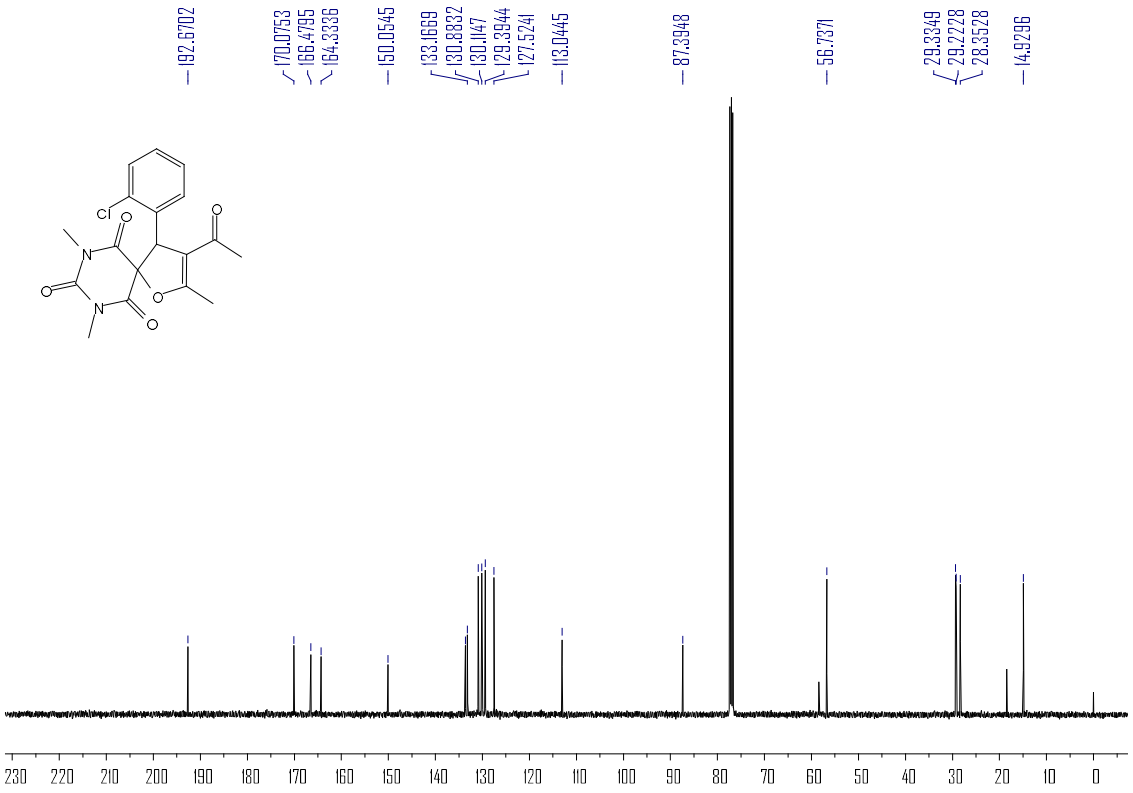
^{1}H NMR of compound **4a**



^{13}C NMR of compound **4a**



^{1}H NMR of compound **4b**



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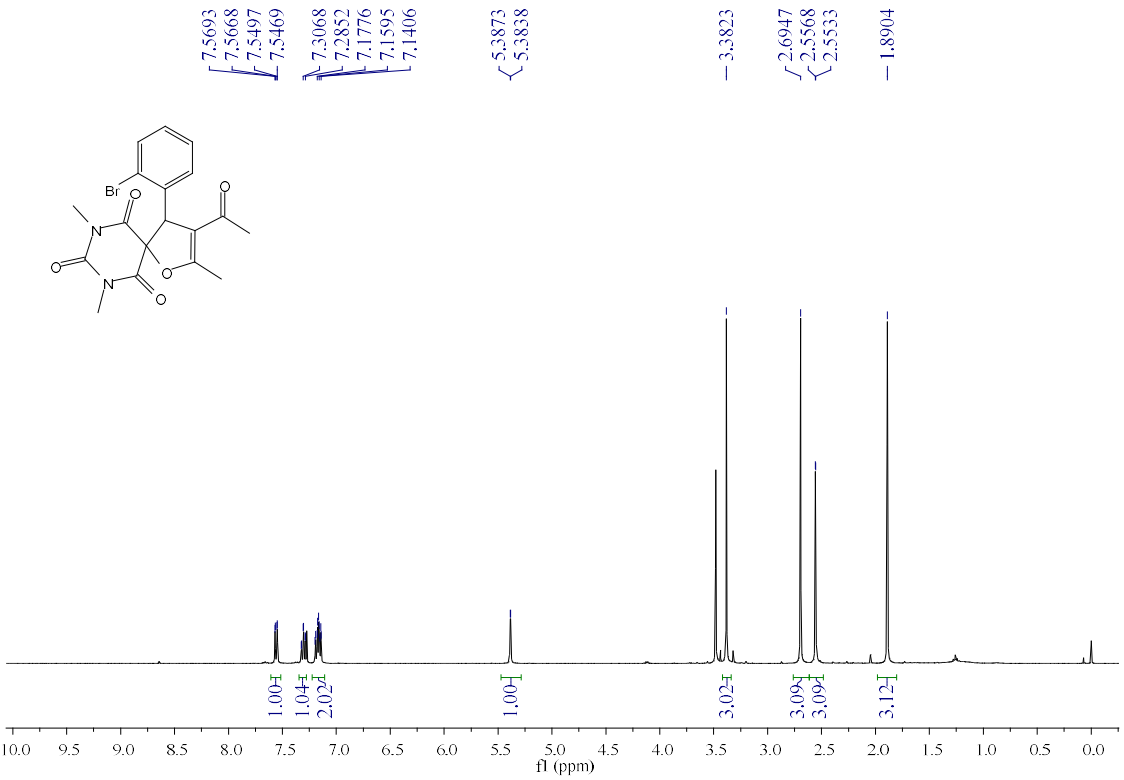
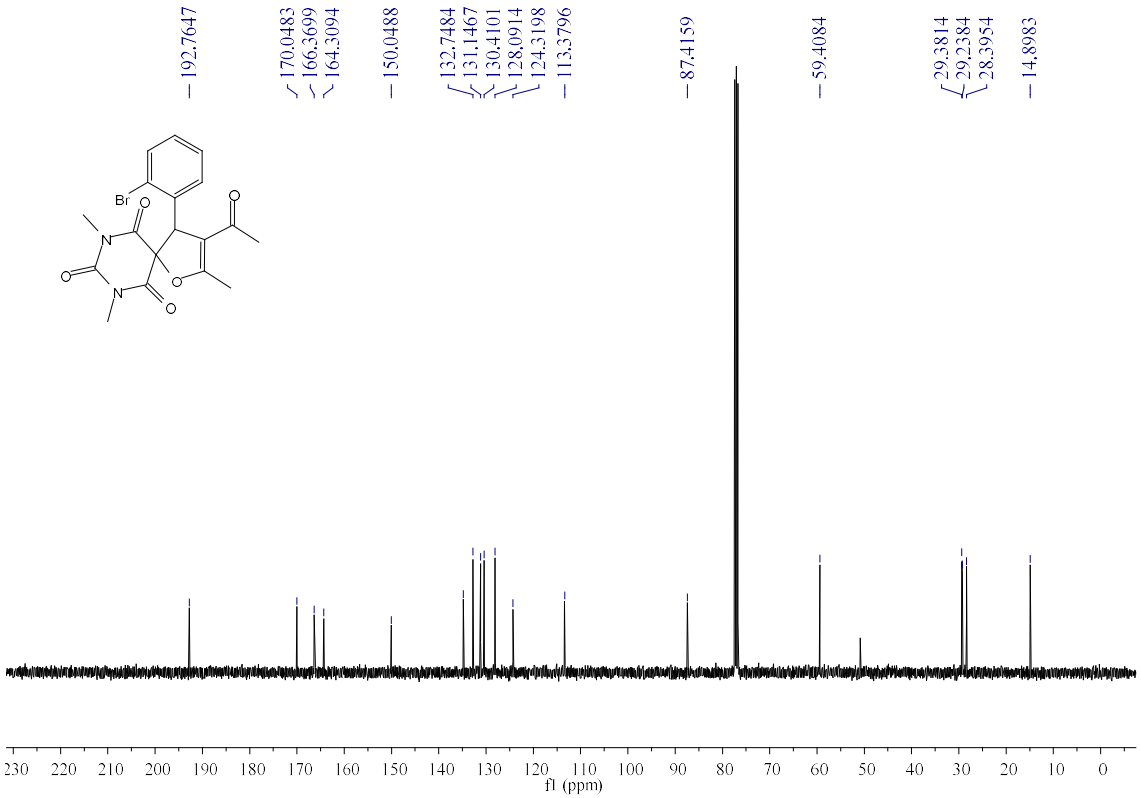


^{1}H NMR of compound **4c**



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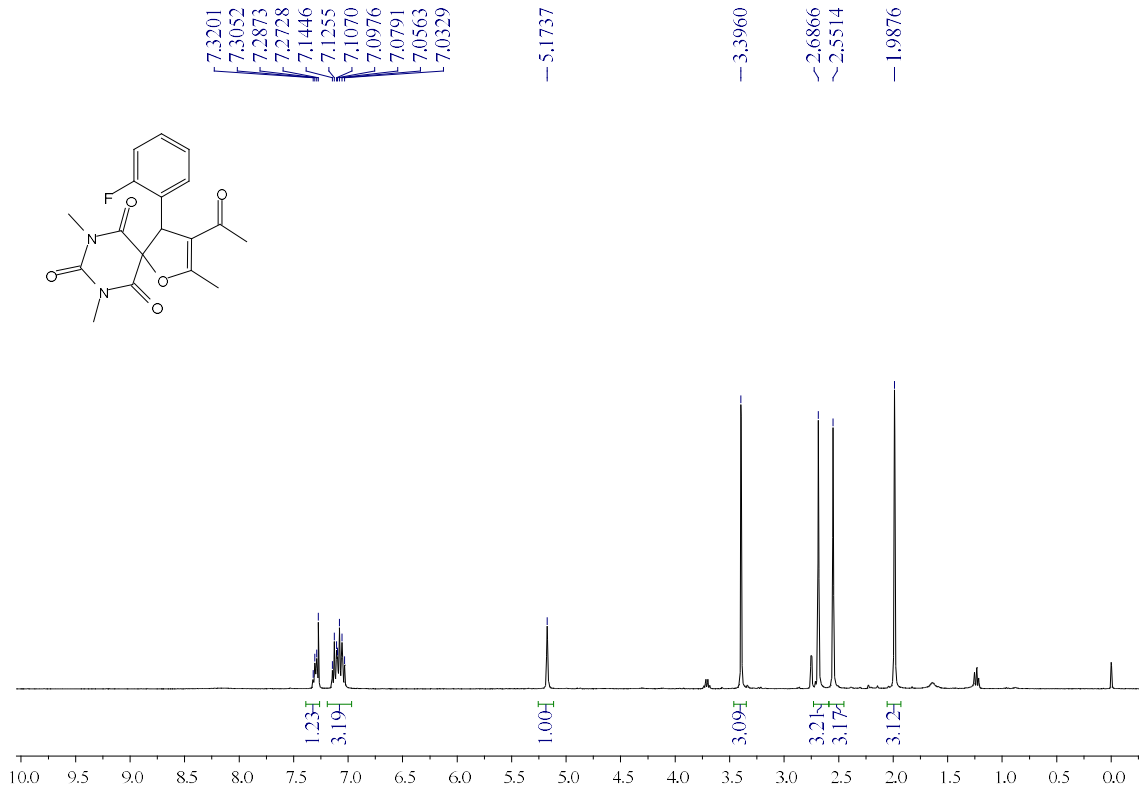

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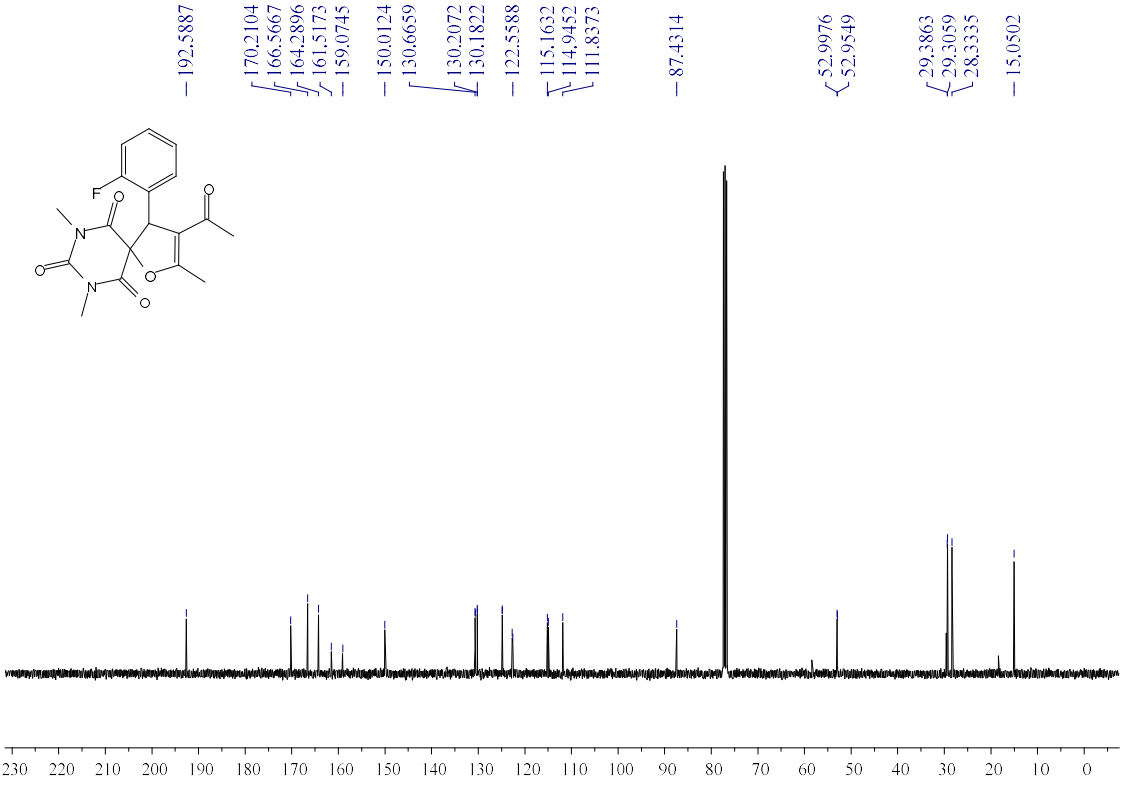

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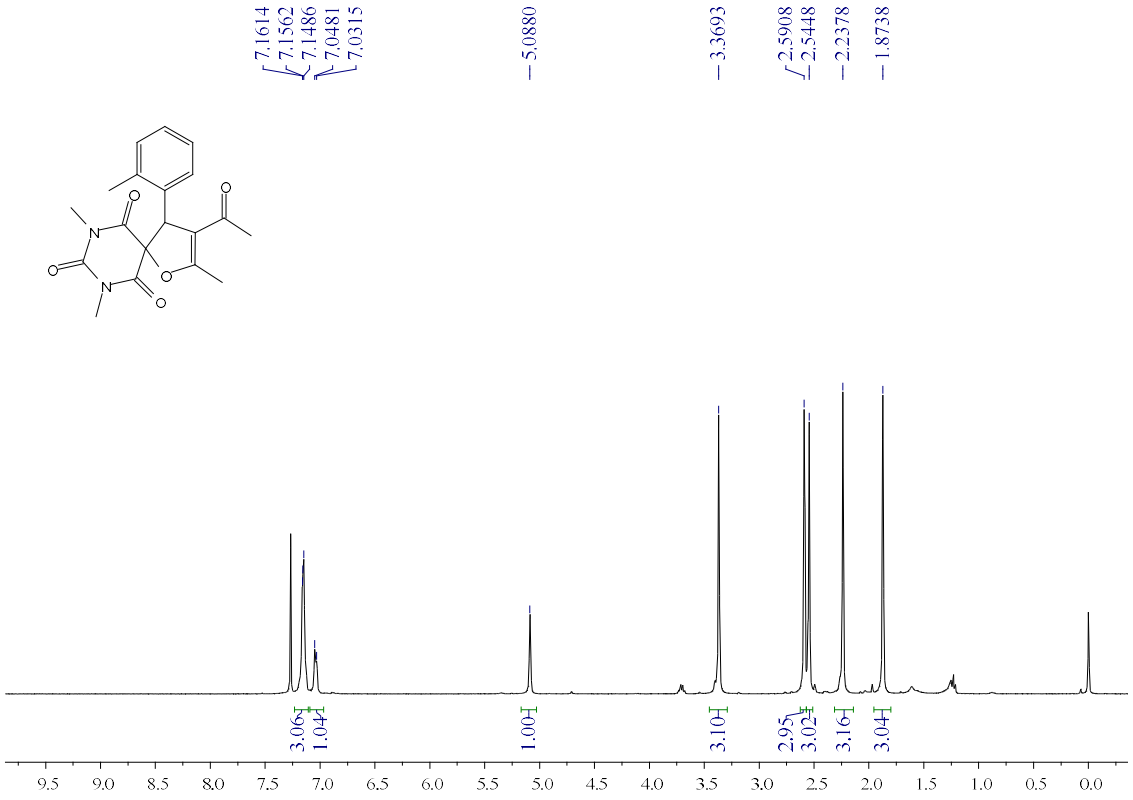

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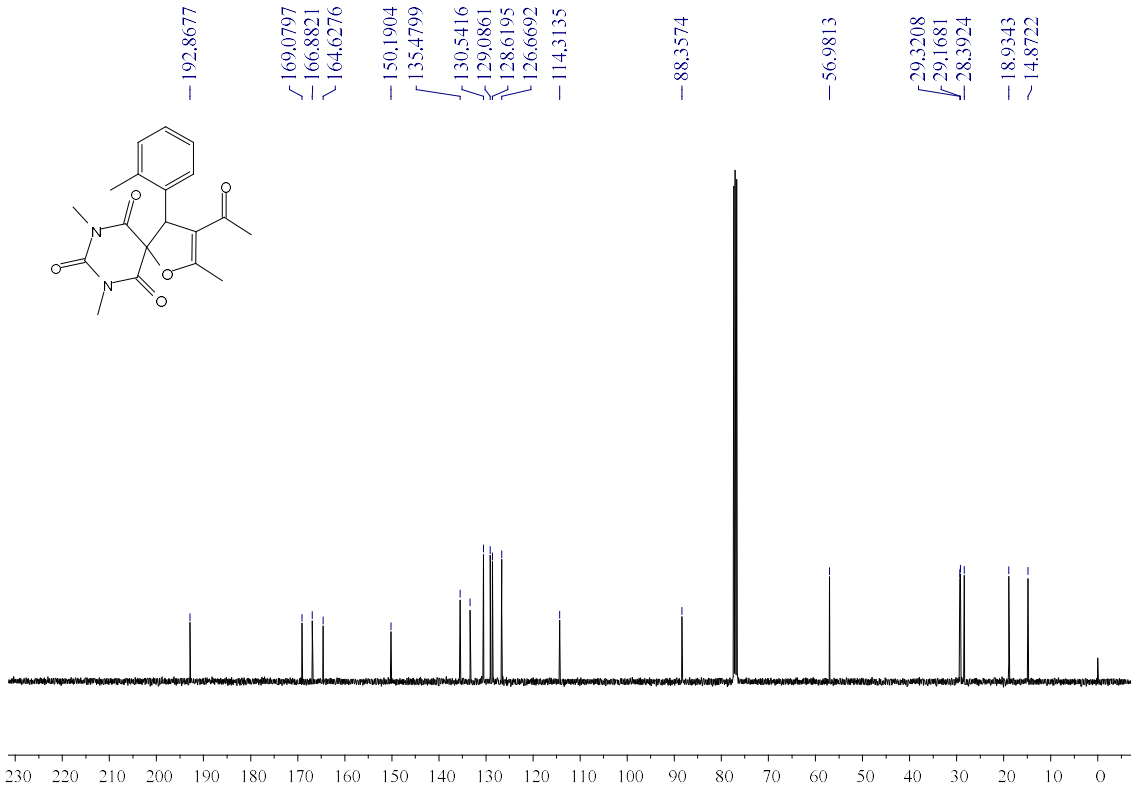

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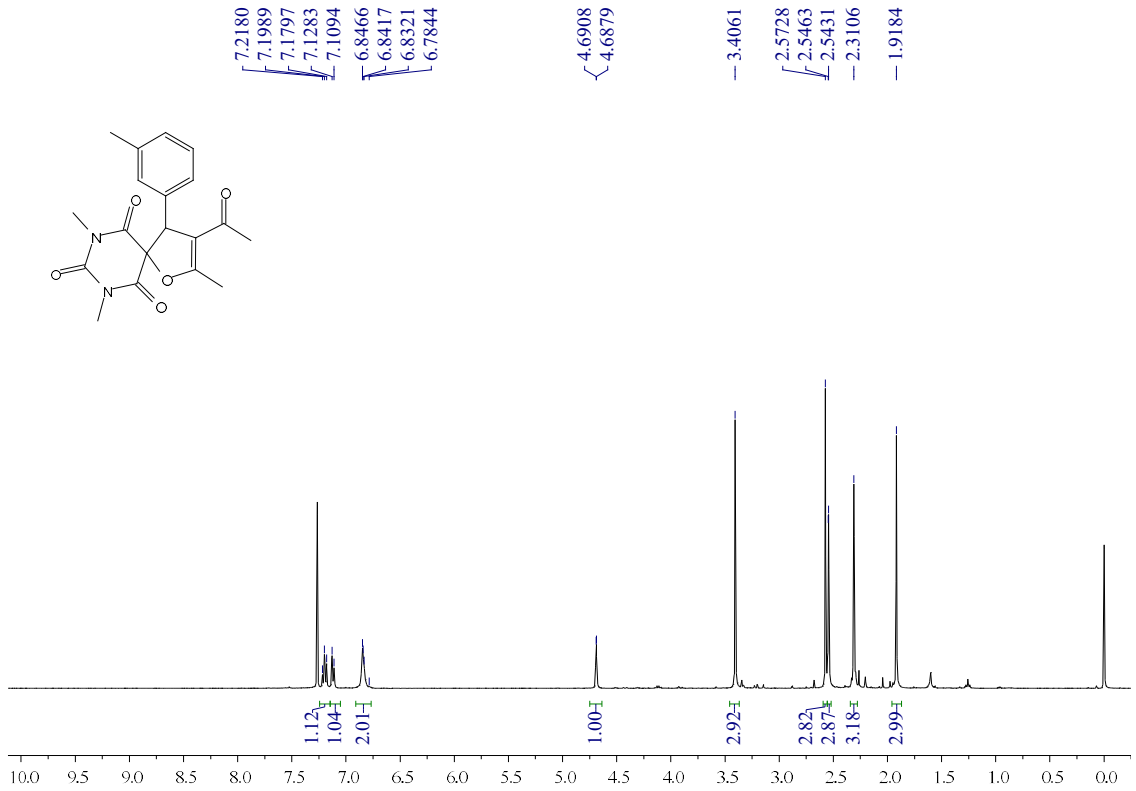

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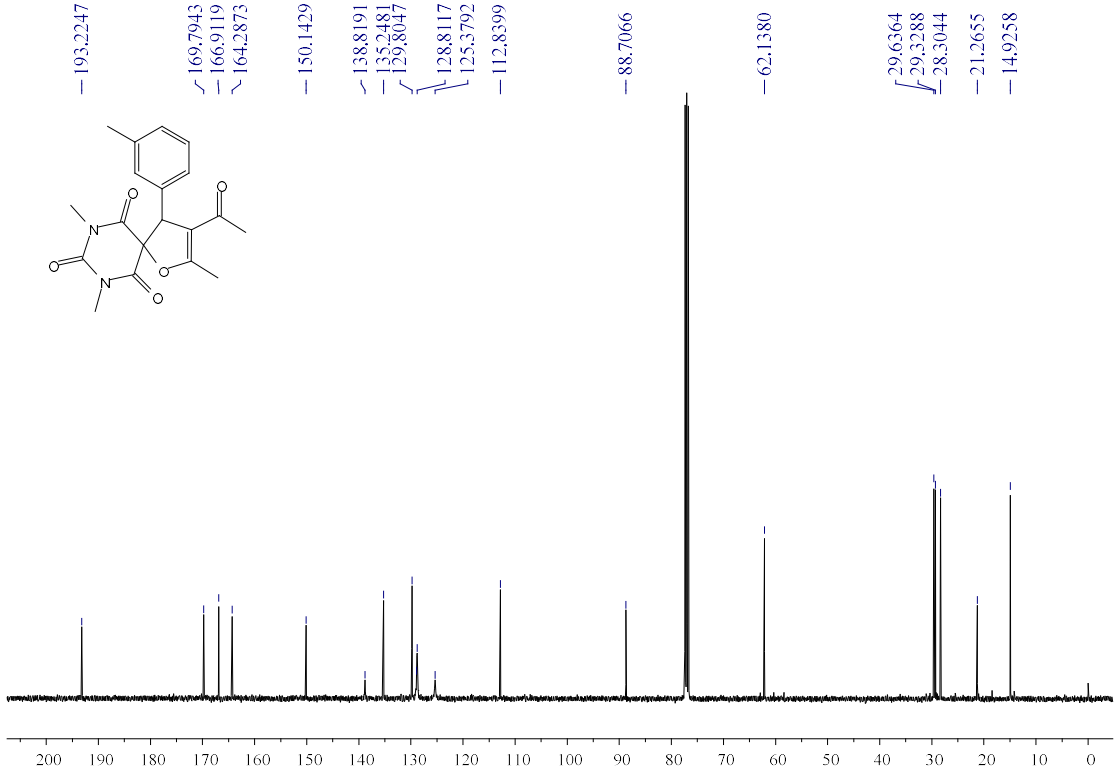

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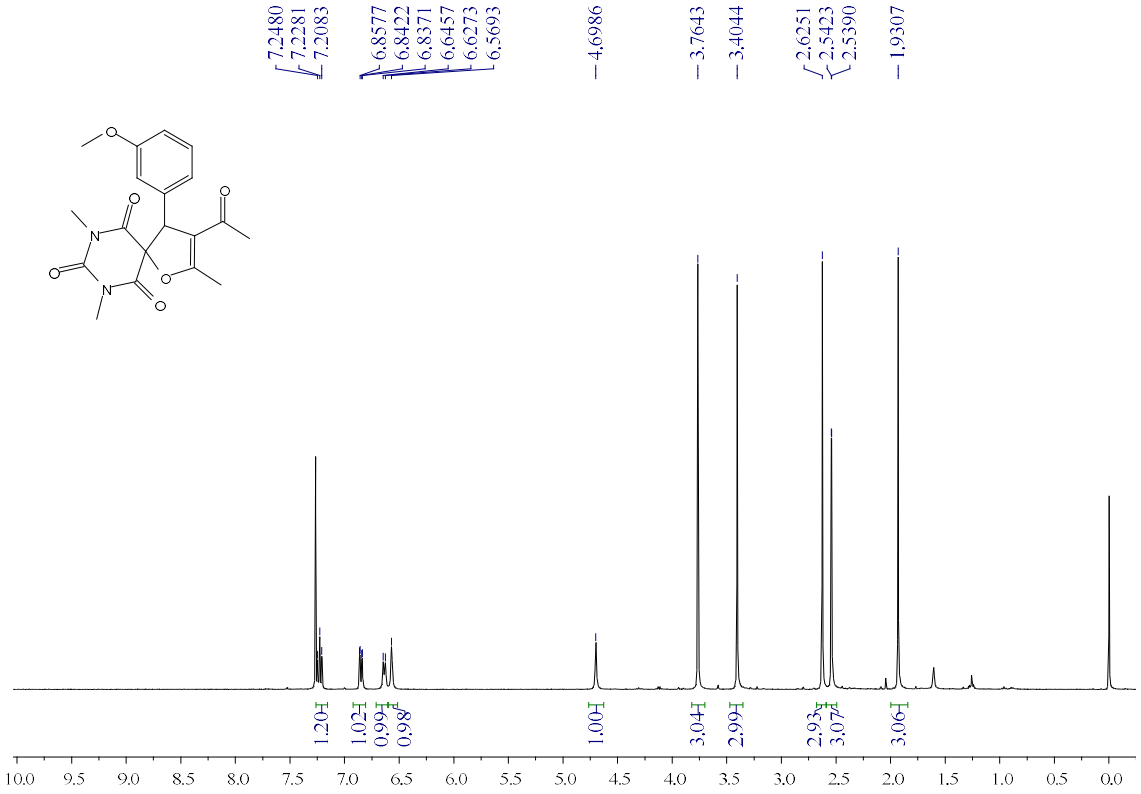
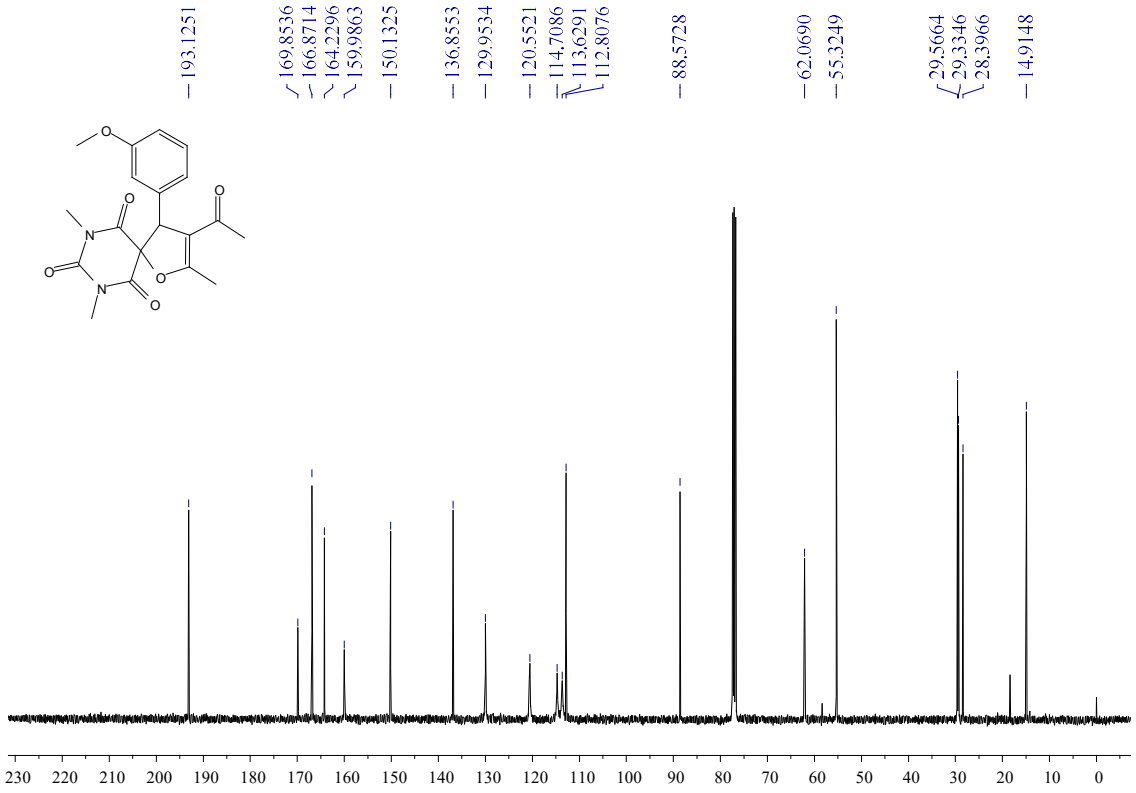


^{1}H NMR of compound **4g**



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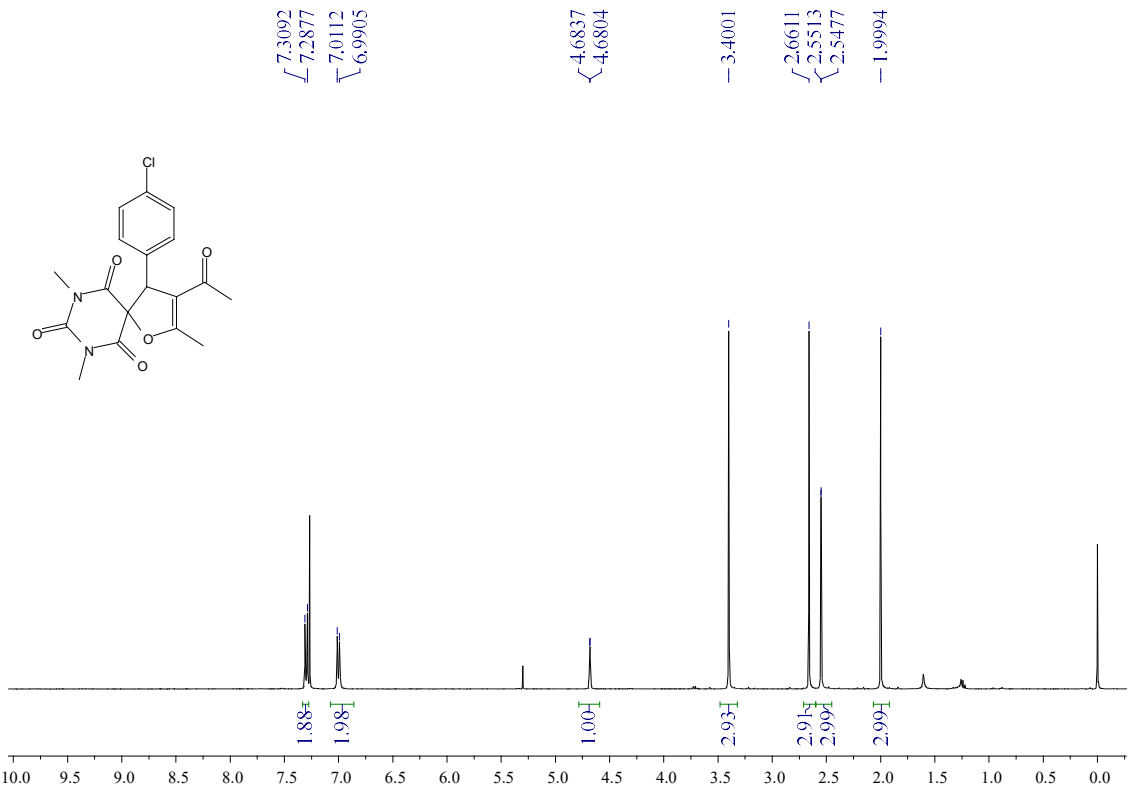
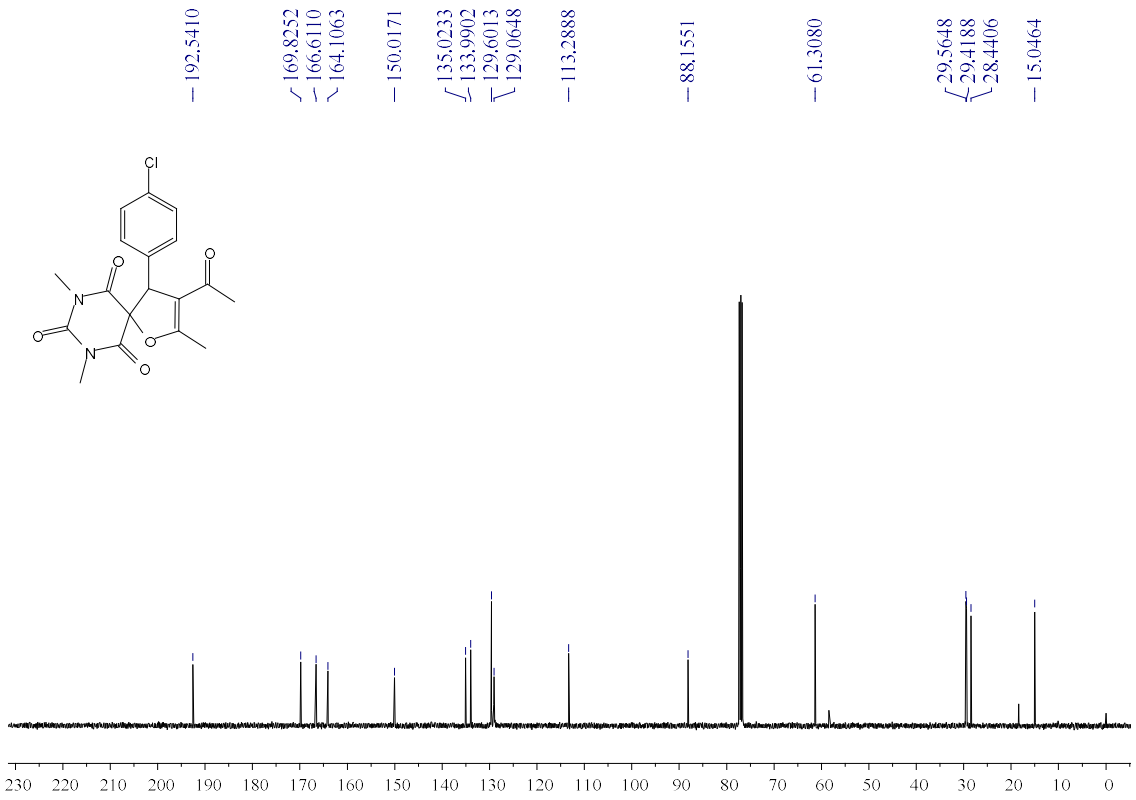
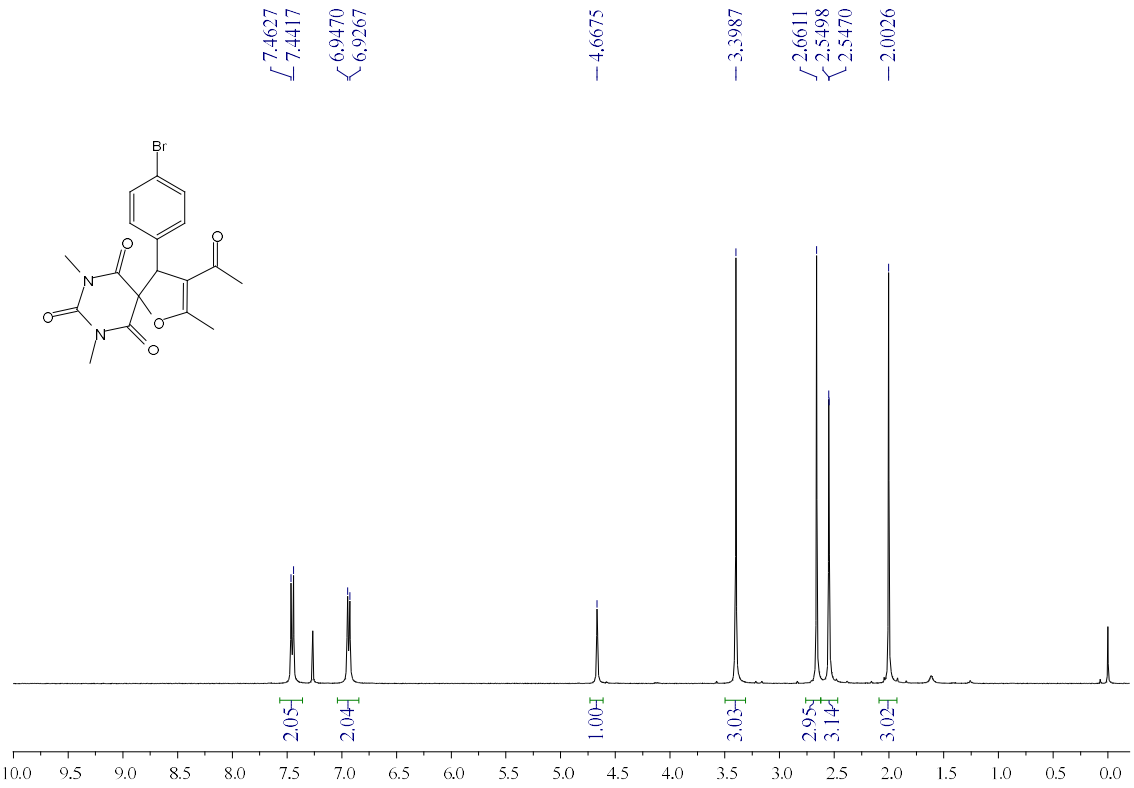


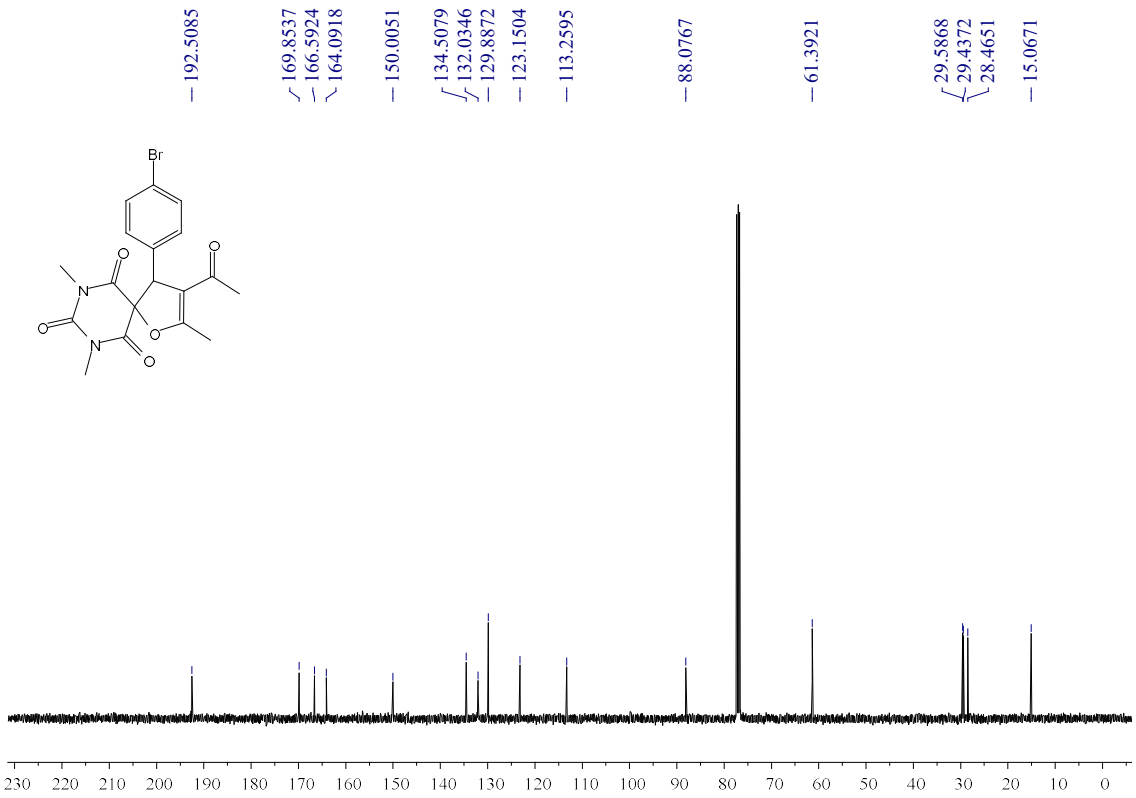
^{1}H NMR of compound **4h**



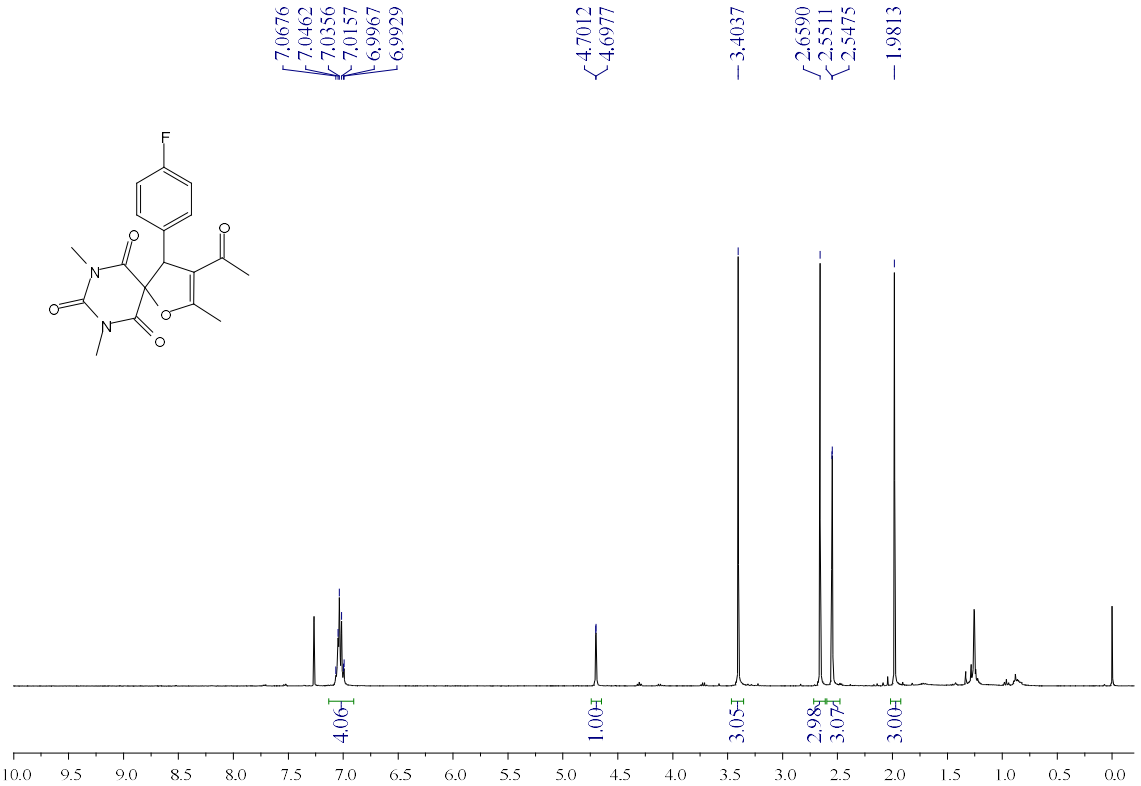
^{13}C NMR of compound **4h**



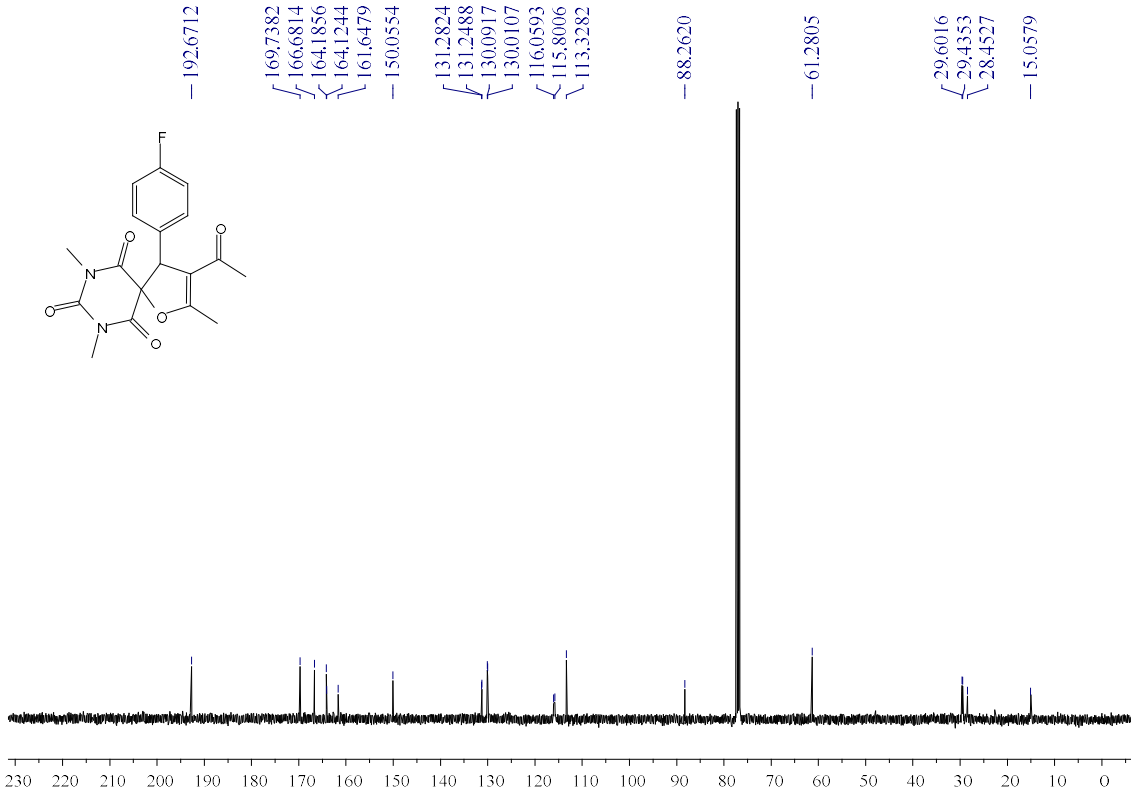
^{1}H NMR of compound **4i**



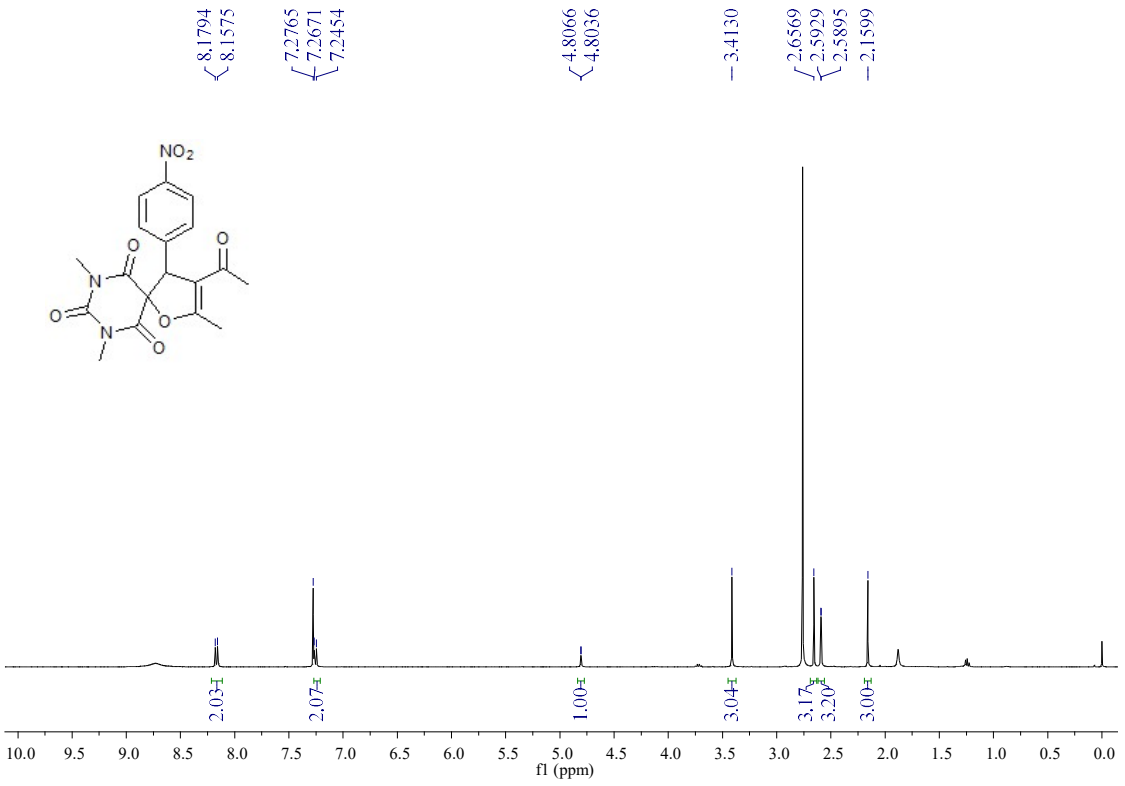
^{13}C NMR of compound **4i**



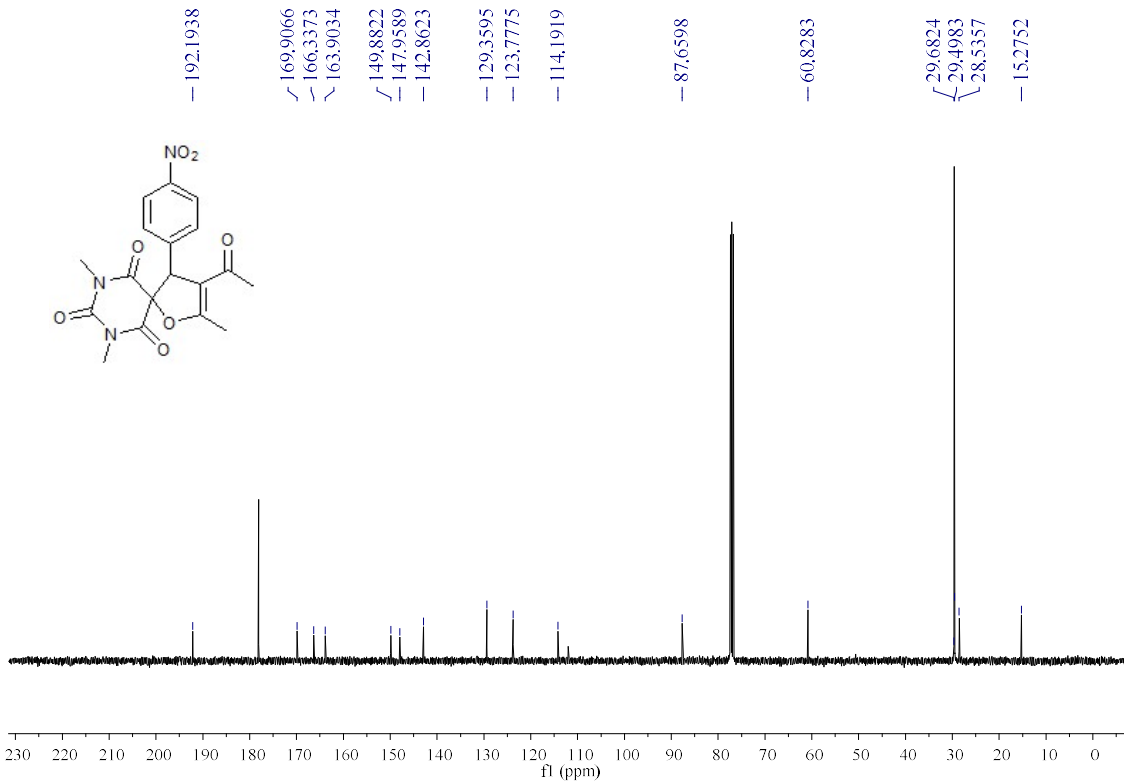
^{1}H NMR of compound **4j**



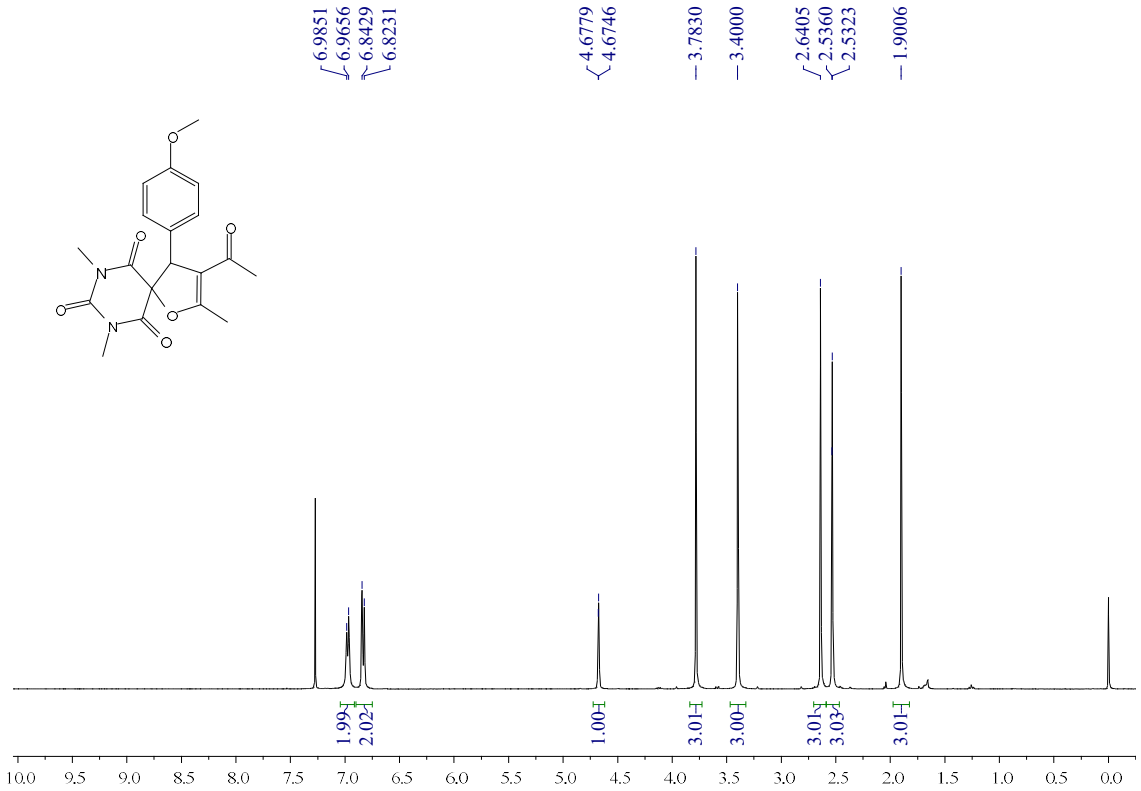
^{13}C NMR of compound **4j**



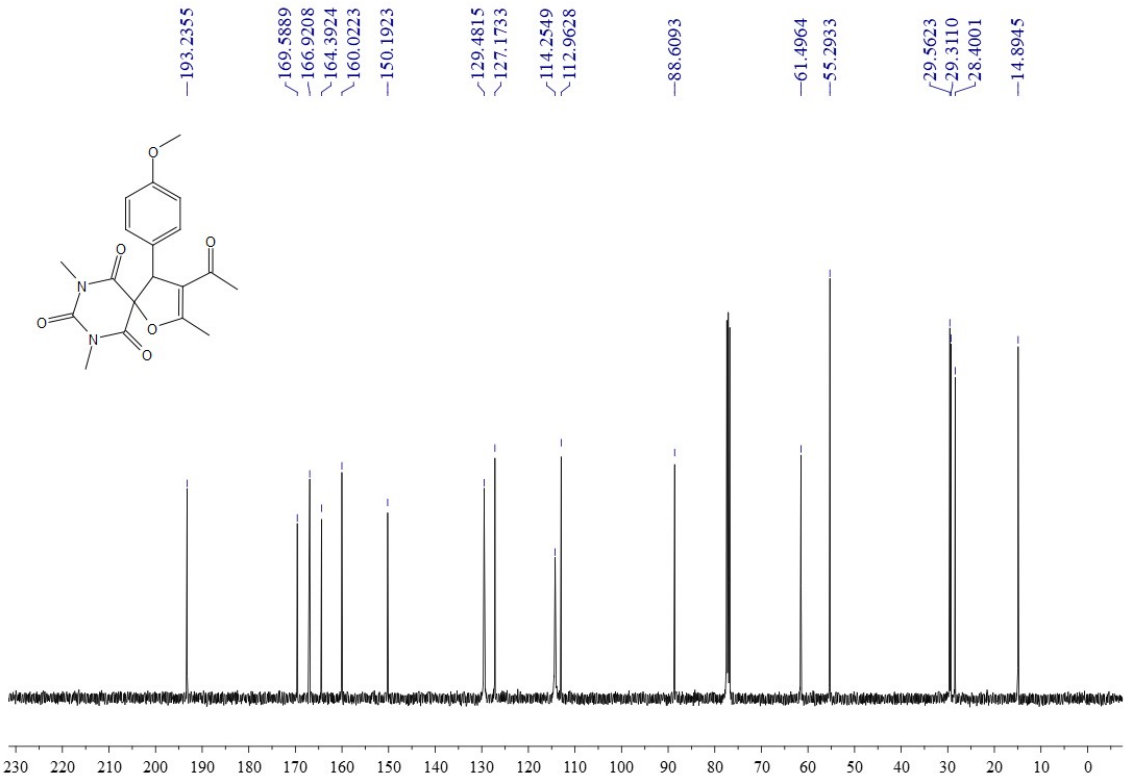
^{1}H NMR of compound **4k**



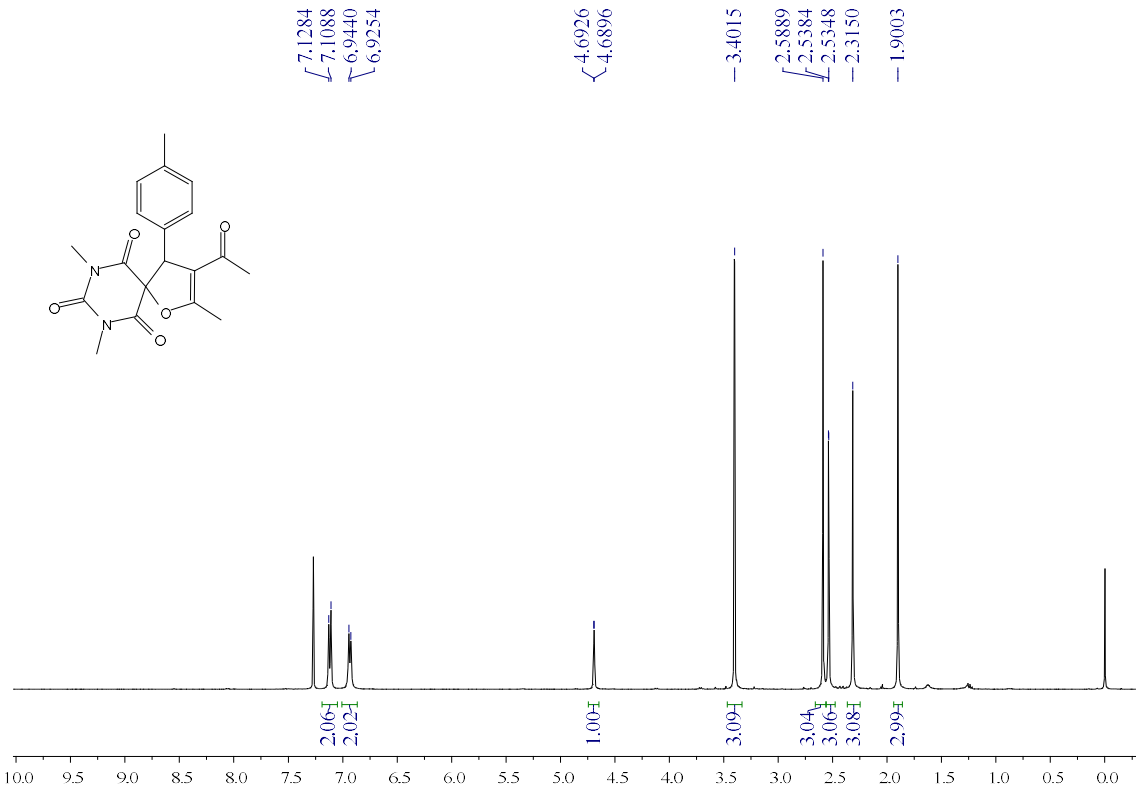
^{13}C NMR of compound **4k**



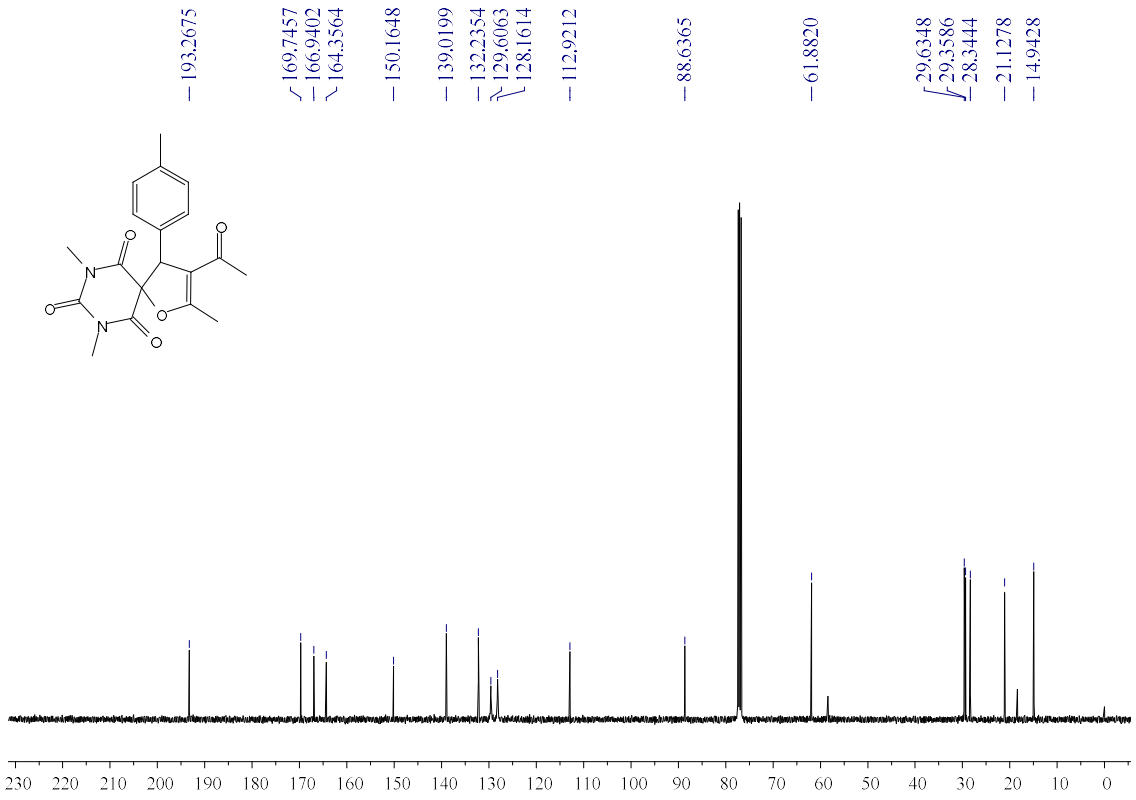
^{1}H NMR of compound **4l**



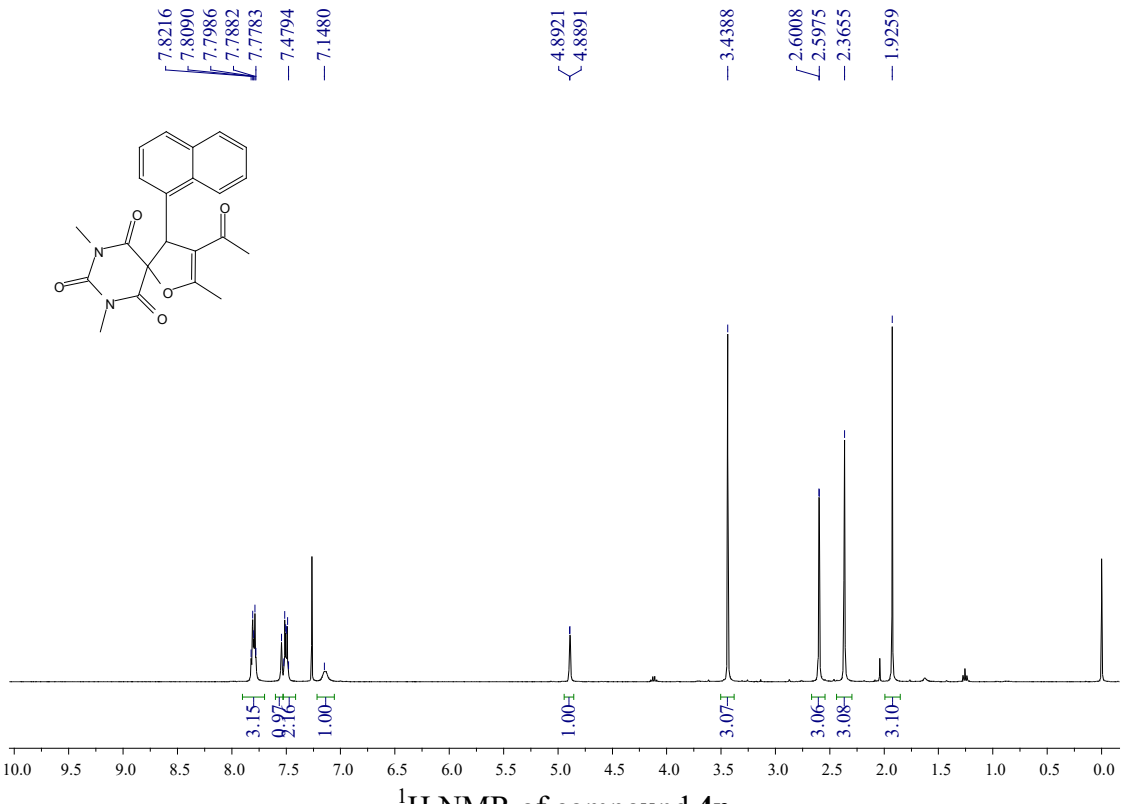
^{13}C NMR of compound **4l**



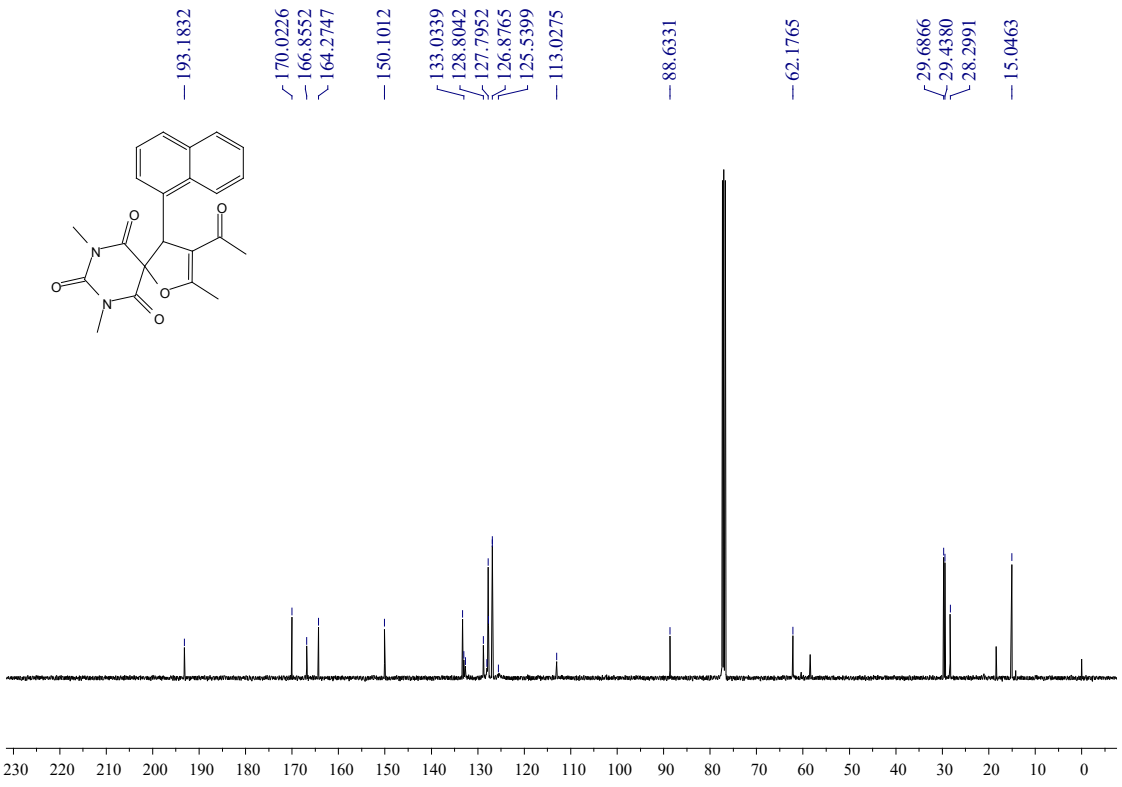
^{1}H NMR of compound **4m**



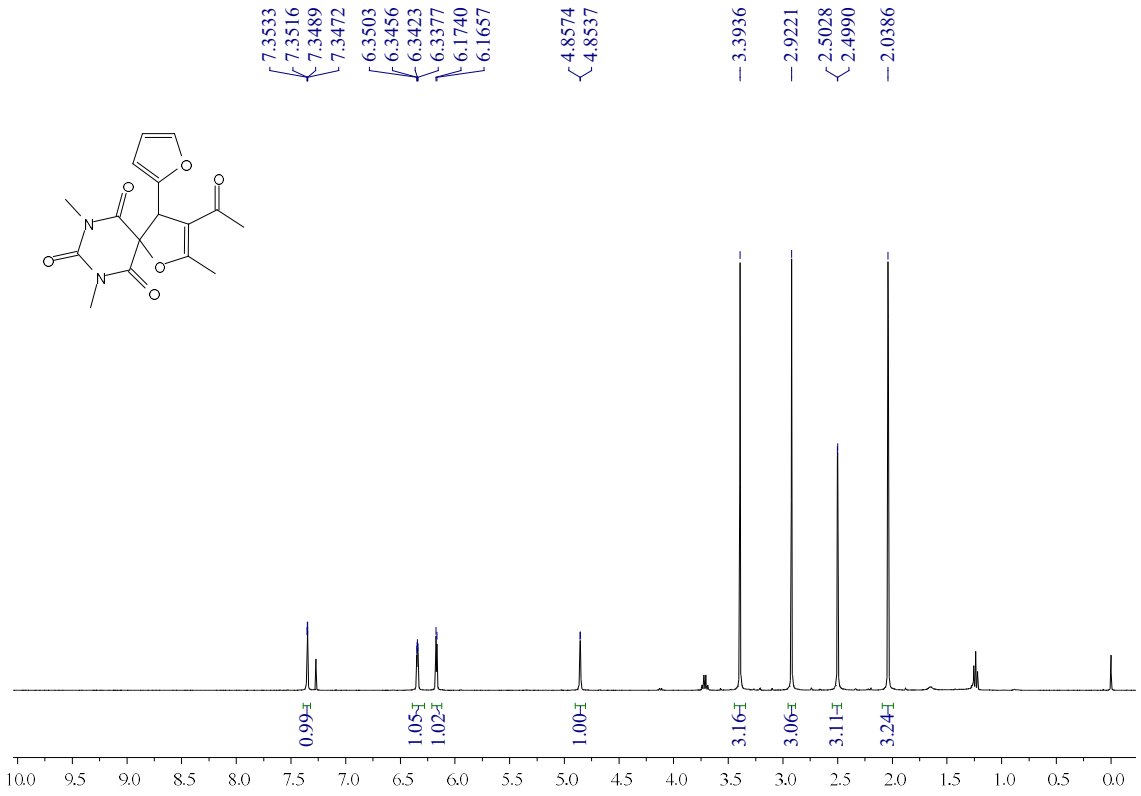
^{13}C NMR of compound **4m**



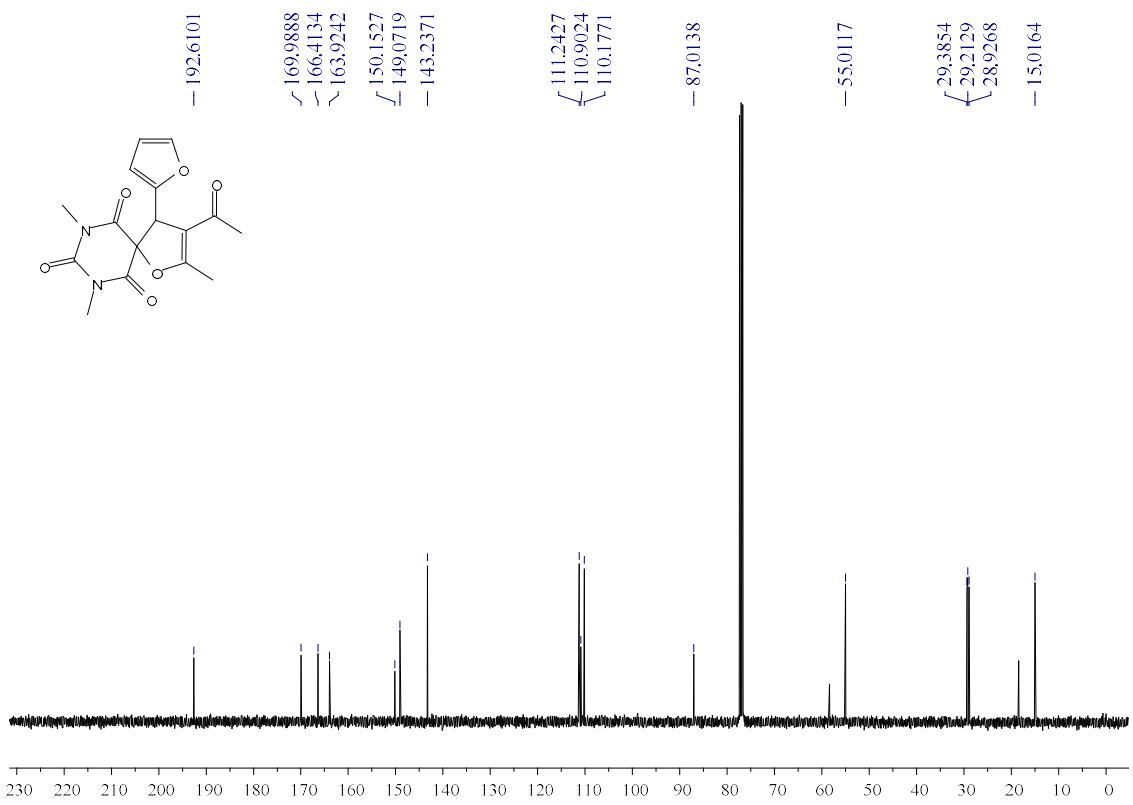
^{1}H NMR of compound **4n**



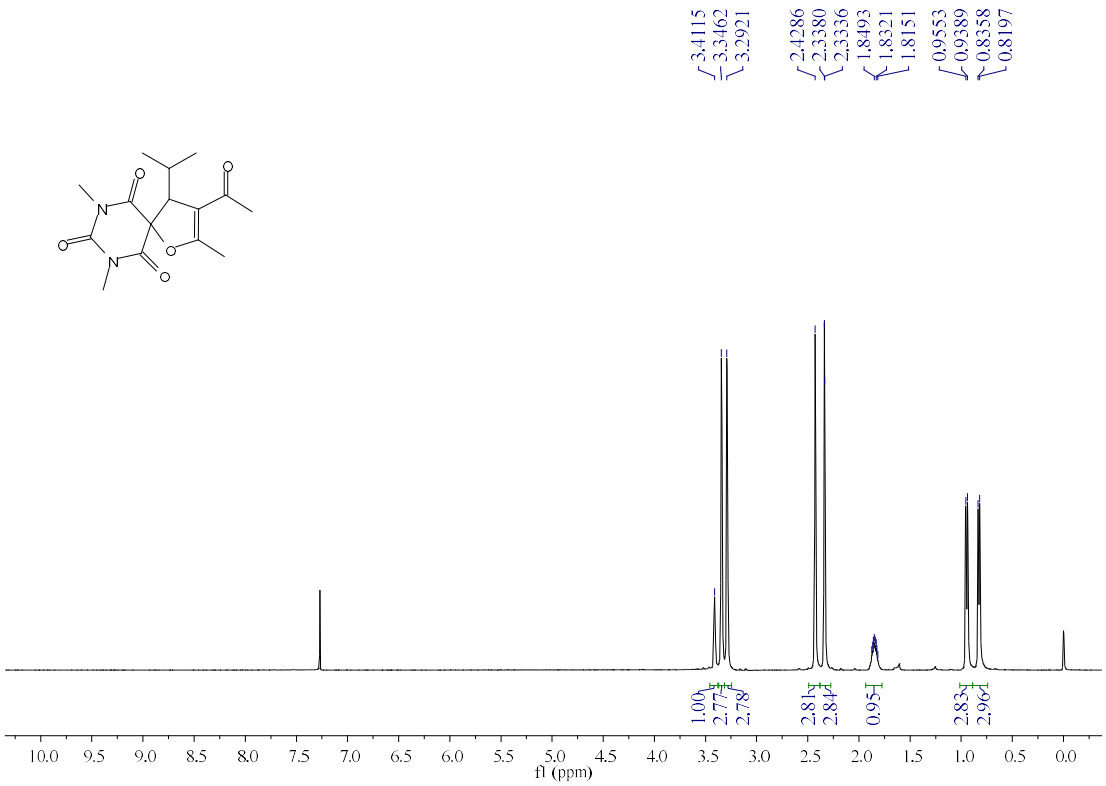
^{13}C NMR of compound **4n**



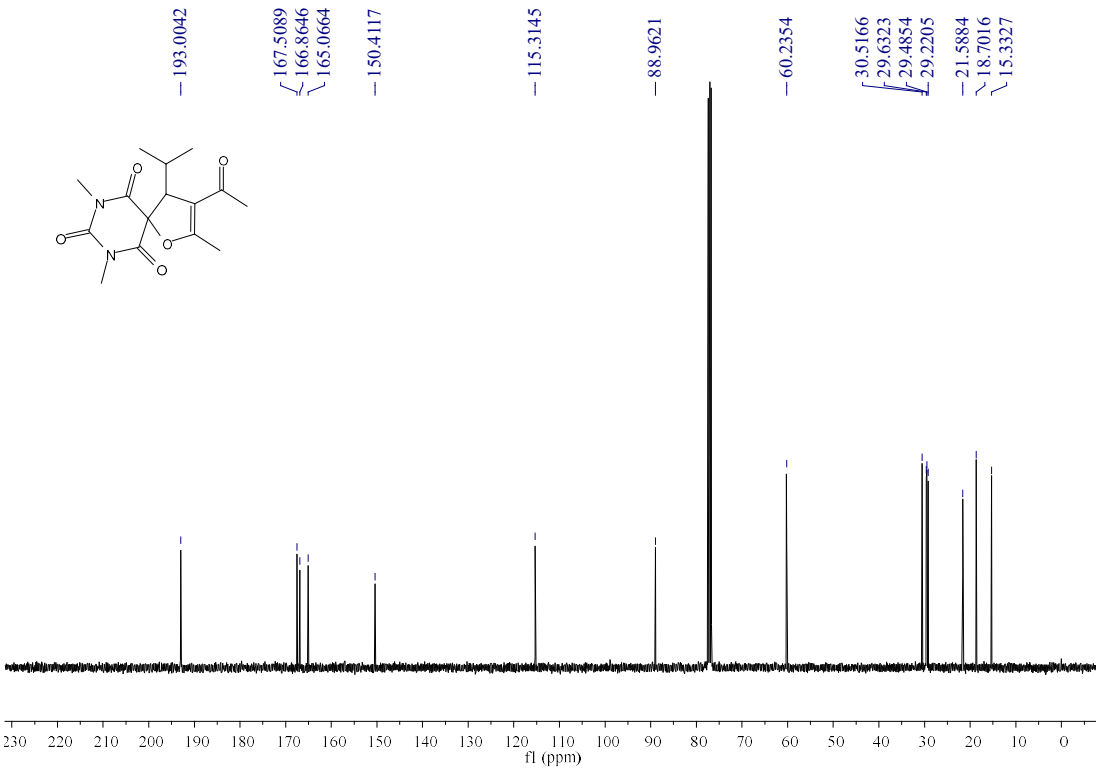
^{1}H NMR of compound **4o**



^{13}C NMR of compound **4o**



^{1}H NMR of compound **4p**



^{13}C NMR of compound **4p**