Selective Divergent Radical Cyclization of 1,6-Dienes with Alkyl Nitriles

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Supporting Information

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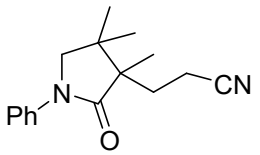
(A) Typical experimental procedure for the radical cyclization

To a Schlenk tube were added 1,6-dienes **1** (0.2 mmol), alkyl nitriles **2** (1.0 mL), $Sc(OTf)_3$ (20 mol%), and Ag_2CO_3 (2.0 equiv). Then the tube was stirred at 130 °C sealed in air for the indicated time until complete consumption of starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the mixture was extracted three times with EtOAc. The organic layer was dried over Na_2SO_4, filtration and evaporation of the solvent. The mixture was purified by flash column chromatography over silica gel (hexane/ethyl acetate = 5:1) to afford the desired products **3** or **5**.

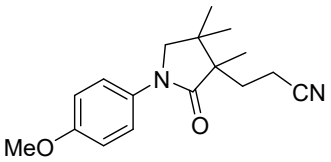
To a Schlenk tube were added 1,6-dienes **1** (0.2 mmol), *α*-methyl-nitriles **2** (1.0 mL), $Sc(OTf)_3$ (20 mol%), Ag_2CO_3 (2.0 equiv), AcONa (2.0 equiv), and H_2O (4.0 equiv). Then the tube was stirred at 130 °C sealed in air for the indicated time until complete consumption of starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the mixture was extracted three times with EtOAc. The organic layer was dried over Na_2SO_4, filtration and evaporation of the solvent. The mixture was purified by flash column chromatography over silica gel (hexane/ethyl acetate = 5:1) to afford the desired products **6**.

(B) Analytical data

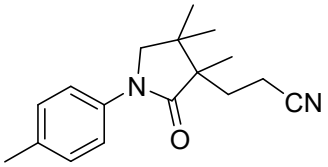


3-(3,4,4-Trimethyl-2-oxo-1-phenylpyrrolidin-3-yl)propanenitrile (3a), yellow oil (0.0410 g, 80% yield); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.16 (t,

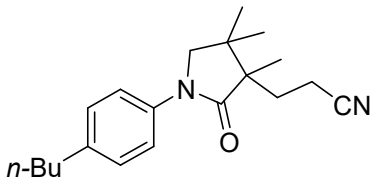
J = 7.5 Hz, 1H), 3.55-3.49 (m, 2H), 2.78-2.71 (m, 1H), 2.56-2.49 (m, 1H), 2.15-2.00 (m, 2H), 1.12 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.6, 139.4, 128.9, 124.7, 120.3, 119.7, 58.7, 49.3, 38.9, 29.2, 23.3, 22.2, 15.3, 12.7; HRMS *m/z* (ESI) calcd for $C_{16}H_{21}N_2O$ ($[M+H]^+$) 257.1648, found 257.1652.



3-(1-(4-Methoxyphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3b), yellow oil (0.0486 g, 85% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.47 (d, *J* = 9.5 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.80 (s, 3H), 3.51-3.44 (m, 2H), 2.79-2.72 (m, 1H), 2.55-2.49 (m, 1H), 2.11-2.07 (m, 2H), 1.11 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 177.4, 155.3, 138.0, 120.5, 113.1, 111.6, 58.1, 54.8, 48.0, 38.0, 32.4, 23.0, 22.2, 14.2, 12.7; HRMS *m/z* (ESI) calcd for $C_{17}H_{23}N_2O_2$ ($[M+H]^+$) 287.1754, found 287.1758.

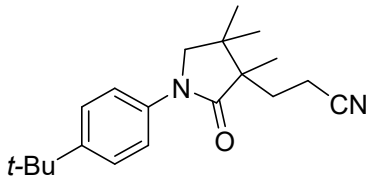


3-(3,4,4-Trimethyl-2-oxo-1-(*p*-tolyl)pyrrolidin-3-yl)propanenitrile (3c), yellow oil (0.0443 g, 82% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.45 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 3.53-3.46 (m, 2H), 2.78-2.71 (m, 1H), 2.55-2.49 (m, 1H), 2.33 (s, 3H), 2.07-2.01 (m, 1H), 1.75-1.71 (m, 1H), 1.11 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.5, 136.8, 134.5, 129.4, 120.3, 119.8, 58.9, 49.2, 39.0, 29.2, 23.3, 22.2, 20.8, 15.3, 12.7; HRMS *m/z* (ESI) calcd for $C_{17}H_{23}N_2O$ ($[M+H]^+$) 271.1805, found 271.1801.

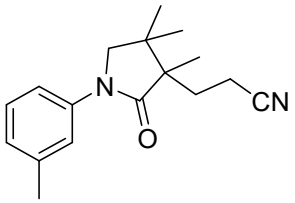


3-(1-(4-Butylphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3d), yellow oil

(0.0487 g, 78% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.48 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 3.53-3.47 (m, 2H), 2.78-2.71 (m, 1H), 2.59 (t, *J* = 8.0 Hz, 2H), 2.55-2.49 (m, 1H), 2.07-2.01 (m, 1H), 1.75-1.69 (m, 1H), 1.61-1.56 (m, 2H), 1.37-1.32 (m, 2H), 1.11 (s, 3H), 1.10 (s, 6H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.4, 139.5, 137.0, 128.8, 120.3, 119.7, 58.8, 49.2, 39.0, 35.0, 33.6, 29.2, 23.3, 22.3, 22.2, 15.3, 13.9, 12.7; HRMS *m/z* (ESI) calcd for $C_{20}H_{29}N_2O$ ($[M+H]^+$) 313.2274, found 313.2272.

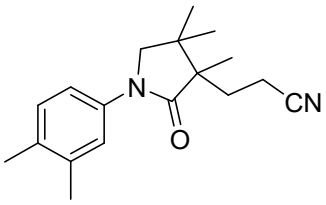


3-(1-(4-(*tert*-Butyl)phenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3e), yellow oil (0.0481 g, 77% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 7.0 Hz, 2H), 3.54-3.47 (m, 2H), 2.76-2.70 (m, 1H), 2.55-2.48 (m, 1H), 2.06-2.00 (m, 1H), 1.75-1.69 (m, 1H), 1.31 (s, 9H), 1.11 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.5, 147.7, 136.8, 125.8, 120.3, 119.4, 58.7, 49.2, 39.0, 34.4, 31.3, 29.2, 23.3, 22.1, 15.2, 12.7; HRMS *m/z* (ESI) calcd for $C_{20}H_{29}N_2O$ ($[M+H]^+$) 313.2274, found 313.2278.

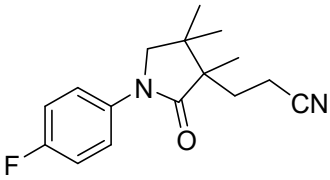


3-(3,4,4-Trimethyl-2-oxo-1-(*m*-tolyl)pyrrolidin-3-yl)propanenitrile (3f), yellow oil (0.0438 g, 81% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.48 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 3.67 (d, *J* = 10.0 Hz, 1H), 3.48 (d, *J* = 9.5 Hz, 1H), 2.47-2.38 (m, 2H), 2.36 (s, 3H), 1.98-1.92 (m, 1H), 1.88-1.82 (m, 1H), 1.13 (s, 6H), 1.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 177.8, 139.3, 138.9,

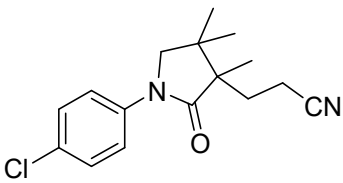
128.8, 125.4, 120.4, 119.5, 116.7, 56.6, 48.4, 40.6, 31.1, 21.6, 20.3, 20.1, 19.3, 13.0; HRMS *m/z* (ESI) calcd for $C_{17}H_{23}N_2O$ ($[M+H]^+$) 271.1805, found 271.1801.



3-(1-(3,4-Dimethylphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3g), yellow oil (0.0472 g, 83% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.41 (d, J = 2.0 Hz, 1H), 7.25-7.23 (m, 1H), 7.12 (d, J = 8.0 Hz, 1H), 3.53-3.46 (m, 2H), 2.79-2.72 (m, 1H), 2.56-2.49 (m, 1H), 2.27 (s, 3H), 2.24 (s, 3H), 2.04-2.01 (m, 1H), 1.75-1.70 (m, 1H), 1.11 (s, 3H), 1.10 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.4, 137.2, 137.1, 133.2, 129.9, 121.3, 120.3, 117.3, 59.0, 49.1, 39.0, 29.2, 23.2, 22.2, 20.0, 19.1, 15.2, 12.7; HRMS *m/z* (ESI) calcd for $C_{18}H_{25}N_2O$ ($[M+H]^+$) 285.1961, found 285.1967.

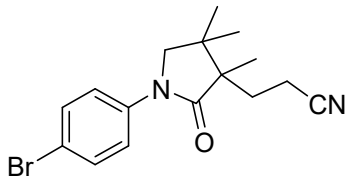


3-(1-(4-Fluorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3h), yellow oil (0.0395 g, 72% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.55-7.52 (m, 2H), 7.08-7.04 (m, 2H), 3.52-3.46 (m, 2H), 2.77-2.71 (m, 1H), 2.55-2.49 (m, 1H), 2.07-2.01 (m, 1H), 1.76-1.70 (m, 1H), 1.12 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.5, 159.6 (d, J_{C-F} = 243.1 Hz), 135.4 (d, J_{C-F} = 2.9 Hz), 121.5 (d, J_{C-F} = 7.9 Hz), 120.2, 115.6 (d, J_{C-F} = 22.4 Hz), 59.0, 49.1, 39.0, 29.1, 23.2, 22.2, 15.3, 12.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ: -117.4; HRMS *m/z* (ESI) calcd for $C_{16}H_{20}FN_2O$ ($[M+H]^+$) 275.1554, found 275.1550.

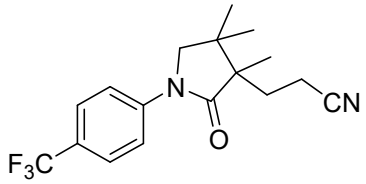


3-(1-(4-Chlorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3i), yellow oil

(0.0406 g, 70% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 9.0 Hz, 2H), 7.33 (d, *J* = 9.0 Hz, 2H), 3.52-3.46 (m, 2H), 2.76-2.69 (m, 1H), 2.55-2.48 (m, 1H), 2.06-2.00 (m, 1H), 1.76-1.70 (m, 1H), 1.12 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.7, 137.9, 129.8, 128.9, 120.8, 120.1, 58.7, 49.3, 38.9, 29.1, 23.2, 22.2, 15.3, 12.7; HRMS *m/z* (ESI) calcd for $C_{16}H_{20}ClN_2O$ ($[M+H]^+$) 291.1259, found 291.1267.

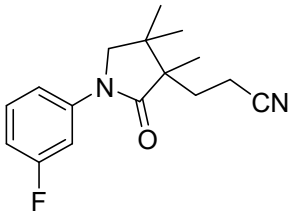


3-(1-(4-Bromophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3j), yellow oil (0.0474 g, 71% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.49 (m, 2H), 7.48-7.46 (m, 2H), 3.51-3.46 (m, 2H), 2.76-2.69 (m, 1H), 2.55-2.48 (m, 1H), 2.06-2.00 (m, 1H), 1.75-1.70 (m, 1H), 1.12 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.8, 138.4, 131.9, 121.1, 120.1, 117.5, 58.6, 49.3, 38.9, 29.1, 23.2, 22.2, 15.3, 12.7; HRMS *m/z* (ESI) calcd for $C_{16}H_{20}BrN_2O$ ($[M+H]^+$) 335.0754, found 335.0758.

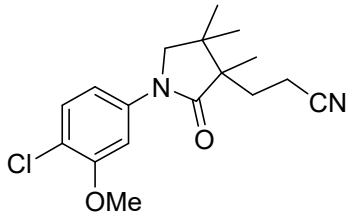


3-(3,4,4-Trimethyl-2-oxo-1-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)propanenitrile (3k), yellow oil (0.0428 g, 66% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 9.0 Hz, 2H), 3.57-3.52 (m, 2H), 2.76-2.69 (m, 1H), 2.56-2.49 (m, 1H), 2.08-2.02 (m, 1H), 1.78-1.72 (m, 1H), 1.14 (s, 3H), 1.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 177.2, 142.3, 126.1 (*q*, $J_{C\text{-}F}$ = 2.8 Hz), 125.1, 122.9, 120.0, 119.1, 58.5, 49.5, 38.9, 29.1, 23.2,

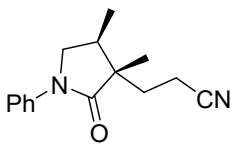
22.2, 15.4, 12.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ: -62.2; HRMS *m/z* (ESI) calcd for $C_{17}H_{20}F_3N_2O$ ($[M+H]^+$) 325.1522, found 325.1516.



3-(1-(3-Fluorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3l), yellow oil (0.0389 g, 71% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.49 (m, 1H), 7.33-7.30 (m, 2H), 6.88-6.84 (m, 1H), 3.53-3.48 (m, 2H), 2.76-2.70 (m, 1H), 2.56-2.49 (m, 1H), 2.07-2.01 (m, 1H), 1.77-1.71 (m, 1H), 1.12 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.9, 162.9 (d, J_{C-F} = 243.6 Hz), 140.8 (d, J_{C-F} = 10.5 Hz), 130.0 (d, J_{C-F} = 9.3 Hz), 120.1, 114.6 (d, J_{C-F} = 3.1 Hz), 111.3 (d, J_{C-F} =21.3 Hz), 107.1 (d, J_{C-F} =26.1 Hz), 58.6, 49.4, 38.8, 29.1, 23.2, 22.2, 15.3, 12.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ: -111.1; HRMS *m/z* (ESI) calcd for $C_{16}H_{20}FN_2O$ ($[M+H]^+$) 275.1554, found 275.1550.



3-(1-(4-Chloro-3-methoxyphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3m), yellow oil (0.0499 g, 78% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.76 (d, *J* = 2.5 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 6.78-6.76 (m, 1H), 3.93 (s, 3H), 3.54-3.47 (m, 2H), 2.76-2.70 (m, 1H), 2.55-2.49 (m, 1H), 2.07-2.01 (m, 1H), 1.77-1.71 (m, 1H), 1.13 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 176.9, 155.1, 139.2, 129.8, 120.1, 118.1, 111.1, 104.4, 58.7, 56.2, 49.5, 38.8, 29.1, 23.3, 22.2, 15.3, 12.7; HRMS *m/z* (ESI) calcd for $C_{17}H_{22}ClN_2O_2$ ($[M+H]^+$) 321.1364, found 321.1368.



3-(3,4-Dimethyl-2-oxo-1-phenylpyrrolidin-3-yl)propanenitrile (3p), yellow oil (0.0329 g, 68% yield, d.r. > 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 9.5 Hz, 2H), 7.38 (t, *J* = 8.5 Hz, 2H), 7.16 (t, *J* = 8.0 Hz,

1H), 3.82 (t, *J* = 10.0 Hz, 1H), 3.42 (t, *J* = 12.0 Hz, 1H), 2.68-2.61 (m, 1H), 2.57-2.49 (m, 1H), 2.39-2.32 (m, 1H), 2.09-2.02 (m, 1H), 1.93-1.86 (m, 1H), 1.11 (d, *J* =8.5 Hz, 3H), 1.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 177.0, 139.1, 128.9, 124.8, 120.1, 119.8, 52.0, 47.0, 34.3, 31.9, 16.7, 12.6, 12.1; HRMS *m/z* (ESI) calcd for $C_{15}H_{19}N_2O$ ($[M+H]^+$) 243.1492, found 243.1498.

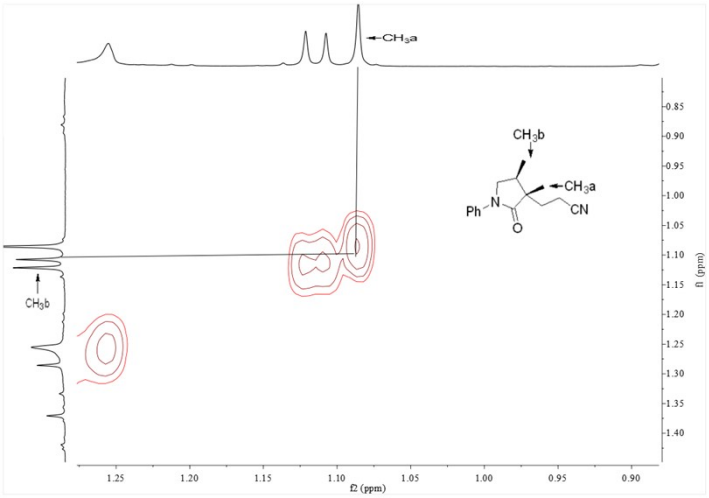
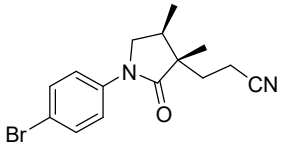
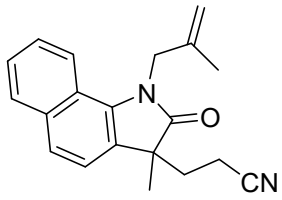


Figure 1. H-H Noesy: there is strong NOE between CH_{3a} and CH_{3b}

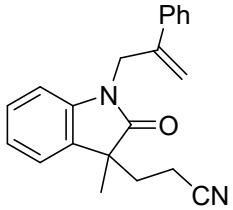


3-(1-(4-Bromophenyl)-3,4-dimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3q), yellow oil (0.0410 g, 64% yield, d.r. > 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.53-7.50 (m, 2H), 7.49-7.46 (m, 2H), 3.80-3.77 (m, 1H), 3.38 (t, *J* = 9.5 Hz, 1H), 2.66-2.60 (m, 1H), 2.55-2.48 (m, 1H), 2.40-2.34 (m, 1H), 2.08-2.02 (m, 1H), 1.92-1.86 (m, 1H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 177.1, 138.2, 131.9, 121.1, 119.9, 117.5, 51.9, 47.0, 34.3, 31.9, 16.7, 12.6, 12.0; HRMS *m/z* (ESI) calcd for $C_{15}H_{18}BrN_2O$ ($[M+H]^+$) 321.0597, found 321.0591.

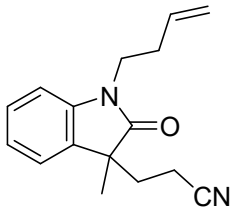


3-(3-Methyl-1-(2-methylallyl)-2-oxo-2,3-dihydro-1*H*-benzo[*g*]indol-3-yl)propanenitrile (4n), yellow oil (0.0474

g, 78% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.77 (d, *J* = 8.0 Hz, 1H), 7.59-7.52 (m, 2H), 7.43-7.39 (m, 2H), 6.91 (d, *J* = 7.5 Hz, 1H), 4.92 (d, *J* = 1.0 Hz, 1H), 4.80 (d, *J* =17.0 Hz, 1H), 4.75 (s, 1H), 4.55 (d, *J* = 17.0 Hz, 1H), 2.89-2.83 (m, 1H), 2.34-2.28 (m, 1H), 2.24-2.18 (m, 1H), 2.14-2.07 (m, 1H), 1.83 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.5, 139.1, 135.5, 135.3, 133.6, 127.1, 127.0, 126.7, 122.9, 122.5, 119.5, 119.1, 110.6, 110.0, 48.1, 47.1, 37.4, 31.7, 20.1, 13.7; HRMS *m/z* (ESI) calcd for $C_{20}H_{21}N_2O$ ($[M+H]^+$) 305.1648, found 305.1656.

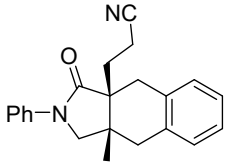


3-(3-Methyl-2-oxo-1-(2-phenylallyl)indolin-3-yl)propanenitrile (4r), yellow oil (0.0512 g, 81% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30-7.27 (m, 2H), 7.25-7.20 (m, 3H), 7.07-7.03 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.58 (s, 1H), 5.23-5.19 (m, 1H), 4.87-4.83 (m, 1H), 2.06-2.00 (m, 1H), 1.77-1.71 (m, 1H), 1.42 (d, *J* = 4.5 Hz, 1H), 1.29 (d, *J* = 5.5 Hz, 1H), 1.17 (s, 3H), 1.14-1.07 (m, 1H), 0.96-0.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 178.4, 141.7 (2), 136.9, 131.1, 129.0, 128.7, 128.5, 127.5, 123.2, 122.4, 118.9, 109.4, 108.9, 47.4, 41.5, 33.3, 23.5, 11.4; HRMS *m/z* (ESI) calcd for $C_{21}H_{21}N_2O$ ($[M+H]^+$) 317.1648, found 317.1652.



3-(1-(But-3-en-1-yl)-3-methyl-2-oxoindolin-3-yl)propanenitrile (4s), yellow oil (0.0422 g, 83% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.33-7.29 (m, 1H), 7.20 (d, *J* = 7.0 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 5.84-5.76 (m, 1H), 5.05-5.02 (m, 2H), 3.87-3.82 (m, 1H), 3.79-3.73 (m, 1H), 2.47-2.43 (m, 2H), 2.33-2.29 (m, 1H), 2.14-2.04 (m, 2H), 1.98-1.93 (m, 1H), 1.38 (s, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ: 178.8, 142.4, 134.5, 131.8, 128.6, 122.9, 122.8, 118.9, 117.7, 108.8, 47.3, 39.2, 33.4, 31.9, 23.8, 12.8; HRMS *m/z* (ESI) calcd for $C_{16}H_{19}N_2O$ ($[M+H]^+$) 255.1492, found 255.1490.



3-(9a-Methyl-3-oxo-2-phenyl-1,2,3,4,9,9a-hexahydro-3a*H*-benzo[*f*]isoindol-3a-yl)propanenitrile (5a), yellow oil (0.0436 g, 66% yield, d.r. > 20:1); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.36 (m, 2H), 7.32-7.29 (m, 2H), 7.18-7.13 (m, 4H), 7.07 (d, *J* = 6.5 Hz, 1H), 3.66 (d, *J* = 8.5 Hz, 1H), 3.46 (d, *J* = 10.0 Hz, 1H), 3.20 (d, *J* = 15.0 Hz, 1H), 2.87-2.78 (m, 2H), 2.69-2.62 (m, 3H), 2.17-2.12 (m, 1H), 1.98-1.92 (m, 1H), 1.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 175.6, 138.8, 135.5, 134.7, 128.9, 128.0, 127.7, 126.9, 126.8, 125.1, 120.4, 120.1, 59.5, 50.4, 42.3, 39.1, 34.3, 30.3, 22.7, 12.8; HRMS *m/z* (ESI) calcd for $C_{22}H_{23}N_2O$ ($[M+H]^+$) 331.1805, found 331.1809.

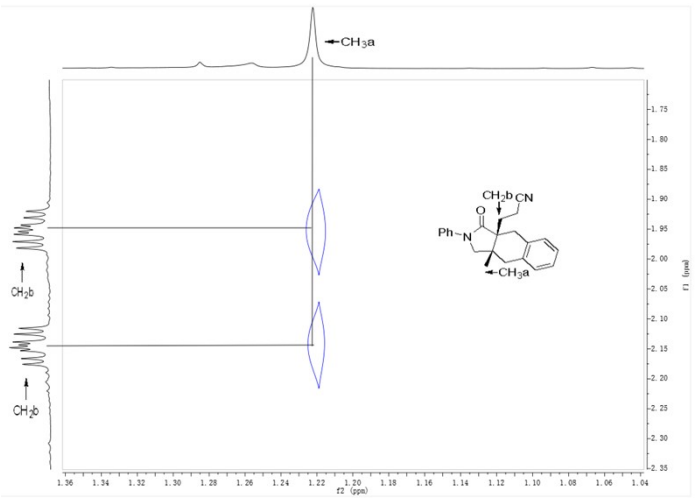
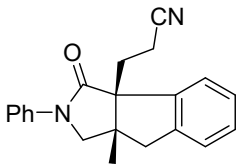
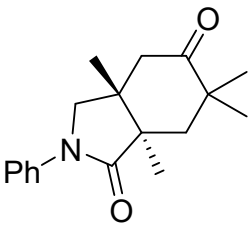


Figure 2. H-H Noesy: there is strong NOE between CH_{3a} and CH_{2b}



3-(8a-Methyl-3-oxo-2-phenyl-2,3,8,8a-tetrahydroindeno[1,2-*c*]pyrrol-3a(1*H*)-yl)propanenitrile (5b), yellow oil (0.0449 g, 71% yied, d.r. > 20:1); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.50

(m, 2H), 7.35-7.31 (m, 3H), 7.30-7.28 (m, 2H), 7.25-7.24 (m, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 3.53 (d, *J* = 10.0 Hz, 1H), 3.46 (d, *J* = 9.5 Hz, 1H), 2.99 (s, 2H), 2.73-2.67 (m, 1H), 2.56-2.50 (m, 1H), 2.30-2.24 (m, 1H), 2.07-2.00 (m, 1H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 173.3, 141.4, 140.1, 139.1, 128.9 (2), 127.9, 125.5, 124.9, 124.8, 119.9, 119.8, 61.6, 59.1, 46.8, 43.5, 28.7, 20.7, 12.8; HRMS *m/z* (ESI) calcd for $C_{21}H_{21}N_2O$ ($[M+H]^+$) 317.1648, found 317.1642.



3a,6,6,7a-Tetramethyl-2-phenylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6a),[1] 0.0405 g, 71% yield, d.r. > 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 3.65 (d, *J* = 10.0 Hz, 1H), 3.37 (d, *J* =10.0 Hz, 1H), 2.95 (d, *J* = 13.5 Hz, 1H), 2.46 (d, *J* = 15.0 Hz, 1H), 2.15 (d, *J* = 14.0 Hz, 1H), 1.58 (d, *J* = 15.0 Hz, 1H), 1.23 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 214.4, 177.3, 139.5, 129.0, 124.7, 119.8, 57.8, 47.4, 46.7, 45.3, 45.1, 43.7, 26.6, 25.9, 21.3, 19.6.

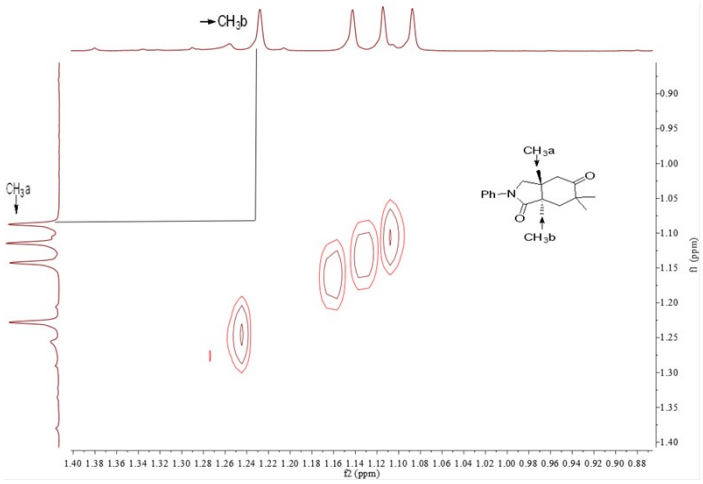
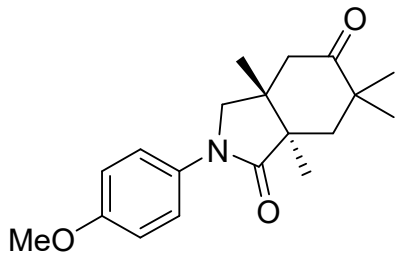
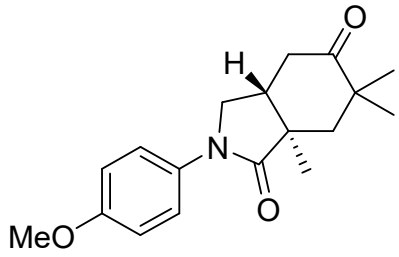


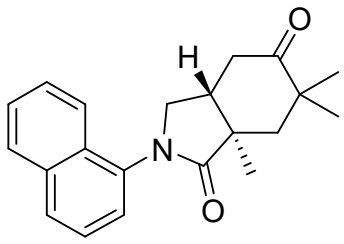
Figure 3. H-H Noesy: there is no NOE between CH_{3a} and CH_{3b}



2-(4-Methoxyphenyl)-3a,6,6,7a-tetramethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6b), yellow oil (0.0460 g, 73% yield, d.r. > 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H), 3.62 (d, *J* = 10.0 Hz, 1H), 3.32 (d, *J* = 9.5 Hz, 1H), 2.95 (d, *J* = 13.5 Hz, 1H), 2.45 (d, *J* = 15.0 Hz, 1H), 2.15 (d, *J* = 13.5 Hz, 1H), 1.60 (d, *J* = 3.0 Hz, 1H), 1.22 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 214.5, 176.9, 156.8, 132.7, 121.6, 114.2, 58.3, 55.5, 47.2, 46.8, 45.4, 45.0, 43.8, 26.5, 26.0, 21.2, 19.8; HRMS *m/z* (ESI) calcd for $C_{19}H_{26}NO_3$ ($[M+H]^+$) 316.1907, found 316.1909.

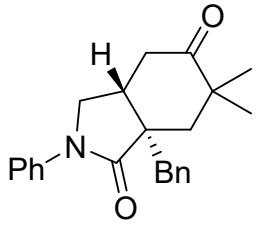


2-(4-Methoxyphenyl)-6,6,7a-trimethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6c),[1] 0.0361 g, 60% yield, d.r. > 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.50 (d, *J* = 9.5 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.05-4.01 (m, 1H), 3.80 (s, 3H), 3.34-3.32 (m, 1H), 2.65-2.62 (m, 2H), 2.54-2.49 (m, 1H), 2.34 (d, *J* = 14.5 Hz, 1H), 1.79 (d, *J* = 15.0 Hz, 1H), 1.34 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215.5, 177.0, 156.9, 132.4, 121.8, 114.2, 55.5, 51.9, 45.6, 43.8 (2), 40.4, 38.7, 26.8, 25.9, 25.4.

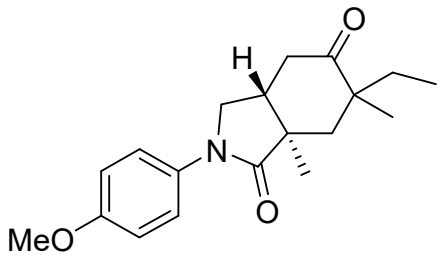


6,6,7a-Trimethyl-2-(naphthalen-1-yl)hexahydro-1*H*-isoindole-1,5(4*H*)-dione (6d),[1] 0.0334 g, 52% yield, d.r. > 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91-7.89 (m, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.56-

7.49 (m, 3H), 7.33 (d, *J* = 7.5 Hz, 1H), 4.14-4.08 (m, 1H), 3.42 (d, *J* = 9.5 Hz, 1H), 2.81-2.76 (m, 2H), 2.72-2.68 (m, 1H), 2.43 (d, *J* = 14.5 Hz, 1H), 1.90 (d, *J* = 14.5 Hz, 1H), 1.53 (s, 3H), 1.24 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215.6, 178.3, 135.1, 134.6, 129.9, 128.7, 128.5, 126.8, 126.4, 125.6, 124.5, 122.2, 54.7, 45.3, 44.0, 43.2, 40.7, 40.0, 27.1, 26.2, 25.5.

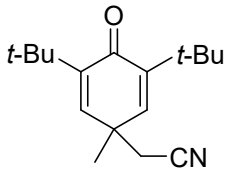


7a-Benzyl-6,6-dimethyl-2-phenylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6e),[1] 0.0368 g, 53% yield, d.r. > 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.31 (m, 4H), 7.24 (t, *J* = 3.0 Hz, 3H), 7.20-7.18 (m, 2H), 7.17-7.14 (m, 1H), 3.24 (d, *J* = 13.5 Hz, 1H), 3.09-3.02 (m, 2H), 2.92-2.87 (m, 1H), 2.76 (d, *J* = 13.5 Hz, 1H), 2.68-2.64 (m, 1H), 2.41-2.35 (m, 2H), 2.00 (d, *J* = 14.5 Hz, 1H), 1.19 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215.7, 176.2, 138.8, 136.4, 130.1, 128.8, 128.4, 127.2, 125.1, 120.6, 52.2, 49.3, 45.4, 45.2, 43.6, 41.3, 33.9, 27.8, 25.1.

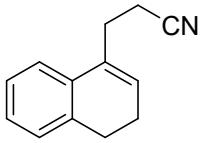


6-Ethyl-2-(4-methoxyphenyl)-6,7a-dimethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6f),[1] 0.0353 g, 56% yield, d.r. = 2:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.53-7.48 (m, 2H), 6.91 (t, *J* = 9.5 Hz, 2H), 4.06-3.98 (m, 1H), 3.81 (s, 1.2H), 3.80 (s, 1.8H), 3.35-3.31 (m, 1H), 2.72-2.62 (m, 1H), 2.56-2.44 (m, 2H), 1.89 (d, *J* = 14.5 Hz, 1H), 1.70-1.62 (m, 2H), 1.56-1.50 (m, 1H), 1.38 (s, 1.2H), 1.30 (s, 1.8H), 1.06 (s, 1.8H), 1.01 (s, 1.2H), 0.86 (t, *J* = 8.0 Hz, 1.8H), 0.79 (t, *J* = 7.5 Hz, 1.2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215.9, 215.2, 177.2, 177.0, 156.9, 156.8, 132.6, 132.3, 121.9, 121.7, 114.2

(2), 55.5 (2), 52.0, 51.8, 47.7, 46.9, 43.8, 43.5, 43.1, 42.8, 41.2, 40.9, 39.4, 38.0, 32.7, 30.9, 26.7, 25.5, 22.8, 22.0, 8.3, 8.1.



2-(3,5-di-*tert*-Butyl-1-methyl-4-oxocyclohexa-2,5-dien-1-yl)acetonitrile (7a),[2] 0.0389 g, 75% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.47 (s, 2H), 2.50 (s, 2H), 1.37 (s, 3H), 1.24 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 185.2, 148.2, 142.0, 116.3, 37.4, 34.9, 29.8, 29.4, 25.8.



3-(3,4-Dihydronaphthalen-1-yl)propanenitrile (8a),[3] 0.0286 g, 78% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36 (s, 1H), 7.17 (s, 2H), 7.12 (d, *J* = 8.5 Hz, 1H), 5.99 (s, 1H), 2.82-2.74 (m, 4H), 2.56 (t, *J* = 8.5 Hz, 2H), 2.29 (t, *J* = 13.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 135.9, 132.0, 127.2, 127.0, 126.5, 126.3, 125.5 (2), 120.8, 27.6, 27.0, 22.0, 15.8.

(C) References

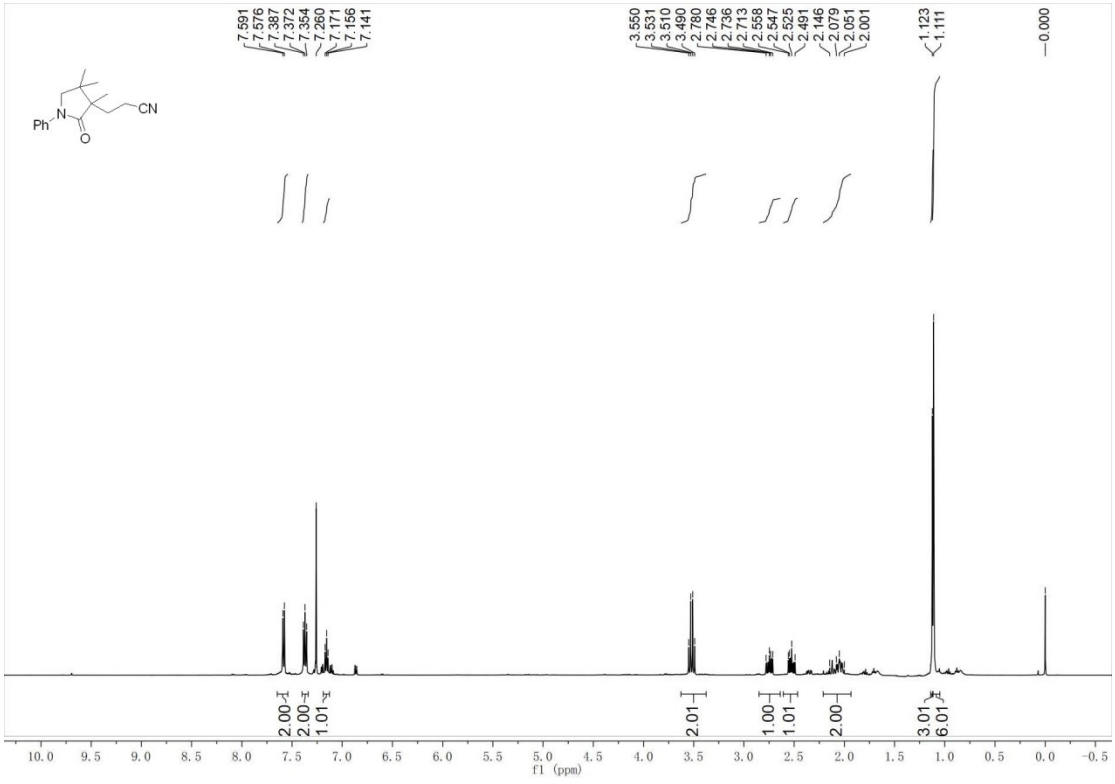
[1] Y. Liu, Y.-N. Meng, X.-J. Huang, F.-H. Qin, D. Wu, Q. Shao, Z. Guo, Q. Li and W.-T. Wei, *Green Chem*. 2020, **22**, 4593.

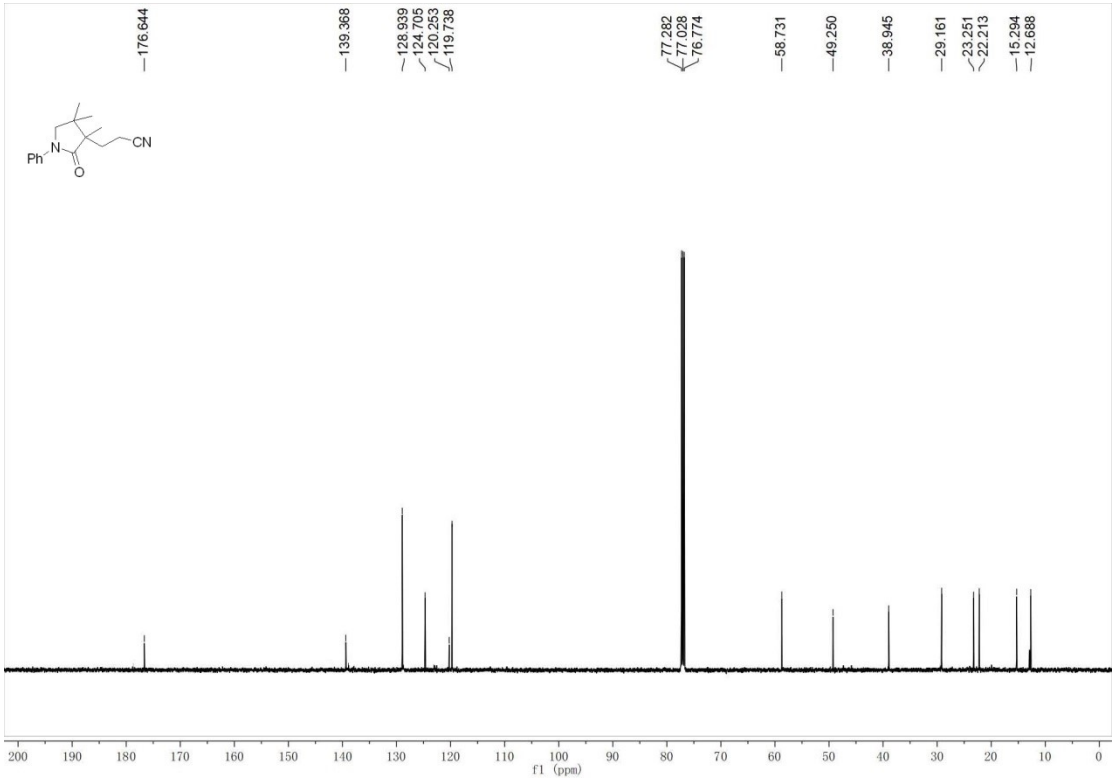
[2] D. Liang, X. Song, L. Xu, Y. Sun, Y. Dong, B. Wang and W. Li, *Tetrahedron*. 2019, **75**, 3495.

[3] Z. Chen, Q. Zhou, Q.-N. Chen, P. Chen, B.-Q. Xiong, Y. Liang, K.-W. Tang, J. Xie and Y. Liu, *Org. Biomol. Chem*. 2020, **18**, 8677.

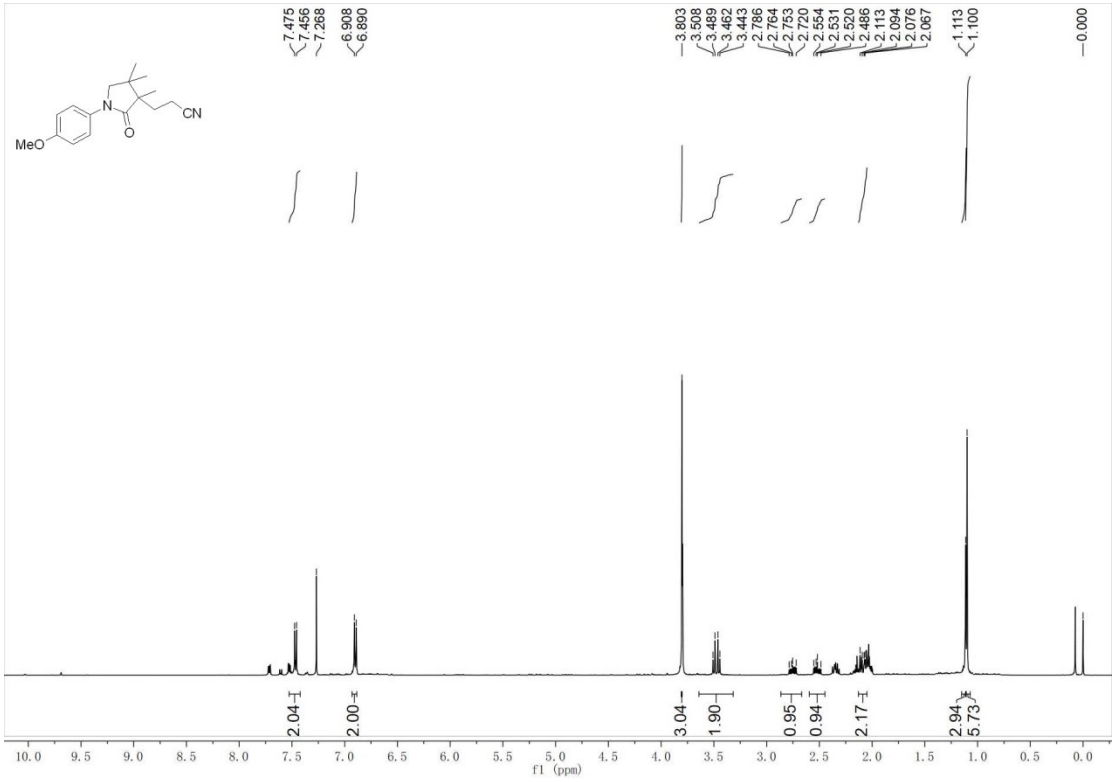
(D) Spectra

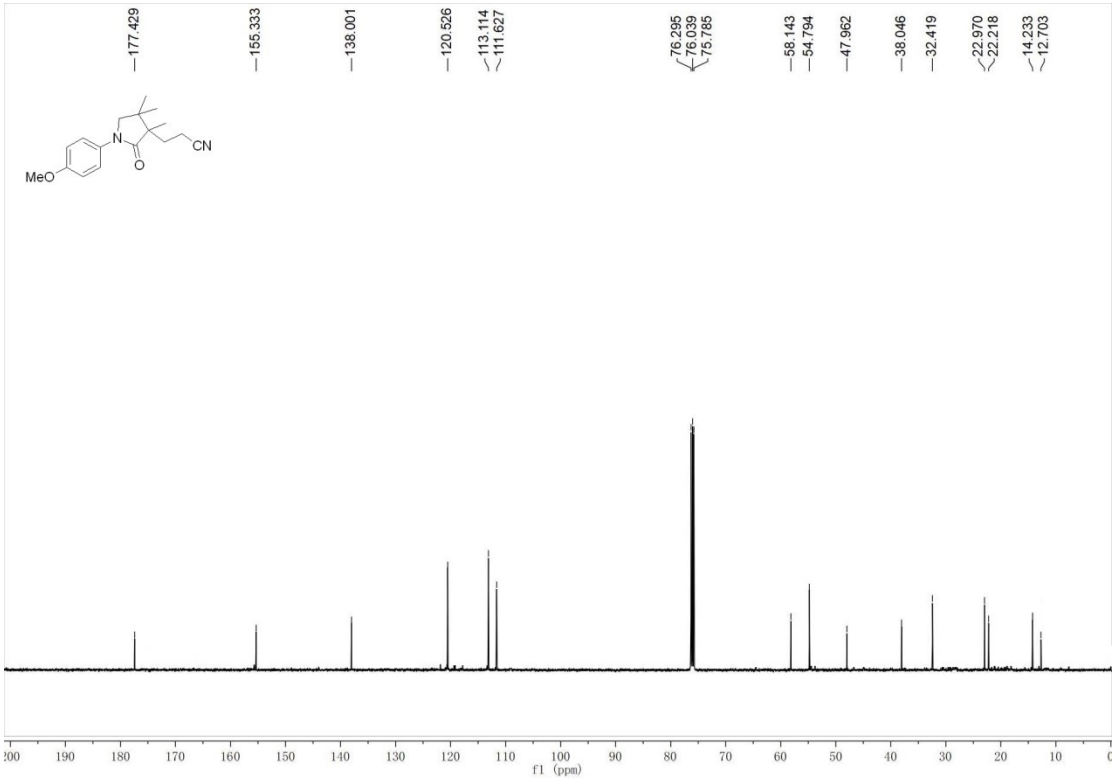
3-(3,4,4-Trimethyl-2-oxo-1-phenylpyrrolidin-3-yl)propanenitrile (3a)



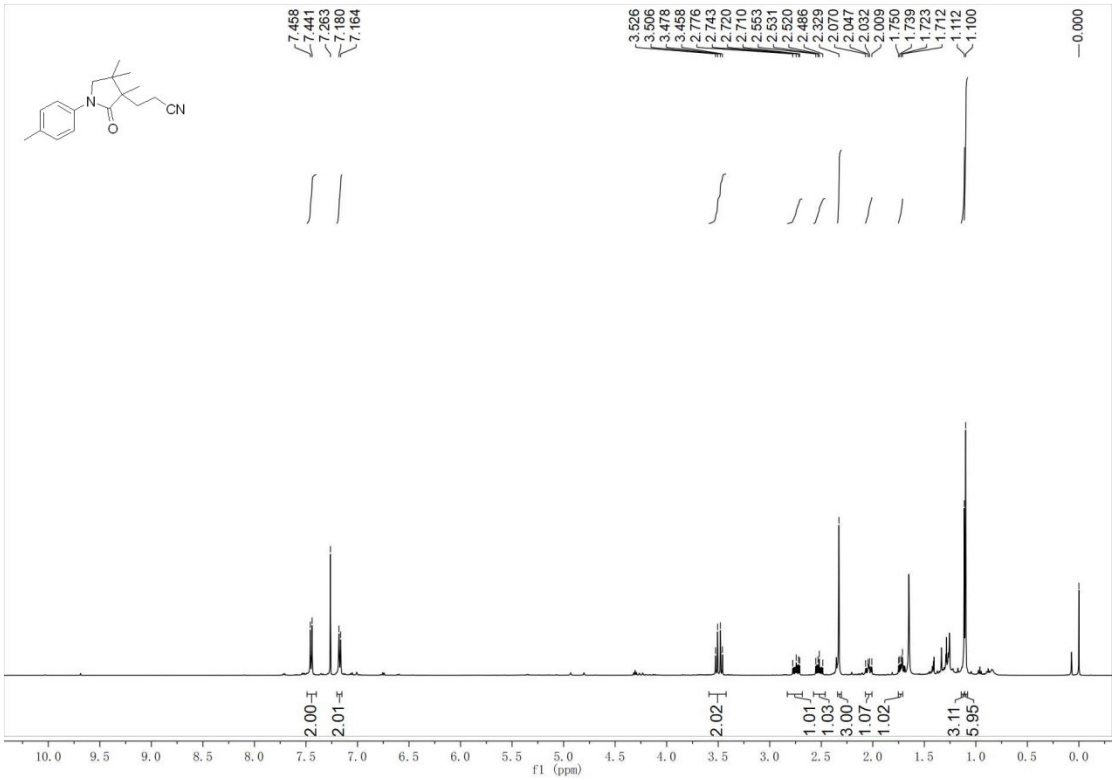


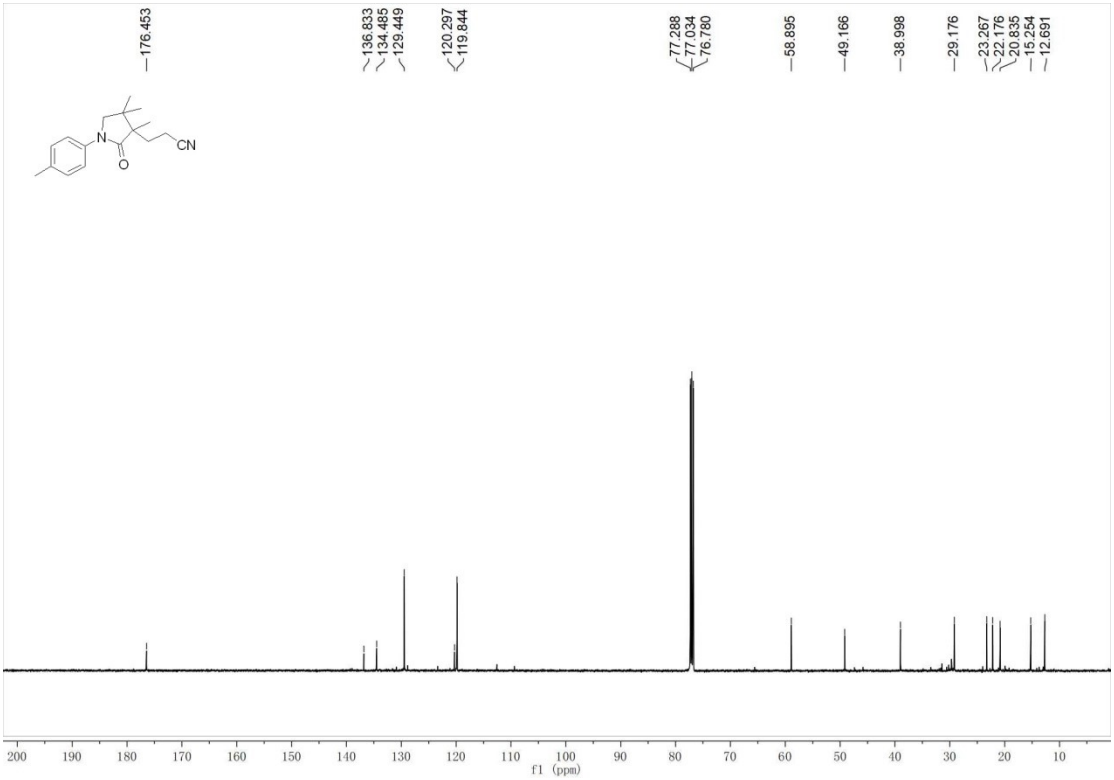
3-(1-(4-Methoxyphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3b)



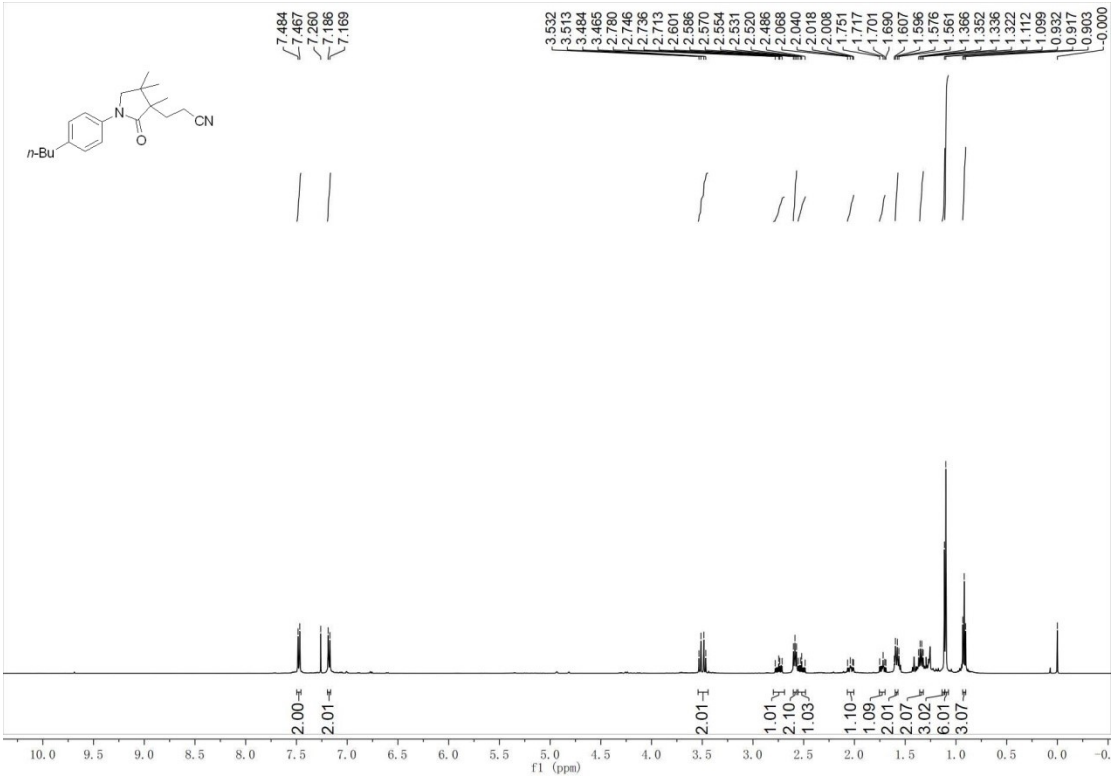


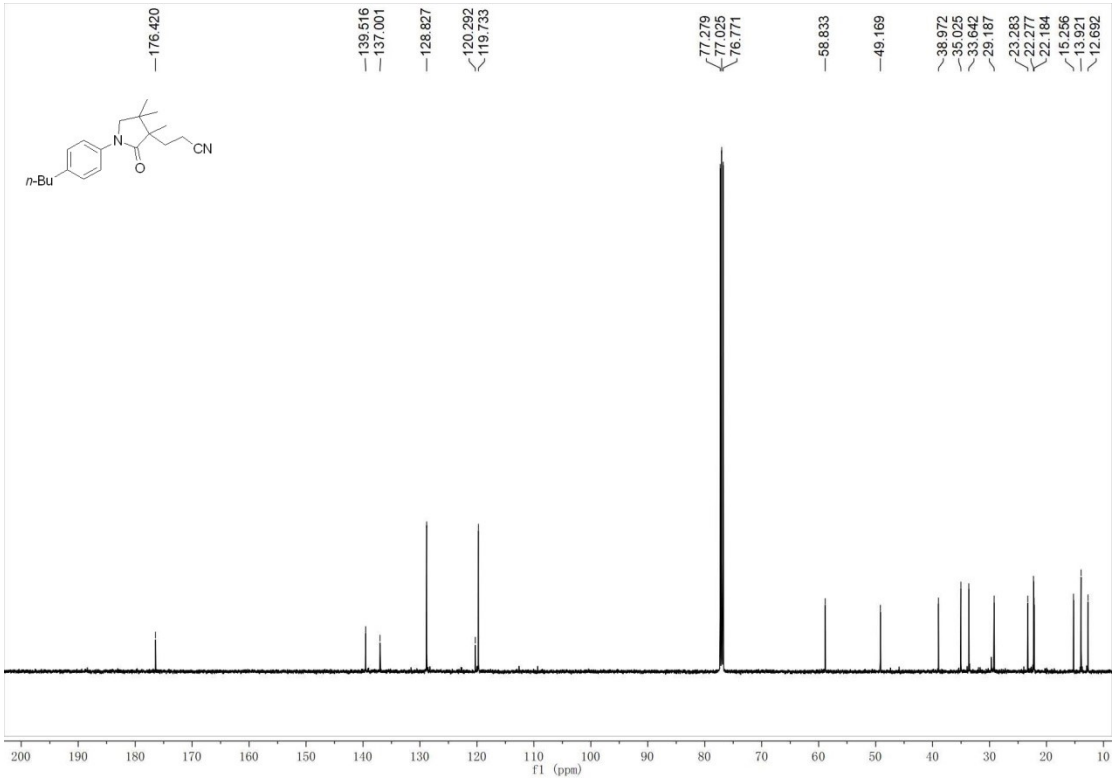
3-(3,4,4-Trimethyl-2-oxo-1-(*p*-tolyl)pyrrolidin-3-yl)propanenitrile (3c)





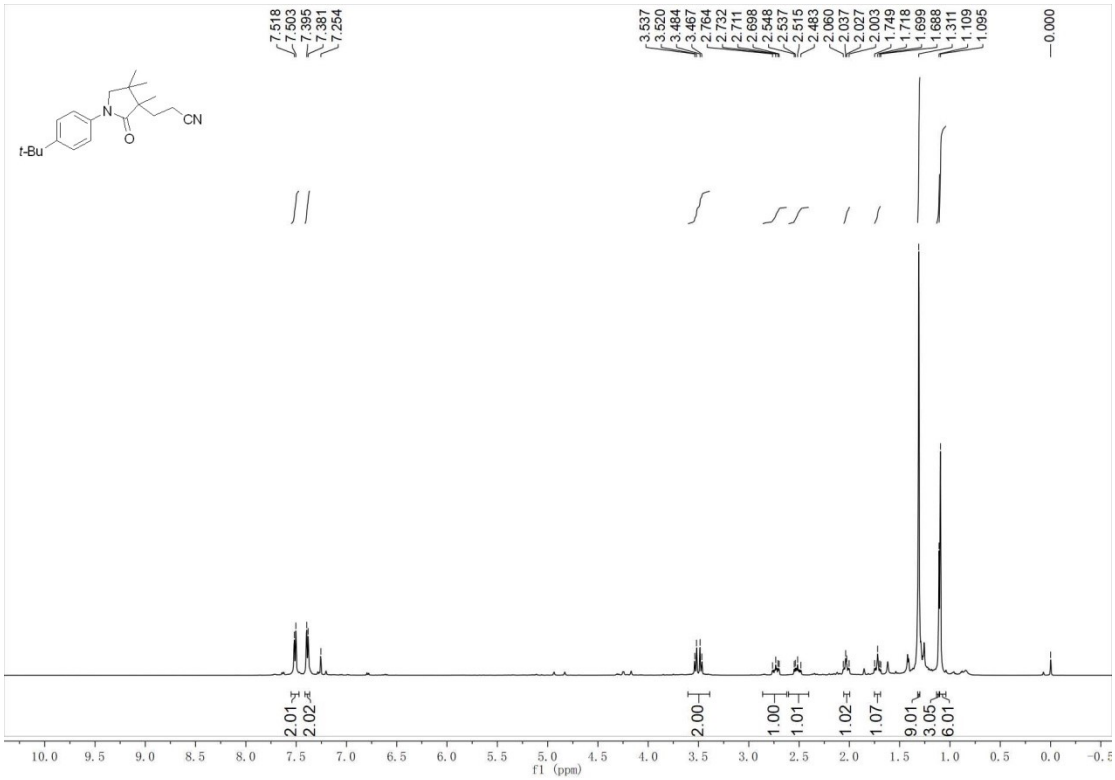
3-(1-(4-Butylphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3d)

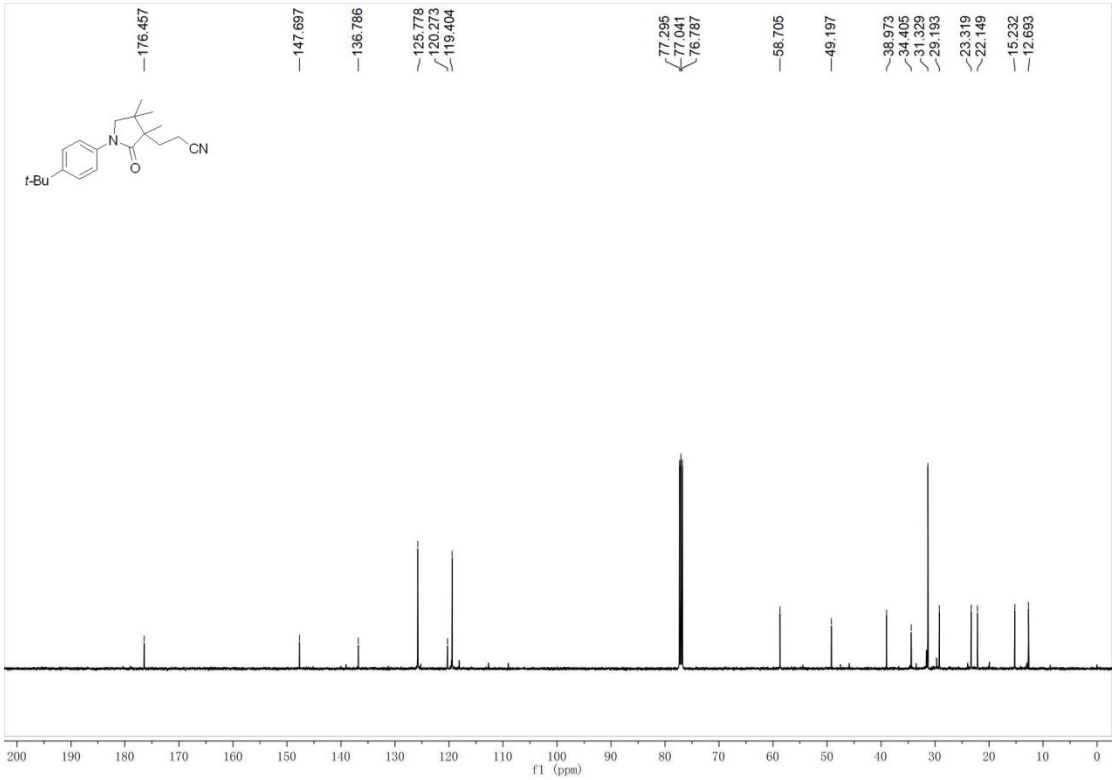




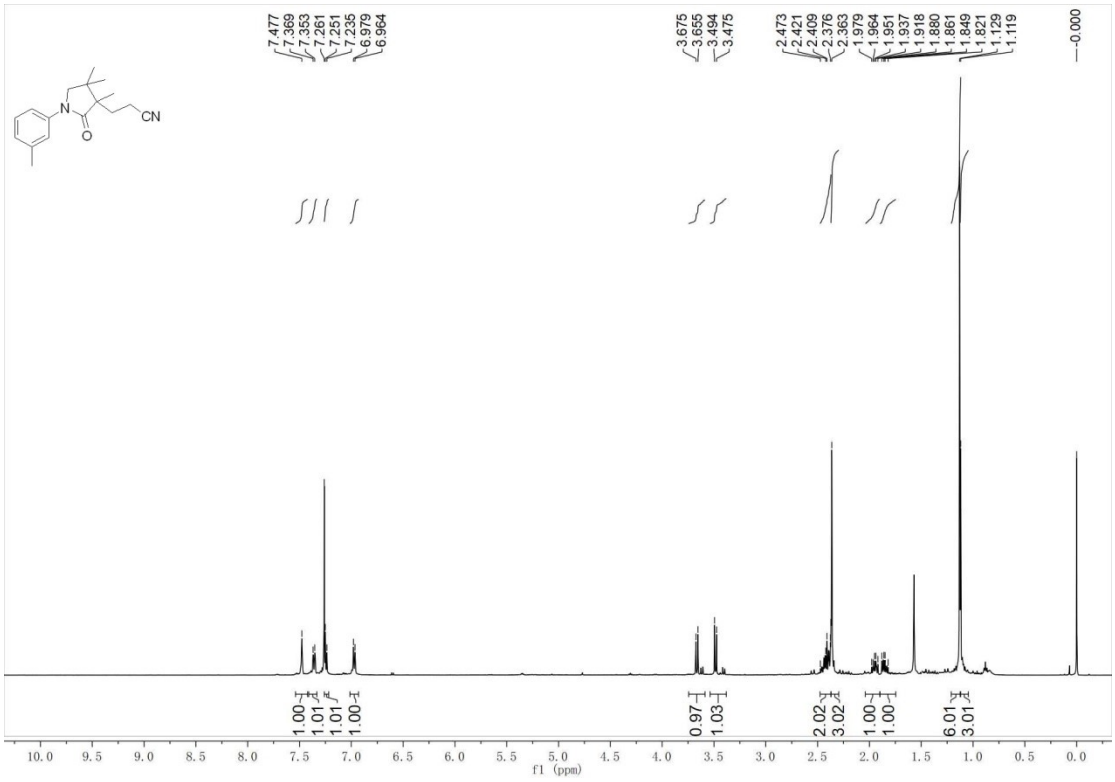
3-(1-(4-(*tert*-Butyl)phenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile

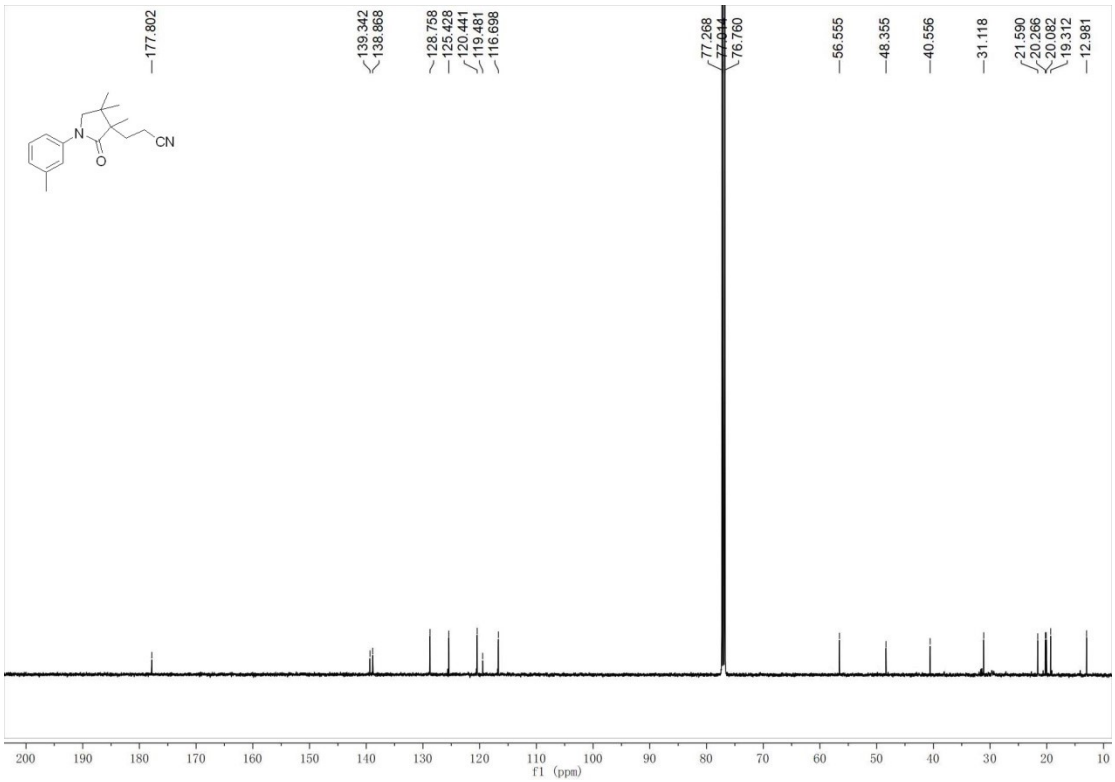
(3e)





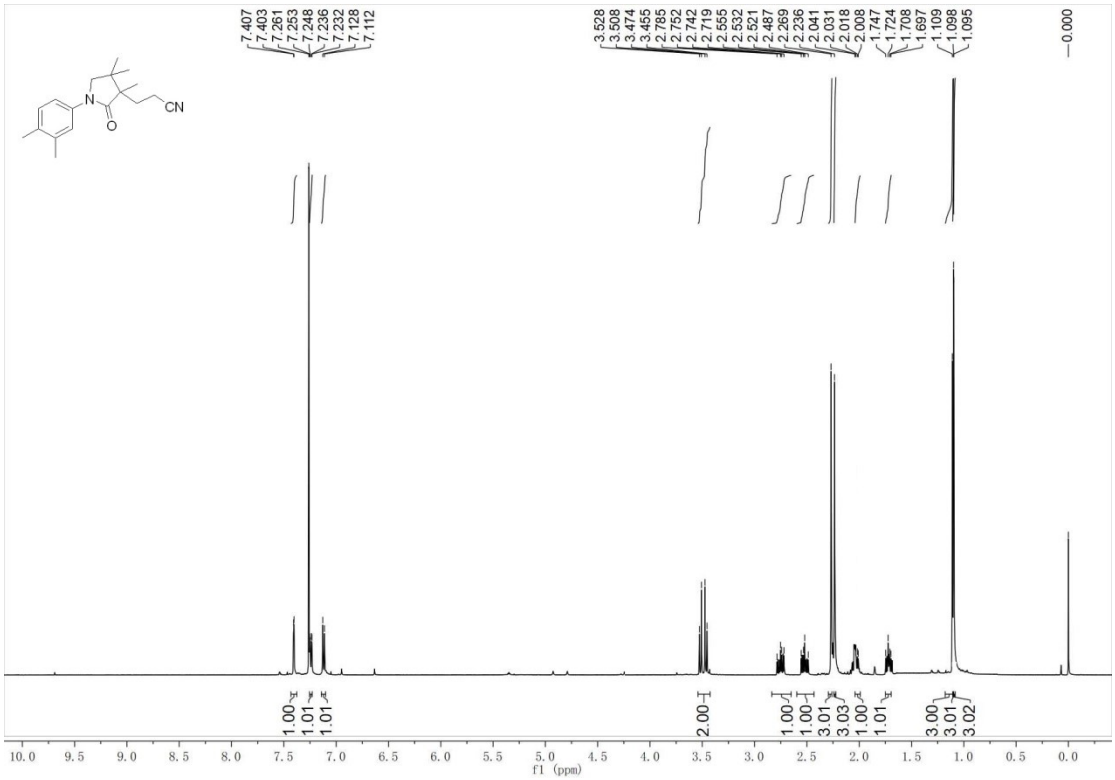
3-(3,4,4-Trimethyl-2-oxo-1-(*m*-tolyl)pyrrolidin-3-yl)propanenitrile (3f)

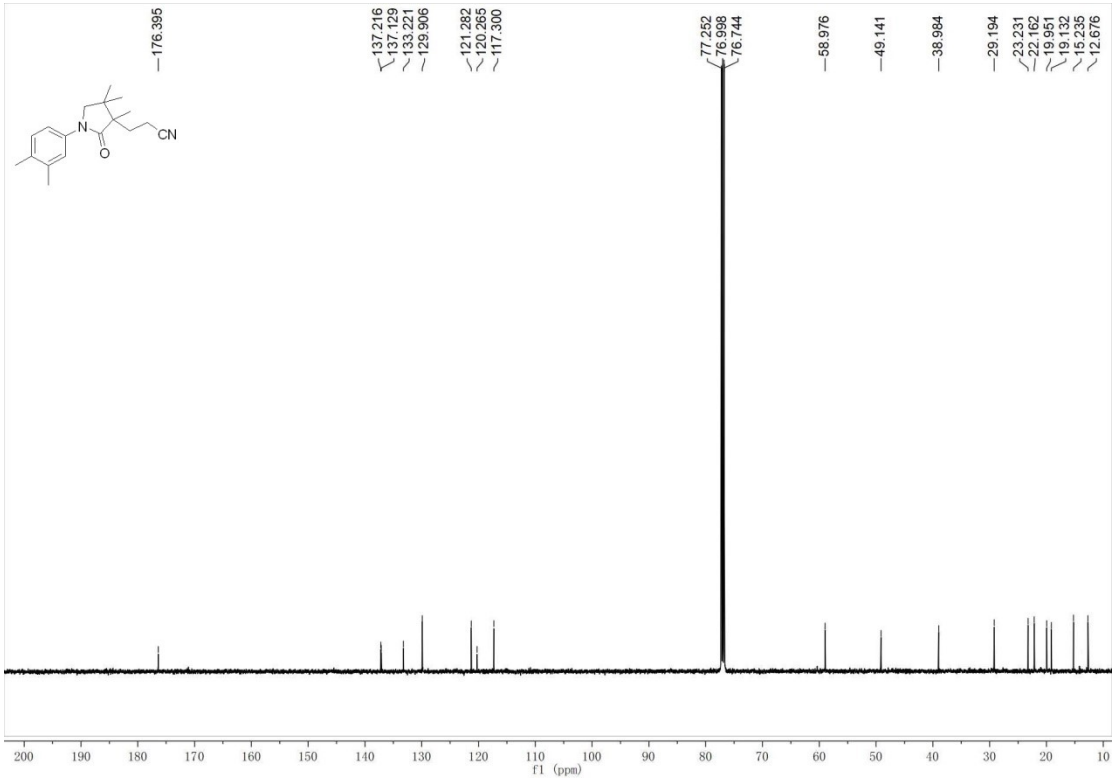




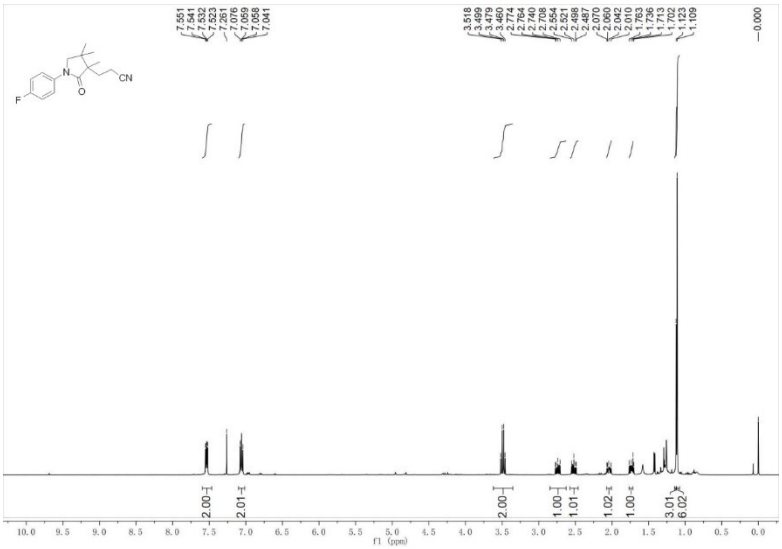
3-(1-(3,4-Dimethylphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile

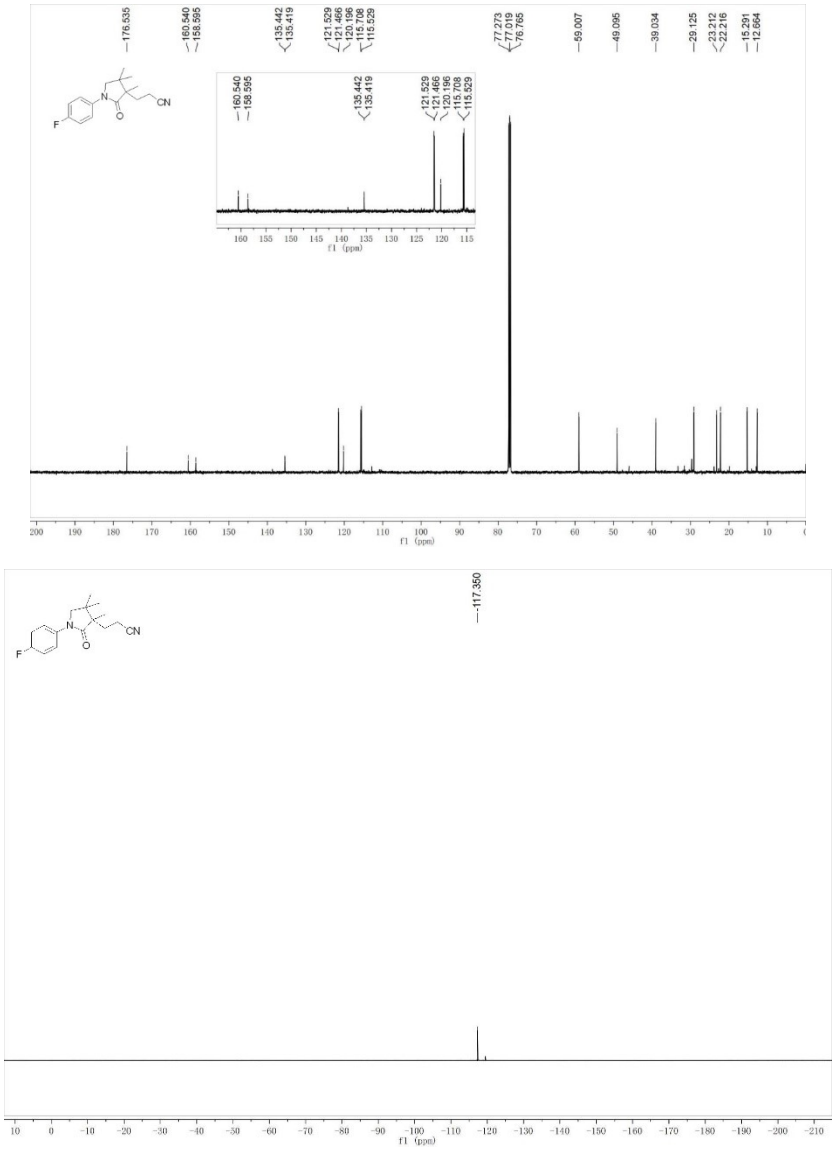
(3g)



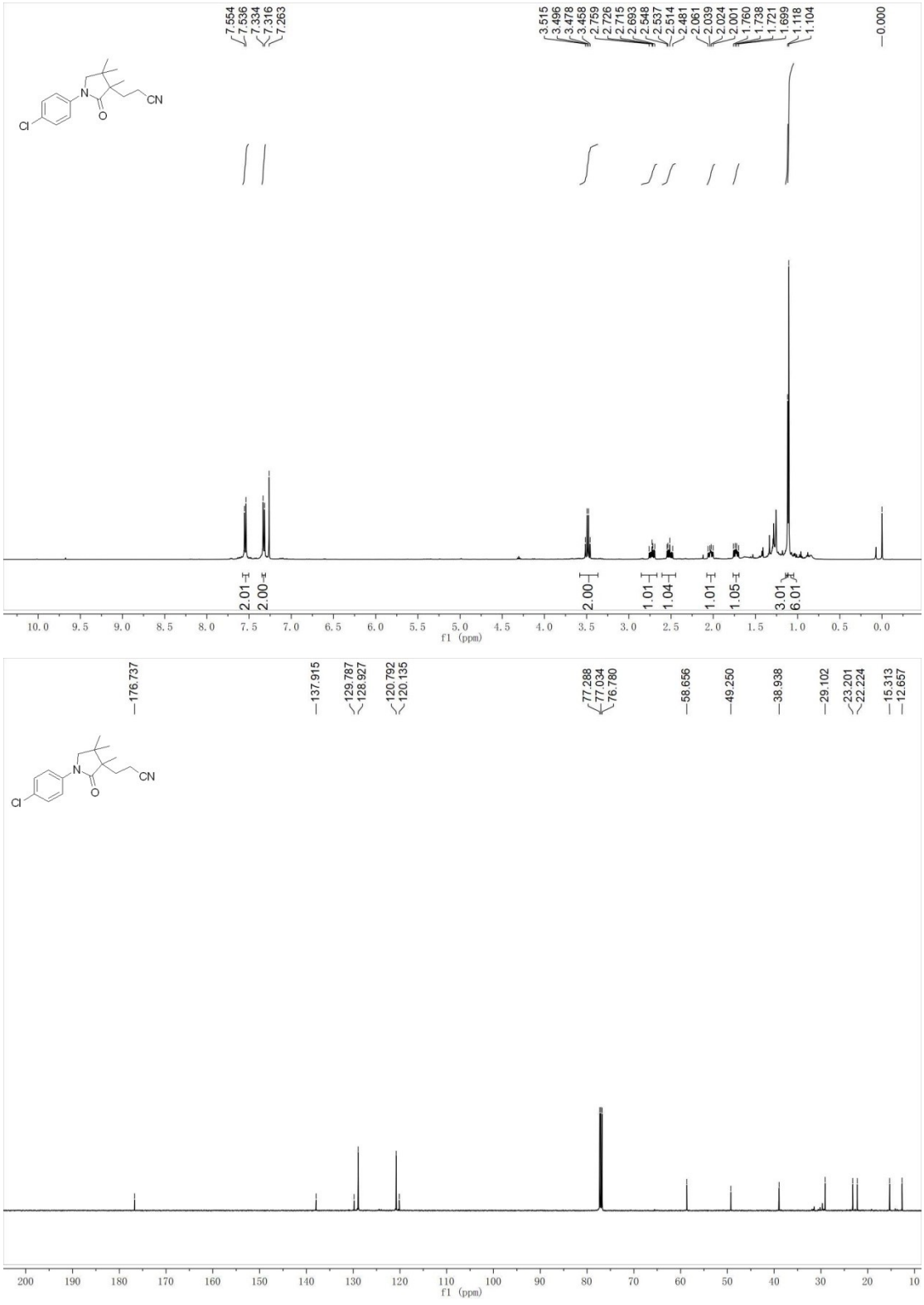


3-(1-(4-Fluorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3h)

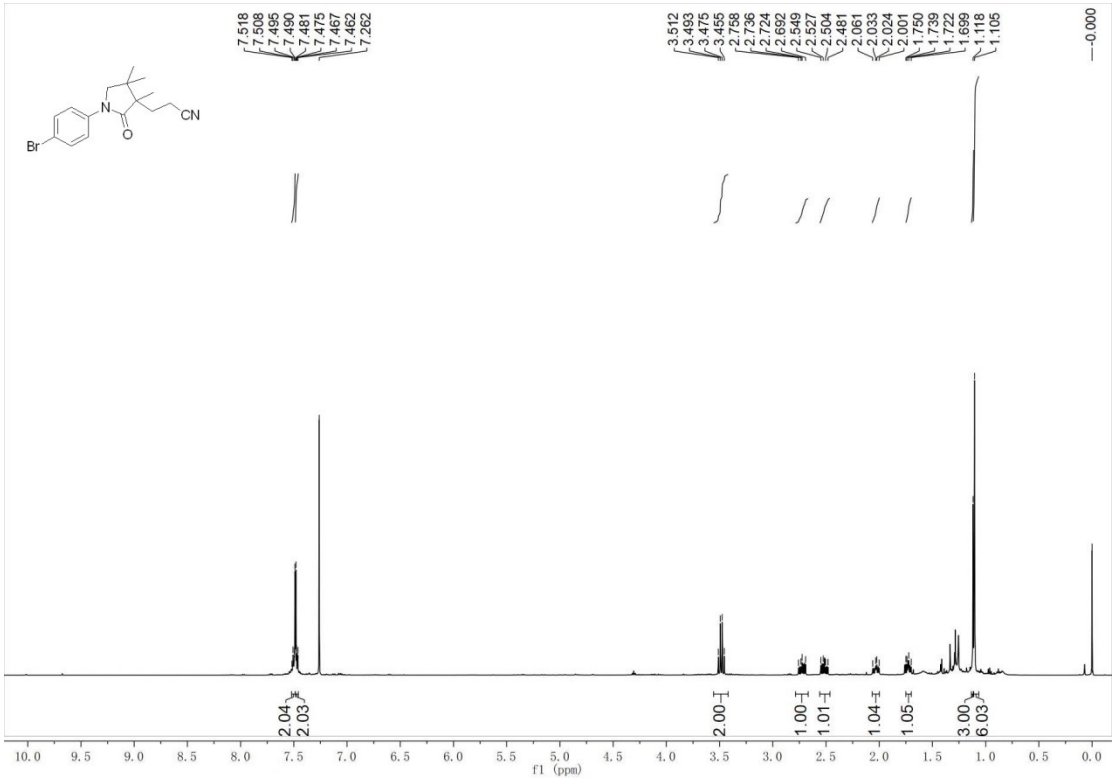


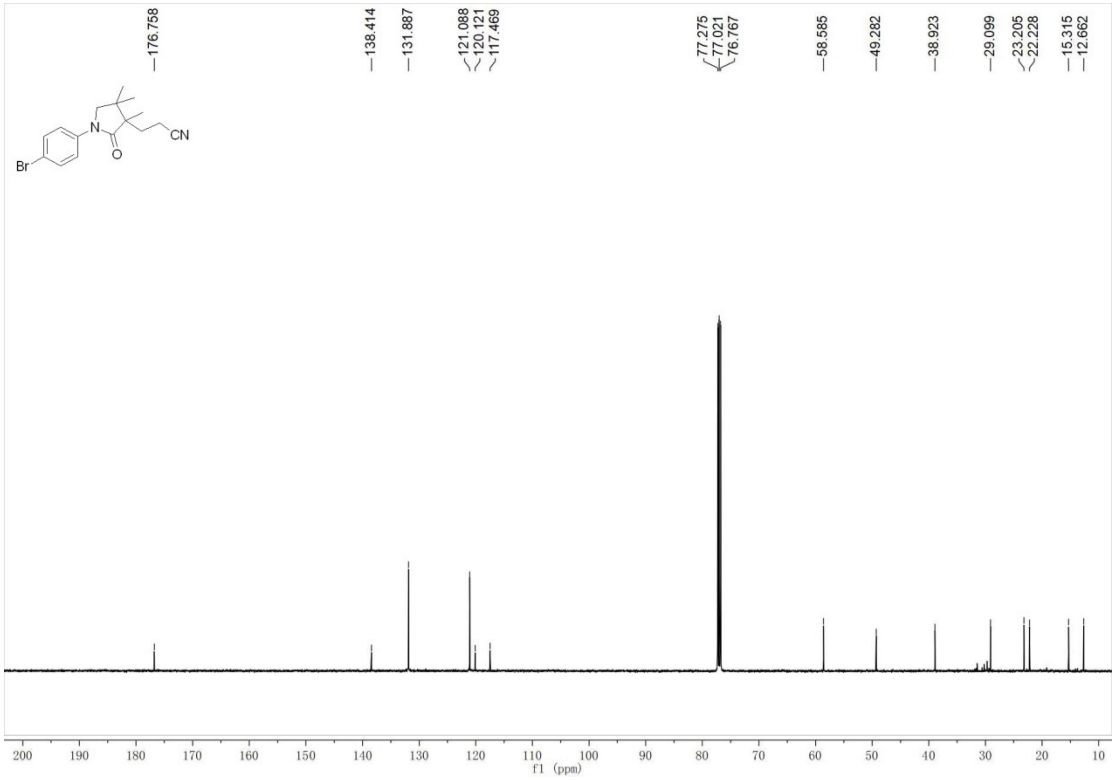


3-(1-(4-Chlorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3i),

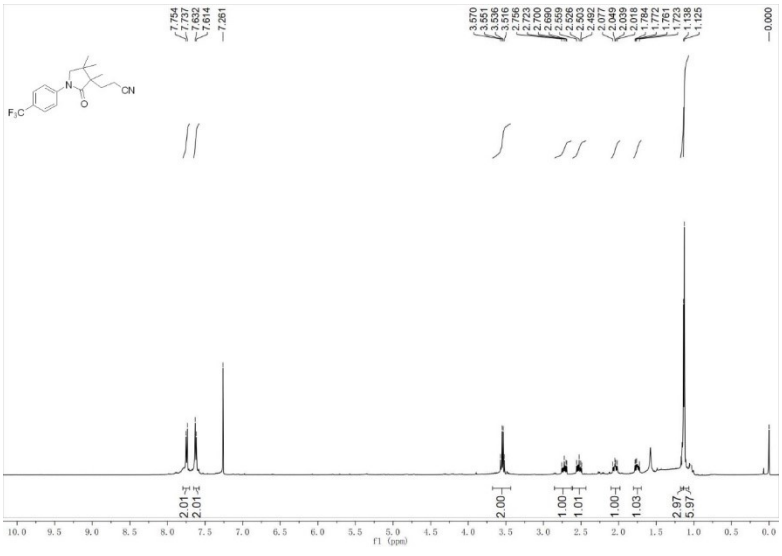


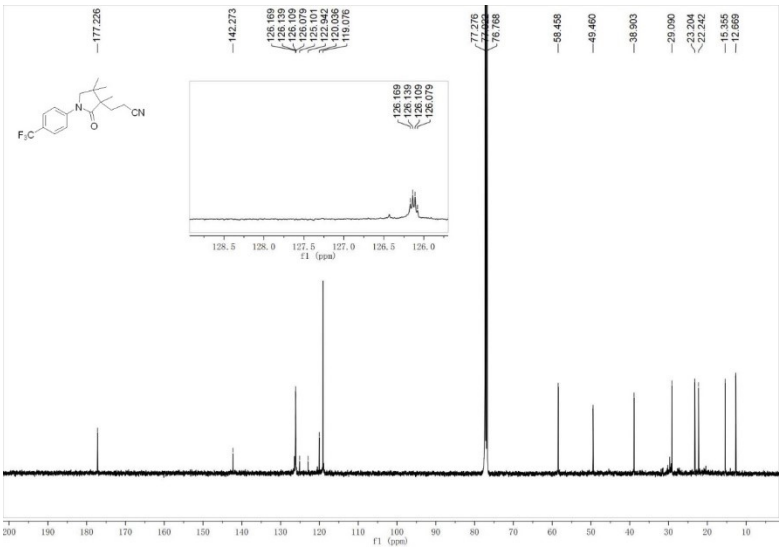
3-(1-(4-Bromophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3j)

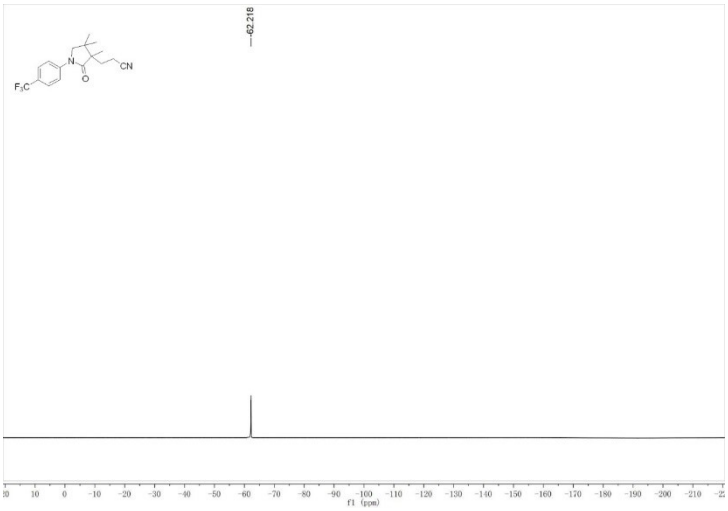




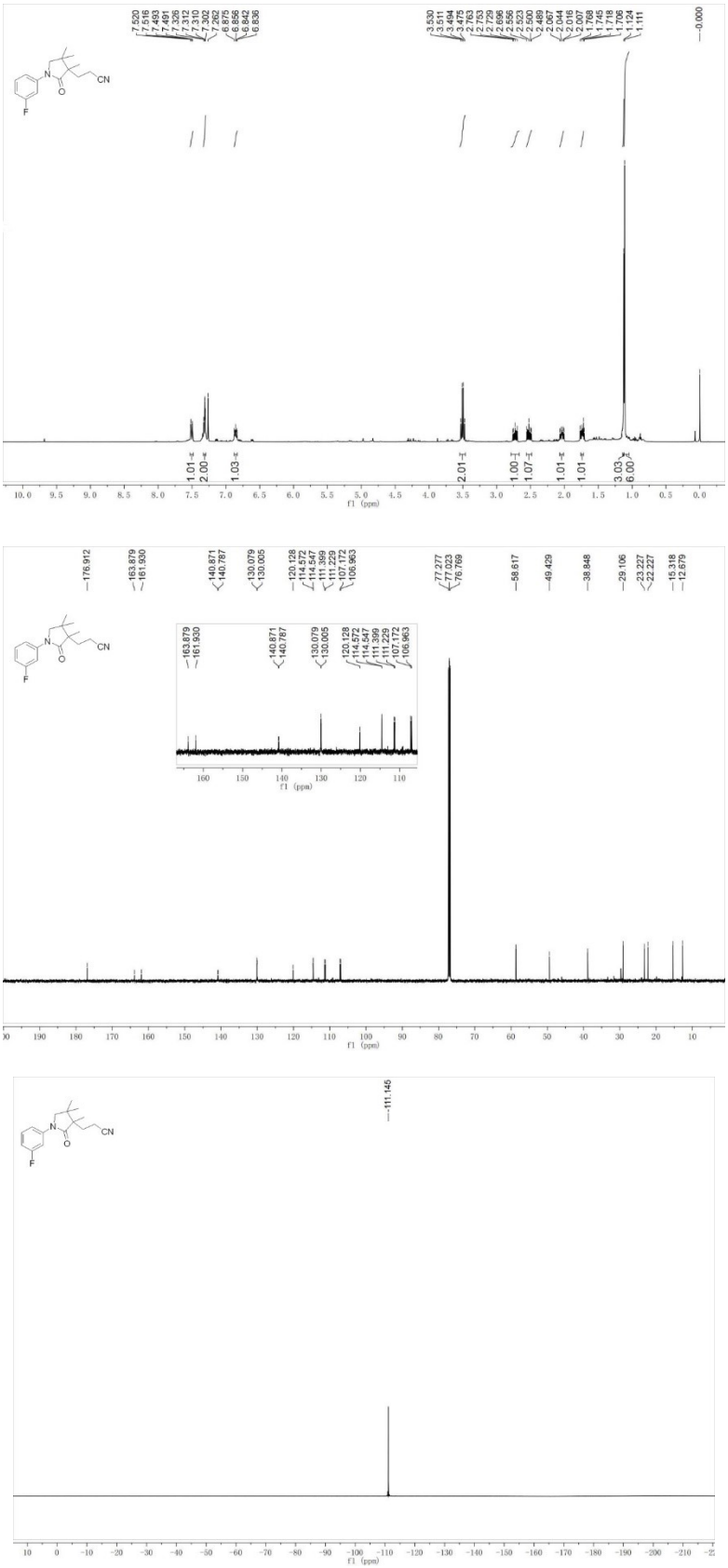
3-(3,4,4-Trimethyl-2-oxo-1-(4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)propanenitrile (3k)



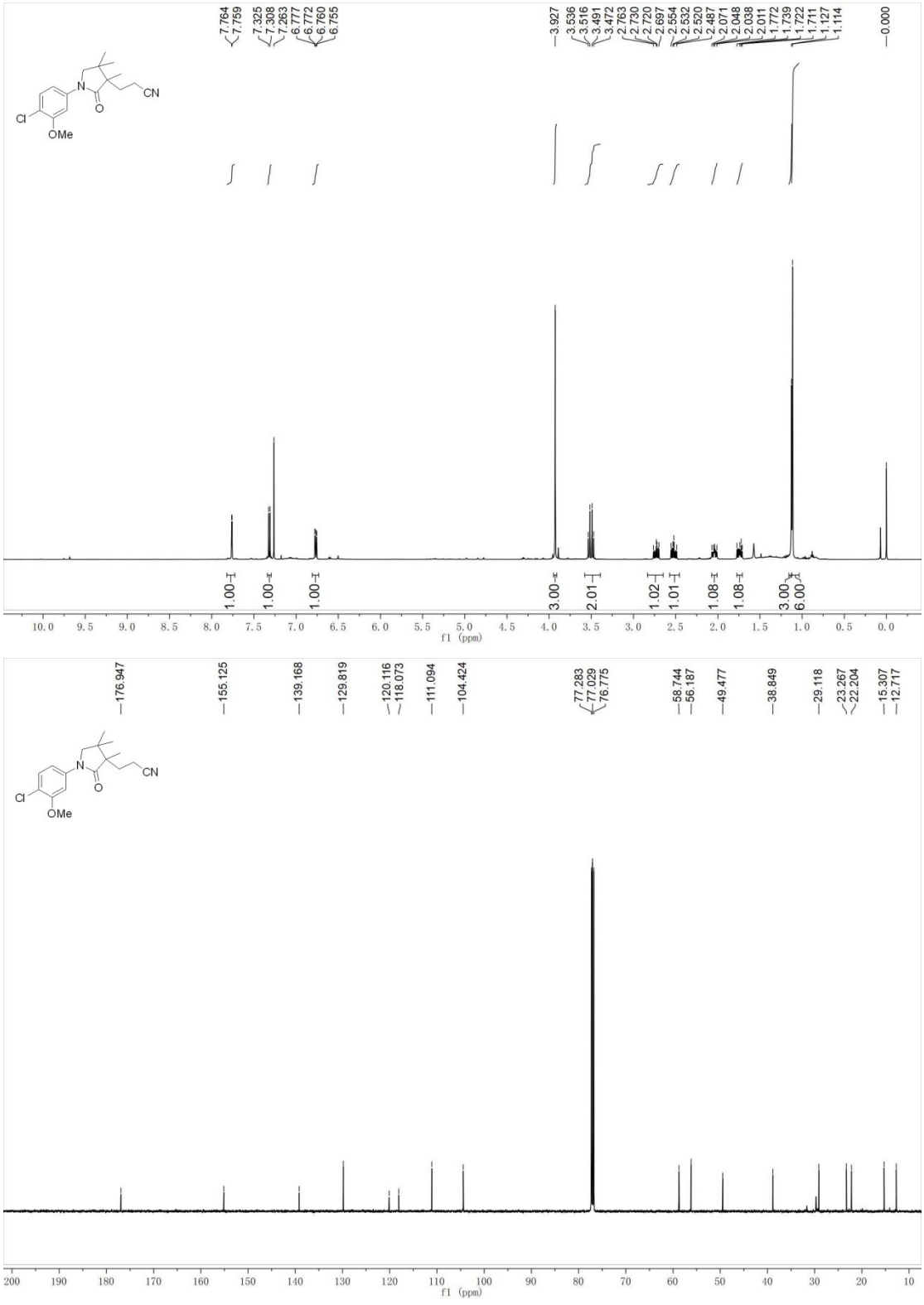




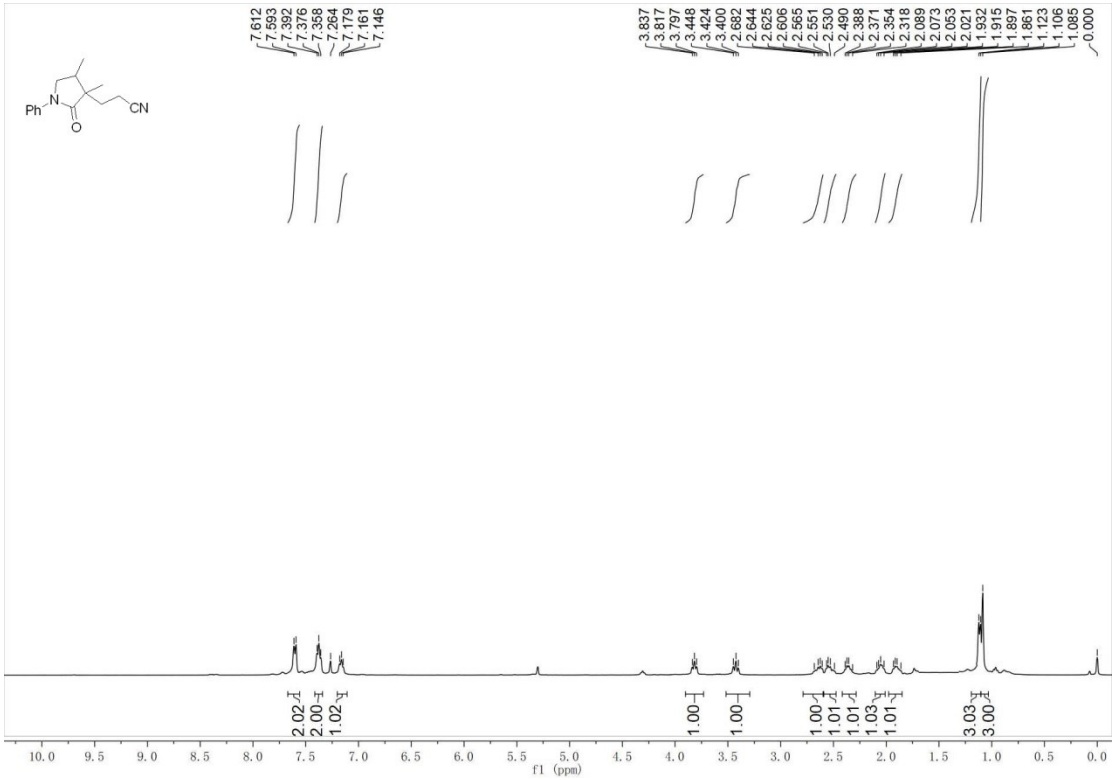
3-(1-(3-Fluorophenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3l)

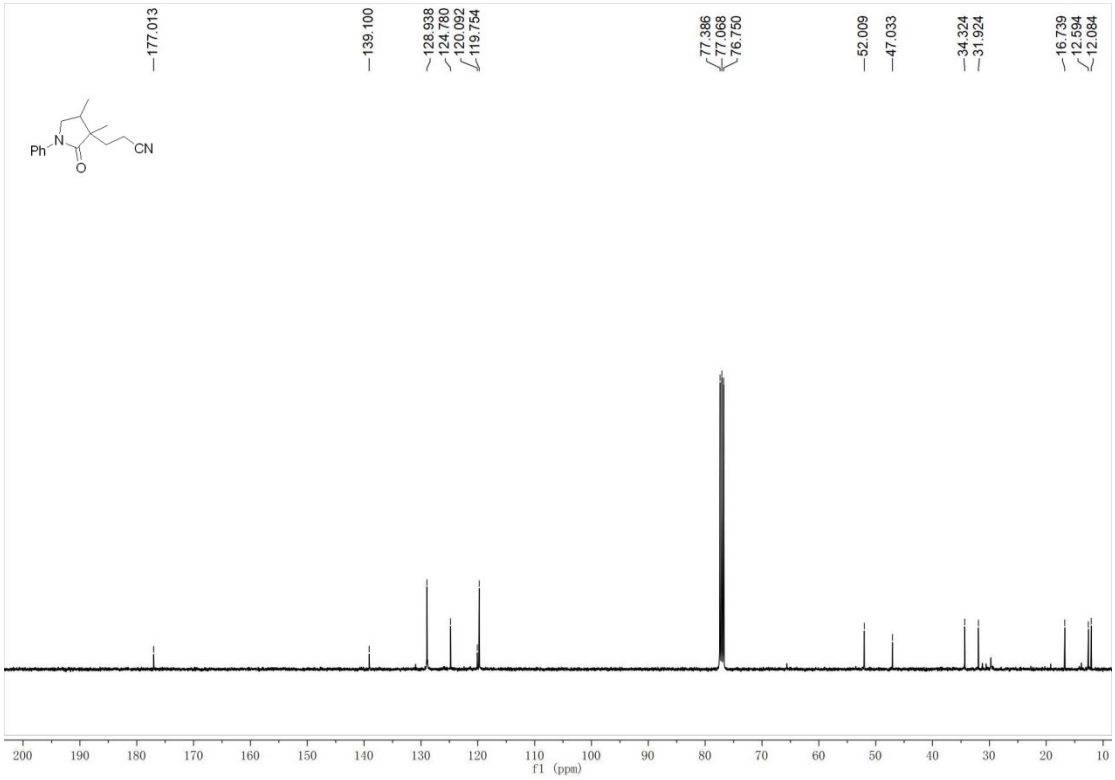


3-(1-(4-Chloro-3-methoxyphenyl)-3,4,4-trimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3m)

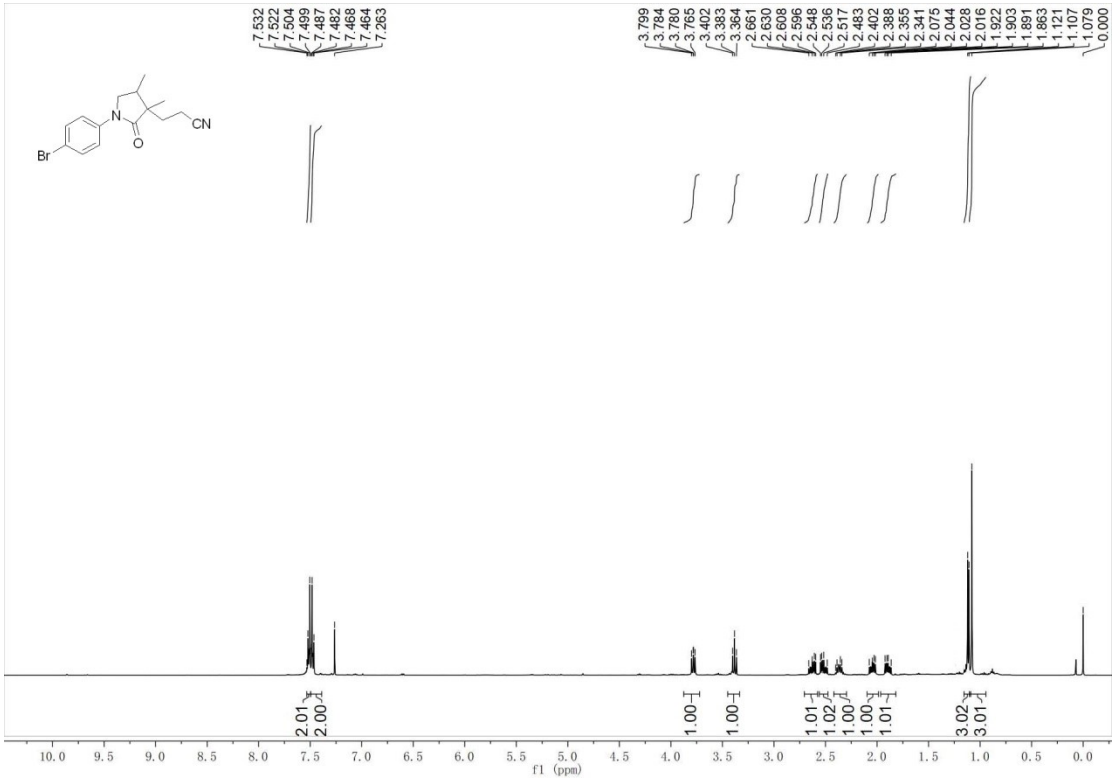


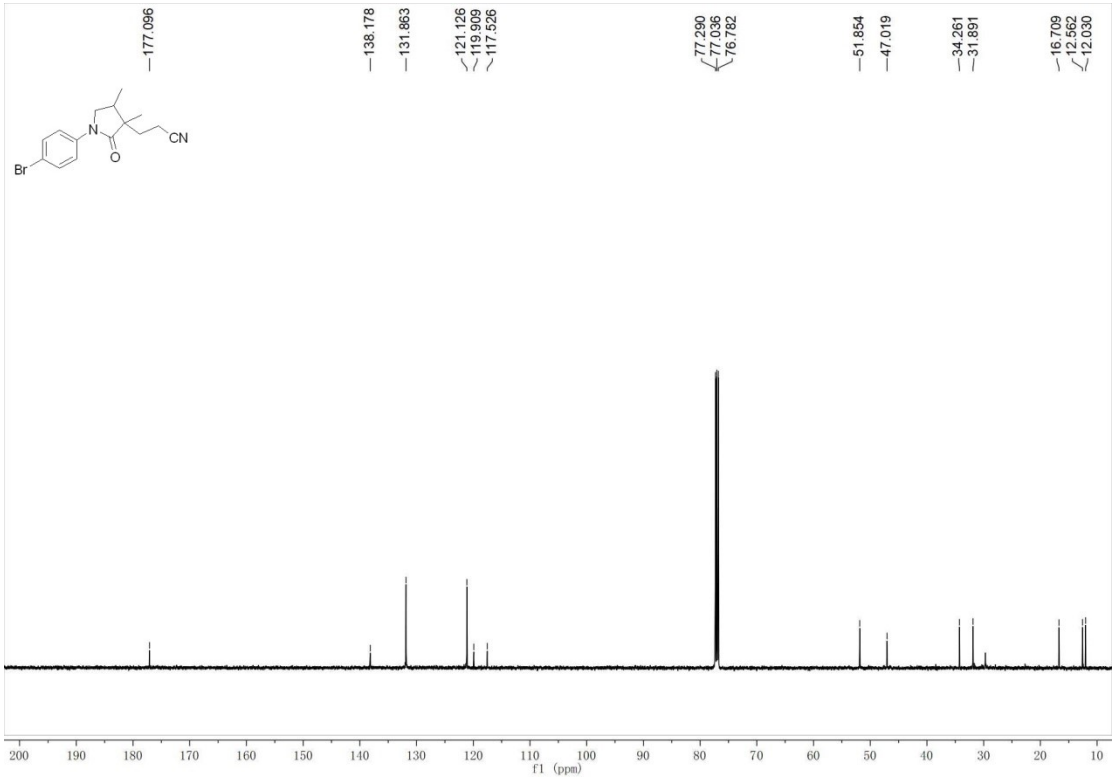
3-(3,4-Dimethyl-2-oxo-1-phenylpyrrolidin-3-yl)propanenitrile (3p)



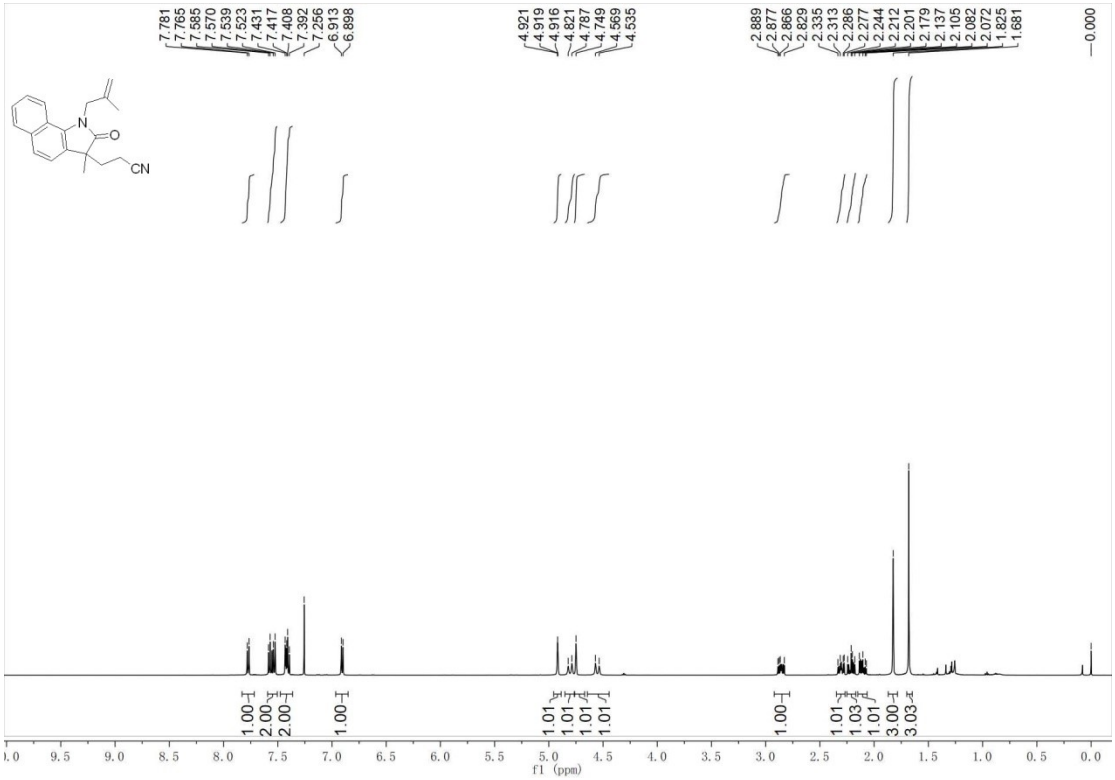


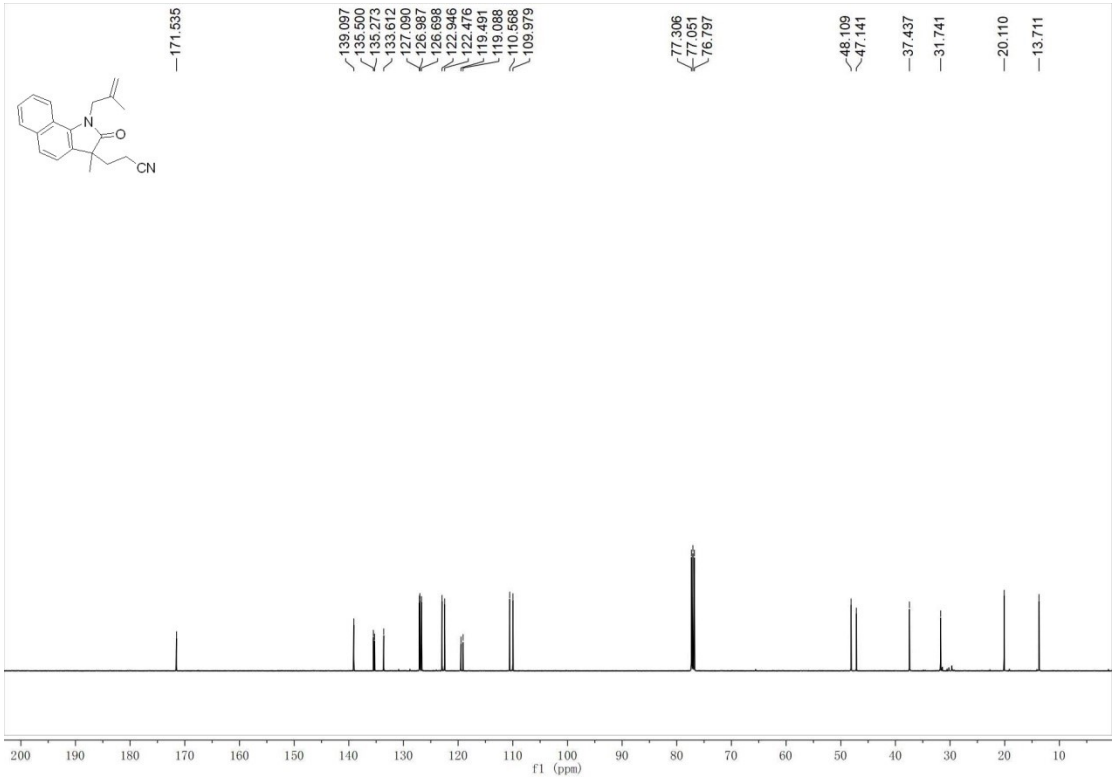
3-(1-(4-Bromophenyl)-3,4-dimethyl-2-oxopyrrolidin-3-yl)propanenitrile (3q)



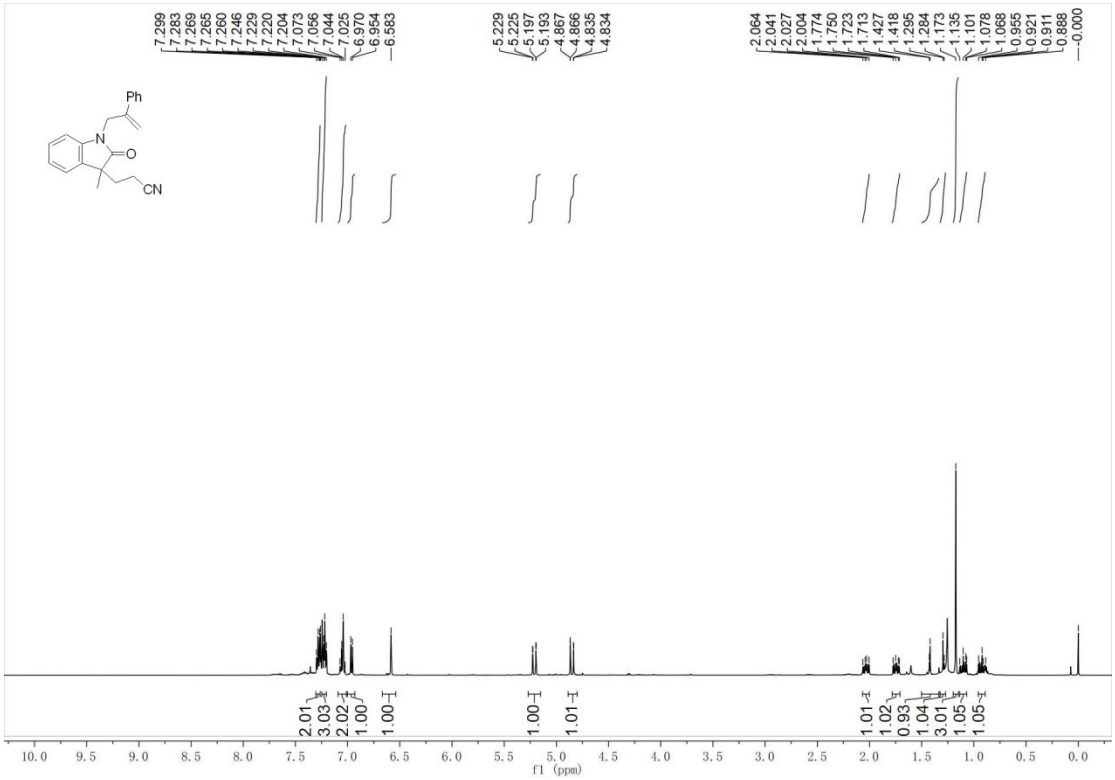


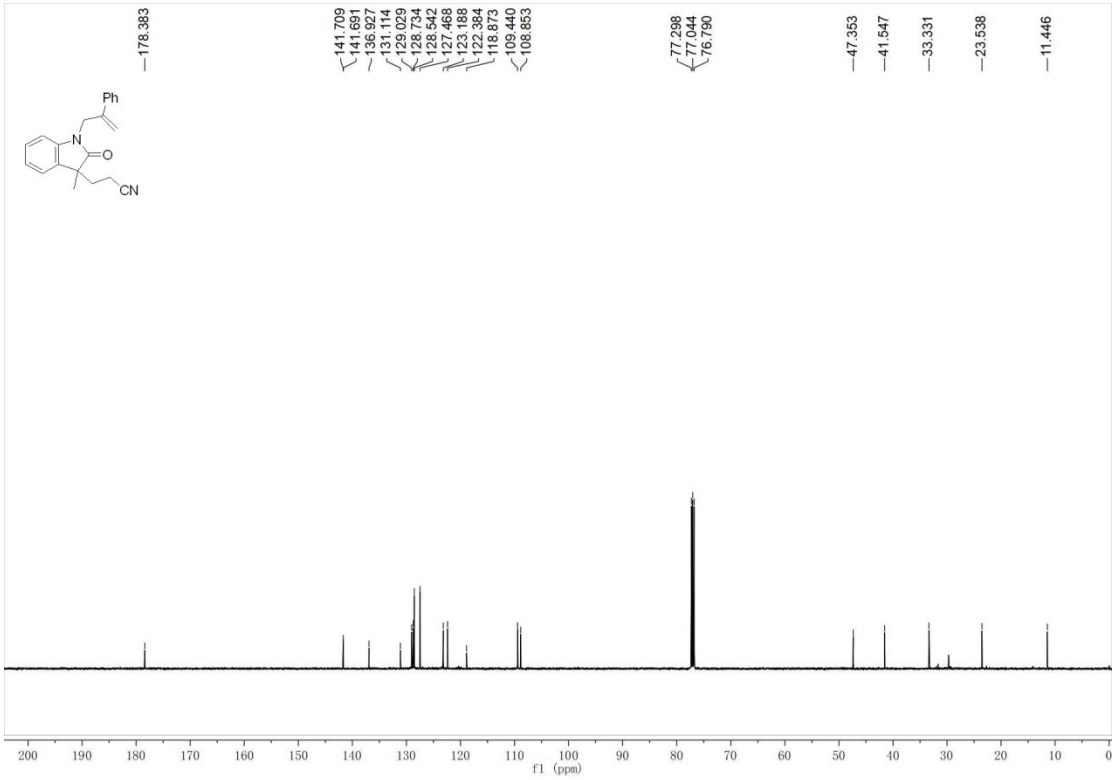
3-(3-Methyl-1-(2-methylallyl)-2-oxo-2,3-dihydro-1*H*-benzo[*g*]indol-3-yl)propanenitrile (4n)



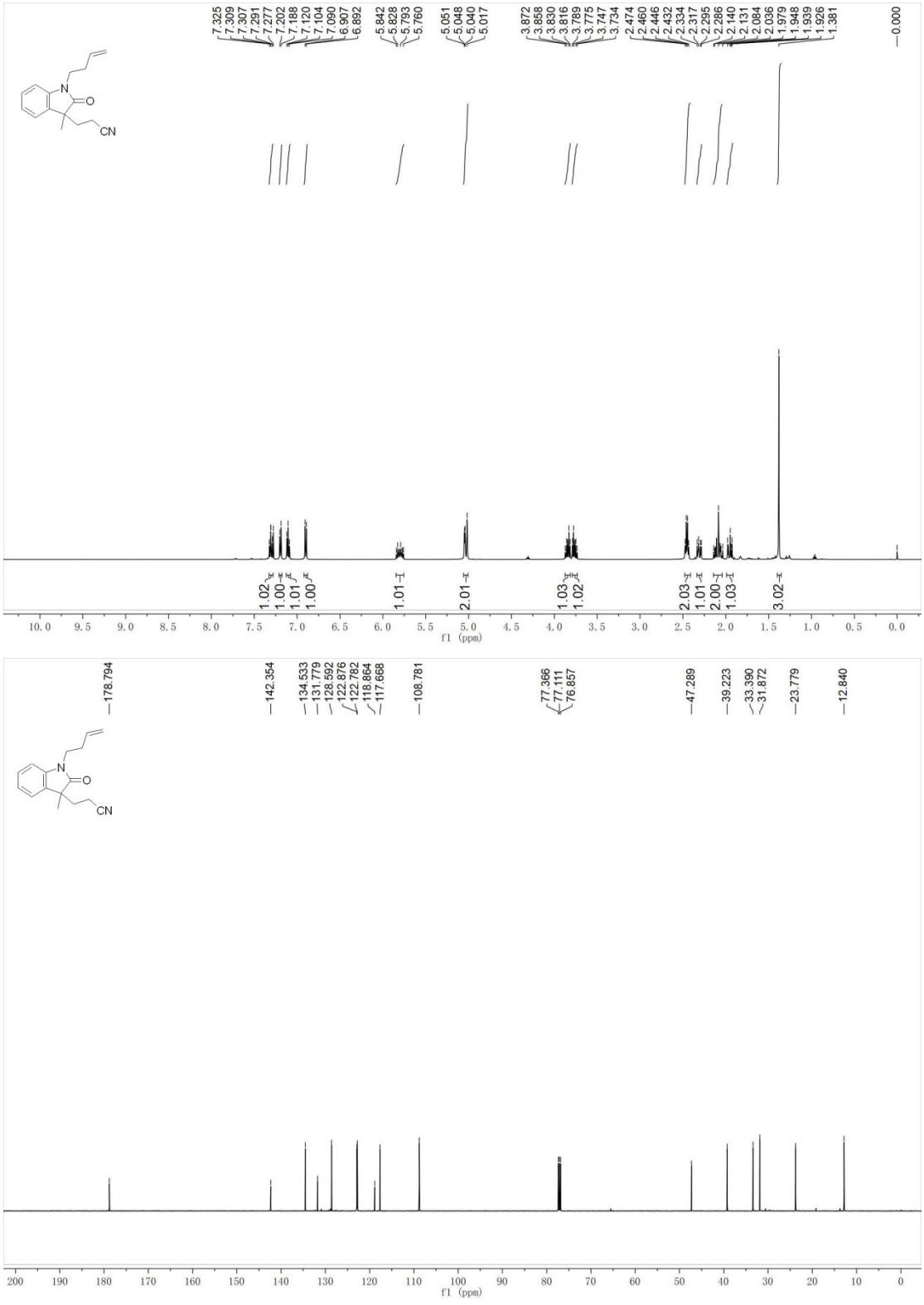


3-(3-Methyl-2-oxo-1-(2-phenylallyl)indolin-3-yl)propanenitrile (4r),

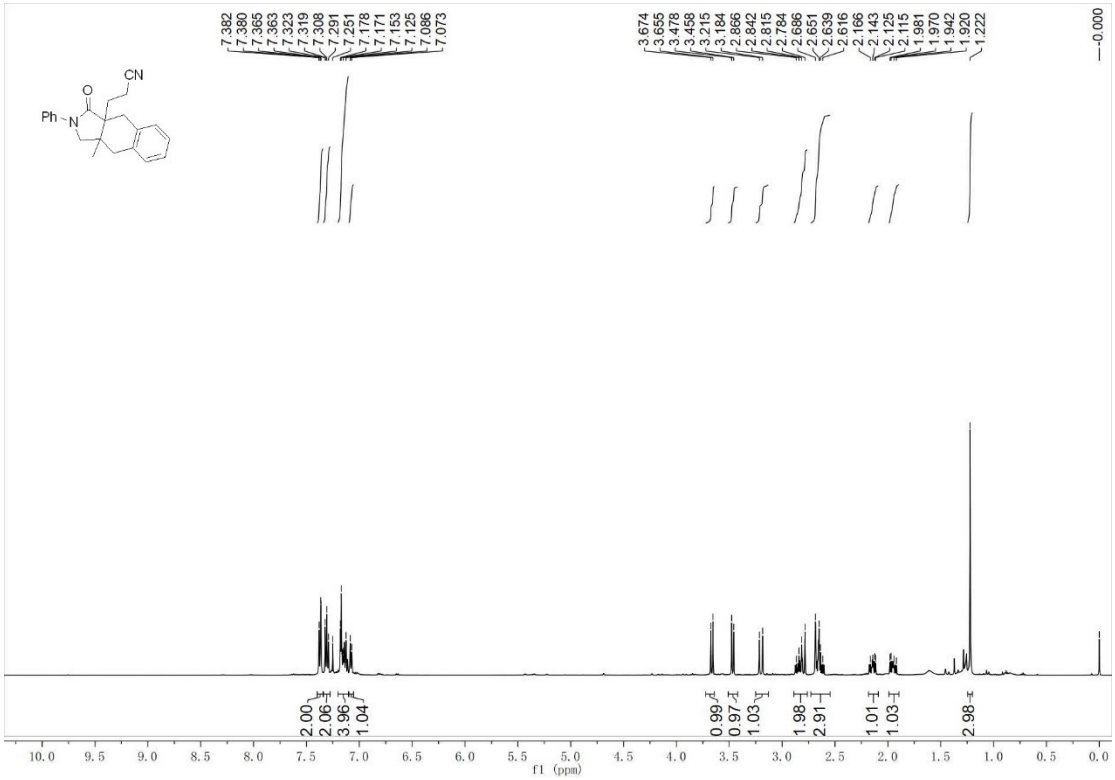


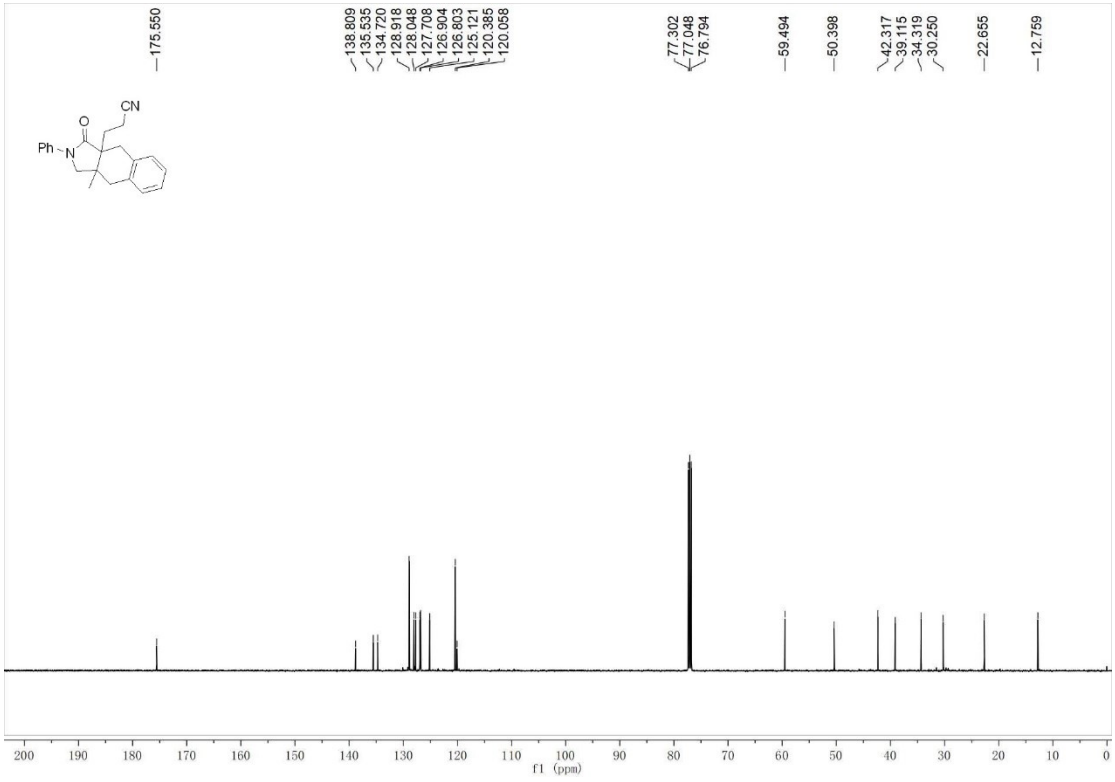


3-(1-(But-3-en-1-yl)-3-methyl-2-oxoindolin-3-yl)propanenitrile (4s)

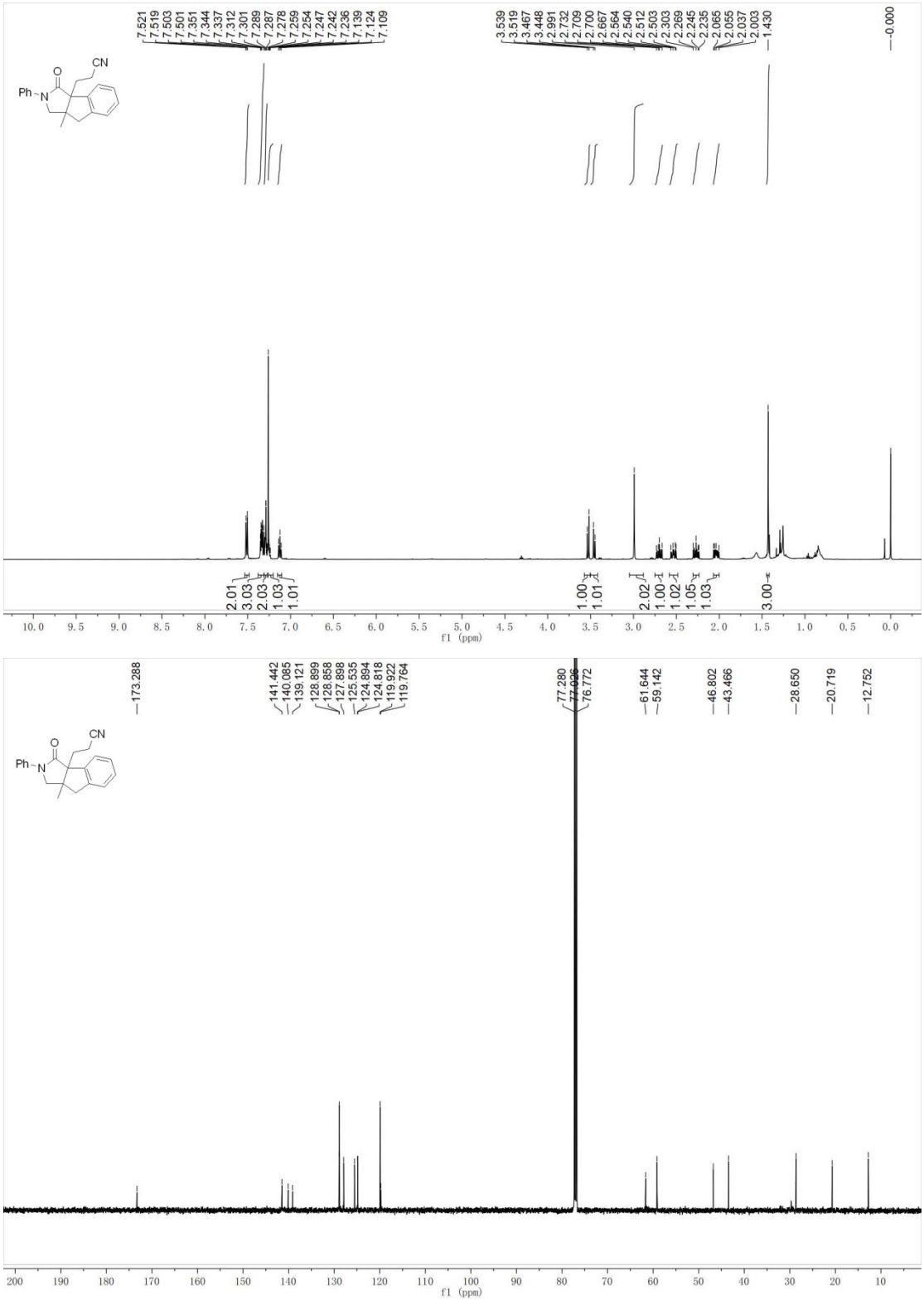


3-(9a-Methyl-3-oxo-2-phenyl-1,2,3,4,9,9a-hexahydro-3a*H*-benzo[*f*]isoindol-3a-yl)propanenitrile (5a)

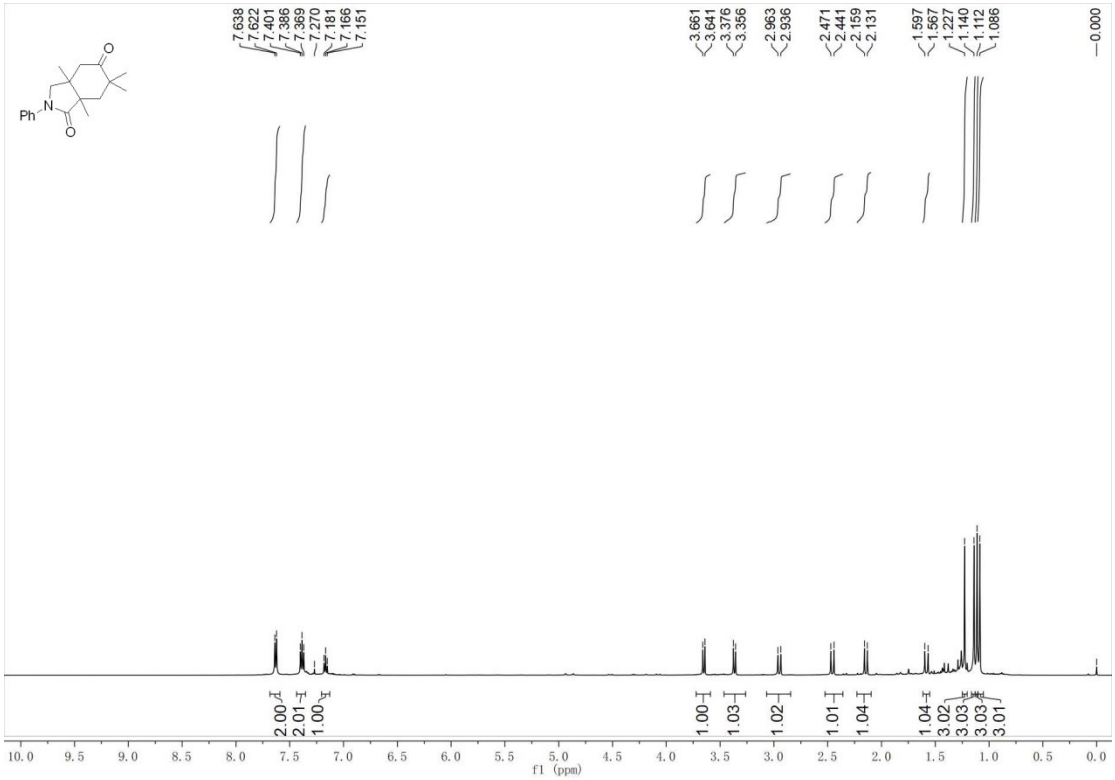


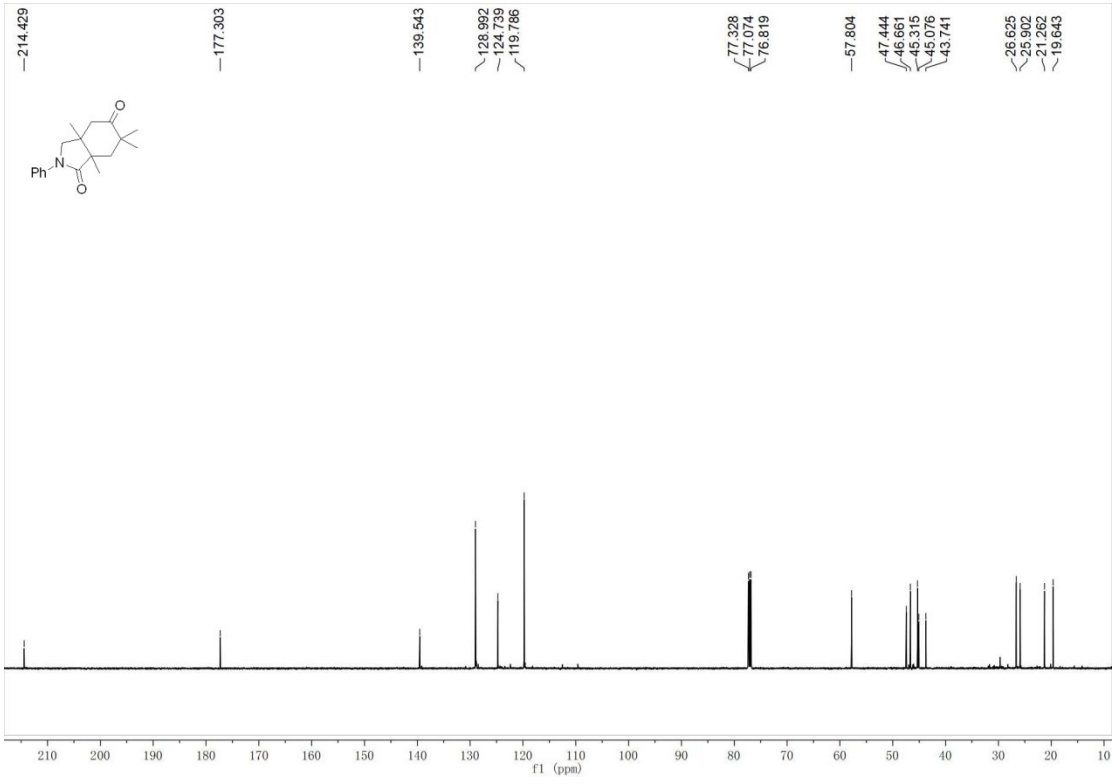


3-(8a-Methyl-3-oxo-2-phenyl-2,3,8,8a-tetrahydroindeno[1,2-*c*]pyrrol-3a(1*H*)-yl)propanenitrile (5b)

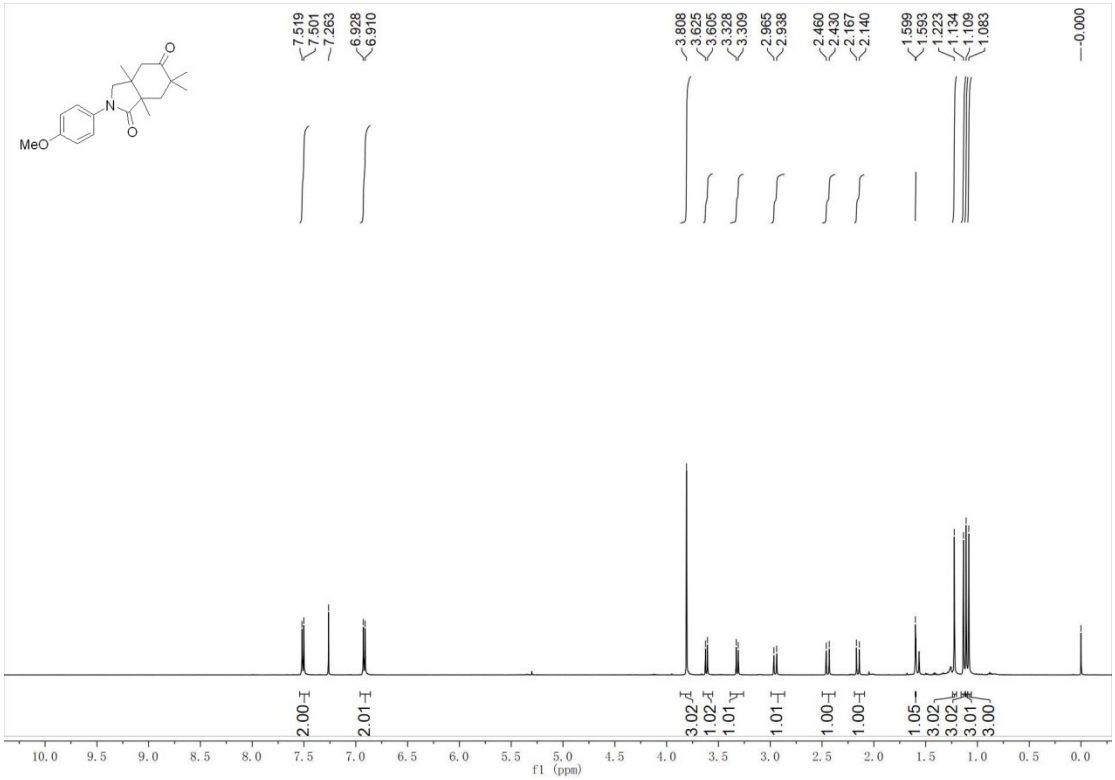


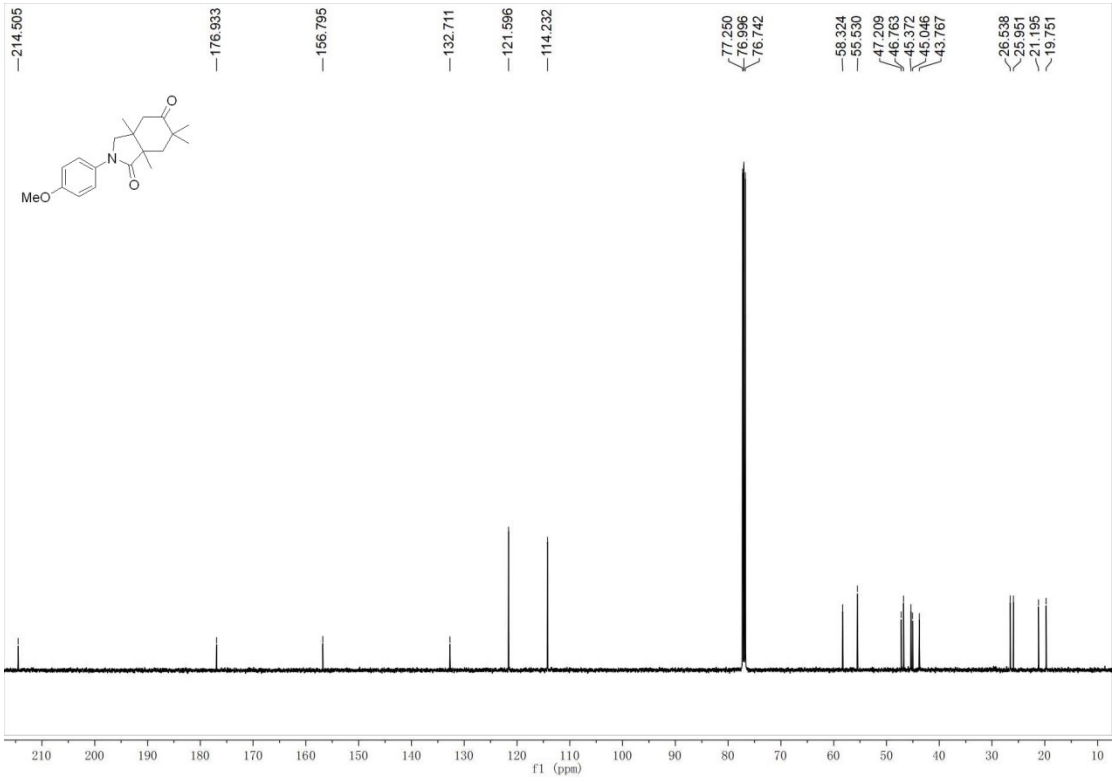
3a,6,6,7a-Tetramethyl-2-phenylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6a)



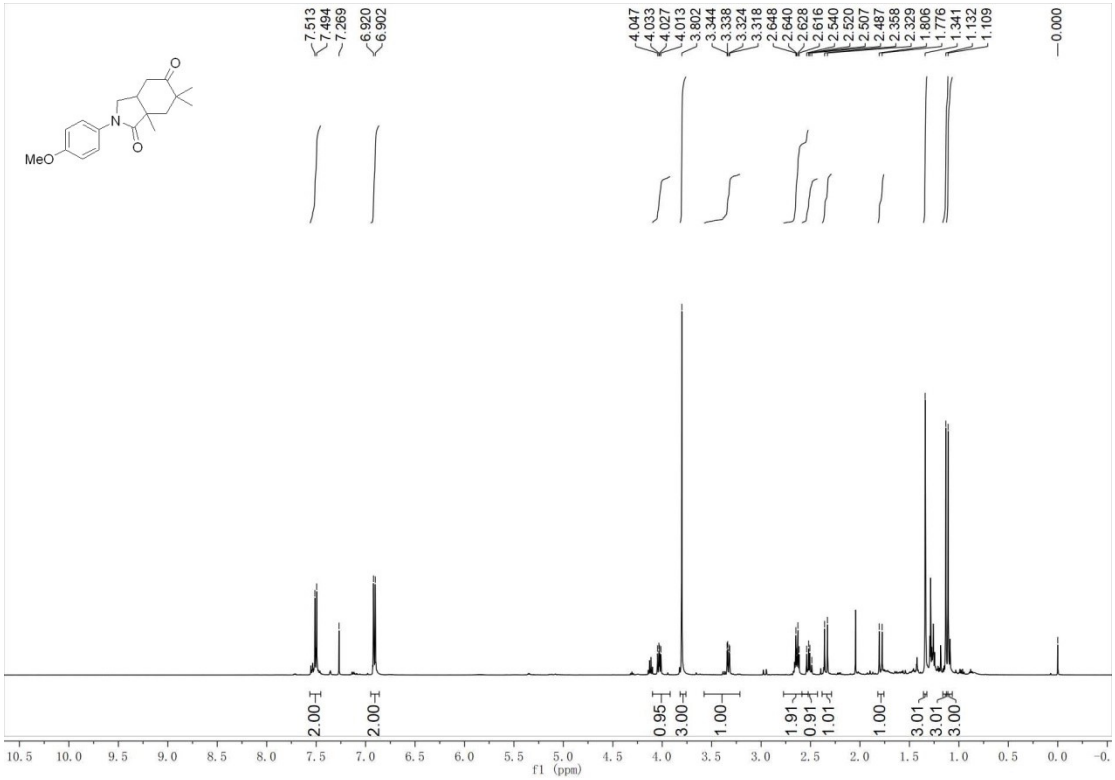


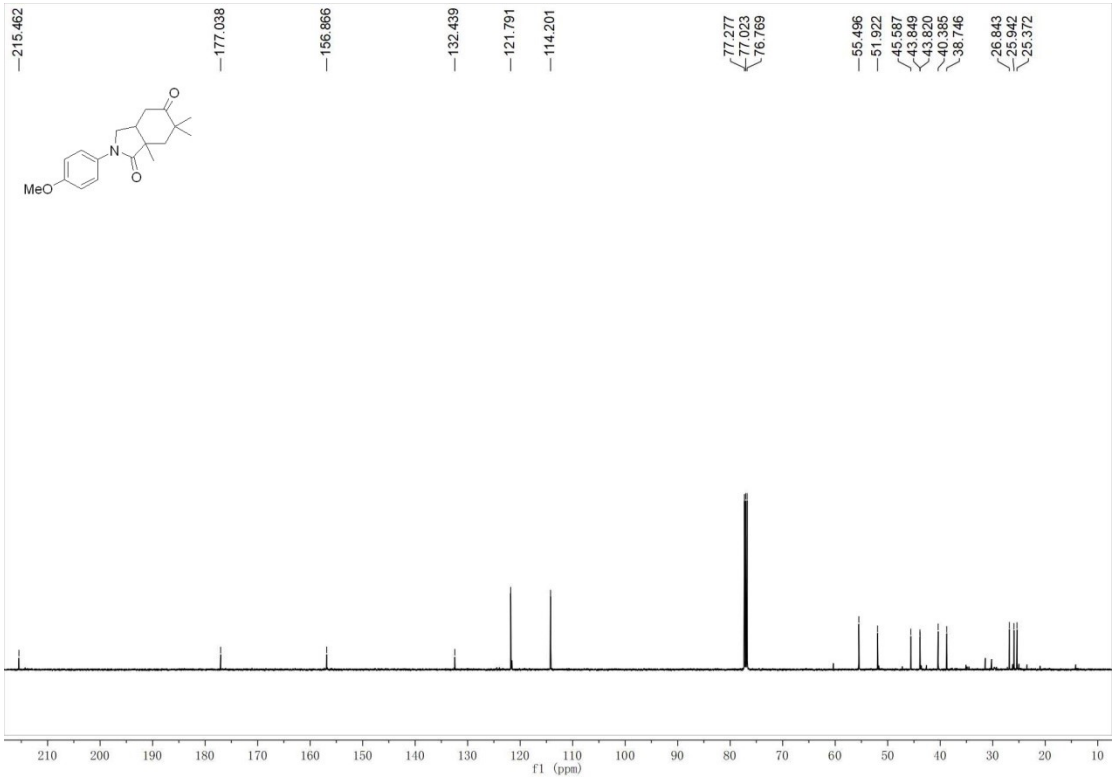
2-(4-Methoxyphenyl)-3a,6,6,7a-tetramethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6b)



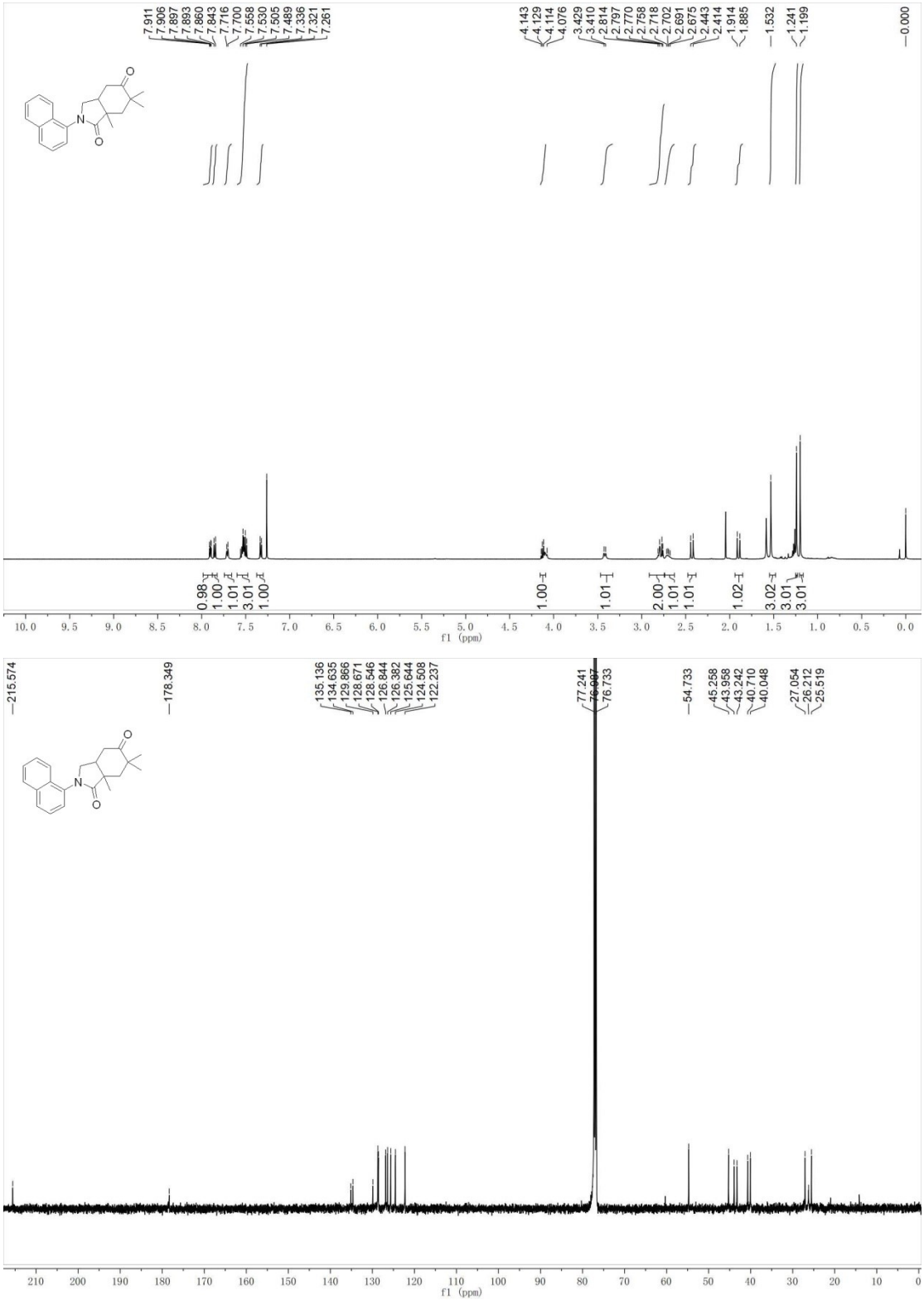


2-(4-Methoxyphenyl)-6,6,7a-trimethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6c)

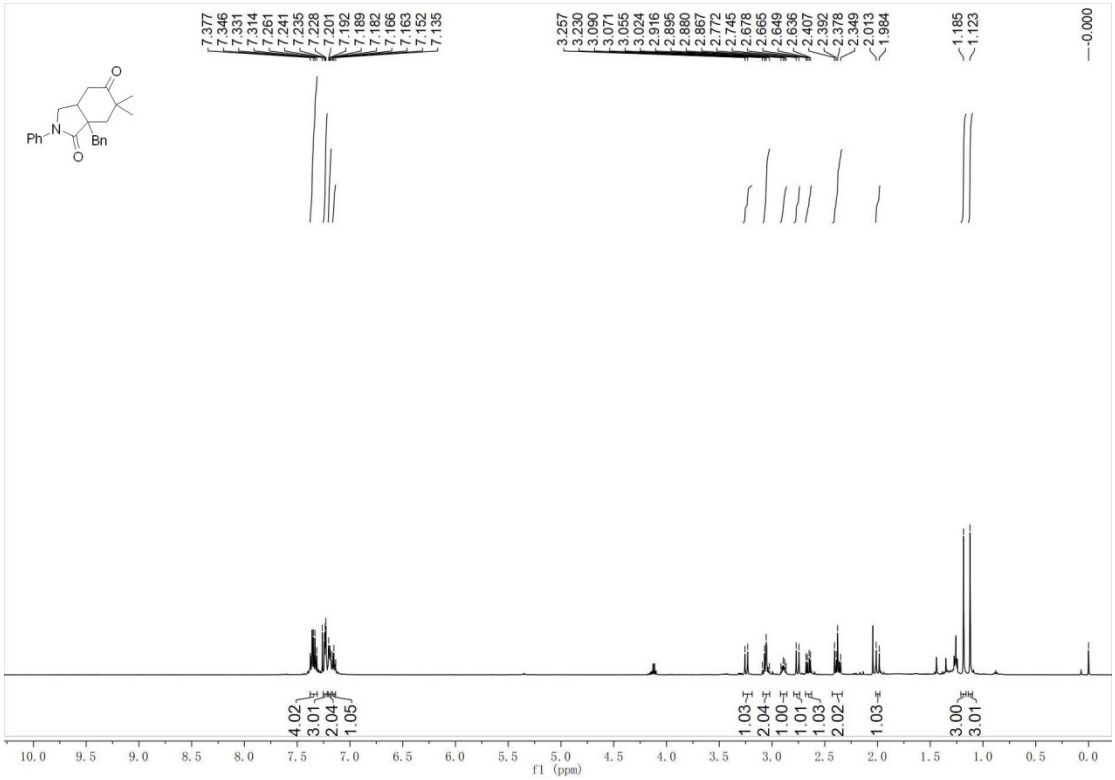


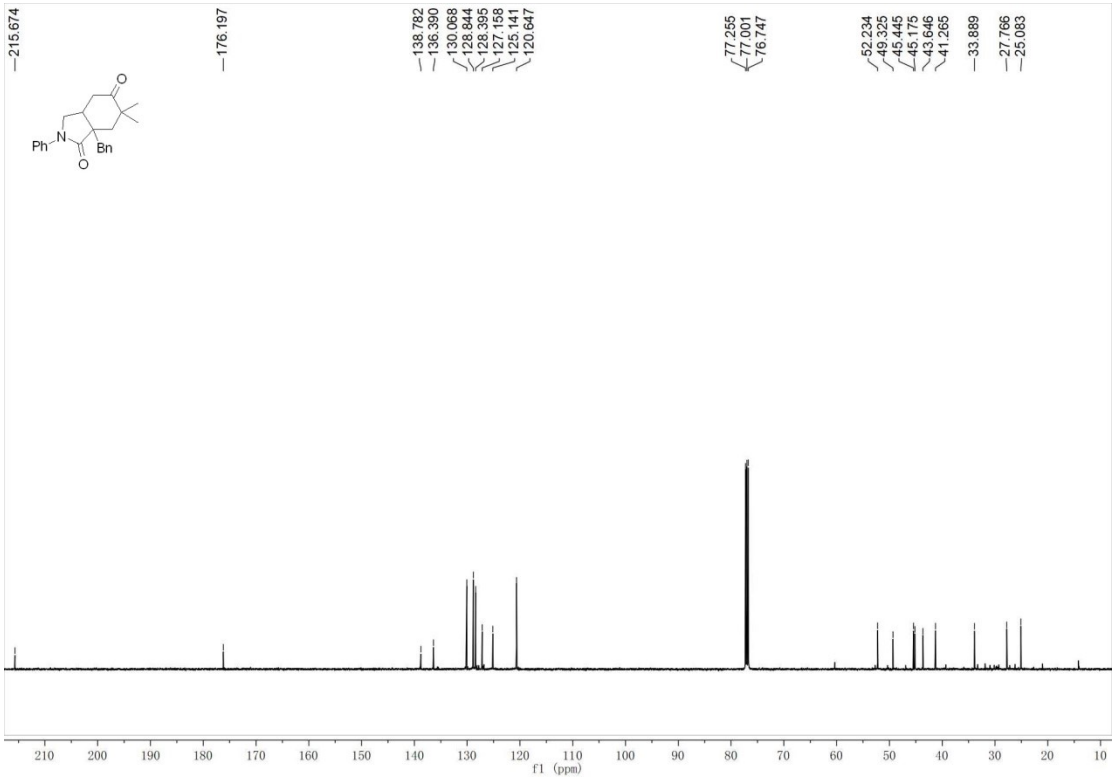


6,6,7a-Trimethyl-2-(naphthalen-1-yl)hexahydro-1*H*-isoindole-1,5(4*H*)-dione (6d)

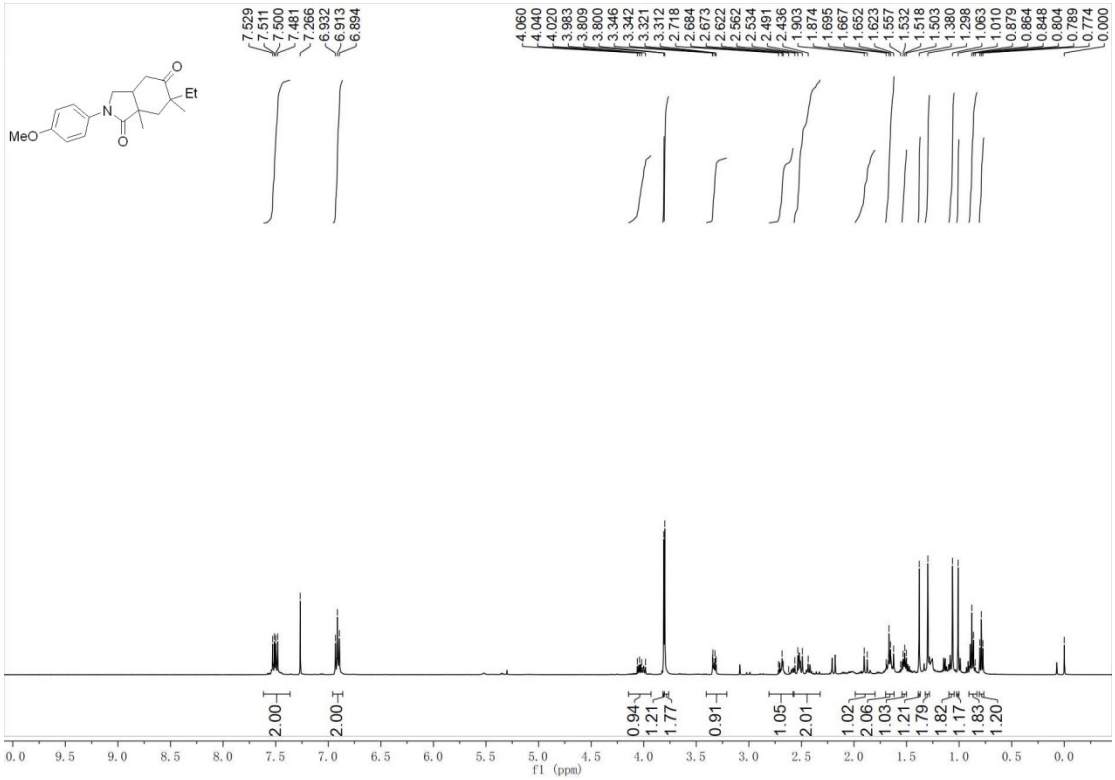


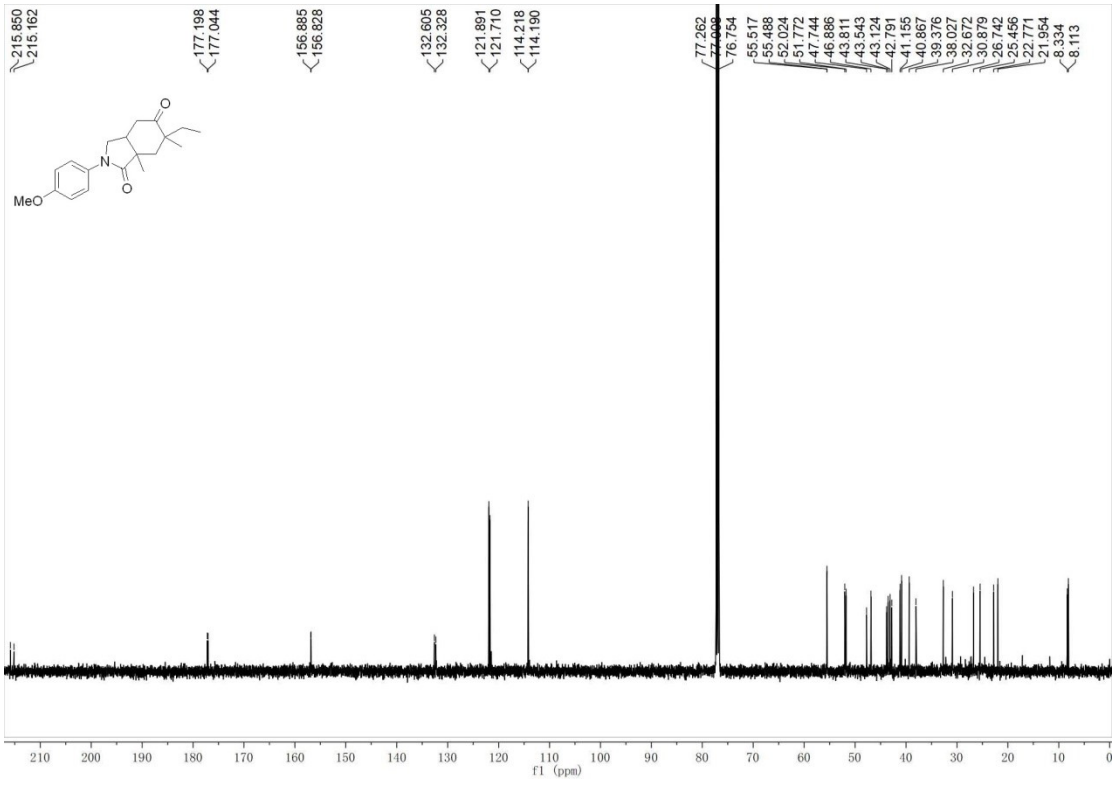
7a-Benzyl-6,6-dimethyl-2-phenylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6e)



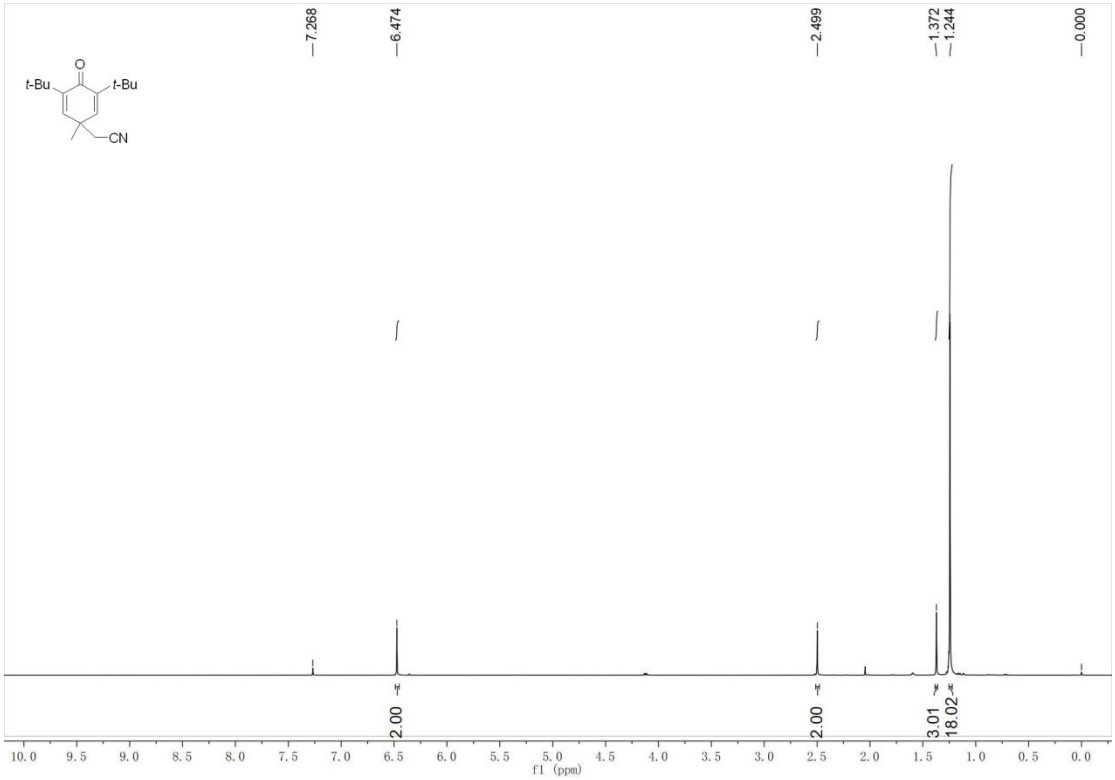


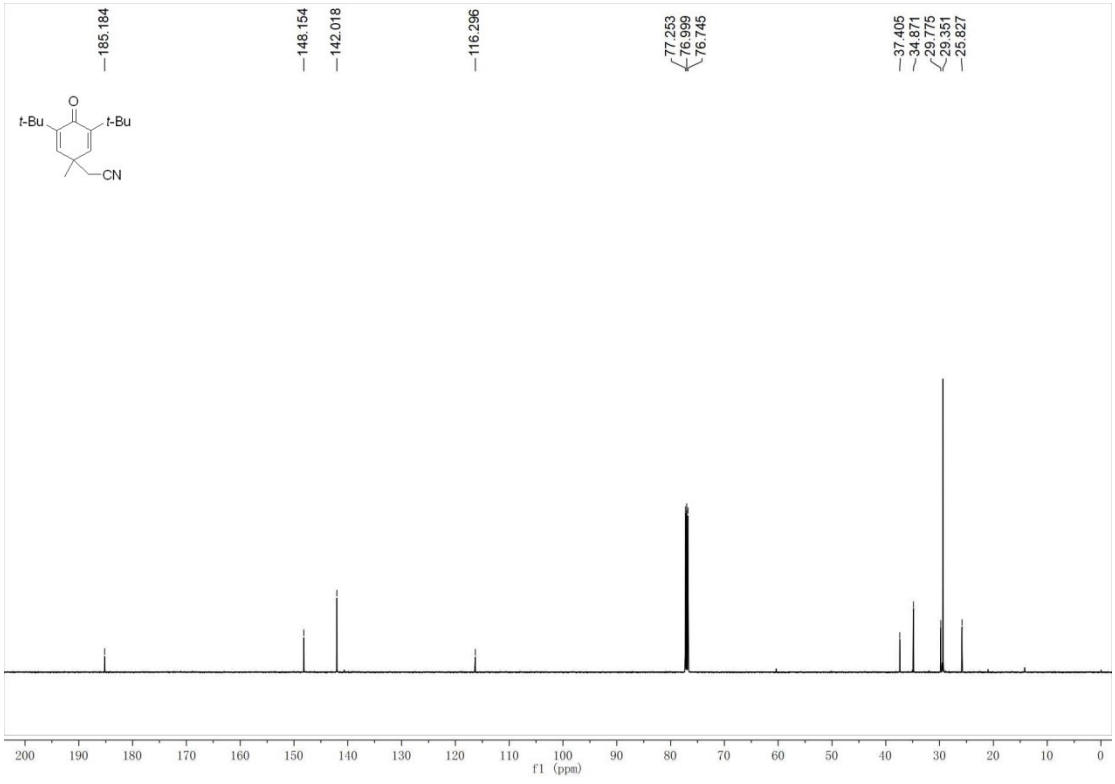
6-Ethyl-2-(4-methoxyphenyl)-6,7a-dimethylhexahydro-1*H*-isoindole-1,5(4*H*)-dione (6f)



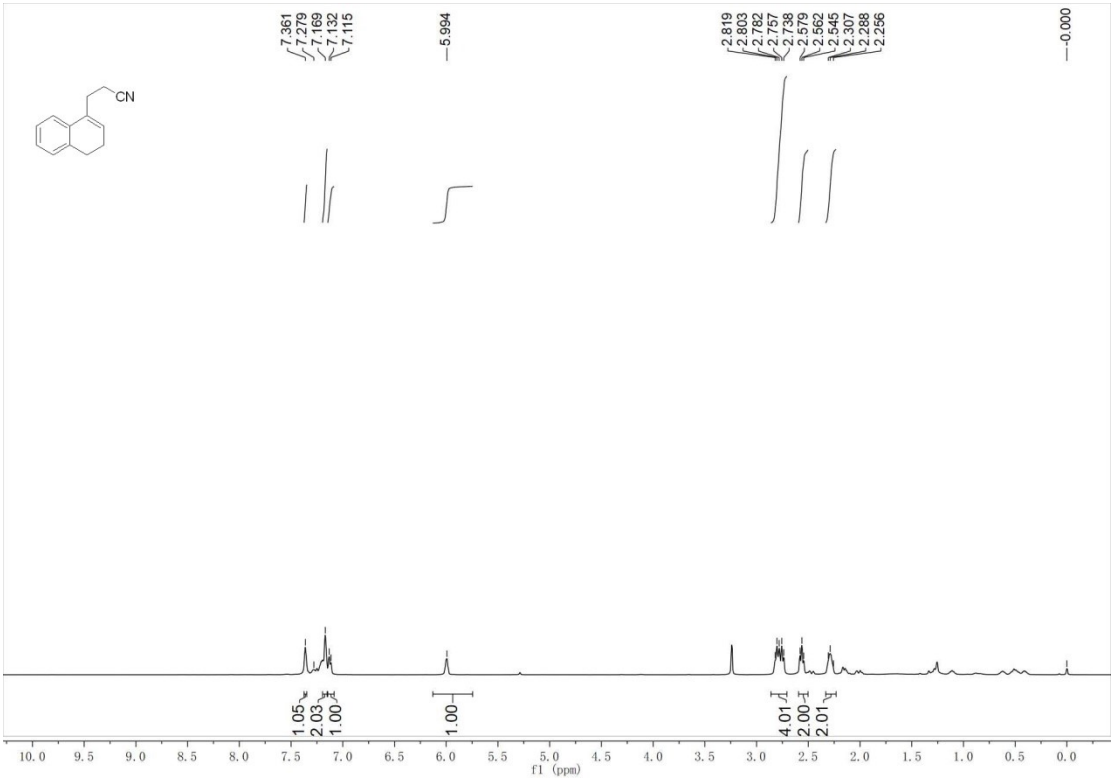


2-(3,5-di-*tert*-Butyl-1-methyl-4-oxocyclohexa-2,5-dien-1-yl)acetonitrile (7a)





3-(3,4-Dihydronaphthalen-1-yl)propanenitrile (8a)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2.579
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2.545
2.307
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2.03
1.00
1.00
4.01
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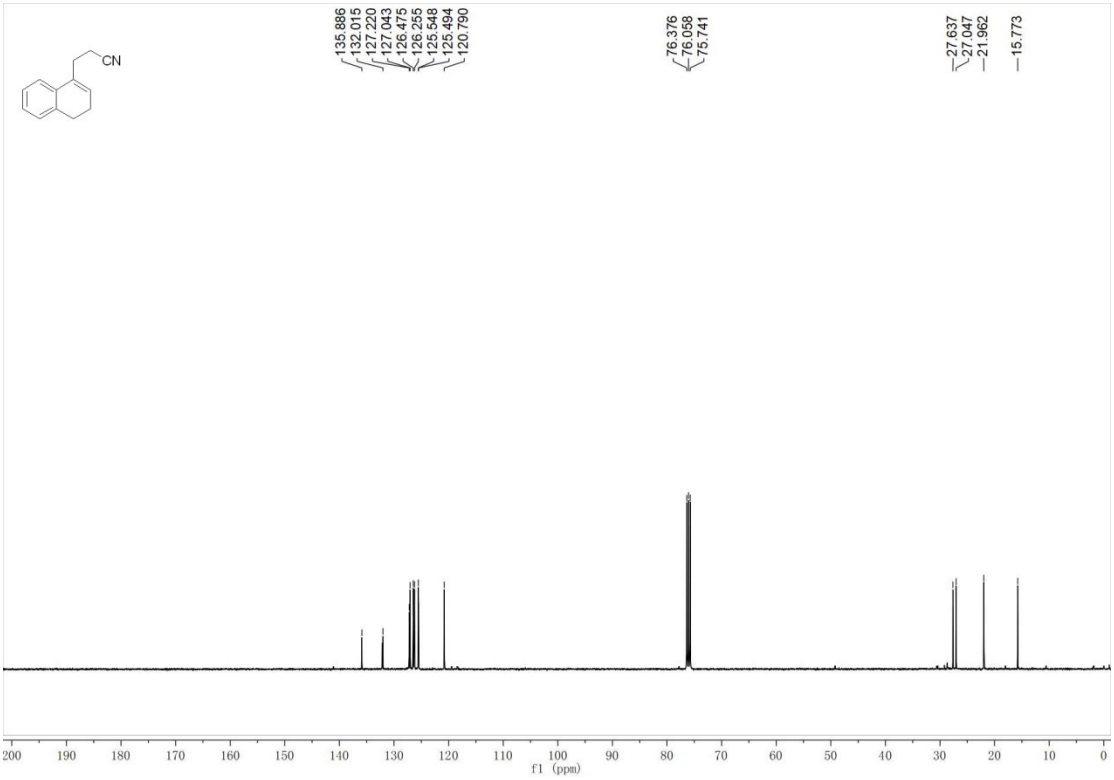
2.01
f1 (ppm)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21.962
15.773
CN
f1 (ppm)