Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Transition-metal-catalyst-free reaction of amides and acetonitriles: Synthesis of ß-ketonitriles

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Contents

1. General Information

All reagents were purchased and used without further purification. ^{1}H spectra were recorded in $CDCl_3$ on 500 or 600 MHz NMR spectrometers and data are reported as follows: chemical shift, multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of a triplets (dt), doublet of quartet(dq), doublet of doublet of doublet (ddd), doublet of doublet of doublet of doublet (dddd), triplet of doublets (td), quartet of doublet (qd), and multiplet (m)], coupling constants (Hz) and integration. ^{13}C spectra were recorded in CDCl3 on 126 or 151 MHz NMR spectrometers and resonances (δ) are given in ppm. High resolution mass spectra was recorded on a time of flight (TOF) mass spectrometer.

2. General procedure for the synthesis of starting materials

Starting materials of amides were synthesized according to corresponding literature. Citations to the references containing characterization data for these compounds are given: **1a**[1], **1a-1**[1], **1a-2**[2], **1a-3**[3], **1a-4**[4], **1a-5**[5], **1a-6**[6], **1a-7**[6], **1a-8**[3], **1a-9**[7], **1a-10**[8], **1a-11**[9], **1a-12**[10], **1a-13**[10], **1a-14**[11], **1a-15**[11], **1a-18**[12], **1a-19**[12], **1a-20**[13]

3. General procedure for the synthesis of ß-ketonitrile (3) from tertiary amides

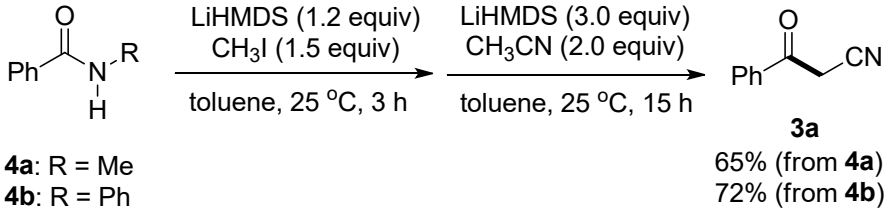
To a 20 mL vial was charged with tertiary amide (1 mmol, 1.0 equiv), acetonitrile (2 mmol, 2.0 equiv) and toluene (3.5 mL), and then LiHMDS (3 mL, 3.0 equiv, 1 M in THF) was added under argon atmosphere. The resulting solution was stirred for 15 h. The reaction was then quenched with saturated NH4Cl (7 mL) and diluted with ethyl acetate (50 mL). The organic layer was washed with brine (20 mL × 2), dried with anhydrous MgSO4, filtered and concentrated under vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate/hexane to afford the product.

4. Gram-scale synthesis of benzoylacetonitrile from *N*-phenyl-*N*-tosylbenzamide

To a 250 mL round-bottom flask was charged with *N*-phenyl-*N*-tosylbenzamide (2.56 g, 7.29 mmol), acetonitrile (597 mg, 14.6 mmol) and toluene (30 mL), and then LiHMDS (21.9 mL, 1 M in THF was slowly added under argon atmosphere. The resulting solution was stirred for 15 h. The reaction solution was concentrated using evaporation and then quenched with saturated aqueous NH_4Cl (40 mL) and diluted with ethyl acetate (100 mL). The organic layer was washed with brine (50 mL × 3), dried with anhydrous $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate/hexane to afford 3a (1.02 g, 7.03 mmol, 96%).

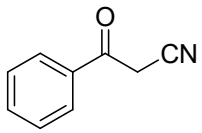
5. General procedure for the synthesis of ß-ketonitrile (3) from secondary amides in one pot

To the solution of N-phenylbenzamide (4a) or N-methylbenzamide (4b) (0.5 mmol, 1.0 equiv) in toluene (3.5 mL) was added LiHMDS (0.6 mL, 0.6 mmol, 1.2 equiv, 1 M in THF) under argon protected. After stirred for 1 h at room temperature, CH_3I (106 mg, 0.75 mmol, 1.5 equiv) was added dropwise. The resulting solution was stirred for 3 h at room temperature. To the mixture was added acetonitrile (41 mg, 1 mmol, 2.0 equiv) and LiHMDS (1.5 mL, 1.5 mmol, 3.0 equiv, 1 M in THF). The resulting solution was stirred for 15 h under argon protected. The reaction was then quenched with saturated NH4Cl (7 mL) and diluted with ethyl acetate (50 mL). The organic layer was washed with brine (10 mL × 2), dried with anhydrous MgSO4, filtered and concentrated under vacuum. The crude product was purified by silica gel column chromatography with ethyl acetate in hexane (10%) to afford 3-oxo-3-phenylpropanenitrile (**3a**) (47.1mg, 0.33 mmol, 65% yield from 4a, 52.2 mg, 0.36 mmol, 72% yield from 4b) as a yellow solid. (Scheme 4)

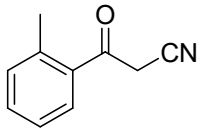


Scheme 4. Sequential reaction with secondary amides

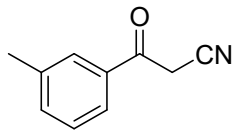
5. Analytical data



3-Oxo-3-phenylpropanenitrile (**3a**)[14]
According to the general procedure using *N*-phenyl-*N*-tosylbenzamide (351 mg, 1.0 mmol), the product **3a** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (138 mg, 0.95 mmol, 95%).
m.p. 79–81 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.69 – 7.64 (m, 1H), 7.55 – 7.50 (m, 2H), 4.09 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 187.12, 134.74, 134.27, 129.16, 128.46, 113.80, 29.41.;
FTIR (neat): 1686 cm^{-1}, 2264 cm^{-1};
MS (EI) m/z = 145.0 (M^+)

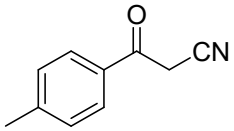


3-Oxo-3-(*o*-tolyl)propanenitrile (**3b**)[14]
According to the general procedure using *tert*-butyl (2-methylbenzoyl)(phenyl)carbamate (311mg, 1.0mmol), the product **3b** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (148 mg, 0.93 mmol, 93%).
m.p. 69 – 71 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 1H), 7.47 (td, *J* = 7.6, 1.2 Hz, 1H), 7.33 – 7.30(m, 2H), 4.06 (s, 2H), 2.56 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 189.33, 140.32, 133.72, 133.23, 132.69, 129.23, 126.10, 114.06, 31.39, 21.75;
FTIR (neat): 1679 cm^{-1}, 2262 cm^{-1};
MS (EI) m/z = 159.0 (M^+)



3-Oxo-3-(*m*-tolyl)propanenitrile (**3c**)[14]
According to the general procedure using *tert*-butyl (3-methylbenzoyl)(phenyl)carbamate (311mg, 1.0mmol), the product **3c** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (146 mg, 0.92 mmol, 92%).
m.p. 71 – 72 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 2H), 7.46 (dddd, *J* = 7.6, 1.8, 1.2, 0.7 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 4.08 (s, 2H), 2.46 – 2.38 (m, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 187.28, 139.08, 135.44, 134.22, 128.91, 128.83, 125.61, 113.91, 29.38, 21.23;
FTIR (neat): 1687 cm^{-1}, 2250 cm^{-1};

MS (EI) m/z = 159.0 (M^+)



3-Oxo-3-(*p*-tolyl)propanenitrile (3d)[14]

According to the general procedure using *tert*-butyl (4-methylbenzoyl)(phenyl)carbamate (311mg, 1.0mmol), the product **3d** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (157 mg, 0.99 mmol, 99%).

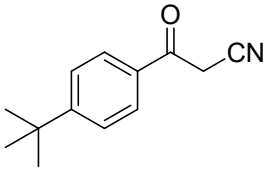
m.p. 94 – 96 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.06 (s, 2H), 2.42 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.75, 145.85, 131.71, 129.69, 128.46, 114.03, 29.22, 21.67;

FTIR (neat): 1682 cm^{-1}, 2250 cm^{-1};

MS (EI) m/z = 159.0 (M^+)



3-(4-(*tert*-Butyl)phenyl)-3-oxopropanenitrile (3e) [14]

According to the general procedure using 4-*tert*-butyl-*N*-phenyl-*N*-tosylbenzamide (407 mg, 1.0 mmol), the product **3e** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (171 mg, 0.85 mmol, 85%).

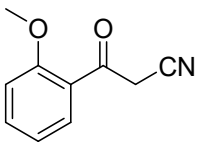
m.p. 75–77 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.84 (m, 2H), 7.55 – 7.51 (m, 2H), 4.05 (s, 2H), 1.35 (d, *J* = 1.9 Hz, 9H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.59, 158.86 , 131.72 , 128.49 , 126.12 , 113.92 , 35.35 , 30.97 , 29.26;

FTIR (neat): 1686 cm^{-1}, 2263 cm^{-1};

MS (EI) m/z = 201.1 (M^+)



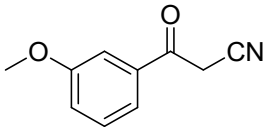
3-(2-Methoxyphenyl)-3-oxopropanenitrile (3f)[15]

According to the general procedure using 2-methoxy-*N*-phenyl-*N*-tosylbenzamide (381 mg, 1.0 mmol), the product **3f** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (173 mg, 0.99 mmol, 99%).

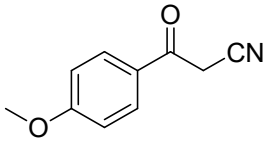
m.p. 87 – 89 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.55 (ddd, *J* = 8.4, 7.3, 1.8 Hz, 1H), 7.06 – 6.97 (m, 2H), 4.08 (s, 2H), 3.95 (s, 3H);

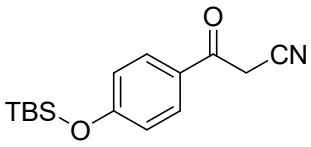
^{13}C NMR (126 MHz, $CDCl_3$) δ 187.95, 159.14, 135.66, 131.13, 124.27, 121.02, 114.55, 111.75, 55.67, 34.02;
FTIR (neat): 1670 cm^{-1}, 2252 cm^{-1};
MS (EI) m/z = 175.0 (M^+)



3-(3-Methoxyphenyl)-3-oxopropanenitrile (3g)[16]
According to the general procedure using 3-methoxy-*N*-phenyl-*N*-tosylbenzamide (381 mg, 1.0 mmol), the product **3g** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (173 mg, 0.99 mmol, 99%).
m.p. 125 – 127 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 3H), 7.17 (ddd, *J* = 7.9, 2.5, 1.3 Hz, 1H), 4.09 (s, 2H), 3.84 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 187.07, 159.98, 135.44, 130.02, 121.03, 120.84, 113.87, 112.57, 55.47, 29.47;
FTIR (neat): 1695 cm^{-1}, 2252 cm^{-1};
MS (EI) m/z = 175.0 (M^+)

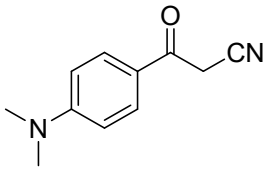


3-(4-Methoxyphenyl)-3-oxopropanenitrile (3h)[14]
According to the general procedure using 4-methoxy-*N*-phenyl-*N*-tosylbenzamide (381 mg, 1.0 mmol), the product **3h** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (173 mg, 0.99 mmol, 99%).
m.p. 126 – 127 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.9 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 4.03 (s, 2H), 3.88 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 185.45, 164.64, 130.84, 127.19, 114.25, 114.10, 55.60, 29.00;
FTIR (neat): 1681 cm^{-1}, 2261 cm^{-1};
MS (EI) m/z = 176.0 (M^+)

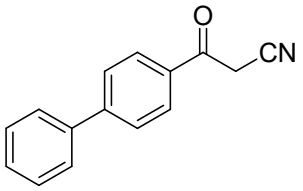


3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-3-oxopropanenitrile (3i)
According to the general procedure using 4-(*tert*-butyldimethylsilyl)oxy-*N*-phenyl-*N*-tosylbenzamide (481 mg, 1.0 mmol), the product was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (190 mg, 0.69 mmol, 69%).

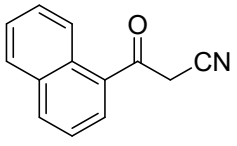
m.p. 55 – 57 °C;
^{1}H NMR (500 MHz, CDCl3) δ 7.87 – 7.82 (m, 2H), 6.93 – 6.89 (m, 2H), 4.01 (s, 2H), 0.99 (s, 9H), 0.25 (s, 6H);
^{13}C NMR (126 MHz, CDCl3) δ 185.45, 161.74, 130.85, 127.75, 120.43, 114.02, 29.03, 25.51, 18.24, -4.36;
FTIR (neat): 1682 cm^{-1}, 2260 cm^{-1};
HRMS (FD-TOF) m/z: $[M]^+$ Calcd for $C_{10}H_8ClNO$ 275.1336; Found 275.1335.



3-(4-Dimethylaminophenyl)-3-oxopropanenitrile (3j)[17]
According to the general procedure using 4-dimethylamino-*N*-phenyl-*N*-tosylbenzamide (395 mg, 1.0 mmol), the product **3j** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a brown solid (130 mg, 0.69 mmol, 69%).
m.p. 164 – 165 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.77 (m, 2H), 6.69 – 6.64 (m, 2H), 3.94 (s, 2H), 3.09 (s, 6H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 184.35, 154.12, 130.84, 122.05, 114.70, 110.89, 40.05, 28.49;
FTIR (neat): 1664 cm^{-1}, 2260 cm^{-1};
MS (EI) m/z = 188.1 (M^+)



3-(4-Biphenylyl)-3-oxopropanenitrile (3k) [14]
According to the general procedure using *N*-phenyl-*N*-tosyl-[1,1'-biphenyl]-4-carboxamide (427 mg, 1.0 mmol), the product **3k** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (212 mg, 0.96 mmol, 96%).
m.p. 112–113 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 – 7.98 (m, 2H), 7.76 – 7.72 (m, 2H), 7.64 – 7.61 (m, 2H), 7.52 – 7.47 (m, 2H), 7.46 – 7.41 (m, 1H), 4.11 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ δ 186.57, 147.47, 139.21, 132.90, 129.09, 128.74, 127.71, 127.31, 113.79, 29.39;
FTIR (neat): 1687 cm^{-1}, 2264 cm^{-1};
MS (EI) m/z = 221.0 (M^+)



3-(Naphthalen-1-yl)-3-oxopropanenitrile (3l) [14]

According to the general procedure using *N*-phenyl-*N*-tosyl-1-naphthamide (401 mg, 1.0 mmol), the product **3l** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (179 mg, 0.41 mmol, 92%).

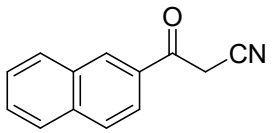
m.p. 96 – 97 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (dd, *J* = 8.7, 0.7 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.66 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.59 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.53 (dd, *J* = 8.2, 7.4 Hz, 1H), 4.19 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.54, 135.20, 134.05, 131.44, 130.31, 129.57, 129.16, 128.70, 127.11, 125.59, 124.19, 114.14, 31.80;

FTIR (neat): 1683 cm^{-1}, 2256 cm^{-1};

MS (EI) m/z = 195.0 (M^+)



3-(Naphthalen-2-yl)-3-oxopropanenitrile (3m) [14]

According to the general procedure using *N*-phenyl-*N*-tosyl-2-naphthamide (401 mg, 1.0 mmol), the product **3m** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (181 mg, 0.93 mmol, 93%).

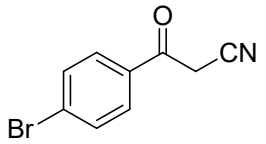
m.p. 107 – 108 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 0.9 Hz, 1H), 8.00 – 7.88 (m, 4H), 7.66 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 4.21 (s, 2H).;

^{13}C NMR (126 MHz, $CDCl_3$) δ 187.01, 136.15, 132.26, 131.62, 130.72, 129.73, 129.53, 129.20, 127.93, 127.43, 123.38, 113.93, 29.47;

FTIR (neat): 1686 cm^{-1}, 2258 cm^{-1};

MS (EI) m/z = 195.0 (M^+)



3-(4-Bromophenyl)-3-oxopropanenitrile (3n) [14]

According to the general procedure using 4-bromo-N-phenyl-N-tosylbenzamide (430 mg, 1.0 mmol), the product **3n** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (201 mg, 0.90 mmol, 90%).

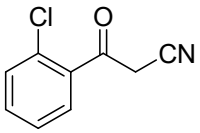
m.p. 153–155 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.69 – 7.66 (m, 2H), 4.05 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.19, 132.95, 132.56, 130.29, 129.86, 113.42, 29.38;

FTIR (neat): 1684 cm^{-1}, 2252 cm^{-1};

MS (EI) m/z = 222.9 (M^+)



3-(2-Chlorophenyl)-3-oxopropanenitrile (3o) [18]

According to the general procedure using 2-chloro-*N*-phenyl-*N*-tosylbenzamide (386 mg, 1.0 mmol), the product **3o** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (133 mg, 0.74 mmol, 74%).

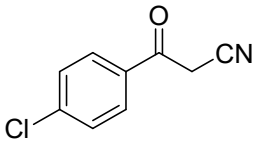
m.p. 95 – 97 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H), 7.52 – 7.45 (m, 2H), 7.39 (ddd, *J* = 7.7, 7.1, 1.5 Hz, 1H), 4.15 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 189.42, 135.63, 133.77, 131.70, 131.02, 130.43, 127.50, 113.44, 32.95;

FTIR (neat): 1693 cm^{-1}, 2264 cm^{-1};

MS (EI) m/z = 179.0 (M^+)



3-(4-Chlorophenyl)-3-oxopropanenitrile (3p) [14]

According to the general procedure using 2-chloro-*N*-phenyl-*N*-tosylbenzamide (386 mg, 1.0 mmol), the product **3p** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (143 mg, 0.80 mmol, 80%).

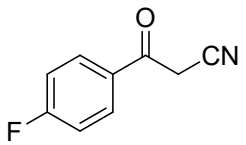
m.p. 123 – 125 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.53 – 7.48 (m, 2H), 4.06 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.01, 141.43, 132.52, 129.80, 129.50, 113.49, 29.40;

FTIR (neat): 1685 cm^{-1}, 2252 cm^{-1};

MS (EI) m/z = 179.6 (M^+)



3-(4-Fluorophenyl)-3-oxopropanenitrile (3q) [14]

According to the general procedure using 4-fluoro-*N*-phenyl-*N*-tosylbenzamide (369 mg, 1.0 mmol), the product **3q** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (139 mg, 0.85 mmol, 85%).

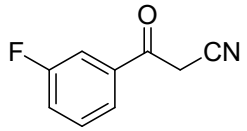
m.p. 73 – 75 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.93 (m, 2H), 7.22 – 7.16 (m, 2H), 4.08 (s, 2H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 185.52, 166.57 (d, J = 258.3 Hz), 131.27 (d, J = 9.7 Hz), 130.68 (d, J = 3.1 Hz), 116.44 (d, J = 22.2 Hz), 113.55, 29.34;

FTIR (neat): 1683 cm^{-1}, 2260 cm^{-1};

MS (EI) m/z = 163.0 (M^+)



3-(3-Fluorophenyl)-3-oxopropanenitrile (3r)[14]

According to the general procedure using 3-fluoro-*N*-phenyl-*N*-tosylbenzamide (369 mg, 1.0 mmol), the product **3r** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (126 mg, 0.77 mmol, 77%).

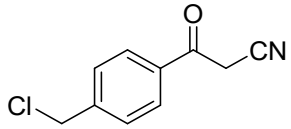
m.p. 69 – 71 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.57 (m, 1H), 7.51 (td, *J* = 8.0, 5.5 Hz, 1H), 7.35 (td, *J* = 8.2, 2.0 Hz, 1H), 4.12 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.23 (d, *J* = 2.4 Hz), 162.78 (d, *J* = 250.2 Hz), 136.08 (d, *J* = 6.5 Hz), 130.89 (d, *J* = 7.7 Hz), 124.19 (d, *J* = 3.1 Hz), 121.77 (d, *J* = 21.5 Hz), 115.09 (d, *J* = 22.8 Hz), 113.52, 29.59;

FTIR (neat): 1690 cm^{-1}, 2258 cm^{-1};

MS (EI) m/z = 163.0 (M^+)



3-(4-(Chloromethyl)phenyl)-3-oxopropanenitrile (3s)

According to the general procedure using 4-(chloromethyl)-*N*-phenyl-*N*-tosylbenzamide (399 mg, 1.0 mmol), the product **3s** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (149 mg, 0.71 mmol, 71%).

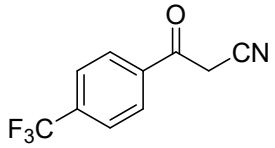
m.p. 115 – 117 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 4.62 (s, 2H), 4.09 (s, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.60, 144.21, 134.01, 129.18, 128.93, 113.70, 44.95, 29.51;

FTIR (neat): 1688 cm^{-1}, 2255 cm^{-1};

HRMS (FD-TOF) m/z: $[M]^+$ Calcd for $C_{10}H_8ClNO$ 193.0289; Found 193.0290.



3-Oxo-3-(4-(trifluoromethyl)phenyl)propanenitrile (3t)[14]

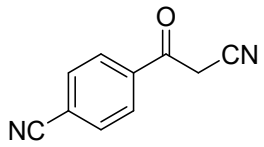
According to the general procedure using *tert*-butyl phenyl(4-(trifluoromethyl)benzoyl)carbamate (365 mg, 1.0 mmol), the product **3t** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (164 mg, 0.77 mmol, 77%).

m.p. 141 – 143 °C;

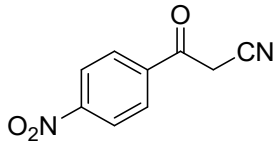
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.8, 0.7 Hz, 2H), 7.79 (dd, *J* = 8.8, 0.6 Hz, 2H), 4.15 (s, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 186.50, 136.77, 136.09 (q, *J* = 32.7 Hz), 128.83, 126.20 (q, *J* = 3.7 Hz), 123.17 (q, *J* = 273.6 Hz), 113.31, 29.72;

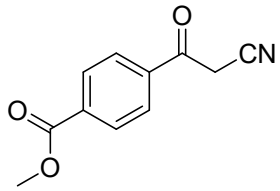
FTIR (neat): 1693 cm^{-1}, 2264 cm^{-1};
MS (EI) m/z = 213.0 (M^+)



4-(2-Cyanoacetyl)benzonitrile (**3u**)[16]
According to the general procedure using *tert*-butyl (4-cyanobenzoyl)(phenyl)carbamate (322 mg, 1.0 mmol), the product **3u** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (122 mg, 0.72 mmol, 72%).
m.p. 121 – 122 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 4.14 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 186.16, 136.98, 132.92, 128.84, 117.92, 117.31, 113.03, 29.74;
FTIR (neat): 1699 cm^{-1}, 2229 cm^{-1}, 2267 cm^{-1};
MS (EI) m/z = 170.0 (M^+)

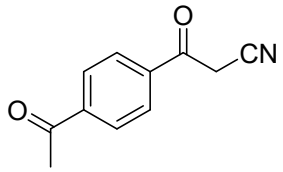


3-(4-Nitrophenyl)-3-oxopropanenitrile (**3v**)[16]
According to the general procedure using *tert*-butyl (4-nitrobenzoyl)(phenyl)carbamate (342 mg, 1.0 mmol), the product **3v** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (131 mg, 0.69 mmol, 69%).
m.p. 123 – 124 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 – 8.35 (m, 2H), 8.13 – 8.09 (m, 2H), 4.17 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 185.95, 151.12, 138.41, 129.60, 124.32, 112.92, 29.93;
FTIR (neat): 1523 cm^{-1}, 1698 cm^{-1}, 2266 cm^{-1};
MS (EI) m/z = 190.0 (M^+)

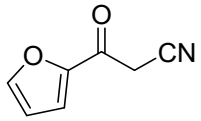


Methyl 4-(2-cyanoacetyl)benzoate (**3w**)[19]
According to the general procedure using methyl 4-(phenyl(tosyl)carbamoyl)benzoate (409 mg, 1.0 mmol), the product **3w** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (95 mg, 0.47 mmol, 47%).
m.p. 98 – 100 °C;
^{1}H NMR (500 MHz, CDCl3) δ 8.20 – 8.16 (m, 2H), 8.00 – 7.97 (m, 2H), 4.11 (s, 2H), 3.97 (s, 3H);
^{13}C NMR (126 MHz, CDCl3) δ 186.63, 165.66, 137.24, 135.36, 130.27, 128.40, 113.25, 52.69, 29.68;
FTIR (neat): 1691 cm^{-1}, 1707 cm^{-1}, 2265 cm^{-1};

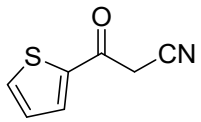
MS (EI) m/z = 203.0 (M^+)



3-(4-Acetylphenyl)-3-oxopropanenitrile (**3x**)[14]
According to the general procedure using 4-acetyl-*N*-phenyl-*N*-tosylbenzamide (393 mg, 1.0 mmol), the product **3x** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (60 mg, 0.32 mmol, 32%).
m.p. 121 – 123 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.05 (m, 2H), 8.03 – 7.99 (m, 2H), 4.13 (s, 2H), 2.65 (s, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 197.00, 186.71, 141.31, 137.17, 128.87, 128.73, 113.34, 29.74, 26.93;
FTIR (neat): 1671 cm^{-1}, 1687 cm^{-1}, 2266 cm^{-1};
MS (EI) m/z = 187.0 (M^+)

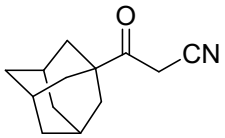


3-(Furan-2-yl)-3-oxopropanenitrile (**3y**)[19]
According to the general procedure using *N*-Phenyl-*N*-tosylfuran-2-carboxamide (341 mg, 1.0 mmol), the product **3y** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (120 mg, 0.89 mmol, 89%).
m.p. 63 – 65 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.36 (dd, *J* = 3.7, 0.8 Hz, 1H), 6.62 (dd, *J* = 3.7, 1.7 Hz, 1H), 3.97 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 175.74, 150.31, 147.77, 119.31, 113.34, 113.27, 28.77;
FTIR (neat): 1669 cm^{-1}, 2258 cm^{-1};
MS (EI) m/z = 135.0 (M^+)

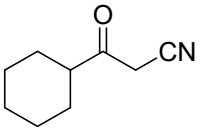


3-Oxo-3-(thiophen-2-yl)propanenitrile (**3z**)[14]
According to the general procedure using *N*-phenyl-*N*-tosylthiophene-2-carboxamide (357 mg, 1.0 mmol), the product **3z** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (121 mg, 0.80 mmol, 80%).
m.p. 137 – 138 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dt, *J* = 3.7, 1.1 Hz, 2H), 7.20 (dd, *J* = 4.9, 3.9 Hz, 1H), 4.01 (s, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 179.50, 140.85, 136.23, 133.67, 128.69, 113.42, 29.54;

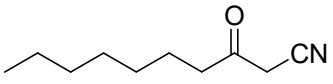
FTIR (neat): 1664 cm^{-1}, 2256 cm^{-1};
MS (EI) m/z = 151.0 (M^+)



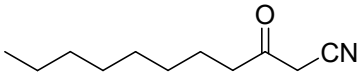
3-(Adamantan-1-yl)-3-oxopropanenitrile (3ab)[18]
According to the general procedure using *N*-phenyl-*N*-tosyladamantane-1-carboxamide (409 mg, 1.0 mmol), the product **3ab** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a white solid (179 mg, 0.86 mmol, 86%).
m.p. 97 – 99 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (s, 2H), 2.08 (s, 3H), 1.82 (d, *J* = 2.6 Hz, 6H), 1.77 (d, *J* = 12.3 Hz, 3H), 1.71 – 1.66 (m, 3H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 202.17, 114.14, 46.85, 37.98, 36.15, 27.62, 27.04;
FTIR (neat): 1702 cm^{-1}, 2259 cm^{-1};
MS (EI) m/z = 203.1 (M^+)



3-Cyclohexyl-3-oxopropionitrile (3ac)[19]
According to the general procedure using *N*-phenyl-*N*-tosylcyclohexanecarboxamide (357 mg, 1.0 mmol), the product **3ac** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a pale yellow oil (113 mg, 0.75 mmol, 75%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 (s, 2H), 2.54 – 2.48 (m, 1H), 1.91 – 1.84 (m, 2H), 1.80 – 1.76 (m, 2H), 1.70 – 1.63 (m, 1H), 1.40 – 1.14 (m, 5H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 200.56, 114.06, 49.98, 30.32, 28.11, 25.49, 25.22;
FTIR (neat): 1719 cm^{-1}, 2258 cm^{-1};
MS (EI) m/z = 151.0 (M^+)



3-Oxo-decanenitrile (3ad)
According to the general procedure using *N*-phenyl-*N*-tosyloctanamide (387 mg, 1.0 mmol), the product **3ad** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow oil (142 mg, 0.85 mmol, 85%).
^{1}H NMR (600 MHz, $CDCl_3$) δ 3.46 (s, 2H), 2.60 – 2.55 (m, 2H), 1.59 (qd, *J* = 7.4, 2.5 Hz, 2H), 1.32 – 1.19 (m, 8H), 0.86 (t, *J* = 7.2 Hz, 3H);
^{13}C NMR (151 MHz, $CDCl_3$) δ 197.68, 113.84, 42.10, 31.87, 31.46, 28.81, 28.71, 23.24, 22.45, 13.93;
FTIR (neat): 1715 cm^{-1}, 2259 cm^{-1};
HRMS (FD-TOF) m/z: $[M]^+$ Calcd for $C_{10}H_{17}NO$ 167.1305; Found 167.1304.



3-Oxo-undecanenitrile (3ae)[20]

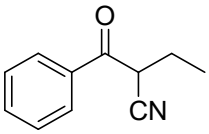
According to the general procedure using *N*-phenyl-*N*-tosylnonanamide (401 mg, 1.0 mmol), the product **3ae** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow oil (168 mg, 0.46 mmol, 93%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.46 (s, 2H), 2.57 (t, *J* = 7.4 Hz, 2H), 1.58 (dq, *J* = 14.7, 7.4 Hz, 2H), 1.33 – 1.16 (m, 10H), 0.85 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.80, 113.94, 42.18, 31.95, 31.72, 29.19, 29.01, 28.84, 23.32, 22.58, 14.04;

FTIR (neat): 1715 cm^{-1}, 2259 cm^{-1};

MS (EI) m/z = 181.1 (M^+)



2-Ethyl-3-oxo-3-phenylpropanenitrile (6a)[21]

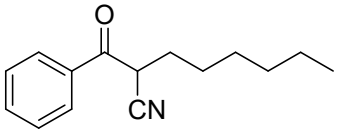
According to the general procedure using *N*-phenyl-*N*-tosylbenzamide (351 mg, 1.0 mmol) and Butyronitrile (138 mg, 2.0 mmol) instead of acetonitrile, the product **6a** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a clear liquid (149 mg, 0.86 mmol, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.67 – 7.61 (m, 1H), 7.54 – 7.48 (m, 2H), 4.32 (dd, *J* = 8.2, 5.6 Hz, 1H), 2.13 – 1.97 (m, 2H), 1.15 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 190.79, 134.38, 133.96, 129.04, 128.64, 117.20, 41.43, 23.53, 11.43;

FTIR (neat): 1736 cm^{-1}, 2248 cm^{-1};

MS (EI) m/z = 173.0 (M^+)



2-Hexyl-3-oxo-3-phenylpropanenitrile (6b)

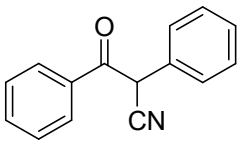
According to the general procedure using *N*-phenyl-*N*-tosylbenzamide (351 mg, 1.0 mmol) and Octanenitrile (250 mg, 2.0 mmol) instead of acetonitrile, the product **6b** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a clear liquid (176 mg, 0.77 mmol, 77%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.9 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.65 Hz, 2H), 4.34 (dd, *J* = 7.9, 6.4 Hz, 1H), 2.05 – 1.94 (m, 2H), 1.63 – 1.47 (m, 2H), 1.38 – 1.25 (m, 6H), 0.89 – 0.86 (t, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 190.86, 134.38, 134.01, 129.06, 128.68, 117.36, 40.03, 31.33, 29.89, 28.67, 27.01, 22.42, 13.94;

FTIR (neat): 1740 cm^{-1}, 2246 cm^{-1};

HRMS (FD-TOF) m/z: $[M]^+$ Calcd for $C_{15}H_{19}NO$ 229.1461; Found 229.1461.



3-Oxo-2,3-diphenylpropanenitrile (6c)[21]

According to the general procedure using *N*-phenyl-*N*-tosylbenzamide (351 mg, 1.0 mmol) and Benzylcyanide (234 mg, 2.0 mmol) instead of acetonitrile, the product **5ab** was purified by chromatography on silica gel eluting with *n*-hexane/EtOAc (12:1) and obtained as a yellow solid (172 mg, 0.78 mmol, 78%).

m.p. 93 – 94 ^{o}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.5, 1.2 Hz, 2H), 7.62 – 7.57 (m, 1H), 7.50 – 7.44 (m, 4H), 7.43 - 7.35 (m, 3H), 5.62 (s, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.84, 134.39, 133.58, 130.31, 129.62, 129.22, 129.10, 128.20, 128.21, 116.51, 46.63;

FTIR (neat): 1690 cm^{-1}, 2250 cm^{-1};

MS (EI) m/z = 221.0 (M^{+})

6. References

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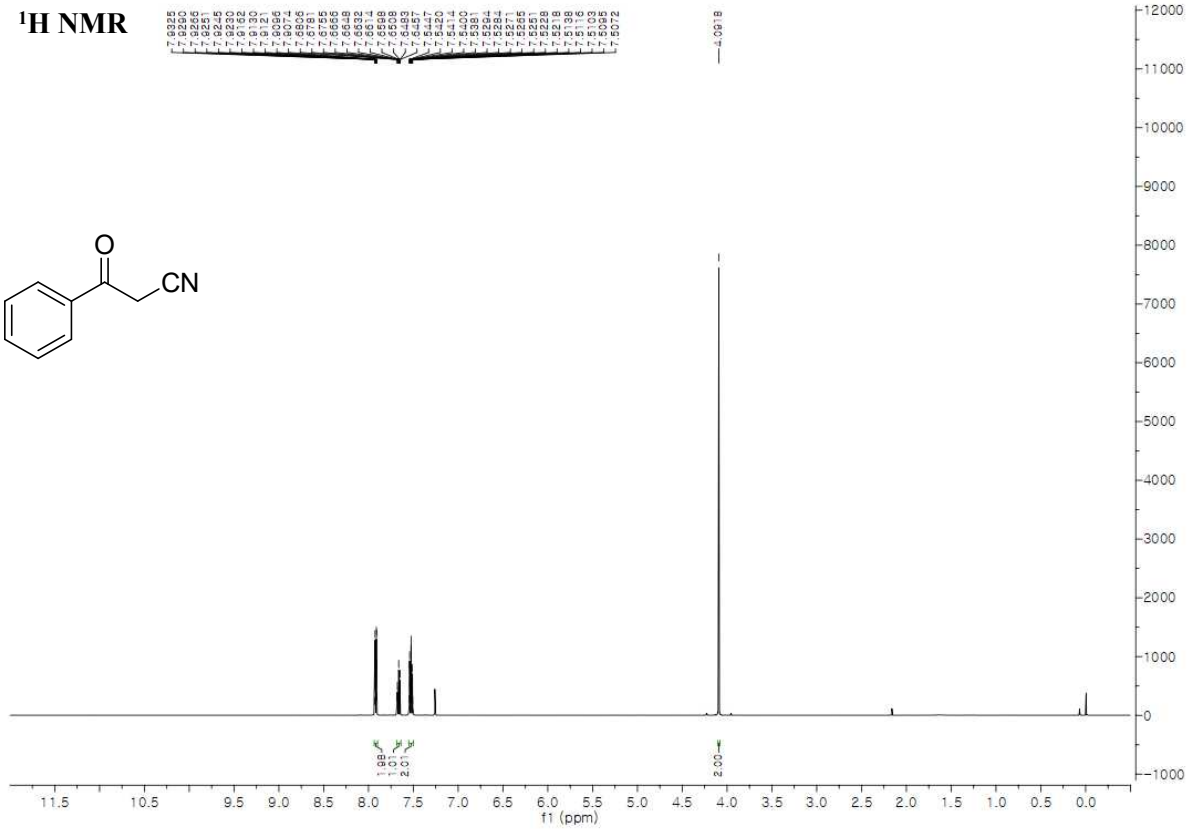
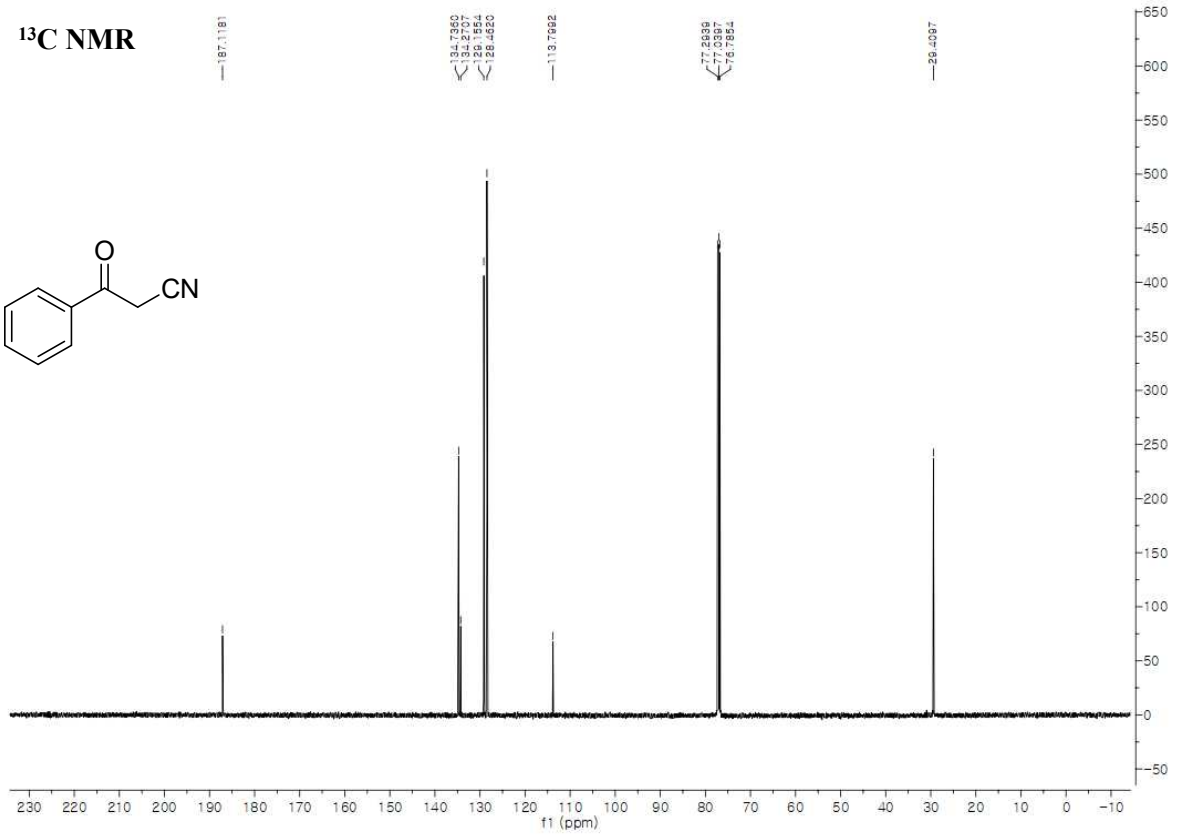
7. ^{1}H and ^{13}C NMR spectra of products

3-Oxo-3-phenylpropanenitrile (3a)

^{1}H NMR

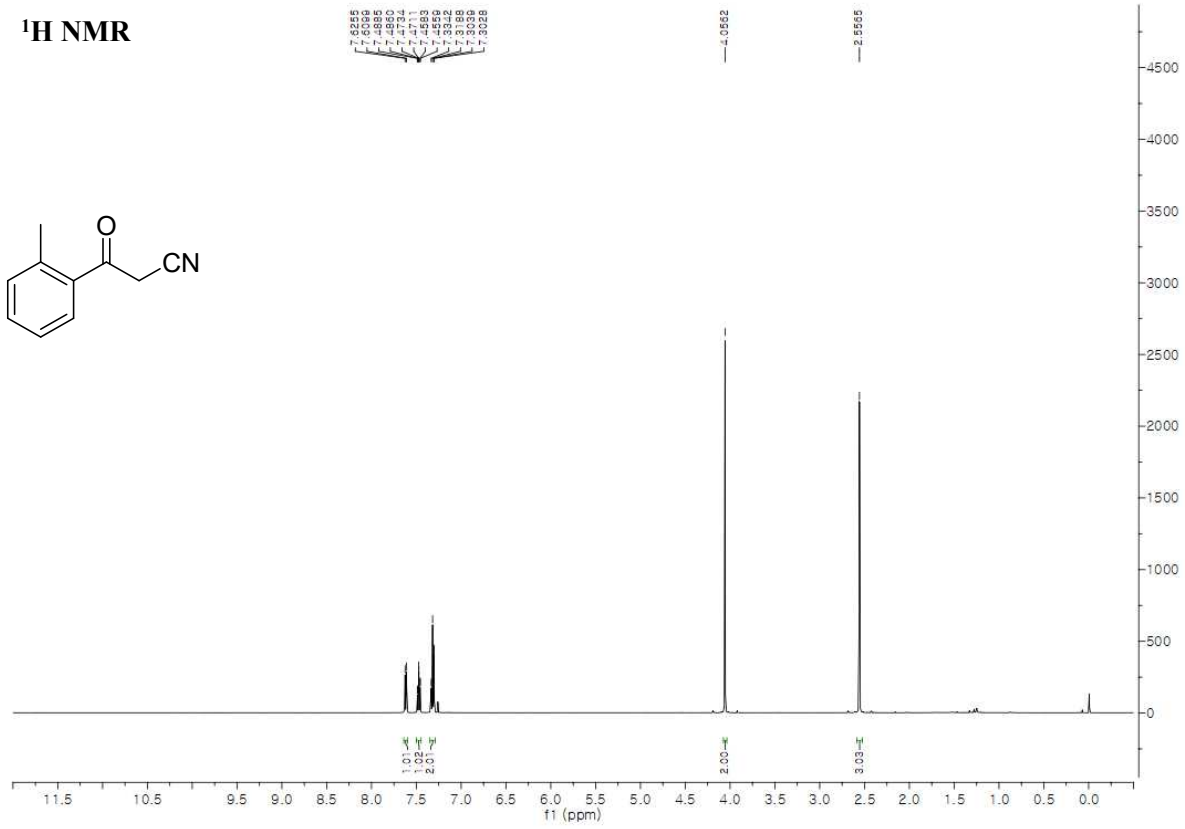


^{13}C NMR

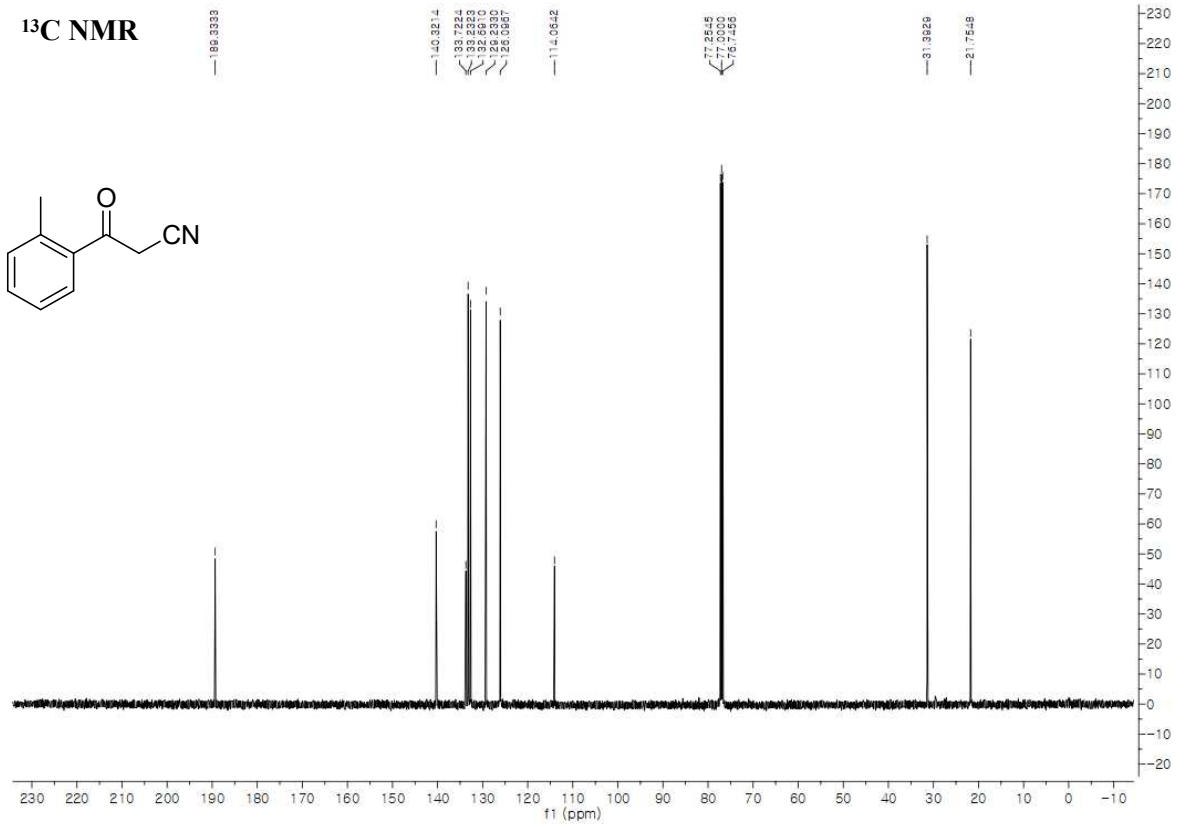


3-Oxo-3-(o-tolyl)propanenitrile (3b)

^{1}H NMR

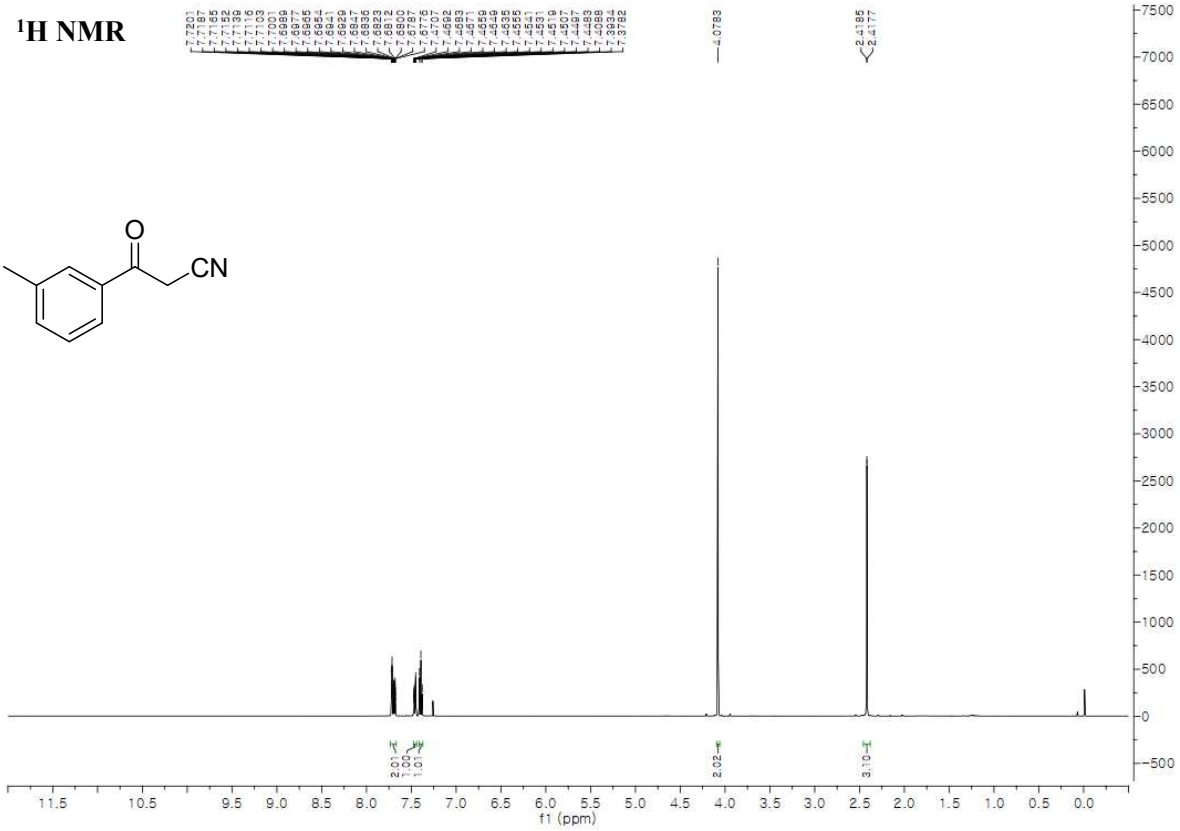


^{13}C NMR

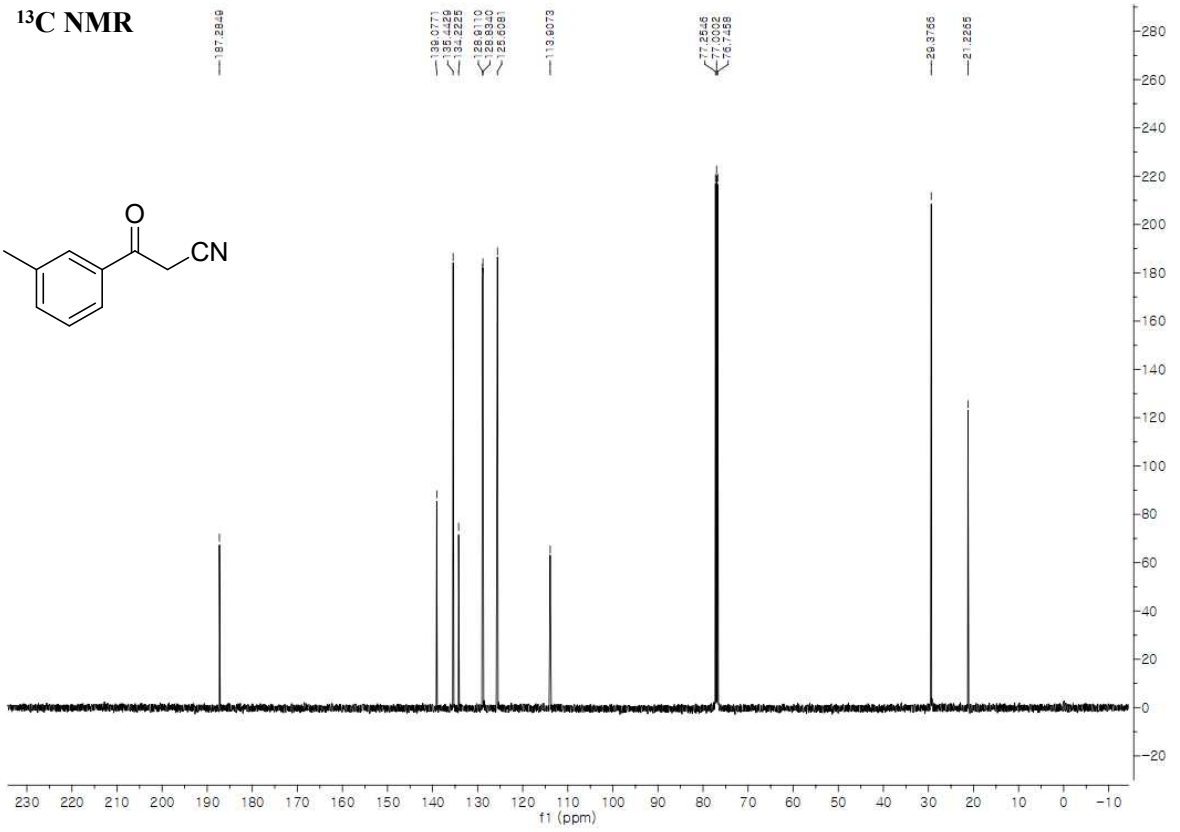


3-Oxo-3-(m-tolyl)propanenitrile (3c)

^{1}H NMR

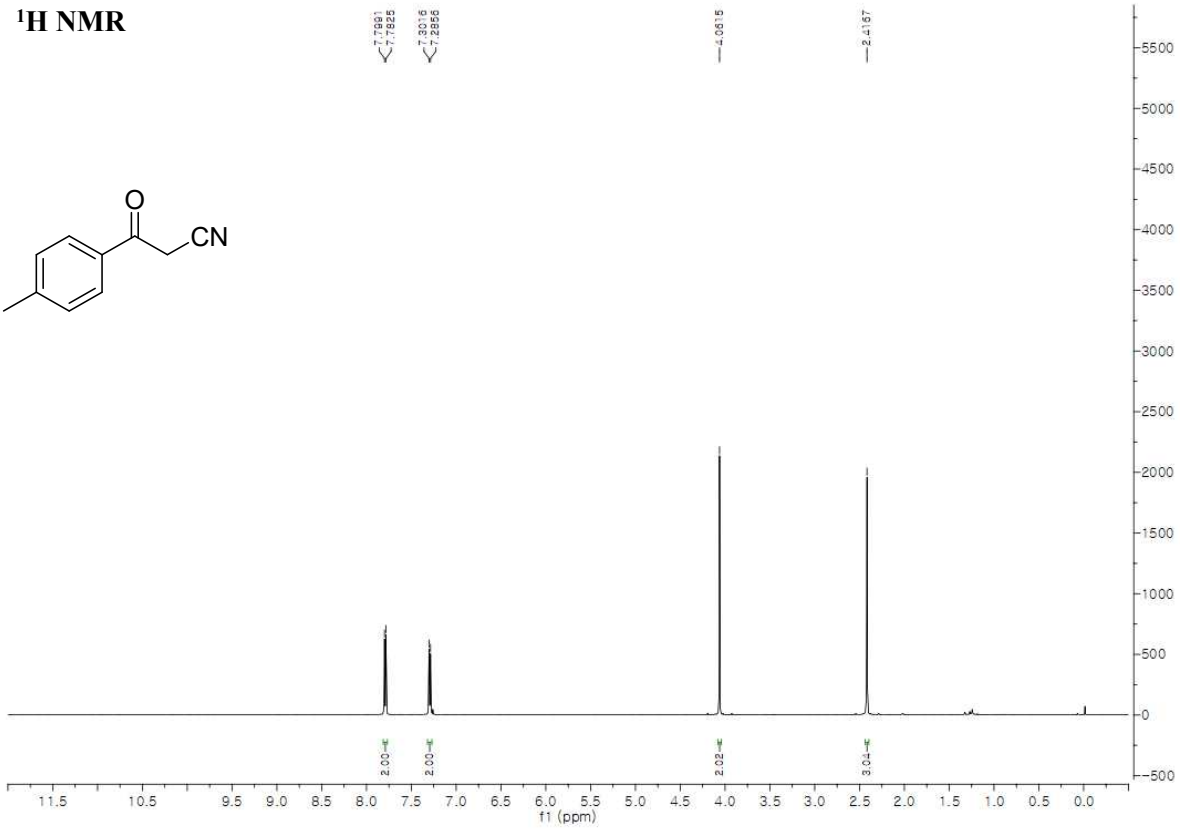


^{13}C NMR

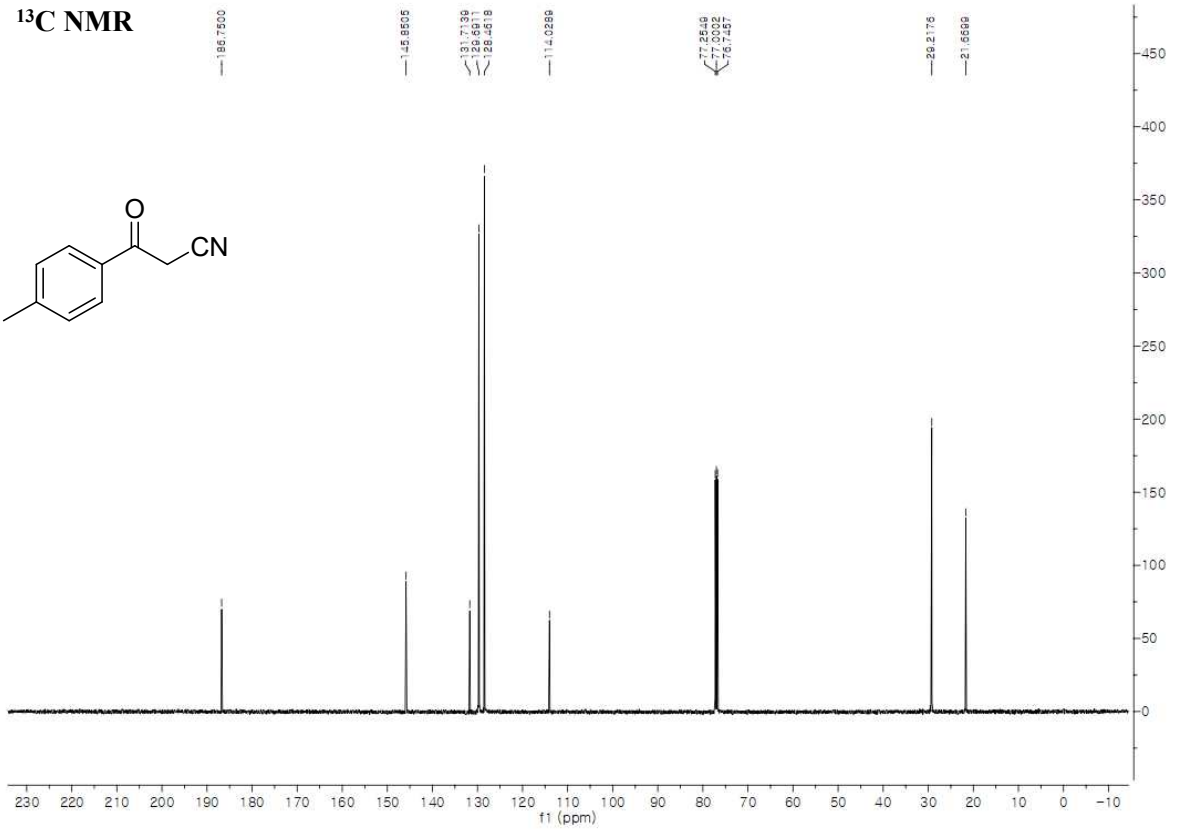


3-Oxo-3-(p-tolyl)propanenitrile (3d)

^{1}H NMR

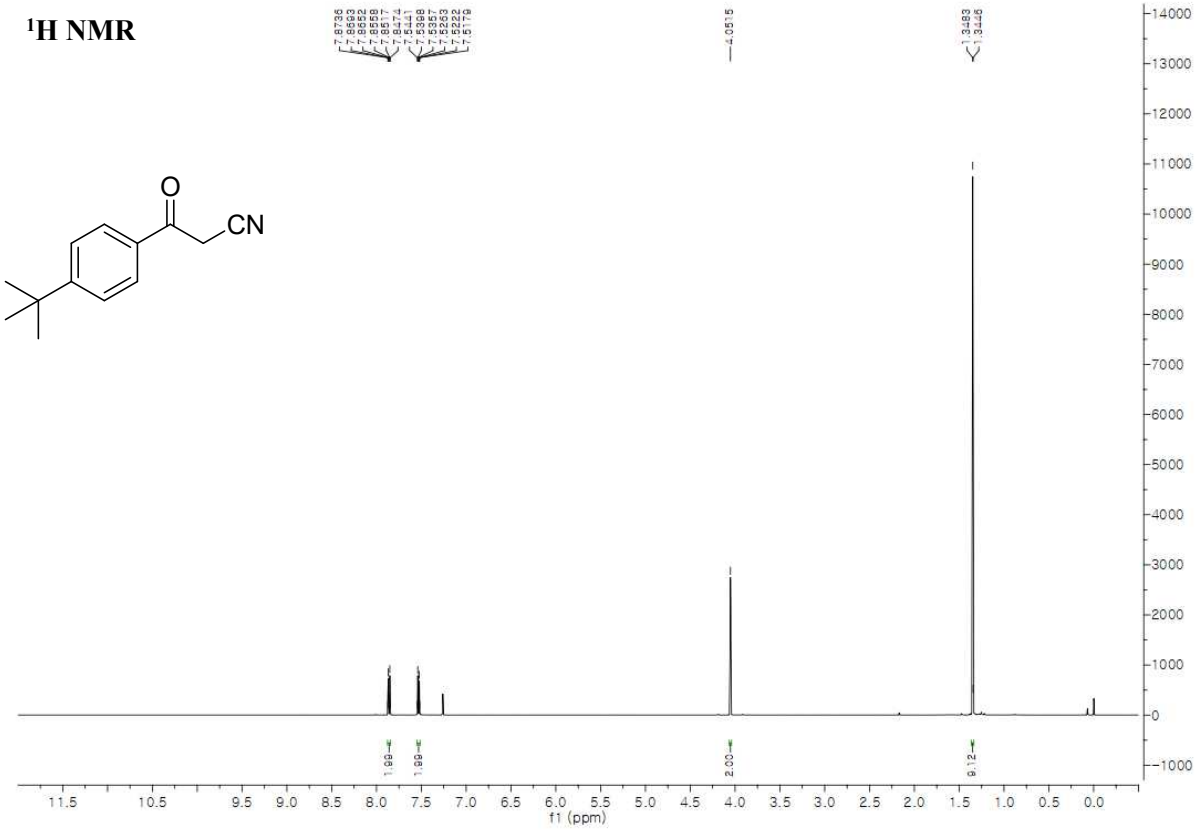


^{13}C NMR

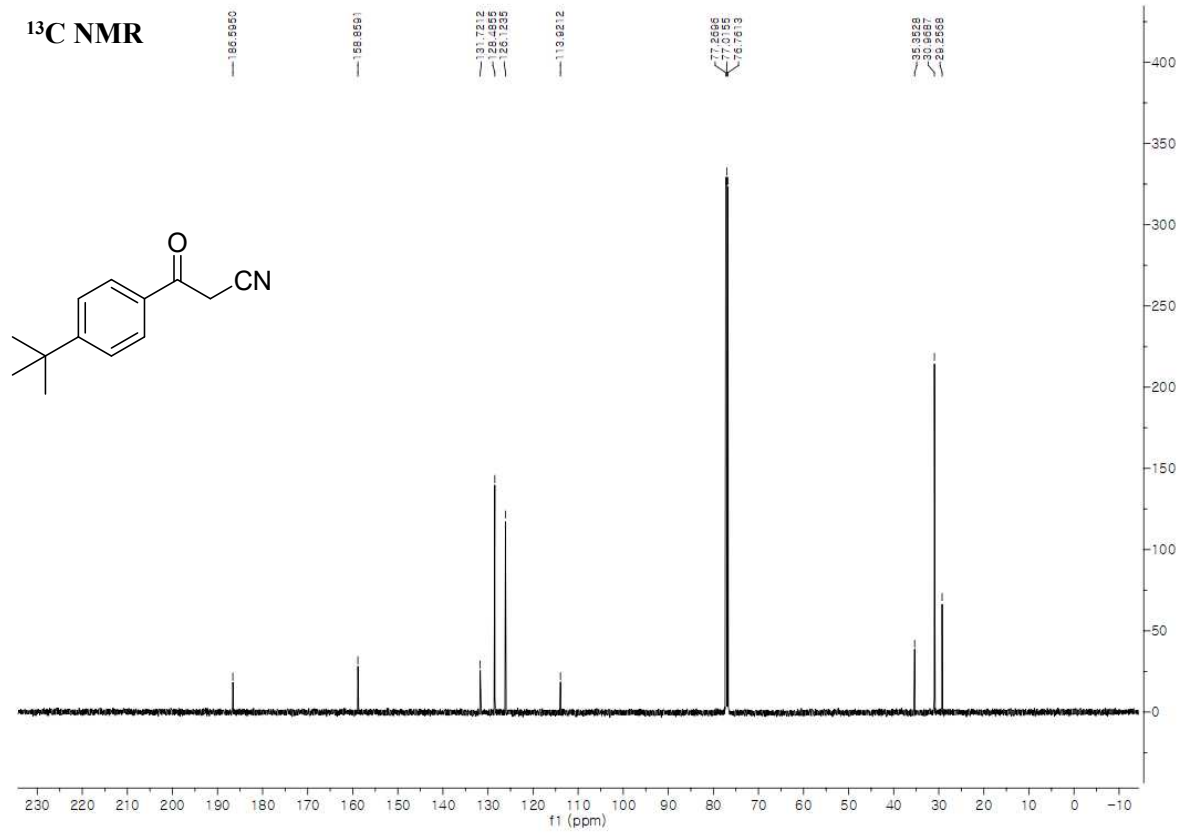


3-(4-(*tert*-Butyl)phenyl)-3-oxopropanenitrile (3e)

^{1}H NMR

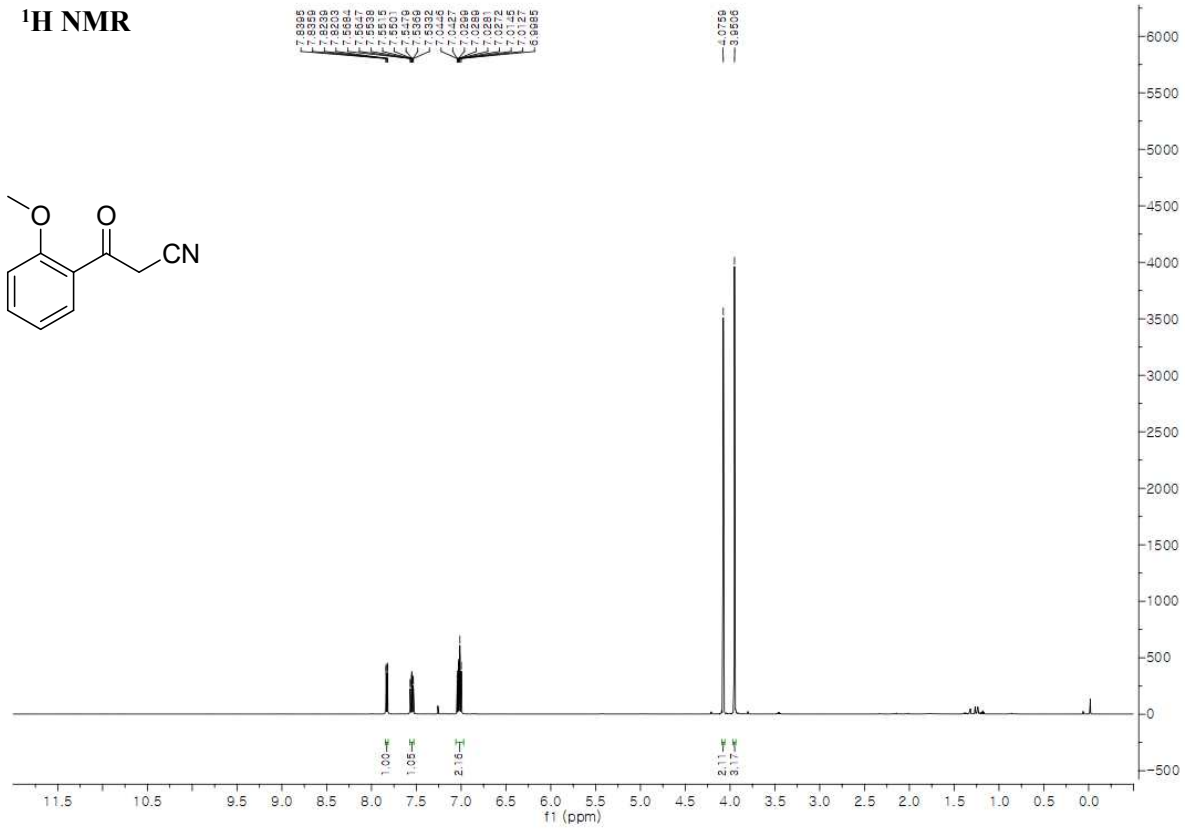


^{13}C NMR

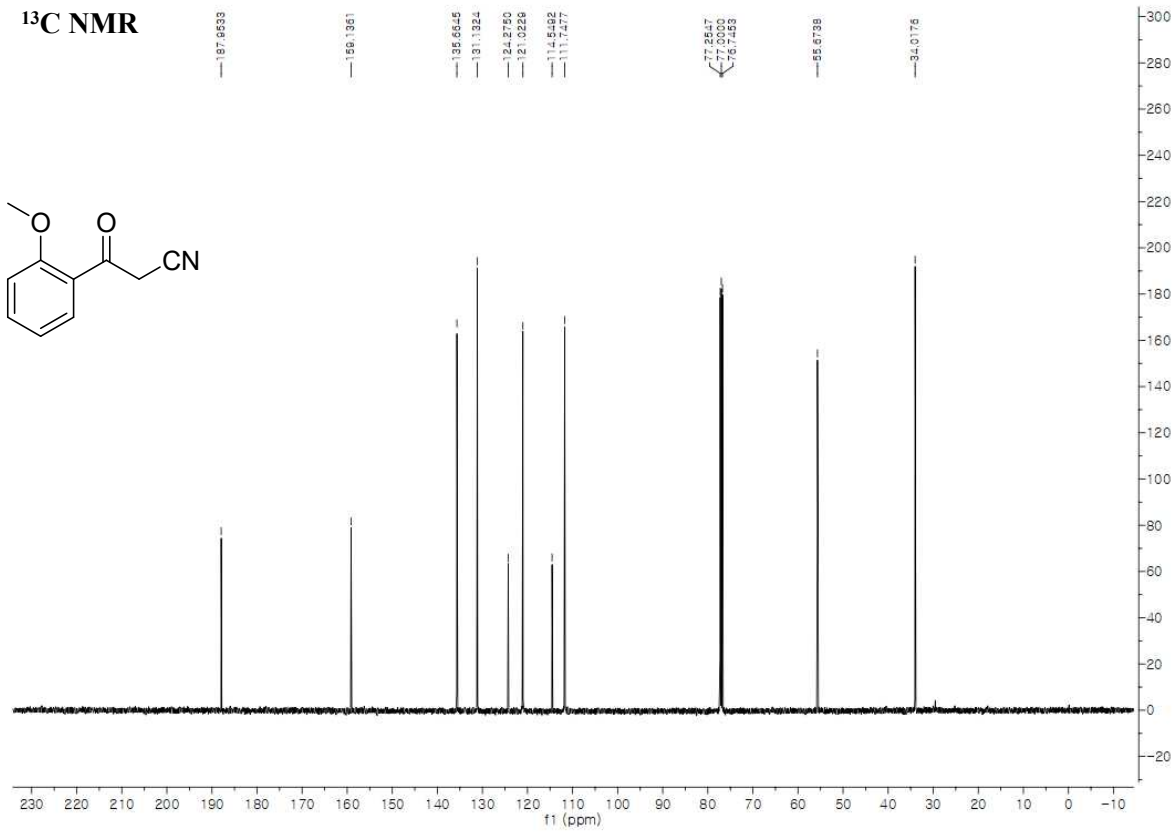


3-(2-Methoxyphenyl)-3-oxopropanenitrile (3f)

^{1}H NMR

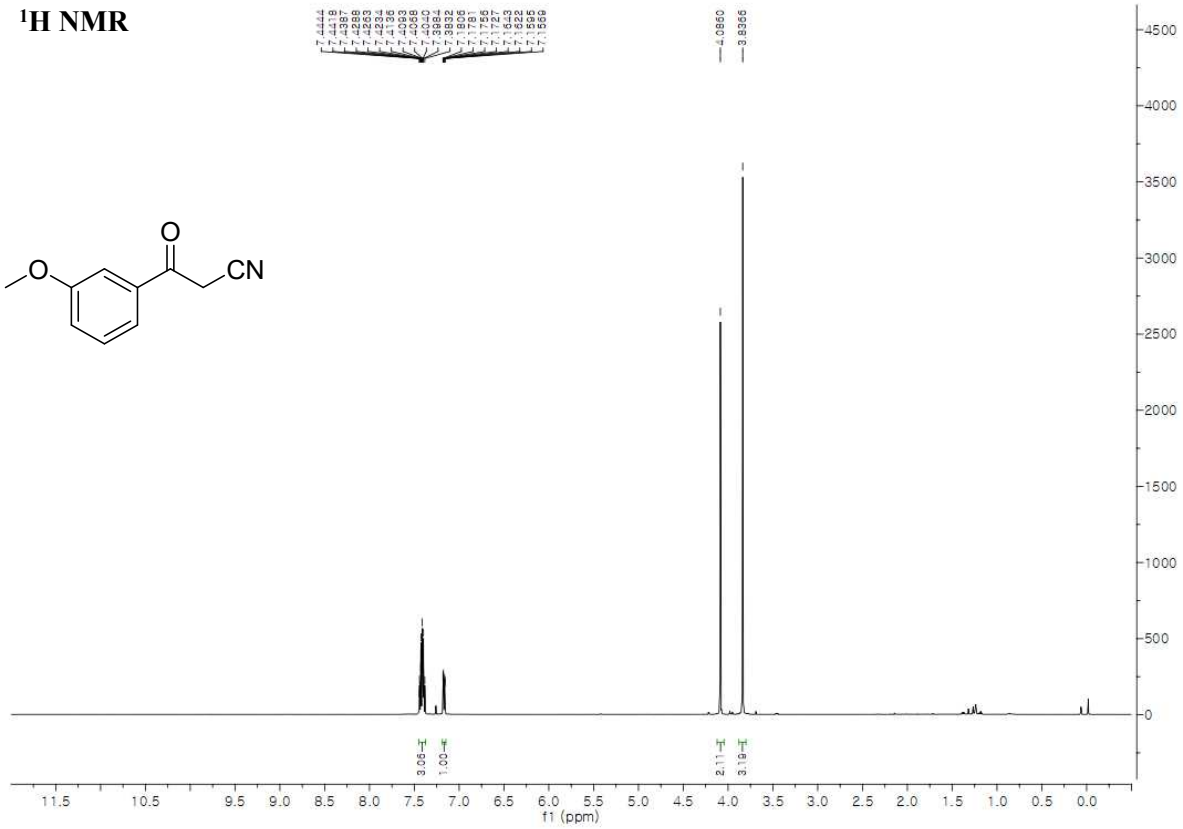


^{13}C NMR

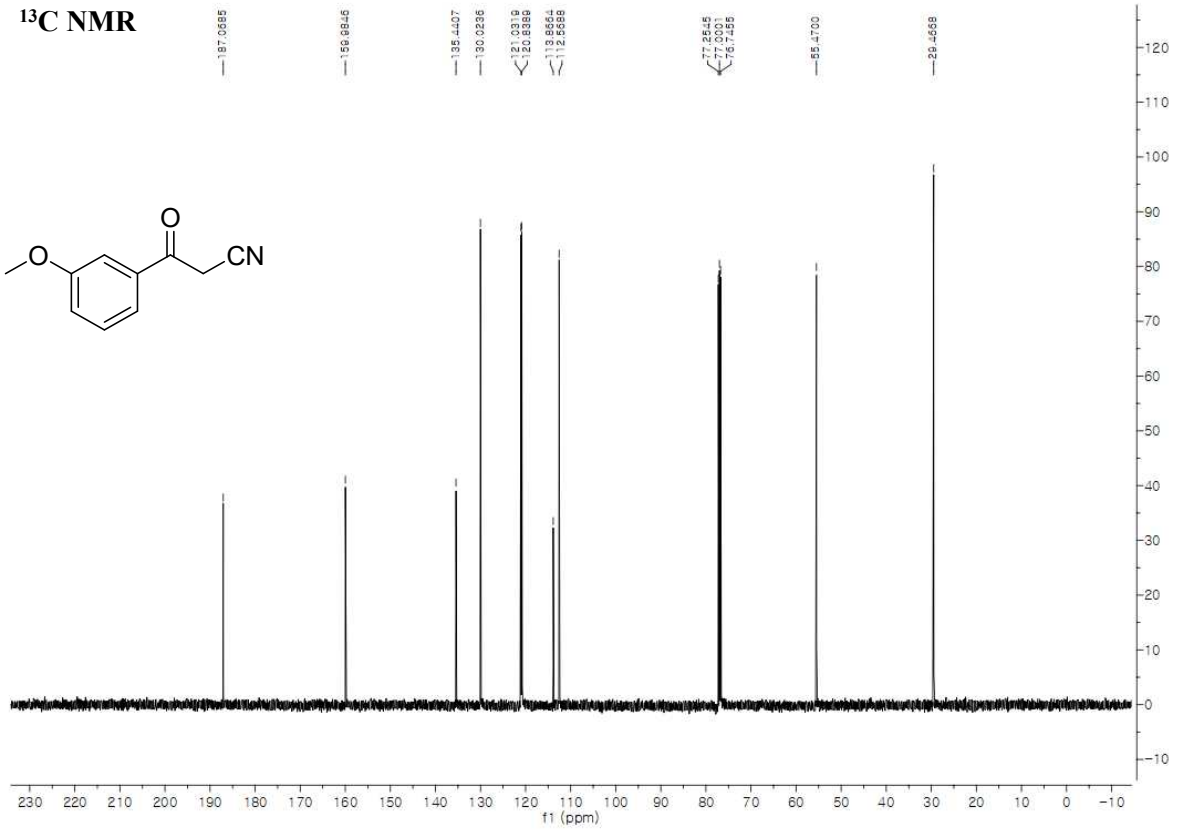


3-(3-Methoxyphenyl)-3-oxopropanenitrile (3g)

^{1}H NMR

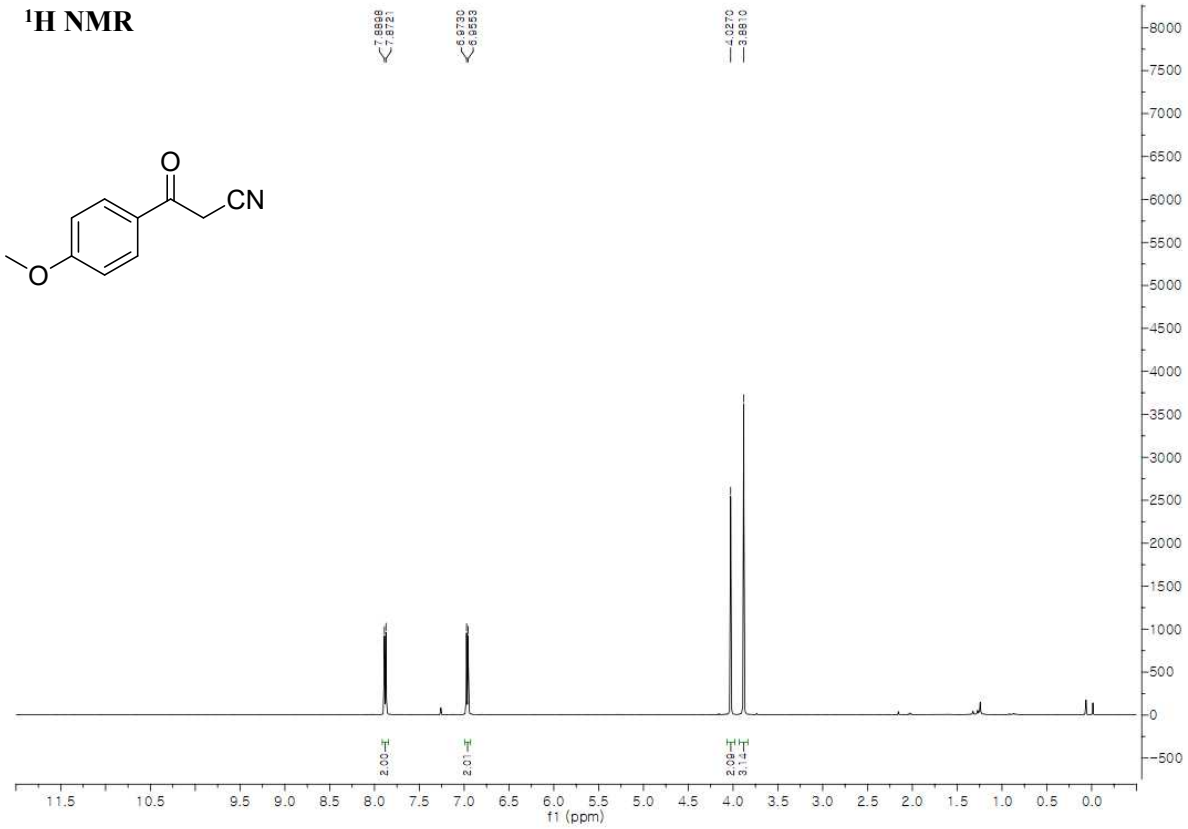


^{13}C NMR

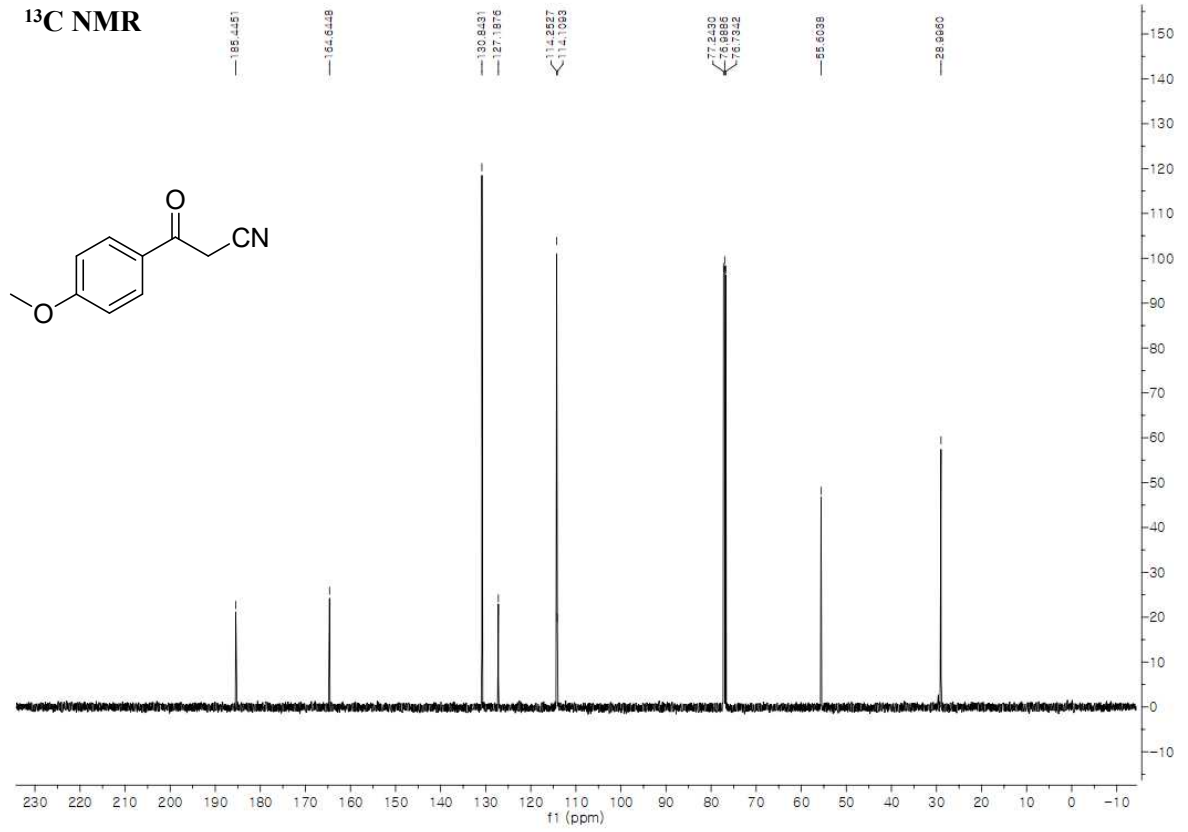


3-(4-Methoxyphenyl)-3-oxopropanenitrile (3h)

^{1}H NMR



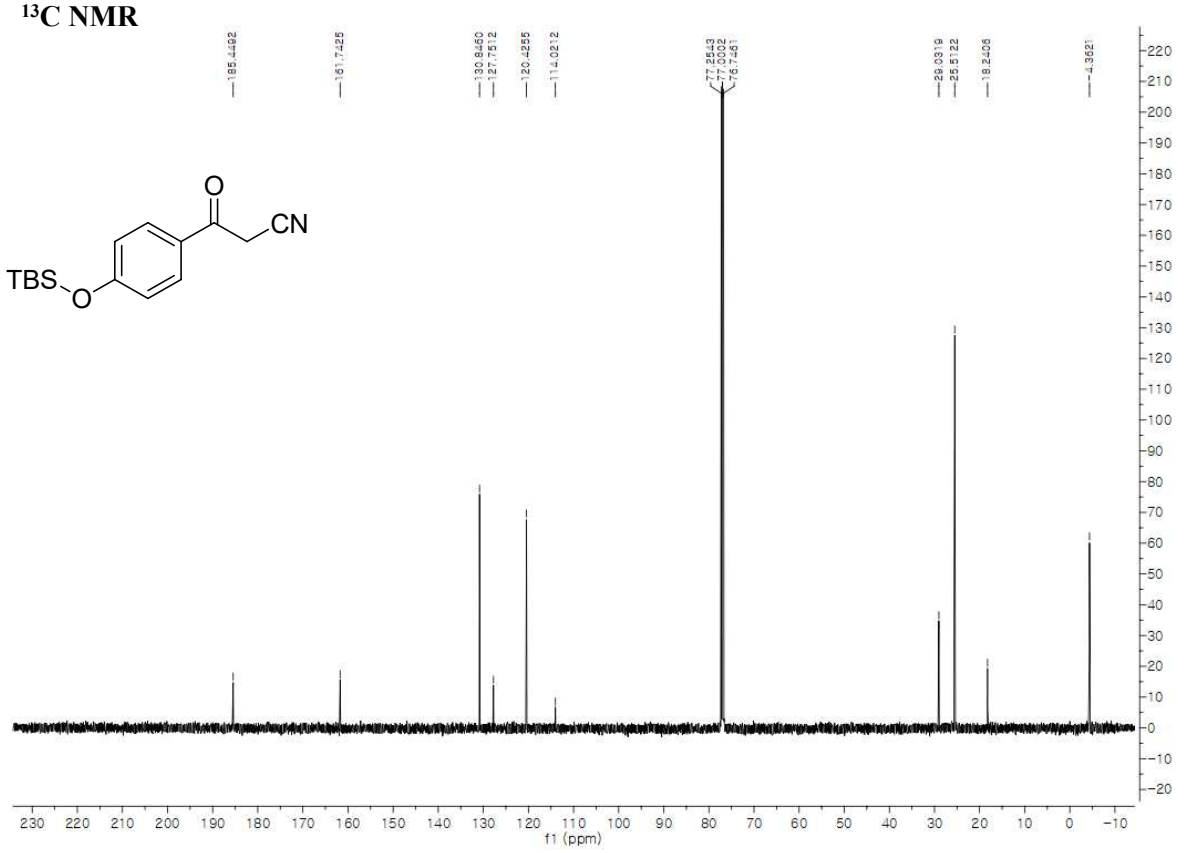
^{13}C NMR



3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-3-oxopropanenitrile (3i)

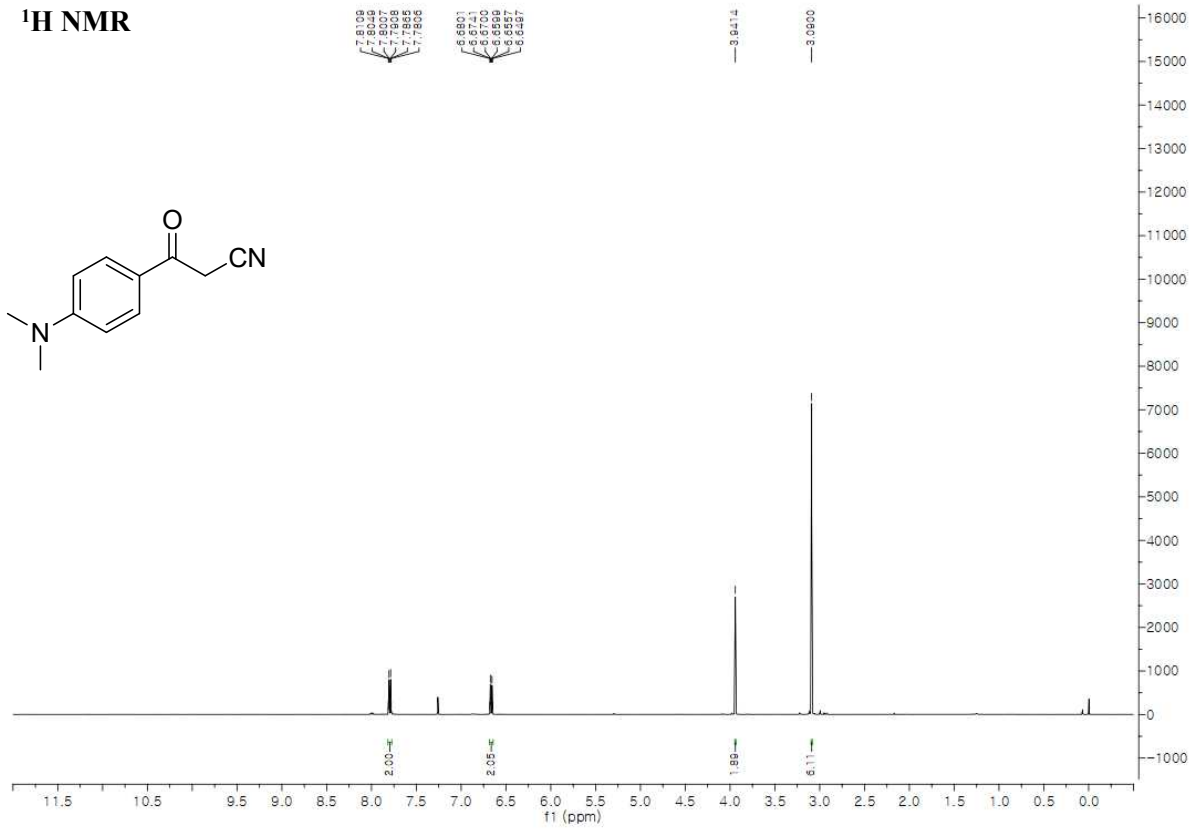
^{1}H NMR

^{13}C NMR

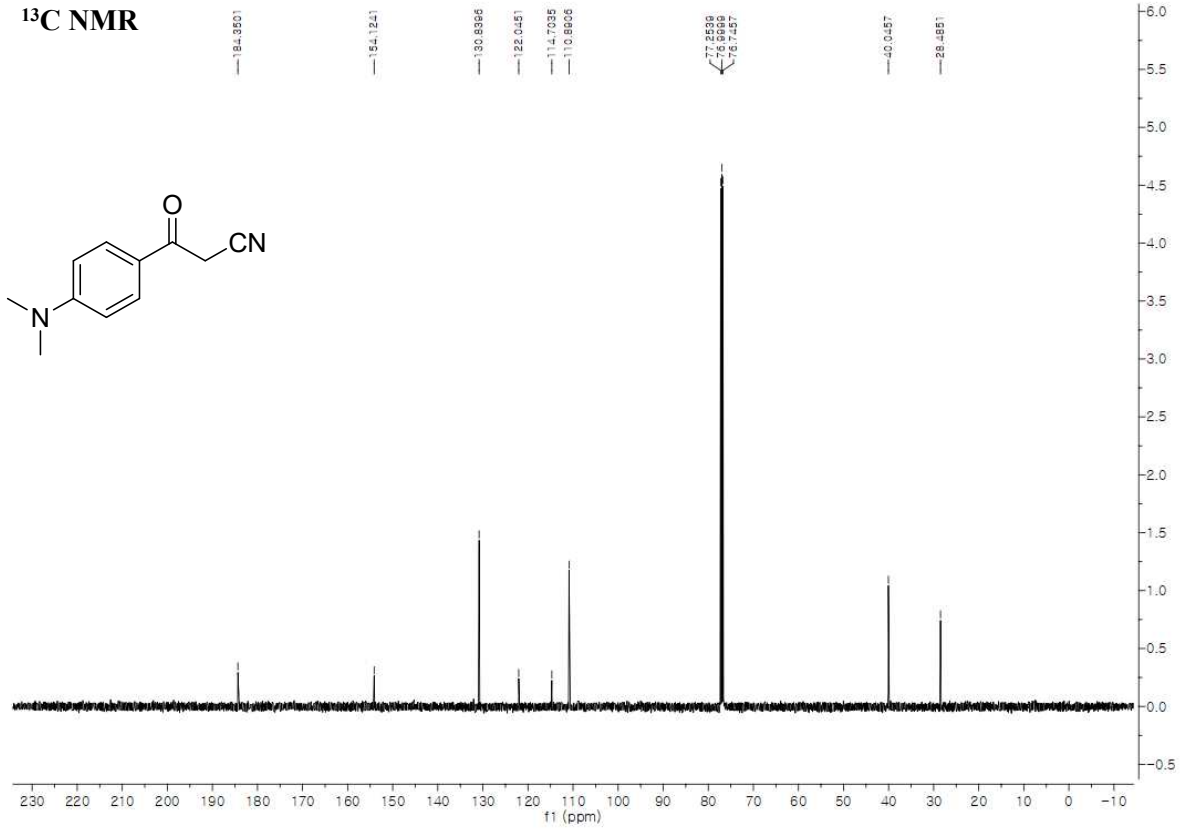


3-(4-Dimethylaminophenyl)-3-oxopropanenitrile (3j)

^{1}H NMR

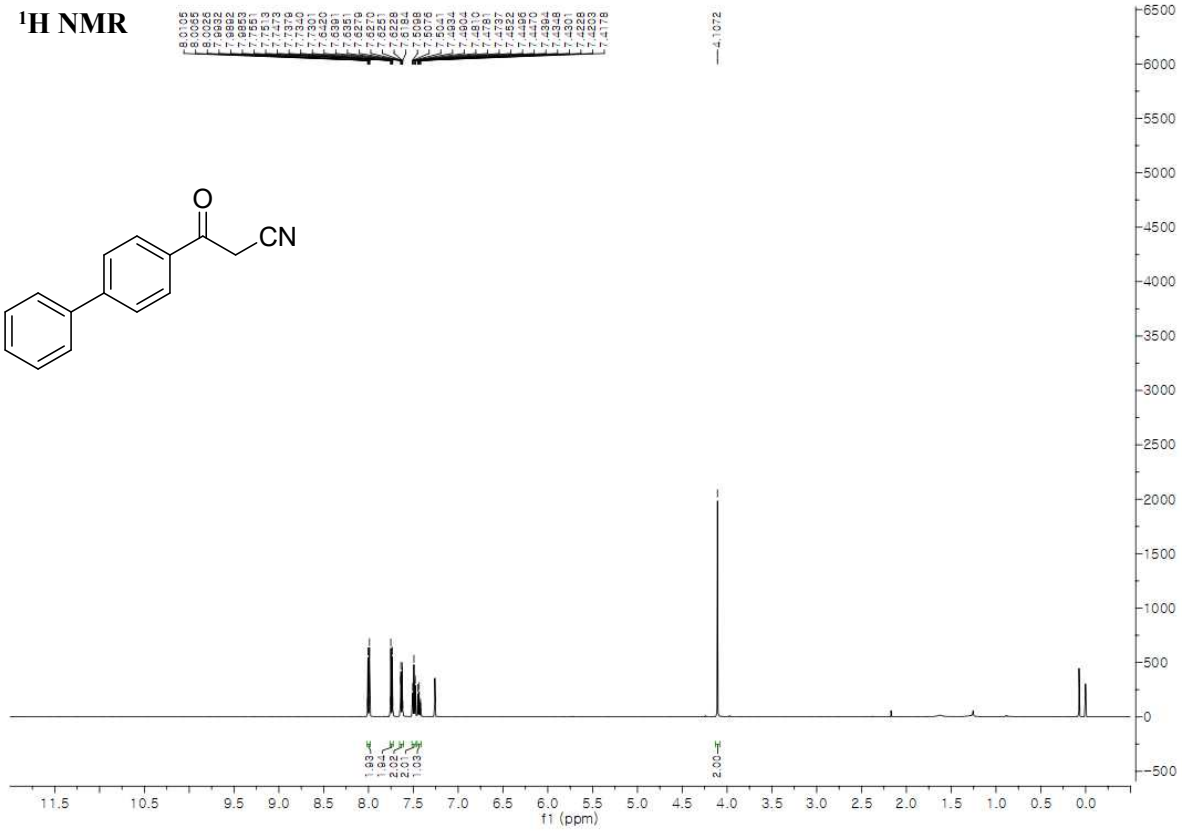


^{13}C NMR

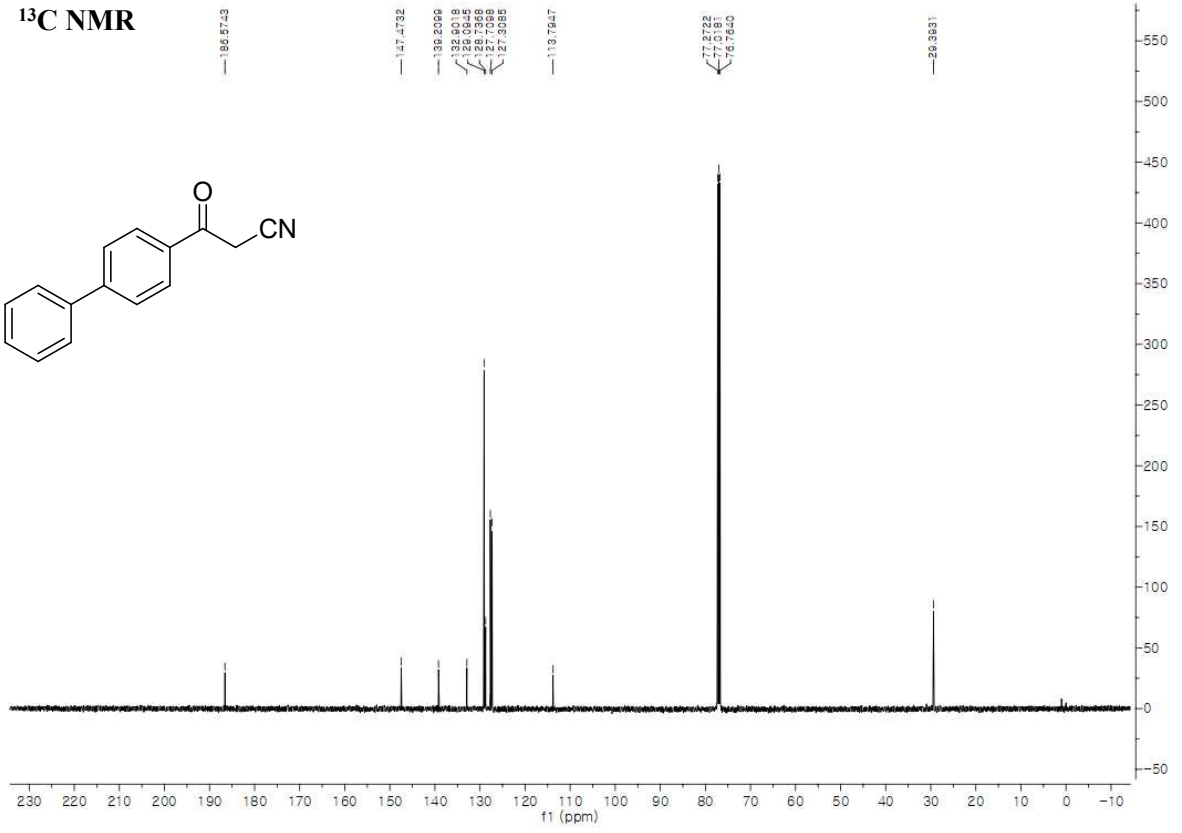


3-(4-Biphenylyl)-3-oxopropanenitrile (3k)

^{1}H NMR

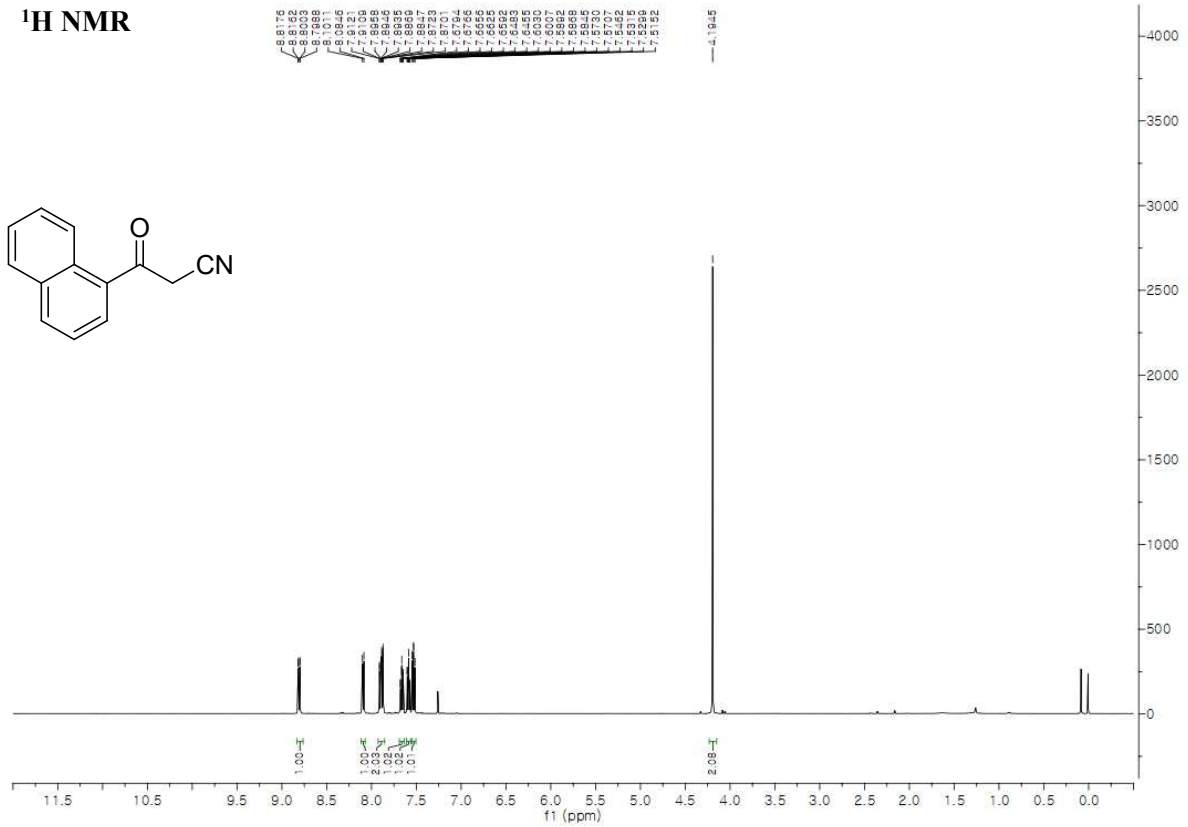


^{13}C NMR



3-(Naphthalen-1-yl)-3-oxopropanenitrile (3l)

^{1}H NMR



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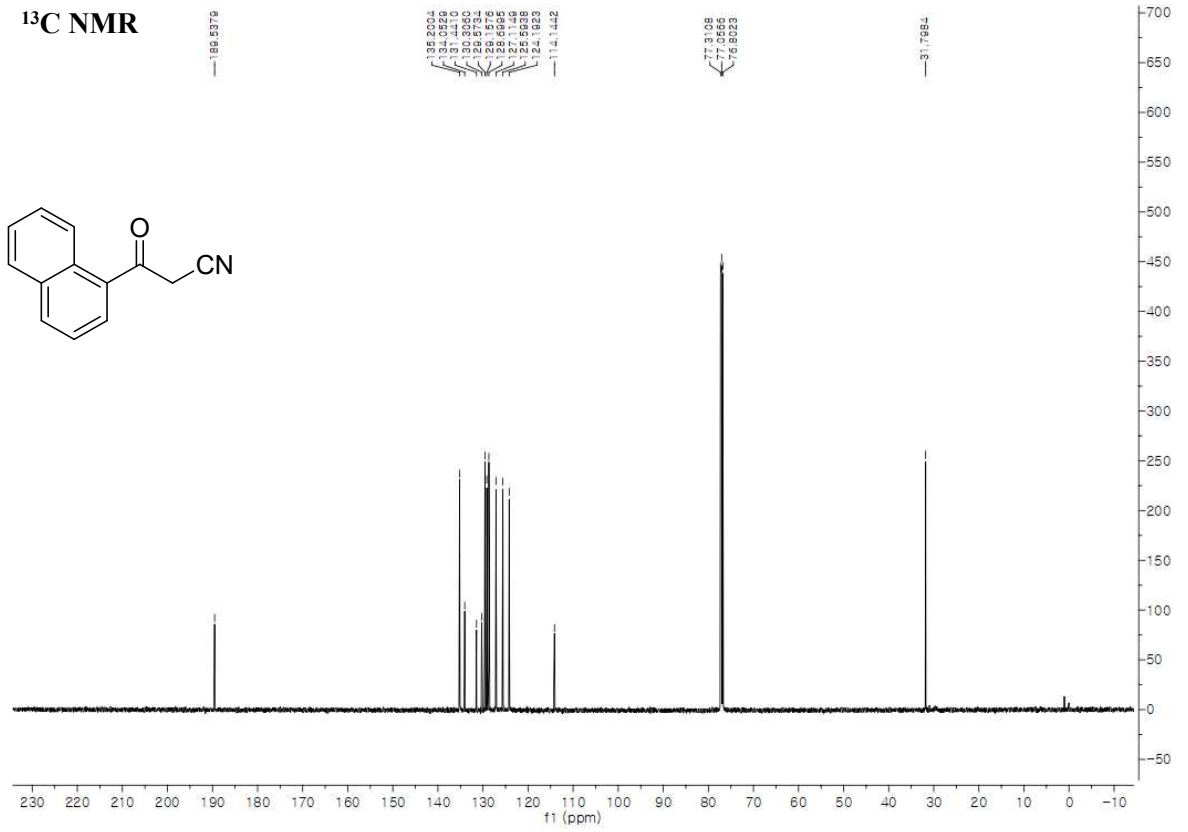
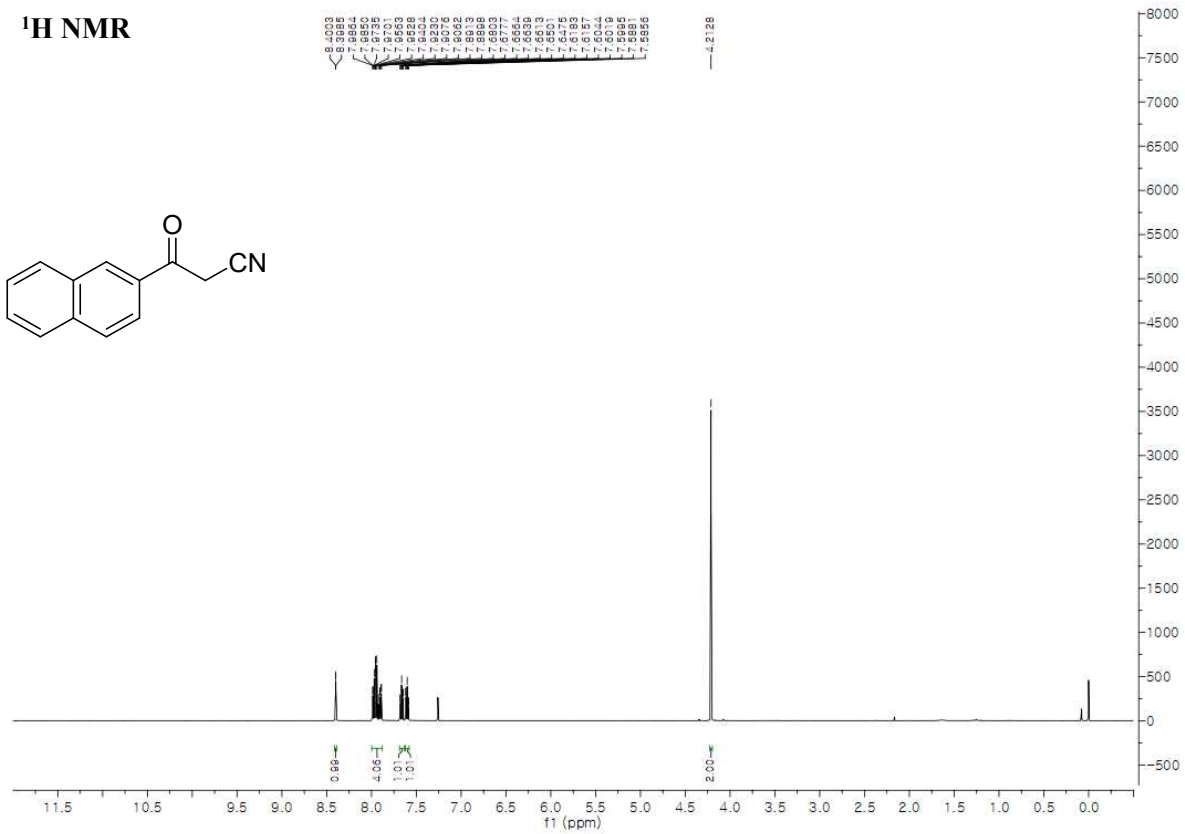
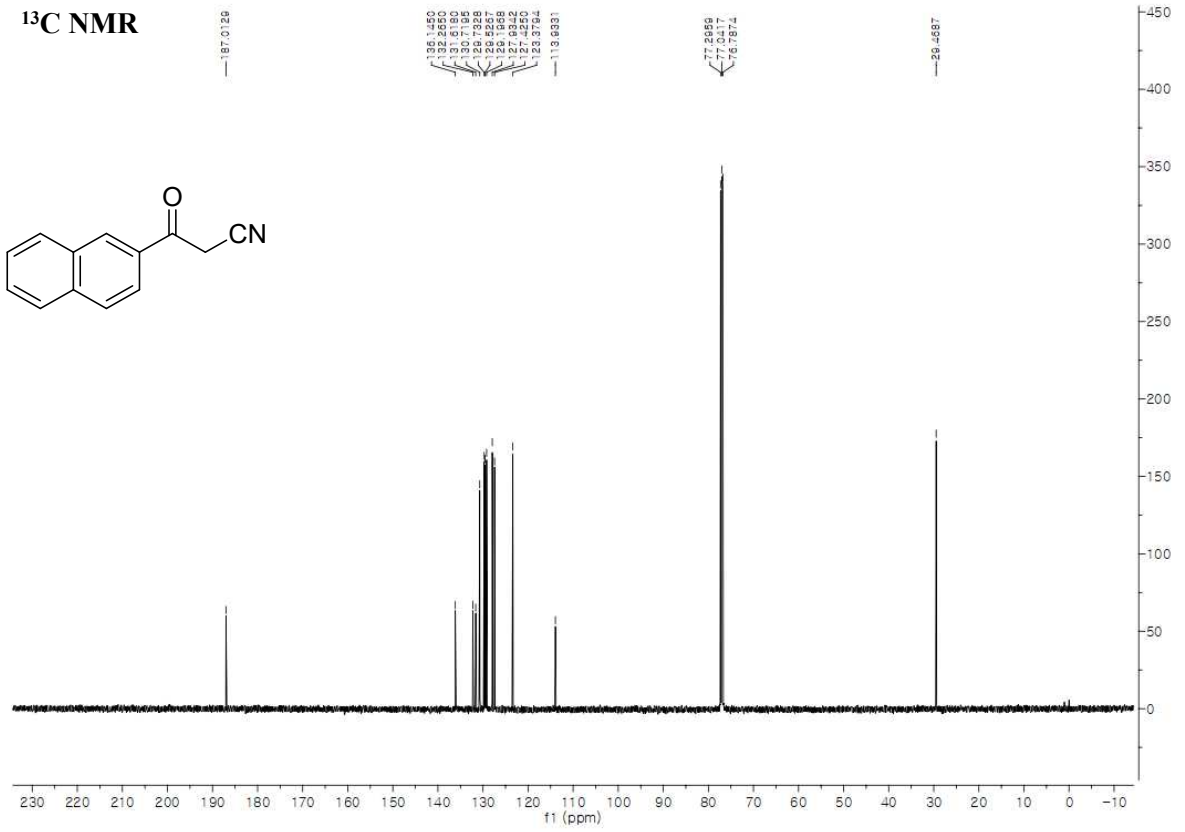


3-(Naphthalen-2-yl)-3-oxopropanenitrile (3m)

^{1}H NMR

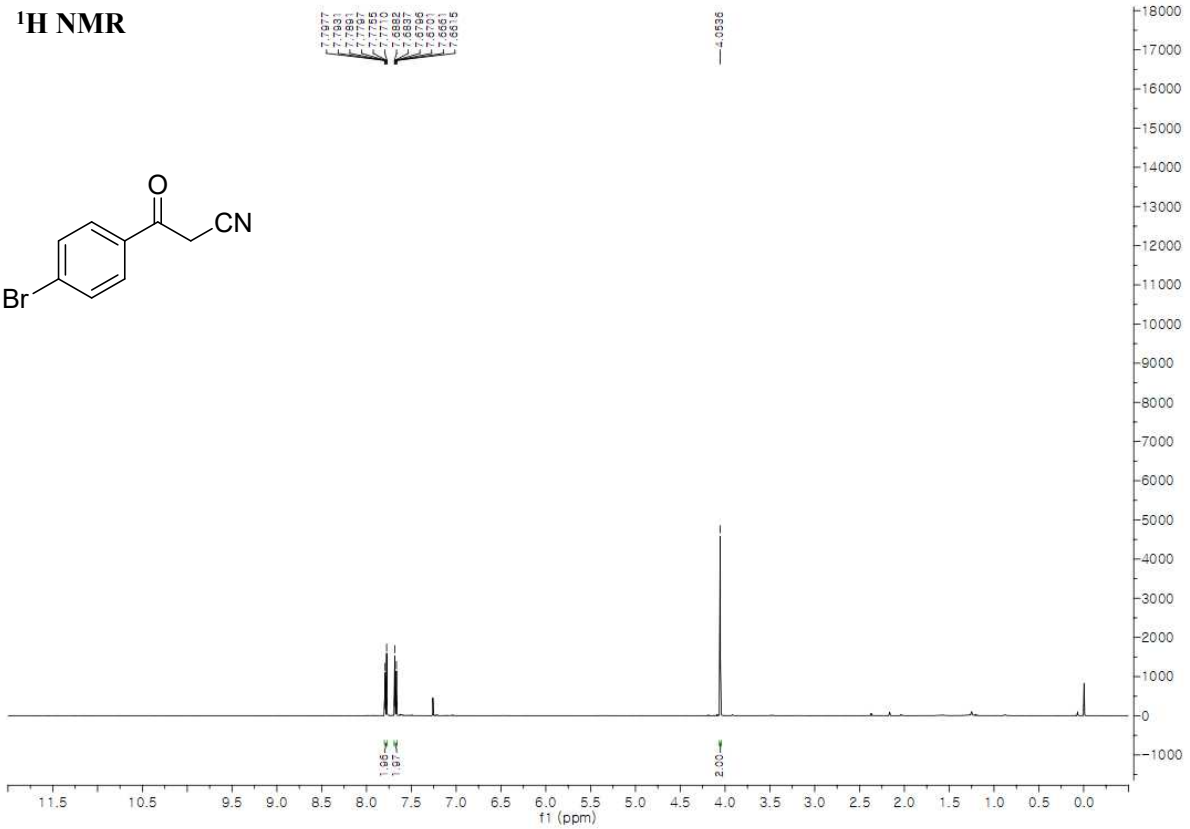


^{13}C NMR

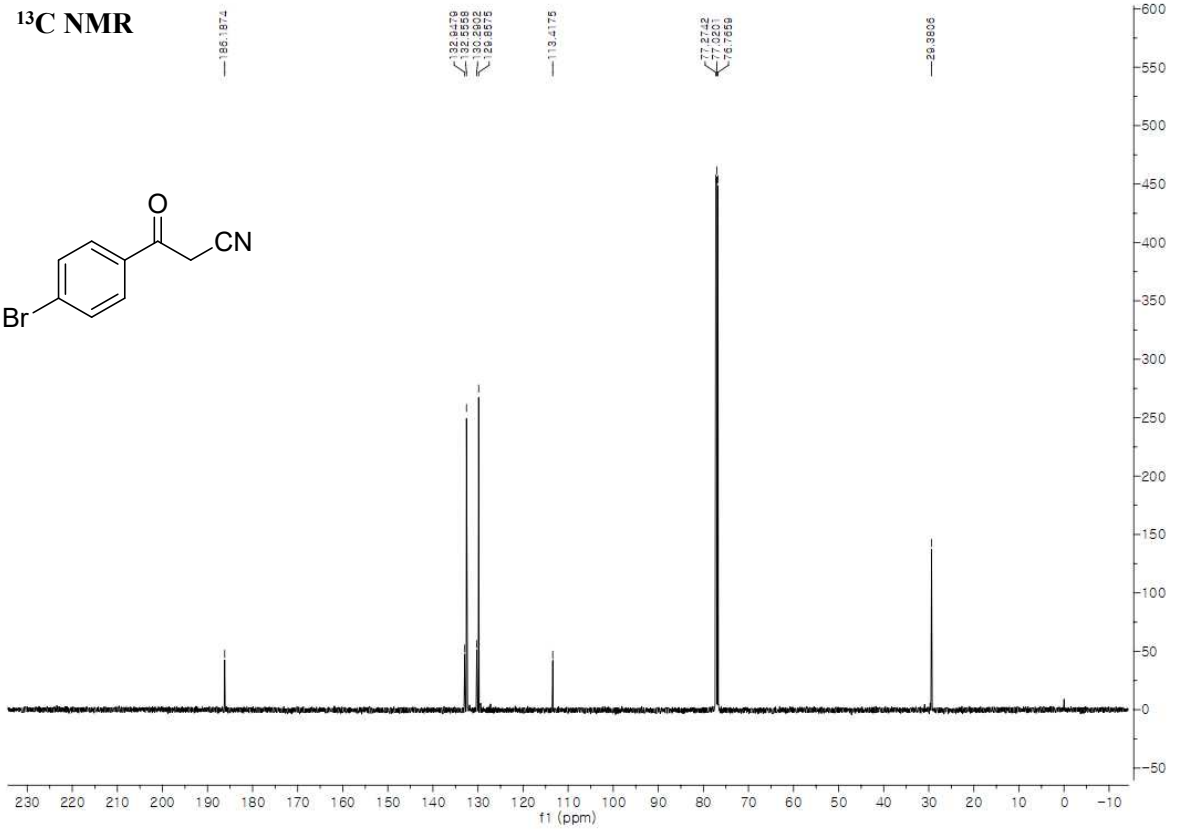


3-(4-Bromophenyl)-3-oxopropanenitrile (3n)

^{1}H NMR

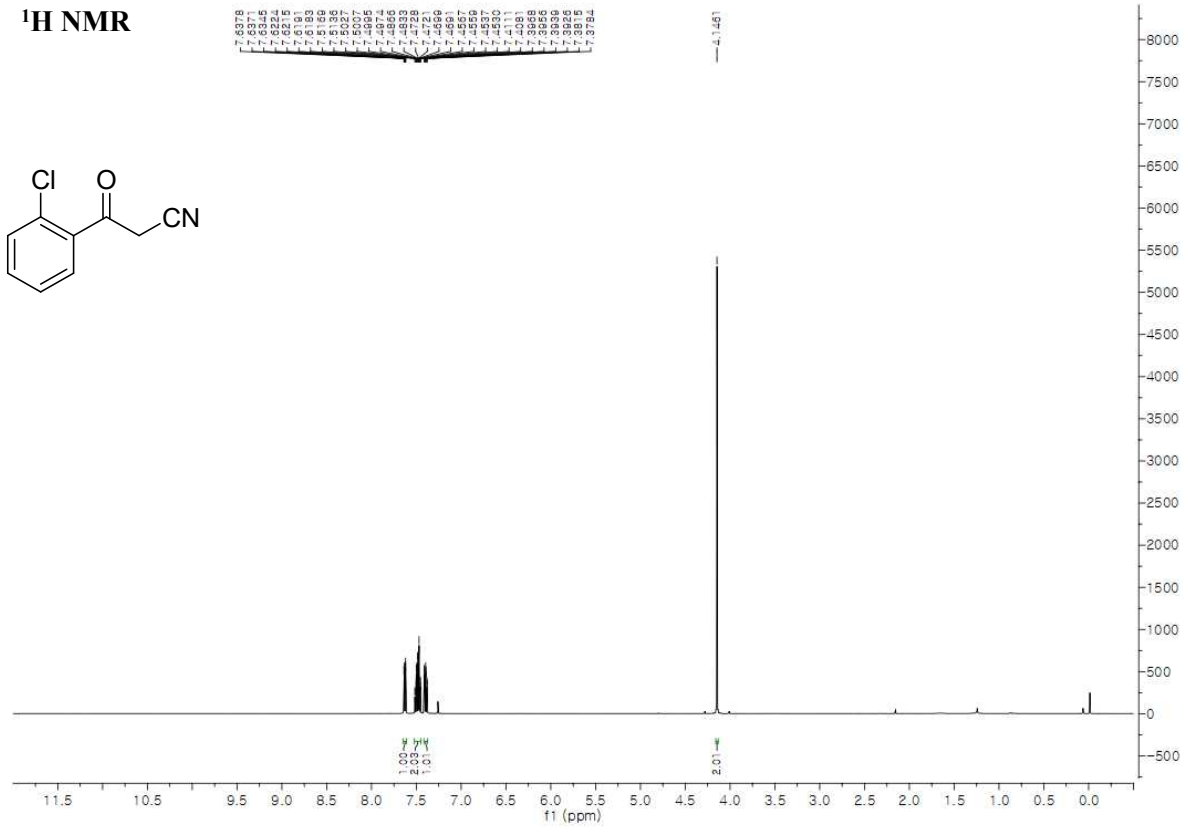


^{13}C NMR

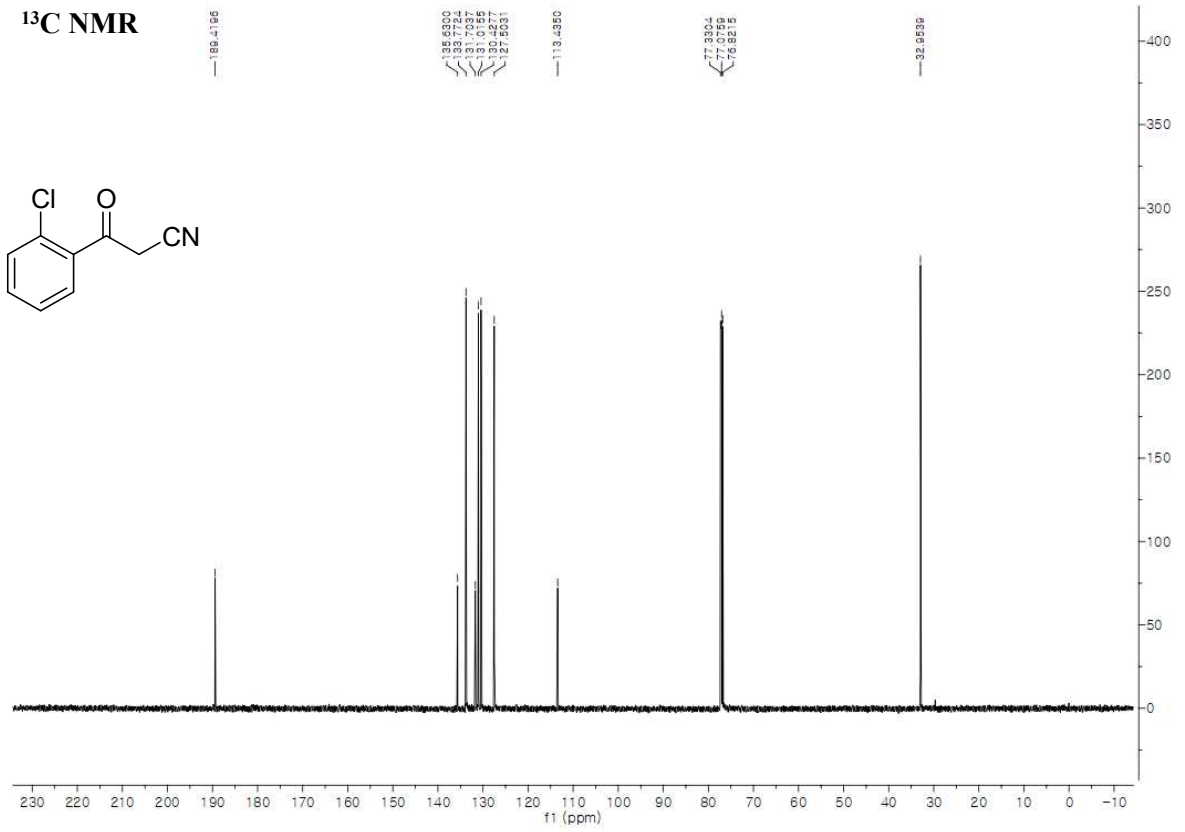


3-(2-Chlorophenyl)-3-oxopropanenitrile (3o)

^{1}H NMR

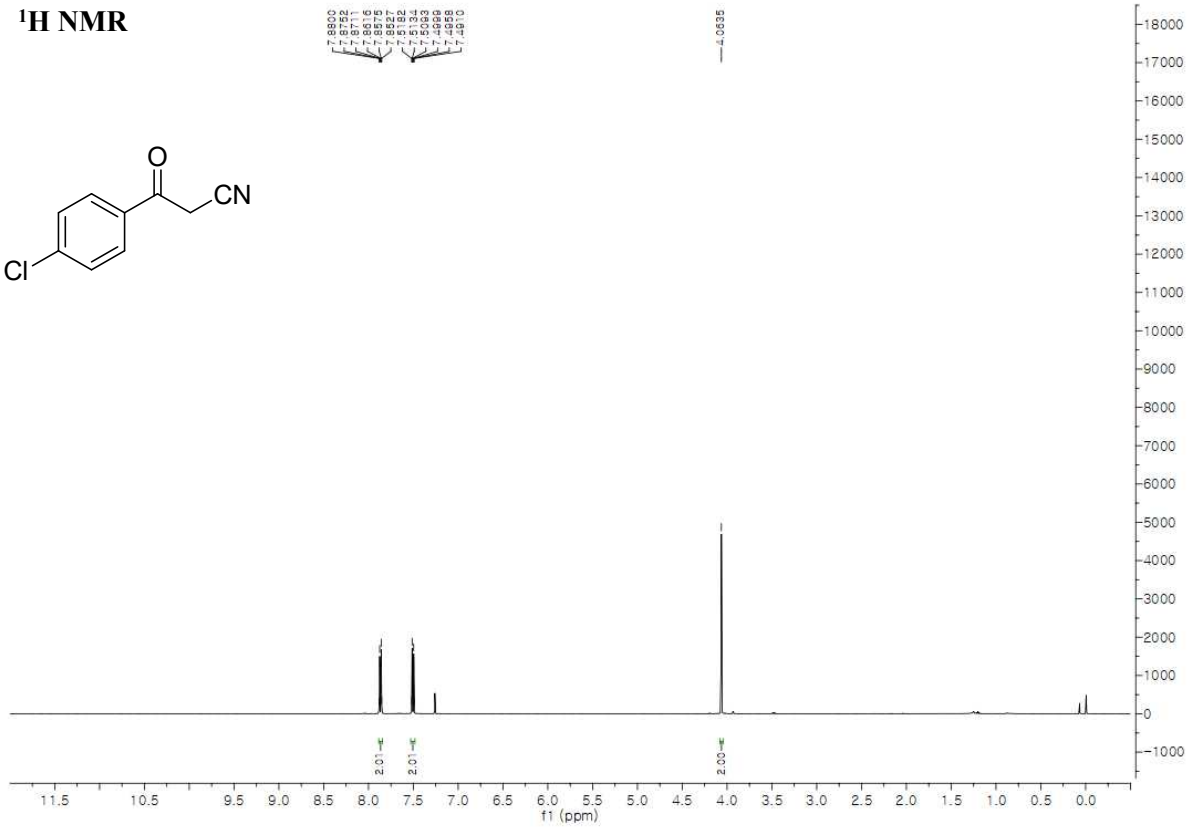


^{13}C NMR

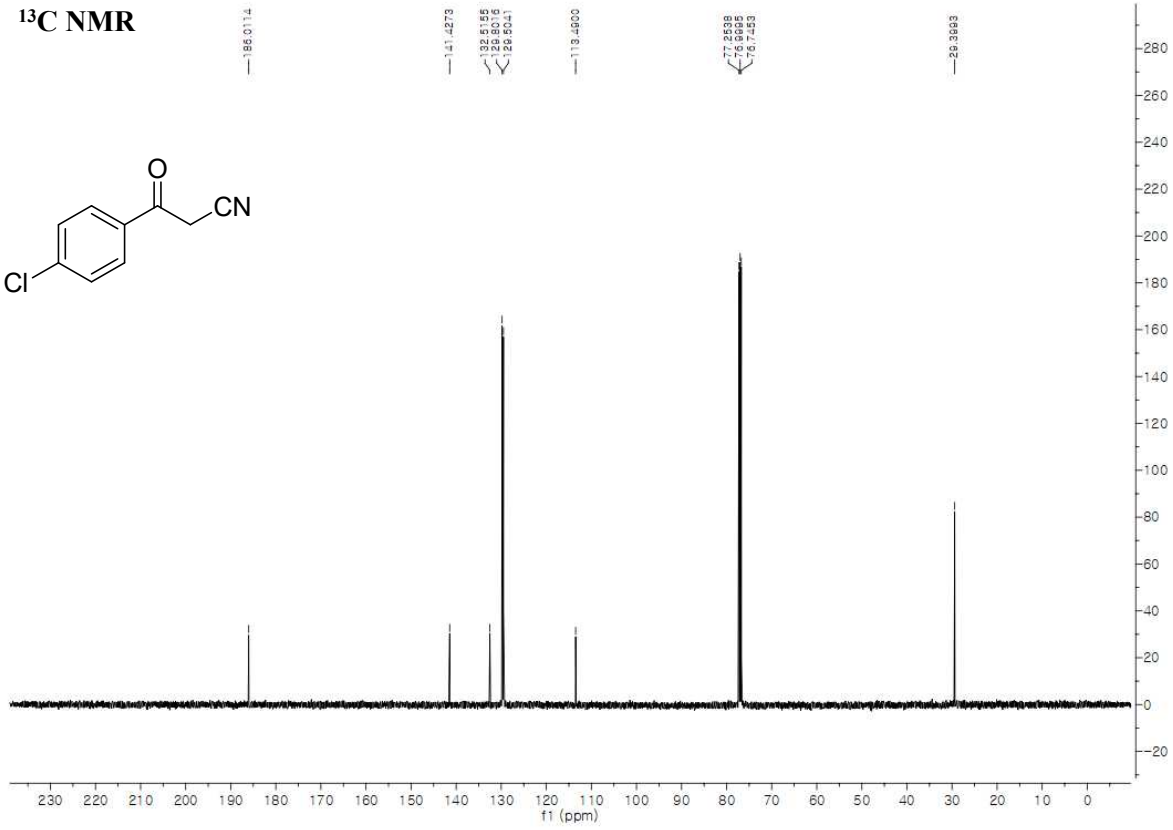


3-(4-Chlorophenyl)-3-oxopropanenitrile (3p)

^{1}H NMR

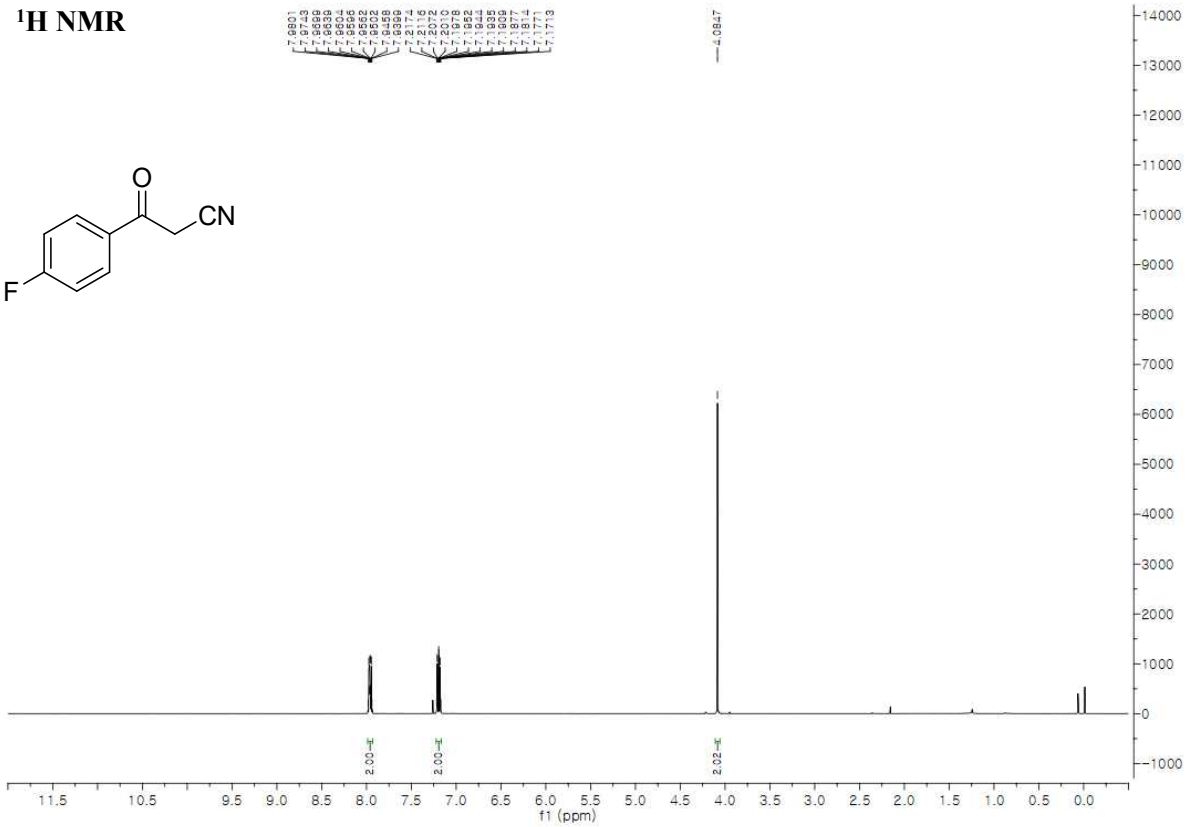


^{13}C NMR



3-(4-Fluorophenyl)-3-oxopropanenitrile (3q)

^{1}H NMR



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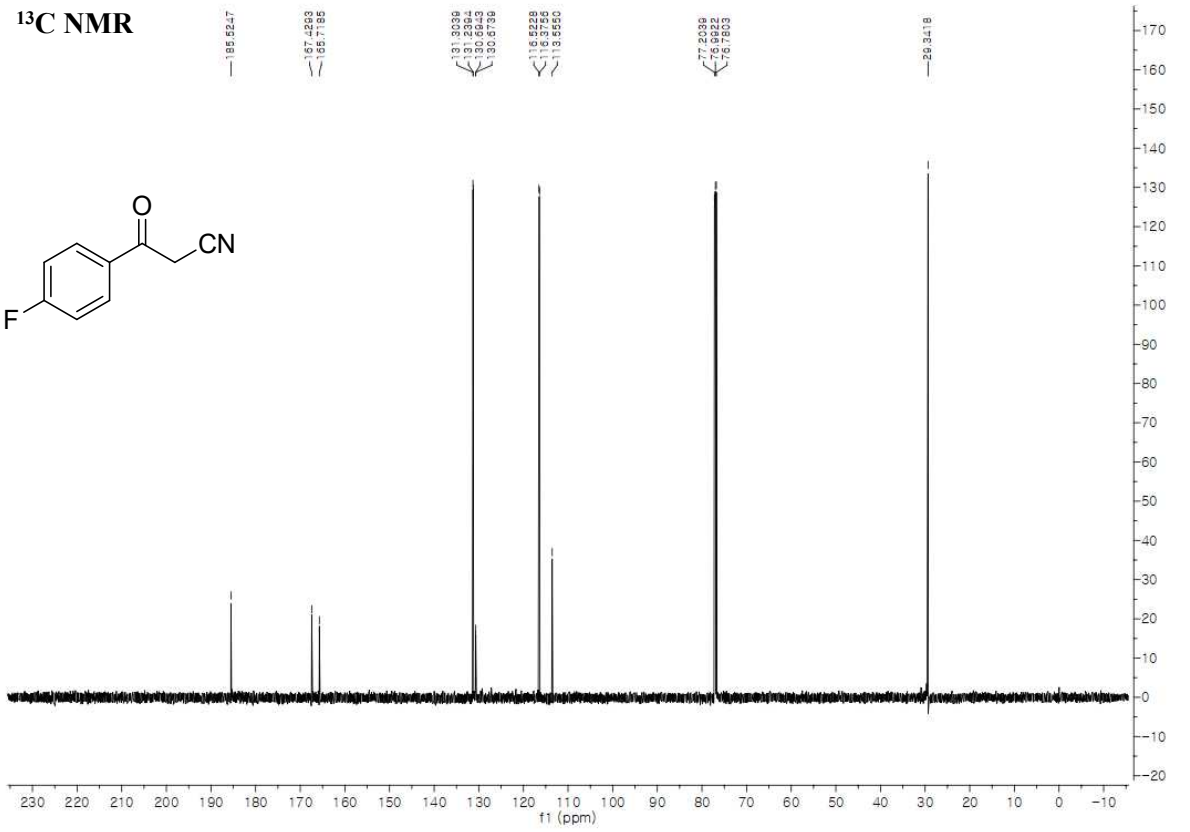
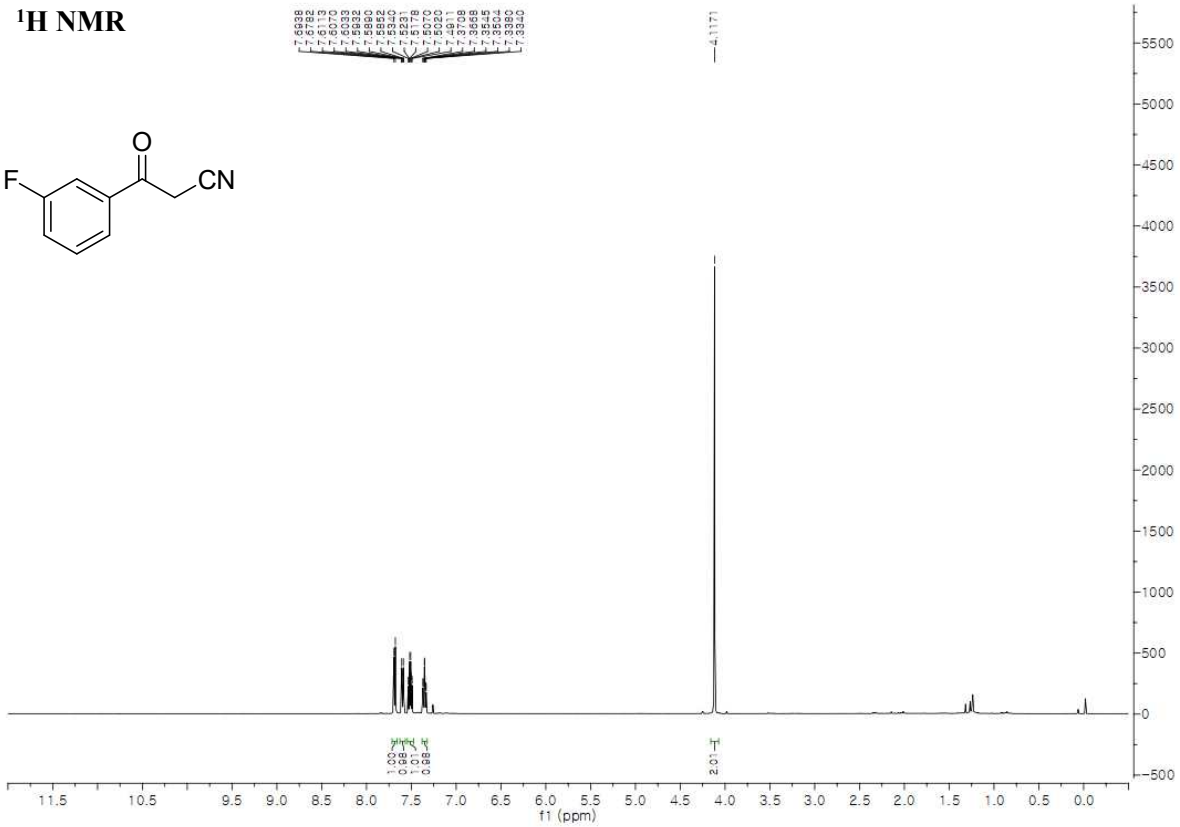
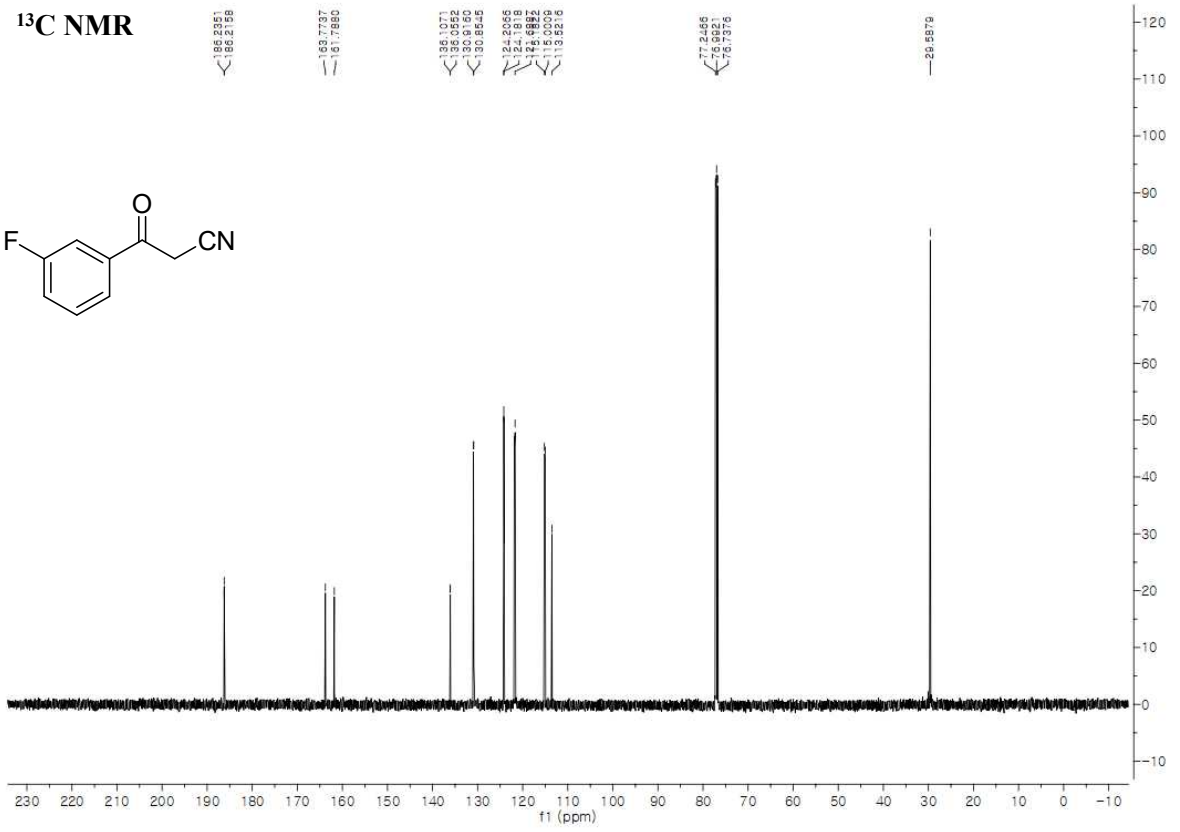


3-(3-Fluorophenyl)-3-oxopropanenitrile (3r)

^{1}H NMR

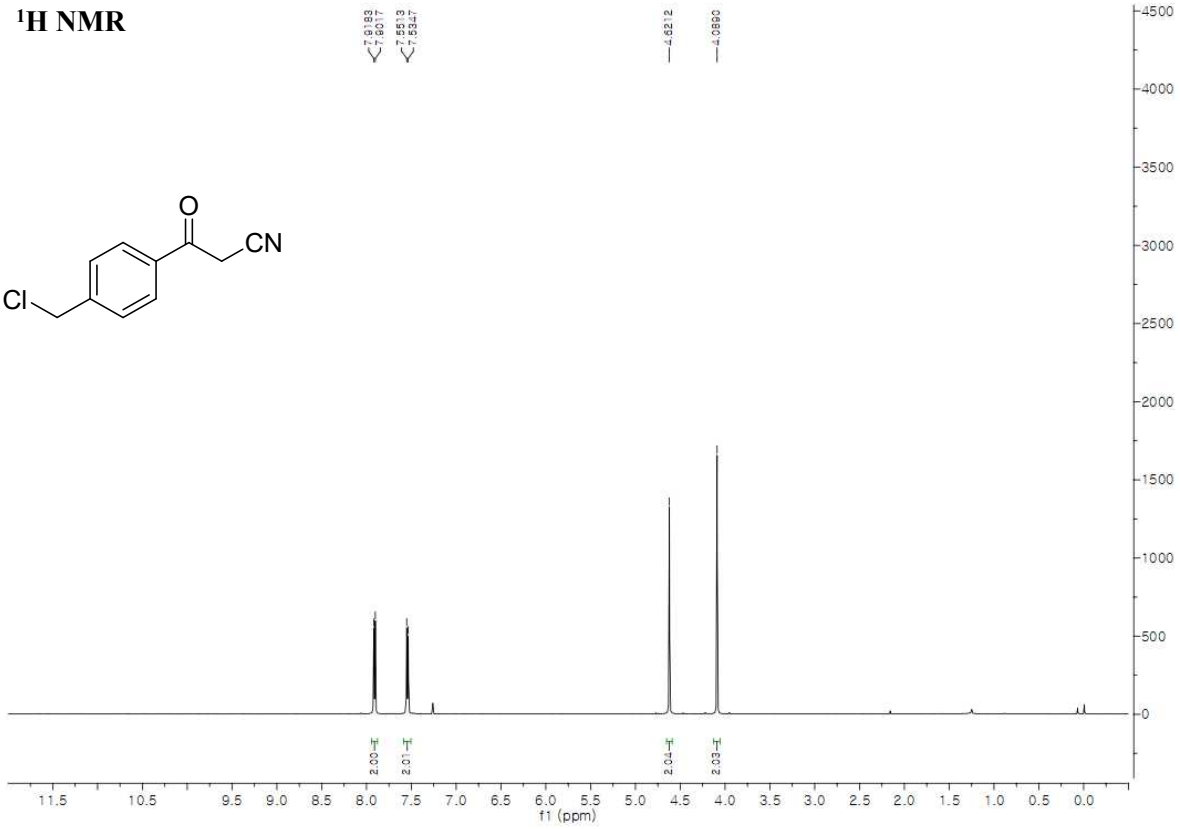


^{13}C NMR

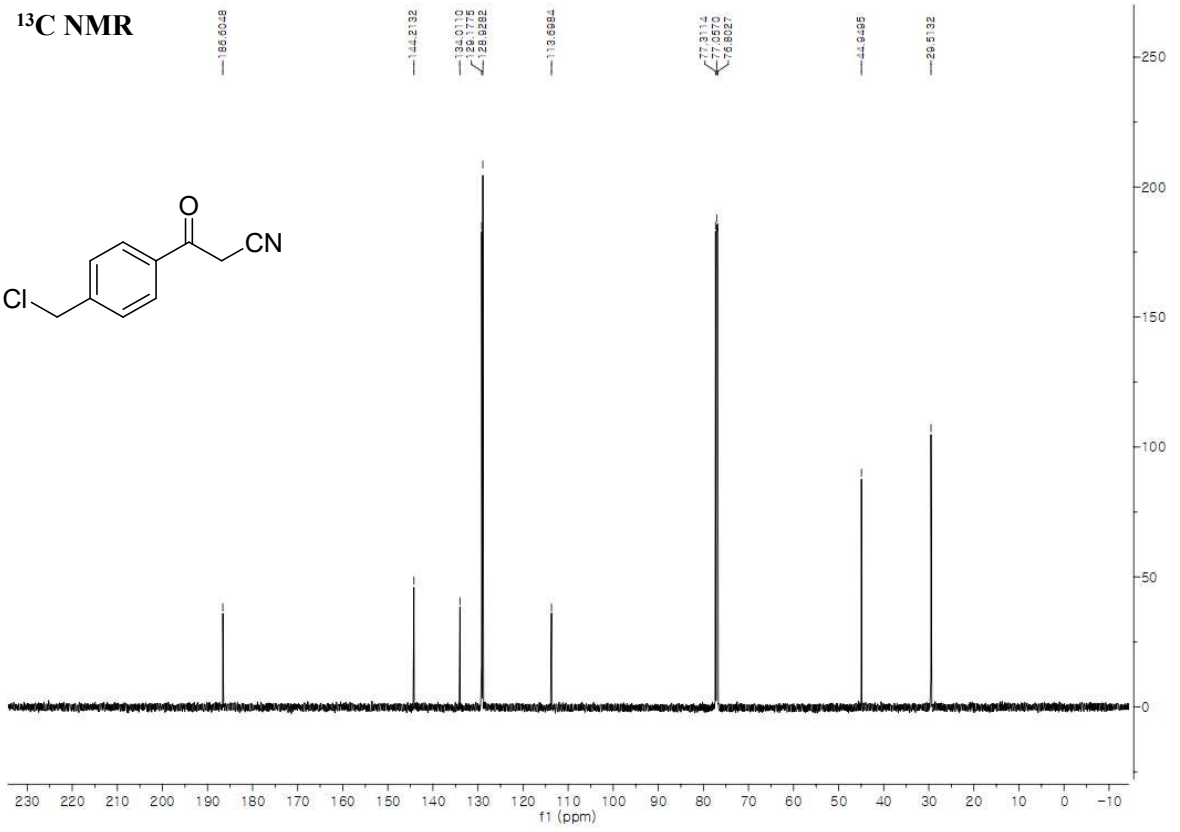


3-(4-(Chloromethyl)phenyl)-3-oxopropanenitrile (3s)

^{1}H NMR

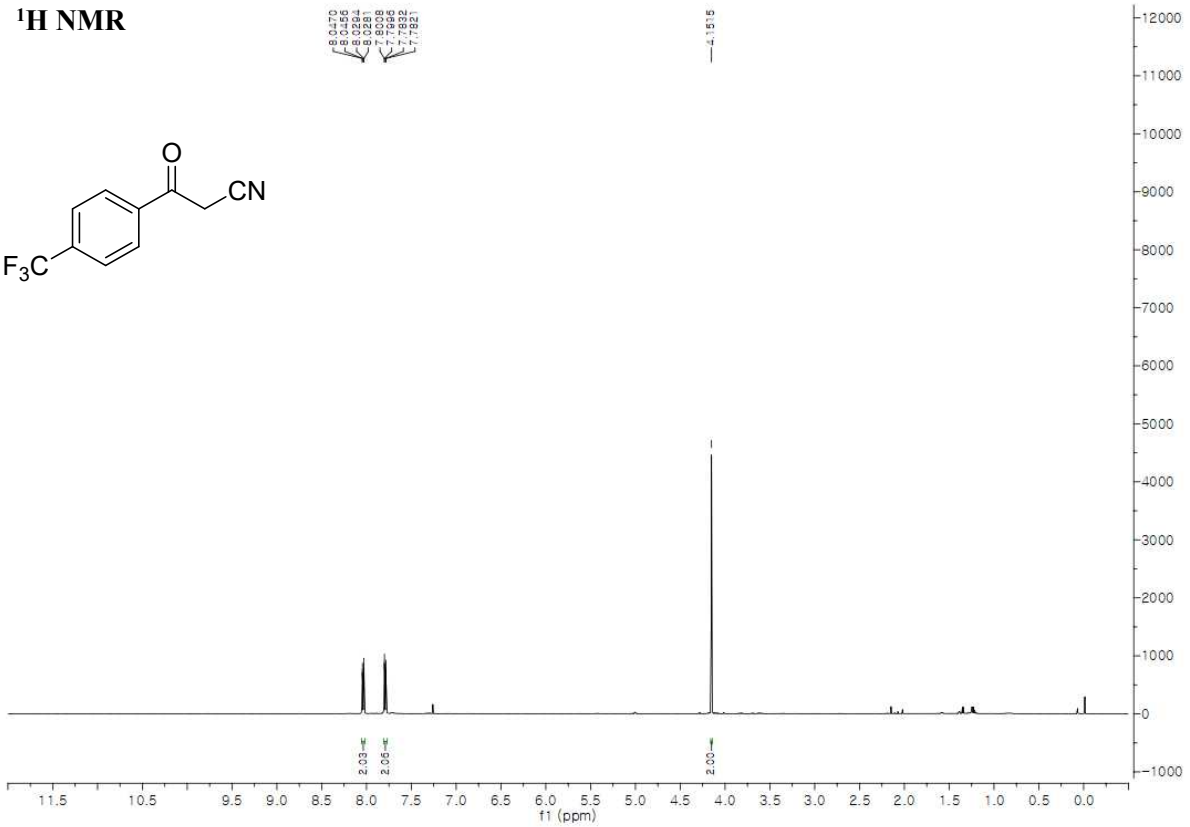


^{13}C NMR

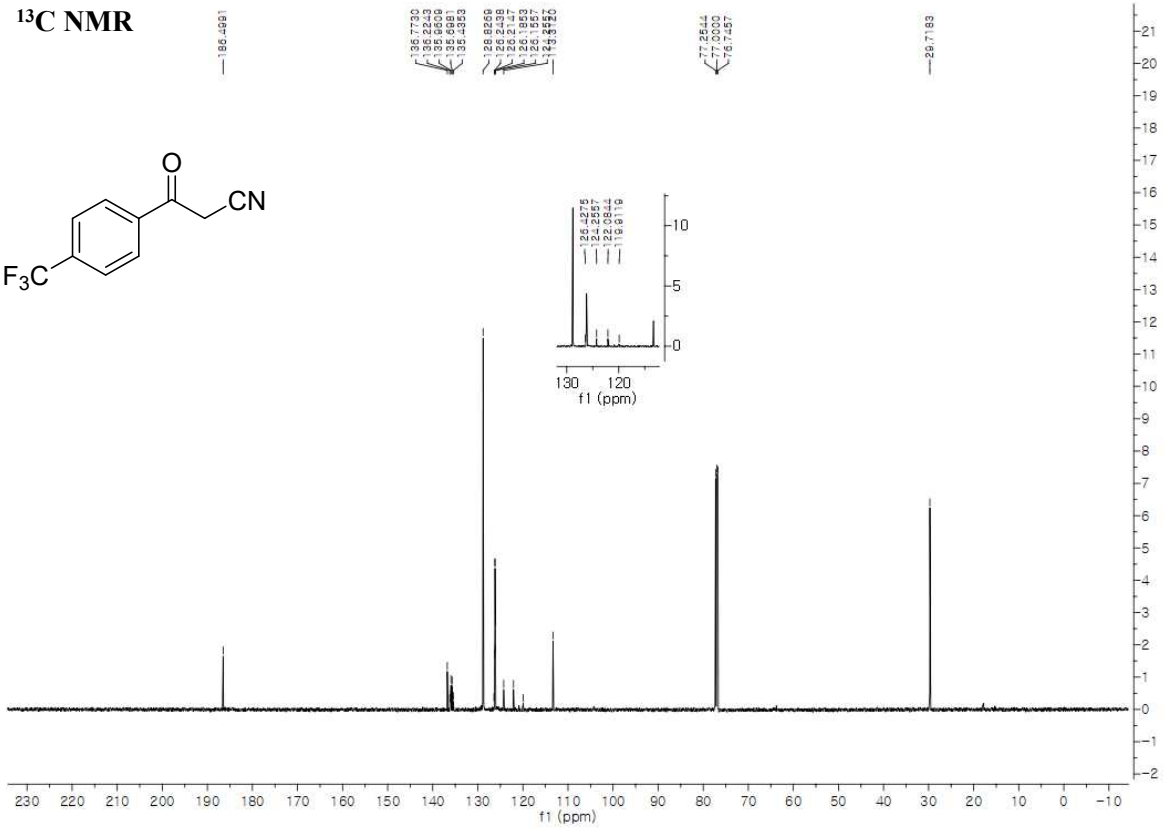


3-Oxo-3-(4-(trifluoromethyl)phenyl)propanenitrile (3t)

^{1}H NMR

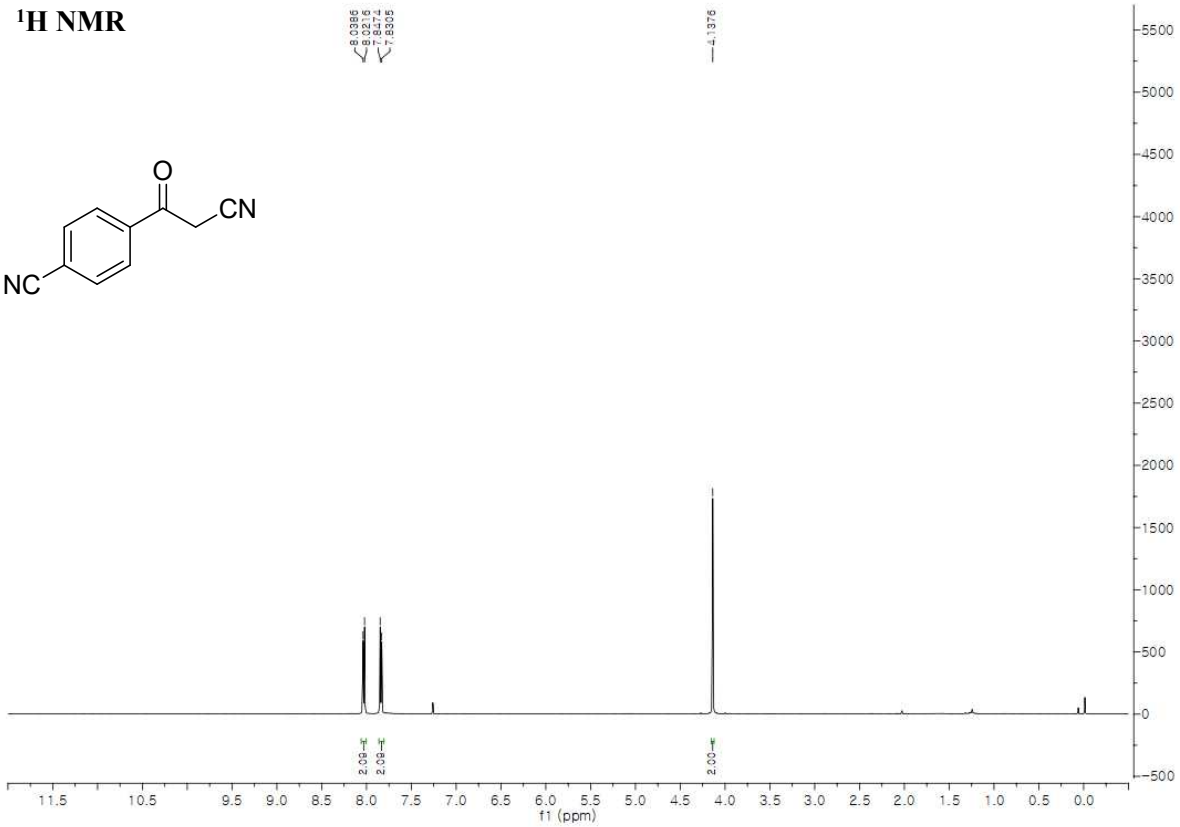


^{13}C NMR

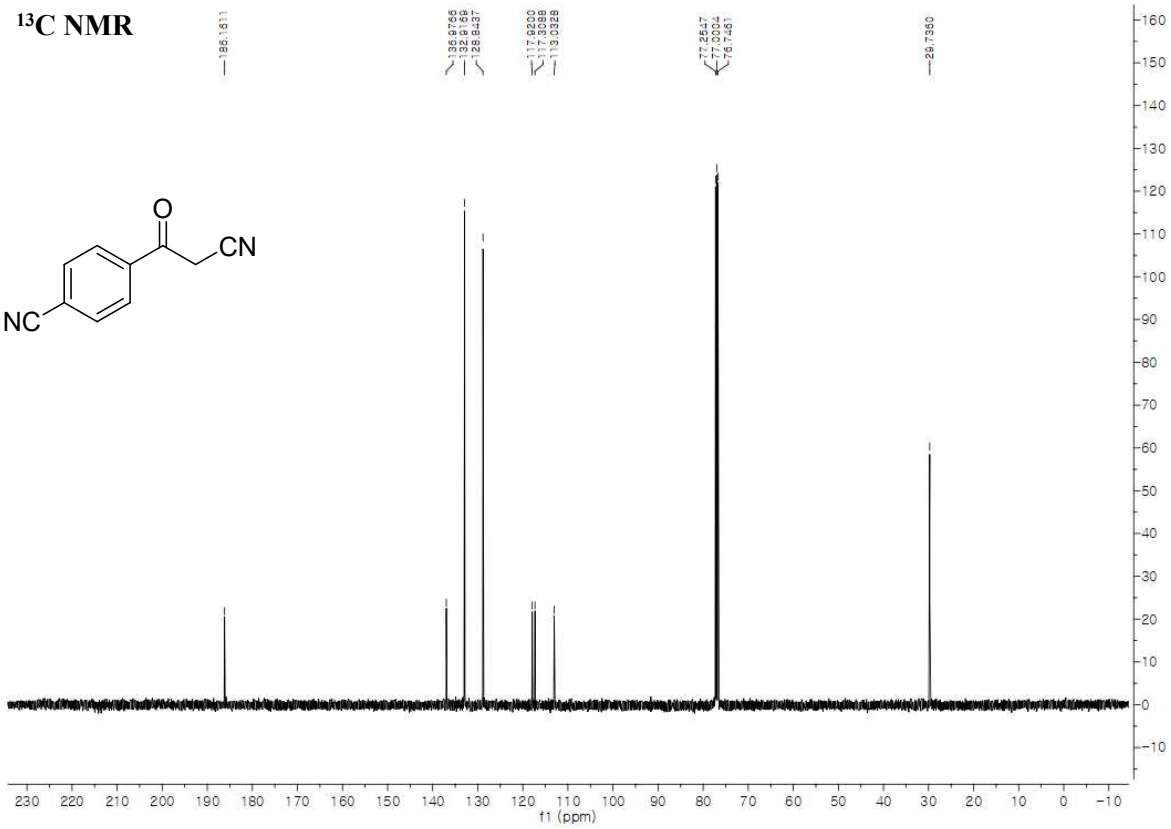


4-(2-Cyanoacetyl)benzonitrile (3u)

^{1}H NMR

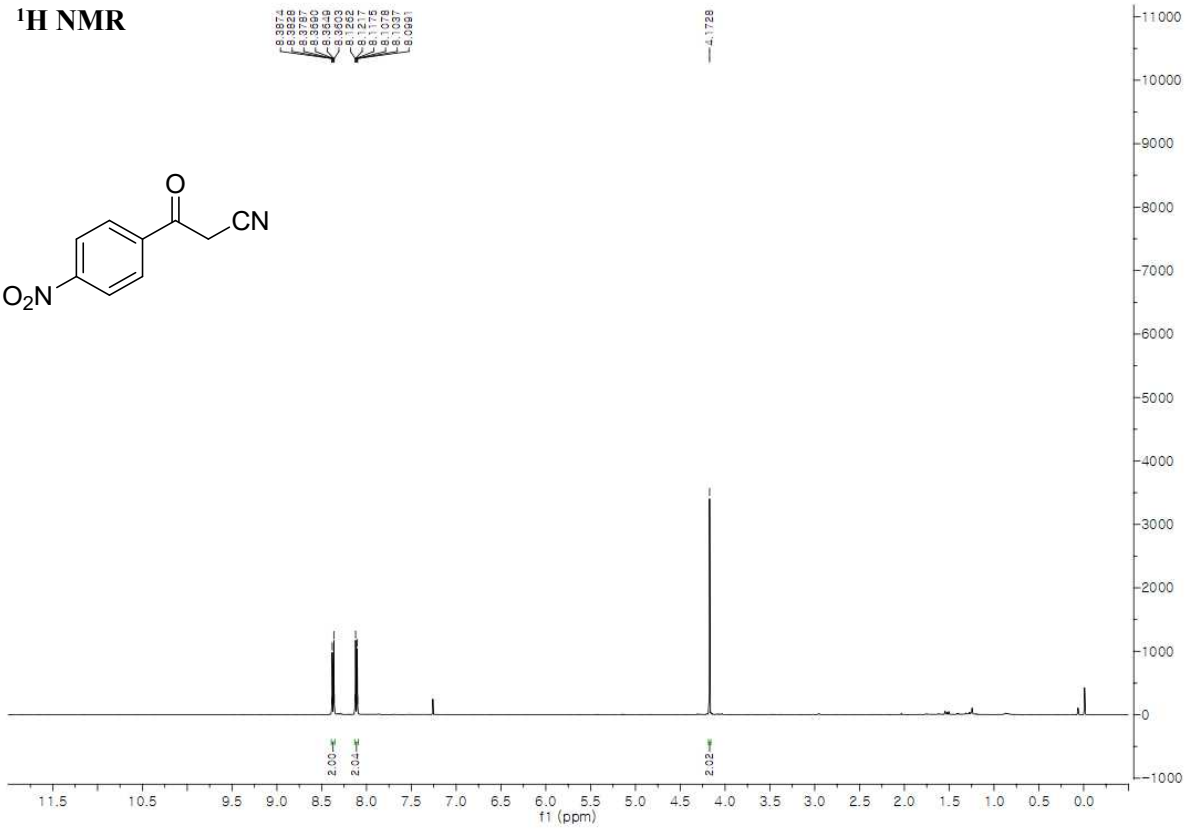


^{13}C NMR

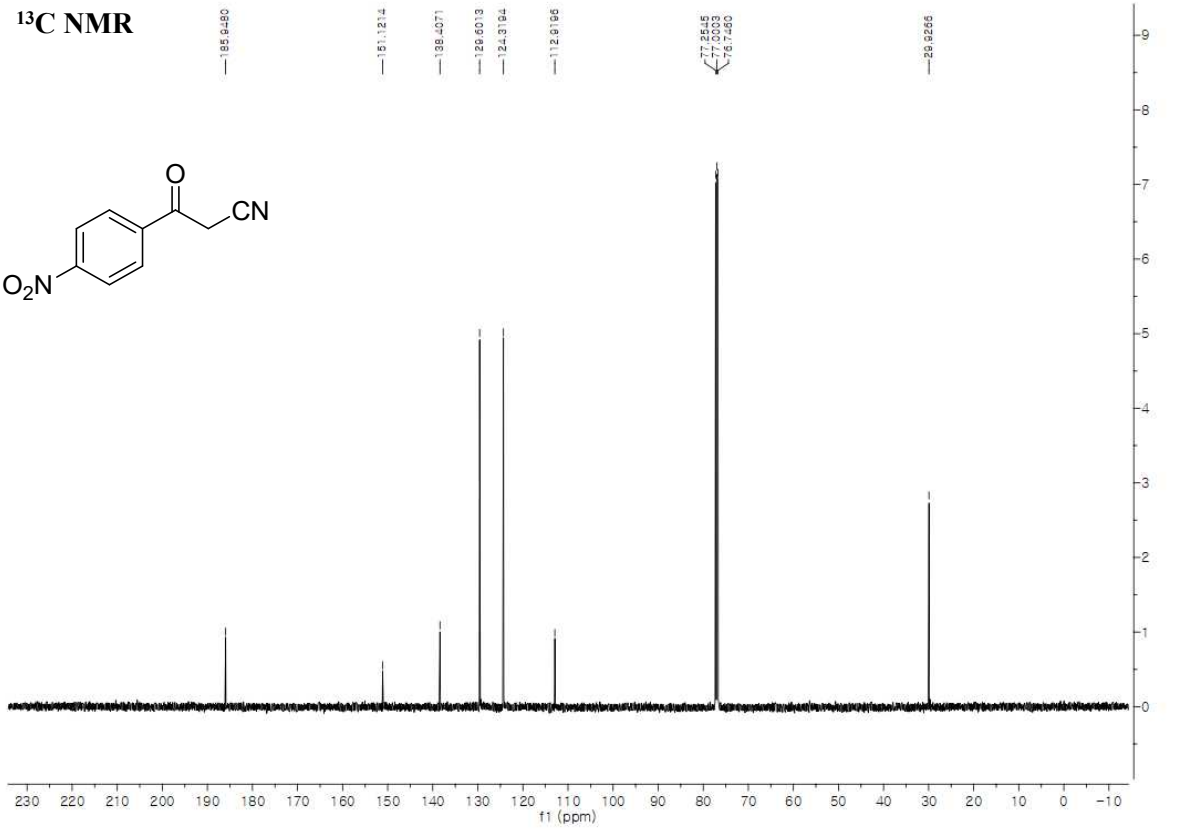


3-(4-Nitrophenyl)-3-oxopropanenitrile (3v)

^{1}H NMR

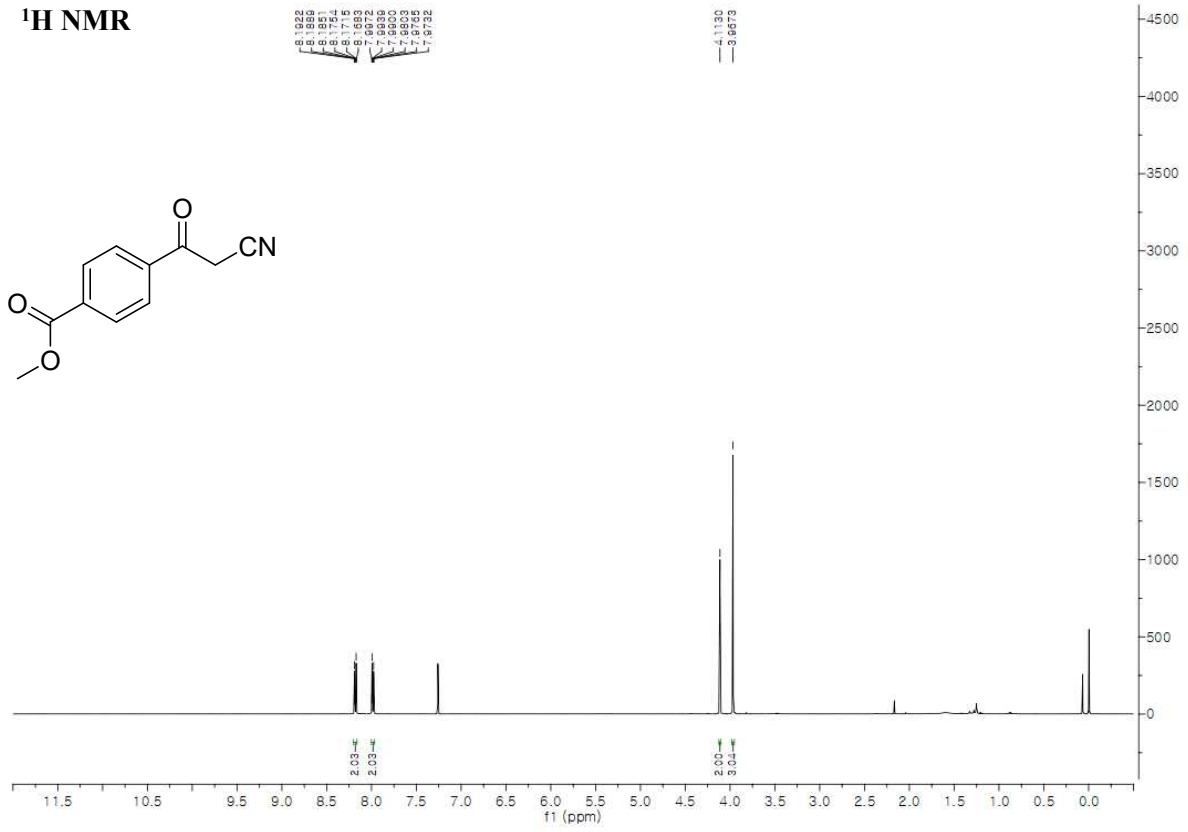


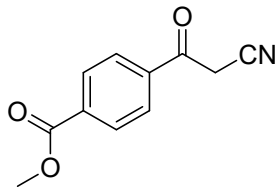
^{13}C NMR

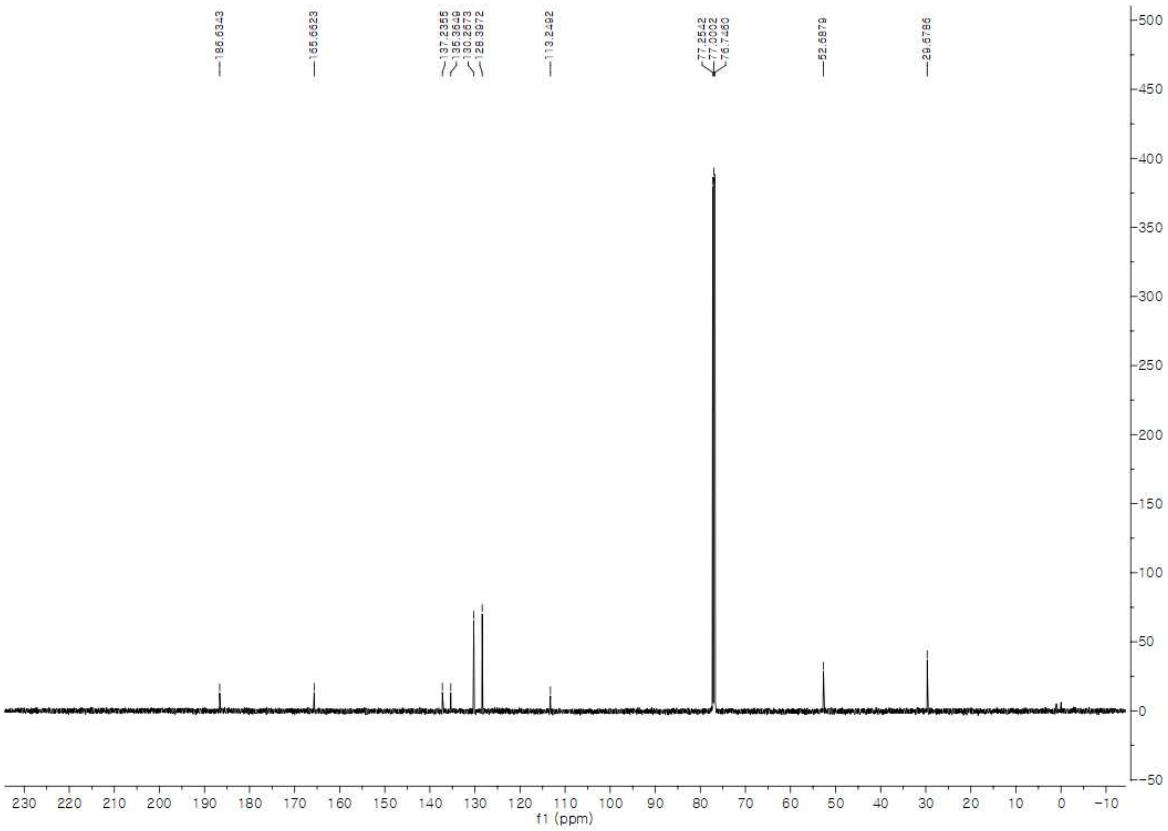


Methyl 4-(2-cyanoacetyl)benzoate (3w)

^{1}H NMR



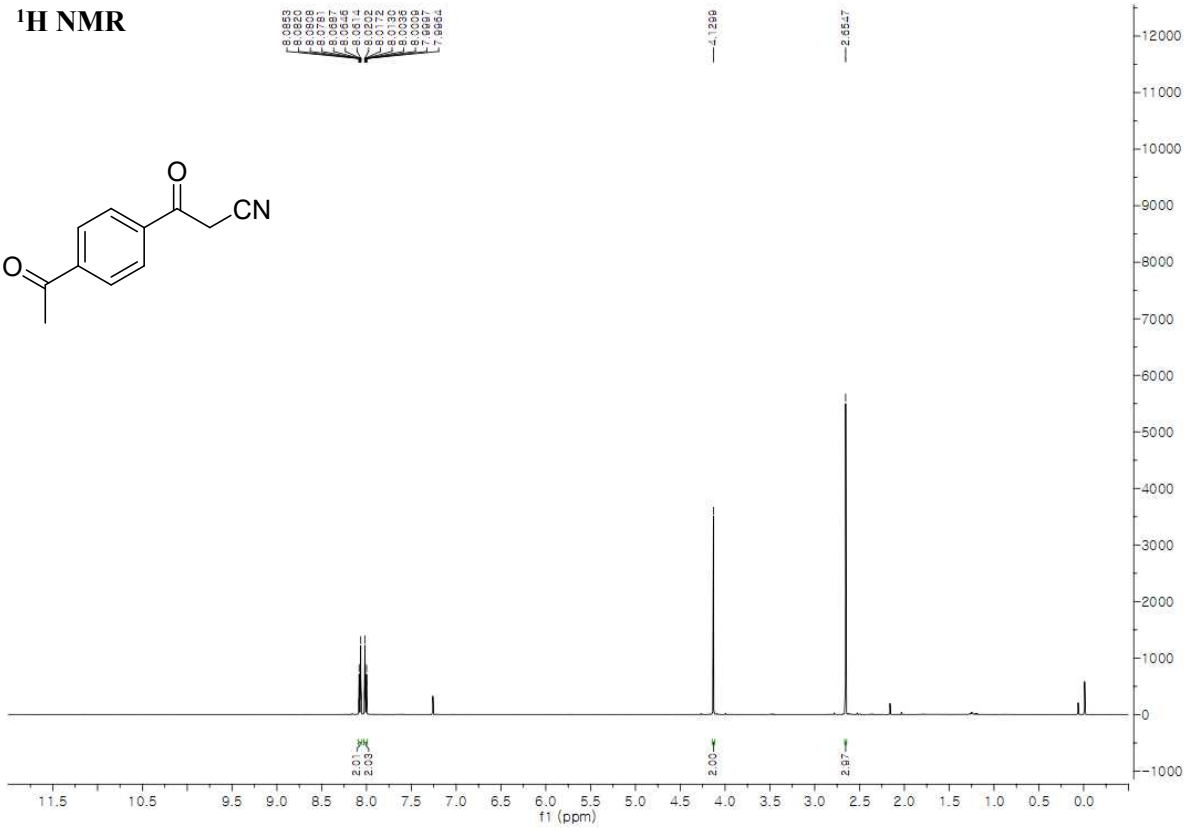



186.6343
165.6623
137.2356
135.5649
130.2673
128.3972
113.2482
77.2542
77.0002
76.7460
52.6879
29.6786
f1 (ppm)

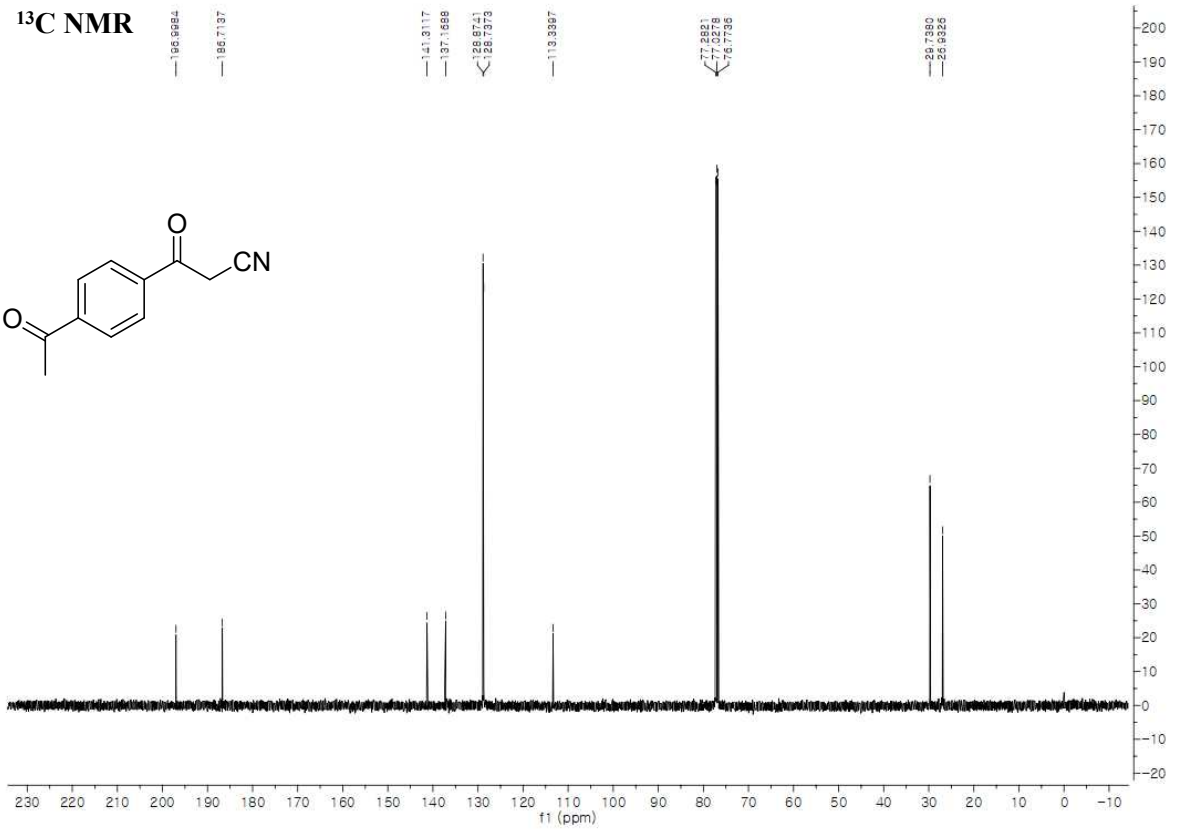
^{13}C NMR

3-(4-Acetylphenyl)-3-oxopropanenitrile (3x)

^{1}H NMR

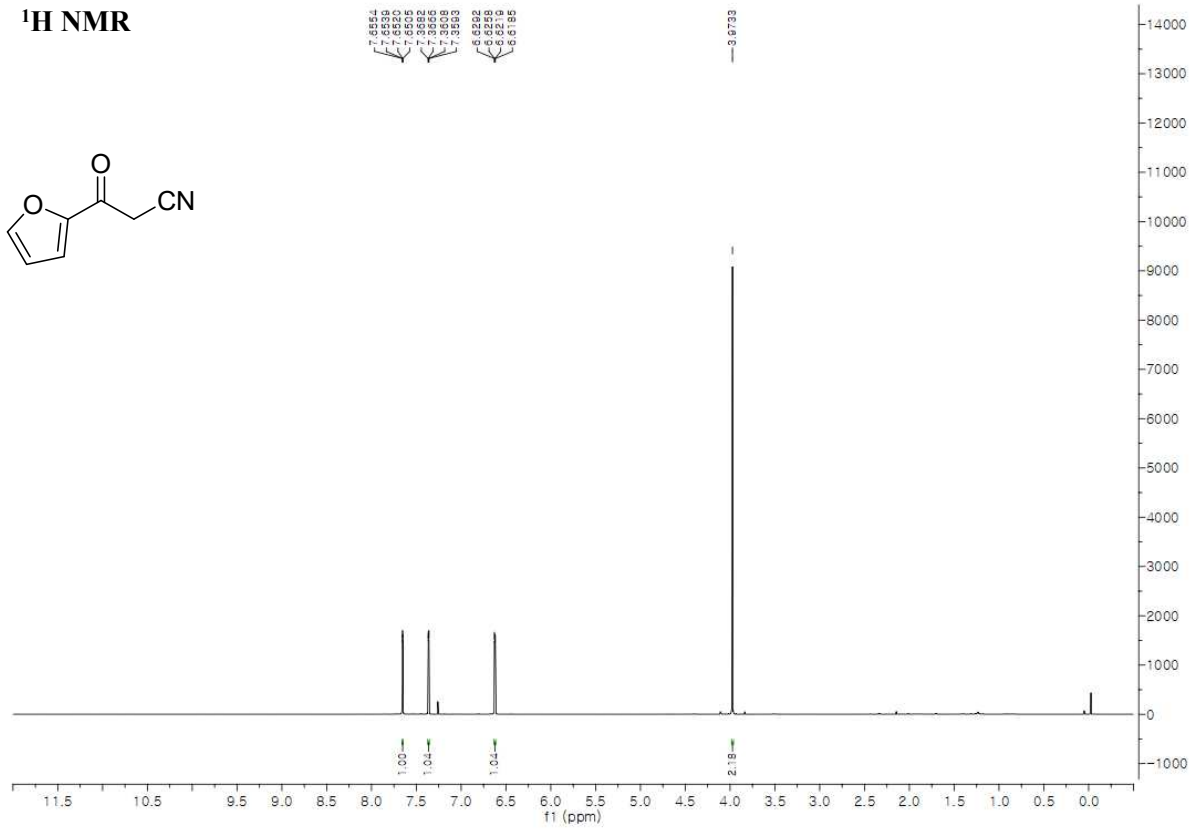


^{13}C NMR

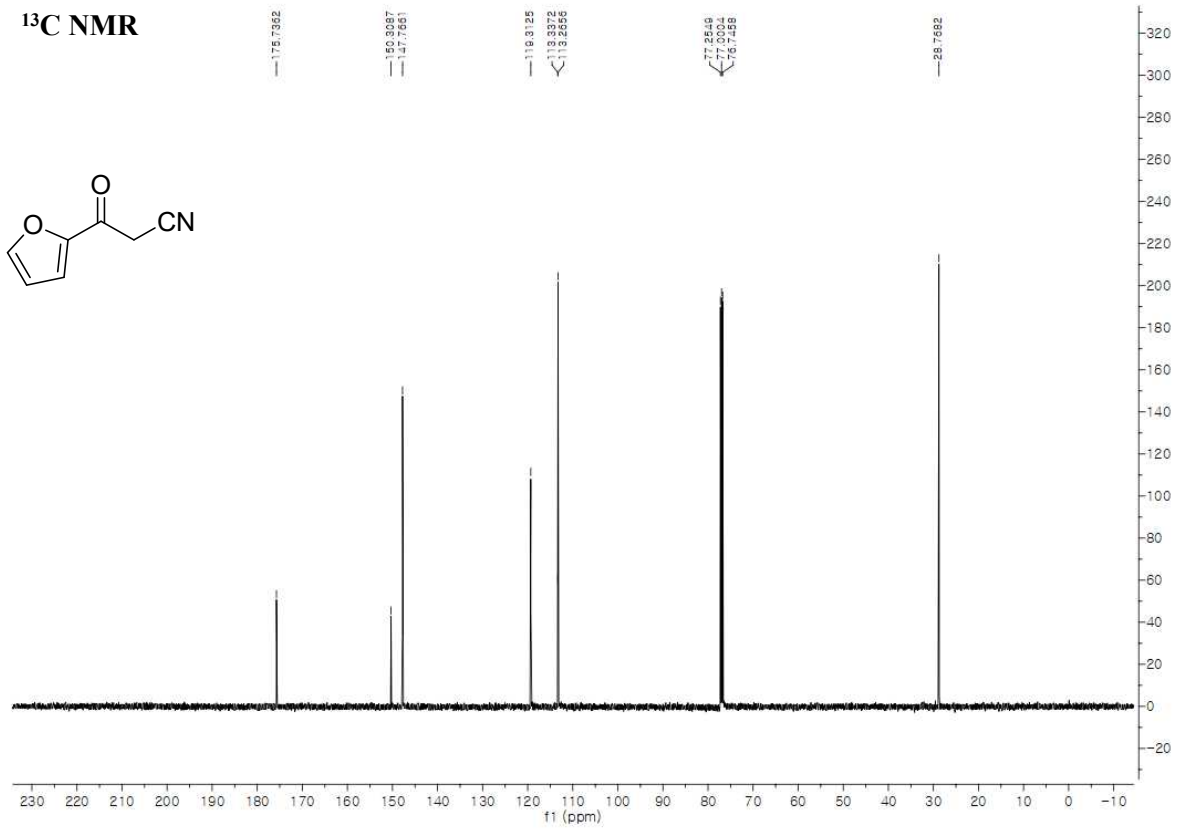


3-(Furan-2-yl)-3-oxopropanenitrile (3y)

^{1}H NMR

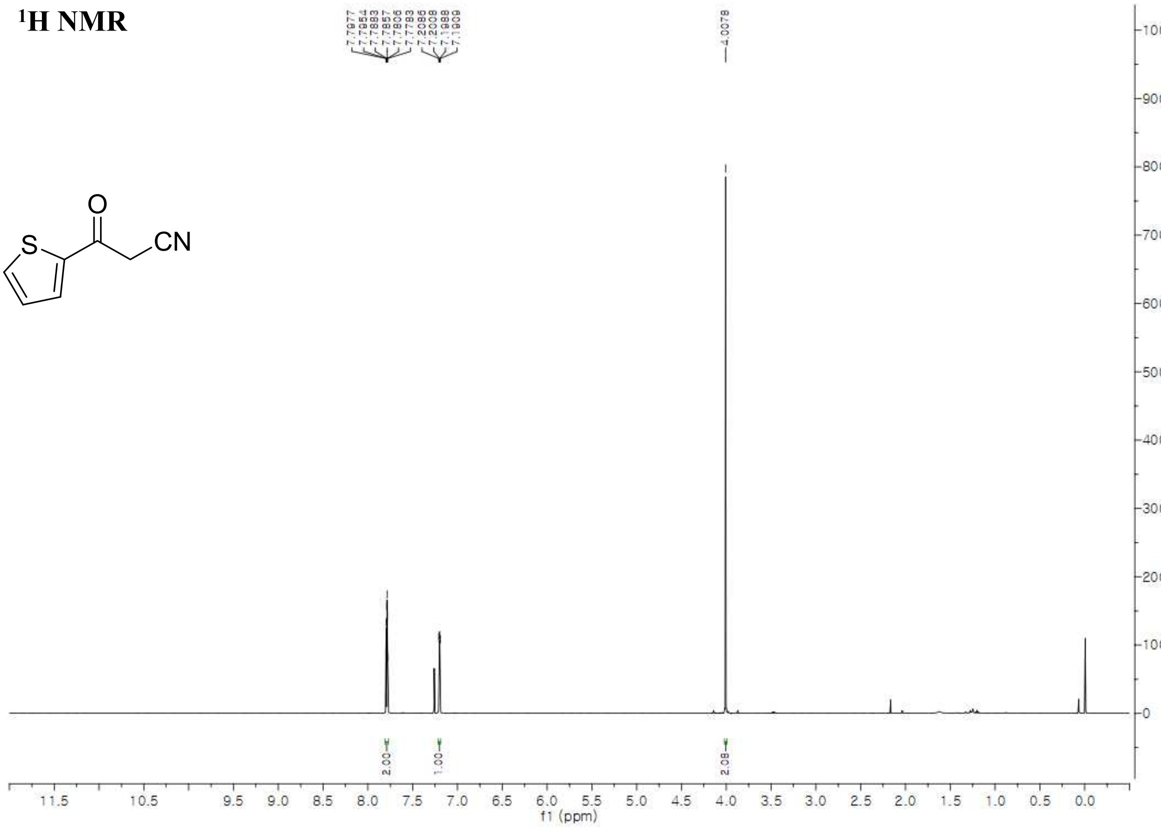


^{13}C NMR

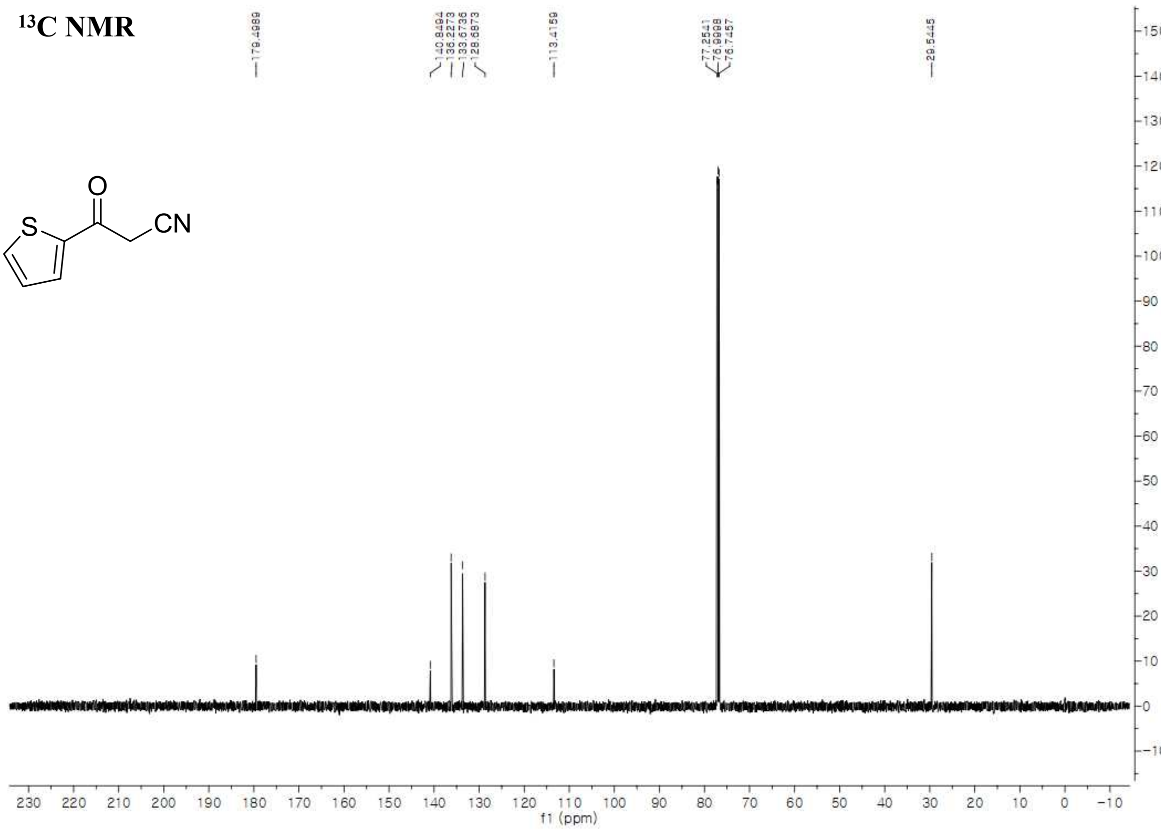


3-Oxo-3-(thiophen-2-yl)propanenitrile (3z)

^{1}H NMR

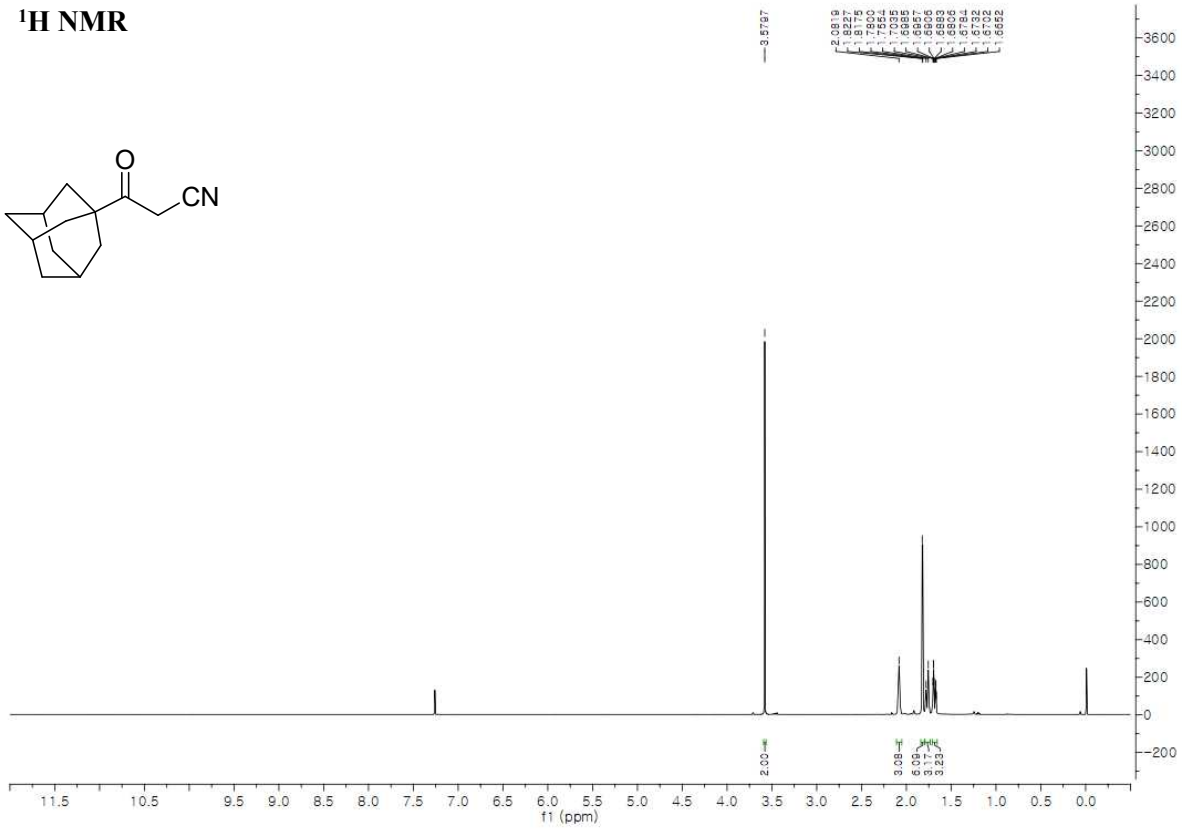


^{13}C NMR

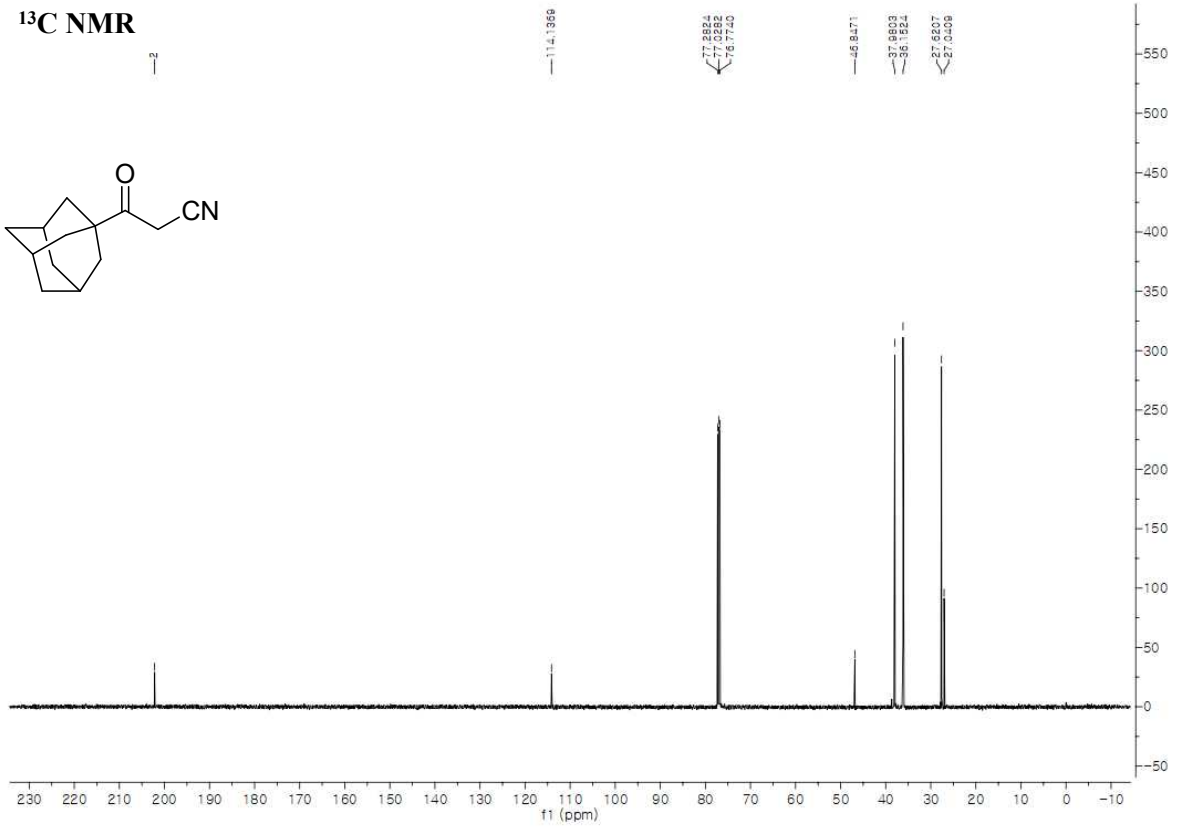


3-(Adamantan-1-yl)-3-oxopropanenitrile (3ab)

^{1}H NMR

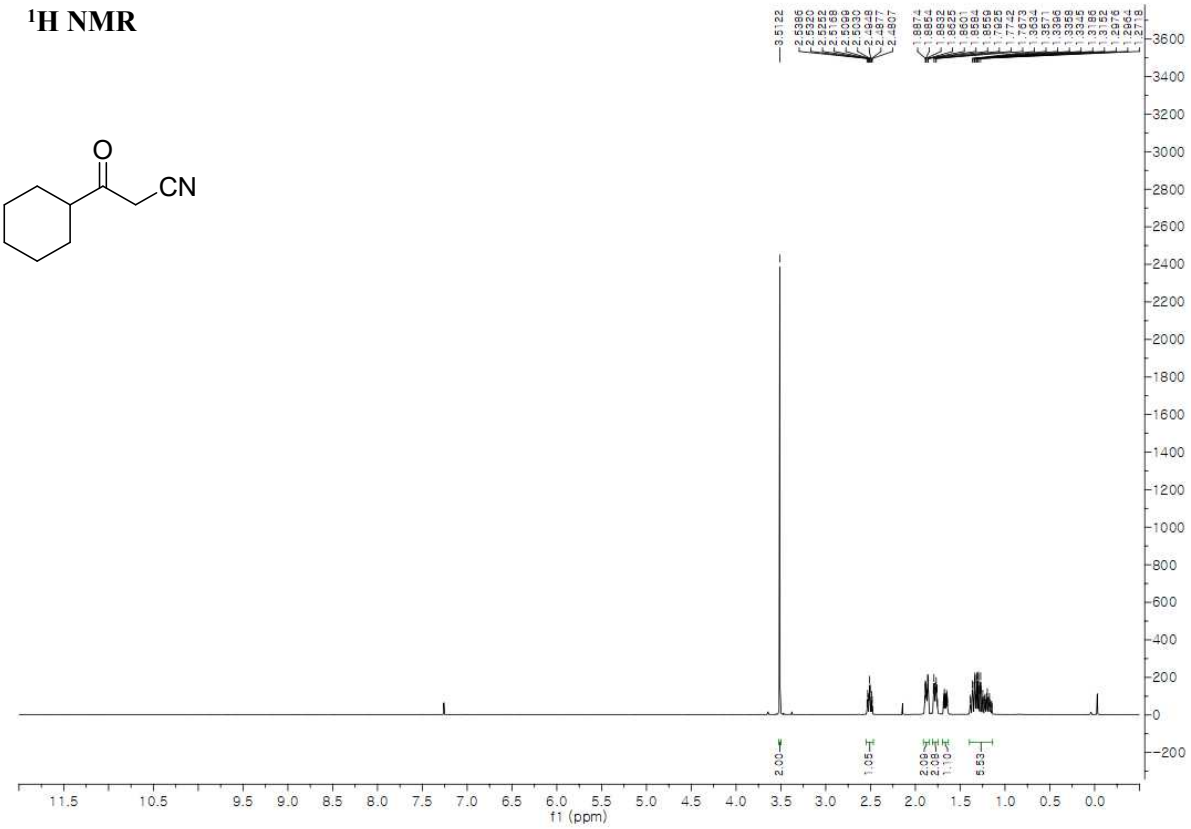


^{13}C NMR

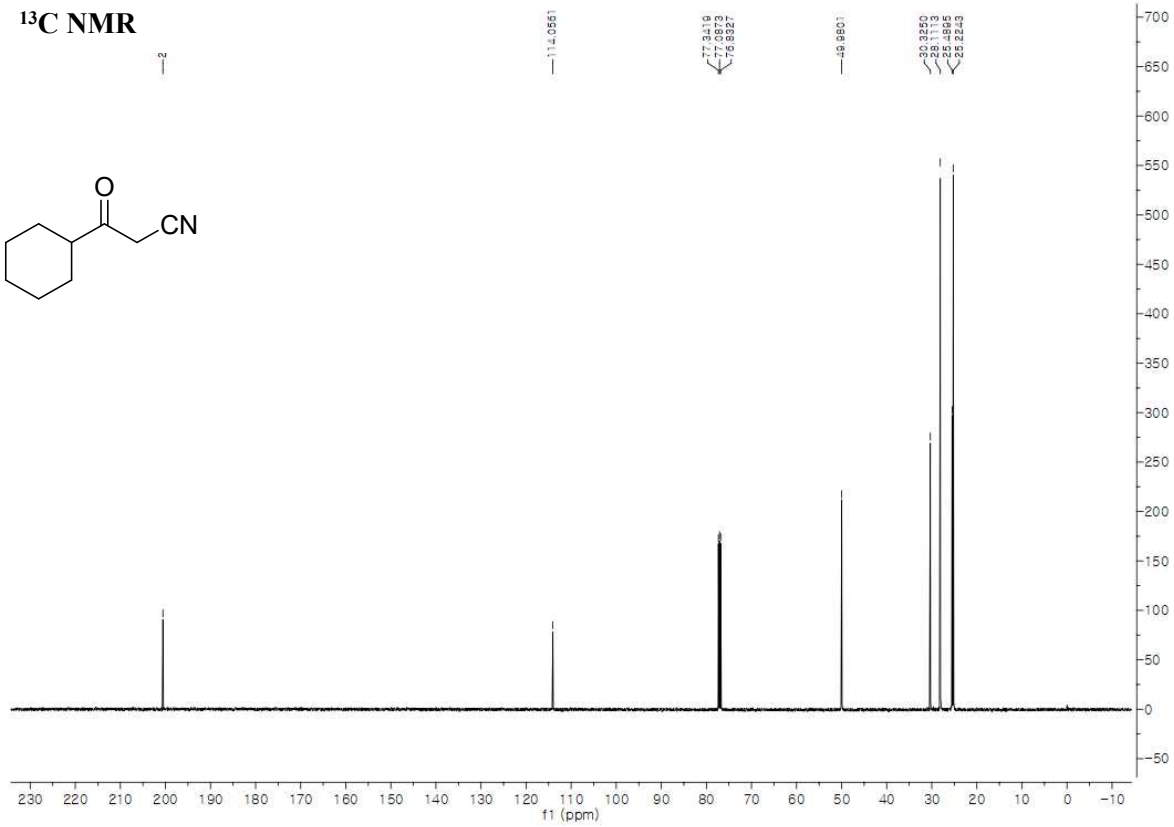


3-Cyclohexyl-3-oxopropionitrile (3ac)

^{1}H NMR

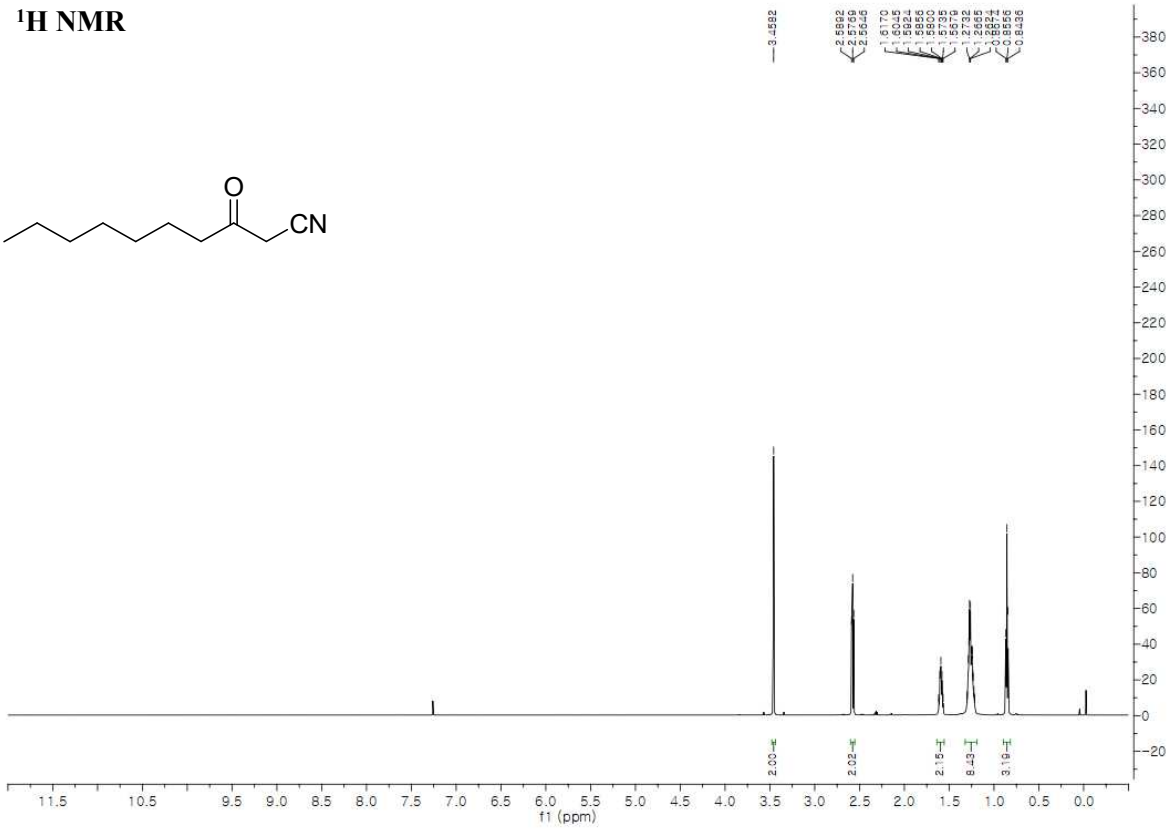


^{13}C NMR

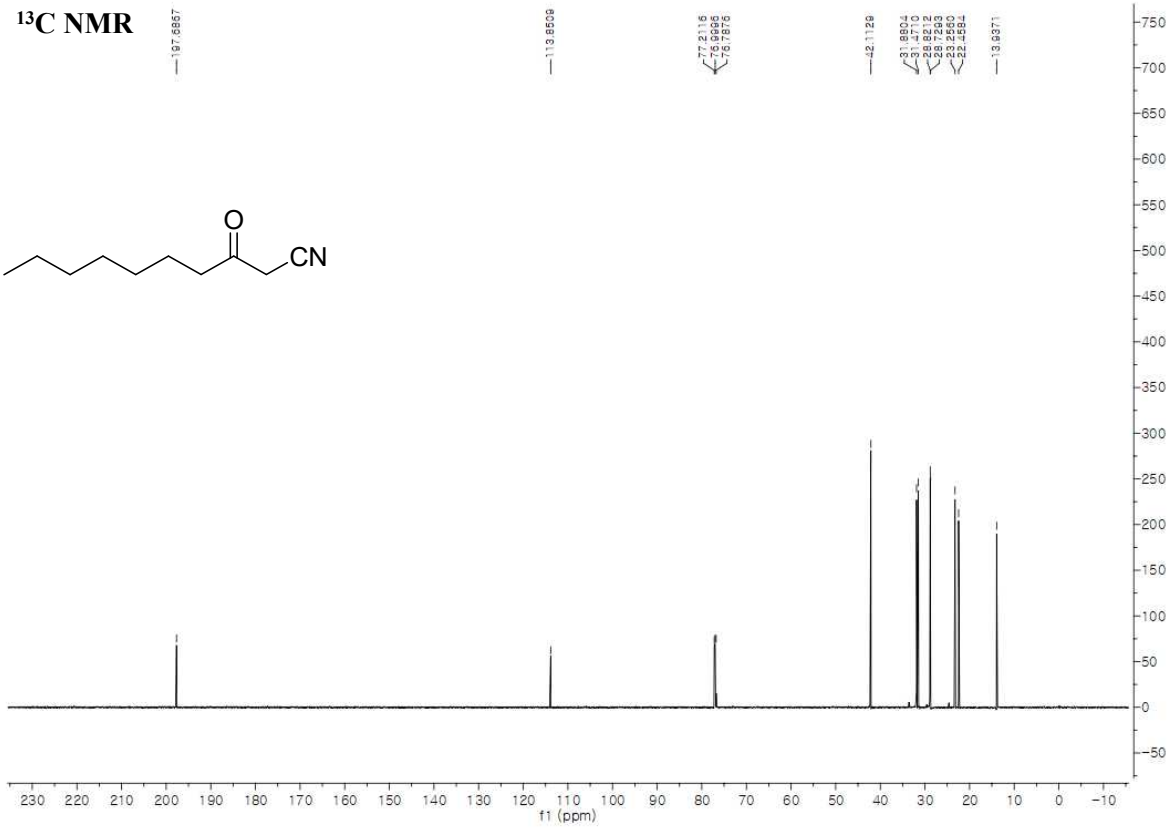


3-Oxo-decanenitrile (3ad)

^{1}H NMR

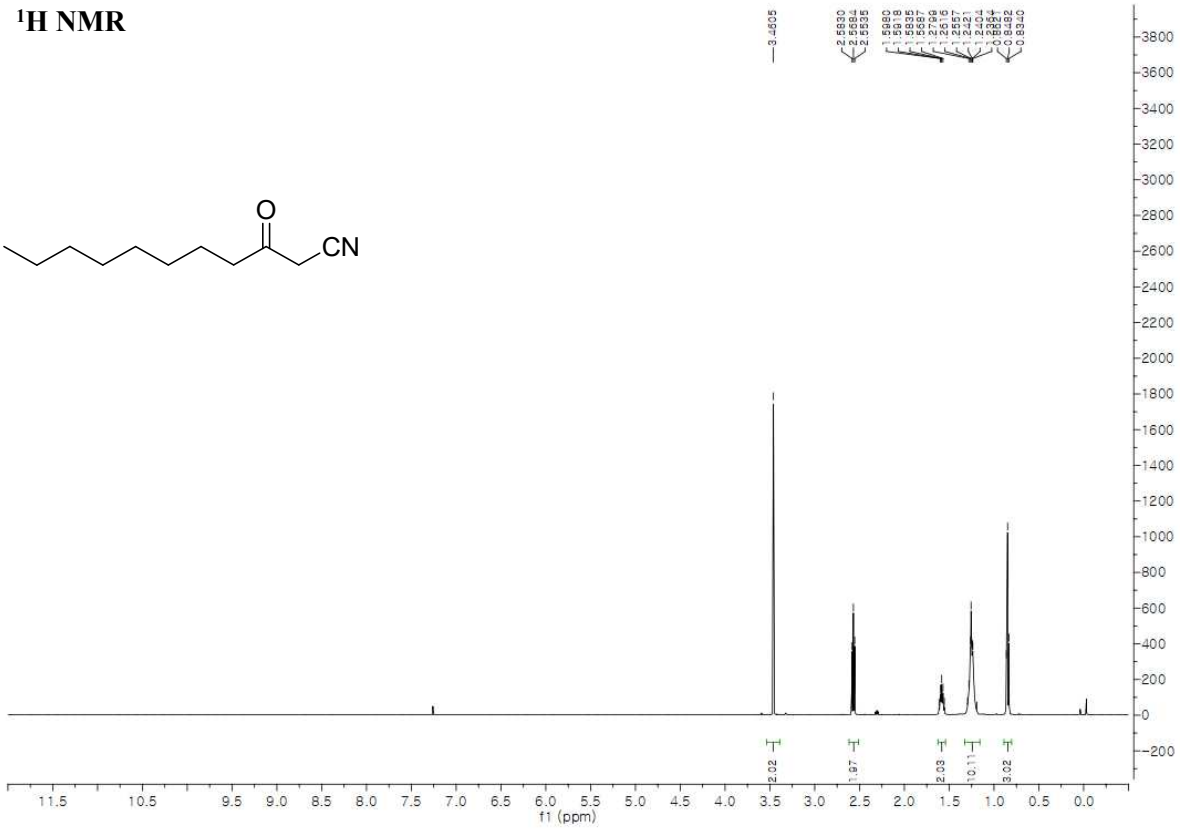


^{13}C NMR

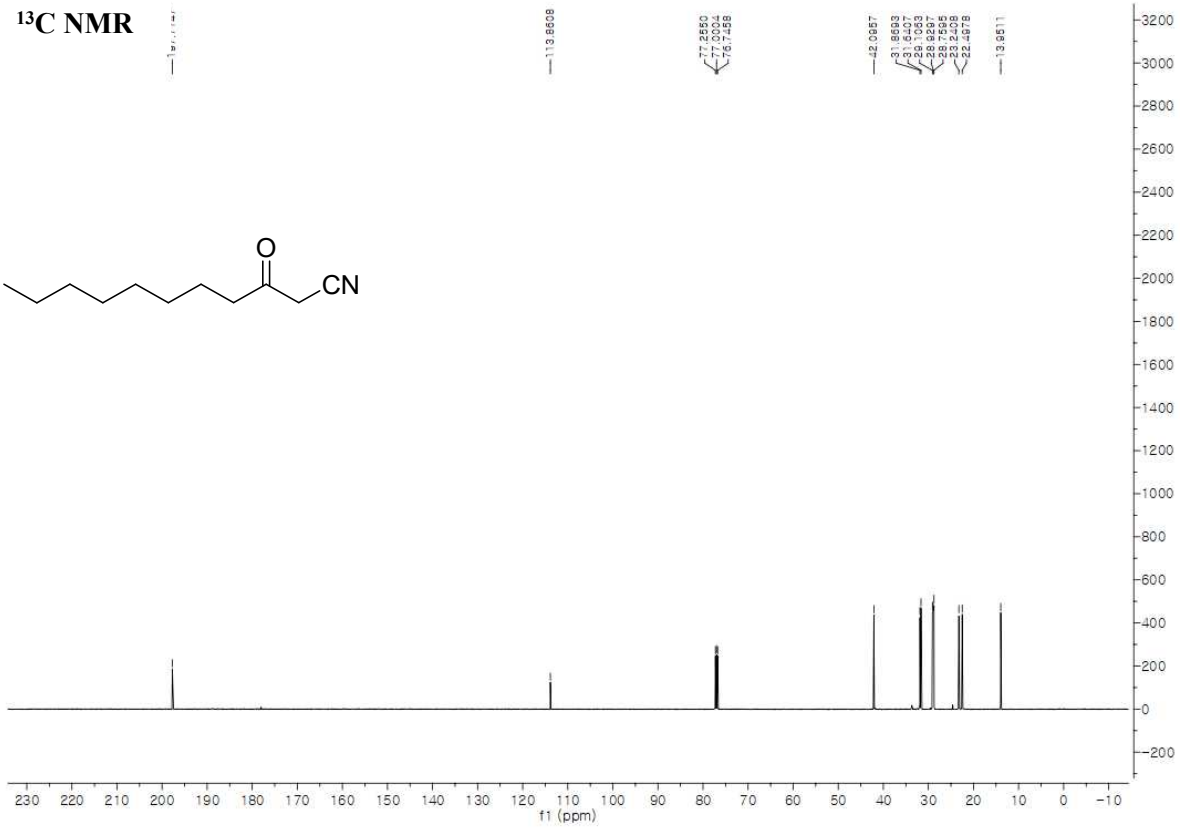


3-Oxo-undecanenitrile (3ae)

^{1}H NMR

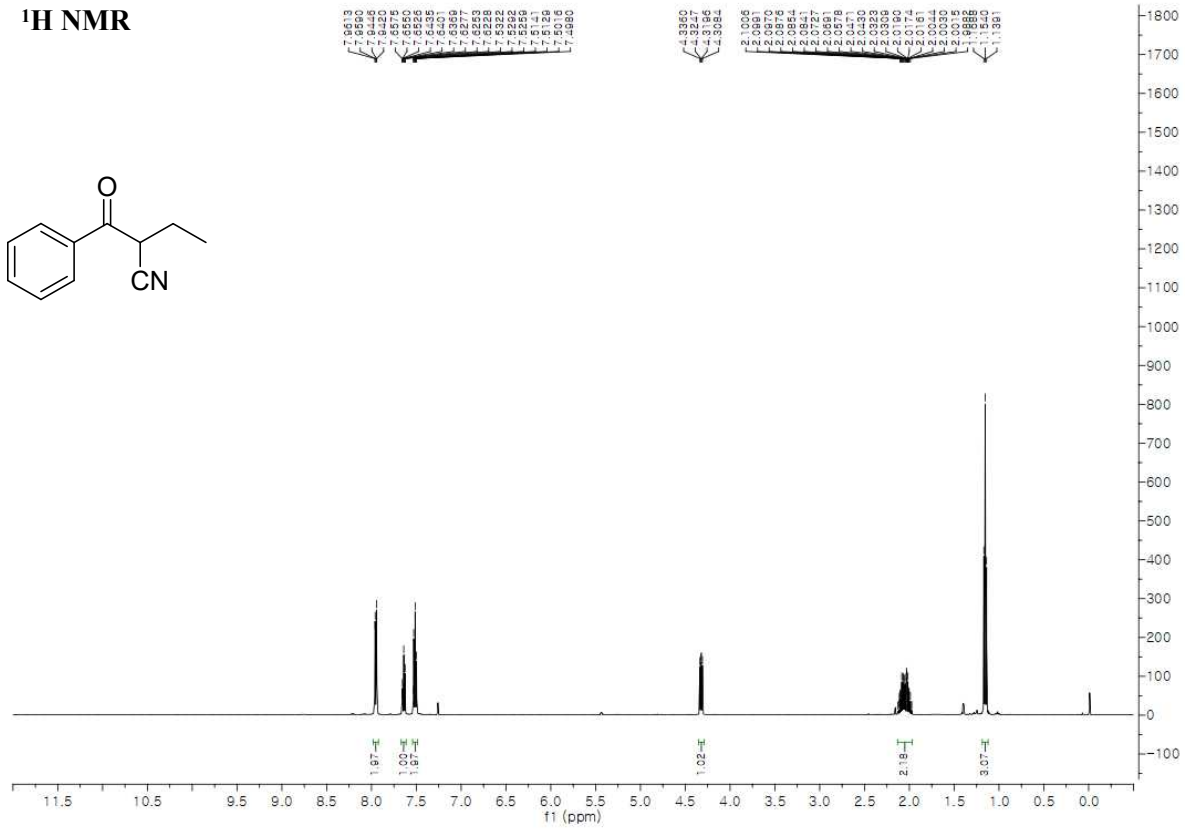


^{13}C NMR

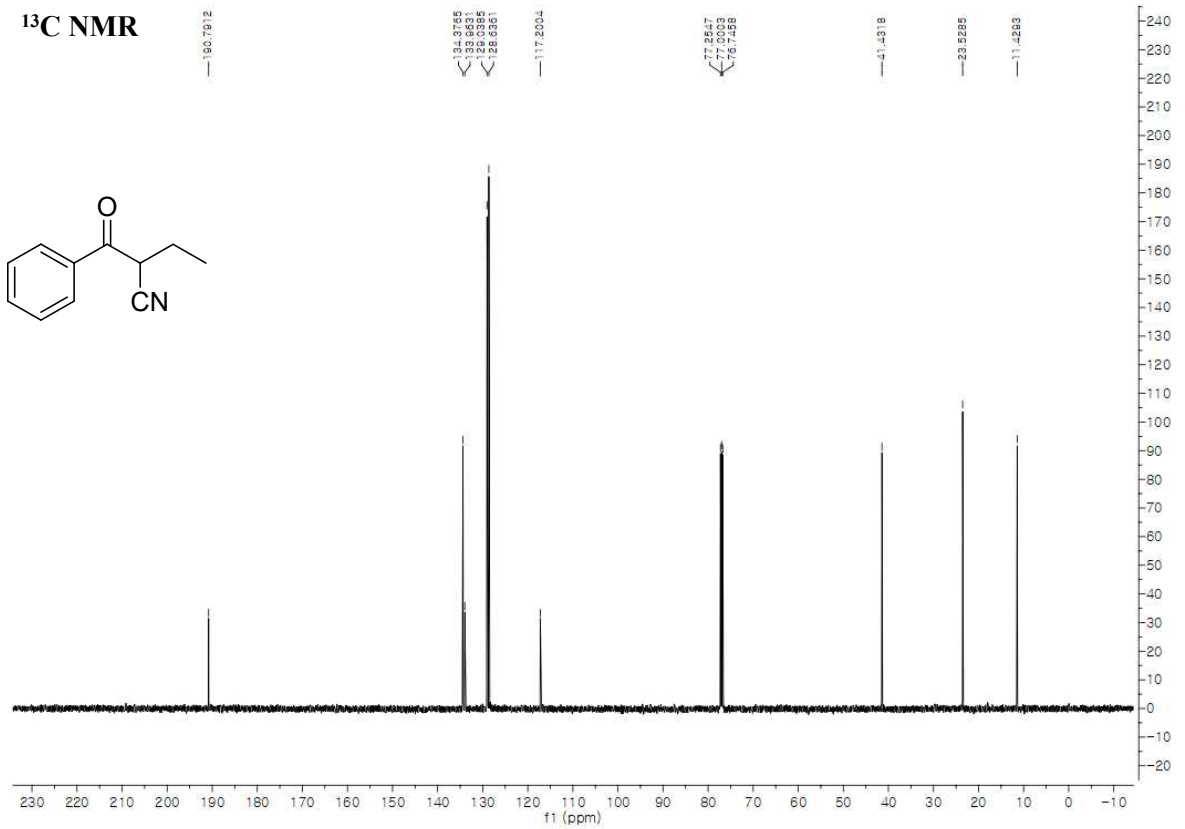


2-Ethyl-3-oxo-3-phenylpropanenitrile (6a)

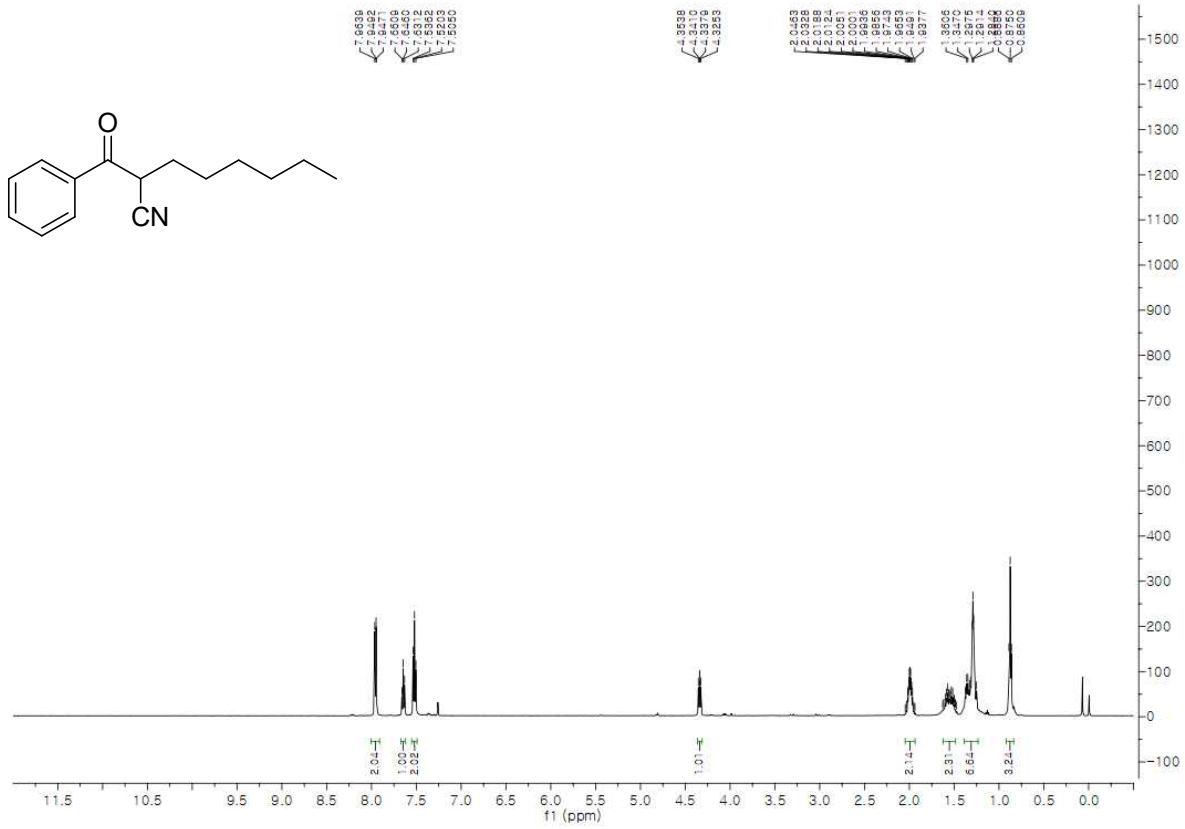
^{1}H NMR

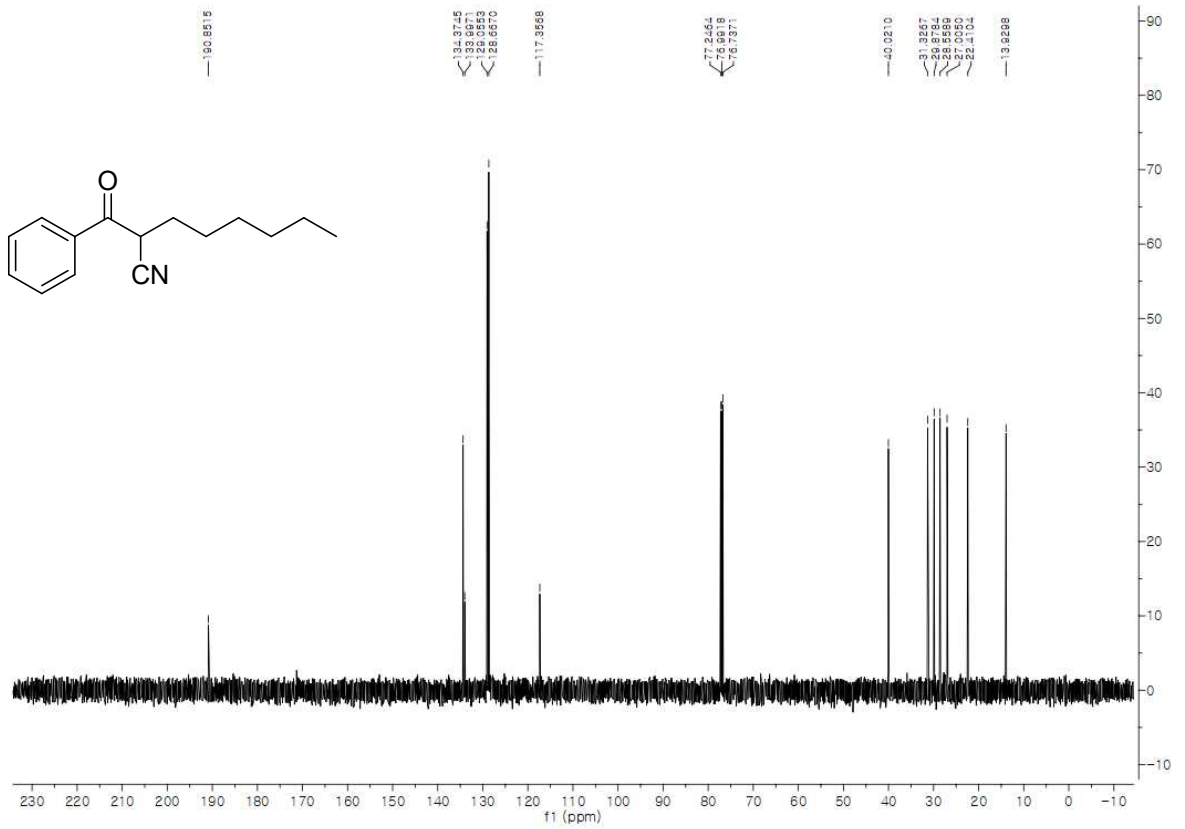


^{13}C NMR



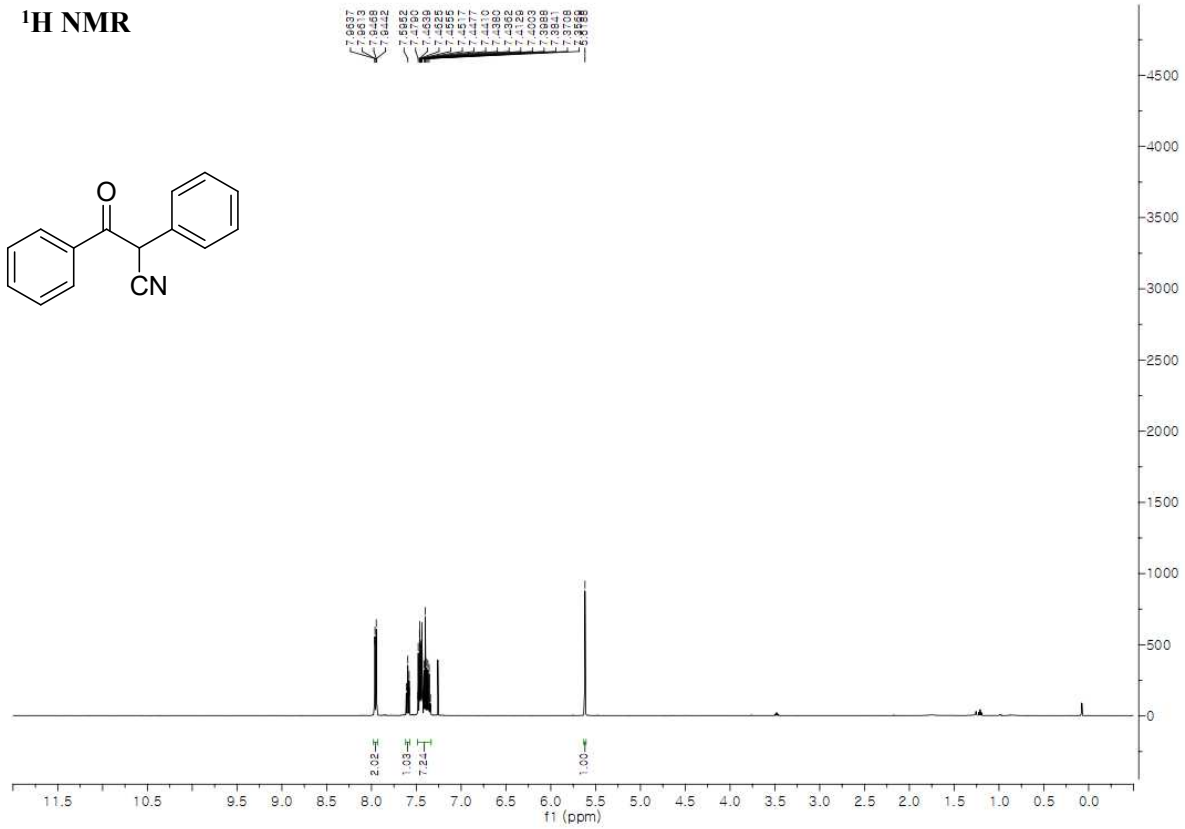
2-Hexyl-3-oxo-3-phenylpropanenitrile (6b)





3-Oxo-2,3-diphenylpropanenitrile (6c)

^{1}H NMR



^{13}C NMR