

Supporting Information

***N*-Heterocyclic Carbene-Catalyzed Radical Ring-Opening Acylation of Oxime Esters with Aldehydes**

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Table of Contents

General Information	s2
Characterization Data for Products	s3
Mechanistic Studies	s10
References	s11
NMR Spectra of Compounds.....	s13

General Information

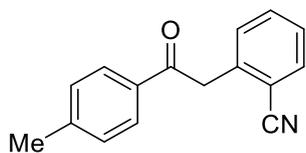
All reactions were performed under an argon or nitrogen atmosphere, unless otherwise stated. Commercially available reagents, unless otherwise noted, were utilized directly as provided. Dry solvents were distilled according to standard laboratory methods prior to usage. All other solvents were used without further purification. Thin-layer chromatography (TLC) analysis was carried out on 0.2 mm silica gel plates (HSGF 254) using a short-wave UV light for visualization. Flash column chromatography was performed with silica gel (200–300 mesh).

NMR spectra were recorded at room temperature on a Bruker AVANCE 400 spectrometer in deuterated solvents as noted. Chemical shifts (δ) are reported in parts per million (ppm) relative to a residual solvent resonance as the internal standard (^1H δ 7.26 for CDCl_3 , δ 2.50 for $\text{DMSO-}d_6$; ^{13}C δ 77.16 for CDCl_3 , δ 39.52 for $\text{DMSO-}d_6$). NMR peak multiplicities are abbreviated as follows: brs = broad signal, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, and m = multiplet. High-resolution mass spectra (HRMS) were recorded on an Agilent Technologies 6520 Q-TOF mass spectrometer using electrospray ionization time-of-flight (ESI-TOF) reflectron experiments. Melting points were determined on a capillary melting point apparatus (Shanghai Precision & Scientific Instrument Co., LTD) in degrees Celsius ($^\circ\text{C}$).

Thiazolium salts **C1–C4** were prepared according to the reported procedure.¹ Carbene precursors **C7** and **C8** were prepared according to a protocol of the group of Gravel.² Benzocyclobutenone-derived oxime ester **2a** and α -aryl-substituted cyclobutanone-derived oxime esters **2b–2d** were prepared by the literatures.^{3,4} The aldehyde derivatives of pregnenolone and diacetone-D-glucose (**1n** and **1o**) were synthesized by the literature.⁵

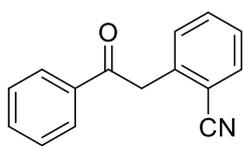
Characterization Data for Products

2-(2-Oxo-2-(*p*-tolyl)ethyl)benzonitrile (**3aa**)



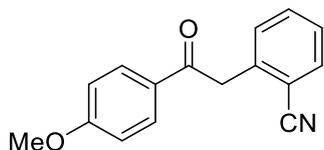
Purification by flash column chromatography (PE/EA, 40:1 to 30:1) furnished **3aa** (22.4 mg, 95% yield) as a colorless solid: $R_f = 0.50$ (PE/EA, 5:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.95 (d, $J = 8.2$ Hz, 2H), 7.70–7.68 (m, 1H), 7.59–7.55 (m, 1H), 7.41–7.37 (m, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 4.53 (s, 2H), 2.43 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 195.2, 144.8, 138.9, 133.9, 132.9, 131.2, 129.7, 128.7, 127.7, 118.1, 113.7, 43.6, 21.9; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{14}\text{NONa}$, 258.0889; found 258.0884. The spectral data were consistent with values reported in the literature⁶.

2-(2-Oxo-2-phenylethyl)benzonitrile (**3ba**)



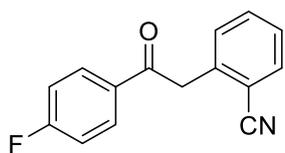
Purification by flash column chromatography (PE/EA, 50:1 to 30:1) furnished **3ba** (19.0 mg, 86% yield) as a colorless solid: $R_f = 0.43$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.08–8.05 (m, 2H), 7.71–7.69 (m, 1H), 7.64–7.56 (m, 2H), 7.53–7.49 (m, 2H), 7.42–7.38 (m, 2H), 4.56 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 195.5, 138.7, 136.3, 133.8, 132.9, 131.2, 129.0, 128.5, 127.8, 118.1, 113.8, 43.7; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{11}\text{NONa}$, 244.0733; found 244.0727. The spectral data were consistent with values reported in the literature⁶.

2-(2-(4-Methoxyphenyl)-2-oxoethyl)benzonitrile (**3ca**)



40 mol% **C1** was used. Purification by flash column chromatography (PE/EA, 40:1 to 10:1) furnished **3ca** (16.3 mg, 65% yield) as a colorless solid: $R_f = 0.42$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.06–8.02 (m, 2H), 7.70–7.68 (m, 1H), 7.59–7.54 (m, 1H), 7.40–7.38 (m, 2H), 6.99–6.95 (m, 2H), 4.50 (s, 2H), 3.89 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.0, 164.1, 139.0, 132.9, 131.1, 130.9, 129.4, 127.6, 118.1, 114.1, 113.7, 55.7, 43.3; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{NO}_2\text{Na}$, 274.0838; found 274.0833. The spectral data were consistent with values reported in the literature⁷.

2-(2-(4-Fluorophenyl)-2-oxoethyl)benzonitrile (**3da**)

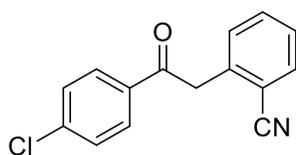


Purification by flash column chromatography (PE/EA, 50:1 to 40:1) furnished

3da (21.8 mg, 91% yield) as a colorless solid: $R_f = 0.46$ (PE/EA, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.11–8.06 (m, 2H), 7.71–7.69 (m, 1H), 7.61–7.57 (m, 1H),

7.43–7.38 (m, 2H), 7.20–7.16 (m, 2H), 4.52 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.0, 166.2 (d, $^1J_{\text{CF}} = 254.2$ Hz), 138.4, 133.02, 132.98, 132.8 (d, $^4J_{\text{CF}} = 3.2$ Hz), 131.3, 131.2 (d, $^3J_{\text{CF}} = 4.2$ Hz), 127.9, 118.0, 116.2 (d, $^2J_{\text{CF}} = 21.8$ Hz), 113.7, 43.6; $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -104.0; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{10}\text{FNONa}$, 262.0639; found 262.0633. The spectral data were consistent with values reported in the literature⁶.

2-(2-(4-Chlorophenyl)-2-oxoethyl)benzonitrile (**3ea**)

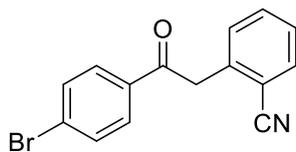


Purification by flash column chromatography (PE/EA, 20:1) furnished **3ea**

(22.2 mg, 87% yield) as a colorless solid: $R_f = 0.28$ (PE/EA, 8:1); mp 93.4–94.2°C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01–7.97 (m, 2H), 7.71–7.68 (m,

1H), 7.60–7.56 (m, 1H), 7.50–7.46 (m, 2H), 7.43–7.36 (m, 2H), 4.52 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.4, 140.4, 138.3, 134.6, 133.02, 132.97, 131.1, 129.9, 129.3, 127.9, 118.0, 113.7, 43.7; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{10}\text{ClNONa}$, 278.0343; found 278.0346.

2-(2-(4-Bromophenyl)-2-oxoethyl)benzonitrile (**3fa**)

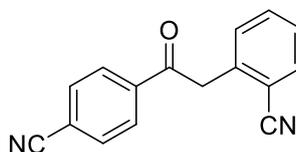


Purification by flash column chromatography (PE/EA, 50:1 to 40:1) furnished

3fa (25.8 mg, 86% yield) as a colorless solid: $R_f = 0.51$ (PE/EA, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.93–7.90 (m, 2H), 7.71–7.69 (m, 1H), 7.67–7.64 (m, 2H),

7.60–7.56 (m, 1H), 7.43–7.36 (m, 2H), 4.51 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.6, 138.2, 135.0, 133.04, 132.99, 132.3, 131.1, 130.0, 129.1, 127.9, 118.0, 113.7, 43.7; HRMS (ESI-TOF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{10}\text{BrNONa}$, 321.9838; found 321.9846. The spectral data were consistent with values reported in the literature⁶.

2-(2-(4-Cyanophenyl)-2-oxoethyl)benzonitrile (**3ga**)

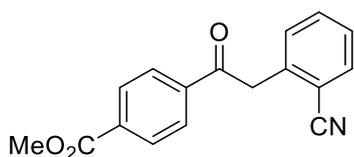


Purification by flash column chromatography (PE/EA, 30:1 to 10:1)

furnished **3ga** (17.5 mg, 71% yield) as a colorless solid: $R_f = 0.56$ (PE/EA, 1:1);

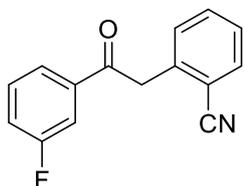
¹H NMR (400 MHz, CDCl₃) δ 8.16–8.13 (m, 2H), 7.84–7.81 (m, 2H), 7.73–7.71 (m, 1H), 7.63–7.59 (m, 1H), 7.46–7.42 (m, 1H), 7.39–7.37 (m, 1H), 4.56 (s, 2H); **¹³C{¹H} (100 MHz, CDCl₃)** δ 194.4, 139.3, 137.6, 133.2, 133.1, 132.9, 131.2, 128.9, 128.2, 117.9, 117.1, 113.7, 44.0; **HRMS (ESI-TOF)** m/z: [M + Na]⁺ calcd for C₁₆H₁₀N₂ONa, 269.0685; found 269.0683. The spectral data were consistent with values reported in the literature⁷.

Methyl 4-(2-(2-Cyanophenyl)acetyl)benzoate (3ha)



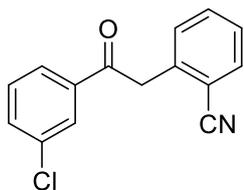
Purification by flash column chromatography (PE/EA, 40:1 to 20:1) furnished **3ha** (20.9 mg, 75% yield) as a colorless solid: *R_f* = 0.36 (PE/EA, 4:1); **¹H NMR (400 MHz, CDCl₃)** δ 8.19–8.16 (m, 2H), 8.12–8.09 (m, 2H), 7.71 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.59 (td, *J* = 7.7, 1.4 Hz, 1H), 7.44–7.37 (m, 2H), 4.58 (s, 2H), 3.96 (s, 3H); **¹³C{¹H} (100 MHz, CDCl₃)** δ 195.1, 166.2, 139.5, 138.1, 134.5, 133.1, 133.0, 131.2, 130.2, 128.4, 128.0, 118.0, 113.8, 52.7, 44.1; **HRMS (ESI-TOF)** m/z: [M + Na]⁺ calcd for C₁₇H₁₃NO₃Na, 302.0788; found 302.0778. The spectral data were consistent with values reported in the literature⁸.

2-(2-(3-Fluorophenyl)-2-oxoethyl)benzonitrile (3ia)



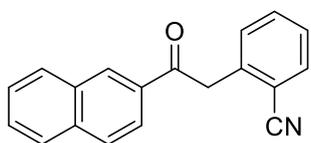
Purification by flash column chromatography (PE/EA, 40:1 to 30:1) furnished **3ia** (21.5 mg, 90% yield) as a colorless solid: *R_f* = 0.46 (PE/EA, 3:1); **¹H NMR (400 MHz, CDCl₃)** δ 8.19–8.16 (m, 2H), 8.12–8.09 (m, 2H), 7.71 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.59 (td, *J* = 7.7, 1.4 Hz, 1H), 7.44–7.37 (m, 2H), 4.58 (s, 2H), 3.96 (s, 3H); **¹³C{¹H} (100 MHz, CDCl₃)** δ 194.3, 163.1 (d, ¹*J*_{CF} = 246.9 Hz), 138.4 (d, ⁵*J*_{CF} = 6.2 Hz), 138.2, 133.03, 132.99, 131.2, 130.7 (d, ⁴*J*_{CF} = 7.6 Hz), 127.9, 124.3 (d, ⁶*J*_{CF} = 2.9 Hz), 120.9 (d, ³*J*_{CF} = 21.2 Hz), 118.0, 115.2 (d, ²*J*_{CF} = 22.3 Hz), 113.8, 43.9; **¹⁹F NMR (376 MHz, CDCl₃)** δ -111.2; **HRMS (ESI-TOF)** m/z: [M + Na]⁺ calcd for C₁₅H₁₀FNONa, 262.0639; found 262.0627. The spectral data were consistent with values reported in the literature⁸.

2-(2-(3-Chlorophenyl)-2-oxoethyl)benzonitrile (3ja)



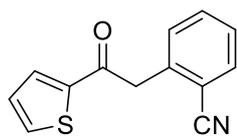
Purification by flash column chromatography (PE/EA, 40:1 to 25:1) furnished **3ja** (22.2 mg, 87% yield) as a light yellow solid: $R_f = 0.46$ (PE/EA, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01 (t, $J = 1.8$ Hz, 1H), 7.95–7.92 (m, 1H), 7.71–7.69 (m, 1H), 7.61–7.57 (m, 2H), 7.46 (t, $J = 7.9$ Hz, 1H), 7.43–7.36 (m, 2H), 4.53 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.3, 138.1, 137.8, 135.3, 133.8, 133.03, 132.99, 131.2, 130.3, 128.6, 127.9, 126.6, 118.0, 113.8, 43.8; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{10}\text{ClN}$ ONa, 278.0343; found 278.0336. The spectral data were consistent with values reported in the literature⁶.

2-(2-(Naphthalen-2-yl)-2-oxoethyl)benzonitrile (**3ka**)



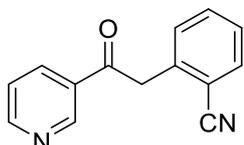
Purification by flash column chromatography (PE/EA, 40:1 to 30:1) furnished **3ka** (22.5 mg, 83% yield) as a colorless solid: $R_f = 0.45$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.63 (s, 1H), 8.09–8.07 (m, 1H), 8.01 (d, $J = 8.0$ Hz, 1H), 7.94–7.88 (m, 2H), 7.71 (d, $J = 7.6$ Hz, 1H), 7.65–7.56 (m, 3H), 7.45–7.38 (m, 2H), 4.69 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 195.5, 138.8, 136.0, 133.6, 133.0, 132.6, 131.2, 130.5, 129.9, 129.0, 128.9, 127.9, 127.8, 127.1, 124.0, 118.2, 113.7, 43.8; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{13}\text{N}$ ONa, 294.0889; found 294.0894. The spectral data were consistent with values reported in the literature⁷.

2-(2-Oxo-2-(thiophen-2-yl)ethyl)benzonitrile (**3la**)



Purification by flash column chromatography (PE/EA, 20:1 to 15:1) furnished **3la** (21.1 mg, 93% yield) as a colorless solid: $R_f = 0.43$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.91 (dd, $J = 3.8, 1.0$ Hz, 1H), 7.71–7.67 (m, 2H), 7.60–7.56 (m, 1H), 7.47–7.45 (m, 1H), 7.41–7.37 (m, 1H), 7.18 (dd, $J = 5.0, 3.8$ Hz, 1H), 4.48 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 188.3, 143.5, 138.1, 134.9, 133.1, 133.0, 132.9, 131.1, 128.6, 127.9, 118.1, 113.6, 44.1; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_9\text{NOS}$ Na, 250.0297; found 250.0296. The spectral data were consistent with values reported in the literature⁸.

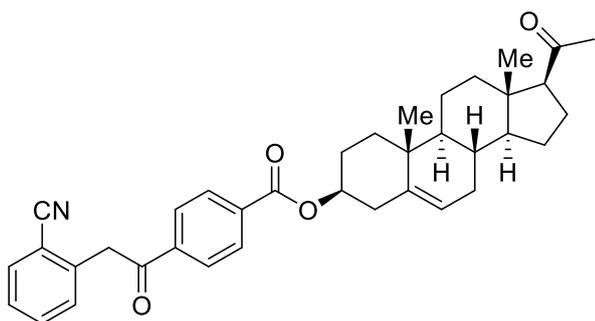
2-(2-Oxo-2-(pyridin-3-yl)ethyl)benzonitrile (**3ma**)



30 mol% **C1** was used. Purification by flash column chromatography (PE/EA, 10:1 to 1:1) furnished **3ma** (19.3 mg, 87% yield) as a yellow solid: $R_f = 0.30$ (PE/EA,

1:1); mp 94.7–96.6°C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.27 (s, 1H), 8.831–8.826 (m, 1H), 8.33–8.30 (m, 1H), 7.71–7.70 (m, 1H), 7.61–7.57 (m, 1H), 7.48–7.44 (m, 1H), 7.44–7.37 (m, 2H), 4.56 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 194.5, 154.1, 149.9, 137.7, 135.8, 133.1, 133.0, 131.7, 131.2, 128.1, 124.0, 117.9, 113.8, 44.0; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{11}\text{N}_2\text{O}$, 223.0866; found 223.0861.

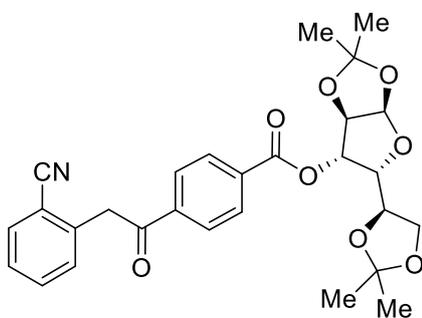
(3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-17-Acetyl-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl 4-(2-(2-cyanophenyl)acetyl)benzoate (**3na**)



30 mol% **C1** was used. Purification by flash column chromatography (PE/DCM, 1:5 to 1:6) furnished **3na** (32.7 mg, 58% yield) as a colorless solid: R_f = 0.46 (DCM/MeOH, 50:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.17–8.08 (m, 4H), 7.71 (d, J = 8.4 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.43–7.37 (m, 2H), 5.43 (d, J = 3.6 Hz, 1H),

4.93–4.85 (m, 1H), 4.57 (s, 2H), 2.57–2.48 (m, 3H), 2.25–2.18 (m, 1H), 2.13 (s, 3H), 2.08–2.01 (m, 3H), 1.97–1.93 (m, 1H), 1.82–1.52 (m, 7H), 1.29–1.14 (m, 5H), 1.08 (s, 3H), 0.64 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 209.8, 195.2, 165.1, 139.5, 139.3, 138.1, 135.2, 133.05, 133.01, 131.2, 130.1, 128.4, 127.9, 122.8, 118.0, 113.7, 75.3, 63.8, 56.9, 50.0, 44.12, 44.06, 38.9, 38.2, 37.1, 36.8, 31.93, 31.91, 31.7, 27.9, 24.6, 22.9, 21.2, 19.5, 13.4; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{37}\text{H}_{41}\text{NO}_4\text{Na}$, 586.2928; found 586.2927. The spectral data were consistent with values reported in the literature⁸.

(3*aR*,5*R*,6*S*,6*aR*)-5-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl 4-(2-(2-cyanophenyl)acetyl)benzoate (**3oa**)

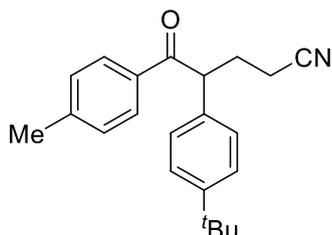


30 mol% **C1** was used. Purification by flash column chromatography (PE/EA, 20:1 to 3:1) furnished **3oa** (15.2 mg, 30% yield) as a colorless oil: R_f = 0.44 (PE/EA, 2:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.17–8.11 (m, 4H), 7.72–7.70 (m, 1H), 7.62–7.58 (m, 1H), 7.44–7.38 (m, 2H), 5.97 (d, J = 3.6 Hz, 1H), 5.52 (d, J = 2.8 Hz, 1H), 4.66 (d, J = 4.0 Hz, 1H), 4.57 (s, 2H), 4.38–4.30 (m, 2H), 4.16–4.07

(m, 2H), 1.57 (s, 3H), 1.42 (s, 3H), 1.33 (s, 3H), 1.27 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 195.0, 164.4,

139.9, 138.0, 133.9, 133.1, 133.0, 131.2, 130.3, 128.6, 128.0, 126.7, 118.0, 113.7, 112.6, 109.7, 105.3, 83.4, 80.1, 72.6, 67.5, 44.1, 27.0, 26.9, 26.3, 25.3; **HRMS (ESI-TOF)** m/z: [M + H]⁺ calcd for C₂₈H₃₀NO₈, 508.1966; found 508.1959.

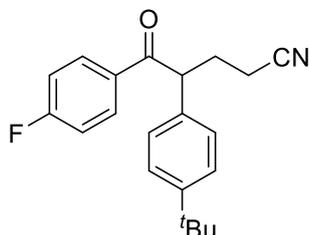
4-(4-(tert-Butyl)phenyl)-5-oxo-5-(p-tolyl)pentanenitrile (3ab)



1.1 equiv of oxime ester **2b** was used. Purification by flash column chromatography (PE/EA, 40:1 to 30:1) furnished **3ab** (30.3 mg, 95% yield) as a light yellow oil: $R_f = 0.49$ (PE/EA, 5:1); **¹H NMR (400 MHz, CDCl₃)** δ 7.89–7.87 (m, 2H), 7.33–7.30 (m, 2H), 7.23–7.18 (m, 4H), 4.69 (t, $J = 7.2$ Hz, 1H), 2.47–2.36 (m, 2H), 2.35 (s, 3H), 2.29–2.12 (m, 2H), 1.26 (s, 9H);

¹³C{¹H} (100 MHz, CDCl₃) δ 198.0, 150.7, 144.3, 134.6, 133.7, 129.5, 129.1, 127.8, 126.4, 119.6, 51.3, 34.6, 31.4, 29.2, 21.7, 15.4; **HRMS (ESI-TOF)** m/z: [M + Na]⁺ calcd for C₂₂H₂₅NONa, 342.1828; found 342.1824.

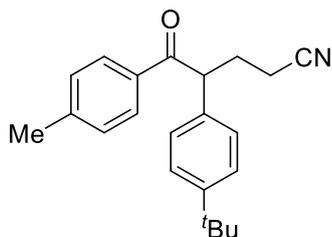
4-(4-(tert-Butyl)phenyl)-5-(4-fluorophenyl)-5-oxopentanenitrile (3db)



1.1 equiv of oxime ester **2b** was used. Purification by flash column chromatography (PE/EA, 50:1 to 35:1) furnished **3db** (27.2 mg, 84% yield) as a light yellow oil: $R_f = 0.43$ (PE/EA, 5:1); **¹H NMR (400 MHz, CDCl₃)** δ 8.01–7.97 (m, 2H), 7.34–7.32 (m, 2H), 7.21–7.19 (m, 2H), 7.08–7.03 (m, 2H), 4.65 (t, $J = 7.0$ Hz, 1H), 2.48–2.36 (m, 2H), 2.29–2.12 (m, 2H), 1.27 (s, 9H);

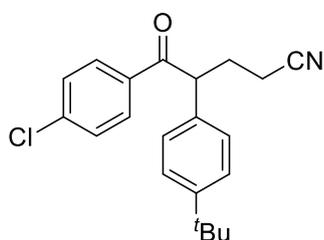
¹³C{¹H} (100 MHz, CDCl₃) δ 196.9, 165.8 (d, $^1J_{CF} = 254.1$ Hz), 151.0, 134.2, 132.6 (d, $^4J_{CF} = 3.0$ Hz), 131.7 (d, $^3J_{CF} = 9.3$ Hz), 127.8, 126.5, 119.5, 115.9 (d, $^2J_{CF} = 21.8$ Hz), 51.5, 34.6, 31.4, 29.1, 15.3; **¹⁹F NMR (376 MHz, CDCl₃)** δ -104.6; **HRMS (ESI-TOF)** m/z: [M + Na]⁺ calcd for C₂₁H₂₂FNONa, 346.1578; found 346.1570.

5-(4-Bromophenyl)-4-(4-(tert-butyl)phenyl)-5-oxopentanenitrile (3fb)



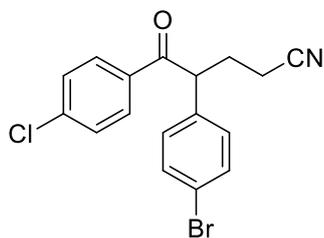
1.1 equiv of oxime ester **2b** was used. Purification by flash column chromatography (PE/EA, 50:1 to 30:1) furnished **3fb** (28.1 mg, 73% yield) as a light yellow oil: $R_f = 0.45$ (PE/EA, 5:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.83–7.80 (m, 2H), 7.54–7.51 (m, 2H), 7.34–7.31 (m, 2H), 7.19–7.16 (m, 2H), 4.63 (t, $J = 6.9$ Hz, 1H), 2.46–2.36 (m, 2H), 2.28–2.14 (m, 2H), 1.27 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 197.4, 151.1, 134.8, 134.0, 132.1, 130.5, 128.6, 127.8, 126.6, 119.5, 51.6, 34.6, 31.4, 29.0, 15.3; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{K}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{BrNOK}$, 422.0516; found 422.0508.

4-(4-(tert-Butyl)phenyl)-5-(4-chlorophenyl)-5-oxopentanenitrile (**3eb**)



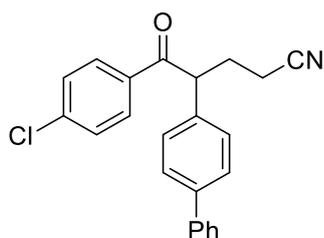
On a 0.2 mmol scale. 1.1 equiv of oxime ester **2b** was used. Purification by flash column chromatography (PE/EA, 50:1 to 30:1) furnished **3eb** (59.2 mg, 87% yield) as a light yellow oil: $R_f = 0.49$ (PE/EA, 6:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.82 (d, $J = 8.4$ Hz, 2H), 7.26 (t, $J = 8.1$ Hz, 4H), 7.11 (d, $J = 8.0$ Hz, 2H), 4.56 (t, $J = 6.8$ Hz, 1H), 2.39–2.28 (m, 2H), 2.21–2.04 (m, 2H), 1.19 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 197.2, 151.0, 139.8, 134.4, 134.0, 130.4, 129.0, 127.8, 126.6, 119.4, 51.6, 34.6, 31.3, 29.0, 15.3; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{22}\text{ClNONa}$, 362.1282; found 362.1276.

4-(4-Bromophenyl)-5-(4-chlorophenyl)-5-oxopentanenitrile (**3ec**)



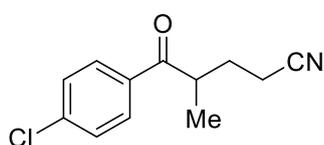
1.1 equiv of oxime ester **2c** was used. Purification by flash column chromatography (PE/EA, 40:1 to 10:1) furnished **3ec** (33.4 mg, 92% yield) as a yellow oil: $R_f = 0.45$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.87–7.84 (m, 2H), 7.48–7.45 (m, 2H), 7.39–7.36 (m, 2H), 7.18–7.14 (m, 2H), 4.65 (t, $J = 7.2$ Hz, 1H), 2.48–2.39 (m, 2H), 2.29–2.20 (m, 1H), 2.18–2.10 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 196.7, 140.2, 136.3, 134.1, 132.9, 130.3, 129.9, 129.2, 122.3, 119.2, 51.4, 28.8, 15.3; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{13}\text{BrClNONa}$, 383.9761; found 383.9761.

4-([1,1'-Biphenyl]-4-yl)-5-(4-chlorophenyl)-5-oxopentanenitrile (**3ed**)



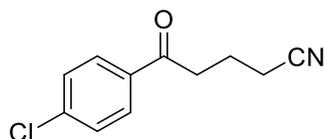
1.1 equiv of oxime ester **2d** was used. Purification by flash column chromatography (PE/EA, 40:1 to 15:1) furnished **3ed** (25.5 mg, 71% yield) as a yellow oil: $R_f = 0.49$ (PE/EA, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.93–7.91 (m, 2H), 7.57–7.52 (m, 4H), 7.44–7.34 (m, 7H), 4.72 (t, $J = 7.0$ Hz, 1H), 2.54–2.42 (m, 2H), 2.34–2.17 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 197.1, 141.1, 140.2, 140.0, 136.2, 134.4, 130.4, 129.2, 129.0, 128.6, 128.4, 127.7, 127.1, 119.4, 51.8, 29.0, 15.3; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{23}\text{H}_{18}\text{ClN}$ ONa, 282.0969; found 282.0963.

5-(4-Chlorophenyl)-4-methyl-5-oxopentanenitrile (**3ee**)



On a 0.2 mmol scale. 1.1 equiv of oxime ester **2e** was used. Purification by flash column chromatography (PE/EA, 40:1 to 15:1) furnished **3ee** (11.5 mg, 26% yield) as a yellow oil: $R_f = 0.43$ (PE/EA, 4:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.87–7.84 (m, 2H), 7.42–7.39 (m, 2H), 3.61–3.52 (m, 1H), 2.43–2.25 (m, 2H), 2.19–2.11 (m, 1H), 1.78–1.69 (m, 1H), 1.18 (d, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 201.4, 140.2, 134.2, 129.9, 129.4, 119.4, 39.4, 28.3, 18.1, 15.4; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{12}\text{ClN}$ ONa, 244.0500; found 244.0513.

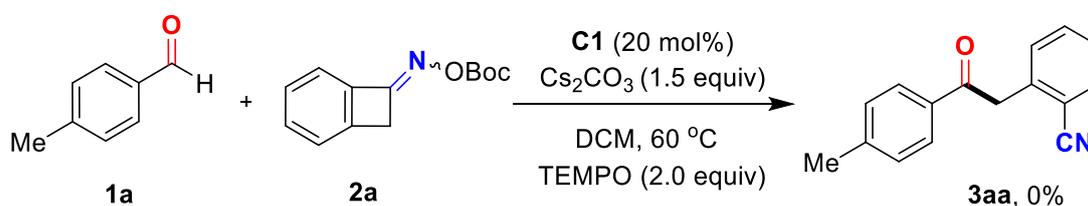
5-(4-Chlorophenyl)-5-oxopentanenitrile (**3ef**)



3.9 mg, 19% yield; a yellow oil; $R_f = 0.46$ (PE/EA, 3:1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.93–7.89 (m, 2H), 7.48–7.44 (m, 2H), 3.16 (t, $J = 6.8$ Hz, 2H), 2.53 (t, $J = 7.0$ Hz, 2H), 2.15–2.08 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 197.1, 140.2, 134.8, 129.5, 129.2, 119.4, 36.4, 19.7, 16.8; **HRMS (ESI-TOF)** m/z : $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{11}\text{ClNO}$, 208.0524; found 208.0519. The spectral data were consistent with values reported in the literature⁹.

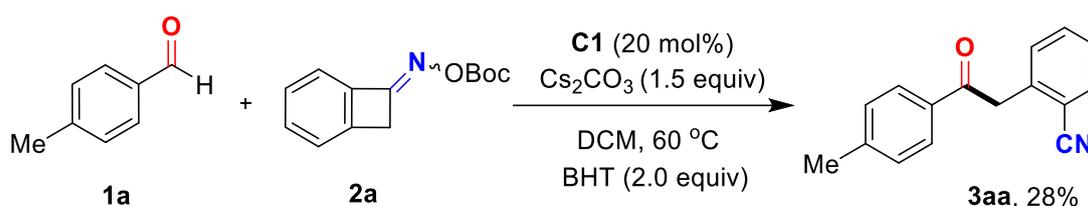
Mechanistic Studies

TEMPO Trapping Experiment



A flame-dried Schlenk tube containing a magnetic stirring bar was charged with **1a** (12.0 mg, 0.1 mmol, 1.0 equiv), **2a** (28.0 mg, 0.12 mmol, 1.2 equiv), NHC precursor **C1** (8.3 mg, 0.02 mmol, 0.1 equiv), Cs₂CO₃ (48.9 mg, 0.15 mmol, 1.5 equiv), TEMPO (31.3 mg, 0.2 mmol, 2.0 equiv), and anhydrous DCM (1.0 mL) under an argon atmosphere. The reaction mixture was stirred at 60 °C for 12 h. After that, no desired product **3aa** was detected by HRMS and NMR.

BHT Trapping Experiment

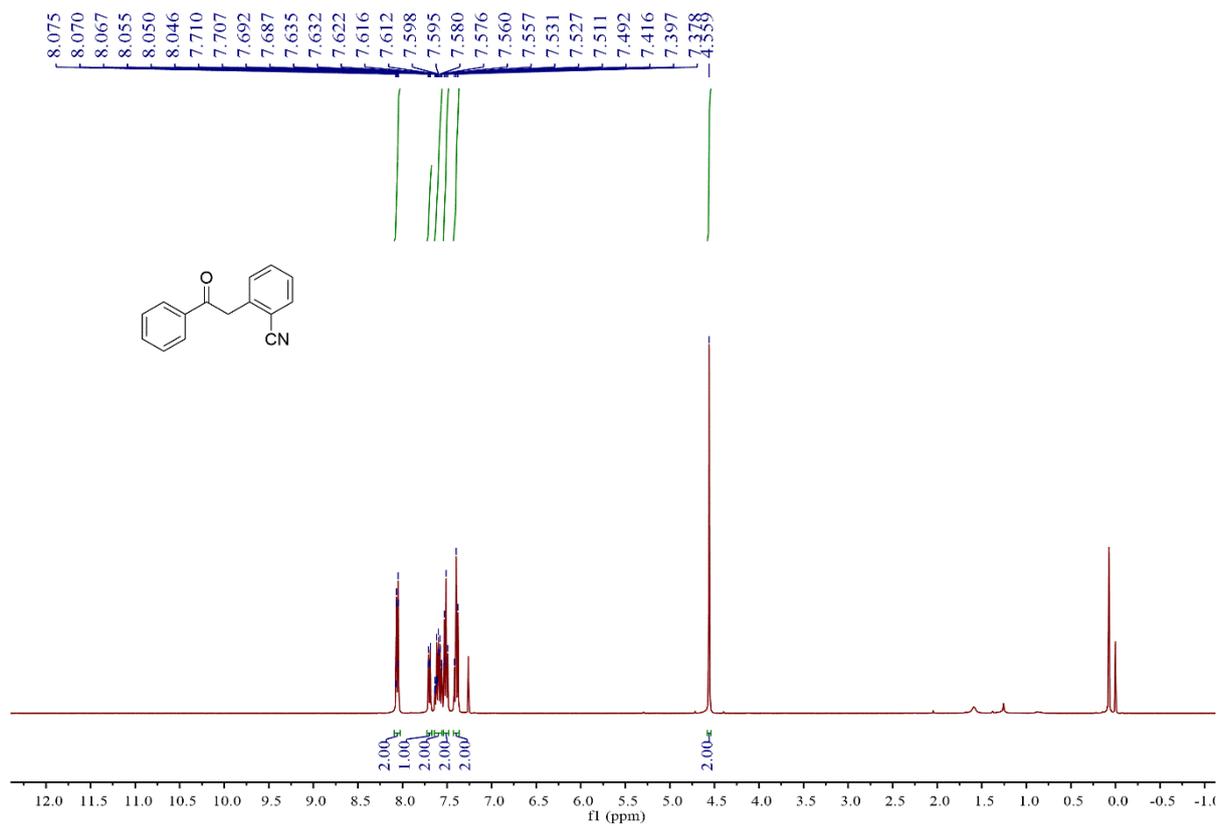


A flame-dried Schlenk tube containing a magnetic stirring bar was charged with **1a** (12.0 mg, 0.1 mmol, 1.0 equiv), **2a** (28.0 mg, 0.12 mmol, 1.2 equiv), NHC precursor **C1** (8.3 mg, 0.02 mmol, 0.1 equiv), Cs₂CO₃ (48.9 mg, 0.15 mmol, 1.5 equiv), BHT (44.1 mg, 0.2 mmol, 2.0 equiv), and anhydrous DCM (1.0 mL) under an argon atmosphere. The reaction mixture was stirred at 60 °C for 12 h. After that, the mixture was concentrated under reduced pressure. The resulting crude product was purified by silica gel flash column chromatography to give the product **3aa** (6.6 mg, 28% yield).

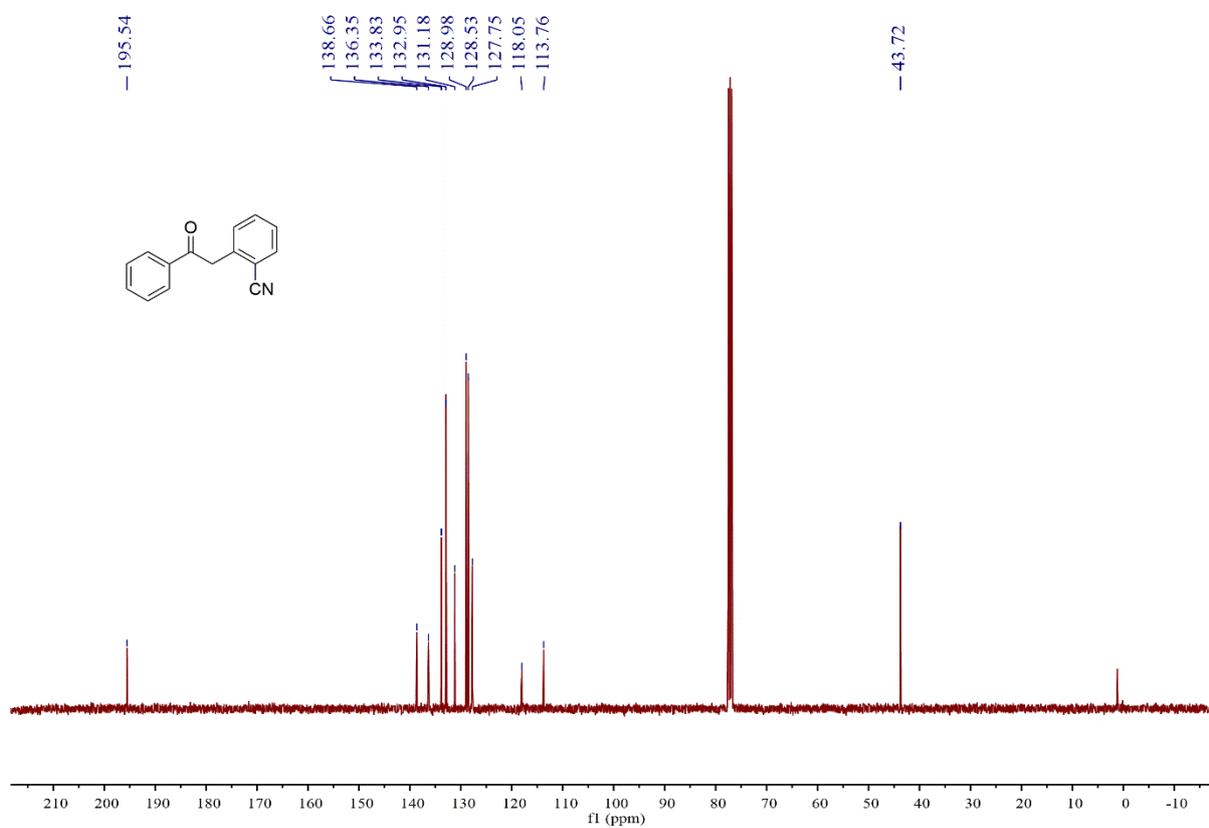
References

1. I. Piel, M. D. Pawelczyk, K. Hirano, R. Fröhlich and F. Glorius, A Family of Thiazolium Salt Derived N-Heterocyclic Carbenes (NHCs) for Organocatalysis: Synthesis, Investigation and Application in Cross-Benzoin Condensation, *Eur. J. Org. Chem.*, 2011, **2011**, 5475-5484.
2. M. M. D. Wilde and M. Gravel, Bis(amino)cyclopropenylidenes as Organocatalysts for Acyl Anion and Extended Umpolung Reactions, *Angew. Chem. Int. Ed.*, 2013, **52**, 12651-12654.
3. Z. Liu, H. Shen, H. Xiao, Z. Wang, L. Zhu and C. Li, Copper-Catalyzed Ring-Opening Radical Trifluoromethylation of Cycloalkanone Oximes, *Org. Lett.*, 2019, **21**, 5201-5205.
4. W. Ai, Y. Liu, Q. Wang, Z. Lu and Q. Liu, Cu-Catalyzed Redox-Neutral Ring Cleavage of Cycloketone O-Acyl Oximes: Chemodivergent Access to Distal Oxygenated Nitriles, *Org. Lett.*, 2018, **20**, 409-412.
5. R.-H. Liu, Z.-Y. Shen, C. Wang, T.-P. Loh and X.-H. Hu, Selective Dehydrogenative Acylation of Enamides with Aldehydes Leading to Valuable β -Ketoenamides, *Org. Lett.*, 2020, **22**, 944-949.

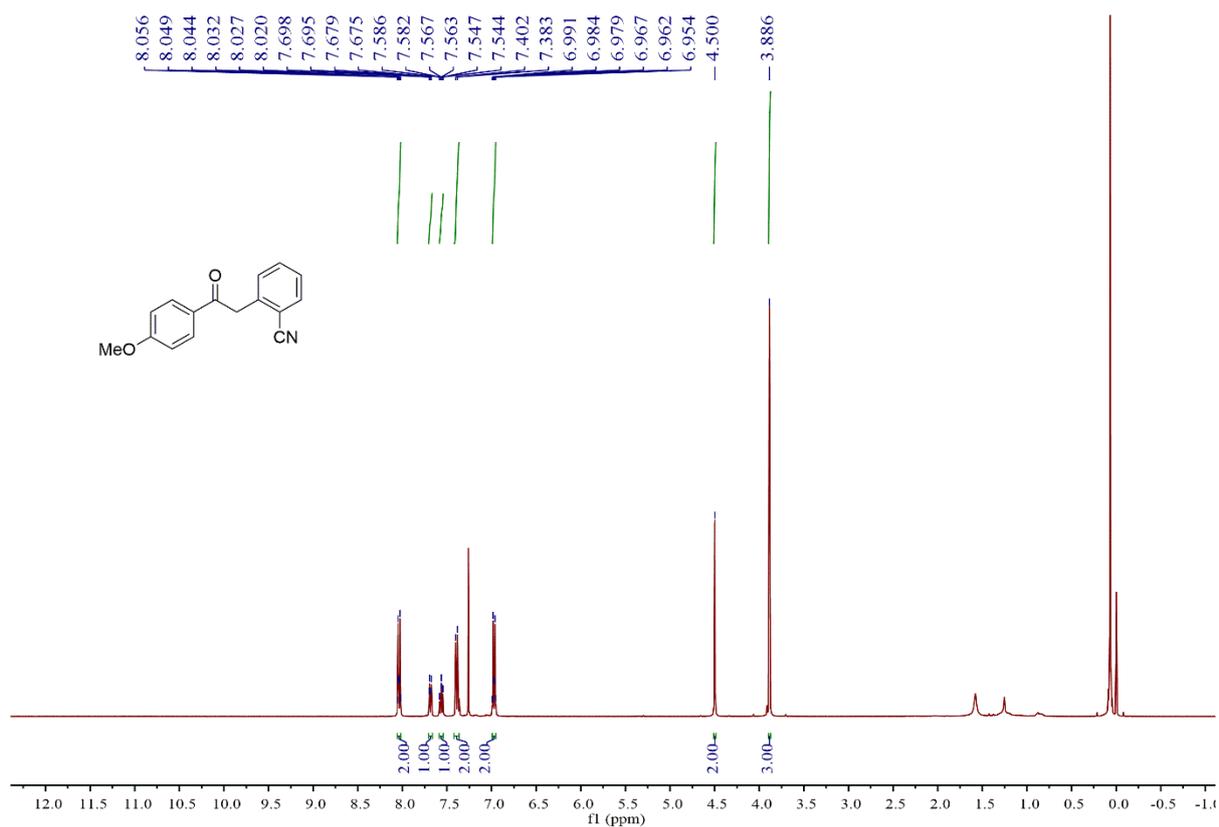
6. K. Yashiro, K. Sakata, I. Hachiya and M. Shimizu, Titanium tetraiodide induced cyclization of cyanoketones into 3-Aryl-1-Iodoisoquinolines. *Heterocycles*. 2016, **92**, 2032–2046.
7. L. Qi, K. Hu, S. Yu, J. Zhu, T. Cheng, X. Wang, J. Chen and H. Wu, Tandem Addition/Cyclization for Access to Isoquinolines and Isoquinolones via Catalytic Carbopalladation of Nitriles, *Org. Lett.*, 2017, **19**, 218-221.
8. T. Wang and N. Jiao, TEMPO-catalyzed aerobic oxygenation and nitrogenation of olefins via C horizontal lineC double-bond cleavage, *J. Am. Chem. Soc.*, 2013, **135**, 11692-11695.
9. D. Ding and C. Wang, Nickel-Catalyzed Reductive Electrophilic Ring Opening of Cycloketone Oxime Esters with Aroyl Chlorides, *ACS Catal.*, 2018, **8**, 11324-11329.



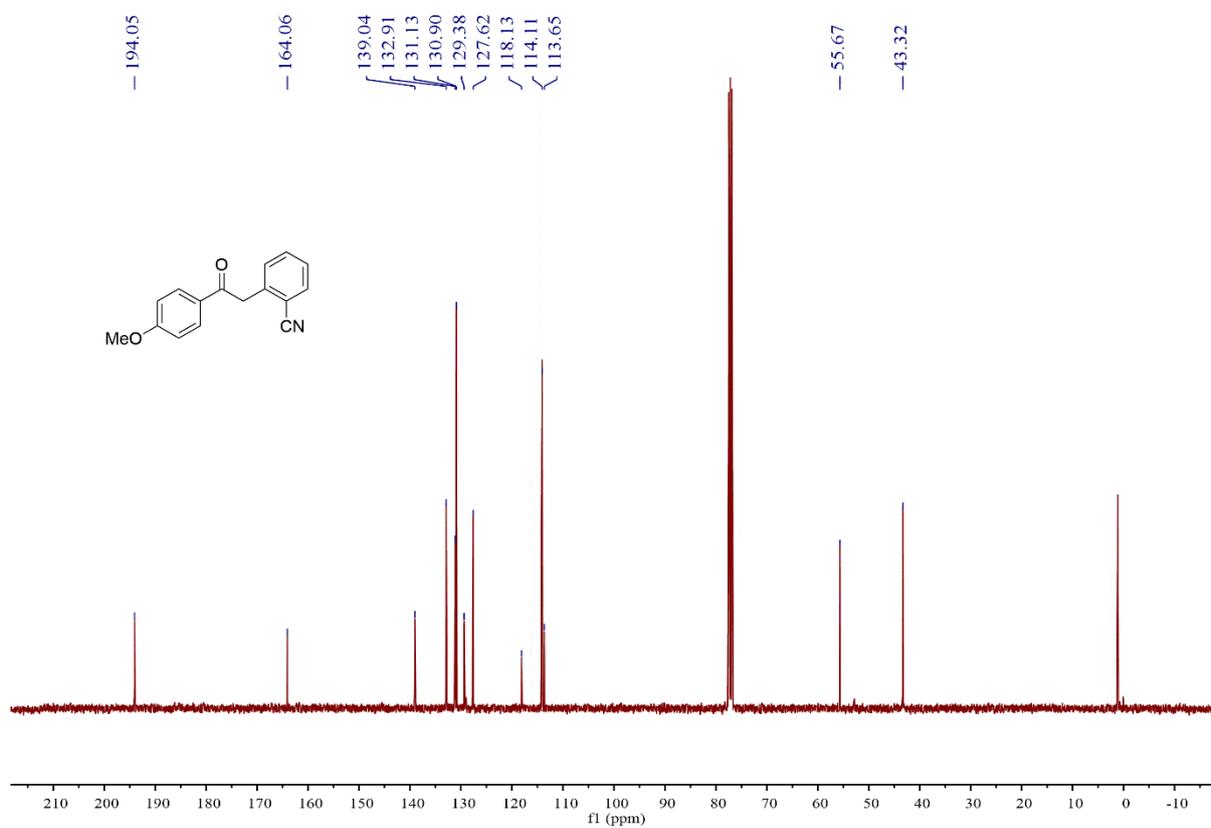
¹H NMR Spectrum of Compound **3ba (400 MHz, CDCl₃)**



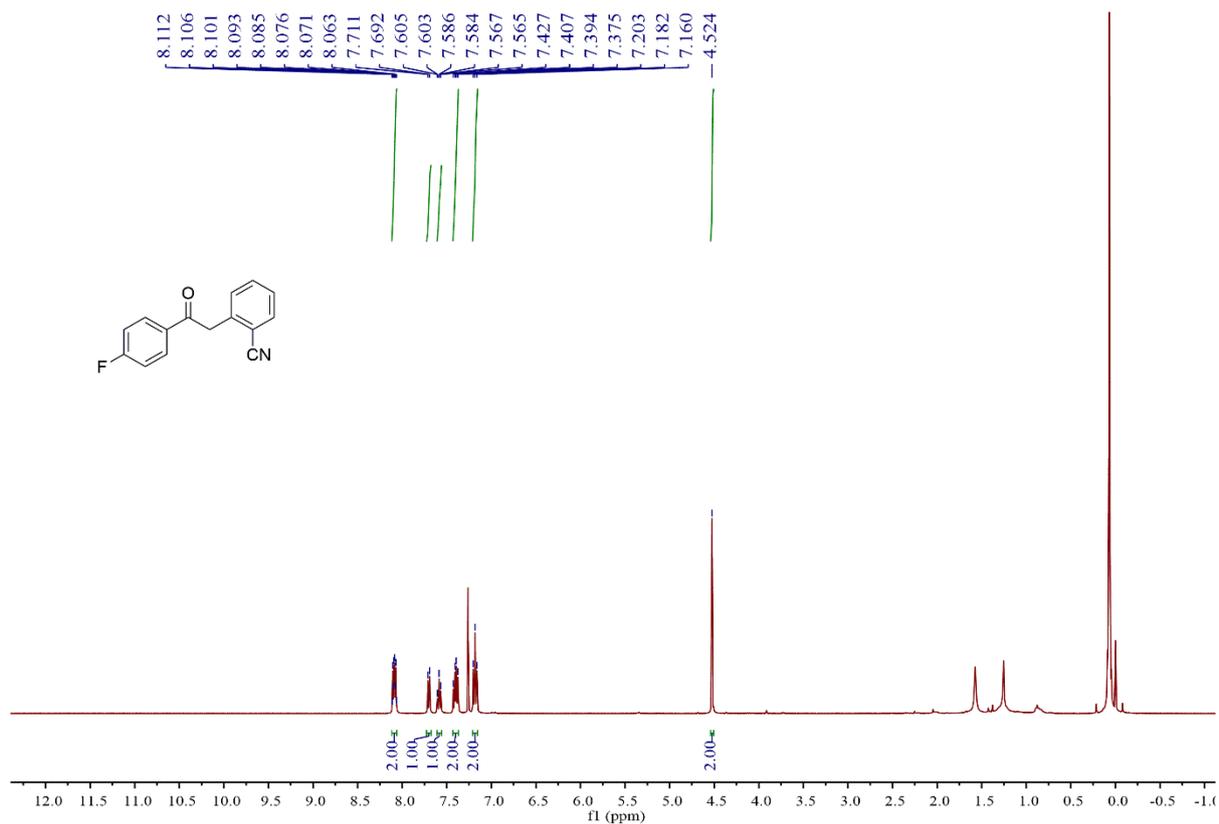
¹³C NMR Spectrum of Compound **3ba (100 MHz, CDCl₃)**



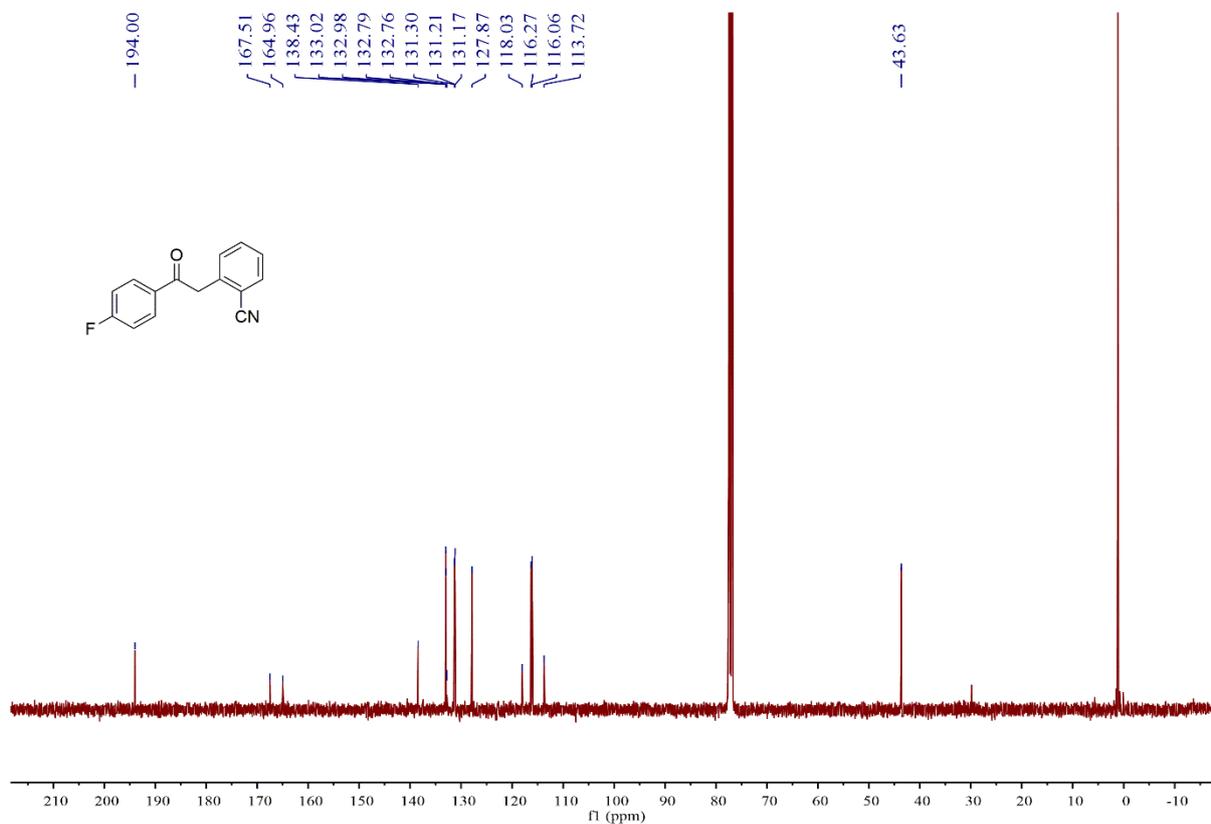
¹H NMR Spectrum of Compound 3ca (400 MHz, CDCl₃)



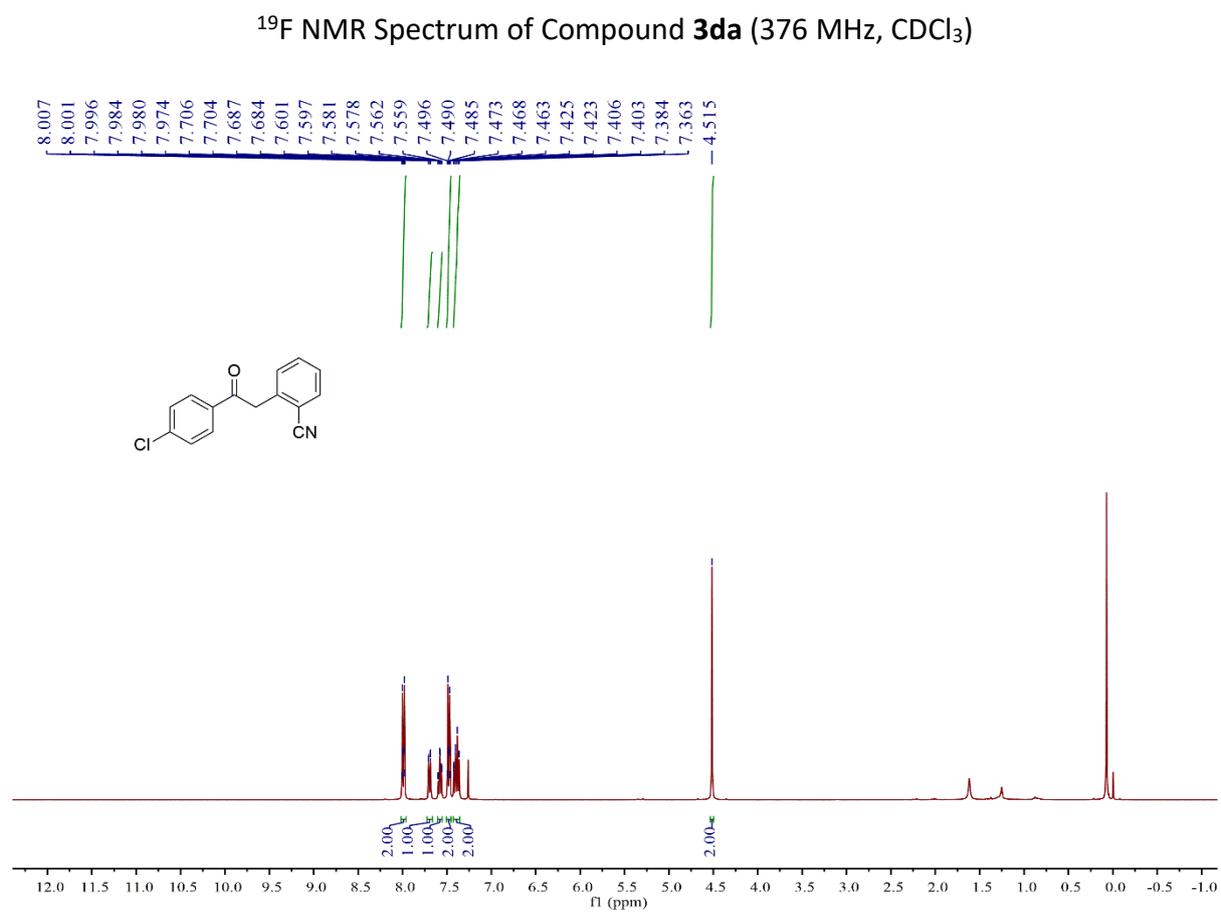
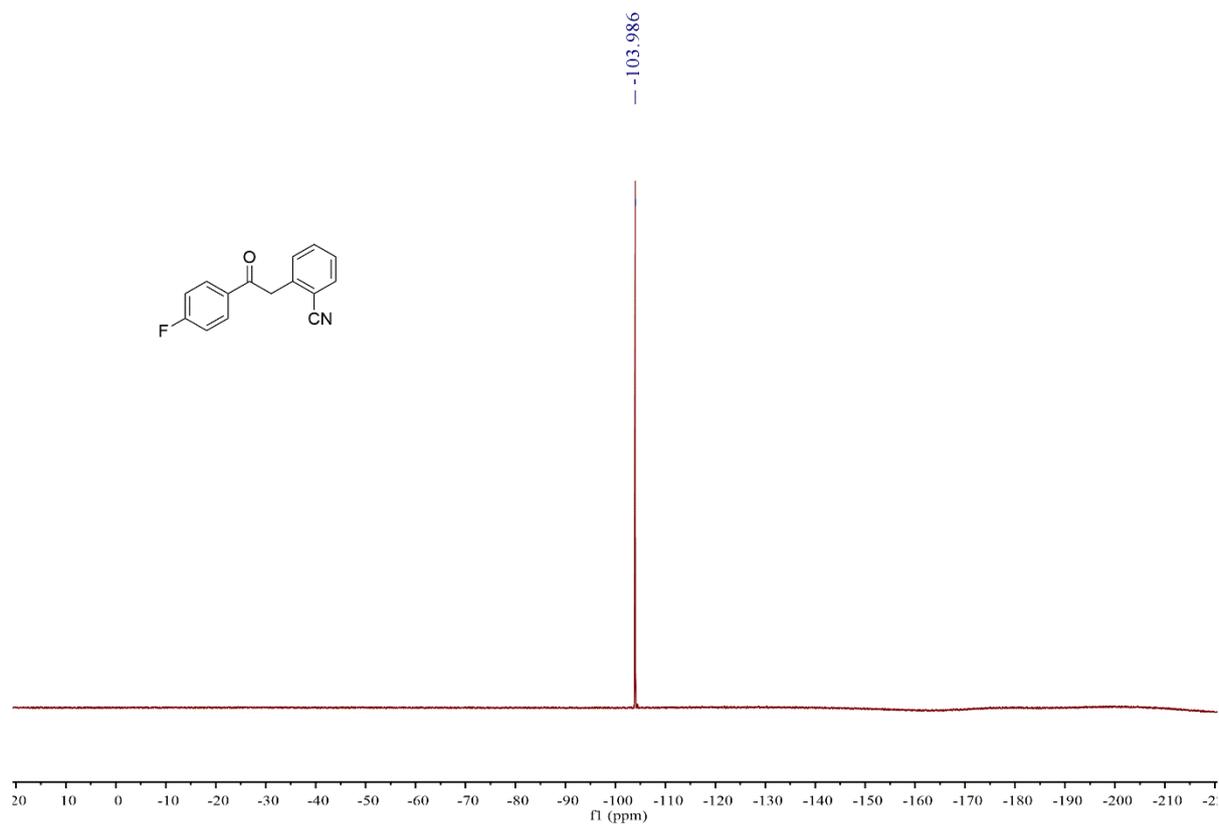
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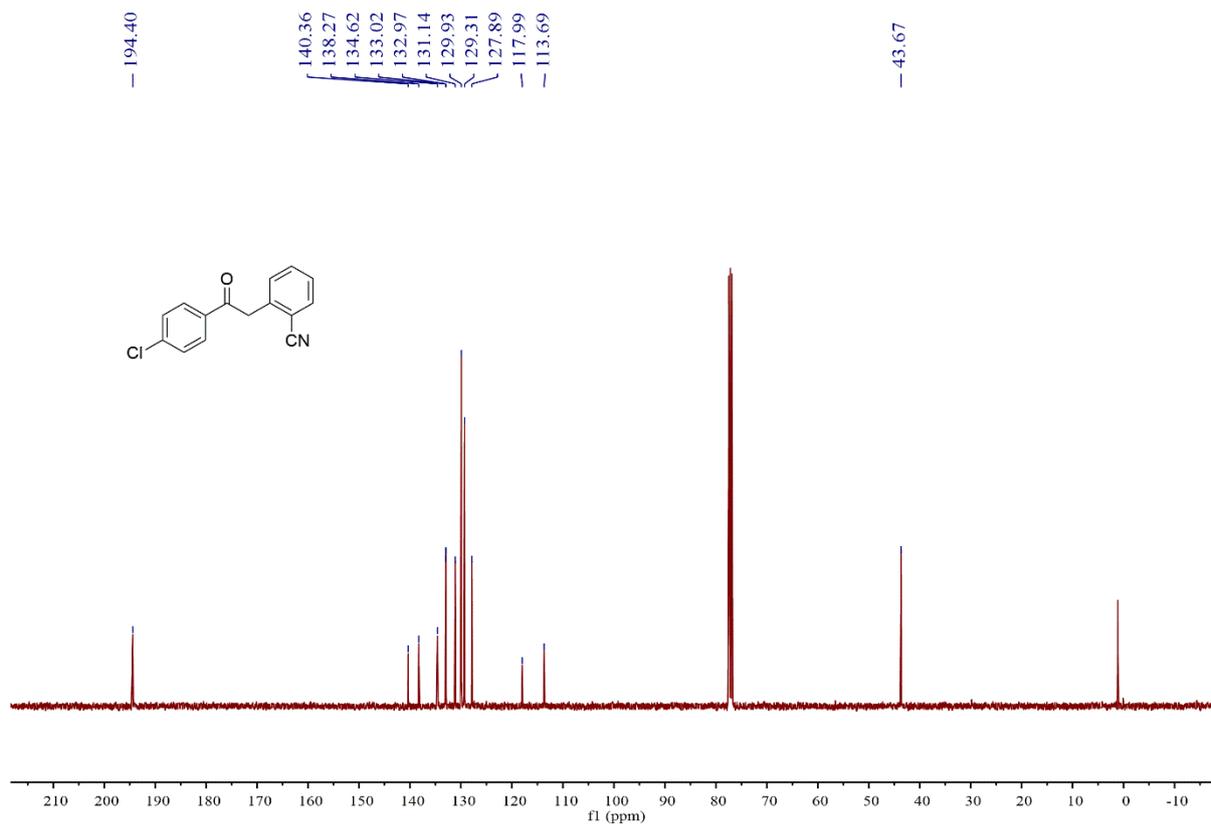


¹H NMR Spectrum of Compound 3da (400 MHz, CDCl₃)

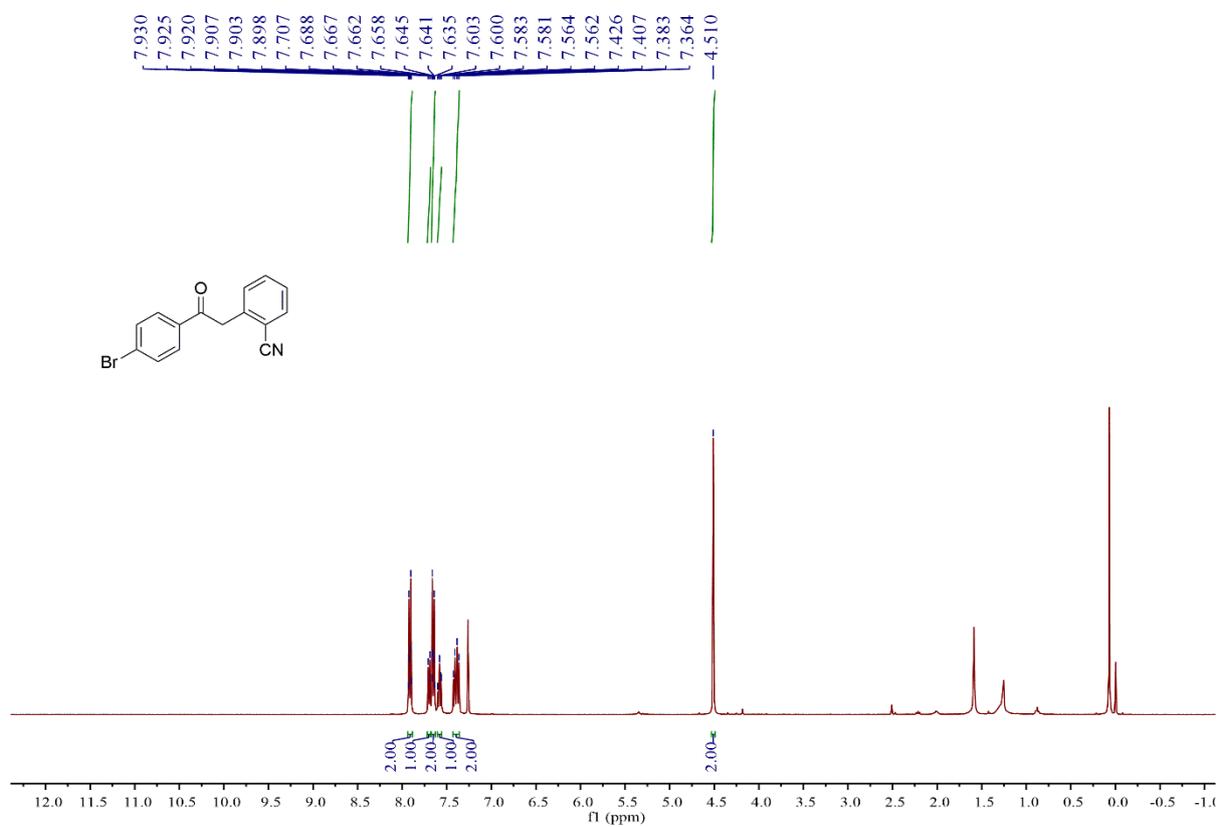


¹³C NMR Spectrum of Compound 3da (100 MHz, CDCl₃)

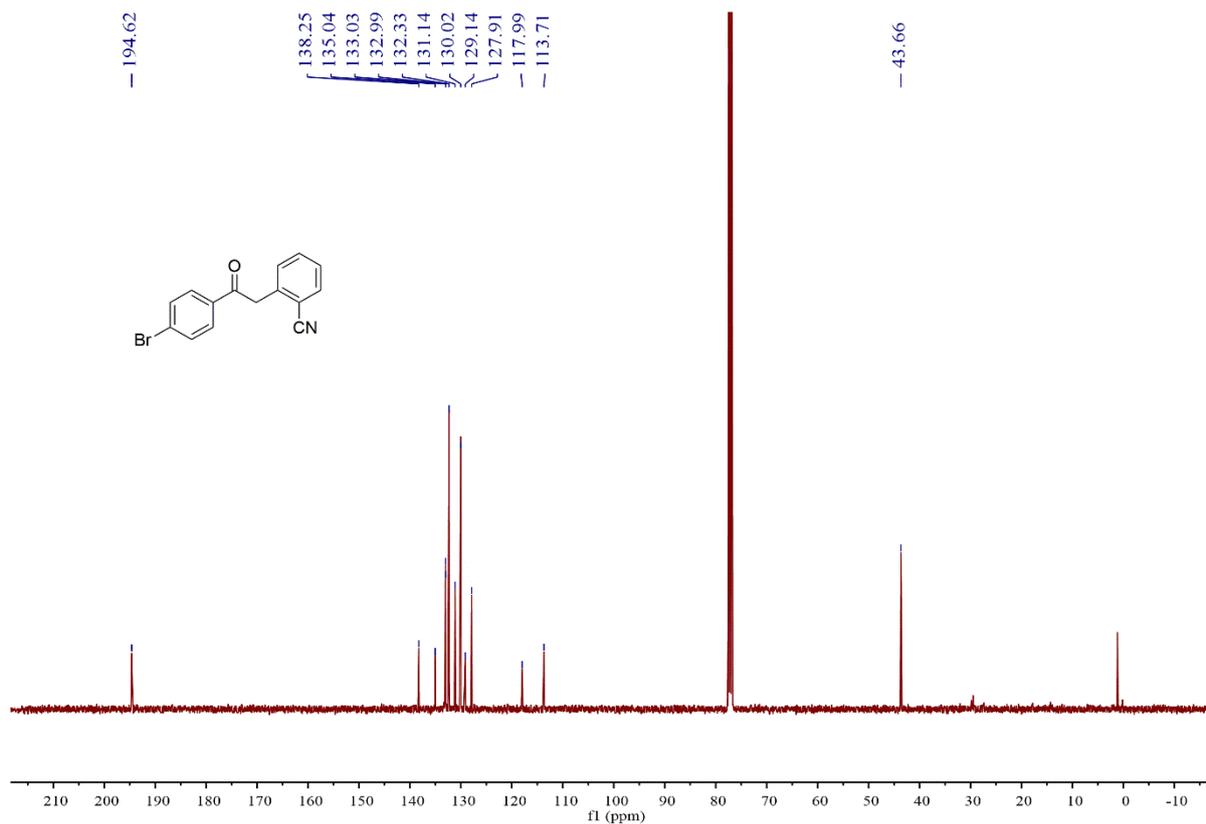




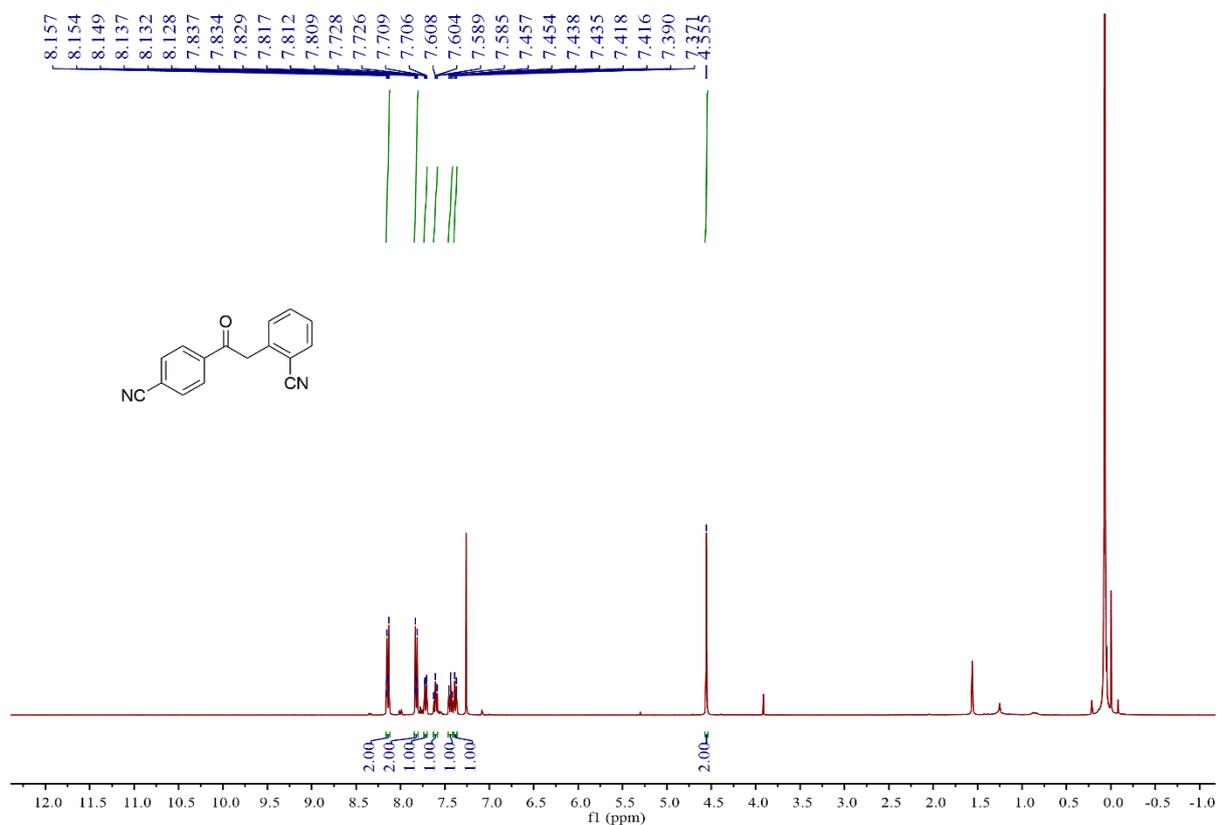
¹³C NMR Spectrum of Compound **3ea** (100 MHz, CDCl₃)



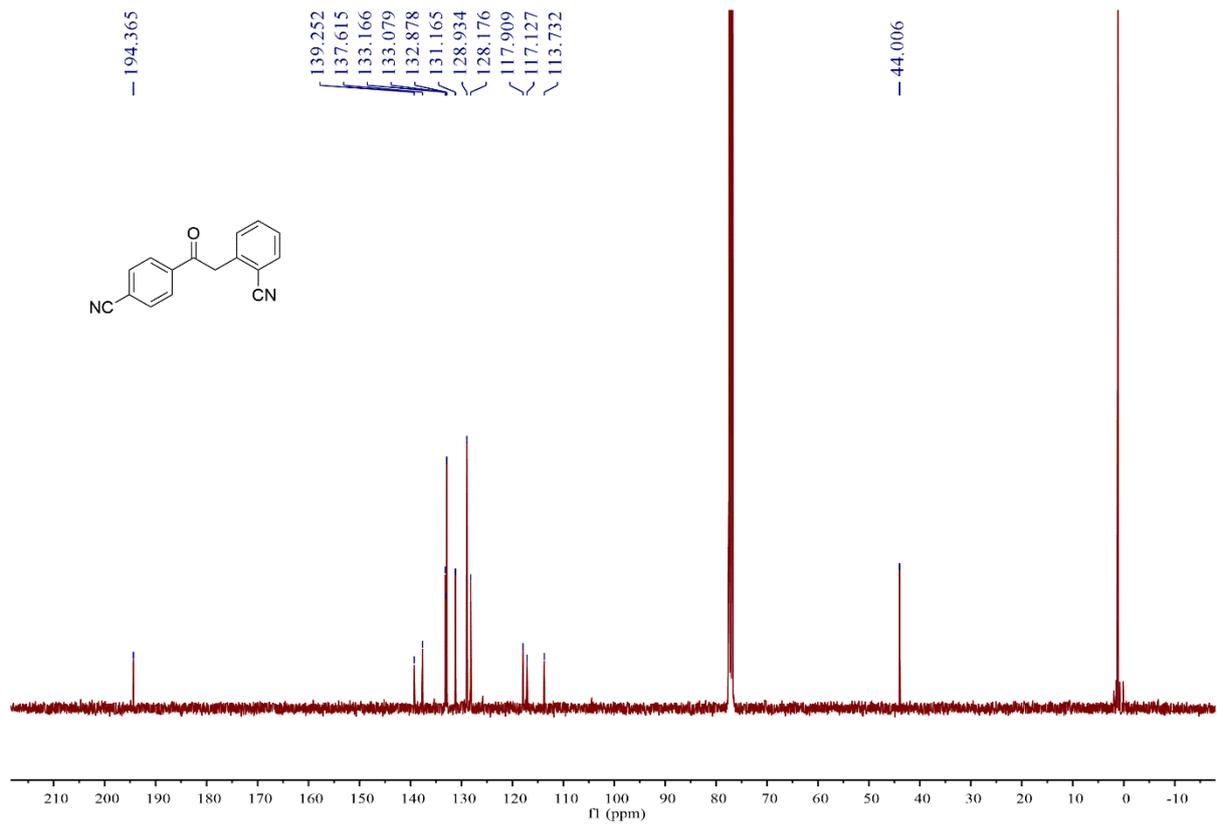
¹H NMR Spectrum of Compound **3fa** (400 MHz, CDCl₃)



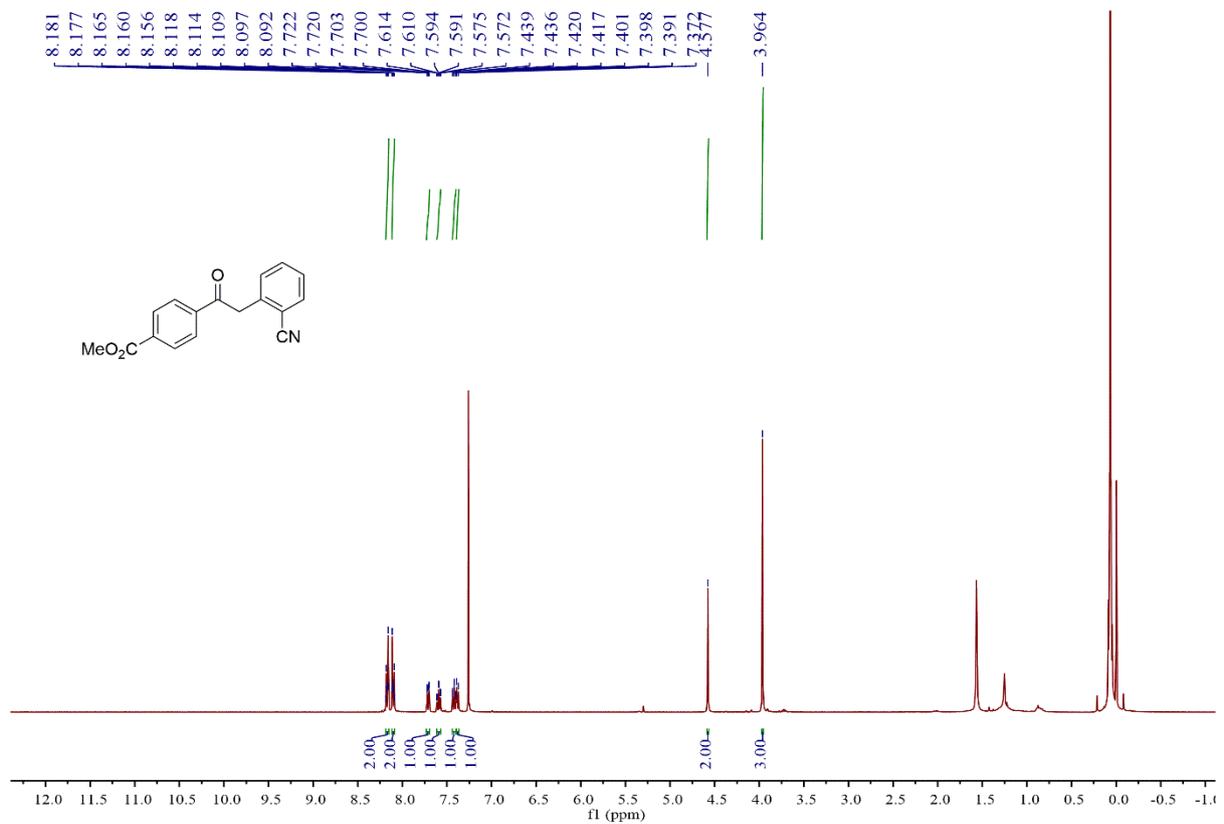
¹³C NMR Spectrum of Compound **3fa** (100 MHz, CDCl₃)



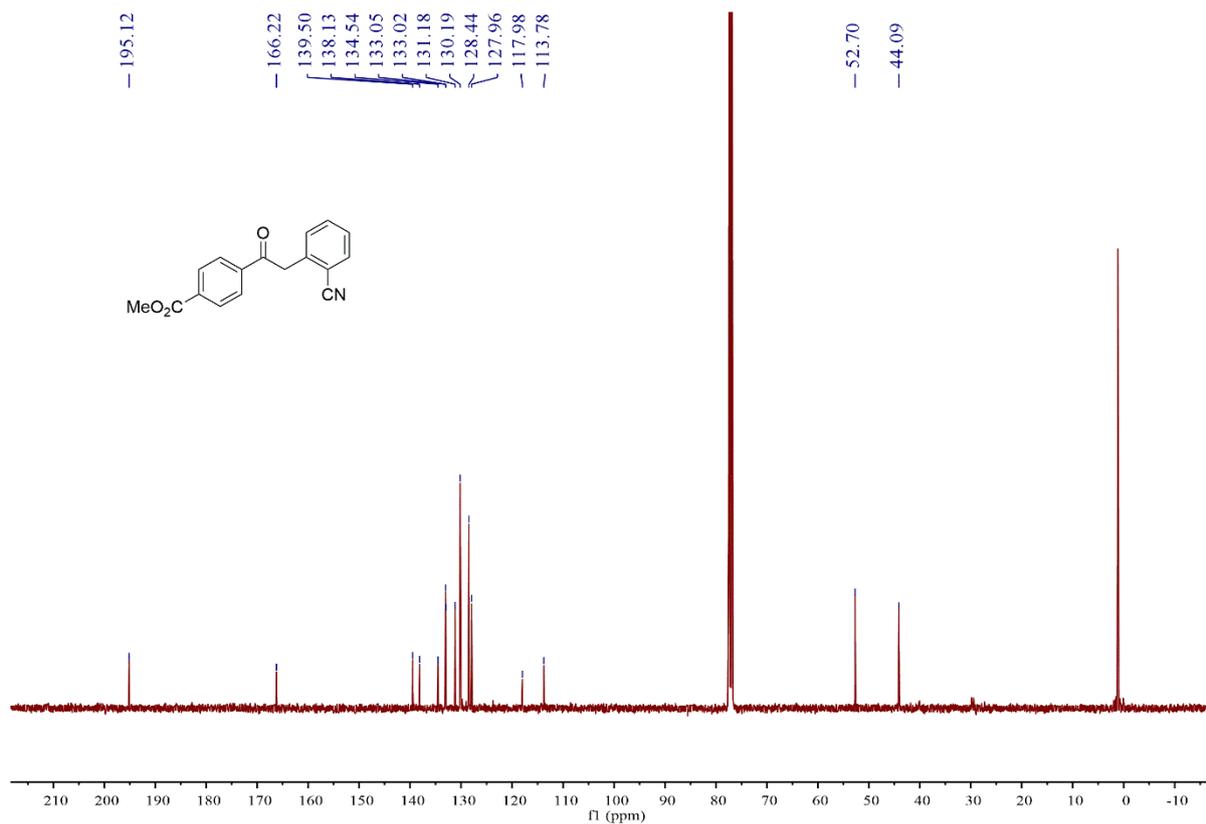
¹H NMR Spectrum of Compound **3ga** (400 MHz, CDCl₃)



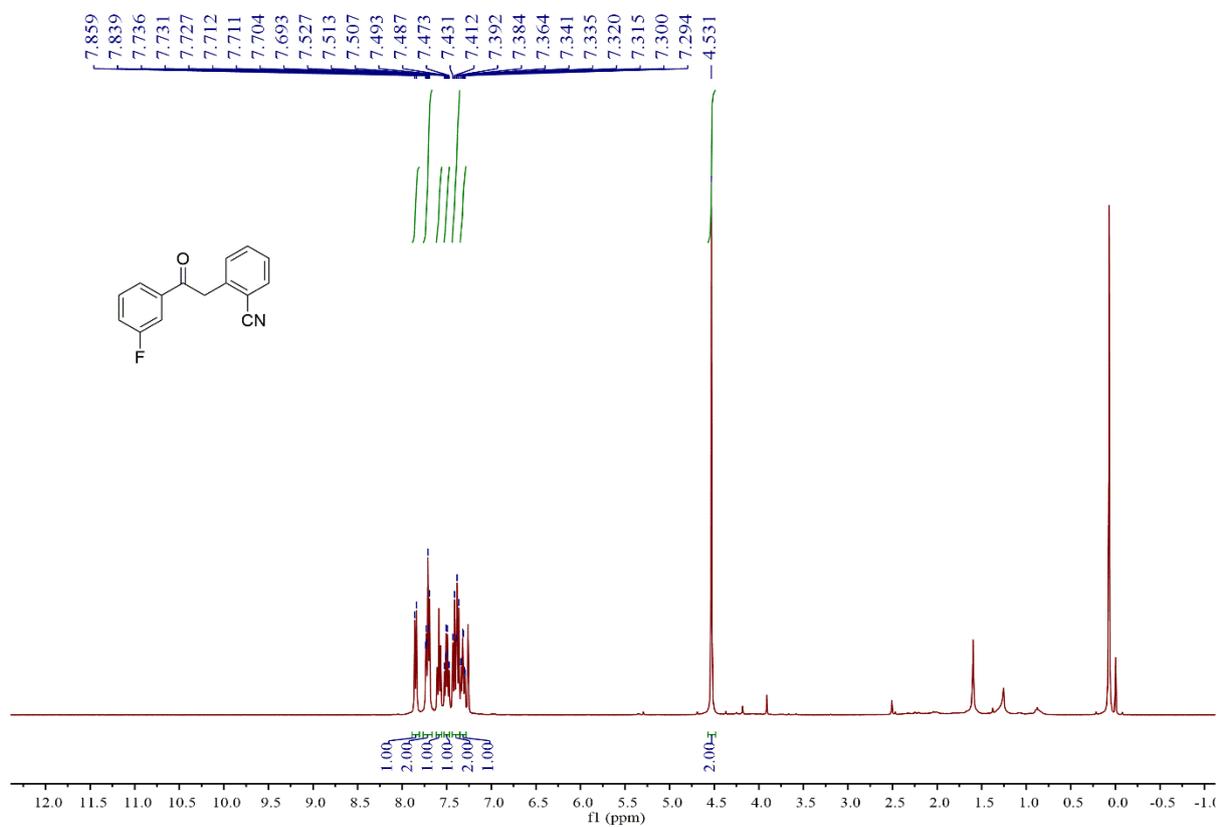
¹³C NMR Spectrum of Compound **3ga** (100 MHz, CDCl₃)



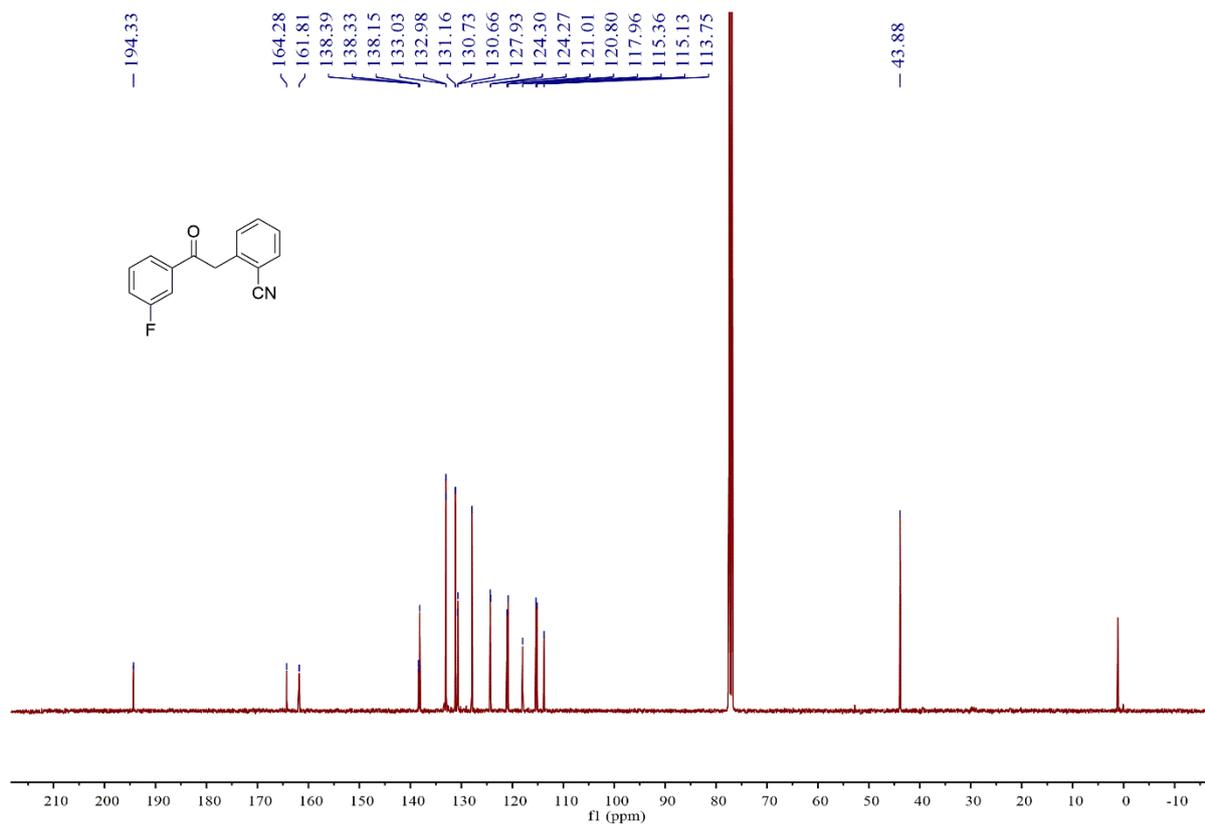
¹H NMR Spectrum of Compound **3ha** (400 MHz, CDCl₃)



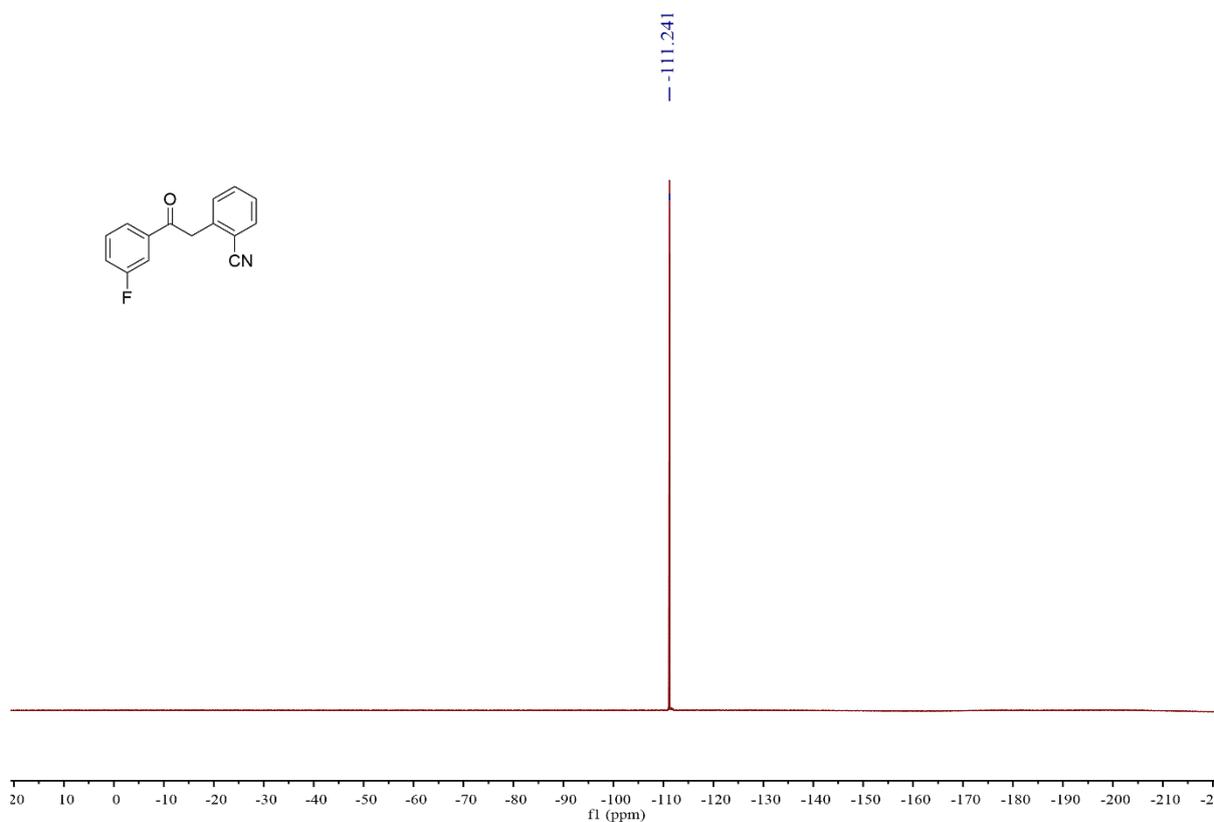
¹³C NMR Spectrum of Compound 3ha (100 MHz, CDCl₃)



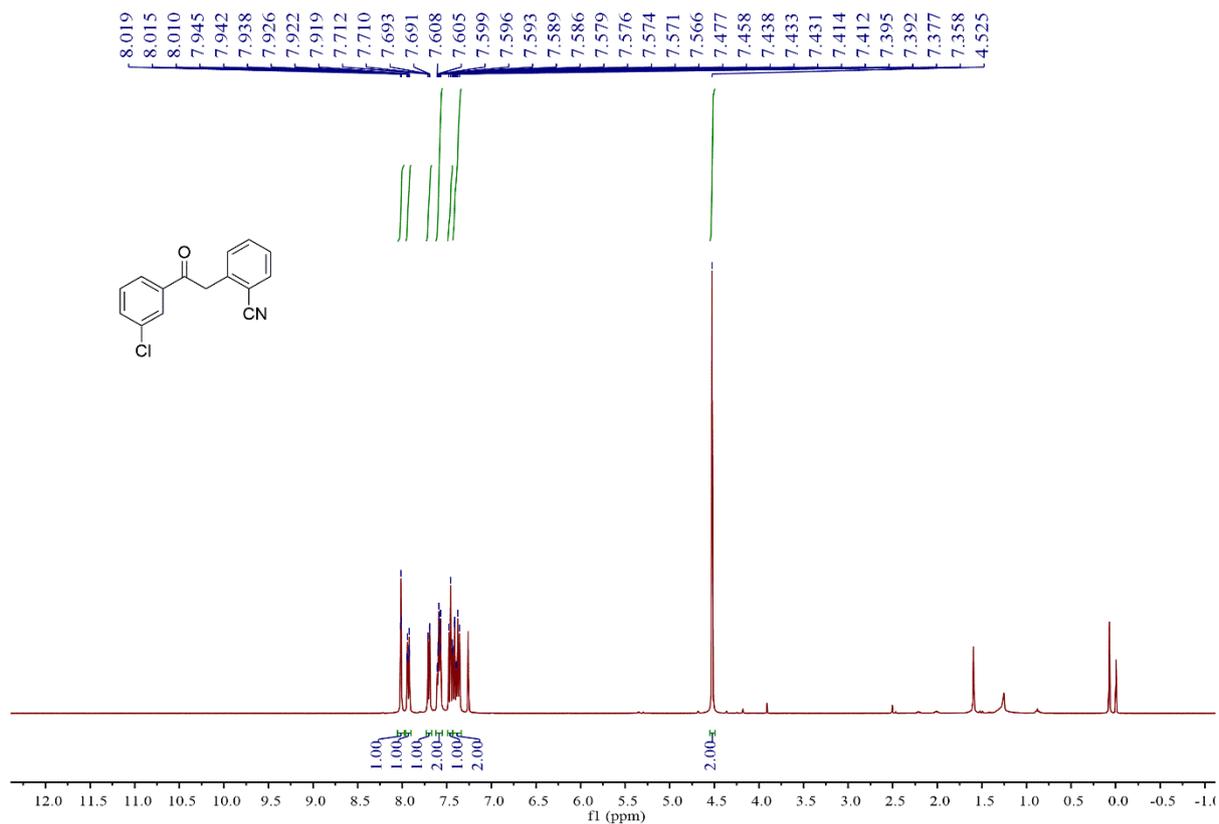
¹H NMR Spectrum of Compound 3ia (400 MHz, CDCl₃)



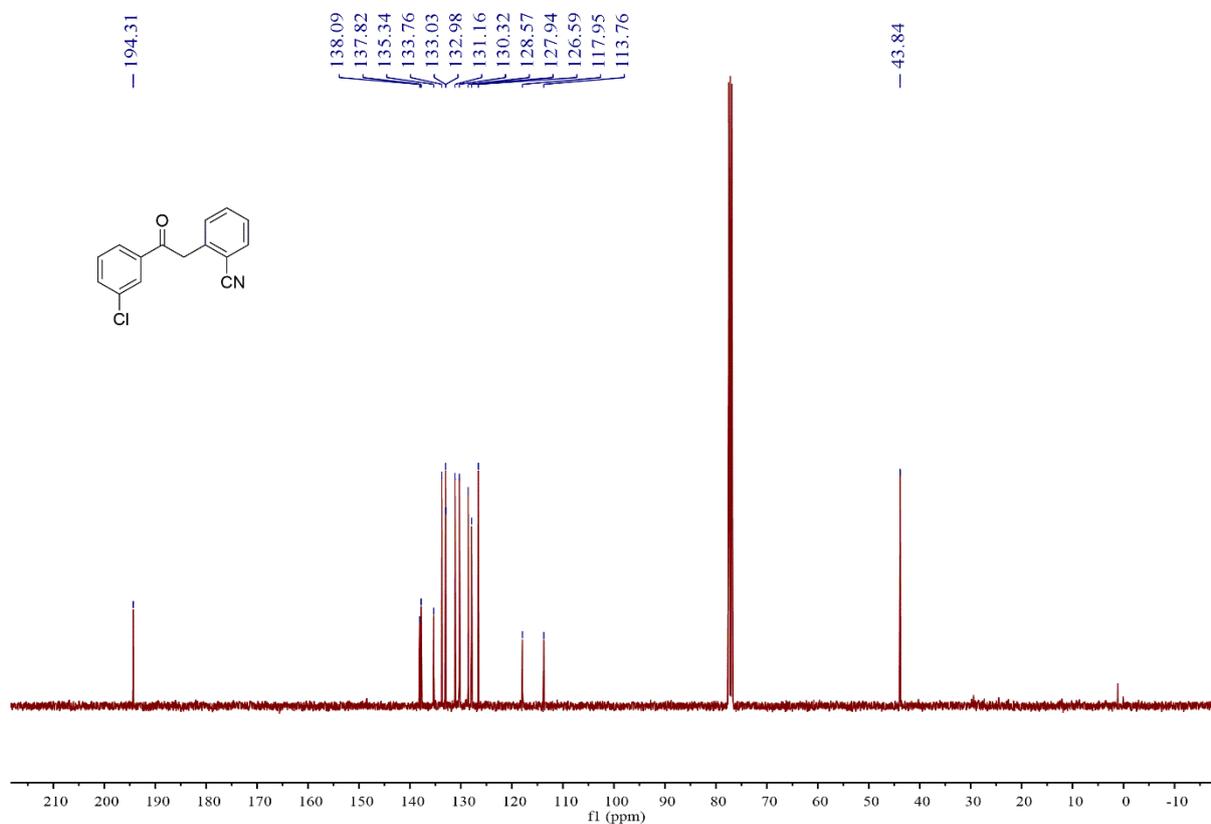
¹³C NMR Spectrum of Compound **3ia** (100 MHz, CDCl₃)



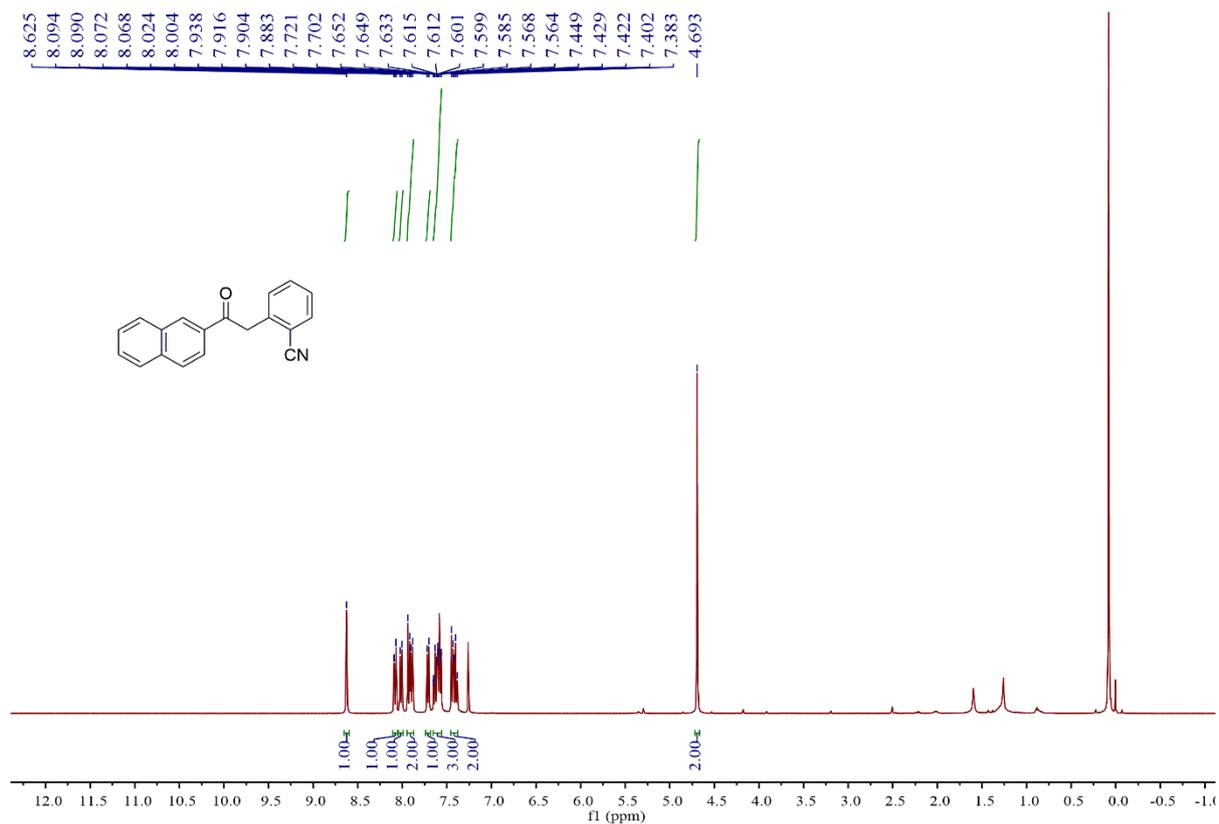
¹⁹F NMR Spectrum of Compound **3ia** (376 MHz, CDCl₃)



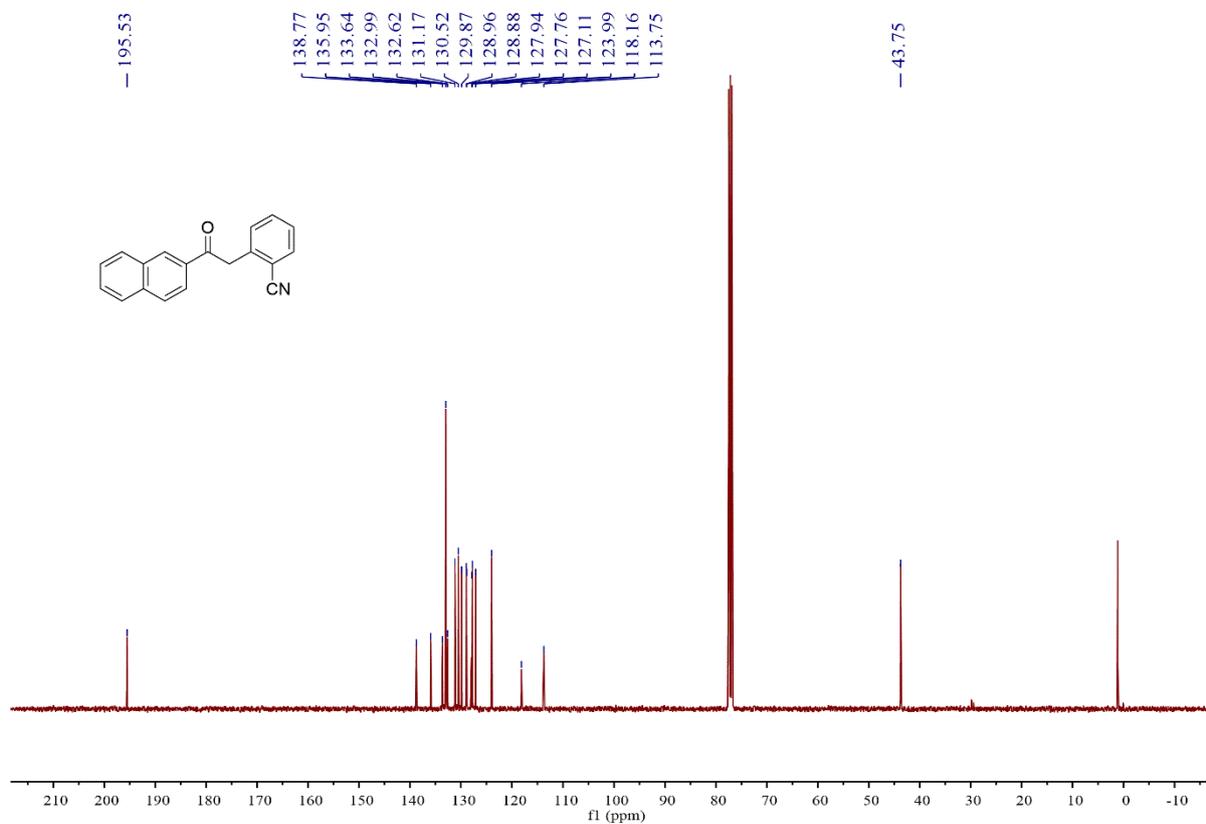
¹H NMR Spectrum of Compound 3ja (400 MHz, CDCl₃)



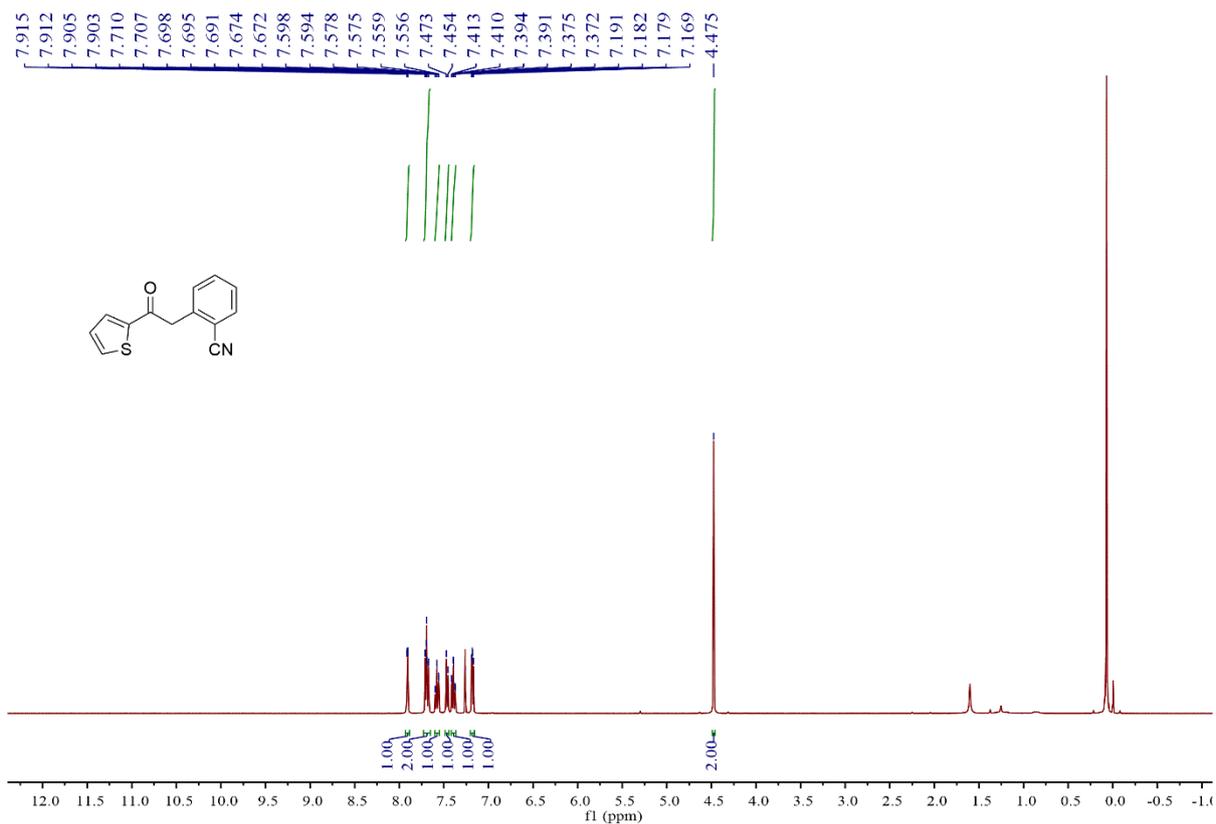
¹³C NMR Spectrum of Compound 3ja (100 MHz, CDCl₃)



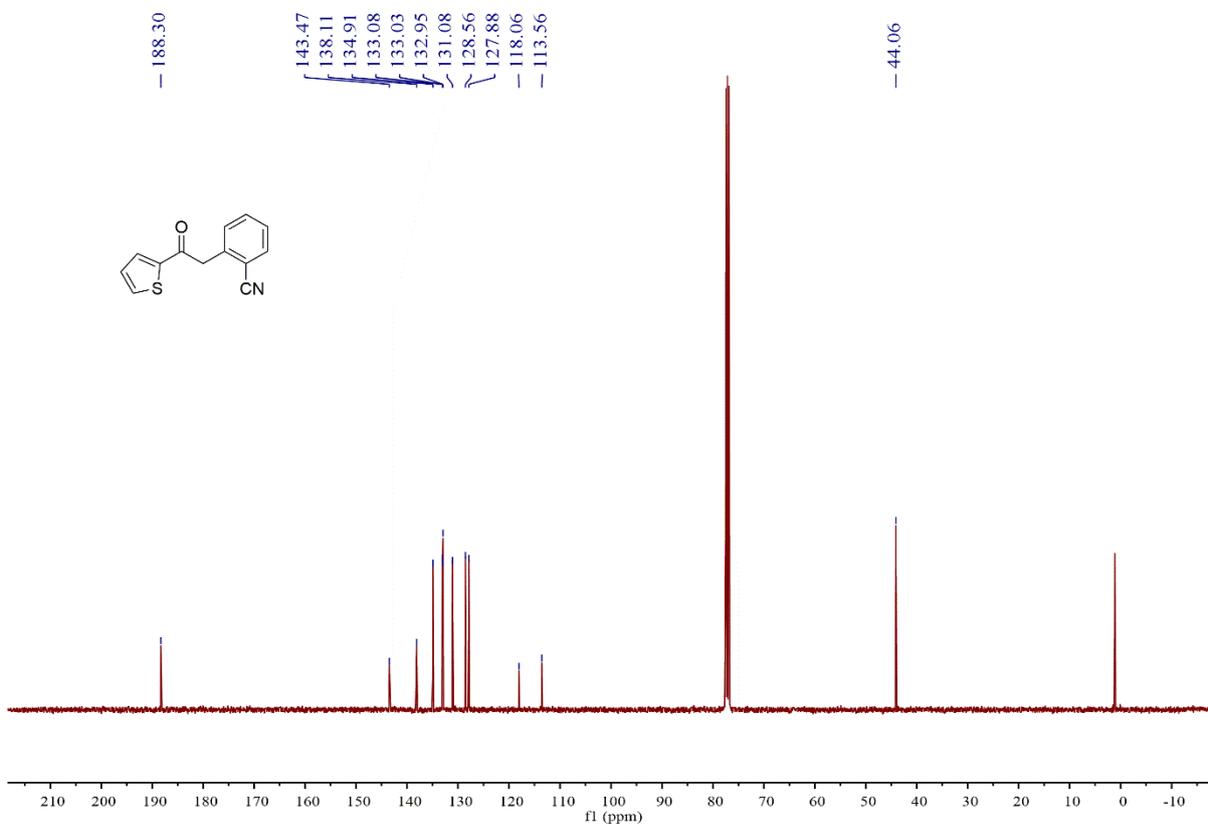
¹H NMR Spectrum of Compound 3ka (400 MHz, CDCl₃)



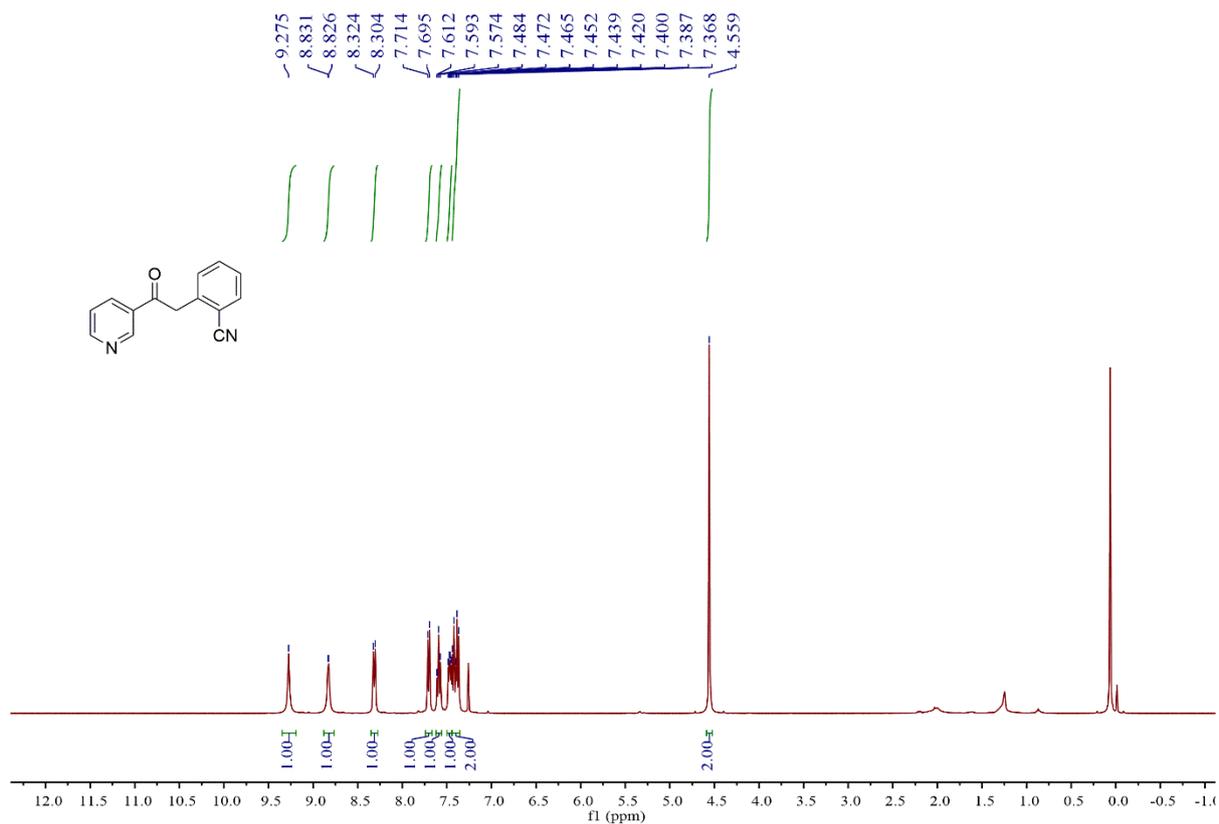
¹³C NMR Spectrum of Compound 3ka (100 MHz, CDCl₃)



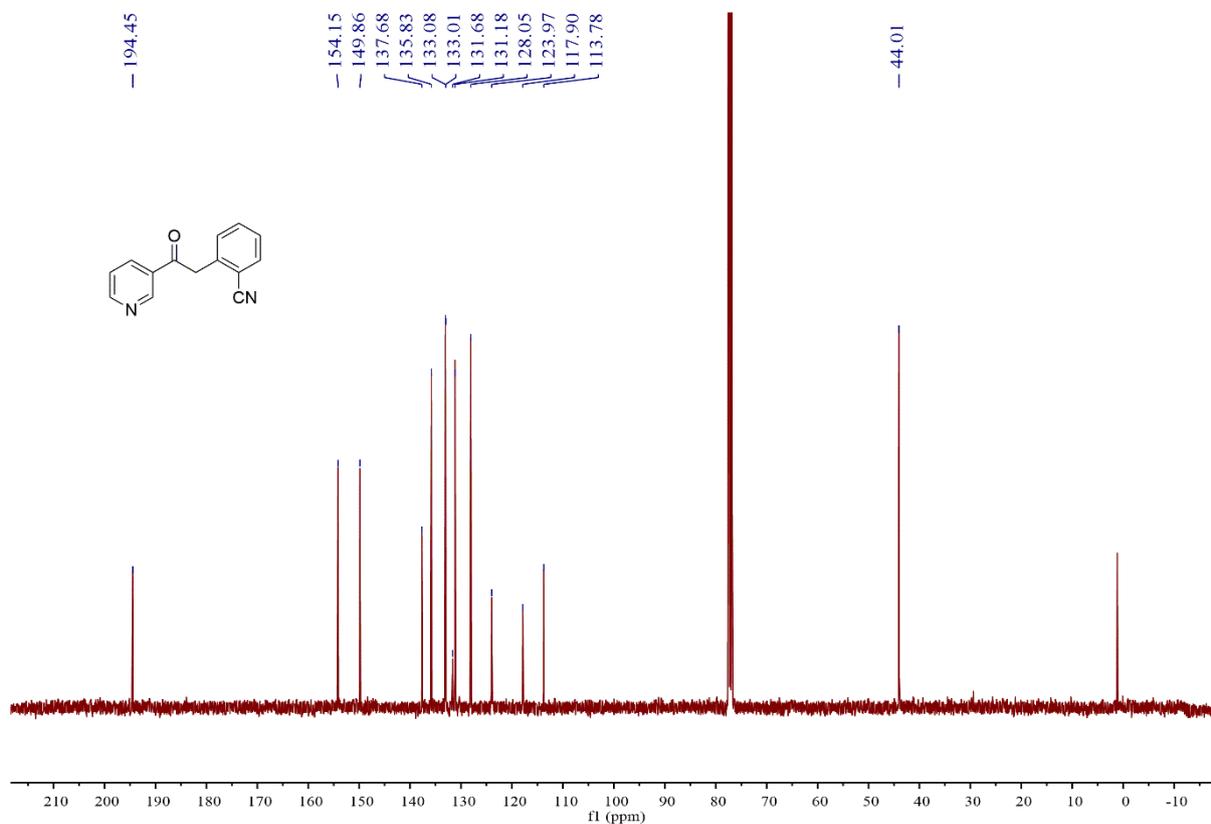
¹H NMR Spectrum of Compound 3la (400 MHz, CDCl₃)



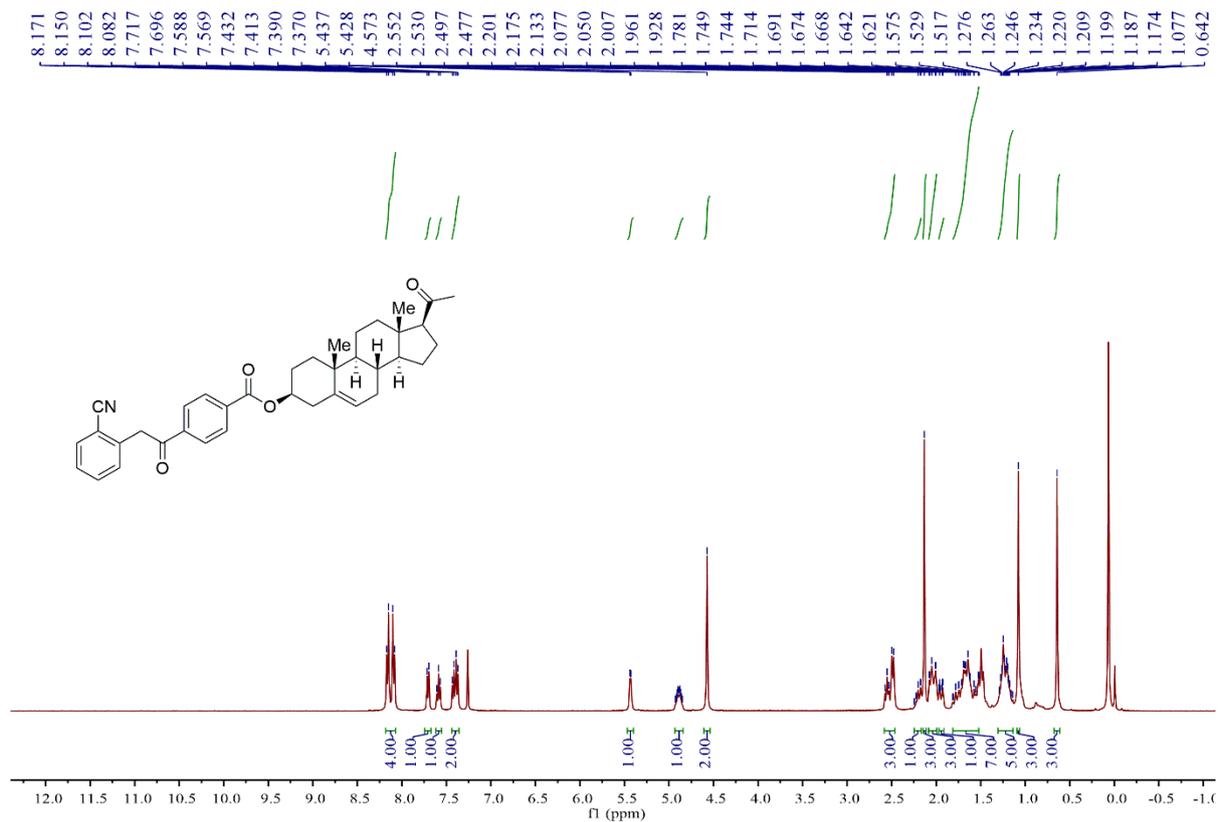
¹³C NMR Spectrum of Compound 3la (100 MHz, CDCl₃)



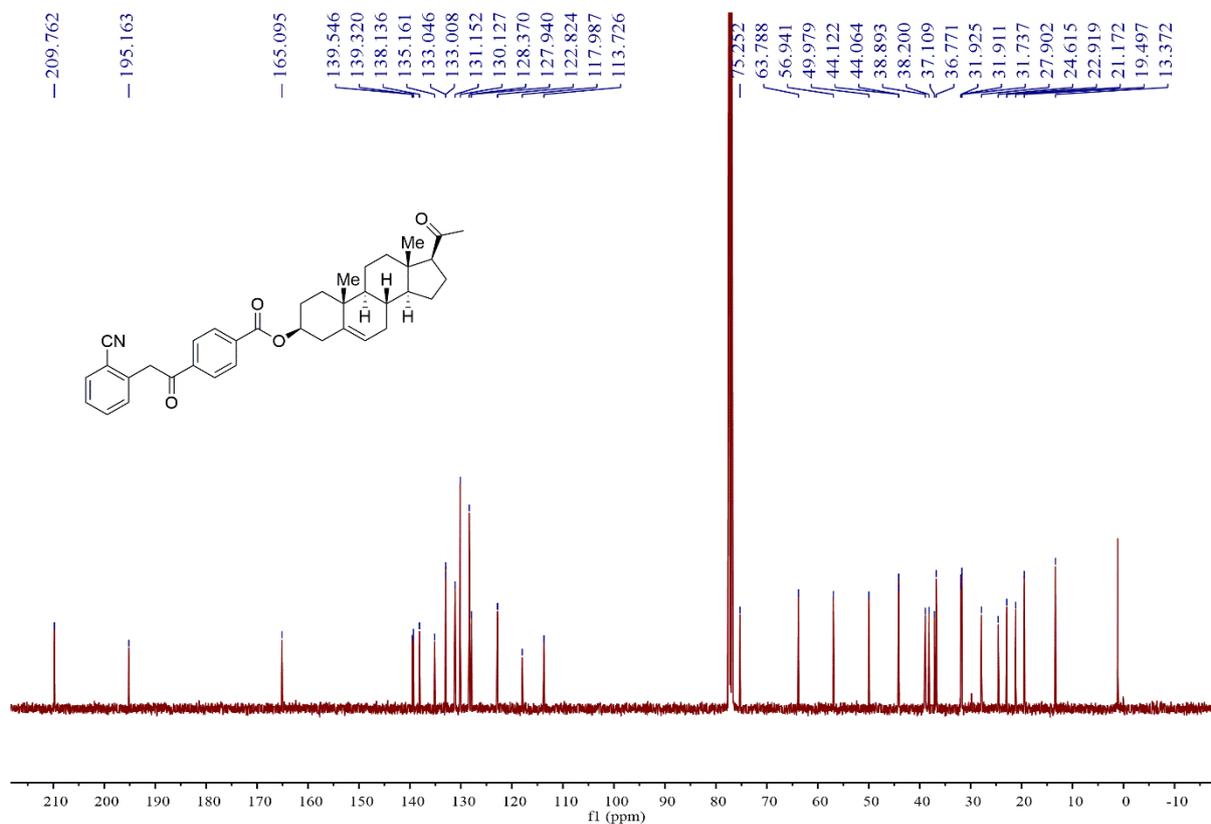
¹H NMR Spectrum of Compound 3ma (400 MHz, CDCl₃)



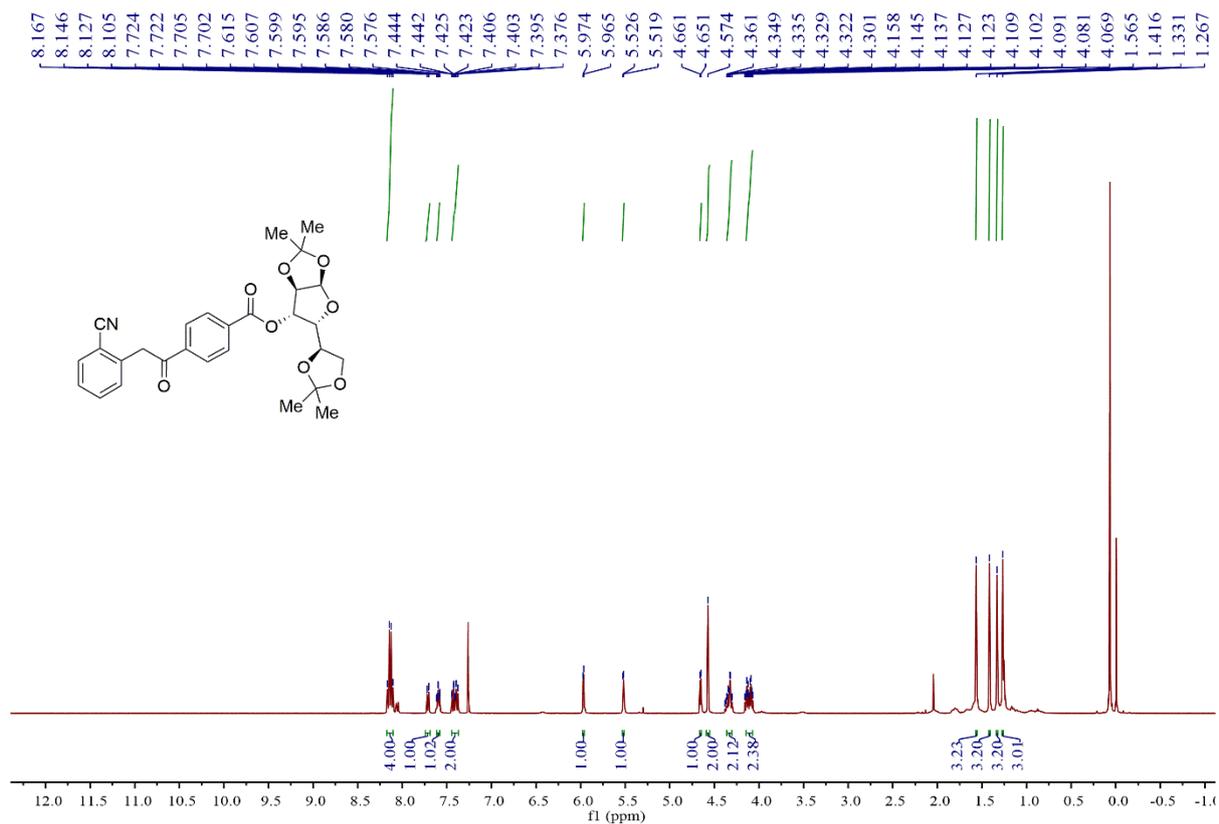
¹³C NMR Spectrum of Compound 3ma (100 MHz, CDCl₃)



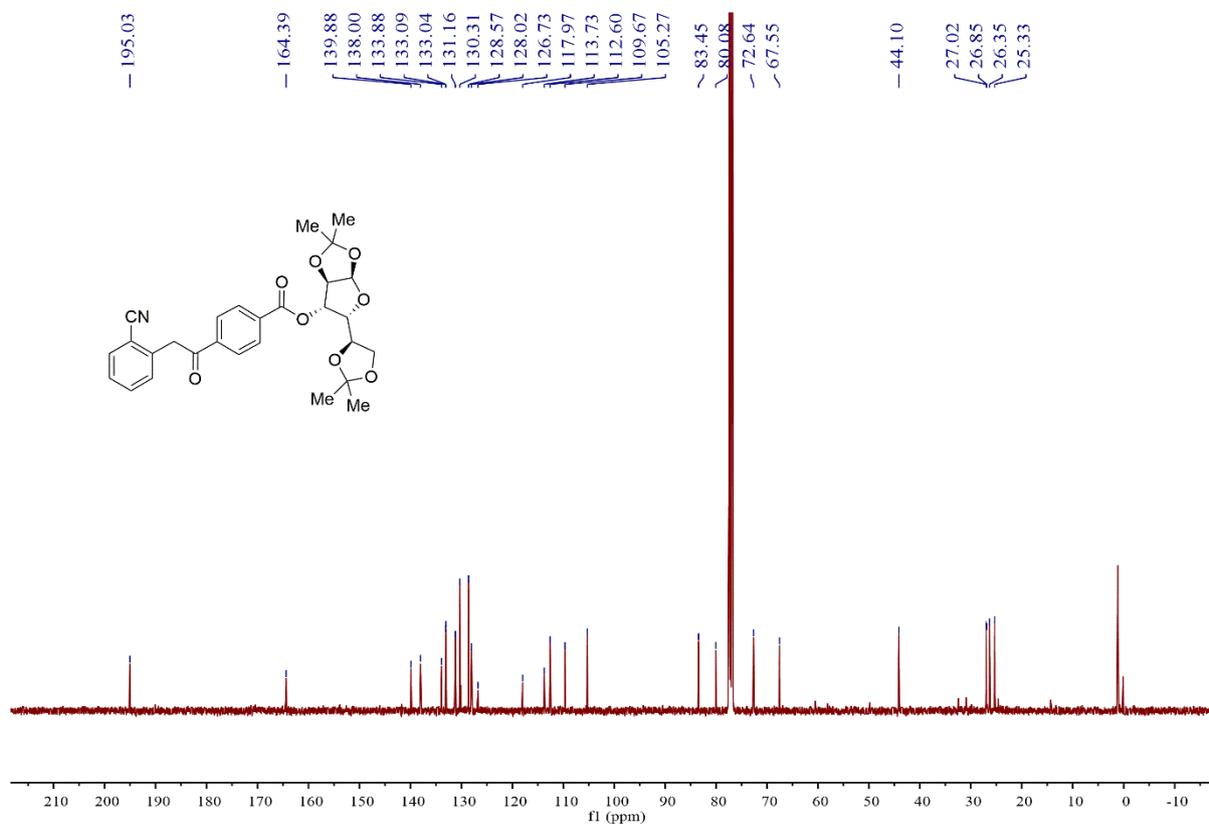
¹H NMR Spectrum of Compound 3na (400 MHz, CDCl₃)



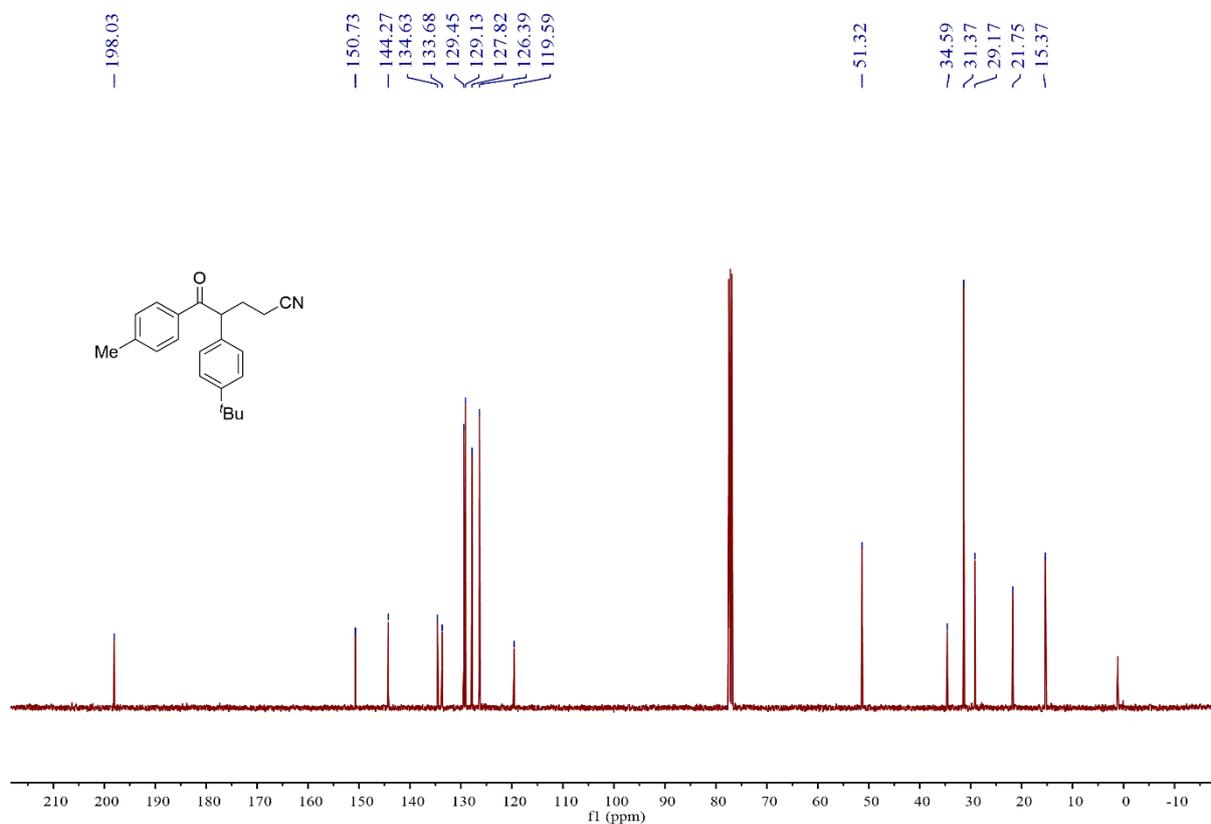
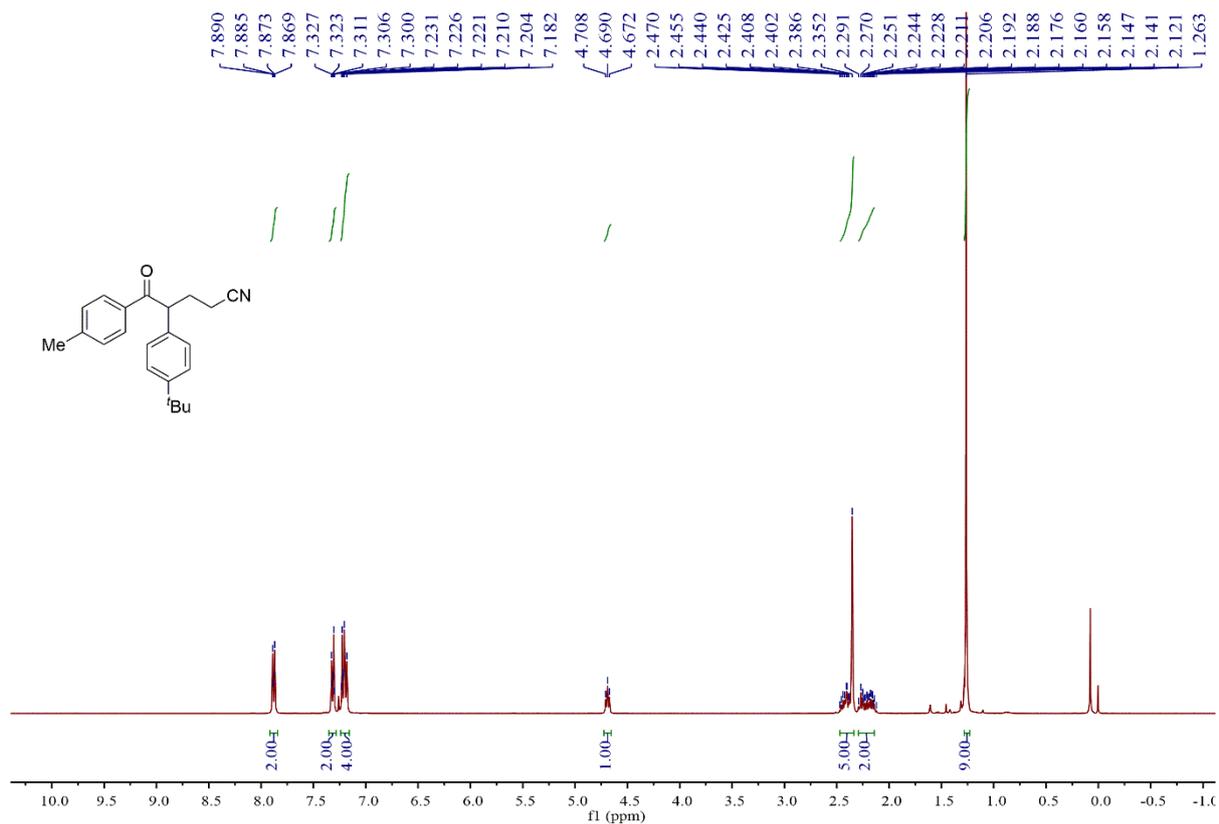
¹³C NMR Spectrum of Compound 3na (100 MHz, CDCl₃)

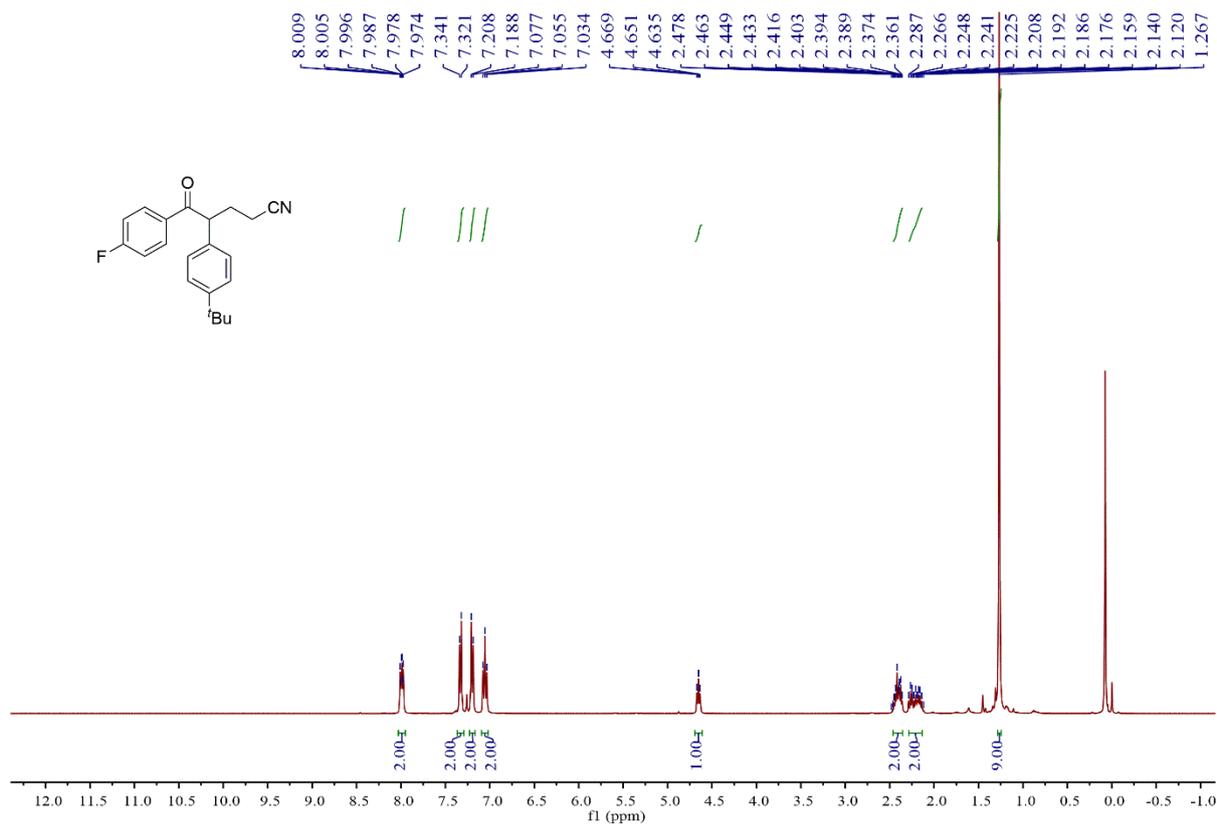


¹H NMR Spectrum of Compound 30a (400 MHz, CDCl₃)

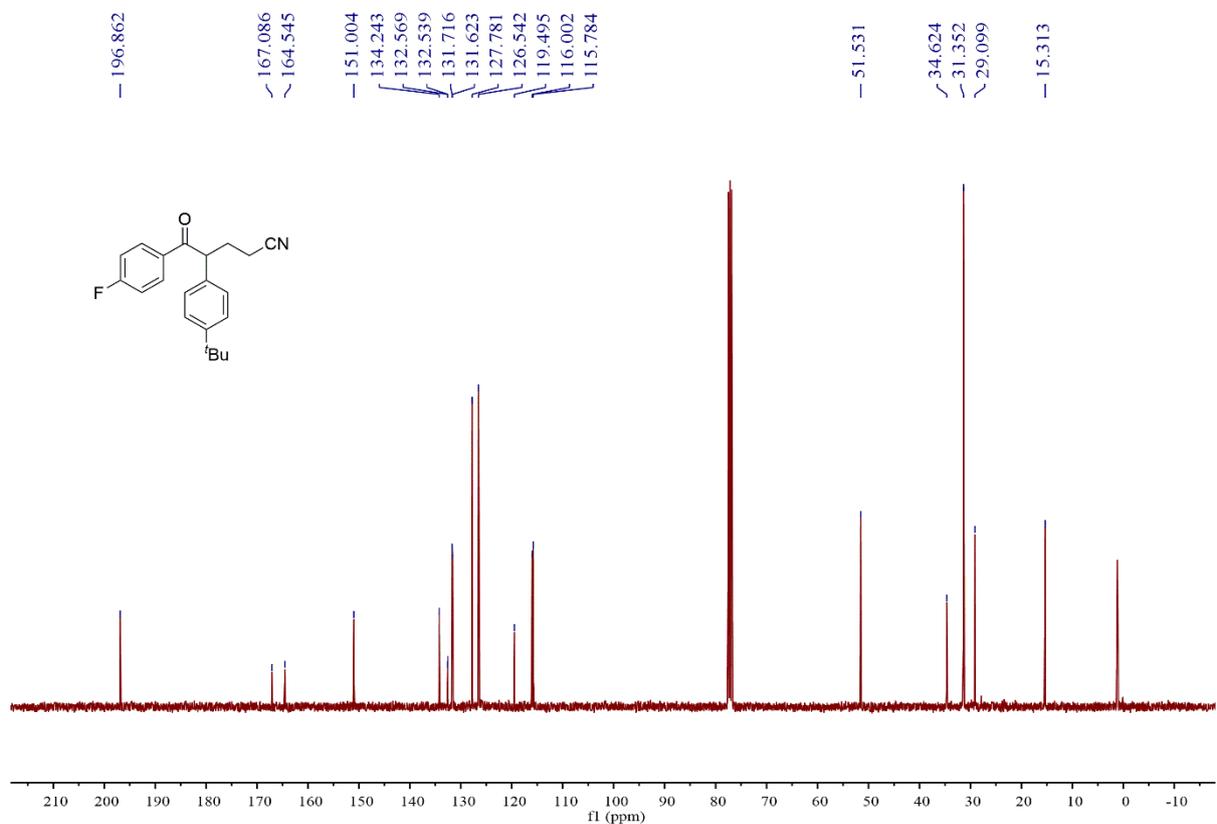


¹³C NMR Spectrum of Compound 30a (100 MHz, CDCl₃)

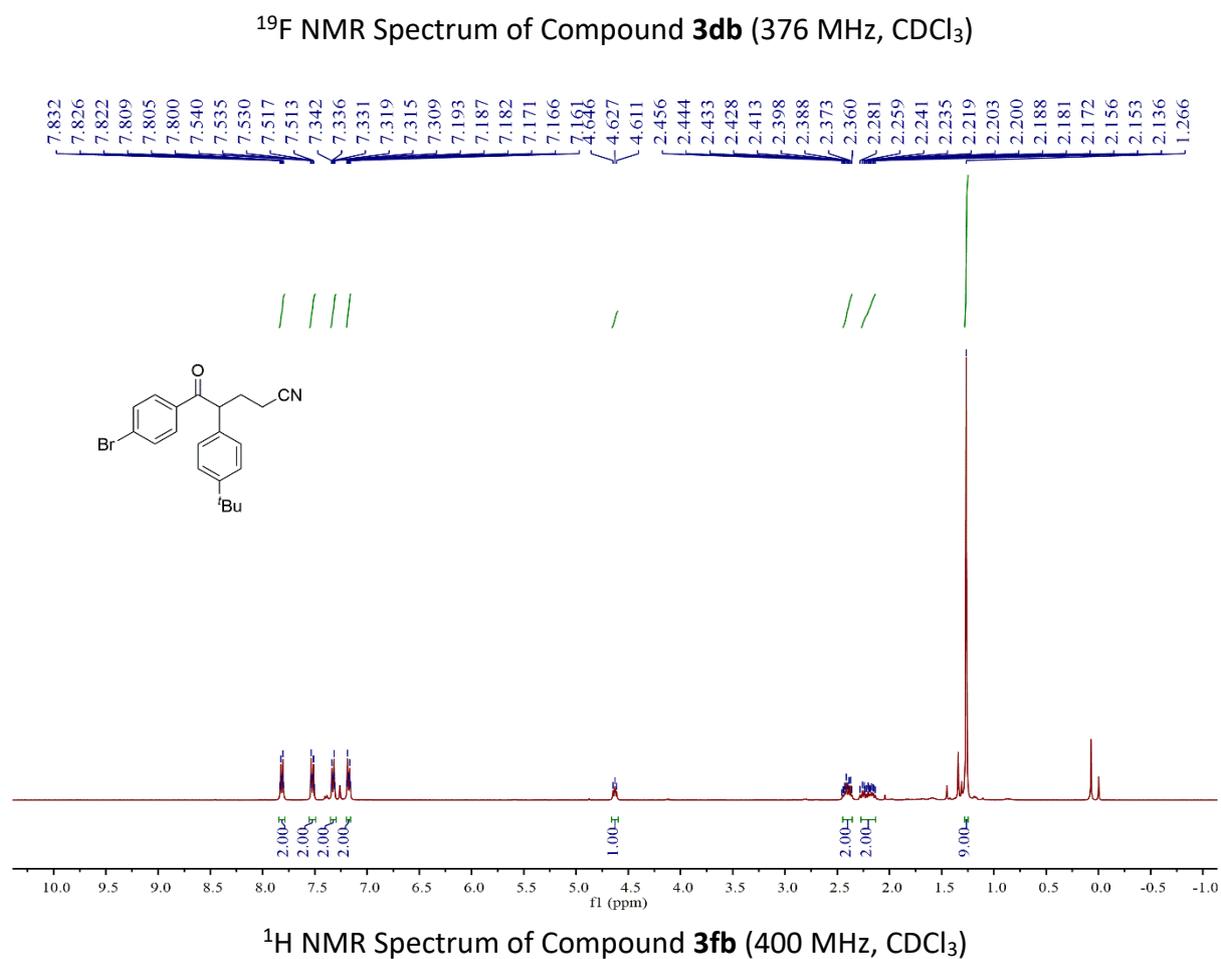
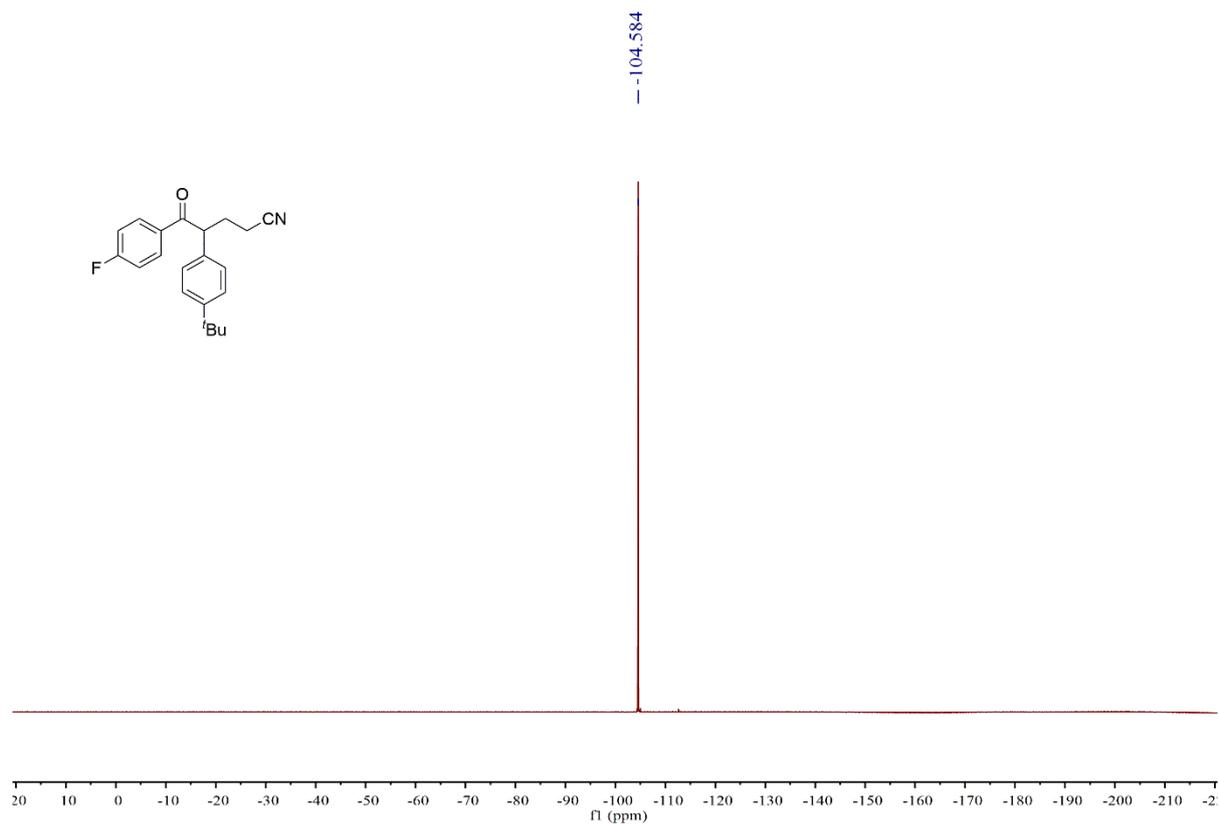


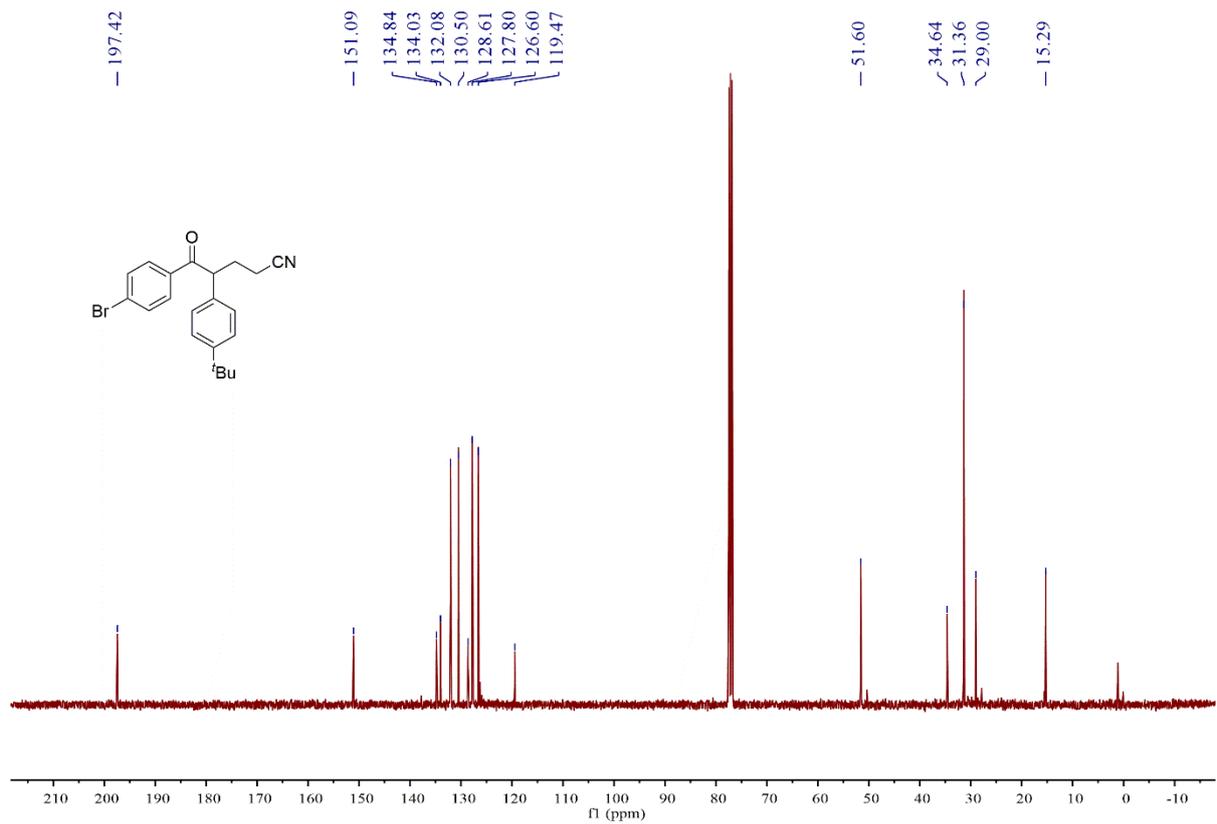


¹H NMR Spectrum of Compound 3db (400 MHz, CDCl₃)

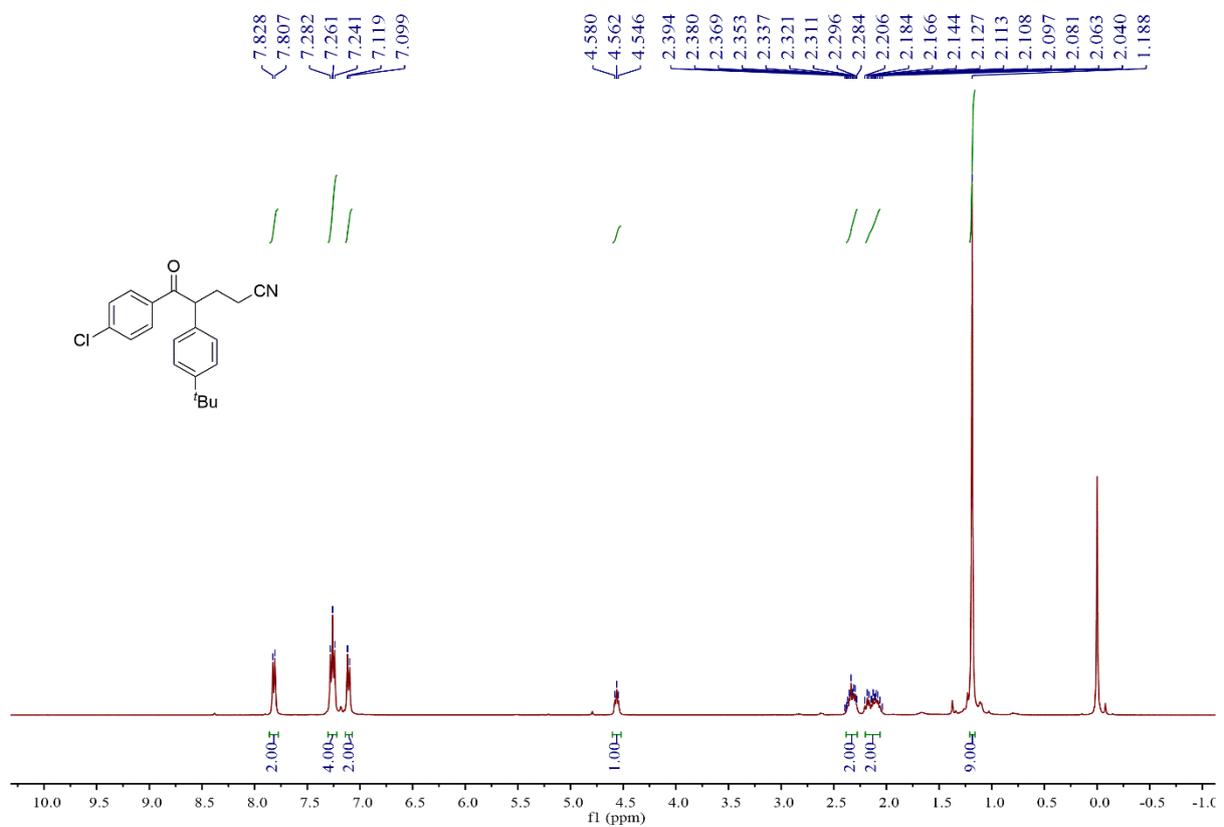


¹³C NMR Spectrum of Compound 3db (100 MHz, CDCl₃)

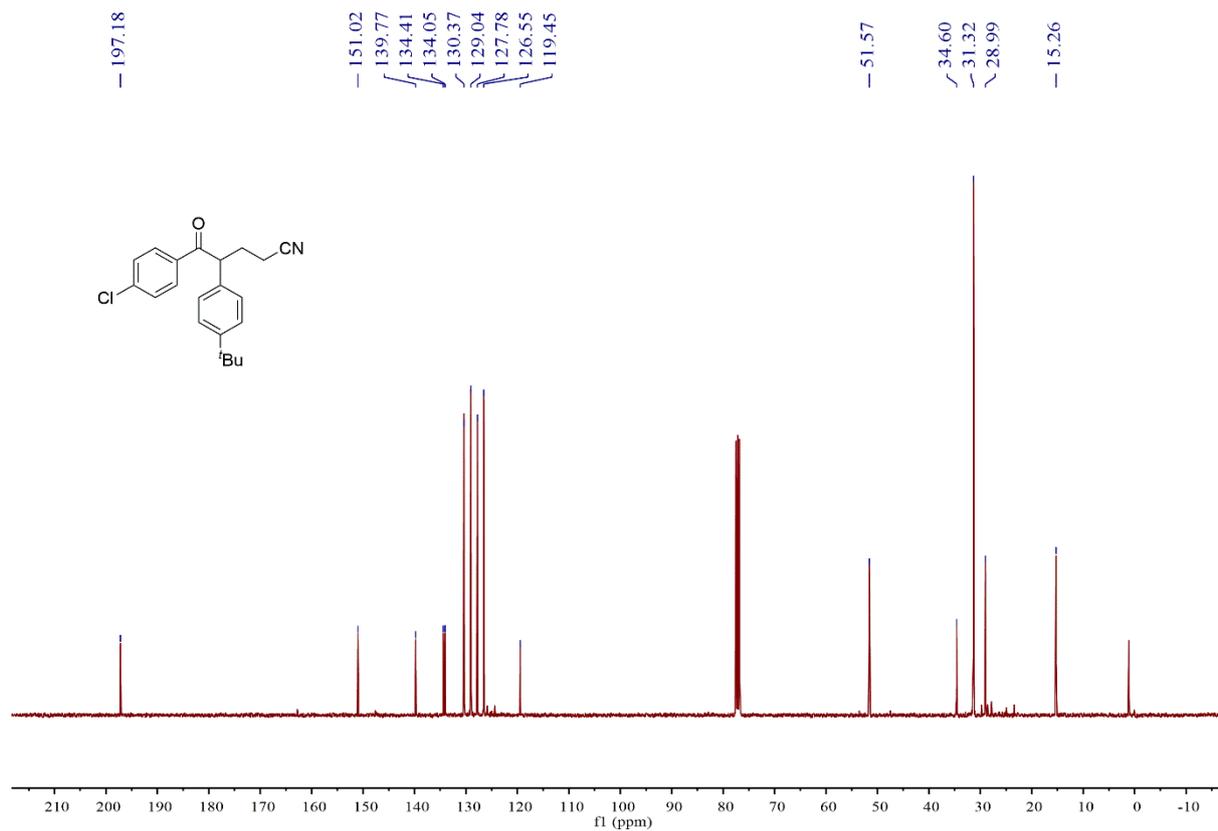




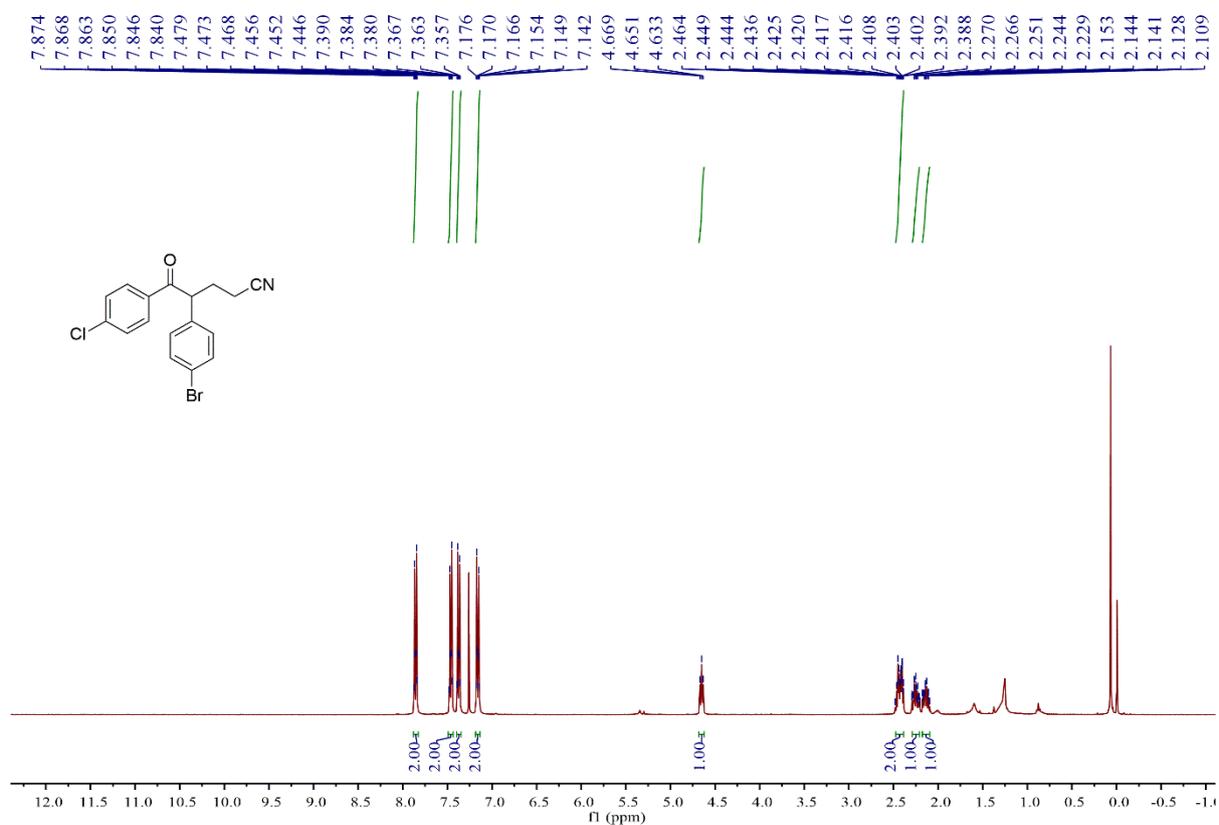
¹³C NMR Spectrum of Compound 3fb (100 MHz, CDCl₃)



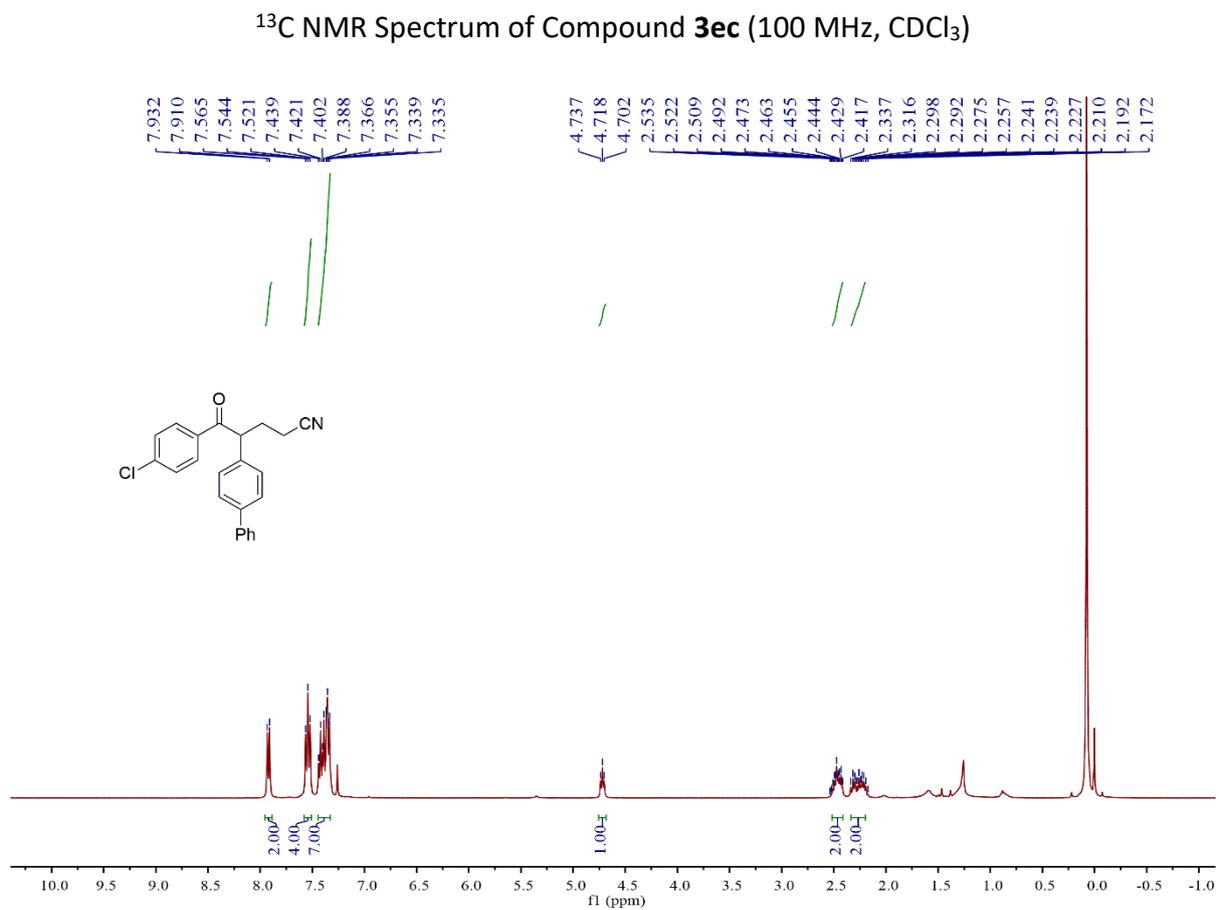
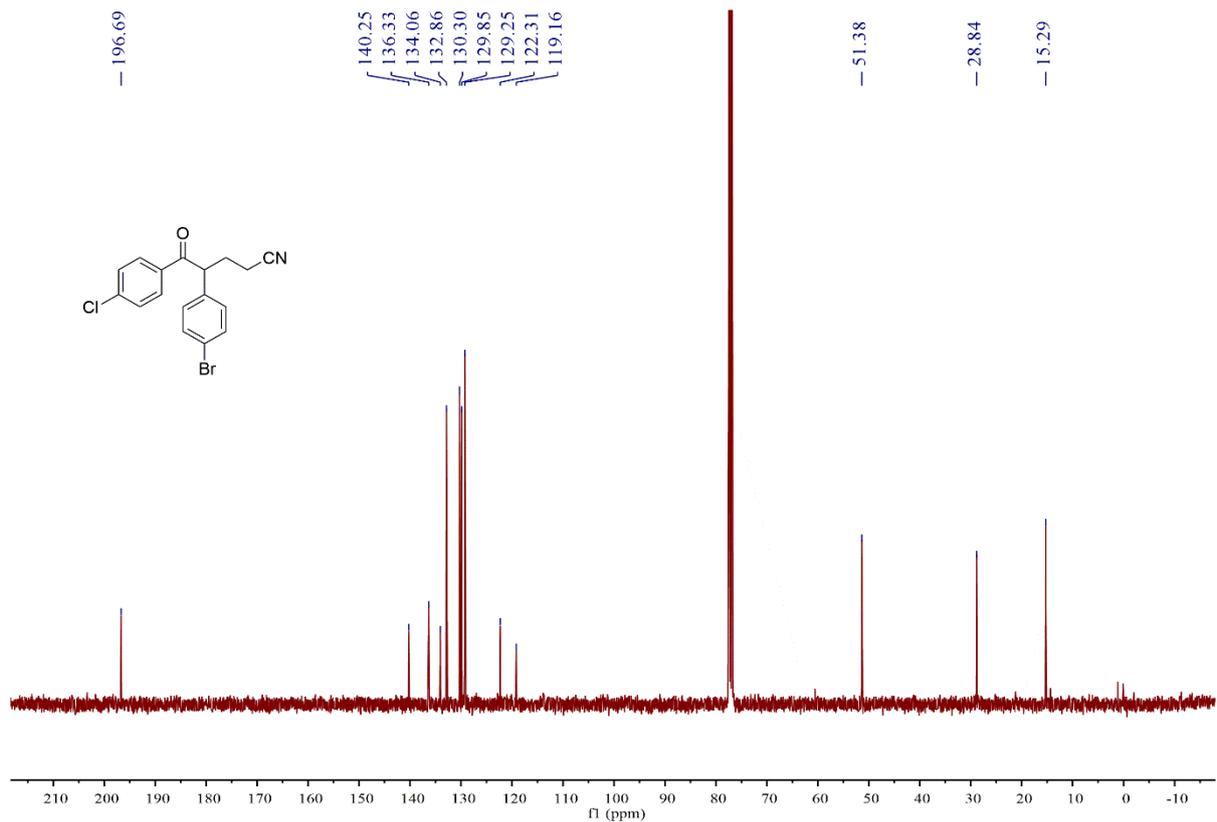
¹H NMR Spectrum of Compound 3eb (400 MHz, CDCl₃)

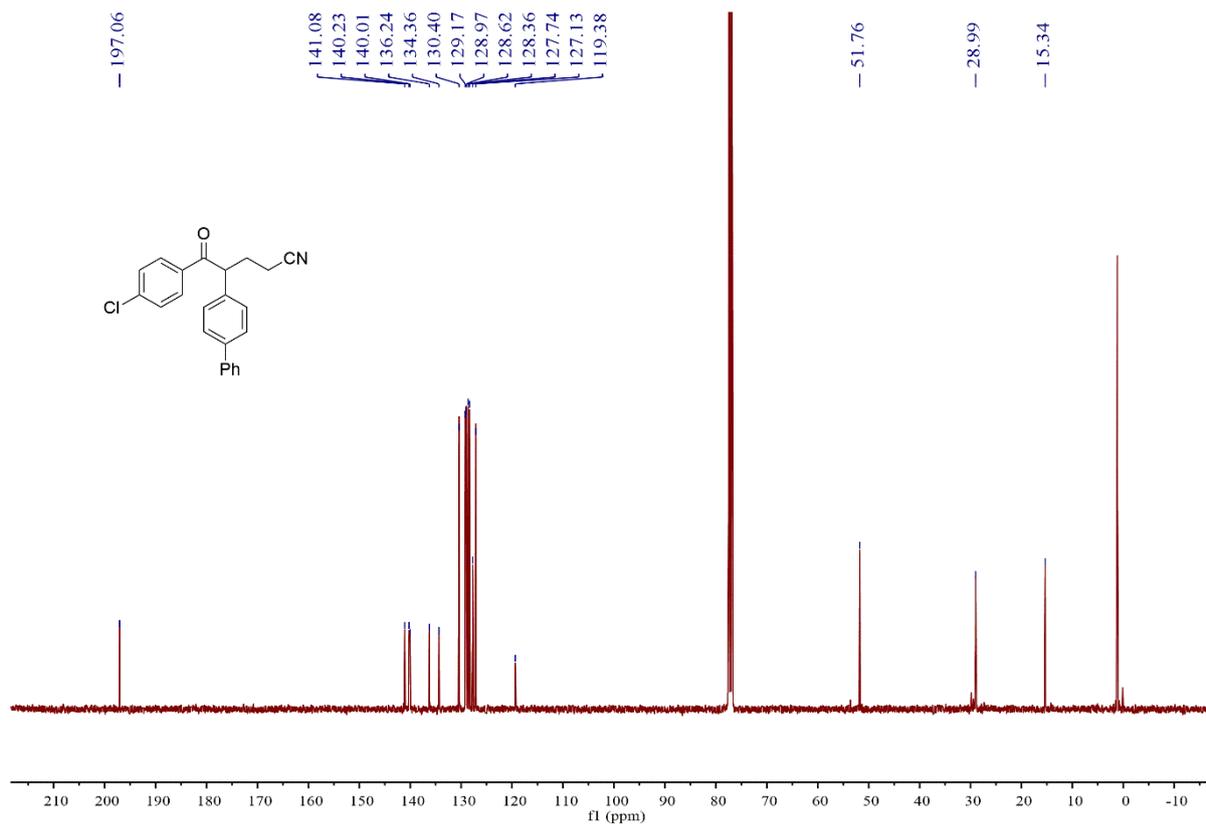


¹³C NMR Spectrum of Compound 3eb (100 MHz, CDCl₃)

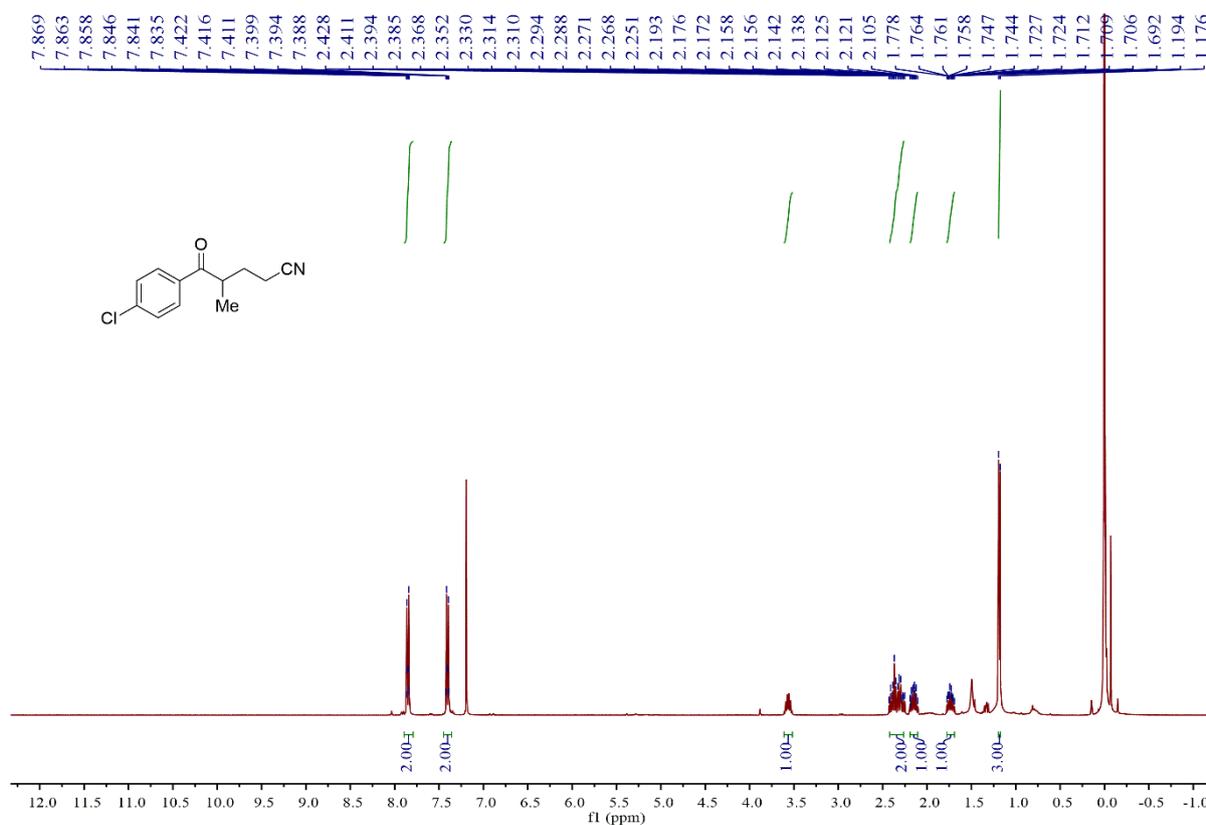


¹H NMR Spectrum of Compound 3ec (400 MHz, CDCl₃)

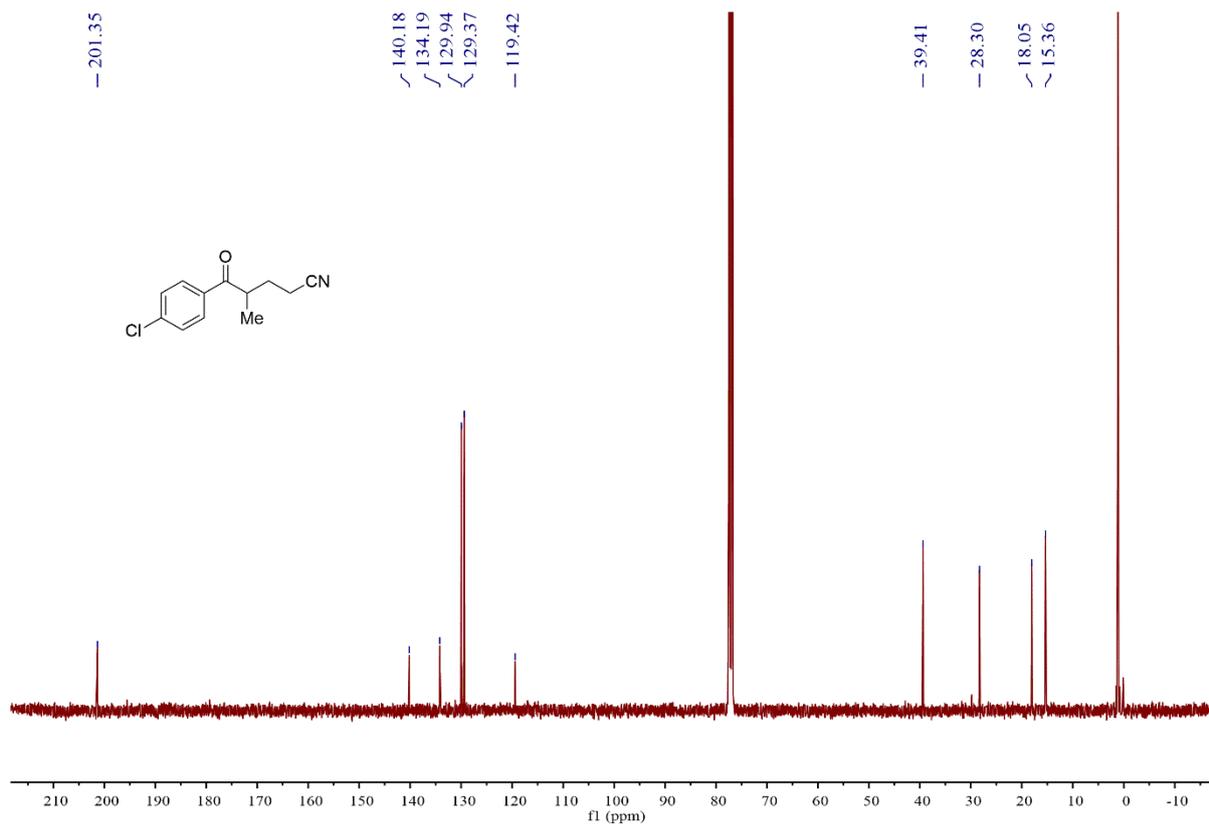




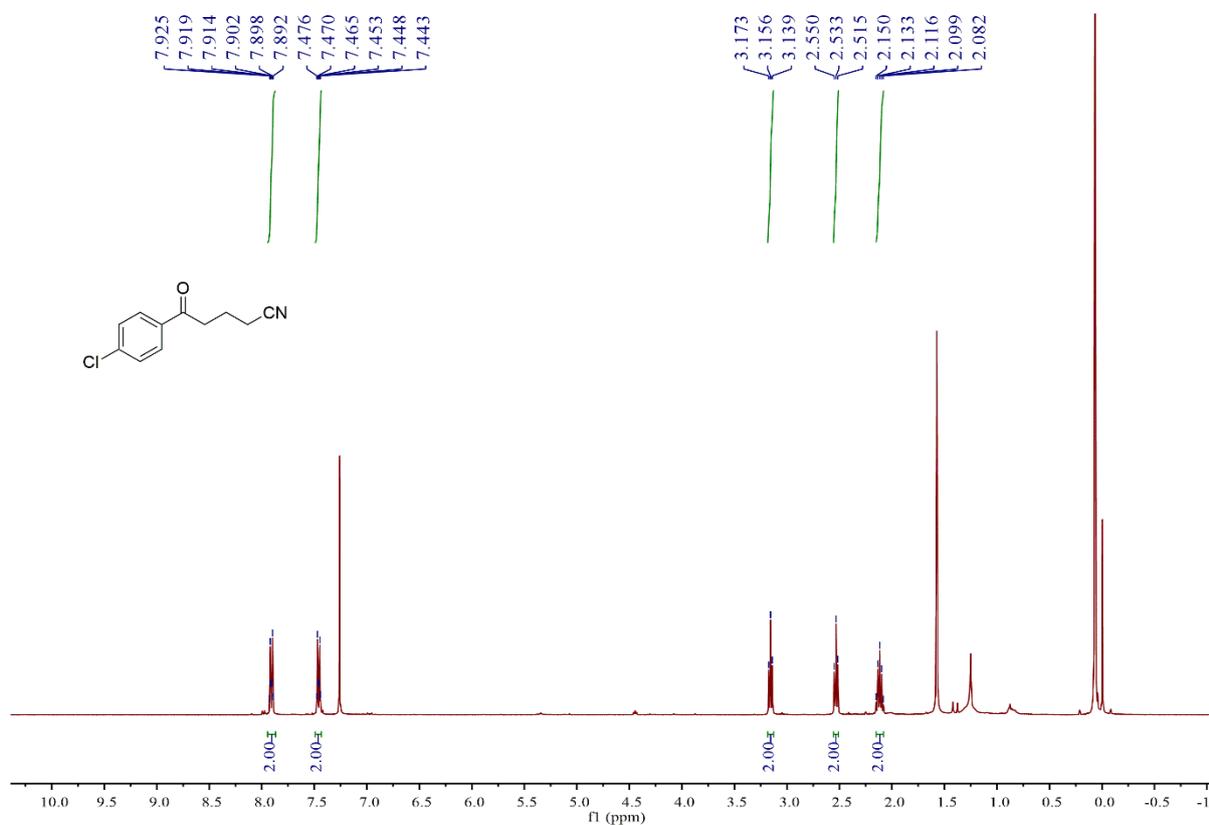
^{13}C NMR Spectrum of Compound 3ed (100 MHz, CDCl_3)



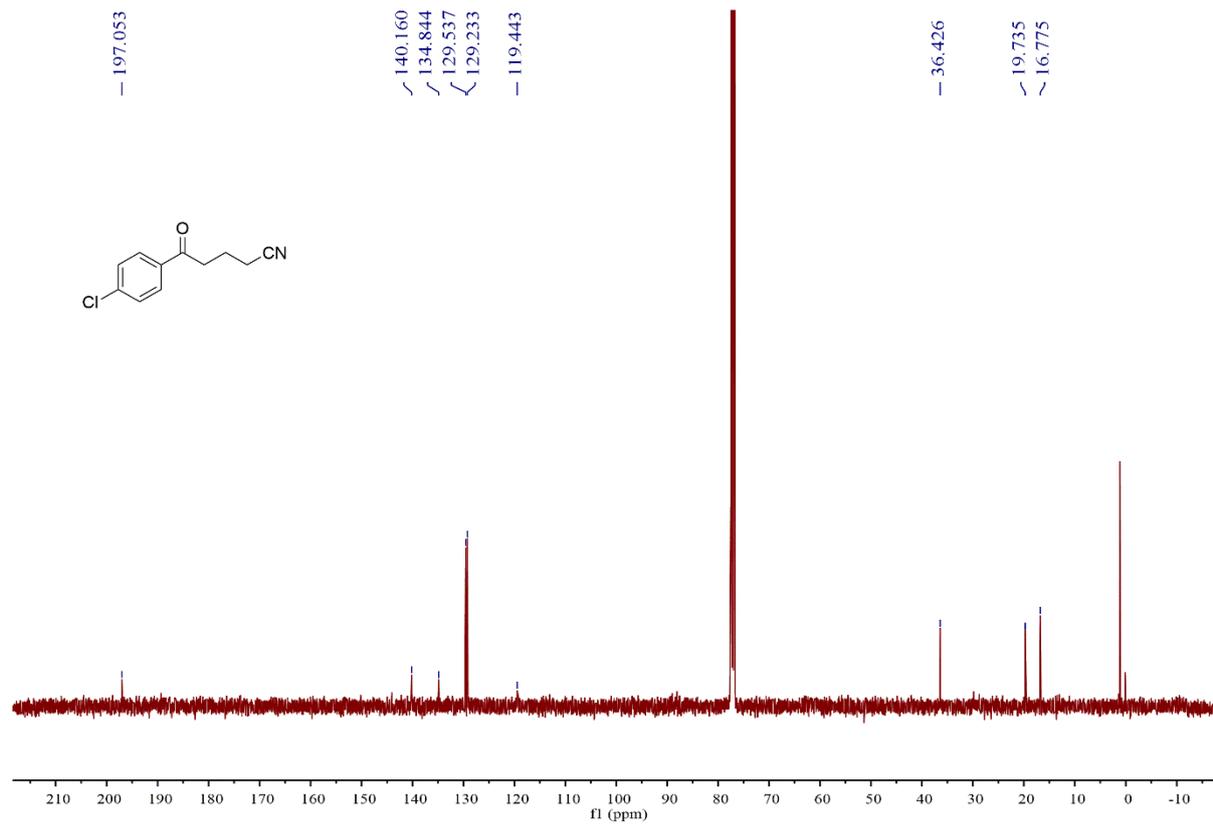
^1H NMR Spectrum of Compound 3ee (400 MHz, CDCl_3)



^{13}C NMR Spectrum of Compound 3ee (100 MHz, CDCl_3)



^1H NMR Spectrum of Compound 3ef (400 MHz, CDCl_3)



¹³C NMR Spectrum of Compound **3ef** (100 MHz, CDCl₃)