

Supporting information

Iodine-TBHP Mediated Efficient Synthesis of α -Ketoamides from Vinyl Azides and Amines under Mild Condition

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Table of contents

1 Experimental Section

1.1 General information.....P2

1.2 Synthesis of azidovinyl benzene.....P2

1.3 General Experimental procedure.....P2

2 Characterization data

2.1. X-ray crystallographic data.....P3

2.2 GC-MS spectra and data.....P4

2.2 ¹H and ¹³C data of the compoundsP7

3 References.....P12

4 Copies of ¹H and ¹³C NMR Spectra.....P14

1. Experimental Section

1.1. General Information

All starting materials and commercial reagent were purchased from Alfa Aesar, Sigma Aldrich, Avra, Spectrochem, TCI. Thin Layer Chromatography plates were visualized by exposure to ultraviolet light (UV) with 254 nm of wavelength and then further analyzed by using iodine chamber. Thin-layer chromatography was performed using pre-coated plates. Column chromatography was performed in 120 to 200 mesh size silica gel. The reactions were carried out in round bottom flask and sealed tube. Crude product was examined by SIMADZU GC-MS (Selected Ion Monitoring) and all NMR spectra were recorded by Bruker Avance 400 spectrometer (^1H at 400 MHz and ^{13}C at 100 MHz). Chemical shifts for ^1H NMR spectra have been reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 : δ 7.26 ppm). Similarly, ^{13}C NMR spectra have been reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (CDCl_3 : δ 77.0 ppm). The ^1H NMR and ^{13}C NMR of the known products were compared with literature reports.

1.2. Synthesis of azidovinyl benzenes 1a-1g:

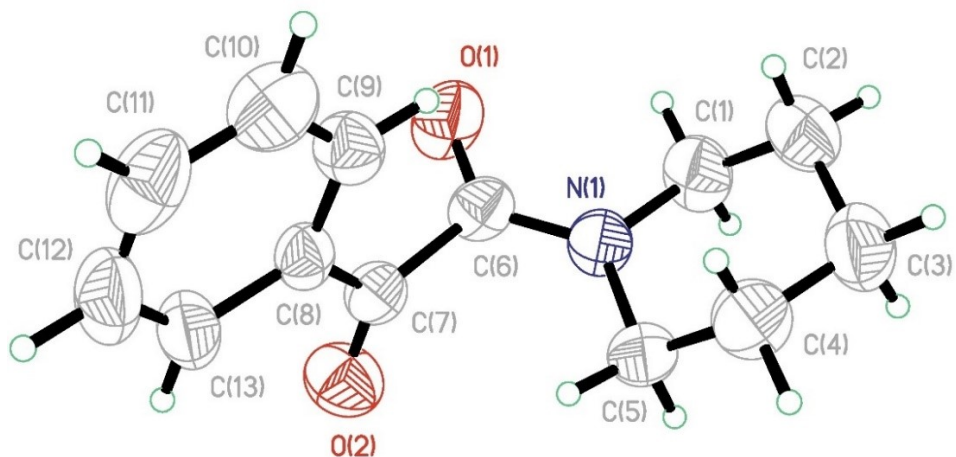
The azidovinyl benzenes (**1a-1g**) were prepared using the literature reports.¹

1.3 General procedure for the synthesis of α -diketoamides (**3a**)

In a 25 mL round bottom flask (1-azidovinyl)benzene 145 mg (1 mmol) was added in a mixture of 2 mL acetonitrile and iodine 50 mg (0.3 mmol) at room temperature. After that piperidine 255 mg (3 mmol) was added dropwise to the stirring reaction mass at 0°C and followed by 30% aqueous solution of *tert*-butyl hydroperoxide 270 mg (3 mmol) was added during a longer period and reaction mixture was stirred in a room temperature for 6 hours. Reaction was monitoring by TLC, after completion of reaction, reaction mass was quenched by saturated aqueous sodium metabisulfite and extracted with EtOAc (3 x 10mL) and combined organic phase was washed with distilled water (2 x 15mL) and dried over anhydrous NaSO_4 followed by concentrating under reduced pressure. Crude product was purified by column chromatography on silica gel (EtOAc: *n*-Hexane ~ 12:88) to afford 186 mg white crystalline solid (86% yield).

2. Characterization data

2.1. X-ray crystallographic data for 3a:



ORTEP diagram for the structure 1-phenyl-2-(piperidin-1-yl)ethane-1,2-dione **3a**

| | |
|----------------------|---|
| Wavelength | 0.71073 |
| Moiety formula | C ₁₃ H ₁₅ NO ₂ |
| Crystal system | Monoclinic |
| Space group | P 21/c |
| Unit cell dimensions | a=9.581(1) b=11.381(1) c=10.941(1) $\alpha=90$ $\beta=103.15(2)$ $\gamma=90$ |
| Volume | 1161.7(2) |
| Z | 4 |
| R-factor (%) | 5.10 |

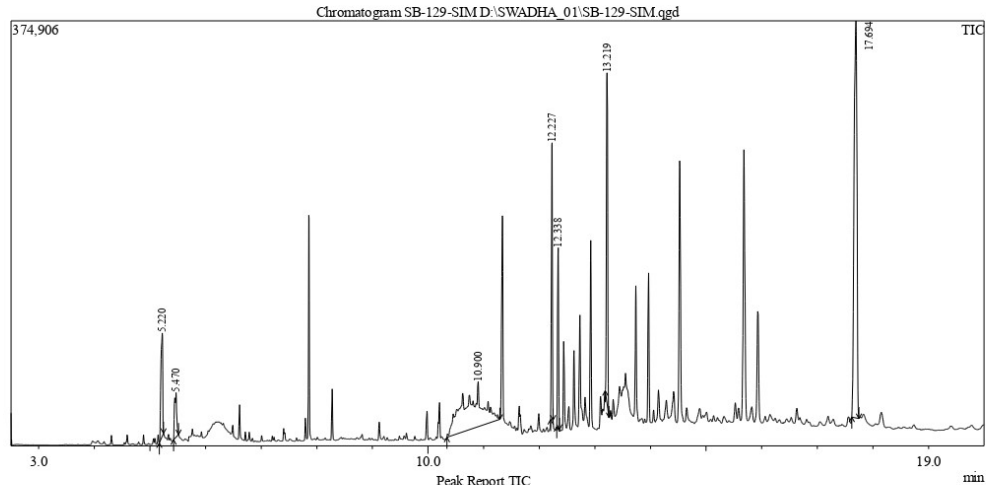
The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with a CCDC reference number **CCDC 2155832**.

2.2. GC-MS spectra and data:

SHIMADZU GC-MS

Test Date : Mar/25/2022 23:39

Sample Information
 Analyzed by : Admin
 Analyzed : 3/25/2022 2:45:45 AM
 Sample Name : SB-129-SIM
 Sample ID : SB-129-SIM
 Vial# : 10
 Injection Volume : 0.50
 Org Data File : D:\SWADHA_01\SB-129-SIM.qgd
 Org Method File : D:\SWADHA_01\EI_METHOD SIM.qgm
 \$EndIf\$Modified by : Admin
 Modified : 3/25/2022 11:07:51 PM



| Peak# | R Time | I Time | F Time | Area | Area% | Height | Height% | A/H | Mark | Name |
|-------|--------|--------|--------|---------|--------|---------|---------|-------|------|------|
| 1 | 5.220 | 5.170 | 5.245 | 214421 | 6.21 | 91175 | 7.50 | 2.35 | MI | |
| 2 | 5.470 | 5.425 | 5.515 | 106434 | 3.08 | 39218 | 3.23 | 2.71 | MI | |
| 3 | 10.900 | 10.340 | 11.290 | 887668 | 25.69 | 39727 | 3.27 | 22.34 | MI | |
| 4 | 12.227 | 12.205 | 12.250 | 312479 | 9.04 | 244354 | 20.11 | 1.28 | MI | |
| 5 | 12.338 | 12.315 | 12.365 | 205911 | 5.96 | 158941 | 13.08 | 1.30 | MI | |
| 6 | 13.219 | 13.185 | 13.255 | 453488 | 13.13 | 291768 | 24.01 | 1.55 | MI | |
| 7 | 17.694 | 17.620 | 17.750 | 1274483 | 36.89 | 350080 | 28.81 | 3.64 | MI | |
| | | | | 3454884 | 100.00 | 1215263 | 100.00 | | | |

Scheme 3



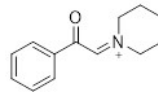
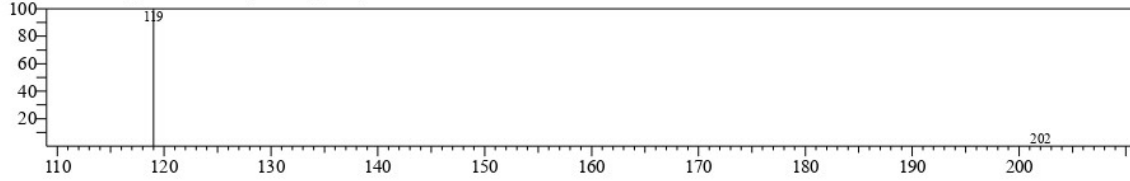
Mol. Wt: 119.1670

<< Intermediate >>

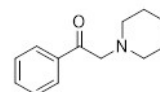
Line# 1 R Time: 5.220(Scan# 545) MassPeaks: 3

RawMode: Averaged 5.215-5.225(544-546) BasePeak: 119.00(87243)

BG Mode: Averaged 5.245-5.255(550-552) Group 1 - Event 1 SIM



Mol. Wt: 202.2765



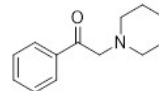
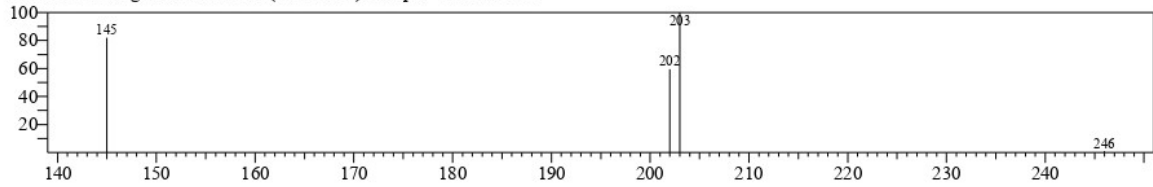
Mol. Wt: 203.2850

<< Intermediate >>

Line# 3 R Time: 10.900(Scan# 1681) MassPeaks: 4

RawMode: Averaged 10.895-10.905(1680-1682) BasePeak: 203.00(12803)

BG Mode: Averaged 11.290-11.300(1759-1761) Group 1 - Event 1 SIM



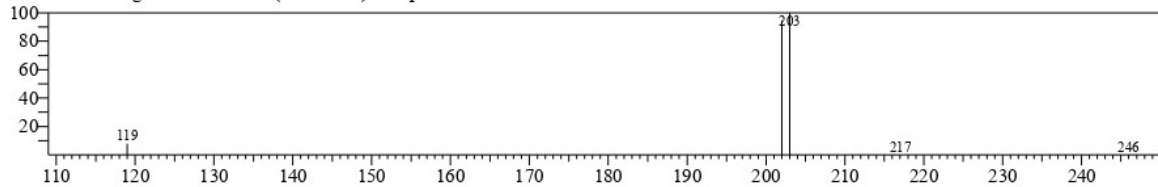
Mol. Wt: 203.2850

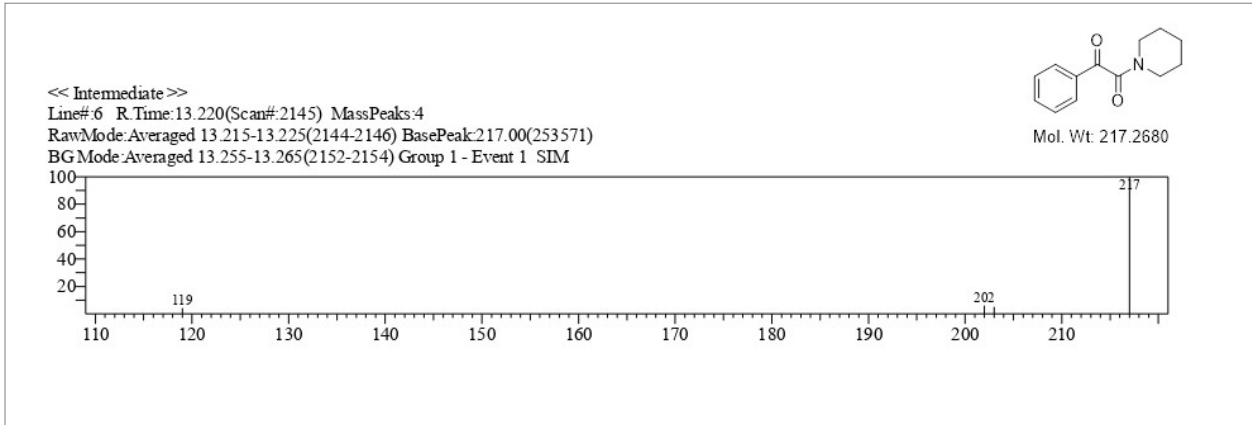
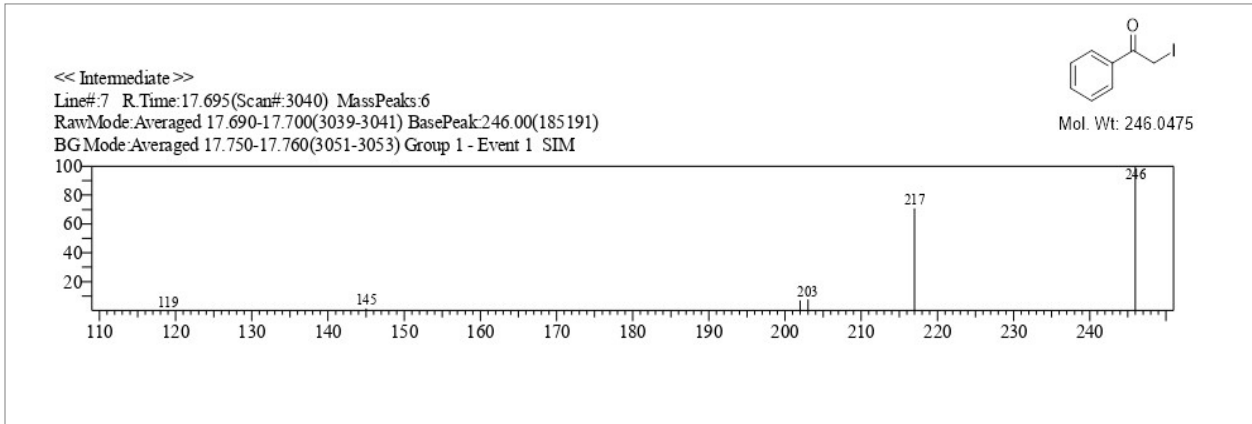
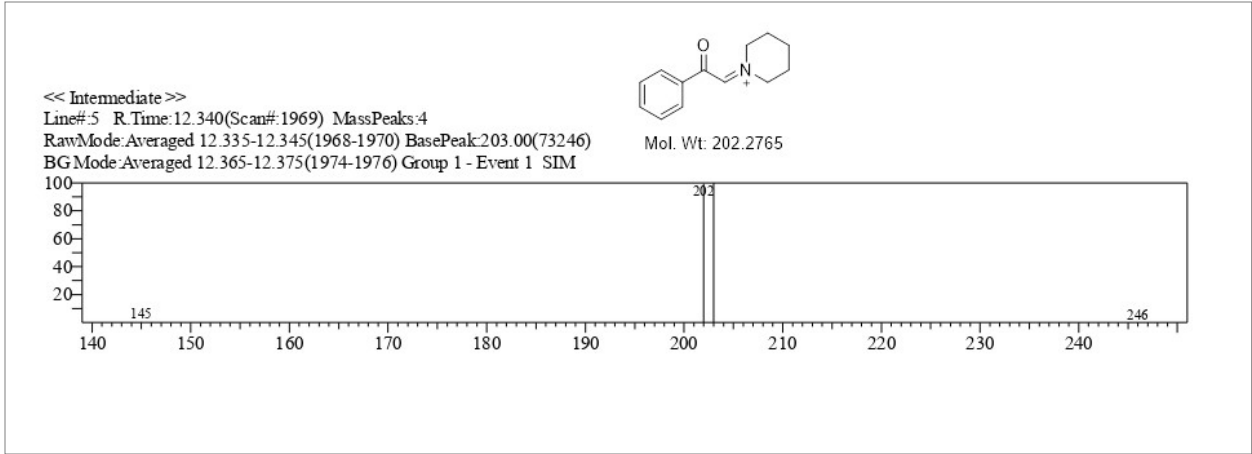
<< Intermediate >>

Line# 4 R Time: 12.225(Scan# 1946) MassPeaks: 5

RawMode: Averaged 12.220-12.230(1945-1947) BasePeak: 203.00(110996)

BG Mode: Averaged 12.250-12.260(1951-1953) Group 1 - Event 1 SIM





2.3. ¹H and ¹³C data of compounds:

1-phenyl-2-(piperidin-1-yl) ethane-1,2-dione (3a)²

White crystalline solid (86%, 186 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.90 – 7.84 (m, 2H), 7.59 – 7.52 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 3.62 (d, *J* = 5.0 Hz, 2H), 3.24 – 3.18 (m, 2H), 1.65 – 1.58 (m, 4H), 1.50 – 1.43 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 191.97, 165.45, 134.66, 133.26, 129.55, 129.15, 129.01, 47.03, 42.14, 26.20, 25.45, 24.37

1-(piperidin-1-yl)-2-(p-tolyl) ethane-1,2-dione (3b)³

Yellow liquid (73%, 168 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 3.60 (d, *J* = 4.8 Hz, 2H), 3.21 – 3.17 (m, 2H), 2.34 (s, 3H), 1.62 – 1.58 (m, 4H), 1.45 (d, *J* = 5.2 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 191.70, 165.65, 145.86, 130.86, 129.70, 129.64, 128.96, 126.90, 47.00, 42.06, 26.17, 25.43, 24.36, 21.84.

1-(2-methoxyphenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3c)⁴ Colourless viscous liquid (65%, 160 mg) ¹H NMR (400 MHz, CDCl₃) δ 7.87 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.54 – 7.44 (m, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 3.81 (s, 3H), 3.61 – 3.54 (m, 2H), 3.29 – 3.22 (m, 2H), 1.63 – 1.49 (m, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 190.70, 167.19, 160.23, 135.99, 131.20, 123.59, 121.26, 112.19, 56.09, 46.71, 41.92, 25.59, 25.32, 24.54.

1-(4-methoxyphenyl)-2-(piperidin-1-yl)ethane-1,2-dione (3d)⁵

Yellow solid (68%, 167 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.80 (m, 2H), 6.92 – 6.87 (m, 2H), 3.80 (s, 3H), 3.61 (d, *J* = 5.0 Hz, 2H), 3.23 – 3.17 (m, 2H), 1.64 – 1.56 (m, 4H), 1.49 – 1.42 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 190.68, 165.79, 164.80, 131.96, 126.33, 114.31, 55.63, 47.04, 42.05, 26.21, 25.45, 24.37

1-(4-chlorophenyl)-2-(piperidin-1-yl) ethane-1,2-dione (3e)⁶

White solid (82%, 205 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 3.69 (d, *J* = 5.1 Hz, 2H), 3.29 – 3.24 (m, 2H), 1.68 (d, *J* = 2.7 Hz, 4H), 1.53 (d, *J* = 3.8 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 190.56, 164.94, 141.28, 131.64, 130.94, 129.42, 47.07, 42.26, 26.25, 25.77, 25.44, 24.34

1-(3-bromophenyl)-2-(piperidin-1-yl) ethane-1,2-dione (3f)³

Yellow solid (80%, 236 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.01 (t, *J* = 1.7 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.68 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 3.62 (t, *J* = 4.9 Hz, 2H), 3.24 – 3.17 (m, 2H), 1.67 – 1.58 (m, 4H), 1.53 – 1.44 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 190.31, 164.65, 137.45, 135.06, 132.22, 130.59, 128.24, 123.27, 47.07, 42.30, 26.23, 25.45, 24.49, 24.34.

1-(4-nitrophenyl)-2-(piperidin-1-yl) ethane-1,2-dione (3g)⁷

Reddish viscous liquid (79%, 206 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.68 (t, *J* = 1.8 Hz, 1H), 8.41 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.24 – 8.17 (m, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 3.66 (d, *J* = 5.1 Hz, 2H), 3.29 – 3.23 (m, 2H), 1.70 – 1.61 (m, 4H), 1.55 – 1.50 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 189.05, 164.00, 148.60, 135.04, 134.74, 130.36, 128.62, 124.27, 47.13, 42.52, 26.30, 25.46, 24.29

1-(piperidin-1-yl)-2-(thiophen-2-yl)ethane-1,2-dione (3h)⁸

Reddish viscous liquid (73%, 162 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.76 (m, 2H), 7.17 (dd, *J* = 4.8, 4.0 Hz, 1H), 3.67 (t, *J* = 5.3 Hz, 2H), 3.39 – 3.35 (m, 2H), 1.72 – 1.64 (m, 4H), 1.57 (dt, *J* = 10.9, 5.5 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 183.93, 164.50, 140.66, 136.21, 135.86, 128.60, 47.22, 42.50, 26.31, 25.47, 24.39

1-morpholino-2-phenylethane-1,2-dione (3i)³

Reddish viscous liquid (81%, 177 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, *J* = 7.8 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 3.79 (s, 4H), 3.67 – 3.64 (m, 2H), 3.40 – 3.36 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 191.20, 165.47, 135.01, 133.02, 129.70, 129.14, 66.75, 66.68, 46.27, 41.63

1-(4-methoxyphenyl)-2-morpholinoethane-1,2-dione (3j)⁸

Reddish viscous liquid (65%, 168 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.88 – 7.81 (m, 2H), 6.92 – 6.88 (m, 2H), 3.81 (s, 3H), 3.70 (s, 4H), 3.59 – 3.55 (m, 2H), 3.33 – 3.28 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 189.82, 165.04, 132.14, 126.14, 125.23, 114.43, 66.77, 66.67, 55.67, 55.57, 46.30, 41.56

1-(4-chlorophenyl)-2-morpholinoethane-1,2-dione (3k)²

Reddish viscous liquid (75%, 189 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.86 – 7.81 (m, 1H), 7.45 – 7.40 (m, 1H), 3.75 – 3.68 (m, 2H), 3.61 – 3.56 (m, 1H), 3.34 – 3.28 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 189.70, 164.91, 141.61, 131.49, 131.05, 129.51, 66.74, 66.65, 46.30, 41.72

1-morpholino-2-(3-nitrophenyl)ethane-1,2-dione (3l)⁹

Reddish viscous liquid (77%, 203 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.80 (d, *J* = 1.5 Hz, 1H), 8.53 – 8.48 (m, 1H), 8.32 (d, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 1H), 3.83 (s, 4H), 3.72 – 3.69 (m, 2H), 3.46 – 3.43 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 188.15, 163.90, 148.63, 135.16, 134.55, 130.39, 128.90, 124.58, 66.76, 66.66, 46.39, 42.00

1-morpholino-2-(thiophen-2-yl) ethane-1,2-dione (3m)²

Reddish viscous liquid (71%, 159 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.75 (t, *J* = 4.3 Hz, 2H), 7.13 – 7.10 (m, 1H), 3.70 – 3.66 (m, 4H), 3.60 – 3.57 (m, 2H), 3.42 – 3.38 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 182.89, 164.33, 140.21, 136.88, 136.34, 128.79, 66.75, 66.57, 46.40, 41.89

1-phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (3n)⁶

Reddish viscous liquid (83%, 168 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.93 – 7.89 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 3.57 (t, *J* = 6.7 Hz, 2H), 3.34 (t, *J* = 6.4 Hz, 2H), 1.90 – 1.83 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 191.60, 164.95, 134.62, 132.90, 129.87, 128.94, 46.67, 45.24, 25.89, 24.01

1-(pyrrolidin-1-yl)-2-(p-tolyl) ethane-1,2-dione (3o)³

Reddish viscous liquid (72%, 156 mg) ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 3.54 (t, *J* = 6.7 Hz, 2H), 3.30 (t, *J* = 6.4 Hz, 2H), 2.32 (s, 3H), 1.88 – 1.79 (m, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 191.33, 165.19, 145.80, 130.44, 129.89, 129.63, 46.60, 45.12, 25.82, 23.96, 21.80

1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3p)⁸

Reddish viscous liquid (70%, 163 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.87 (m, 2H), 6.92 – 6.87 (m, 2H), 3.81 (s, 3H), 3.57 (t, *J* = 6.7 Hz, 2H), 3.34 (t, *J* = 6.4 Hz, 2H), 1.92 – 1.82 (m,

4H); ^{13}C NMR (101 MHz, CDCl_3) δ 190.30, 165.33, 164.78, 132.36, 126.01, 114.26, 55.63, 46.70, 45.19, 25.91, 24.04

2-(4-fluorophenyl)-1-(pyrrolidin-1-yl) ethan-1-one (3q)¹⁰

Reddish viscous liquid (79%, 174 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.02 – 7.95 (m, 1H), 7.13 – 7.07 (m, 1H), 3.58 (t, $J = 6.9$ Hz, 1H), 3.37 (t, $J = 6.6$ Hz, 1H), 1.93 – 1.85 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 189.77, 166.6 (d, $J = 256$ Hz), 165.37, 164.49, 132.79 (d, $J = 9.7$ Hz), 129.52, 116.34, 116.12, 46.78, 45.39, 25.95, 24.00

1-(4-chlorophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (3r)²

Reddish viscous liquid (76%, 180 mg); ^1H NMR (400 MHz, CDCl_3) δ 7.89 – 7.85 (m, 1H), 7.41 – 7.38 (m, 1H), 3.56 (dd, $J = 8.4, 5.6$ Hz, 1H), 3.35 (dd, $J = 8.2, 5.3$ Hz, 1H), 1.90 – 1.84 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 190.07, 164.25, 141.14, 131.41, 131.29, 129.27, 46.74, 45.37, 25.91, 23.96

1-(3-nitrophenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3s)²

Reddish viscous liquid (74%, 208 mg); ^1H NMR (400 MHz, CDCl_3) δ 8.77 (t, $J = 1.8$ Hz, 1H), 8.39 (dd, $J = 8.2, 2.2$ Hz, 1H), 8.30 (d, $J = 7.8$ Hz, 1H), 7.65 (t, $J = 8.0$ Hz, 1H), 3.60 (dd, $J = 8.9, 5.0$ Hz, 2H), 3.45 (dd, $J = 8.8, 4.6$ Hz, 2H), 1.96 – 1.89 (m, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 188.53, 163.08, 148.59, 135.58, 134.69, 130.21, 128.55, 124.86, 47.03, 45.80, 26.06, 23.99

1-(3-bromophenyl)-2-(pyrrolidin-1-yl) ethane-1,2-dione (3t)³

Reddish viscous liquid (81%, 200 mg) ^1H NMR (400 MHz, CDCl_3) δ 8.07 (t, $J = 1.7$ Hz, 1H), 7.89 – 7.84 (m, 1H), 7.68 (ddd, $J = 8.0, 1.9, 1.0$ Hz, 1H), 7.31 (t, $J = 7.9$ Hz, 1H), 3.58 (t, $J = 6.9$ Hz, 2H), 3.37 (t, $J = 6.7$ Hz, 2H), 1.94 – 1.85 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 189.82, 163.98, 137.39, 134.83, 132.65, 130.48, 128.58, 123.16, 46.79, 45.46, 25.94, 23.98

1-(pyrrolidin-1-yl)-2-(thiophen-2-yl) ethane-1,2-dione (3u)¹¹

Reddish viscous liquid (72%, 150 mg); ^1H NMR (400 MHz, CDCl_3) δ 7.90 (dd, $J = 3.9, 1.2$ Hz, 1H), 7.70 (dd, $J = 4.9, 1.2$ Hz, 1H), 7.10 (dd, $J = 4.9, 3.9$ Hz, 1H), 3.60 – 3.50 (m, 4H), 1.93 –

1.82 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 182.64, 163.06, 139.88, 136.62, 136.46, 128.41, 47.3, 46.06, 26.17, 23.87

1-(4-(1H-benzo[d]imidazol-2-yl)piperidin-1-yl)-2-(3-nitrophenyl)ethane-1,2-dione (3v)

White solid (78%, 294 mg, mp: 228-232 °C); ¹H NMR (400 MHz, DMSO) δ 12.27 (s, 1H), 8.60 (d, *J* = 7.0 Hz, 2H), 8.34 (d, *J* = 7.8 Hz, 1H), 7.94 (t, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.13 (p, *J* = 6.1 Hz, 2H), 4.46 (d, *J* = 13.2 Hz, 1H), 3.64 (d, *J* = 13.7 Hz, 1H), 3.24 (ddd, *J* = 15.0, 12.2, 5.1 Hz, 2H), 2.21 (dd, *J* = 13.3, 2.3 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.85 (dtd, *J* = 20.5, 11.5, 6.6 Hz, 2H); ¹³C NMR (100 MHz, DMSO) δ 190.14, 164.17, 157.22, 148.78, 143.39, 135.97, 134.64, 134.25, 131.84, 129.65, 123.77, 122.14, 121.40, 118.83, 111.37, 45.55, 35.70, 30.92, 30.26; HRMS (ESI) calcd for C₂₀H₁₈N₄O₄ [M+H]⁺ 379.1401, found 379.1411

1-(3,4-dihydroisoquinolin-2(1H)-yl)-2-phenylethane-1,2-dione (3w)¹² White solid (71%, 101 mg) ¹H NMR (400 MHz, CDCl₃) δ 8.00 (dd, *J* = 12.9, 7.7 Hz, 2H), 7.66 (dd, *J* = 10.3, 7.7 Hz, 1H), 7.53 (dt, *J* = 13.0, 7.7 Hz, 2H), 7.33 – 7.10 (m, 4H), 4.94 (s, 1H), 4.57 (s, 1H), 4.02 (t, *J* = 6.1 Hz, 1H), 3.65 (t, *J* = 5.9 Hz, 1H), 3.03 (t, *J* = 6.0 Hz, 1H), 2.89 (t, *J* = 5.8 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 191.49 (d, *J* = 14.5 Hz), 166.12, 165.81, 134.88 (d, *J* = 4.2 Hz), 134.22, 133.45, 133.10 (d, *J* = 7.2 Hz), 131.85, 131.57, 129.76 (d, *J* = 1.2 Hz), 129.02 (dd, *J* = 15.6, 9.9 Hz), 127.26, 126.79 (dd, *J* = 20.6, 5.7 Hz), 126.12, 47.37, 43.51 (d, *J* = 8.3 Hz), 39.39, 29.26, 28.29.

N,N-dimethyl-2-oxo-2-phenylacetamide (3x)¹³ Yellow viscous liquid (57%, 101 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 3.04 (s, 3H), 2.89 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 191.84, 167.06, 134.77, 133.03, 129.66, 129.04, 37.06, 34.00.

N,N-diethyl-2-oxo-2-phenylacetamide (3y)¹³ Yellow viscous liquid (61%, 125 mg) ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 3.50 (q, *J* = 7.2 Hz, 2H), 3.18 (q, *J* = 7.1 Hz, 2H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 191.62, 134.60, 133.27, 129.66, 128.98, 42.13, 38.81, 14.13, 12.87.

1-(4-(4-((5-chloro-4-((2-(isopropylsulfonyl)phenyl)amino)pyrimidin-2-yl)amino)-5-isopropoxy-2-methylphenyl)piperidin-1-yl)-2-phenylethane-1,2-dione (3ab) (White solid, 58%, 399 mg) ¹H NMR (400 MHz, CDCl₃) δ 9.65 (s, 1H), 8.57 (d, *J* = 8.3 Hz, 1H), 8.15 (s, 1H), 7.97 (dt, *J* = 42.9, 15.4 Hz, 5H), 7.66 (dt, *J* = 15.4, 7.5 Hz, 2H), 7.32 – 7.28 (m, 1H), 6.74 (s, 1H), 4.89 (d, *J* = 13.0 Hz, 1H), 4.60 (dt, *J* = 11.8, 5.8 Hz, 1H), 3.74 (d, *J* = 13.0 Hz, 1H), 3.31 – 3.20 (m, 2H), 2.96 (dt, *J* = 24.0, 12.0 Hz, 2H), 2.19 (s, 3H), 1.96 (d, *J* = 13.3 Hz, 1H), 1.82 – 1.67 (m, 3H), 1.40 (d, *J* = 2.8 Hz, 6H), 1.34 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 191.88, 165.55, 156.63, 155.57, 153.46, 145.20, 138.13, 136.70, 134.86, 134.66, 133.20, 131.36, 129.68, 129.08, 127.54, 126.78, 125.10, 123.71, 123.53, 121.25, 110.89, 105.85, 71.82, 55.59, 46.97, 42.17, 38.30, 32.84, 32.28, 22.24, 18.98, 15.37; HRMS (ESI) calcd for C₃₆H₄₀ClN₅O₅S [M+H]⁺ 690.2511, found 690.2523.

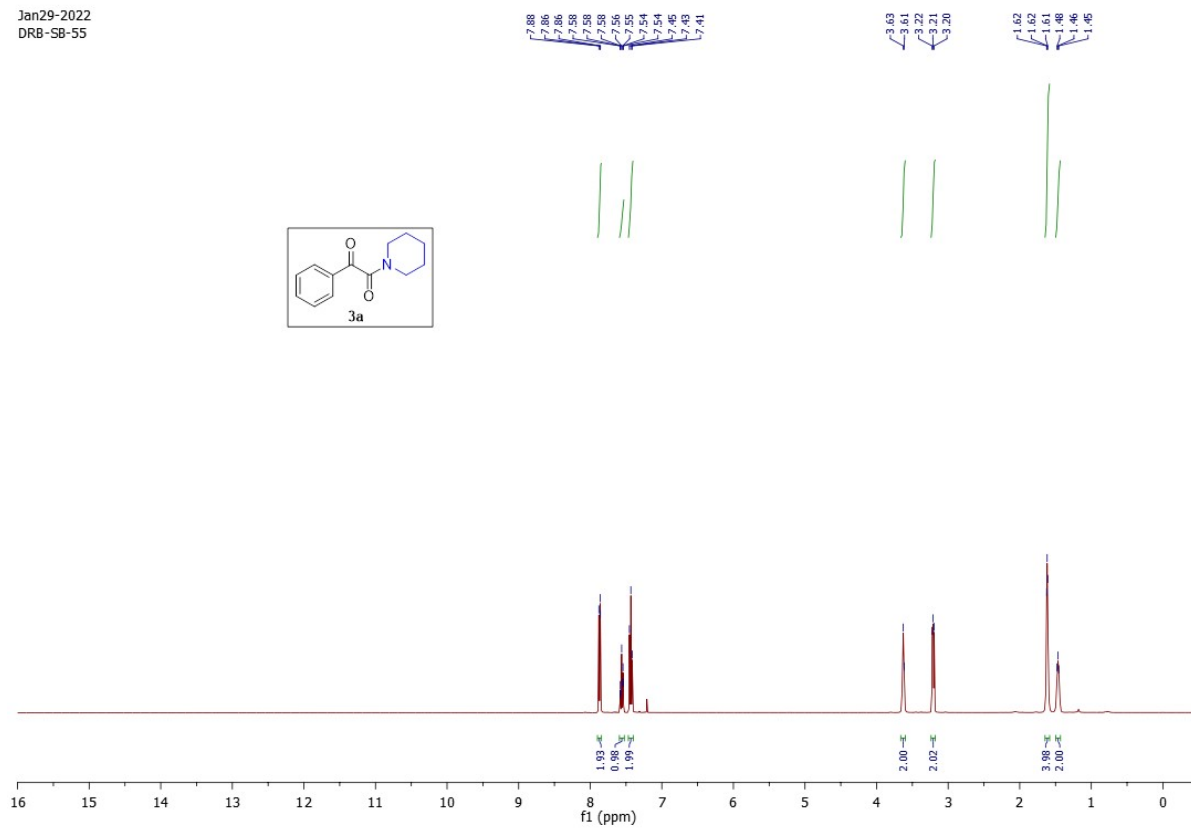
3. References

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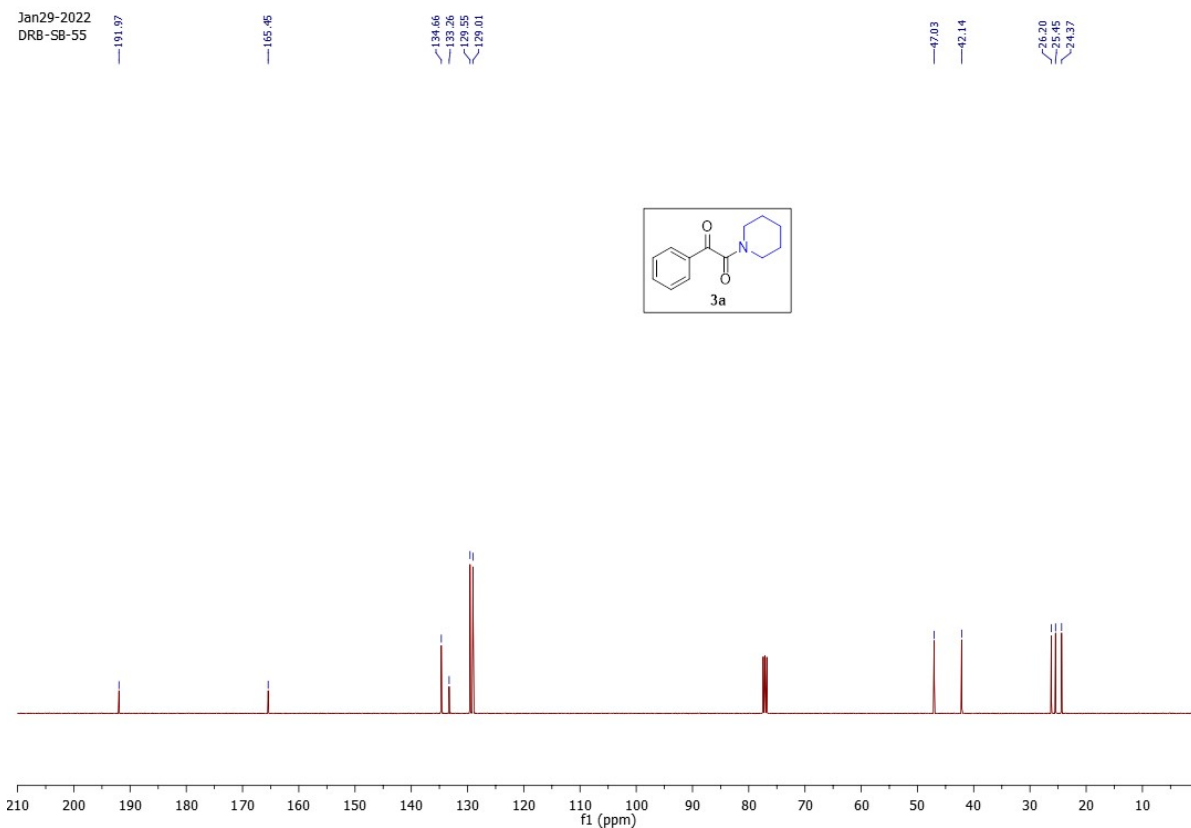
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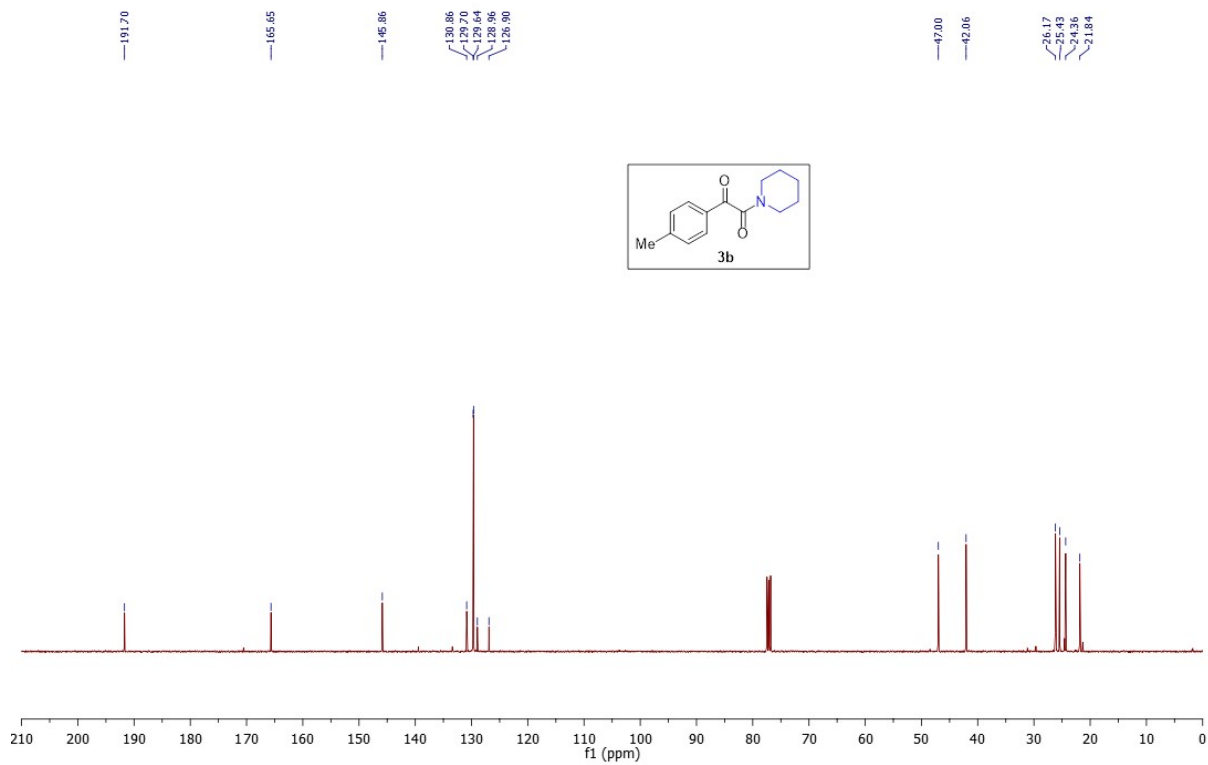
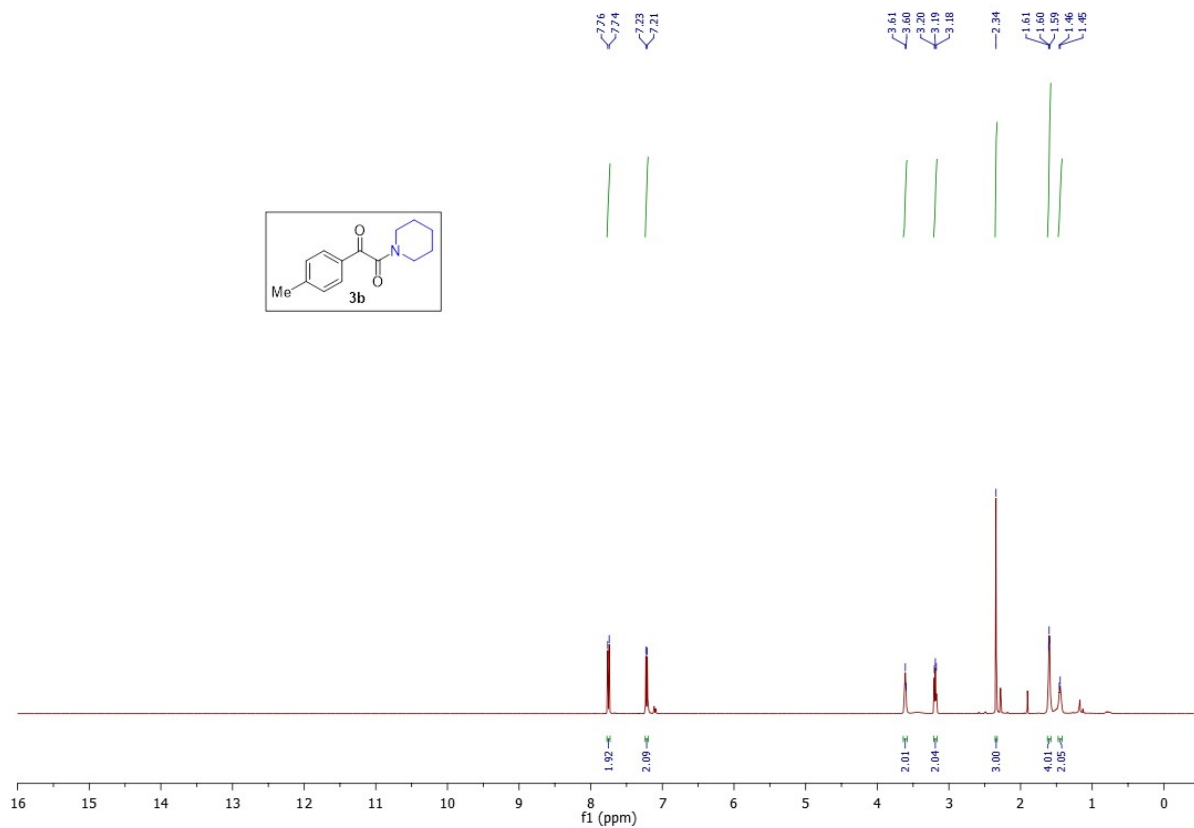
3. ^1H and ^{13}C NMR Spectra of Compounds

Jan29-2022
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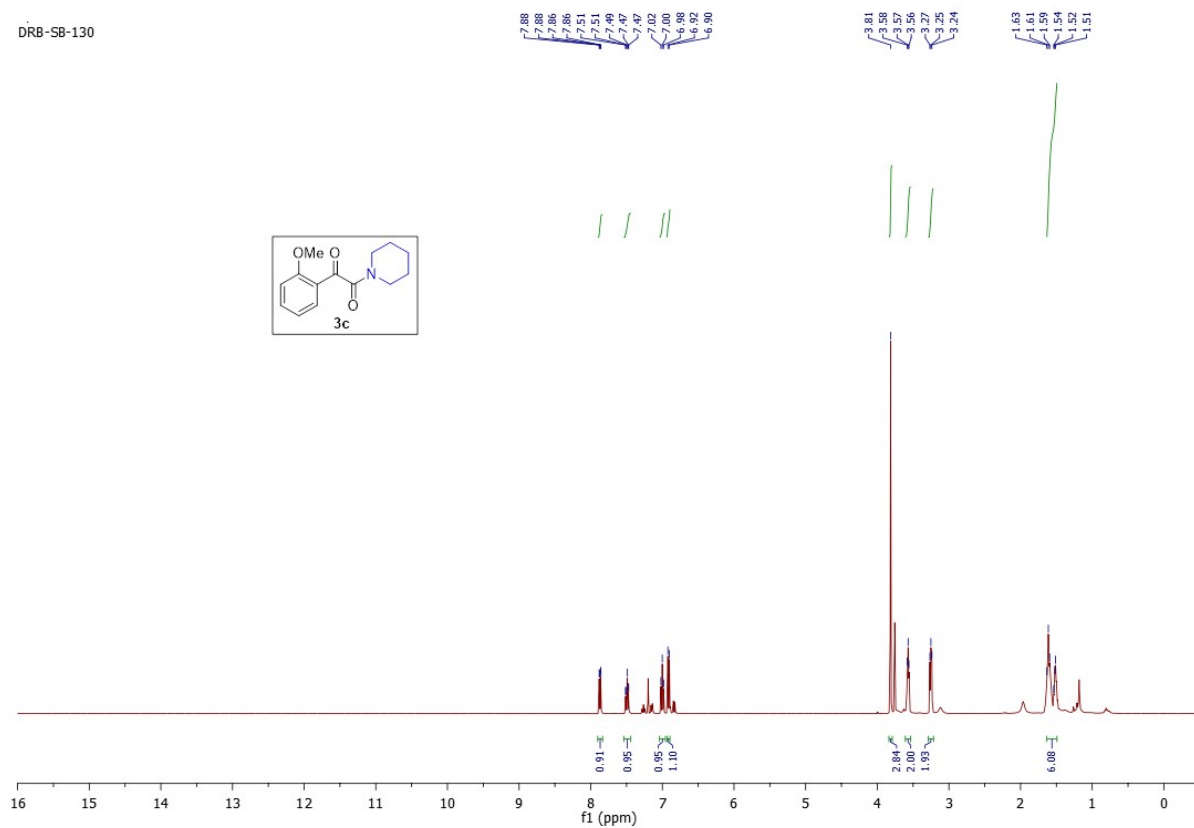


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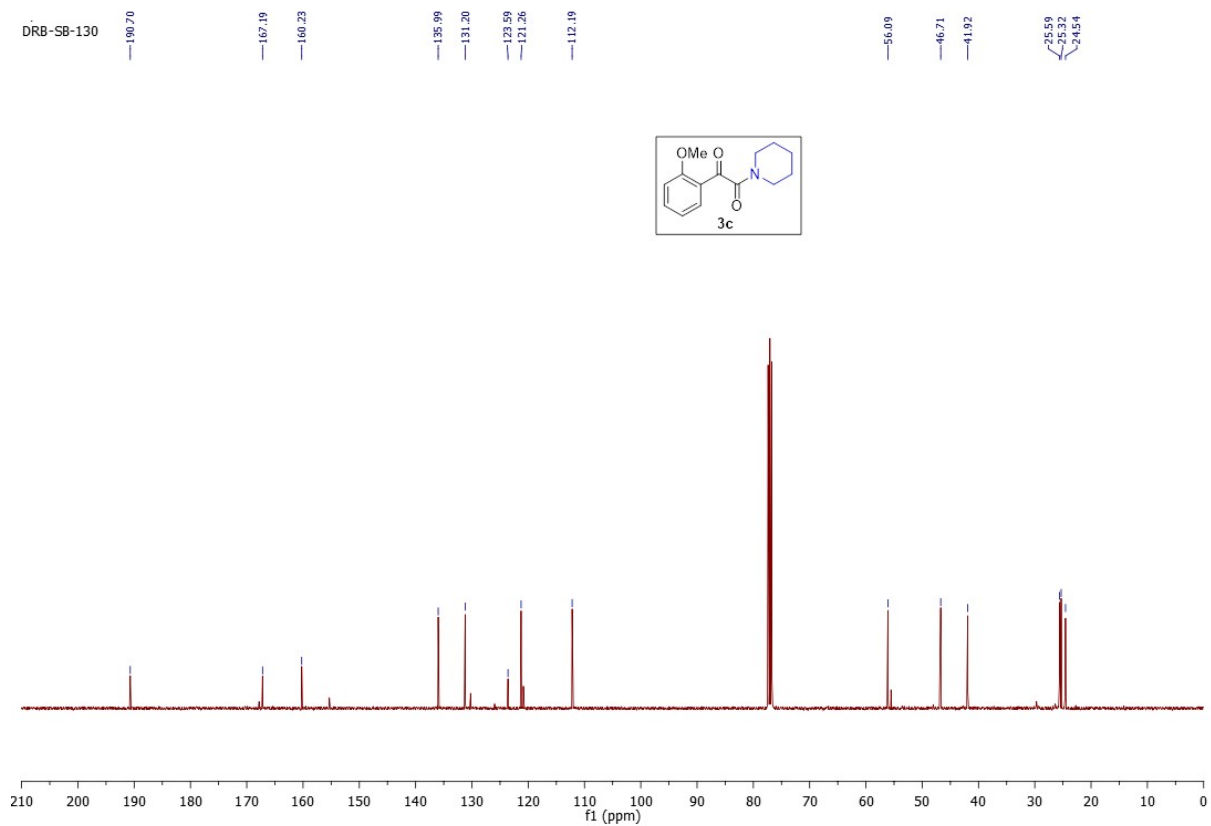




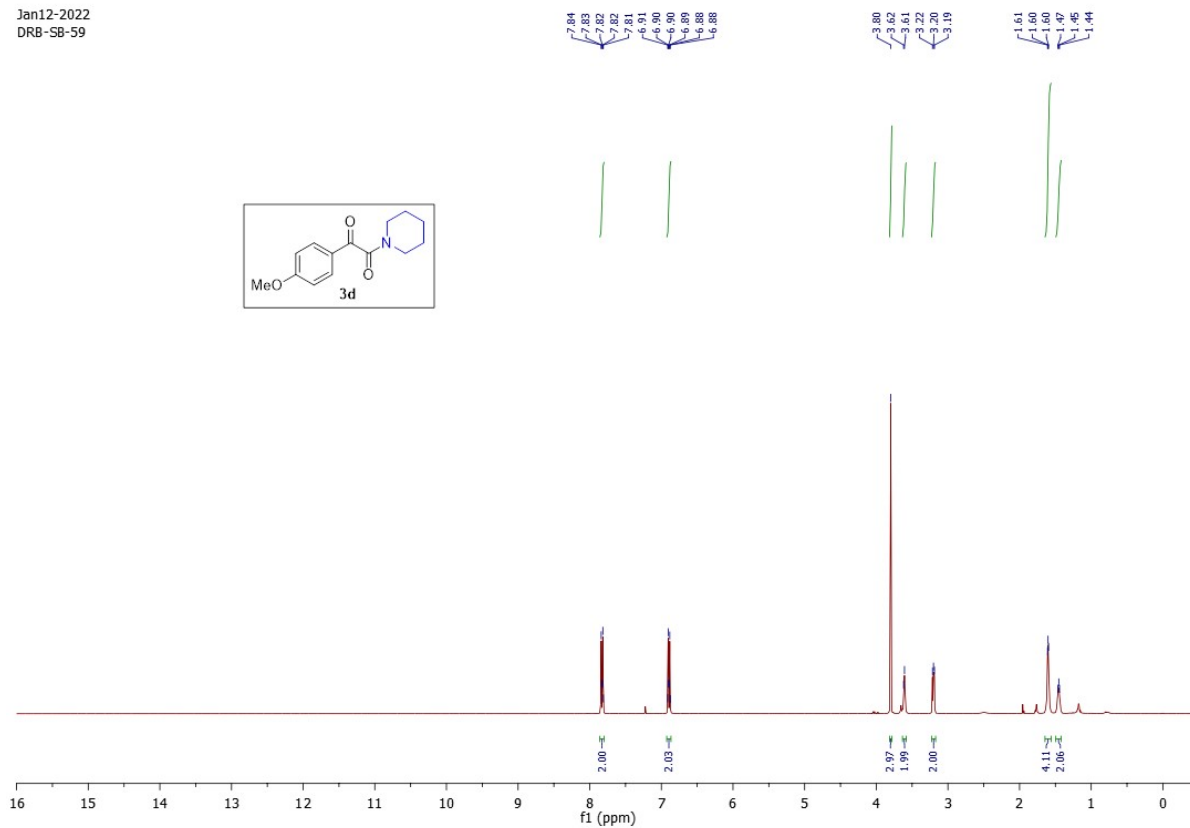
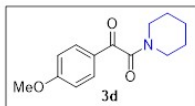
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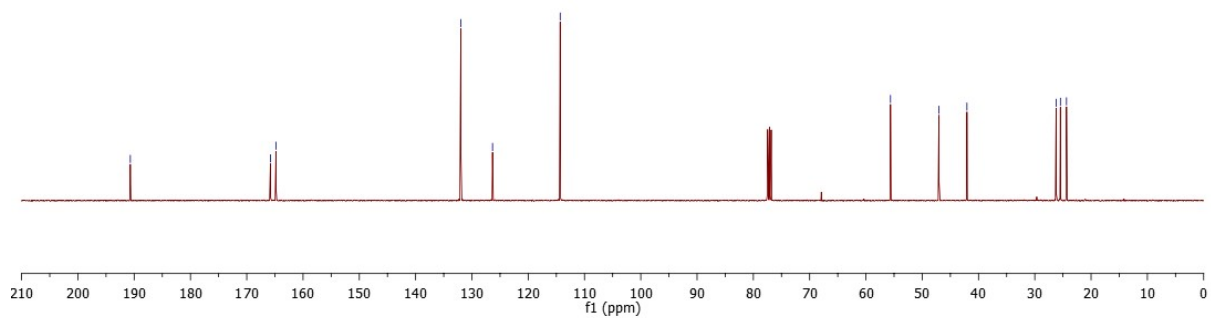
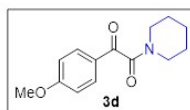
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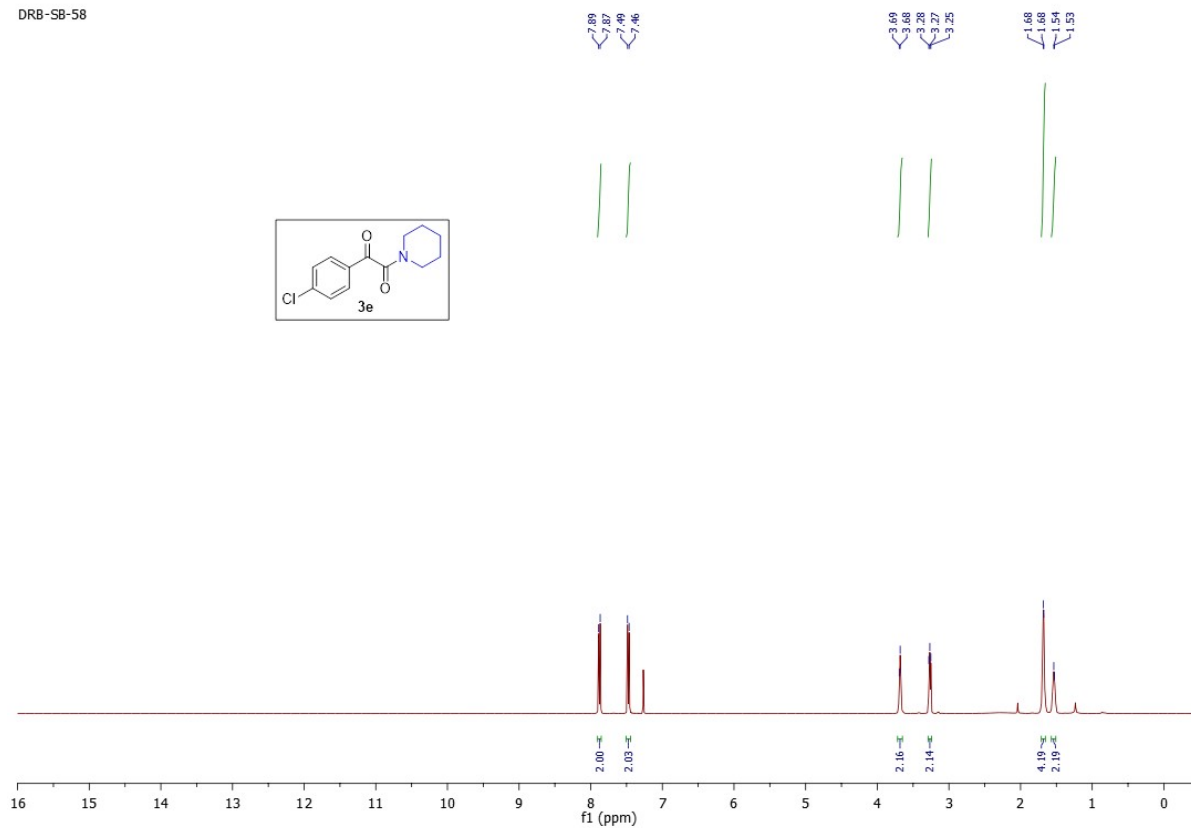
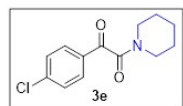
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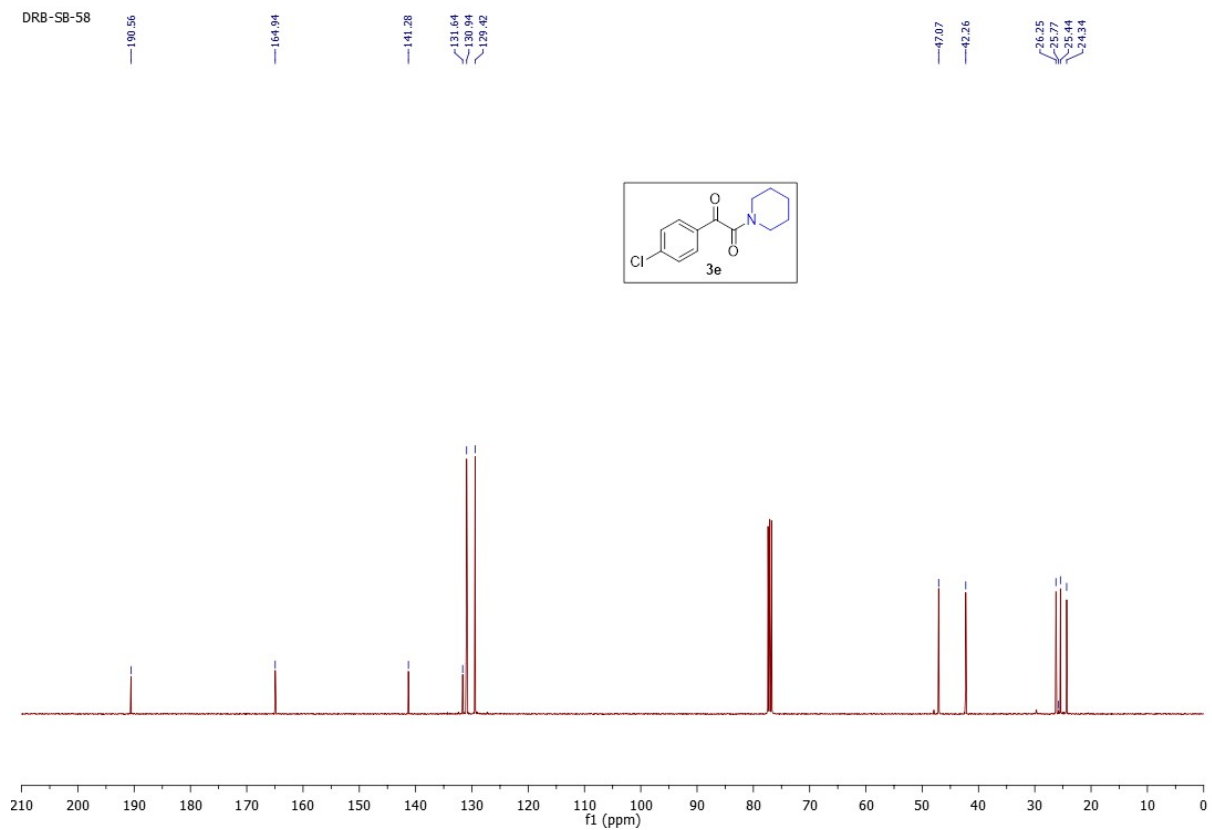
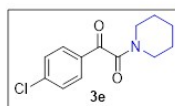
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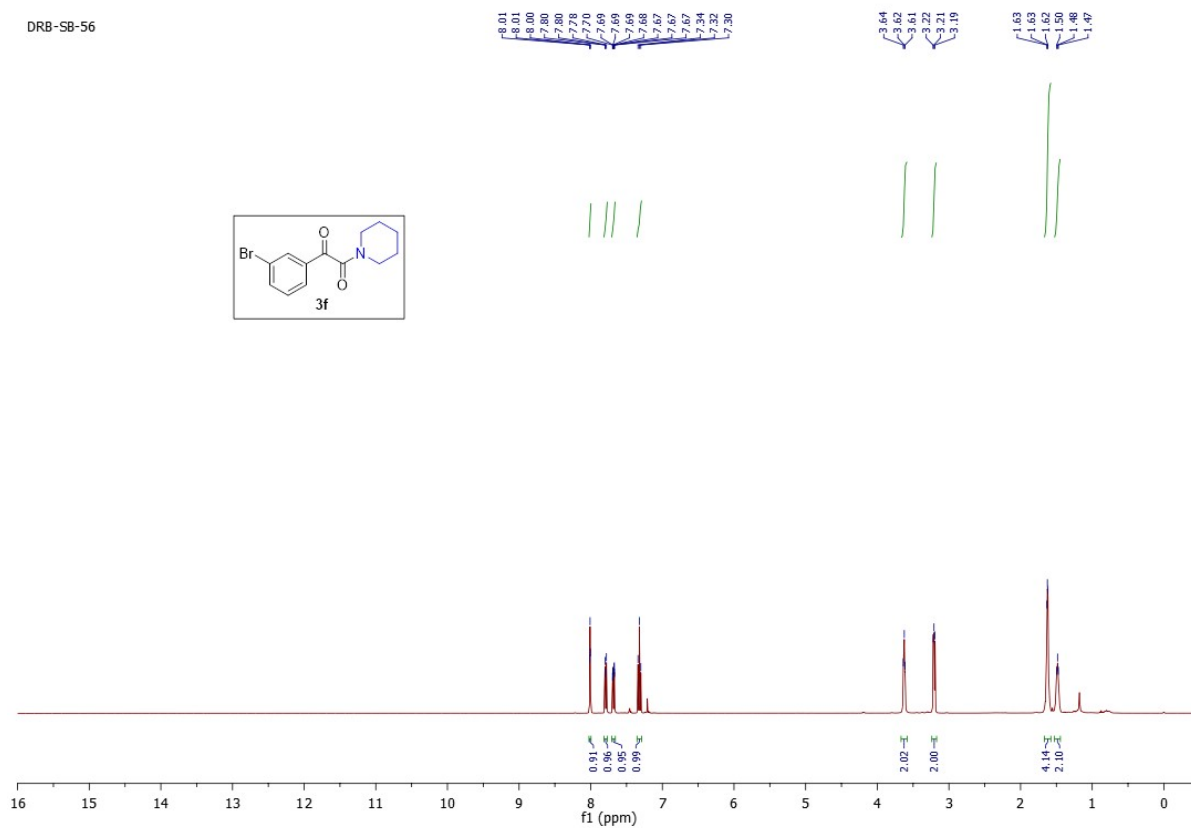
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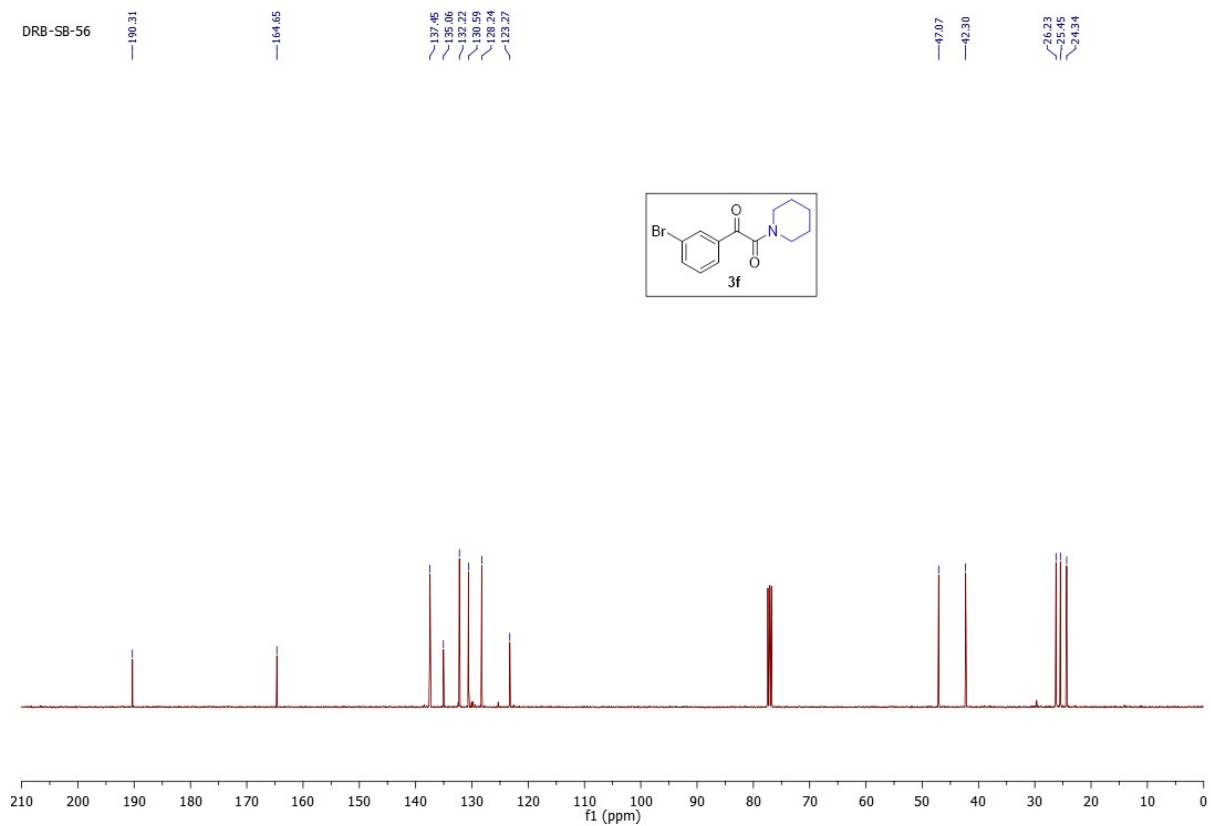
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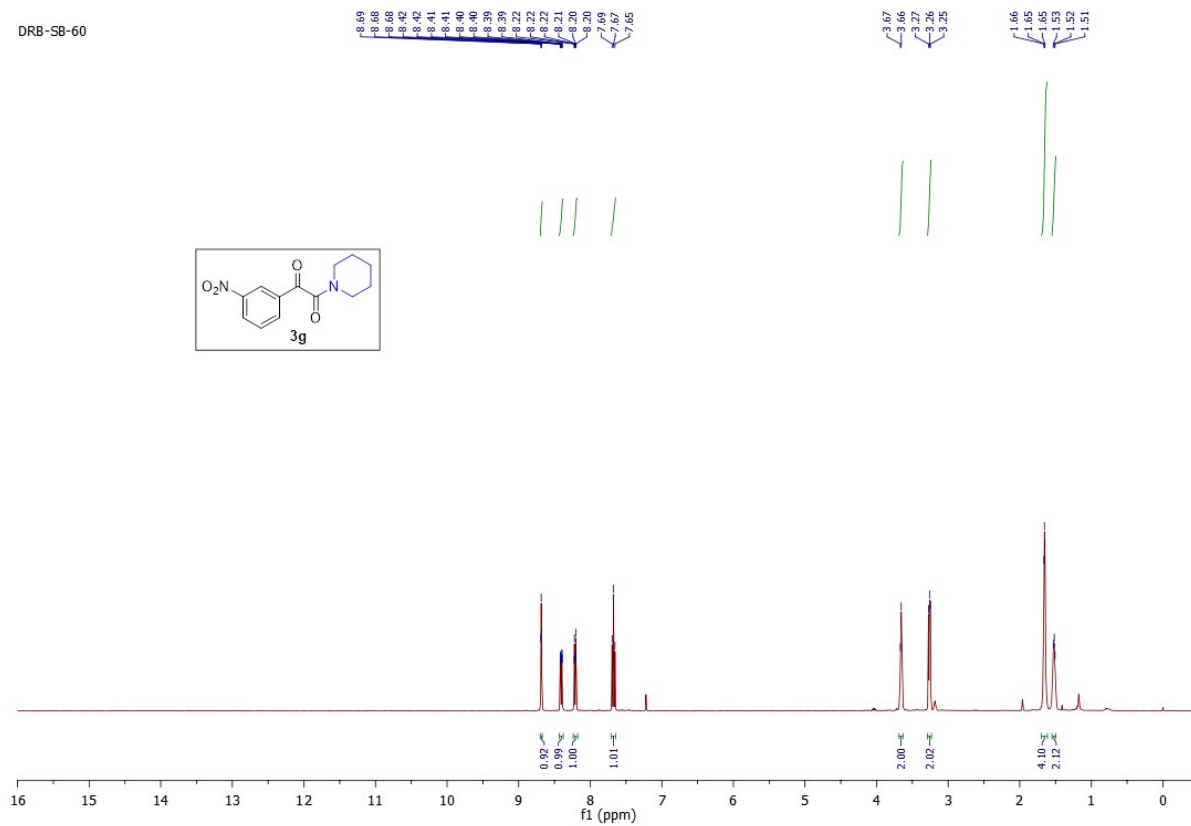
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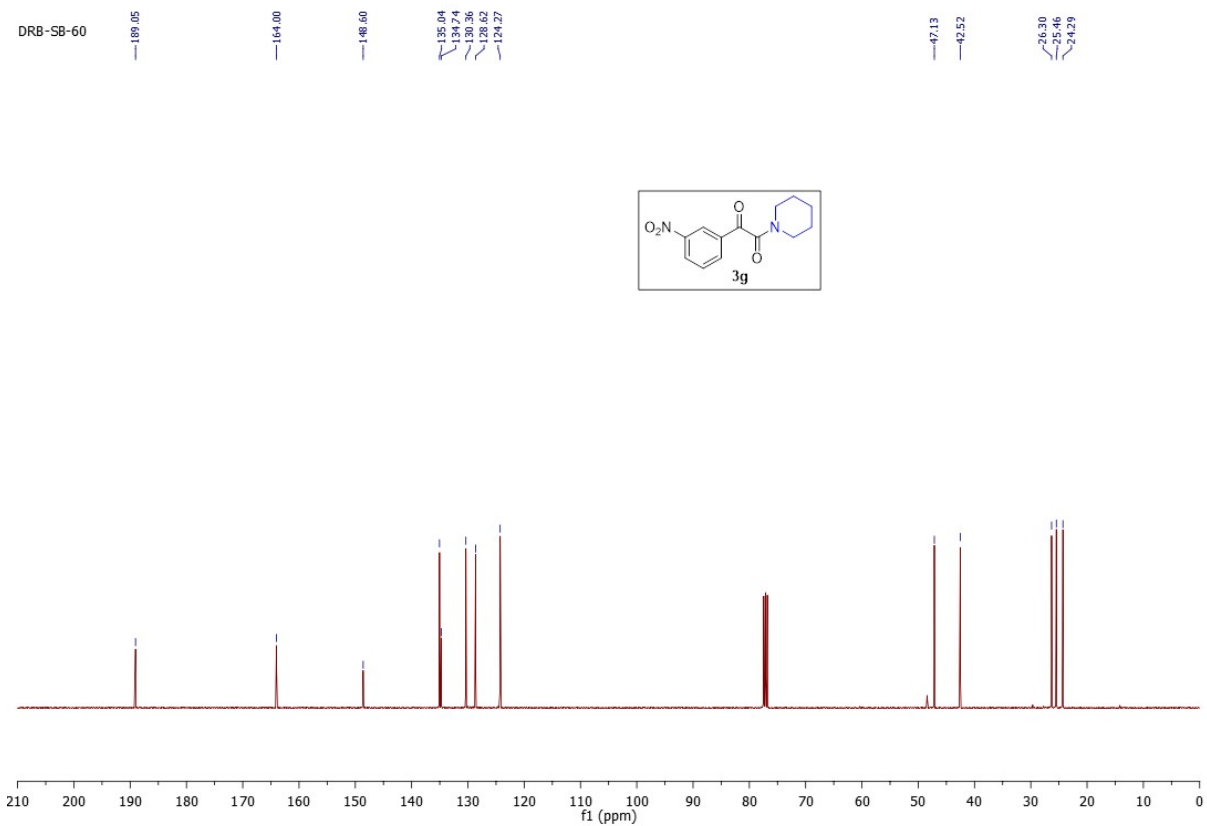
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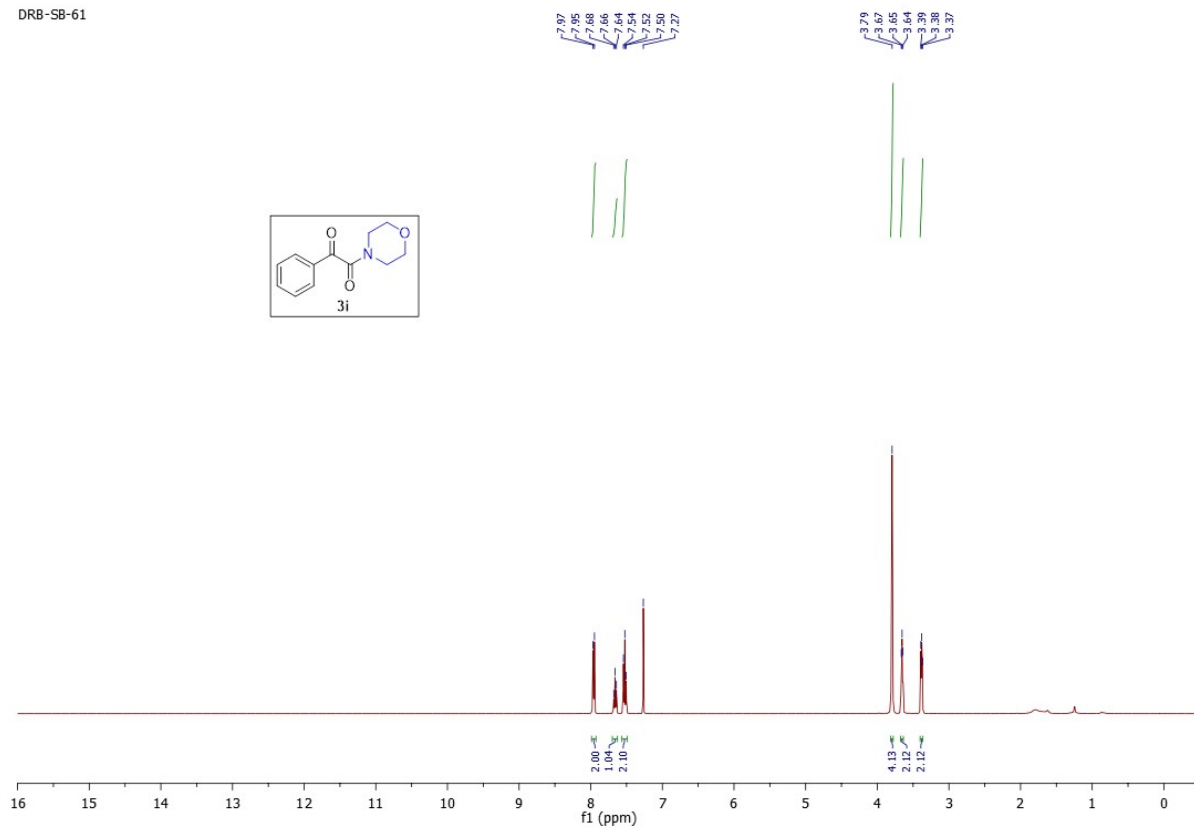
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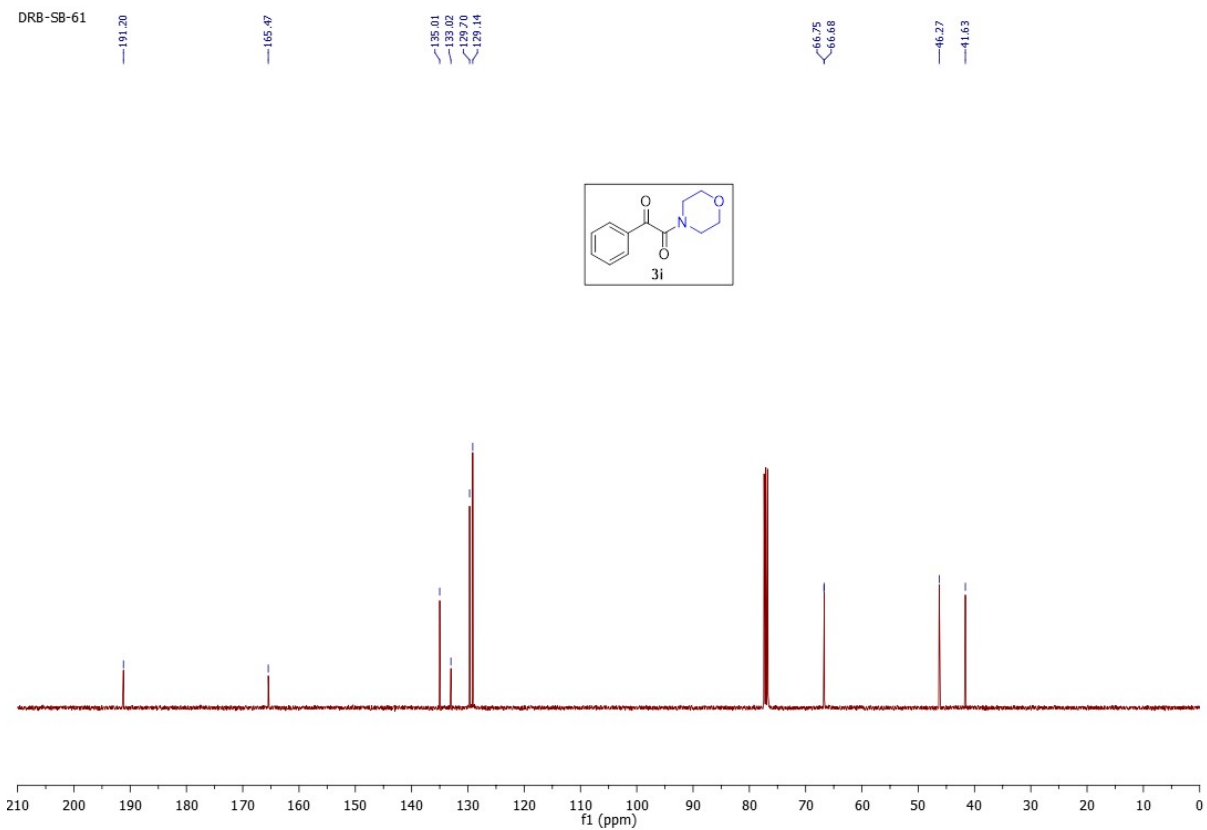
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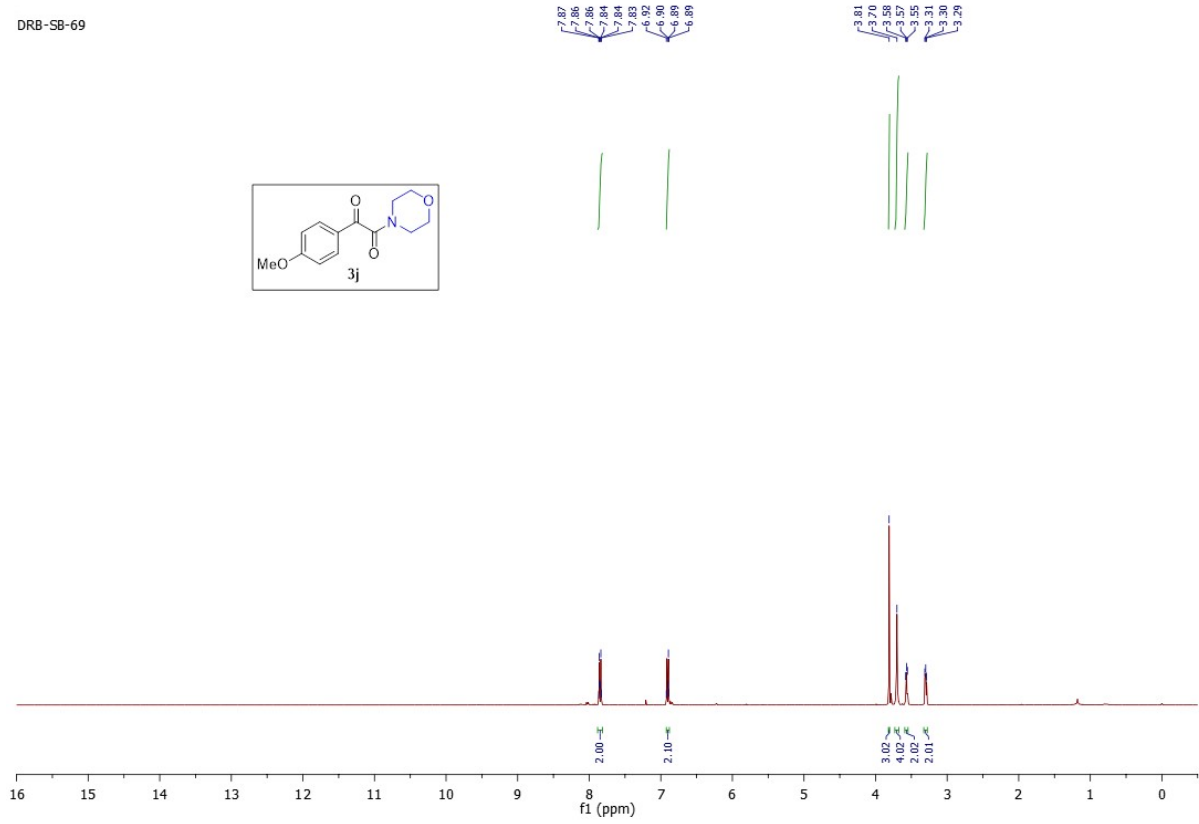
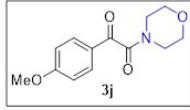
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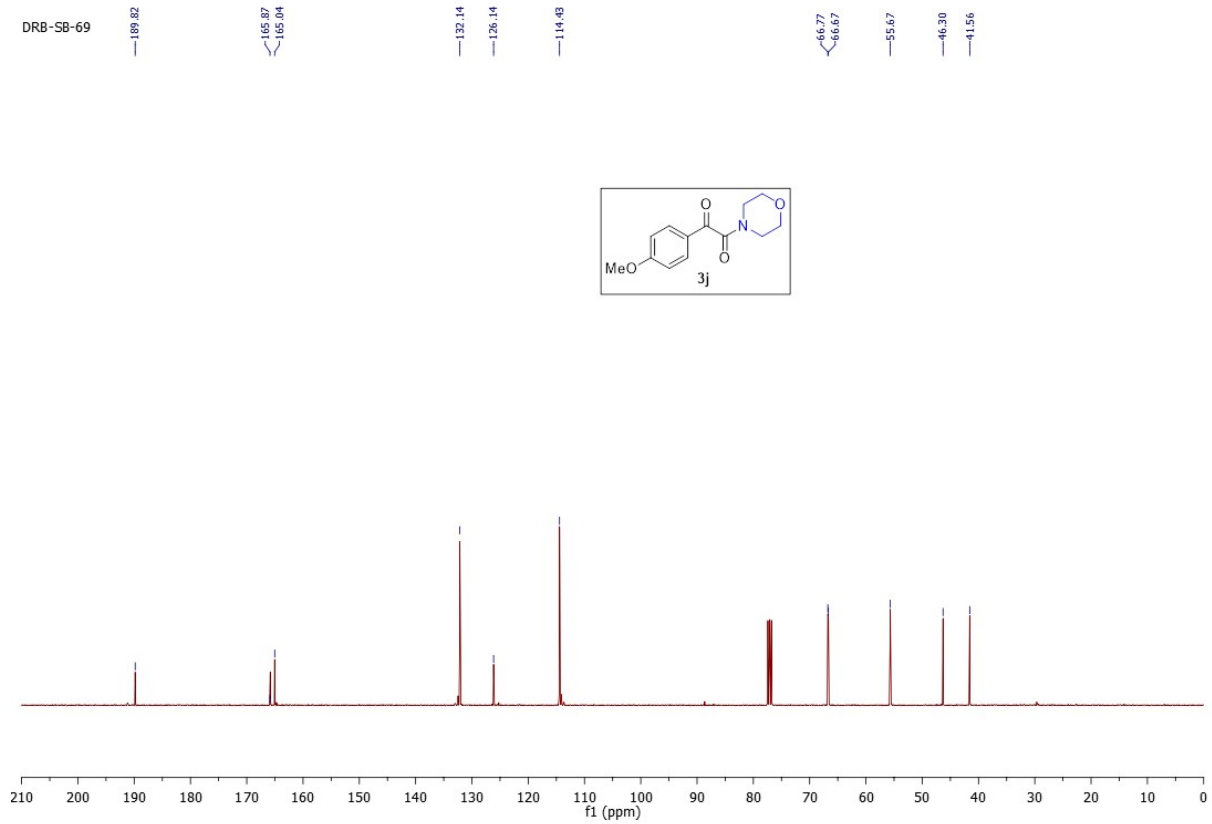
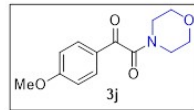
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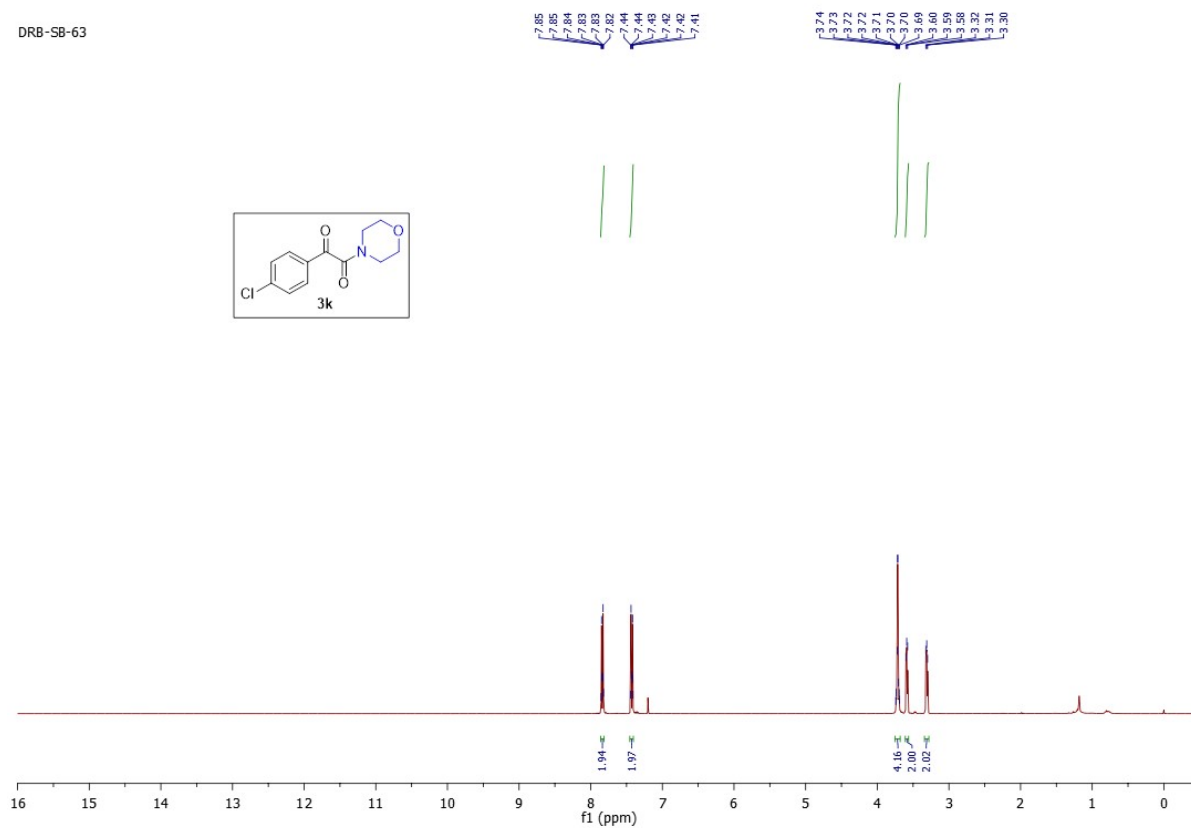
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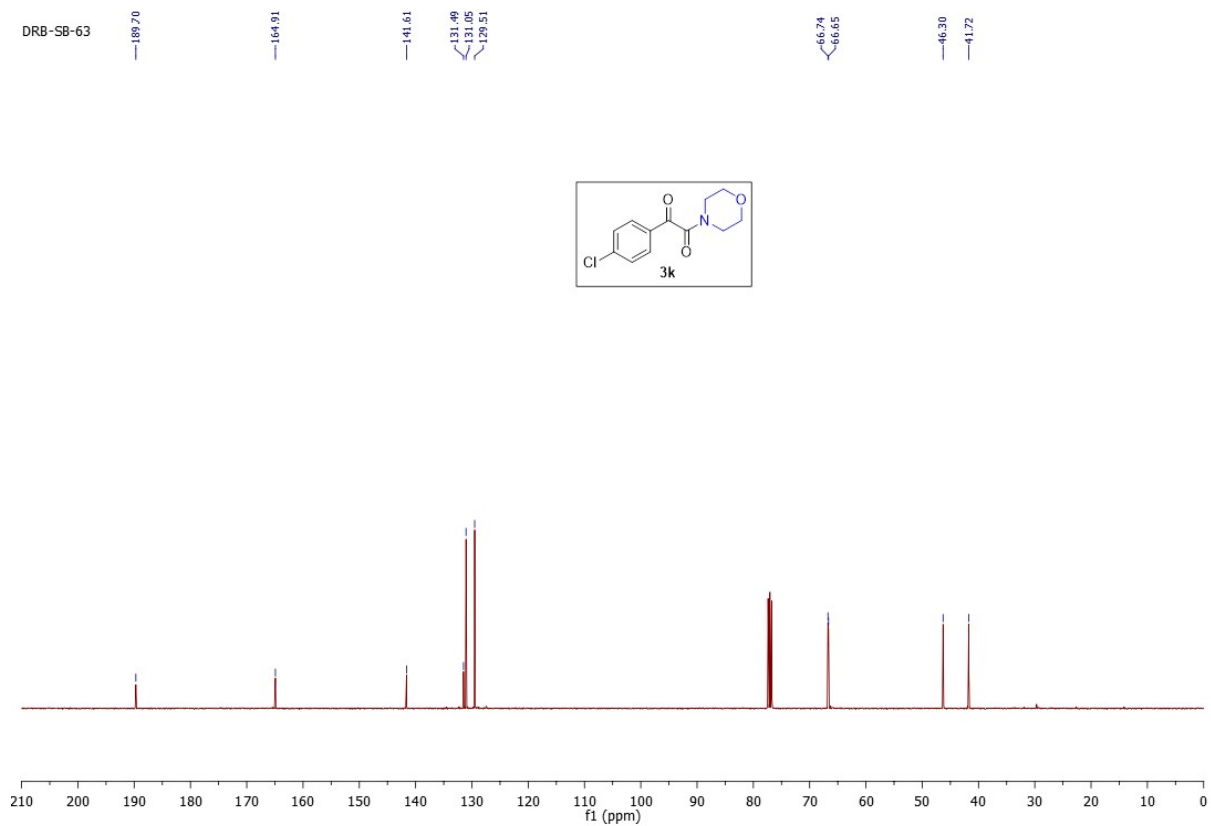
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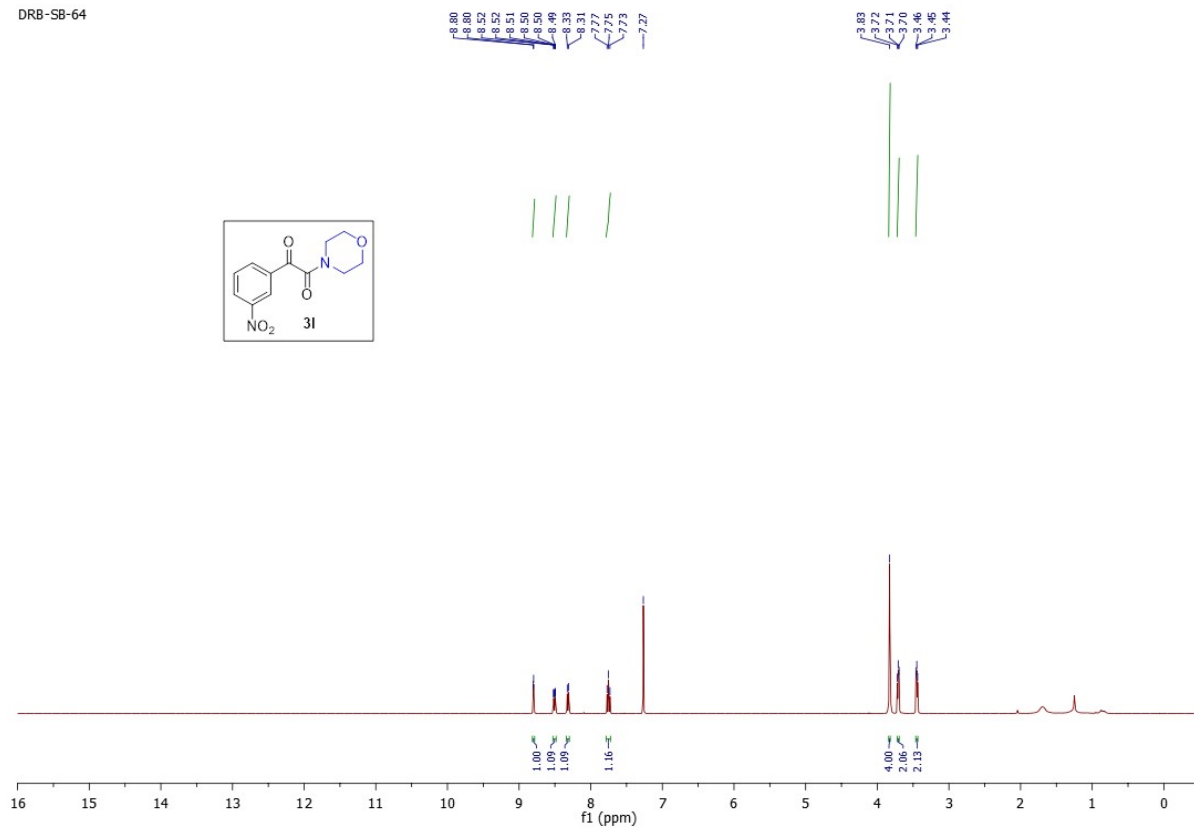
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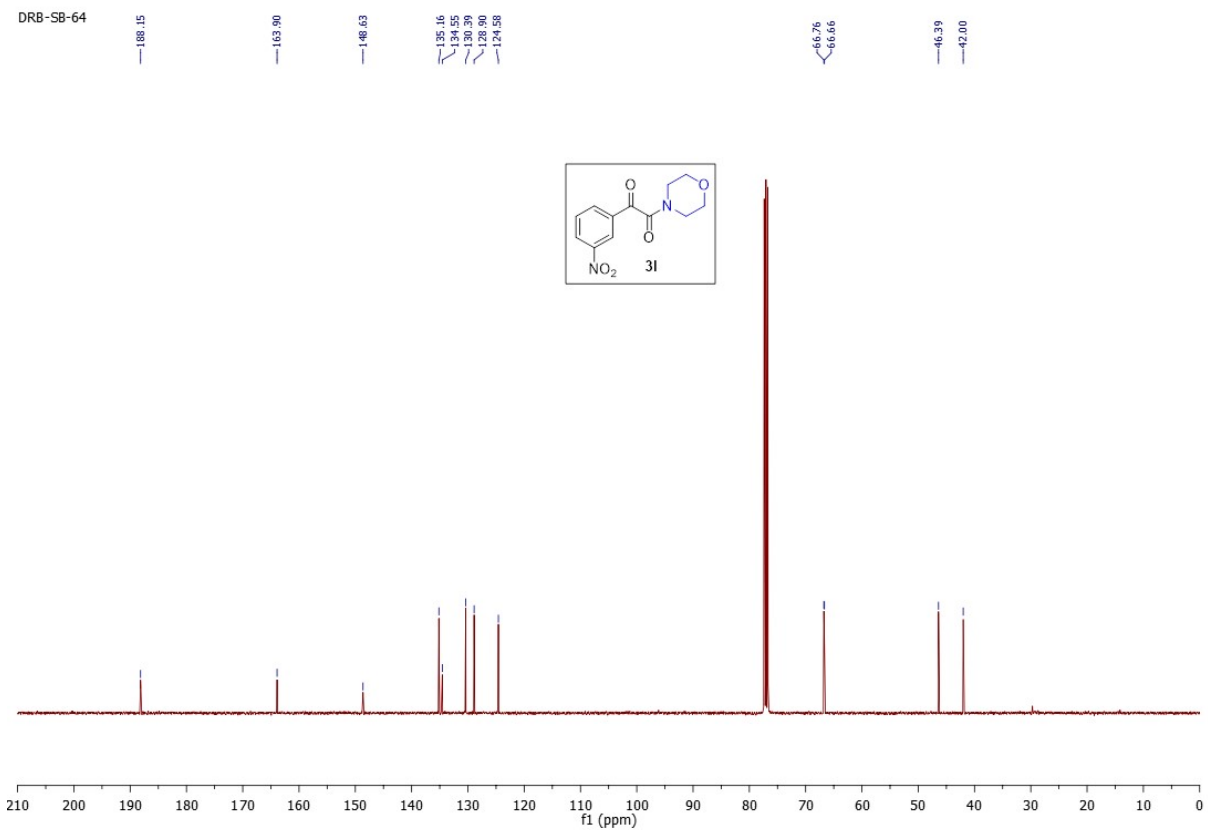
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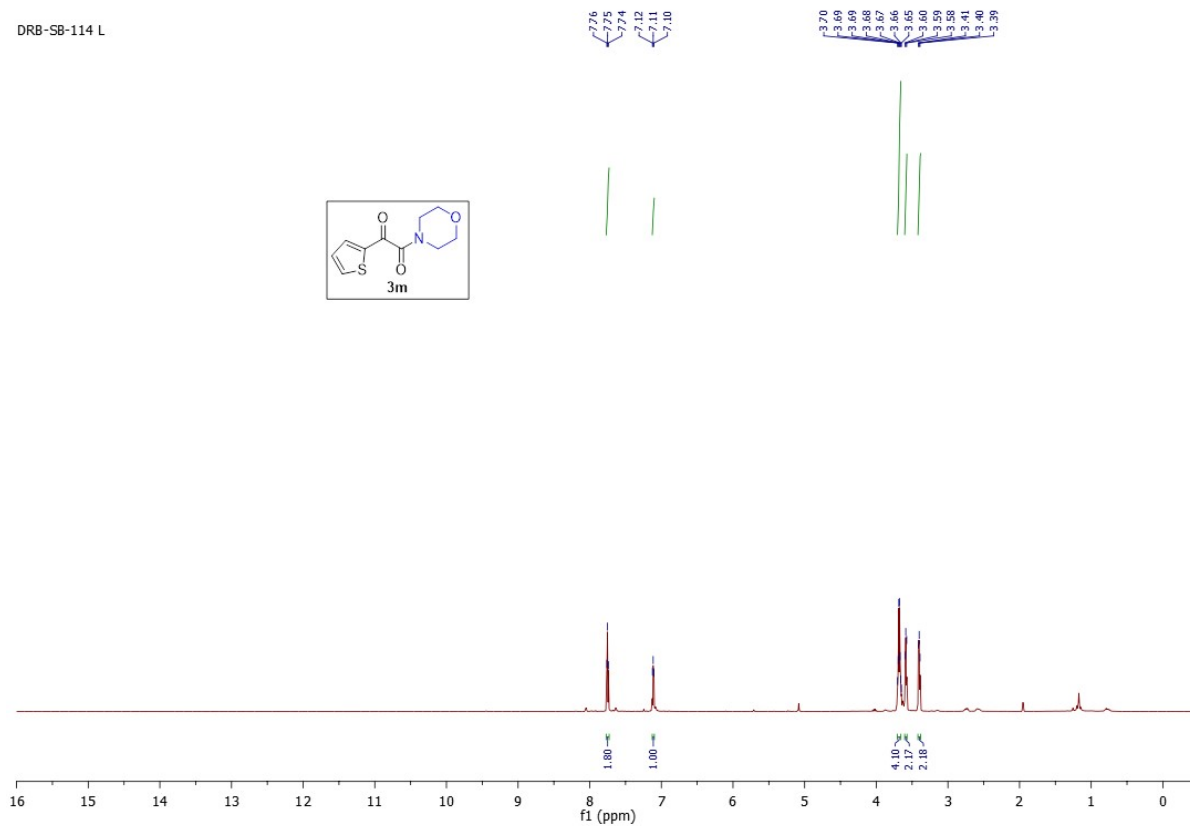
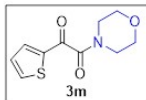
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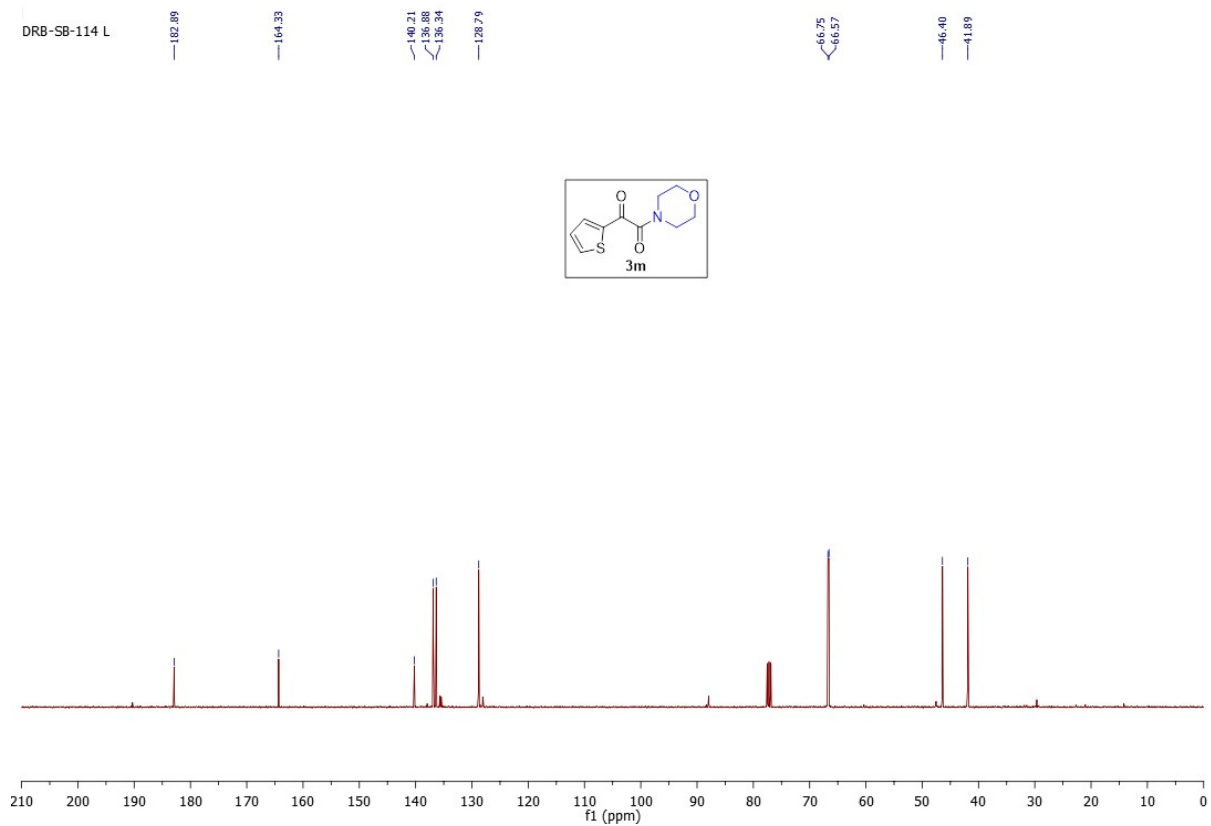
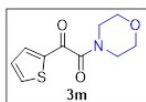
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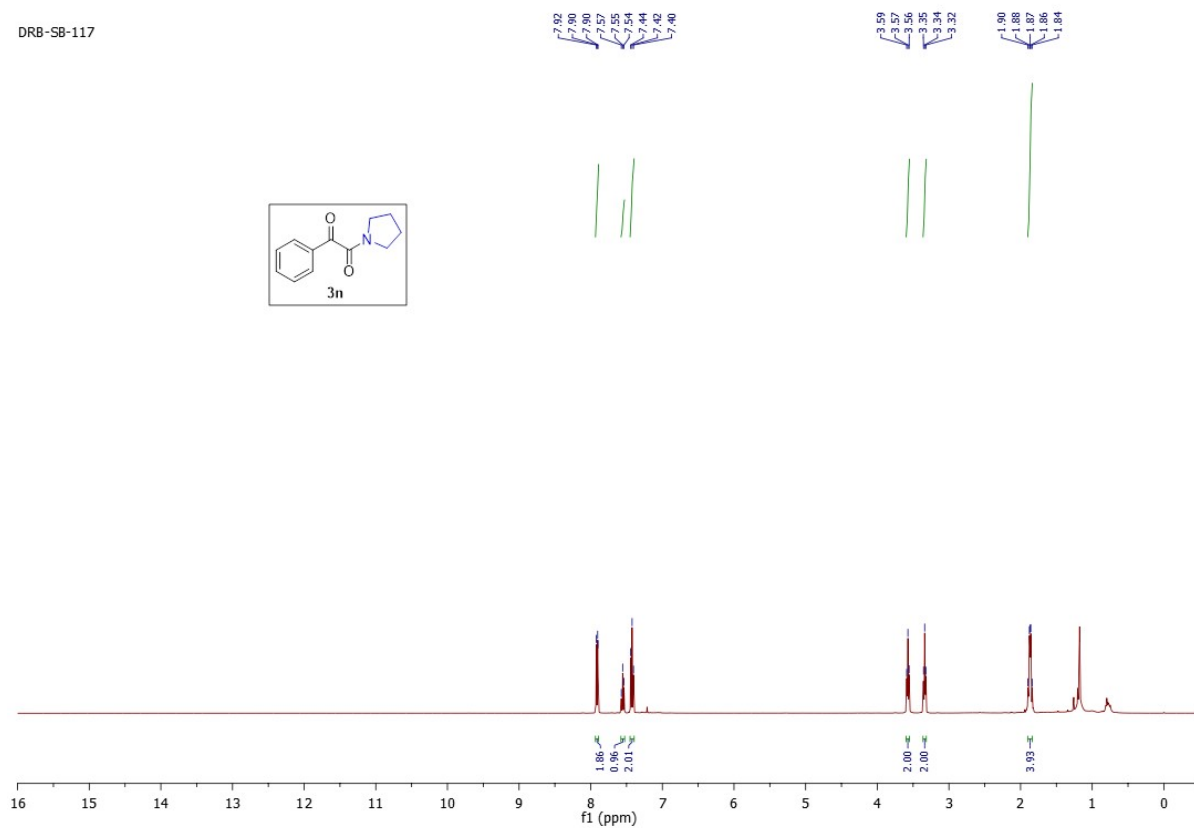
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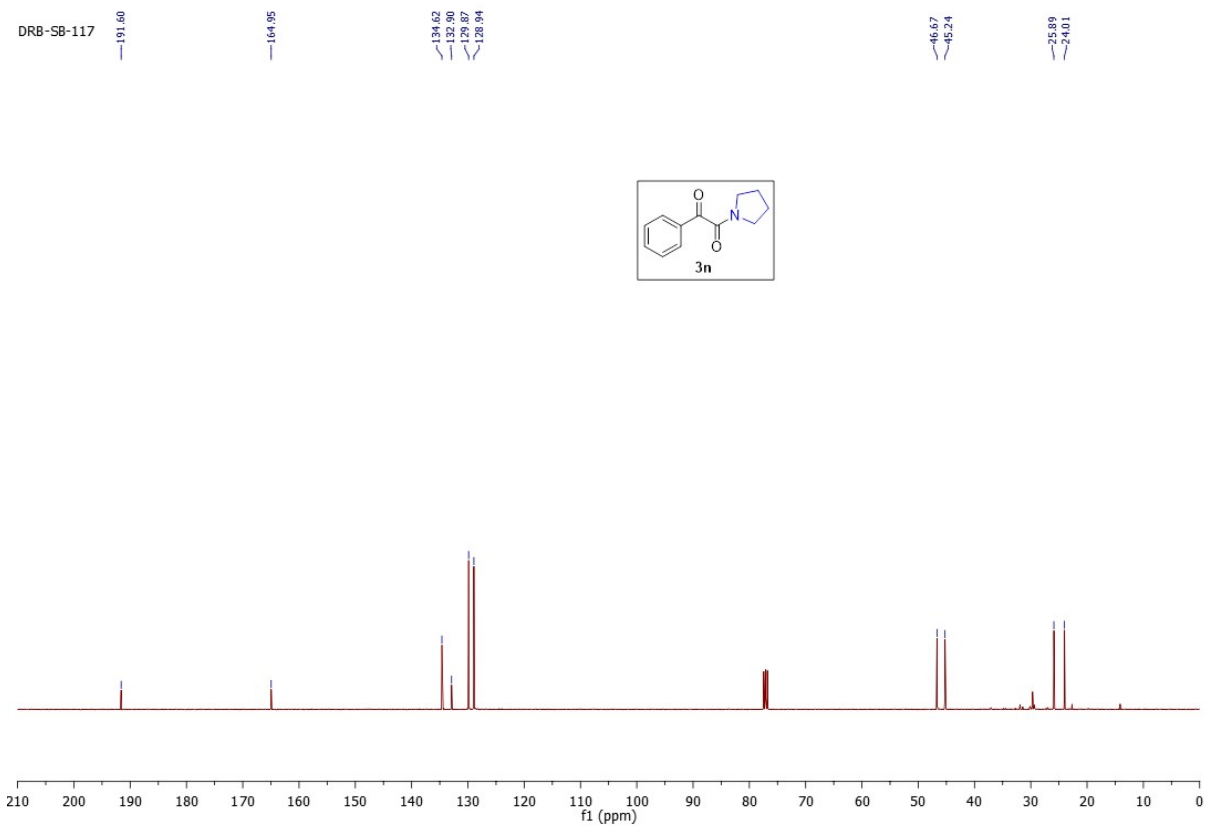
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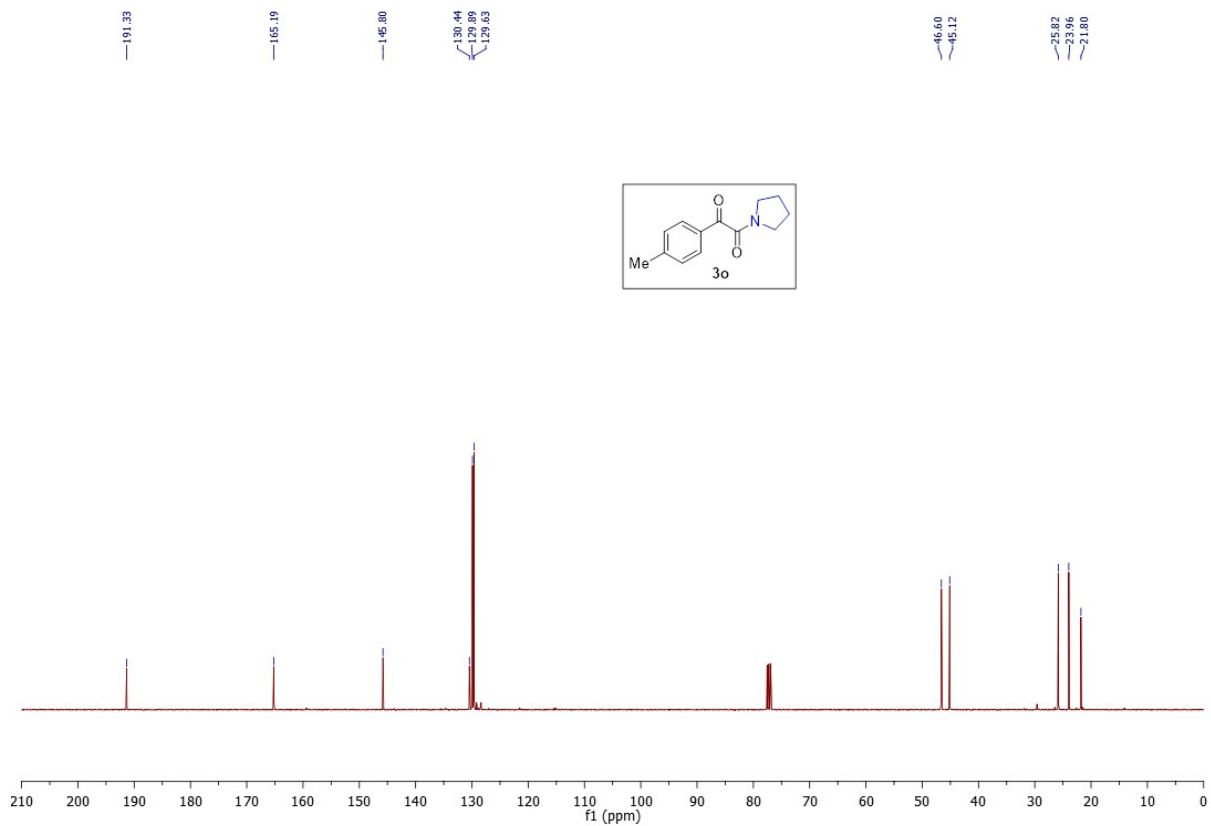
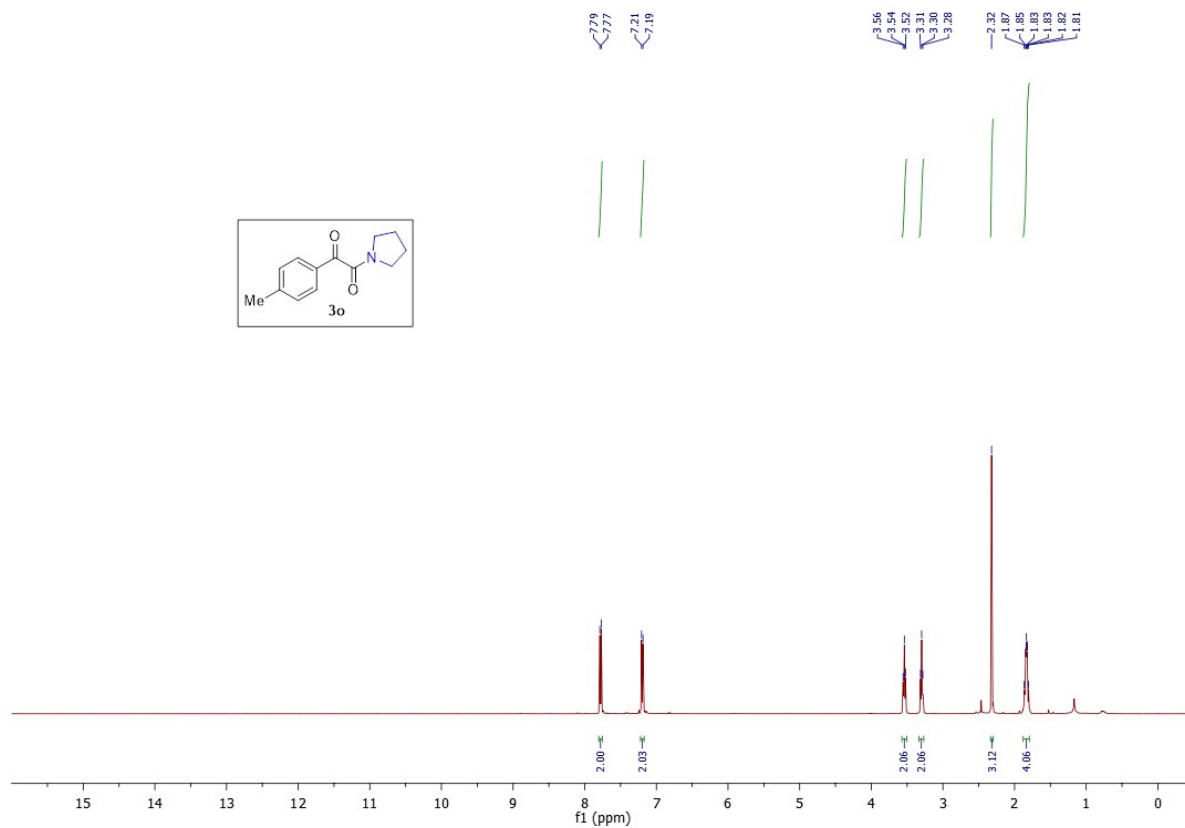


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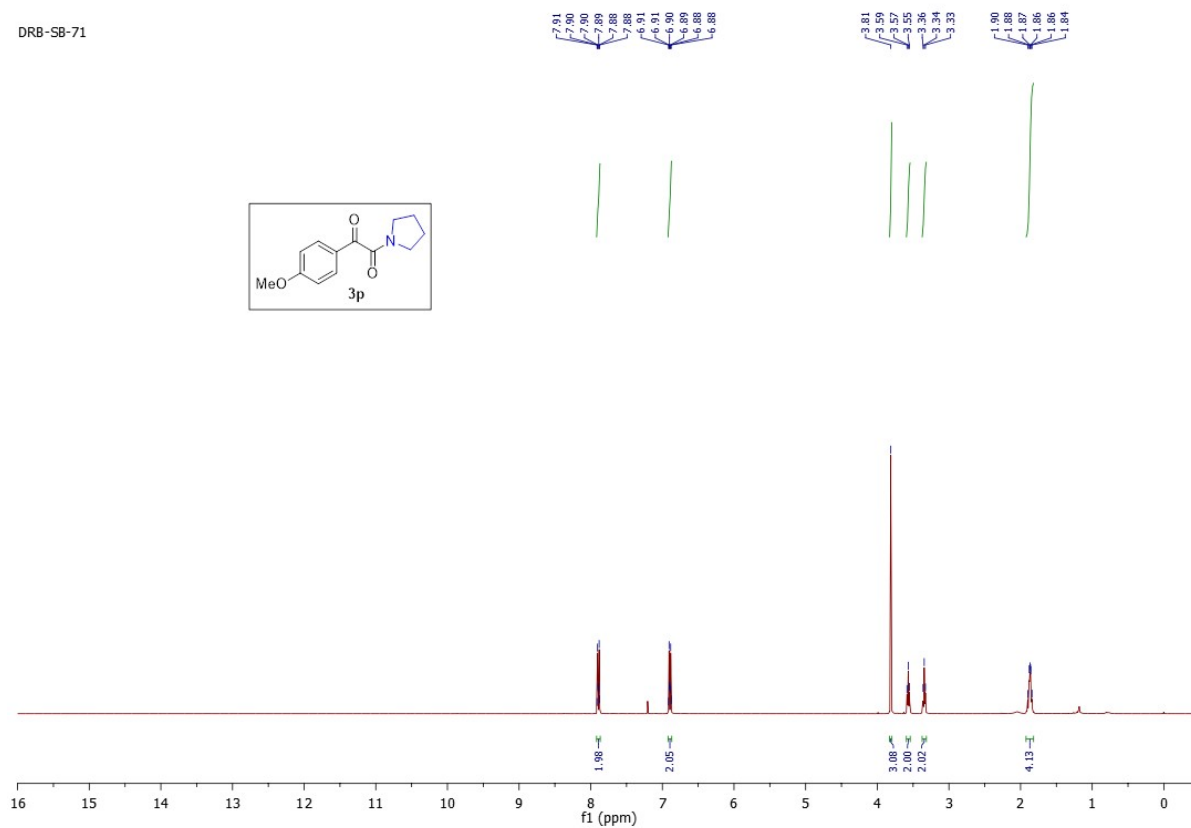
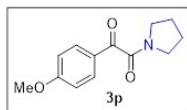


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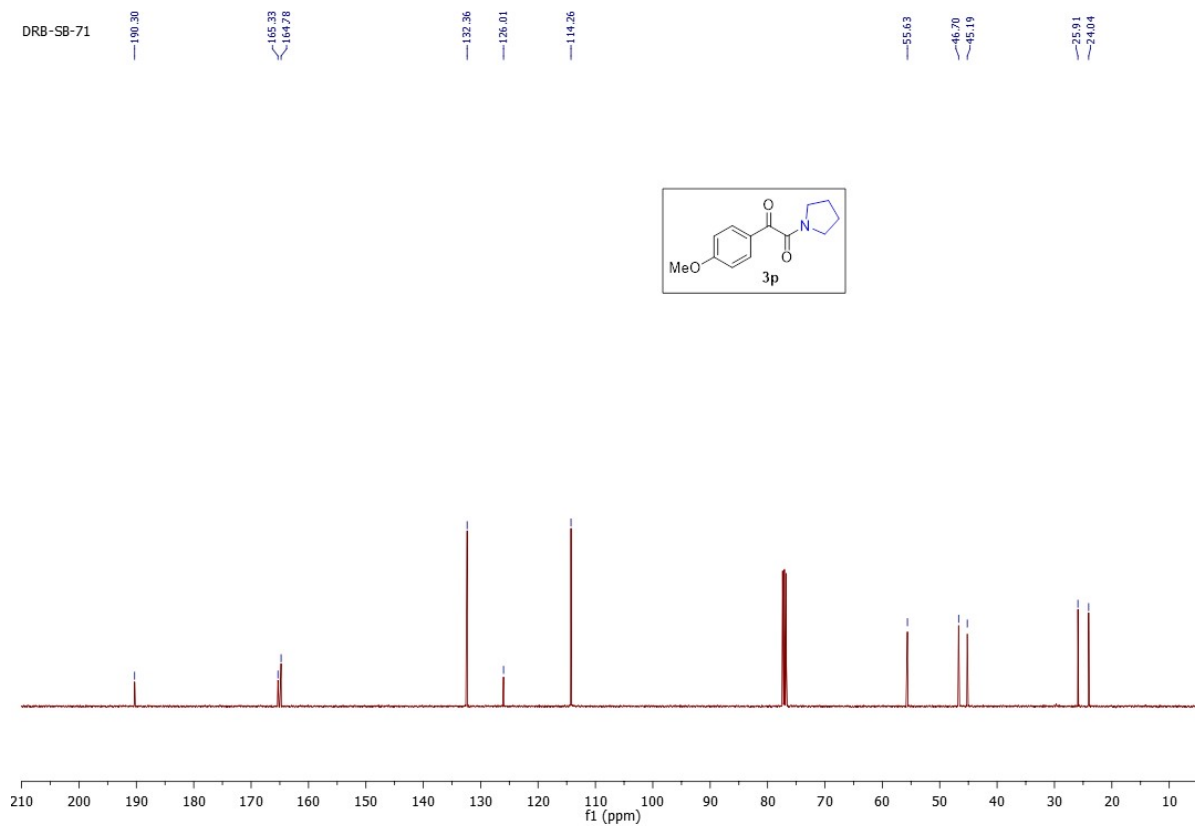
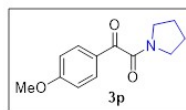




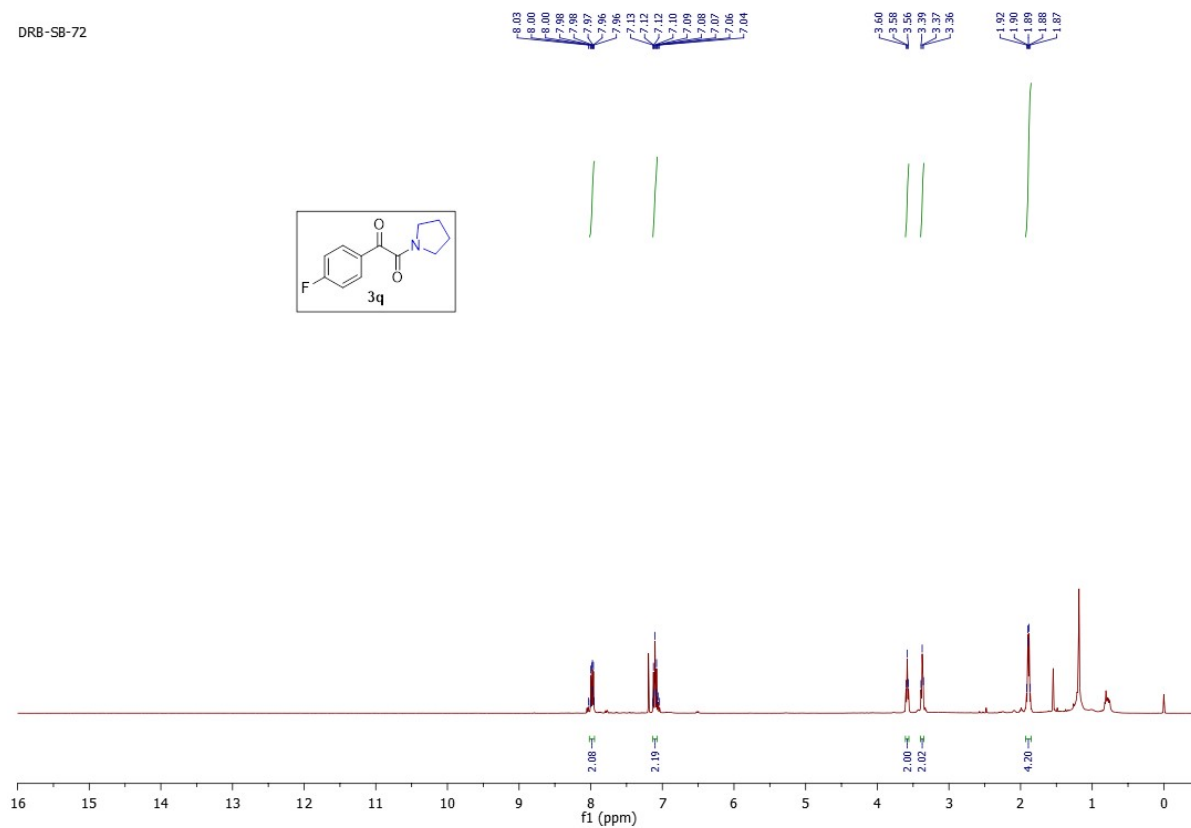
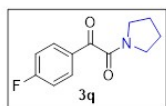
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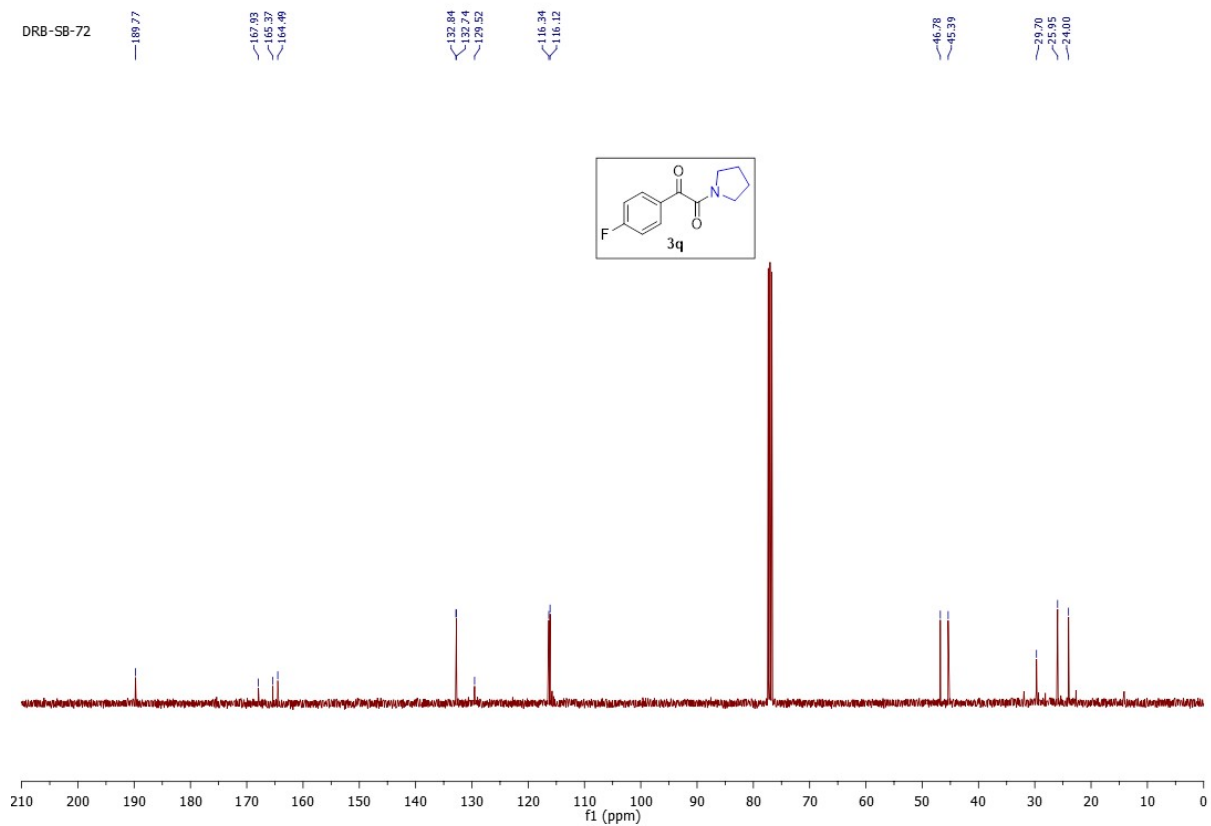
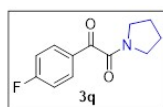
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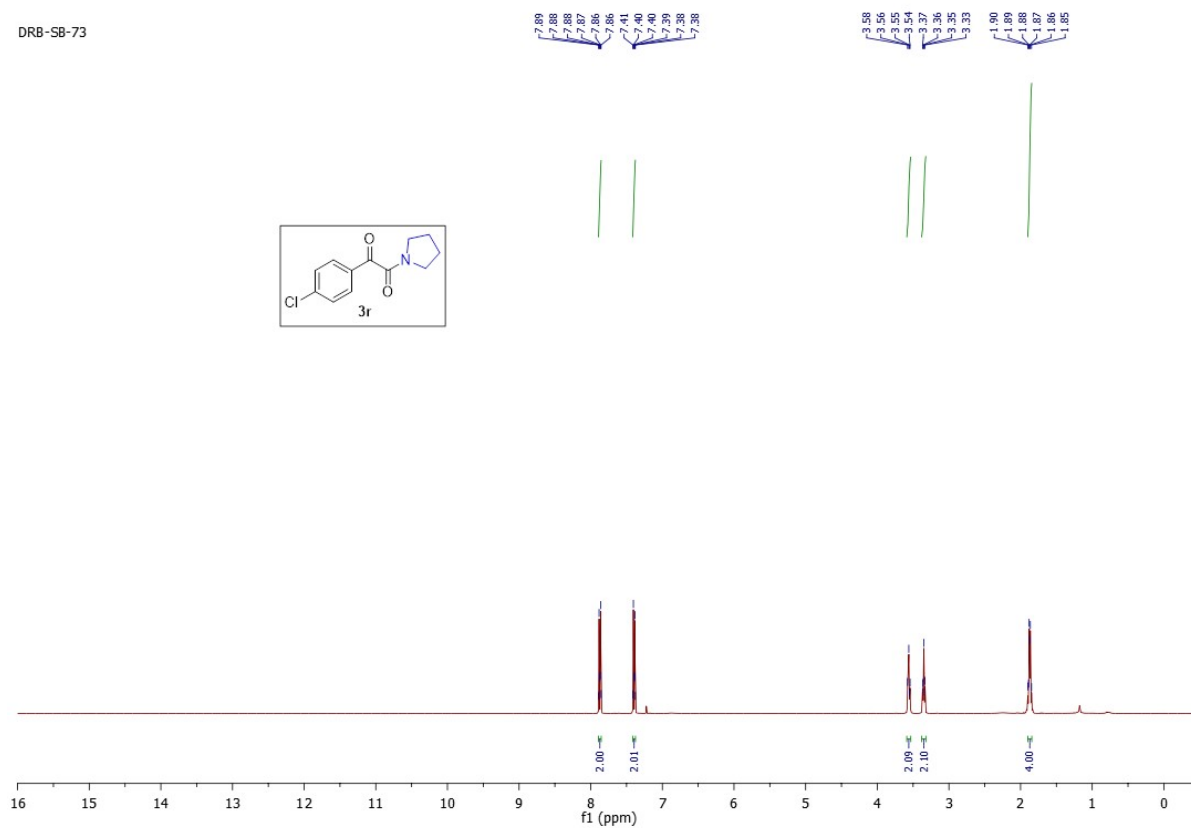
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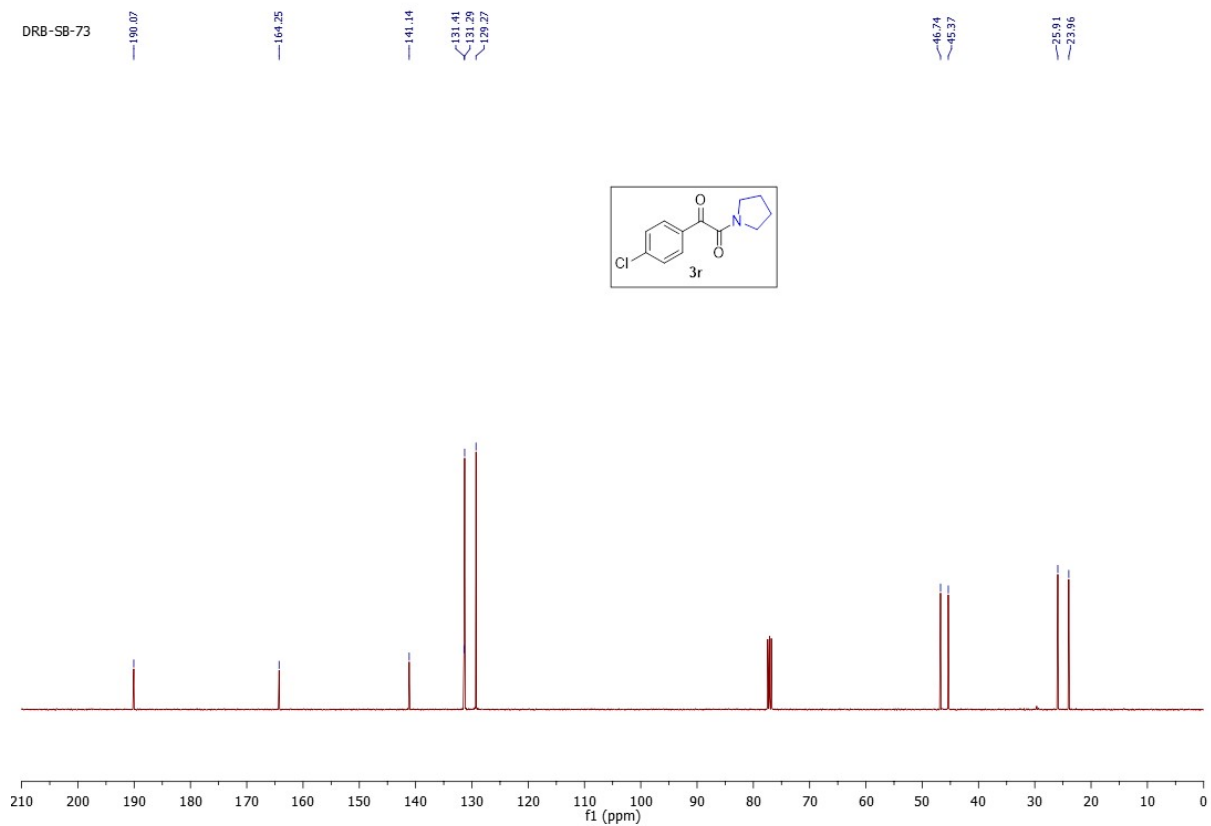
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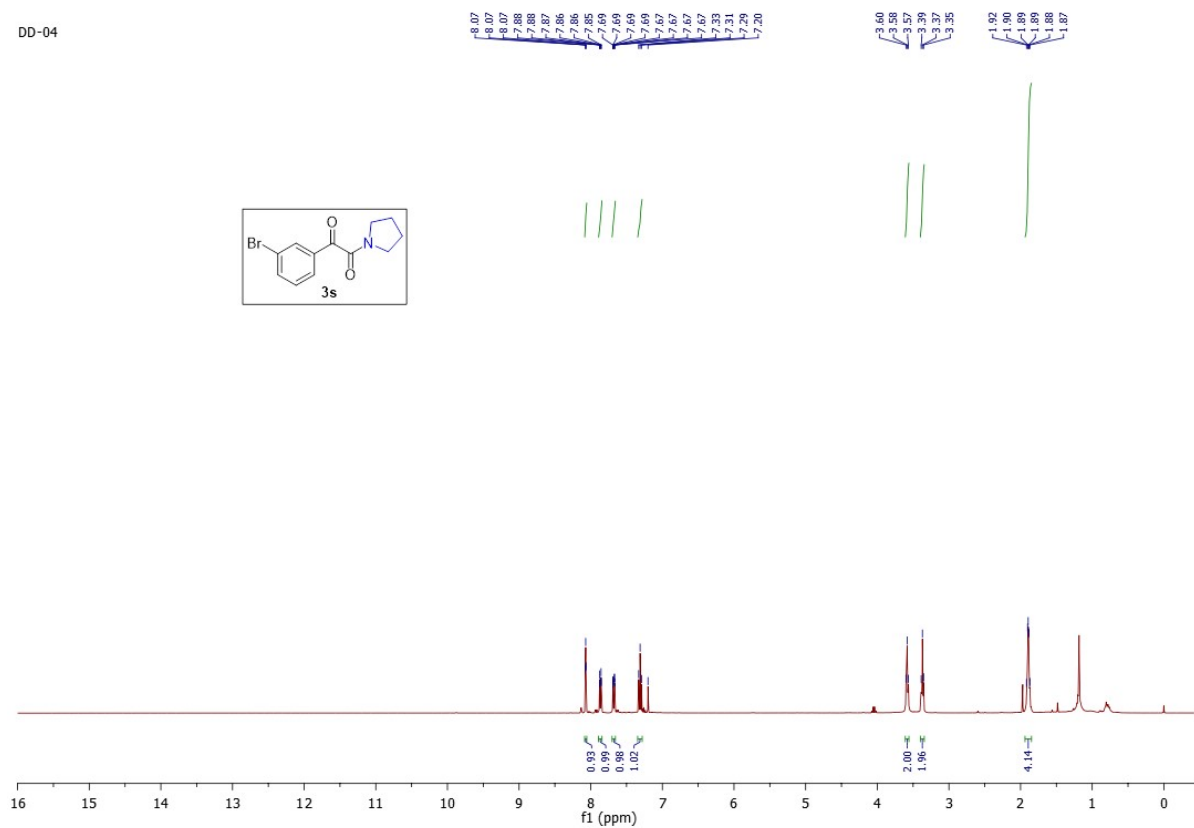
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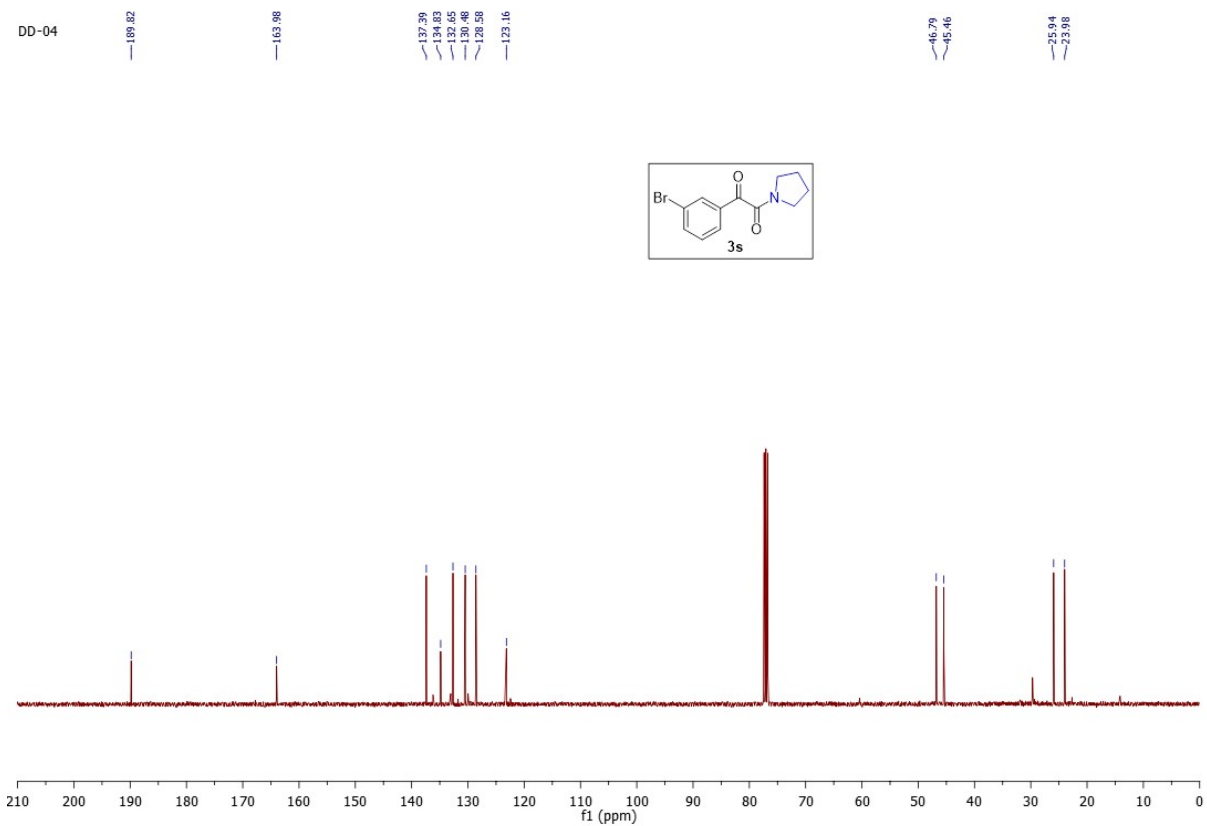
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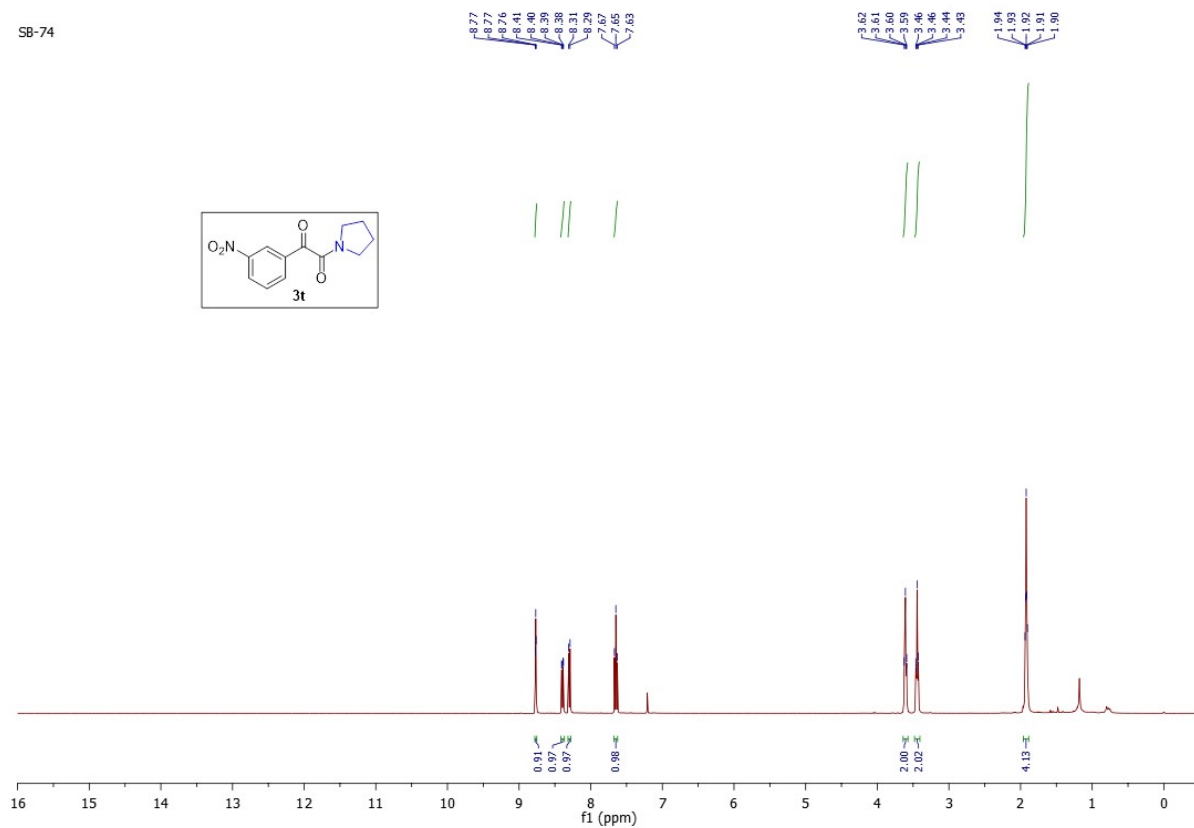
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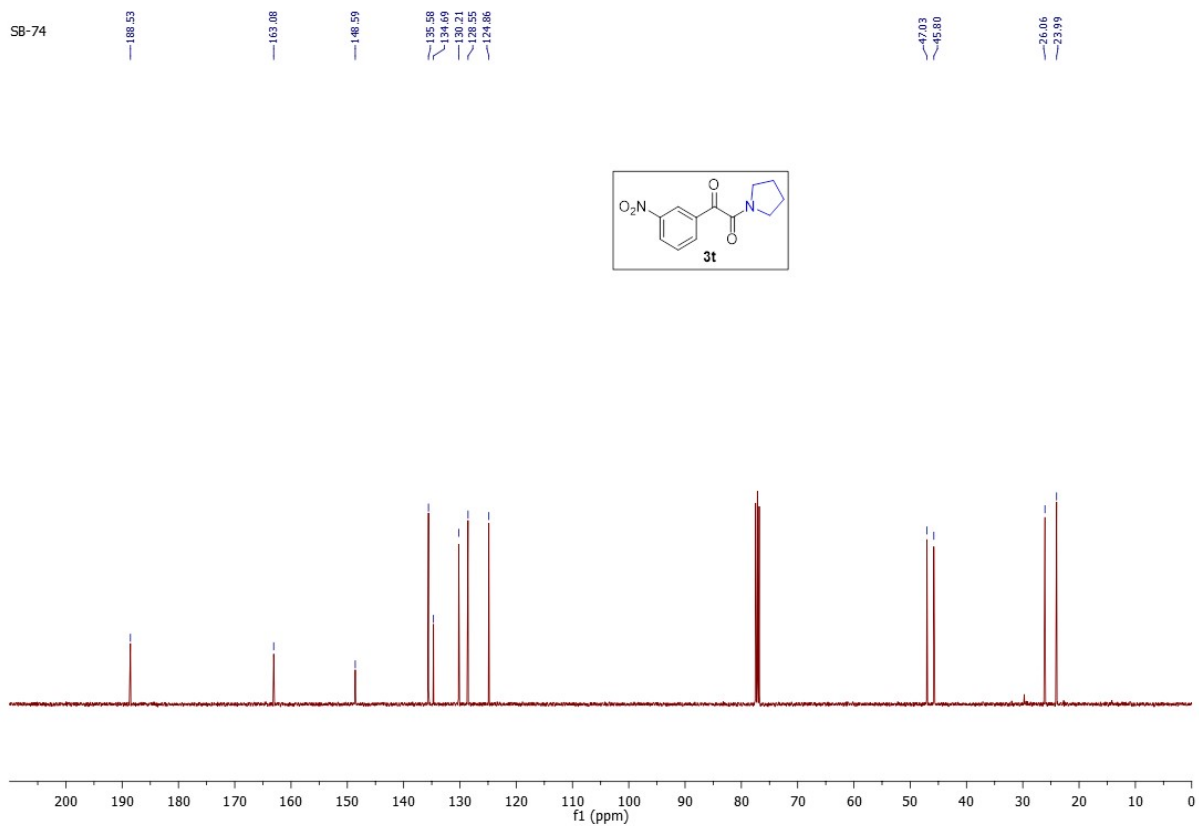
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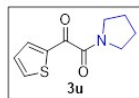
SB-74



SB-74



DRB-SB-89



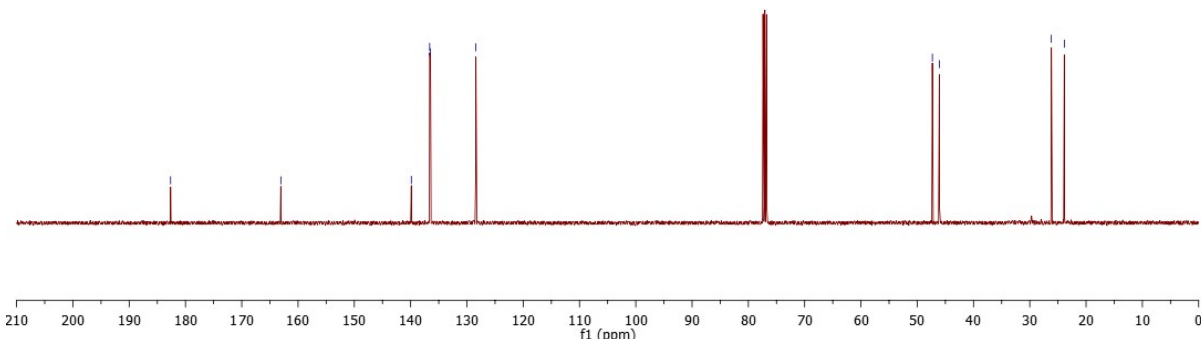
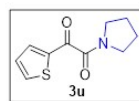
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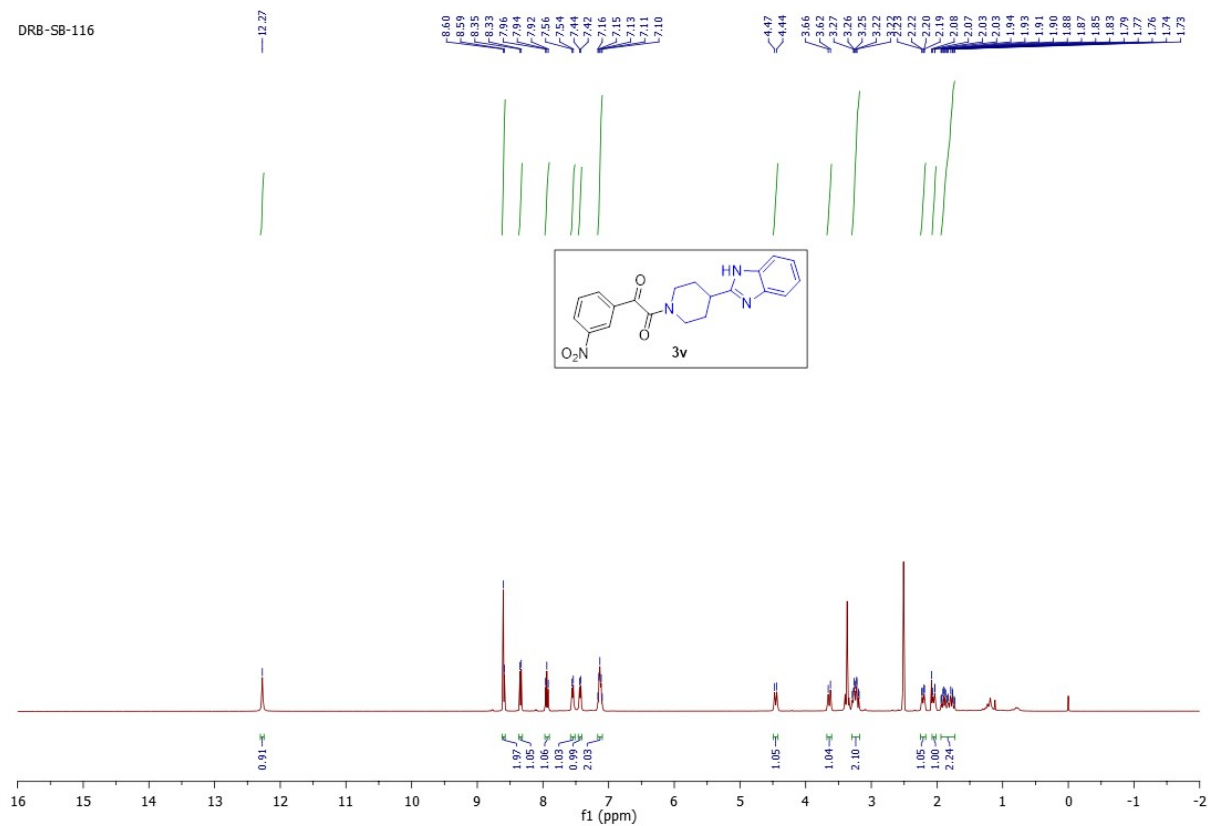
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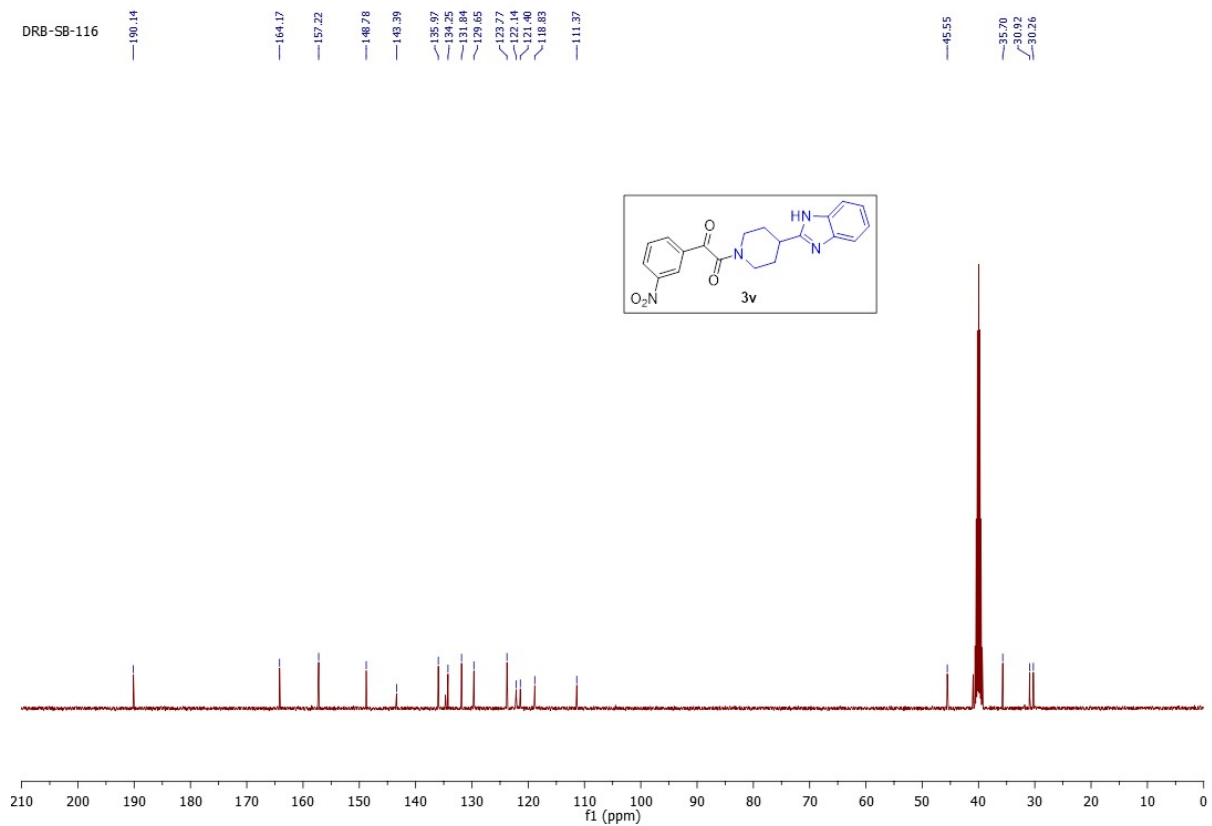
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DRB-SB-116



DRB-SB-116

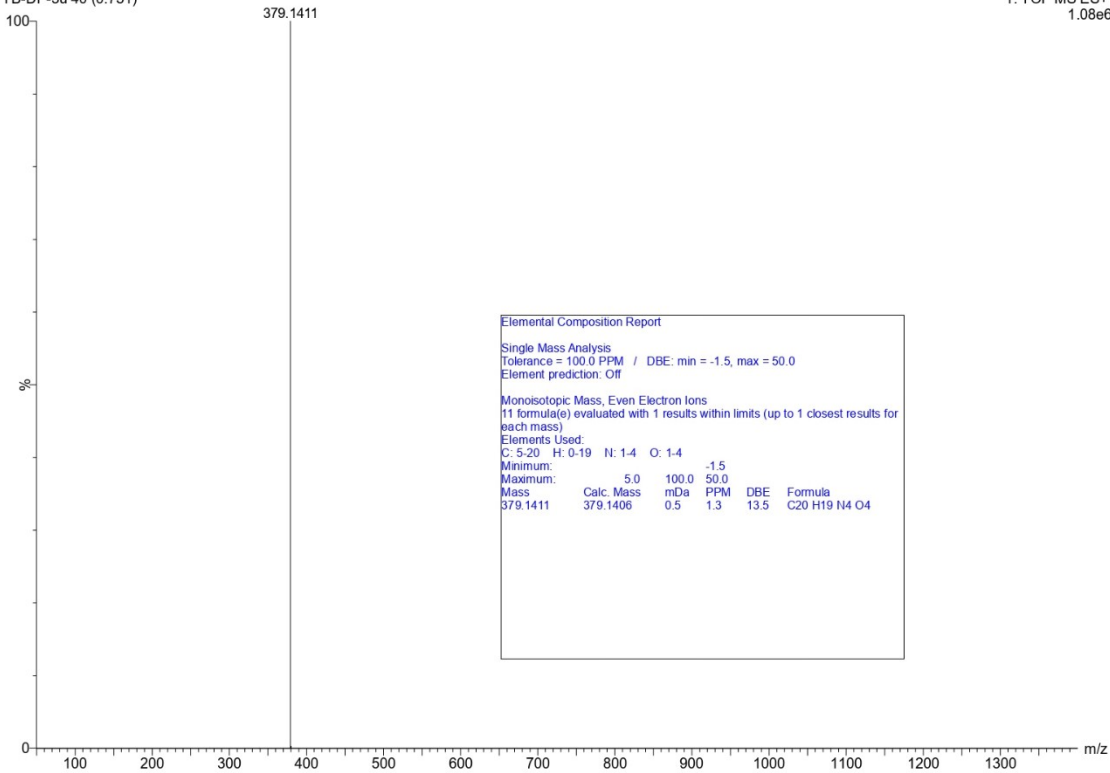


TB

05-Apr-2022 15:18:18

TB-DP-3u 40 (0.751)

1: TOF MS ES+
1.08e6



Elemental Composition Report

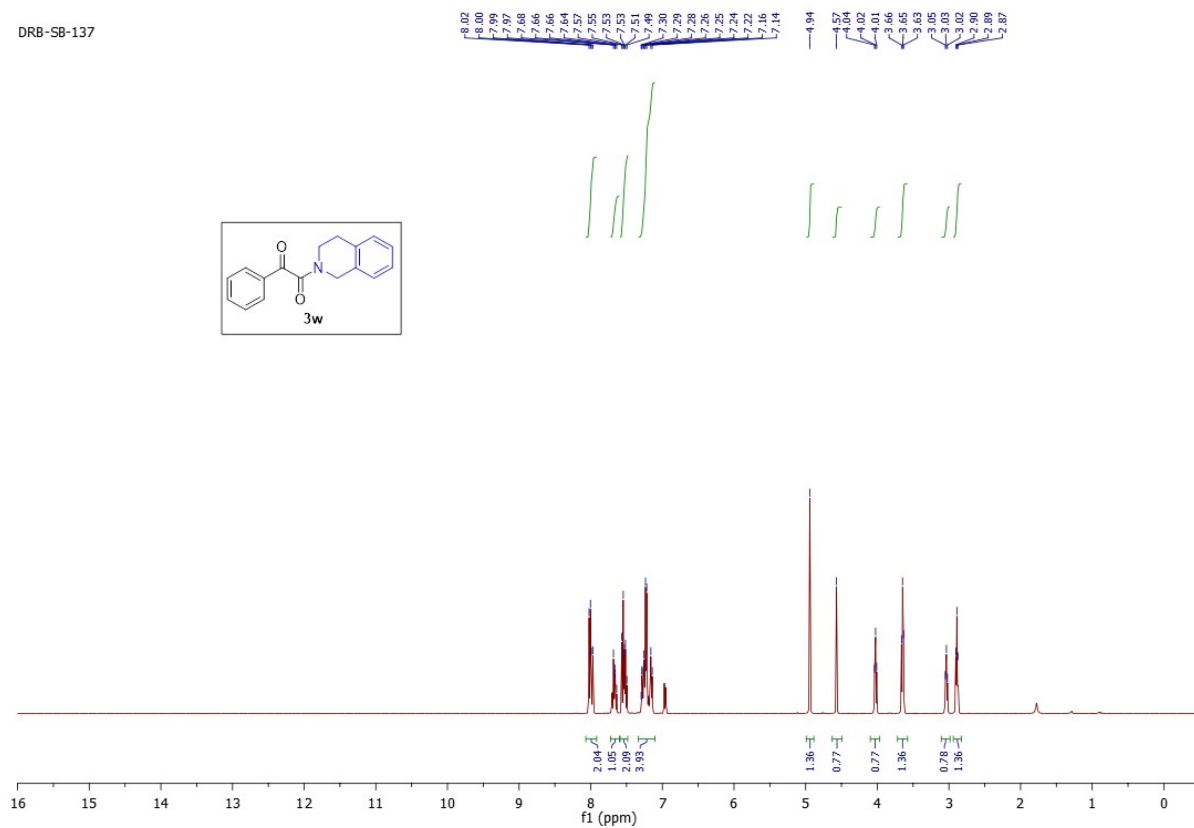
Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
11 formula(e) evaluated with 1 results within limits (up to 1 closest results for each mass)

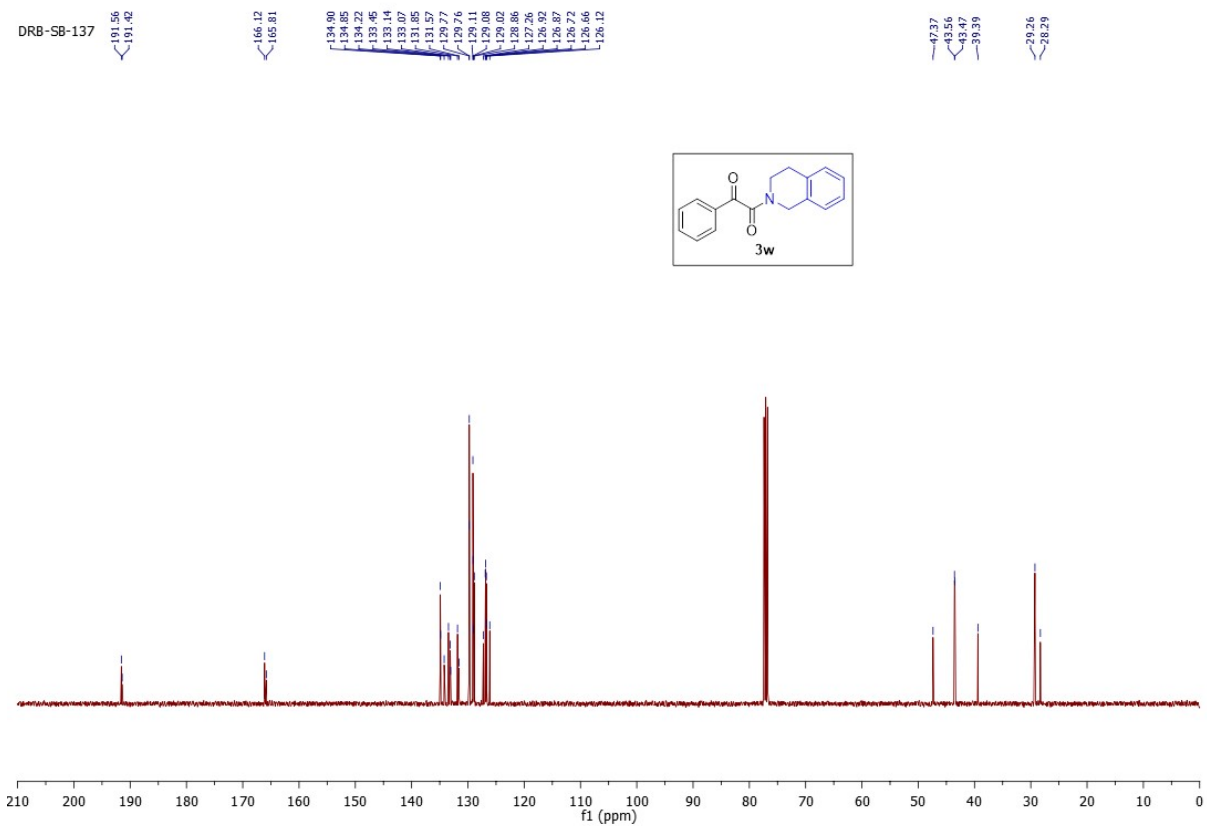
Elements Used:
C: 5-20 H: 0-19 N: 1-4 O: 1-4

| Minimum: | 5.0 | 100.0 | 50.0 | -1.5 | | |
|----------|------------|-------|------|------|---------------|--|
| Mass | Calc. Mass | mDa | PPM | DBE | Formula | |
| 379.1411 | 379.1406 | 0.5 | 1.3 | 13.5 | C20 H19 N4 O4 | |

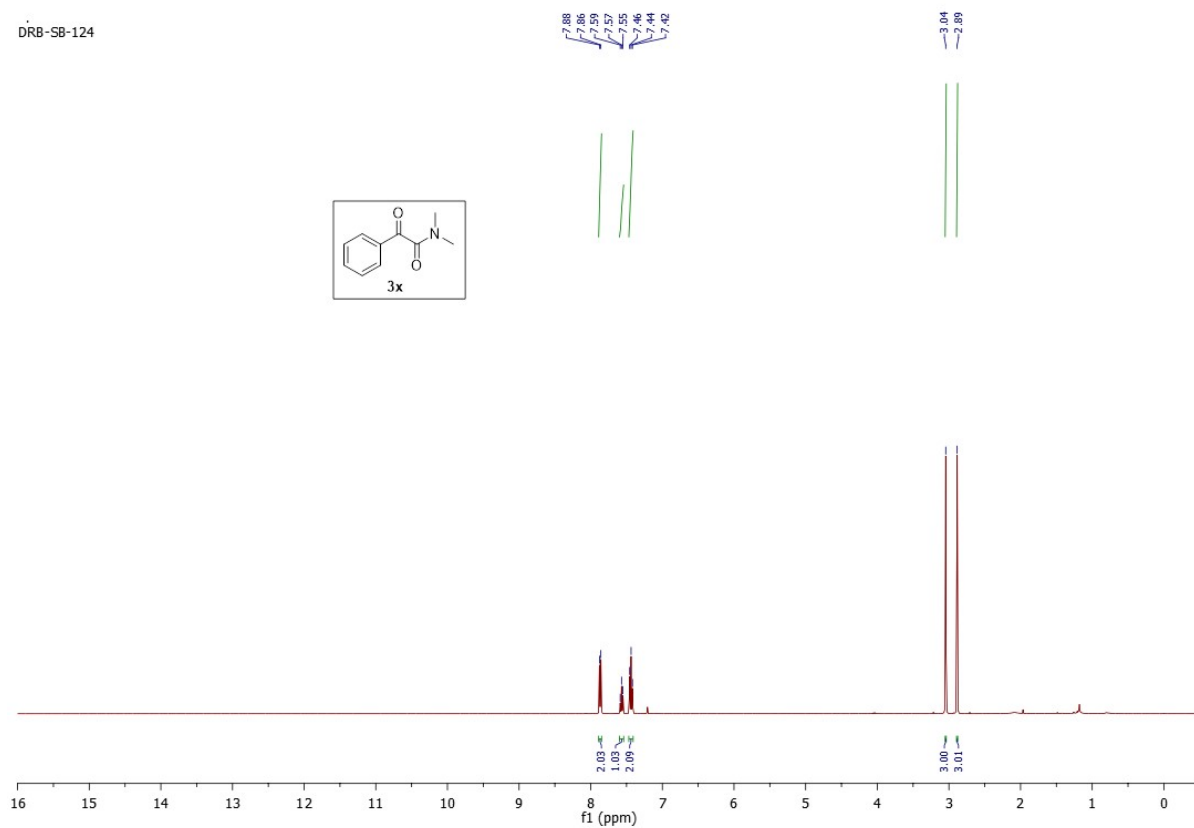
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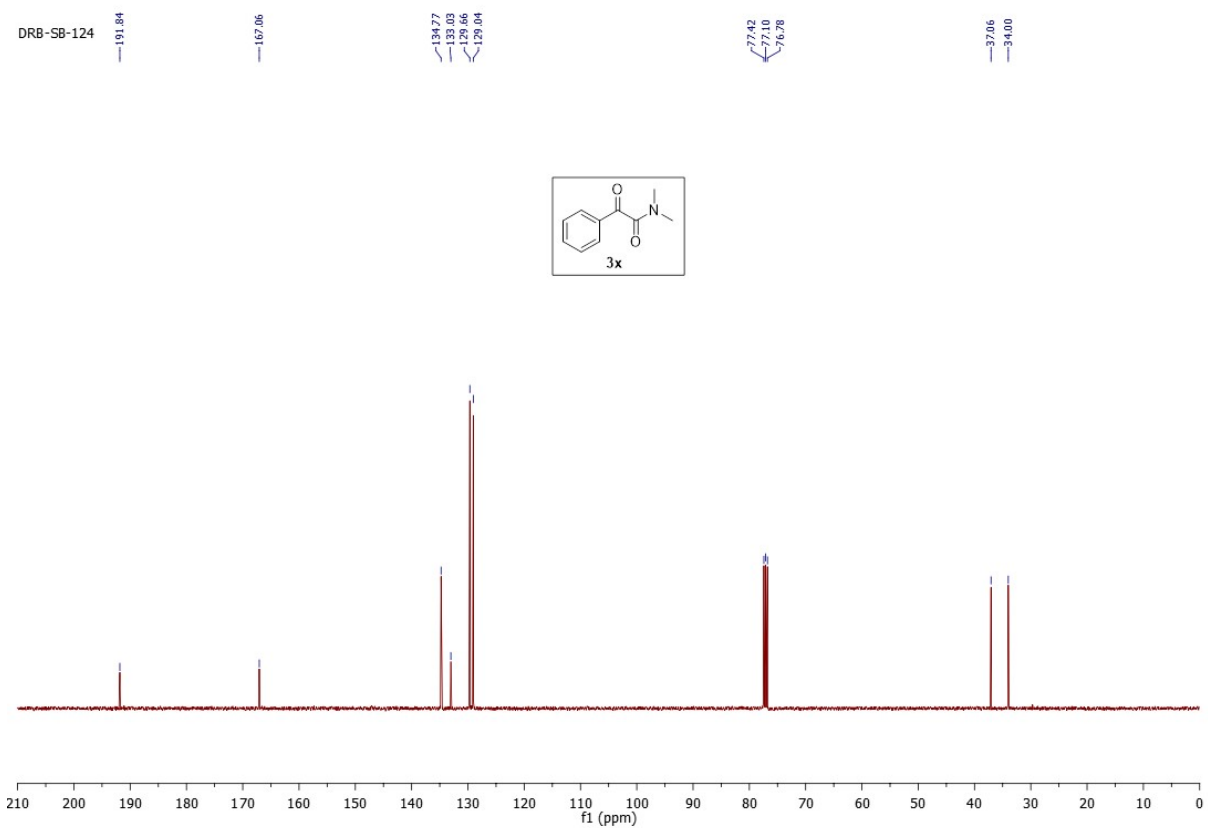
DRB-SB-137



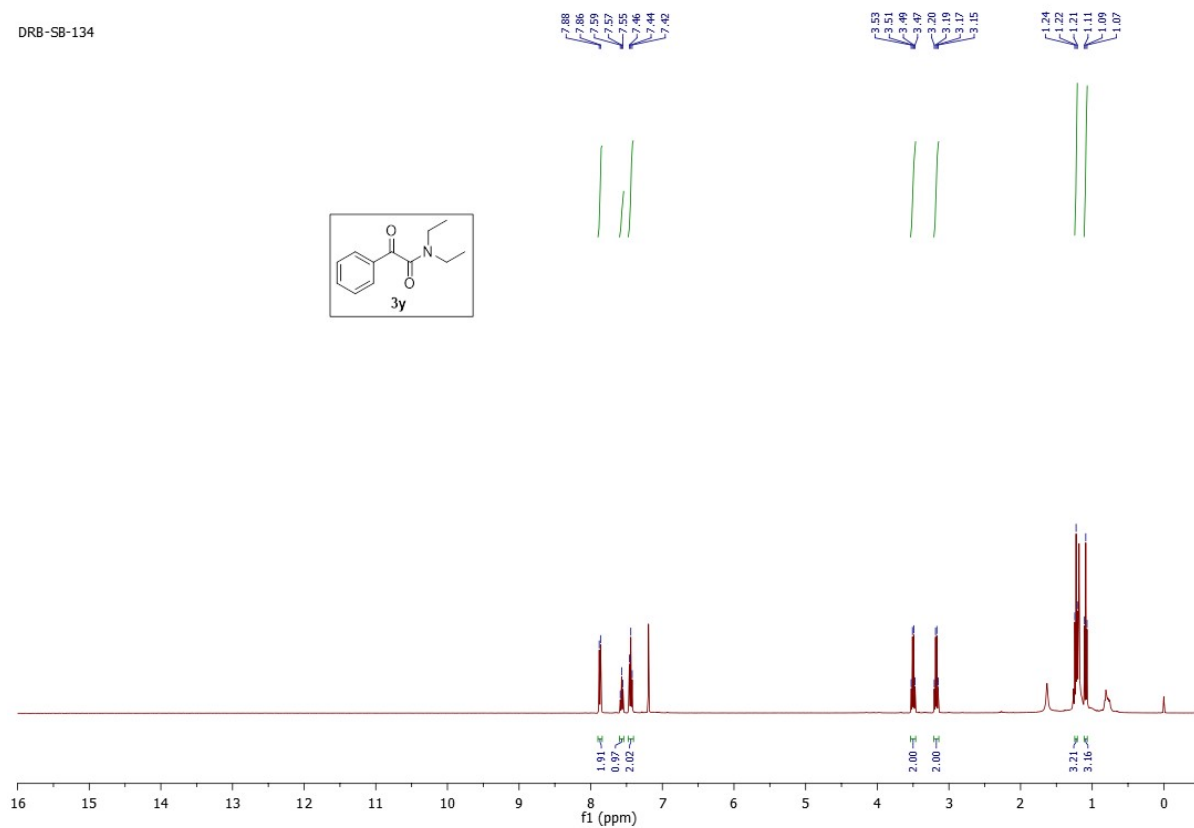
DRB-SB-124



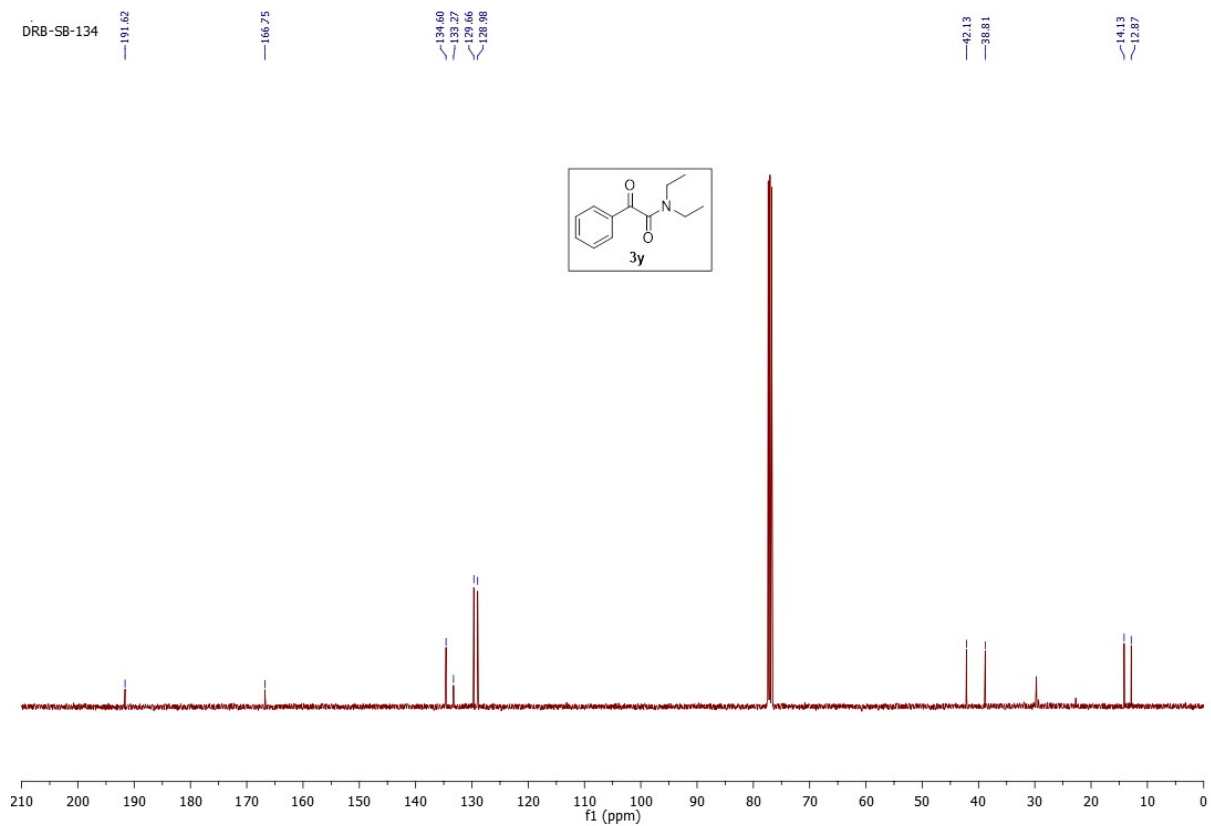
DRB-SB-124



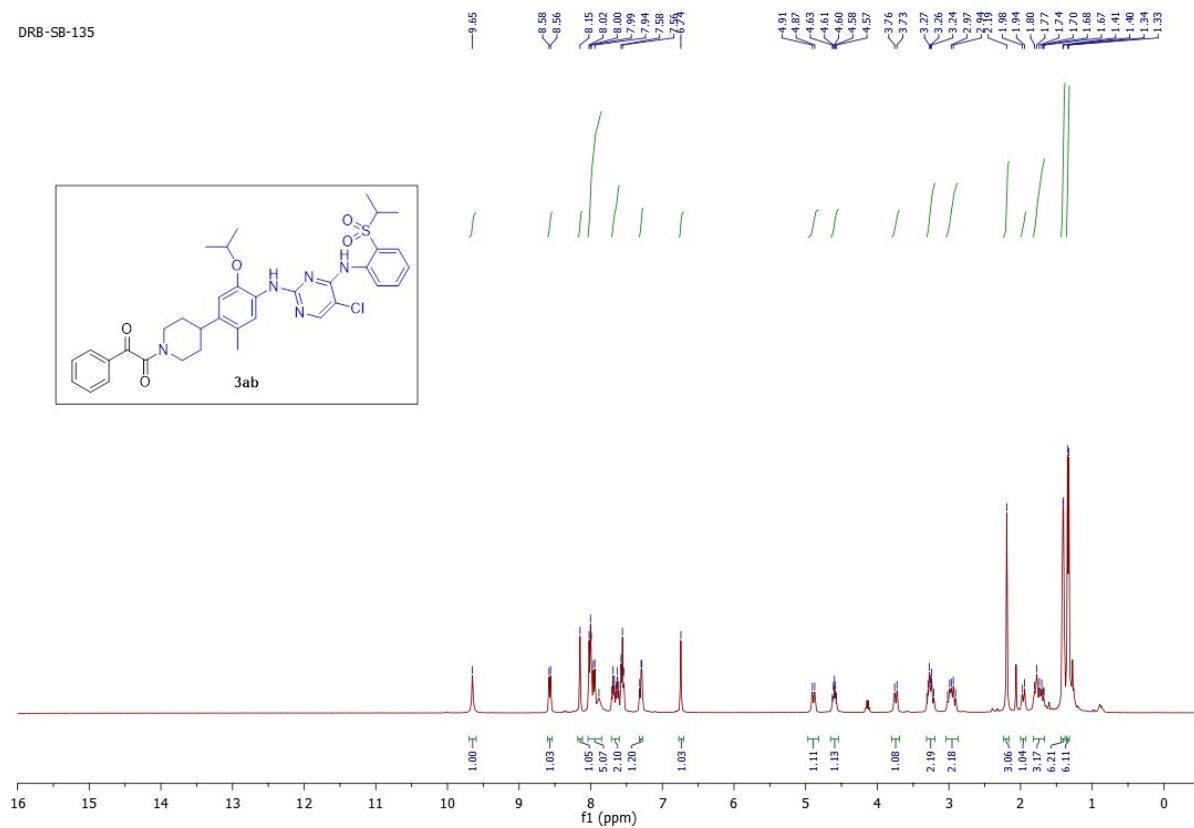
DRB-SB-134



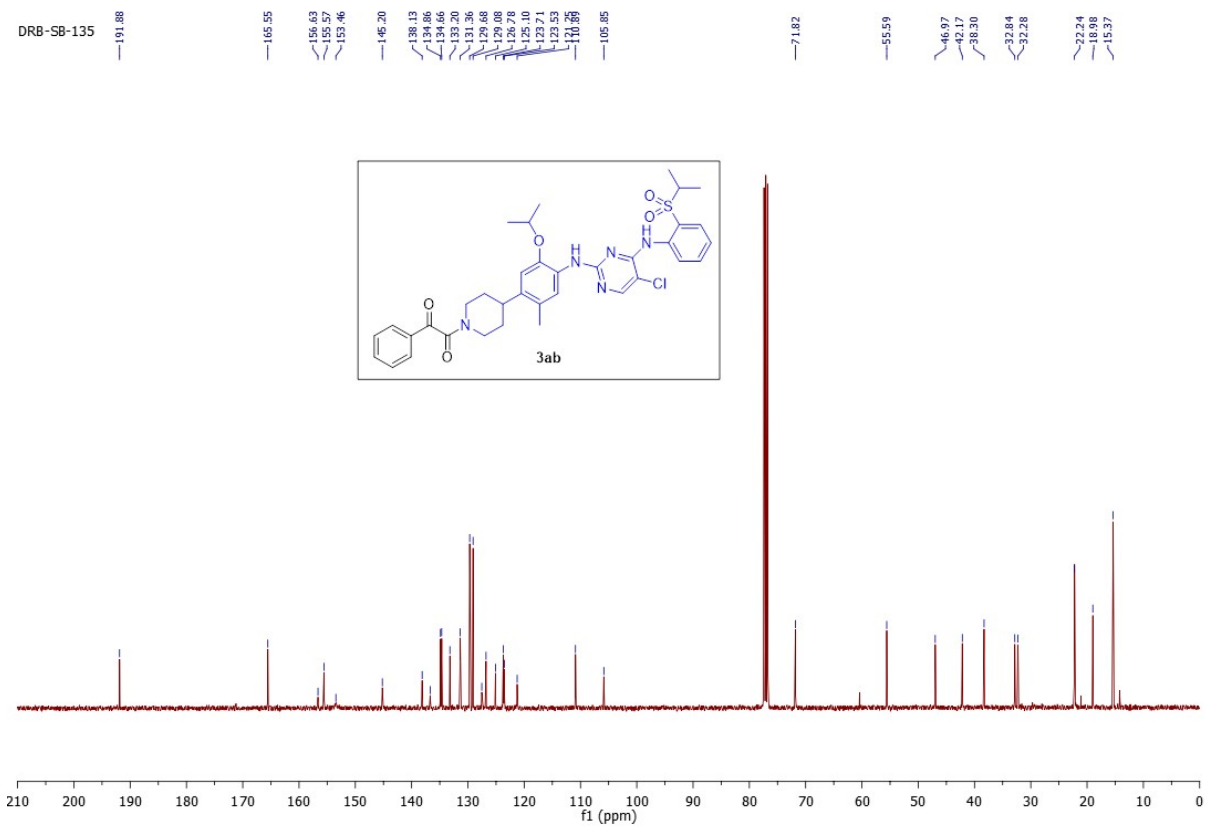
DRB-SB-134



DRB-SB-135



DRB-SB-135

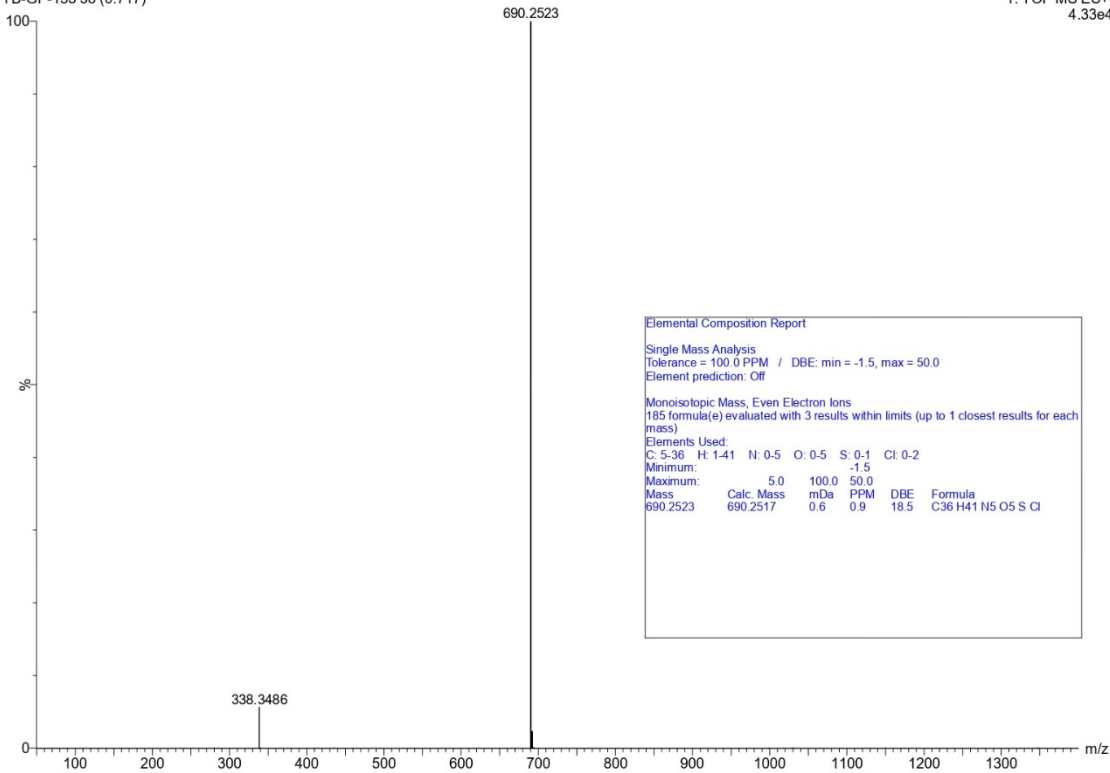


TB

12-Apr-2022 11:35:15

TB-GP-135 38 (0.717)

1: TOF MS ES+
4.33e4



Elemental Composition Report

Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
185 formula(e) evaluated with 3 results within limits (up to 1 closest results for each mass)

Elements Used:
C: 5-36 H: 1-41 N: 0-5 O: 0-5 S: 0-1 Cl: 0-2

| Mass | Calc. Mass | mDa | PPM | DBE | Formula |
|----------|------------|-----|-----|------|--|
| 690.2523 | 690.2517 | 0.6 | 0.9 | 18.5 | C ₃₆ H ₄₁ N ₅ O ₅ S Cl |