Supporting information

for

Copper-TEMPO-catalyzed synthesis of α-ketoamide via tandem sp^3C-H aerobic oxidation and amination of phenethyl alcohol derivatives

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General experimental information

Reagents and solvents: Commercially available reagents were used without any further purification. All organic solvents were also of reagent grade quality without any further purification.

Chromatography: Flash column chromatography was performed using silicycle silica gel (200-300 mesh).

Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates (HSGF 254) and visualized using a UV lamp (254 nm or 365 nm).

Nuclear Magnetic Resonance Spectroscopy:

^{1}H NMR was recorded on magnet system 400'54 ascend purchased from Bruker Biospin AG. ^{1}H NMR spectra chemical shifts (δ) are reported in parts per million (ppm) referenced to TMS (0 ppm).

^{13}C NMR spectra chemical shifts (δ) are reported in parts per million (ppm) were referenced to carbon resonances in the NMR solvent.

ESI-MS spectra were recorded on Agilent Q-TOF 6520.

Scheme S1 Traditional methods for the synthesis of α-ketoamides

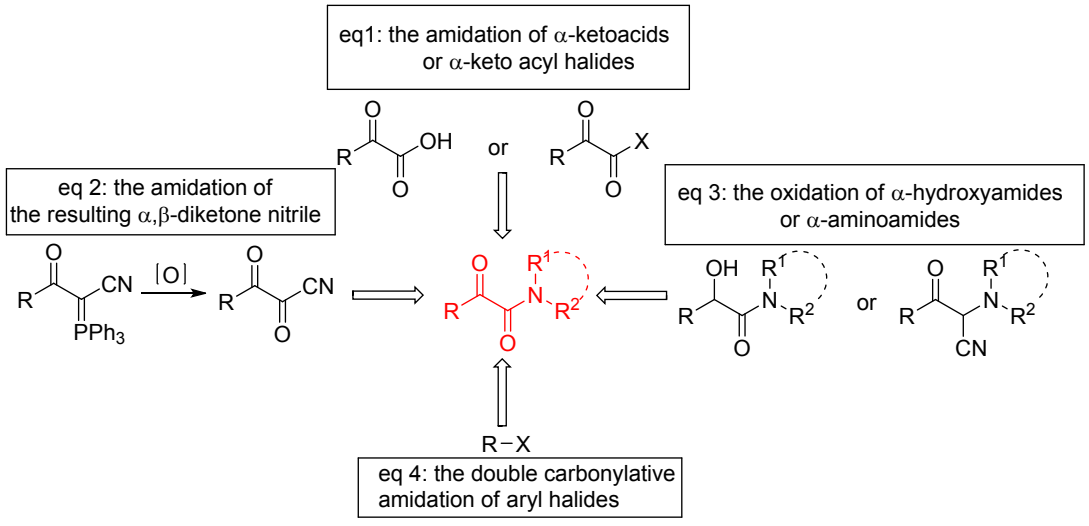
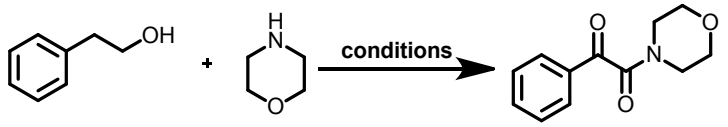


Table S1 optimization of the reaction condition[a]

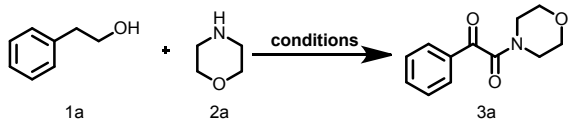


1a 2a 3a

Entry	Catalyst	Additive	Solvent	T(℃)	Yield (%)[b]
1	$CuBr_2$	pyridine	Toluene	90	8
2	CuI	pyridine	Toluene	90	trace
3	$CuBr_2$/CuI	pyridine	Toluene	90	76
4	CuBr	pyridine	Toluene	90	88
5	CuO	pyridine	Toluene	90	NO
6	$NiBr_2$	pyridine	Toluene	90	NO
7[c]	CuBr	pyridine	Toluene	90	52
8[d]	CuBr	pyridine	Toluene	90	NO
9	CuBr		Toluene	90	4
10	CuBr	TEA	Toluene	90	70
11	CuBr	DIPEA	Toluene	90	73
12	CuBr	K_2CO_3	Toluene	90	86
13	CuBr	Cs_2CO_3	Toluene	90	34
14	CuBr	K_2CO_3	DMSO	90	85
15	CuBr	K_2CO_3	DMF	90	72
16	CuBr	K_2CO_3	Dioxane	90	62
17	CuBr	K_2CO_3	DMSO	80	85
18	CuBr	K_2CO_3	DMSO	70	86
19	CuBr	K_2CO_3	DMSO	60	72
20[e]	CuBr	K_2CO_3	DMSO	70	84

[a]Reaction condition: 1a (1 mmol), 2a (3 mmol), catalyst (0.1 mmol), additive (2 mmol), TEMPO (0.2 mmol) and solvent (3 mL) were heated under O_2 (O_2 balloon) for 12h. [b]Yields of the isolated product. [c]In the absence of TEMPO. [d]Under N_2. [e]Under air.

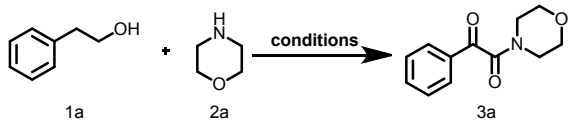
Table S2: the equiv. of TEMPO screening[a]



Entry	Equiv. of TEMPO	Yield[b] (%)
1	0.2	86
2	0.15	85
3	0.1	78
4	0.05	83

[a]reaction conditions: 1a (1 mmol), 2a (3 mmol), CuBr (10 mmol%), TEMPO, K_2CO_3 (2 mmol) in DMSO (3 mL) at 70℃ under air for 12h.
[b]ioslated yield.
[c]24h.

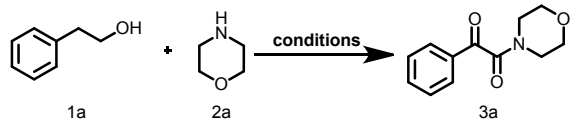
Table S3: the equiv. of CuBr screening[a]



Entry	Equiv. of CuBr	Yield[b] (%)
1	0.1	86
2	0.08	82
3	0.05	72
4	0.02	85[c]

[a]reaction conditions: 1a (1 mmol), 2a (3 mmol), CuBr, TEMPO (15 mmol%), K_2CO_3 (2 mmol) in DMSO (3 mL) at 70℃ under air for 12h.
[b]ioslated yield.
[c]24h.

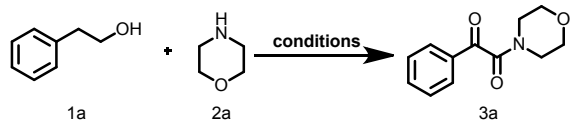
Table S4: the equiv. of K_2CO_3 screening[a]



Entry	Equiv. of K_2CO_3	Yield[b] (%)
1	2	86
2	1.5	83
3	1	84

[a]reaction conditions: 1a (1 mmol), 2a (3 mmol), CuBr (8 mmol%), TEMPO (15 mmol%), K_2CO_3 in DMSO (3 mL) at 70℃ under air for 12h.
[b]ioslated yield.

Table S5: the equiv. of amine screening[a]



Entry	Equiv. of amine	Yield[b] (%)
1	3	86
2	2.5	88
3	2	84
4	1.5	85

[a]reaction conditions: 1a (1 mmol), 2a, CuBr (8 mmol%), TEMPO (15 mmol%), K_2CO_3 (1 mmol) in DMSO (3 mL) at 70℃ under air for 12h.
[b]ioslated yield.

General experimental details for the synthesis of α-ketoamides

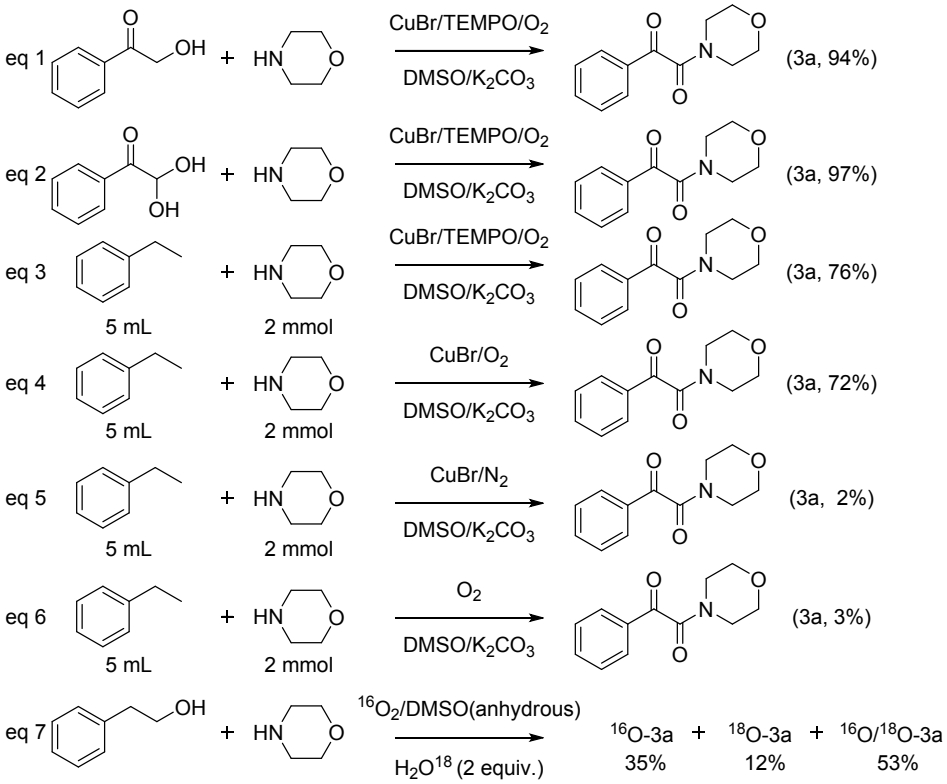
aliphatic amines used as the substrates

The specific phenethyl alcohol derivative (1 mmol, 1.0 eq), aliphalic amine (1.5 mmol, 1.5 eq) and TEMPO (0.15 mmol, 0.15 eq) were dissolved in DMSO (3 mL). Then, CuBr (0.08 mmol, 0.08 eq) and K_2CO_3 (1 mmol, 1 eq) were added to the reaction mixture and stirred for a certain time in a preheated oil batch at 70℃ under air. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL) or dichloromethane (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate or dichloromethane/methanol to afford the desired product.

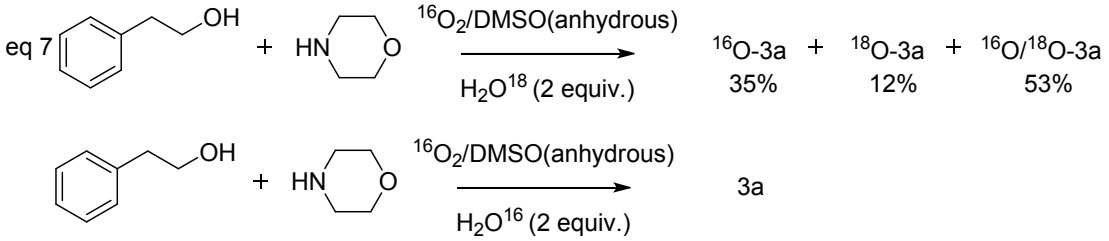
substituted anilines used as the substrates

The specific phenethyl alcohol derivative (1 mmol, 1.0 eq), substituted anilines (1.5 mmol, 1.5 eq) and TEMPO (0.15 mmol, 0.15 eq) were dissolved in toluene (3 mL). Then, CuBr (0.08 mmol, 0.08 eq) and pyridine (2 mmol, 2 eq) were added to the reaction mixture and stirred for a certain time in a preheated oil batch at 70℃ under air. The reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate to afford the desired product.

Figure S1 control experiments

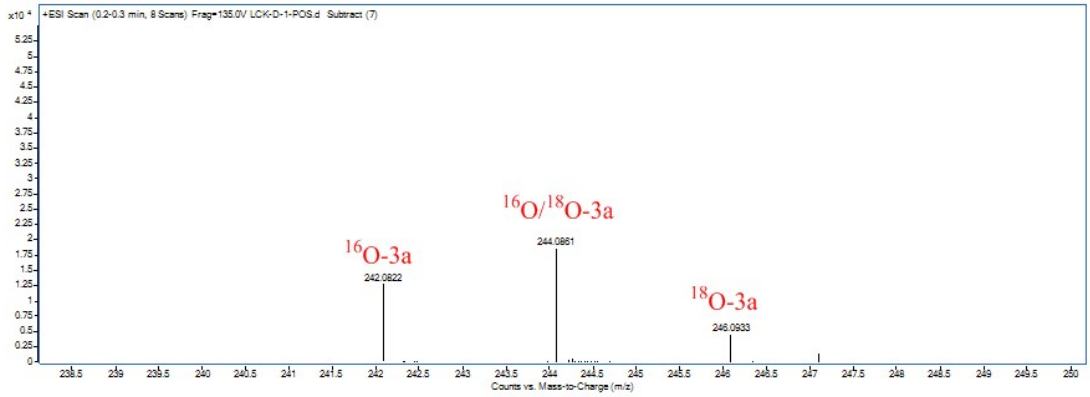


The label experiment of eq 7



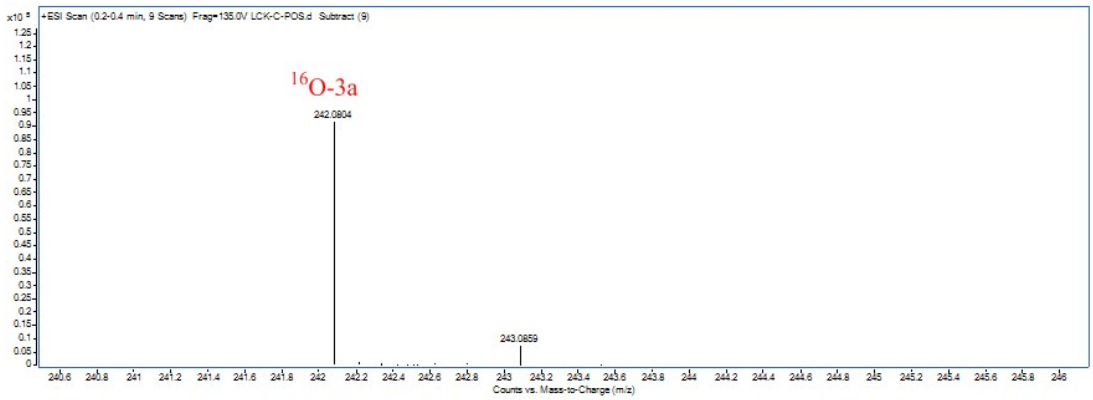
The ^{18}O was determined by HRMS.

The HRMS spectra of 3a for the reaction under H_2O^{18}



Reaction condition: CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol (122.2 mg, 1 mmol), 1-oxa-4-azacyclohexane (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) and H_2O^{18} (36.0 mg, 2 mmol) were mixed in anhydrous DMSO (3 mL) under air (air balloon). The reaction mixture was stirred at 70 °C for 2 h.

The HRMS spectra of 3a for the reaction under H_2O^{16}



Reaction condition: CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol (122.2 mg, 1 mmol), 1-oxa-4-azacyclohexane (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) and H_2O^{16} (36.0 mg, 2 mmol) were mixed in anhydrous DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 2 h.

The detailed mechanism in Jiao's report

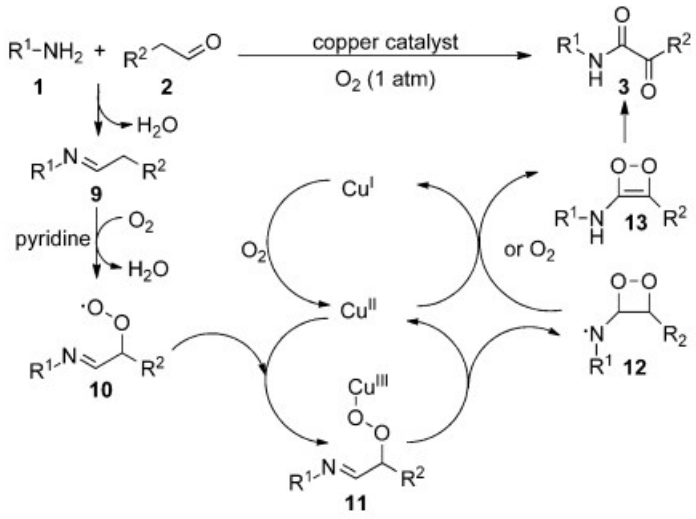
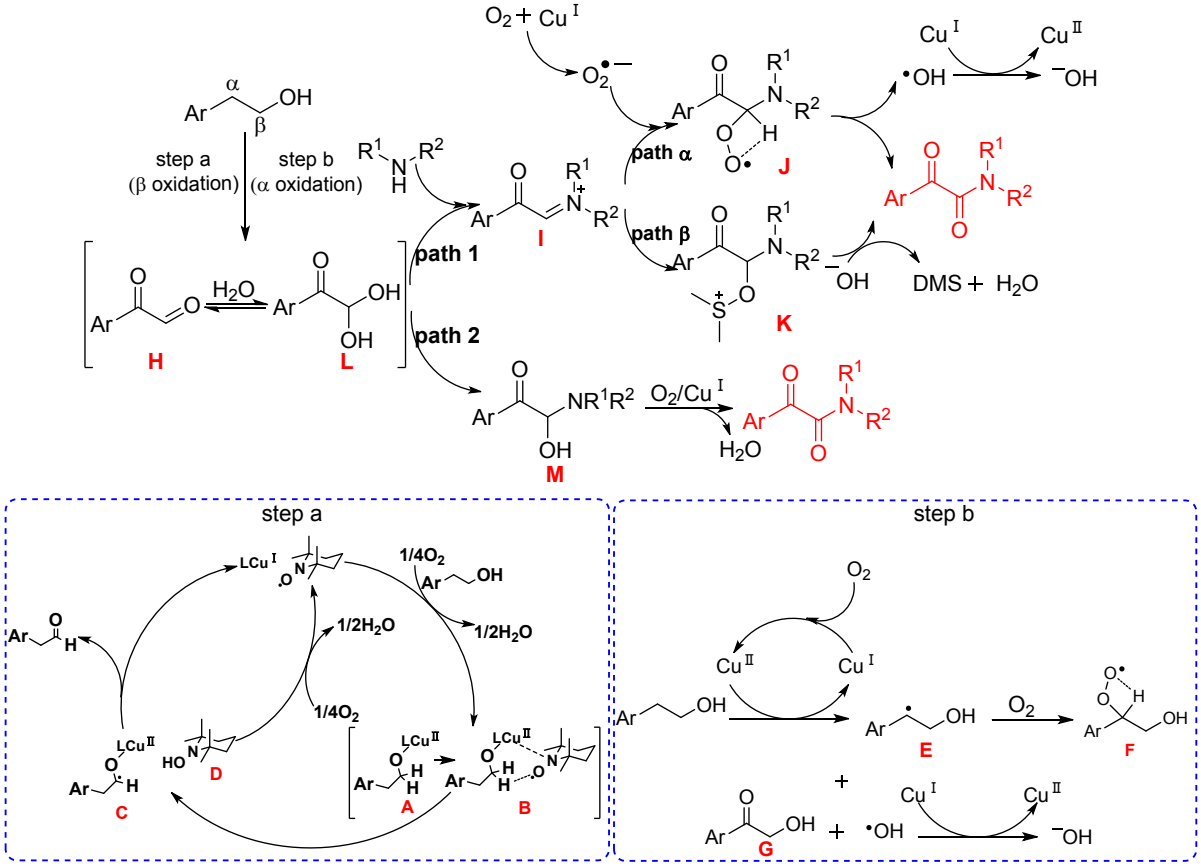
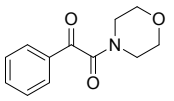


Figure S2: a plausible mechanism for our system



Analytical data for compounds 3 and P



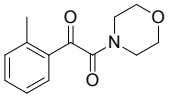
3a

1)

1-Morpholino-2-phenylethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (188.4 mg, 86% yield); mp 89-91℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.3 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 3.78 (br, s, 4H), 3.67 – 3.60 (m, 2H), 3.40 – 3.33 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 191.29, 165.59, 135.08, 133.20, 129.82, 129.24, 66.88, 66.81, 46.41, 41.76; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{13}NO_3$ 242.0788 found 242.0783.



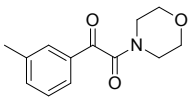
3b

2)

1-Morpholino-2-(*o*-tolyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2-methyl-benzeneethano 1b (136.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (191.3 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 6.8 Hz, 1H),7.50 (t, J = 6.9 Hz, 1H), 7.33 (dd, J = 10.0, 7.7 Hz, 2H), 3.79 (d, J = 3.1 Hz, 4H), 3.69 – 3.65 (m, 2H), 3.42 – 3.37 (m, 2H), 2.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.21, 166.30, 141.75, 134.00, 132.82, 131.80, 131.58, 126.33, 66.77, 66.75, 46.38, 41.72, 21.94; HRMS (TOF) m/z [M + H]$^+$Calcd for $C_{13}H_{15}NO_3$ 234.1125 found 234.1122.



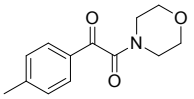
3c

3)

1-Morpholino-2-(*m*-tolyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 3-methylphenethyl alcohol 1c (136.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

White solid (195.9 mg, 84% yield); ^{1}H NMR (300 MHz, DMSO) δ 7.71 (s, 2H), 7.55 (dd, *J* = 19.2, 7.1 Hz, 2H), 3.68 (dd, *J* = 14.2, 3.5 Hz, 4H), 3.52 (t, *J* = 4.2 Hz, 2H), 3.28 (t, *J* = 5.1 Hz, 2H), 2.41 (s, 3H);^{13}C NMR (75 MHz, DMSO) δ 191.70 (s), 164.97, 138.98, 135.83, 132.69, 129.24, 126.72, 66.03, 65.83, 45.67, 40.99, 20.71; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{13}H_{15}NO_3$ 234.1125 found 234.1112.

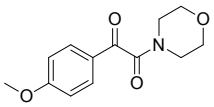
4) 

3d

1-Morpholino-2-(*p*-tolyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2-(4-methyphenyl)ethanol 1d (136.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

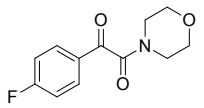
Yellow solid (188.8 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 3.77 (br, s, 4H), 3.64 – 3.60 (m, 2H), 3.37 – 3.33 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 190.98, 165.75, 146.36, 130.73, 129.90, 129.86, 66.82, 66.74, 46.34, 41.64, 22.00; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{13}H_{15}NO_3$ 234.1125 found 234.1106.

5) 

3e

1-(4-Methoxyphenyl)-2-morpholinoethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 4-methoxyphenethyl alcohol 1e (152.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. Only trace amount of product was detected.



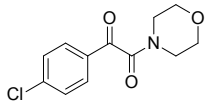
3f

6)

1-(4-fluorophenethyl)-2-morpholinoethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 4-fluorophenethyl alcohol 1f (140.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (170.7 mg, 72% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.95 (m, 2H), 7.19 (t, J = 8.5 Hz, 2H), 3.79 (s, 4H), 3.70 – 3.62 (m, 2H), 3.43 – 3.34 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 189.50, 166.94 (d, J=256.7), 165.22, 132.69 (d, J=9.8), 129.75 (d, J=2.8), 116.70, 116.48, 66.89, 66.79, 46.44, 41.84; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{12}H_{12}FNO_3$ 238.0874 found 238.0876.



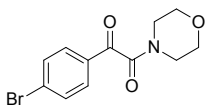
3g

7)

1-(4-Chlorophenyl)-2-morpholinoethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 4-chlorophenethylalcohol 1g (156.6 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (192.3 mg, 76% yield); mp 112-114℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.85 (m, 2H), 7.56 – 7.46 (m, 2H), 3.82 – 3.74 (m, 4H), 3.69 – 3.63 (m, 2H), 3.42 – 3.34 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 188.83, 164.04, 140.76, 130.61, 130.18, 128.64, 65.88, 65.79, 45.43, 40.85; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{12}H_{12}ClNO_3$ 276.0398 found 276.0374.



3h

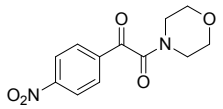
8)

1-(4-bromophenethyl)-2-morpholinoethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 4-bromophenethyl alcohol 1h (200.1 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg,

1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

White solid (243.5 mg, 82% yield); mp 122-124℃; ^{1}H NMR (300 MHz, DMSO) δ 7.84 (s, 4H), 3.74-3.68 (m, 2H), 3.67-3.62 (m, 2H), 3.53 (t, *J* = 4.2 Hz, 2H), 3.30 (t, *J* = 4.5 Hz, 2H); ^{13}C NMR (75 MHz, DMSO) δ 190.51 (s), 164.42 (s), 132.53 (s), 131.65 (s), 131.16 (s), 129.52 (s), 66.05 (s), 65.77 (s), 45.66 (s), 41.09 (s); HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{12}BrNO_3$ 319.9893 found 3199872.



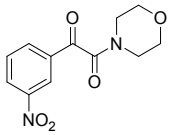
3i

9)

1-Morpholino-2-(4-nitrophenyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 4-nitrobenzeneethanol 1i (167.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (4:1) to afford the desired product.

Yellow solid (119.9mg, 42% yield); mp 142-144℃; ^{1}H NMR (400 MHz, DMSO) δ 8.41 (d, *J* = 8.4 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 2H), 3.74 (t, *J* = 4.4 Hz, 2H), 3.67 (t, *J* = 5.2 Hz, 2H), 3.56 (t, *J* = 4.4 Hz, 2H), 3.36 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 189.78 (s), 163.89 (s), 150.90 (s), 136.96 (s), 130.84 (s), 124.37 (s), 66.05 (s), 65.73 (s), 45.66 (s), 41.23 (s); HRMS (TOF) m/z [M + K]$^+$ Calcd for $C_{12}H_{12}N_2O_5$ 303.0378 found 303.0330.



3j

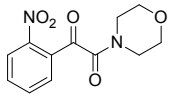
10)

1-Morpholino-2-(3-nitrophenyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 3-nitrobenzeneethanol 1j (167.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (4:1) to afford the desired product.

Yellow solid (103.0mg, 39% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (t, J = 1.8 Hz, 1H), 8.48

(ddd, J = 8.2, 2.2, 1.0 Hz, 1H), 8.34 – 8.27 (m, 1H), 7.74 (t, J = 8.0 Hz, 1H), 3.83 – 3.79 (m, 4H), 3.72 – 3.67 (m, 2H), 3.46 – 3.42 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 188.25, 164.00, 148.73, 135.24, 134.66, 130.48, 128.96, 124.64, 66.85, 66.74 46.48, 42.10; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{12}N_2O_5$ 287.0638 found 287.0623.



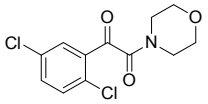
3k

11)

1-Morpholino-2-(2-nitrophenyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2-nitrophenethyl alcohol 1k (167.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (4:1) to afford the desired product.

Yellow solid (95.1mg, 36% yield); ^{1}H NMR (400 MHz, DMSO) δ 8.19 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.95 (td, *J* = 7.5, 1.1 Hz, 1H), 7.91 – 7.82 (m, 2H), 3.75 (d, *J* = 1.2 Hz, 4H), 3.65 (t, *J* = 4.4 Hz 2H), 3.55 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 187.03 (s), 161.75 (s), 147.07 (s), 134.83 (s), 133.48 (s), 131.71 (s), 131.14 (s), 124.15 (s), 66.01 (d, *J* = 16.8 Hz), 45.98 (s), 42.11 (s); HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{12}H_{12}N_2O_5$ 287.0638 found 287.0637.



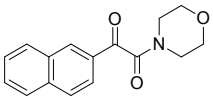
3l

12)

1-Morpholino-2-(2,5-dichloropheneyl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2,5-dichlorophenethyl alcohol 1l (191.0 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (186.6 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.5 Hz, 1H), 7.39 (dd, J = 9.4, 7.7 Hz, 1H), 7.34 – 7.25 (m, 1H), 3.74 – 3.61 (m, 6H), 3.47 (d, J = 3.9 Hz, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 187.39, 163.81, 134.03, 133.29, 132.93, 130.92, 130.90, 130.67, 65.38, 65.33, 45.28, 41.13; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{12}H_{11}Cl_2NO_3$ 288.0189 found 288.0165.



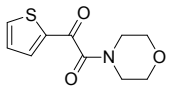
3m

13)

1-Morpholino-2-(naphthalen-2-yl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2-naphthaleneethanol 1m (172.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (220.7 mg, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.04 – 7.86 (m, 4H), 7.61 (dt, J = 28.4, 7.3 Hz, 2H), 3.84 (s, 4H), 3.72 – 3.61 (m, 2H), 3.47 – 3.36 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 191.34, 165.70, 136.54, 133.16, 132.53, 130.53, 130.02, 129.66, 129.30, 128.08, 127.35, 123.68, 66.87, 66.82, 46.47, 41.83; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{16}H_{15}NO_3$ 270.1125 found 270.1140.



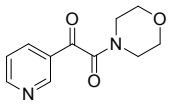
3n

14)

1-Morpholino-2-(thiophen-2-yl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 2-thiopheneethanol 1n (128.2 mg, 1 mmol), 1-oxa-4-azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow oil (155.3 mg, 69% yield); mp 93-95℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (ddd, J = 5.9, 4.4, 1.0 Hz, 2H), 7.17 (dd, J = 4.8, 4.0 Hz, 1H), 3.78 – 3.71 (m, 4H), 3.69 – 3.62 (m, 2H), 3.51 – 3.44 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 182.90, 164.41, 140.36, 136.87, 136.37, 128.82, 66.89, 66.70, 46.52, 42.03; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{10}H_{11}NO_3S$ 226.0532 found 226.0552.



3o

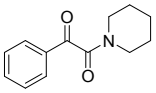
15)

1-Morpholino-2-(pyridine-3-yl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), 3-(2-hydroxyethyl)pyridine 1o (123.2 mg, 1 mmol), 1-oxa-4-

azacyclohexane 2a (130.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (4:1) to afford the desired product.

Yellow solid (121.0 mg, 55% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.81 – 8.75 (m, 1H), 8.19 (dd, J = 8.0, 2.0 Hz, 1H), 7.46 – 7.37 (m, 1H), 3.72 (s, 4H), 3.63 – 3.58 (m, 2H), 3.38 – 3.33 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 189.45, 164.13, 154.80, 151.17, 136.73, 128.77, 123.92, 66.68, 66.55, 46.25, 41.79; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{11}H_{12}N_2O_3$ 221.0921 found 221.0928.

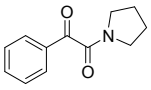


16) 3p

1-Phenyl-2-(piperidin-1-yl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), azocyclohexane 2b (127.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (184.5 mg, 85% yield); mp 94-96℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 1.4 Hz, 2H), 7.65 – 7.59 (m, 1H), 7.49 (t, J = 7.7 Hz, 2H), 3.69 (s, 2H), 3.31 – 3.23 (m, 2H), 1.71 – 1.64 (m, 4H), 1.57 – 1.47 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 192.05, 165.54, 134.74, 133.36, 129.65, 129.09, 47.12, 42.24, 26.29, 25.54, 24.47; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{13}H_{15}NO_2$ 218.1184 found 218.1184.

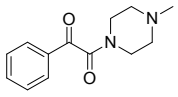


17) 3q

1-Phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), tetrahydro pyrrole 2c (106.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (168.6 mg, 83% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.94 (m, 2H), 7.62 (t, J = 8.0 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 3.64 (t, J = 6.8 Hz, 2H), 3.40 (t, J = 6.2 Hz, 2H), 2.00 – 1.87 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.59, 164.93, 134.59, 132.86, 129.80, 128.91, 46.62, 45.19, 25.85, 23.96; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{12}H_{13}NO_2$ 204.1019 found 204.1026.

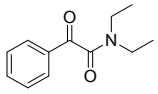


18) 3r

1-(4-Methylpiperazin-1-yl)-2-phenylethane-1,2-dione:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 1-methylpiperazine 2d (150.3 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by dichloromethane (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using dichloromethane/methanol (30:1) to afford the desired product.

Yellow solid (188.0 mg, 81% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 3.82 – 3.71 (m, 2H), 3.39 – 3.28 (m, 2H), 2.51 – 2.45 (m, 2H), 2.36 – 2.32 (m, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 191.54, 165.44, 134.88, 133.16, 129.69, 129.11, 54.95, 54.49, 46.04, 45.81, 41.20; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{13}H_{16}N_2O_2$ 233.1285 found 233.1281.

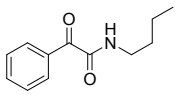


19) 3s

N,N-Diethyl-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), diethylamine 2e (219.4 mg, 3 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air (air balloon). The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (6:1) to afford the desired product.

Yellow solid (108.7 mg, 53% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.85 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 3.53 (q, J = 7.2 Hz, 2H), 3.21 (q, J = 7.1 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 191.66, 166.80, 134.64, 133.28, 129.64, 129.01, 42.16, 38.85, 14.14, 12.87; HRMS (TOF) m/z [M + H]$^+$ Calcd for $C_{12}H_{15}NO_2$ 206.1176 found 206.1191.

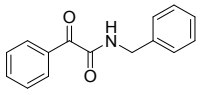


20) 3t

N-Butyl-2-oxo-2- phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), butylamine 2f (219.4 mg, 3 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air (air balloon). The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (7:1) to afford the desired product.

Yellow oil (41.0 mg, 20% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.23 (m, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.07 (s, 1H), 3.32 (dd, *J* = 13.4, 7.0 Hz, 2H), 1.56 – 1.47 (m, 2H), 1.38-1.28 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.93, 160.75, 133.32, 132.35, 130.17, 127.44, 38.13, 30.30, 19.03, 12.68; HRMS (TOF) m/z $[M + H]^+$ Calcd for $C_{12}H_{15}NO_2$ 206.1176 found 206.1193.

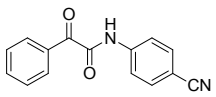


21) 3u

N-Benzyl-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), benzylamine 2g (160.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and K_2CO_3 (138.2 mg, 1 mmol) were mixed in DMSO (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (20:1) to afford the desired product.

Yellow solid (35.8 mg, 15% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.24 (m, 2H), 7.54 (tt, 7.6, 1.2,1H), 7.43 – 7.35 (m, 3H), 7.30 – 7.20 (m, 5H), 4.48 (d, *J* = 6.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.53, 160.55, 136.08, 133.42, 132.25, 130.19, 127.80, 127.47, 126.86, 126.79, 42.42; HRMS (TOF) m/z $[M + Na]^+$ Calcd for $C_{15}H_{13}NO_2$ 262.0838 found 262.0861.



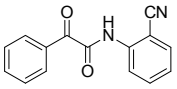
22) 3v

N-(4-Cyanophenyl)-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 4-aminobenzonitrile 2h (177.2 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol)

were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (10:1) to afford the desired product.

Yellow solid (210.0 mg, 84% yield); ^{1}H NMR (300 MHz, DMSO/ $CDCl_3$) δ 10.33 (s, 1H), 8.18 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.62-7.55 (m, 3H), 7.45 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, DMSO/$CDCl_3$) δ 187.28, 161.02, 141.23, 134.30, 132.65, 132.39, 130.45, 128.27, 120.04, 118.39, 107.19; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{15}H_{10}N_2O_2$ 249.0670 found 249.0747.

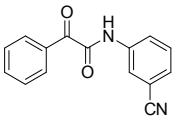


23) 3w

N-(2-Cyanophenyl)-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 2-aminobenzonitrile 2i (177.2 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (10:1) to afford the desired product.

Yellow solid (215.1 mg, 86% yield); ^{1}H NMR (300 MHz, DMSO) δ 11.27 (s, 1H), 8.15 (d, *J* = 7.4 Hz, 2H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.84 – 7.74 (m, 3H), 7.65 (t, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 188.86, 163.49, 138.51, 134.90, 134.06, 133.39, 132.54, 129.95, 128.99, 126.88, 125.95, 116.63, 108.10; HRMS (TOF) m/z [M + Na]$^+$ Calcd for $C_{15}H_{10}N_2O_2$ 273.0634 found 273.0692.

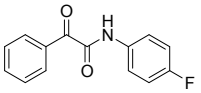


24) 3x

N-(3-Cyanophenyl)-2-oxo-2-phenylacetamide:

CuBr (177.2 mg, 1.5 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 3-aminobenzonitrile 2j (354.4 mg, 3 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (10:1) to afford the desired product.

White solid (210.0 mg, 84% yield); ^{1}H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 8.25 (s, 1H), 8.15 – 8.07 (m, 2H), 8.03 (dt, *J* = 6.5, 2.3 Hz, 1H), 7.78 (t, *J* = 7.4 Hz, 1H), 7.65-7.60 (m, 4H); ^{13}C NMR (75 MHz, DMSO) δ 188.71, 163.24, 138.47, 134.86, 132.41, 130.36, 130.07, 128.98, 128.07, 124.77, 122.99, 118.43, 111.77; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{15}H_{10}N_2O_2$ 249.0670 found 249.0743.



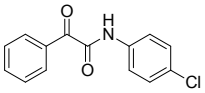
3y

25)

2-Oxo-2-phenyl-N-(4-fluorophenyl)acetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 4-fluoroaniline 2k (166.7 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (30:1) to afford the desired product.

^{1}H NMR (400 MHz, DMSO) δ 11.05 (s, 1H), 8.08 (d, *J* = 8.2 Hz, 2H), 7.84 – 7.74 (m, 3H), 7.62 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 189.32 (s), 163.01 (s), 159.95 (s), 157.55 (s), 134.77 (s), 134.06 (d, *J* = 2.5 Hz), 132.58 (s), 129.97 (s), 129.02 (s), 122.00 (d, *J* = 8.0 Hz), 115.68 (s), 115.45 (s); HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{14}H_{10}FNO_2$ 242.0623 found 242.0669.



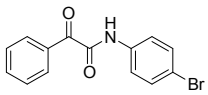
3z

26)

2-Oxo-2-phenyl-N-(4-chlorophenyl)acetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 4-chloroaniline 2l (191.4 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (30:1) to afford the desired product.

Yellow solid (165.8 mg, 64% yield); ^{1}H NMR (400 MHz, DMSO) δ 11.11 (s, 1H), 8.08 – 8.03 (m, 2H), 7.82 – 7.73 (m, 3H), 7.61 (t, *J* = 7.7 Hz, 2H), 7.49 – 7.43 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 189.13, 163.17, 136.62, 134.85, 132.48, 129.98, 129.05, 128.86, 128.29, 121.69; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{14}H_{10}ClNO_2$ 258.0327 found 258.0399.



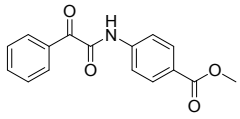
3aa

27)

2-Oxo-2-phenyl-N-(4-bromophenyl)acetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 4-bromoaniline 2m (258.1 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (30:1) to afford the desired product.

Yellow solid (187.8 mg, 62% yield); ^{1}H NMR (400 MHz, DMSO) δ 11.12 (s, 1H), 8.10 – 8.05 (m, 2H), 7.80 – 7.73 (m, 3H), 7.65 – 7.58 (m, 4H); ^{13}C NMR (101 MHz, DMSO) δ 189.10, 163.18, 137.05, 134.83, 132.48, 131.77, 129.99, 129.04, 122.05, 116.42; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{14}H_{10}BrNO_2$ 301.9822 found 301.9772.



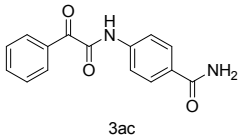
3ab

28)

2-Oxo-2-phenyl-N-(4-(methoxycarbonyl)phenyl)acetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 4-(methoxycarbonyl)aniline 2n (226.8 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (8:1) to afford the desired product.

Yellow solid (223.6 mg, 79% yield); ^{1}H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 8.12 – 8.06 (m, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.78 (t, *J* = 7.4 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.90, 165.66, 163.53, 141.98, 134.84, 132.40, 130.29, 129.96, 129.03, 125.28, 119.63, 51.91; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{16}H_{13}NO_4$ 282.0772 found 282.0825.



3ac

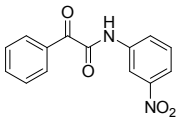
29)

2-Oxo-2-phenyl-N-(4-(aminocarbonyl)phenyl)acetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), p-aminobenzamide 2o (204.2 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After

cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (5:1) to afford the desired product.

White solid (198.4 mg, 74% yield); ^{1}H NMR (300 MHz, DMSO) δ 11.16 (s, 1H), 8.09 (d, *J* = 7.8 Hz, 2H), 7.96 (d, *J* = 8.3 Hz, 3H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.77 (t, *J* = 7.0 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 2H), 7.35 (s, 1H); ^{13}C NMR (75 MHz, DMSO) δ 189.13, 167.31, 163.43, 140.23, 134.84, 132.50, 130.15, 129.98, 129.06, 128.49, 119.38; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{15}H_{12}N_2O_3$ 267.0775 found 267.0852.



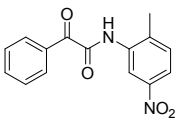
3ad

30)

N-(3-nitrophenyl)-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 3-nitroaniline 2p (207.3 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (5:1) to afford the desired product.

Yellow solid (202.5 mg, 75% yield); ^{1}H NMR (300 MHz, DMSO) δ 11.42 (s, 1H), 8.79 (t, *J* = 1.9 Hz, 1H), 8.14 – 8.07 (m, 3H), 8.03 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.81 – 7.59 (m, 4H); ^{13}C NMR (75 MHz, DMSO) δ 188.60, 163.28, 147.95, 138.80, 134.89, 132.39, 130.33, 130.11, 129.00, 126.15, 119.05, 114.36; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{14}H_{10}N_2O_4$ 269.0568 found 269.0601.



3ae

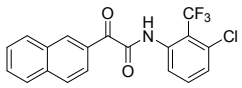
31)

N-(2-methyl-5-nitrophenyl)-2-oxo-2-phenylacetamide:

CuBr (11.5 mg, 0.08 mmol), phenethyl alcohol 1a (122.2 mg, 1 mmol), 2-methyl-5-nitroaniline 2q (228.2 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (5:1) to afford the desired product.

Yellow solid (238.6 mg, 84% yield); ^{1}H NMR (300 MHz, DMSO) δ 10.70 (s, 1H), 8.58 (d, *J* =

2.2 Hz, 1H), 8.14 – 8.09 (m, 2H), 8.05 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.78 (t, *J* = 7.4 Hz, 1H), 7.62 (dd, *J* = 18.3, 8.2 Hz, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 189.04, 163.97, 145.82, 139.96, 135.75, 134.82, 132.63, 131.69, 129.98, 129.06, 120.51, 119.05, 18.06; HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{15}H_{12}N_2O_4$ 283.0724 found 283.0758.

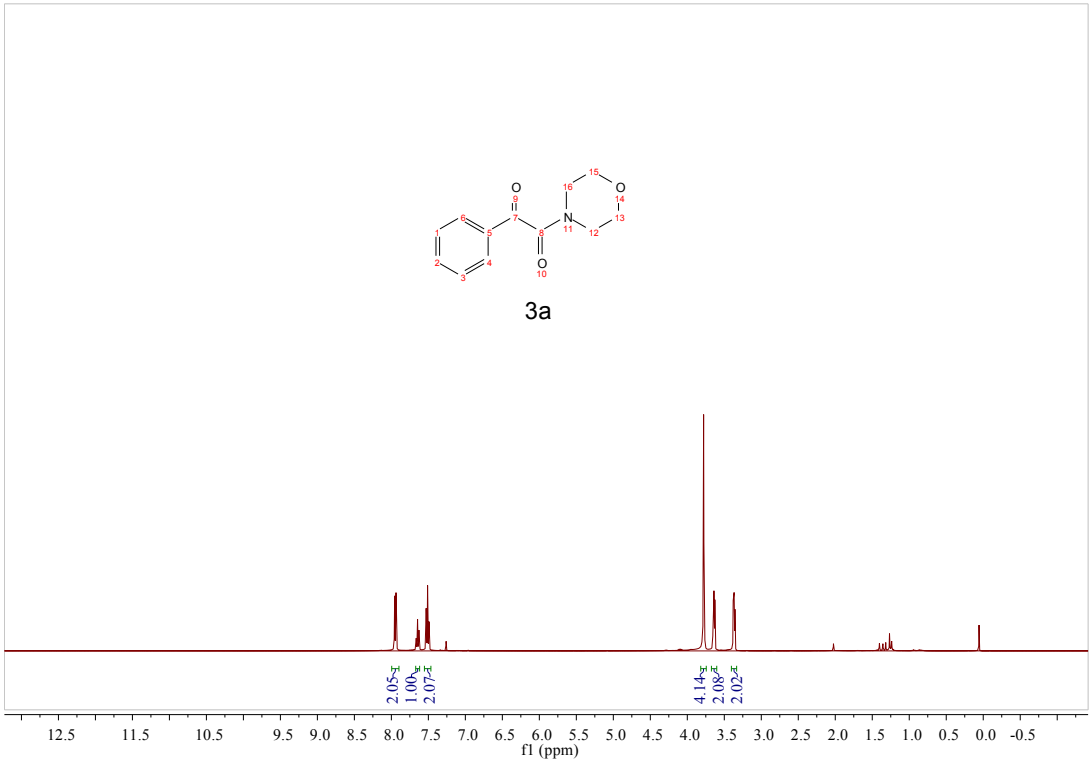


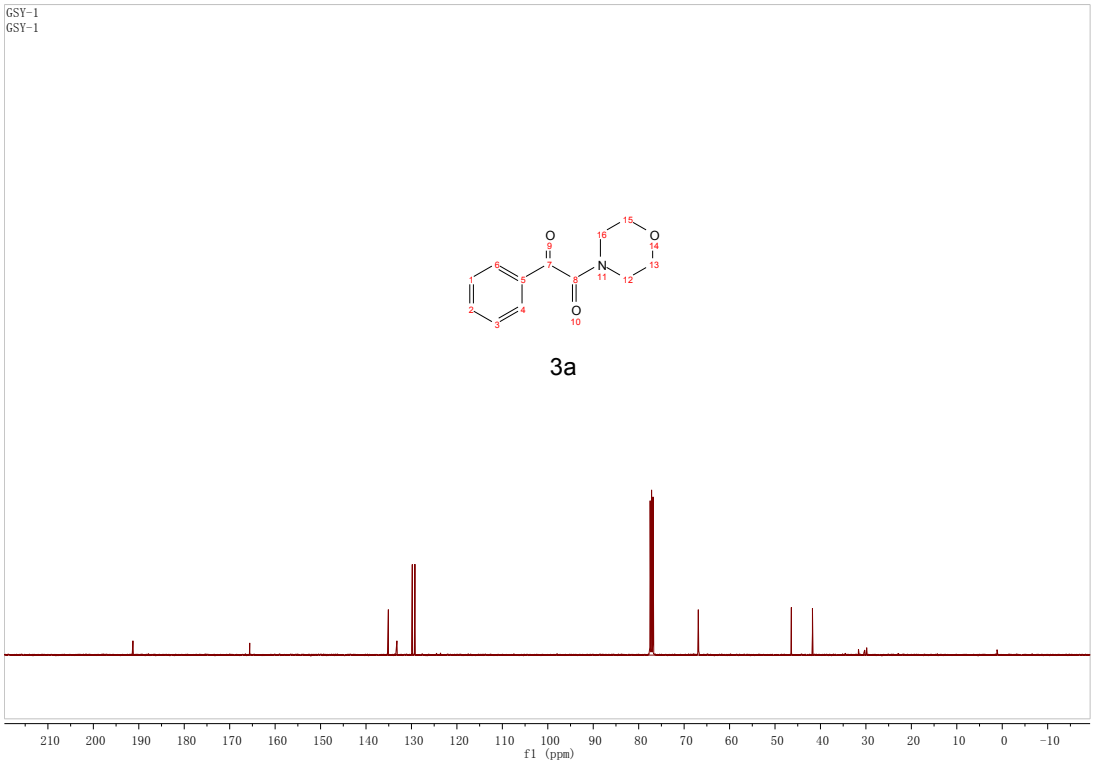
32) **P**

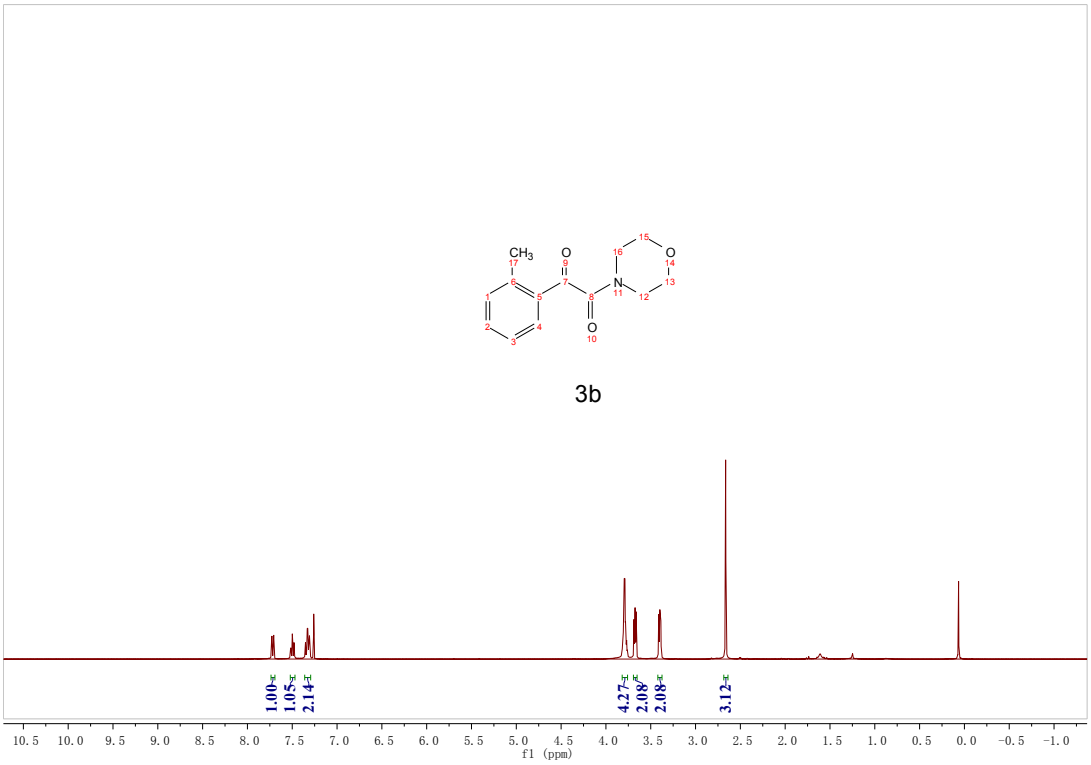
CuBr (11.5 mg, 0.08 mmol), 2-naphthaleneethanol (172.1 mg, 1 mmol), 2-amino-6-chlorobenzotrifluoride (292.5 mg, 1.5 mmol), TEMPO (23.4 mg, 0.15 mmol) and pyridine (158.2 mg, 2 mmol) were mixed in toluene (3 mL) under air. The reaction mixture was stirred at 70 °C for 12 h. After cooling down to room temperature, the reaction mixture was diluted with H_2O (30 mL) and extracted by ethyl acetate (30 mL). The separated organic layers were dried over by anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was chromatographed on silica gel using hexane/ethyl acetate (40:1) to afford the desired product.

Yellow solid (207.4 mg, 55% yield); ^{1}H NMR (400 MHz, DMSO) δ 11.12 (s, 1H), 8.79 (s, 1H), 8.20 (d, *J* = 8.1 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.9 Hz, 2H), 7.79 – 7.66 (m, 5H); ^{13}C NMR (101 MHz, DMSO) δ 188.90 (s), 163.74 (s), 135.97 – 135.85 (m), 135.70 (s), 133.73 (s), 133.21 (s), 132.47 – 132.35 (m), 131.89 (s), 130.61 – 130.54 (m), 129.99 (s), 129.84 (s), 129.69 (s), 128.90 (d, *J* = 7.9 Hz), 127.85 (s), 127.38 (s), 124.00 (s). HRMS (TOF) m/z [M - H]$^-$ Calcd for $C_{19}H_{11}NO_4F_3Cl$ 376.0358 found 376.0385.

^{1}H NMR and ^{13}C NMR spectra of those compounds



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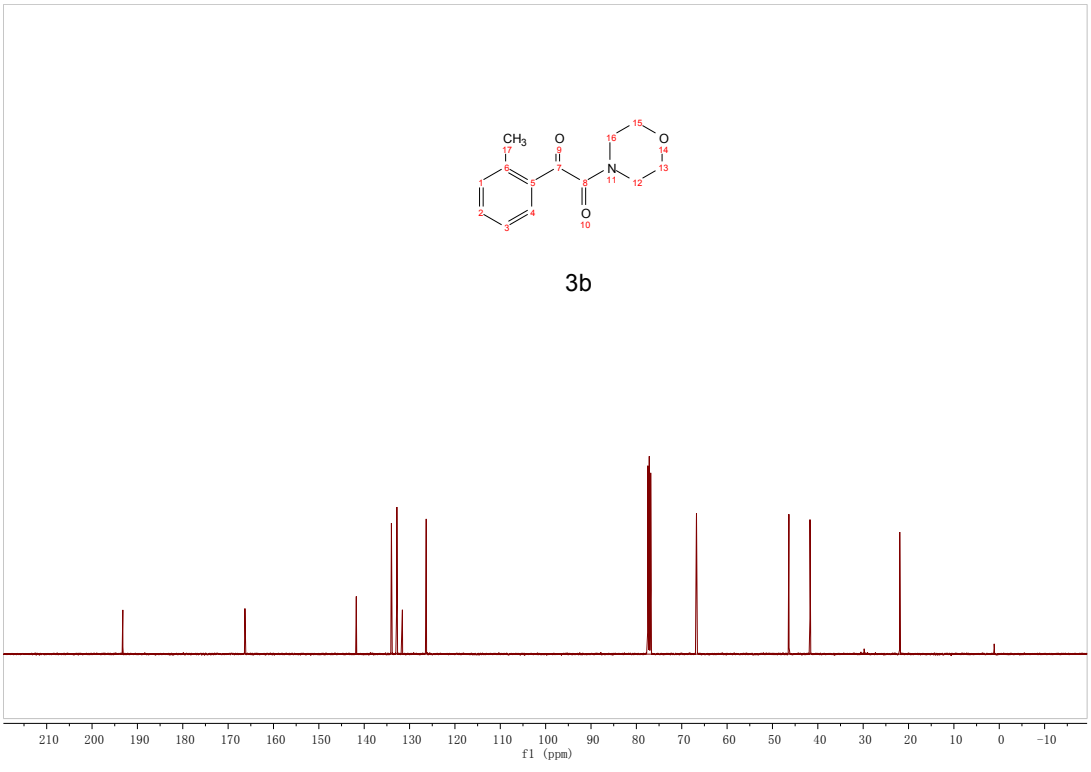
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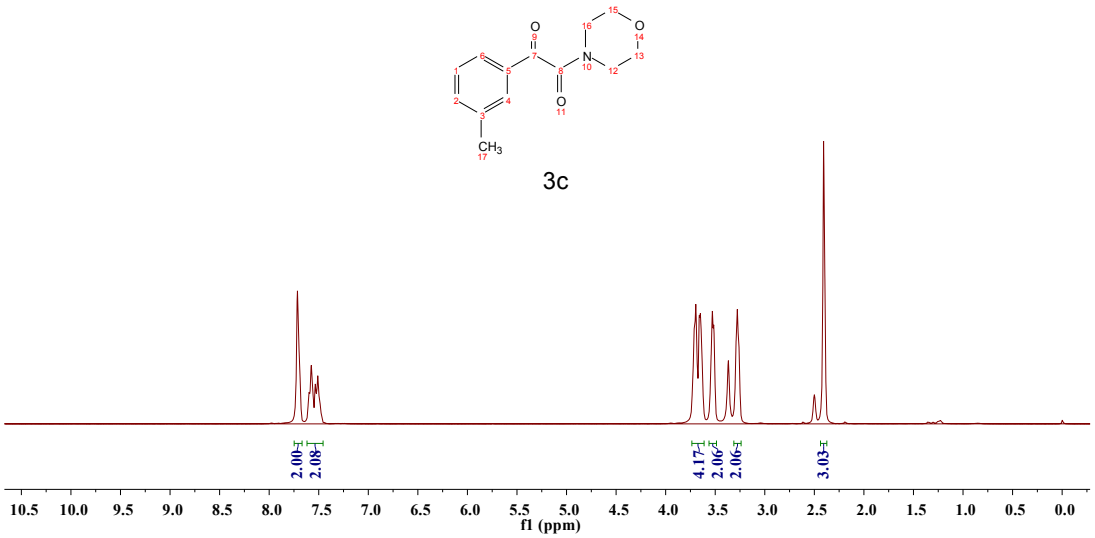

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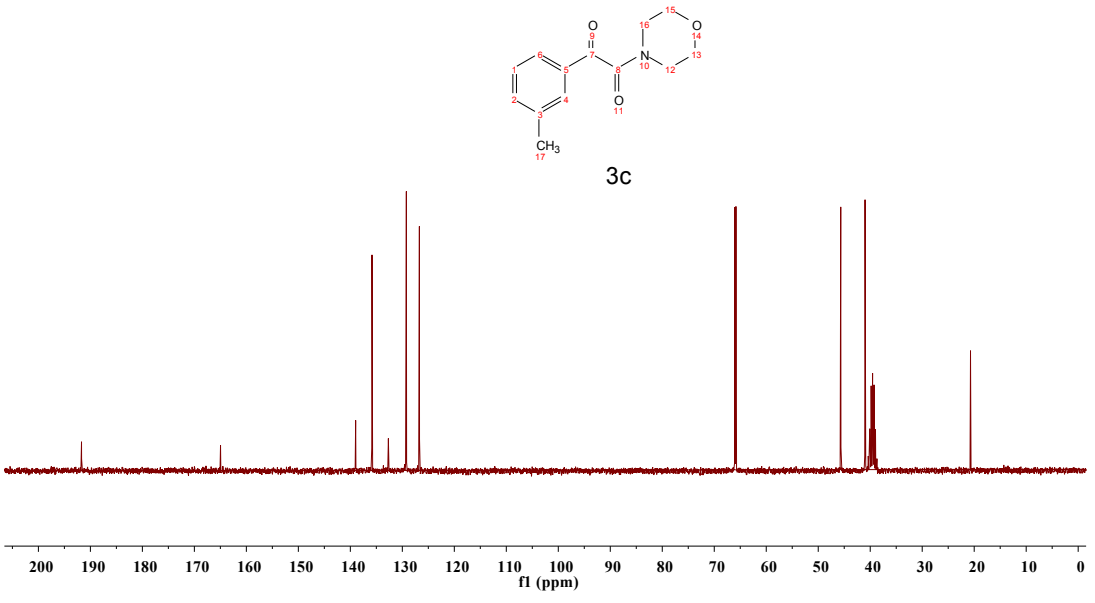

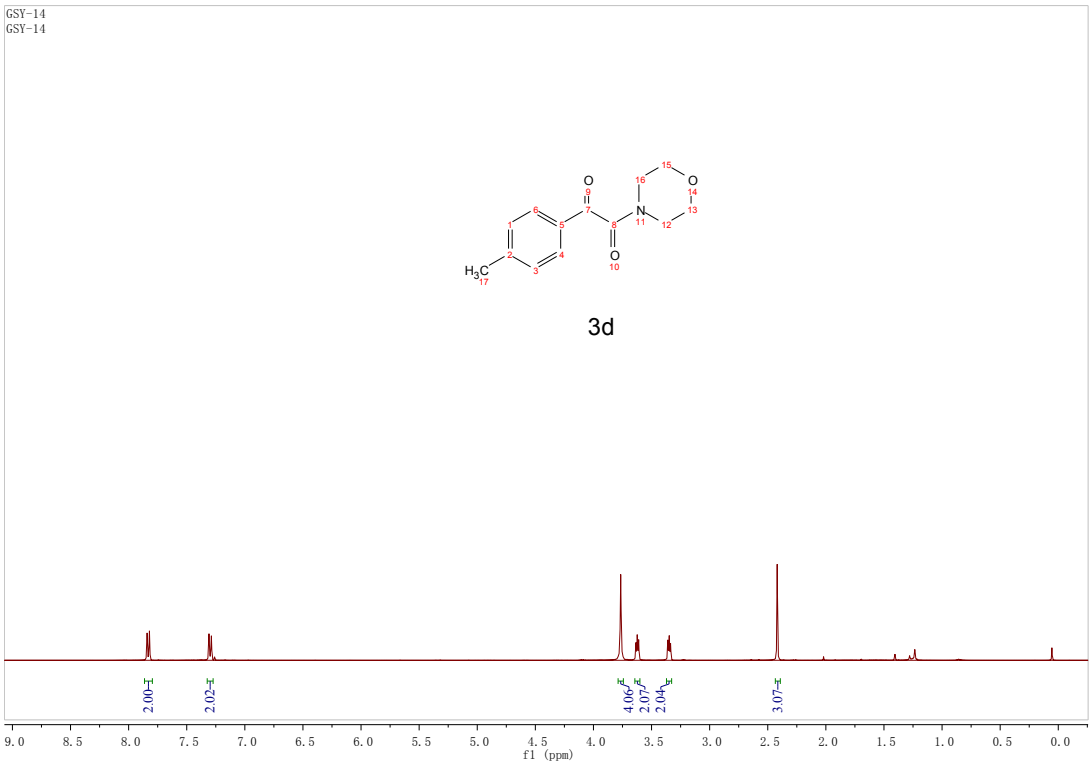
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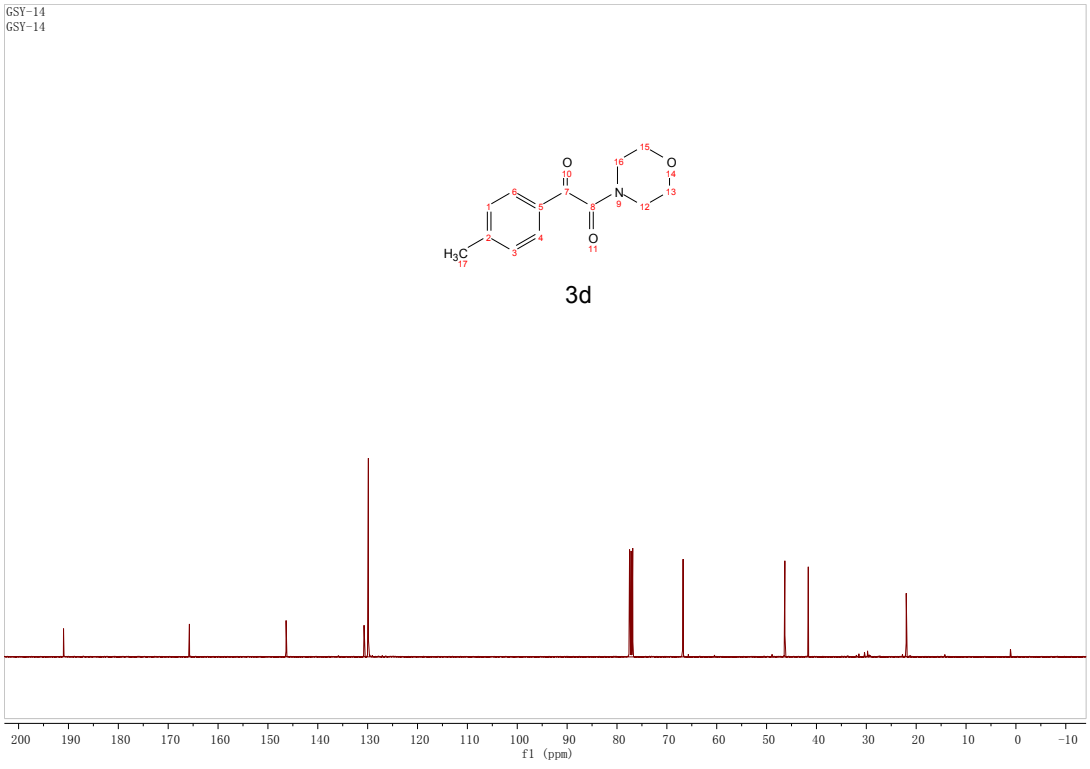
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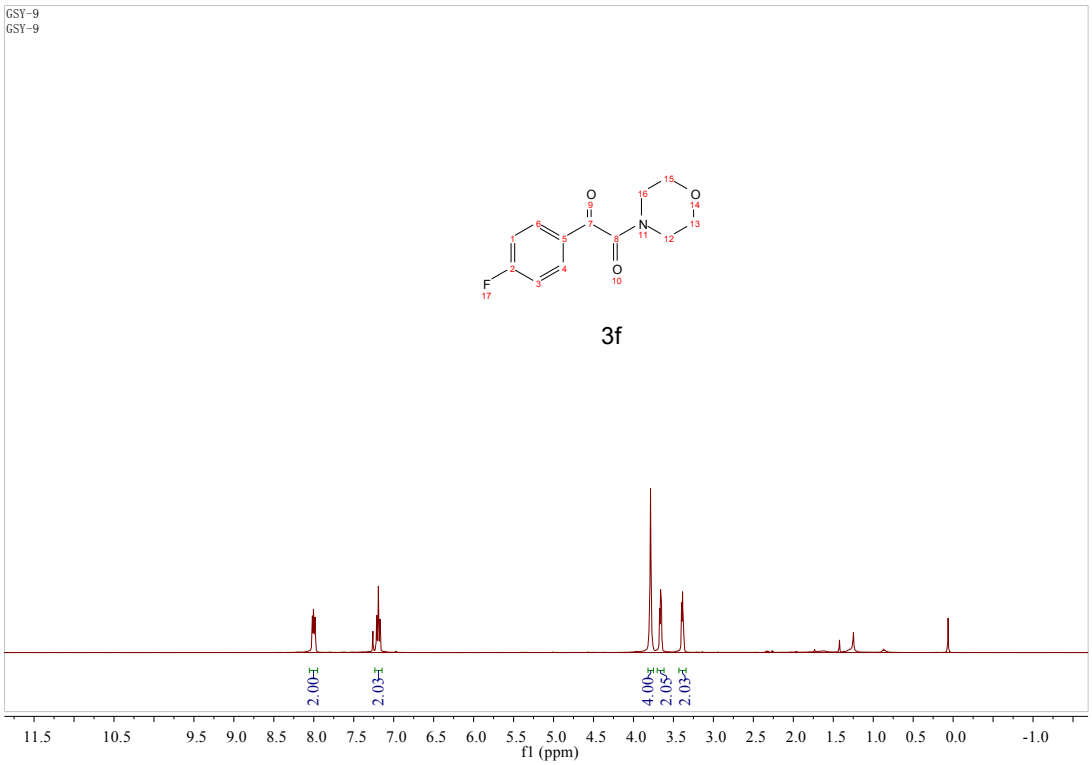
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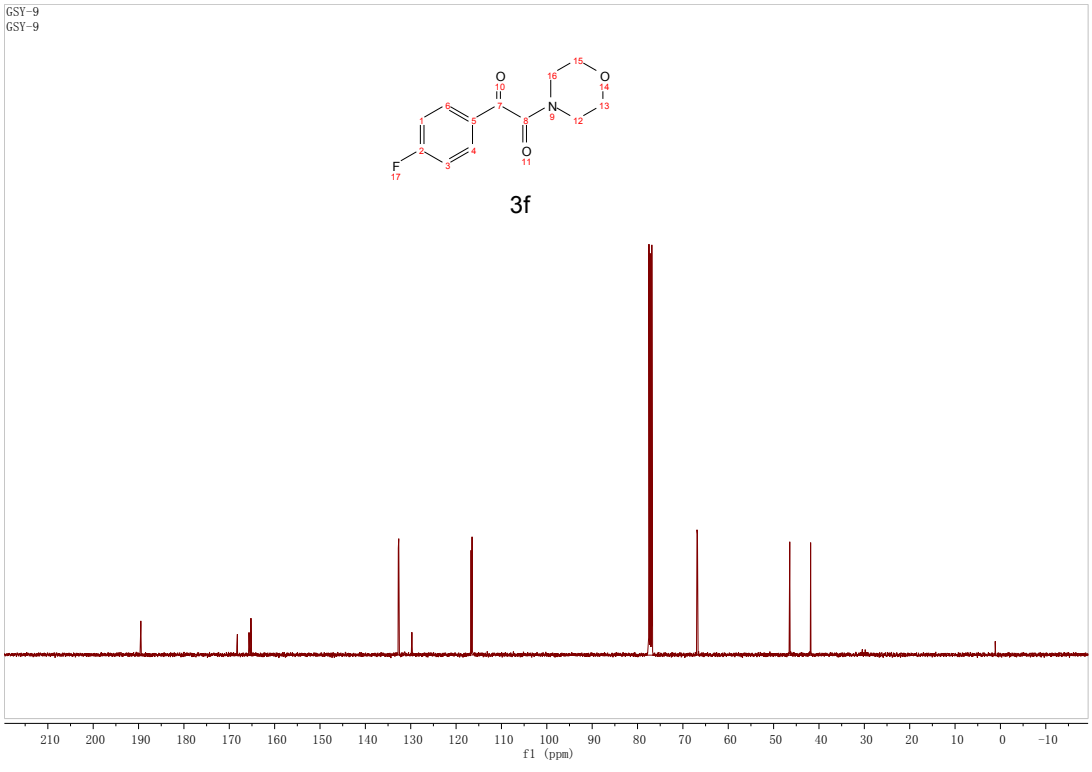
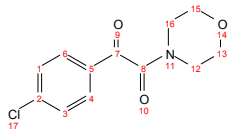
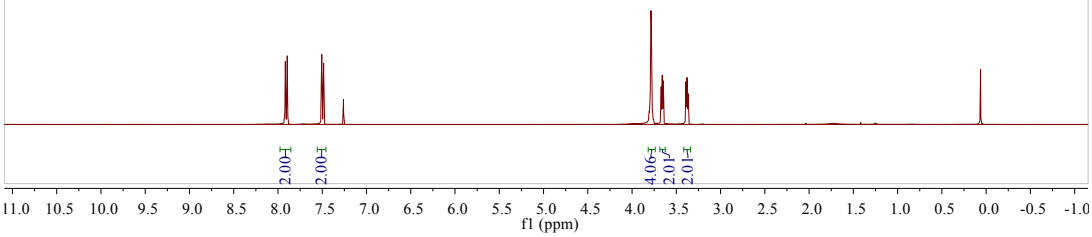
2.03
f1 (ppm)


GSY-9
GSY-9
3f
f1 (ppm)

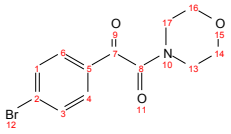
GSY-2
GSY-2



3g

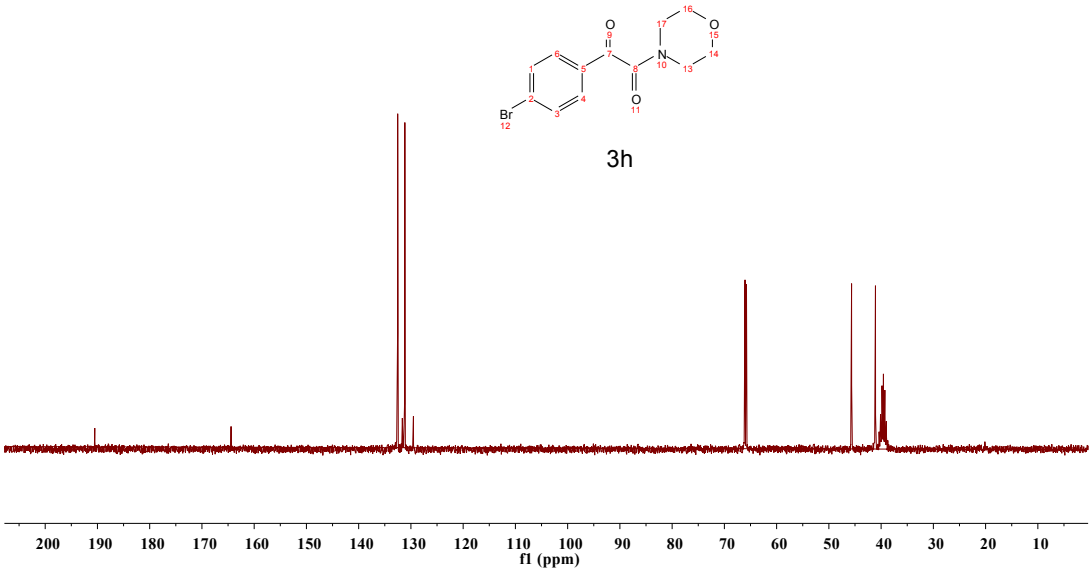


160424-gk
LCK-78 1H-NMR DMSO 303K AV-300



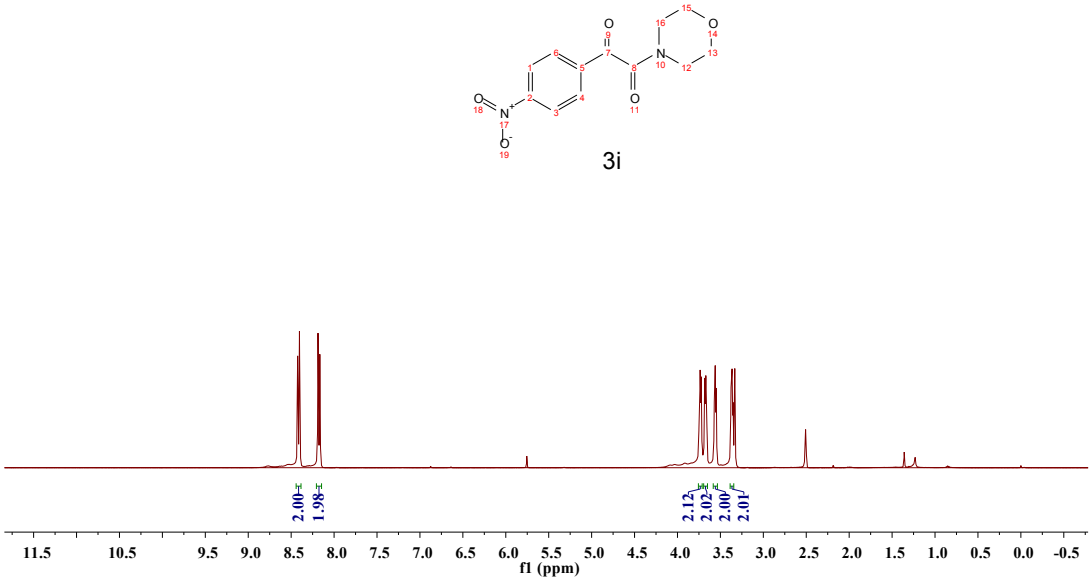
3h

160424-gk
LCK-78 13C-NMR DMSO 303K AV-300



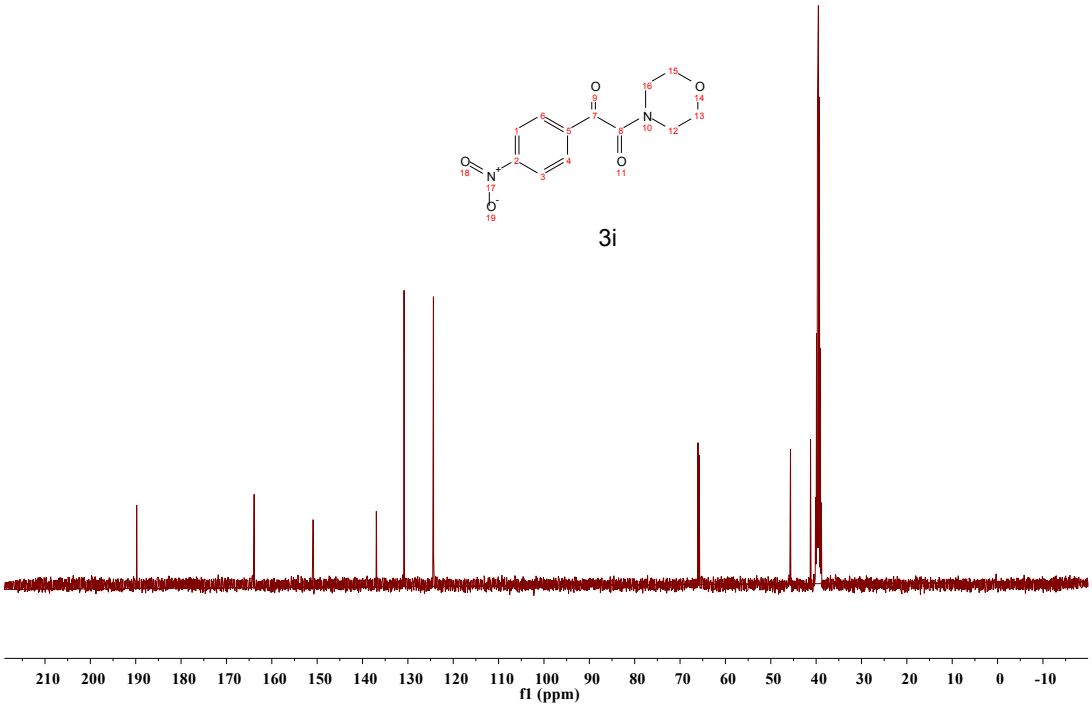
3h

LCK-82
LCK-82

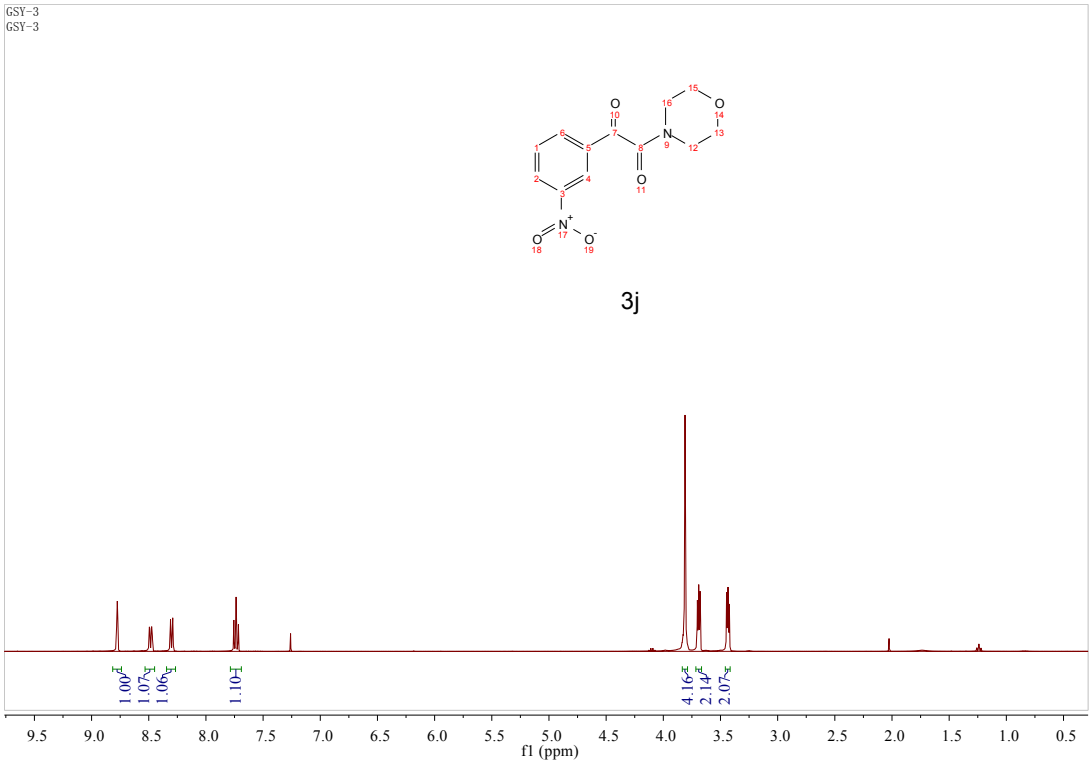


3i

LCK-82
LCK-82

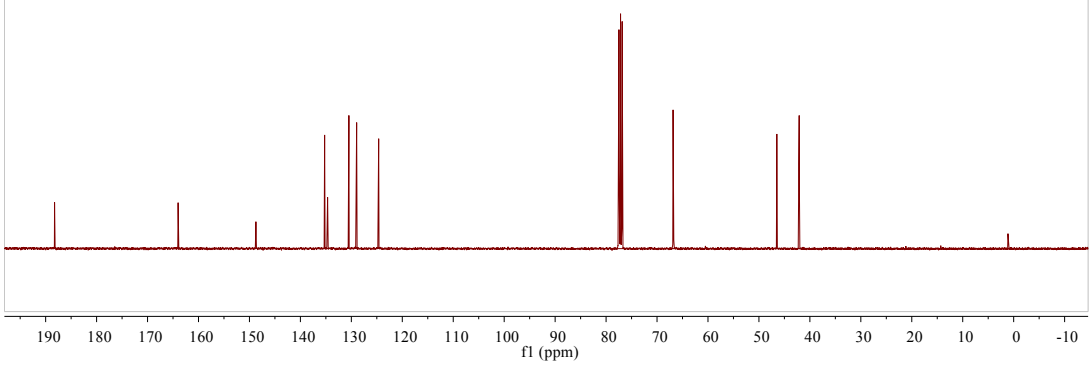


GSY-3
GSY-3

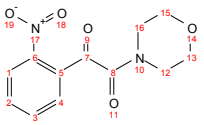


GSY-3
GSY-3

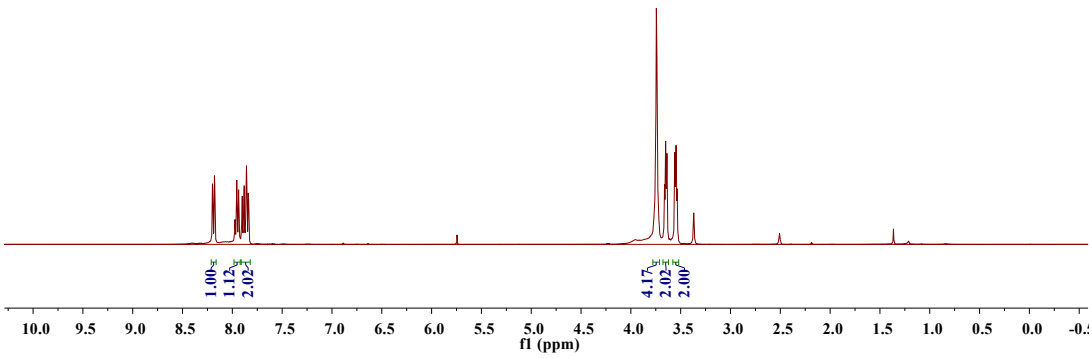
3j



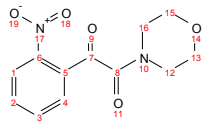
LCK-83
LCK-83



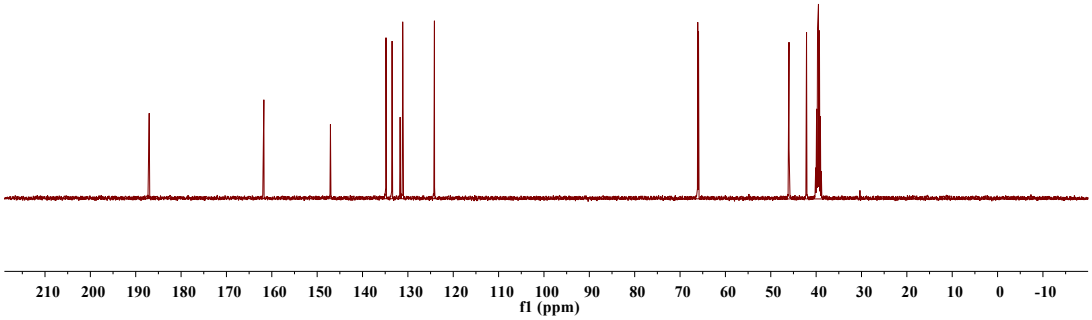
3k



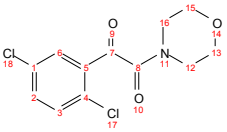
LCK-83
LCK-83



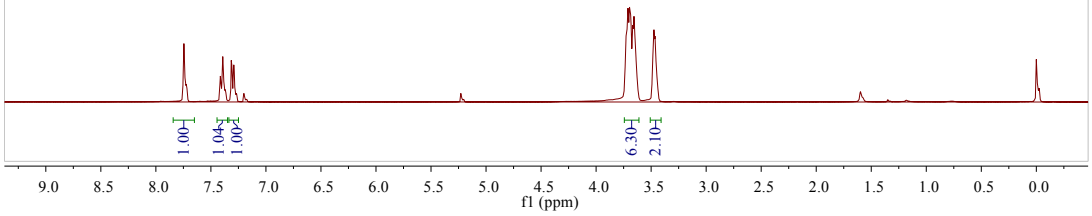
3k

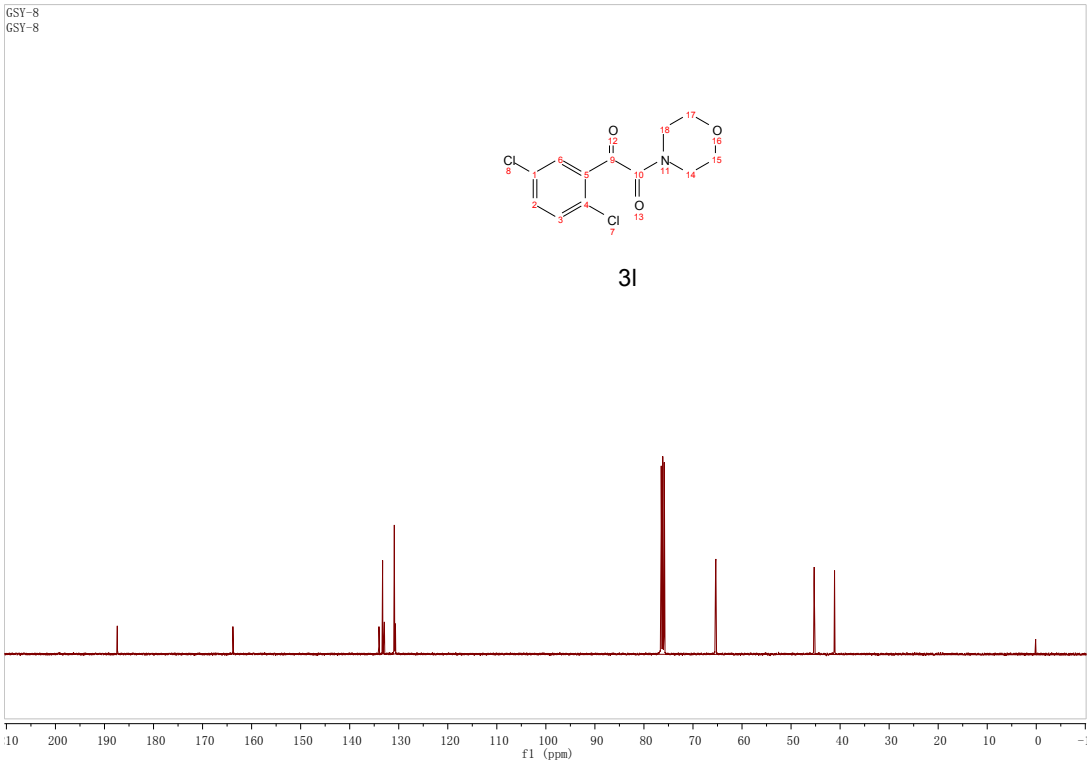


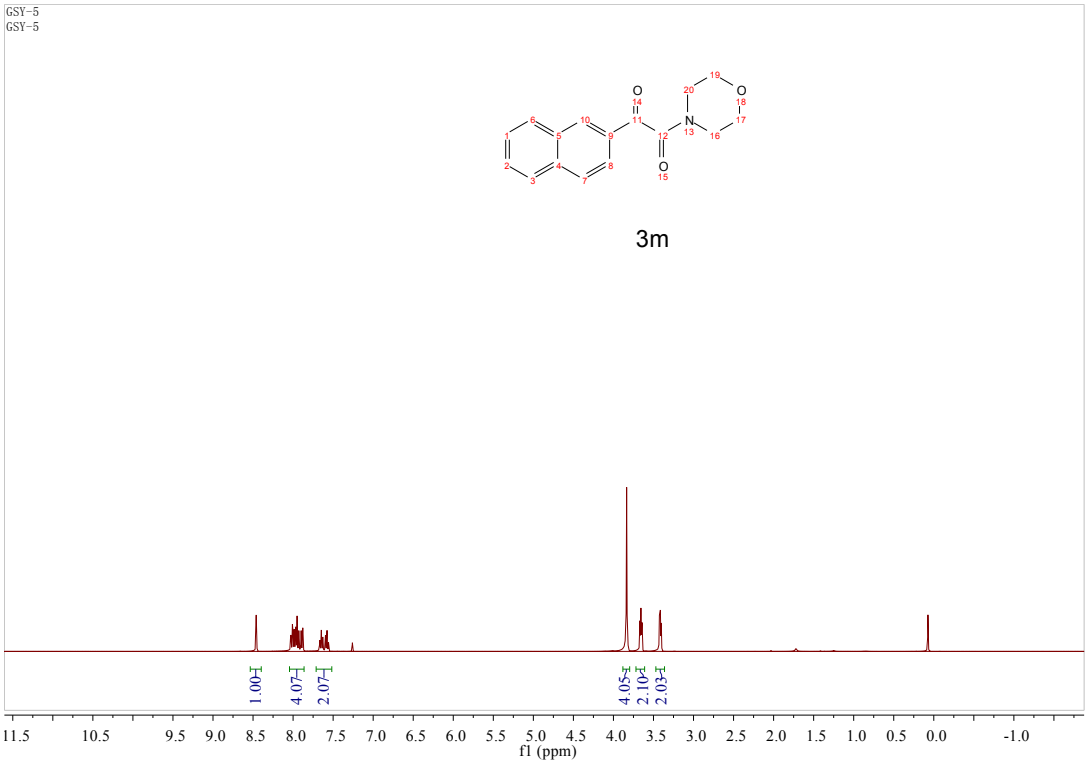
GSY-8
GSY-8

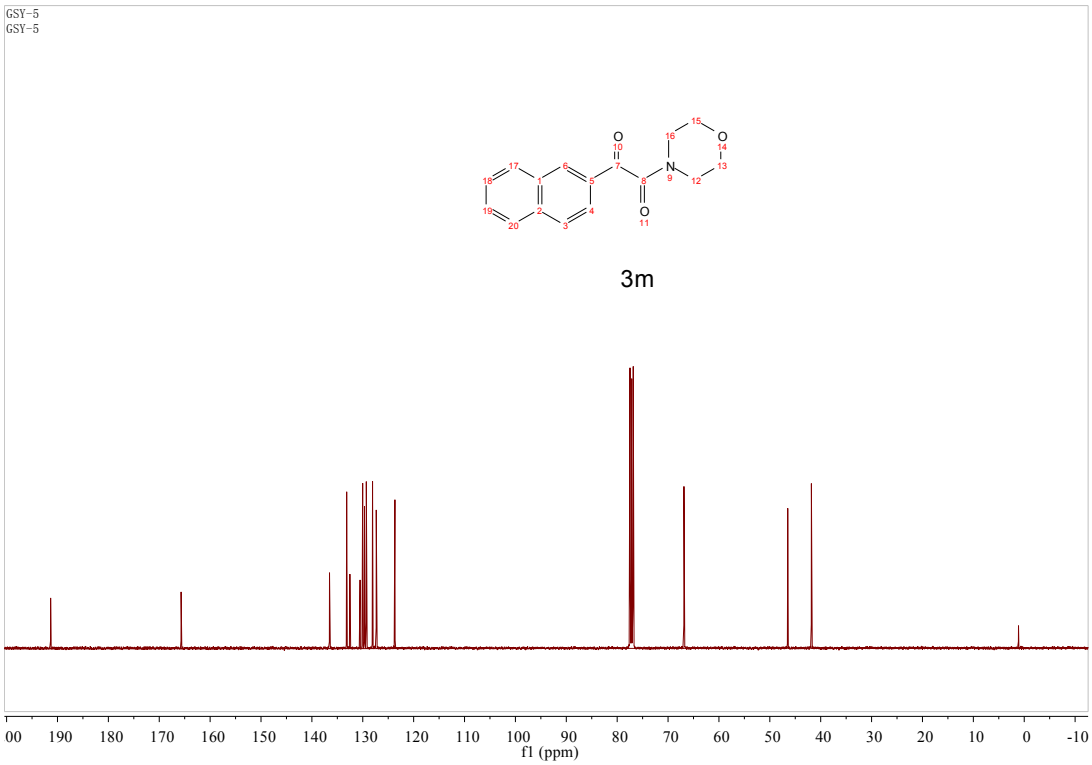


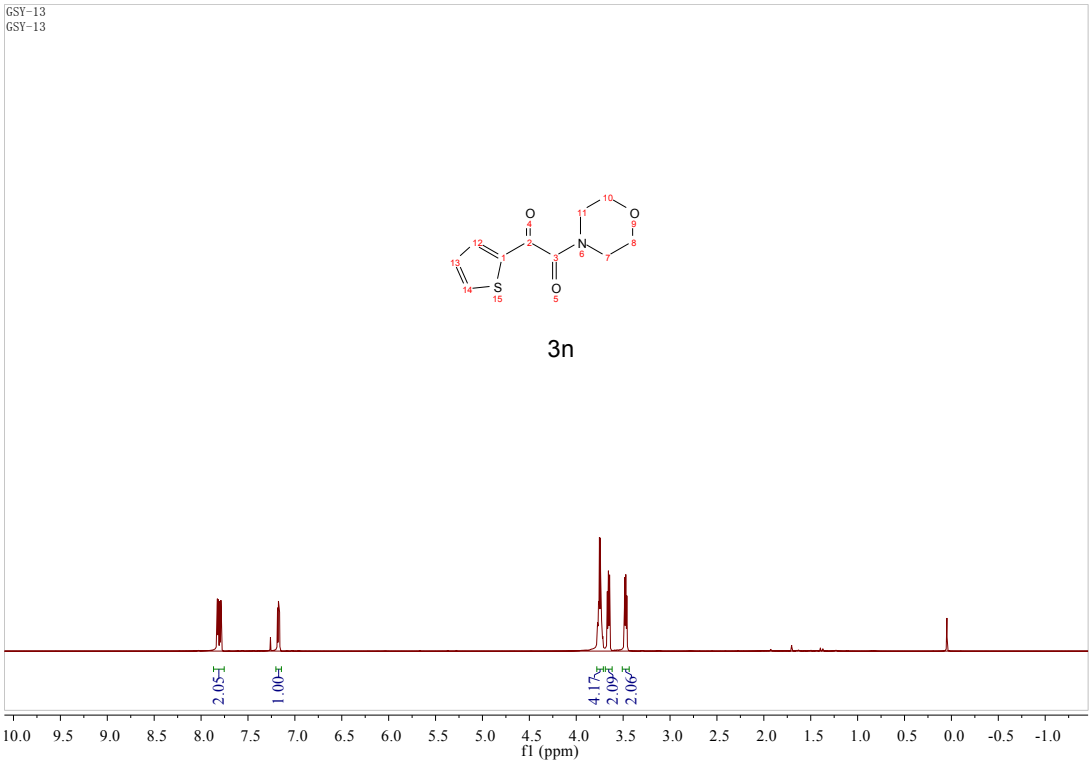
3l

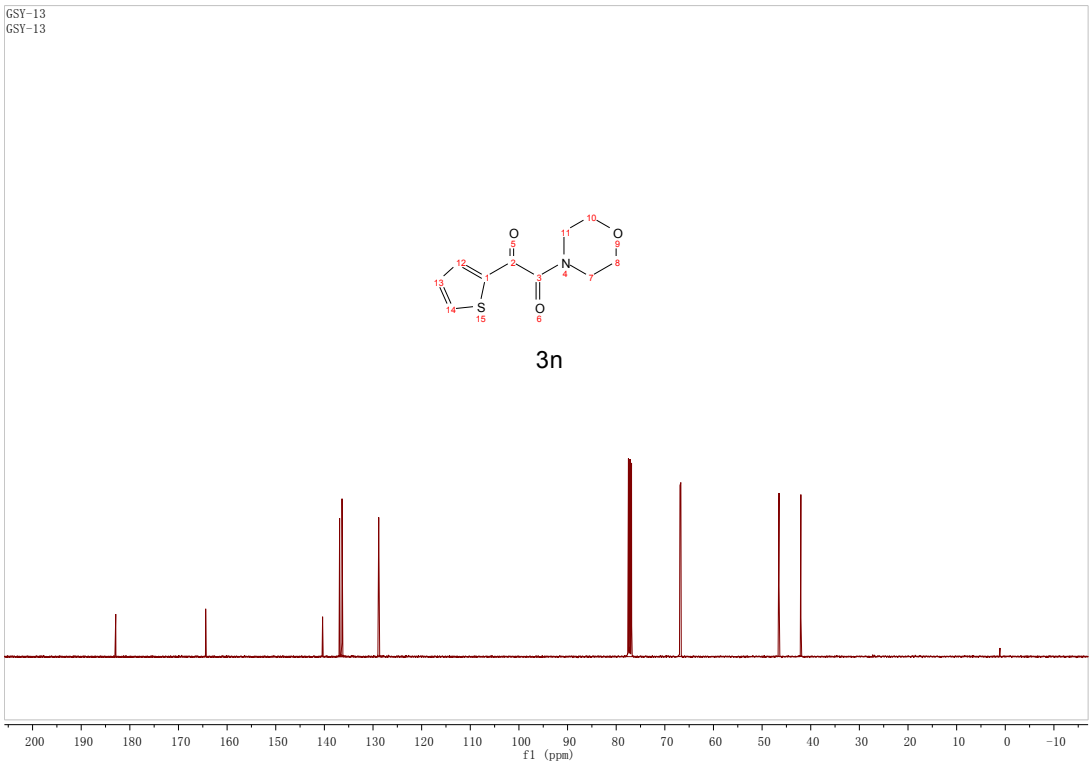


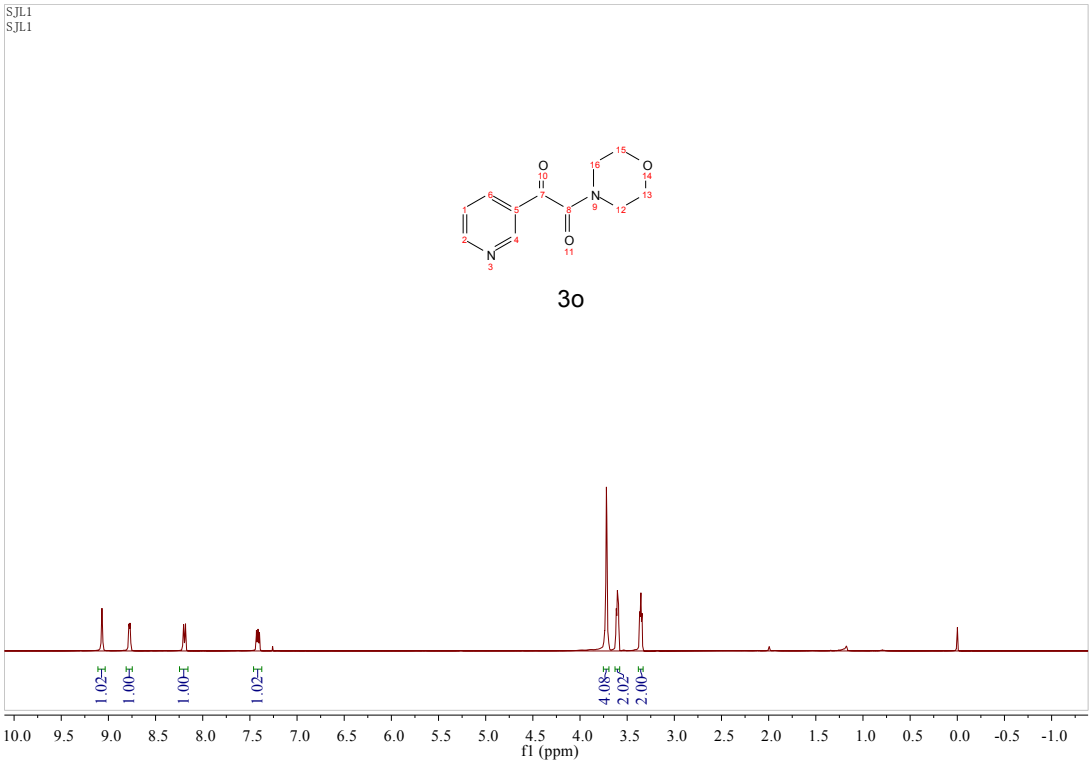

GSY-8
GSY-8
3l
f1 (ppm)

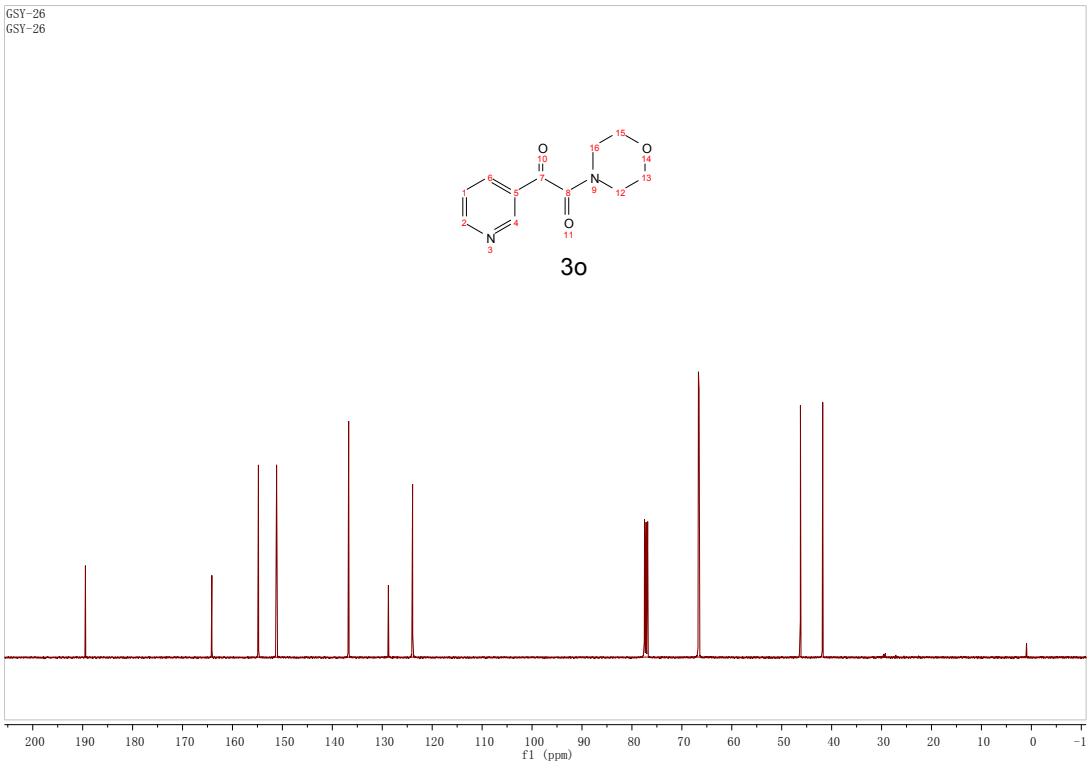

GSY-5
GSY-5
3m
1.00
4.07
2.07
4.05
2.10
2.03
f1 (ppm)

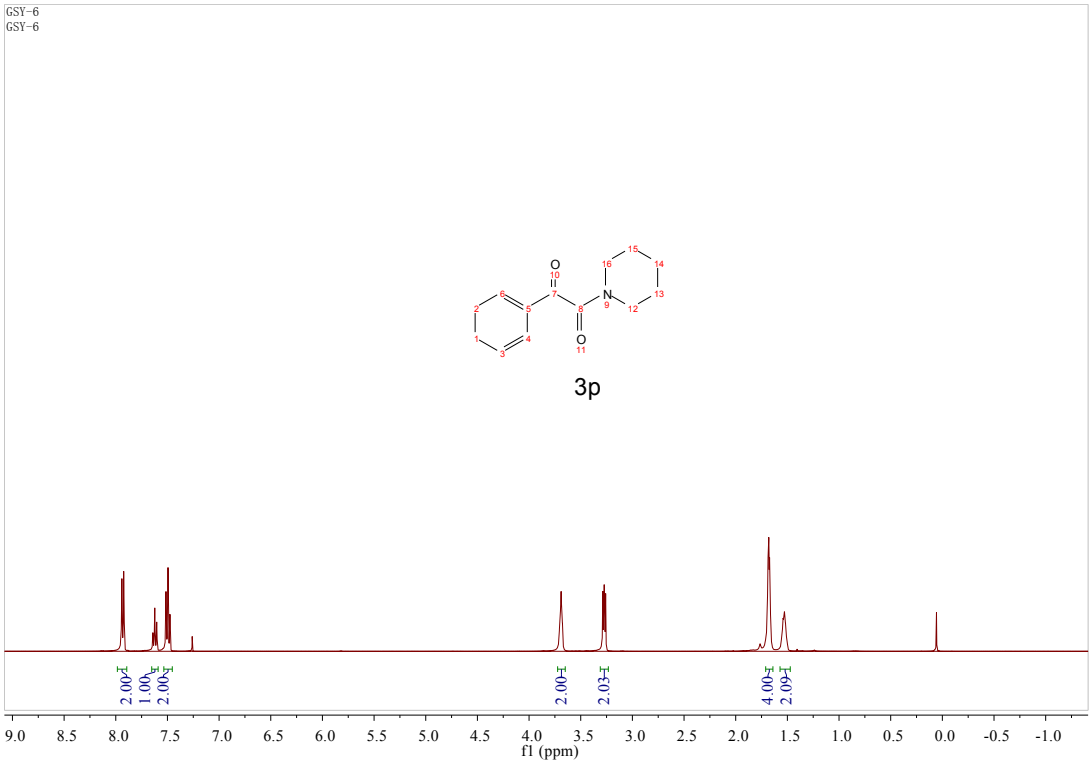

GSY-5
GSY-5
3m
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


GSY-13
GSY-13
3n
2.05
1.00
4.17
2.09
2.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

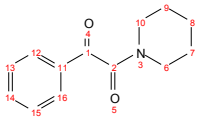

GSY-13
GSY-13
3n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SJL1
SJL1
3o
1.02
1.00
1.00
1.02
4.08
2.02
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

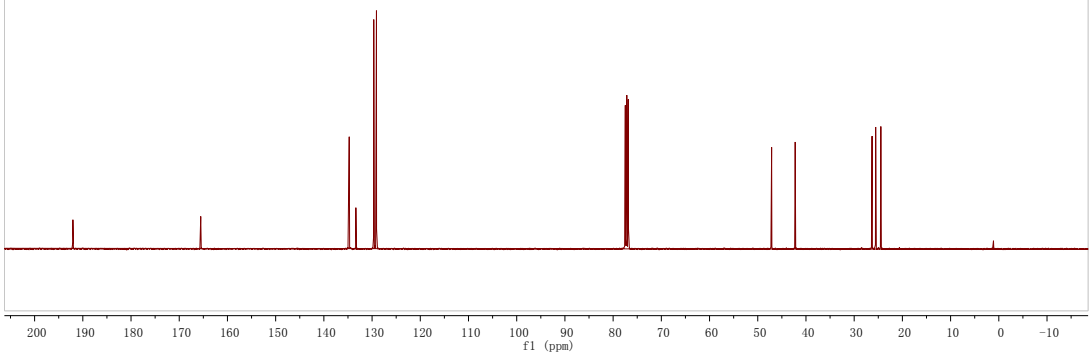

GSY-26
GSY-26
3o
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


GSY-6
GSY-6
3p
2.00
1.00
2.00
2.00
2.03
4.00
2.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

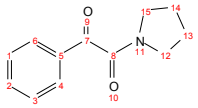
GSY-6
GSY-6



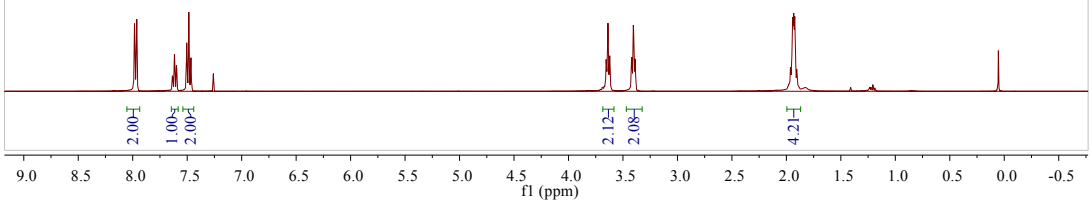
3p

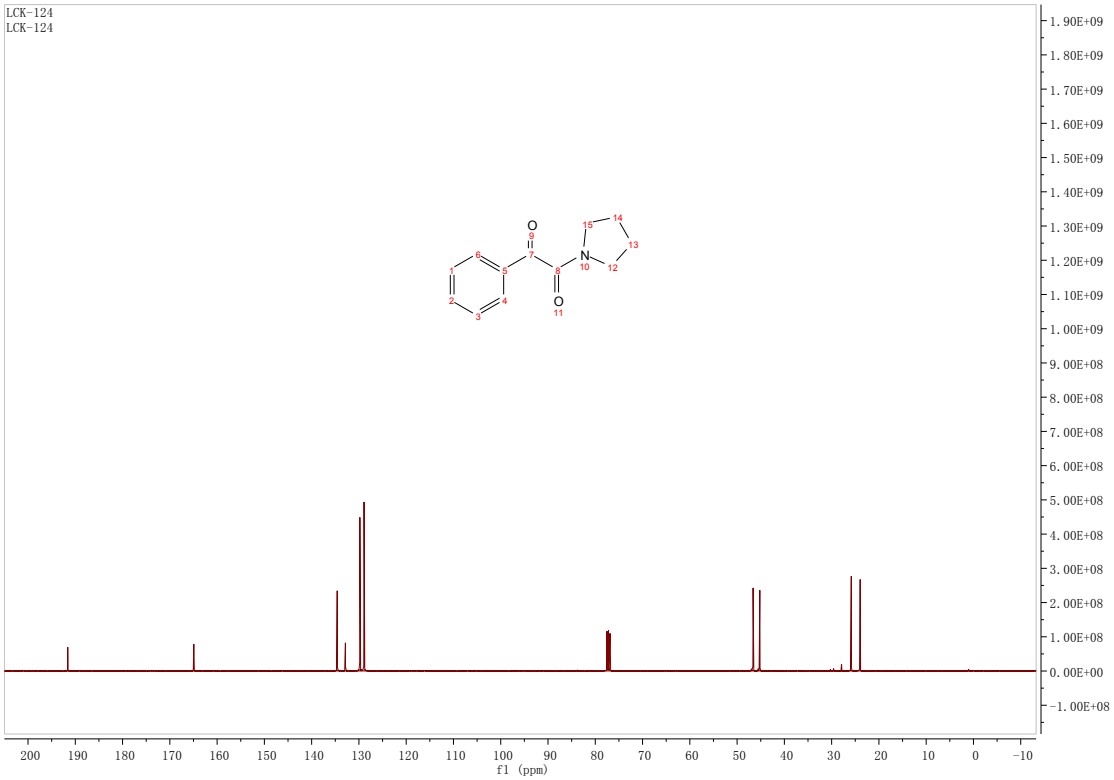


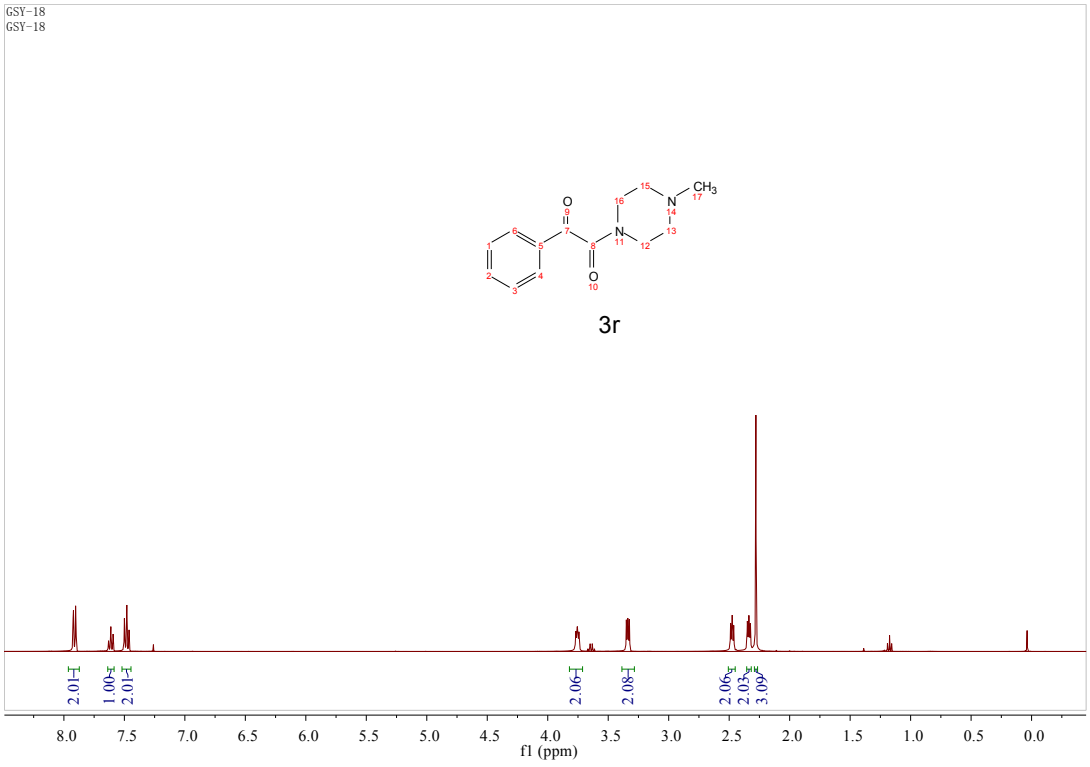
GSY-15
GSY-15

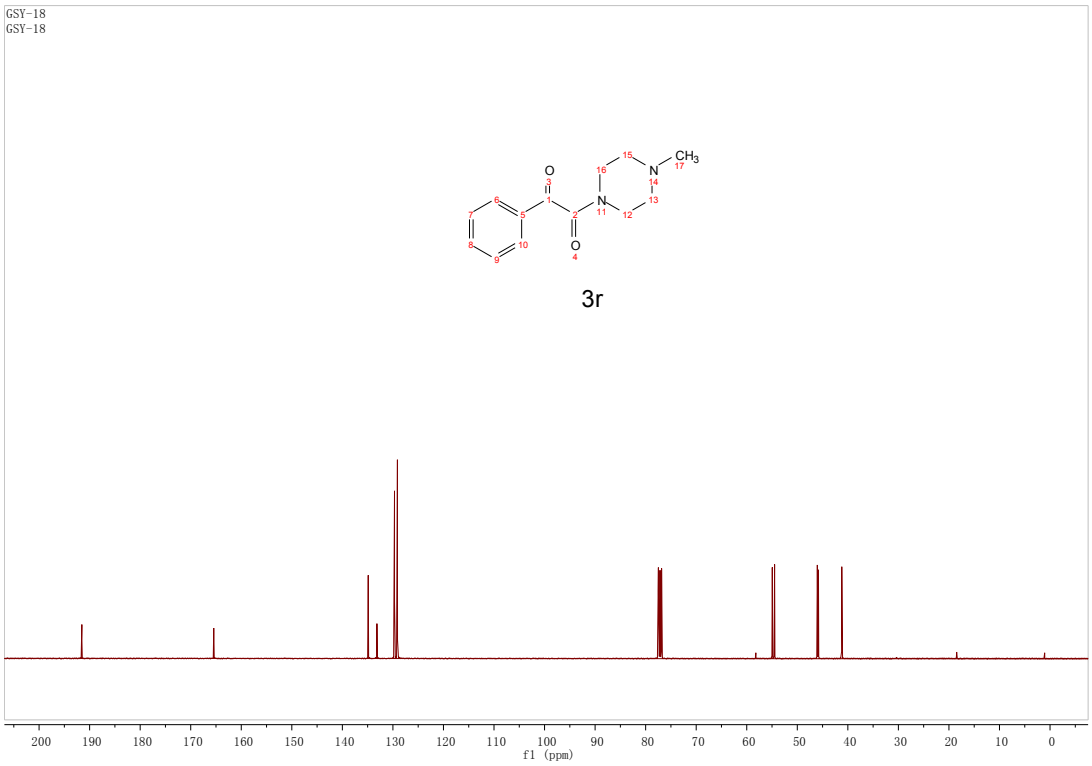


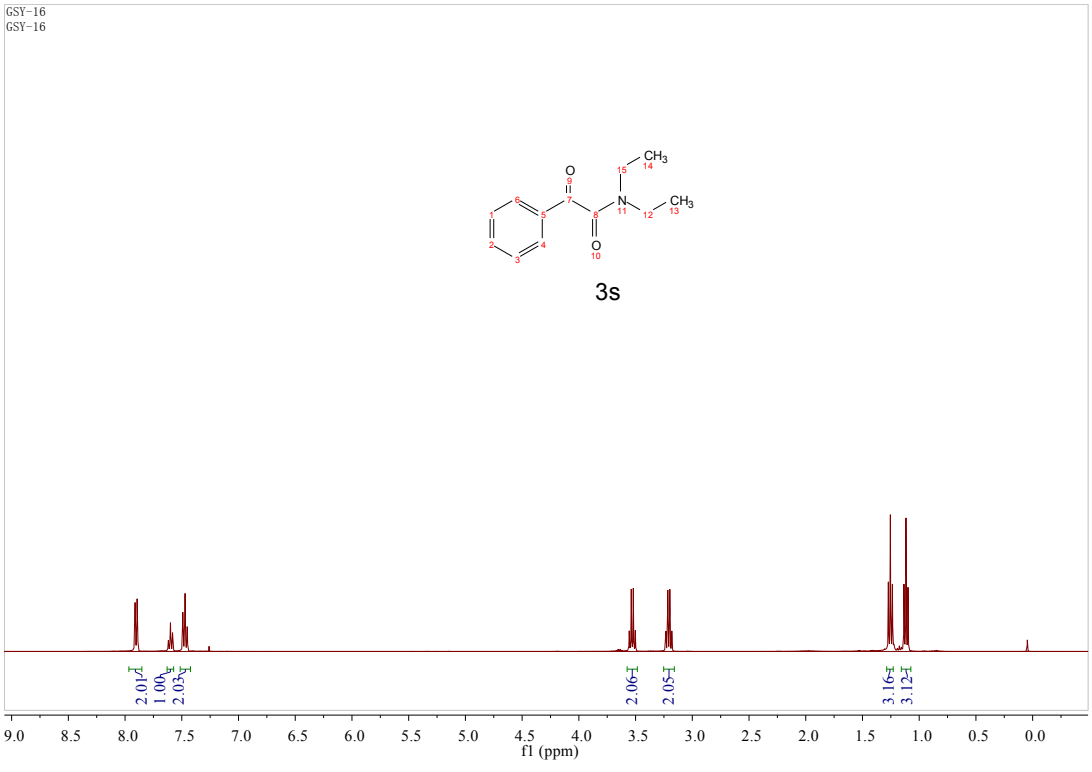
3q



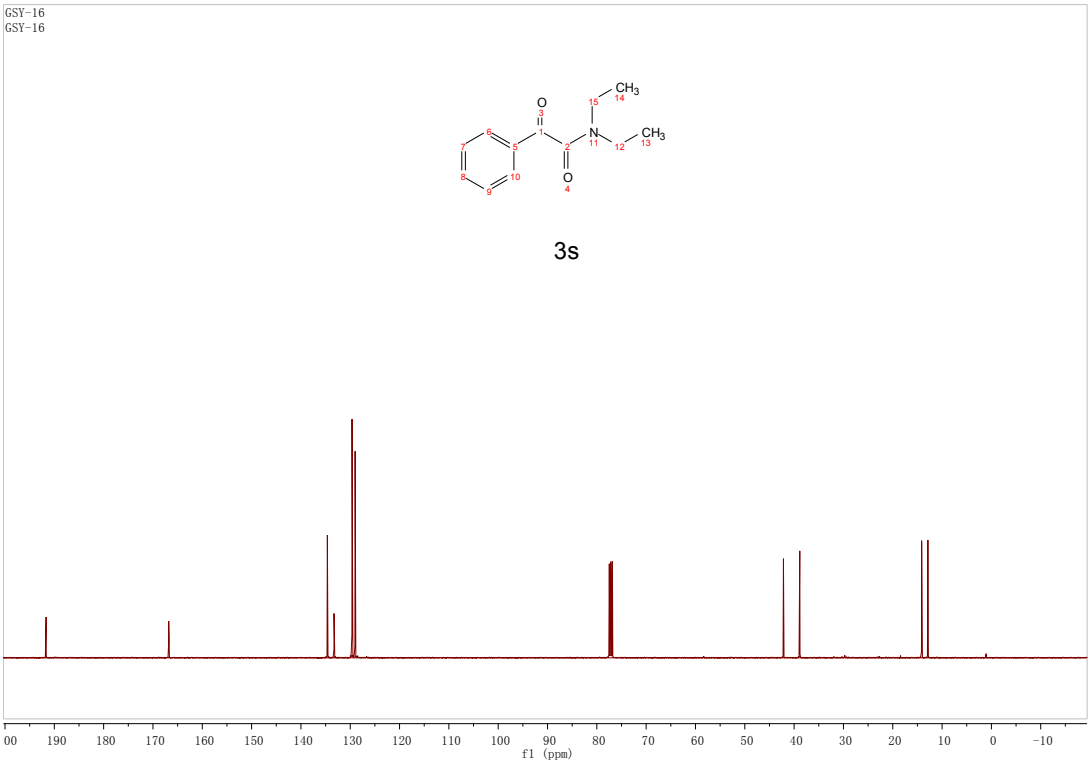

LCK-124
LCK-124
f1 (ppm)


GSY-18
GSY-18
3r
2.01
1.00
2.01
2.06
2.08
2.06
2.03
3.09
f1 (ppm)

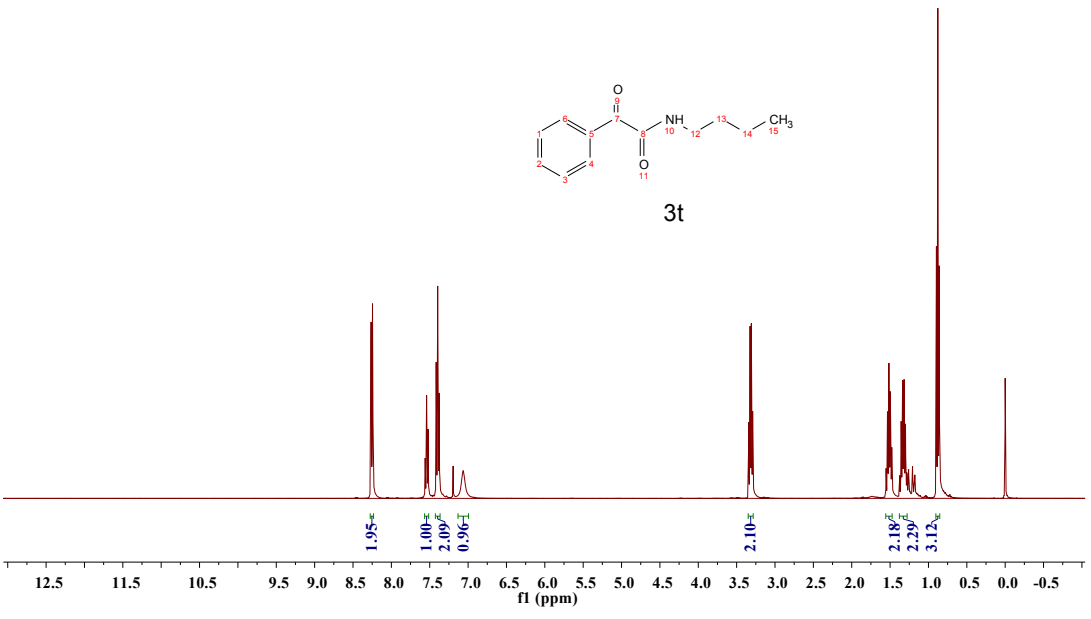

GSY-18
GSY-18
3r
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


GSY-16
GSY-16
3s
2.01
1.00
2.03
2.06
2.05
3.16
3.12
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

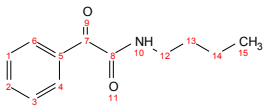
GSY-16
GSY-16



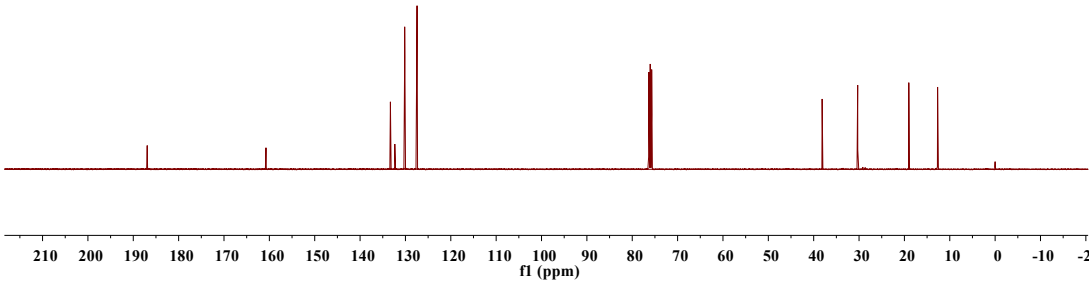
GSY-44
GSY-44



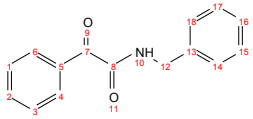
GSY-44
GSY-44



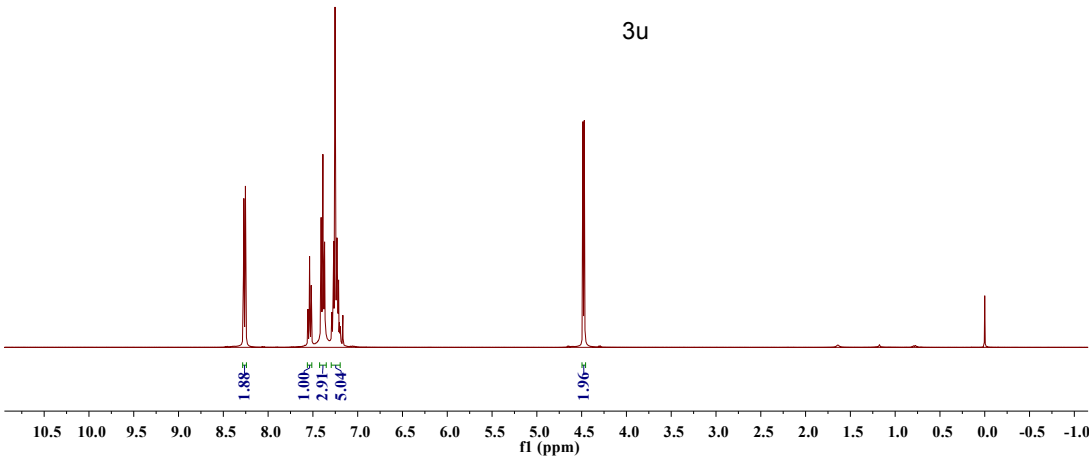
3t



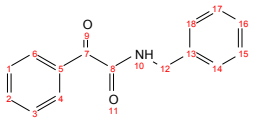
GSY-34
GSY-34



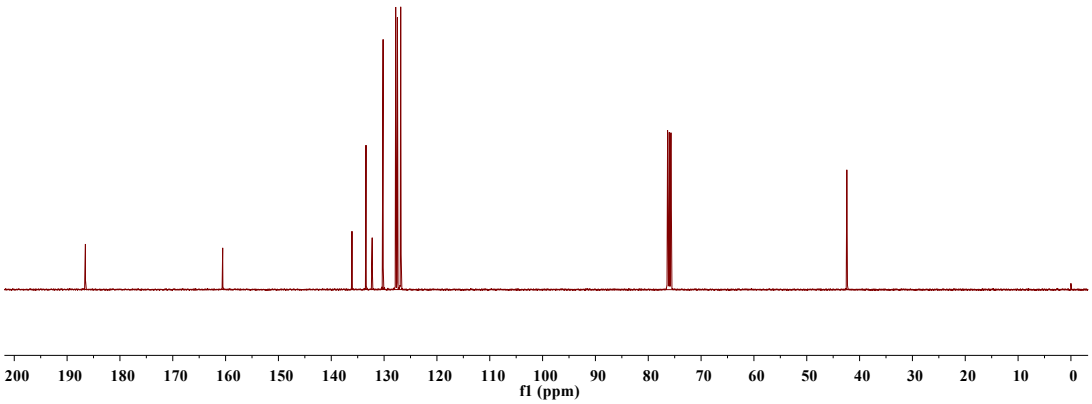
3u



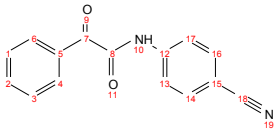
GSY-34
GSY-34



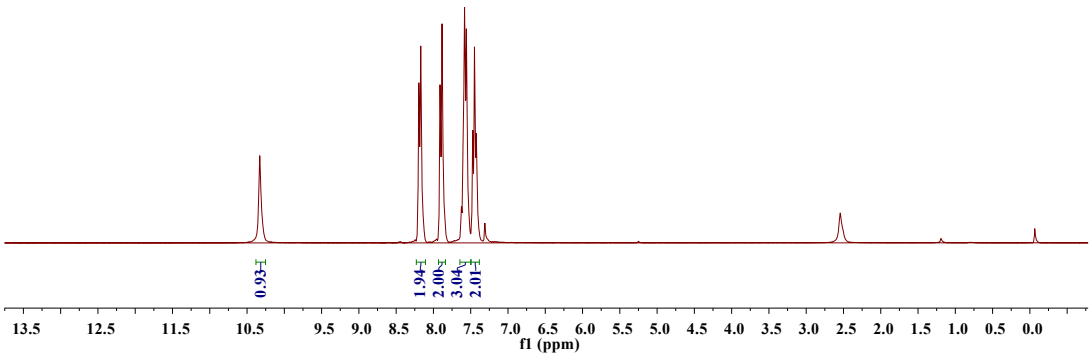
3u



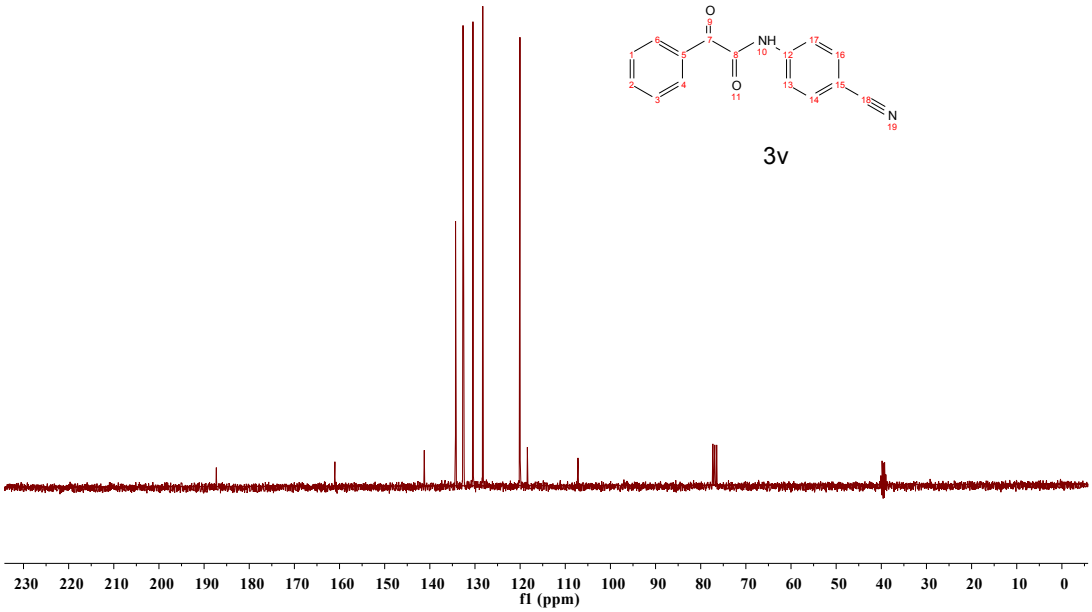
160323-gk
LCK-65 1H-NMR CDC13+DMSO 303K AV-300



3v

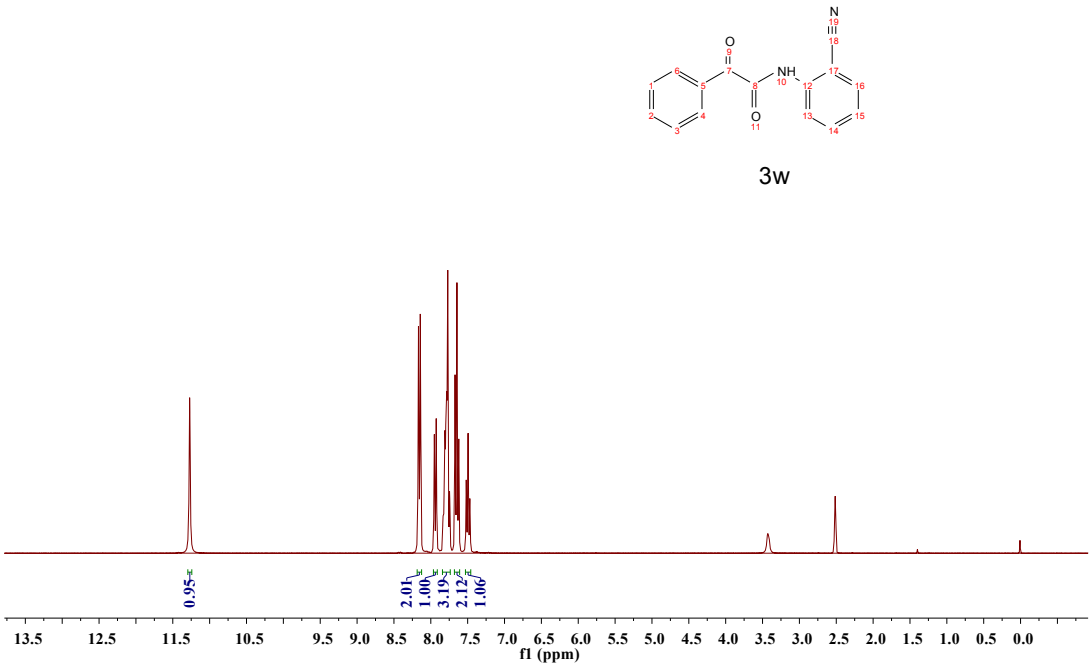


160323-gk
LCK-65 13C-NMR CDCl3+DMSO 303K AV-300



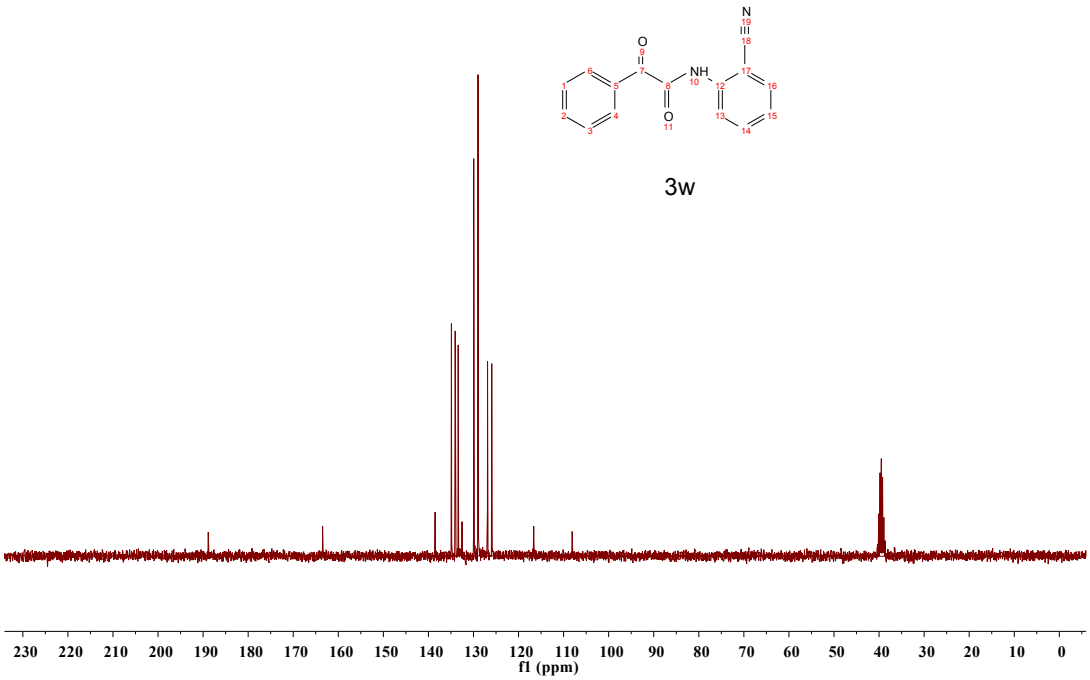
3v

160323-gk
LCK-66 1H-NMR DMSO 303K AV-300

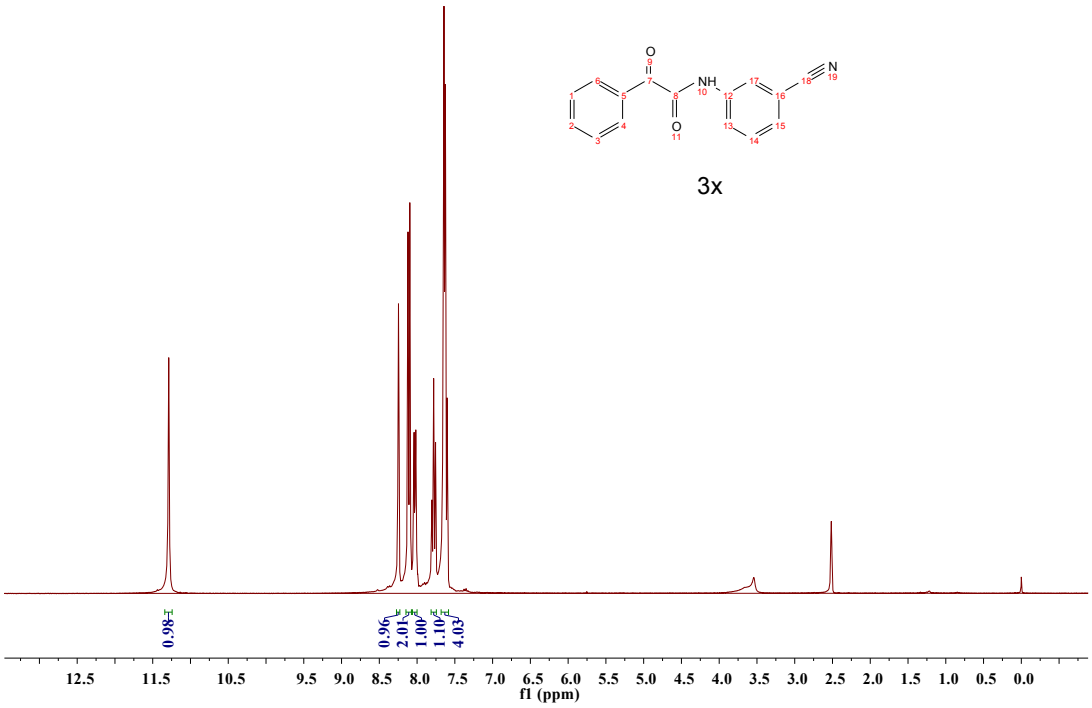


3w

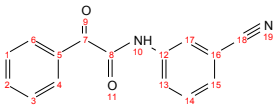
160323-gk
LCK-66 13C-NMR DMSO 303K AV-300



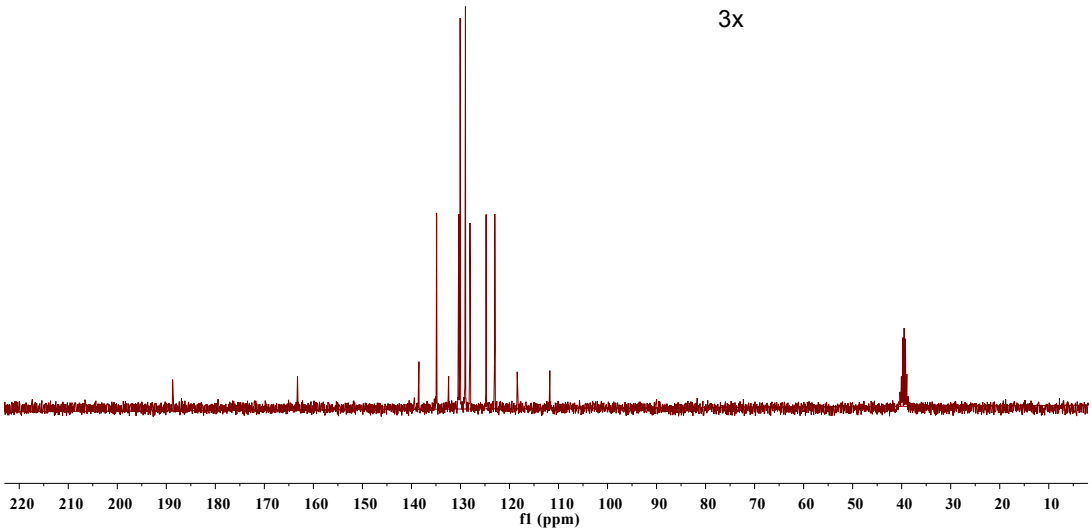
160323-gk
LCK-67 1H-NMR DMSO 303K AV-300



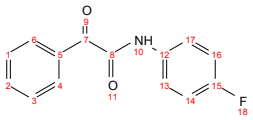
160323-gk
LCK-67 13C-NMR DMSO 303K AV-300



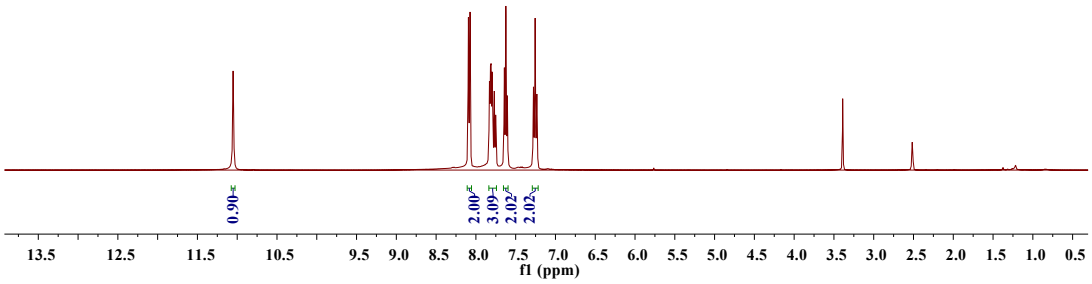
3x



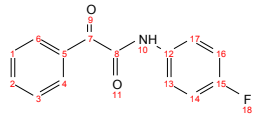
LCK-80
LCK-80



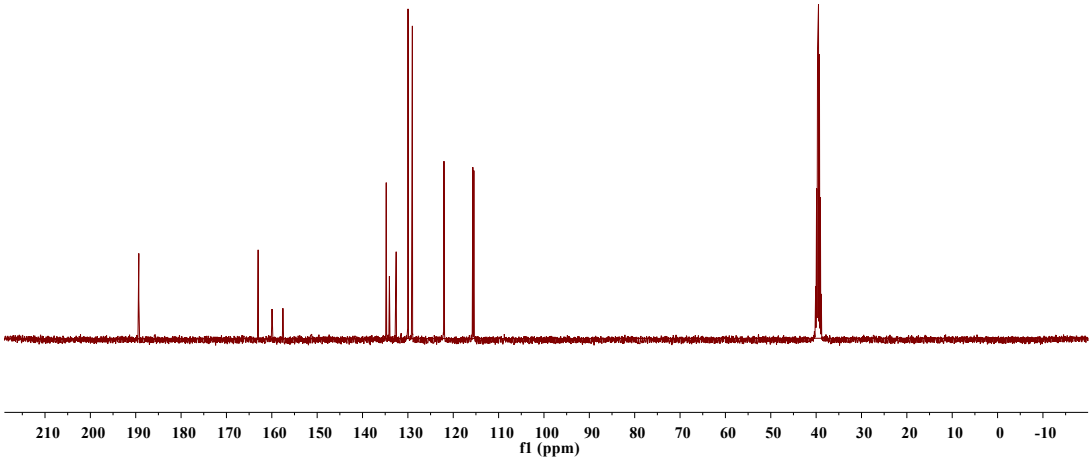
3y



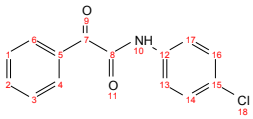
LCK-80
LCK-80



3y



LCK-76



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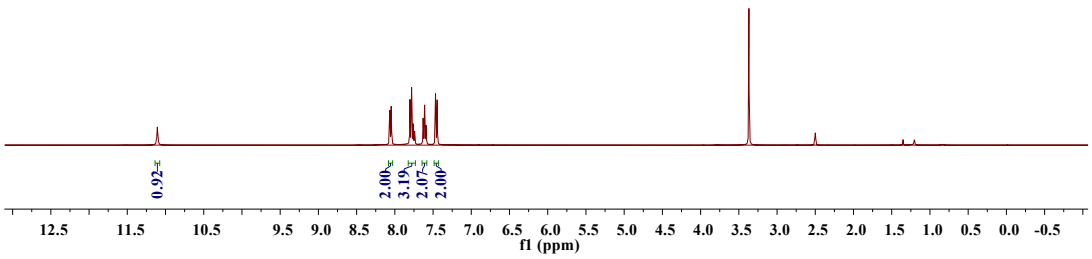
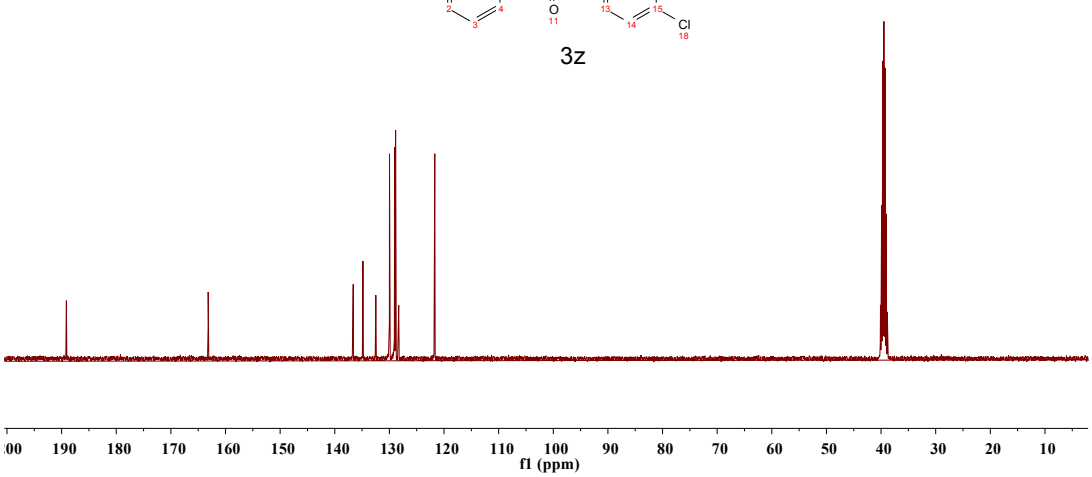


LCK-76
LCK-76

3z



LCK-77
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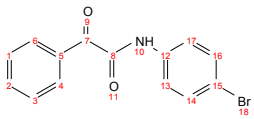

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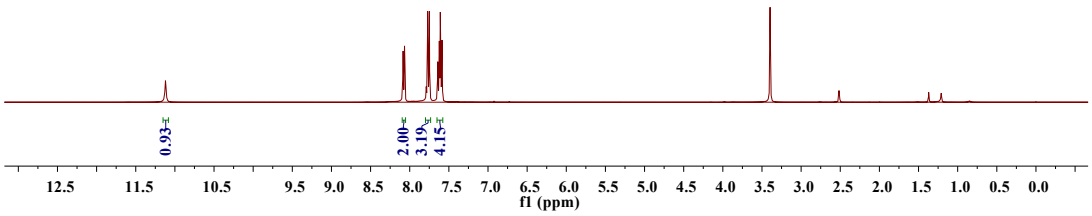
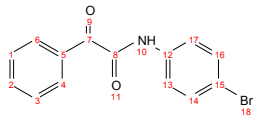


LCK-77
LCK-77



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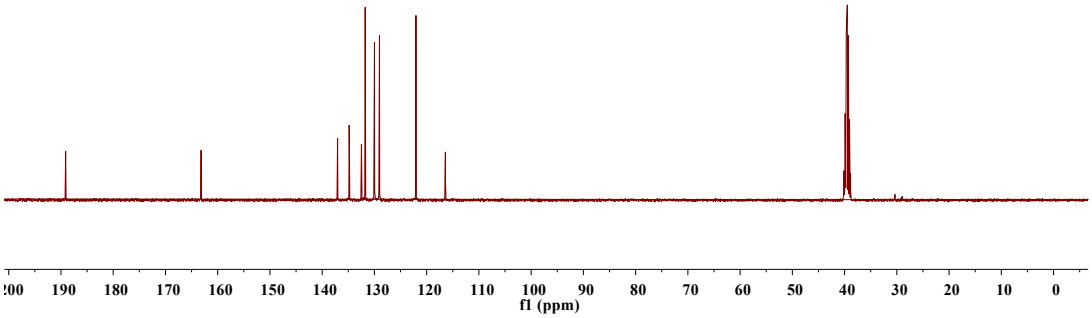
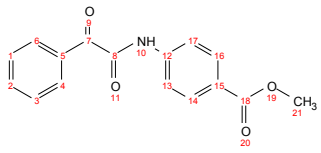


160323-gk
LCK-68 1H-NMR DMSO 303K AV-300



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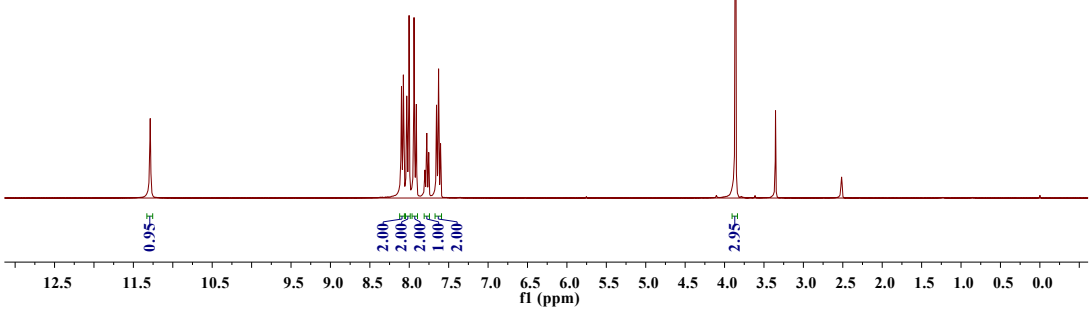
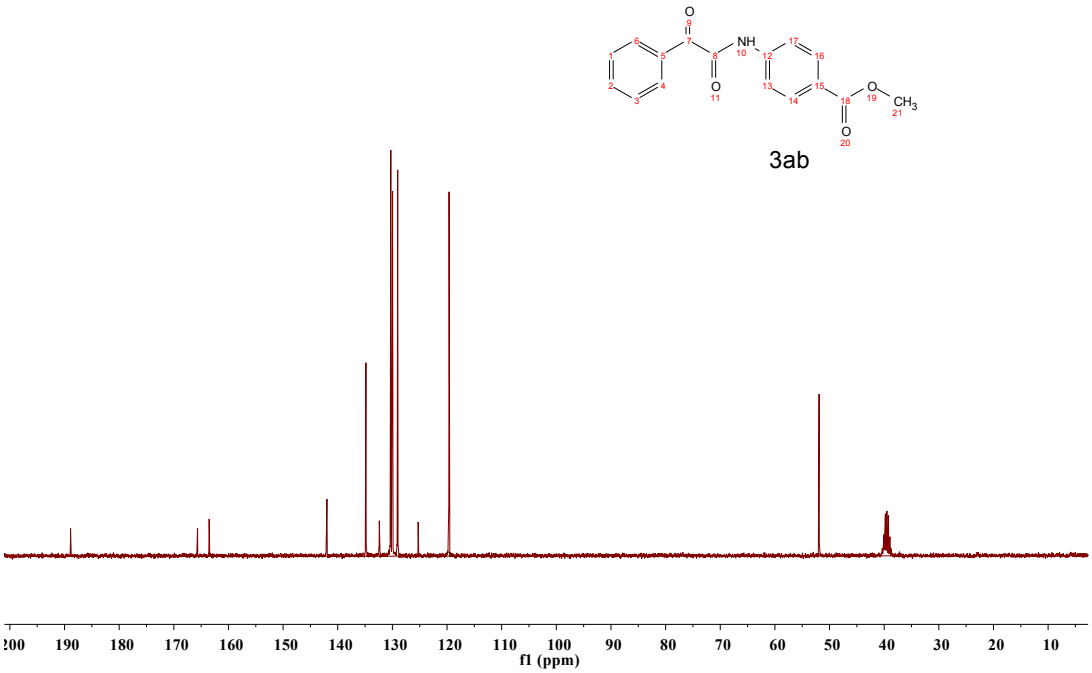


160323-gk
LCK-68 13C-NMR DMSO 303K AV-300



160323-gk
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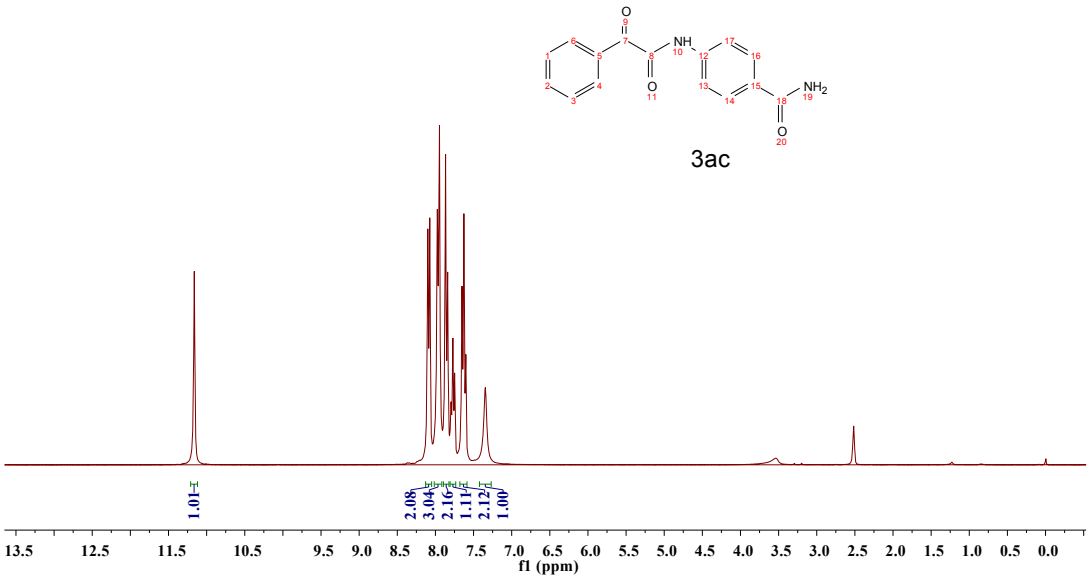
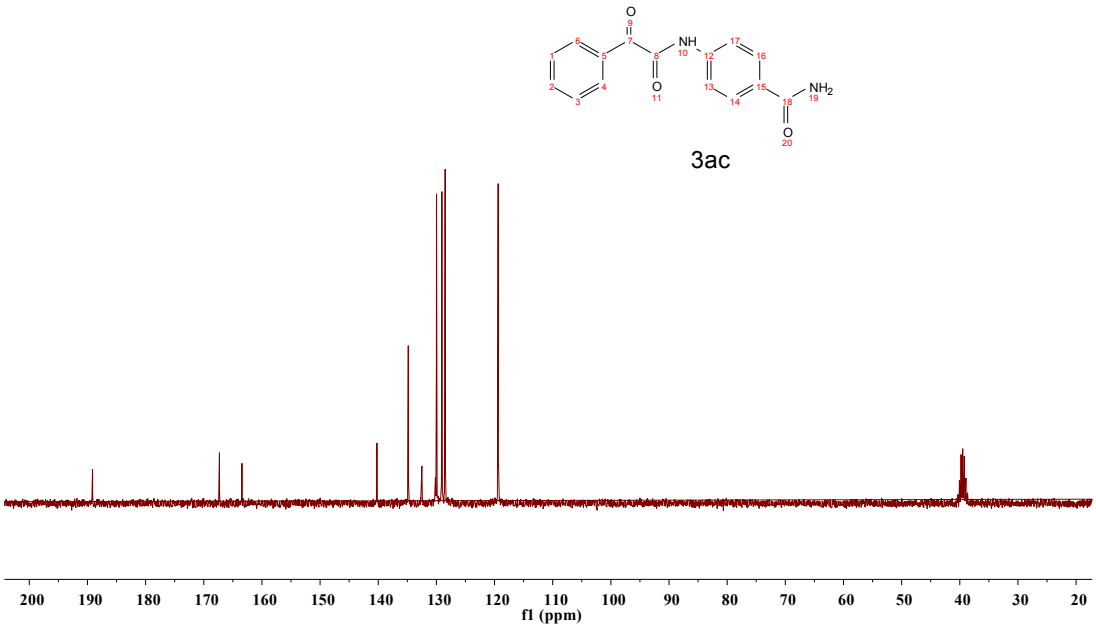
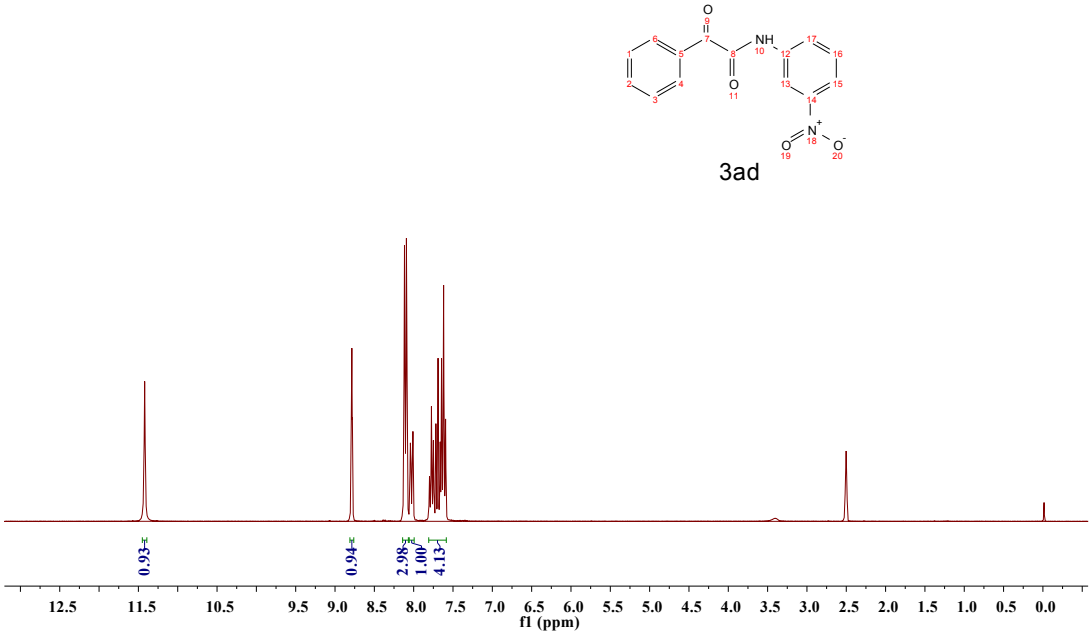


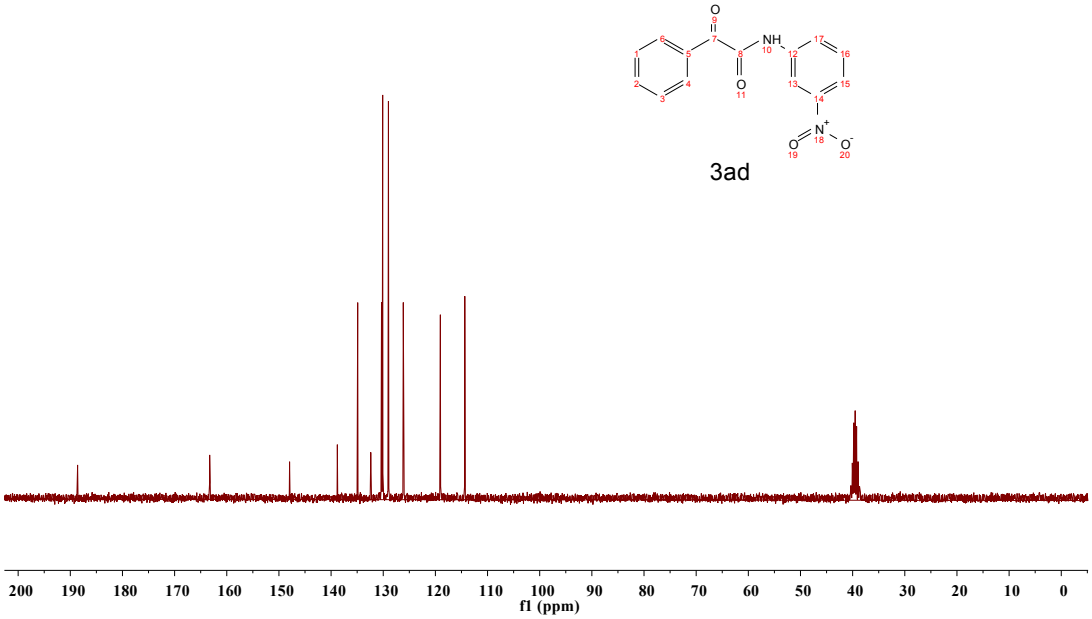
160323-gk
LCK-69 13C-NMR DMSO 303K AV-300



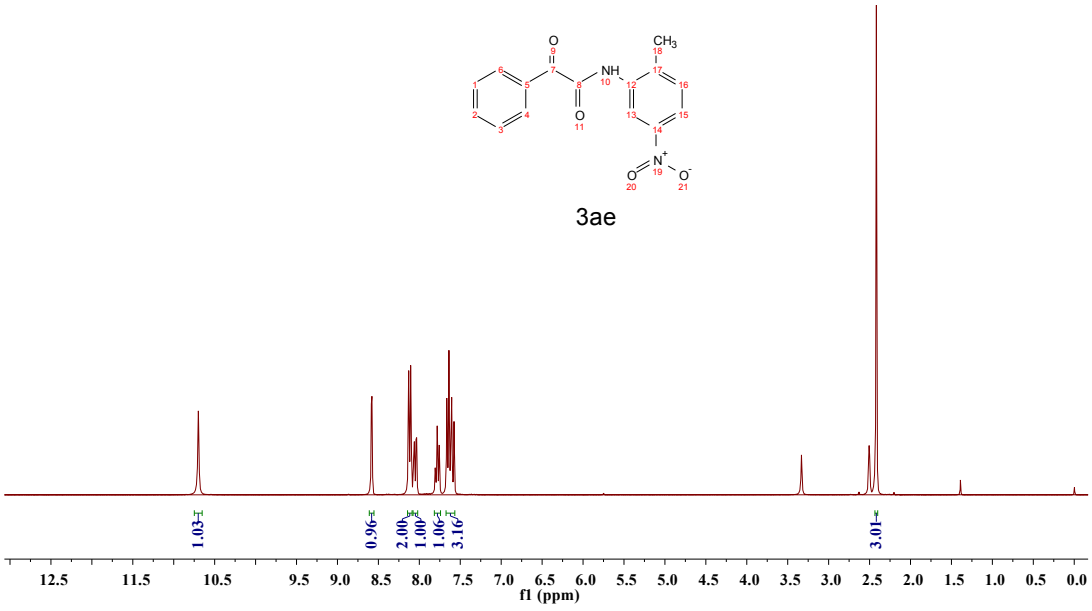
160419-gk
LCK-74 1H-NMR DMSO 303K AV-300



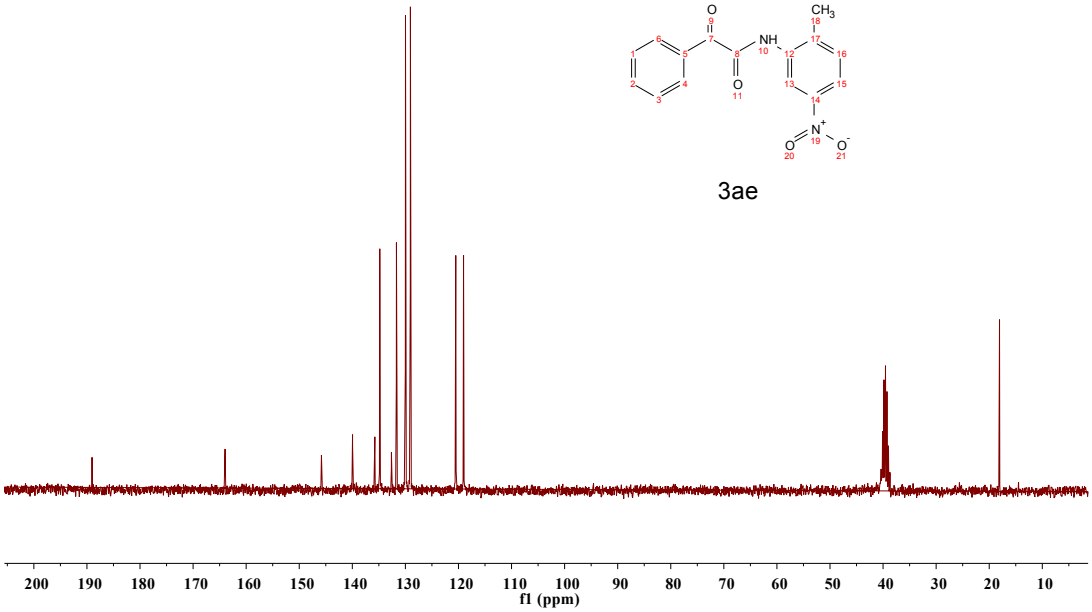
160419-gk
LCK-74 13C-NMR DMSO 303K AV-300



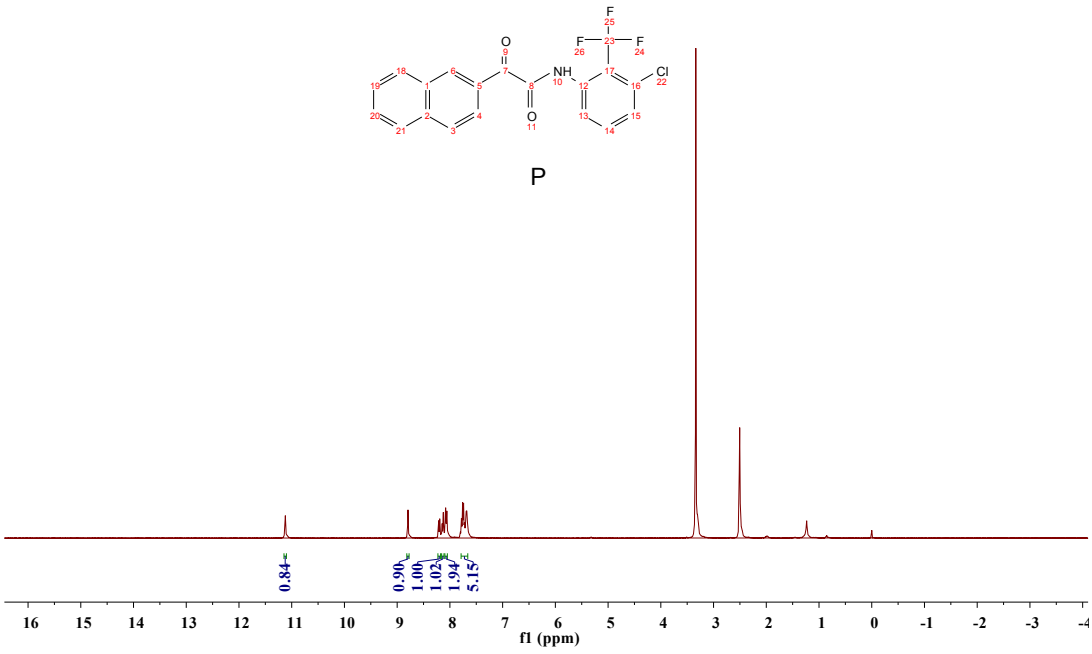
160419-gk
LCK-75 1H-NMR DMSO 303K AV-300

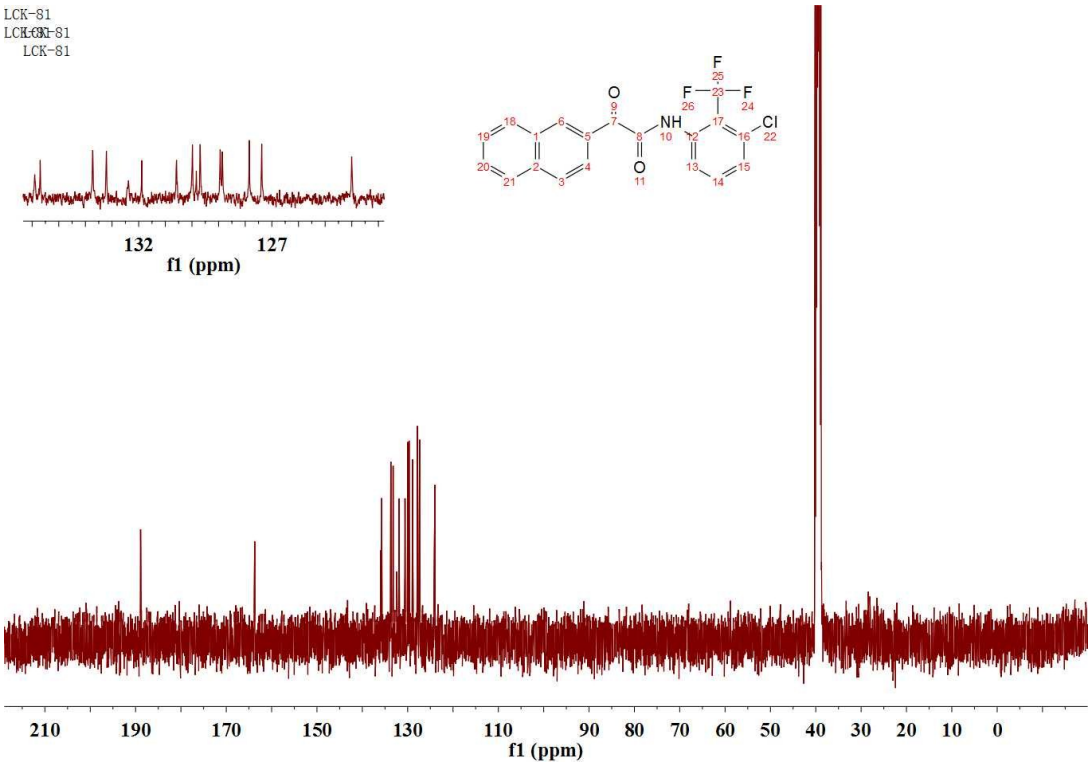


160419-gk
LCK-75 13C-NMR DMSO 303K AV-300



LCK-81
LCK-81




LCK-81
LCK-81
LCK-81
132
127
f1 (ppm)
O
NH
F
F
F
Cl
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)