Supplementary Information for

A Green and Efficient Monoacylation Strategy for Symmetrical Diamines in Microreactors

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Part 1. Details of each reagent

Table S1. details of each reagent.

Entry	Abbreviation	Specification	CAS No.	Matching additives /base
1	$SOCl_2$	Thionyl chloride	7719-09-7	Triethylamine (TEA)
2	TsCl	*p*-Toluenesulfonyl chloride	98-59-9	Triethylamine (TEA)
3	PivCl	Trimethylacetyl chloride	3282-30-2	Triethylamine (TEA)
4	IBCF	Isobutyl chloroformate	543-27-1	*N*-methylmorpholine (NMM)
5	EEDQ	2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline	16357-59-8	-
6	DPPCl	Diphenylphosphinic Chloride	1499-21-4	*N*-methylmorpholine (NMM)
7	CDI	1,1′-Carbonyldiimidazole	530-62-1	-
8	DCC	Dicyclohexylcarbodiimide	538-75-0	1-Hydroxybenzotriazole (HOBt)
9	DIC	*N,N*-Diisopropylcarbodiimide	693-13-0	1-Hydroxybenzotriazole (HOBt)
10	EDCI	*N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride	25952-53-8	1-Hydroxybenzotriazole (HOBt)
11	PyBOP	1*H*-benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate	128625-52-5	Triethylamine (TEA)
12	HATU	2-(7-azabenzotriazole)-*N,N,N′,N′*-tetramethylurea hexafluorophosphate	148893-10-1	Triethylamine (TEA)
13	HBTU	2-(1*H*-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate	94790-37-1	Triethylamine (TEA)
14	TPTU	2-(2-Oxo-1(2H)-pyridyl)-1,1,3,3-tetramethyluronium Tetrafluoroborate	125700-71-2	Triethylamine (TEA)

In order to deprotonate carboxylic acid, in general, additional bases or additives were added in the acylation reactions. 1 eq. additional bases or additives were used in Table S1.[1]

Part 2. The kinetics research of the monoacylation between acyl imidazole and 2a in microreactor

According to literature, all the reactions are in first order with respect to each reactant.[2] Thus, the kinetic equations are as follows:

$$r_1 = k_1 C_A C_{2a} \quad (1)$$

$$r_2 = k_2 C_A C_{3a} \quad (2)$$

$$\frac{dC_A}{dt} = -r_1 - r_2 \quad (3)$$

$$\frac{dC_{2a}}{dt} = -r_1 \quad (4)$$

$$\frac{dC_{3a}}{dt} = r_1 - r_2 \quad (5)$$

$$\frac{dC_{4a}}{dt} = r_2 \quad (6)$$

Where r_1 is the reaction rate of the monoacylation between acyl imidazole and **2a**, r_2 is the reaction rate of the re-acylation between acyl imidazole and **3a**. k_1 and k_2 stand for the corresponding reaction rate constant, where the subscripts A, 2a, 3a and 4a stand for acyl imidazole, **2a**, **3a** and **4a**, respectively.

The yields of **3a** and **4a** were collected at different temperatures and residence times in microreactor, and the results were shown in Fig. S1.

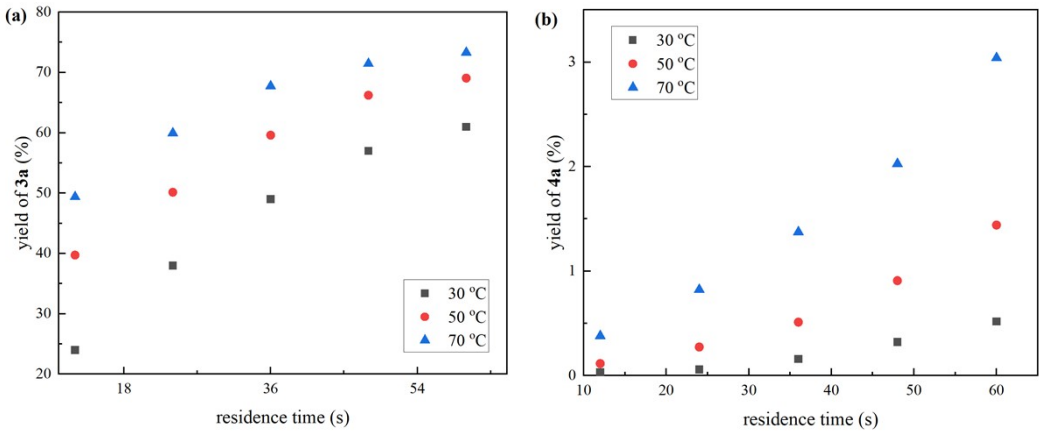


Fig. S1. The yields of **3a** and **4a** at different temperatures and residence times.

The reaction kinetics data was analyzed in MATLAB 2019a software to solve the partial differential equations Eqs.(3) – (6), the fitting results of k_1 and k_2 were shown in Table S2.

Table S2. Values of k_1 and k_2 at different temperatures.

Temperature (°C)	30	50	70
Values of k_1 (L mol^{-1}s^{-1})	2.2355	3.0217	4.4348
Values of k_2 (L mol^{-1}s^{-1})	0.0658	0.0995	0.01418

After getting k_1 and k_2 at different temperatures, according to the Arrhenius equation, the fittings of ln(k) and 1/T were shown in Fig. S2. According to the fitting results, the pre-exponential factors (A_1 and A_2) and activation energy values (E_1 and E_2) were derived, and the results were shown in Table S3.

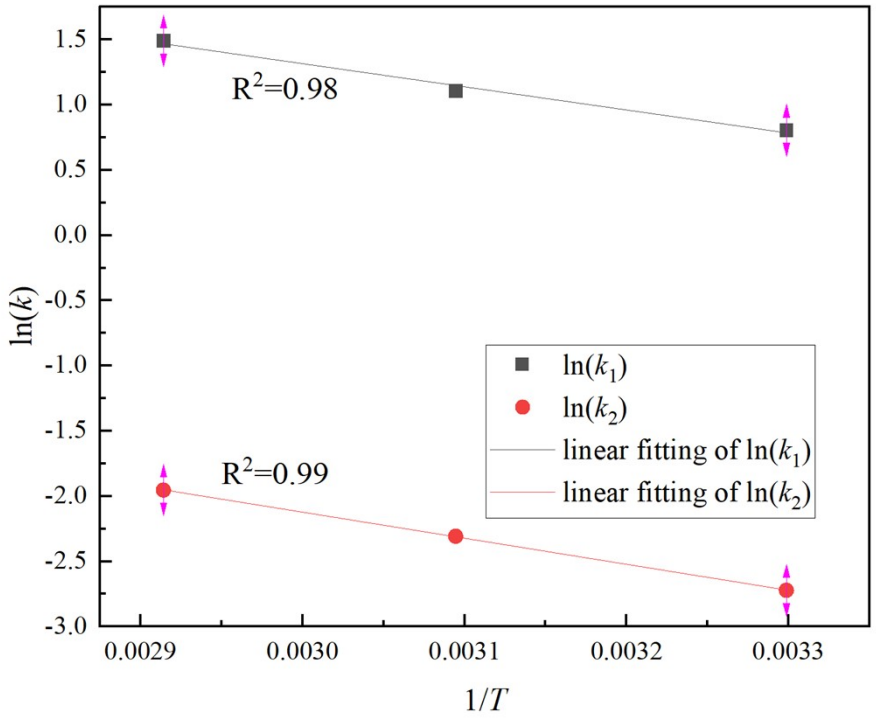


Fig. S2 The plot of ln(k) and 1/T.

Table S3. Values of the pre-exponential factors and activation energies.[a]

Factors	E_1 (kJ/mol)	A_1 (L mol^{-1} s^{-1})	E_2 (kJ/mol)	A_2 (L mol^{-1} s^{-1})
Values	14.76	7.65×10^2	16.61	4.79×10

[a]: E_1 and A_1 are the activation energy and pre-exponential factor in the monoacylation reaction; E_2 and A_2 are the activation energy and pre-exponential factor in the re-acylation reaction.

Part 3. The comparisons of different additives in the reaction between 4-chlorophenoxyacetic acid and 2a.

Table S4. The comparisons of different additives[a]

Entry	additives	eq.	conv. (%)	**3b:4b**
1	HOBt	0.5	99	71:28
2	DBU	0.5	76	73:3
3	DIPEA	0.5	100	84:16
4	DMAP	0.5	99	85:14
5	2-hydroxy-5-nitropyridine	0.5	99	79:20

[a]: microreactor, C_0 = 0.167 M, T_2 = 30 °C, t_{res} = 10 min, d_{in} = 0.38 mm, Q_t= 0.226 mL/min.

Part 4. The optimization of the substitution reaction between monoacylation product (3a) and benzyl chloride

The schematic diagram of the reaction device is shown in Scheme 5.

Table S5. The comparisons of different additives

Entry	benzyl chloride (eq.) [a]	residence time (min)	temperature (°C)	overall yield of befuraline (%) [b]
1	1	15	80	62
2	1.1	15	80	70
3	1.2	15	80	76
4	1.3	15	80	81
5	1.4	15	80	85

[a]: the eq. of benzyl chloride was controlled by adjusted the flow rate of pump.

[b]: the yield was determined by LC-MS.

Part 5. HPLC chromatograms

The HPLC chromatograms of the all products are shown here, labelled with the carboxylic acid starting material and the amide product.

HPLC equipment: LC-2030C, 3D Plus, Shimadzu

Table S6. HPLC testing conditions.

chromatographic column	C18 (5 μm, 4.6 × 250 mm, XB-C18, Wlech)		
mobile phase	A: 0.1 wt% aqueous formic acid solution, B: MeOH		
	min.	A%	B%
	0	90	10
	0-15.00	0	100
	15.01	90	10
	15.01-20.00	90	10
column temperature	30 °C		
detection wavelength	275 nm		
flow rate	1 mL/min		
injection volume	1 μL		

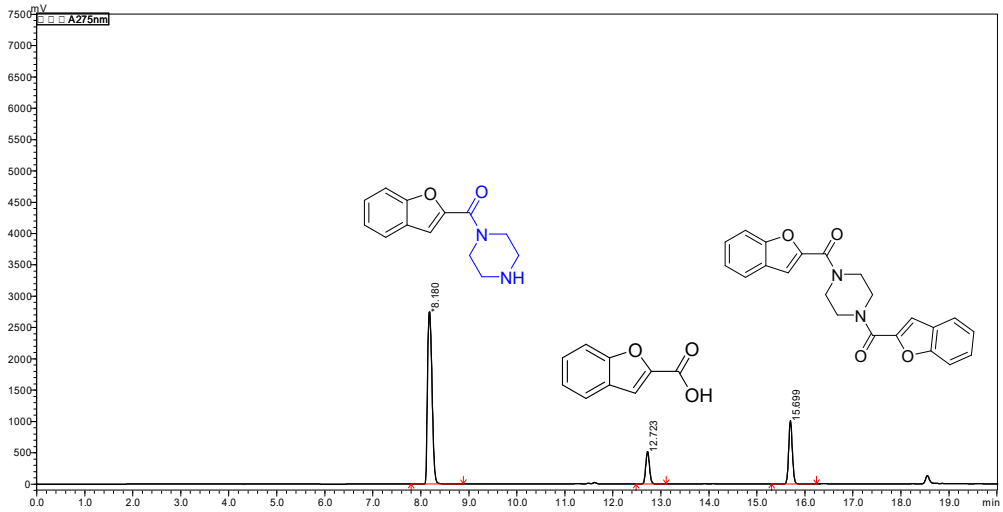


Fig. S2. The monoacylation between 1a with 2a using 1 eq. CDI in batch [a]

[a] Conditions: flask, solvent: DMA. acid activation: benzofuran-2-carboxylic acid (1a, 12.5 mmol) dissolved in 25 mL solvent, was charged into a 150 mL flask and a solution of CDI (**12.5 mmol**, dissolved in 25 mL solvent) was added, reaction temperature (T_1) = 70 °C, reaction time (t_1) = 30 min.

amine coupling: a solution of piperazine (1b, 12.5 mmol, 25 mL) was added before quenching with water, reaction temperature = 30 °C, reaction time = 30 min.

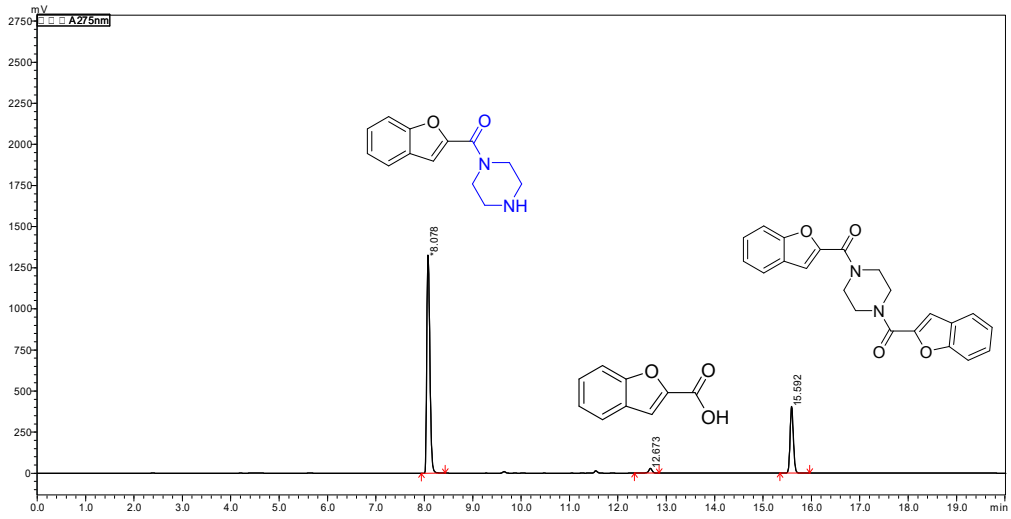


Fig. S3 The monoacylation between 1a with 2a using 1.2 eq. CDI in batch [a]

[a] Conditions: flask, solvent: DMA. acid activation: benzofuran-2-carboxylic acid (1a, 12.5 mmol) dissolved in 25 mL solvent, was charged into a 150 mL flask and a solution of CDI (**15 mmol**, dissolved in 25 mL solvent) was added, reaction temperature (T_1) = 70 °C, reaction time (t_1) = 30 min.

amine coupling: a solution of piperazine (1b, 12.5 mmol, 25 mL) was added before quenching with water, reaction temperature = 30 °C, reaction time = 30 min.

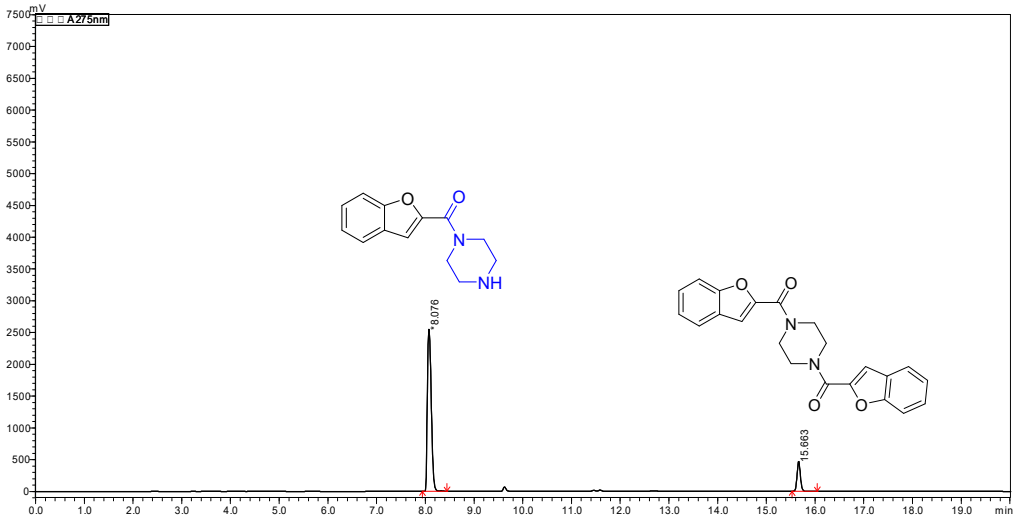


Fig. S4 The monoacylation between 1a with 2a using 1.2 eq. CDI in microreactor [a]

[a] Conditions: microreactor, solvent: DMA. solution A: benzofuran-2-carboxylic acid (1a, 12.5 mmol) dissolved in 25 mL solvent, was charged into a 150 mL flask and a solution of CDI (**15 mmol**, dissolved in 25 mL solvent) was added, reaction temperature (T_1) = 70 °C, reaction time (t_1) = 30 min. solution B: a solution of piperazine (1b, 12.5 mmol, 25 mL). d_{in} (inner diameter of reaction tube): 0.25 mm; Q_A (volume flow rate of solution A) = 0.180 mL/min; Q_B (volume flow rate of solution B) = 0.090 mL/min; T_2 (reaction temperature) = 30 °C; t_{res} (residence time) = 1 min.

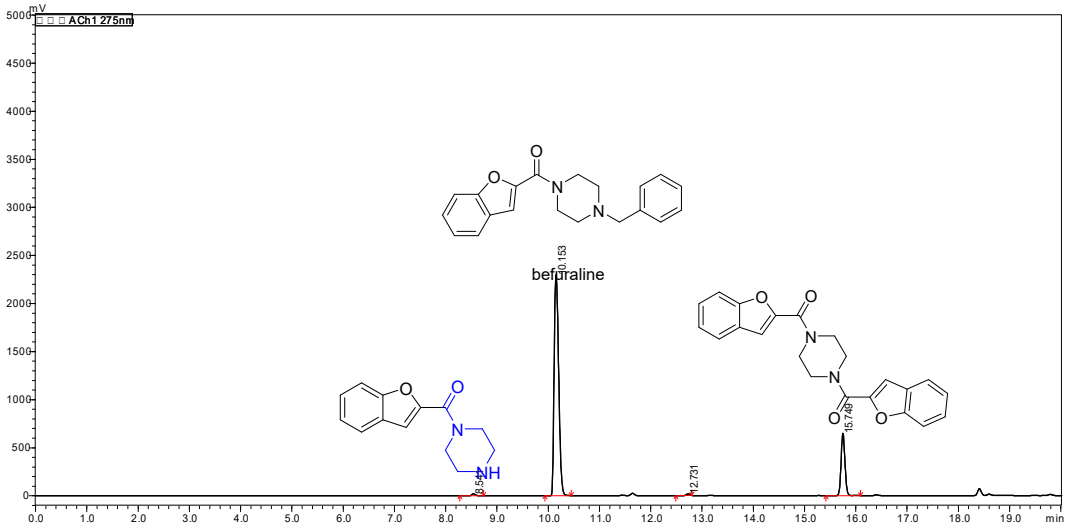


Fig. S5 two-step cascade continuous-flow process to synthesize benzfuraline

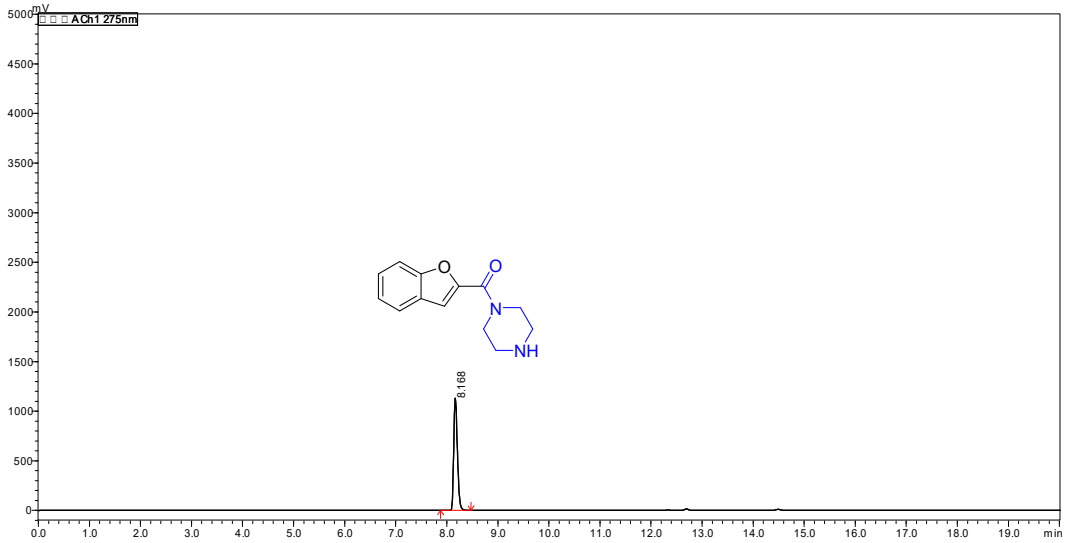


Fig. S6. benzofuran-2-yl(piperazin-1-yl)methanone (monoacylation product of 1a with 2a).

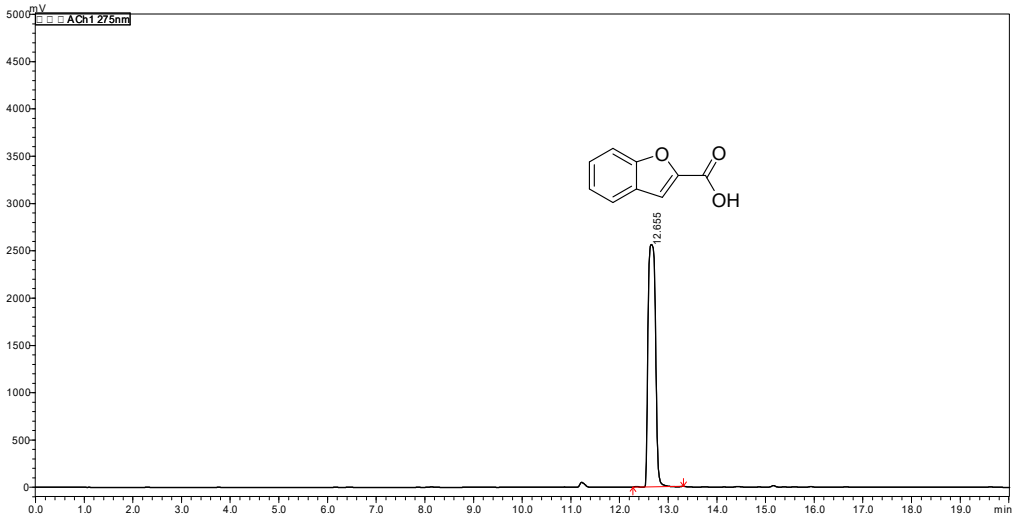


Fig. S7. benzofuran-2-carboxylic acid (1a).

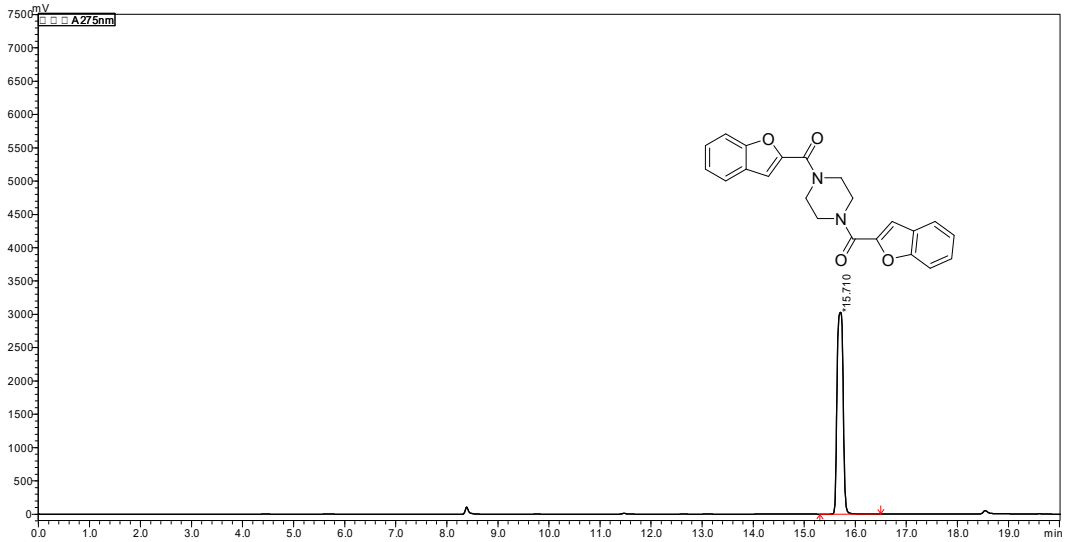


Fig. S8. diacylation byproduct of 1a with 2a.

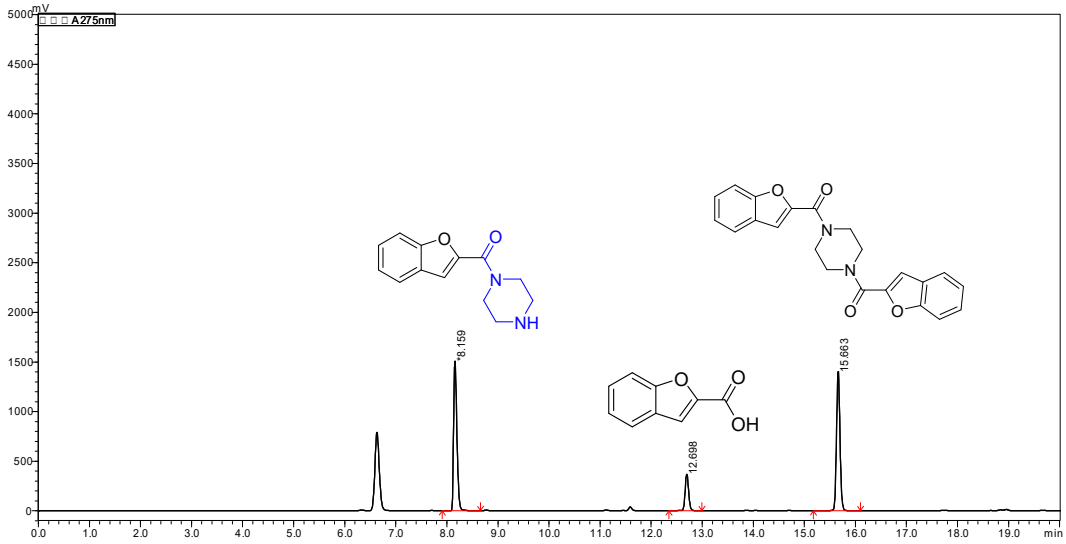


Fig. S9 The monoacylation between 1a with 2a using 1 eq. HATU in batch

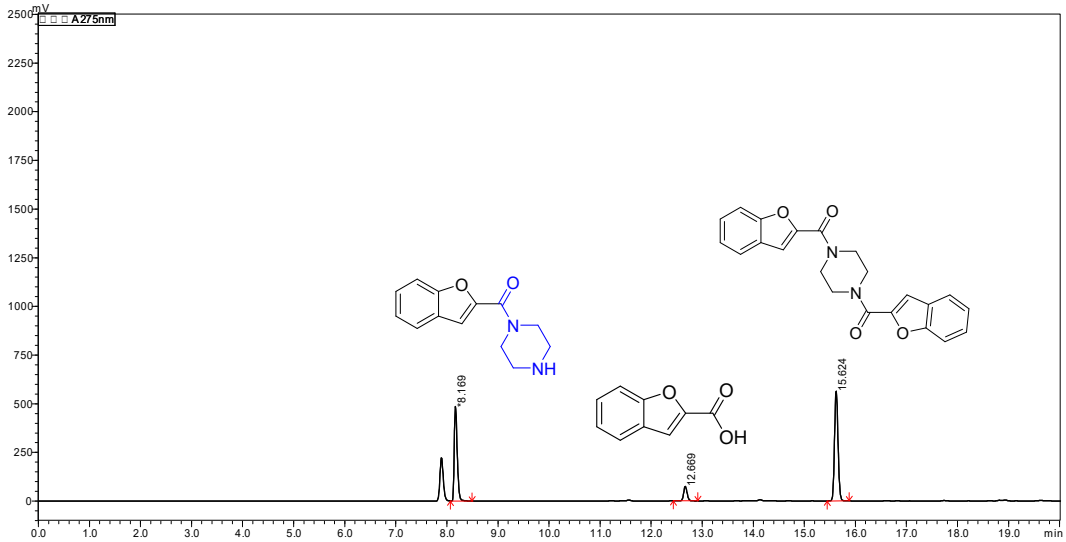


Fig. S10 The monoacylation between 1a with 2a using 1 eq. PyBOP in batch

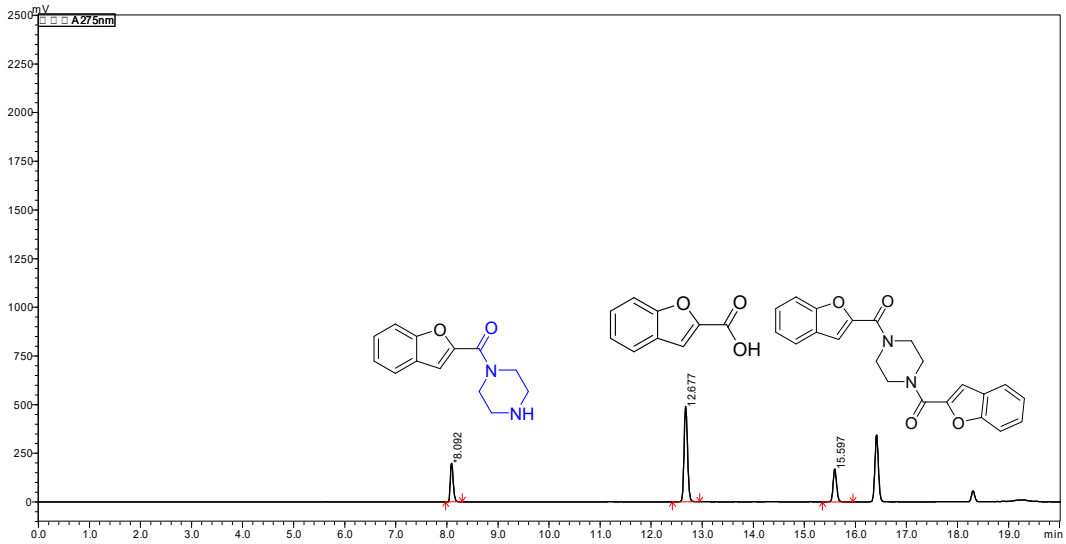


Fig. S11 The monoacylation between 1a with 2a using 1 eq. IBCF in batch

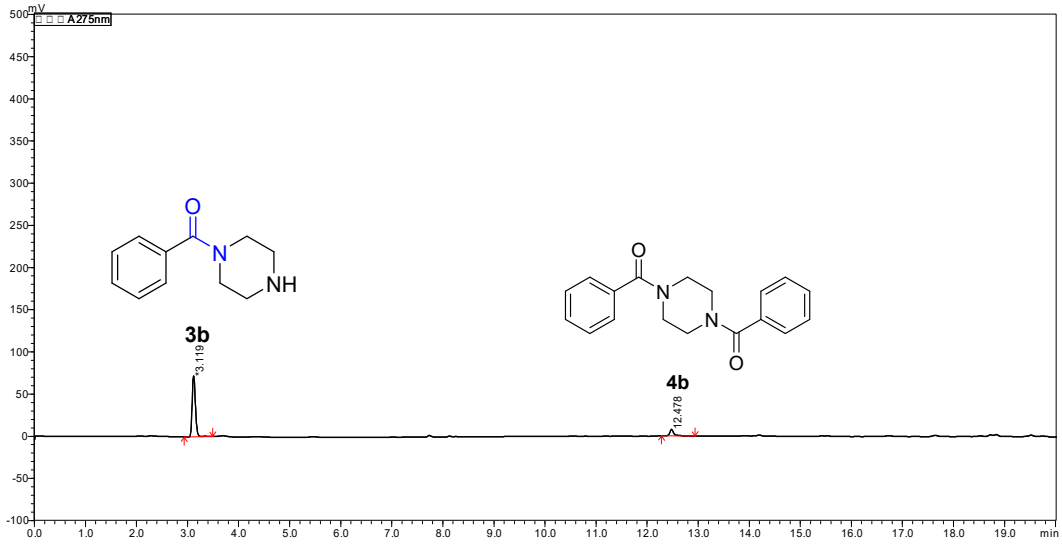


Fig. S12 The monoacylation between 1b with 2a in microreactor under optimized conditions [a]

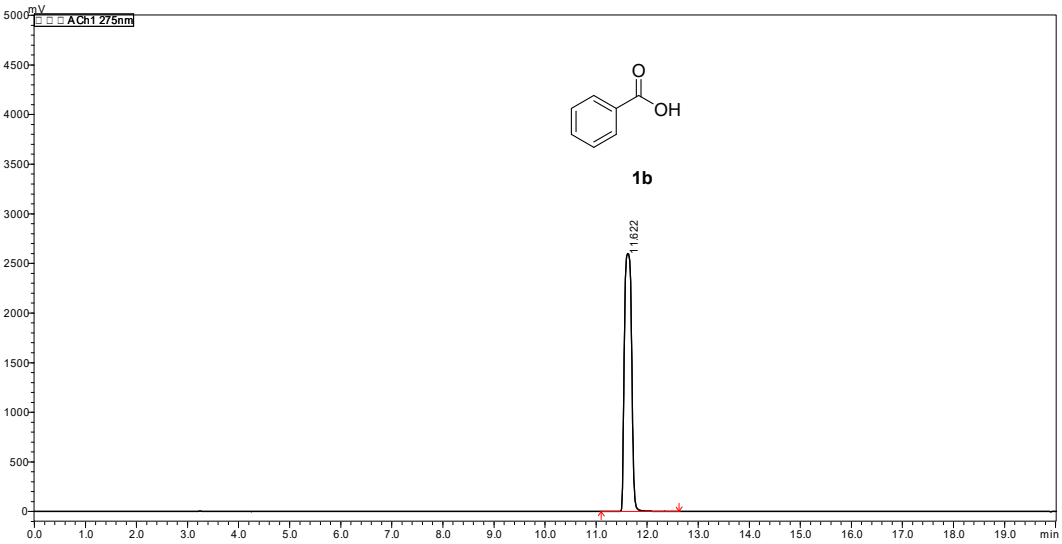


Fig. S13 Benzoic acid (1b)

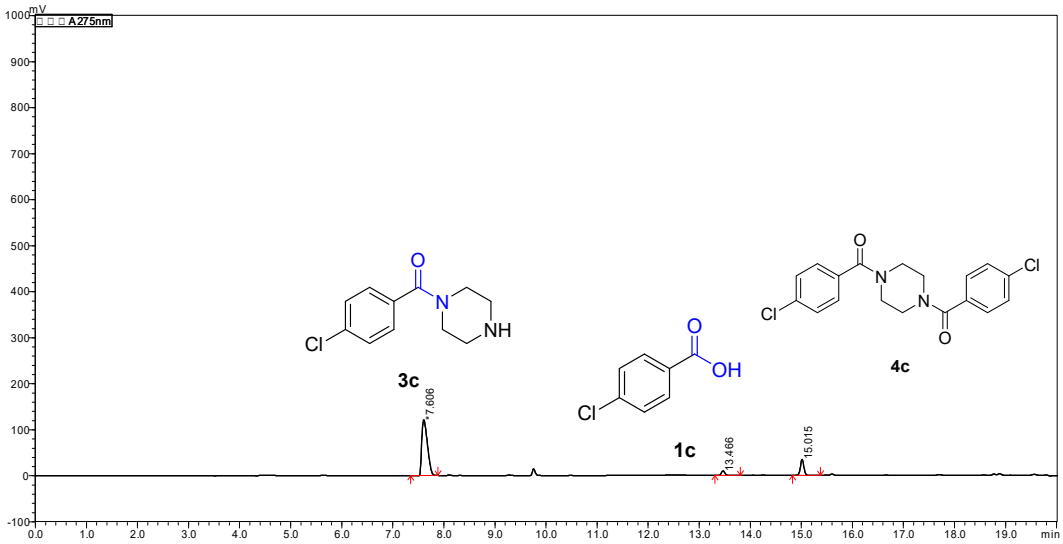


Fig. S14 The monoacylation between 1c with 2a in microreactor under optimized condition.

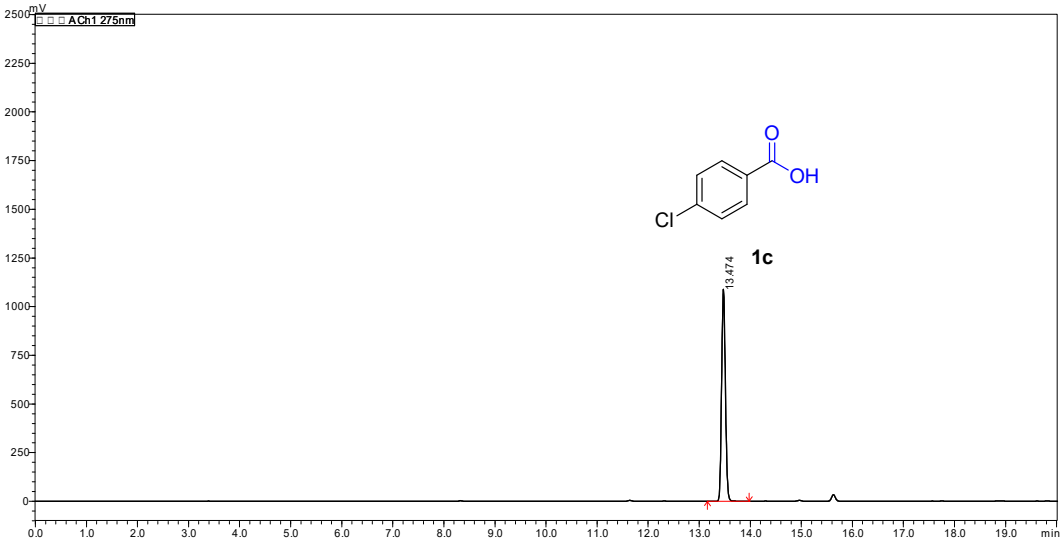


Fig. S15 4-Chlorobenzoic acid (1c)

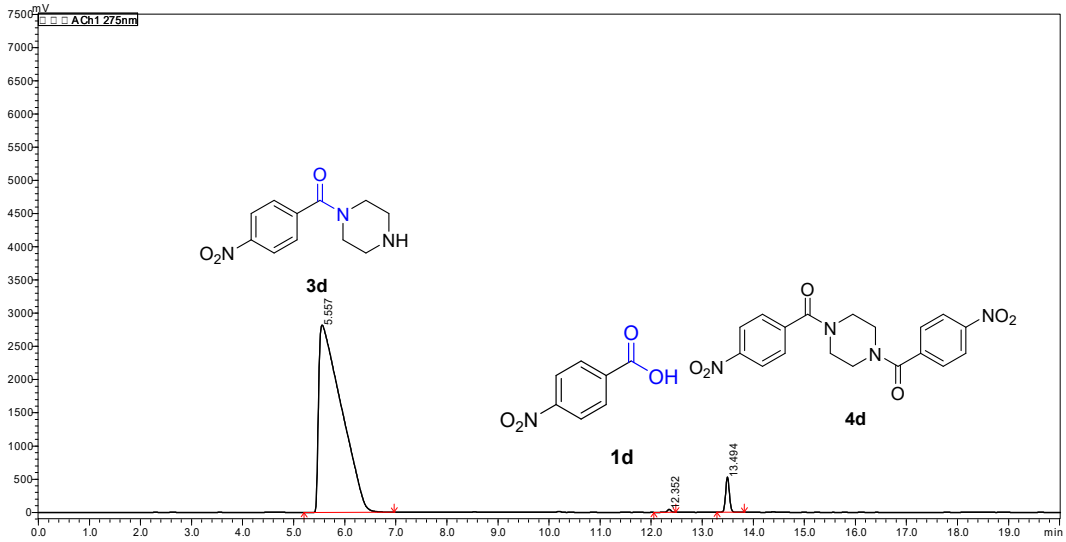


Fig. S16 The monoacylation between 1d with 2a in microreactor under optimized condition.

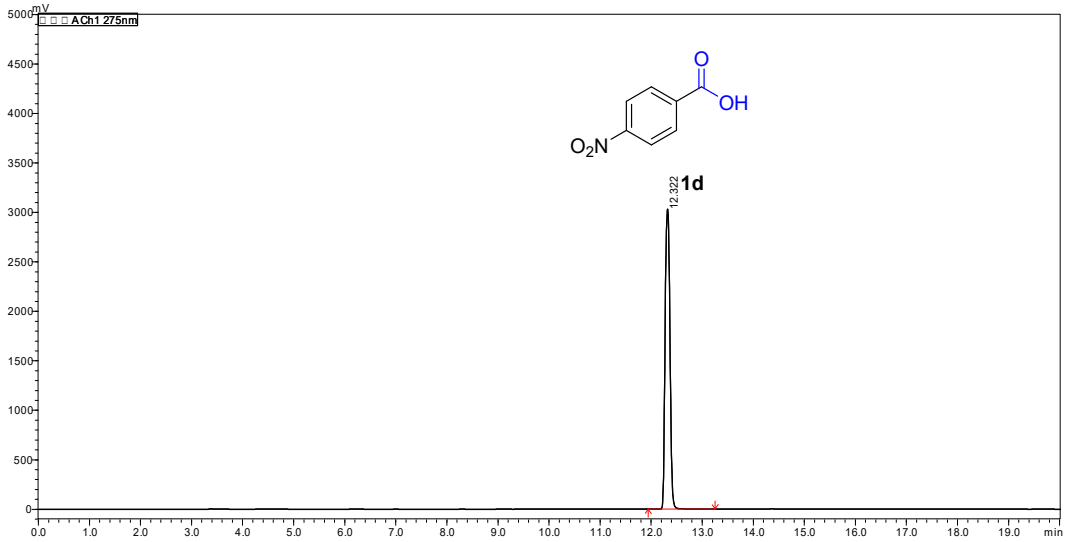


Fig. S17 4-Nitrobenzoic acid (1d)

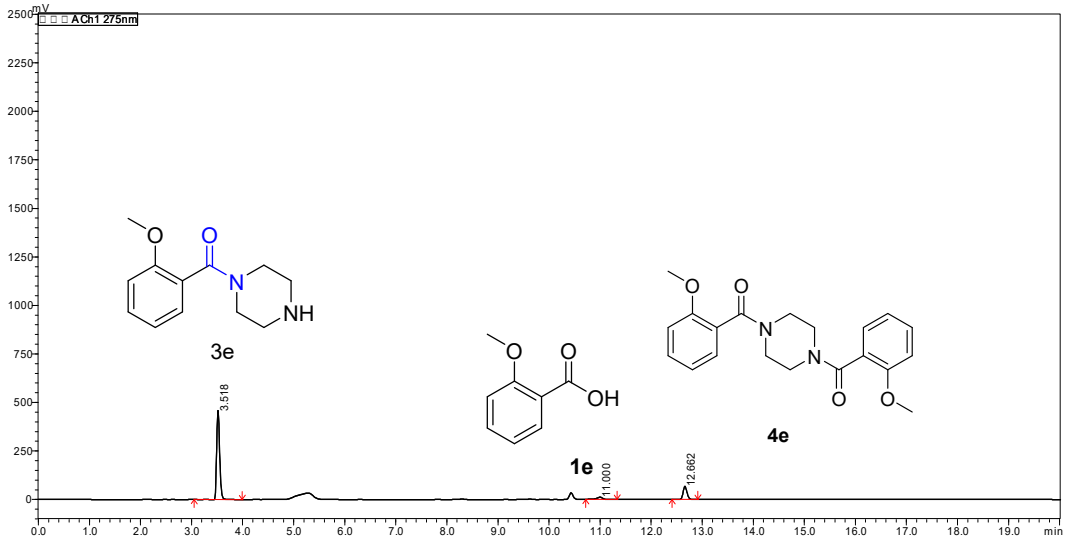


Fig. S18 The monoacylation between 1e with 2a in microreactor under optimized condition.

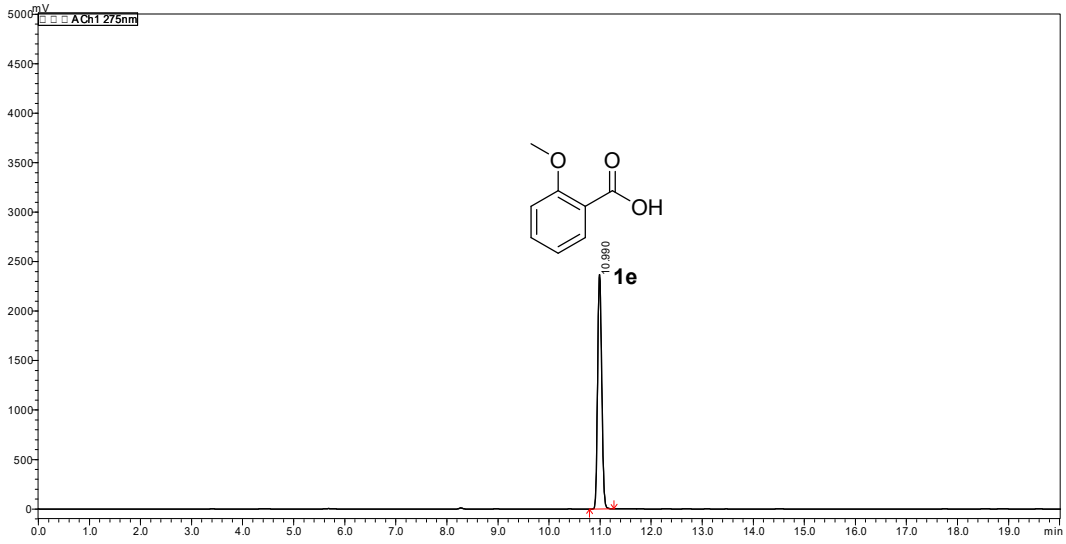


Fig. S19 2-Methoxybenzoic acid (1e)

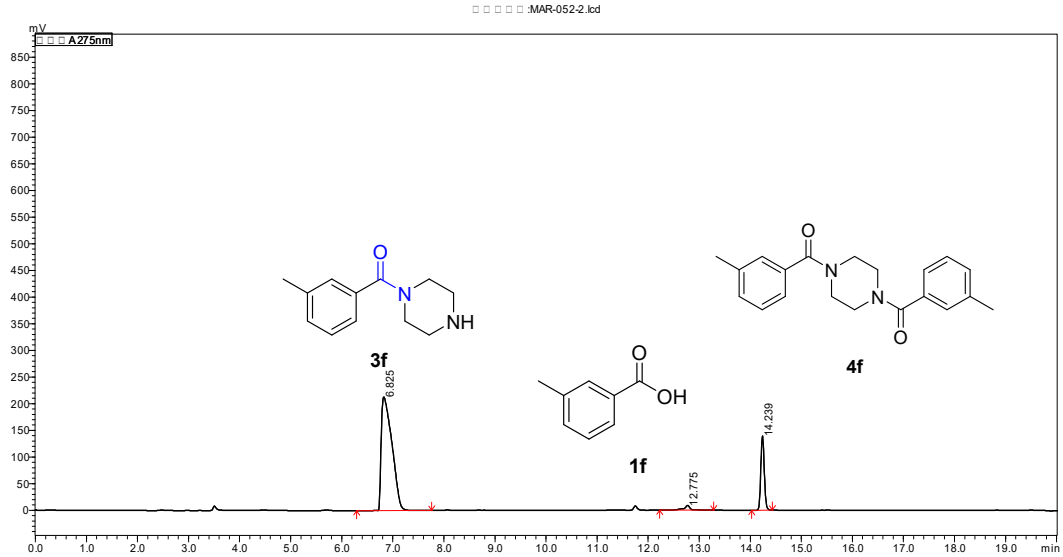


Fig. S20 The monoacylation between 1f with 2a in microreactor under optimized condition.

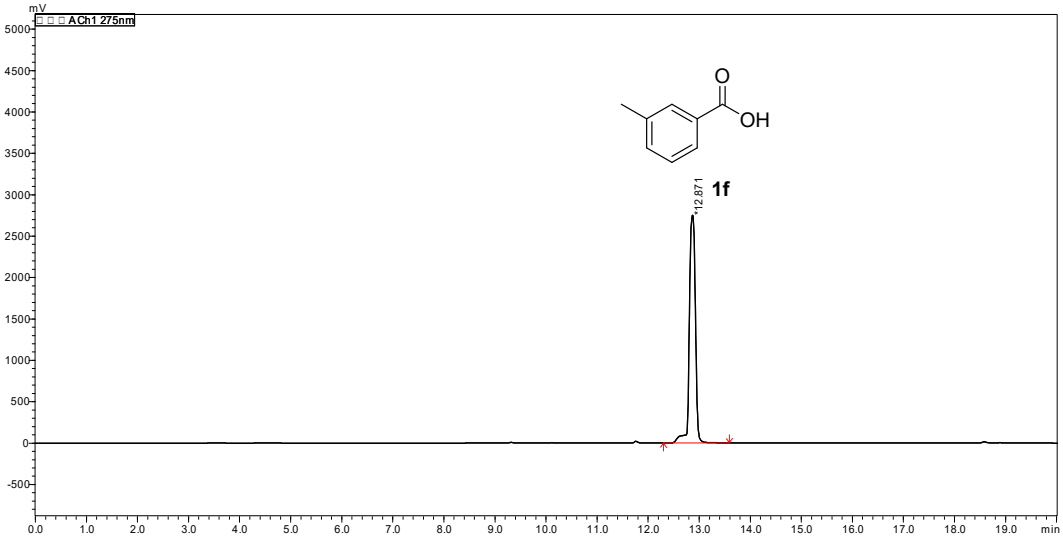


Fig. S21 3-Methylbenzoic acid (1f)

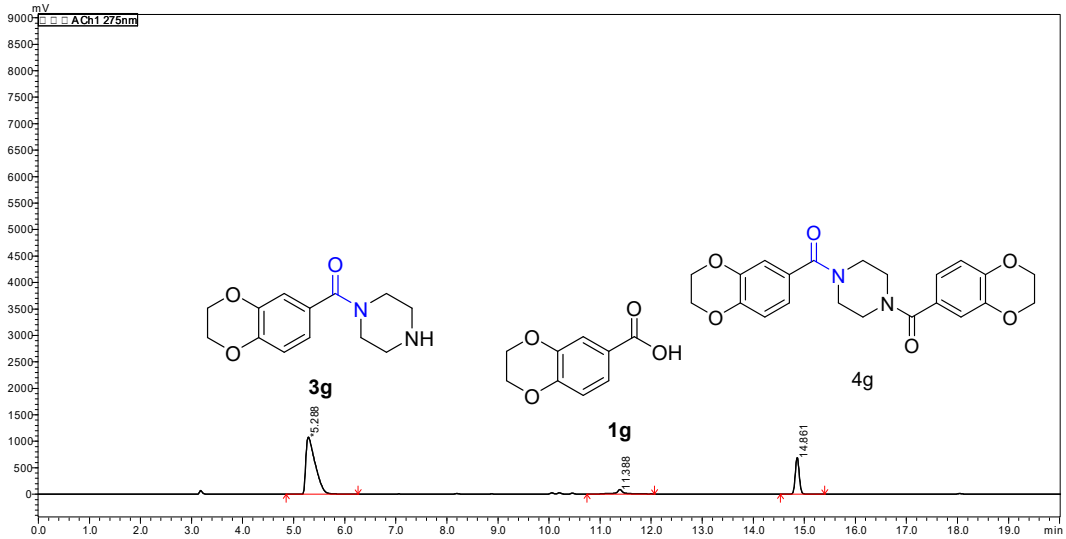


Fig. S22 The monoacylation between 1g with 2a in microreactor under optimized condition.

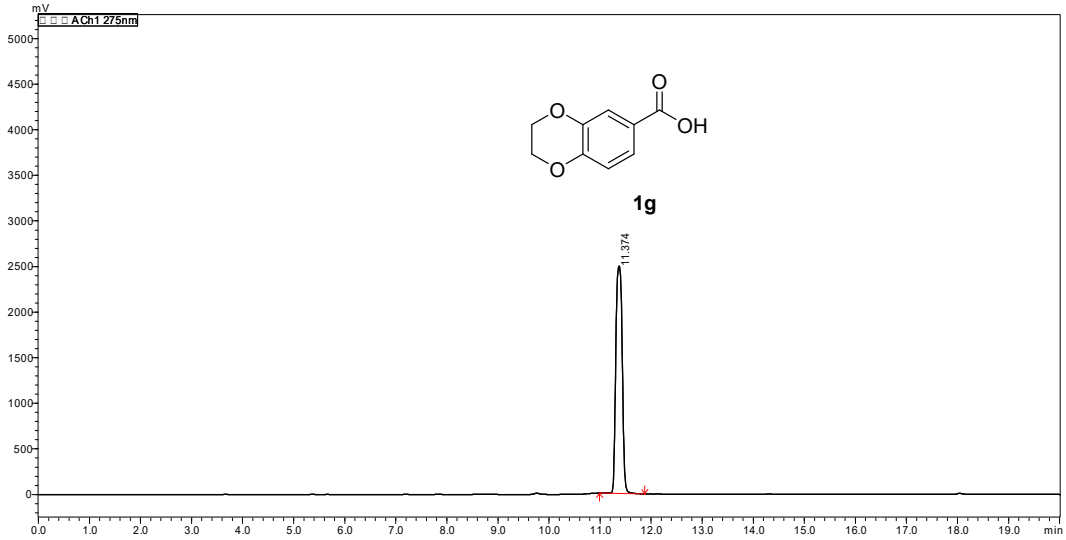


Fig. S23 1,4-Benzodioxane-6-carboxylic acid (1f)

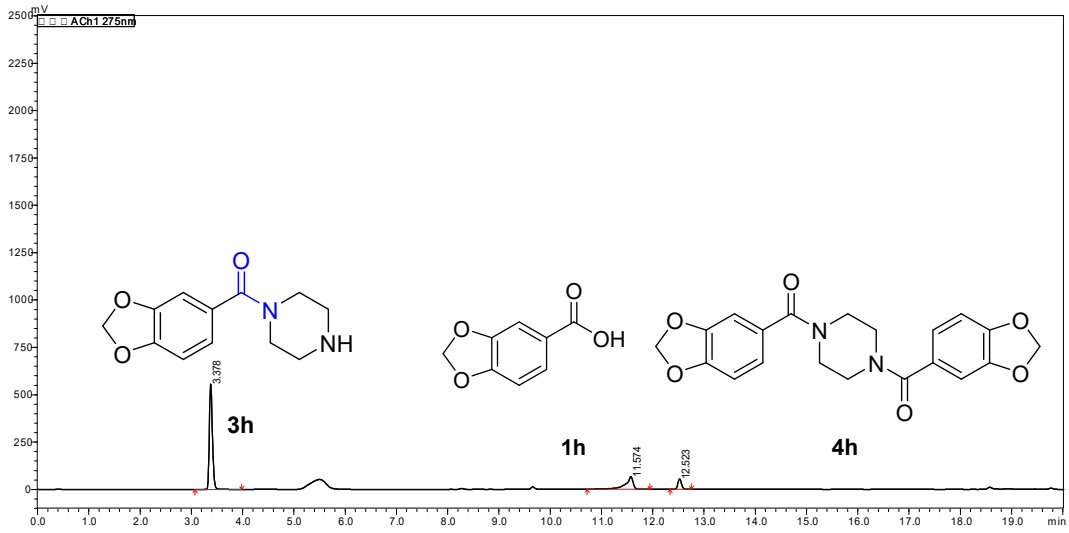


Fig. S24 The monoacylation between 1h with 2a in microreactor under optimized condition.

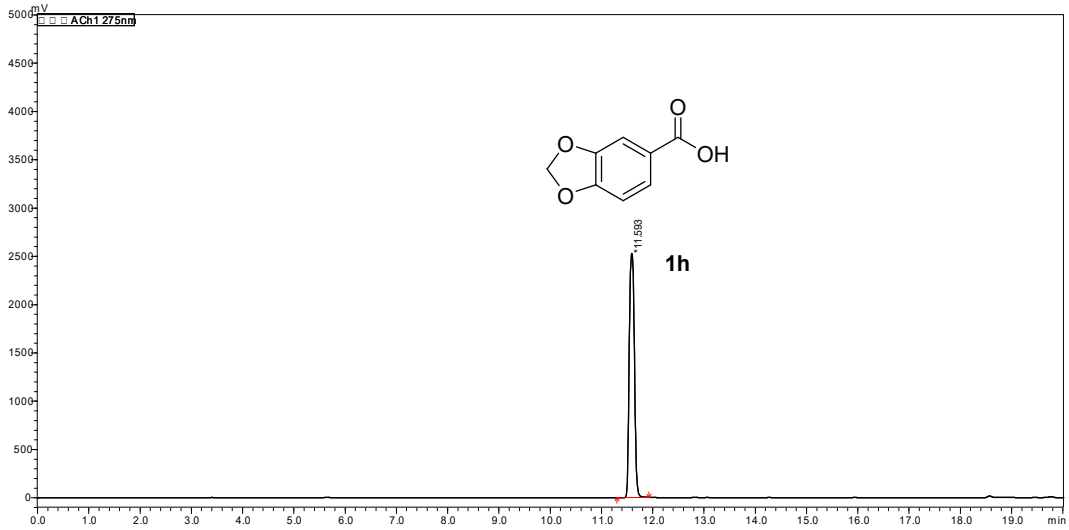


Fig. S25 3,4-Methylenedioxybenzoic acid (1h).

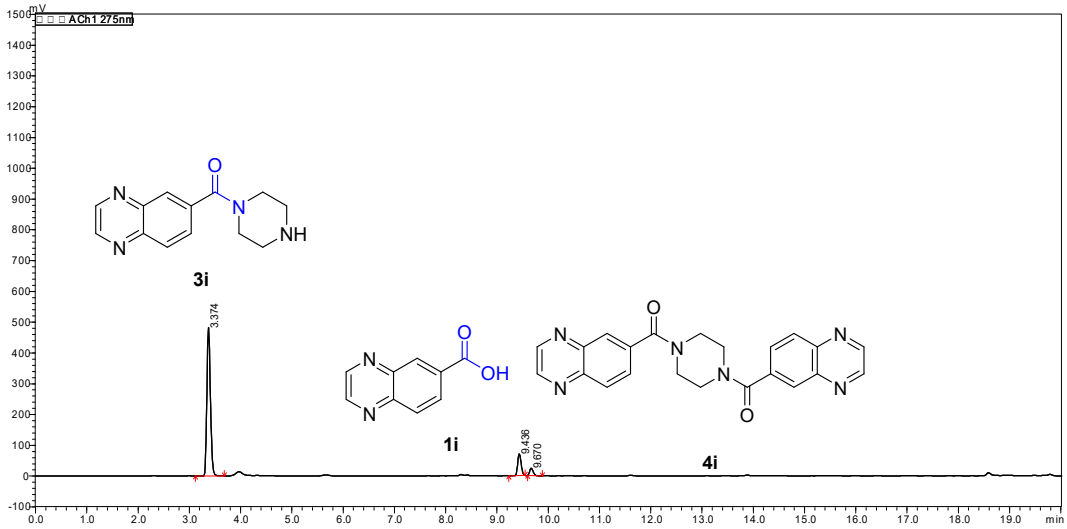


Fig. S26 The monoacylation between 1i with 2a in microreactor under optimized condition.

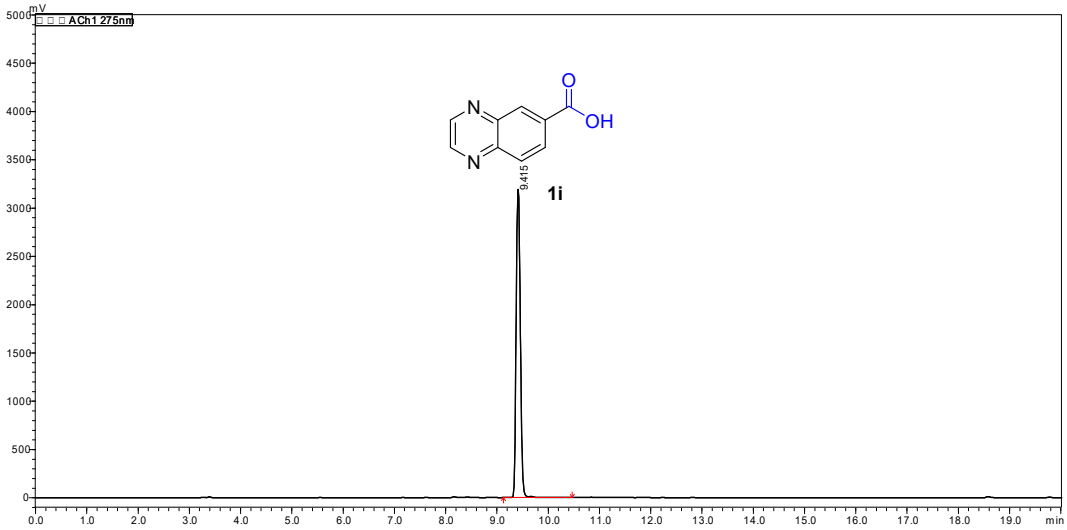


Fig. S27 6-Quinoxaline carboxylic acid (1i).

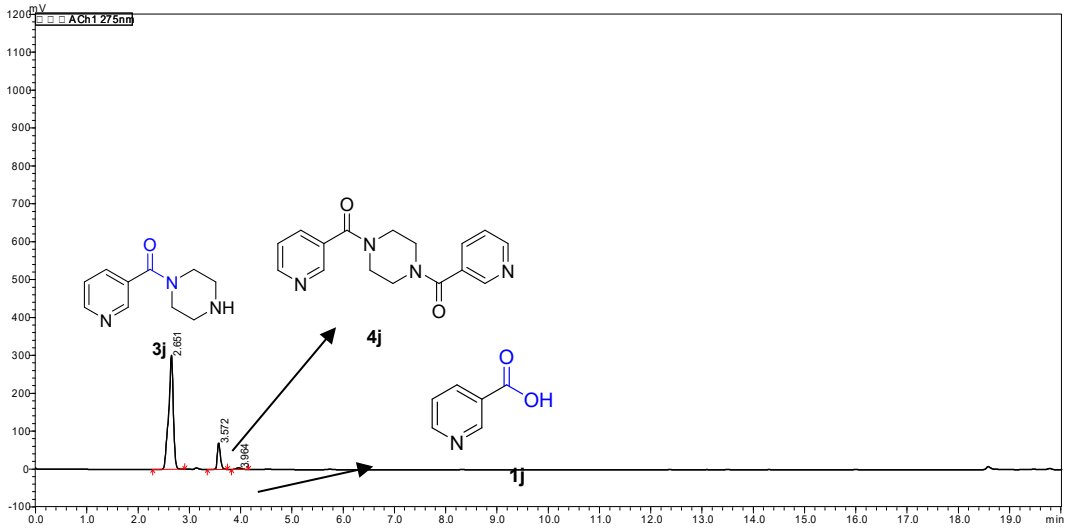


Fig. S28 The monoacylation between 1j with 2a in microreactor under optimized condition.

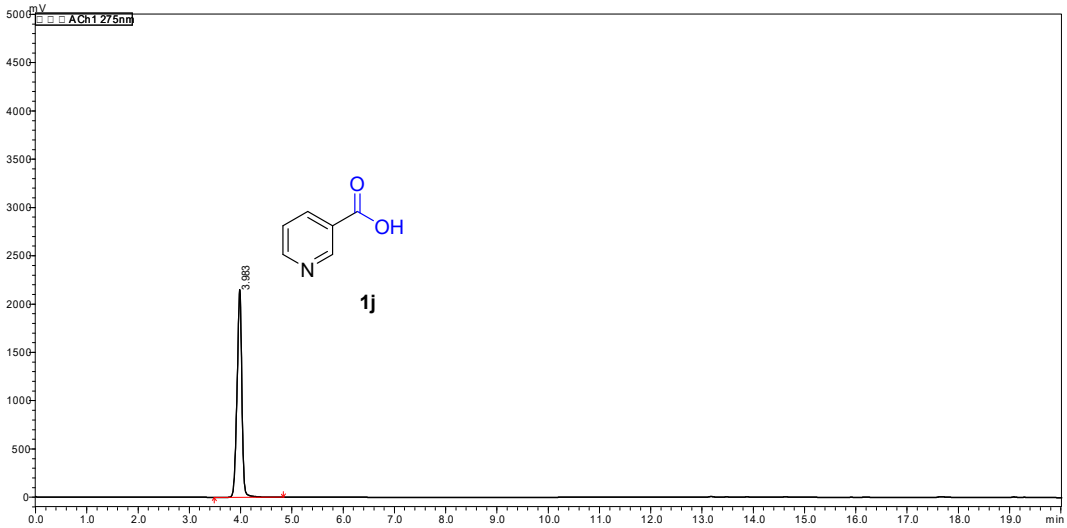


Fig. S29 6-Quinoxaline carboxylic acid (1i).

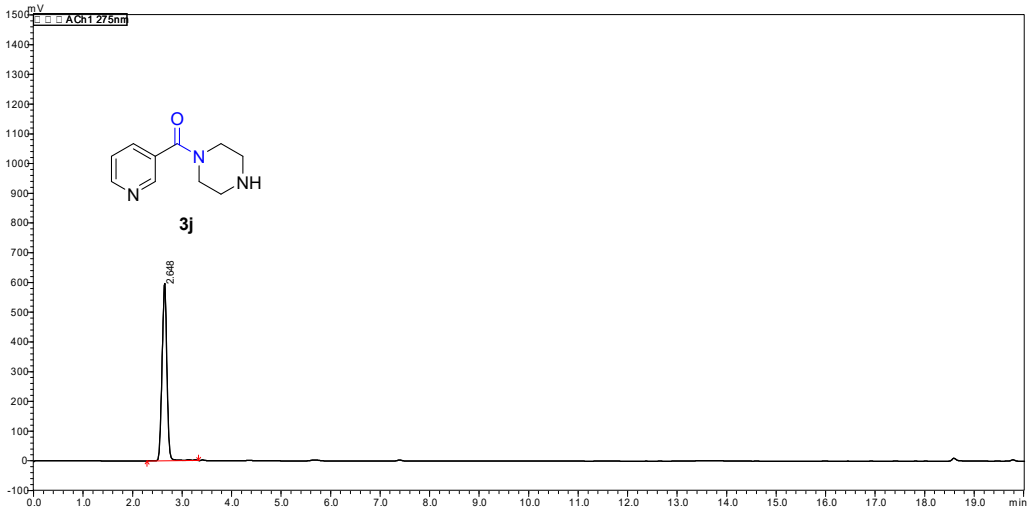


Fig. S30 monoacylation product of 1j with 2a (3j).

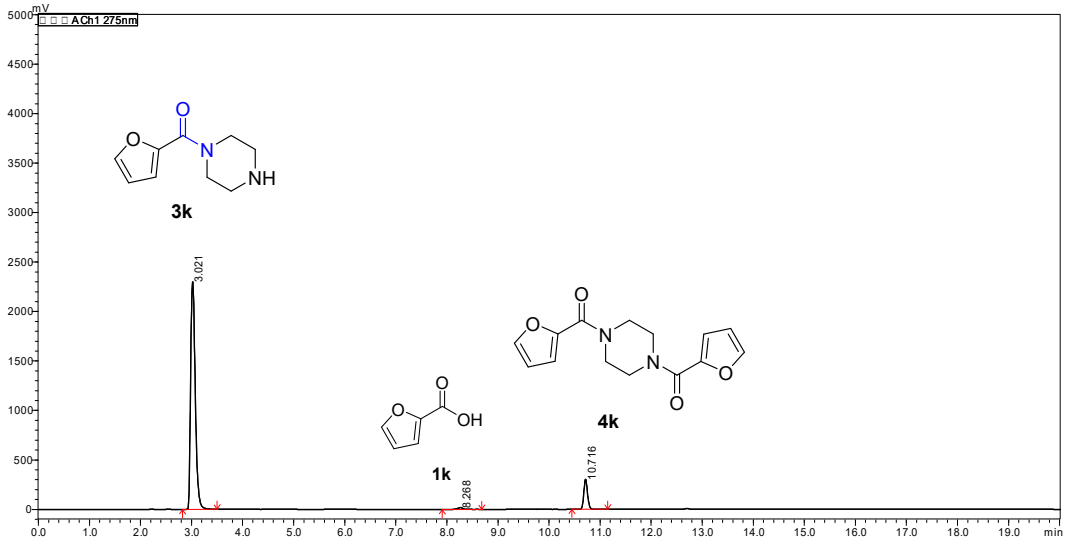


Fig. S31 The monoacylation between 1k with 2a in microreactor under optimized condition.

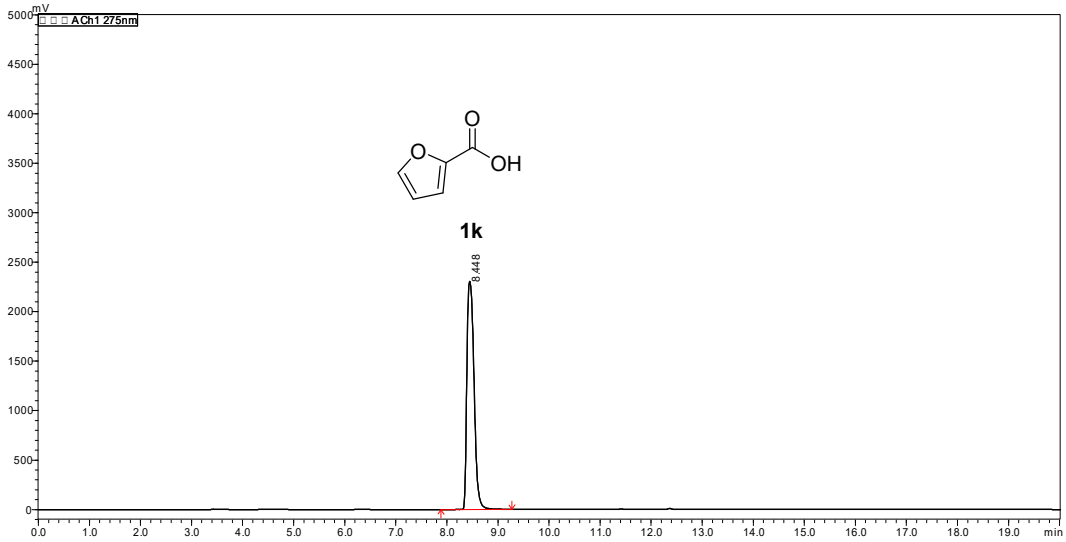


Fig. S32 2-furoic acid (1k).

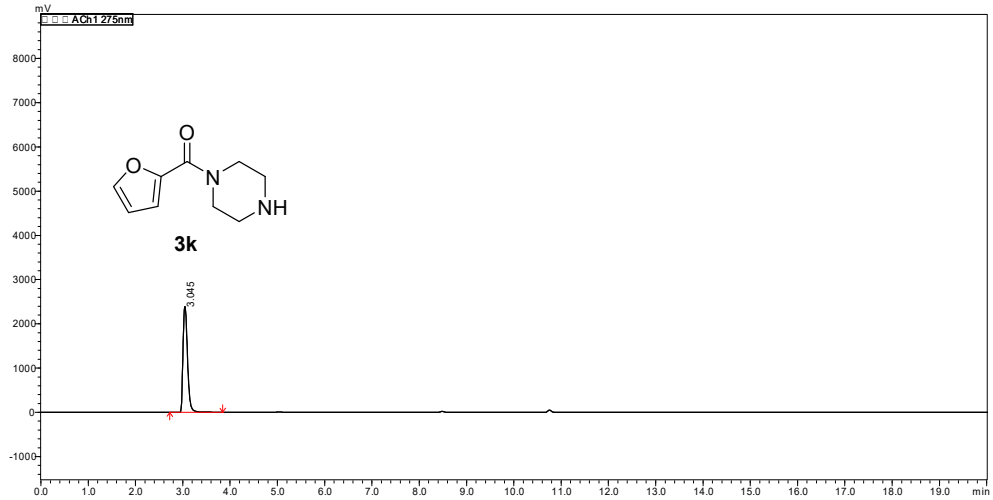


Fig. S33 monoacylation product of 1k with 2a (3k).

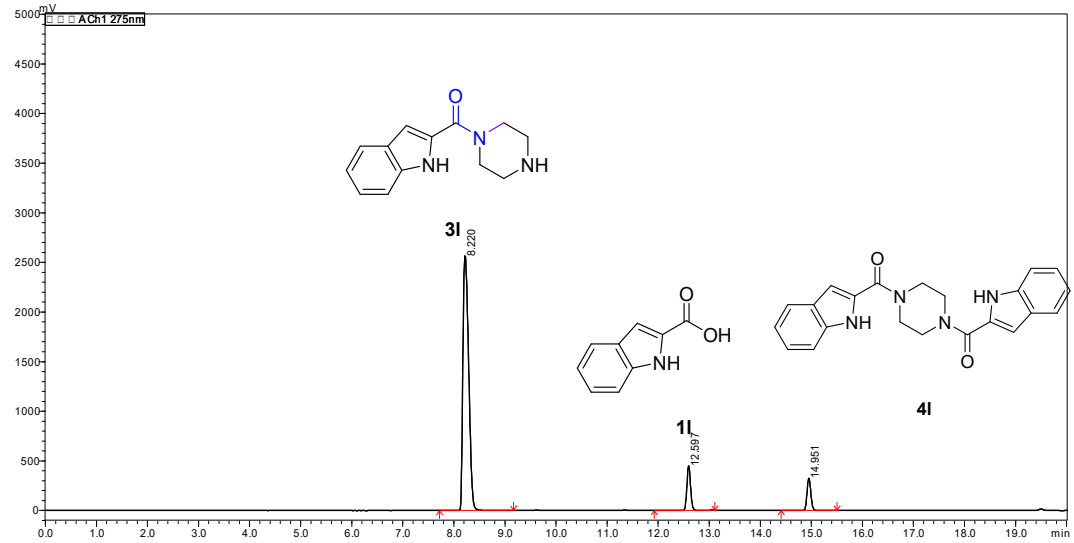


Fig. S34 The monoacylation between 1i with 2a in microreactor under optimized condition.

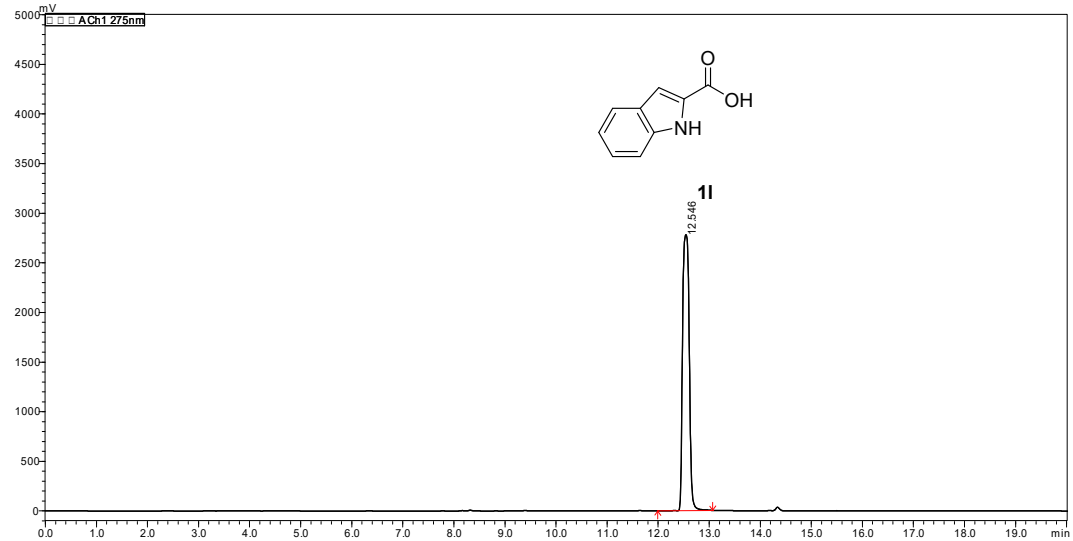


Fig. S35 Indole-2-carboxylic acid (1i).

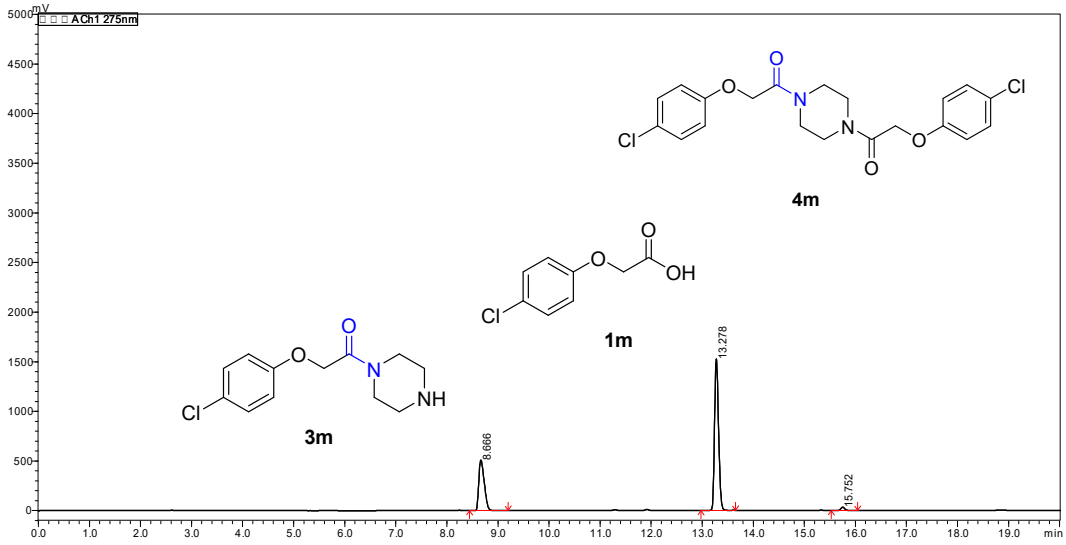


Fig. S36 The monoacylation between 1m with 2a in microreactor with none catalysis

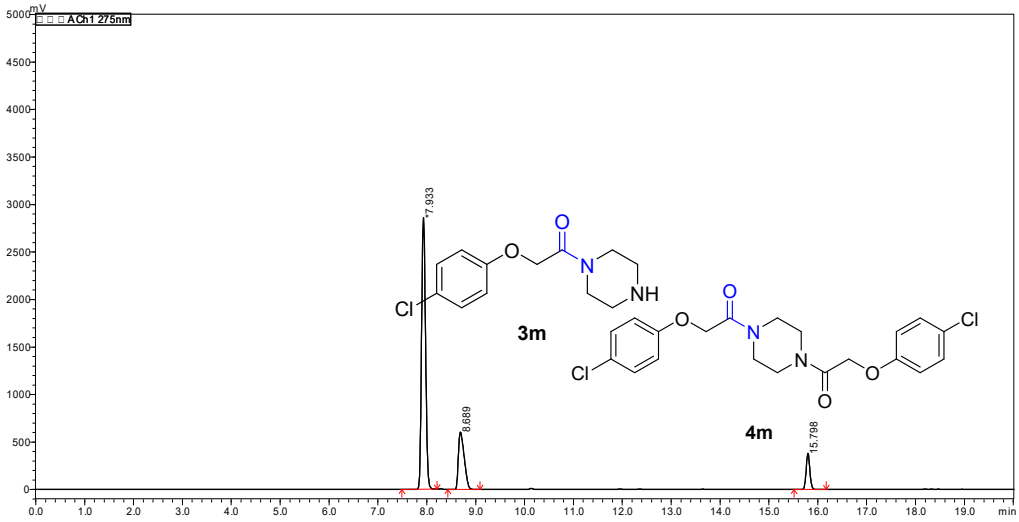


Fig. S37 The monoacylation between 1m with 2a in microreactor with 1 eq. HOBt

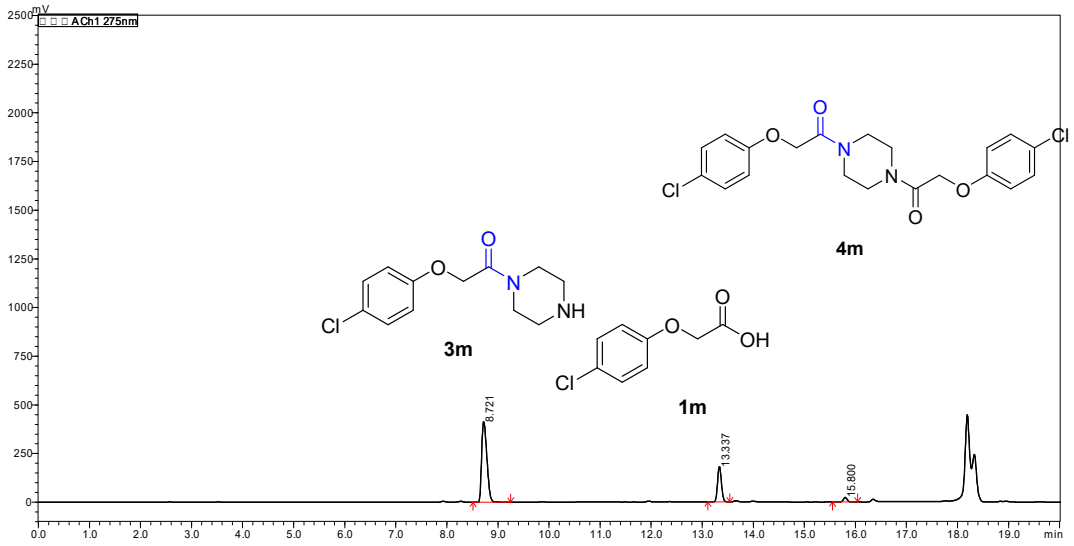


Fig. S38 The monoacylation between 1m with 2a in microreactor with 1 eq. DBU

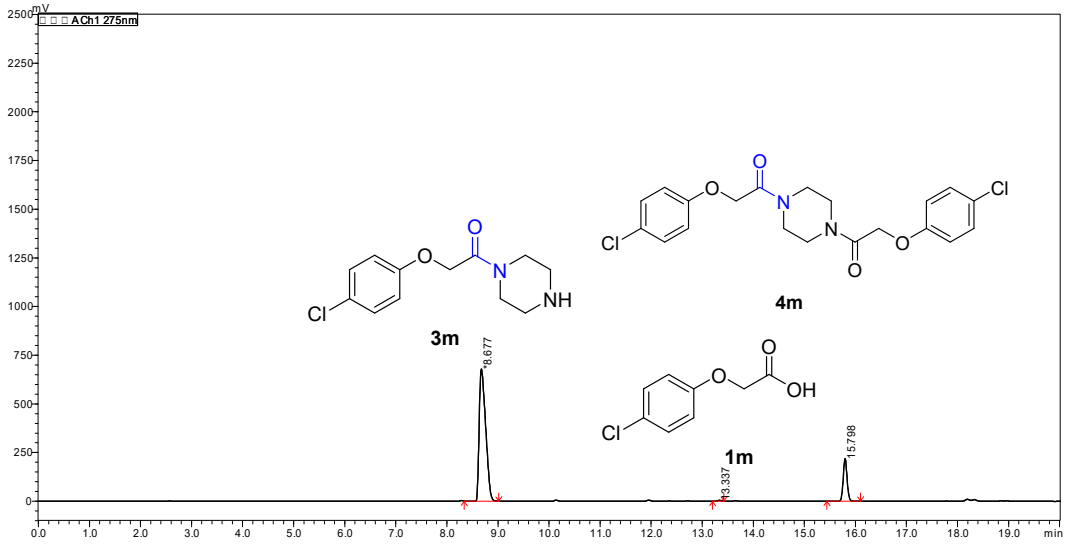


Fig. S39 The monoacylation between 1m with 2a in microreactor with 1 eq. DIPEA

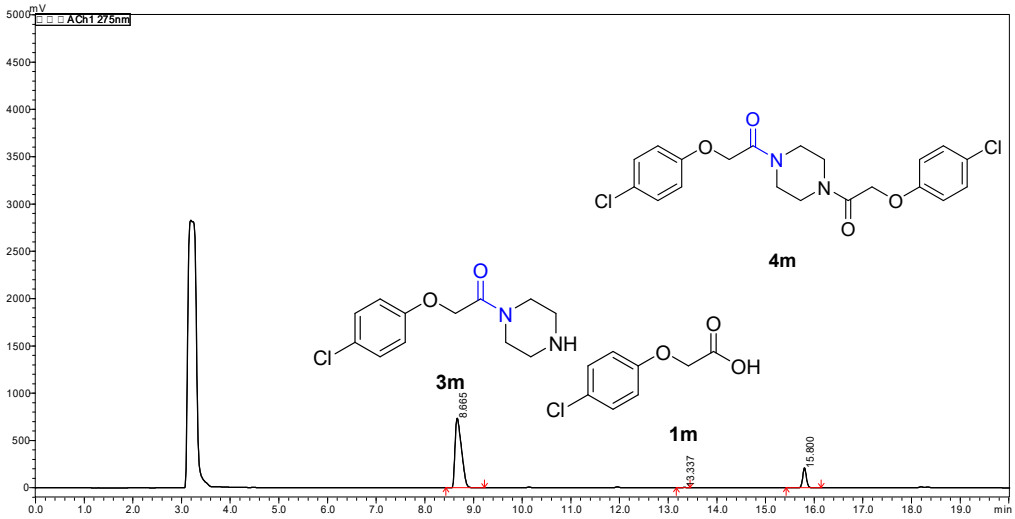


Fig. S40 The monoacylation between 1m with 2a in microreactor with 1 eq. DMAP

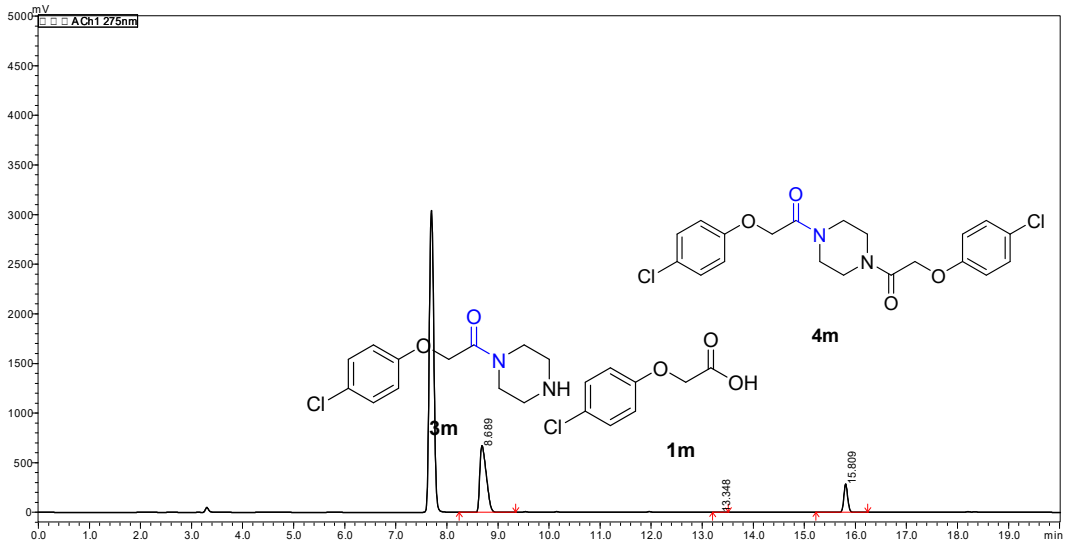


Fig. S41 The monoacylation between 1m with 2a in microreactor with 1 eq. 2-hydroxy-5-nitropyridine

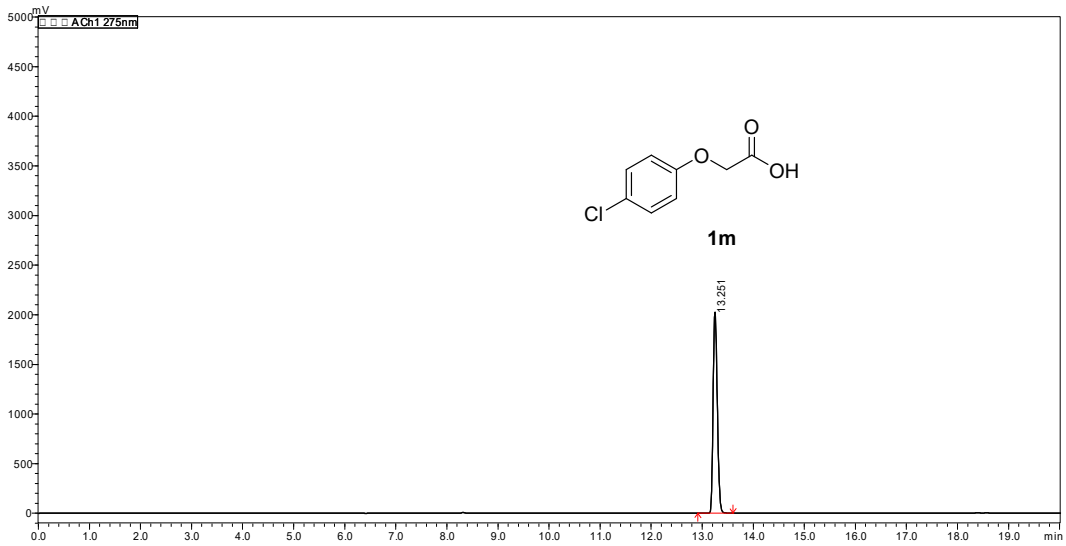


Fig. S42 4-Chlorophenoxyacetic acid (1m)

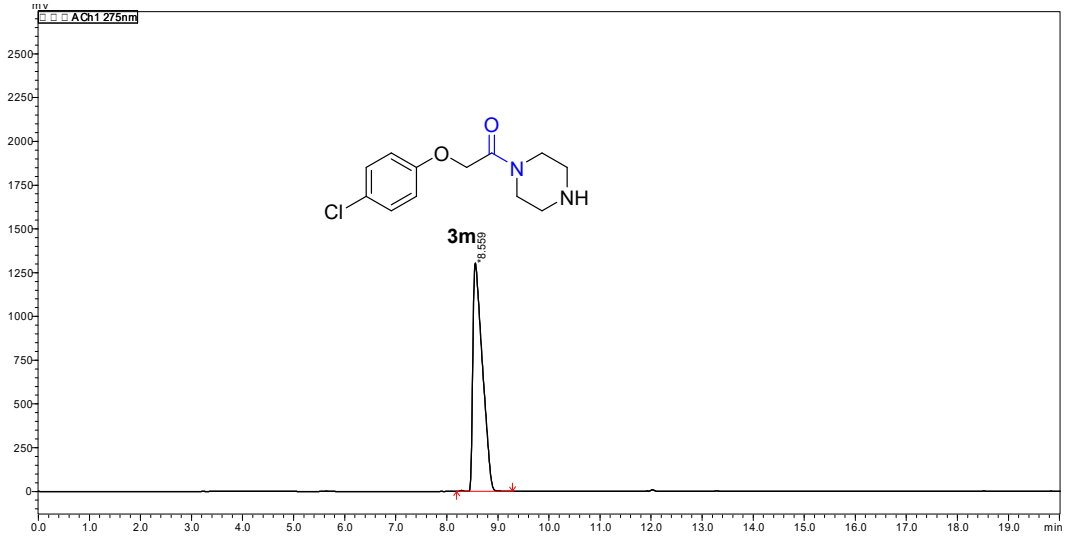


Fig. S43 The monoacylation product between 1m with 2a

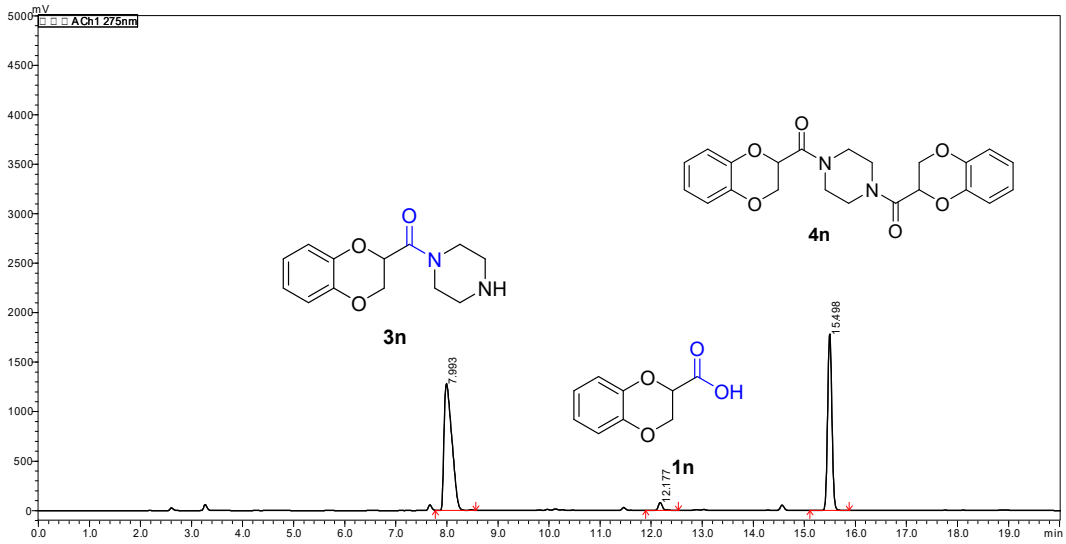


Fig. S44 The monoacylation between 1n with 2a in microreactor

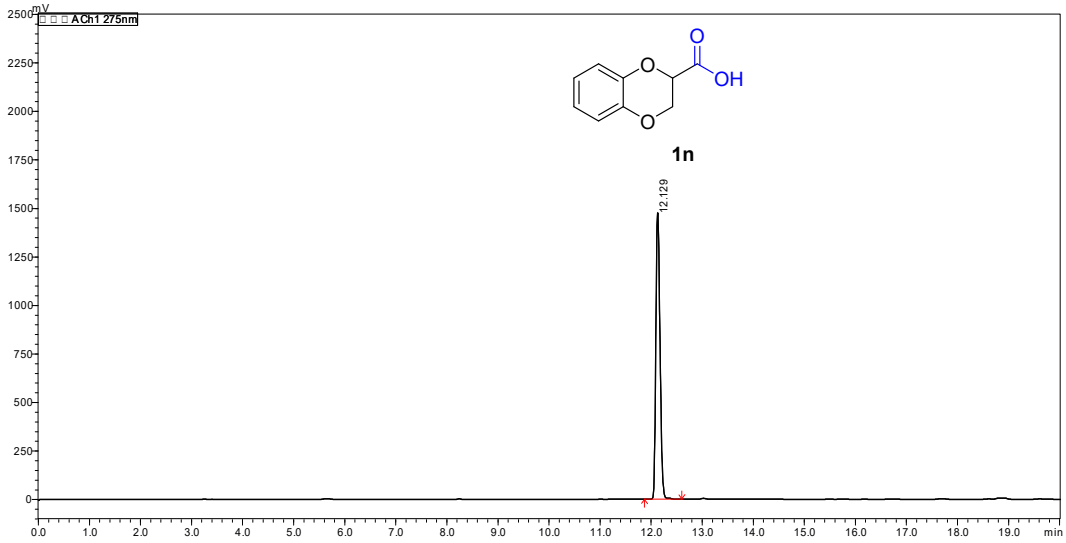


Fig. S45 1,4-Benzodioxane-2-carboxylic acid (1n)

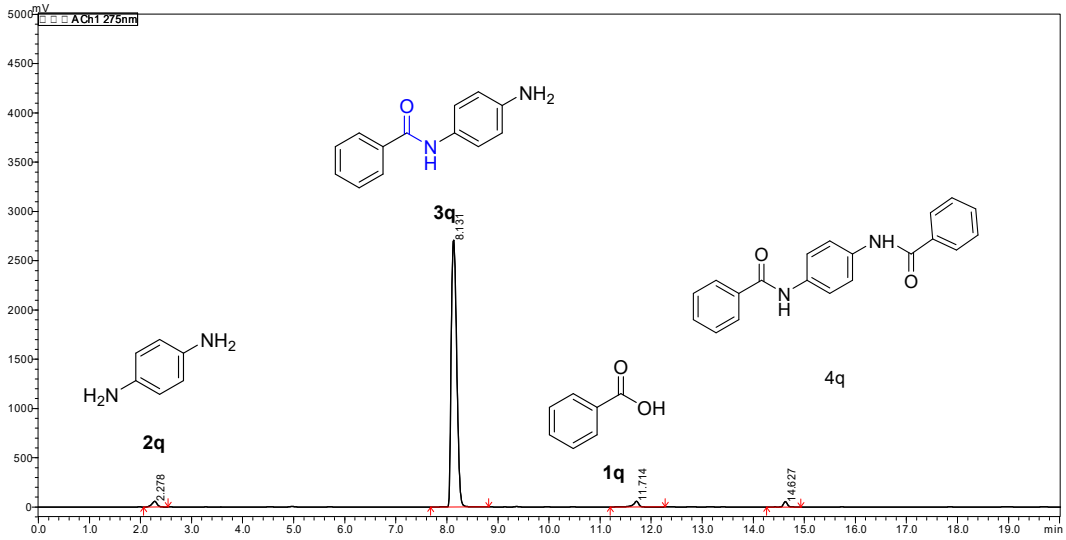


Fig. S46 The monoacylation between benzoic acid and *p*-phenylenediamine in microreactor

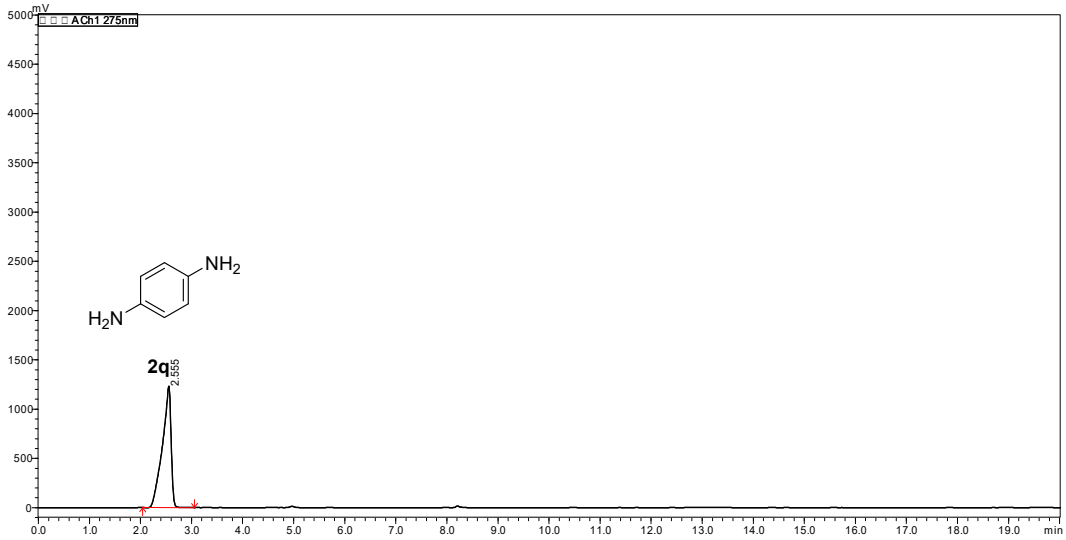


Fig. S47 *p*-phenylenediamine (2q)

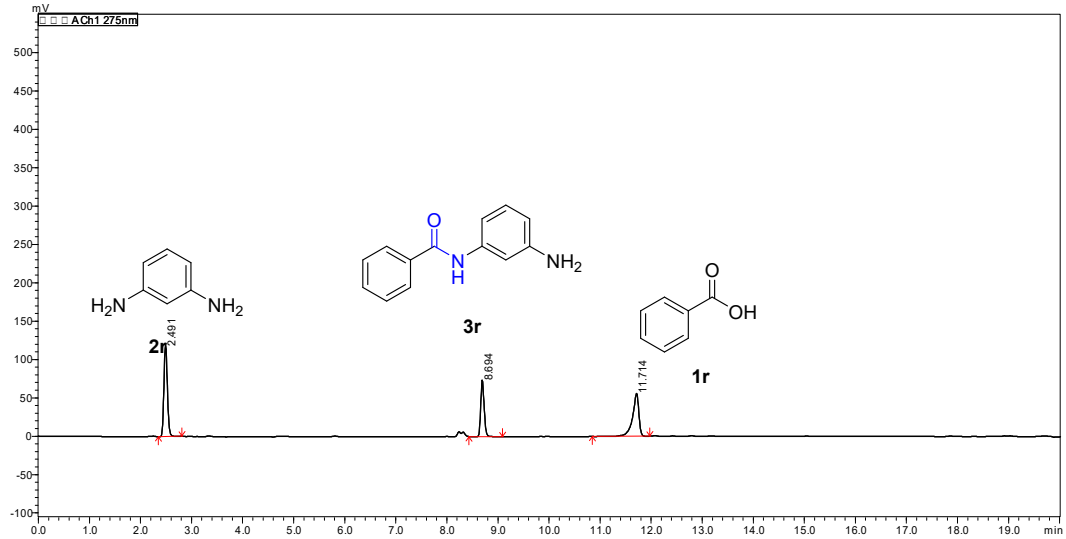


Fig. S48 The monoacylation between benzoic acid and *m*-phenylenediamine in microreactor

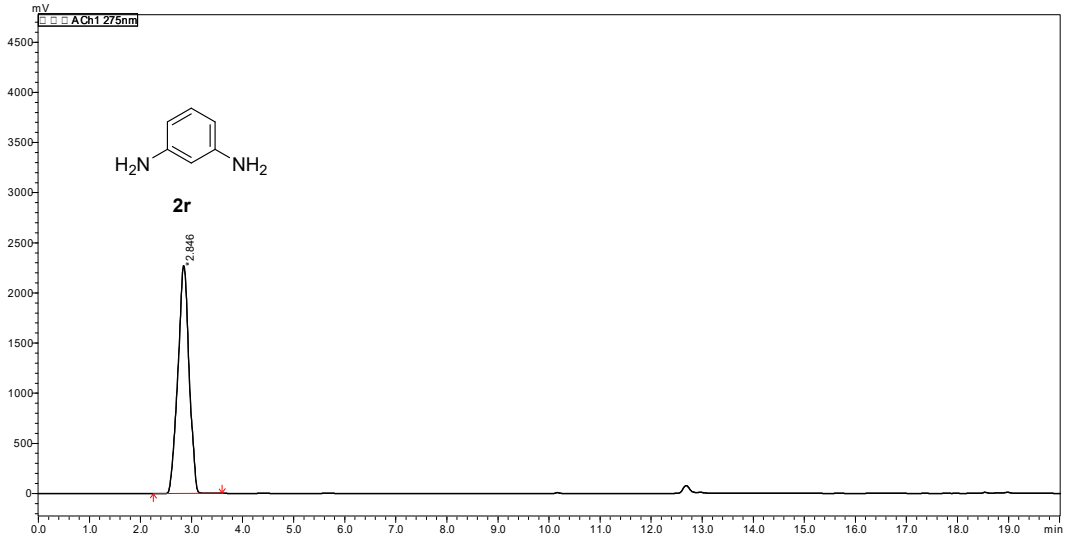


Fig. S49 *m*-phenylenediamine (2r)

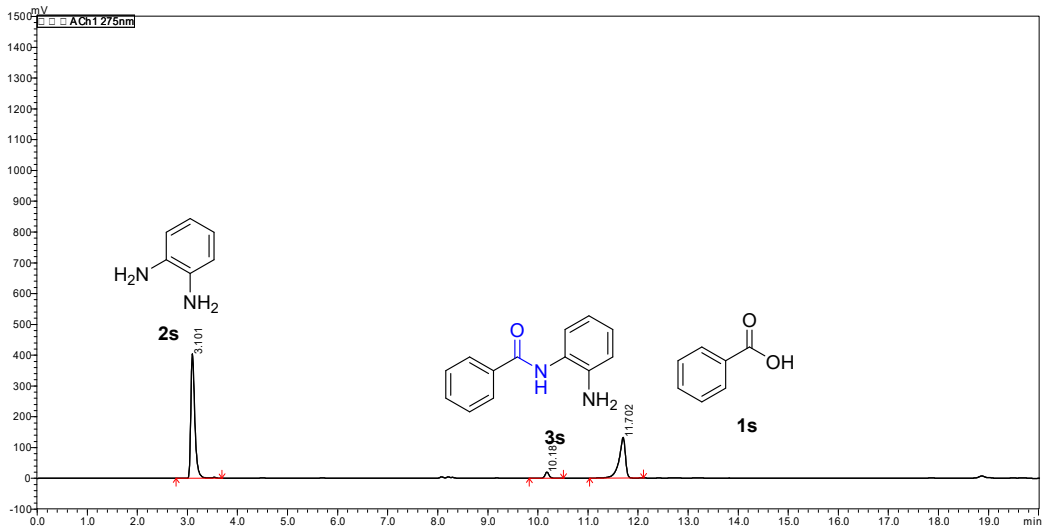


Fig. S50 The monoacylation between benzoic acid and *o*-phenylenediamine in microreactor

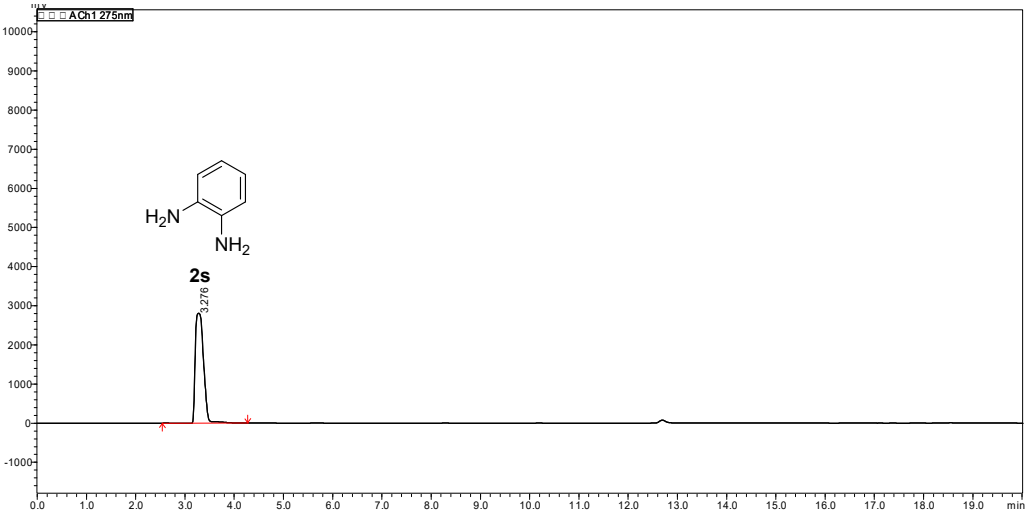


Fig. S51 *m*-phenylenediamine (2s)

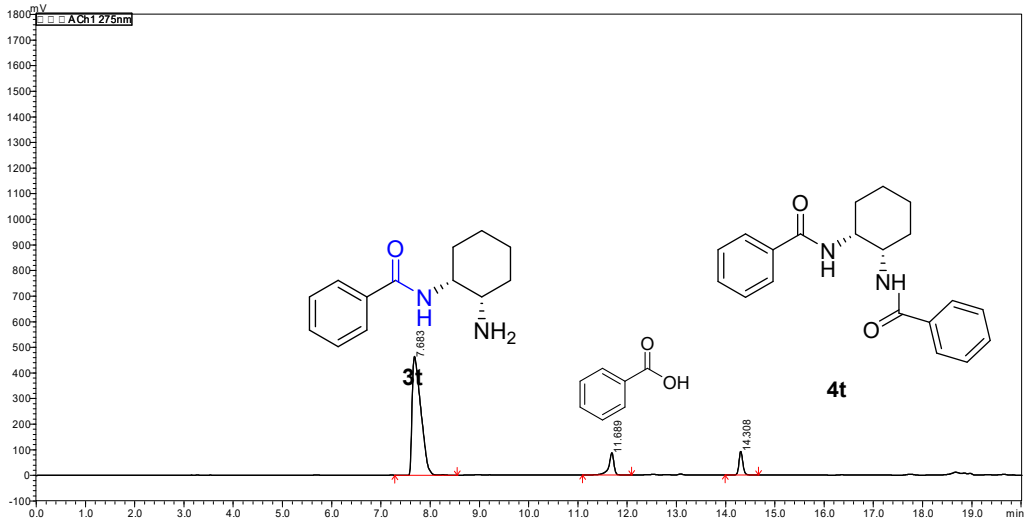


Fig. S52 The monoacylation between benzoic acid and cis-cyclohexanediamine in microreactor

Part 6. Product identification by LC-MS or HRMS

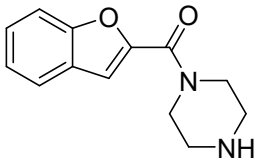
LC-MS conditions:

Instrument:: Waters, Liquid phase 2695-2996, mass spectrometry ZQ2000
Ion source: ESI
Scanning mode SCAN: 50-1500 (depending on the situation)
Source Temperature: 140 ° C
Desolvation Temperature: 350 ° C
Capital: 3.0 KV
Core: 10 V
Extractor: 5 V
RF Lens: 0.3 V
Gas (Desolvation): 800 L/h
Gas (Core): 50 L/h

Mass spectrometry conditions:

Instrument: Waters G2-XS Qtof
Positive mode: voltage 2kV
Ion source temperature 110 ℃
Desolvent temperature 400 ℃
Nitrogen flow rate: 800L/h
Collection quality range 50-1200
Collision voltage: 20-40V

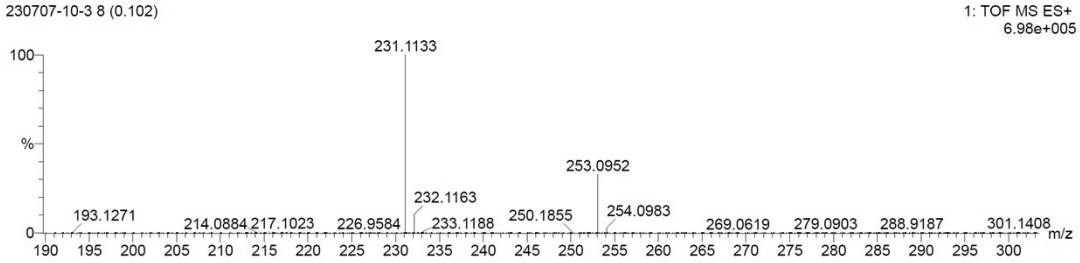
Negative mode: voltage 1.5kV
Ion source temperature 110 ℃
Desolvent temperature 400 ℃
Nitrogen flow rate: 800L/h
Collection quality range 50-1200
Collision voltage: 20-40V



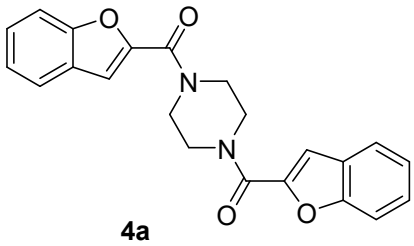
3a

Chemical Formula: $C_{13}H_{14}N_2O_2$
Exact Mass: 230.11

Monoisotopic Mass, Even Electron Ions
219 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 13-13 H: 15-15 N: 0-100 O: 0-100 Na: 0-1
3
230707-10-3 8 (0.102)



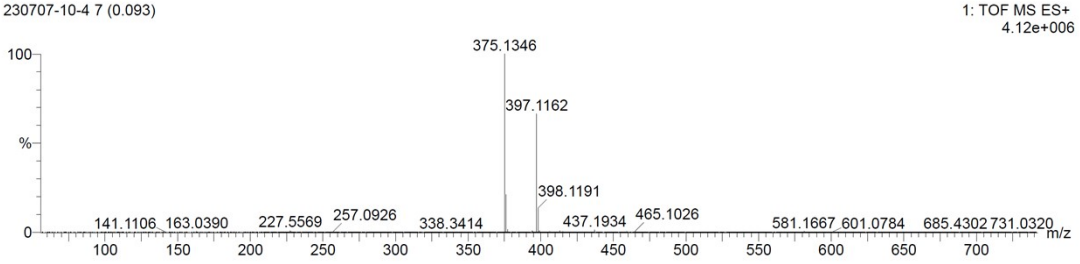
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
231.1133	231.1134	-0.1	-0.4	7.5	271.9	n/a	n/a	C13 H15 N2 O2



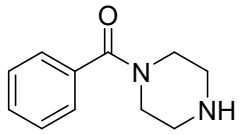
4a

Chemical Formula: $C_{22}H_{18}N_2O_4$
Exact Mass: 374.13

Monoisotopic Mass, Even Electron Ions
586 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 22-22 H: 19-19 N: 0-100 O: 0-100 Na: 0-1
3
230707-10-4 7 (0.093)

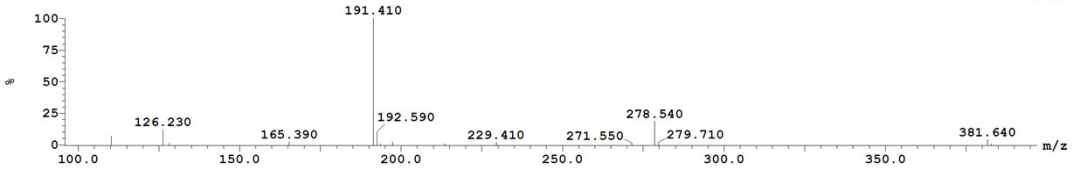


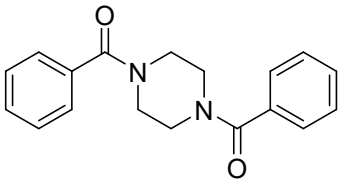
Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
375.1346	375.1345	0.1	0.3	14.5	387.6	n/a	n/a	C22 H19 N2 O4



3b

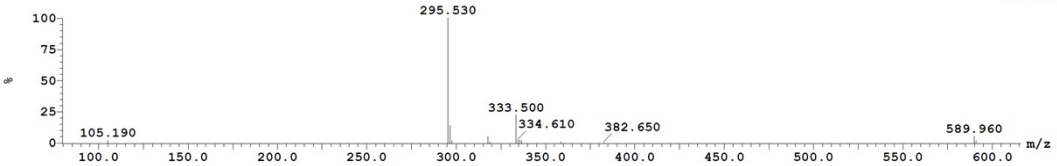
Chemical Formula: $C_{11}H_{14}N_2O$
Exact Mass: 190.11

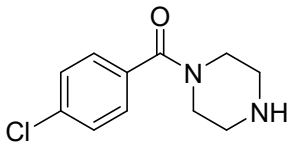




4b

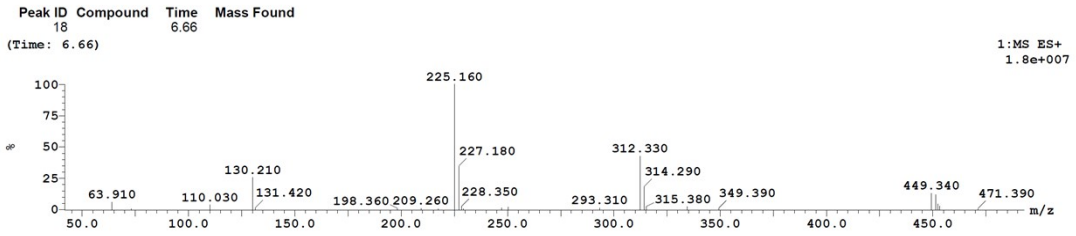
Chemical Formula: $C_{18}H_{18}N_2O_2$
Exact Mass: 294.14

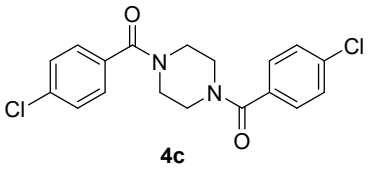




3c

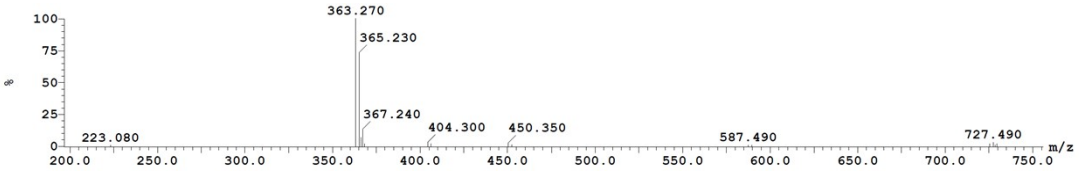
Chemical Formula: $C_{11}H_{13}ClN_2O$
Exact Mass: 224.07

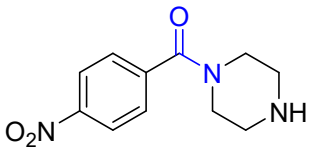




4c

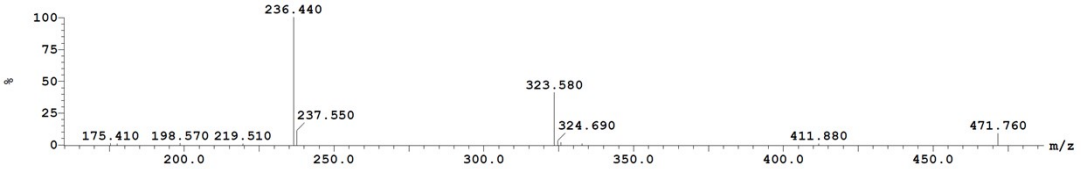
Chemical Formula: $C_{18}H_{16}Cl_2N_2O_2$
Exact Mass: 362.06

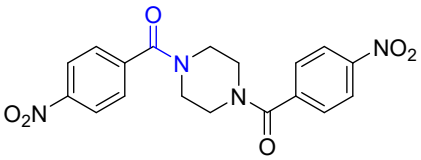




3d

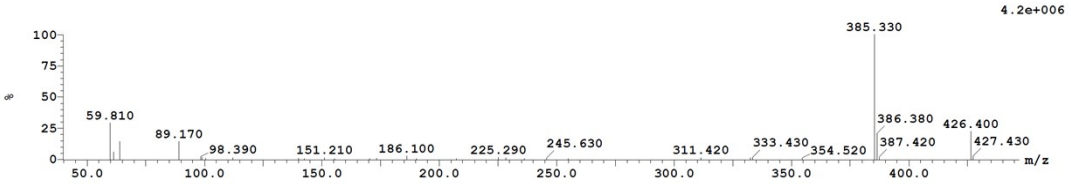
Chemical Formula: $C_{11}H_{13}N_3O_3$
Exact Mass: 235.10

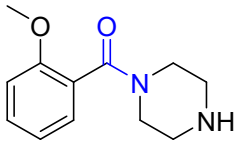




4d

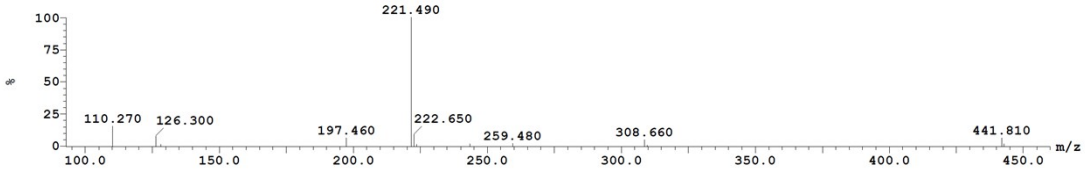
Chemical Formula: $C_{18}H_{16}N_4O_6$
Molecular Weight: 384.35

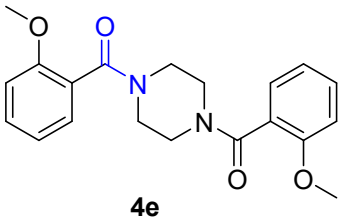




3e

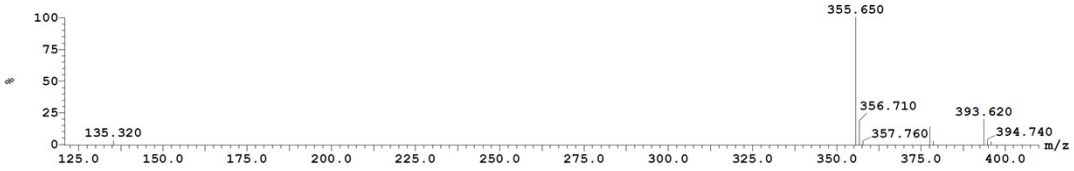
Chemical Formula: $C_{12}H_{16}N_2O_2$
Exact Mass: 220.12

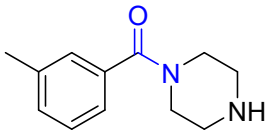




4e

Chemical Formula: $C_{20}H_{22}N_2O_4$
Exact Mass: 354.16

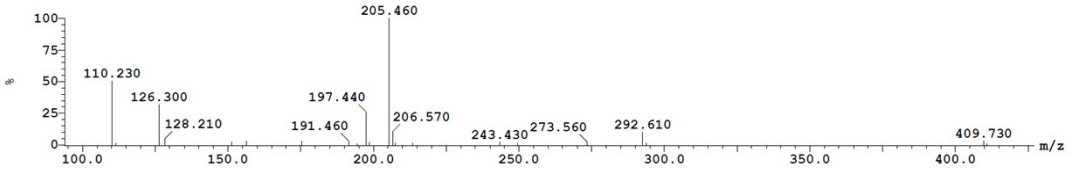


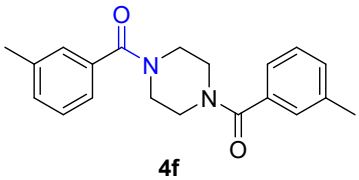


3f

Chemical Formula: $C_{12}H_{16}N_2O$

Exact Mass: 204.13

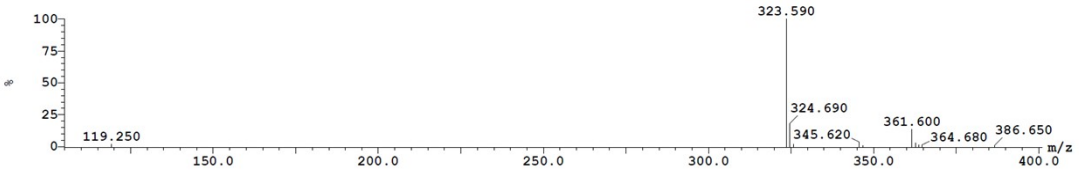


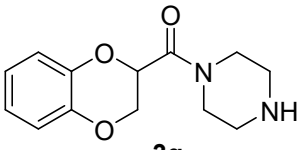


4f

Chemical Formula: $C_{20}H_{22}N_2O_2$

Exact Mass: 322.17

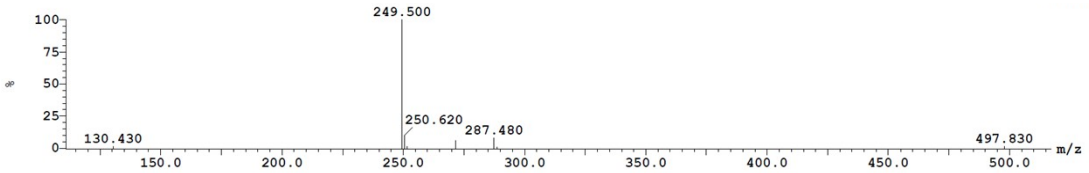


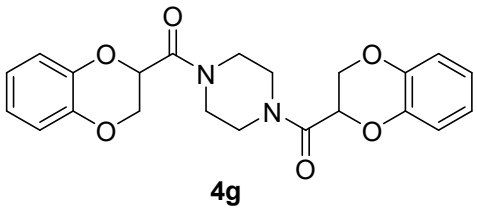


3g

Chemical Formula: $C_{13}H_{16}N_2O_3$

Exact Mass: 248.12

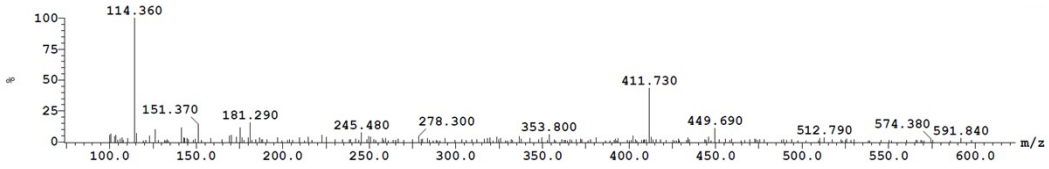


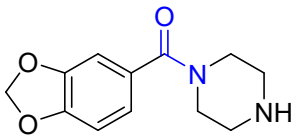


4g

Chemical Formula: $C_{22}H_{22}N_2O_6$

Exact Mass: 410.15

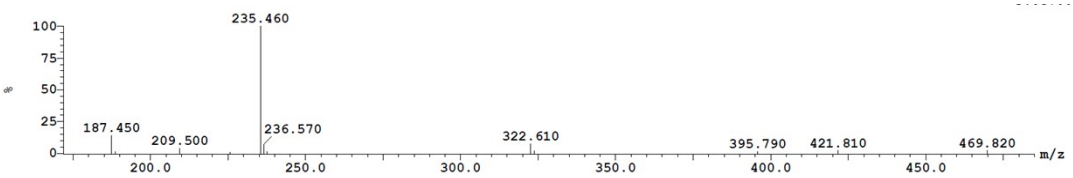


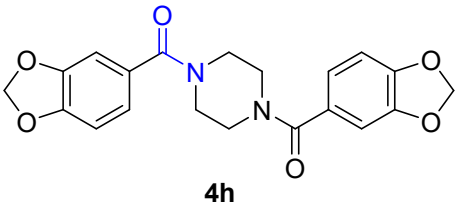


3h

Chemical Formula: $C_{12}H_{14}N_2O_3$

Exact Mass: 234.10

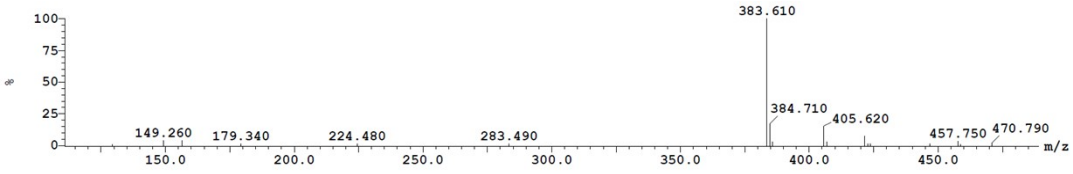


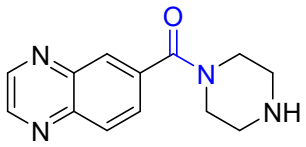


4h

Chemical Formula: $C_{20}H_{18}N_2O_6$

Exact Mass: 382.12

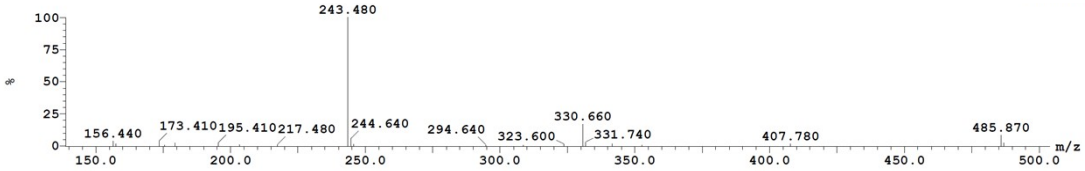


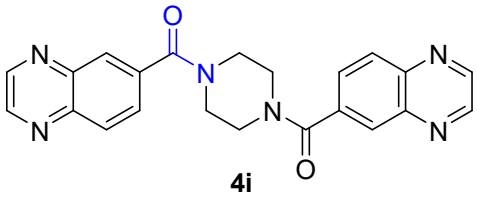


3i

Chemical Formula: $C_{13}H_{14}N_4O$

Exact Mass: 242.12

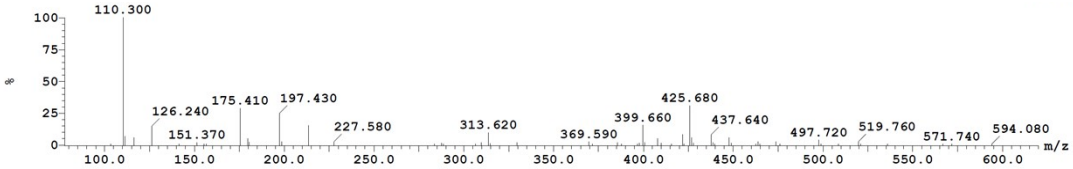


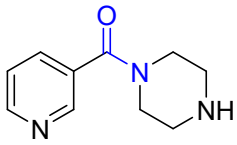


4i

Chemical Formula: $C_{22}H_{18}N_6O_2$

Exact Mass: 398.15

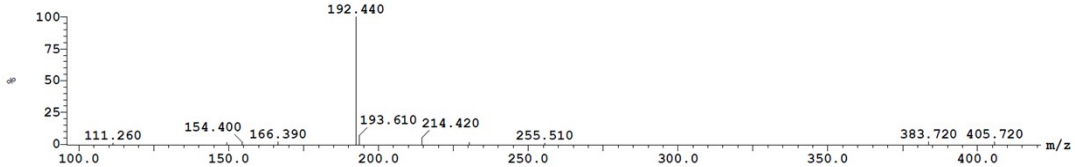


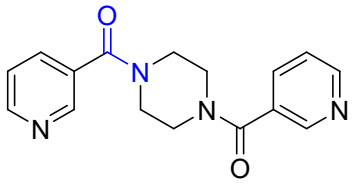


3j

Chemical Formula: $C_{10}H_{13}N_3O$

Exact Mass: 191.11

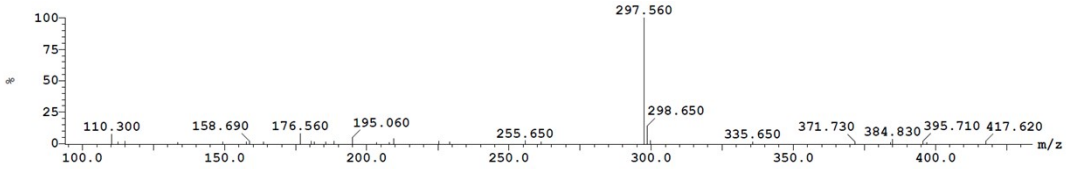


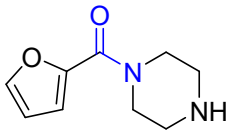


4j

Chemical Formula: $C_{16}H_{16}N_4O_2$

Exact Mass: 296.13

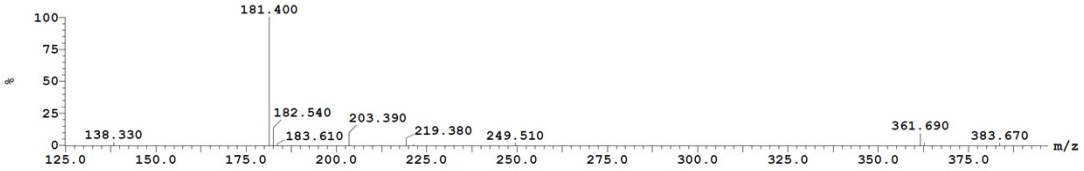


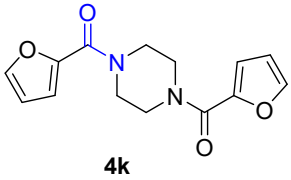


3k

Chemical Formula: $C_9H_{12}N_2O_2$

Exact Mass: 180.09

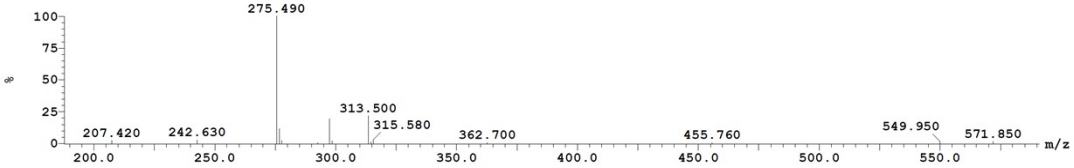


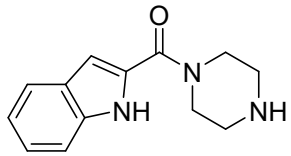


4k

Chemical Formula: $C_{14}H_{14}N_2O_4$

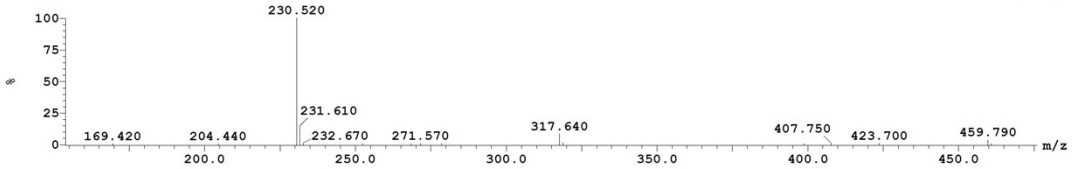
Exact Mass: 274.10

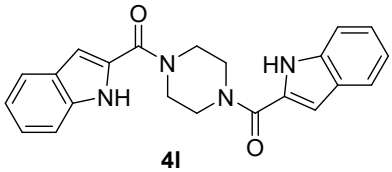




3l

Chemical Formula: $C_{13}H_{15}N_3O$
Exact Mass: 229.12

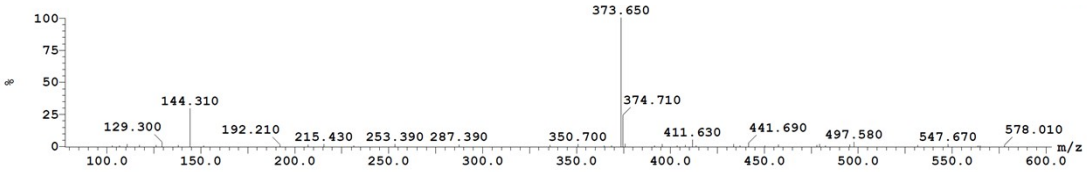


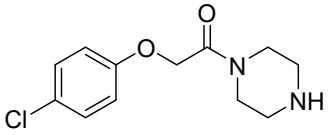


4l

Chemical Formula: $C_{22}H_{20}N_4O_2$

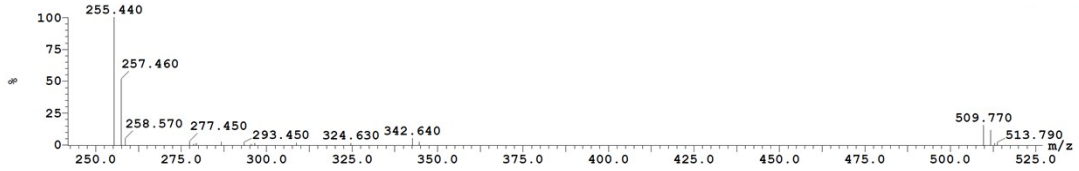
Exact Mass: 372.16

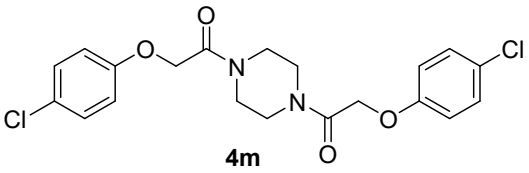




3m

Chemical Formula: $C_{12}H_{15}ClN_2O_2$
Exact Mass: 254.08

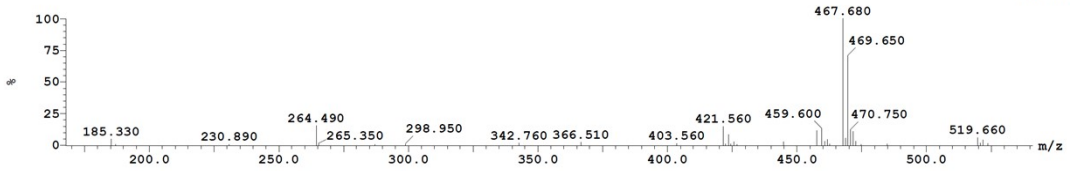




4m

Chemical Formula: $C_{20}H_{20}Cl_2N_2O_4$

Exact Mass: 422.08



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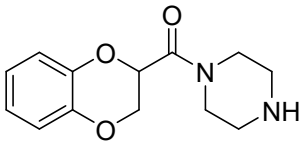
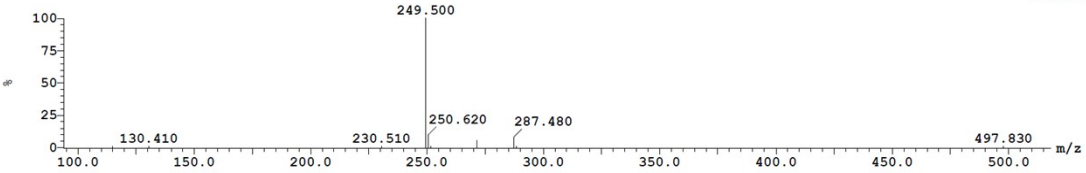
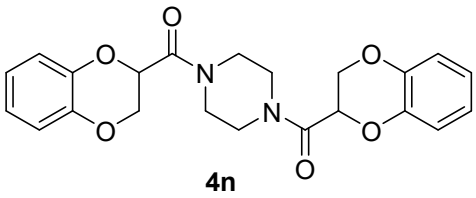


3n

Chemical Formula: $C_{13}H_{16}N_2O_3$

Exact Mass: 248.12

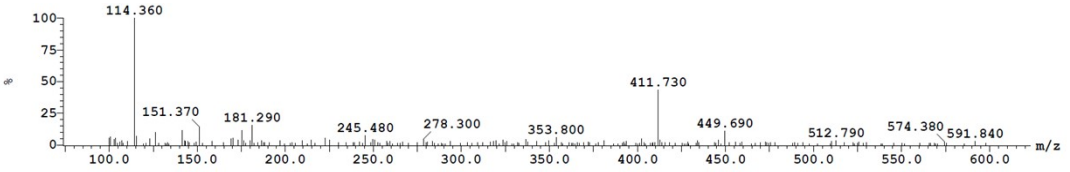


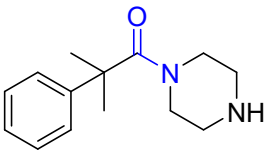


4n

Chemical Formula: $C_{22}H_{22}N_2O_6$

Exact Mass: 410.15

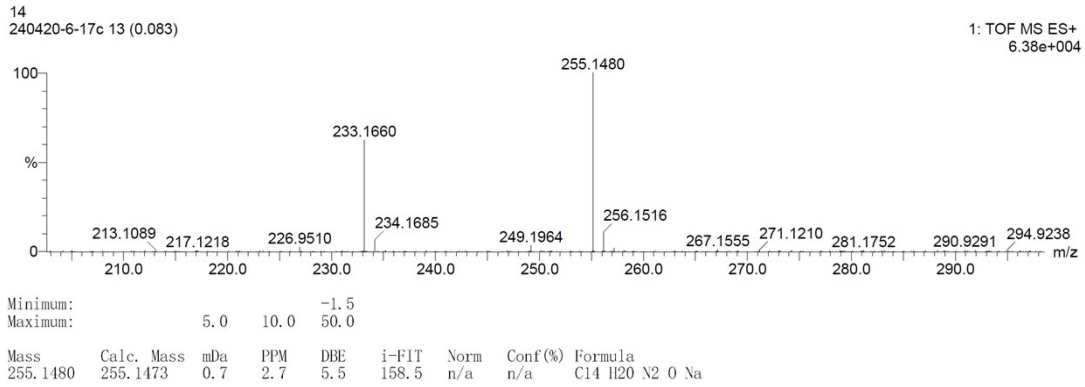




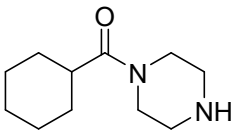
3o

Chemical Formula: $C_{14}H_{20}N_2O$

Exact Mass: 232.16



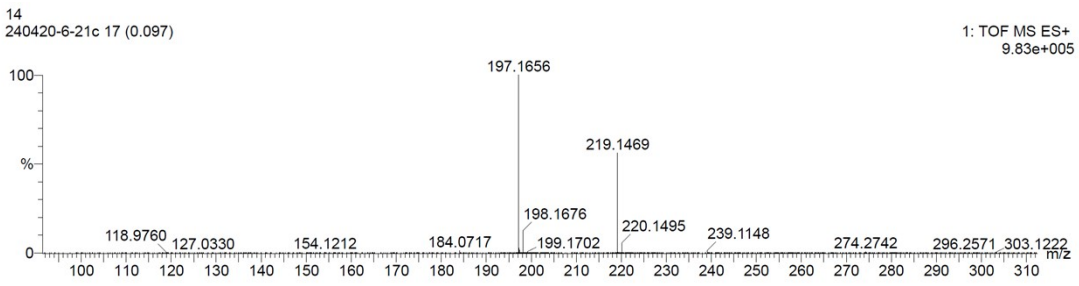
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
255.1480	255.1473	0.7	2.7	5.5	158.5	n/a	n/a	C14 H20 N2 O Na



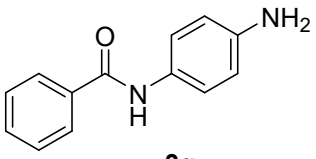
3p

Chemical Formula: $C_{11}H_{20}N_2O$

Exact Mass: 196.16



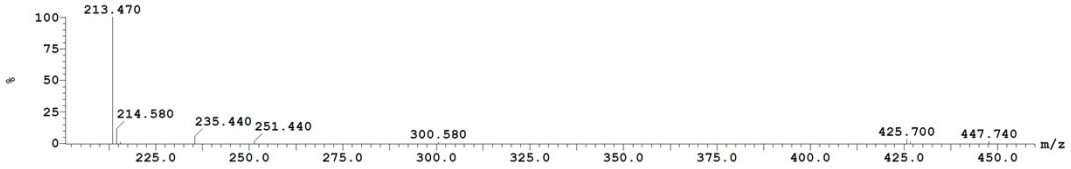
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
197.1656	197.1654	0.2	1.0	2.5	577.7	n/a	n/a	C11 H21 N2 O

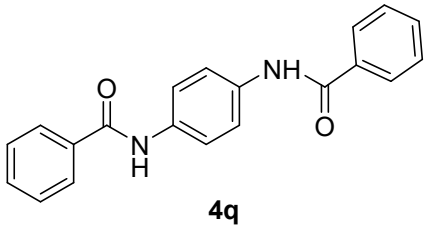


3q

Chemical Formula: $C_{13}H_{12}N_2O$

Exact Mass: 212.09

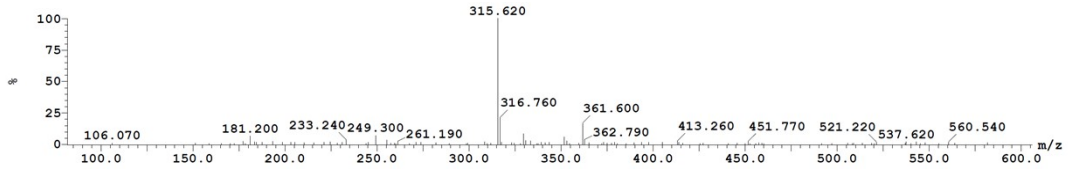




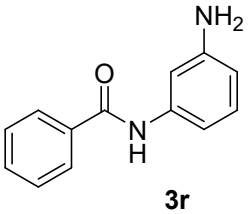
4q

Chemical Formula: $C_{20}H_{16}N_2O_2$

Exact Mass: 316.12



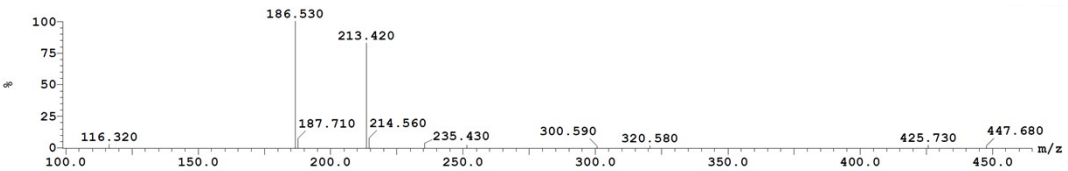
（ES-）

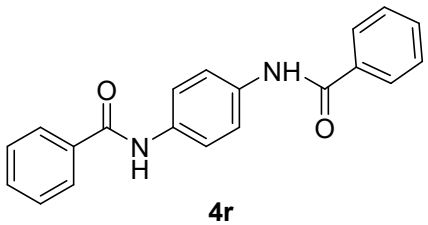


3r

Chemical Formula: $C_{13}H_{12}N_2O$

Exact Mass: 212.09

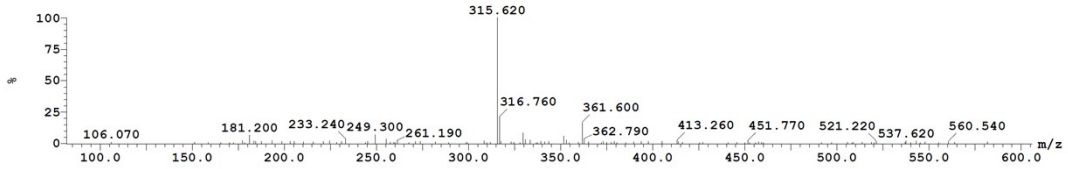


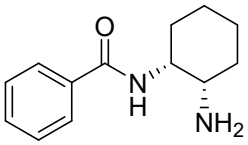


4r

Chemical Formula: $C_{20}H_{16}N_2O_2$

Exact Mass: 316.12

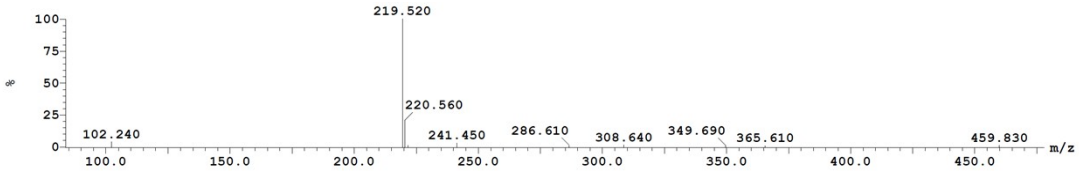


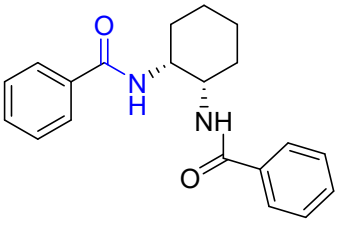


3t

Chemical Formula: $C_{13}H_{18}N_2O$

Exact Mass: 218.14

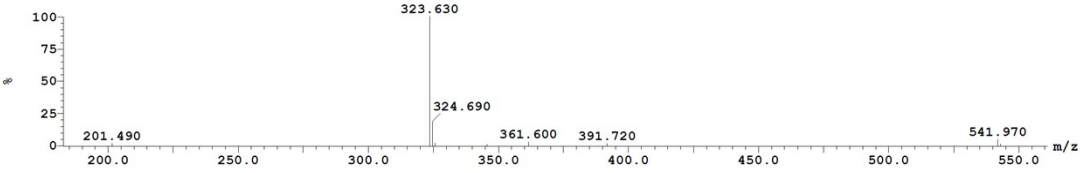


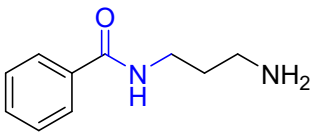


4t

Chemical Formula: $C_{20}H_{22}N_2O_2$

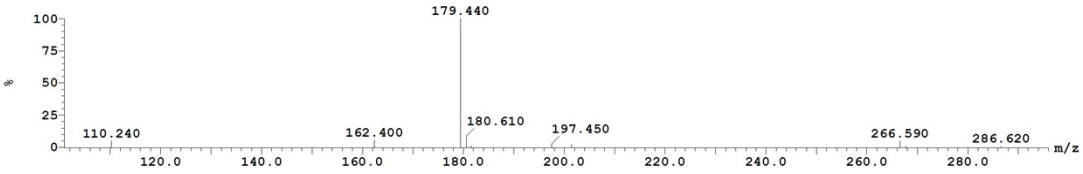
Exact Mass: 322.17

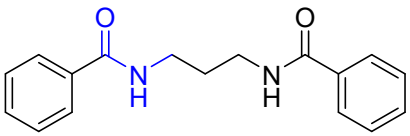




3u

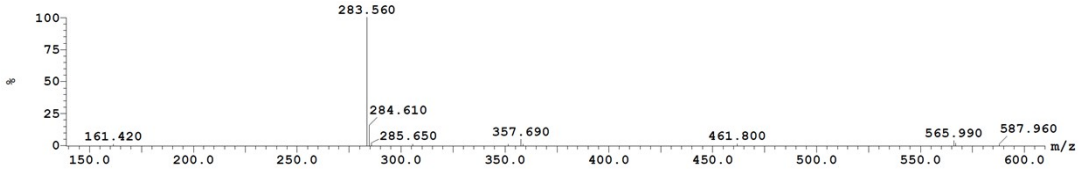
Chemical Formula: $C_{10}H_{14}N_2O$
Exact Mass: 178.11



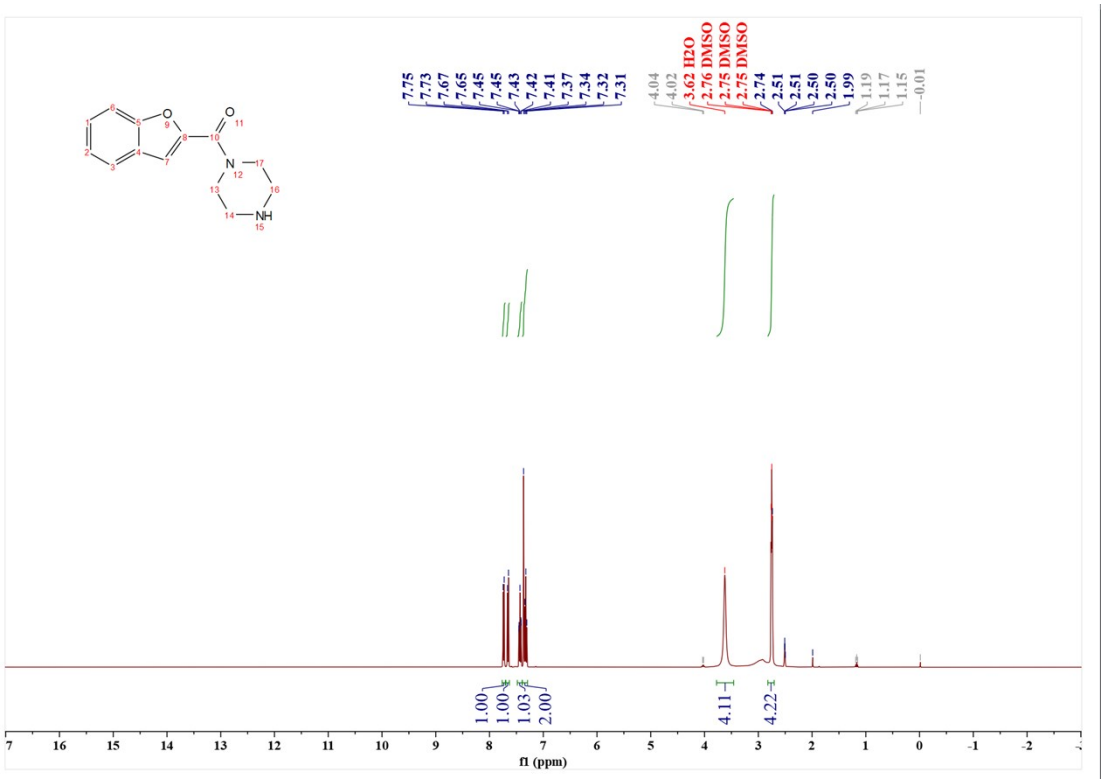


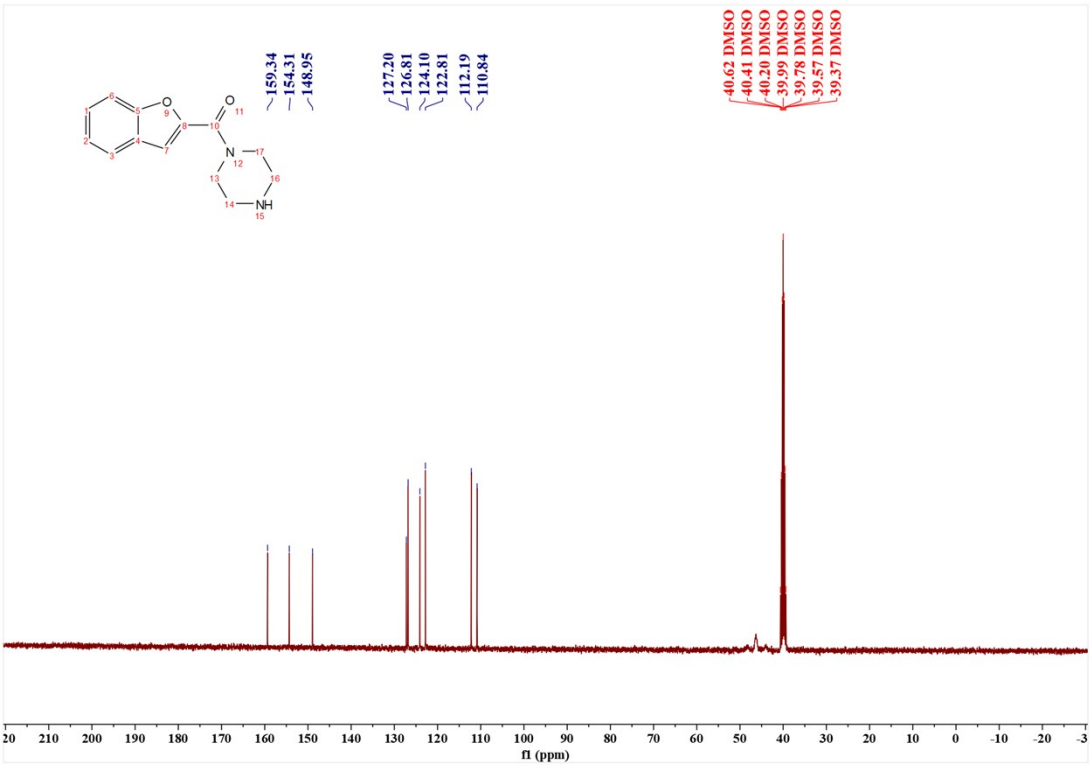
4u

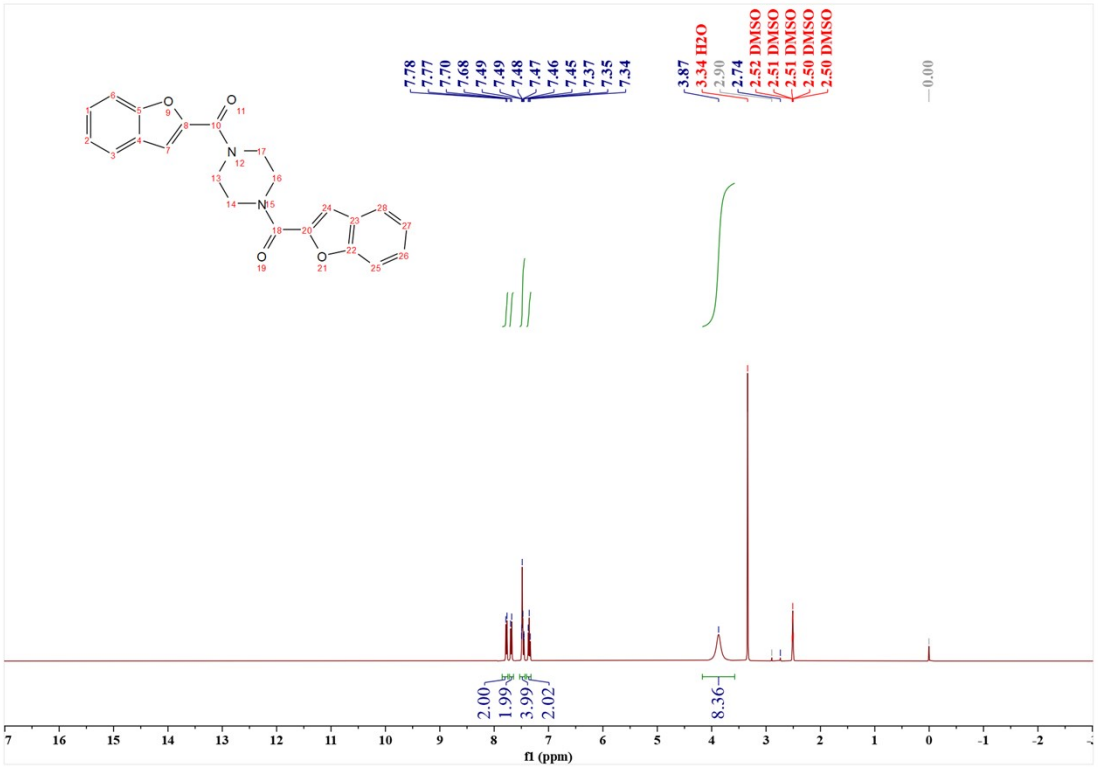
Chemical Formula: $C_{17}H_{18}N_2O_2$
Exact Mass: 282.14

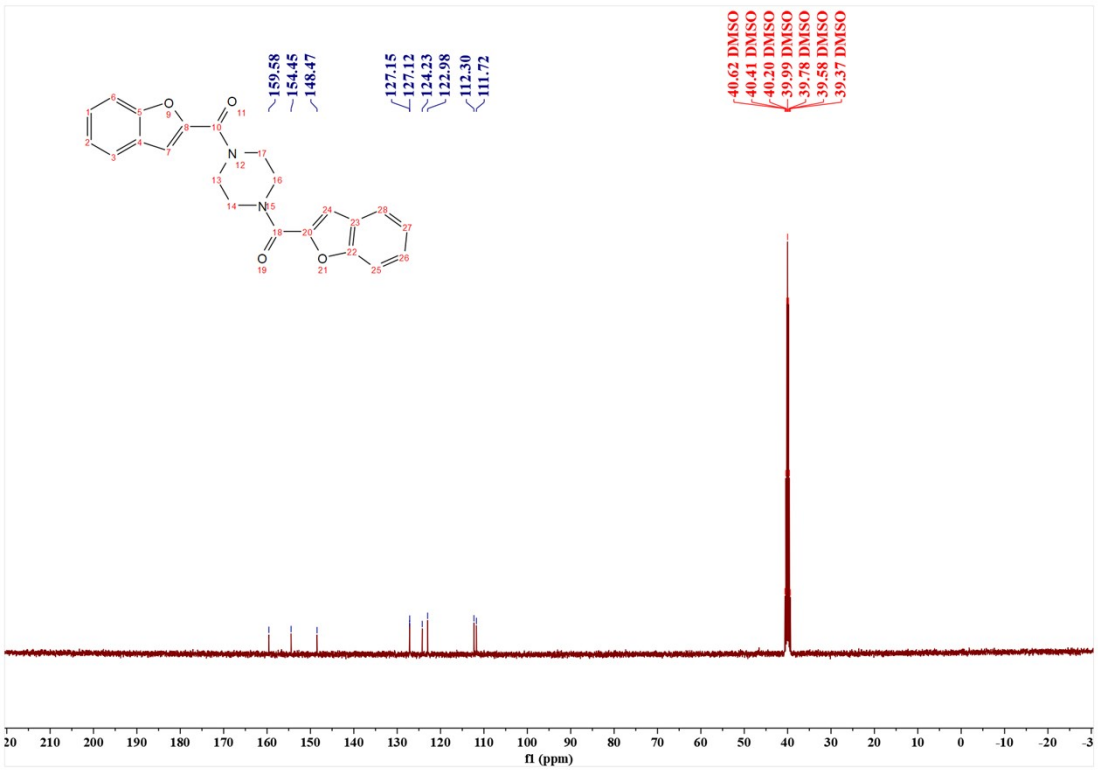


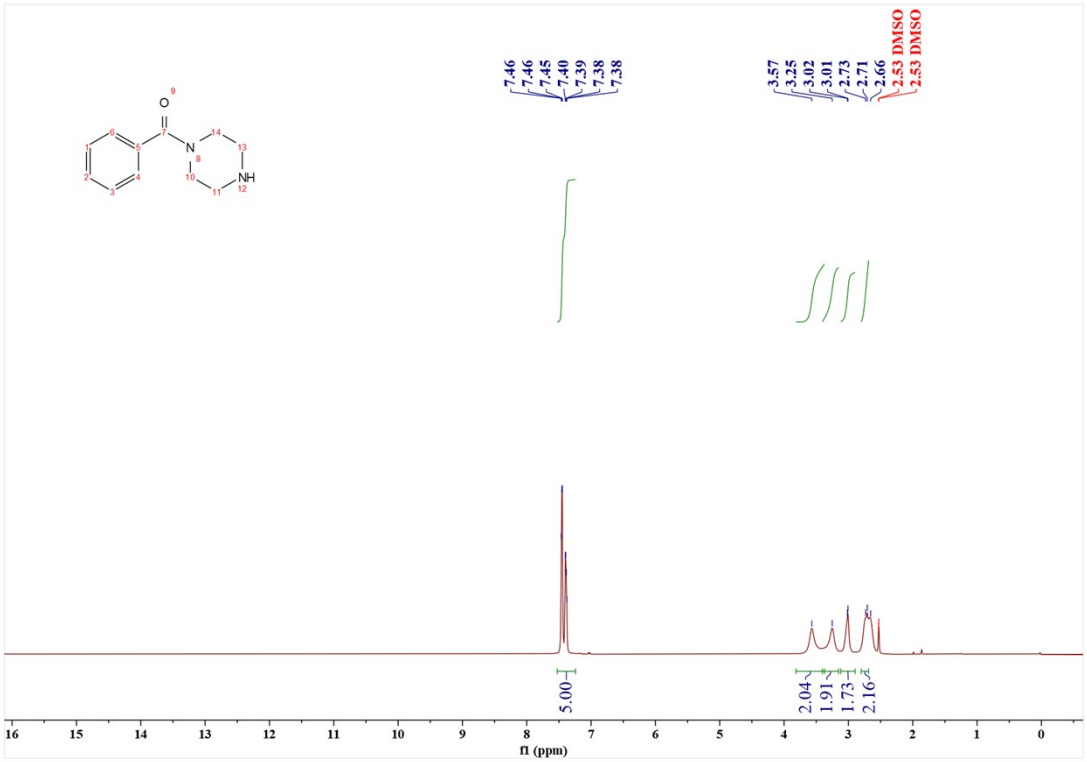
Part 7. Compound spectras

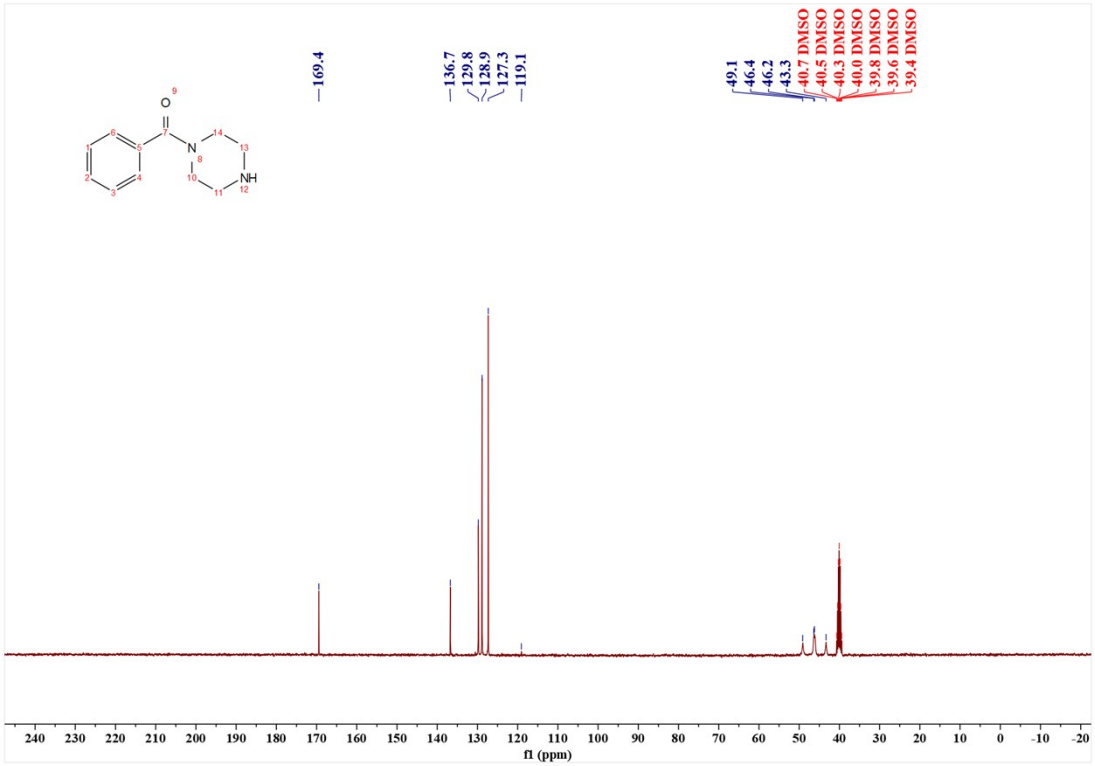


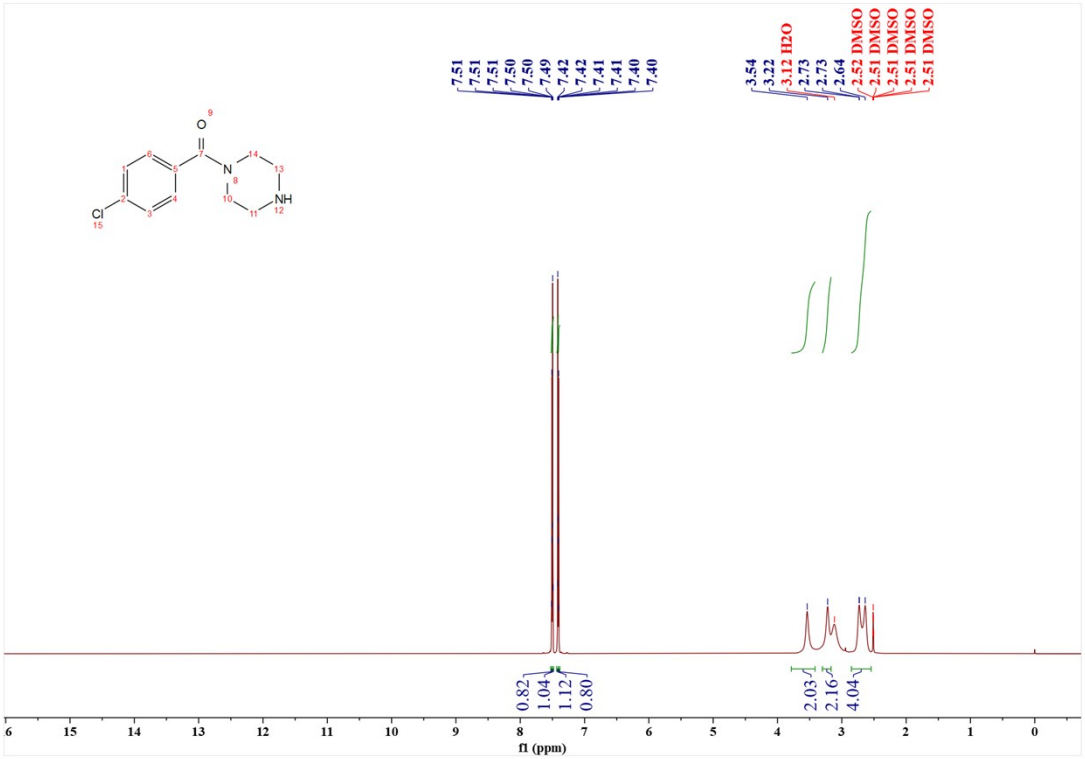


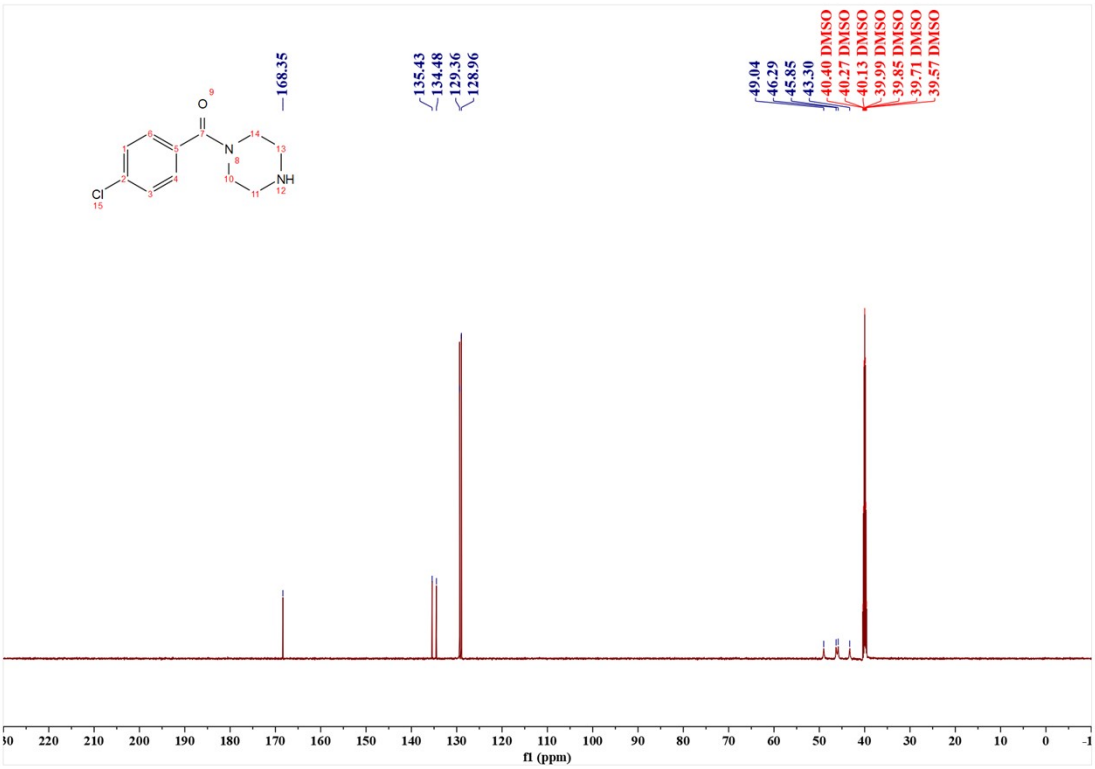

7.78
7.77
7.70
7.68
7.49
7.49
7.48
7.47
7.46
7.45
7.37
7.35
7.34
3.87
3.34 H2O
2.90
2.74
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
0.00
2.00
1.99
3.99
2.02
8.36
f1 (ppm)

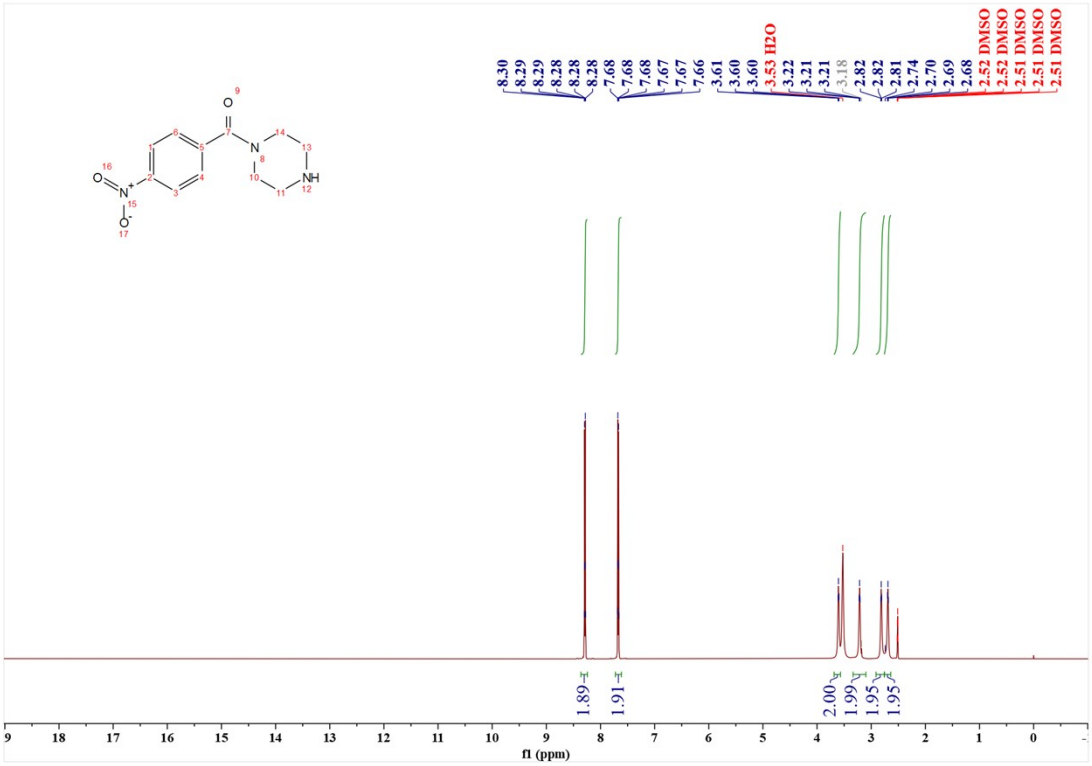

159.58
154.45
148.47
127.15
127.12
124.23
122.98
112.30
111.72
40.62 DMSO
40.41 DMSO
40.20 DMSO
39.99 DMSO
39.78 DMSO
39.58 DMSO
39.37 DMSO
f1 (ppm)


7.46
7.46
7.45
7.40
7.39
7.38
7.38
3.57
3.25
3.02
3.01
2.73
2.71
2.66
2.53 DMSO
2.53 DMSO
5.00
2.04
1.91
1.73
2.16
f1 (ppm)


169.4
136.7
129.8
128.9
127.3
119.1
49.1
46.4
46.2
43.3
40.7 DMSO
40.5 DMSO
40.3 DMSO
40.0 DMSO
39.8 DMSO
39.6 DMSO
39.4 DMSO
f1 (ppm)


7.51
7.51
7.51
7.50
7.50
7.49
7.42
7.42
7.41
7.41
7.40
7.40
3.54
3.22
3.12 H2O
2.73
2.73
2.64
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
0.82
1.04
1.12
0.80
2.03
2.16
4.04
f1 (ppm)


168.35
135.43
134.48
129.36
128.96
49.04
46.29
45.85
43.30
40.40 DMSO
40.27 DMSO
40.13 DMSO
39.99 DMSO
39.85 DMSO
39.71 DMSO
39.57 DMSO
f1 (ppm)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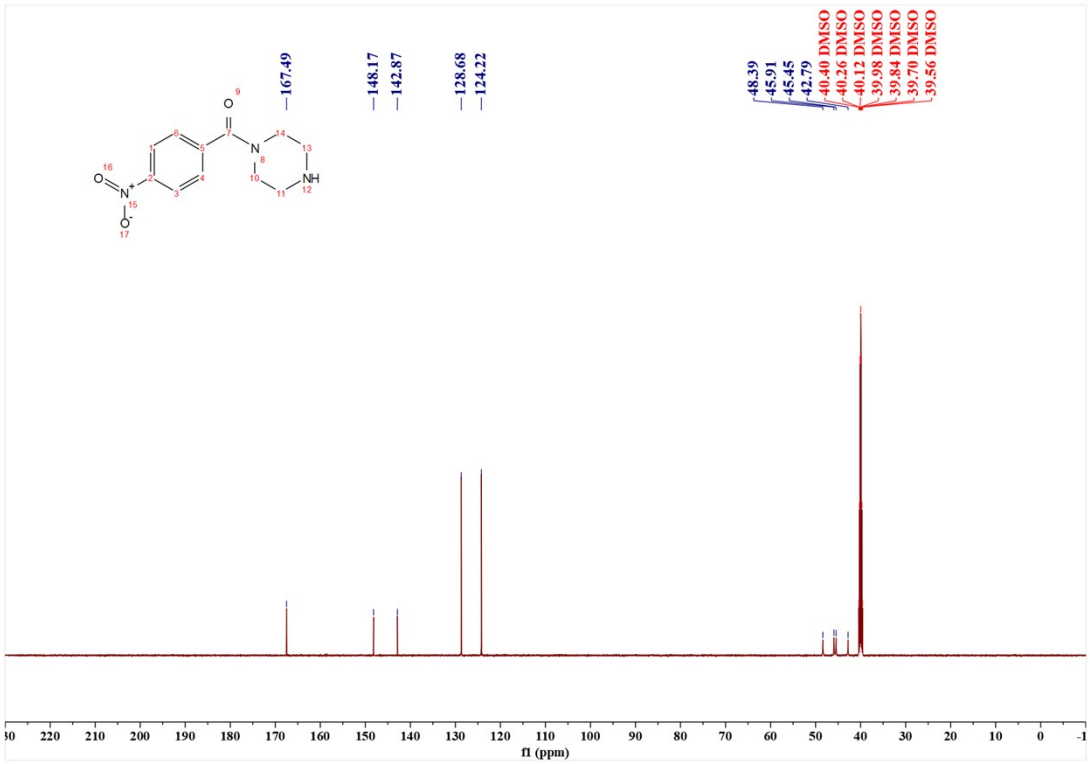
8.29
8.29
8.28
8.28
8.28
7.68
7.68
7.68
7.67
7.67
7.66
3.61
3.60
3.60
3.53 H2O
3.22
3.21
3.21
3.18
2.82
2.82
2.81
2.74
2.70
2.69
2.68
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
1.89
1.91
2.00
1.99
1.95
1.95
f1 (ppm)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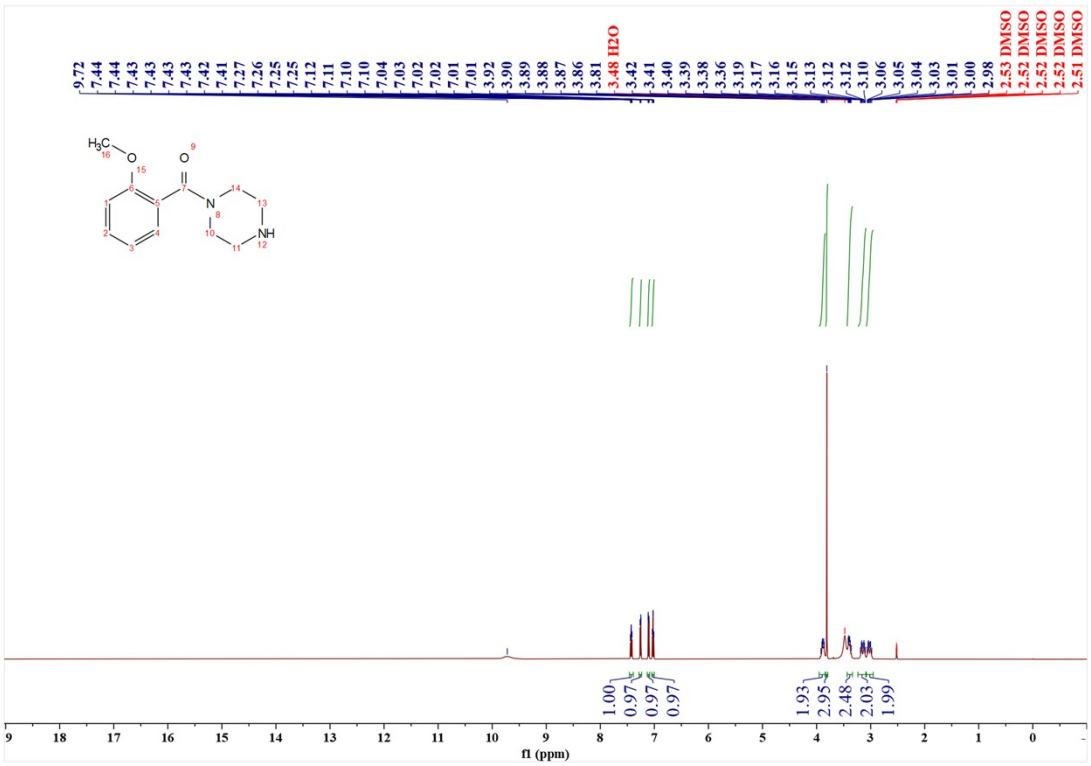
148.17
142.87
128.68
124.22
48.39
45.91
45.45
42.79
40.40 DMSO
40.26 DMSO
40.12 DMSO
39.98 DMSO
39.84 DMSO
39.70 DMSO
39.56 DMSO
f1 (ppm)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7.43
7.42
7.41
7.27
7.26
7.25
7.25
7.12
7.11
7.10
7.10
7.04
7.03
7.02
7.02
7.01
7.01
3.92
3.90
3.89
3.88
3.87
3.86
3.81
3.48 H2O
3.42
3.41
3.40
3.39
3.38
3.36
3.19
3.17
3.16
3.15
3.13
3.12
3.10
3.06
3.05
3.04
3.03
3.01
3.00
2.98
2.53 DMSO
2.52 DMSO
2.52 DMSO
2.52 DMSO
2.51 DMSO
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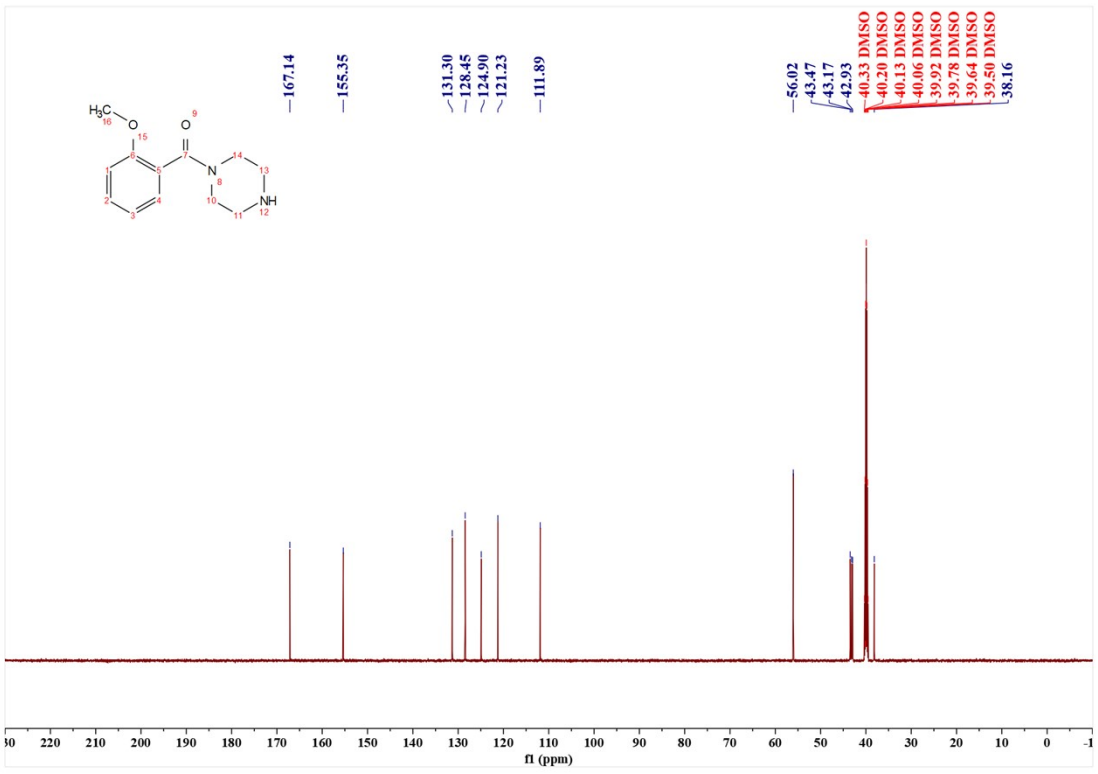
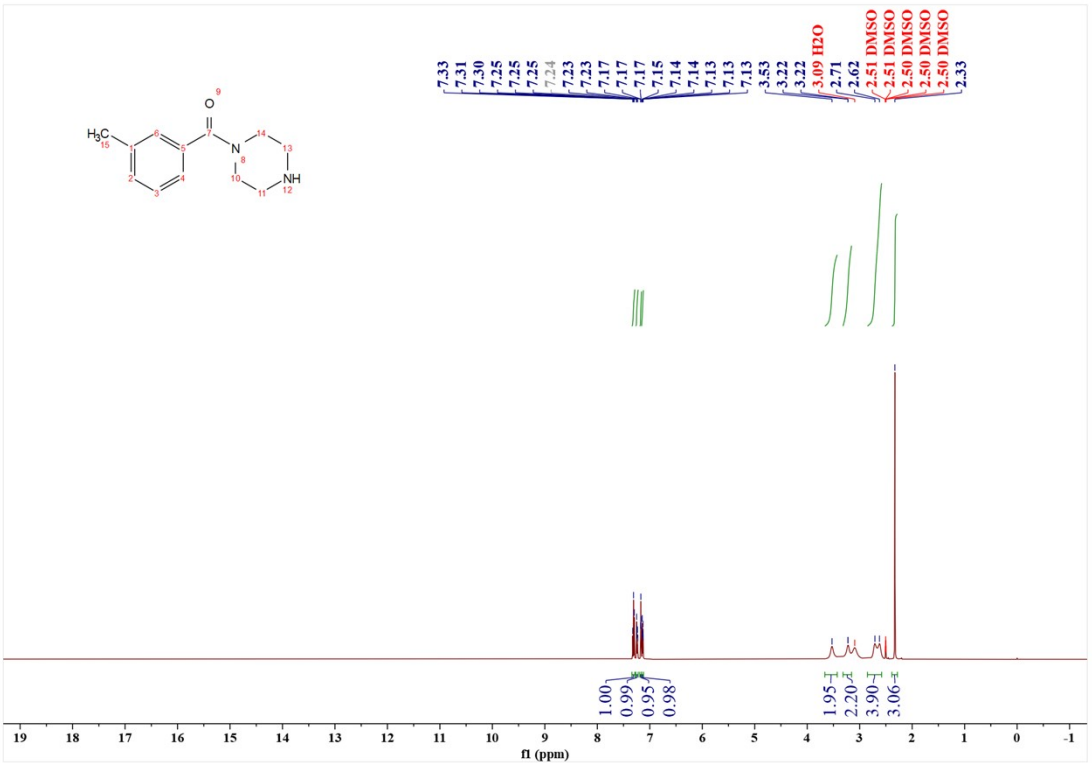
0.97
0.97
0.97
1.93
2.95
2.48
2.03
1.99
f1 (ppm)


167.14
155.35
131.30
128.45
124.90
121.23
111.89
56.02
43.47
43.17
42.93
40.33 DMSO
40.20 DMSO
40.13 DMSO
40.06 DMSO
39.92 DMSO
39.78 DMSO
39.64 DMSO
39.50 DMSO
38.16
f1 (ppm)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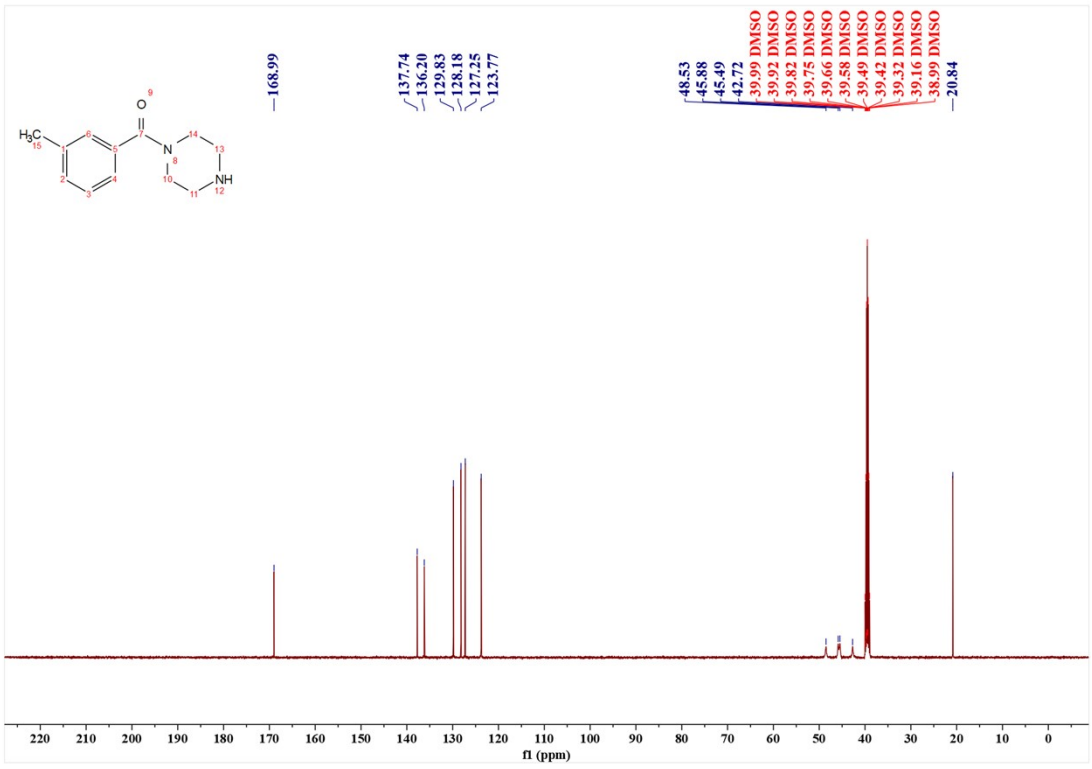
7.31
7.30
7.25
7.25
7.25
7.24
7.23
7.23
7.17
7.17
7.17
7.15
7.14
7.14
7.13
7.13
7.13
3.53
3.22
3.22
3.09 H2O
2.71
2.62
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.33
1.00
0.99
0.95
0.98
1.95
2.20
3.90
3.06
f1 (ppm)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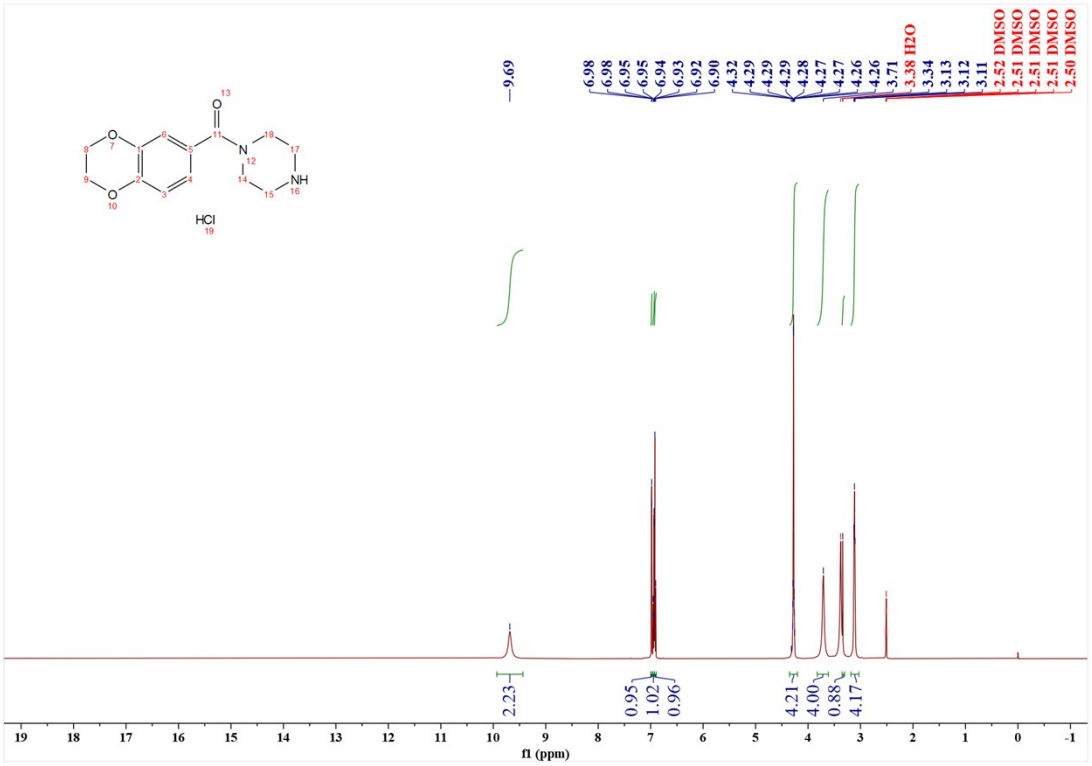
137.74
136.20
129.83
128.18
127.25
123.77
48.53
45.88
45.49
42.72
39.99 DMSO
39.92 DMSO
39.82 DMSO
39.75 DMSO
39.66 DMSO
39.58 DMSO
39.49 DMSO
39.42 DMSO
39.32 DMSO
39.16 DMSO
38.99 DMSO
20.84
f1 (ppm)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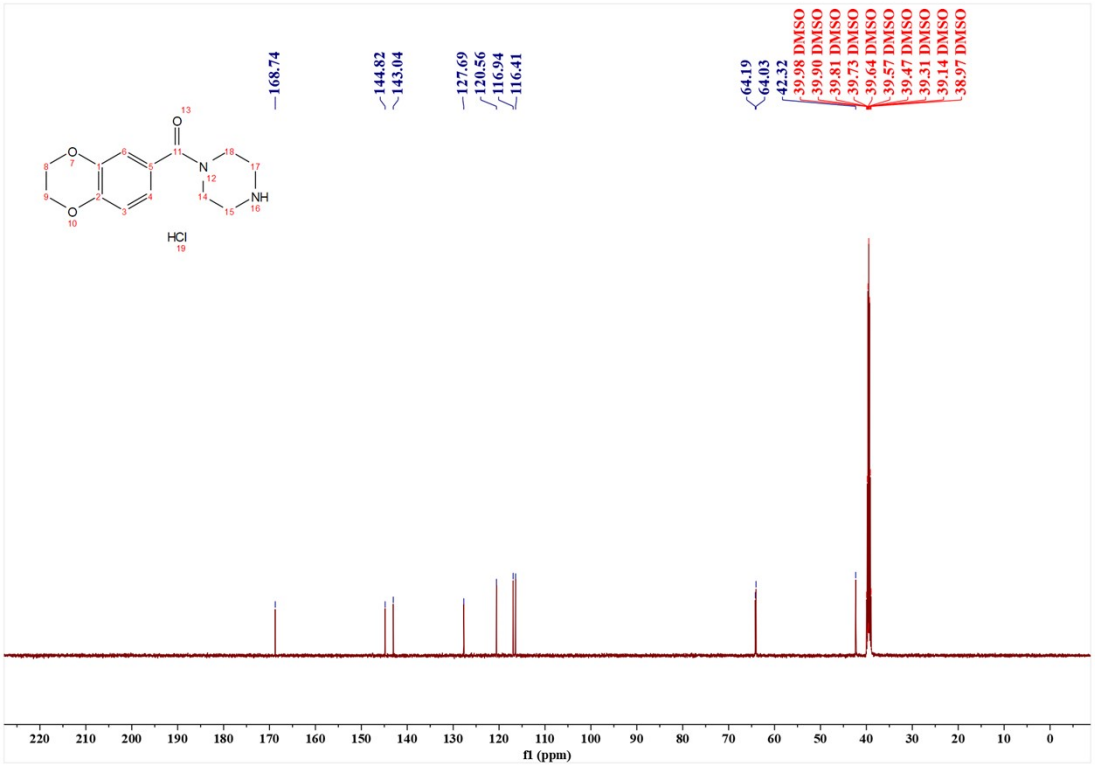
6.98
6.98
6.95
6.95
6.94
6.93
6.92
6.90
4.32
4.29
4.29
4.29
4.28
4.27
4.27
4.26
4.26
3.71
3.38 H2O
3.34
3.13
3.12
3.11
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
HCl
2.23
0.95
1.02
0.96
4.21
4.00
0.88
4.17
f1 (ppm)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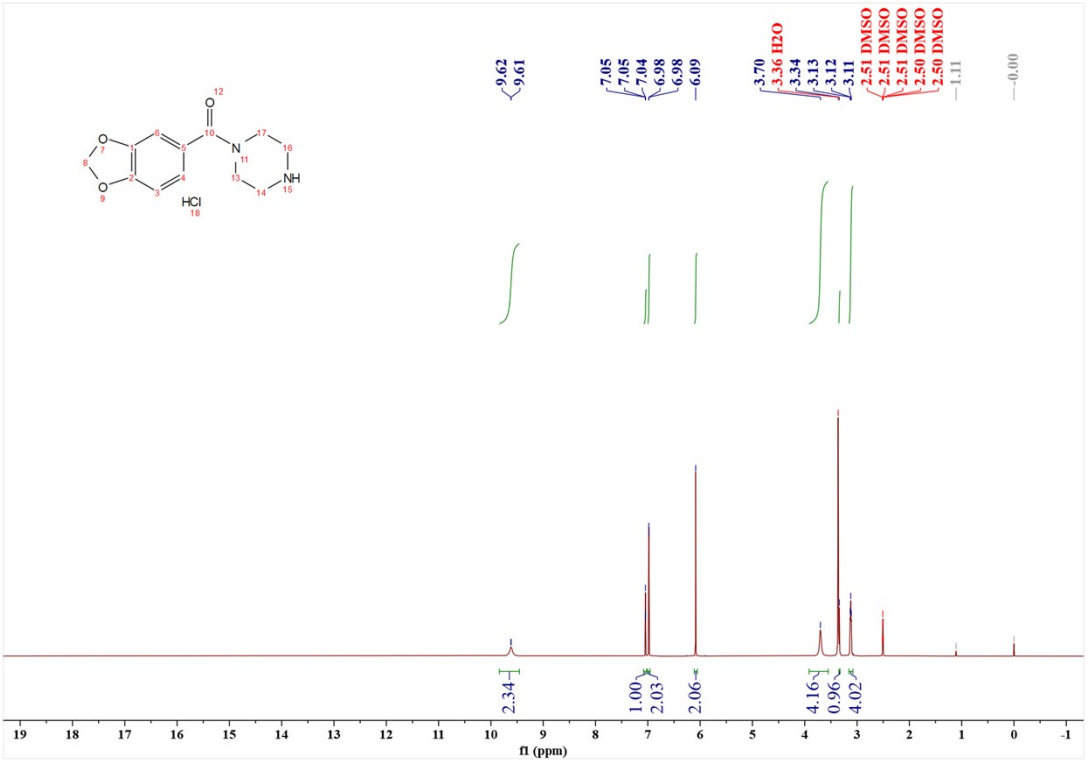
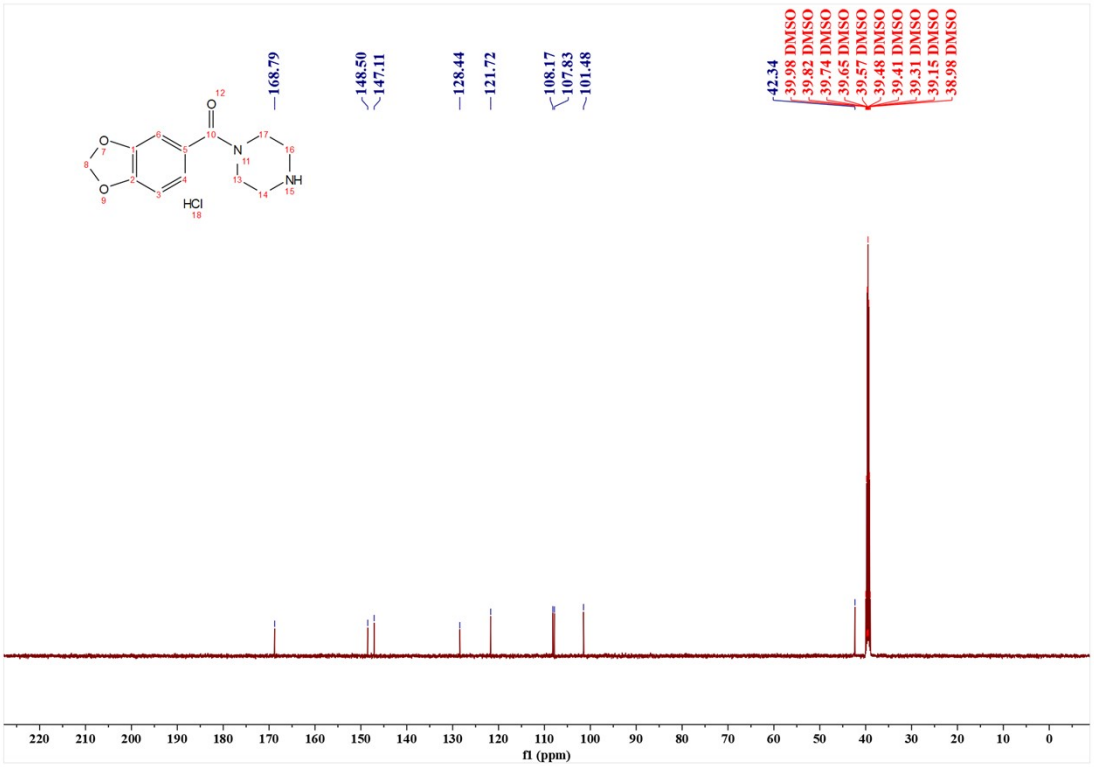
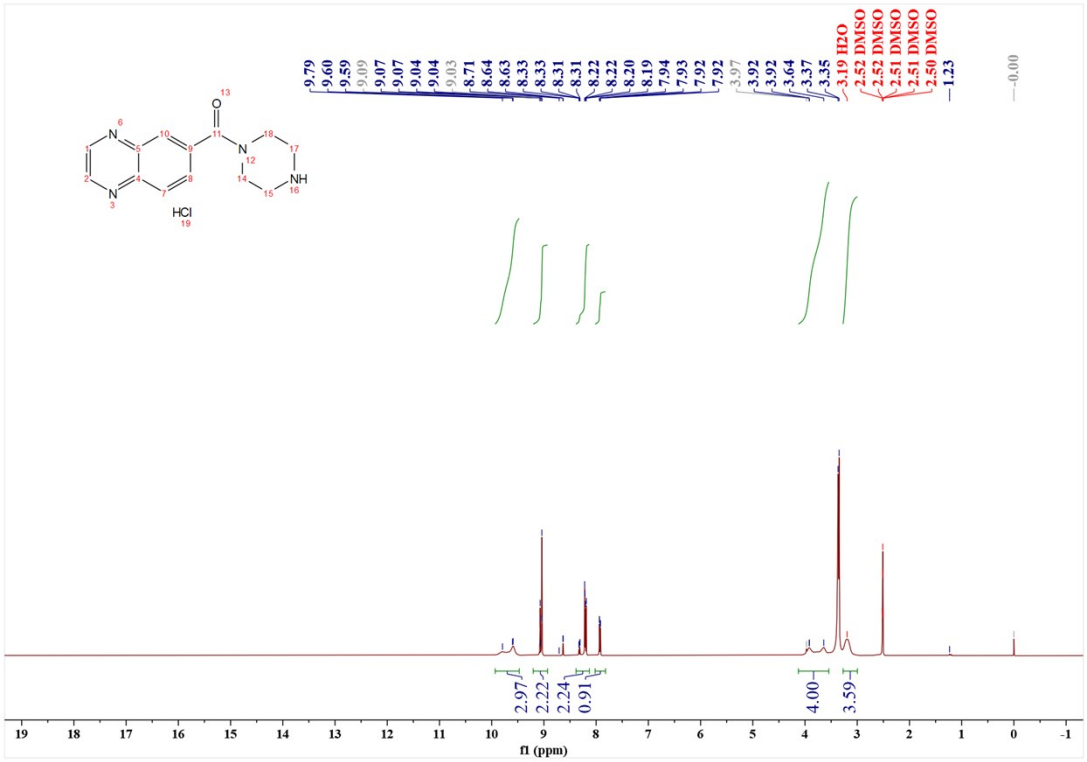
144.82
143.04
127.69
120.56
116.94
116.41
64.19
64.03
42.32
39.98 DMSO
39.90 DMSO
39.81 DMSO
39.73 DMSO
39.64 DMSO
39.57 DMSO
39.47 DMSO
39.31 DMSO
39.14 DMSO
38.97 DMSO
HCl
f1 (ppm)


9.62
9.61
7.05
7.05
7.04
6.98
6.98
6.09
3.70
3.36 H2O
3.34
3.13
3.12
3.11
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
1.11
0.00
HCl
2.34
1.00
2.03
2.06
4.16
0.96
4.02
f1 (ppm)


168.79
148.50
147.11
128.44
121.72
108.17
107.83
101.48
42.34
39.98 DMSO
39.82 DMSO
39.74 DMSO
39.65 DMSO
39.57 DMSO
39.48 DMSO
39.41 DMSO
39.31 DMSO
39.15 DMSO
38.98 DMSO
HCl
f1 (ppm)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9.09
9.07
9.07
9.04
9.04
9.03
8.71
8.64
8.63
8.33
8.33
8.31
8.31
8.22
8.22
8.20
8.19
7.94
7.93
7.92
7.92
7.92
3.97
3.92
3.92
3.64
3.37
3.35
3.19 H2O
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.23
0.00
HCl
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2.22
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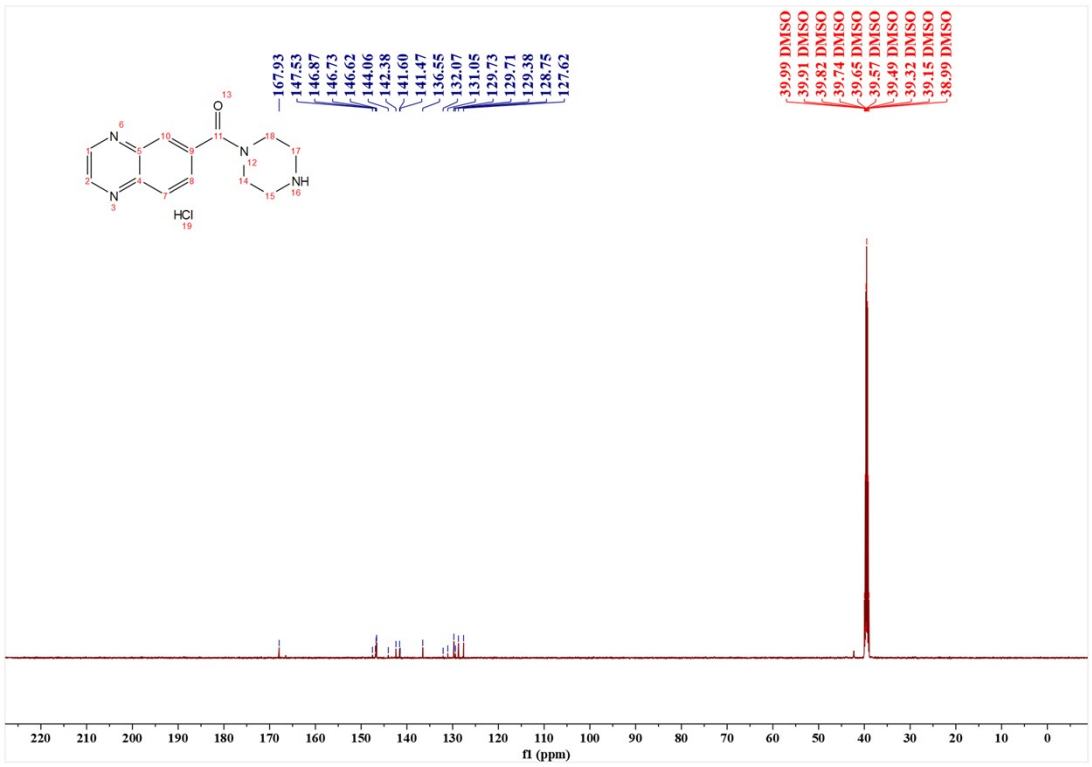
0.91
4.00
3.59
f1 (ppm)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147.53
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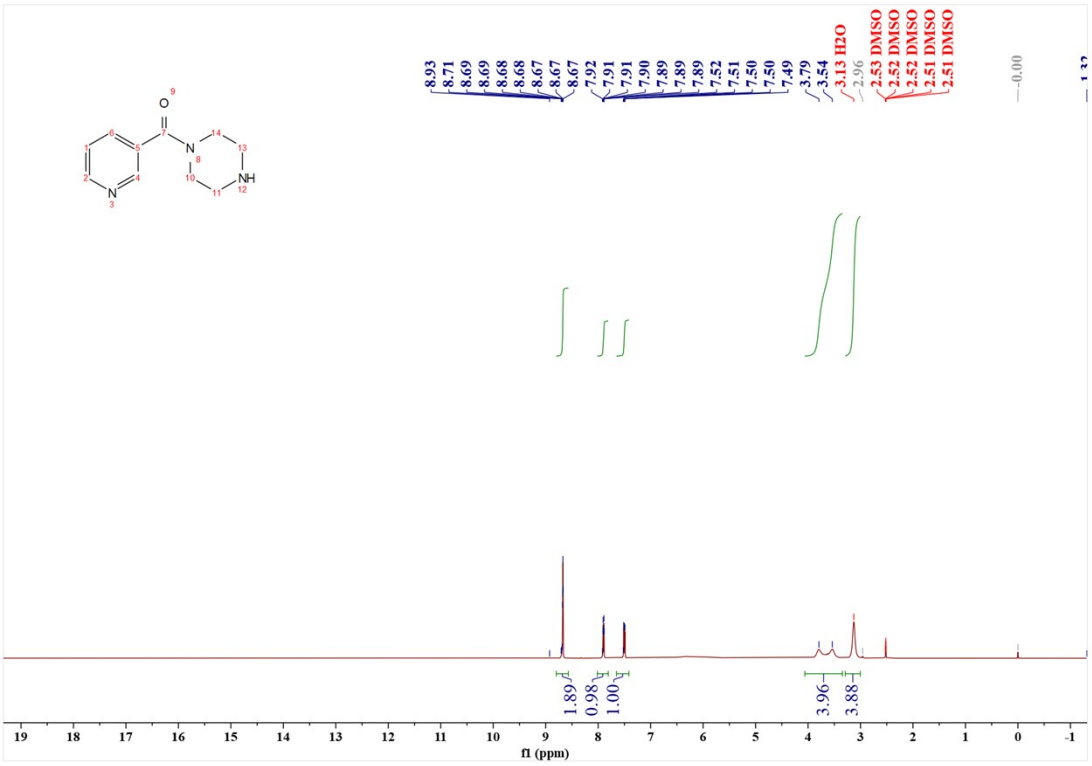
146.73
146.62
144.06
142.38
141.60
141.47
136.55
132.07
131.05
129.73
129.71
129.38
128.75
127.62
39.99 DMSO
39.91 DMSO
39.82 DMSO
39.74 DMSO
39.65 DMSO
39.57 DMSO
39.49 DMSO
39.32 DMSO
39.15 DMSO
38.99 DMSO
HCl
f1 (ppm)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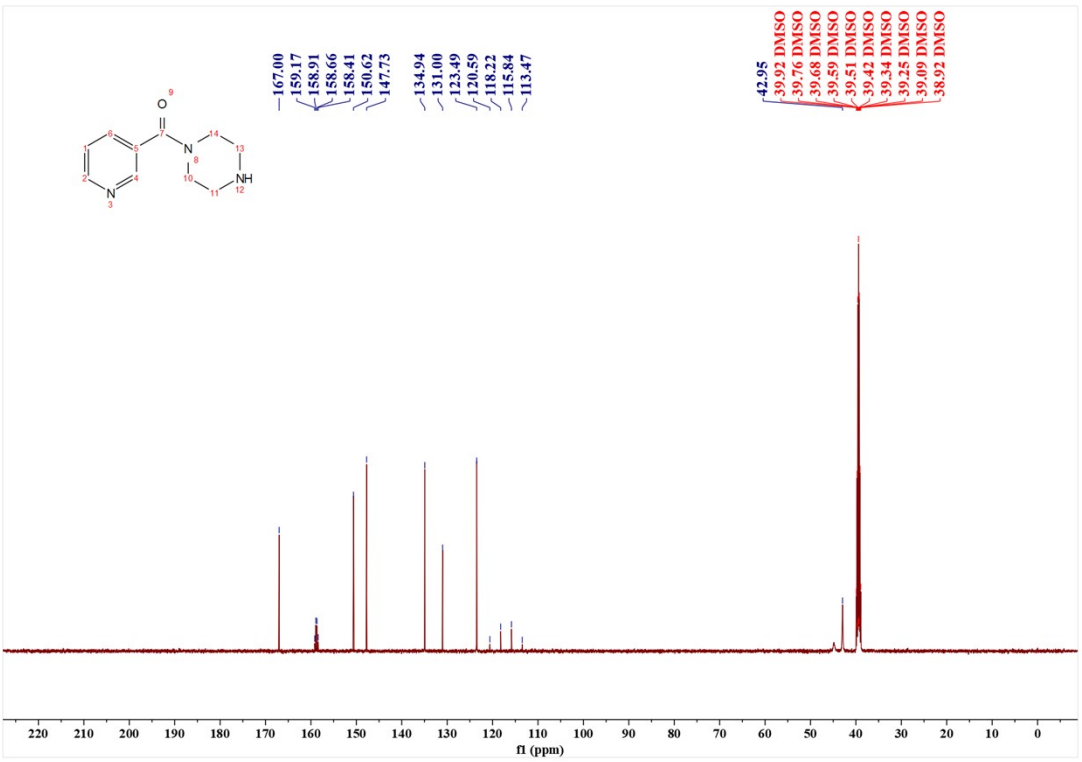
8.71
8.69
8.69
8.68
8.68
8.67
8.67
8.67
7.92
7.91
7.91
7.90
7.89
7.89
7.89
7.52
7.51
7.50
7.50
7.49
3.79
3.54
3.13 H2O
2.96
2.53 DMSO
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
0.00
1.89
0.98
1.00
3.96
3.88
f1 (ppm)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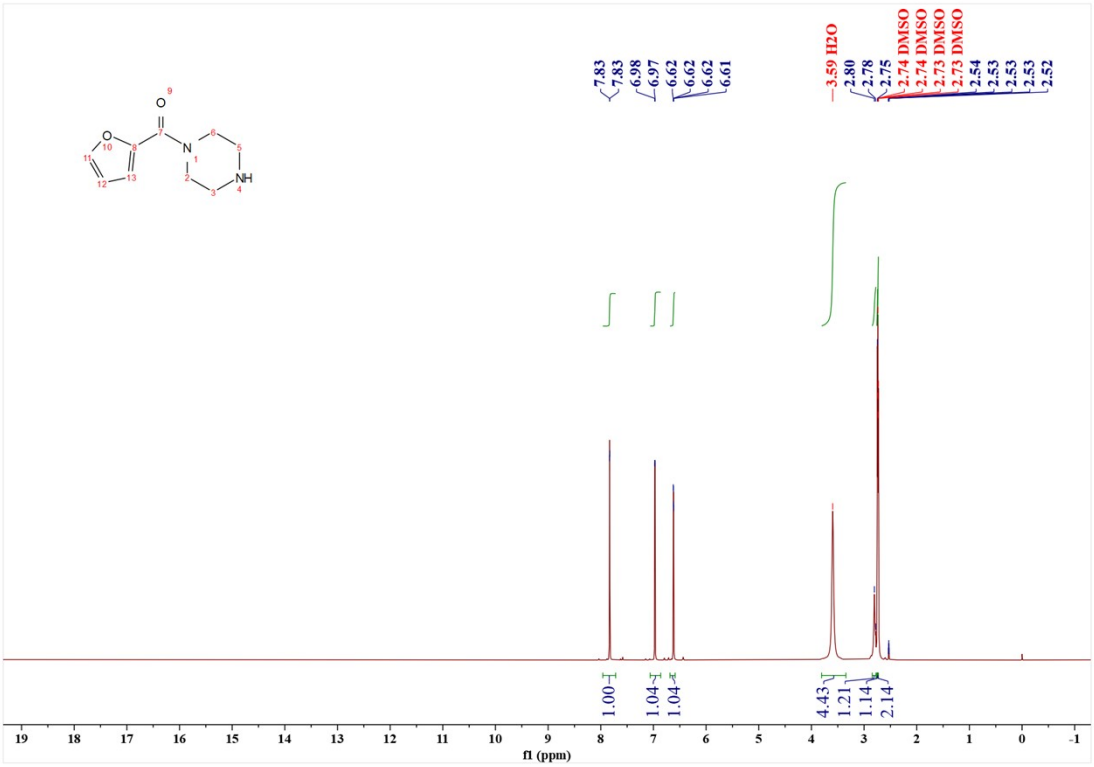
158.91
158.66
158.41
150.62
147.73
134.94
131.00
123.49
120.59
118.22
115.84
113.47
42.95
39.92 DMSO
39.76 DMSO
39.68 DMSO
39.59 DMSO
39.51 DMSO
39.42 DMSO
39.34 DMSO
39.25 DMSO
39.09 DMSO
38.92 DMSO
f1 (ppm)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6.97
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6.62
6.62
6.61
3.59 H2O
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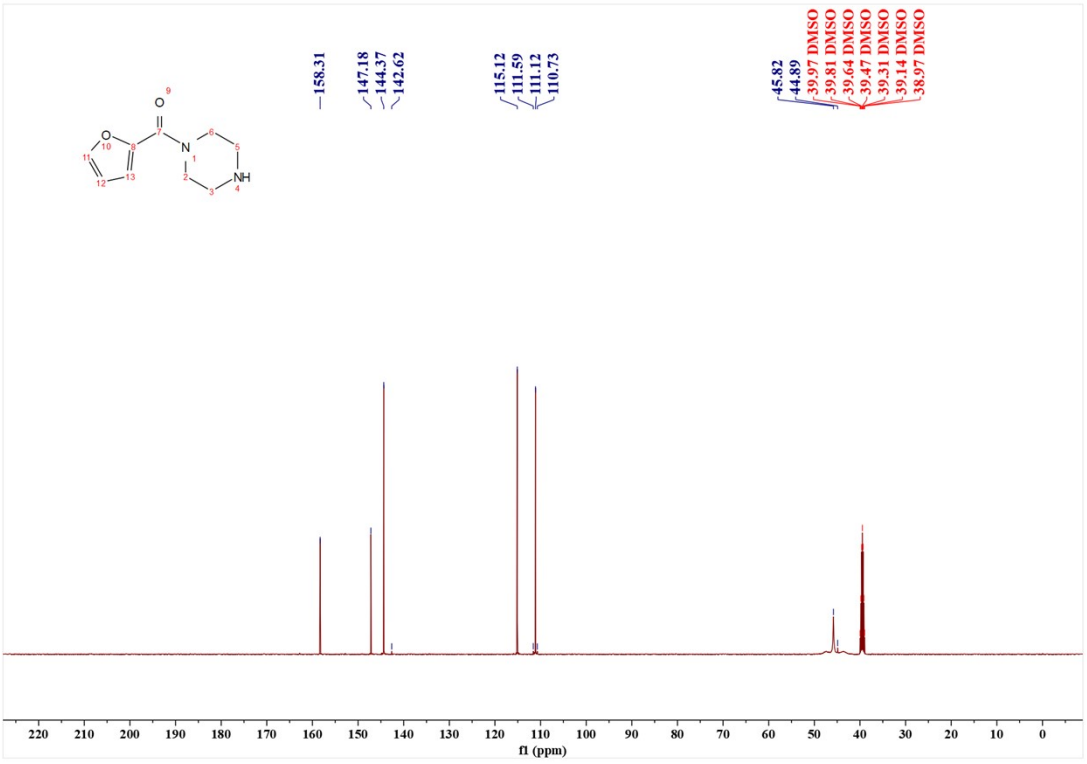
2.78
2.75
2.74 DMSO
2.74 DMSO
2.73 DMSO
2.73 DMSO
2.54
2.53
2.53
2.53
2.52
1.00
1.04
1.04
4.43
1.21
1.14
2.14
f1 (ppm)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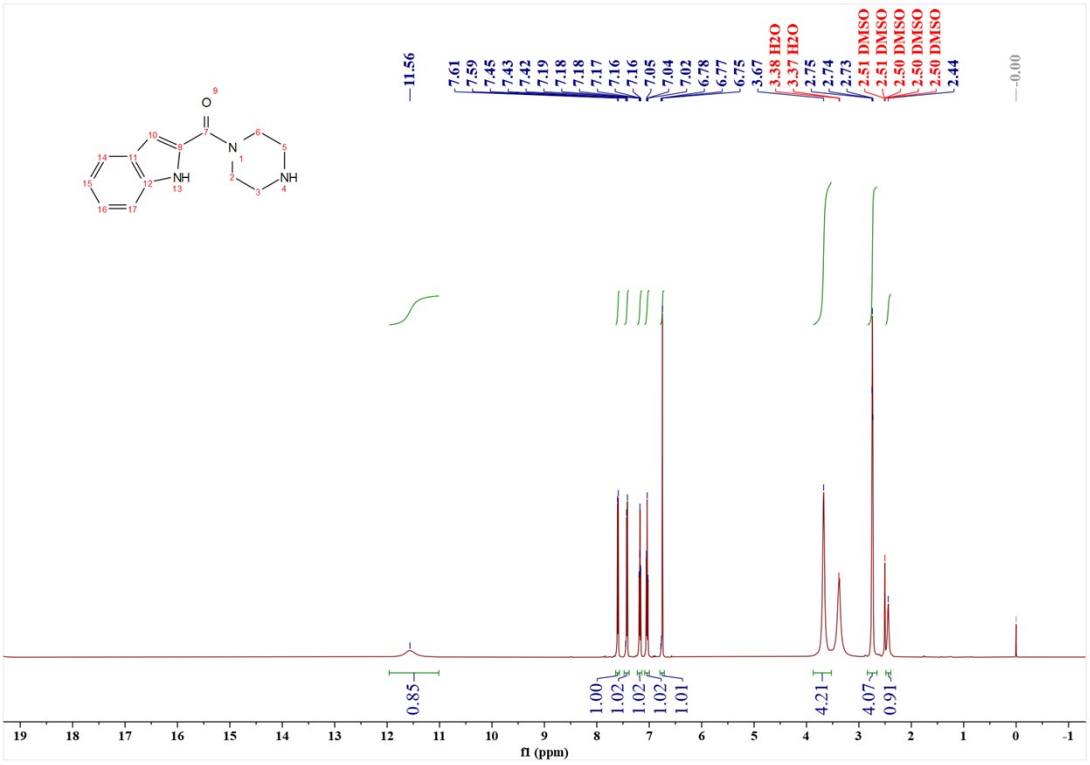
147.18
144.37
142.62
115.12
111.59
111.12
110.73
45.82
44.89
39.97 DMSO
39.81 DMSO
39.64 DMSO
39.47 DMSO
39.31 DMSO
39.14 DMSO
38.97 DMSO
f1 (ppm)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7.61
7.59
7.45
7.43
7.42
7.19
7.18
7.18
7.17
7.16
7.16
7.05
7.04
7.02
6.78
6.77
6.75
3.67
3.38 H2O
3.37 H2O
2.75
2.74
2.73
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.44
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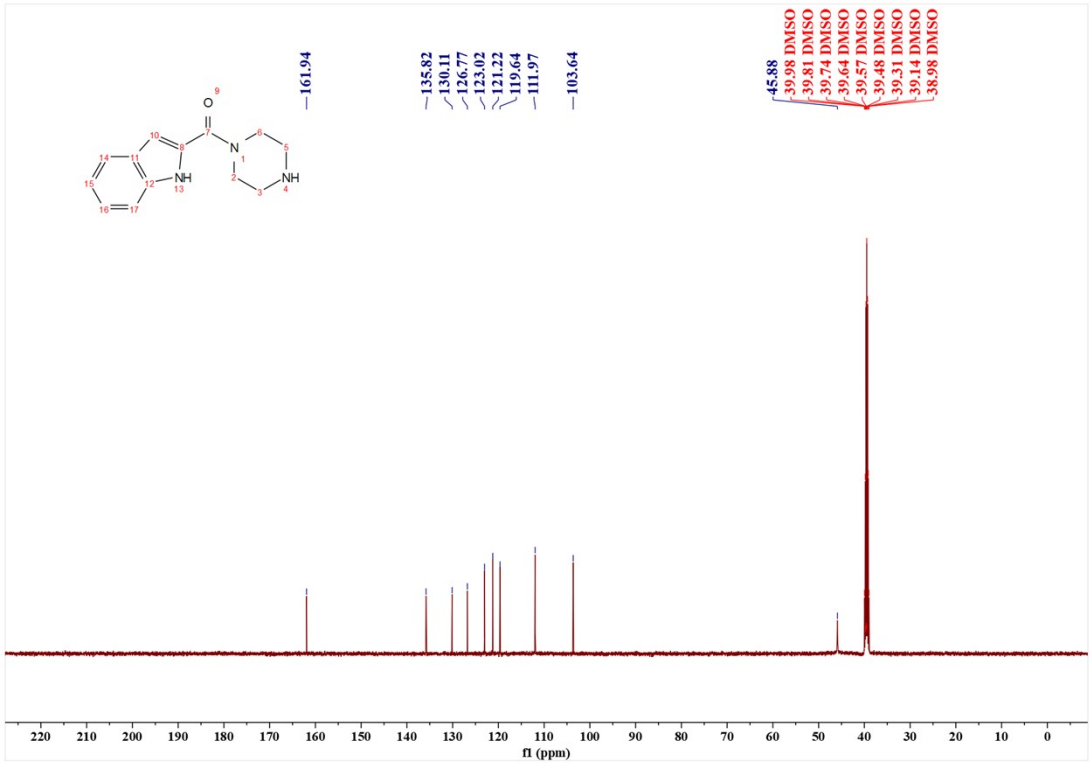
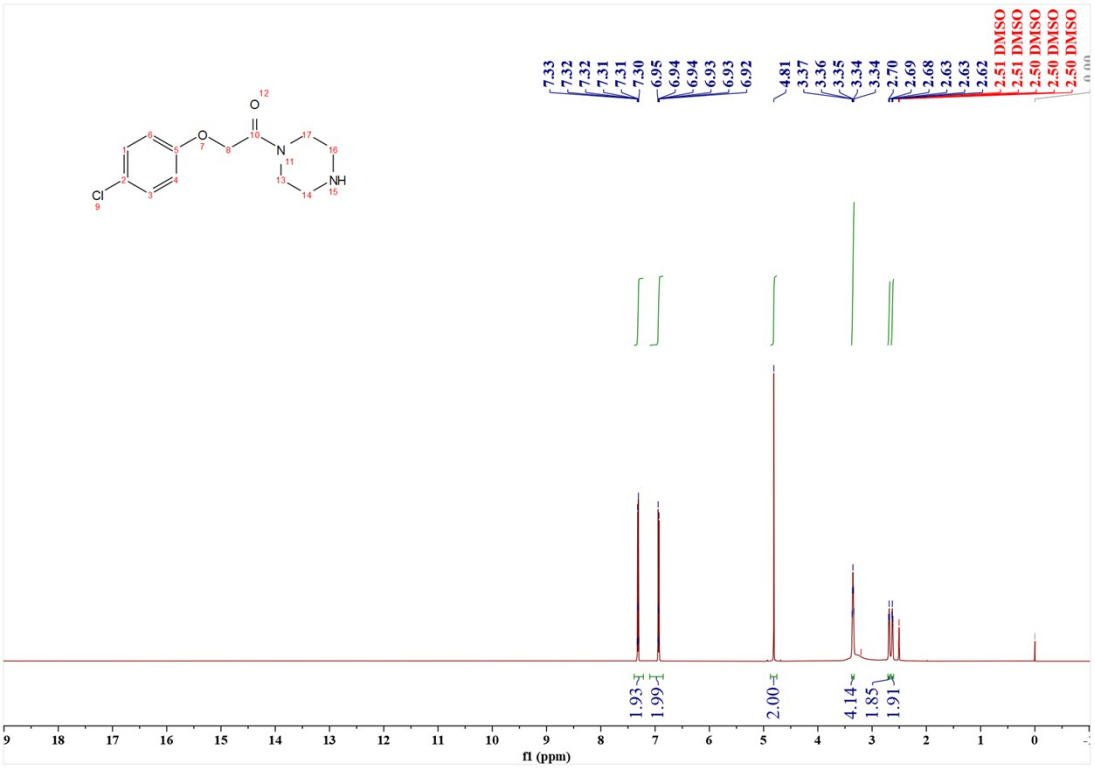
1.00
1.02
1.02
1.02
1.01
4.21
4.07
0.91
f1 (ppm)


161.94
135.82
130.11
126.77
123.02
121.22
119.64
111.97
103.64
45.88
39.98 DMSO
39.81 DMSO
39.74 DMSO
39.64 DMSO
39.57 DMSO
39.48 DMSO
39.31 DMSO
39.14 DMSO
38.98 DMSO
f1 (ppm)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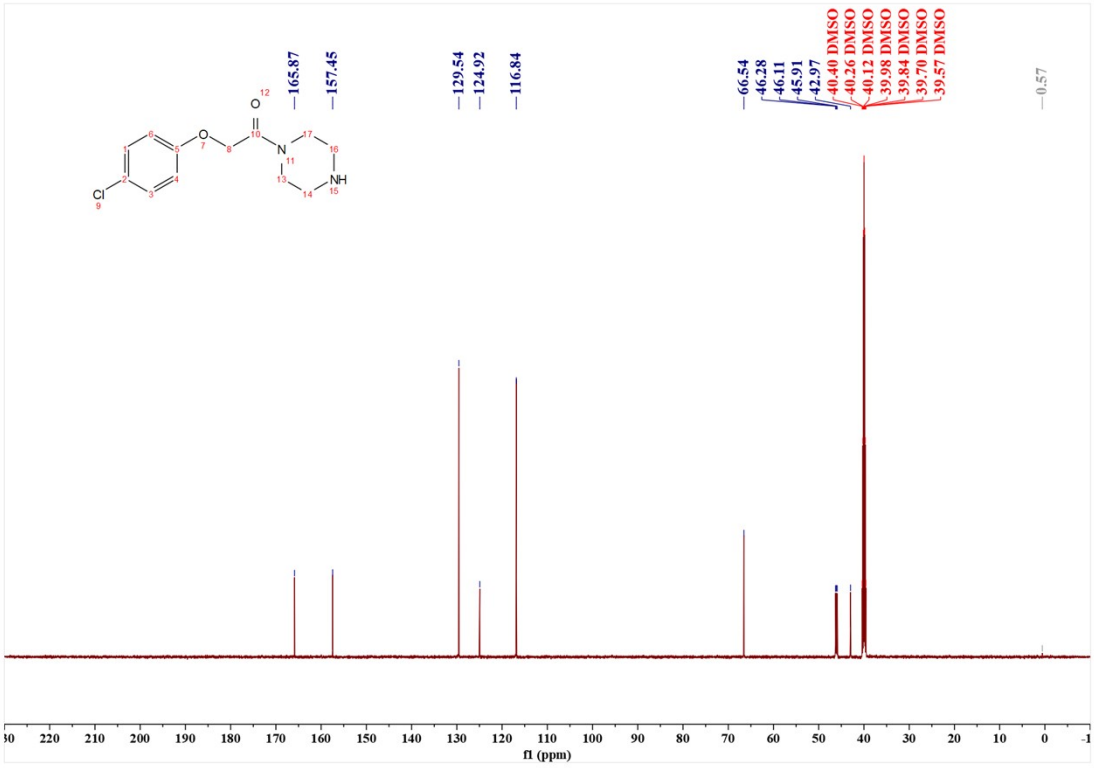
6.94
6.94
6.93
6.93
6.92
4.81
3.37
3.36
3.35
3.34
3.34
2.70
2.69
2.68
2.63
2.63
2.62
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
1.93
1.99
2.00
4.14
1.85
1.91
f1 (ppm)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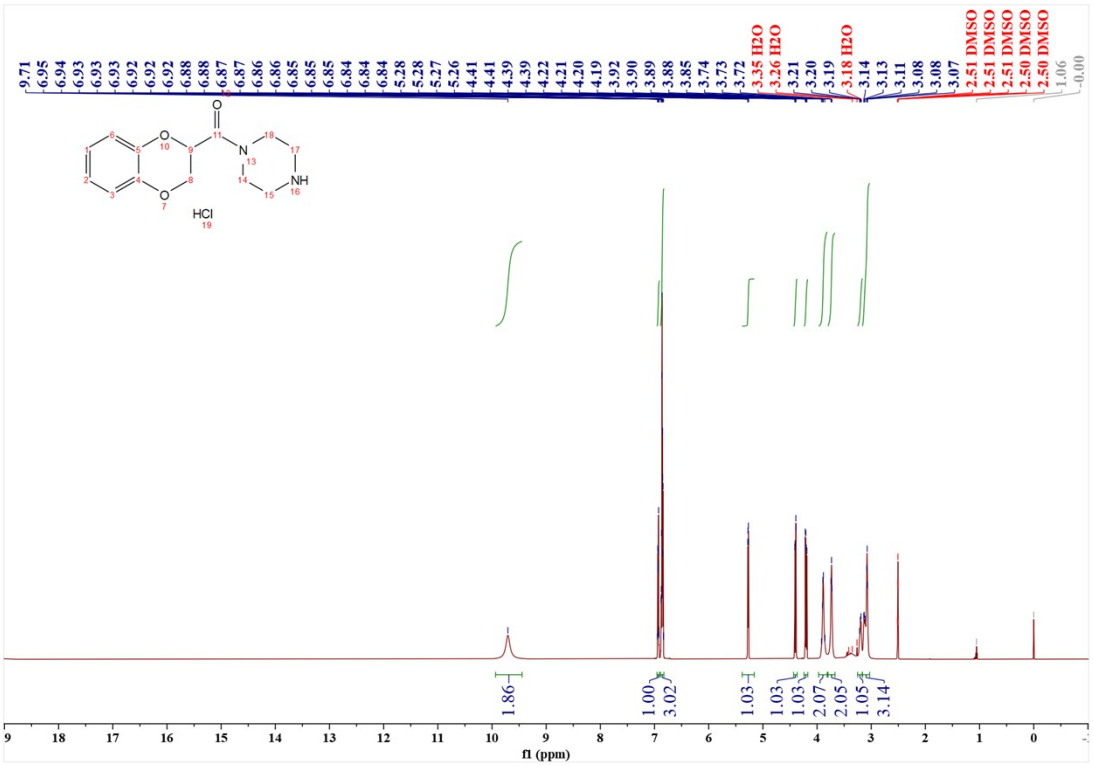
129.54
124.92
116.84
66.54
46.28
46.11
45.91
42.97
40.40 DMSO
40.26 DMSO
40.12 DMSO
39.98 DMSO
39.84 DMSO
39.70 DMSO
39.57 DMSO
0.57
f1 (ppm)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6.88
6.88
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6.86
6.86
6.85
6.85
6.85
6.84
6.84
6.84
5.28
5.27
5.26
4.41
4.41
4.39
4.39
4.22
4.21
4.20
4.19
3.92
3.90
3.89
3.88
3.85
3.74
3.73
3.72
3.35 H2O
3.26 H2O
3.21
3.20
3.19
3.18 H2O
3.14
3.13
3.11
3.08
3.08
3.07
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
1.06
0.00
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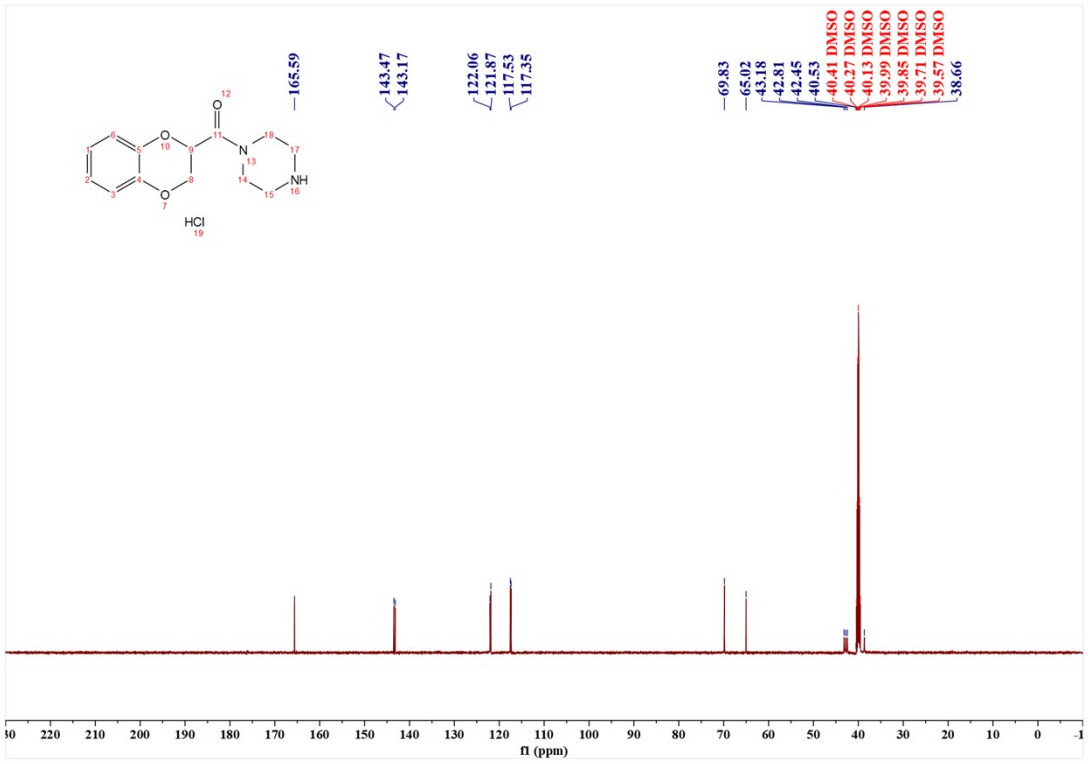
1.00
3.02
1.03
1.03
1.03
2.07
2.05
1.05
3.14
fl (ppm)


165.59
143.47
143.17
122.06
121.87
117.53
117.35
69.83
65.02
43.18
42.81
42.45
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40.27 DMSO
40.13 DMSO
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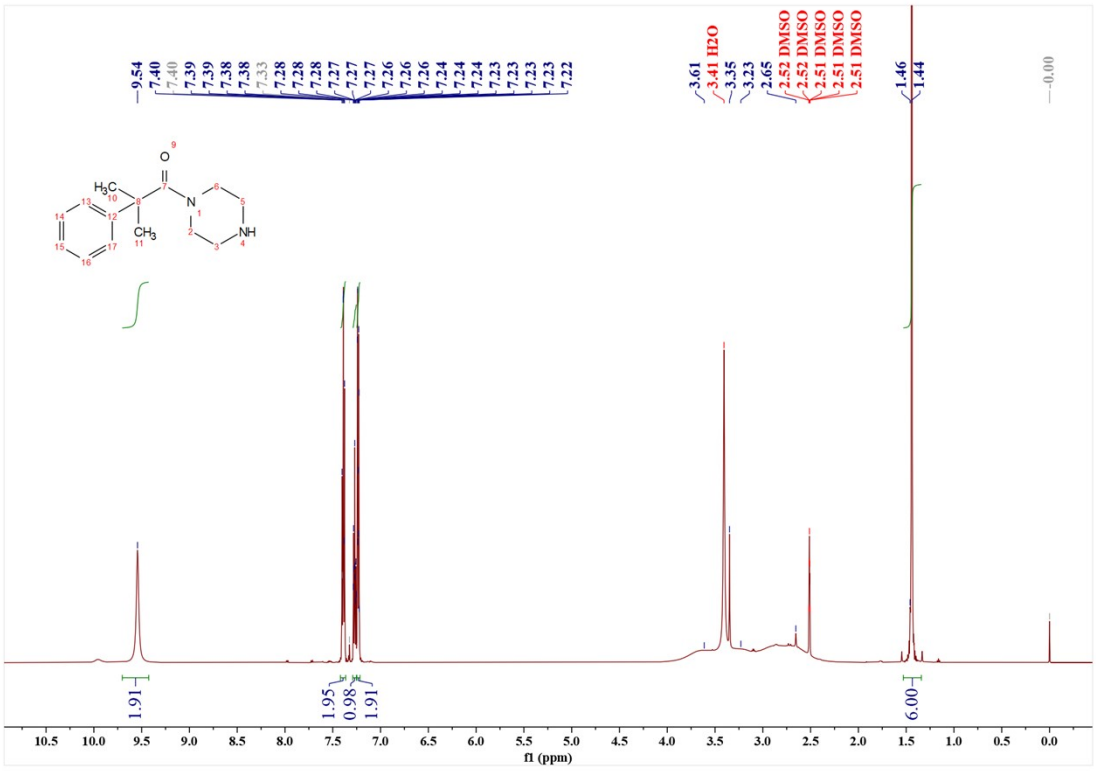
39.71 DMSO
39.57 DMSO
38.66
HCl
fl (ppm)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7.38
7.33
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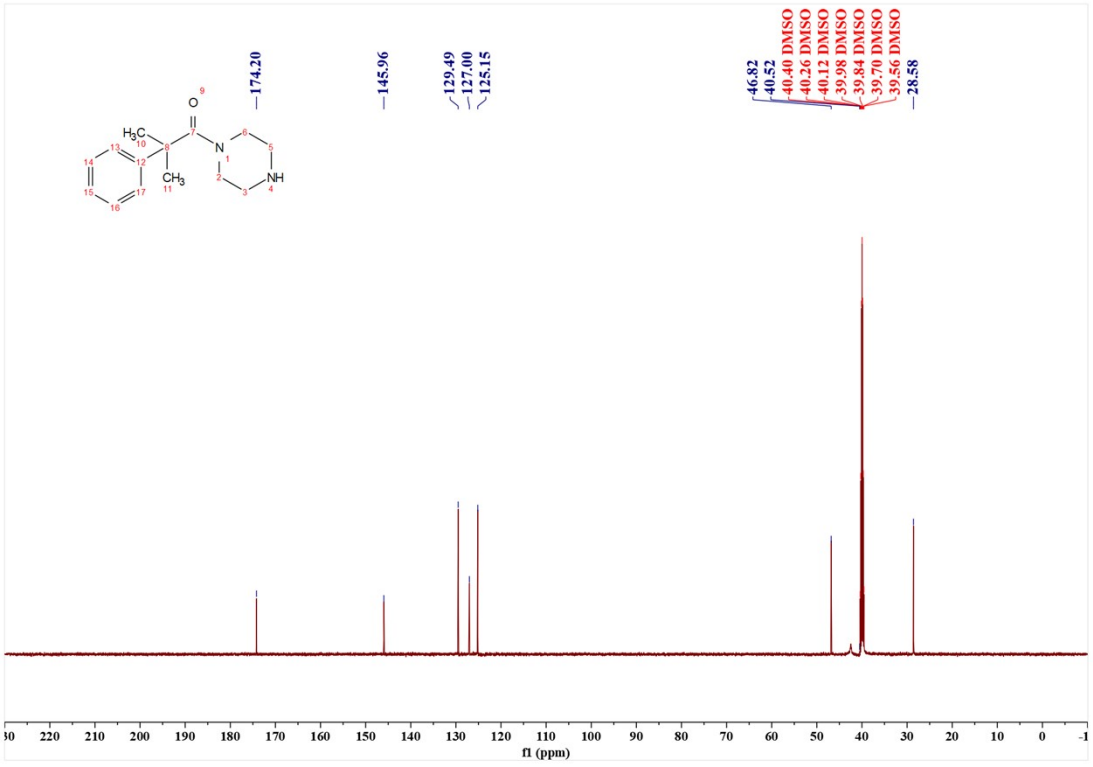
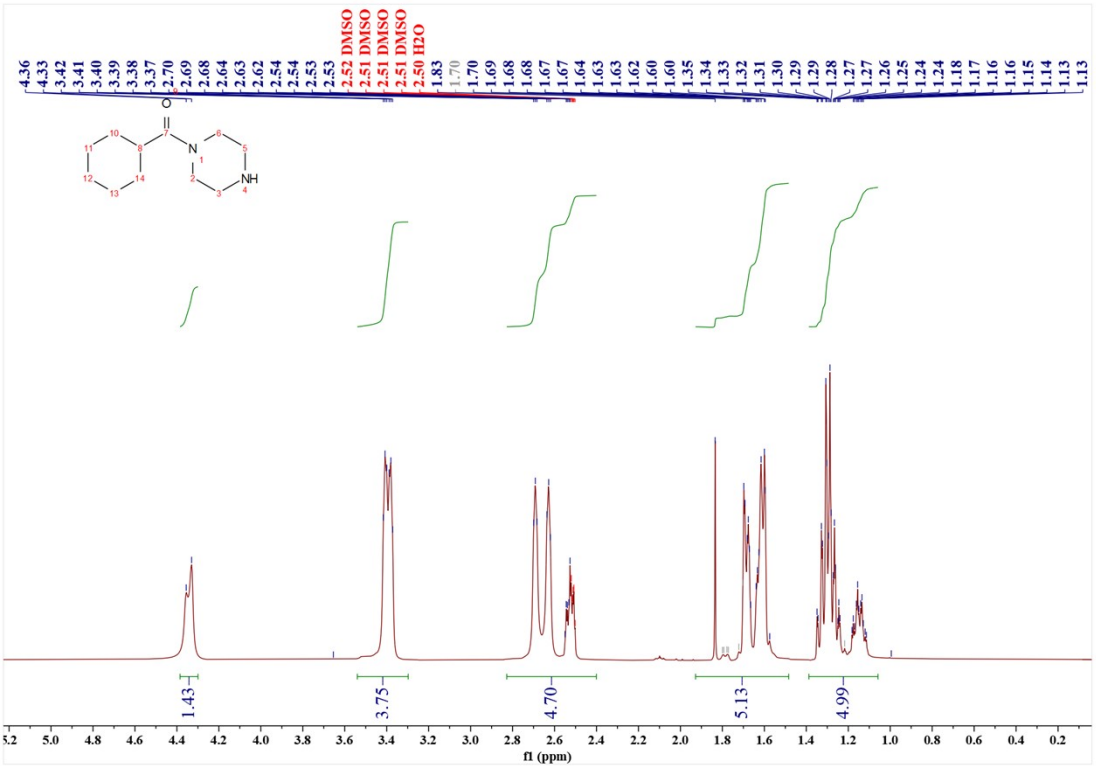
7.28
7.28
7.27
7.27
7.27
7.26
7.26
7.26
7.24
7.24
7.24
7.23
7.23
7.23
7.22
3.61
3.41 H2O
3.35
3.23
2.65
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
1.46
1.44
0.00
1.91
1.95
0.98
1.91
6.00
f1 (ppm)


174.20
145.96
129.49
127.00
125.15
46.82
40.52
40.40 DMSO
40.26 DMSO
40.12 DMSO
39.98 DMSO
39.84 DMSO
39.70 DMSO
39.56 DMSO
28.58
f1 (ppm)


4.36
4.33
3.42
3.41
3.40
3.39
3.38
3.37
2.70
2.69
2.68
2.64
2.63
2.62
2.54
2.54
2.53
2.53
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 H2O
1.83
1.70
1.70
1.69
1.68
1.68
1.67
1.67
1.64
1.63
1.63
1.62
1.60
1.60
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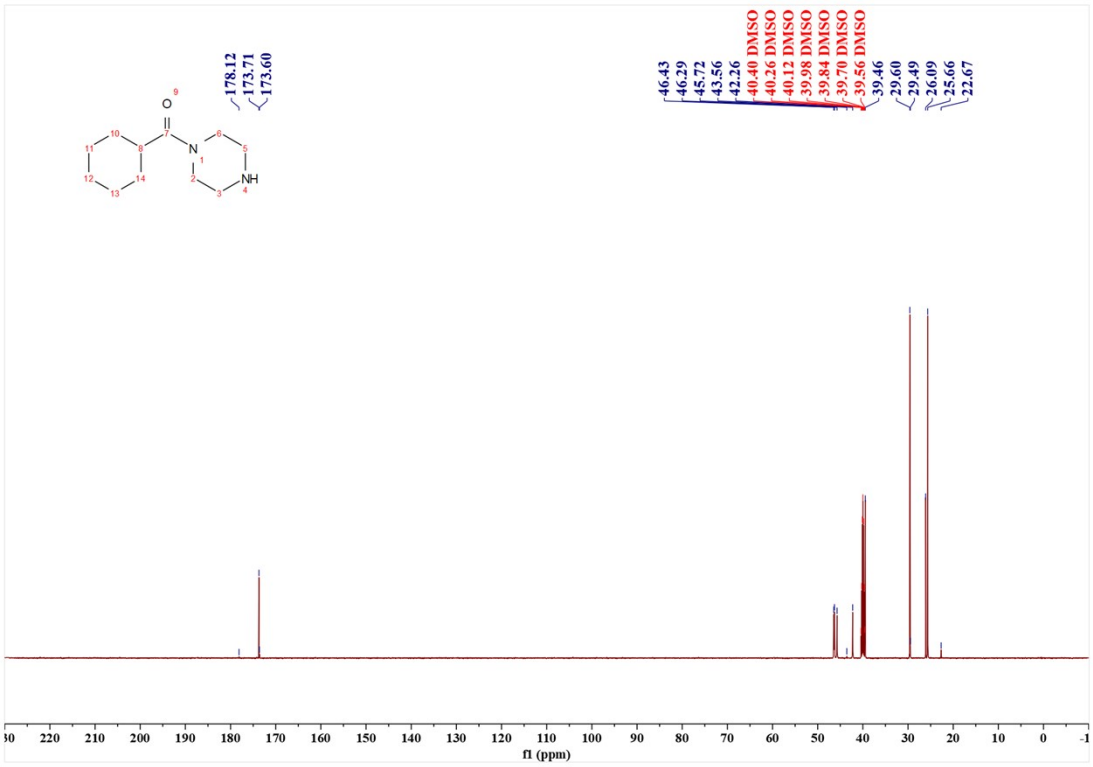
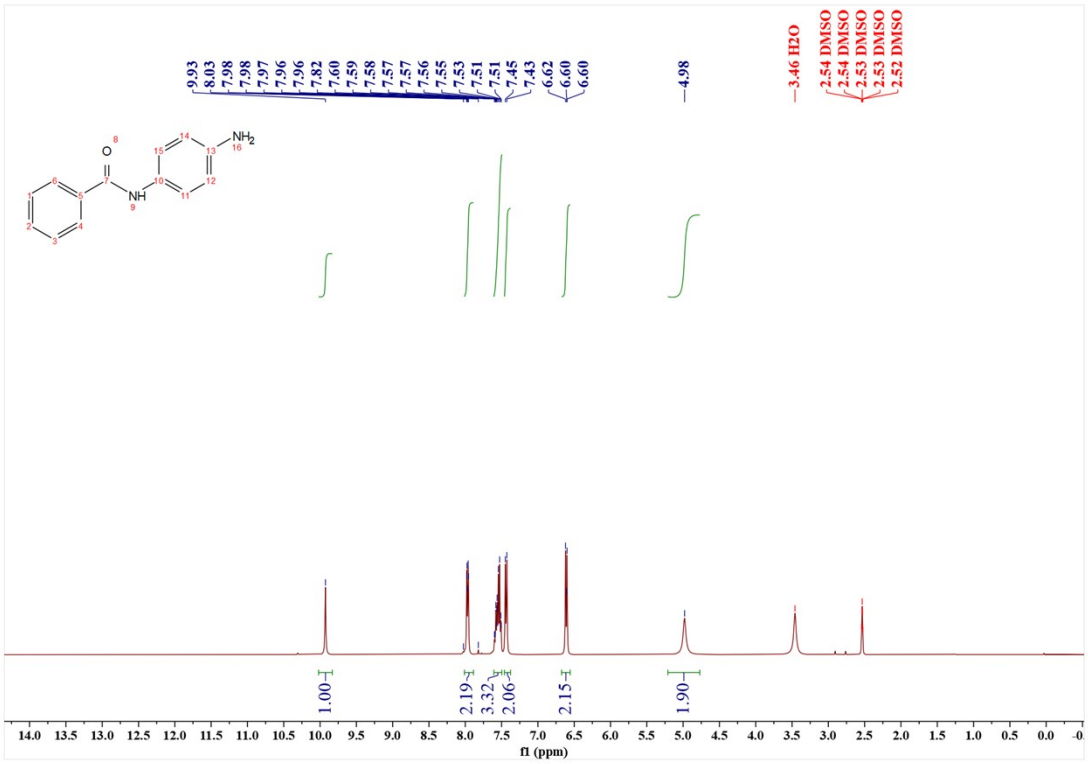
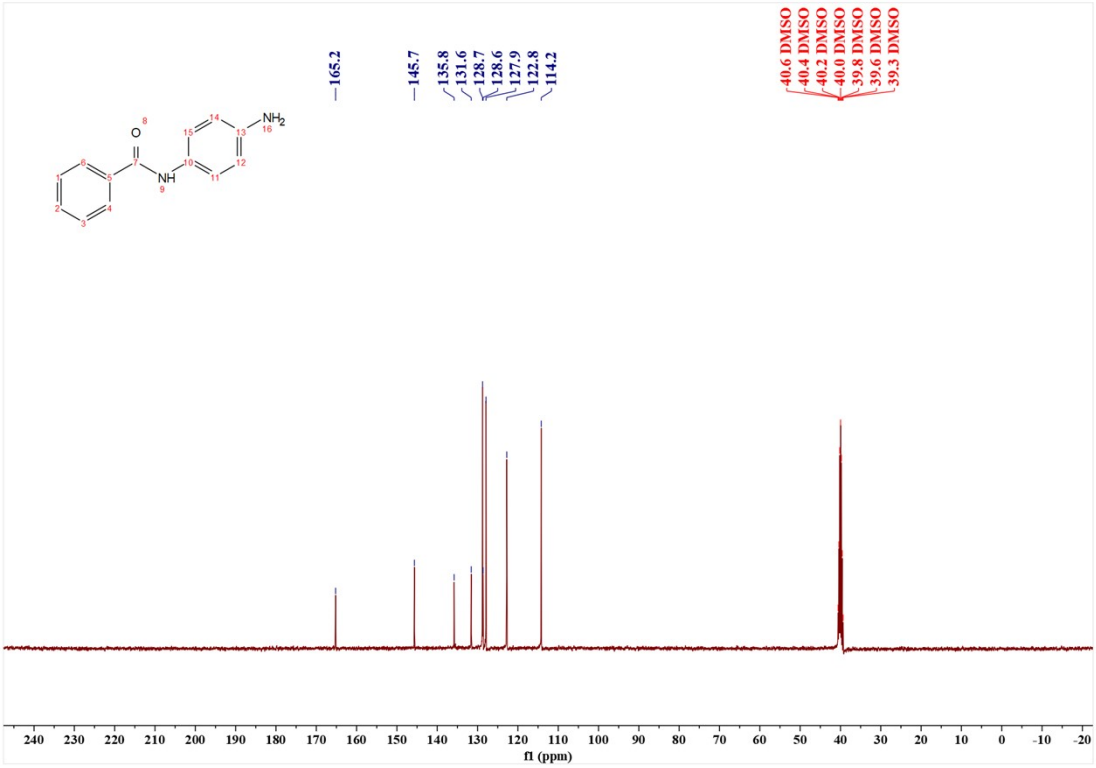
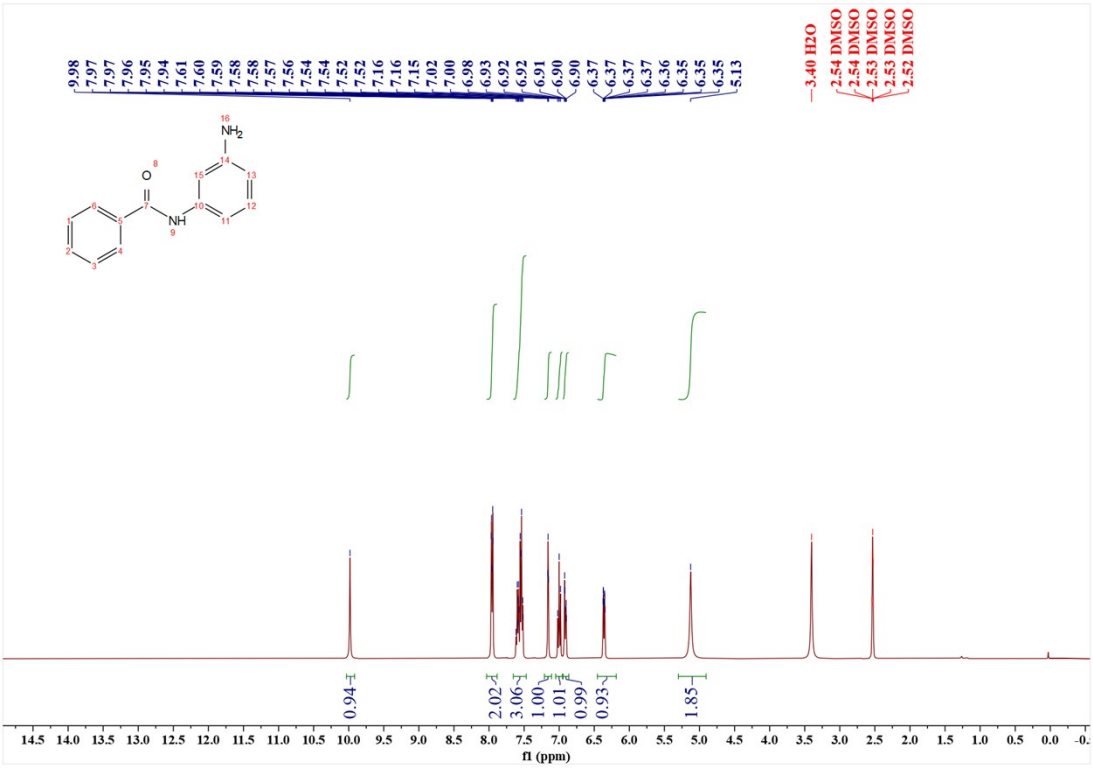
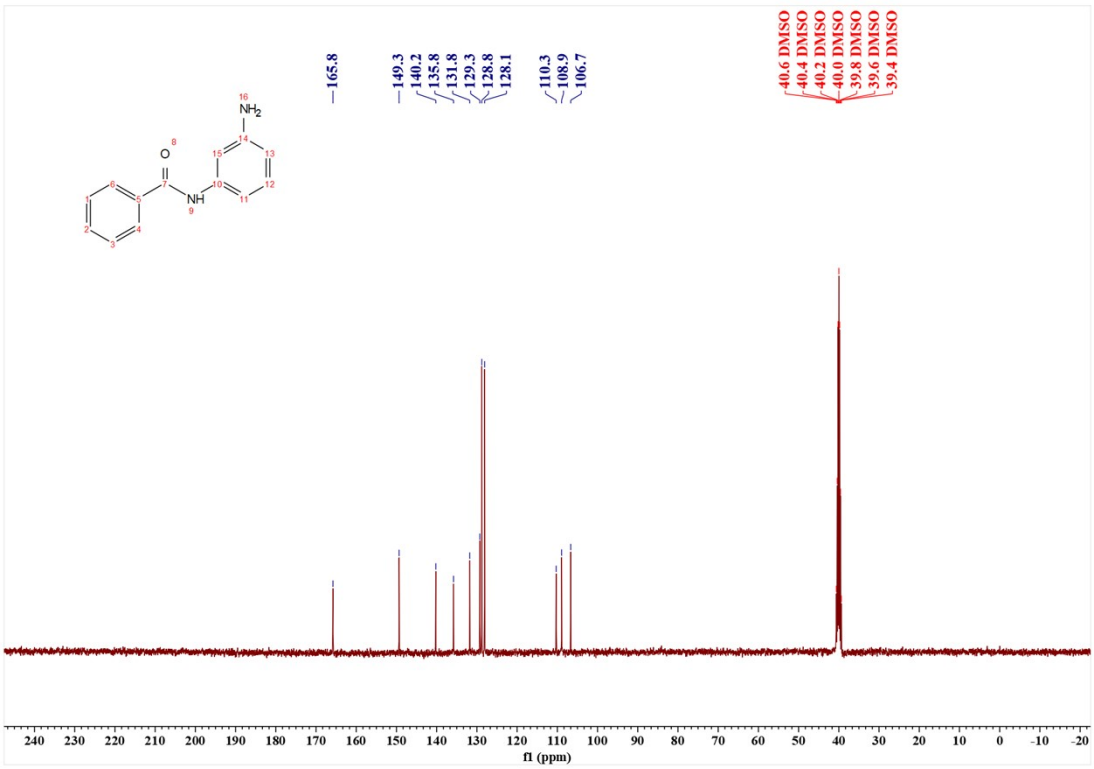
1.27
1.27
1.26
1.25
1.24
1.24
1.18
1.17
1.16
1.16
1.15
1.14
1.13
1.13
O
N
NH
1.43
3.75
4.70
5.13
4.99
f1 (ppm)

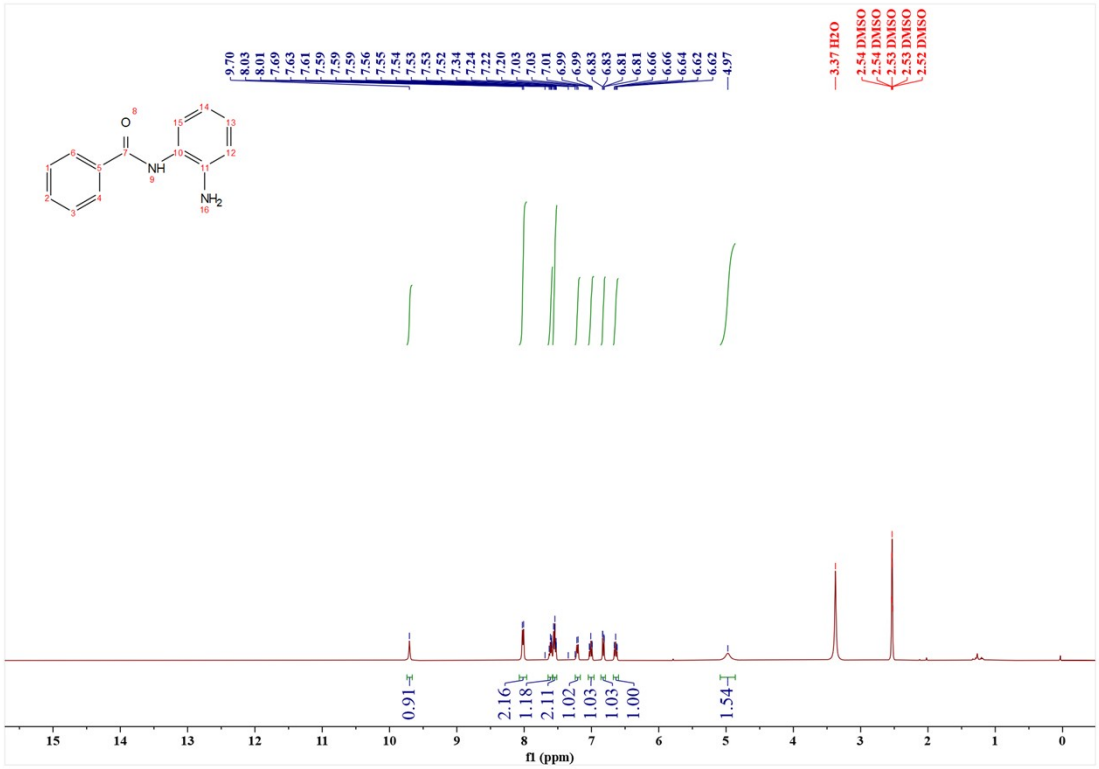

178.12
173.71
173.60
O
N
NH
46.43
46.29
45.72
43.56
42.26
40.40 DMSO
40.26 DMSO
40.12 DMSO
39.98 DMSO
39.84 DMSO
39.70 DMSO
39.56 DMSO
39.46
29.60
29.49
26.09
25.66
22.67
f1 (ppm)

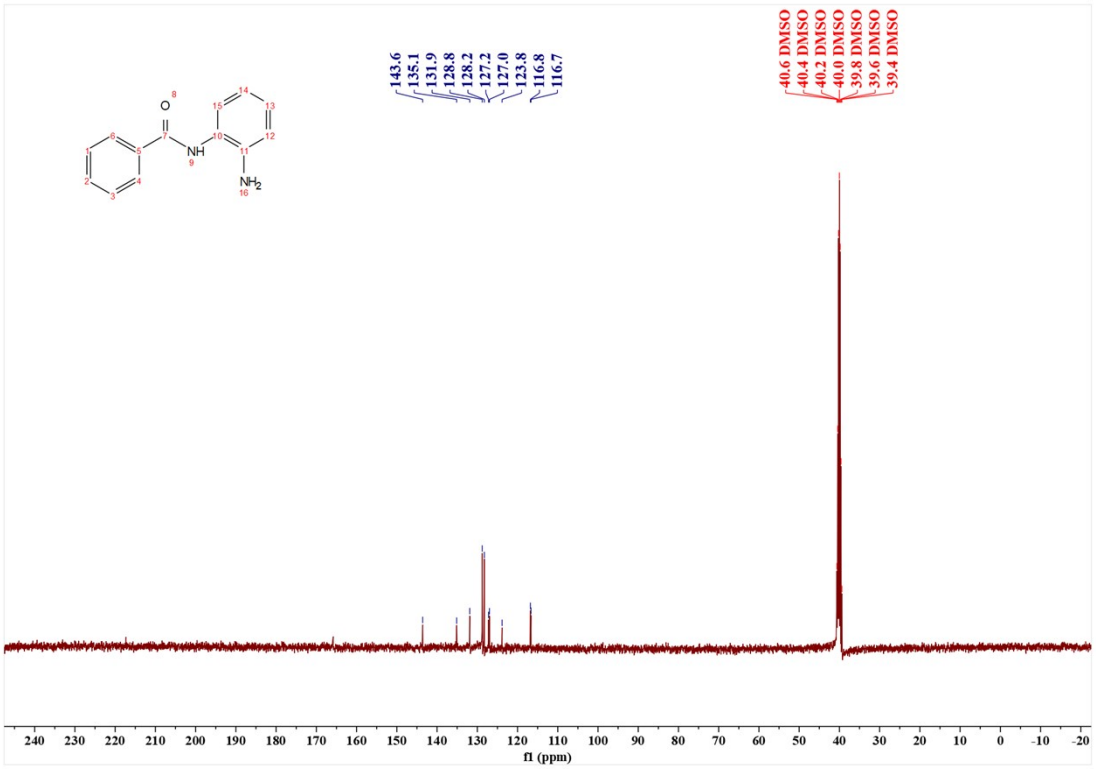

9.93
8.03
7.98
7.98
7.97
7.96
7.96
7.82
7.60
7.59
7.58
7.57
7.57
7.56
7.55
7.53
7.51
7.51
7.45
7.43
6.62
6.60
6.60
4.98
3.46 H2O
2.54 DMSO
2.54 DMSO
2.53 DMSO
2.53 DMSO
2.52 DMSO
1.00
2.19
3.32
2.06
2.15
1.90
f1 (ppm)

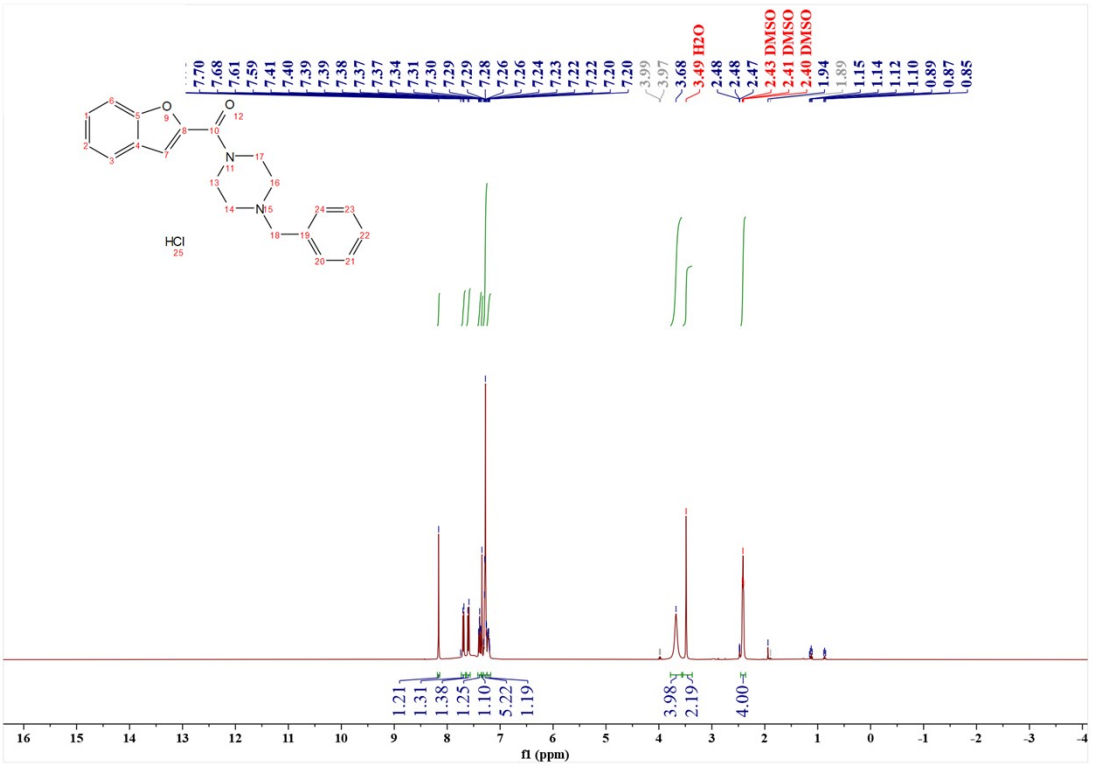

165.2
145.7
135.8
131.6
128.7
128.6
127.9
122.8
114.2
40.6 DMSO
40.4 DMSO
40.2 DMSO
40.0 DMSO
39.8 DMSO
39.6 DMSO
39.3 DMSO
f1 (ppm)


9.98
7.97
7.97
7.96
7.95
7.94
7.61
7.60
7.59
7.58
7.58
7.57
7.56
7.54
7.54
7.52
7.52
7.16
7.16
7.15
7.02
7.00
6.98
6.93
6.92
6.92
6.91
6.90
6.90
6.37
6.37
6.37
6.37
6.36
6.35
6.35
6.35
5.13
3.40 H2O
2.54 DMSO
2.54 DMSO
2.53 DMSO
2.53 DMSO
2.52 DMSO
NH2
O
NH
0.94
2.02
3.06
1.00
1.01
0.99
0.93
1.85
f1 (ppm)


165.8
149.3
140.2
135.8
131.8
129.3
128.8
128.1
110.3
108.9
106.7
40.6 DMSO
40.4 DMSO
40.2 DMSO
40.0 DMSO
39.8 DMSO
39.6 DMSO
39.4 DMSO
NH2
O
NH
f1 (ppm)


9.70
8.03
8.01
7.69
7.63
7.61
7.59
7.59
7.59
7.59
7.56
7.55
7.54
7.53
7.53
7.52
7.34
7.24
7.22
7.20
7.03
7.03
7.01
6.99
6.99
6.83
6.83
6.81
6.81
6.66
6.66
6.64
6.62
6.62
4.97
3.37 H2O
2.54 DMSO
2.54 DMSO
2.53 DMSO
2.53 DMSO
2.52 DMSO
O
NH
NH2
0.91
2.16
1.18
2.11
1.02
1.03
1.03
1.00
1.54
f1 (ppm)


143.6
135.1
131.9
128.8
128.2
127.2
127.0
123.8
116.8
116.7
40.6 DMSO
40.4 DMSO
40.2 DMSO
40.0 DMSO
39.8 DMSO
39.6 DMSO
39.4 DMSO
O
NH
NH2
f1 (ppm)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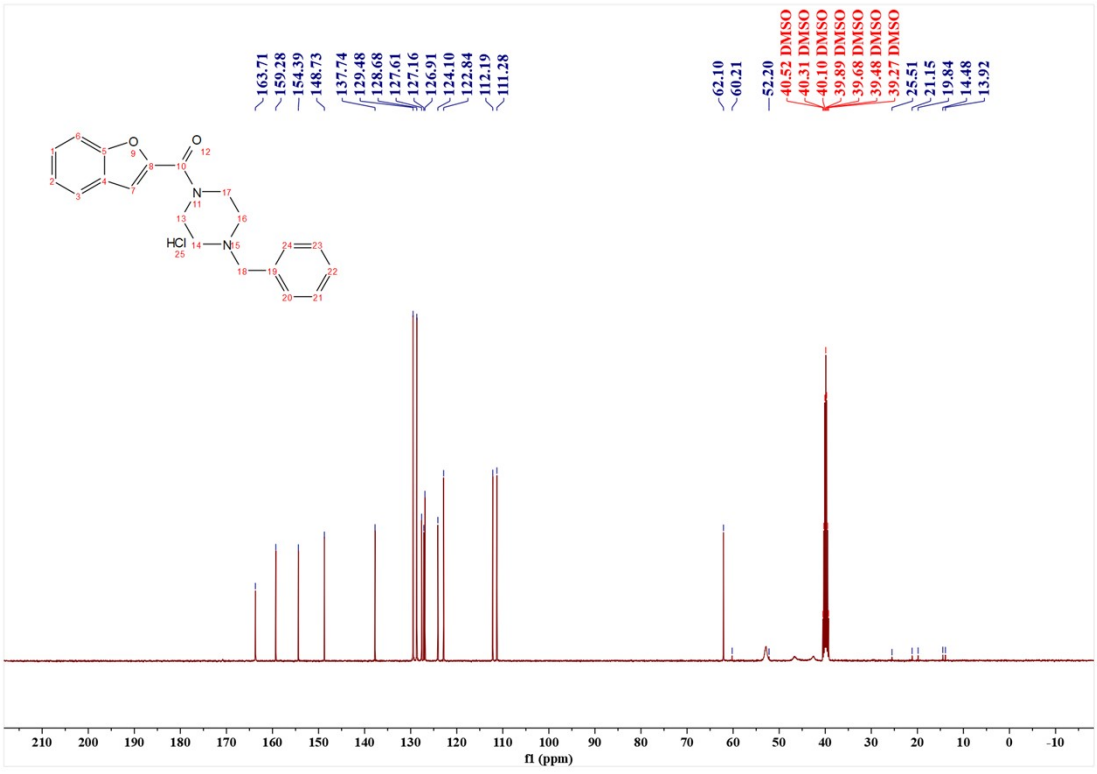
7.68
7.61
7.59
7.41
7.40
7.39
7.39
7.38
7.37
7.37
7.34
7.31
7.30
7.29
7.29
7.28
7.26
7.26
7.24
7.23
7.22
7.22
7.20
7.20
3.99
3.97
3.68
3.49 H2O
2.48
2.48
2.47
2.43 DMSO
2.41 DMSO
2.40 DMSO
1.94
1.89
1.15
1.14
1.12
1.10
0.89
0.87
0.85
HCl
1.21
1.31
1.38
1.25
1.10
5.22
1.19
3.98
2.19
4.00
f1 (ppm)


163.71
159.28
154.39
148.73
137.74
129.48
128.68
127.61
127.16
126.91
124.10
122.84
112.19
111.28
62.10
60.21
52.20
40.52 DMSO
40.31 DMSO
40.10 DMSO
39.89 DMSO
39.68 DMSO
39.48 DMSO
39.27 DMSO
25.51
21.15
19.84
14.48
13.92
HCl
f1 (ppm)

References

1. J. Magano, *Org. Process Res. Dev.*, 2022, **26**, 1562-1689.

2. Q. L. Xu, J. Chen, Z. H. Wang, Y. J. Zang, G. S. Li, F. C. Zhu, D. Liu and C. Y. Sun, *Chem. Eng. J.*, 2023, **471**, 144304-144313.