Supporting Information

Application of Bis(oxazoline) in Asymmetric β-Amination of Chalcones

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1. General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^{1}H NMR spectra were recorded at 500 MHz using $CDCl_3$ as solvent. Elemental analysis was performed on a Vario EL III recorder. Mass spectra were obtained with an automated Fininigan TSQ Advantage mass spectrometer. Most of the products were known compounds and were identified by comparison of their physical and spectra data with those of authentic samples. The enantiomeric excess of the β-imidoketones was determined by HPLC on Ultron ES-OVM column.

2. General procedure

*2.1 Synthesis of chalcones(**1a** as an example)*

A mixture of acetophenone (10 mmol) and benzaldehyde (1.1 equiv) in anhydrous EtOH (15 mL) was stirred at room temperature for 5 min. Then, NaOH (3 equiv) was added. The reaction mixture was stirred at room temperature overnight until aldehyde consumption. After that, HCl (10%) was added until neutrality. Then dichloromethane was added to dilute the reaction mixture. The organic layer was dried over anhydrous Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography to give **1a**.

2.2 Typical procedure for the β-amination of chalcones

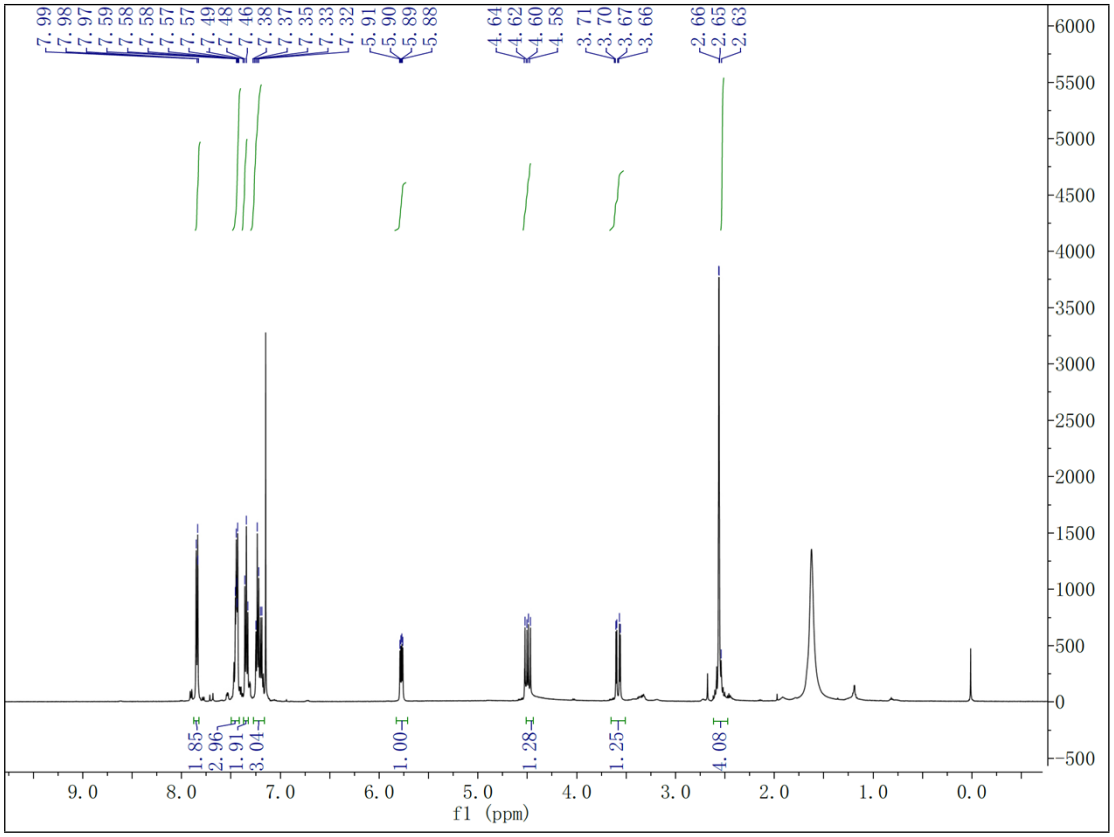
General procedure for the preparation of **2** (**2a** as an example): A mixture of chalcone **1a** (208 mg, 1.0 mmol), L3 (30.6 mg, 0.1 mmol), and DBU (0.18 mL, 1.2 mmol) in MeCN (2.0 mL) was stirred at room temperature. To the mixture were then added NBS (213 mg, 1.2 mmol). After the starting material **1a** was consumed as indicated by TLC, the reaction mixture was poured into water and then extracted with CH_2Cl_2 (3 × 10mL). The combined organic phase was washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The

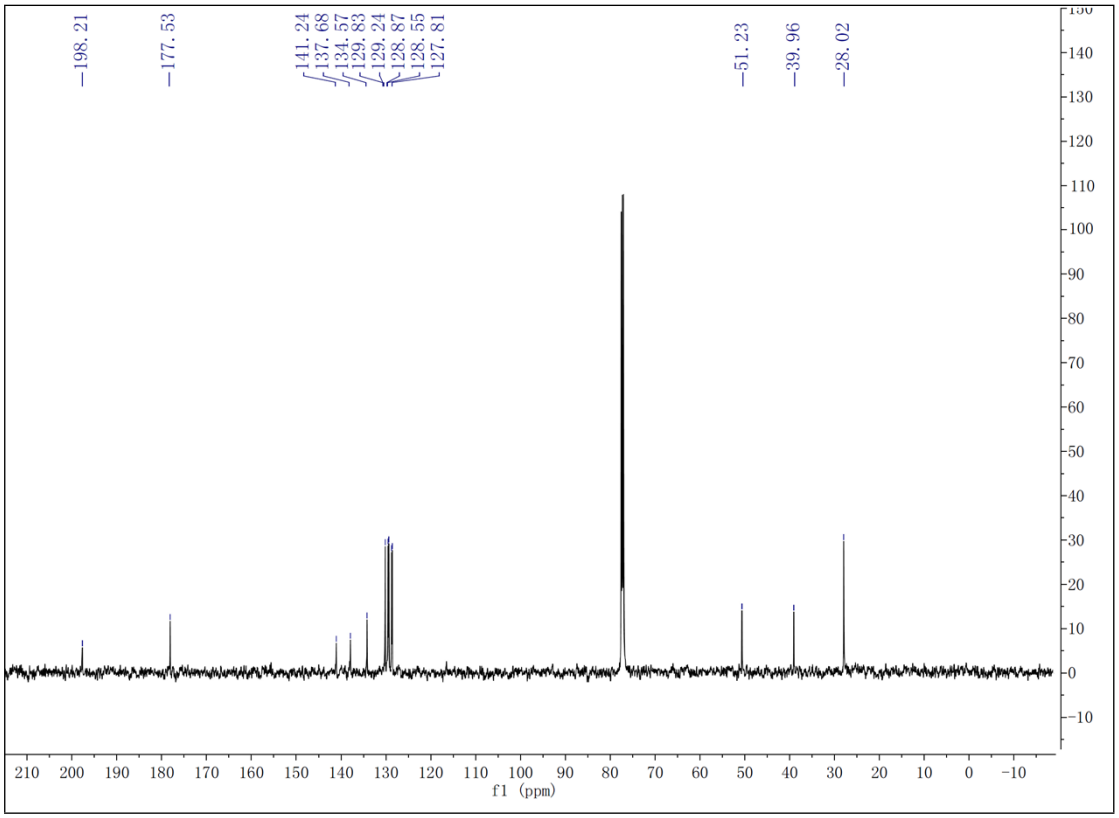
crude product was purified by flash chromatography.

3. ^{1}H, ^{13}C NMR spectras and HPLC chromatograms

*3.1 1-(3-Oxo-1,3-diphenylpropyl)pyrrolidine-2,5-dione (**2a**)*

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (76% yield); m.p. 118-120ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ : 7.99-7.97 (m, 2H), 7.59-7.57 (m, 3H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.38-7.31 (m, 3H), 5.91-5.88 (m, 1H), 4.64-4.58 (m, 1H), 3.71-3.66 (m, 1H), 2.66-2.63 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ: 28.0, 40.0, 51.2, 127.8, 128.6, 128.9, 129.2, 129.8, 134.6, 137.7, 141.2, 177.5, 198.2. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm,major enantiomer t_1 = 1.87 min, minor enantiomer t_2 = 0.72 min; 90% *ee*.

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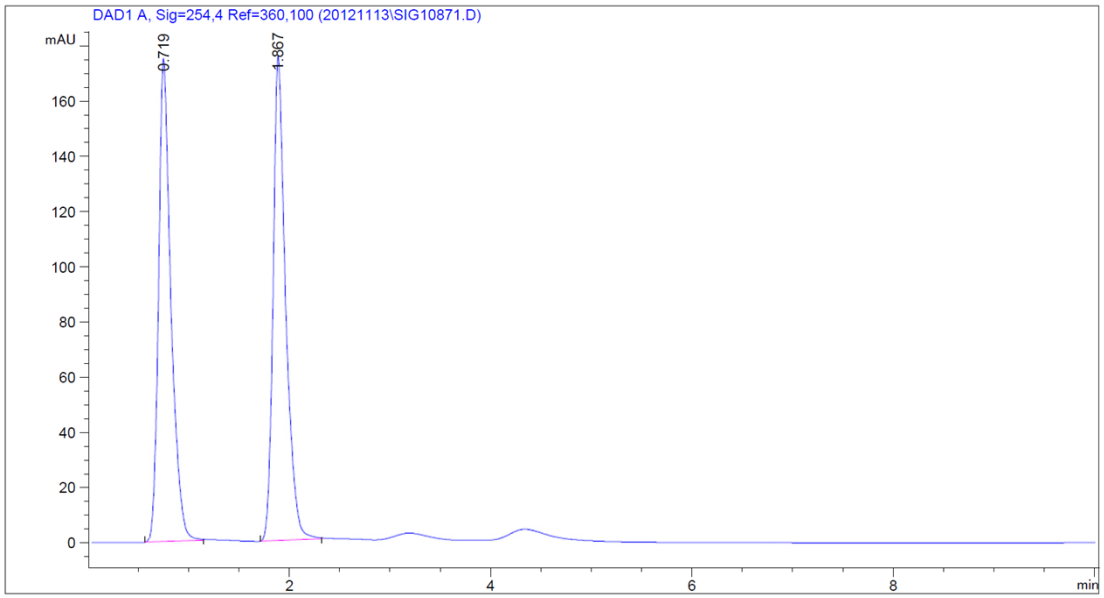
28.02
f1 (ppm)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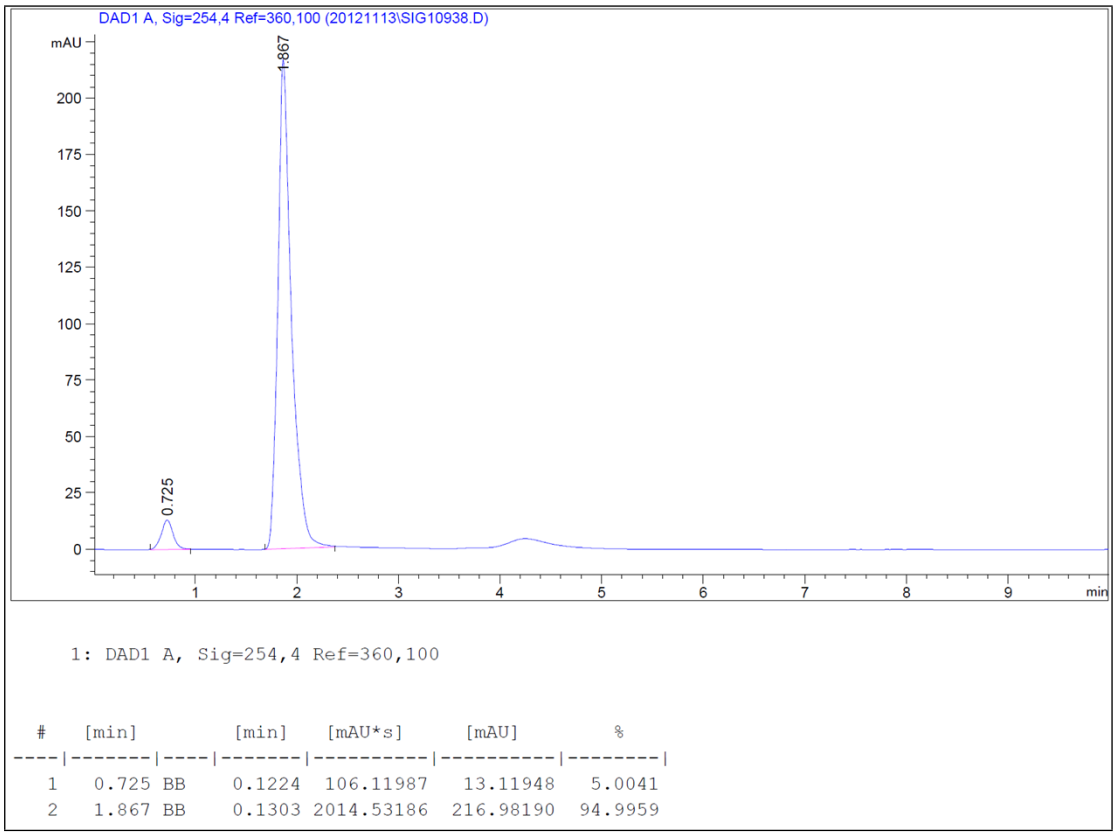
min



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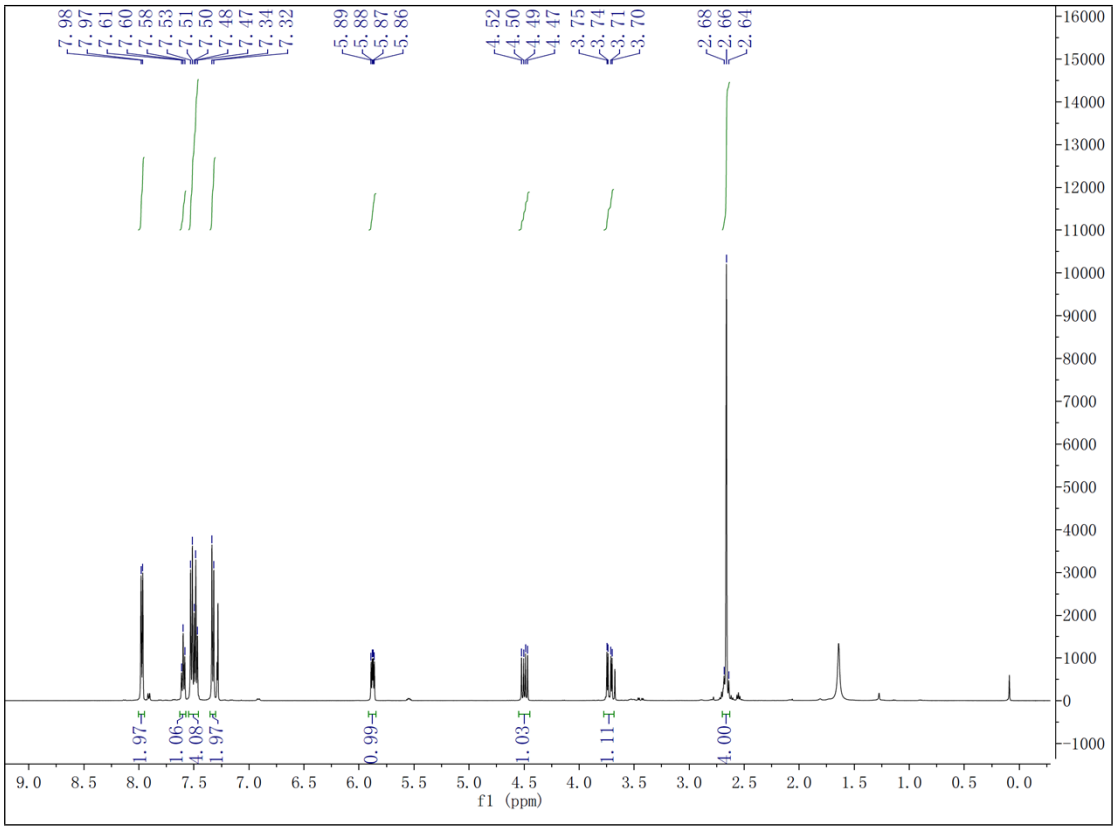
2	1.867	BB	0.1303	2014.53186	216.98190	94.9959

*3.2 1-(1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione(**2b**)*

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (83% yield); m.p. 142-144ºC. ^{1}H NMR (500 MHz, $CDCl_3$): δ : 7.97 (d, J = 7.6 Hz, 2H), 7.61-7.58 (m, 2H), 7.54-7.46 (m, 4H), 7.34-7.28 (d, J = 8.3 Hz, 2H), 5.89-5.86 (m, 1H), 4.52-4.47 (m, 2H), 3.75-3.67 (m, 2H), 2.68-2.64 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 28.3, 39.2, 49.9, 127.4, 128.0, 128.7, 129.2, 133.5, 134.1, 136.6, 137.1, 176.5, 196.1. HPLC analysis: Ultron ES-OVM column, 32:68 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.5 ml/min, UV = 273nm,major enantiomer t_1 = 3.49 min, minor enantiomer t_2 = 2.34 min; 94% *ee*.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7.61
7.60
7.58
7.53
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7.50
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7.47
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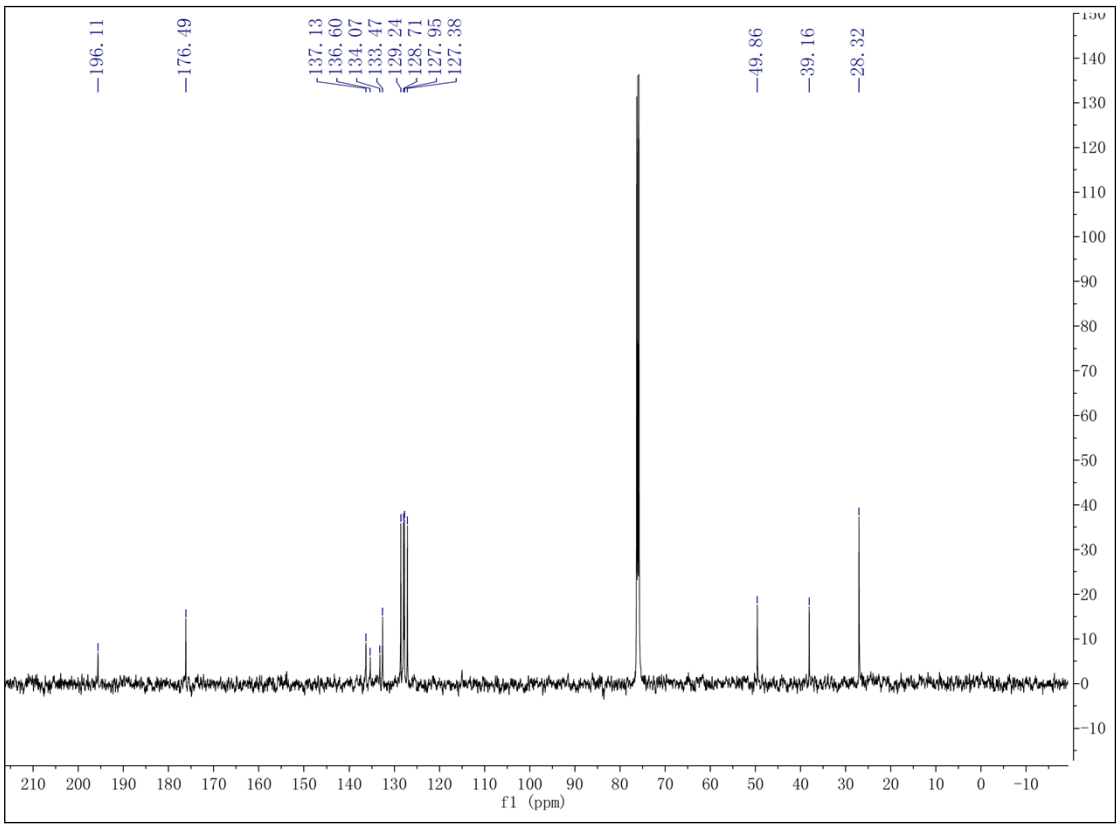
5.89
5.88
5.87
5.86
4.52
4.50
4.49
4.47
3.75
3.74
3.71
3.70
2.68
2.66
2.64
1.97
1.06
4.08
1.97
0.99
1.03
1.11
4.00
f1 (ppm)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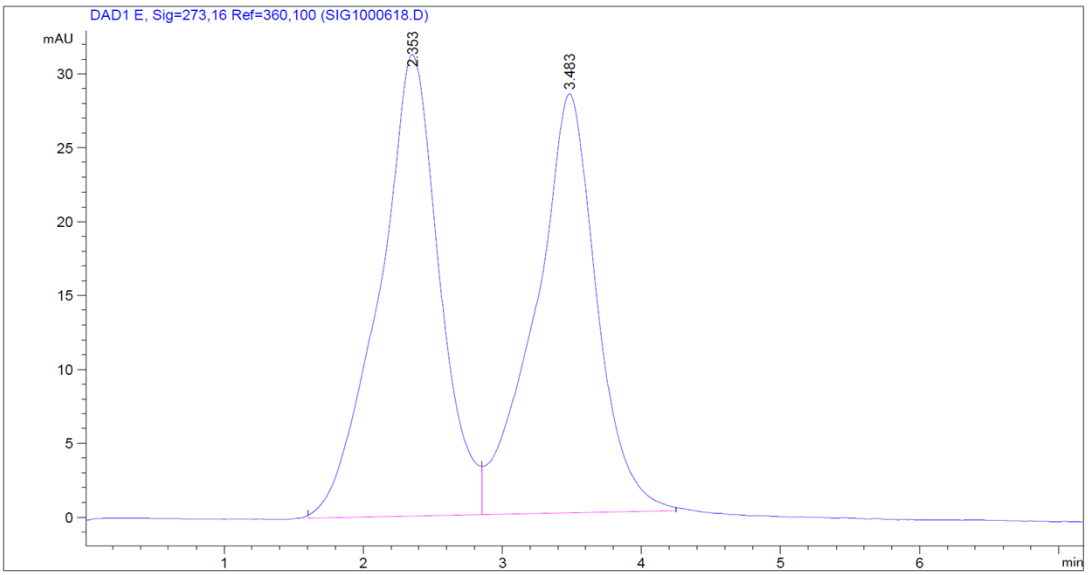
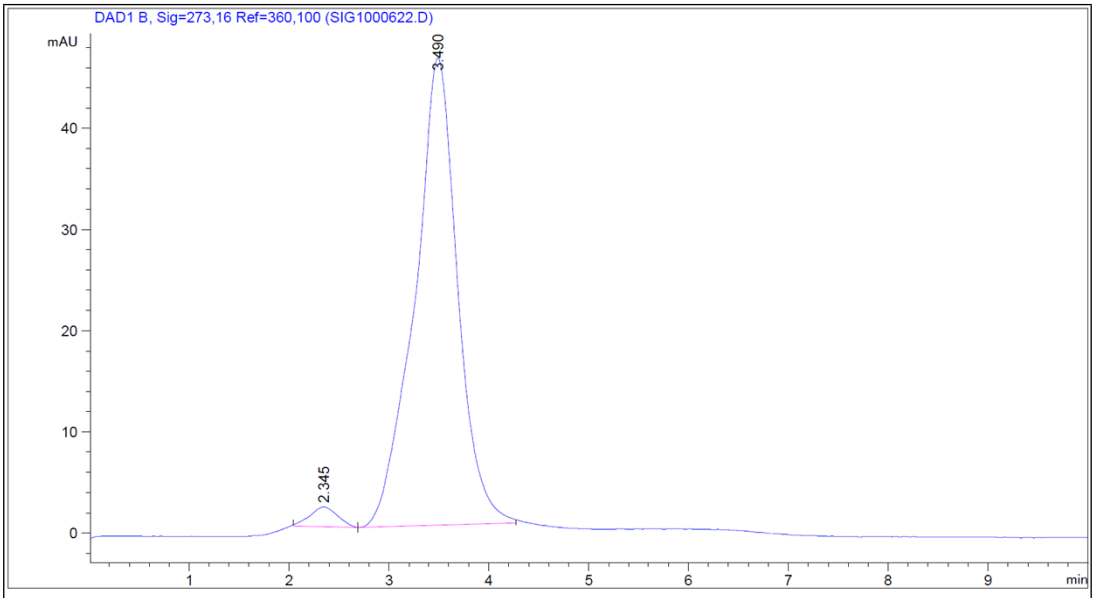
28.32
f1 (ppm)





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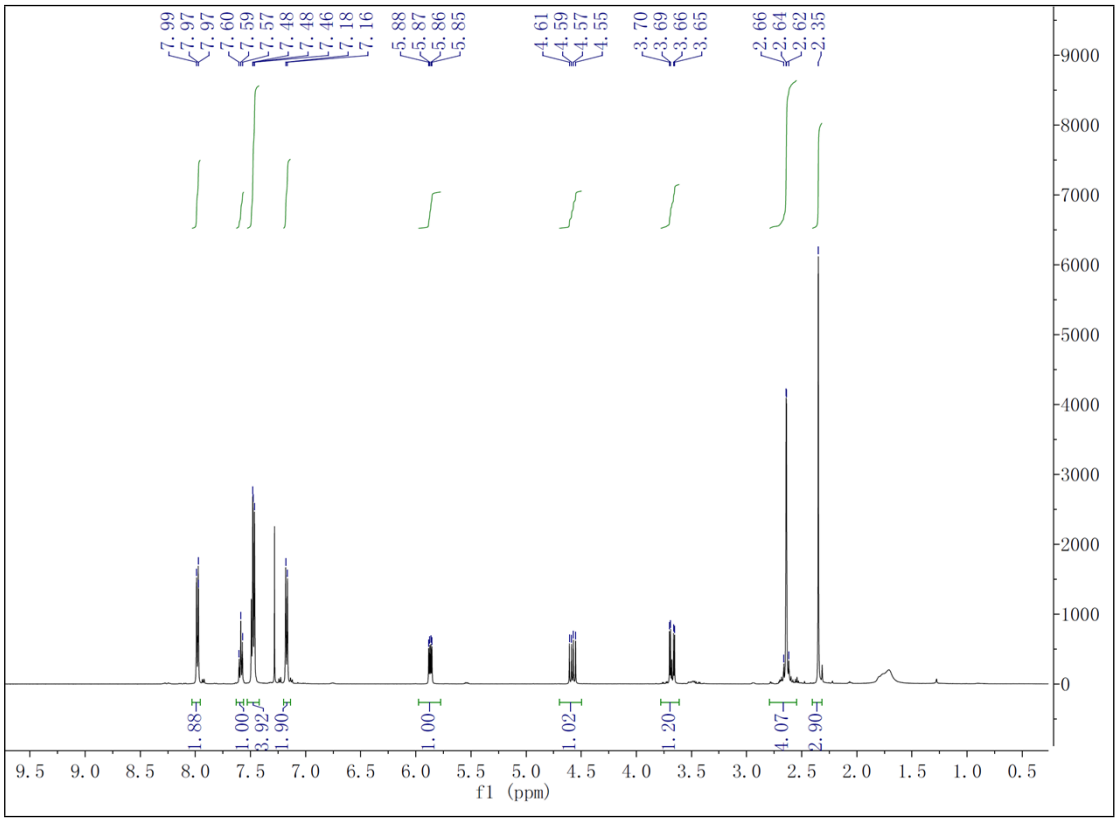
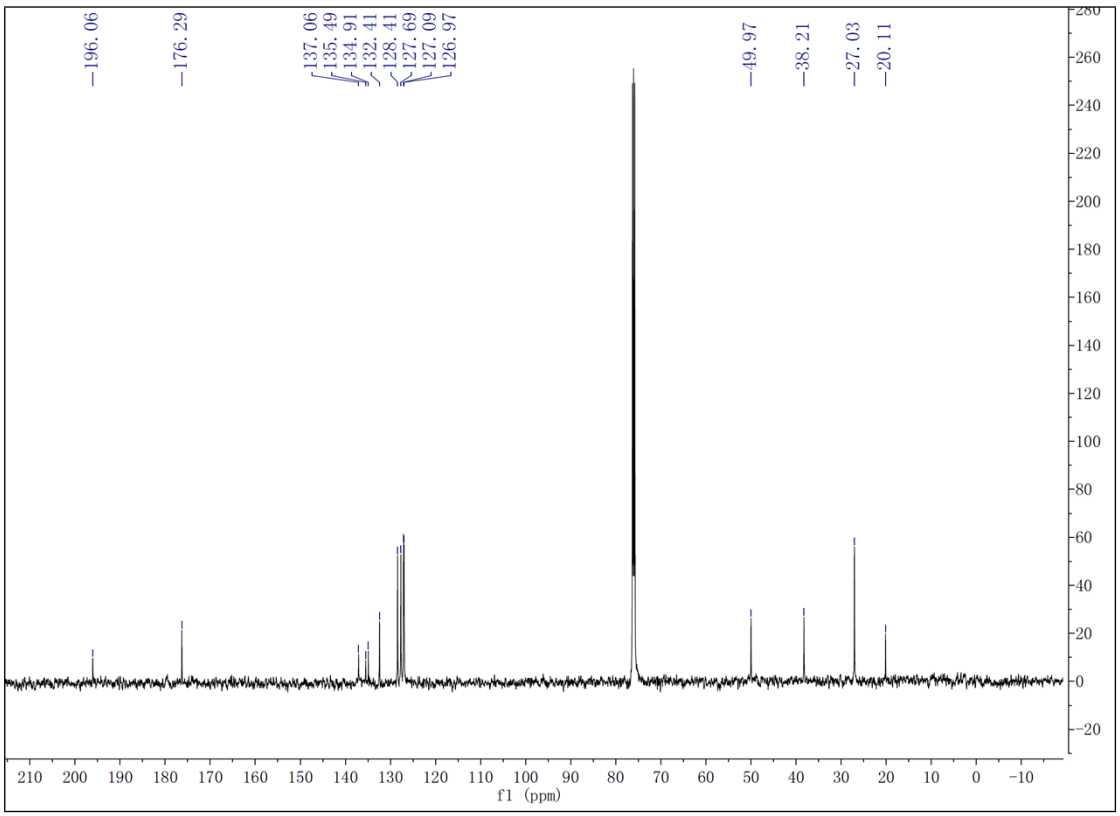
1	2.345	BV	0.2834	37.37333	1.95172	2.6449
2	3.490	VB	0.4294	1375.63831	46.19231	97.3551

*3.3 1-(3-Oxo-3-phenyl-1-(p-tolyl)propyl)pyrrolidine-2,5-dione**(2c)***

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 7 : 1) to give a white solid (73% yield); m.p. 120-122ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.03-7.92 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.53-7.42 (m, 4H), 7.17 (d, J = 7.9 Hz, 2H), 5.88-5.85 (m, 1H),

4.61-4.55(m, 1H), 3.70-3.65 (m, 1H), 2.66-2.62 (m, 4H), 2.35 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 20.1, 27.0, 38.2, 50.0, 127.0, 127.1, 127.7, 128.4, 132.4, 135.0, 135.5, 137.1, 176.3, 196.1. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm, major enantiomer t_1 = 1.84 min, minor enantiomer t_2 = 0.71 min; 80% *ee*.

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49.97
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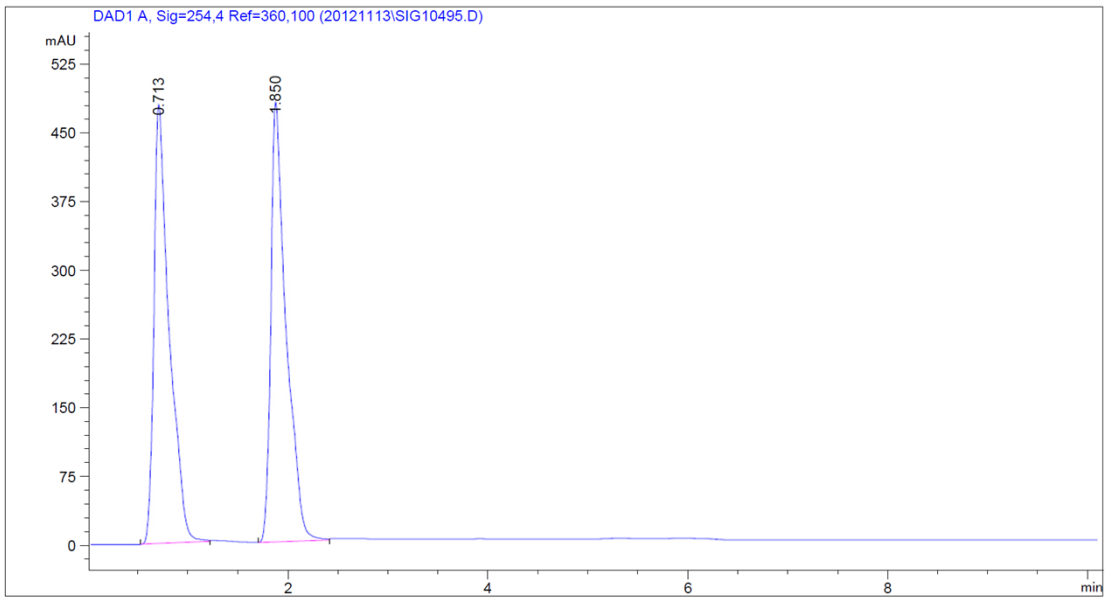
27.03
20.11
f1 (ppm)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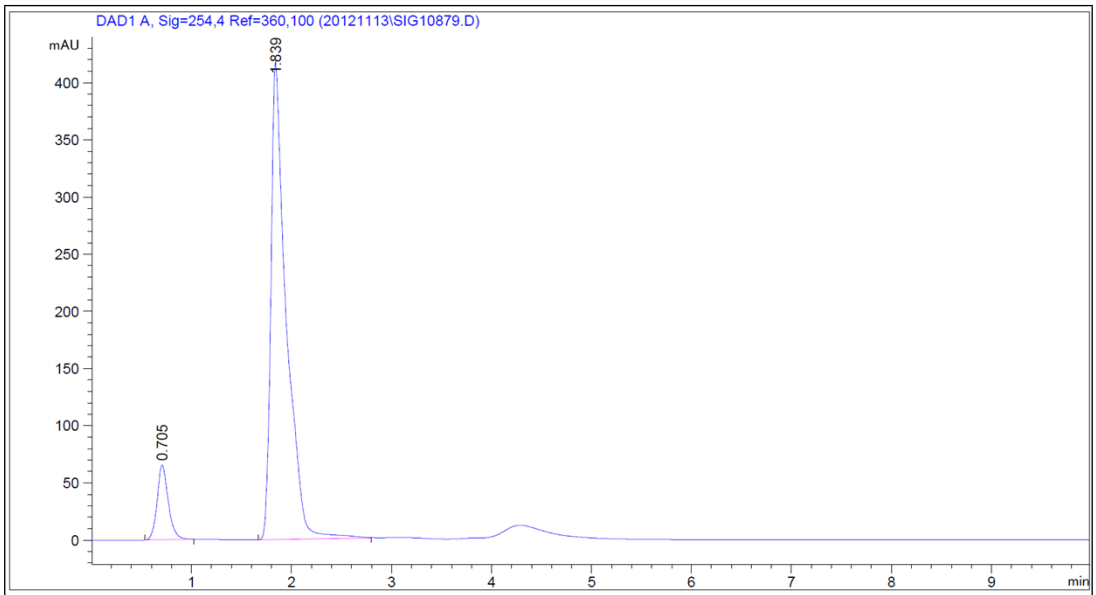
min



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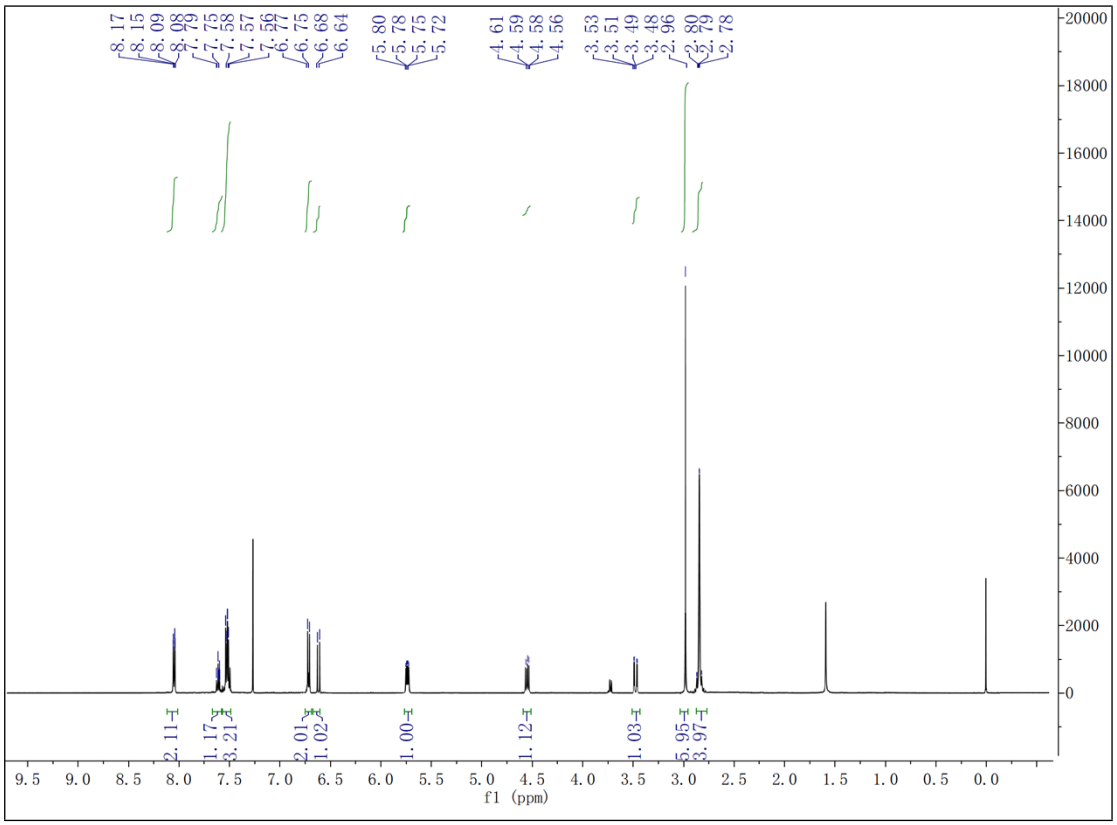
2	1.839	BB	0.1480	4446.89795	418.36777	89.7196

3.4 1-(1-(4-(Dimethylamino)phenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione ***(2d)***

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 8 : 1) to give a white solid (62% yield); m.p. 147-149ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ:8.17-8.08(m, 2H), 7.77(d, *J* = 5.0 Hz, 1H), 7.58-7.56 (m, 3H), 6.76 (d, *J* = 2.5Hz, 2H), 6.66 (d, *J* = 5.0 Hz, 1H), 5.80-5.72(m, 1H), 4.61-4.56(m, 1H), 3.53-3.48 (m, 1H), 2.96 (s, 6H), 2.80-2.78 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 27.8, 38.8, 40.5, 50.9, 111.9, 127.5, 128.5, 128.9, 129.2, 132.1, 138.9, 148.3, 177.5, 197.8. ESI-MS *(m/z)*: 351 ($[M+H]^+$). Anal. calcd. for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99. Found: C, 71.77; H, 6.43; N, 8.11. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.8 ml/min, UV = 254 nm, major enantiomer t_1 = 0.65 min, minor enantiomer t_2 = 1.82 min; 40% *ee*.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1.12
1.03
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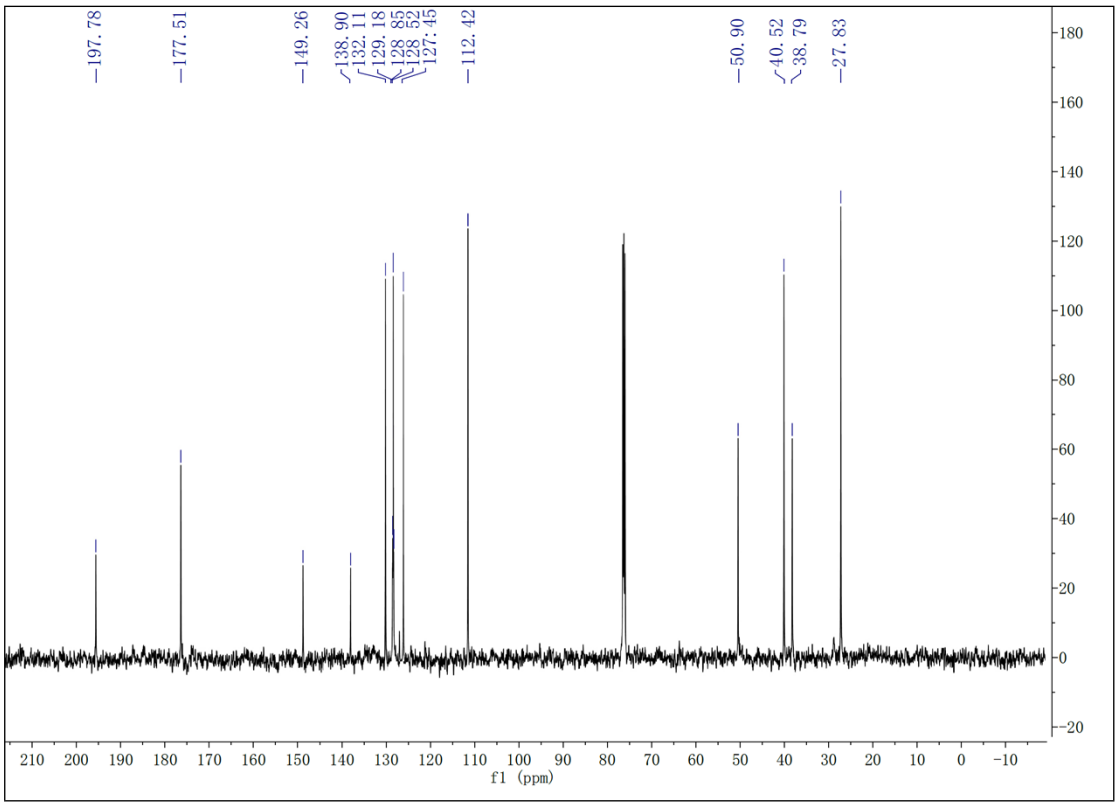
f1 (ppm)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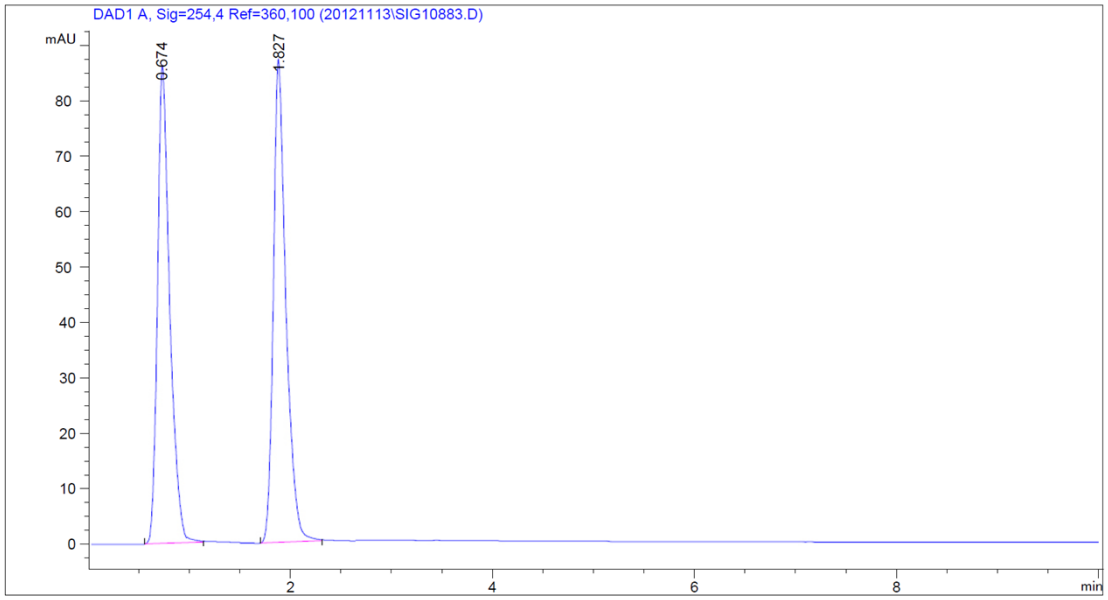

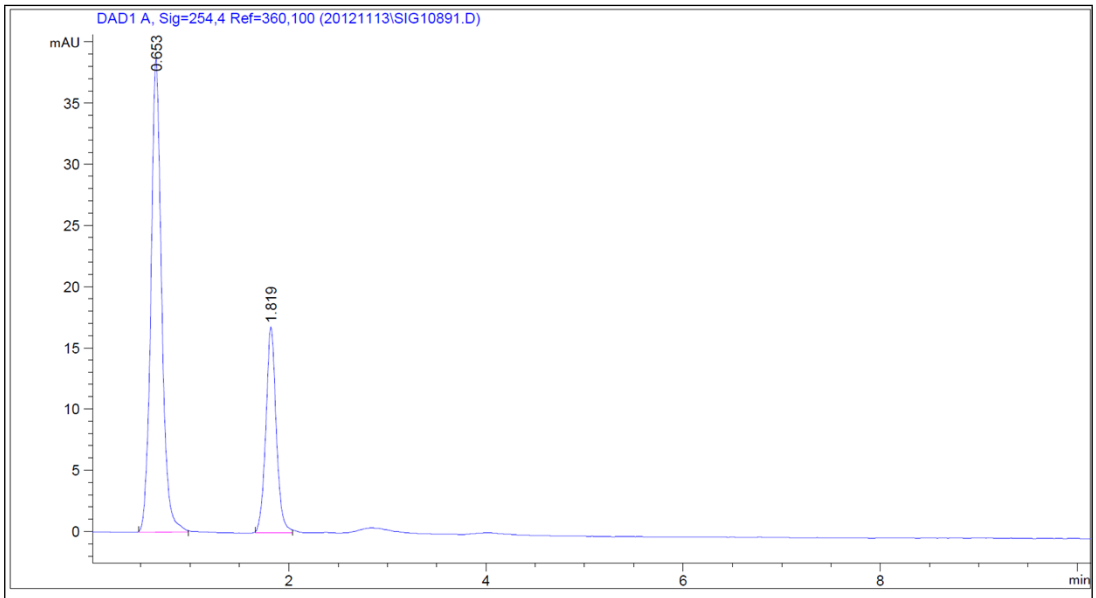

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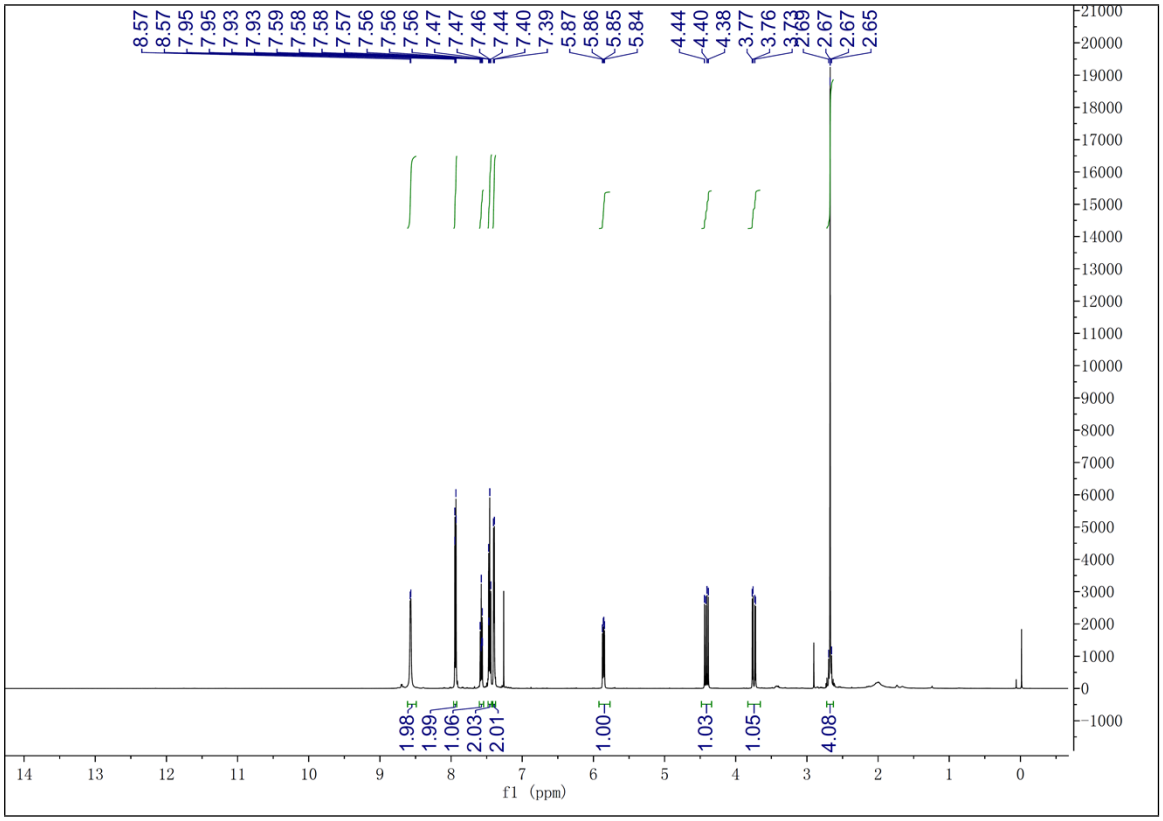
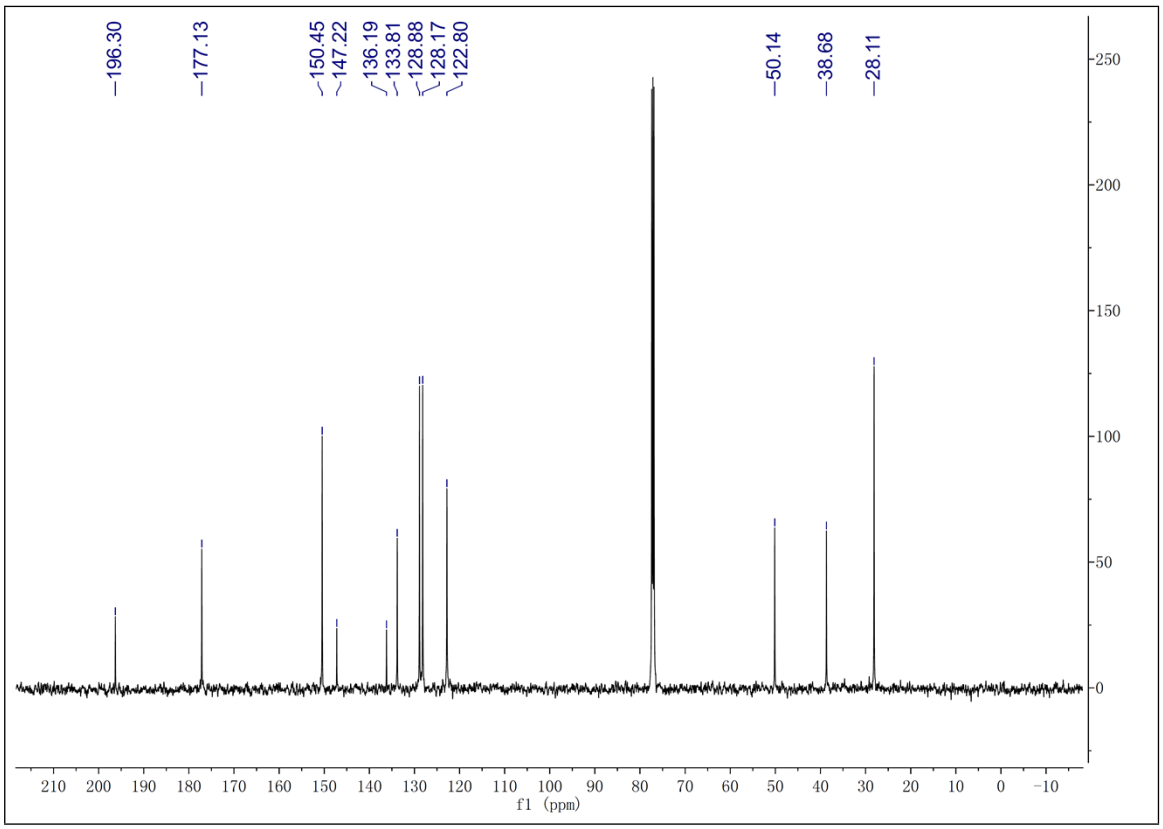
2	1.819	BB	0.1115	123.31005	16.83071	29.6661

3.5 *1-(3-oxo-3-phenyl-1-(pyridin-4-yl)propyl)pyrrolidine-2,5-dione* ***(2e)***

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a yellow solid (67% yield); m.p. 140-142ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J = 4.5 Hz, 2H), 7.95-7.93 (m, 2H), 7.59-7.56 (m, 1H), 7.47-7.44 (m, 2H), 7.40 (d, J = 6.0 Hz, 2H), 5.87-

5.84 (m, 1H), 4.44-4.38 (m, 1H), 3.77-3.72 (m, 1H), 2.69-2.65 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 28.1, 38.7, 50.1, 122.8, 128.7, 128.9, 133.8, 136.2, 147.2, 150.5, 177.1, 196.3. ESI-MS (m/z): 309 ($[M+H]^+$). Anal. calcd. for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.31; H, 5.15; N, 9.23. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.5 ml/min, UV = 280 nm, major enantiomer t_1 = 5.78 min, minor enantiomer t_2 = 4.40 min; 64% *ee*.

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128.17
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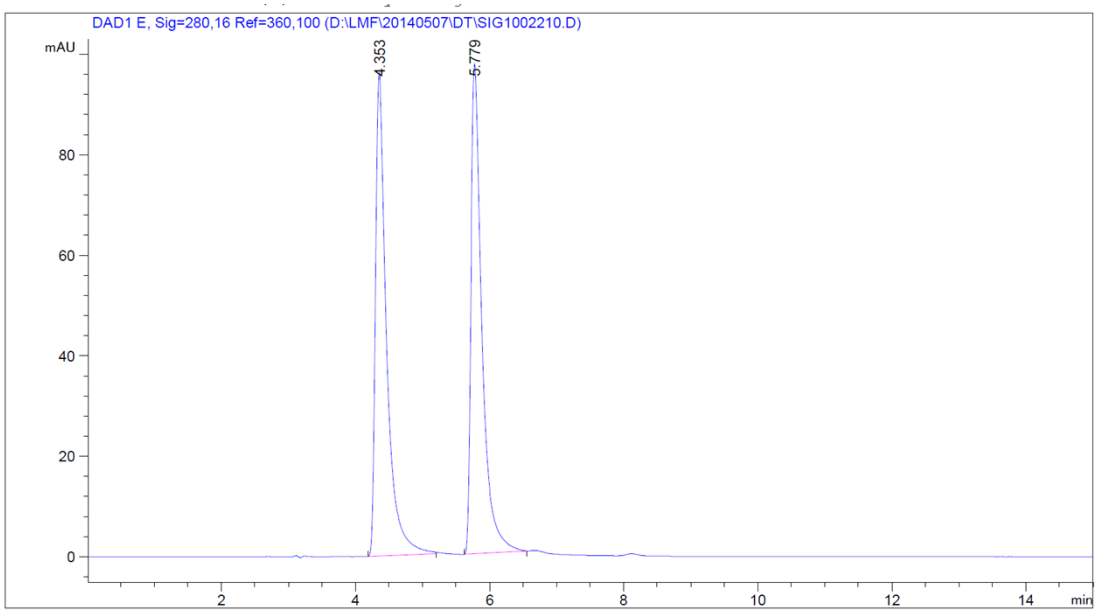
50.14
38.68
28.11
f1 (ppm)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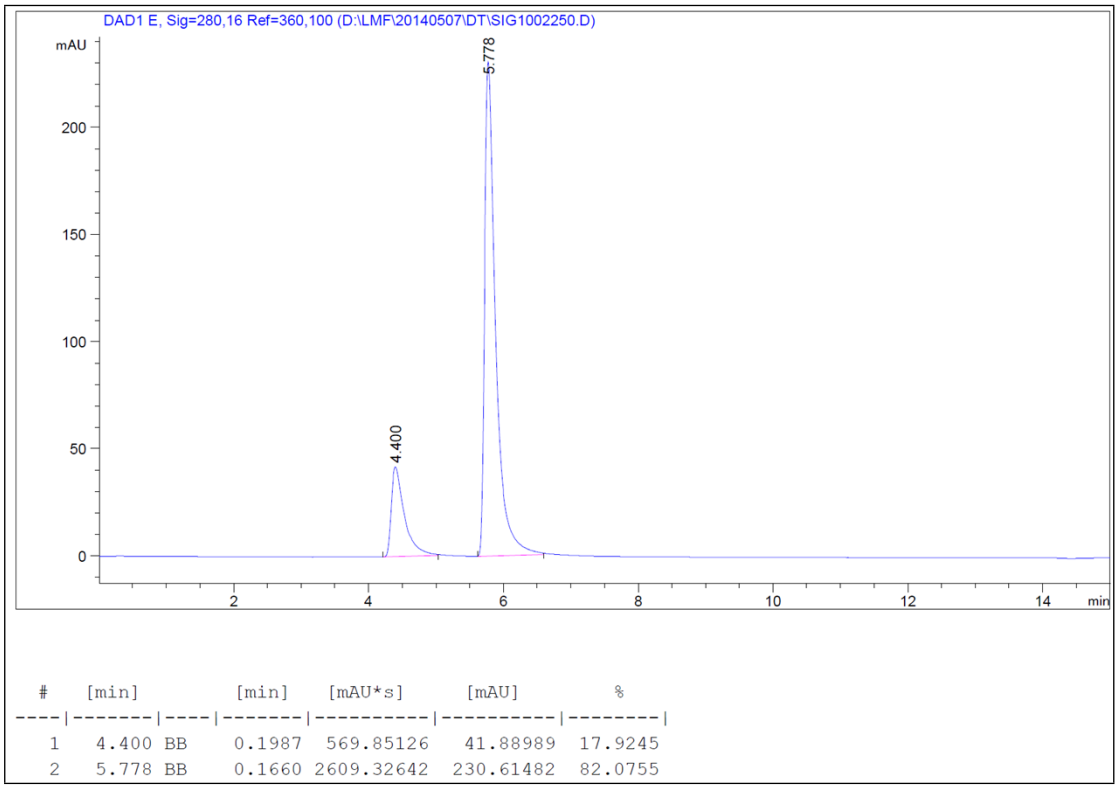

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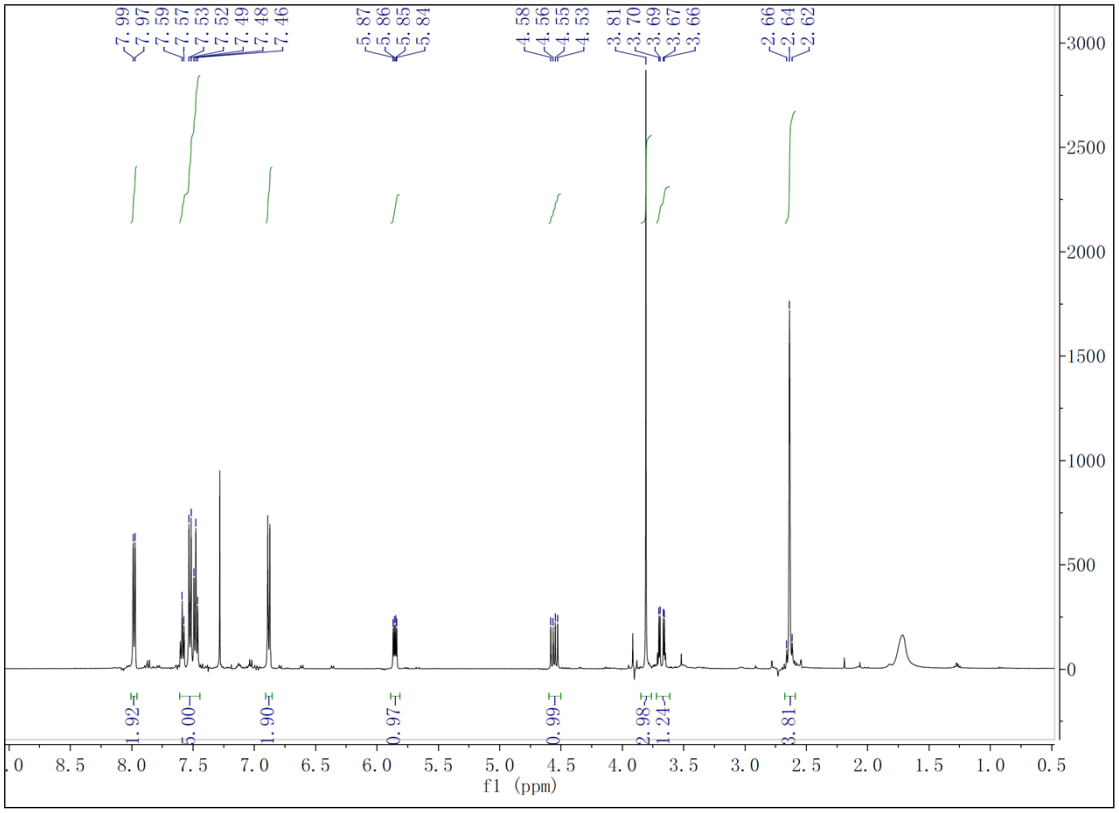
1	4.400	BB	0.1987	569.85126	41.88989	17.9245
2	5.778	BB	0.1660	2609.32642	230.61482	82.0755

3.6 *1-(3-(4-Methoxyphenyl)-3-oxo-1-phenylpropyl)pyrrolidine-2,5-dione* ***(2f)***

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (52% yield); m.p. 127-129ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.98 (d, J = 7.4 Hz, 2H), 7.65-7.37 (m, 5H), 6.88 (d, J = 8.7 Hz, 2H), 5.87-5.84 (m, 1H), 4.58-4.53 (m, 1H), 3.81 (s, 3H), 3.71-3.61 (m, 1H), 2.69-2.62 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 27.0, 38.3, 49.7, 54.3, 113.0, 127.1, 127.7, 128.4, 130.1, 132.4, 135.5, 158.4, 176.3, 196.0. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 2.0 ml/min, UV = 254 nm, major enantiomer t_1 = 1.86 min, minor enantiomer t_2 = 0.71min; 80% *ee*.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7.52
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4.55
4.53
3.81
3.70
3.69
3.67
3.66
2.66
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2.62
1.92
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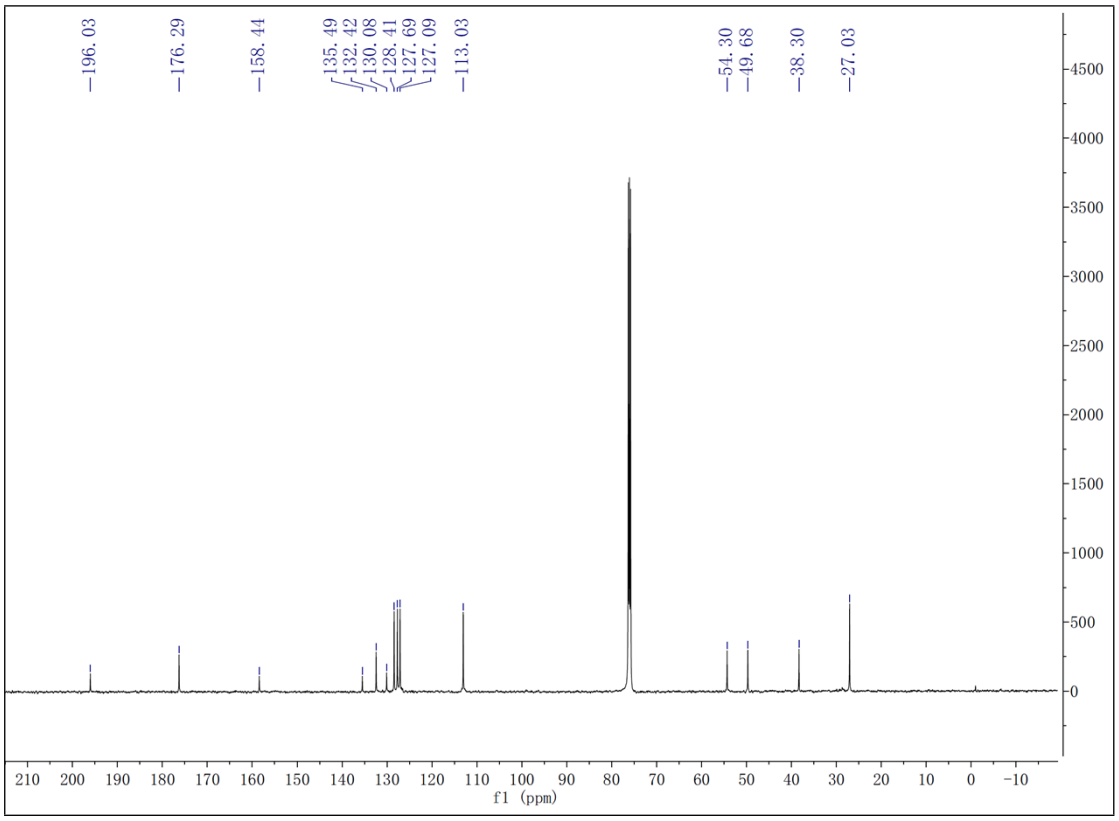
1.90
0.97
0.99
2.98
1.24
3.81
f1 (ppm)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127.09
113.03
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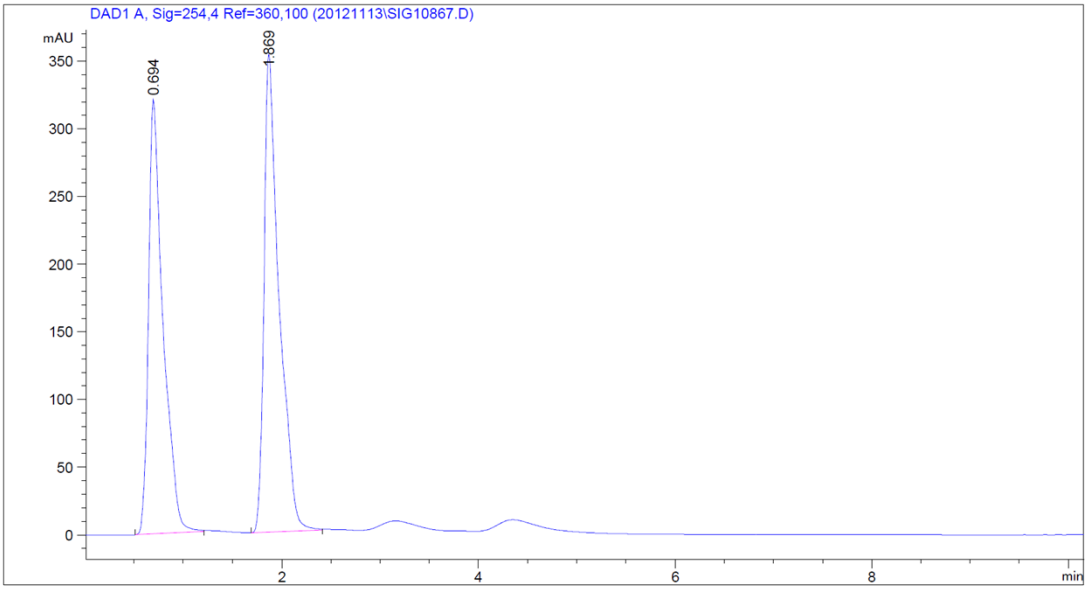
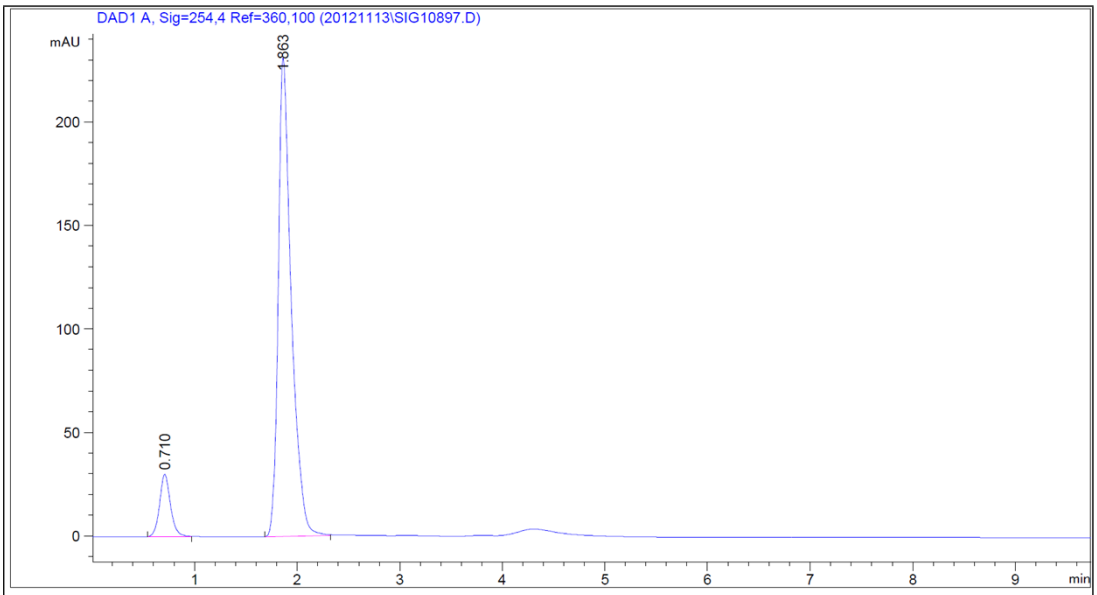
49.68
38.30
27.03
f1 (ppm)





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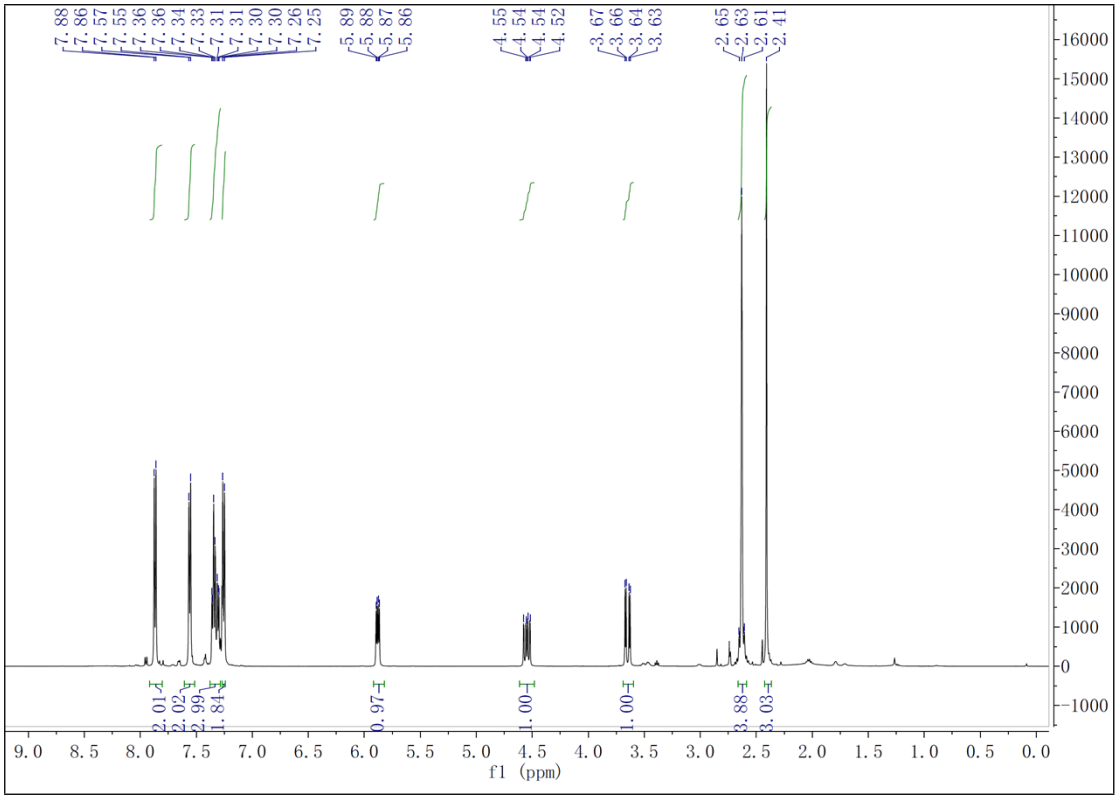
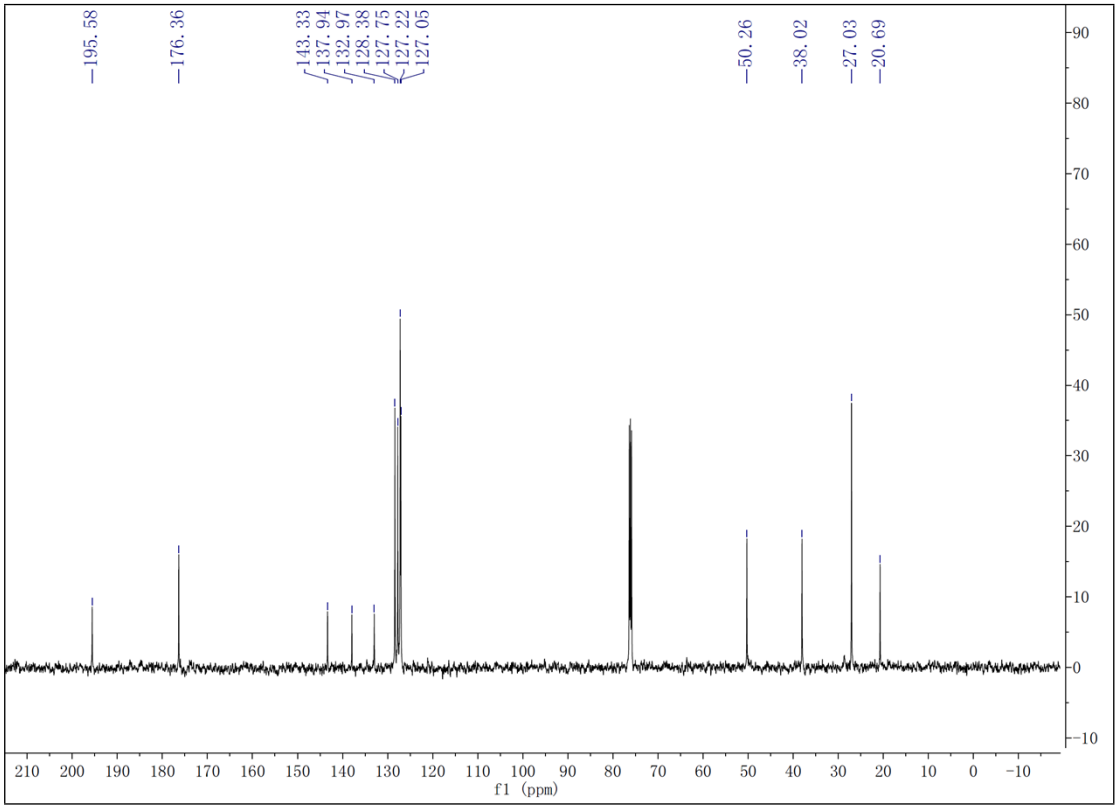
2	1.863	BB	0.1287	2038.55078	231.63240	90.1062

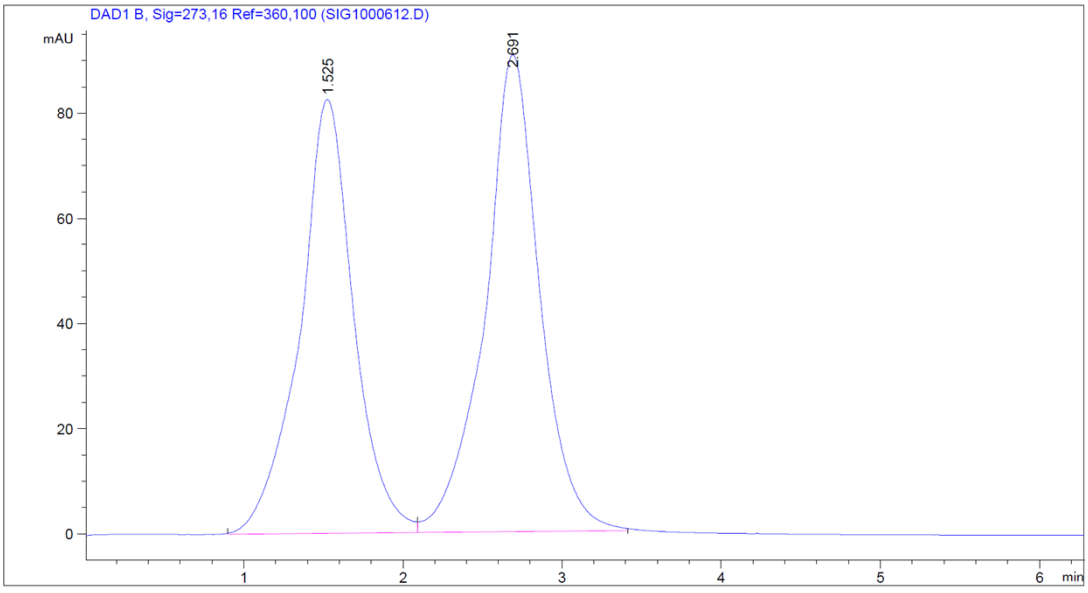
3.7 1-(3-(4-Methylphenyl)-3-oxo-1-phenylpropyl)pyrrolidine-2,5-dione ***(2g)***

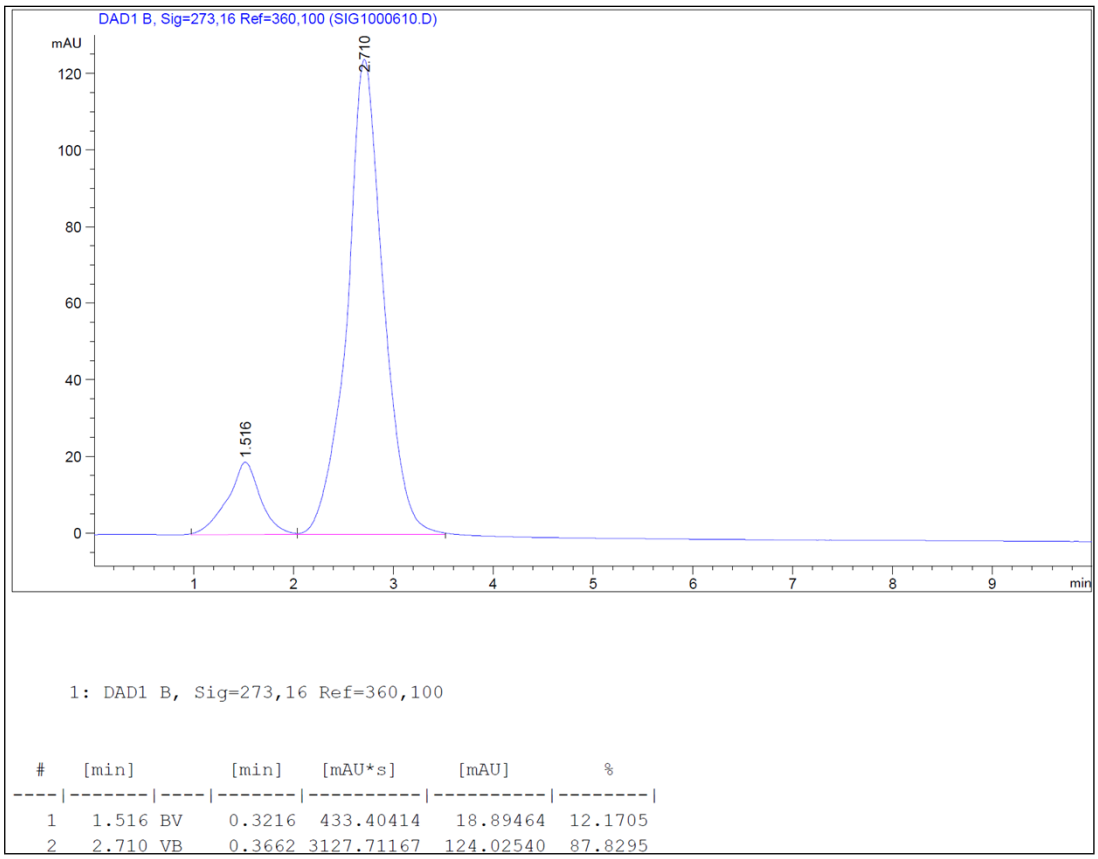
This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 6 : 1) to give a white solid (71% yield); m.p. 131-133ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ:7.87 (d, J = 7.8 Hz, 2H),

7.56 (d, J = 7.9 Hz, 2H), 7.36-7.30 (m, 3H), 7.26 (d, J = 7.9 Hz, 2H), 5.89-5.86 (m, 1H), 4.55-4.52 (m, 1H), 3.67-3.63 (m, 1H), 2.65-2.61 (m, 4H), 2.41 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 20.7, 27.0, 38.0, 50.3, 127.1, 127.2, 127.8, 128.4, 133.0, 138.0, 143.3, 176.4, 195.6. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.025 mol/L), flow rate = 1.2 ml/min, UV = 273 nm, major enantiomer t_1 = 2.71 min, minor enantiomer t_2 = 1.52min; 76% *ee*.




195.58
176.36
143.33
137.94
132.97
128.38
127.75
127.22
127.05
50.26
38.02
27.03
20.69
f1 (ppm)


DAD1 B, Sig=273,16 Ref=360,100 (SIG1000612.D)
mAU
1.525
2.691
min

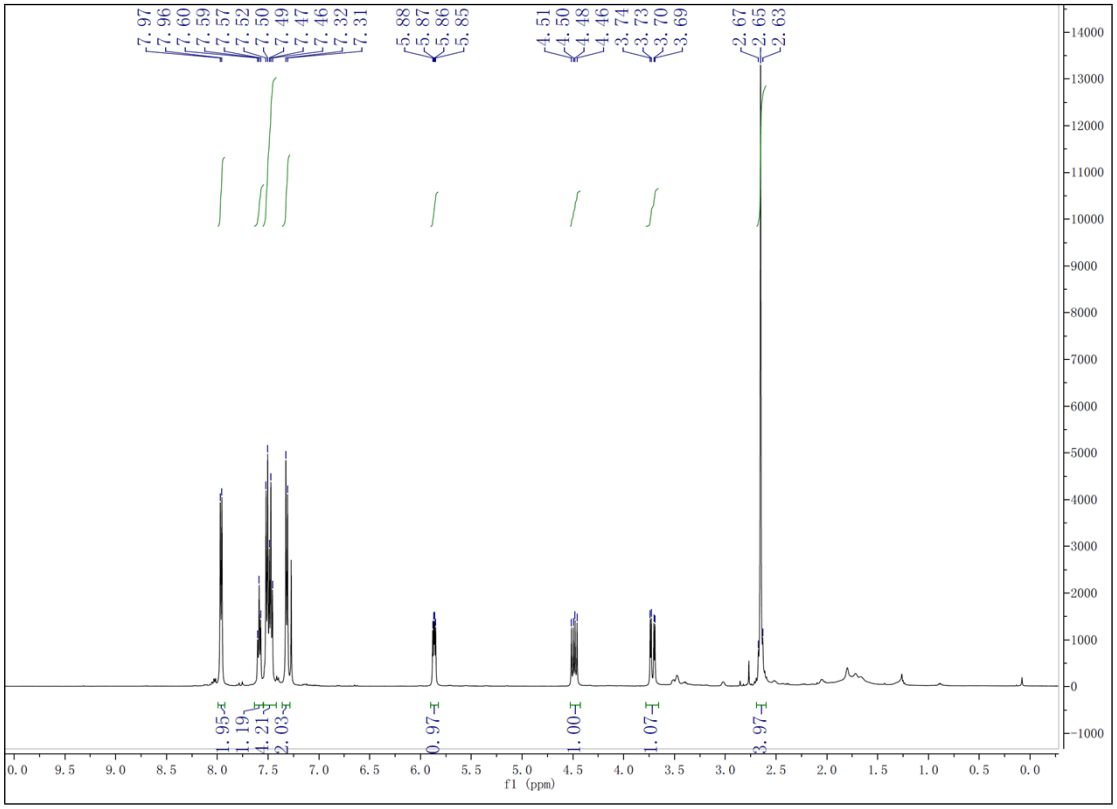


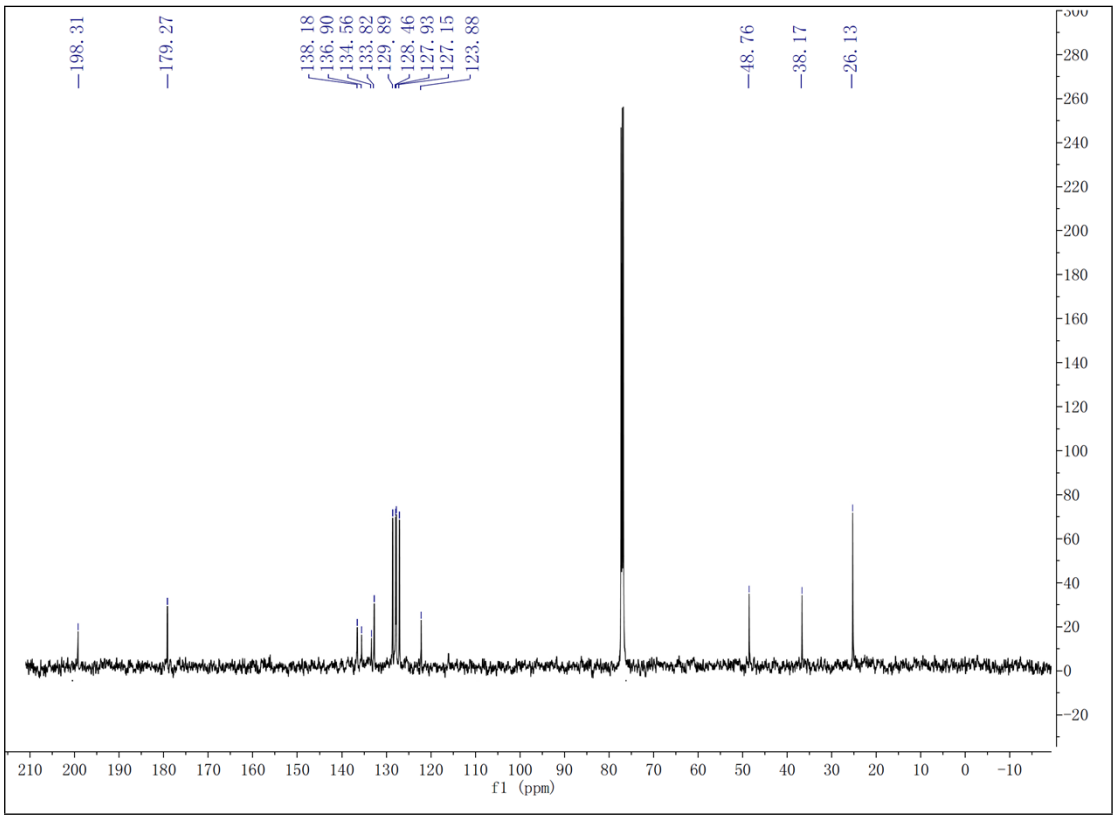
1: DAD1 B, Sig=273,16 Ref=360,100

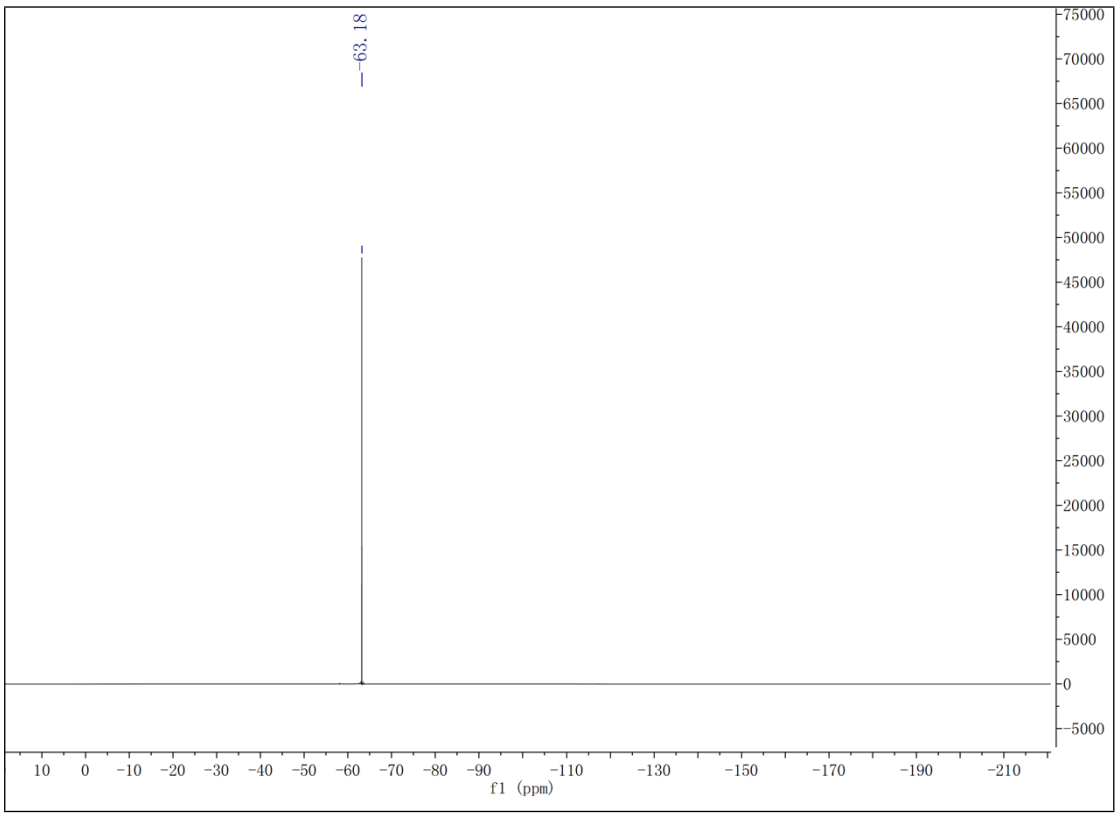
#	[min]		[min]	[mAU*s]	[mAU]	%
1	1.516	BV	0.3216	433.40414	18.89464	12.1705
2	2.710	VB	0.3662	3127.71167	124.02540	87.8295

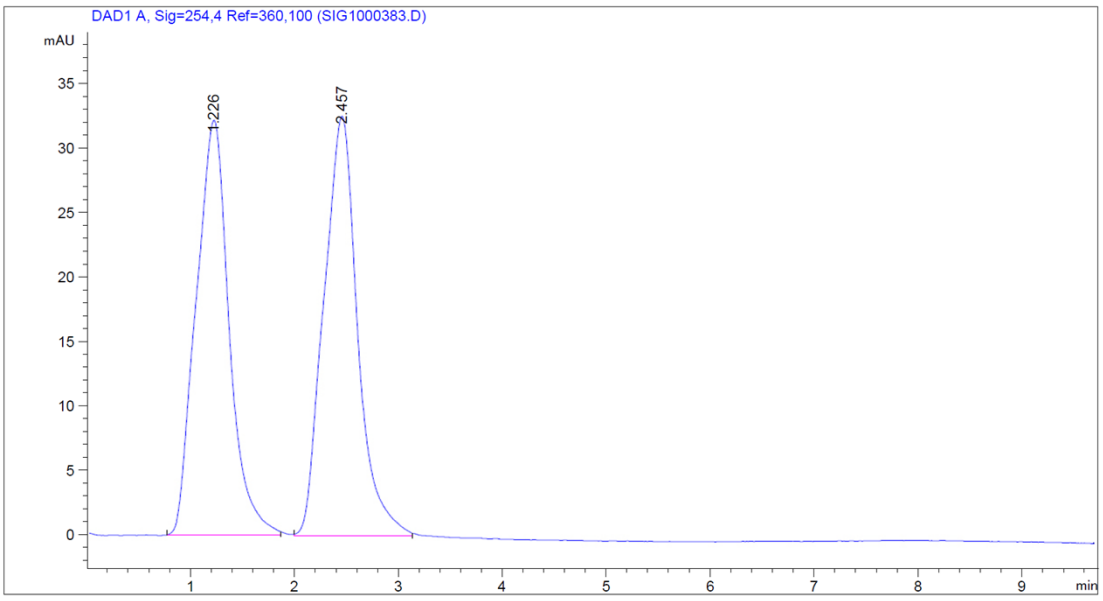
*3.8 1-(3-(4-(Trifluoromethyl)-3-oxo-1-phenylpropyl) pyrrolidine-2,5-dione(**2h**)*

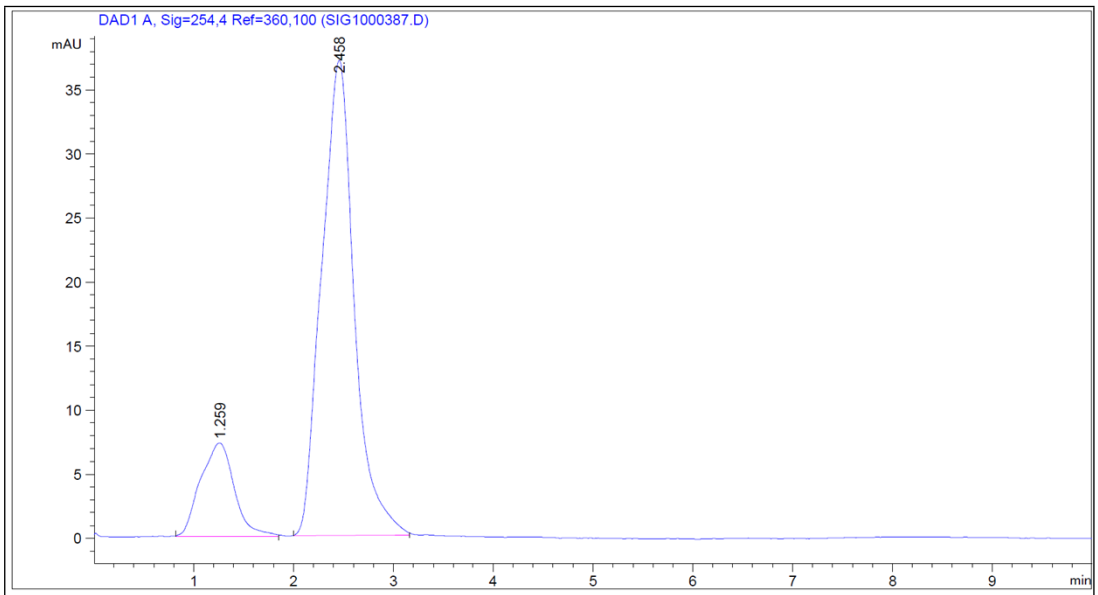
This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 8 : 1) to give a white solid (60% yield); m.p. 144-146ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.96 (d, J = 7.5 Hz, 2H), 7.60-7.57 (m, 1H), 7.52-7.47 (m, 4H), 7.32 (d, J = 8.4 Hz, 2H), 5.88-5.85 (m, 1H), 4.51-4.46 (m, 1H), 3.74-3.69 (m, 1H), 2.67-2.63 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 26.1, 38.2, 48.8, 123.9, 127.2, 127.9, 128.5, 129.9, 133.8, 134.6, 136.9, 138.2, 179.3, 198.3. ^{19}F NMR (500 MHz, $CDCl_3$) δ: -63.18. ESI-MS (m/z): 376 ($[M+H]^+$). Anal. calcd. for $C_{20}H_{16}F_3NO_3$: C, 64.00; H, 4.30; N, 3.73. Found: C, 64.18; H, 4.22; N, 3.67. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.025 mol/L), flow rate = 1.5 ml/min, UV = 254 nm, major enantiomer t_1 = 2.46 min, minor enantiomer t_2 = 1.26min; 66% *ee*.


7.97
7.96
7.60
7.59
7.57
7.52
7.50
7.49
7.47
7.46
7.32
7.31
5.88
5.87
5.86
5.85
4.51
4.50
4.48
4.46
3.74
3.73
3.70
3.69
2.67
2.65
2.63
1.95
1.19
4.21
2.03
0.97
1.00
1.07
3.97
f1 (ppm)


198.31
179.27
138.18
136.90
134.56
133.82
129.89
128.46
127.93
127.15
123.88
48.76
38.17
26.13
f1 (ppm)


-63.18
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)


DAD1 A, Sig=254,4 Ref=360,100 (SIG1000383.D)
mAU
35
30
25
20
15
10
5
0
1.226
2.457
1 2 3 4 5 6 7 8 9 min

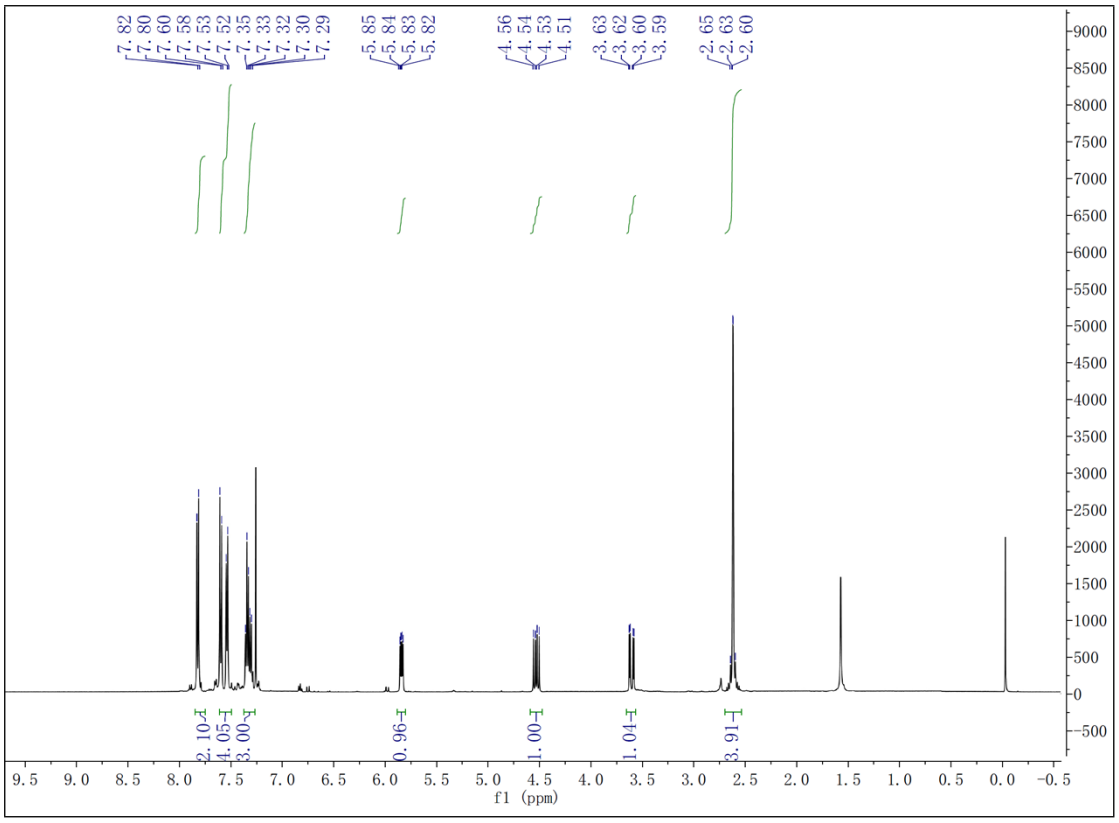


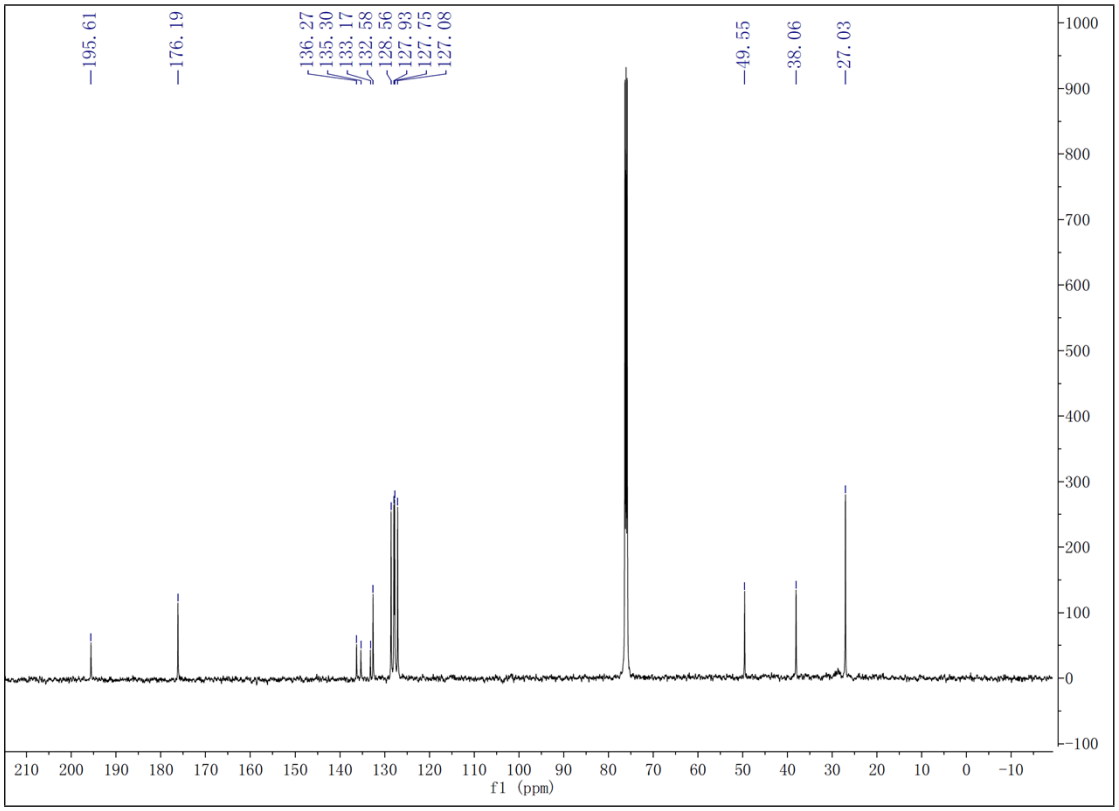
1: DAD1 A, Sig=254,4 Ref=360,100

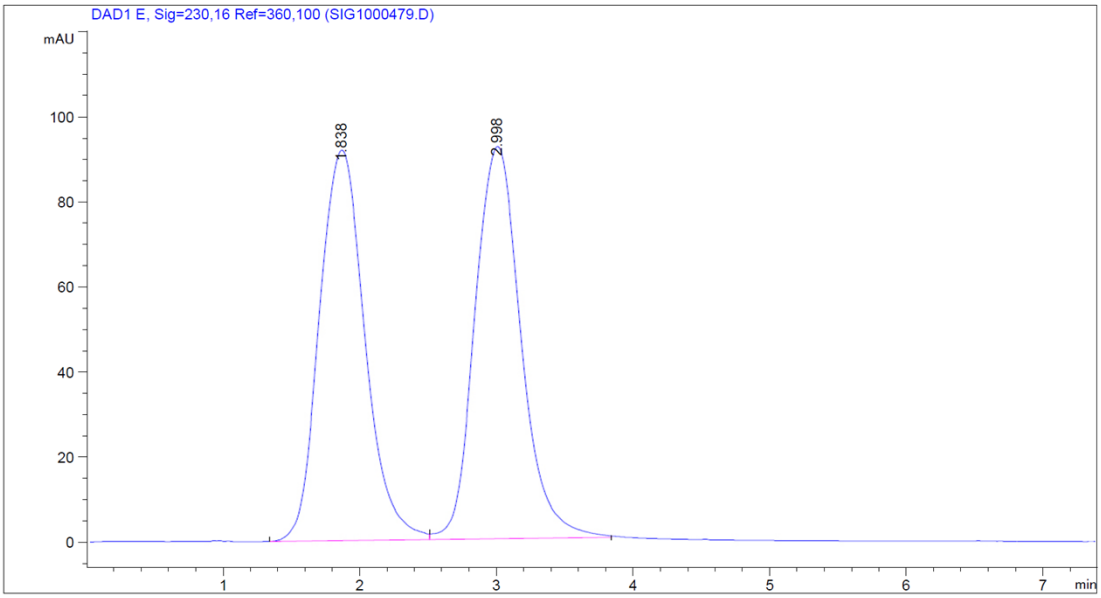
#	[min]		[min]	[mAU*s]	[mAU]	%
1	1.259	BB	0.3322	169.43143	7.26208	16.7776
2	2.458	BB	0.3243	840.43506	37.10258	83.2224

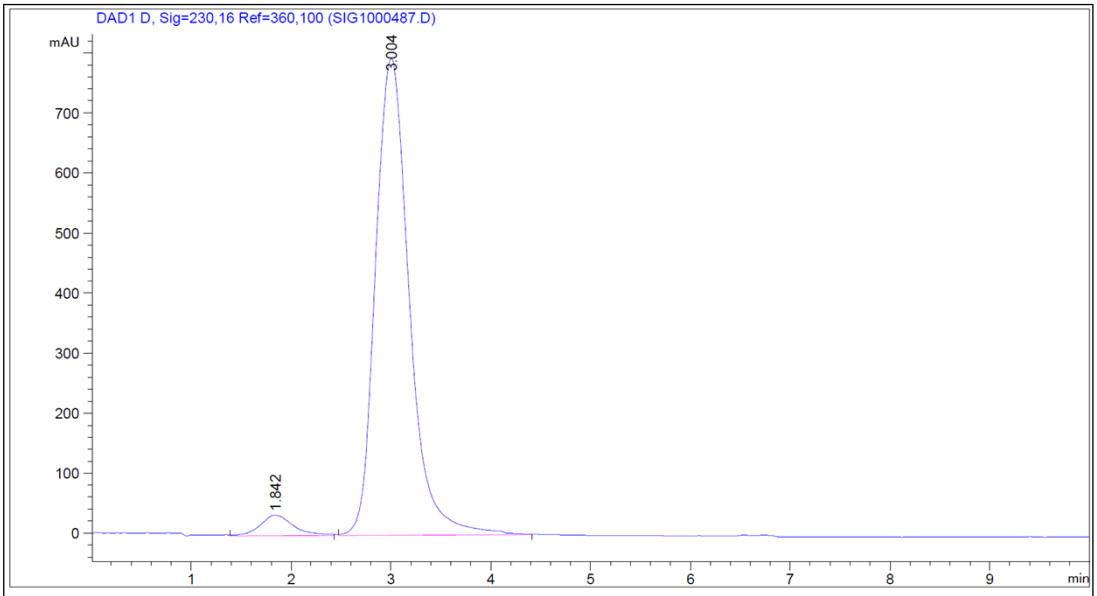
*3.9 1-(3-(4-Bromophenyl)-3-oxo-1-phenylpropyl)pyrrolidine-2,5-dione(**2i**)*

This compound was prepared according to the Section 2.2 and purified by column chromatography (petroleum ether : ethyl acetate = 7 : 1) to give a white solid (72% yield); m.p. 149-151ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.81(d, J = 10 Hz, 2H), 7.60-7.52 (m,4H), 7.35-7.29 (m, 3H), 5.85-5.82 (m, 1H), 4.56-4.51 (m, 1H), 3.63-3.59 (m, 1H), 2.65-2.60 (m, 4H). ^{13}C NMR (125MHz, $CDCl_3$) δ: 27.0, 38.1, 49.6, 127.1, 127.8, 128.0, 132.6, 133.2, 135.3, 136.3, 176.2, 195.6. HPLC analysis: Ultron ES-OVM column, 30:70 alcohol/KH_2PO_4 (0.02 mol/L), flow rate = 1.2 ml/min, UV = 230 nm, major enantiomer t_1 = 3.00 min, minor enantiomer t_2 = 1.64min; 92% *ee*.


7.82
7.80
7.60
7.58
7.53
7.52
7.35
7.33
7.32
7.30
7.29
5.85
5.84
5.83
5.82
4.56
4.54
4.53
4.51
3.63
3.62
3.60
3.59
2.65
2.63
2.60
2.10
4.05
3.00
0.96
1.00
1.04
3.91
f1 (ppm)


195.61
176.19
136.27
135.30
133.17
132.58
128.56
127.93
127.75
127.08
49.55
38.06
27.03
f1 (ppm)





1: DAD1 D, Sig=230,16 Ref=360,100

#	[min]		[min]	[mAU*s]	[mAU]	%
1	1.842	VB	0.3261	797.54169	34.20163	4.0981
2	3.004	BB	0.3721	1.86637e4	794.35223	95.9019