Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information for

The First N-Ligands Assisted Pd Catalyzed Asymmetric Synthesis of 3-Arylsuccinimides as Novel Antifungal Leads

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Content

1. General Information

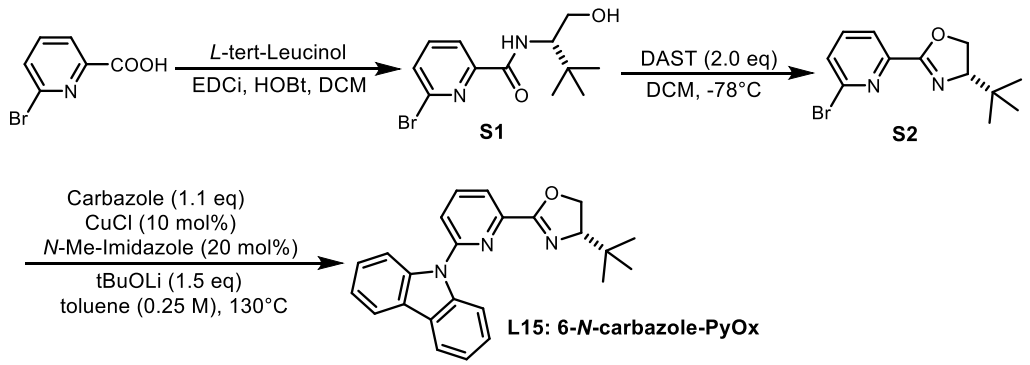
Unless otherwise stated, all solvents and reagents were purchased from commercial sources (Energy or Meryer Chemicals etc.), they were analytically pure and used without further purification. Anhydrous solvents were dried and distilled by standard techniques before use or were purchased from commercial sources (Energy Chemicals etc.).

Silica gel GF_{254} and column chromatography silica gel for isolation (200-300 mesh) were both purchased from Qingdao Broadchem Industrial Co., Ltd. Reaction progress was monitored by thin-layer chromatography (TLC) on silica gel GF_{254} with ultraviolet (UV_{254nm} or UV_{365nm}) detection. ^{1}HNMR and ^{13}CNMR spectra were recorded on a Bruker AV 400 spectrometers with $CDCl_3$ as solvent and tetramethylsilane as the internal standard. The chemical shifts (δ) were recorded in parts per million (ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ: ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet), coupling constant (Hz), integration and assignment (*H*). Data for ^{13}C NMR are reported in terms of chemical shift (δ: ppm).

The agriculturally important plant pathogens were provided by the College of Plant Protection, Nanjing Agricultural University (Nanjing, China).

2. Synthesis and Structural Elucidation of Ligands

2.1 Synthesis of Ligand L15



To a dried Schlenk flask charged with 6-Br-pyridine-2-carboxylic acid (10 mmol, 2.04 g) and *L*-tert-Leucinol (10 mmol, 1.17 g) was added anhydrous dichloromethane (100 mL) for dissolution. Hydroxybenzotriazole (HOBt) (1.75 g, 13 mmol) and *N*-(3-(dimethyl amino)-propyl)-*N*′-ethylcarbodiimide hydrochloride (EDC-HCl) (2.50 g, 13 mmol) were then added while the reaction flask was in an ice bath. The mixture was allowed to gradually warm to room temperature, and it was stirred overnight until full consumption of the carboxylic acid detected by thin layer chromatography (TLC). The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (50 mL) and separated. The water phase was extracted with dichloromethane (50 mL × 3), and the combined organic phase was sequentially washed with water (30 mL × 2) and saturated aqueous NaCl (30 mL), dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography on silica gel with hexane/EtOAc (2:1, v/v) as the eluent gave the amide **S1** in 63% yield as white solid.

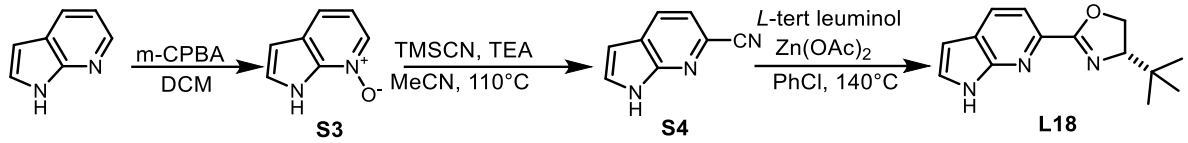
To a Schlenk tube charged the amide (5.0 mmol) was added anhydrous DCM (20.0 mL) under N_2 atmosphere. Diethylaminosulfur trifluoride (DAST) (1.6 g, 10 mmol) was added dropwise at -78°C. The reaction mixture was stirred at -78°C until the full consumption of

the starting material was detected by TLC. The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (20 mL) and separated, The water phase was extracted with dichloromethane (20 mL × 3), and the combined organic phase was sequentially washed with water (20 mL × 2) and saturated aqueous NaCl (20 mL), dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography on silica gel (200-300 m) with hexane/EtOAc (2:1, v/v) as the eluent gave the ligand **S2** in 65% yield as white solid.

To a Schlenk tube charged the **S2** (0.2 mmol), tBuOLi (0.3 mmol, 1.5 equiv), CuCl (0.02 mmol, 10 mol%), *N*-Me-Imidazole (0.04 mmol, 20 mol%) and carbazole (0.22 mmol, 1.1 equiv) was added anhydrous toluene (0.8 mL, 0.25 M) under N_2 atmosphere. The reaction mixture was stirred at 130^o C until the full consumption of the starting material was detected by TLC. The mixture was quenched by the addition of H_2O (5 mL) and separated, the water phase was extracted with EtOAc (5 mL × 3), dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography on silica gel (200-300 m) with hexane/EtOAc (15:1, v/v) as the eluent gave the ligand **L15** in 53% yield as white solid.

M.p.75-76 ^{o}C. ^{1}HNMR (500 MHz, $CDCl_3$) δ 8.13-8.08 (m, 3H), 7.99 (t, J = 7.8 Hz, 1H), 7.92 (d, J = 6.6 Hz, 2H), 7.75 (dd, J_1 = 8.1 Hz, J_2 = 0.9 Hz, 1H), 7.47 - 7.44 (m, 2H), 7.34-7.31 (m, 2H), 4.50 (dd, J_1 = 10.2 Hz, J_2 = 8.7 Hz, 1H), 4.36 (t, J = 8.5 Hz, 1H), 4.17 (dd, J_1 = 10.2 Hz, J_2 = 8.3 Hz, 1H), 1.01 (s, 9H). ^{13}CNMR (126 MHz, $CDCl_3$) δ 162.5, 151.6, 147.0, 139.5, 139.1, 126.5, 124.6, 121.3, 121.2, 120.4, 120.3, 111.4, 69.6, 34.2, 26.1.

2.2 Synthesis of Ligand L16, L17 and L18



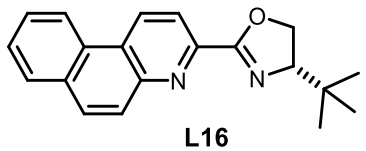
To a dried Schlenk flask charged with 7-azaindole (10 mmol, 1.18 g) was added anhydrous dichloromethane (100 mL) for dissolution. m-CPBA (15 mmol, 1.5 equiv) was then added while the reaction flask was in an ice bath. The mixture was allowed to gradually warm to room temperature, and it was stirred overnight until full consumption of the pyridine-2-ethyl detected by thin layer chromatography (TLC). The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (100 mL) and separated. The water phase was extracted with dichloromethane (100 mL × 3), dried over anhydrous sodium sulfate, and concentrated under vacuum to give the product **S3**, which can be used in next step without further purification.

To a Schlenk flask charged the nitrogen oxide **S3** (5.0 mmol) and TMSCN (18 mmol, 3.6 equiv) was added anhydrous MeCN (20 mL). Triethylamine (TEA) (7.5 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred at 110℃ until the full consumption of the starting material was detected by TLC. The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (30 mL) and separated, The water phase was extracted with EtOAc (30 mL × 3), and the combined organic phase was sequentially washed with water (20 mL × 2) and saturated aqueous NaCl (20 mL), dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography on silica gel (200-300m) with hexane/EtOAc (10:1, v/v) as the eluent gave the cyanated compound

S4 (47% yield in two steps) as white solid.

To a Schlenk flask charged the compound **S4** (1.0 mmol) and $Zn(OAc)_2$ (0.2 mmol, 0.2 equiv) was added anhydrous PhCl (5 mL). Then *L*-tert-Leucinol (1.5 mmol, 1.5 equiv) was added. The reaction mixture was stirred at 140℃ until the full consumption of the starting material was detected by TLC. The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (5 mL) and separated. The water phase was extracted with EtOAc (5 mL × 3), and the combined organic phase was sequentially washed with water (5 mL × 2), dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification by silica gel column chromatography on silica gel (200-300m) with hexane/EtOAc (5:1, v/v) as the eluent gave the I Ligand **L18** as white solid in 61% yield. M.p.189-192°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J_1 = 0.7 Hz, J_2 = 0.7 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.63 (dd, J_1 = 3.4 Hz, J_2 = 2.6 Hz, 1H), 6.55 (dd, J_1 = 3.4 Hz, J_2 = 1.9 Hz , 1H), 4.54 (dd, J_1 = 10.2 Hz J_2 = 8.4 Hz, 1H), 4.43 (t, J = 8.1 Hz, 1H), 4.21 (dd, J_1 = 10.1 Hz, J_2 = 7.8 Hz, 1H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 148.3, 138.9, 129.6, 128.9, 122.9, 116.2, 100.3, 76.6, 69.2, 34.3, 26.1.

Ligands **L16** and **L17** were synthesized according to the same procedure as above.

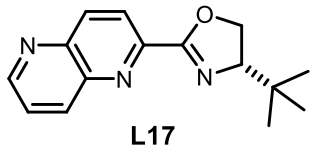


L16

White solid. M.p.111 - 113°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 – 9.27 (m, 1H), 8.37 (d, J = 8.3 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.92 – 7.89 (m, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.77

– 7.69 (m, 3H), 4.59 (dd, J_1 = 10.3 Hz, J_2 = 8.6 Hz, 1H), 4.44 (t, J = 8.5 Hz, 1H), 4.21 (dd, J_1 = 10.3 Hz, J_2 = 8.4 Hz, 1H), 1.03 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 146.1, 145.7, 136.4, 133.8, 131.6, 129.4, 128.7, 127.9, 127.5, 127.4, 125.1, 125.0, 122.1, 69.7, 34.3, 26.2.

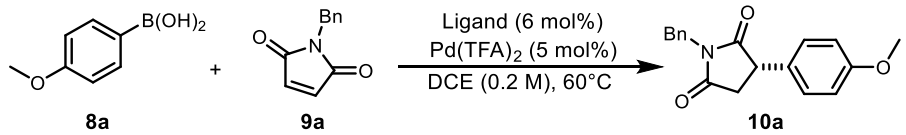


L17

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (dd, J_1 = 4.1 Hz, J_2 = 1.7 Hz, 1H), 8.40 (m, 2H), 8.33 (m, 1H), 7.65 (dd, J_1 = 8.6 Hz, J_2 = 4.2 Hz, 1H), 4.12 – 3.98 (m, 2H), 3.74 (dd, J_1 = 10.2 Hz, J_2 = 8.0 Hz, 1H), 1.04 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 152.5, 150.3, 144.5, 142.0, 138.7, 137.8, 125.0, 122.6, 62.9, 60.4, 34.1, 27.1.

3. Enantioselective Addition of Arylboronic Acid to Maleamide

3.1. General Procedure



8a **9a** **10a**

To a Schlenk tube charged with $Pd(TFA)_2$ (0.01 mmol, 3.3 mg, 5 mol%), ligand (0.012 mmol, 6 mol%) and 4-OMe-$PhB(OH)_2$ (60.8 mg, 0.4 mmol, 2.0 eq) was added DCE (0.5 mL). The mixture was stirred at 60 ℃ for 15 min to afford the catalyst solution.

To the above solution was added *N*-Bn-Maleimide (37.4 mg, 0.2 mmol) and 0.5 mL DCE (The volume of DCE is 1.0 mL). The tube was placed in the modules of the reactor which

was set at 60℃. After stirring for 36 h, the solvent was removed by rotary evaporation.

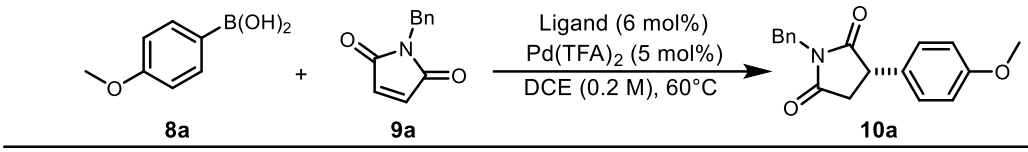
The residue was purified by column chromatography (petroleum ether/EtOAc = 10/1, v/v) to give the desired chiral pyrrolidine-2,5-dione product 10a as white solid.

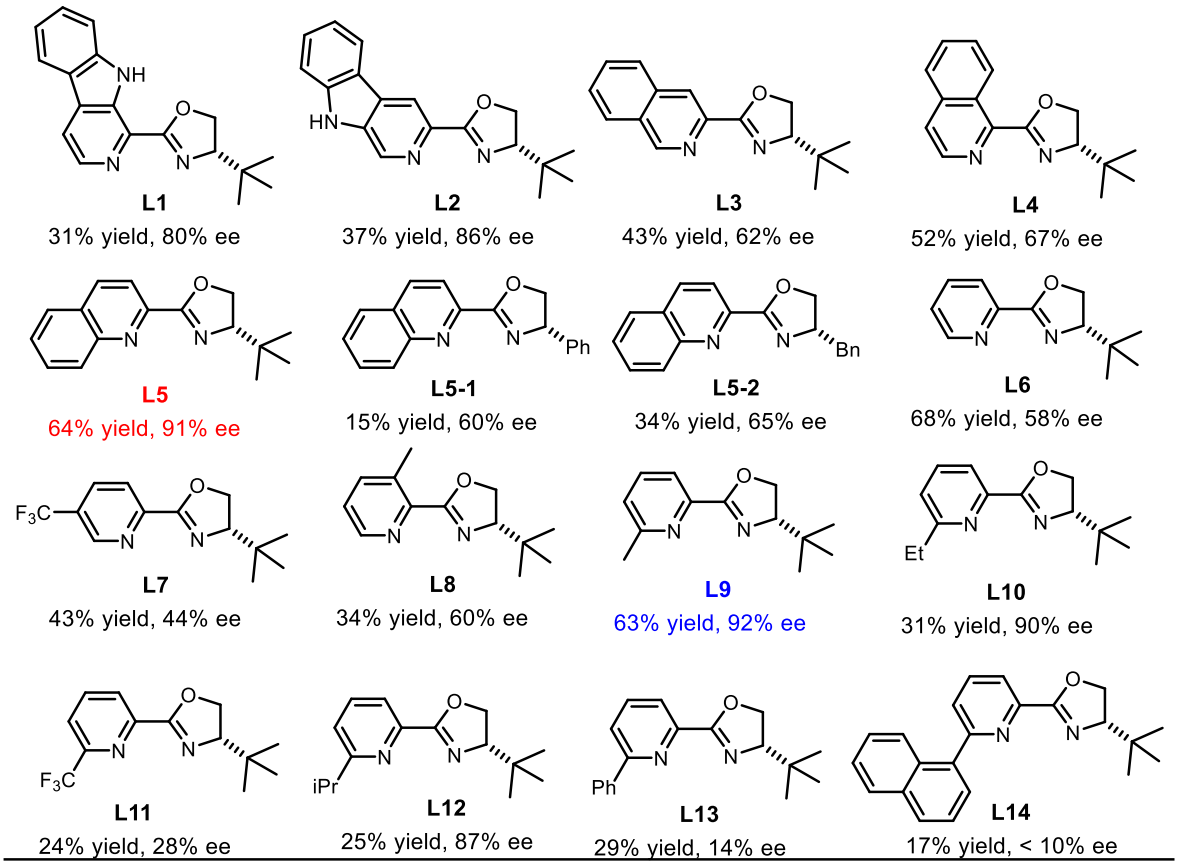
Bpy (2,2- Bipyridine) was utilized as a ligand for the preparation of the racemic products.

3.2. Optimization of the Reaction Conditions

3.2.1 Ligand Screening[a, b]

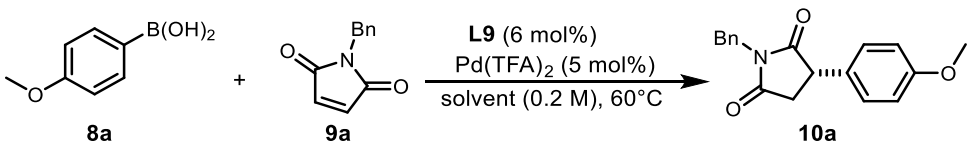
To select the appropriate chiral nitrogen-containing chiral ligand(s), *N*-benzylmaleimide and 4-methoxyphenylboronic acid were chosen as benchmark reaction partners. Versatile chiral ligands developed by our groups or synthesized according to the previous reports, were thoroughly tested.





a All reactions were run at 0.2 mmol scale. *b* Isolated yield and ee determined by HPLC on a chiral stationary phase.

3.2.2 Solvent Screening [a]

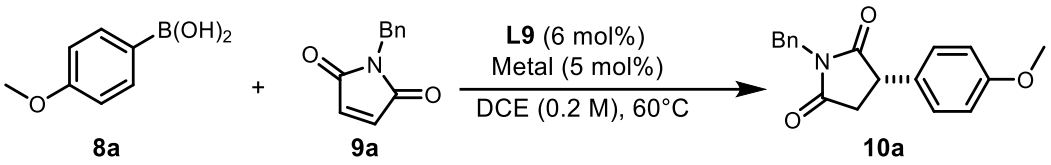


entry	solvent	Yield (%) [b]	ee (%) [b]
1	DMF	19%	46%
2	THF	31%	20%
3	Toluence	19%	63%

4	MeCN	15%	34%
5	DMSO	N.D.	
6	Butyl acetate	17%	61%
7	$CHCl_3$	9%	57%
8[c]	MeOH	22%	17%
9[d]	DCM	53%	78%

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase. c β^1-CarOx as Ligand. d temp as 40℃. N.D. = not detected.

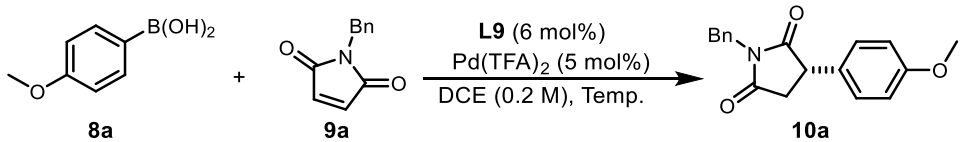
3.2.3 Metal Screening [a]



entry	metal	Yield (%) [b]	ee (%) [b]
1	$Pd(OAc)_2$	17%	84%
2	$PdCl_2$	N.D.	
3	$Cu(TFA)_2{\cdot}H_2O$	N.D.	
4	$Ni(OAc)_2{\cdot}4H_2O$	N.D.	
5	Ag_2OTf	N.D.	

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase. N.D. = not detected.

3.2.4 Temperature Screening [a]

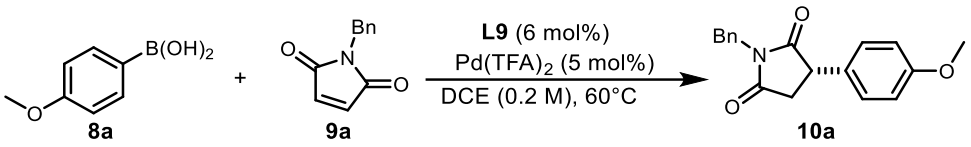


entry	Temp. (℃)	Yield (%) [b]	ee (%) [b]
1	40	17%	83%
2	60	63%	91%
3	80	9%	77%

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral

stationary phase.

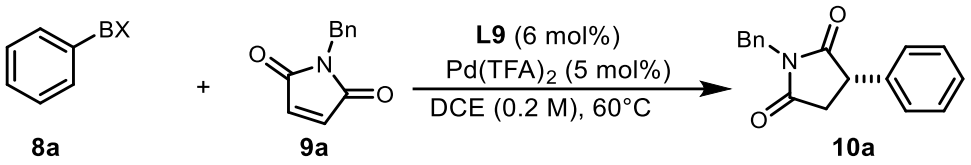
3.2.5 The Effect of the Amount of PMP-B(OH)$_2$ [a]



entry	Amount of PMP-B(OH)$_2$	Yield (%) [b]	ee (%) [b]
1	1.5 eq	46%	92%
2	2.0 eq	63%	92%
3	3.0 eq	33%	89%
4	4.0 eq	31%	89%

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase.

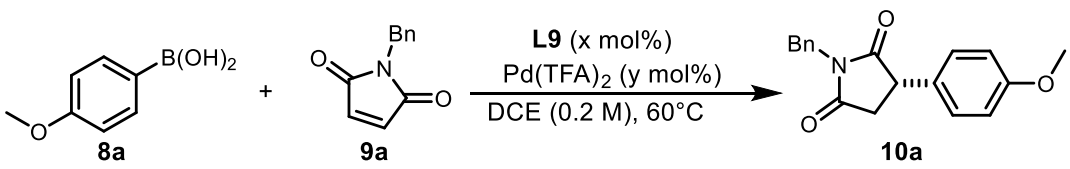
3.2.6 The Effect of Aryl Boron Variants [a]



entry	PhBX	Yield (%) [b]	ee (%) [b]
1	PhBPin	N.D.	
2	$PhBF_3K$	N.D.	
3	$(PhBO)_3$	N.D.	
4	PhBneop	N.D.	

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase. N.D. = not detected.

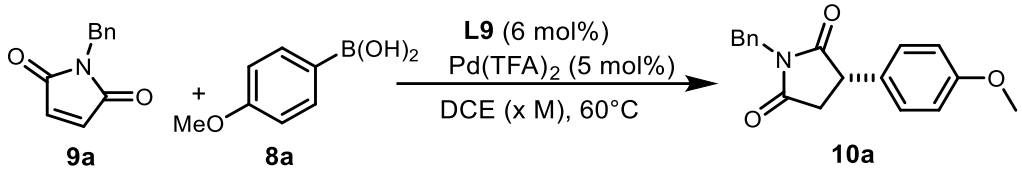
3.2.7 The Effect of the ratio of L11 to Pd(TFA)$_2$ [a]



entry	$Pd(TFA)_2$/mol%	**L9**/mol%	Yield(%) [b]	ee (%) [b]
1	5%	7.5%	29%	72%
2	5%	6%	63%	92%
3	10%	12%	46%	77%

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase.

3.2.8 The Effect of the Reaction Concentration [a]

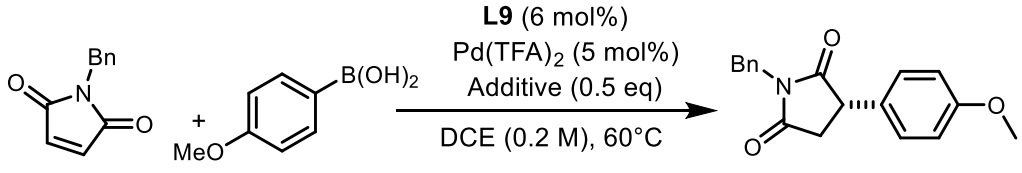


9a **8a** **10a**

entry	Amount of DCE	Yield (%) [b]	ee (%) [b]
1	0.4 M (0.5 mL)	70%	83%
2	0.2 M (1.0 mL)	63%	92%
3	0.1 M (2.0 mL)	55%	96%

a All reactions were run at 0.2 mmol scale. b Isolated yield and ee determined by HPLC on a chiral stationary phase.

3.2.9 Screening of Additive [a]



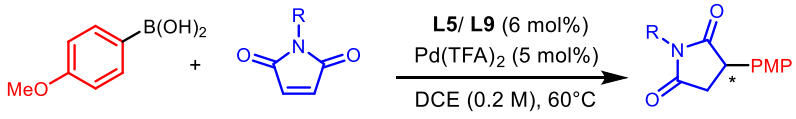
9a **8a** **10a**

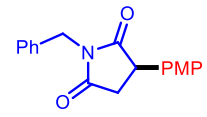
entry	Additive	Yield (%) [b]	ee (%) [b]
1	K_2CO_3	89%	30.2%
2	tBuOk	57%	79.9%
3	PhCOOH	N.D.	

a All reactions were run at 0.2 mmol scale. *b* Isolated yield and ee determined by HPLC on a chiral stationary phase. N.D. = not detected.

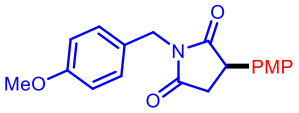
4. Substrate Scopes of this Methodology

4.1 Substrate Scope of Maleimides

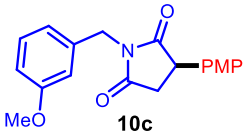




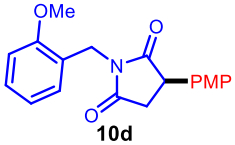
10a
L5: 64% yield, 91% ee
L9: 63% yield, 92% ee



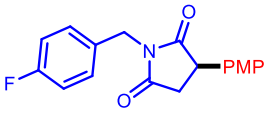
10b
L5: 38% yield, 87% ee
L9: 46% yield, 99% ee



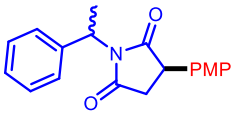
10c
L5: 36% yield, 88% ee
L9: 33% yield, 63% ee



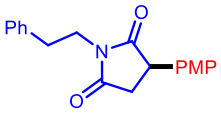
10d
L5: 32% yield, 88% ee
L9: 43% yield, 51% ee



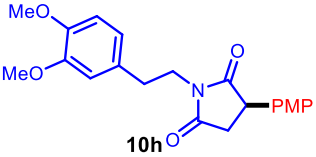
10e
L5: 46% yield, 86% ee
L9: 32% yield, 44% ee



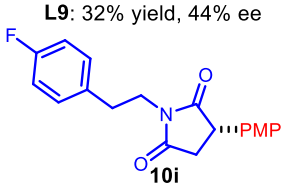
10f
L5: 43% yield, 90% ee
L9: 36% yield, 79% ee



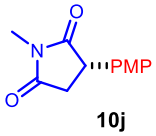
10g
L5: 58% yield, 90% ee
L9: 49% yield, 83% ee



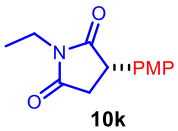
10h
L5: 45% yield, 92% ee
L9: 48% yield, 82% ee



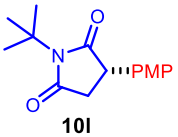
10i
L5: 58% yield, 89% ee
L9: 53% yield, 91% ee



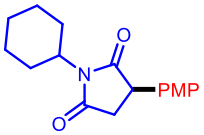
10j
L5: 56% yield, 98% ee
L9: 34% yield, 85% ee



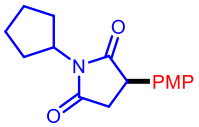
10k
L5: 59% yield, 94% ee
L9: 62% yield, 88% ee



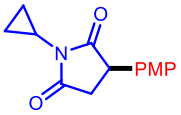
10l
L5: 72% yield, 95% ee
L9: 65% yield, 91% ee



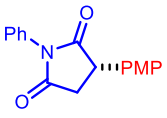
10m
L5: 56% yield, 84% ee
L9: 72% yield, 84% ee



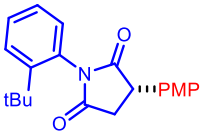
10n
L9: 62% yield; 62% ee



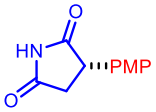
10o
L9: 58% yield; 58% ee



10p
L5: 57% yield, 81% ee
L9: 64% yield, 84% ee

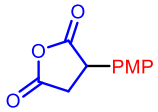


10q
L5: 37% yield, 74% ee
L9: 48% yield; 76% ee

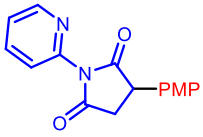


10r
L5: 58% yield, 87% ee
L9: 44% yield, 73% ee

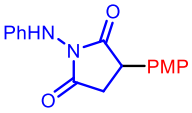
Unsuccessful examples



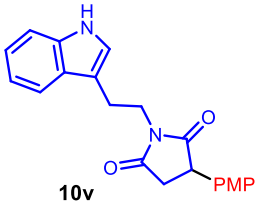
10s



10t

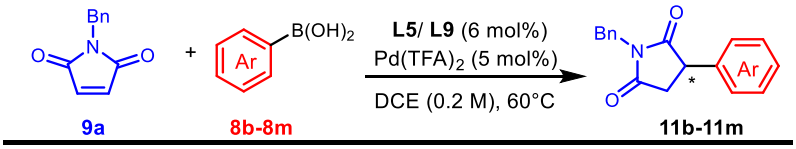


10u

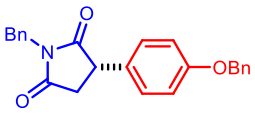


10v

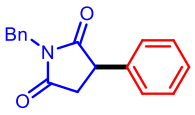
4.2 Substrate Scope of Ar-B(OH)$_2$



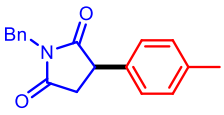
9a **8b-8m** **11b-11m**



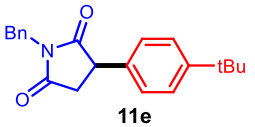
11b
L5: 63% yield, 75% ee
L9: 56% yield, 67% ee



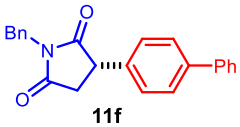
11c
L5: 68% yield, 65% ee
L9: 61% yield, 45% ee



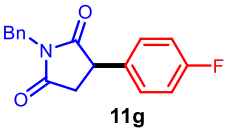
11d
L5: 57% yield, 84% ee
L9: 48% yield, 57% ee



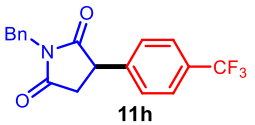
11e
L5: 54% yield, 75% ee
L9: 46% yield, 47% ee



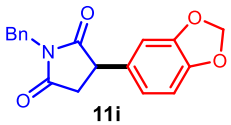
11f
L5: 78% yield, 54% ee
L9: 82% yield, 61% ee



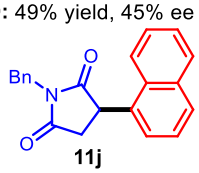
11g
L5: < 5% yield, n.d.
L9: 49% yield, 45% ee



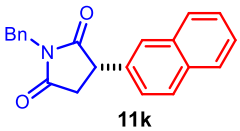
11h
L5: 46% yield, 46% ee
L9: 37% yield, 0 ee



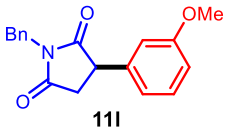
11i
L5: 40% yield, 88% ee
L9: 45% yield, 60% ee



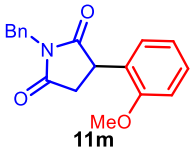
11j
L5: 42% yield, 53% ee
L9: 55% yield, 95% ee



11k
L5: 54% yield, 80% ee
L9: 47% yield, 61% ee



11l
L5: 58% yield, 38% ee
L9: 66% yield, 46% ee



11m
L5: < 5% yield, n.d.
L9: < 5% yield, n.d.

5. Antifungal Bioassay of 3-Arylsuccinimides

5.1 Initial Antifungal Screening

The antifungal activity of the target compounds was tested in *vitro* against the plant pathogenic fungi using the mycelium growth rate test. All the tested compounds were dissolved in DMSO at a concentration of mmol/mL. The media containing compounds at a concentration of 0.1 mmol/mL were then poured into Petri dishes for initial screening.

$$\text{Inhibition rate (\%)} = (C-T) / (C-5\text{ mm}) \times 100\%$$

Where *C*: The average diameter (in mm) of mycelia in the blank test, *T*: The average diameter (in mm) of mycelia on treated PDA with tested compounds.

Compds.	Inhibitory Rate at 100 uM (%)				
	R.s	*S.s*	*B.c*	*F.g*	*P.o*
rac -10a	7.9	23.6	6.3	32	*11.3*
10a	90.3	66.7	90.9	33.6	58.1
rac -10b	3.4	17.9	1.1	40.8	30.9
10b	70.9	30.5	90.9	14.1	44.8
rac-10e	30.3	43.8	13.5	29.1	30.9
10e	74.8	71.4	70.1	28.9	52.4
rac -10g	23.6	46.1	15.6	57.3	30.9
10g	43.7	23.8	90.9	18.8	29.5
rac -10h	64.1	76.4	43.8	57.3	54.6
10h	86.4	53.3	75.6	30.5	61.9
rac -10i	0	31.5	21.9	20	29.9
10i	42.1	32.6	16.7	4.9	27.8

rac-10j	43.2	34.8	32.3	33.9	25.8
10j	8.7	0	29.3	0	20
rac-10k	24.3	23.6	35.4	24.3	29.9
10k	39.8	12.4	26.8	0	16.2
rac-10l	75.3	40.8	33.3	41.7	33
10l	64.1	2.9	29.9	7.8	26.7
rac-10m	44.9	62.9	16.7	22.3	34
10m	98.1	98.1	36.6	35.9	60
rac-10n	19.7	42.7	8.2	18.4	23.7
10n	0	14.6	2.8	29.1	11.2
rac-10o	75.3	10.1	1.1	30.1	11.3
10o	40.4	28.1	0	30.1	9.3
rac-10p	64.1	55.1	41.7	36.9	25.8
10p	67	26.7	50.1	10.9	25.7
rac-11c	43.8	60.7	26	39.8	37.1
11c	84.5	46.7	90.9	26.6	60
rac-11d	37.1	40.4	37.5	39.8	58
11d	90.3	81	90.9	23.4	60.9
rac-11f	20.2	34.8	27.1	36.9	27.8
11f	43.7	29.5	90.9	25	41
rac-11g	31.5	55.1	15.6	32	23.7
11g	76.4	97.7	47.9	47.6	65
rac-11h	64.1	83.1	37.4	46.6	62.3
11h	98.1	98.1	90.9	59.3	71.4
rac-11j	75.7	60.9	64.6	8.6	78
11j	98.1	73.3	90.9	37.5	82
S-11j	65	41.9	79.3	23.4	71.4
boscalid	93.4	88.6	90.9	30.5	81.9

5.2 Precise Antifungal Test

In the precision antifungal test, the 20 mg/mL stock solution was diluted to 100, 50, 25, 12.5, 6.25, 3.125 uM and the above experiments were repeated for three times, the inhibition rates were calculated separately. The statistical analyses were performed by SPSS software version 20.0. Inhibition rate was calculated as follows,

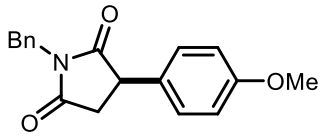
$$\text{Inhibition rate (\%)} = (C-T) / (C-5\text{ mm}) \times 100\%$$

Where C: The average diameter (in mm) of mycelia in the blank test, T: The average diameter (in mm) of mycelia on treated PDA with tested compounds.

Compds.	EC_{50} (uM)			
	R.s	*S.s*	*B.c*	*P.o*
rac-10m	69.83	39.99	214.04	128.76
10m	39.31	25.71	304.51	328.26
rac-11d	93.68	134.38	107.06	40.91
11d	46.99	43.01	43.99	46.79
rac-11h	18.24	14.32	33.27	29.65
11h	32.03	13.33	15.14	22.27
rac-11j	127.52	34.98	73.34	11.83
11j	26.31	50.11	44.41	16.12
S-11j	118.7	70.7	163.7	21.2
boscalid	1.22	1.56	5.38	1.02

6. Characterization of Chiral 3-Arylsuccinimides

(*R*)-1-benzyl-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10a)



White solid. Yield: 64% yield (**L5**); 63% yield (**L9**).

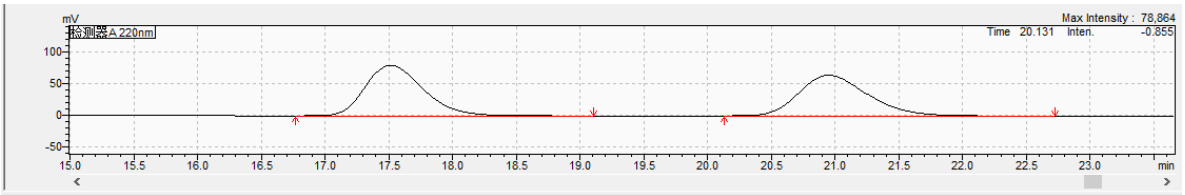
The ^{1}H NMR data is in accordance with that of previous publications. (*Chem. Eur. J.* **2015**, 21, 11050-11055)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.39 (m, 2H), 7.34-7.29 (m, 3H), 7.10-7.07 (m, 2H), 6.89-6.86 (m, 2H), 4.72 (dd, J_1 = 29.3 Hz, J_2 = 14.1 Hz, 2H), 3.98 (dd, J_1 = 9.6 Hz, J_2 = 4.8 Hz, 1H), 3.79 (s, 3H), 3.18 (dd, J_1 = 18.5 Hz, J_2 = 9.5 Hz, 1H), 2.79 (dd, J_1 = 18.5 Hz, J_2 = 4.8 Hz, 1H).

HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 17.4 min (major), t_{R2} = 20.8 min (minor); ee = 90.5%.

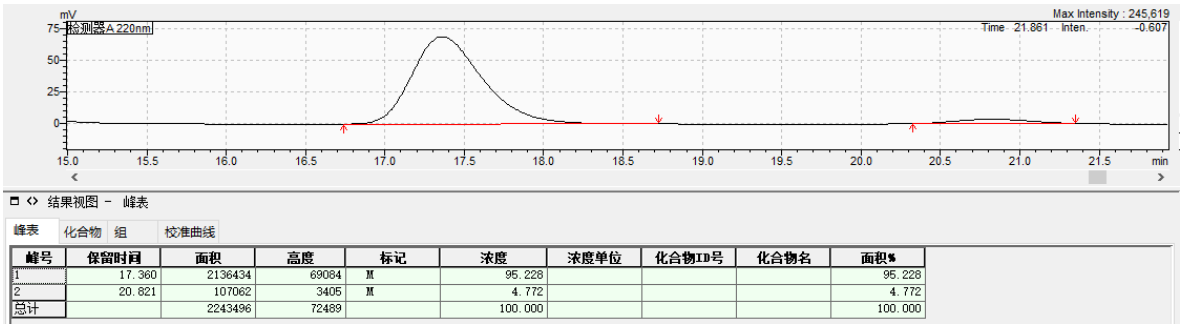
L9: t_{R1} = 17.0 min (major), t_{R2} = 20.6 min (minor); ee = 91.7%.



结果视图 - 峰表

峰表 | 化合物 | 组 | 校准曲线

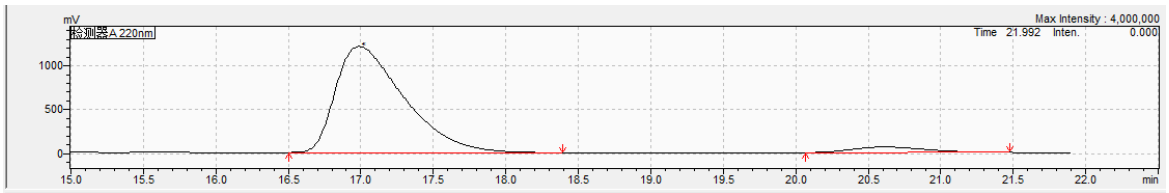
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.511	2500141	79722		50.954				50.954
2	20.951	2406519	64090		49.046				49.046
总计		4906660	143811		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.360	2136434	69084	M	95.228				95.228
2	20.821	107062	3405	M	4.772				4.772
总计		2243496	72489		100.000				100.000

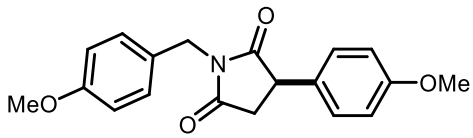


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	16.988	39687545	1211053	M	94.617				94.617
2	20.616	2257964	63741	M	5.383				5.383
总计		41945509	1274794		100.000				100.000

(*R*)-1-(4-methoxybenzyl)-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10b)



Colorless oil. Yield: 38% yield (**L5**); 46% yield (**L9**).

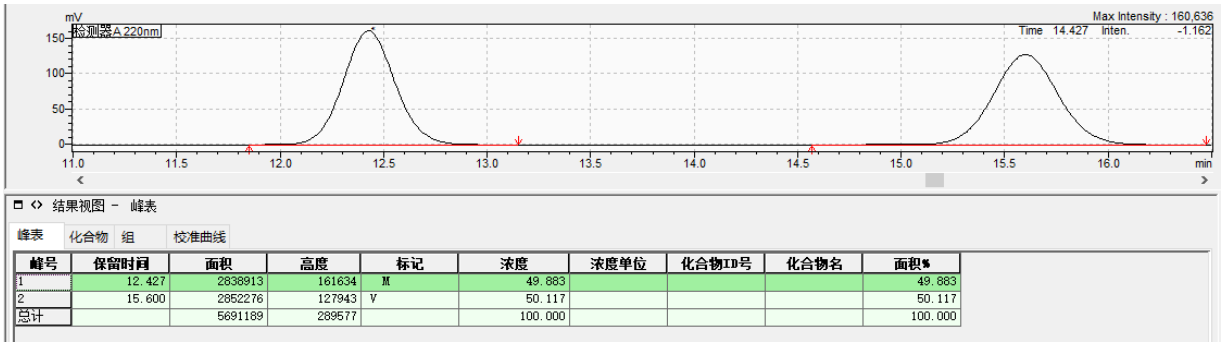
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 2H), 7.12 – 6.99 (m, 2H), 6.89-6.82 (m, 4H), 4.70 – 4.59 (dd, J = 2H), 3.94 (dd, J_1= 9.5 Hz, J_2 = 4.7 Hz, 1H), 3.78 (s, 6H), 3.15 (dd, J_1= 18.0 Hz, J_2 = 9.6 Hz, 1H), 2.75 (dd, J_1= 18.5 Hz, J_2 = 4.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.9, 176.1, 159.5, 159.3, 130.5, 129.3, 128.6, 128.3, 114.7, 114.1, 55.5, 55.4, 45.3, 42.3, 37.4.

HPLC trace: Daicel chiralcel AD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 12.4 min (minor), t_{R2} = 15.6 min (major); ee = 86.6%.

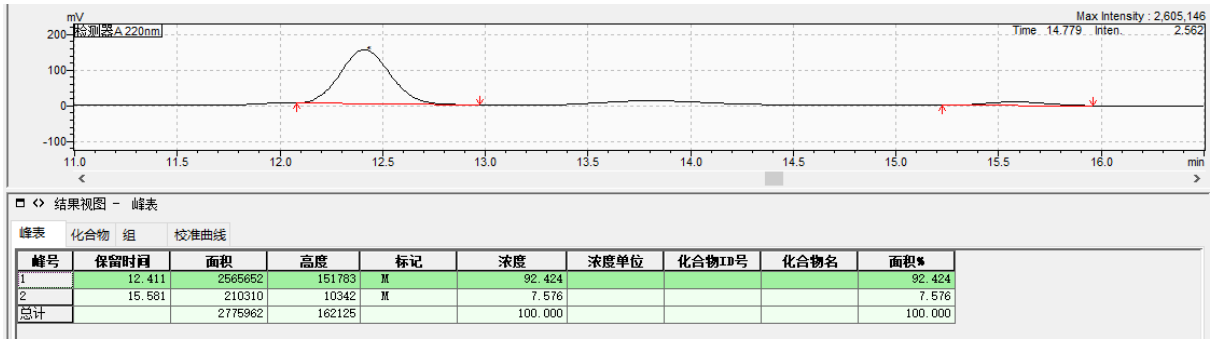
L9: t_{R1} = 12.2 min (minor), t_{R2} = 15.2 min (major); ee = 98.6%.



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.427	2838913	161634	M	49.883				49.883
2	15.600	2852276	127943	V	50.117				50.117
总计		5691189	289577		100.000				100.000



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

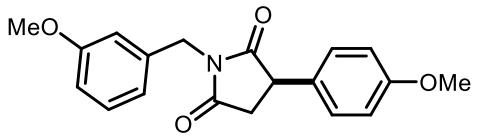
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.411	2565652	151783	M	92.424				92.424
2	15.581	210310	10342	M	7.576				7.576
总计		2775962	162125		100.000				100.000

结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.248	295124	7383	M	99.301				99.301
2	15.243	2079	111	M	0.699				0.699
总计		297203	7494		100.000				100.000

(*R*)-1-(3-methoxybenzyl)-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10c)



Colorless oil. Yield: 36% yield (**L5**); 33% yield (**L9**).

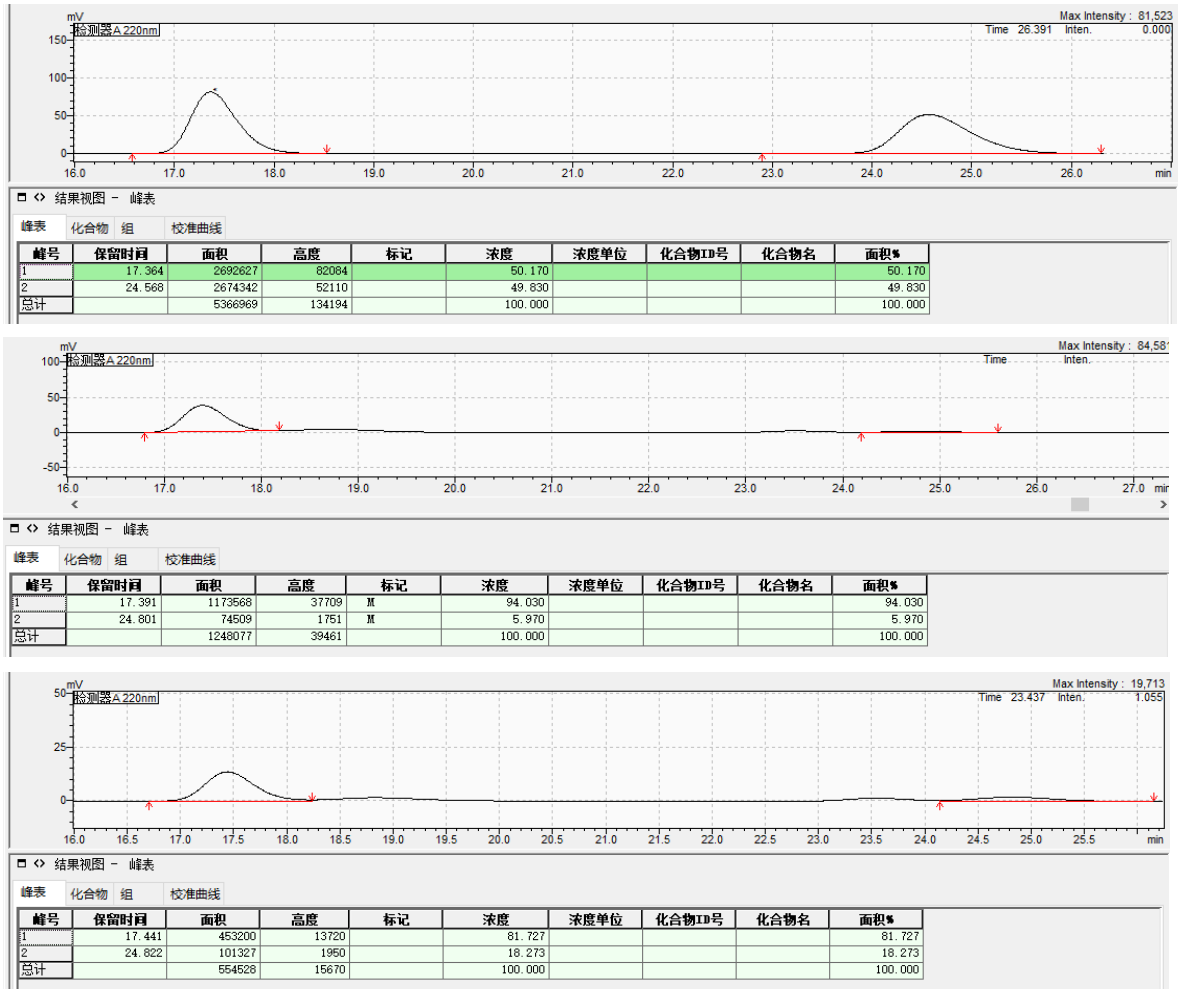
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.35 (m, 1H), 7.32 – 7.19 (m, 2H), 7.18 – 7.08 (m, 2H), 7.08 – 6.93 (m, 3H), 4.94 – 4.75 (m, 2H), 4.13 (dd, J_1= 9.5 Hz, J_2 = 4.8 Hz, 1H), 3.94 (d, J = 3.6 Hz, 6H), 3.34 (dd, J_1= 18.0 Hz, J_2 = 9.6 Hz, 1H), 2.94 (dd, J_1= 18.5 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 176.0, 159.8, 159.3, 137.3, 129.8, 129.2, 128.5, 121,0, 114.6, 114.1, 113.8, 55.4, 55.3, 45.2, 42.7, 37.3.

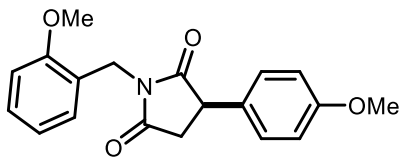
HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 17.4 min (major), t_{R2} = 24.8 min (minor); ee = 88.0%.

L9: t_{R1} = 17.4 min (major), t_{R2} = 24.8 min (minor); ee = 63.4%.



(*R*)-1-(2-methoxybenzyl)-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10d)



Colorless oil. Yield: 32% yield (**L5**); 43% yield (**L9**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.13 (m, 1H), 7.10 – 7.00 (m, 3H), 6.86 – 6.76 (m, 4H), 4.79 – 4.62 (m, 2H), 3.92 (dd, J_1= 9.5 Hz, J_2 = 4.7 Hz, 1H), 3.72 (d, J = 3.4 Hz, 6H), 3.13 (dd, J_1= 18.4 Hz, J_2 = 9.6 Hz, 1H), 2.73 (dd, J_1= 18.5 Hz, J_2 = 4.7 Hz, 1H).

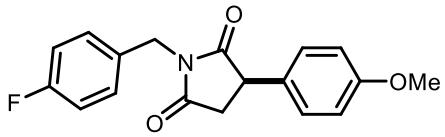
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 175.1, 158.3, 156.3, 128.5, 128.1, 128.1, 127.6, 122.5, 119.5, 113.7, 109.6, 54.5, 54.5, 44.3, 37.3, 36.3.

HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 9.6 min (major), t_{R2} = 19.5 min (minor); ee = 87.8%.

L9: t_{R1} = 9.6 min (major), t_{R2} = 19.5 min (minor); ee = 50.6%.

(*R*)-1-(4-fluorobenzyl)-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10e)



Colorless oil. Yield: 46% yield (**L5**); 32% yield (**L9**).

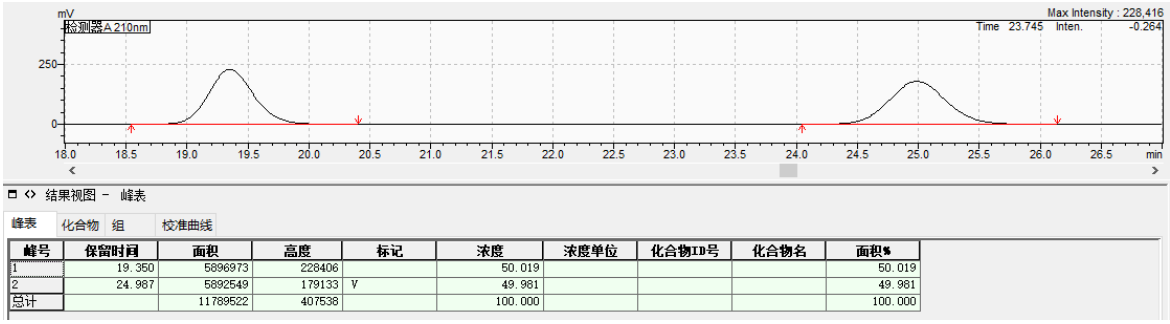
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.36 (m, 2H), 7.12 – 7.03 (m, 2H), 7.03 – 6.96 (m, 2H), 6.94 – 6.79 (m, 2H), 4.80 – 4.58 (m, 2H), 3.96 (dd, J_1= 9.5 Hz, J_2 = 4.7 Hz, 1H), 3.79 (s, 3H), 3.18 (dd, J_1= 18.5 Hz, J_2 = 9.5 Hz, 1H), 2.78 (dd, J_1= 18.5 Hz, J_2 = 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 176.0, 162.6 (d, J = 247.8 Hz), 159.4, 131.8 (d, J = 3.3 Hz), 130.9 (d, J = 8.2 Hz), 129.1, 128.5, 115.7 (d, J = 21.7 Hz), 114.8, 55.5, 45.3, 42.1, 37.4.

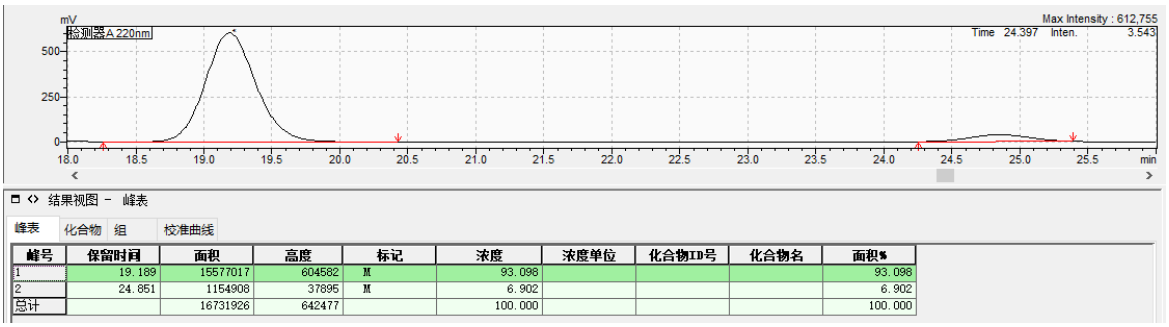
HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 19.2 min (major), t_{R2} = 24.7 min (minor); ee = 86.2%.

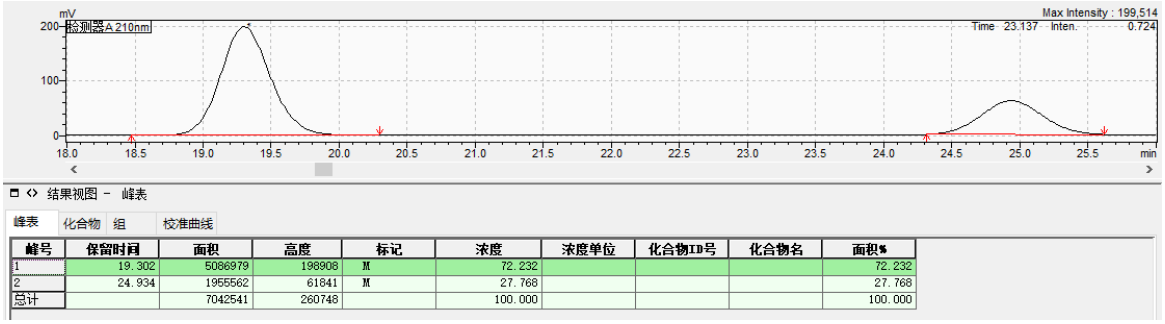
L9: t_{R1} = 19.3 min (major), t_{R2} = 24.9 min (minor); ee = 44.4%.



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.350	5896973	228406		50.019				50.019
2	24.987	5892549	179133	V	49.981				49.981
总计		11789522	407538		100.000				100.000

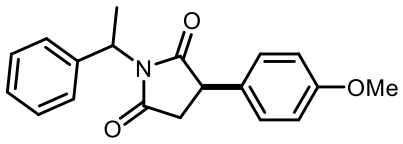


峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.189	15577017	604582	M	93.098				93.098
2	24.851	1154908	37895	M	6.902				6.902
总计		16731926	642477		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.302	5086979	198908	M	72.232				72.232
2	24.934	1955562	61841	M	27.768				27.768
总计		7042541	260748		100.000				100.000

(3*R*)-3-(4-methoxyphenyl)-1-(1-phenylethyl) pyrrolidine-2,5-dione (10f)



White solid. Yield: 43% yield (**L5**); 36% yield (**L9**).

^{1}H NMR (500 MHz, $CHCl_3$) δ 7.38 (d, J = 7.3 Hz, 2H), 7.28 – 7.16 (m, 3H), 7.02 – 6.93 (m, 2H), 6.82 – 6.74 (m, 2H), 5.42-5.36 (m, 1H), 3.80 (ddd, J_1= 12.2 Hz, J_2 = 9.7 Hz, J_3= 4.8 Hz, 1H), 3.70 (d, J = 4.7 Hz, 3H), 3.03 (dt, J_1= 18.4 Hz, J_2 = 9.4 Hz, 1H), 2.64 (ddd, J_1= 18.3 Hz, J_2 = 8.5 Hz, J_3= 4.6 Hz, 1H), 1.76 (dd, J_1= 12.6 Hz, J_2 = 7.4 Hz , 3H).

^{13}C NMR (126 MHz, $CHCl_3$) δ 178.0, 177.9, 176.1, 176.1, 159.3, 159.3, 139.7, 139.6, 129.5, 128.6, 128.5, 128.0, 127.9, 127.7, 127.6, 114.7, 114.6, 55.4, 50.8, 50.5, 45.0, 37.3, 37.2, 16.8, 16.5.

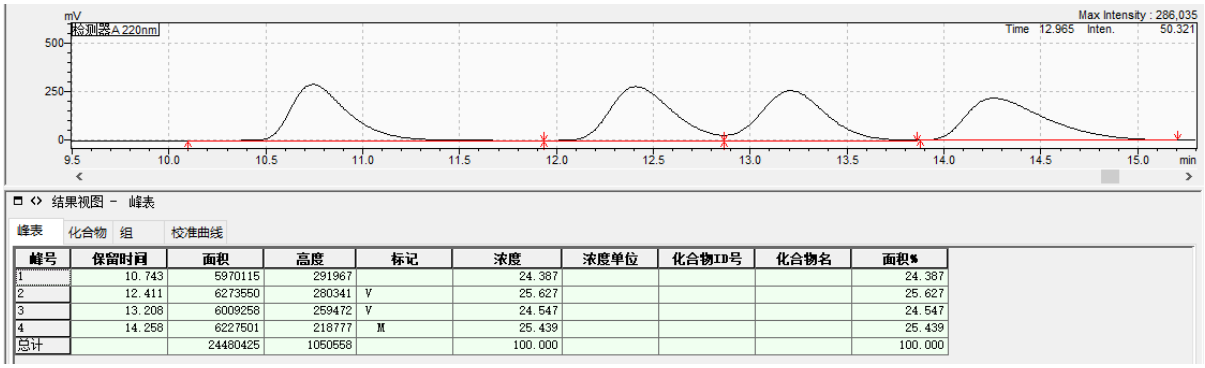
HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 10.8 min (major), t_{R2} = 13.2 min (minor), ee = 90.2%.

t_{R1} = 12.5 min (major), t_{R2} = 14.6 min (minor), ee = 89.0%.

L9: t_{R1} = 10.9 min (major), t_{R2} = 13.2 min (minor), ee = 83.8%.

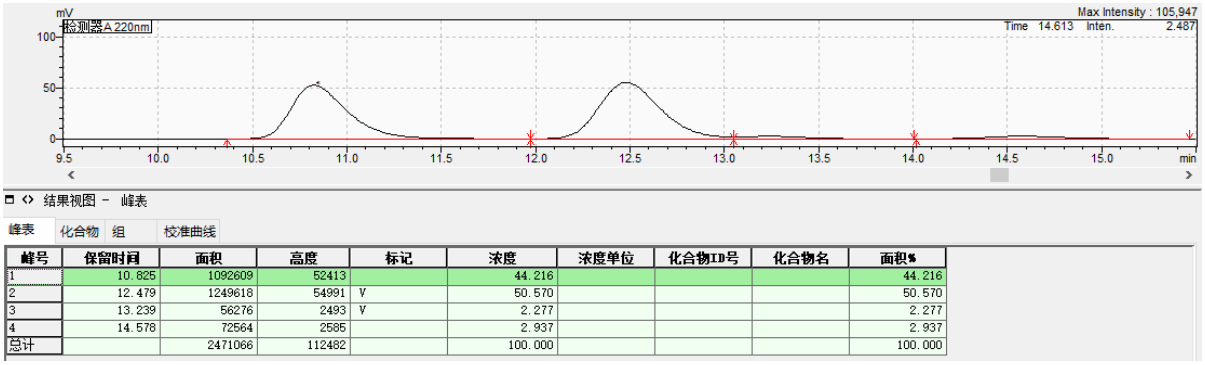
t_{R1} = 12.5 min (major), t_{R2} = 14.6 min (minor), ee = 75.2%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	10.743	5970115	291967		24.387				24.387
2	12.411	6273550	280341	V	25.627				25.627
3	13.208	6009258	259472	V	24.547				24.547
4	14.258	6227501	218777	M	25.439				25.439
总计		24480425	1050558		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

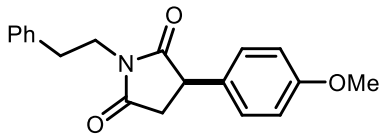
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	10.825	1092609	52413		44.216				44.216
2	12.479	1249618	54991	V	50.570				50.570
3	13.239	56276	2493	V	2.277				2.277
4	14.578	72564	2585		2.937				2.937
总计		2471066	112482		100.000				100.000

结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	10.936	57341	2439		43.542				43.542
2	12.543	60691	2324		46.086				46.086
3	13.229	5064	240	V	3.846				3.846
4	14.590	8594	332		6.526				6.526
总计		131691	5336		100.000				100.000

(*R*)-3-(4-methoxyphenyl)-1-phenethylpyrrolidine-2,5-dione (10g)



White solid. Yield: 58% yield (**L5**); 49% yield (**L9**).

^{1}H NMR (500 MHz, $CHCl_3$) δ 7.21 (dd, J_1= 7.9 Hz, J_2 = 6.4 Hz, 2H), 7.18 – 7.08 (m, 3H), 6.87 (d, J = 8.7 Hz, 2H), 6.76 (d, J = 8.7 Hz, 2H), 3.83 – 3.71 (m, 3H), 3.71 (s, 3H), 3.01 (dd,

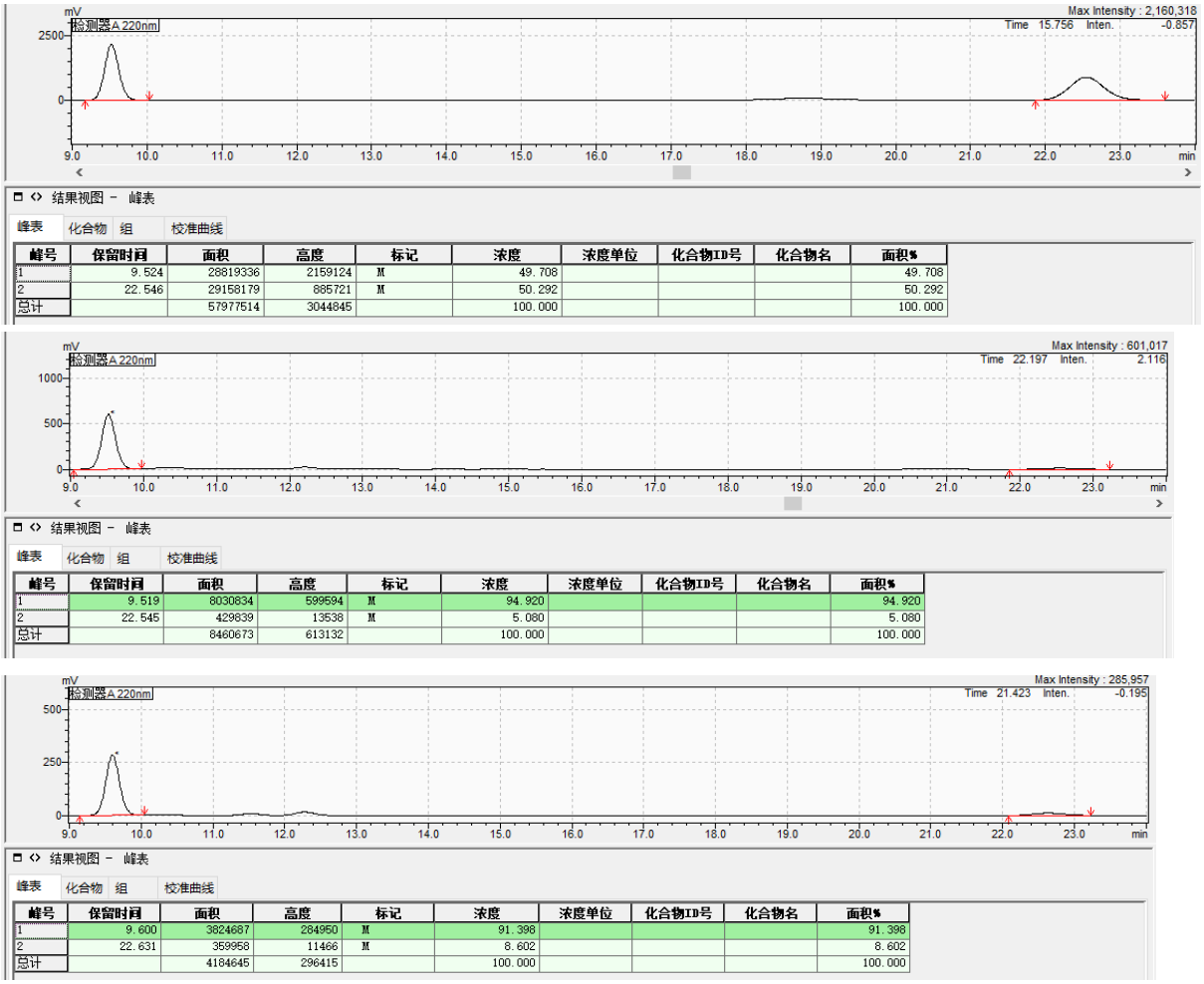
J_1= 18.4 Hz, J_2 = 9.6 Hz, 1H), 2.87 (t, J = 7.8 Hz, 2H), 2.59 (dd, J_1= 18.4 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (126 MHz, $CHCl_3$) δ 178.0, 176.2, 159.3, 137.7, 129.3, 129.1, 128.7, 128.5, 126.9, 114.6, 55.4, 45.1, 40.1, 37.3, 33.4.

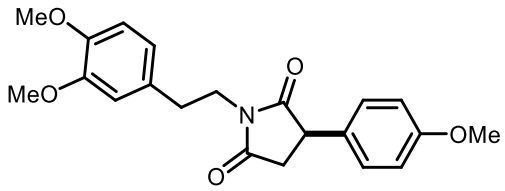
HPLC trace: Daicel chiralcel AD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 9.5 min (major), t_{R2} = 22.5 min (minor); ee = 89.8%.

L9: t_{R1} = 9.6 min (major), t_{R2} = 22.6 min (minor); ee = 82.8%.



(*R*)-1-(3,4-dimethoxyphenethyl)-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10h)



Colorless oil. Yield: 45% yield (**L5**); 48% yield (**L9**).

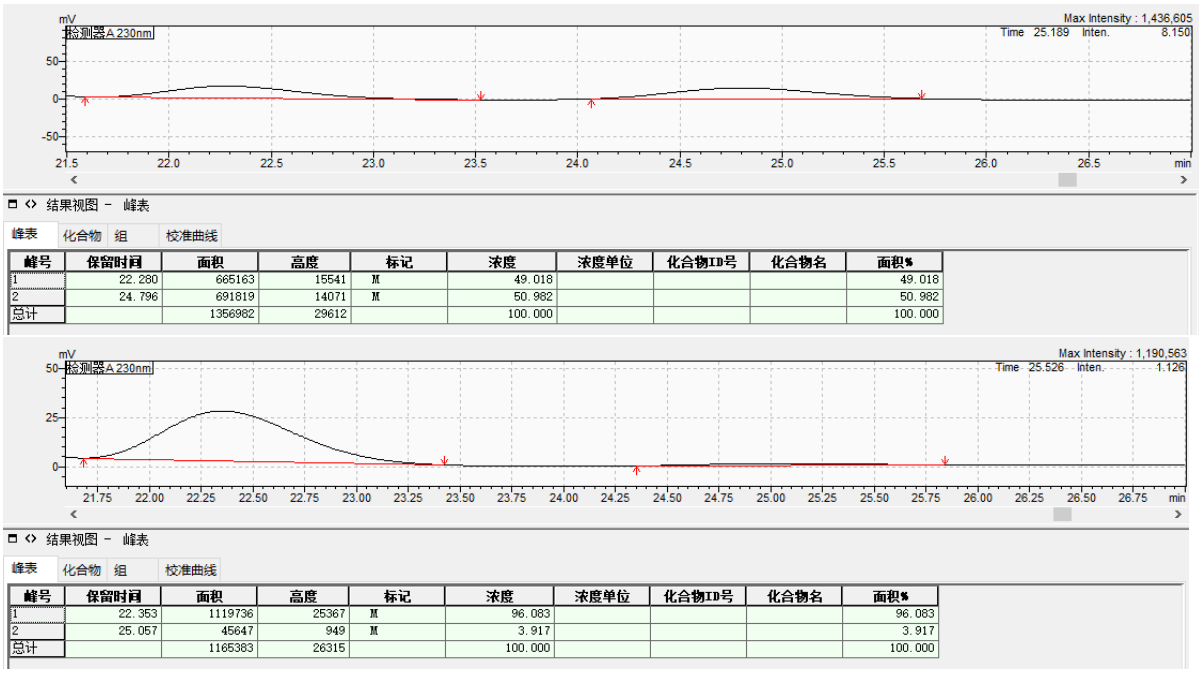
The ^{1}H NMR data is in accordance with that of previous publications. (*Chem. Eur. J.* **2015**, 21, 11050-11055.)

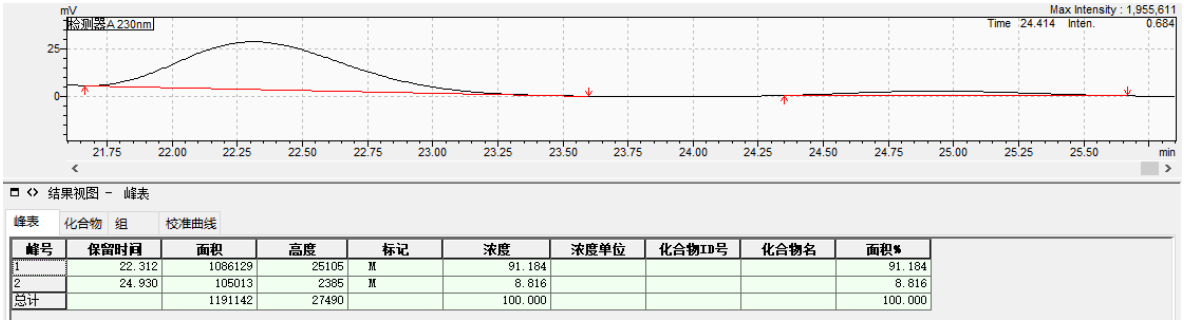
^{1}H NMR (400 MHz, $CHCl_3$) δ 8.32-8.27 (m, 2H), 7.79-7.75 (m, 1H), 7.64-7.60 (m, 1H), 6.82 – 6.69 (m, 3H), 5.36 (dd, J_1= 8.7 Hz, J_2 = 4.7 Hz, 1H), 4.09 – 3.98 (m, 2H), 3.87 (s, 3H), 3.86-3.83 (m, 3H), 3.80 – 3.70 (m, 3H), 3.10 (dd, J_1= 18.3 Hz, J_2 = 8.7 Hz, 1H), 2.90 – 2.81 (m, 2H), 2.61 (dd, J_1= 18.3 Hz, J_2 = 4.8 Hz, 1H).

HPLC trace: Daicel chiralcel AD-H, hexane/ *i*-PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 9.5 min (major), t_{R2} = 22.5 min (minor); ee = 92.2%.

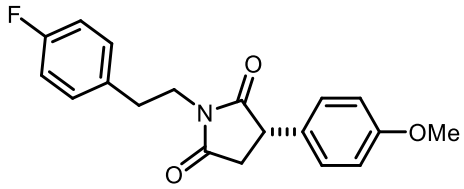
L9: t_{R1} = 9.6 min (major), t_{R2} = 22.6 min (minor); ee = 82.4%.





峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	22.312	1086129	25105	M	91.184				91.184
2	24.930	105013	2385	M	8.816				8.816
总计		1191142	27490		100.000				100.000

(*S*)-1-(4-fluorophenethyl)-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10i)



Colorless oil. Yield: 58% yield (**L5**); 53% yield (**L9**).

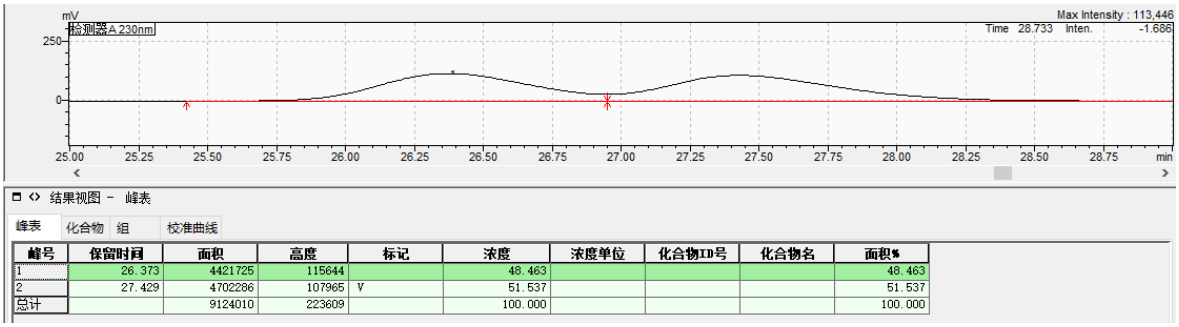
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.13 (m, 2H), 7.02 – 6.91 (m, 4H), 6.89 – 6.82 (m, 2H), 3.88 (dd, J_1= 9.6 Hz, J_2 = 4.6 Hz, 1H), 3.86 – 3.74 (m, 5H), 3.11 (dd, J_1= 18.5 Hz, J_2 = 9.5 Hz, 1H), 2.94 (td, J_1= 7.4 Hz, J_2 = 1.7 Hz, 2H), 2.68 (dd, J_1= 18.5 Hz, J_2 = 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.0, 176.2, 162.5 (d, J = 245.7 Hz), 159.3, 133.3 (d, J = 3.2 Hz), 130.6, 130.5 (d, J = 8.1 Hz), 129.2, 128.5, 115.5 (d, J = 21.3 Hz), 114.7, 55.5, 45.1, 40.0, 37.2, 32.6.

HPLC trace: Daicel chiralcel AD-H, hexane/ *i* -PrOH = 70/30, 220 nm, 1.0 mL/min.

L5: t_{R1} = 26.5 min (minor), t_{R2} = 27.5 min (major); ee = 89.2%.

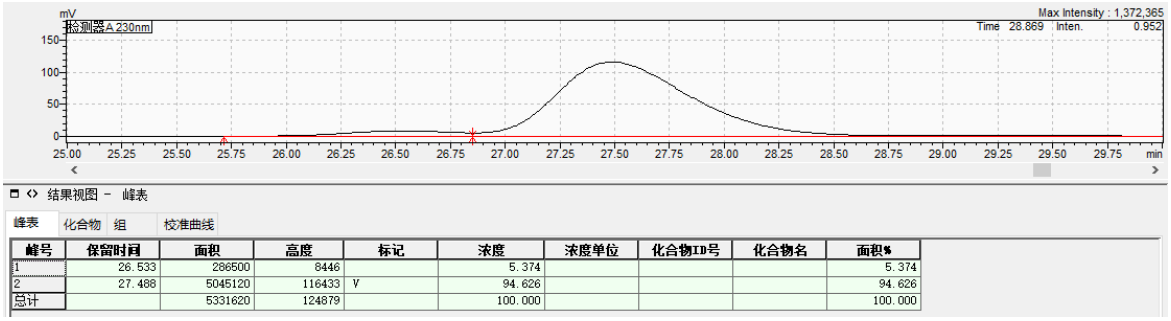
L9: t_{R1} = 26.6 min (minor), t_{R2} = 27.6 min (major); ee = 91.2%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

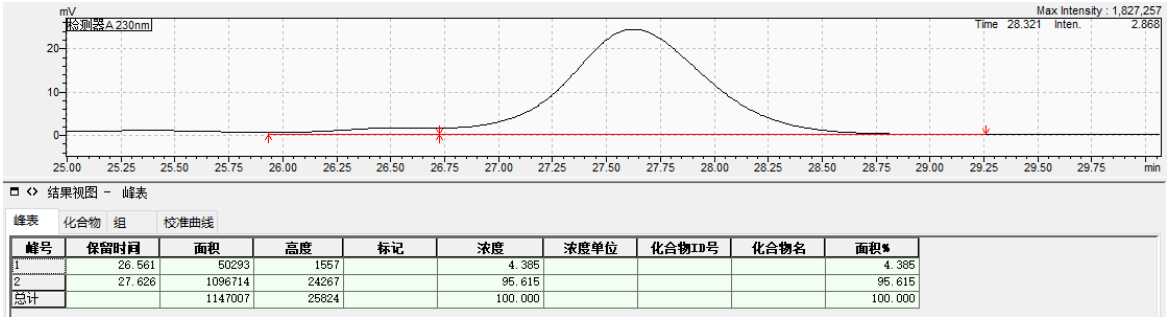
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	26.373	4421725	115644		48.463				48.463
2	27.429	4702286	107965	V	51.537				51.537
总计		9124010	223609		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	26.533	286500	8446		5.374				5.374
2	27.488	5045120	116433	V	94.626				94.626
总计		5331620	124879		100.000				100.000

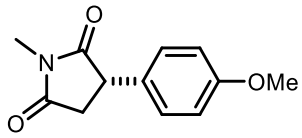


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	26.561	50293	1557		4.385				4.385
2	27.626	1096714	24267		95.615				95.615
总计		1147007	25824		100.000				100.000

(*S*)-3-(4-methoxyphenyl)-1-methylpyrrolidine-2,5-dione (10j)



Colorless oil. Yield: 56% yield (**L5**); 34% yield (**L9**).

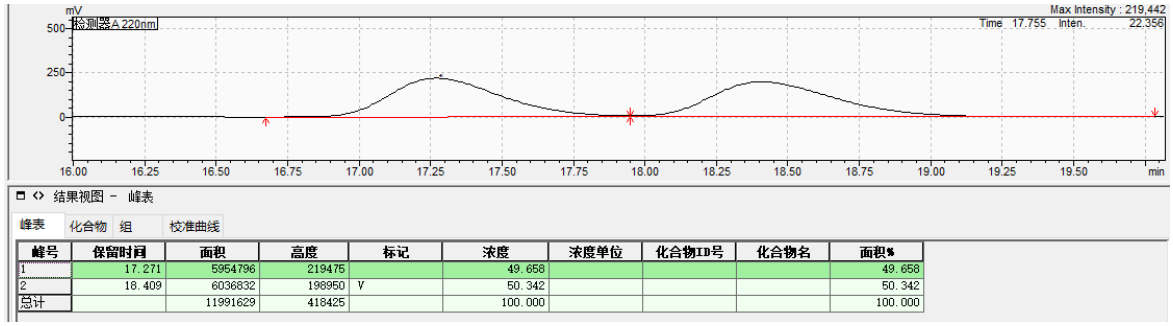
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16-7.13 (m, 2H), 6.91-6.88 (m, 2H), 3.98 (dd, J_1 = 9.6 Hz, J_2 = 4.8 Hz, 1H), 3.80 (s, 3H), 3.20 (dd, J_1 = 18.5 Hz, J_2 = 9.6 Hz, 1H), 3.06 (s, 3H), 2.80 (dd, J_1 = 18.5 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 178.3, 176.5, 159.3, 129.1, 128.6, 114.7, 55.4, 45.3, 37.3, 25.3.

HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 17.6 min (major), t_{R2} = 18.8 min (minor); ee = 97.6%.

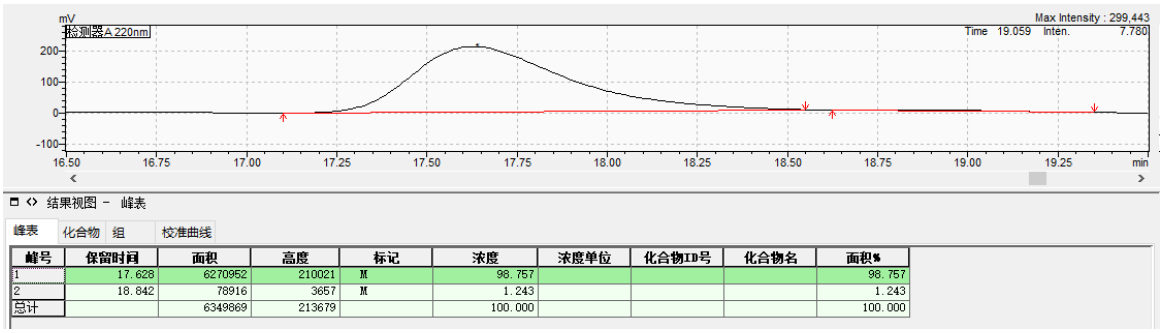
L9: t_{R1} = 17.4 min (major), t_{R2} = 18.6 min (minor); ee = 85.0%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

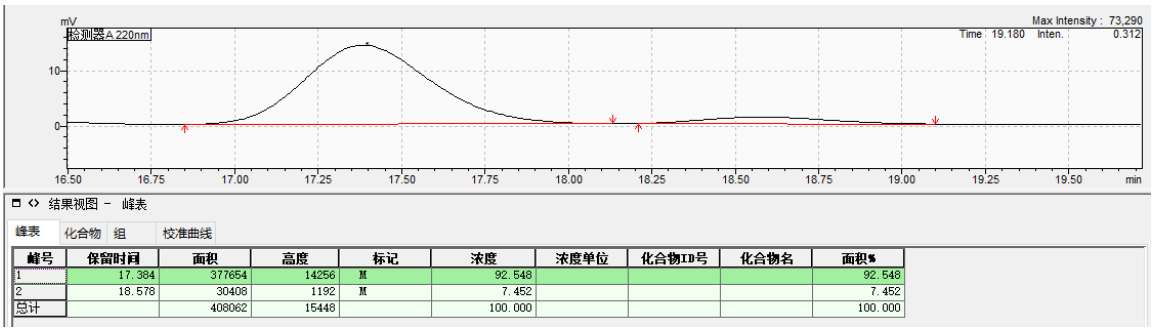
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.271	5954796	219475		49.658				49.658
2	18.409	6036832	198950	V	50.342				50.342
总计		11991629	418425		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.628	6270952	210021	M	98.757				98.757
2	18.842	78916	3657	M	1.243				1.243
总计		6349869	213679		100.000				100.000

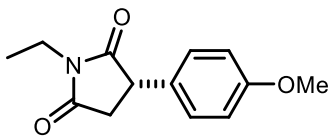


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.384	377654	14256	M	92.548				92.548
2	18.578	30408	1192	M	7.452				7.452
总计		408062	15448		100.000				100.000

(*S*)-1-ethyl-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10k)



Colorless oil. Yield: 59% yield (**L5**); 62% yield (**L9**).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14-7.11 (m, 2H), 6.91-6.88 (m, 2H), 3.95 (dd, J_1 = 9.7 Hz, J_2 = 4.6 Hz, 1H), 3.80 (s, 3H), 3.63 (dd, J_1 = 14.4 Hz, J_2 = 7.9 Hz, 2H), 3.16 (dd, J_1 = 18.4

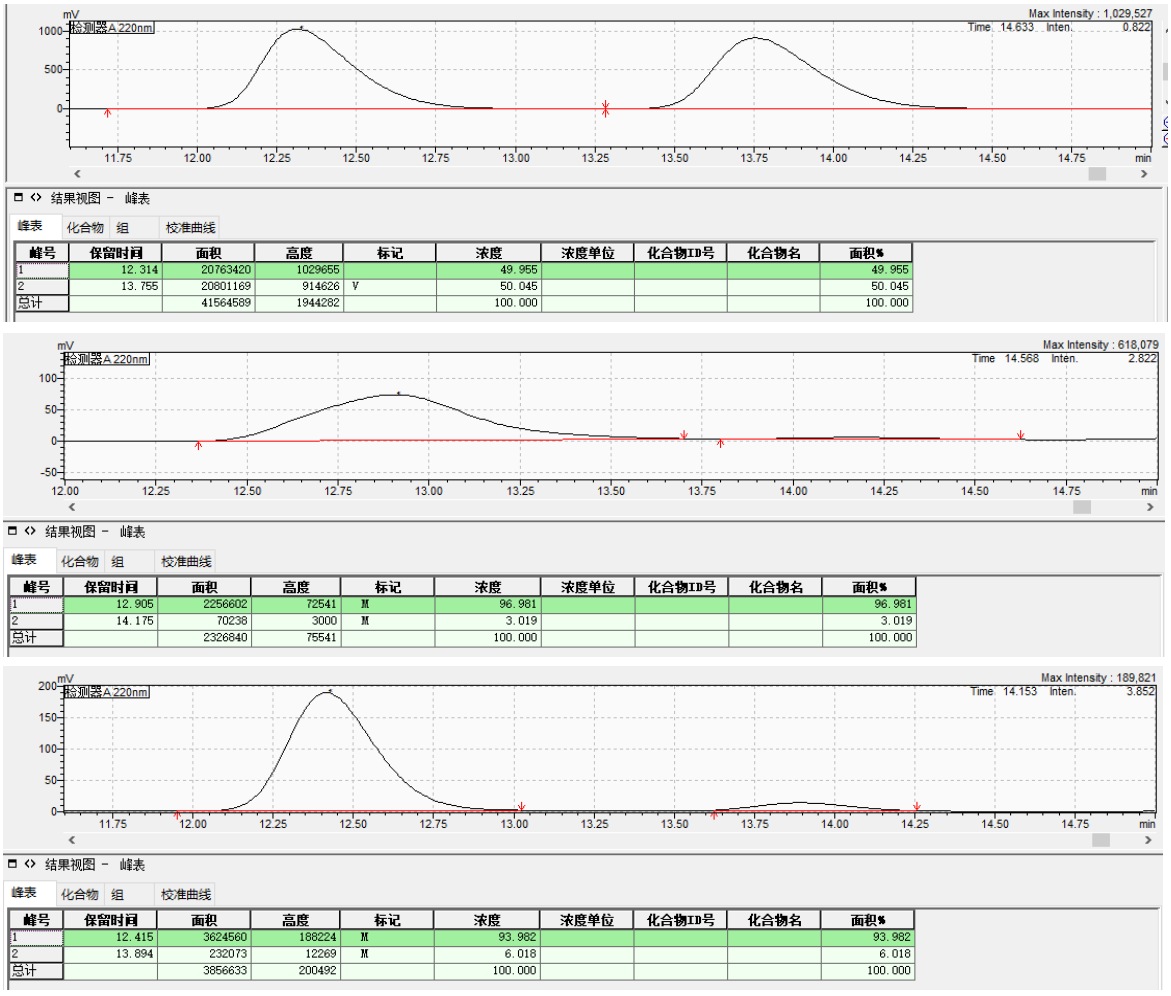
Hz, J_2 = 9.8 Hz, 1H), 2.77 (dd, J_1 = 18.3 Hz, J_2 = 4.5 Hz, 1H), 1.21 (t, J = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 178.0, 176.3, 159.3, 129.3, 128.5, 114.7, 55.4, 45.2, 37.4, 34.1, 13.2.

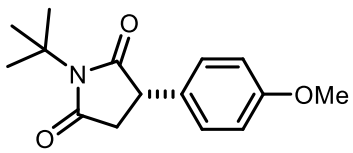
HPLC trace: Daicel chiralcel OD-H, hexane/ *i* -PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 12.9 min (major), t_{R2} = 14.2 min (minor); ee = 93.9%.

L9: t_{R1} = 12.4 min (major), t_{R2} = 13.9 min (minor); ee = 88.0%.



(*S*)-1-(tert-butyl)-3-(4-methoxyphenyl) pyrrolidine-2,5-dione (10l)



Colorless oil. Yield: 72% yield (**L5**); 65% yield (**L9**).

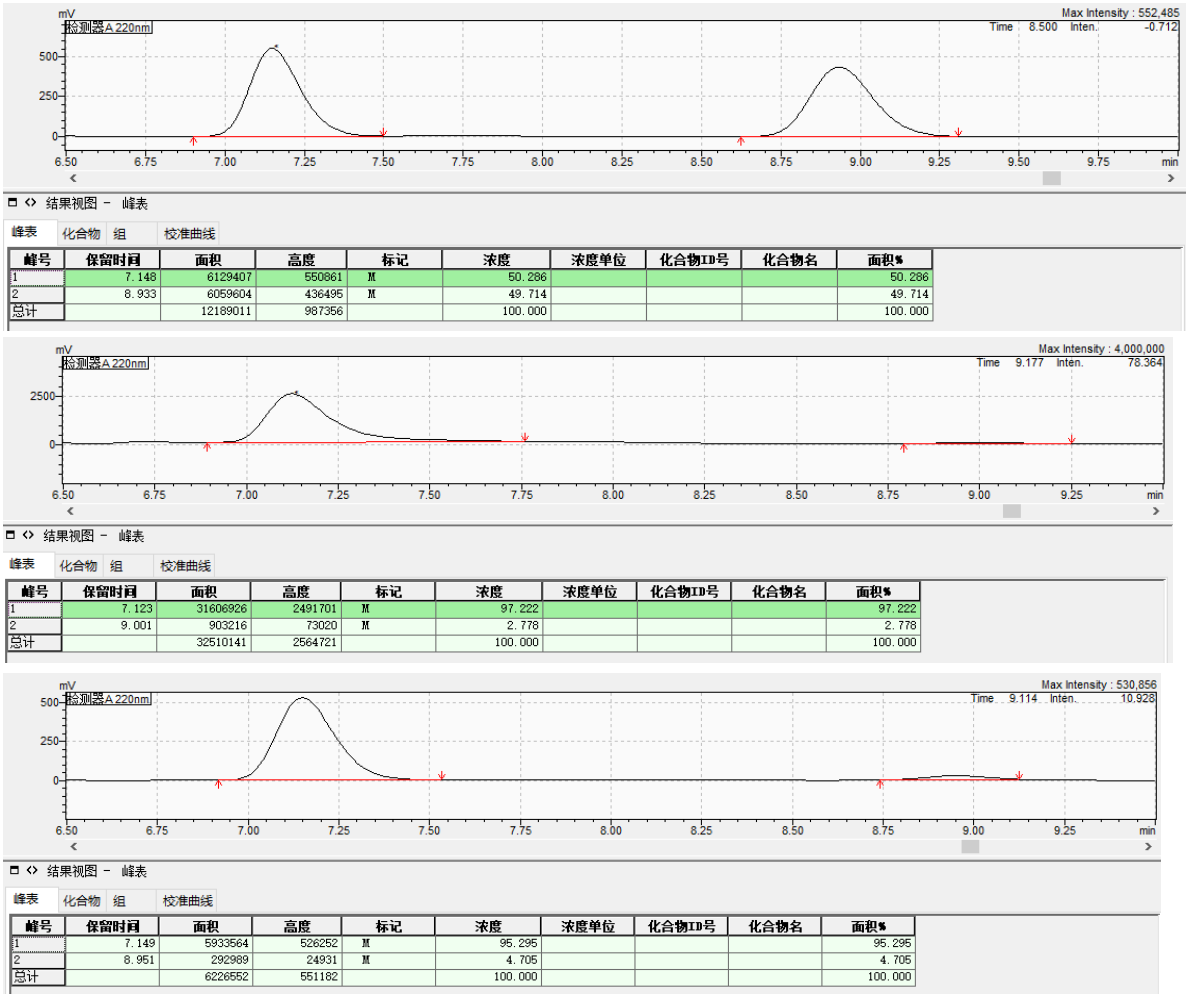
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14-7.11 (m, 2H), 6.91-6.88 (m, 2H), 3.82-3.79 (m, 4H), 3.06 (dd, J_1 = 17.9 Hz, J_2 = 9.8 Hz, 1H), 2.69 (dd, J_1 = 18.3 Hz, J_2 = 4.9 Hz, 1H), 1.60 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 179.3, 177.5, 159.2, 130.0, 128.4, 114.6, 58.6, 55.4, 45.3, 37.6, 28.5.

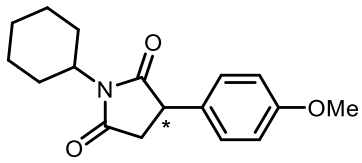
HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 7.1 min (major), t_{R2} = 9.0 min (minor); ee = 94.5%.

L9: t_{R1} = 7.1 min (major), t_{R2} = 9.0 min (minor); ee = 90.6%.



1-cyclohexyl-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10m)



White solid. Yield: 56% yield (**L5**); 72% yield (**L9**).

^{1}H NMR (500 MHz, $CHCl_3$) δ 7.13 – 7.07 (m, 2H), 6.92 – 6.84 (m, 2H), 4.05- 4.02 (m, 1H), 3.88 (dd, J_1 = 9.6 Hz, J_2 = 4.5 Hz, 1H), 3.79 (s, 3H), 3.12 (dd, J_1 = 18.4 Hz, J_2 = 9.6 Hz, 1H), 2.71 (dd, J_1 = 18.4 Hz, J_2 = 4.6 Hz, 1H), 2.26 – 2.09 (m, 2H), 1.82 (m, 2H), 1.63 (m, 3H), 1.34 – 1.21 (m, 3H).

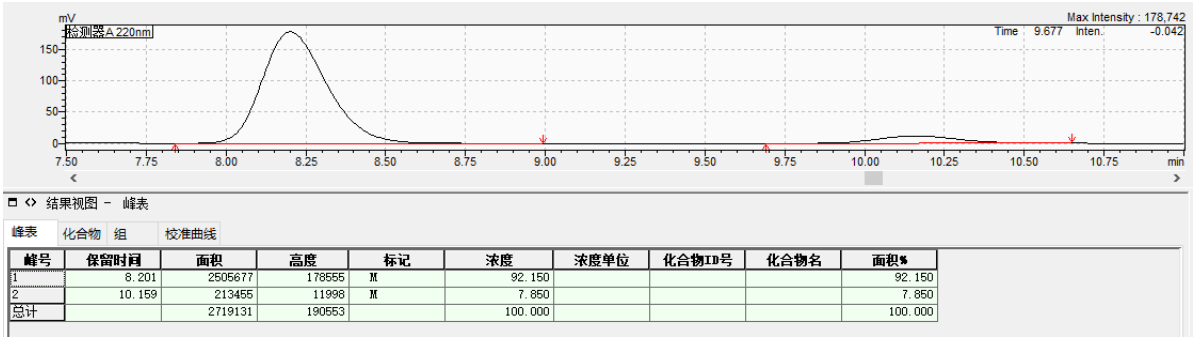
^{13}C NMR (126 MHz, $CHCl_3$) δ 178.3, 176.7, 159.3, 129.8, 128.4, 114.7, 55.4, 52.1, 44.9, 37.3, 29.0, 28.8, 26.0, 25.9, 25.1.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

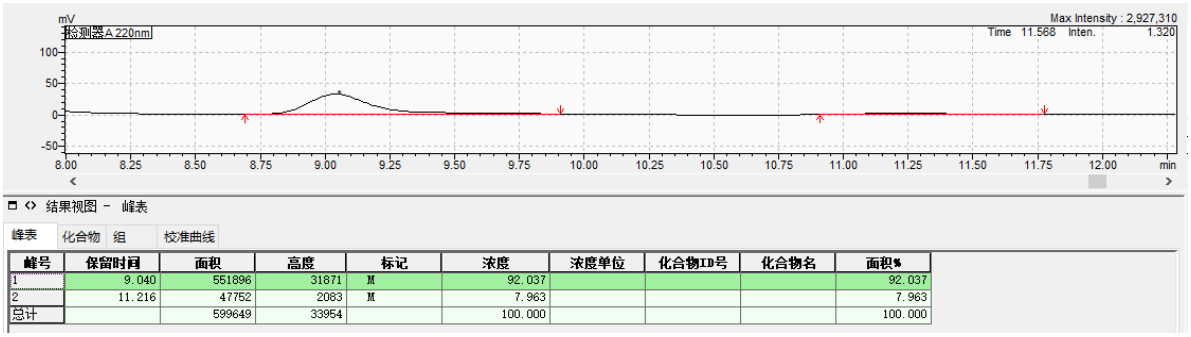
L5: t_{R1} = 8.2 min (minor), t_{R2} = 10.2 min (major); ee = 84.3%.

L9: t_{R1} = 9.0 min (major), t_{R2} = 11.2 min (minor); ee = 84.0%.

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	8.958	13012906	770134	M	49.666				49.666
2	11.109	13187848	645313	M	50.334				50.334
总计		26200753	1415447		100.000				100.000

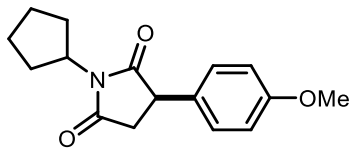


峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	8.201	2505677	178555	M	92.150				92.150
2	10.159	213455	11998	M	7.850				7.850
总计		2719131	190553		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	9.040	551896	31871	M	92.037				92.037
2	11.216	47752	2083	M	7.963				7.963
总计		599649	33954		100.000				100.000

(*R*)-1-cyclopentyl-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10n)



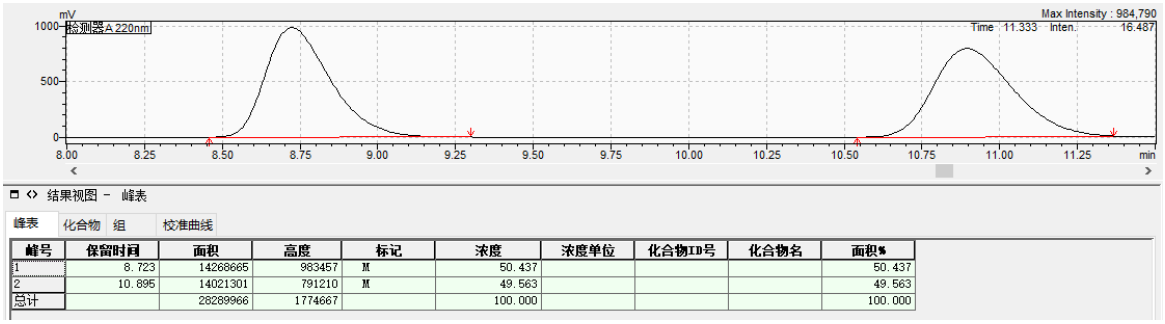
White solid. Yield: 62% yield (**L9**).

^{1}H NMR (500 MHz, $CHCl_3$) δ 7.14 – 7.08 (m, 2H), 6.91 – 6.86 (m, 2H), 4.57-4.50 (m, 1H), 3.88 (dd, J_1 = 9.7 Hz, J_2 = 4.6 Hz, 1H), 3.78 (s, 3H), 3.12 (dd, J_1 = 18.3 Hz, J_2 = 9.7 Hz, 1H), 2.72 (dd, J_1 = 18.3 Hz, J_2 = 4.6 Hz, 1H), 2.01 (m, 2H), 1.93 – 1.79 (m, 4H), 1.64 – 1.51 (m, 2H).

^{13}C NMR (126 MHz, $CHCl_3$) δ 178.3, 176.5, 159.3, 129.6, 128.5, 114.7, 55.4, 51.9, 44.9, 37.2, 28.9, 28.8, 25.4.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.0 mL/min.

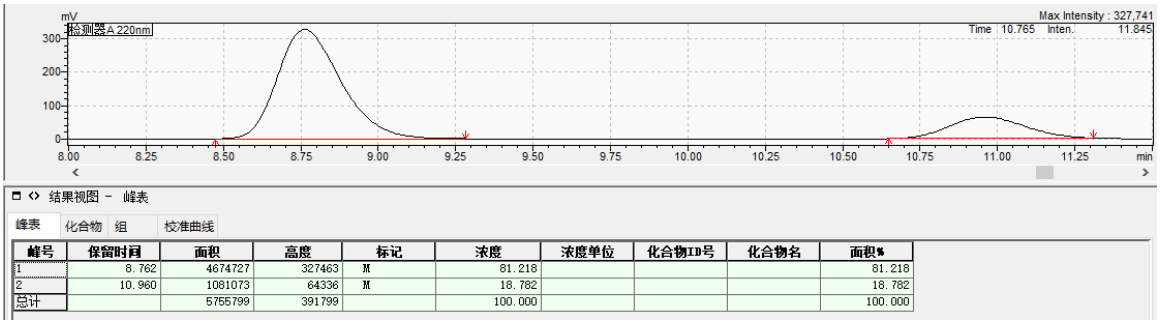
L9: t_{R1} = 8.8 min (major), t_{R2} = 11.0 min (minor); ee = 62.4%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	8.723	14268665	983457	M	50.437				50.437
2	10.895	14021301	791210	M	49.563				49.563
总计		28289966	1774667		100.000				100.000

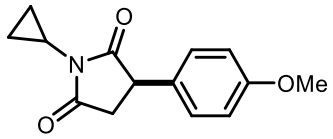


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	8.762	4674727	327463	M	81.218				81.218
2	10.960	1081073	64336	M	18.782				18.782
总计		5755799	391799		100.000				100.000

(*R*)-1-cyclopropyl-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10o)



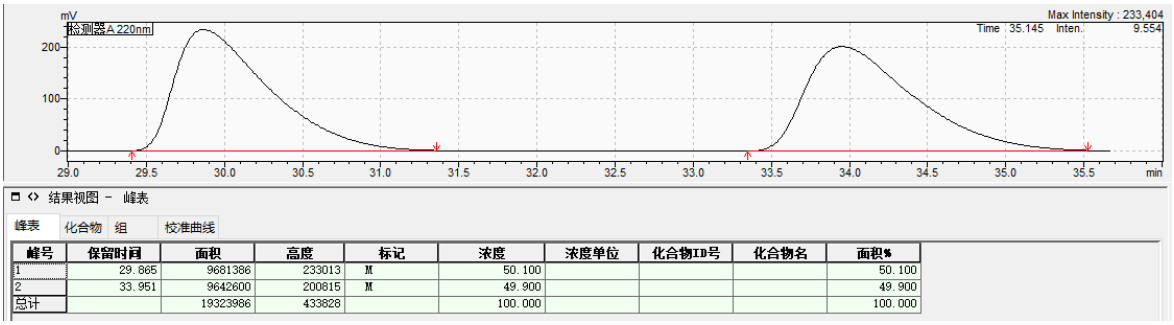
White solid. Yield: 58% yield (**L9**).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 – 7.07 (m, 2H), 6.92 – 6.85 (m, 2H), 3.89 (dd, J_1 = 9.6 Hz, J_2 = 4.8 Hz, 1H), 3.79 (s, 3H), 3.12 (dd, J_1 = 18.5 Hz, J_2 = 10.2 Hz, 1H), 2.73 (dd, J_1 = 18.5 Hz, J_2 = 9.8 Hz, 1H), 2.70 – 2.63 (m, 1H), 1.01 – 0.93 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 176.8, 159.4, 129.3, 128.5, 114.7, 55.5, 44.8, 37.1, 22.7, 5.04, 5.01.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.0 mL/min.

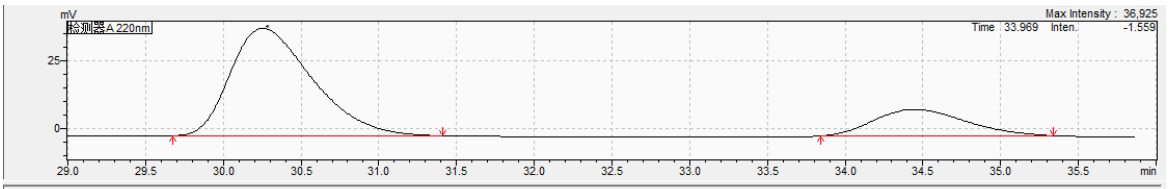
L9: t_{R1} = 30.3 min (major), t_{R2} = 34.4 min (minor); ee = 57.8%.



结果视图 - 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	29.865	9681386	233013	M	50.100				50.100
2	33.951	9642600	200815	M	49.900				49.900
总计		19323986	433828		100.000				100.000

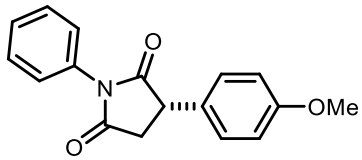


结果视图 - 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	30.253	1448516	39496	M	78.387				78.387
2	34.448	399388	9763	M	21.613				21.613
总计		1847904	49259		100.000				100.000

(*S*)-3-(4-methoxyphenyl)-1-phenylpyrrolidine-2,5-dione (10p)



Yellow solid. Yield: 57% yield (**L5**); 64% yield (**L9**).

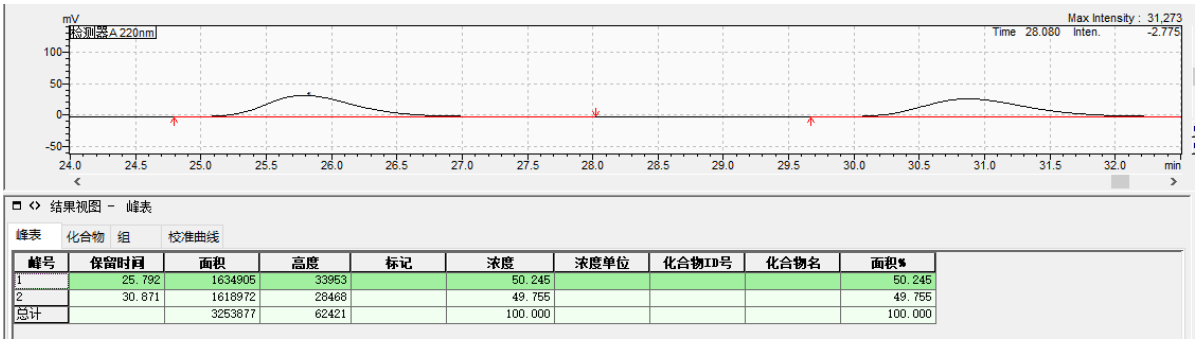
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.46 (m, 2H), 7.42-7.38 (m, 1H), 7.33-7.31 (m, 2H), 7.25-7.21 (m, 2H,), 6.94-6.91 (m, 2H), 4.14 (dd, J_1 = 9.7 Hz, J_2 = 4.8 Hz, 1H), 3.81 (s, 3H), 3.35 (dd, J_1 = 18.5 Hz, J_2 = 9.8 Hz, 1H), 2.96 (dd, J_1 = 18.6 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 177.1, 175.4, 159.4, 132.0, 129.3, 129.1, 128.8, 128.6, 126.6, 114.8, 55.5, 45.3, 37.4.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5*:* t_{R1} = 26.4 min (major), t_{R2} = 31.8 min (minor); ee = 81.4%.

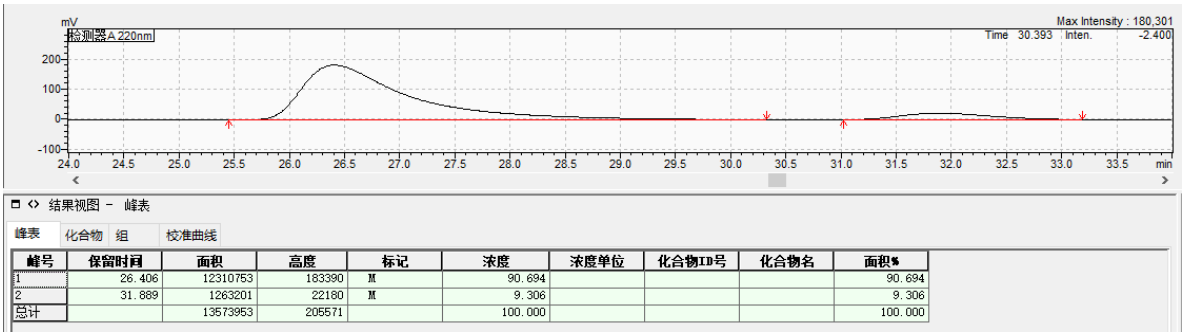
L9: t_{R1} = 25.8 min (major), t_{R2} = 30.9 min (minor); ee = 84.4%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

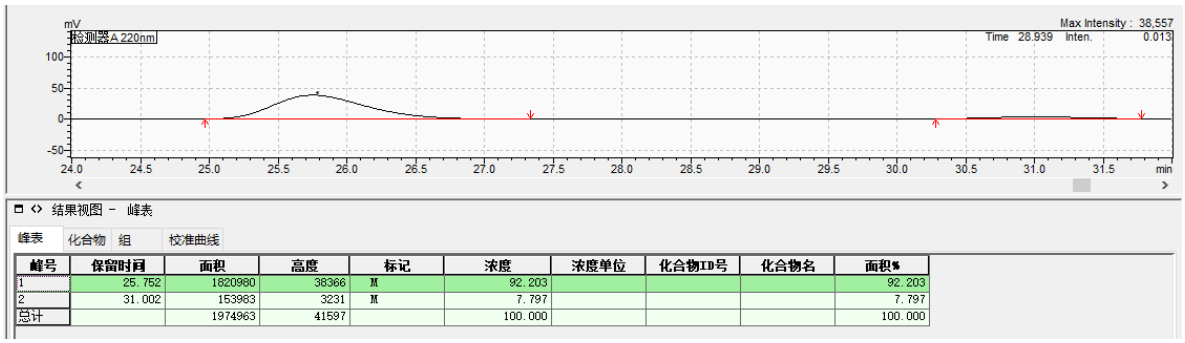
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	25.792	1634905	33953		50.245				50.245
2	30.871	1618972	28468		49.755				49.755
总计		3253877	62421		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	26.406	12310753	183390	M	90.694				90.694
2	31.889	1263201	22180	M	9.306				9.306
总计		13573953	205571		100.000				100.000

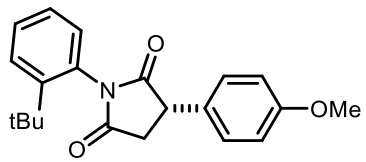


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	25.752	1820980	38366	M	92.203				92.203
2	31.002	153983	3231	M	7.797				7.797
总计		1974963	41597		100.000				100.000

(*S*)-1-(2-(tert-butyl)phenyl)-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10q)



White solid. Yield: 37% yield (**L5**); 48% yield (**L9**).

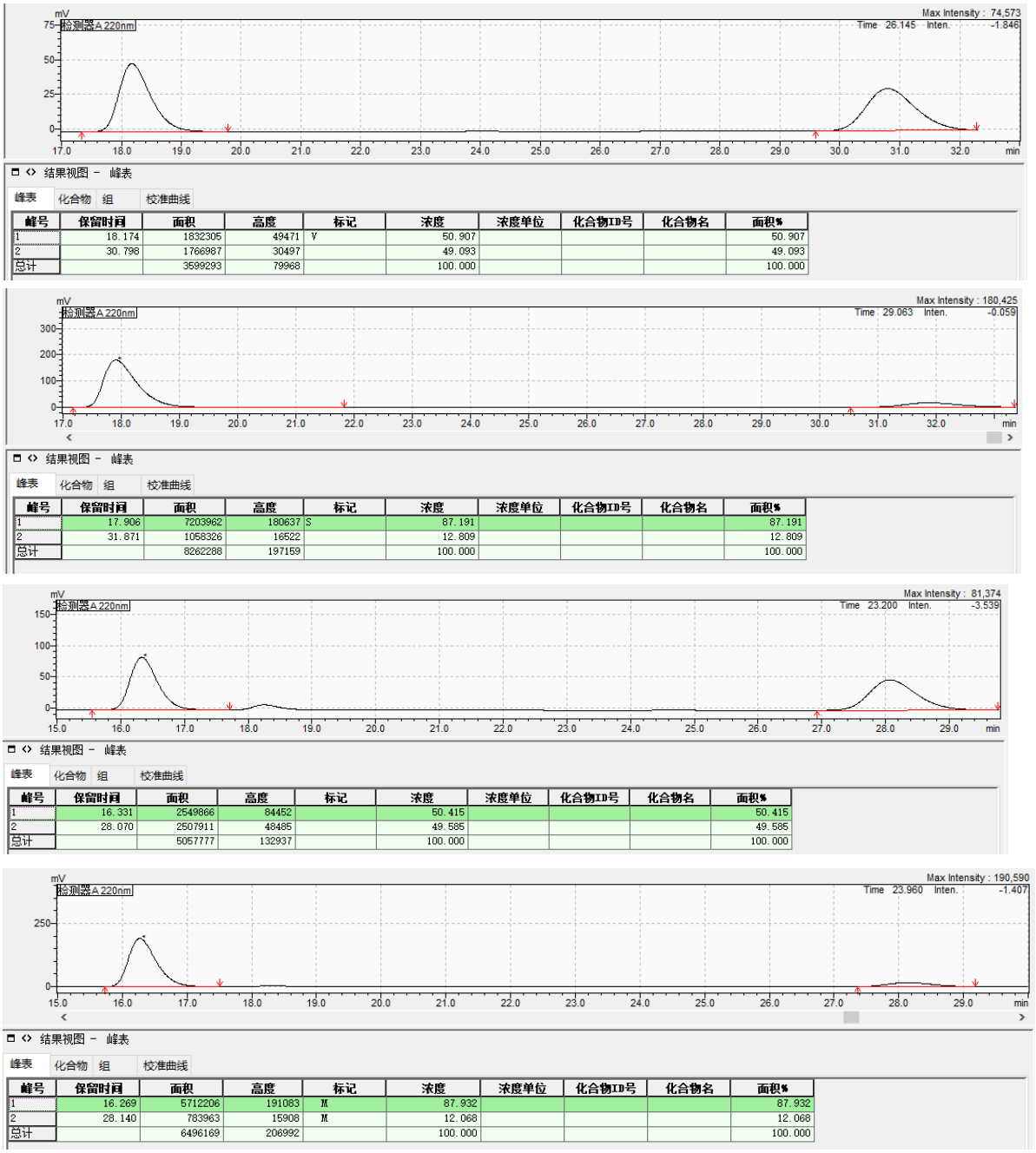
^{1}H NMR (400 MHz, $CHCl_3$) δ 7.58 (dd, J_1 = 8.2 Hz, J_2 = 1.5 Hz, 1H), 7.44 – 7.33 (m, 1H), 7.31 – 7.19 (m, 3H), 6.98 – 6.88 (m, 2H), 6.84 (dd, J_1 = 7.7 Hz, J_2 = 1.5 Hz 1H), 4.13 (dd, J_1 = 9.8 Hz, J_2 = 4.6 Hz, 1H), 3.80 (s, 3H), 3.35 (dd, J_1 = 18.8 Hz, J_2 = 9.6 Hz, 1H), 2.96 (dd, J_1 = 18.6 Hz, J_2 = 4.6 Hz, 1H), 1.33 (s, 9H).

^{13}C NMR (101 MHz, $CHCl_3$) δ 178.2, 176.7, 159.5, 148.2, 130.9, 130.5, 129.9, 129.2, 129.1, 128.7, 127.6, 114.8, 55.5, 45.7, 37.9, 35.8, 31.8.

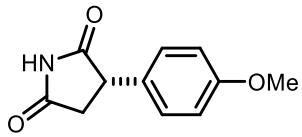
HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 90/10, 220 nm, 1.0 mL/min.

L5: t_{R1} = 17.9 min (major), t_{R2} = 31.9 min (minor); ee = 74.4%.

L9: t_{R1} = 16.3 min (major), t_{R2} = 28.1 min (minor); ee = 75.8%.



(*S*)-3-(4-methoxyphenyl)pyrrolidine-2,5-dione (10r)



White solid. Yield: 56% yield (**L5**); 44% yield (**L9**).

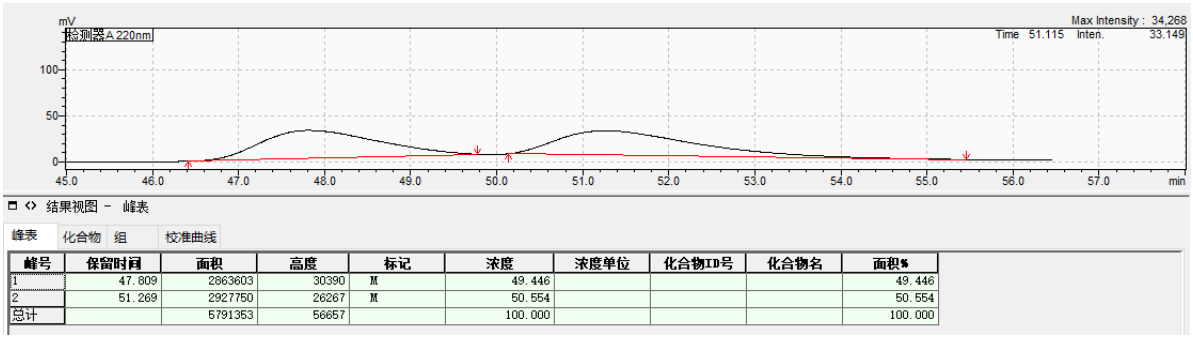
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.21 – 7.10 (m, 2H), 6.98 – 6.80 (m, 2H), 4.04 (dd, J_1 = 9.7 Hz, J_2 = 5.1 Hz, 1H), 3.80 (s, 3H), 3.23 (dd, J_1 = 18.6 Hz, J_2 = 9.6 Hz, 1H), 2.85 (dd, J_1 = 18.6 Hz, J_2 = 5.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.6, 176.6, 159.4, 128.7, 128.6, 114.7, 55.5, 46.7, 38.4.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 90/10, 220 nm, 1.1 mL/min.

L5: t_{R1} = 46.9 min (major), t_{R2} = 58.0 min (minor); ee = 87.0%.

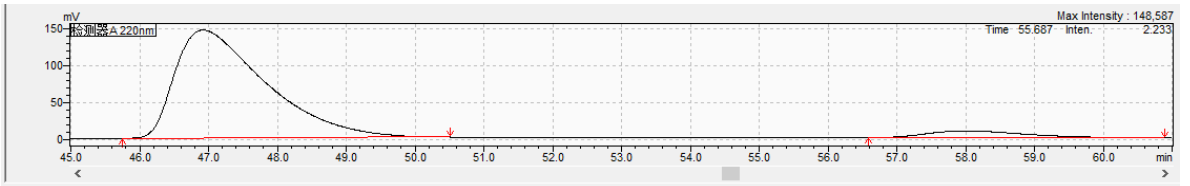
L9: t_{R1} = 48.0 min (minor), t_{R2} = 51.2 min (major); ee = 73.4%.



结果视图 - 峰表

峰表 | 化合物 | 组 | 校准曲线

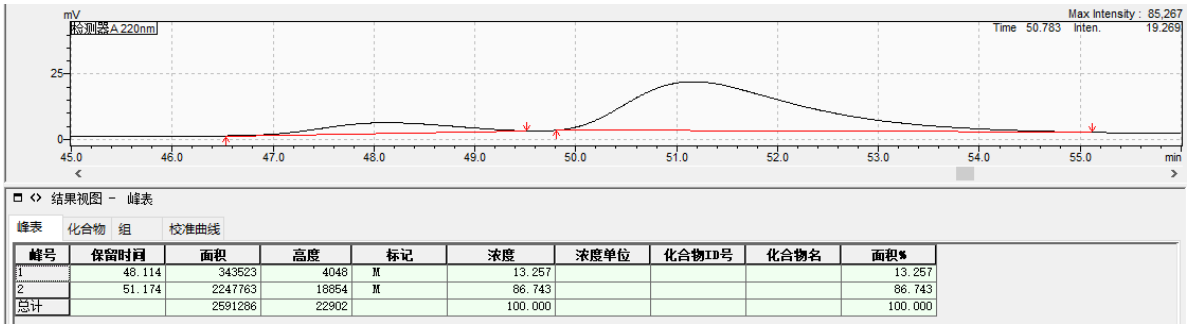
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	47.809	2863603	30390	M	49.446				49.446
2	51.269	2927750	26267	M	50.554				50.554
总计		5791353	56657		100.000				100.000



结果视图 - 峰表

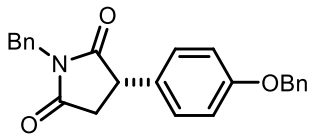
峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	46.918	13361763	146467	M	93.485				93.485
2	57.996	931228	9389	M	6.515				6.515
总计		14292991	155856		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	48.114	343523	4048	M	13.257				13.257
2	51.174	2247763	18854	M	86.743				86.743
总计		2591286	22902		100.000				100.000

(*S*)-1-benzyl-3-(4-(benzyloxy)phenyl)pyrrolidine-2,5-dione (11b)



White solid. Yield: 63% yield (**L5**); 56% yield (**L9**).

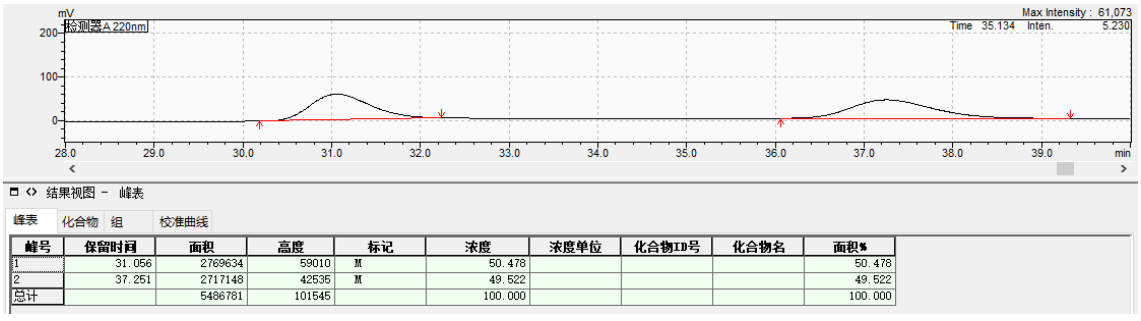
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.32 – 7.22 (m, 6H), 7.14 – 7.09 (m, 2H), 4.76 – 4.60 (m, 2H), 3.97 (dd, J_1= 9.6 Hz, J_2 = 4.7 Hz, 1H), 3.15 (dd, J_1= 18.5 Hz, J_2 = 9.7 Hz, 1H), 2.77 (dd, J_1= 18.0 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 175.9, 137.3, 135.9, 129.3, 128.9, 128.8, 128.2, 128.1, 127.5, 45.9, 42.8, 37.3.

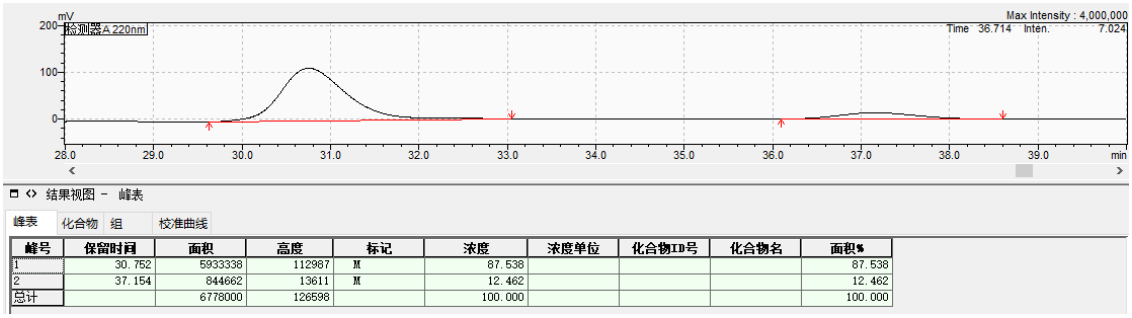
HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 70/30, 220 nm, 1.1 mL/min.

L5: t_{R1} = 30.8 min (minor), t_{R2} = 37.2 min (major); ee = 75.0%.

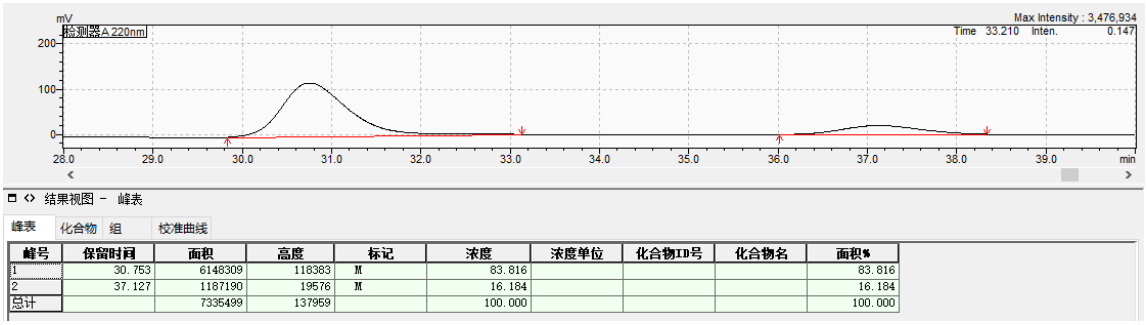
L9: t_{R1} = 30.7 min (minor), t_{R2} = 37.1 min (major); ee = 66.6%.



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	31.056	2769634	59010	M	50.478				50.478
2	37.251	2717148	42535	M	49.522				49.522
总计		5486781	101545		100.000				100.000

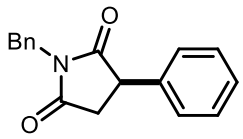


峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	30.752	5933338	112987	M	87.538				87.538
2	37.154	844662	13611	M	12.462				12.462
总计		6778000	126598		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	30.753	6148309	118383	M	83.816				83.816
2	37.127	1187190	19576	M	16.184				16.184
总计		7335499	137959		100.000				100.000

(*R*)-1-benzyl-3-phenylpyrrolidine-2,5-dione (11c)



White solid. Yield: 68% yield (**L5**); 61% yield (**L9**).

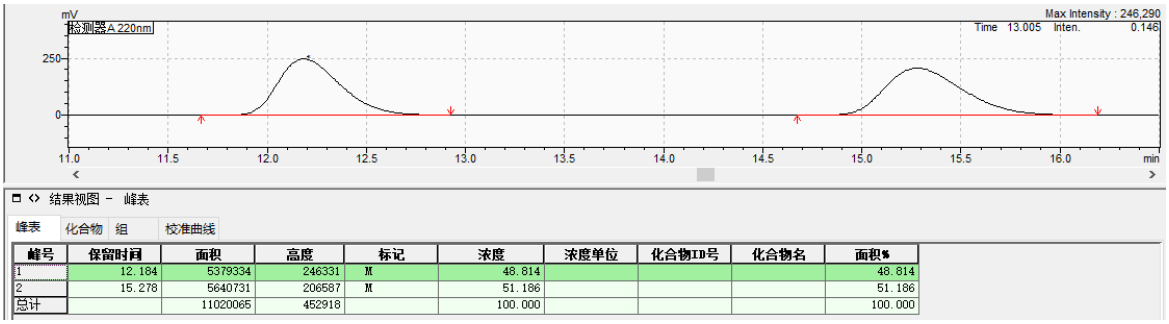
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.39 (m, 2H), 7.36-7.28 (m, 6H), 7.16-7.14 (m, 2H), 4.71 (dd, J_1 = 29.6 Hz, J_2 = 14.2 Hz, 2H), 4.01 (dd, J_1 = 9.8 Hz, J_2 = 4.8 Hz, 1H), 3.20 (dd, J_1 = 18.3 Hz, J_2 = 9.7 Hz, 1H), 2.82 (dd, J_1 = 18.3 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 177.6, 175.9, 137.3, 135.8, 129.3, 129.1, 128.9, 128.8, 128.2, 128.1, 127.5, 46.0, 42.8, 37.3.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 12.2 min (minor), t_{R2} = 15.1 min (major); ee = 64.6%.

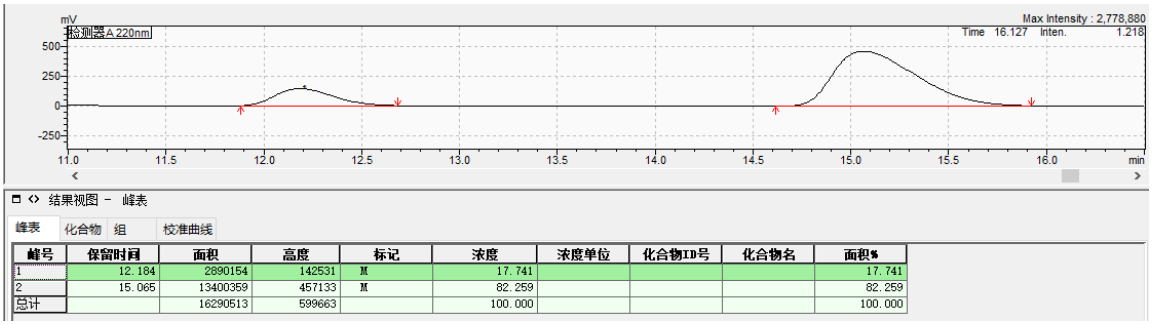
L9: t_{R1} = 12.3 min (minor), t_{R2} = 15.3 min (major); ee = 45.2%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

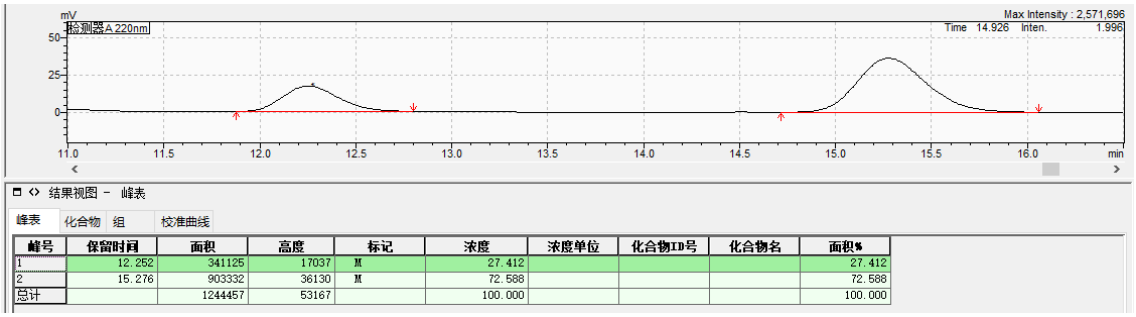
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.184	5379334	246331	M	48.814				48.814
2	15.278	5640731	206587	M	51.186				51.186
总计		11020065	452918		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.184	2890154	142531	M	17.741				17.741
2	15.065	13400359	457133	M	82.259				82.259
总计		16290513	599663		100.000				100.000

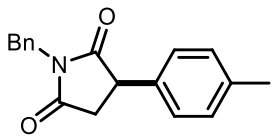


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.252	341125	17037	M	27.412				27.412
2	15.276	903332	36130	M	72.588				72.588
总计		1244457	53167		100.000				100.000

(*R*)-1-benzyl-3-(*p*-tolyl)pyrrolidine-2,5-dione (11d)



White solid. Yield: 57% yield (**L5**); 48% yield (**L9**).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.39 (m, 2H), 7.34-7.29 (m, 3H), 7.14 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 4.73 (dd, J_1 = 29.8 Hz, J_2 = 14.0 Hz, 2H), 3.98 (dd, J_1 = 9.6 Hz, J_2 = 4.6 Hz, 1H), 3.19 (dd, J_1 = 18.5 Hz, J_2 = 9.3 Hz, 1H), 2.80 (dd, J_1 = 18.7 Hz, J_2 = 5.0 Hz, 1H).

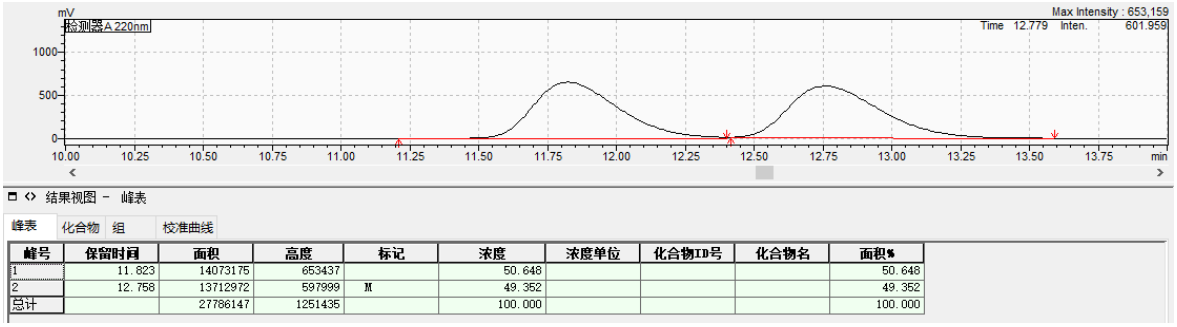
^{13}C NMR (126 MHz, $CDCl_3$): δ 177.8, 176.1, 137.9, 135.9, 134.2, 130.0, 128.9, 128.8, 128.1,

127.3, 45.6, 42.8, 37.3, 21.2.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 11.9 min (minor), t_{R2} = 12.8 min (major); ee = 84.0%.

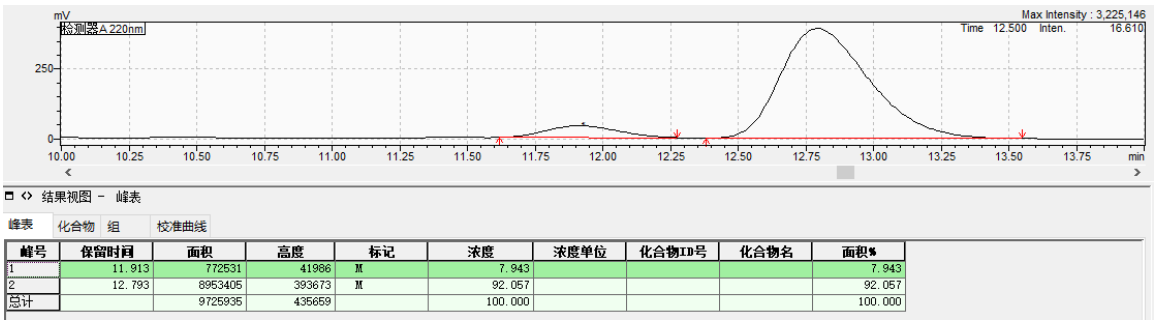
L9: t_{R1} = 11.9 min (minor), t_{R2} = 12.8 min (major); ee = 56.8%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

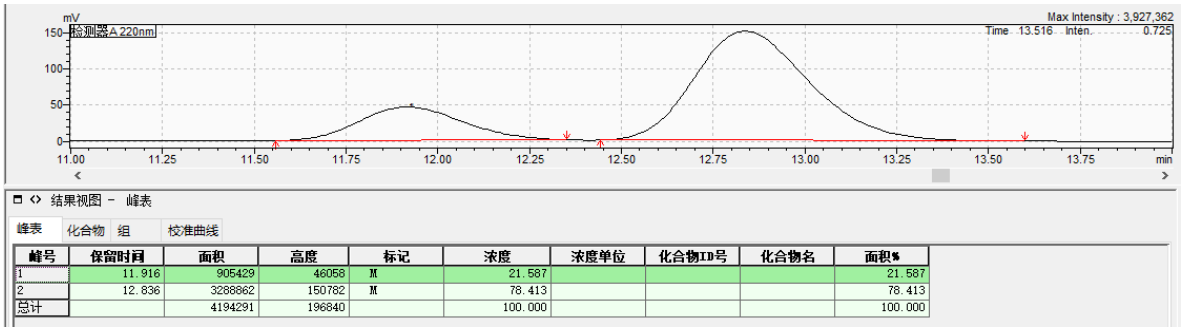
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	11.823	14073175	653437		50.648				50.648
2	12.758	13712972	597999	M	49.352				49.352
总计		27786147	1251435		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	11.913	772531	41986	M	7.943				7.943
2	12.793	8953405	393673	M	92.057				92.057
总计		9725935	435659		100.000				100.000

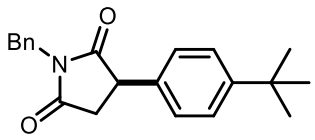


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	11.916	905429	46058	M	21.587				21.587
2	12.836	3288862	150782	M	78.413				78.413
总计		4194291	196840		100.000				100.000

(*R*)-1-benzyl-3-(4-(tert-butyl)phenyl)pyrrolidine-2,5-dione (11e)



White solid. Yield: 54% yield (**L5**); 46% yield (**L9**).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.38 – 7.28 (m, 5H), 7.12 – 7.07 (m, 2H), 4.89 – 4.60 (m, 2H), 4.00 (dd, J_1 = 9.5 Hz, J_2 = 4.8 Hz, 1H), 3.18 (dd, J_1 = 18.6 Hz, J_2 = 9.5 Hz, 1H), 2.82 (dd, J_1 = 18.6 Hz, J_2 = 4.7 Hz, 1H), 1.30 (s, 9H).

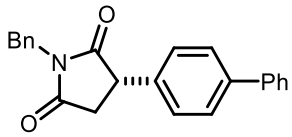
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.8, 176.1, 151.0, 135.9, 134.1, 128.9, 128.8, 128.1, 127.1, 126.3, 45.6, 42.8, 37.3, 34.7, 31.4.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 9.6 min (minor), t_{R2} = 11.4 min (major); ee = 75.2%.

L9: t_{R1} = 9.6 min (minor), t_{R2} = 11.4 min (major); ee = 46.6%.

(*S*)-3-([1,1'-biphenyl]-4-yl)-1-benzylpyrrolidine-2,5-dione (11f)



White solid. Yield: 78% yield (**L5**); 82% yield (**L9**).

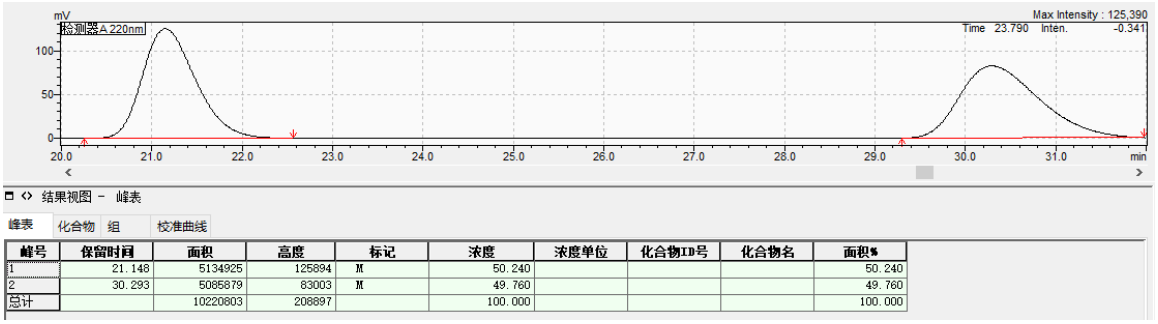
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 4H), 7.50 – 7.39 (m, 4H), 7.39 – 7.27 (m, 4H), 7.26 – 7.22 (m, 2H), 4.86 – 4.65 (m, 2H), 4.07 (dd, J_1 = 9.5 Hz, J_2 = 4.8 Hz, 1H), 3.24 (dd, J_1 = 18.5 Hz, J_2 = 9.6 Hz, 1H), 2.87 (dd, J_1 = 18.5 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 175.9, 141.1, 140.5, 136.2, 135.9, 129.0, 128.9, 128.9, 128.2, 128.1, 127.9, 127.7, 127.2, 45.7, 42.9, 37.3.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 21.2 min (major), t_{R2} = 30.5 min (minor); ee = 54.0%.

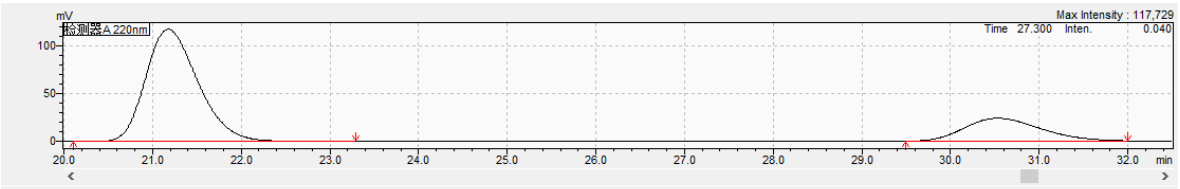
L9: t_{R1} = 21.2 min (major), t_{R2} = 30.5 min (minor); ee = 61.4%.



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

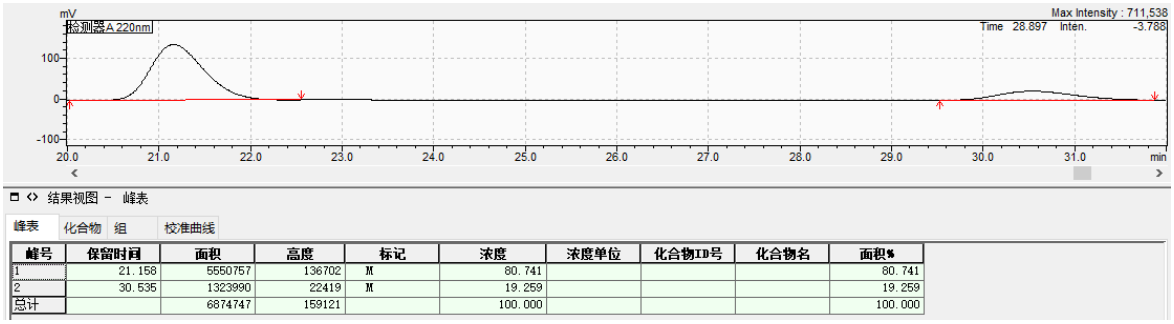
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	21.148	5134925	125894	M	50.240				50.240
2	30.293	5085879	83003	M	49.760				49.760
总计		10220803	208897		100.000				100.000



结果视图 – 峰表

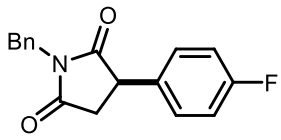
峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	21.176	4808366	117582	M	77.067				77.067
2	30.533	1430816	23974	M	22.933				22.933
总计		6239182	141556		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	21.158	5550757	136702	M	80.741				80.741
2	30.535	1323990	22419	M	19.259				19.259
总计		6874747	159121		100.000				100.000

(*R*)-1-benzyl-3-(4-fluorophenyl)pyrrolidine-2,5-dione (11g)



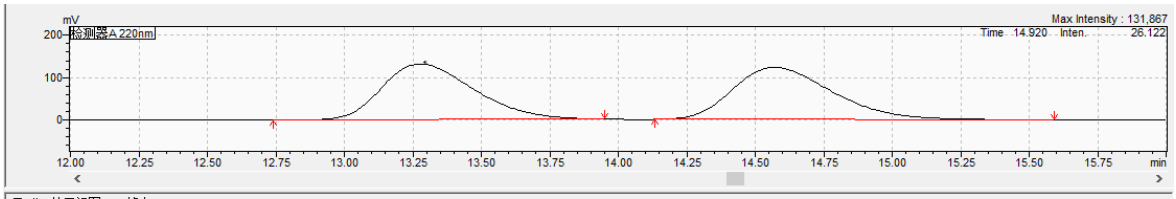
White solid. Yield: 49% yield (**L9**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.37 (m, 2H), 7.37 – 7.27 (m, 3H), 7.18 – 7.09 (m, 2H), 7.08 – 6.98 (m, 2H), 4.80 – 4.62 (m, 2H), 4.01 (dd, J_1 = 9.6 Hz, J_2 = 4.9 Hz, 1H), 3.20 (dd, J_1 = 18.5 Hz, J_2 = 9.6 Hz, 1H), 2.78 (dd, J_1 = 18.5 Hz, J_2 = 4.8 Hz, 1H).

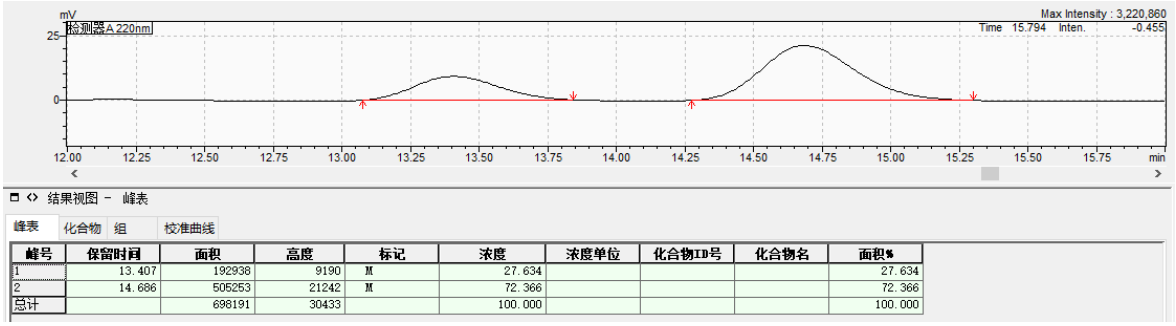
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 175.6, 162.5 (d, J = 63.7 Hz), 135.8, 132.9 (d, J = 3.4 Hz), 129.1 (d, J = 8.2 Hz), 128.9, 128.8, 128.2, 116.3 (d, J = 15.7 Hz), 45.2, 42.9, 37.2.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L9: t_{R1} = 13.4 min (minor), t_{R2} = 14.7 min (major); ee = 44.8%.

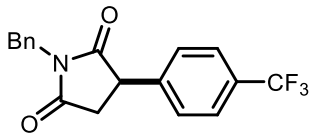


峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	13.277	3070371	131902	M	49.675				49.675
2	14.570	3110502	123521	M	50.325				50.325
总计		6180873	255423		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	13.407	192938	9190	M	27.634				27.634
2	14.686	505253	21242	M	72.366				72.366
总计		698191	30433		100.000				100.000

(*R*)-1-benzyl-3-(4-(trifluoromethyl)phenyl)pyrrolidine-2,5-dione (11h)



White solid. Yield: 46% yield (**L5**); 37% yield (**L9**)

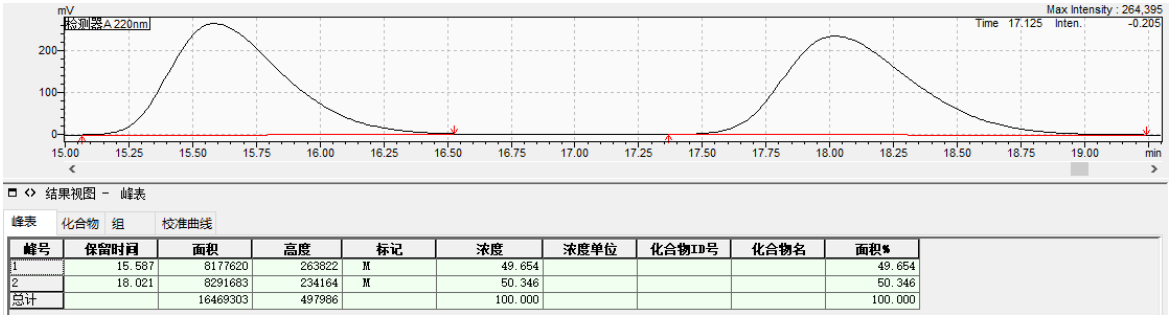
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 2H), 7.36 (dd, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 2H), 7.33 – 7.23 (m, 5H), 4.75 – 4.62 (m, 2H), 4.05 (dd, J_1 = 9.6 Hz, J_2 = 4.9 Hz, 1H), 3.20 (dd, J_1 = 18.5 Hz, J_2 = 9.6 Hz, 1H), 2.77 (dd, J_1 = 18.5 Hz, J_2 = 4.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 175.3, 141.1, 135.7, 130.4 (d, J = 251.2 Hz), 128.9 (d, J = 115.0 Hz), 128.32, 128.01, 126.3 (dd, J_1 = 77.1 Hz, J_2 = 38.6 Hz), 125.0, 122.9, 45.7, 43.0, 36.9.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 15.8 min (major), t_{R2} = 18.2 min (minor); ee = 46.4%.

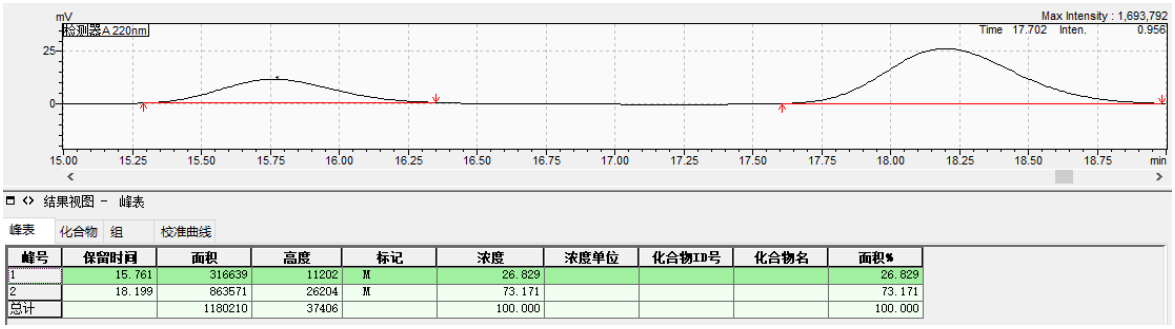
L9: t_{R1} = 15.7 min, t_{R2} = 18.2 min; ee = 0.



结果视图 – 峰表

峰表 化合物 组 校准曲线

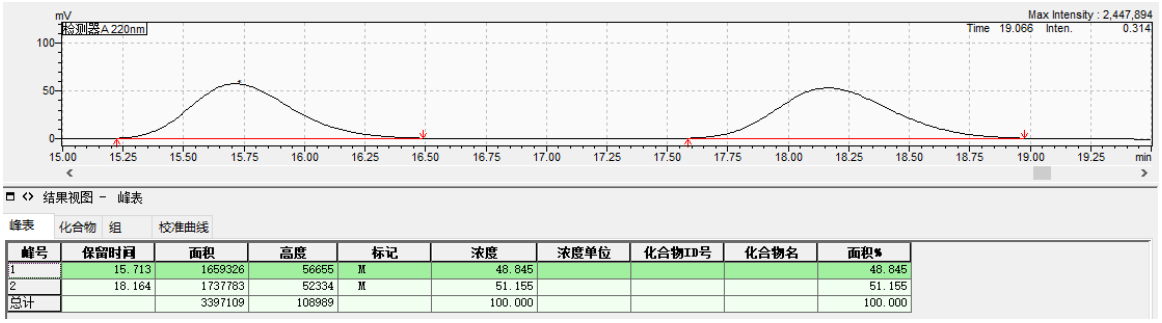
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.587	8177620	263822	M	49.654				49.654
2	18.021	8291683	234164	M	50.346				50.346
总计		16469303	497986		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.761	316639	11202	M	26.829				26.829
2	18.199	863571	26204	M	73.171				73.171
总计		1180210	37406		100.000				100.000

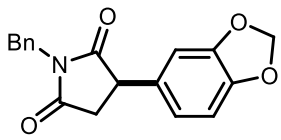


结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.713	1659326	56655	M	48.845				48.845
2	18.164	1737783	52334	M	51.155				51.155
总计		3397109	108989		100.000				100.000

(*R*)-3-(benzo[d][1,3]dioxol-5-yl)-1-benzylpyrrolidine-2,5-dione (11i)



White solid. Yield: 40% yield **(L5)**; 45% yield (**L9**)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.33 (m, 2H), 7.32 – 7.23 (m, 3H), 6.79 – 6.66 (m, 1H), 6.62 – 6.51 (m, 2H), 5.90 (s, 2H), 4.75 – 4.59 (m, 2H), 3.88 (dd, J_1 = 9.5 Hz, J_2 = 4.8 Hz, 1H), 3.13 (dd, J_1 = 18.5 Hz, J_2 = 9.5 Hz, 1H), 2.71 (dd, J_1 = 18.5 Hz, J_2 = 4.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 175.8, 148.4, 147.5, 135.8, 130.8, 128.9, 128.8, 128.2, 120.9, 108.9, 107.8, 101.4, 45.7, 42.8, 37.4.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

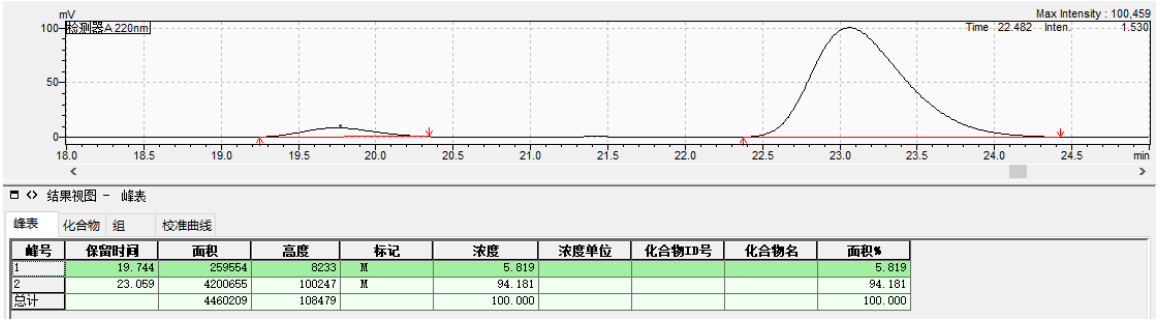
L5: t_{R1} = 19.7 min (minor), t_{R2} = 23.1 min (major); ee = 88.4%.

L9: t_{R1} = 19.6 min (minor), t_{R2} = 23.0 min (major); ee = 59.6%.

结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.567	3428723	96873	M	49.944				49.944
2	23.035	3436464	82389	M	50.056				50.056
总计		6865187	179261		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

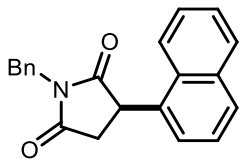
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.744	259554	8233	M	5.819				5.819
2	23.059	4200655	100247	M	94.181				94.181
总计		4460209	108479		100.000				100.000

结果视图 – 峰表

峰表 化合物 组 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.562	27872	896	M	20.205				20.205
2	22.962	110074	2729	M	79.795				79.795
总计		137946	3625		100.000				100.000

(*R*)-1-benzyl-3-(naphthalen-1-yl)pyrrolidine-2,5-dione (11j)



White solid. Yield: 42% yield (**L5**); 55% yield (**L9**)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, J_1 = 8.1 Hz, J_2 = 1.4 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 8.5 Hz, 1H), 7.55 – 7.47 (m, 3H), 7.47 – 7.31 (m, 5H), 7.21 (dd, J_1 = 7.1

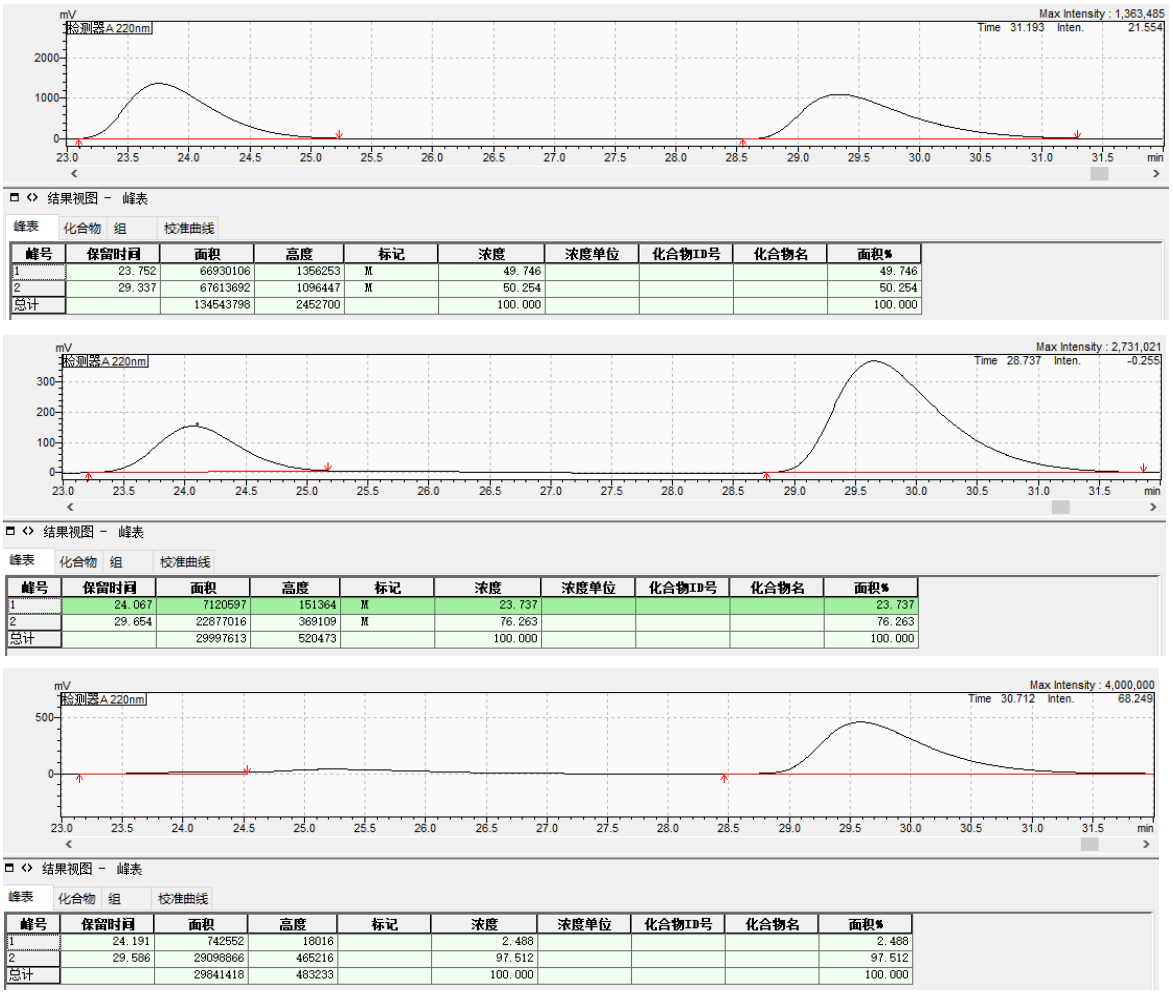
Hz, J_2 = 1.2 Hz, 1H), 4.83 (dd, J_1 = 13.8 Hz, J_2 = 2.3 Hz, 2H), 4.70 (dd, J_1 = 9.7 Hz, J_2 = 5.0 Hz, 1H), 3.35 (dd, J_1 = 18.5 Hz, J_2 = 9.7 Hz, 1H), 2.82 (dd, J_1 = 18.5 Hz, J_2 = 5.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 175.8, 148.4, 147.5, 135.8, 130.8, 128.9, 128.8, 128.2, 120.9, 108.9, 107.8, 101.4, 45.7, 42.8, 37.4.

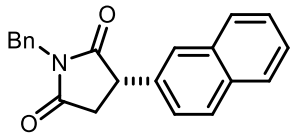
HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 24.0 min (minor), t_{R2} = 29.7 min (major); ee = 52.6%.

L9: t_{R1} = 24.2 min (minor), t_{R2} = 29.6 min (major); ee = 95.0%.



(*S*)-1-benzyl-3-(naphthalen-2-yl)pyrrolidine-2,5-dione (11k)



White solid. Yield: 54% yield (**L5**); 47% yield (**L9**)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 2H), 7.82 – 7.76 (m, 1H), 7.66 (d, J = 1.8 Hz, 1H), 7.56 – 7.47 (m, 4H), 7.42 – 7.33 (m, 3H), 7.25 (dd, J_1 = 8.5 Hz, J_2 = 1.9 Hz, 1H), 4.81 (dd, J_1 = 28.5 Hz, J_2 = 14.1 Hz, 2H), 4.17 (dd, J_1 = 9.5 Hz, J_2 = 4.7 Hz, 1H), 3.26 (dd, J_1 = 18.5 Hz, J_2 = 9.6 Hz, 1H), 2.92 (dd, J_1 = 18.5 Hz, J_2 = 4.7 Hz, 1H).

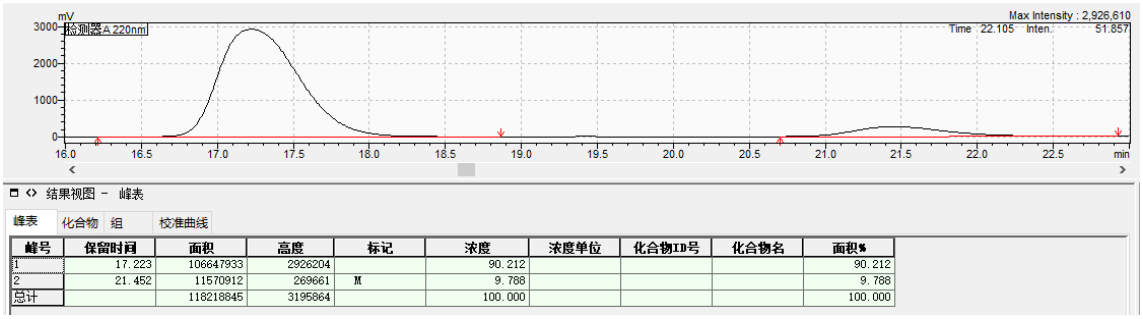
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 175.9, 135.9, 134.6, 133.4, 132.8, 129.3, 128.9, 128.8, 128.1, 127.8, 127.7, 126.6, 126.6, 126.4, 124.8, 46.0, 42.8, 37.2.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

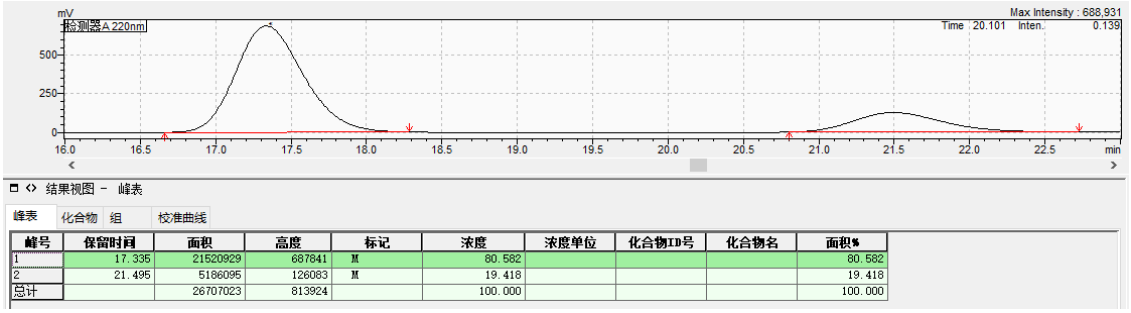
L5: t_{R1} = 17.2 min (major), t_{R2} = 21.5 min (minor); ee = 80.4%.

L9: t_{R1} = 17.1 min (major), t_{R2} = 21.5 min (minor); ee = 61.2%.

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.371	5127958	164701	M	50.112				50.112
2	21.497	5105131	123195	M	49.888				49.888
总计		10233089	287896		100.000				100.000

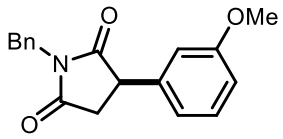


峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.223	106647933	2926204		90.212				90.212
2	21.452	11570912	269661	M	9.788				9.788
总计		118218845	3195864		100.000				100.000



峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	17.335	21520929	687841	M	80.582				80.582
2	21.495	5186095	126083	M	19.418				19.418
总计		26707023	813924		100.000				100.000

(*R*)-1-benzyl-3-(3-methoxyphenyl)pyrrolidine-2,5-dione (11l)



White solid. Yield: 58% yield (**L5**); 66% yield **(L9**)

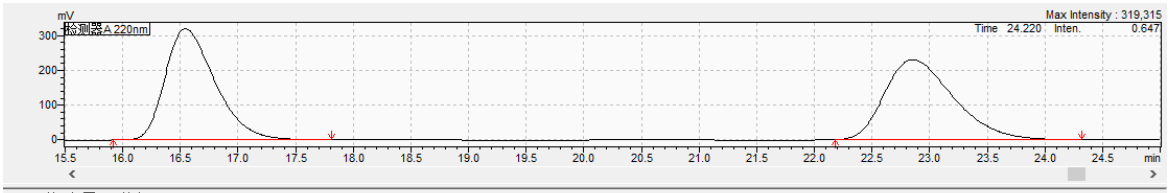
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 2H), 7.27 – 7.09 (m, 4H), 6.74 (dd, J_1 = 8.1 Hz, J_2 = 2.5 Hz, 1H), 6.68 – 6.60 (m, 1H), 6.57 (t, J = 2.2 Hz, 1H), 4.72 – 4.52 (m, 2H), 3.88 (dd, J_1 = 9.5 Hz, J_2 = 4.6 Hz 1H), 3.64 (s, 3H), 3.09 (dd, J_1 = 18.5 Hz, J_2 = 9.5 Hz, 1H), 2.71 (dd, J_1 = 18.5 Hz, J_2 = 4.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 175.9, 160.2, 138.8, 135.9, 130.4, 128.9, 128.8, 128.1, 119.6, 113.5, 113.2, 55.3, 46.0, 42.8, 37.3.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

L5: t_{R1} = 16.6 min (minor), t_{R2} = 22.8 min (major); ee = 37.6%.

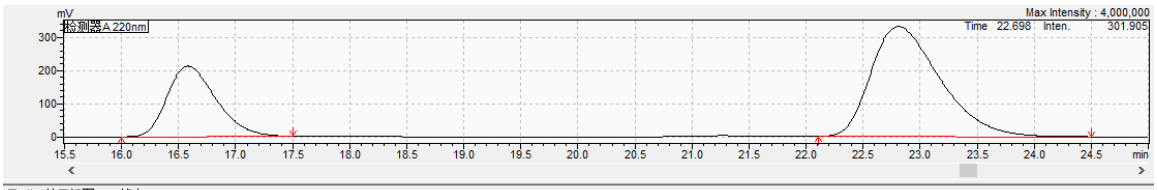
L9: t_{R1} = 16.6 min (minor), t_{R2} = 22.8 min (major); ee = 45.6%.



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

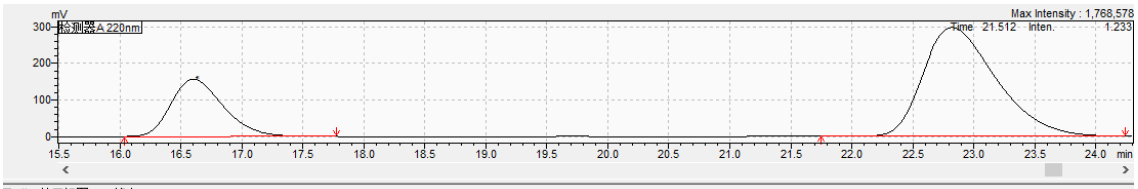
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	16.545	9628609	319514	M	50.162				50.162
2	22.853	9566604	230628	M	49.838				49.838
总计		19195213	550142		100.000				100.000



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	16.582	6323563	213091	M	31.155				31.155
2	22.810	13973507	332295	M	68.845				68.845
总计		20297070	545386		100.000				100.000

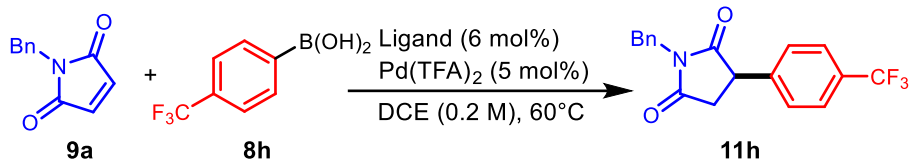


结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

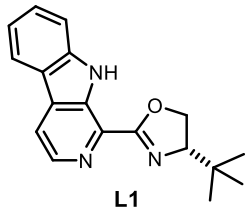
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	16.603	4626873	156533	M	27.159				27.159
2	22.825	12409629	297313	M	72.841				72.841
总计		17036502	453846		100.000				100.000

7. Heterocycle-oxazolines for Asymmetric Synthesis of 11h

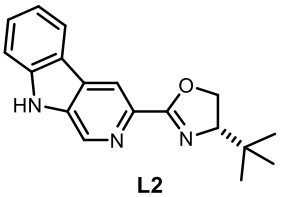


9a 8h 11h

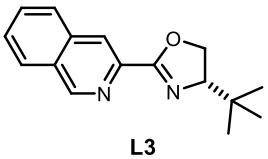
Ligand Screening



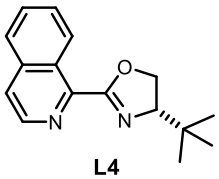
L1
16% yield, 55% ee



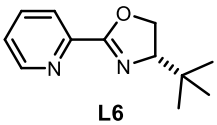
L2
N.D.



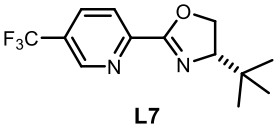
L3
45% yield, < 10% ee



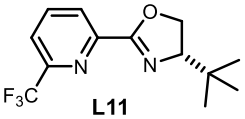
L4
28% yield, 32% ee



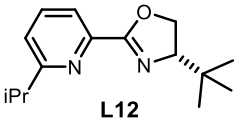
L6
17% yield, 61% ee



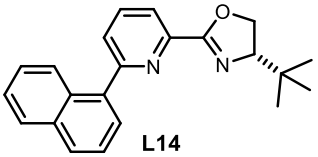
L7
N.D.



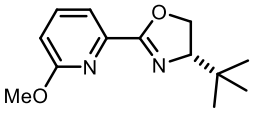
L11
10% yield, < 10% ee



L12
25% yield, 13% ee

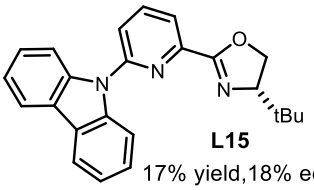


L14
17% yield, < 10% ee

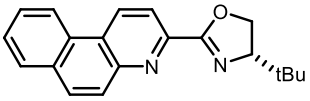


L21
25% yield, 25% ee

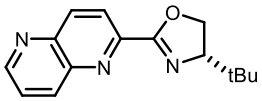
New heterocycle-oxazolines Ligand



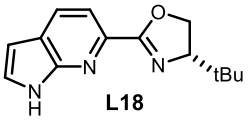
L15
17% yield,18% ee



L16
52% yield, 0 ee



L17
29% yield, 0 ee

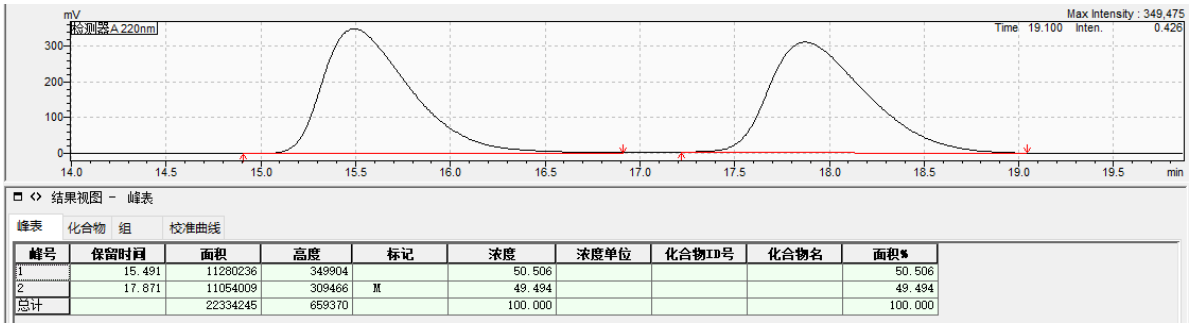


L18
38% yield, 83% ee
48% yield [b], 83% ee

a, unless otherwise mentioned, the yields referred to HPLC yield. The ee values were determined by HPLC analysis on a chiral phase. b, Isolated yield. N.D. = not detected.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.1 mL/min.

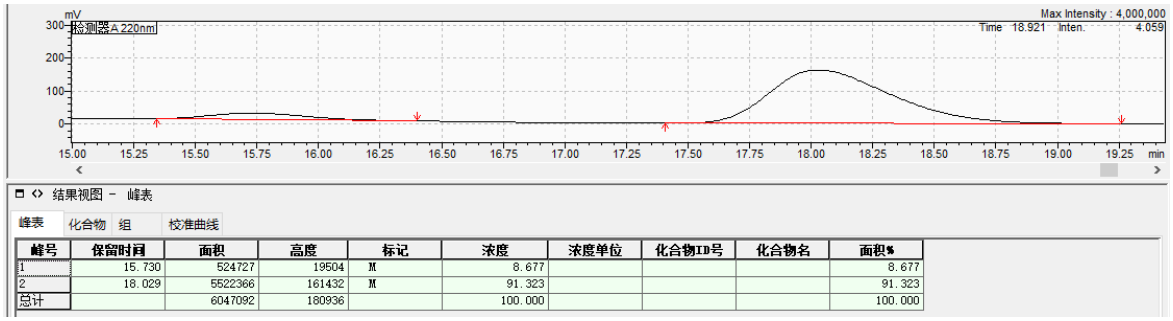
L18: t_{R1} = 15.7 min (minor), t_{R2} = 18.0 min (major); ee = 82.7%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

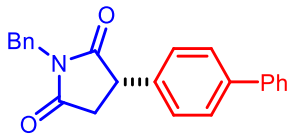
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.491	11280236	349904		50.506				50.506
2	17.871	11054009	309466	M	49.494				49.494
总计		22334245	659370		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

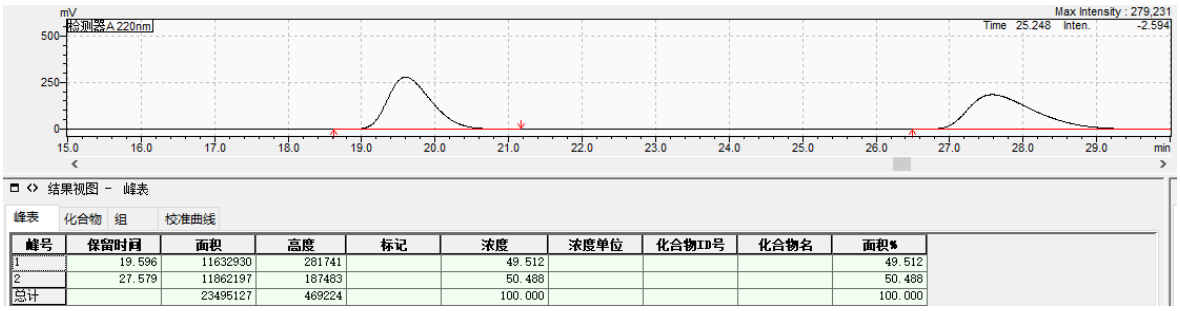
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.730	524727	19504	M	8.677				8.677
2	18.029	5522366	161432	M	91.323				91.323
总计		6047092	180936		100.000				100.000



11f: 76% isolated yield.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.2 mL/min.

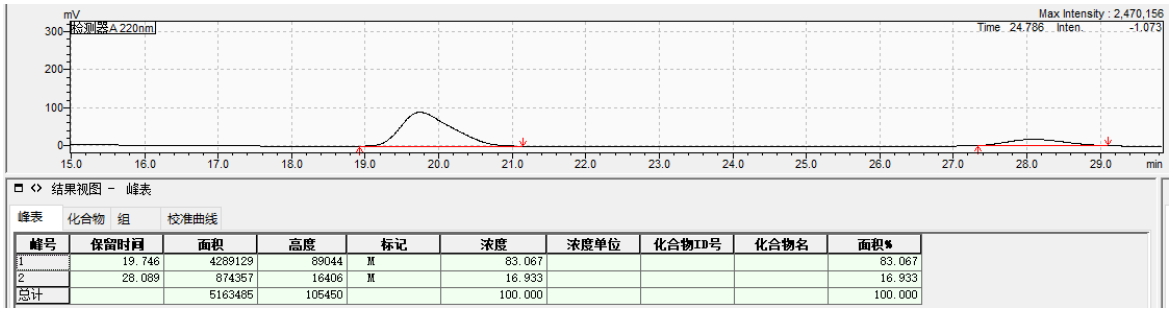
L18: t_{R1} = 19.7 min (major), t_{R2} = 28.1 min (minor); ee = 66.0%.



结果视图 – 峰表

峰表 化合物 组 校准曲线

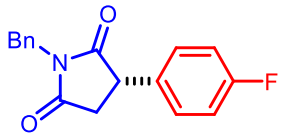
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.596	11632930	281741		49.512				49.512
2	27.579	11862197	187483		50.488				50.488
总计		23495127	469224		100.000				100.000



结果视图 – 峰表

峰表 化合物 组 校准曲线

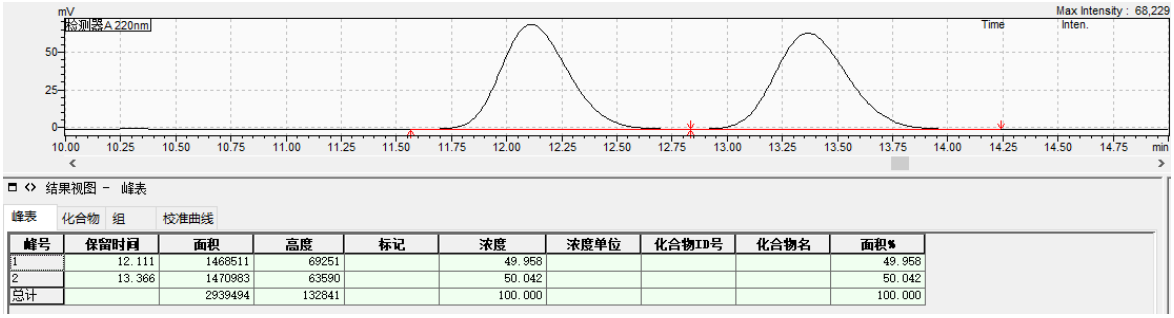
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	19.746	4289129	89044	M	83.067				83.067
2	28.089	874357	16406	M	16.933				16.933
总计		5163485	105450		100.000				100.000



11g： 58% isolated yield.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.2 mL/min.

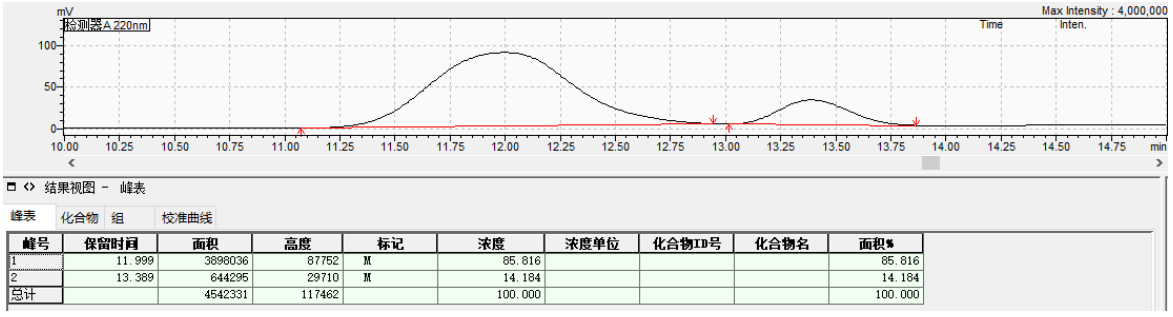
L18: t_{R1} = 12.0 min (major), t_{R2} = 13.4 min (minor); ee = 71.6%.



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

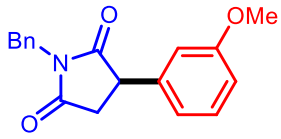
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	12.111	1468511	69251		49.958				49.958
2	13.366	1470983	63590		50.042				50.042
总计		2939494	132841		100.000				100.000



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

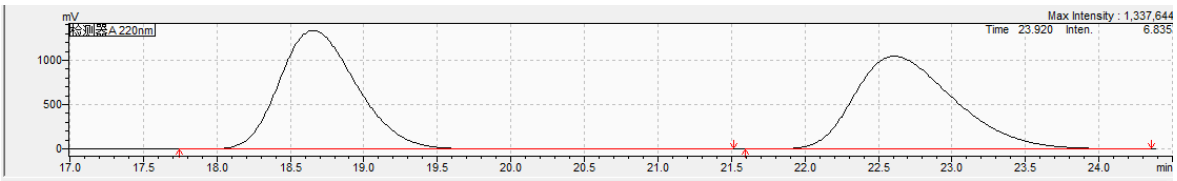
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	11.999	3898036	87752	M	85.816				85.816
2	13.389	644295	29710	M	14.184				14.184
总计		4542331	117462		100.000				100.000



11l： 53% isolated yield.

HPLC trace: Daicel chiralcel OD-H, hexane/*i*-PrOH = 80/20, 220 nm, 1.2 mL/min.

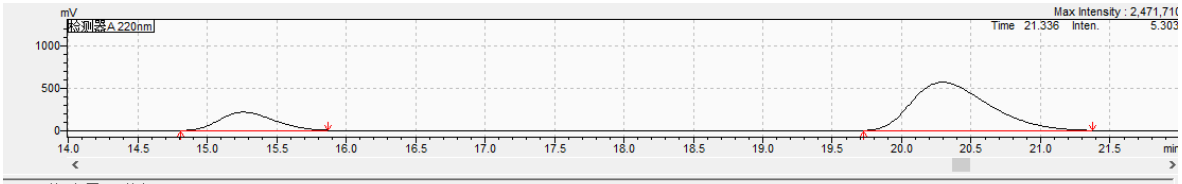
L18: t_{R1} = 15.3 min (minor), t_{R2} = 20.3 min (major); ee = 57.6%.



结果视图 – 峰表

峰表 | 化合物 | 组 | 校准曲线

峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	18.654	48985574	1341065		49.820				49.820
2	22.608	49339544	1048541		50.180				50.180
总计		98325118	2389605		100.000				100.000

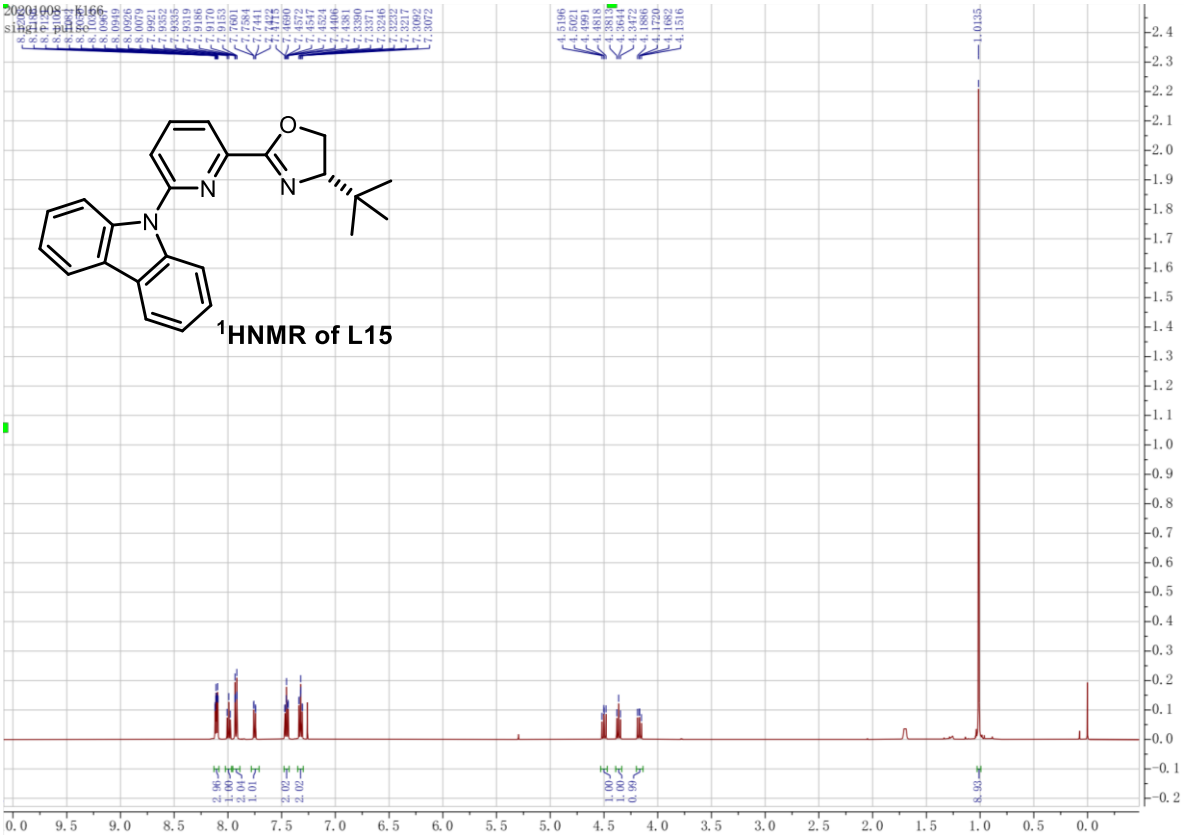


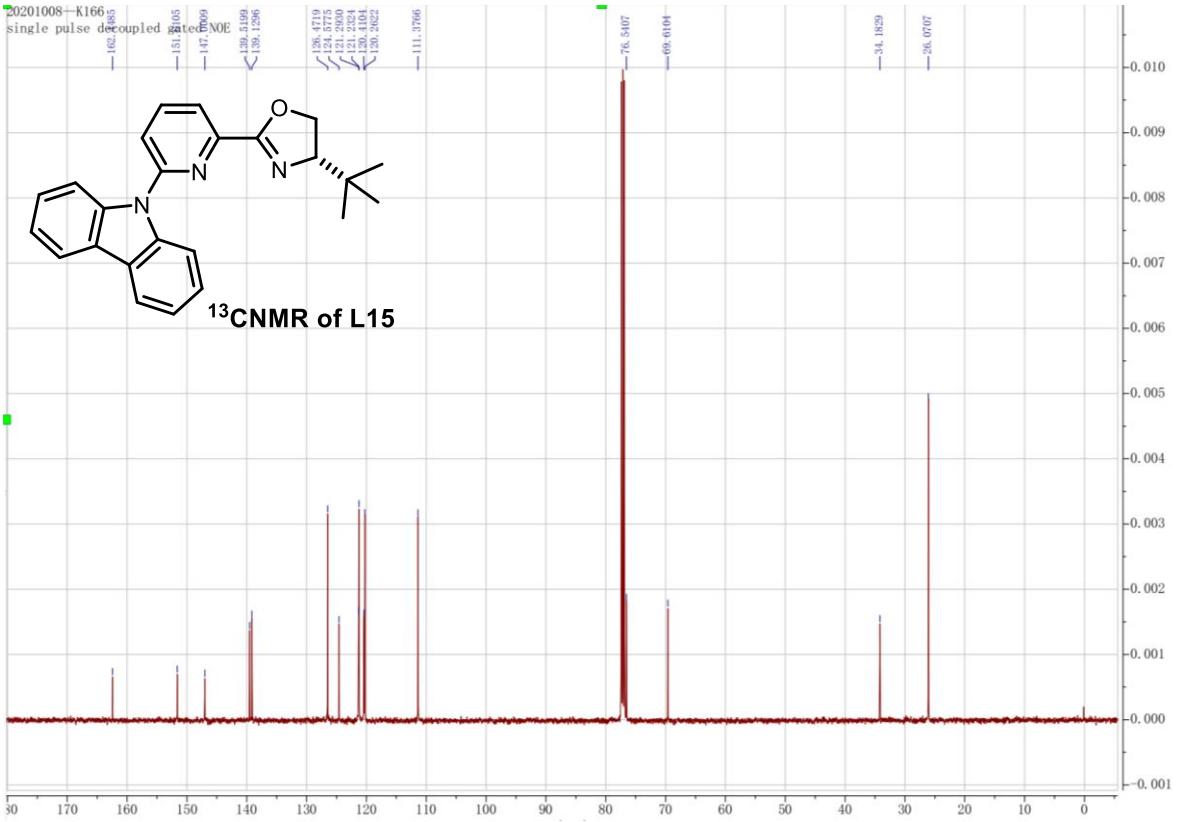
结果视图 – 峰表

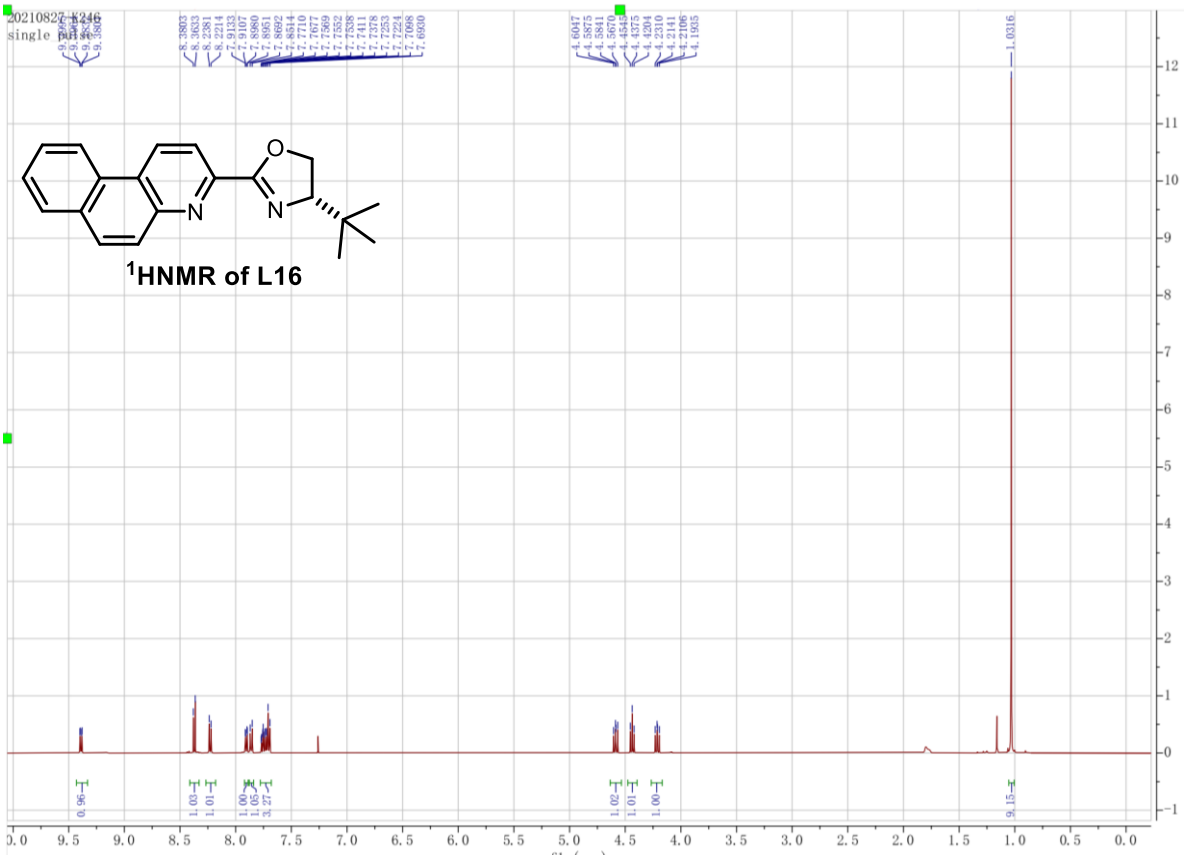
峰表 化合物 组 校准曲线

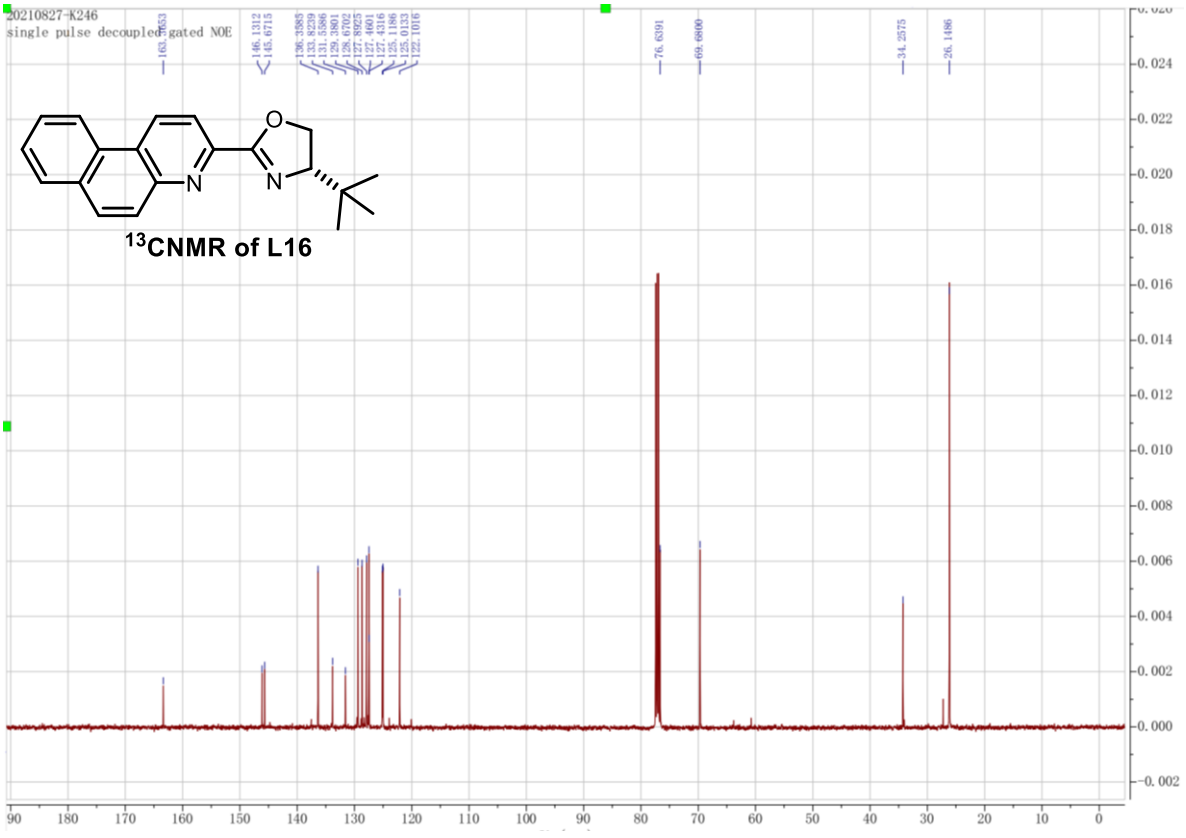
峰号	保留时间	面积	高度	标记	浓度	浓度单位	化合物ID号	化合物名	面积%
1	15.261	5869458	215913	M	21.159				21.159
2	20.292	21870696	567968	M	78.841				78.841
总计		27740154	783881		100.000				100.000

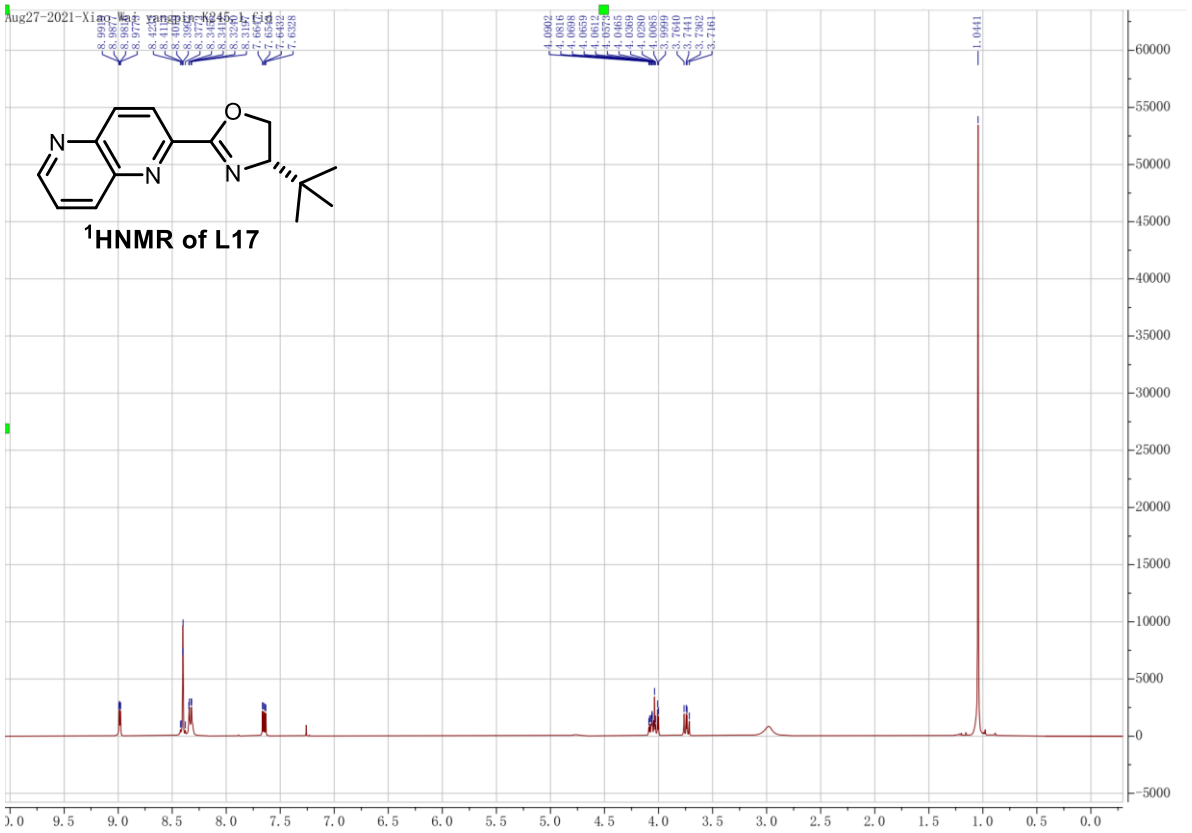
8. NMR spectra



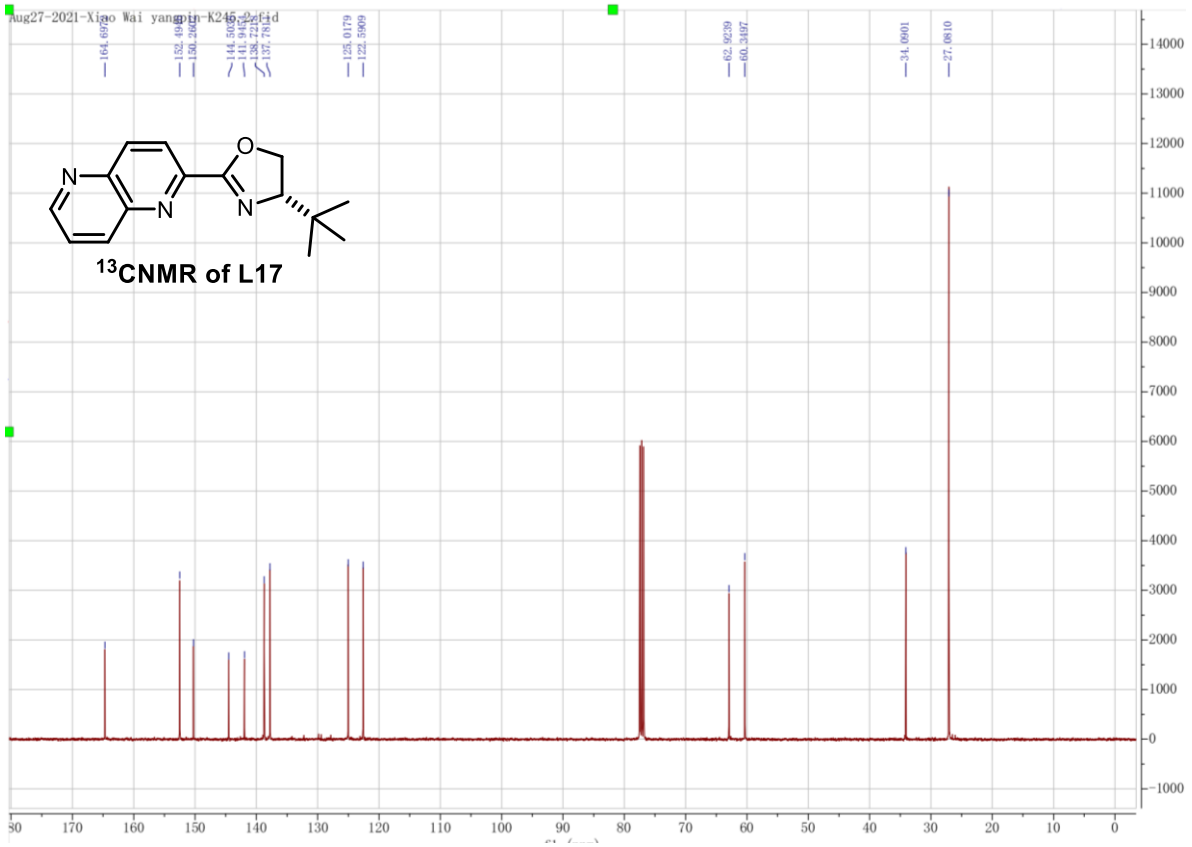



20210827-K246
single pulse
O
N
N
1HNMR of L16

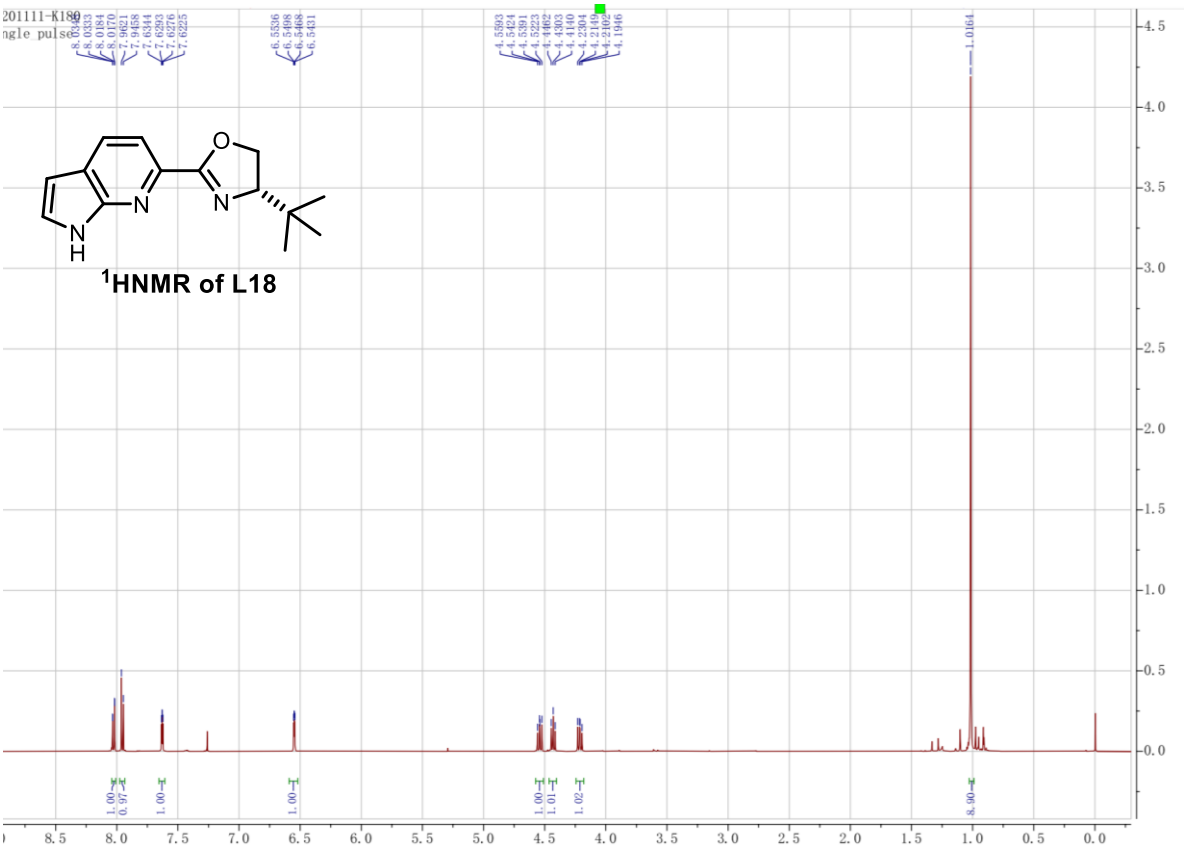

20210827-K246
single pulse decoupled gated NOE
O
N
N
13CNMR of L16



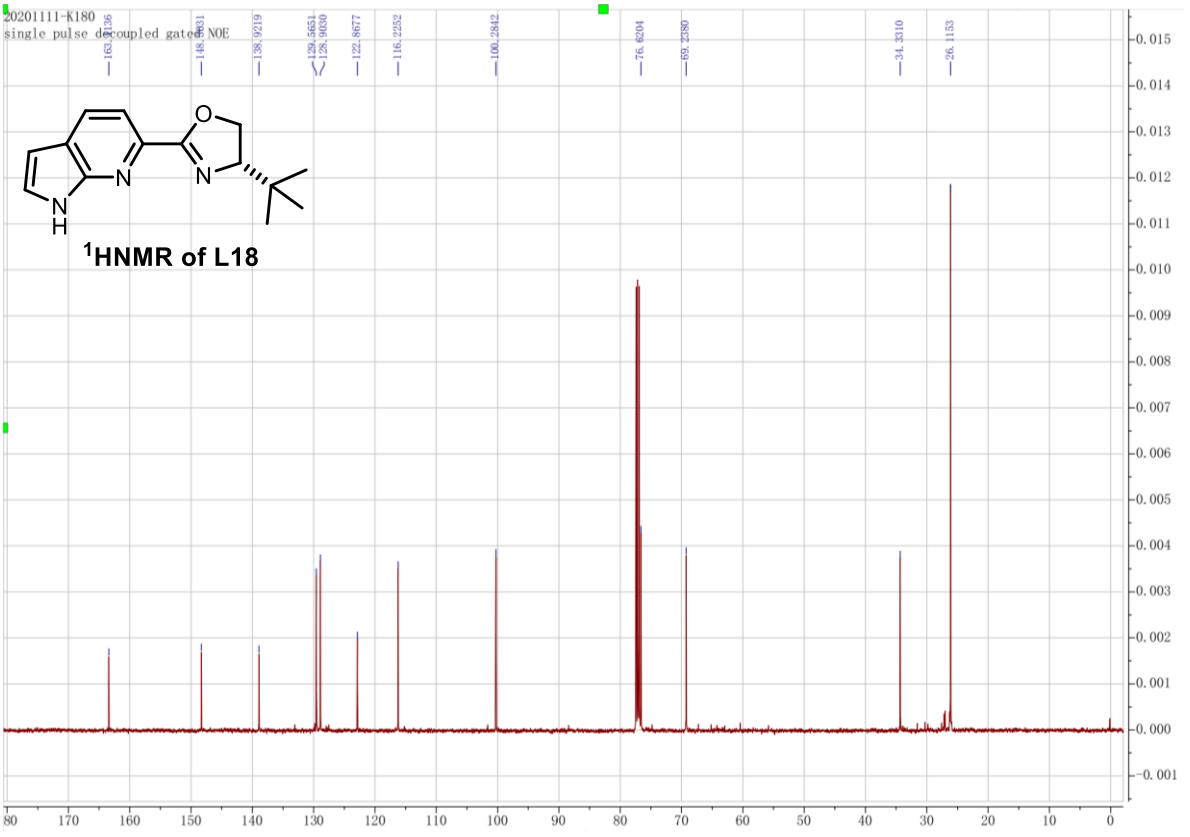
^{1}HNMR of L17



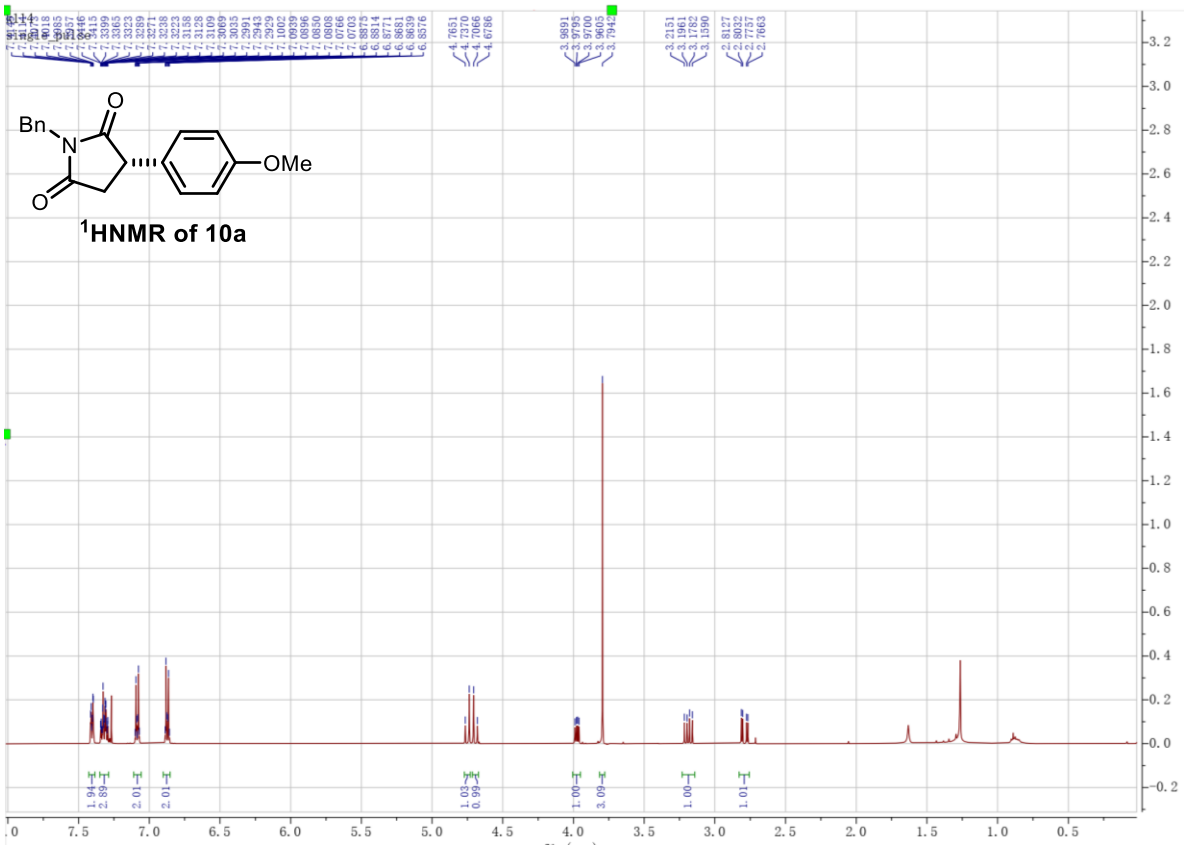
^{13}CNMR of L17

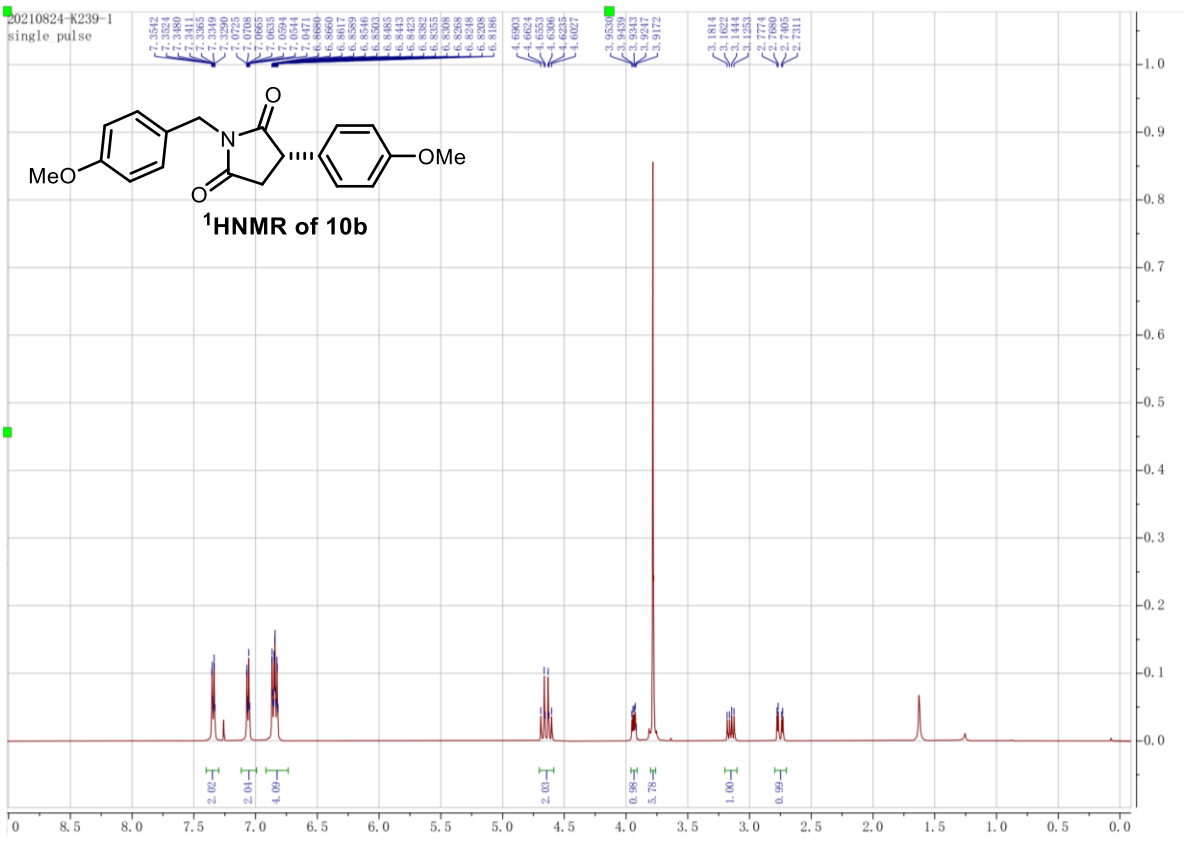


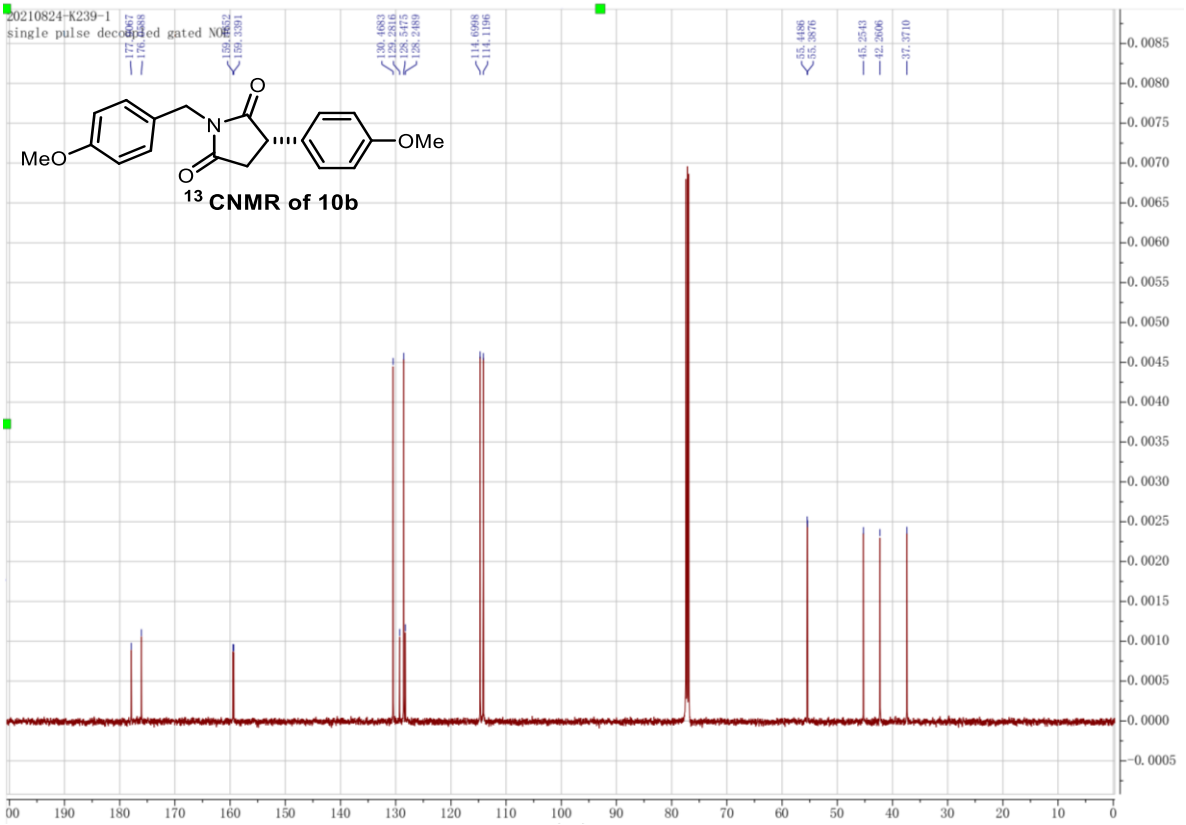
^{1}HNMR of L18

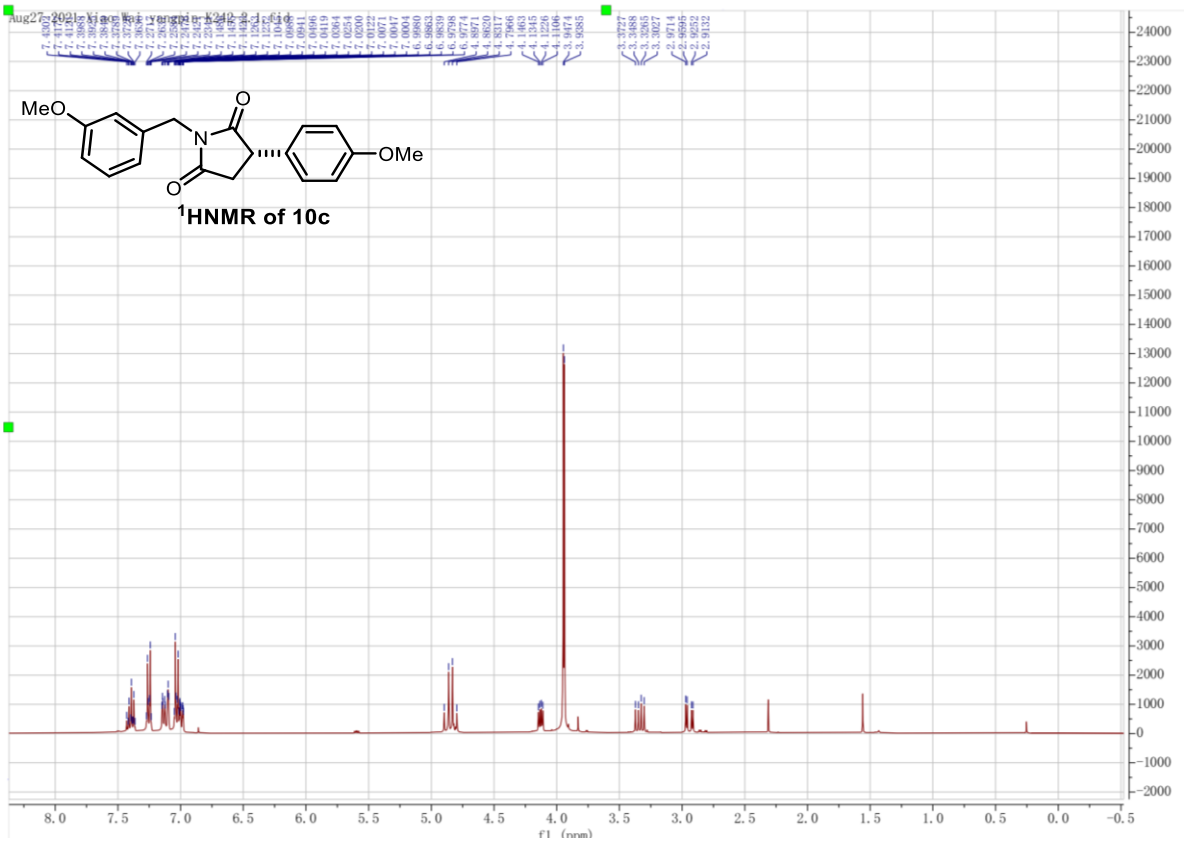


^{1}HNMR of L18

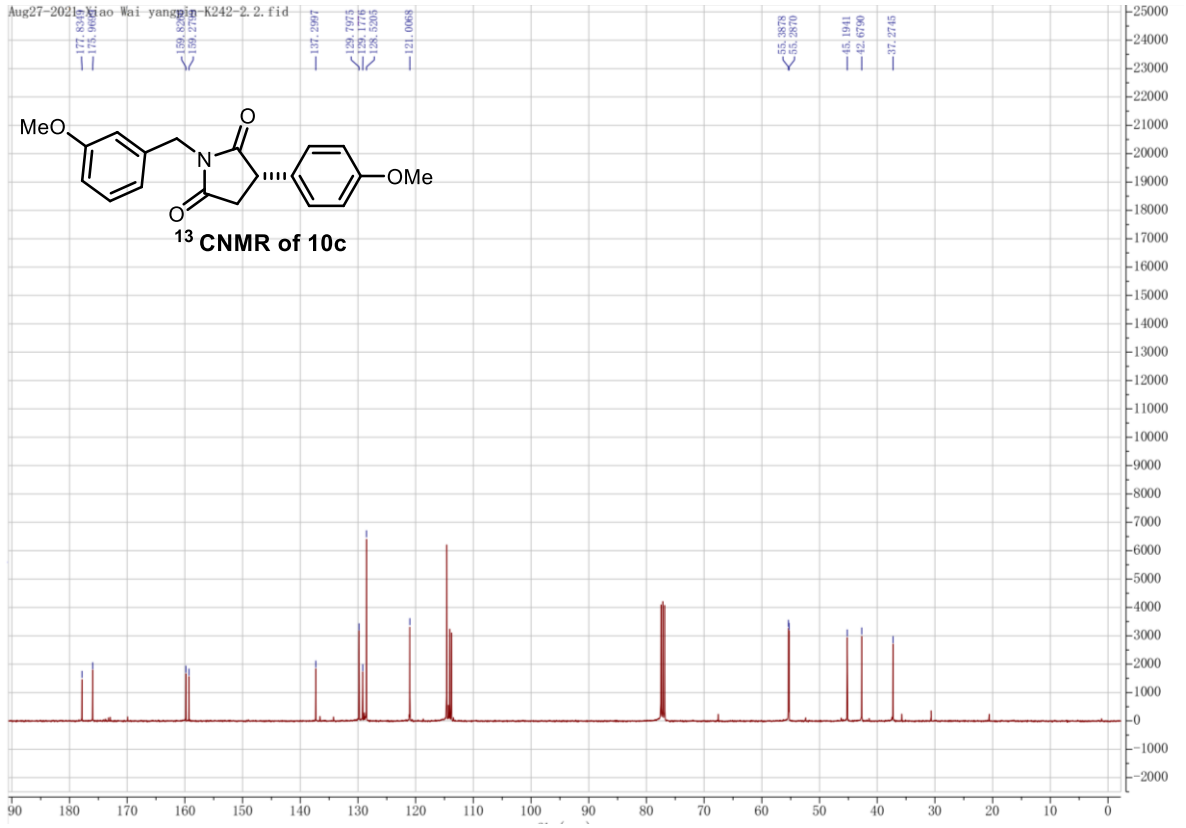

Bn
N
O
O
OMe
1HNMR of 10a


20210824-K239-1
single pulse
MeO
OMe
O
N
O
1HNMR of 10b

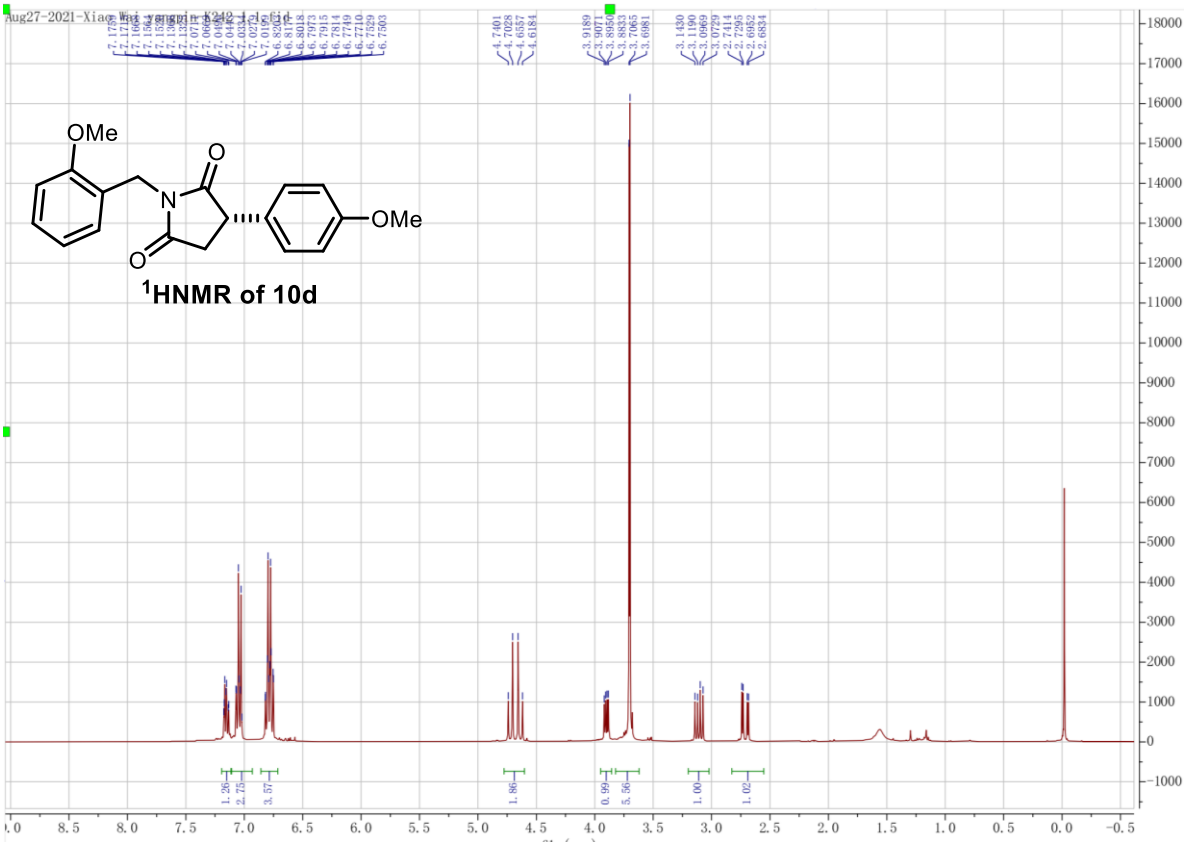

20210824-K239-1
single pulse decoupled gated NOE
MeO
OMe
O
N
O
13 CNMR of 10b

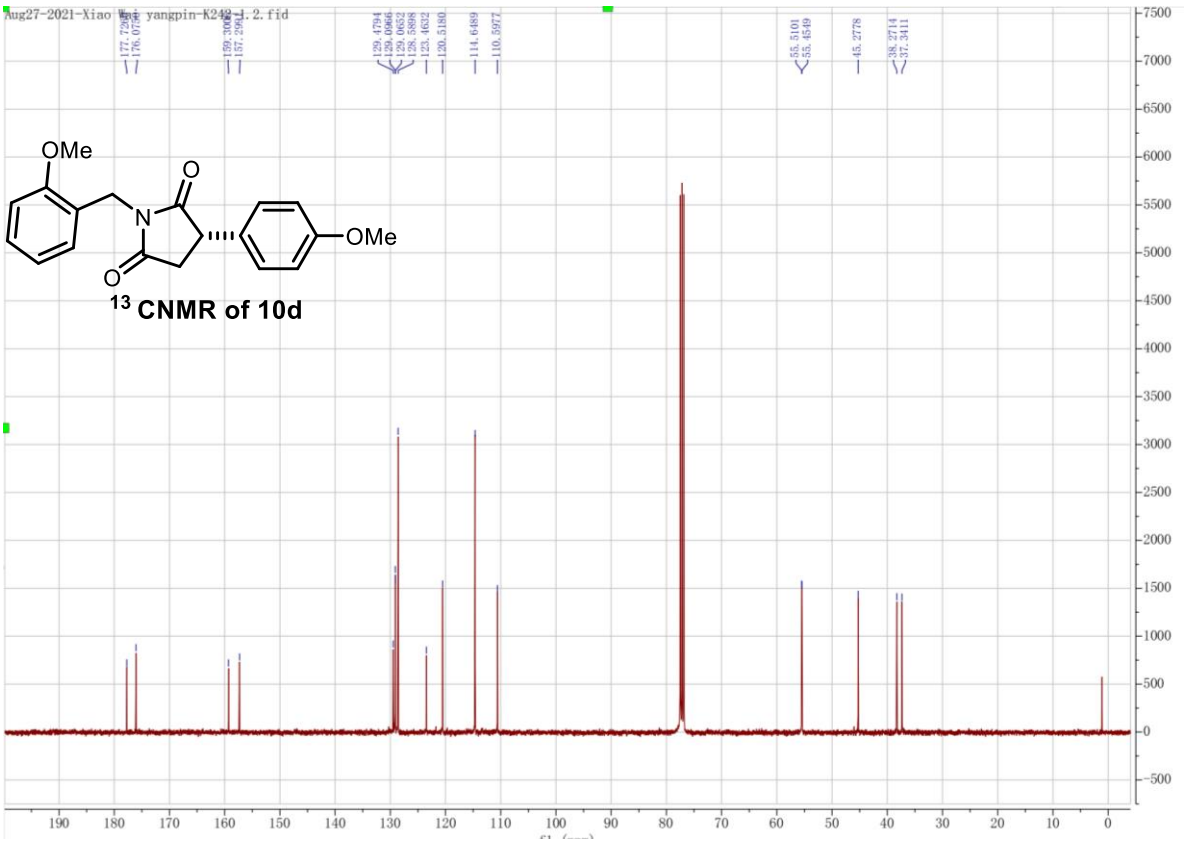


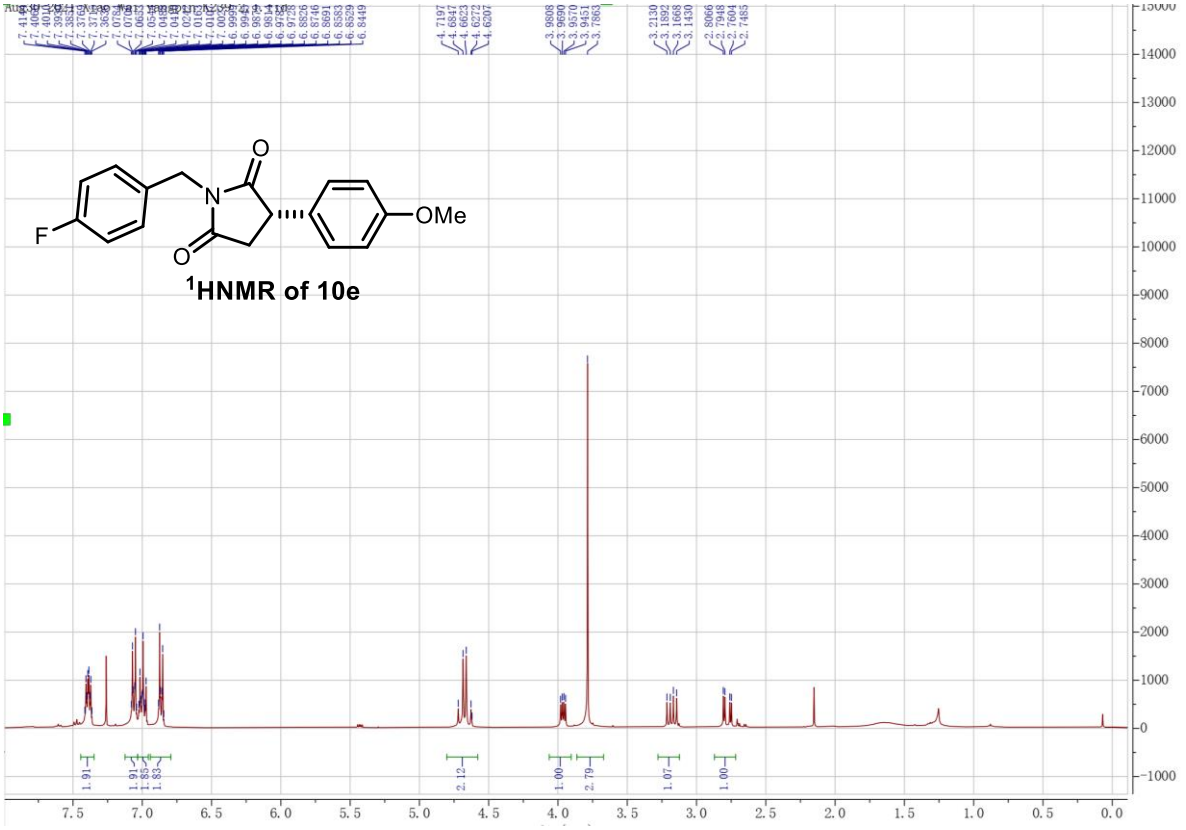
^{1}HNMR of 10c

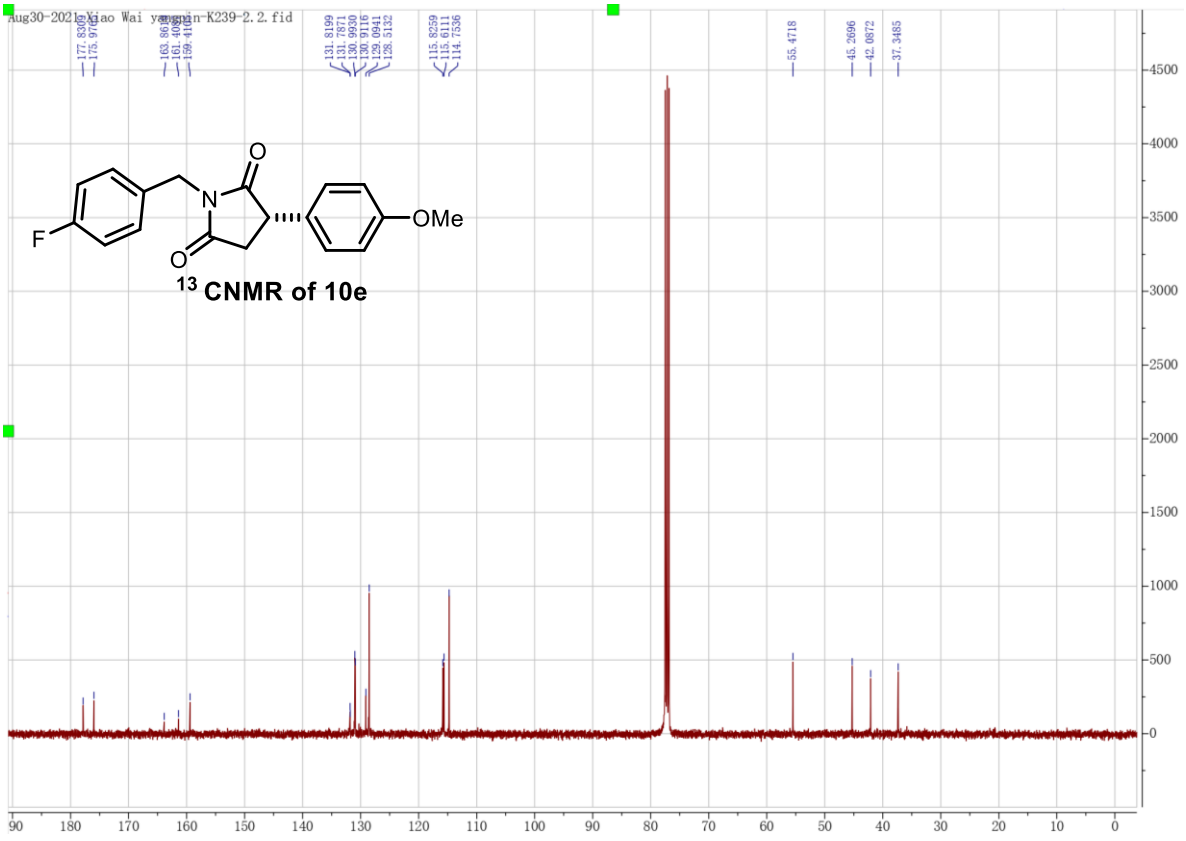


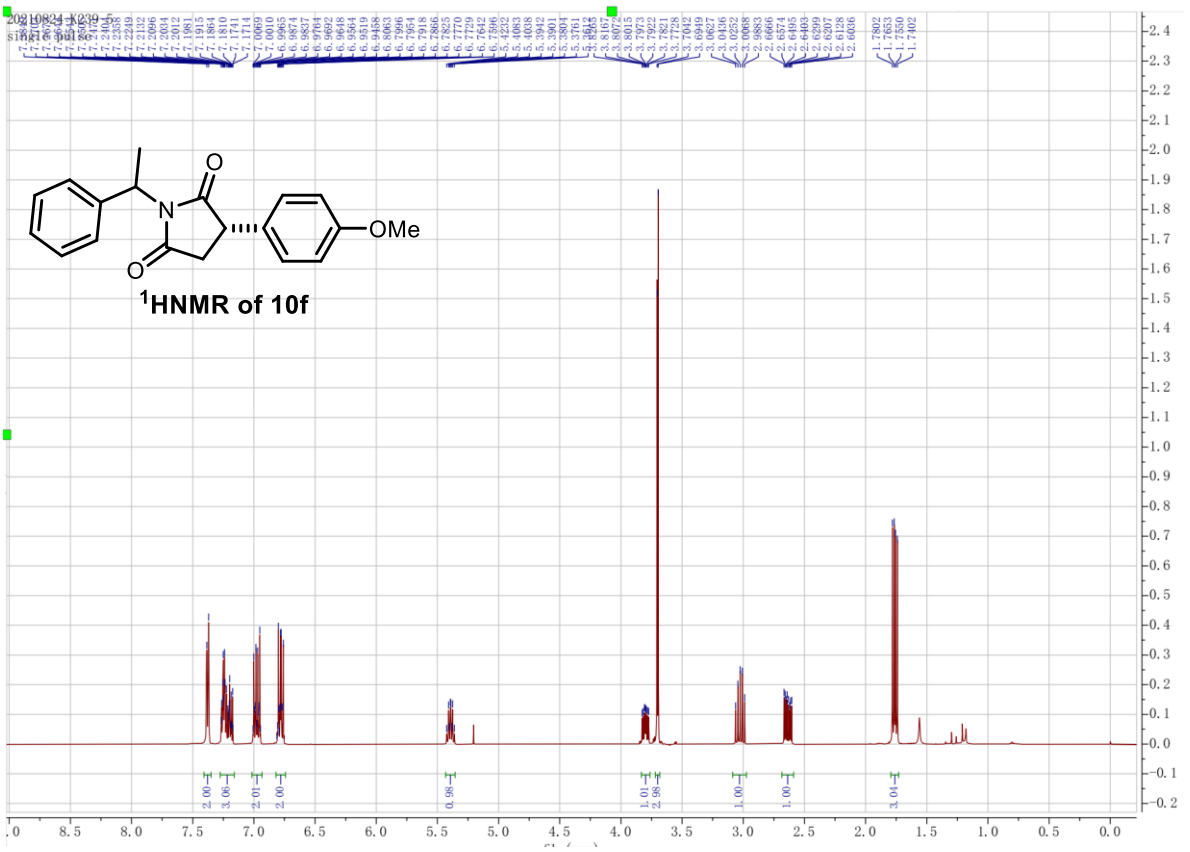
^{13}CNMR of 10c

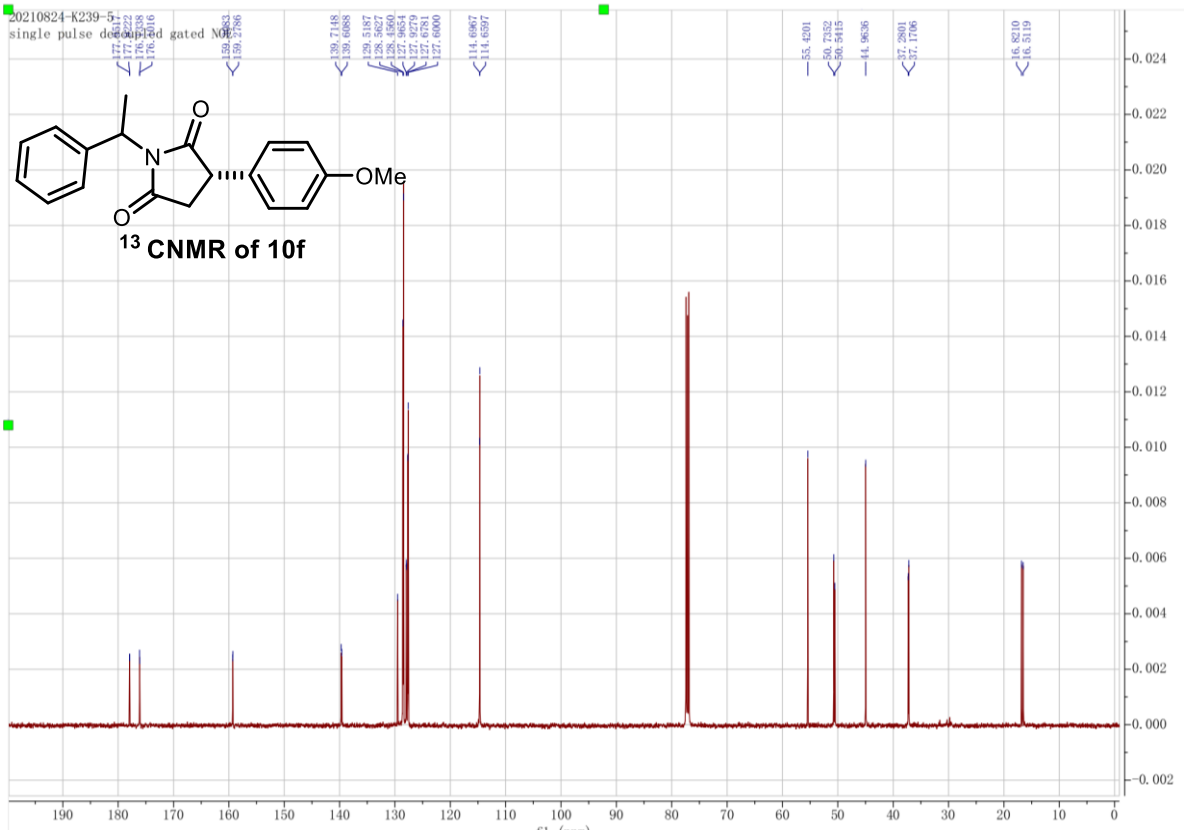

OMe
O
N
O
OMe
1HNMR of 10d

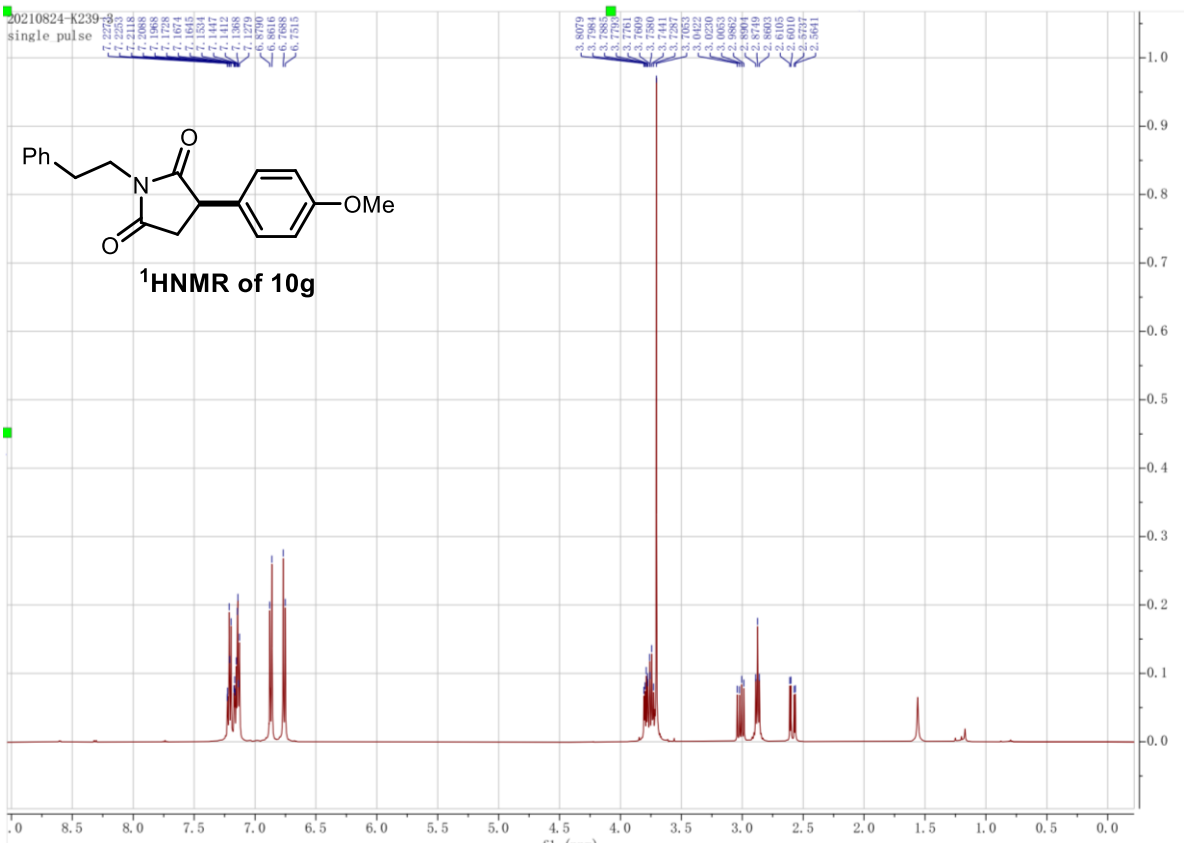

OMe
O
N
O
OMe
13 CNMR of 10d

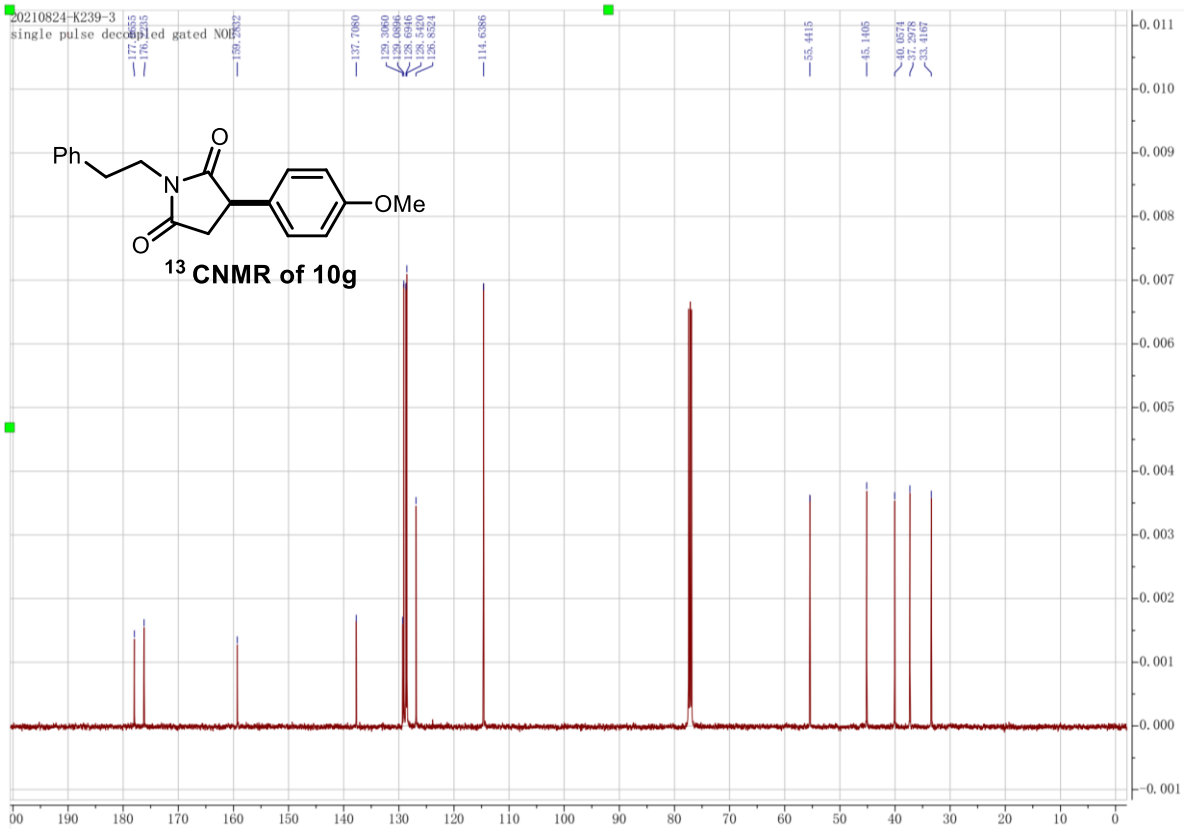

F
N
O
O
OMe
1HNMR of 10e

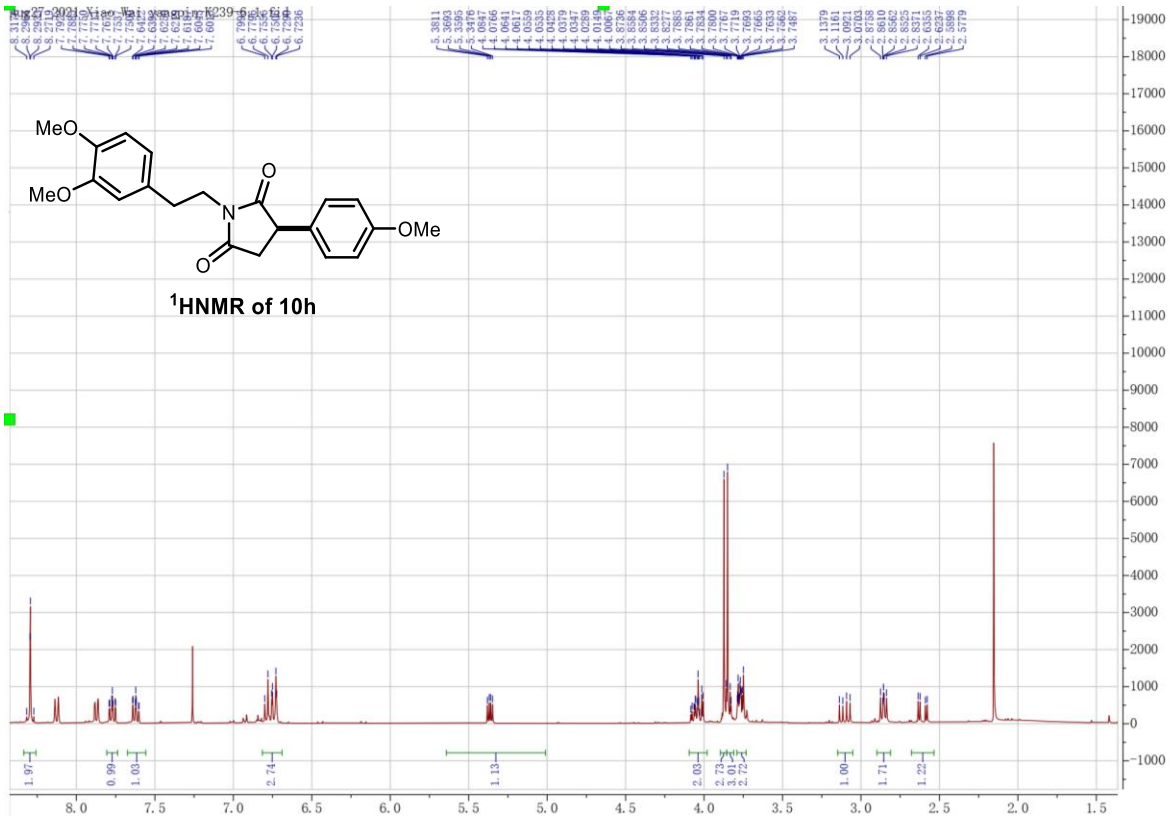

F
N
O
O
OMe
13 CNMR of 10e

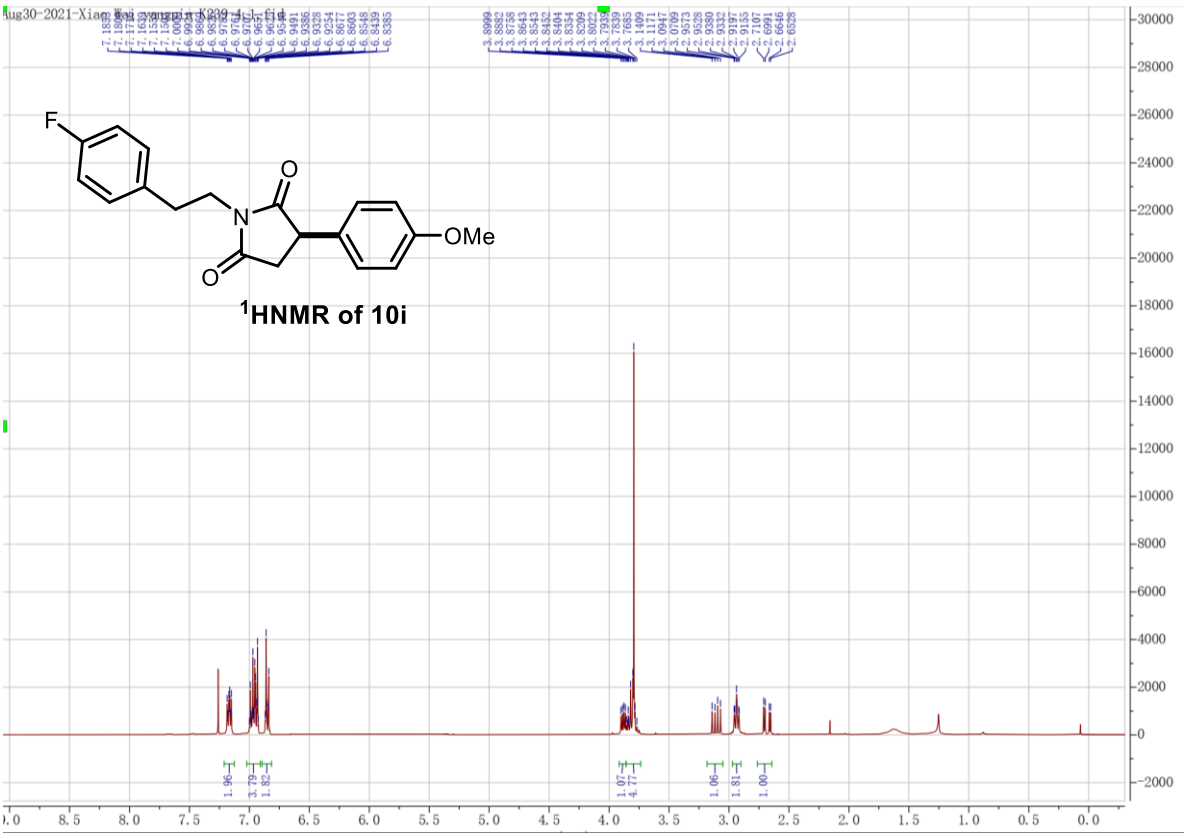

OMe
1HNMR of 10f

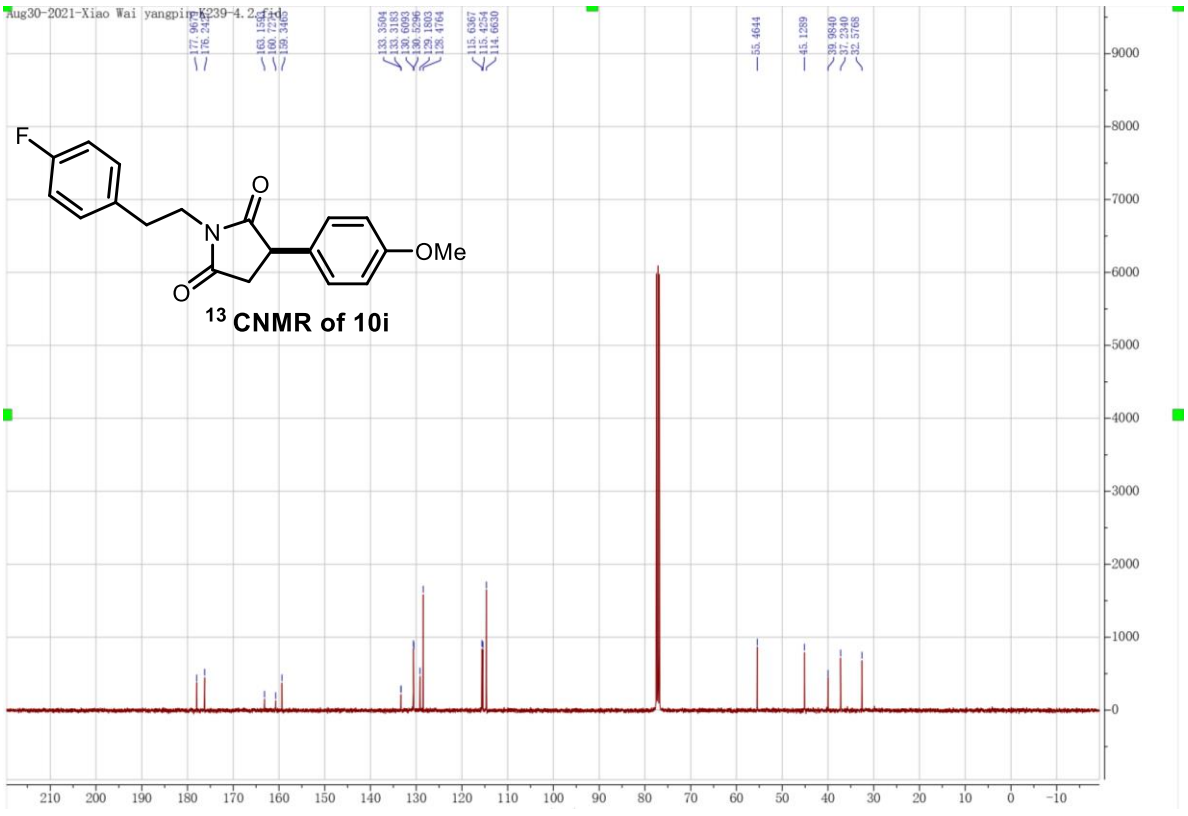

OMe
13 CNMR of 10f

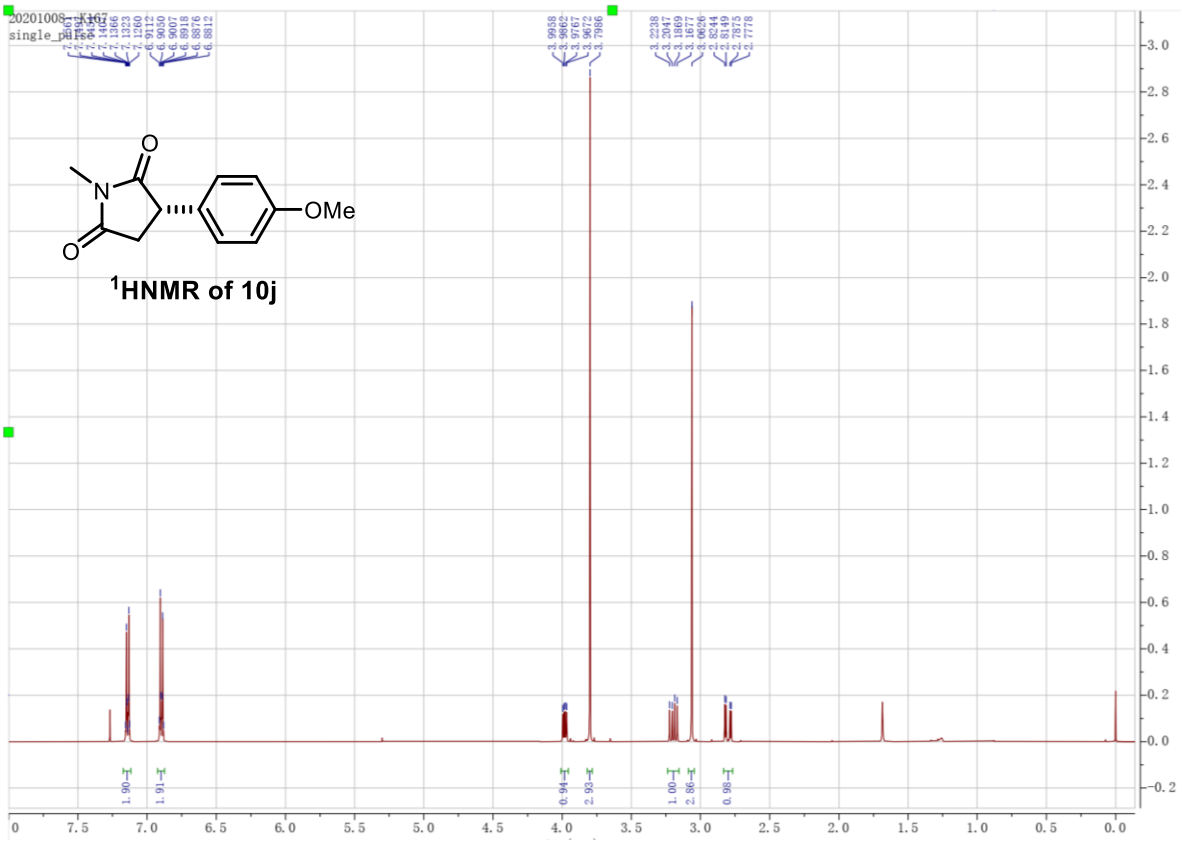

20210824-K239-3
single pulse
Ph
N
O
O
OMe
1HNMR of 10g

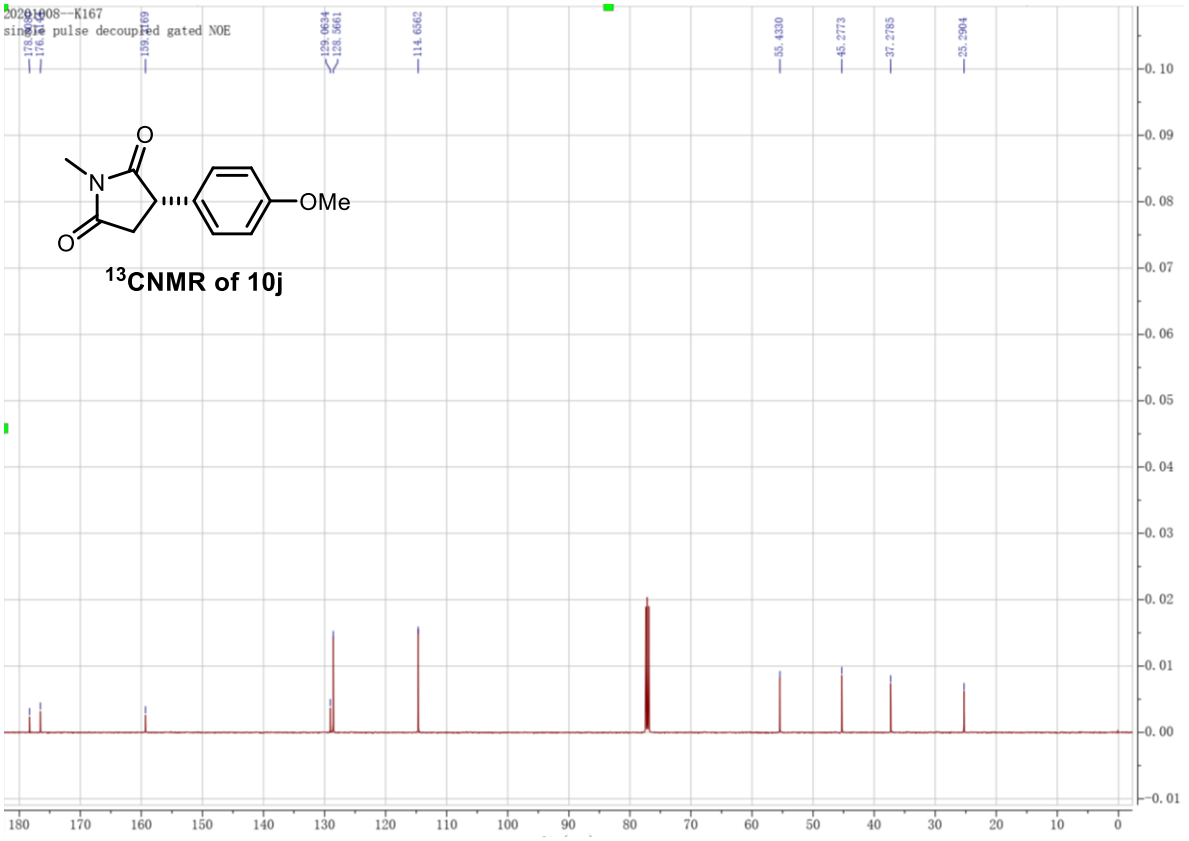

20210824-K239-3
single pulse decoupled gated NOE
Ph
N
O
O
OMe
13 CNMR of 10g

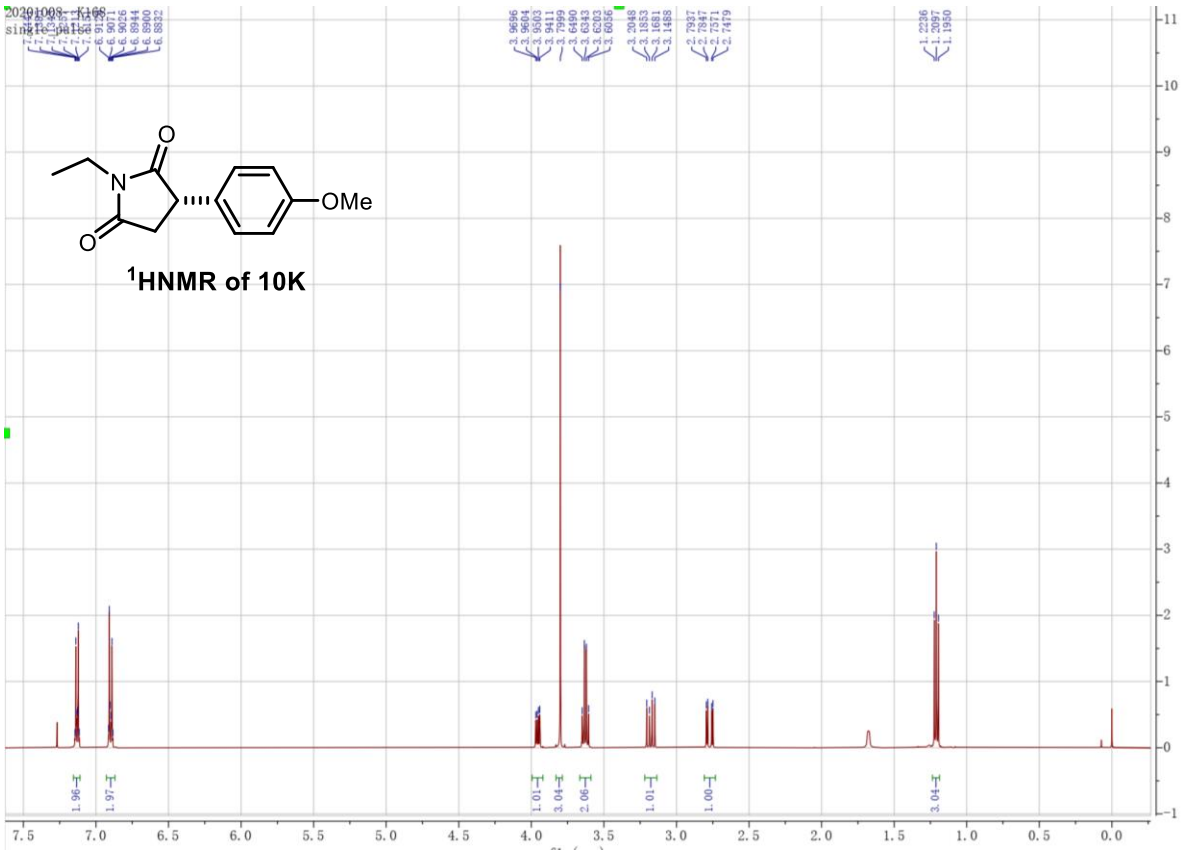

MeO
MeO
O
N
O
OMe
1HNMR of 10h

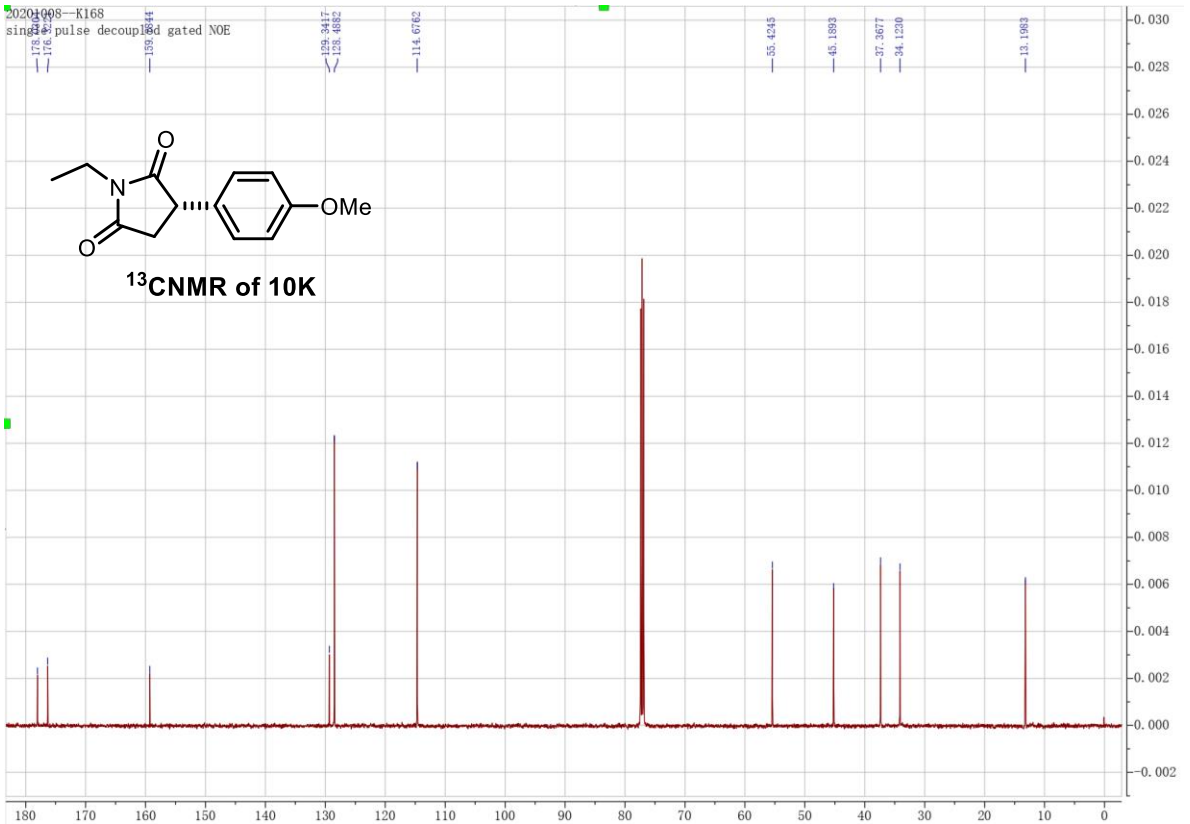

F
O
N
O
OMe
1HNMR of 10i

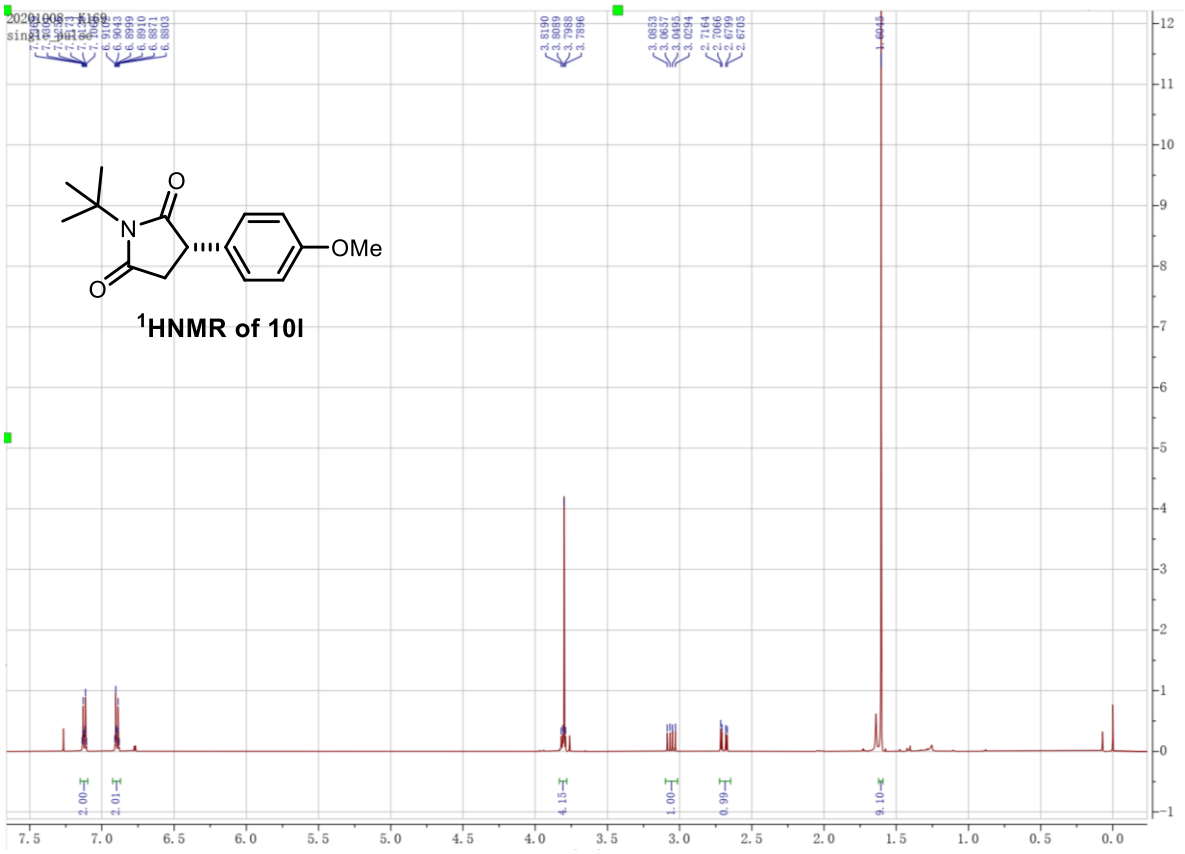

F
O
N
O
OMe
13 CNMR of 10i


OMe
1HNMR of 10j

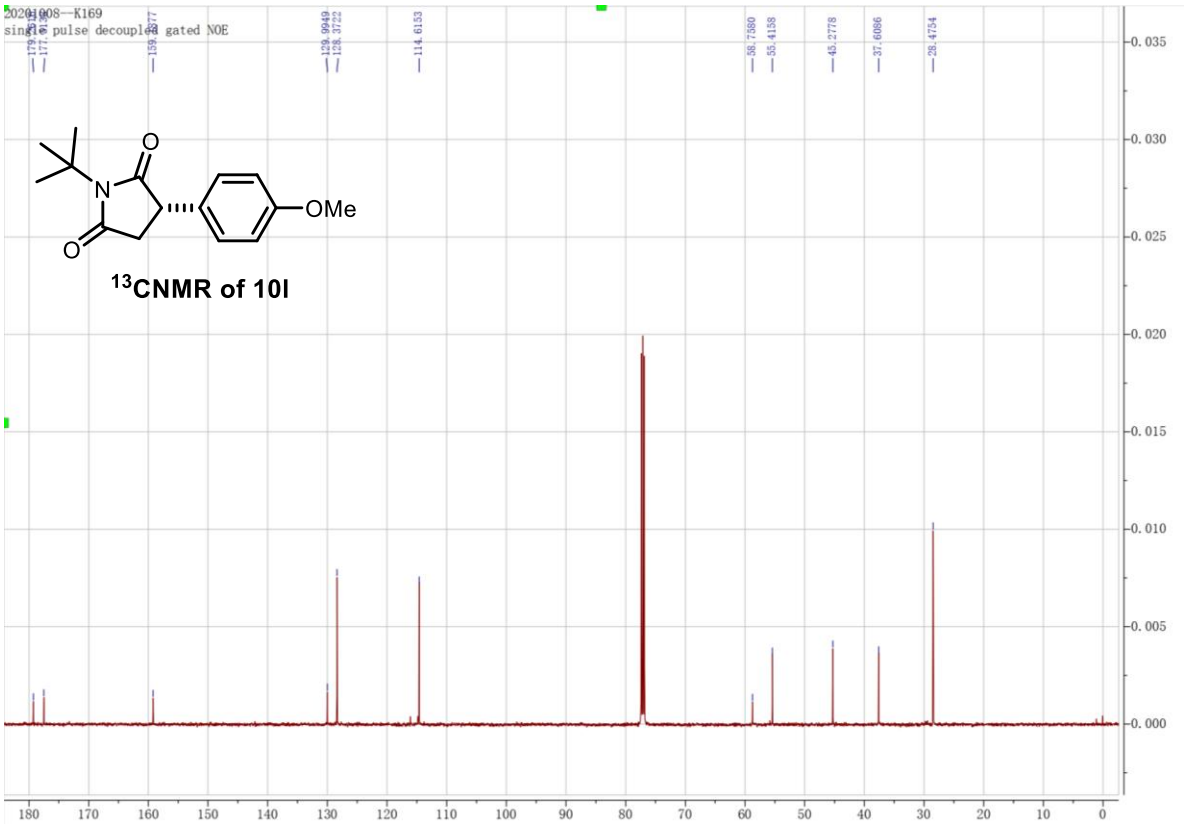

OMe
13CNMR of 10j


O
N
O
OMe
1HNMR of 10K

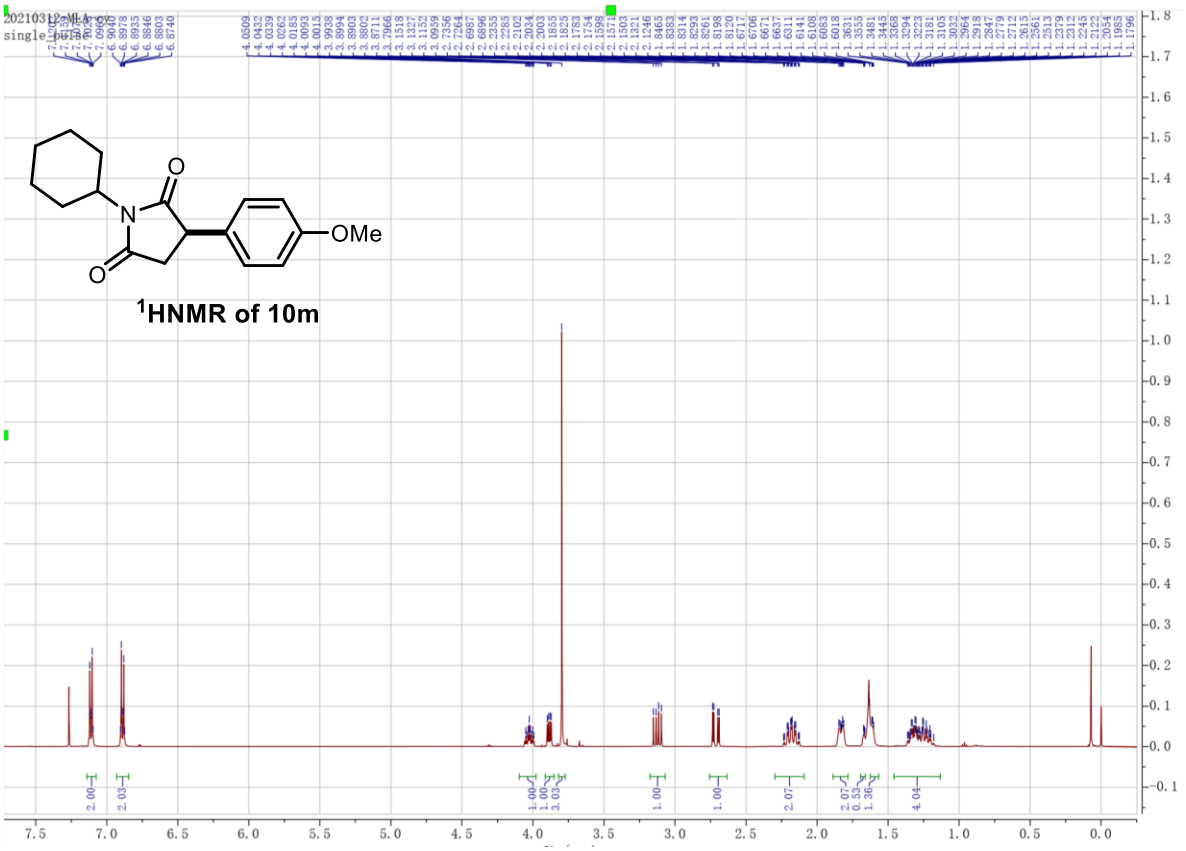

O
N
O
OMe
13CNMR of 10K



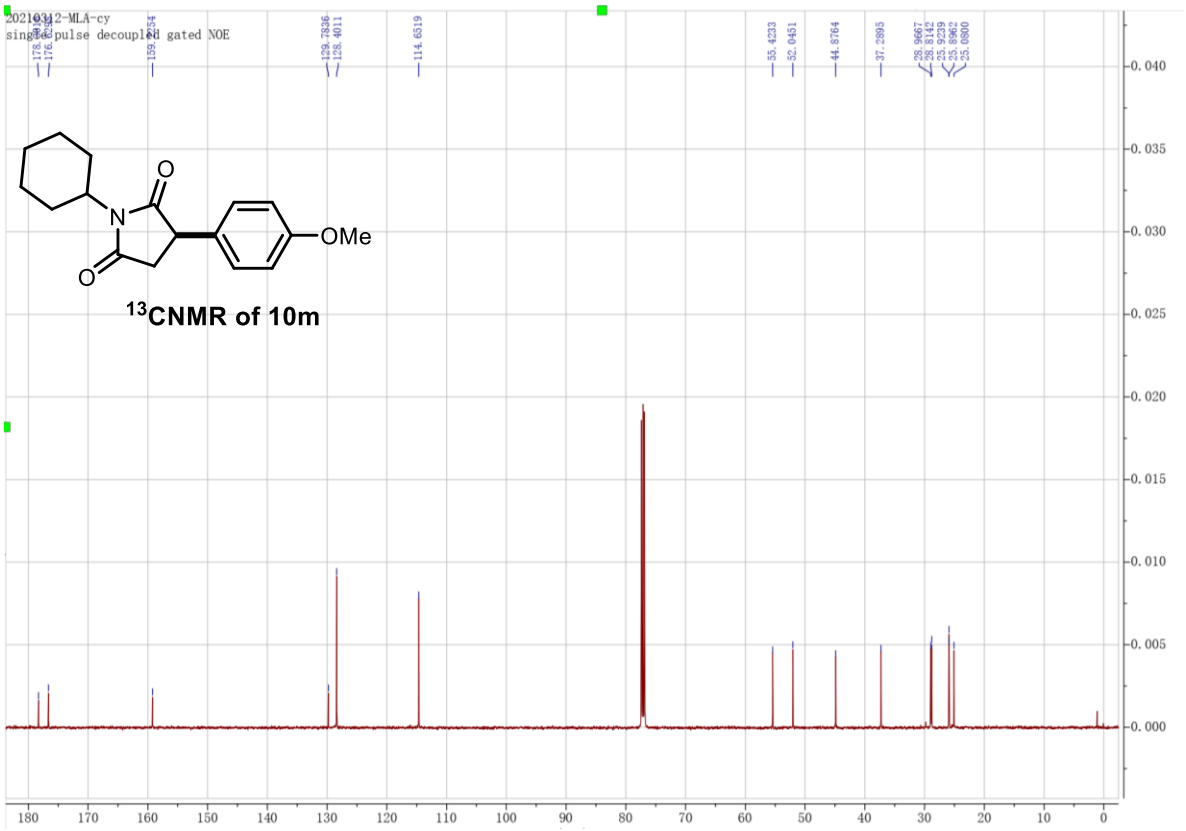
^{1}HNMR of 10l



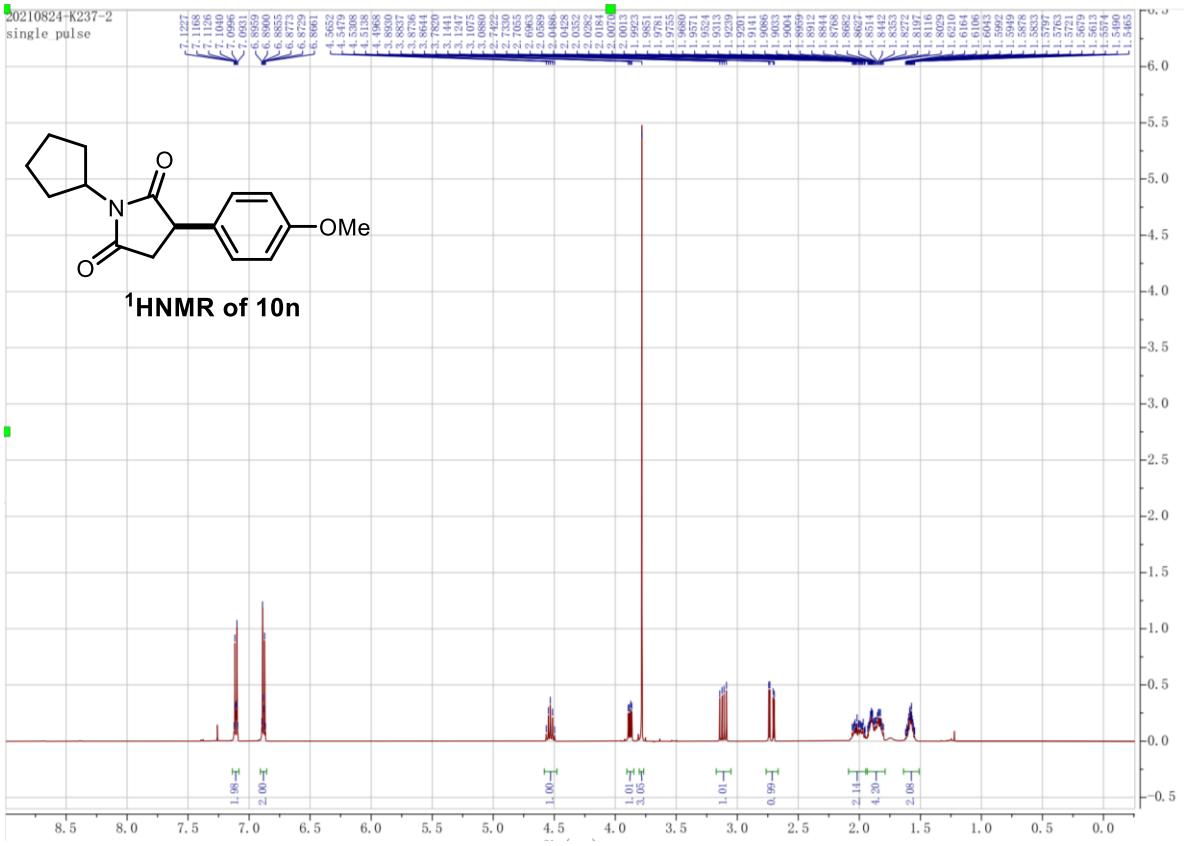
^{13}CNMR of 10l



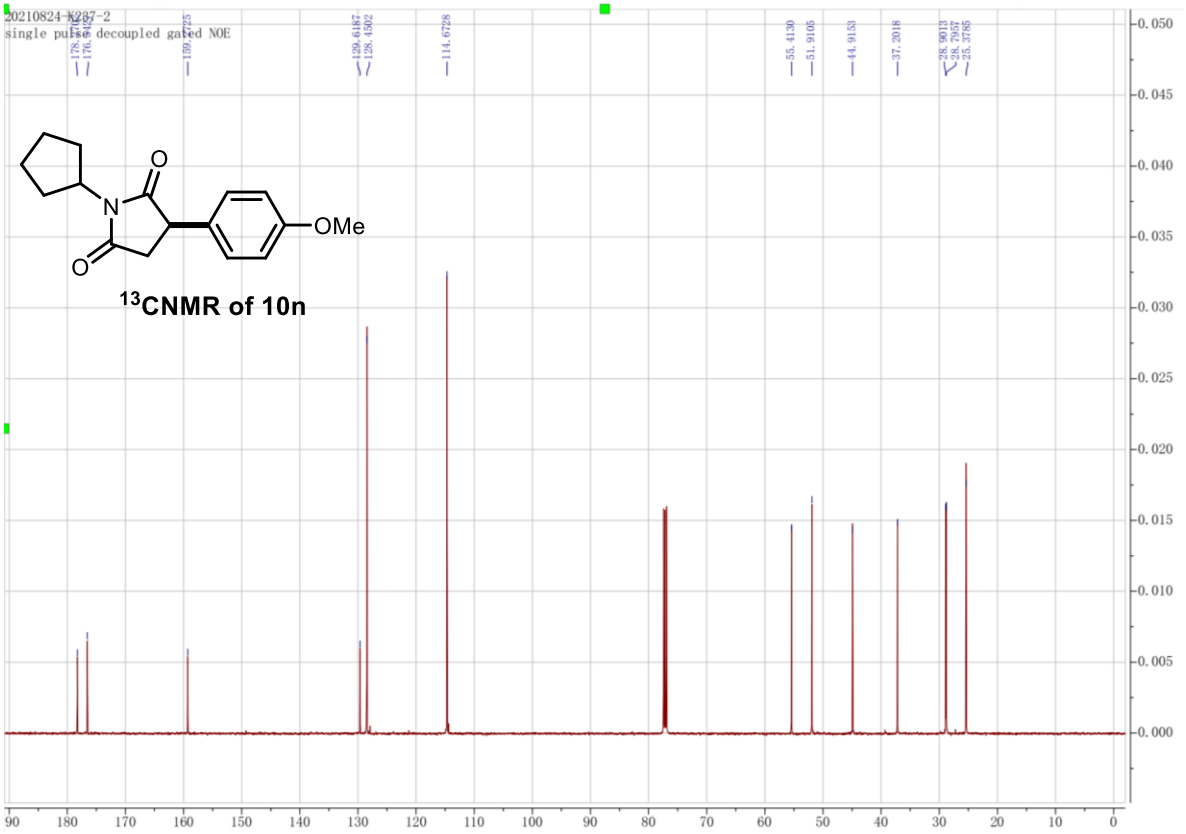
^{1}HNMR of 10m



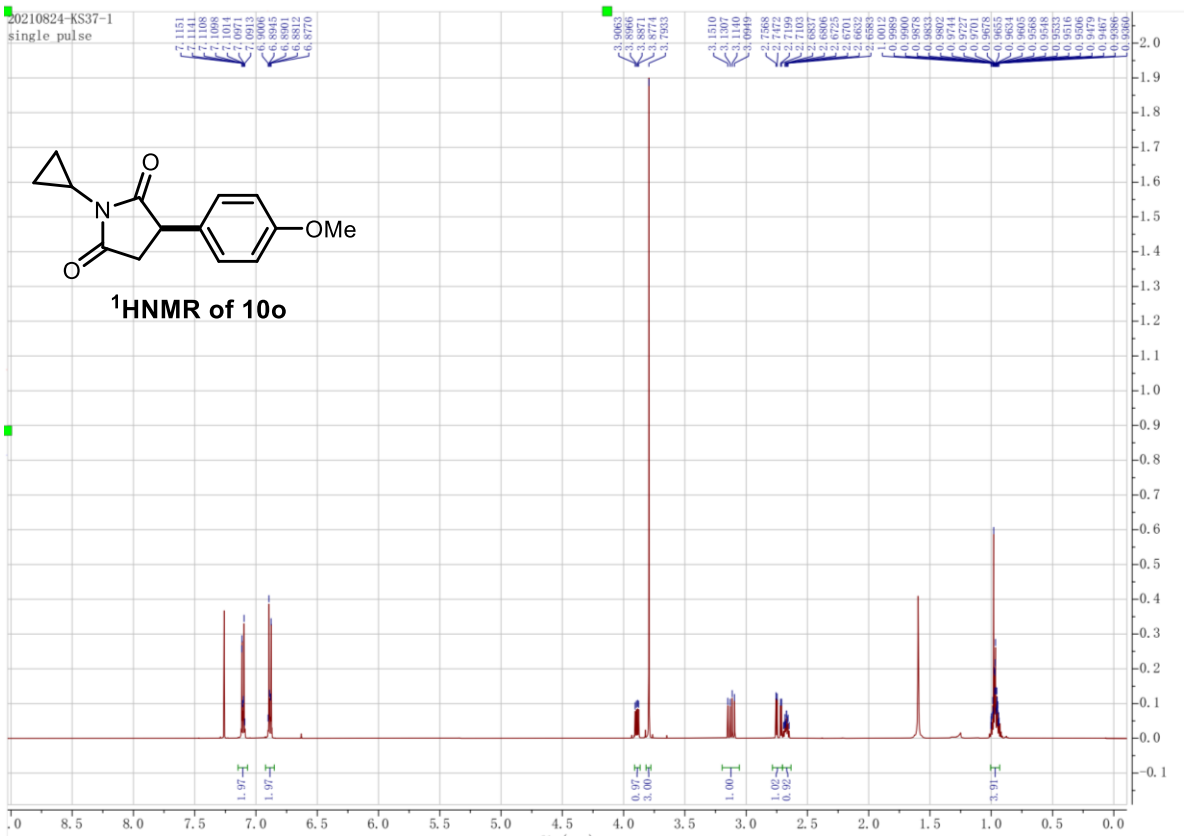
^{13}CNMR of 10m

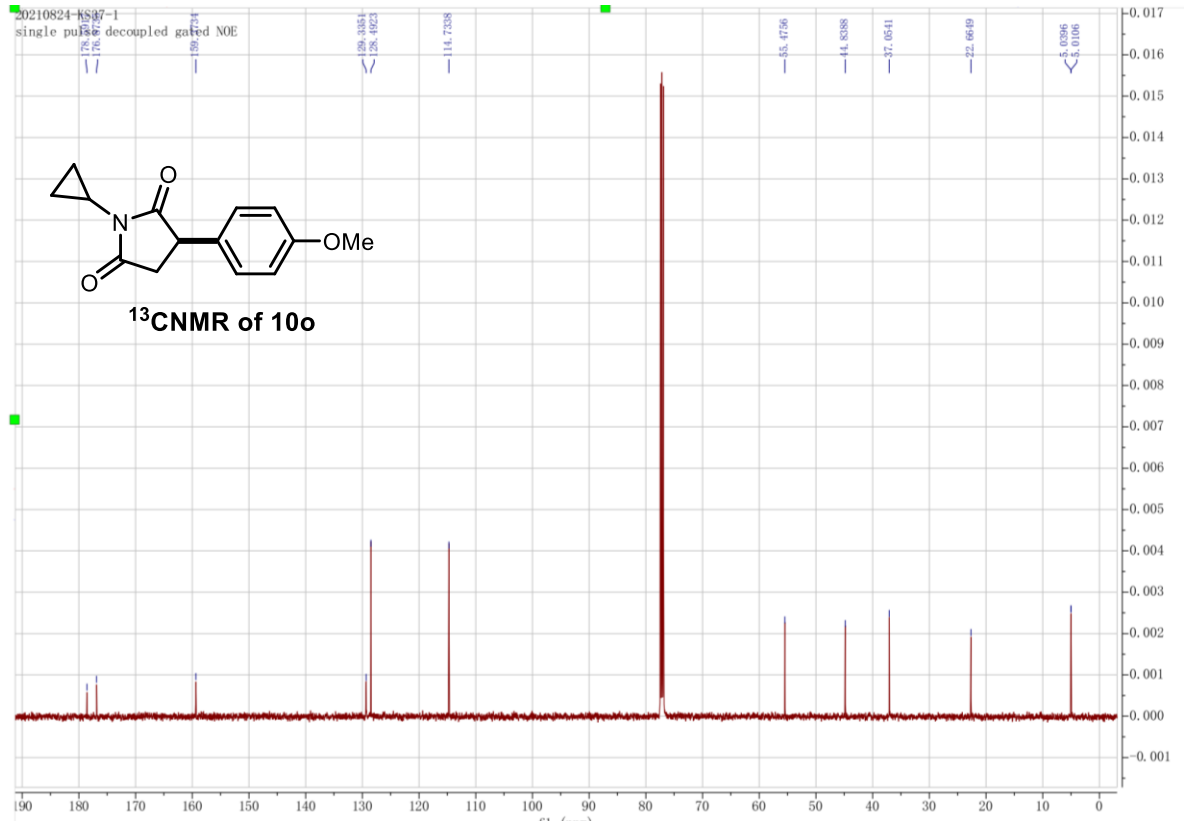


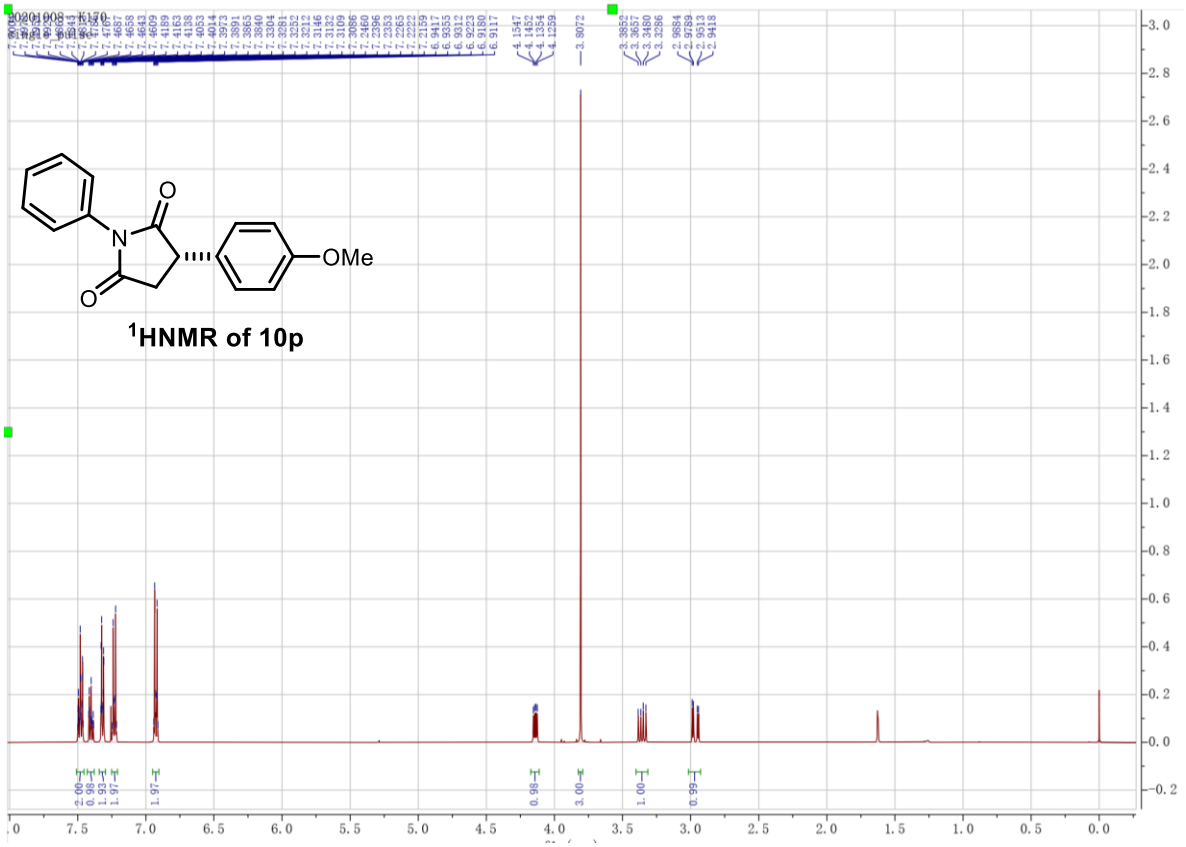
^{1}HNMR of 10n



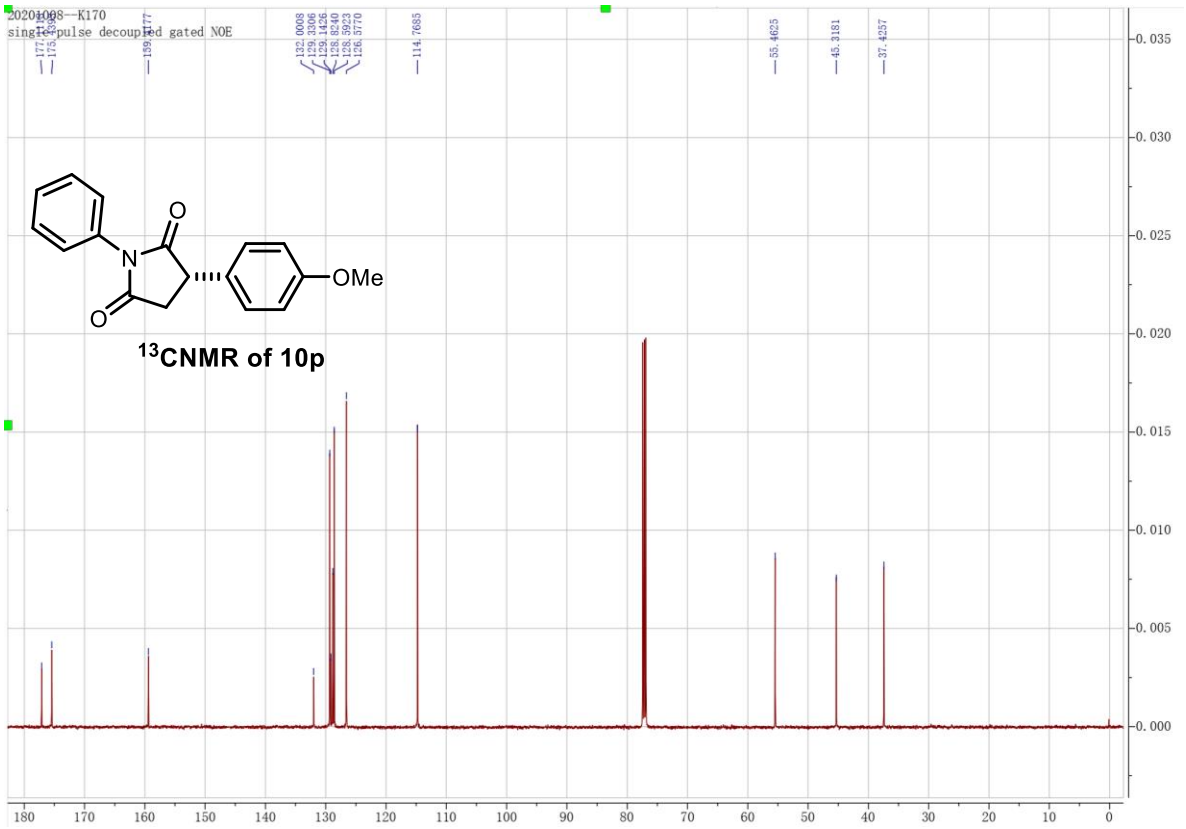
^{13}CNMR of 10n


20210824-KS37-1
single pulse
OMe
1HNMR of 10o

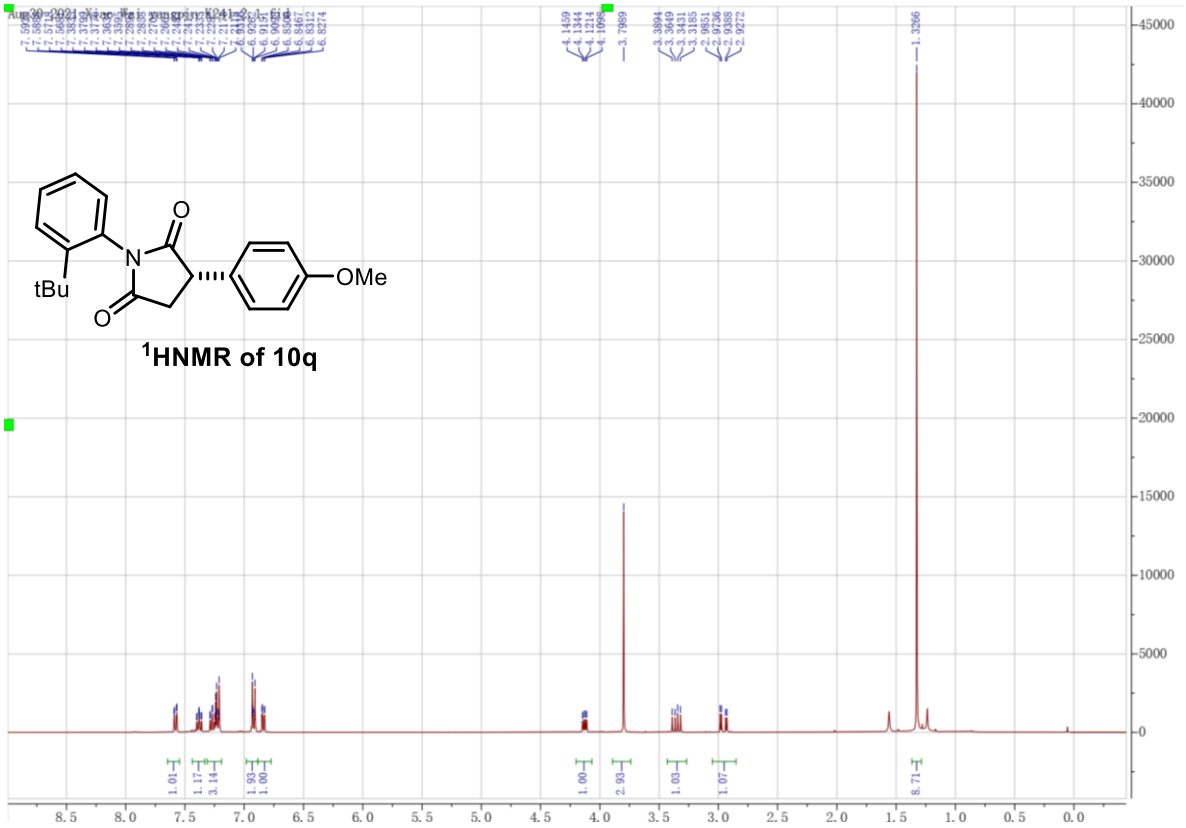

20210824-KS37-1
single pulse decoupled gated NOE
OMe
13CNMR of 10o



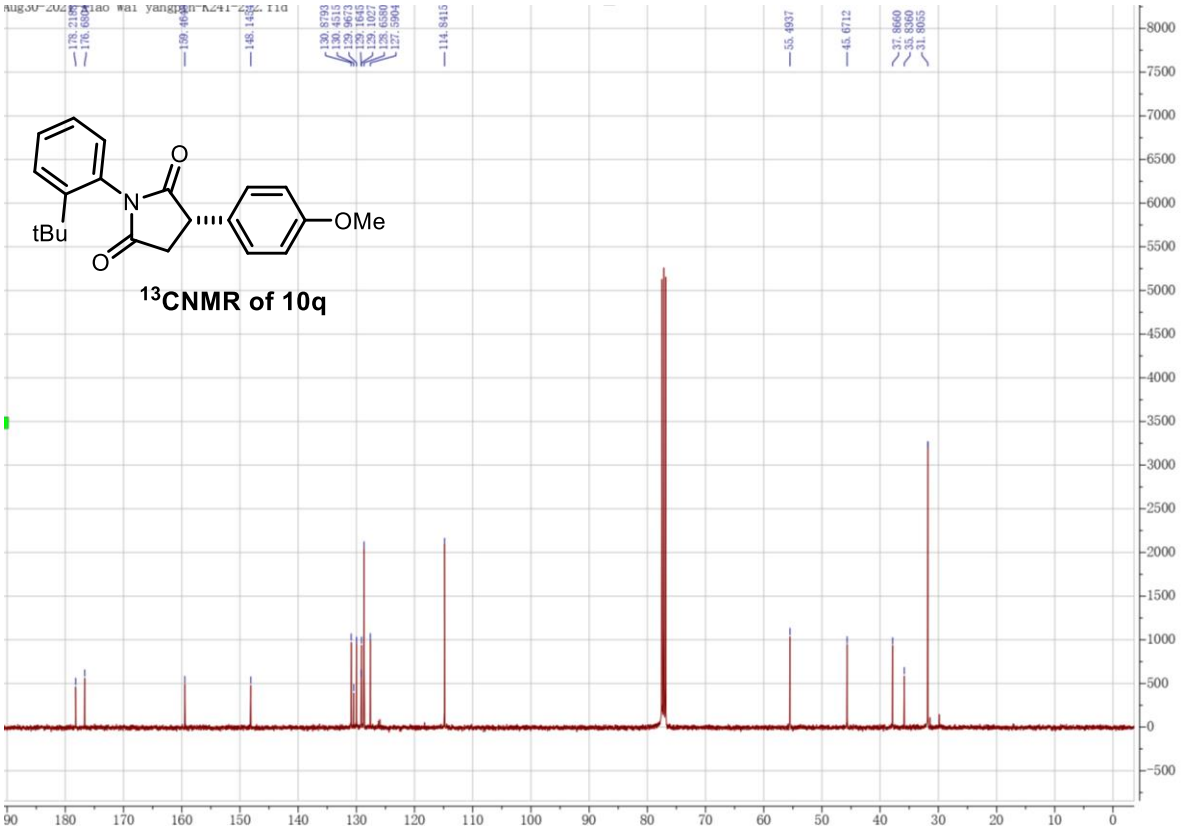
^{1}HNMR of 10p



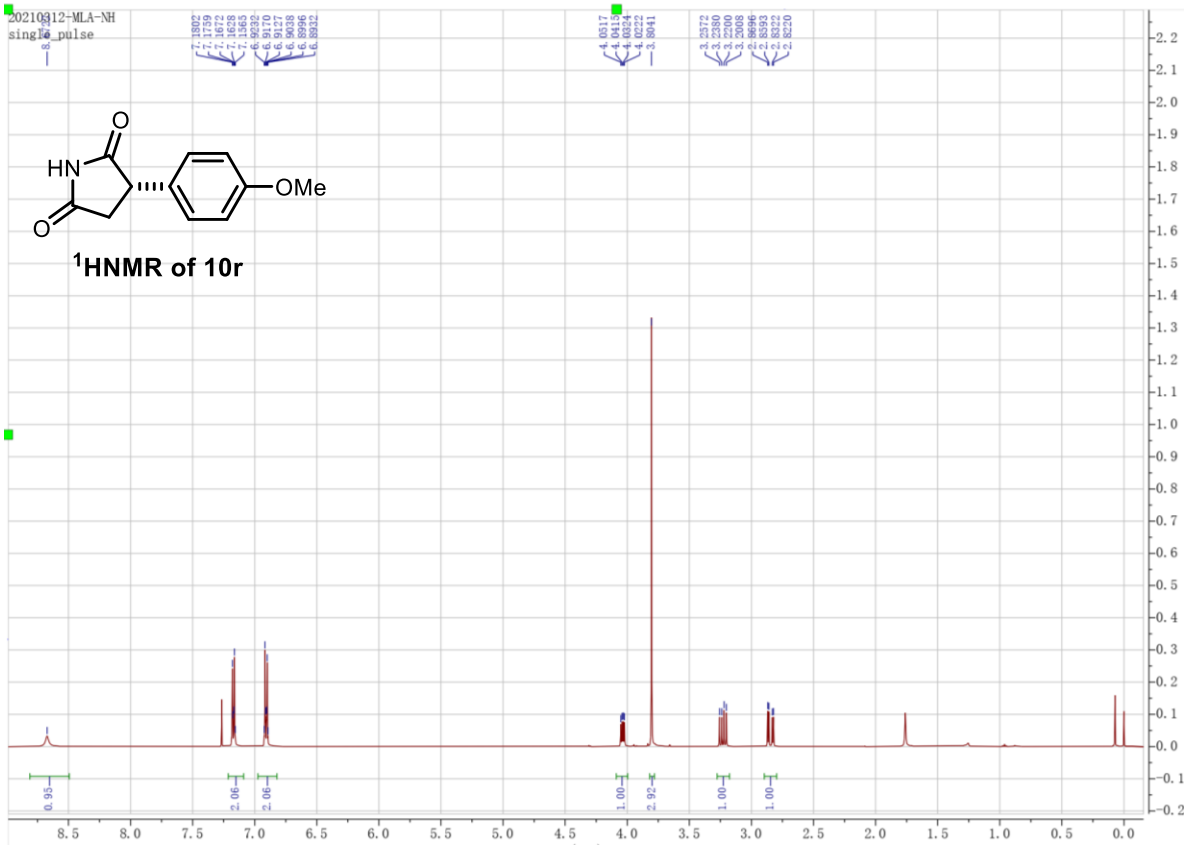
^{13}CNMR of 10p

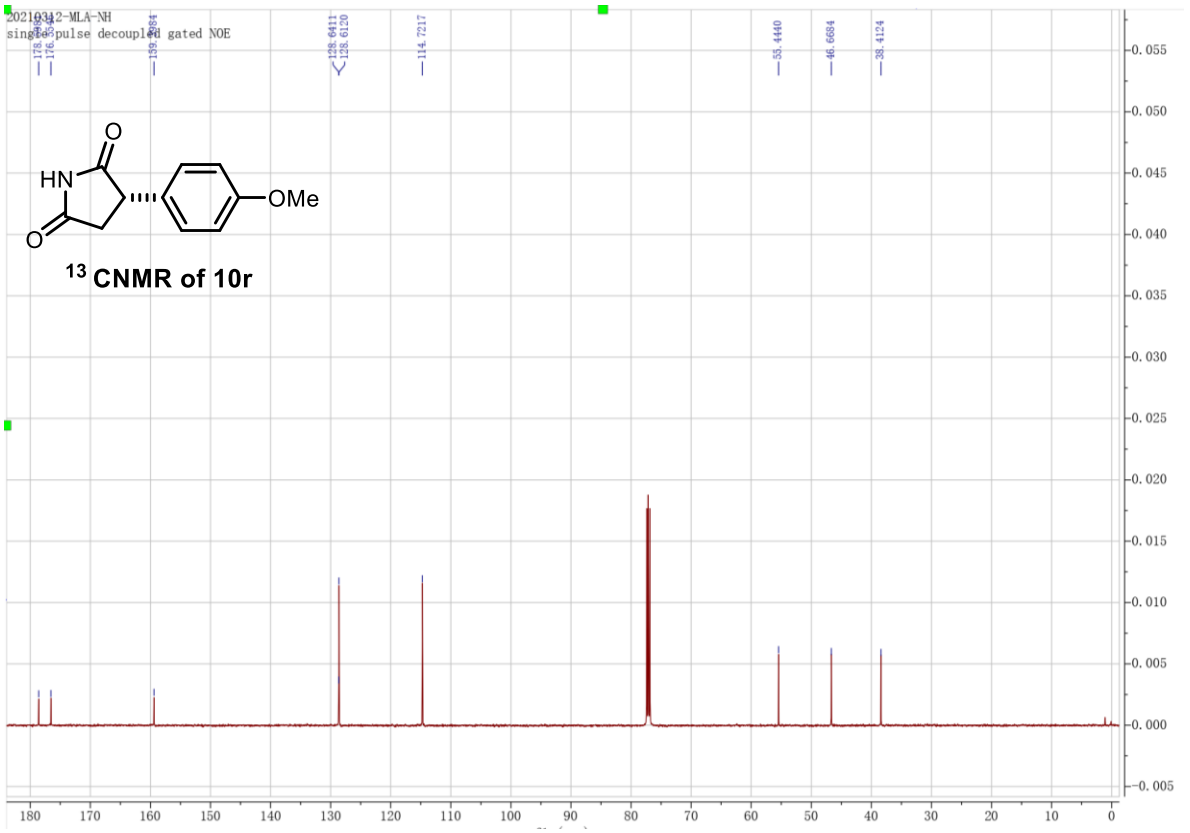


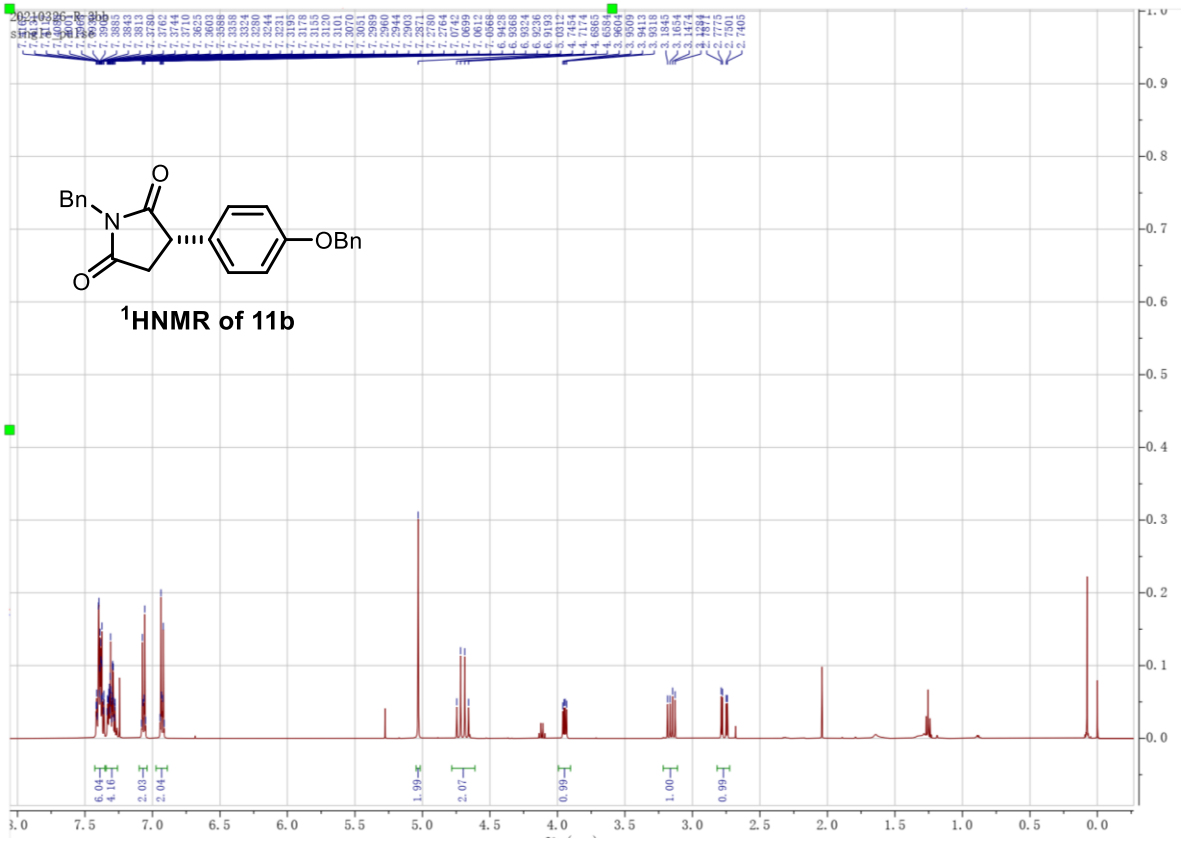
^{1}HNMR of 10q



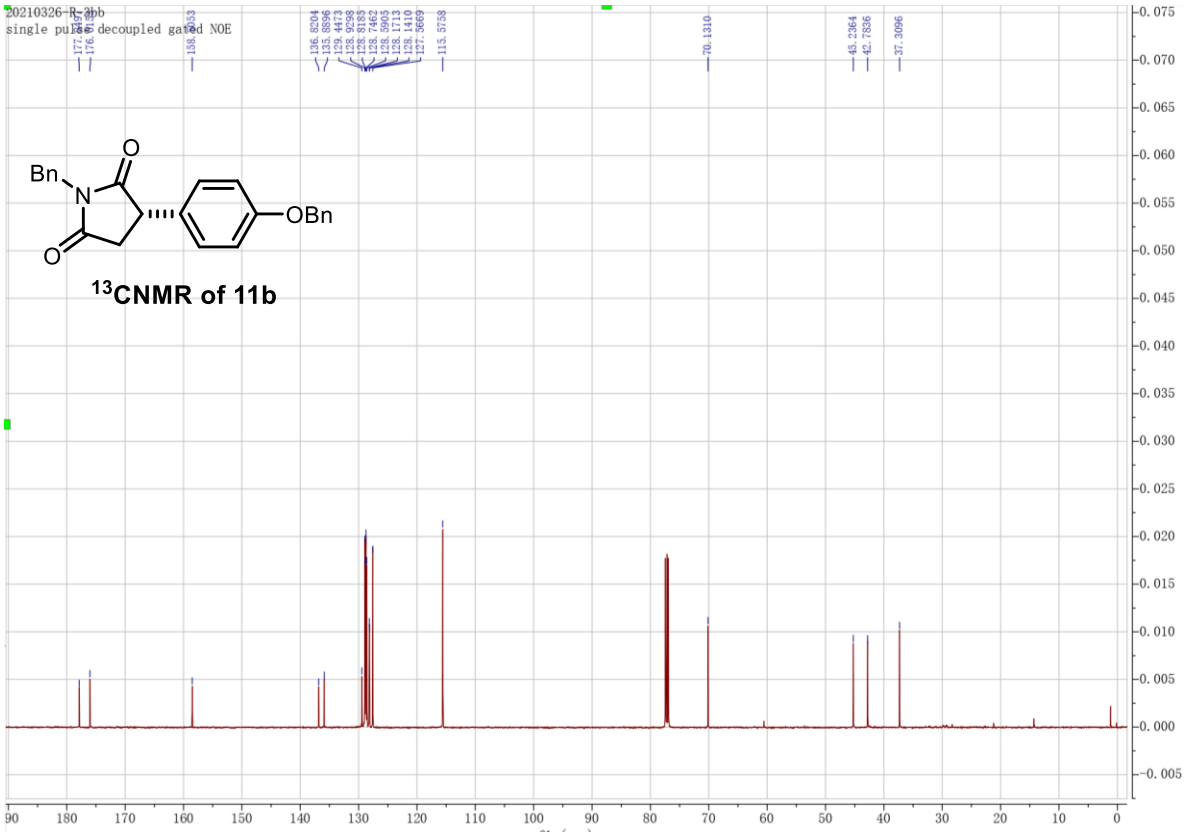
^{13}CNMR of 10q


20210312-MLA-NH
single_pulse
HN
O
O
OMe
1HNMR of 10r

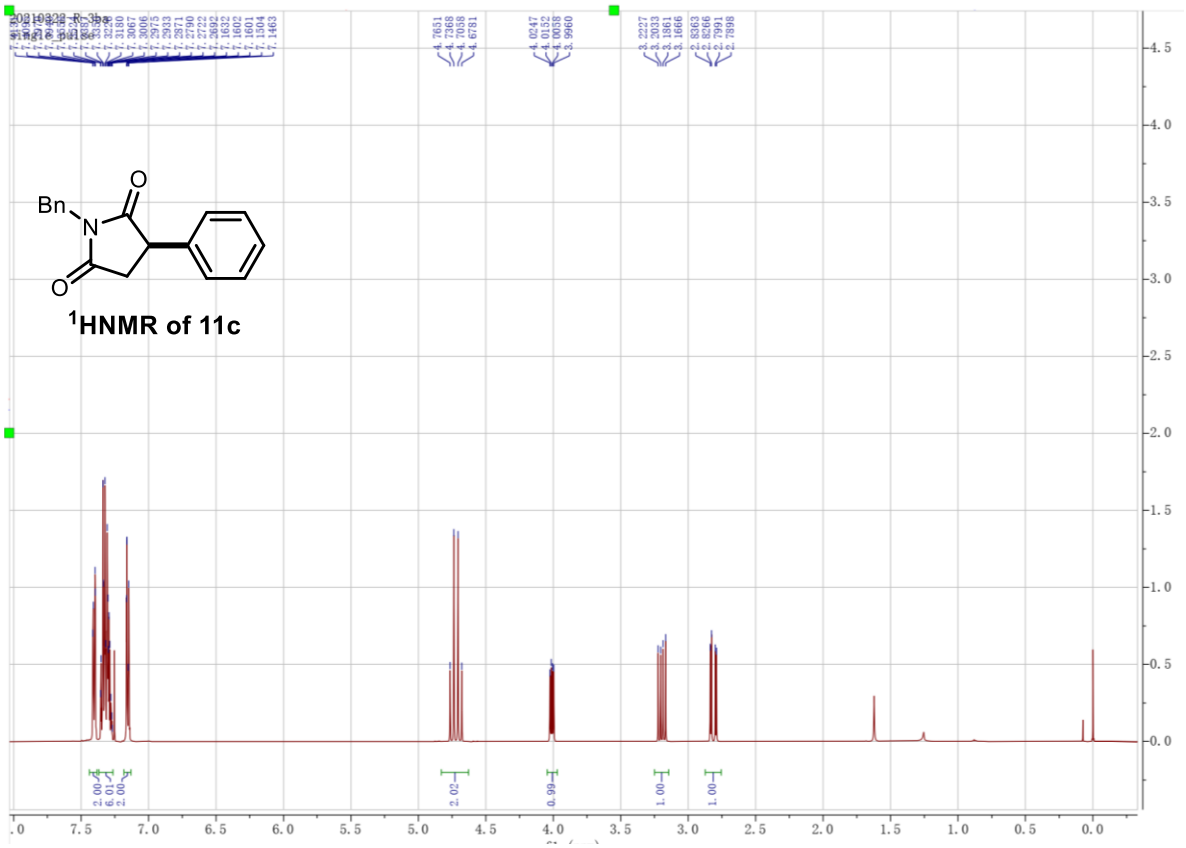

20210312-MLA-NH
single_pulse decoupled gated NOE
HN
O
O
OMe
13 CNMR of 10r

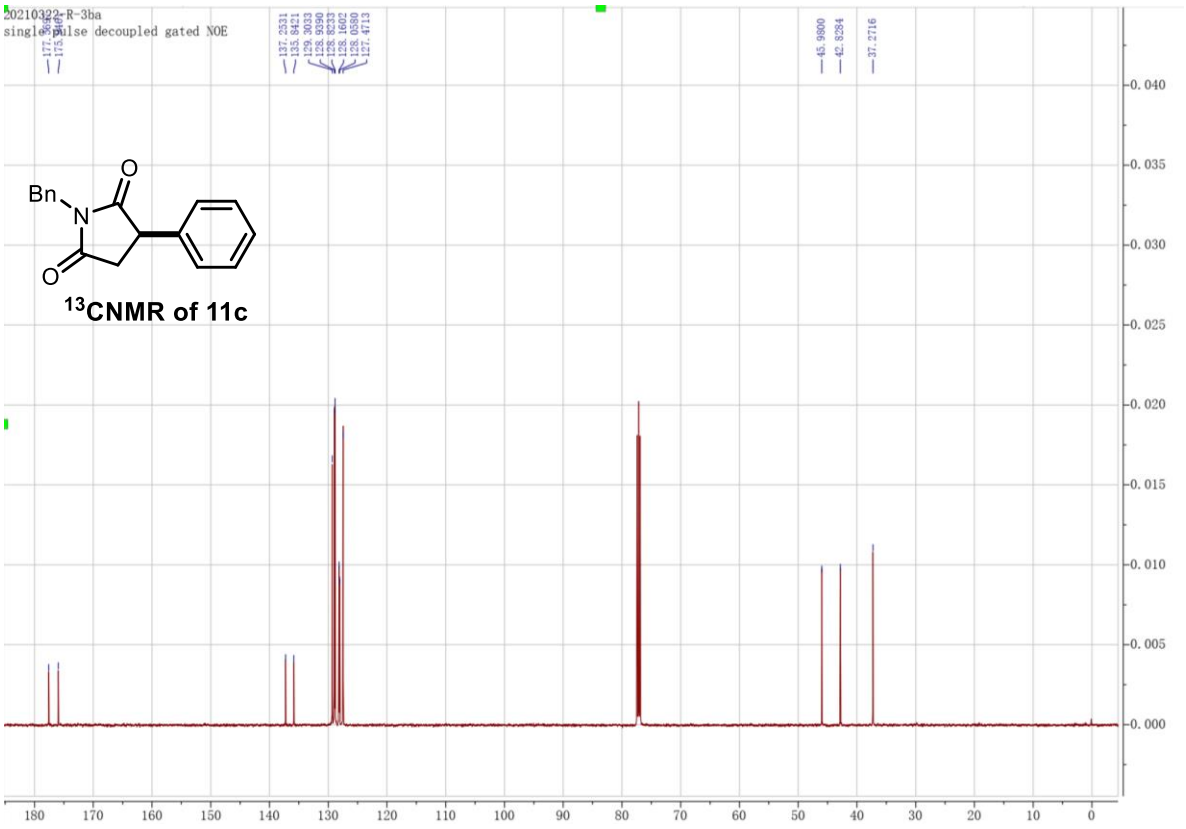


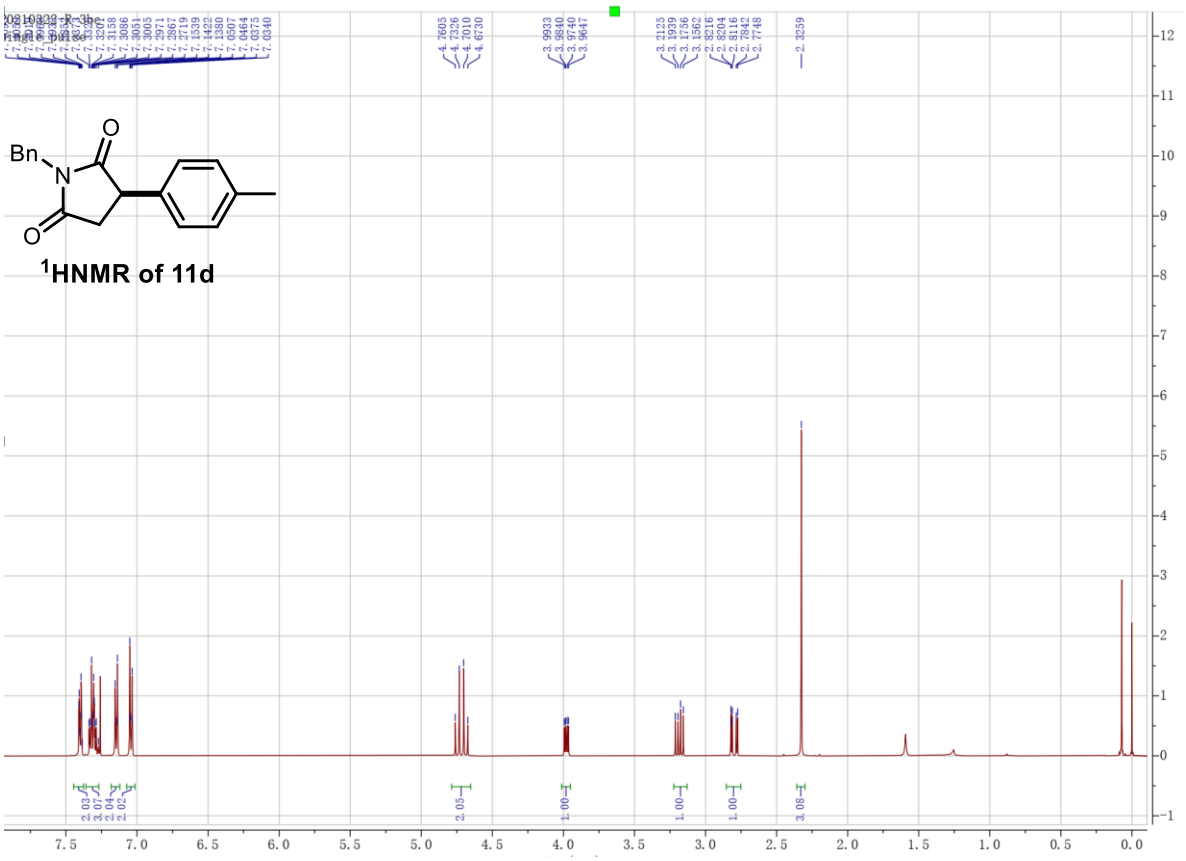
^{1}HNMR of 11b

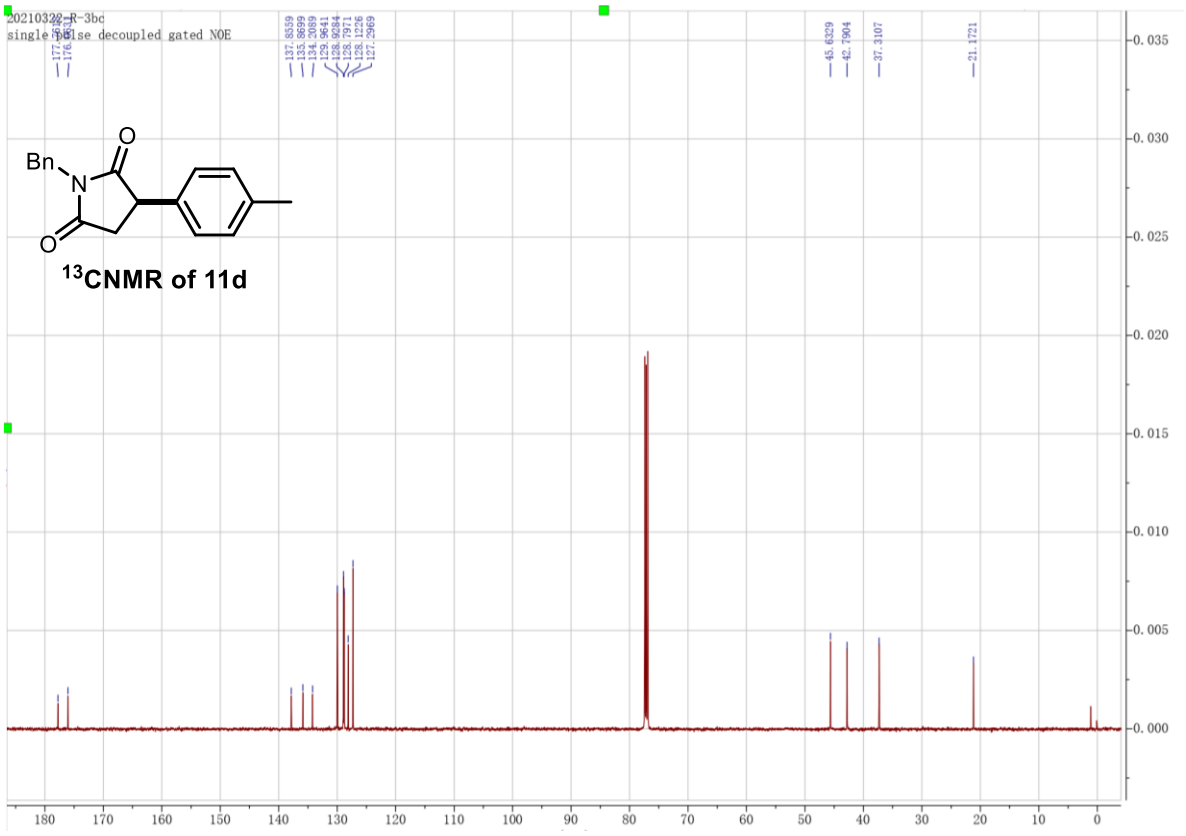


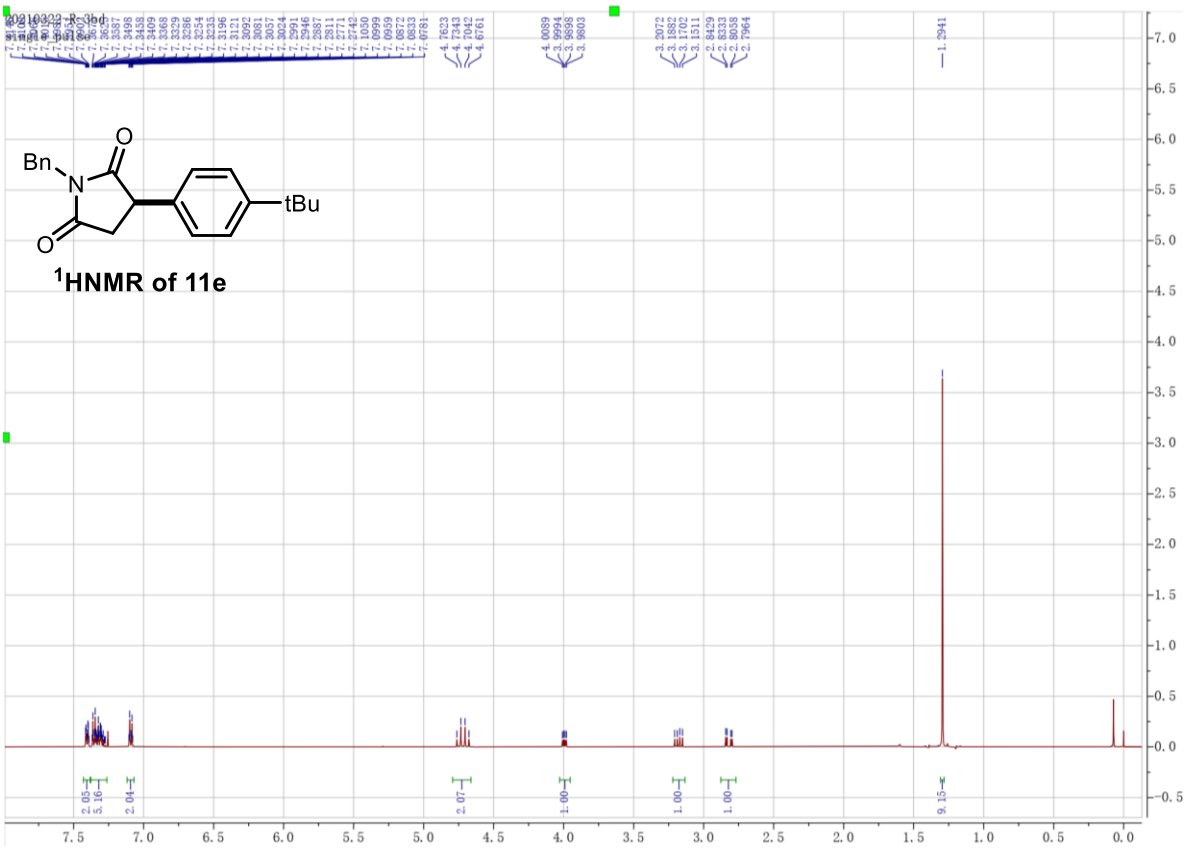
^{13}CNMR of 11b


Bn
N
O
O
1HNMR of 11c

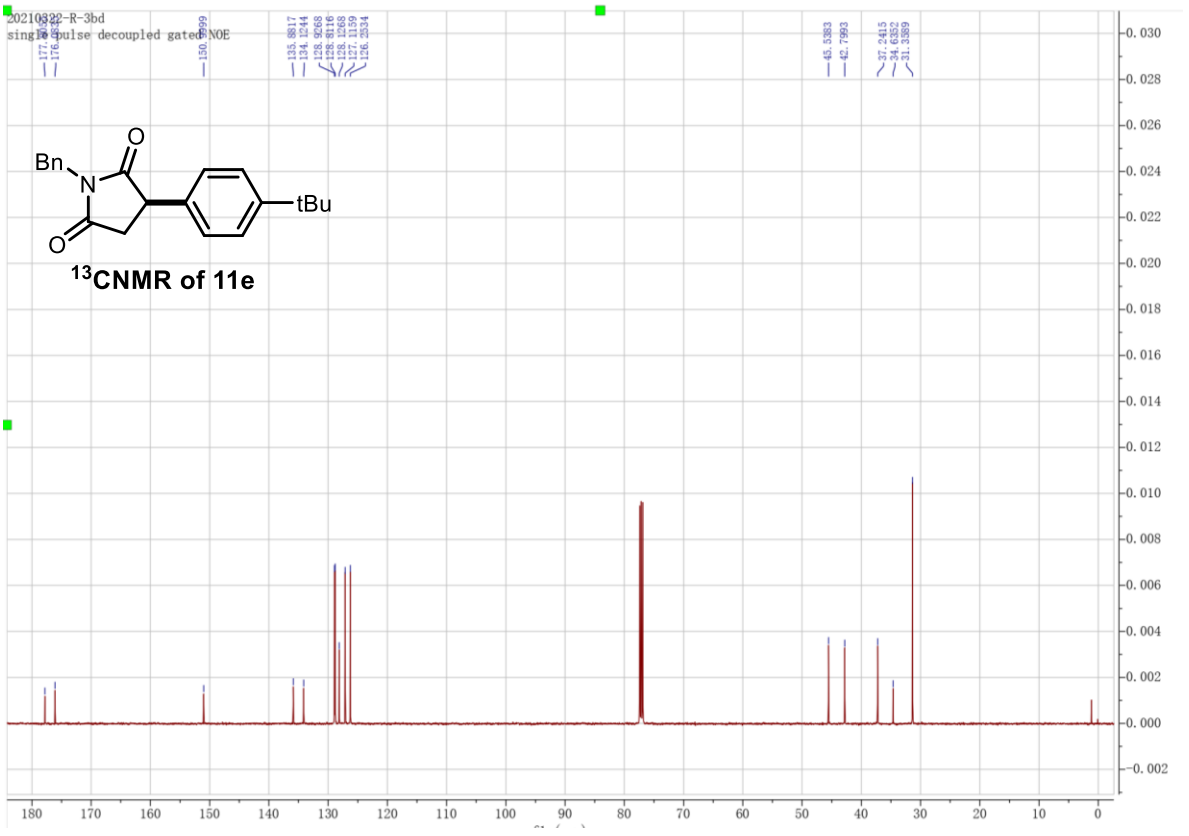

20210322-R-3ba
single pulse decoupled gated NOE
Bn
N
O
O
13CNMR of 11c


Bn
N
O
O
1HNMR of 11d


Bn
N
O
O
13CNMR of 11d

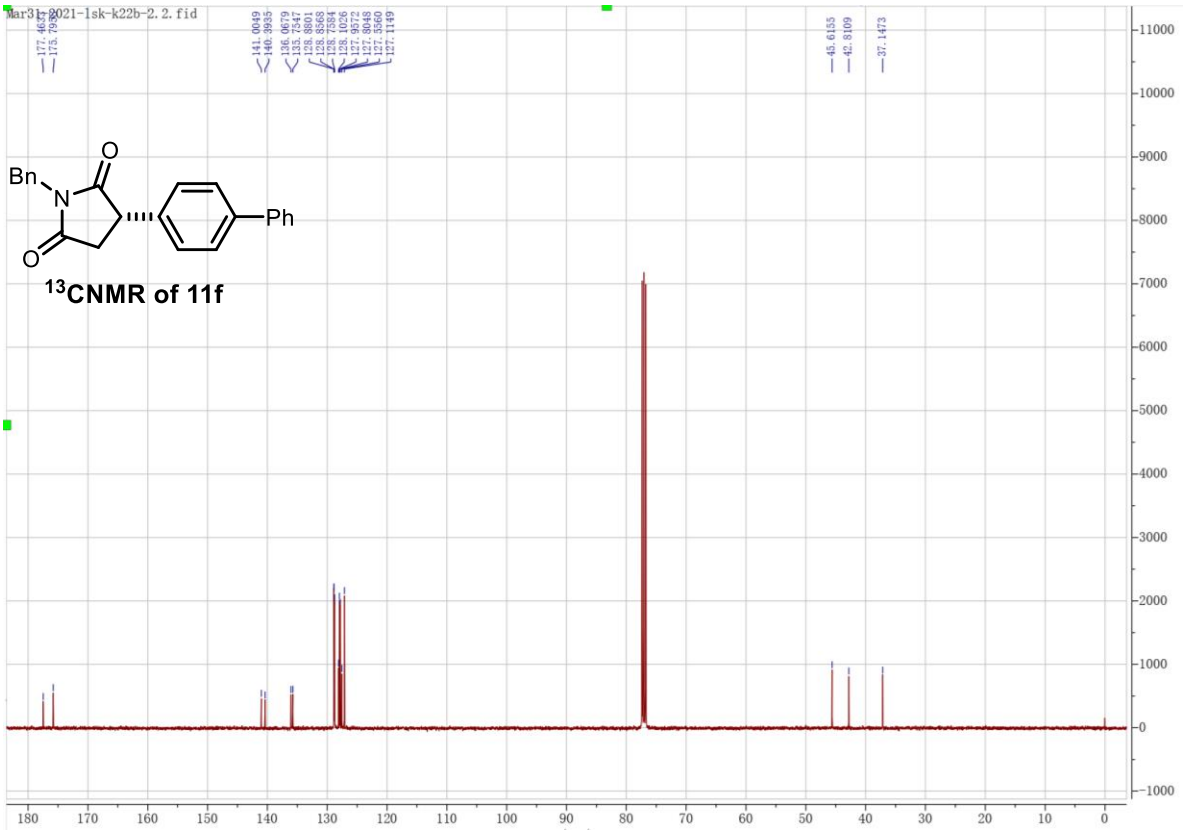


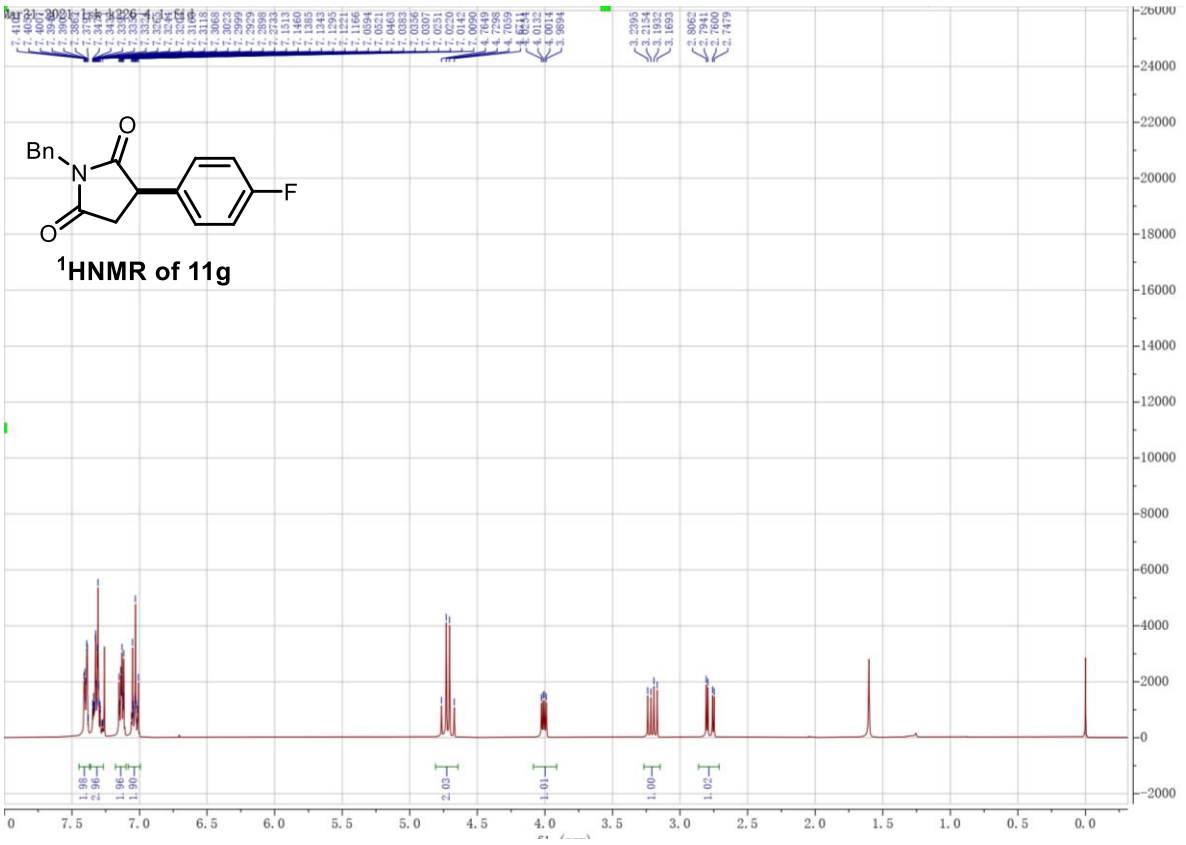
^{1}HNMR of 11e



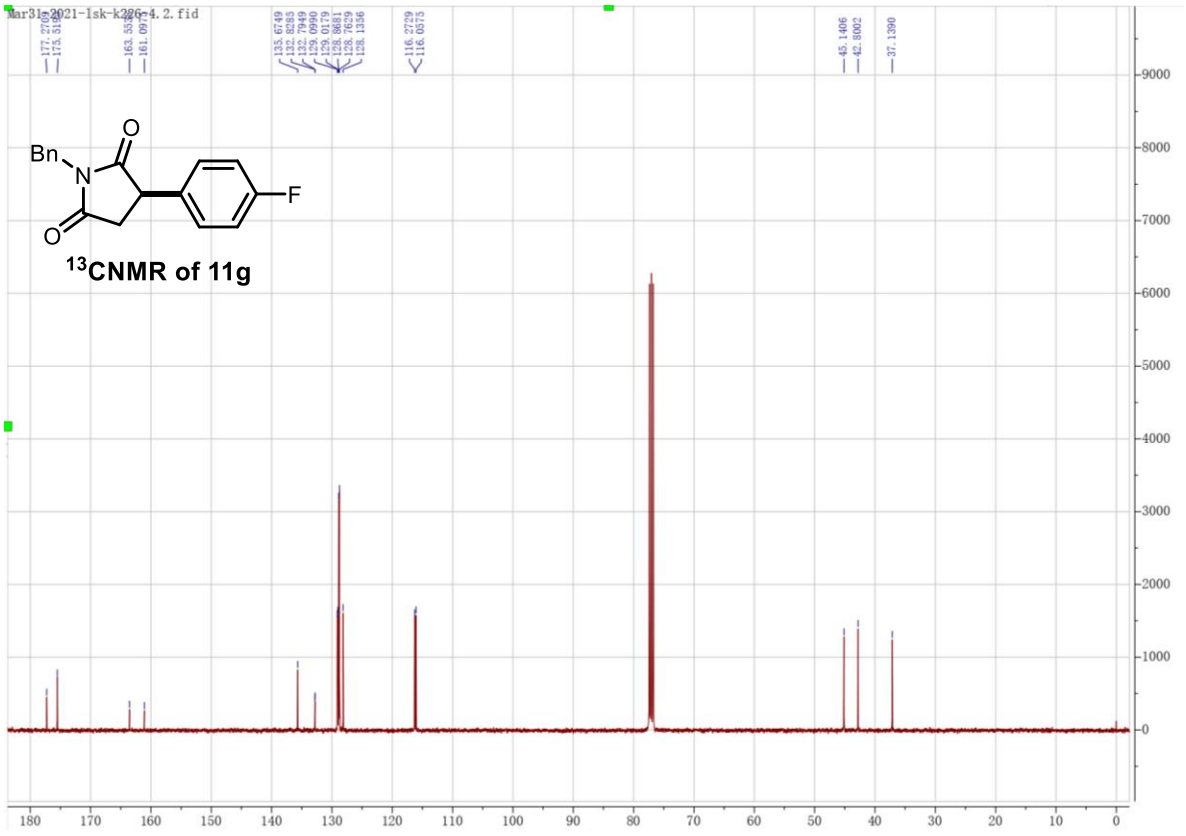
^{13}CNMR of 11e


Bn
N
O
O
Ph
1HNMR of 11f

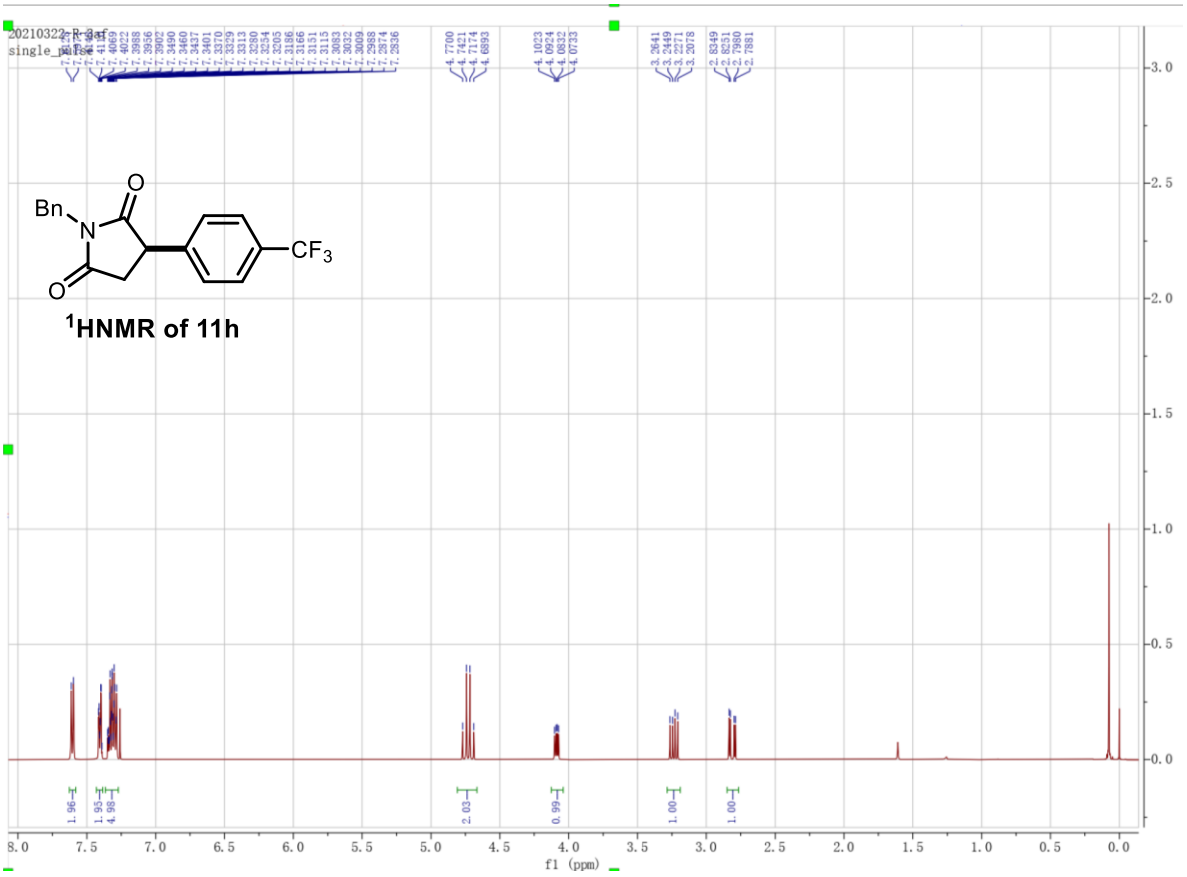

Bn
N
O
O
Ph
13CNMR of 11f



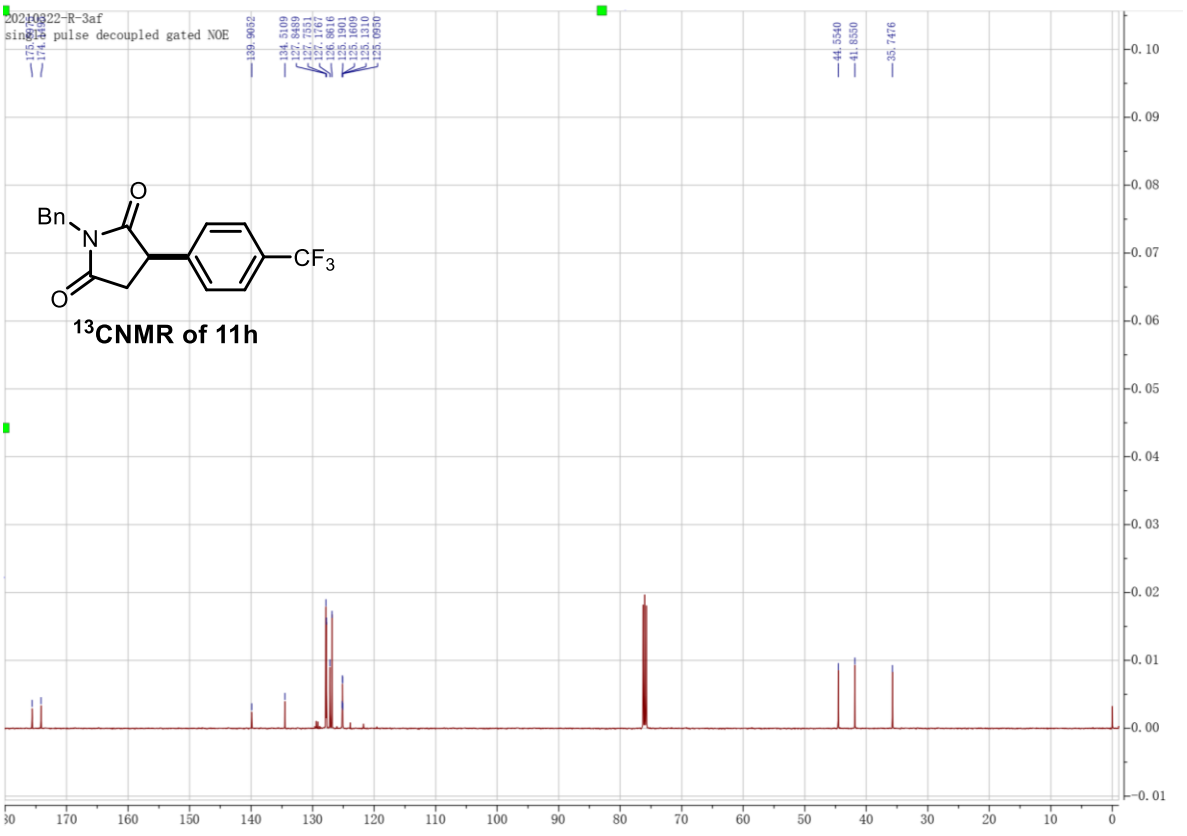
^{1}HNMR of 11g



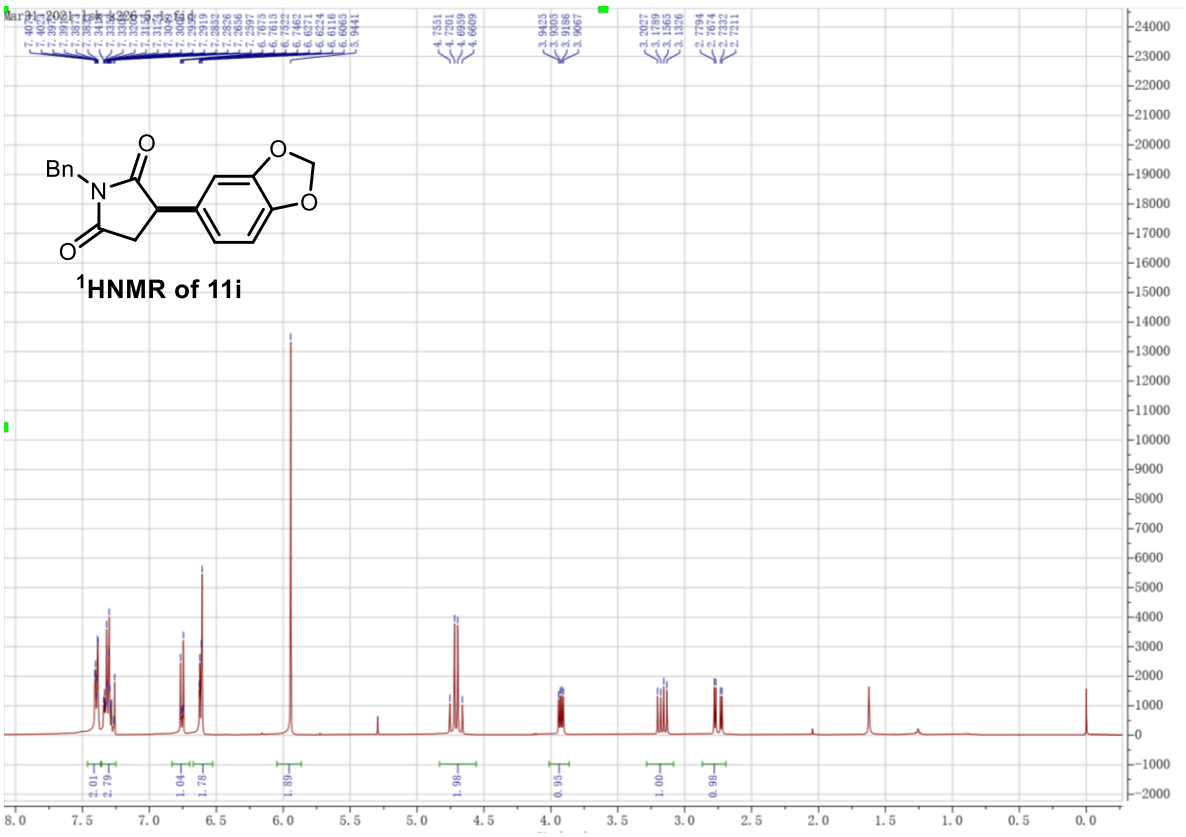
^{13}CNMR of 11g

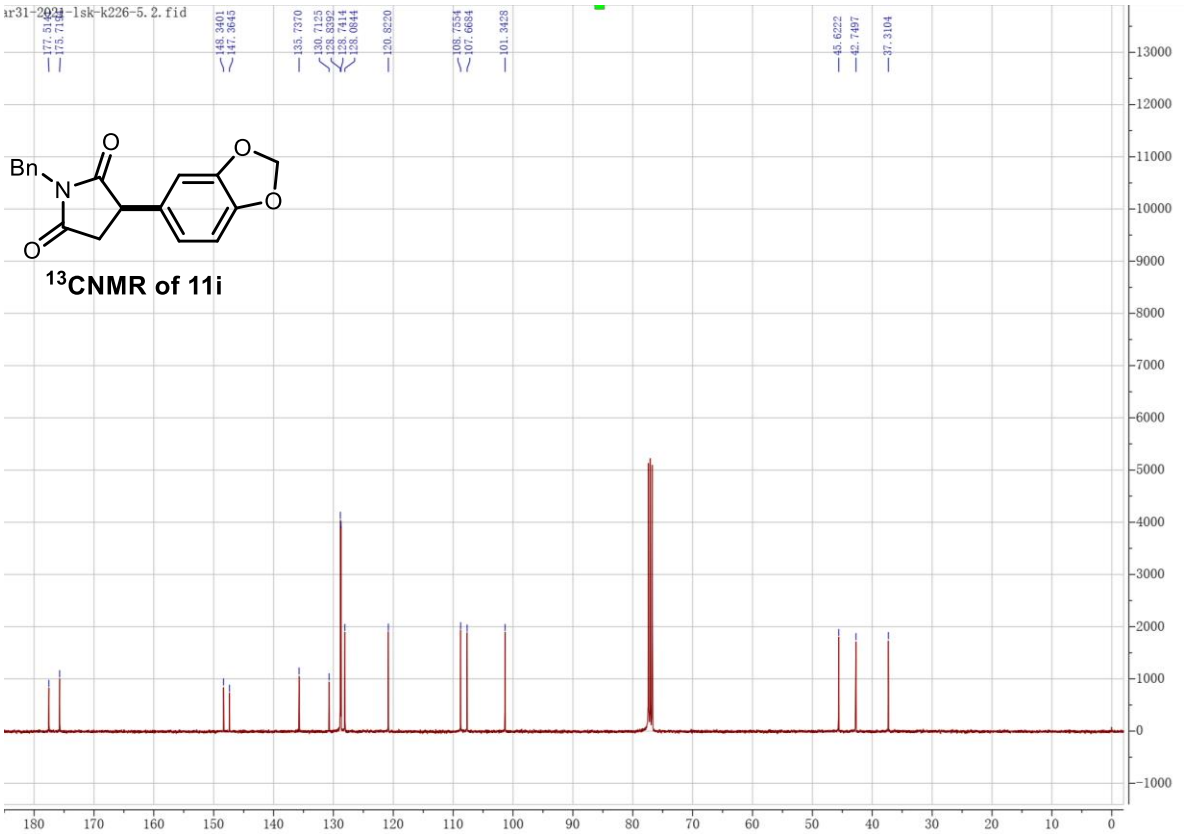


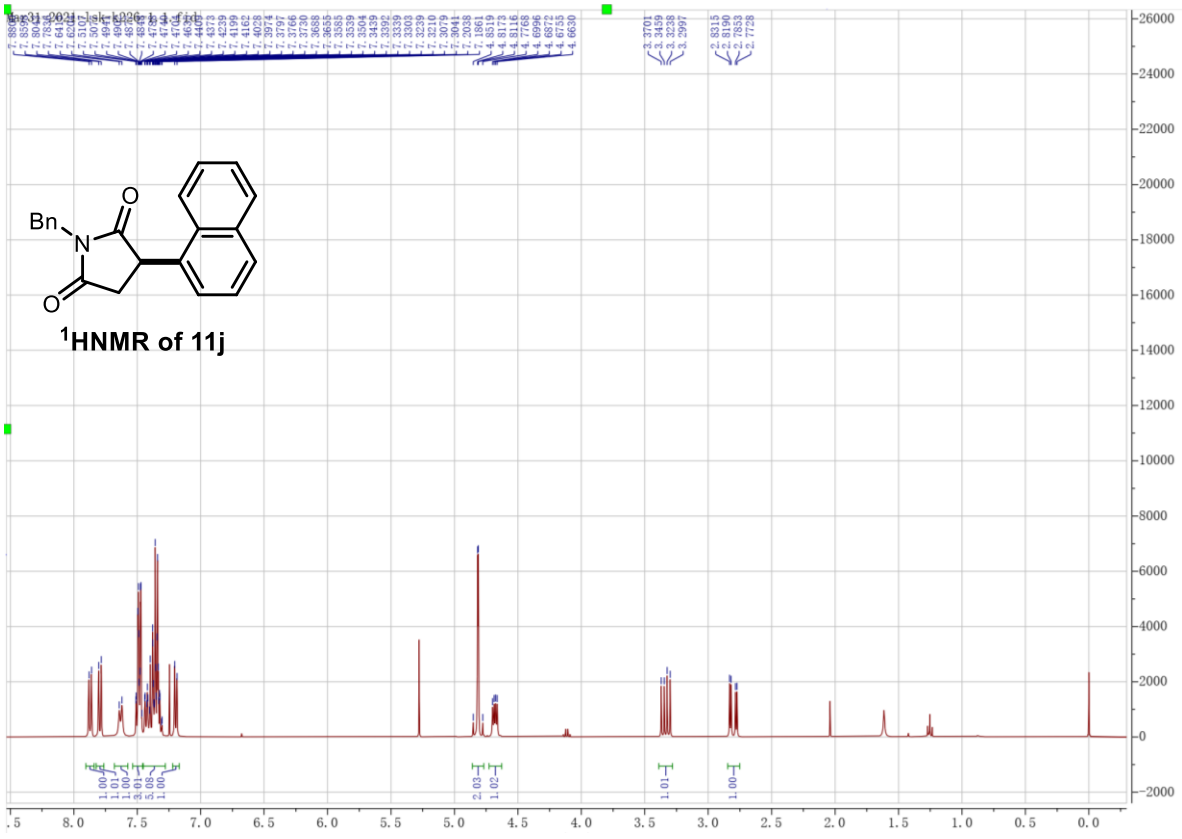
^{1}HNMR of 11h

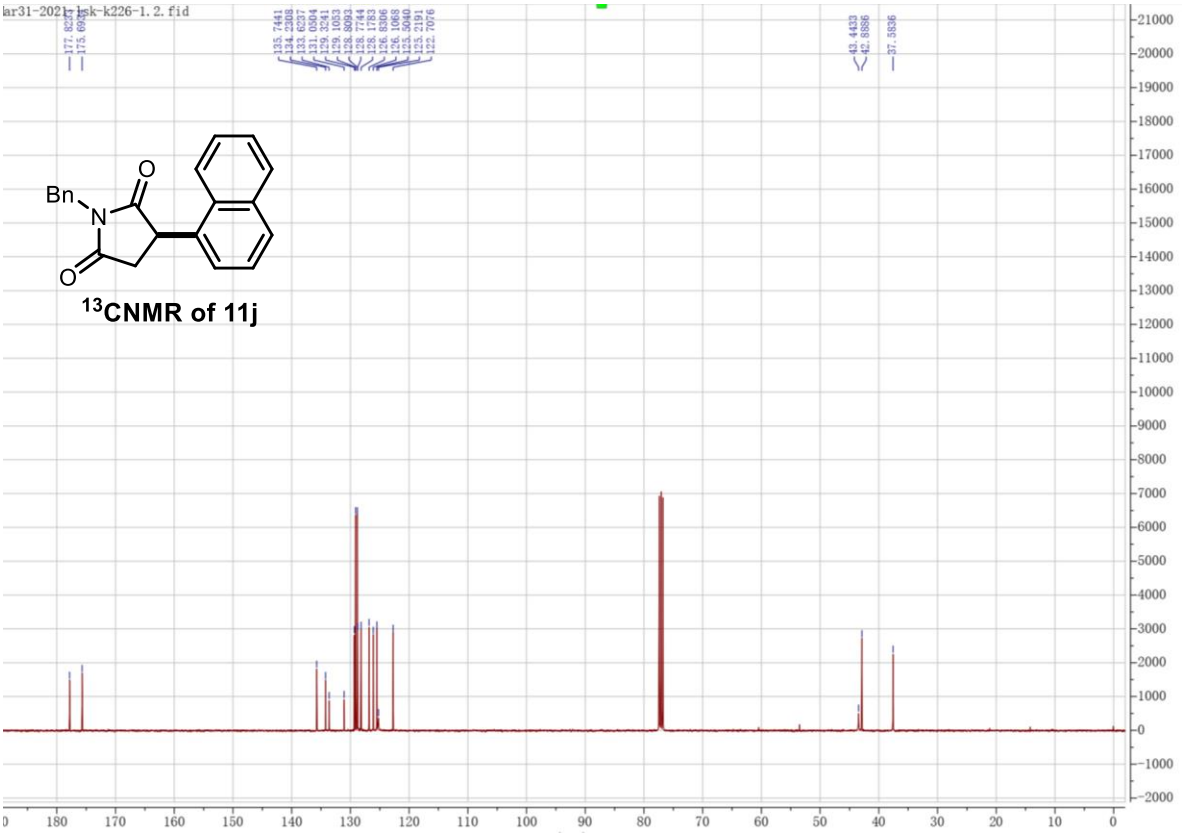


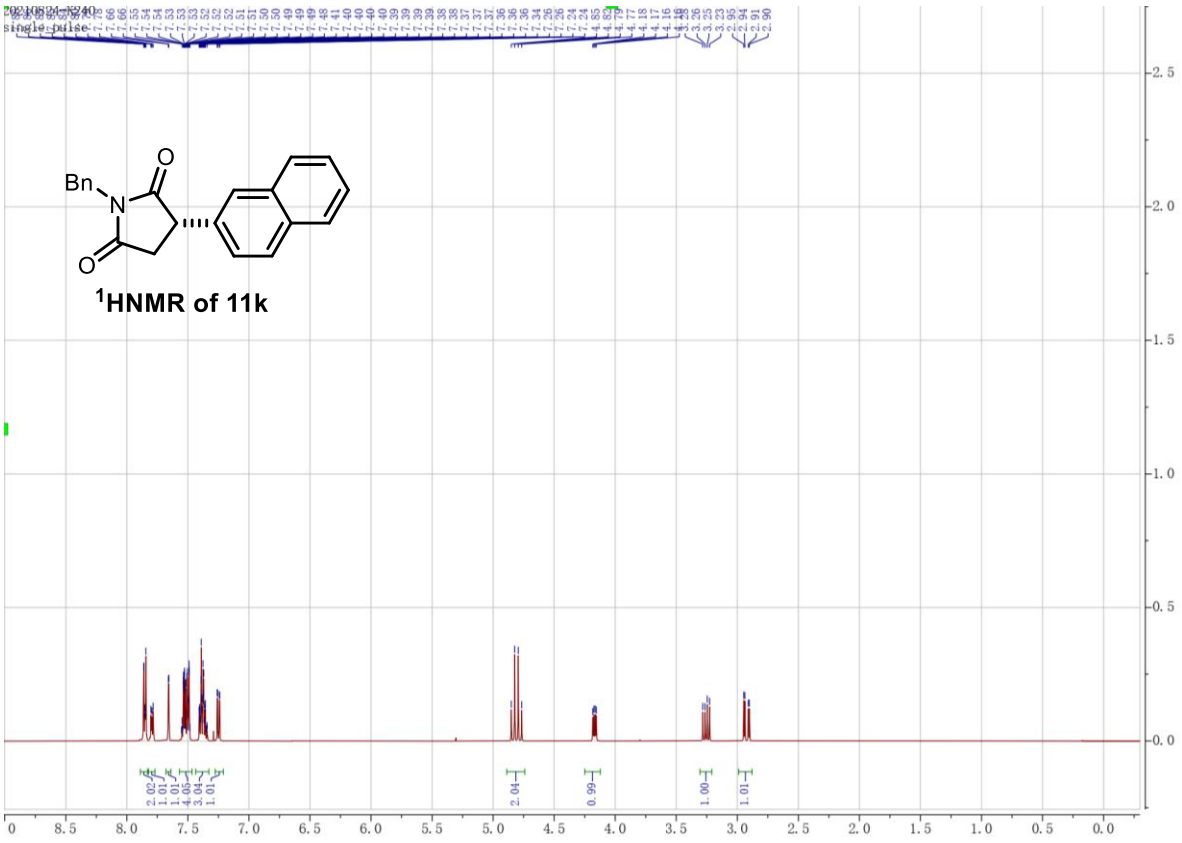
^{13}CNMR of 11h

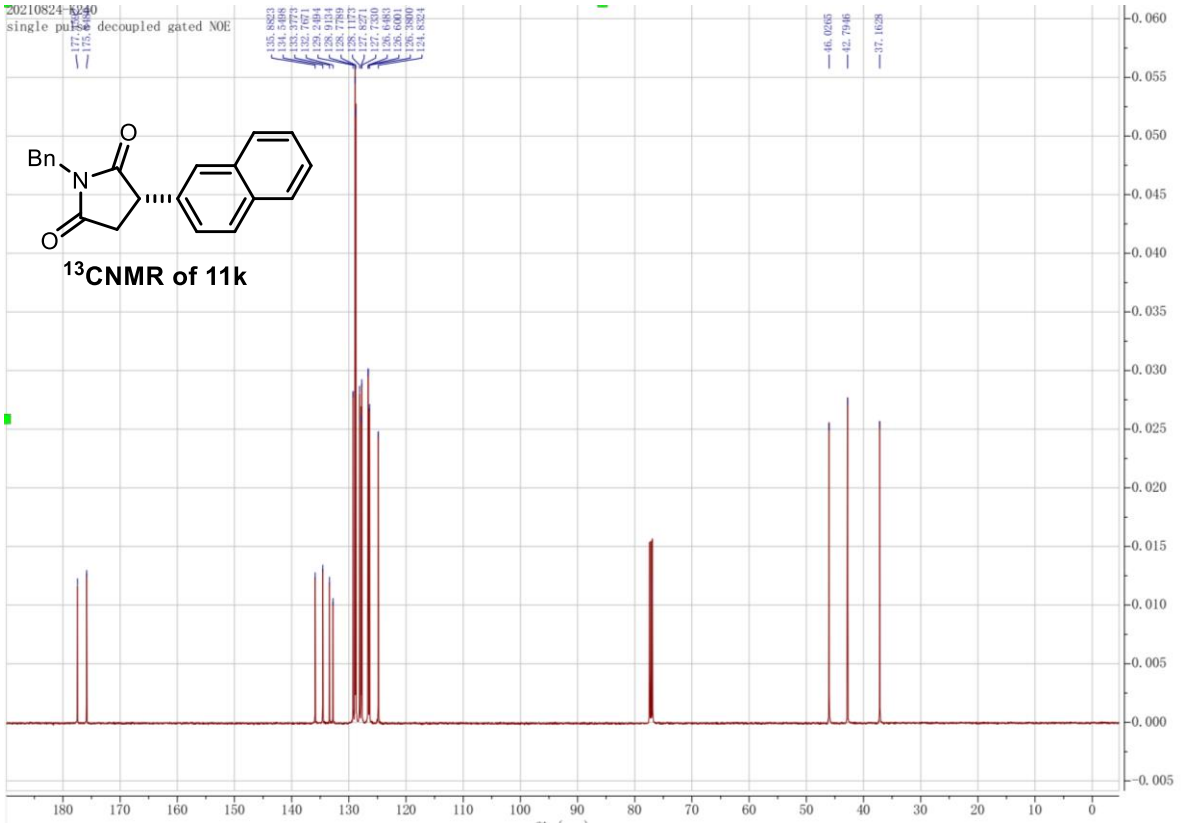

Bn
N
O
O
O
O
O
^{1}HNMR of 11i

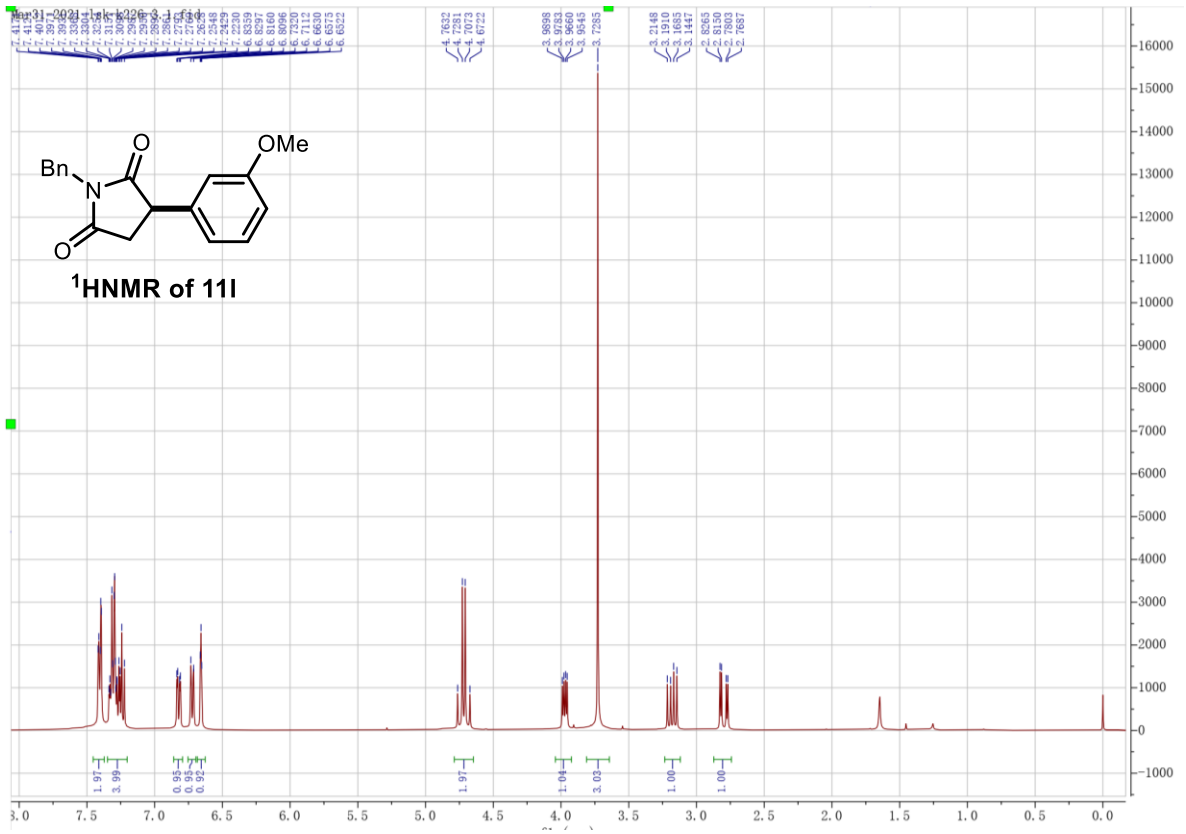

Bn
N
O
O
O
O
O
^{13}CNMR of 11i


Bn
N
O
O
1HNMR of 11j

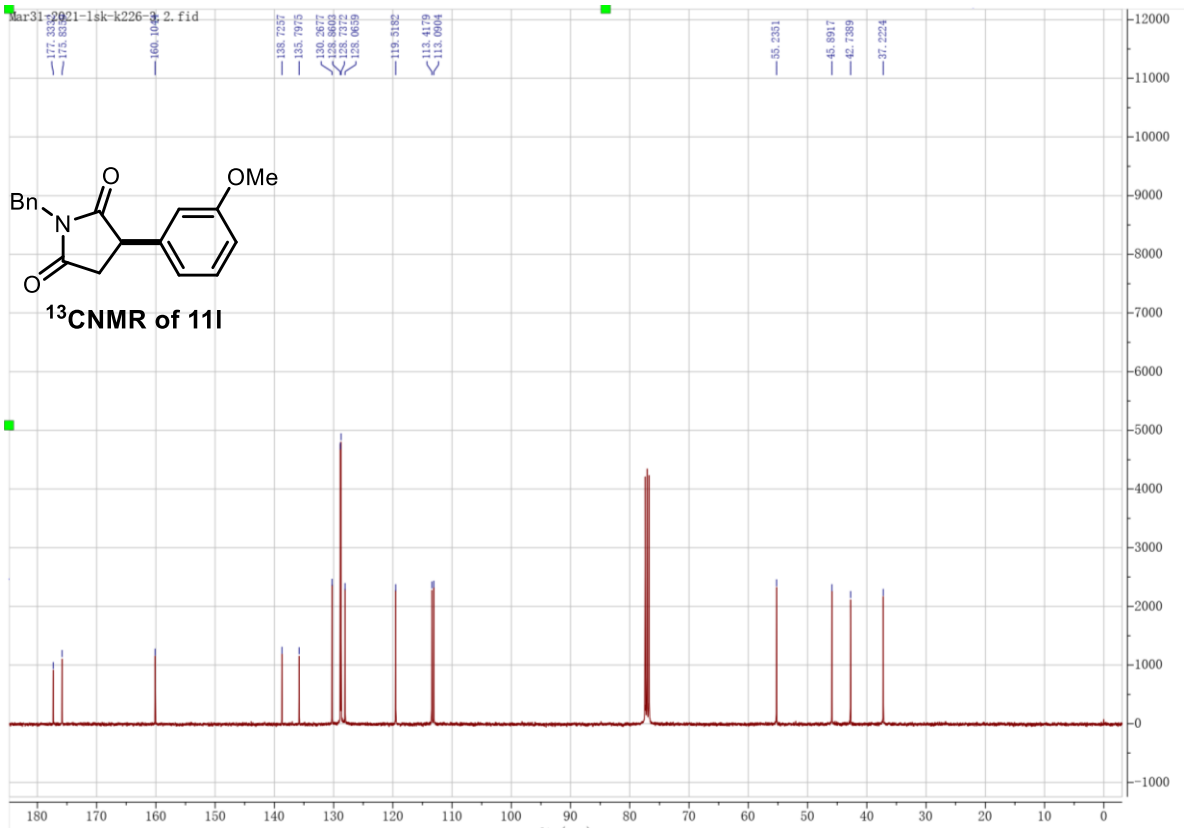

Bn
N
O
O
13CNMR of 11j


Bn
N
O
O
1HNMR of 11k


single pulse decoupled gated NOE
Bn
N
O
O
13CNMR of 11k



^{1}HNMR of 11l



^{13}CNMR of 11l