

**Enantioselective synthesis of chiral α,β -unsaturated
 γ -substituted butyrolactams by organocatalyzed direct
asymmetric vinylogous Michael addition of α,β -unsaturated
 γ -butyrolactam to 2-enoylpyridines**

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Xiao-Mei Zhang^a and Wei-Cheng Yuan*^a

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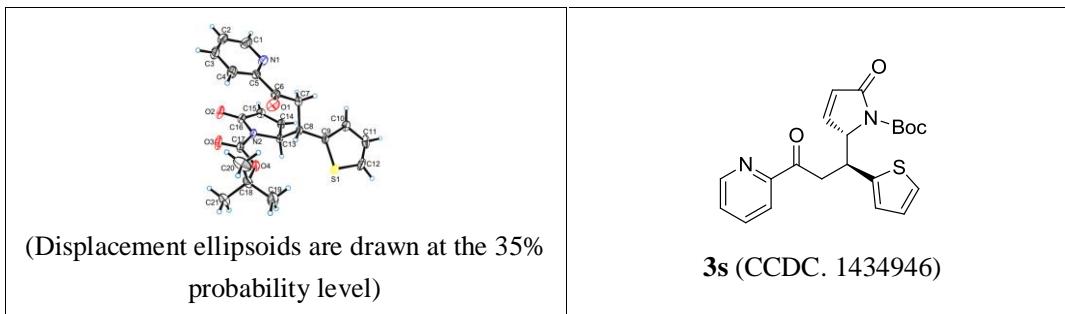
xuxy@cioc.ac.cn

Supporting Information

Table of Contents

1. X-ray crystal structure of compound 3s	S1
2. ^1H , ^{13}C NMR and HPLC spectra for compounds 3a-x and compounds 4 , 5 , and 6	S2

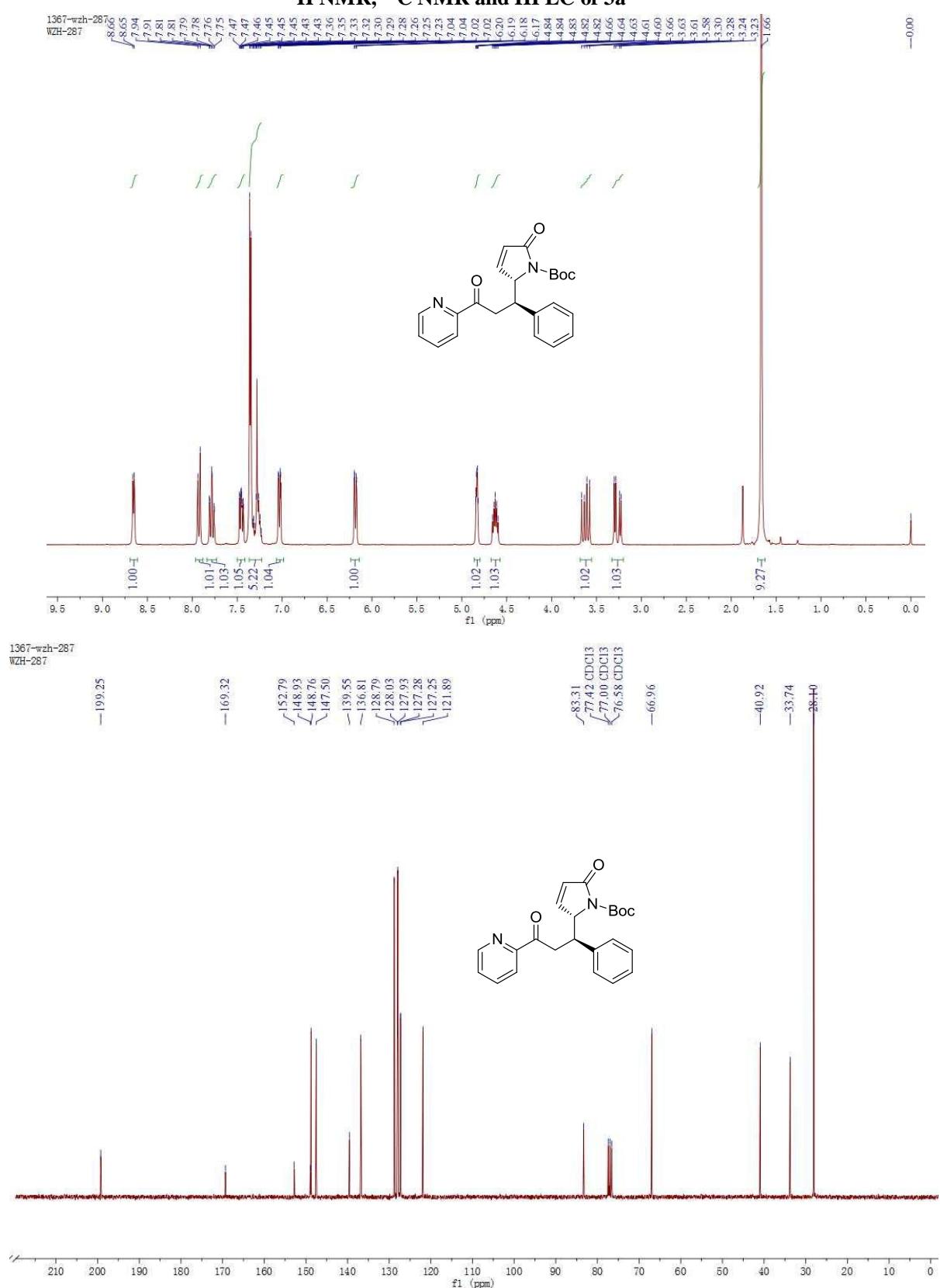
1. X-ray crystallography of compound 3s

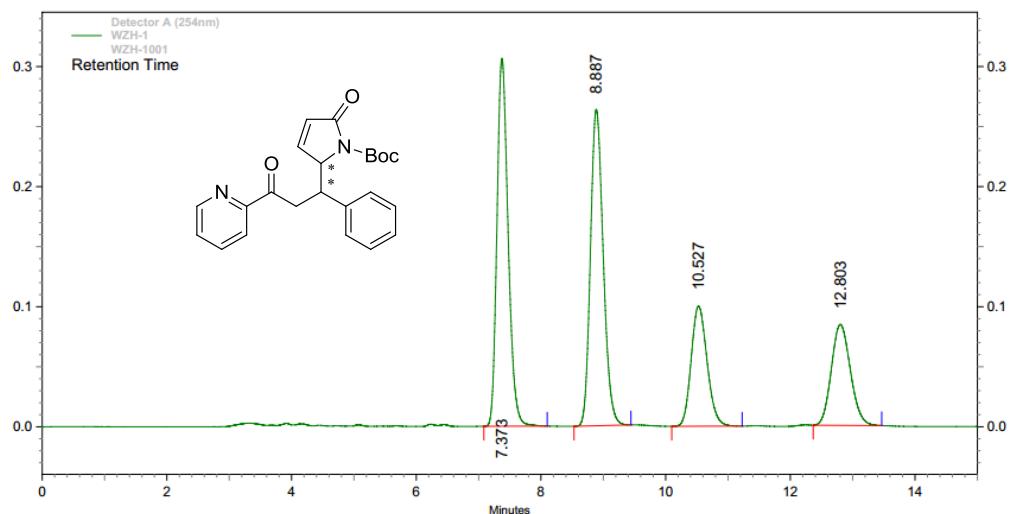


Identification code	3s
Empirical formula	C ₂₁ H ₂₂ N ₂ O ₄ S
Formula weight	398.46
Temperature/K	291(2)
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	8.291(5)
b/Å	10.918(5)
c/Å	22.462(5)
α/°	90.000(5)
β/°	90.000(5)
γ/°	90.000(5)
Volume/Å ³	2033.3(16)
Z	4
ρ _{calc} g/cm ³	1.302
μ/mm ⁻¹	1.659
F(000)	840.0
Crystal size/mm ³	0.420 × 0.400 × 0.350
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.872 to 139.54
Index ranges	-9 ≤ h ≤ 7, -12 ≤ k ≤ 10, -25 ≤ l ≤ 26
Reflections collected	5986
Independent reflections	3612 [R _{int} = 0.0283, R _{sigma} = 0.0348]
Data/restraints/parameters	3612/2/260
Goodness-of-fit on F ²	1.087
Final R indexes [I>=2σ (I)]	R ₁ = 0.0454, wR ₂ = 0.1149
Final R indexes [all data]	R ₁ = 0.0552, wR ₂ = 0.1357
Largest diff. peak/hole / e Å ⁻³	0.19/-0.21
Flack parameter	0.058(19)

2 ^1H , ^{13}C NMR, and HPLC spectra for compounds 3a-v, and compounds 4, 5, and 6.

^1H NMR, ^{13}C NMR and HPLC of 3a



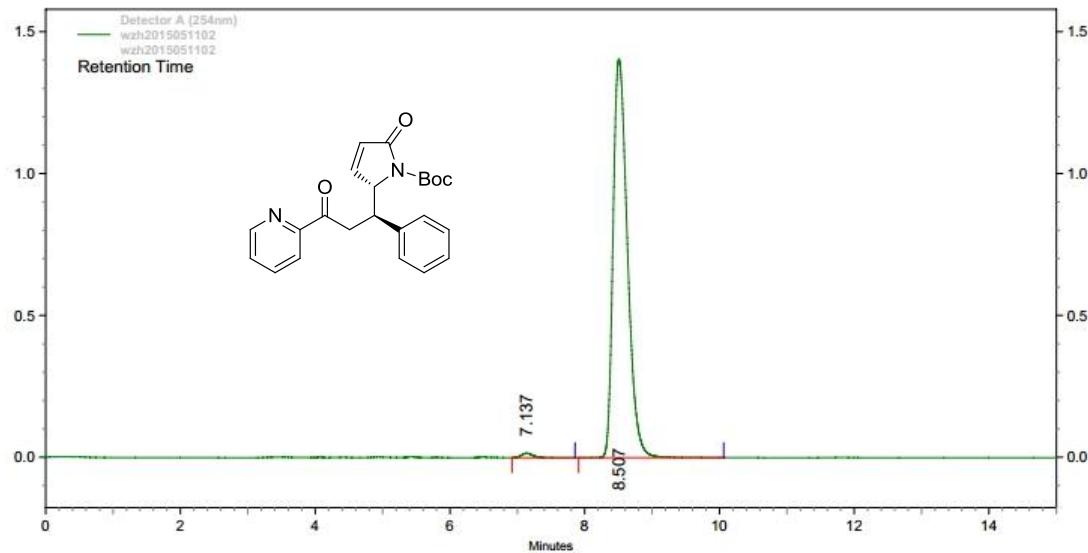


Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.373	306412	40.64	3806931	34.22
2	8.887	263451	34.94	3752158	33.73
3	10.527	100048	13.27	1780326	16.00
4	12.803	84028	11.15	1784165	16.04
Totals		753939	100.00	11123580	100.00



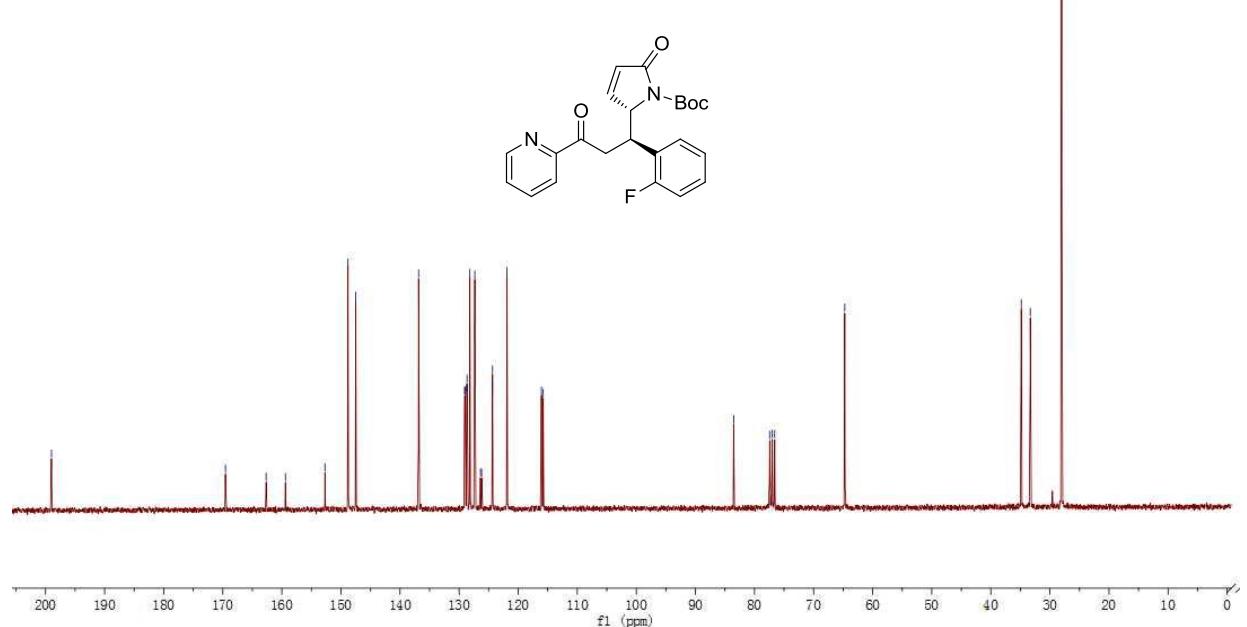
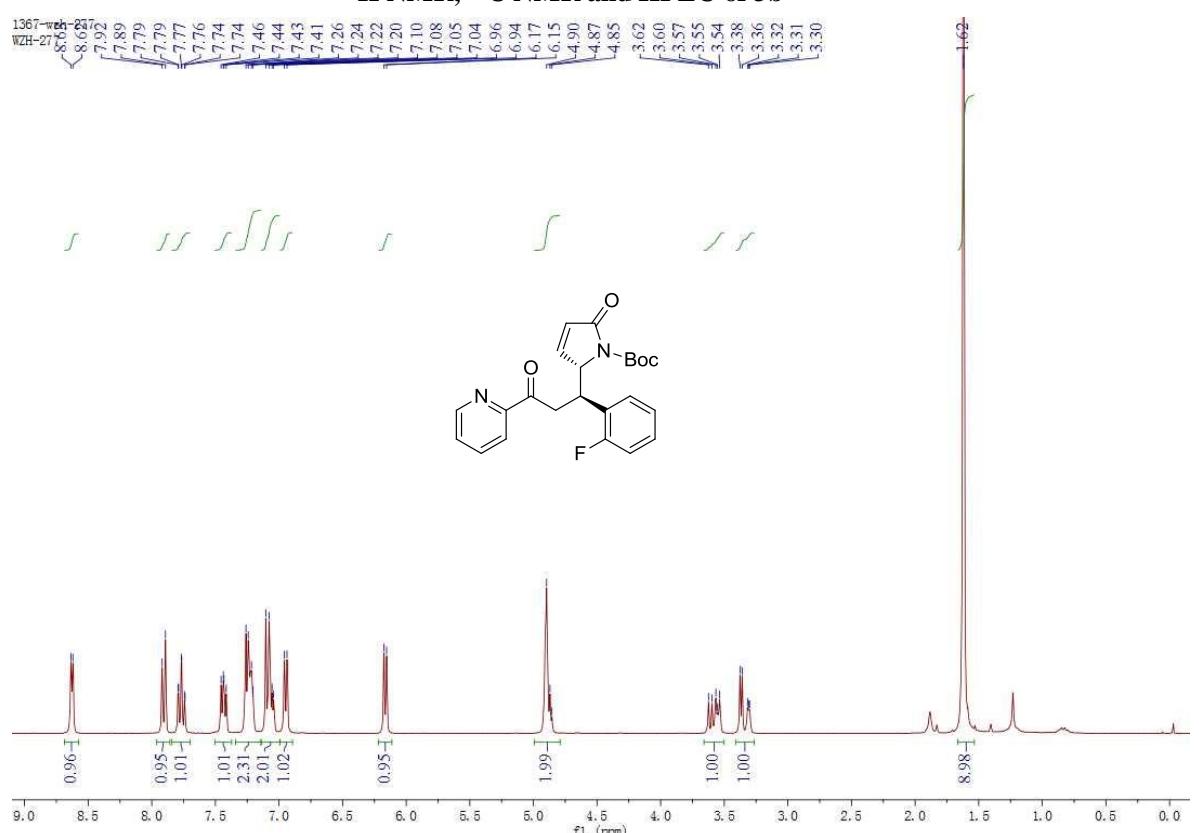
Detector

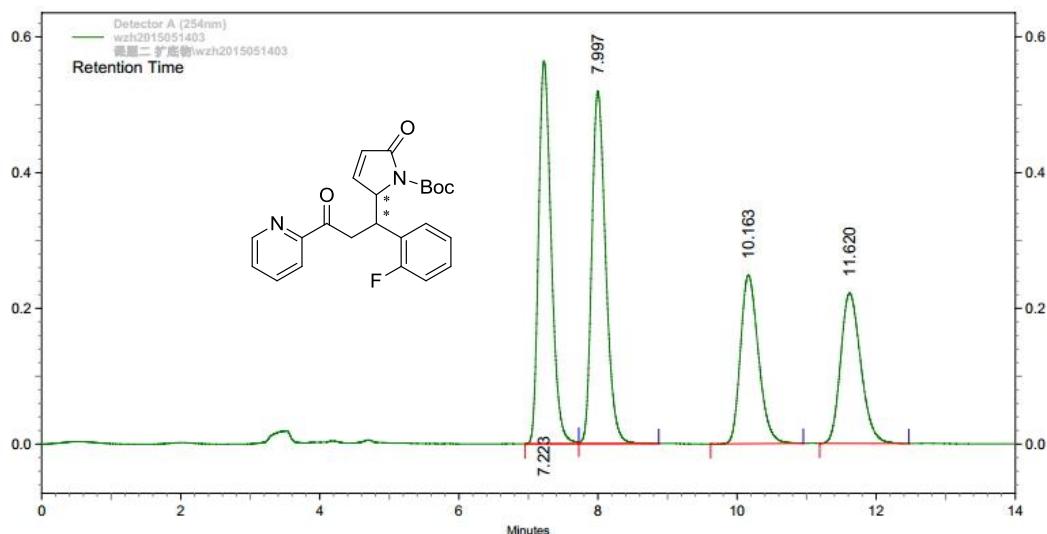
A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.137	15747	1.11	184096	0.88
2	8.507	1404848	98.89	20741869	99.12
Totals		1420595	100.00	20925965	100.00

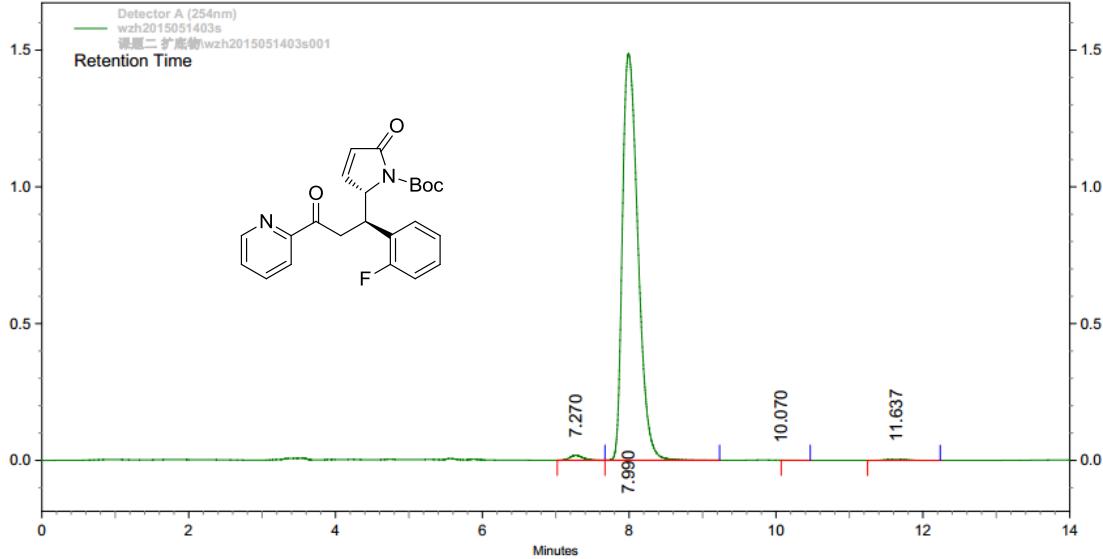
¹H NMR, ¹³C NMR and HPLC of 3b




Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.223	564153	36.30	7107613	30.60
2	7.997	519849	33.45	7188509	30.95
3	10.163	248489	15.99	4469084	19.24
4	11.620	221523	14.25	4463507	19.22

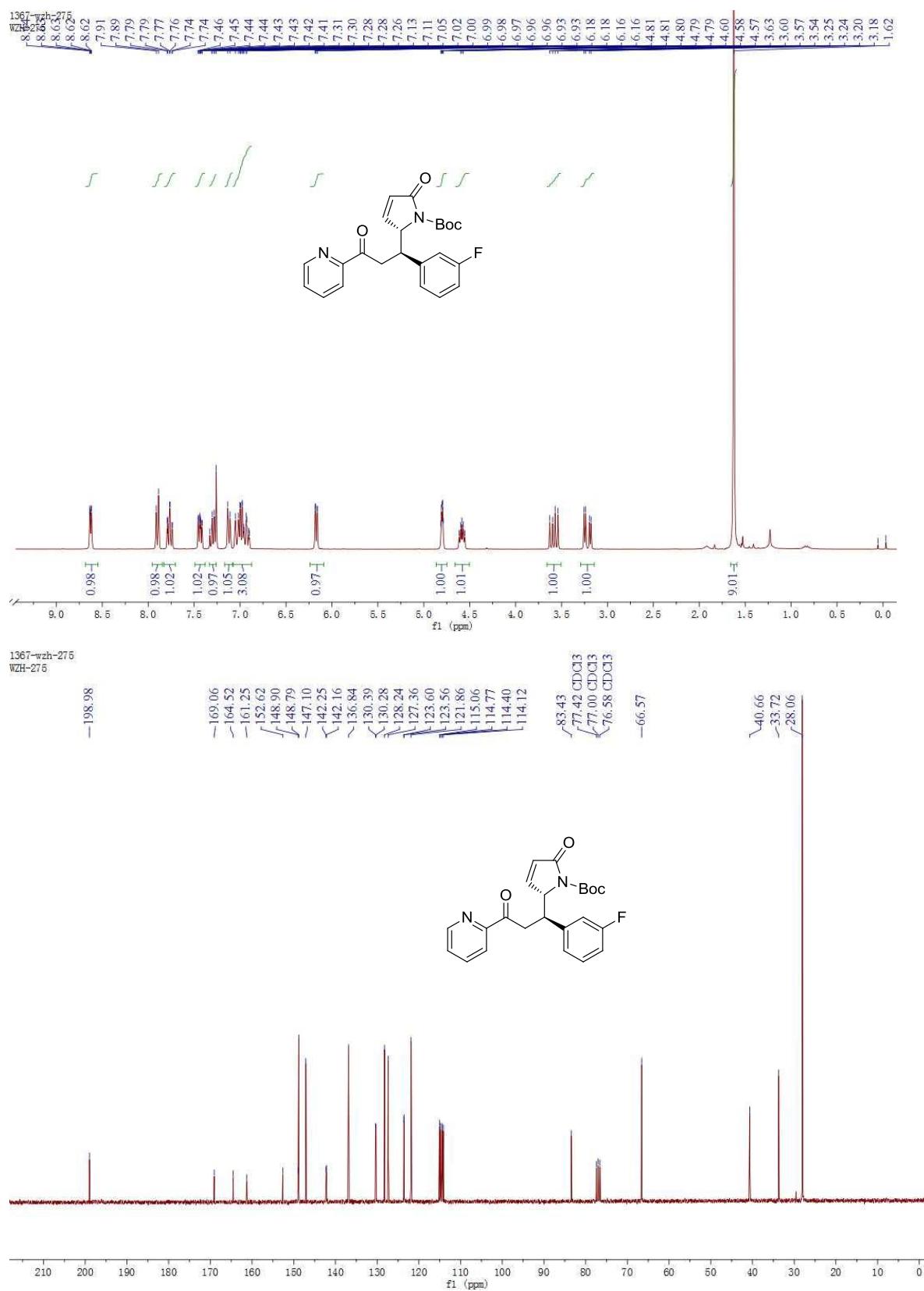
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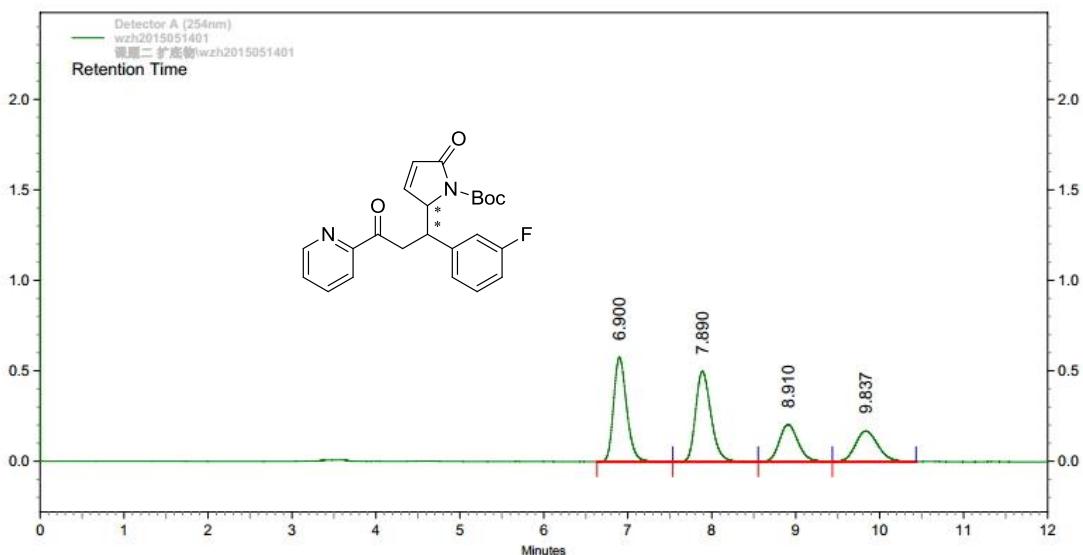

Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.270	18079	1.20	218254	0.99
2	7.990	1486950	98.56	21823731	98.69
3	10.070	0	0.00	622	0.00
4	11.637	3595	0.24	71071	0.32

Totals	1508624	100.00	22113678	100.00
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¹H NMR, ¹³C NMR and HPLC of 3c

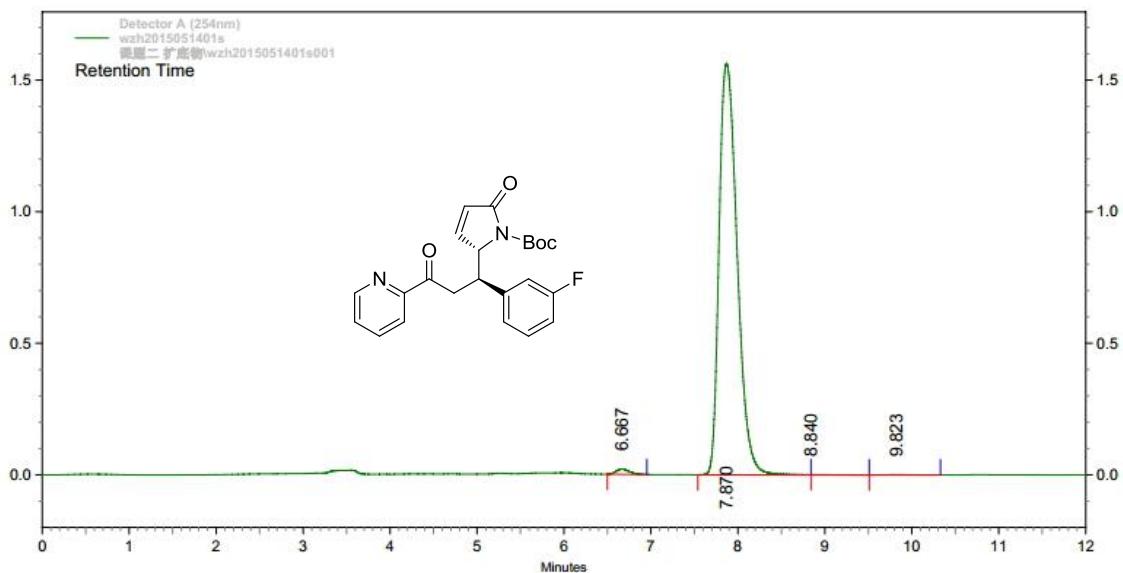




**Detector
A
(254nm)**

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.900	576543	39.78	6239686	33.00
2	7.890	499172	34.44	6328172	33.46
3	8.910	204401	14.10	3179973	16.82
4	9.837	169109	11.67	3162919	16.73

Totals	1449225	100.00	18910750	100.00
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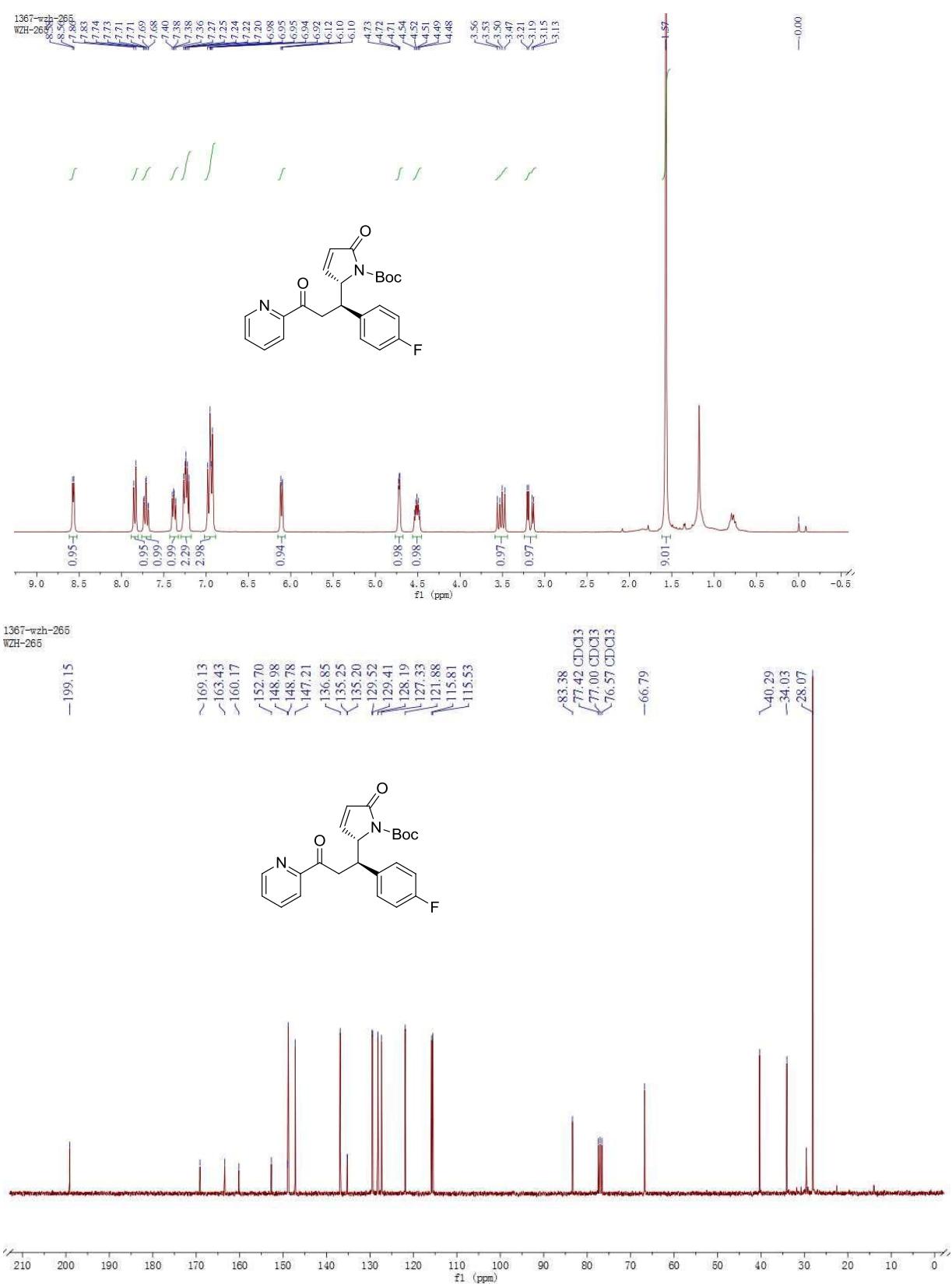


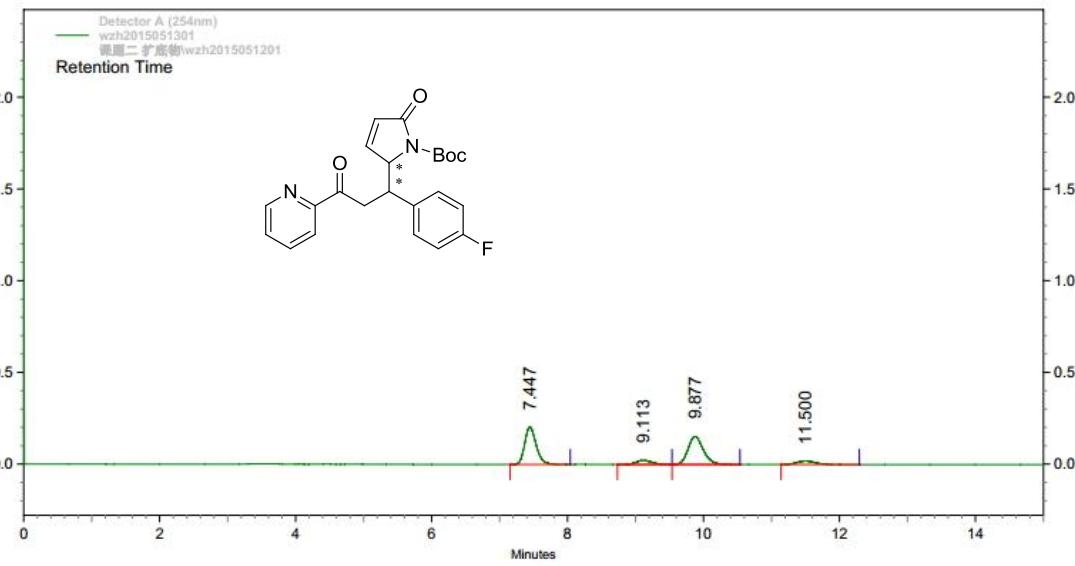
**Detector
A
(254nm)**

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.667	19973	1.26	212389	0.93
2	7.870	1562741	98.65	22524536	98.97
3	8.840	618	0.04	9808	0.04
4	9.823	810	0.05	12874	0.06

Totals	1584142	100.00	22759607	100.00
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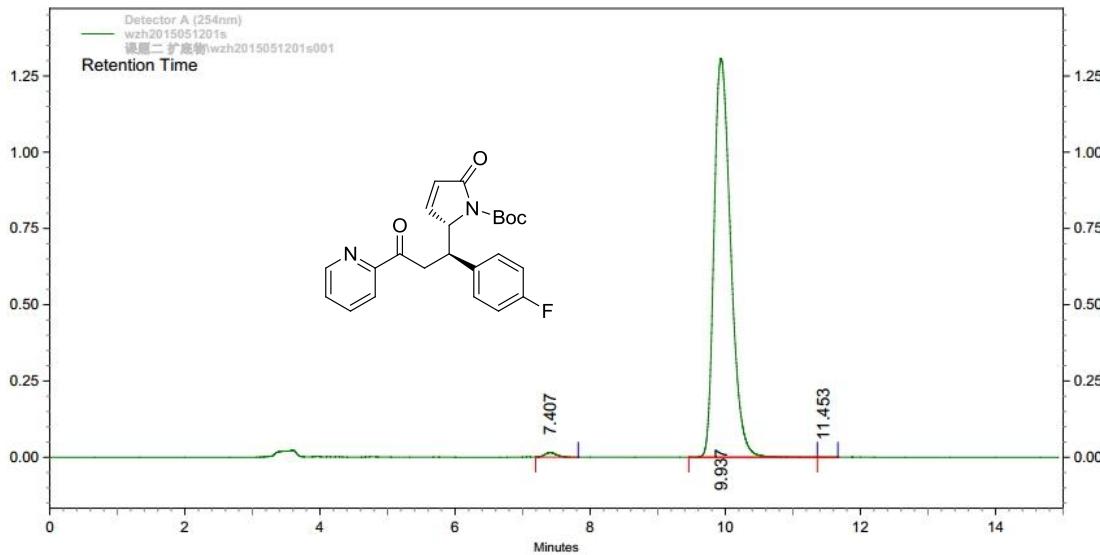
¹H NMR, ¹³C NMR and HPLC of 3d





Detector
A
(254nm)

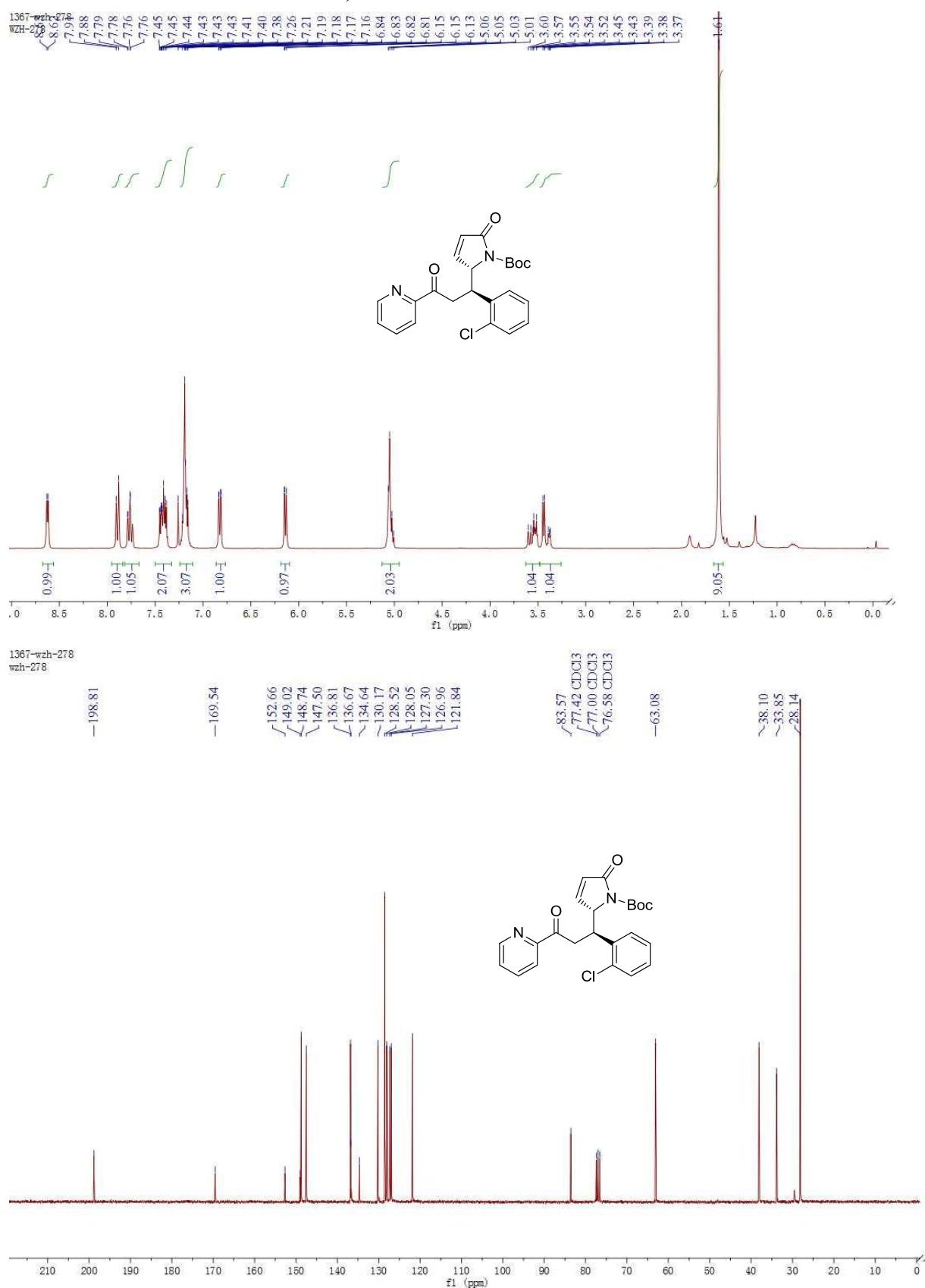
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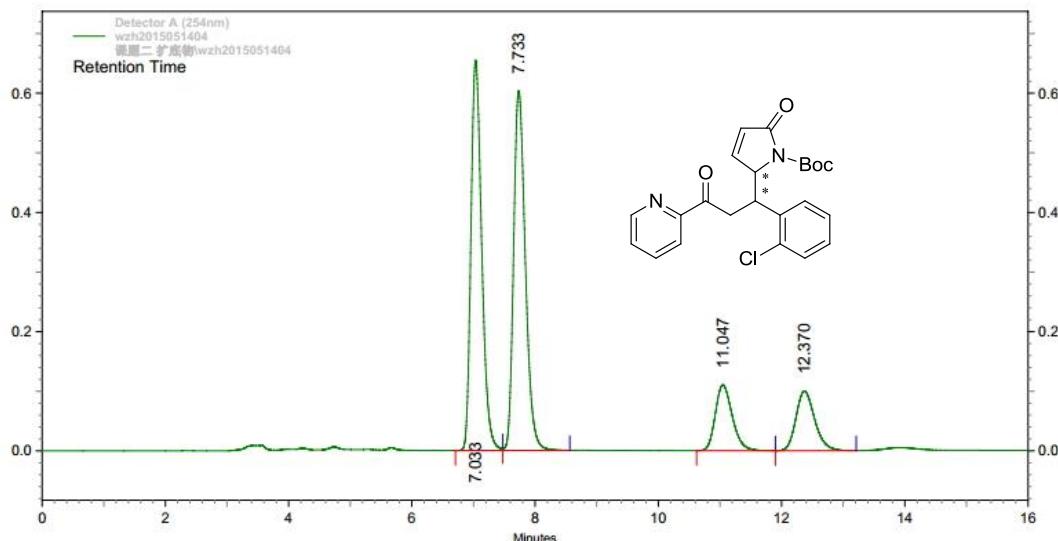


Detector
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(254nm)

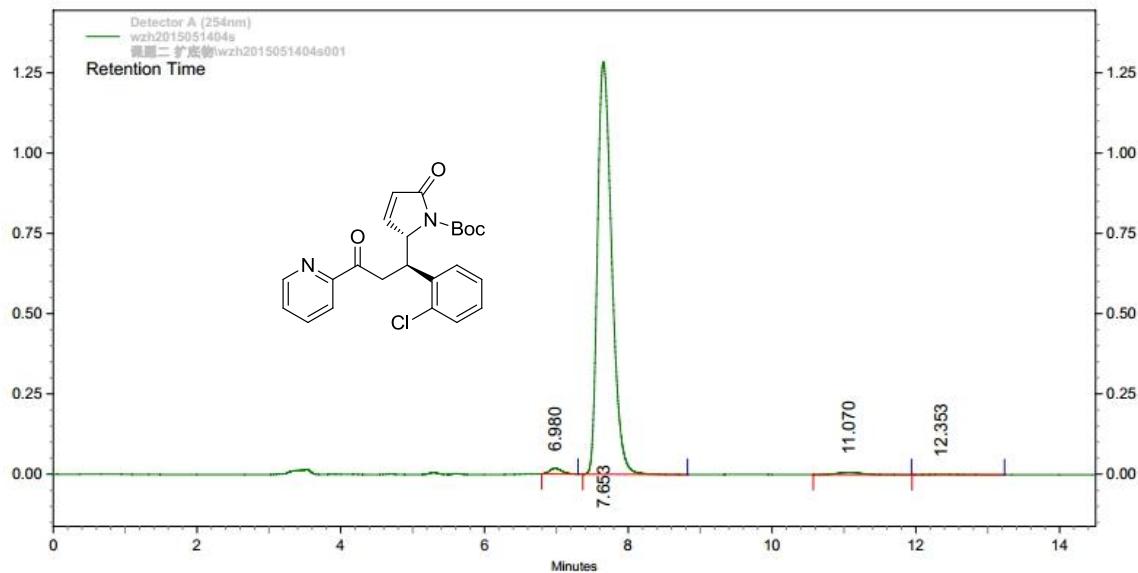
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Totals		1321967	100.00	22540591	100.00

¹H NMR, ¹³C NMR and HPLC of 3e



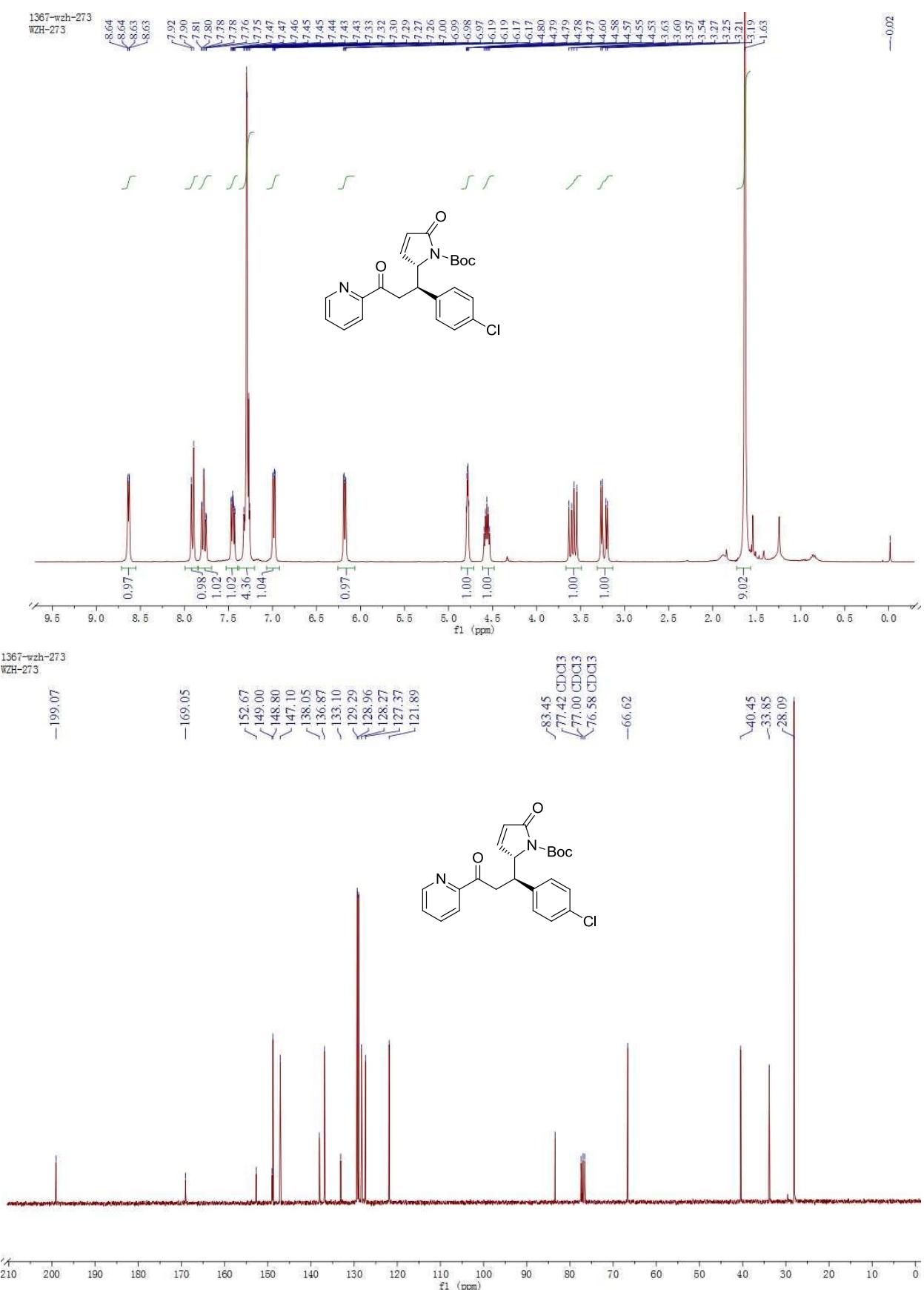

Detector
A
(254nm)

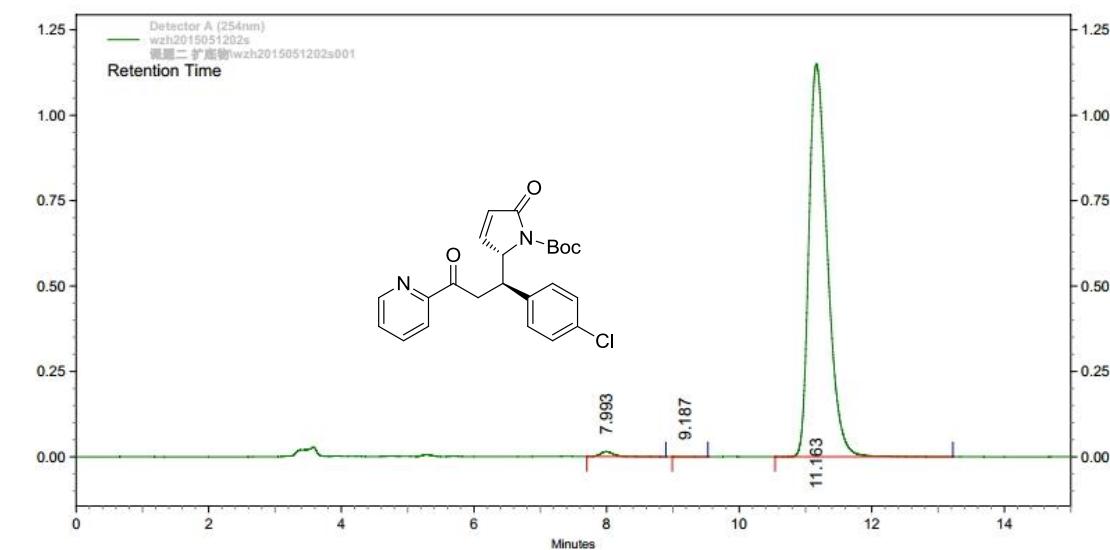
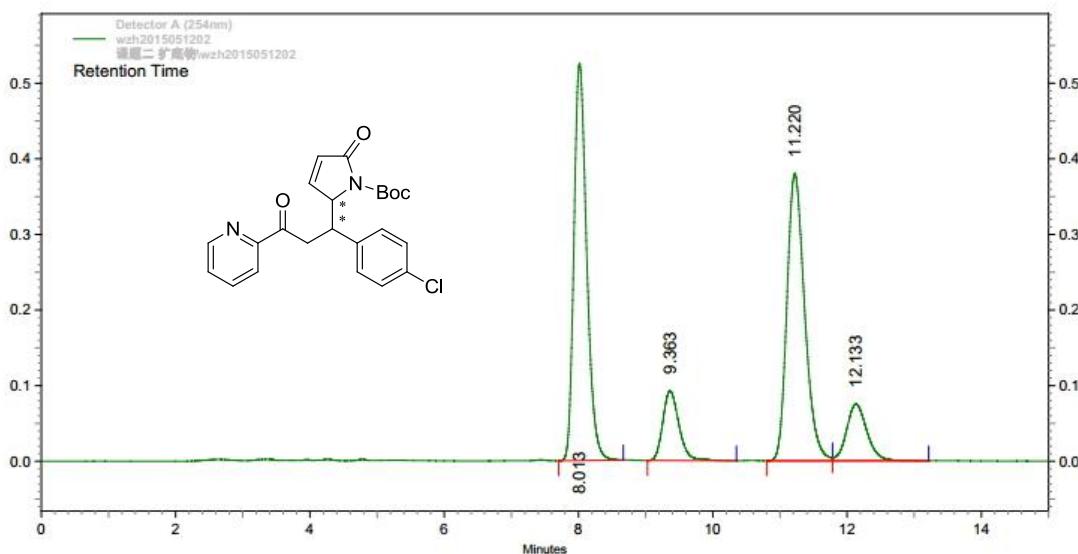
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.033	654650	44.57	7927210	39.37
2	7.733	603751	41.10	7976260	39.62
3	11.047	110376	7.51	2113577	10.50
4	12.370	100071	6.81	2115751	10.51
Totals		1468848	100.00	20132798	100.00


Detector
A
(254nm)

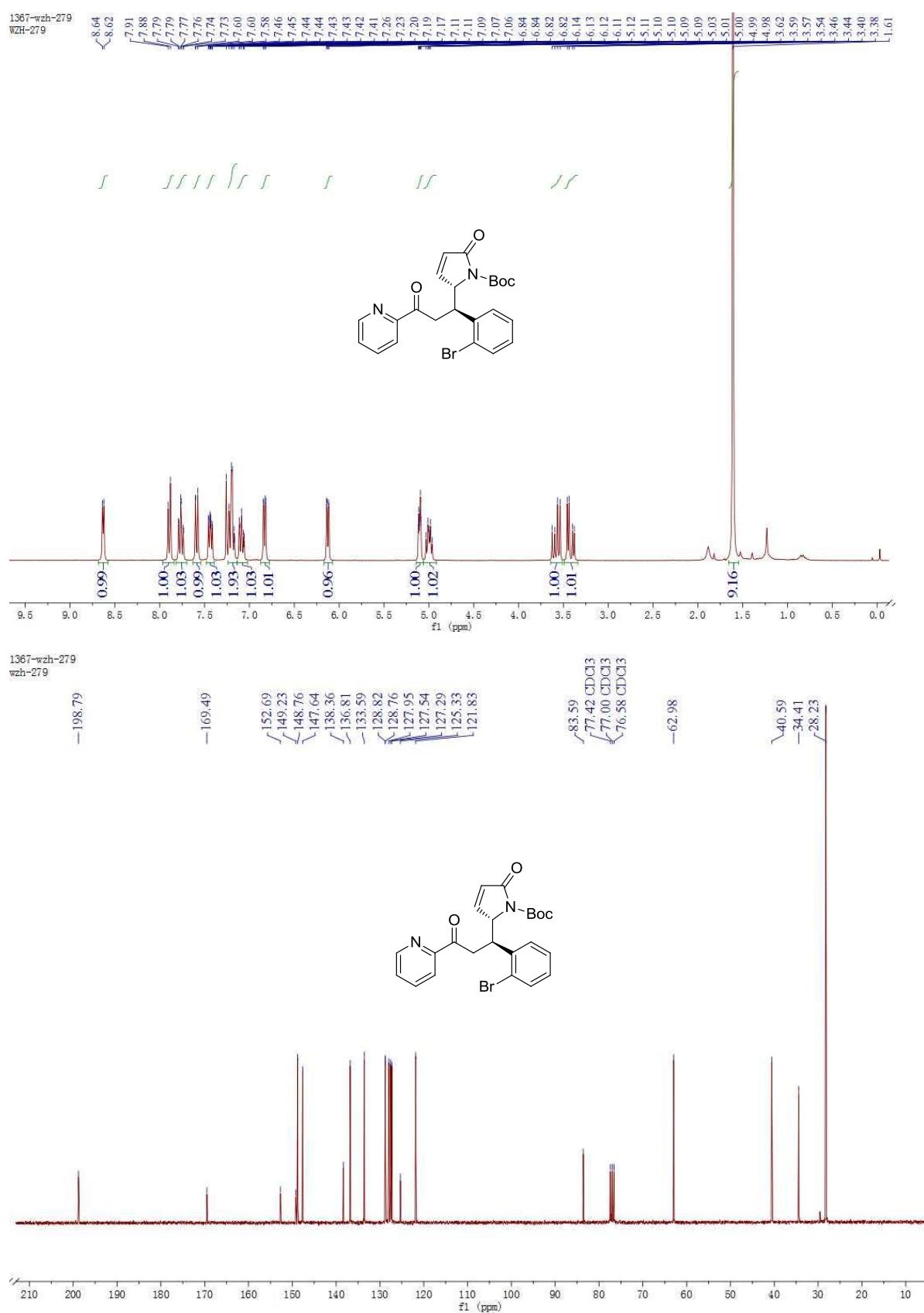
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.980	18031	1.38	210891	1.17
2	7.653	1284123	98.03	17616069	97.78
3	11.070	6476	0.49	156782	0.87
4	12.353	1243	0.09	31613	0.18
Totals		1309873	100.00	18015355	100.00

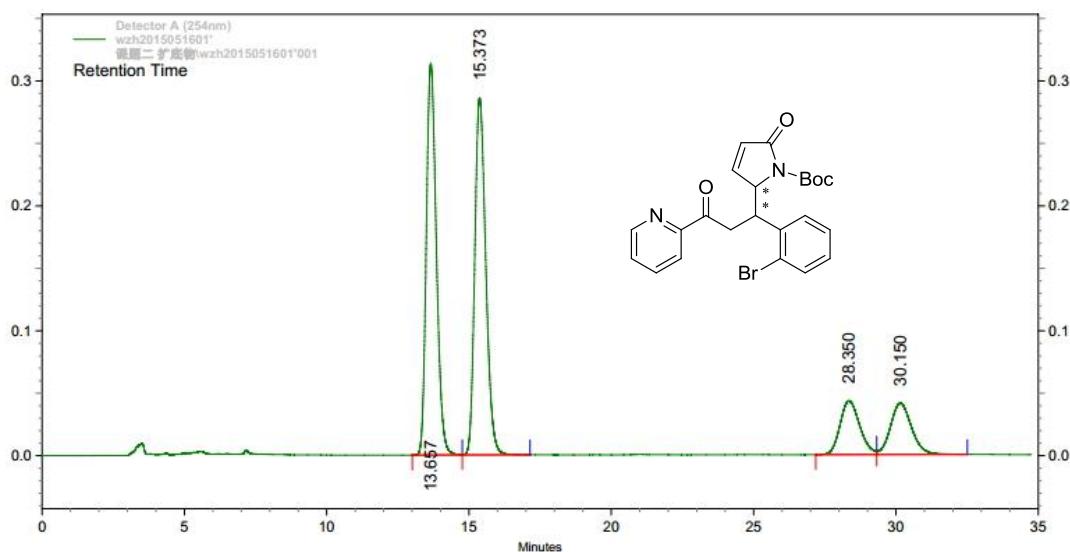
¹H NMR, ¹³C NMR and HPLC of 3f





¹H NMR, ¹³C NMR and HPLC of 3g



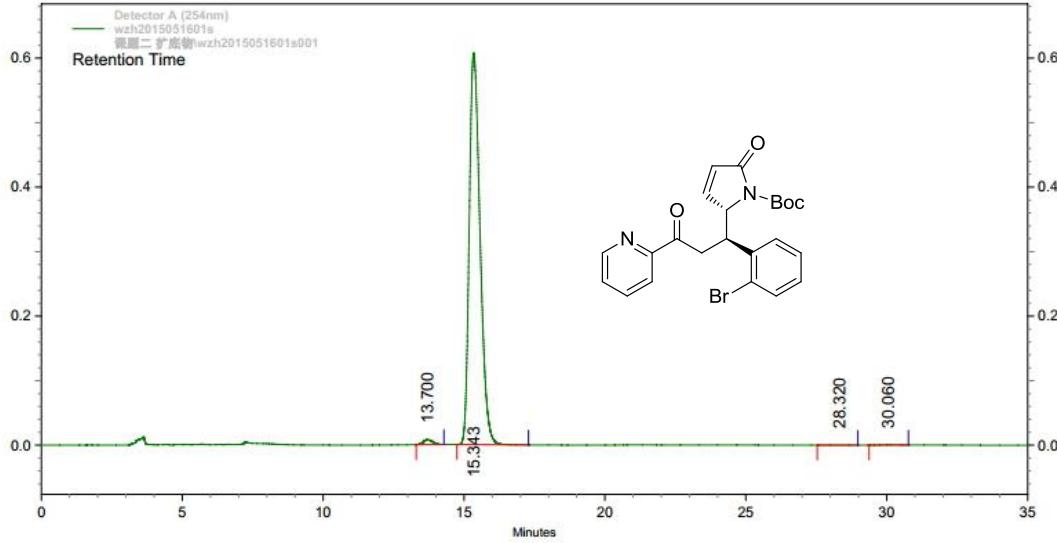


Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	13.657	313185	45.83	7646386	39.21
2	15.373	285893	41.84	7672613	39.35
3	28.350	43129	6.31	2059919	10.56
4	30.150	41091	6.01	2121297	10.88
Totals		683298	100.00	19500215	100.00



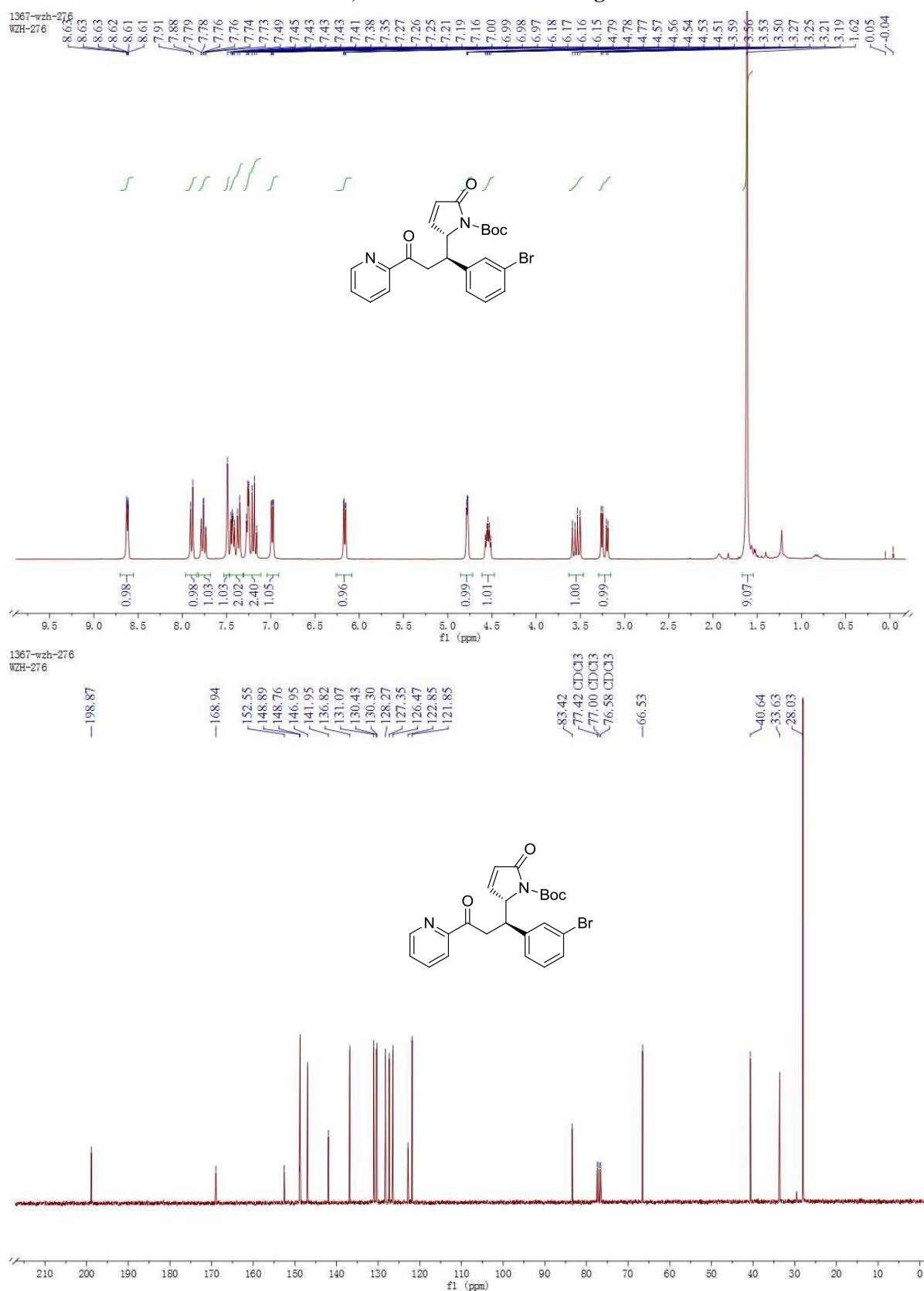
Detector

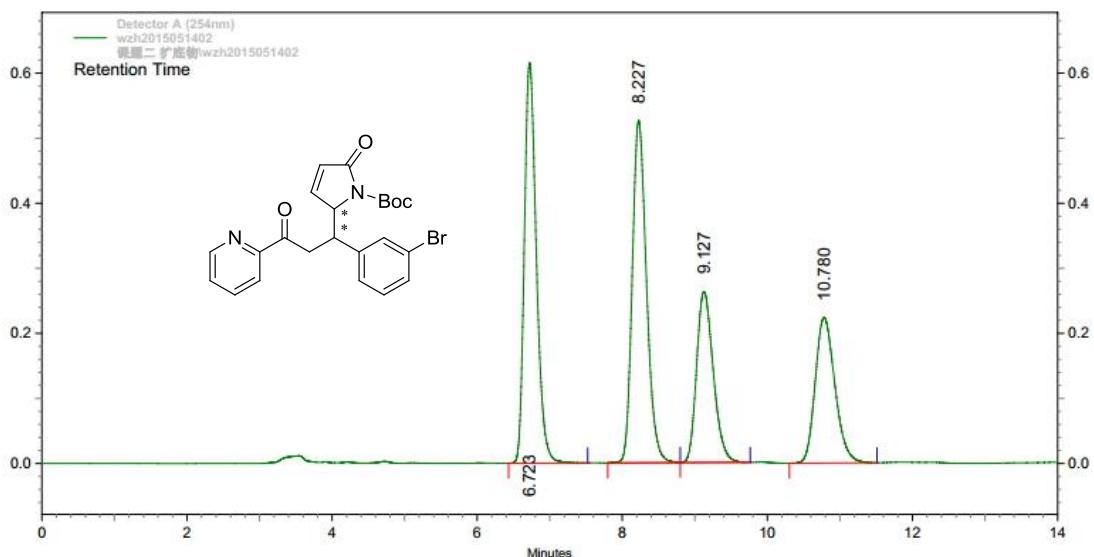
A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	13.700	7509	1.22	173730	1.06
2	15.343	607113	98.72	16148732	98.84
3	28.320	39	0.01	1611	0.01
4	30.060	352	0.06	14365	0.09
Totals		615013	100.00	16338438	100.00

¹H NMR, ¹³C NMR and HPLC of 3g





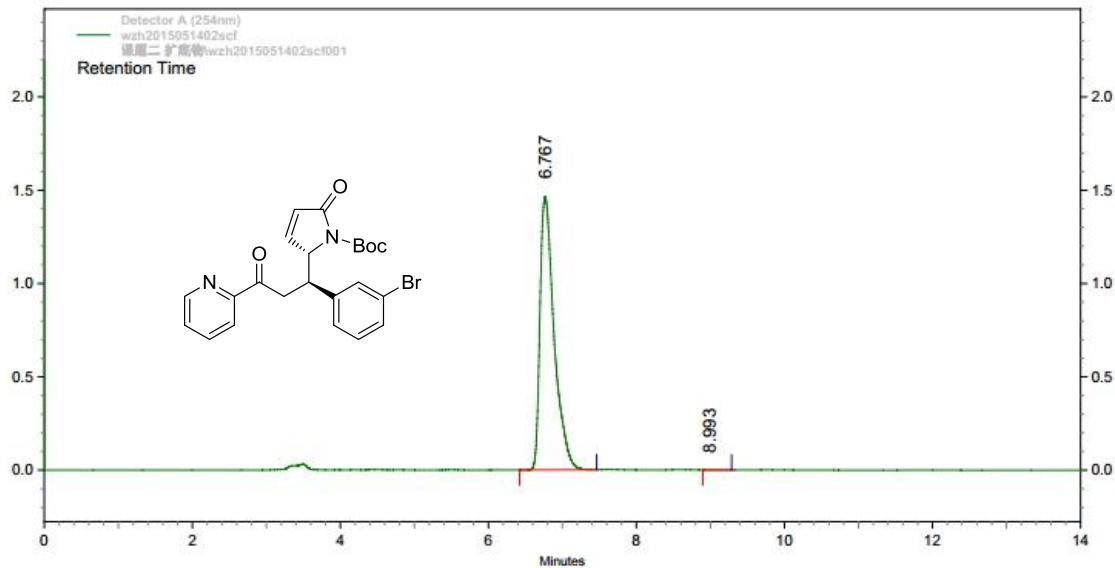
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.723	615481	37.81	7060131	31.18
2	8.227	525953	32.31	7163135	31.63
3	9.127	262877	16.15	4200967	18.55
4	10.780	223579	13.73	4220843	18.64

Totals	1627890	100.00	22645076	100.00
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Detector

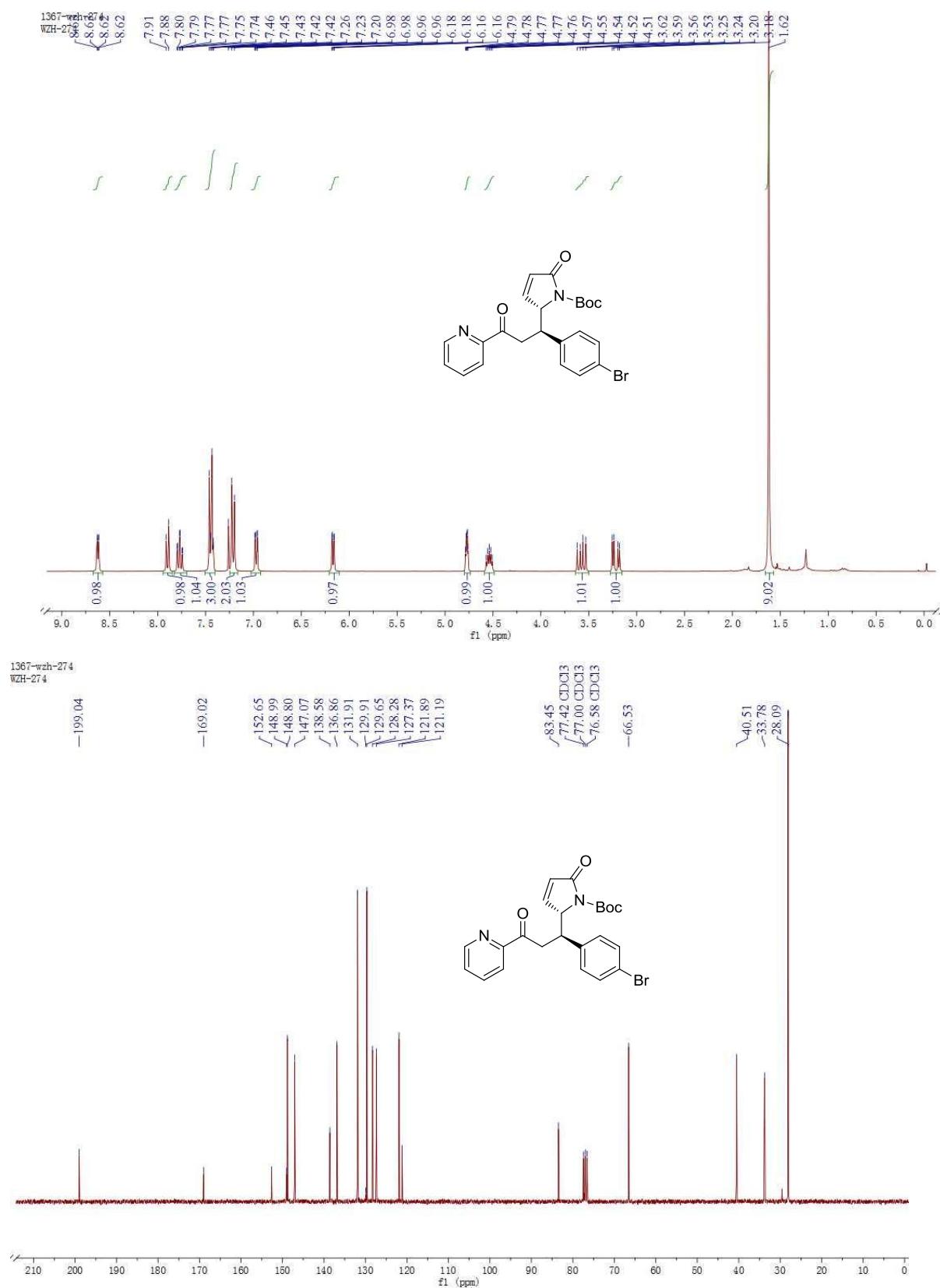
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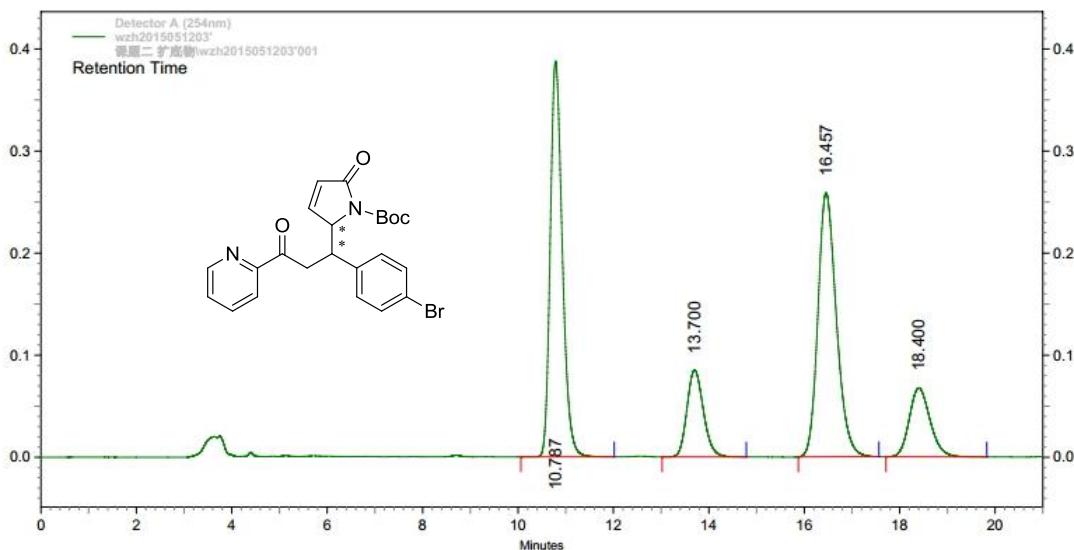
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	6.767	1462803	99.99	19413273	100.00
2	8.993	108	0.01	801	0.00

Totals	1462911	100.00	19414074	100.00
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¹H NMR, ¹³C NMR and HPLC of 3i





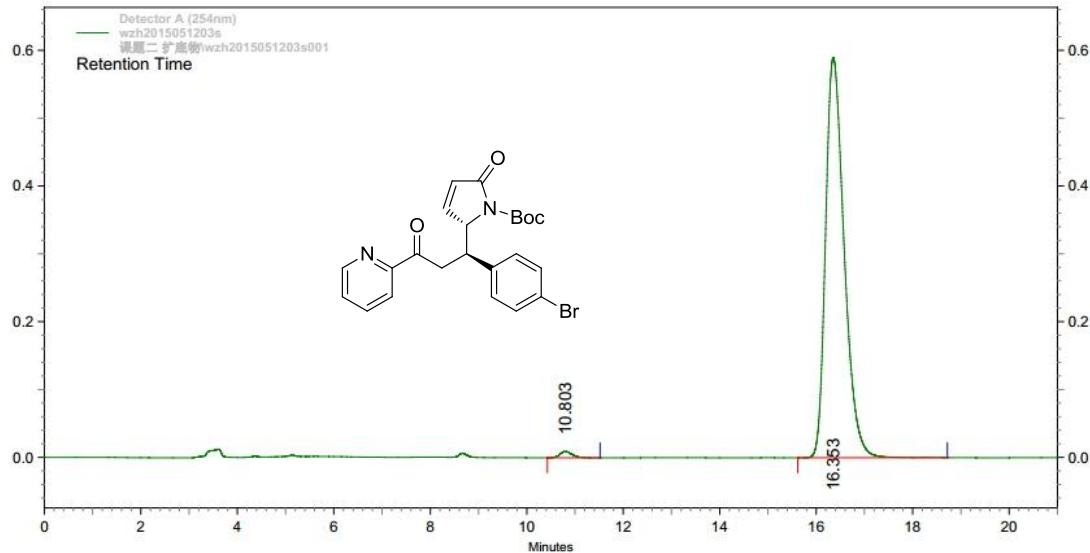
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.787	387528	48.50	6792135	38.09
2	13.700	85158	10.66	2037524	11.43
3	16.457	258788	32.38	6951749	38.99
4	18.400	67630	8.46	2049459	11.49

Totals	799104	100.00	17830867	100.00
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Detector

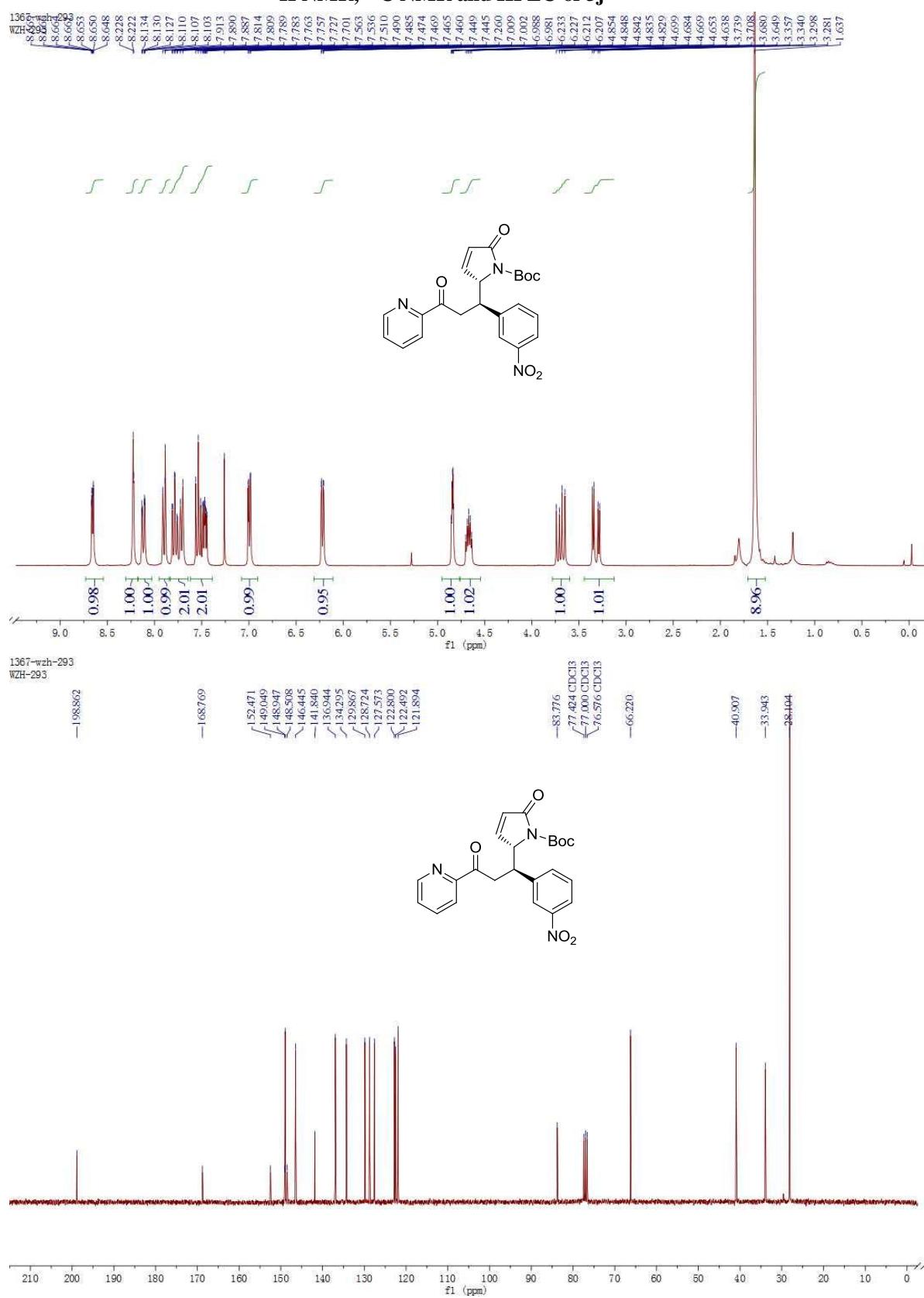
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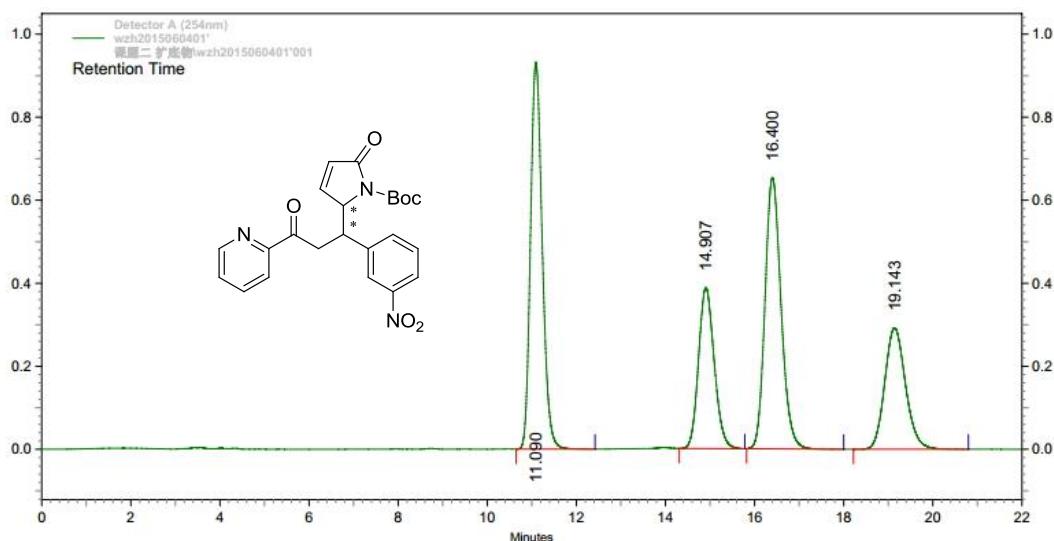
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.803	9293	1.55	162931	1.02
2	16.353	590018	98.45	15782073	98.98

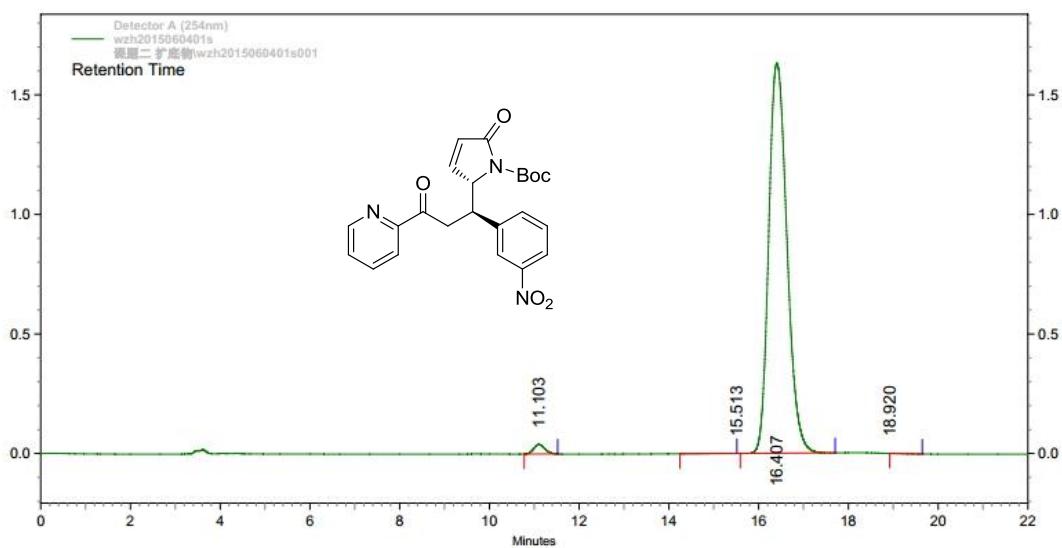
Totals		599311	100.00	15945004	100.00
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¹H NMR, ¹³C NMR and HPLC of 3j



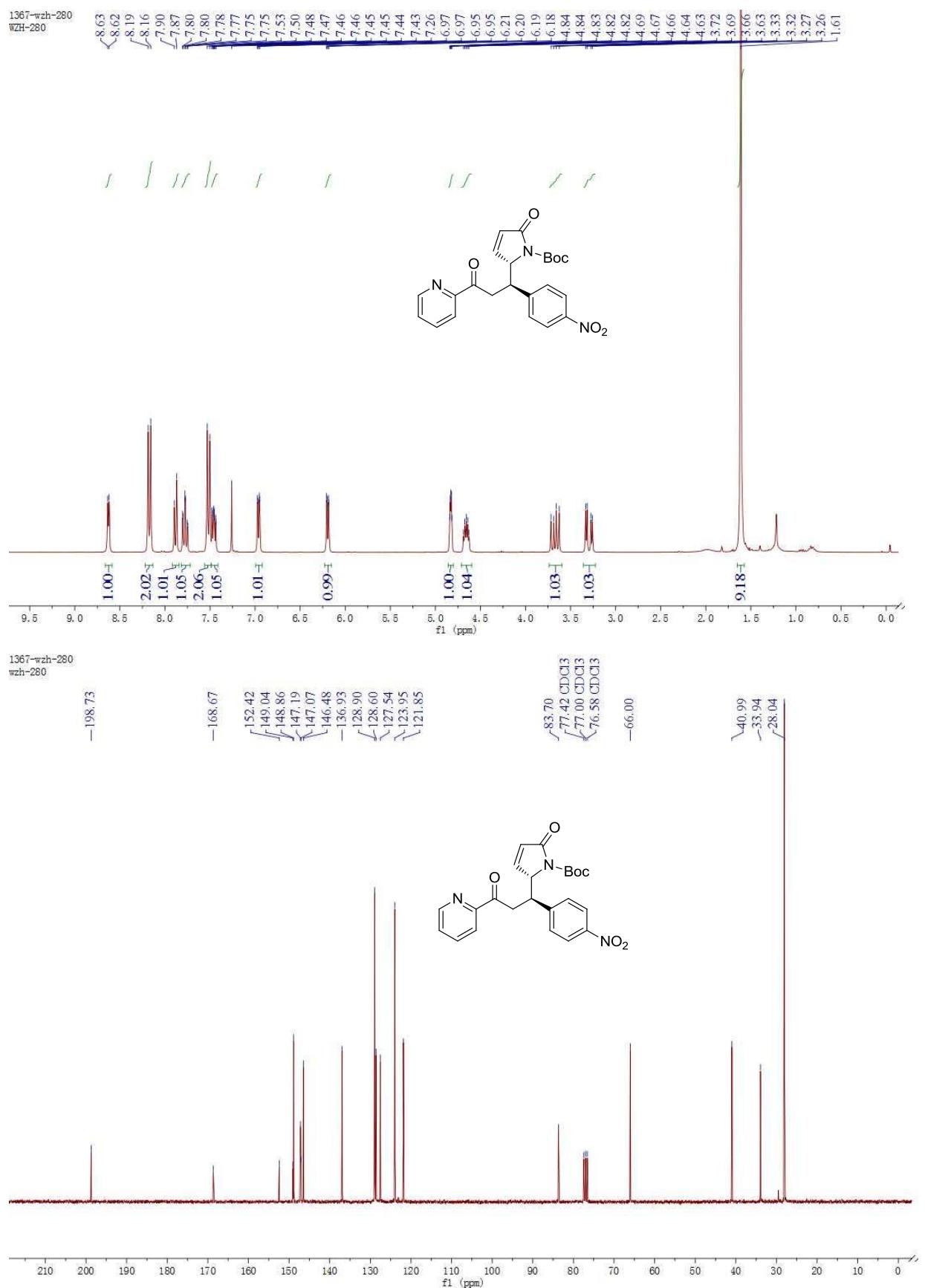

Detector
A
(254nm)

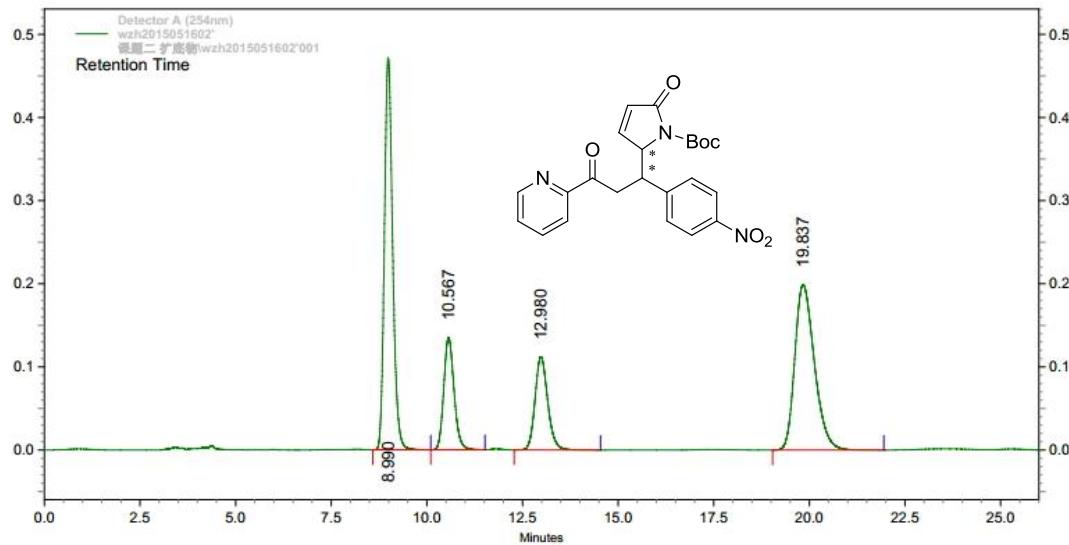
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Detector
A
(254nm)

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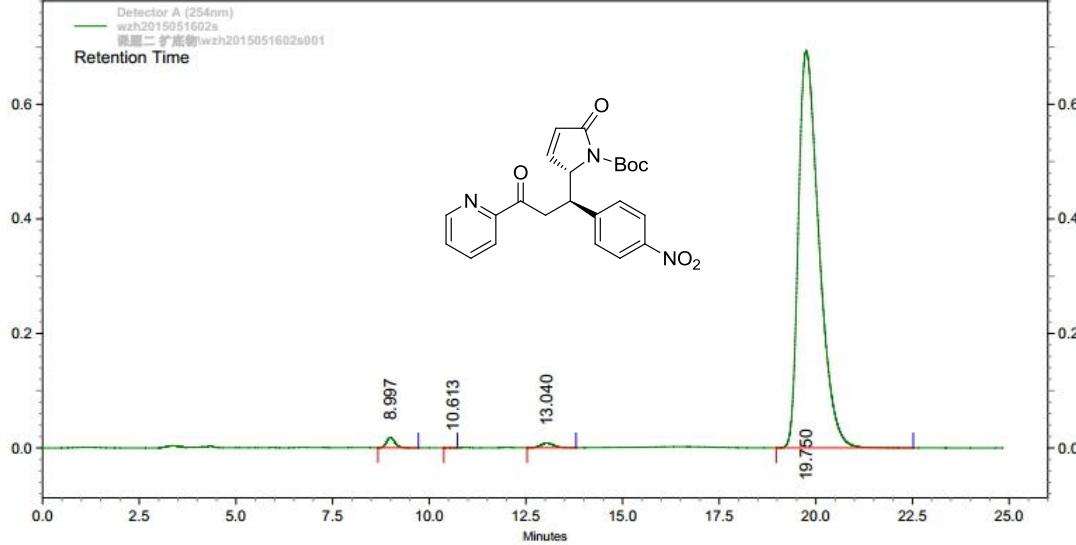
¹H NMR, ¹³C NMR and HPLC of 3k





Detector
A
(254nm)

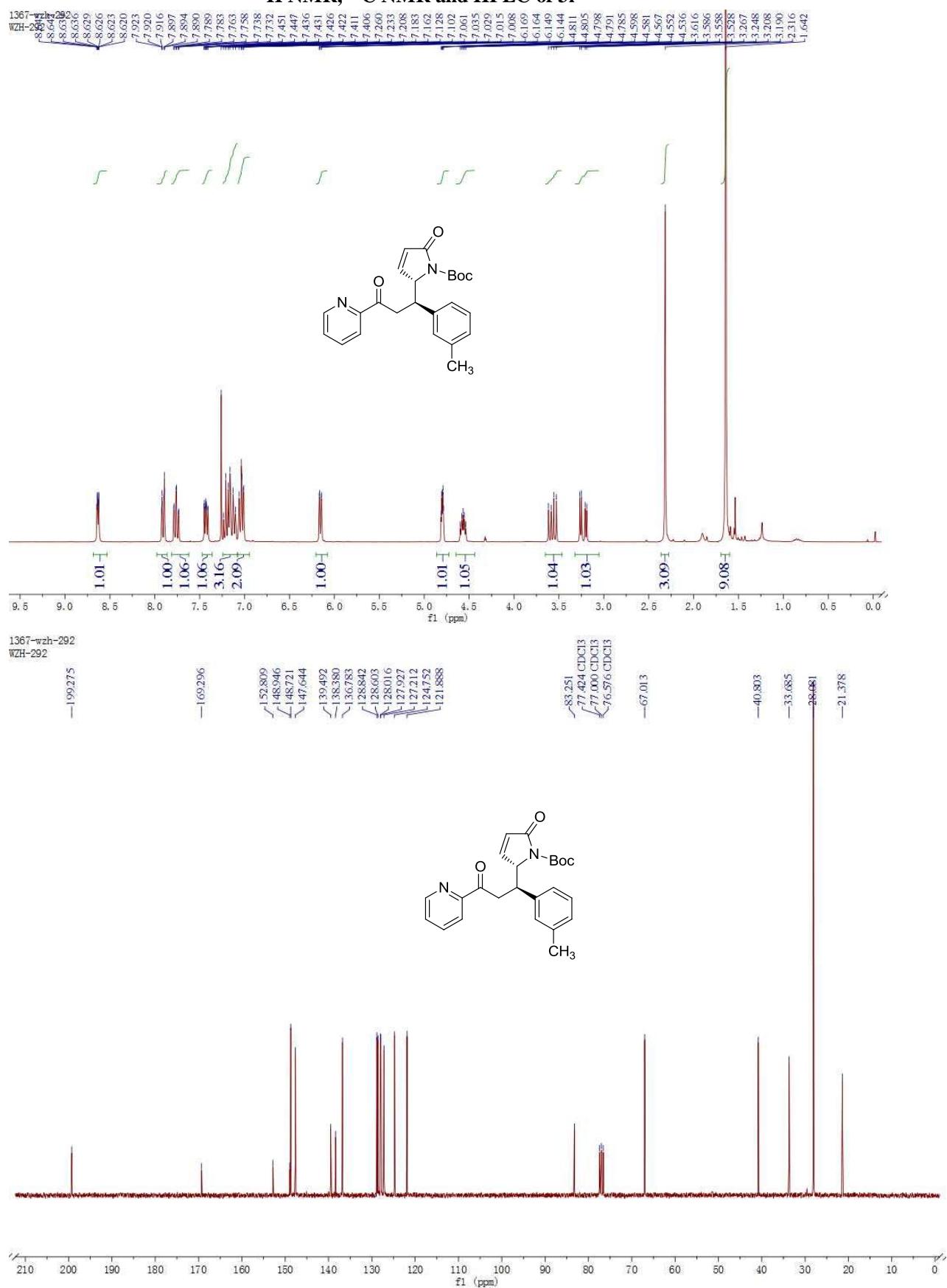
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	8.990	471259	51.34	7072191	36.68
2	10.567	135201	14.73	2530481	13.12
3	12.980	112205	12.22	2584101	13.40
4	19.837	199267	21.71	7093916	36.79
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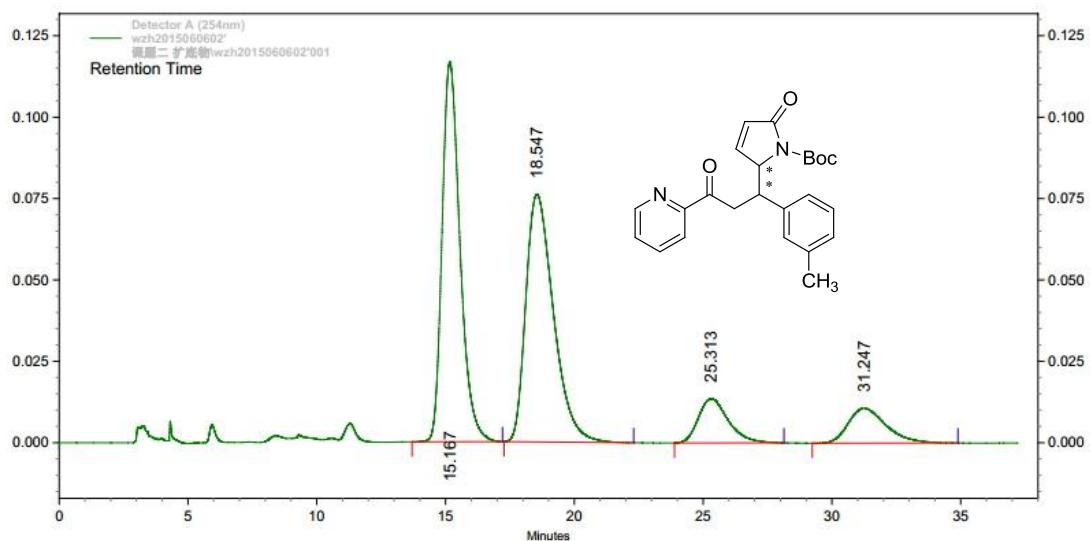


Detector
A
(254nm)

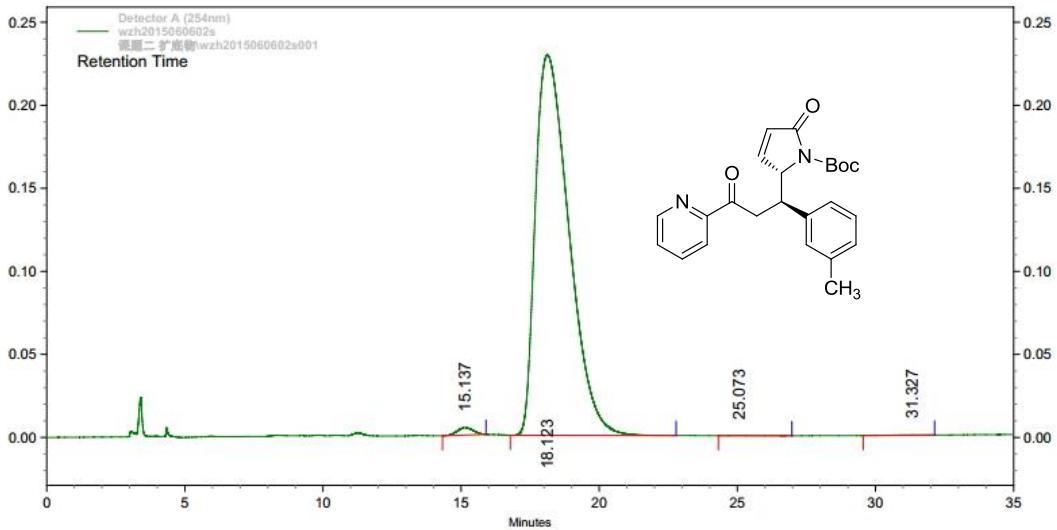
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	8.997	18198	2.53	269772	1.04
2	10.613	96	0.01	1186	0.00
3	13.040	8164	1.13	187235	0.72
4	19.750	693476	96.32	25598553	98.24
Totals		719934	100.00	26056746	100.00

¹H NMR, ¹³C NMR and HPLC of 3l



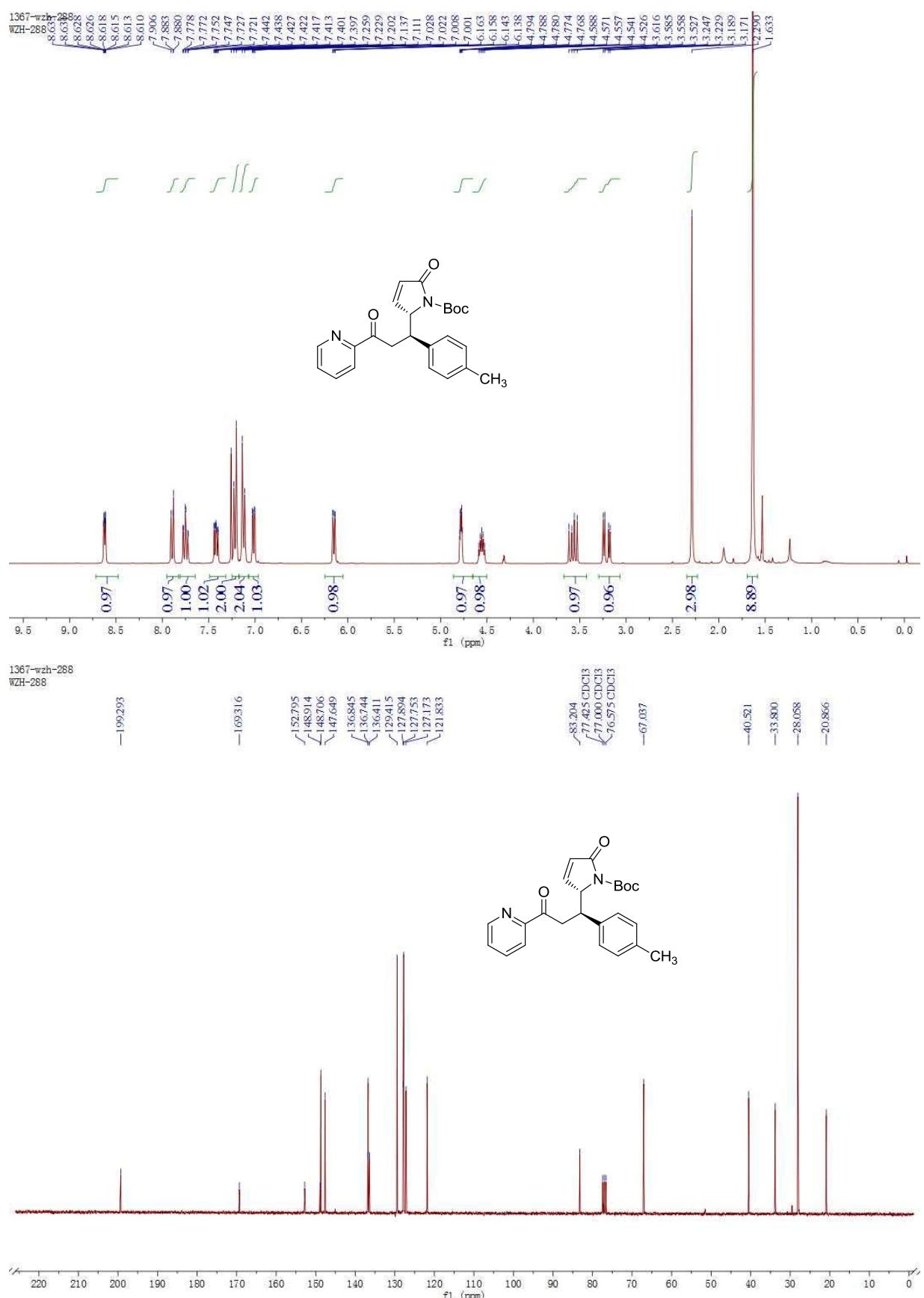

Detector
A
(254nm)

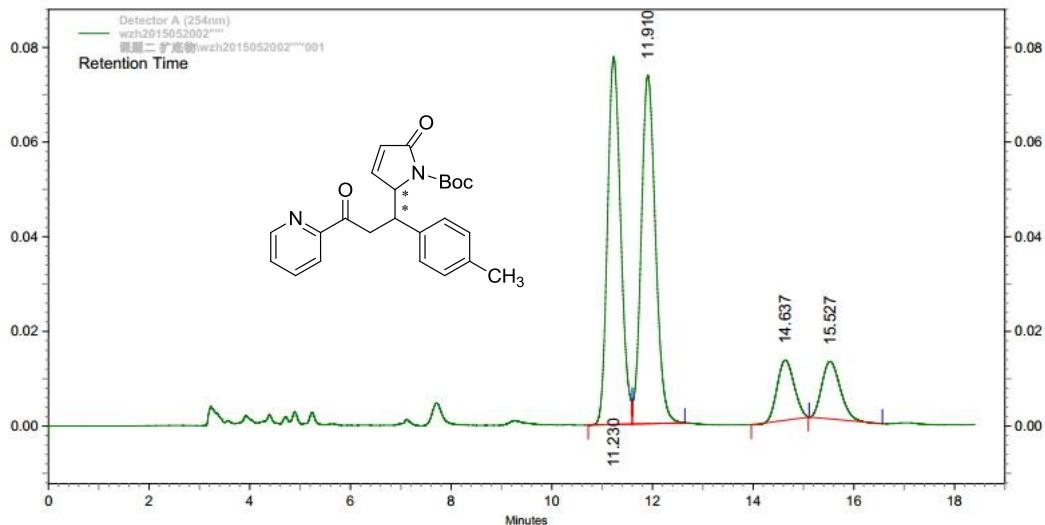
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	15.167	116621	53.74	5636469	41.74
2	18.547	76061	35.05	5677470	42.05
3	25.313	13590	6.26	1094784	8.11
4	31.247	10728	4.94	1093623	8.10
Totals		217000	100.00	13502346	100.00


Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	15.137	4416	1.89	178082	0.91
2	18.123	229009	98.05	19318581	99.04
3	25.073	20	0.01	1299	0.01
4	31.327	114	0.05	8634	0.04
Totals		233559	100.00	19506596	100.00

¹H NMR, ¹³C NMR and HPLC of 3m

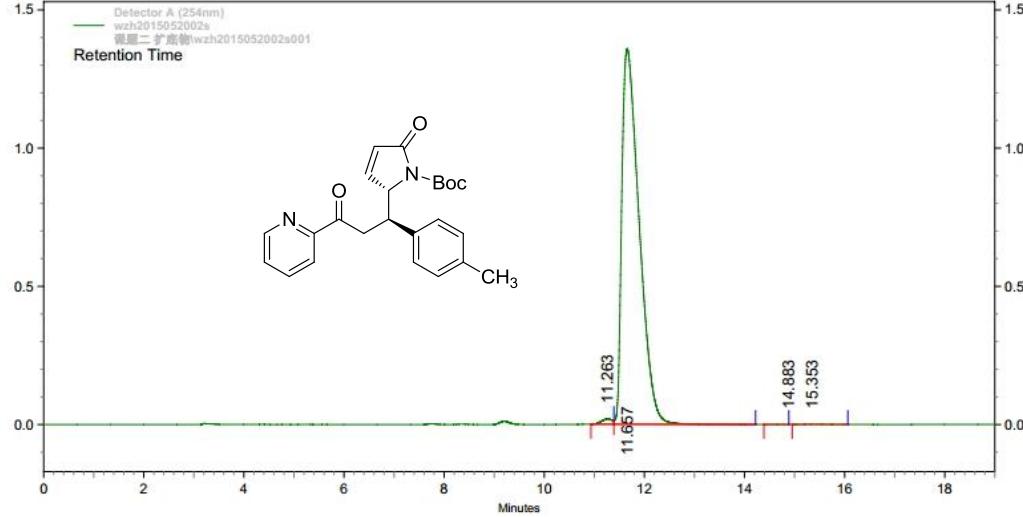



Detector
A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.230	77660	44.09	1412523	40.79
2	11.910	73605	41.79	1446005	41.76
3	14.637	12708	7.22	296359	8.56
4	15.527	12148	6.90	307806	8.89

Totals	176121	100.00	3462693	100.00
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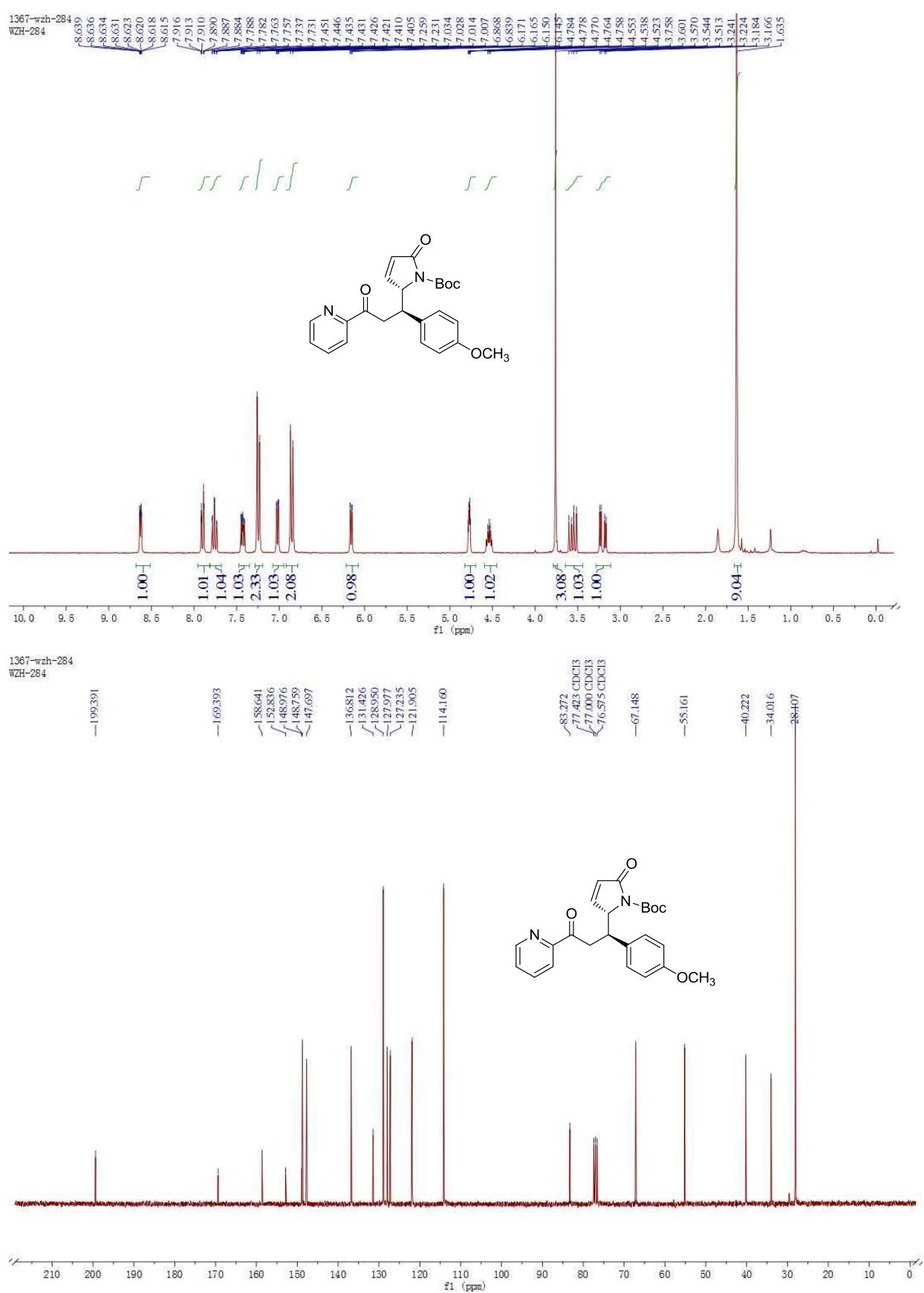

Detector
A

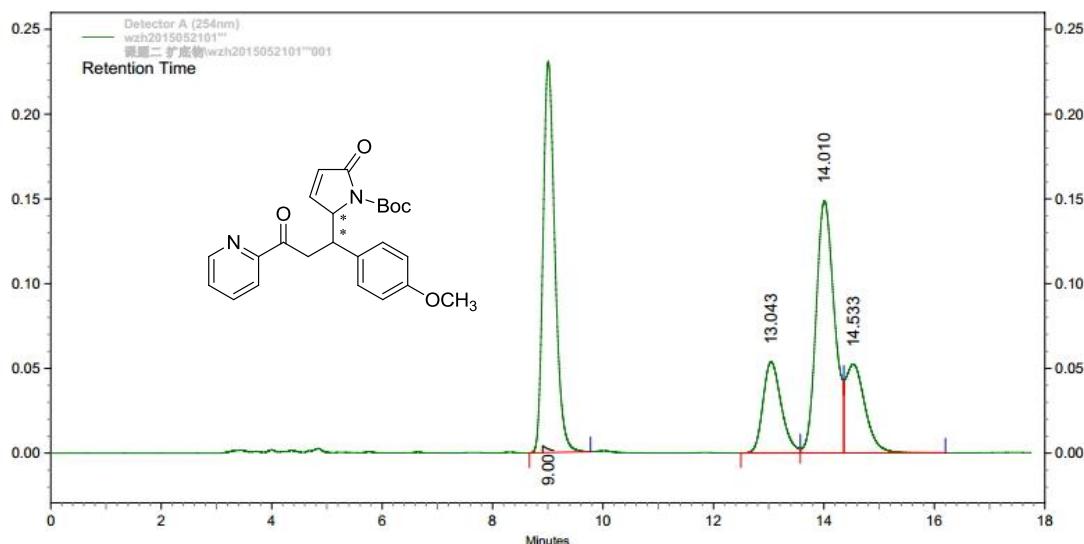
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.263	18953	1.37	283215	0.86
2	11.657	1358722	98.57	32690912	99.07
3	14.883	1	0.00	123	0.00
4	15.353	809	0.06	24716	0.07

Totals	1378485	100.00	32998966	100.00
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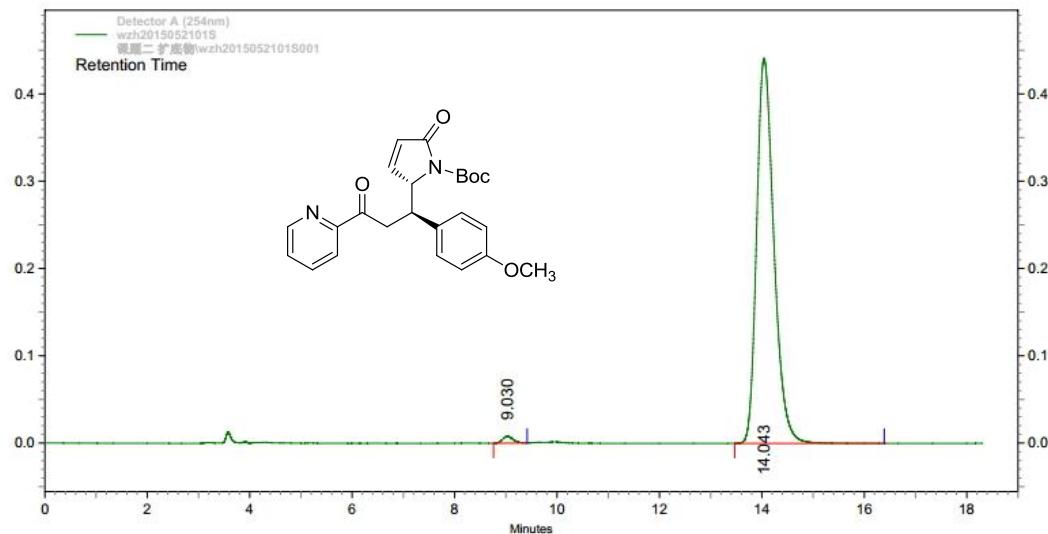
¹H NMR, ¹³C NMR and HPLC of 3n




Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	9.007	230589	47.48	3428799	36.55
2	13.043	53892	11.10	1234372	13.16
3	14.010	148743	30.63	3430677	36.57
4	14.533	52443	10.80	1287529	13.72

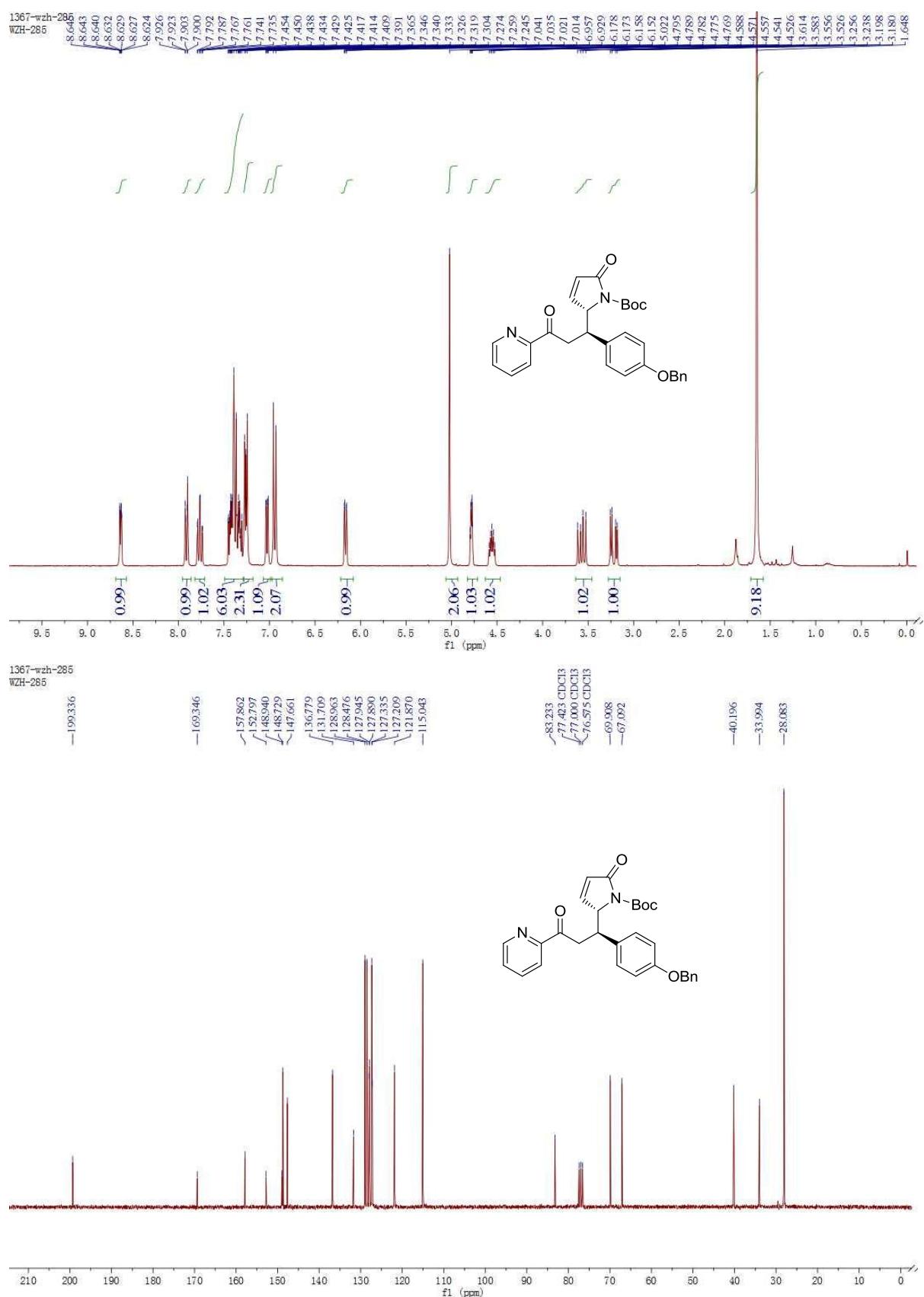
Totals		485667	100.00	9381377	100.00
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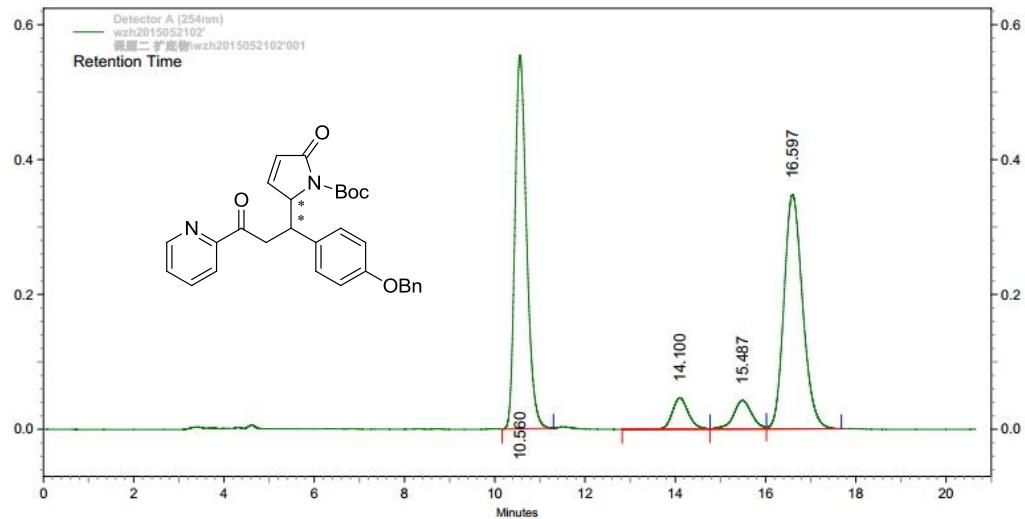

Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	9.030	7967	1.77	112198	1.07
2	14.043	441060	98.23	10327556	98.93

Totals		449027	100.00	10439754	100.00
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¹H NMR, ¹³C NMR and HPLC of 3o



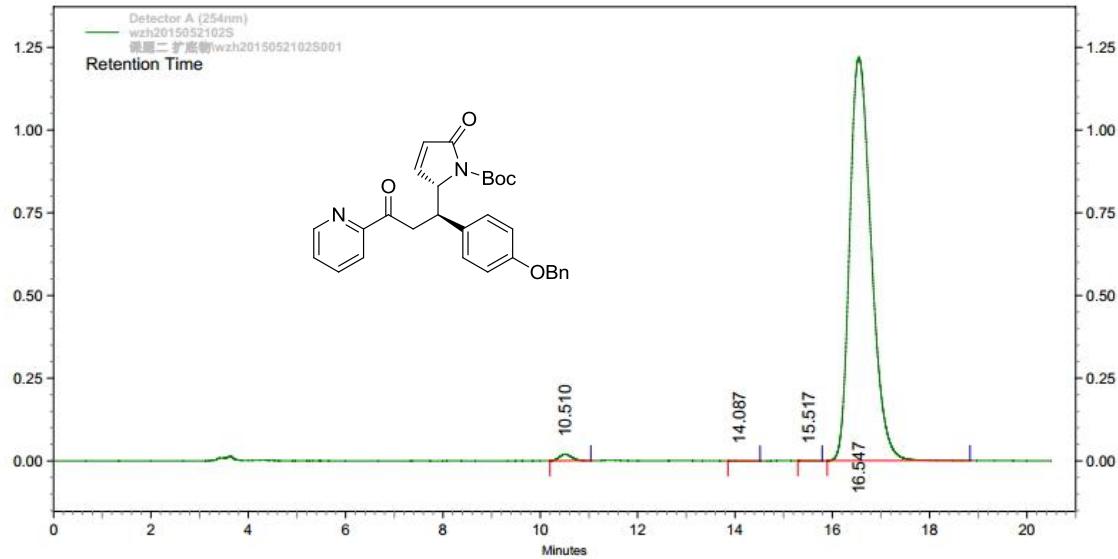


Detector

A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.560	554029	55.94	9916468	44.58
2	14.100	46433	4.69	1150910	5.17
3	15.487	42378	4.28	1184371	5.32
4	16.597	347642	35.10	9992020	44.92

Totals	990482	100.00	22243769	100.00
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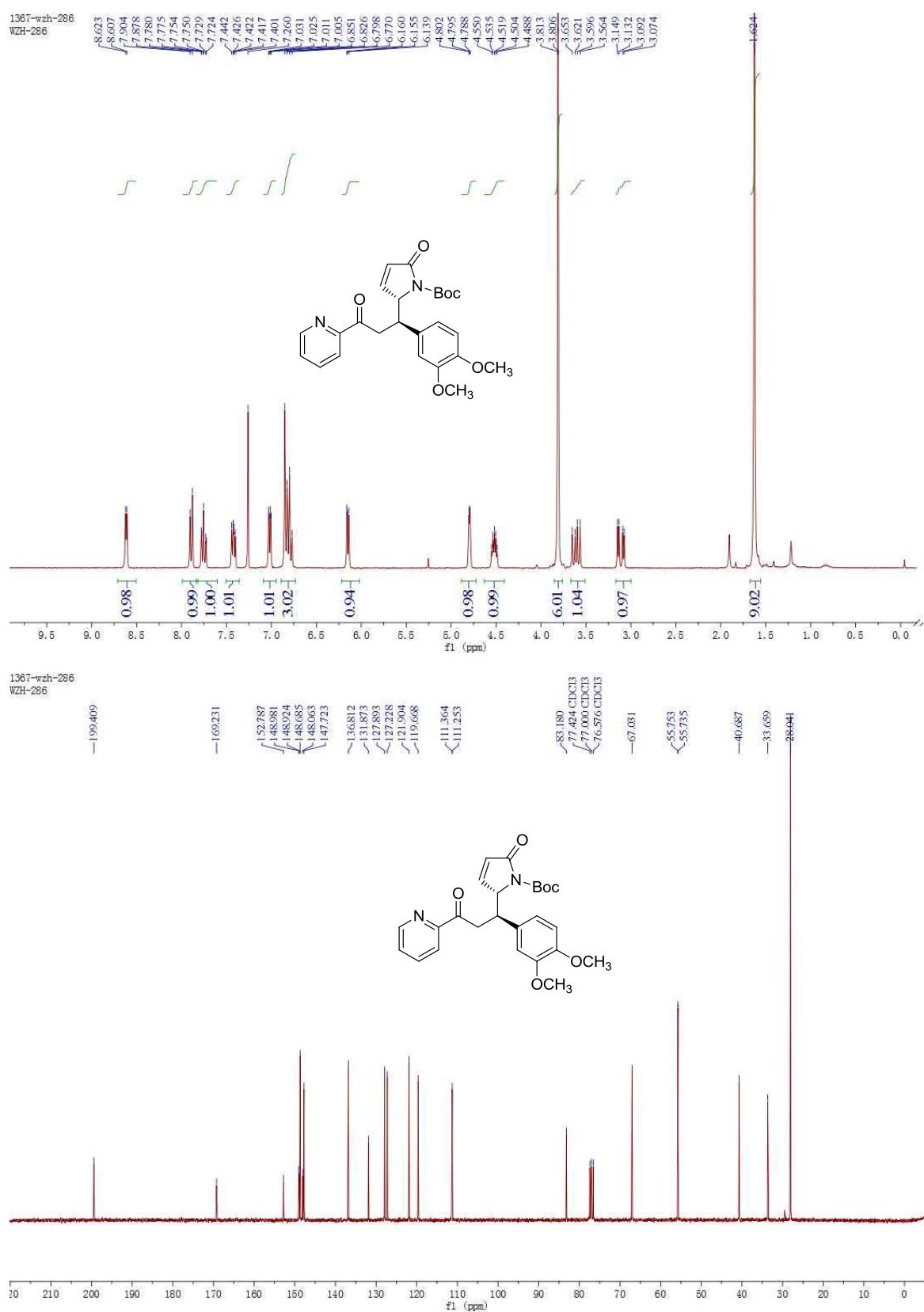
Detector

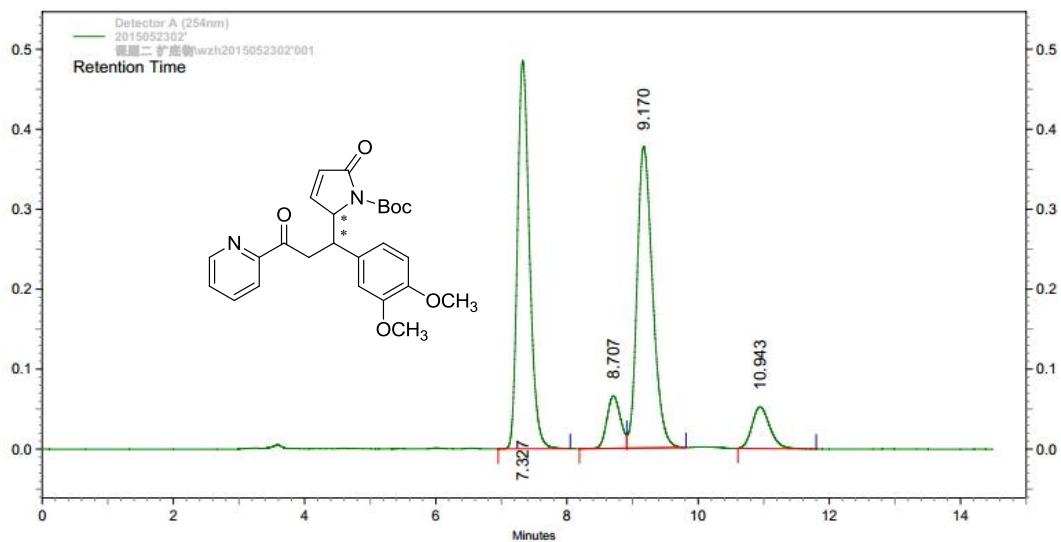
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.510	19717	1.59	342459	0.91
2	14.087	34	0.00	587	0.00
3	15.517	129	0.01	2076	0.01
4	16.547	1219382	98.40	37378826	99.09

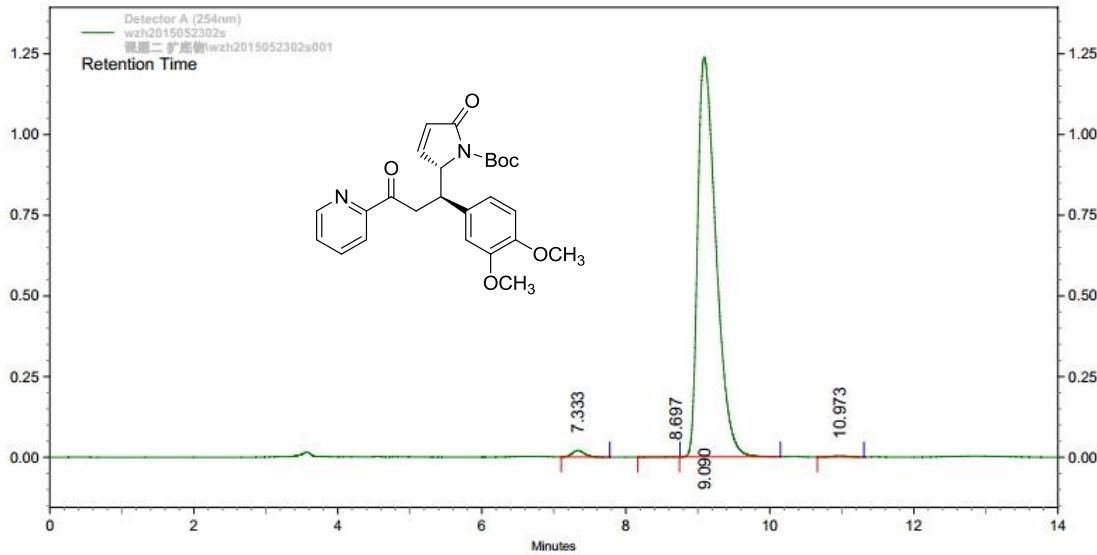
Totals	1239262	100.00	37723948	100.00
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¹H NMR, ¹³C NMR and HPLC of 3p



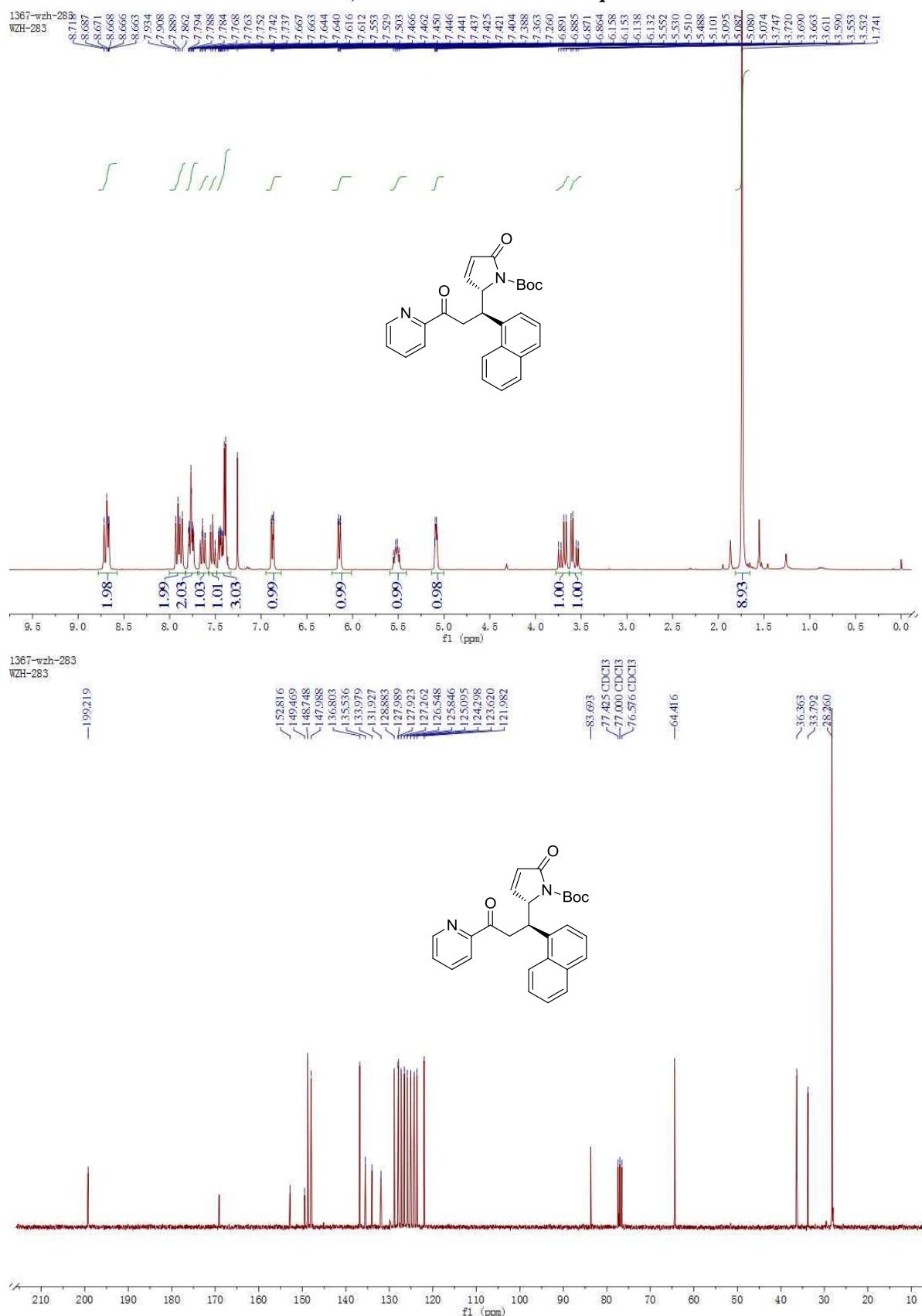

Detector
A
(254nm)

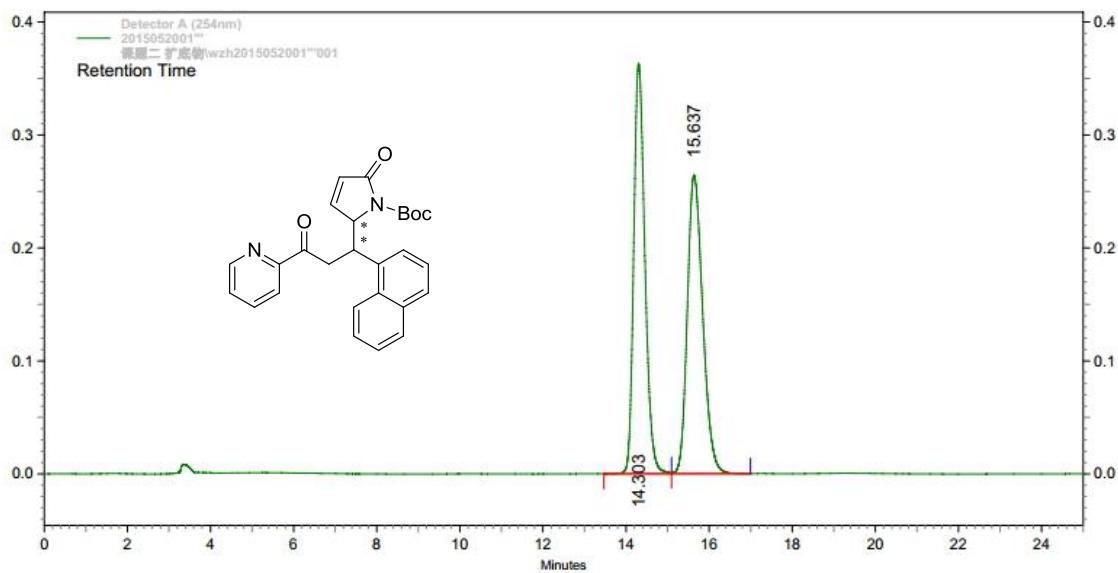
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.327	485630	49.52	6154621	43.10
2	8.707	65620	6.69	942539	6.60
3	9.170	377158	38.46	6202145	43.43
4	10.943	52247	5.33	981384	6.87
Totals		980655	100.00	14280689	100.00


Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.333	20097	1.59	244055	1.10
2	8.697	59	0.00	2836	0.01
3	9.090	1237775	98.11	21870085	98.61
4	10.973	3715	0.29	62281	0.28
Totals		1261646	100.00	22179257	100.00

¹H NMR, ¹³C NMR and HPLC of 3q





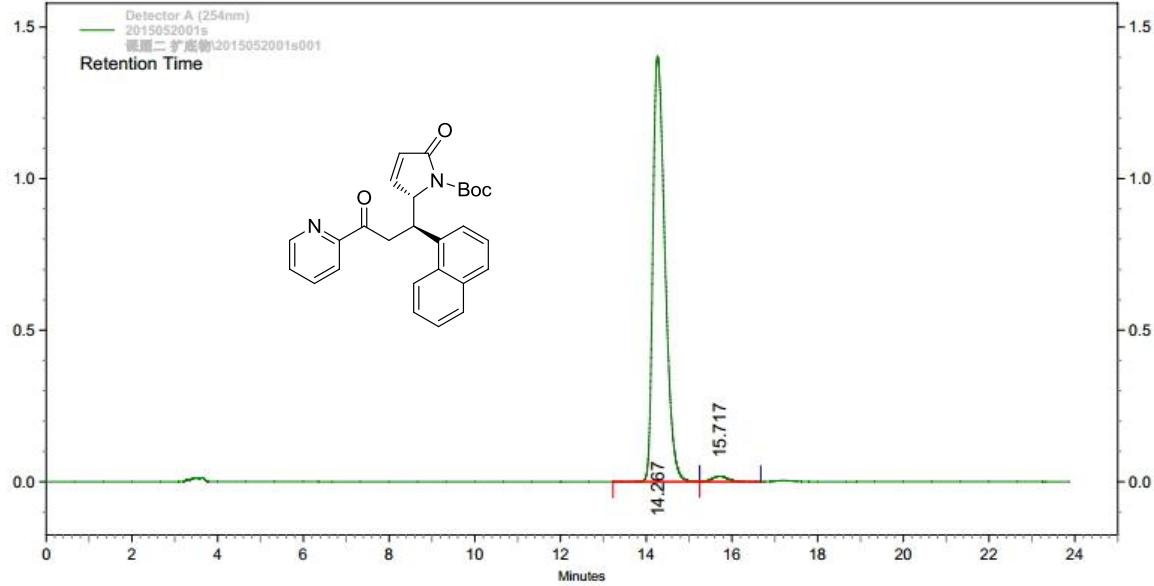
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	14.303	363075	57.87	6780270	49.97
2	15.637	264298	42.13	6789101	50.03

Totals	627373	100.00	13569371	100.00
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Detector

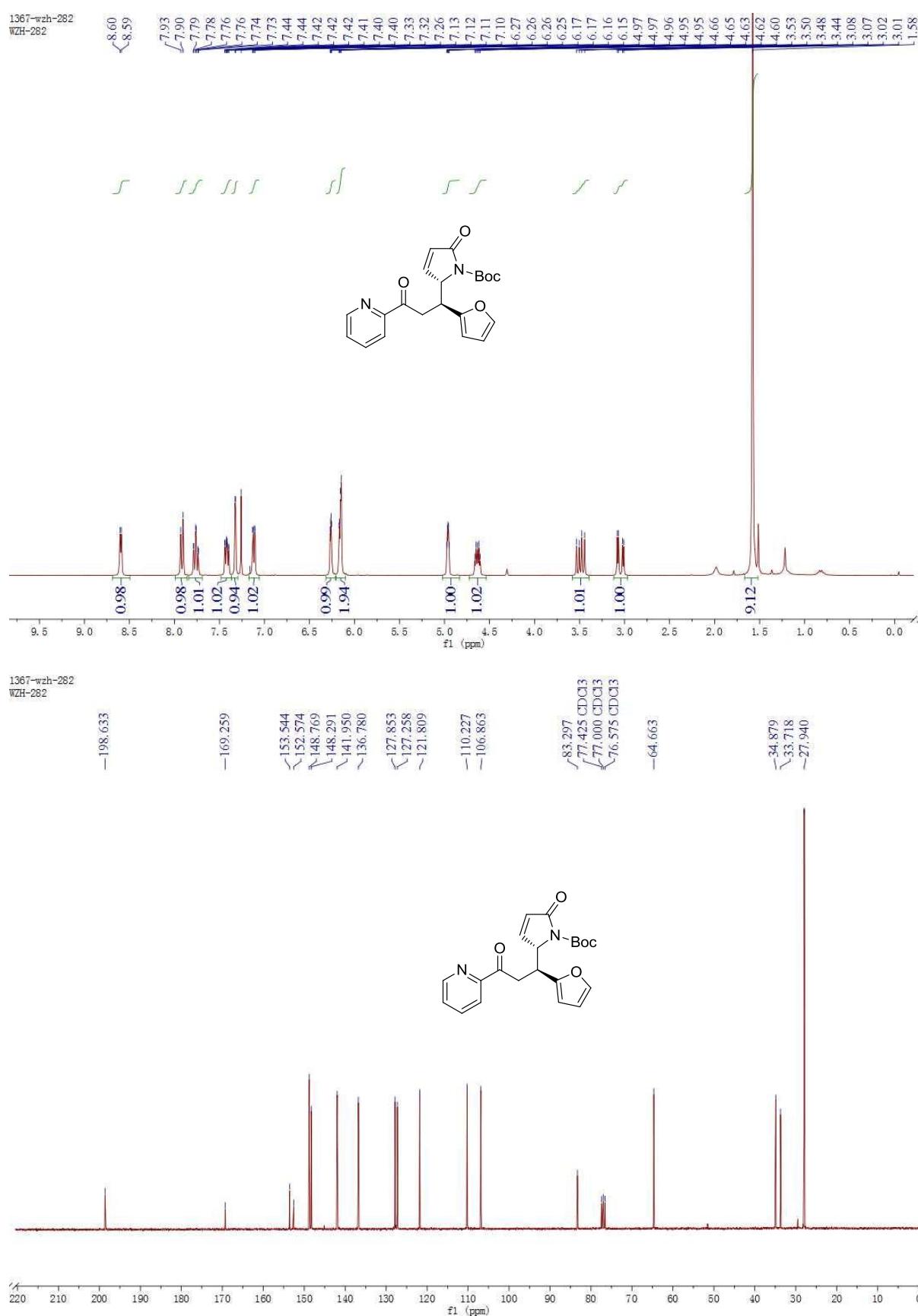
A

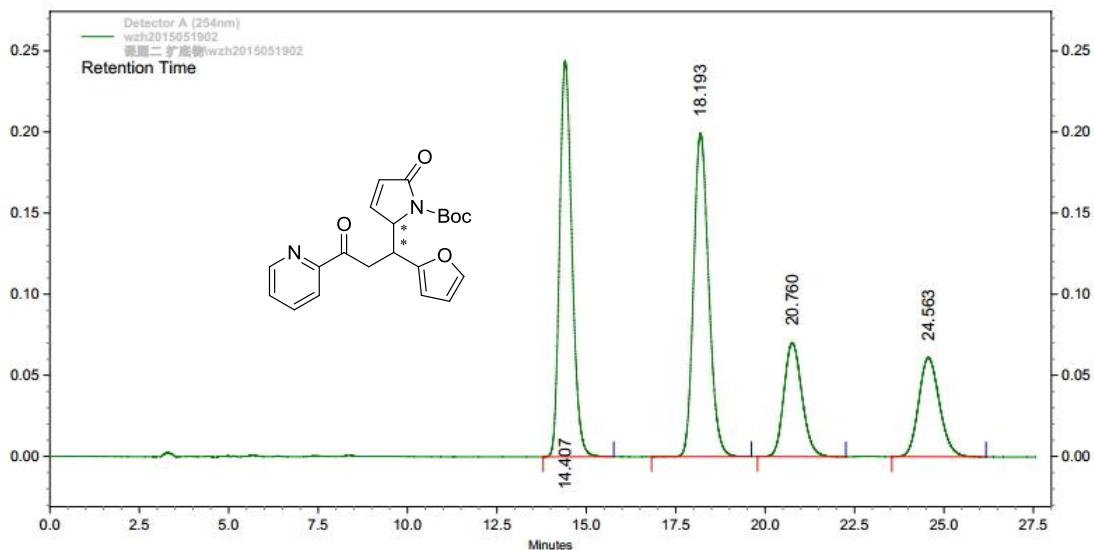
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	14.267	1402950	98.75	27544760	98.34
2	15.717	17829	1.25	464940	1.66

Totals	1420779	100.00	28009700	100.00
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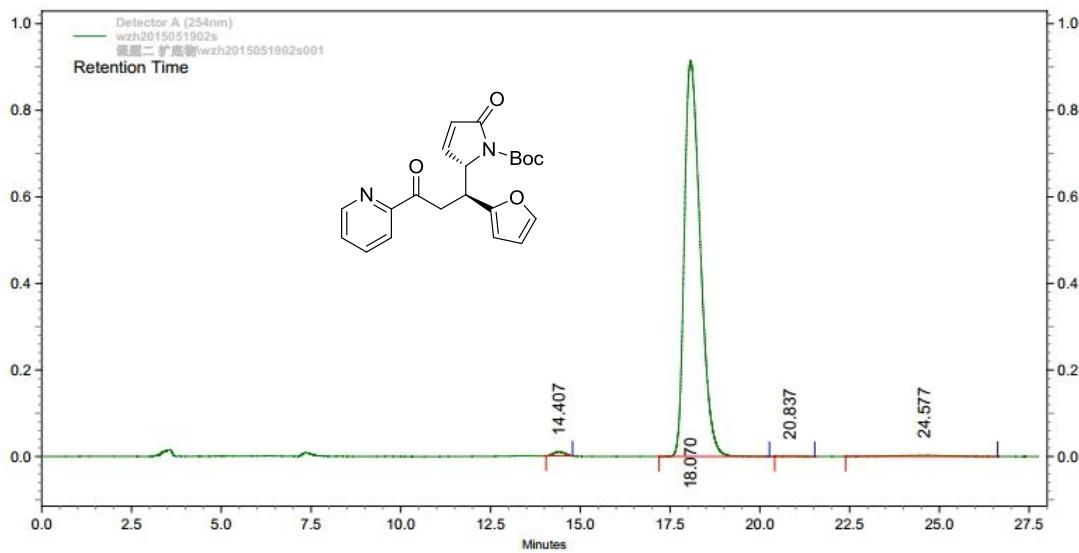
¹H NMR, ¹³C NMR and HPLC of 3r





Detector A (254nm)

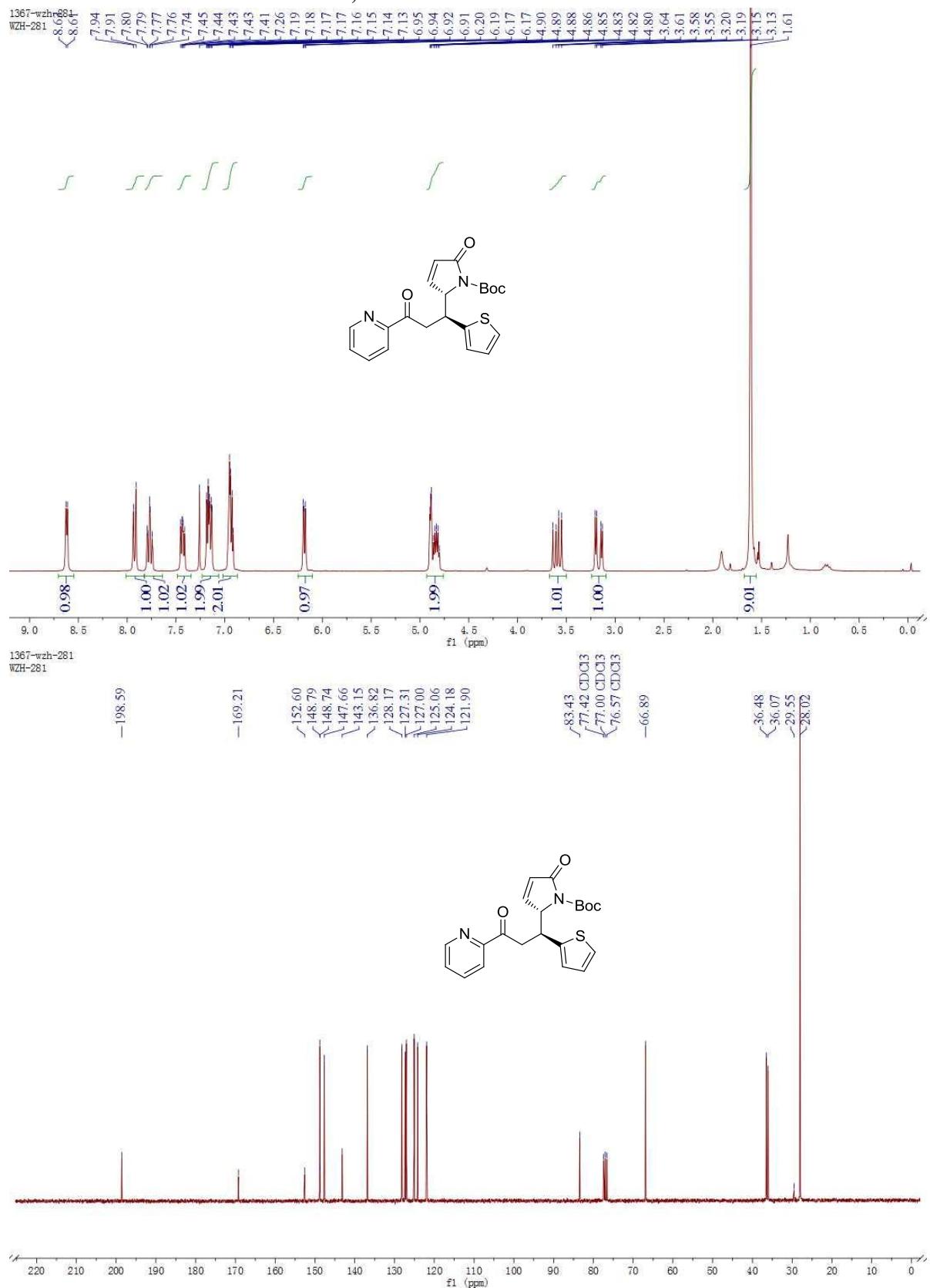
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	14.407	243953	42.46	5850972	35.14
2	18.193	199292	34.68	5853974	35.16
3	20.760	70264	12.23	2469604	14.83
4	24.563	61086	10.63	2473580	14.86
Totals		574595	100.00	16648130	100.00

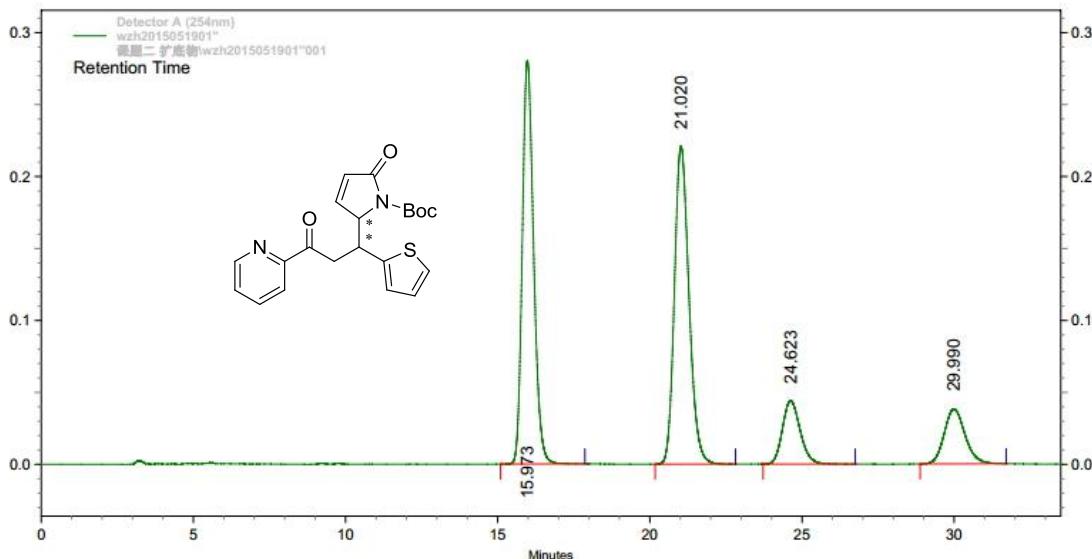


Detector A (254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	14.407	9628	1.04	205502	0.72
2	18.070	914809	98.63	28144643	98.20
3	20.837	567	0.06	15675	0.05
4	24.577	2493	0.27	294596	1.03
Totals		927497	100.00	28660416	100.00

¹H NMR, ¹³C NMR and HPLC of 3s





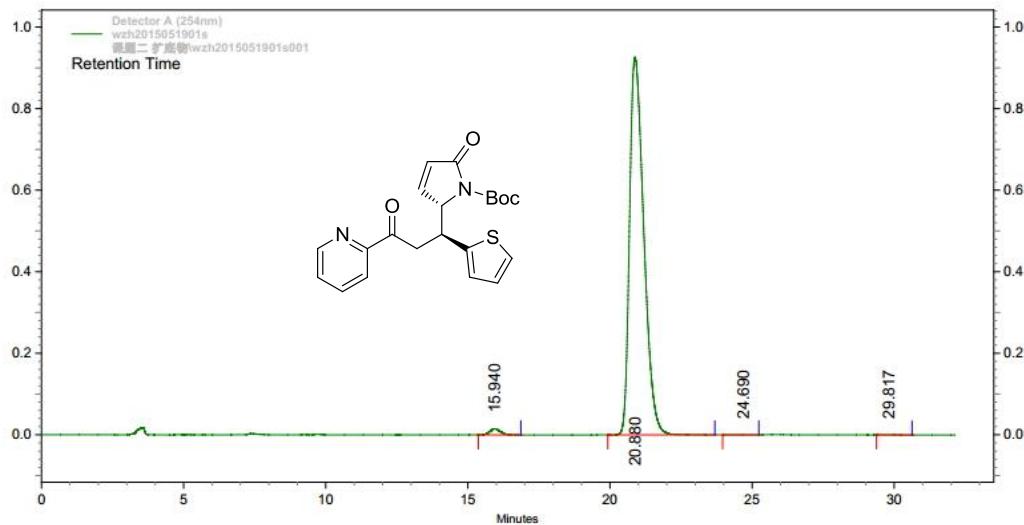
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	15.973	280152	48.03	7237116	39.81
2	21.020	220962	37.88	7344958	40.41
3	24.623	44023	7.55	1783903	9.81
4	29.990	38156	6.54	1811739	9.97

Totals	583293	100.00	18177716	100.00
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Detector

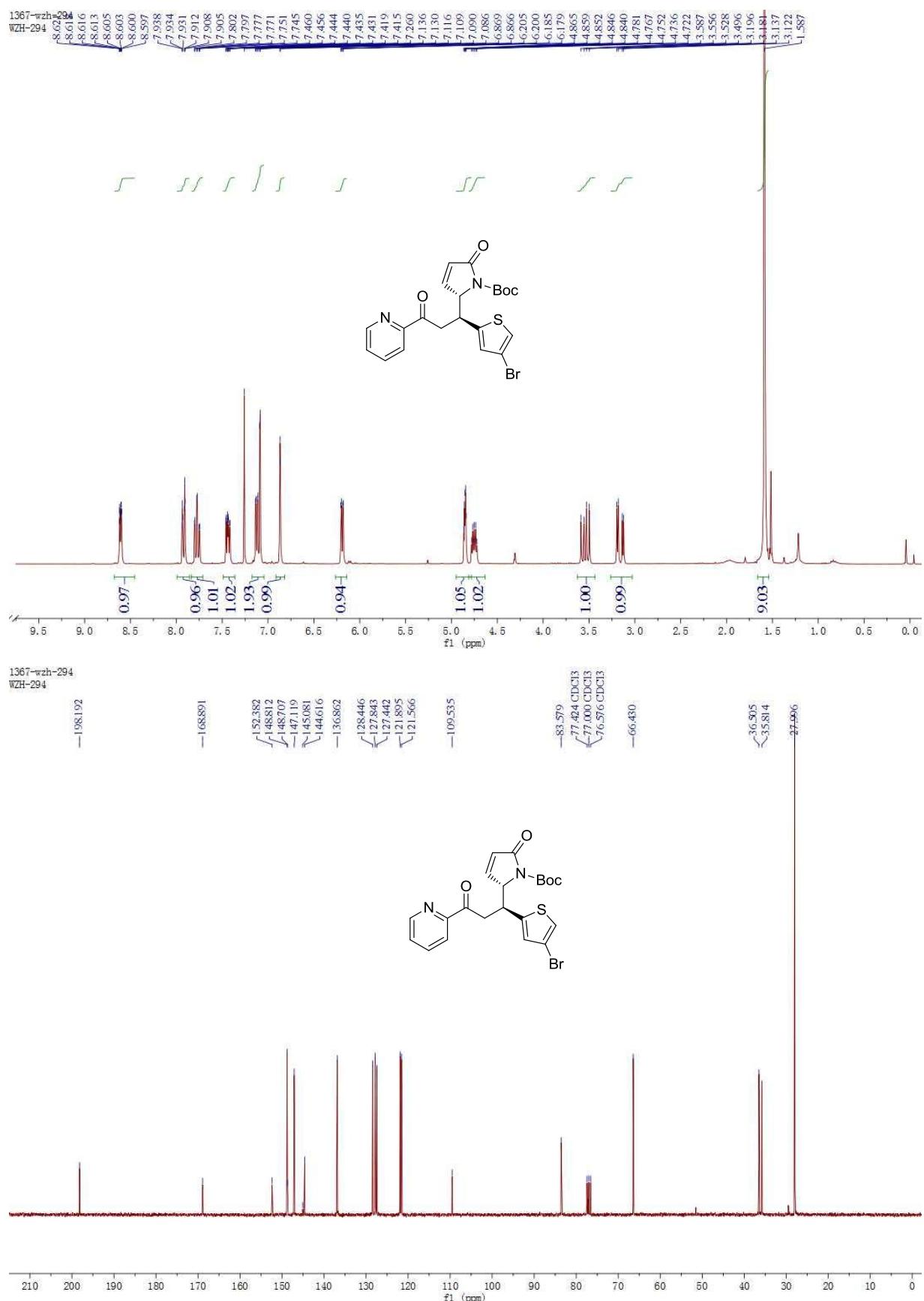
A

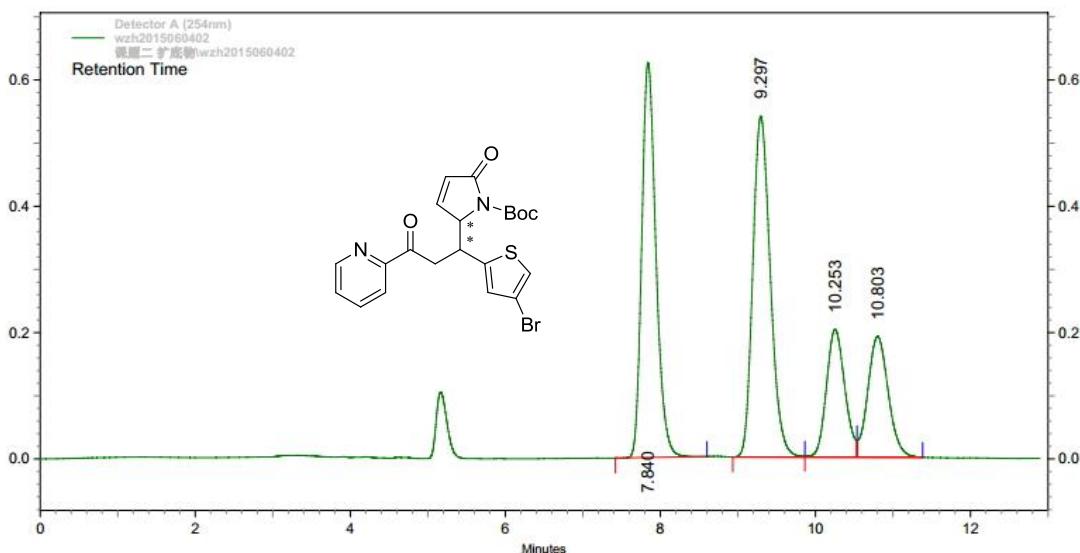
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	15.940	15105	1.60	388974	1.19
2	20.880	926290	98.37	32252531	98.78
3	24.690	48	0.01	1476	0.00
4	29.817	202	0.02	7774	0.02

Totals	941645	100.00	32650755	100.00
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¹H NMR, ¹³C NMR and HPLC of 3t





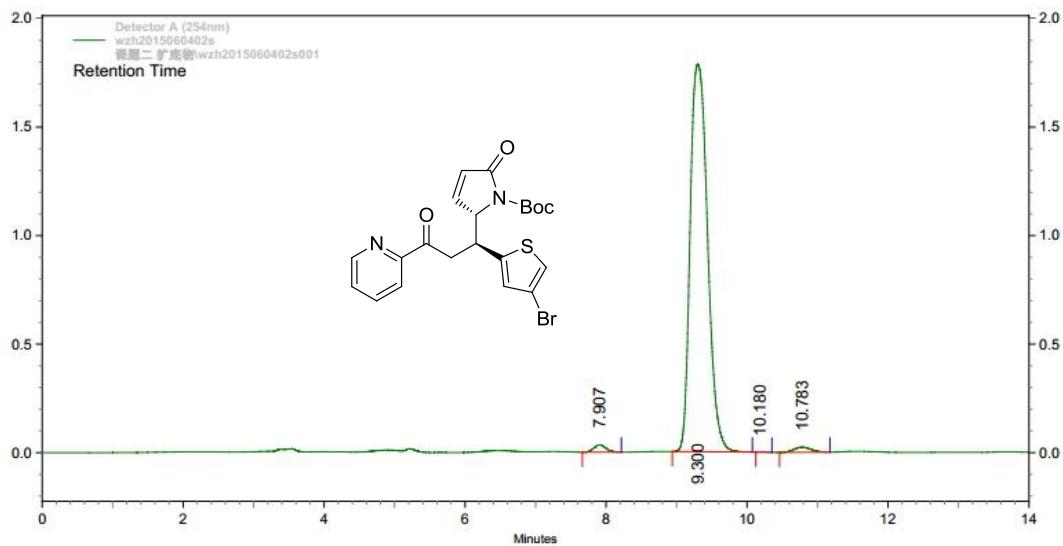
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.840	625414	40.12	7928185	34.15
2	9.297	539911	34.63	8450827	36.40
3	10.253	202386	12.98	3330928	14.35
4	10.803	191331	12.27	3508647	15.11

Totals	1559042	100.00	23218587	100.00
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Detector

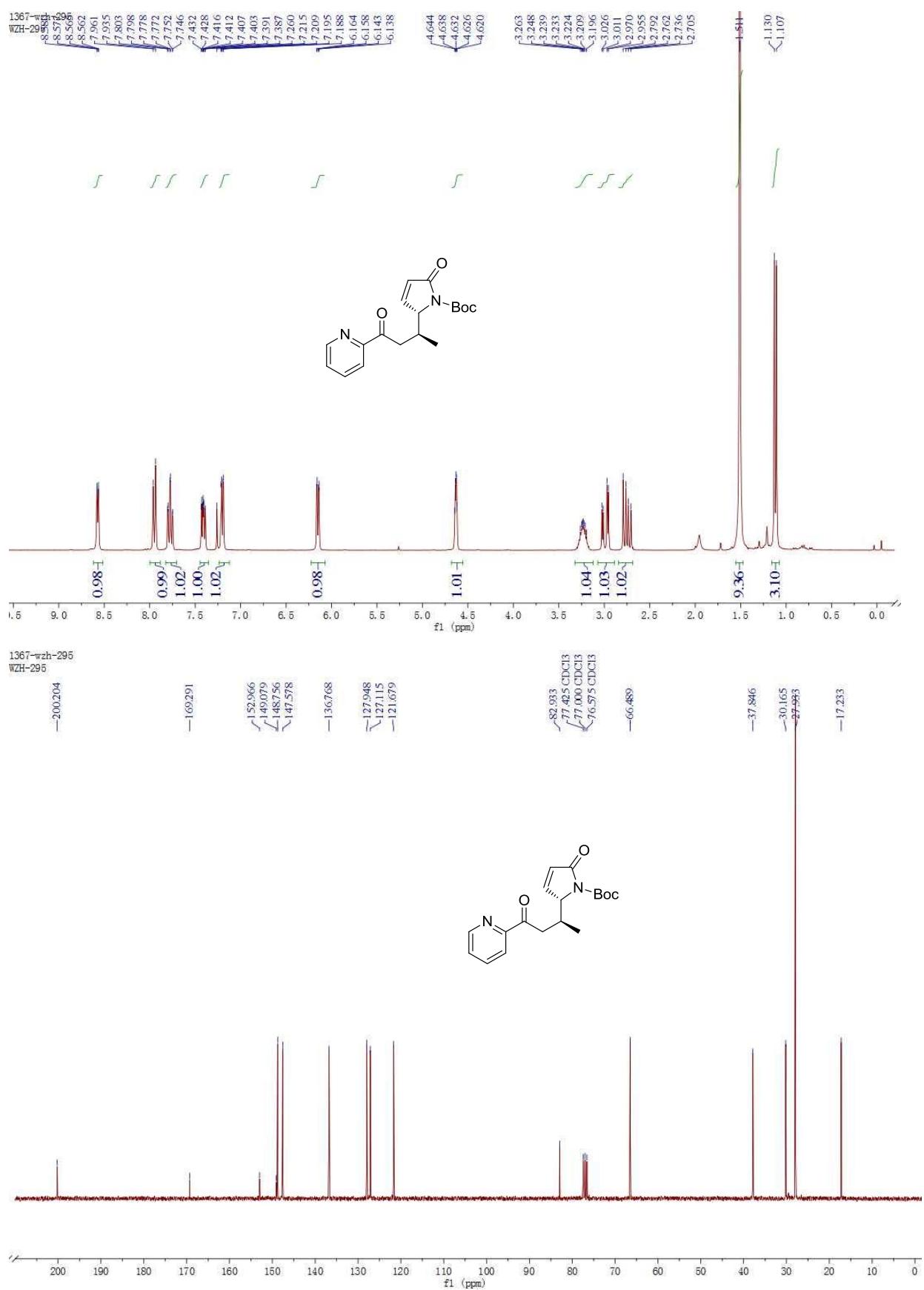
A

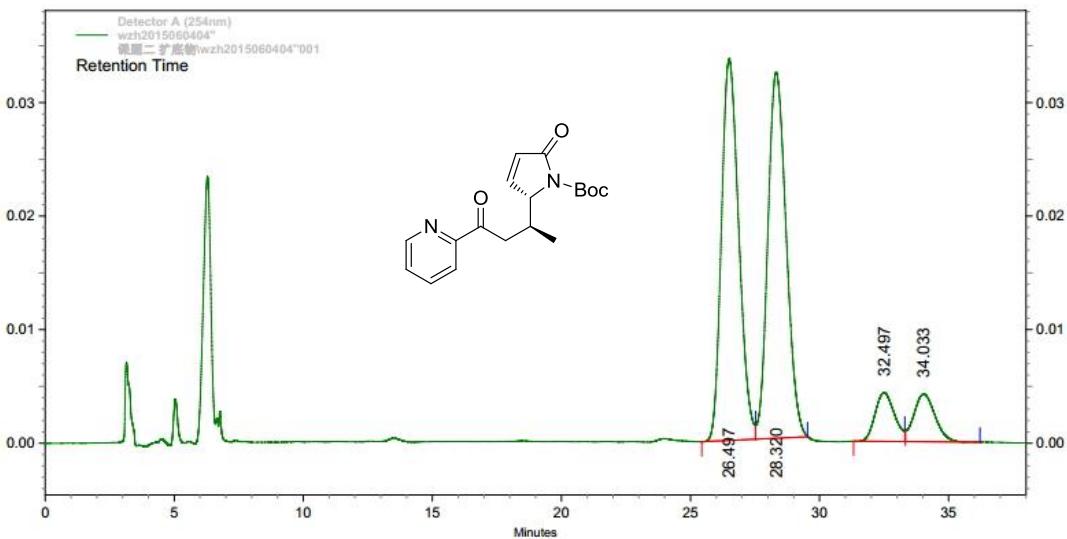
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	7.907	33741	1.83	400558	1.28
2	9.300	1785513	96.88	30577934	97.46
3	10.180	274	0.01	3595	0.01
4	10.783	23505	1.28	392594	1.25

Totals	1843033	100.00	31374681	100.00
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¹H NMR, ¹³C NMR and HPLC of 3u



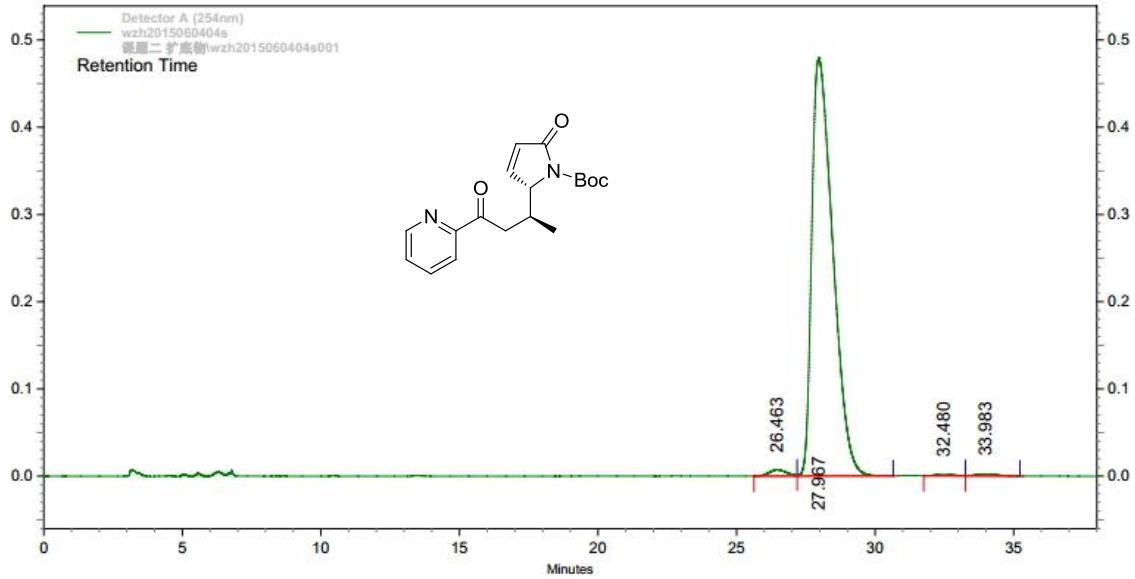


Detector

A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	26.497	33593	45.21	1564004	43.22
2	28.320	32239	43.39	1593745	44.04
3	32.497	4279	5.76	222437	6.15
4	34.033	4191	5.64	238624	6.59

Totals	74302	100.00	3618810	100.00
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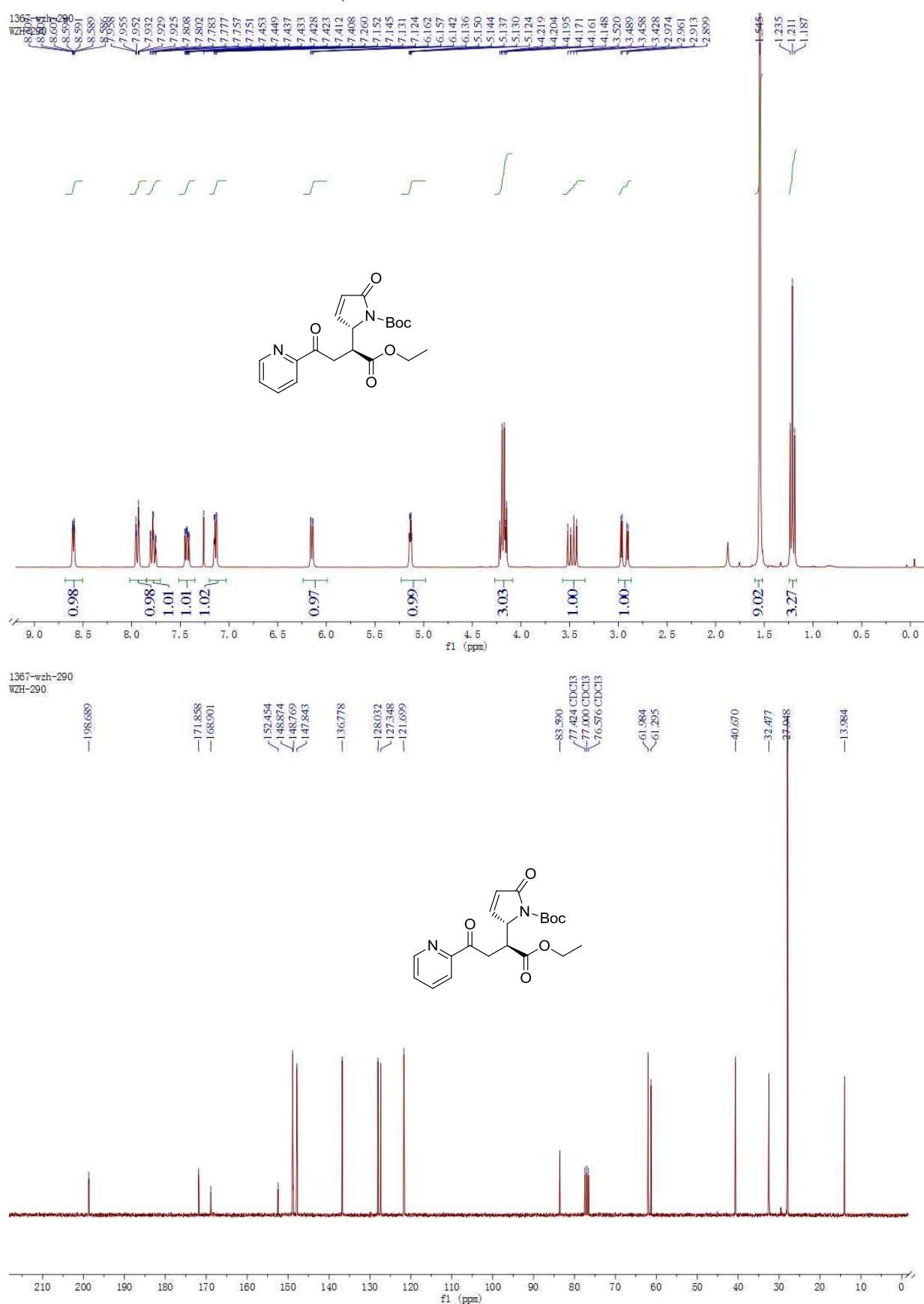
Detector

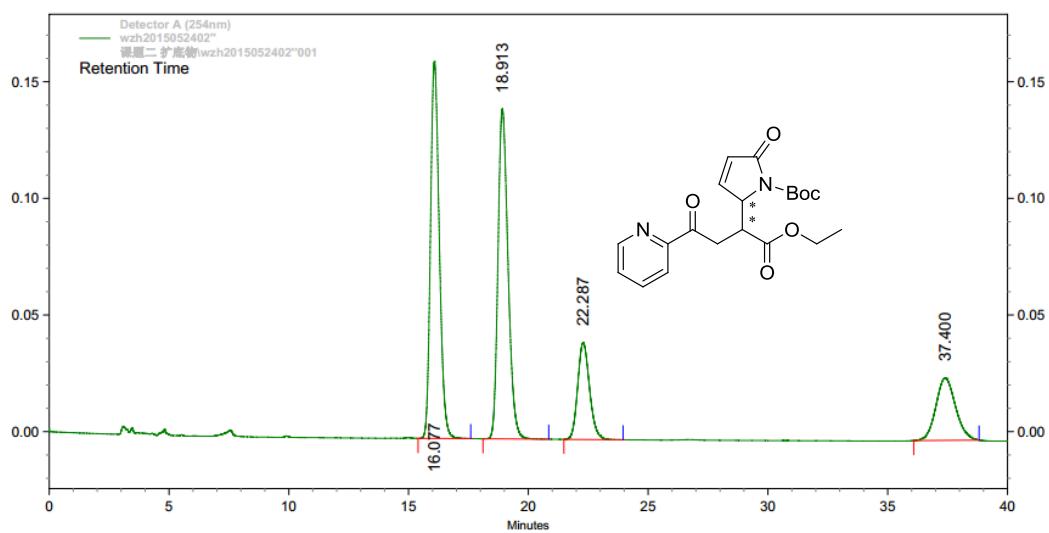
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	26.463	7104	1.45	310926	1.21
2	27.967	478768	97.77	25230314	98.01
3	32.480	1624	0.33	79985	0.31
4	33.983	2207	0.45	121513	0.47

Totals	489703	100.00	25742738	100.00
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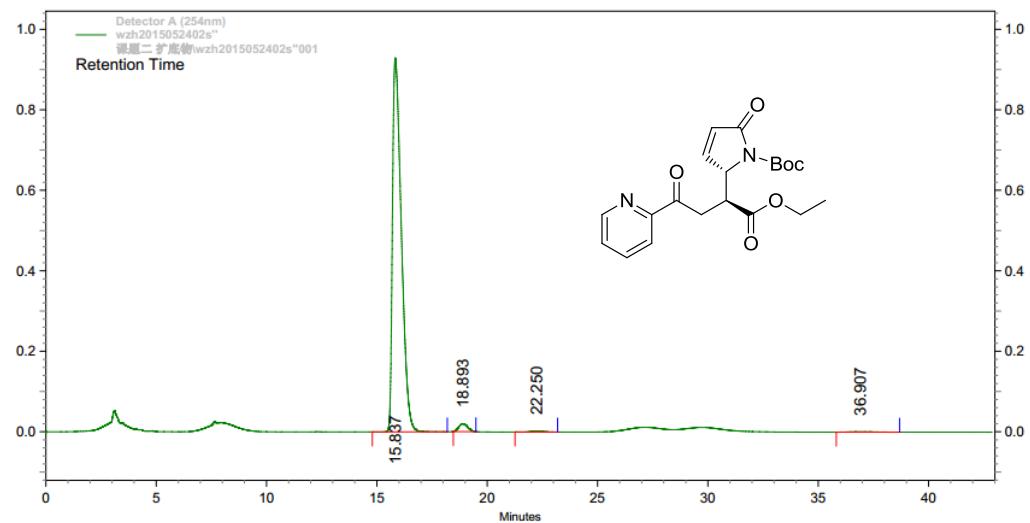
¹H NMR, ¹³C NMR and HPLC of 3v





Detector
A
(254nm)

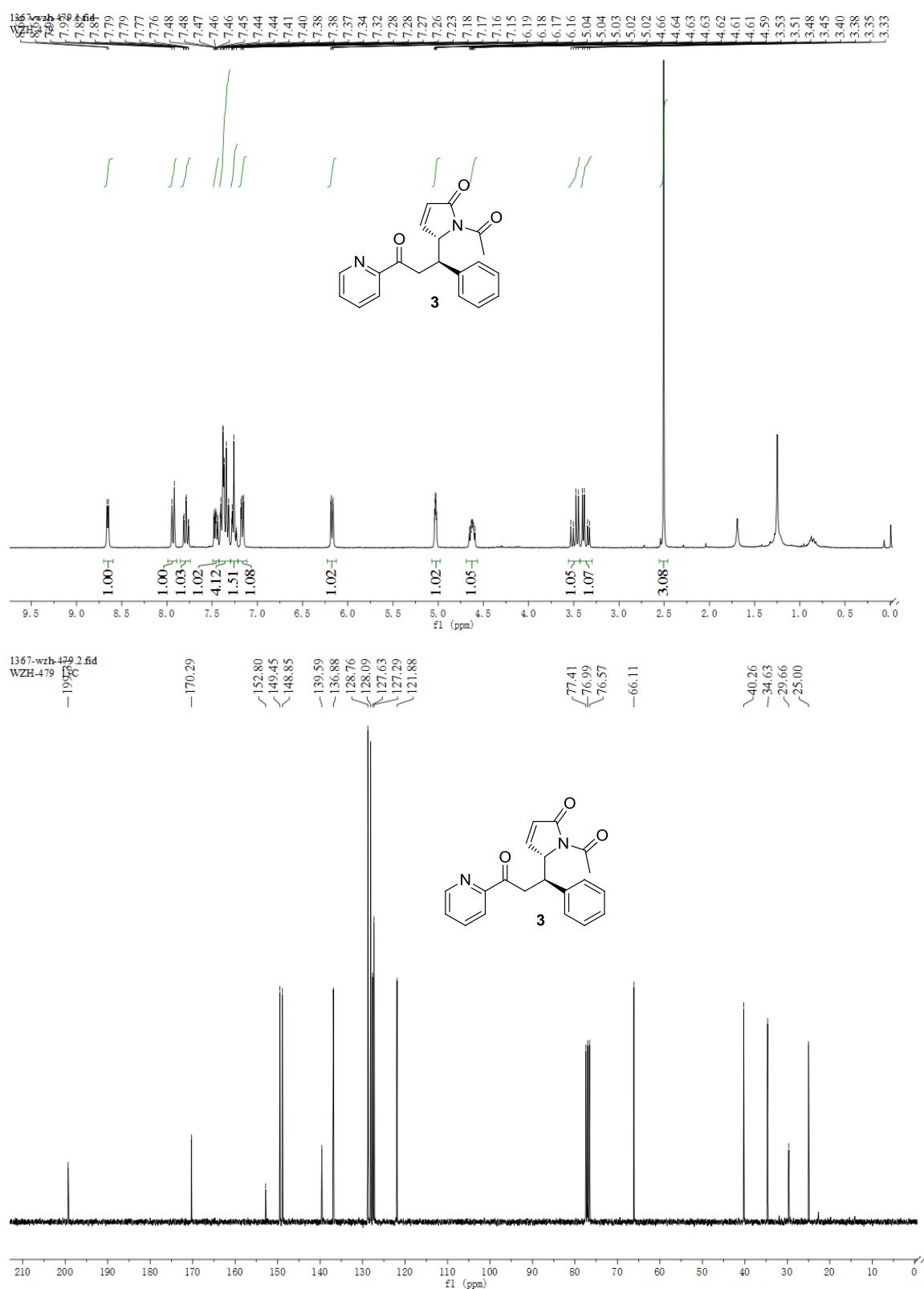
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	16.077	161539	43.51	4119014	36.79
2	18.913	141424	38.09	4120621	36.81
3	22.287	41553	11.19	1426871	12.74
4	37.400	26758	7.21	1529194	13.66
Totals		371274	100.00	11195700	100.00

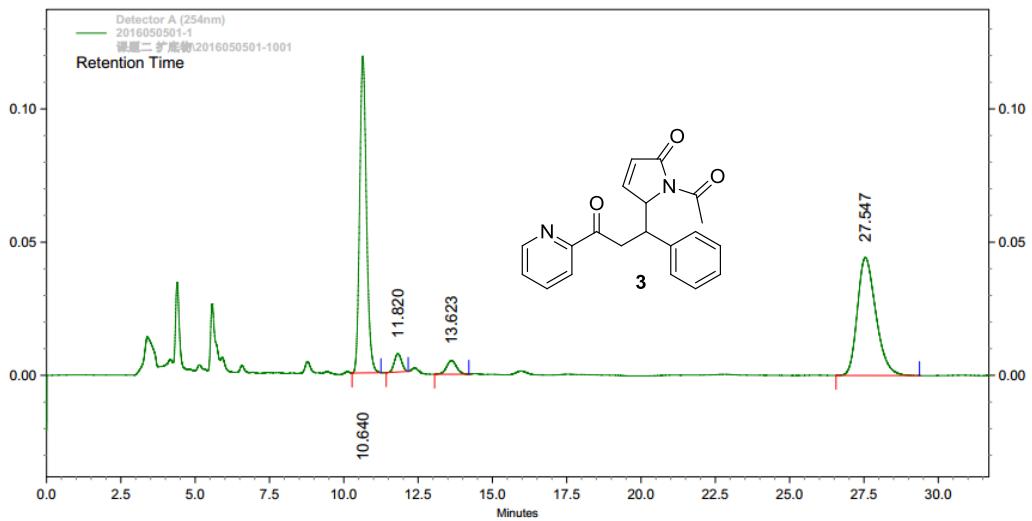


Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	15.837	928993	97.56	25995923	97.34
2	18.893	19710	2.07	539615	2.02
3	22.250	2526	0.27	92342	0.35
4	36.907	1029	0.11	79578	0.30
Totals		952258	100.00	26707458	100.00

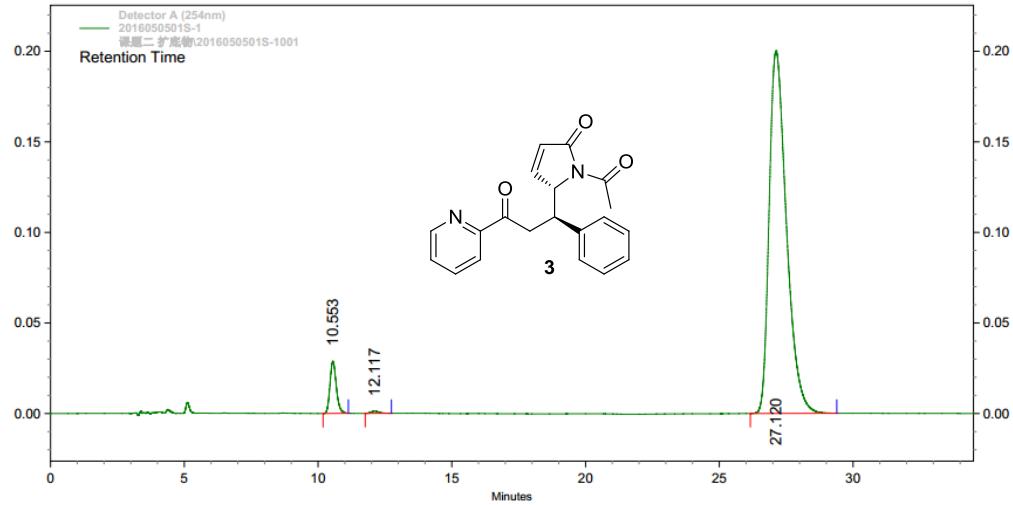
¹H NMR, ¹³C NMR and HPLC of 3w




Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.640	118855	67.87	1884218	46.70
2	11.820	6848	3.91	117149	2.90
3	13.623	5149	2.94	118684	2.94
4	27.547	44262	25.28	1914316	47.45

Totals	175114	100.00	4034367	100.00
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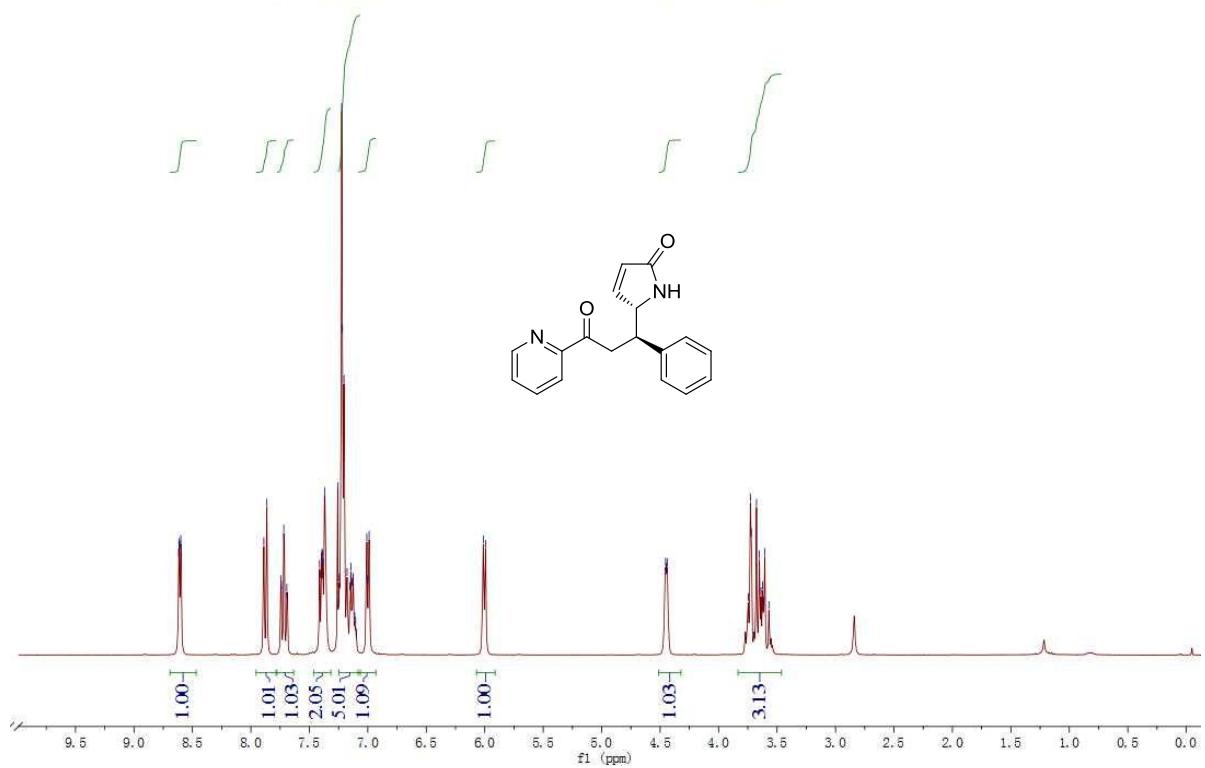

Detector
A
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	10.553	28833	12.53	473764	5.00
2	12.117	1207	0.52	24193	0.26
3	27.120	200151	86.95	8983057	94.75

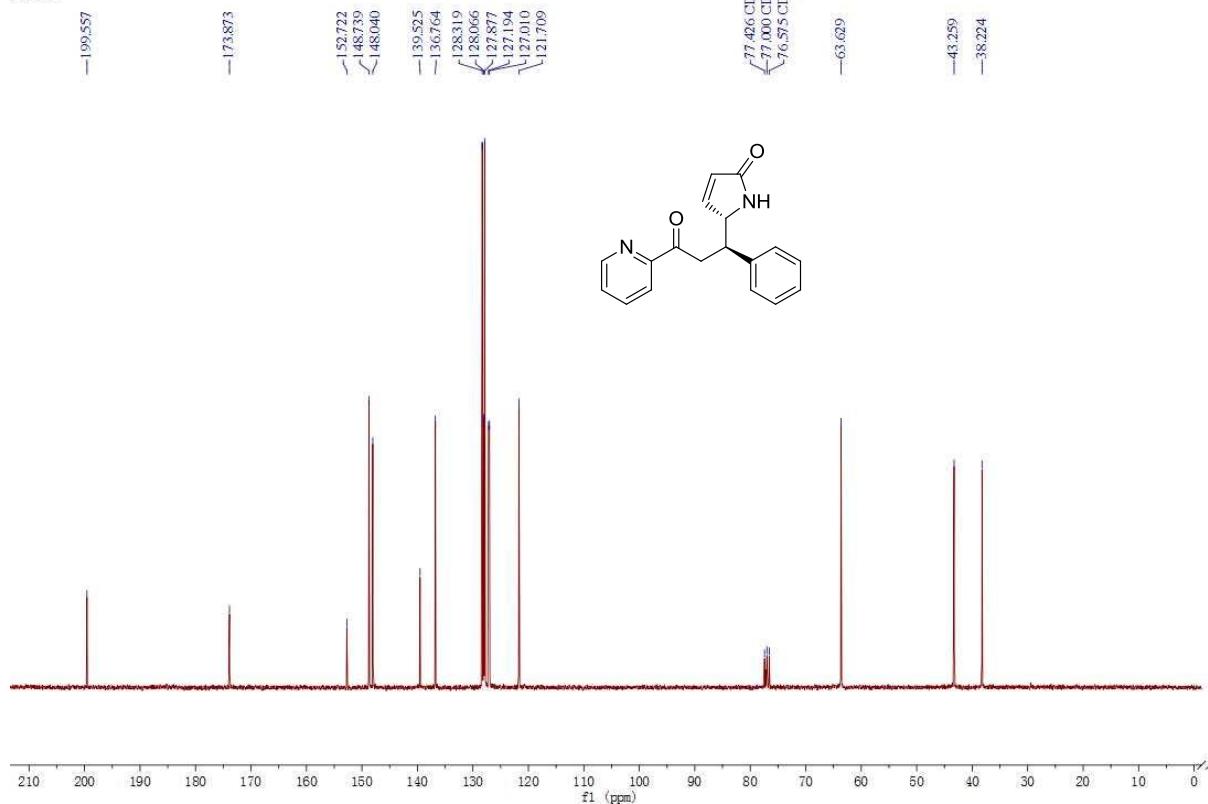
Totals	230191	100.00	9481014	100.00
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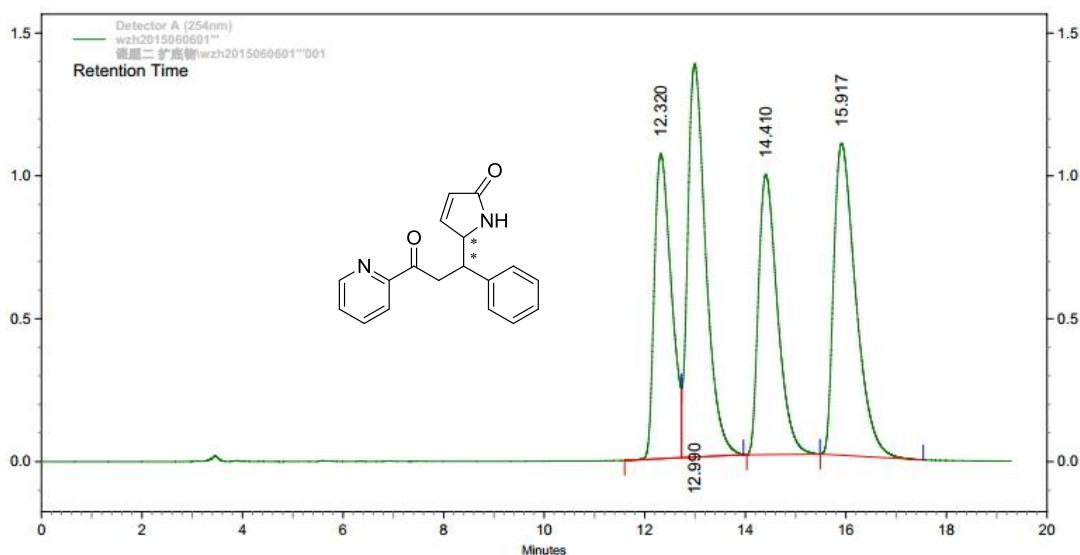
¹H NMR, ¹³C NMR and HPLC of 4

1367-wzh-291
WZH-291



1367-wzh-291
WZH-291





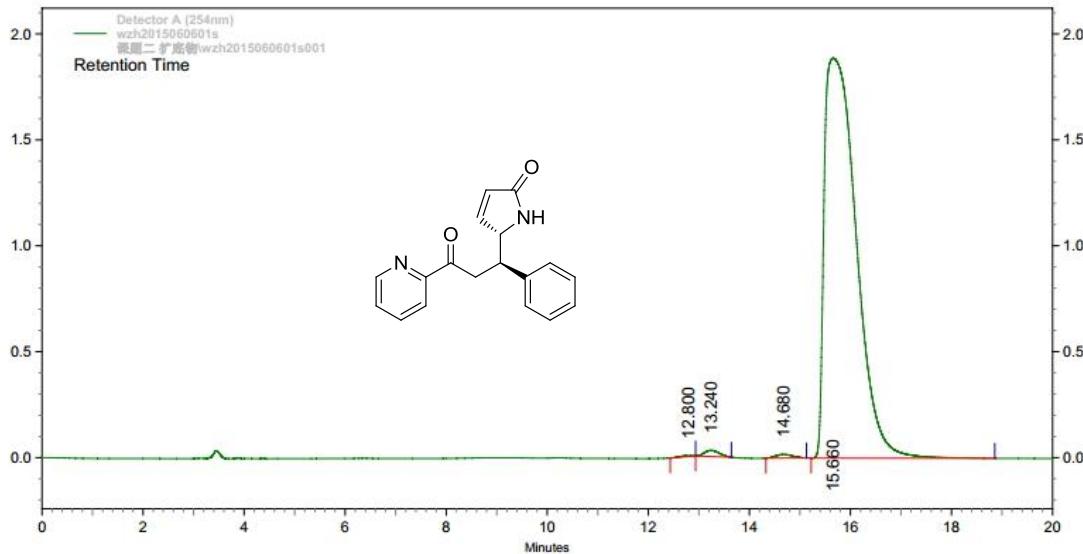
Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	12.320	1067333	23.64	25003393	21.11
2	12.990	1376092	30.48	34540922	29.17
3	14.410	979735	21.70	25716421	21.71
4	15.917	1091456	24.18	33170086	28.01

Totals	4514616	100.00	118430822	100.00
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Detector

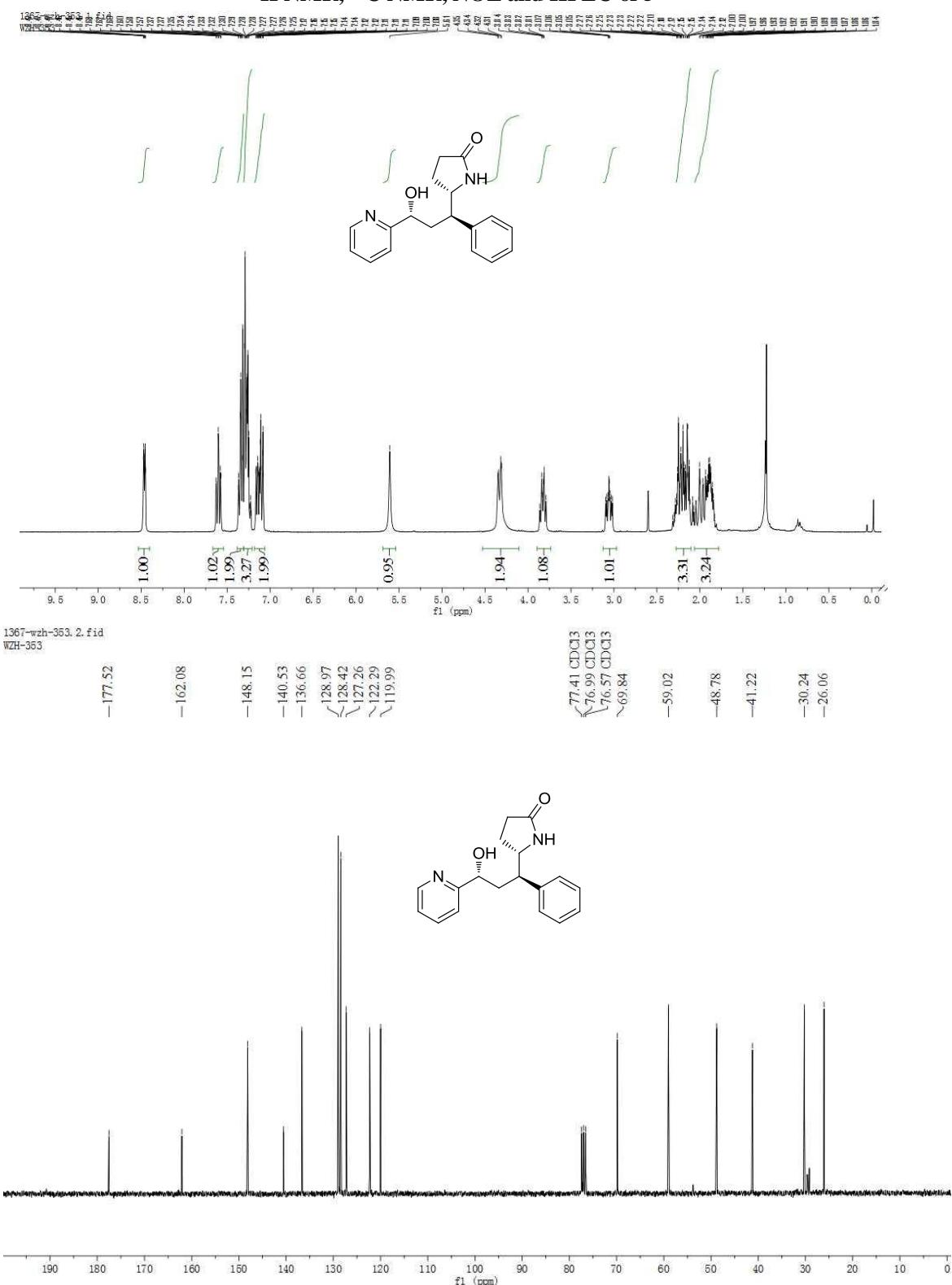
A

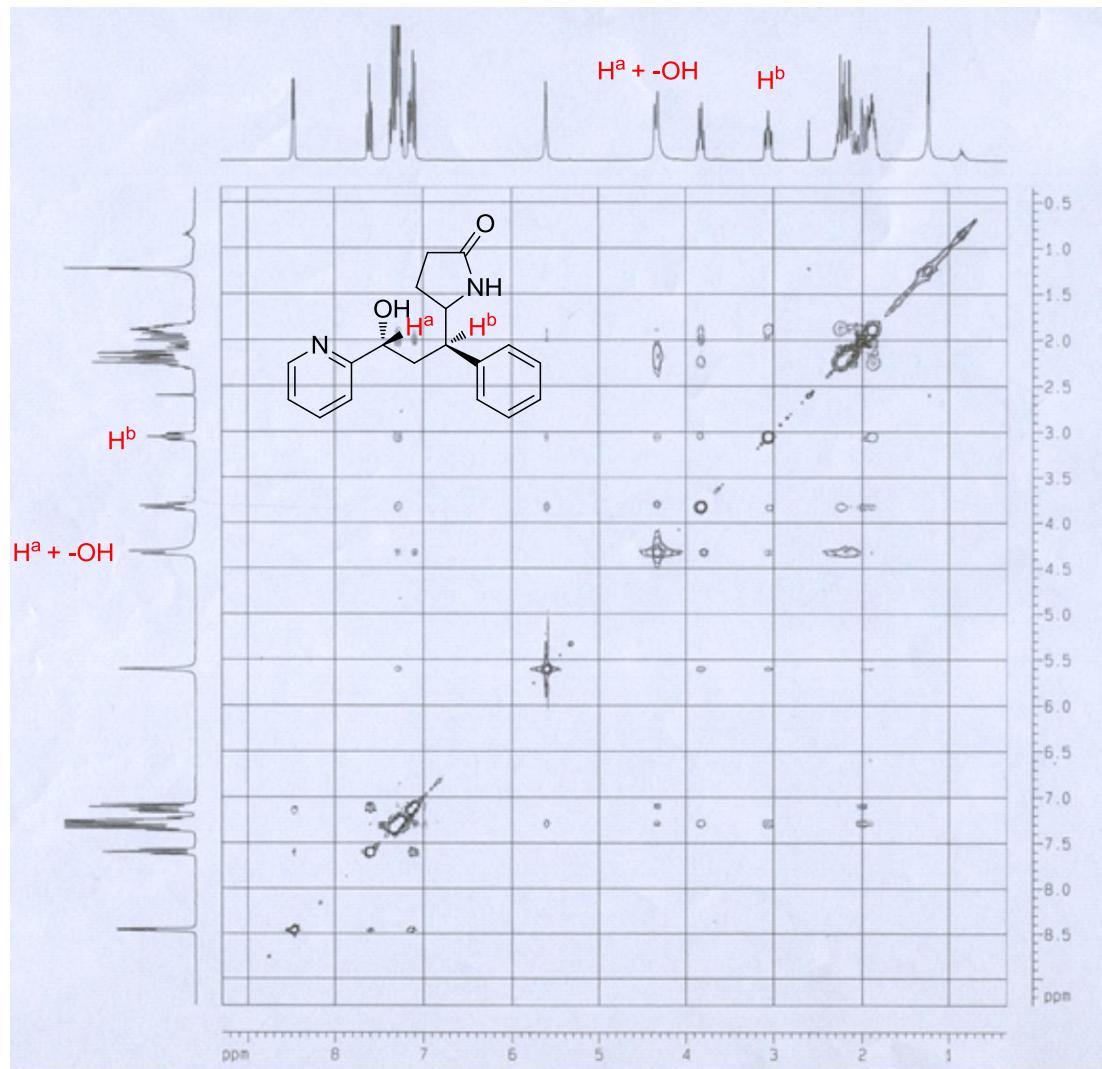
(254nm)

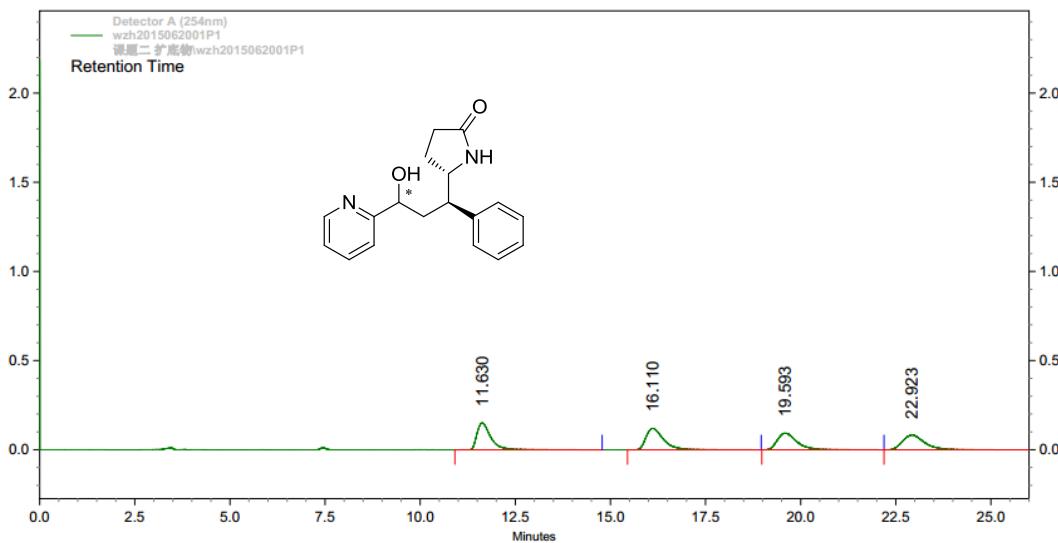
Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	12.800	4399	0.23	72450	0.09
2	13.240	29226	1.51	592974	0.71
3	14.680	17457	0.90	408249	0.49
4	15.660	1888200	97.37	82653223	98.72

Totals	1939282	100.00	83726896	100.00
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¹H NMR, ¹³C NMR, NOE and HPLC of 5





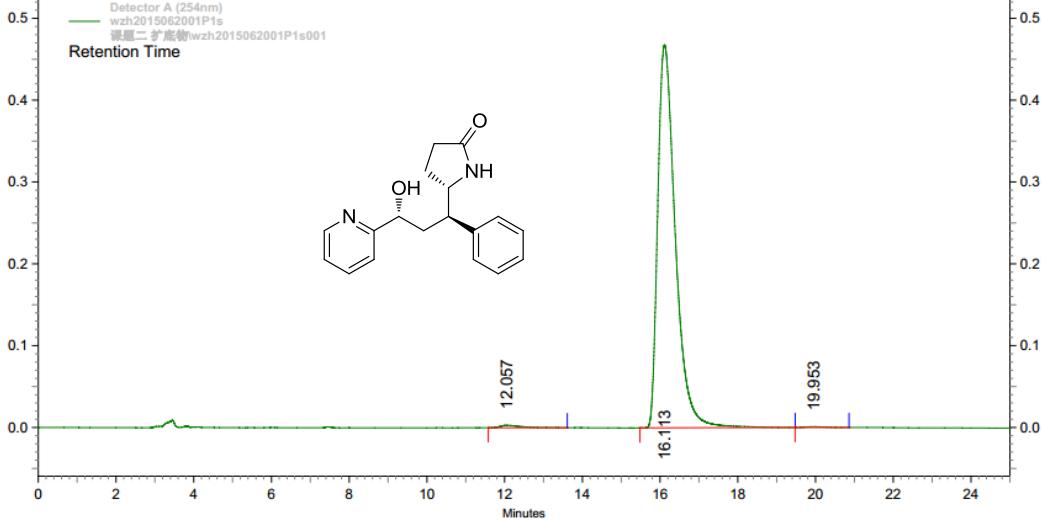


Detector

A

(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	11.630	150176	33.72	3841800	26.48
2	16.110	119889	26.92	3892792	26.83
3	19.593	93310	20.95	3380523	23.30
4	22.923	82021	18.42	3394057	23.39
Totals		445396	100.00	14509172	100.00



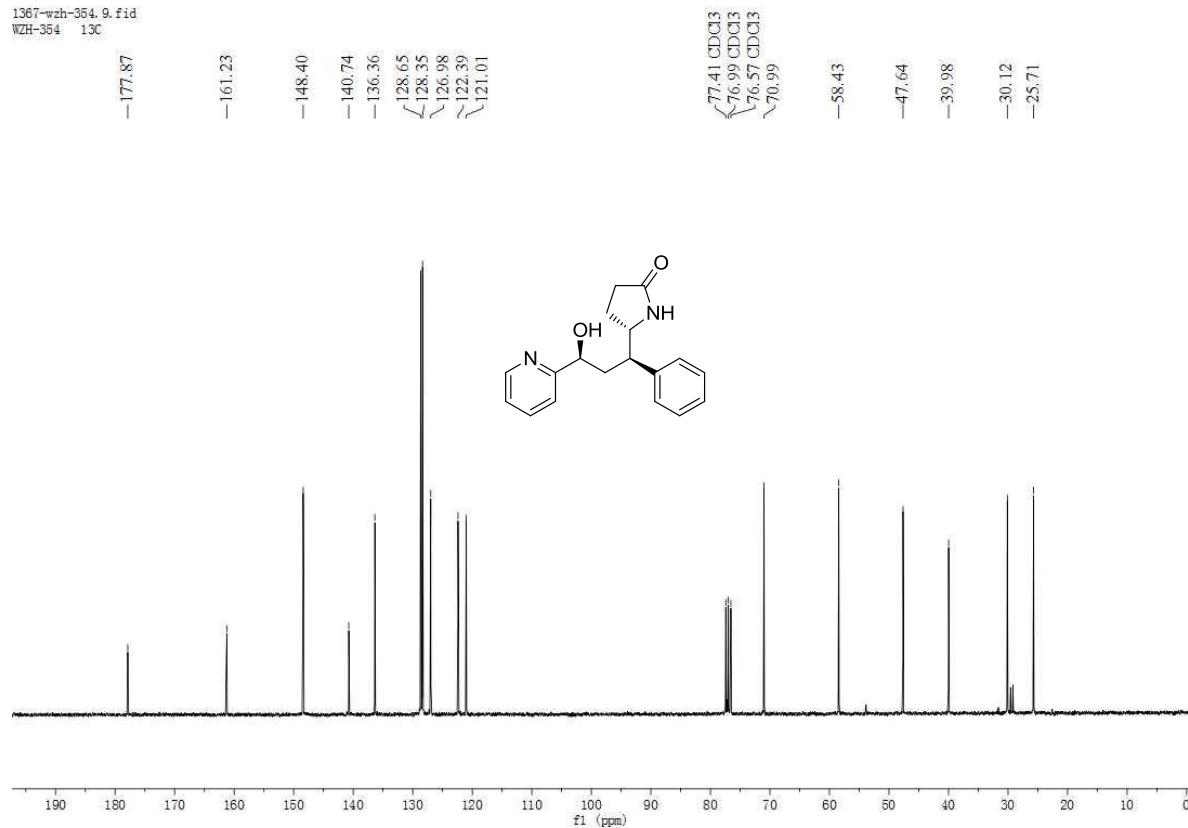
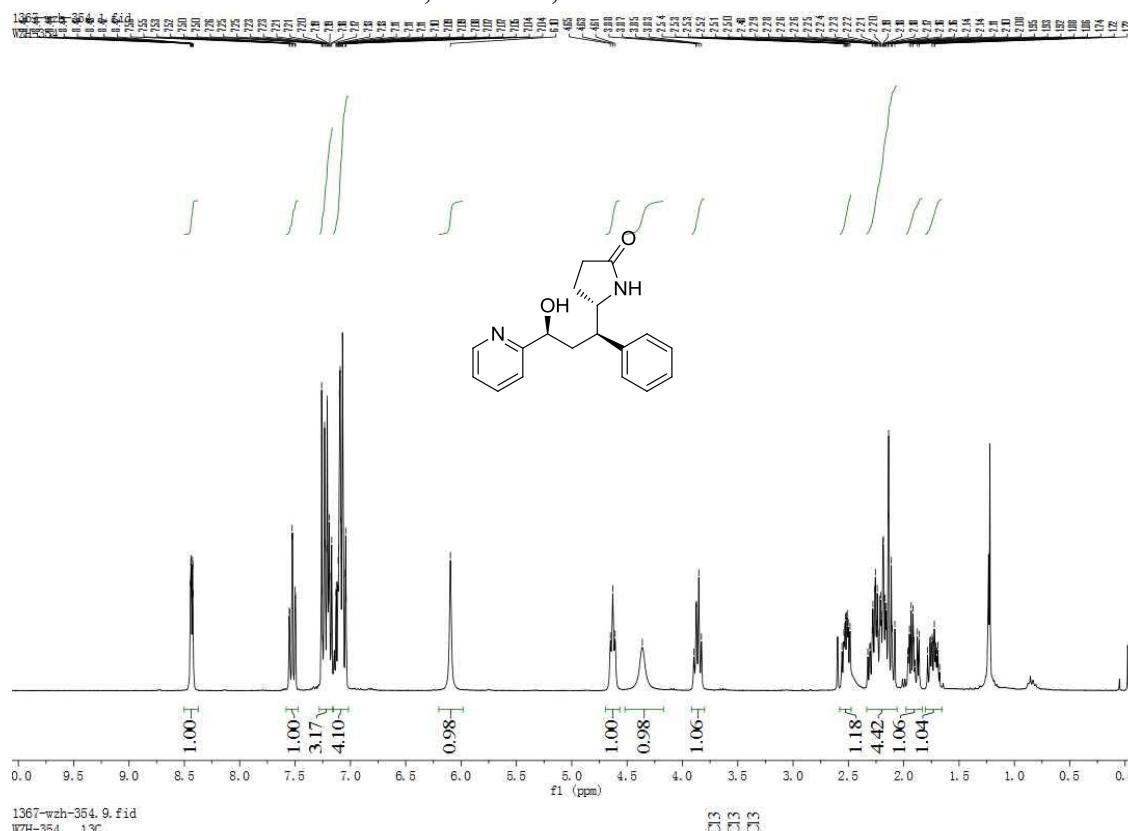
Detector

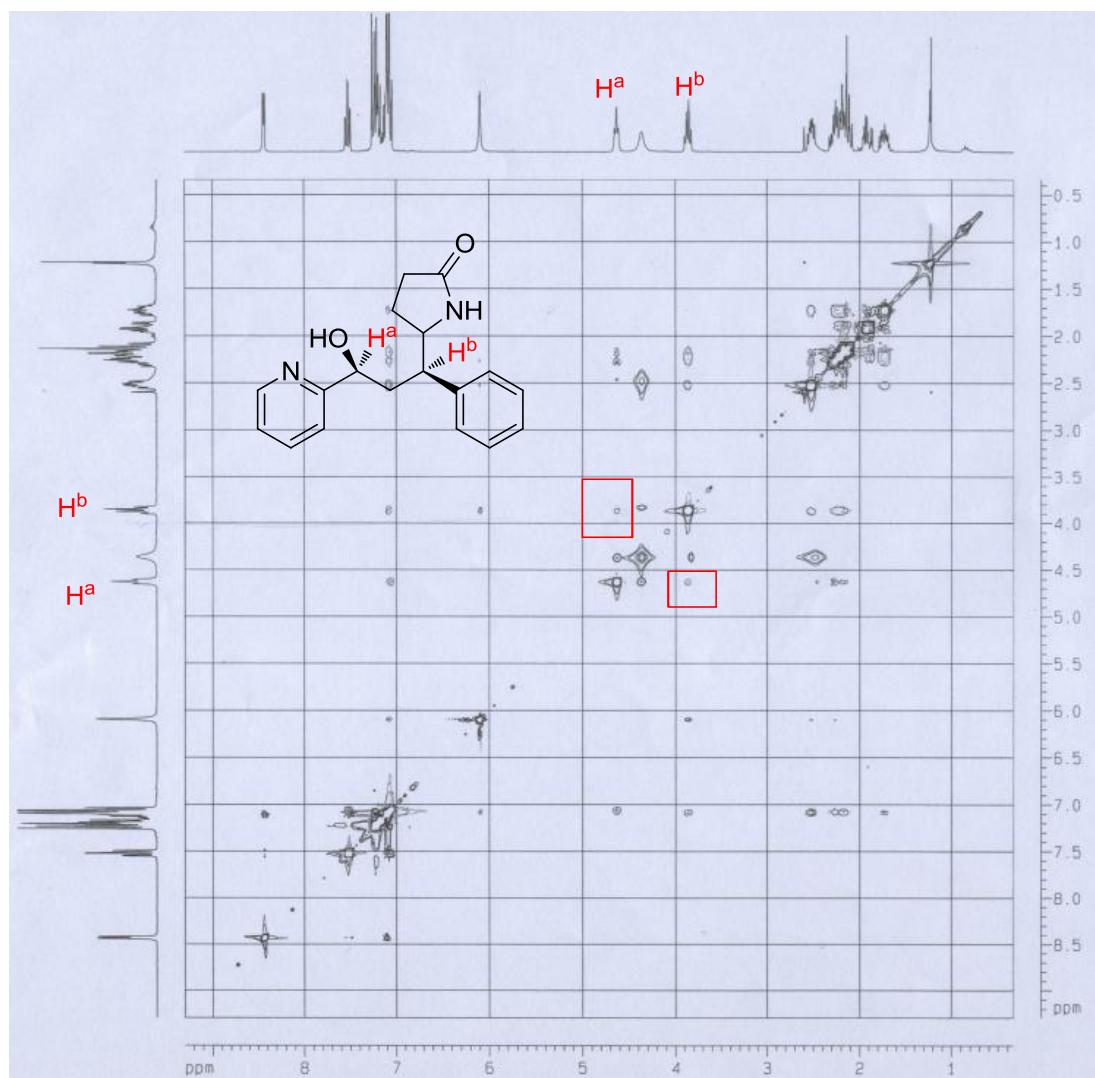
A

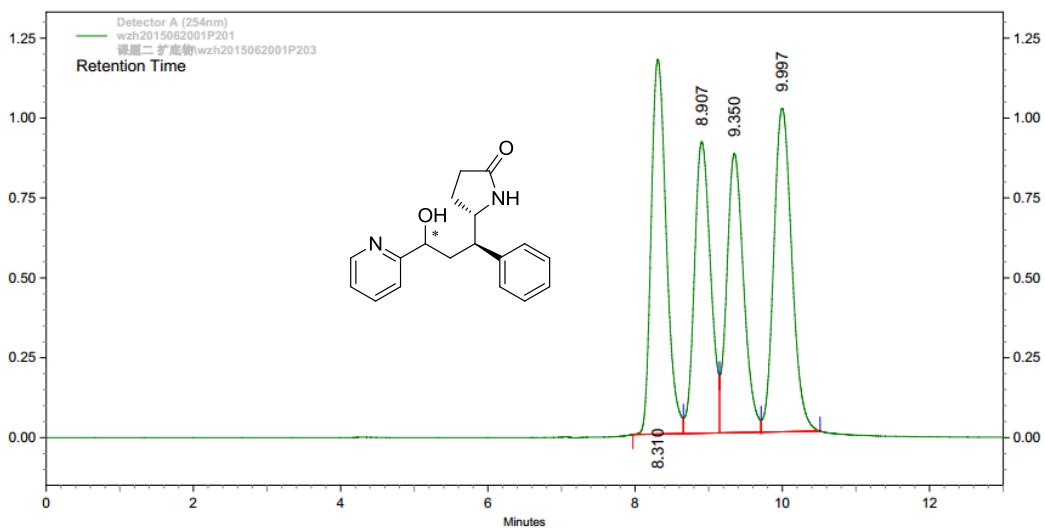
(254nm)

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	12.057	2979	0.63	108269	0.73
2	16.113	467882	99.17	14741615	99.04
3	19.953	934	0.20	34921	0.23
Totals		471795	100.00	14884805	100.00

¹H NMR, ¹³C NMR, NOE and HPLC of 6

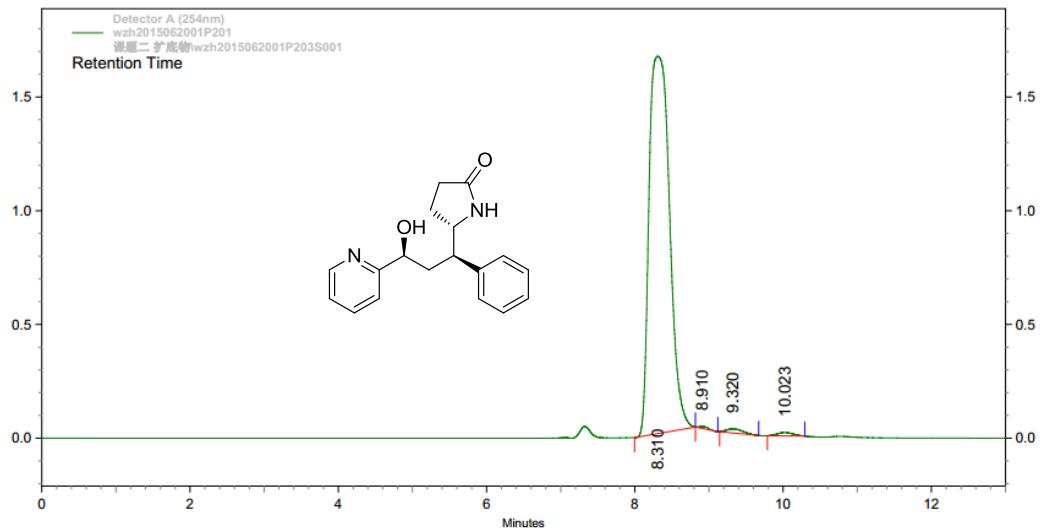






**Detector
A
(254nm)**

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	8.310	1172339	29.53	16718002	27.00
2	8.907	911725	22.97	13933173	22.50
3	9.350	873336	22.00	14009402	22.62
4	9.997	1012377	25.50	17264851	27.88
Totals		3969777	100.00	61925428	100.00



**Detector
A
(254nm)**

Pk #	Retention Time	Height	Height Percent	Area	Area Percent
1	8.310	1658558	97.58	31844789	98.20
2	8.910	8299	0.49	77066	0.24
3	9.320	18061	1.06	286113	0.88
4	10.023	14793	0.87	219195	0.68
Totals		1699711	100.00	32427163	100.00