Squaramide-Catalyzed Asymmetric Michael Addition/Cyclization Reaction for the Synthesis of Chiral Bisspiro Barbituric Acid-Oxindoles

De-Jun Qiao, Da-Ming Du*

Key Laboratory of Medicinal Molecule Science and Pharmaceutical Engineering, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing 100081, China

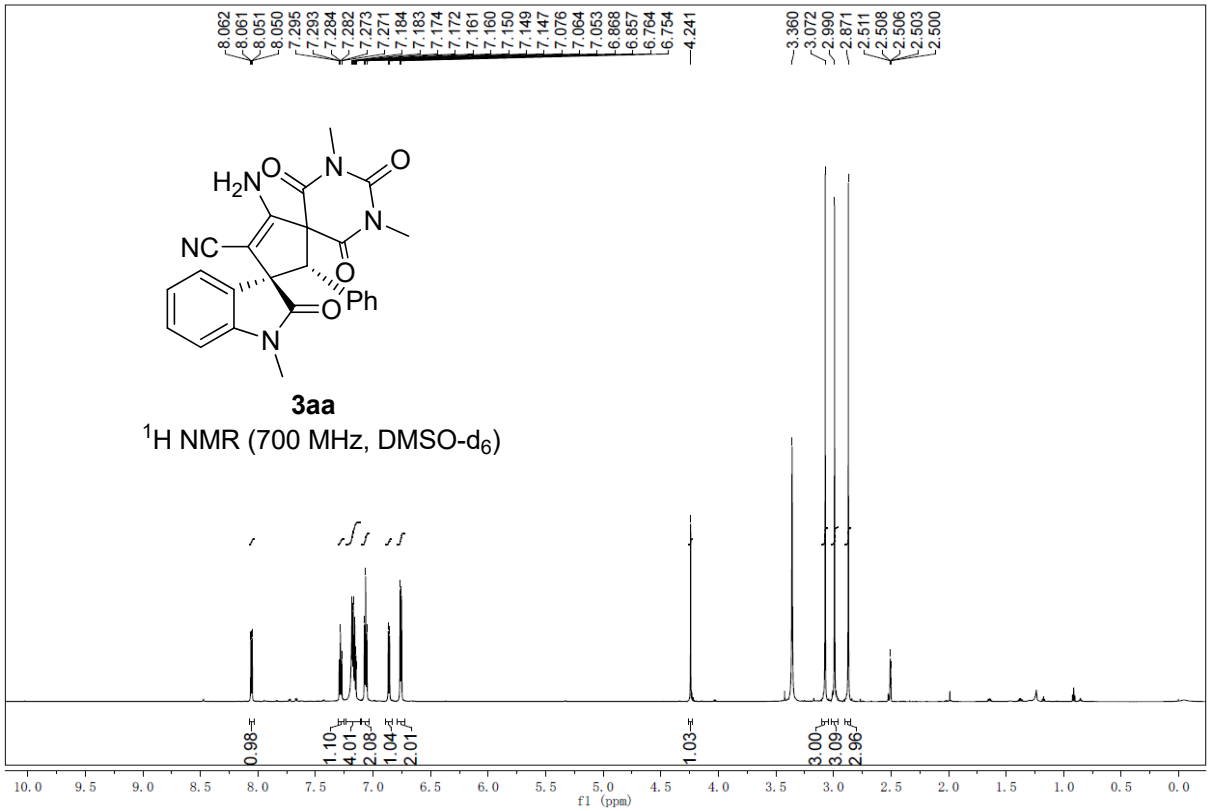
E-mail: dudm@bit.edu.cn

Supporting Information

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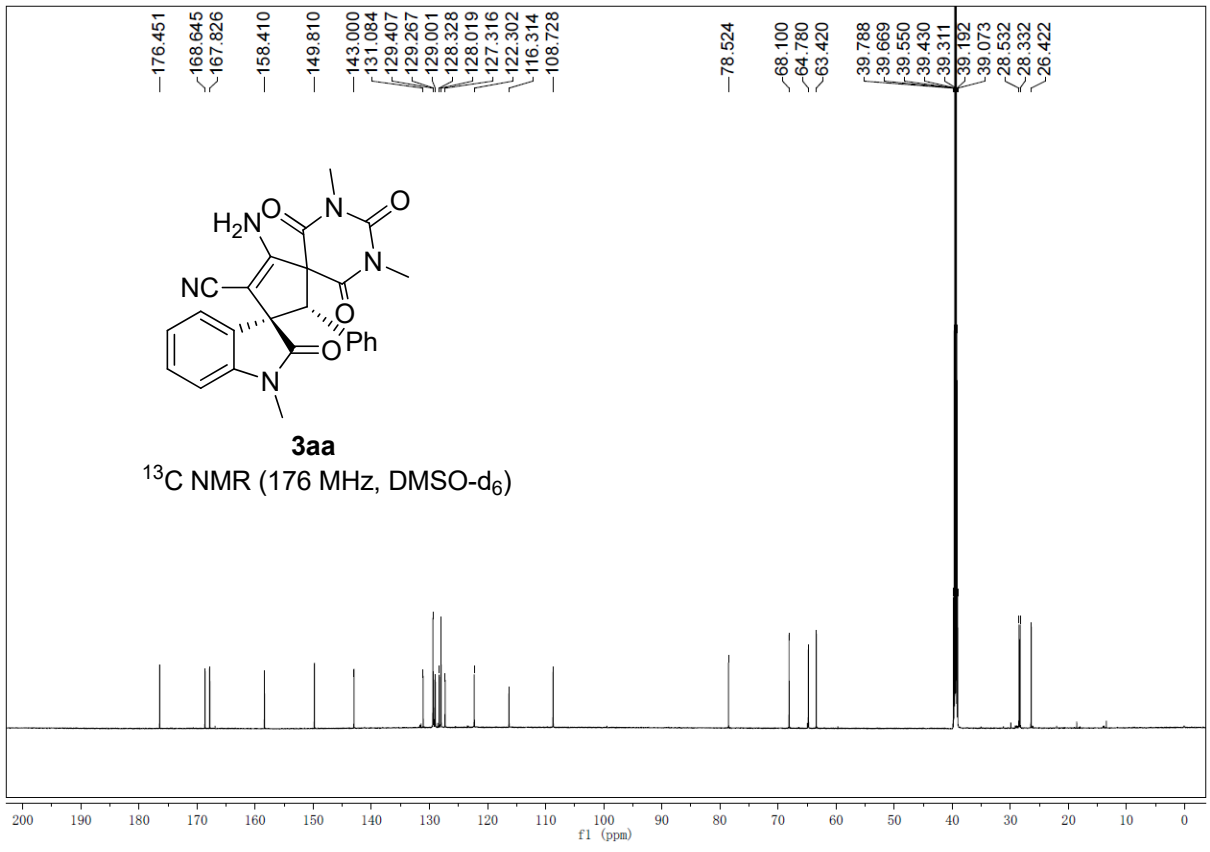
1. Copies of ^{1}H and ^{13}C NMR spectra of new compounds…….....S1
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1. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra of new compounds



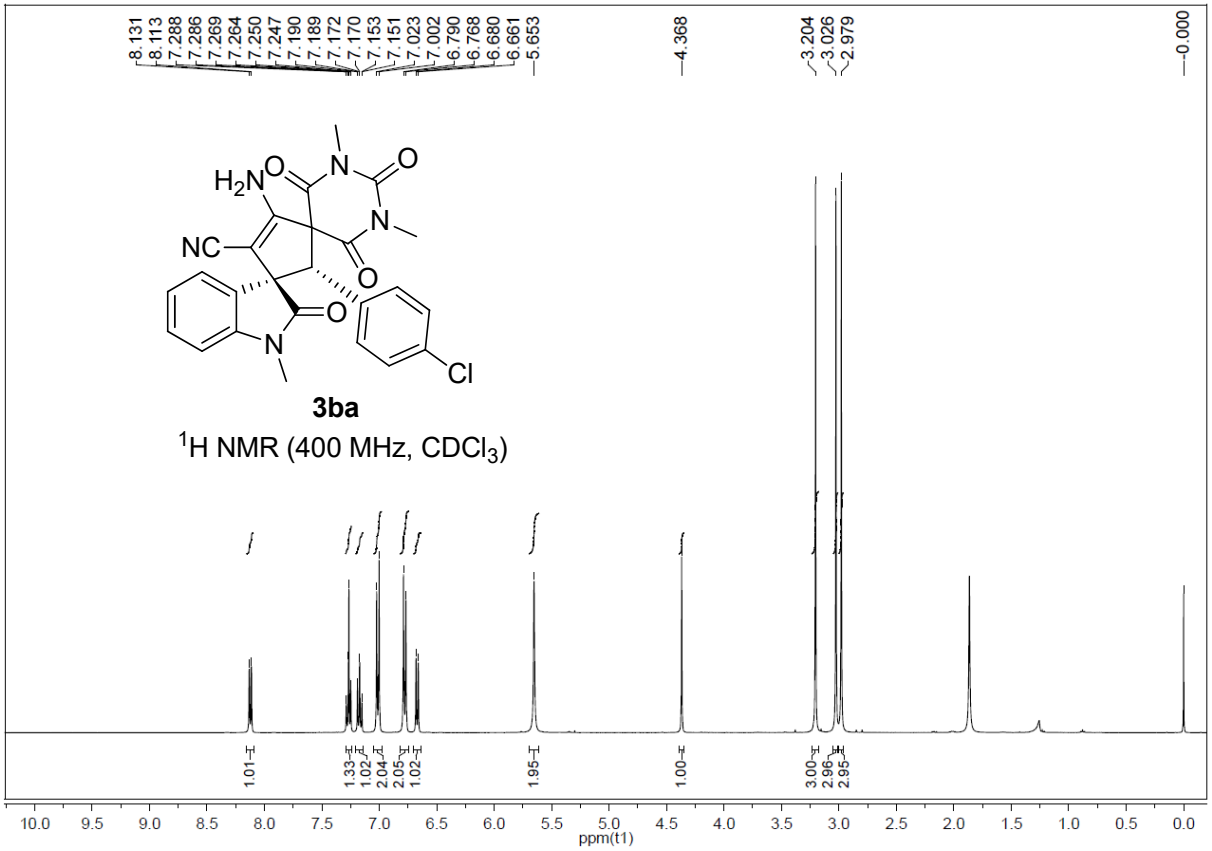
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^{1}H NMR (700 MHz, DMSO-d_6)



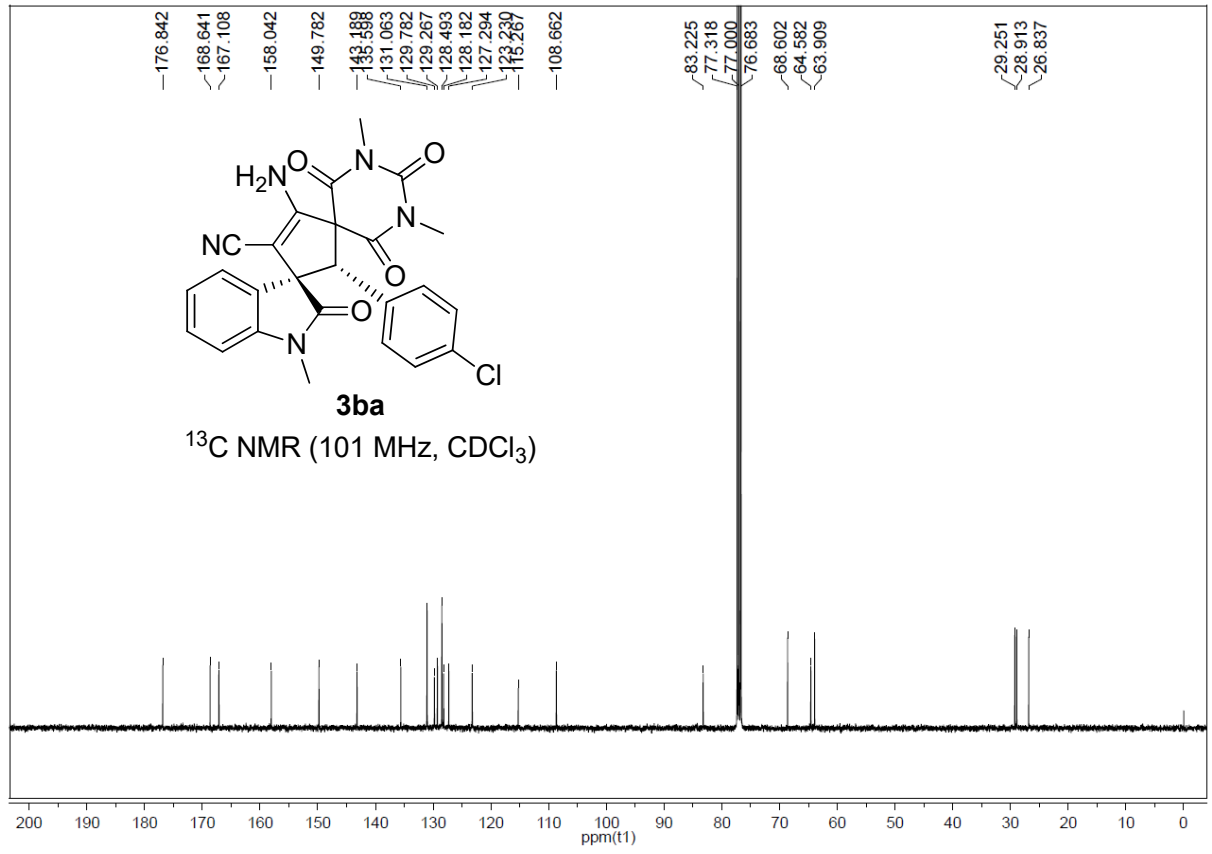
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^{13}C NMR (176 MHz, DMSO-d_6)



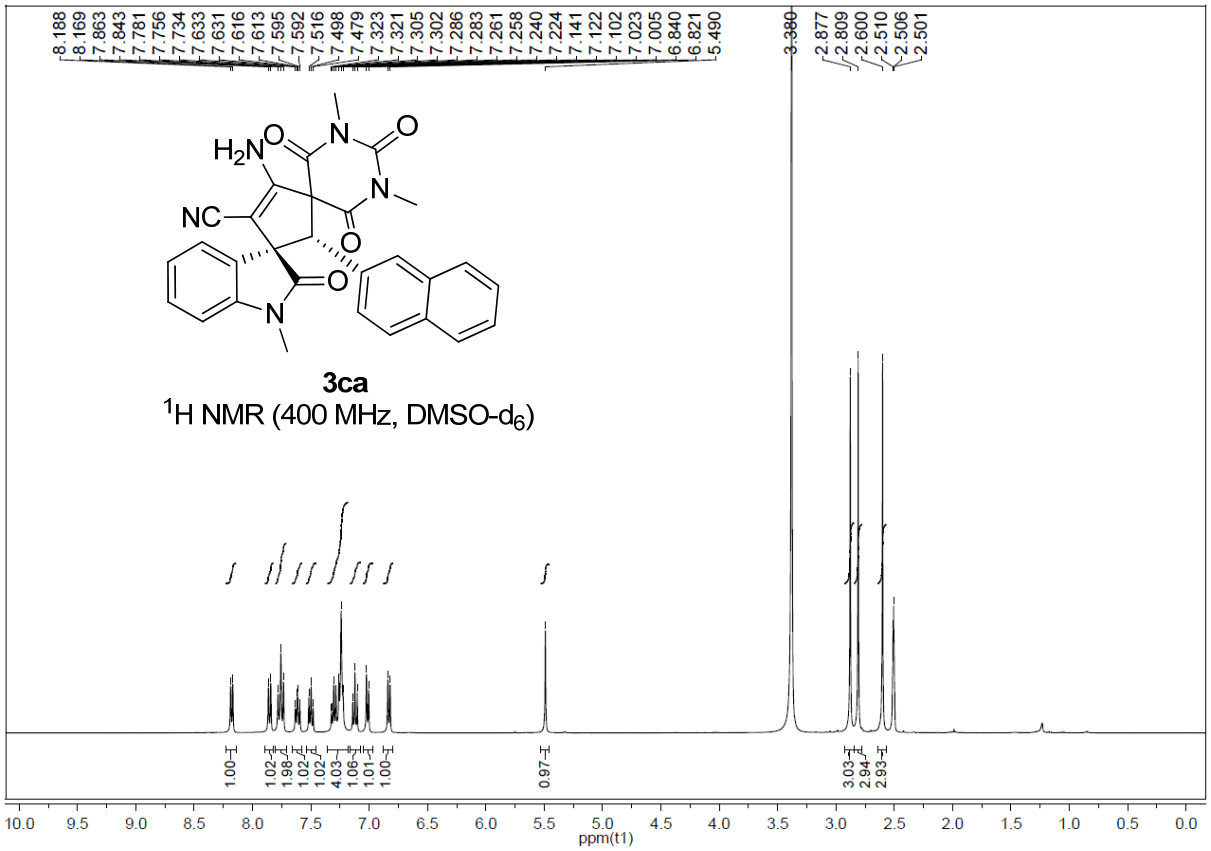
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^{1}H NMR (400 MHz, $CDCl_3$)



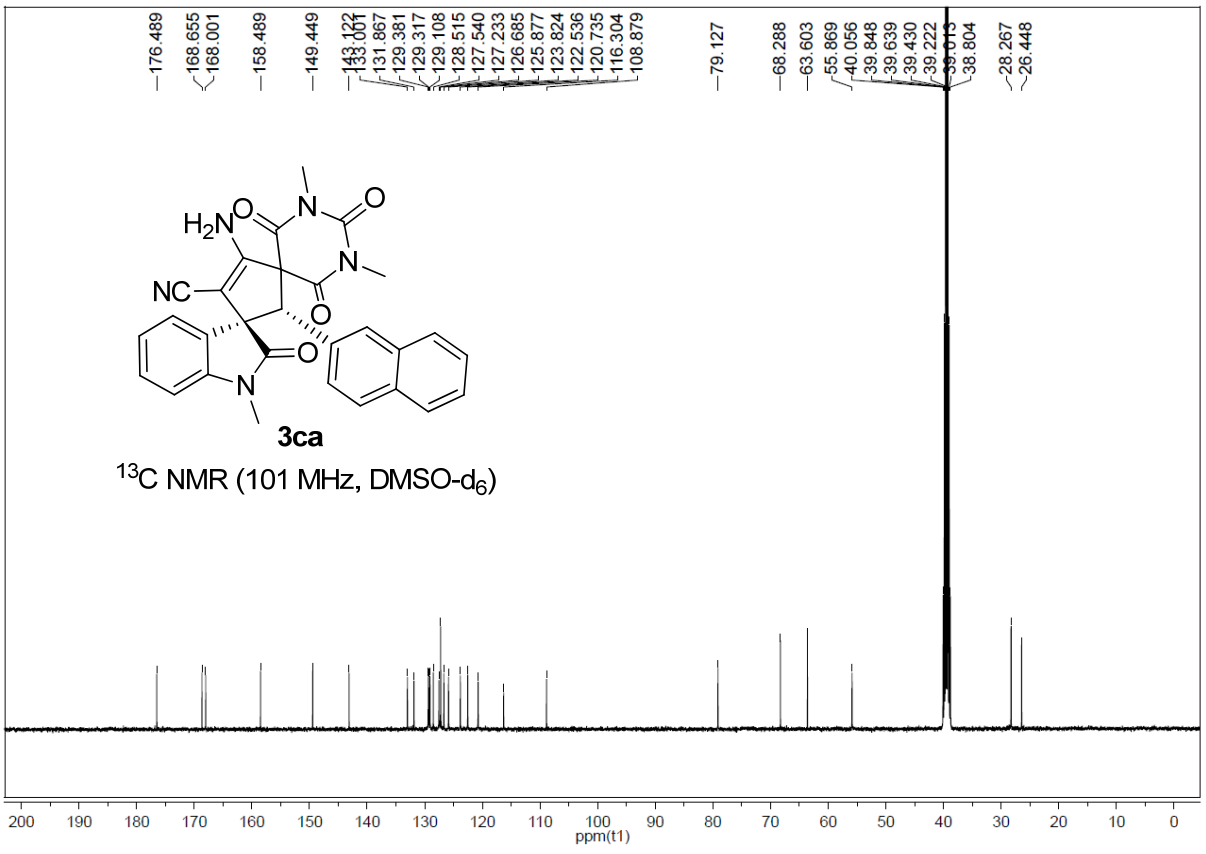
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^{13}C NMR (101 MHz, $CDCl_3$)



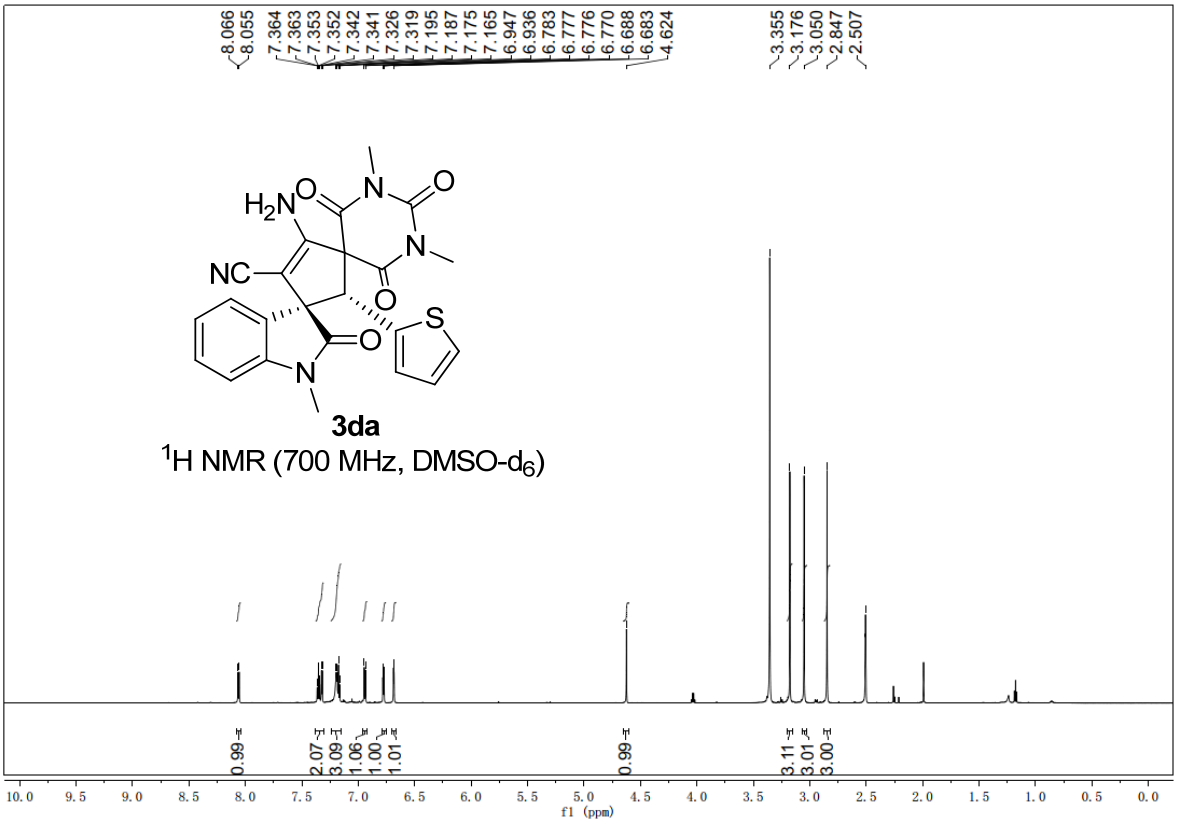
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^{1}H NMR (400 MHz, DMSO-d_6)



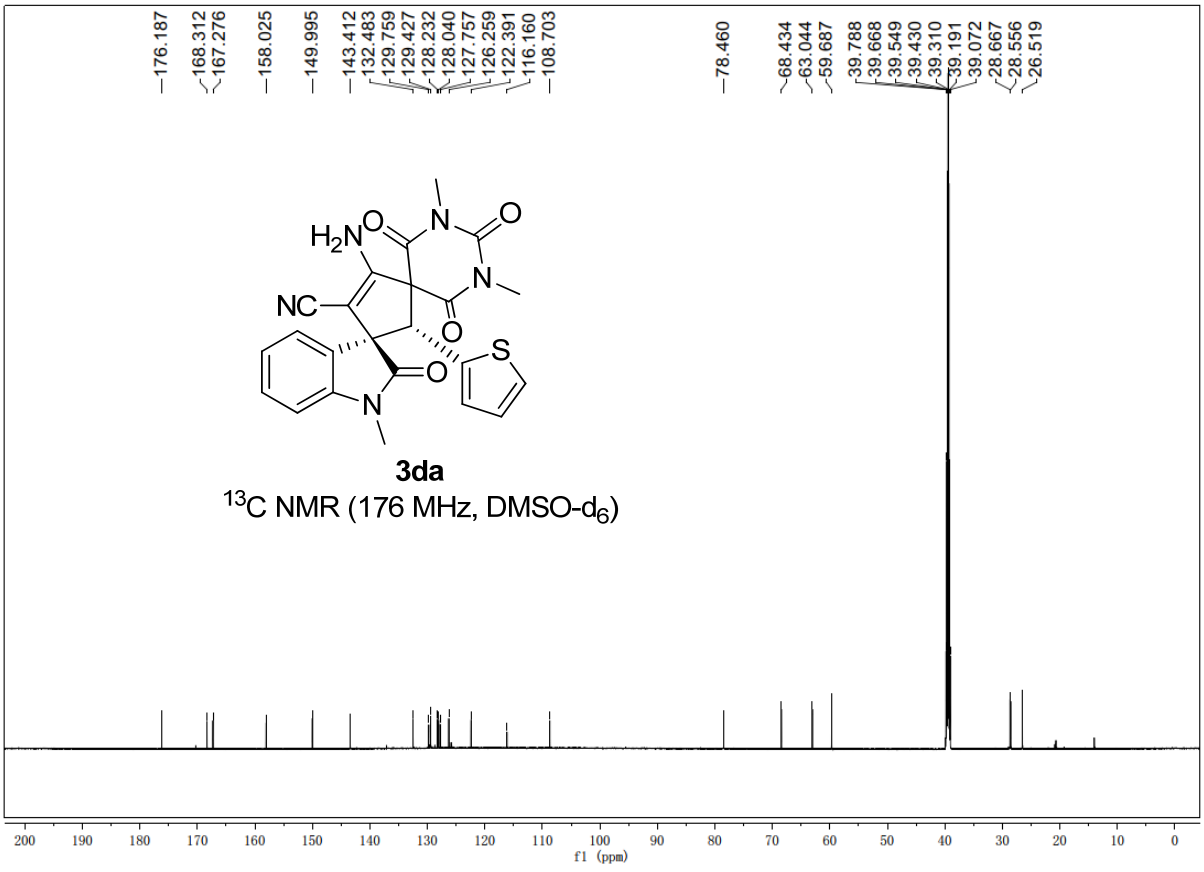
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^{13}C NMR (101 MHz, DMSO-d_6)



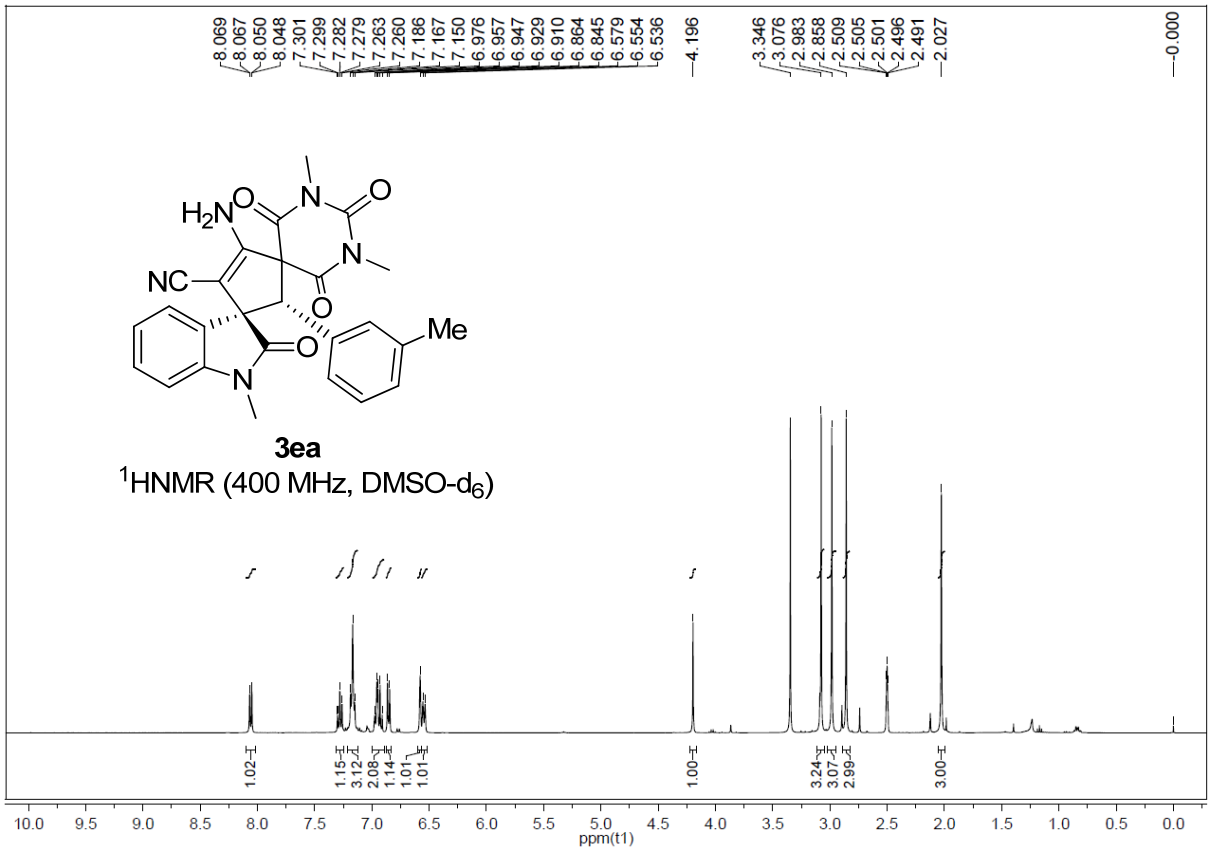
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^{1}H NMR (700 MHz, DMSO-d_6)



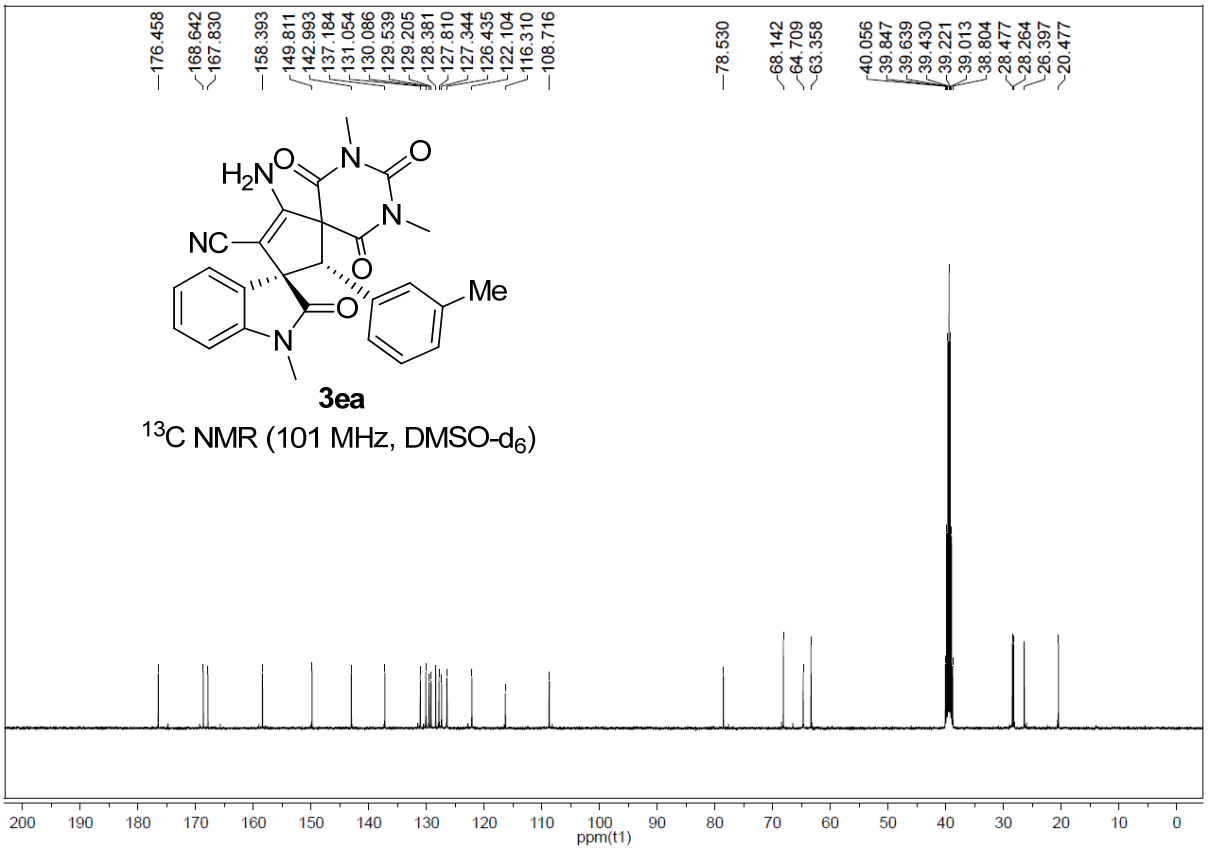
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^{13}C NMR (176 MHz, DMSO-d_6)



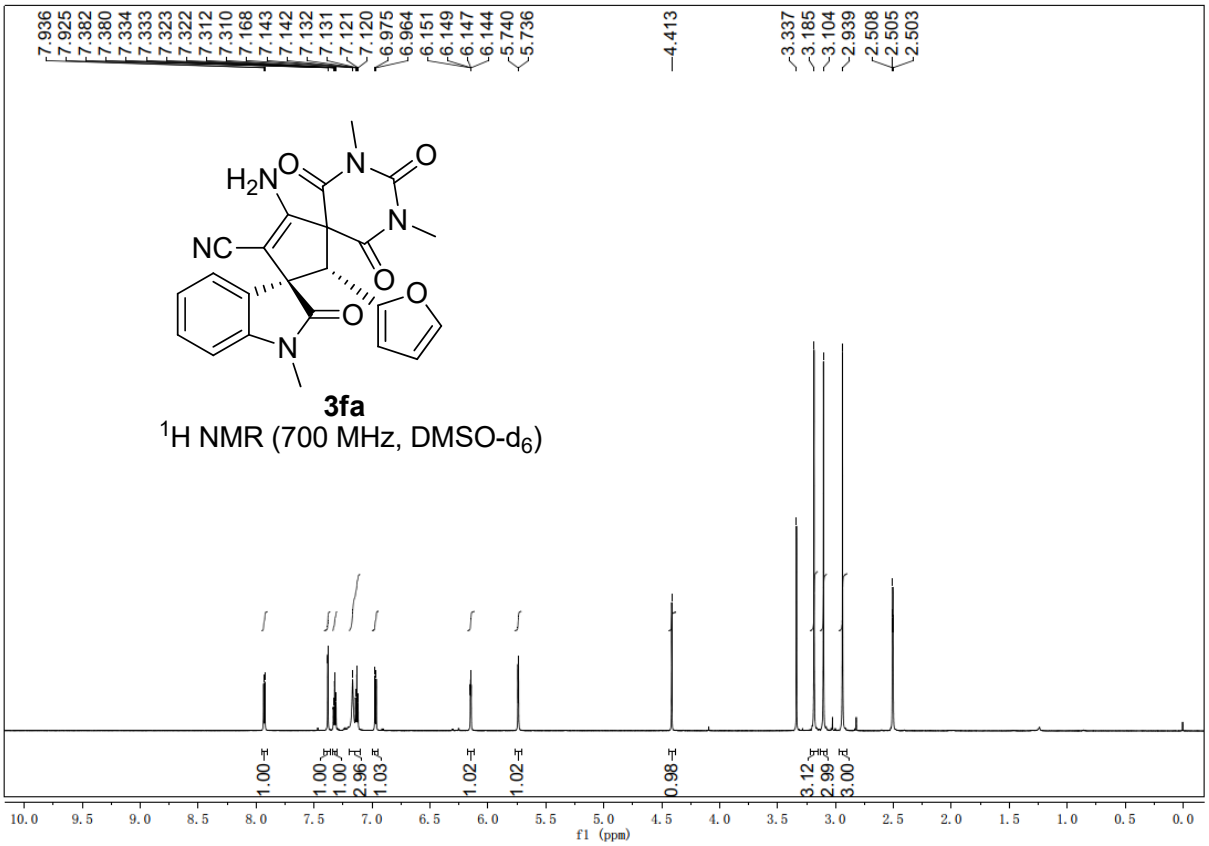
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^{1}HNMR (400 MHz, DMSO-d_6)



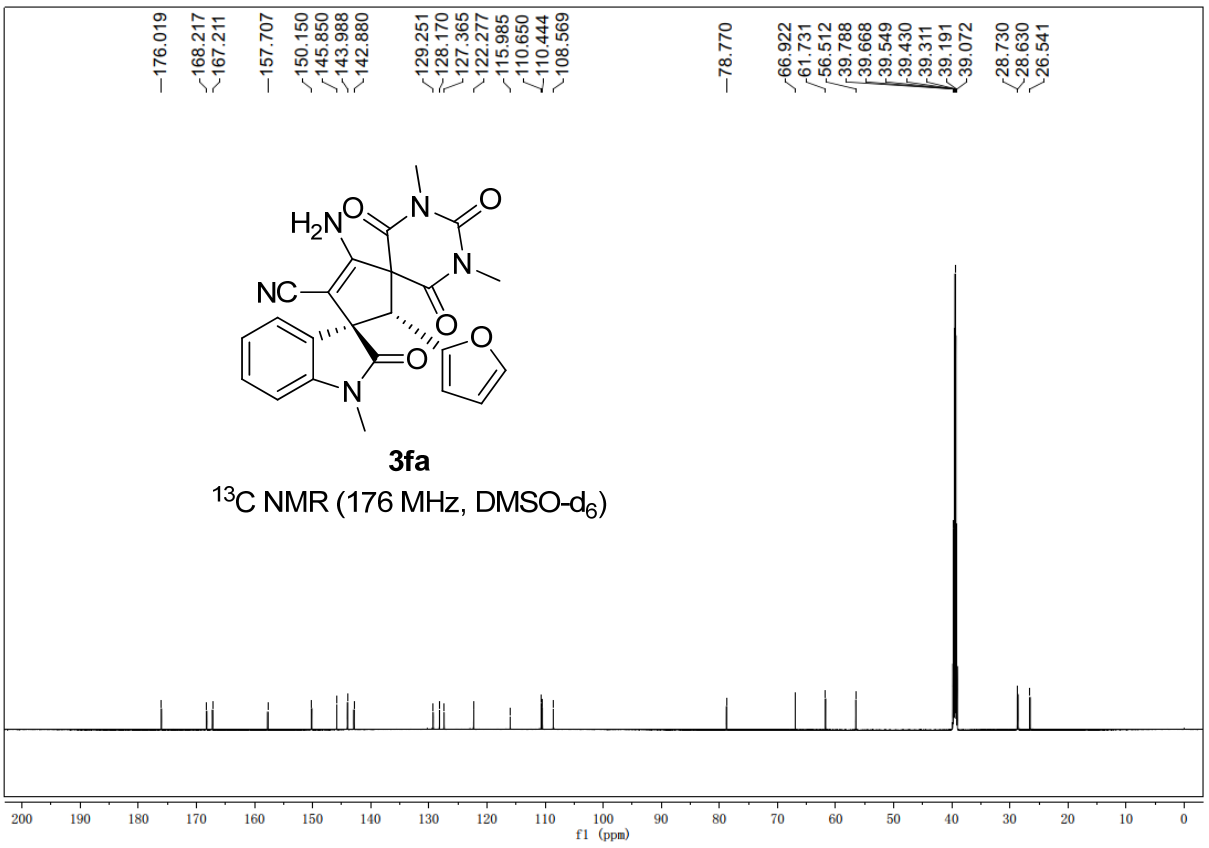
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^{13}C NMR (101 MHz, DMSO-d_6)



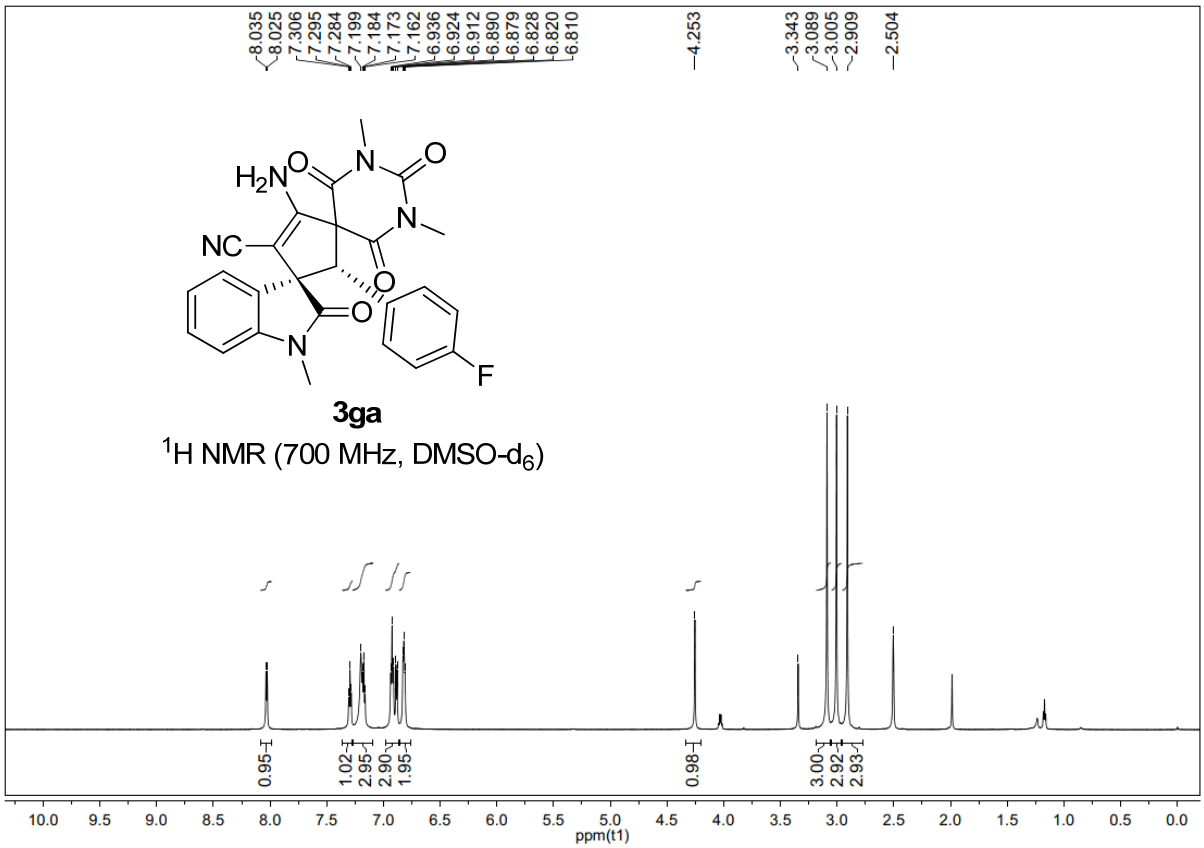
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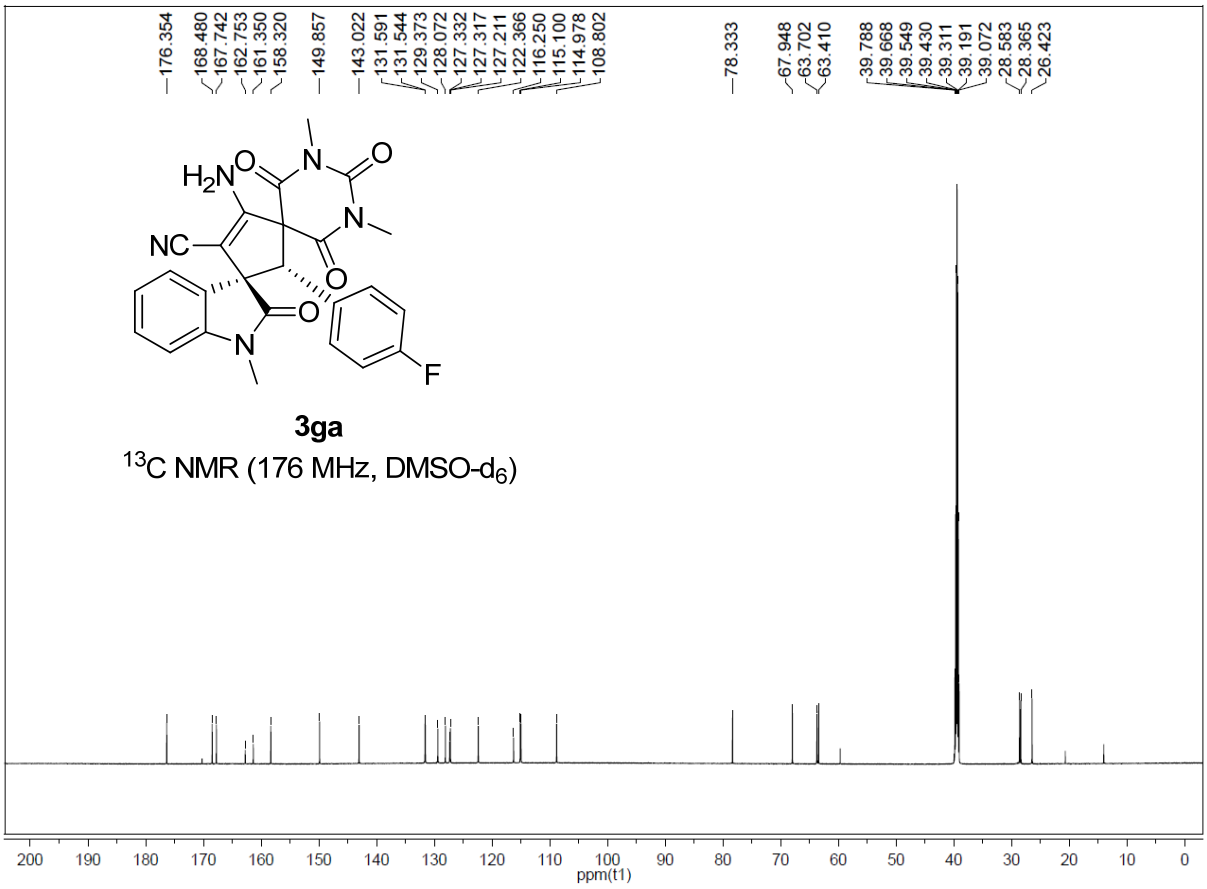
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^{13}C NMR (176 MHz, DMSO-d_6)



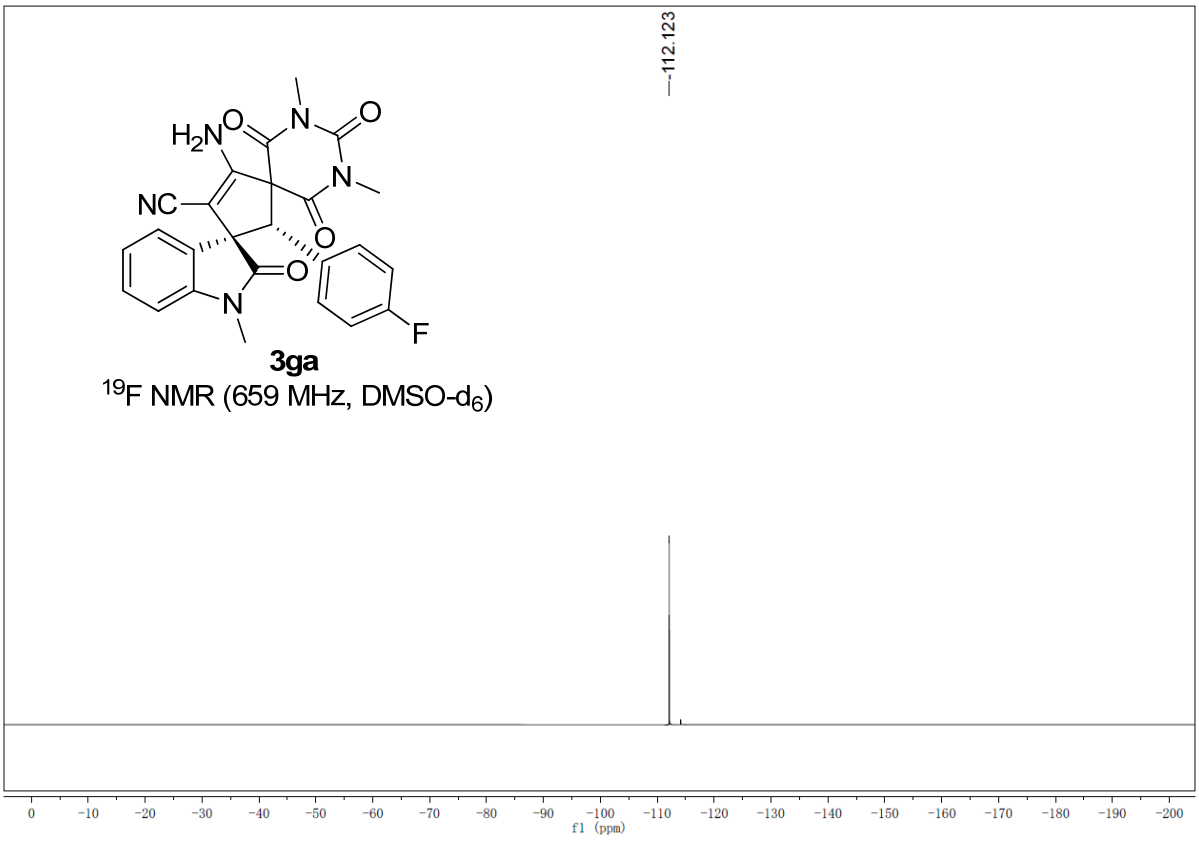
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^{1}H NMR (700 MHz, DMSO-d_6)



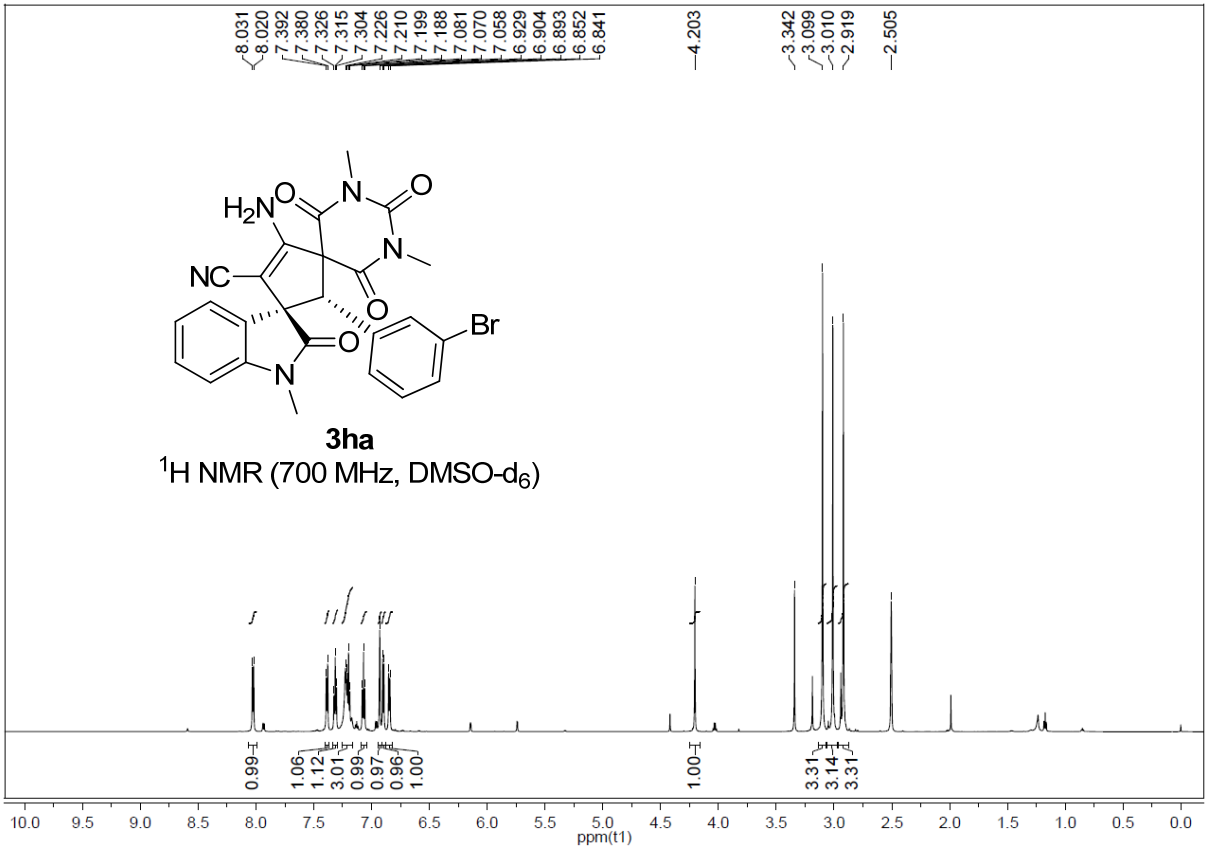
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^{13}C NMR (176 MHz, DMSO-d_6)



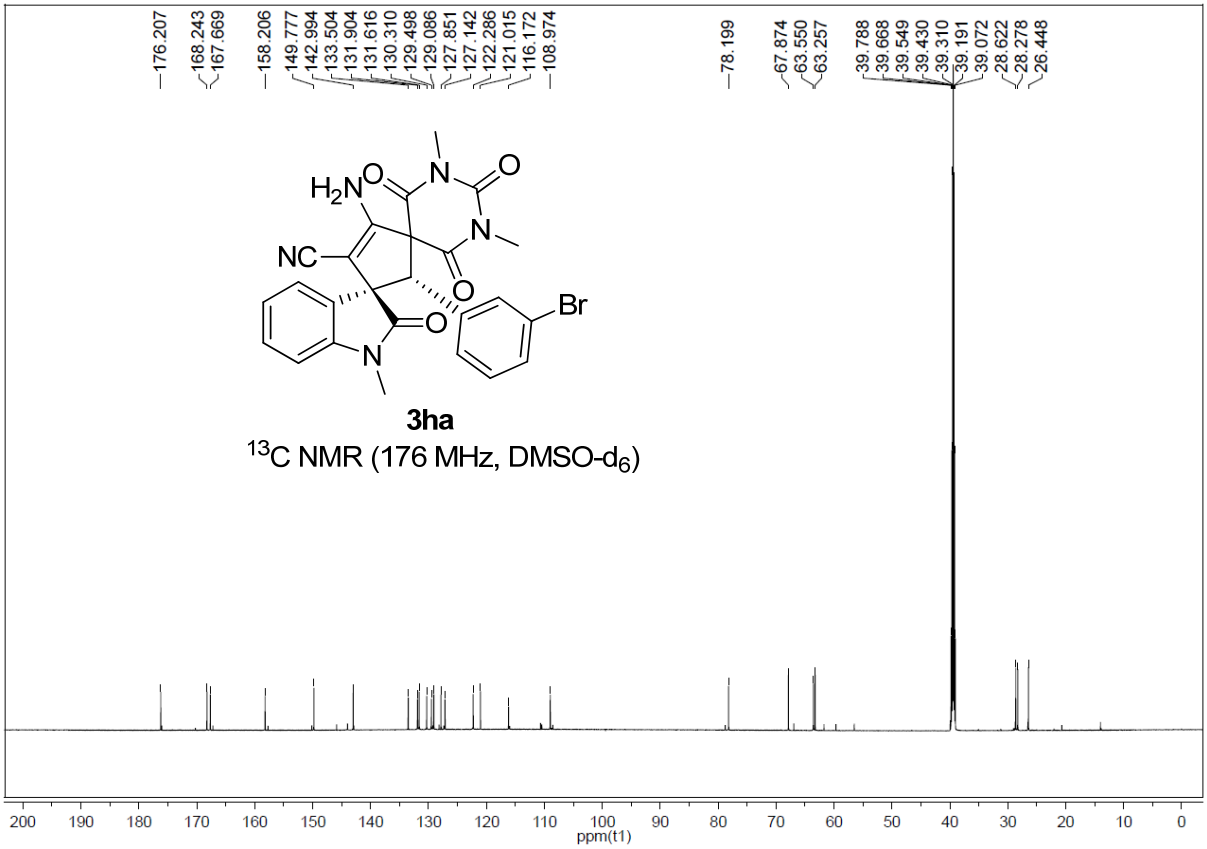
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^{19}F NMR (659 MHz, DMSO-d_6)



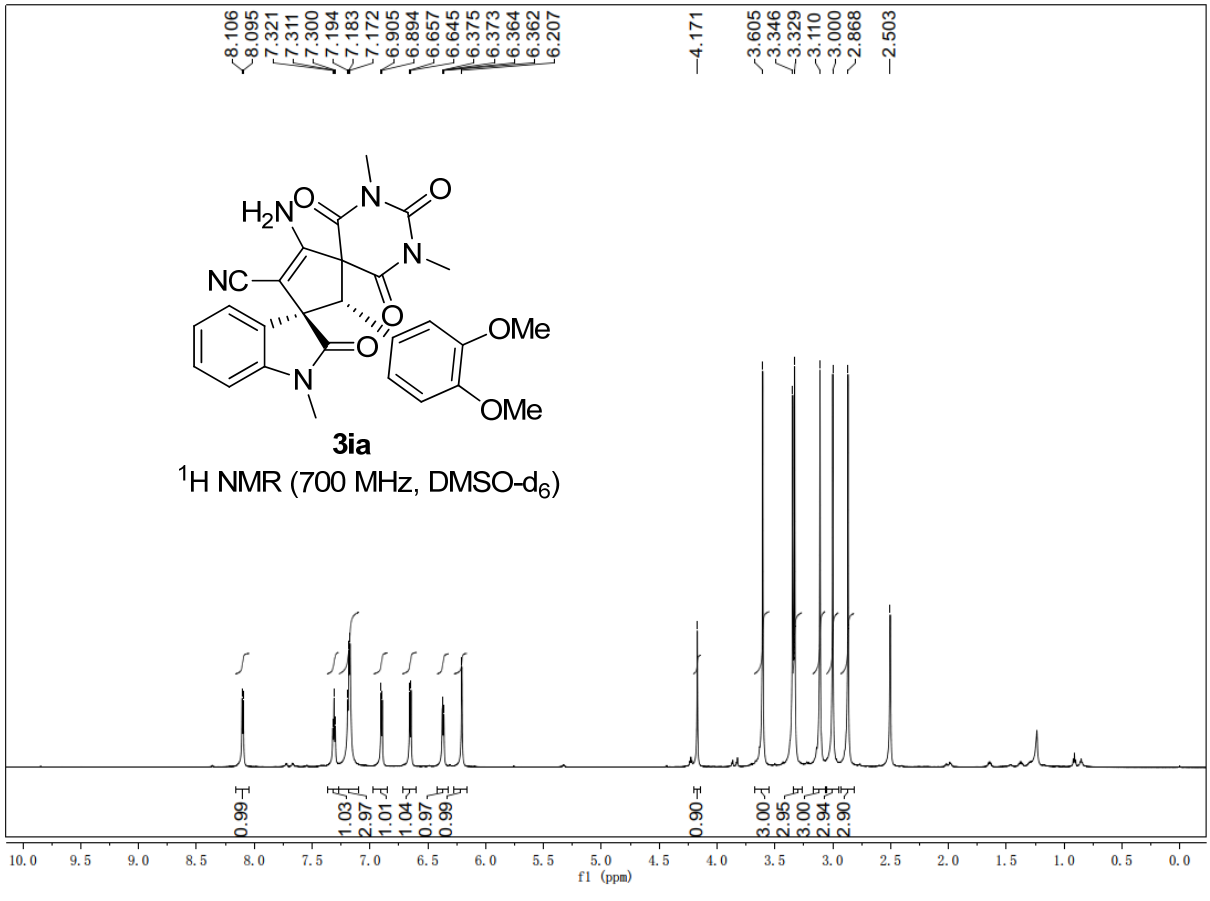
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^{1}H NMR (700 MHz, DMSO-d_6)



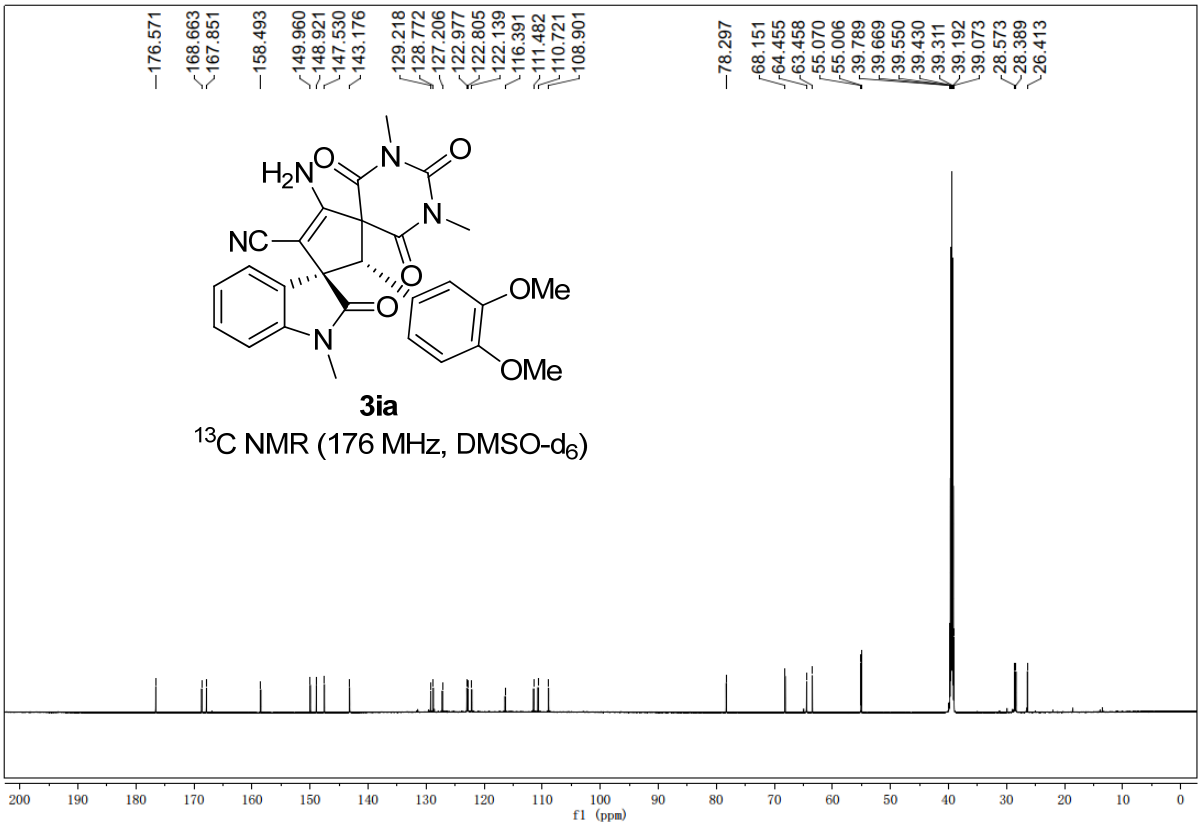
3ha

^{13}C NMR (176 MHz, DMSO-d_6)



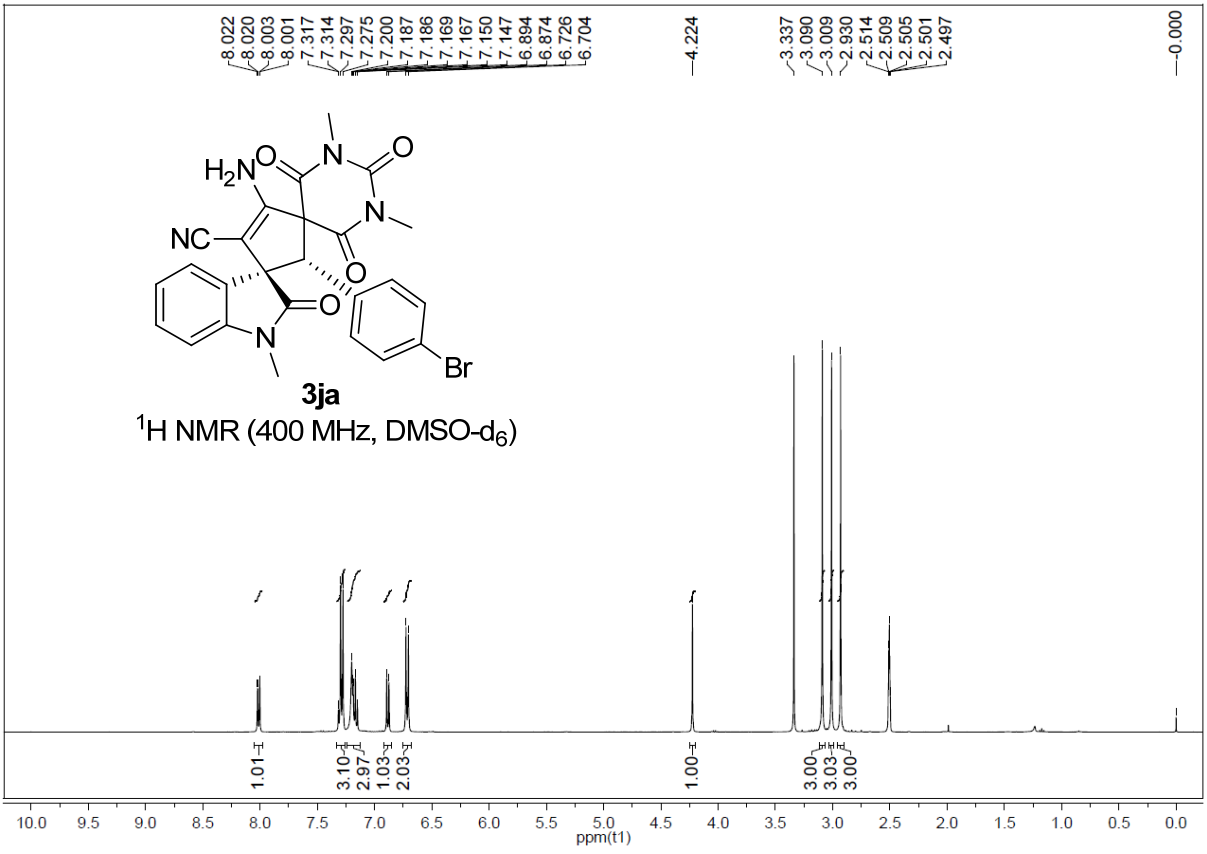
3ia

^{1}H NMR (700 MHz, DMSO-d_6)



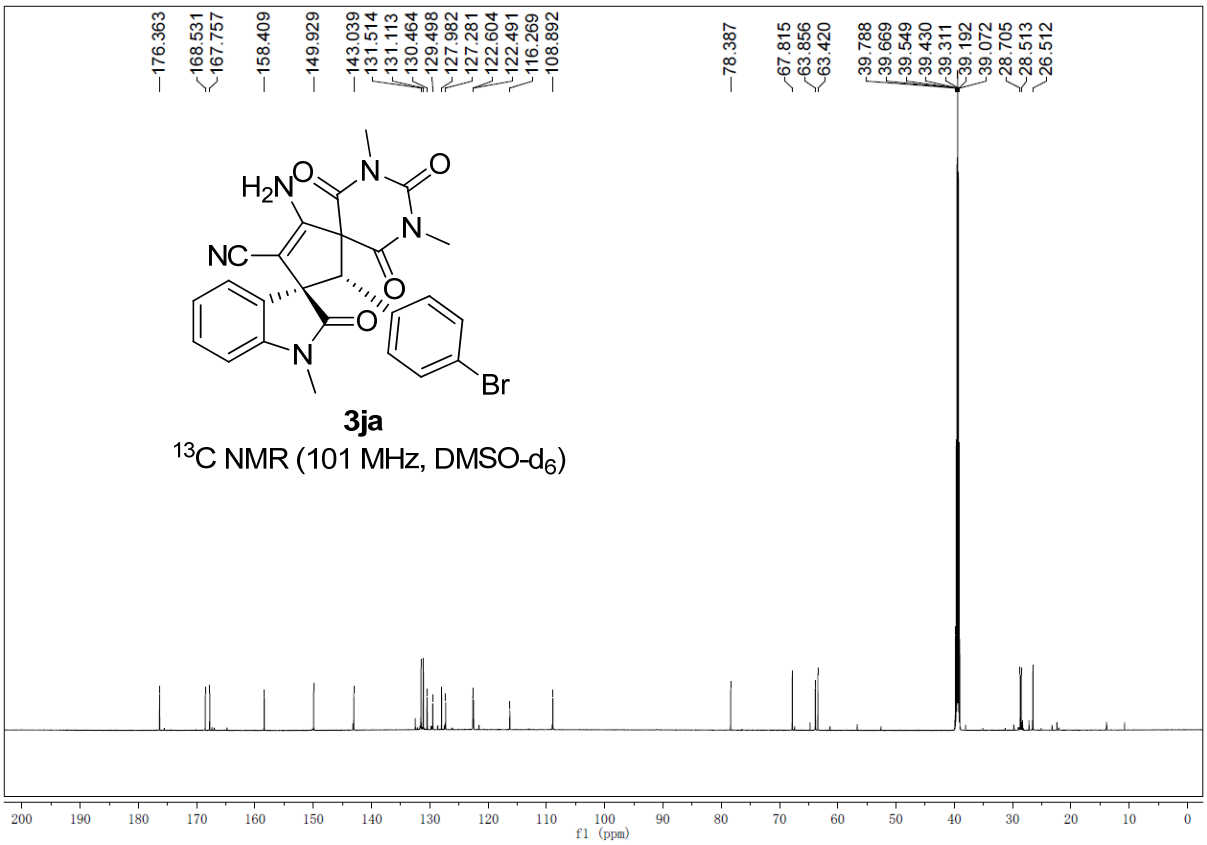
3ia

^{13}C NMR (176 MHz, DMSO-d_6)



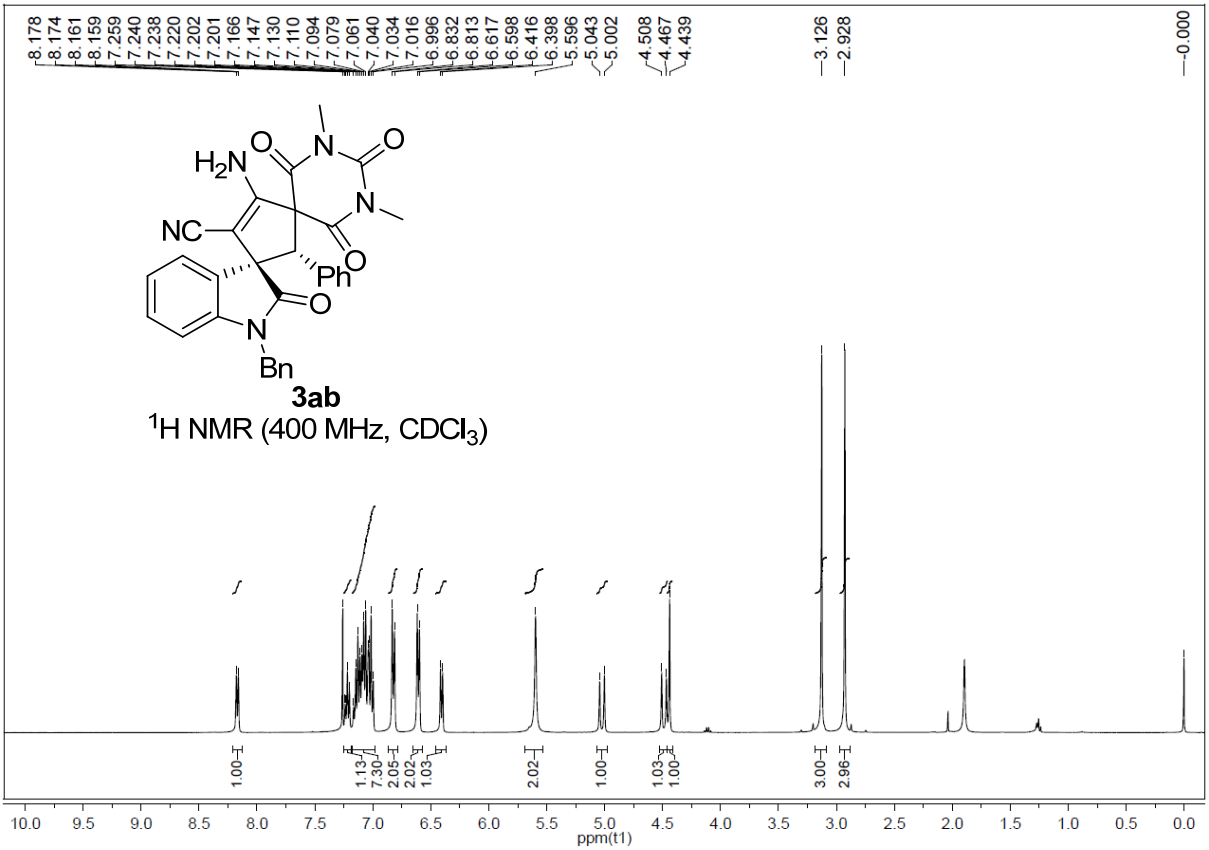
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^{1}H NMR (400 MHz, DMSO-d_6)



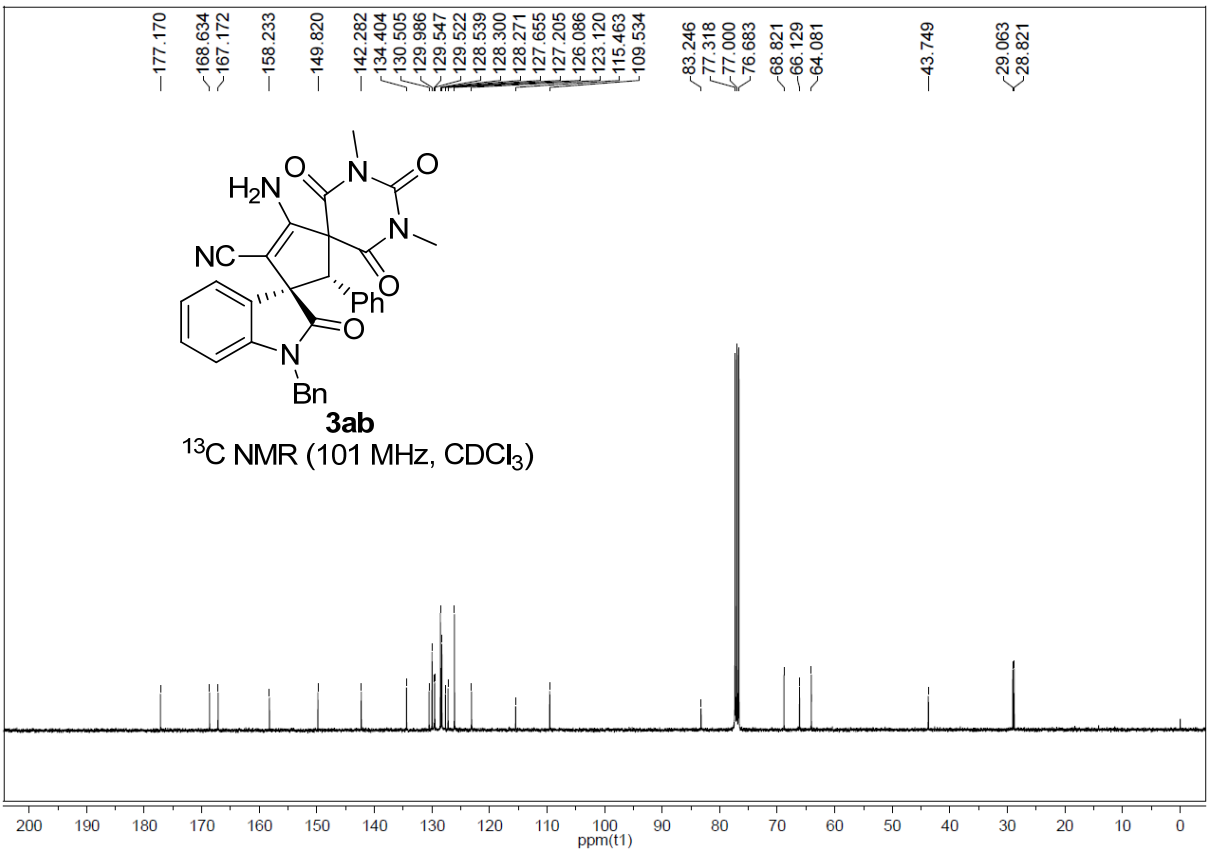
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^{13}C NMR (101 MHz, DMSO-d_6)



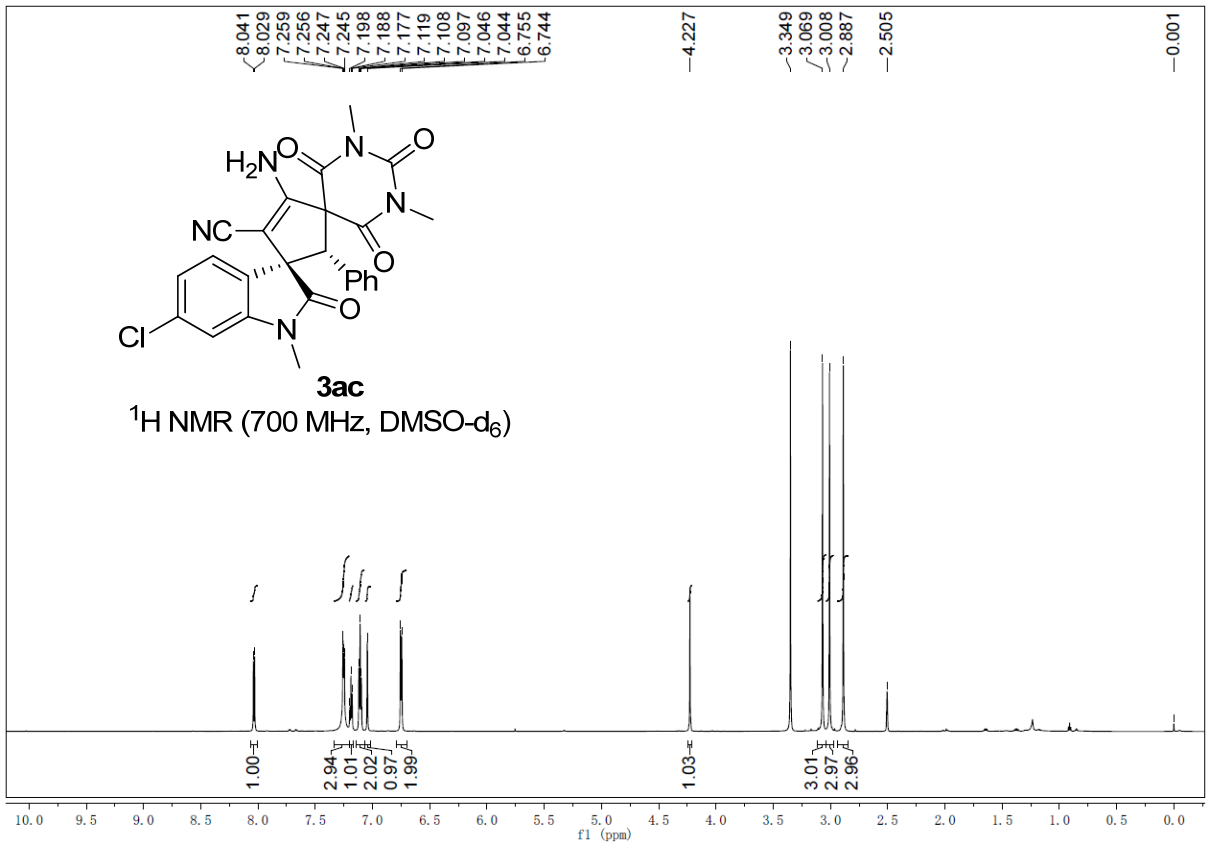
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^{1}H NMR (400 MHz, $CDCl_3$)



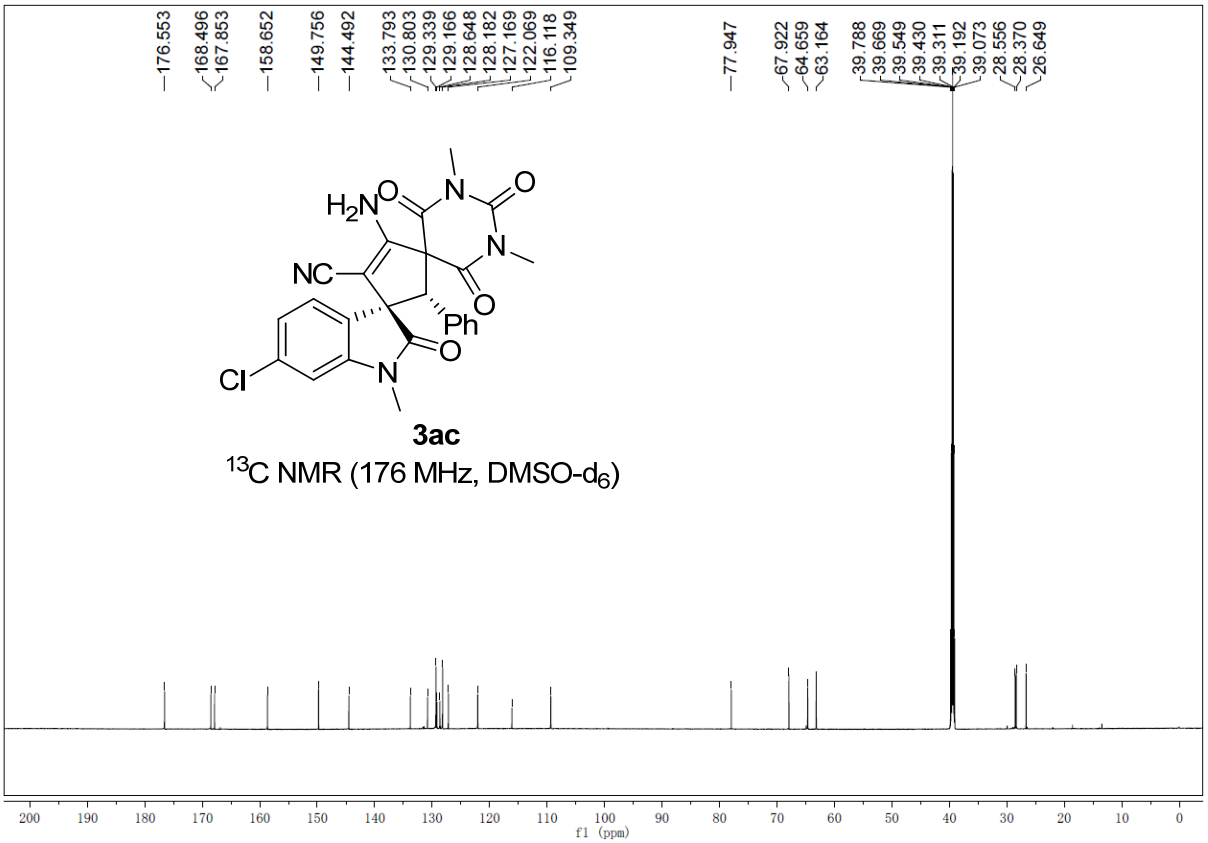
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^{13}C NMR (101 MHz, $CDCl_3$)



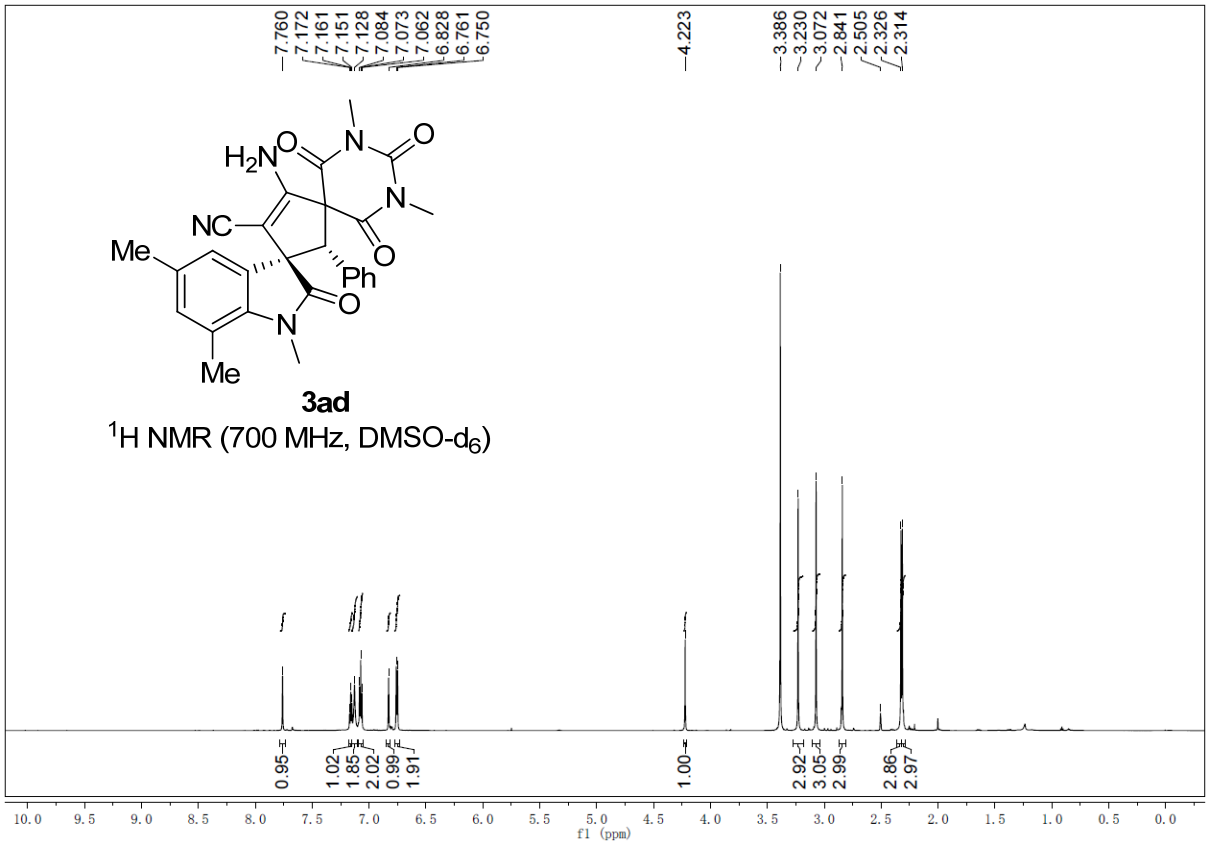
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^{1}H NMR (700 MHz, DMSO-d_6)



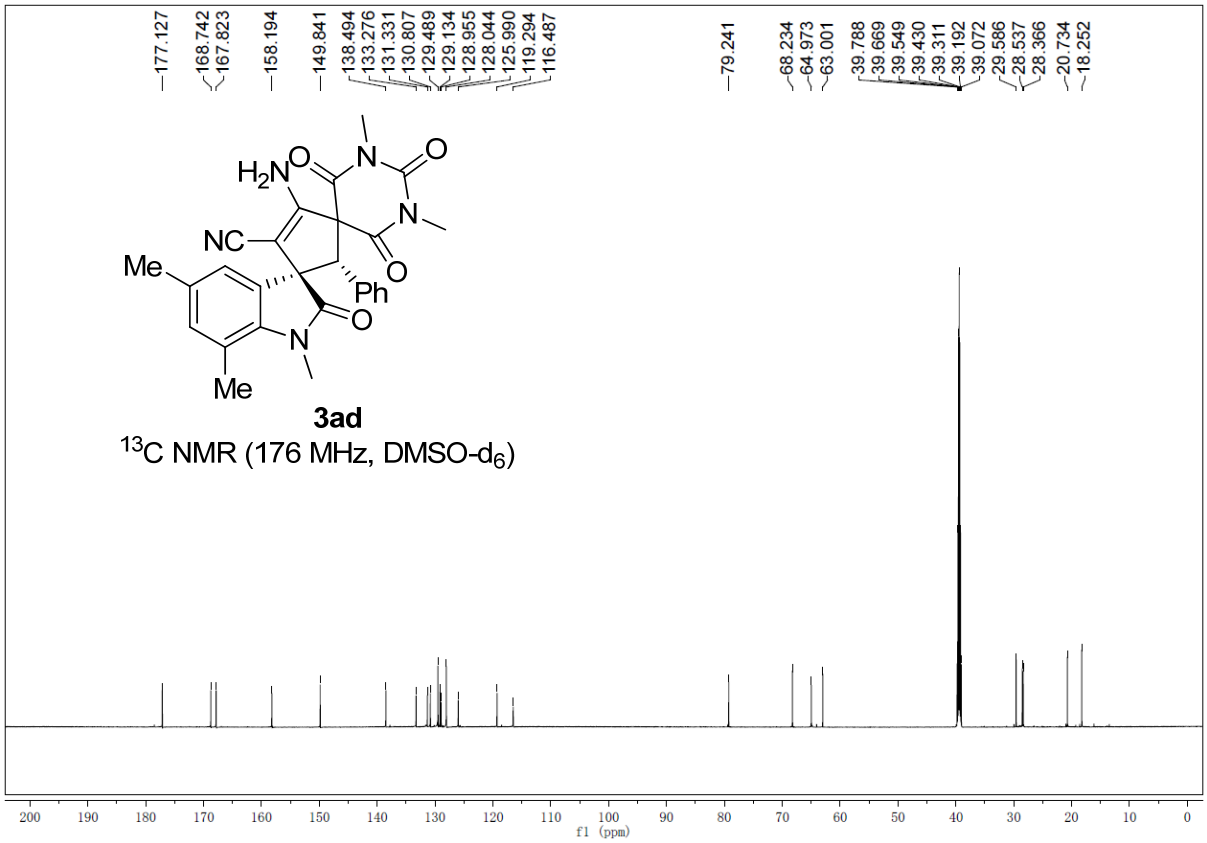
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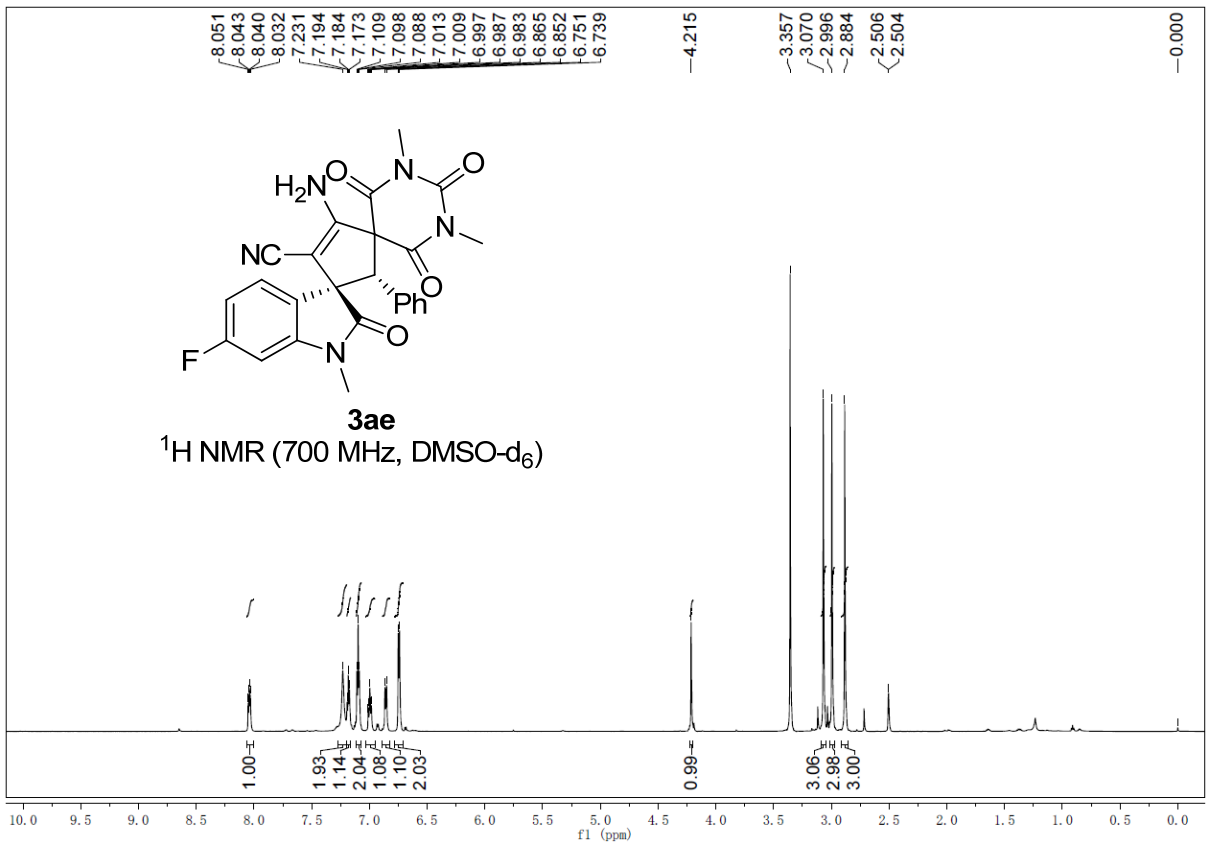
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^{1}H NMR (700 MHz, DMSO-d_6)



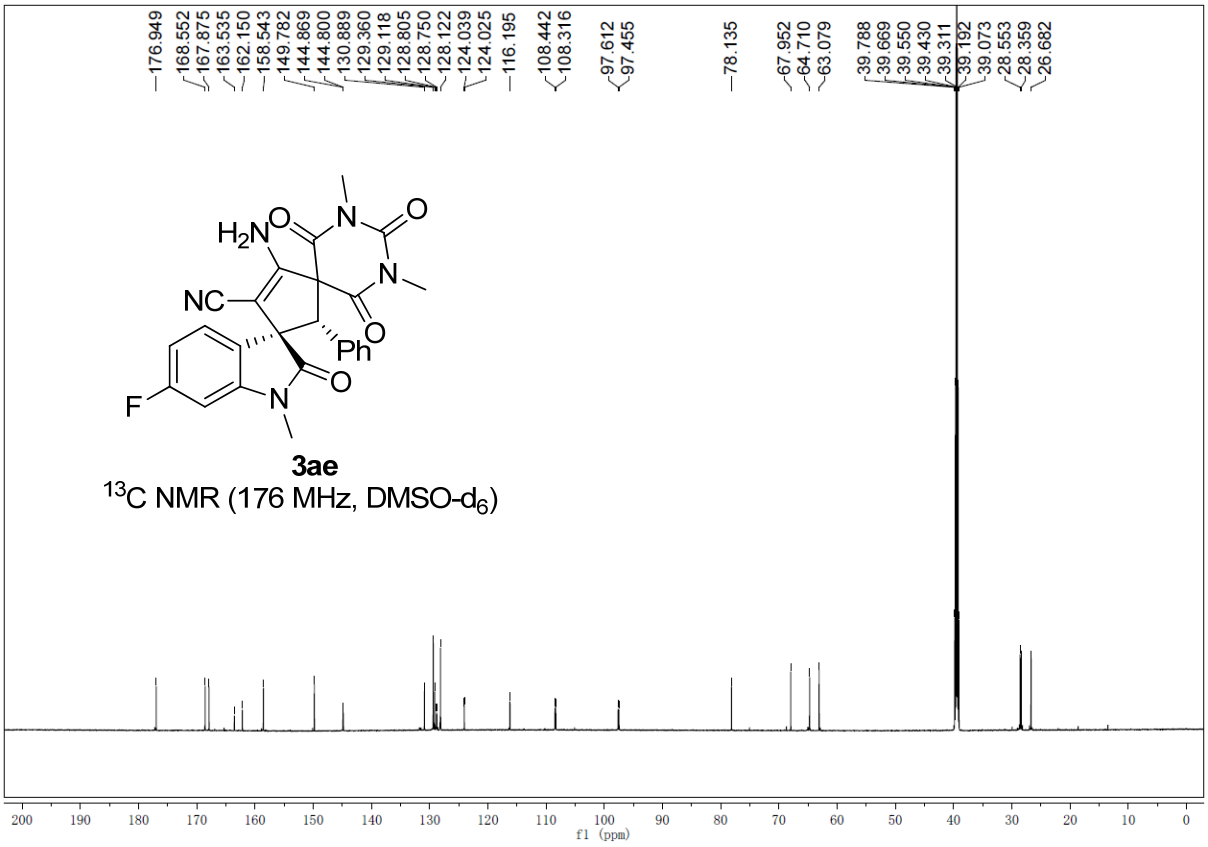
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^{13}C NMR (176 MHz, DMSO-d_6)



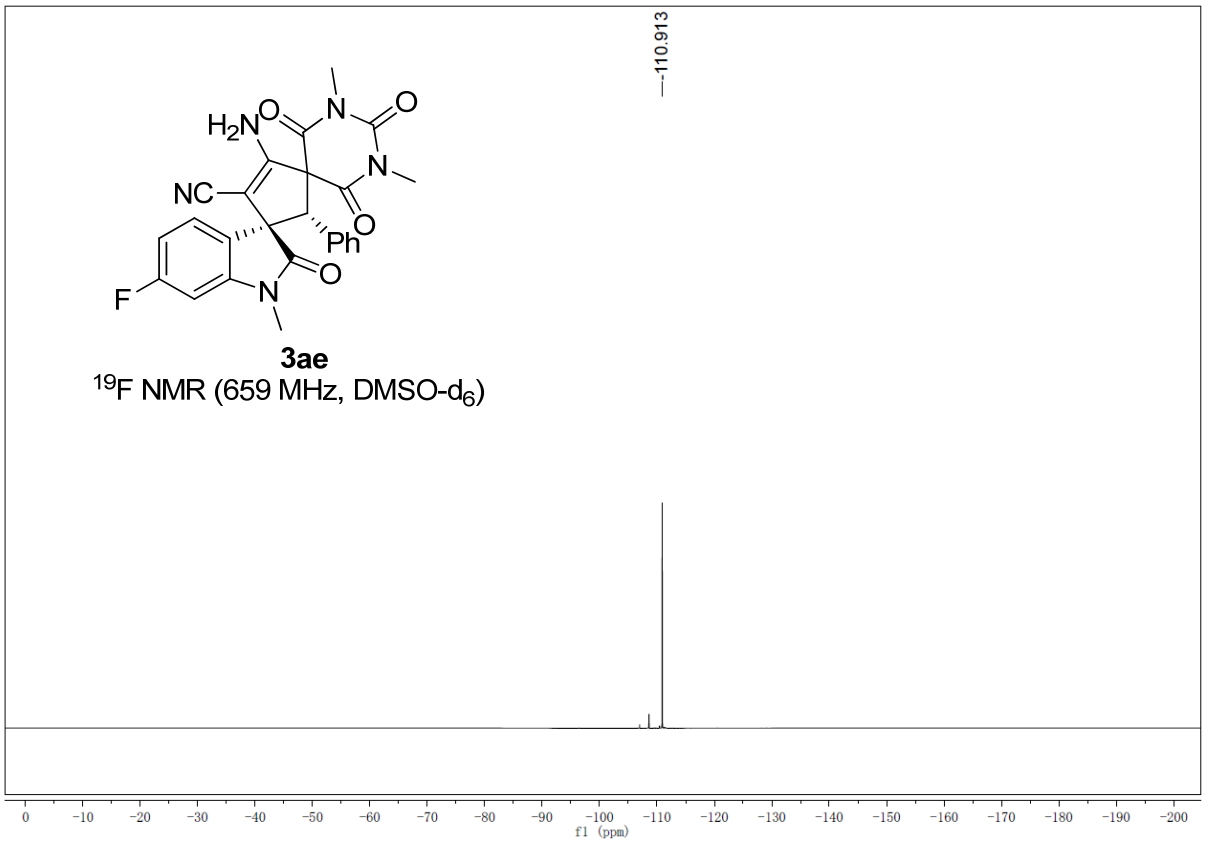
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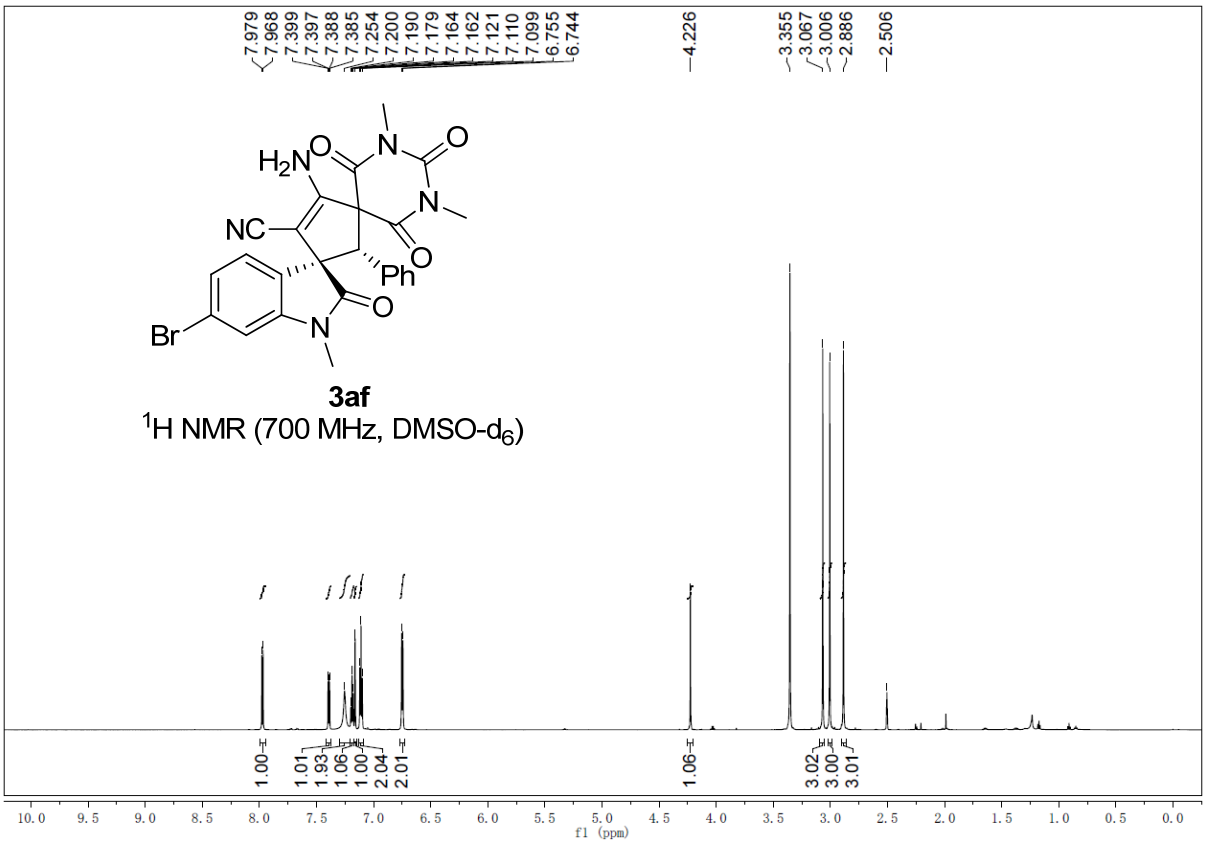
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^{13}C NMR (176 MHz, DMSO-d_6)



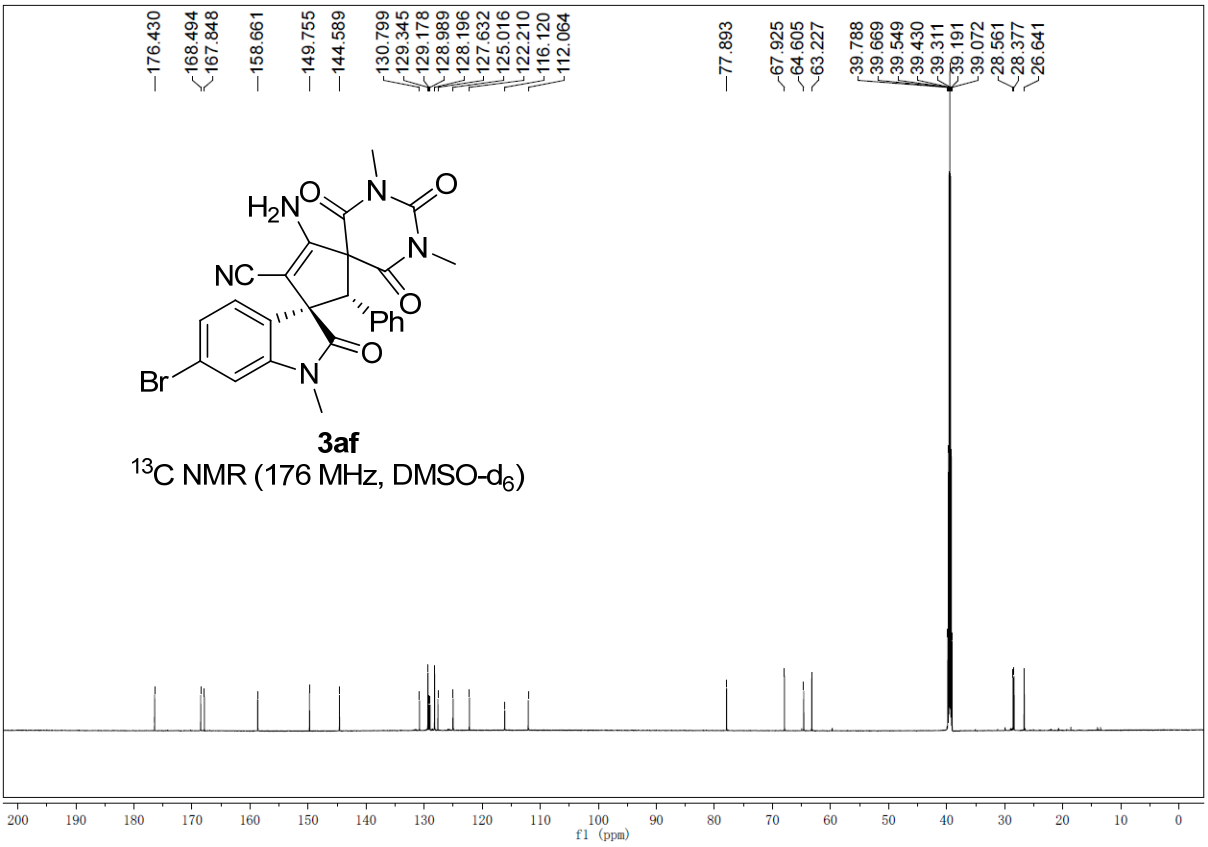
3ae

^{19}F NMR (659 MHz, DMSO-d_6)



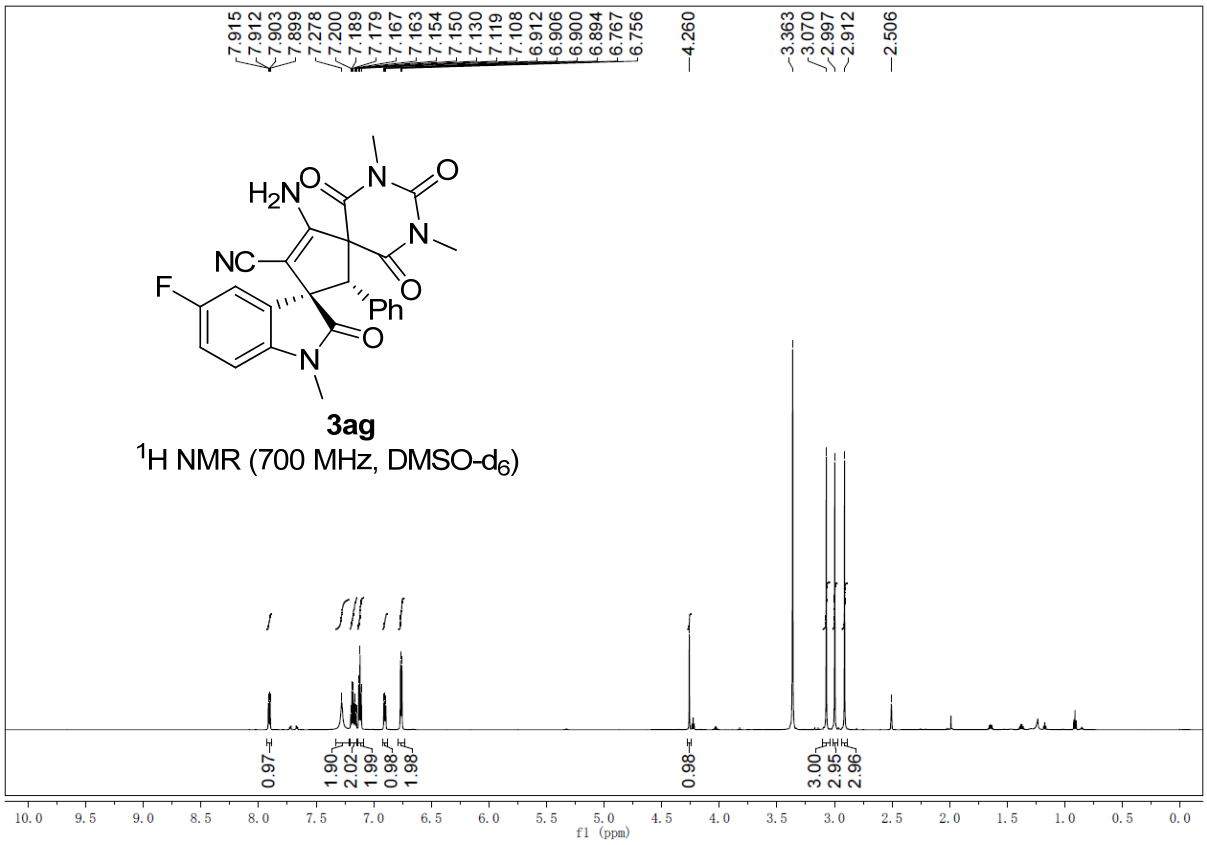
3af

^{1}H NMR (700 MHz, DMSO-d_6)



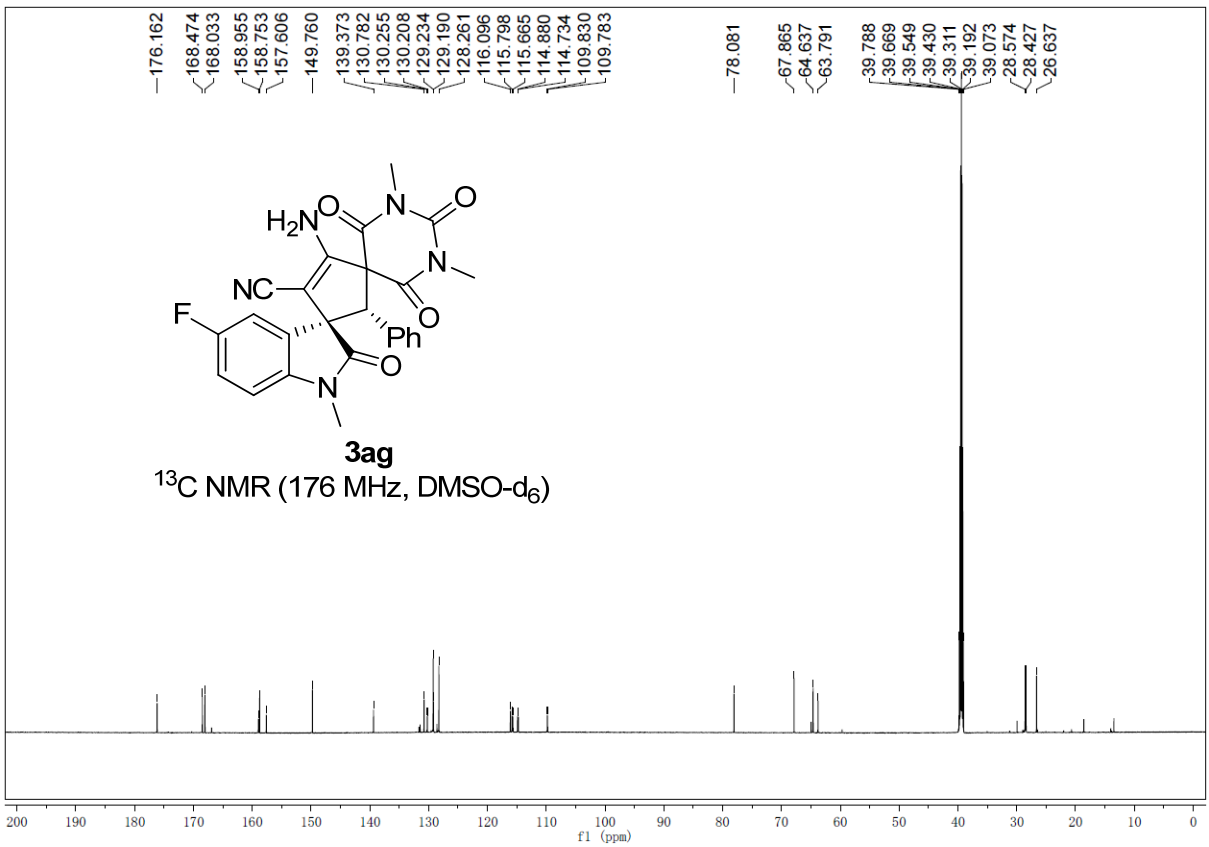
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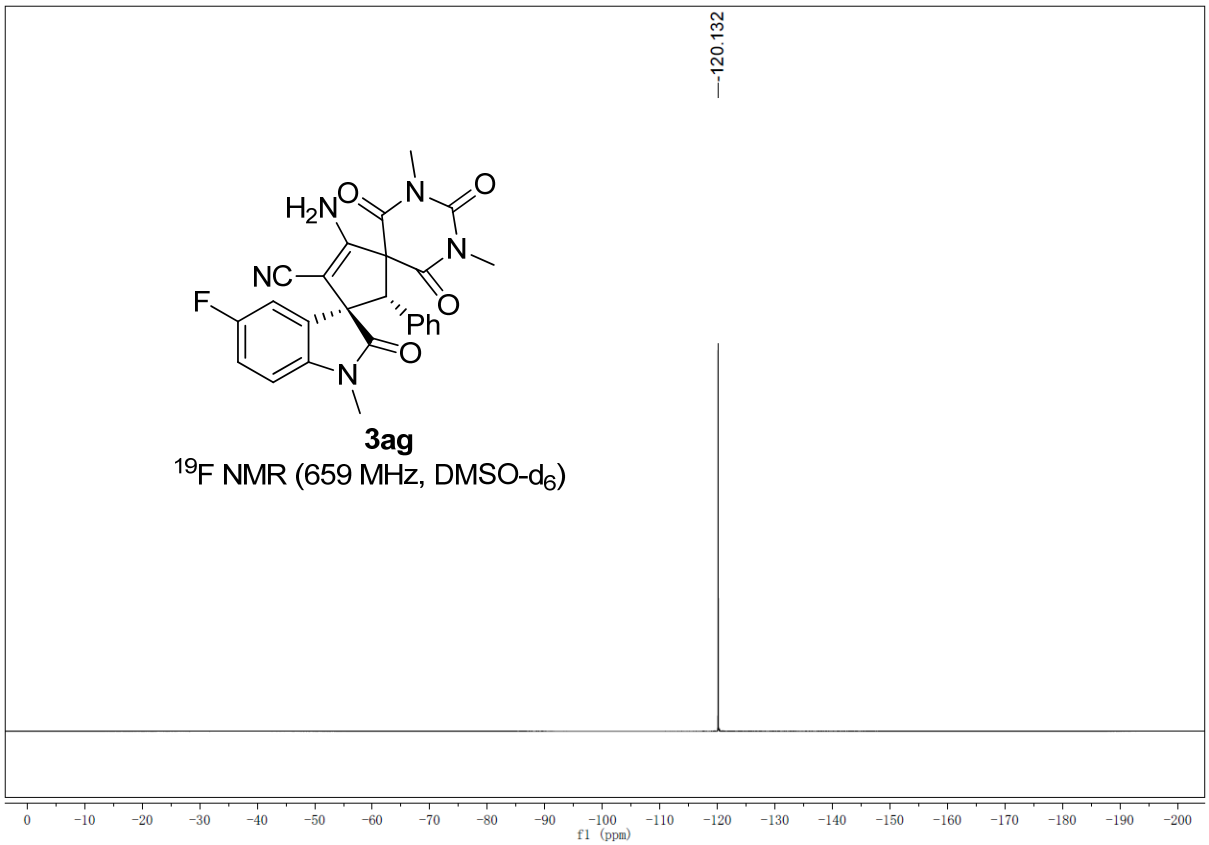
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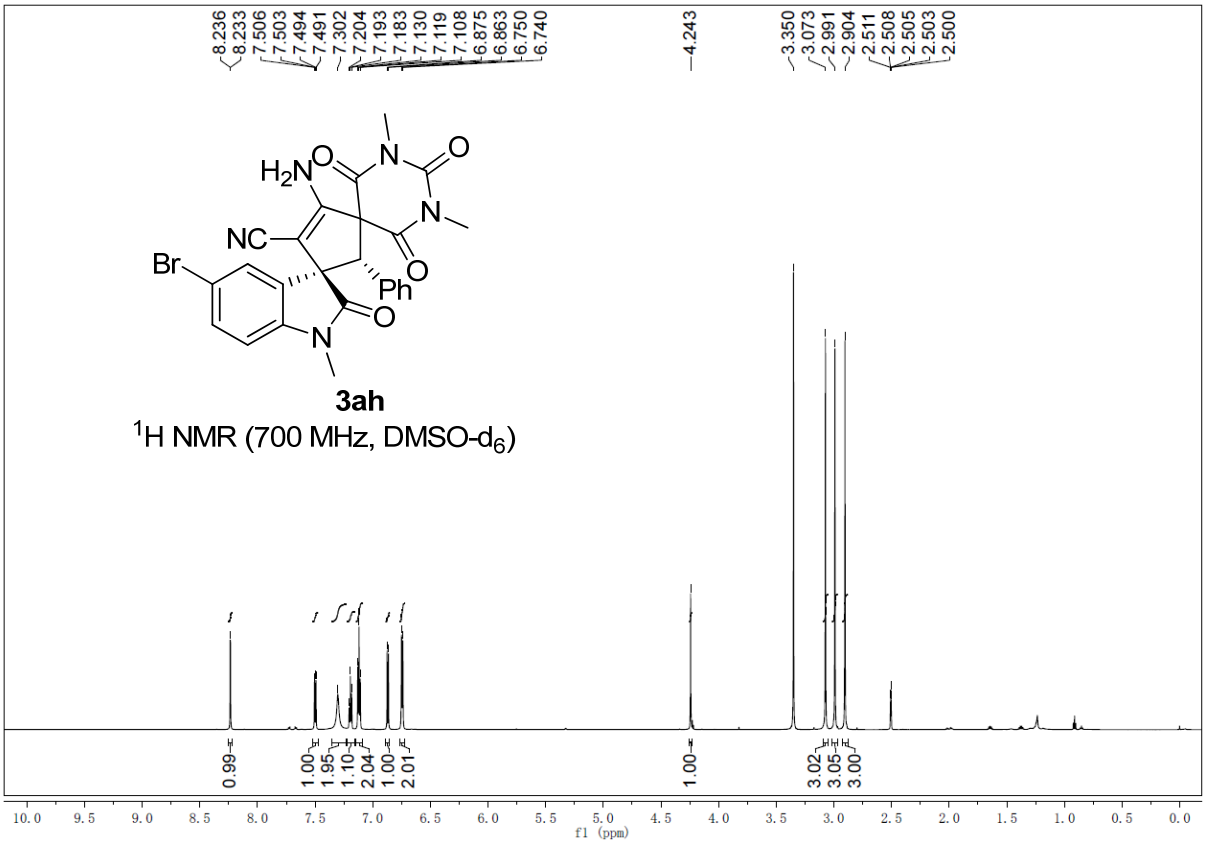
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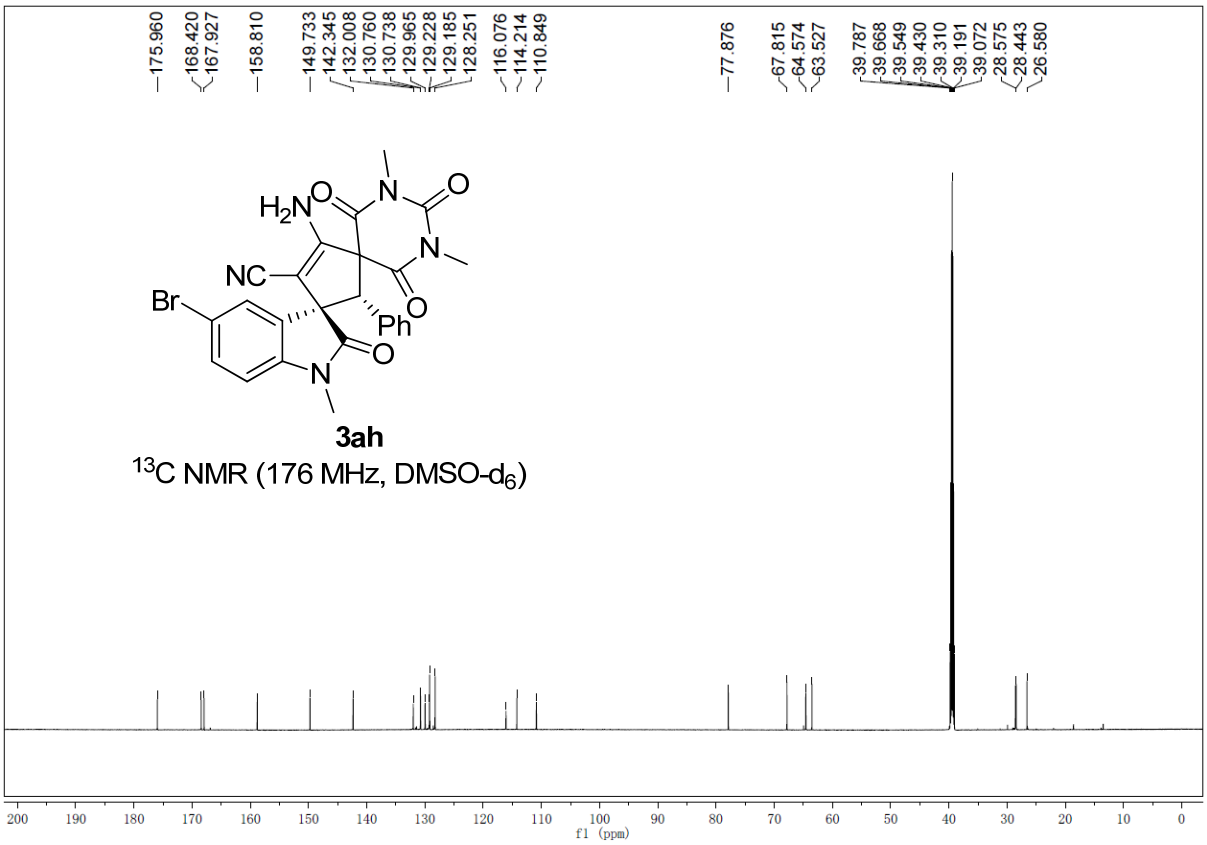
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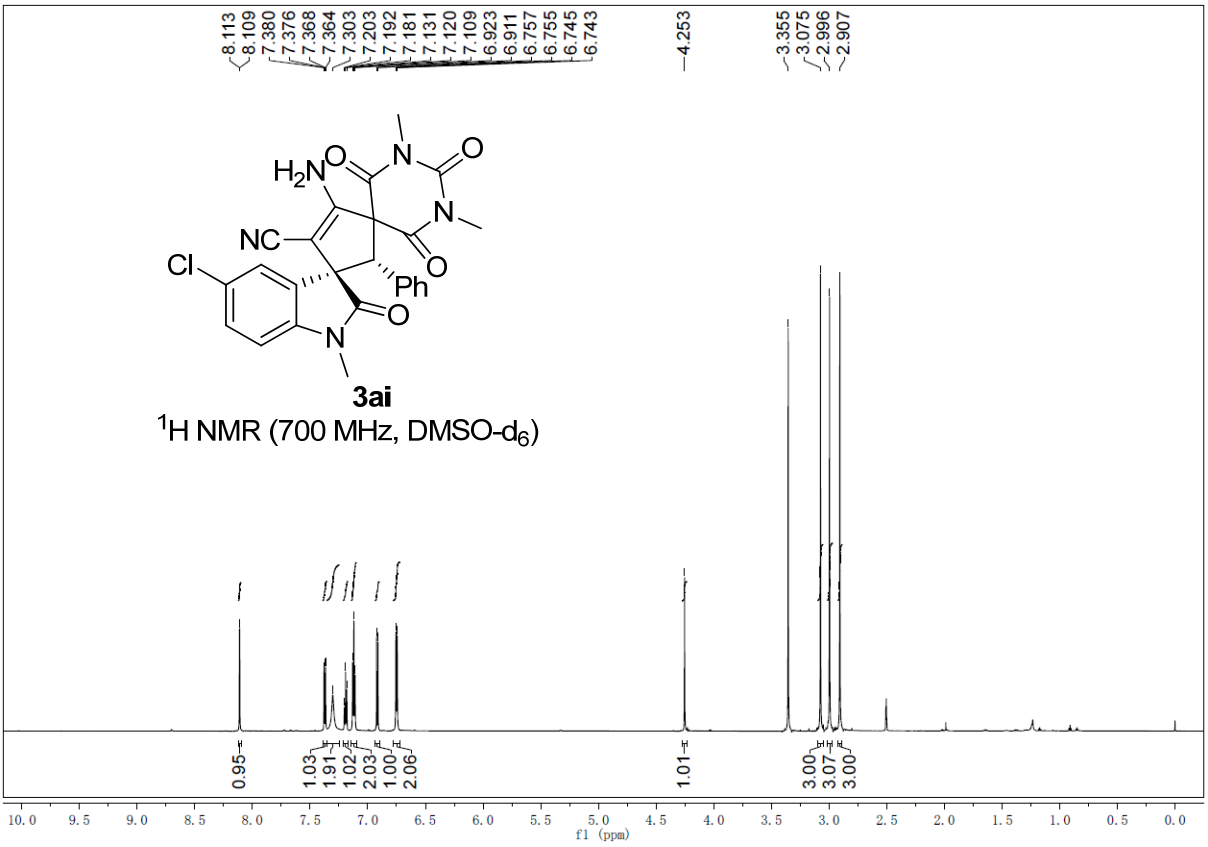
3ah

^{1}H NMR (700 MHz, DMSO-d_6)



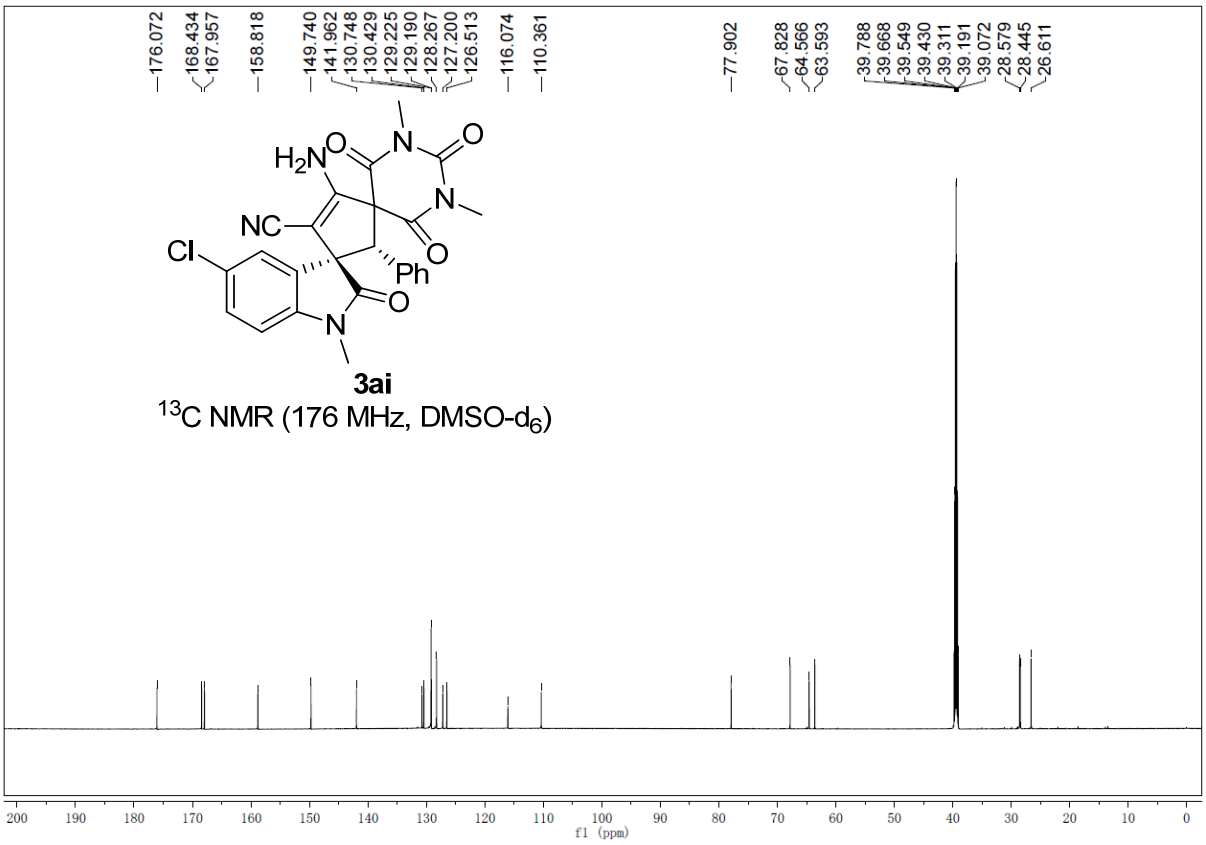
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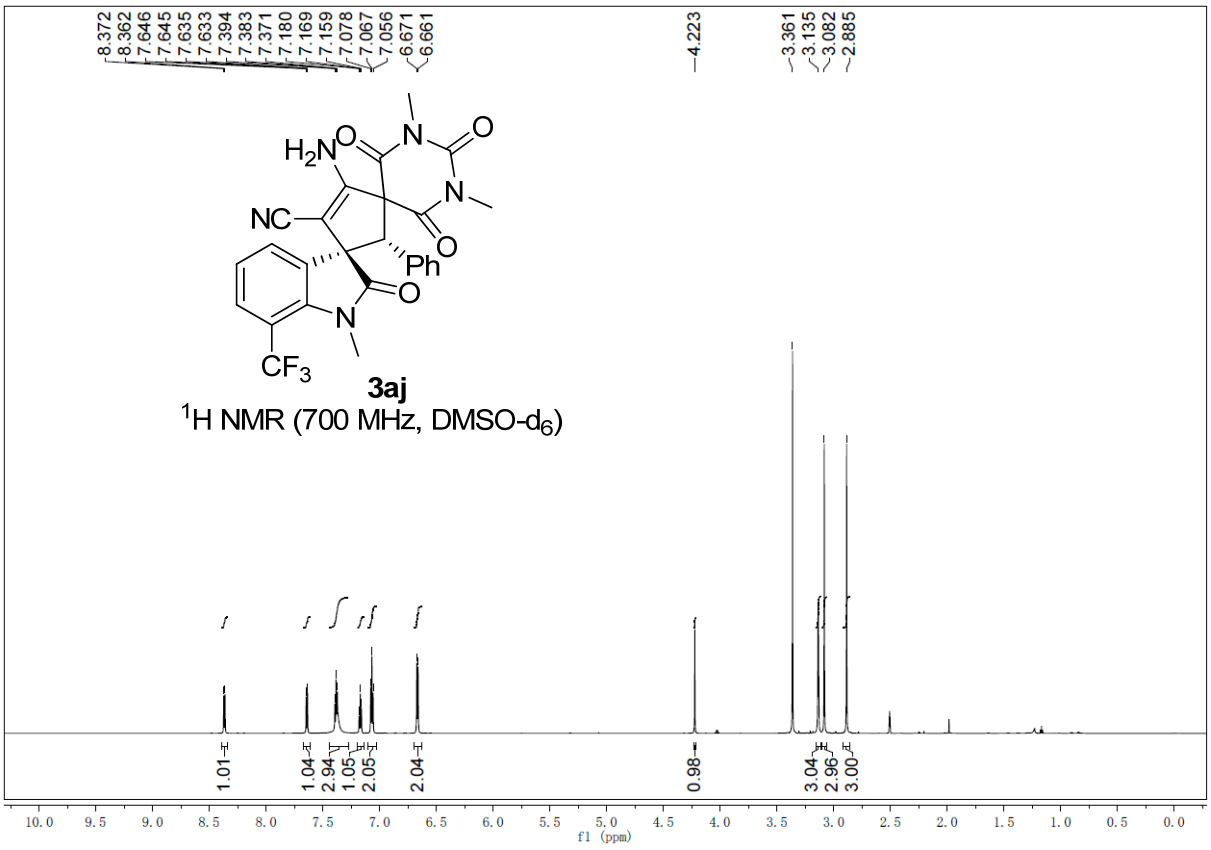
^{13}C NMR (176 MHz, DMSO-d_6)

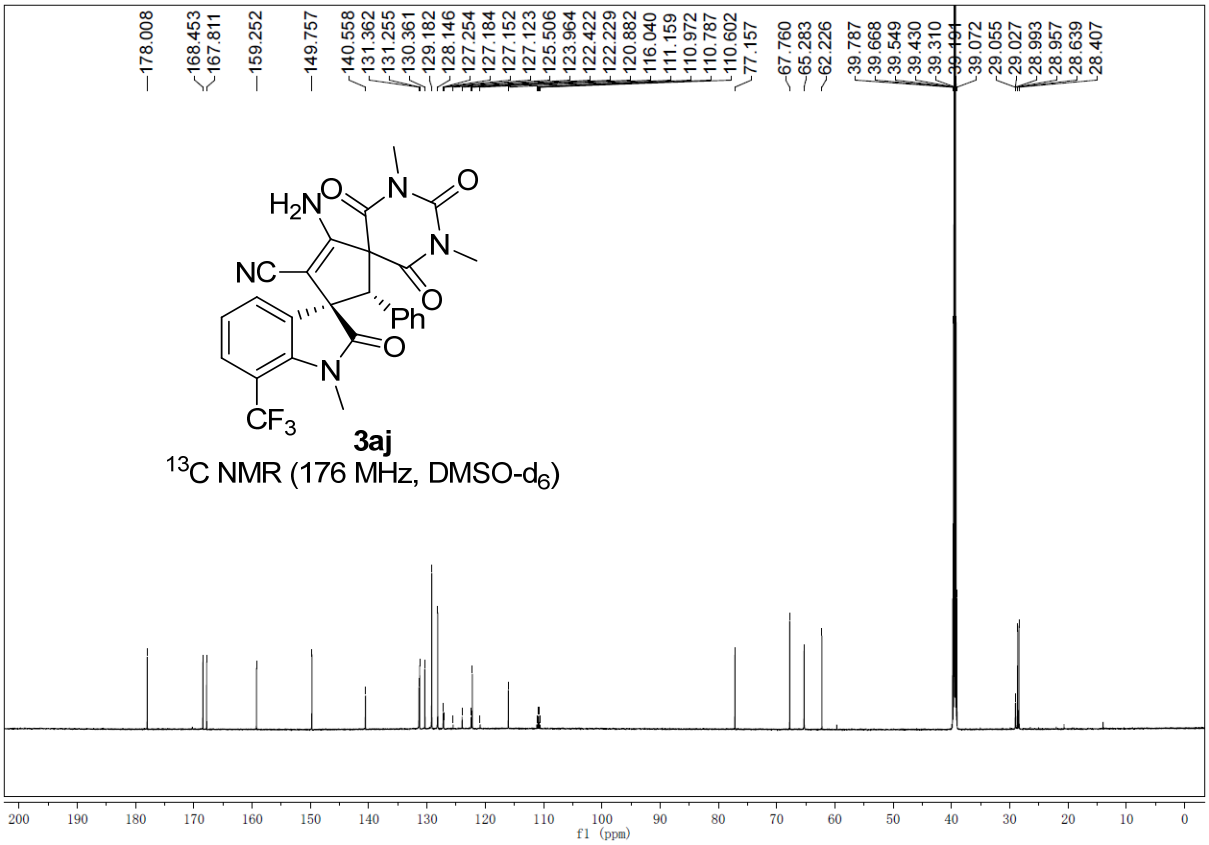


3ai

^{1}H NMR (700 MHz, DMSO-d_6)

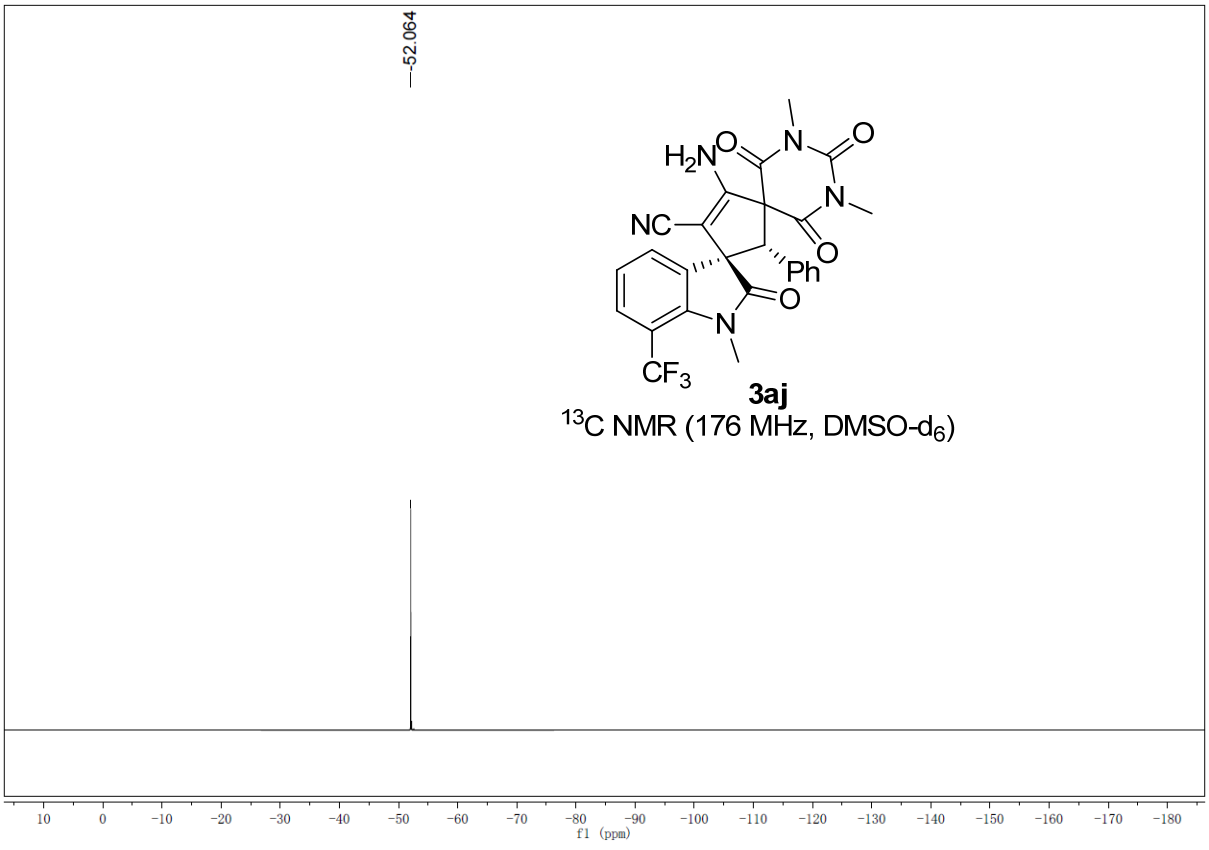

176.072
168.434
167.957
158.818
149.740
141.962
130.748
130.429
129.225
129.190
128.267
127.200
126.513
116.074
110.361
77.902
67.828
64.566
63.593
39.788
39.668
39.549
39.430
39.311
39.191
39.072
28.579
28.445
26.611
H2N
O
N
O
N
O
NC
Cl
Ph
O
N
3ai
13C NMR (176 MHz, DMSO-d6)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.372
8.362
7.646
7.645
7.635
7.633
7.394
7.383
7.371
7.180
7.169
7.159
7.078
7.067
7.056
6.671
6.661
4.223
3.361
3.135
3.082
2.885
H2N
O
N
O
N
O
NC
Ph
O
N
CF3
3aj
1H NMR (700 MHz, DMSO-d6)
1.01
1.04
2.94
1.05
2.05
2.04
0.98
3.04
2.96
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



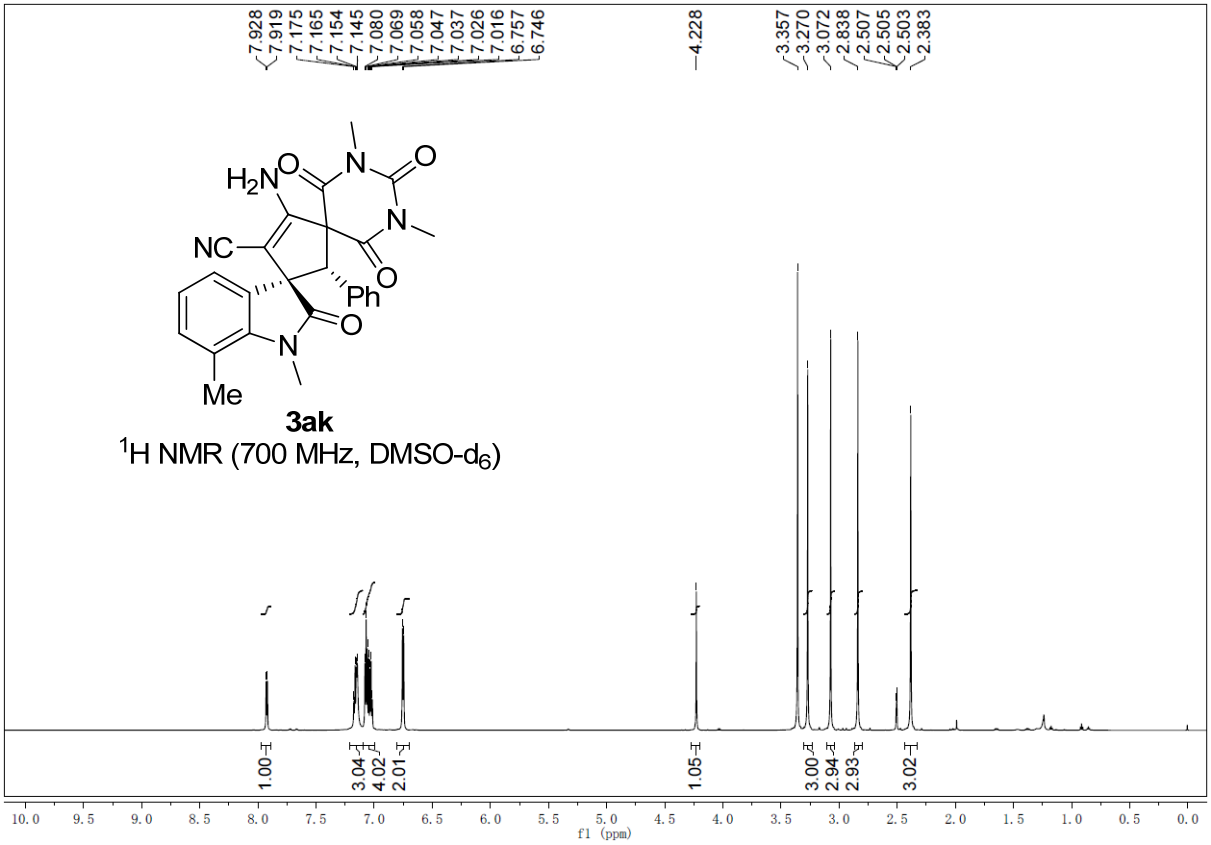
3aj

^{13}C NMR (176 MHz, DMSO-d_6)



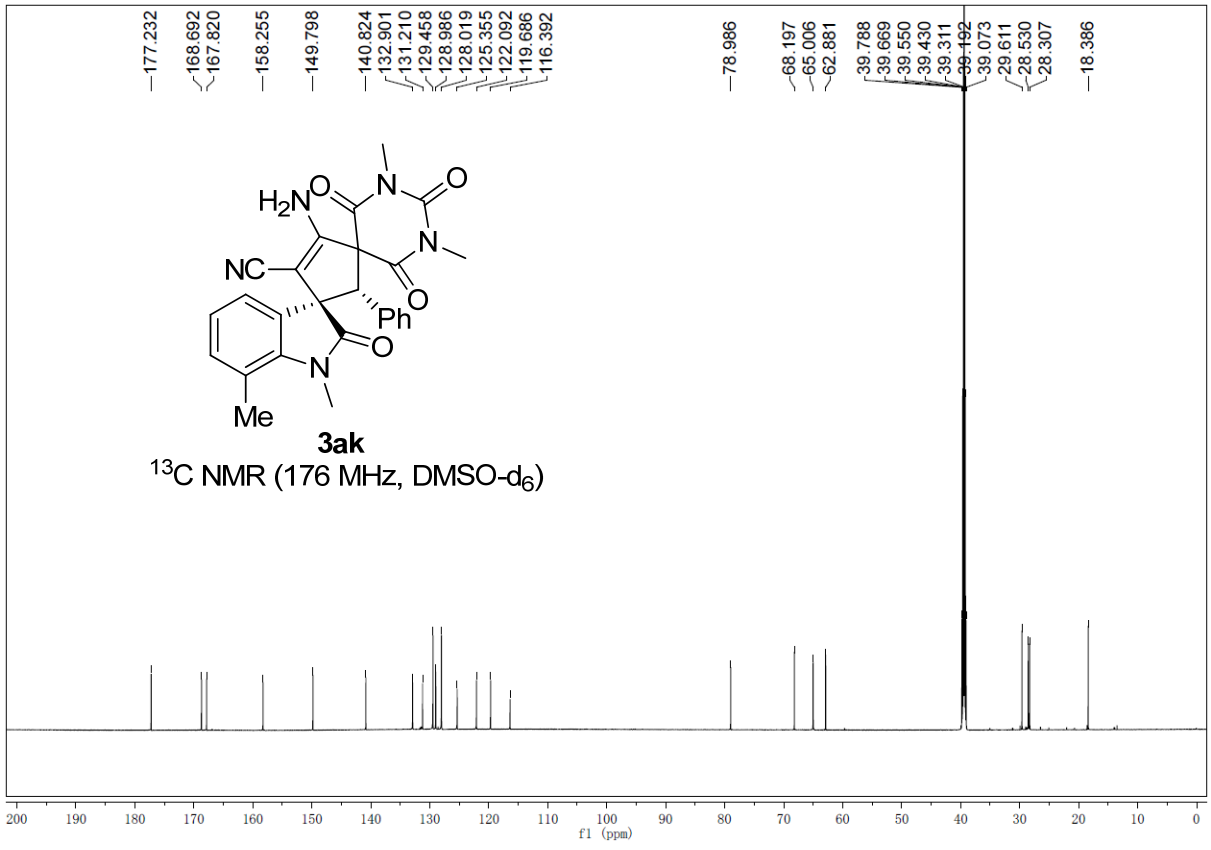
3aj

^{13}C NMR (176 MHz, DMSO-d_6)



3ak

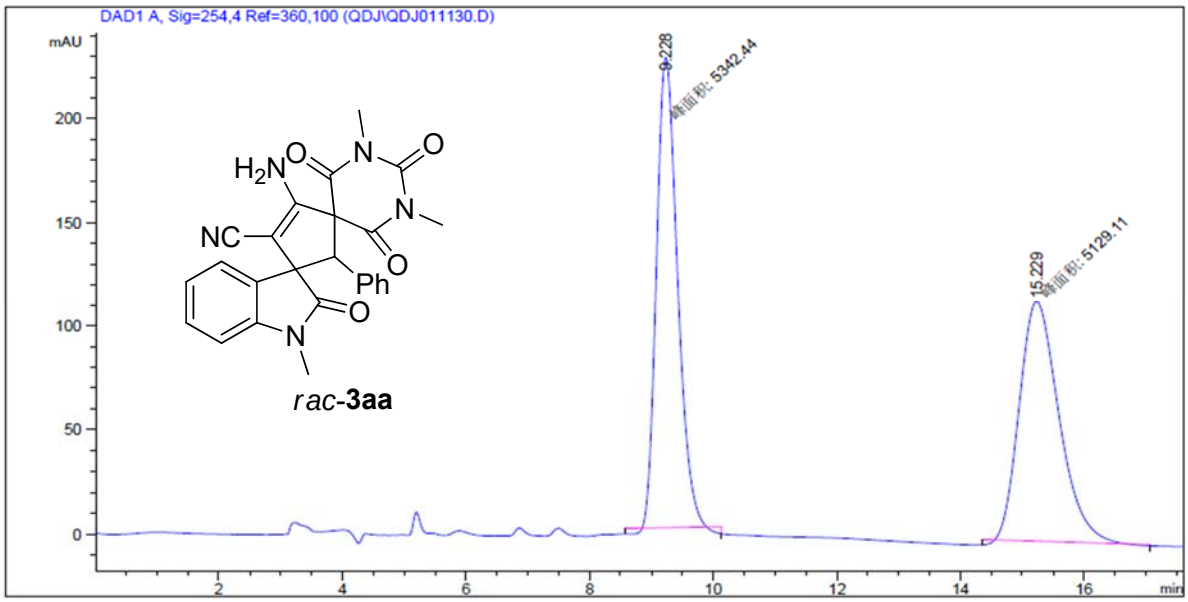
^{1}H NMR (700 MHz, DMSO-d_6)



3ak

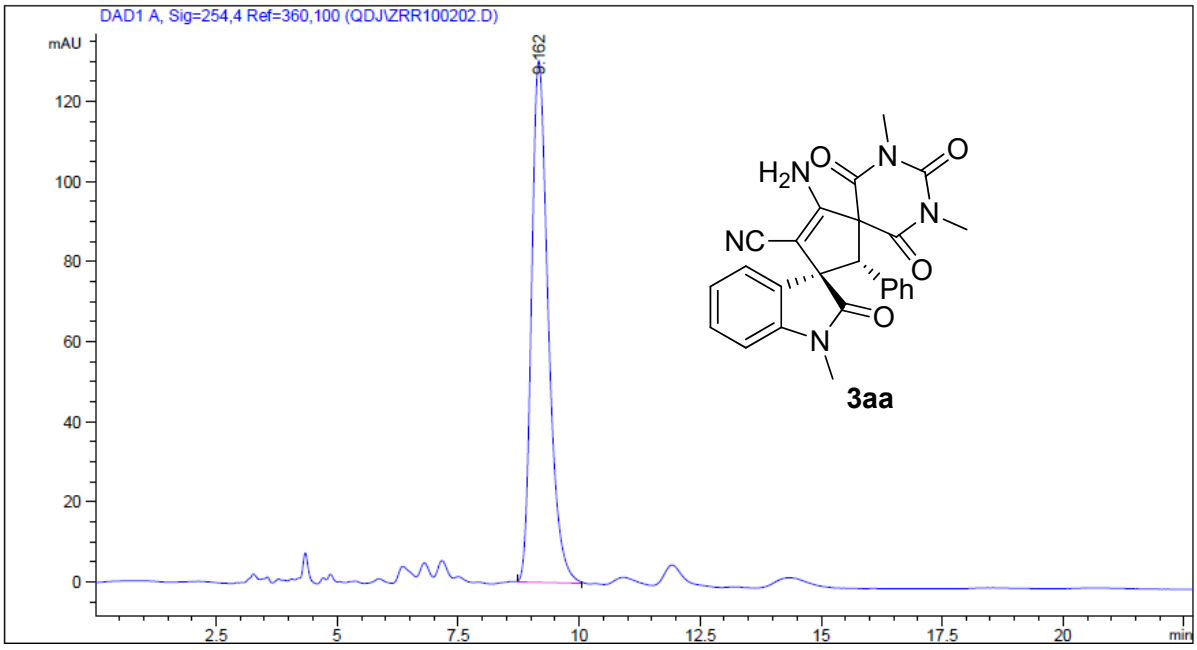
^{13}C NMR (176 MHz, DMSO-d_6)

2. Copies of HPLC chromatograms

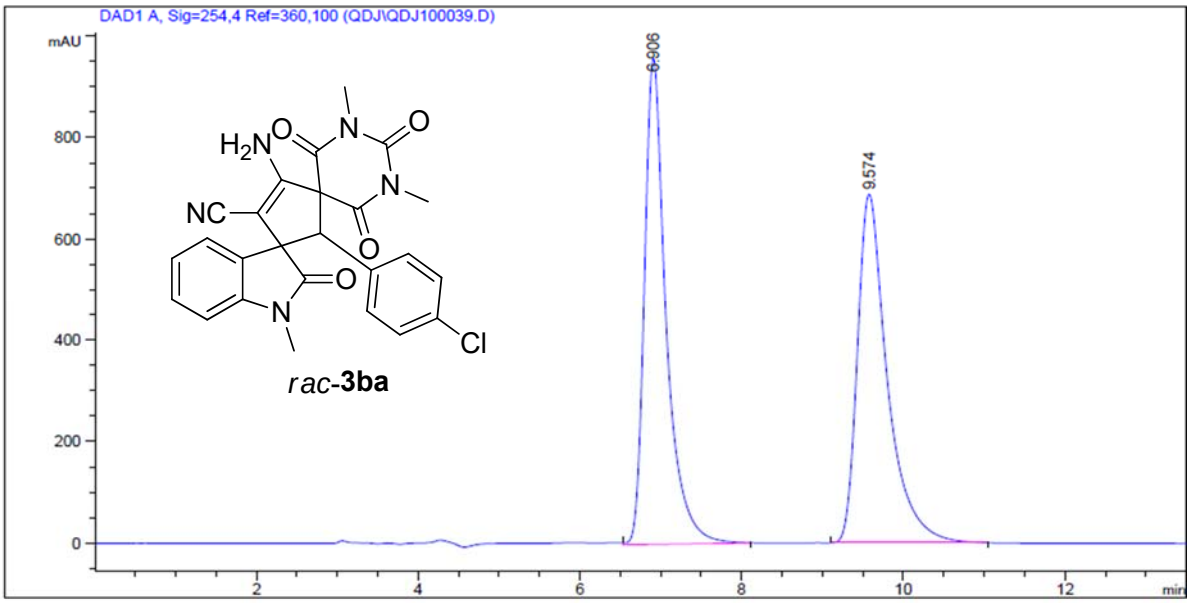


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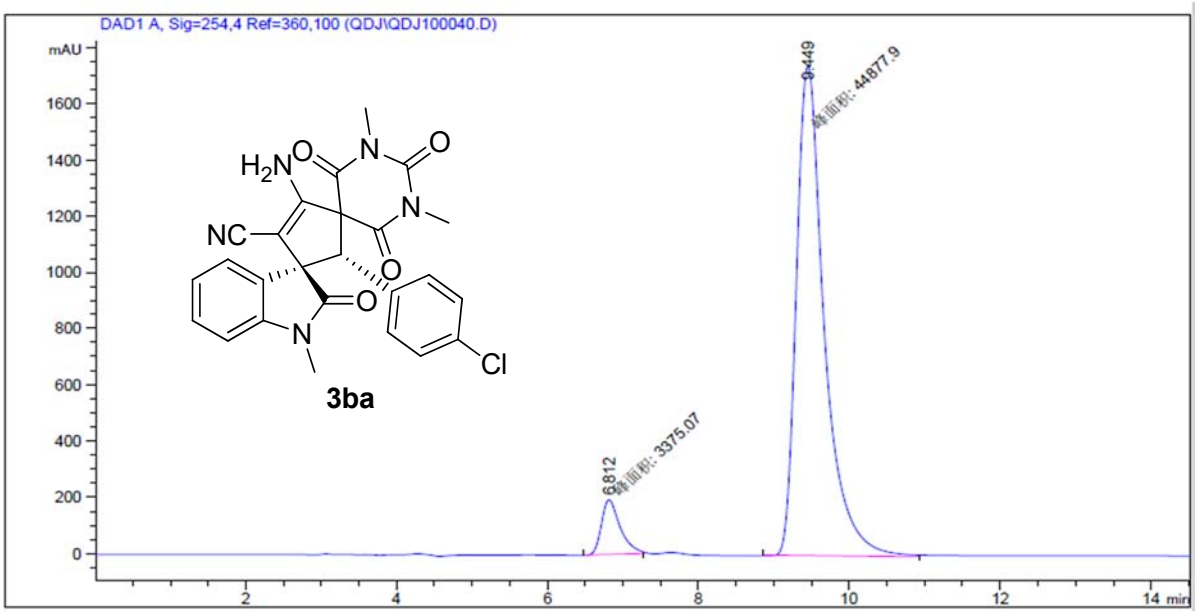
（峰面积：peak area）



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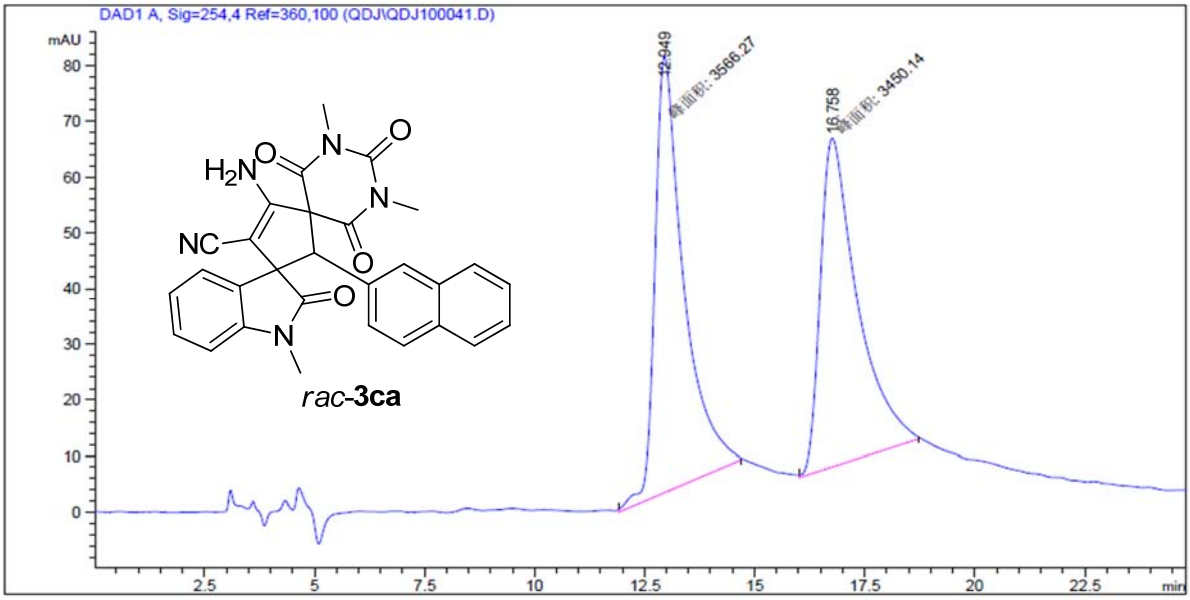


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1	6.906	VB	0.2751	1.78500e4	959.07739	50.2701
2	9.574	BB	0.3793	1.76582e4	688.23169	49.7299



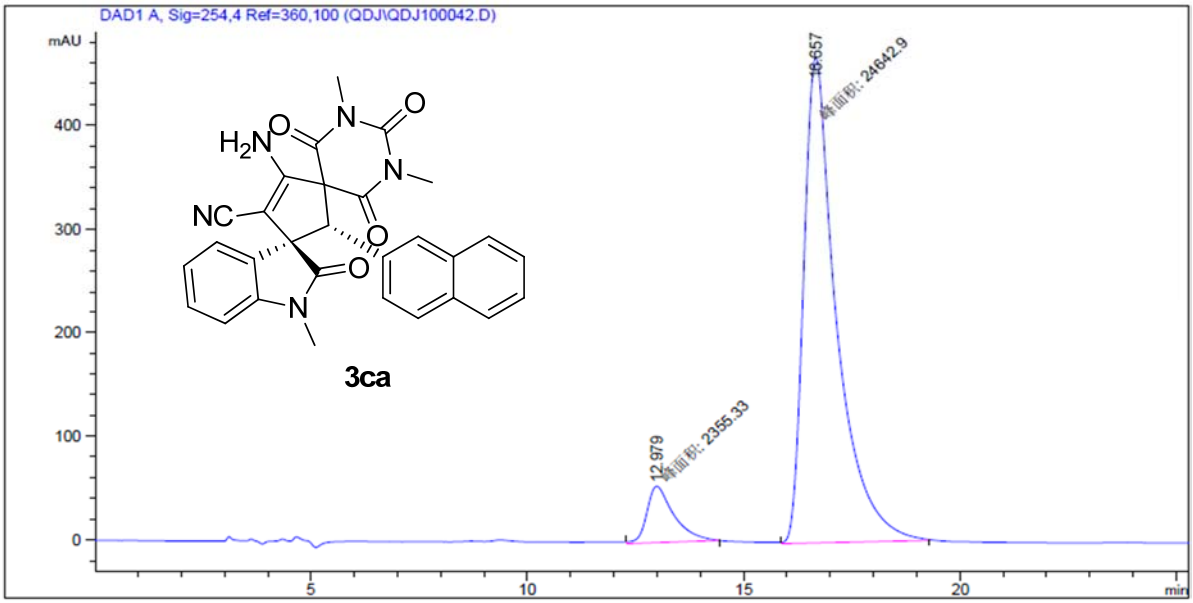
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.812	MM	0.2888	3375.06982	194.74199	6.9945
2	9.449	MM	0.4298	4.48779e4	1740.22803	93.0055

（峰面积：peak area）



rac-**3ca**

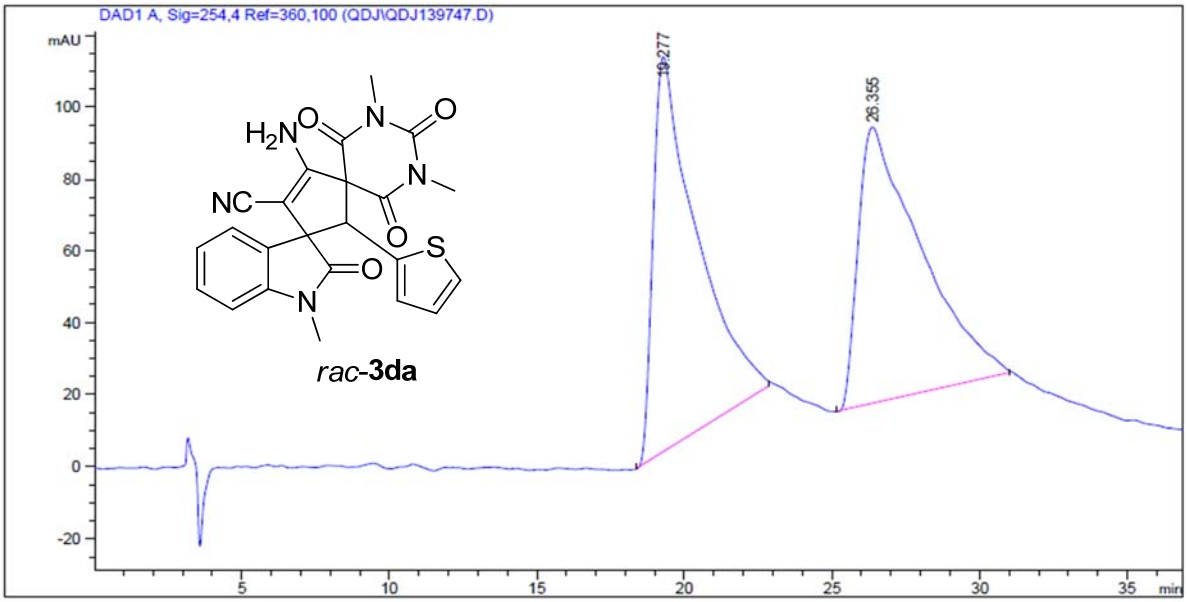
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.949	MM	0.7603	3566.27319	78.18192	50.8276
2	16.758	MM	0.9760	3450.13721	58.91587	49.1724



3ca

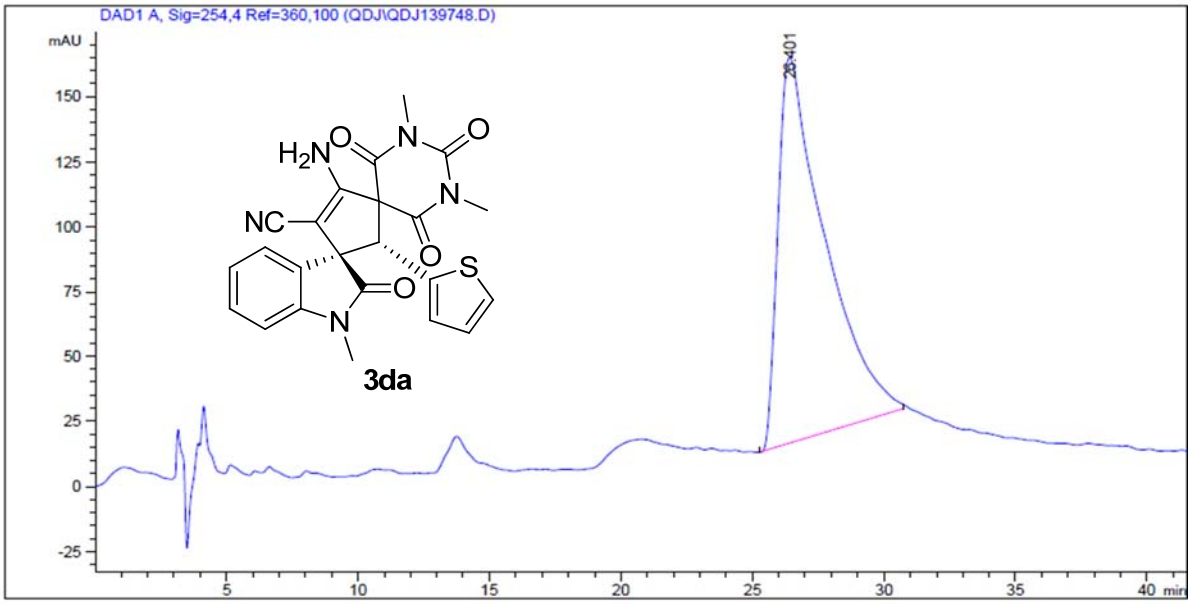
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.979	MM	0.7227	2355.32739	54.31891	8.7240
2	16.657	MM	0.8775	2.46429e4	468.03088	91.2760

（峰面积：peak area）



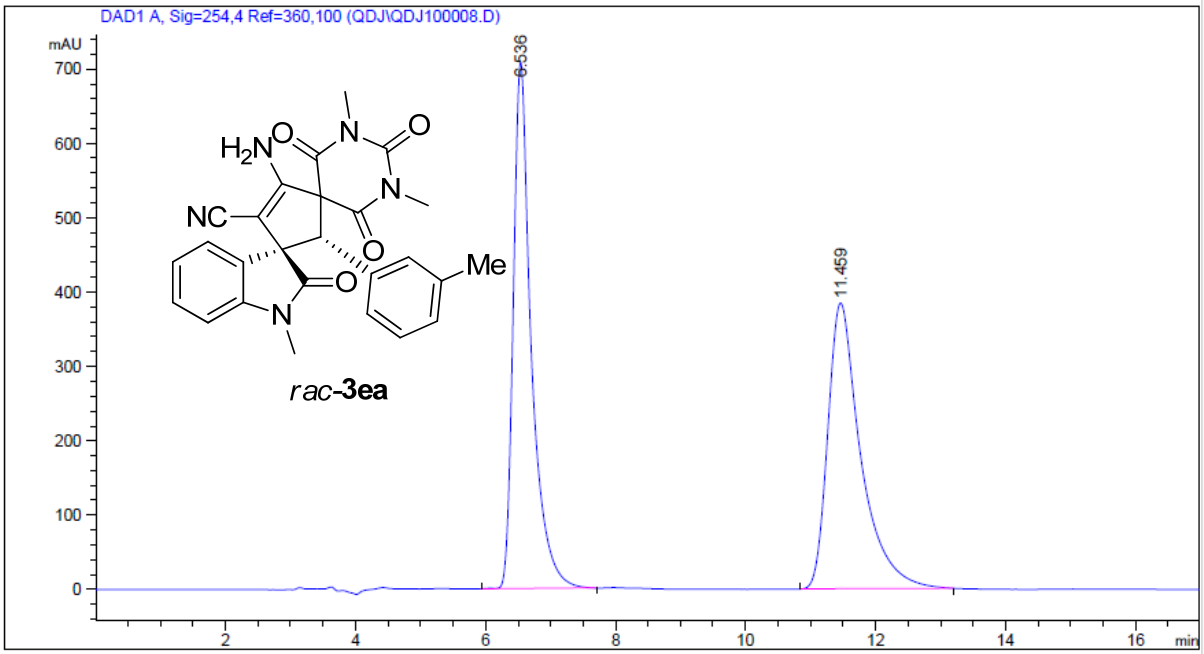
rac-**3da**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.277	BB	1.3767	1.13497e4	109.91280	50.0510
2	26.355	BB	1.7334	1.13266e4	76.94252	49.9490

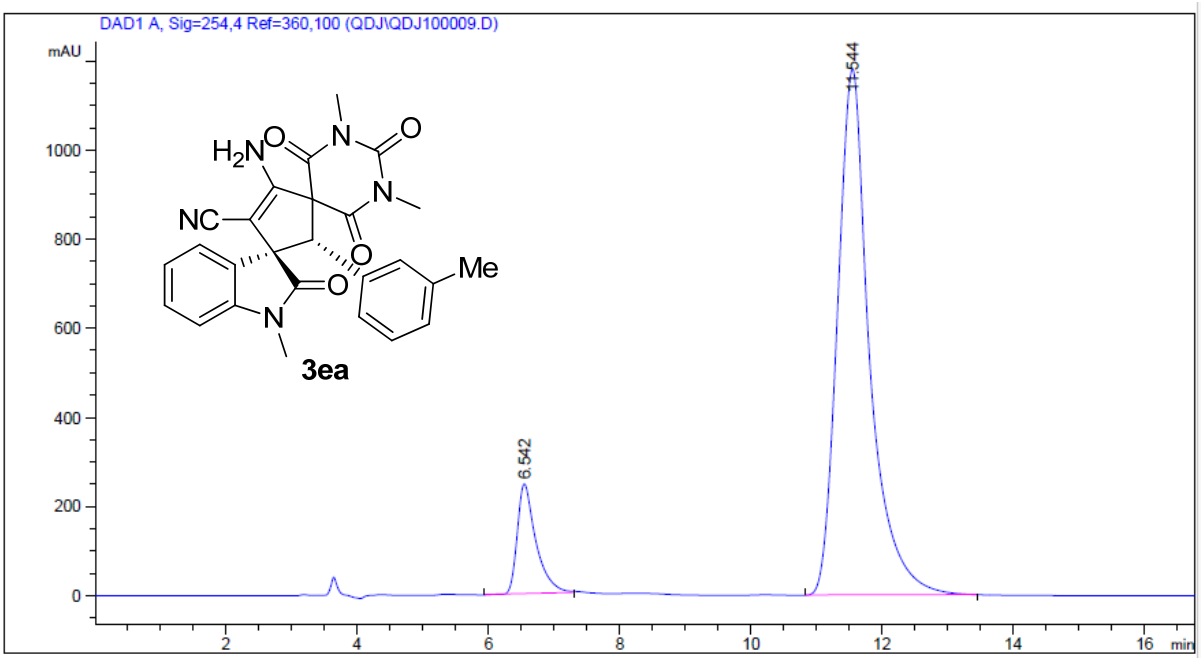


3da

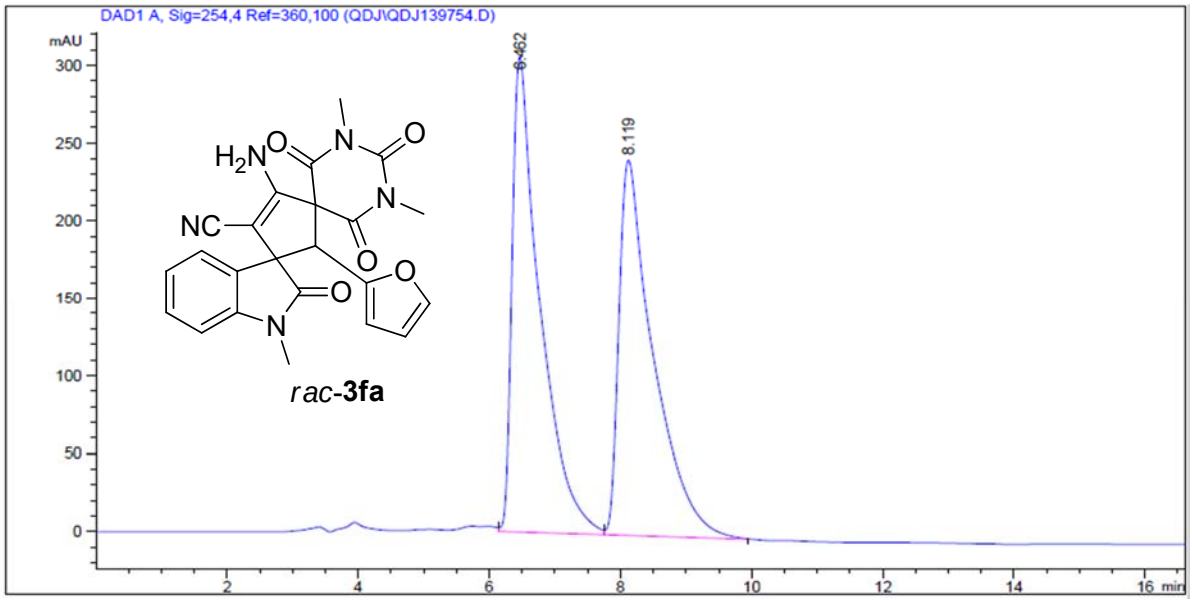
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.401	BB	1.6792	1.84783e4	148.75494	100.0000



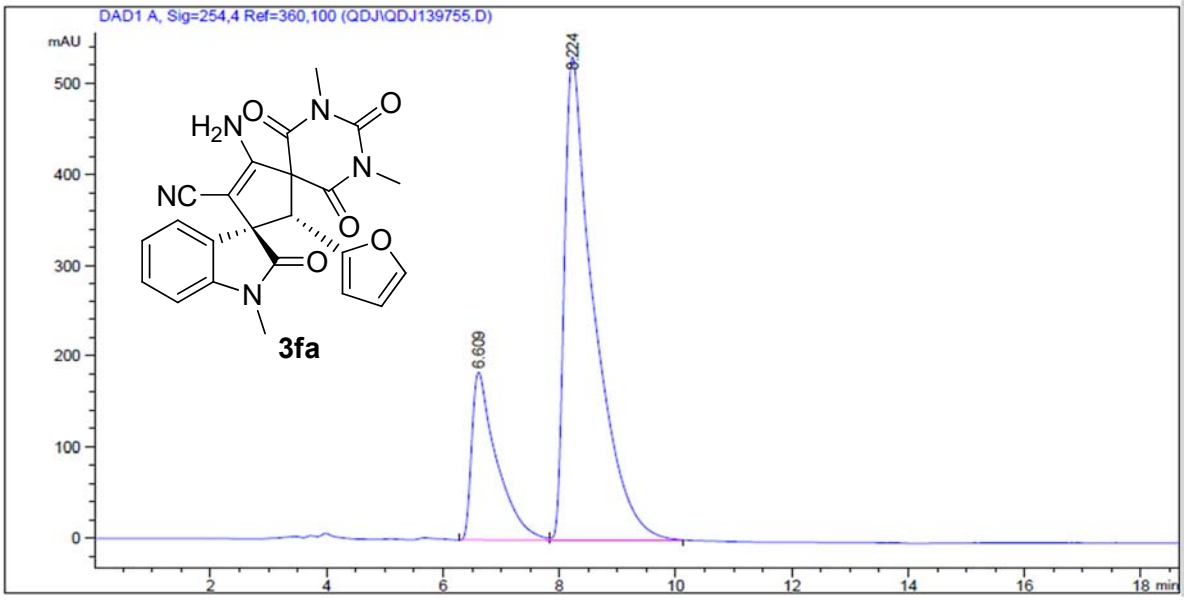
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.536	BB	0.2800	1.36046e4	708.44281	50.0884
2	11.459	BB	0.5170	1.35566e4	384.83334	49.9116



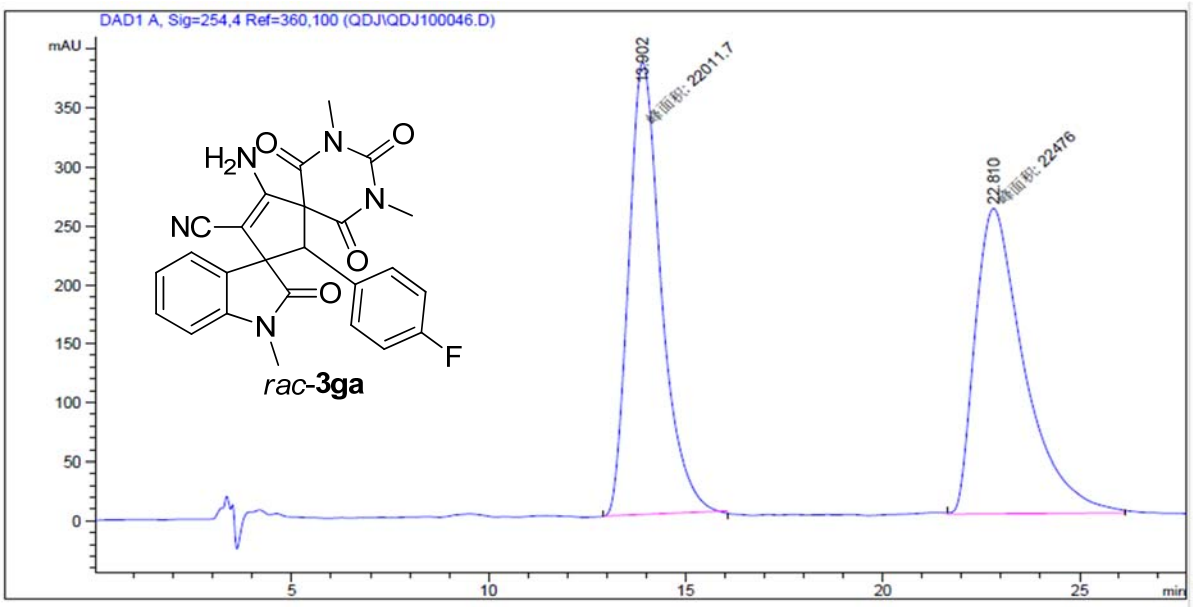
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.542	BB	0.2887	4879.15039	246.73080	10.8513
2	11.544	BB	0.5039	4.00844e4	1181.15967	89.1487



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.462	VV	0.4131	9056.08105	306.17358	50.6287
2	8.119	VB	0.5098	8831.16016	241.98680	49.3713

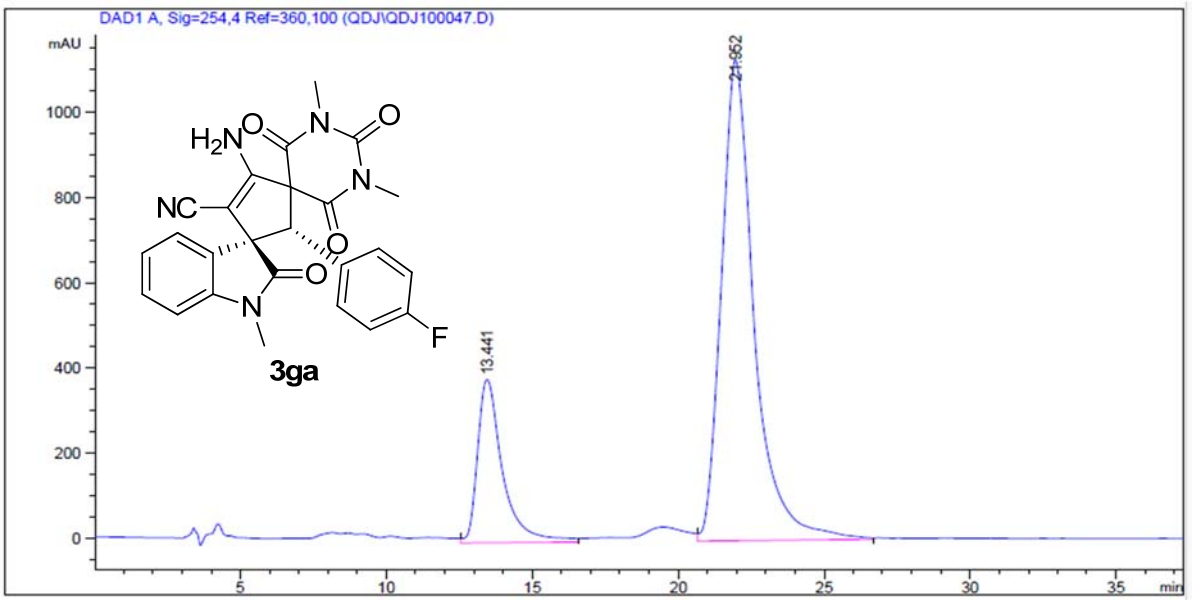


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.609	VV	0.4177	5481.59229	183.90752	22.4785
2	8.224	VB	0.4974	1.89043e4	530.94720	77.5215

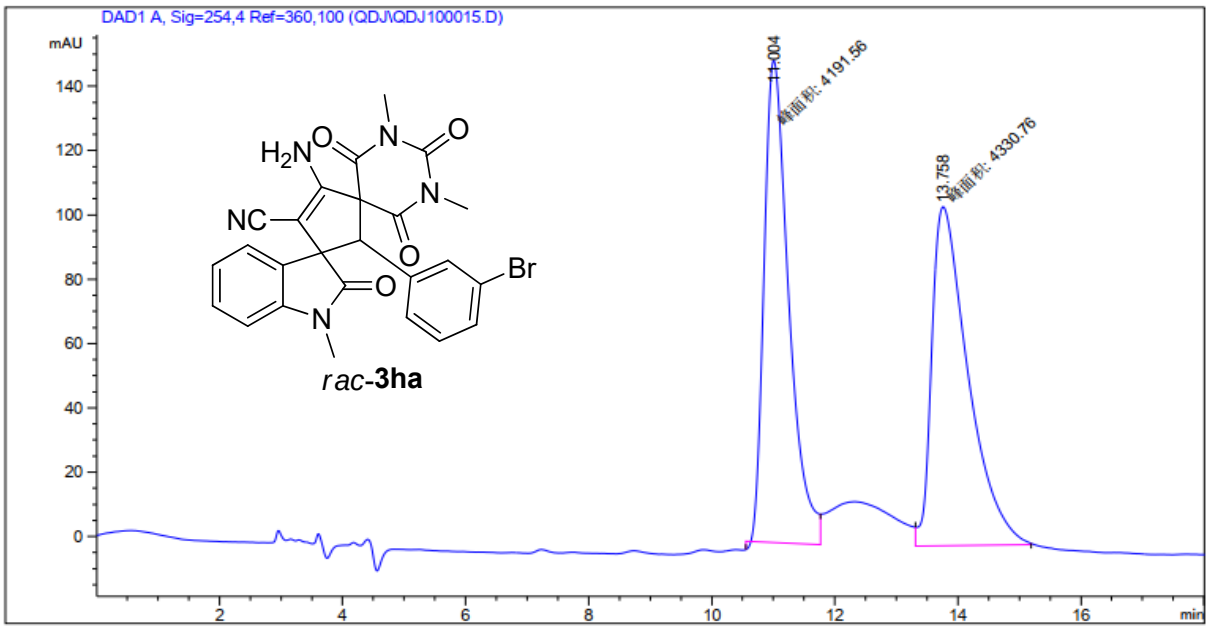


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.902	MM	0.9575	2.20117e4	383.16333	49.4782
2	22.810	MM	1.4452	2.24760e4	259.20590	50.5218

（峰面积：peak area）

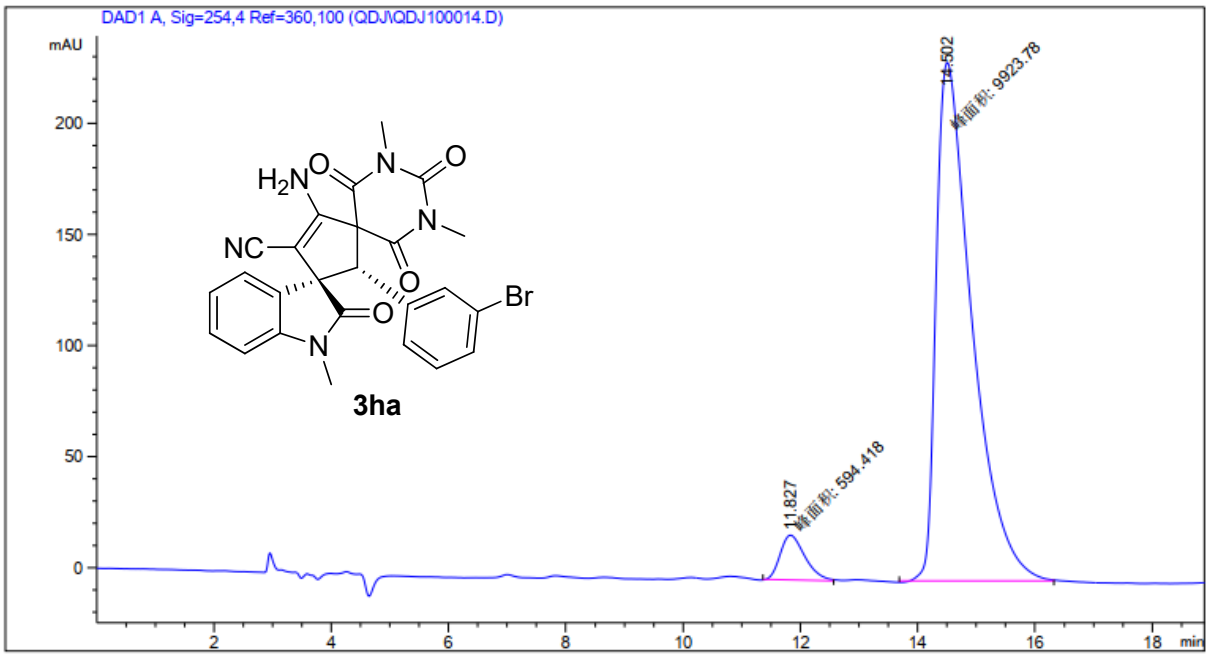


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.441	VV	0.8871	2.29297e4	382.65372	20.6138
2	21.952	VV	1.1859	8.83051e4	1127.34204	79.3862

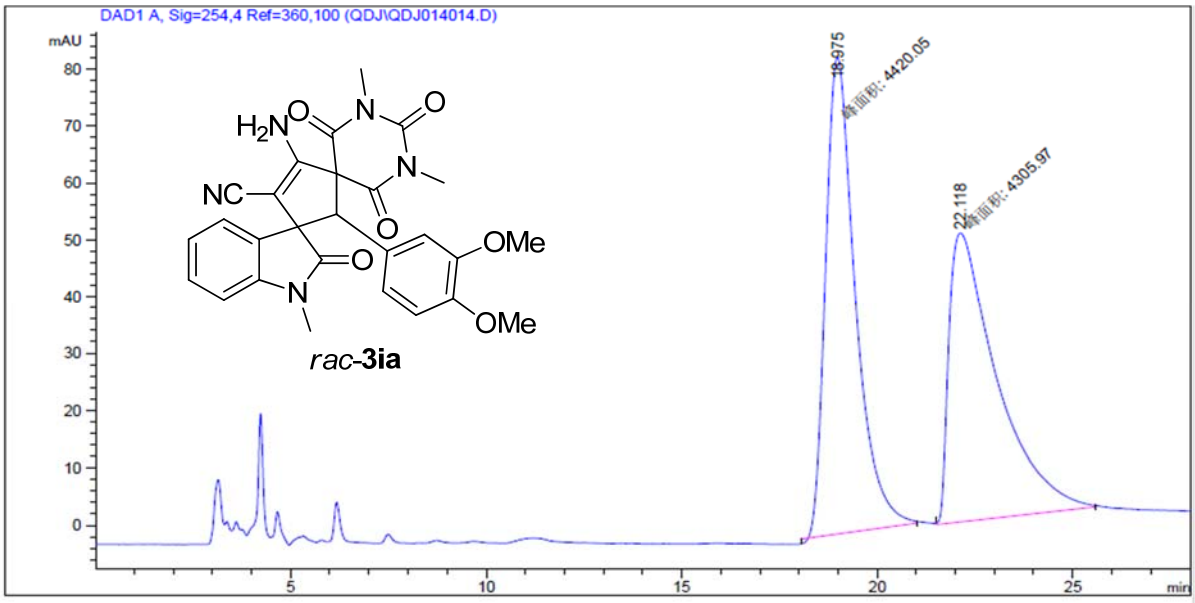


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.004	MM	0.4658	4191.56250	149.97838	49.1834
2	13.758	MM	0.6843	4330.75586	105.48135	50.8166

（峰面积：peak area）



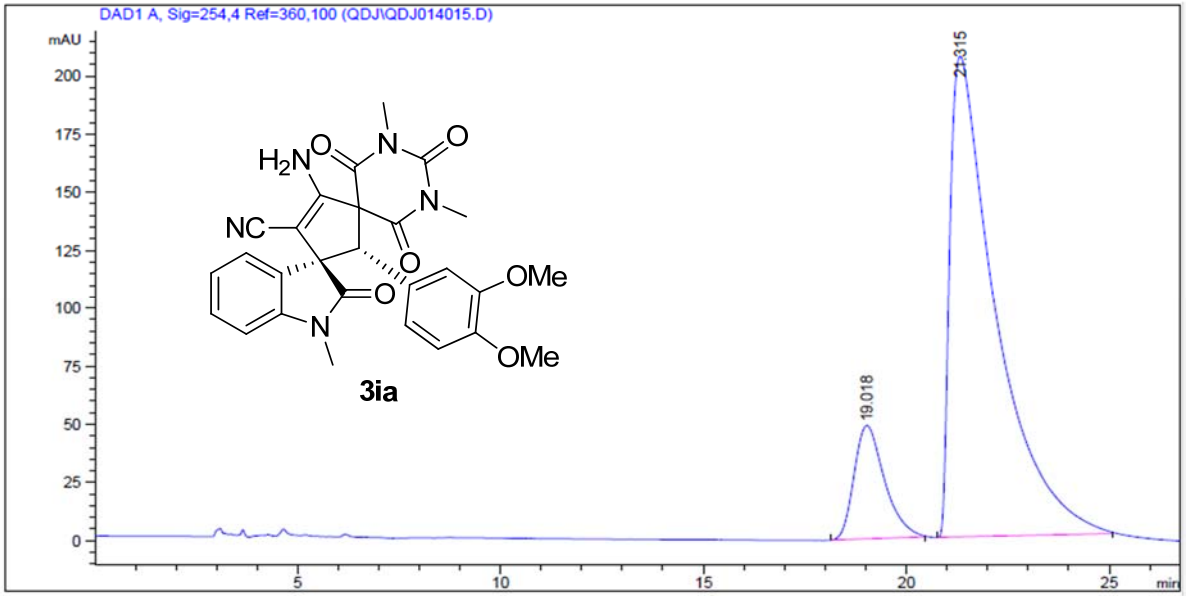
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.827	MM	0.4914	594.41797	20.16006	5.6513
2	14.502	MM	0.7088	9923.77539	233.34561	94.3487



rac-**3ia**

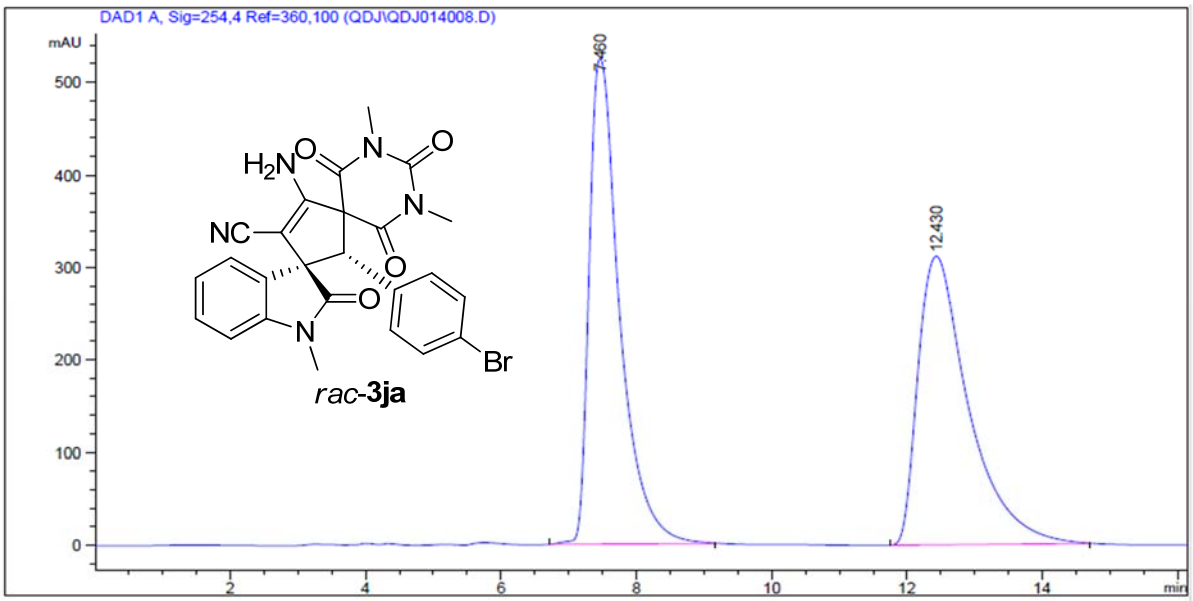
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.975	MM	0.8815	4420.04590	83.57407	50.6537
2	22.118	MM	1.4172	4305.96973	50.64063	49.3463

（峰面积：peak area）

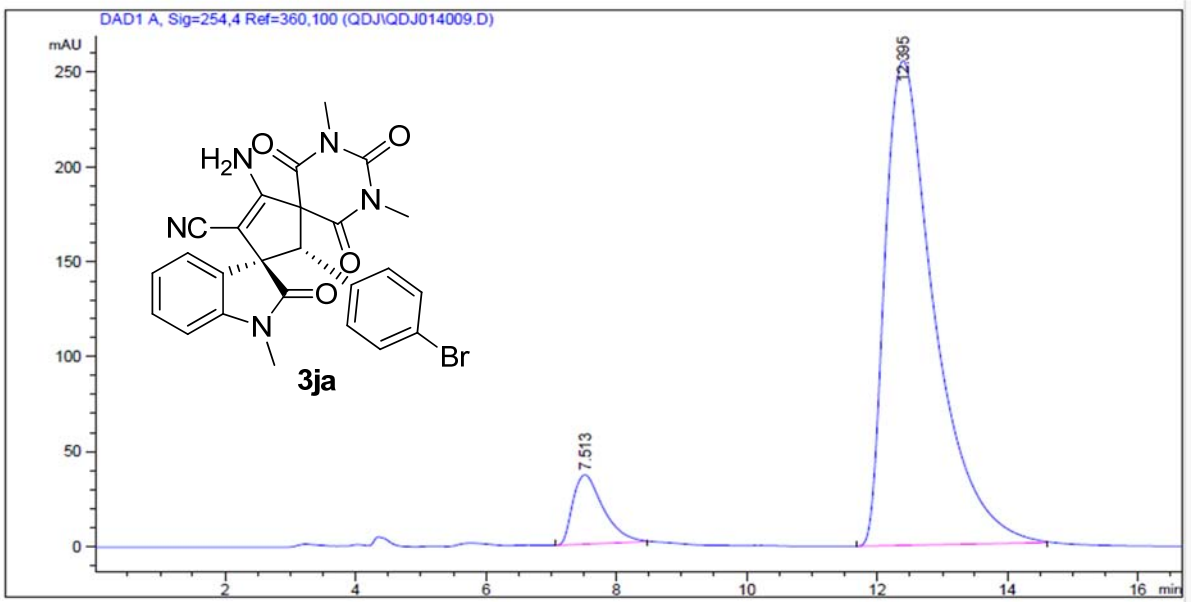


3ia

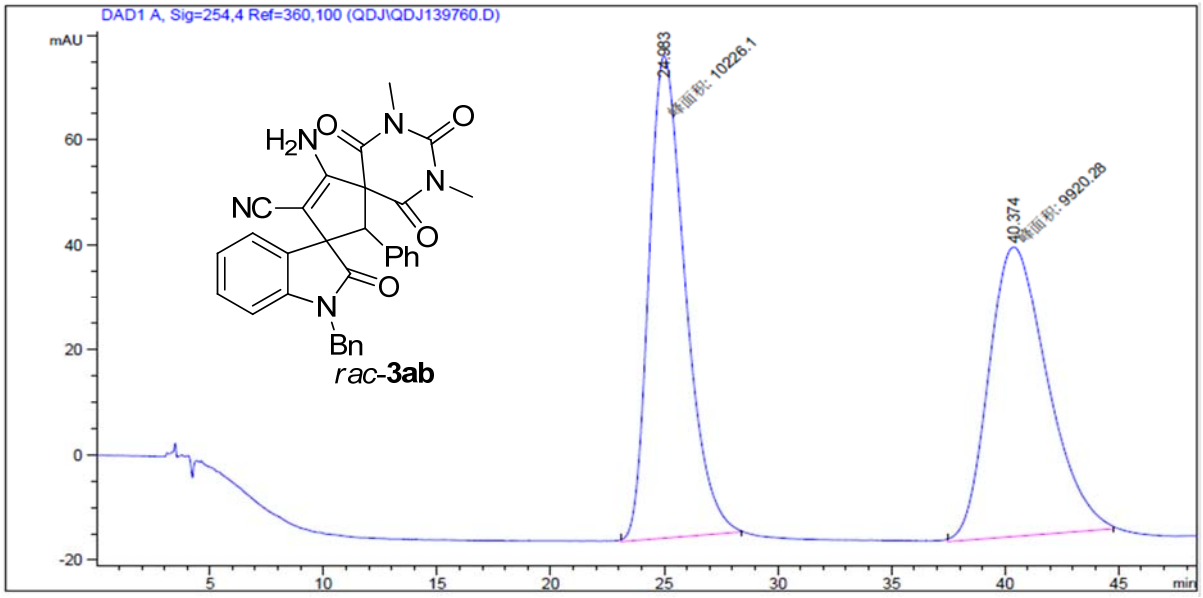
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.018	BB	0.7754	2555.64233	48.76661	13.5908
2	21.315	BB	1.0894	1.62486e4	207.09192	86.4092



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.460	BB	0.4683	1.64594e4	524.27692	50.3802
2	12.430	BB	0.7778	1.62110e4	312.17899	49.6198

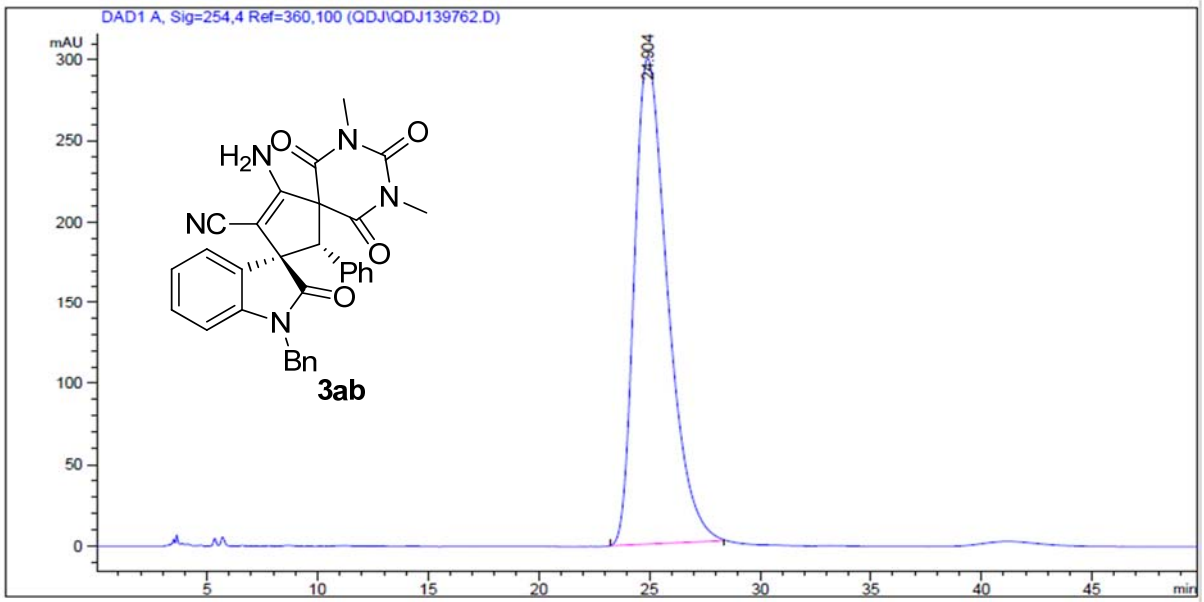


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.513	BB	0.4975	1191.26038	36.43427	8.1437
2	12.395	BB	0.7894	1.34368e4	255.57106	91.8563

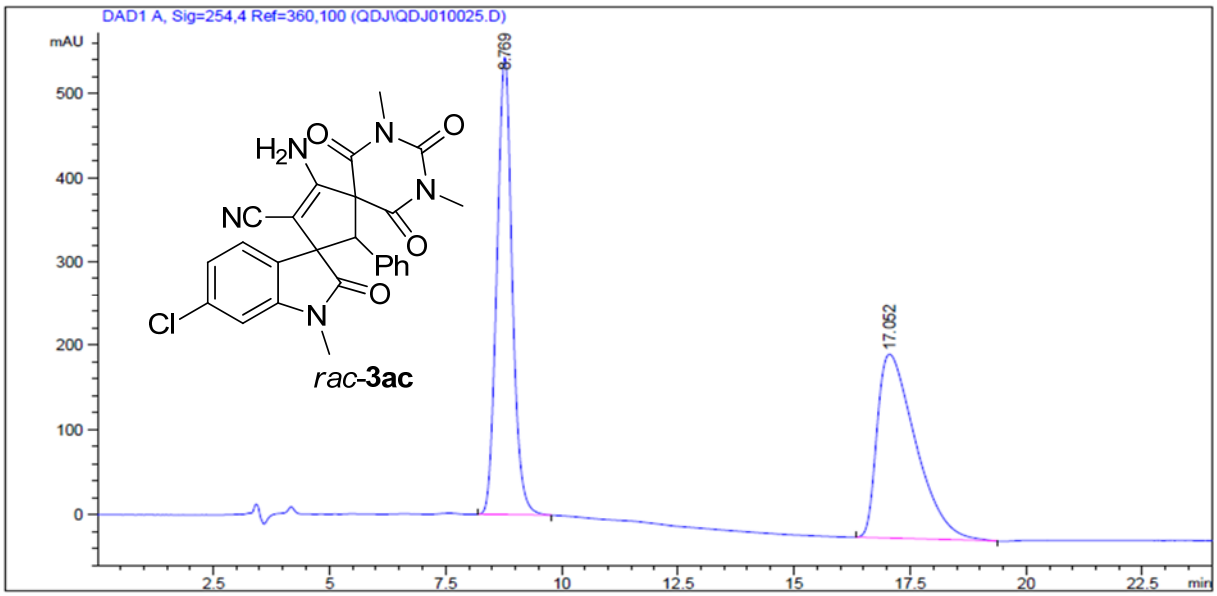


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.983	MM	1.8545	1.02261e4	91.90362	50.7590
2	40.374	MM	2.9952	9920.27930	55.20137	49.2410

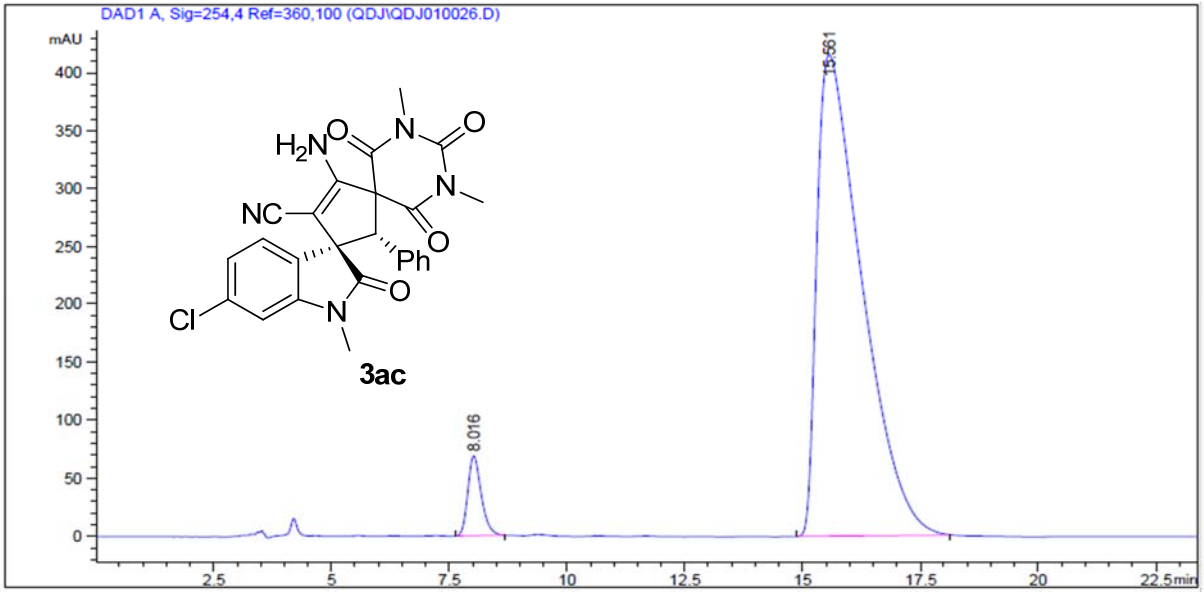
（峰面积：peak area）



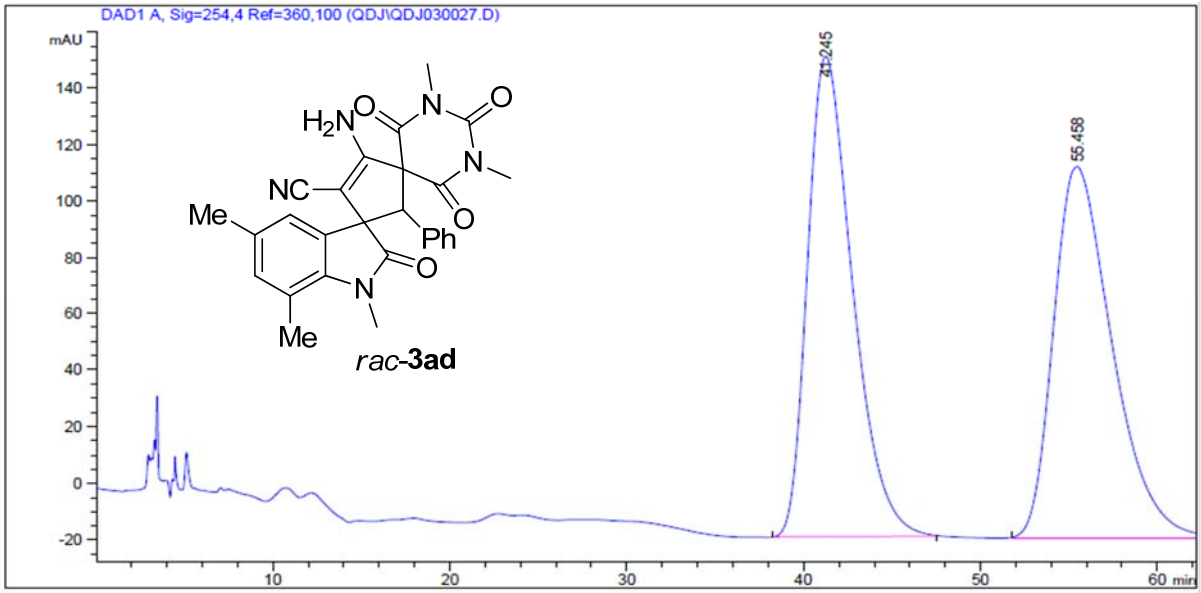
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.904	BB	1.5472	3.13476e4	299.96777	100.0000



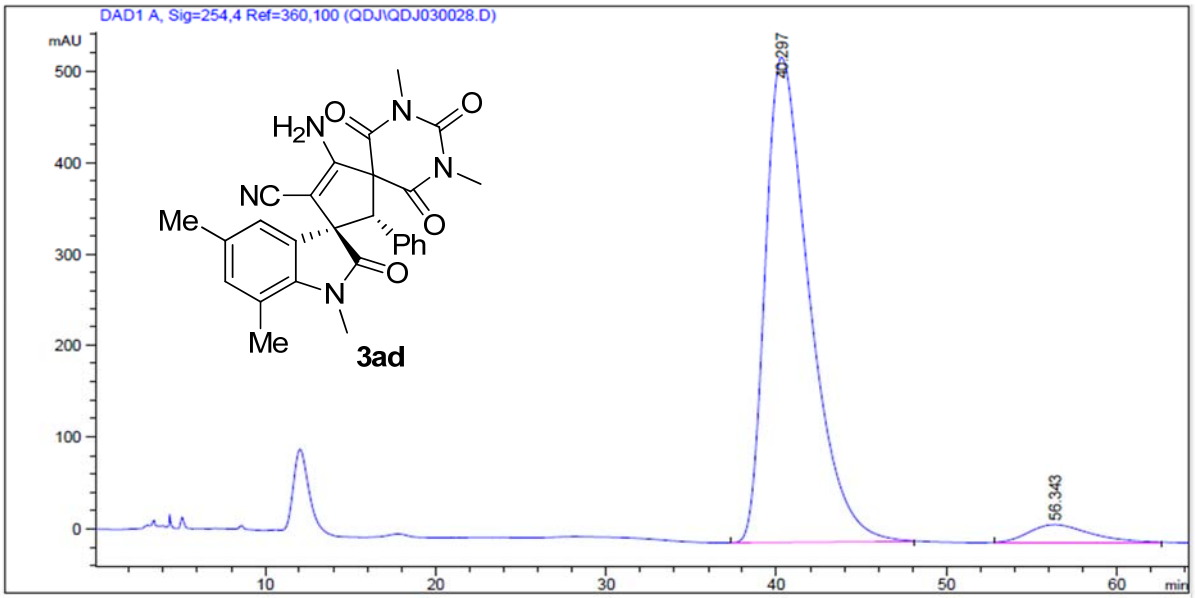
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.769	BB	0.3498	1.24712e4	543.22906	49.8799
2	17.052	BB	0.8575	1.25313e4	217.06197	50.1201



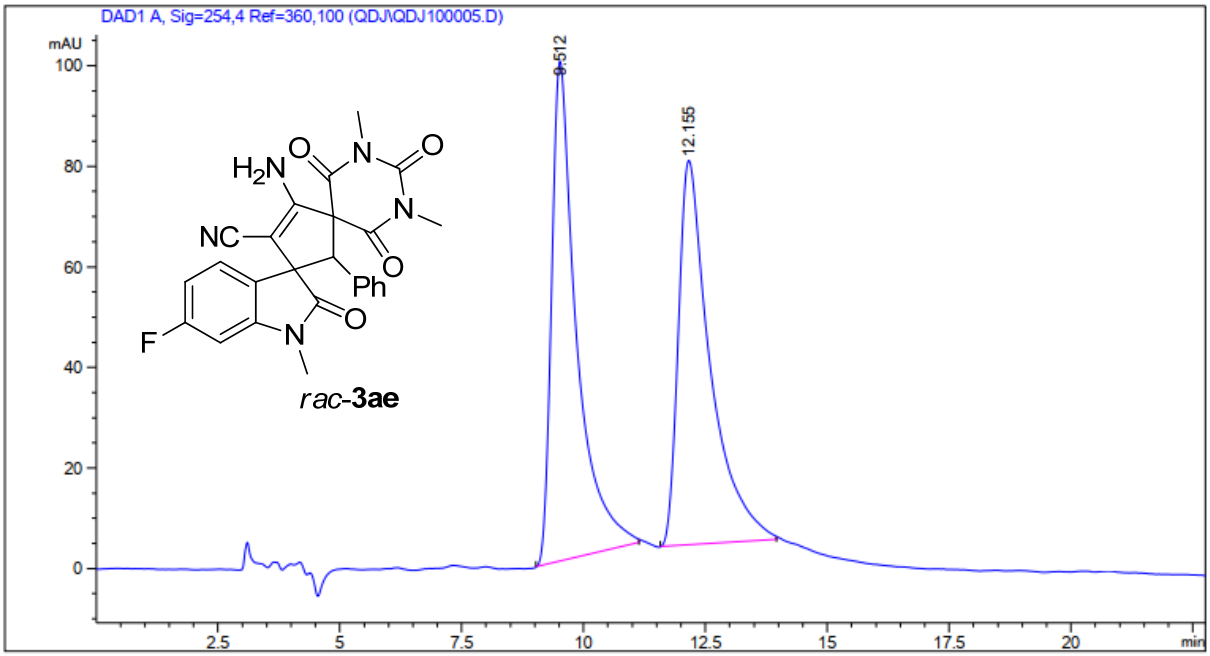
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.016	BB	0.3022	1366.07776	68.63458	4.7117
2	15.561	BB	0.9721	2.76274e4	415.32861	95.2883



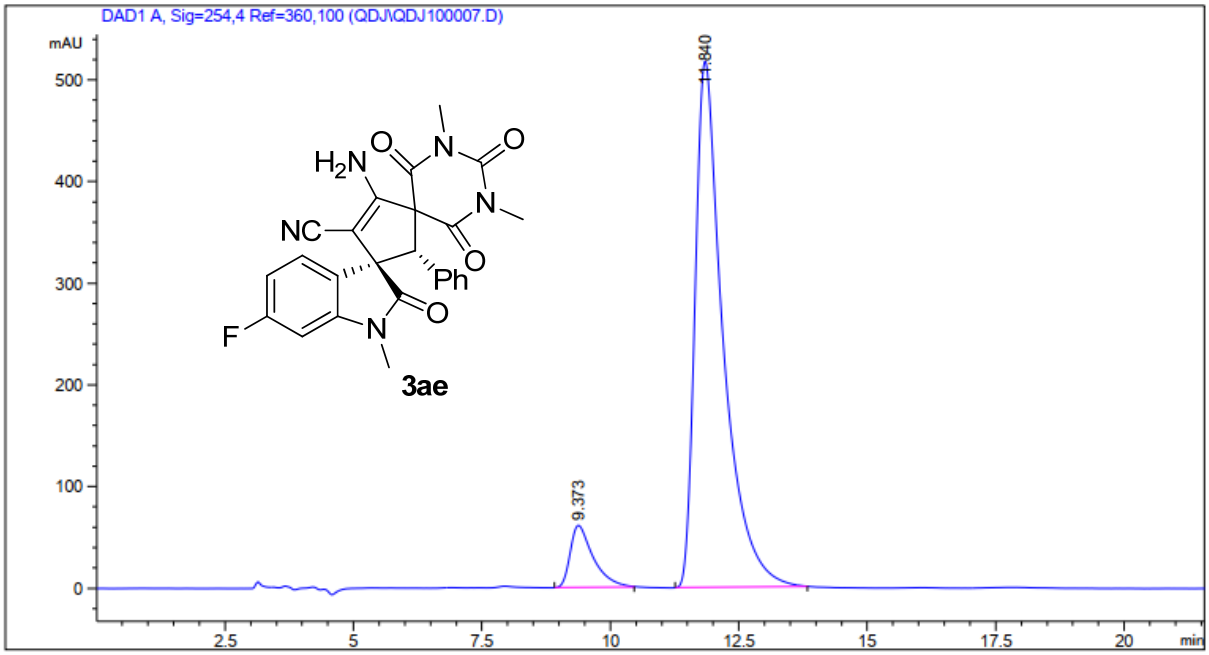
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.245	BB	2.6767	3.01995e4	170.31615	50.0102
2	55.458	BBA	3.2760	3.01871e4	131.60959	49.9898



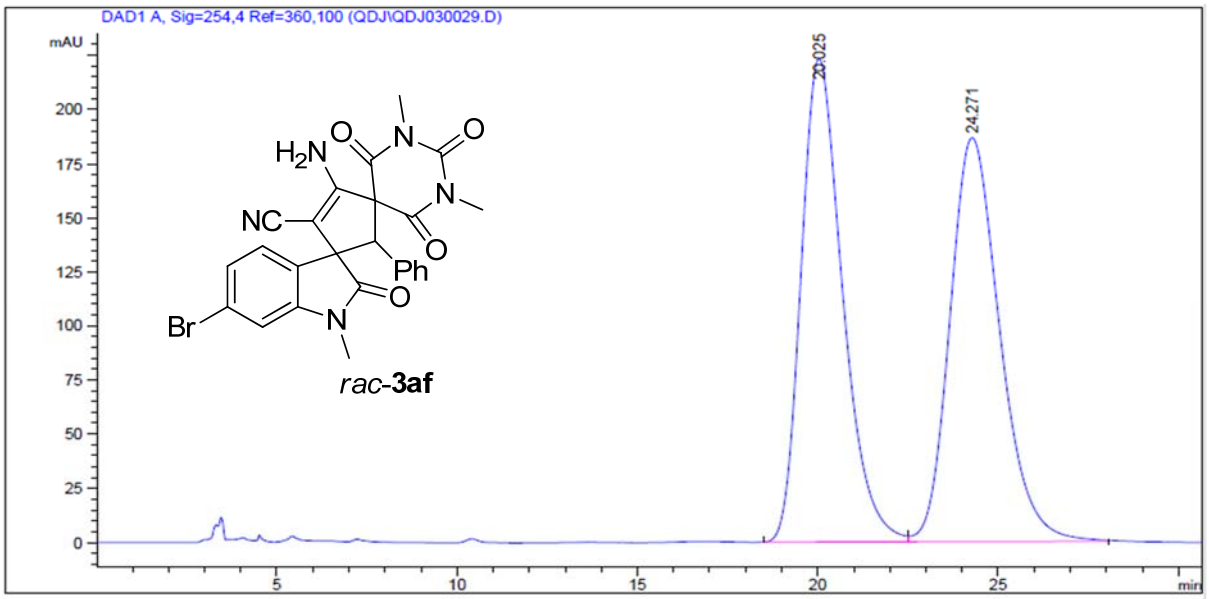
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.297	BB	2.5981	9.52733e4	529.76904	95.1467
2	56.343	BB	2.9537	4859.77344	19.40564	4.8533



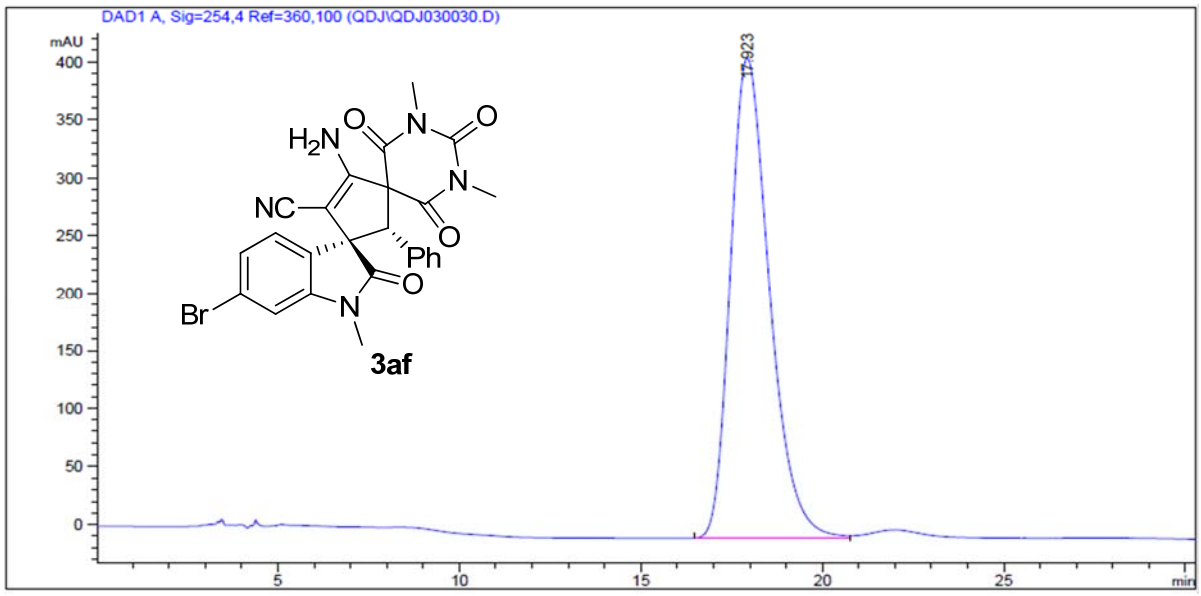
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.512	BB	0.5082	3548.33496	99.45790	50.4480
2	12.155	BB	0.6417	3485.31934	76.47534	49.5520



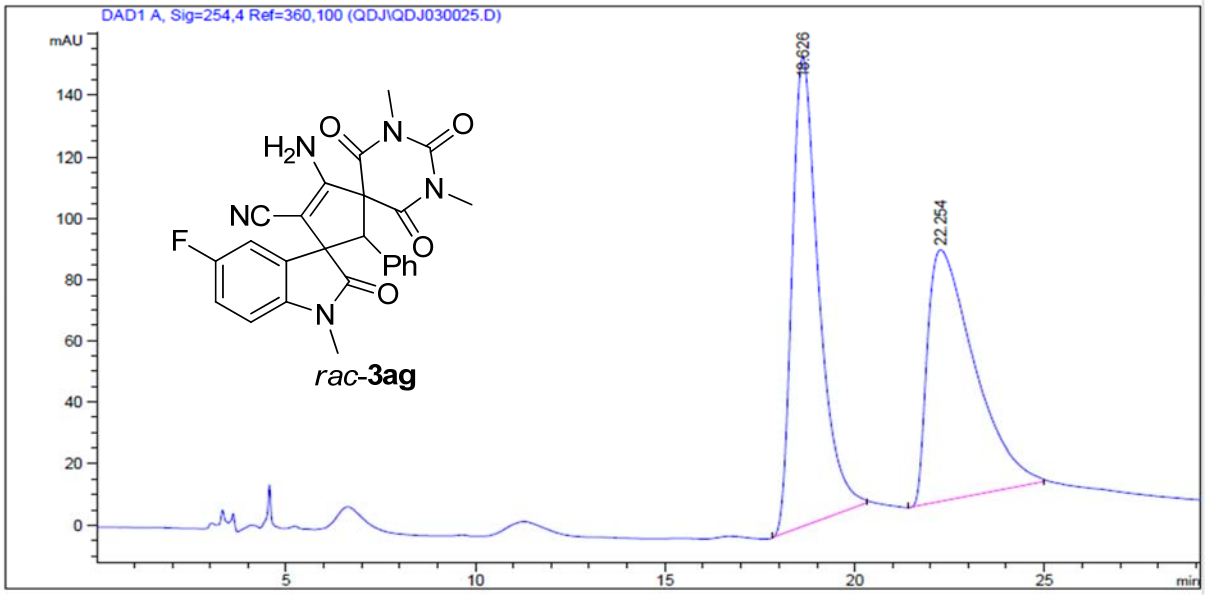
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.373	BB	0.4560	1905.36243	61.07478	8.8196
2	11.840	BB	0.5538	1.96984e4	517.87146	91.1804



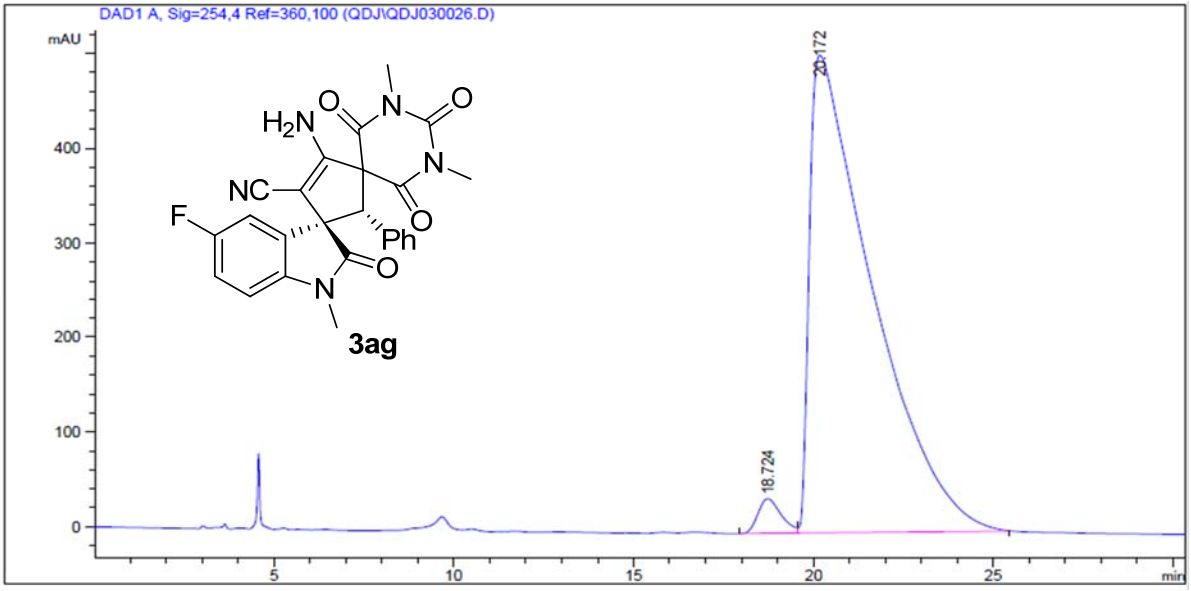
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.025	BV	1.2337	1.77821e4	223.15535	49.8288
2	24.271	VB	1.4969	1.79042e4	186.35692	50.1712



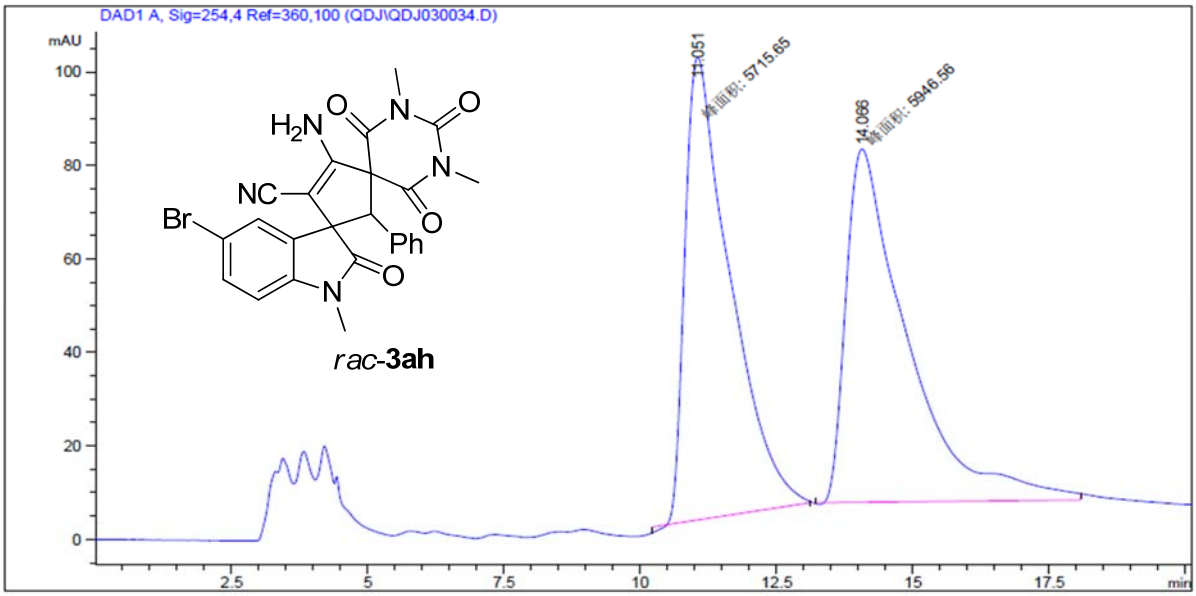
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.923	BV	1.1583	3.11083e4	415.12875	100.0000



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.626	BB	0.7333	7511.52148	152.84779	51.5522
2	22.254	BB	1.1707	7059.18018	82.13405	48.4478

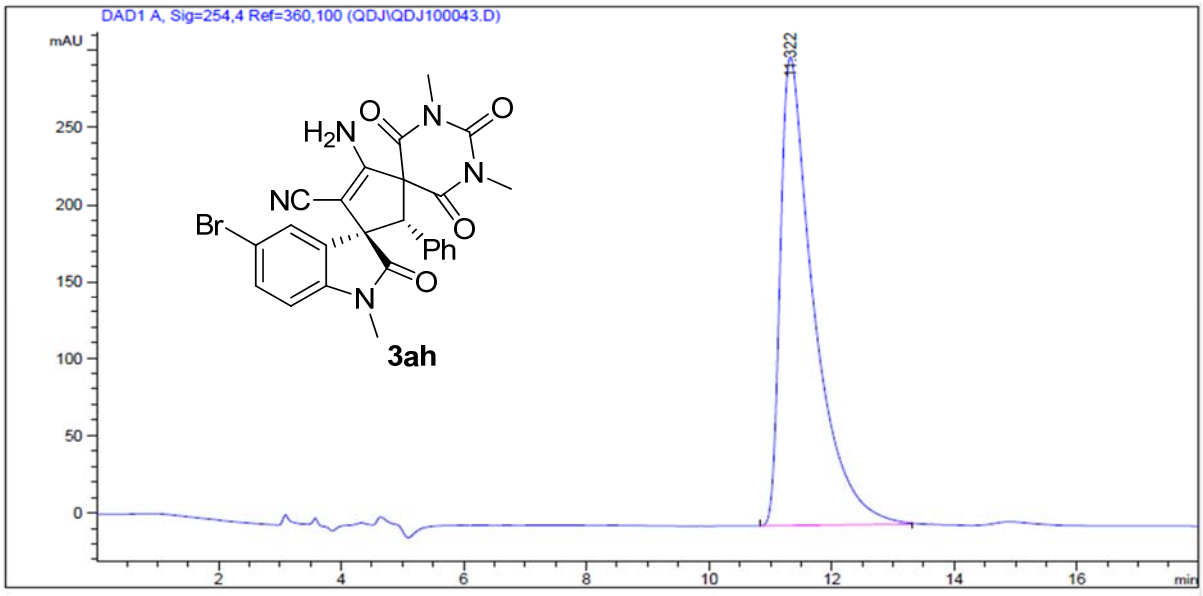


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.724	BV	0.6600	1654.62842	36.70240	2.6251
2	20.172	VB	1.6145	6.13763e4	504.79556	97.3749

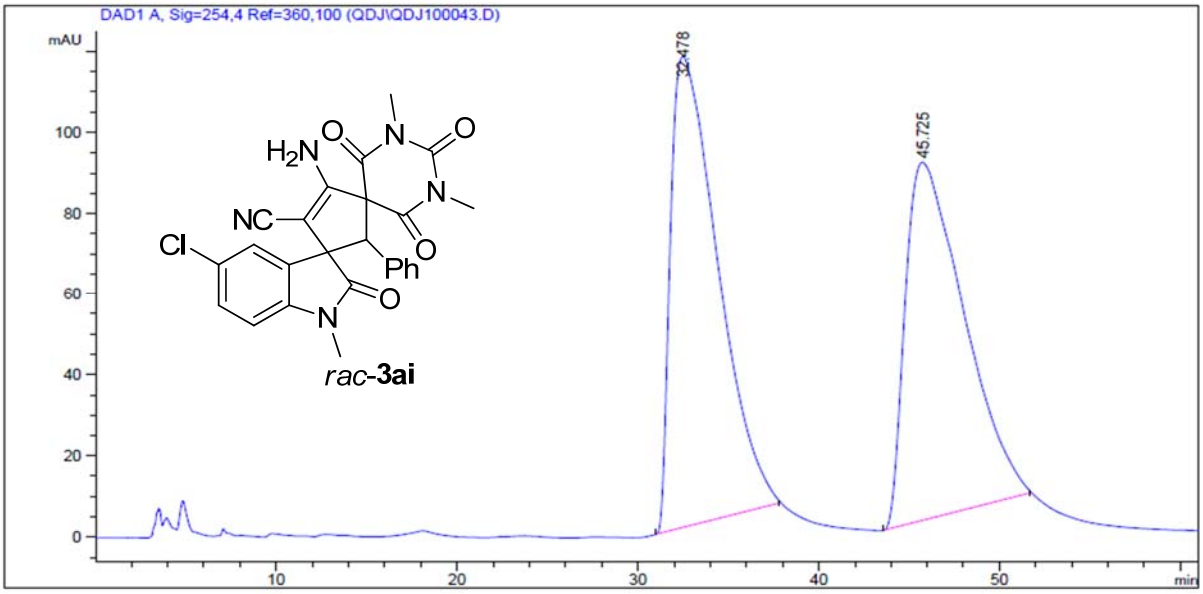


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.051	MM	0.9620	5715.64941	99.02480	49.0100
2	14.066	MM	1.3109	5946.55664	75.60430	50.9900

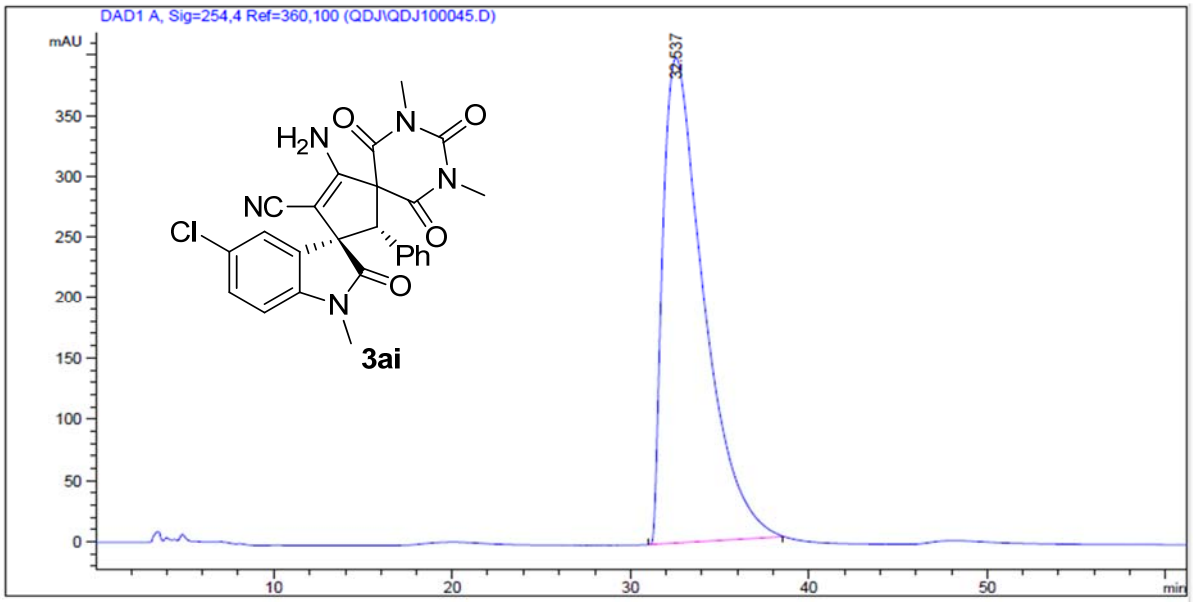
（峰面积：peak area）



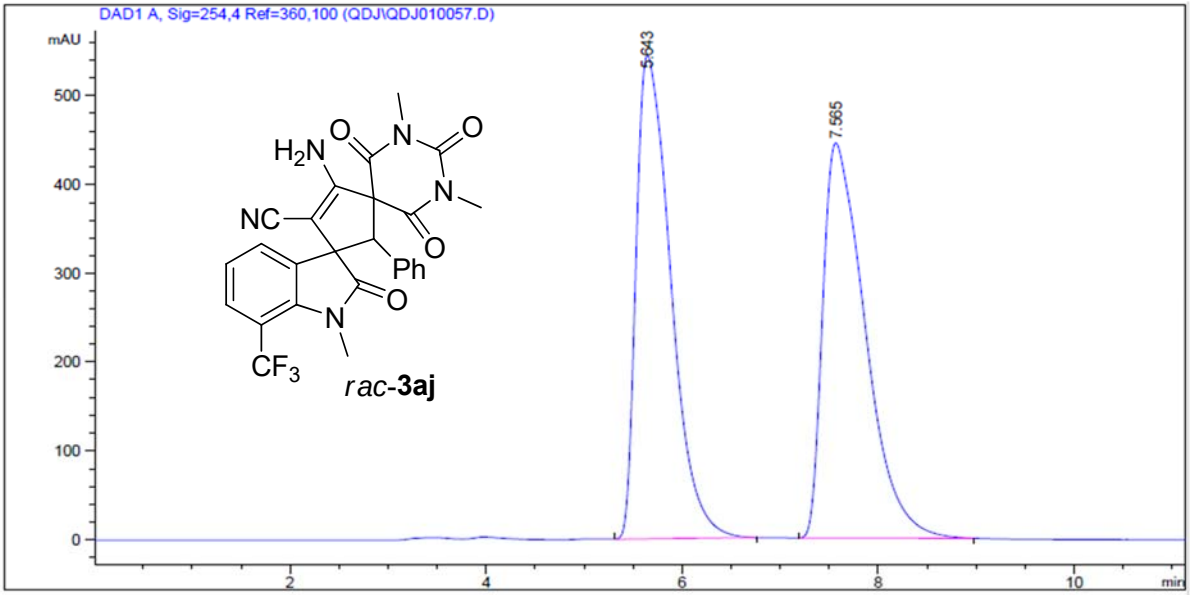
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.322	BB	0.5471	1.15330e4	303.65527	100.0000



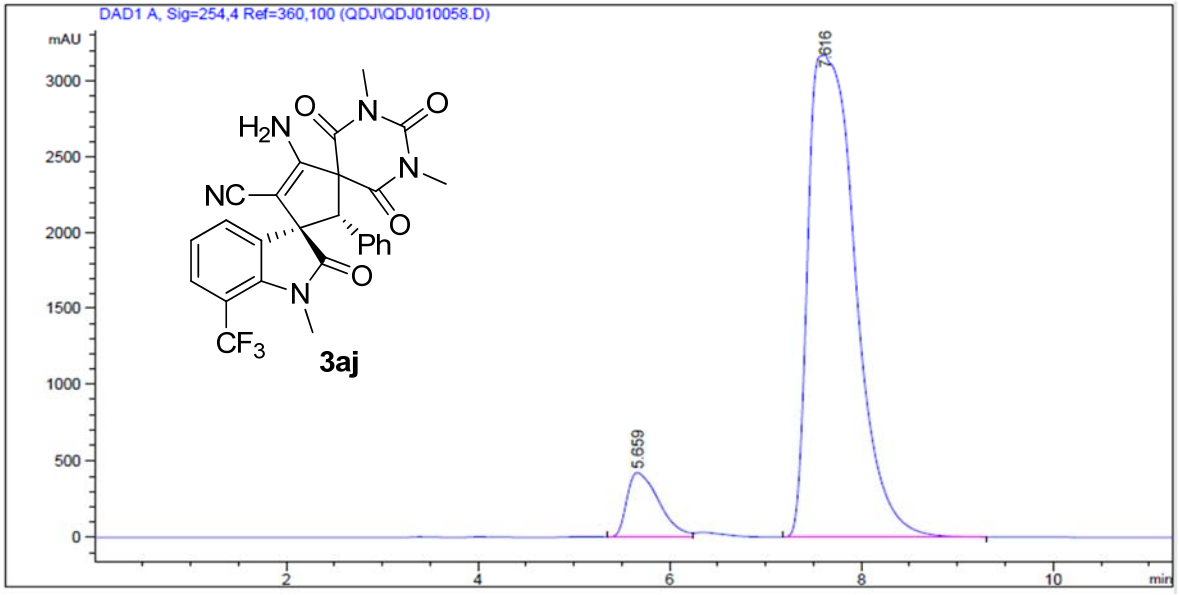
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.478	BB	2.3825	2.10775e4	116.40337	51.4196
2	45.725	BB	2.6385	1.99137e4	88.59107	48.5804



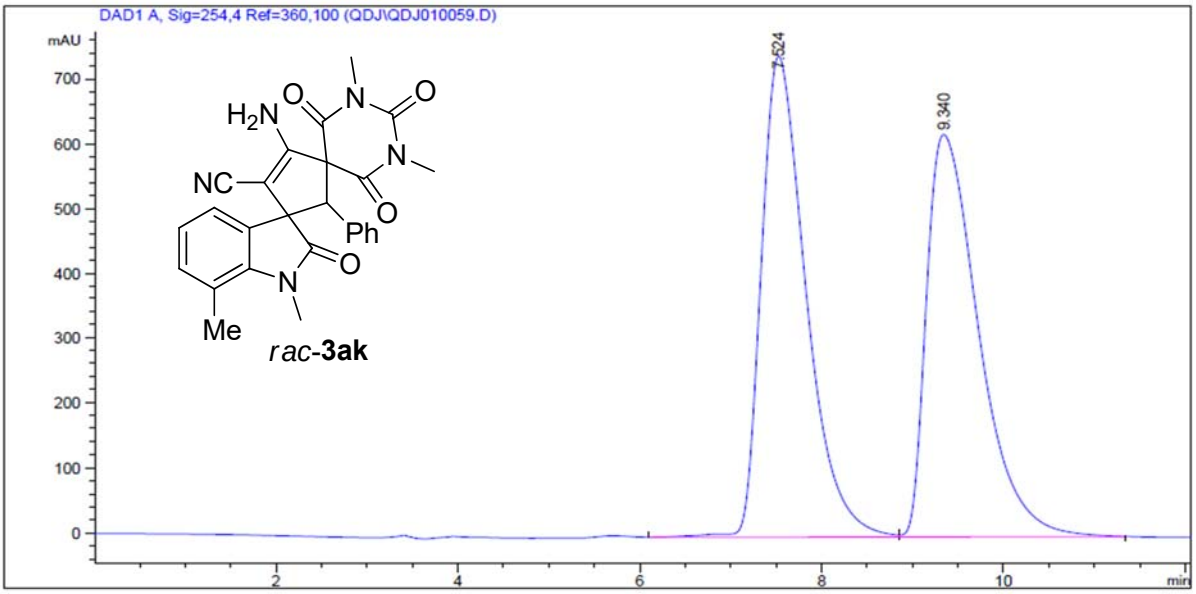
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.537	BB	2.2505	6.34293e4	398.61462	100.0000



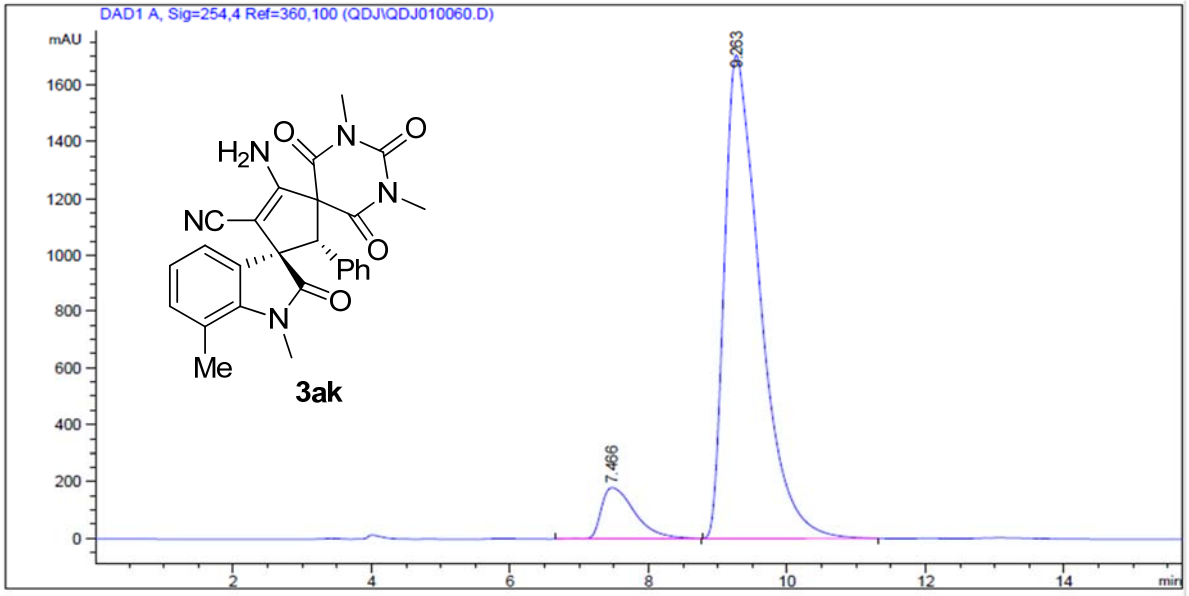
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.643	BB	0.3903	1.33540e4	544.08850	49.9590
2	7.565	BB	0.4788	1.33759e4	444.82416	50.0410



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.659	VV	0.3716	9878.32910	424.39972	8.3496
2	7.616	BB	0.4088	1.08430e5	3171.68530	91.6504



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.524	VV	0.5310	2.53685e4	741.74432	50.7140
2	9.340	VB	0.6177	2.46541e4	620.24689	49.2860



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.466	BB	0.5302	6140.44238	180.81670	9.1617
2	9.263	BB	0.5163	6.08822e4	1706.40686	90.8383