

Supporting Information

N-Heterocyclic carbene-catalyzed [4+2] cyclization of α,β -unsaturated carboxylic acids bearing γ -H with isatins: An enantioselective synthesis of spirocyclic oxindole–dihydropyranones

Ling Zhu, Chenxia Yu, Tuanjie Li, Yuhong Wang, Yinan Lu, Wenjing Wang and Changsheng Yao*

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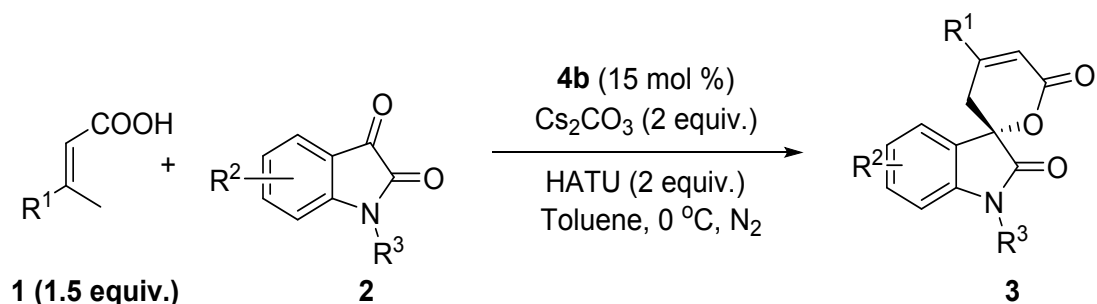
1. General methods

Common reagents and materials were purchased from commercial sources and purified by recrystallization or distillation. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a FT-IR-Tensor 27 spectrometer in KBr pellets and reported in cm^{-1} . ^1H NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in CDCl_3 (100 MHz, ^{13}C NMR) with chemical shift (δ) given in ppm relative to TMS as internal standard. High-resolution mass spectra (HRMS) were obtained on a microTOF-Q II HRMS/MS instrument (Bruker) with the technique of electrospray ionization.

2. Abstract

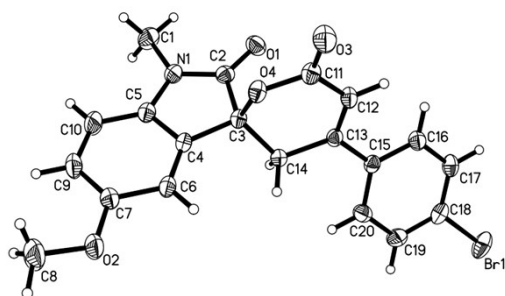
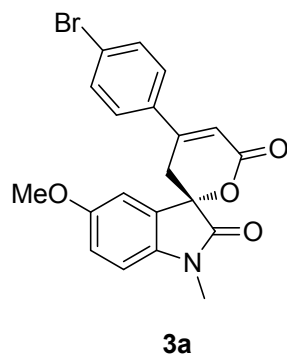
An NHC-catalyzed asymmetric [4+2] annulation of isatins and α,β -unsaturated carboxylic acids bearing γ -H gave spirocyclic oxindole-dihydropyranones successfully via in situ activation strategy. This protocol featured easy availability of raw materials, good yields and excellent enantioselectivities (up to 99% ee).

3. Experimental section



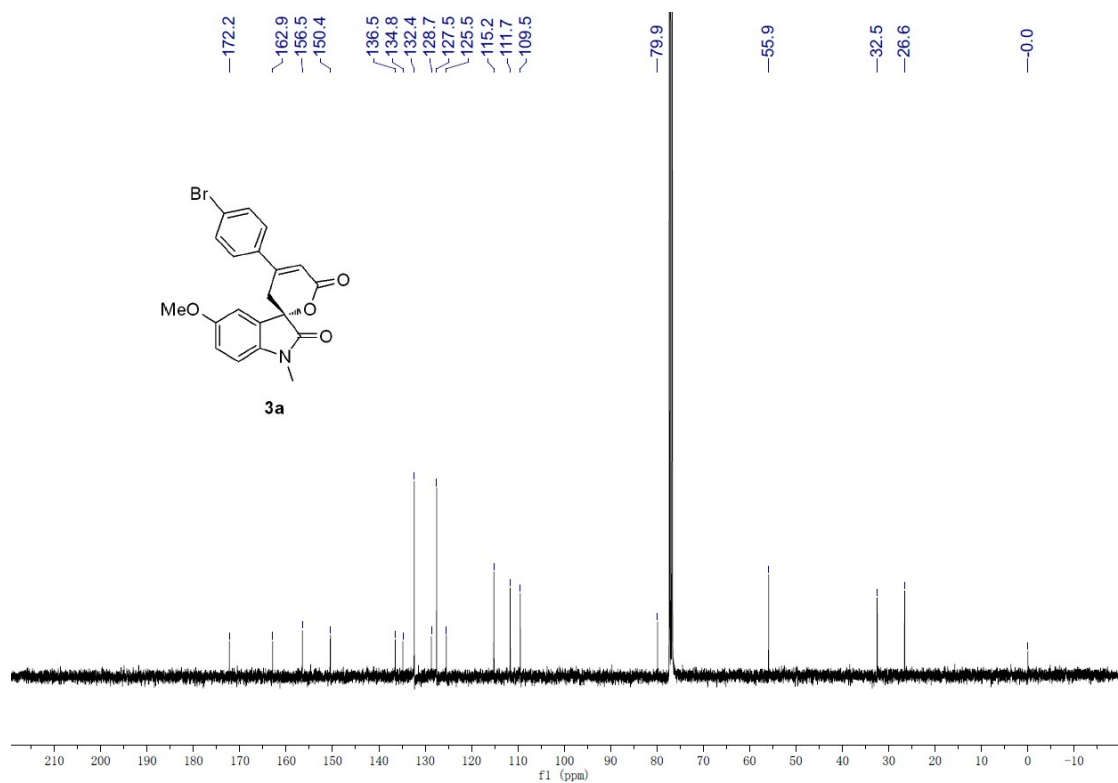
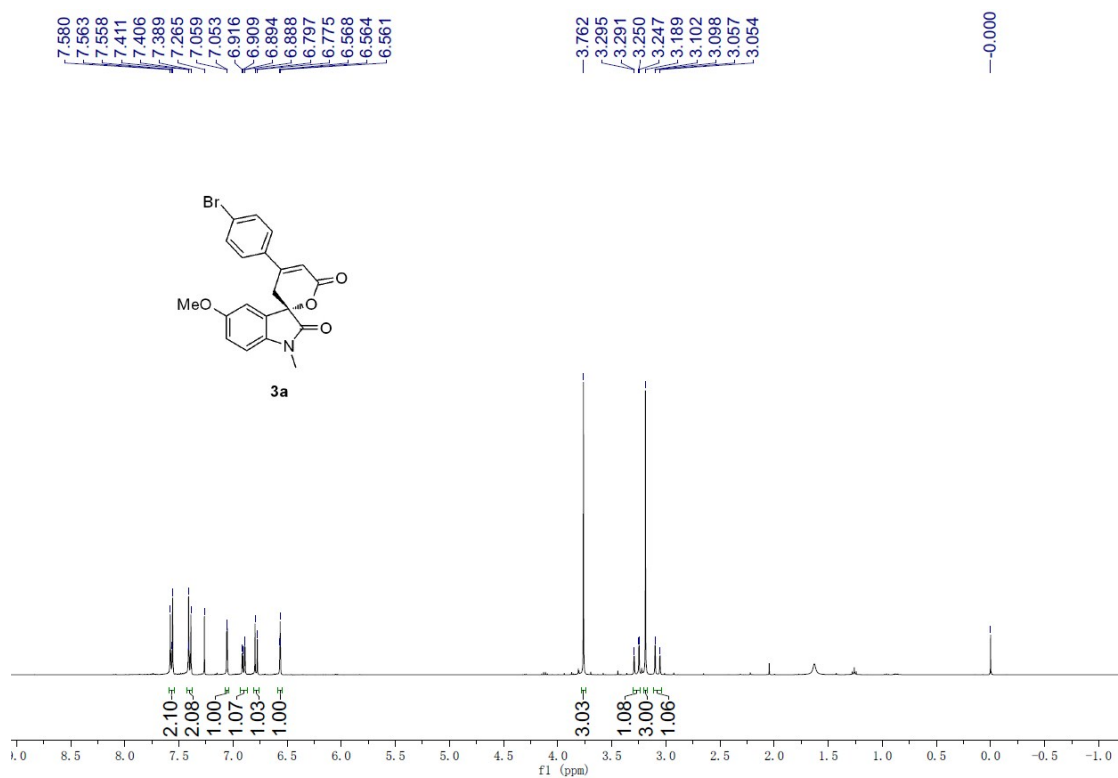
An oven-dried 10-mL Schlenk tube equipped with a magnetic stir bar was charged with triazolium salt **4b** (12.6 mg, 0.03 mmol), Cs_2CO_3 (130 mg, 0.4 mmol), α,β -unsaturated carboxylic acid **1** (0.3 mmol), isatin **2** (0.2 mmol) and HATU (228 mg, 0.6 mmol). This tube was closed with a septum, evacuated, and refilled with nitrogen. To this mixture was added freshly distilled toluene (2 mL) with a syringe. Then the mixture was stirred at 0°C until completion (monitored by TLC). After removal of the solvent under reduced pressure, the resulting crude residue was purified by column chromatography (silicagel, mixtures of petroleum ether/ethyl acetate, 3:1, v/v) to afford the desired product **3**.

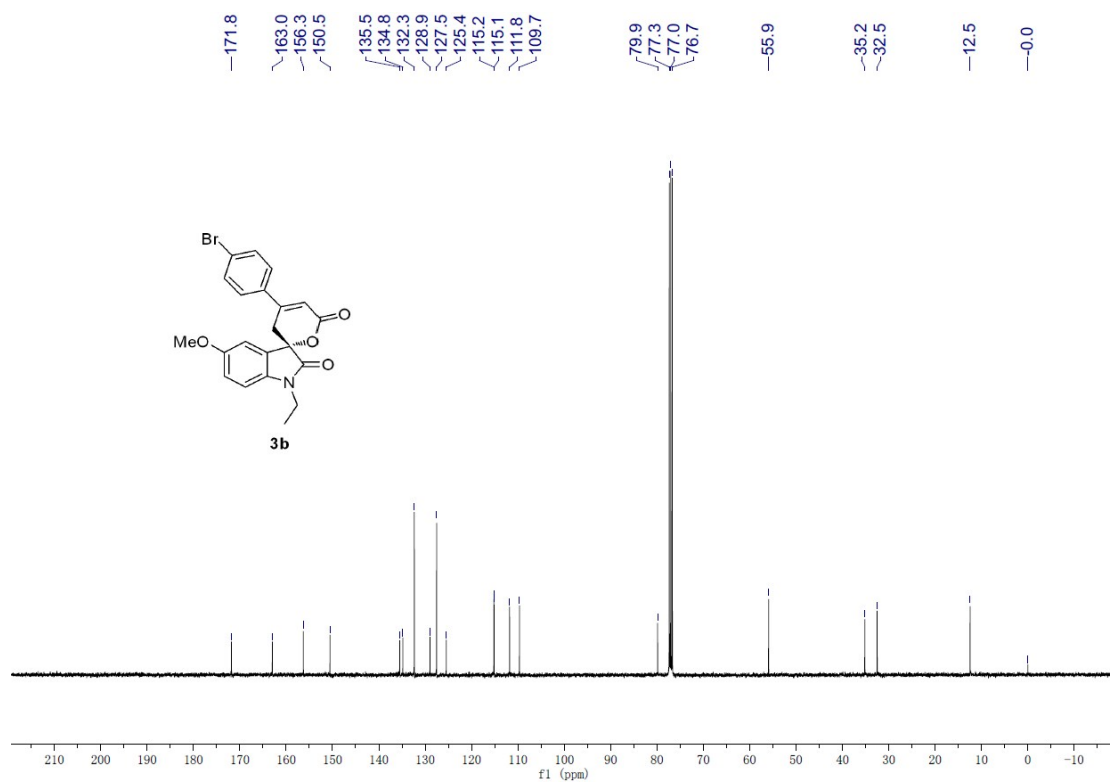
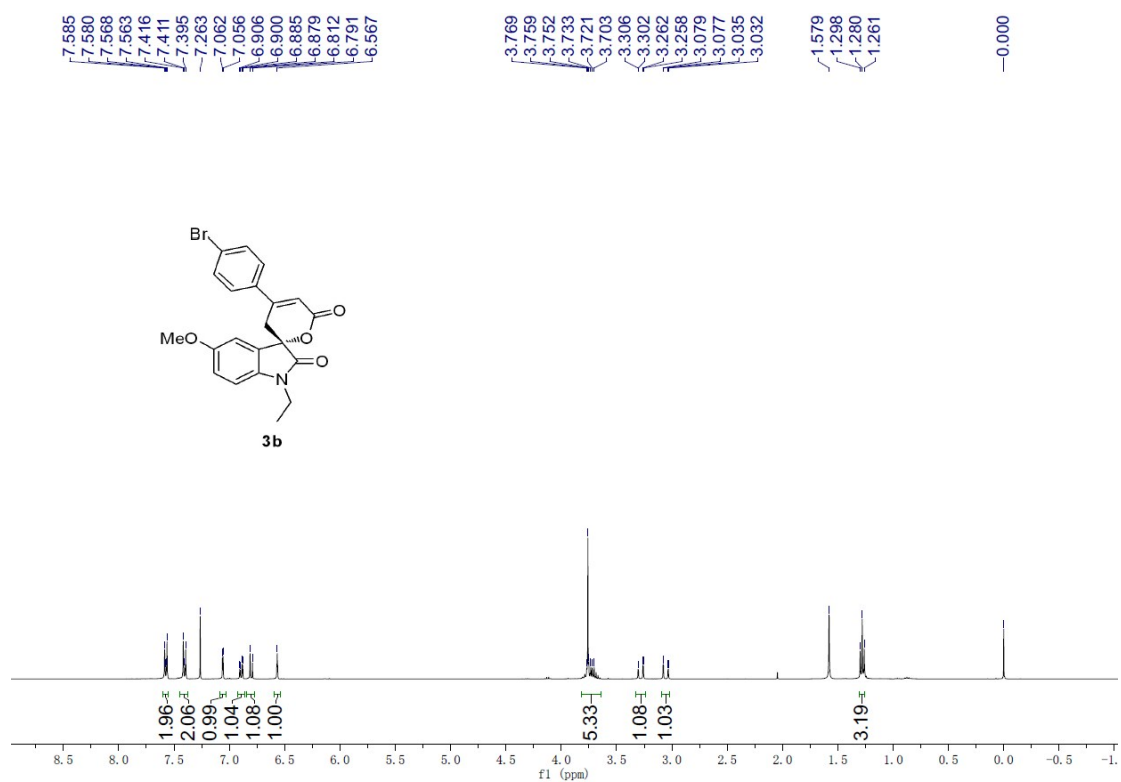
4. X-ray structure of 3a

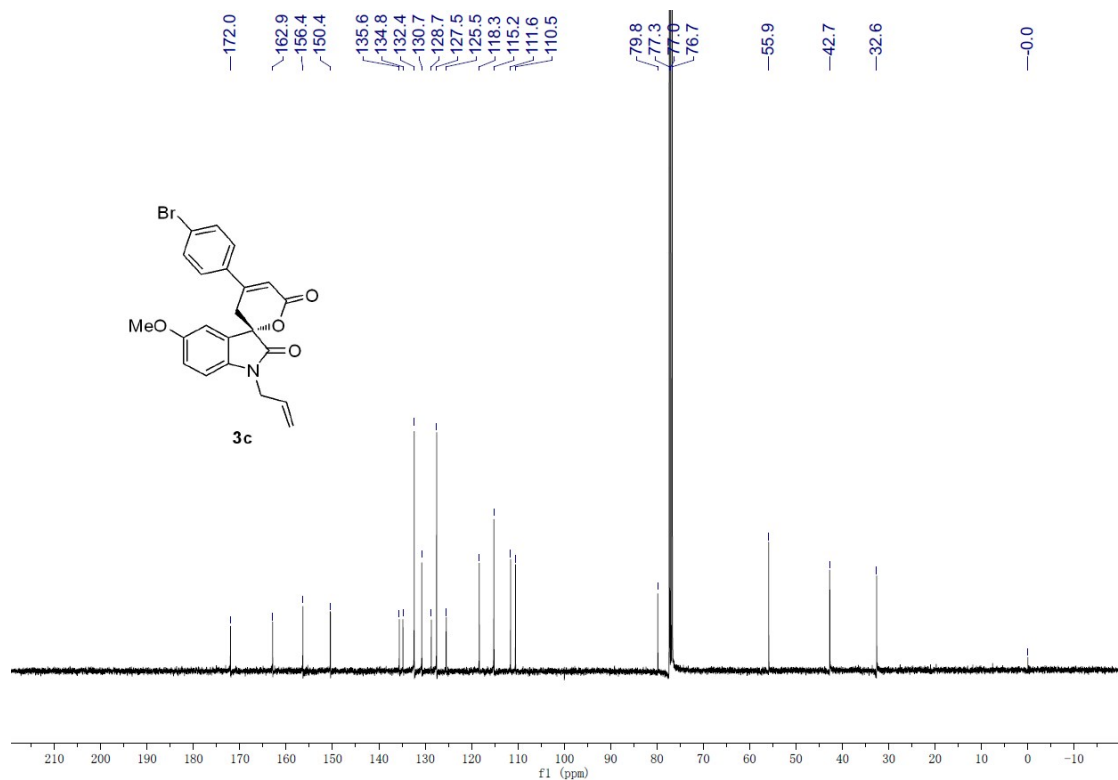
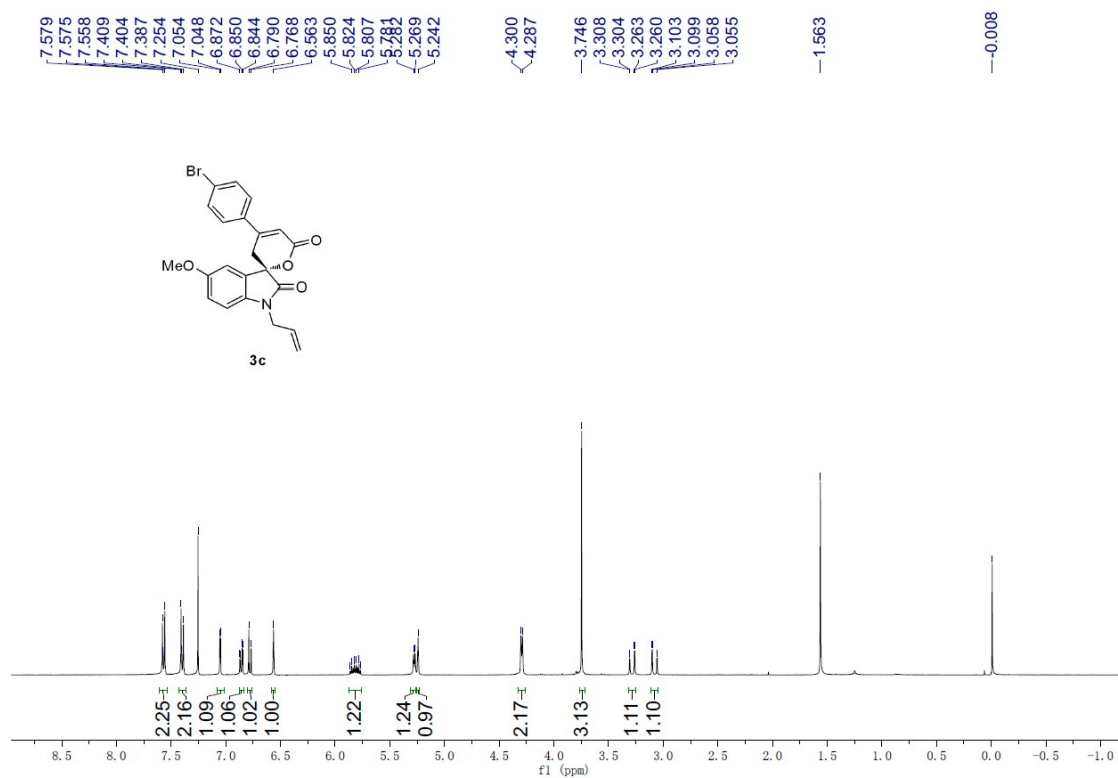


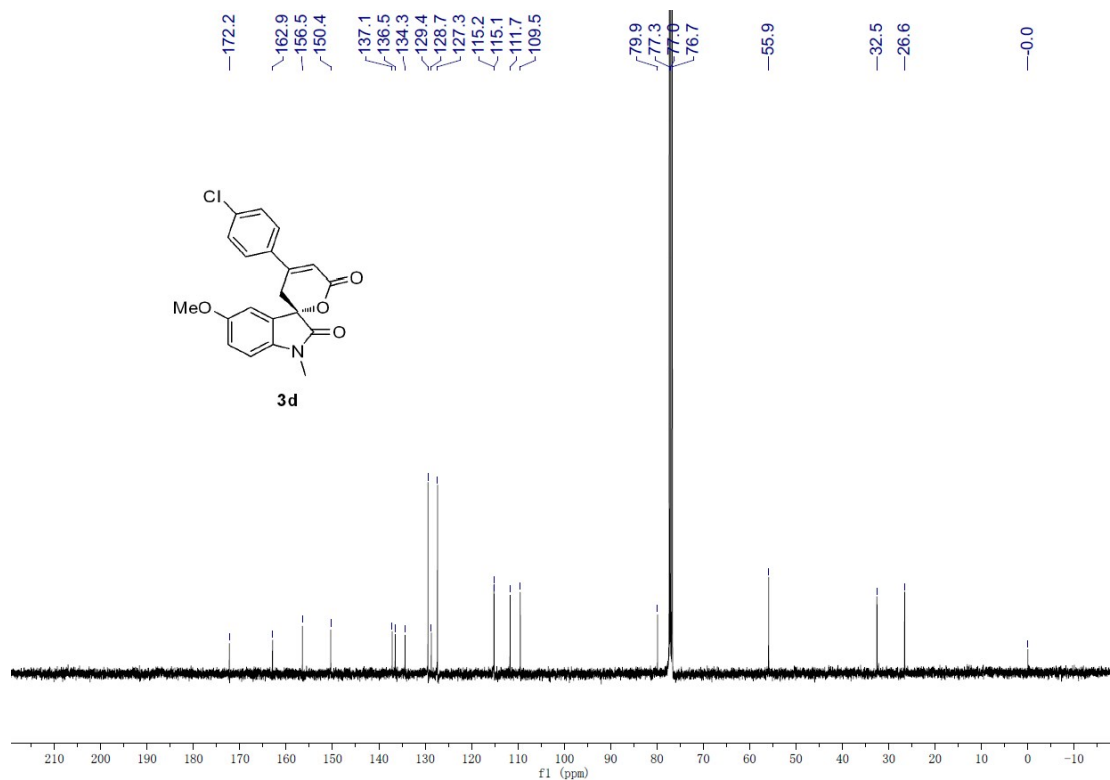
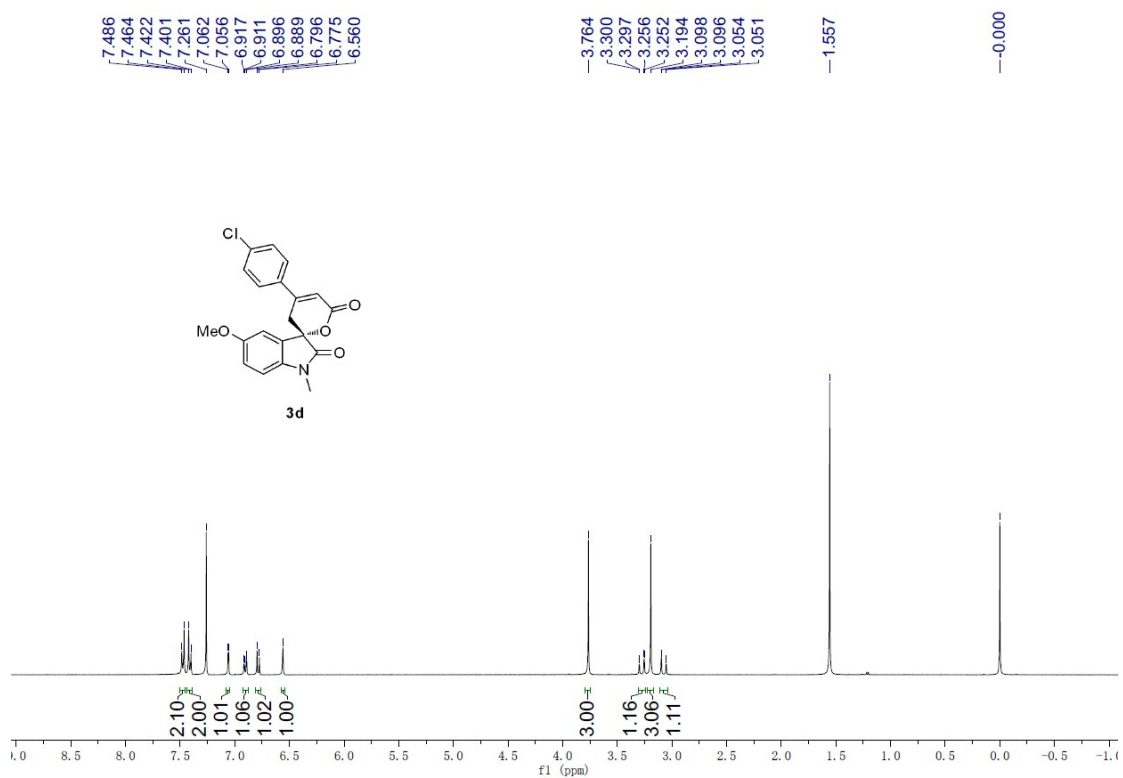
The crystal of compound **3a** was prepared from the solution in petroleum ether/ethyl acetate (M.P.: 207-208 °C). Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1046964. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 1223 336033 or email: deposit@ccdc.cam.ac.uk).

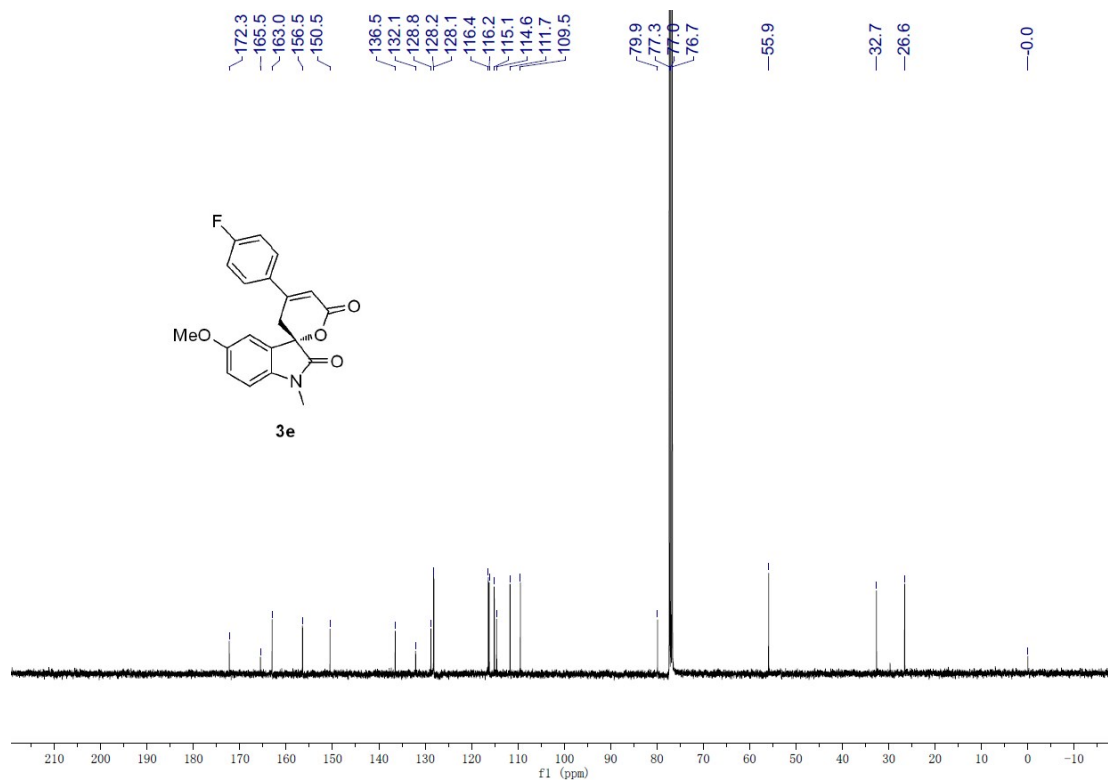
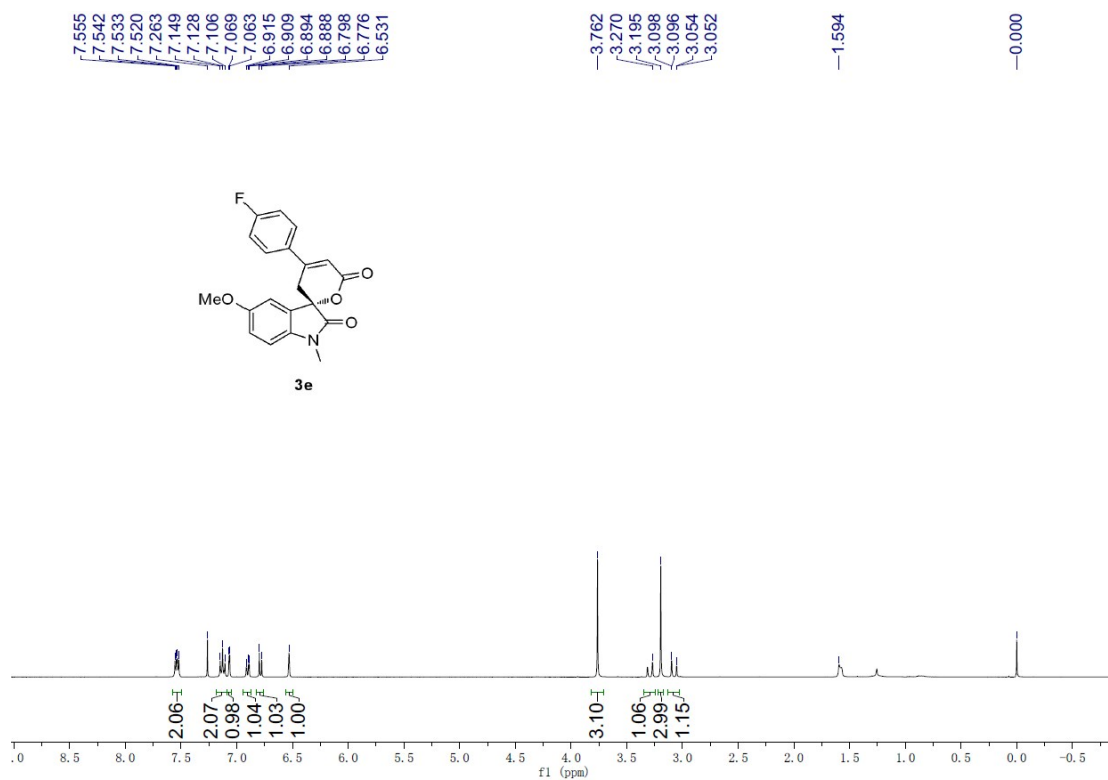
5. NMR Spectures

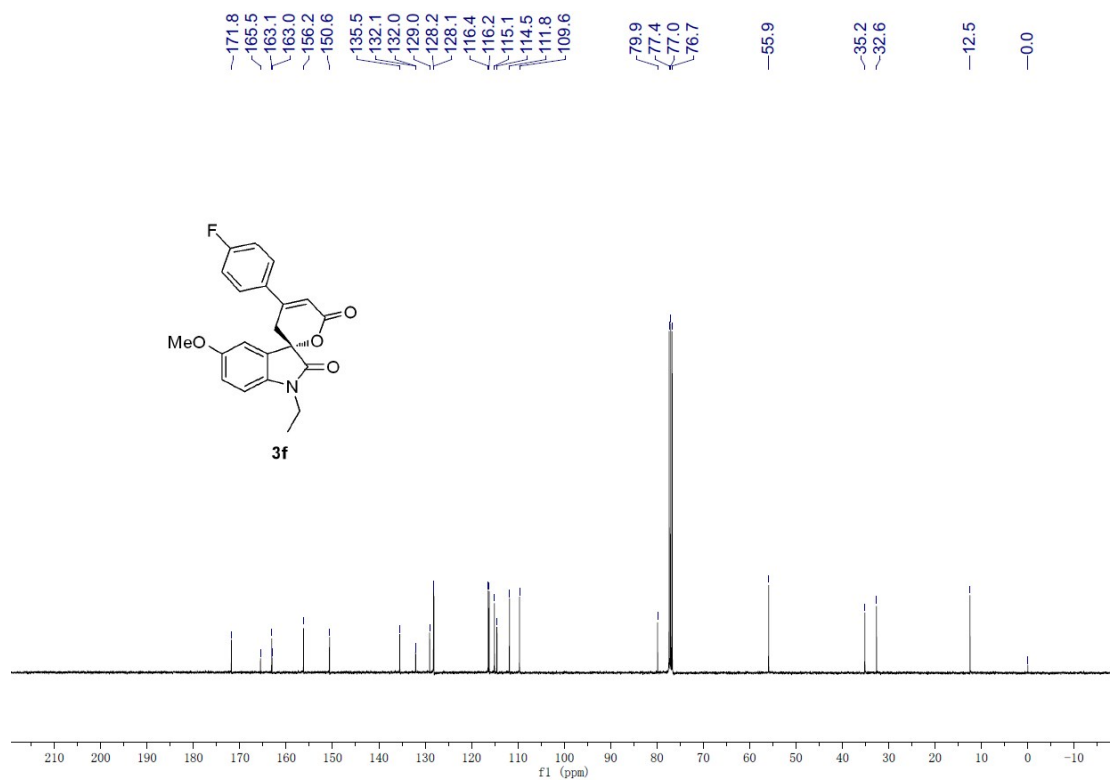
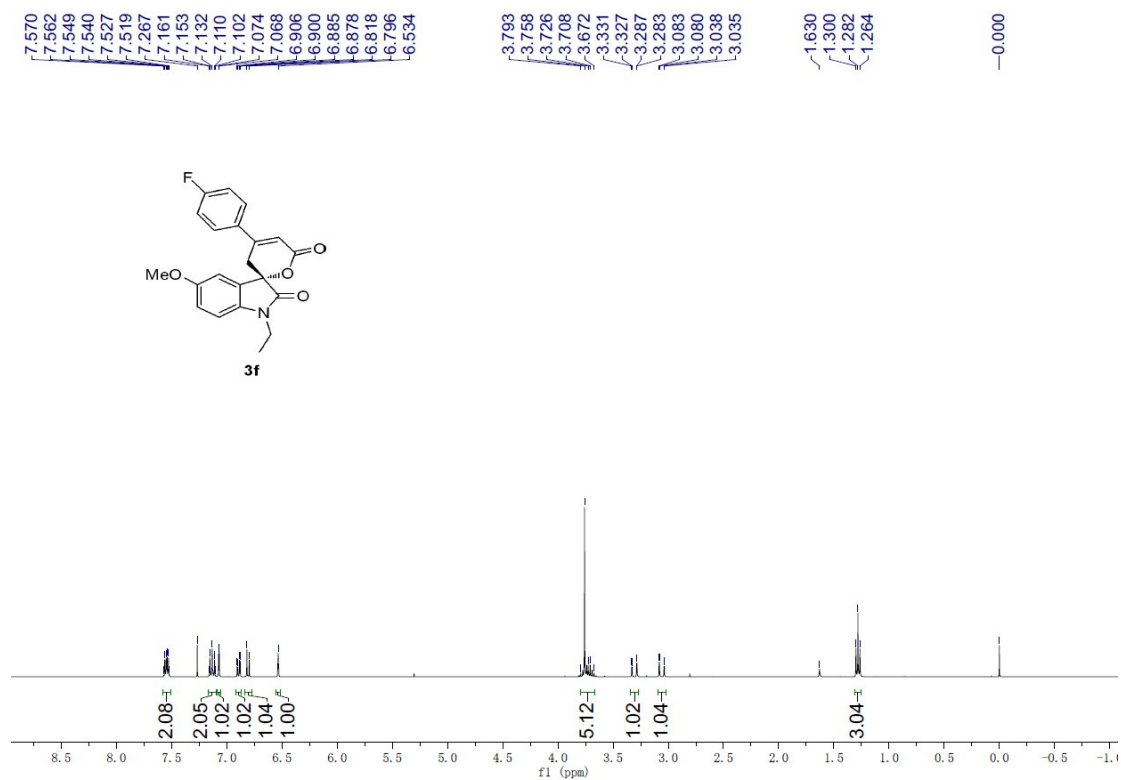


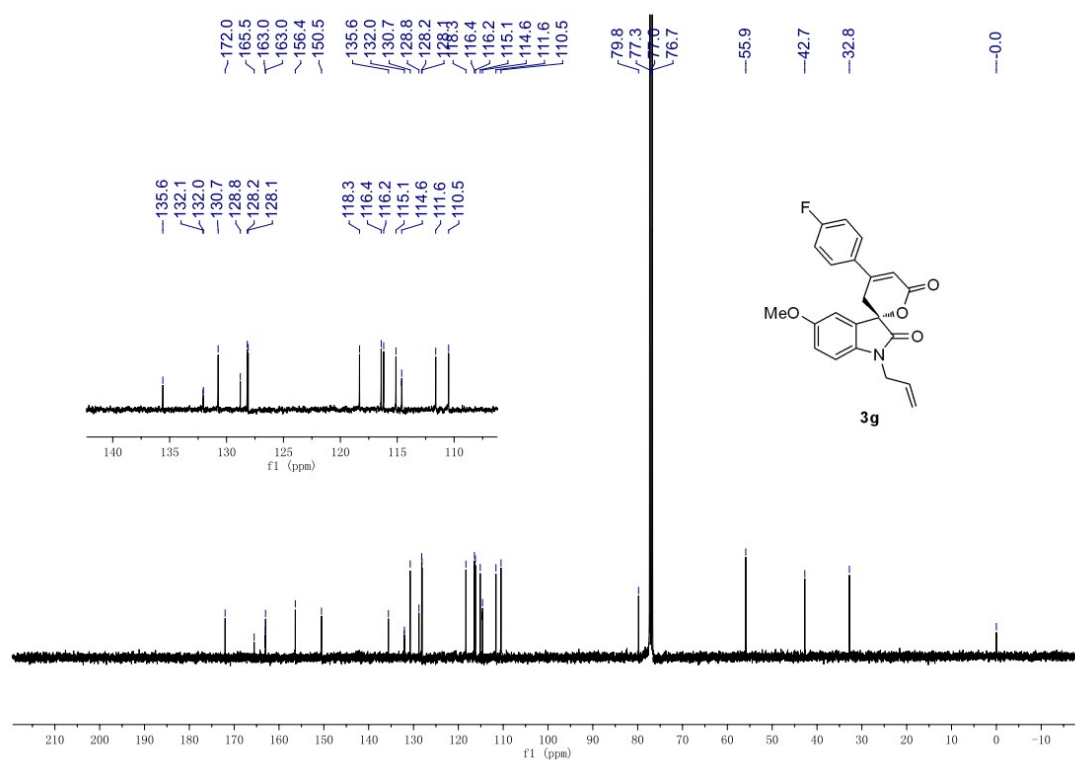
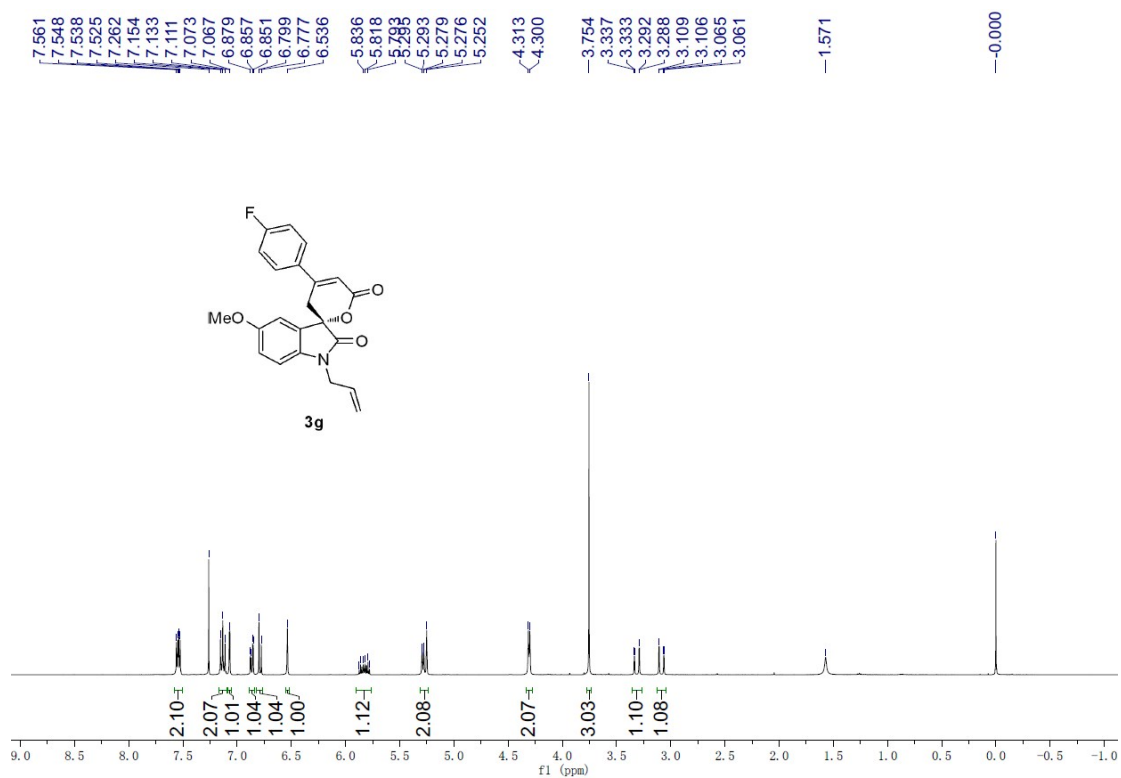


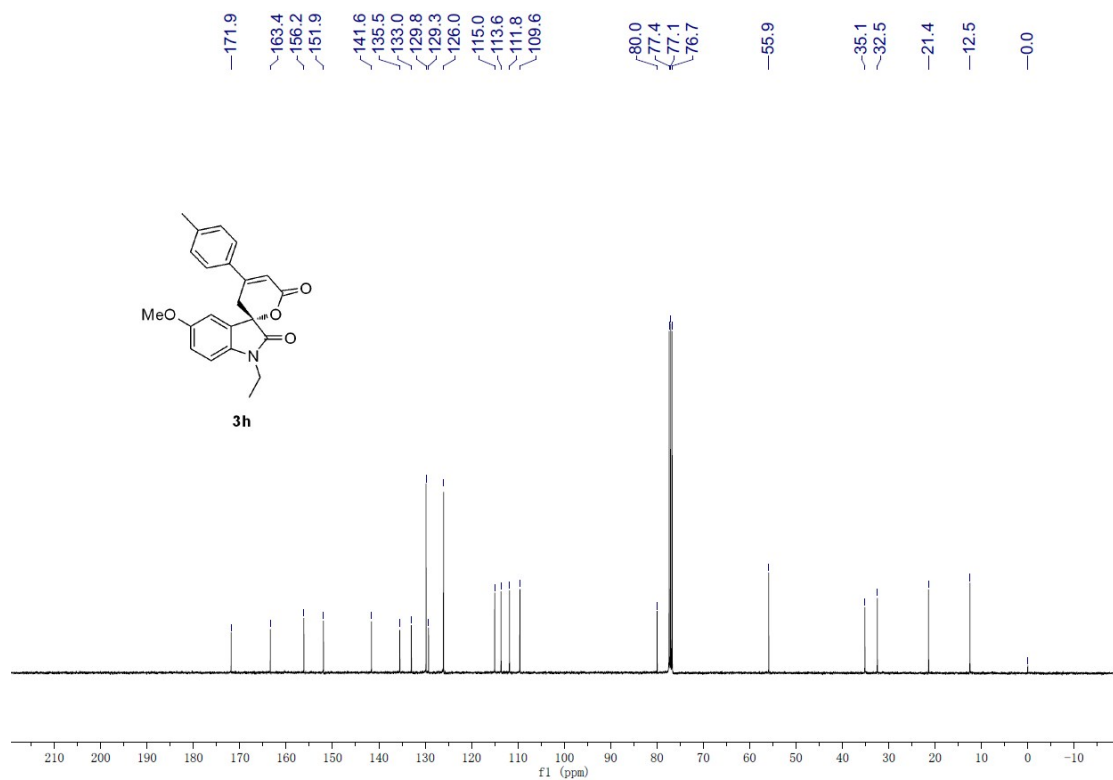
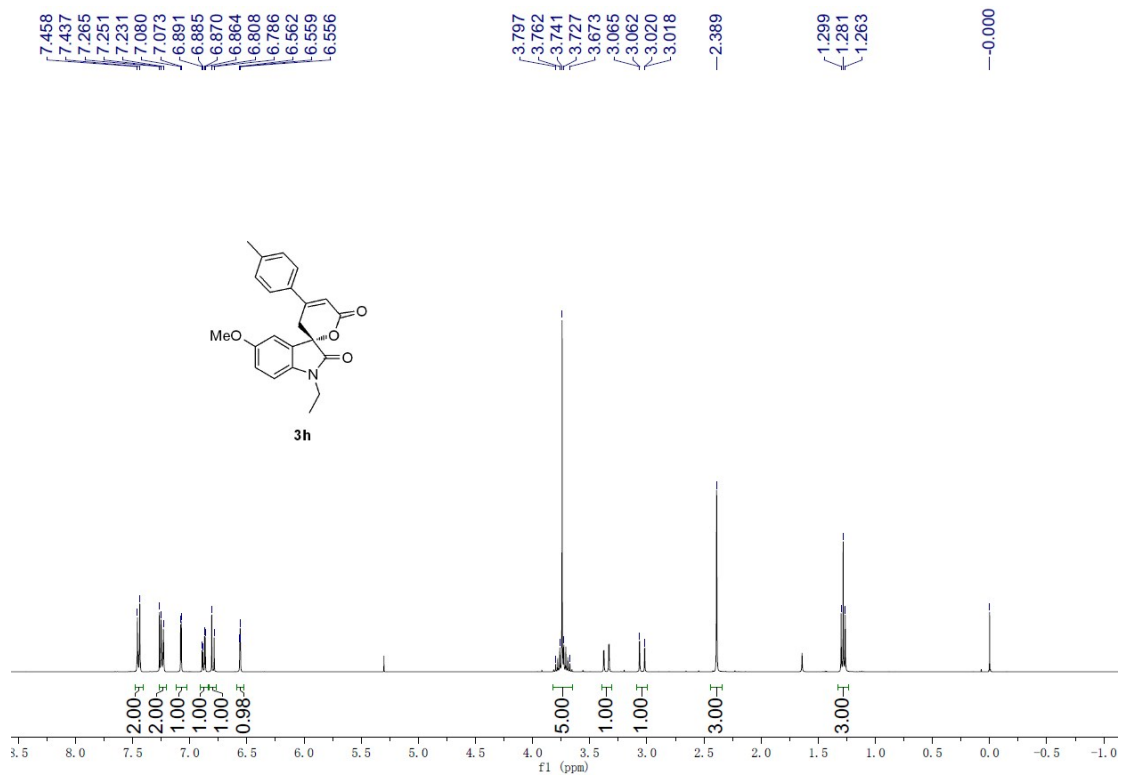


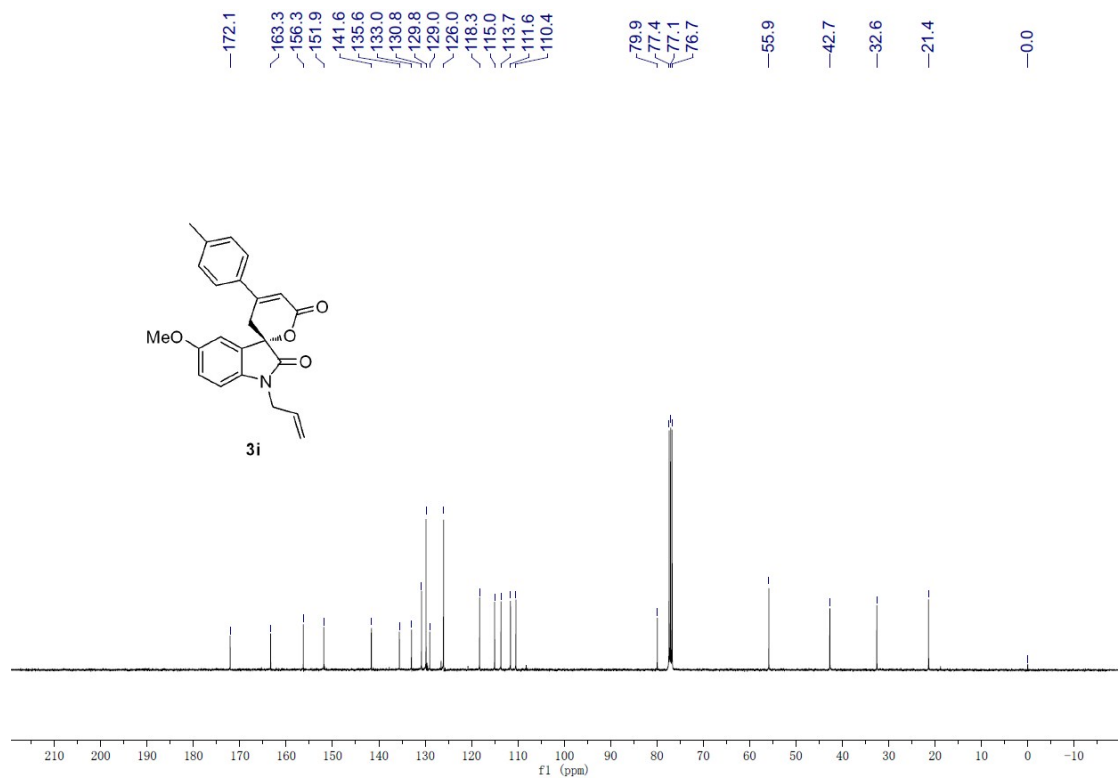
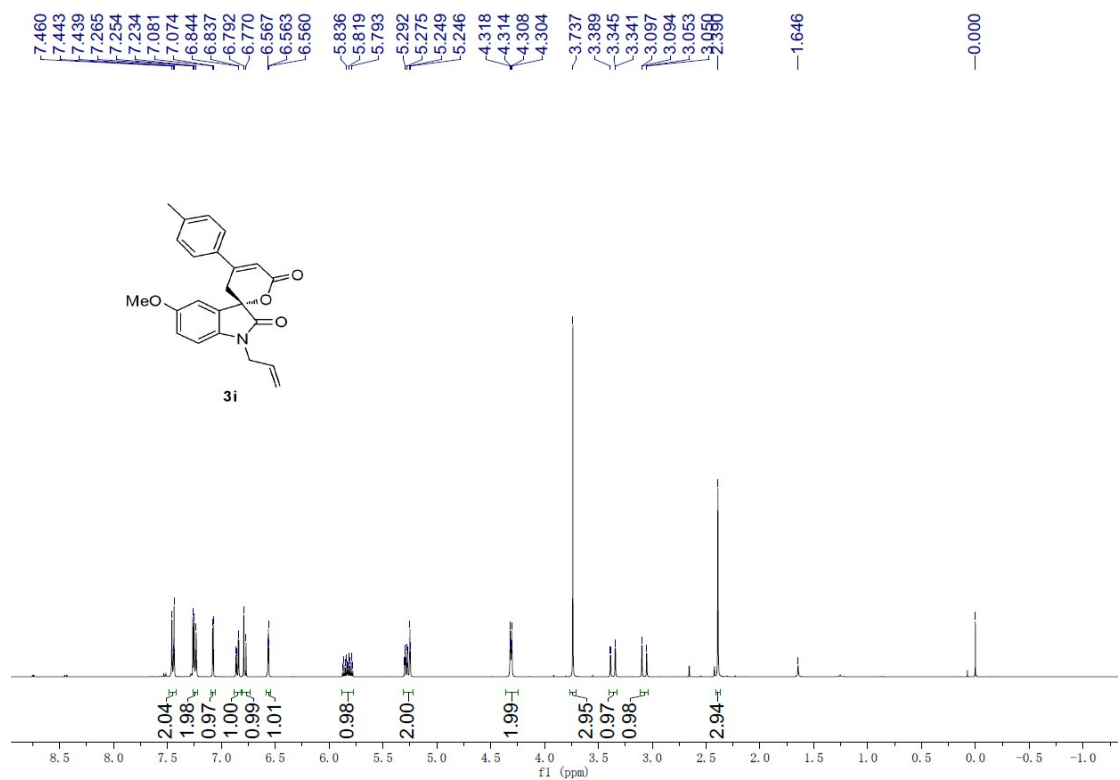


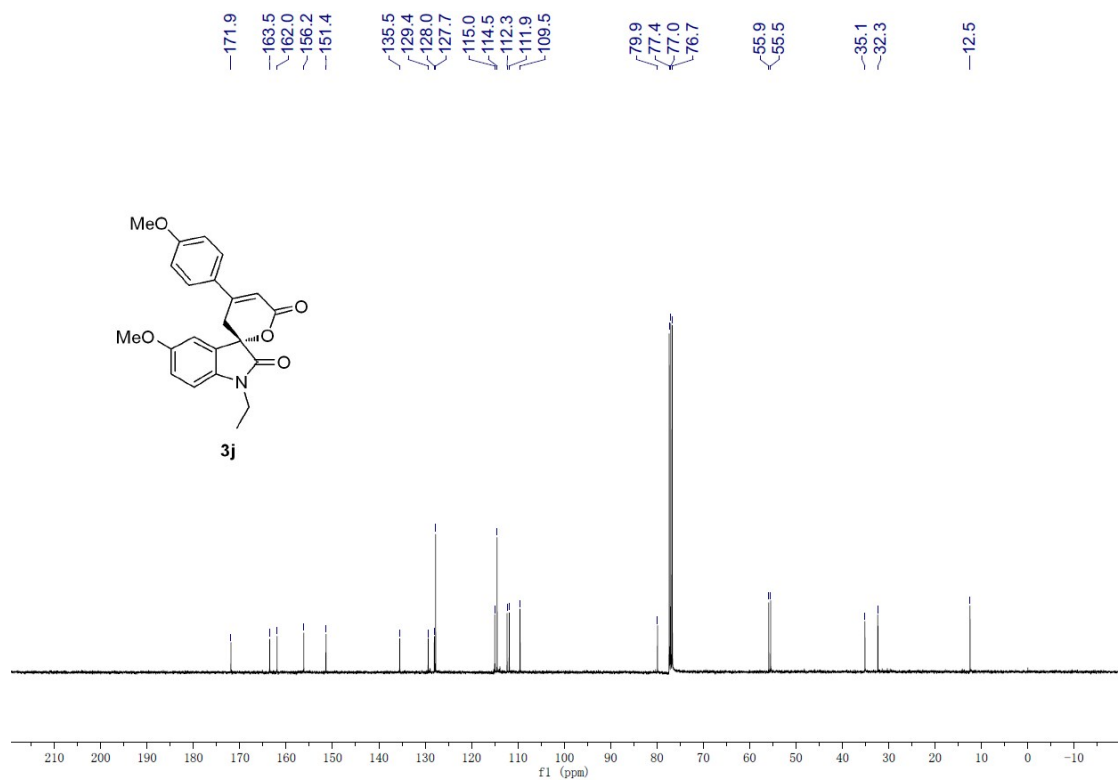
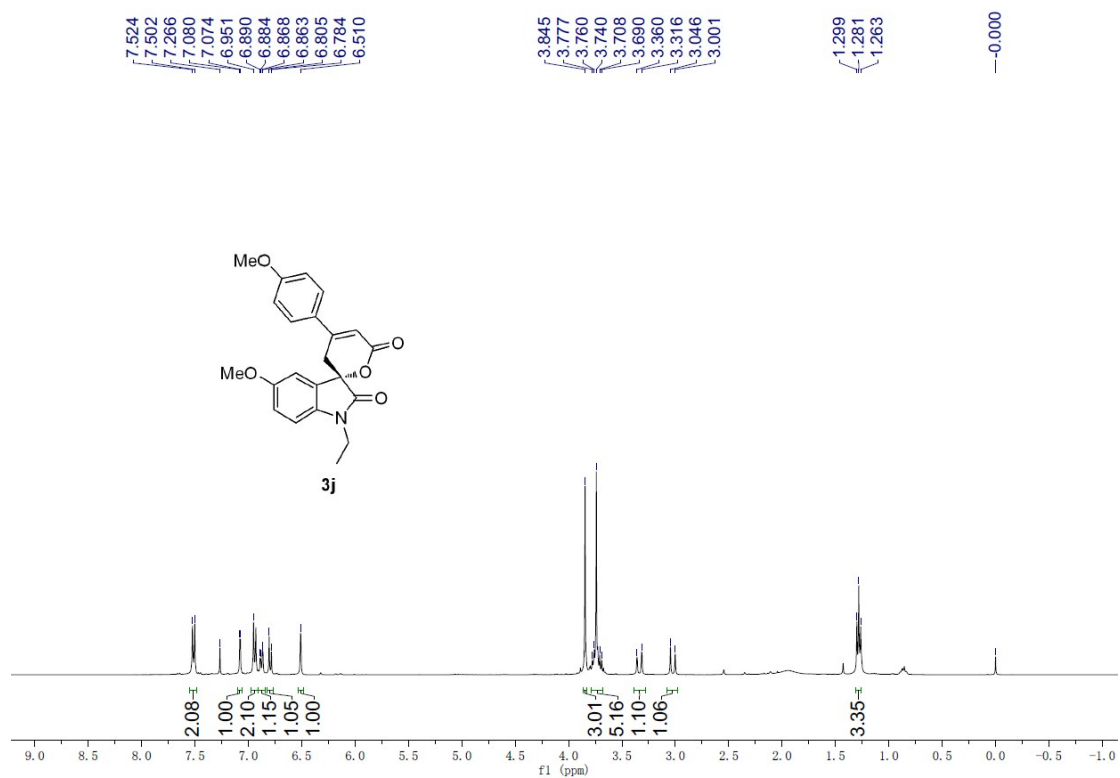


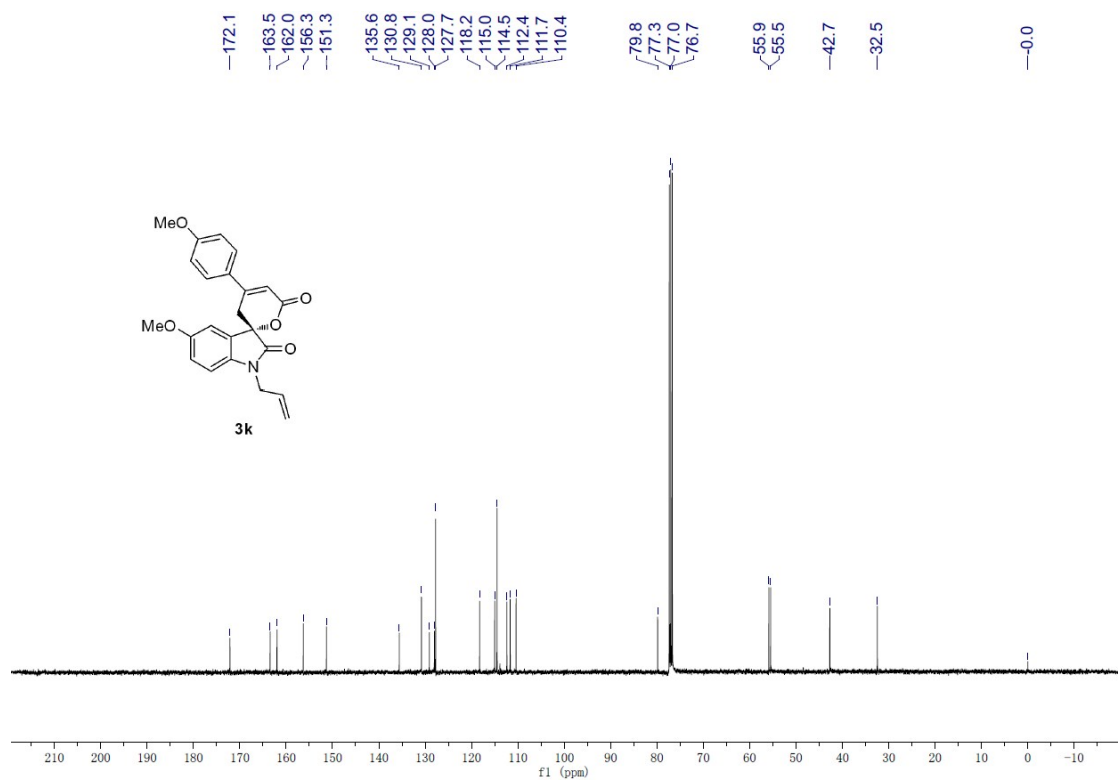
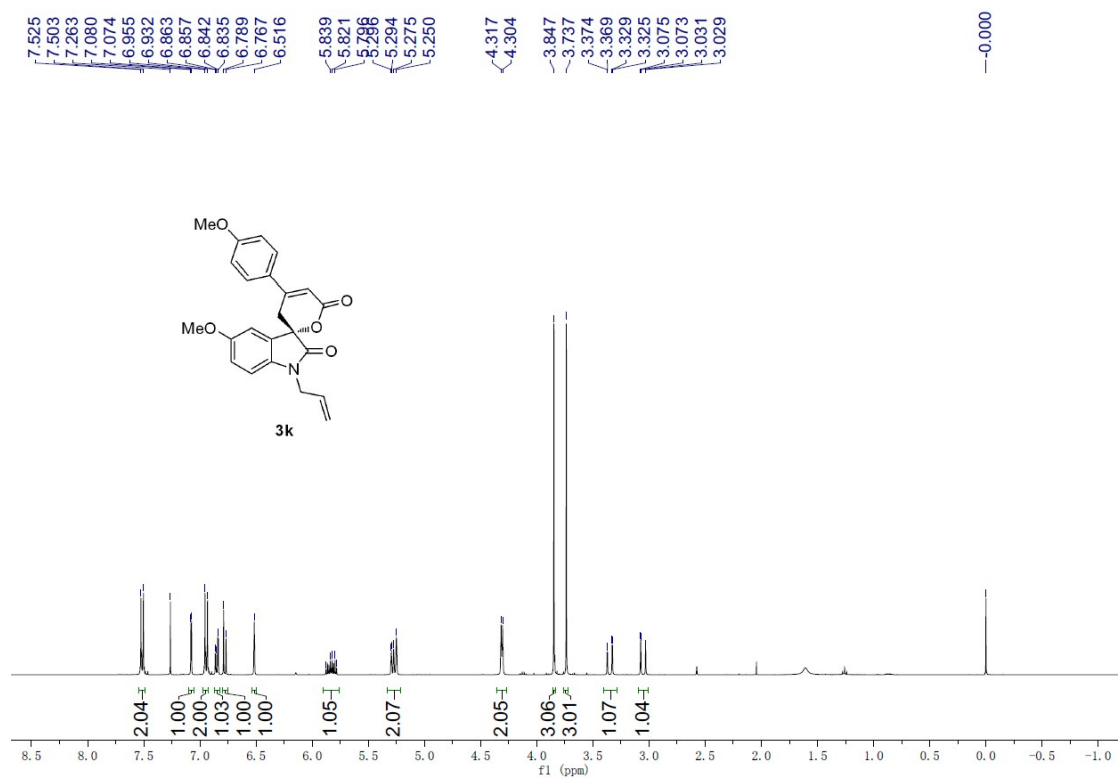


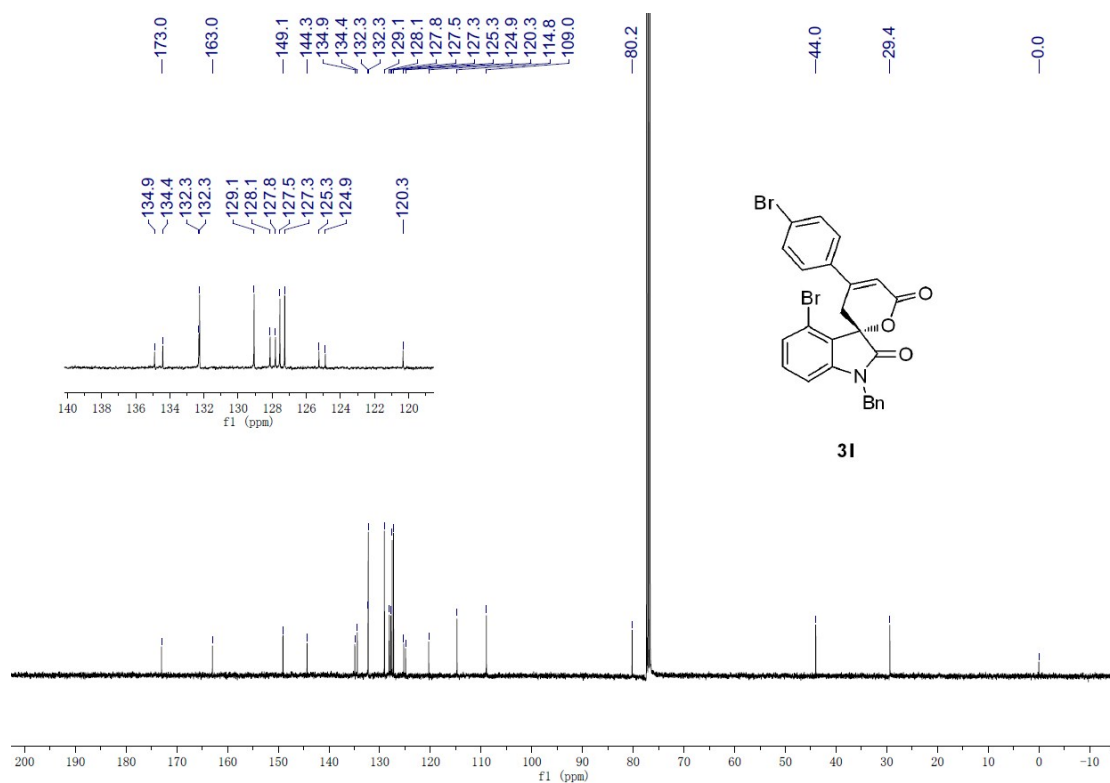
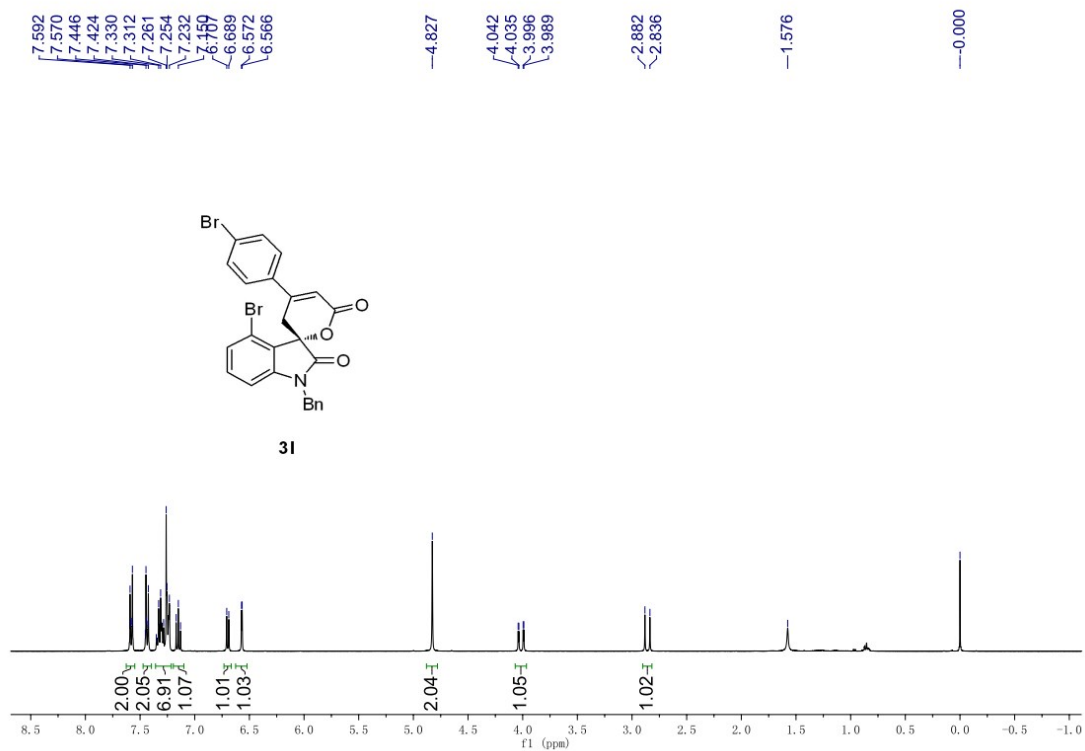


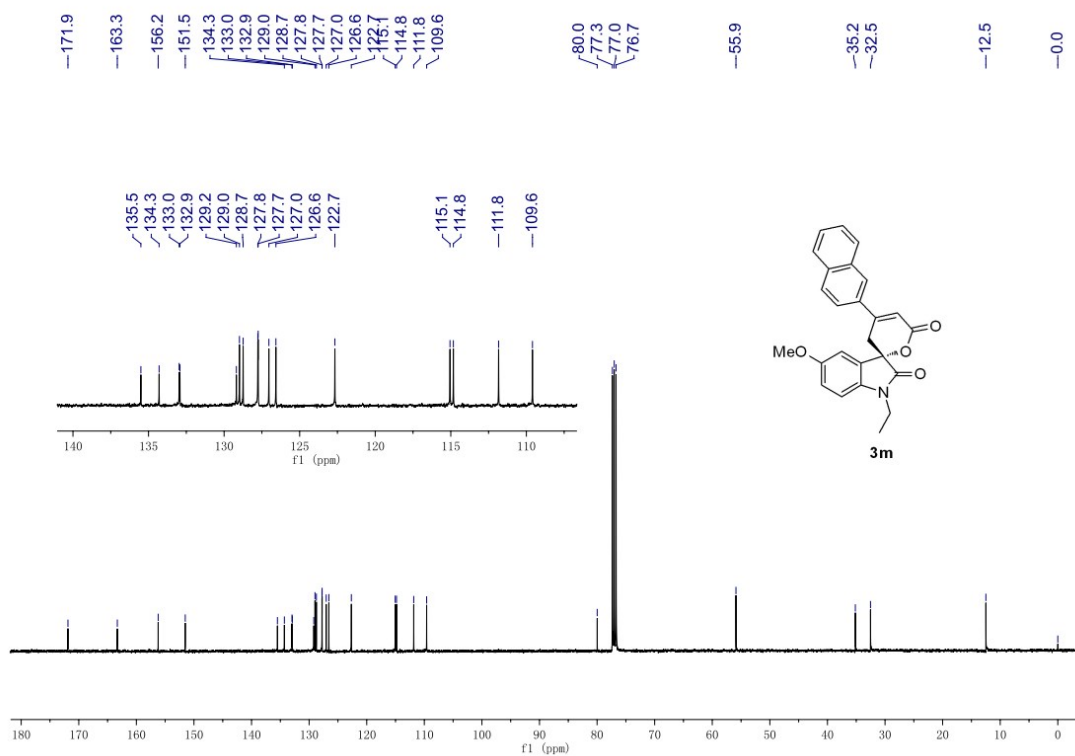
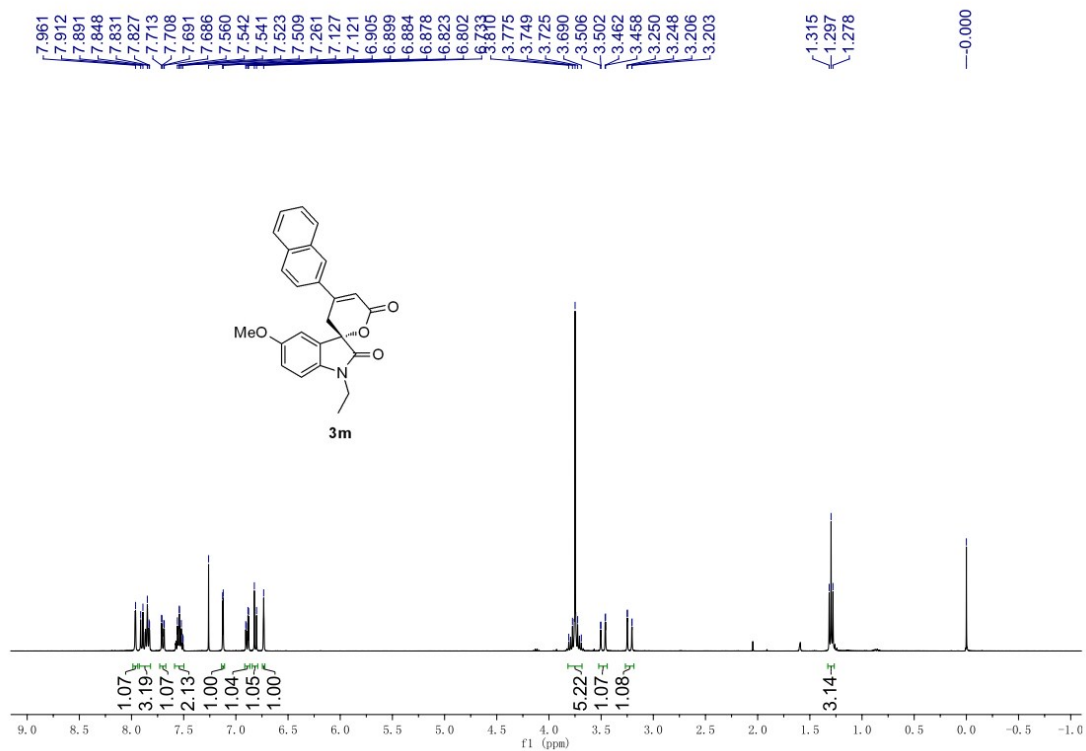


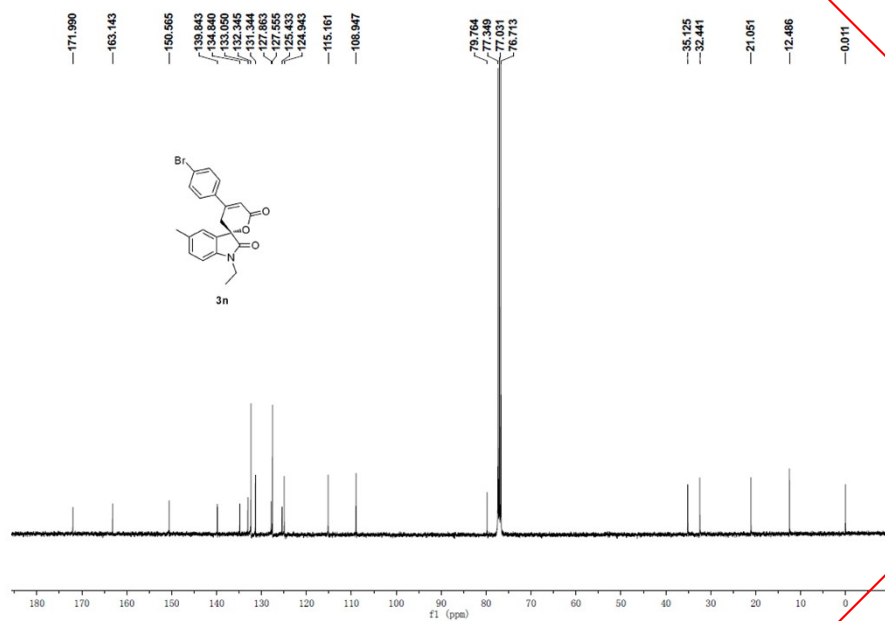
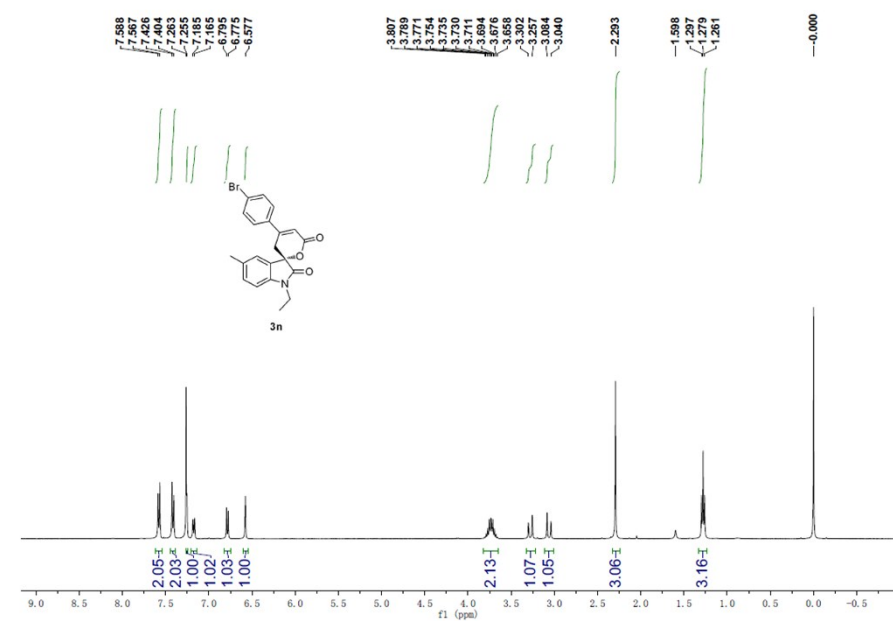




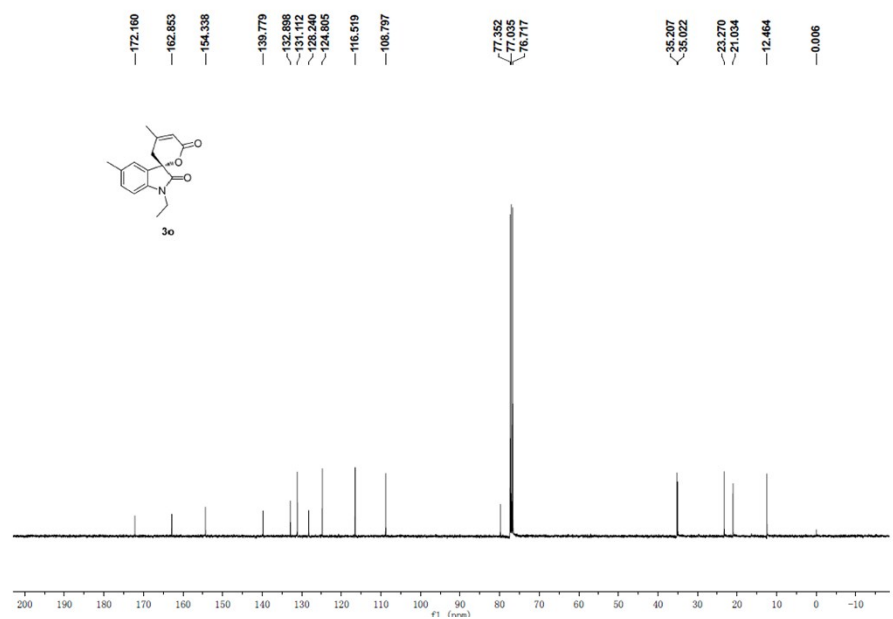
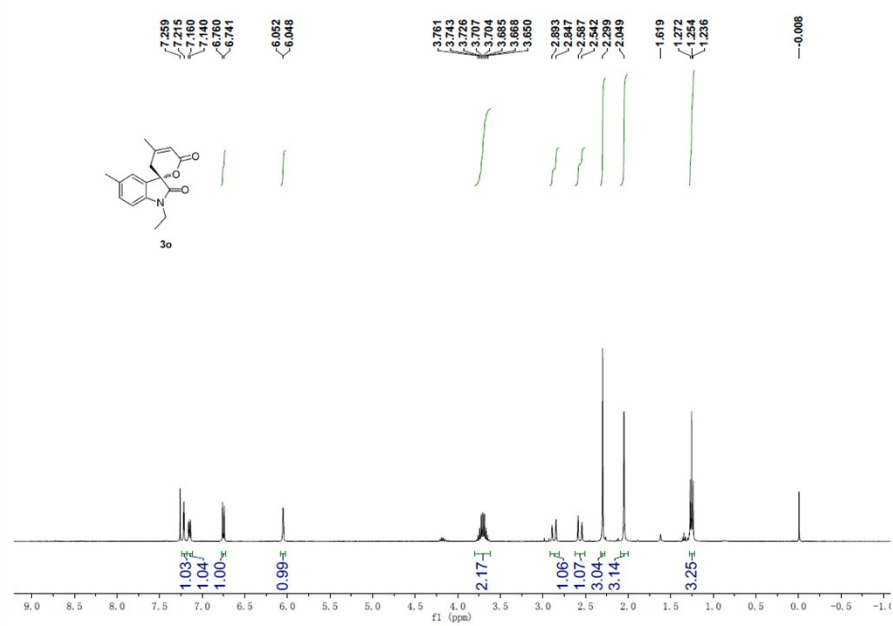






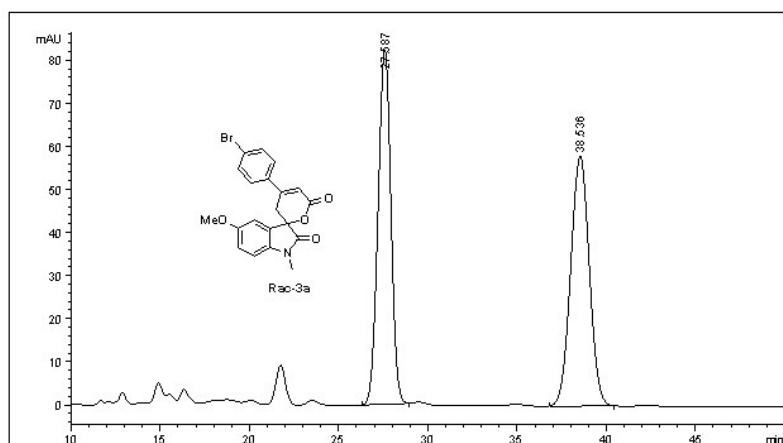


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6. HPLC Spectures



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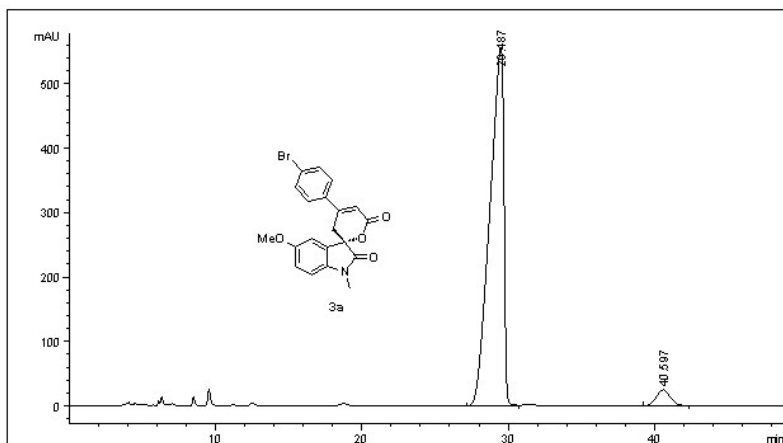
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 C, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.587	BB	0.7812	4128.06299	82.30220	49.5387
2	38.536	BB	1.1140	4204.93848	57.98717	50.4613

Totals : 8333.00146 140.28937

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Area Percent Report

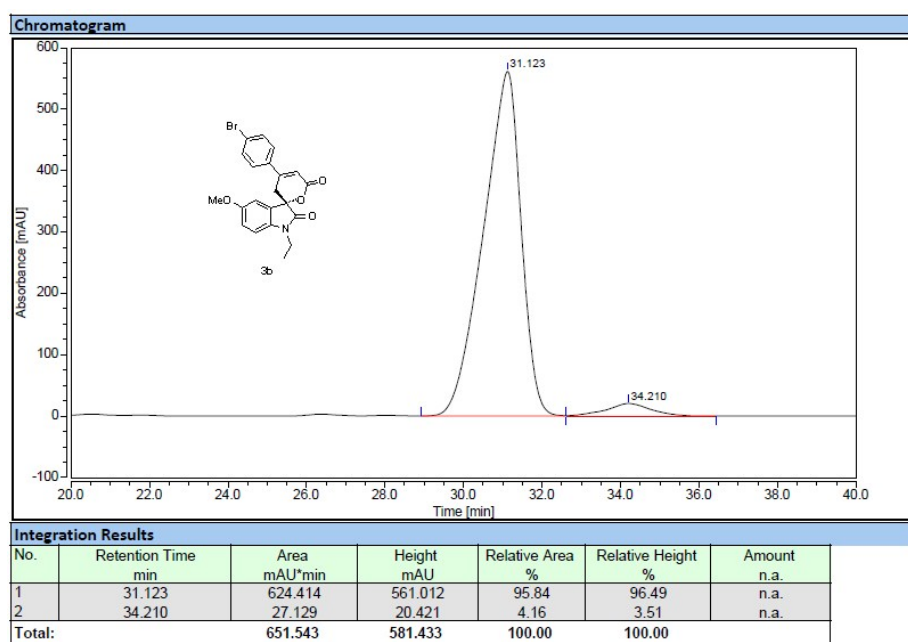
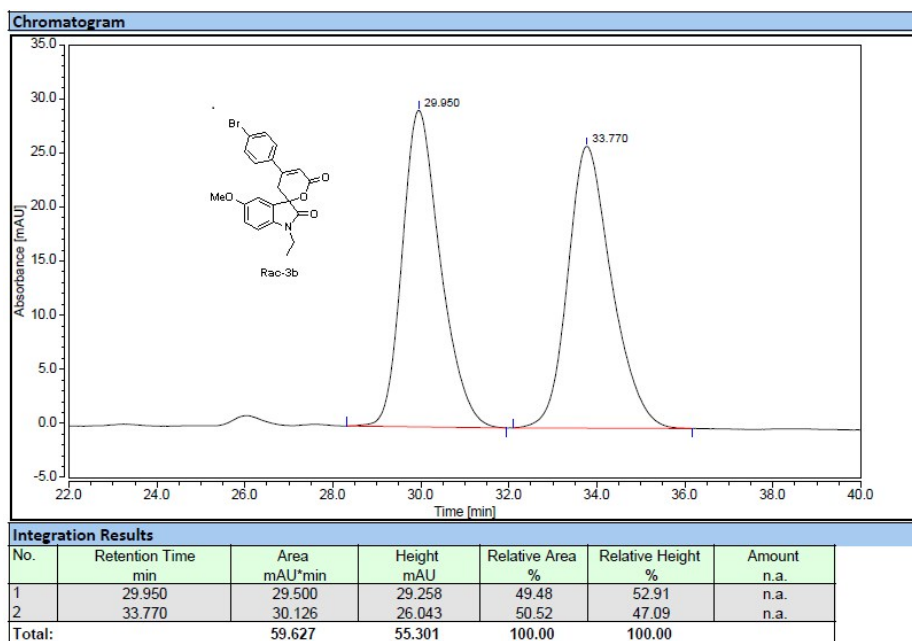
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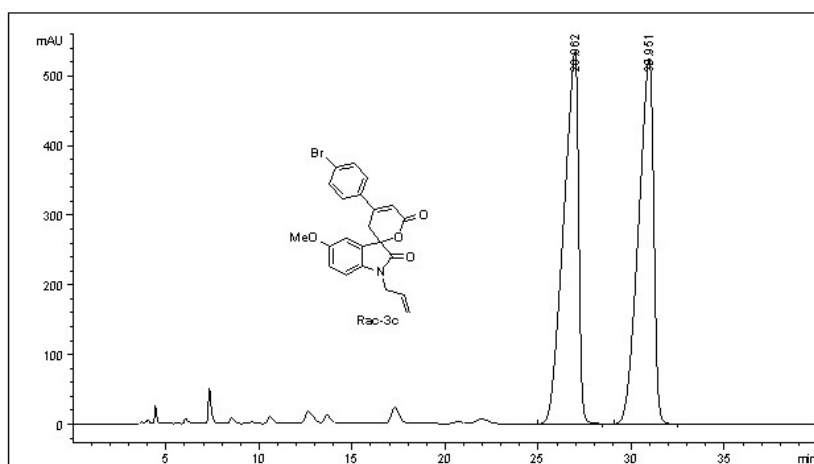
Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.487	BV	0.9737	3.69045e4	556.48242	95.7478
2	40.597	BB	1.0262	1638.94983	24.69736	4.2522

Totals : 3.85434e4 581.17978

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Area Percent Report
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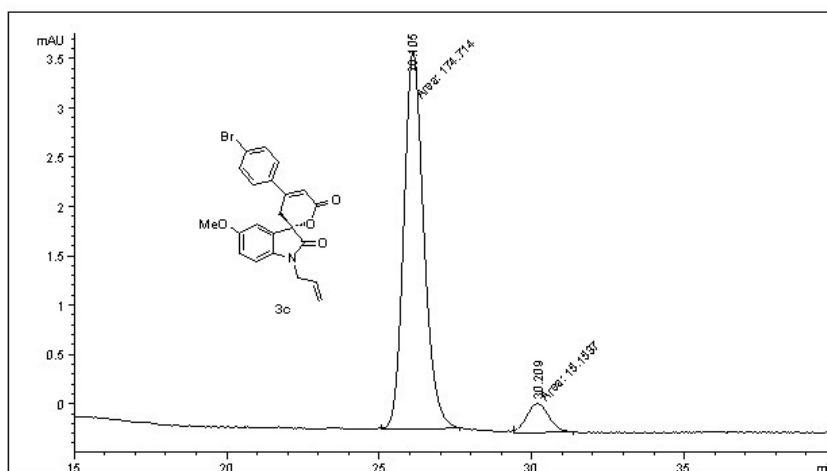
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.962	BB	0.8284	2.96685e4	533.86200	50.0135
2	30.951	BB	0.8625	2.96524e4	523.80133	49.9865

Totals : 5.93209e4 1057.66333

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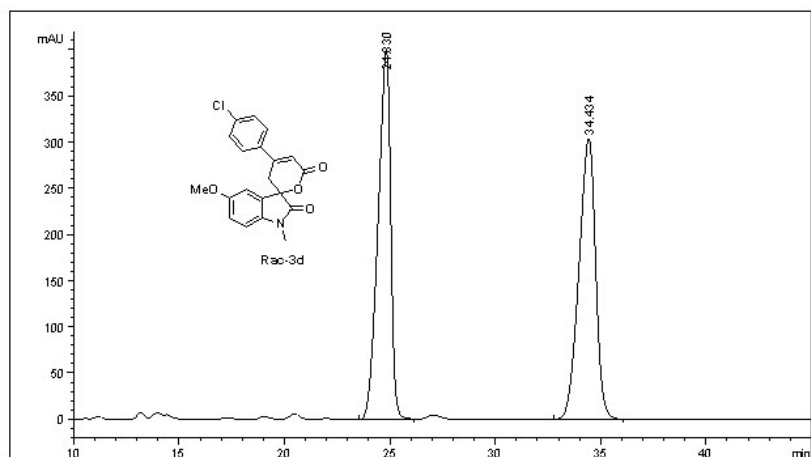
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.105	NM	0.7624	174.71397	3.81949	92.0188
2	30.209	NM	0.8540	15.15374	2.95725e-1	7.9812

Totals : 189.86772 4.11521

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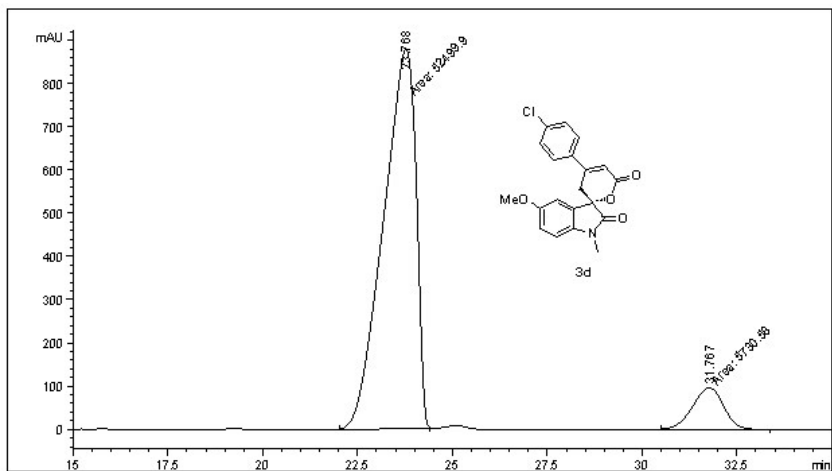
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.830	BB	0.6353	1.66245e4	399.61536	49.9328
2	34.434	BB	0.8462	1.66692e4	303.78613	50.0672

Totals : 3.32936e4 703.40149

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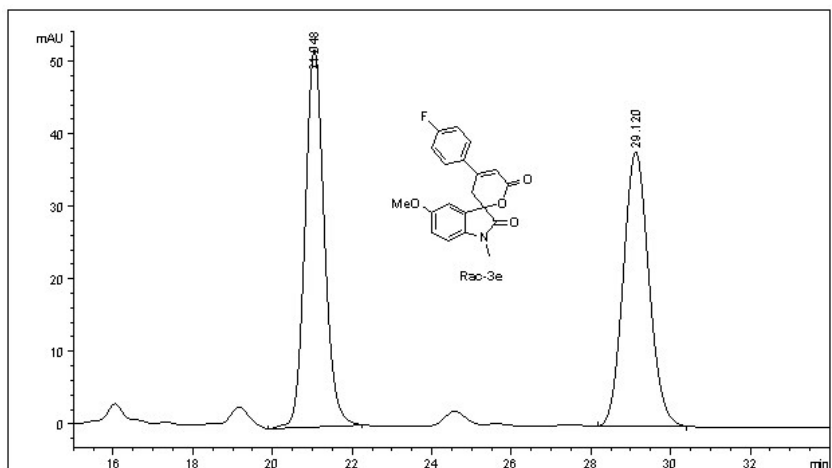
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Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.768	MM	0.9969	5.24999e4	877.75183	90.1588
2	31.767	MM	0.9754	5730.57520	97.92017	9.8412

Totals : 5.82305e4 975.67200

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Area Percent Report

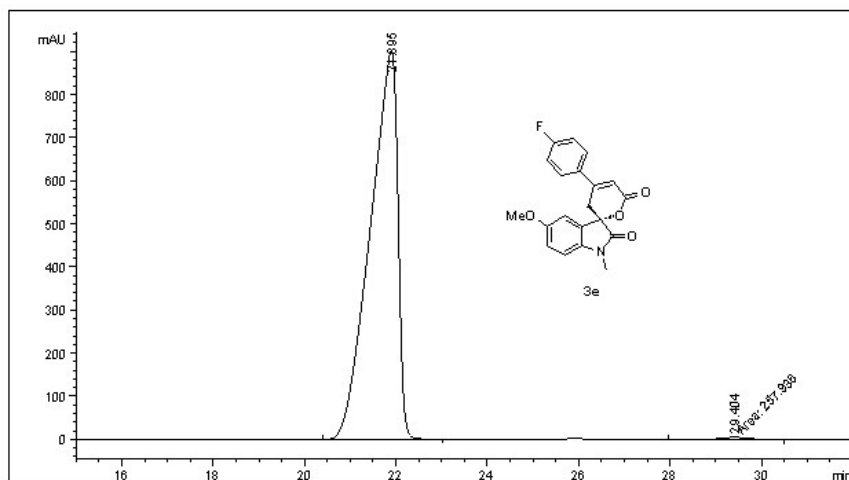
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Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.048	VB	0.5161	1748.11902	52.01600	50.7963
2	29.120	BB	0.6899	1693.31055	37.85235	49.2037

Totals : 3441.42957 89.86835

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Area Percent Report

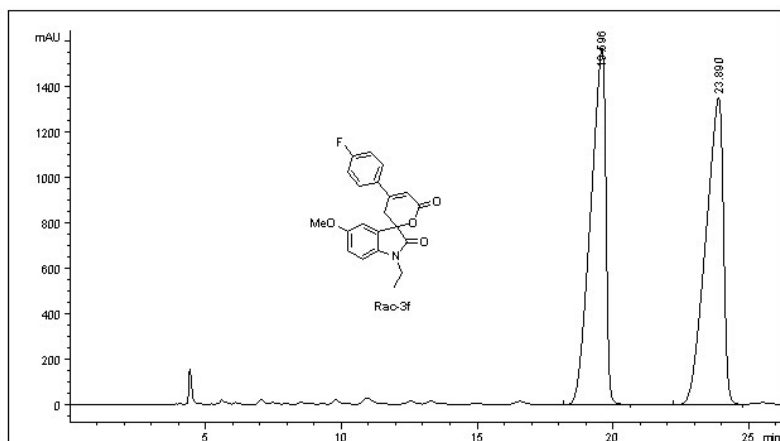
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Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.895	BB	0.6214	3.77943e4	900.97162	99.3222
2	29.404	MM	0.7785	257.93561	5.52185	0.6778

Totals : 3.80523e4 906.49347

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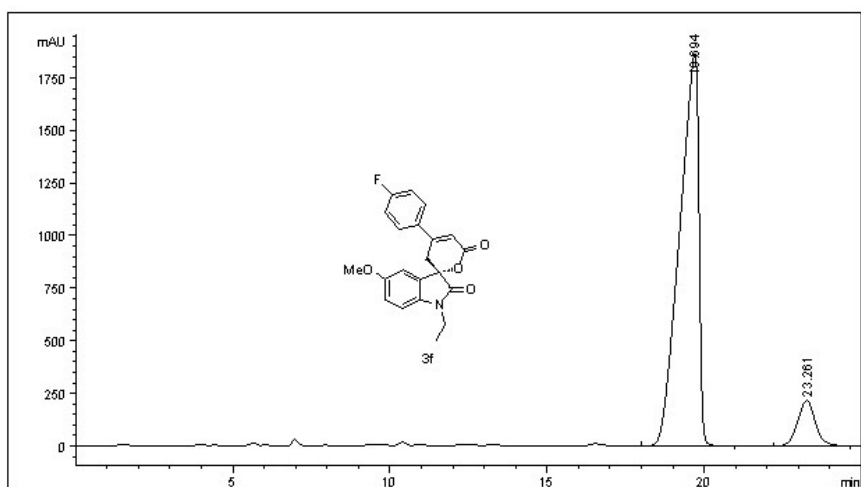
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Tvpe	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.596	BB	0.5832	6.03765e4	1568.22717	49.9238
2	23.890	VV	0.6897	6.05610e4	1349.05664	50.0762

Totals : 1.20938e5 2917.28381

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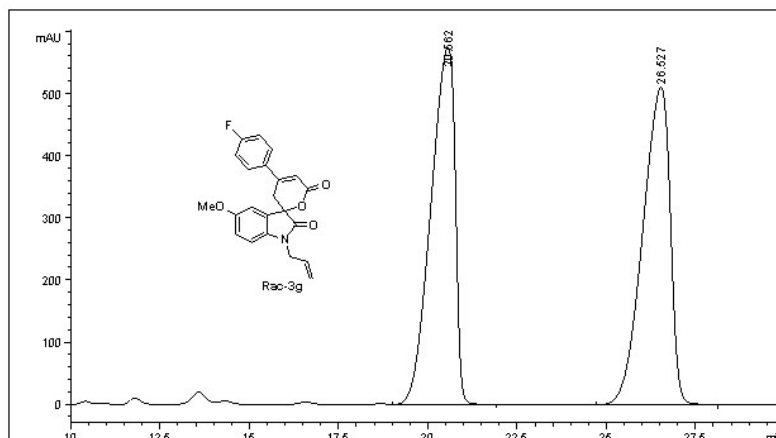
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Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Tvpe	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.694	BB	0.6592	7.88383e4	1864.83313	90.3110
2	23.261	BV	0.5959	8458.11621	216.46432	9.6890

Totals : 8.72964e4 2081.29745

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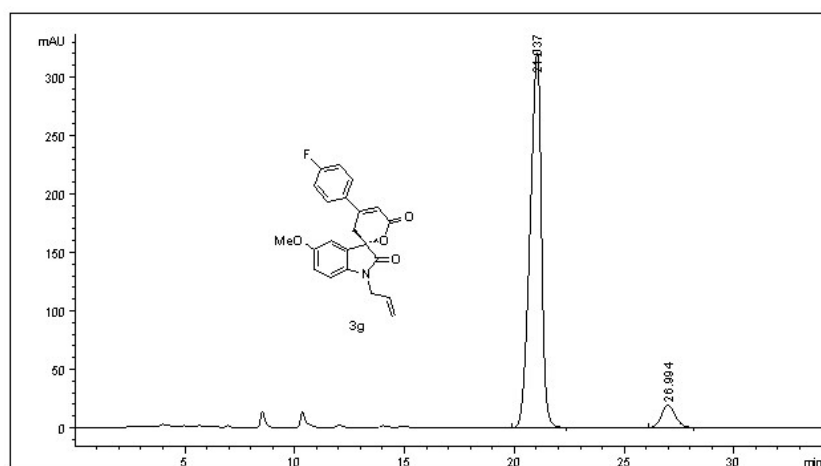
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Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.562	VB	0.7524	2.72063e4	574.63806	49.9459
2	26.527	BB	0.8510	2.72652e4	510.56363	50.0541

Totals : 5.44714e4 1085.20169

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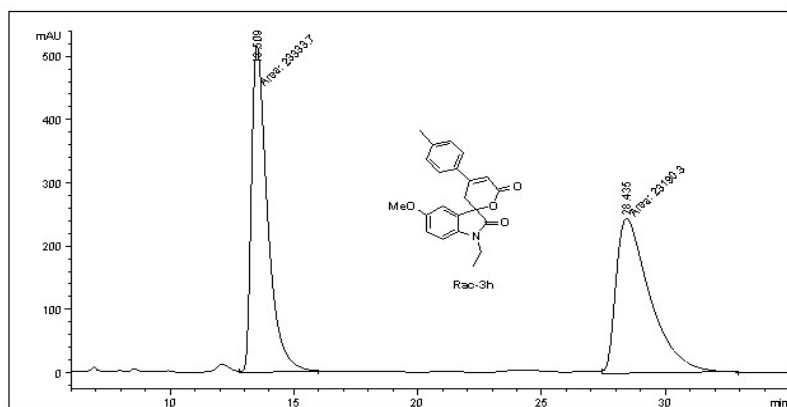
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Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.037	BB	0.5444	1.15011e4	320.72775	93.1653
2	26.994	BB	0.6665	843.73578	19.05745	6.8347

Totals : 1.23448e4 339.78520

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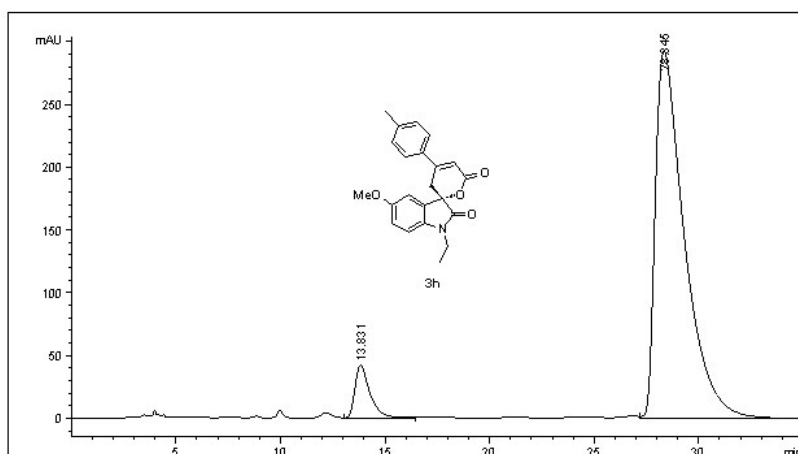
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Sorted By : Signal
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Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.509	MM	0.7533	2.33337e4	516.22260	50.1541
2	28.435	MM	1.5816	2.31903e4	244.38194	49.8459
Totals :				4.65240e4	760.60454	

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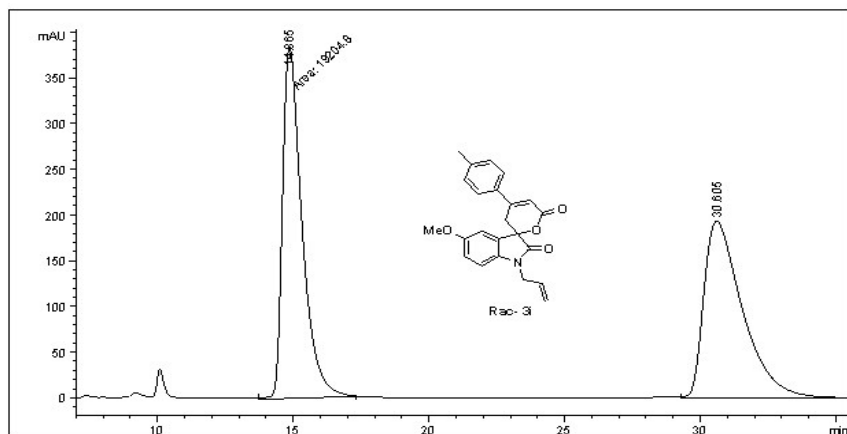
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.831	VV	0.7563	2173.01929	42.51846	7.1279
2	28.345	VB	1.4326	2.83131e4	292.68225	92.8721
Totals :				3.04861e4	335.20071	

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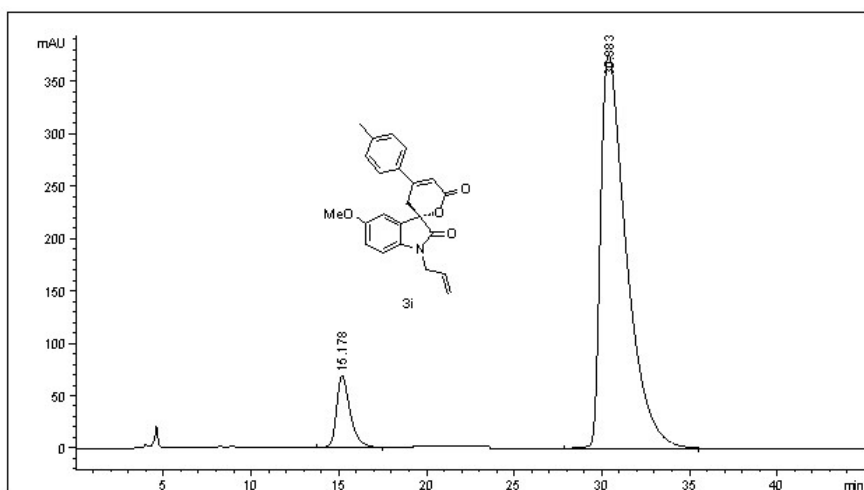
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.865	MM	0.8315	1.92048e4	384.91962	50.0780
2	30.605	VBA	1.4895	1.91449e4	193.64267	49.9220
Totals :				3.83497e4	578.56229	

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*** End of Report ***



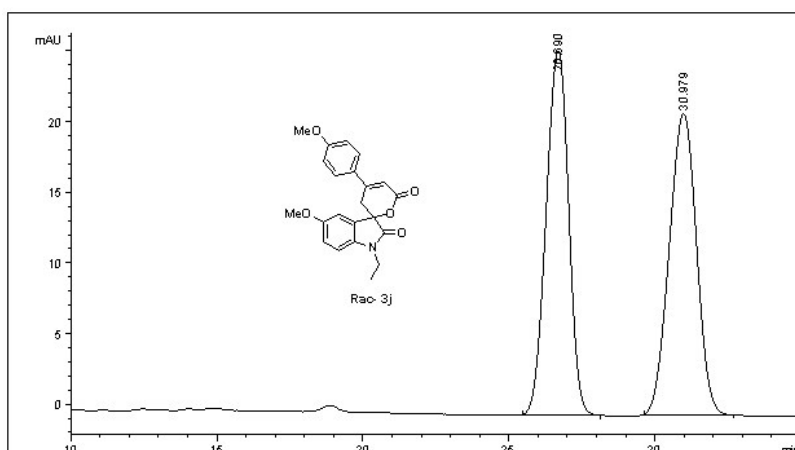
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.178	VB	0.8163	3769.61206	69.11324	8.9597
2	30.383	BB	1.4859	3.83032e4	376.17947	91.0403
Totals :				4.20728e4	445.29271	

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*** End of Report ***



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Area Percent Report
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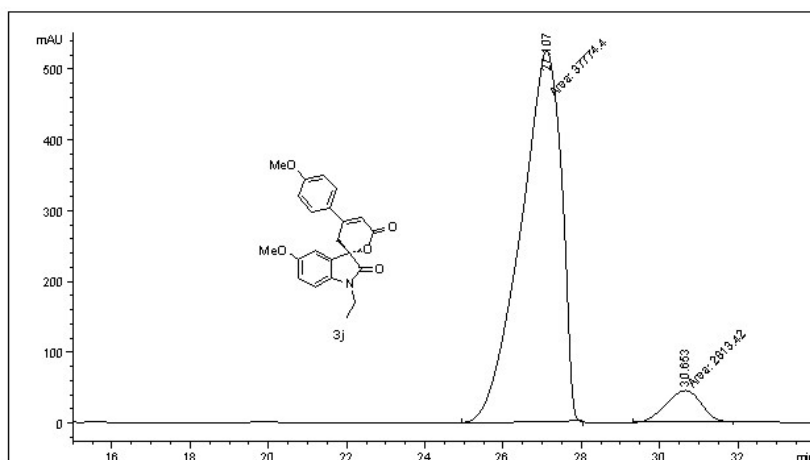
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Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 C, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.690	BB	0.8448	1380.28467	25.77466	49.9018
2	30.979	BB	0.9802	1385.71448	21.32373	50.0982

Totals : 2765.99915 47.09839

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*** End of Report ***



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Area Percent Report
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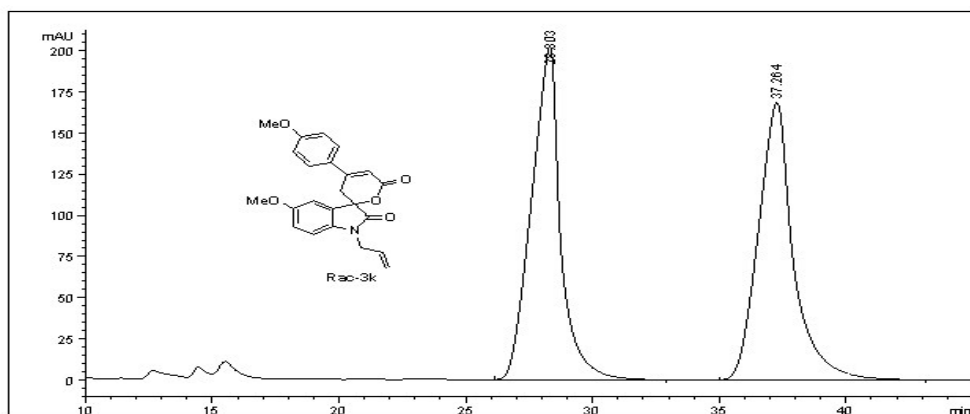
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 C, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.107	MM	1.2025	3.77744e4	523.54712	93.0683
2	30.653	MM	1.0544	2813.41675	44.47123	6.9317

Totals : 4.05878e4 568.01835

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*** End of Report ***



Area Percent Report

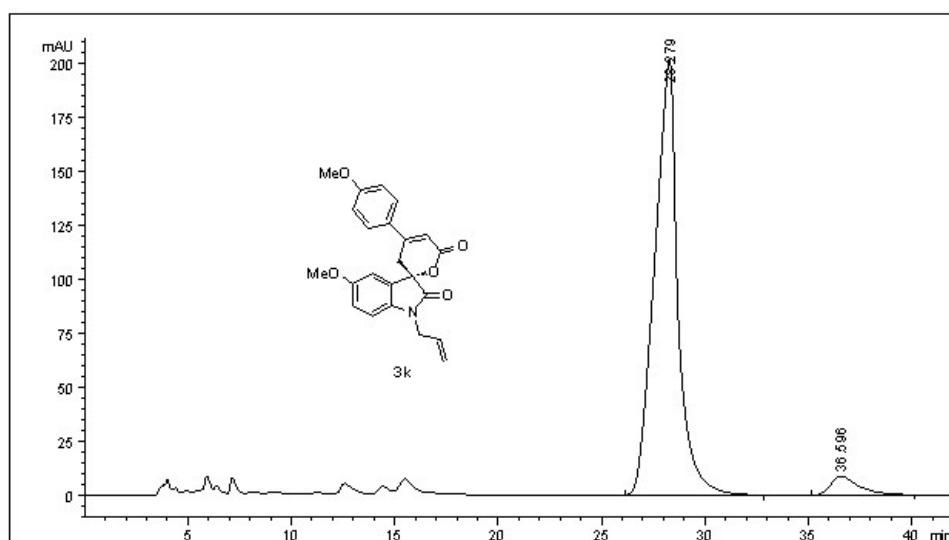
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.303	BB	1.1845	1.61094e4	202.40913	49.9908
2	37.264	BB	1.4119	1.61153e4	168.48386	50.0092

Totals : 3.22246e4 370.89299

*** End of Report ***



Area Percent Report

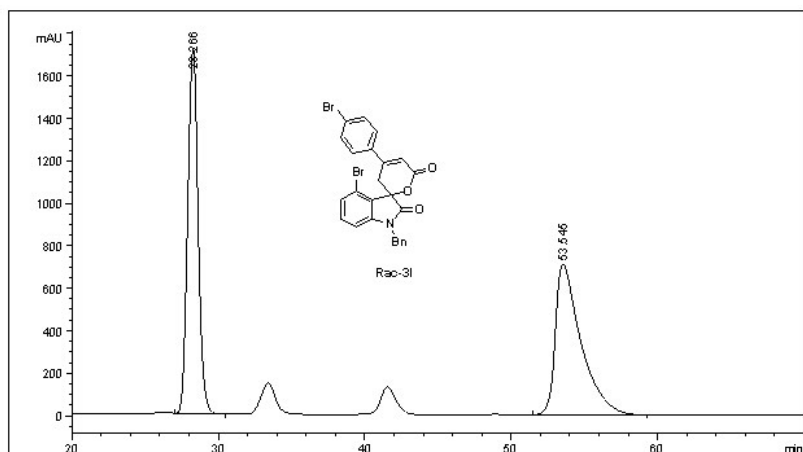
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.279	BB	1.1466	1.58190e4	201.78352	94.8655
2	36.596	BB	1.4181	856.19135	8.77700	5.1345

Totals : 1.66751e4 210.56052

*** End of Report ***



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Area Percent Report
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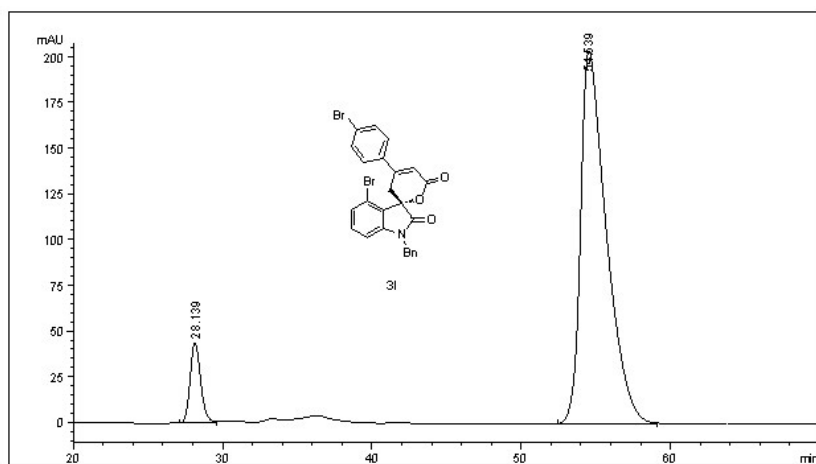
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.266	VB	0.7769	8.52484e4	1718.11914	49.8320
2	53.545	BB	1.6828	8.58232e4	708.73456	50.1680

Totals : 1.71072e5 2426.85370

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*** End of Report ***



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Area Percent Report
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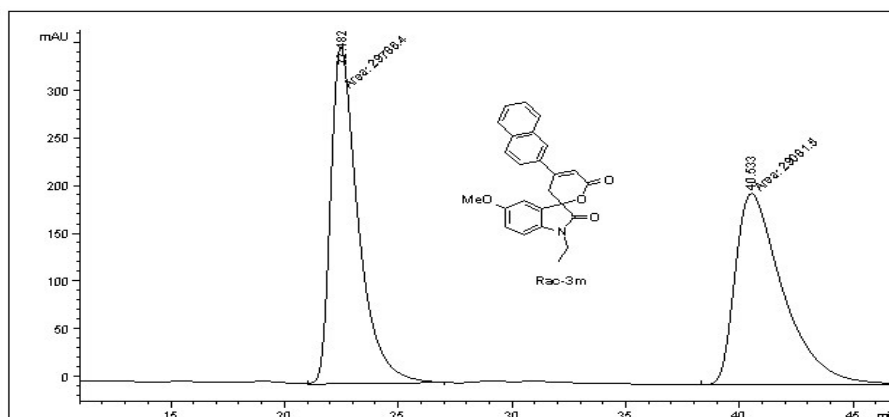
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.139	BB	0.7528	2125.80151	43.75694	8.0333
2	54.539	BB	1.7072	2.43365e4	203.79347	91.9667

Totals : 2.64623e4 247.55042

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*** End of Report ***



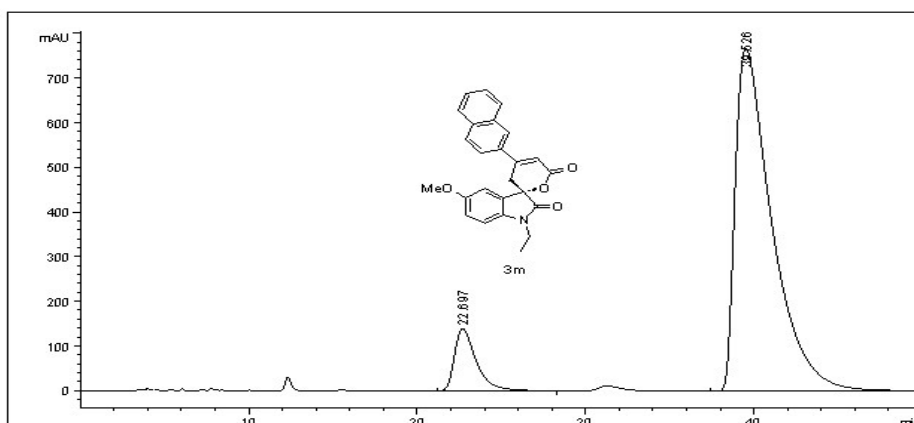
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.482	MM	1.4042	2.97864e4	353.55222	50.5987
2	40.533	MM	2.4251	2.90815e4	199.86505	49.4013
Totals :				5.88680e4	553.41727	

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*** End of Report ***



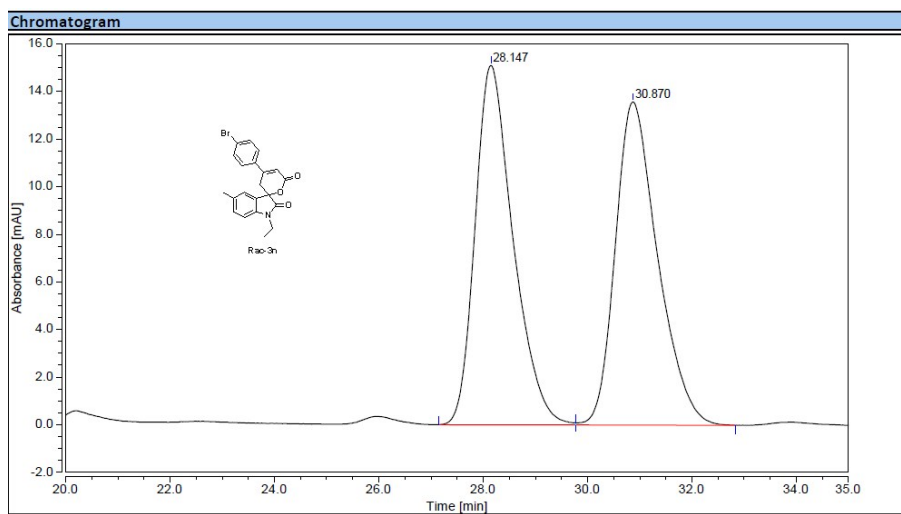
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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

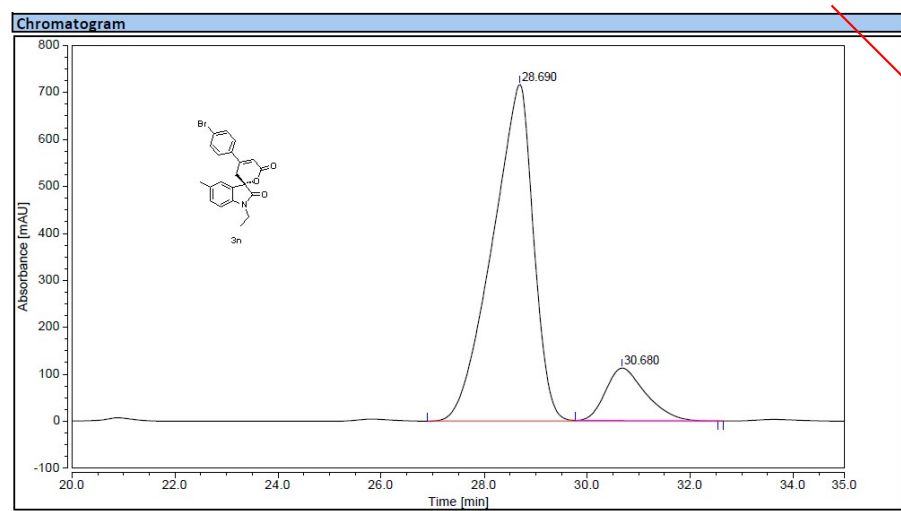
Signal 1: MWD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.697	BB	1.3626	1.26716e4	139.65680	9.8353
2	39.526	BBA	2.2446	1.16167e5	768.04095	90.1647
Totals :				1.28838e5	907.69775	

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*** End of Report ***

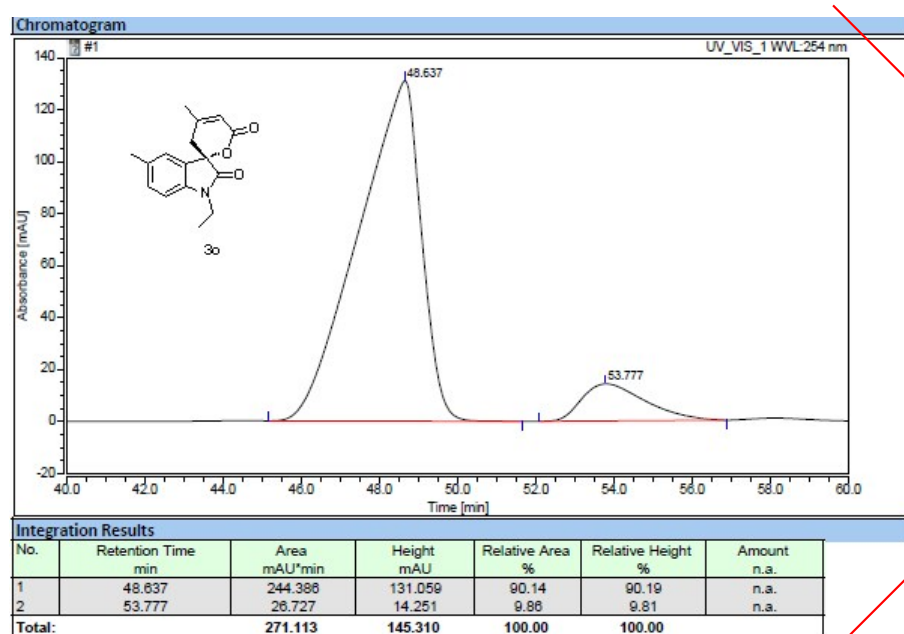
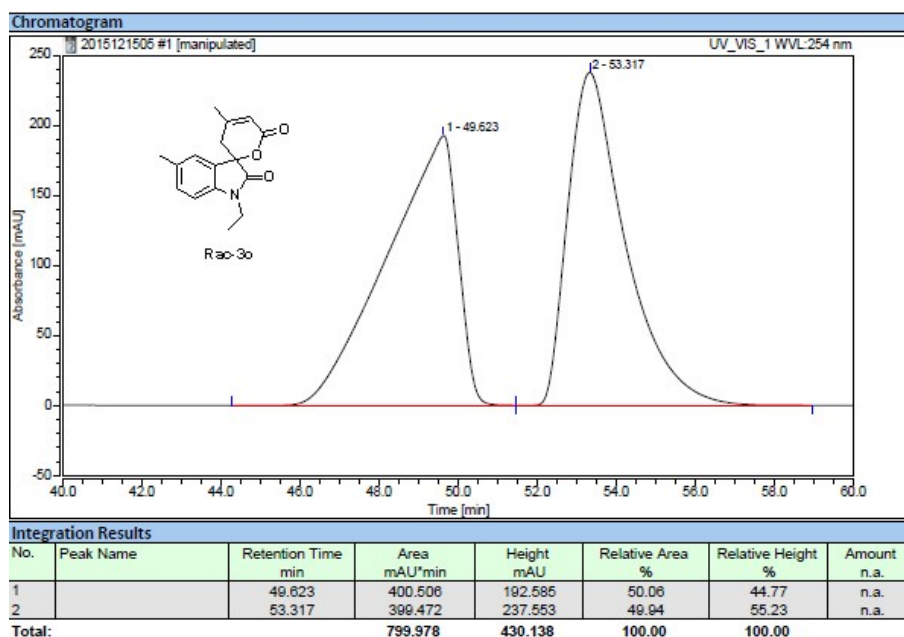


Integration Results						
No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1	28.147	12.748	15.104	49.96	52.65	n.a.
2	30.870	12.768	13.583	50.04	47.35	n.a.
Total:		25.516	28.687	100.00	100.00	



Integration Results						
No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1	28.690	663.247	716.804	86.86	86.52	n.a.
2	30.680	100.372	111.666	13.14	13.48	n.a.
Total:		763.619	828.469	100.00	100.00	

Comment [D]: 新增化合物 3n



Comment [D]: 新增化合物 3o