

Asymmetric Mannich reaction of α -Diazocarbonyl compounds and *N*-sulfonyl Cyclic Ketimines Catalyzed by Complexes Generated from Chiral and Achiral Phosphines with Gold(I)

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China

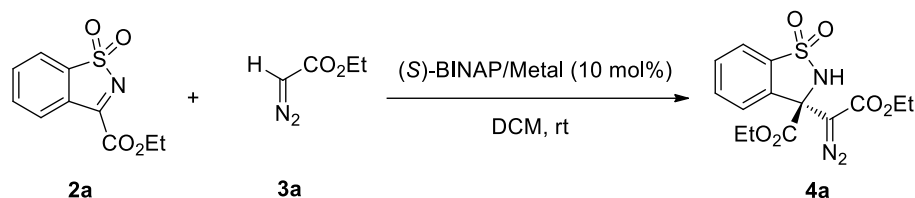
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1. Optimization of the reaction conditions

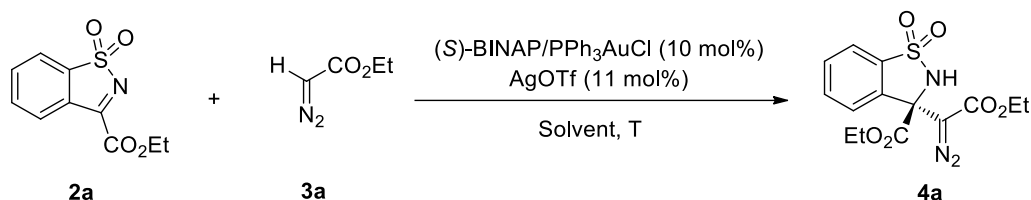
1.1 The effect of metal salts on the nucleophile addition between α -diazocarbonyl with *N*-sulfonyl ketimines



entry ^a	metal salt (mol %)	yield(%) ^b	ee(%) ^c
1	Sc(OTf) ₃	trace	-
2	NiCl ₂ (PPh ₃) ₂	65	0
3	IrCl ₃ (10)+AgClO ₄ (30)	70	50
4	Ag ₂ CO ₃	65	71
5	Ag ₂ O	59	30
6	AgClO ₄	NR	-
7	AgOTf	91	60

^a Reactions were carried out with **2a** (0.2 mmol), **3a** (0.4 mmol), metal salt and catalyst (10 mol%), DCM (0.1 M). ^b Isolated yield. ^c Determined by HPLC analysis.

1.2 The effect of solvents on the Mannich reaction of α -diazocarbonyl with *N*-sulfonyl ketimines

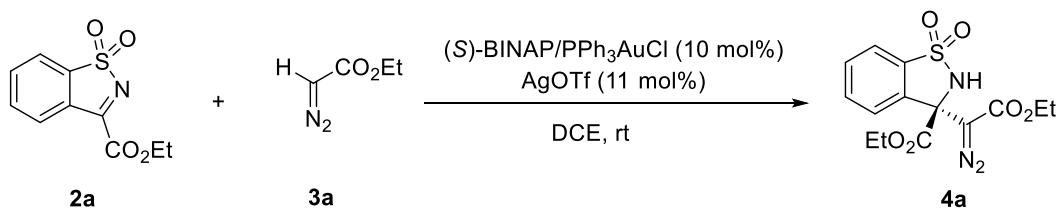


entry ^a	solvent	Temp(°C)	Time(h)	yield(%) ^b	ee(%) ^c
1	DCM	rt	24	74	78
2	CHCl ₃	rt	24	NR	-
3	THF	rt	24	trace	-
4	CH ₃ CN	rt	24	51	57
5	Et ₂ O	rt	24	trace	-
6	Toluene	rt	24	NR	-
7	DCE	rt	24	97	85
8	DCE	0	72	75	82
9	DCE	40	12	60	81

^a Reactions were carried out with **2a** (0.2 mmol), **3a** (0.4 mmol), metal salt and catalyst (10 mol%), solvent (0.1 M). ^b Isolated yield. ^c Determined by HPLC analysis.

1.3 Effect of conducting orders of procedure

In order to investigate the effect of conducting orders of procedure, the control experiments were carried out as follows.



entry ^a	conducting orders	yield(%) ^b	ee(%) ^c
1	The mixture of (<i>S</i>)-BINAP, PPh ₃ AuCl, AgOTf, 2a and 3a was stirred in DCE together.	84	83
2	The mixture of (<i>S</i>)-BINAP, AgOTf, 2a and 3a was stirred in DCE first, and then PPh ₃ AuCl was added.	82	83

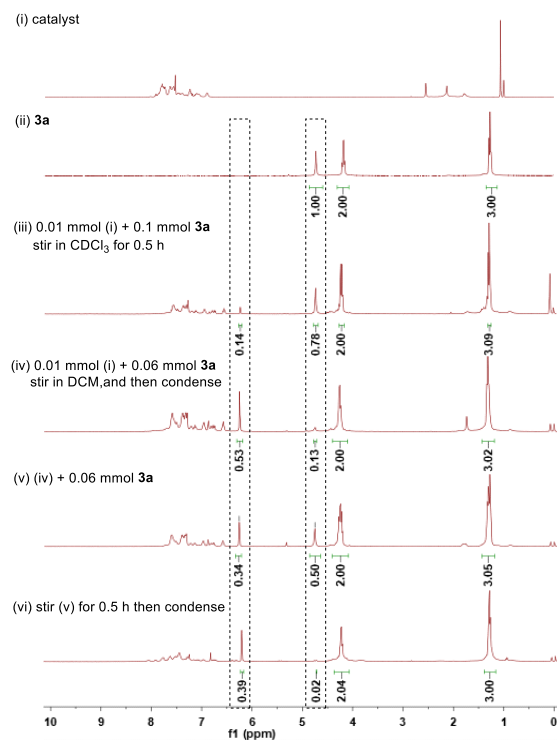
^a The reactions were carried out with **2a** (0.1 mmol), **3a** (0.2 mmol), PPh₃AuCl (10 mol%), AgOTf (11 mol%) and (*S*)-BINAP (11 mol%) in DCE (0.1 M) at rt for 24 h. ^b Isolated yield. ^c Determined by HPLC analysis.

2. Control NMR experiments

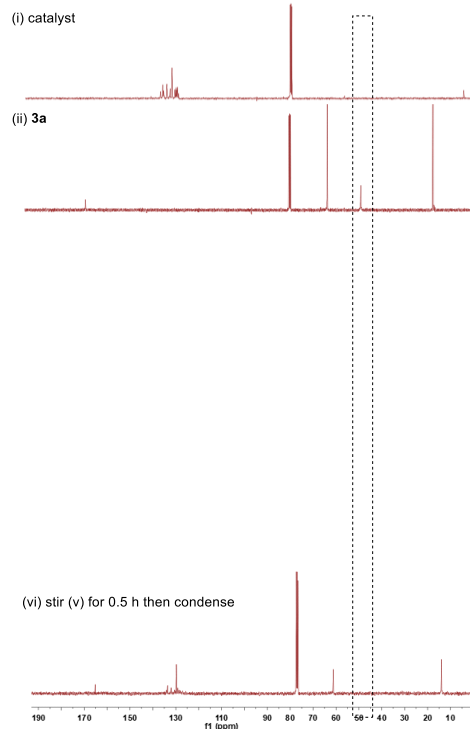
2.1 ^1H , ^{13}C NMR of catalytic mixture

To gain insight into the mechanism of Mannich reaction of α -diazocarbonyl compounds and *N*-sulfonyl cyclic ketimines catalyzed by gold(I) complex, NMR analysis was attempted. The preparation procedures and analysis of catalyst samples for NMR were as follows.

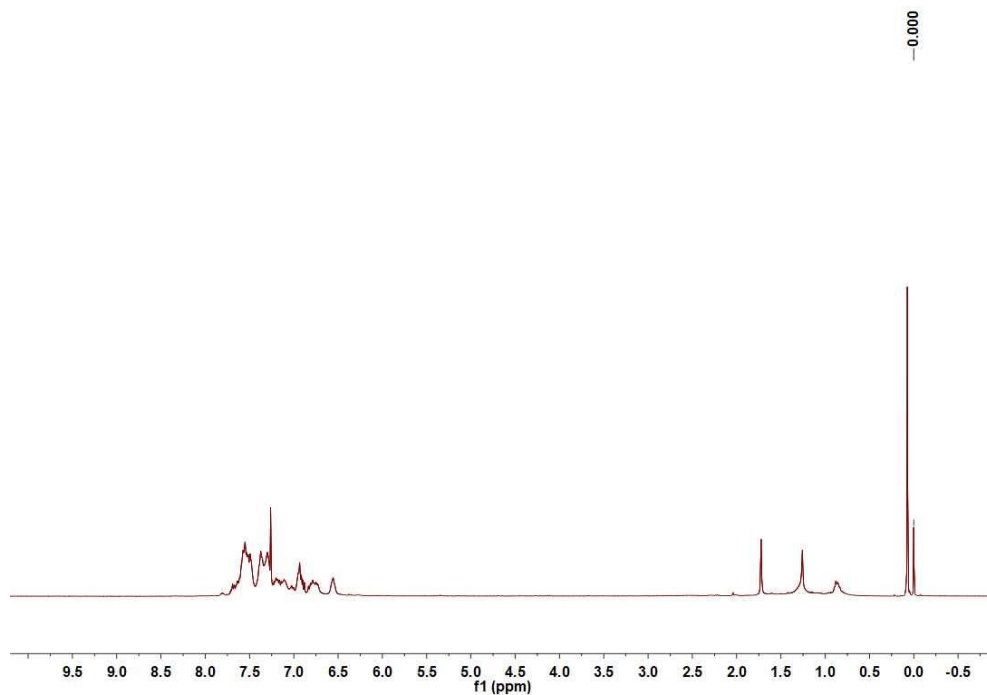
(a) ^1H NMR Analysis of Catalyst Solution

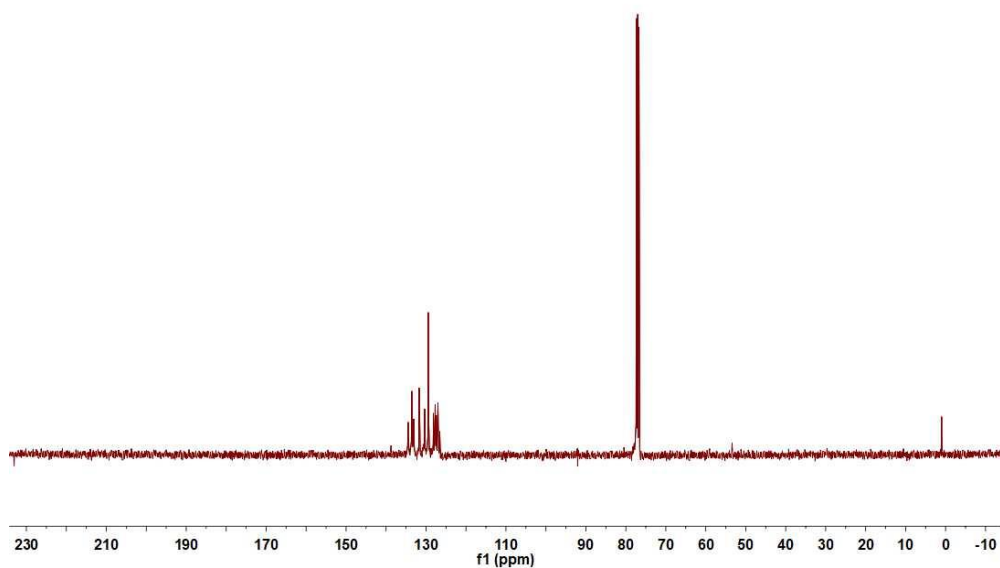


(b) ^{13}C NMR Analysis of Catalyst Solution



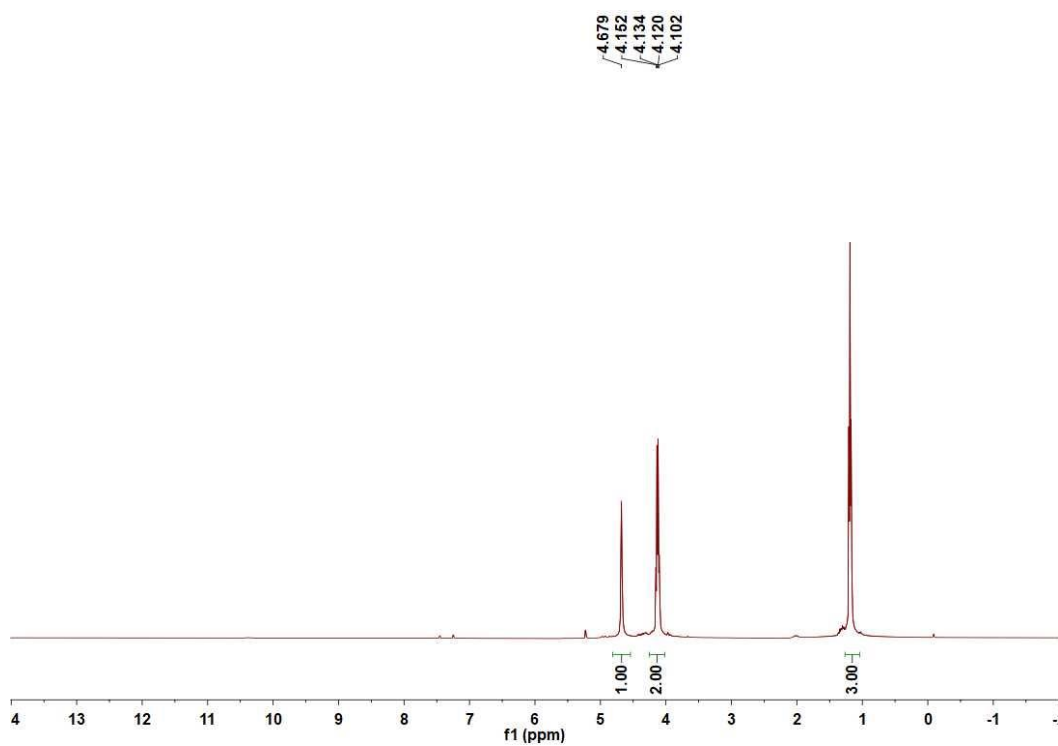
Sample i: (*S*)-BINAP (0.01 mmol, 6.3 mg), PPh_3AuCl (0.01 mmol, 5.0 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml DCM at room temperature for 10 min. The filtrate was concentrated in vacuo. The resulting compound dissolved in CDCl_3 (0.5 ml) and transferred to a dry NMR tube. ^1H NMR and ^{13}C NMR were taken with the sample at 25 $^\circ\text{C}$.

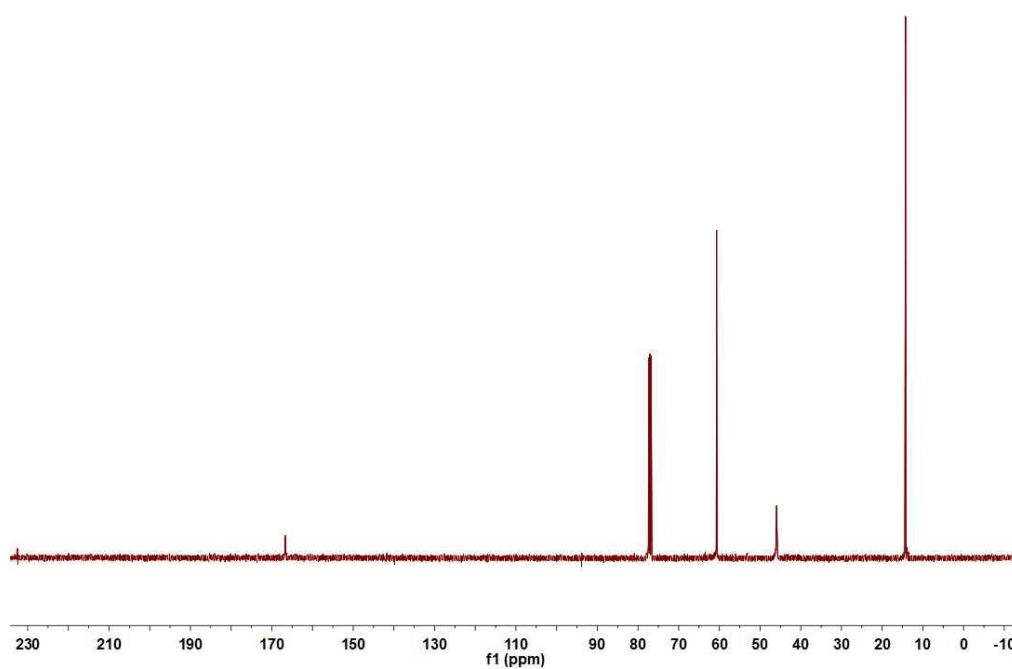




^1H NMR, ^{13}C NMR analysis of sample i

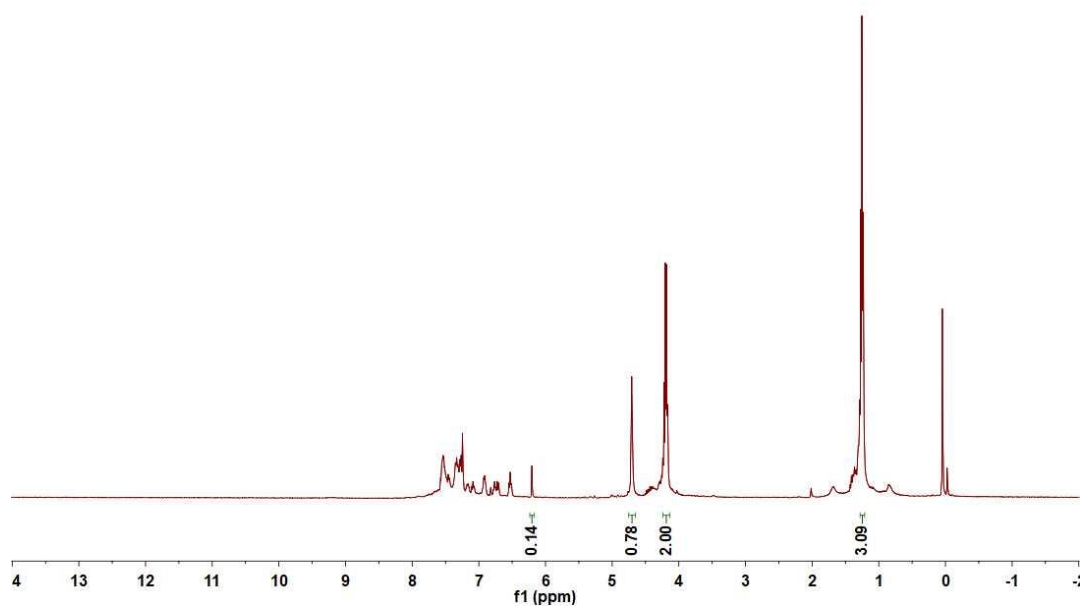
Sample ii: Dissolved **3a** in CDCl_3 and transferred to a dried NMR tube. ^1H NMR and ^{13}C NMR were taken with the sample at 25 °C.





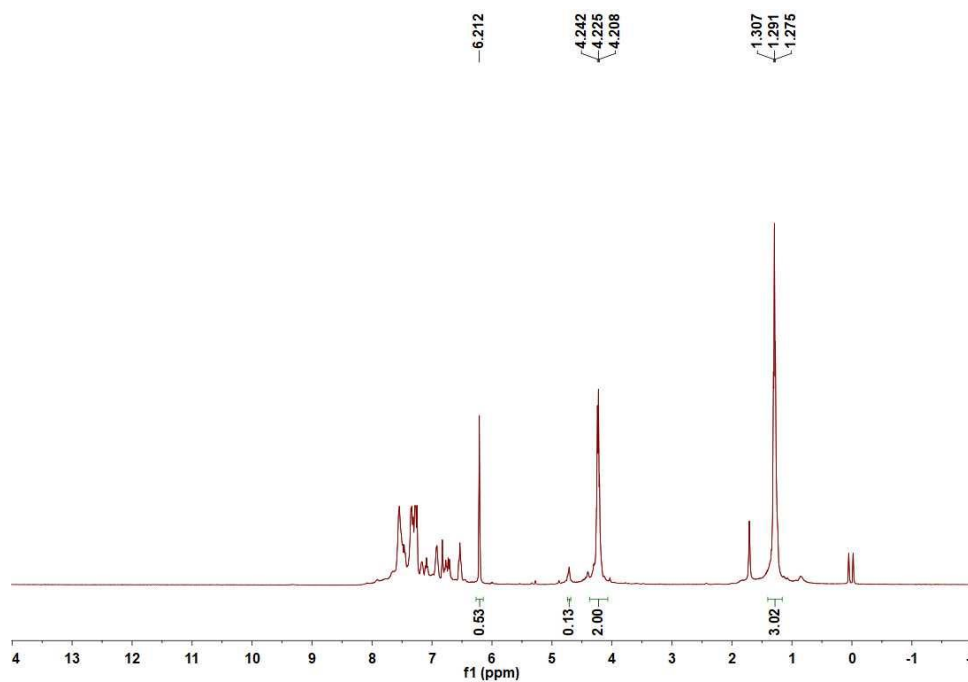
^1H NMR, ^{13}C NMR analysis of sample ii

Sample iii: (*S*)-BINAP (0.01 mmol, 6.3 mg), PPh_3AuCl (0.01 mmol, 5.0 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml CDCl_3 at room temperature for 10 min then filtered. **3a** (0.1 mmol, 25 μl) was added, and then stirred the mixture for 0.5 h. The mixture transferred directly to a dry NMR tube. ^1H NMR was taken with the sample at 25 $^\circ\text{C}$.



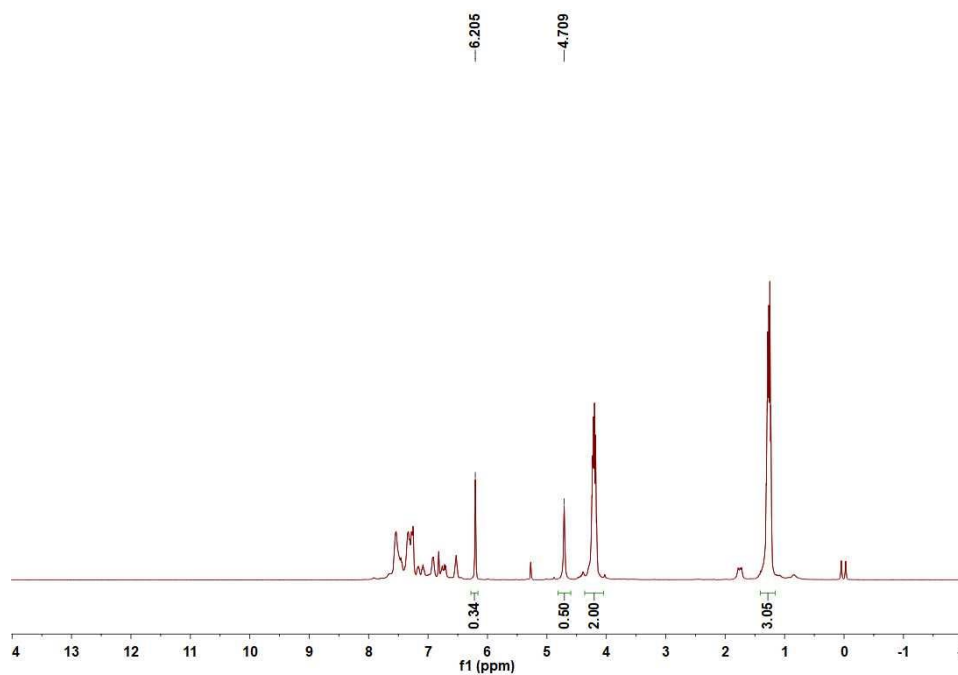
^1H NMR analysis of sample iii

Sample iv: (*S*)-BINAP (0.01 mmol, 6.3 mg), PPh₃AuCl (0.01 mmol, 5.0 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml DCM at room temperature for 10 min then filtered. **3a** (0.06 mmol, 15 µl) was added. Stirred the resulting mixture for 0.5 h and then concentrated in vacuo. The resulting compound dissolved in CDCl₃ (0.5 ml) and transferred to a dry NMR tube. ¹H NMR was taken with the sample at 25 °C.



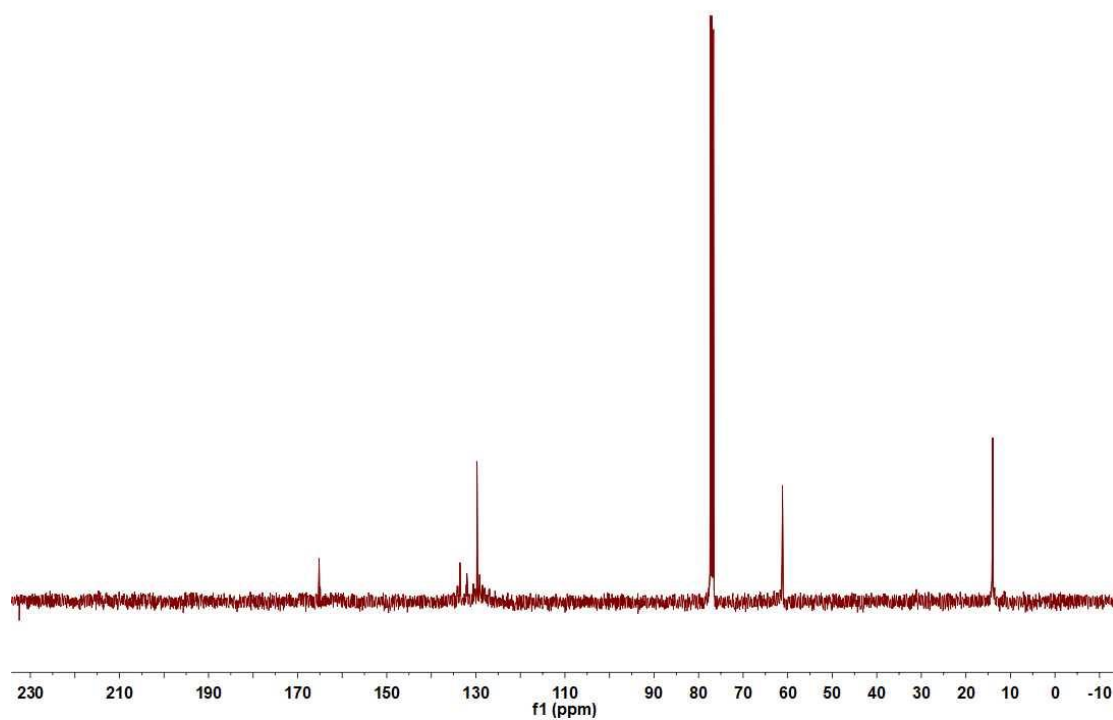
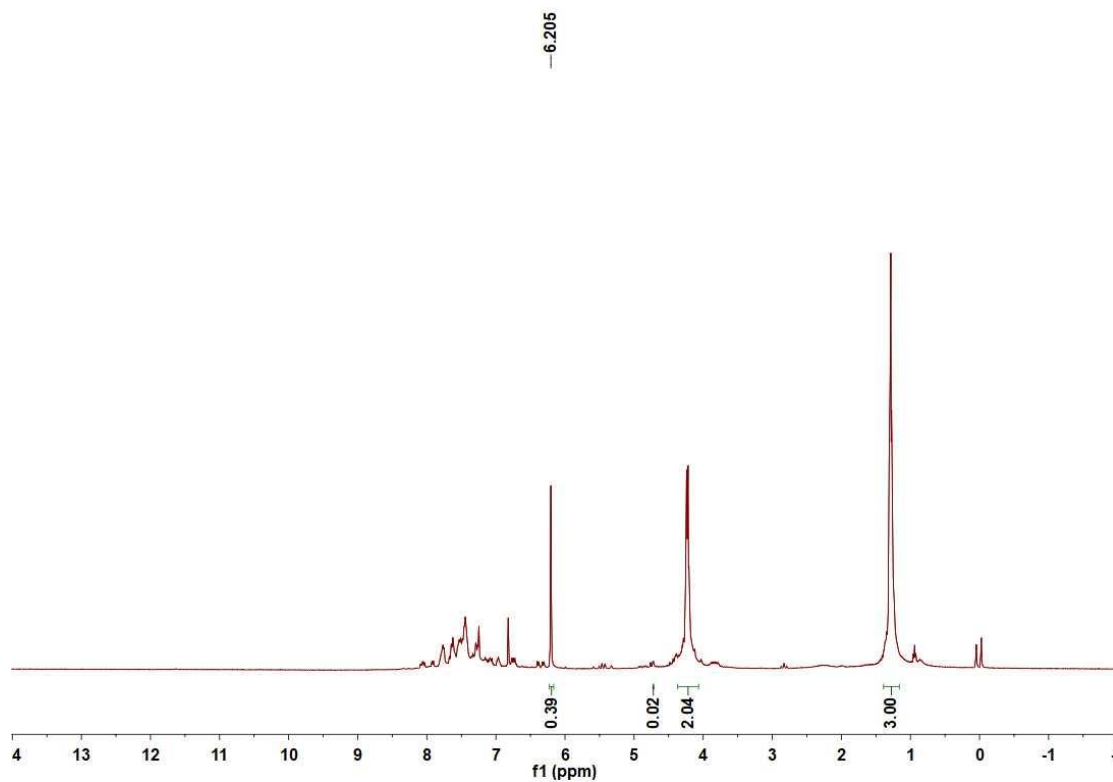
¹H NMR analysis of sample iv

Sample v: **3a** (0.06 mmol, 15 µl) was added directly to the NMR tube of sample iv. ¹H NMR was taken with the sample at 25 °C.



¹H NMR analysis of sample v

Sample vi: Removed CDCl_3 of sample v and dissolved the compounds in 1.0 ml DCM. Stirred the resulting mixture for 0.5 h and then concentrated in vacuo. The resulting compounds dissolved again in CDCl_3 (0.5 ml) and transferred to a dry NMR tube. ^1H NMR and ^{13}C NMR were taken with the sample at 25 °C.



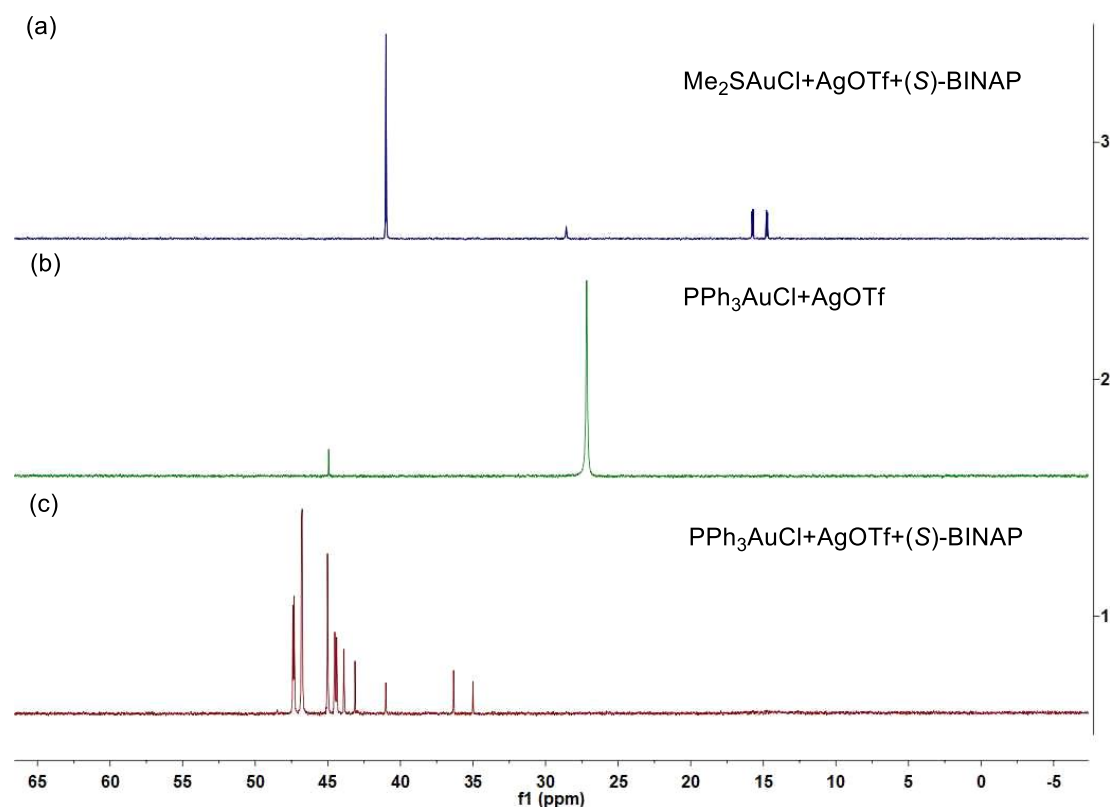
^1H NMR, ^{13}C NMR analysis of sample vi

2.2 ^{31}P NMR of catalytic mixture

(a) (*S*)-BINAP (0.01 mmol, 6.3 mg), Me_2SAuCl (0.01 mmol, 2.9 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml DCM at room temperature for 10 min, and then the filtrate concentrated in vacuo. The resulting compound dissolved in CDCl_3 (0.5 ml) and transferred to a dried NMR tube. ^{31}P NMR was taken with the sample at 25 °C.

(b) (*S*)-BINAP (0.01 mmol, 6.3 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml DCM at room temperature for 10 min, and then the filtrate concentrated in vacuo. The resulting compound dissolved in CDCl_3 (0.5 ml) and transferred to a dried NMR tube. ^{31}P NMR was taken with the sample at 25 °C.

(c) (*S*)-BINAP (0.01 mmol, 6.3 mg), PPh_3AuCl (0.01 mmol, 5.0 mg), AgOTf (0.011 mmol, 2.8 mg) were stirred in 1.0 ml DCM at room temperature for 10 min, and then the filtrate concentrated in vacuo. The resulting compound dissolved in CDCl_3 (0.5 ml) and transferred to a dry NMR tube. ^{31}P NMR was taken with the sample at 25 °C.

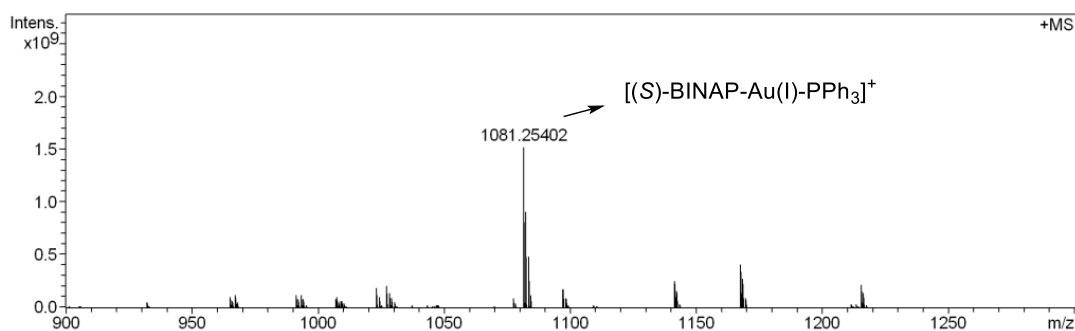


^{31}P NMR of catalyst mixture

3. ESI-QFT MS Analysis of Catalytic Solution

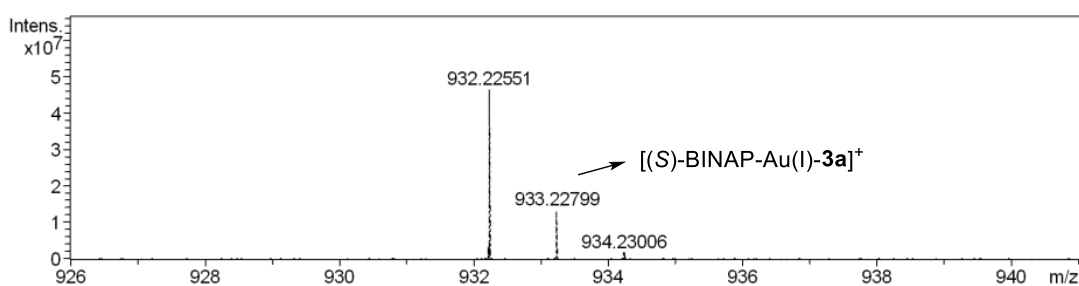
The catalytic composition of (*S*)-BINAP, Au(I)PPh_3 and diazocarbonyl compound **3a** was investigated by using ESIMS. The results indicated that an MS peak at 1081.2540 (HR-ESIMS: m/z calcd for $[\text{C}_{62}\text{H}_{47}\text{AuP}_3]^+$: 1081.2556) could be assigned to complex $[(\text{S})\text{-BINAP-Au(I)PPh}_3]^+$.

ESI-QFT MS Analysis of Catalytic Solution



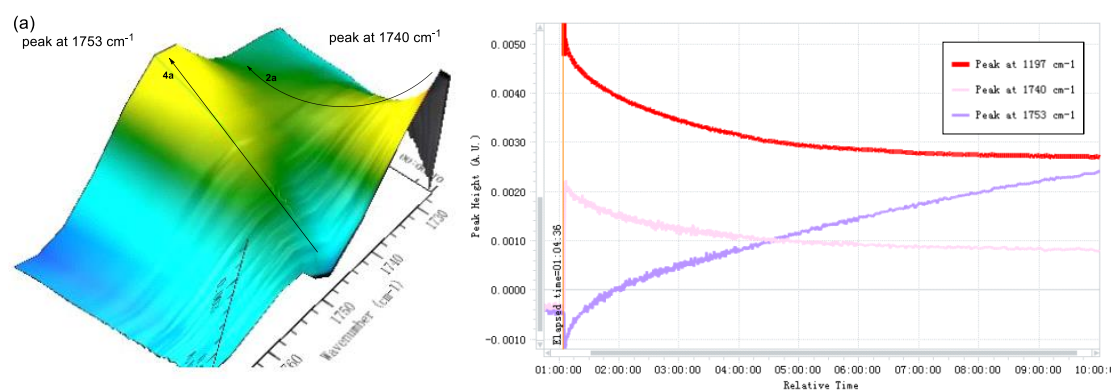
Additionally, another MS peak at 933.2279 (ESIMS: m/z calcd for $[\text{C}_{48}\text{H}_{38}\text{AuN}_2\text{O}_2\text{P}_2]^+$: 933.2074) also could be assigned to possible intermediate $[(S)\text{-BINAP-Au(I)-3a}]^+$.

ESI-QFT MS Analysis of Catalytic Solution

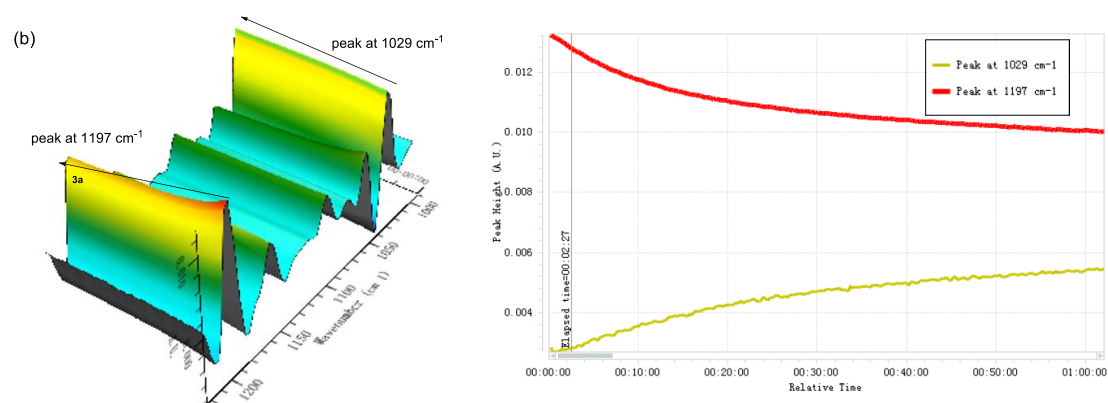


4. IR experiment

In Operando IR experiment, it was demonstrated that the amount of Mannich product **4a** increased with the consumption of *N*-sulfonyl cyclic ketimine **2a** and diazocarbonyl compound **3a**.

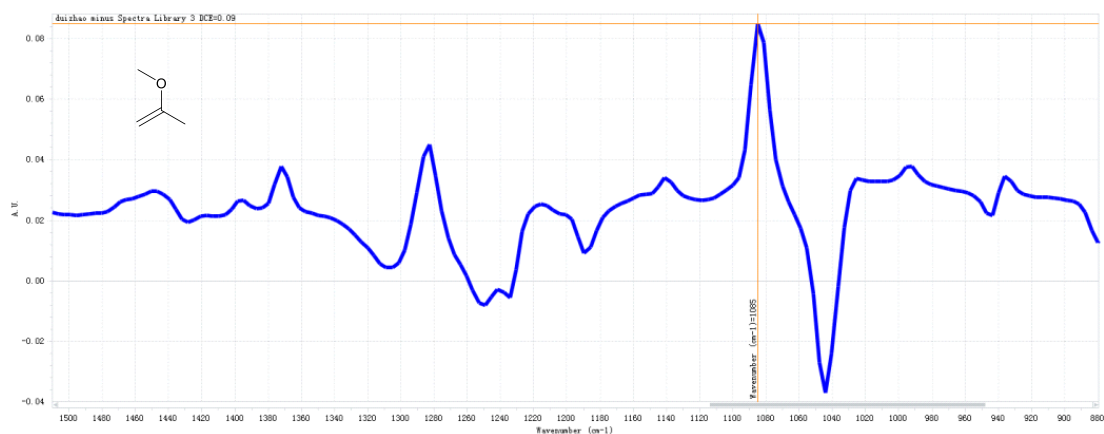


Operando IR experiment: (a) **2a** was added to the stirring mixture of gold(I) complex and **3a** after 1 h.



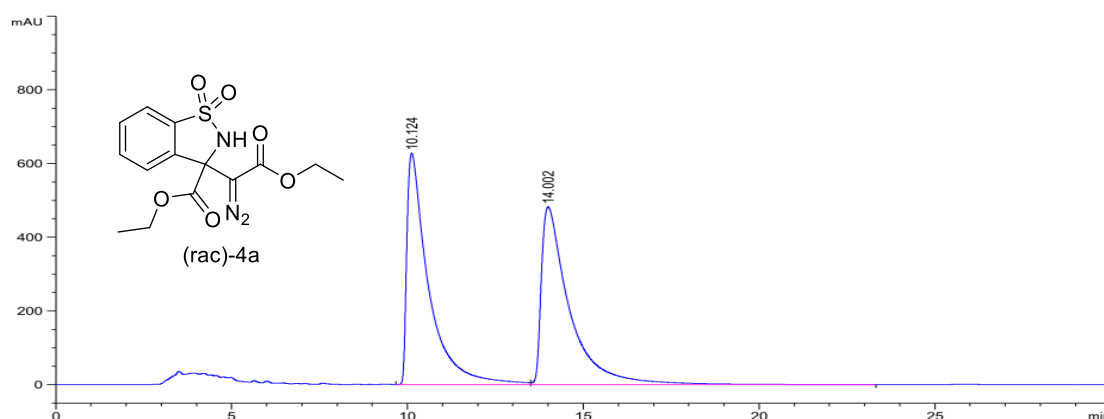
Operando IR experiment: (b) Stirring gold(I) complex and **3a** for 1 h.

The intermediate was detected by Operando IR experiment (Peak at 1029 cm^{-1}). 2-Methoxy-1-propene was used as analogue of intermediate in Operando IR experiment. The IR experiment analysis of 2-Methoxy-1-propene was as follows. The characteristic peak of 2-Methoxy-1-propene was at 1085 cm^{-1} (peak of intermediate was found at 1029 cm^{-1}).

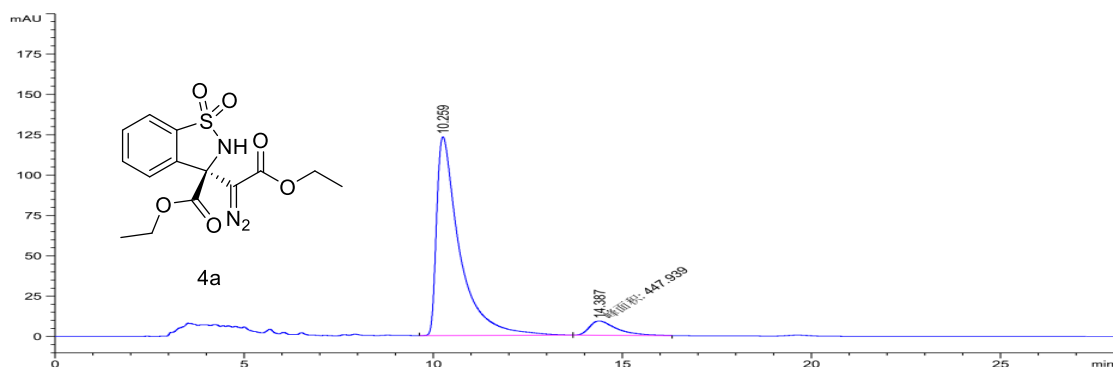


IR experiment analysis of 2-Methoxy-1-propene

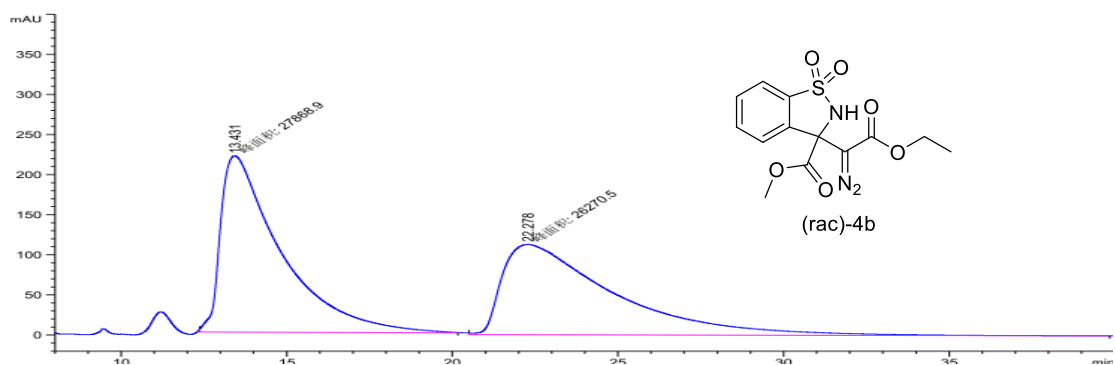
5. The analytical and spectral characterization data for the product



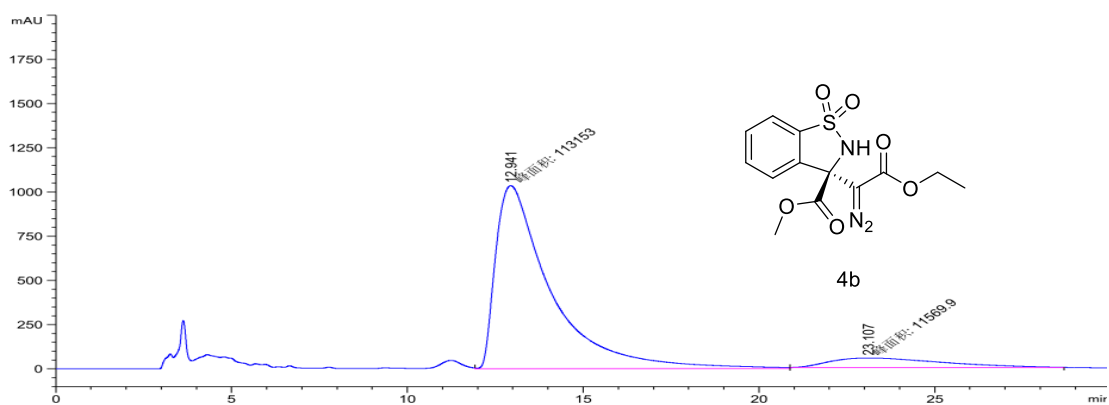
	Retention time (min)	Area (mAu + s)	%Area
1	10.124	2.68555e4	50.0936
2	14.002	2.67551e4	49.9064



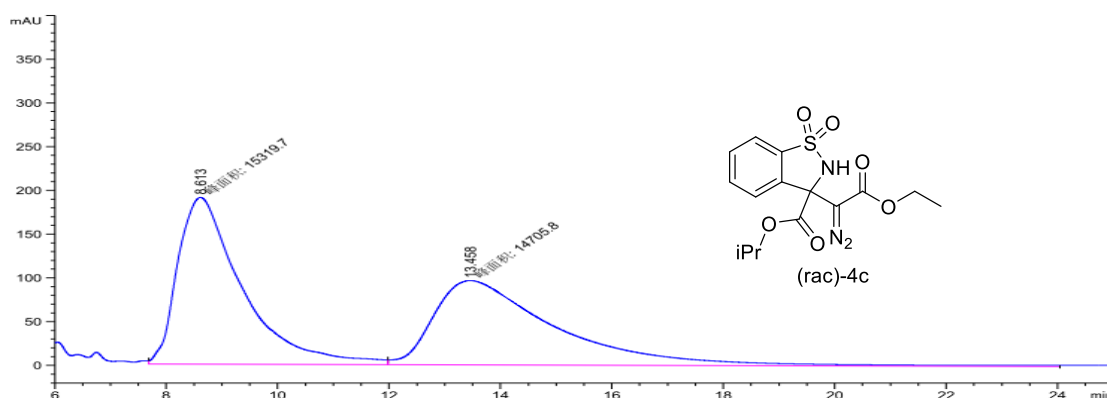
	Retention time (min)	Area (mAu + s)	%Area
1	10.259	5176.67285e4	92.0361
2	14.387	447.93936e4	7.9639



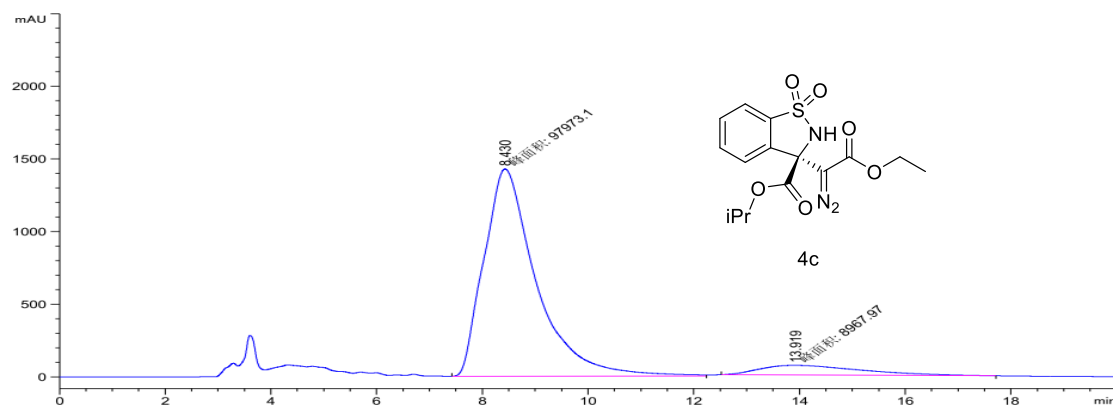
	Retention time (min)	Area (mAu + s)	%Area
1	13.431	2.78689e4	51.4762
2	22.278	2.62705e4	48.5238



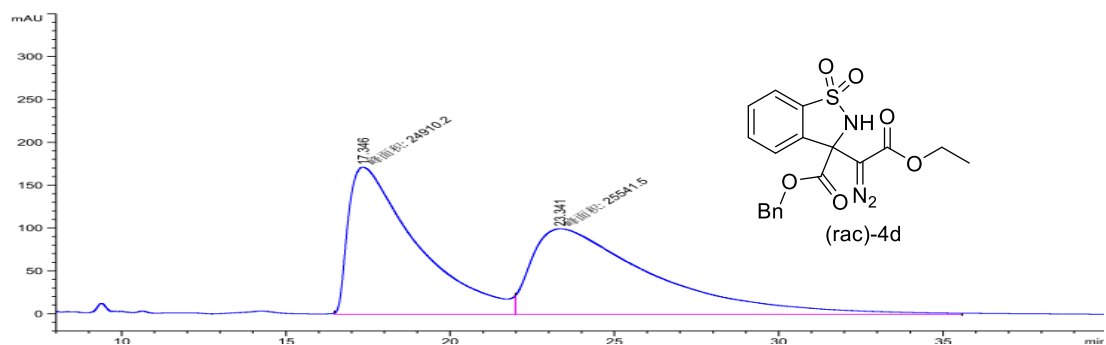
	Retention time (min)	Area (mAu + s)	%Area
1	12.941	1.13153e5	90.7235
2	23.107	1.15699e4	9.2765



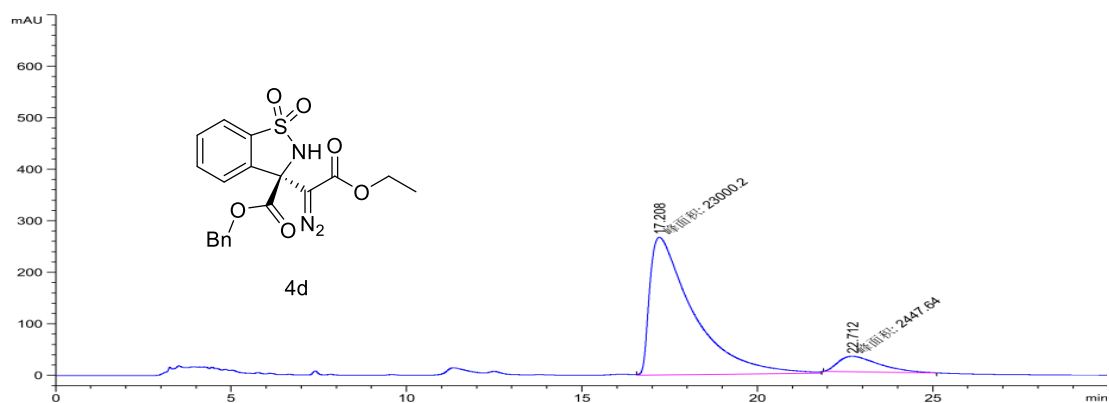
	Retention time (min)	Area (mAu + s)	%Area
1	8.613	1.53197e4	51.0224
2	13.458	1.47058e4	48.9776



	Retention time (min)	Area (mAu + s)	%Area
1	8.430	9.79731e4	91.6141
2	13.919	8967.97461	8.3859

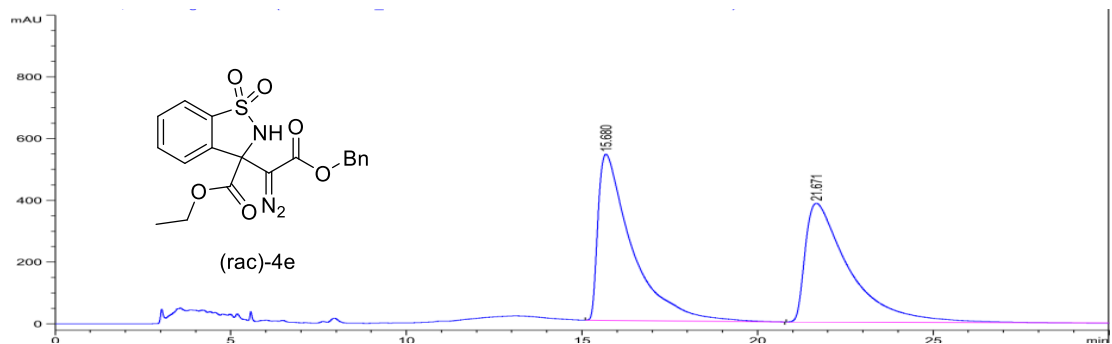


	Retention time (min)	Area (mAu + s)	%Area
1	17.346	2.49102e4	49.3744
2	23.341	2.55415e4	50.6256

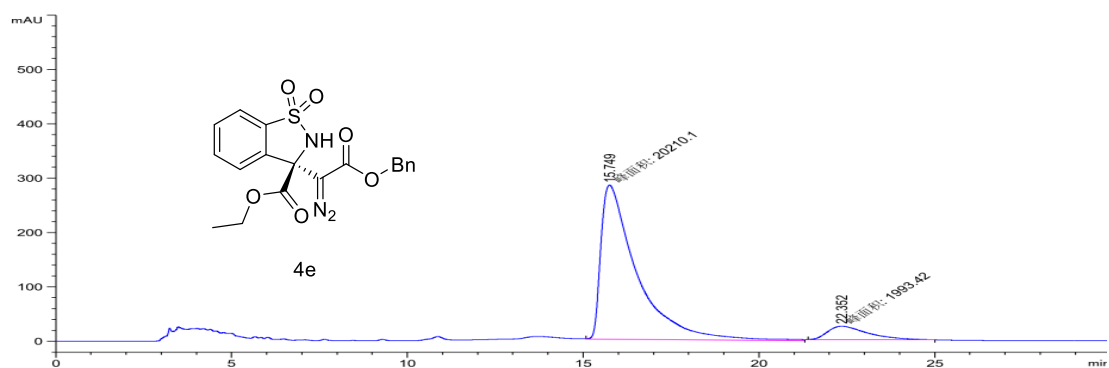


	Retention time (min)	Area (mAu + s)	%Area
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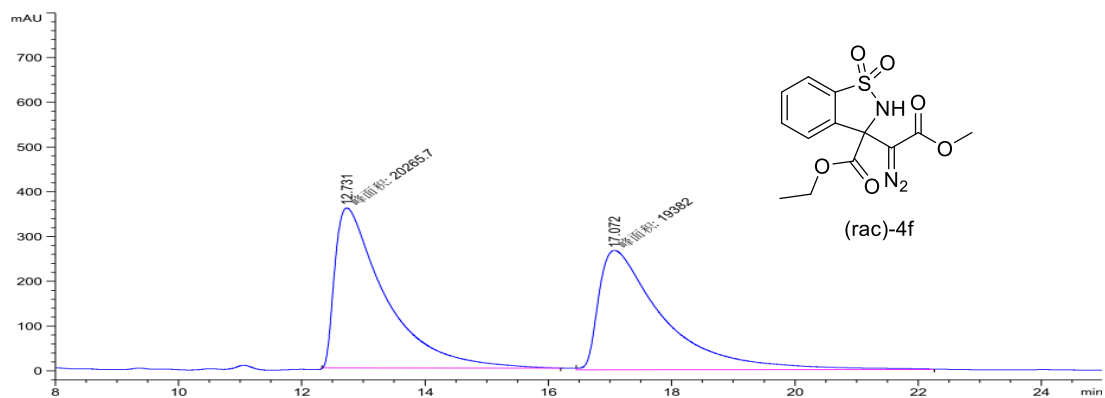
1	17.208	2.30002e4	90.3817
2	22.712	2447.64038	9.6183



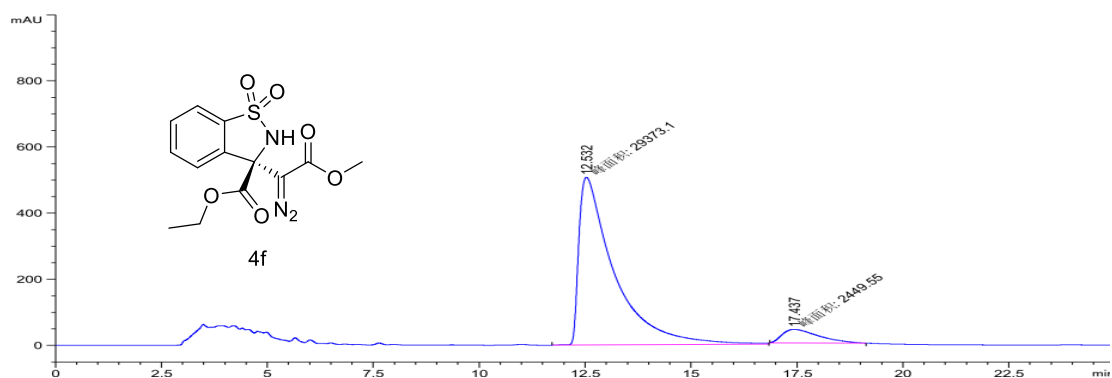
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1	15.680	3.61998e4	51.8893
2	21.671	3.35637e4	48.1107



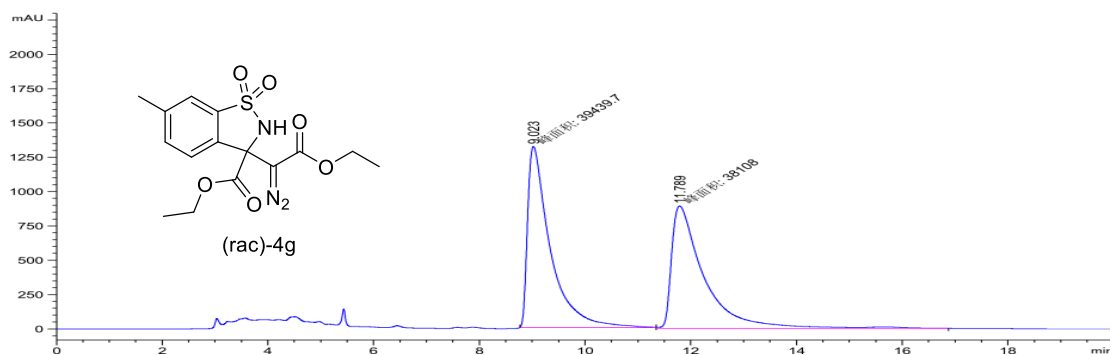
	Retention time (min)	Area (mAu + s)	%Area
1	15.749	2.02101e4	91.0221
2	22.352	1993.41882	8.9779



	Retention time (min)	Area (mAu + s)	%Area
1	12.731	2.02657e4	51.1144
2	17.072	1.93820e4	48.8856

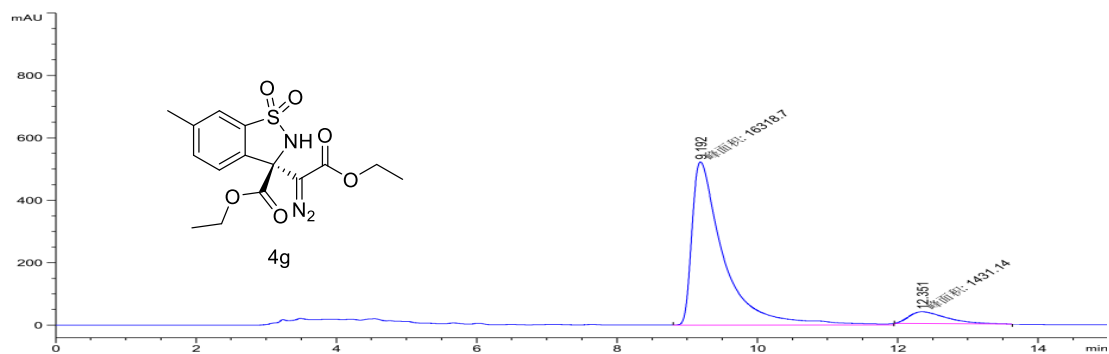


	Retention time (min)	Area (mAu + s)	%Area
1	12.532	2.93731e4	92.3025
2	17.437	2449.55225	7.6975

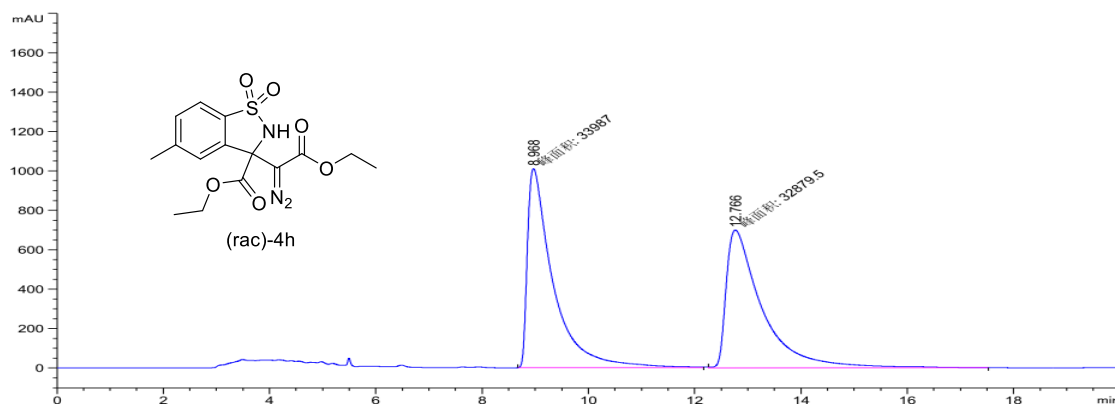


	Retention time (min)	Area (mAu + s)	%Area
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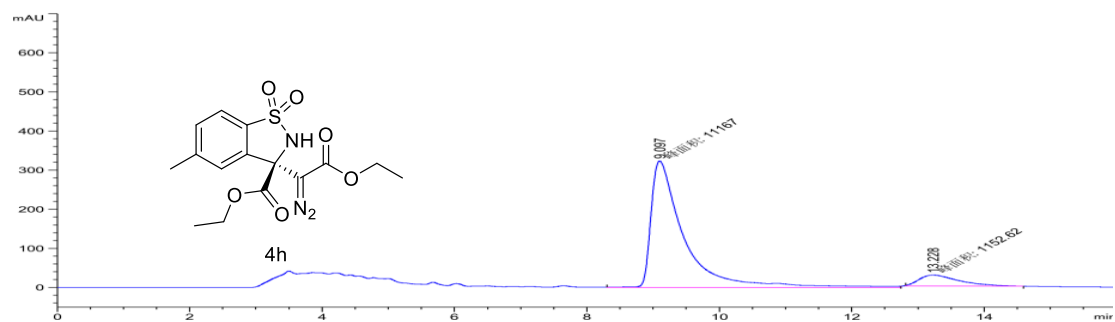
1	9.023	3.94397e4	50.8586
2	11.789	3.81080e4	49.1414



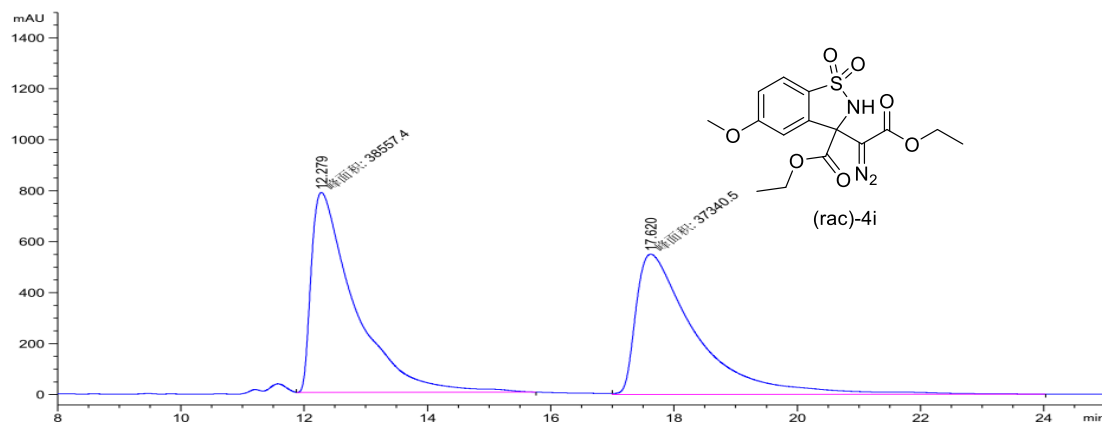
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1	9.192	1.63187e4	91.9372
2	12.351	1431.14148	8.0628



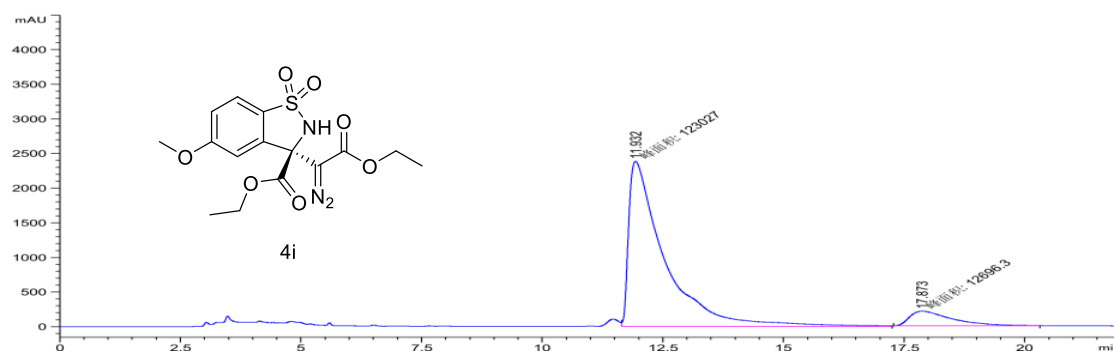
	Retention time (min)	Area (mAu + s)	%Area
1	8.968	3.39870e4	50.8281
2	12.766	3.28795e4	49.1719



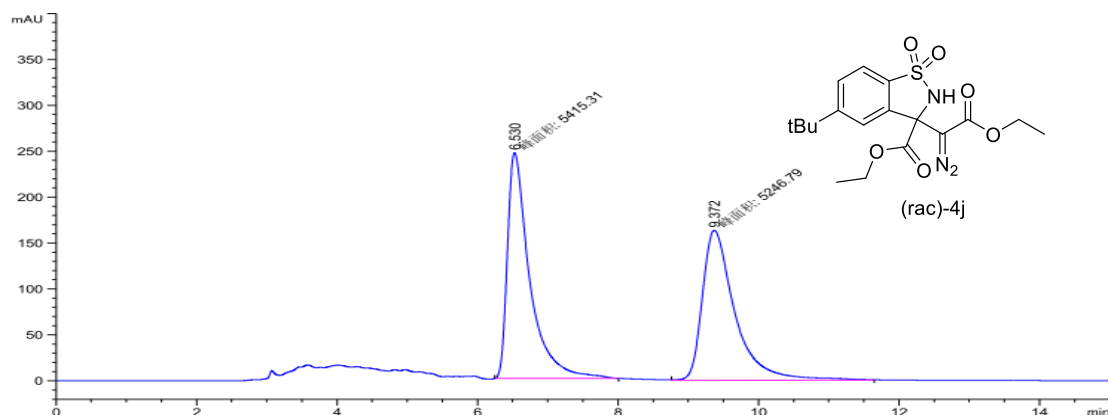
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1	9.097	1.11670e4	90.6441
2	13.228	1152.61780	9.3559



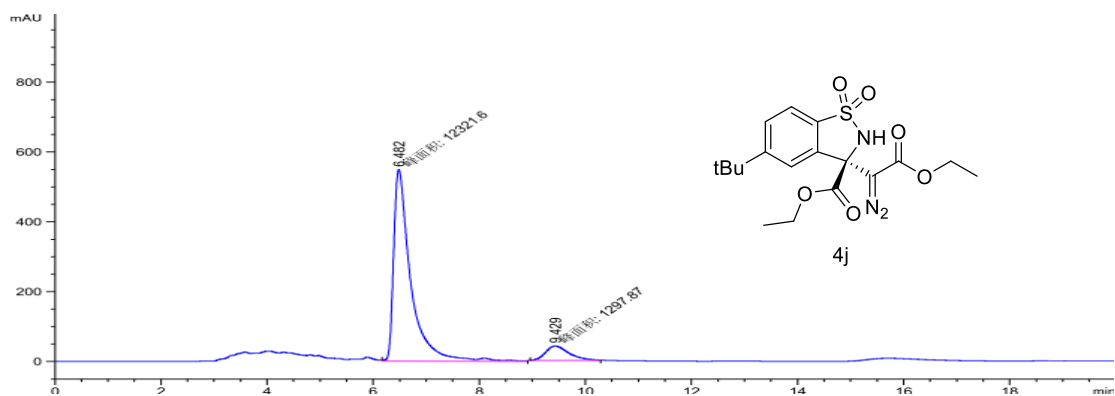
	Retention time (min)	Area (mAu + s)	%Area
1	12.279	3.85574e4	50.8016
2	17.620	3.73405e4	49.1984



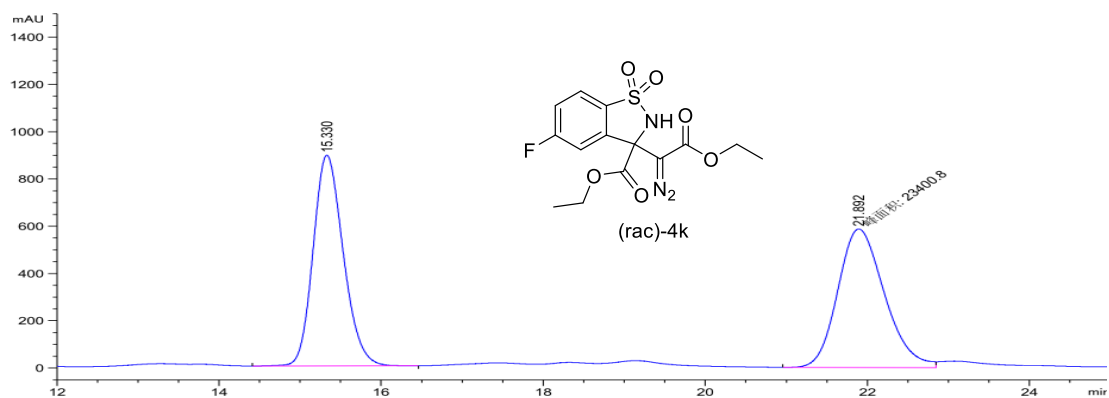
	Retention time (min)	Area (mAu + s)	%Area
1	11.932	1.23027e5	90.6454
2	17.873	1.26963e4	9.3546



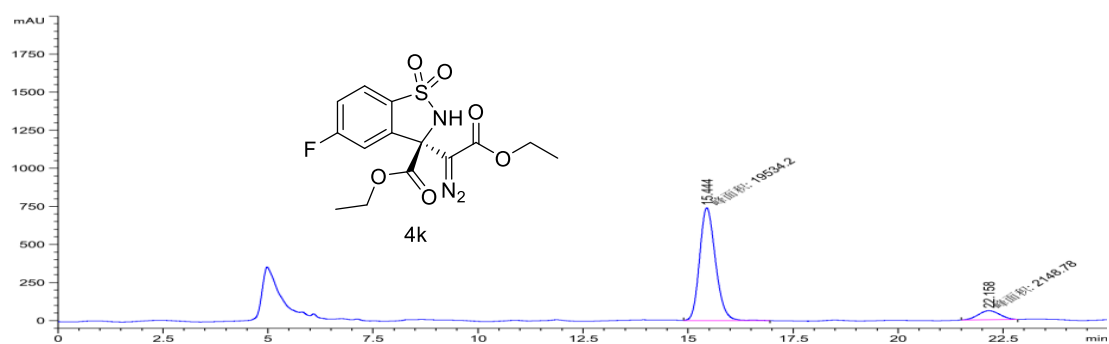
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1	6.530	5415.31201	50.7903
2	9.372	5246.79102	49.2097



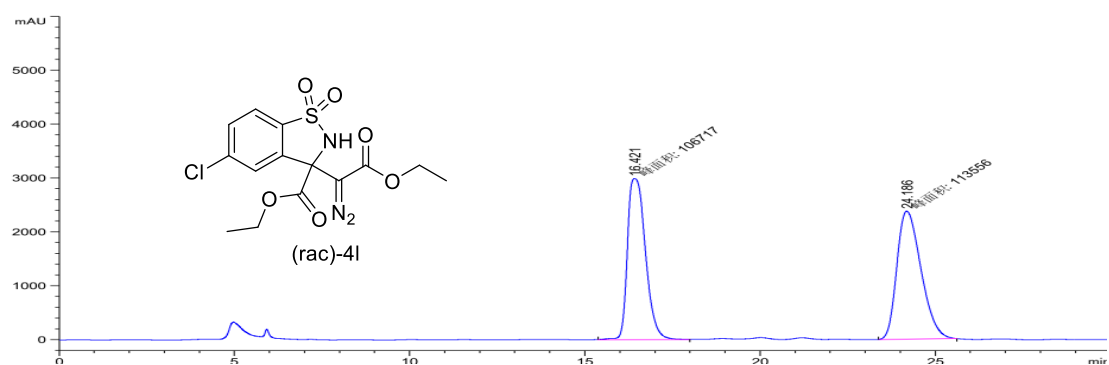
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1	6.482	1.23216e4	90.4704
2	9.429	1297.87061	9.5296



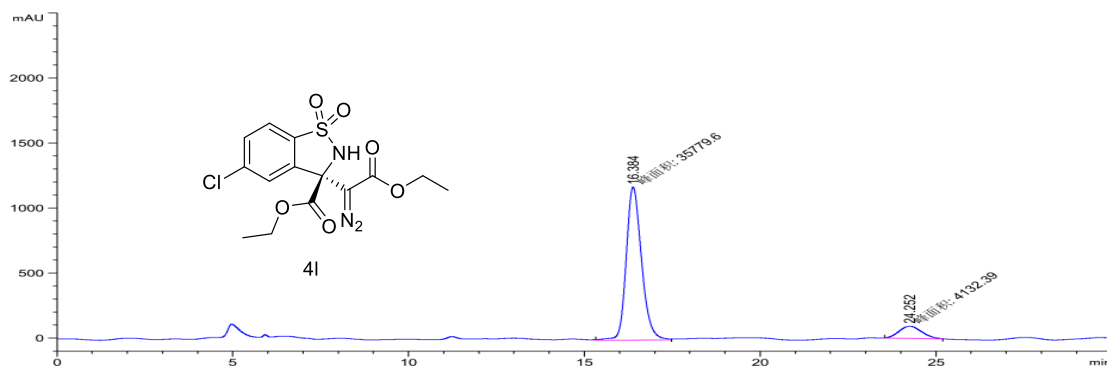
	Retention time (min)	Area (mAu + s)	%Area
1	15.330	2.30161e4	49.5857
2	21.892	2.34008e4	50.4143



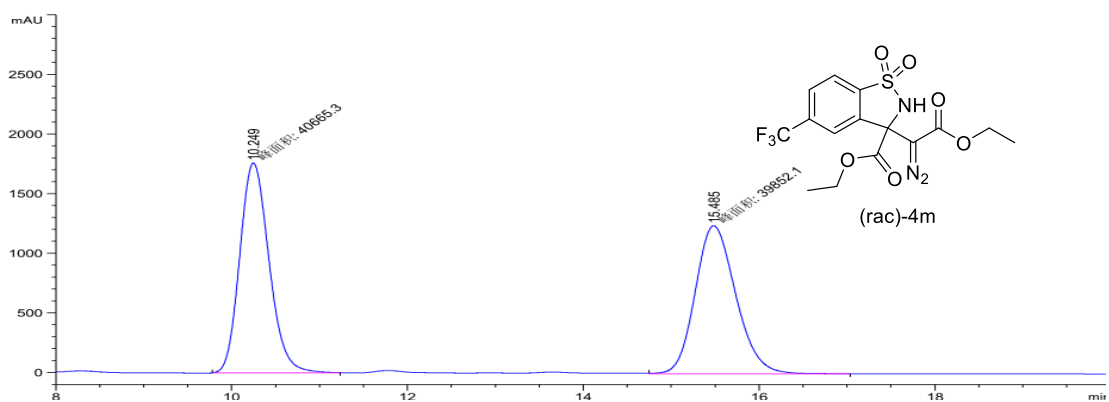
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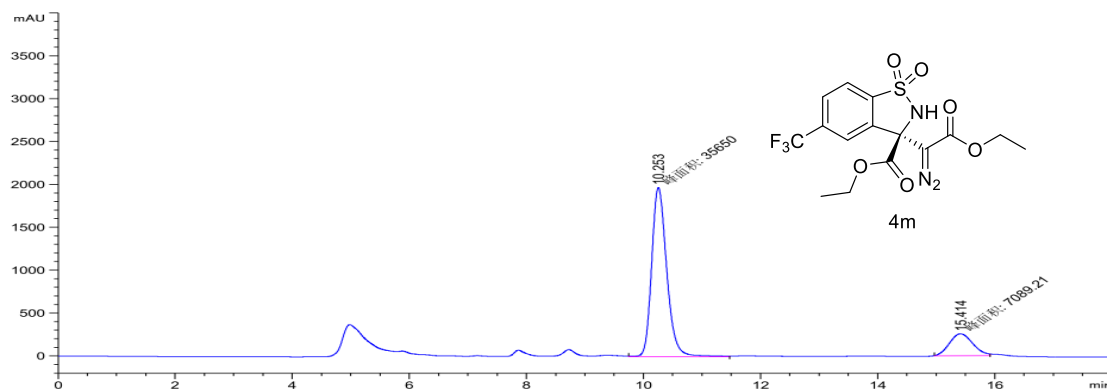
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2	24.186	1.13556e5	51.5523



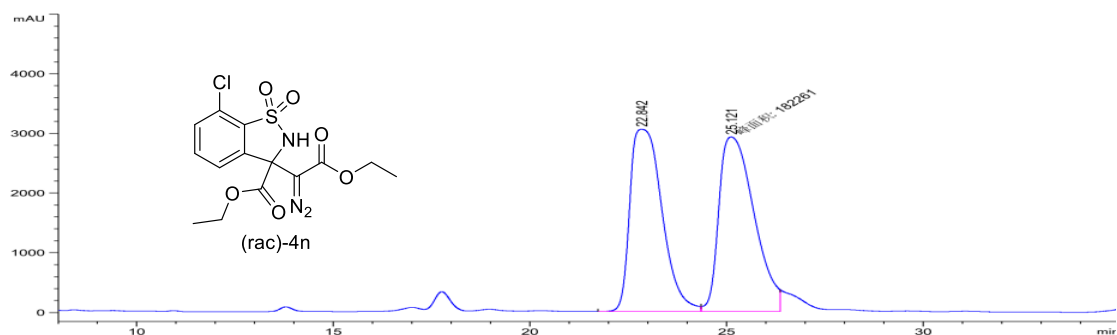
	Retention time (min)	Area (mAu + s)	%Area
1	16.384	3.57796e4	89.6463
2	24.252	4132.39160	10.3537



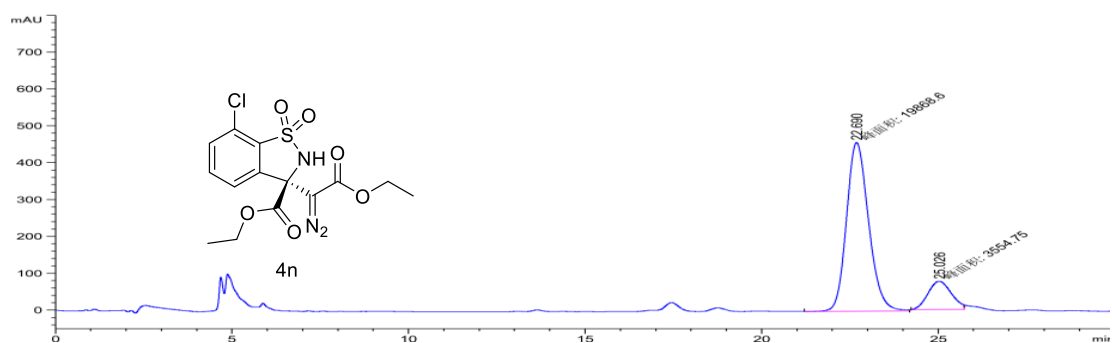
	Retention time (min)	Area (mAu + s)	%Area
1	10.249	4.06653e4	50.5050
2	15.485	3.98521e4	49.4950



	Retention time (min)	Area (mAu + s)	%Area
1	10.253	3.56500e4	83.4129
2	15.414	7089.20801	16.5871

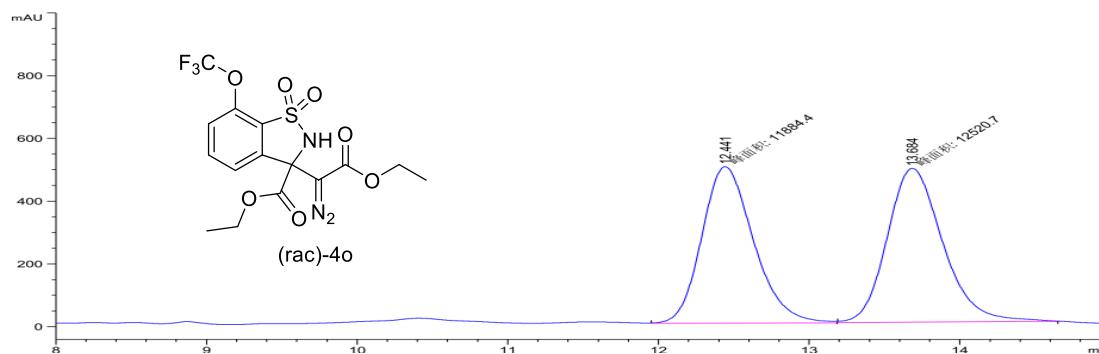


	Retention time (min)	Area (mAu + s)	%Area
1	22.842	1.73668e5	48.7930
2	25.121	1.82261e5	51.2070

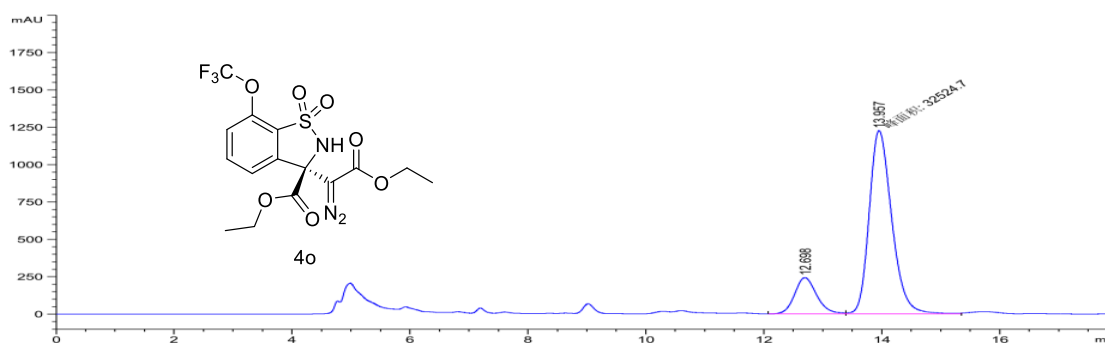


	Retention time (min)	Area (mAu + s)	%Area
1	22.690	1.98686e4	84.8239

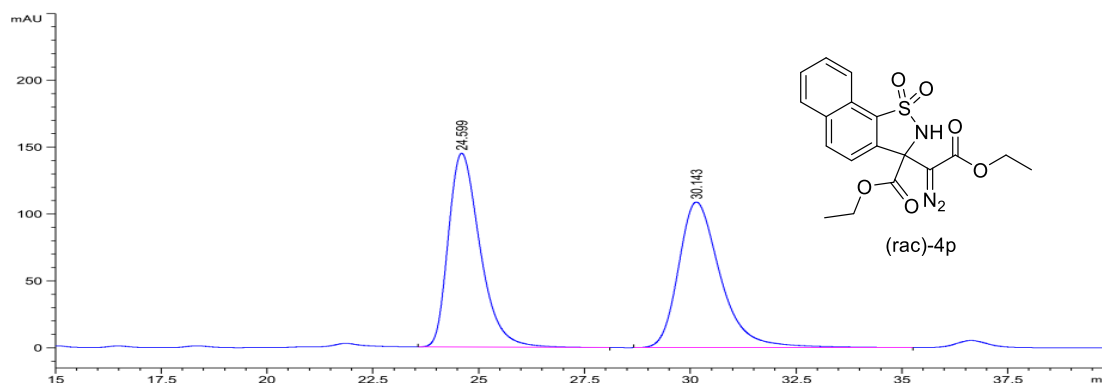
2	25.026	3554.74658	15.1761
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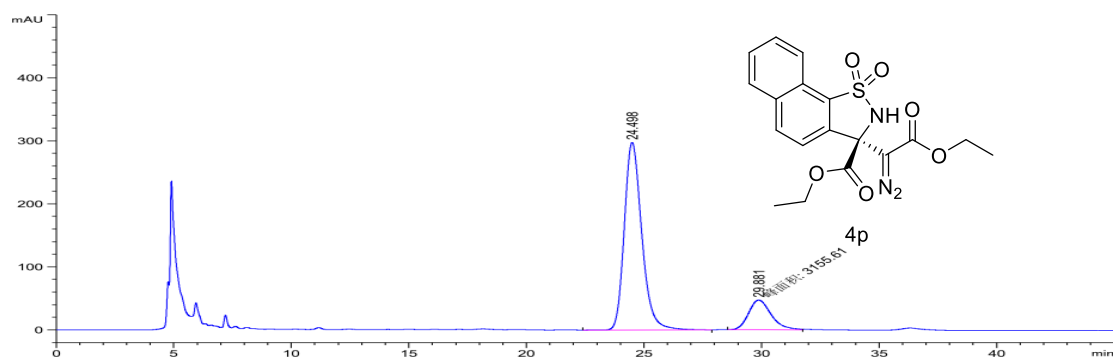
	Retention time (min)	Area (mAu + s)	%Area
1	12.441	1.18844e4	48.6964
2	13.684	1.25207e4	51.3036



	Retention time (min)	Area (mAu + s)	%Area
1	12.698	6261.78613	16.1442
2	13.957	3.25247e4	83.8558

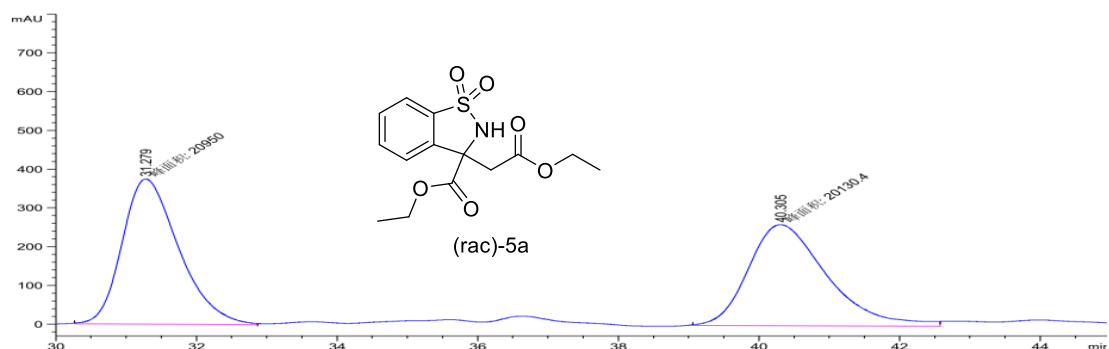


	Retention time (min)	Area (mAu + s)	%Area
1	24.599	7549.71533	50.2366
2	30.143	7478.61377	49.7634

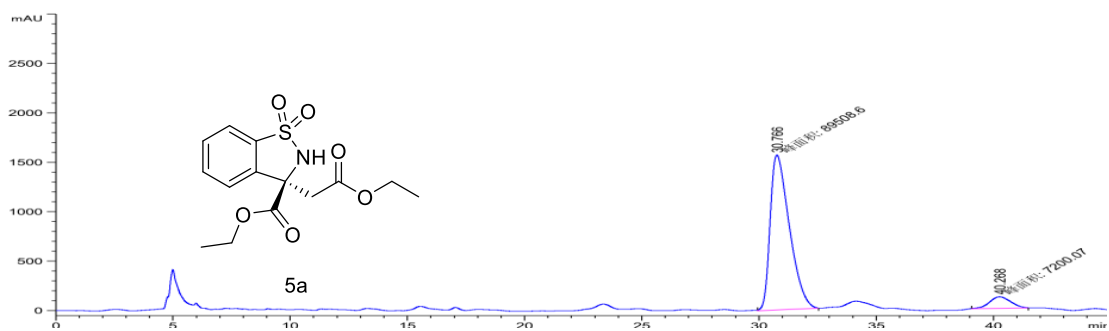


	Retention time (min)	Area (mAu + s)	%Area
1	24.498	1.53924e4	82.9868
2	29.881	3155.61377	17.0132

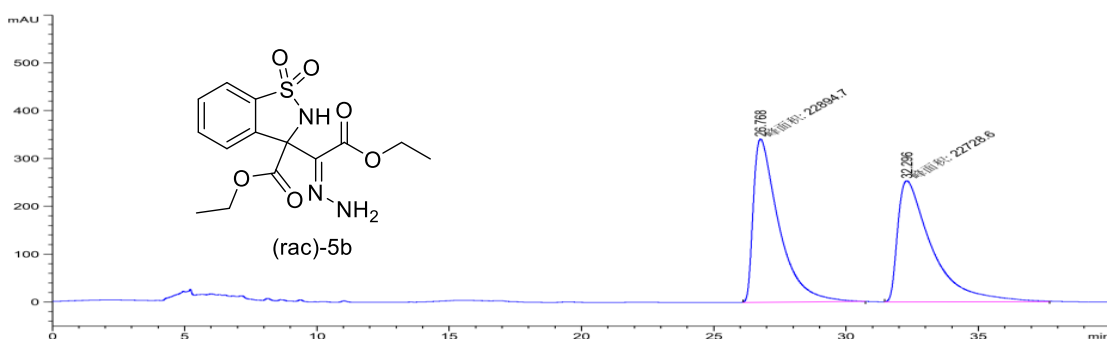
6. The analytical and spectral characterization data for the derivatives



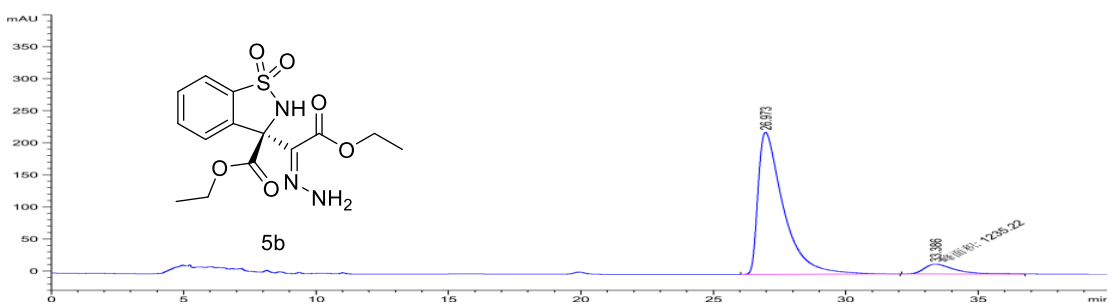
	Retention time (min)	Area (mAu + s)	%Area
1	31.279	2.09500e4	50.9976
2	40.305	2.01304e4	49.0024



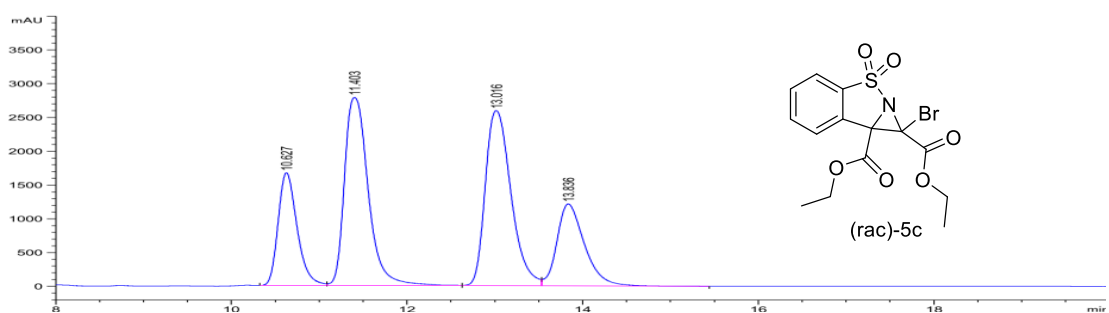
	Retention time (min)	Area (mAu + s)	%Area
1	30.766	8.9508e4	92.5549
2	40.268	7200.07373	7.4451



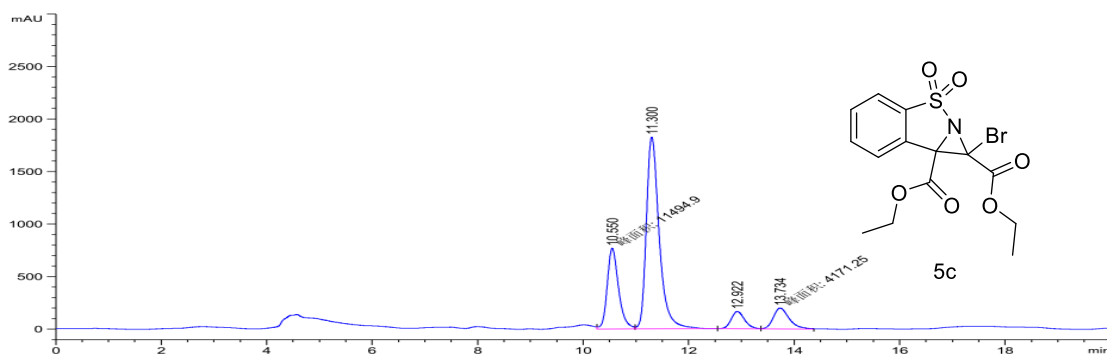
	Retention time (min)	Area (mAu + s)	%Area
1	26.768	2.28947e4	50.1819
2	32.296	2,27286e4	49.8181



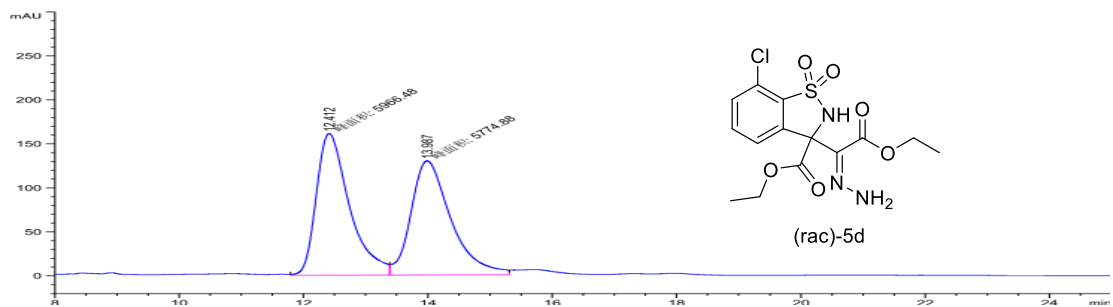
	Retention time (min)	Area (mAu + s)	%Area
1	26.973	1.47281e4	92.2621
2	33.386	1235.22302	7.7379



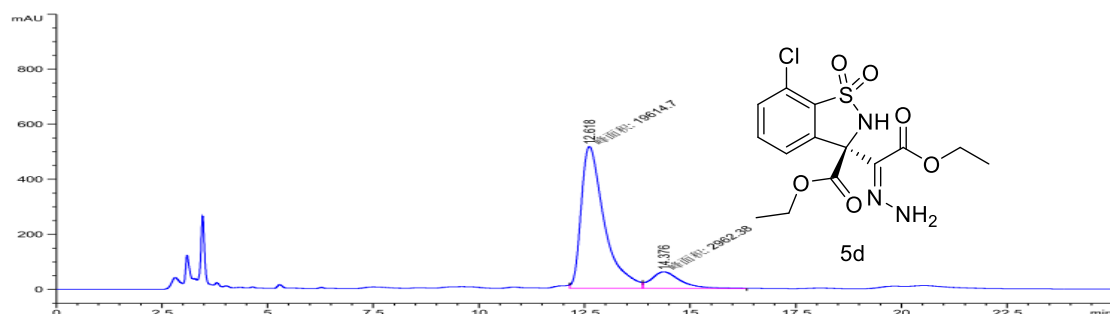
	Retention time (min)	Area (mAu + s)	%Area
1	10.627	2.50178e4	16.0581
2	11.403	5.20874e4	33.4334
3	13.016	5.24056e4	33.6376
4	13.836	2.62840e4	16.8709



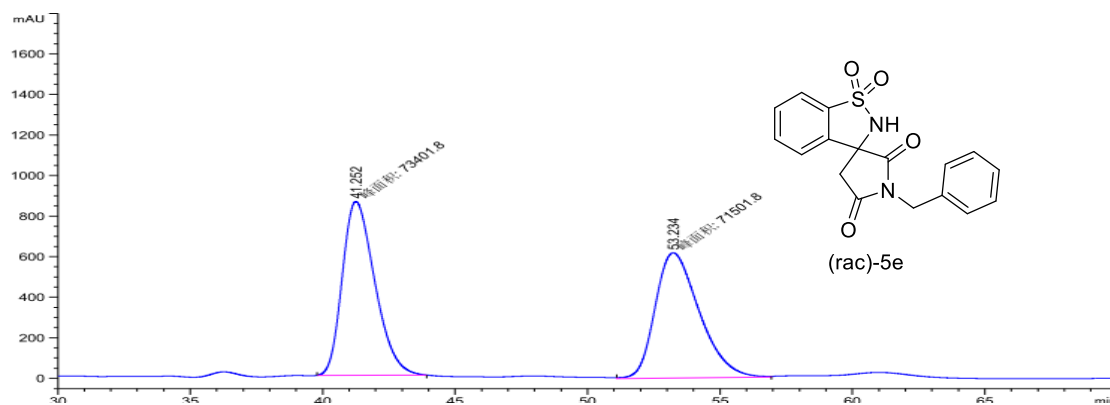
	Retention time (min)	Area (mAu + s)	%Area
1	10.550	1.14949e4	23.1973
2	11.300	3.10101e4	62.5802
3	12.922	2876.36304	5.8047
4	13.734	4171.25391	8.4178



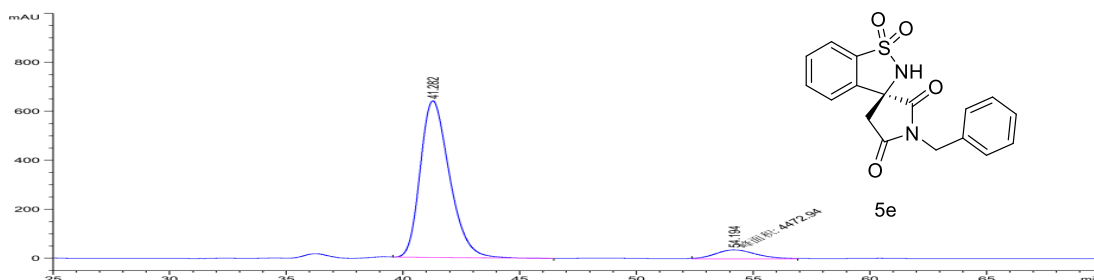
	Retention time (min)	Area (mAu + s)	%Area
1	12.412	5966.47900	50.8159
2	13.987	5774.88428	49.1841



	Retention time (min)	Area (mAu + s)	%Area
1	12.618	1.96147e4	86.8788
2	14.376	2962.38110	13.1212



	Retention time (min)	Area (mAu + s)	%Area
1	41.252	7.34018e4	50.6556
2	53.234	7.15018e4	49.3444



	Retention time (min)	Area (mAu + s)	%Area
1	41.282	5.56462e4	92.5599
2	54.194	4472.94189	7.4401

7. X-ray crystal structure for 5d

CCDC 1580590 (**5d**) contain the supplementary crystallographic data of adducts for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

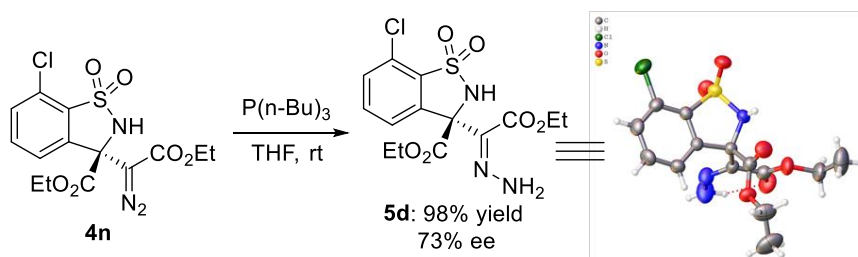


Table 1 Crystal data and structure refinement for 5d.

Identification code	5d
Empirical formula	C ₁₄ H ₁₆ ClN ₃ O ₆ S
Formula weight	389.81
Temperature/K	293.15
Crystal system	triclinic
Space group	P-1
a/Å	7.8621(4)
b/Å	10.1290(5)
c/Å	12.5926(5)
α/°	70.829(4)
β/°	76.104(4)
γ/°	67.503(5)
Volume/Å ³	867.55(8)
Z	2
ρ _{calc} /g/cm ³	1.492
μ/mm ⁻¹	0.377

F(000)	404.0
Crystal size/mm ³	0.3 × 0.25 × 0.02
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/°	5.834 to 52.738
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 12, -15 ≤ l ≤ 15
Reflections collected	7194
Independent reflections	3544 [R_{int} = 0.0194, R_{sigma} = 0.0424]
Data/restraints/parameters	3544/0/240
Goodness-of-fit on F^2	1.098
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0492, wR_2 = 0.1246
Final R indexes [all data]	R_1 = 0.0752, wR_2 = 0.1343
Largest diff. peak/hole / e Å ⁻³	0.67/-0.50

8. NMR Spectra of the Compounds 4-5

