

Supporting Information

The Effects of Solvent on Switchable Stereoselectivity: Copper-Catalyzed Asymmetric Conjugate Addition Using *D*₂-Symmetric Biphenyl Phosphoramidite Ligand

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Table of Contents

1. General Experimental Conditions.....	S2
2. General Procedure for Preparation of the Substrates.....	S2
3. General Procedure for Copper-Catalyzed Enantioselective Conjugate Addition...S2	
4. Screening of <i>trans</i> - L3-5	S4
5. NMR Charts of New Compounds.....	S5
6. HPLC Data of Copper-Catalyzed Conjugate Addition Products	S7

1. General Experimental Conditions

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen. Toluene, PhCF₃, DMF, THF, Et₂O, DIPE, MTBE, and dichloromethane were dried according to published procedures. Commercially available reagents were used without further purification. All reactions were performed under a nitrogen atmosphere, and the workup was carried out in air unless otherwise stated.

NMR spectra were recorded on a Varian MERCURY plus-400 spectrometer. The chemical shifts were reported in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Coupling constants are reported in Hz and refer to apparent peak multiplicities. Optical rotations were measured with a SPSI SGW-1 polarimeter. All *ee* values were determined by HPLC using a Daicel Chiralcel OJ-H or AD-H column.

2. General Procedure for Preparation of the Substrates¹

To a solution of 2.2 g of NaOH in 20 mL of H₂O and 43 mmol of aromatic ketone in 12 mL ethanol at 0 °C was gradually added 1 equiv of aromatic aldehyde (43 mmol). The mixture was then allowed to warm to room temperature and stirred for 4 h, after which a precipitate of the product formed. The product was collected by suction filtration on a Buchner funnel and washed repeatedly with cold water in order to remove all traces of sodium hydroxide. Recrystallization of the product from ethanol afforded enones **1a-n**. All spectroscopic data of enones **1a-n** are in good agreement with reported literature data.¹

3. General Procedure for Copper-Catalyzed Enantioselective Conjugate Addition

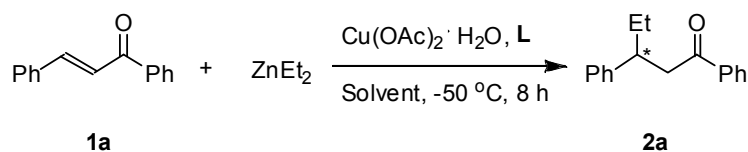
A flame dried Schlenk tube was charged with Cu(OAc)₂·H₂O (1.0 mg, 0.005 mmol) and *trans*-**L2** (7.8 mg, 0.01 mmol) under a N₂ atmosphere, and the mixture was dissolved in dry toluene (1.5 mL). The solution was stirred at 25 °C for 30 min and then cooled to -50 °C. Et₂Zn (0.75 mmol, 0.75 mL of 1 M hexane solution) was added dropwise to the above solution. The colour of the solution gradually turned to light yellow after 5 min at -50 °C. The substrate **1a** (0.50 mmol dissolved in 1.0 mL dry toluene) was then added dropwise. The mixture was stirred at -50 °C for 16 h before quenching with aqueous saturated NH₄Cl. The layers were separated and the aqueous layer was extracted with ethyl acetate (5 mL×2). The combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the addition product. The enantiomeric excess of the product was determined by chiral HPLC.

References

1. (a) *Vogel's Textbook of Practical Organic Chemistry (ELBS)*, 5th ed.; Longman Group: UK, 1989, 1034; (b) E. P. Kohler and H. M. Chadwell, *Org. Synth. Coll.*, 1941, **1**, 78; (c) W. Davey and D. J. Tivey, *J. Chem. Soc.*, 1958, 1230; (d) T. A. Forester and I. M. Heiborn, *J. Chem. Soc.*, 1924, 340; (e) H. Xian, X. Linghong and I. N. Hong, *J. Org. Chem.*, 1988, **53**,

4862; (f) M. Brenan, I. Hunt, T. C. Jarvis, C. D. Johnson and P. D. McDonell, *Can. J. Chem.*, 1990, **68**, 1780; (g) K. V. Auwers and H. Brink, *Annalen*, 1932, **493**, 218; (h) X. Hu, H. Chen and X. Zhang, *Angew. Chem. Int. Ed.*, 1999, **38**, 3518; (i) M. Shi, C. Wang and W. Zhang, *Chem. Eur. J.*, 2004, **10**, 5507; (j) L. Liu and M. Wang, *Tetrahedron: Asymmetry*, 2006, **17**, 136; (k) A. Isleyen and Z. Dogan, *Tetrahedron: Asymmetry*, 2007, **18**, 679; (l) W. Zhang and M. Shi, *Synlett*, 2007, 19; (m) Y. Xie, H. Huang and X. Hu, *Tetrahedron: Asymmetry*, 2009, **20**, 1425.

4. Screening of *trans*-L3-5^a



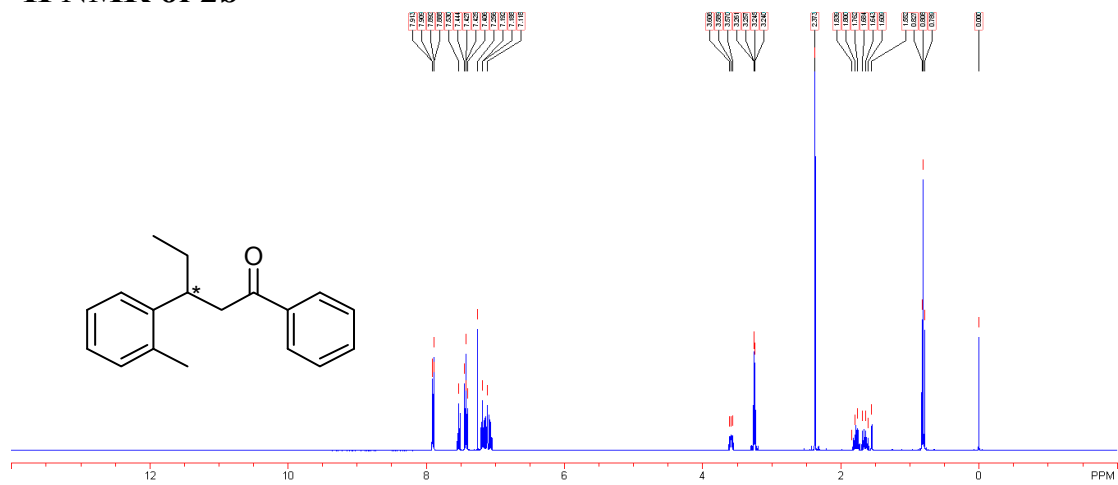
Entry	L	Solvent	Yield (%) ^b	<i>Ee</i> (%) ^c
1	<i>trans</i> -L3	Toluene	95	82 (<i>R</i>)
2	<i>trans</i> -L3	THF	95	75 (<i>S</i>)
3	<i>trans</i> -L4	Toluene	94	73 (<i>R</i>)
4	<i>trans</i> -L4	THF	96	61 (<i>S</i>)
5	<i>trans</i> -L5	Toluene	91	65 (<i>R</i>)
6	<i>trans</i> -L5	THF	93	53 (<i>S</i>)

^a1 mol% Cu salt, 2 mol% *trans*-L, 1.5 eq. ZnEt₂. ^bYield of the isolated product.

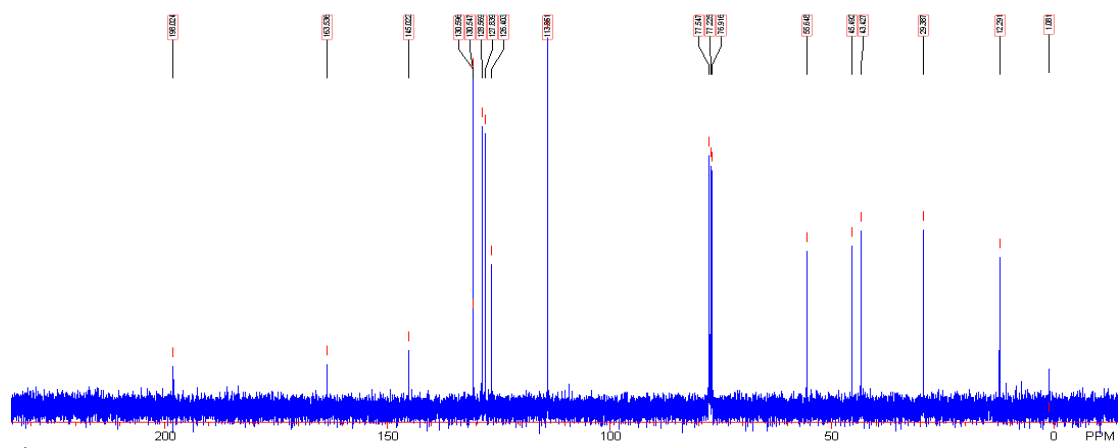
^cDetermined by HPLC, Chiralcel AD-H column. The absolute configuration was determined by comparison with literature data.

5. NMR Charts of New Compounds

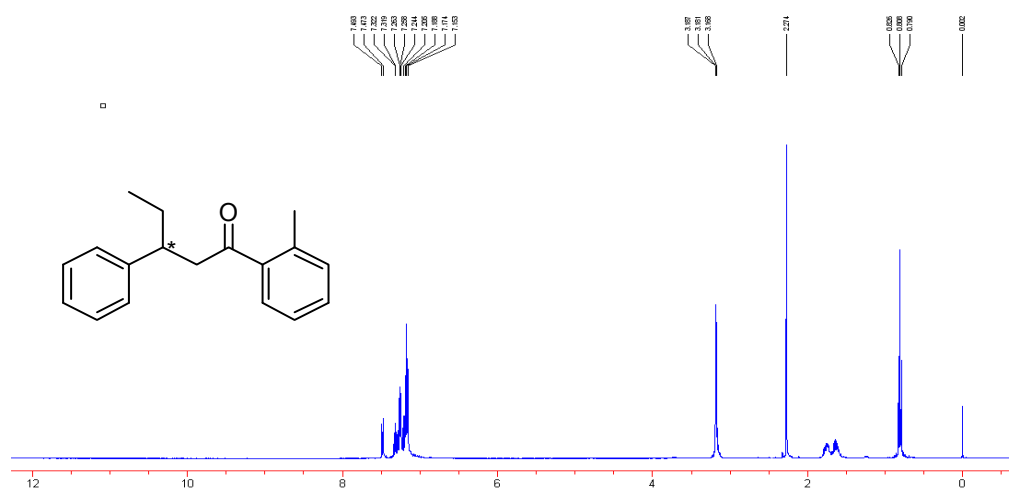
^1H NMR of 2b



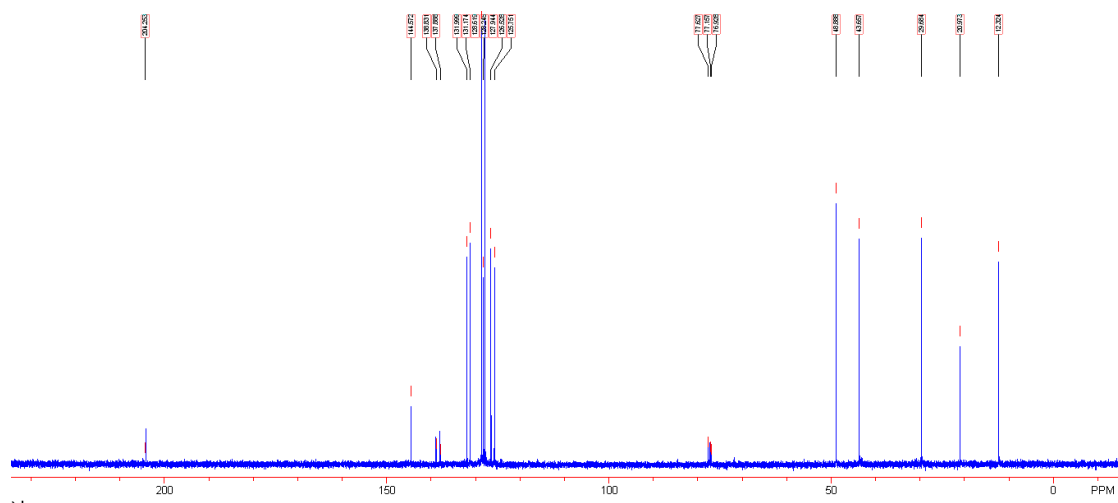
^{13}C NMR of 2b



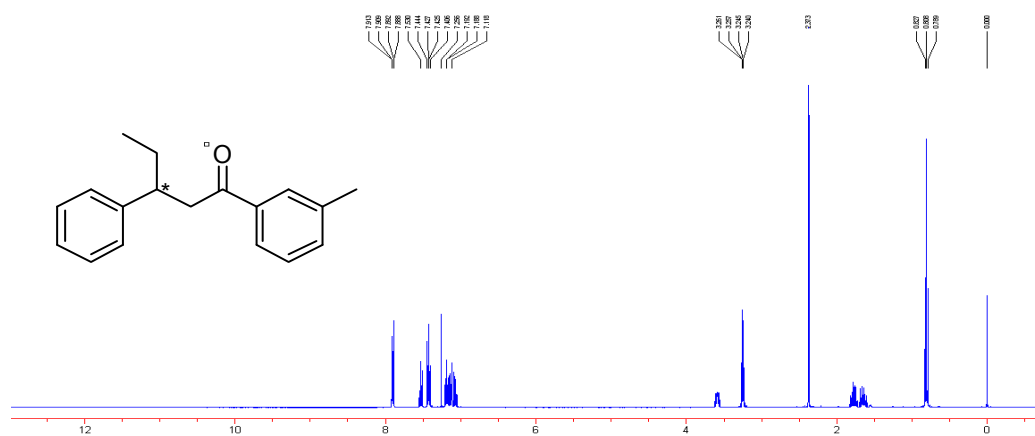
^1H NMR of 2h



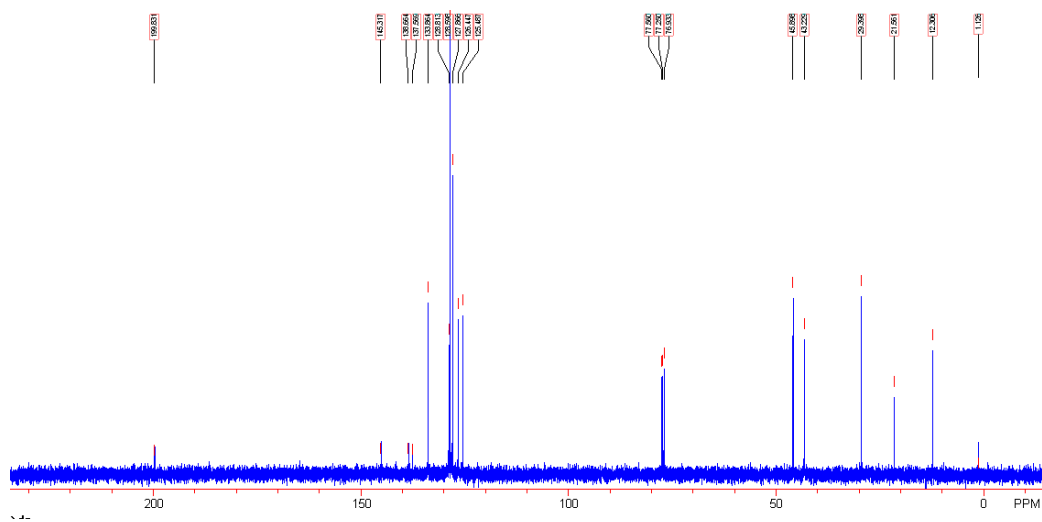
^{13}C NMR of 2h



^1H NMR of 2i

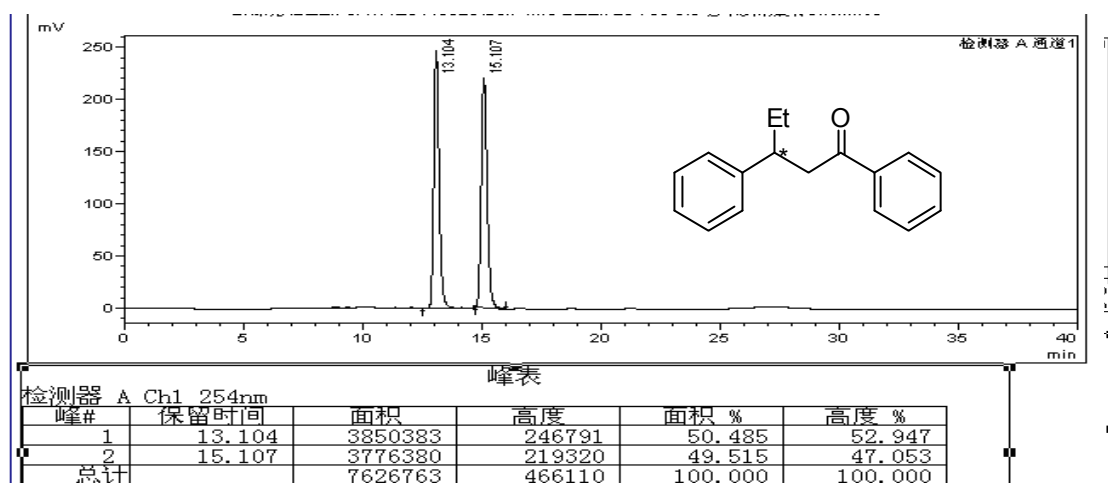


^{13}C NMR of 2i

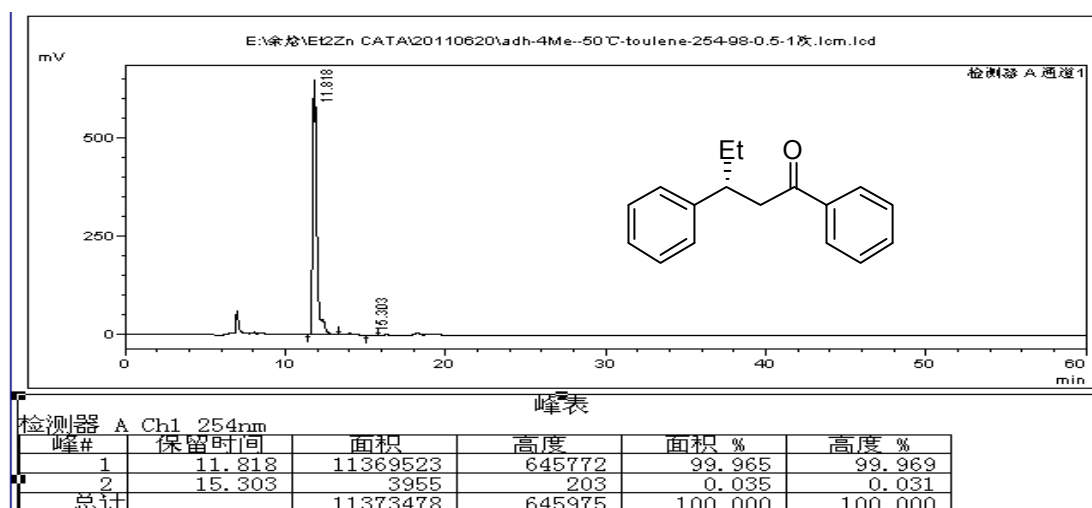


6. HPLC Date of Copper-Catalyzed Conjugate Addition Products

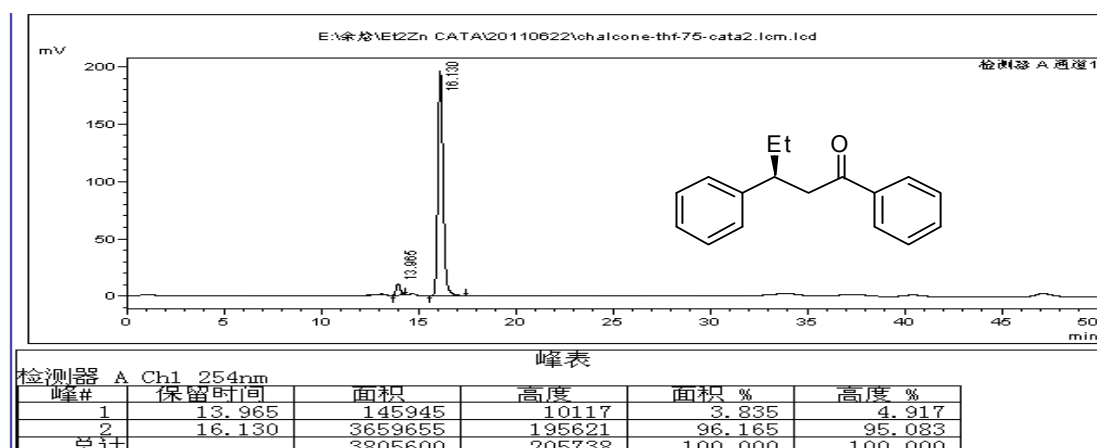
HPLC data of 2a, racemic sample



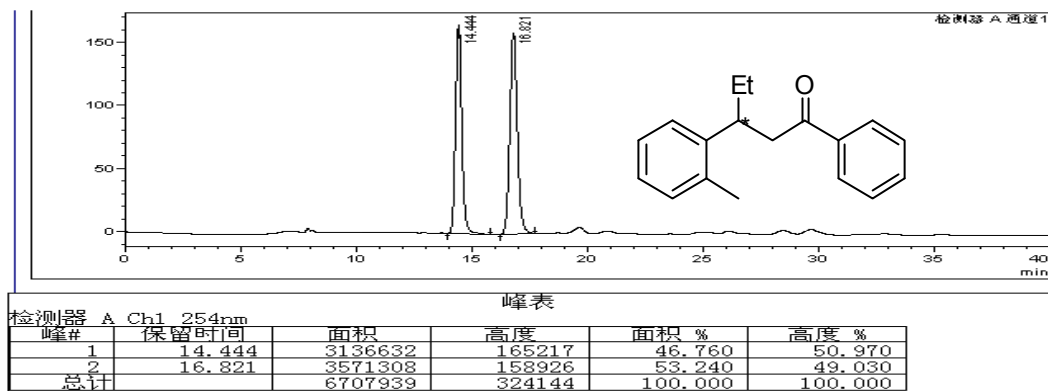
Toluene as solvent



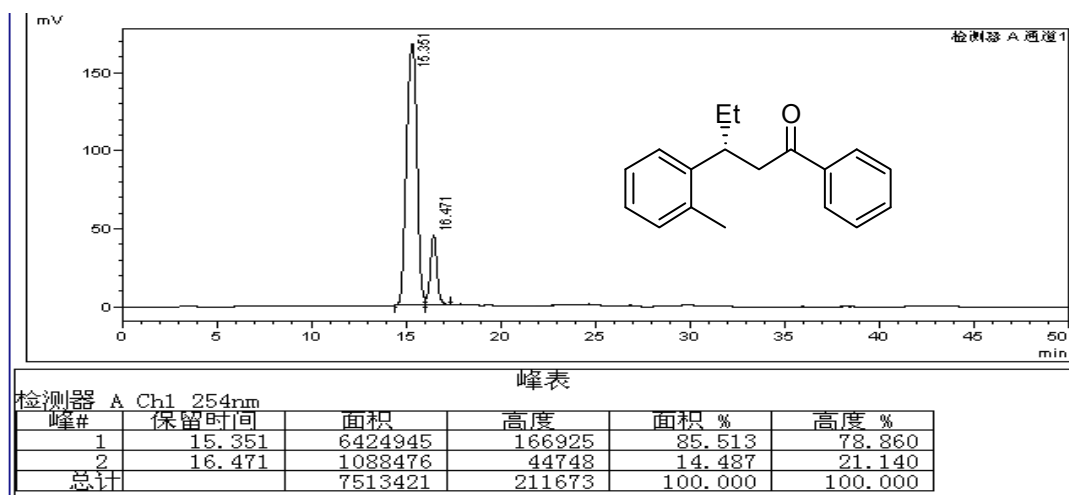
THF as solvent



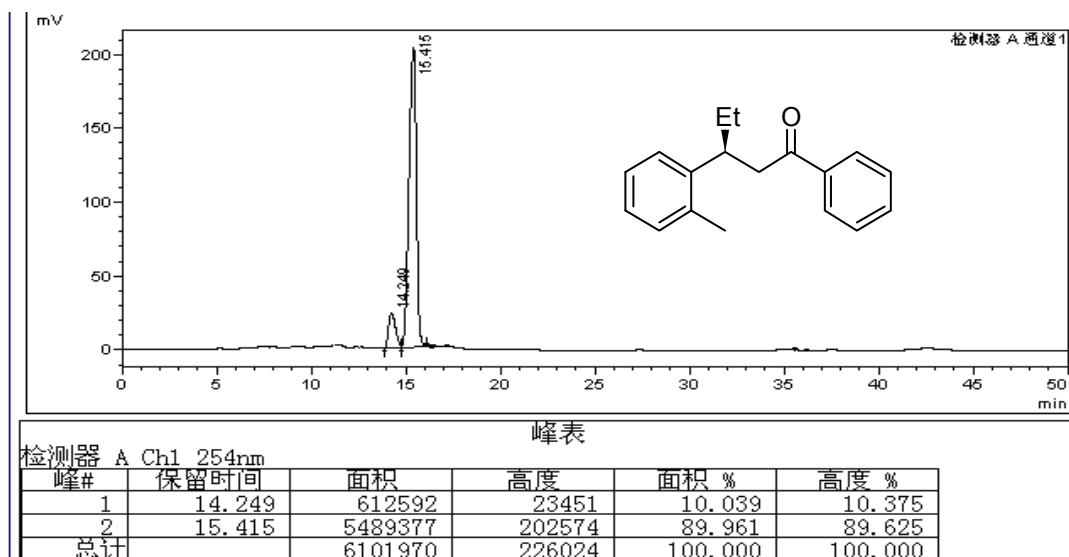
HPLC data of 2b, racemic sample



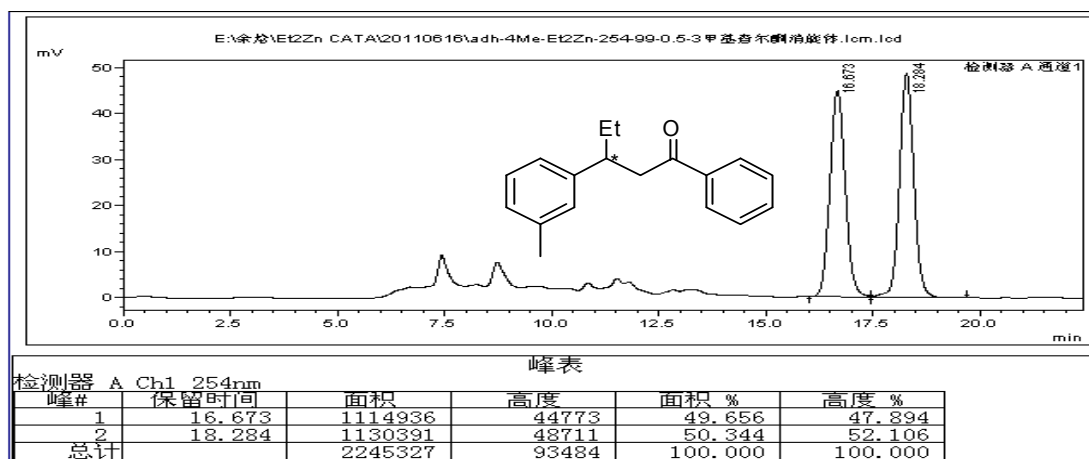
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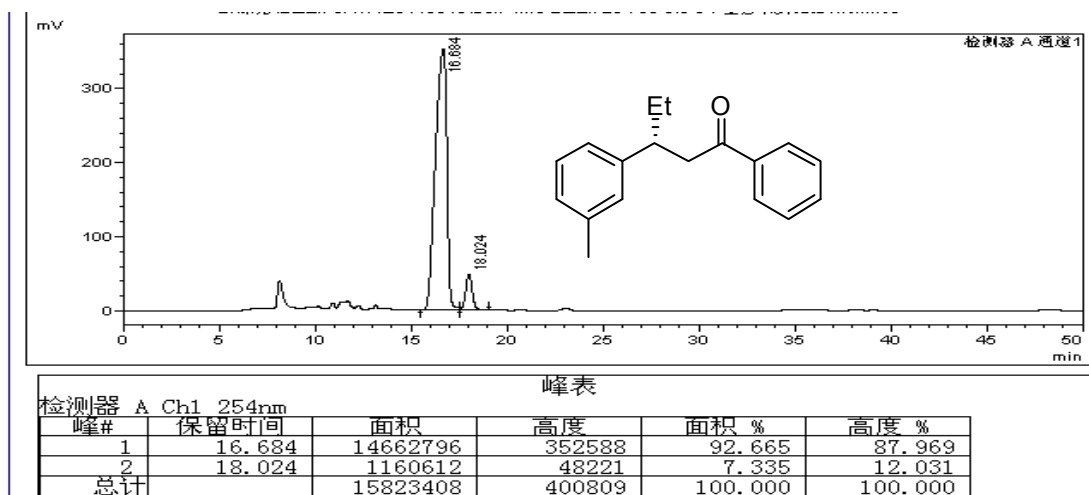
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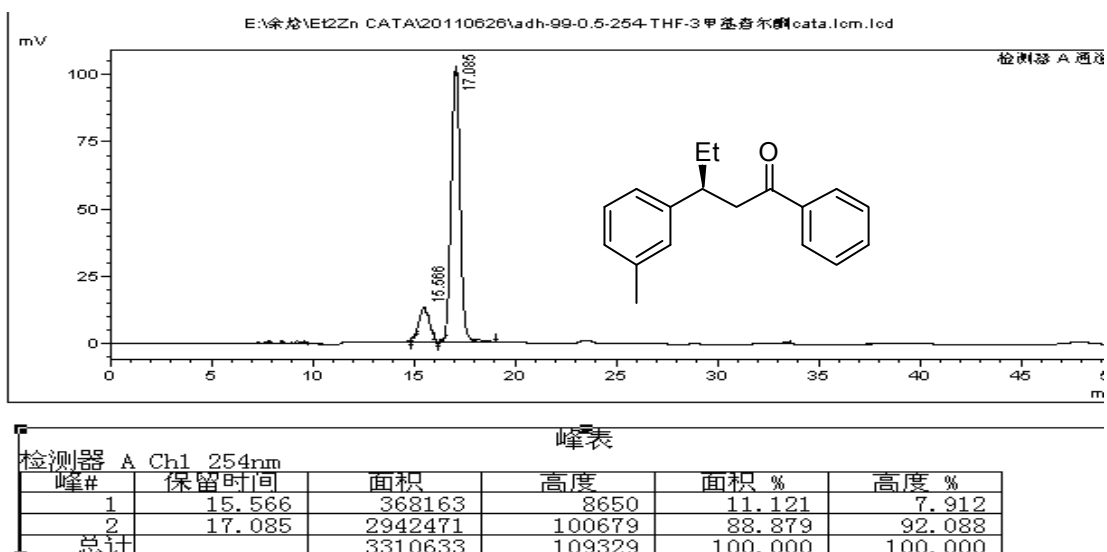
HPLC data of 2c, racemic sample



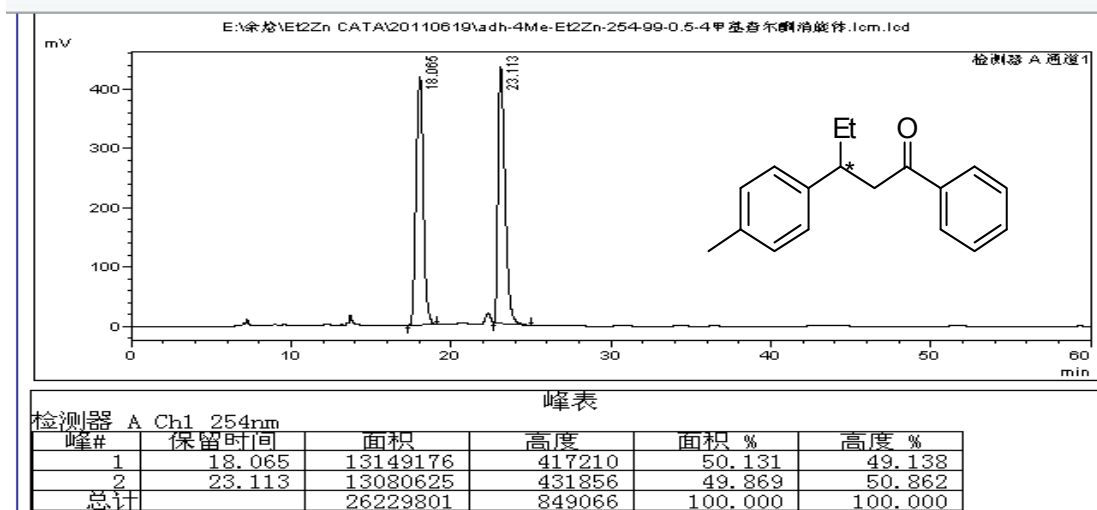
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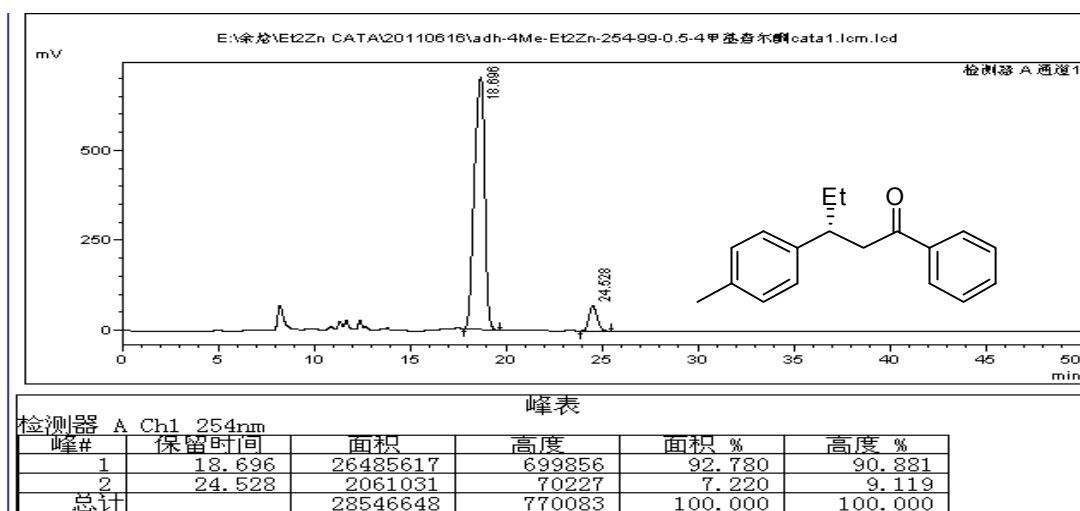
THF as solvent



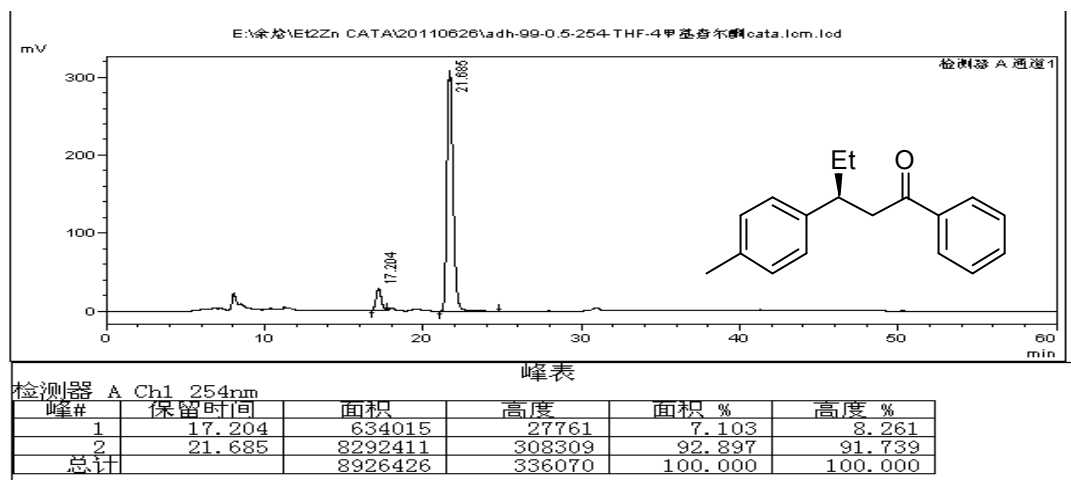
HPLC data of 2d, racemic sample



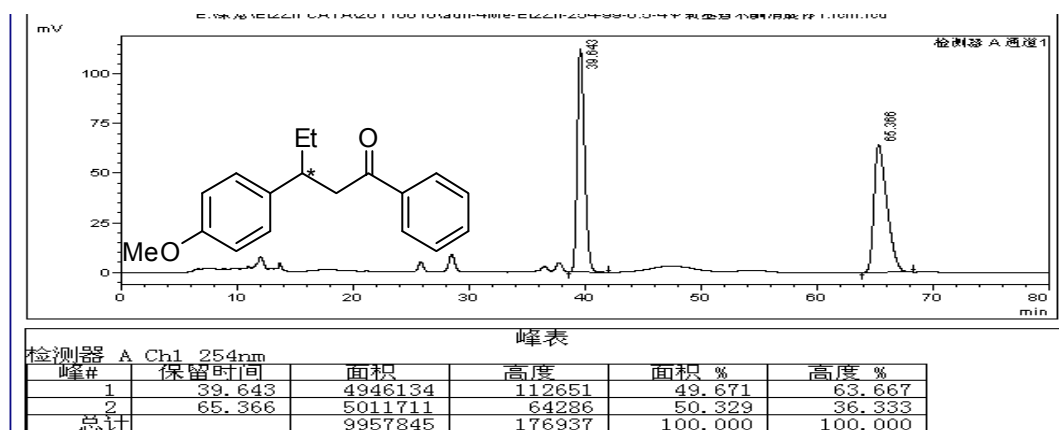
Toluene as solvent



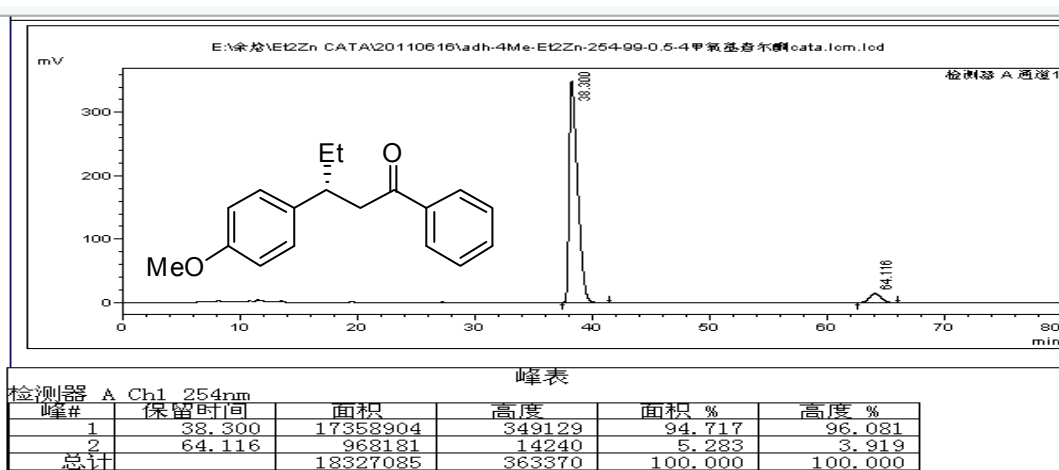
THF as solvent



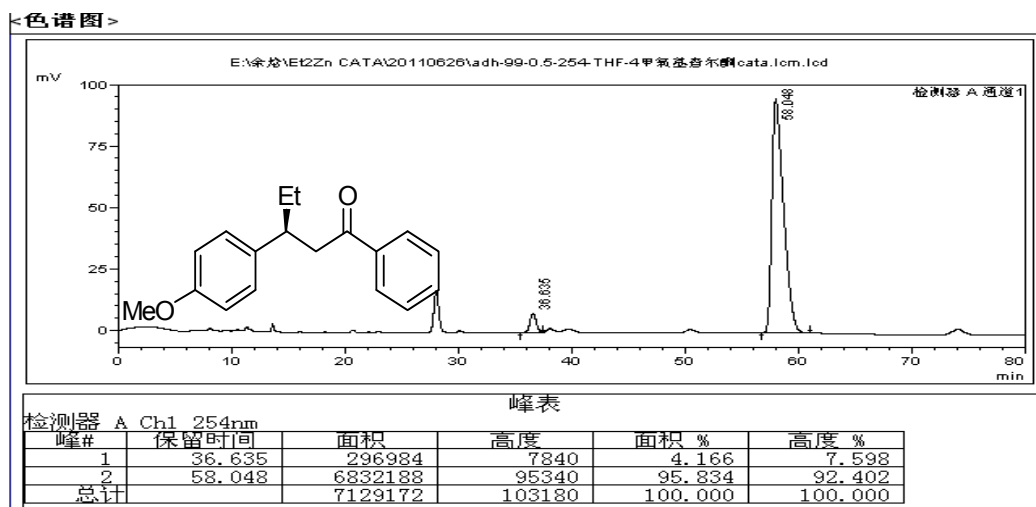
HPLC data of 2e, racemic sample



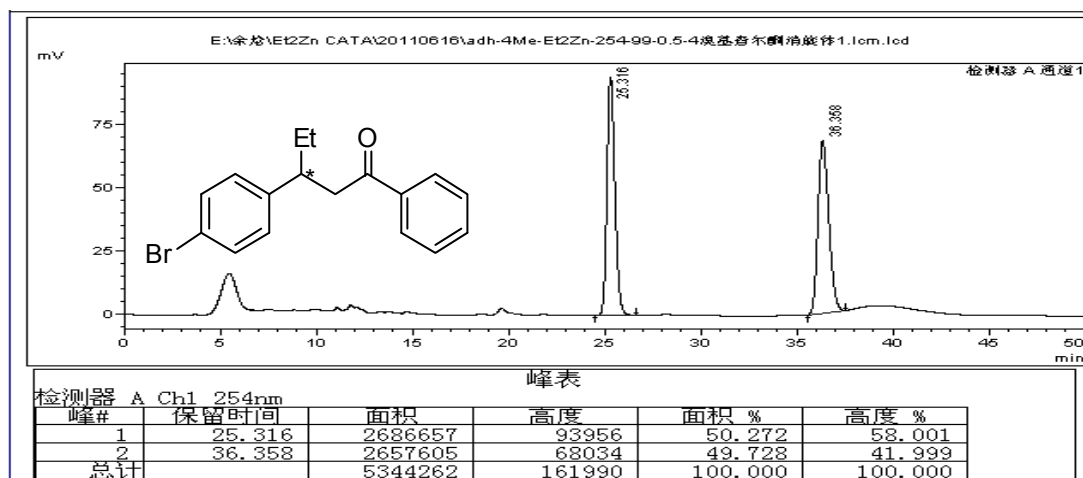
Toluene as solvent



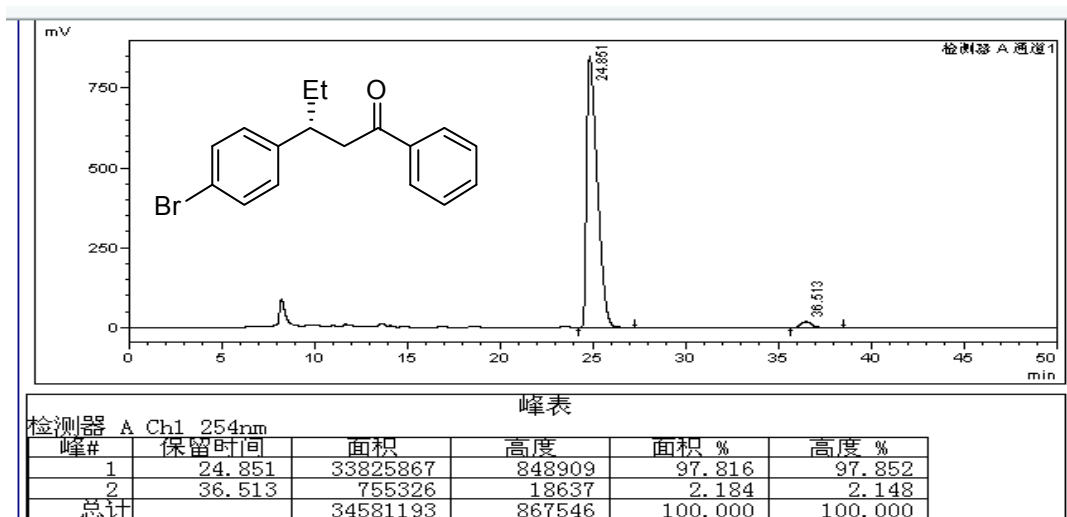
THF as solvent



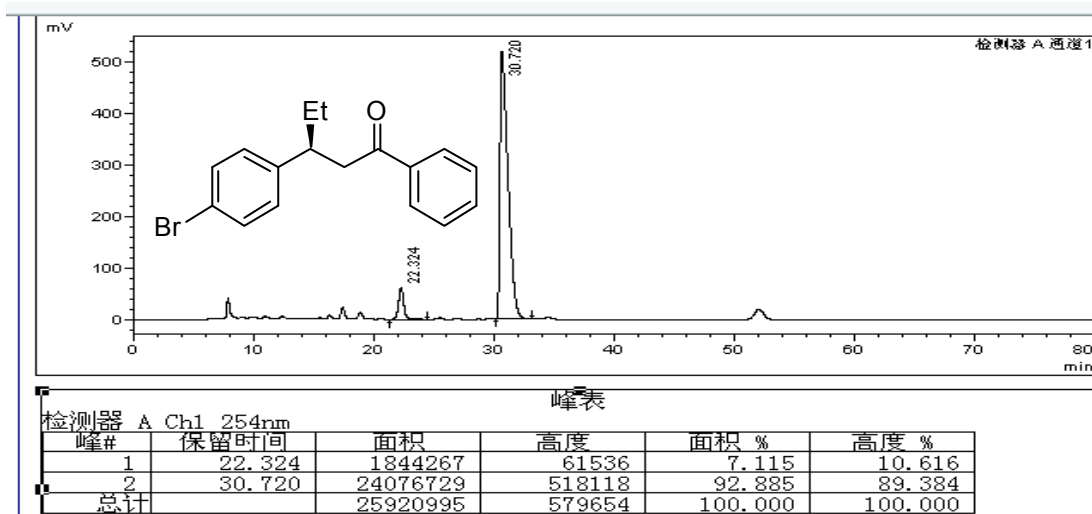
HPLC data of 2f, racemic sample



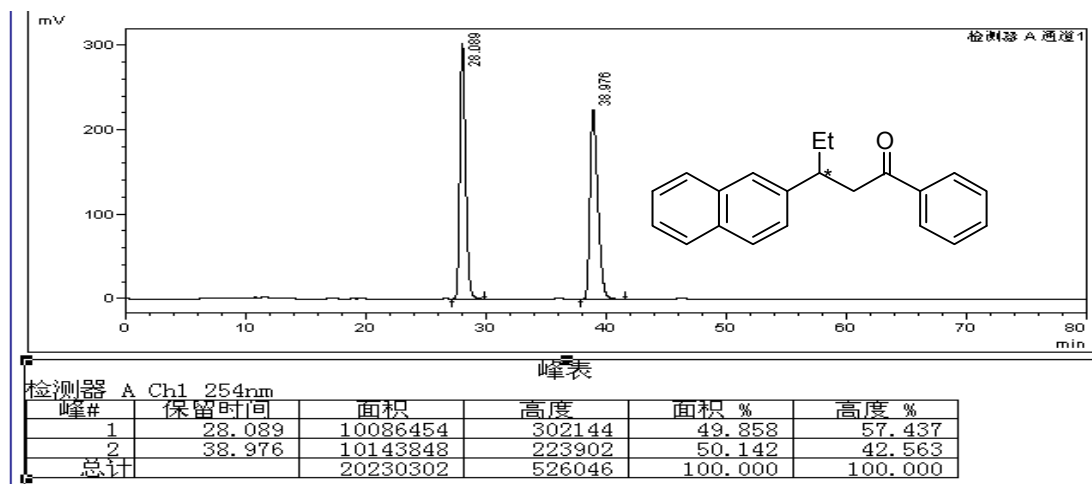
Toluene as solvent



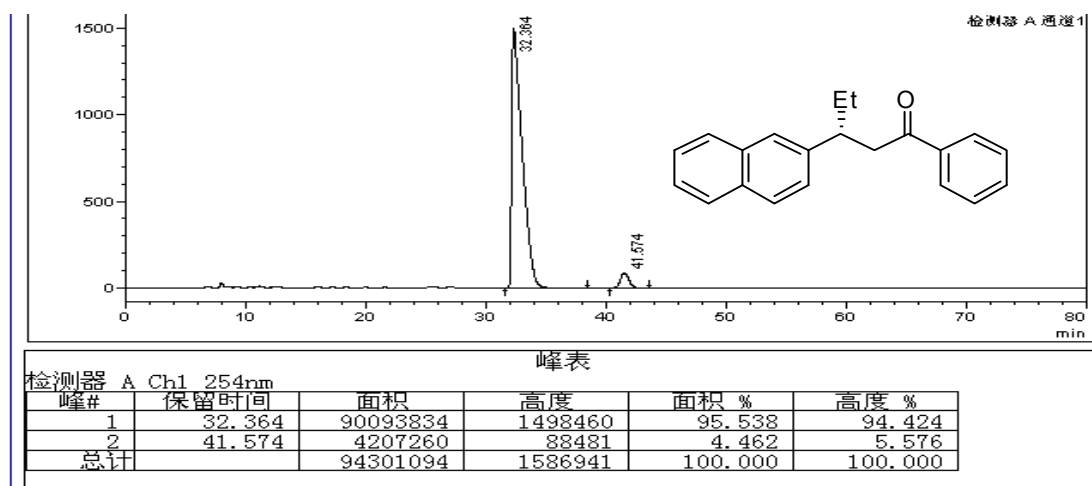
THF as solvent



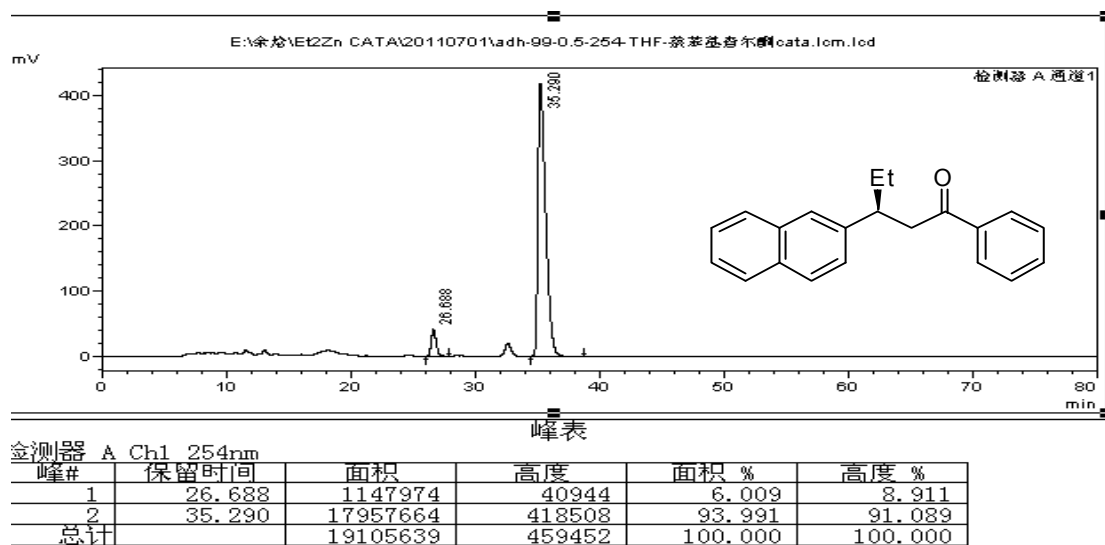
HPLC data of 2g, racemic sample



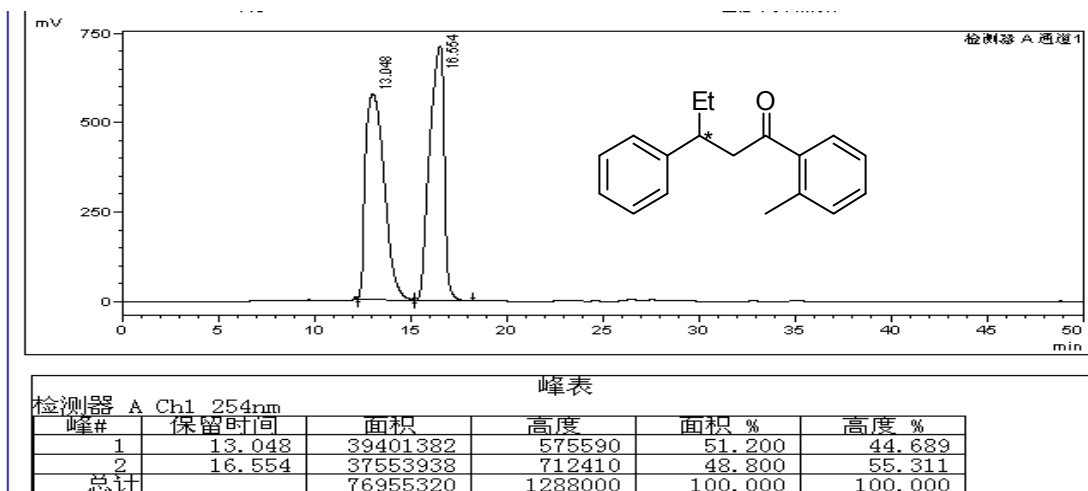
Toluene as solvent



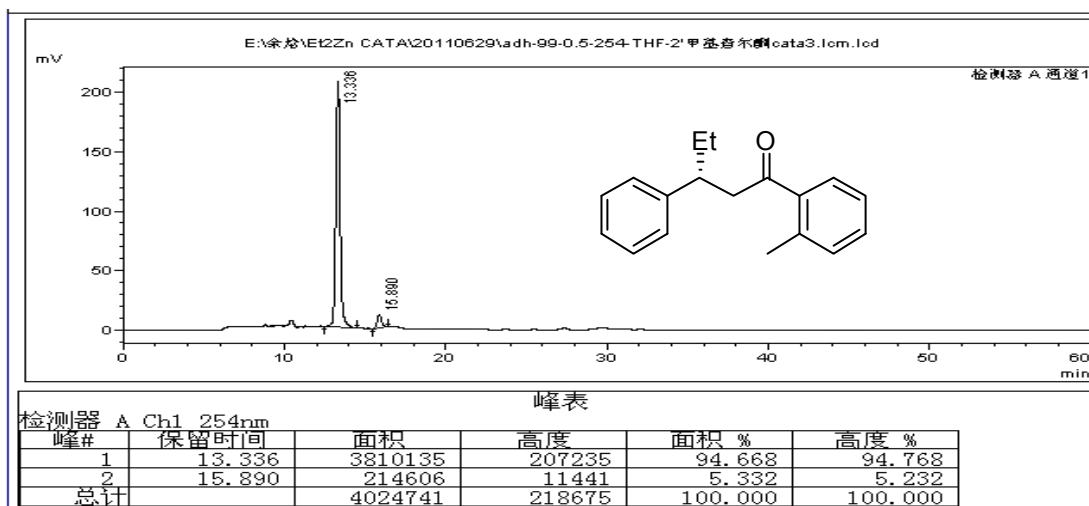
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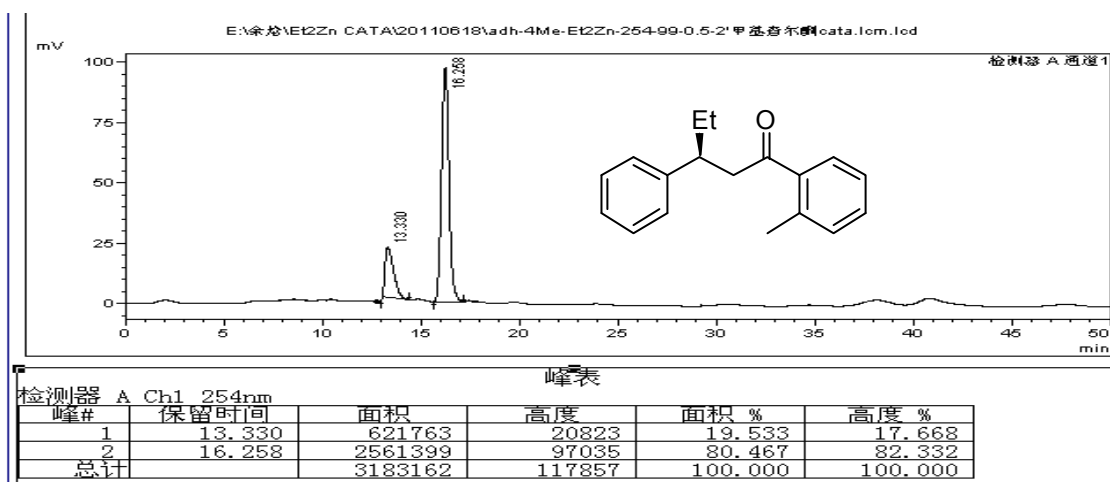
HPLC data of 2h, racemic sample



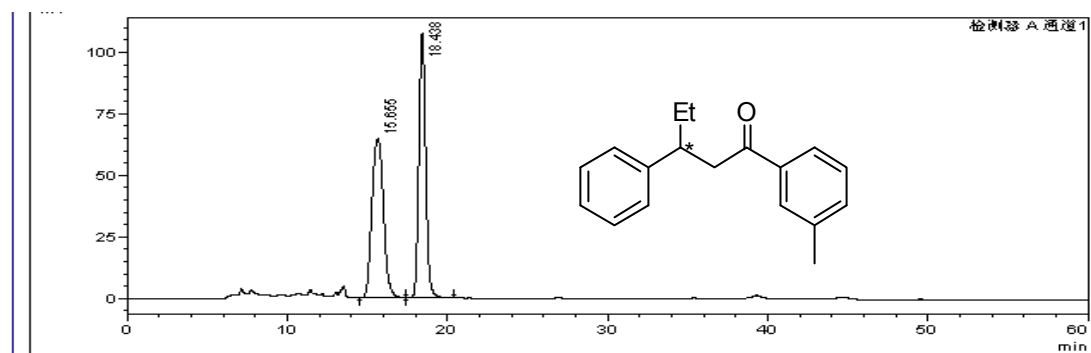
Toluene as solvent



THF as solvent



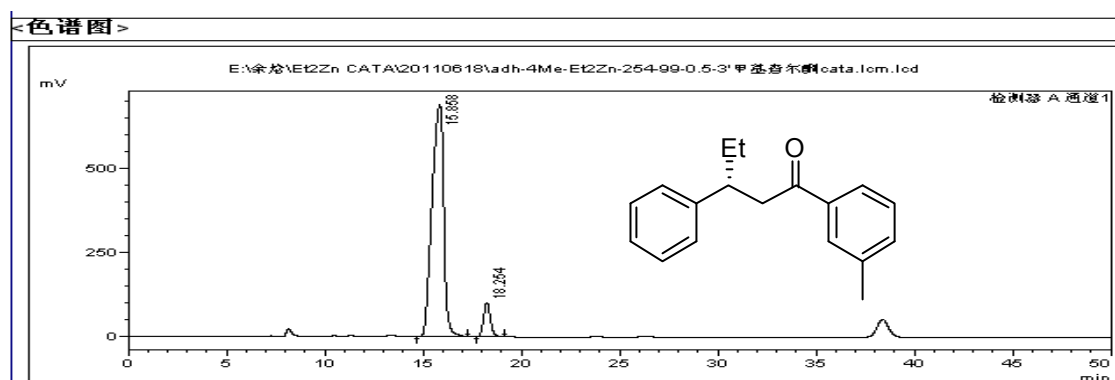
HPLC data of 2i, racemic sample



峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	15.655	3250281	64547	50.351	37.520
2	18.438	3204970	107485	49.649	62.480
总计		6455252	172033	100.000	100.000

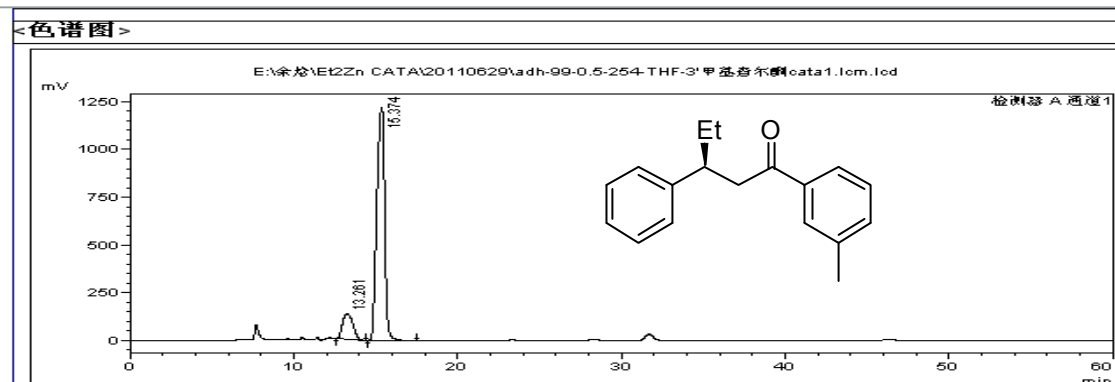
Toluene as solvent



峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	15.858	28776106	691553	92.117	87.121
2	18.254	2462384	102235	7.883	12.879
总计		31238489	793788	100.000	100.000

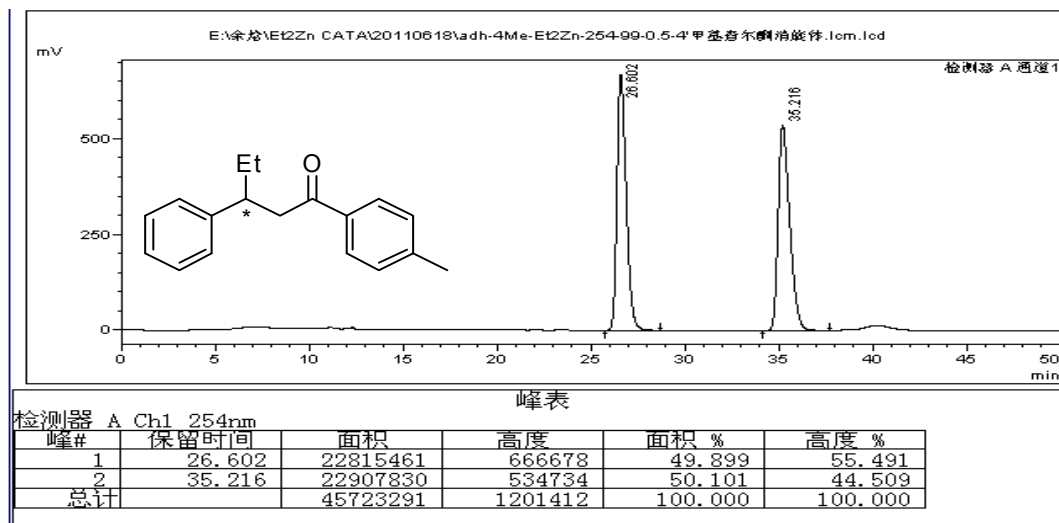
THF as solvent



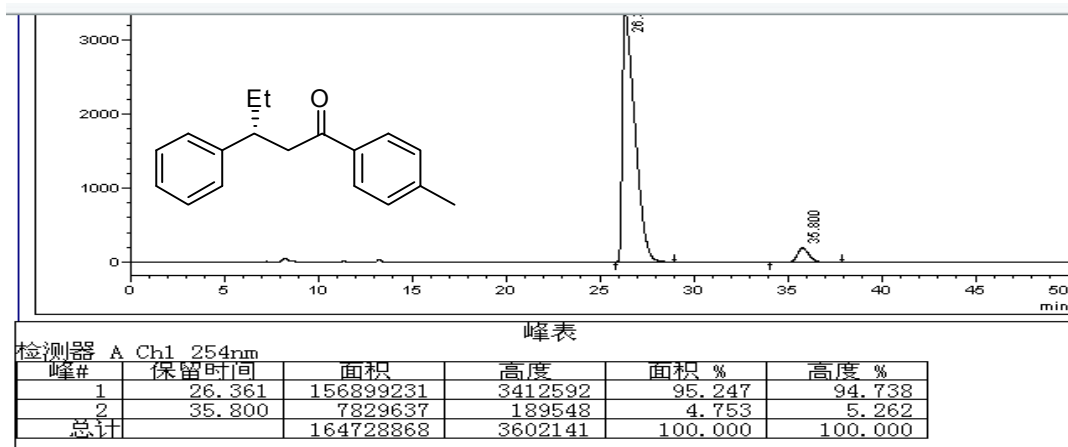
峰表

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1	13.261	5953682	134361	12.789	9.932
2	15.374	40598498	1218518	87.211	90.068
总计		46552180	1352879	100.000	100.000

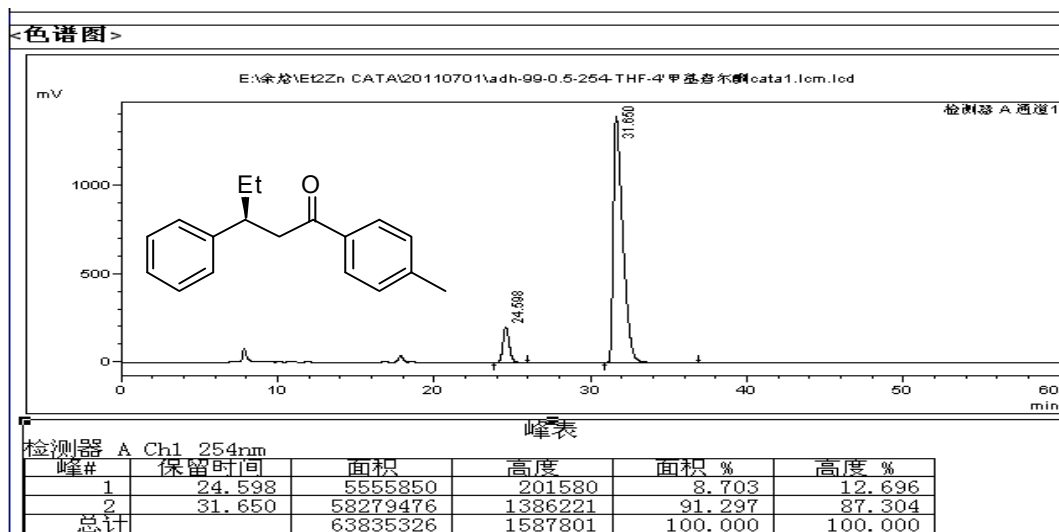
HPLC data of 2j, racemic sample



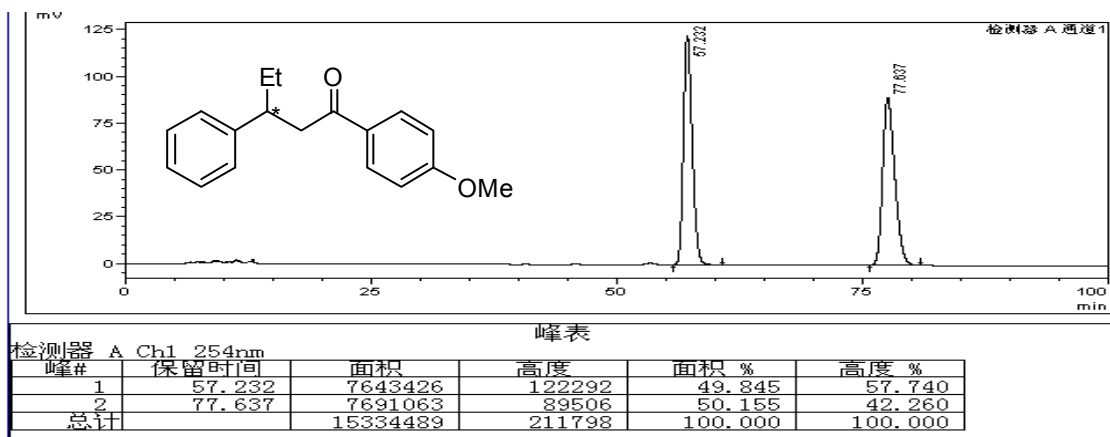
Toluene as solvent



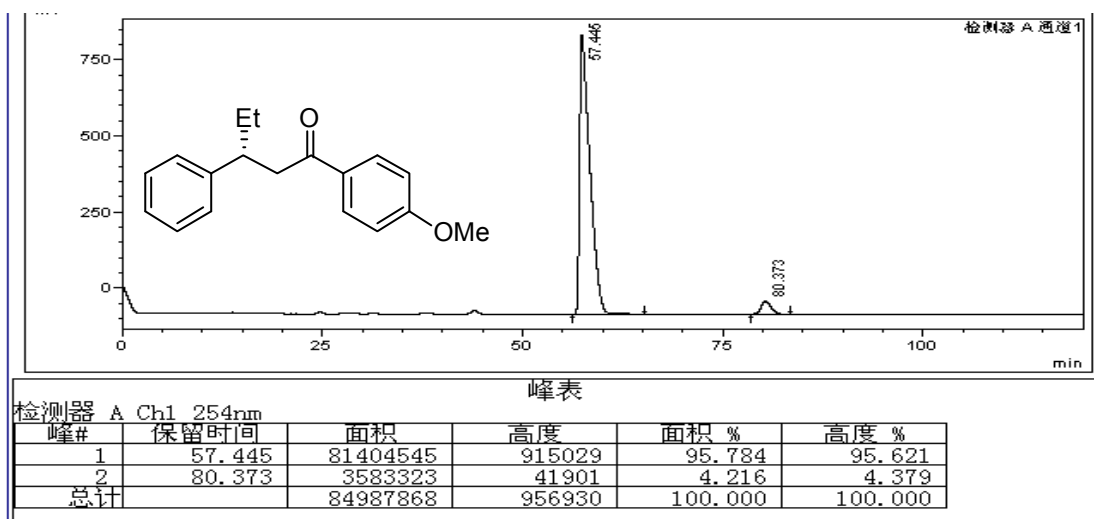
THF as solvent



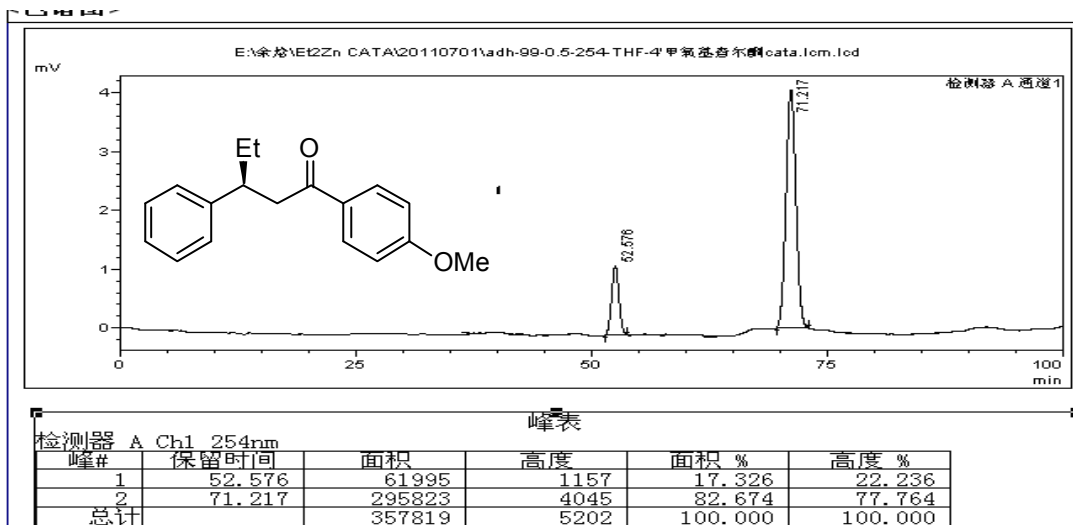
HPLC data of 2k, racemic sample



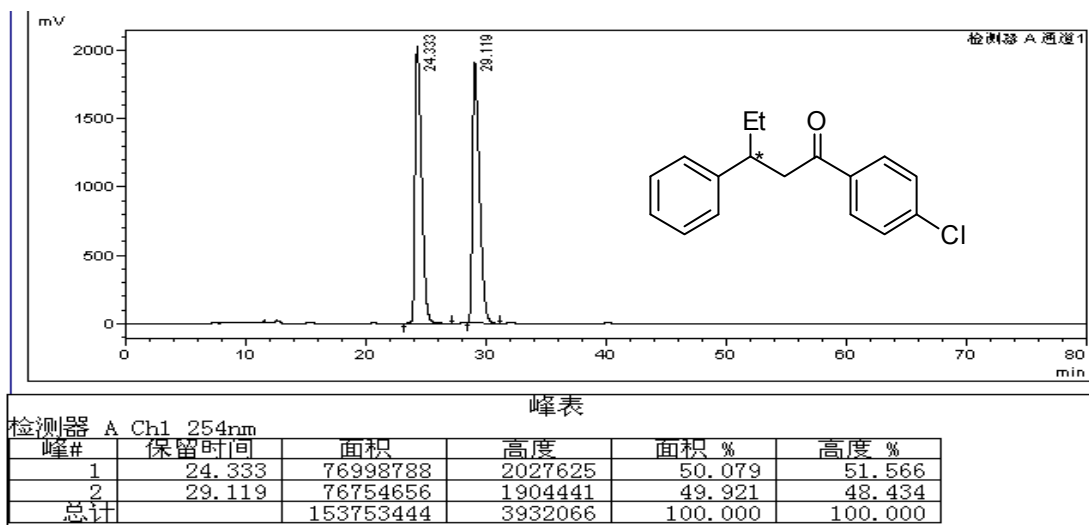
Toluene as solvent



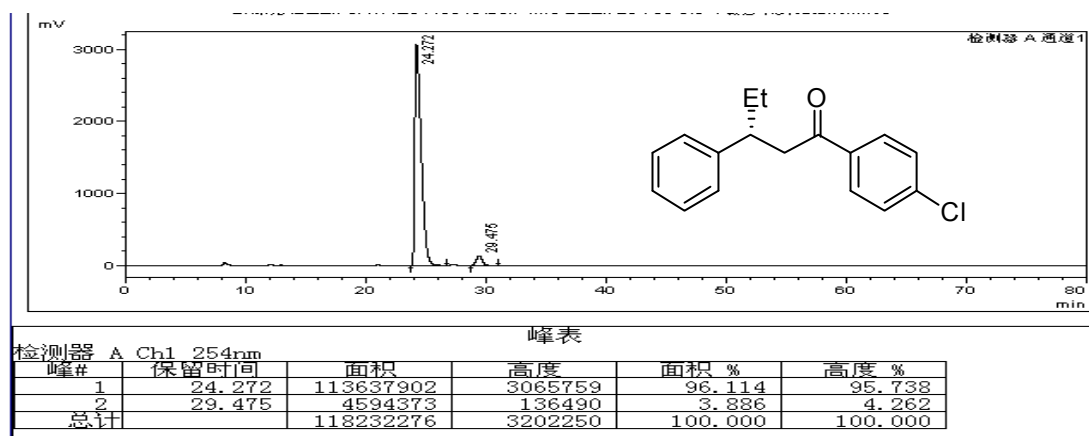
THF as solvent



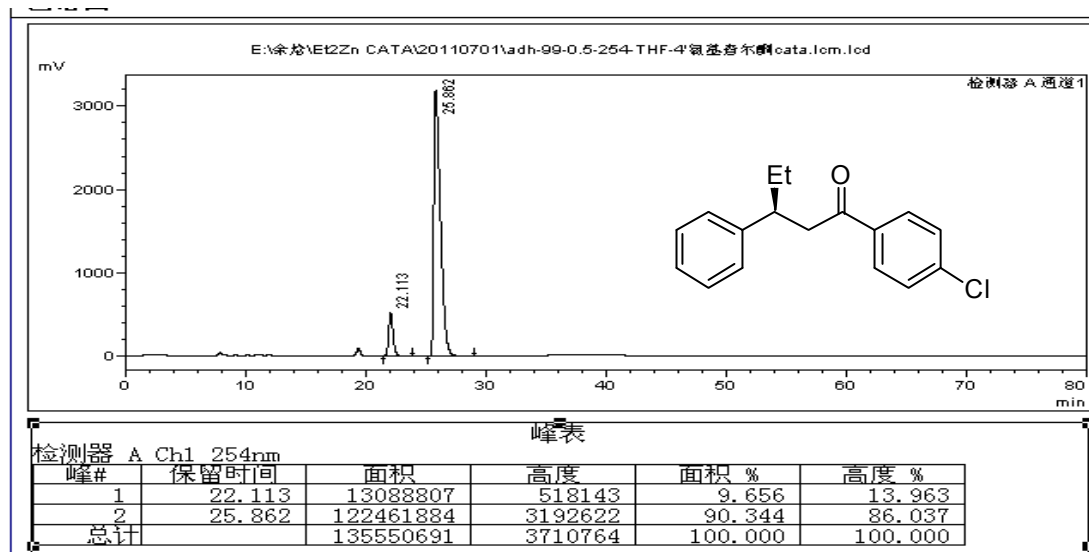
HPLC data of 2l, racemic sample



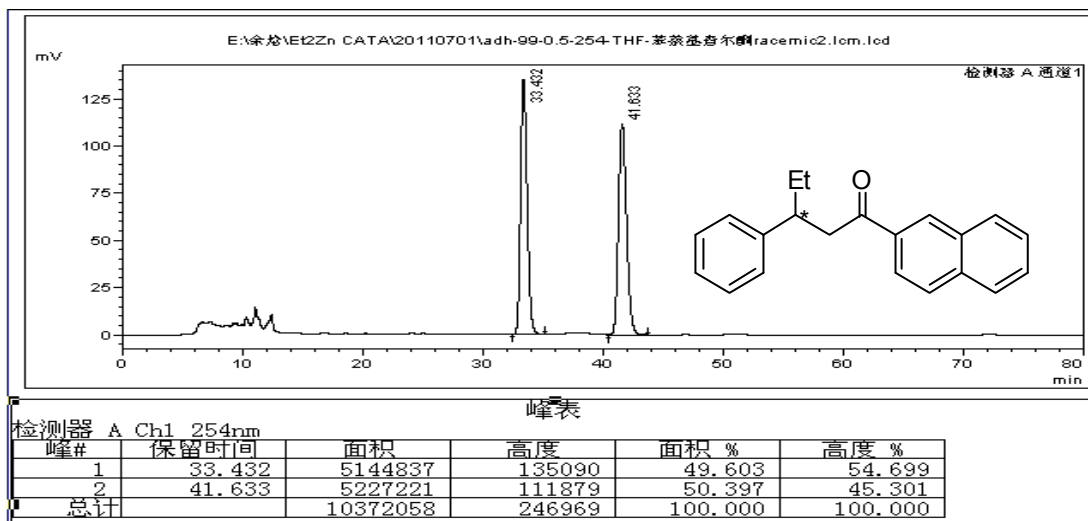
Toluene as solvent



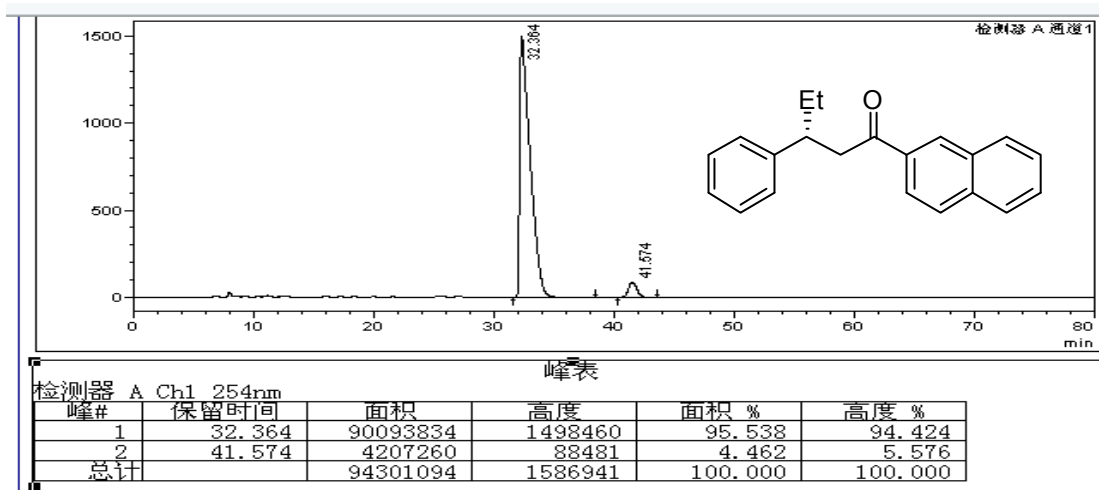
THF as solvent



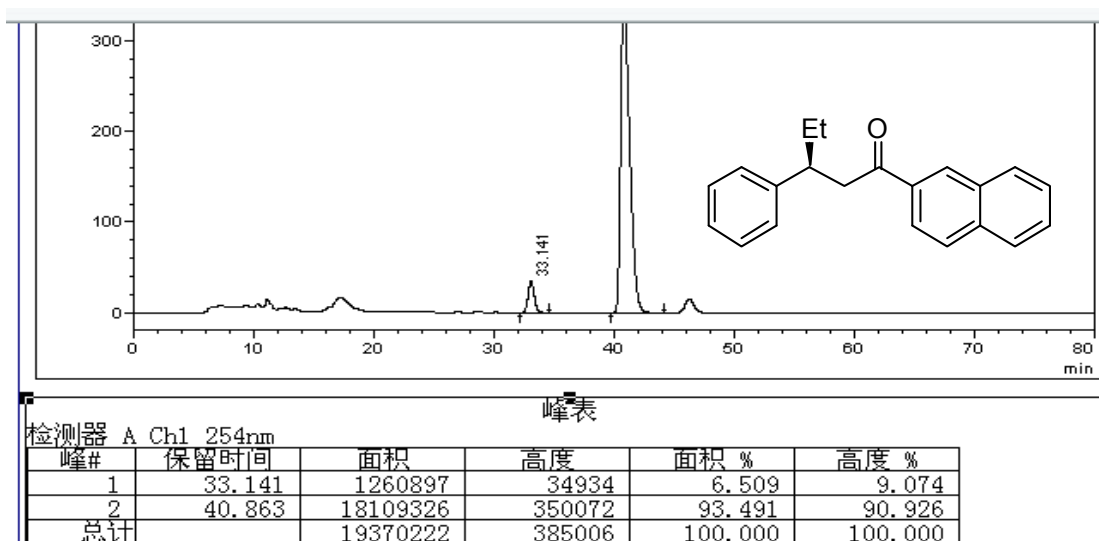
HPLC data of 2m, racemic sample



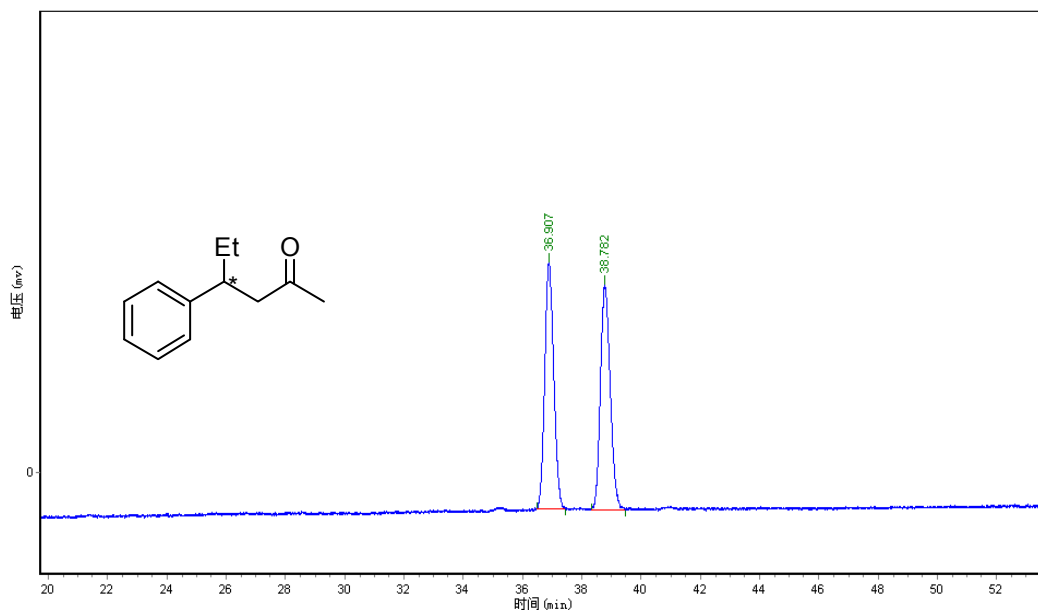
Toluene as solvent



THF as solvent

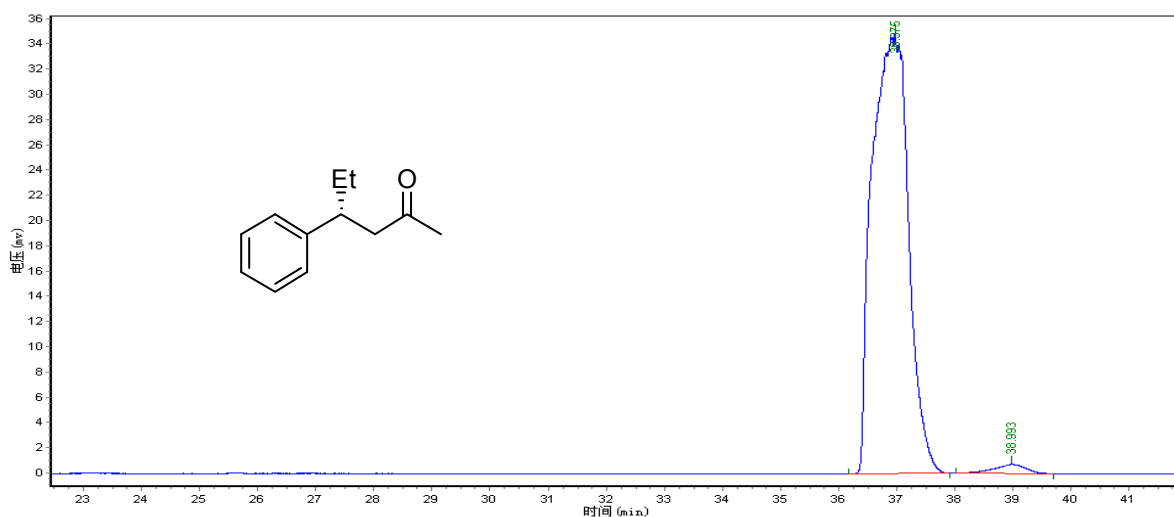


HPLC data of 2n, racemic sample



Entry	Retention Time	Height	Area	Area%
1	36.893	438.563	9278.300	50.1722
2	38.772	405.000	9214.600	49.8278

Toluene as solvent



Entry	Retention Time	Height	Area	Area%
1	36.975	34889.023	1508947.625	98.4880
2	38.993	680.827	23165.000	1.5120

Entry	Retention Time	Height	Area	Area%
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1	36.800	530.254	40125.000	6.6730
2	38.970	35038.746	1467320.631	93.3270

THF as solvent

