

Supporting Information

Chiral Phosphine-Squaramide as Enantioselective Catalyst for the Intramolecular Morita-Baylis-Hillman Reaction

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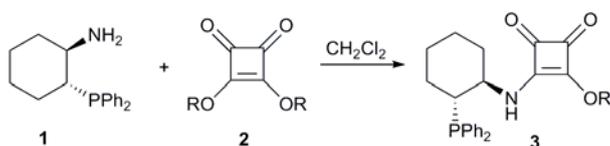
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1. General Information

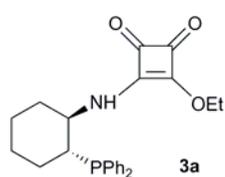
Melting points were taken without correction. Optical rotations were measured on a WZZ-2A digital polarimeter at the wavelength of the sodium D-line (589 nm). ^1H NMR spectra were referenced to tetramethylsilane (d, 0.00 ppm) using CDCl_3 as solvent. ^{13}C NMR spectra were referenced to solvent carbons (77.0 ppm for CDCl_3). ^{31}P NMR spectra were referenced to an external H_3PO_4 signal (0.0 ppm). IR spectra were recorded on Nicolet Magna-I 550 spectrometer. High Resolution Mass spectra (HRMS) were recorded on Micromass GCT with Electron Ionization (EI) resource. HPLC analysis was performed on Waters 510 with 2487 detector using Daicel Chiralcel OD-H, Chiralpak AS-H or Chiralpak AD-H column.

Toluene, *n*-hexane and ether were freshly distilled from sodium-benzophenone. Dichloromethane, chloroform, acetonitrile were freshly distilled from CaH_2 . Methanol, ethanol and isopropanol were distilled from magnesium. Thin-layer chromatography (TLC) was performed on 10-40 μm silica gel plates. Column chromatography was performed using silica gel (300-400 mesh) eluting with ethyl acetate, petroleum ether and CH_2Cl_2 .

2. Synthesis of Chiral Phosphine-Squaramide Catalysts

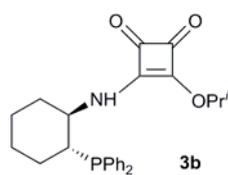


General procedure: To a solution of the squarate $\mathbf{2}^1$ (0.59 mmol, 1.2 eq.) in CH_2Cl_2 (4 mL) was added dropwise a solution of (*R,R*)-2-amino-1-(diphenylphosphino)-cyclohexane ($\mathbf{1}^2$) (140 mg, 0.49 mmol) in CH_2Cl_2 (4 mL). The reaction mixture was stirring at room temperature or under reflux (monitoring by TLC), then the resulting solution was concentrated and purified by silica gel column chromatography to give the phosphine-squaramide $\mathbf{3}$.

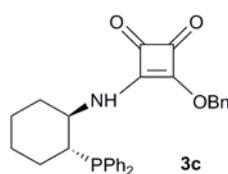


White solid, 89% yield. M.p.: 69.4-71.5 $^\circ\text{C}$. $[\alpha]_{\text{D}}^{28} = +20.5$ (*c* 2.0, CH_2Cl_2). ^1H NMR ($\text{DMSO}-d_6$, 400 MHz, rt): δ 8.85 (d, $J = 8.3$ Hz, 0.5H), 8.46 (d, $J = 8.3$ Hz, 0.5H), 7.46-7.33 (m, 10H), 4.68-4.63 (m, 1H), 4.51-4.46 (m, 1H), 3.86-3.83 (m, 0.5H), 3.35 (m, 0.5H, part in water peak), 2.56-2.50 (m, 1H, part in $\text{DMSO}-d_6$ residual peak), 1.86 (s, 1H), 1.68-1.48 (m, 4H), 1.39-1.28 (m, 3H), 1.23-1.11 (m, 2H), 0.83 (s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 189.6, 181.9, 176.7, 170.8, 136.3 (d, $J = 12.8$ Hz), 134.9 (d, $J = 15.8$ Hz), 134.5 (d, $J = 21.2$ Hz), 132.6 (d, $J = 18.4$ Hz), 129.0, 128.3-128.1 (m), 69.4, 56.8 (d, $J = 15.7$ Hz), 40.4 (d, $J = 15.7$ Hz), 34.8 (d, $J = 6.9$ Hz), 27.6 (d, $J = 3.8$ Hz), 25.1 (d, $J = 4.2$ Hz), 24.5, 15.8; ^{31}P NMR (CDCl_3 , 202 MHz): δ -6.50; IR (KBr, cm^{-1}): ν 3251, 3050, 2931, 2855, 1802, 1704, 1604, 1520, 1494, 1479, 1434, 1384, 1344, 1117, 1091, 1024, 999, 869, 883,

742, 699, 508; HRMS Calcd for C₂₄H₂₆NO₃P ([M]⁺): 407.1650, Found: 407.1669.



White solid, 69% yield. M.p.: 74.4-76.6 °C. [α]_D³⁰ = + 25.7 (*c* 1.5, CH₂Cl₂). ¹H NMR (DMSO-*d*₆, 400 MHz, rt): δ 8.89 (d, *J* = 9.0 Hz, 0.5H), 8.46 (d, *J* = 9.1 Hz, 0.5H), 7.48-7.31 (m, 10H), δ 5.25 (heptet, *J* = 6.2 Hz, 0.5H), δ 5.08 (heptet, *J* = 6.2 Hz, 0.5H), 3.92-3.82 (m, 0.5H), 3.43-3.33 (m, 0.5H, part in water peak), 2.58-2.50 (m, 1H, part in DMSO-*d*₆ residual peak), 1.89-1.86 (m, 1H), 1.70-1.45 (m, 4H), 1.38 (dd, *J* = 11.8 Hz, 6.2 Hz, 3H), 1.31 (q, *J* = 3.2 Hz, 3H), 1.24-1.06 (m, 2H), 0.86-0.78 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 189.7, 181.7, 176.6, 171.1, 136.3 (d, *J* = 13.0 Hz), 135.1 (d, *J* = 16.1 Hz), 134.4 (d, *J* = 20.8 Hz), 132.5 (d, *J* = 18.4 Hz), 129.0, 128.4-128.1 (m), 60.3, 56.7 (d, *J* = 16.4 Hz), 40.2 (d, *J* = 16.1 Hz), 35.0 (d, *J* = 7.0 Hz), 27.7 (d, *J* = 3.4 Hz), 25.2 (d, *J* = 4.3 Hz), 22.9-22.8 (m), 20.9, 14.1; ³¹P NMR (CDCl₃, 162 MHz): δ -6.77 (major), -7.39 (minor); IR (KBr, cm⁻¹): ν 3251, 3051, 2980, 2932, 2855, 1801, 1703, 1601, 1520, 1480, 1434, 1412, 1387, 1332, 1094, 908, 808, 742, 698, 509; HRMS Calcd for C₂₅H₂₈NO₃P ([M]⁺): 421.1807, Found: 421.1815.



White solid, 39% yield. [α]_D¹⁷ = + 21.0 (*c* 0.69, CH₂Cl₂). ¹H NMR (DMSO-*d*₆, 400 MHz, rt): δ 8.90 (d, *J* = 8.9 Hz, 0.5H), 8.54 (d, *J* = 9.1 Hz, 0.5H), 7.53-7.27 (m, 15H), 5.71 (s, 1H), 5.52 (s, 1H), 3.90-3.80 (m, 0.5H), 3.41-3.32 (m, 0.5H, part in water peak), 2.55-2.50 (m, 1H, part in DMSO-*d*₆ residual peak), 1.88-1.82 (m, 1H), 1.68-1.44 (m, 4H), 1.23-1.03 (m, 2H), 0.89-0.74 (m, 1H); ¹H NMR (DMSO-*d*₆, 400 MHz, 333K): δ 8.71 (s, 0.5H), 8.38 (s, 0.5H), 7.45-7.27 (m, 15H), 5.71 (s, 1H), 5.53 (s, 1H), 3.88 (s, 0.5H), 3.41 (s, 0.5H), 2.57-2.50 (m, 1H, part in DMSO-*d*₆ residual peak), 1.86 (s, 1H), 1.70-1.48 (m, 4H), 1.25-1.07 (m, 2H), 0.88 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 189.6, 182.3, 176.4, 171.0, 136.5 (d, *J* = 12.8 Hz), 135.2 (d, *J* = 16.2 Hz), 134.5 (d, *J* = 21.0 Hz), 132.9 (d, *J* = 19.1 Hz), 129.1 (d, *J* = 4.4 Hz), 128.9, 128.8, 128.6 (d, *J* = 3.1 Hz), 128.5 (d, *J* = 6.5 Hz), 128.3 (d, *J* = 7.6 Hz), 74.5, 57.3 (d, *J* = 16.6 Hz), 40.6 (d, *J* = 15.8 Hz), 34.9 (d, *J* = 6.8 Hz), 28.0 (d, *J* = 5.4 Hz), 25.3 (d, *J* = 4.9 Hz), 24.7; ³¹P NMR (CDCl₃, 162 MHz): δ -6.78 (major), -7.53 (minor); HRMS (ESI) Calcd for C₂₉H₂₈NO₃PNa ([M+Na]⁺): 492.1704, Found: 492.1708.

3. General Procedure for the Enantioselective Intramolecular MBH Reaction

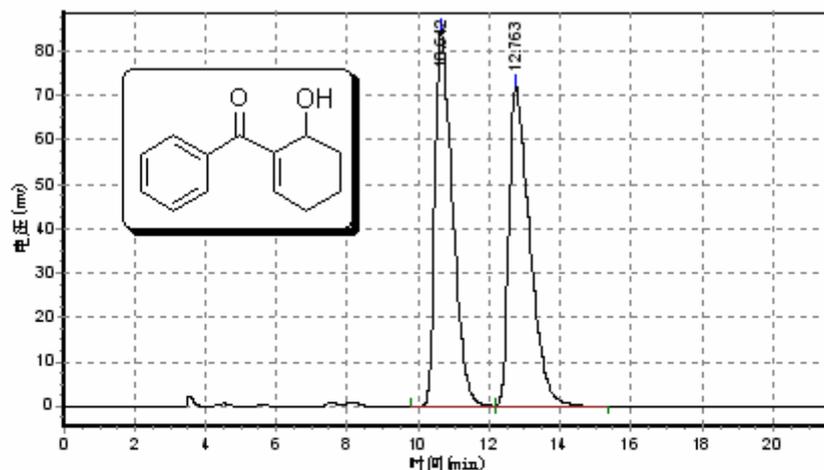
Phosphine-Squaramide **3a** (2.4 mg, 0.006 mmol) and EtOH (1.0 mL) were added to a vessel containing substrate **4** (0.20 mmol) and stirred at 25°C. After the reaction was completed (monitoring by TLC), the solvent was removed under reduced pressure and the residue was

purified by column chromatography on silica gel to afford the intramolecular MBH adduct **5** and the ee values were determined by HPLC analysis using chiral column.³

4. References

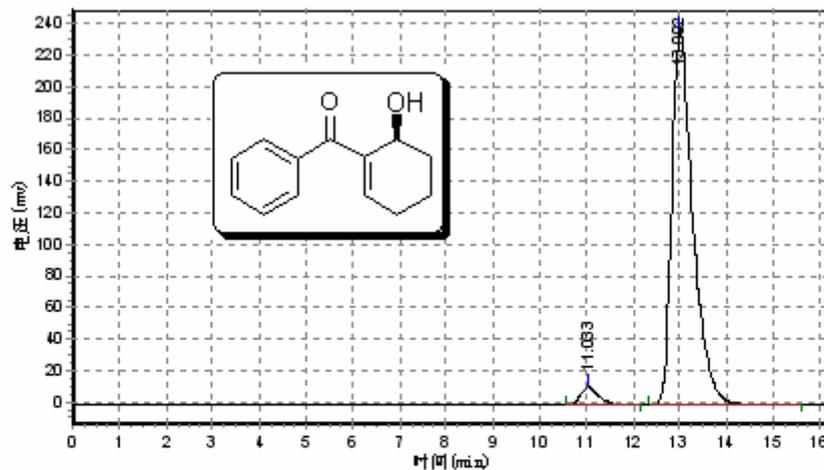
- 1 N. Fu, A. D. Allen, S. Kobayashi, T. T. Tidwell and S. Vukovic, *J. Org. Chem.* 2008, **73**, 1768-1773.
- 2 (a) A. Caiazzo, S. Dalili and A. K. Yudin, *Org. Lett.*, 2002, **4**, 2597-2600; (b) Y.-Q. Fang and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2008, **130**, 5660-5661; (c) K. Yuan, L. Zhang, H.-L. Song, Y. Hu and X.-Y. Wu, *Tetrahedron Lett.*, 2008, **49**, 6262-6264.
- 3 The analytical data of the intramolecular MBH products **4** could be found in our recent publication: J.-J. Gong, K. Yuan, H.-L. Song, and X.-Y. Wu, *Tetrahedron*, 2010, **66**, 2439-2443.

5. HPLC Spectra for the MBH Products



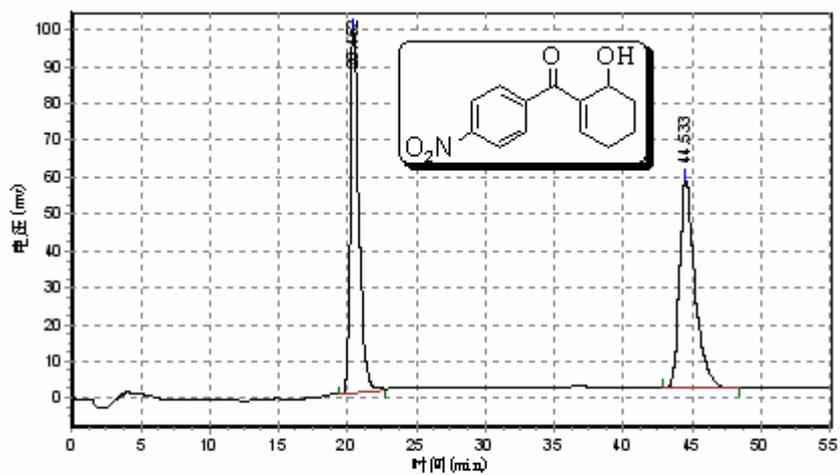
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		10.642	84548.453	2934675.500	49.9637
2		12.763	71940.625	2938942.500	50.0363
总计			156489.078	5873618.000	100.0000



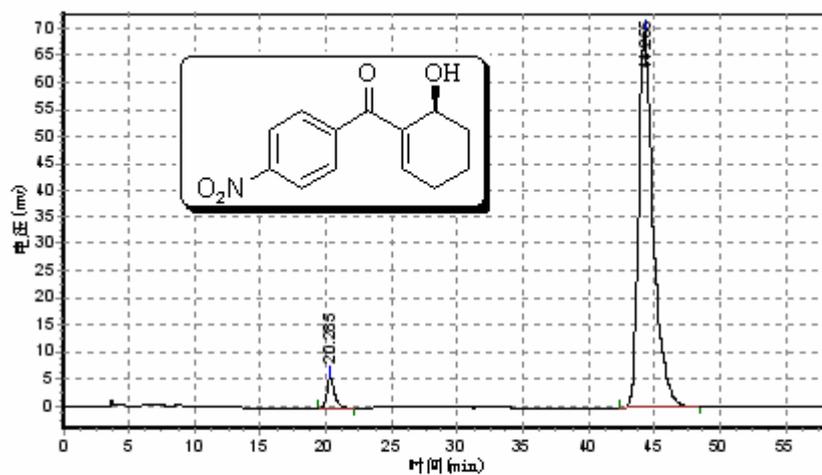
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.033	10688.000	279528.719	3.6141
2		13.002	238311.953	7454806.000	96.3859
总计			248999.953	7734334.719	100.0000



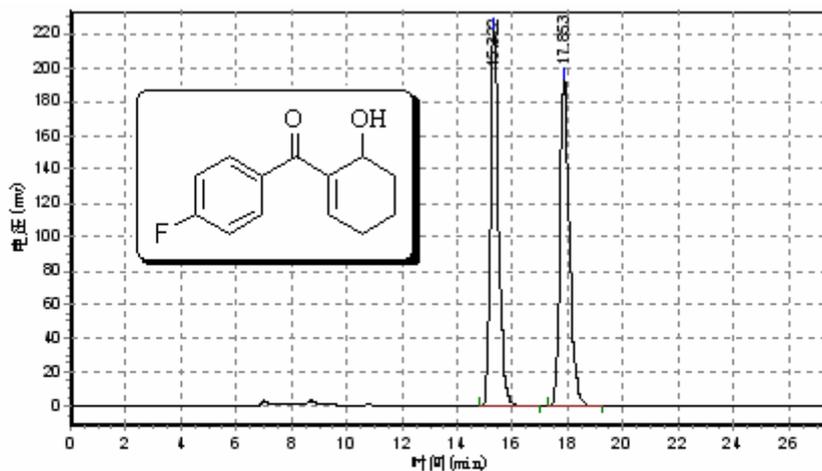
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		20.452	98324.961	4341880.000	49.6548
2		44.533	56373.234	4402254.500	50.3452
总计			154698.195	8744134.500	100.0000



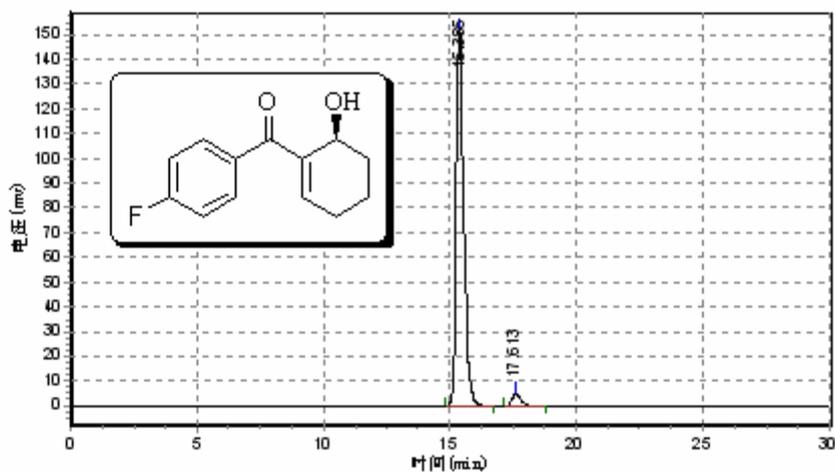
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		20.285	5455.848	226086.750	3.9970
2		44.255	69682.680	5430376.000	96.0030
总计			75138.528	5656462.750	100.0000



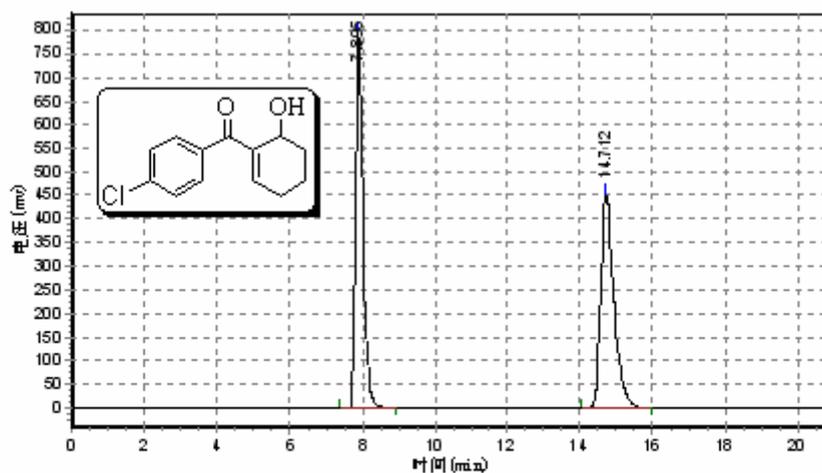
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		15.322	221951.484	4632682.000	50.0403
2		17.853	191978.016	4625211.500	49.9597
总计			413929.500	9257893.500	100.0000



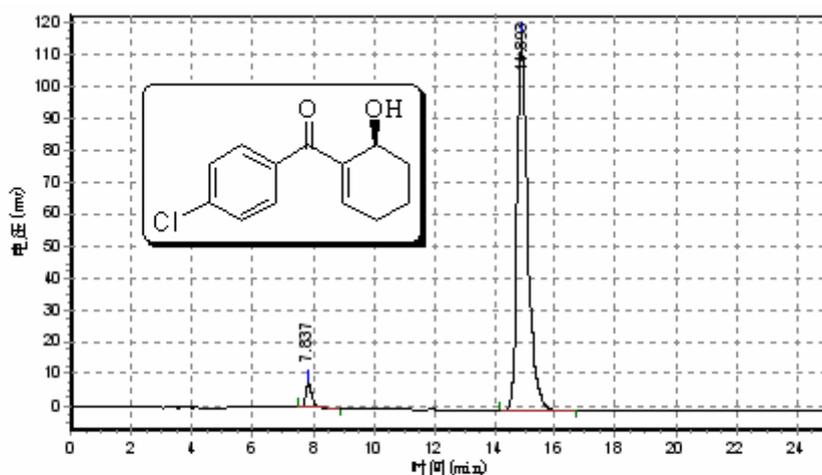
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		15.385	151661.766	3187319.750	96.4632
2		17.613	4920.406	116863.703	3.5368
总计			156582.171	3304183.453	100.0000



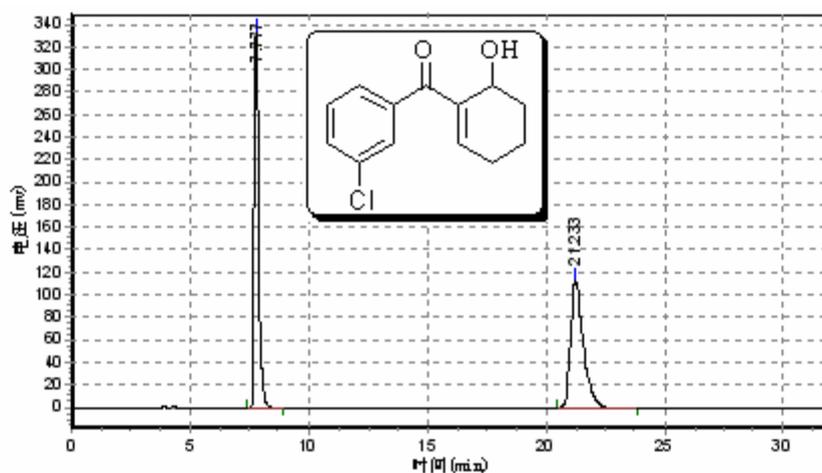
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.895	795895.938	11324862.000	49.9533
2		14.712	450383.125	11346019.000	50.0467
总计			1246279.063	22670881.000	100.0000



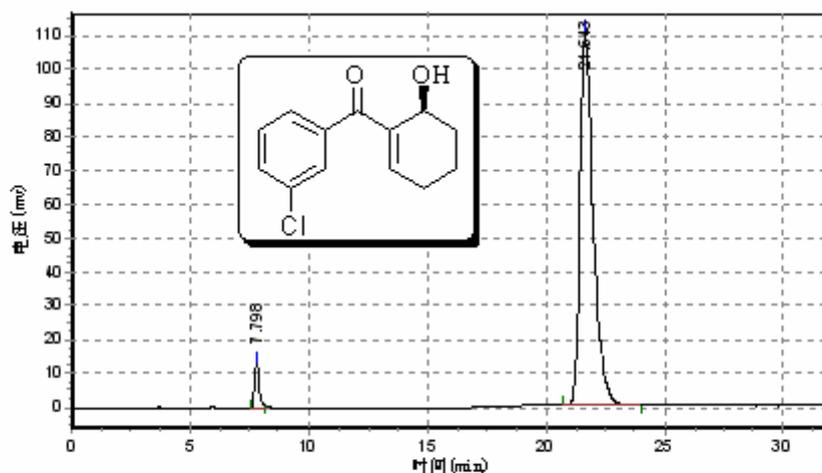
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峰号	峰名	保留时间	峰高	峰面积	含量
1		7.837	7873.555	102177.742	3.4670
2		14.893	117478.563	2844986.250	96.5330
总计			125352.118	2947163.992	100.0000



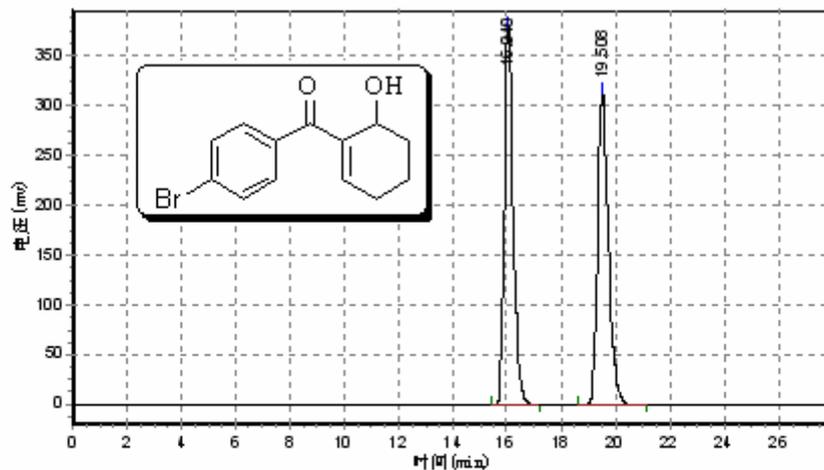
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峰号	峰名	保留时间	峰高	峰面积	含量
1		7.777	332568.656	4218205.000	50.0763
2		21.233	111346.500	4205348.500	49.9237
总计			443915.156	8423553.500	100.0000



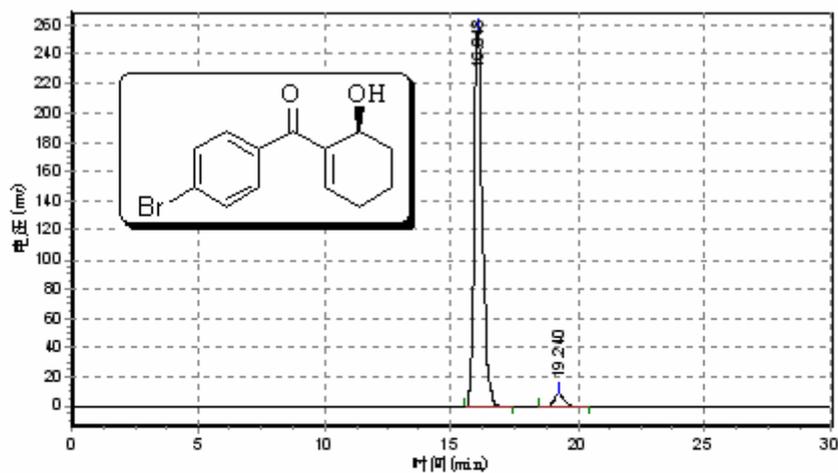
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1		7.798	12905.007	166948.219	3.7572
2		21.643	110464.789	4276447.000	96.2428
总计			123369.796	4443395.219	100.0000



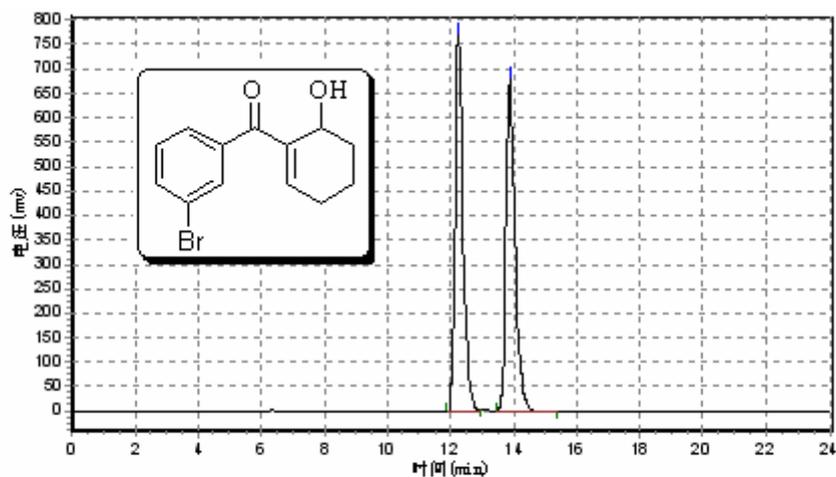
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		16.040	376694.594	8647735.000	49.8362
2		19.508	311377.125	8704573.000	50.1638
总计			688071.719	17352308.000	100.0000



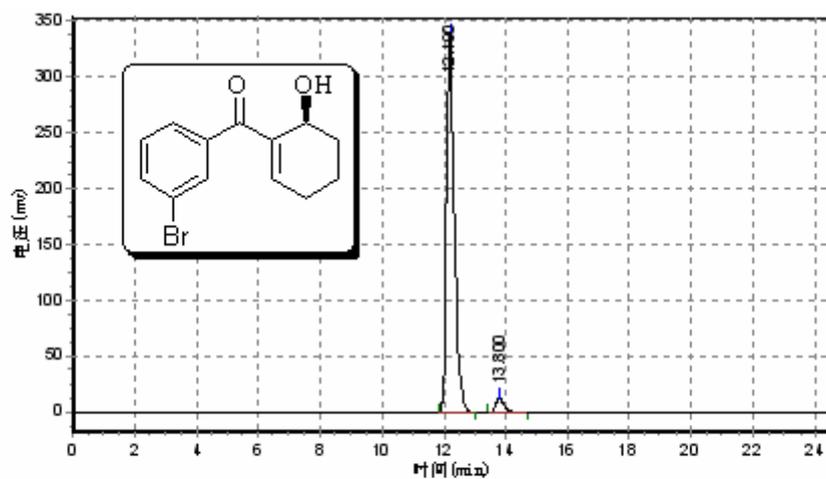
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		16.048	256509.469	5899752.000	95.9891
2		19.240	8917.200	246522.203	4.0109
总计			265426.669	6146274.203	100.0000



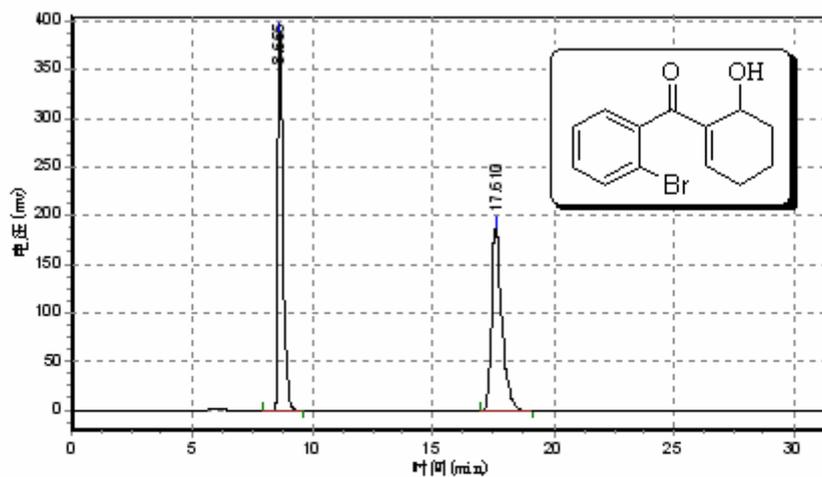
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1		12.245	768069.188	13626761.000	49.9474
2		13.880	681994.438	13655438.000	50.0526
总计			1450063.625	27282199.000	100.0000



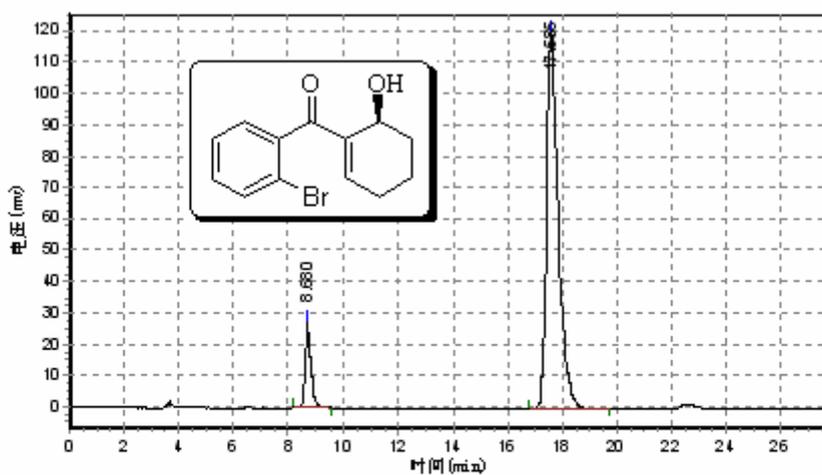
分析结果表

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1		12.190	336583.938	5933501.000	96.1554
2		13.800	11902.874	237239.766	3.8446
总计			348486.812	6170740.766	100.0000



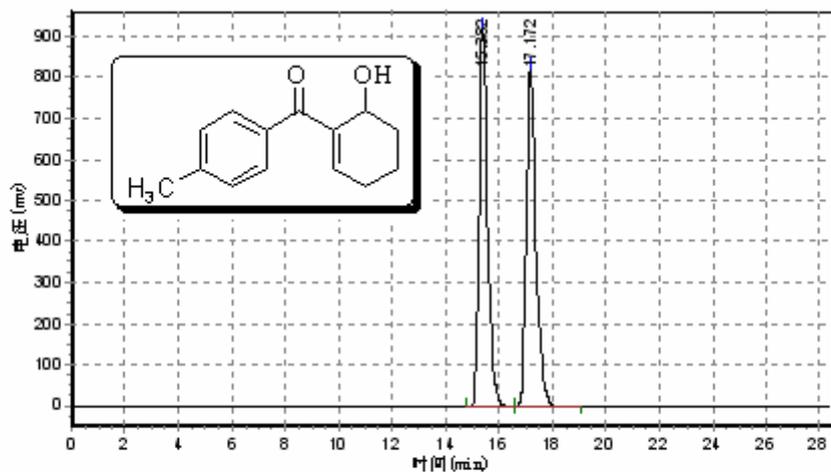
分析结果表

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1		8.655	385038.344	5570692.000	49.9753
2		17.610	186561.781	5576208.000	50.0247
总计			571600.125	11146900.000	100.0000



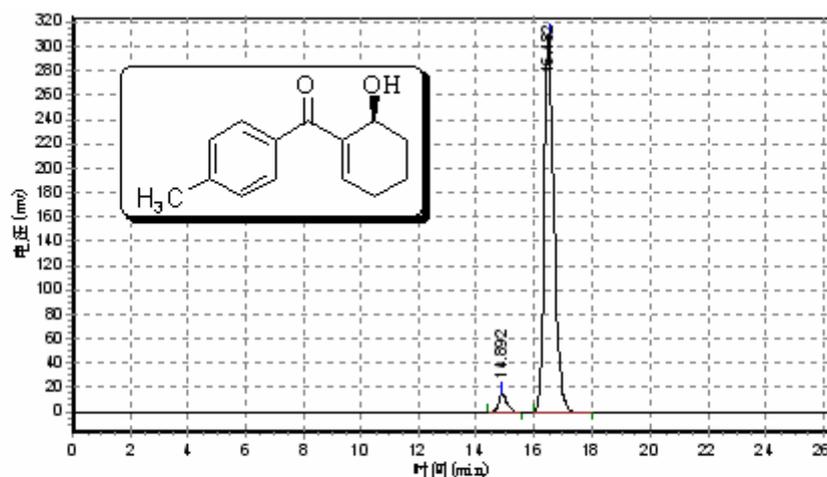
分析结果表

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1		8.680	27040.830	391106.688	9.9290
2		17.585	119912.258	3547917.250	90.0710
总计			146953.088	3939023.938	100.0000



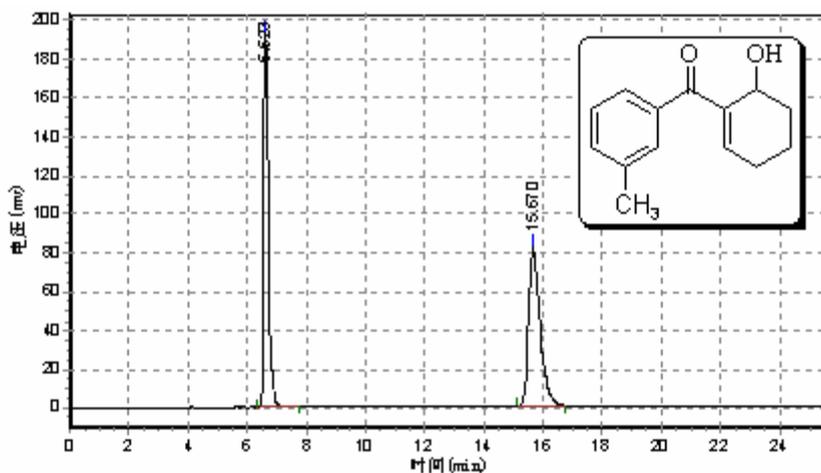
分析结果表

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1		15.382	916672.313	20368818.000	49.9483
2		17.172	817900.563	20410990.000	50.0517
总计			1734572.875	40779808.000	100.0000



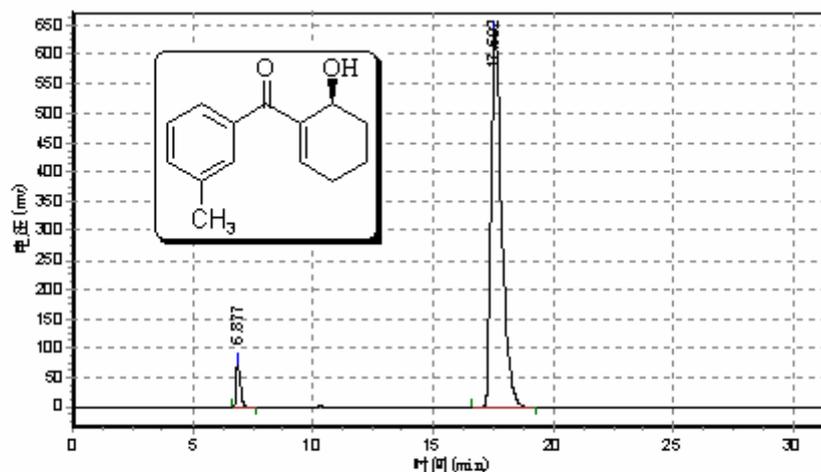
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1		14.892	14475.043	308946.156	4.0699
2		16.482	309095.875	7282146.500	95.9302
总计			323570.918	7591092.656	100.0000



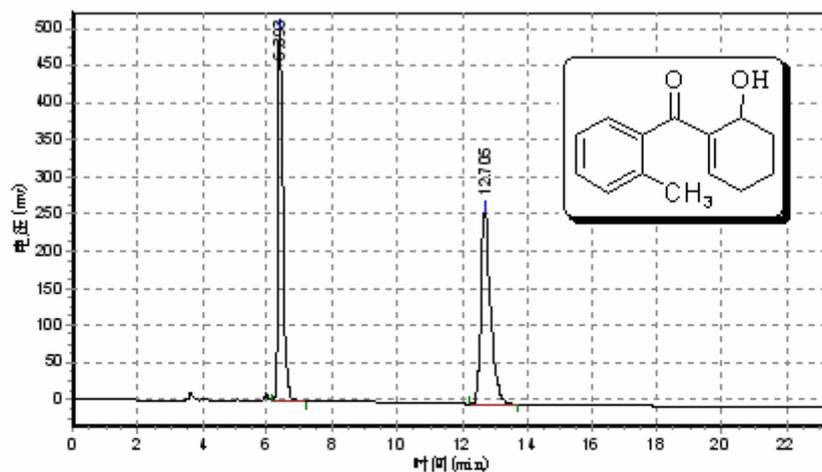
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1		6.623	192924.578	2111698.000	49.9086
2		15.670	82058.695	2119429.250	50.0914
总计			274983.273	4231127.250	100.0000



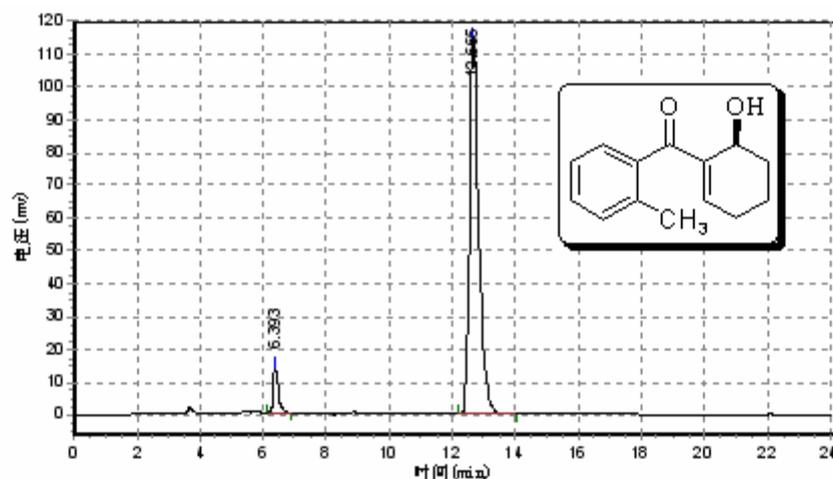
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1		6.877	72249.586	866866.313	4.1760
2		17.592	640215.625	19891390.000	95.8240
总计			712465.211	20758256.313	100.0000



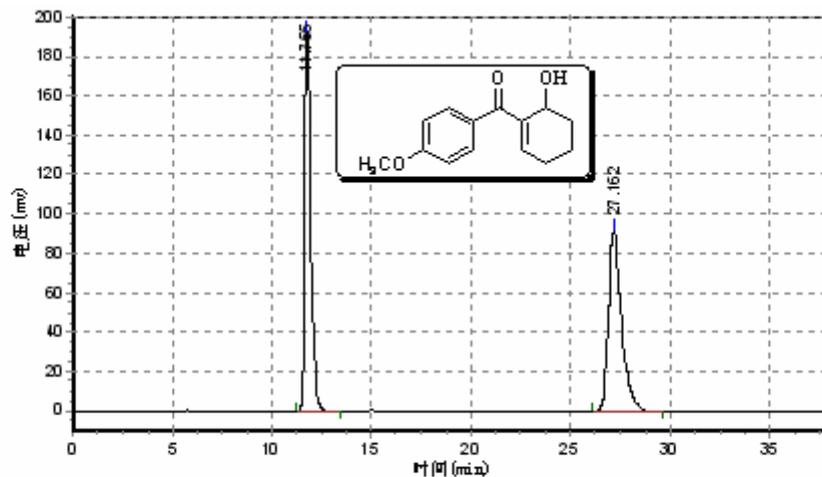
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.393	498386.250	5317947.500	49.9226
2		12.705	258437.641	5334432.500	50.0774
总计			756823.891	10652380.000	100.0000



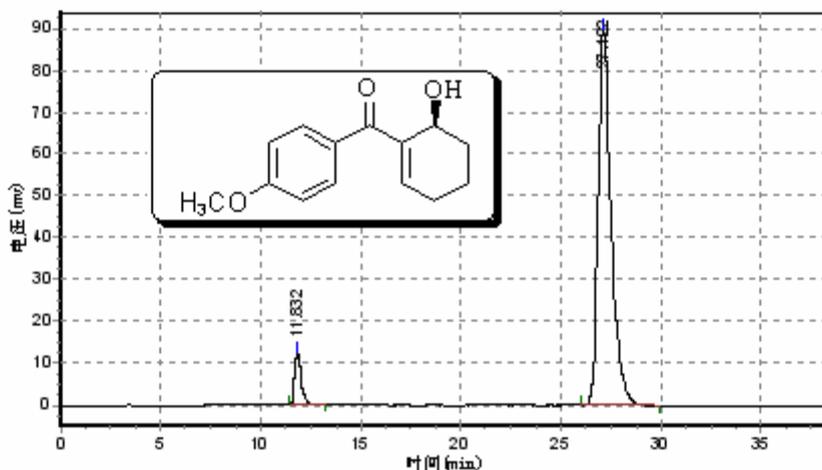
分析结果表

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1		6.393	13302.870	146191.500	5.8478
2		12.665	113932.766	2353752.750	94.1522
总计			127235.636	2499944.250	100.0000



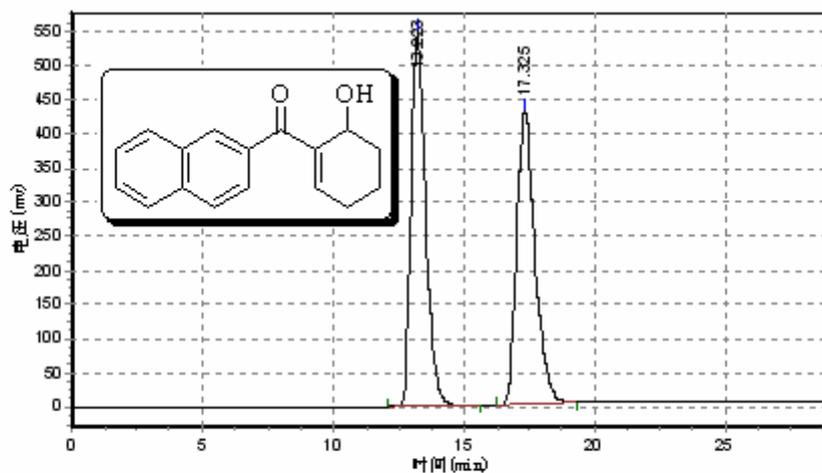
分析结果表

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1		11.755	190892.094	4169246.750	49.9537
2		27.162	91167.531	4176967.250	50.0463
总计			282059.625	8346214.000	100.0000



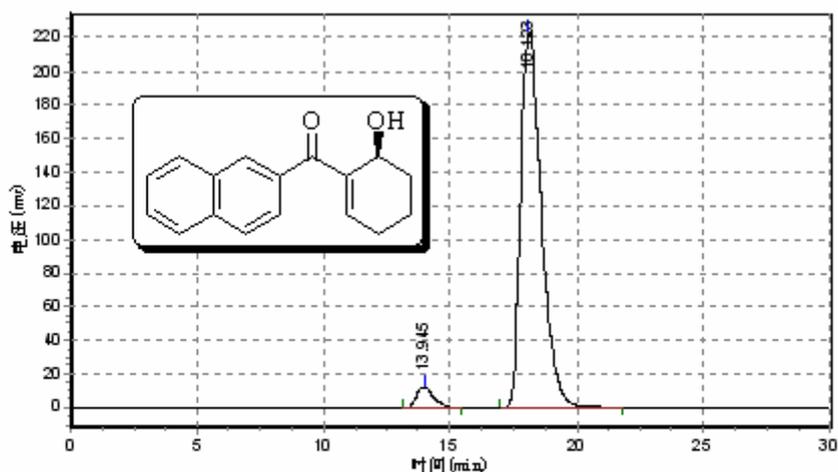
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.832	12028.707	254763.406	5.9292
2		27.122	89329.836	4041964.000	94.0708
总计			101358.543	4296727.406	100.0000



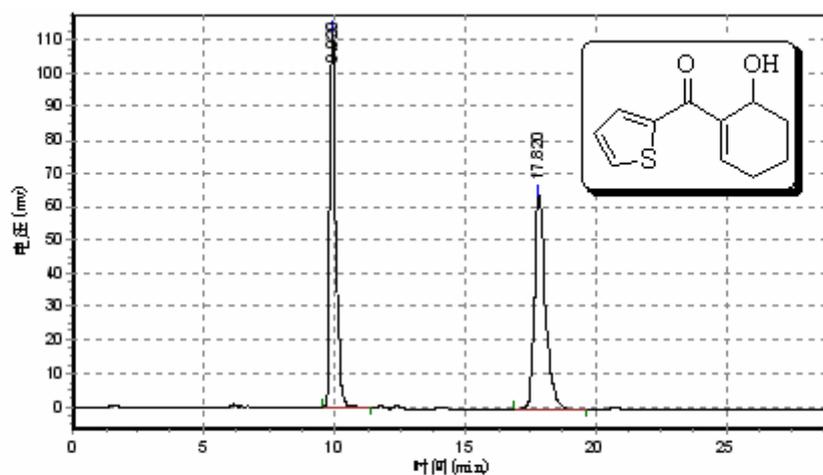
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		13.223	549064.438	20679280.000	49.9560
2		17.325	428966.844	20715708.000	50.0440
总计			978031.281	41394988.000	100.0000



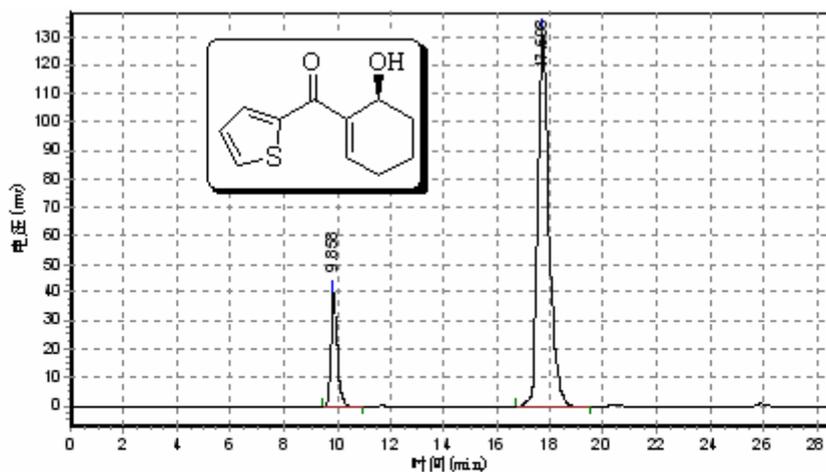
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		13.945	12074.282	528100.813	4.0608
2		18.123	222864.344	12476867.000	95.9392
总计			234938.626	13004967.813	100.0000



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		9.920	112334.445	1805897.375	49.9957
2		17.820	63703.195	1806209.750	50.0043
总计			176037.641	3612107.125	100.0000



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		9.858	40421.715	676629.313	15.0986
2		17.698	132321.547	3804775.500	84.9014
总计			172743.262	4481404.813	100.0000

