

Supporting Information

Asymmetric Tandem Michael Addition/Ylide Olefination Reaction for the Synthesis of Optically Active Cyclohexa-1,3-diene Derivatives

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General Information. All reaction flasks were dried by flame and all reactions
were carried out under N₂ unless otherwise noted. All solvents were purified
according to standard methods unless otherwise noted.

NMR spectra were recorded on a VARIAN Mercury 300 MHz spectrometer in
chloroform-d₃. The data is being reported as (s = singlet, d = doublet, t = triplet, m =
multiplet or unresolved, brs = broad singlet, coupling constant(s) in Hz, integration).

phosphonium **2** (Derived from chiral phosphine (*R*)-**1d**, R = Me as an example):
[α]_D²⁰ = -64.8° (c = 1.50, CHCl₃). IR ν /cm⁻¹ 2907 (m), 1728 (m), 1591 (m), 1418 (m),
1041 (m); ¹H NMR (300 MHz, CDCl₃, TMS): δ 7.59-6.40 (m, 24H), 6.28-6.15 (m,
1H), 5.18 (dd, *J* = 16.8 and 21.6 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.66 (s, 3H), 3.63
(s, 3H), 3.60 (s, 3H), 3.31 (s, 3H), 3.10 (s, 3H); ³¹P NMR (121.5 MHz, CDCl₃): δ 34.5,
-0.47. MS (ESI, positive mode, *m/z*) 401 ((M⁺+2H⁺)/2-Br). HRMS (MALDI/DHB)

calcd for C₄₇H₄₇O₈P₂ (M⁺-Br): 801.2719; Found: 801.2741.

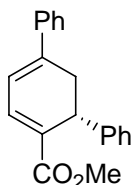
Synthesis of optically active 4,6-diphenyl-cyclohexa-1,3-dienecarbaldehyde 5:²

DIBAL (1.0 M in toluene, 0.6 mL, 0.6 mmol) was added dropwise to a solution of **4a** (58 mg, 0.20 mmol) in dry dichloromethane (1.0 mL) at -78 °C. After 1 h, the reaction mixture was cooled to 0 °C and quenched with 2.5 mL of Rochelle's salt solution. The mixture was stirred vigorously for 2 h and the layers were separated. The aqueous layer was extracted with dichloromethane (2 x 10 mL). The organic layers were combined, dried with sodium sulfate, and concentrated to give the crude alcohol.

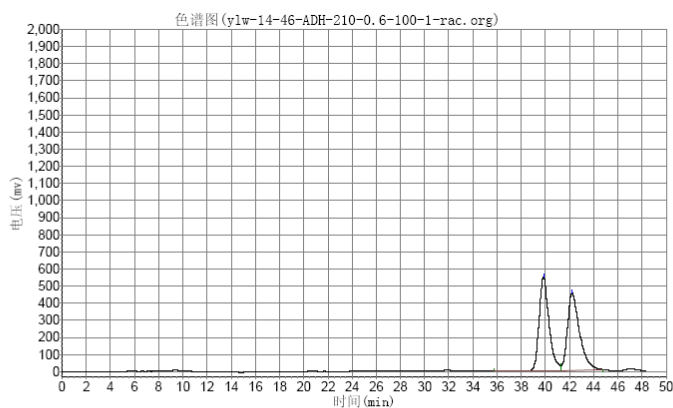
To a flame-dried 25 mL of round bottom flask was added a solution of the crude alcohol in 5 mL of dichloromethane, followed by Dess-Martin periodinane (DMP) (102 mg, 0.24 mmol). The solution was allowed to stir at ambient temperature for 10 min,, filtered through Celite 545, then concentrated in vacuo. The residue was purified to column chromatography to provide **5** as pale yellow liquid.

Reference:

1. L.-W. Ye, X. Han, X.-L. Sun and Y. Tang, *Tetrahedron*, 2008, **64**, 8149.
2. C. M. H. Watanabe and B. J. Bench, US 2007232813, 2007; *Chem. Abstr.*, 2007, **147**, 427217.

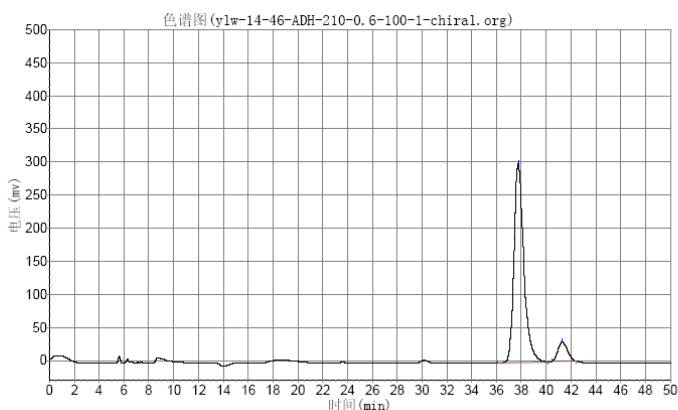


4a: 62% yield (white solid, 48 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.44-7.13 (m, 11H), 6.53 (dd, $J = 6.0$ and 3.0 Hz, 1H), 4.18 (dd, $J = 1.8$ and 9.9 Hz, 1H), 3.70 (s, 3H), 3.29-3.19 (m, 1H), 3.02 (dd, $J = 18$ and 2.7 Hz, 1H); $[\alpha]_{\text{D}}^{20} = -113.5^\circ$ ($c = 0.96$, CHCl_3). 83% ee (determined by HPLC: Chiralcel AD-H Column, 1/100 i PrOH /hexane, 0.6 mL/min, 210 nm; $T_{\text{R}} = 37.75$ min (major), 41.30 min (minor)). (Table 2, Entry 1).



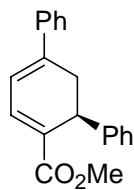
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		39.838	546564.875	31246918.000	49.9563
2		42.205	450574.875	31301564.000	50.0437
总计			997139.750	62548482.000	100.0000

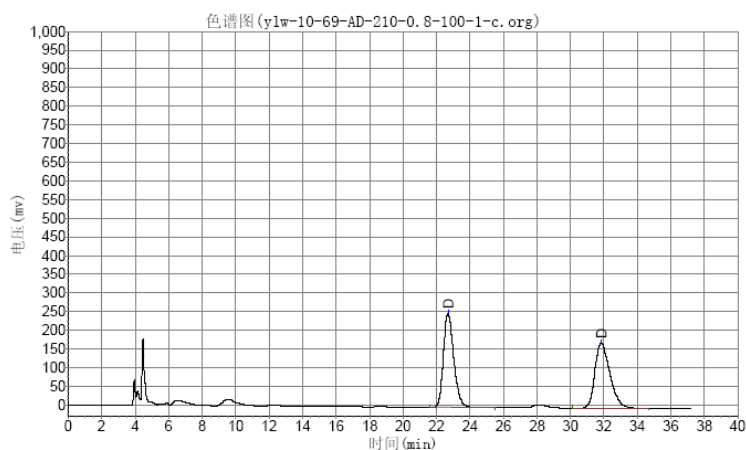


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		37.748	300175.688	16538174.000	91.4230
2		41.303	29228.383	1551559.500	8.5770
总计			329404.070	18089733.500	100.0000

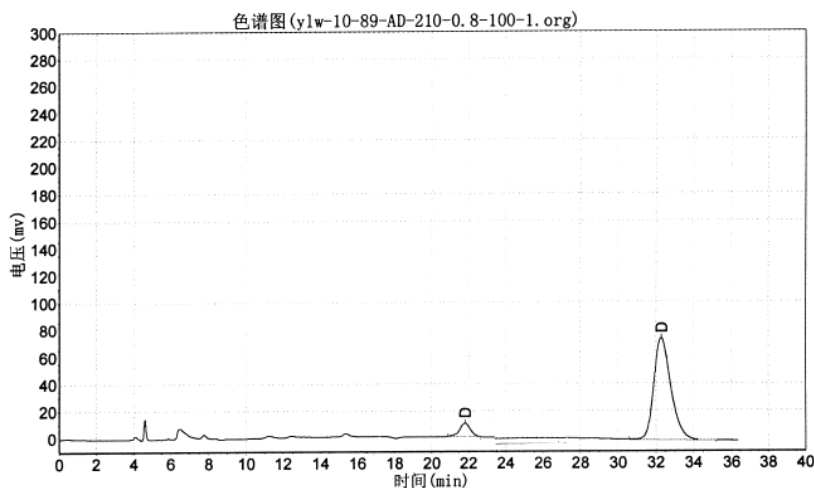


Ent-4a: 64% yield (white solid, 57 h). $[\alpha]_D^{20} = 137.2^\circ$ ($c = 1.10$, CHCl_3). -84% ee (determined by HPLC: Chiralcel AD Column, 1/100 *i*PrOH /hexane, 0.8 mL/min, 210 nm; $T_R = 32.29$ min (major), 21.80 min (minor)). (Table 2, Entry 2).



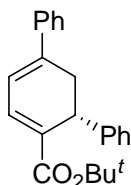
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1	D	22.682	252389.281	10759889.000	50.0206
2	D	31.835	173291.000	10751013.000	49.9794
总计			425680.281	21510902.000	100.0000



分析结果表

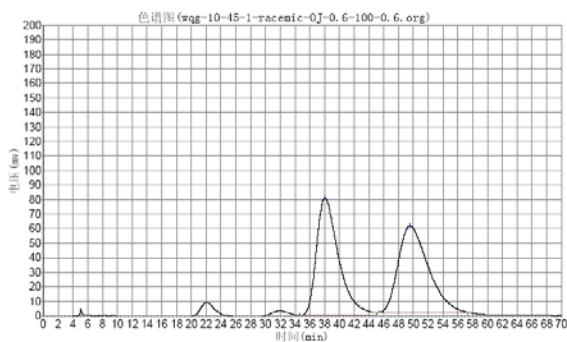
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1	D	21.802	9993.084	399799.469	7.8573
2	D	32.287	74842.906	4688488.000	92.1428
总计			84835.990	5088287.469	100.0000



4a': 55% yield (colorless oil, 70 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.42-7.39 (m, 2H), 7.33-7.15 (m, 9H), 6.51 (dd, $J = 6.0$ and 2.7 Hz, 1H), 4.12 (dd, $J = 2.1$ and 9.9 Hz, 1H), 3.27-3.17 (m, 1H), 2.99 (dd, $J = 17.7$ and 2.7 Hz, 1H), 1.40 (s, 9H); $[\alpha]_{\text{D}}^{20} = -39.9^\circ$ ($c = 0.91$, CHCl_3). 79% ee (determined by HPLC: Chiralcel AD-H Column, 0.6/100 i PrOH /hexane, 0.6 mL/min, 210 nm; $T_{\text{R}} = 48.8$ min (major), 36.7 min (minor)). (Table 2, Entry 3).

实验时间: 2008-10-30, 23:53:28 实验者: 2008-12-29, 15:48:52
谱图文件: E:\HPLC\wqg\wqg-10-45-1-racemic-0J-0.6-100-0.6.org 积分方法: 面积归一法

使用仪器类型: 气相色谱 检测器: FID 进样器: 分流
柱温: 程序升温

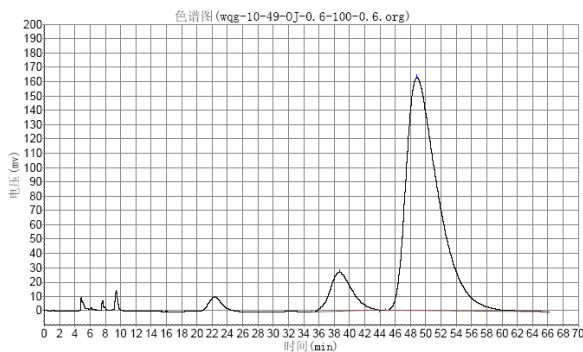


分析结果表

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1		38.042	80570.117	16718097.000	49.9860
2		49.538	59495.762	16727445.000	50.0140
总计			140065.879	33445542.000	100.0000

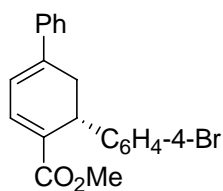
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使用仪器类型: 气相色谱 检测器: FID 进样器: 分流
柱温: 程序升温

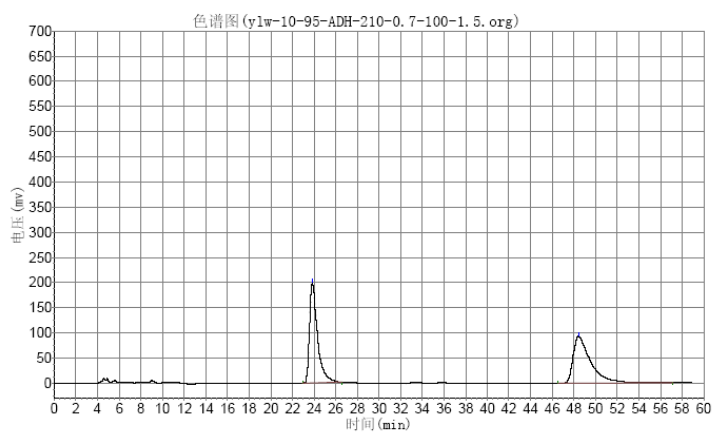


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		38.682	27170.500	5470373.500	10.3782
2		48.835	162730.625	47239712.000	89.6218
总计			189901.125	52710085.500	100.0000

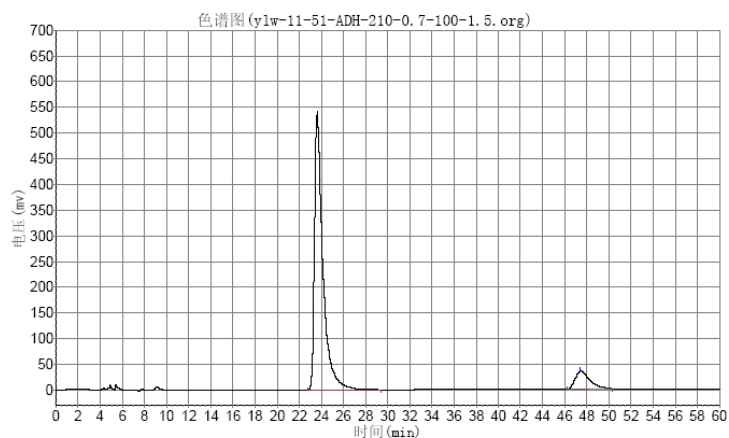


4b: 73% yield (white solid, 68 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.43-7.23 (m, 8H), 7.16 (d, $J = 8.4$ Hz, 2H), 6.52 (dd, $J = 6.0$ and 3.0 Hz, 1H), 4.12 (d, $J = 9.9$ Hz, 1H), 3.70 (s, 3H), 3.27-3.17 (m, 1H), 2.96 (dd, $J = 17.7$ and 1.8 Hz, 1H); $[\alpha]_{\text{D}}^{20} = -27.8^\circ$ ($c = 0.83$, CHCl_3). 80% ee (determined by HPLC: Chiralcel AD-H Column, 1.5/100 i PrOH /hexane, 0.7 mL/min, 210 nm; $T_{\text{R}} = 23.61$ min (major), 47.46 min (minor)). (Table 2, Entry 4).



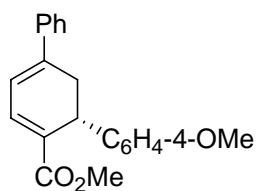
分析结果表

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1		23.848	200641.703	10581931.000	49.8641
2		48.448	93831.898	10639617.000	50.1359
总计			294473.602	21221548.000	100.0000

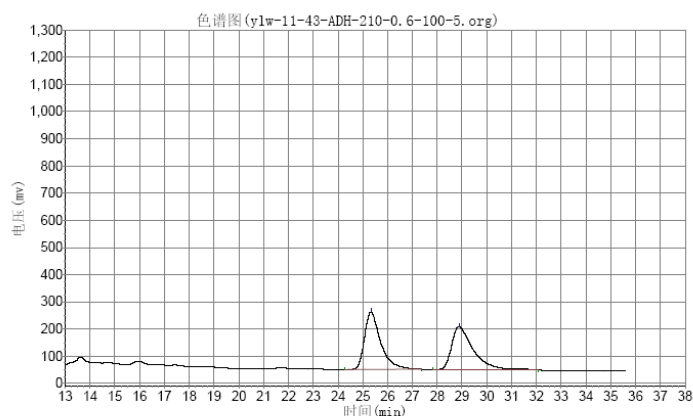


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		23.610	536883.313	28700542.000	90.0424
2		47.455	34545.043	3173928.500	9.9576
总计			571428.355	31874470.500	100.0000

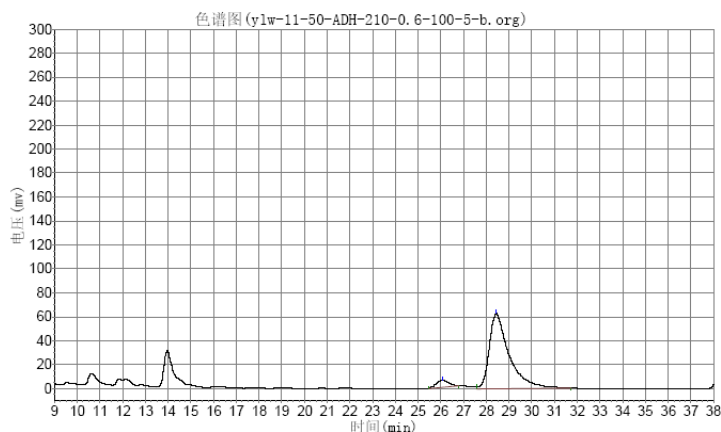


4c: 65% yield (white solid, 62 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.43-7.19 (m, 8H), 6.75 (d, $J = 8.7$ Hz, 2H), 6.52 (dd, $J = 6.0$ and 3.0 Hz, 1H), 4.13 (d, $J = 9.6$ Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.27-3.17 (m, 1H), 2.99 (dd, $J = 17.4$ and 1.5 Hz, 1H); $[\alpha]_{\text{D}}^{20} = -117.9^\circ$ ($c = 0.81$, CHCl_3). 90% ee (determined by HPLC: Chiralcel AD-H Column, 5/100 i PrOH /hexane, 0.6 mL/min, 210 nm; $T_{\text{R}} = 28.43$ min (major), 26.06 min (minor)). (Table 2, Entry 5).



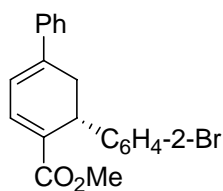
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		25.325	211170.188	9668081.000	49.8195
2		28.880	159536.172	9738127.000	50.1805
总计			370706.359	19406208.000	100.0000

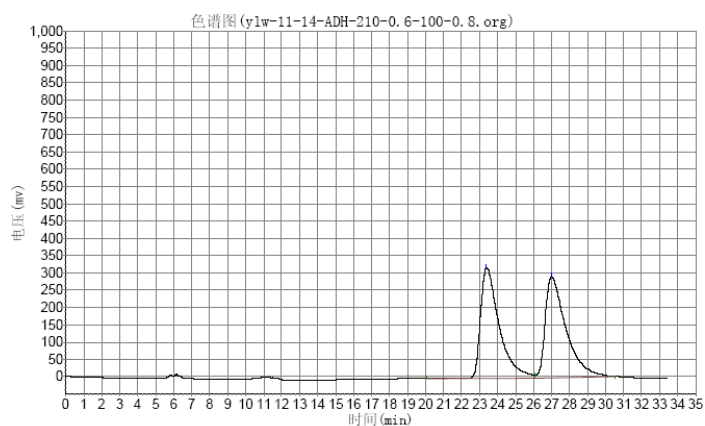


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		26.058	5502.266	208149.094	5.1670
2		28.432	62767.941	3820283.000	94.8330
总计			68270.207	4028432.094	100.0000

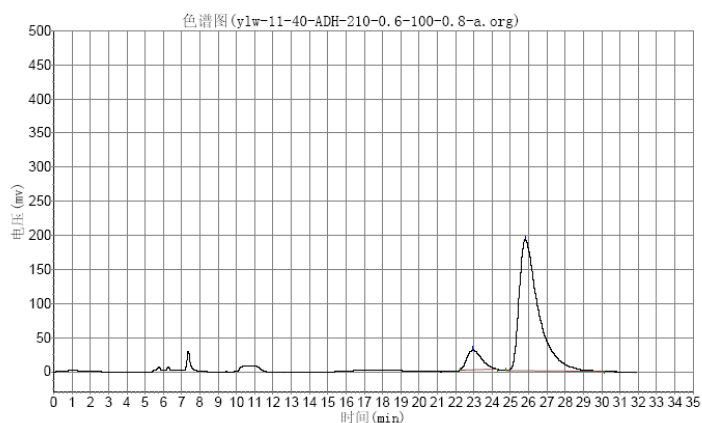


4d: 60% yield (white solid, 63 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.58-7.55 (m, 2H), 7.37-7.22 (m, 5H), 7.17-7.08 (m, 2H), 7.04-6.98 (m, 1H), 6.54 (dd, $J = 6.3$ and 3.0 Hz, 1H), 4.67 (dd, $J = 10.8$ and 1.8 Hz, 1H), 3.68 (s, 3H), 3.25-3.15 (m, 1H), 2.99 (dd, $J = 17.7$ and 2.1 Hz, 1H); $[\alpha]_{\text{D}}^{20} = -11.5^\circ$ ($c = 1.60$, CHCl_3). 80% ee (determined by HPLC: Chiralcel AD-H Column, 0.8/100 i PrOH /hexane, 0.6 mL/min, 210 nm; $T_{\text{R}} = 25.82$ min (major), 22.95 min (minor)). (Table 2, Entry 6).



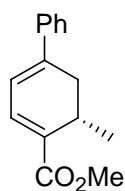
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		23.390	320771.031	23180500.000	49.6282
2		26.993	292993.375	23527804.000	50.3718
总计			613764.406	46708304.000	100.0000

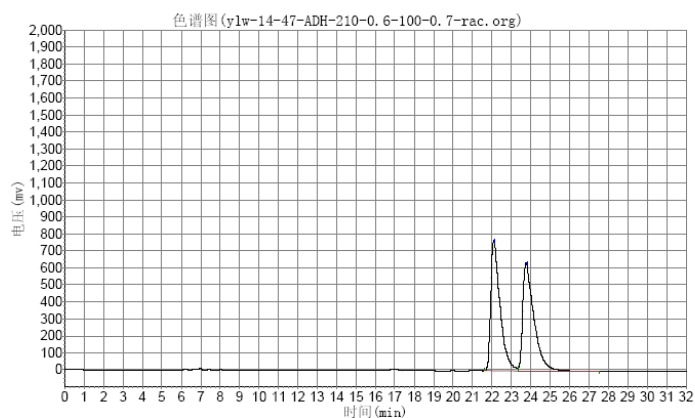


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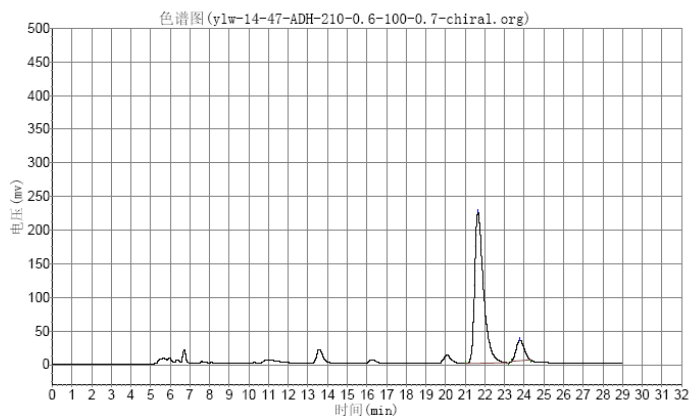
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1		22.950	28821.621	1606735.750	10.2314
2		25.818	192071.953	14097226.000	89.7686
总计			220893.574	15703961.750	100.0000



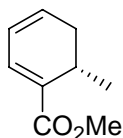
4e: 53% yield (colorless oil, 72 h). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.42 (d, $J = 7.2$ Hz, 2H), 7.31-7.17 (m, 3H), 7.05 (d, $J = 6.3$ Hz, 1H), 6.36 (dd, $J = 5.7$ and 2.7 Hz, 1H), 3.70 (s, 3H), 2.94-2.76 (m, 2H), 2.54 (d, $J = 17.0$ Hz, 1H), 0.95 (d, $J = 6.6$ Hz, 3H); $[\alpha]_{\text{D}}^{20} = -14.1^\circ$ ($c = 0.78$, CHCl_3). 78% ee (determined by HPLC: Chiralcel AD-H Column, 0.6/100 i PrOH /hexane, 0.7 mL/min, 210 nm; $T_{\text{R}} = 21.65$ min (major), 23.78 min (minor)). (Table 2, Entry 7).



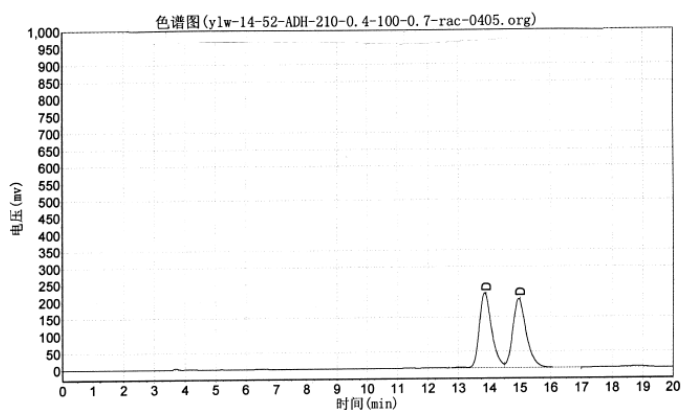
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峰号	峰名	保留时间	峰高	峰面积	含量
1		22.132	765321.438	25506950.000	50.0674
2		23.798	633031.688	25438282.000	49.9326
总计			1398353.125	50945232.000	100.0000



分析结果表					
峰号	峰名	保留时间	峰高	峰面积	含量
1		21.652	223715.078	7040714.000	88.9384
2		23.778	30415.143	875680.688	11.0616
总计			254130.221	7916394.688	100.0000

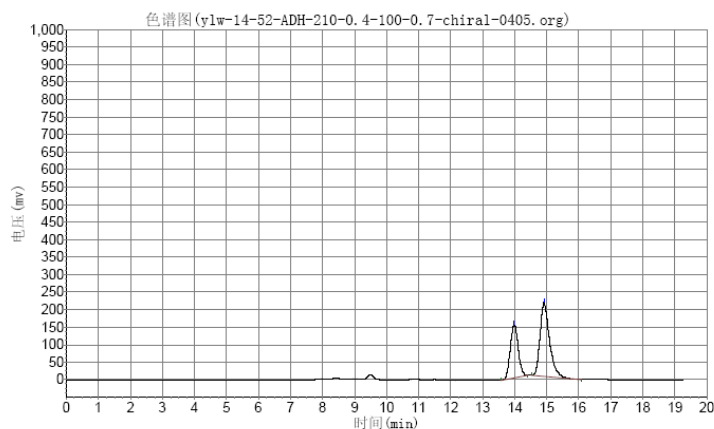


4f: 67% yield (colorless oil, 72 h). ¹H NMR (300 MHz, CDCl₃, TMS): δ 6.98-6.96 (m, 1H), 6.03 (t, *J* = 3.0 Hz, 2H), 3.76 (s, 3H), 2.85-2.75 (m, 1H), 2.57-2.48 (m, 1H), 2.22-2.14 (m, 1H), 0.99 (d, *J* = 7.2 Hz, 3H); [α]_D²⁰ = -11.6° (c = 0.66, CHCl₃). 25% ee (determined by HPLC: Chiralcel AD-H Column, 0.7/100 ⁱPrOH/hexane, 0.4 mL/min, 210 nm; T_R = 14.92 min (major), 13.99 min (minor)). (Table 2, Entry 8).



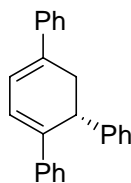
分析结果表

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1		13.898	218031.531	6179433.000	50.1003
2		14.998	200511.375	6154690.000	49.8997
总计			418542.906	12334123.000	100.0000

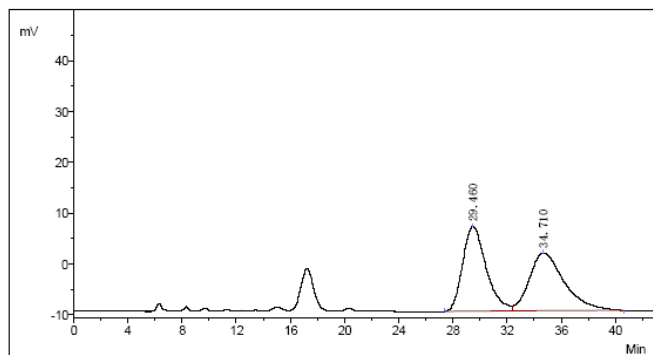


分析结果表

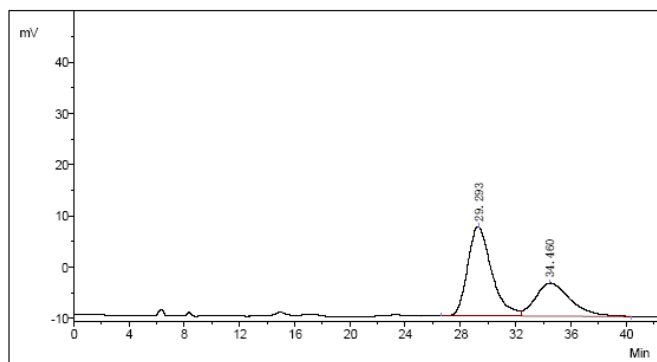
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1		13.985	150104.531	2595883.000	37.6933
2		14.915	210003.250	4290979.000	62.3067
总计			360107.781	6886862.000	100.0000



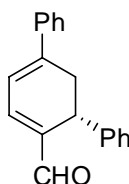
4h: 79% yield. ^1H NMR (300 MHz, CDCl_3 , TMS): δ 7.43-6.55 (m, 15H), 6.87 (d, $J = 6.0$, 1H), 6.57 (q, $J = 3.0$, 1H), 6.87 (d, $J = 6.0$, 1H), 4.14 (dd, $J = 1.8$ and 9.0, 1H), 3.29 (ddd, $J = 2.7$, 9.0 and 16.8, 1H), 2.96 (dd, $J = 2.1$ and 16.8, 1H); ^{13}C NMR (75 MHz, CDCl_3). 142.2, 140.5, 139.9, 137.1, 134.2, 128.4, 128.37, 128.33, 127.5, 127.13, 127.07, 126.4, 125.3, 125.0, 123.0, 121.4, 41.5, 35.5; IR (KBr) ν/cm^{-1} : 3057 (w), 1491 (m), 1445 (m), 752 (s), 690 (s). MS (EI): m/z (% relative intensity): 308 (M^+ , 196.47), 217 (100); HRMS (EI): Calcd for $\text{C}_{24}\text{H}_{20}$: 308.1563, Found: 308.1565. $[\alpha]_{\text{D}}^{20} = +22.9^\circ$ ($c = 1.0$, CHCl_3). 30% ee (determined by HPLC: Chiralcel OJ-H Column, 30/70 iPrOH /hexane, 0.5 mL/min, 230 nm; TR = 29.29 min (major), 34.46 min (minor)).



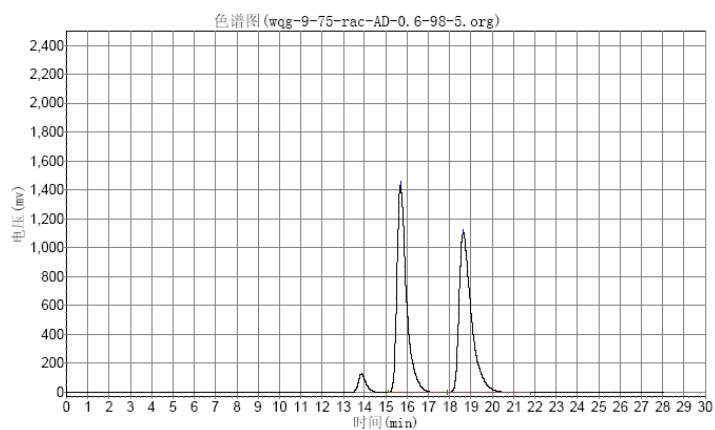
No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	29.460	16709.7	2022080.8	49.5997
2	2	Unknown	34.710	11409.6	2054718.8	50.4003
Total				28119.3	4076799.5	100.0000



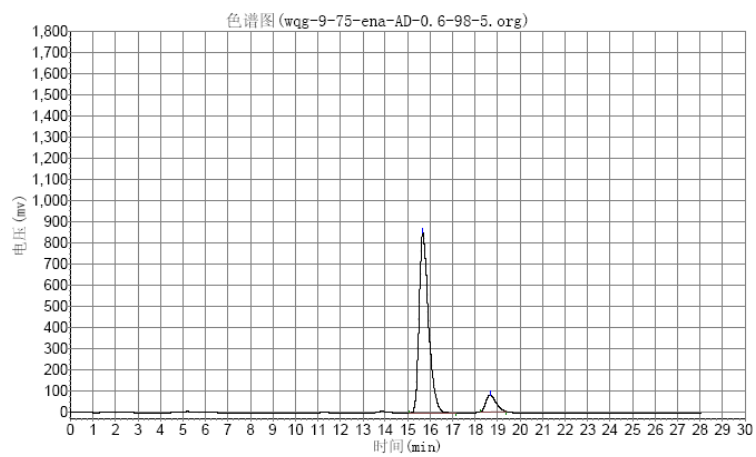
No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	Per Cent
1	1	Unknown	29.293	17473.3	2109970.6	64.7352
2	2	Unknown	34.460	6517.0	1149417.8	35.2648
Total				23990.3	3259388.4	100.0000



5: 83% yield (two steps). ^1H NMR (300 MHz, CDCl_3 , TMS): δ 9.58 (s, 1H), 7.45 (dd, $J = 8.1$ and 1.8 Hz, 2H), 7.36-7.05 (m, 9H), 6.63 (dd, $J = 6.0$ and 2.4 Hz, 1H), 4.22 (dd, $J = 9.0$ and 2.1 Hz, 1H), 3.24-3.05 (m, 2H); $[\alpha]_{\text{D}}^{20} = -31.8^\circ$ ($c = 0.56$, CHCl_3). 82% ee (determined by HPLC: Chiralcel AD Column, 5/98 i PrOH /hexane, 0.6 mL/min, 230 nm; $T_{\text{R}} = 15.67$ min (major), 18.66 min (minor)).



峰号	峰名	保留时间	峰高	峰面积	含量
1		15.683	1433499.500	44062708.000	50.0268
2		18.633	1103522.375	44015444.000	49.9732
总计			2537021.875	88078152.000	100.0000



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		15.670	851204.250	24772180.000	90.7736
2		18.663	80125.367	2517905.500	9.2264
总计			931329.617	27290085.500	100.0000