Supporting Information for

_N_-Alkylation of Indole _via_ Ring-Closing Metathesis/Isomerization/Mannich Cascade under Ruthenium/Chiral Phosphoric Acid Sequential Catalysis

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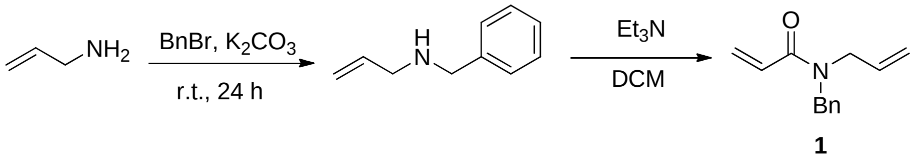
General Methods. Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (300 MHz and 75 MHz, 400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm).

Procedures for preparation of substrate 1

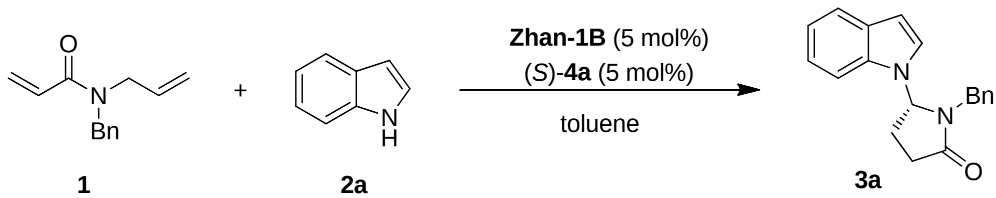


***N*-allyl-benzyl-amine** was synthesized from allylamine and benzyl bromide according to reported procedures.[1]

Synthesis of diene **1**: A solution of acryloylchloride (2.0 g, 22.4 mmol) in dichloromethane was added dropwise to a mixture of *N*-allyl-benzyl-amine (3.0 g, 20.4 mmol) and triethylamine (2.5 g, 24.5 mmol) in dried dichloromethane (50 mL) at 0 ^{o}C. The reaction was stirred at 0 ^{o}C for 1 h and then warmed to r.t. for 2 h. Then the reaction mixture was quenched with aqueous $NaHCO_3$, the dichloromethane layer was washed with brine, dried over Na_2SO_4 and filtrated. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ethyl acetate / petroleum = 1/10, v/v) to afford **1** (4.0 g, 98% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (m, J = 2.4 Hz, 1H), 4.07 (m, J = 5.7 Hz, 1H), 4.58 (s, 1H), 4.66 (s, 1H), 5.11-5.29 (m, 2H), 5.67-5.83 (m, 2H), 6.45 (dd, J_1 = 2.4 Hz, J_2 = 16.5 Hz, 1H), 6.55 (dd, J_1 = 9.9 Hz, J_2 = 16.8 Hz, 1H), 7.17-7.38 (m, 5H). Spectroscopic data were in agreement with those previously reported.[2]

Complete optimization data

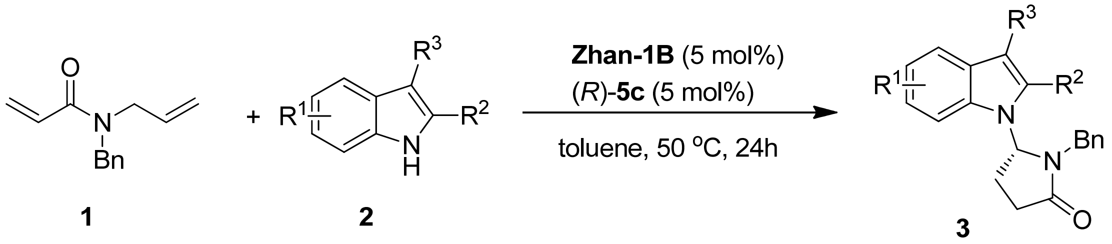
Table 1. Conditions Optimization



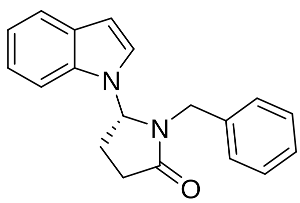
entry[a]	temp (^{o}C)	time (day)	yield (%)[b]	*ee* (%)[c]
1	rt	3	23	78
2	rt	7	52	78

[a] Reaction conditions: **1** (0.2 mmol), **2a** (1.2 equiv), **Zhan-1B** (5 mol%), **4** or **5** (5 mol%) in 1.5 mL toluene. [b] Isolated yield. [c] Determined by HPLC analysis.

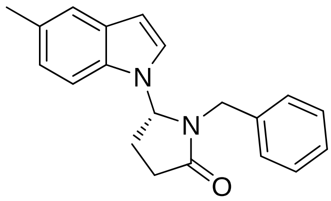
General procedure for asymmetric cascade reaction



Under argon, a round bottom flask was charged with *N*-allyl-*N*-benzylacrylamide **1** (0.20 mmol), indole **2** (0.24 mmol), and chiral phosphoric acid (*R*)-**5c** (7.2 mg, 0.01 mmol), then dry toluene (1.5 mL) were added. The mixture was heated to 50 °C and then **Zhan-1B** (7.3 mg, 0.01 mmol) was added. The reaction was stirred 50 °C for 24 h. After the reaction was complete (monitored by TLC), the solvent was removed under reduced pressure. The residue was purified by flash chromatography to afford the product **3**.

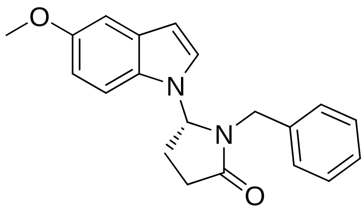


(*R*)-1-benzyl-5-(1*H*-indol-1-yl)pyrrolidin-2-one[3]
White solid (44.1 mg, 76% yield, 92% *ee*). Analytical data for **3a**: Mp = 41-43 °C; $[\alpha]_D^{20}$ = 105.4 (c = 0.2 CH_2Cl_2, 92% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18-2.26 (m, 1H), 2.52-2.71 (m, 2H), 2.77-2.89 (m, 1H), 3.31 (d, *J* = 14.7 Hz, 1H), 5.07 (d, *J* = 15.0 Hz, 1H), 5.77-5.80 (m, 1H), 6.60 (d, *J* = 3.0 Hz, 1H), 7.02-7.13 (m, 4H), 7.13-7.17 (m, 2H), 7.26-7.30 (m, 3H), 7.64-7.67 (m, 1H); The enantiomeric excess was determined by Daicel Chiralcel AD-H (25 cm), Hexanes / IPA = 90 / 10, 0.6 mL/min, λ = 254 nm, t (major) = 13.41 min, t (minor) = 15.46 min.



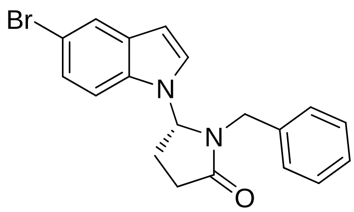
(*R*)-1-benzyl-5-(5-methyl-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (38.5 mg, 63% yield, 94% *ee*). Analytical data for **3b**: Mp = 34-36 ^{o}C; $[\alpha]_D^{20}$ = 118.8 (c = 0.2 CH_2Cl_2, 94% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18-2.26 (m, 1H), 2.47 (s, 3H), 2.53-2.68 (m, 2H), 2.76-2.89 (m, 1H), 3.30 (d, *J* = 14.7 Hz, 1H), 5.08 (d, *J* = 14.7 Hz, 1H), 5.73-5.76 (m, 1H), 6.53 (d, *J* = 3.0 Hz, 1H), 6.98-7.01 (m, 3H), 7.02-7.08 (m, 2H), 7.26-7.30 (m, 3H), 7.49 (s, 1H). The enantiomeric excess was determined by Daicel Chiralcel AD-H (25 cm), Hexanes / IPA = 95 / 5, 1.0 mL/min, λ = 254 nm, t (major) = 12.94 min, t (minor) = 14.23 min.



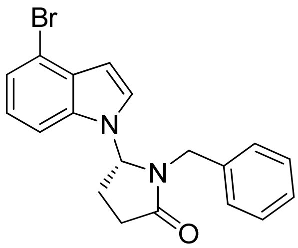
(*R*)-1-benzyl-5-(5-methoxy-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (55.3 mg, 86% yield, 93% *ee*). Analytical data for **3c**: Mp = 94-96 ^{o}C; $[\alpha]_D^{20}$ = 102.0 (c = 0.2 CH_2Cl_2, 93% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09-2.20 (m, 1H), 2.41-2.60 (m, 2H), 2.67-2.79 (m, 1H), 3.22 (d, *J* = 14.4 Hz, 1H), 3.77 (s, 3H), 4.98 (d, *J* = 14.7 Hz, 1H), 5.61-5.64 (m, 1H), 6.43 (d, *J* = 2.1 Hz, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.87-6.90 (m, 2H), 6.98 (brs, 2H), 7.03 (s, 1H), 7.20 (brs, 3H). The enantiomeric excess was determined by Daicel Chiralcel OD-H (25 cm) (25 cm), CH_3CN / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 28.86 min, t (minor) = 48.99 min.



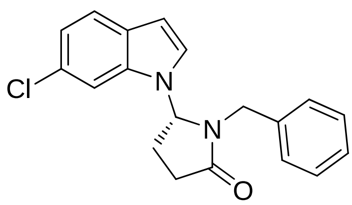
(*R*)-1-benzyl-5-(5-bromo-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (51.3 mg, 70% yield, 88% *ee*). Analytical data for **3d**: Mp = 40-42 °C; $[\alpha]_D^{20}$ = 67.8 (c = 0.2 CH_2Cl_2, 88% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17-2.29 (m, 1H), 2.54-2.72 (m, 2H), 2.78-2.90 (m, 1H), 3.31 (d, *J* = 14.4 Hz, 1H), 5.18 (d, *J* = 15.0 Hz, 1H), 5.74-5.76 (m, 1H), 6.56 (d, *J* = 2.7 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 7.04-7.05 (m, 3H), 7.29-7.31 (m, 4H), 7.80 (s, 1H). The enantiomeric excess was determined by Daicel Chiralcel AD-H (25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 11.43 min, t (minor) = 13.49 min.



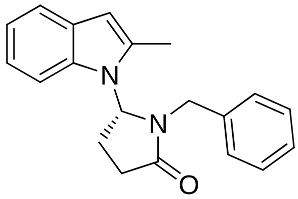
(*R*)-1-benzyl-5-(4-bromo-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (24 mg, 33% yield, 90% *ee*). Analytical data for **3e**: Mp = 108-110 °C; $[\alpha]_D^{20}$ = 83.8 (c = 0.2 CH_2Cl_2, 90% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17-2.24 (m, 1H), 2.55-2.71 (m, 2H), 2.77-2.89 (m, 1H), 3.30 (d, *J* = 14.7 Hz, 1H), 5.06 (d, *J* = 14.7 Hz, 1H), 5.71-5.75 (m, 1H), 6.66 (d, *J* = 3.3 Hz, 1H), 7.02-7.04 (m, 4H), 7.07-7.08 (d, *J* = 3.6 Hz, 1H), 7.26-7.34 (m, 4H). The enantiomeric excess was determined by Daicel Chiralcel IA (25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 10.42 min, t (minor) = 11.33 min.



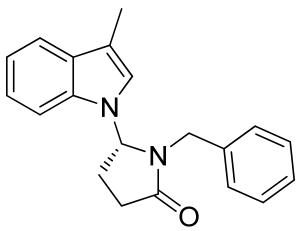
(*R*)-1-benzyl-5-(6-chloro-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (33.4 mg, 52% yield, 93% *ee*). Analytical data for **3f**: Mp = 97-99 °C; $[\alpha]_D^{20}$ = 155.7 (c = 0.2 CH_2Cl_2, 93% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17-2.23 (m, 1H), 2.55-2.70 (m, 2H), 2.76-2.87 (m, 1H), 3.32 (d, *J* = 14.4 Hz, 1H), 5.05 (d, *J* = 15.0 Hz, 1H), 5.69-5.71 (m, 1H), 6.58 (d, *J* = 3.0 Hz, 1H), 7.00-7.02 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.28-7.30 (m, 3H), 7.53 (d, *J* = 8.4 Hz, 1H). The enantiomeric excess was determined by Daicel Chiralcel AD-H (25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 16.32 min, t (minor) = 18.70 min.



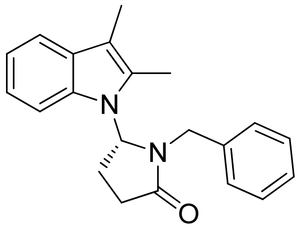
(*R*)-1-benzyl-5-(2-methyl-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (40.5 mg, 67% yield, 95% *ee*). Analytical data for **3g**: Mp = 39-41 ^{o}C; $[\alpha]_D^{20}$ = 126.9 (c = 0.2 CH_2Cl_2, 95% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ1.91 (s, 3H), 2.38-2.55 (m, 2H), 2.61-2.78 (m, 1H), 2.82-2.93 (m, 1H), 3.17 (d, *J* = 15.0 Hz, 1H), 5.16 (d, *J* = 15.0 Hz, 1H), 5.65 (t, *J* = 6.9 Hz, 1H), 6.22 (s, 1H), 6.88-7.04 (m, 2H), 7.08-7.15 (m, 3H), 7.20-7.30 (m, 3H), 7.53-7.56 (m, 1H). The enantiomeric excess was determined by Daicel Chiralcel IC (25 cm), CH_3CN / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 23.62 min, t (minor) = 18.69 min.



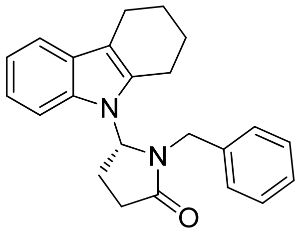
(*R*)-1-benzyl-5-(3-methyl-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (56.0 mg, 92% yield, 85% *ee*). Analytical data for **3h**: Mp = 75-77 ^{o}C; $[\alpha]_D^{20}$ = 90.2 (c = 0.2 CH_2Cl_2, 85% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.19-2.21 (m, 1H), 2.32 (s, 3H), 2.54-2.68 (m, 2H), 2.79-2.82 (m, 1H), 3.35 (d, *J* = 15.0 Hz, 1H), 5.03 (d, *J* = 14.7 Hz, 1H), 5.73-5.77 (m, 1H), 6.79 (s, 1H), 7.02-7.06 (m, 3H), 7.16-7.19 (m, 2H), 7.26-7.29 (m, 3H), 7.57-7.60 (m, 1H). The enantiomeric excess was determined by Daicel Chiralcel OJ-H (25 cm), Hexanes / IPA = 90 / 10, 0.8 mL/min, λ = 254 nm, t (major) = 24.01 min, t (minor) = 35.22 min.



(*R*)-1-benzyl-5-(2,3-dimethyl-1*H*-indol-1-yl)pyrrolidin-2-one[3]

White solid (54.2 mg, 85% yield, 89% *ee*). Analytical data for **3i**: Mp = 90-92 ^{o}C; $[\alpha]_D^{20}$ = 128.7 (c = 0.2 CH_2Cl_2, 89% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90 (s, 3H), 2.25 (s, 3H), 2.30-2.55 (m, 2H), 2.60-2.94 (m, 2H), 3.22 (d, J = 14.4 Hz, 1H), 5.16 (d, J = 15.0 Hz, 1H), 5.69 (dd, J_1 = 6.6 Hz, J_2 = 7.8 Hz, 1H), 6.89-7.08 (m, 2H), 7.12-7.22 (m, 3H), 7.24-7.32 (m, 3H), 7.51-7.56 (m, 1H). The enantiomeric excess was determined by Daicel Chiralcel AD-H (25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 7.01 min, t (minor) = 7.77 min.



(*R*)-1-benzyl-5-(3,4-dihydro-1*H*-carbazol-9(2*H*)-yl)pyrrolidin-2-one[3]

White solid (59.1 mg, 86% yield, 85% *ee*). Analytical data for **3j**: Mp = 88-90 ^{o}C; $[\alpha]_D^{20}$ = 113.5 (c = 0.2 CH_2Cl_2, 85% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.61-1.85 (m, 5H), 2.10-2.49 (m, 2H), 2.52-2.70 (m, 4H), 2.74-2.85 (m, 1H), 3.10 (d, J = 14.7 Hz, 1H), 5.05 (d, J = 14.7 Hz, 1H), 5.52 (t, J = 7.2 Hz, 1H), 6.84-6.96 (m, 2H), 7.03-7.13 (m, 3H), 7.17-7.22 (m, 3H), 7.42-7.43 (m, 1H). The enantiomeric excess was determined by Daicel Chiralcel OD-H (25 cm), Hexanes / IPA = 90 / 10, 1.0 mL/min, λ = 254 nm, t (major) = 12.99 min, t (minor) = 11.32 min.

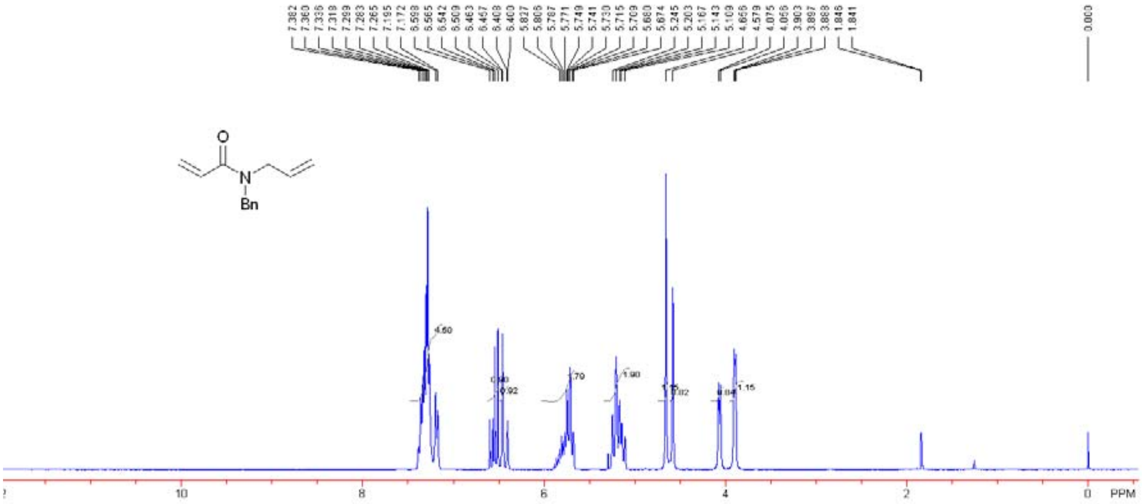
References

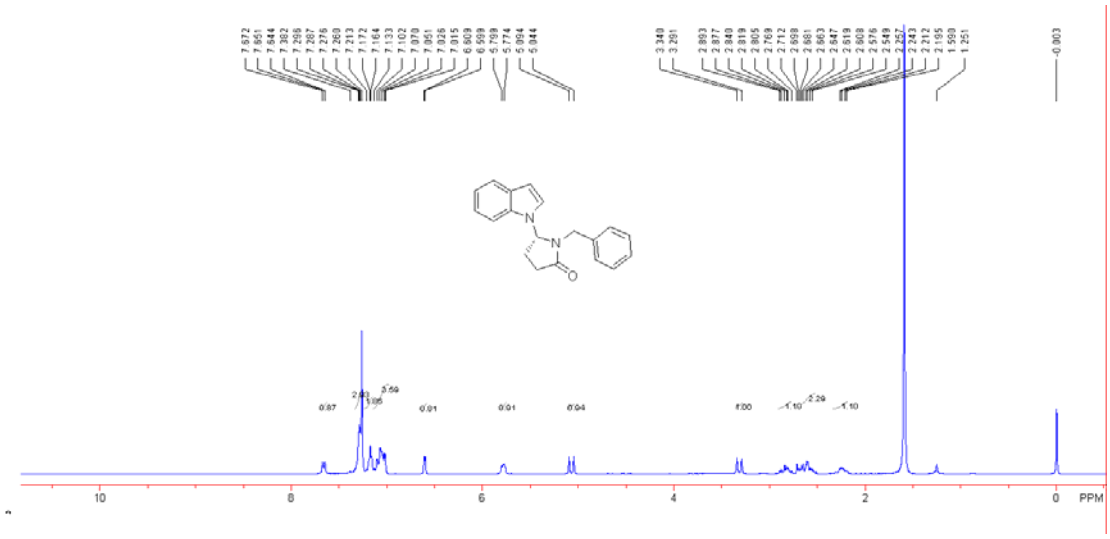
1. S. Mukherjee and B. List, *J. Am. Chem. Soc.* 2007, **129**, 11336.
2. (a) I. D. Riggi, S. Gastaldi, J.-M. Surzur, M. P. Bertrand and A. Virgili, *J. Org. Chem.* 1992, **57**, 6118. (b) E. Benedetti, M. Lomazzi, F. Tibiletti, P. Giovanni, J.-P.

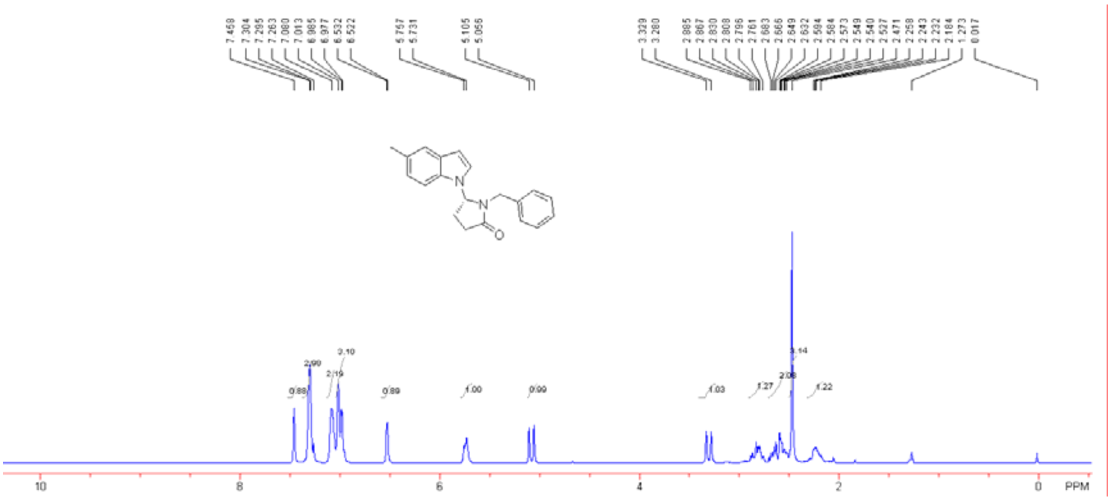
Goddard, M. Fensterbank, G. Palmisano and A. Penoni, *Synthesis* 2012, **44**, 3523.

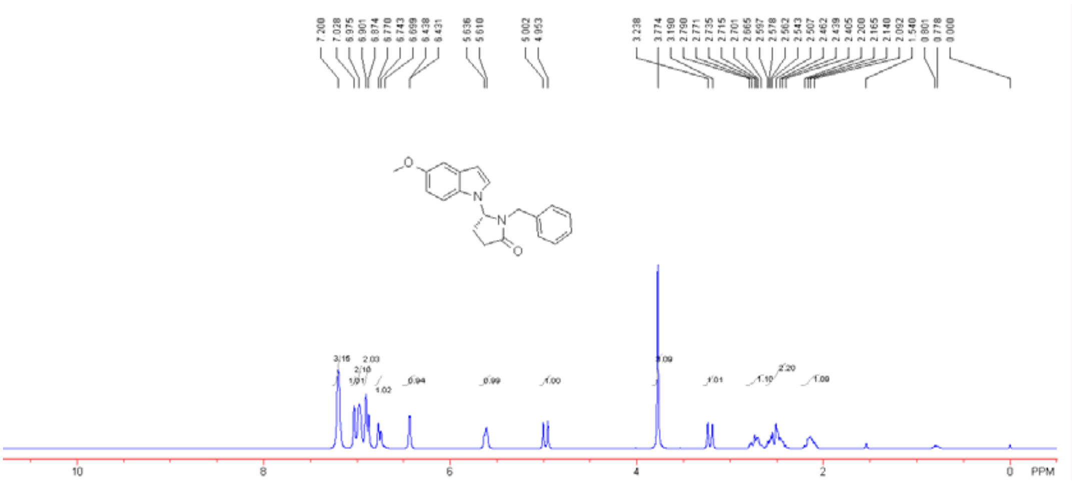
3. Y. Xie, Y. Zhao, B. Qian, L. Yang, C. Xia and H. Huang, *Angew. Chem., Int. Ed.* 2011, **50**, 5682.

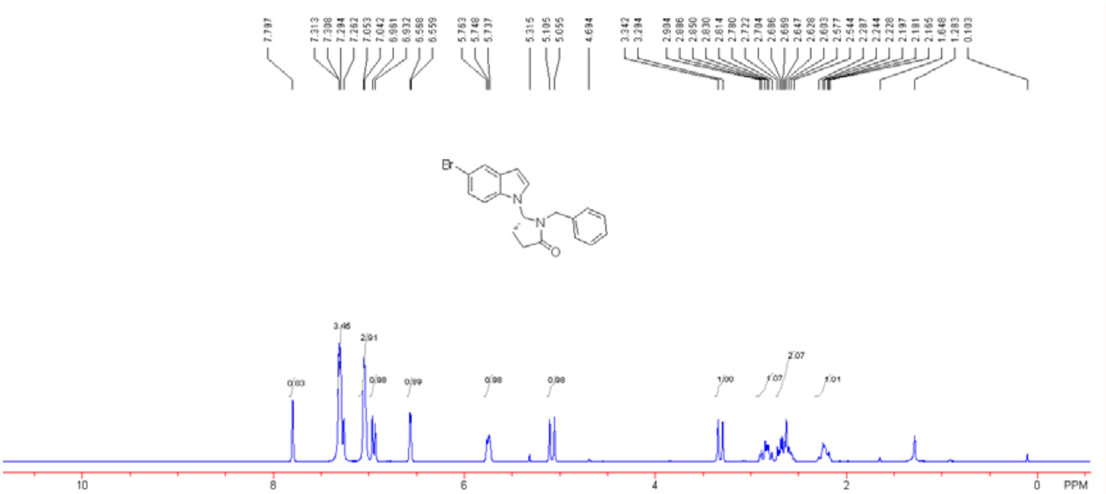
4. Copies of NMR spectra and HPLC

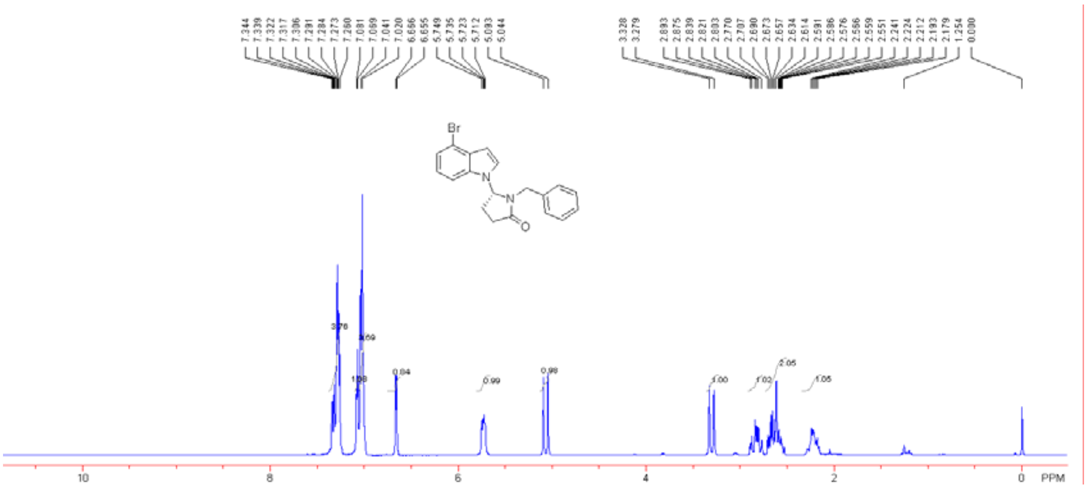


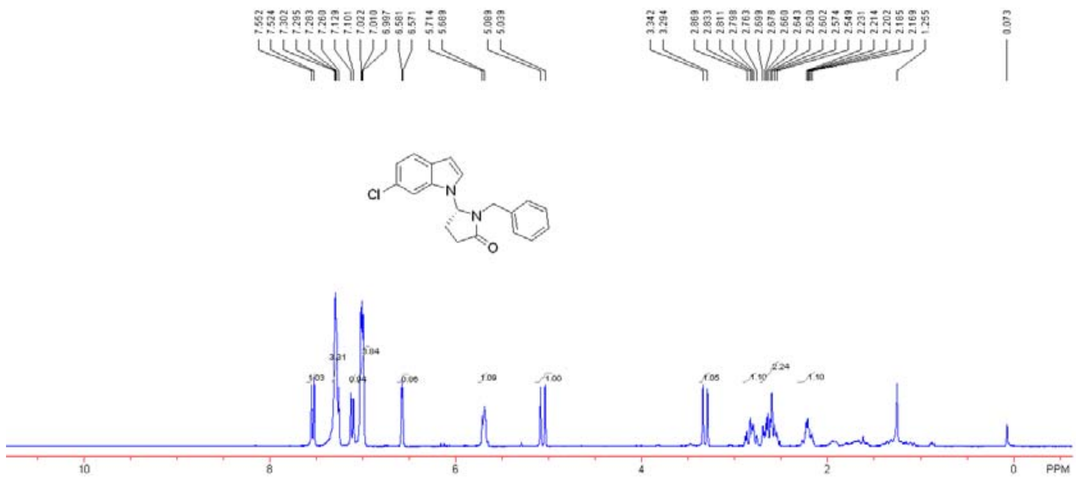


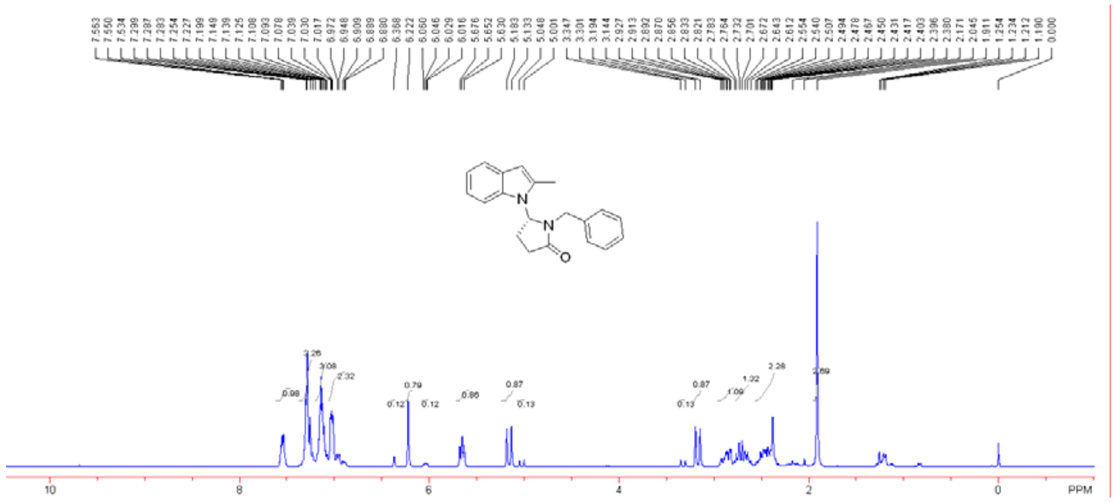


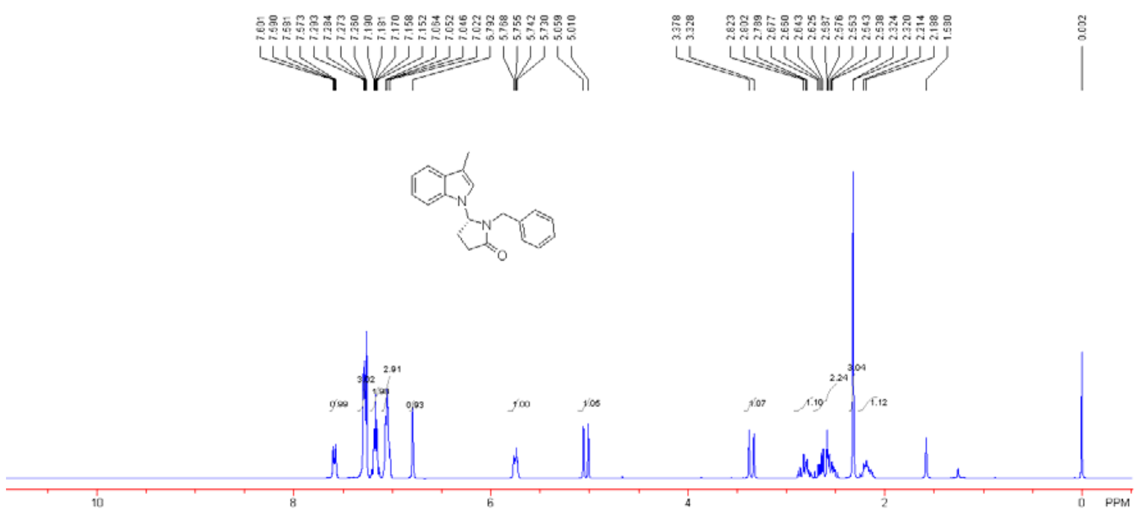


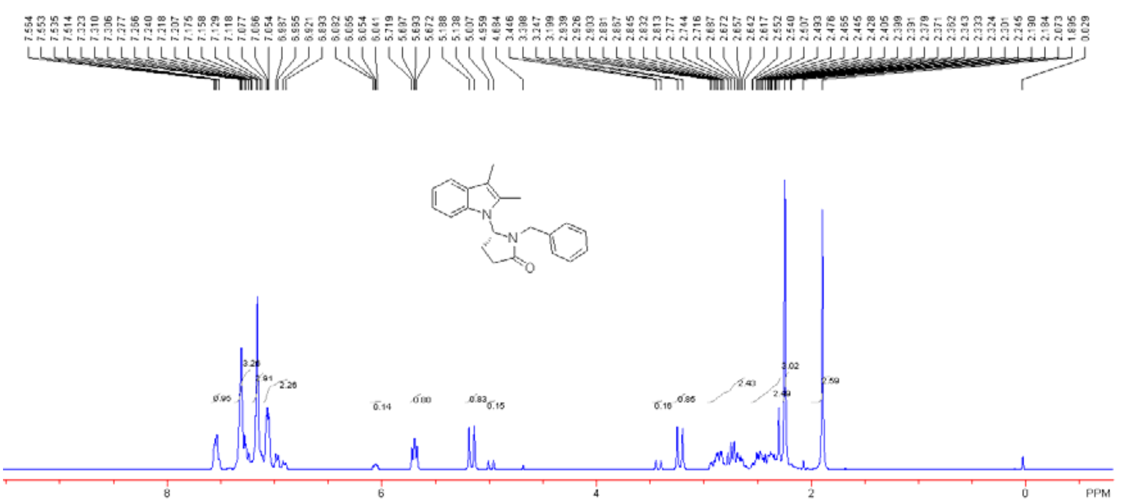


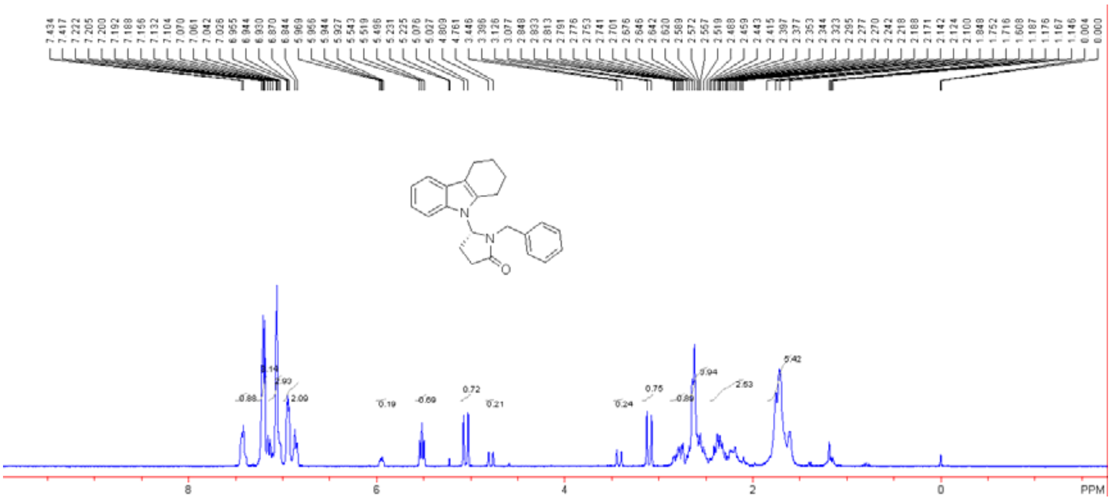


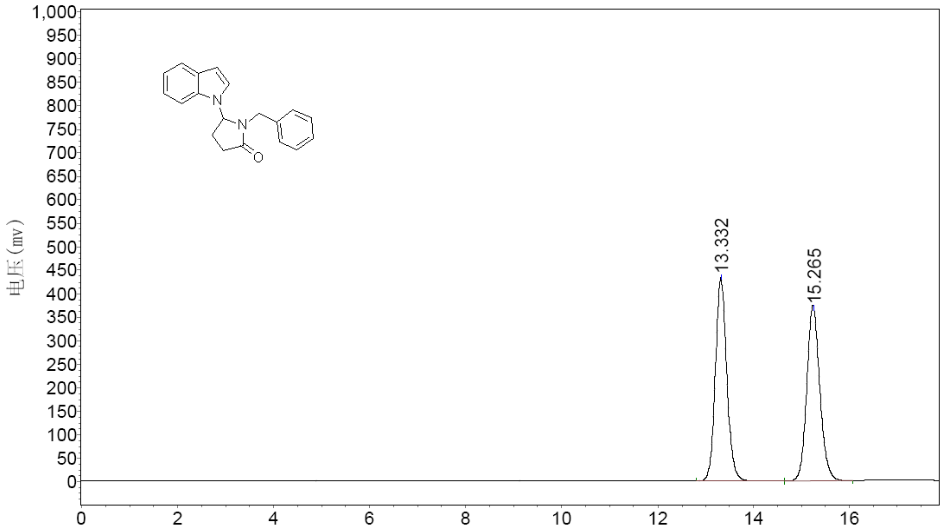












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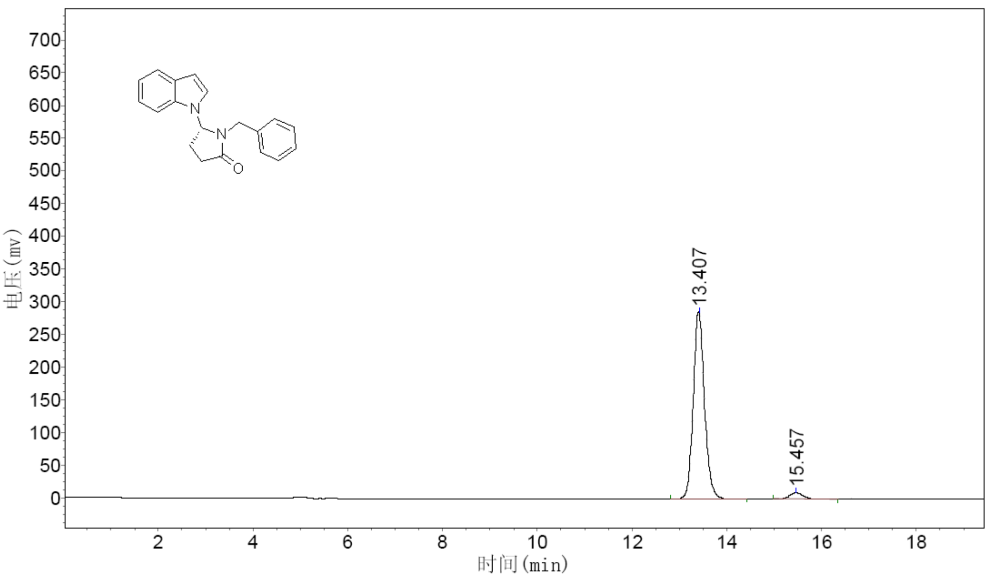

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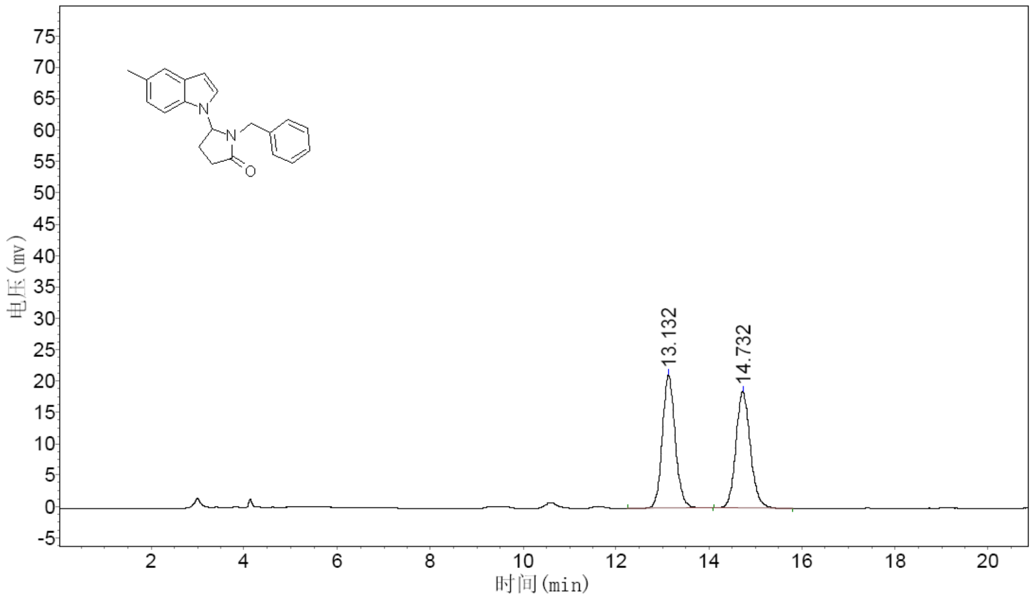

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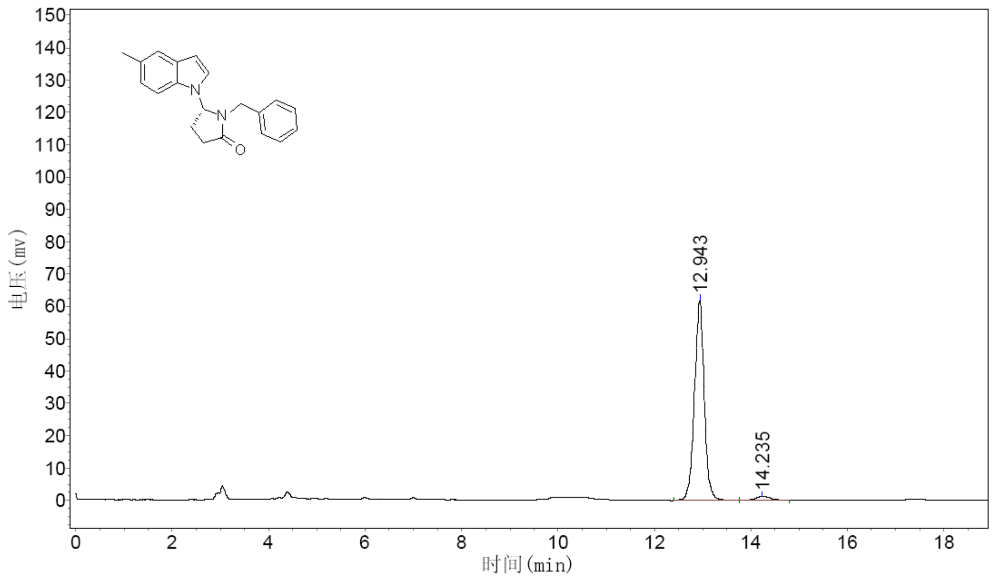

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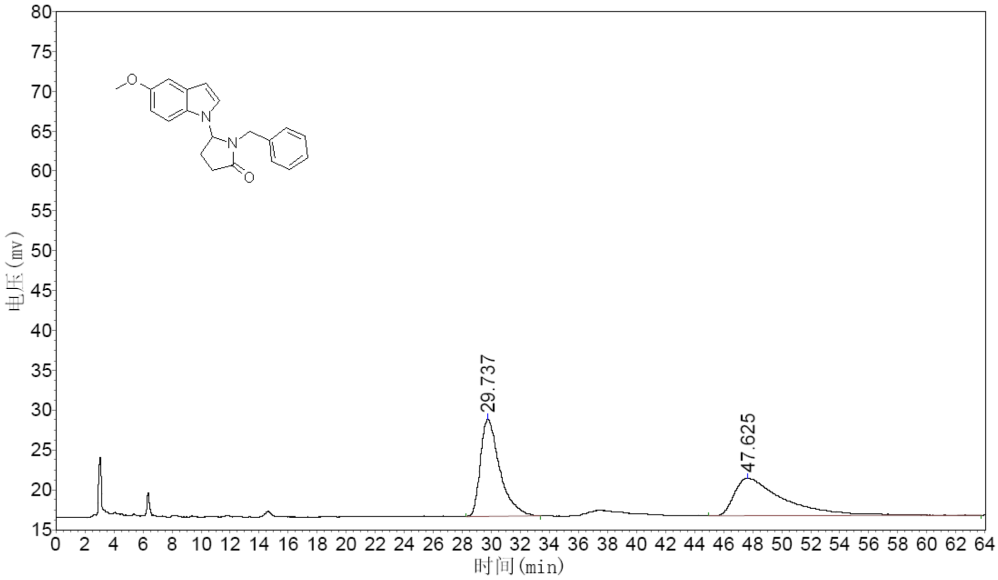

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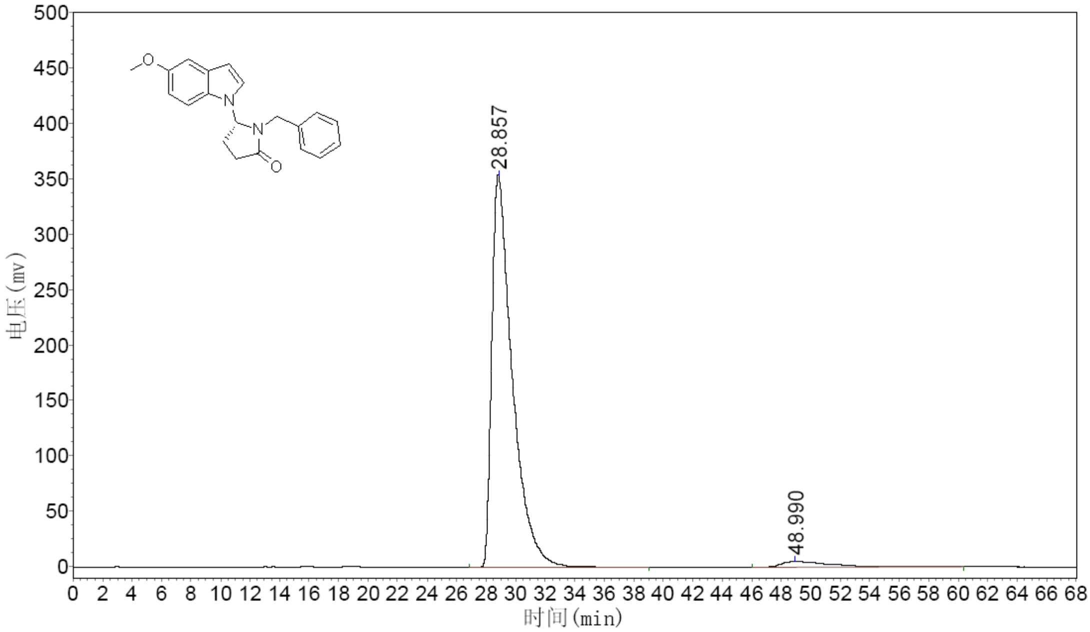
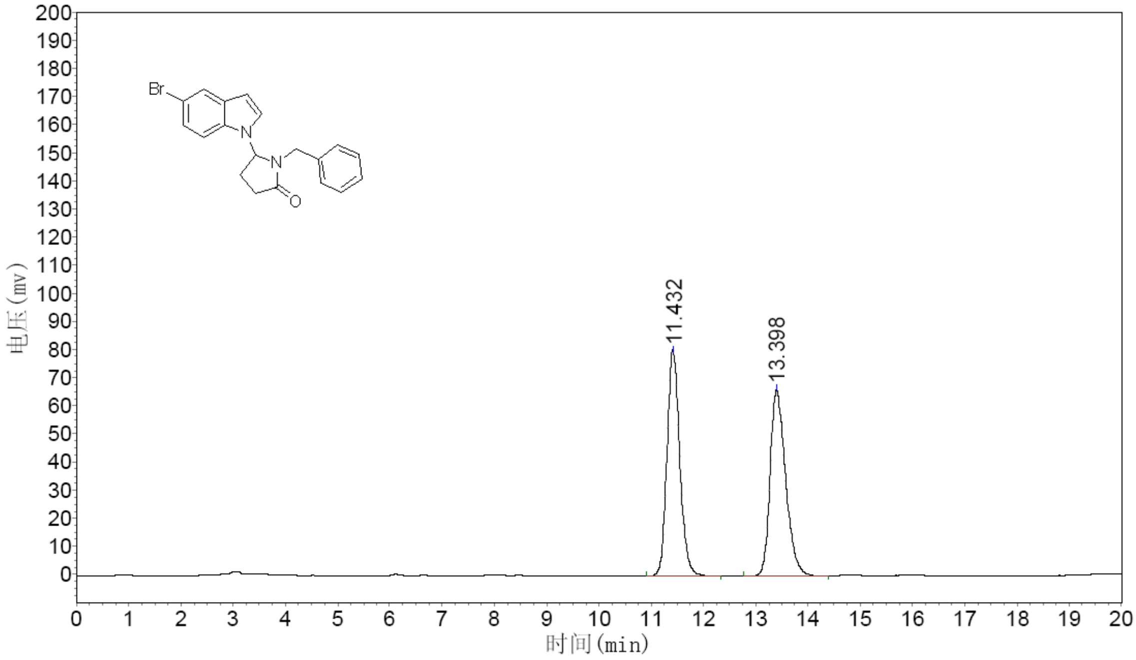
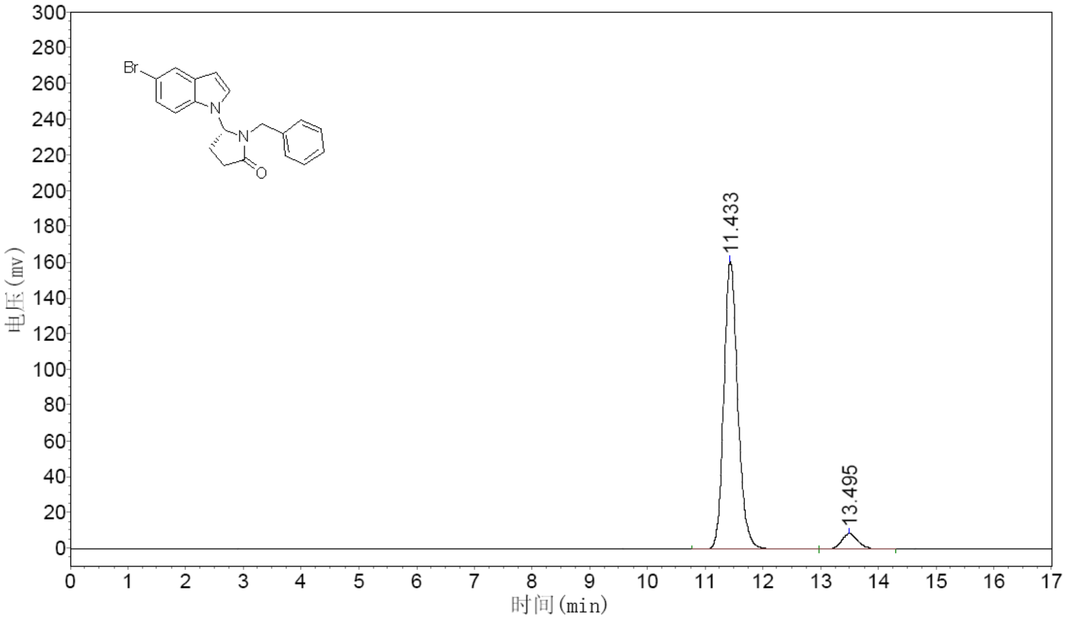
2	47. 625	4703. 648	1092695. 375	49. 2107
Total		16877. 213	2220443. 000	100. 0000



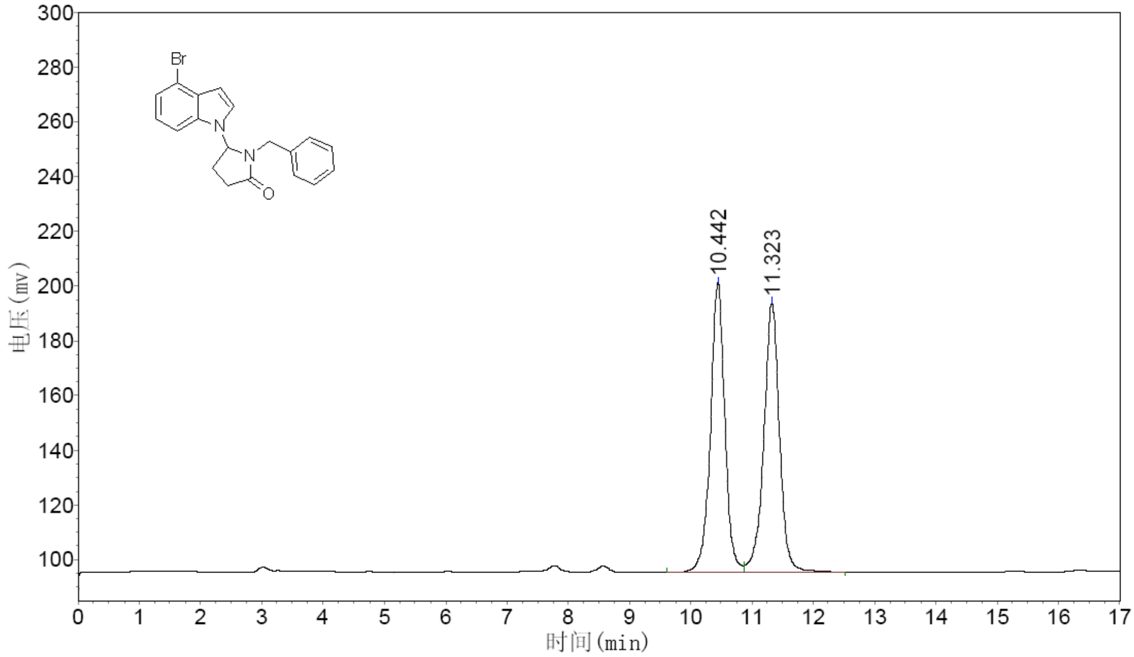
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	28. 857	353637. 375	34109952. 000	96. 4071
2	48. 990	5304. 093	1271205. 500	3. 5929
Total		358941. 468	35381157. 500	100. 0000



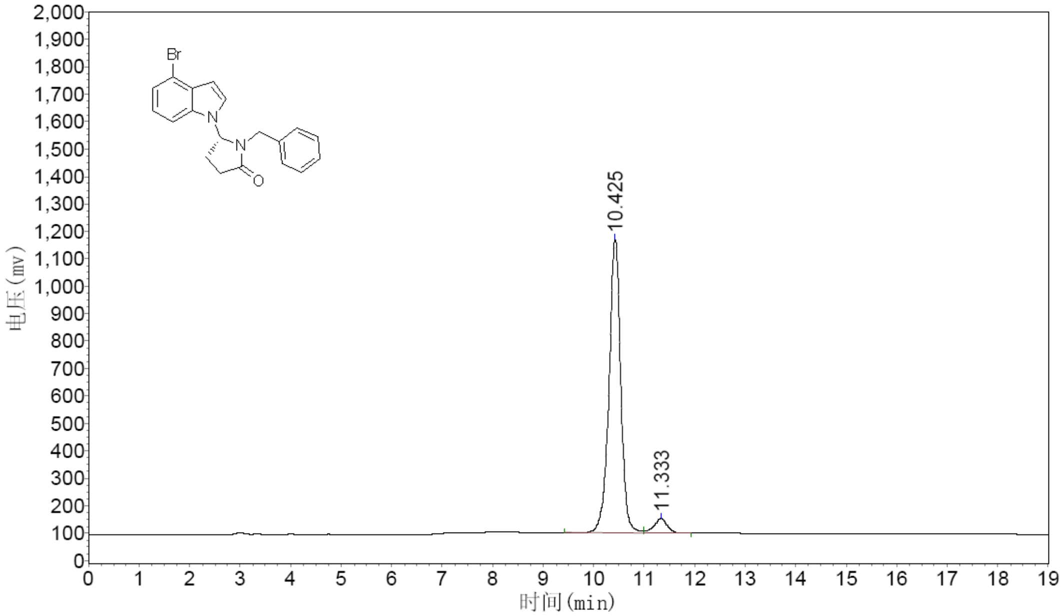
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	11.432	80170.469	1360811.000	50.0118
2	13.398	65333.020	1360166.875	49.9882
Total		145503.488	2720977.875	100.0000



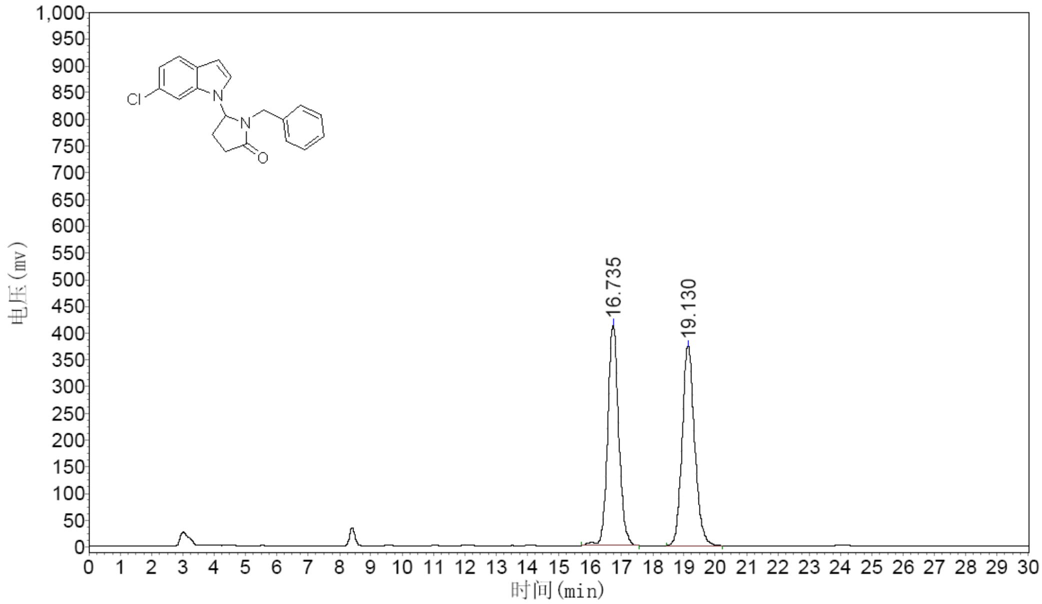
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	11.433	161255.719	2709575.750	94.0319
2	13.495	8639.966	171975.109	5.9681
Total		169895.685	2881550.859	100.0000



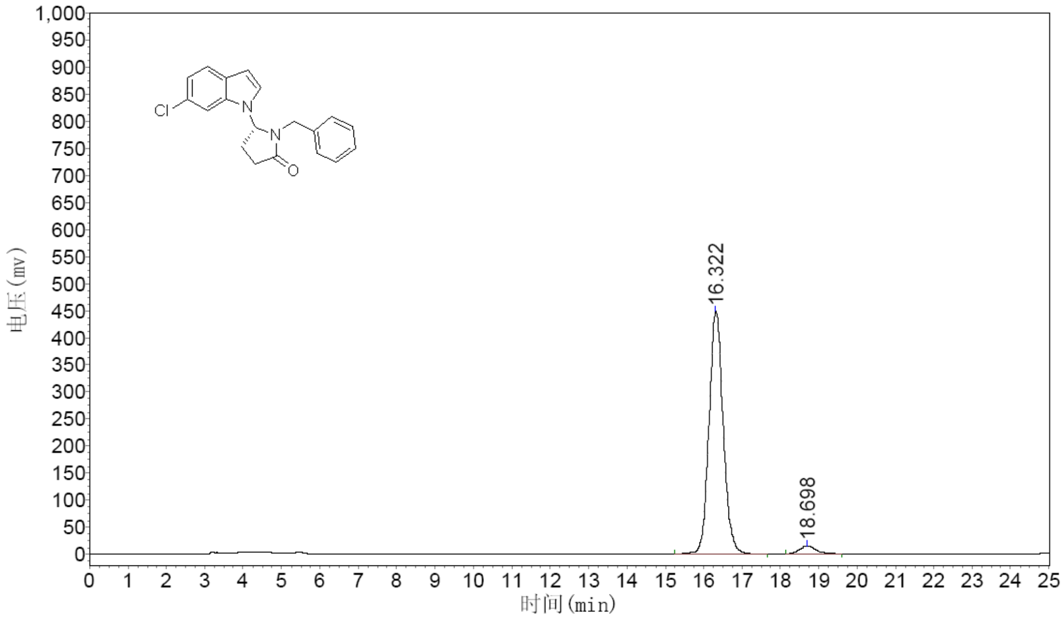
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	10. 442	105789. 547	1724715. 750	49. 7218
2	11. 323	98232. 039	1744014. 125	50. 2782
Total		204021. 586	3468729. 875	100. 0000



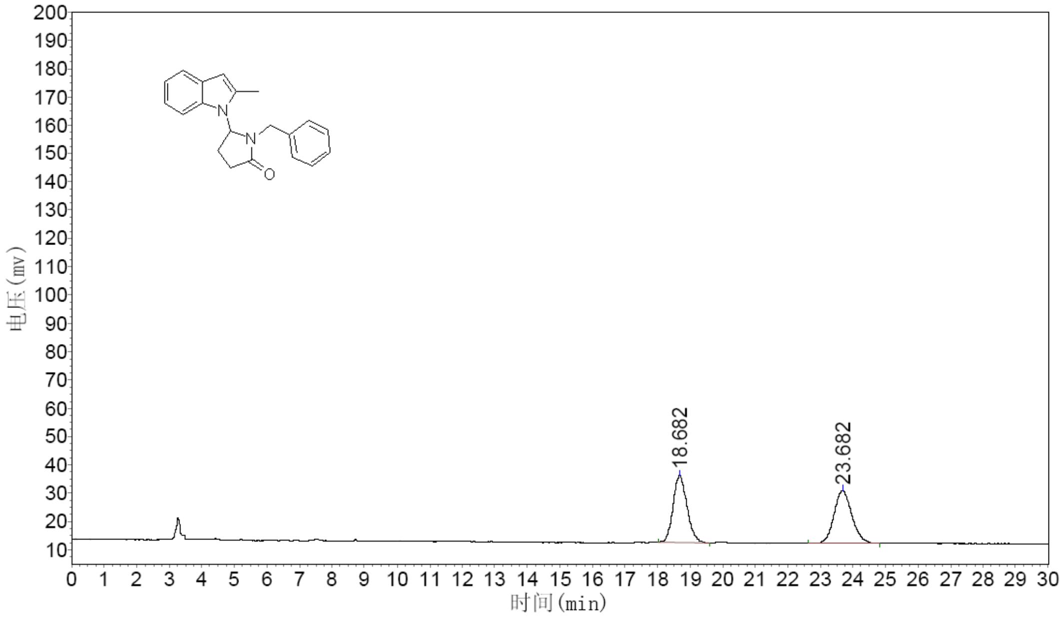
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	10. 425	1068083. 750	17293008. 000	94. 8127
2	11. 333	52901. 547	946110. 250	5. 1873
Total		1120985. 297	18239118. 250	100. 0000



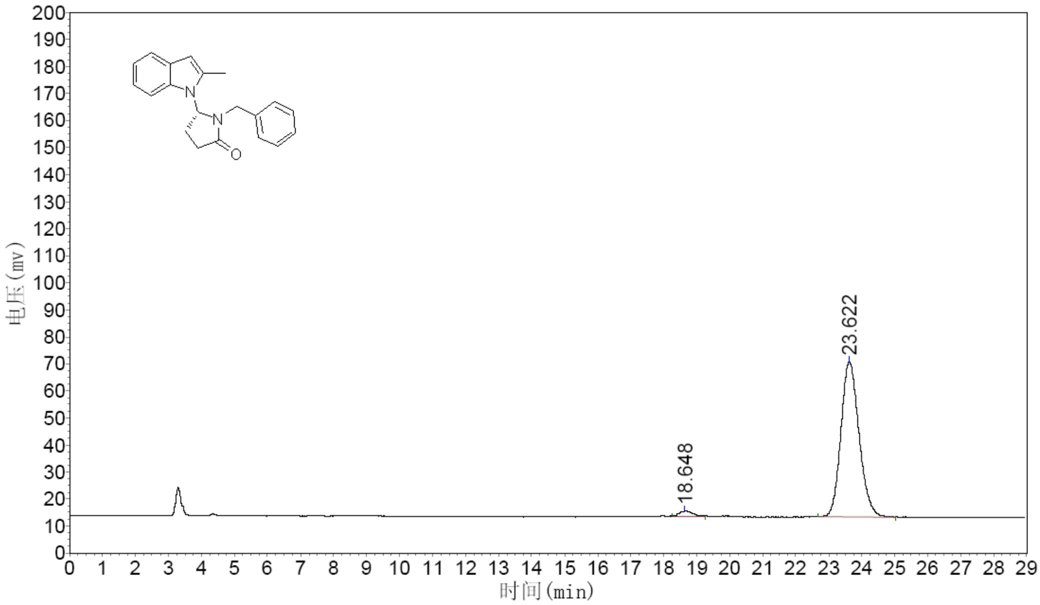
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	16. 735	413272. 656	10126263. 000	49. 2261
2	19. 130	373819. 750	10444643. 000	50. 7739
Total		787092. 406	20570906. 000	100. 0000



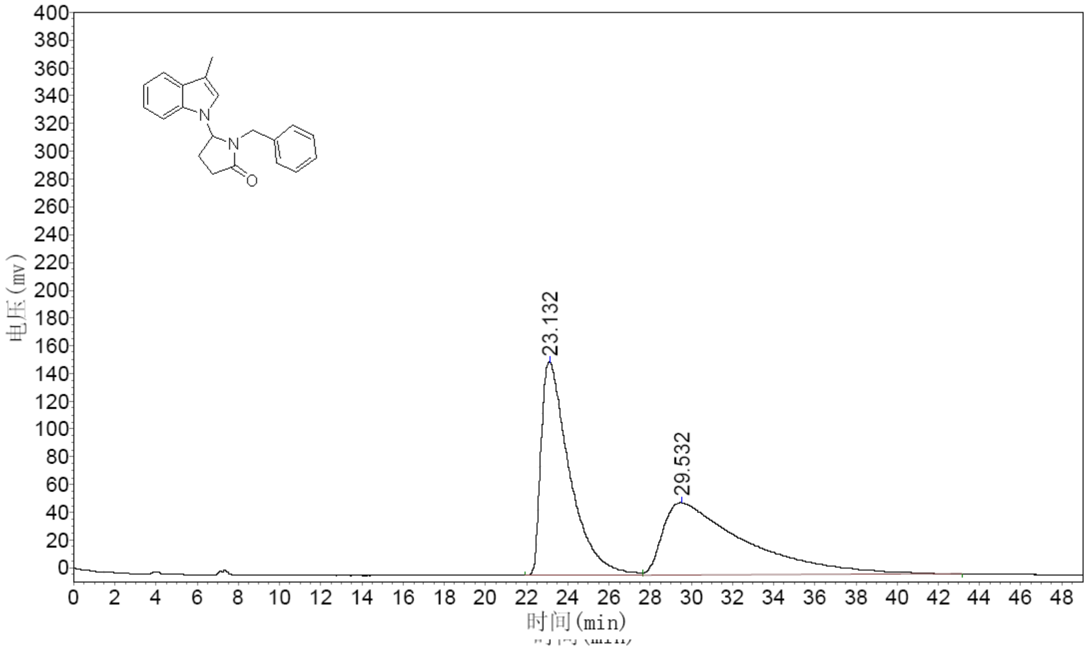
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	16. 322	446545. 344	11402348. 000	96. 5969
2	18. 698	14294. 431	401697. 750	3. 4031
Total		460839. 774	11804045. 750	100. 0000



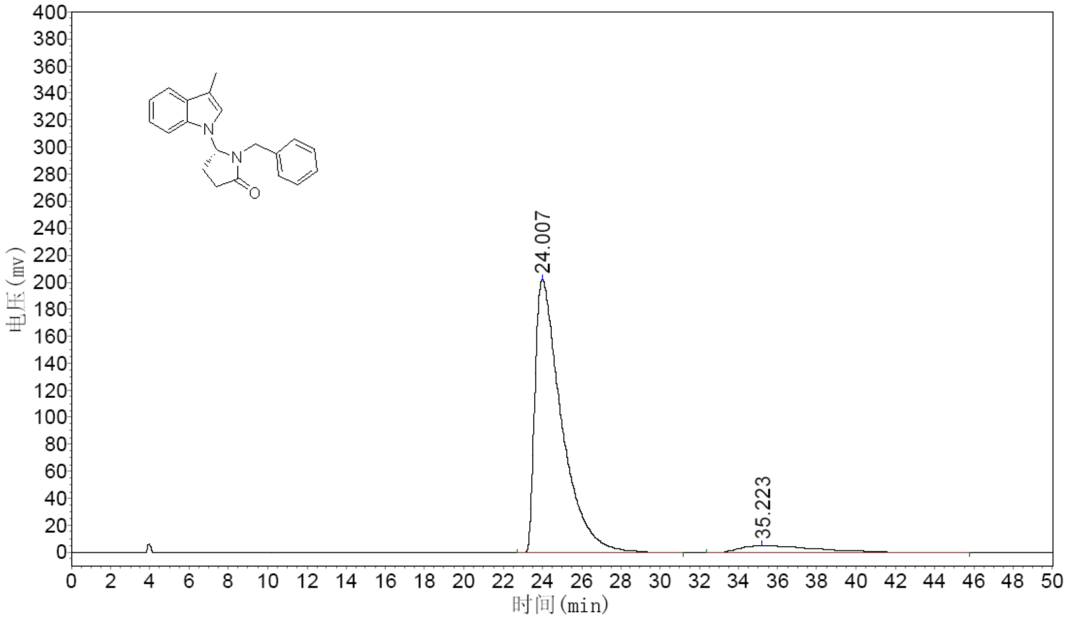
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	18. 682	23587. 672	707969. 938	49. 7014
2	23. 682	18678. 090	716476. 625	50. 2986
Total		42265. 762	1424446. 563	100. 0000



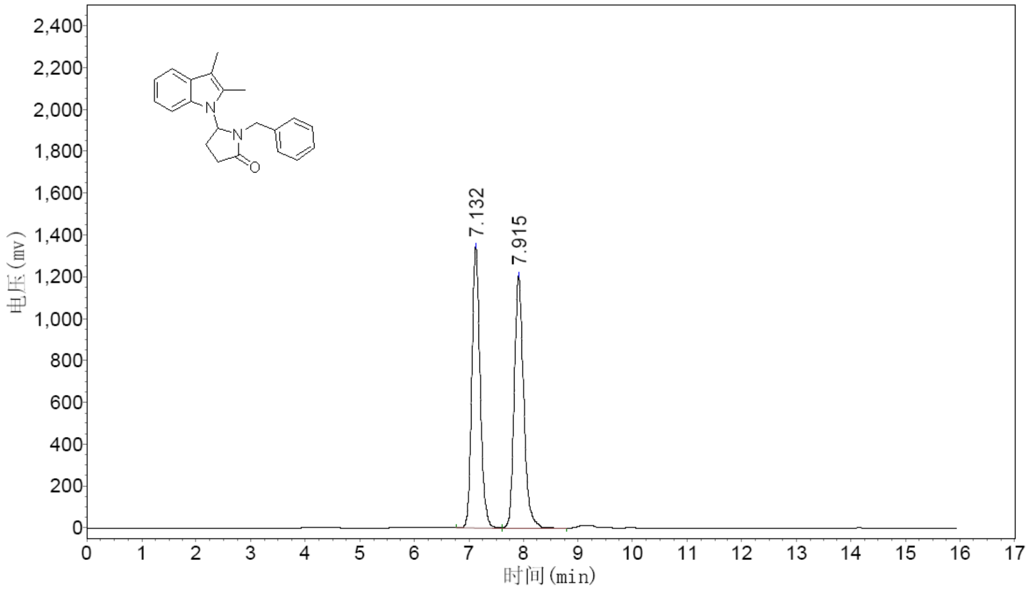
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	18. 648	1928. 792	53261. 691	2. 3793
2	23. 622	57314. 895	2185278. 500	97. 6207
Total		59243. 687	2238540. 191	100. 0000



PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	23. 132	153642. 109	14820001. 000	49. 9567
2	29. 532	52119. 984	14845718. 000	50. 0433
Total		205762. 094	29665719. 000	100. 0000

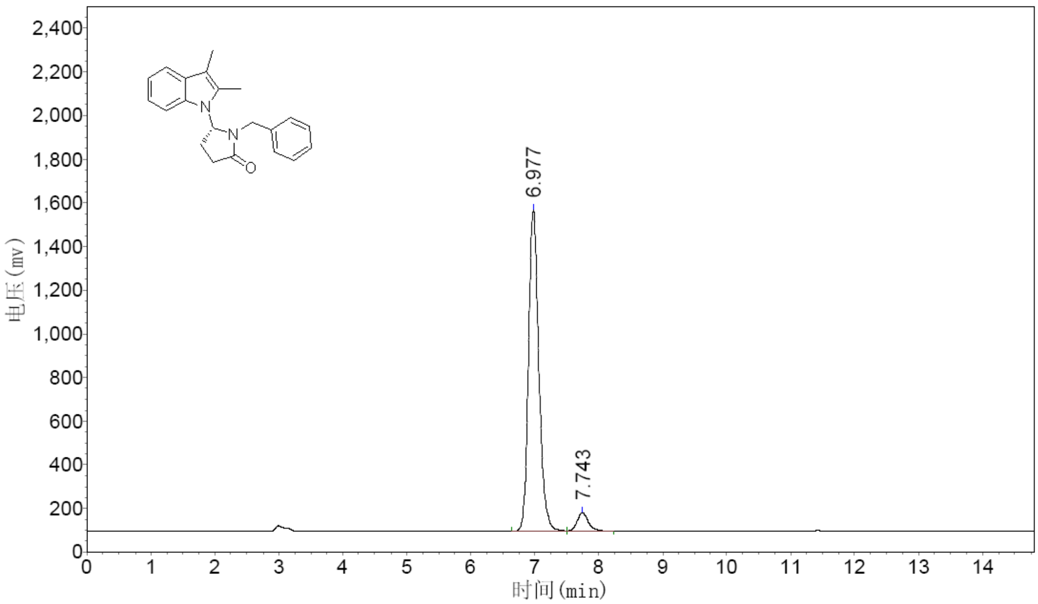


PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	24. 007	202406. 531	19204228. 000	92. 2946
2	35. 223	5498. 350	1603293. 500	7. 7054
Total		207904. 881	20807521. 500	100. 0000

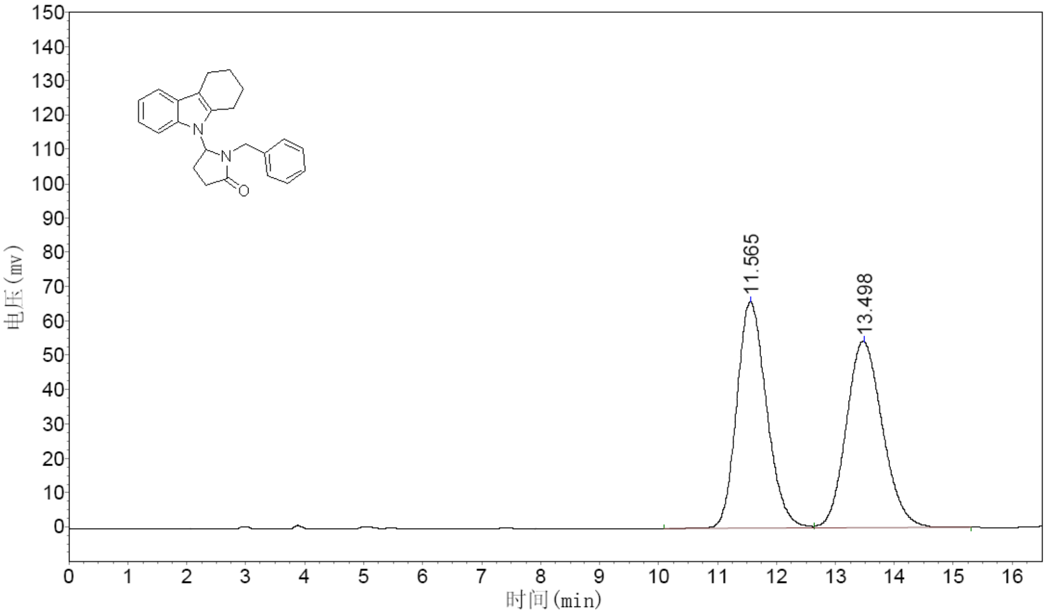


时间(min)

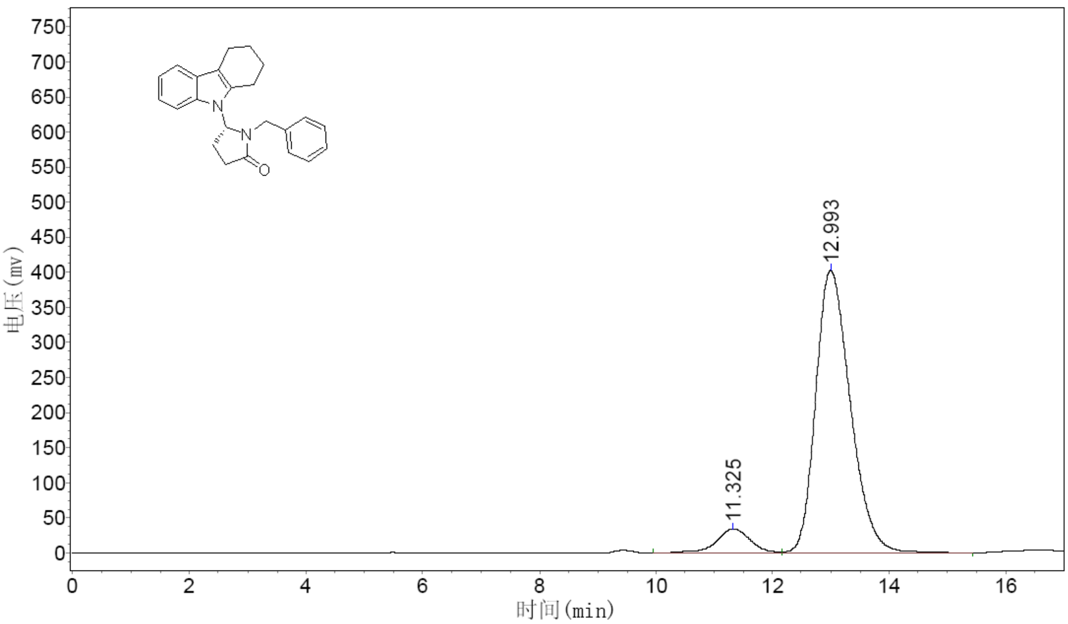
PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	7.132	1342126.500	14265561.000	49.4600
2	7.915	1203448.375	14577088.000	50.5400
Total		2545574.875	28842649.000	100.0000



PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	7.010	861599.375	8952446.000	94.2979
2	7.777	46750.176	541340.938	5.7021
Total		908349.551	9493786.938	100.0000



PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	11. 565	65910. 055	2328262. 000	50. 0113
2	13. 498	54349. 348	2327212. 000	49. 9887
Total		120259. 402	4655474. 000	100. 0000



PeakNo	R. Time	PeakHeight	PeakArea	PerCent
1	11. 325	34248. 852	1344506. 875	7. 5331
2	12. 993	402886. 500	16503517. 000	92. 4669
Total		437135. 352	17848023. 875	100. 0000