Supplementary Materials for

Merging DNA repair with bioorthogonal conjugation enables accessible and superior asymmetric DNA catalysis

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General Information

Synthesis and Chemicals

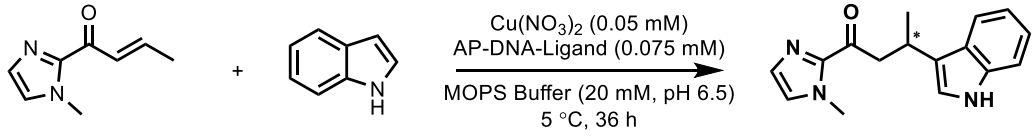
All chemicals were purchased from Sigma-Aldrich, TCI chemicals and BLD Pharm and used without further purification. All reagents were weighed and handled in air. *E. coli* Uracil DNA Glycosylase (UDG) was purchased from New England Biolabs. All oligonucleotides were purchased from Integrated DNA Technologies (IDT) with standard desalting purification and used without further purification.

Analytical Methods

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz spectrometer (400 MHz for ^{1}H; 101 MHz for ^{13}C) or Bruker 500 MHz spectrometer (500 MHz for ^{1}H; 126 MHz for ^{13}C) in $CDCl_3$ unless otherwise noted. Signal positions were recorded in ppm with the abbreviations s, d, t, dd, dt, tt and m denoting singlet, doublet, triplet, doublet of doublets, doublet of triplets, triplets of triplets and multiplet respectively. All NMR chemical shifts were referenced to residual solvent peaks or to $Si(CH_3)_4$ as an internal standard. For ^{1}H NMR: $CDCl_3$ = δ 7.26 ppm. For ^{13}C NMR: $CDCl_3$ = δ 77.00 ppm. High-resolution mass spectrometric data was obtained using 6546 LC-QTOF (Agilent). Oligonucleotide mass spectra were acquired by MALDI-TOF using a JEOL SpiralTOF JMS-S3000 in negative ion mode or by ESI on a Thermo Scientific LCQ Fleet LCMS. GC-MS analysis was performed on an Aglient 7890 GC/MS gas chromatograph mass spectrometer. Oligonucleotide concentrations were determined by UV-absorption on a Nano-Drop One Microvolume UV-Vis Spectrophotometer (Thermo Fisher Scientific). Organic solutions were concentrated under reduced pressure on IKA rotary evaporator. Analytical TLC was performed on ready-to-use plates with silica gel 60 (Merck, F254), Flash column chromatography was performed over Fisher Scientific silica gel (grade 60, 230-400 mesh). Preparative TLC was performed on silica gel Xinnuo $HSGF_{254}$ preparative TLC plates. Silica gel (200–300 mesh) was purchased from Qingdao Haiyang Chemical Co., China.

Optimization of Reaction Conditions

Table S1. Evaluation of the AP DNA-Ligands



1a: 1 mM **2**: 5 mM **3a**

entry	Ligand	SM (%)	3a (%)	ee (%)
1	L1	0	99	80
2	L2	0	99	78
3	L3	0	99	30
4	L4	0	99	38

Conversion and ee were determined by HPLC; DNA sequence: 5'-CGC**U**GAGGAACTCCGCG-3'

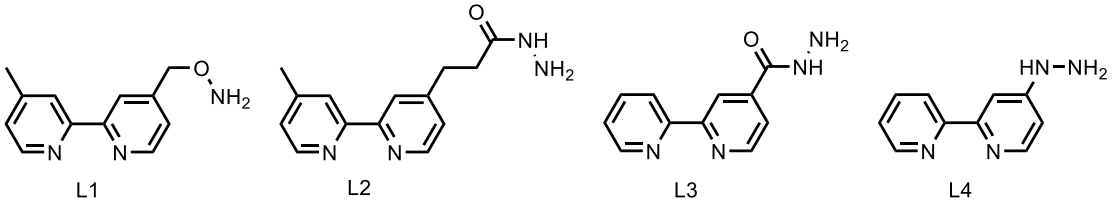
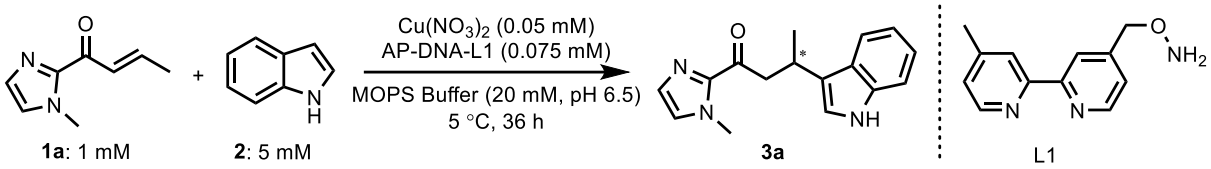


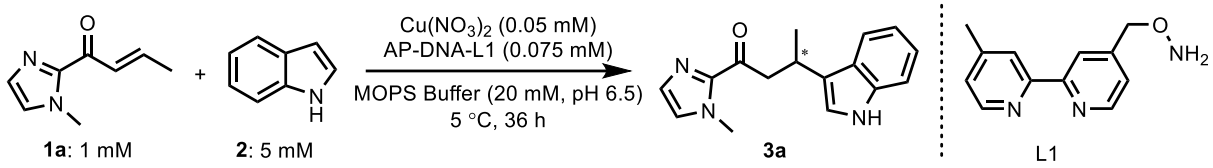
Table S2. Evaluation of the opposite bases



entry	DNA sequence	SM (%)	3a (%)	ee (%)
1	5'-CGC**U**GAGGAACTC**C**GCG-3'	0	99	79
2	5'-CGC**U**GAGGAACTC**A**GCG-3'	0	99	75
3	5'-CGC**U**GAGGAACTC**G**GCG-3'	0	99	67
4	5'-CGC**U**GAGGAACTC**T**GCG-3'	0	99	82

Conversion and ee were determined by HPLC

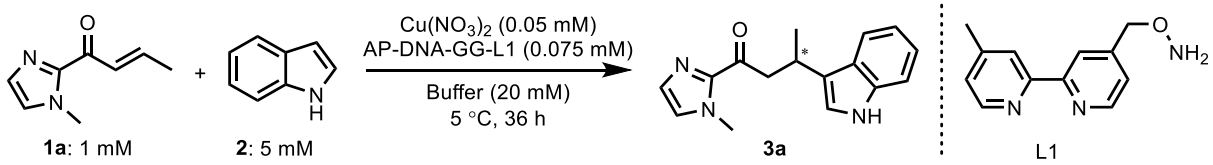
Table S3. Evaluation of the neighboring base pairs



entry	DNA sequence	3a (%)	ee (%)
1	5'-CGTUTAGGAACTATACG-3'	99	77
2	5'-CGGUTAGGAACTATCCG-3'	99	29
3	5'-CGGUCAGGAACTGTCCG-3'	99	80
4	5'-CGTUAAGGAACTTTACG-3'	99	49
5	5'-CGGUAAGGAACTTTCCG-3'	99	14
6	5'-CGTUGAGGAACTCTACG-3'	99	88
7	5'-CGGUGAGGAACTCTCCG-3'	99	92
8	5'-CGAUCAGGAACTGTTCG-3'	99	47
9	5'-CGAUAAGGAACTTTTCG-3'	99	51
10	5'-CGCUCAGGAACTGTGCG-3'	99	40
11	5'-CGCUTAGGAACTATGCG-3'	99	59
12	5'-CGTUCAGGAACTGTACG-3'	99	24
13	5'-CGCUAAGGAACTTTGCG-3'	99	46
14	5'-CGAUTAGGAACTATTCG-3'	99	59
15	5'-CGAUGAGGAACTCTTCG-3'	99	88

Conversion and ee were determined by HPLC

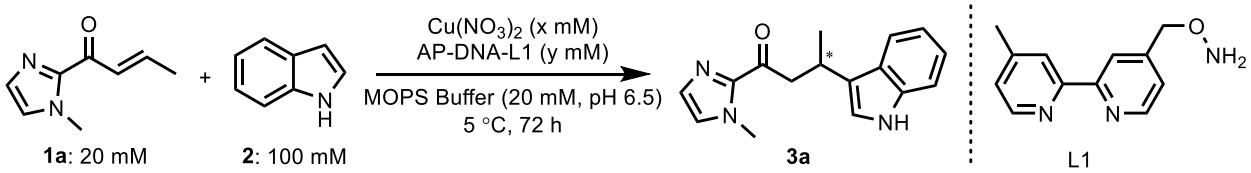
Table S4. Evaluation of buffer



entry	Buffer	3a (%)	ee (%)
1	MOPS (pH 6.5)	99	94
2	MES (pH 6.5)	99	92
3	Borate (pH 9.5)	99	91
4	TEAA (pH 7.0)	99	91
5	TB (pH 8.0)	99	90
6	PB (pH 7.5)	99	92
7	Tris (pH 6.8)	99	92
8	Tris (pH 8.0)	99	93
9	PBS (pH 6.5-6.9)	99	92
10	TBS (pH 7.2-7.6)	99	93
11[a]	MOPS (pH 6.5)	99	85
12[a]	MES (pH 6.5)	99	85

Conversion and ee were determined by HPLC; AP-DNA-GG sequence: 5'-CGGUGAGGAACTCTCCG-3'
[a] Reaction was performed at 37 °C

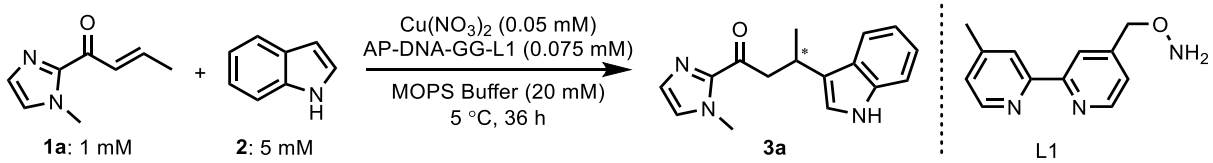
Table S5. Evaluation of the catalyst loadings



entry	[Cu] (x mM)	AP-DNA-L1 (y mM)	SM (%)	3a (%)	ee (%)
1	0.04	0.06	0	99	93
2	0.02	0.03	0	99	92
3	0.008	0.012	0	99	94

Conversion and ee were determined by HPLC; DNA sequence: 5'-CGGUGAGGAACTCTCCG-3'

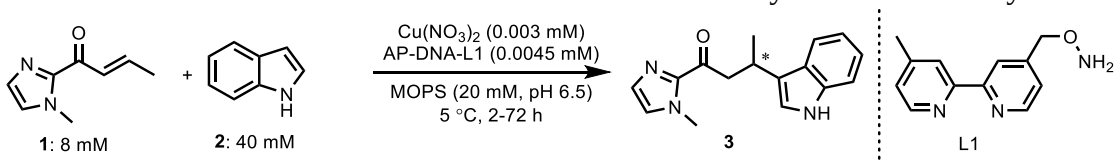
Table S6. Control experiments



entry	Variation from standard conditon	3a (%)	ee (%)
1	None	99	94
2	[Cu]/DNA was added in 2.5 mol%	99	93
3	[Cu]/DNA was added in 1.0 mol%	99	94
4	[Cu]/DNA was added in 0.5 mol%	94	92
5	[Cu]/DNA was added in 0.1 mol%	85	93
6	[Cu] was not added	0	–
7	AP DNA-GG-L1 was not added	67	2
8	dmbpy instead of AP DNA-GG-L1	99	1

Conversion and ee were determined by HPLC; Ratio of [Cu]/DNA was 1:1.5; AP-DNA-GG sequence: 5'-CG**G**U**G**AGGAACT**C**T**C**CG-3'

Table S7. Effects on reaction rate and enantioselectivity of different catalysts



entry	Variation from standard condition
1	none
2	st-DNA/dmbpy instead of AP-DNA-L1
3	Hairpin DNA/dmbpy instead of AP-DNA-L1
4	Hairpin DNA-CHO/dmbpy instead of AP-DNA-L1
5	dmbpy instead of AP-DNA-L1
6	AP-DNA-L1 was not added
7	AP-DNA-GC-L1 was used
8	AP-DNA-GA-L1 was used
9	AP-DNA-CT-L1 was used

Conversion and *ee* were determined by HPLC; AP-DNA-GG sequence: 5'-CG**G**U**G**AGGAACT**C**T**C**CG-3'

Reaction time	Entry 1		Entry 2		Entry 3		Entry 4		Entry 5		Entry 6		Entry 7		Entry 8		Entry 9	
	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**	Yield(%)	**ee(%)**
2h	12	**92**	0	**/**	0	**/**	1	**/**	0	**/**	0	**/**	7	**80**	6	**10**	5	**60**
4h	30	**92**	3	**43**	6	**37**	6	**85**	1	**0**	2	**3**	17	**85**	19	**8**	19	**59**
6h	42	**90**	4	**53**	8	**34**	19	**85**	1	**0**	2	**7**	31	**80**	30	**9**	23	**57**
8h	49	**91**	11	**65**	19	**40**	23	**83**	4	**0**	5	**7**	43	**81**	45	**11**	40	**53**
10h	56	**89**	18	**60**	23	**49**	27	**85**	5	**5**	5	**3**	50	**83**	50	**11**	50	**59**
12h	65	**89**	20	**47**	27	**55**	35	**80**	10	**11**	12	**5**	63	**79**	59	**10**	64	**57**
15h	74	**89**	23	**30**	27	**30**	46	**76**	16	**9**	18	**6**	67	**83**	62	**9**	70	**56**
18h	79	**90**	25	**38**	28	**29**	50	**73**	18	**3**	19	**2**	75	**81**	70	**9**	73	**57**
21h	81	**91**	31	**30**	28	**35**	57	**85**	19	**10**	20	**8**	81	**81**	83	**11**	82	**61**
24h	83	**91**	36	**48**	36	**43**	64	**85**	25	**13**	23	**3**	82	**83**	85	**12**	85	**60**
30h	87	**91**	44	**50**	49	**43**	69	**73**	30	**9**	29	**3**	88	**83**	88	**12**	88	**59**
36h	92	**90**	51	**49**	55	**35**	73	**71**	35	**15**	33	**3**	90	**81**	93	**11**	93	**59**
42h	93	**91**	57	**45**	63	**45**	79	**75**	43	**1**	44	**3**	95	**83**	95	**12**	94	**59**
48h	96	**92**	60	**49**	67	**39**	80	**72**	50	**3**	53	**4**	95	**83**	97	**12**	95	**59**
60h	98	**92**	65	**47**	71	**41**	81	**69**	55	**5**	61	**3**	97	**81**	98	**10**	95	**58**
72h	99	**91**	80	**49**	83	**45**	86	**71**	60	**2**	70	**1**	99	**83**	99	**11**	98	**59**

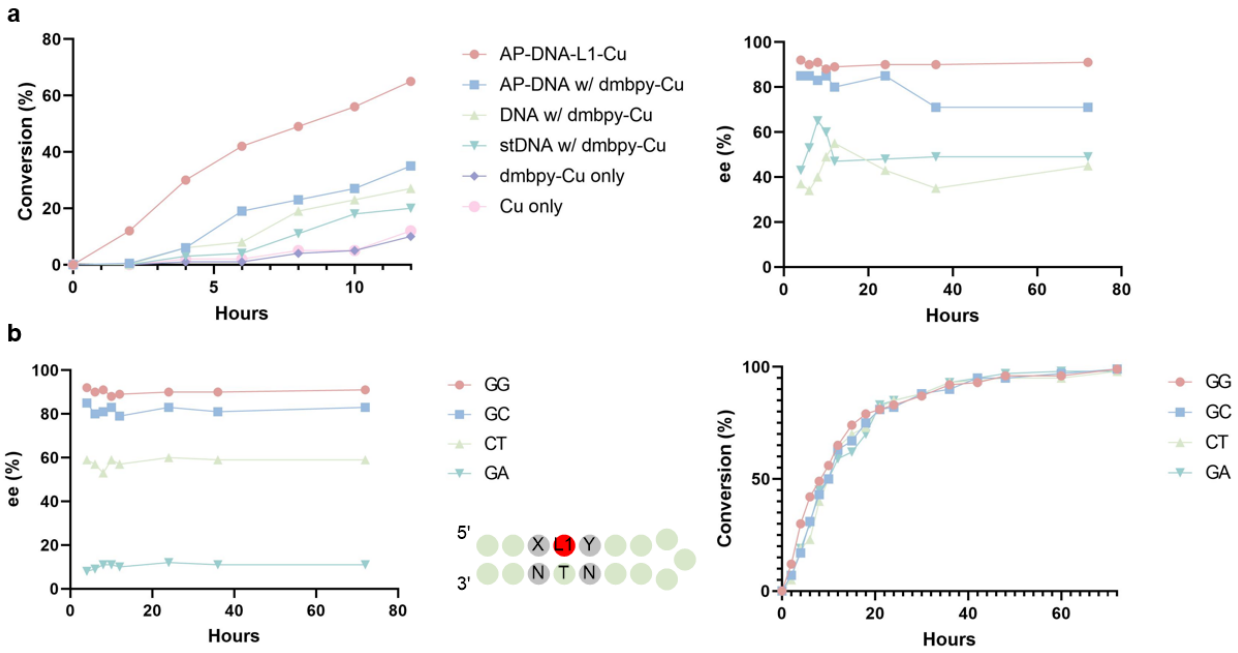
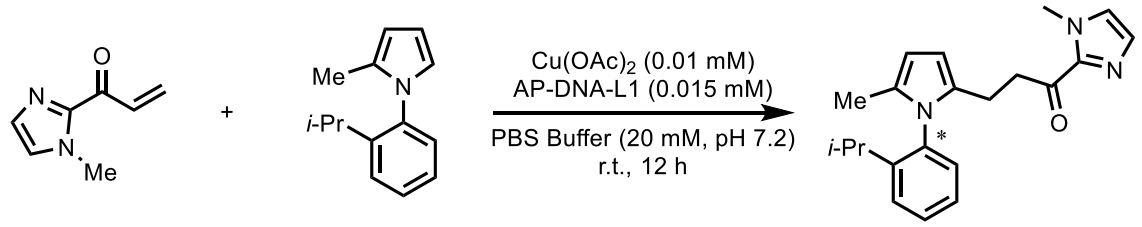


Figure S1. (a) Effects on reaction rate and enantioselectivity of different catalysts. (b) Neighboring sequence on reaction rate.

Table S8. Effects on reaction rate and enantioselectivity of different catalysts



7: 1 mM **8a**: 5 mM **9a**

entry	DNA sequence	9a (%)	ee (%)
1	5'-CG**T**U**T**AGGAACT**A**T**A**CG-3'	99	76
2	5'-CG**G**U**T**AGGAACT**A**T**C**CG-3'	99	-25
3	5'-CG**G**U**C**AGGAACT**G**T**C**CG-3'	99	-29
4	5'-CG**T**U**A**AGGAACT**T**T**A**CG-3'	99	-26
5	5'-CG**G**U**A**AGGAACT**T**T**C**CG-3'	99	45
6	5'-CG**T**U**G**AGGAACT**C**T**A**CG-3'	99	52
7	5'-CG**G**U**G**AGGAACT**C**T**C**CG-3'	99	-65
8	5'-CG**A**U**C**AGGAACT**G**T**T**CG-3'	99	-18
9	5'-CG**A**U**A**AGGAACT**T**T**T**CG-3'	99	10
10	5'-CG**C**U**C**AGGAACT**G**T**G**CG-3'	99	6
11	5'-CG**C**U**T**AGGAACT**A**T**G**CG-3'	99	-35
12	5'-CG**T**U**C**AGGAACT**G**T**A**CG-3'	99	-6
13	5'-CG**C**U**A**AGGAACT**T**T**G**CG-3'	99	4
14	5'-CG**A**U**T**AGGAACT**A**T**T**CG-3'	99	-13
15	5'-CG**A**U**G**AGGAACT**C**T**T**CG-3'	99	33
16	5'-CG**C**U**G**AGGAACT**C**T**G**CG-3'	99	39

Conversion and *ee* were determined by HPLC

Preparation of Materials

Racemic Friedel-Crafts alkylation with indole or pyrrole

An oven-dried 3 ml vial was charged with $Cu(NO_3)_2 \cdot 3H_2O$ (0.1 equiv.) or $Sc(OTf)_3$ (0.1 equiv. for for products **4a-f**) and 4,4'-dimethyl-2,2'-bipyridyl (dmbpy, 0.12 equiv.) and acetonitrile (1.00 mL). The mixture was stirred at room temperature for 10 min then the α,β-unsaturated substrate[1] (0.1 mmol, 1.00 equiv.) and indole (2.00 equiv.) were added. The solution was stirred at room temperature until completion of the reaction (monitored by TLC). The solvent was evaporated, and the crude product was purified by flash column chromatography over silica gel.

Racemic Friedel-Crafts alkylation with N-aryl pyrrole

An oven-dried 3 ml vial was charged with $Sc(OTf)_3$ (0.1 equiv.) and 4,4'-dimethyl-2,2'-bipyridyl (dmbpy, 0.12 equiv.) and acetonitrile (1.00 mL). The mixture was stirred at room temperature for 10 min then the α,β-unsaturated substrate **7**[2] (0.1 mmol, 1.00 equiv.) and N-Ar-Pyrrole[3] (2.00 equiv.) were added. The solution was stirred at room temperature until completion of the reaction (monitored by TLC). The solvent was evaporated, and the crude product was purified by flash column chromatography over silica gel.

General procedure for the preparation of DNA AP site[4]

A dU-containing oligonucleotide (100 μM) was dissolved in 50 mM Tris pH 7.0. The DNA solution was heated at 95 °C for 5 min and cooled to room temperature. The solution was then treated with *E. Coli* UDG (50 U/mL) for 0.5 h at 37 °C. The generated AP site-containing DNA was directly proceeded to next step without purification.

General procedure for the preparation of DNA hybrid catalysts[4]

To a solution of AP site-containing oligonucleotide (50 μM) was added ligands (L1-L16, 1000 μM) and incubated at room temperature overnight. The conjugate was then purified by ethanol precipitation by adding 0.1x (v:v) of 3 M NaOAc (pH 5.2) and 3.75x (v:v) of absolute EtOH. The mixture was incubated at -80 °C for 3 h, and the conjugate pellet was obtained by centrifuging (21,000 RCF) for 1 h at 4 °C. The supernatant was removed, and the pellet was washed 3 times with 75% EtOH and centrifuged (21,000 RCF) for 10 min at 4 °C. The supernatant was removed, and the pellet was dried in air for 0.5 h. The conjugate was dissolved in nuclease-free water and stored at -80 °C for further analysis. The concentration was determined by Nano-Drop.

Preparation of a 100 mM stock solution of MOPS buffer (pH 6.5)

3-(N-morpholino) propane sulfonic acid (2.09 g, 10.0 mmol) was dissolved in nuclease-free H_2O (80.0 mL). The pH was adjusted to 6.5 using an aqueous solution of NaOH (C = 0.10 M, MW = 39.40 g/mol). To the resulting solution was added a given volume of nuclease-free H_2O to obtain a 100 mM concentration.

Preparation of a 100 mM stock solution of MES buffer (pH 5.0)

2-(N-morpholino) ethane sulfonic acid (1.95 g, 10.0 mmol) was dissolved in nuclease-free H_2O (80.0 mL). The pH was adjusted to 5.0 using an aqueous solution of NaOH (C = 0.10 M, MW = 39.40 g/mol). To the resulting solution was added a given volume of nuclease-free H_2O to obtain a 100 mM concentration.

General procedure for the enantioselective Friedel-Crafts reactions

The solution of hairpin DNA-Ligand (~300 μM, 3.75 nmol, 0.0375 equiv.) and nuclease-free H_2O were successively added to a 1.5 mL Eppendorf® safe-lock tube. MOPS buffer solution (20.0 μL,

100 mM in nuclease-free H_2O, pH 6.5) or MES buffer solution (20.0 μL, 100 mM in nuclease-free H_2O, pH 5.0) and $Cu(NO_3)_2$, $Sc(OTf)_3$ (for products **4a-f**), or $Cu(OAc)_2$ (for products **9a-m**) solution (2.5 μL, 1.00 mM in nuclease-free H_2O, 0.025 equiv.) were then added. The resulting mixture was stirred at room temperature for 30 min and frozen at −20 °C for 30 min. The Eppendorf® safe-lock tube was brought into the cold room and the desired enone (2.00 μL, 0.05 M in DMSO, 100 nmol, 1.00 equiv.) and indole (2.00 μL, 0.25 M in DMSO, 500 nmol, 5.00 equiv.) were finally added. The resulting solution was stirred at 5 °C for 36 h or -5 °C for 60 h (for products **3h**, **3k**, **3m**, **3n**, **3o**, **3r**, **3s**, **3t**, **3u**, **3ab**, **3ac**, **3ad**, **4a-f**, and **6i**) on a thermos shaker placed in a cold room. The mixture was then transferred into another 1.5 mL Eppendorf® safe-lock tube. The reaction was diluted with H_2O (200 μL) and extracted with ethyl acetate (three times). The combined organic layers were dried over anhydrous Na_2SO_4, syringe-filtered and concentrated under reduced pressure using Eppendorf® Concentrator plus. After evaporation of ethyl acetate, the sample was dissolved in *n*-Hexane/*i*-PrOH (50 μL/50 μL) subjected to HPLC analysis for conversion and enantiomeric excess data.

List of oligonucleotides

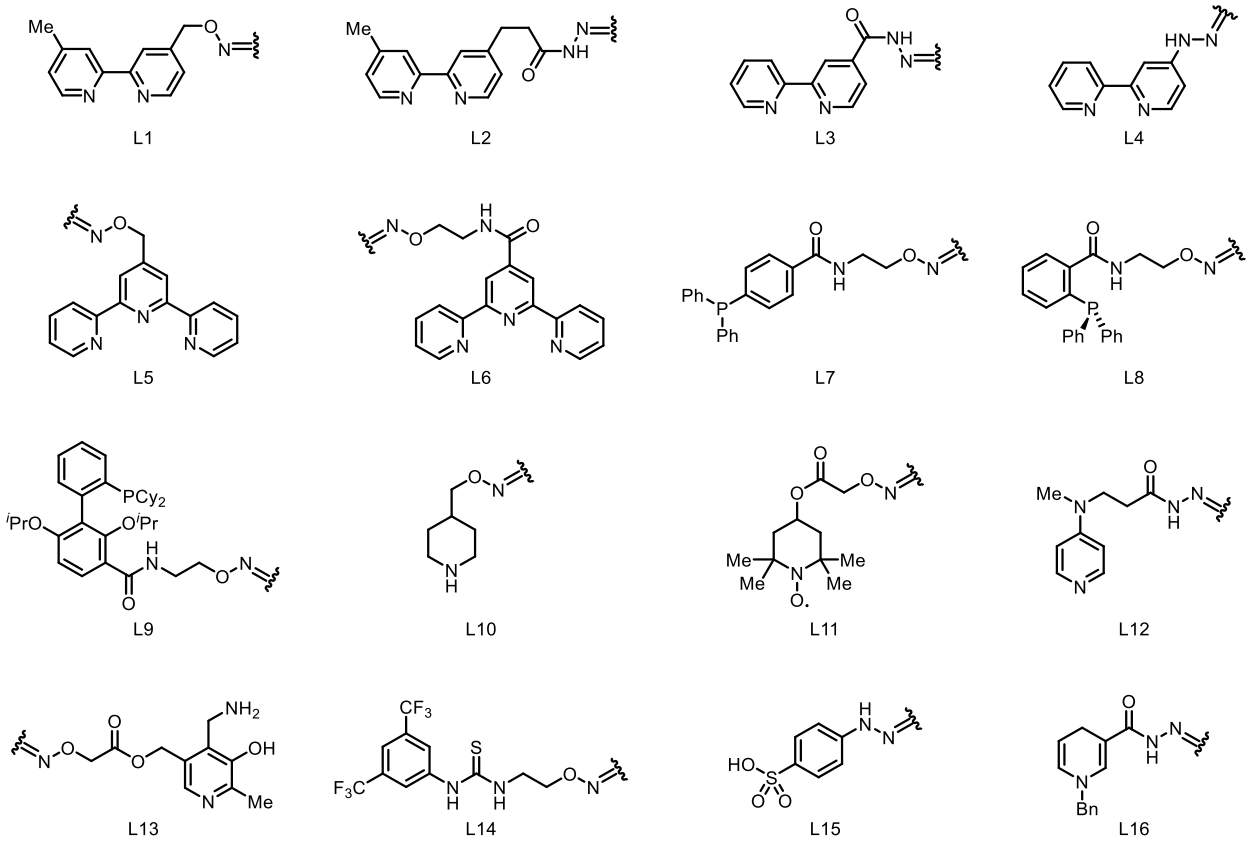
All oligonucleotides were purchased from Integrated DNA Technologies (IDT) with standard desalting purification and used without further purification.

Table S9. List of oligonucleotides.

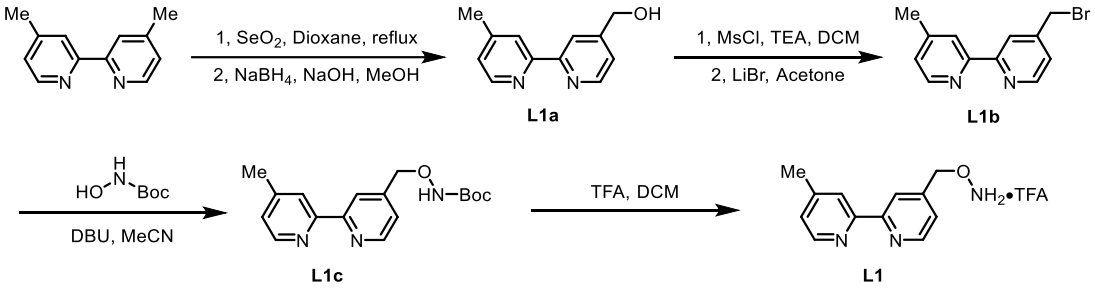
Oligo	Name	Sequence (5'→3')
1	hp-CG DNA (oppo A)	CGC UGA GGA ACT CAG CG
2	hp-CG DNA (oppo T)	CGC UGA GGA ACT CTG CG
3	hp-CG DNA (oppo G)	CGC UGA GGA ACT CGG CG
4	hp-CG DNA (oppo C)	CGC UGA GGA ACT CCG CG
5	hp-TT DNA	CGT UTA GGA ACT ATA CG
6	hp-GT DNA	CGG UTA GGA ACT ATC CG
7	hp-GC DNA	CGG UCA GGA ACT GTC CG
8	hp-TA DNA	CGT UAA GGA ACT TTA CG
9	hp-GA DNA	CGG UAA GGA ACT TTC CG
10	hp-TG DNA	CGT UGA GGA ACT CTA CG
11	hp-GG DNA	CGG UGA GGA ACT CTC CG
12	hp-AC DNA	CGA UCA GGA ACT GTT CG
13	hp-AA DNA	CGA UAA GGA ACT TTT CG
14	hp-CC DNA	CGC UCA GGA ACT GTG CG
15	hp-CT DNA	CGC UTA GGA ACT ATG CG
16	hp-TC DNA	CGT UCA GGA ACT GTA CG
17	hp-CA DNA	CGC UAA GGA ACT TTG CG
18	hp-AT DNA	CGA UTA GGA ACT ATT CG
19	hp-AG DNA	CGA UGA GGA ACT CTT CG
20	DNA aptamer-1	CGA CGC CAG UTT GAA GGT TCG TTC GCA GGT GTG GAG TGA CGT CG
21	DNA aptamer-2	CGA CGC CAG TTT GAA GGT TCG TUC GCA GGT GTG GAG TGA CGT CG
22	DNA aptamer-3	CGA CGC CAG TTT GAA GGT TCG TTC GCA GGT GTG GAG UGA CGT CG
23	DNA aptamer-4	CGA CGC CAG TTT GAA GGT TCG TTC GCA GGT GTG GAG TGA CGU CG

Table of ligands

Table S10. Chemical structures of ligands.



Preparation of Ligands



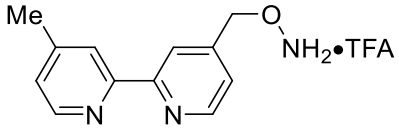
To a stirred suspension of 4,4'-dimethyl-2,2'-bipyridyl (10 mmol) in 1,4-dioxane (100 mL) was added SeO_2 (20 mmol). The solution was refluxed for 48 h under Argon protection. After cooling to room temperature, the mixture was filtered, the solvent was removed in vacuo. The resulting solid was dissolved in chloroform, and the suspension was filtered to remove selenium containing byproducts. After three successive dissolution and filtration treatments, the crude product was obtained. The resulting solid was suspended in methanol (40 mL), and sodium borohydride (10 mmol) in NaOH solution (5 mmol, 5 mL) was added dropwise at 0 °C. The mixture was then stirred at room temperature for 5 h. The reaction was extracted with chloroform and the combined

organic layer was washed with water. The organic layer was concentrated and purified by flash column chromatography (DCM/MeOH/ammonium, 94/5/1) to give the product **L1a** as a white solid.

A flask was charged with **L1a** (10 mmol), methane sulfonyl chloride (12 mmol), and CH_2Cl_2 (30 mL). To this stirring solution was added NEt_3 (12 mmol). Stirring was continued for 1 h, and then LiBr (100 mmol) and acetone (30 mL) were added. The reaction mixture was stirred for an additional 24 h, and then the solvents were removed by rotary evaporation. The contents were partitioned between EtOAc and H_2O, and the EtOAc layer was washed with 0.1M $KHSO_4$ and brine, dried, filtered, evaporated to dryness, and placed under vacuum to give the product **L1b** as a white solid.

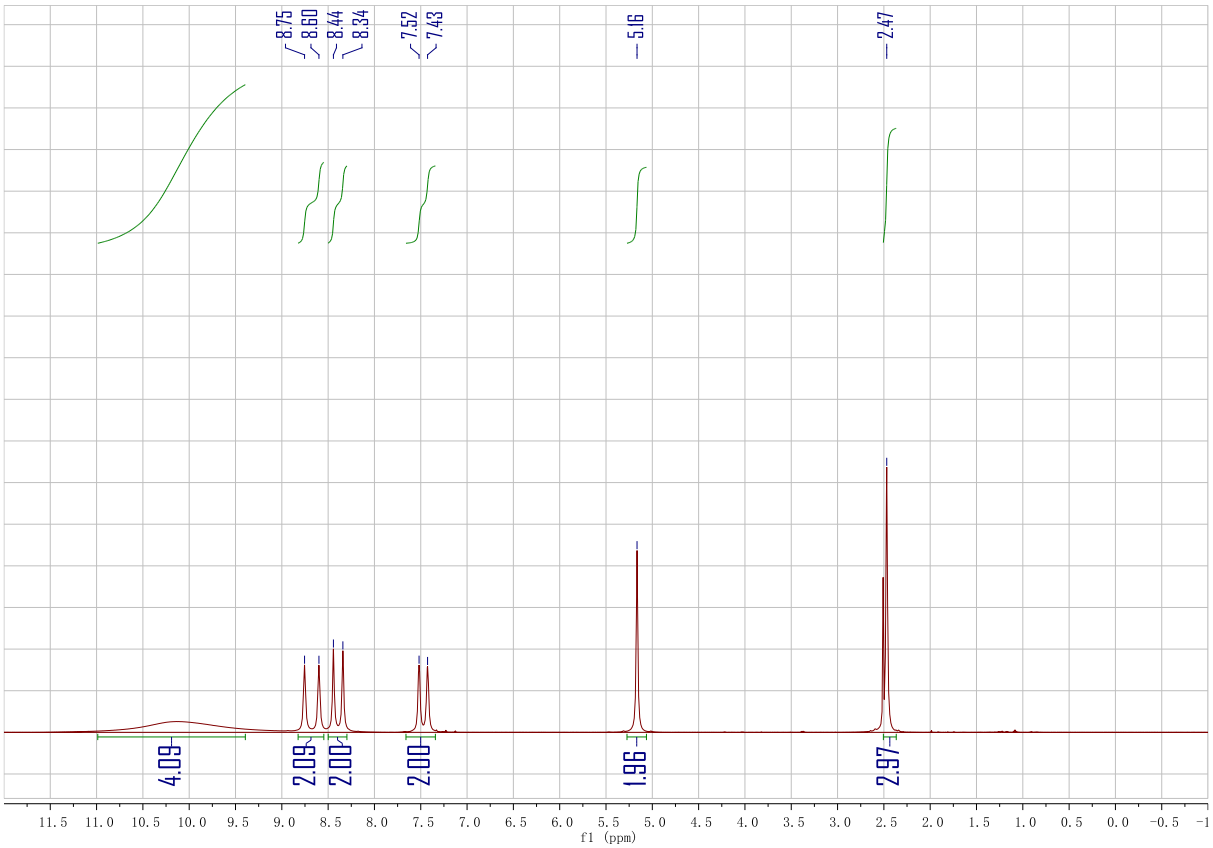
A flask was charged with N-Boc-hydroxylamine (7.5 mmol), DBU (10 mmol), and MeCN (10 mL). To this stirring solution was added **L1b** (5 mmol), and the walls of the flask was rinsed with additional MeCN (5 mL). Stirring was continued for 15 min, and then the solvent was removed by rotary evaporation. The concentrated mixture was stirred for an additional 24 h and then partitioned between EtOAc and water. The EtOAc layer was washed with 0.1 M $KHSO_4$, 0.1 M NaOH and brine, and then dried, filtered, and evaporated. The organic layer was concentrated and purified by flash column chromatography (DCM/MeOH/ammonium, 94/5/1) to give the product **L1c** as a white solid.

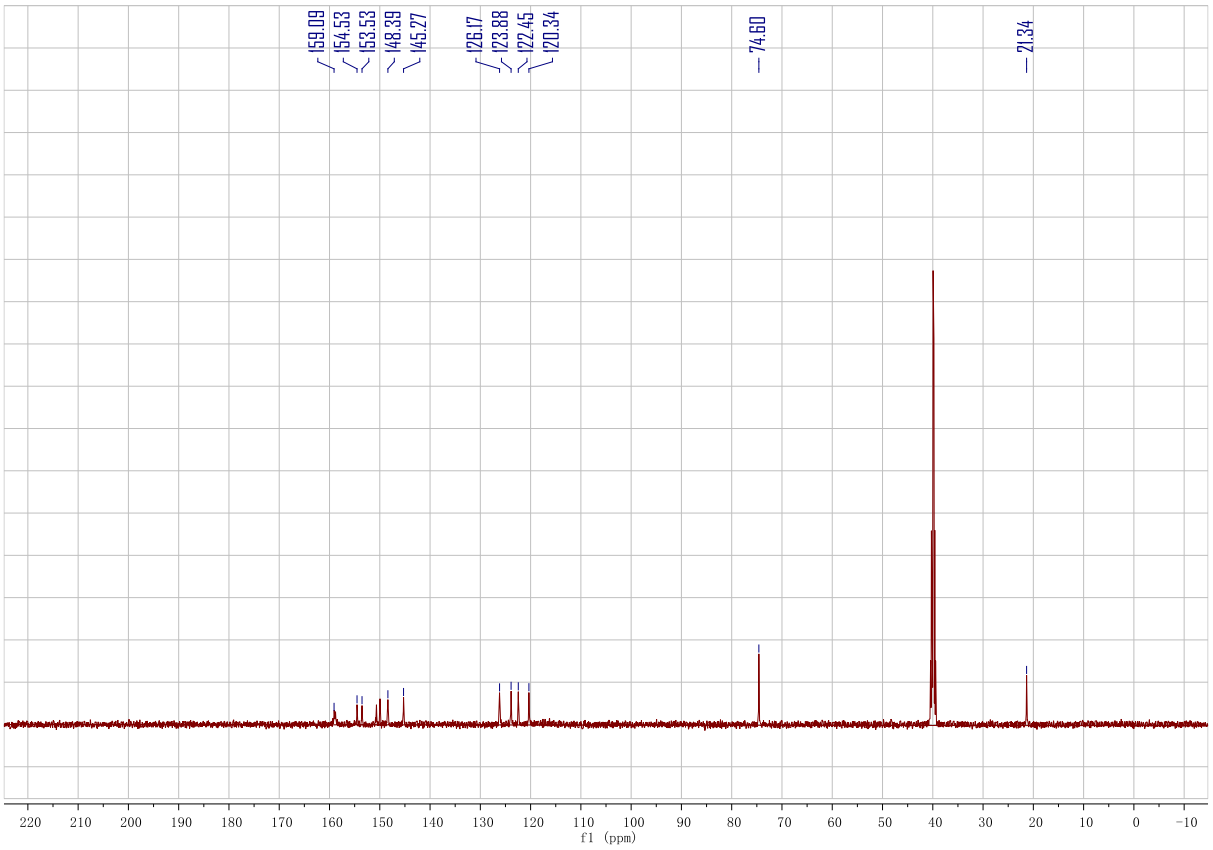
A flask was charged with **L1c** (2 mmol), dry DCM (5 mL) and TFA (5 mL) were added under Argon atmosphere. After 4 hours stirring, the volatiles were removed by rotary evaporation. Remaining TFA was co-evaporated by the addition of 1 mL toluene for three times and dry under vacuum to give the product **L1** as a pink solid.

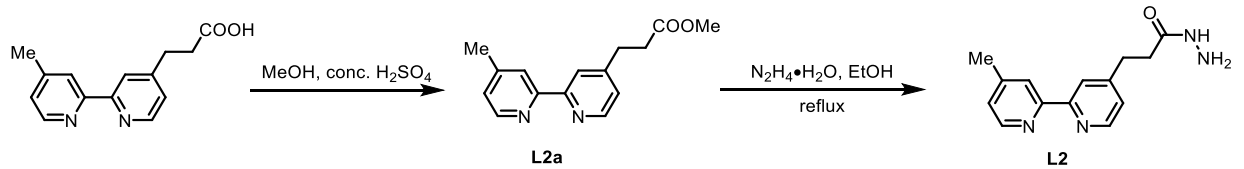


^{1}H NMR (500 MHz, DMSO) δ 10.13 (brs, 4H), 8.68 (d, *J* = 77.7 Hz, 2H), 8.39 (d, *J* = 51.0 Hz, 2H), 7.47 (d, *J* = 46.0 Hz, 2H), 5.16 (s, 2H), 2.47 (s, 3H).

^{13}C NMR (126 MHz, DMSO) δ 159.07 (s), 154.53 (s), 153.53 (s), 150.66 (s), 149.95 (s), 148.39 (s), 145.27 (s), 126.17 (s), 123.88 (s), 122.45 (s), 120.34 (s), 74.60 (s), 21.34 (s).

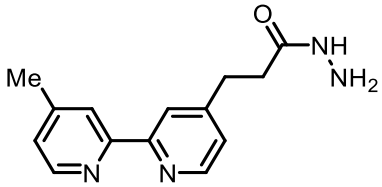

8.75
8.60
8.44
8.34
7.52
7.43
5.16
2.47
4.09
2.09
2.00
2.00
1.96
2.97
f1 (ppm)


159.09
154.53
153.53
148.39
145.27
126.17
123.88
122.45
120.34
74.60
21.34
f1 (ppm)



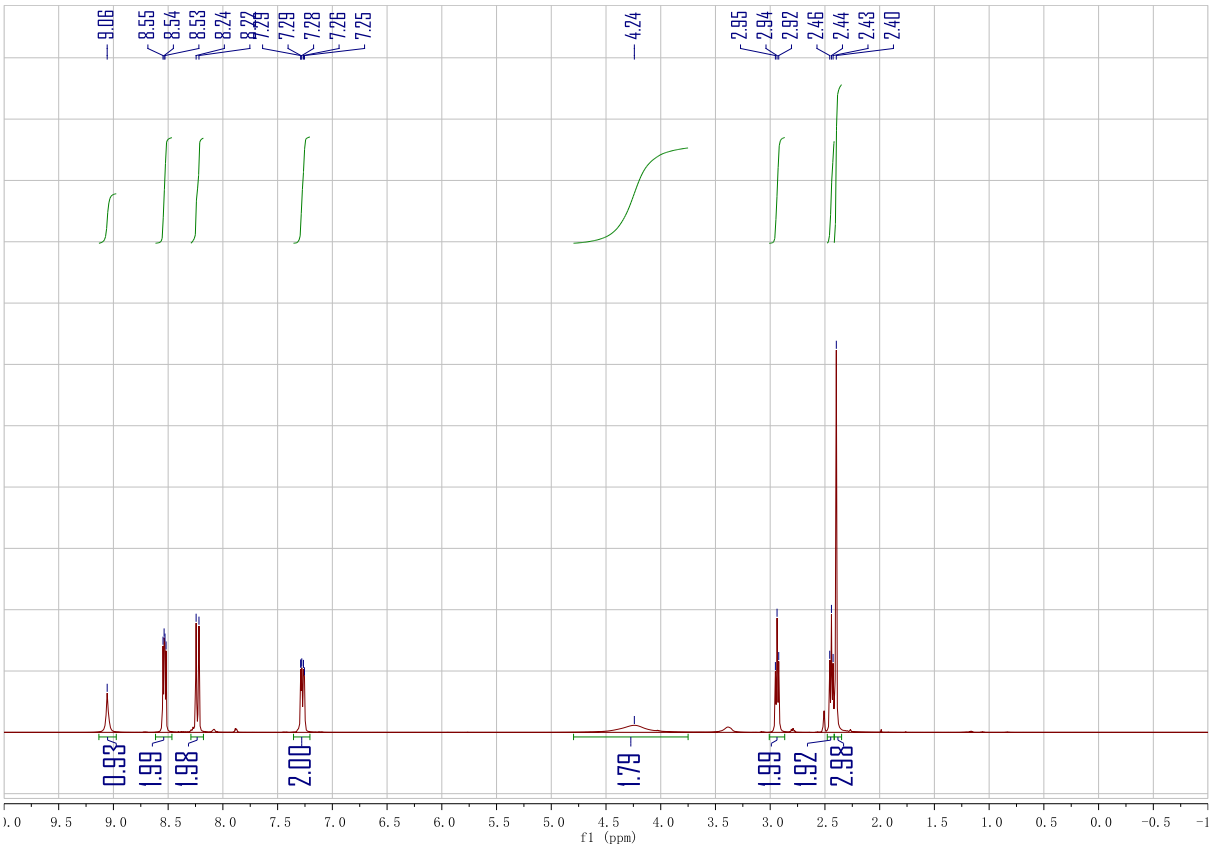
To a stirred mixture of 4,4'-dimethyl-2,2'-bipyridyl[5] (10 mmol) in MeOH (50 mL) was added conc. H_2SO_4 (0.5 mL) slowly. Stirring was continued for 2 hours and then the solvent was partly removed by rotary evaporation. The concentrated mixture was quenched by water and then extracted by EtOAc. The EtOAc layer was washed with $NaHCO_3$ and brine, and then dried, filtered, and evaporated. The organic layer was concentrated and purified by flash column chromatography (DCM/MeOH/ammonium, 94/5/1) to give the product **L2a** as a white solid.

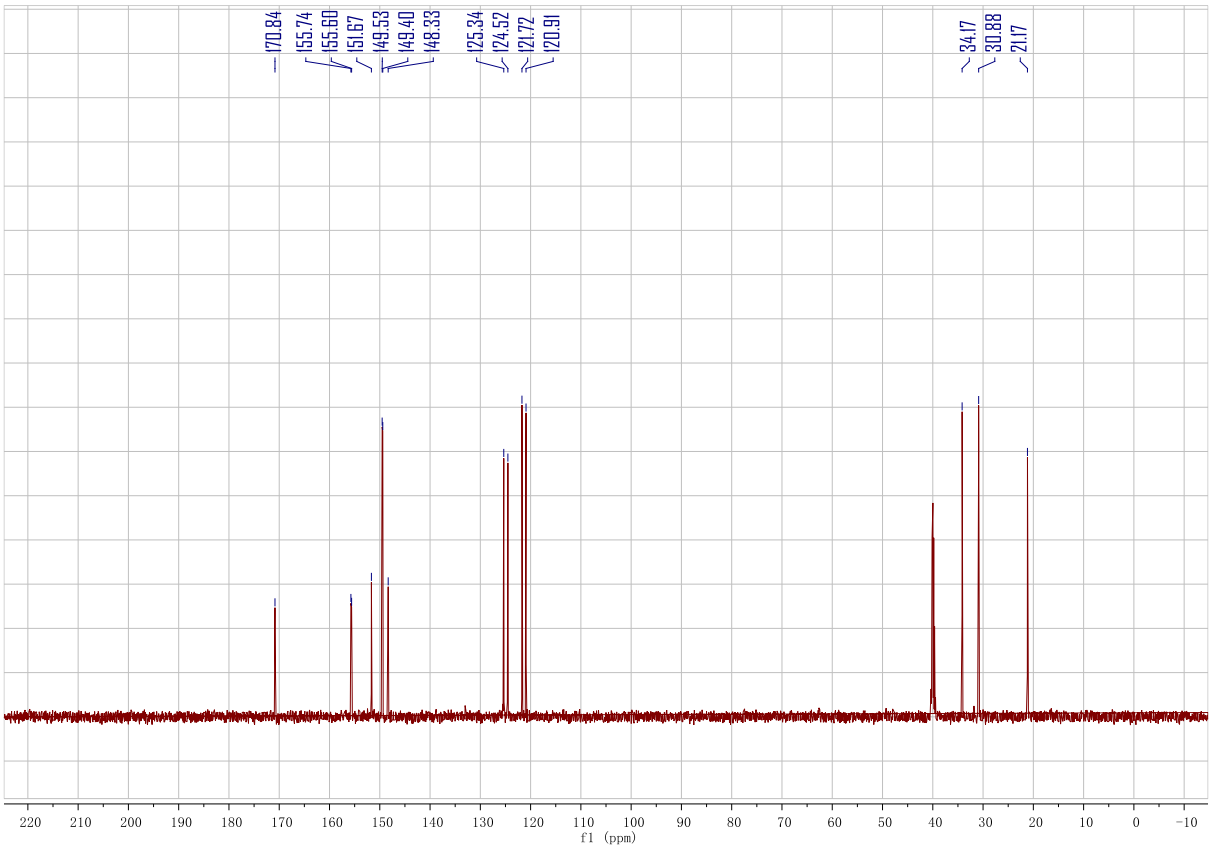
A flask was charged with **L2a** (5 mmol) and dry Ethanol (20 mL). To this stirring solution was added hydrazine hydrate (20 mmol) in one portion under Argon atmosphere and the resulting solution was heated under reflux for 12 hours. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The crude product was recrystallized through MeOH to give the product **L2** as a white solid.

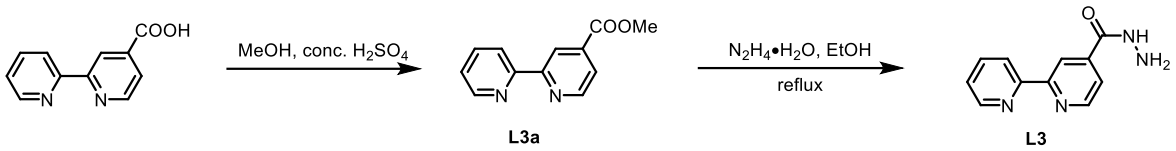


^{1}H NMR (500 MHz, DMSO) δ 9.06 (s, 1H), 8.53 (dd, J = 9.0, 4.9 Hz, 2H), 8.23 (d, J = 13.0 Hz, 2H), 7.35 – 7.20 (m, 2H), 4.24 (brs, 2H), 2.94 (t, J = 7.6 Hz, 2H), 2.44 (t, J = 7.6 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (126 MHz, DMSO) δ 170.84 (s), 155.74 (s), 155.60 (s), 151.67 (s), 149.53 (s), 149.40 (s), 148.33 (s), 125.34 (s), 124.52 (s), 121.72 (s), 120.91 (s), 34.17 (s), 30.88 (s), 21.17 (s).

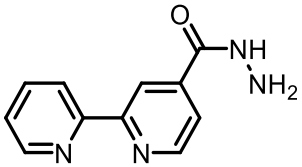

9.06
8.55
8.54
8.53
8.24
7.29
7.28
7.26
7.25
4.24
2.95
2.94
2.92
2.46
2.44
2.43
2.40
0.93
1.99
1.98
2.00
1.79
1.99
1.92
2.98
f1 (ppm)


170.84
155.74
155.60
151.67
149.53
149.40
148.33
125.34
124.52
121.72
120.91
34.17
30.88
21.17
f1 (ppm)



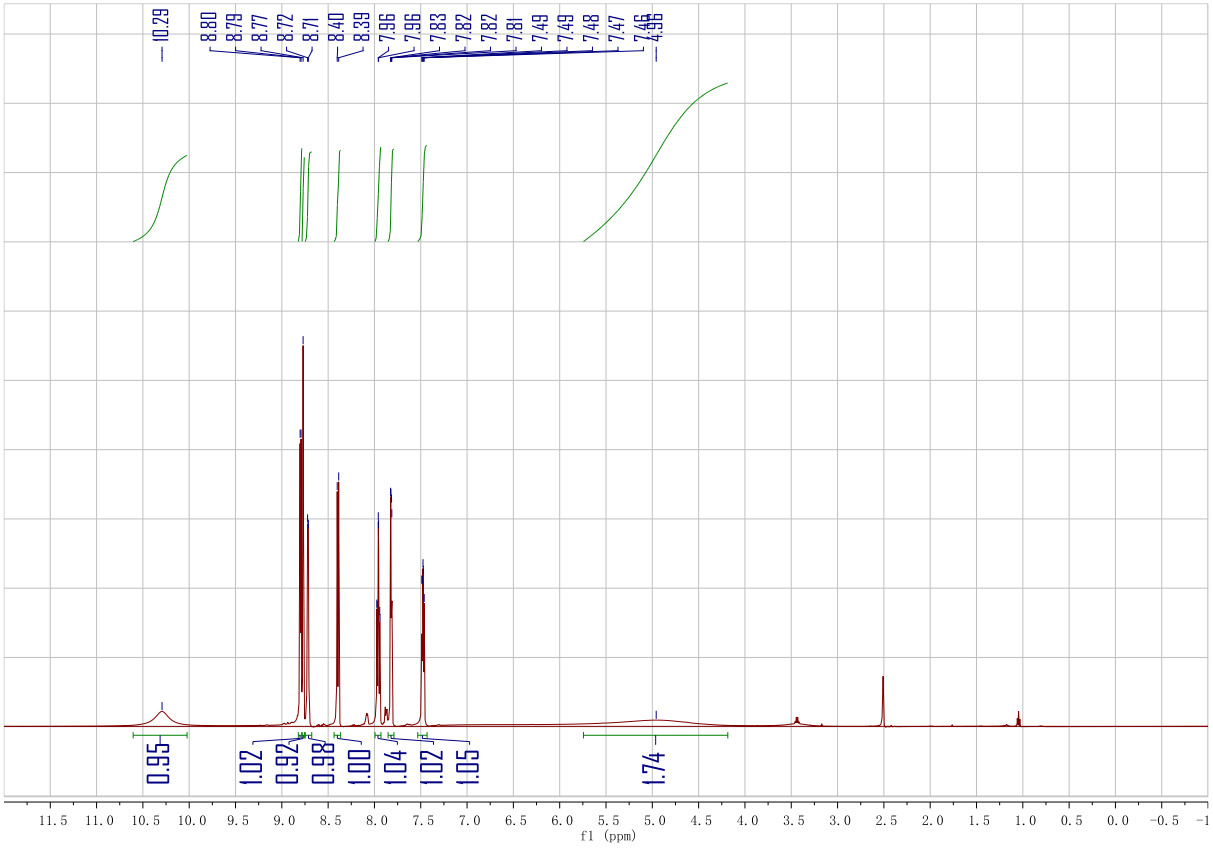
L3a L3

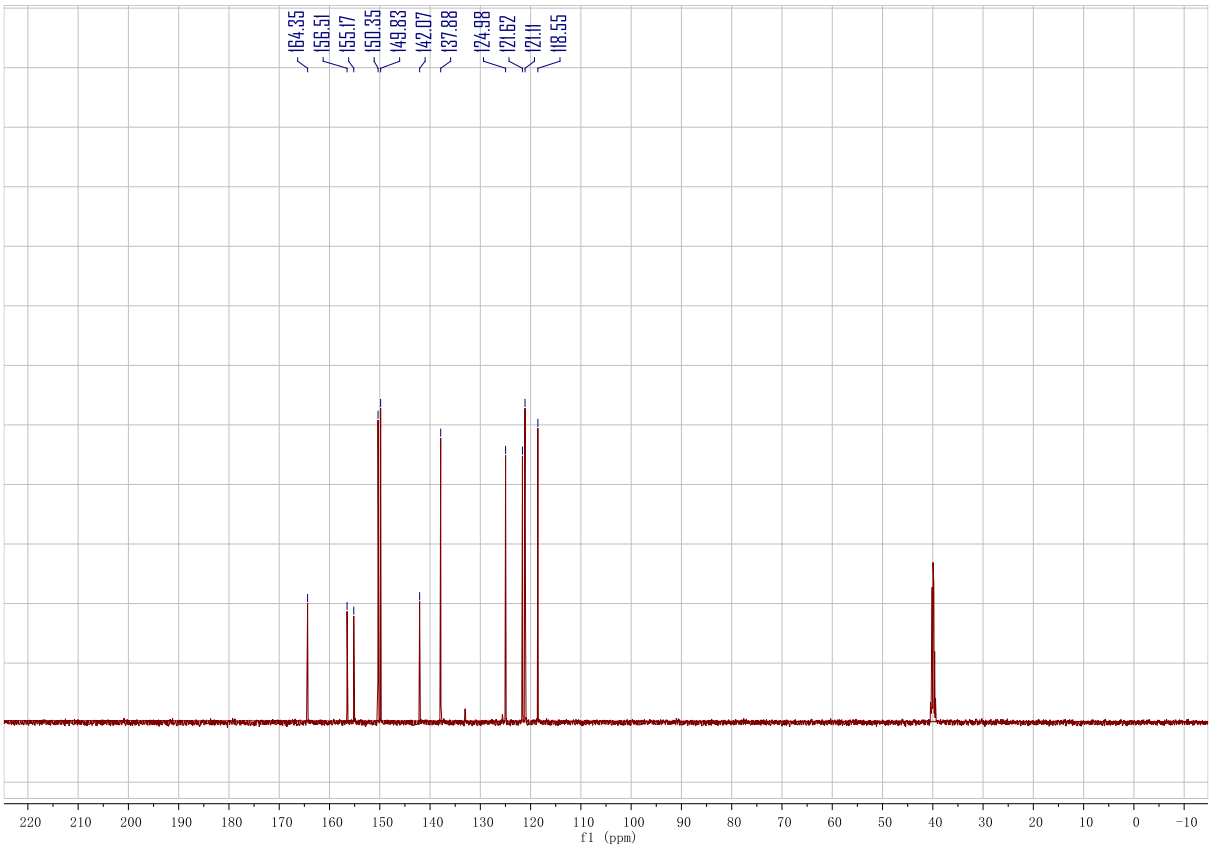
Ligand **L3** was synthesized following the procedure of **L2** using 2,2'-bipyridine-4-carboxylic acid.

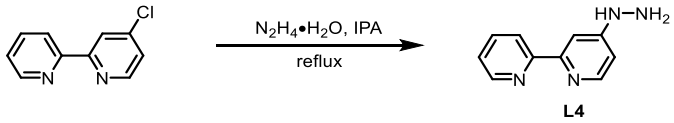


^{1}H NMR (500 MHz, DMSO) δ 10.29 (s, 1H), 8.80 (d, J = 5.0 Hz, 1H), 8.77 (s, 1H), 8.72 (d, J = 4.2 Hz, 1H), 8.39 (d, J = 7.9 Hz, 1H), 7.96 (td, J = 7.8, 1.7 Hz, 1H), 7.82 (dd, J = 5.0, 1.6 Hz, 1H), 7.53 – 7.43 (m, 1H), 4.96 (brs, 2H).

^{13}C NMR (126 MHz, DMSO) δ 164.35 (s), 156.51 (s), 155.17 (s), 150.35 (s), 149.83 (s), 142.07 (s), 137.88 (s), 124.98 (s), 121.62 (s), 121.11 (s), 118.55 (s).

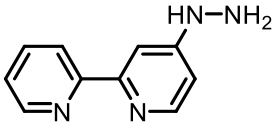






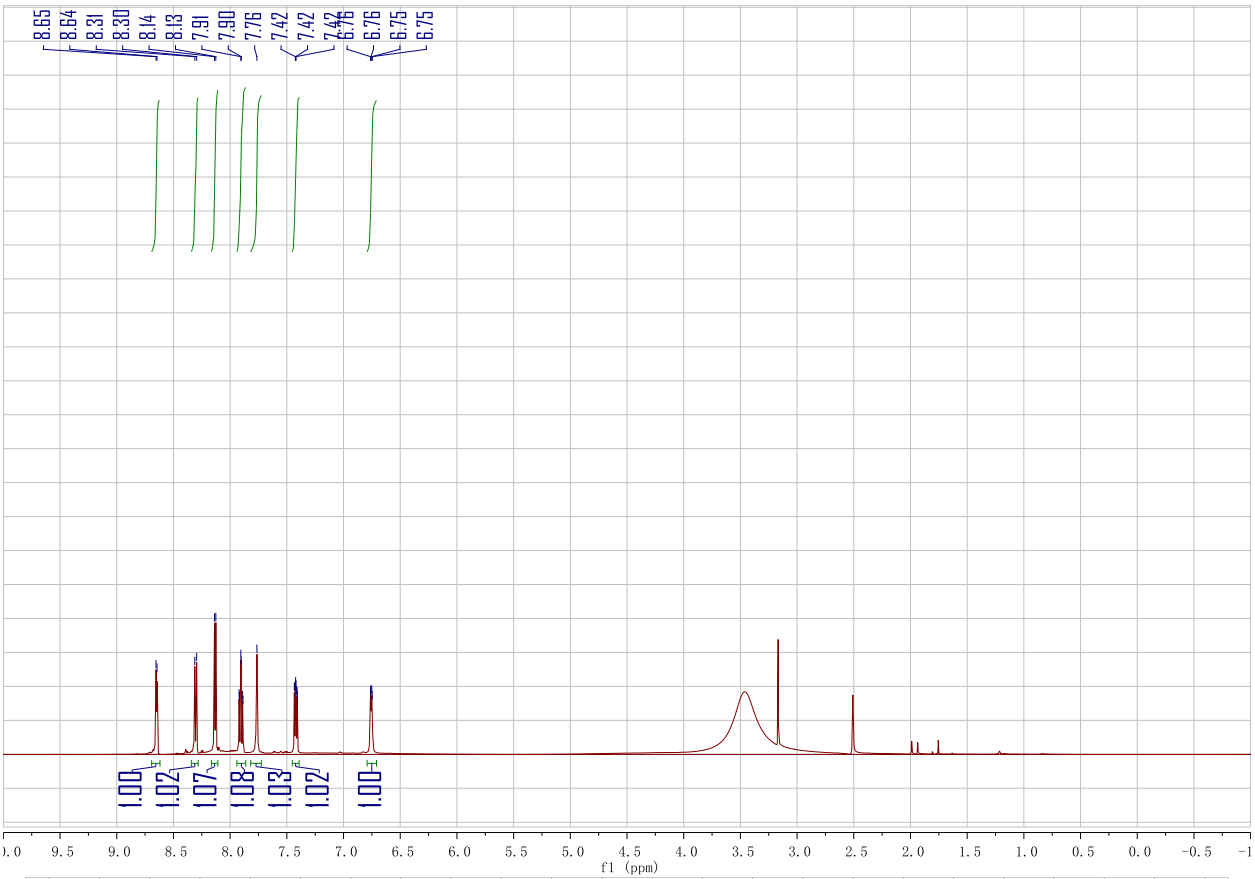
L4

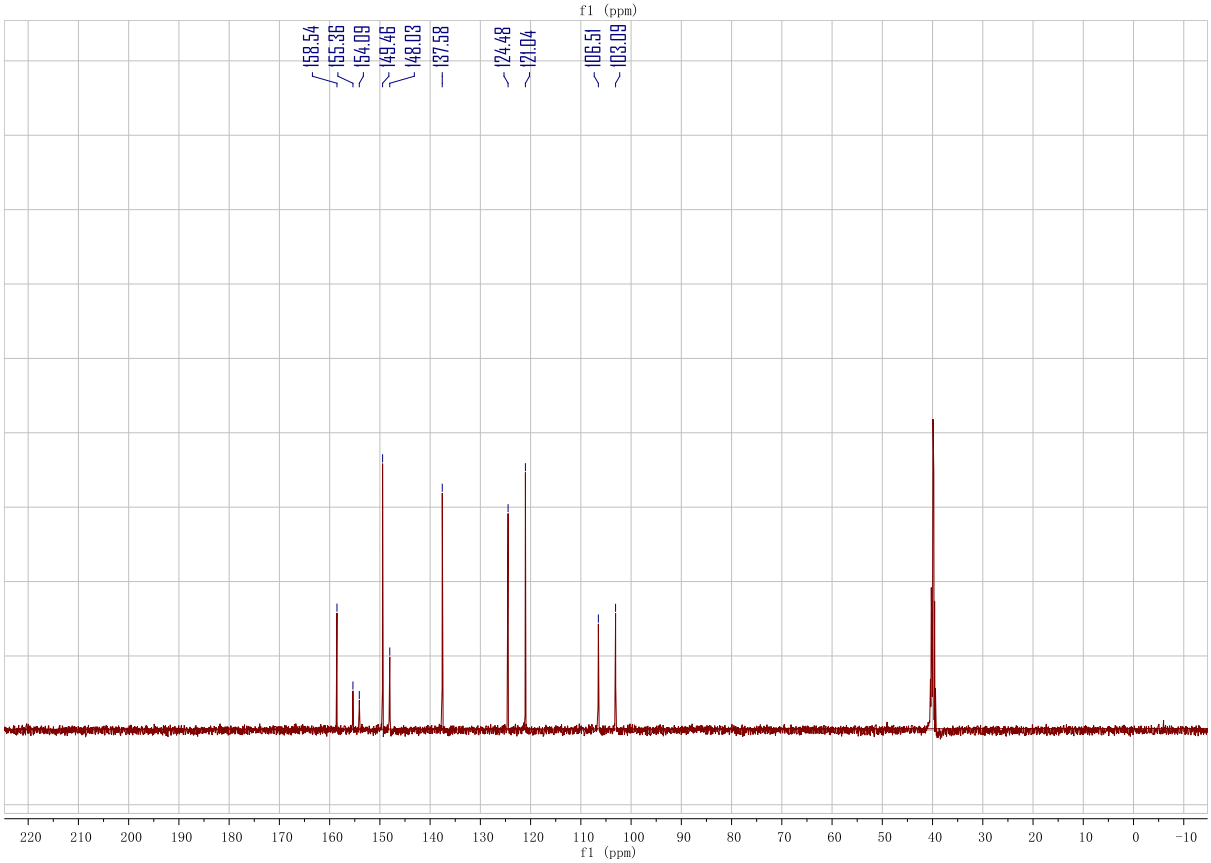
A flask was charged with 4-chloro-2,2'-bipyridine (2 mmol) and dry IPA (3 mL). To this stirring solution was added hydrazine hydrate (20 mmol) in one portion under Argon atmosphere and the resulting solution was heated under reflux for 12 hours. The reaction mixture was cooled to room temperature and the volatiles were removed by rotary evaporation. The crude product was recrystallized through MeOH to give the product **L4** as a brown solid.

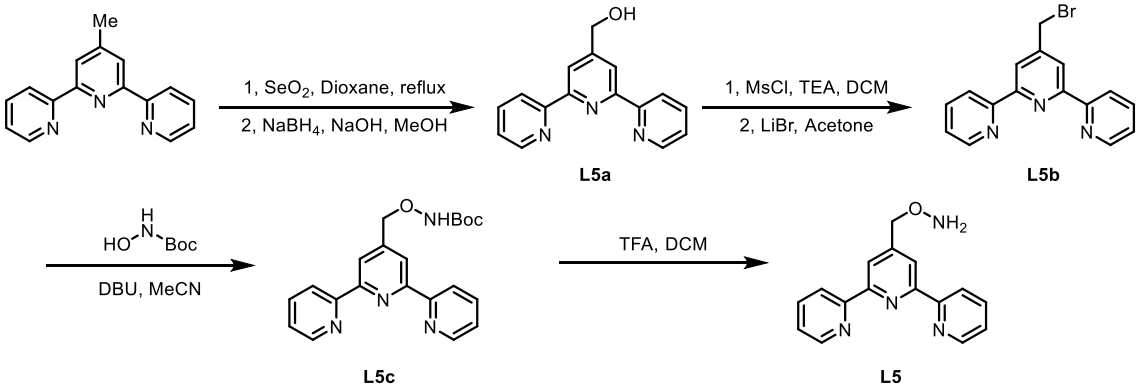


^{1}H NMR (500 MHz, DMSO) δ 8.65 (d, J = 4.5 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 5.8 Hz, 1H), 7.90 (td, J = 7.7, 1.8 Hz, 1H), 7.76 (s, 1H), 7.42 (ddd, J = 7.4, 4.8, 0.9 Hz, 1H), 6.75 (dd, J = 5.6, 1.8 Hz, 1H).

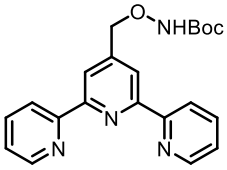
^{13}C NMR (126 MHz, DMSO) δ 158.54 (s), 155.36 (s), 154.09 (s), 149.46 (s), 148.03 (s), 137.58 (s), 124.48 (s), 121.04 (s), 106.51 (s), 103.09 (s).


8.65
8.64
8.31
8.30
8.14
8.13
7.91
7.90
7.76
7.42
7.42
7.42
6.76
6.75
6.75
1.00
1.02
1.07
1.08
1.03
1.02
1.00
f1 (ppm)


158.54
155.36
154.09
149.46
148.03
137.58
124.48
121.04
106.51
103.09
f1 (ppm)

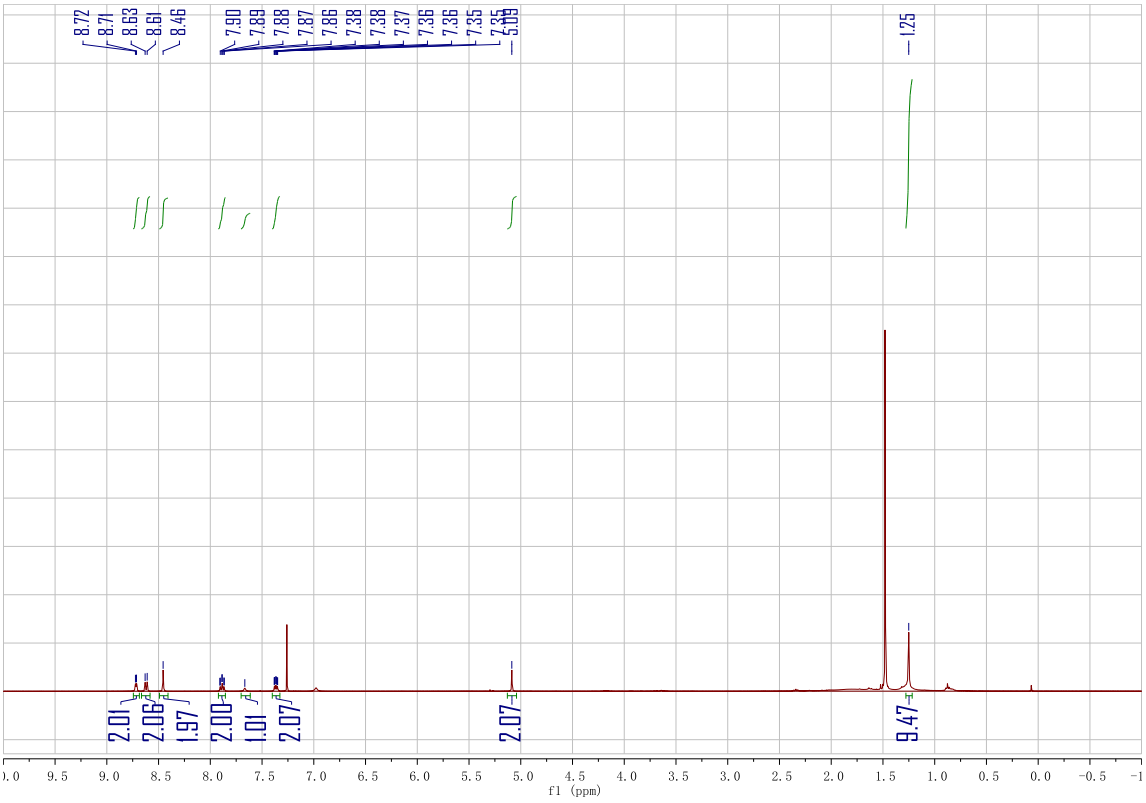


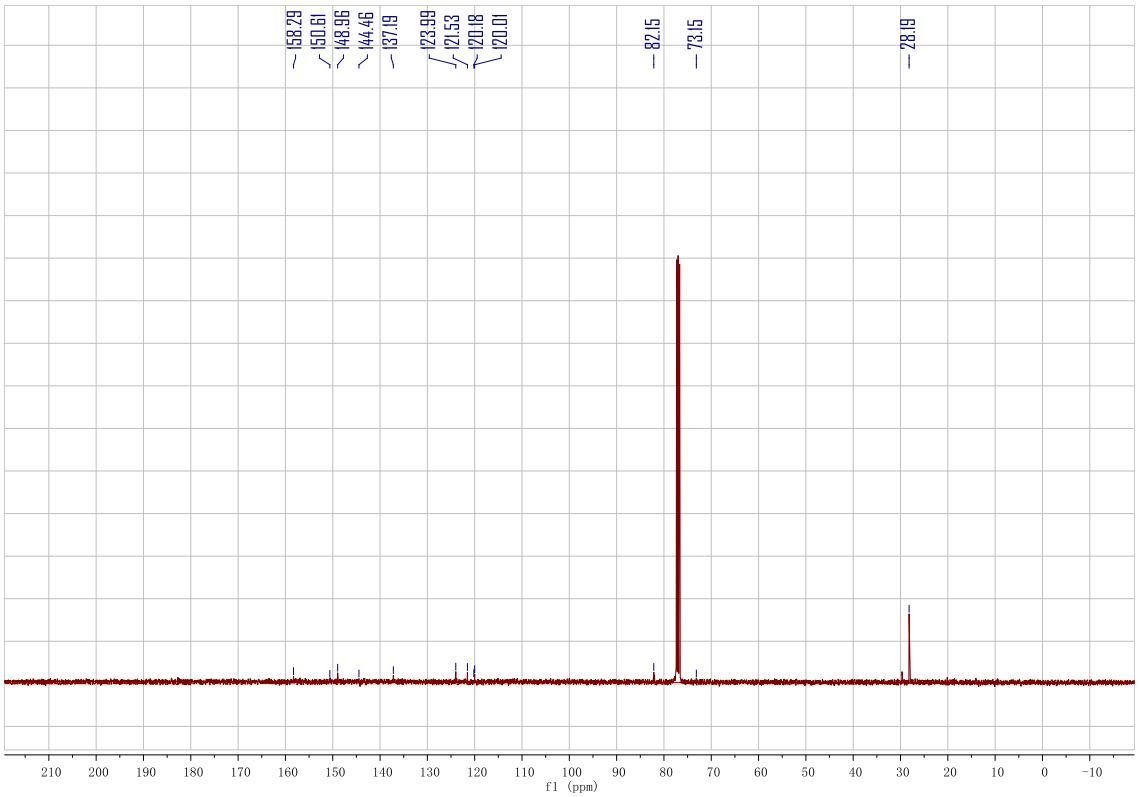
Ligand **L5** was synthesized following the procedure of **L1** using 4'-methyl-2,2':6',2"-terpyridine. (Note: Compound **L5** is not very stable at room temperature, we characterized the Boc-protected version **L5c,** which was later deprotected using TFA/DCM system.)

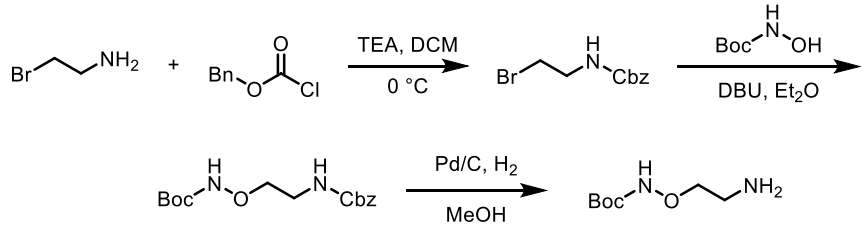


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.1 Hz, 2H), 8.62 (d, J = 8.0 Hz, 2H), 8.46 (s, 2H), 7.89 (td, J = 7.8, 1.7 Hz, 2H), 7.67 (s, 1H), 7.40 – 7.34 (m, 2H), 5.09 (s, 2H), 1.25 (s, 9H).

^{13}C NMR 13C NMR (101 MHz, CDCl3) δ 158.29 (s), 150.61 (s), 148.96 (s), 144.46 (s), 137.19 (s), 123.99 (s), 121.53 (s), 120.18 (s), 120.01 (s), 82.15 (s), 73.15 (s), 28.19 (s).



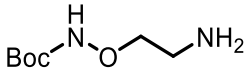




2-Bromoethylamine hydrobromide (48.8 mmol), TEA (148.5 mmol) and DCM (100 mL) were added to a dried two-necked flask under Argon atmosphere. The solution was cooled to 0 °C and then Benzyl chloroformate (58.6 mmol, 8.3 mL) was added dropwise. After the completion of the addition, the reaction mixture was kept at 0 °C and reacted for 2 hours. After the completion of the reaction, the mixture was diluted with water and extracted with DCM. The combined organic phases were washed with saturated $NaHCO_3$ and NaCl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain the benzyl (2-bromoethyl) carbamate as a white solid.

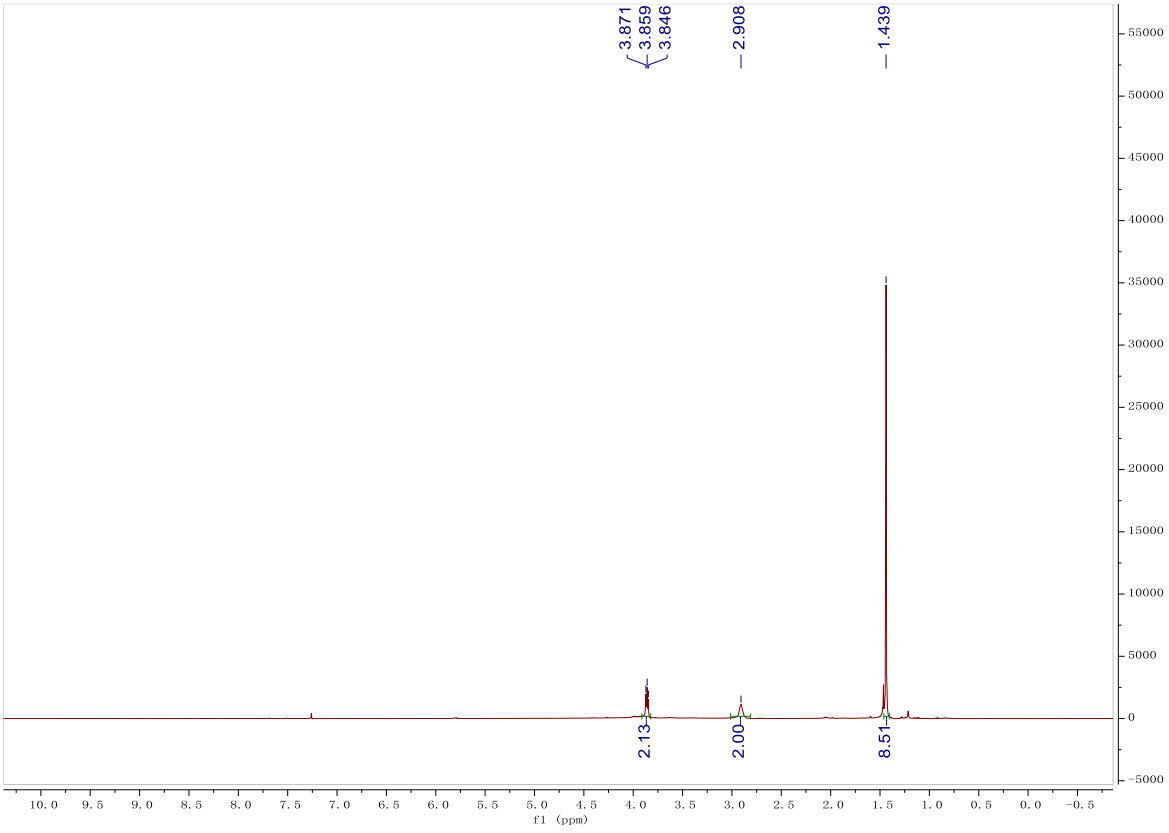
The tert-butyl hydroxy carbamate (35.0 mmol), DBU (52.5 mmol) and Et_2O (60 mL) were added to a dried two-necked flask under Argon atmosphere. Then the benzyl (2-bromoethyl) carbamate (37.4 mmol) was added dropwise. After the completion of the addition, the reaction mixture was stirred at room temperature for 1 hour. Then, the Et_2O was evaporated under reduced pressure. The neat solution was continued to stir at room temperature overnight. The resulted crude was purified by flash column chromatograph to obtain the tert-butyl (2-(((benzyloxy) carbonyl) amino) ethoxy) carbamate as a colorless oil.

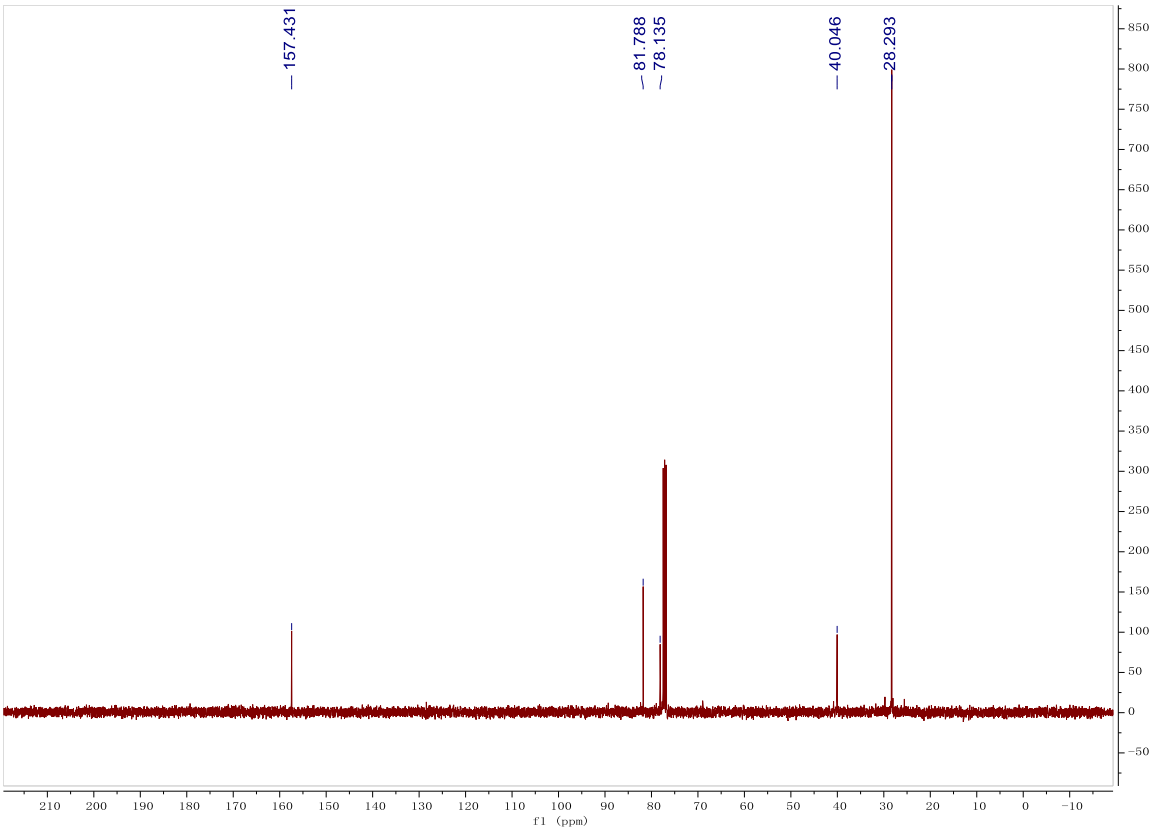
The tert-butyl (2-(((benzyloxy)carbonyl) amino) ethoxy) carbamate (13.0 mmol), Pd/C (800 mg) and MeOH (20 mL) were added to a dried two-necked flask under H_2 atmosphere with a balloon. The solution was continued to stir at room temperature overnight. The reaction was monitored by thin layer chromatography (TLC). After the completion of the reaction, the solution was filtered. The filtrate was evaporated concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain the tert-butyl (2-aminoethoxy) carbamate as a colorless oil.

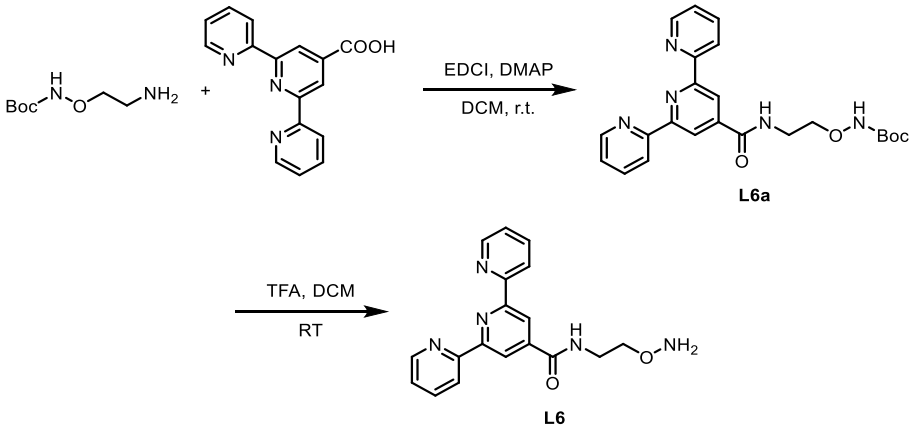


^{1}H NMR (400 MHz, $CDCl_3$) δ**:** 3.86 (t, *J* = 7.2 Hz, 2H), 2.92-2.87 (m, 2H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ**:** 157.4 (s), 81.8 (s), 78.1 (s), 40.0 (s), 28.3 (s).



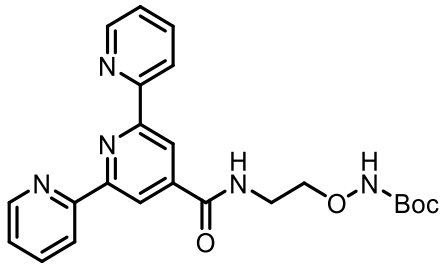




(2,2':6',2"-terpyridine)-4'-carboxylic acid (1.0 mmol), tert-butyl (2-aminoethoxy) carbamate (1.2 mmol) and DCM (60 mL) were added to a dried two-necked flask under Argon atmosphere. The solution was cooled to 0 °C and then EDCI (2.0 mmol) and DMAP (0.1 mmol) were added. After the completion of the addition, the reaction mixture was stirred at room temperature overnight. The reaction was monitored by thin layer chromatography (TLC). And after the completion of the reaction, the mixture was diluted with water (100 mL) and extracted with DCM (50 mL x 3). The combined organic phases were washed with saturated $NaHCO_3$ (100 mL) and NaCl (50 mL) solution, dried over Na_2SO_4 and concentrated under reduced pressure. The resulted crude was

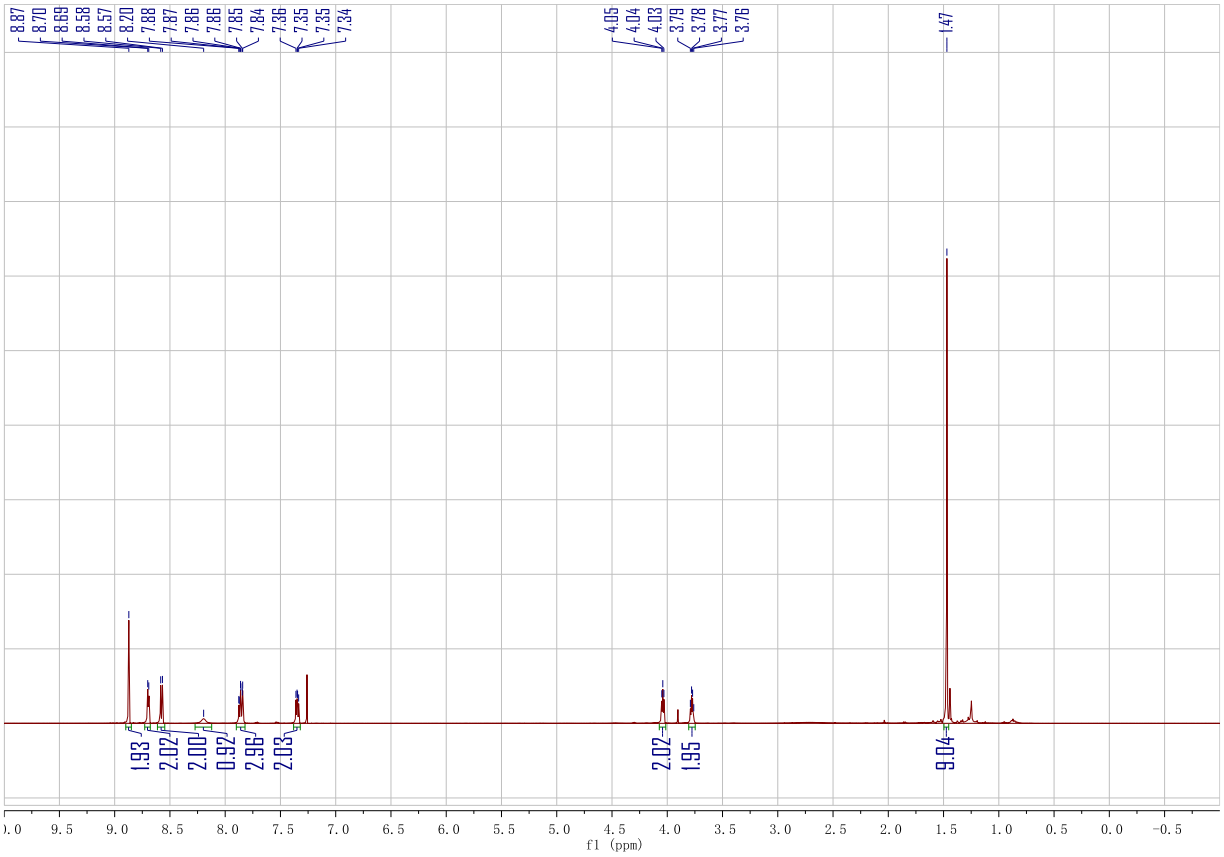
purified by flash column chromatograph to obtain the tert-butyl (2-((2,2':6',2''-terpyridine)-4'-carboxamido) ethoxy) carbamate **L6a** as a white solid.

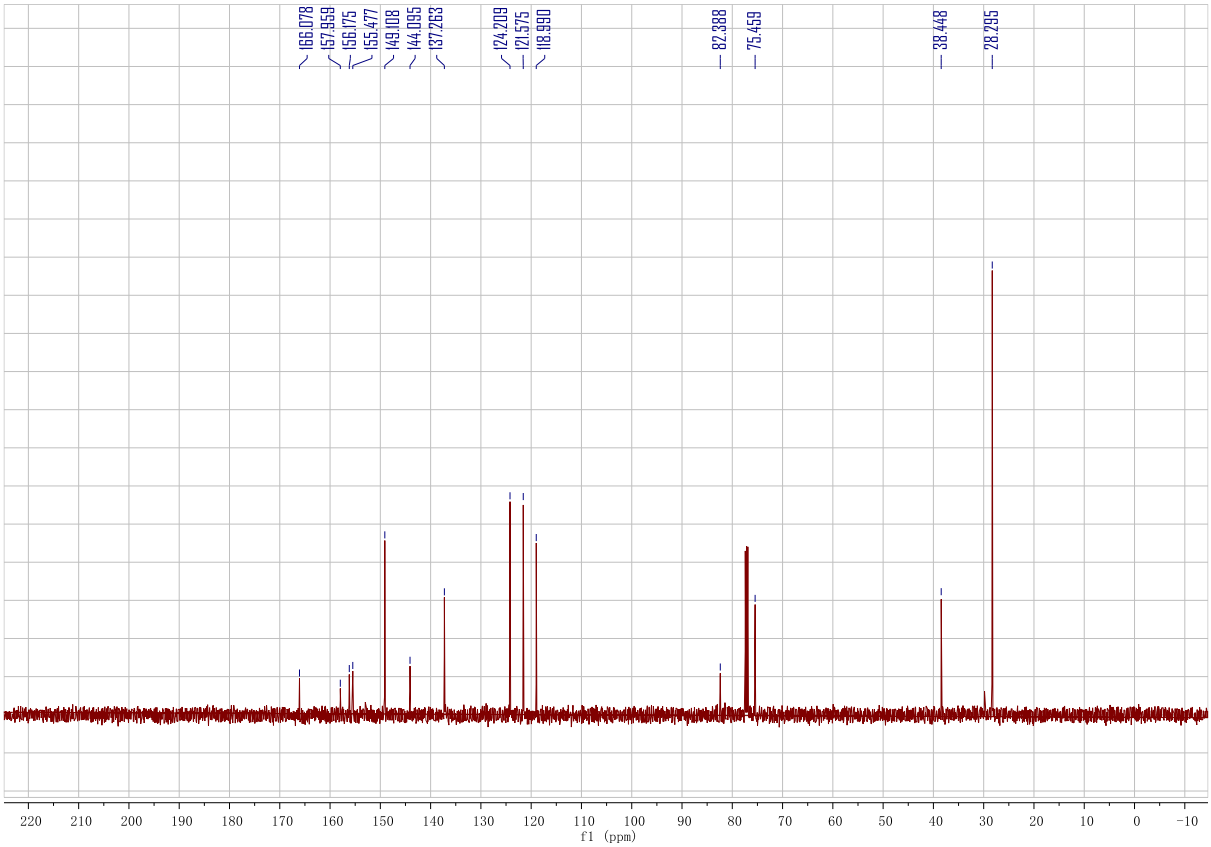
A flask was charged with **L6a** (2 mmol), dry DCM (10 mL) and TFA (10 mL) were added under Argon atmosphere. After 4 hours stirring, the volatiles were removed by rotary evaporation. Remaining TFA was co-evaporated by the addition of 1 mL toluene for three times and dry under vacuum to give the product **L6** as a white solid. (Note: Compound **L6** is not very stable at room temperature, we characterized the Boc-protected version **L6a,** which was later deprotected using TFA/DCM system.)

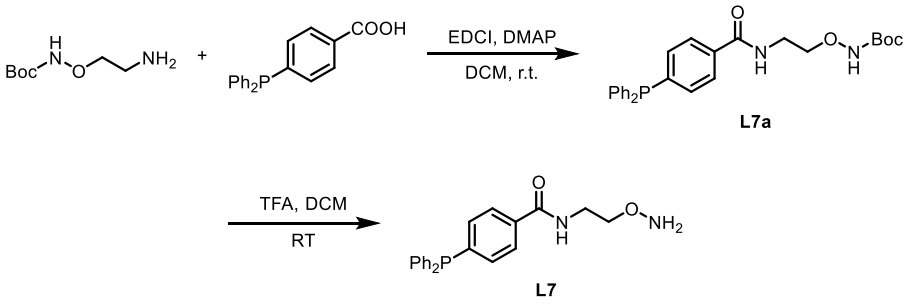


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 2H), 8.70 (d, J = 4.7 Hz, 2H), 8.58 (d, J = 7.9 Hz, 2H), 8.20 (brs, 1H), 7.90 – 7.82 (m, 3H), 7.36-7.33 (m, 2H), 4.04 (t, J = 4.8 Hz, 2H), 3.78 (dd, J = 10.0, 5.3 Hz, 2H), 1.47 (s, 9H).

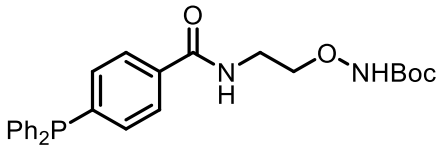
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.08 (s), 157.96 (s), 156.17 (s), 155.48 (s), 149.11 (s), 144.10 (s), 137.26 (s), 124.21 (s), 121.58 (s), 118.99 (s), 82.39 (s), 75.46 (s), 38.45 (s), 28.29 (s).





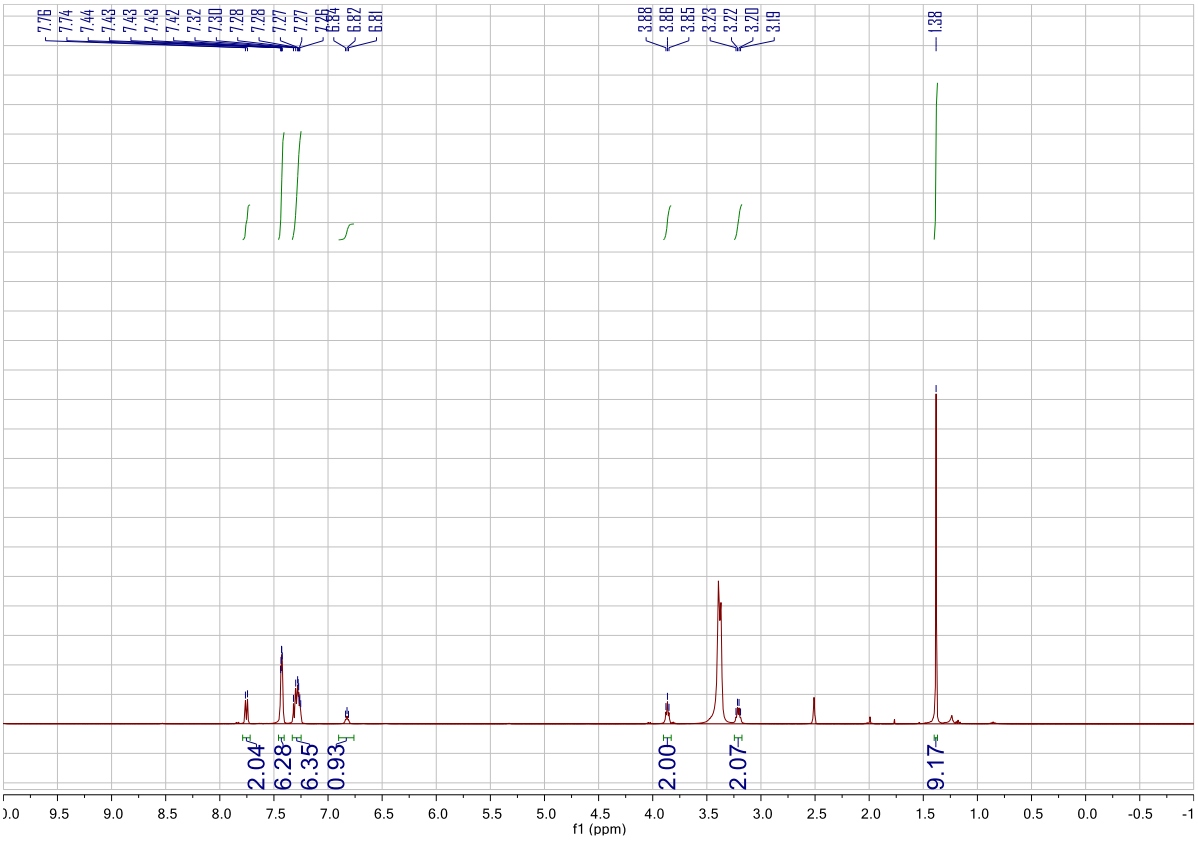


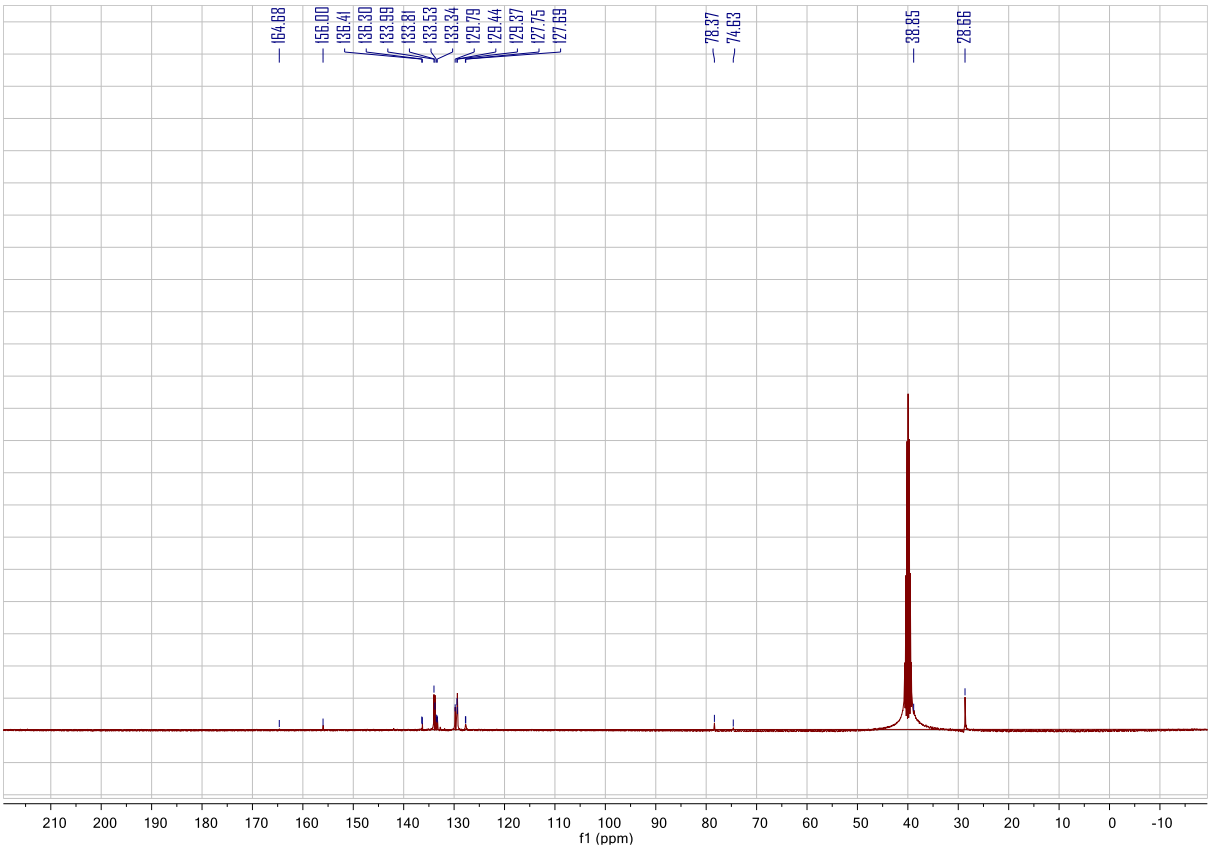
Ligand **L7** was synthesized following the procedure of **L6** using 4-(diphenylphosphanyl) benzoic acid. (Note: Compound **L7** is not very stable at room temperature, we characterized the Boc-protected version **L7a,** which was later deprotected using TFA/DCM system.)

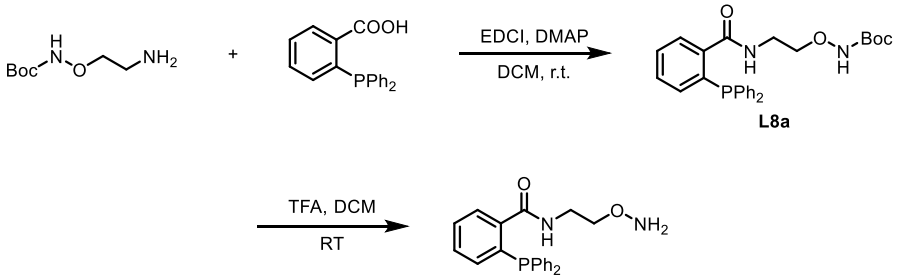


^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, J = 7.6 Hz, 2H), 7.46 – 7.41 (m, 6H), 7.33 – 7.25 (m, 6H), 6.82 (t, J = 5.5 Hz, 1H), 3.86 (t, J = 5.6 Hz, 2H), 3.21 (dd, J = 11.3, 5.6 Hz, 2H), 1.38 (s, 9H).

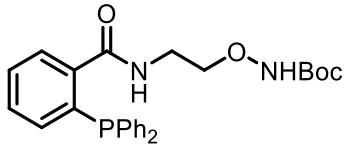
^{13}C NMR (101 MHz, DMSO) δ 164.68 (s), 156.00 (s), 136.36 (d, J = 11.1 Hz), 133.99 (s), 133.81 (s), 133.44 (d, J = 19.1 Hz), 129.79 (s), 129.44 (s), 129.37 (s), 127.72 (d, J = 6.1 Hz), 78.37 (s), 74.63 (s), 38.85 (s), 28.66 (s).





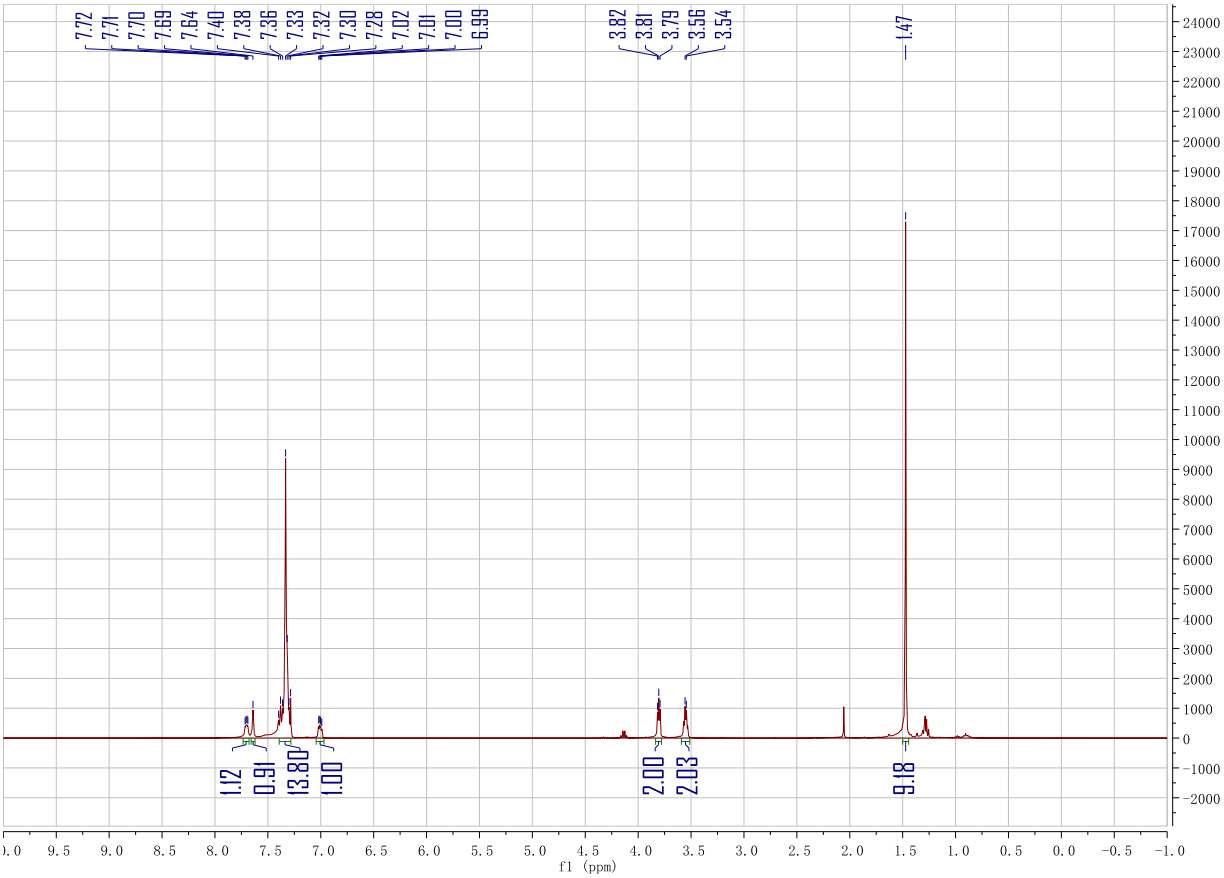


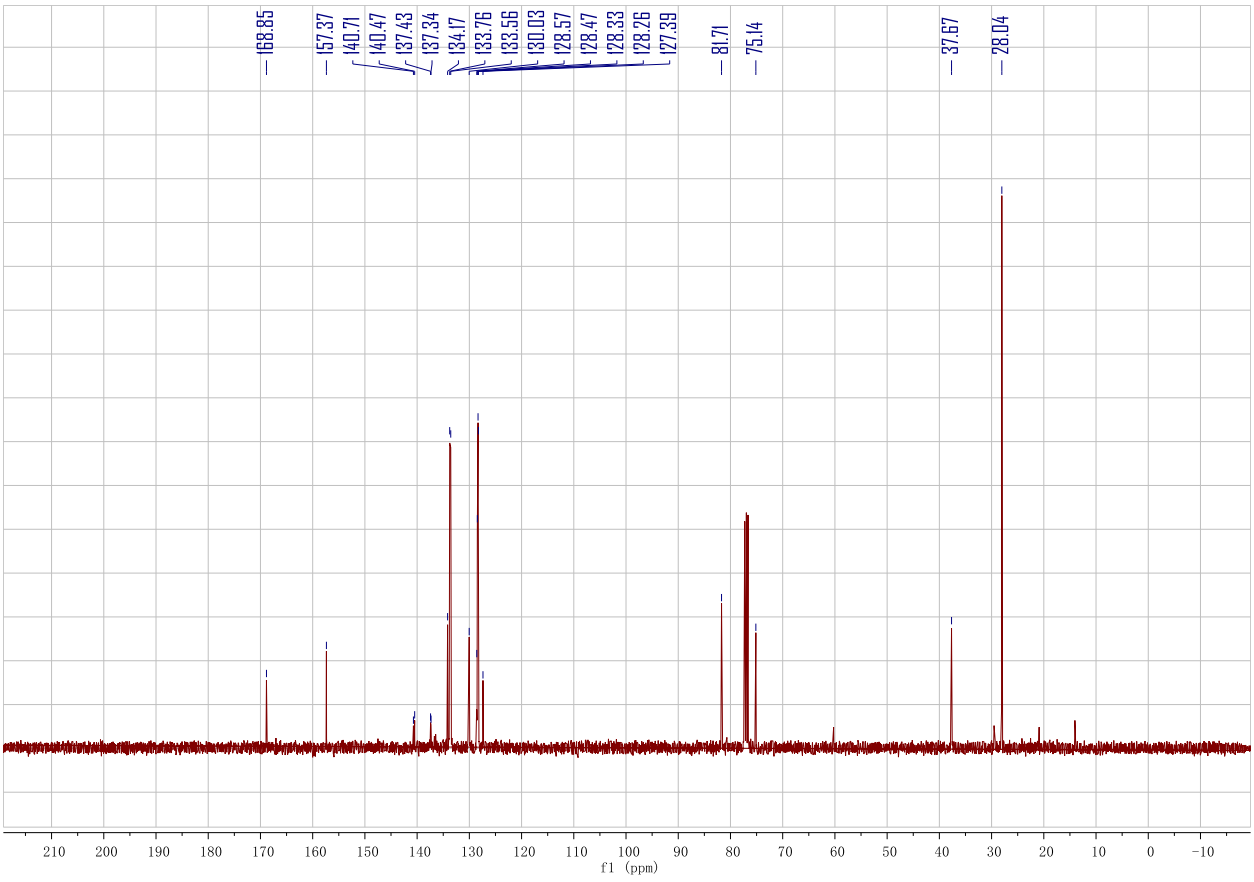
Ligand **L8** was synthesized following the procedure of **L6** using 2-(diphenylphosphanyl) benzoic acid. (Note: Compound **L8** is not very stable at room temperature, we characterized the Boc-protected version **L8a,** which was later deprotected using TFA/DCM system.)

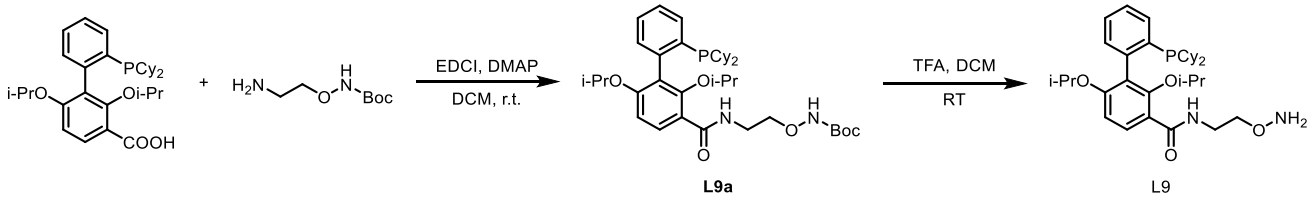


^{1}H NMR (400 MHz, CDCl3) δ: 7.69-7.66 (m, 1H), 7.61 (s, 1H), 7.37-7.27 (m, 13H), 6.99-6.97 (m, 1H), 3.78 (t, J = 4.8 Hz, 2H), 3.54-3.51 (m, 2H), 1.47 (s, 9H).

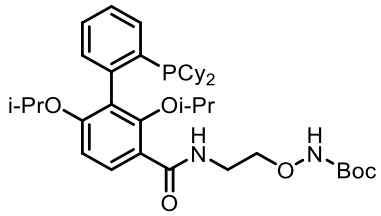
^{13}C NMR (100 MHz, CDCl3) δ: 168.8 (s), 157.4 (s), 140.6 (d, J = 23.7 Hz), 137.4 (d, J = 9.0 Hz), 134.2 (s), 133.8 (s), 133.6 (s), 130.0 (s), 128.6 (s), 128.5 (s), 128.3 (d, J = 7.1 Hz), 127.3 (d, J = 4.5 Hz), 81.7 (s), 75.1 (s), 37.7 (s), 28.0 (s).







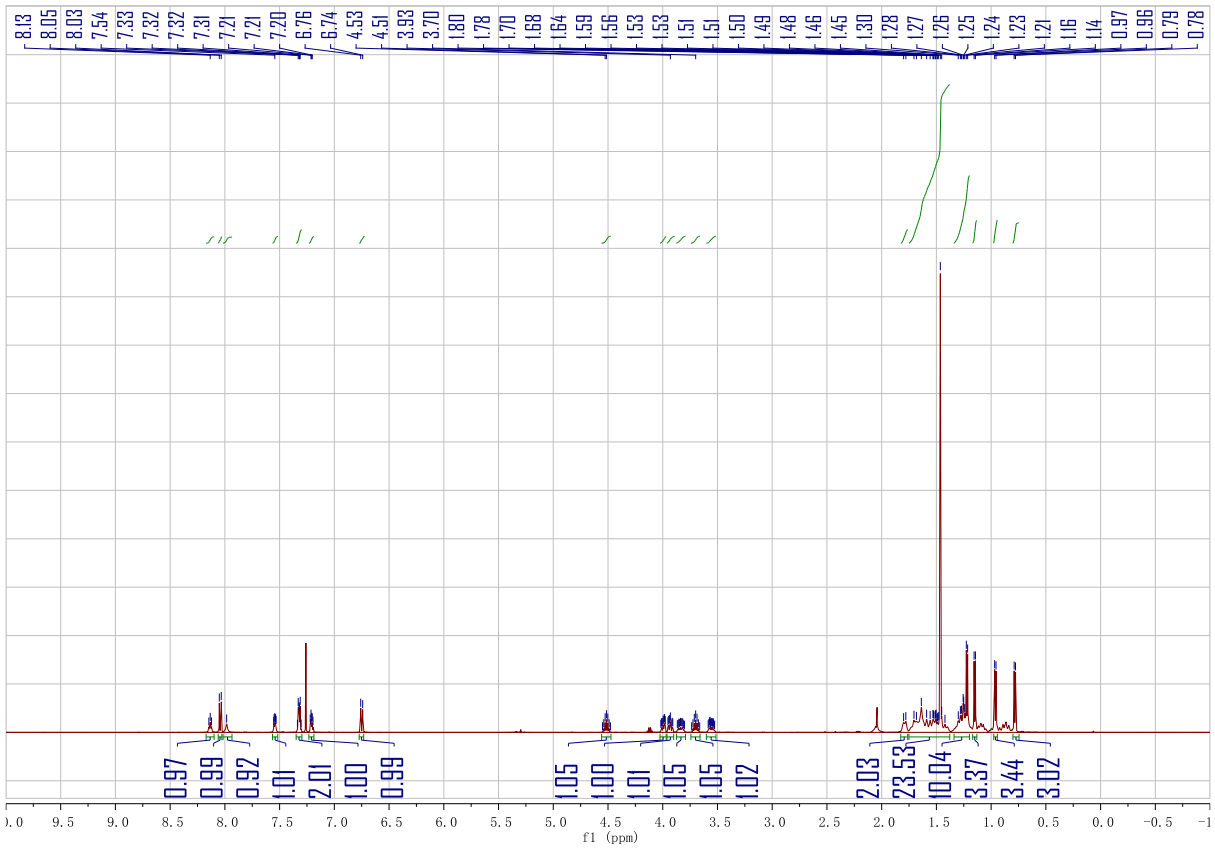
Ligand **L9** was synthesized following the procedure of **L6** using RuPhos benzoic acid[6]. (Note: Compound **L9** is not very stable at room temperature, we characterized the Boc-protected version **L9a,** which was later deprotected using TFA/DCM system.)

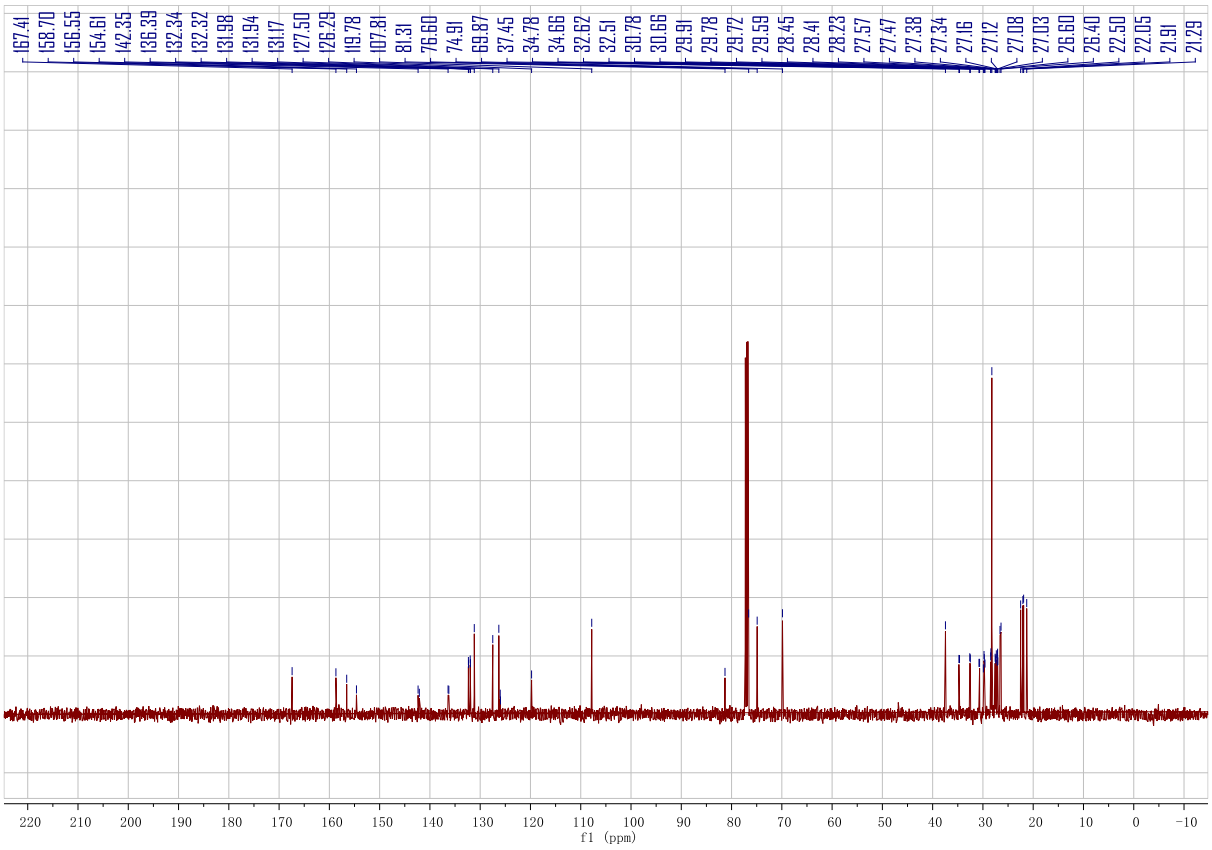


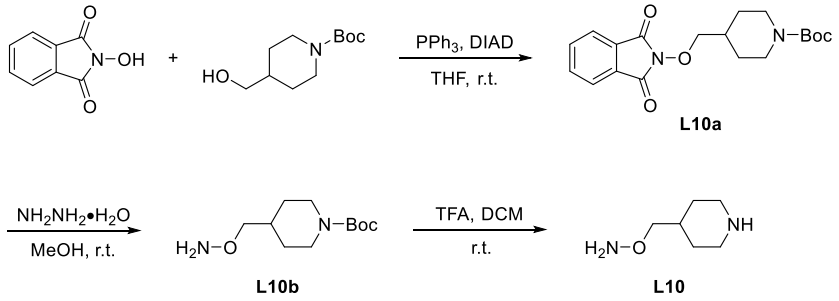
<u>^{1}H NMR</u> (500 MHz, $CDCl_3$) δ 8.13 (t, J = 6.1 Hz, 1H), 8.04 (d, *J* = 8.9 Hz, 1H), 7.98 (s, 1H), 7.58 – 7.50 (m, 1H), 7.35 – 7.30 (m, 2H), 7.23 – 7.19 (m, 1H), 6.75 (d, J = 9.1 Hz, 1H), 4.51 (hept, J = 6.1 Hz, 1H), 4.00 (ddd, J = 11.0, 5.5, 3.6 Hz, 1H), 3.93 (ddd, J = 11.1, 7.6, 3.3 Hz, 1H), 3.83 (dtd, J = 14.4, 7.2, 3.6 Hz, 1H), 3.70 (hept, J = 6.1 Hz, 1H), 3.56 (dtd, J = 14.7, 5.6, 3.4 Hz,

1H), 1.79 (d, J = 10.2 Hz, 2H), 1.75 – 1.39 (m, 22H), 1.33 – 1.20 (m, 10H), 1.15 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 6.2 Hz, 3H), 0.78 (d, J = 6.2 Hz, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 167.41 (s), 158.70 (s), 156.55 (s), 154.61 (s), 142.23 (d, J = 31.1 Hz), 136.31 (d, J = 19.4 Hz), 132.33 (d, J = 3.3 Hz), 131.96 (d, J = 5.7 Hz), 131.17 (s), 127.50 (s), 126.29 (s), 125.99 (d, J = 6.9 Hz), 119.78 (s), 107.81 (s), 81.31 (s), 76.60 (s), 74.91 (s), 69.87 (s), 37.45 (s), 34.72 (d, J = 15.0 Hz), 32.56 (d, J = 13.6 Hz), 30.72 (d, J = 14.9 Hz), 29.85 (d, J = 15.9 Hz), 29.66 (d, J = 16.5 Hz), 28.43 (d, J = 5.4 Hz), 28.23 (s), 27.52 (d, J = 12.4 Hz), 27.36 (d, J = 6.0 Hz), 27.14 (d, J = 5.9 Hz), 27.06 (d, J = 6.1 Hz), 26.60 (s), 26.40 (s), 22.50 (s), 22.05 (s), 21.91 (s), 21.29 (s).



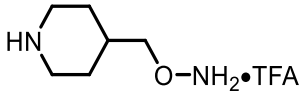




Tert-butyl 4-(hydroxymethyl) piperidine-1-carboxylate (2.5 mmol), 2-hydroxyisoindoline-1,3-dione (3.0 mmol) and triphenylphosphine (3 mmol) were dissolved in dry THF (10 mL). The solution was cooled to 0 °C and then Diisopropyl azodicarboxylate (DIAD) (3 mmol) was dissolved in 1.5 mL dry THF and added dropwise. The reaction mixture was then stirred overnight at room temperature and was monitored by thin layer chromatography (TLC). After the completion of the reaction, the mixture was evaporated under reduced pressure. The residue was subjected to column chromatography to give product **L10a**.

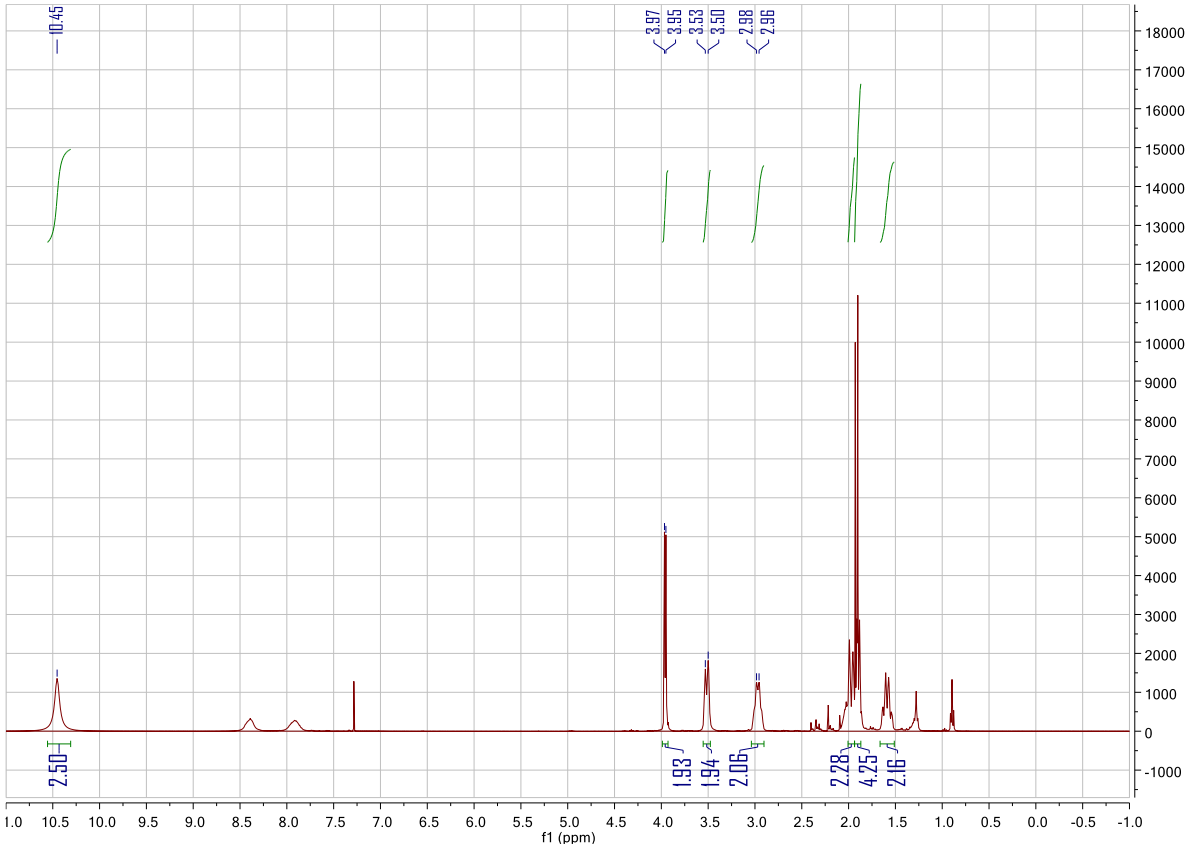
Compound **L10a** (1.0 mmol) and hydrazine hydrate (10 mmol) were dissolved in methanol (1.5 mL) and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then evaporated under reduced pressure to get compound **L10b**.

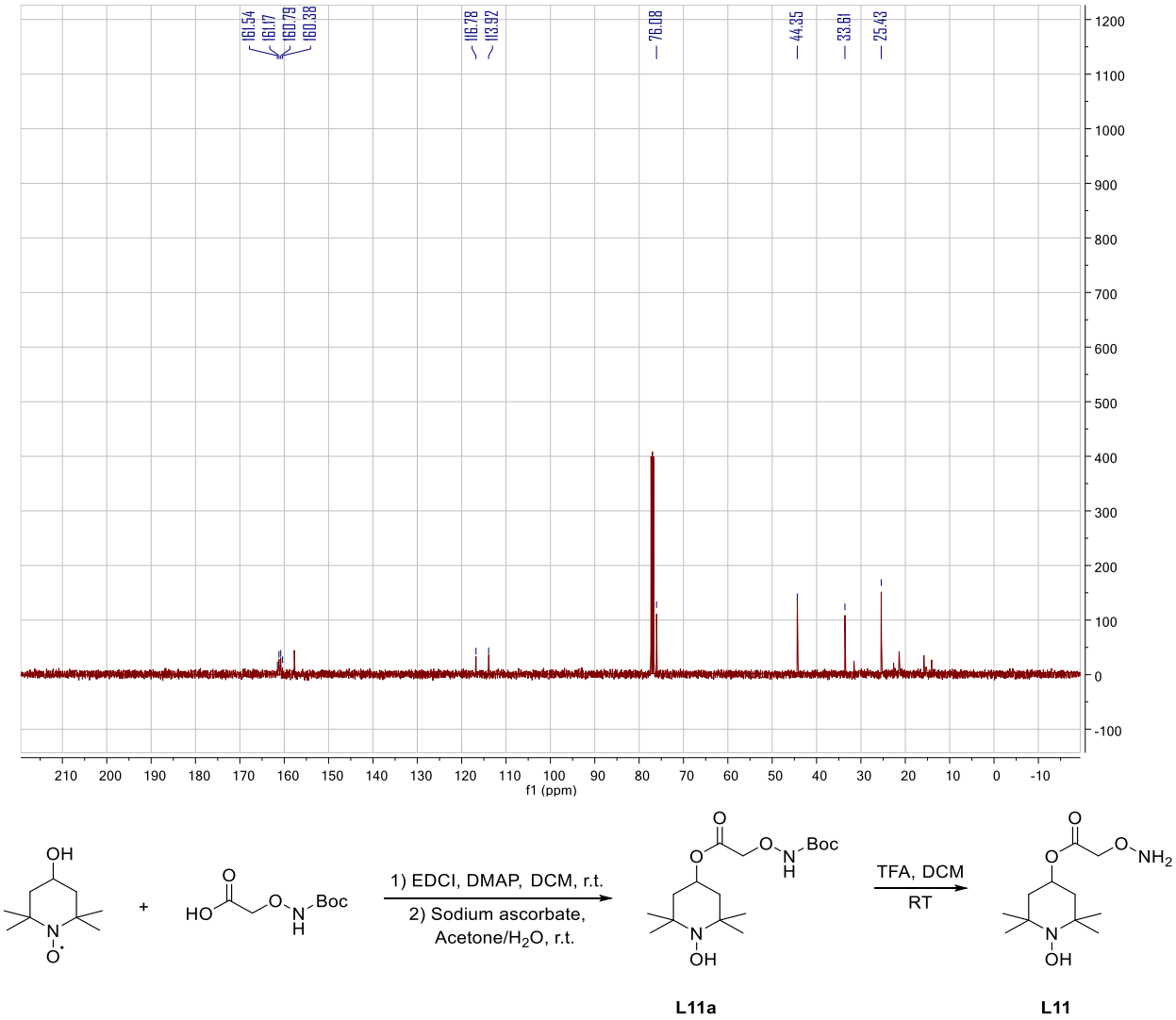
Compound **L10b** (0.87 mmol) was dissolved in 3 mL DCM and then 3 mL trifluoroacetic acid was added. The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The obtained oil was washed with hexane to give final product **L10**.



^{1}H NMR (400 MHz, CDCl3) δ 10.45 (s, 2H), 3.96 (d, J = 6.1 Hz, 2H), 3.51 (d, J = 12.3 Hz, 2H), 2.97 (d, J = 10.8 Hz, 2H), 1.97 (d, J = 14.9 Hz, 2H), 1.94 – 1.87 (m, 4H), 1.58 (dt, J = 14.7, 7.3 Hz, 2H).

^{13}C NMR (101 MHz, CDCl3) δ 160.98 (q, J = 38.8 Hz), 115.35 (q, J = 287.7 Hz), 76.08 (s), 44.35 (s), 33.61 (s), 25.43 (s).



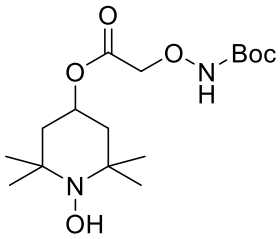


the TEMPO-4-OH (2.0 mmol), 2-(((tert-butoxycarbonyl)amino)oxy) acetic acid (3.0 mmol) and DCM (60 mL) were added to a dried two-necked flask under Argon atmosphere. The solution was cooled to 0 °C and then EDCI (8.0 mmol) and DMAP (0.1 mmol) was added. After the completion of the addition, the reaction mixture was stirred at room temperature overnight. The reaction was monitored by thin layer chromatography (TLC). And after the completion of the reaction, the mixture was diluted with water (100 mL) and extracted with DCM (50 mL x 3). The combined organic phases were washed with saturated $NaHCO_3$ (100 mL) and NaCl (50 mL) solution, dried over Na_2SO_4 and concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain the desired product.

The product of last step and Acetone (4 mL) were added to a dried round-bottom flask. Sodium ascorbate (2 mmol) and H_2O (10 mL) were added stepwise. The reaction mixture was stirred at room temperature for 2 hours. The reaction was monitored by thin layer chromatography (TLC). And after the completion of the reaction, the mixture was extracted with Ethyl Acetate (50 mL x 3), dried over Na_2SO_4 and concentrated under reduced pressure. The resulted crude was purified

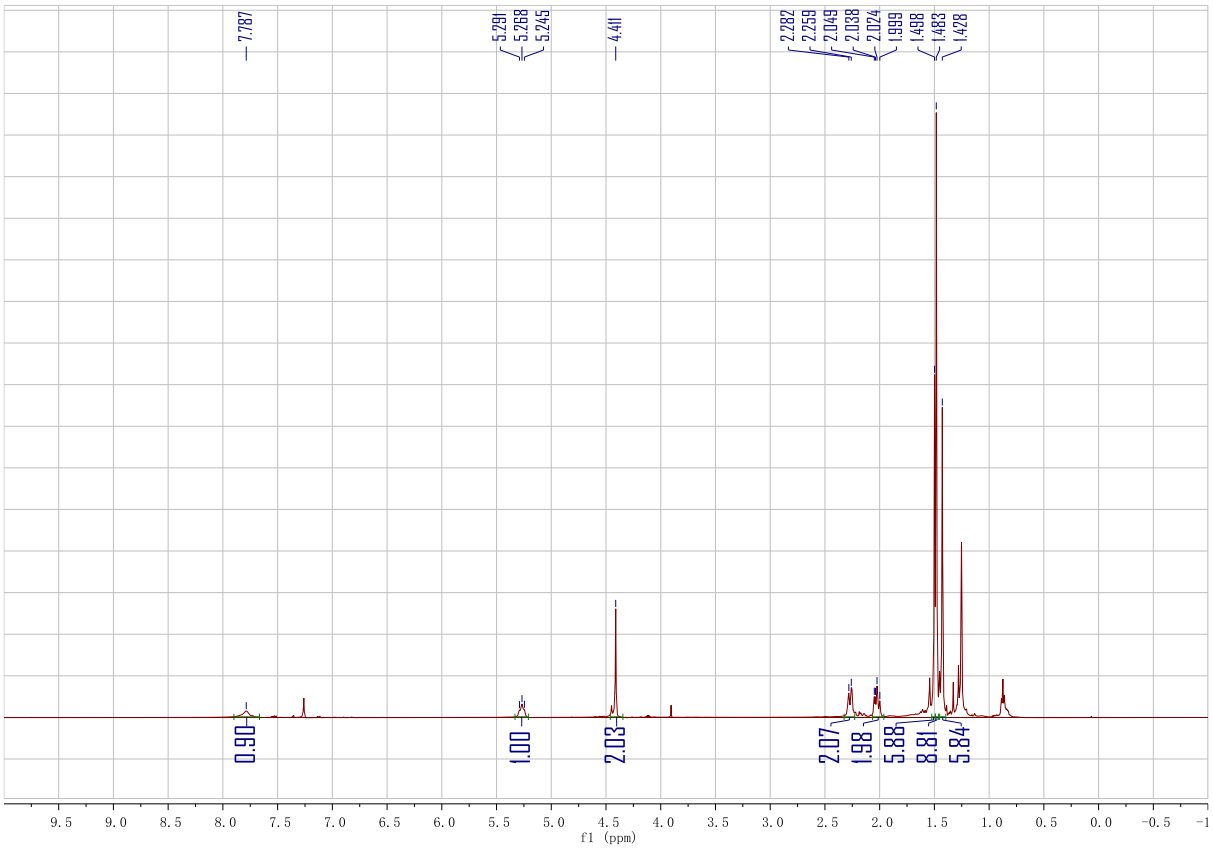
by flash column chromatograph to obtain the 1-hydroxy-2,2,6,6-tetramethylpiperidin-4-yl 2-(((tert-butoxycarbonyl)amino)oxy)acetate **L11a**.

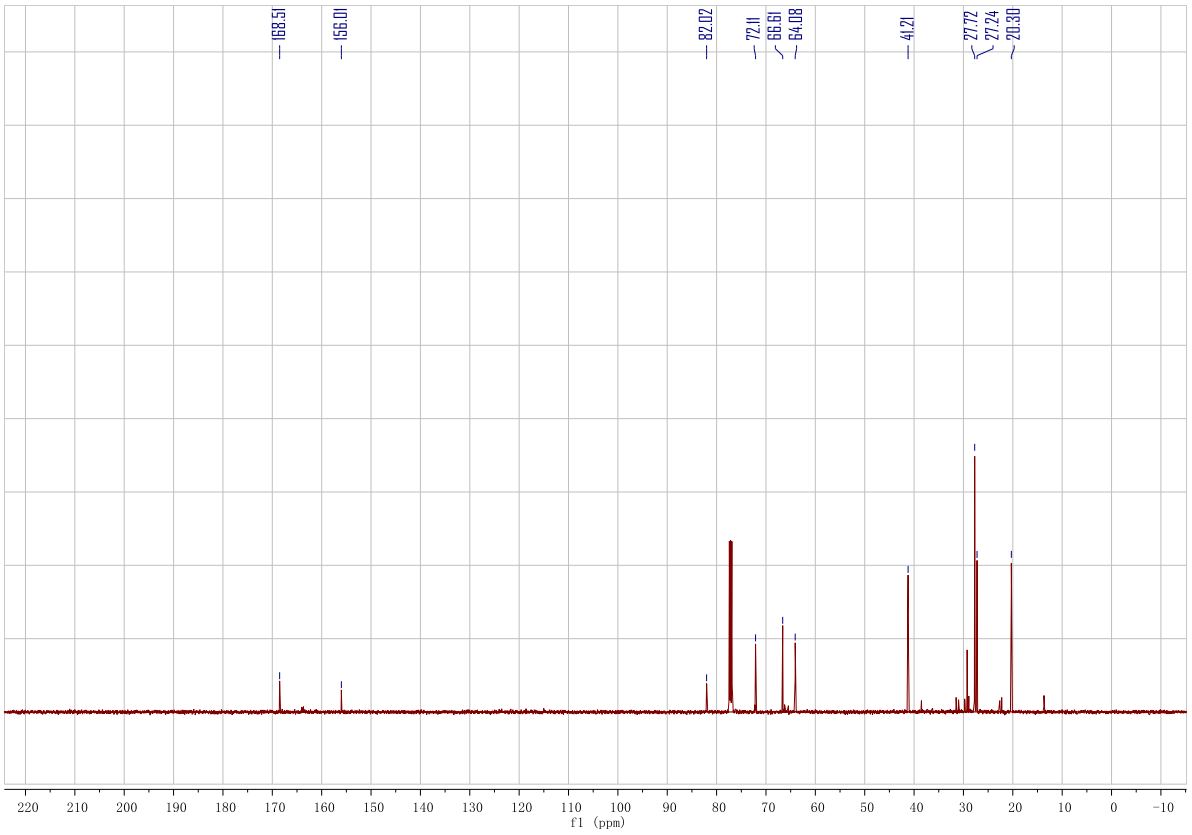
Compound **L11a** (1.0 mmol) was dissolved in 3 mL DCM and then 3 mL trifluoroacetic acid was added. The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The obtained oil was washed with hexane to give final product **L11**. (Note: Compound **L11** is not very stable at room temperature, we characterized the Boc-protected version **L11a,** which was later deprotected using TFA/DCM system.)

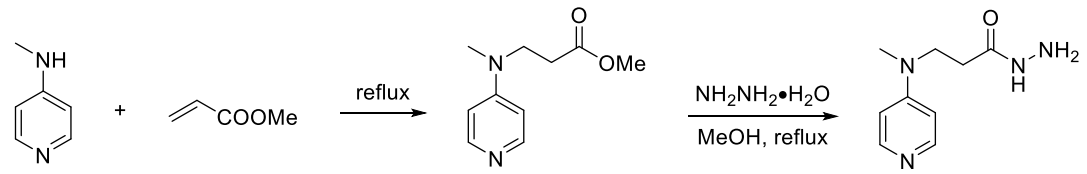


^{1}H NMR (500 MHz, CDCl3) δ 7.79 (s, 1H), 5.27 (t, J = 11.3 Hz, 1H), 4.41 (s, 2H), 2.27 (d, J = 11.2 Hz, 2H), 2.03 (dd, J = 16.1, 9.1 Hz, 2H), 1.50 (s, 6H), 1.48 (s, 9H), 1.43 (s, 6H).

^{13}C NMR (126 MHz, CDCl3) δ 168.51 (s), 156.01 (s), 82.02 (s), 72.11 (s), 66.61 (s), 64.08 (s), 41.21 (s), 27.72 (s), 27.24 (s), 20.30 (s).



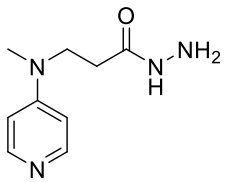




L12a **L12**

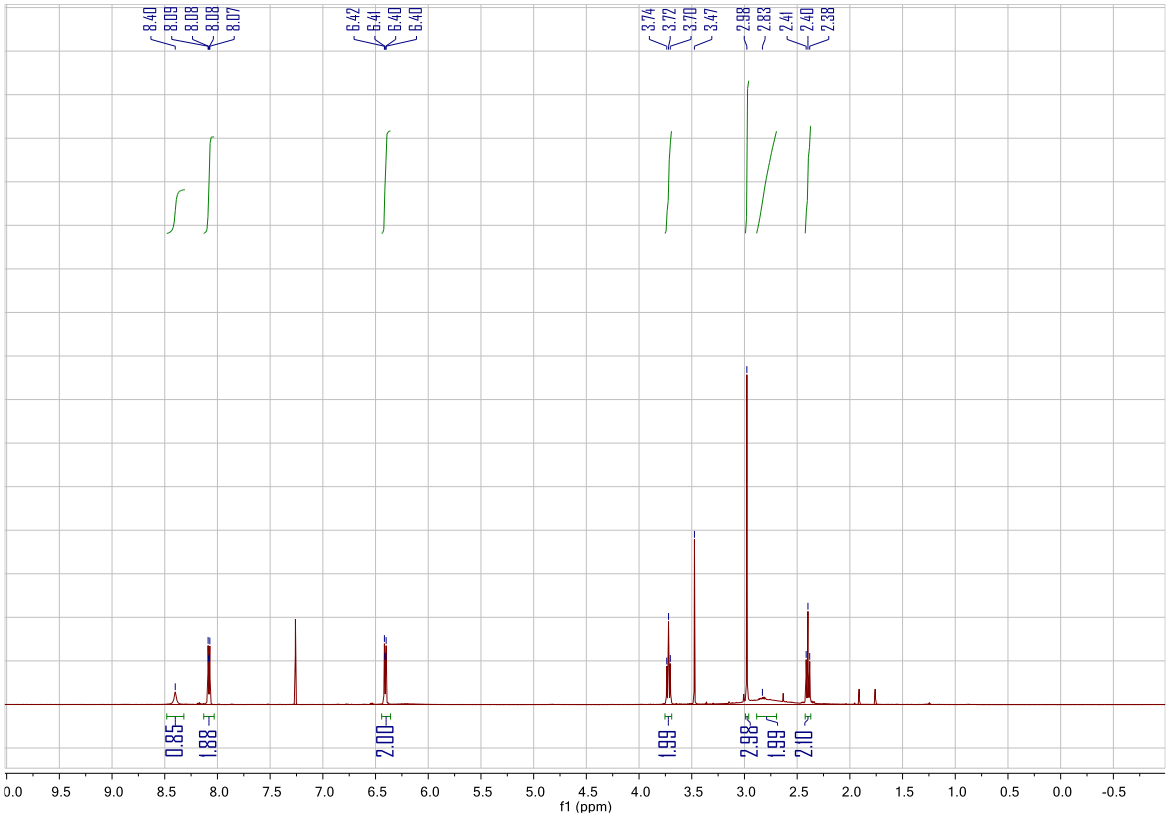
4-(methylamino) pyridine (5 mmol) was dissolved in methanol (10 mL) and methyl acrylate (100 mmol) was added into the reaction mixture and stirred under reflux for 18 hours. After the reaction was finished, the volatiles were removed under reduced pressure to afford crude product, which was then purified by flash column chromatograph to give the product **L12a**.

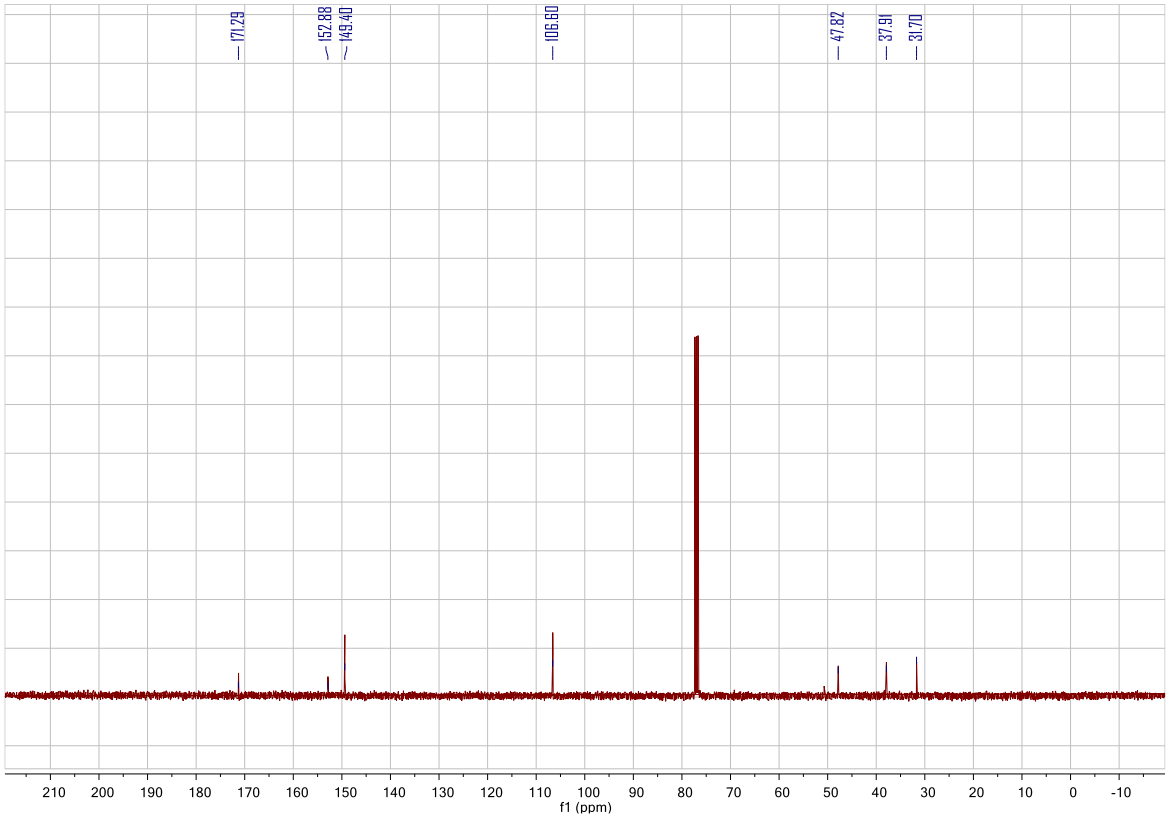
To a stirred solution of **L12a** (4 mmol) in methanol (15 mL) was added hydrazine monohydrate (40 mmol) and solution was stirred under reflux for 24 hours. The reaction mixture was evaporated in vacuo to remove volatiles and hexane was added for precipitation to give **L12** as white solid.

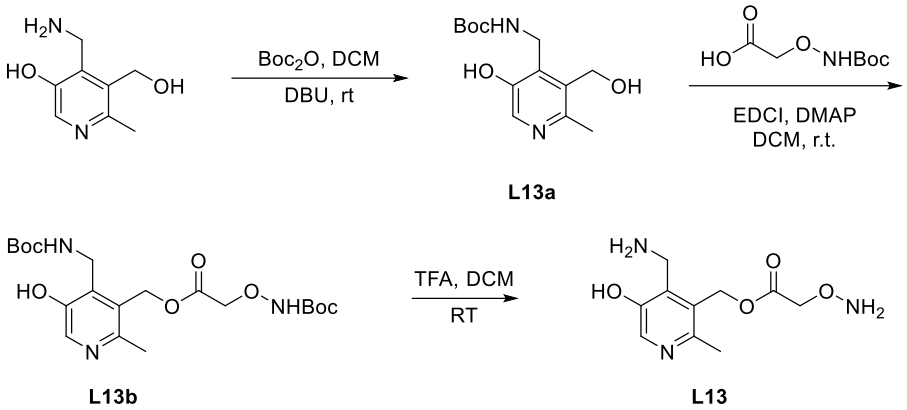


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (brs, 1H), 8.08 (dd, J = 5.0, 1.6 Hz, 2H), 6.41 (dd, J = 5.1, 1.6 Hz, 2H), 3.72 (t, J = 6.7 Hz, 2H), 2.98 (s, 3H), 2.83 (brs, 2H), 2.40 (t, J = 6.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.29 (s), 152.88 (s), 149.40 (s), 106.60 (s), 47.82 (s), 37.91 (s), 31.70 (s).



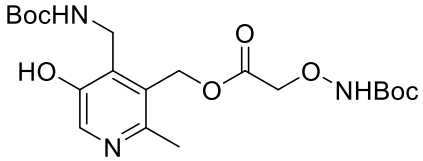




Pyridoxamine (10.0 mmol) was dissolved in 50 mL DCM and di-tert-butyl decarbonate (11 mmol) and DBU were added into the reaction mixture, which was stirred at room temperature overnight. The reaction was monitored by thin layer chromatography (TLC). And after the completion of the reaction, the mixture was diluted with water and extracted with EA. The combined organic phases were washed with saturated NaCl solution, dried and concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain the desired product **L13a**.

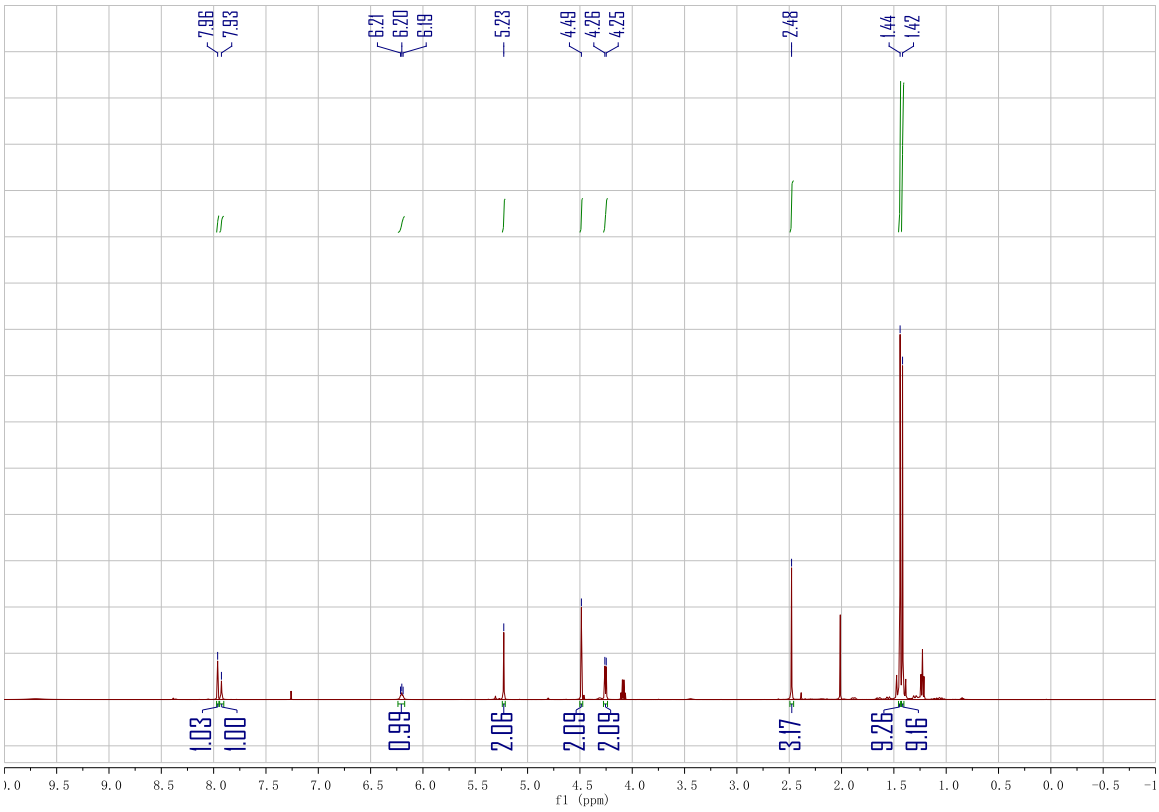
L13a (5.0 mmol), 2-(((tert-butoxycarbonyl)amino)oxy) acetic acid (6.0 mmol) and DCM (60 mL) were added to a dried two-necked flask under Argon atmosphere. The solution was cooled to 0 °C and then EDCI (6.0 mmol) and DMAP (0.1 mmol) was added. After the completion of the addition, the reaction mixture was stirred at room temperature overnight. After the completion of the reaction, the mixture was diluted with water and extracted with EA. The combined organic phases were washed with saturated $NaHCO_3$ and NaCl solution, dried over Na_2SO_4 and concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain the desired product **L13b**.

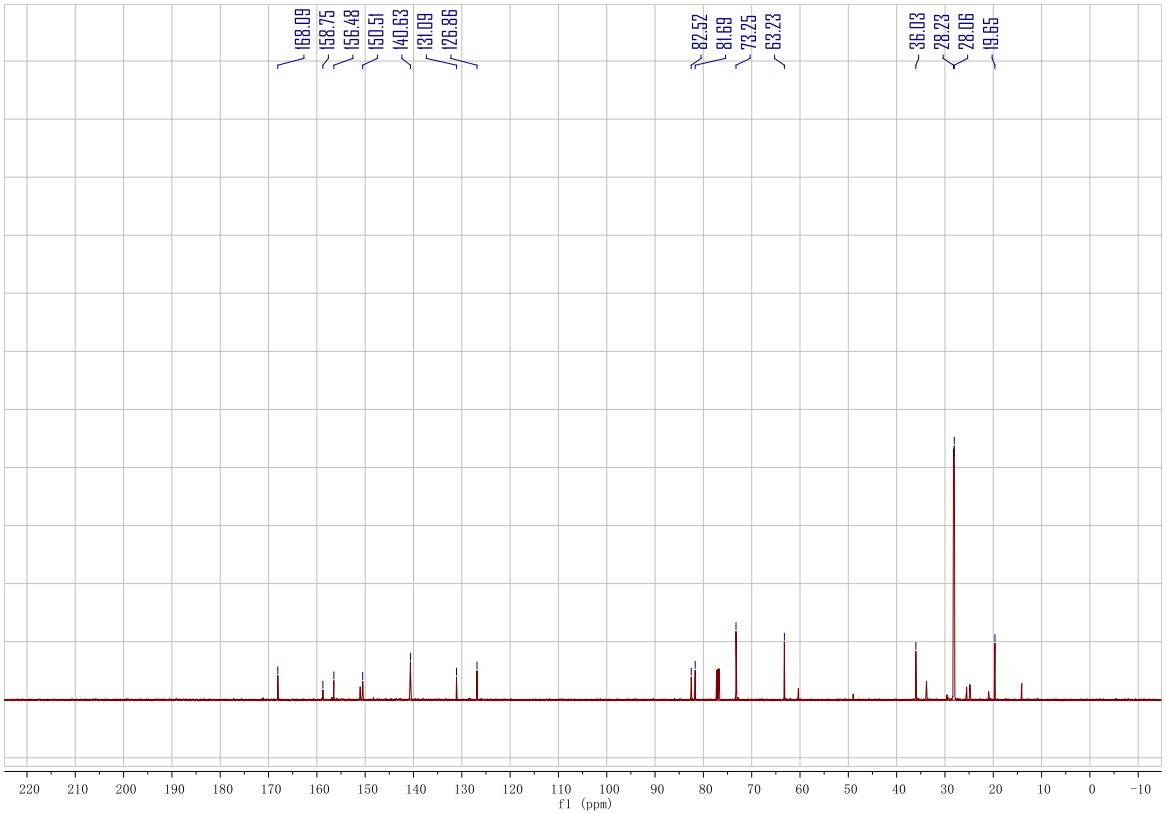
L13b (1.0 mmol) was dissolved in 3 mL DCM and then 3 mL trifluoroacetic acid was added. The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The obtained oil was washed with hexane to give final product **L13**. (Note: Compound **L13** is not very stable at room temperature, we characterized the Boc-protected version **L13b,** which was later deprotected using TFA/DCM system.)

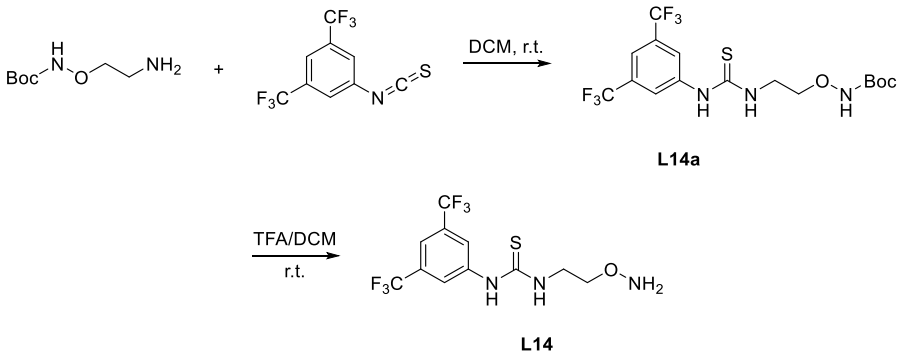


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.93 (s, 1H), 6.20 (t, *J* = 6.1 Hz, 1H), 5.23 (s, 2H), 4.49 (s, 2H), 4.26 (d, *J* = 6.7 Hz, 2H), 2.48 (s, 3H), 1.44 (s, 9H), 1.42 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.09 (s), 158.75 (s), 156.48 (s), 150.51 (s), 140.63 (s), 131.09 (s), 126.86 (s), 82.52 (s), 81.69 (s), 73.25 (s), 63.23 (s), 36.03 (s), 28.23 (s), 28.06 (s), 19.65 (s).

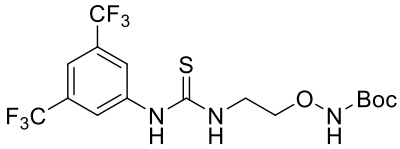

7.96
7.93
6.21
6.20
6.19
5.23
4.49
4.26
4.25
2.48
1.44
1.42
1.03
1.00
0.99
2.06
2.09
2.09
3.17
9.26
9.16
f1 (ppm)


168.09
158.75
156.48
150.51
140.63
131.09
126.86
82.52
81.69
73.25
63.23
36.03
28.23
28.06
19.65
f1 (ppm)



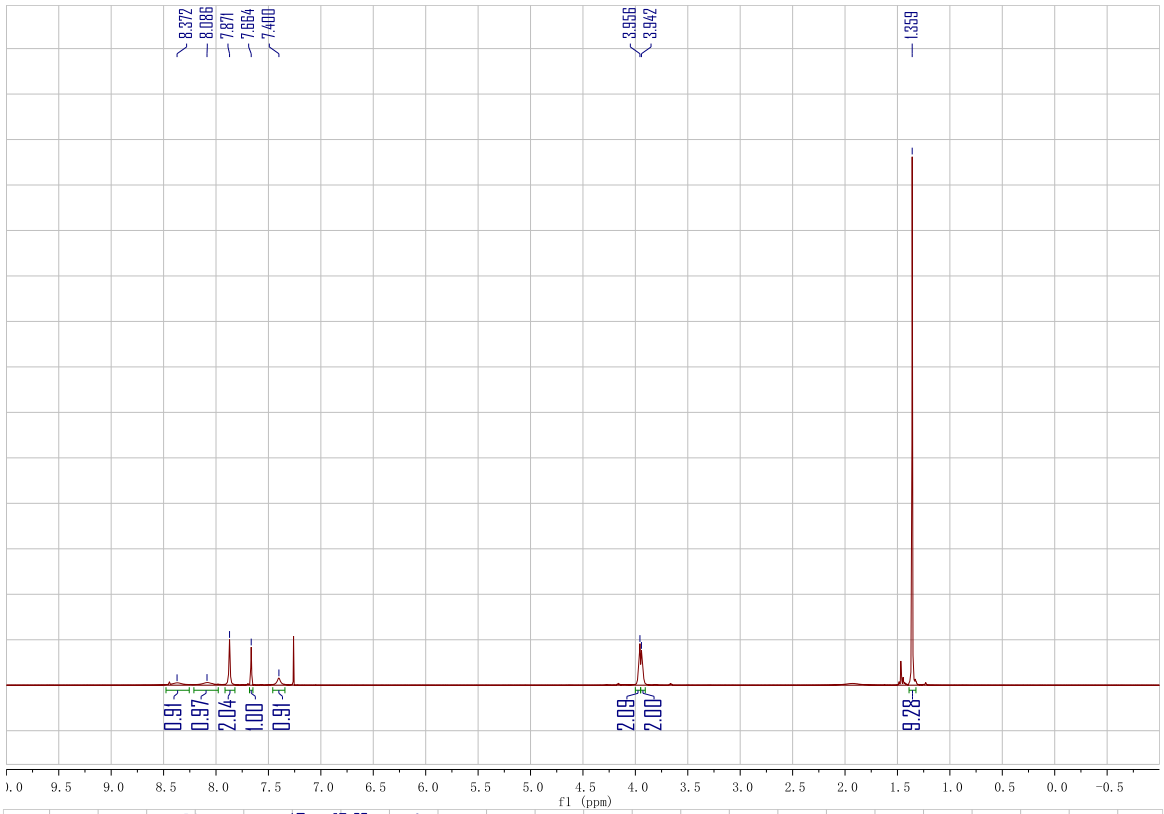
1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (2.0 mmol) and DCM (20 mL) were added to a dried two-necked flask under Argon atmosphere. The solution was cooled to 0 °C and then tert-butyl (2-aminoethoxy) carbamate (2.2 mmol) was added. After the completion of the addition, the reaction mixture was stirred at room temperature for 30 min. After the completion of the reaction, the mixture was concentrated under reduced pressure. The resulted crude was purified by flash column chromatograph to obtain **L14a** as a white solid.

L14a (1.0 mmol) was dissolved in 3 mL DCM and then 3 mL trifluoroacetic acid was added. The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure. The obtained oil was washed with hexane to give final product **L14**. (Note: Compound **L14** is not very stable at room temperature, we characterized the Boc-protected version **L14a,** which was later deprotected using TFA/DCM system.)



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (brs, 1H), 8.09 (brs, 1H), 7.87 (s, 2H), 7.66 (s, 1H), 7.40 (brs, 1H), 3.96 (s, 2H), 3.94 (s, 2H), 1.36 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.77 (s), 158.54 (s), 139.13 (s), 132.78 (q, *J* = 32.6 Hz), 124.24 (q, *J* = 2.9 Hz), 123.09 (q, *J* = 272.9 Hz), 119.18 (q, *J* = 2.4 Hz), 83.11 (s), 43.46 (s), 28.03 (s).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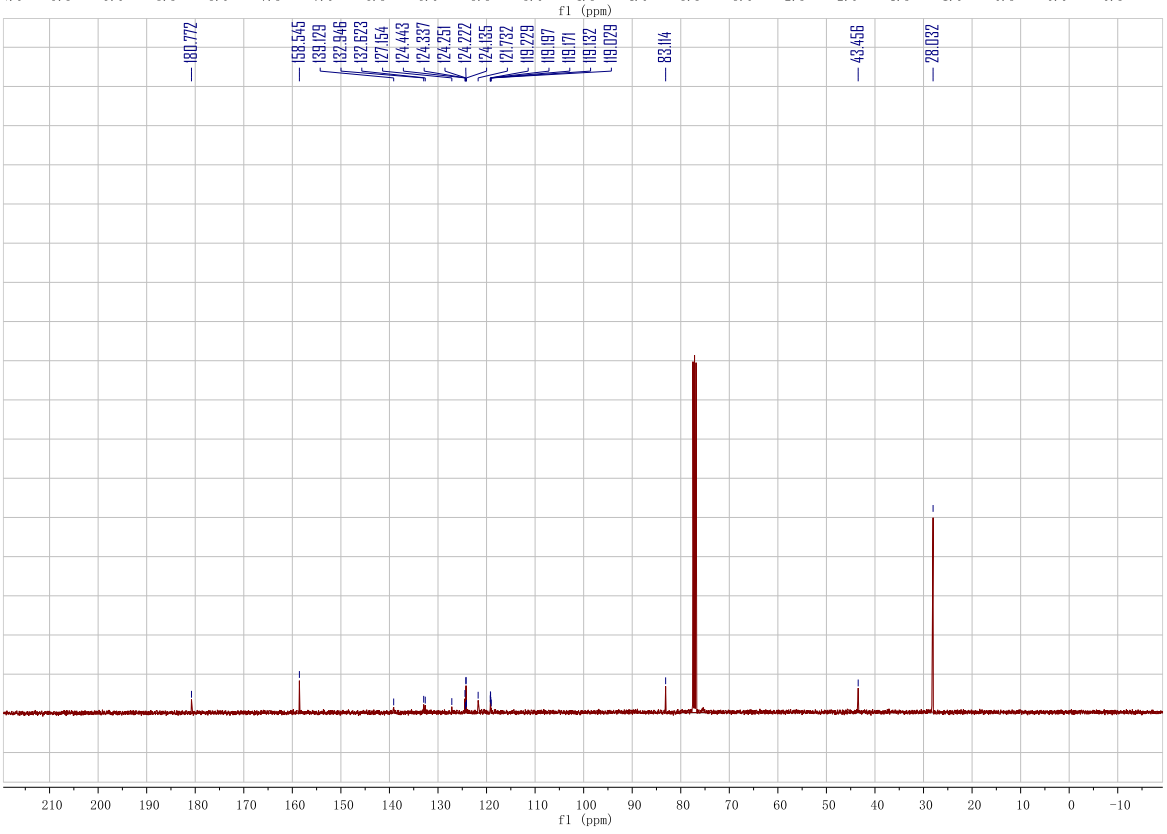
8.086
7.871
7.664
7.400
3.956
3.942
1.359
0.91
0.97
2.04
1.00
0.91
2.09
2.00
9.28
f1 (ppm)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132.623
127.154
124.443
124.337
124.251
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124.135
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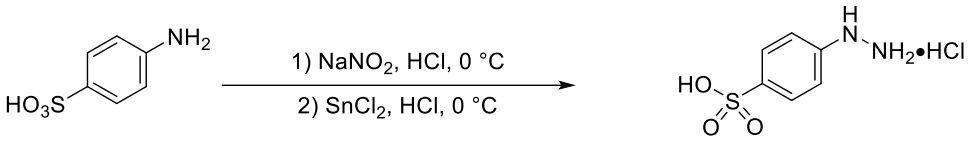
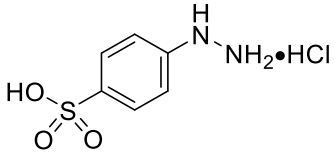
119.229
119.197
119.171
119.132
119.029
83.114
43.456
28.032
f1 (ppm)



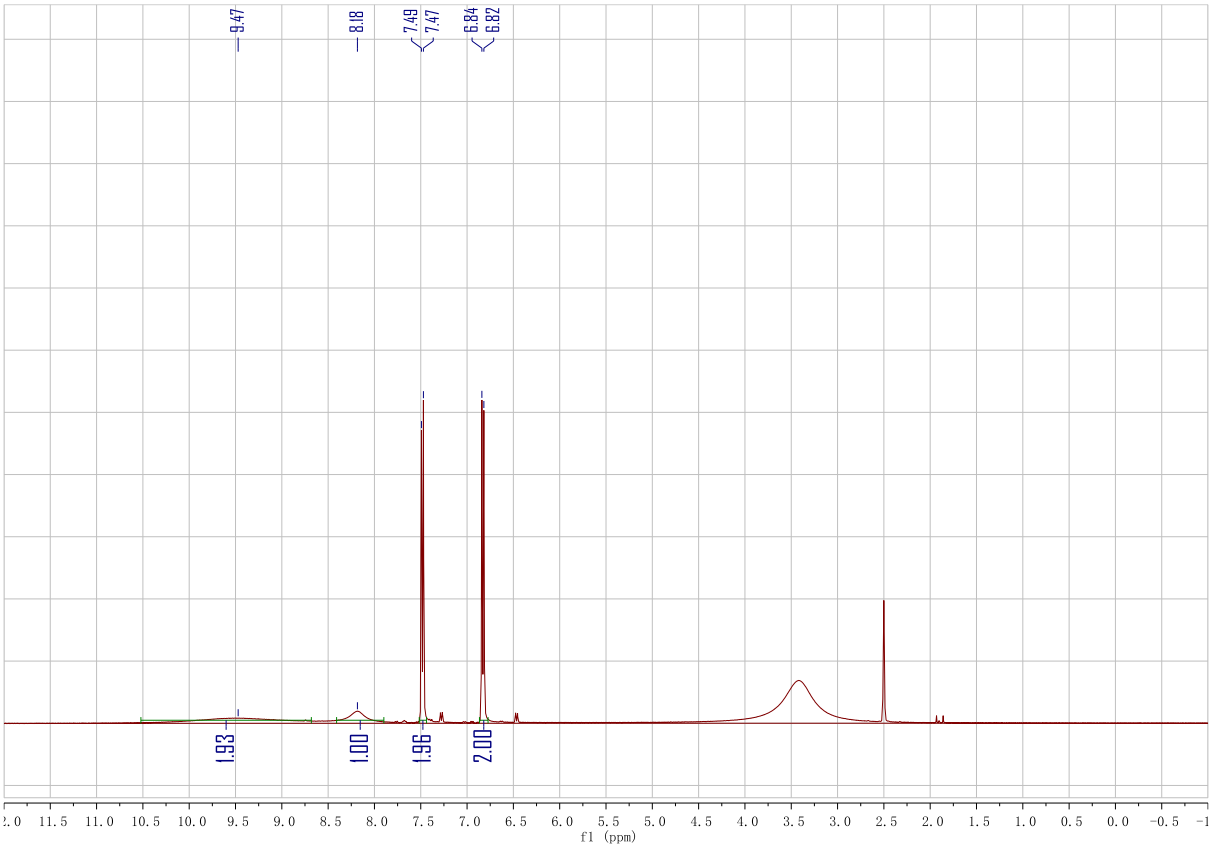
L15

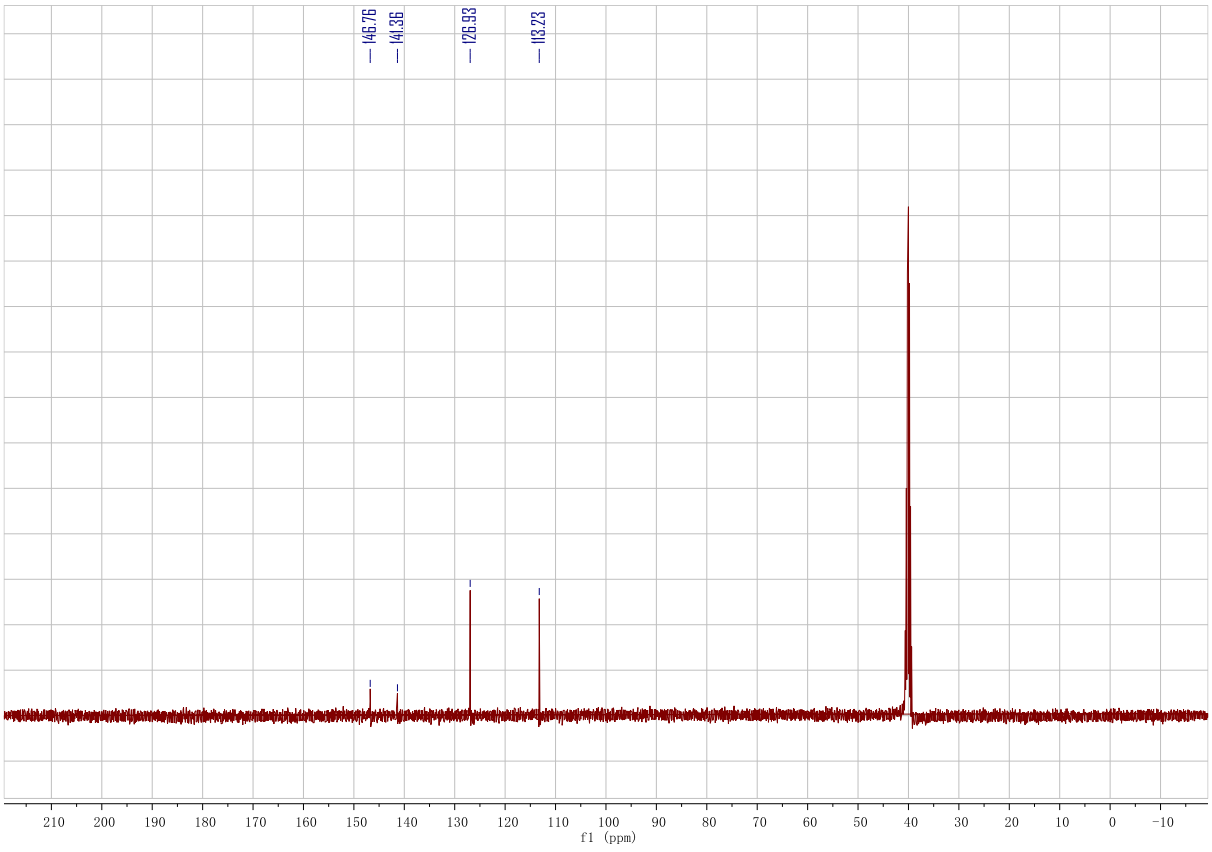
4-Aminobenzenesulfonic acid (6.0 mmol) and concentrated HCl (10 mL) were added to a round bottom flask. The solution was cooled to 0 °C and then $NaNO_2$ (6.38 mmol) was dissolved in ice-water (2.5 mL) and added dropwise for 15 min. After the completion of the addition, the reaction mixture was kept at 0 °C for 30 min. Then $SnCl_2$ (13.3 mmol) was dissolved in concentrated HCl (3.0mL) and added dropwise for 10 min. After the completion of the addition, the reaction mixture was kept at 0 °C and react for 1 hour. Then, the solution was filtered. The filtrate was dried under 45 °C overnight to get **L15** as a white solid.



^{1}H NMR (400 MHz, DMSO) δ 9.47 (brs, 1H), 8.18 (brs, 1H), 7.48 (d, J = 8.5 Hz, 1H), 6.83 (d, J = 8.6 Hz, 1H).

^{13}C NMR (101 MHz, DMSO) δ 146.76 (s), 141.36 (s), 126.93 (s), 113.23 (s).



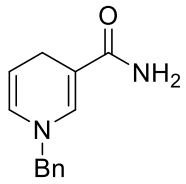


Nicotinamide (10 mmol) was dissolved in MeCN (20 mL) and benzyl bromide (12 mmol) was added into the reaction mixture and stirred under reflux overnight. After the reaction was finished, the solution was cooled to room temperature and volatiles were removed under reduced pressure to afford crude product. Diethyl ether (50 mL) was added for precipitation to give **L16a** as a brown solid.

Compound **L16a** (10 mmol) was dissolved in water (30 mL) and sodium bicarbonate (25 mmol) was added under Argon atmosphere. The solution was stirred for 20 min, then sodium dithionite (25 mmol) was added slowly into the suspension and stirred for 4 hours without light. After the reaction was finished, cold water (50 mL) was added and filtered to get the undissolved solid. Diethyl ether (50 mL) was added for precipitation to give **L16b** as a brown solid.

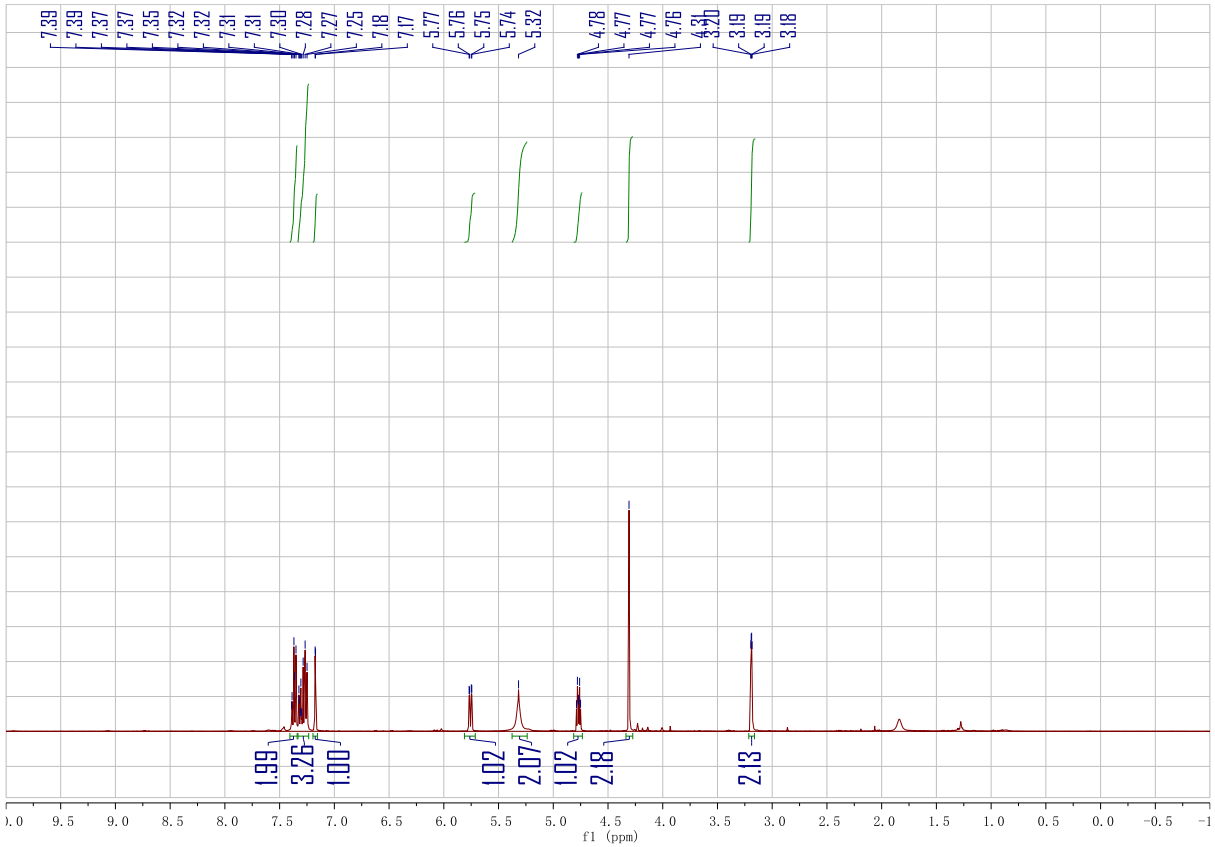
To a stirred solution of **L16b** (5 mmol) in ethanol (15 mL) was added hydrazine monohydrate (40 mmol) and solution was stirred under reflux for 24 hours. The reaction mixture was evaporated in vacuo to remove volatiles and hexane was added for precipitation to give **L16** as brown solid.

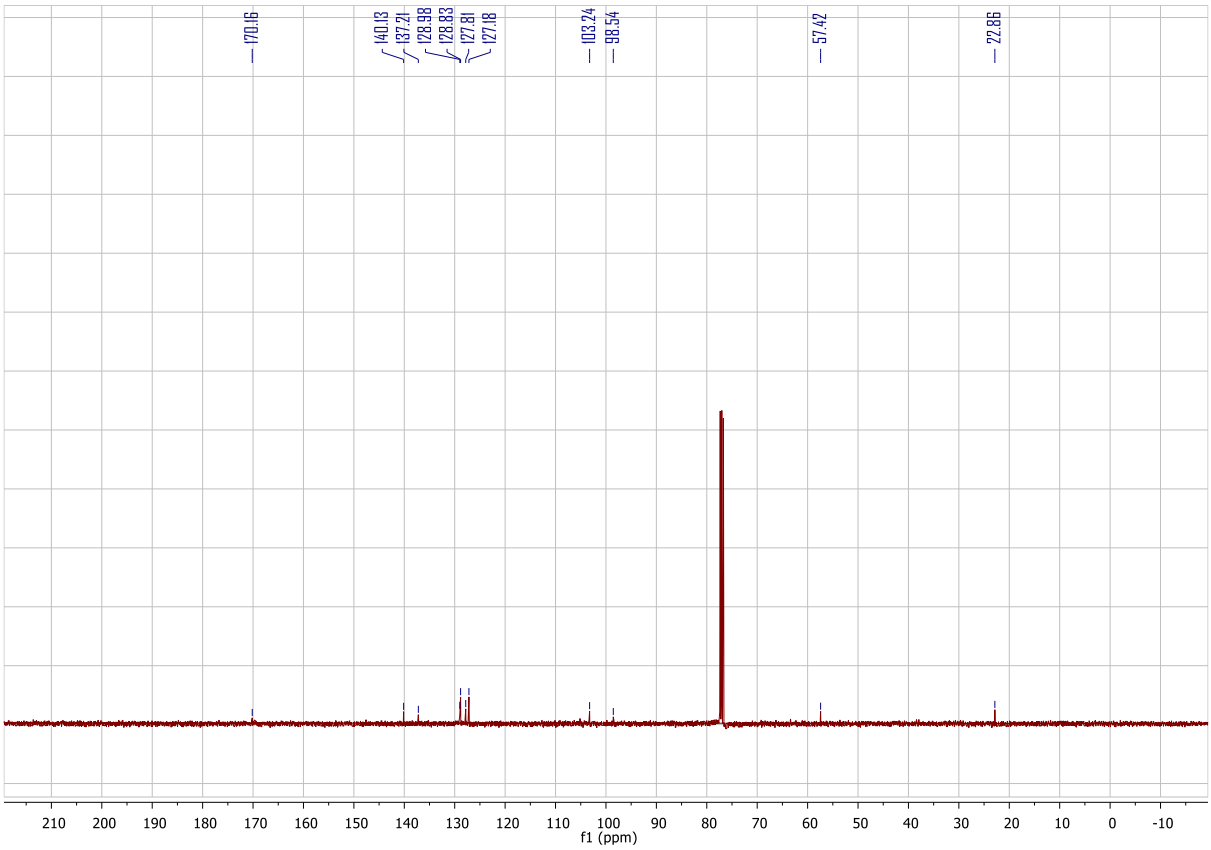
(Note: Compound **L16** is not very stable at room temperature, we characterized the compound **L16b**, which can be reliably transformed to **L16** using a reported protocol[7])



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.30 (ddd, *J* = 19.6, 9.5, 4.1 Hz, 3H), 7.17 (d, *J* = 1.4 Hz, 1H), 5.76 (dd, *J* = 8.1, 1.7 Hz, 1H), 5.32 (brs, 2H), 4.77 (dt, *J* = 7.9, 3.4 Hz, 1H), 4.31 (s, 2H), 3.19 (dd, *J* = 3.2, 1.5 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.16 (s), 140.13 (s), 137.21 (s), 128.98 (s), 128.83 (s), 127.81 (s), 127.18 (s), 103.24 (s), 98.54 (s), 57.42 (s), 22.86 (s).

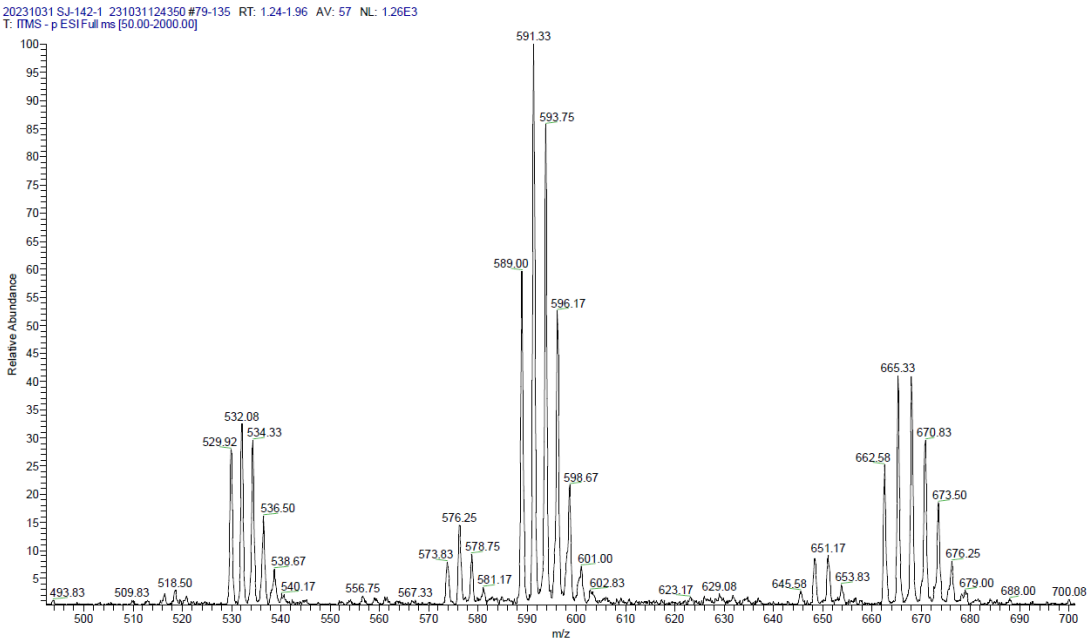



170.16
140.13
137.21
128.98
128.83
127.81
127.18
103.24
98.54
57.42
27.86
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Mass spectrometry analysis

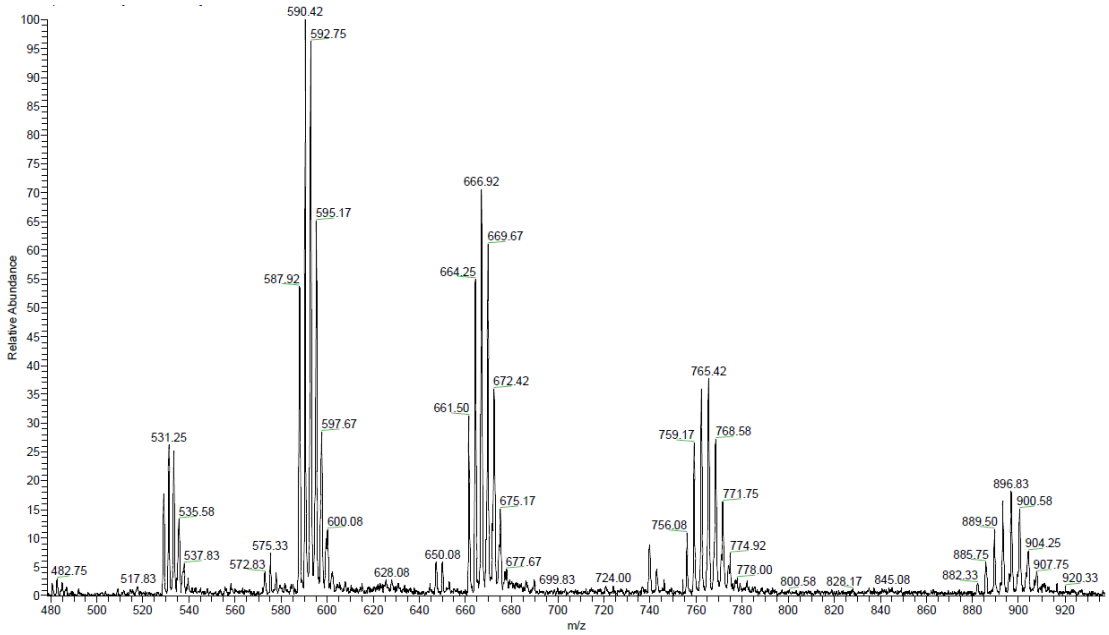
ESI Analysis: hp-CG DNA (oppo A)-L1

Species	Calculated (m/z)	Observed (m/z)
[hp-CG DNA (oppo A)-L1]$^{10-}$	530.05	529.92
[hp-CG DNA (oppo A)-L1]$^{9-}$	589.06	589.00
[hp-CG DNA (oppo A)-L1]$^{8-}$	662.81	662.58



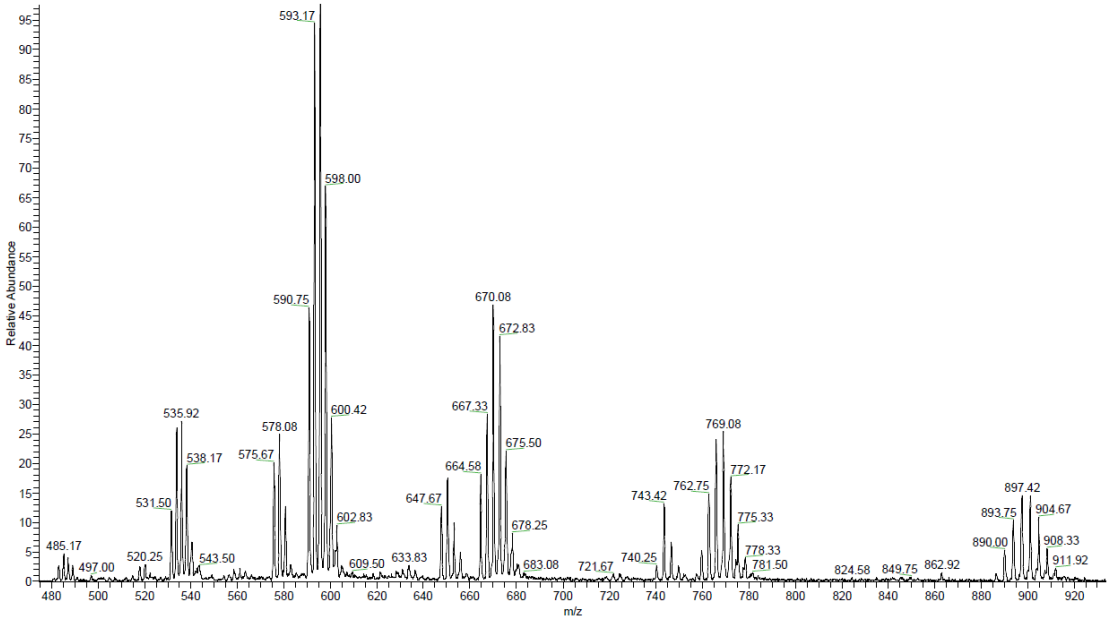
ESI Analysis: hp-CG DNA (oppo T)-L1

Species	Calculated (m/z)	Observed (m/z)
[hp-CG DNA (oppo T)-L1]$^{10-}$	529.15	529.20
[hp-CG DNA (oppo T)-L1]$^{9-}$	588.06	587.92
[hp-CG DNA (oppo T)-L1]$^{8-}$	661.69	661.50
[hp-CG DNA (oppo T)-L1]$^{7-}$	756.36	756.08
[hp-CG DNA (oppo T)-L1]$^{6-}$	882.58	882.33



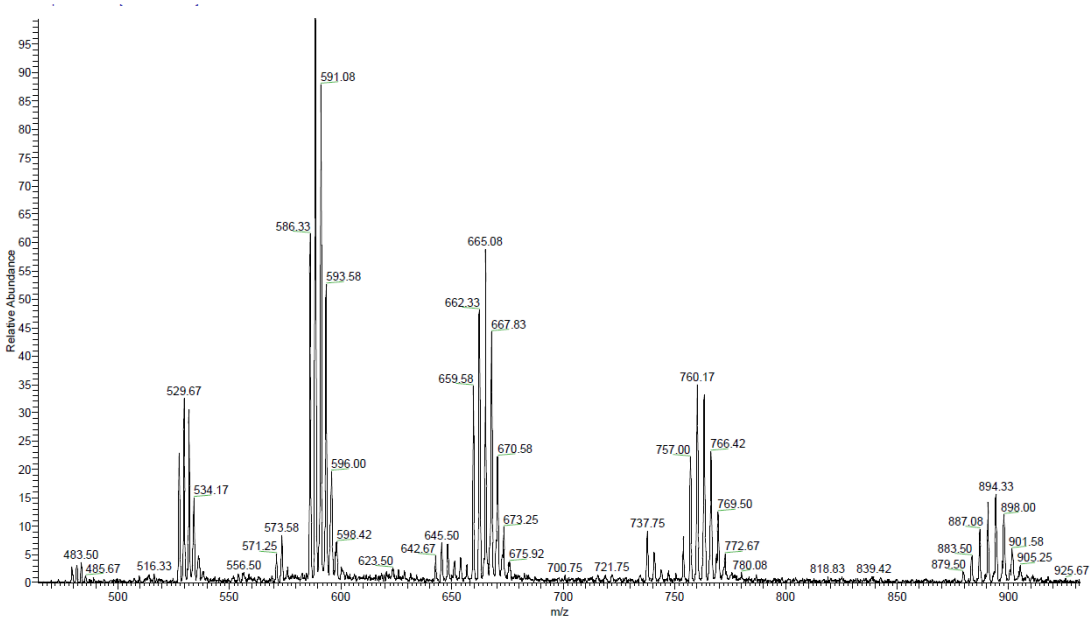
ESI Analysis: hp-CG DNA (oppo G)-L1

Species	Calculated (m/z)	Observed (m/z)
[hp-CG DNA (oppo G)-L1]$^{10-}$	531.65	531.50
[hp-CG DNA (oppo G)-L1]$^{9-}$	590.83	590.75
[hp-CG DNA (oppo G)-L1]$^{8-}$	664.81	664.85
[hp-CG DNA (oppo G)-L1]$^{7-}$	759.93	760.05



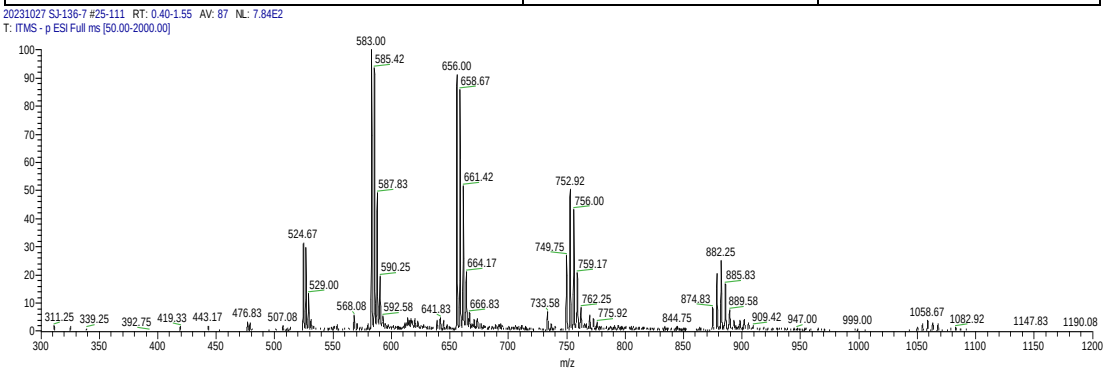
ESI Analysis: hp-CG DNA (oppo C)-L1

Species	Calculated (m/z)	Observed (m/z)
[hp-CG DNA (oppo C)-L1]$^{10-}$	527.65	527.50
[hp-CG DNA (oppo C)-L1]$^{9-}$	586.39	586.33
[hp-CG DNA (oppo C)-L1]$^{8-}$	659.81	659.58
[hp-CG DNA (oppo C)-L1]$^{7-}$	754.21	754.13
[hp-CG DNA (oppo C)-L1]$^{6-}$	880.08	879.50



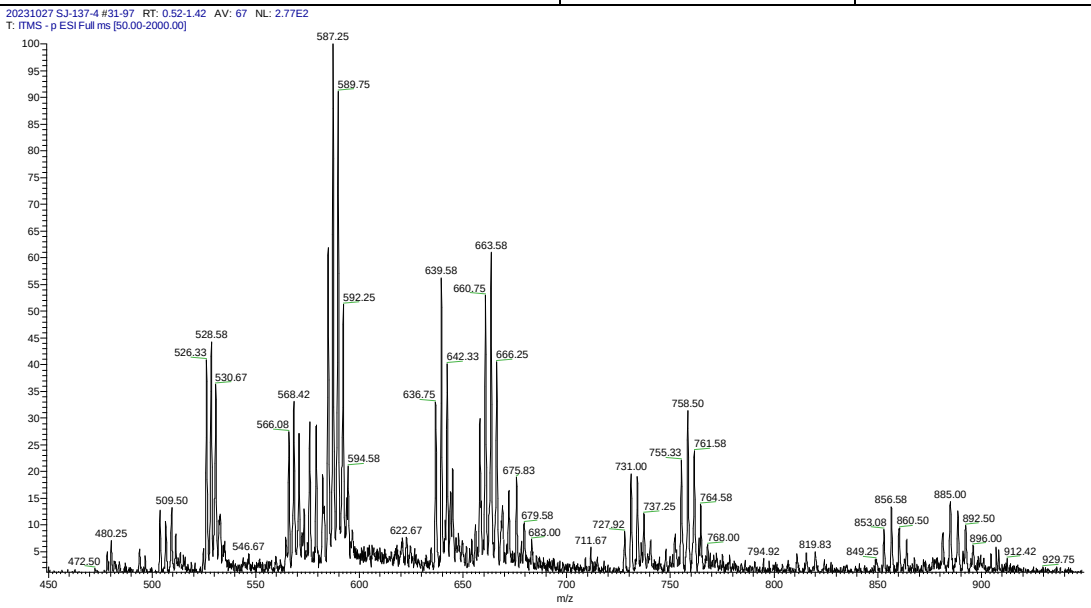
ESI Analysis: hp-CG DNA (oppo C)-L4

Species	Calculated (m/z)	Observed (m/z)
[hp-CG DNA (oppo C)-L4]$^{10-}$	524.8	524.7
[hp-CG DNA (oppo C)-L4]$^{9-}$	583.2	583.0
[hp-CG DNA (oppo C)-L4]$^{8-}$	656.2	656.0
[hp-CG DNA (oppo C)-L4]$^{7-}$	750.1	749.8
[hp-CG DNA (oppo C)-L4]$^{6-}$	875.3	874.8



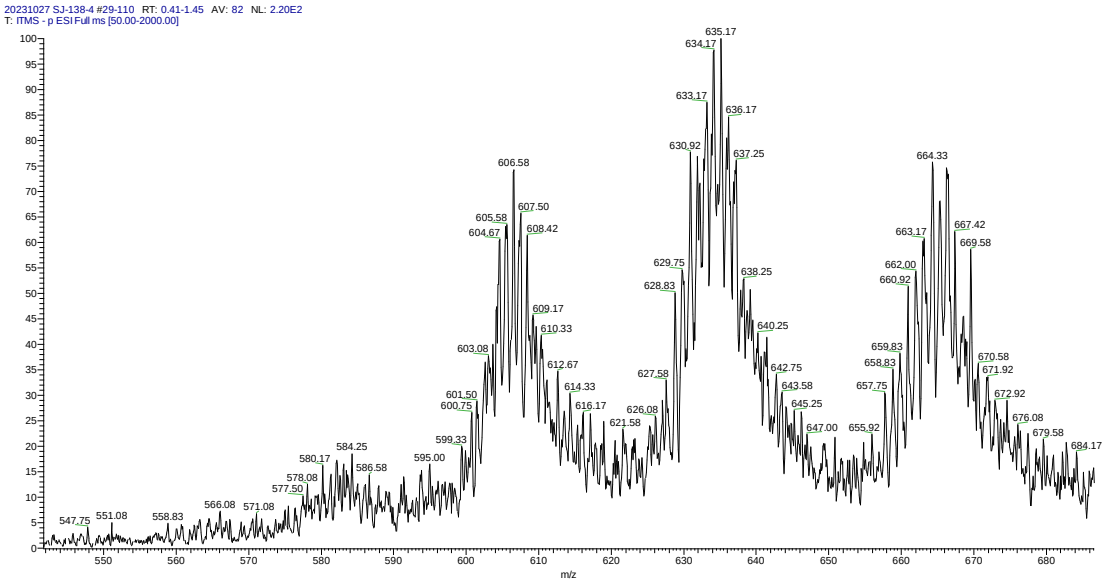
ESI Analysis: hp-GG DNA-L16 (The other set of peaks come from the decomposition of hydrazone during ESI experiment)

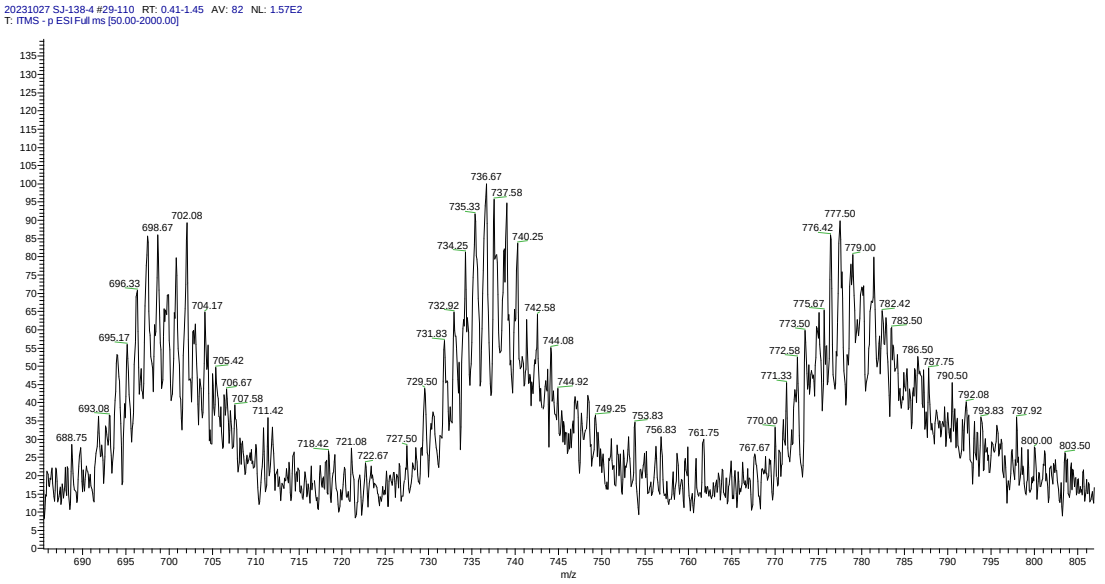
Species	Calculated (m/z)	Observed (m/z)
$[\text{hp-GG DNA-L16}]^{10-}$	530.5	530.7
$[\text{hp-GG DNA-L16}]^{9-}$	589.5	589.8
$[\text{hp-GG DNA-L16}]^{8-}$	663.3	663.6
$[\text{hp-GG DNA-L16}]^{7-}$	758.2	758.5
$[\text{hp-GG DNA-L16}]^{6-}$	884.8	885.0



ESI Analysis: DNA Aptamer-1-L13

Species	Calculated (m/z)	Observed (m/z)
$[\text{DNA Aptamer-1-L13}]^{23-}$	598.64	599.33
$[\text{DNA Aptamer-1-L13}]^{22-}$	625.90	626.08
$[\text{DNA Aptamer-1-L13}]^{21-}$	655.75	655.92
$[\text{DNA Aptamer-1-L13}]^{20-}$	688.59	688.75
$[\text{DNA Aptamer-1-L13}]^{19-}$	724.88	727.5
$[\text{DNA Aptamer-1-L13}]^{18-}$	766.21	767.67


20231027 SJ-138-4 #29-110 RT: 0.41-1.45 AV: 82 NL: 2.20E2
T: ITMS - p ESI Full ms [50.00-2000.00]
m/z

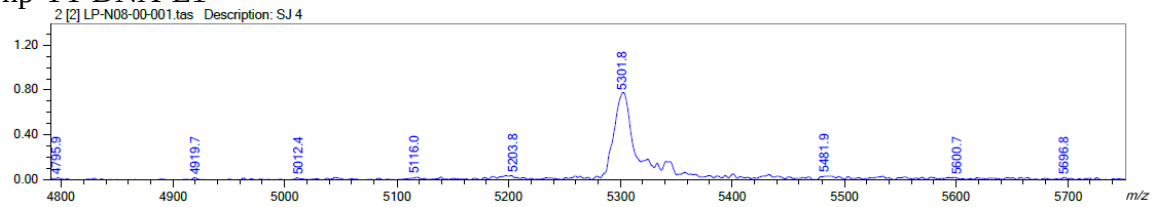

20231027 SJ-138-4 #29-110 RT: 0.41-1.45 AV: 82 NL: 1.57E2
T: ITMS - p ESI Full ms [50.00-2000.00]
m/z

MALDI-TOF Analysis

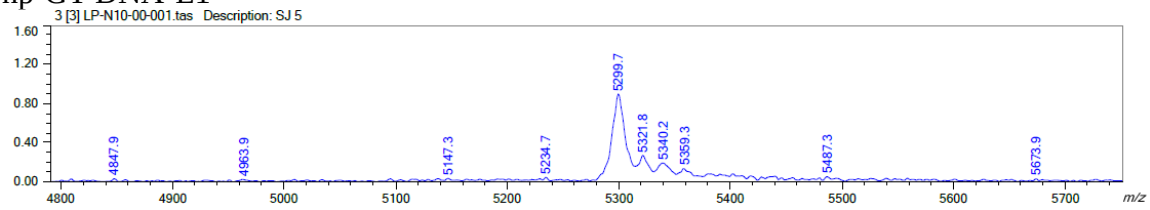
Entry	Name	Calculated	Observed
1	hp-TT DNA-L1	5299.5	5301.8
2	hp-GT DNA-L1	5300.5	5299.7
3	hp-GC DNA-L1	5301.5	5302.9
4	hp-TA DNA-L1	5299.5	5302.5
5	hp-GA DNA-L1	5300.5	5298.6
6	hp-TG DNA-L1	5300.5	5296.7
7	hp-GG DNA-L1	5301.5	5296.6
8	hp-AC DNA-L1	5300.5	5300.2
9	hp-AA DNA-L1	5299.5	5288.7
10	hp-CC DNA-L1	5301.5	5301.4
11	hp-CT DNA-L1	5300.5	5300.3
12	hp-TC DNA-L1	5300.5	5302.7
13	hp-CA DNA-L1	5300.5	5300.5
14	hp-AT DNA-L1	5299.5	5304.2
15	hp-AG DNA-L1	5300.5	5303.6
16	hp-CG DNA (oppo C)-L2	5327.6	5325.7
17	hp-CG DNA (oppo C)-L3	5285.5	5283.8
18	hp-GG DNA-L5	5364.5	5364.3
19	hp-GG DNA-L6	5421.5	5423.5
20	hp-GG DNA-L7	5450.6	5458.8
21	hp-GG DNA-L8	5450.5	5448.8
22	hp-GG DNA-L9	5663.8	5663.2
23	hp-GG DNA-L10	5214.4	5212.9
24	hp-GG DNA-L11	5331.6	5342.9
25	hp-GG DNA-L12	5278.4	5276.1
26	hp-GG DNA-L13	5427.5	5426.5
27	hp-GG DNA-L14	5433.5	5427.1
28	hp-GG DNA-L15	5274.4	5288.1
29	DNA Aptamer-1-L1	13765.9	13781.3
30	DNA Aptamer-1-L5	13828.9	13833.1
31	DNA Aptamer-1-L7	13914.9	13917.7
32	DNA Aptamer-1-L6	13885.9	13893.2
33	DNA Aptamer-2-L6	13885.9	13895.3
34	DNA Aptamer-3-L6	13885.9	13900.1

35	DNA Aptamer-4-L6	13885.9	13897.8

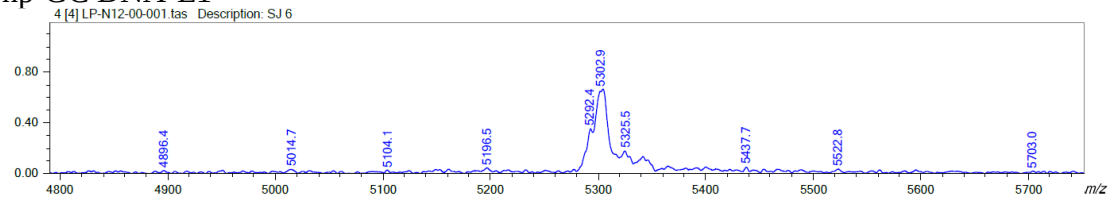
hp-TT DNA-L1



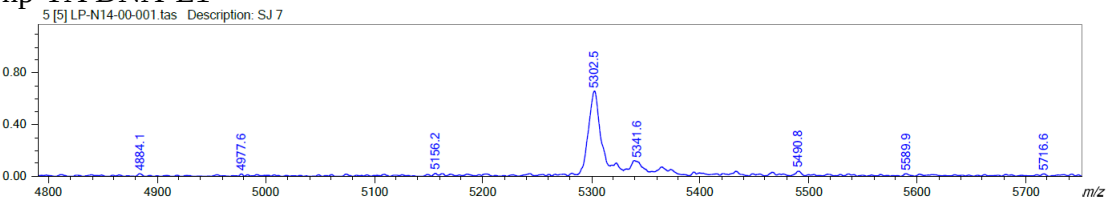
hp-GT DNA-L1



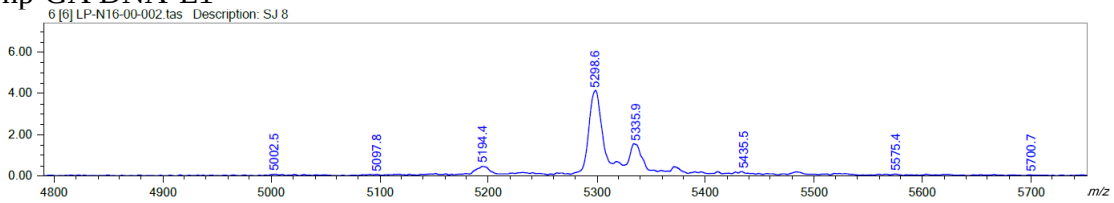
hp-GC DNA-L1



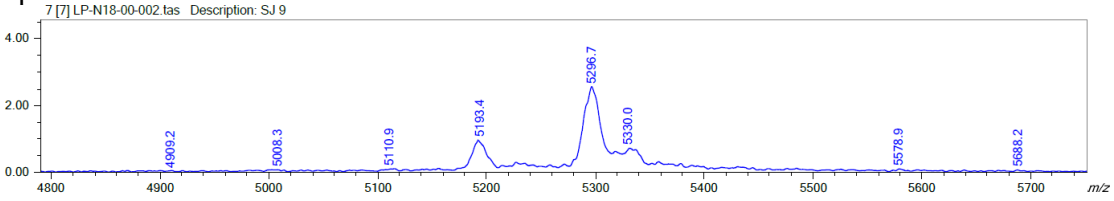
hp-TA DNA-L1



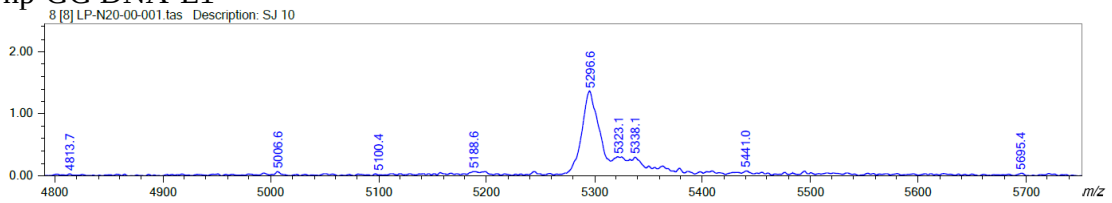
hp-GA DNA-L1



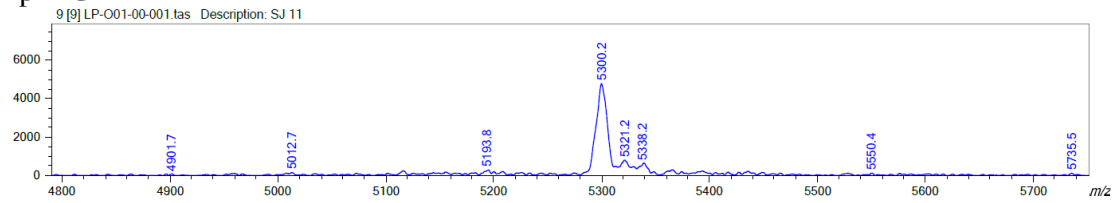
hp-TG DNA-L1



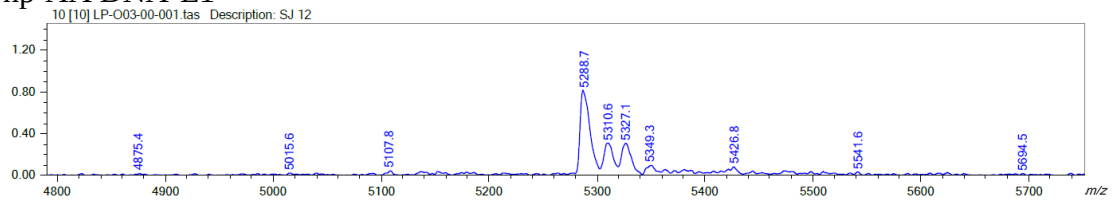
hp-GG DNA-L1



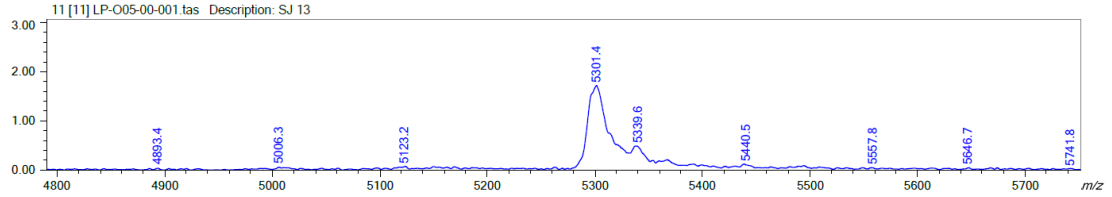
hp-AC DNA-L1



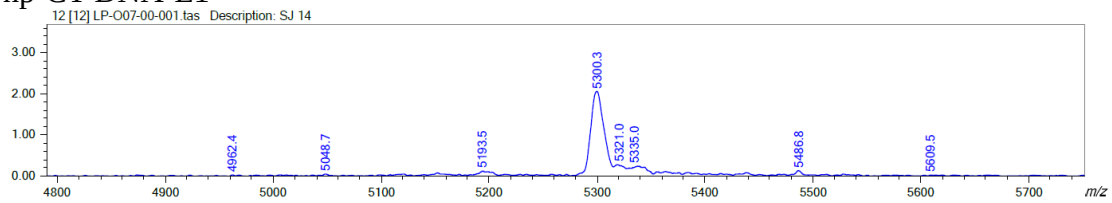
hp-AA DNA-L1



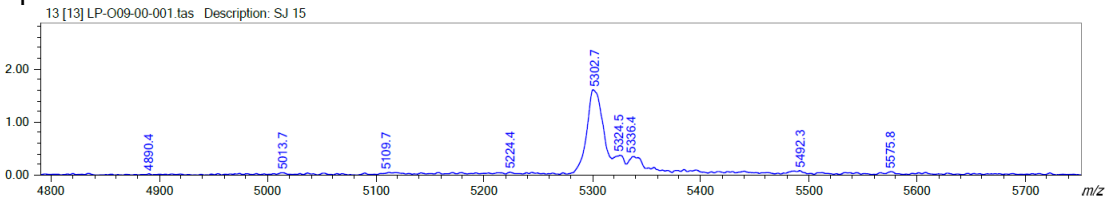
hp-CC DNA-L1



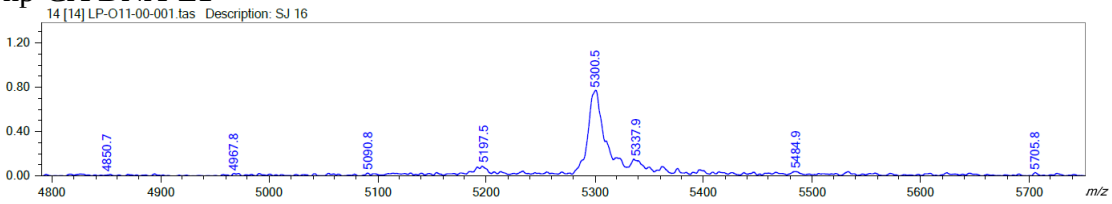
hp-CT DNA-L1



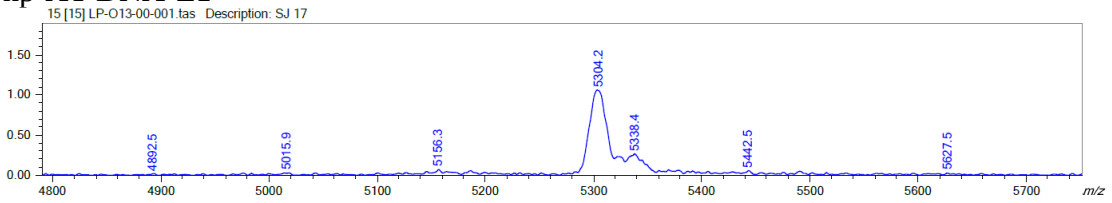
hp-TC DNA-L1



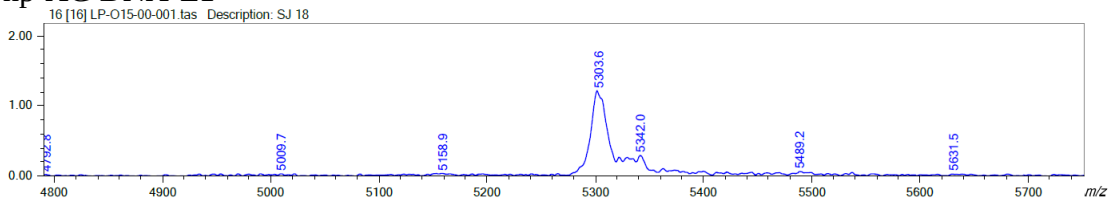
hp-CA DNA-L1



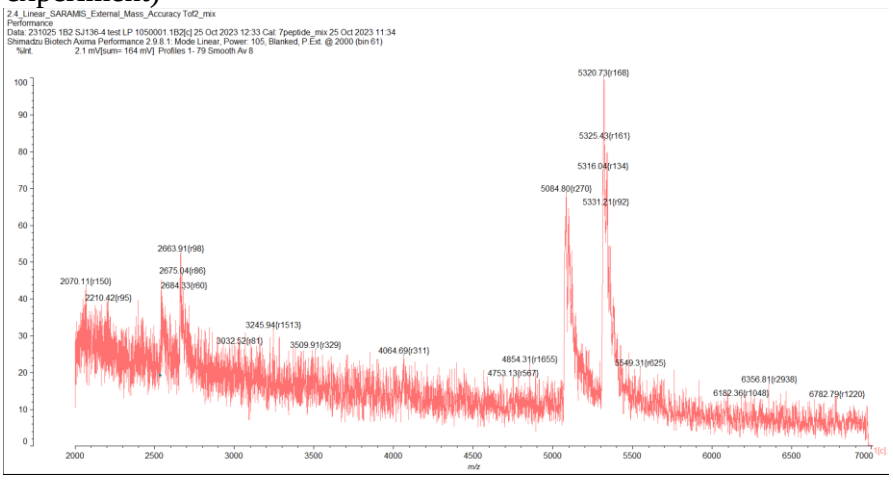
hp-AT DNA-L1



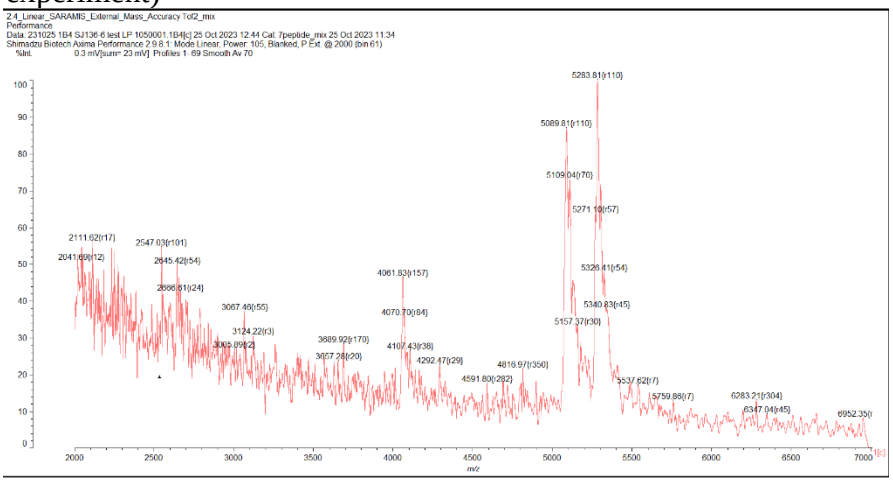
hp-AG DNA-L1



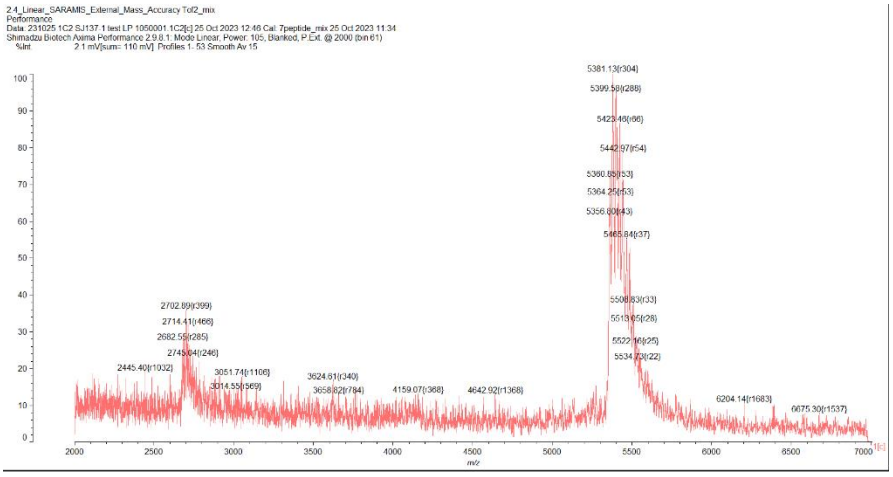
hp-CG DNA (oppo C)-L2 (The other peak comes from the decomposition of hydrazone during MALDI-TOF experiment)



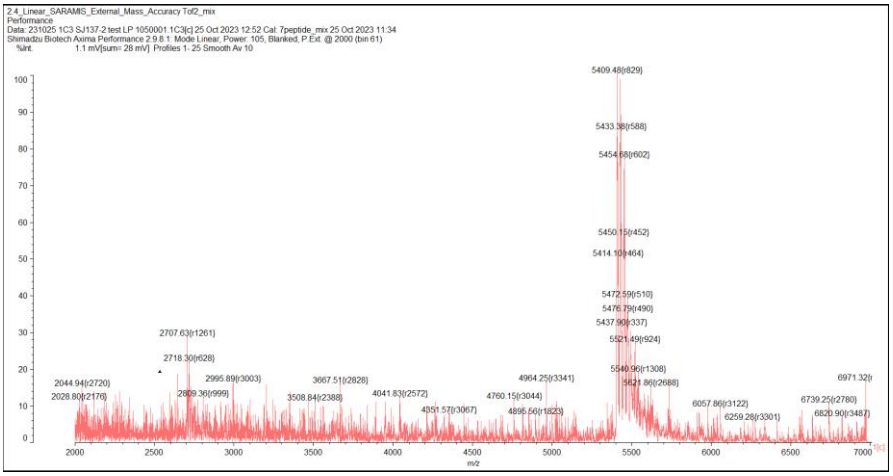
hp-CG DNA (oppo C)-L3 (The other peak comes from the decomposition of hydrazone during MALDI-TOF experiment)



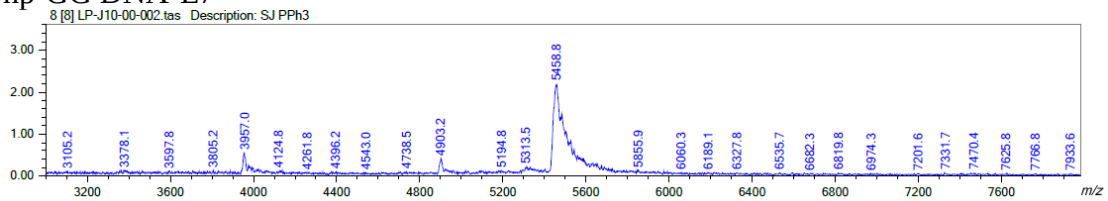
hp-GG DNA-L5



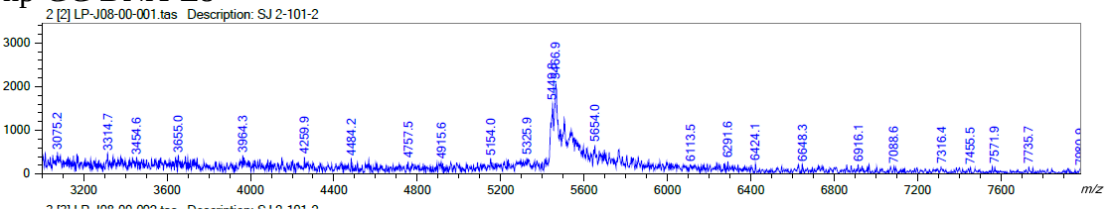
hp-GG DNA-L6



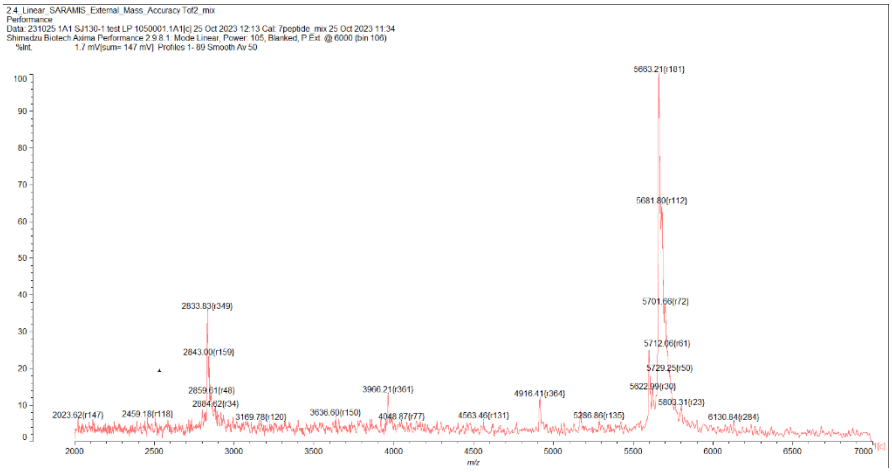
hp-GG DNA-L7



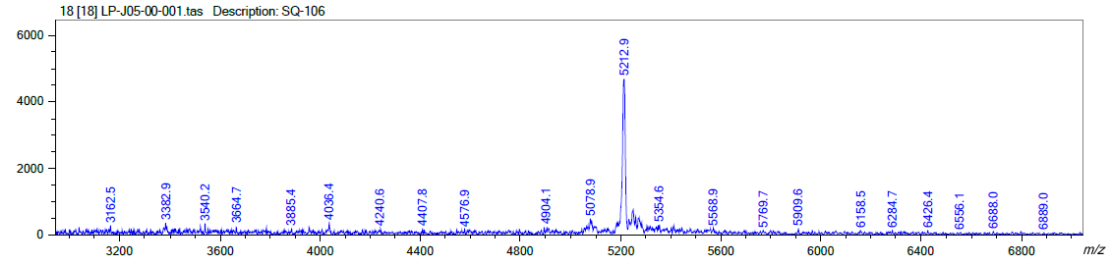
hp-GG DNA-L8



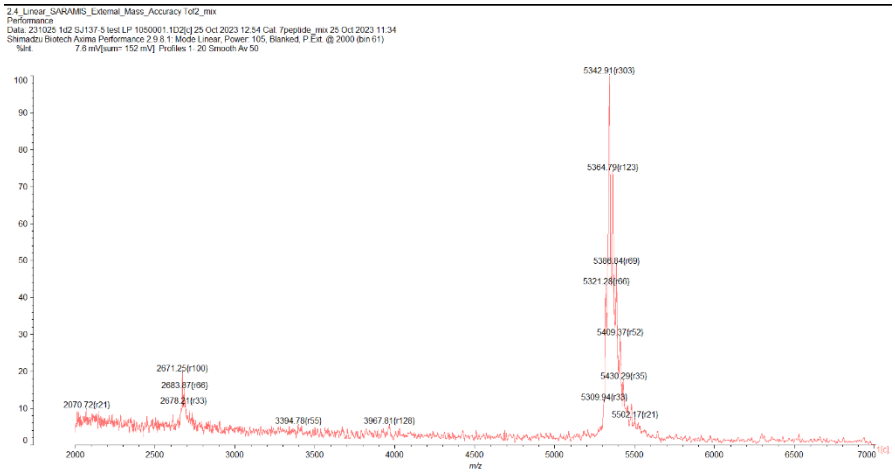
hp-GG DNA-L9



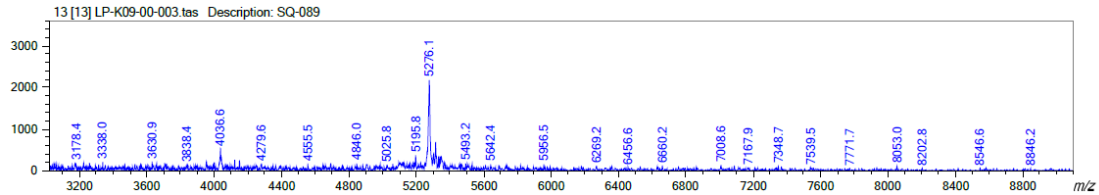
hp-GG DNA-L10



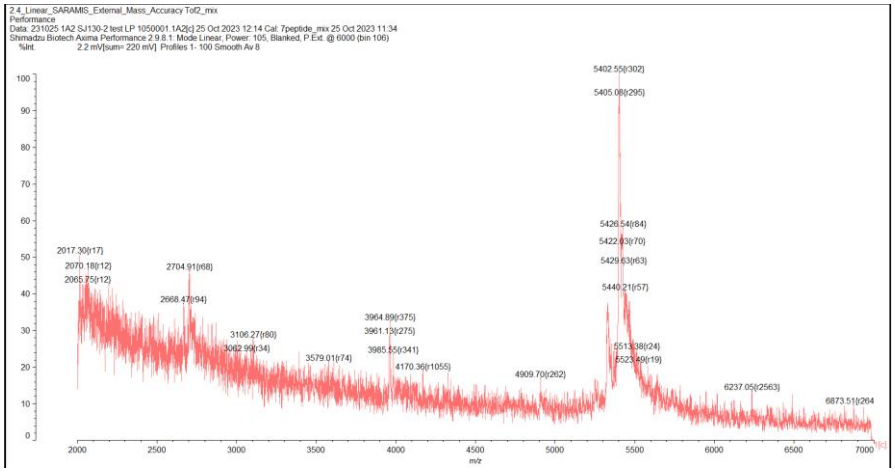
hp-GG DNA-L11



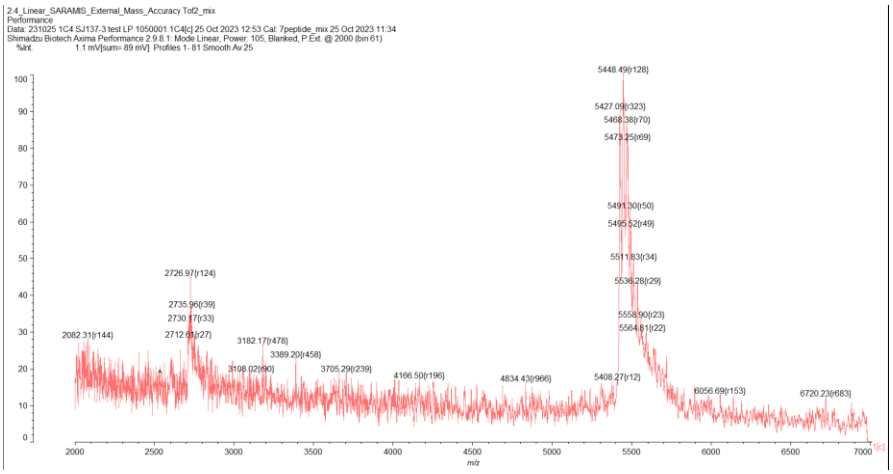
hp-GG DNA-L12



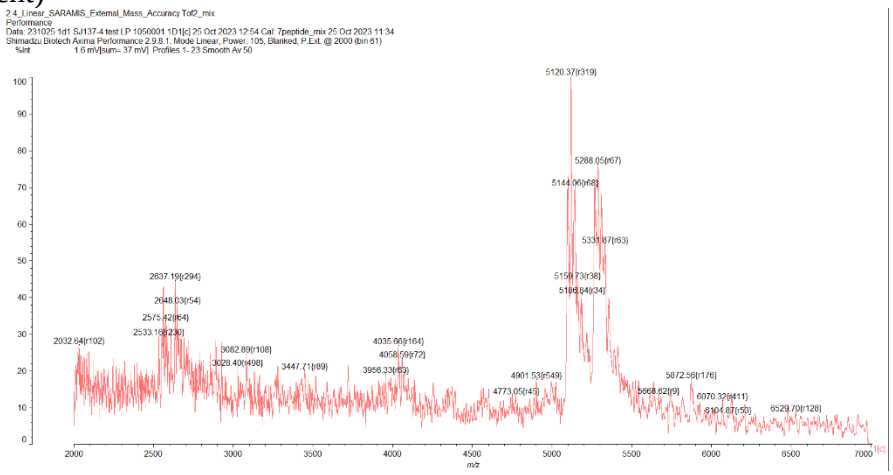
hp-GG DNA-L13



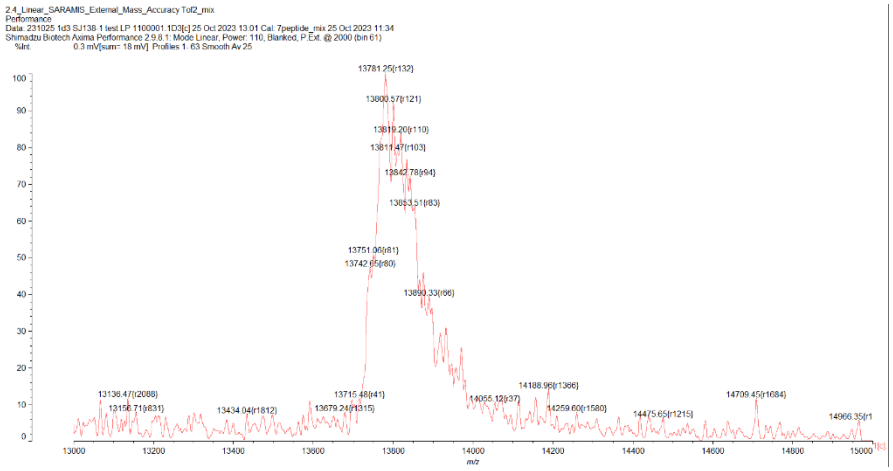
hp-GG DNA-L14



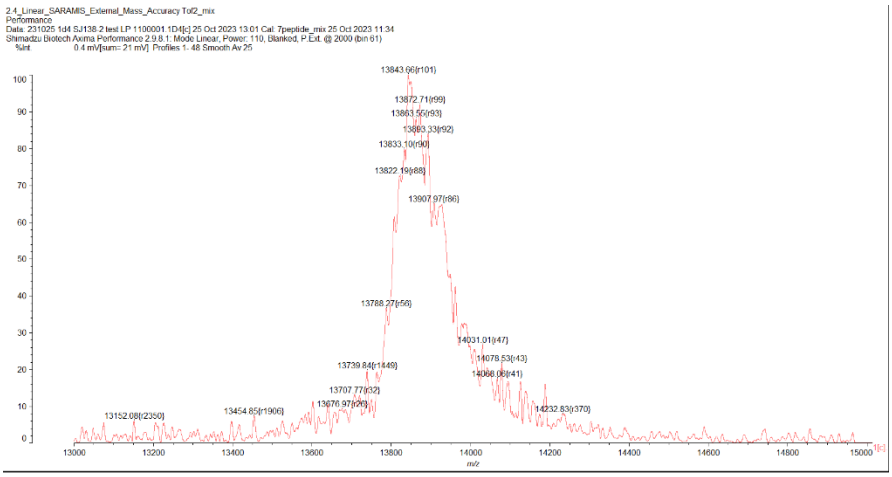
hp-GG DNA-L15 (The other peak comes from the decomposition of hydrazone during MALDI-TOF experiment)



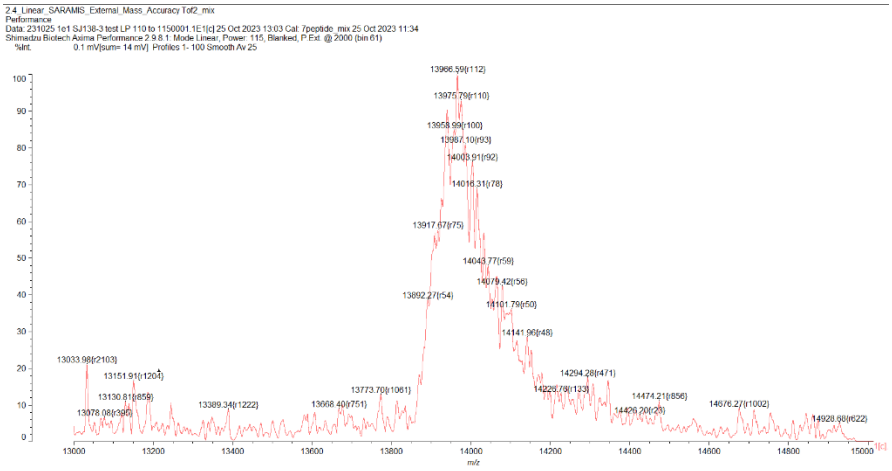
DNA Aptamer-1-L1



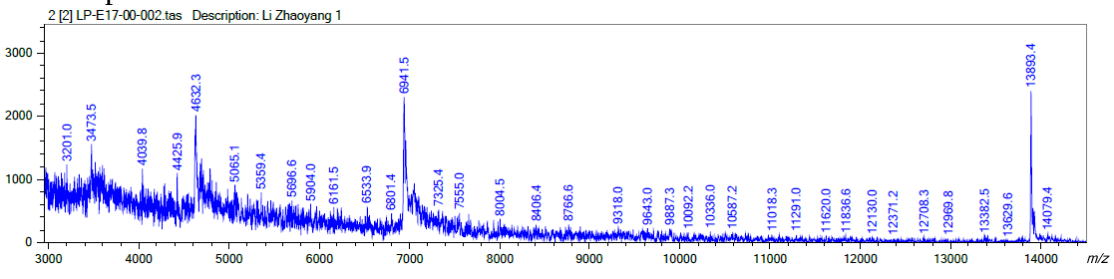
DNA Aptamer-1-L5



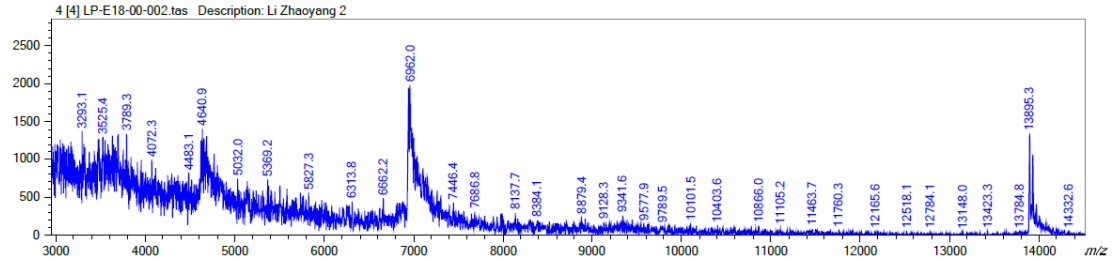
DNA Aptamer-1-L7



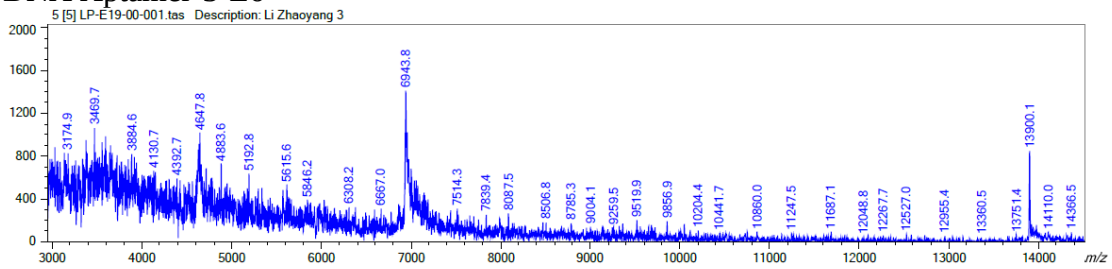
DNA Aptamer-1-L6



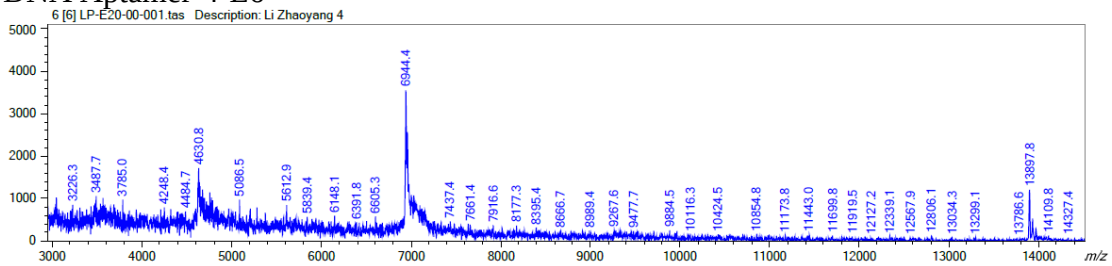
DNA Aptamer-2-L6



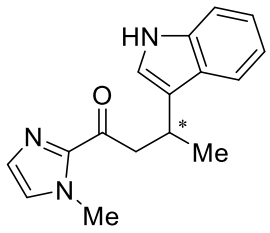
DNA Aptamer-3-L6



DNA Aptamer-4-L6



Characterization of Products



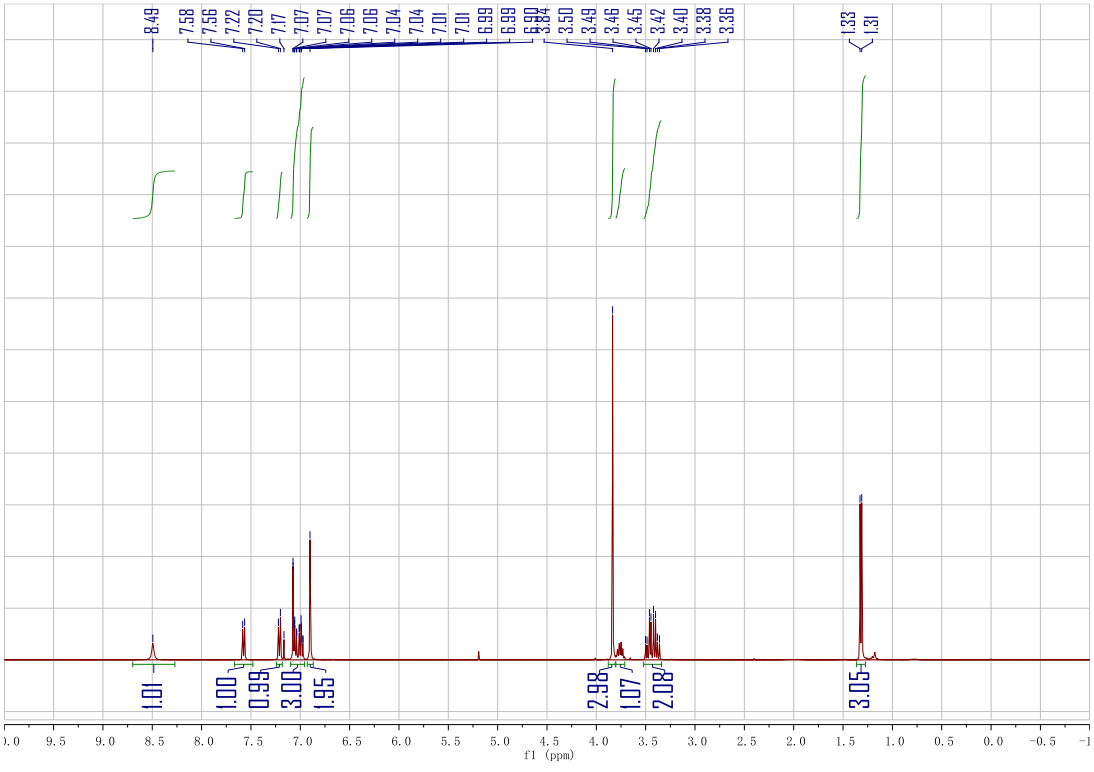
3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3a).

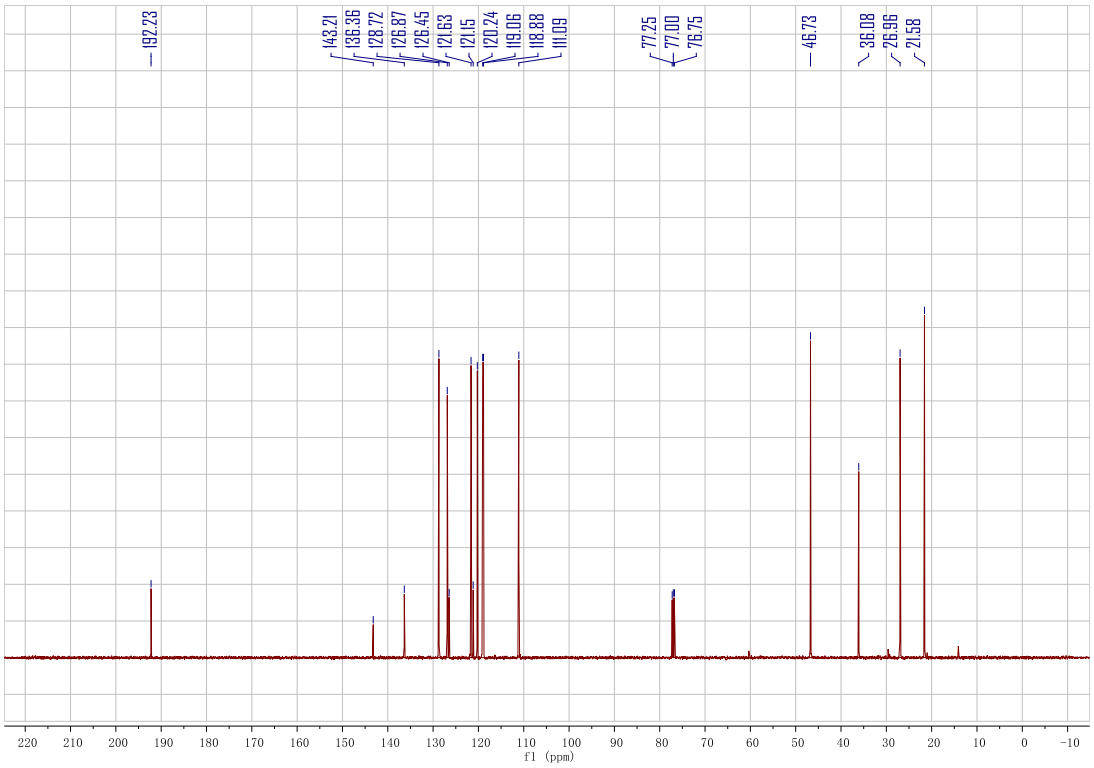
The racemic product was synthesized as described using **1a** and indole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.10 – 6.96 (m, 3H), 6.90 (s, 2H), 3.84 (s, 3H), 3.80 – 3.71 (m, 1H), 3.43 (qd, *J* = 15.9, 7.3 Hz, 2H), 1.32 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.23 (s), 143.21 (s), 136.36 (s), 128.72 (s), 126.87 (s), 126.45 (s), 121.63 (s), 121.15 (s), 120.24 (s), 119.06 (s), 118.88 (s), 111.09 (s), 46.73 (s), 36.08 (s), 26.96 (s), 21.58 (s).

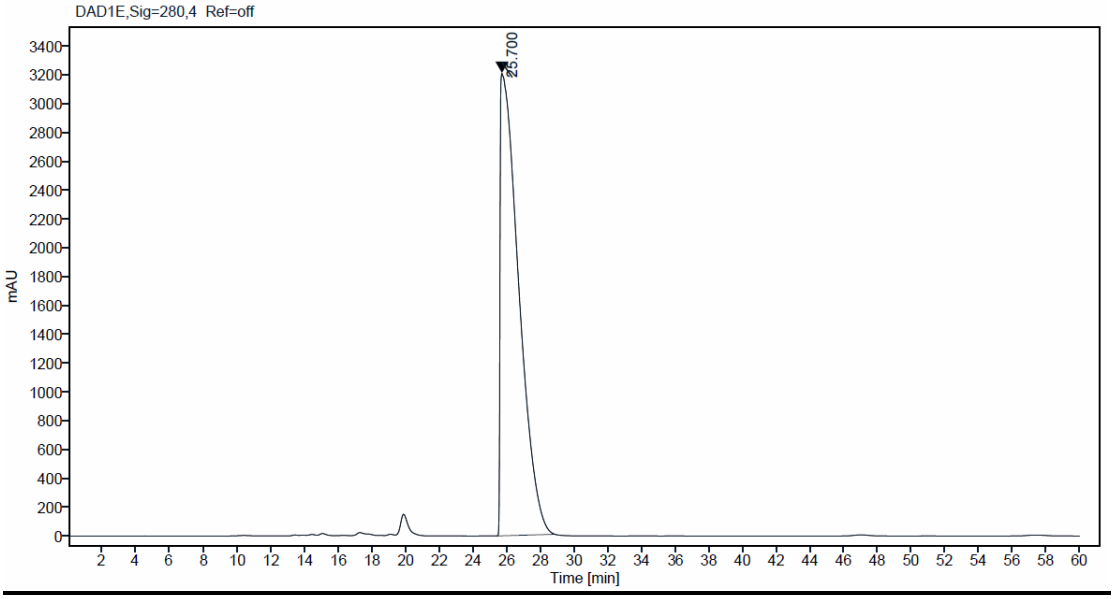
HRMS (ESI) calcd. for $C_{16}H_{18}N_3O$ $[M+H]^+$: m/z 268.1450, found: 268.1444.



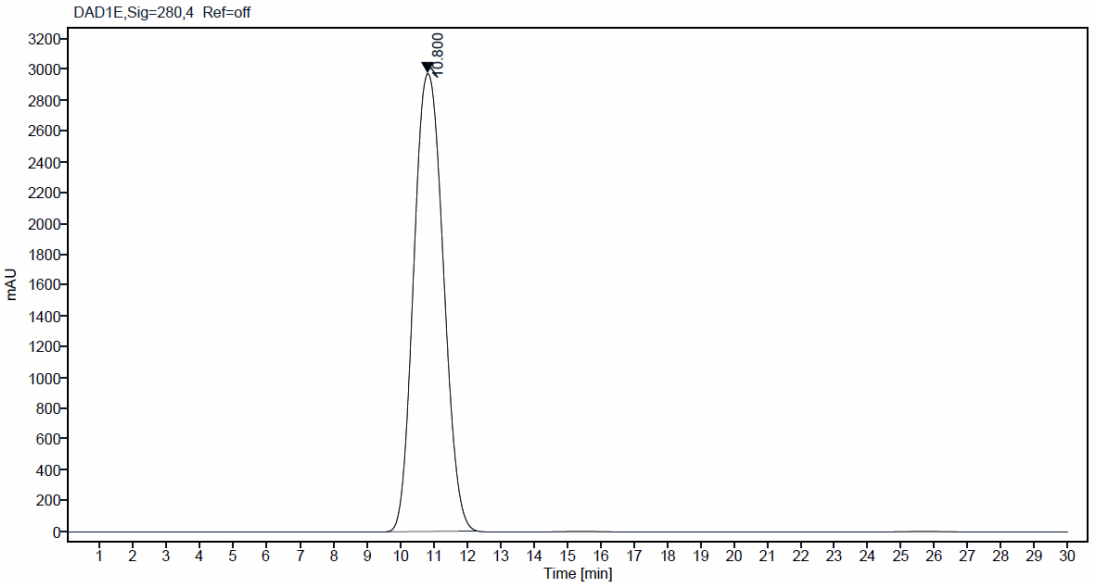


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

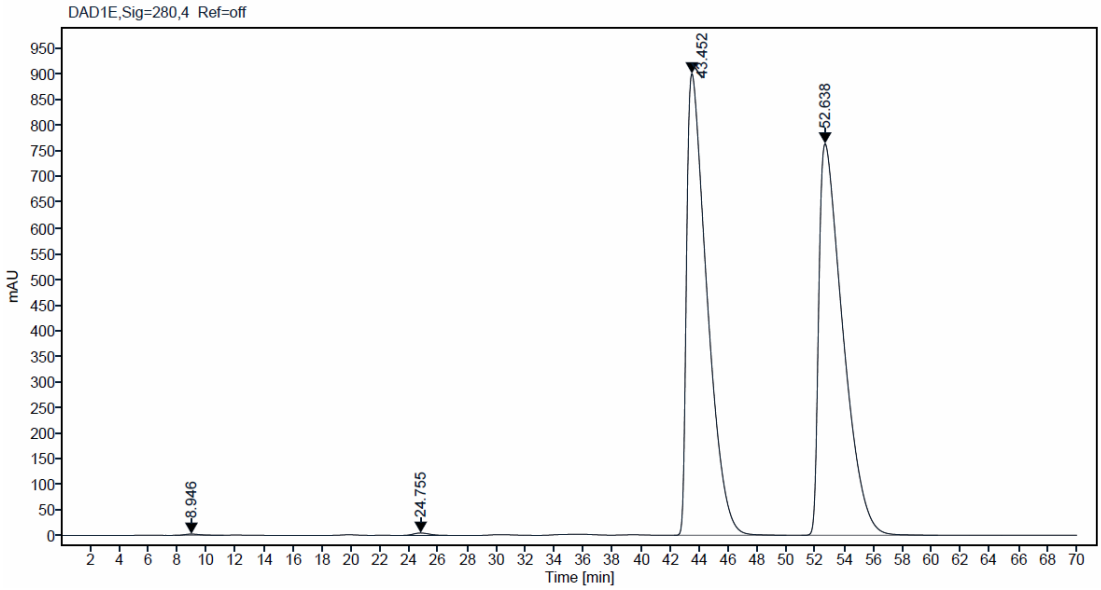
Starting Material (1a): Retention time = 25.700 min



Indole: Retention time = 10.800 min

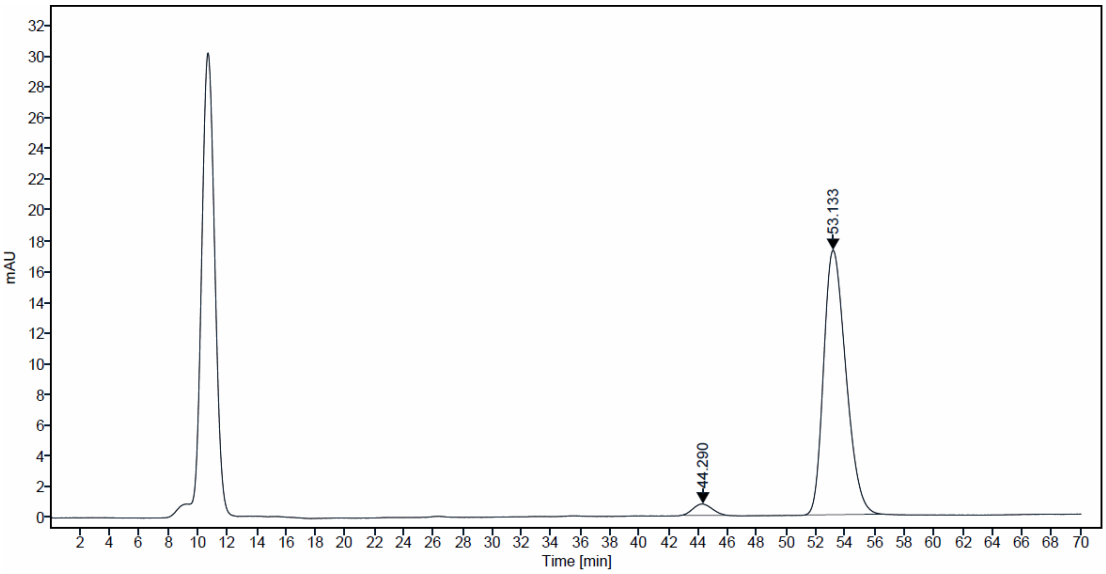


Racemic: Retention time: 43.452 min; 52.638 min

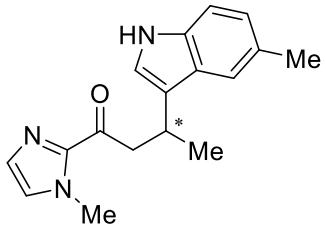


Peak	Retention time (min)	Rel. area (%)
1	43.452	50.2
2	52.638	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3a** < 1:99 and an enantiomeric excess of 94% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 44.290 min; 53.133 min



Peak	Retention time (min)	Rel. area (%)
1	44.290	3.1
2	53.133	96.9



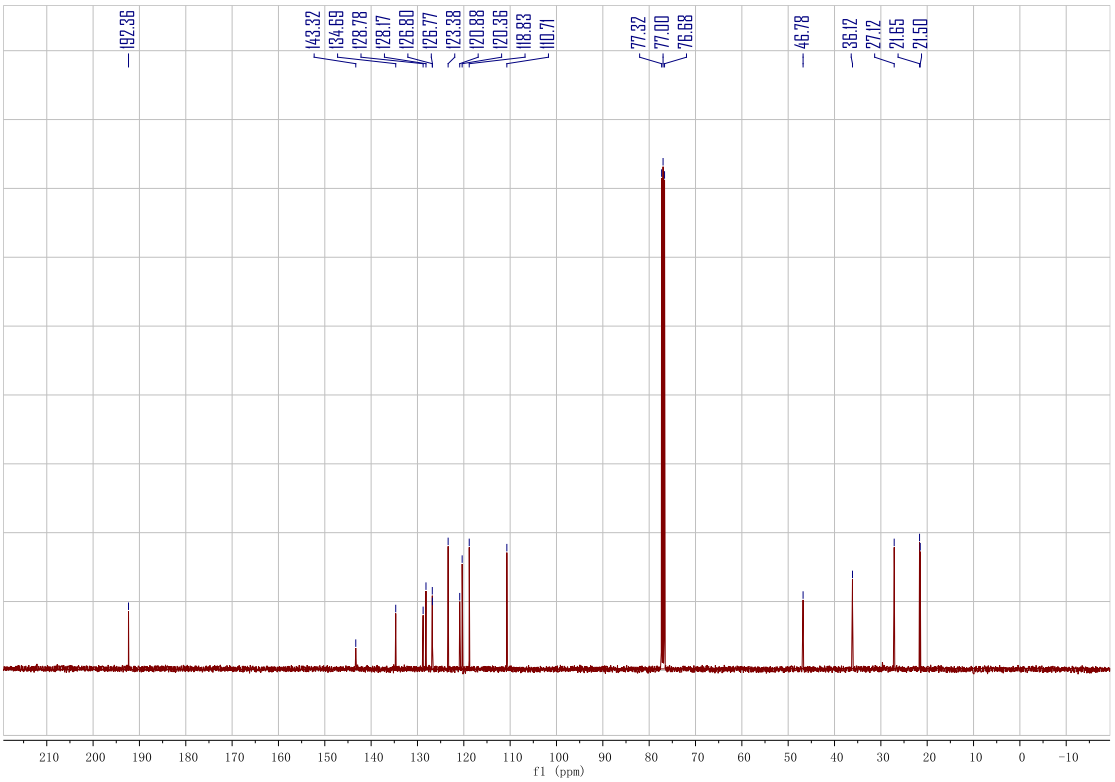
1-(1-methyl-1H-imidazol-2-yl)-3-(5-methyl-1H-indol-3-yl)butan-1-one (3b).

The racemic product was synthesized as described using **1a** and 5-Me-indole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.34 (s, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.08 (s, 1H), 6.90 (m, 3H), 3.85 (s, 3H), 3.79 – 3.68 (m, 1H), 3.51 – 3.35 (m, 2H), 2.36 (s, 3H), 1.33 (d, *J* = 6.9 Hz, 3H).

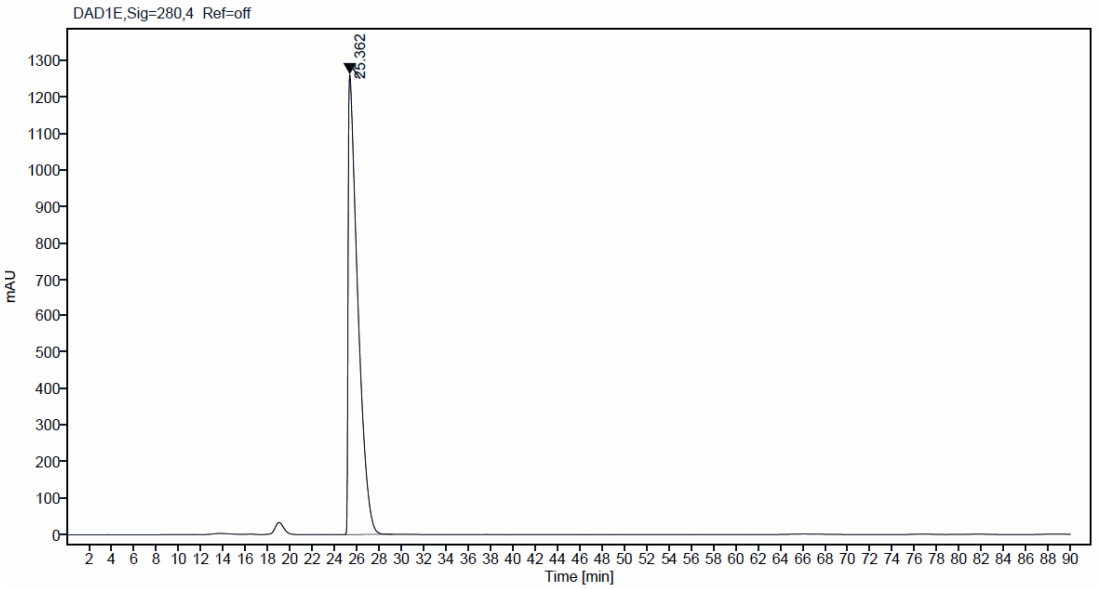
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.36 (s), 143.32 (s), 134.69 (s), 128.78 (s), 128.17 (s), 126.80 (s), 126.77 (s), 123.38 (s), 120.88 (s), 120.36 (s), 118.83 (s), 110.71 (s), 46.78 (s), 36.12 (s), 27.12 (s), 21.65 (s), 21.50 (s).

HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$ $[M+H]^+$: m/z 282.1606, found: 282.1602.

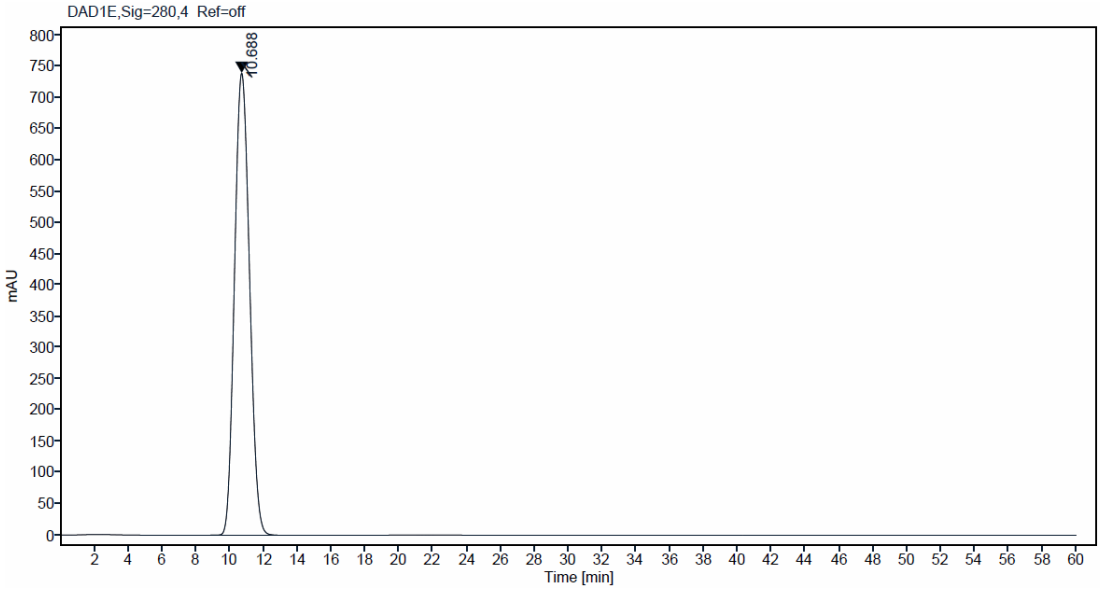


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

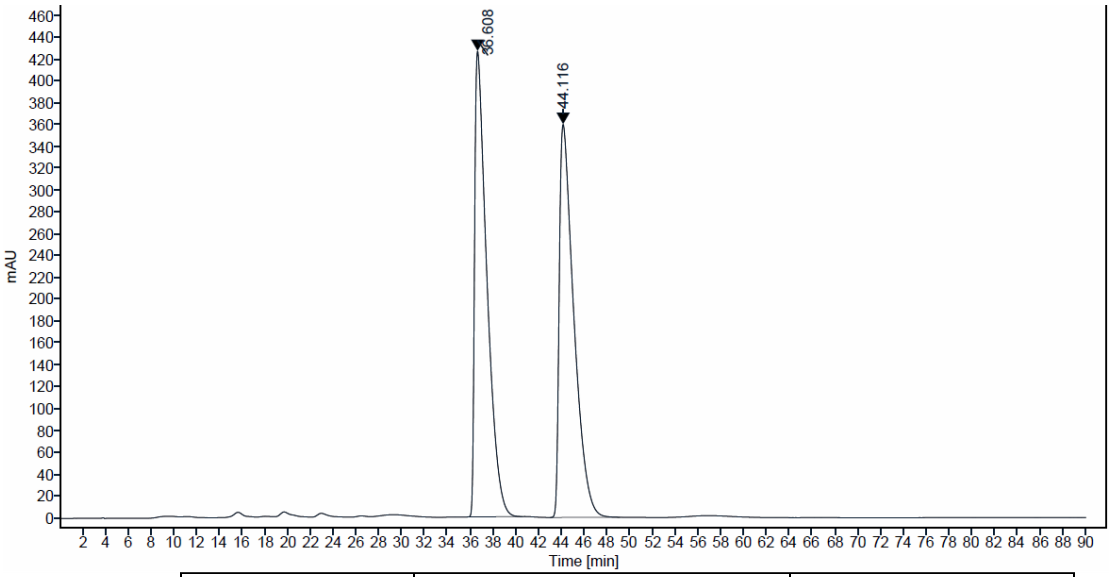
Starting Material (1a): Retention time = 25.362 min



5-Me-Indole: Retention time = 10.688 min

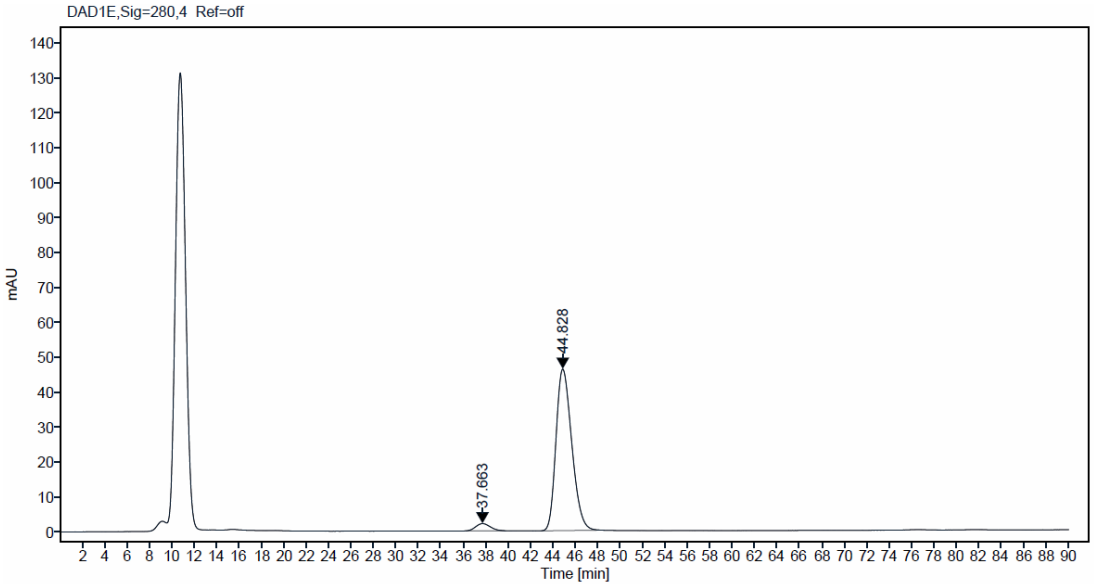


Racemic: Retention time: 36.608 min; 44.119 min

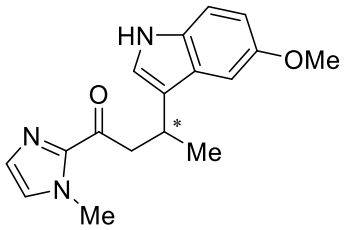


Peak	Retention time (min)	Rel. area (%)
1	36.608	50.1
2	44.119	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3b** < 1:99 and an enantiomeric excess of 92% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 44.265 min; 53.134 min



Peak	Retention time (min)	Rel. area (%)
1	37.663	3.9
2	44.828	96.1



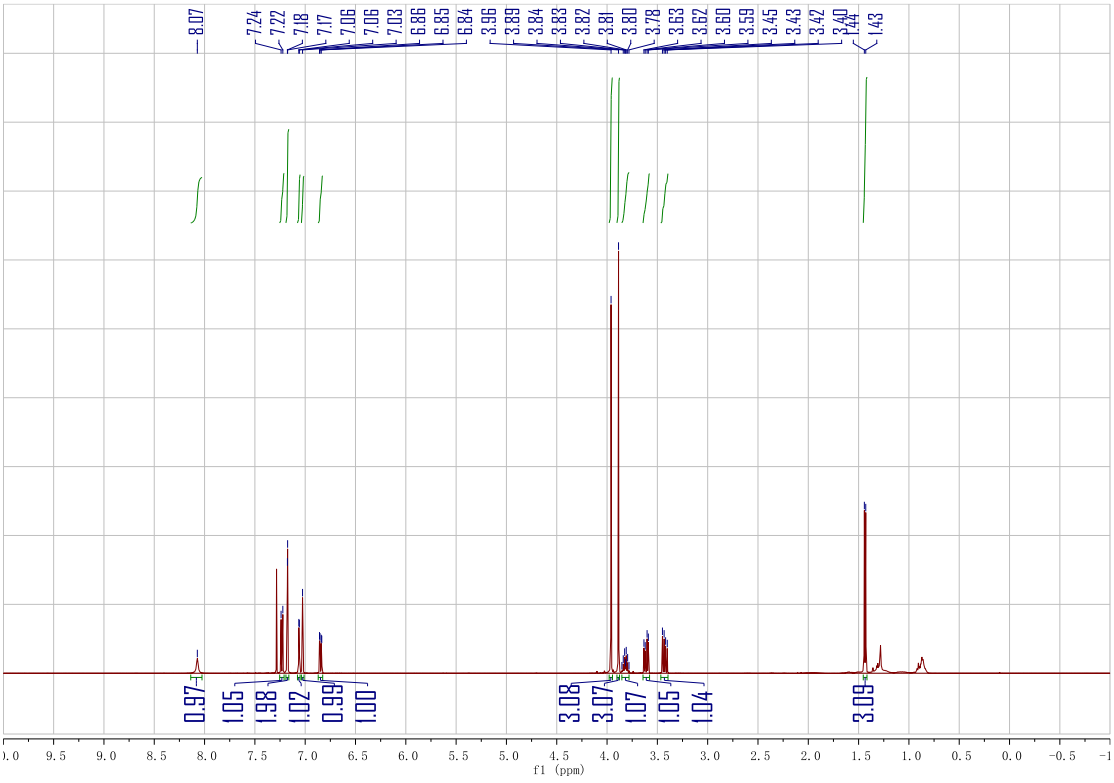
3-(5-methoxy-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3c).

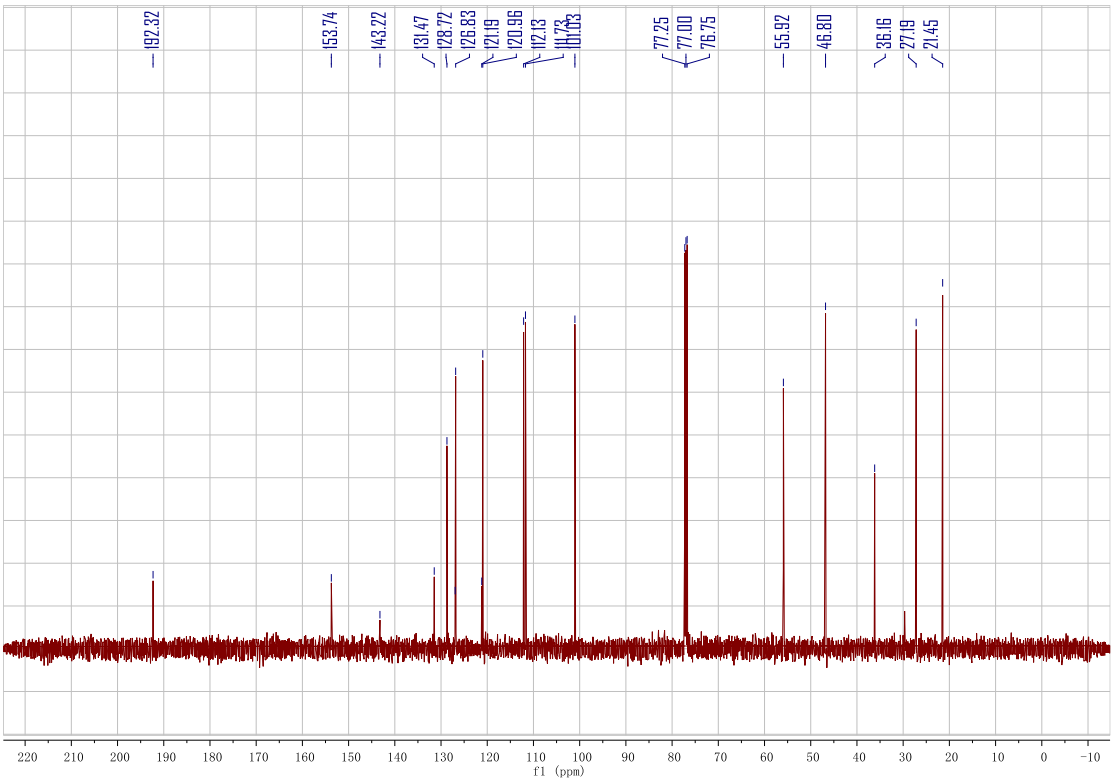
The racemic product was synthesized as described using **1a** and 5-OMe-indole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.23 (d, *J* = 8.7 Hz, 1H), 7.18 (d, *J* = 0.9 Hz, 2H), 7.06 (d, *J* = 2.3 Hz, 1H), 7.03 (s, 1H), 6.85 (dd, *J* = 8.7, 2.4 Hz, 1H), 3.96 (s, 3H), 3.89 (s, 3H), 3.86 – 3.78 (m, 1H), 3.61 (dd, *J* = 15.6, 6.3 Hz, 1H), 3.43 (dd, *J* = 15.6, 8.3 Hz, 1H), 1.44 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.32 (s), 153.74 (s), 143.22 (s), 131.47 (s), 128.72 (s), 126.95 (s), 126.83 (s), 121.19 (s), 120.96 (s), 112.13 (s), 111.73 (s), 101.03 (s), 55.92 (s), 46.80 (s), 36.16 (s), 27.19 (s), 21.45 (s).

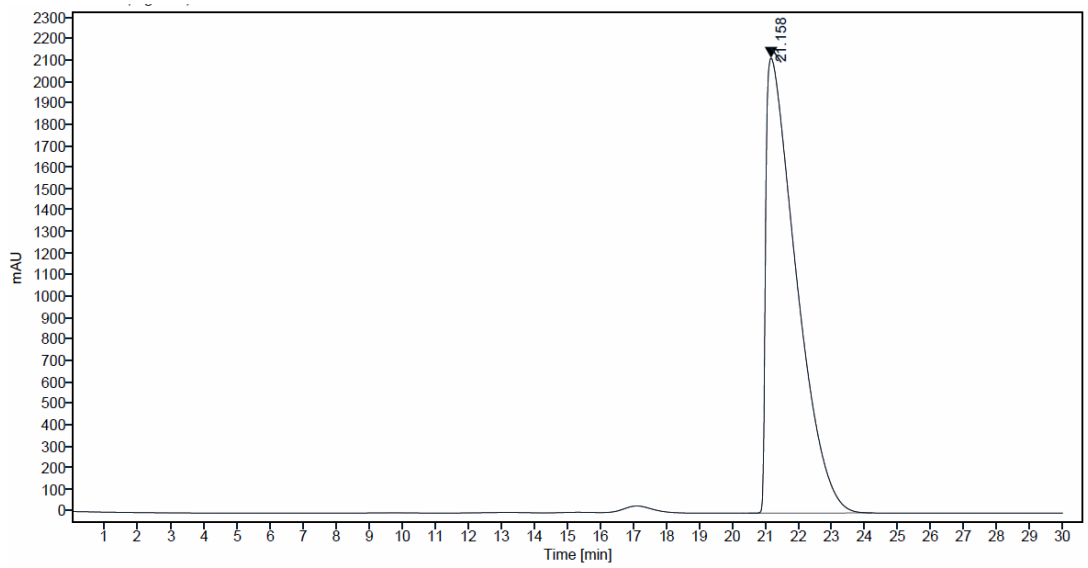
HRMS (ESI) calcd. for $C_{17}H_{20}N_3O_2$ $[M+H]^+$: m/z 298.1556, found: 298.1550.



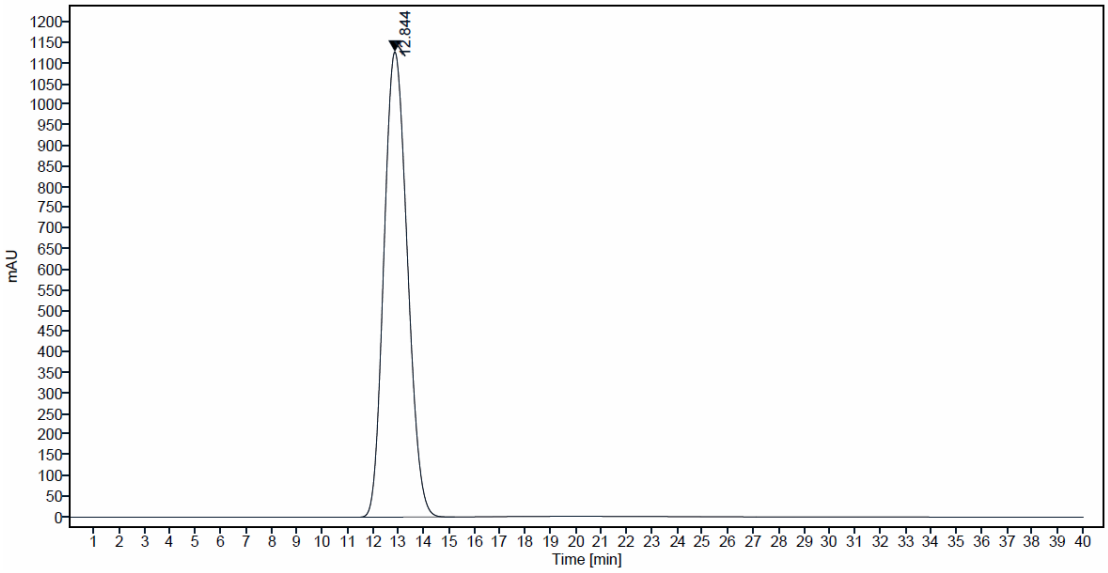


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.5 mL/min, λ = 280 nm

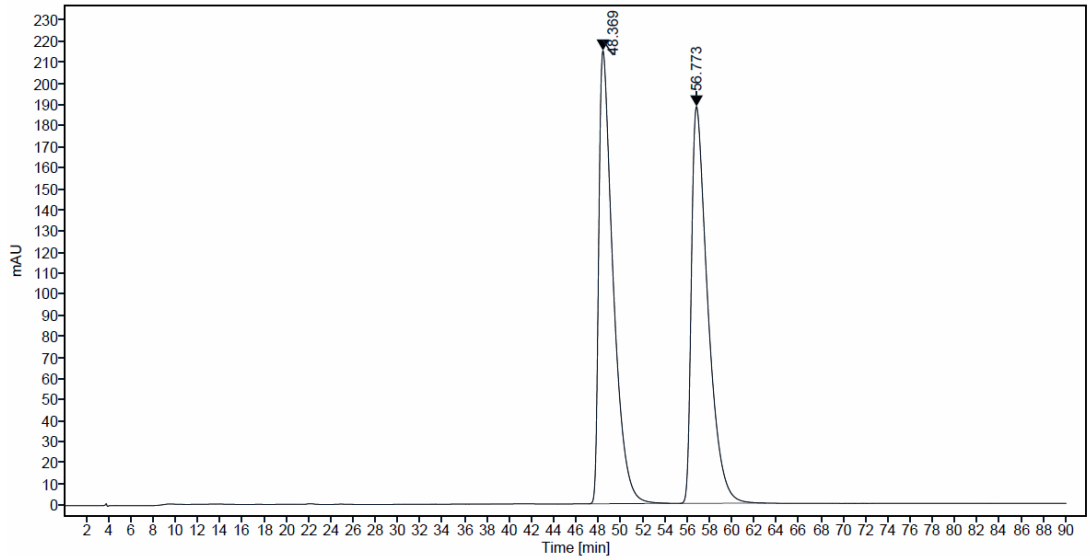
Starting Material (1a): Retention time = 21.158 min



5-OMe-Indole: Retention time = 12.844 min

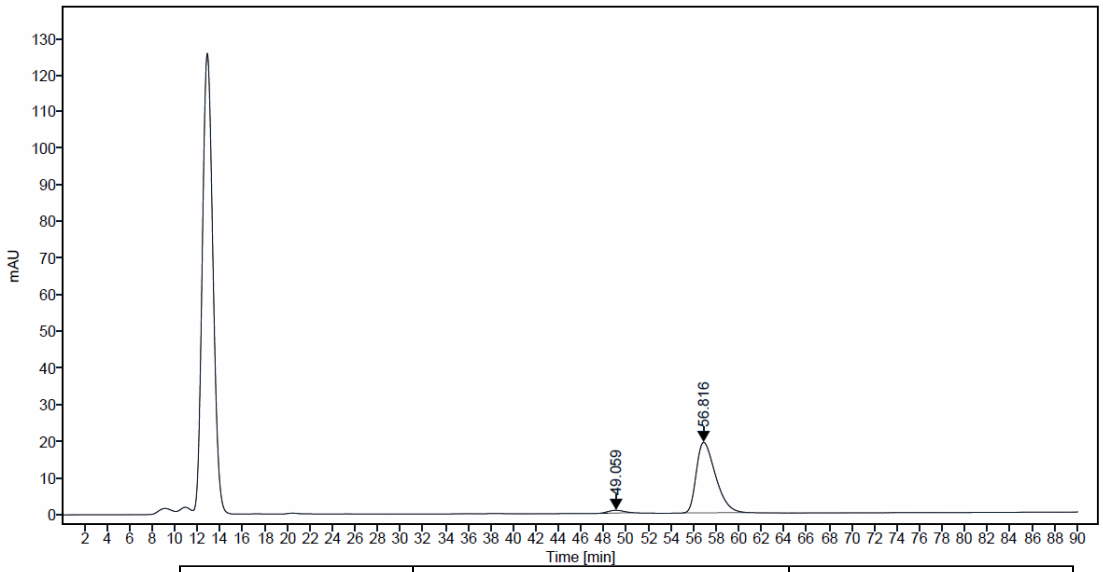


Racemic: Retention time: 48.369 min; 56.773 min

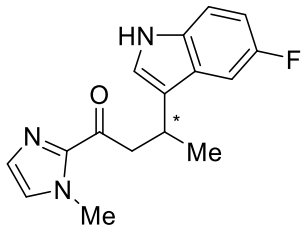


Peak	Retention time (min)	Rel. area (%)
1	48.369	49.6
2	56.773	50.4

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3c** < 1:99 and an enantiomeric excess of 93% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 90:10, 0.5 mL/min, λ = 280 nm]. Retention time: 49.059 min; 56.816 min



Peak	Retention time (min)	Rel. area (%)
1	49.059	3.5
2	56.816	96.5



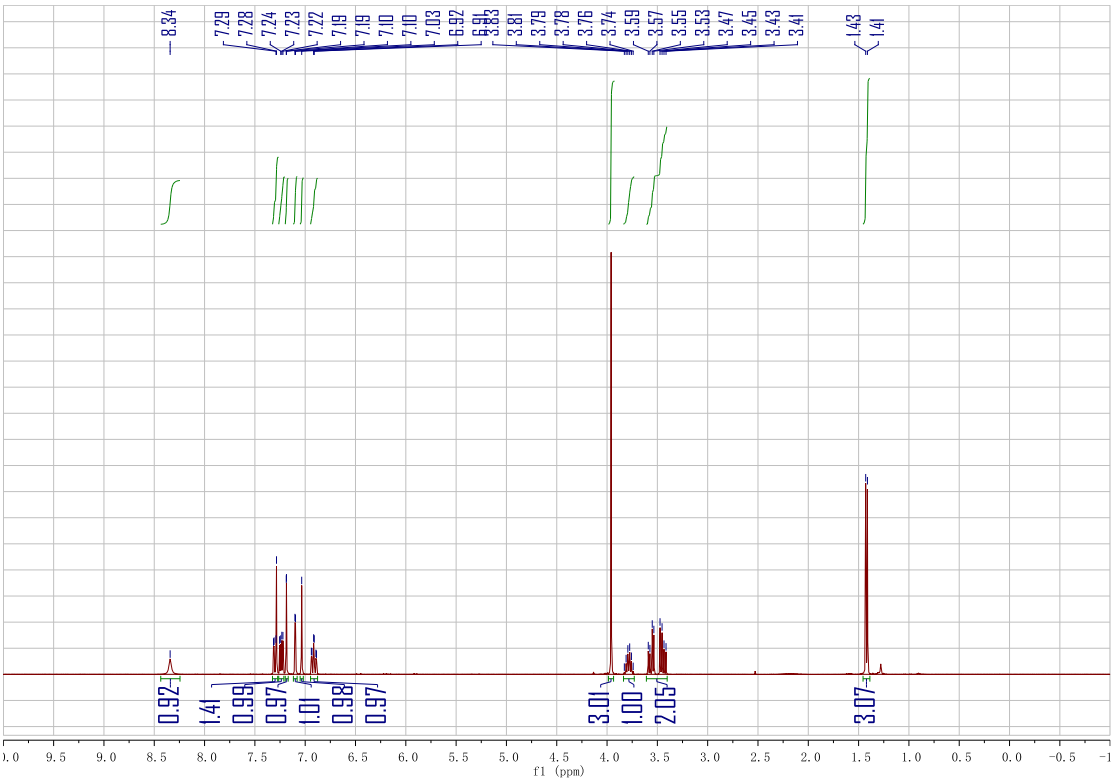
3-(5-fluoro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3d).

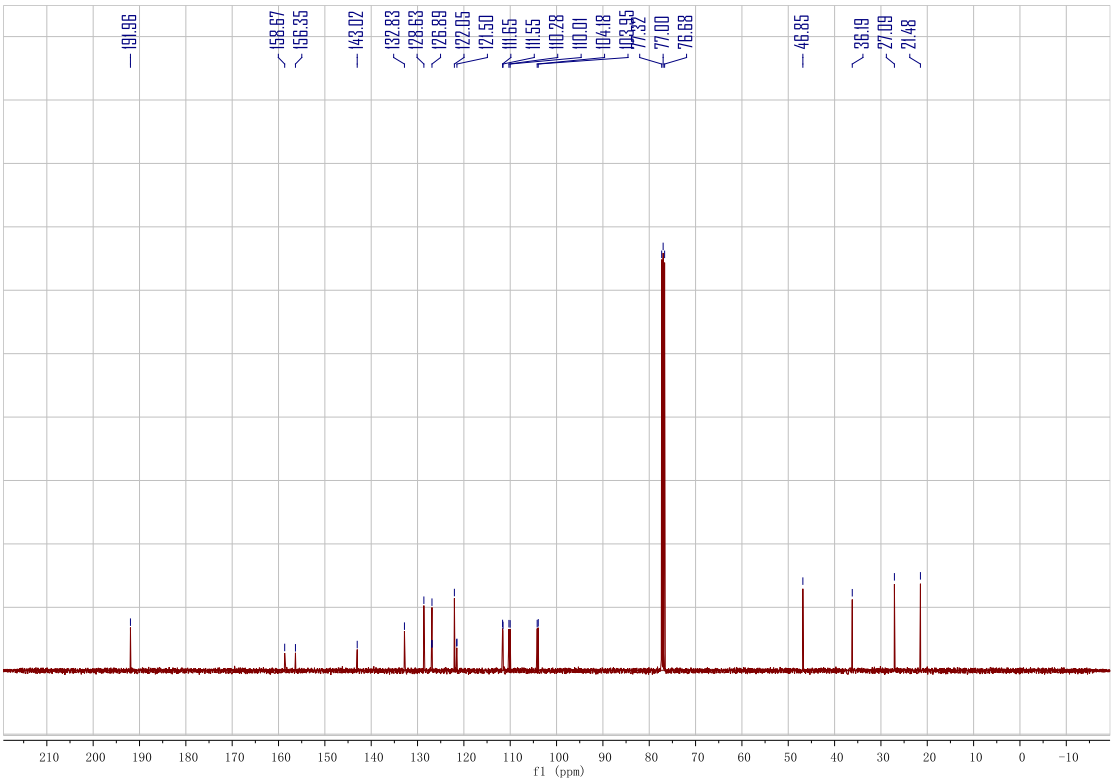
The racemic product was synthesized as described using **1a** and 5-F-indole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.32 – 7.27 (m, 1H), 7.24 (dd, *J* = 8.8, 4.4 Hz, 1H), 7.19 (d, *J* = 0.7 Hz, 1H), 7.10 (d, *J* = 2.3 Hz, 1H), 7.03 (s, 1H), 6.91 (td, *J* = 9.0, 2.5 Hz, 1H), 3.96 (s, 3H), 3.85 – 3.73 (m, 1H), 3.50 (ddd, *J* = 23.8, 15.8, 7.3 Hz, 2H), 1.42 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.96 (s), 157.51 (d, *J* = 233.9 Hz), 143.02 (s), 132.83 (s), 128.63 (s), 126.90 (d, *J* = 9.5 Hz), 126.89 (s), 122.05 (s), 121.53 (d, *J* = 4.8 Hz), 111.60 (d, *J* = 9.7 Hz), 110.15 (d, *J* = 26.4 Hz), 104.07 (d, *J* = 23.5 Hz), 46.85 (s), 36.19 (s), 27.09 (s), 21.48 (s).

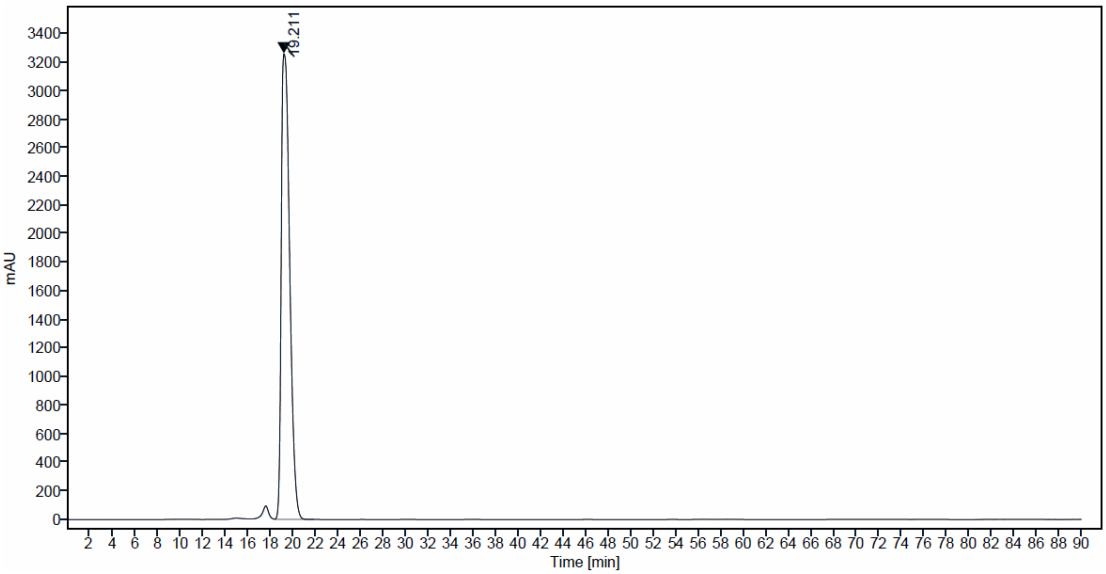
HRMS (ESI) calcd. for $C_{16}H_{17}FN_3O_2$ $[M+H]^+$: m/z 286.1356, found: 286.1350.



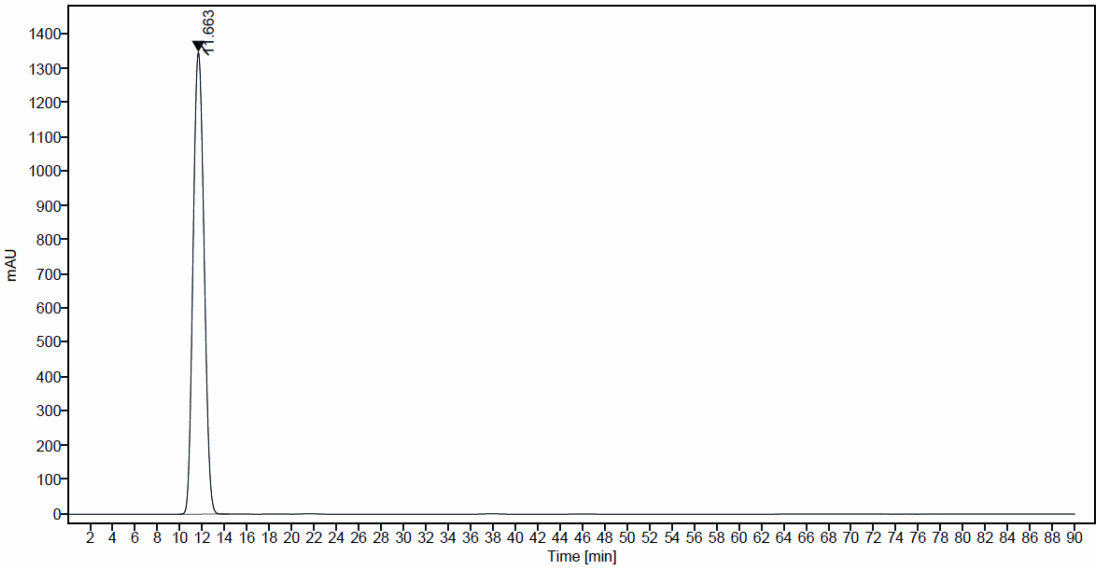


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

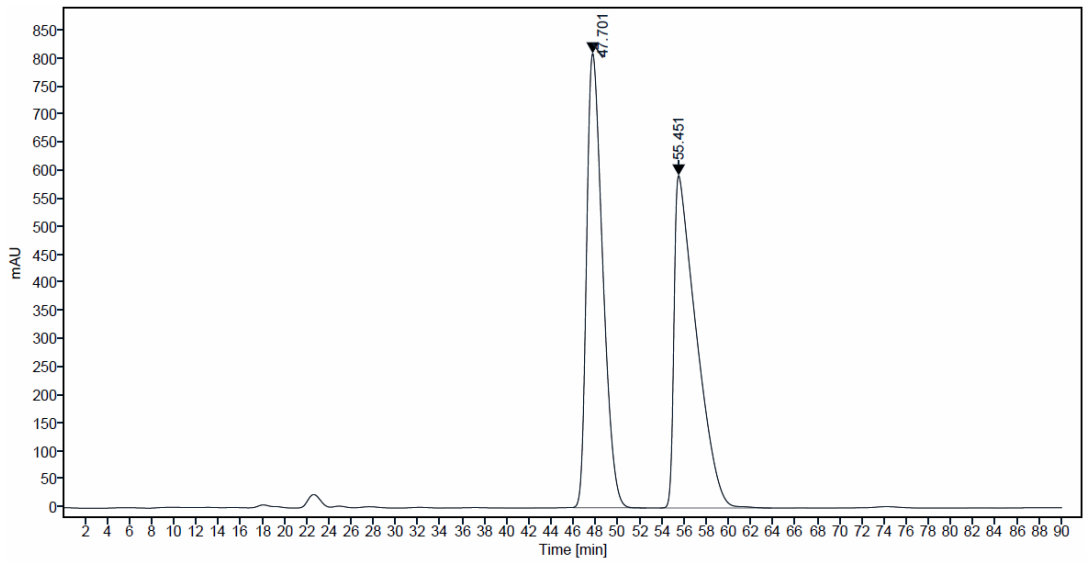
Starting Material (1a): Retention time = 19.211 min



5-F-Indole: Retention time = 11.663 min

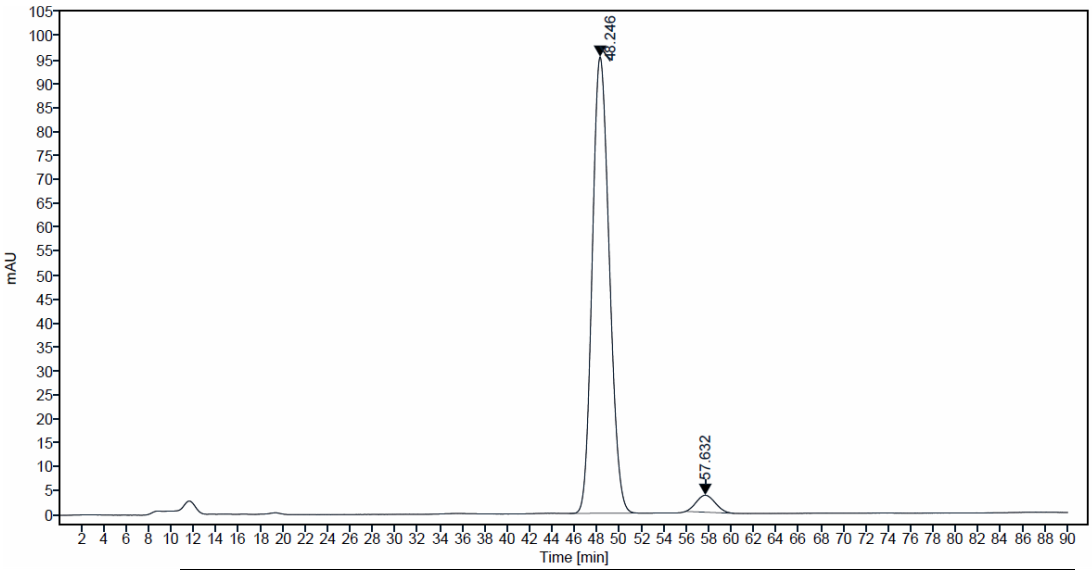


Racemic: Retention time: 47.701 min; 55.451 min

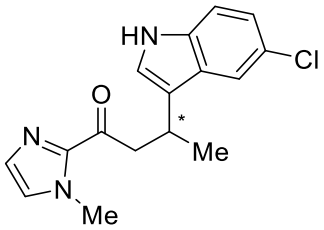


Peak	Retention time (min)	Rel. area (%)
1	47.701	49.8
2	55.451	50.2

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3d** < 1:99 and an enantiomeric excess of 93% [CHIRALCEL IG column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 48.246 min; 57.632 min



Peak	Retention time (min)	Rel. area (%)
1	48.246	96.4
2	57.632	3.6



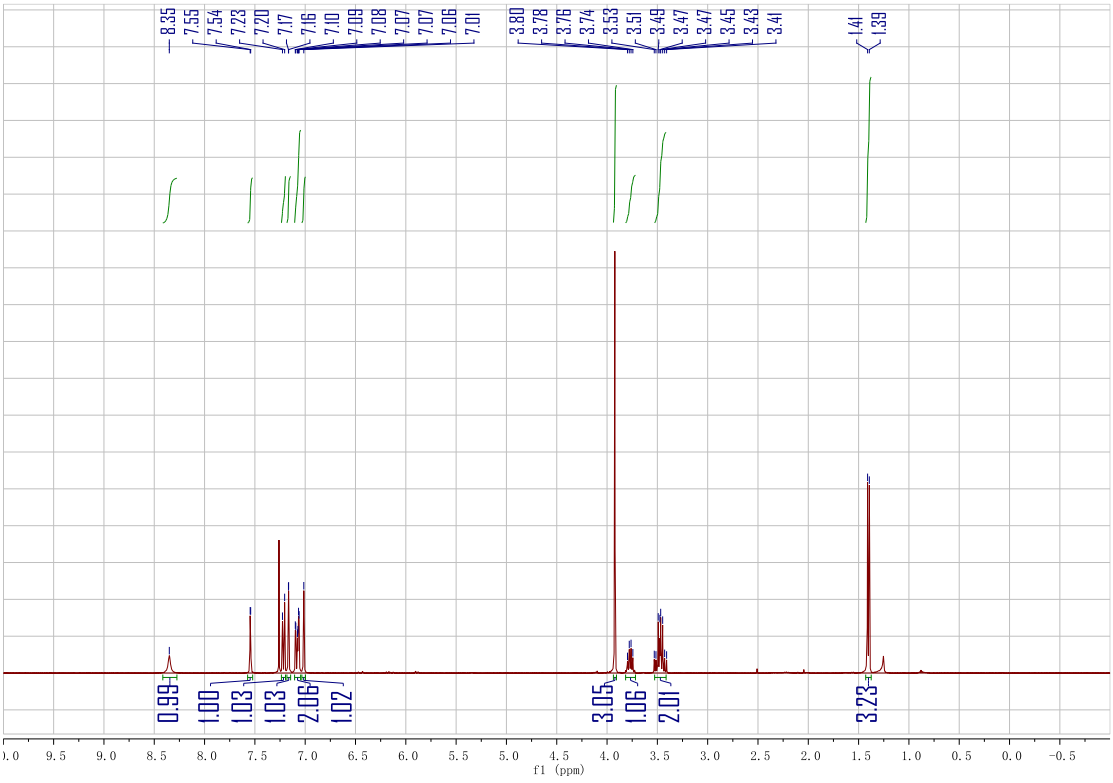
3-(5-chloro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)-butan-1-one (3e).

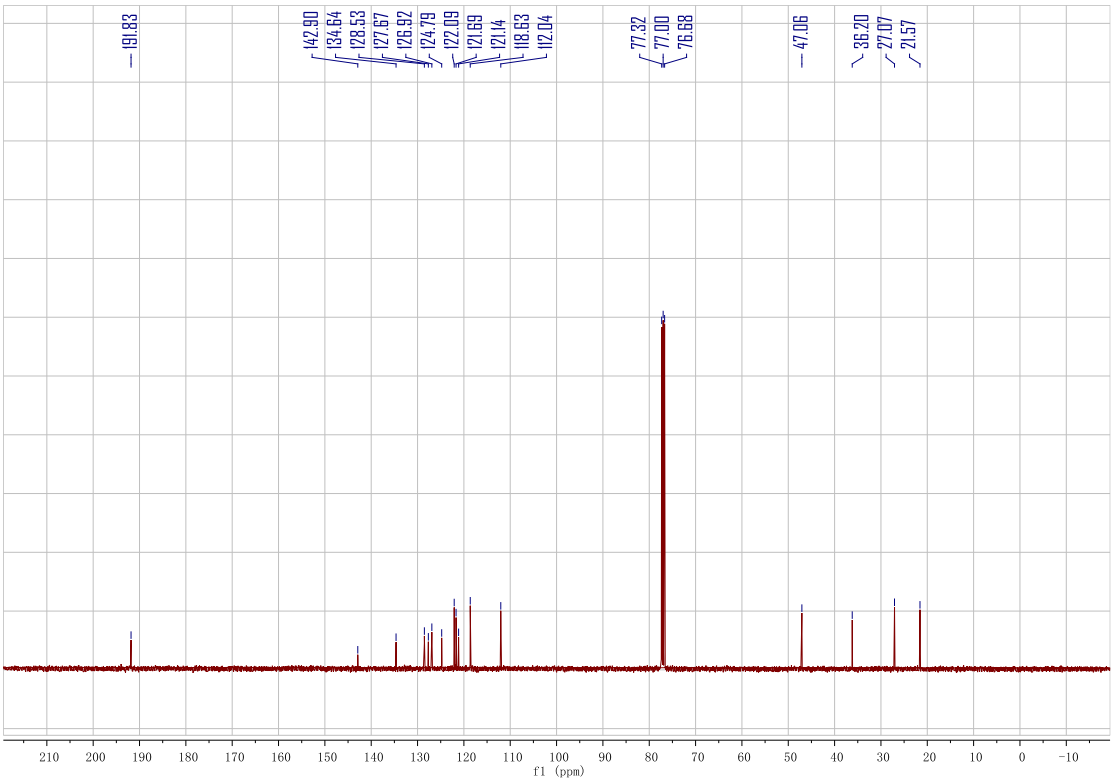
The racemic product was synthesized as described using **1a** and 5-Cl-indole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.54 (d, *J* = 1.9 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.17 (d, *J* = 0.6 Hz, 1H), 7.11 – 7.05 (m, 2H), 7.01 (s, 1H), 3.92 (s, 3H), 3.77 (dd, *J* = 14.2, 7.1 Hz, 1H), 3.53 – 3.41 (m, 2H), 1.40 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.83 (s), 142.90 (s), 134.64 (s), 128.53 (s), 127.67 (s), 126.92 (s), 124.79 (s), 122.09 (s), 121.69 (s), 121.14 (s), 118.63 (s), 112.04 (s), 47.06 (s), 36.20 (s), 27.07 (s), 21.57 (s).

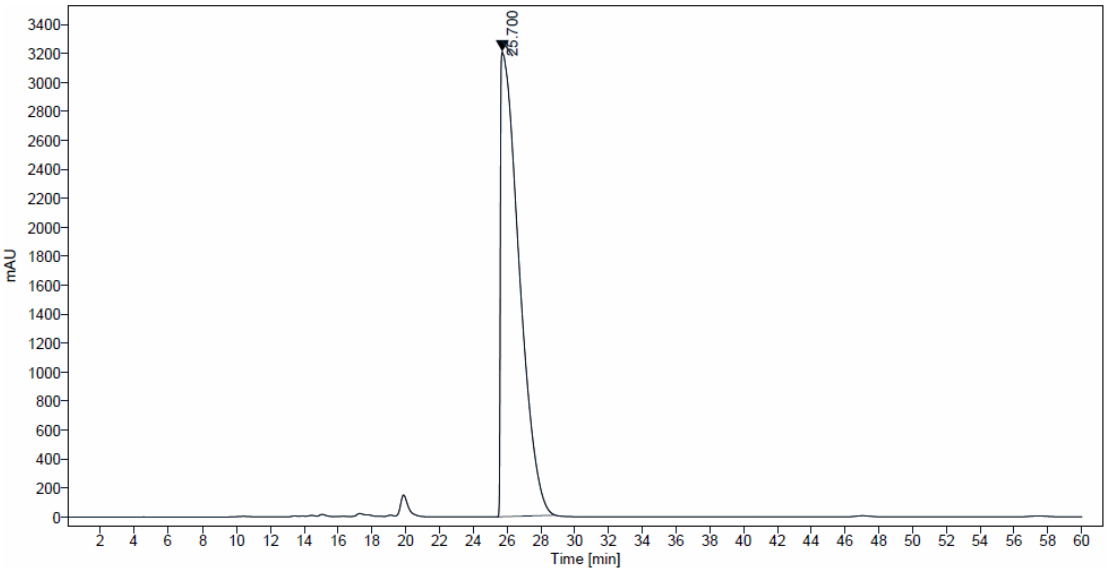
HRMS (ESI) calcd. for $C_{16}H_{17}ClN_3O$ $[M+H]^+$: m/z 302.1060, found: 302.1055.



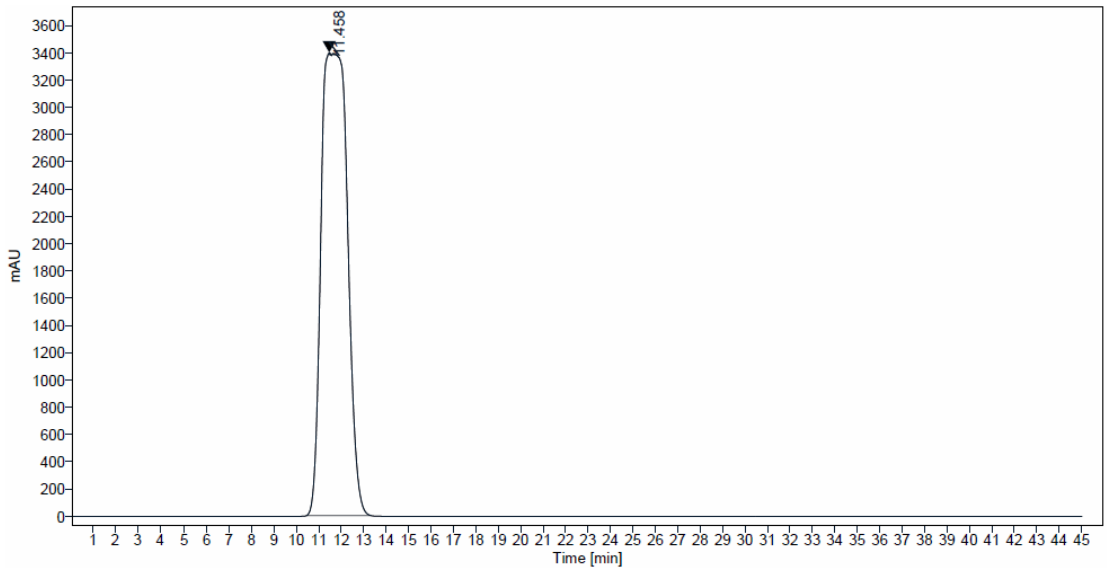


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

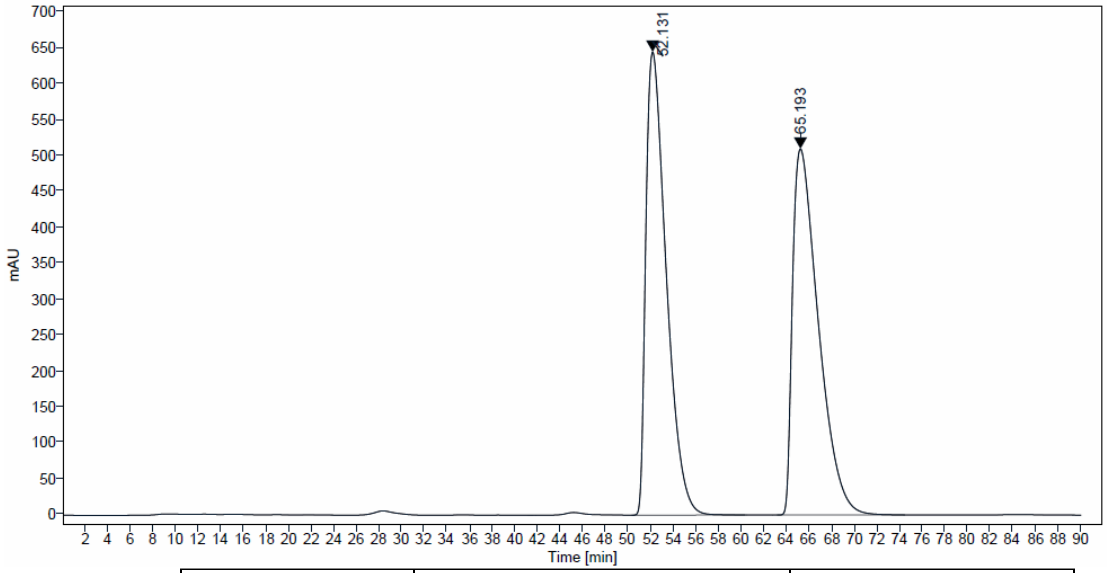
Starting Material (1a): Retention time = 25.700 min



5-Cl-Indole: Retention time = 11.458 min

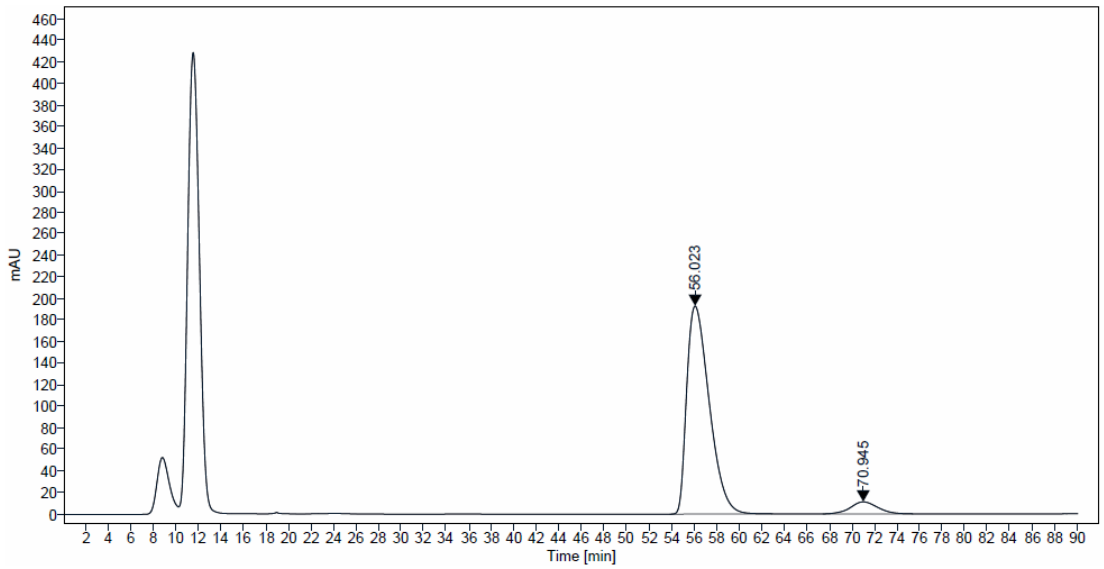


Racemic: Retention time: 52.131 min; 65.193 min

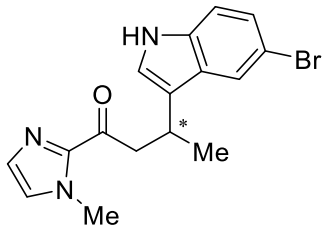


Peak	Retention time (min)	Rel. area (%)
1	52.131	50.7
2	65.193	49.3

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3e** < 1:99 and an enantiomeric excess of 94% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 56.023 min; 70.945 min



Peak	Retention time (min)	Rel. area (%)
1	56.023	96.9
2	70.945	3.1



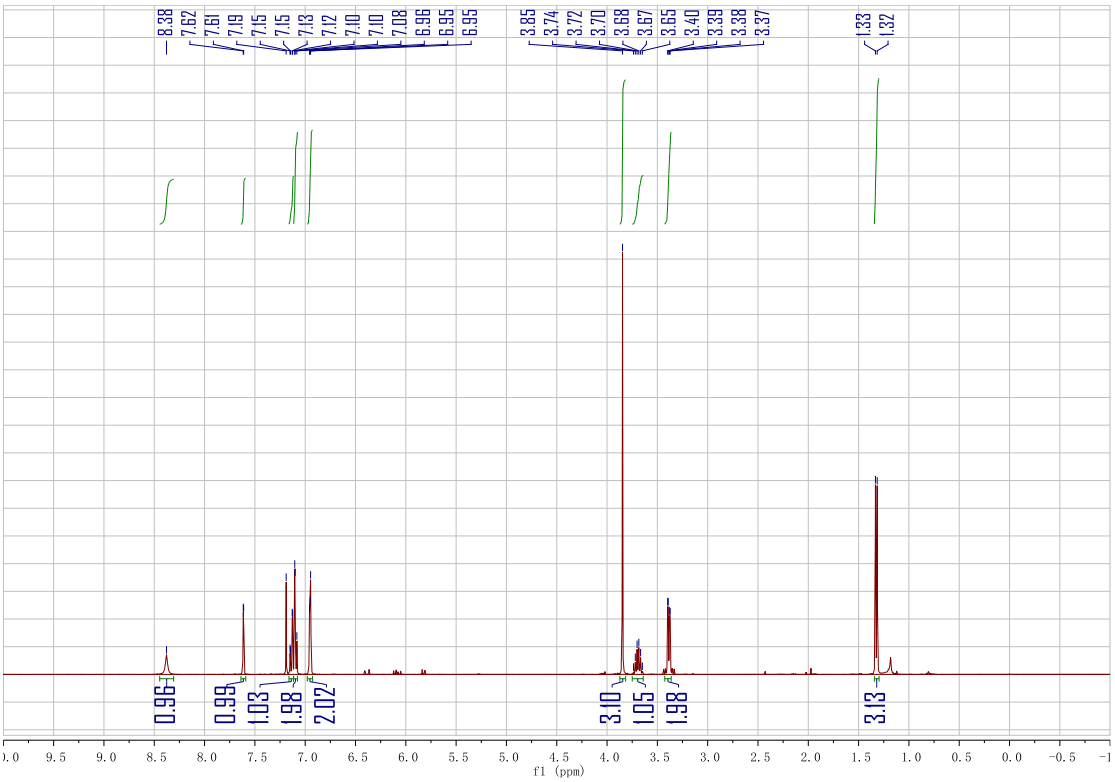
3-(5-bromo-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3f).

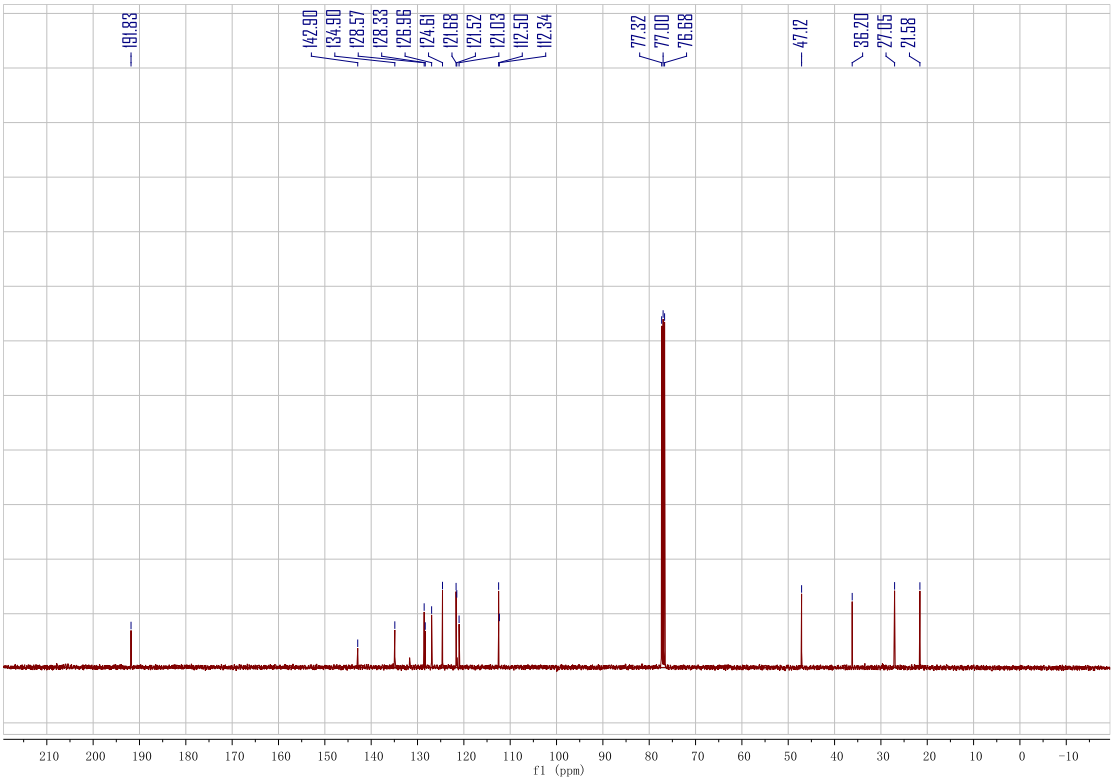
The racemic product was synthesized as described using **1a** and 5-Br-indole. The desired product was obtained as a brown solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.61 (d, *J* = 1.5 Hz, 1H), 7.14 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.11 – 7.08 (m, 2H), 6.98 – 6.93 (m, 2H), 3.85 (s, 3H), 3.69 (h, *J* = 7.0 Hz, 1H), 3.39 (dd, *J* = 7.3, 2.8 Hz, 2H), 1.32 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.83 (s), 142.90 (s), 134.90 (s), 128.57 (s), 128.33 (s), 126.96 (s), 124.61 (s), 121.68 (s), 121.52 (s), 121.03 (s), 112.50 (s), 112.34 (s), 47.12 (s), 36.20 (s), 27.05 (s), 21.58 (s).

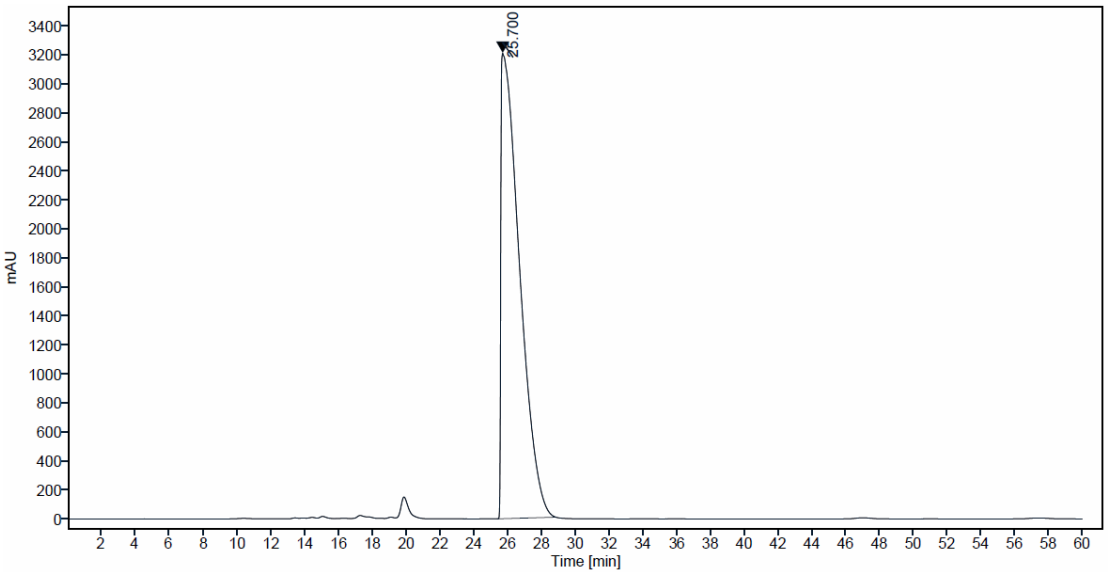
HRMS (ESI) calcd. for $C_{16}H_{17}BrN_3O$ $[M+H]^+$: m/z 346.0555, found: 346.0549.



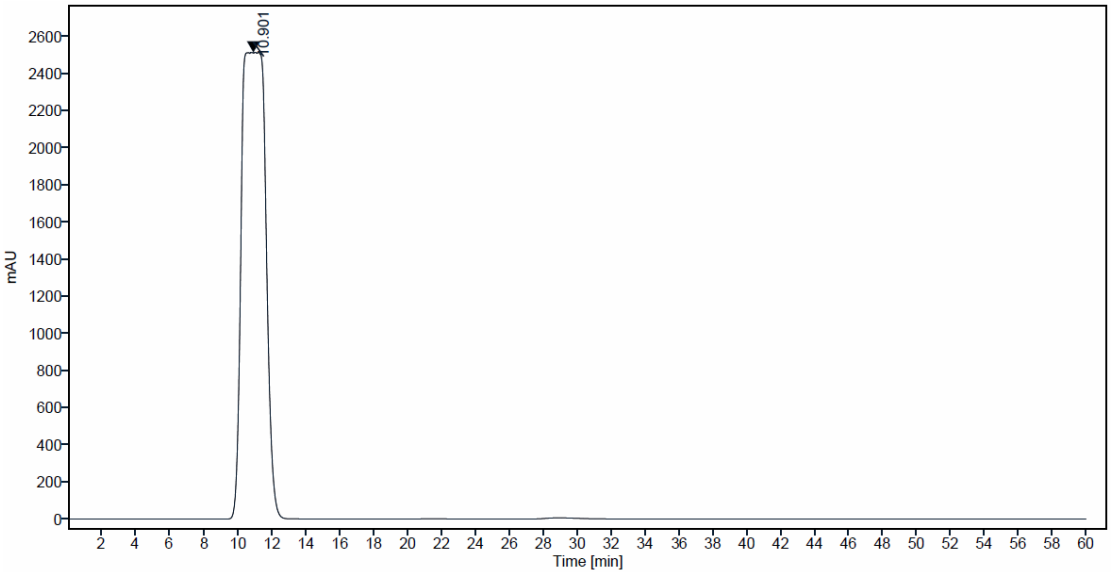


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

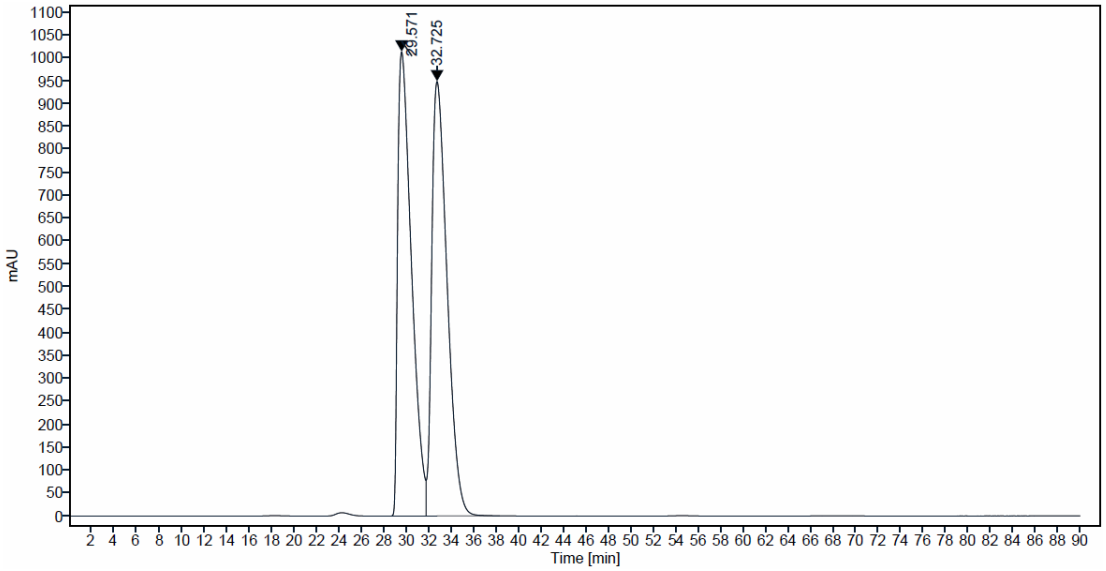
Starting Material (1a): Retention time = 25.700 min



5-Br-Indole: Retention time = 10.901min

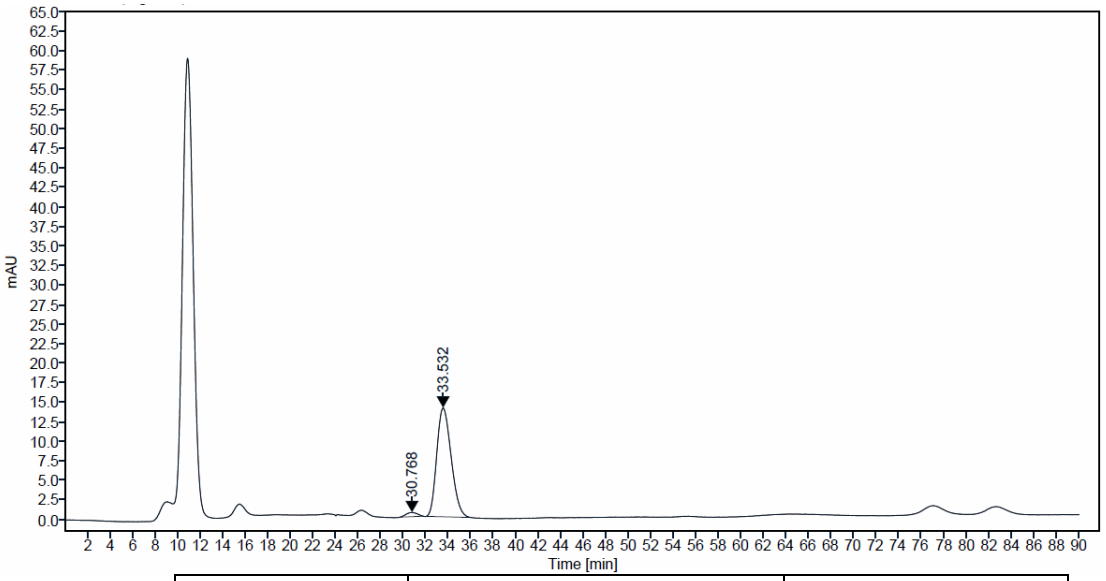


Racemic: Retention time: 29.571 min; 32.725 min

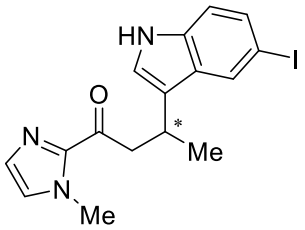


Peak	Retention time (min)	Rel. area (%)
1	29.571	48.9
2	32.725	51.1

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3f** < 1:99 and an enantiomeric excess of 92% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 30.788 min; 33.532 min



Peak	Retention time (min)	Rel. area (%)
1	30.788	4.1
2	33.532	95.9



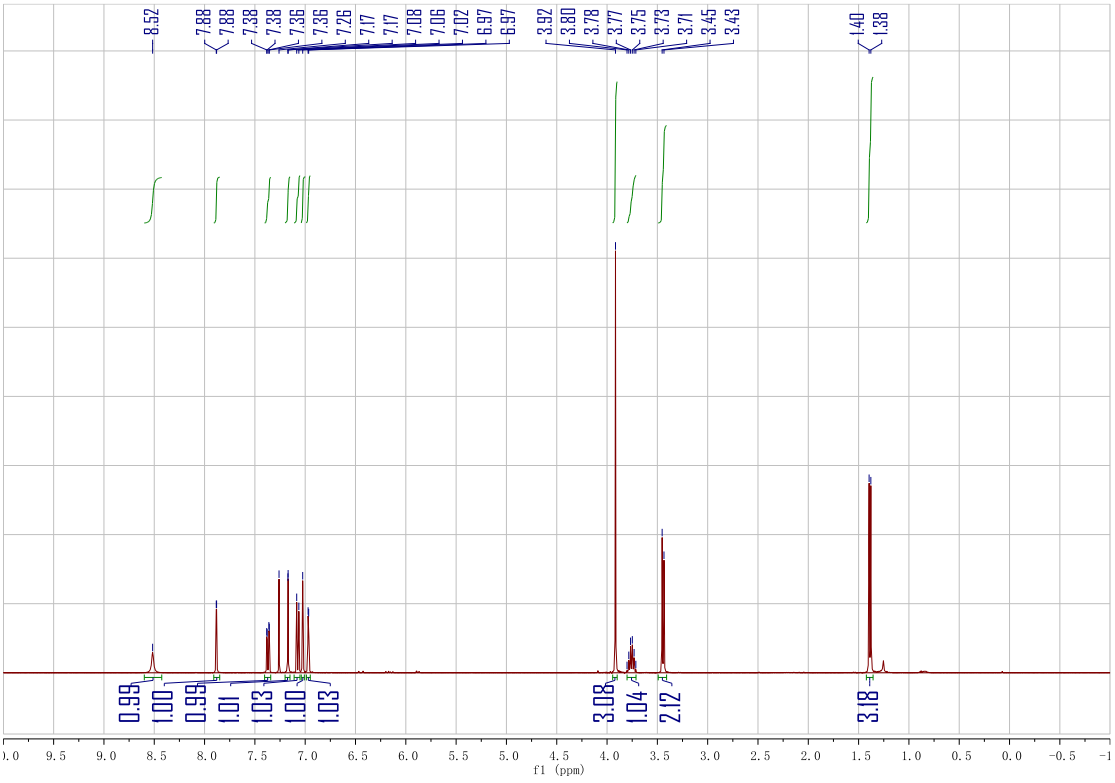
3-(5-iodo-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3g).

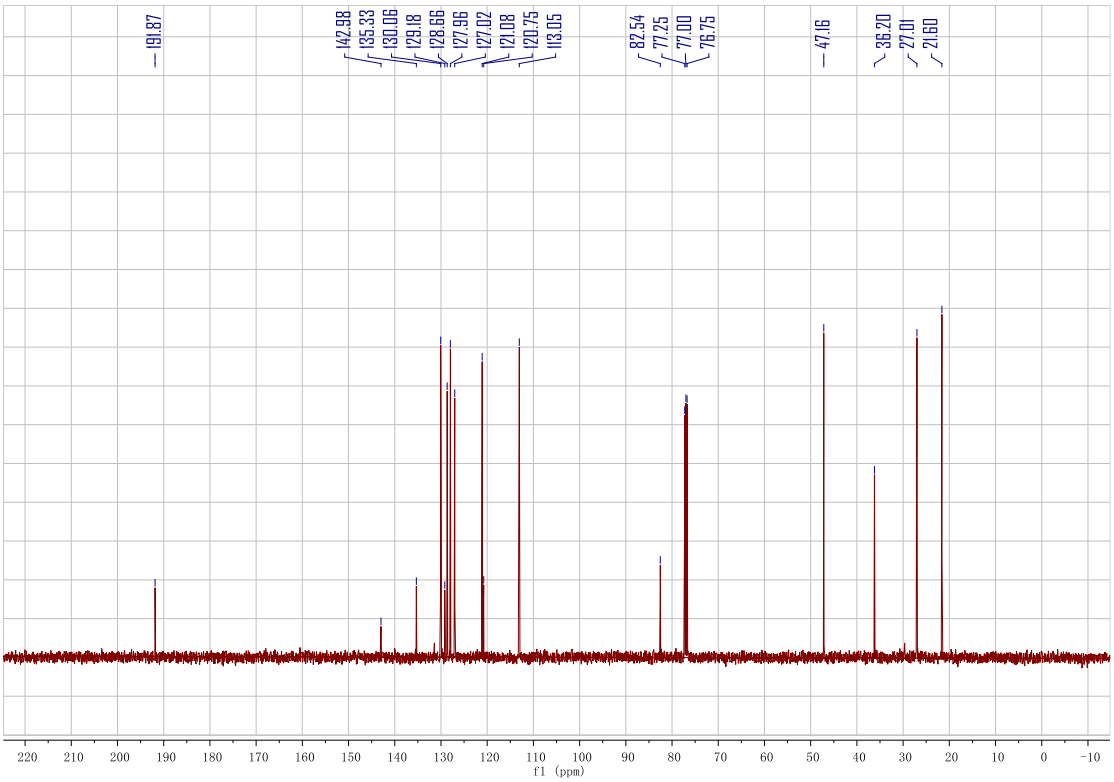
The racemic product was synthesized as described using **1a** and 5-I-indole. The desired product was obtained as a brown solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.88 (d, *J* = 1.3 Hz, 1H), 7.37 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.17 (d, *J* = 0.7 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 7.02 (s, 1H), 6.97 (d, *J* = 2.3 Hz, 1H), 3.92 (s, 3H), 3.80 – 3.71 (m, 1H), 3.44 (d, *J* = 7.3 Hz, 2H), 1.39 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 191.87 (s), 142.98 (s), 135.33 (s), 130.06 (s), 129.18 (s), 128.66 (s), 127.96 (s), 127.02 (s), 121.08 (s), 120.75 (s), 113.05 (s), 82.54 (s), 47.16 (s), 36.20 (s), 27.01 (s), 21.60 (s).

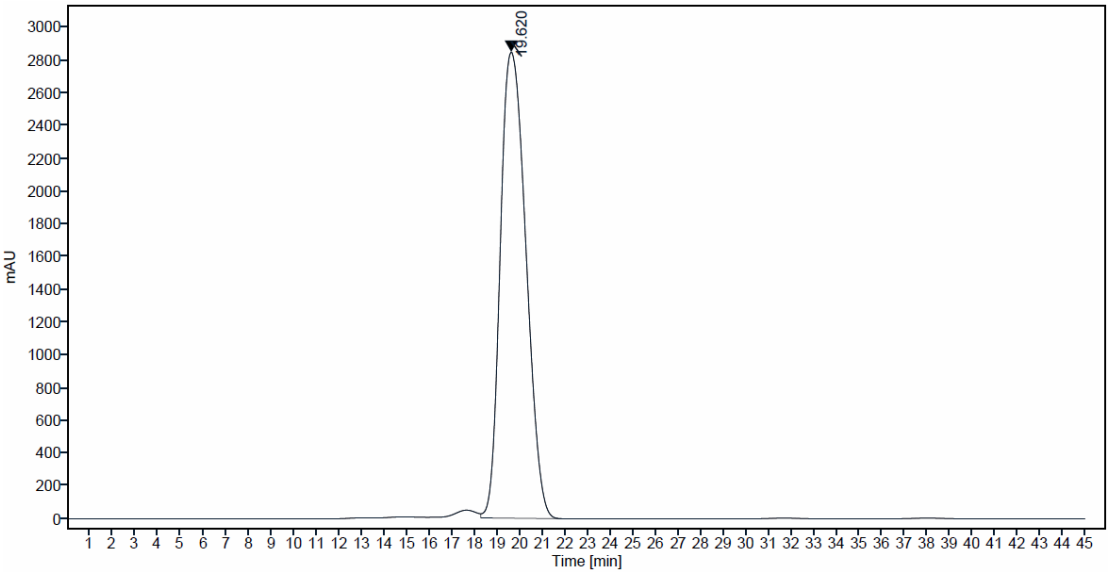
HRMS (ESI) calcd. for $C_{16}H_{17}IN_3O$ $[M+H]^+$: m/z 394.0411, found: 394.0408.



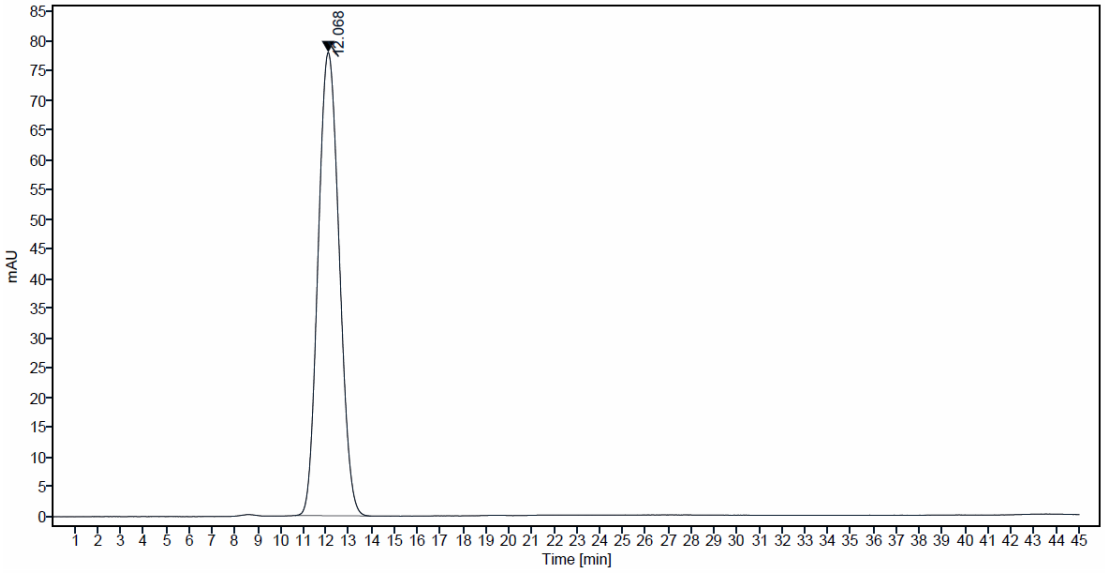


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

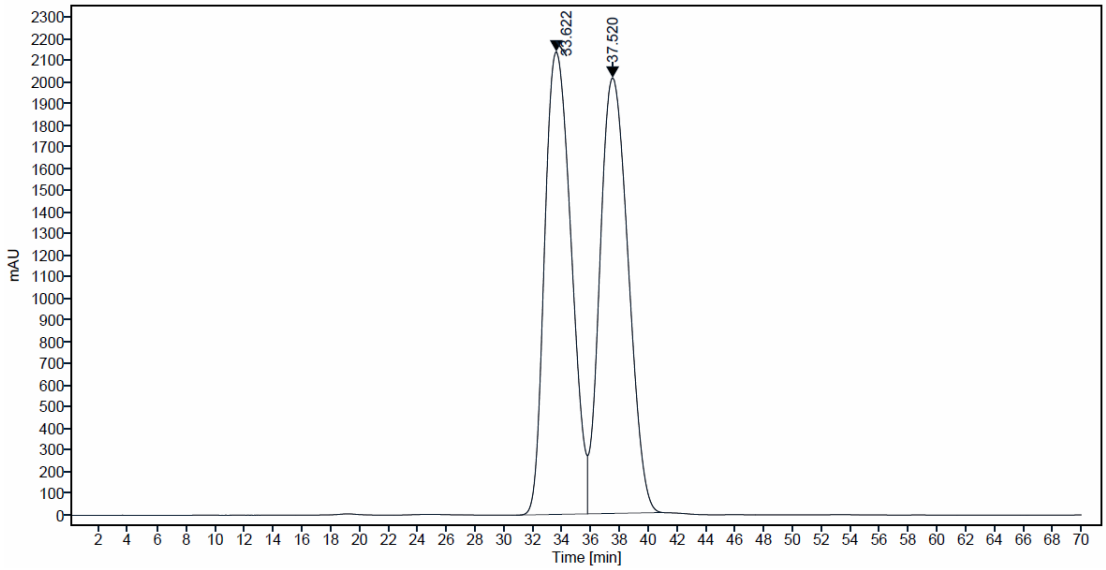
Starting Material (1a): Retention time = 19.620 min



5-I-Indole: Retention time = 12.068 min

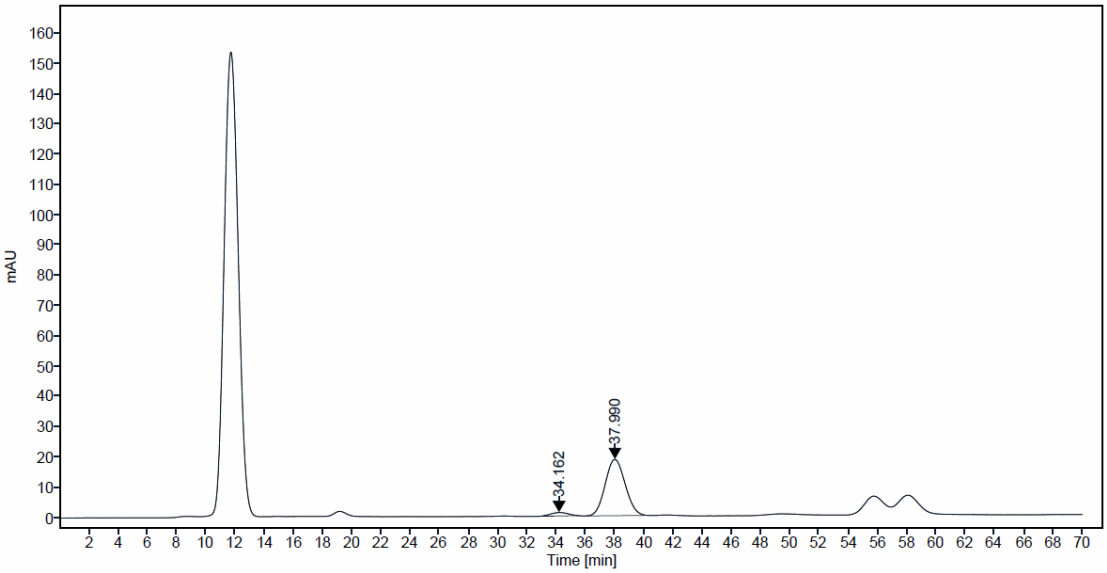


Racemic: Retention time: 33.622 min; 37.520 min

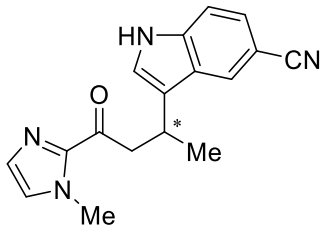


Peak	Retention time (min)	Rel. area (%)
1	33.622	50.2
2	37.520	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3g** as 5:95 and an enantiomeric excess of 90% [CHIRALCEL IG column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 30.788 min; 33.532 min



Peak	Retention time (min)	Rel. area (%)
1	34.162	4.9
2	37.990	95.1



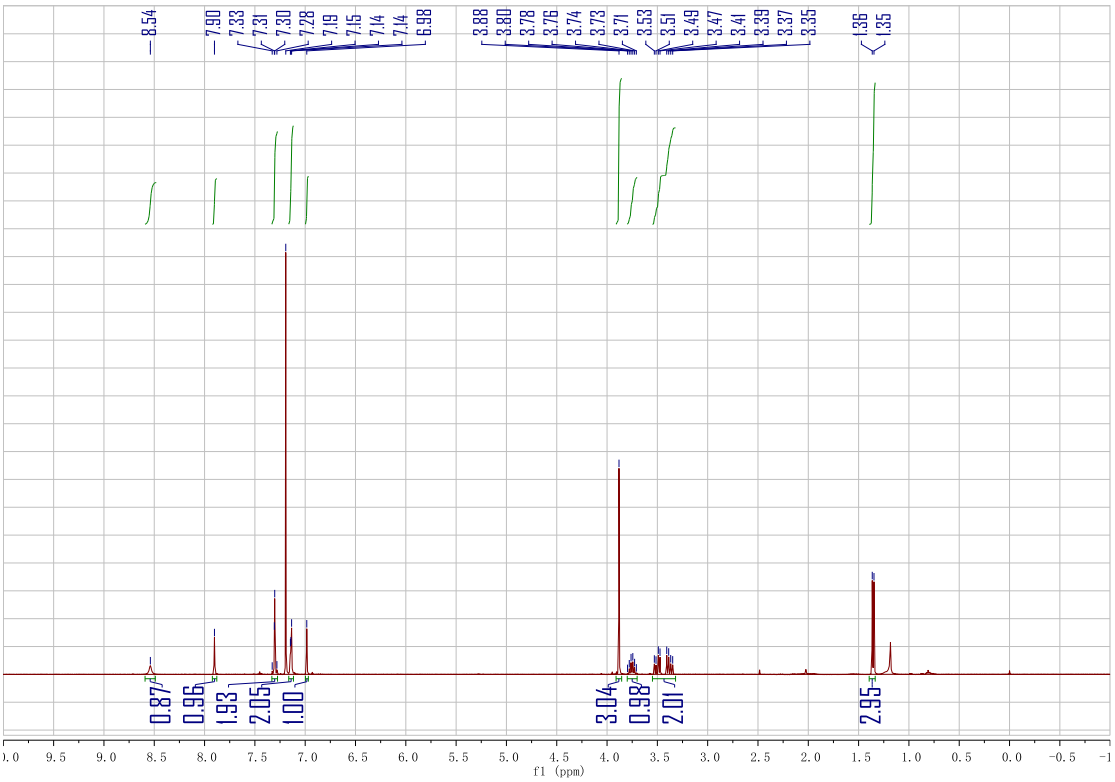
3-(4-(1-methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)-1H-indole-5-carbonitrile (3h).

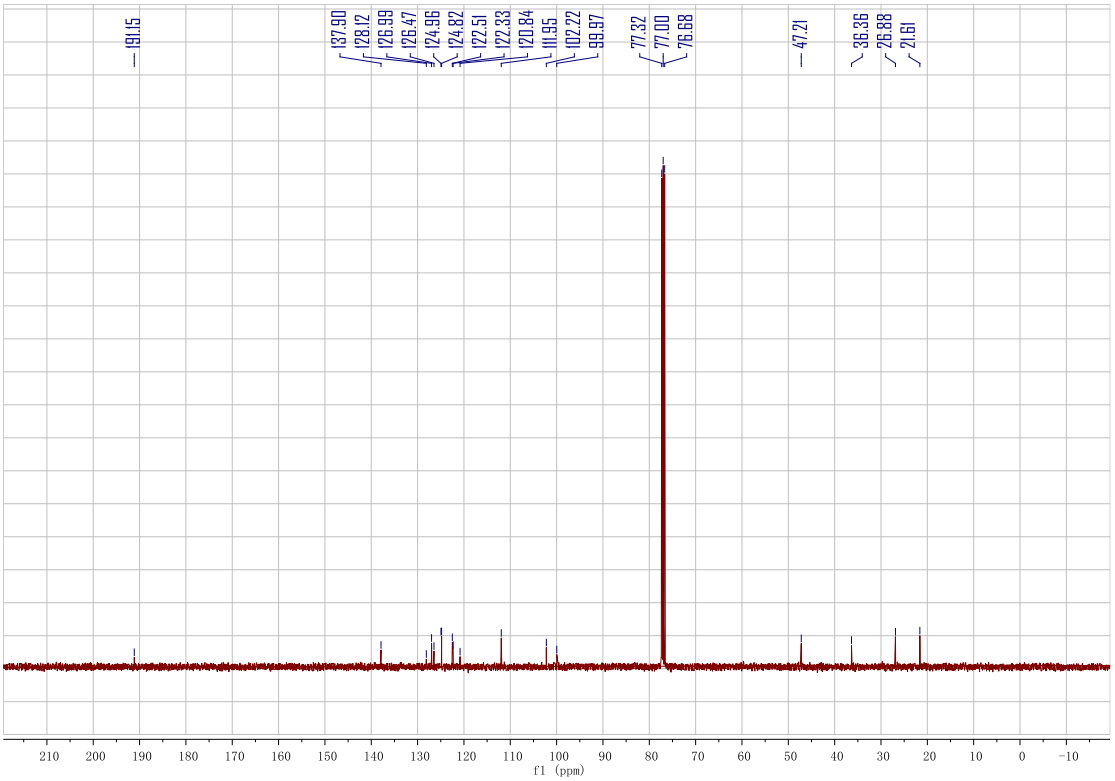
The racemic product was synthesized as described using **1a** and 5-CN-indole. The desired product was obtained as a brown solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.90 (s, 1H), 7.33 – 7.27 (m, 2H), 7.16 – 7.12 (m, 2H), 6.98 (s, 1H), 3.88 (s, 3H), 3.75 (h, *J* = 6.9 Hz, 1H), 3.44 (ddd, *J* = 23.7, 15.9, 7.2 Hz, 2H), 1.36 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.15 (s), 137.90 (s), 128.12 (s), 126.99 (s), 126.47 (s), 124.96 (s), 124.82 (s), 122.51 (s), 122.33 (s), 120.84 (s), 111.95 (s), 102.22 (s), 99.97 (s), 47.21 (s), 36.36 (s), 26.88 (s), 21.61 (s).

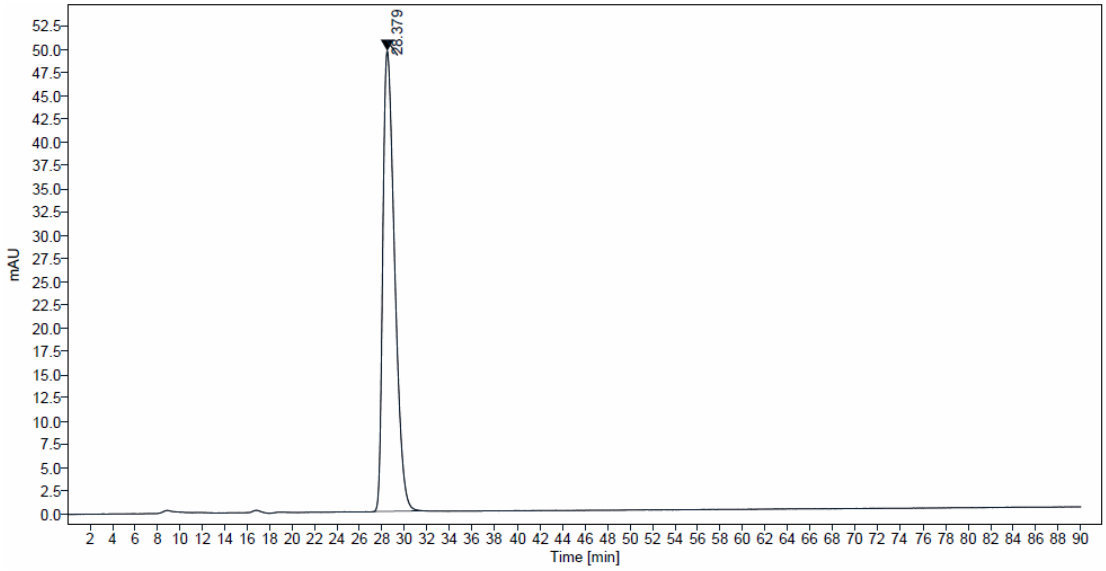
HRMS (ESI) calcd. for $C_{17}H_{17}N_4O$ $[M+H]^+$: m/z 293.1397, found: 293.1396.



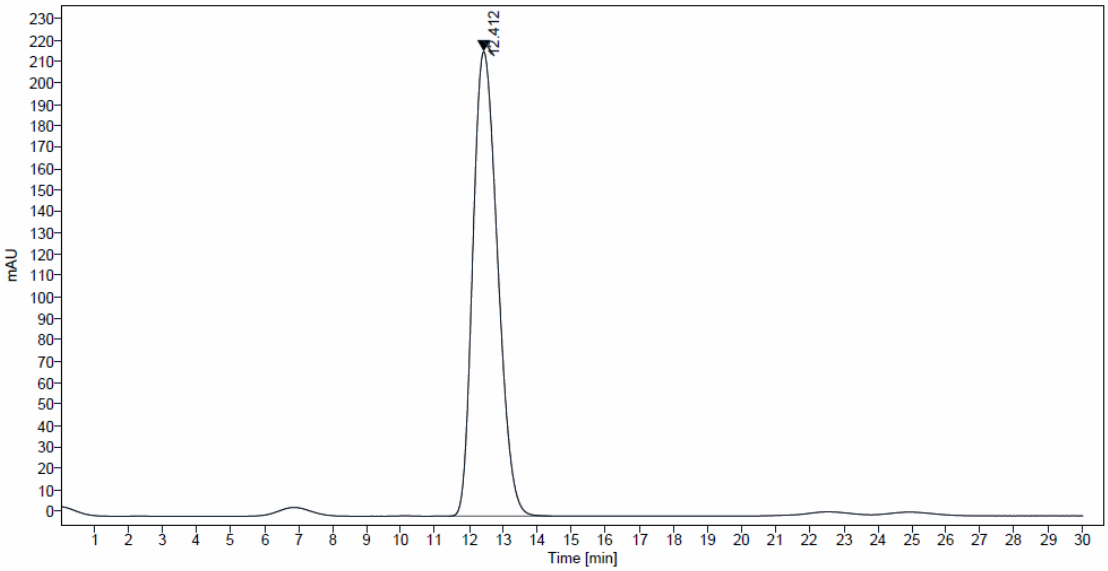


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 96:04, 0.4 mL/min, λ = 280 nm

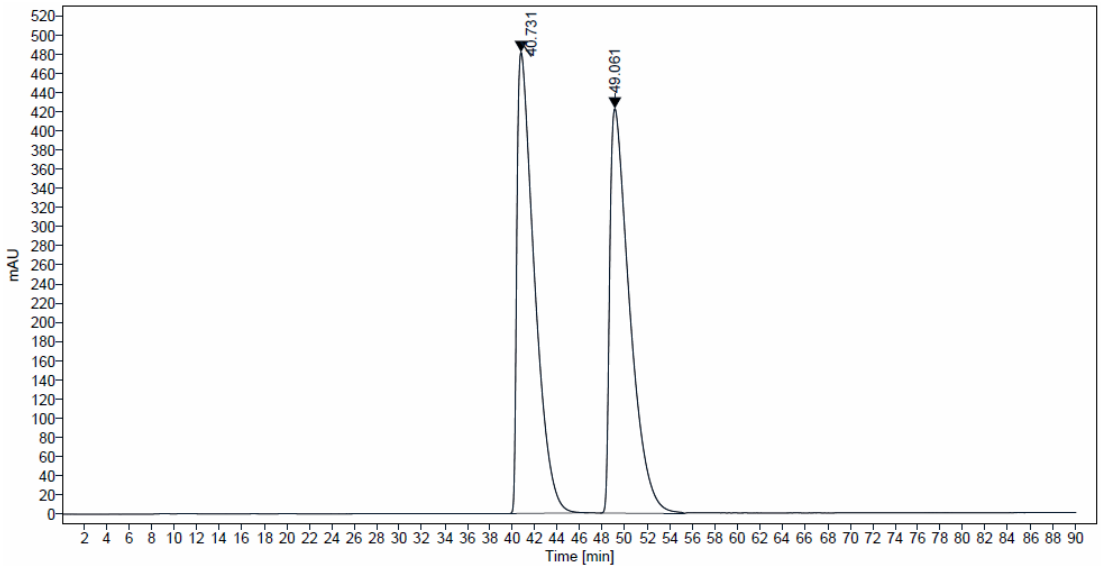
Starting Material (1a): Retention time = 28.379 min



5-CN-Indole: Retention time = 12.412 min

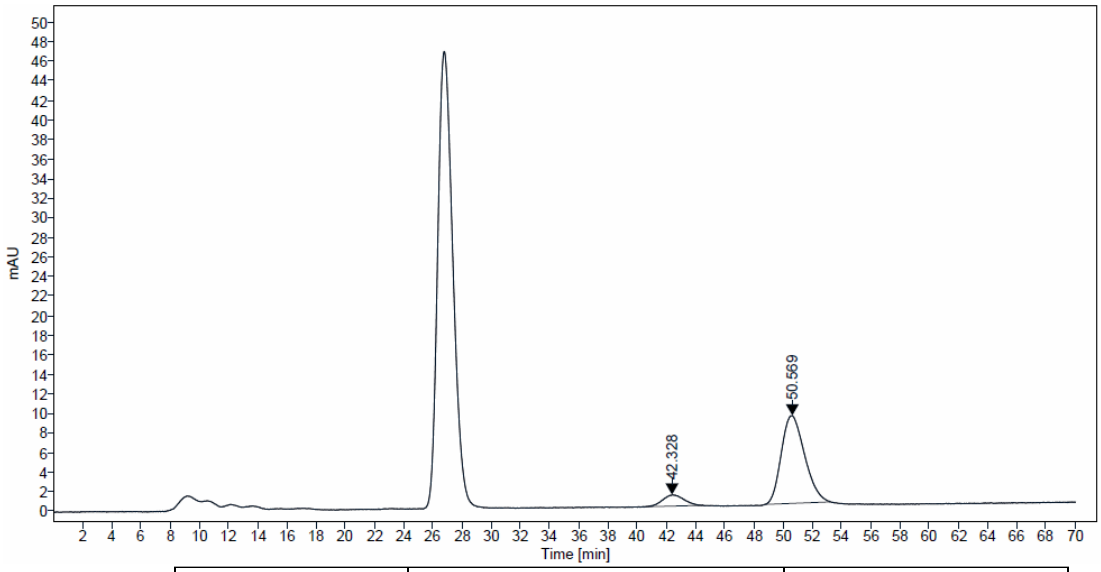


Racemic: Retention time: 40.731 min; 49.061 min

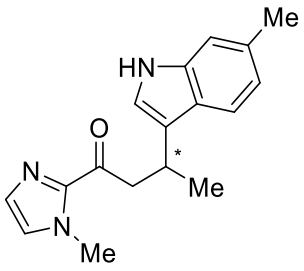


Peak	Retention time (min)	Rel. area (%)
1	40.731	50.5
2	49.061	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3h** as 64:36 and an enantiomeric excess of 77% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 96:04, 0.4 mL/min, λ = 280 nm]. Retention time: 42.328 min; 50.569 min



Peak	Retention time (min)	Rel. area (%)
1	42.328	11.5
2	50.569	88.5



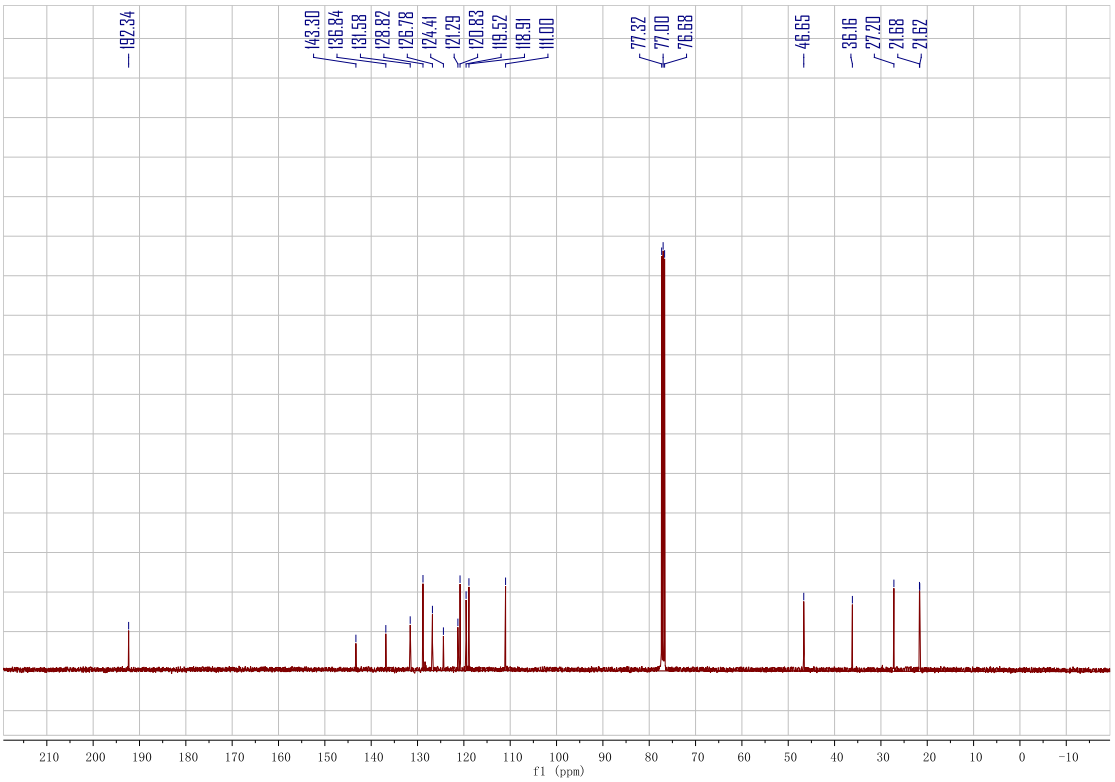
1-(1-methyl-1H-imidazol-2-yl)-3-(6-methyl-1H-indol-3-yl)butan-1-one (3i).

The racemic product was synthesized as described using **1a** and 6-Me-indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.18 (s, 1H), 7.14 (s, 1H), 7.01 (s, 1H), 6.99 (d, *J* = 2.1 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 3.95 (s, 3H), 3.88 – 3.78 (m, 1H), 3.53 (ddd, *J* = 24.0, 15.9, 7.3 Hz, 2H), 2.46 (s, 3H), 1.43 (d, *J* = 6.9 Hz, 3H).

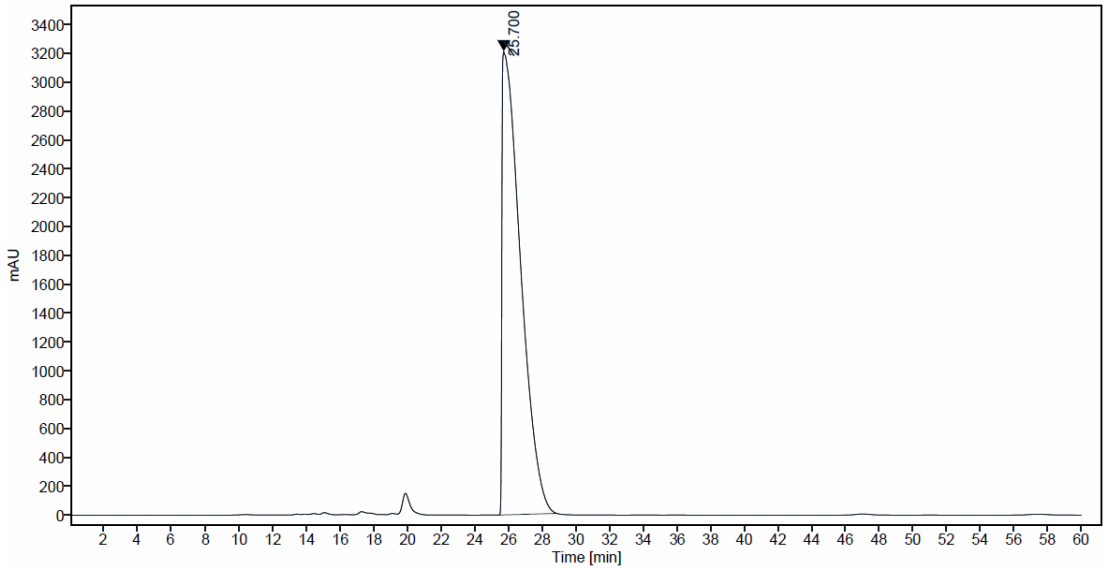
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.34 (s), 143.30 (s), 136.84 (s), 131.58 (s), 128.82 (s), 126.78 (s), 124.41 (s), 121.29 (s), 120.83 (s), 119.52 (s), 118.91 (s), 111.00 (s), 46.65 (s), 36.16 (s), 27.20 (s), 21.68 (s), 21.62 (s).

HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$ $[M+H]^+$: m/z 282.1601, found: 282.1602.

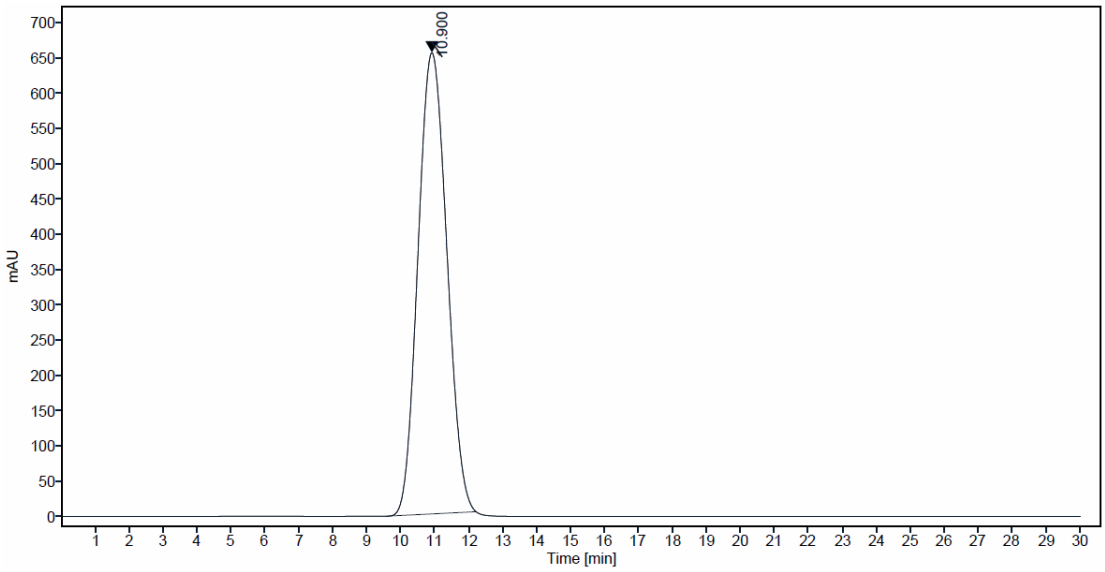


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

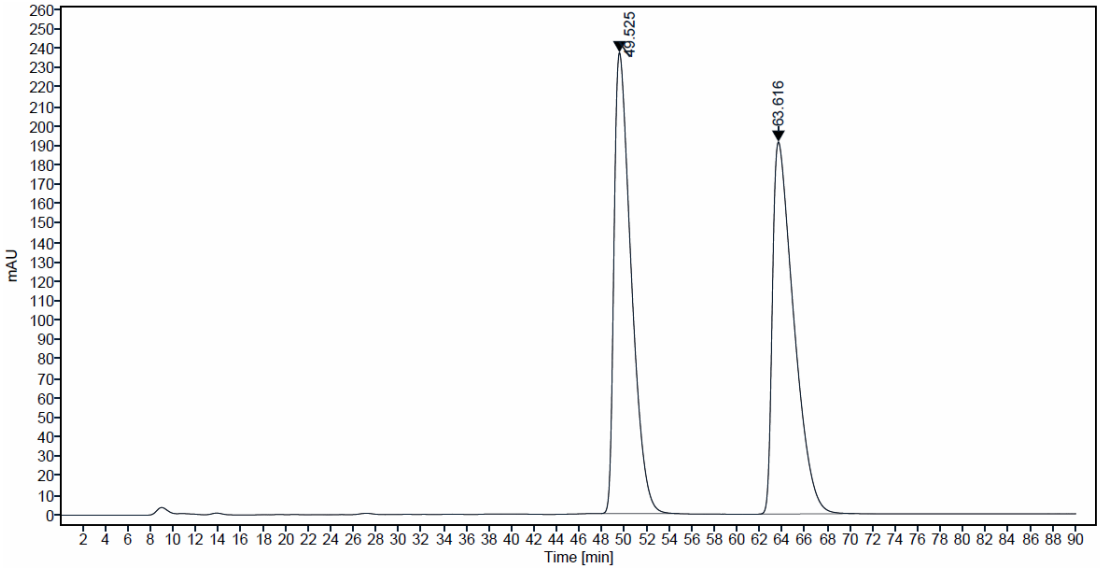
Starting Material (1a): Retention time = 25.700 min



6-Me-Indole: Retention time = 10.900 min

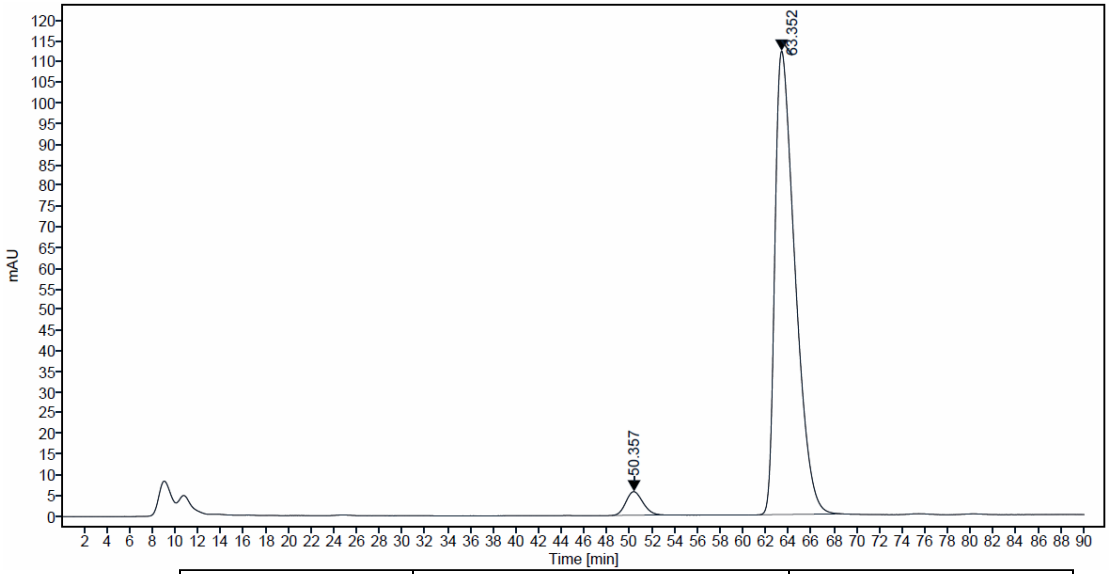


Racemic: Retention time: 49.525 min; 63.616 min

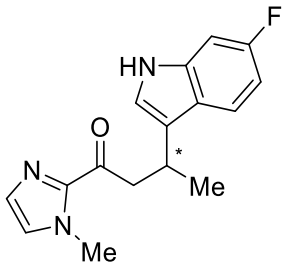


Peak	Retention time (min)	Rel. area (%)
1	49.525	50.4
2	63.616	49.6

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3i** < 1:99 and an enantiomeric excess of 92% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 50.357 min; 63.352 min



Peak	Retention time (min)	Rel. area (%)
1	50.357	3.9
2	63.352	96.1



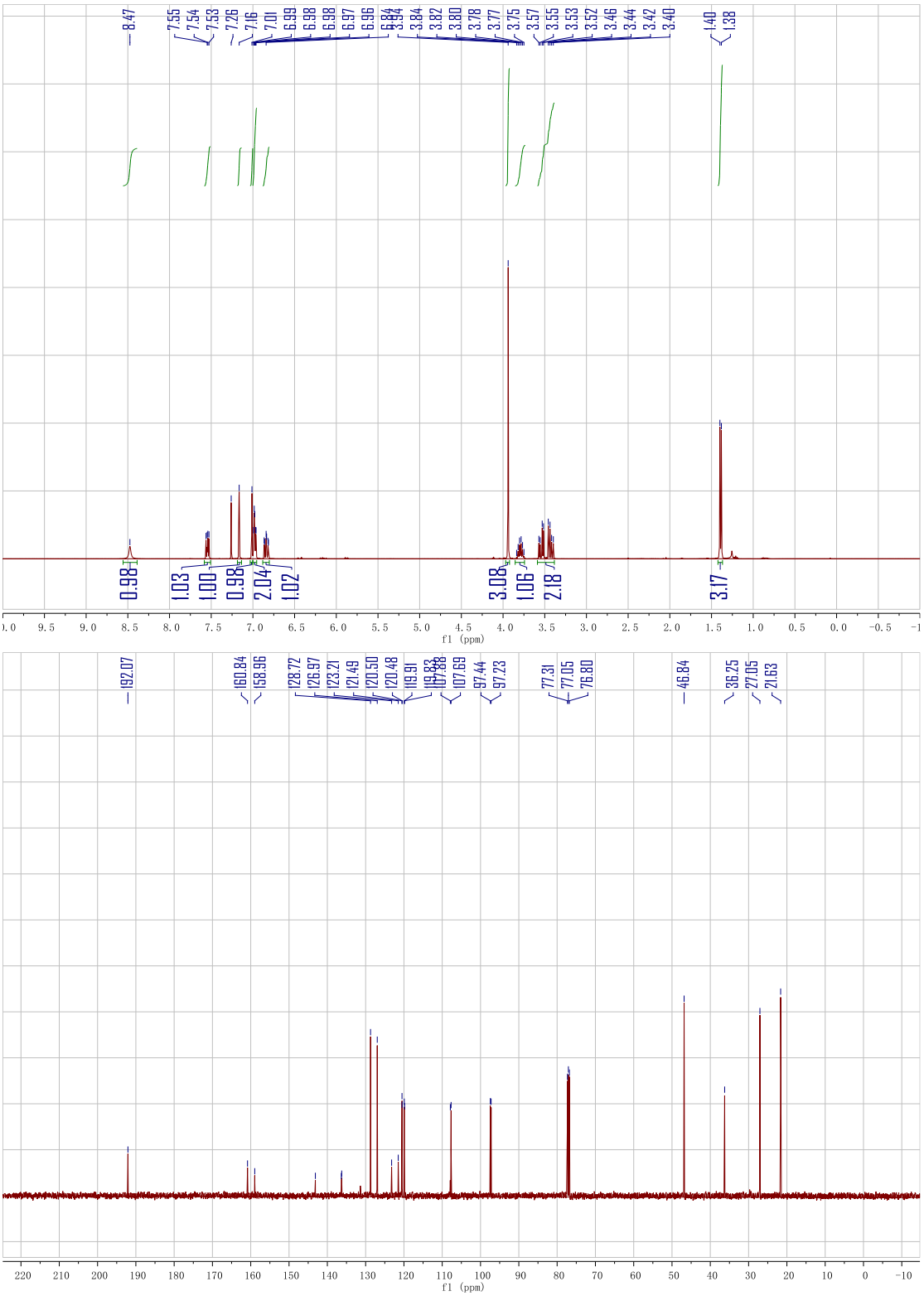
3-(6-fluoro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3j).

The racemic product was synthesized as described using **1a** and 6-F-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.54 (dd, *J* = 8.7, 5.4 Hz, 1H), 7.16 (s, 1H), 7.01 (s, 1H), 7.00 – 6.95 (m, 2H), 6.88 – 6.80 (m, 1H), 3.94 (s, 3H), 3.85 – 3.74 (m, 1H), 3.49 (ddd, *J* = 24.1, 15.9, 7.3 Hz, 2H), 1.39 (d, *J* = 6.9 Hz, 3H).

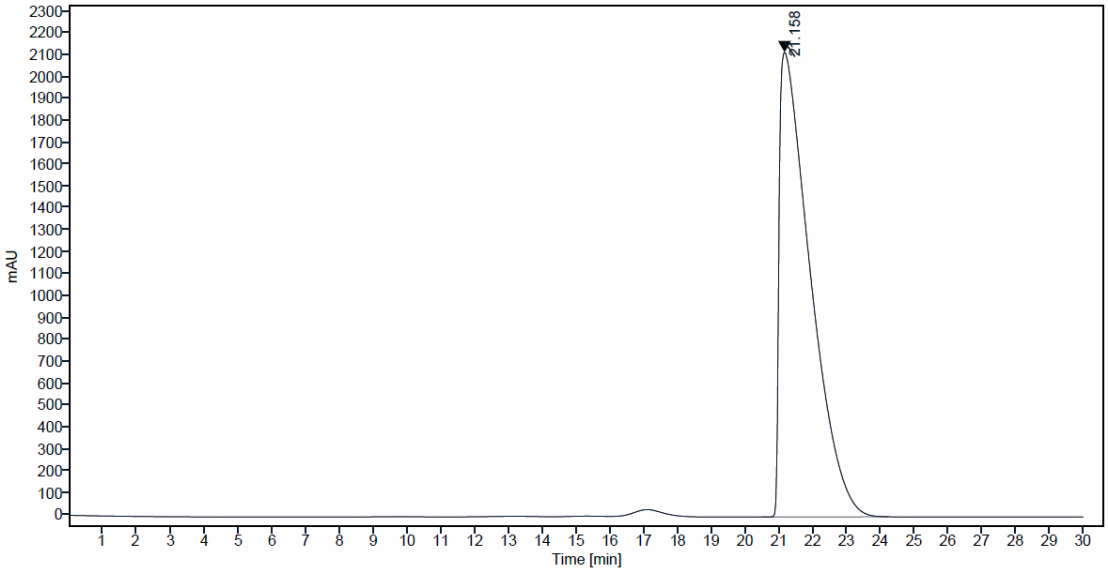
^{13}C NMR (126 MHz, $CDCl_3$) δ 192.07 (s), 159.90 (d, *J* = 237.1 Hz), 143.13 (s), 136.30 (d, *J* = 12.4 Hz), 128.72 (s), 126.97 (s), 123.21 (s), 121.49 (s), 120.49 (d, *J* = 3.4 Hz), 119.87 (d, *J* = 10.2 Hz), 107.78 (d, *J* = 24.4 Hz), 97.33 (d, *J* = 25.9 Hz), 46.84 (s), 36.25 (s), 27.05 (s), 21.63 (s).

HRMS (ESI) calcd. for $C_{16}H_{17}FN_3O$ $[M+H]^+$: m/z 286.1350, found: 286.1350.

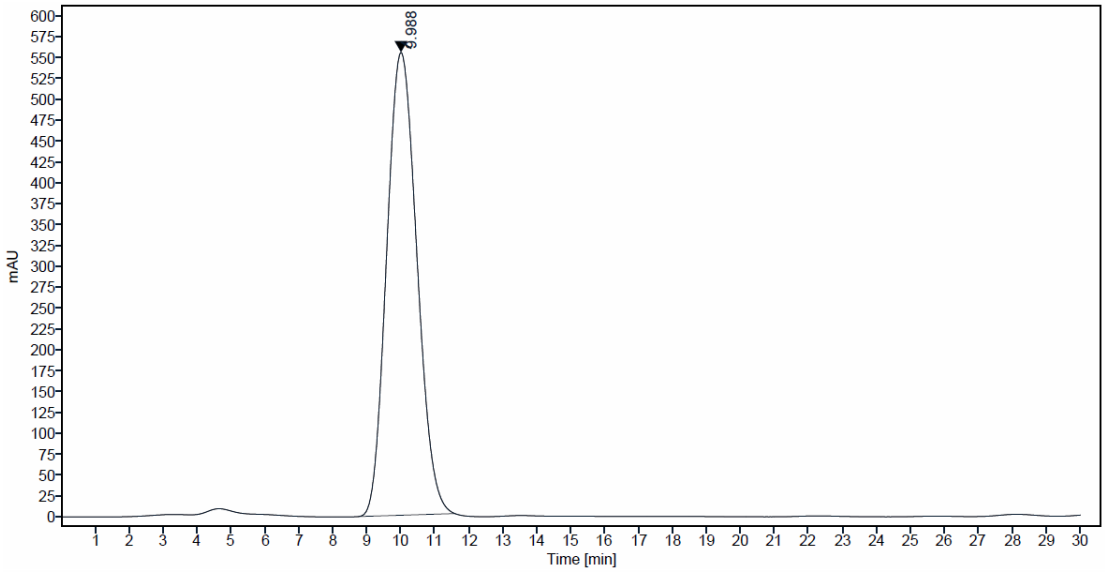


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.5 mL/min, λ = 280 nm

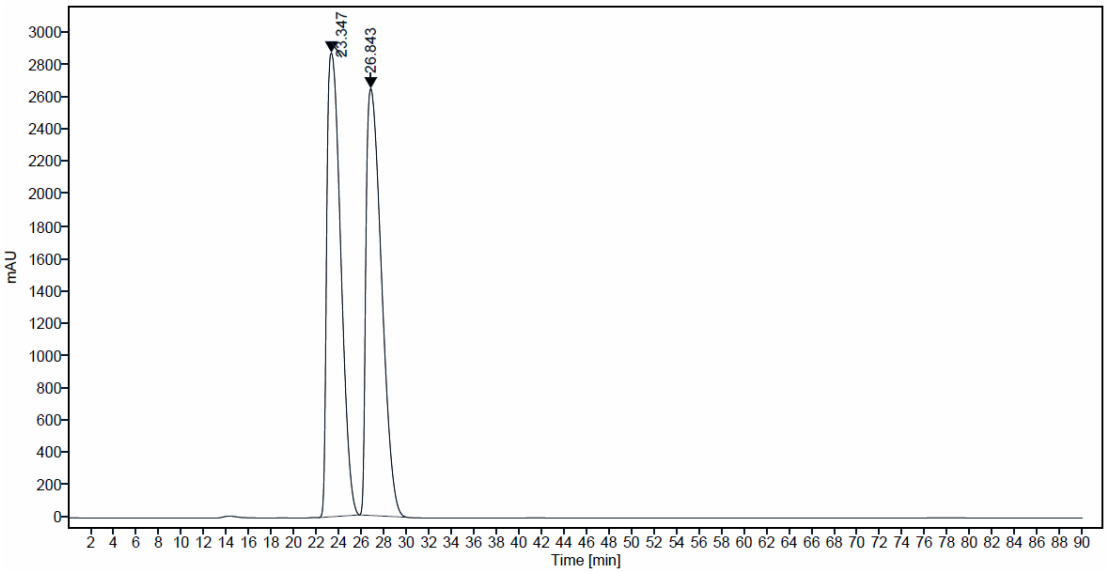
Starting Material (1a): Retention time = 21.158 min



6-F-Indole: Retention time = 9.988 min

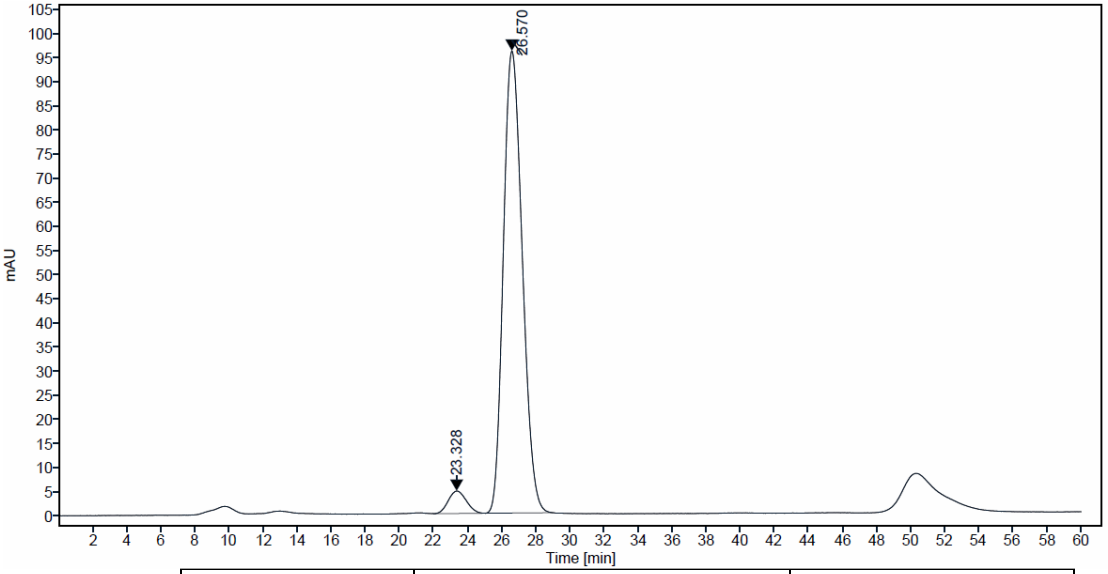


Racemic: Retention time: 23.347min; 26.843 min

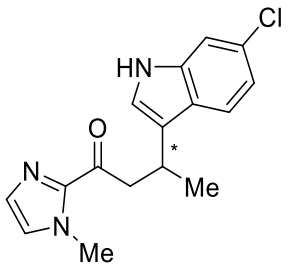


Peak	Retention time (min)	Rel. area (%)
1	23.347	50.1
2	26.843	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3j** < 1:99 and an enantiomeric excess of 91% [CHIRALCEL ID column, T=25 °C, n-Hexane/i-PrOH = 90:10, 0.5 mL/min, λ = 280 nm]. Retention time: 23.328 min; 26.570 min



Peak	Retention time (min)	Rel. area (%)
1	23.328	4.5
2	26.570	95.5



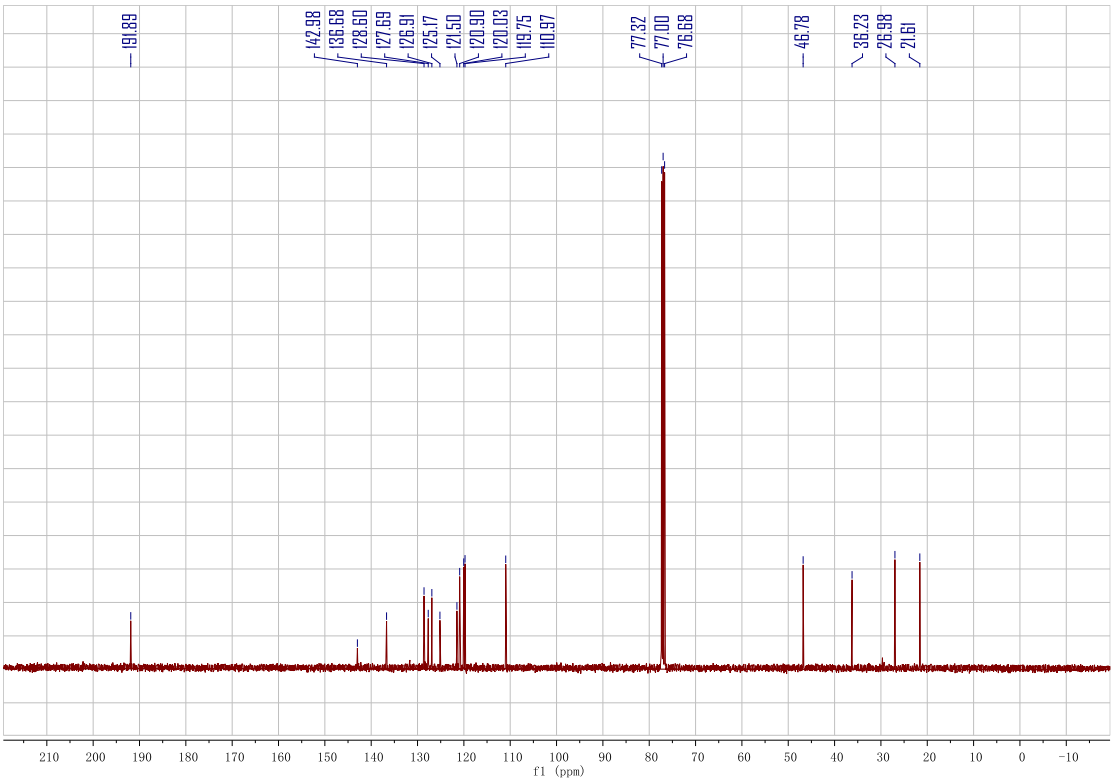
3-(6-chloro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3k).

The racemic product was synthesized as described using **1a** and 6-Cl-indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.22 (d, *J* = 1.6 Hz, 1H), 7.09 (d, *J* = 0.7 Hz, 1H), 7.00 – 6.92 (m, 3H), 3.86 (s, 3H), 3.77 – 3.66 (m, 1H), 3.41 (ddd, *J* = 24.0, 15.9, 7.3 Hz, 2H), 1.32 (d, *J* = 6.9 Hz, 3H).

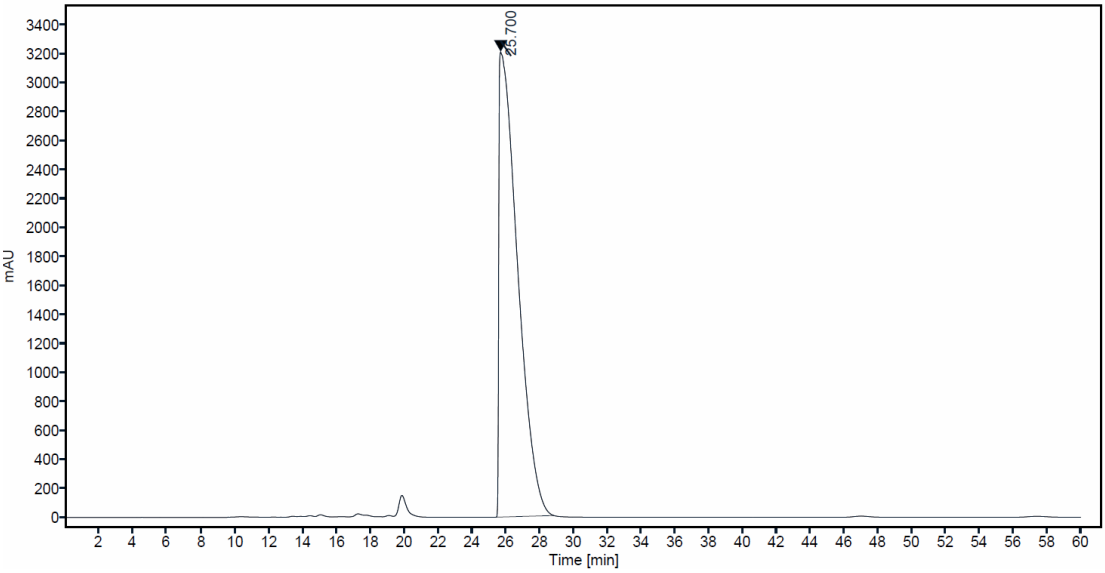
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.89 (s), 142.98 (s), 136.68 (s), 128.60 (s), 127.69 (s), 126.91 (s), 125.17 (s), 121.50 (s), 120.90 (s), 120.03 (s), 119.75 (s), 110.97 (s), 46.78 (s), 36.23 (s), 26.98 (s), 21.61 (s).

HRMS (ESI) calcd. for $C_{16}H_{17}ClN_3O$ $[M+H]^+$: m/z 302.1060, found: 302.1055.

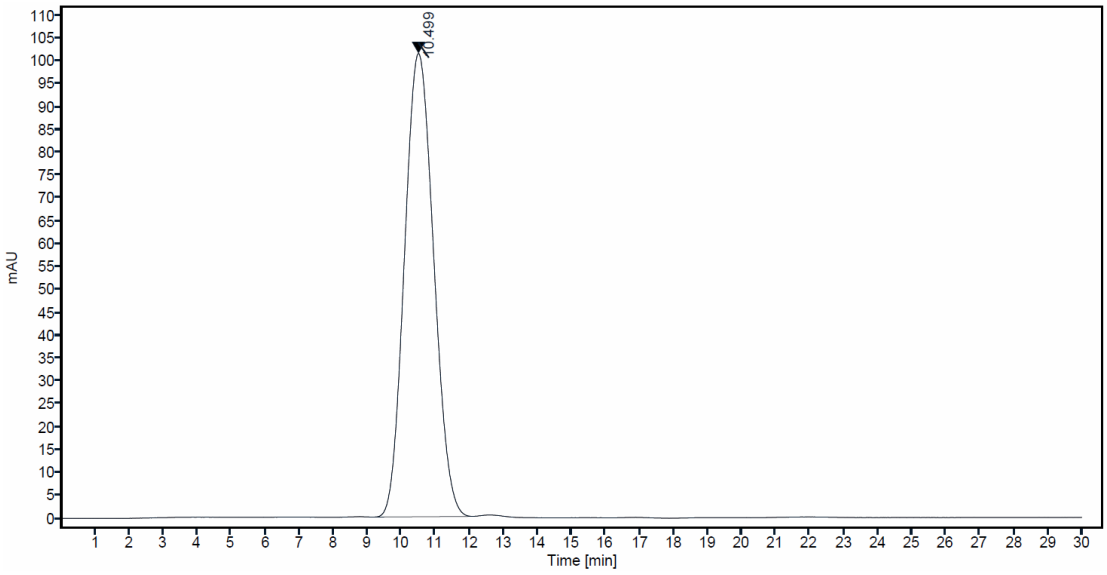


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

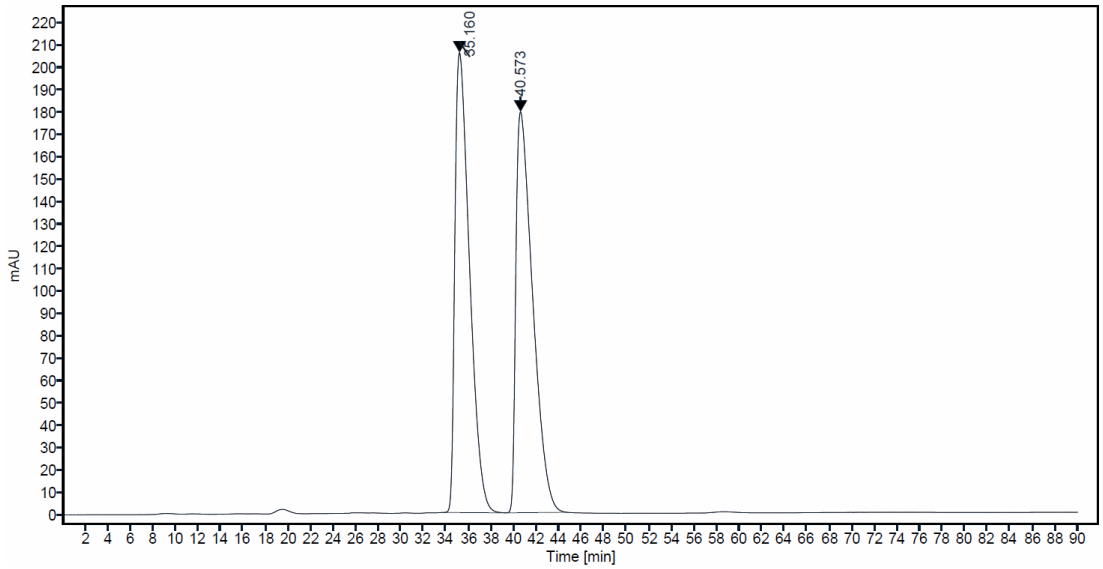
Starting Material (1a): Retention time = 25.692 min



6-Cl-Indole: Retention time = 10.499 min

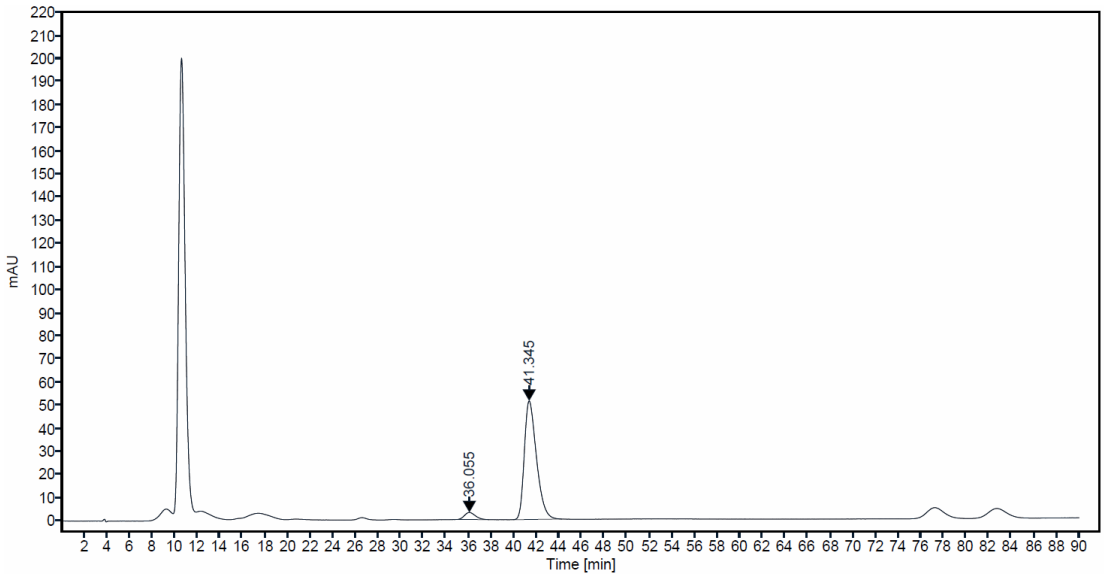


Racemic: Retention time: 35.160 min; 40.573 min

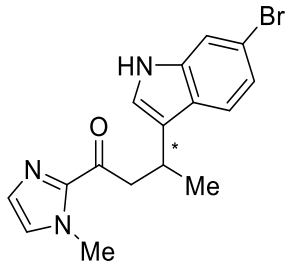


Peak	Retention time (min)	Rel. area (%)
1	35.160	50.2
2	40.573	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3k** as 3:97 and an enantiomeric excess of 90% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 36.055 min; 41.345min



Peak	Retention time (min)	Rel. area (%)
1	36.055	5.1
2	41.345	94.9



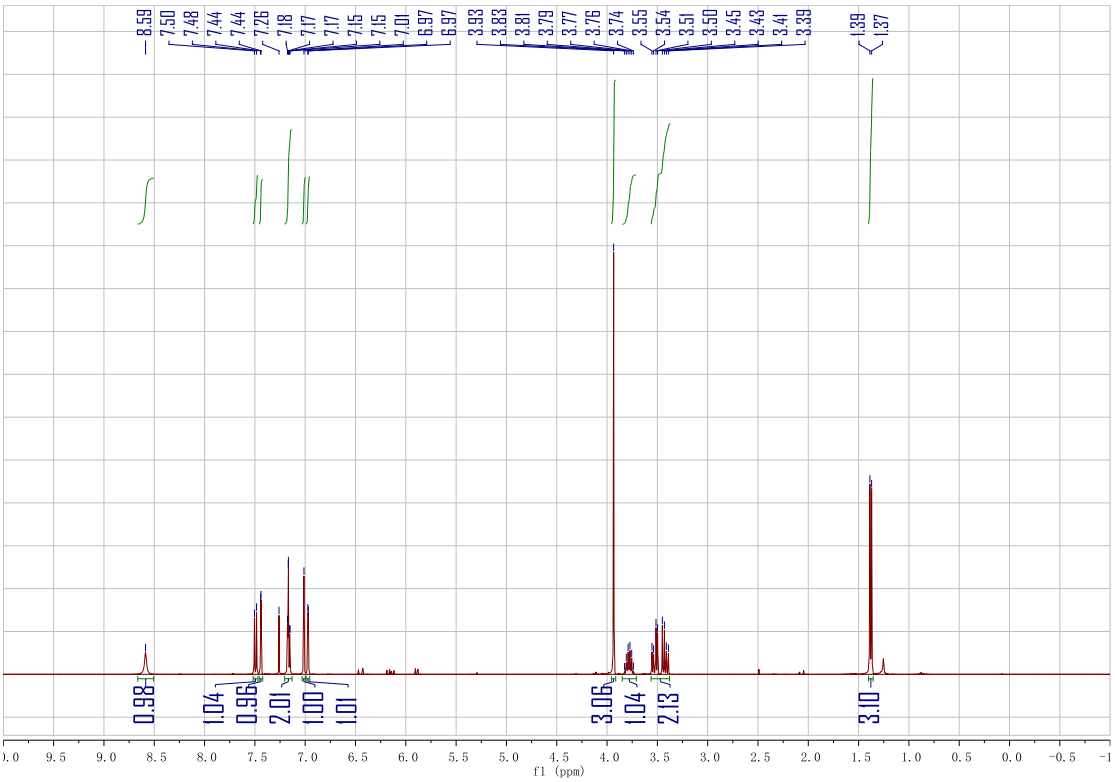
3-(6-bromo-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3l).

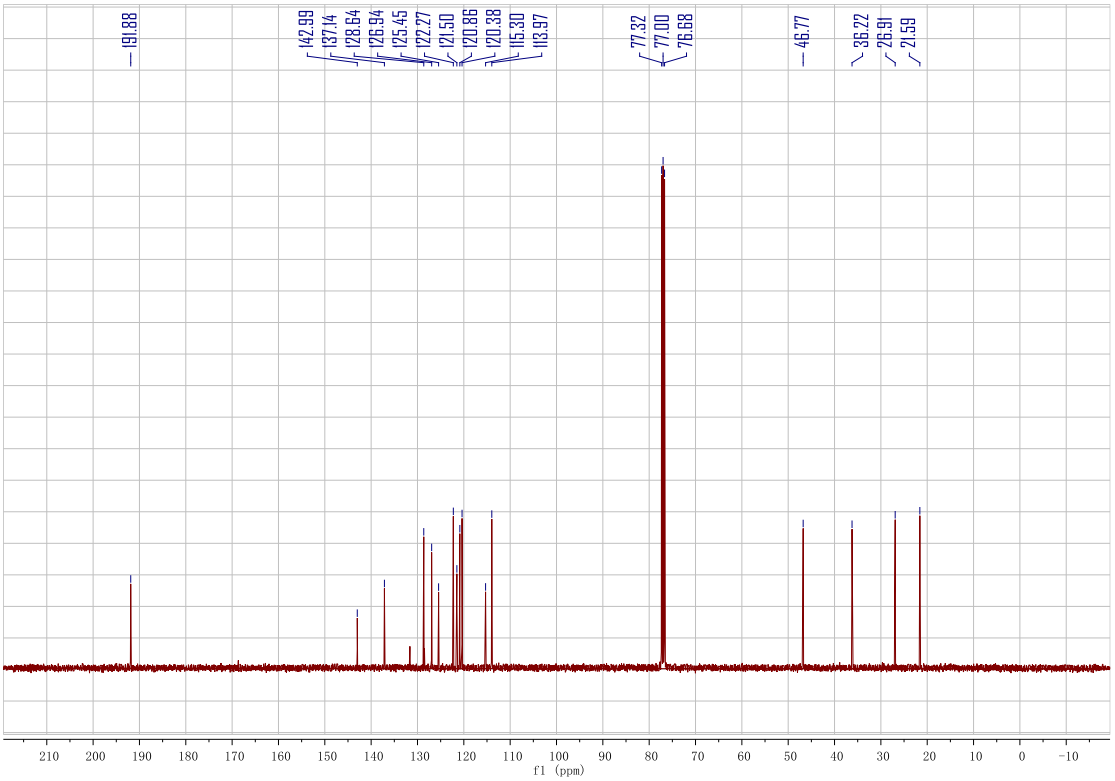
The racemic product was synthesized as described using **1a** and 6-Br-indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.44 (d, *J* = 1.4 Hz, 1H), 7.20 – 7.13 (m, 2H), 7.01 (s, 1H), 6.97 (d, J = 2.1 Hz, 1H), 3.93 (s, 3H), 3.85 – 3.71 (m, 1H), 3.47 (ddd, *J* = 24.1, 15.9, 7.3 Hz, 2H), 1.38 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.88 (s), 142.99 (s), 137.14 (s), 128.64 (s), 126.94 (s), 125.45 (s), 122.27 (s), 121.50 (s), 120.86 (s), 120.38 (s), 115.30 (s), 113.97 (s), 46.77 (s), 36.22 (s), 26.91 (s), 21.59 (s).

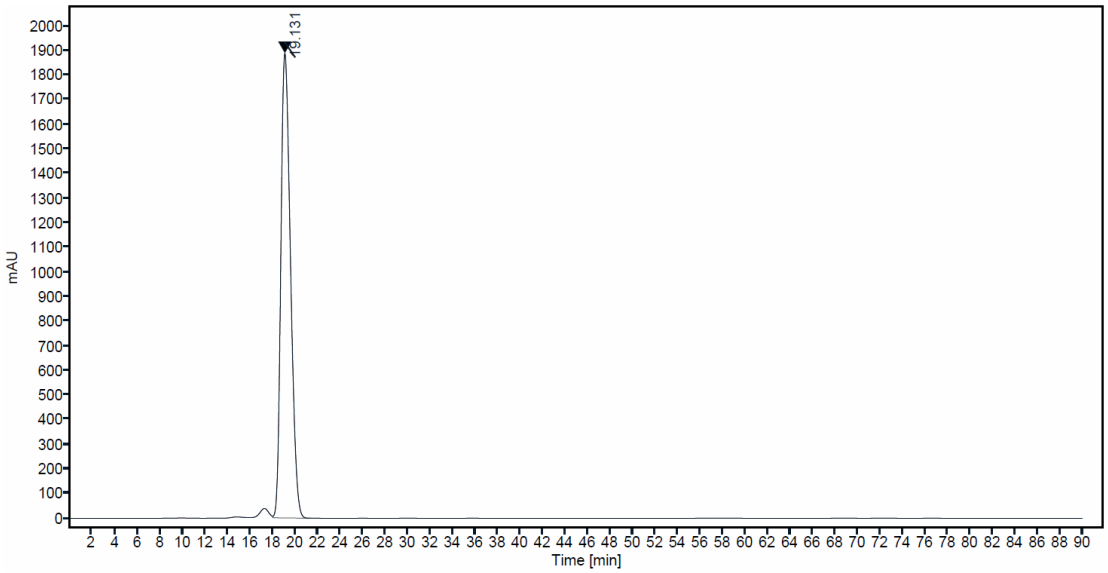
HRMS (ESI) calcd. for $C_{16}H_{17}BrN_3O$ $[M+H]^+$: m/z 346.0555, found: 346.0549.



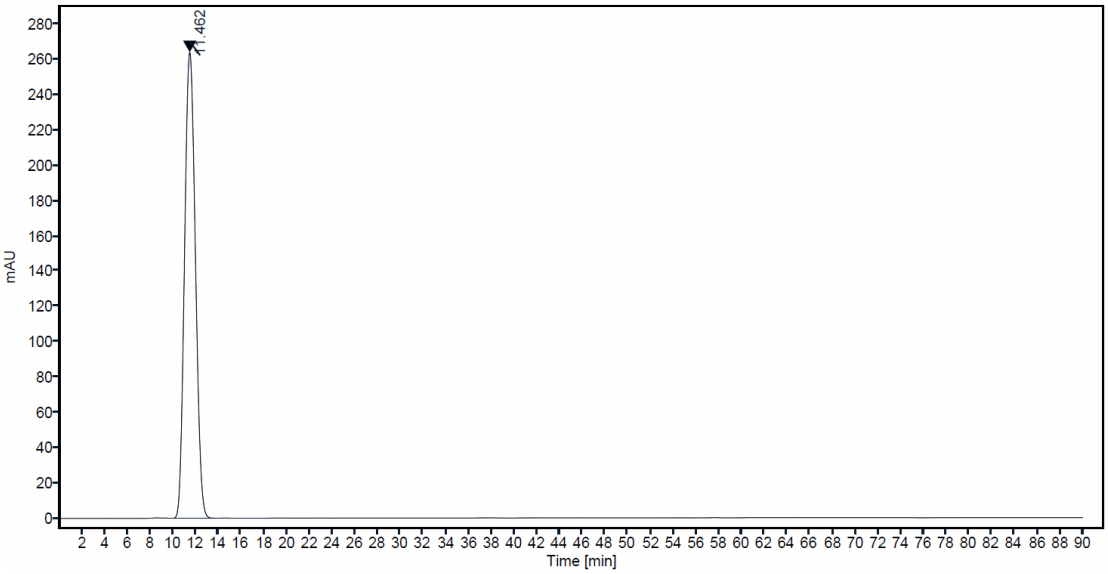


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

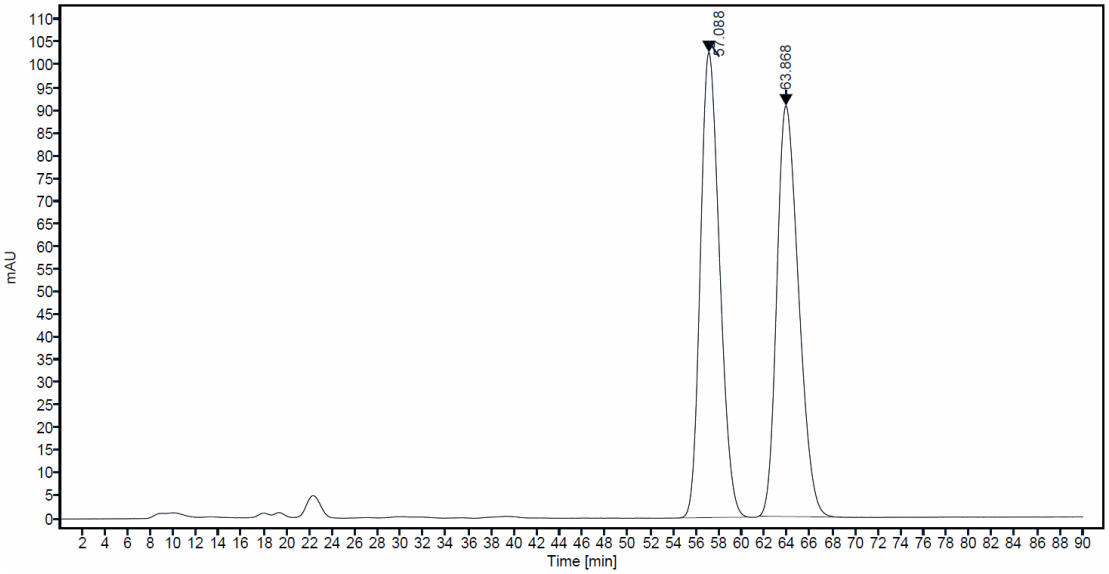
Starting Material (1a): Retention time = 19.131 min



6-Br-Indole: Retention time = 11.462 min

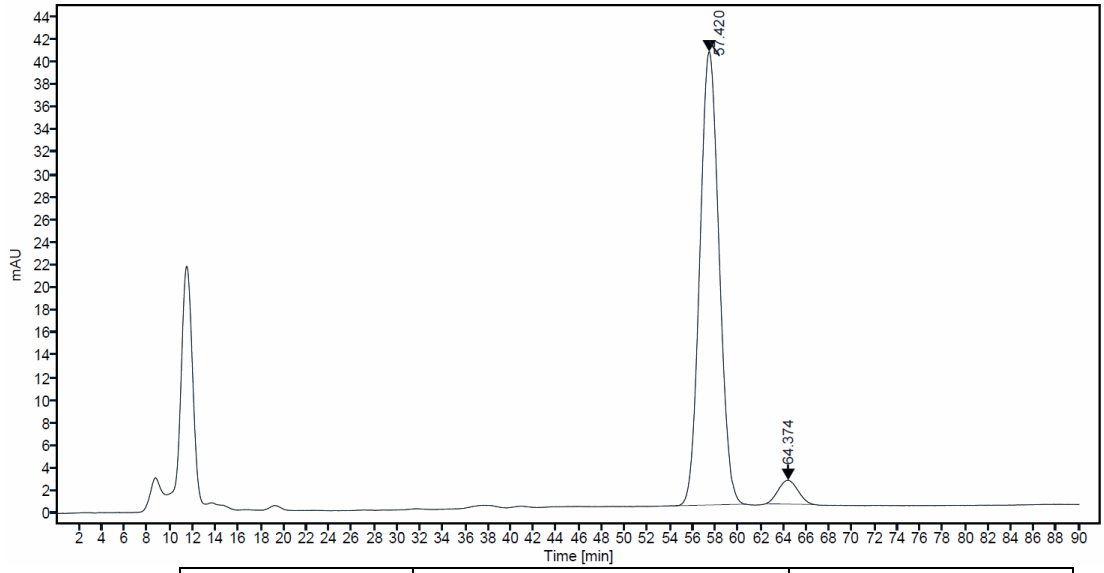


Racemic: Retention time: 57.088 min; 63.868 min

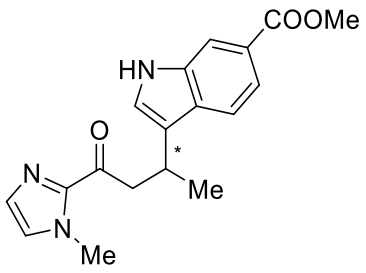


Peak	Retention time (min)	Rel. area (%)
1	57.088	50.1
2	63.868	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3l** as 5:95 and an enantiomeric excess of 90% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 57.420 min; 64.374 min



Peak	Retention time (min)	Rel. area (%)
1	57.420	95.1
2	64.374	4.9



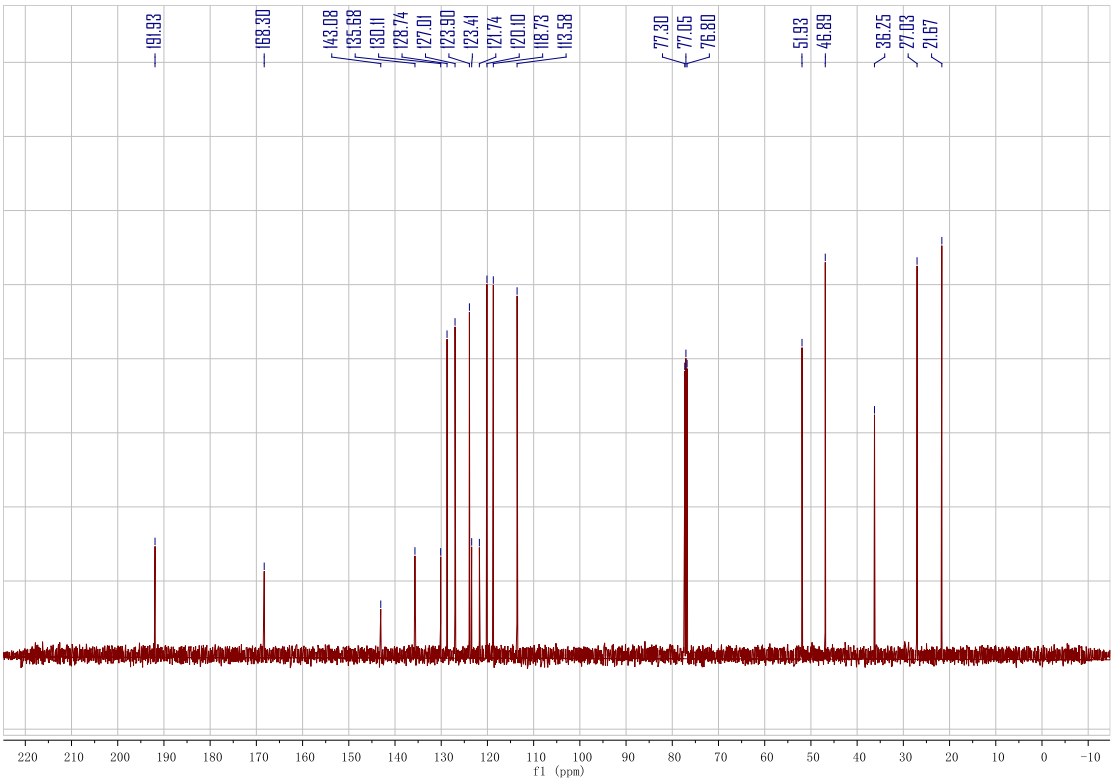
methyl 3-(4-(1-methyl-1H-imidazol-2-yl)-4-oxobutan-2-yl)-1H-indole-6-carboxylate (3m).

The racemic product was synthesized as described using **1a** and 6-COOMe-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 30:70).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.99 (d, *J* = 0.7 Hz, 1H), 7.68 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 7.09 (d, *J* = 0.6 Hz, 1H), 6.93 (s, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.76 (dt, *J* = 14.0, 7.0 Hz, 1H), 3.43 (ddd, *J* = 23.9, 15.8, 7.3 Hz, 2H), 1.33 (d, *J* = 6.9 Hz, 3H).

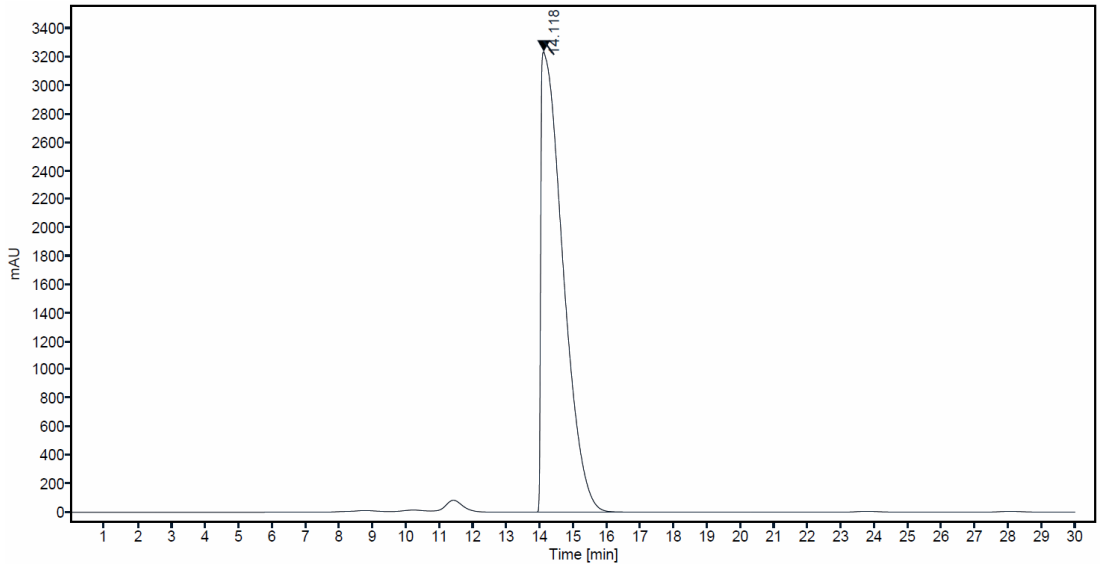
^{13}C NMR (126 MHz, $CDCl_3$) δ 191.93 (s), 168.30 (s), 143.08 (s), 135.68 (s), 130.11 (s), 128.74 (s), 127.01 (s), 123.90 (s), 123.41 (s), 121.74 (s), 120.10 (s), 118.73 (s), 113.58 (s), 51.93 (s), 46.89 (s), 36.25 (s), 27.03 (s), 21.67 (s).

HRMS (ESI) calcd. for $C_{18}H_{20}N_3O_3$ $[M+H]^+$: m/z 326.1499, found: 326.1498.

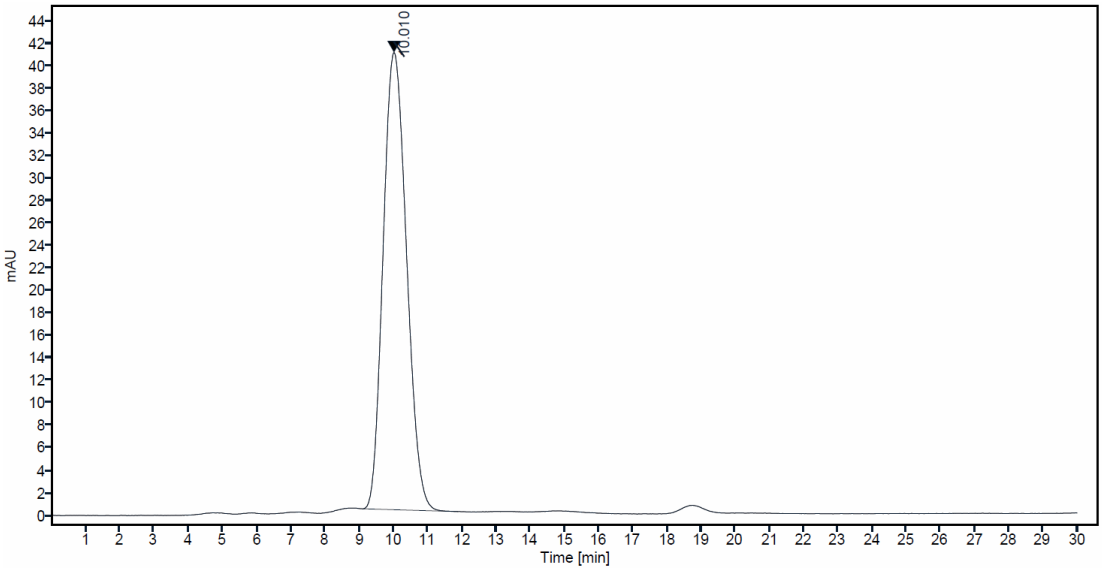


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.75 mL/min, λ = 280 nm

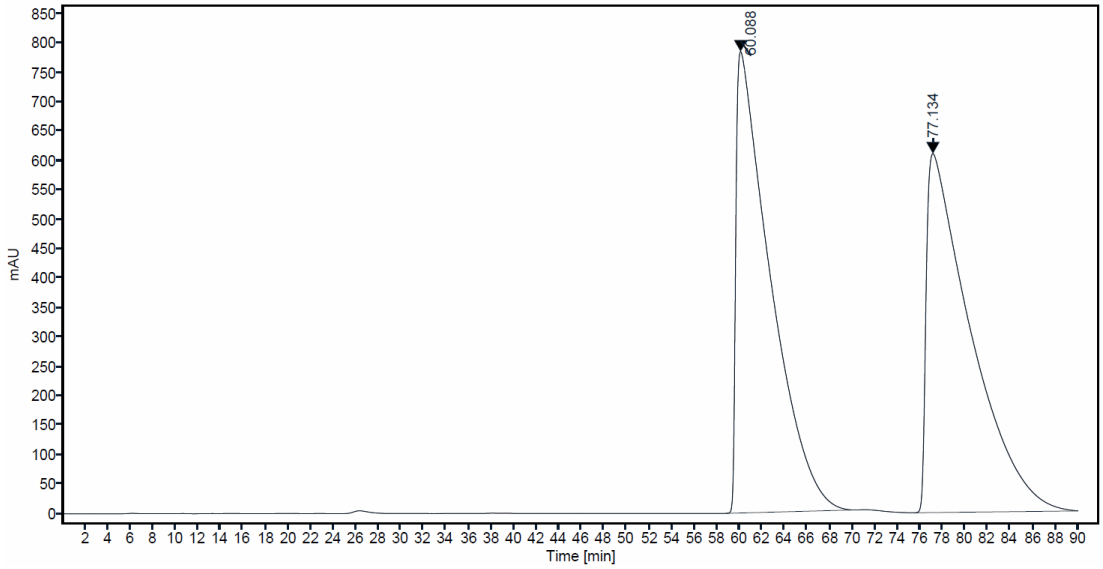
Starting Material (1a): Retention time = 14.118 min



6-COOMe-Indole: Retention time = 10.010 min

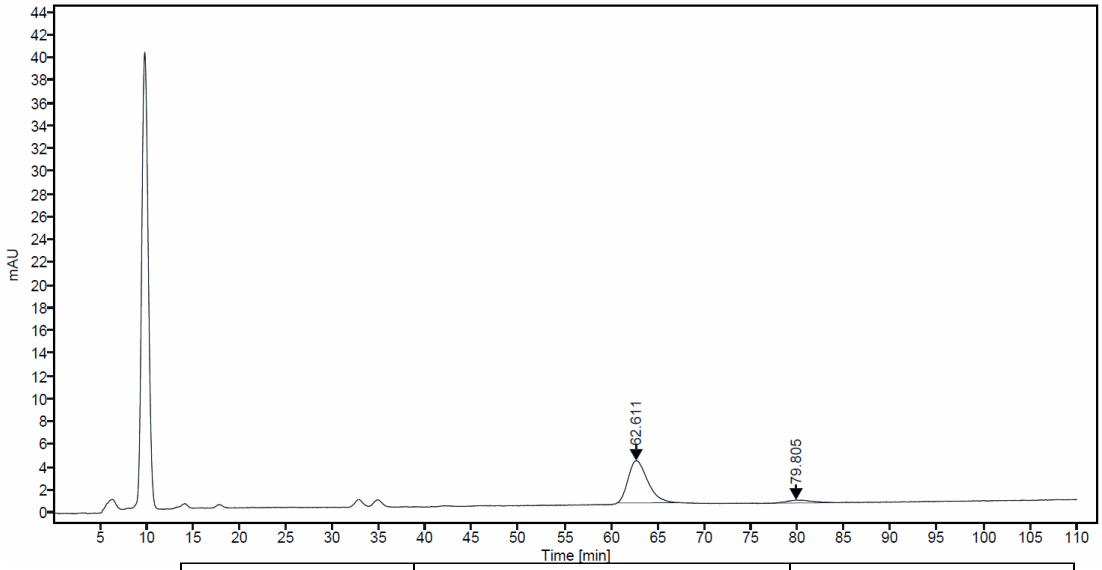


Racemic: Retention time: 60.088 min; 77.134 min

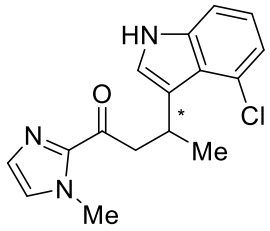


Peak	Retention time (min)	Rel. area (%)
1	60.088	50.0
2	77.134	50.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3m** as 8:92 and an enantiomeric excess of 85% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.75 mL/min, λ = 280 nm]. Retention time: 62.611 min; 79.805 min



Peak	Retention time (min)	Rel. area (%)
1	62.611	92
2	79.805	8



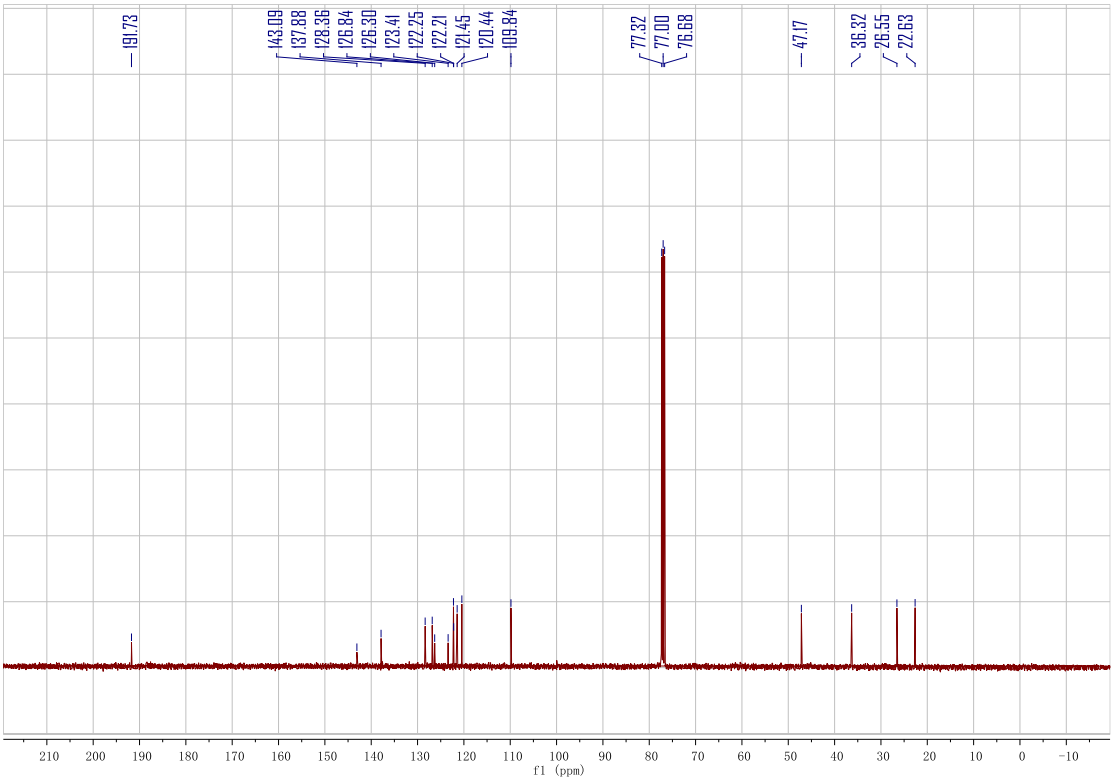
3-(4-chloro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3n).

The racemic product was synthesized as described using **1a** and 4-Cl-indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.20 (dd, *J* = 6.7, 2.3 Hz, 1H), 7.17 (t, *J* = 2.0 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.05 – 6.98 (m, 3H), 4.43 – 4.33 (m, 1H), 4.00 (s, 3H), 3.54 (ddd, *J* = 25.6, 16.8, 7.2 Hz, 2H), 1.38 (d, *J* = 6.8 Hz, 3H)..

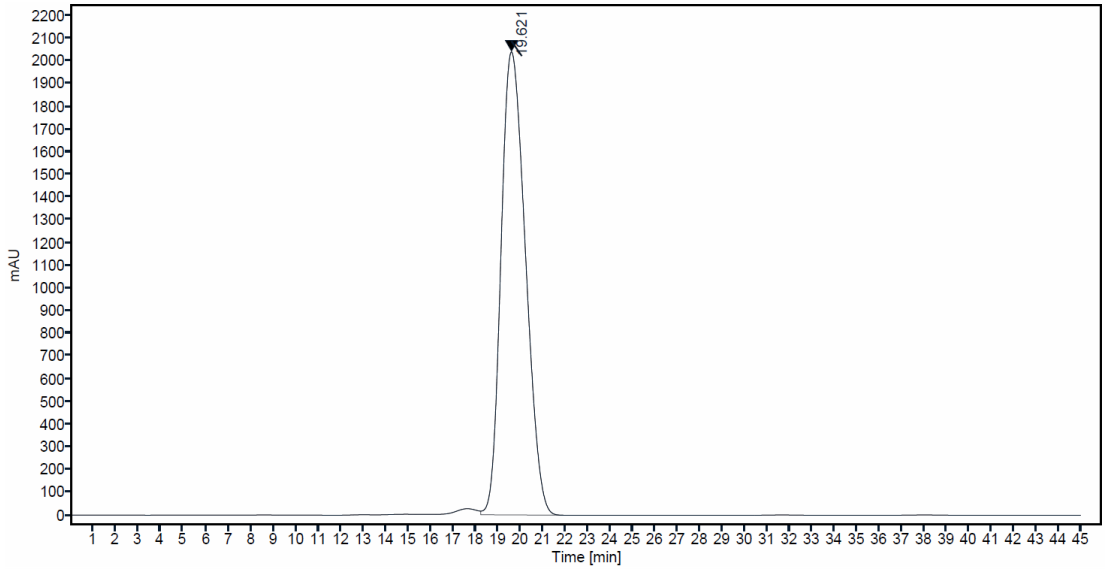
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.73 (s), 143.09 (s), 137.88 (s), 128.36 (s), 126.84 (s), 126.30 (s), 123.41 (s), 122.25 (s), 122.21 (s), 121.45 (s), 120.44 (s), 109.84 (s), 47.17 (s), 36.32 (s), 26.55 (s), 22.63 (s).

HRMS (ESI) calcd. for $C_{16}H_{17}ClN_3O$ $[M+H]^+$: m/z 302.1055, found: 302.1052.

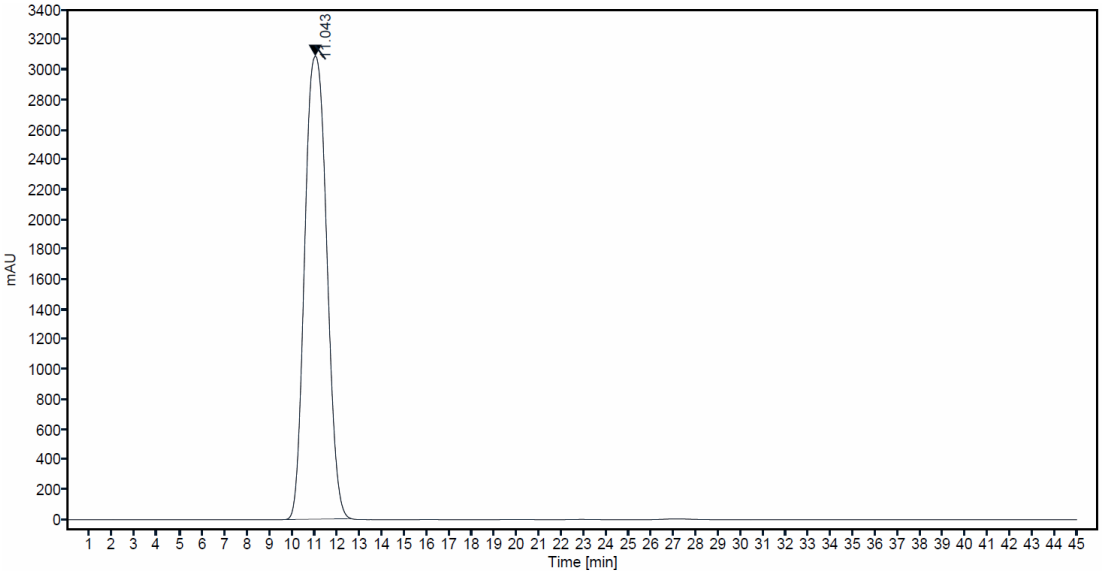


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

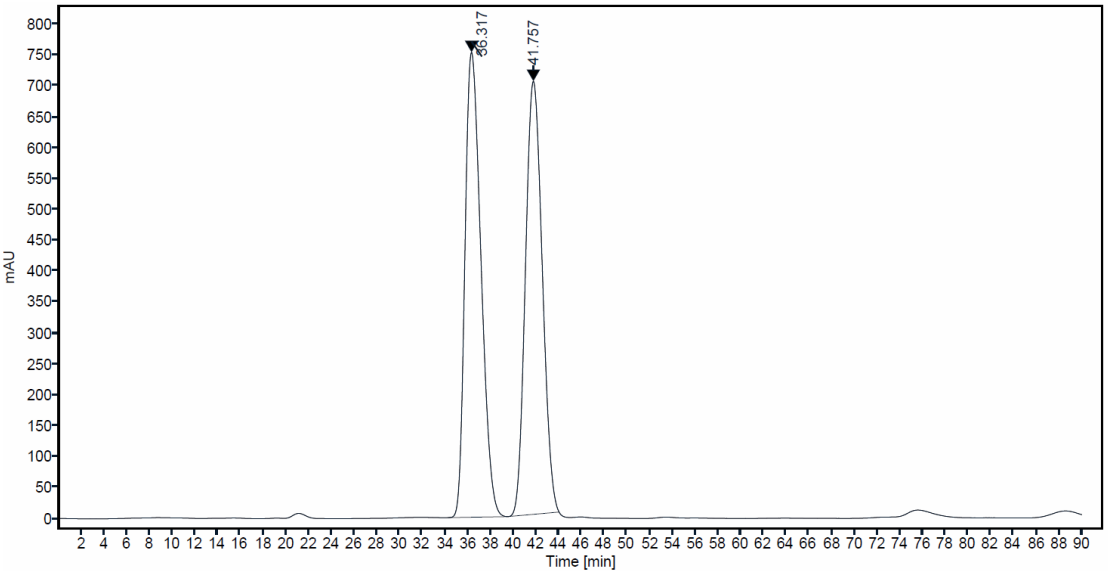
Starting Material (1a): Retention time = 19.621min



4-Cl-Indole: Retention time = 11.043 min

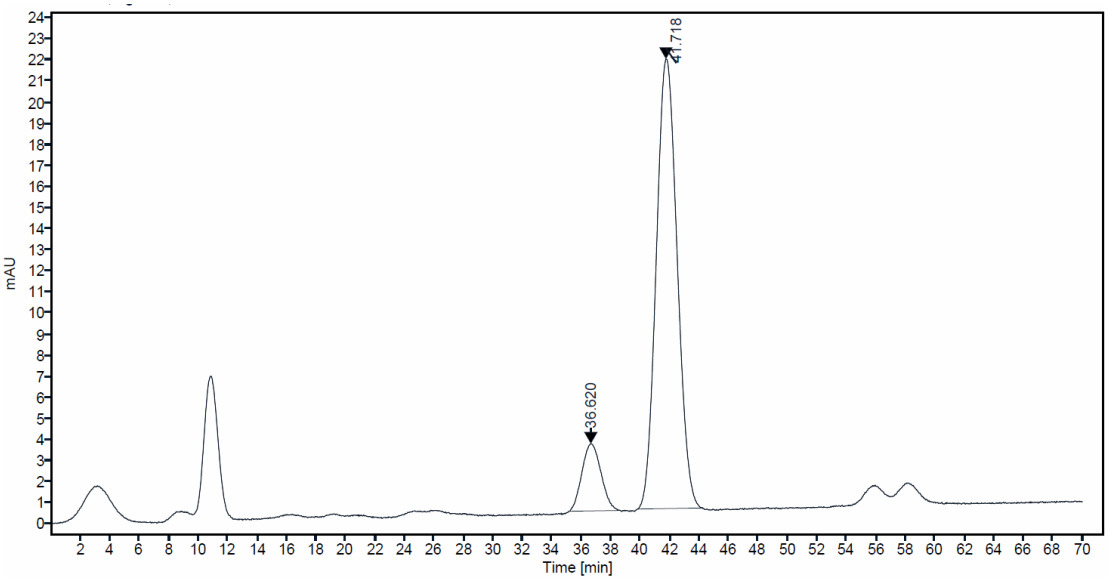


Racemic: Retention time: 36.317 min; 41.757 min

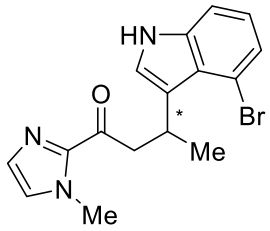


Peak	Retention time (min)	Rel. area (%)
1	36.317	50.3
2	41.757	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3n** < 1:99 and an enantiomeric excess of 76% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 36.620 min; 41.718 min



Peak	Retention time (min)	Rel. area (%)
1	36.620	12.2
2	41.718	87.8



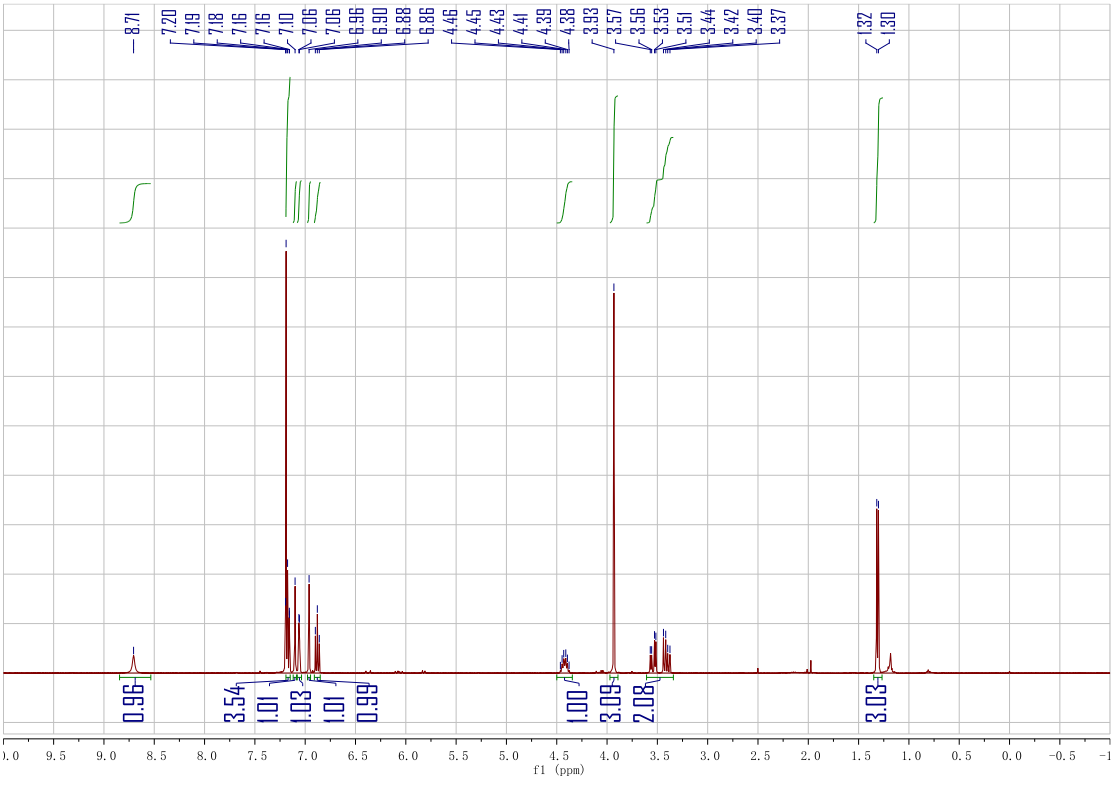
3-(4-bromo-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3o).

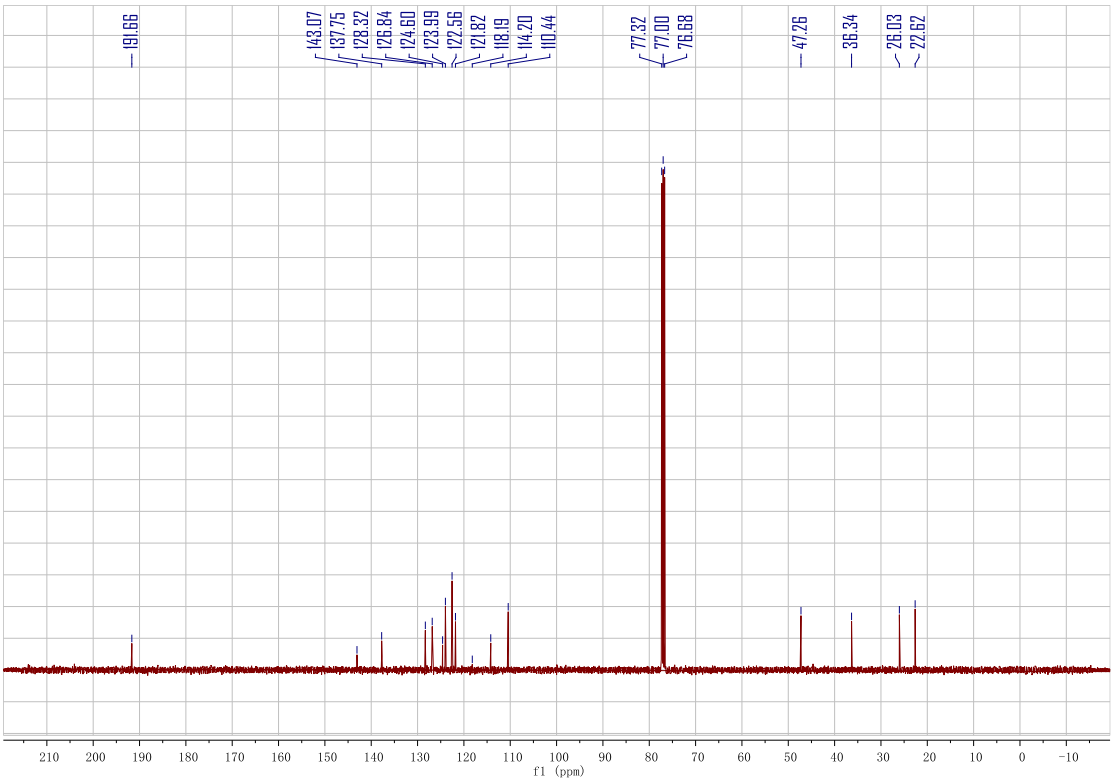
Racemic synthesized through known method using **1a** and 4-Br-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.21 – 7.15 (m, 2H), 7.10 (s, 1H), 7.06 (d, *J* = 2.0 Hz, 1H), 6.96 (s, 1H), 6.88 (t, *J* = 7.8 Hz, 1H), 4.50 – 4.35 (m, 1H), 3.93 (s, 3H), 3.47 (ddd, *J* = 25.8, 16.9, 7.2 Hz, 2H), 1.31 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.70 (s), 143.11 (s), 137.78 (s), 128.36 (s), 126.87 (s), 124.63 (s), 124.03 (s), 122.59 (s), 121.86 (s), 118.23 (s), 114.24 (s), 110.48 (s), 47.29 (s), 36.38 (s), 26.06 (s), 22.66 (s).

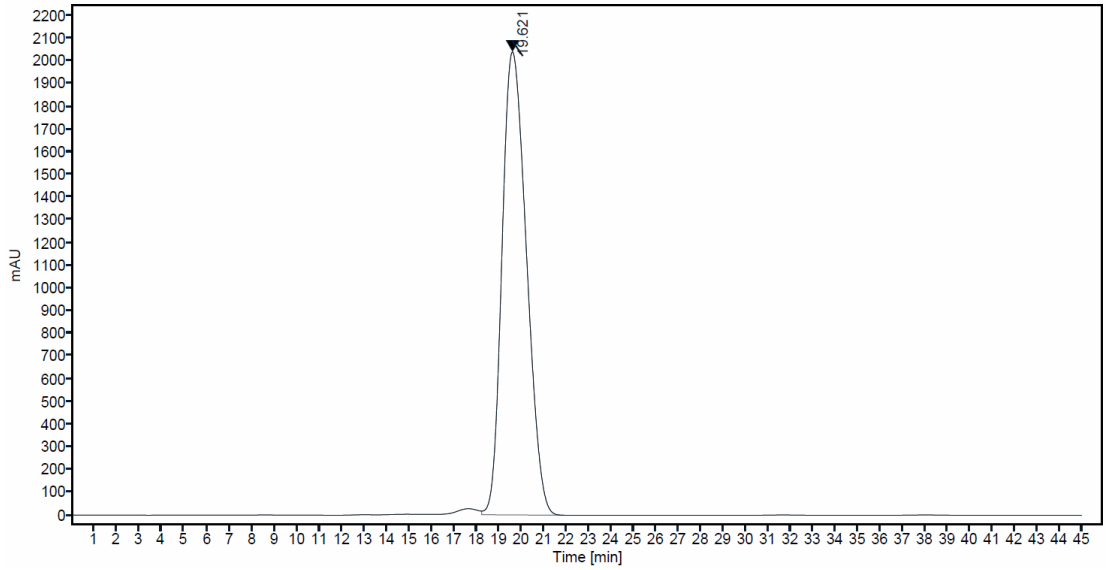
HRMS (ESI) calcd. for $C_{16}H_{17}BrN_3O$ $[M+H]^+$: m/z 346.0550, found: 346.0549.



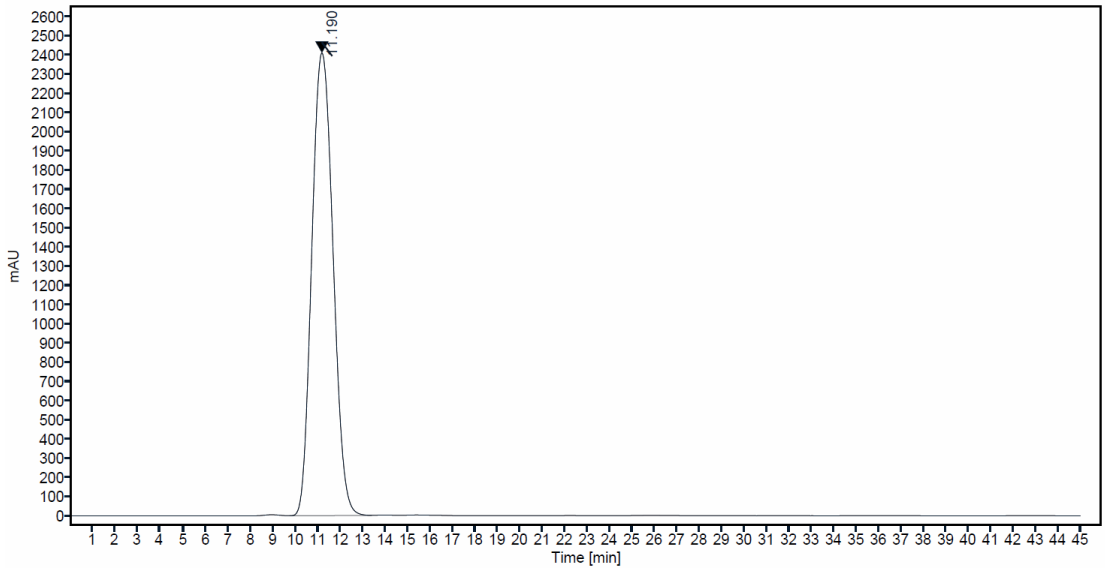


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

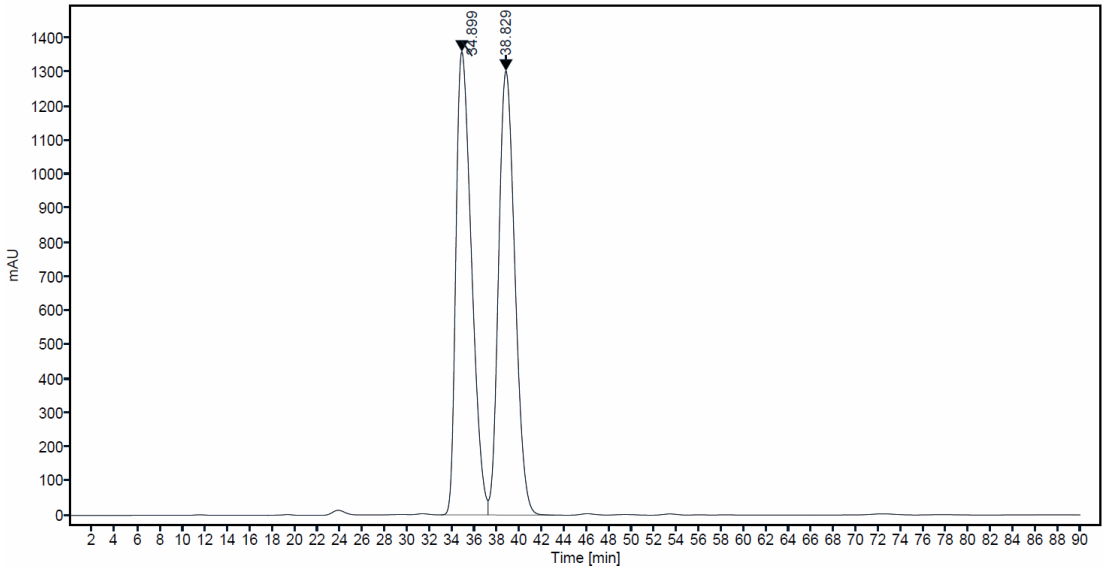
Starting Material (1a): Retention time = 19.621min



4-Br-Indole: Retention time = 11.190 min

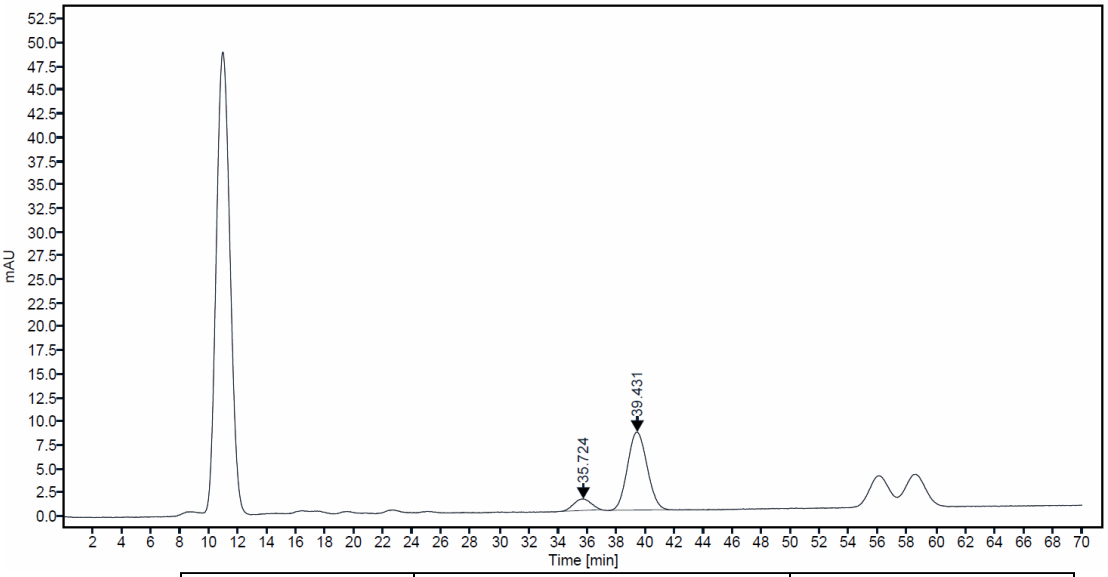


Racemic: Retention time: 34.899 min; 38.829 min

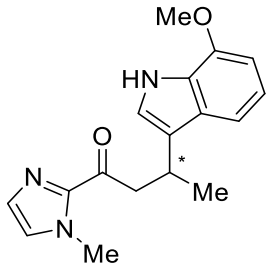


Peak	Retention time (min)	Rel. area (%)
1	34.899	50.0
2	38.829	50.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3o** < 1:99 and an enantiomeric excess of 77% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 35.724 min; 39.431 min



Peak	Retention time (min)	Rel. area (%)
1	35.724	11.6
2	39.432	88.4



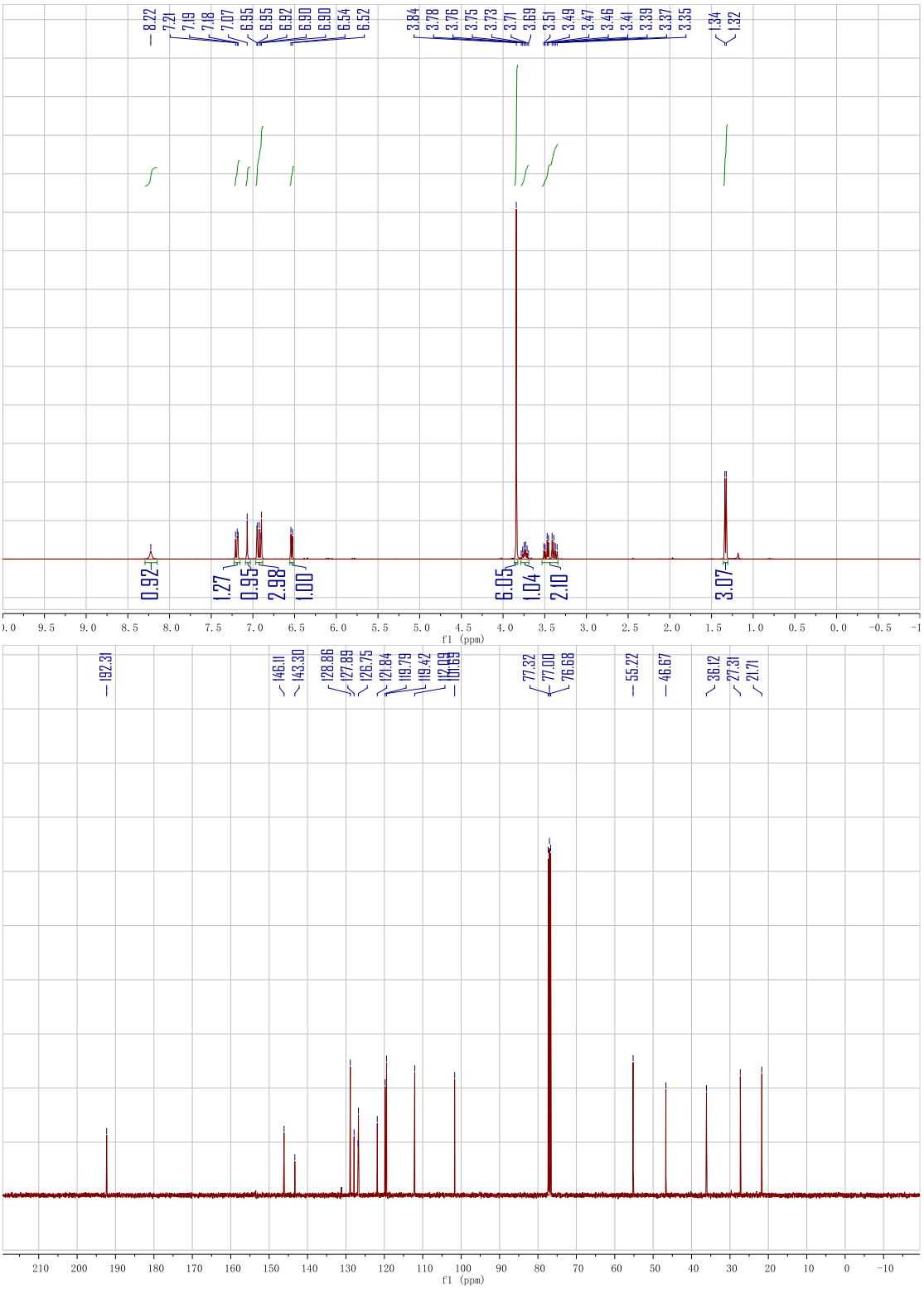
3-(7-methoxy-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3p).

The racemic product was synthesized as described using **1a** and 7-OMe-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.22 – 7.15 (m, 1H), 7.07 (s, 1H), 6.97 – 6.88 (m, 3H), 6.53 (d, *J* = 7.7 Hz, 1H), 3.84 (s, 6H), 3.79 – 3.69 (m, 1H), 3.43 (ddd, *J* = 24.0, 15.9, 7.3 Hz, 2H), 1.33 (d, *J* = 6.9 Hz, 3H).

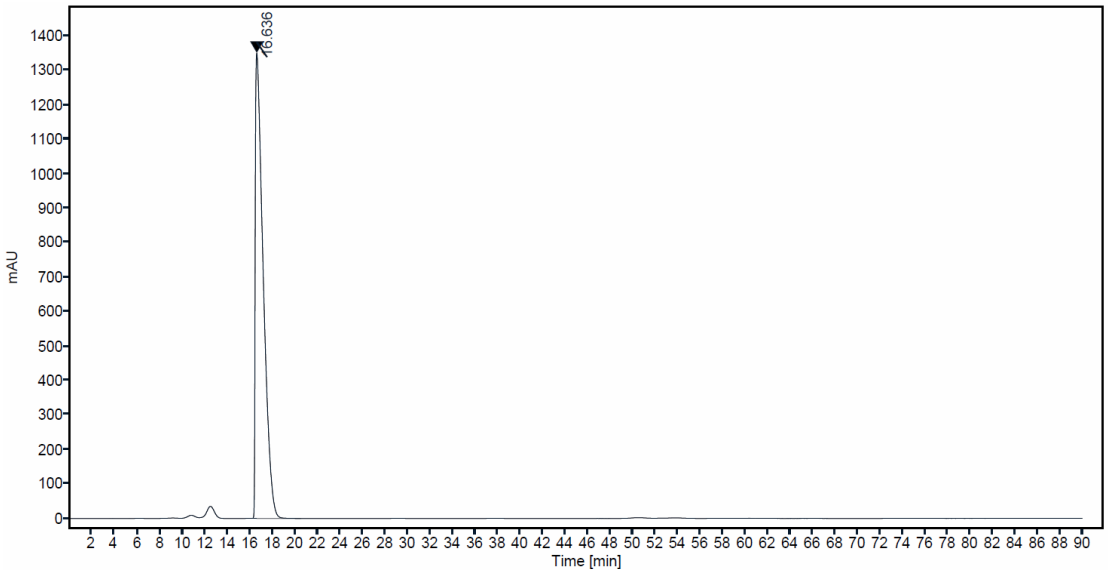
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.31 (s), 146.11 (s), 143.30 (s), 128.86 (s), 127.89 (s), 126.84 (s), 126.75 (s), 121.84 (s), 119.79 (s), 119.42 (s), 112.09 (s), 101.69 (s), 55.22 (s), 46.67 (s), 36.12 (s), 27.31 (s), 21.71 (s).

HRMS (ESI) calcd. for $C_{17}H_{20}N_3O_2$ $[M+H]^+$: m/z 298.1556, found: 298.1550.

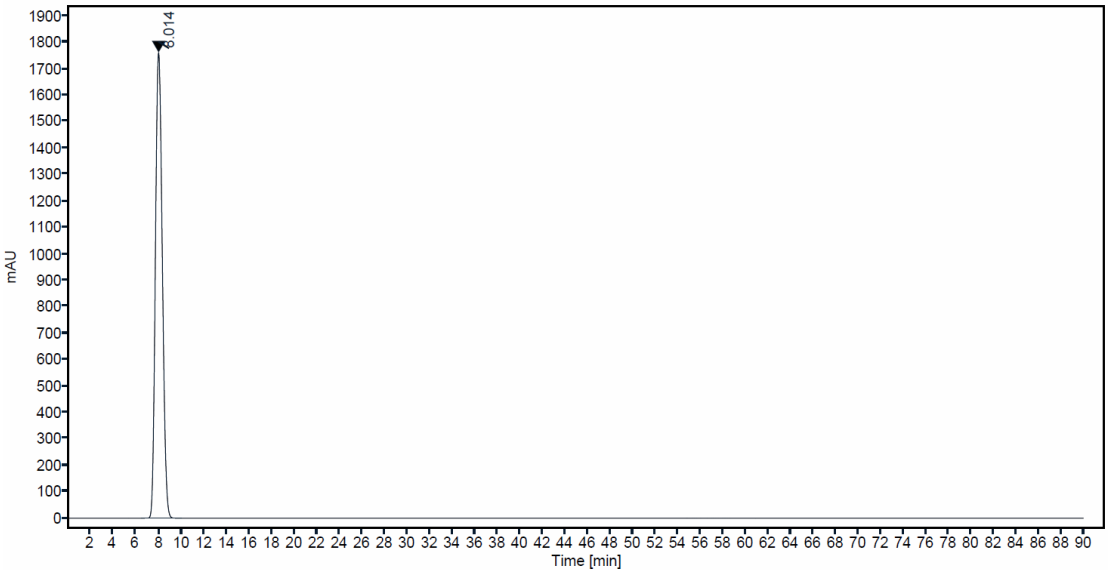


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm

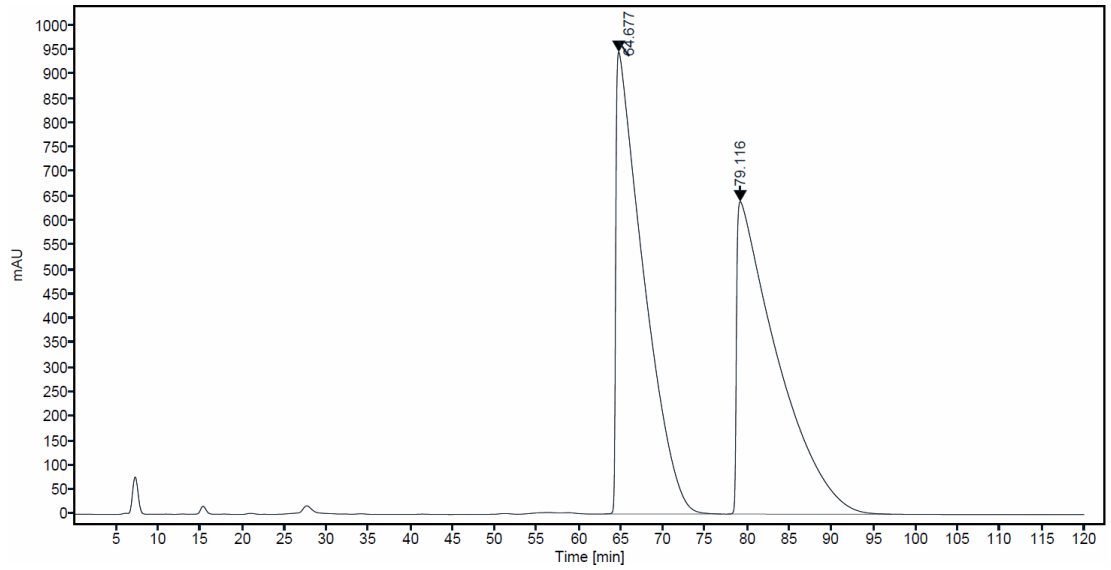
Starting Material (1a): Retention time = 16.636 min



7-OMe-Indole: Retention time = 6.014 min

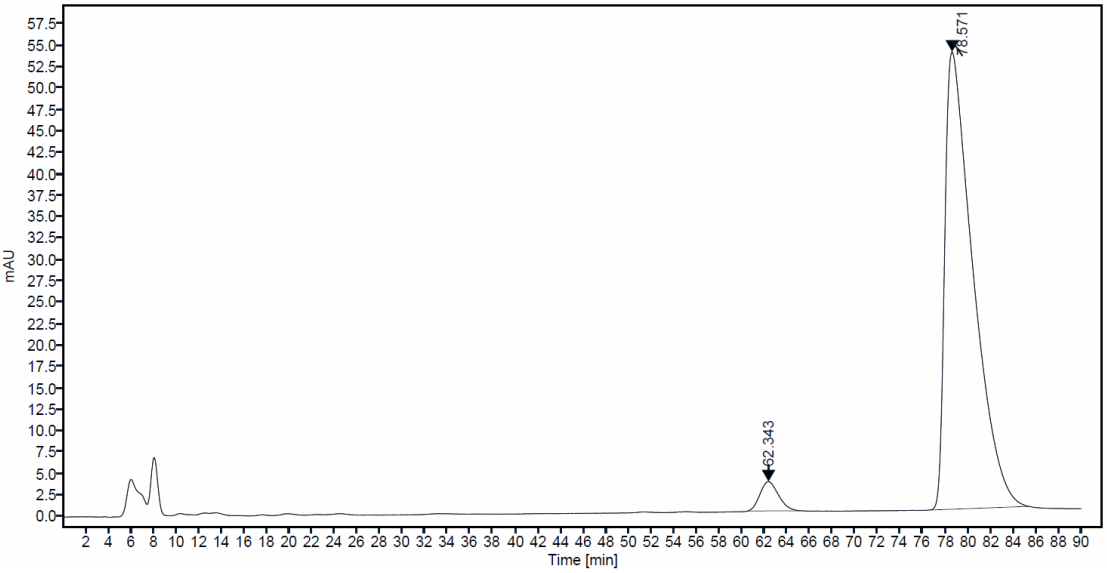


Racemic: Retention time: 64.877 min; 79.116 min

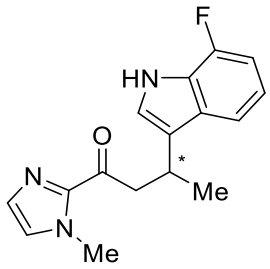


Peak	Retention time (min)	Rel. area (%)
1	64.877	50.3
2	79.116	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3p** < 1:99 and an enantiomeric excess of 92% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm]. Retention time: 62.343 min; 78.571 min



Peak	Retention time (min)	Rel. area (%)
1	62.343	4.1
2	78.571	95.9



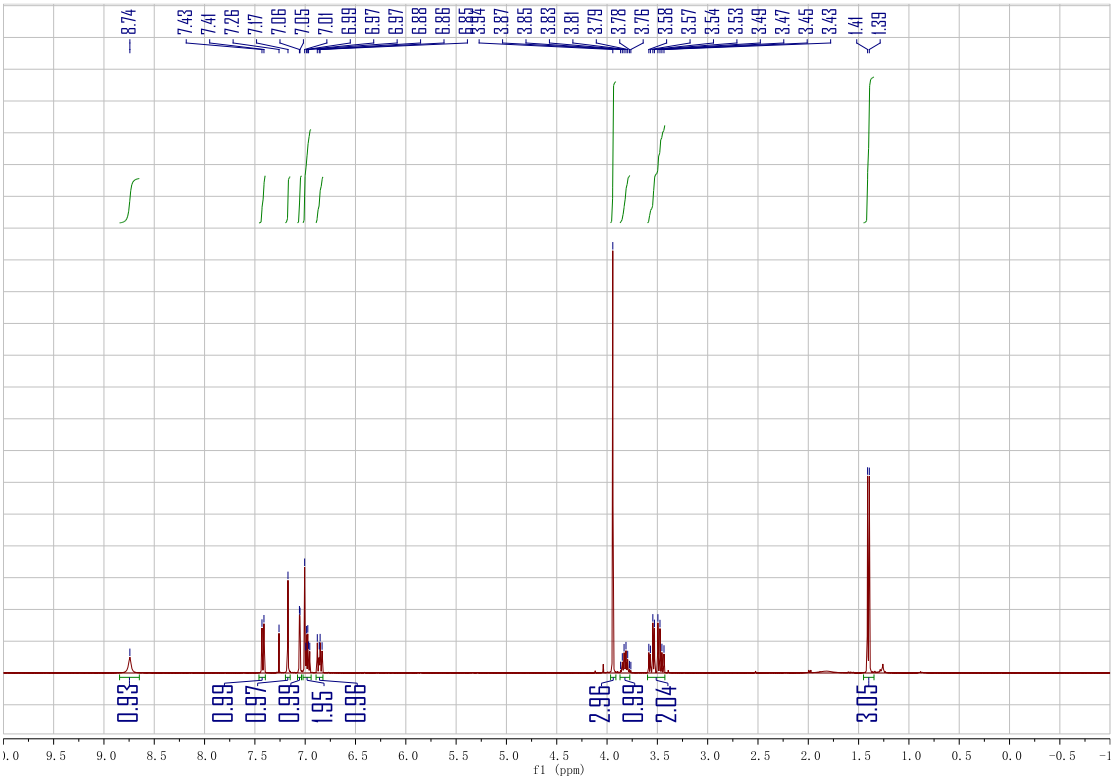
3-(7-fluoro-1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3q).

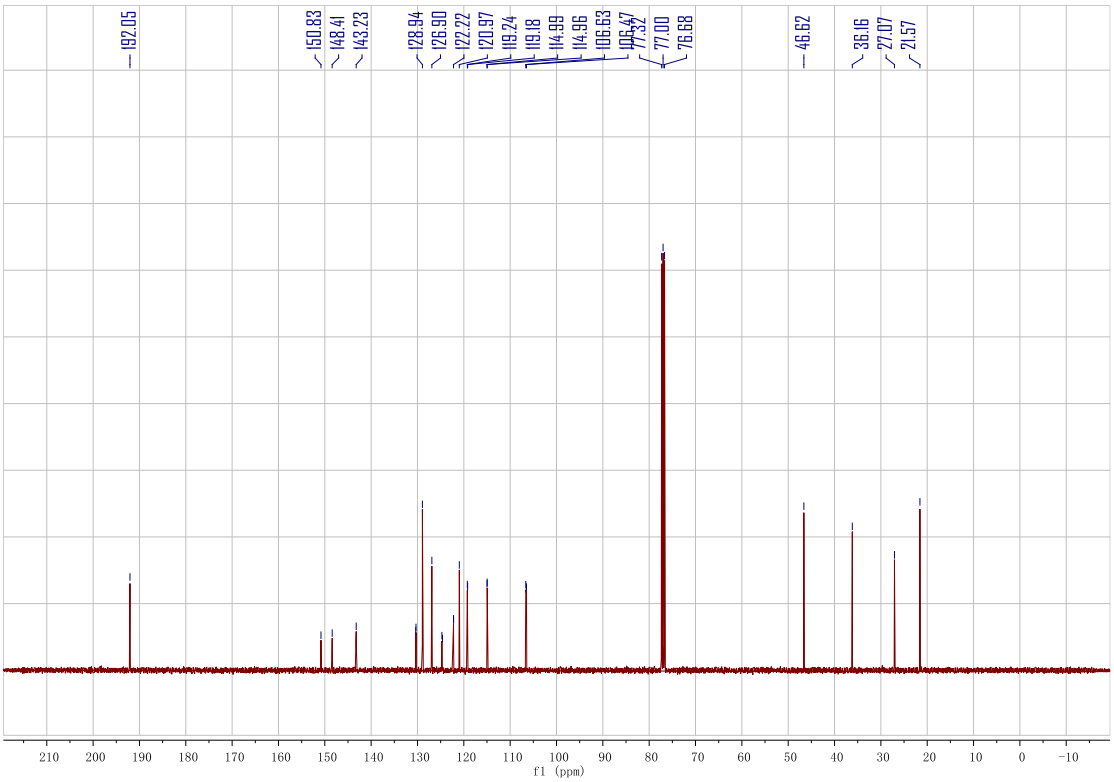
The racemic product was synthesized as described using **1a** and 7-F-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.17 (s, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 7.02 – 6.94 (m, 2H), 6.86 (dd, *J* = 11.2, 7.8 Hz, 1H), 3.94 (s, 3H), 3.87 – 3.77 (m, 1H), 3.51 (ddd, *J* = 24.2, 16.0, 7.3 Hz, 2H), 1.40 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.05 (s), 149.62 (d, *J* = 243.5 Hz), 143.23 (s), 130.35 (d, *J* = 5.4 Hz), 128.94 (s), 126.90 (s), 124.67 (d, *J* = 13.1 Hz), 122.21 (d, *J* = 2.0 Hz), 120.97 (s), 119.21 (d, *J* = 6.1 Hz), 114.97 (d, *J* = 3.3 Hz), 106.55 (d, *J* = 16.1 Hz), 46.62 (s), 36.16 (s), 27.07 (s), 21.57 (s).

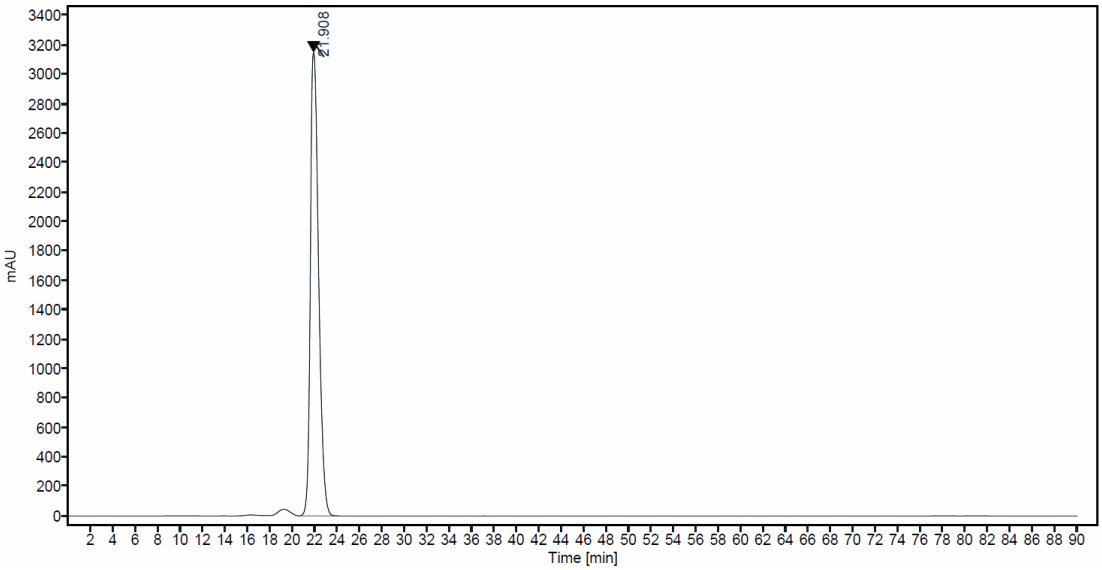
HRMS (ESI) calcd. for $C_{16}H_{17}FN_3O$ $[M+H]^+$: m/z 286.1356, found: 286.1350.



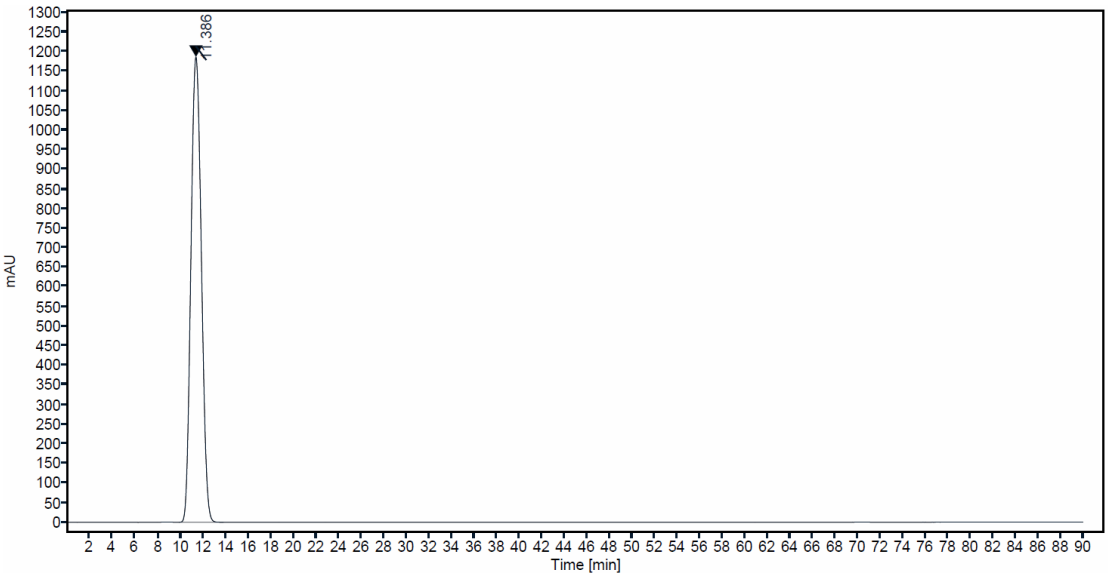


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

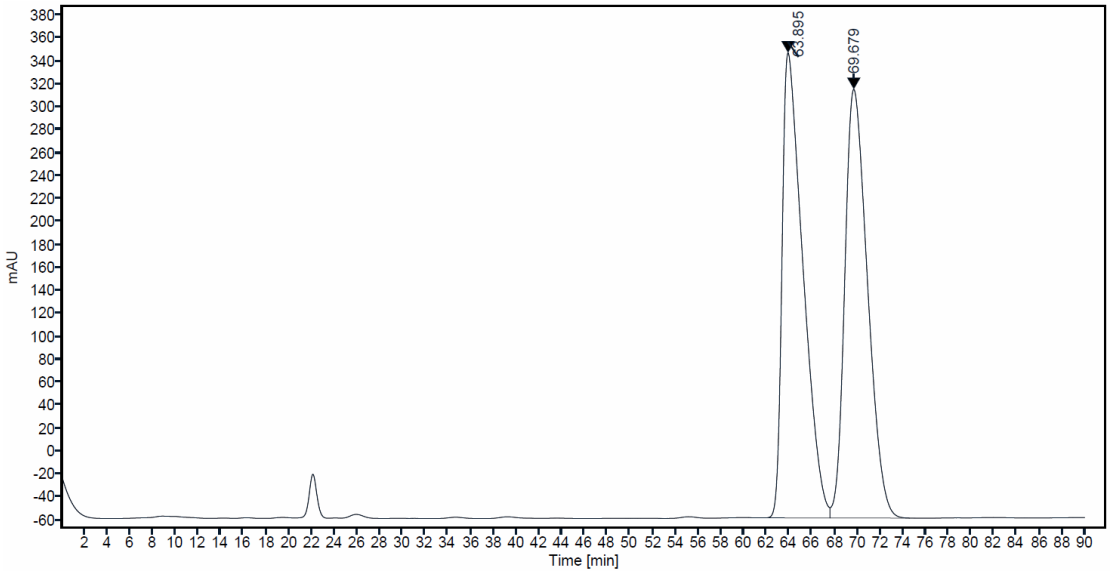
Starting Material (1a): Retention time = 21.908 min



7-F-Indole: Retention time = 11.386 min

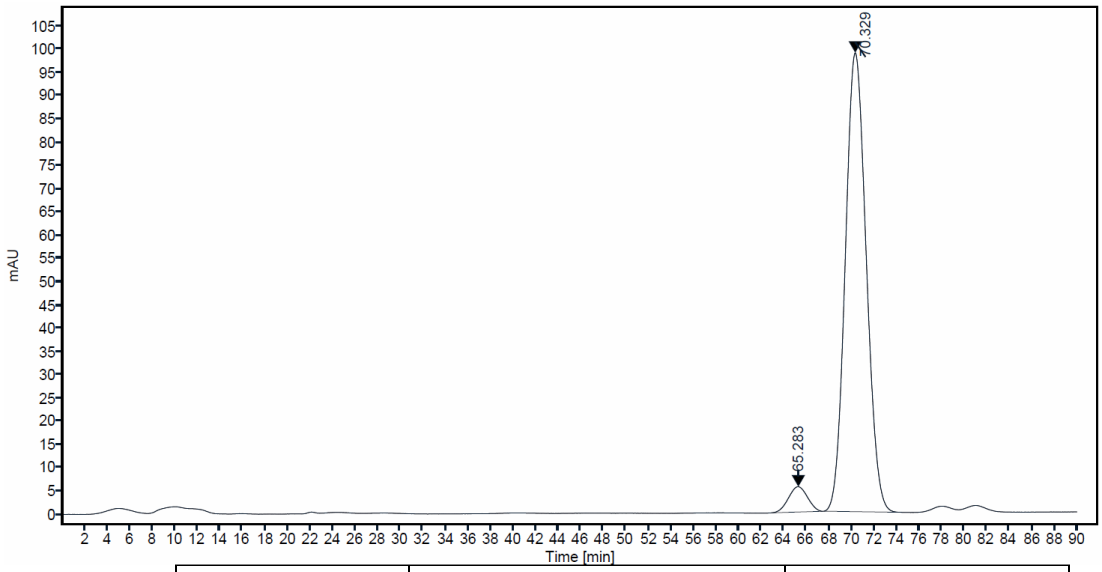


Racemic: Retention time: 63.895 min; 69.679 min

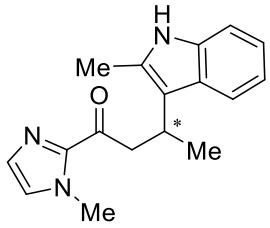


Peak	Retention time (min)	Rel. area (%)
1	63.895	50.2
2	69.679	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3q** < 1:99 and an enantiomeric excess of 91% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 65.283 min; 70.329 min



Peak	Retention time (min)	Rel. area (%)
1	65.283	4.6
2	70.329	95.4



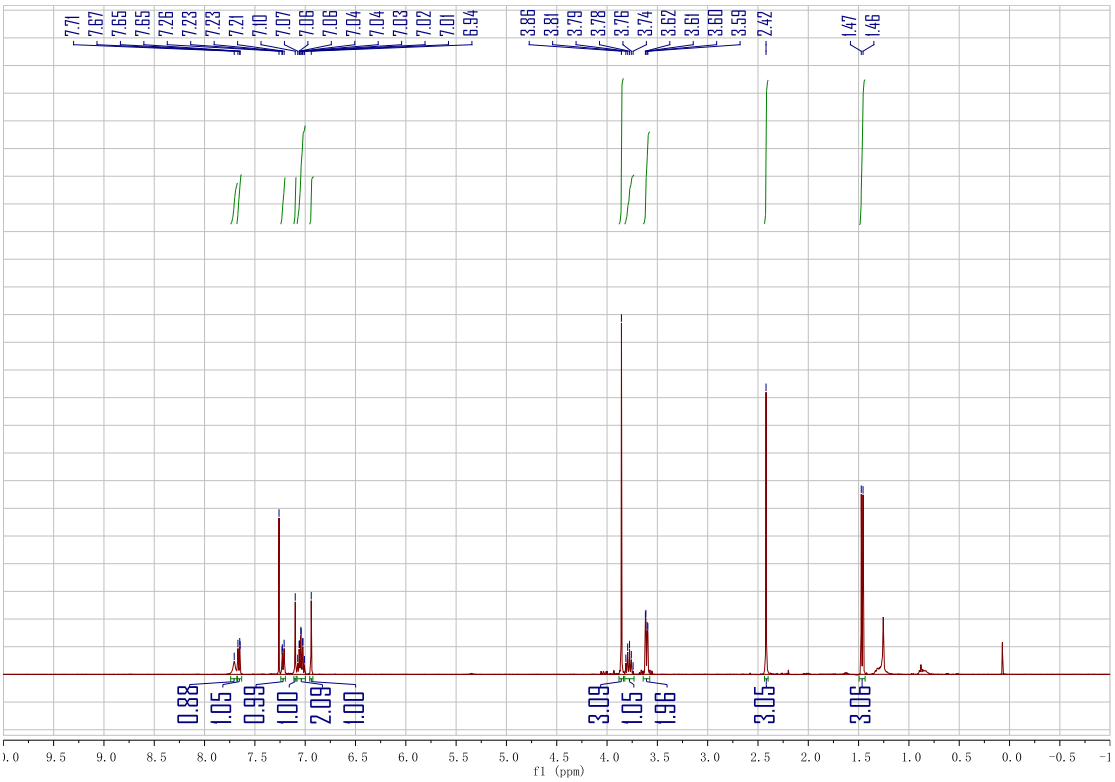
1-(1-methyl-1H-imidazol-2-yl)-3-(2-methyl-1H-indol-3-yl)butan-1-one (3r).

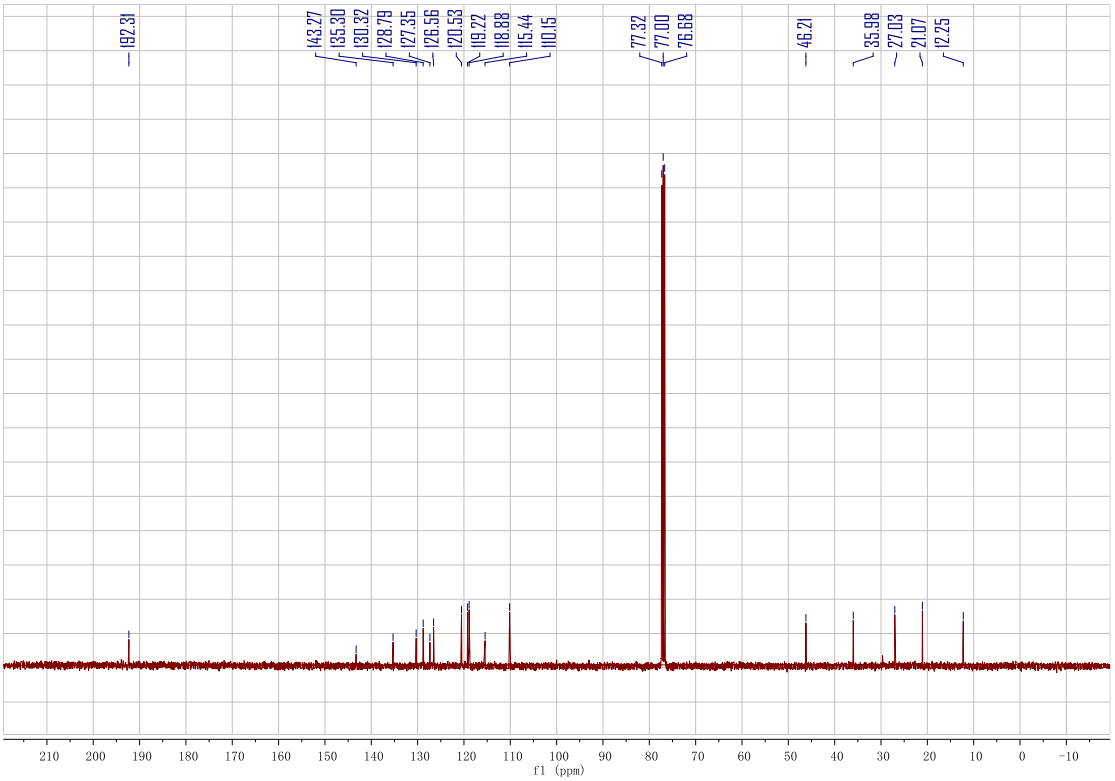
The racemic product was synthesized as described using **1a** and 2-Me-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.68 – 7.63 (m, 1H), 7.24 – 7.20 (m, 1H), 7.10 (s, 1H), 7.08 – 7.00 (m, 2H), 6.94 (s, 1H), 3.86 (s, 3H), 3.78 (dt, *J* = 14.2, 7.2 Hz, 1H), 3.61 (dd, *J* = 7.4, 2.5 Hz, 2H), 2.42 (s, 3H), 1.46 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.31 (s), 143.27 (s), 135.30 (s), 130.32 (s), 128.79 (s), 127.35 (s), 126.56 (s), 120.53 (s), 119.22 (s), 118.88 (s), 115.44 (s), 110.15 (s), 46.21 (s), 35.98 (s), 27.03 (s), 21.07 (s), 12.25 (s).

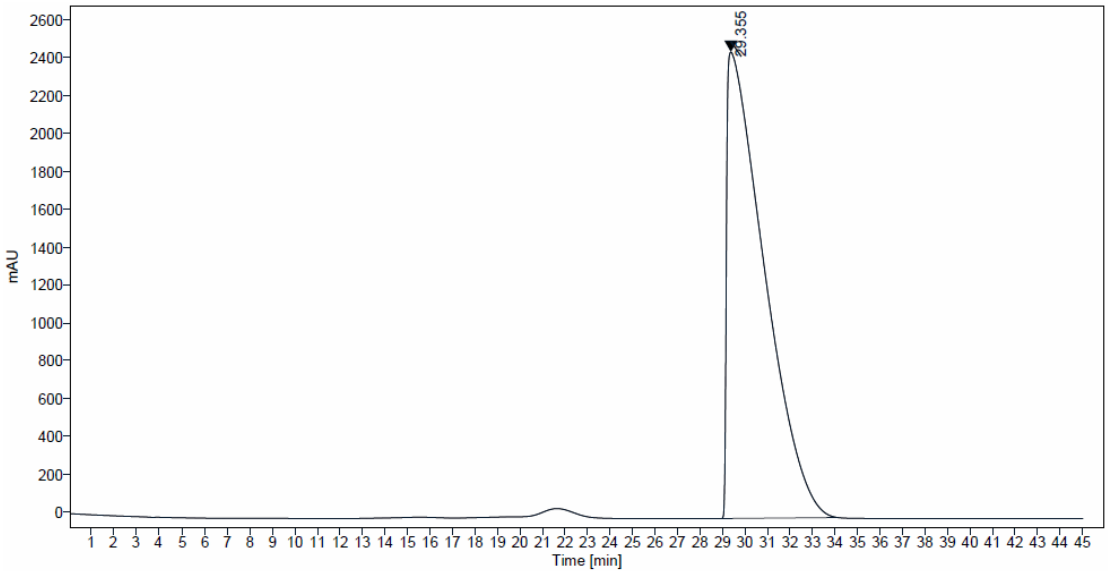
HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$ $[M+H]^+$: m/z 282.1601, found: 282.1602.



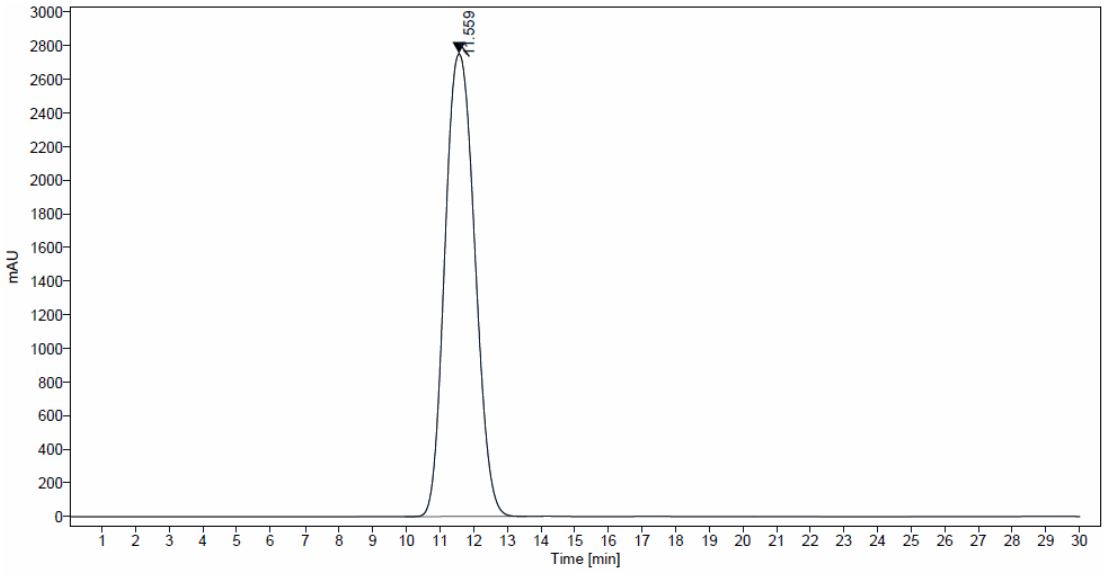


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

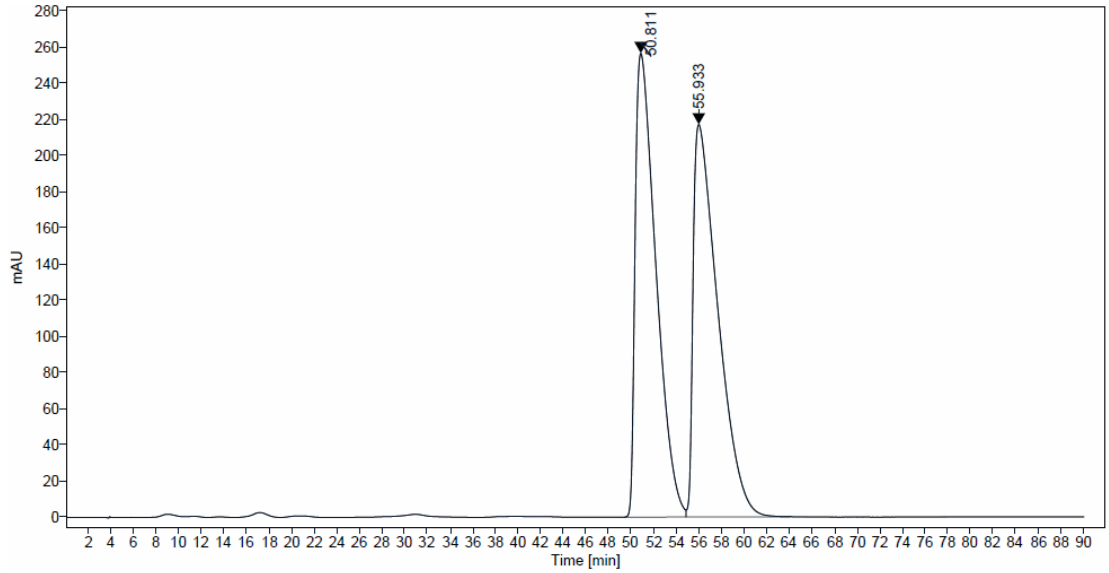
Starting Material (1a): Retention time = 29.355 min



2-Me-Indole: Retention time = 11.559 min

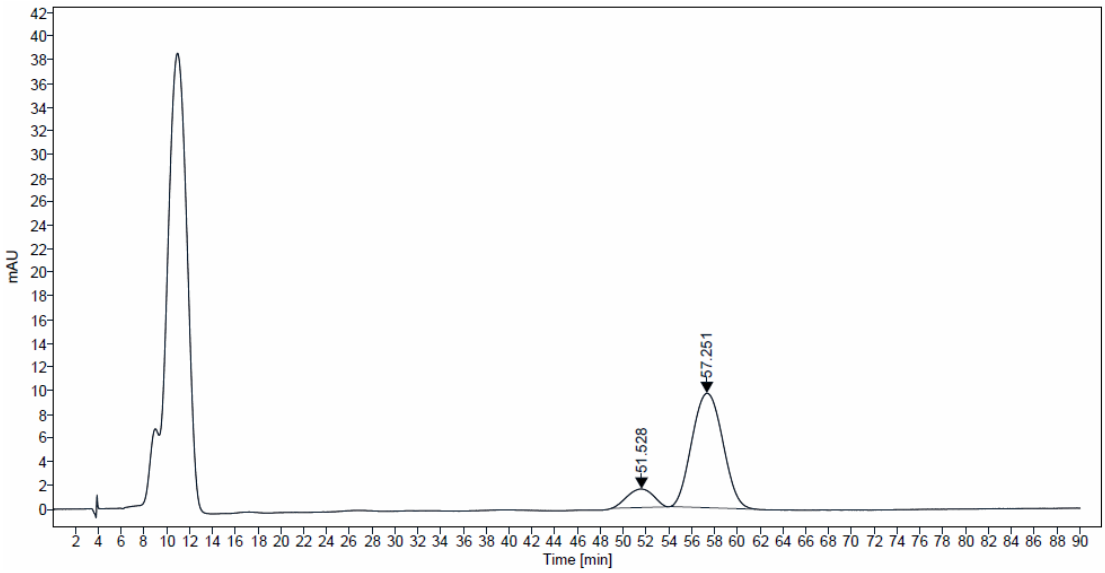


Racemic: Retention time: 50.811 min; 55.933 min

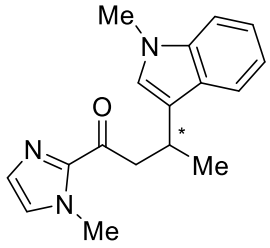


Peak	Retention time (min)	Rel. area (%)
1	50.811	50.4
2	55.933	49.6

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3r** < 1:99 and an enantiomeric excess of 78% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 51.528 min; 57.251 min



Peak	Retention time (min)	Rel. area (%)
1	51.528	10.9
2	57.251	89.1



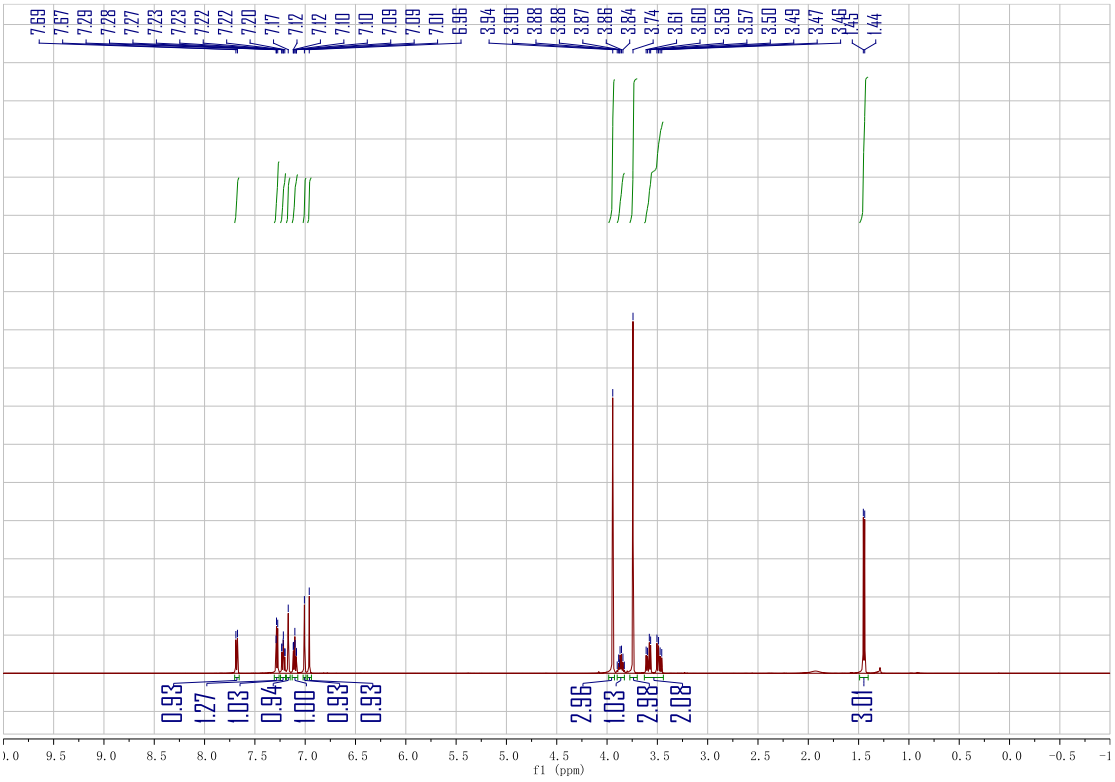
1-(1-methyl-1H-imidazol-2-yl)-3-(1-methyl-1H-indol-3-yl)butan-1-one (3s).

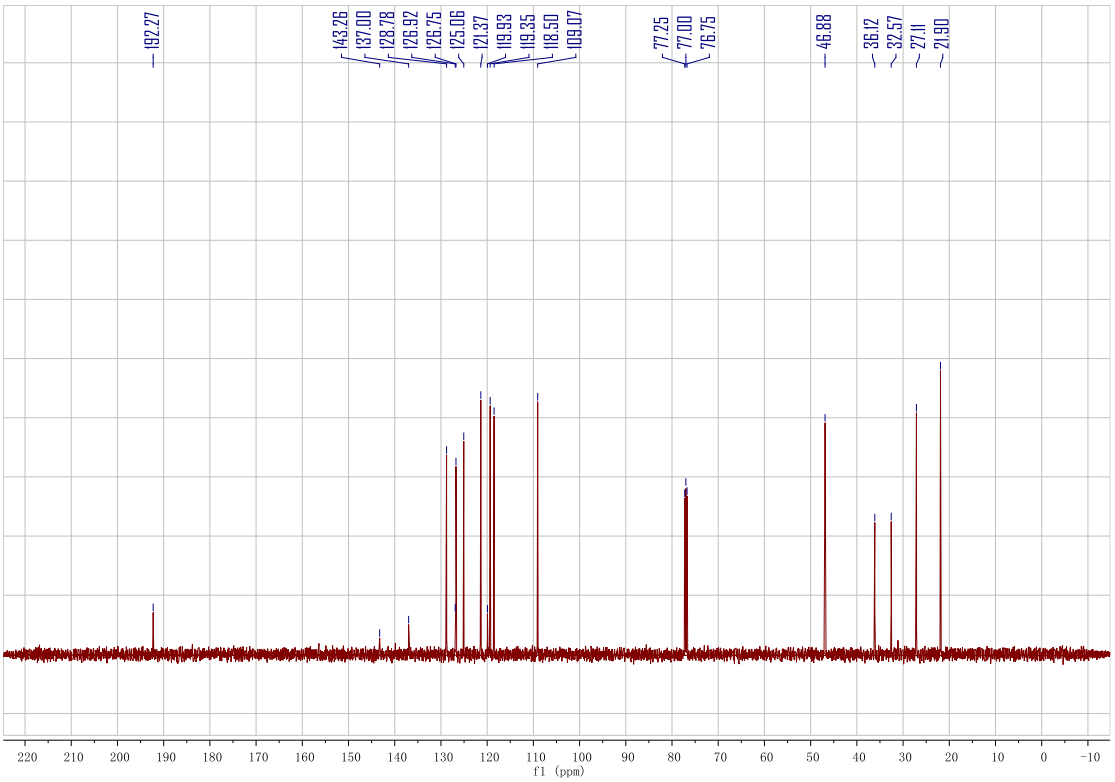
The racemic product was synthesized as described using **1a** and 1-Me-indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.25 – 7.20 (m, 1H), 7.17 (s, 1H), 7.13 – 7.07 (m, 1H), 7.01 (s, 1H), 6.96 (s, 1H), 3.94 (s, 3H), 3.90 – 3.83 (m, 1H), 3.74 (s, 3H), 3.53 (ddd, *J* = 23.8, 15.8, 7.3 Hz, 2H), 1.45 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.27 (s), 143.26 (s), 137.00 (s), 128.78 (s), 126.92 (s), 126.75 (s), 125.06 (s), 121.37 (s), 119.93 (s), 119.35 (s), 118.50 (s), 109.07 (s), 46.88 (s), 36.12 (s), 32.57 (s), 27.11 (s), 21.90 (s).

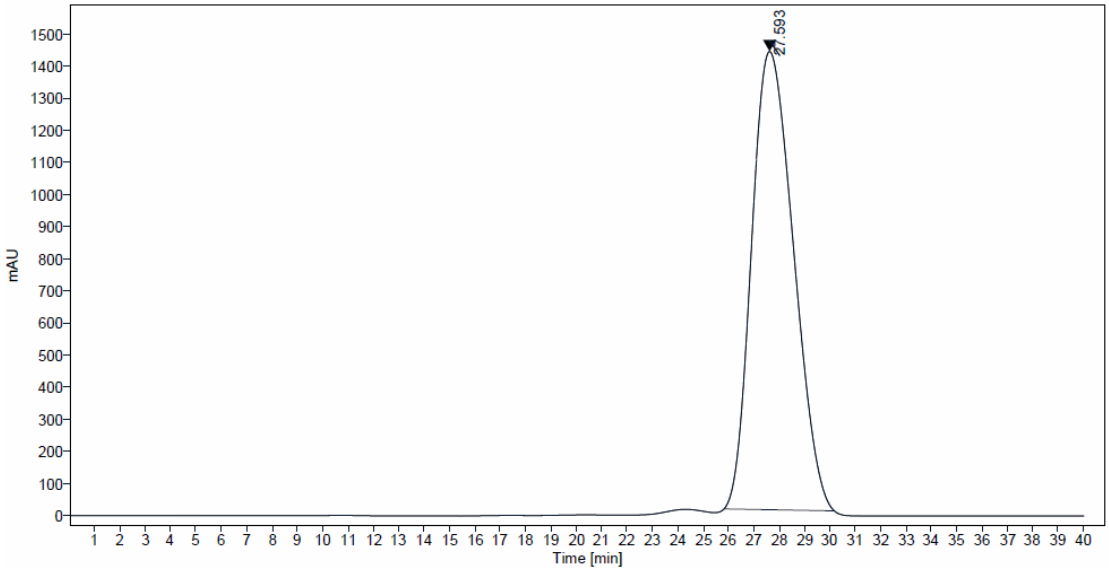
HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$ $[M+H]^+$: m/z 282.1601, found: 282.1598.



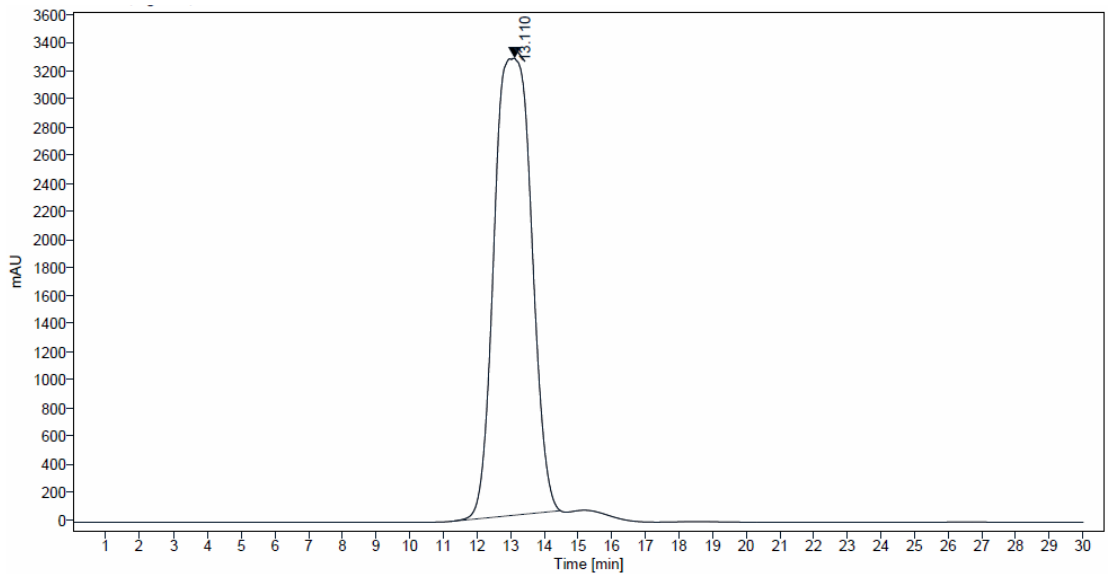


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.4 mL/min, λ = 280 nm

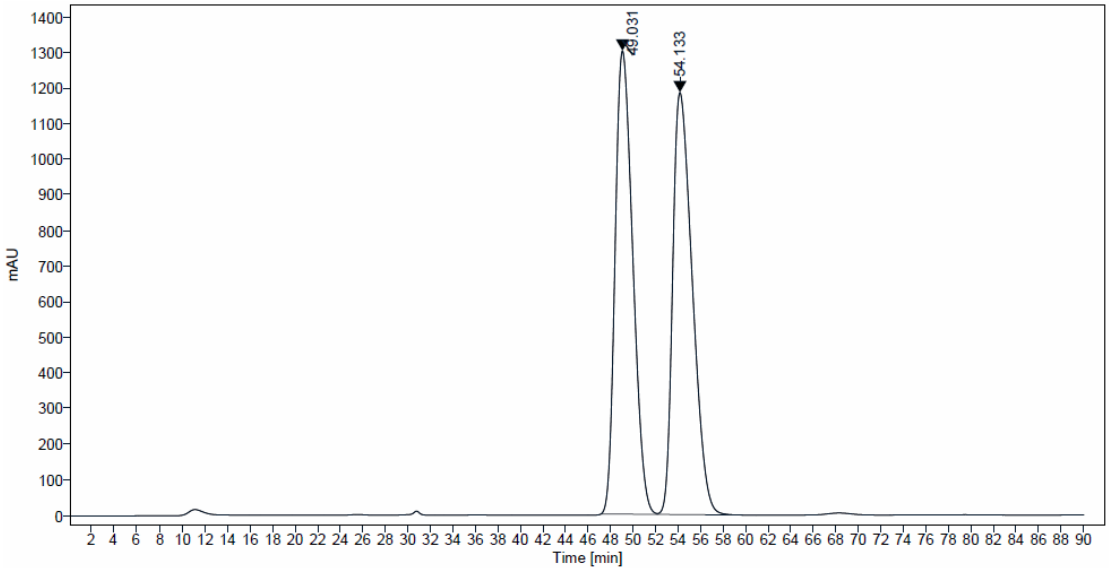
Starting Material (1a): Retention time = 27.593 min



1-Me-Indole: Retention time = 13.110 min

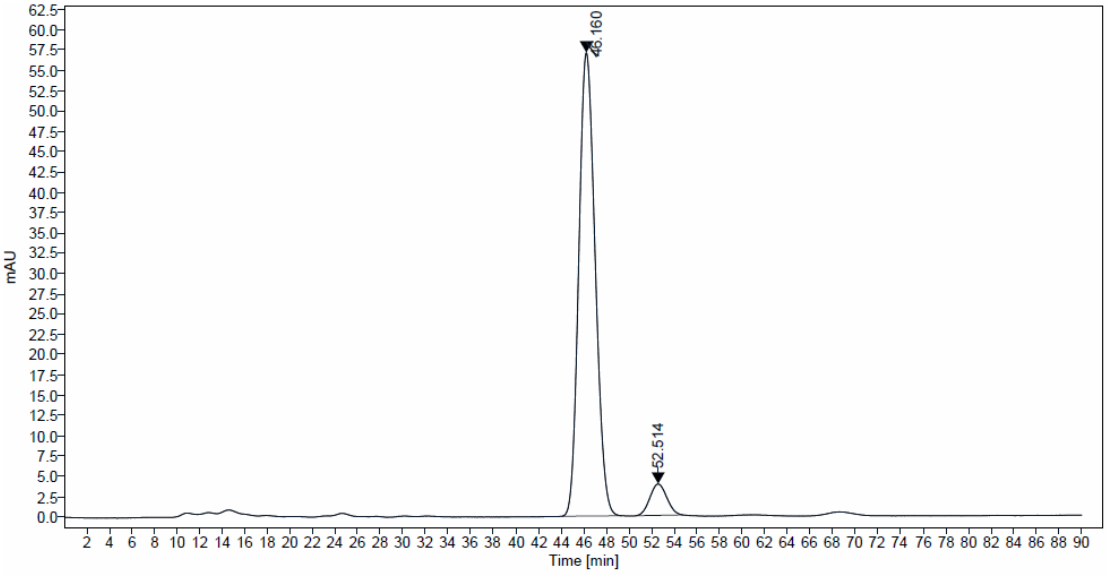


Racemic: Retention time: 49.031 min; 54.133 min

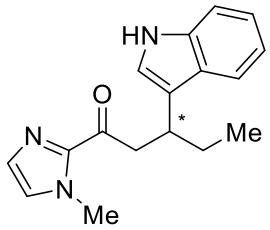


Peak	Retention time (min)	Rel. area (%)
1	49.031	50.1
2	54.133	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3s** < 1:99 and an enantiomeric excess of 89% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.4 mL/min, λ = 280 nm]. Retention time: 46.160 min; 52.514min



Peak	Retention time (min)	Rel. area (%)
1	46.160	94.5
2	52.514	5.5



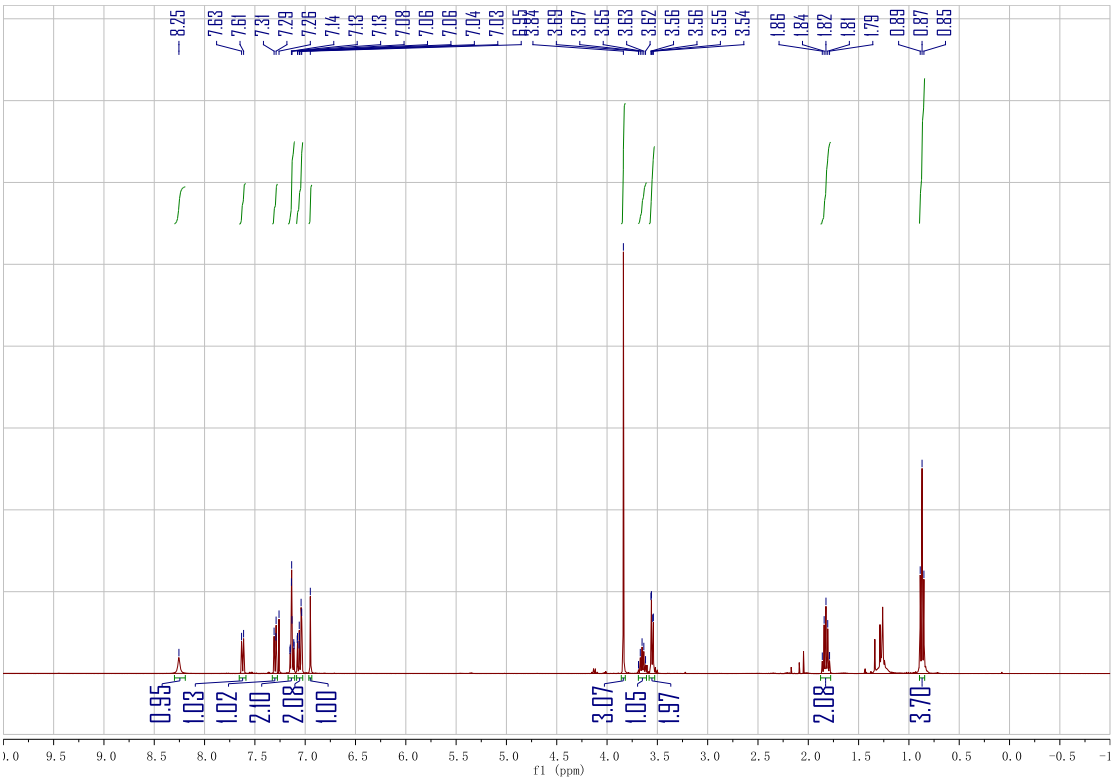
3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)pentan-1-one (3t).

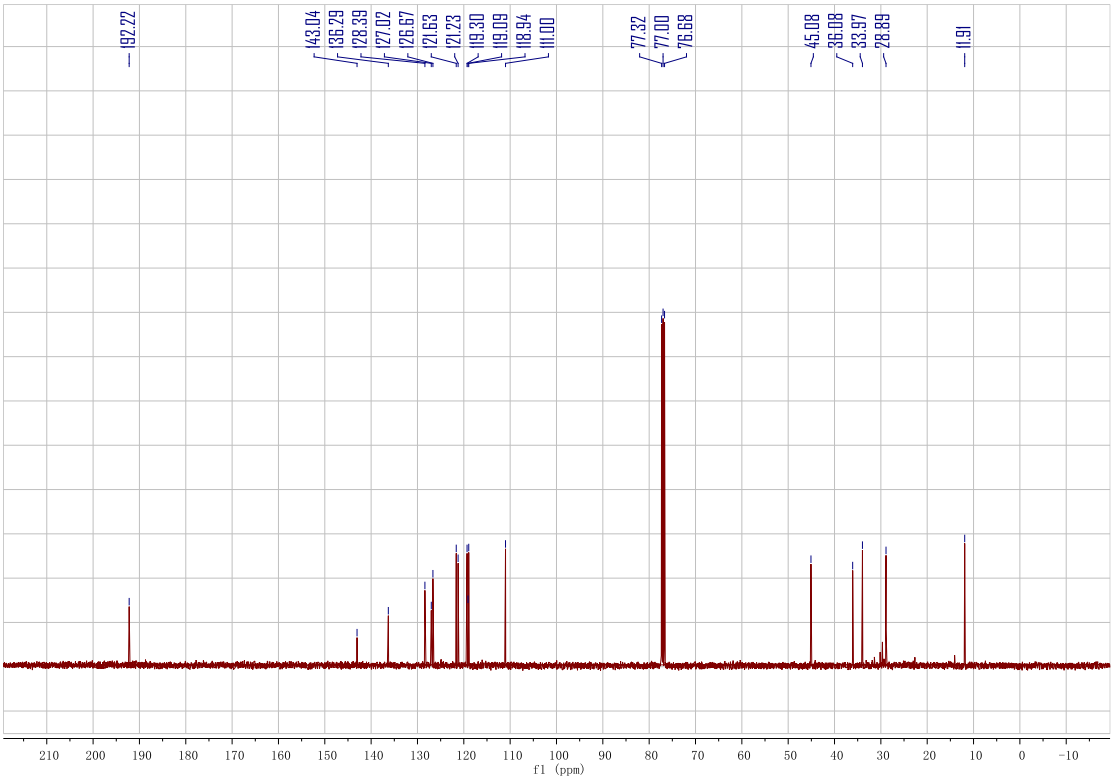
The racemic product was synthesized as described using **1b** and Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.17 – 7.10 (m, 2H), 7.09 – 7.02 (m, 2H), 6.95 (s, 1H), 3.84 (s, 3H), 3.69 – 3.61 (m, 1H), 3.55 (dd, *J* = 7.3, 2.3 Hz, 2H), 1.82 (p, *J* = 7.3 Hz, 2H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.22 (s), 143.04 (s), 136.29 (s), 128.39 (s), 127.02 (s), 126.67 (s), 121.63 (s), 121.23 (s), 119.30 (s), 119.09 (s), 118.94 (s), 111.00 (s), 45.08 (s), 36.08 (s), 33.97 (s), 28.89 (s), 11.91 (s).

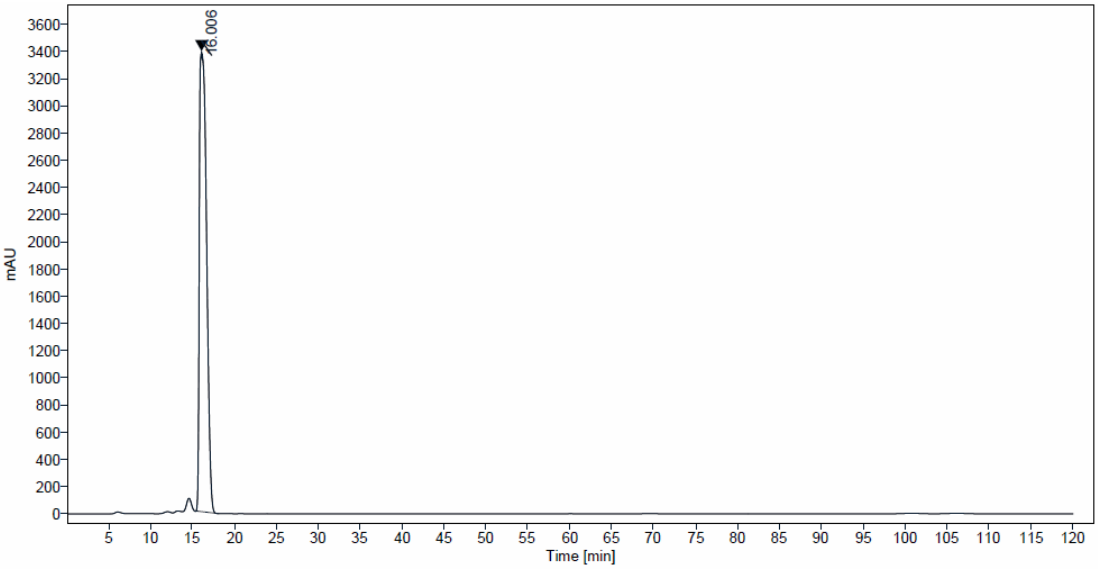
HRMS (ESI) calcd. for $C_{17}H_{20}N_3O$ $[M+H]^+$: m/z 282.1601, found: 282.1602.



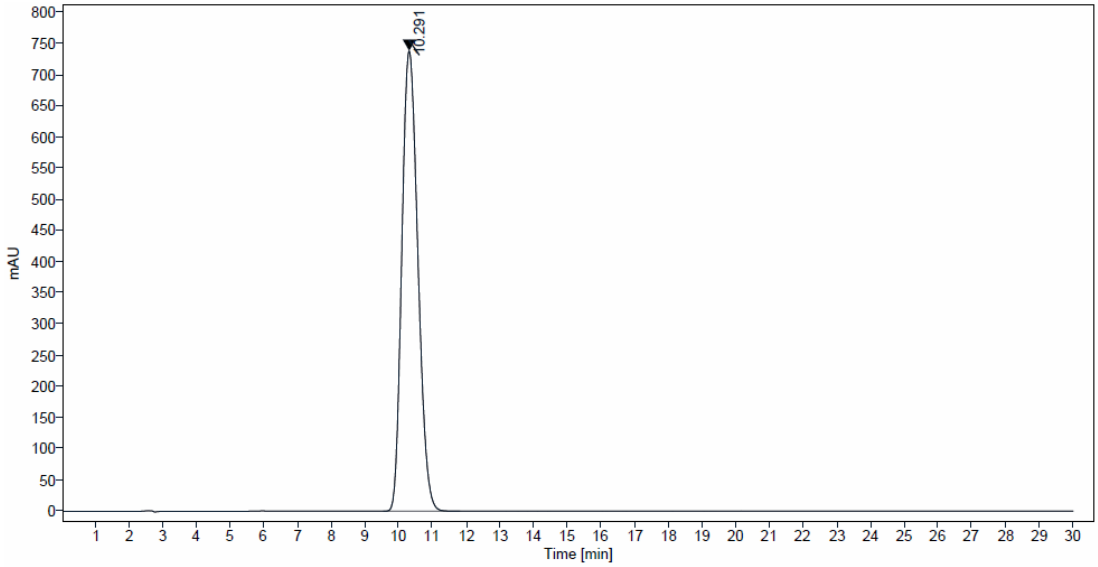


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.75 mL/min, λ = 280 nm

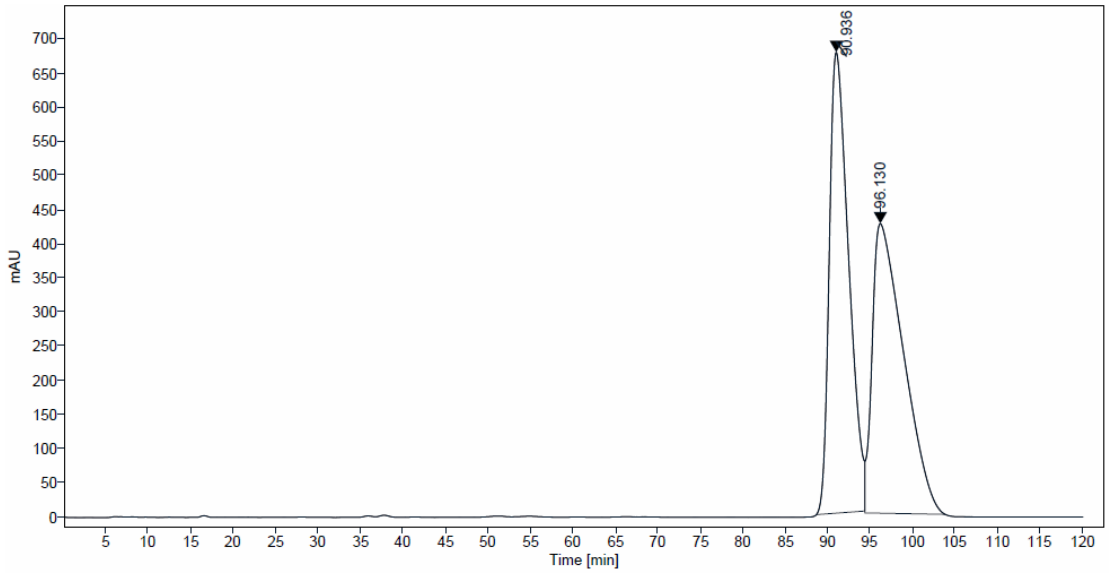
Starting Material (1b): Retention time = 16.006 min



Indole: Retention time = 10.291 min

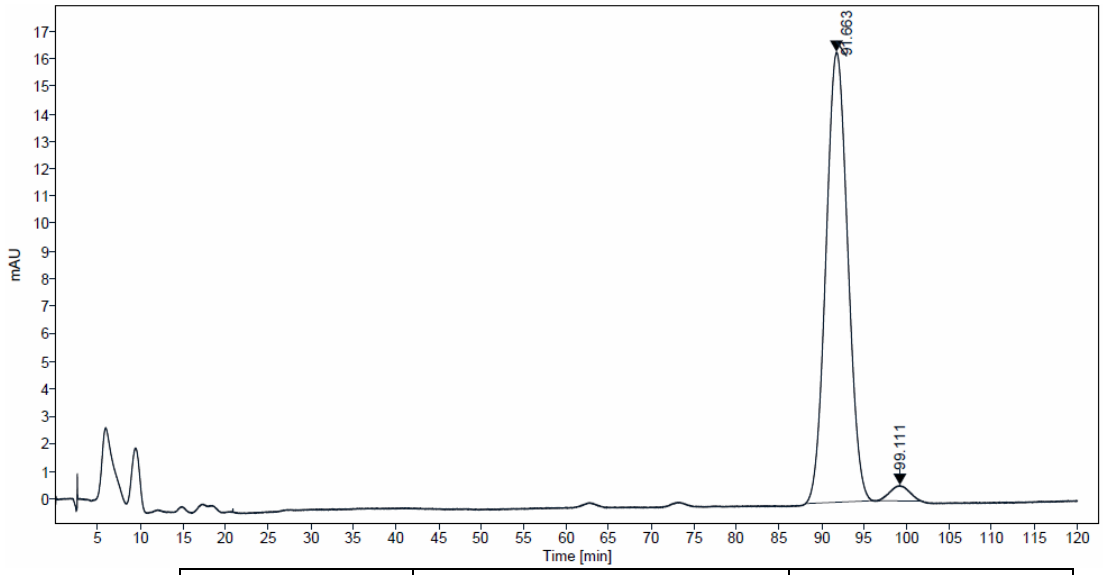


Racemic: Retention time: 90.936 min; 96.130 min

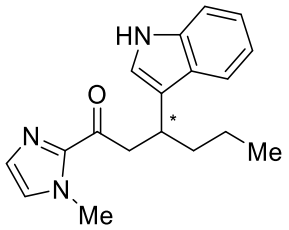


Peak	Retention time (min)	Rel. area (%)
1	90.936	51.5
2	96.130	48.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3t** < 1:99 and an enantiomeric excess of 94% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.75 mL/min, λ = 280 nm]. Retention time: 91.663 min; 99.111 min



Peak	Retention time (min)	Rel. area (%)
1	91.663	97.1
2	99.111	2.9



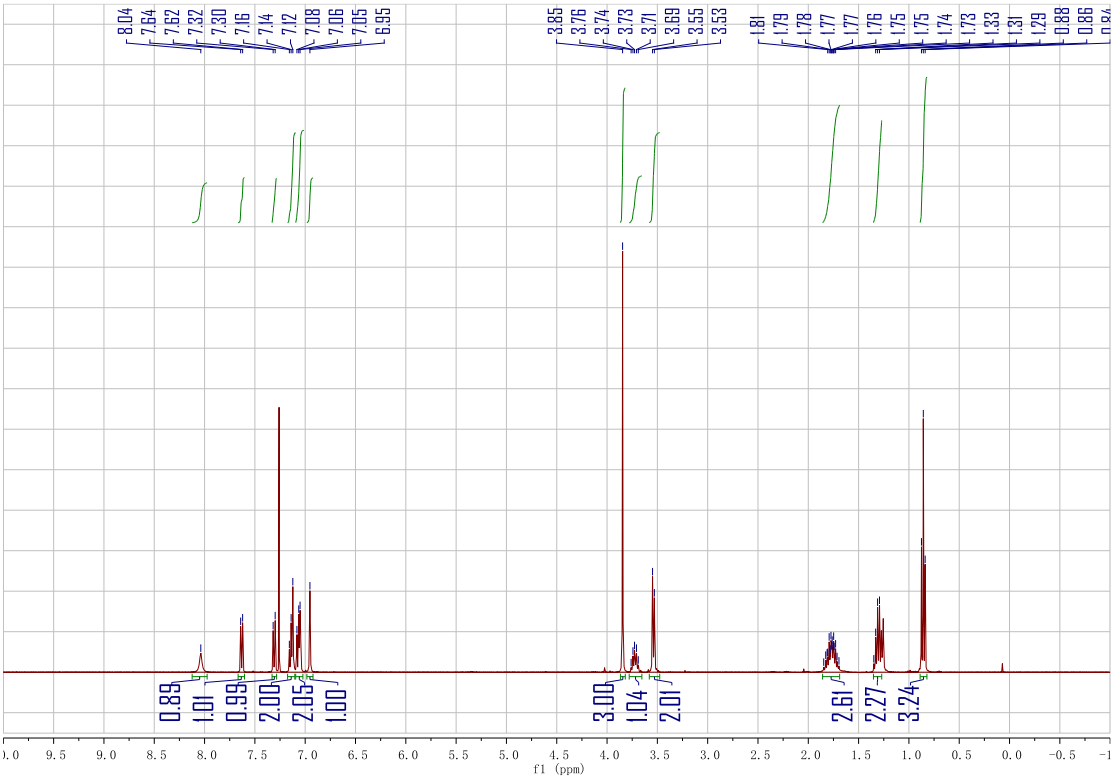
3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)hexan-1-one (3u).

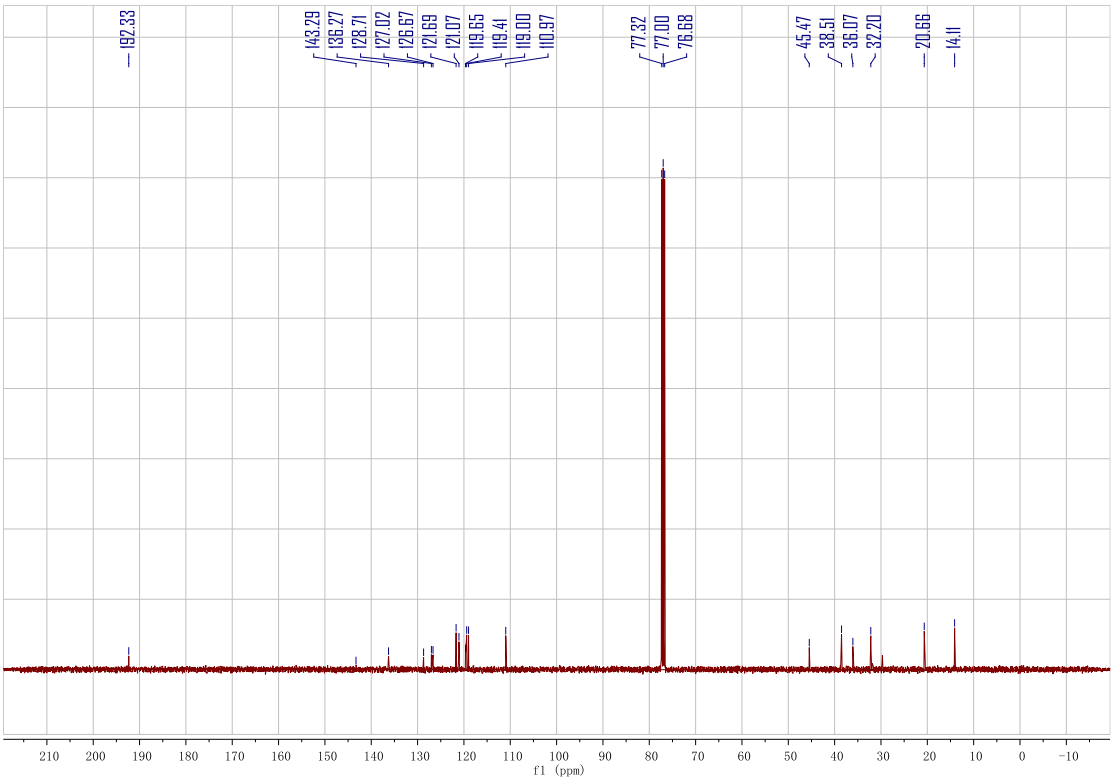
The racemic product was synthesized as described using **1c** and Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 40:60).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.10 (m, 2H), 7.09 – 7.02 (m, 2H), 6.95 (s, 1H), 3.85 (s, 3H), 3.78 – 3.65 (m, 1H), 3.54 (d, *J* = 7.3 Hz, 2H), 1.86 – 1.69 (m, 2H), 1.35 – 1.24 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.33 (s), 143.29 (s), 136.27 (s), 128.71 (s), 127.02 (s), 126.67 (s), 121.69 (s), 121.07 (s), 119.65 (s), 119.41 (s), 119.00 (s), 110.97 (s), 45.47 (s), 38.51 (s), 36.07 (s), 32.20 (s), 20.66 (s), 14.11 (s).

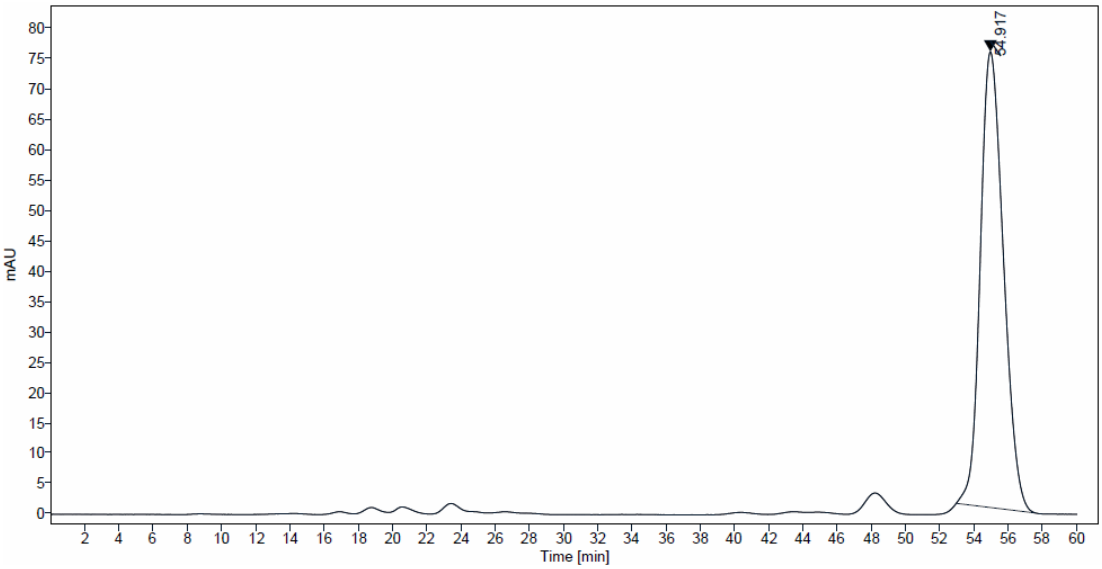
HRMS (ESI) calcd. for $C_{18}H_{22}N_3O$ $[M+H]^+$: m/z 296.1757, found: 296.1758.



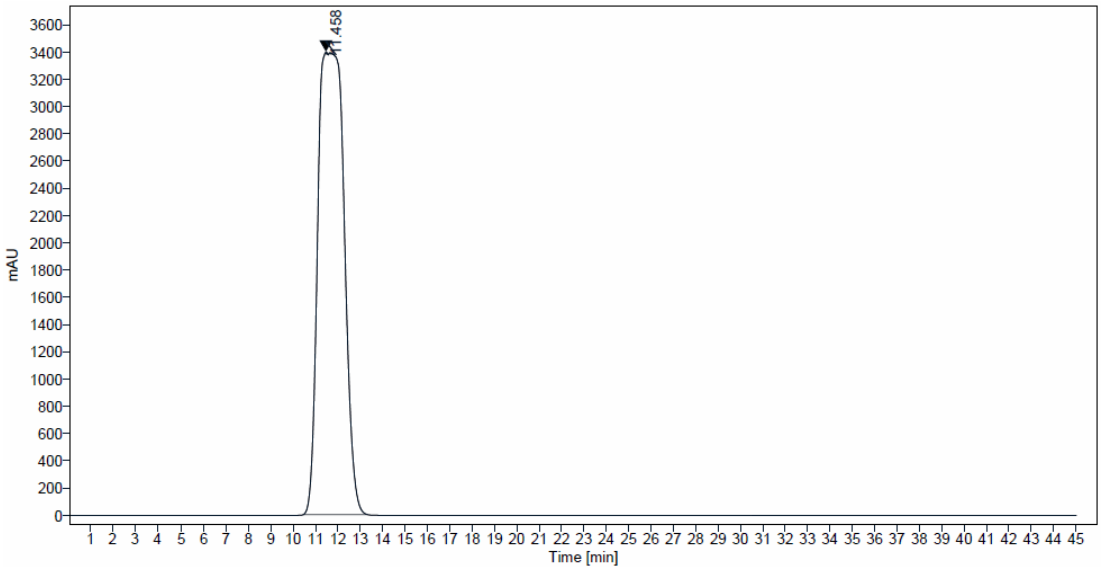


HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

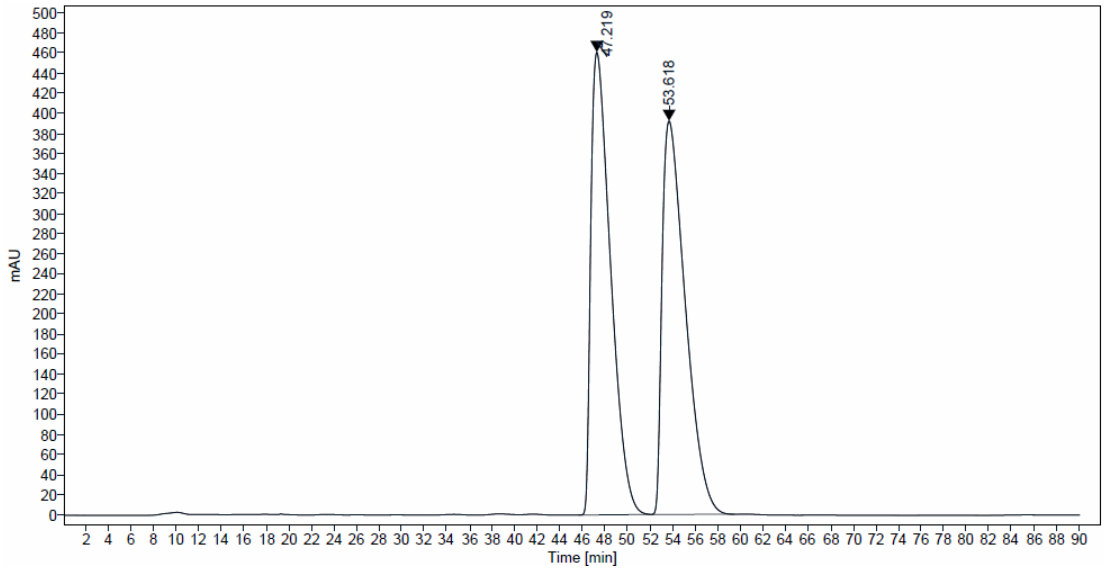
Starting Material (1c): Retention time = 54.917 min



Indole: Retention time = 11.458 min

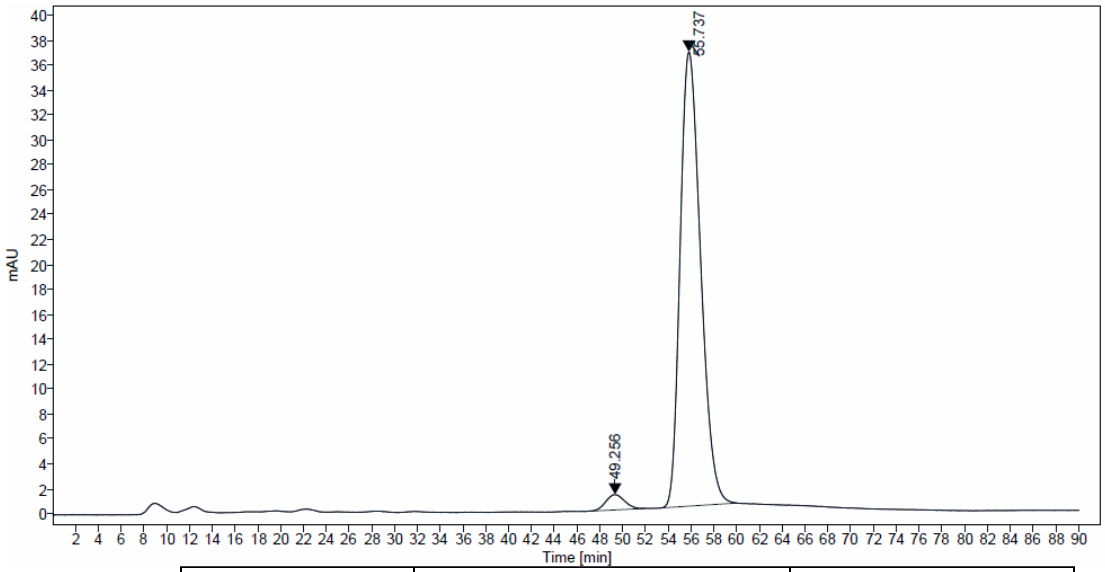


Racemic: Retention time: 47.219 min; 53.618 min

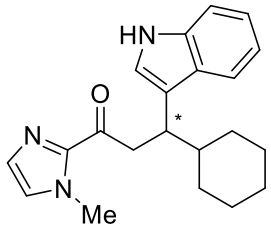


Peak	Retention time (min)	Rel. area (%)
1	47.219	50.1
2	53.618	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3u** < 1:99 and an enantiomeric excess of 94% [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 49.256 min; 55.737 min



Peak	Retention time (min)	Rel. area (%)
1	49.256	3.0
2	55.737	97.0



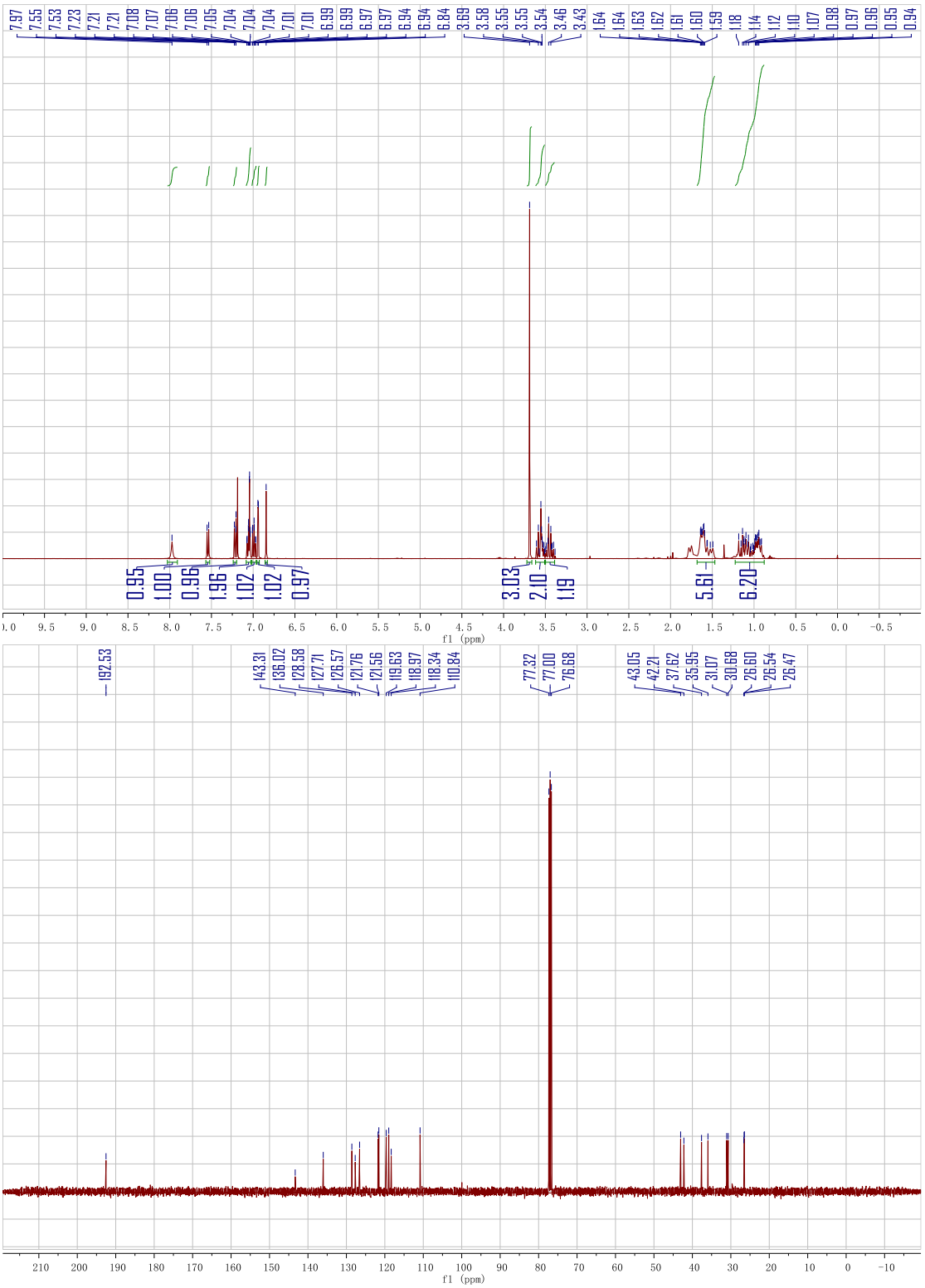
3-cyclohexyl-3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (3v).

The racemic product was synthesized as described using **1d** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.08 – 7.03 (m, 2H), 7.01 – 6.96 (m, 1H), 6.94 (d, *J* = 2.4 Hz, 1H), 6.84 (s, 1H), 3.69 (s, 3H), 3.62 – 3.51 (m, 2H), 3.50 – 3.38 (m, 1H), 1.68 – 1.47 (m, 5H), 1.23 – 0.88 (m, 6H).

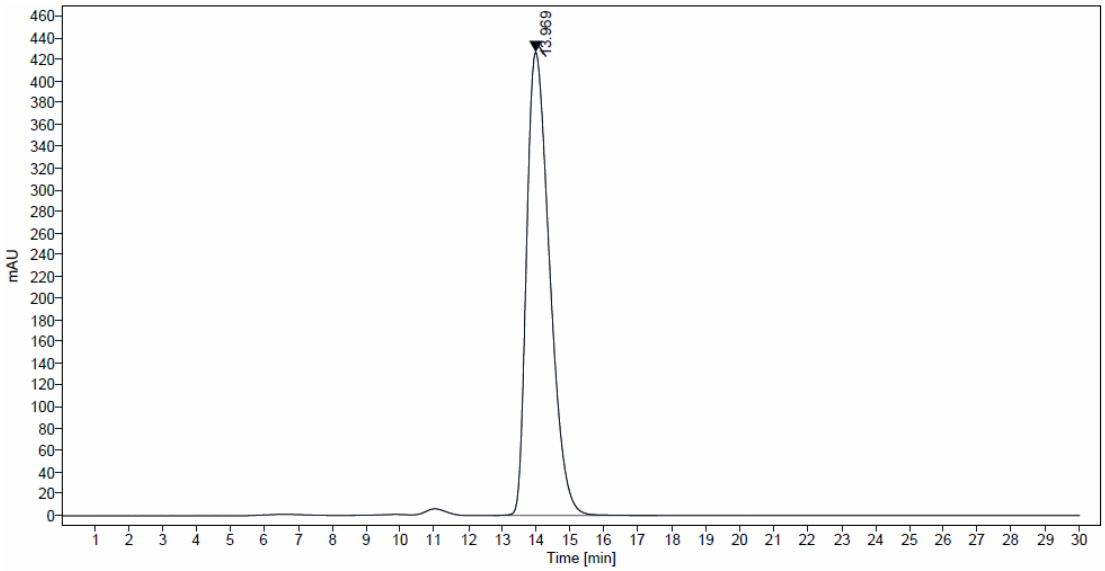
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.53 (s), 143.31 (s), 136.02 (s), 128.58 (s), 127.71 (s), 126.57 (s), 121.76 (s), 121.56 (s), 119.63 (s), 118.97 (s), 118.34 (s), 110.84 (s), 43.05 (s), 42.21 (s), 37.62 (s), 35.95 (s), 31.07 (s), 30.68 (s), 26.60 (s), 26.54 (s), 26.47 (s).

HRMS (ESI) calcd. for $C_{21}H_{26}N_3O$ $[M+H]^+$: m/z 336.2070, found: 336.2072.

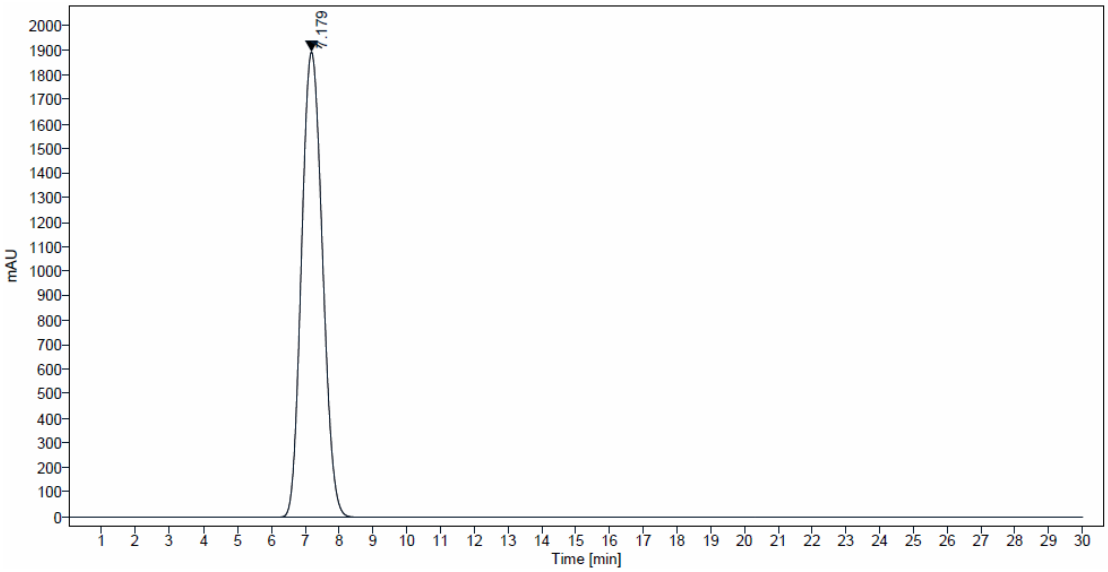


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm

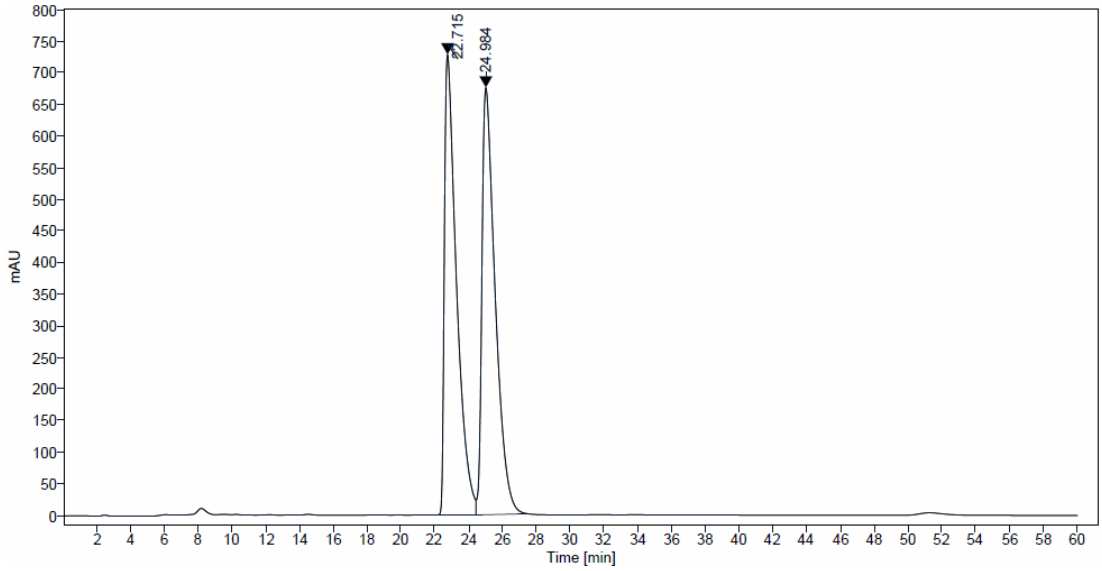
Starting Material (1d): Retention time = 13.969 min



Indole: Retention time = 7.179 min

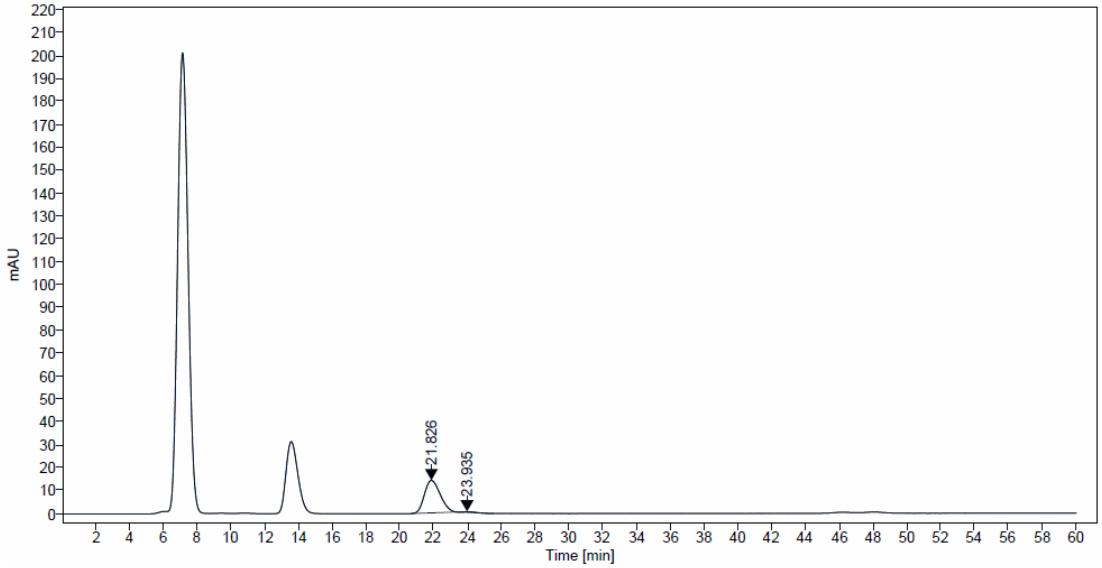


Racemic: Retention time: 22.715 min; 24.984 min

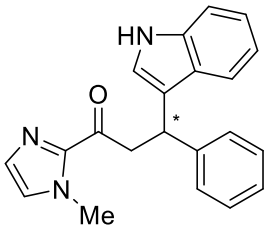


Peak	Retention time (min)	Rel. area (%)
1	22.715	50.5
2	24.984	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3v** as 73:27 and an enantiomeric excess of 98% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm]. Retention time: 21.826 min; 23.935 min



Peak	Retention time (min)	Rel. area (%)
1	21.826	98.8
2	23.935	1.2



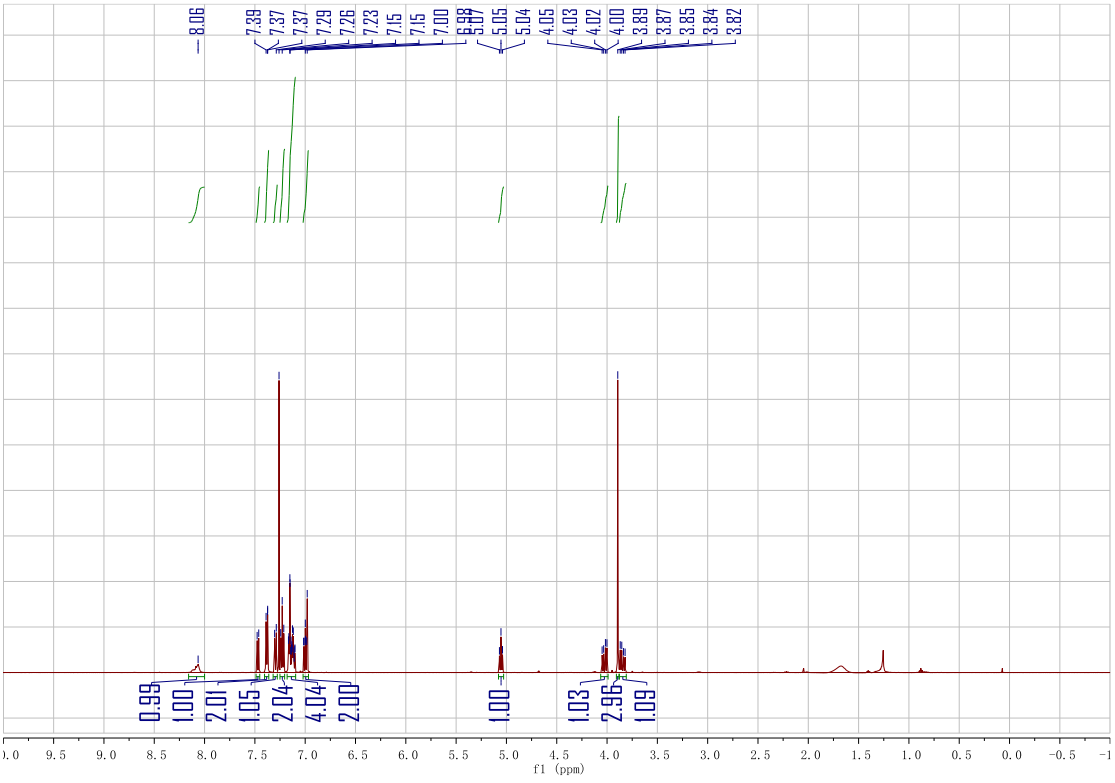
3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)-3-phenylpropan-1-one (3w).

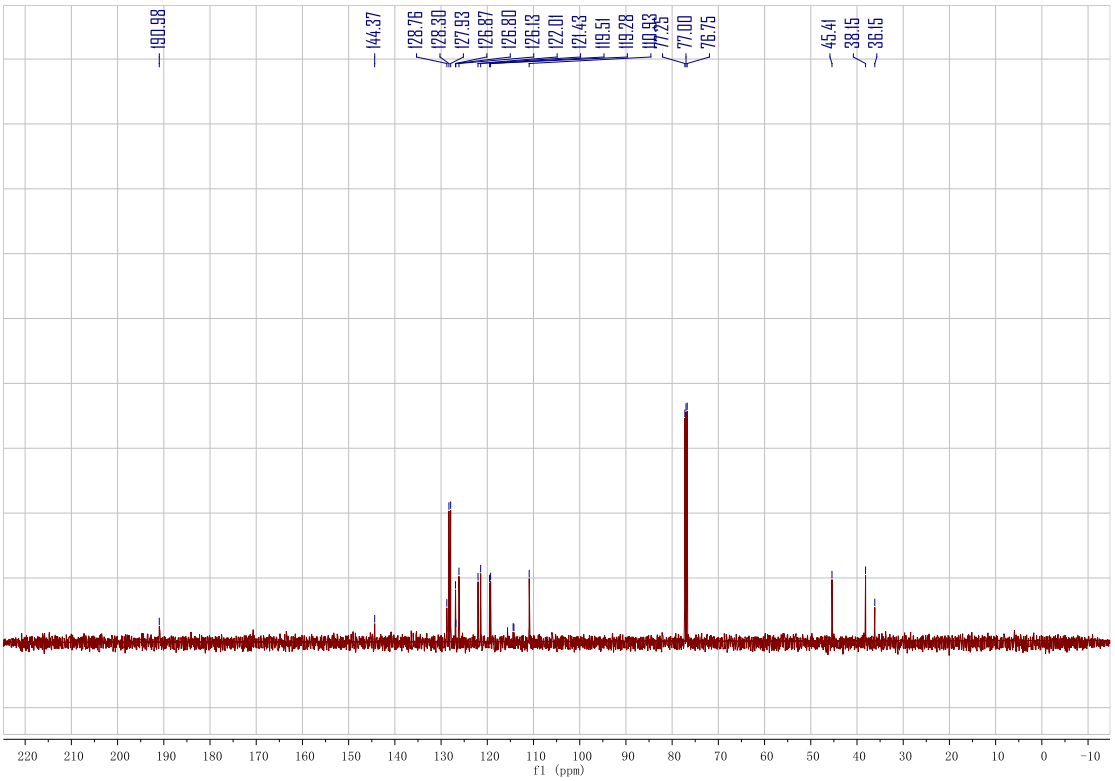
The racemic product was synthesized as described using **1e** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.13 (dddd, *J* = 8.1, 5.3, 4.8, 1.5 Hz, 4H), 7.02 – 6.97 (m, 2H), 5.05 (t, *J* = 7.6 Hz, 1H), 4.02 (dd, *J* = 16.4, 7.6 Hz, 1H), 3.89 (s, 3H), 3.84 (dd, *J* = 16.4, 7.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 190.98 (s), 144.37 (s), 128.76 (s), 128.30 (s), 127.93 (s), 126.87 (s), 126.80 (s), 126.13 (s), 122.01 (s), 121.43 (s), 119.51 (s), 119.28 (s), 115.61 (s), 114.41 (s), 114.24 (s), 110.93 (s), 45.41 (s), 38.15 (s), 36.15 (s).

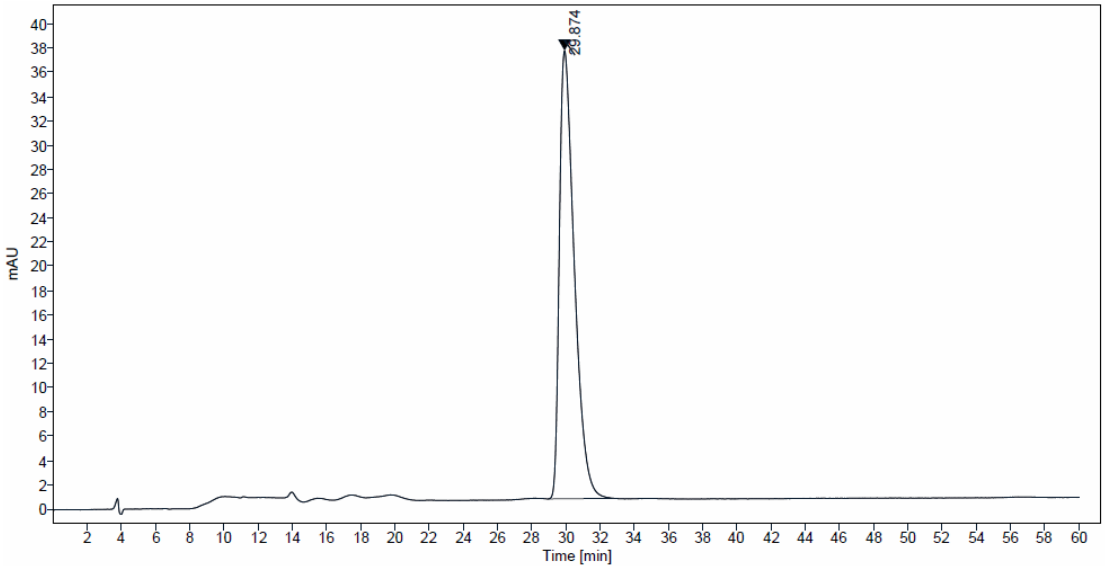
HRMS (ESI) calcd. for $C_{21}H_{20}N_3O$ $[M+H]^+$: m/z 330.1601, found: 330.1598.



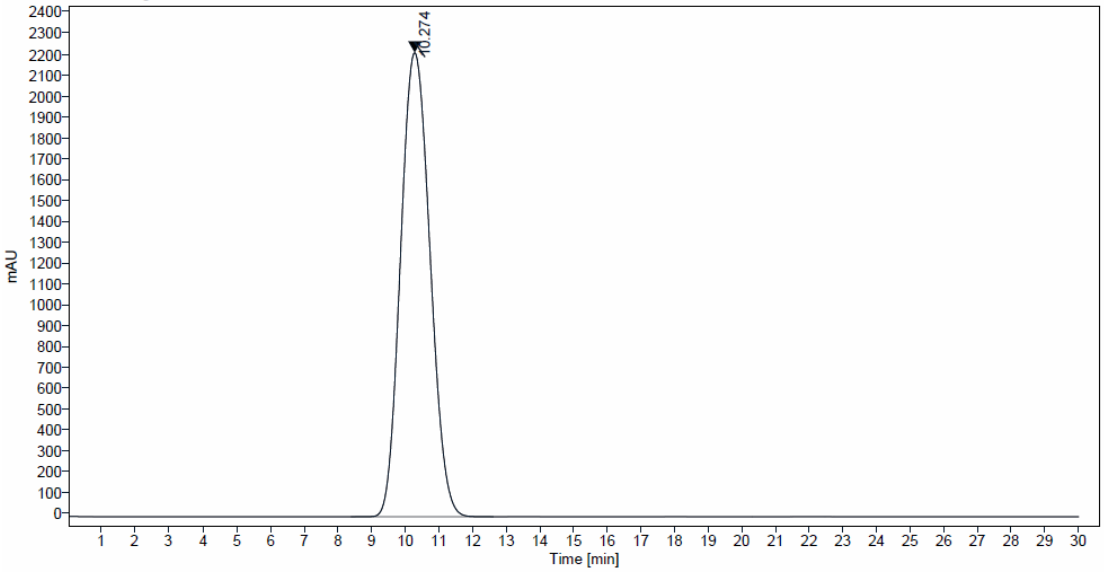


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.5 mL/min, λ = 280 nm

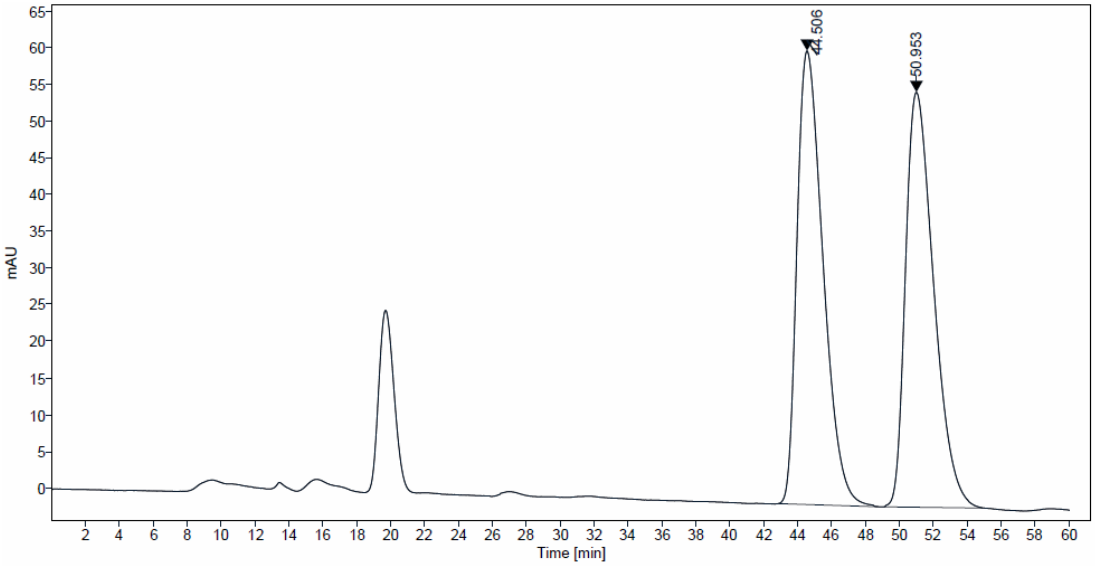
Starting Material (1e): Retention time = 29.874 min



Indole: Retention time = 10.274 min

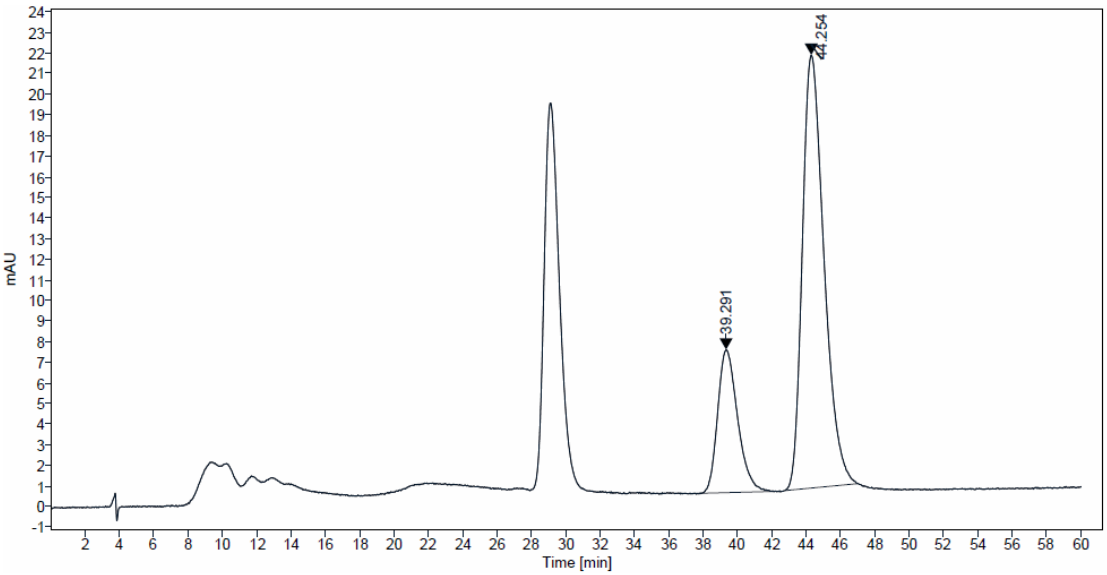


Racemic: Retention time: 44.506 min; 50.953 min

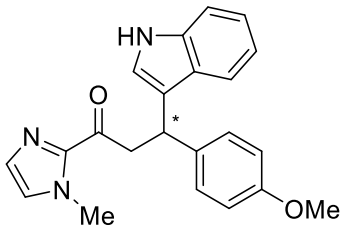


Peak	Retention time (min)	Rel. area (%)
1	44.506	50.1
2	50.953	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3w** as 32:68 and an enantiomeric excess of 75% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.5 mL/min, λ = 280 nm]. Retention time: 39.291 min; 44.254 min



Peak	Retention time (min)	Rel. area (%)
1	39.291	12.5
2	44.254	87.5



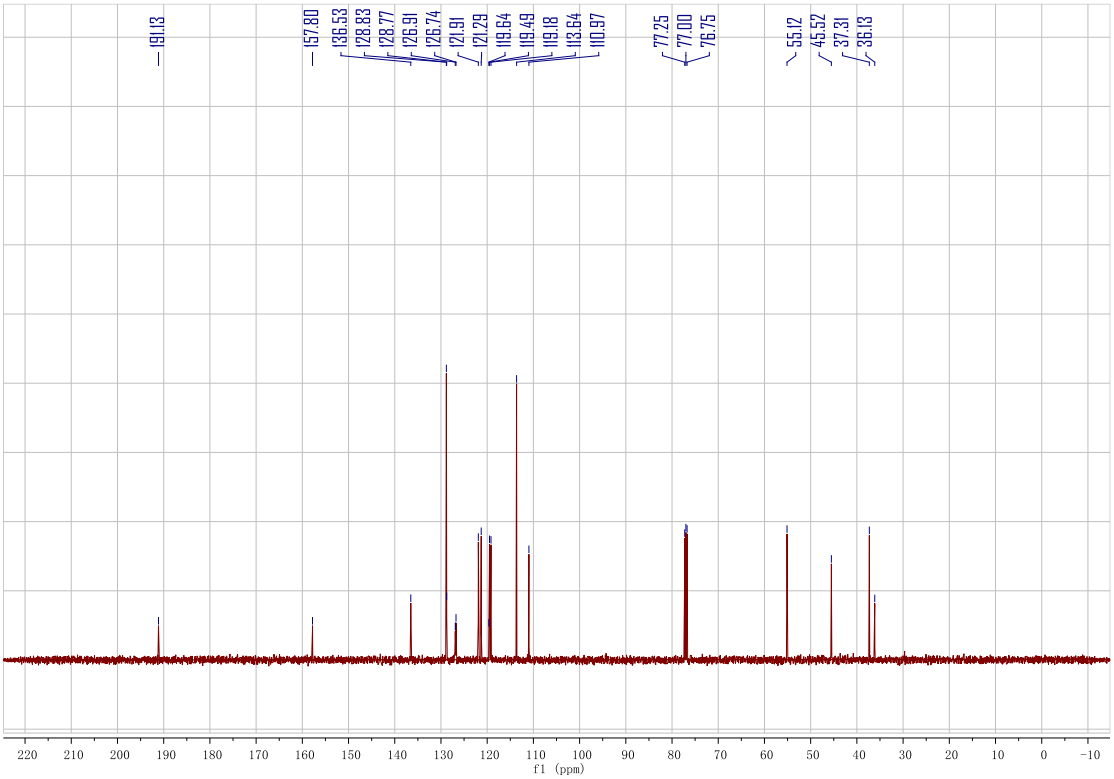
3-(1H-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (3x).

The racemic product was synthesized as described using **1f** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 34.0 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 8.1, 5.5 Hz, 3H), 7.18 (s, 1H), 7.15 – 7.11 (m, 2H), 7.02 (dd, *J* = 12.7, 4.7 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.03 (t, *J* = 7.5 Hz, 1H), 3.98 (dd, *J* = 16.3, 7.0 Hz, 1H), 3.91 (s, 3H), 3.88 (dd, *J* = 16.4, 8.2 Hz, 1H), 3.75 (s, 3H).

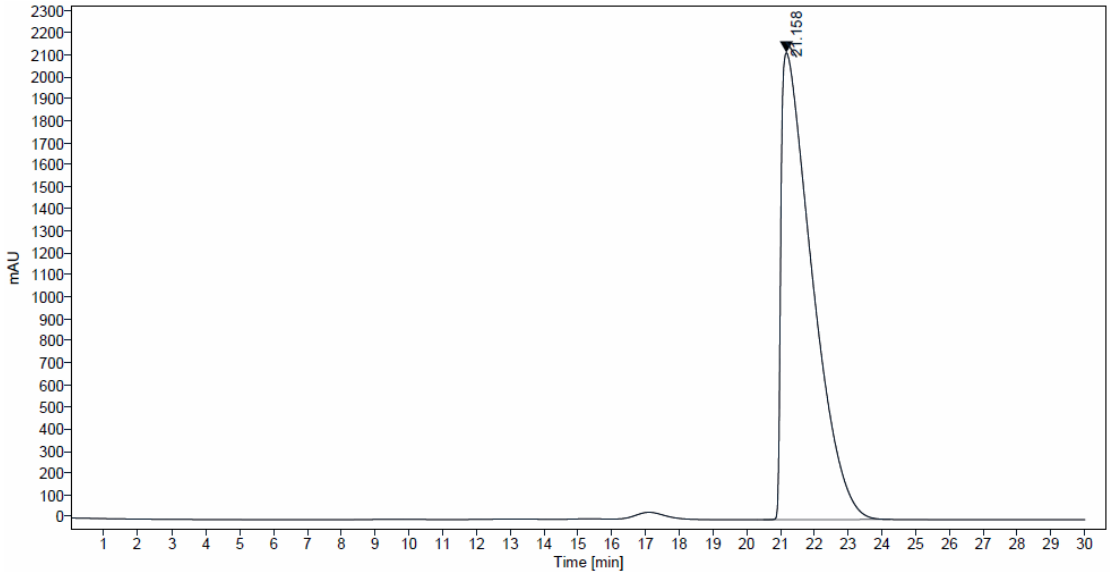
^{13}C NMR (126 MHz, $CDCl_3$) δ 191.13 (s), 157.80 (s), 136.53 (s), 128.83 (s), 128.77 (s), 126.91 (s), 126.74 (s), 121.91 (s), 121.29 (s), 119.64 (s), 119.49 (s), 119.18 (s), 113.64 (s), 110.97 (s), 77.25 (s), 77.00 (s), 76.75 (s), 55.12 (s), 45.52 (s), 37.31 (s), 36.13 (s).

HRMS (ESI) calcd. for $C_{22}H_{22}N_3O_2$ $[M+H]^+$: m/z 360.1707, found: 360.1706.

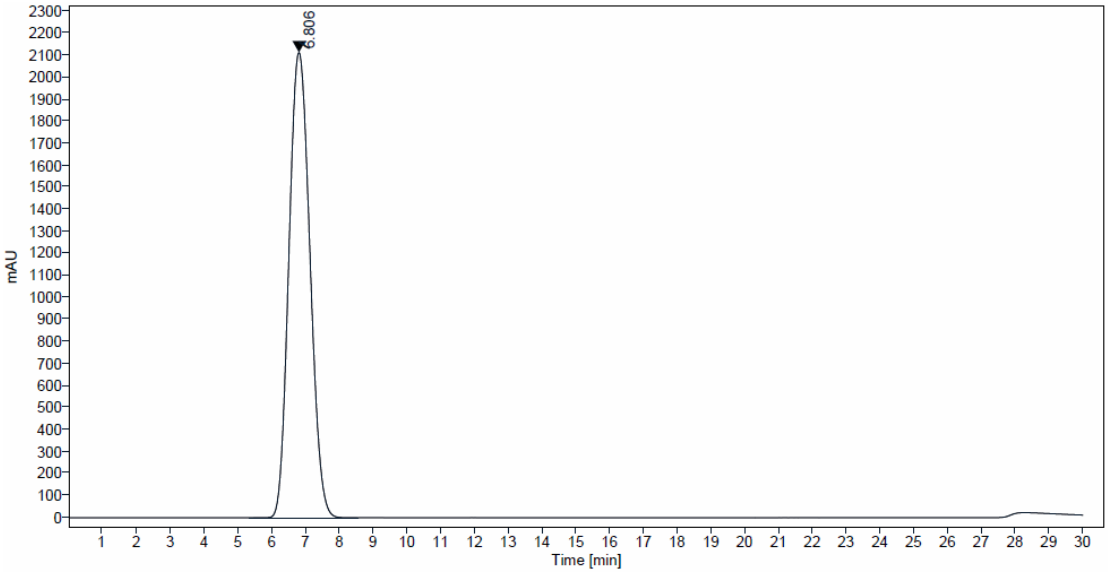


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.75 mL/min, λ = 280 nm

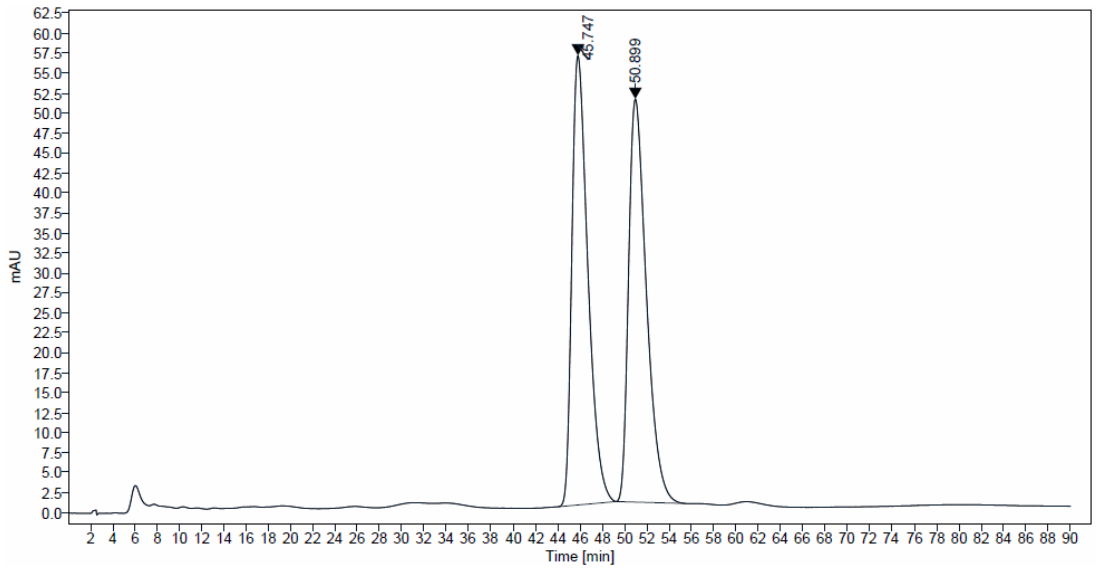
Starting Material (1f): Retention time = 21.158 min



Indole: Retention time = 6.806 min

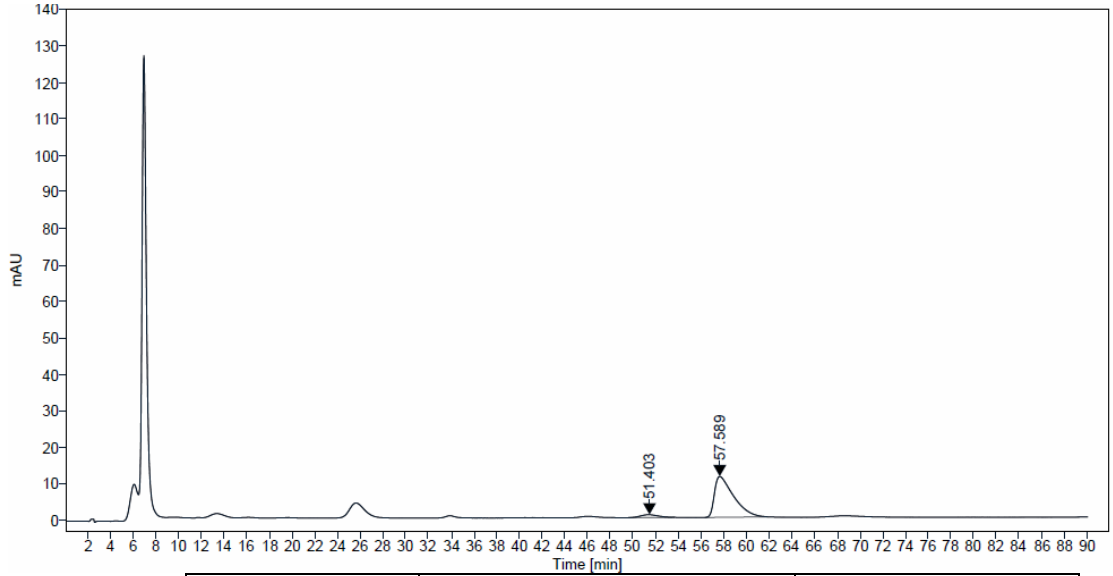


Racemic: Retention time: 45.747 min; 50.899 min

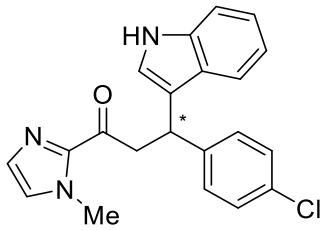


Peak	Retention time (min)	Rel. area (%)
1	45.747	50.1
2	50.899	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3x** as 9:91 and an enantiomeric excess of 91% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 0.75 mL/min, λ = 280 nm]. Retention time: 39.291 min; 44.254 min



Peak	Retention time (min)	Rel. area (%)
1	51.403	4.5
2	57.589	95.5



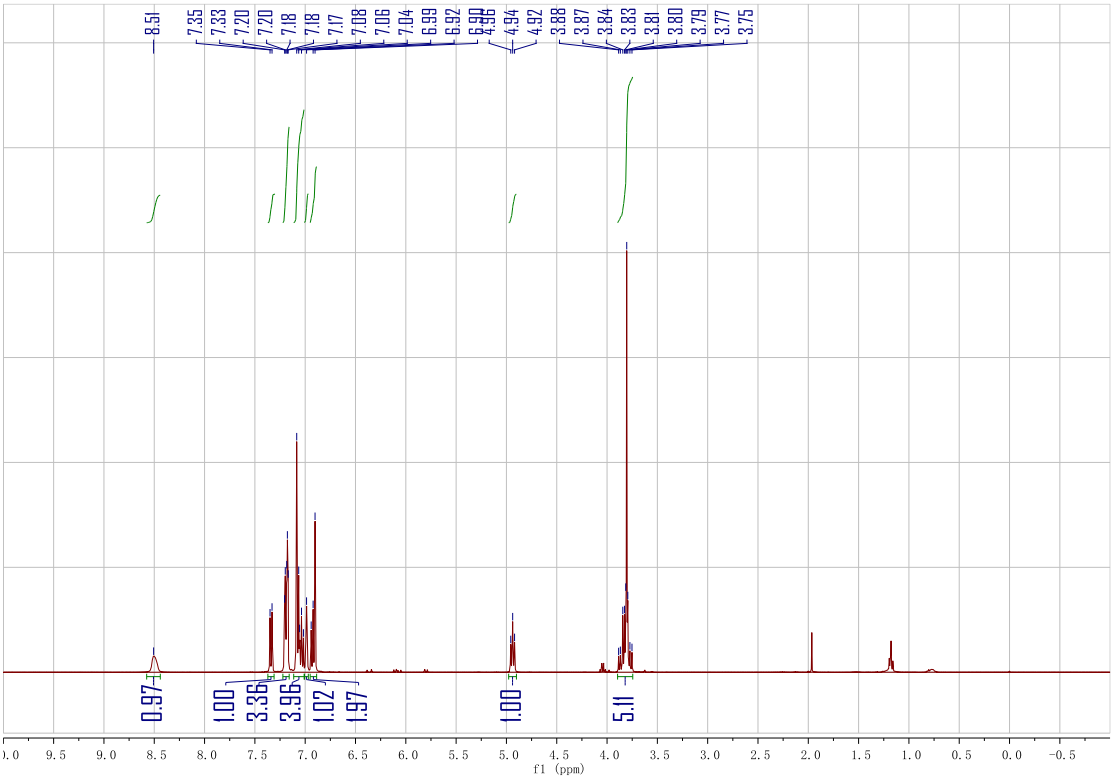
3-(4-chlorophenyl)-3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (3y).

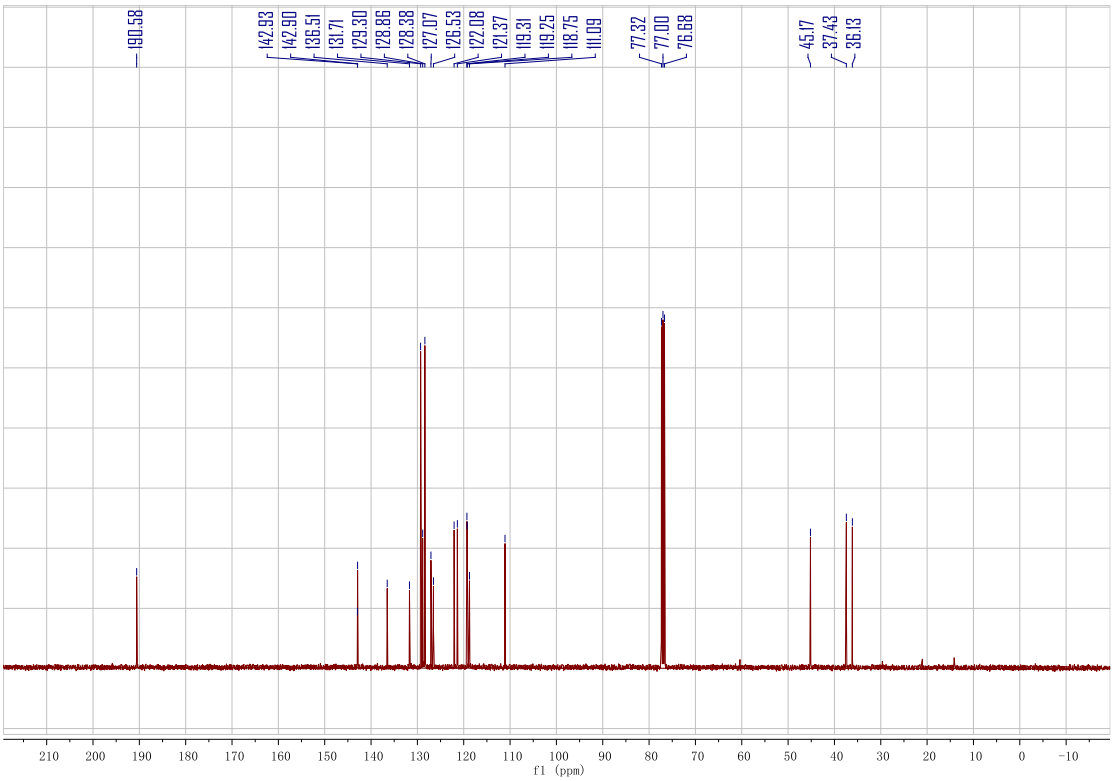
The racemic product was synthesized as described using **1g** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.11 – 7.01 (m, 4H), 6.99 (s, 1H), 6.95 – 6.89 (m, 2H), 4.94 (t, *J* = 7.6 Hz, 1H), 3.90 – 3.74 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.58 (s), 142.93 (s), 142.90 (s), 136.51 (s), 131.71 (s), 129.30 (s), 128.86 (s), 128.38 (s), 127.07 (s), 126.53 (s), 122.08 (s), 121.37 (s), 119.31 (s), 119.25 (s), 118.75 (s), 111.09 (s), 45.17 (s), 37.43 (s), 36.13 (s).

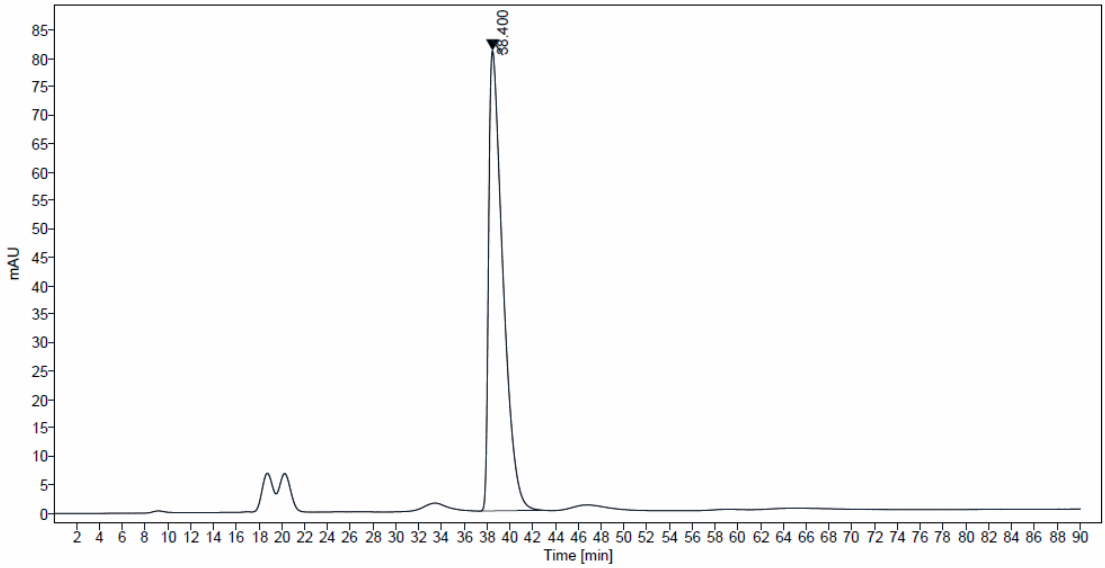
HRMS (ESI) calcd. for $C_{21}H_{19}ClN_3O$ $[M+H]^+$: m/z 364.1211, found: 364.1210.



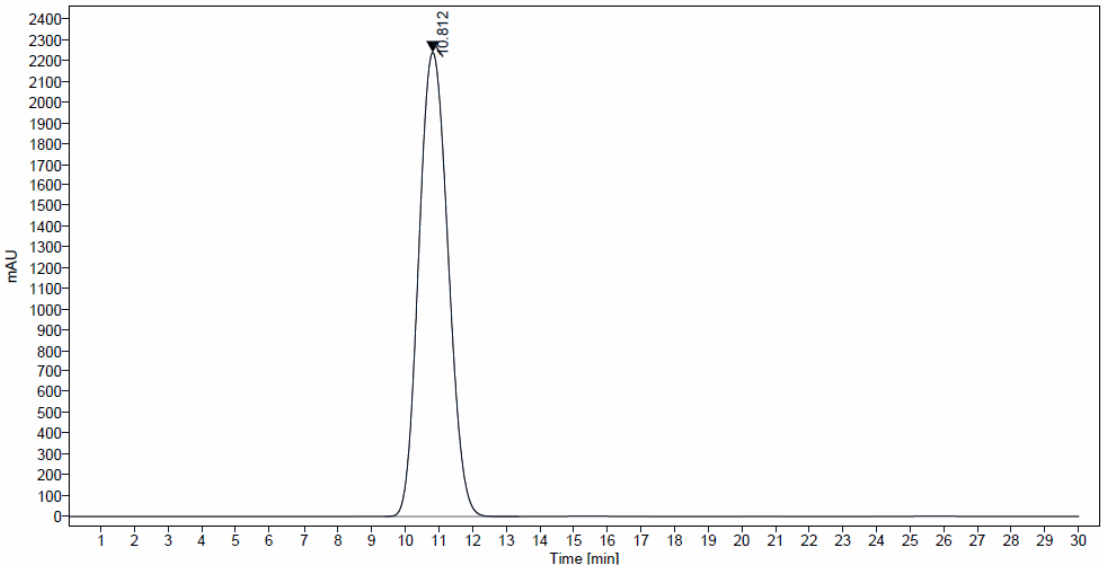


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

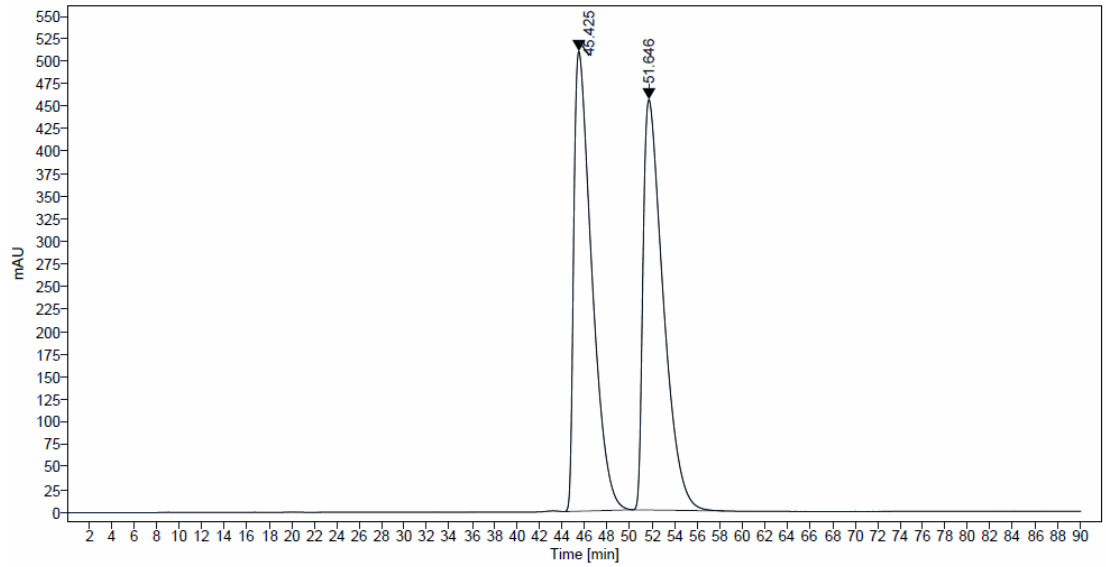
Starting Material (1g): Retention time = 38.400 min



Indole: Retention time = 10.812 min

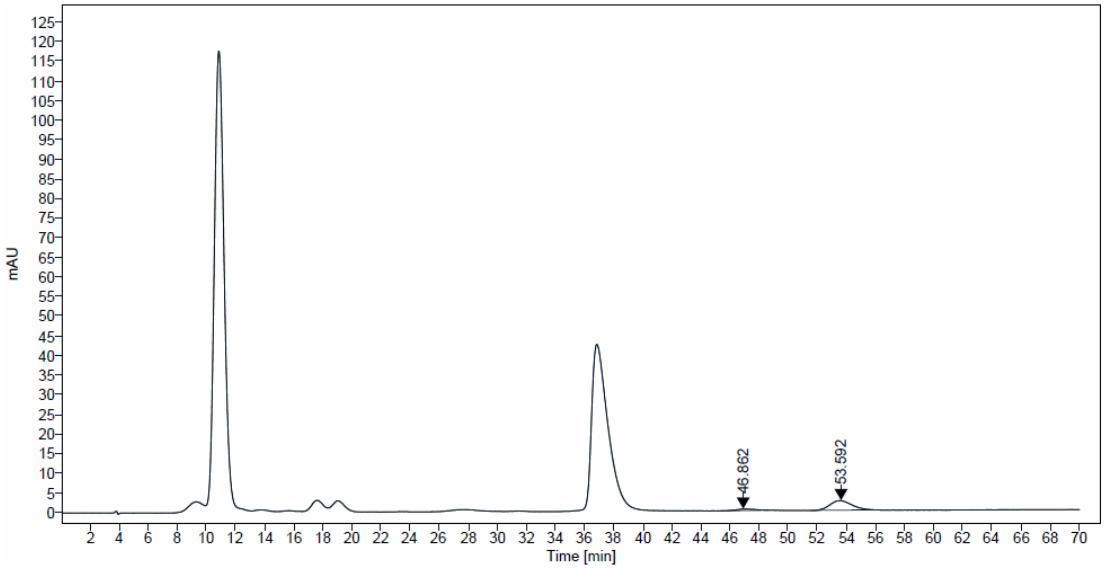


Racemic: Retention time: 45.425 min; 51.646 min

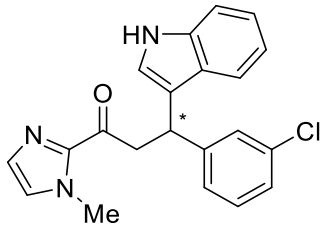


Peak	Retention time (min)	Rel. area (%)
1	45.425	50.0
2	51.646	50.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3y** as 85:15 and an enantiomeric excess of 73% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 46.882 min; 53.592 min



Peak	Retention time (min)	Rel. area (%)
1	46.882	13.5
2	53.592	86.5



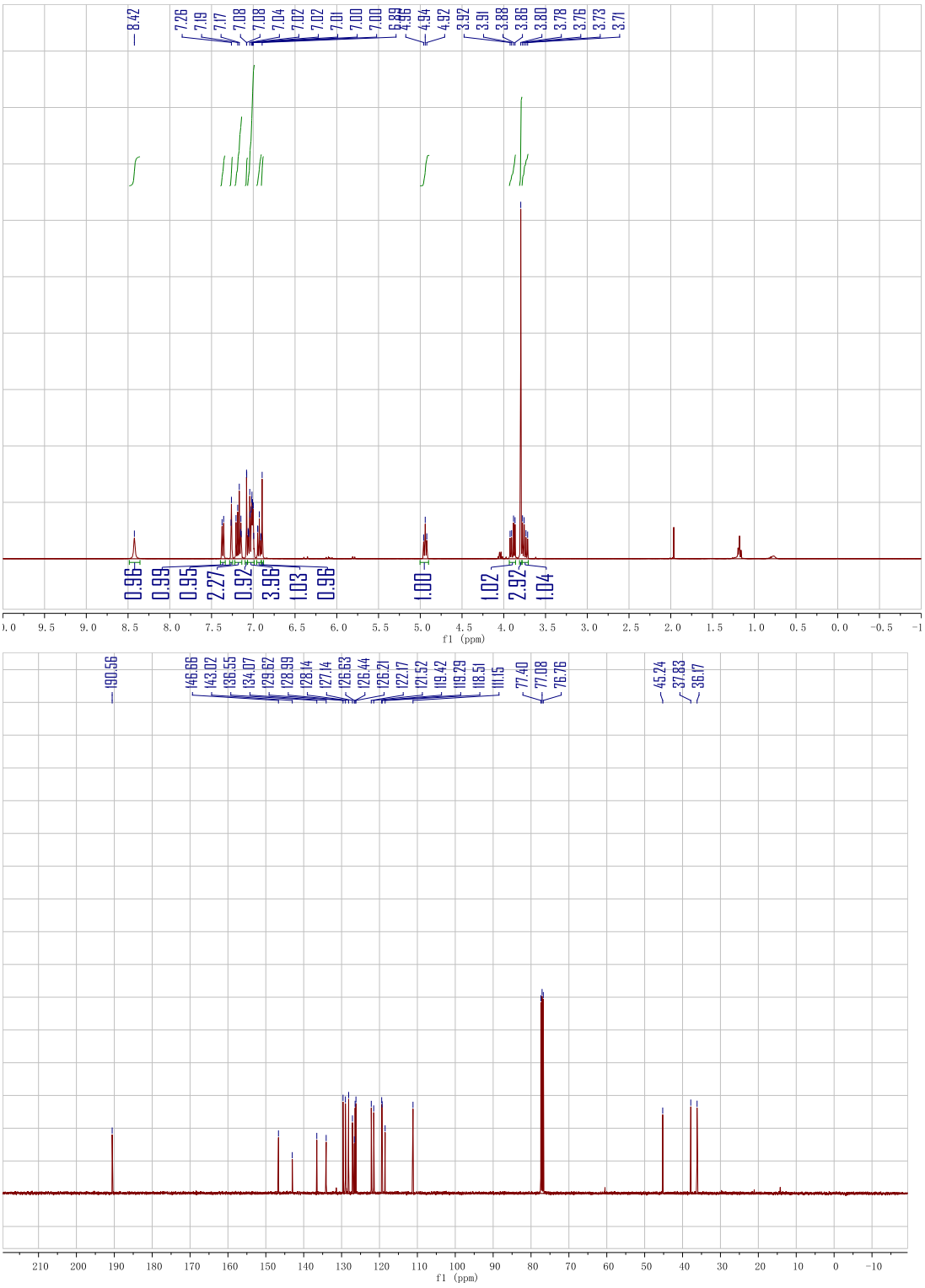
3-(3-chlorophenyl)-3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (3z).

The racemic product was synthesized as described using **1h** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 1.7 Hz, 1H), 7.22 – 7.14 (m, 2H), 7.08 (d, *J* = 0.8 Hz, 1H), 7.07 – 6.99 (m, 4H), 6.96 – 6.90 (m, 1H), 6.89 (s, 1H), 4.94 (t, *J* = 7.6 Hz, 1H), 3.89 (dd, *J* = 16.6, 7.2 Hz, 1H), 3.80 (s, 3H), 3.74 (dd, *J* = 16.6, 8.0 Hz, 1H).

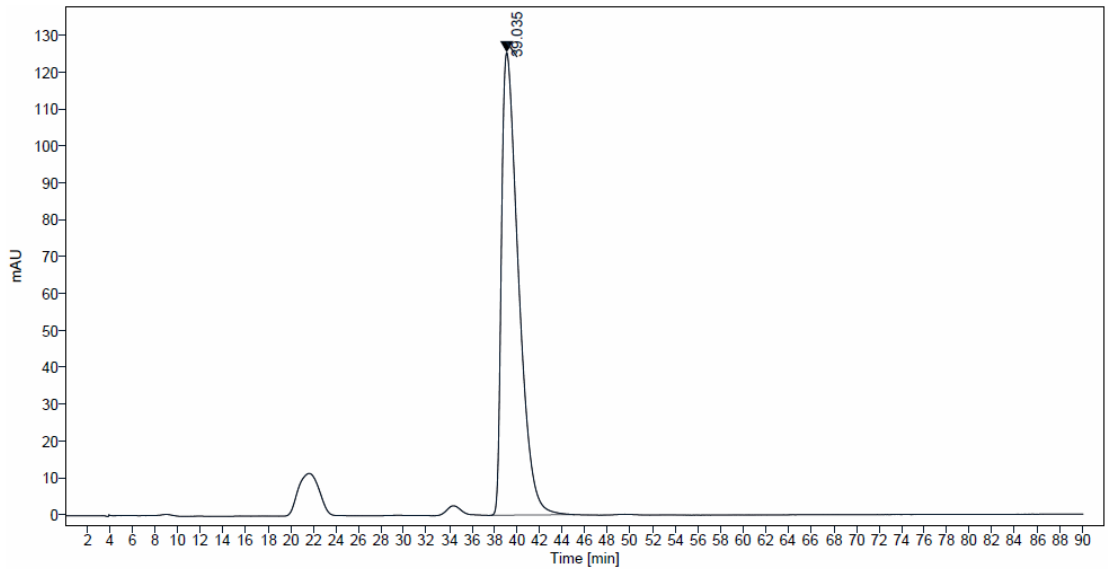
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.56 (s), 146.66 (s), 143.02 (s), 136.55 (s), 134.07 (s), 129.62 (s), 128.99 (s), 128.14 (s), 127.14 (s), 126.63 (s), 126.44 (s), 126.21 (s), 122.17 (s), 121.52 (s), 119.42 (s), 119.29 (s), 118.51 (s), 111.15 (s), 45.24 (s), 37.83 (s), 36.17 (s).

HRMS (ESI) calcd. for $C_{21}H_{19}ClN_3O$ $[M+H]^+$: m/z 364.1211, found: 364.1213.

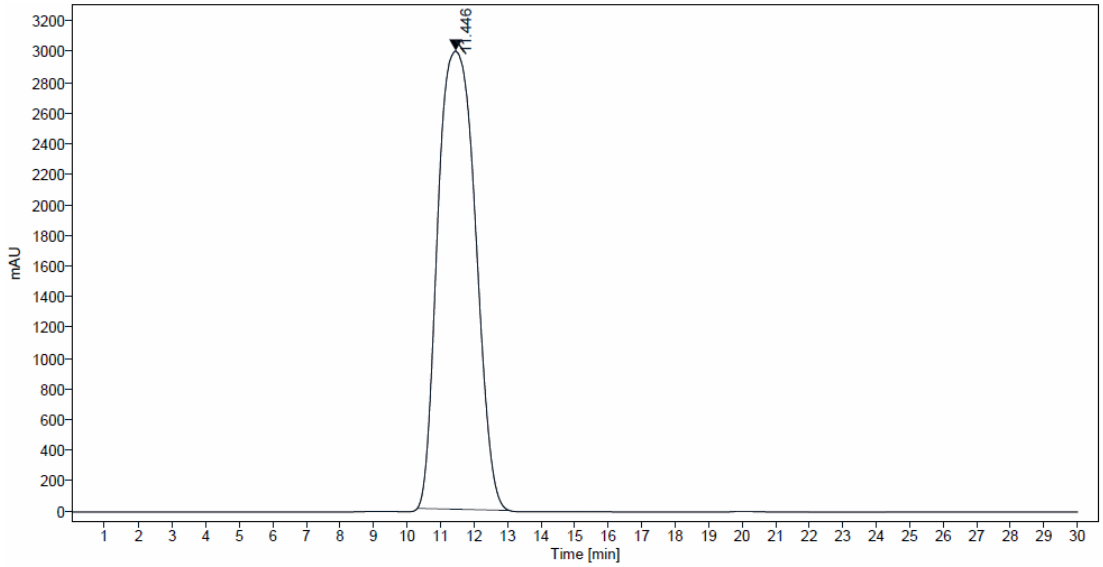


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

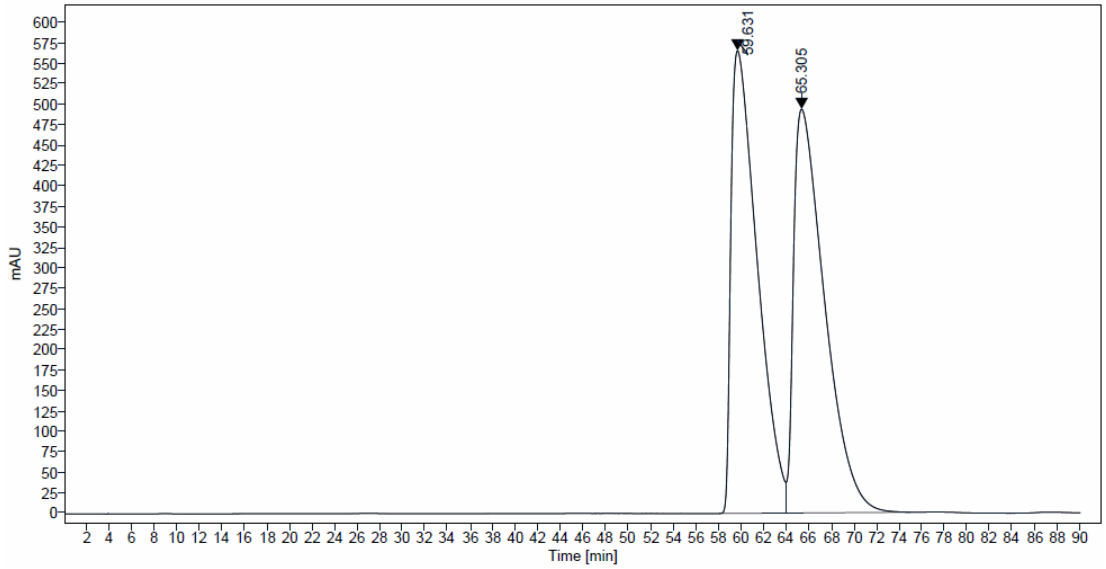
Starting Material (1h): Retention time = 39.035 min



Indole: Retention time = 11.446 min

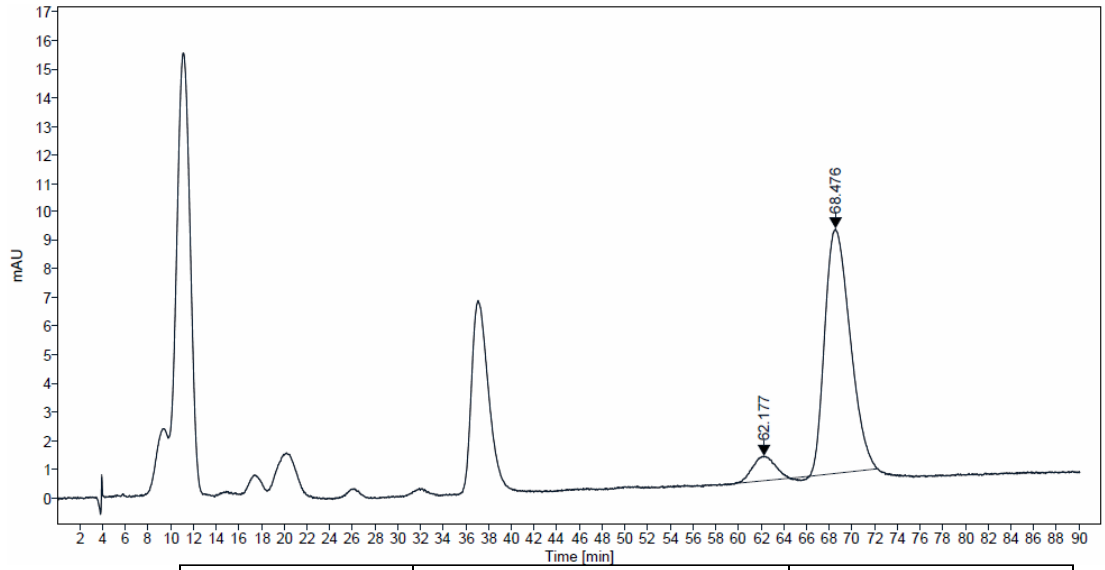


Racemic: Retention time: 59.631 min; 65.305 min

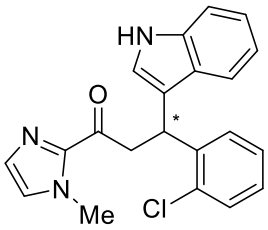


Peak	Retention time (min)	Rel. area (%)
1	59.631	51.0
2	65.305	49.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3z** as 23:77 and an enantiomeric excess of 81% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 62.177 min; 68.478 min



Peak	Retention time (min)	Rel. area (%)
1	62.177	9.5
2	68.478	90.5



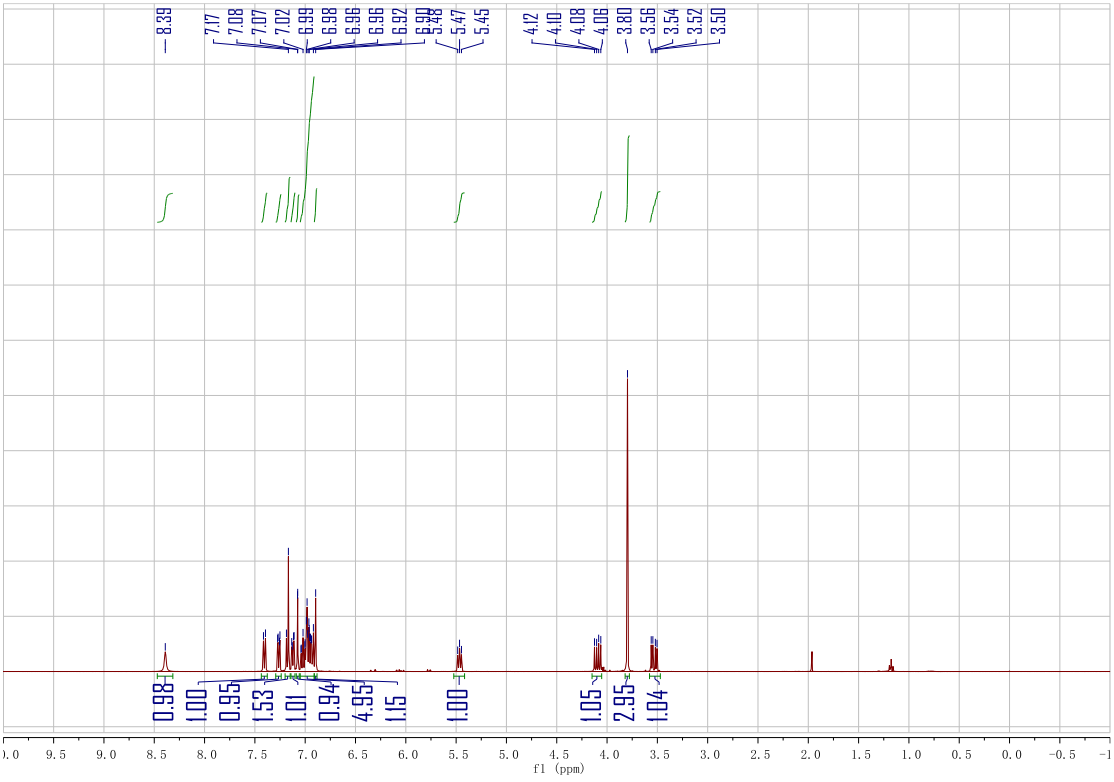
3-(2-chlorophenyl)-3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (3aa).

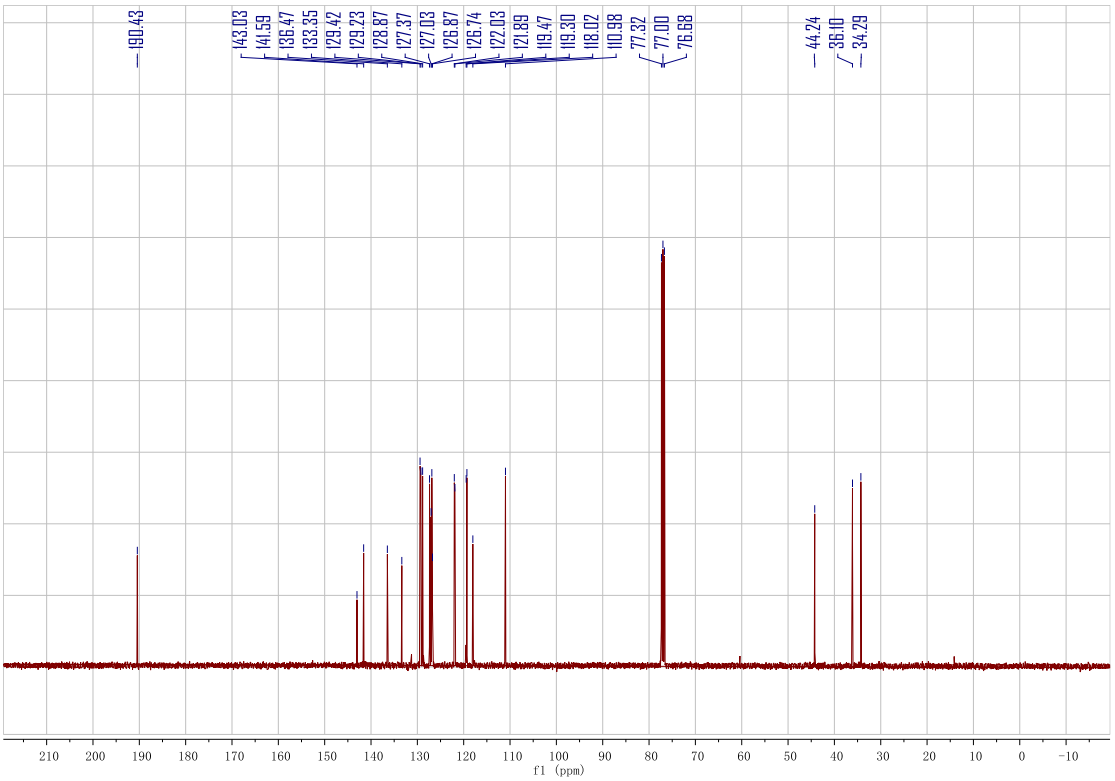
The racemic product was synthesized as described using **1i** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.26 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.18 (d, *J* = 7.7 Hz, 1H), 7.12 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.08 (d, *J* = 0.6 Hz, 1H), 7.05 – 6.91 (m, 5H), 6.90 (s, 1H), 5.52 – 5.42 (m, 1H), 4.09 (dd, *J* = 16.6, 8.5 Hz, 1H), 3.80 (s, 3H), 3.53 (dd, *J* = 16.6, 6.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.43 (s), 143.03 (s), 141.59 (s), 136.47 (s), 133.35 (s), 129.42 (s), 129.23 (s), 128.87 (s), 127.37 (s), 127.03 (s), 126.87 (s), 126.74 (s), 122.03 (s), 121.89 (s), 119.47 (s), 119.30 (s), 118.02 (s), 110.98 (s), 44.24 (s), 36.10 (s), 34.29 (s).

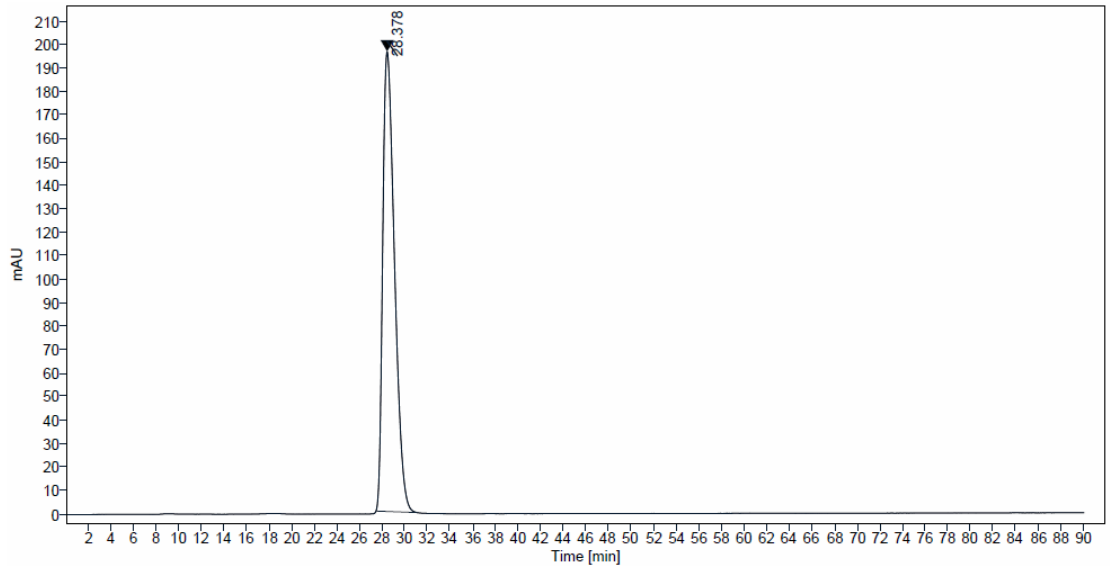
HRMS (ESI) calcd. for $C_{21}H_{19}ClN_3O$ $[M+H]^+$: m/z 364.1211, found: 364.1215.



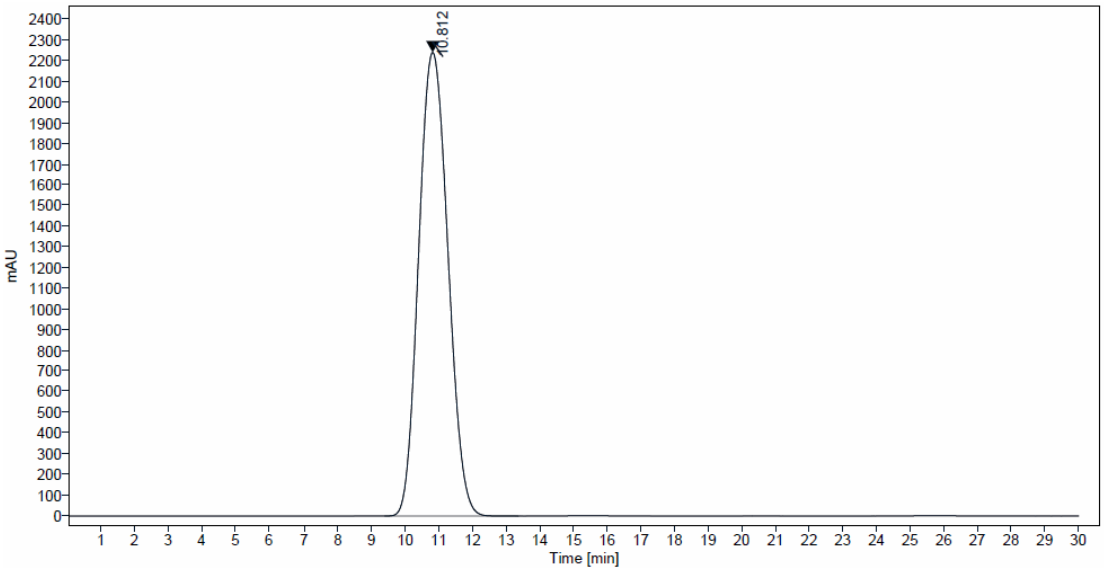


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

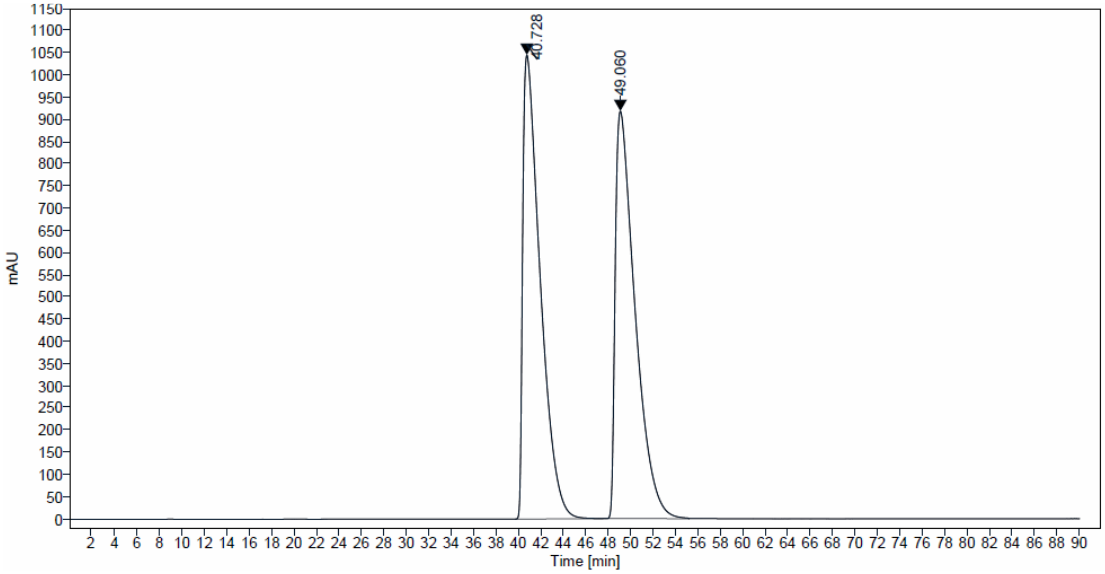
Starting Material (1h): Retention time = 28.378 min



Indole: Retention time = 10.812 min

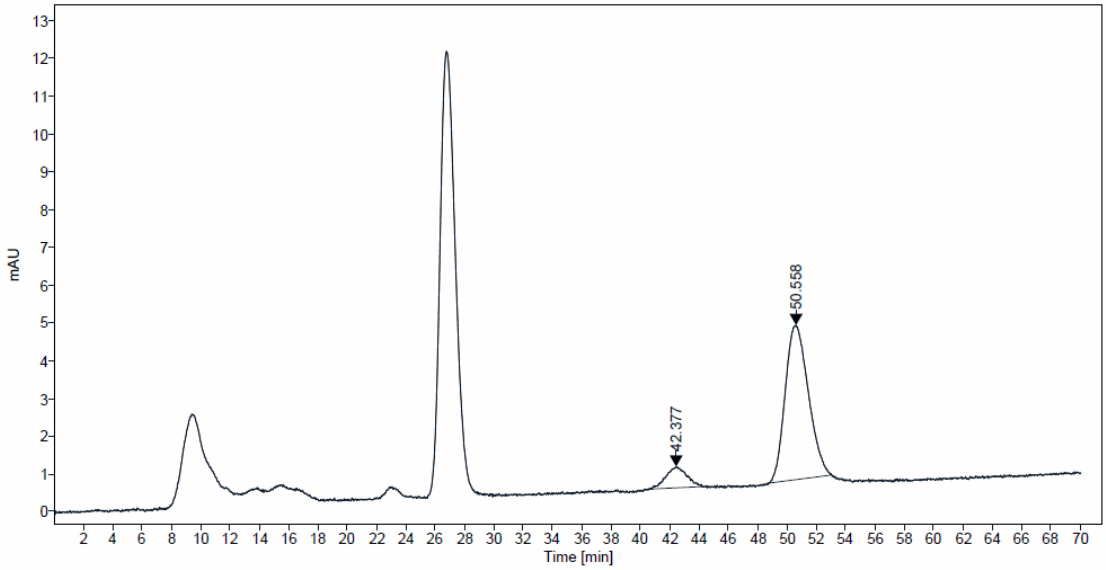


Racemic: Retention time: 40.728 min; 49.060 min

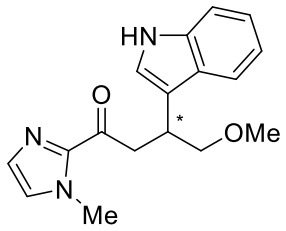


Peak	Retention time (min)	Rel. area (%)
1	40.728	50.2
2	49.060	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3aa** as 40:60 and an enantiomeric excess of 78% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 42.377 min; 50.558 min



Peak	Retention time (min)	Rel. area (%)
1	42.377	11.1
2	50.558	88.9



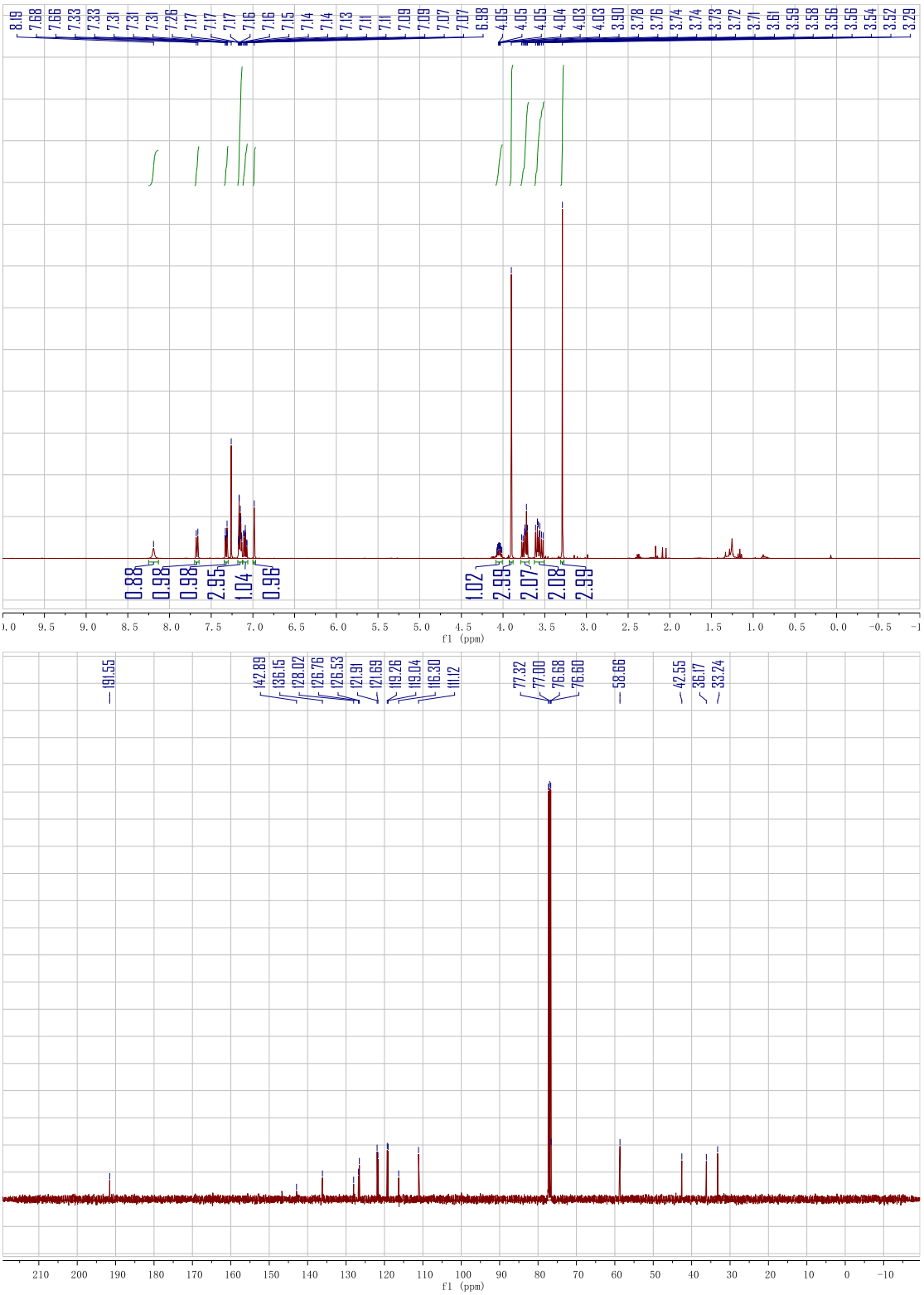
3-(1H-indol-3-yl)-4-methoxy-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (3ab).

The racemic product was synthesized as described using **1j** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.18 – 7.13 (m, 3H), 7.12 – 7.06 (m, 1H), 6.98 (s, 1H), 4.09 – 4.01 (m, 1H), 3.90 (s, 3H), 3.79 – 3.69 (m, 2H), 3.62 – 3.51 (m, 2H), 3.29 (s, 3H).

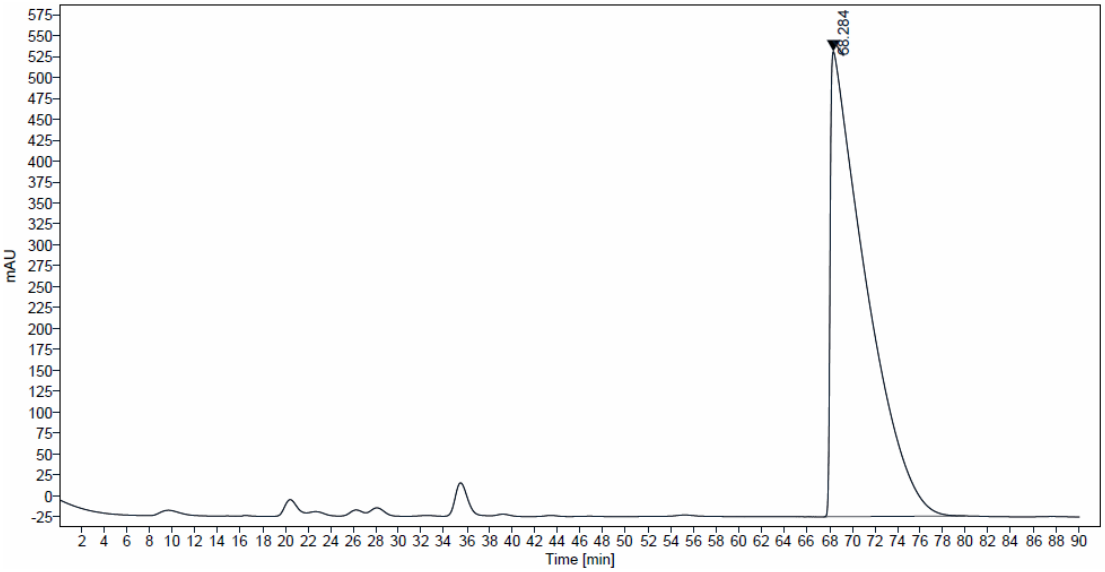
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.55 (s), 142.89 (s), 136.15 (s), 128.02 (s), 126.76 (s), 126.53 (s), 121.91 (s), 121.69 (s), 119.26 (s), 119.04 (s), 116.30 (s), 111.12 (s), 76.60 (s), 58.66 (s), 42.55 (s), 36.17 (s), 33.24 (s).

HRMS (ESI) calcd. for $C_{17}H_{20}N_3O_2$ $[M+H]^+$: m/z 298.1550, found: 298.1552.

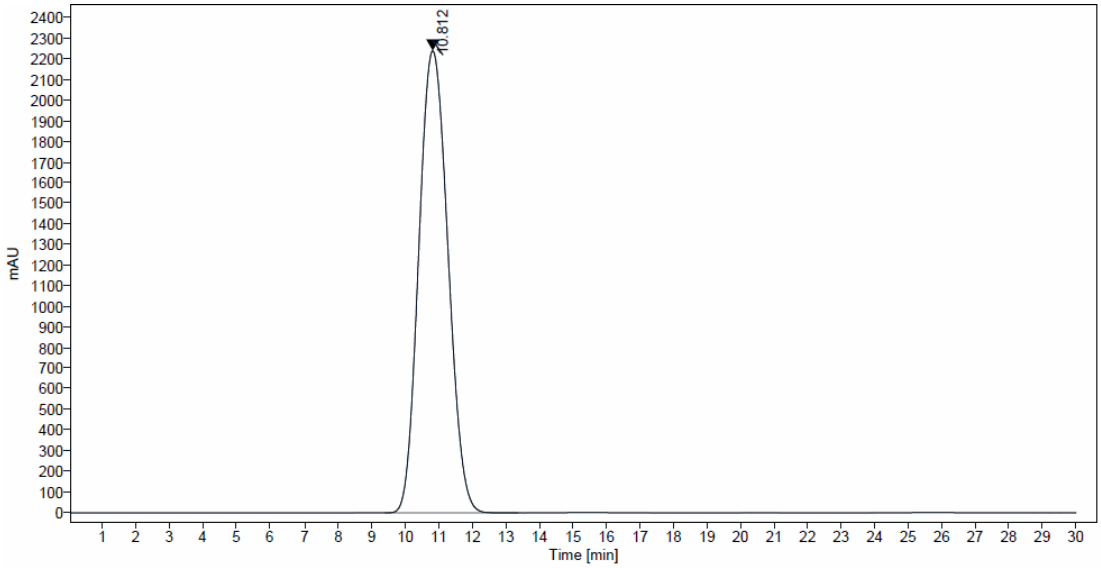


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm

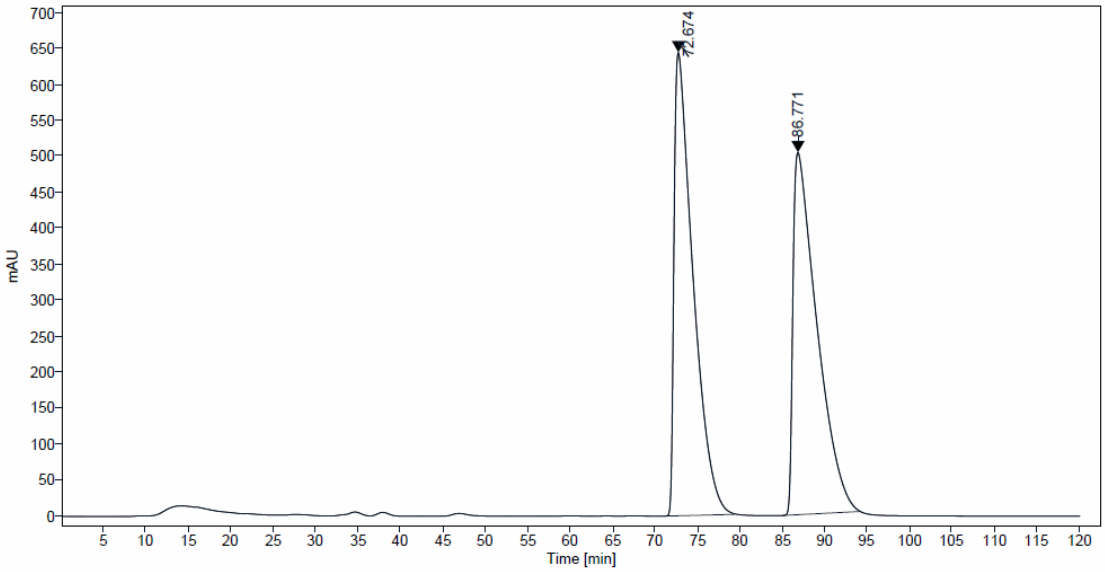
Starting Material (1j): Retention time = 68.284 min



Indole: Retention time = 10.812 min

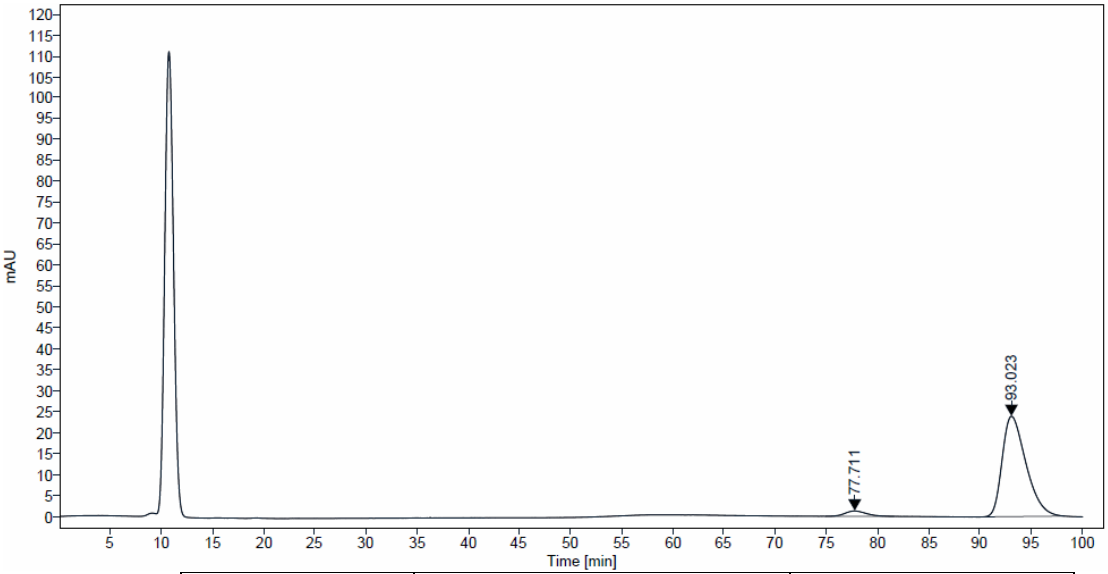


Racemic: Retention time: 72.674 min; 86.771 min

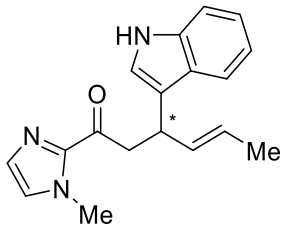


Peak	Retention time (min)	Rel. area (%)
1	72.674	49.9
2	86.771	50.1

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3ab** < 1:99 and an enantiomeric excess of 90% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.5 mL/min, λ = 280 nm]. Retention time: 42.377 min; 50.558 min



Peak	Retention time (min)	Rel. area (%)
1	77.711	5.1
2	93.023	94.9



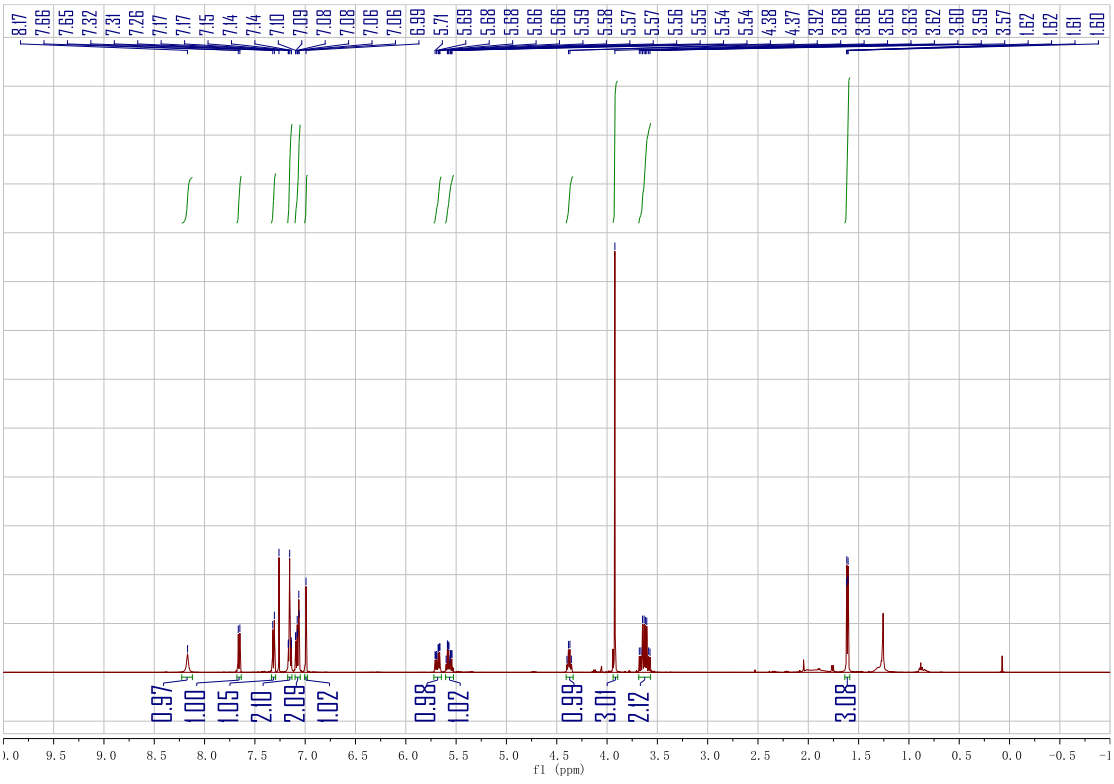
(E)-3-(1H-indol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)hex-4-en-1-one (3ac).

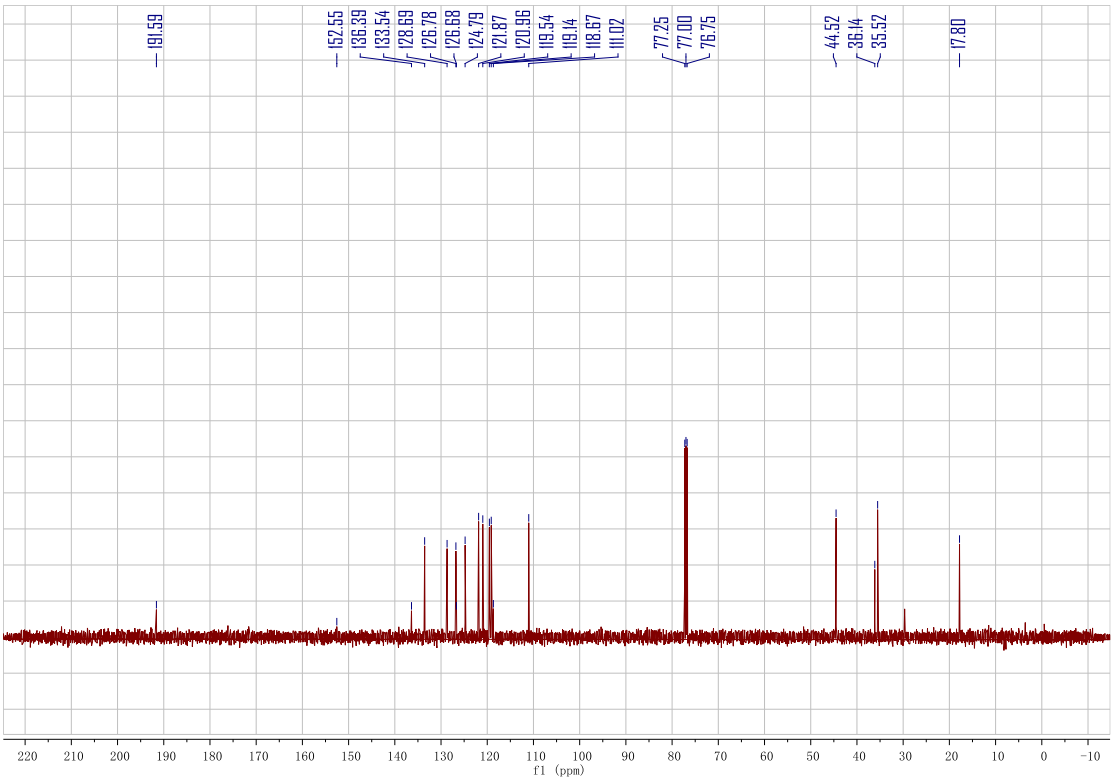
The racemic product was synthesized as described using **1l** and Indole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.13 (m, 2H), 7.10 – 7.05 (m, 2H), 6.99 (s, 1H), 5.68 (ddd, *J* = 15.2, 7.3, 1.5 Hz, 1H), 5.60 – 5.53 (m, 1H), 4.38 (q, *J* = 7.4 Hz, 1H), 3.92 (s, 3H), 3.63 (qd, *J* = 15.9, 7.4 Hz, 2H), 1.61 (dd, *J* = 6.3, 0.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 191.59 (s), 152.55 (s), 136.39 (s), 133.54 (s), 128.69 (s), 126.78 (s), 126.68 (s), 124.79 (s), 121.87 (s), 120.96 (s), 119.54 (s), 119.14 (s), 118.67 (s), 111.02 (s), 44.52 (s), 36.14 (s), 35.52 (s), 17.80 (s).

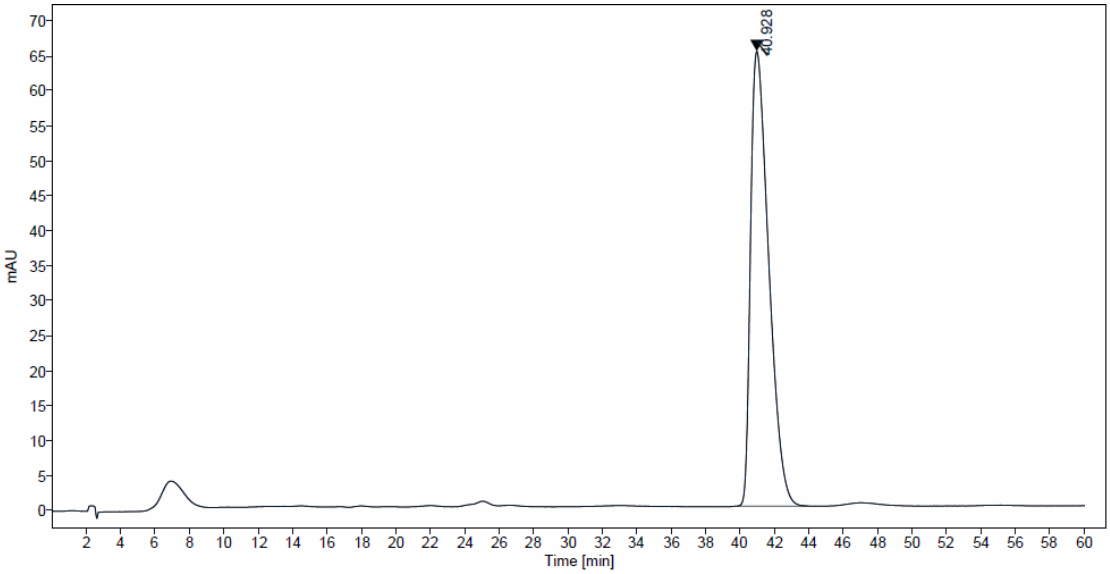
HRMS (ESI) calcd. for $C_{18}H_{20}N_3O$ $[M+H]^+$: m/z 294.1601, found: 294.1600.



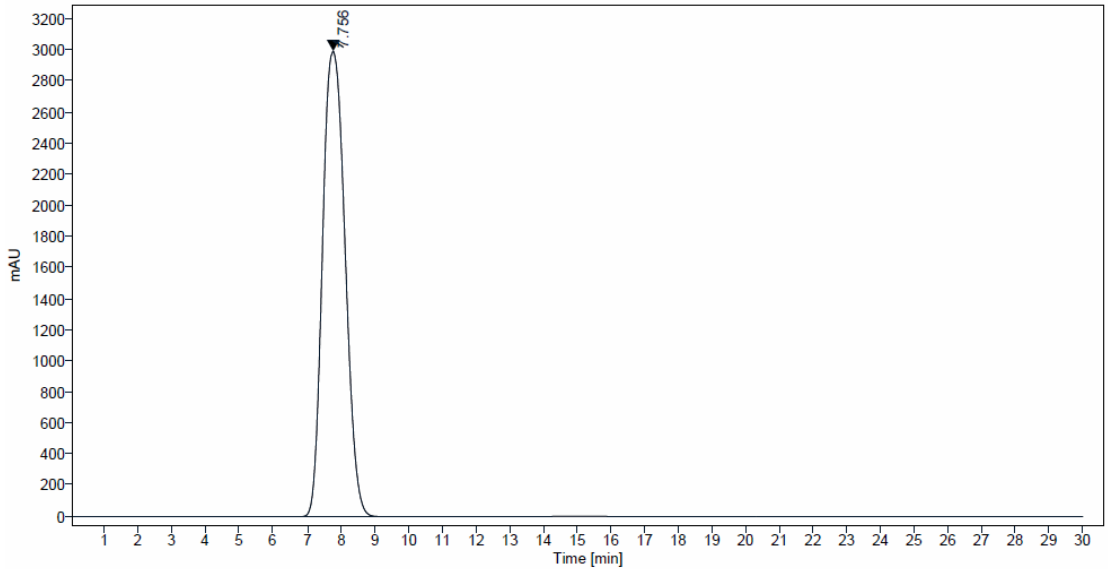


HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm

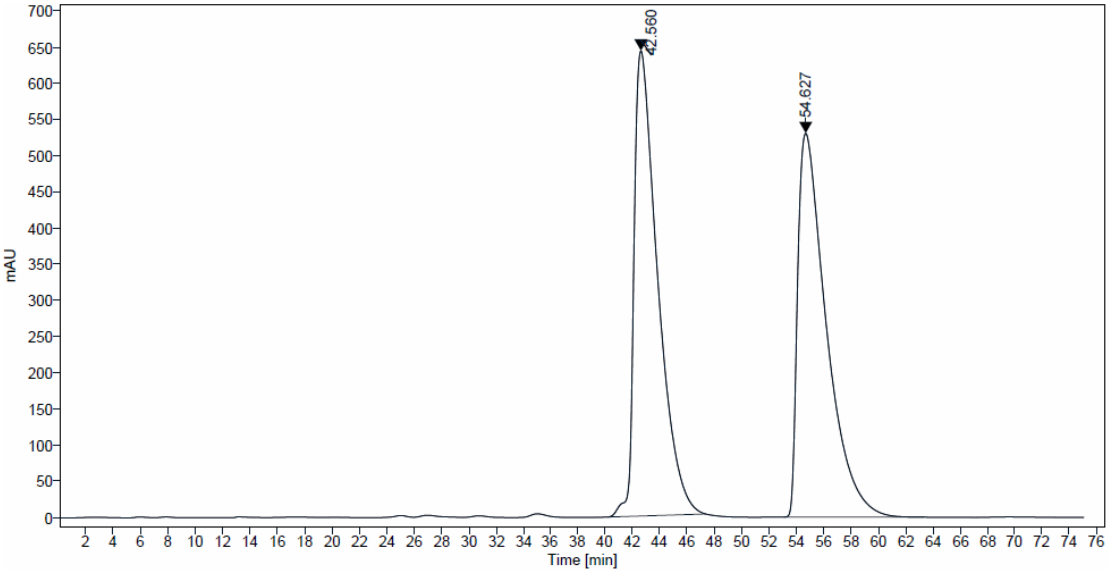
Starting Material (1k): Retention time = 40.928 min



Indole: Retention time = 7.756 min

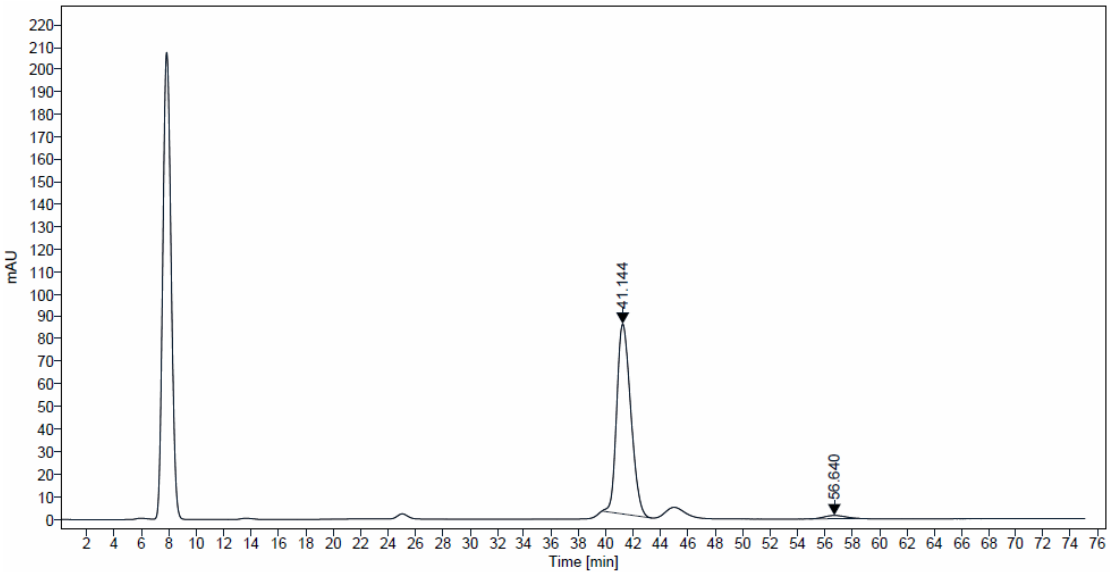


Racemic: Retention time: 42.560 min; 54.627 min

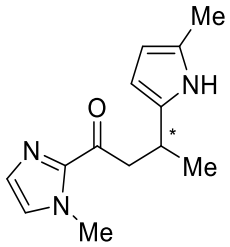


Peak	Retention time (min)	Rel. area (%)
1	42.560	51.5
2	54.627	48.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**3ac** < 1:99 and an enantiomeric excess of 96% [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm]. Retention time: 37.631 min; 41.036 min



Peak	Retention time (min)	Rel. area (%)
1	41.144	97.9
2	56.640	2.1



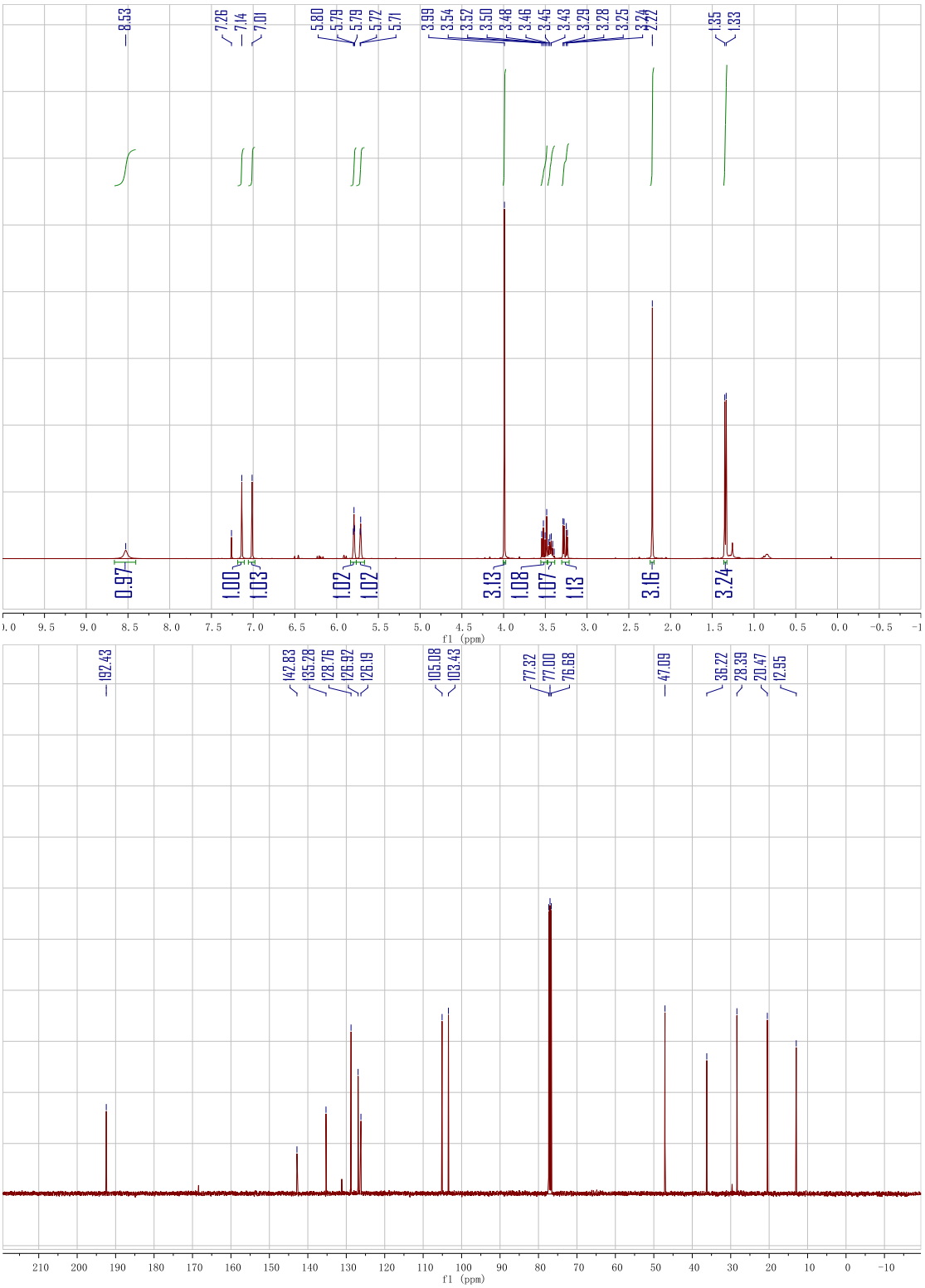
1-(1-methyl-1H-imidazol-2-yl)-3-(5-methyl-1H-pyrrol-2-yl)butan-1-one (4a).

The racemic product was synthesized as described using **1a** and 2-Me-Pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.14 (s, 1H), 7.01 (s, 1H), 5.79 (t, *J* = 2.8 Hz, 1H), 5.72 (d, *J* = 2.4 Hz, 1H), 3.99 (s, 3H), 3.51 (dd, *J* = 16.0, 7.6 Hz, 1H), 3.47 – 3.39 (m, 1H), 3.26 (dd, *J* = 15.9, 5.3 Hz, 1H), 2.22 (s, 3H), 1.34 (d, *J* = 6.9 Hz, 3H).

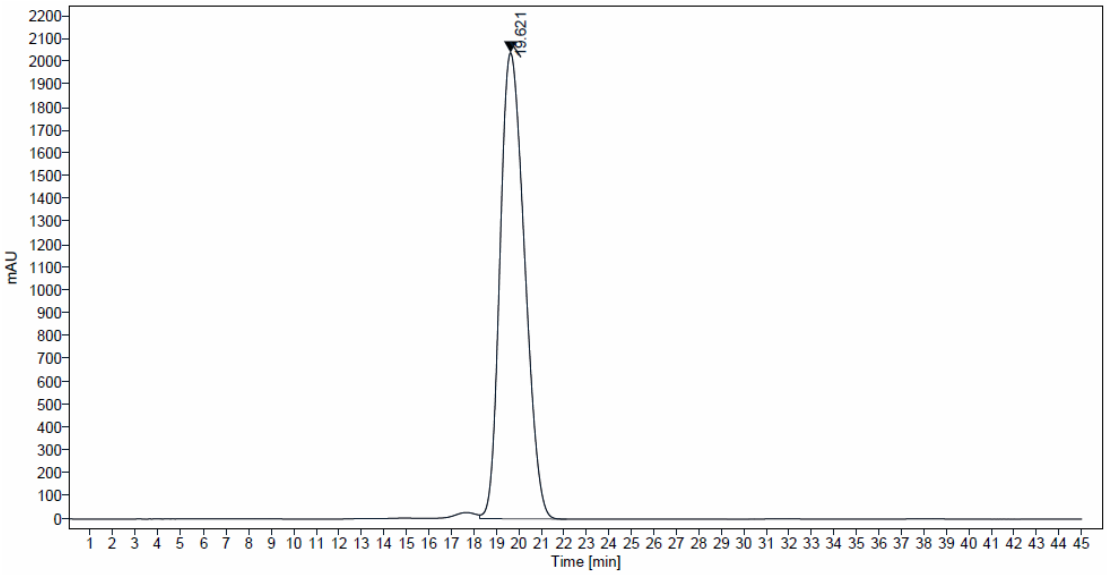
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.43 (s), 142.83 (s), 135.28 (s), 128.76 (s), 126.92 (s), 126.19 (s), 105.08 (s), 103.43 (s), 47.09 (s), 36.22 (s), 28.39 (s), 20.47 (s), 12.95 (s).

HRMS (ESI) calcd. for $C_{13}H_{18}N_3O$ $[M+H]^+$: m/z 232.1444, found: 232.1447.

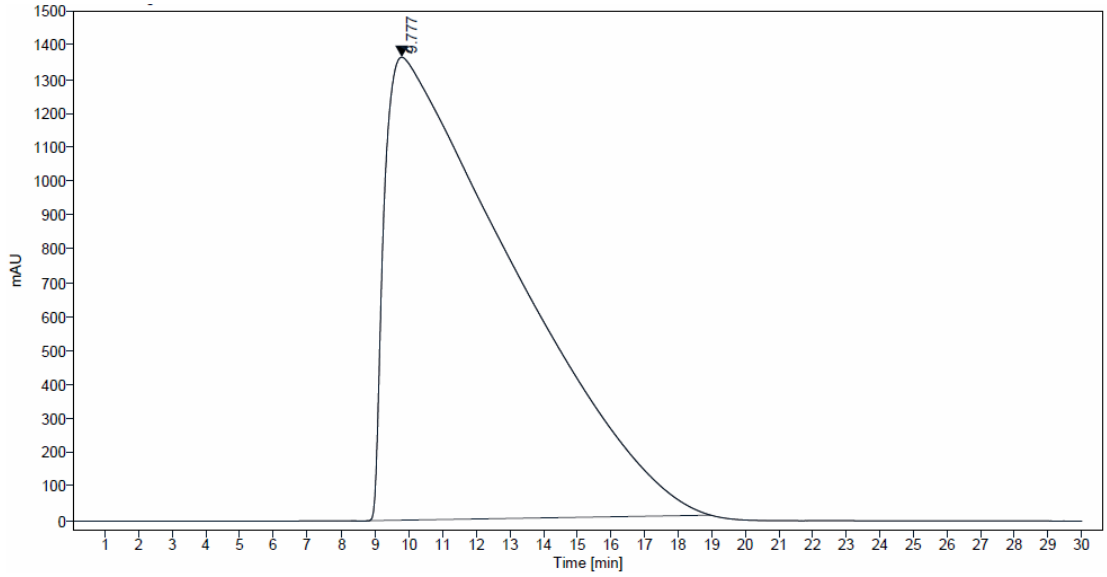


HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

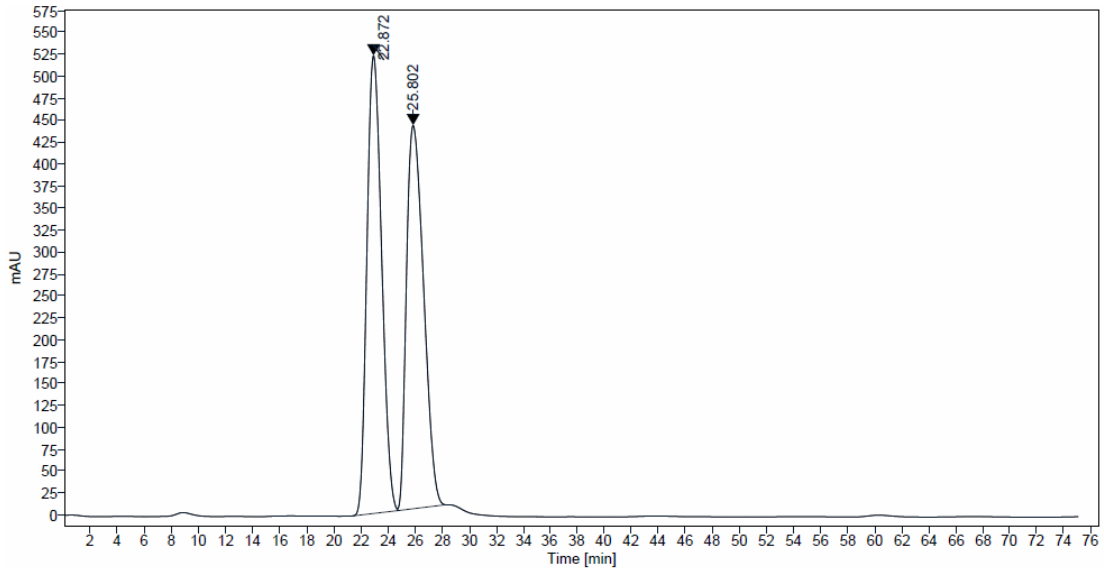
Starting Material (1a): Retention time = 19.621 min



2-Me-Pyrrole: Retention time = 9.777 min

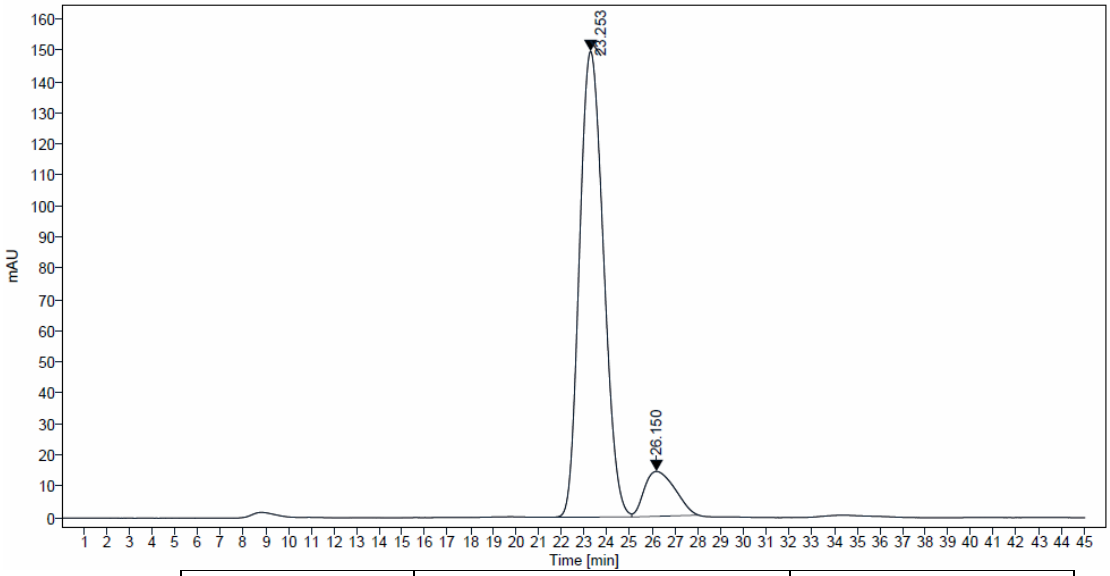


Racemic: Retention time: 22.872 min; 25.802 min

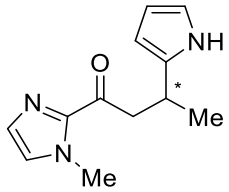


Peak	Retention time (min)	Rel. area (%)
1	22.872	50.5
2	25.802	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4a** < 1:99 and an enantiomeric excess of 82% [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 23.253 min; 26.150 min



Peak	Retention time (min)	Rel. area (%)
1	23.253	90.8
2	26.150	9.2



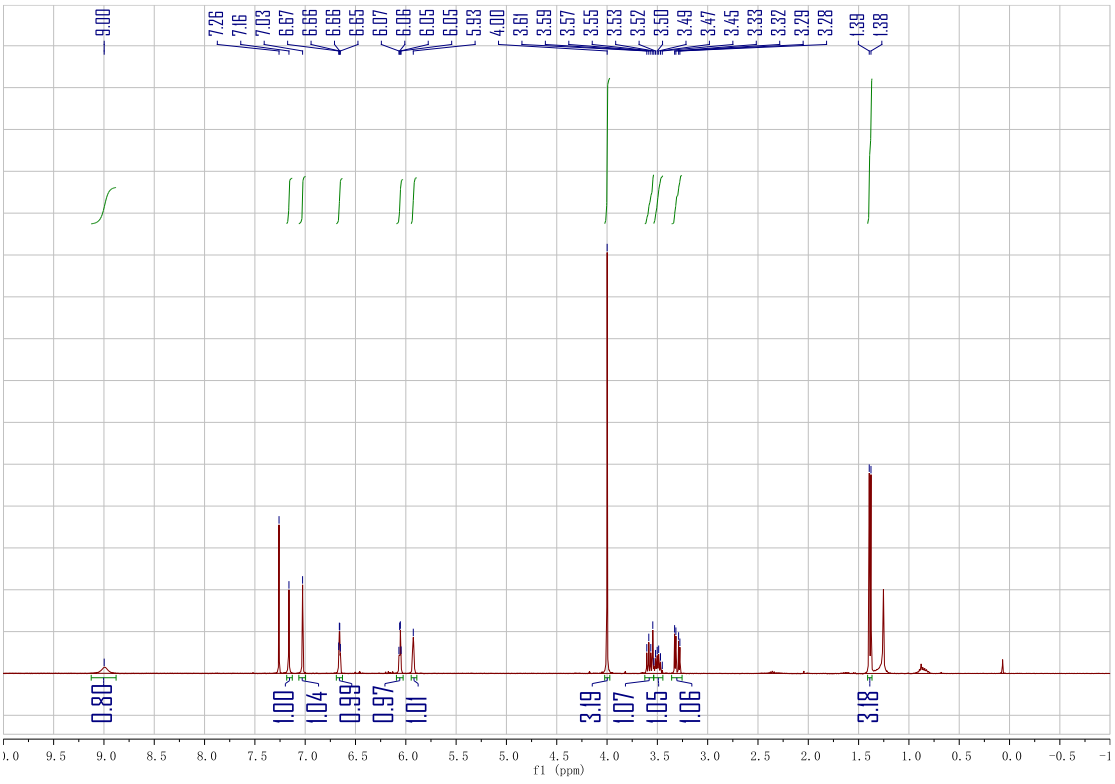
1-(1-methyl-1H-imidazol-2-yl)-3-(1H-pyrrol-2-yl)butan-1-one (4b).

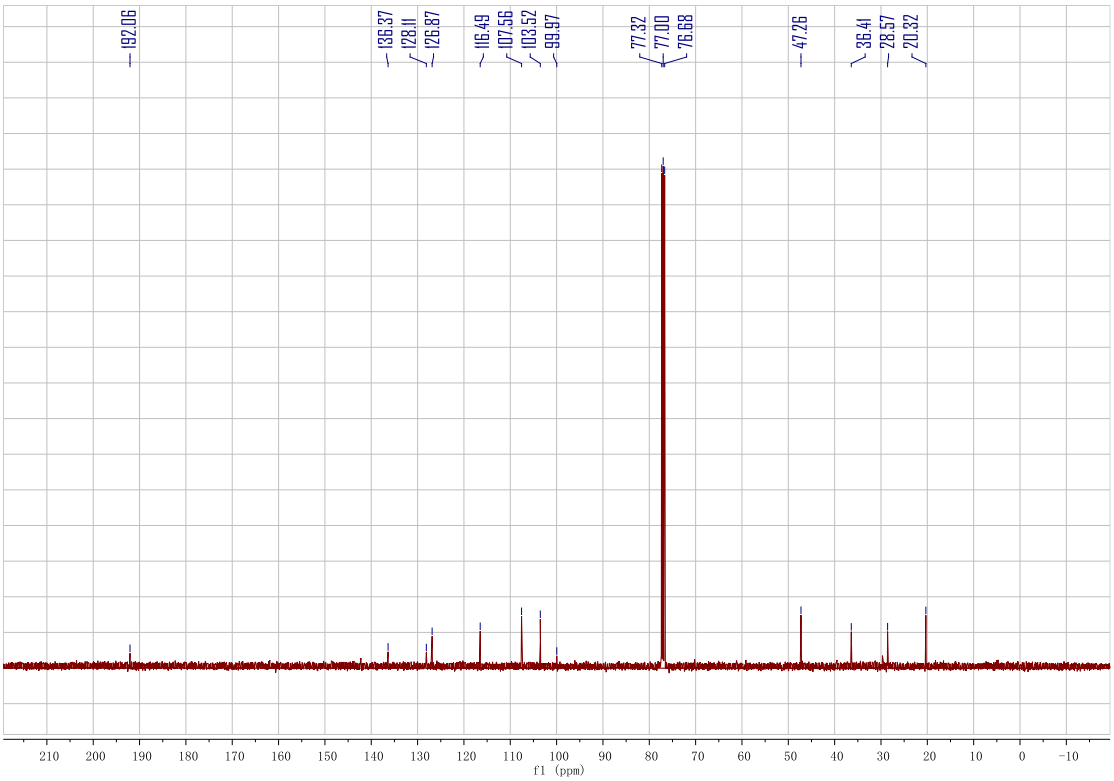
The racemic product was synthesized as described using **1a** and Pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.16 (s, 1H), 7.03 (s, 1H), 6.66 (dd, *J* = 4.1, 2.5 Hz, 1H), 6.06 (dd, *J* = 5.7, 2.8 Hz, 1H), 5.93 (s, 1H), 4.00 (s, 3H), 3.58 (dd, *J* = 15.9, 7.9 Hz, 1H), 3.54 – 3.45 (m, 1H), 3.30 (dd, *J* = 15.9, 5.0 Hz, 1H), 1.39 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.06 (s), 136.37 (s), 128.11 (s), 126.87 (s), 116.49 (s), 107.56 (s), 103.52 (s), 99.97 (s), 47.26 (s), 36.41 (s), 28.57 (s), 20.32 (s).

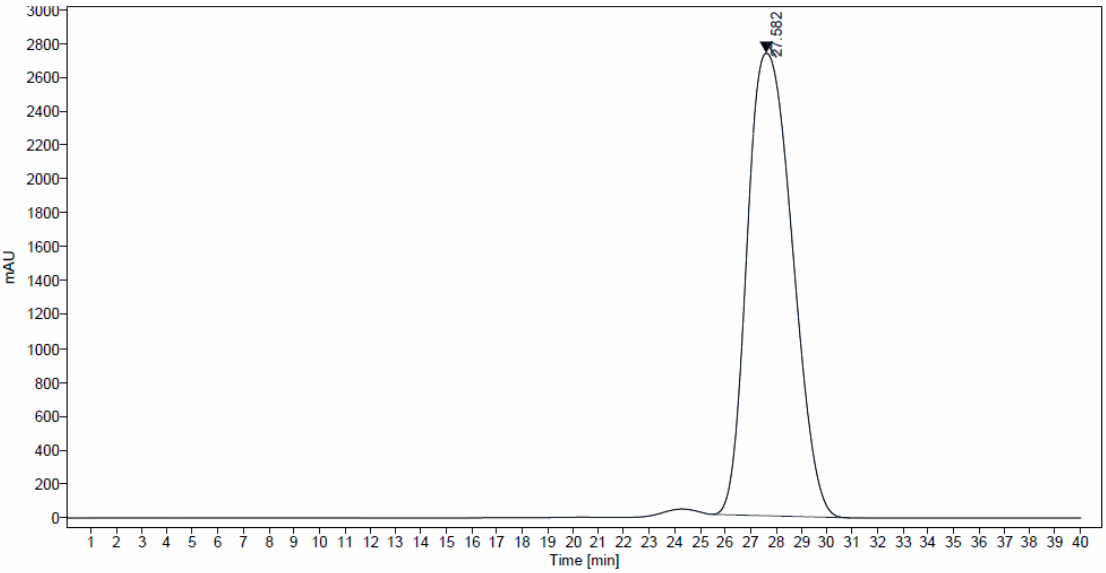
HRMS (ESI) calcd. for $C_{12}H_{16}N_3O$ $[M+H]^+$: m/z 218.1288, found: 218.1288.



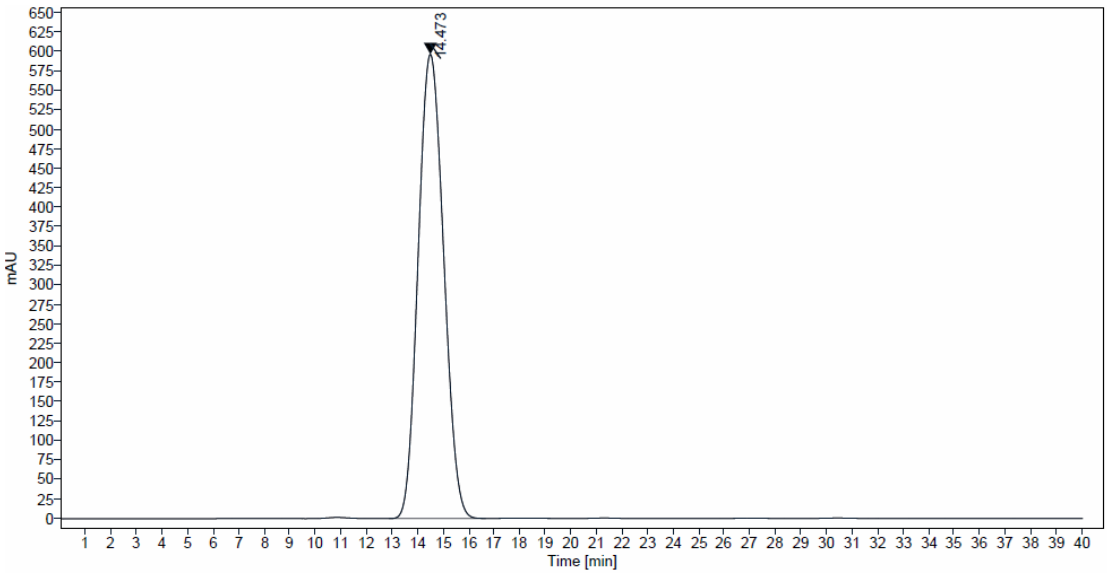


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.4 mL/min, λ = 280 nm

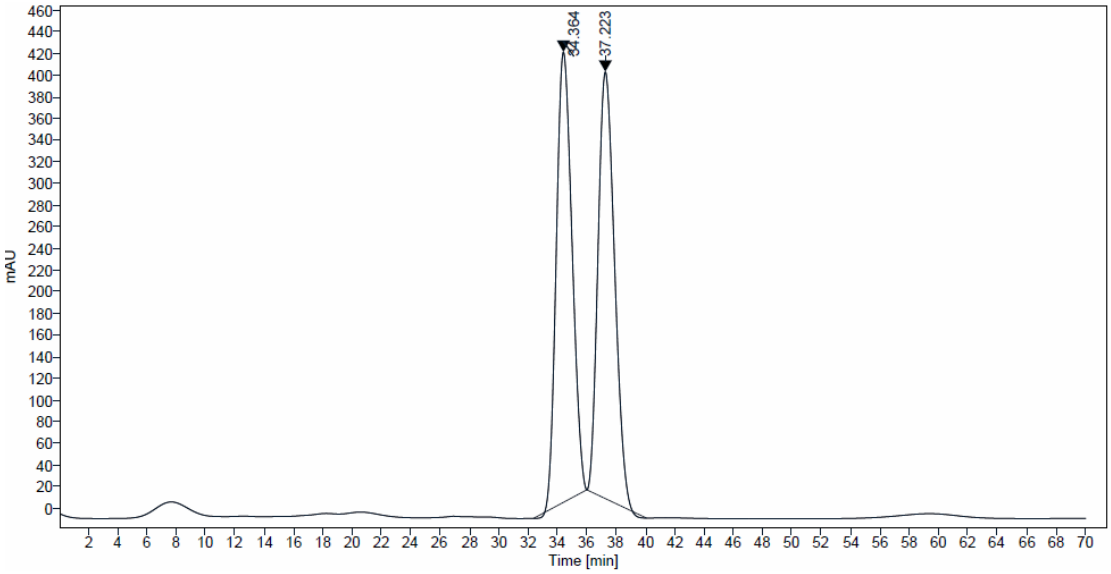
Starting Material (1a): Retention time = 27.582 min



Pyrrole: Retention time = 14.473 min

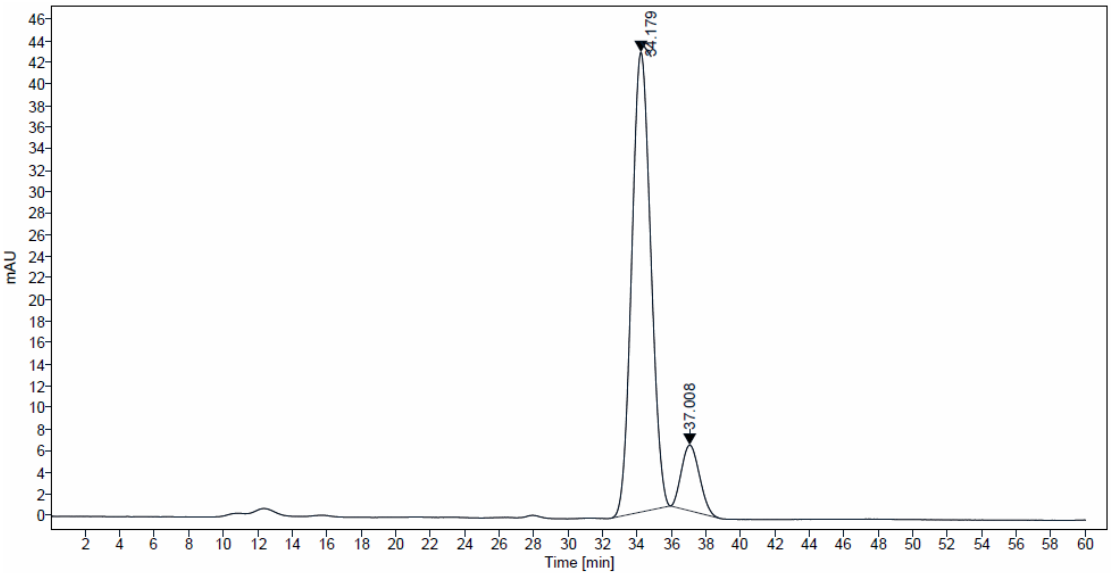


Racemic: Retention time: 34.364 min; 37.223 min

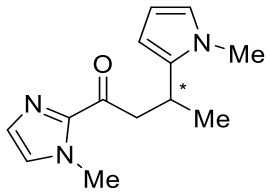


Peak	Retention time (min)	Rel. area (%)
1	34.364	50.1
2	37.223	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4b** < 1:99 and an enantiomeric excess of 75% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.4 mL/min, λ = 280 nm]. Retention time: 34.179 min; 37.008 min



Peak	Retention time (min)	Rel. area (%)
1	34.179	87.5
2	37.008	12.5



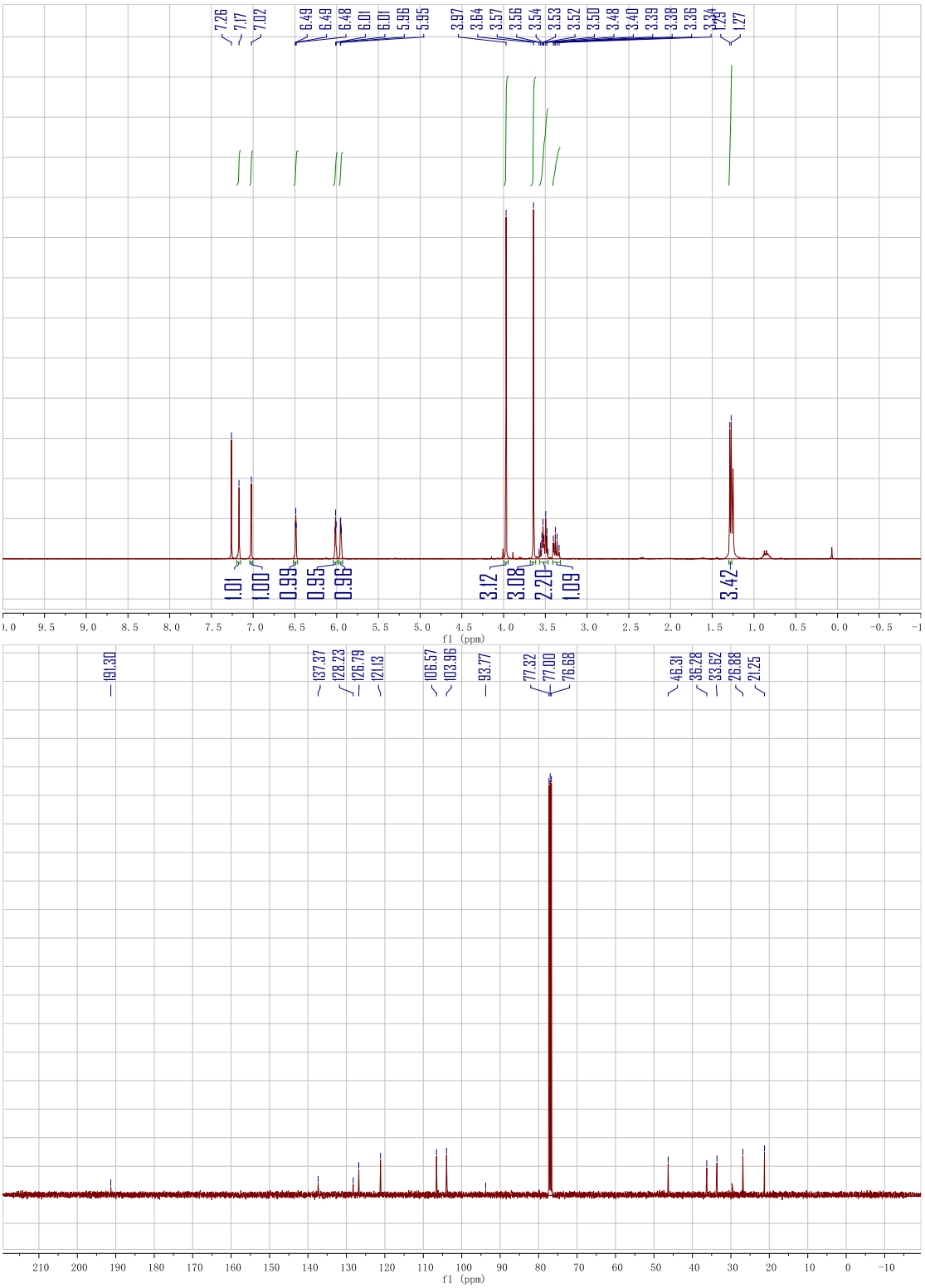
1-(1-methyl-1H-imidazol-2-yl)-3-(1-methyl-1H-pyrrol-2-yl)butan-1-one (4c).

The racemic product was synthesized as described using **1a** and 1-Me-Pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 7.02 (s, 1H), 6.52 – 6.47 (m, 1H), 6.01 (t, *J* = 3.1 Hz, 1H), 5.95 (dd, *J* = 3.5, 1.7 Hz, 1H), 3.97 (s, 3H), 3.64 (s, 3H), 3.57 – 3.47 (m, 2H), 3.41 – 3.32 (m, 1H), 1.28 (d, *J* = 6.7 Hz, 3H).

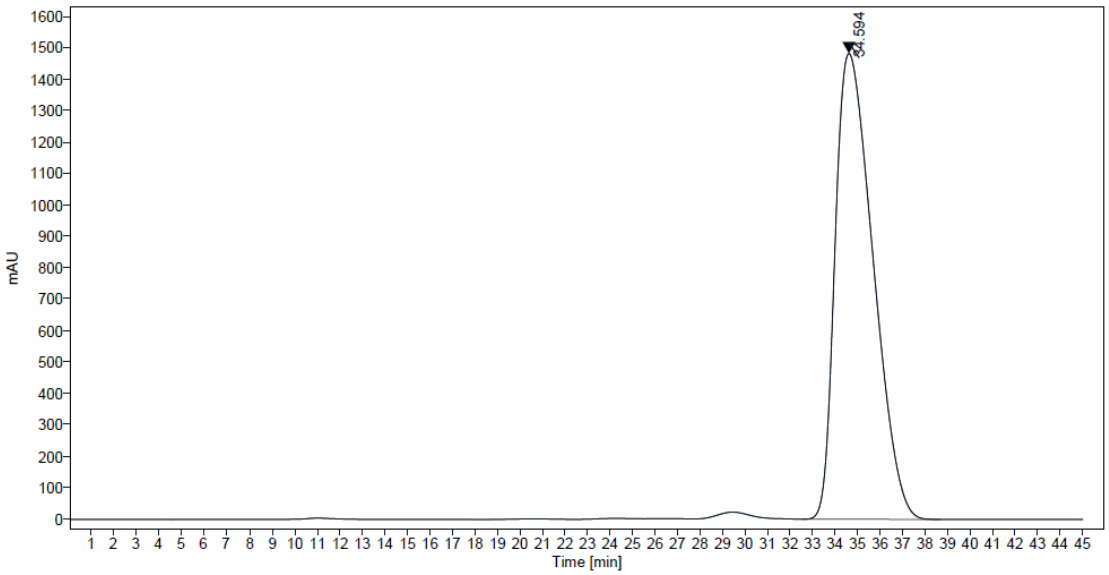
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.30 (s), 137.37 (s), 128.23 (s), 126.79 (s), 121.13 (s), 106.57 (s), 103.96 (s), 93.77 (s), 46.31 (s), 36.28 (s), 33.62 (s), 26.88 (s), 21.25 (s).

HRMS (ESI) calcd. for $C_{13}H_{18}N_3O$ $[M+H]^+$: m/z 232.1444, found: 232.1443.

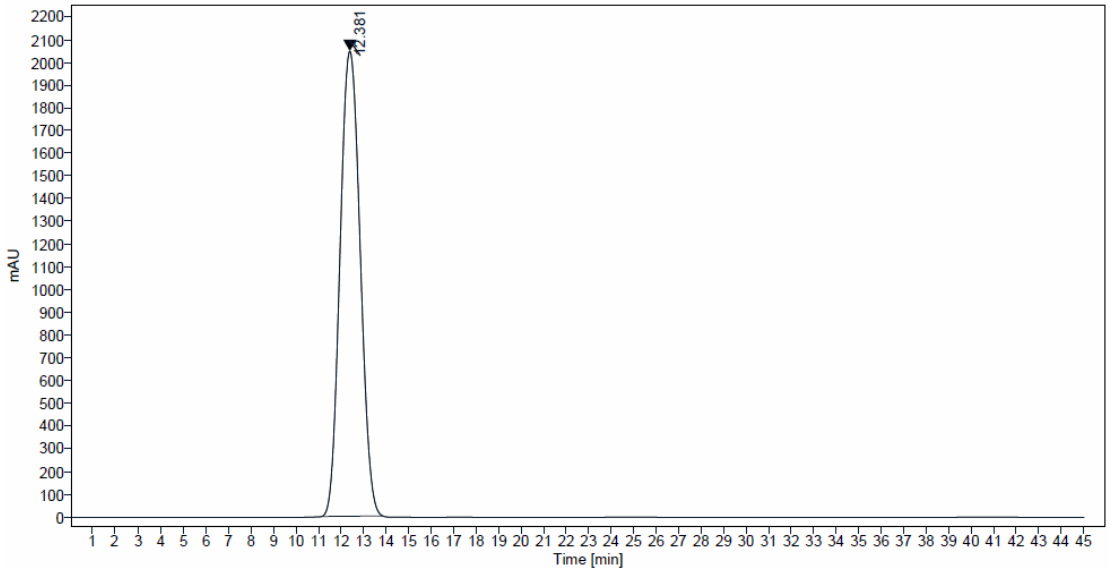


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm

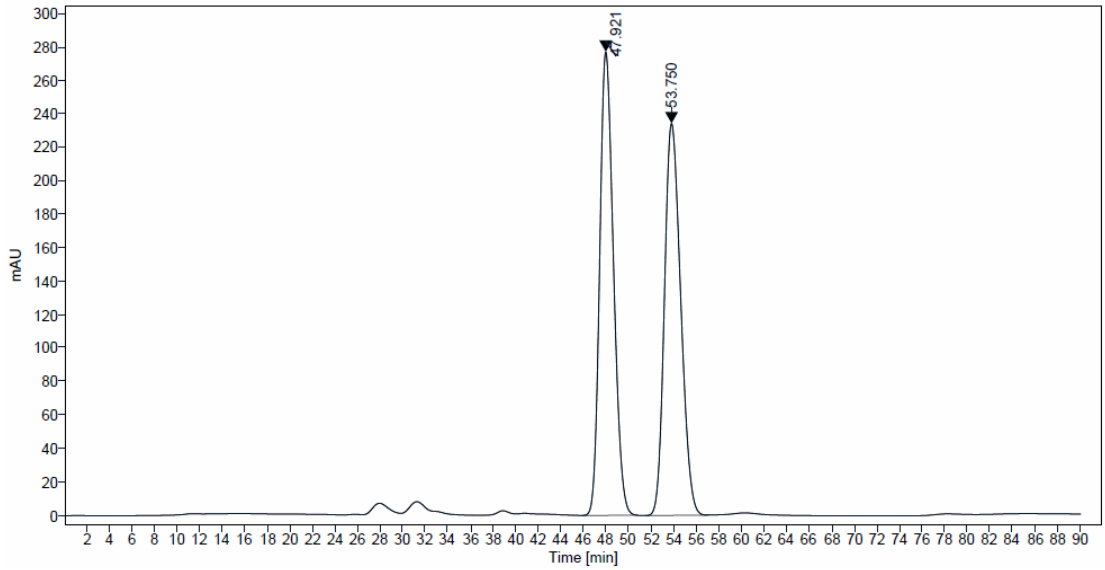
Starting Material (1a): Retention time = 34.594 min



1-Me-Pyrrole: Retention time = 12.381 min

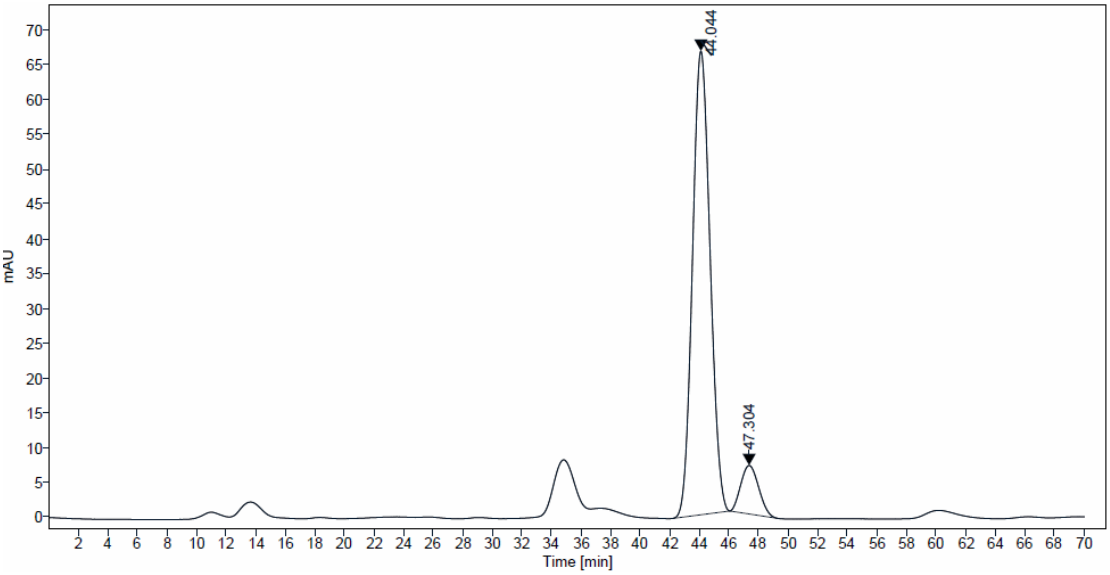


Racemic: Retention time: 47.921 min; 53.750 min

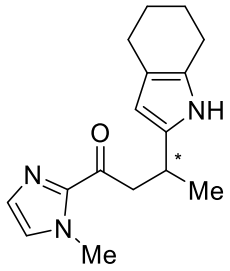


Peak	Retention time (min)	Rel. area (%)
1	47.921	50.3
2	53.750	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4c** as 10:90 and an enantiomeric excess of 82% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm]. Retention time: 44.044 min; 47.304 min



Peak	Retention time (min)	Rel. area (%)
1	44.044	91.0
2	47.304	9.0



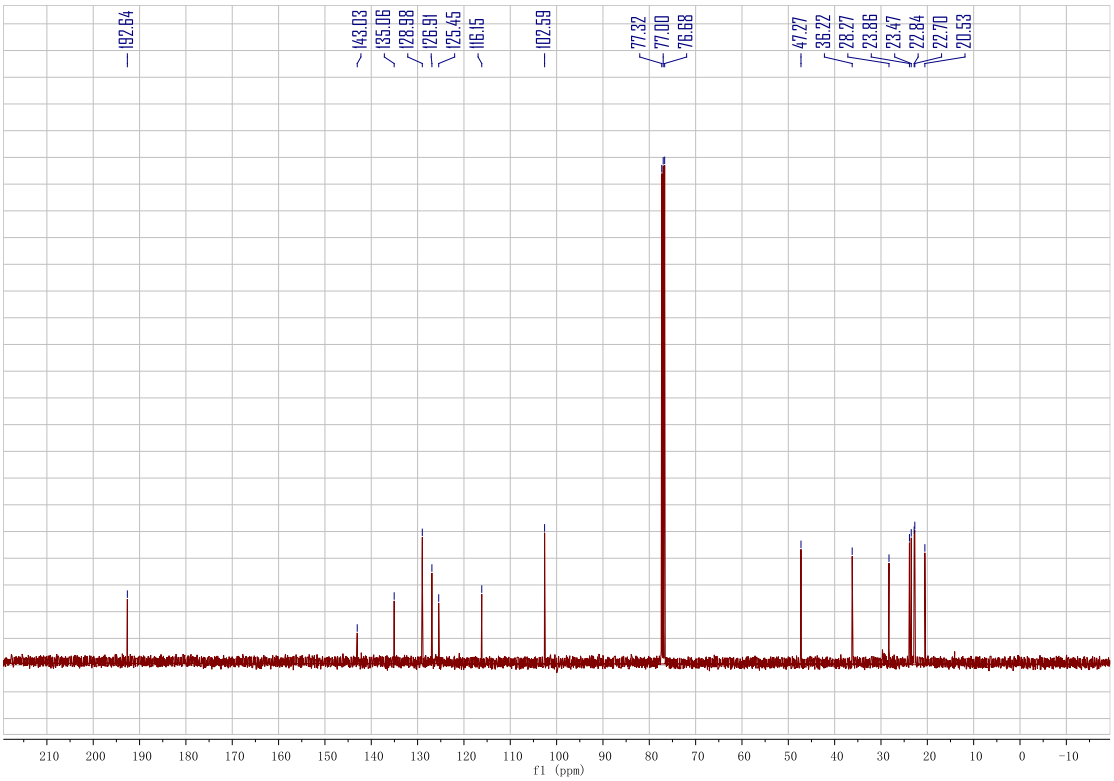
1-(1-methyl-1H-imidazol-2-yl)-3-(4,5,6,7-tetrahydro-1H-indol-2-yl)butan-1-one (4d).

The racemic product was synthesized as described using **1a** and Tetrahydro Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.15 (d, *J* = 0.7 Hz, 1H), 7.04 (s, 1H), 5.71 (d, *J* = 2.5 Hz, 1H), 4.02 (s, 3H), 3.52 (dd, *J* = 16.3, 7.6 Hz, 1H), 3.49 – 3.42 (m, 1H), 3.31 (dd, *J* = 16.3, 5.3 Hz, 1H), 2.55 (t, *J* = 5.9 Hz, 2H), 2.48 (t, *J* = 5.8 Hz, 2H), 1.83 – 1.78 (m, 2H), 1.77 – 1.71 (m, 2H), 1.37 (d, *J* = 6.9 Hz, 3H).

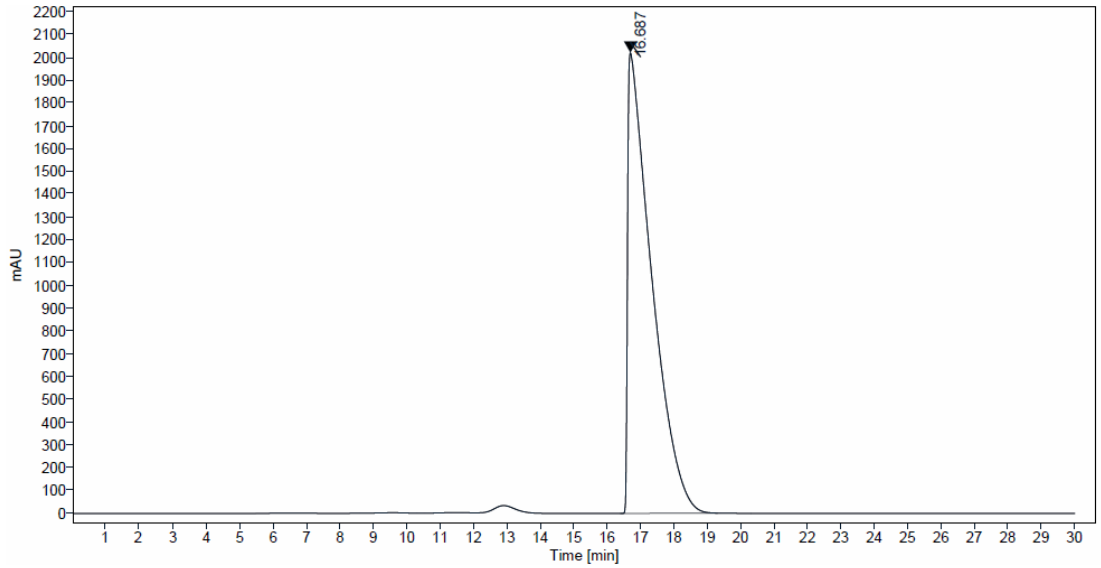
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.64 (s), 143.03 (s), 135.06 (s), 128.98 (s), 126.91 (s), 125.45 (s), 116.15 (s), 102.59 (s), 47.27 (s), 36.22 (s), 28.27 (s), 23.86 (s), 23.47 (s), 22.84 (s), 22.70 (s), 20.53 (s).

HRMS (ESI) calcd. for $C_{16}H_{20}N_3O$ $[M+H]^+$: m/z 270.1601, found: 270.1599.

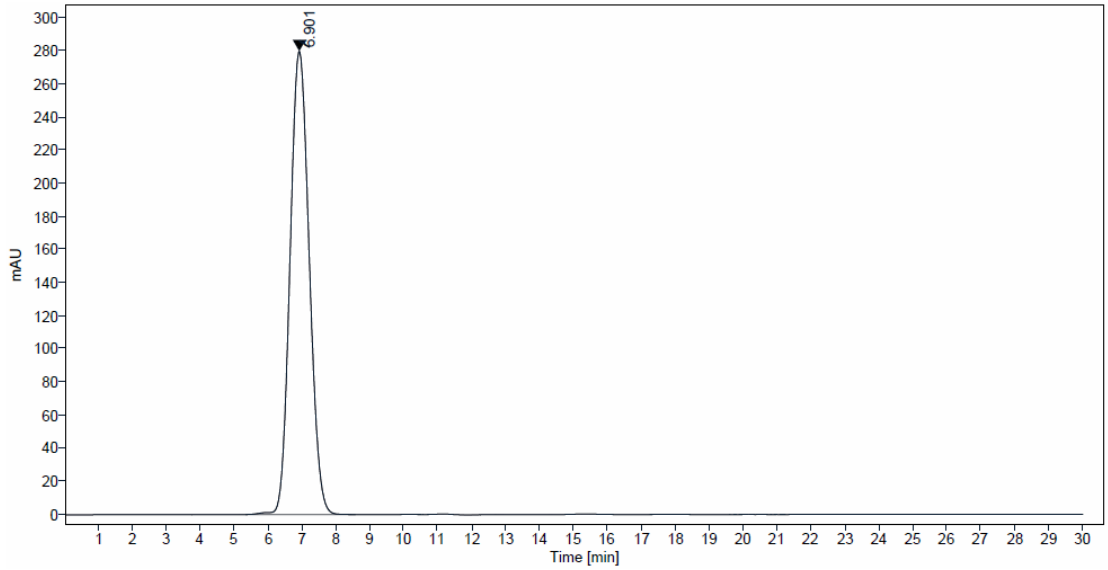


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm

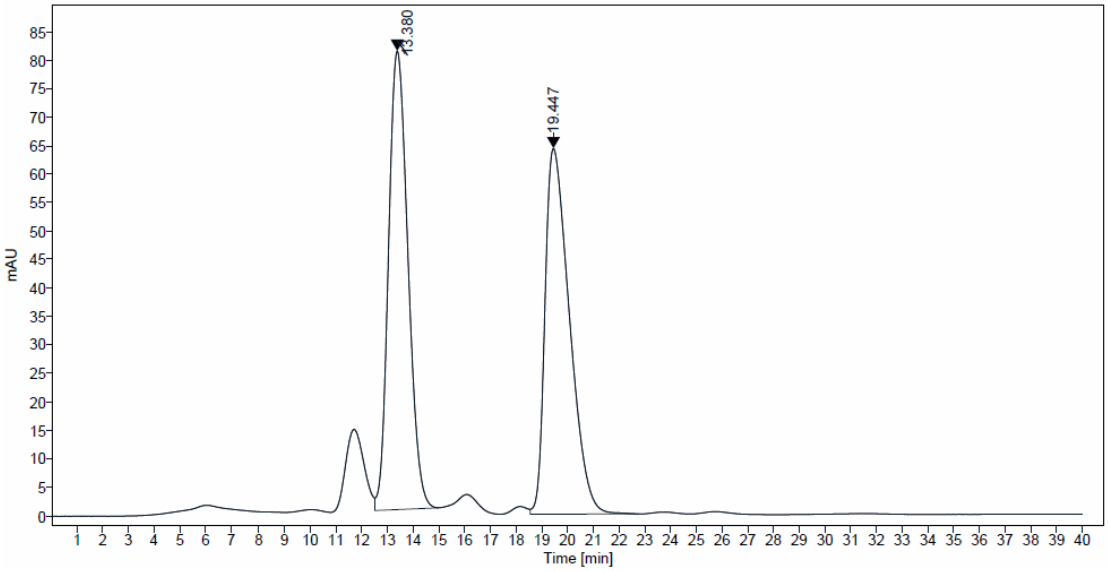
Starting Material (1a): Retention time = 16.687 min



Tetrahydro Indole: Retention time = 6.901 min

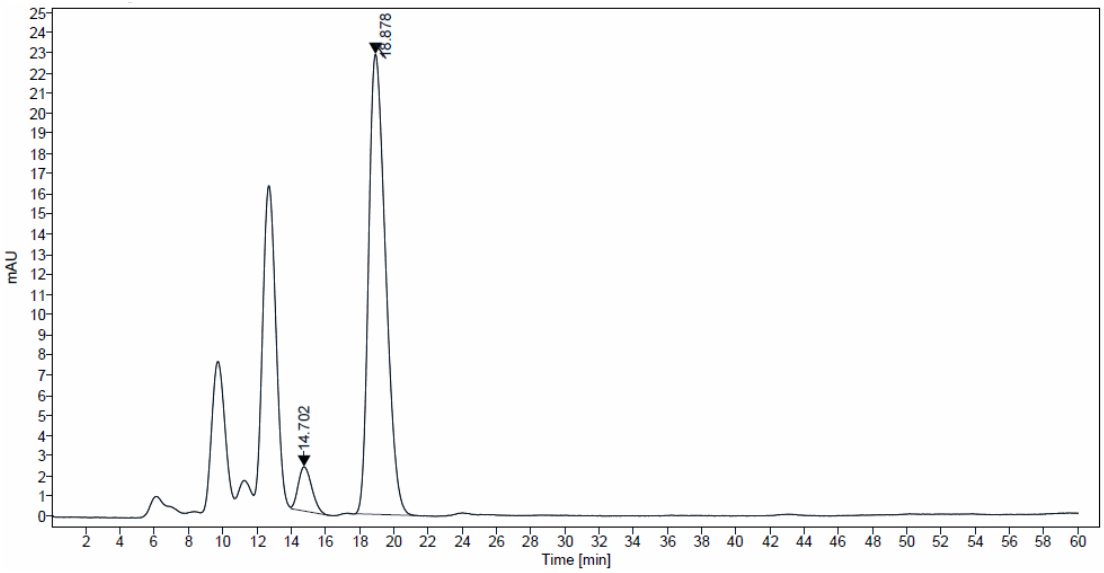


Racemic: Retention time: 13.380 min; 19.447 min

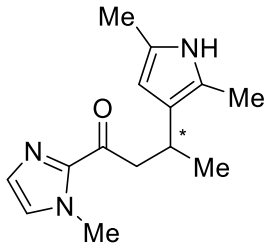


Peak	Retention time (min)	Rel. area (%)
1	13.380	51.0
2	19.447	49.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4d** as 33:67 and an enantiomeric excess of 86% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm]. Retention time: 14.702 min; 18.878 min



Peak	Retention time (min)	Rel. area (%)
1	14.702	7.1
2	18.878	92.9



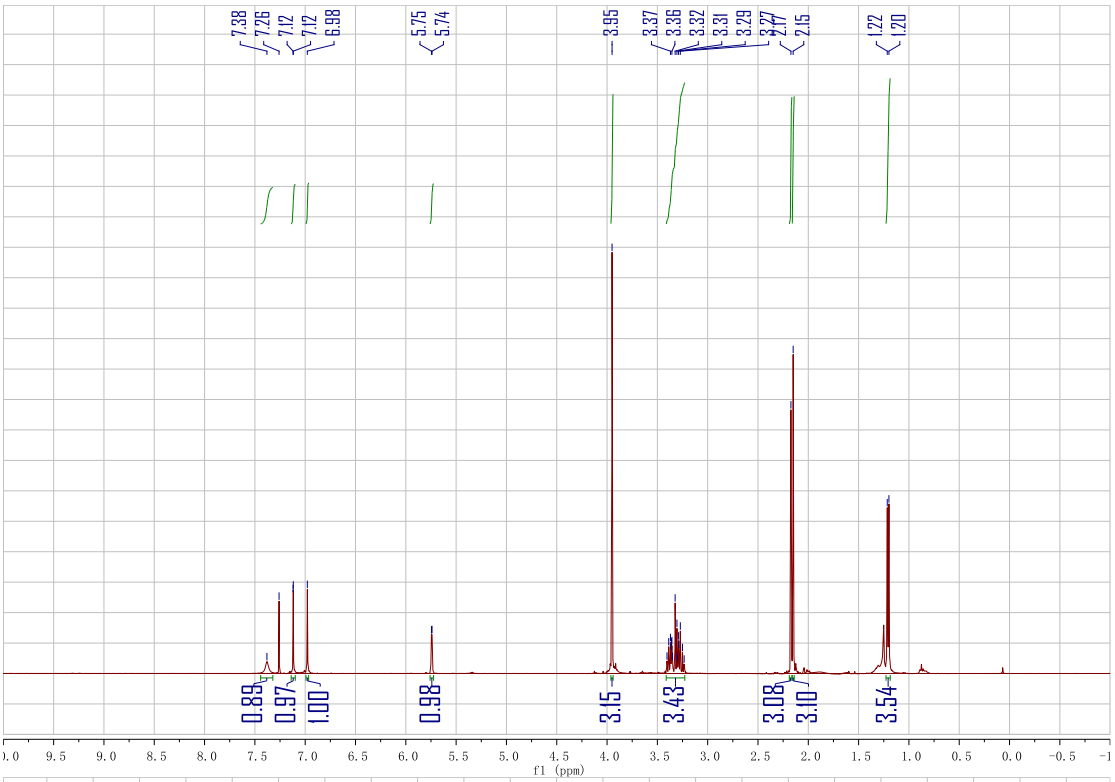
3-(2,5-dimethyl-1H-pyrrol-3-yl)-1-(1-methyl-1H-imidazol-2-yl)butan-1-one (4e).

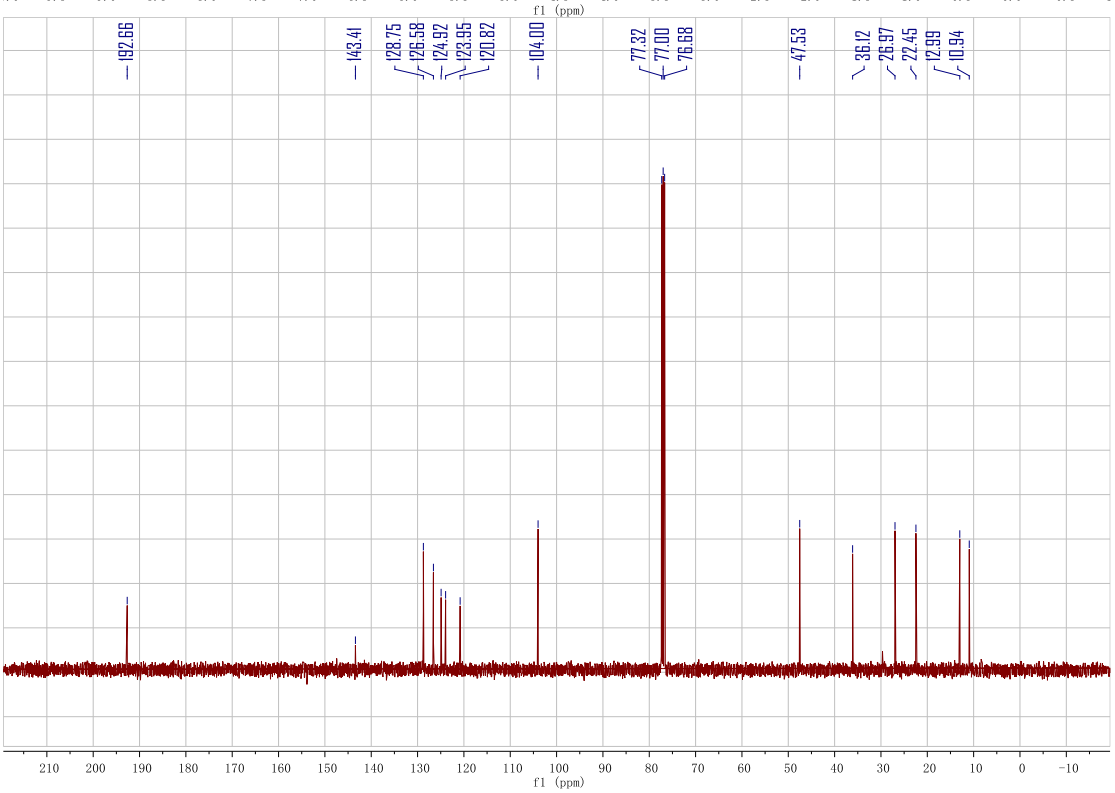
The racemic product was synthesized as described using **1a** and 2,5-Di-Me-Pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.12 (d, *J* = 0.7 Hz, 1H), 6.98 (s, 1H), 5.74 (d, *J* = 2.3 Hz, 1H), 3.95 (s, 3H), 3.41 – 3.23 (m, 3H), 2.17 (s, 3H), 2.15 (s, 3H), 1.21 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.66 (s), 143.41 (s), 128.75 (s), 126.58 (s), 124.92 (s), 123.95 (s), 120.82 (s), 104.00 (s), 47.53 (s), 36.12 (s), 26.97 (s), 22.45 (s), 12.99 (s), 10.94 (s).

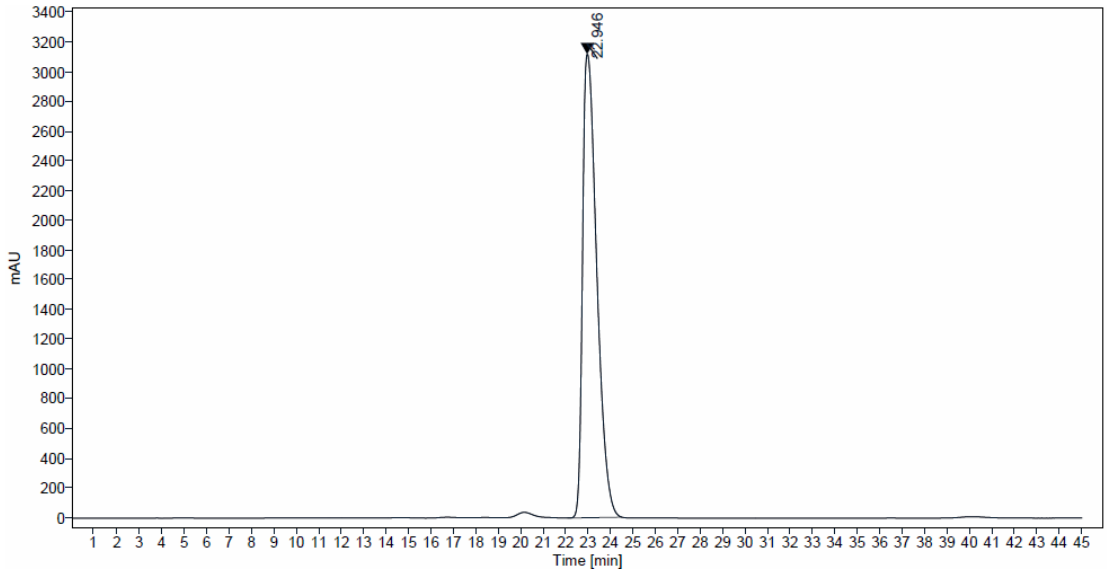
HRMS (ESI) calcd. for $C_{14}H_{20}N_3O$ $[M+H]^+$: m/z 246.1606, found: 246.1602.



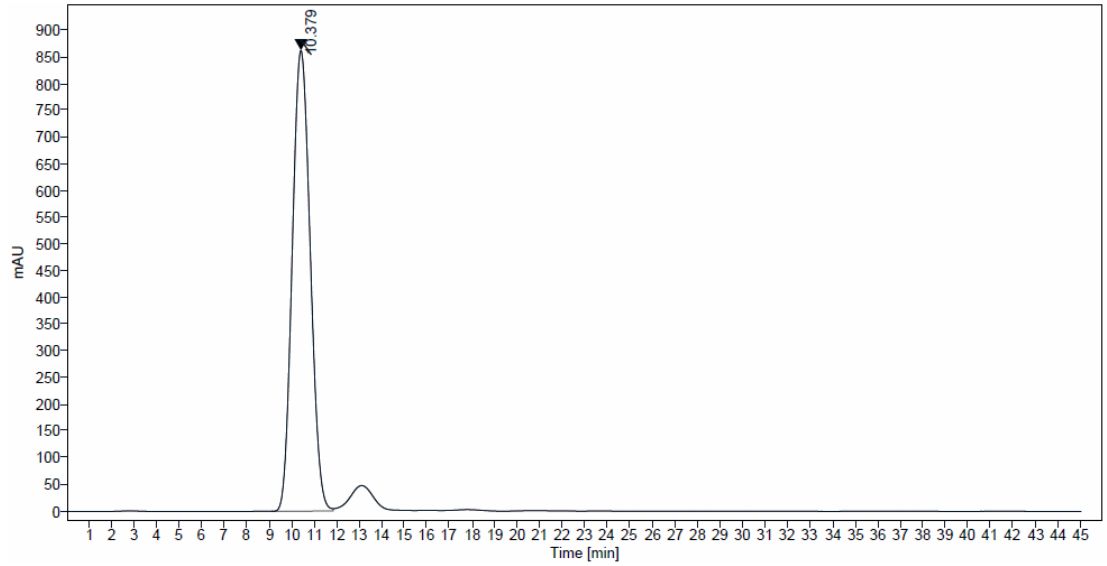


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

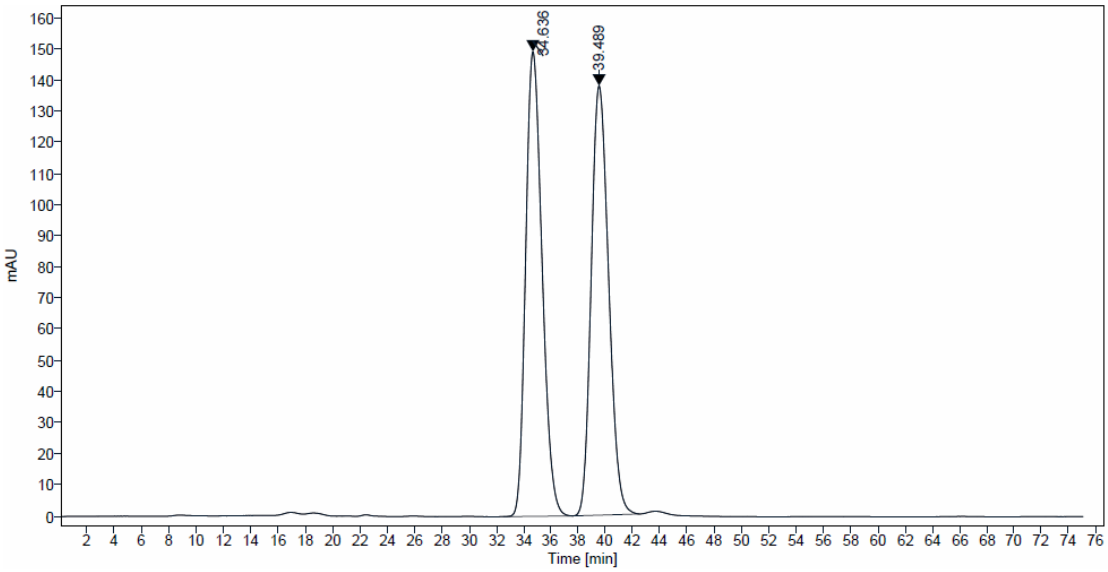
Starting Material (1a): Retention time = 22.946 min



2,5-Di-Me-Pyrrole: Retention time = 10.379 min

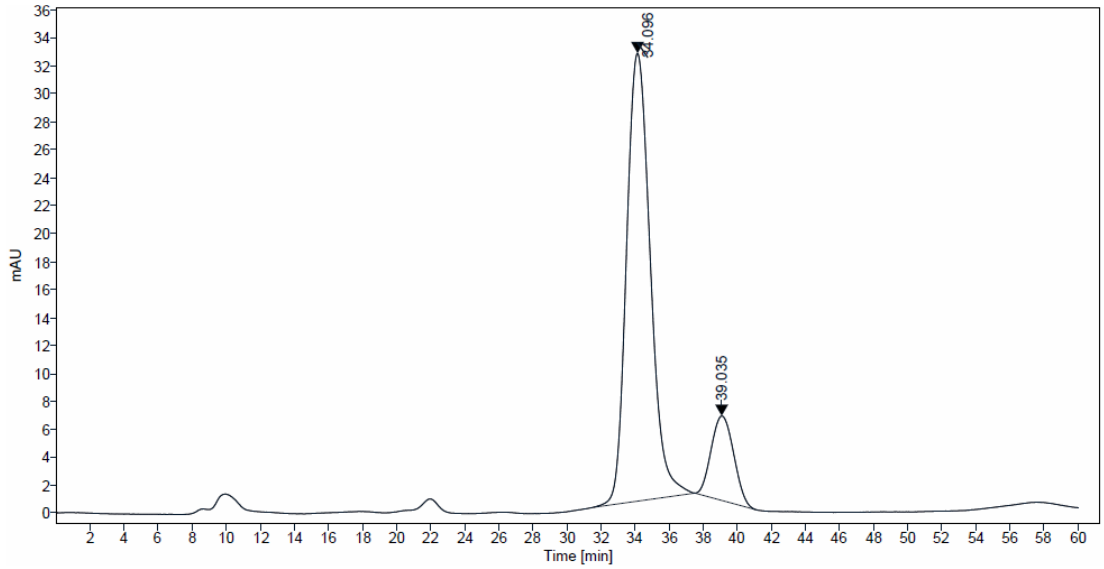


Racemic: Retention time: 34.636 min; 39.489min

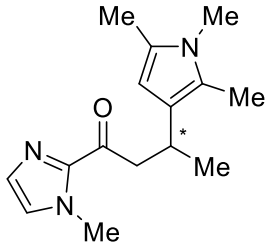


Peak	Retention time (min)	Rel. area (%)
1	34.636	50.0
2	39.489	50.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4e** as 3:97 and an enantiomeric excess of 70% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 34.096 min; 39.035 min



Peak	Retention time (min)	Rel. area (%)
1	34.096	85.0
2	39.035	15.0



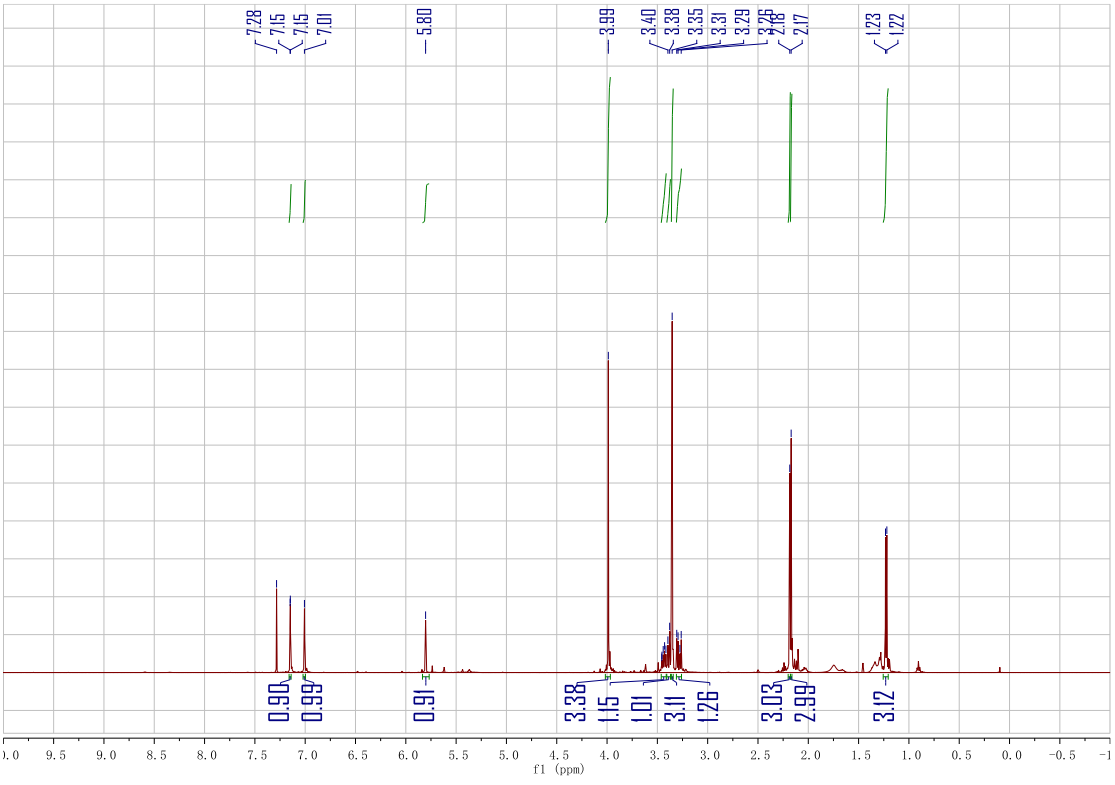
1-(1-methyl-1H-imidazol-2-yl)-3-(1,2,5-trimethyl-1H-pyrrol-3-yl)butan-1-one (4f).

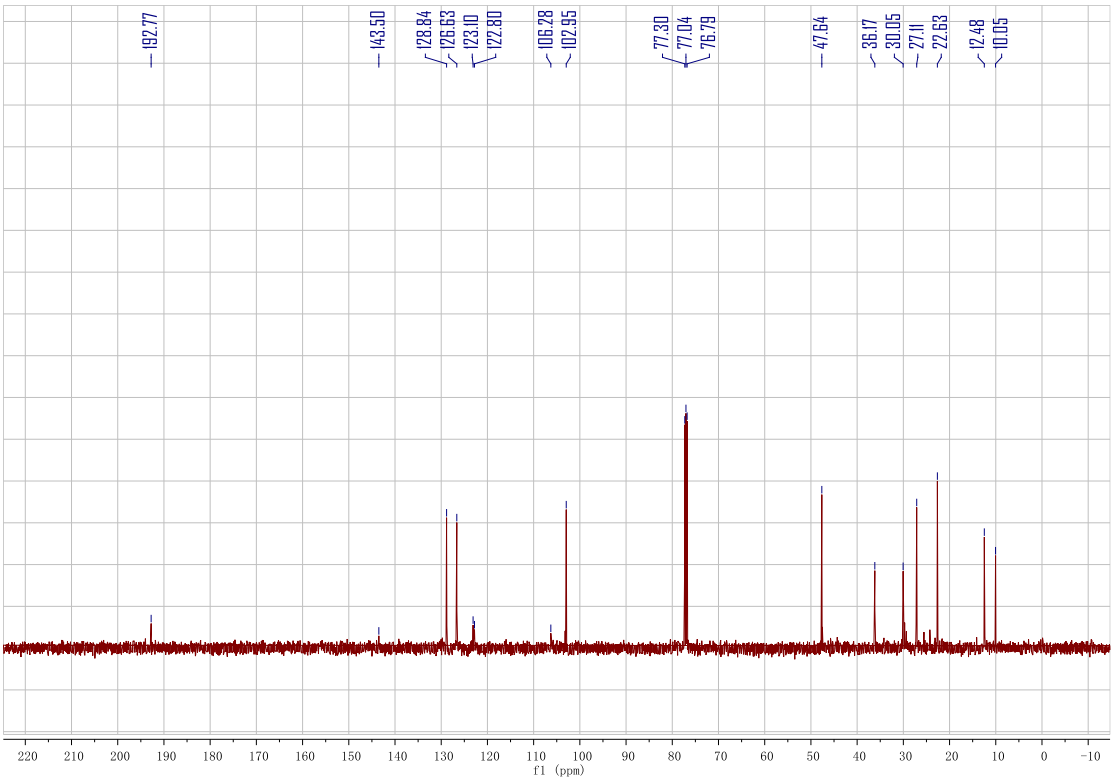
The racemic product was synthesized as described using **1a** and 1,2,5-Tri-Me-Pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 0.8 Hz, 1H), 7.01 (s, 1H), 5.80 (s, 1H), 3.99 (s, 3H), 3.46 – 3.41 (m, 1H), 3.39 (d, *J* = 8.8 Hz, 1H), 3.35 (s, 3H), 3.29 (dd, *J* = 15.7, 6.4 Hz, 1H), 2.18 (s, 3H), 2.17 (s, 3H), 1.23 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.77 (s), 143.50 (s), 128.84 (s), 126.63 (s), 123.10 (s), 122.80 (s), 106.28 (s), 102.95 (s), 47.64 (s), 36.17 (s), 30.05 (s), 27.11 (s), 22.63 (s), 12.48 (s), 10.05 (s).

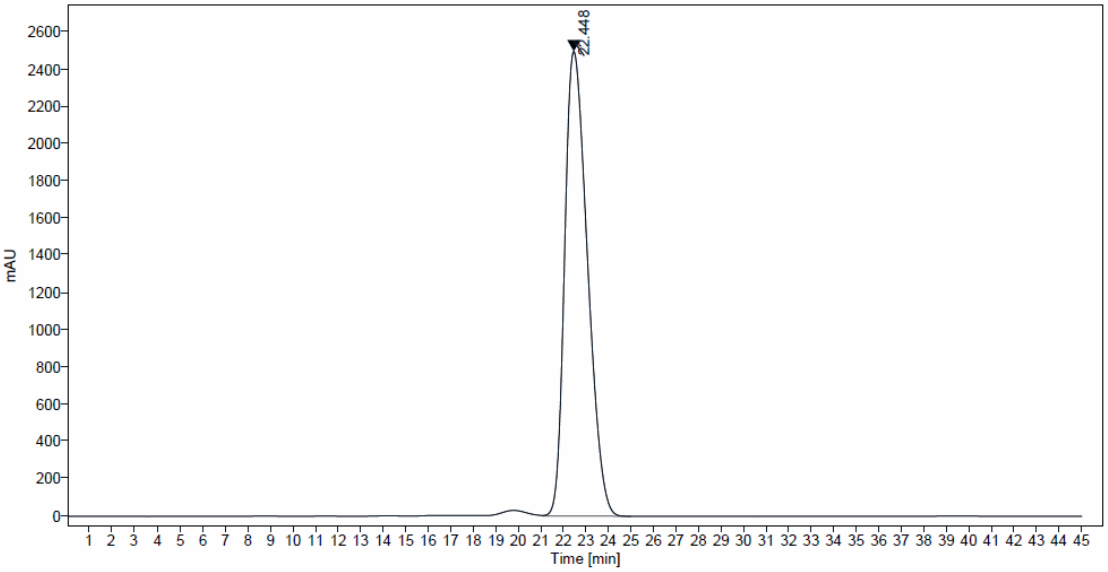
HRMS (ESI) calcd. for $C_{15}H_{22}N_3O$ $[M+H]^+$: m/z 260.1763, found: 260.1760.



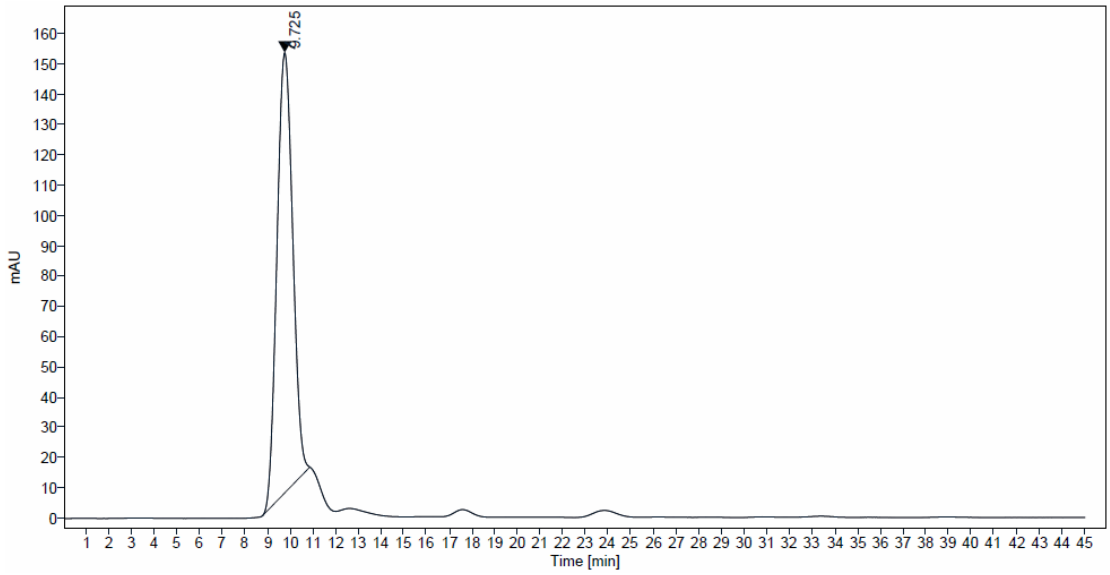


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

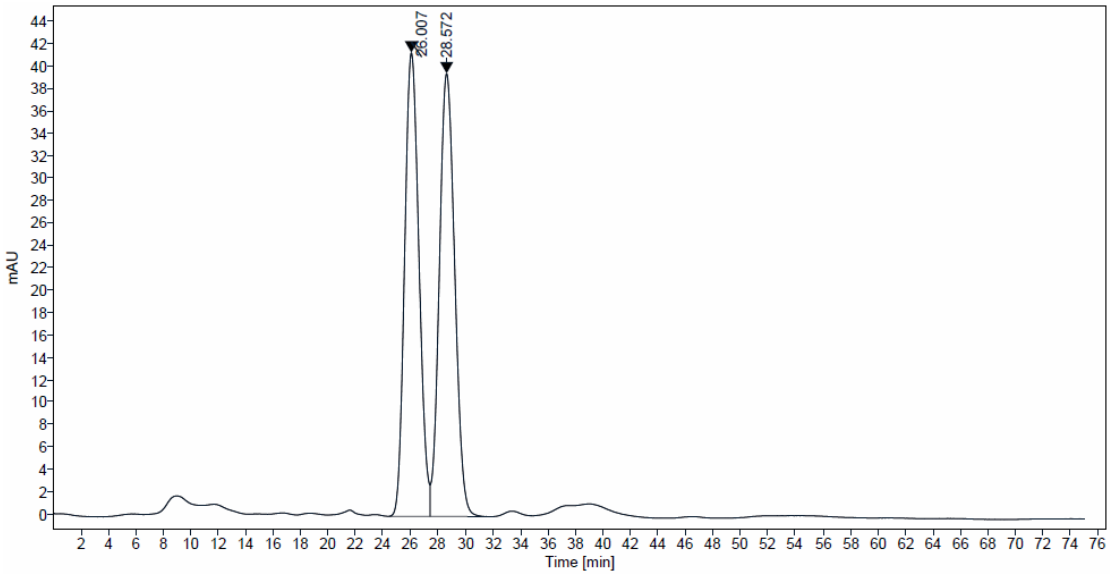
Starting Material (1a): Retention time = 22.448 min



1,2,5-Tri-Me-Pyrrole: Retention time = 9.725 min

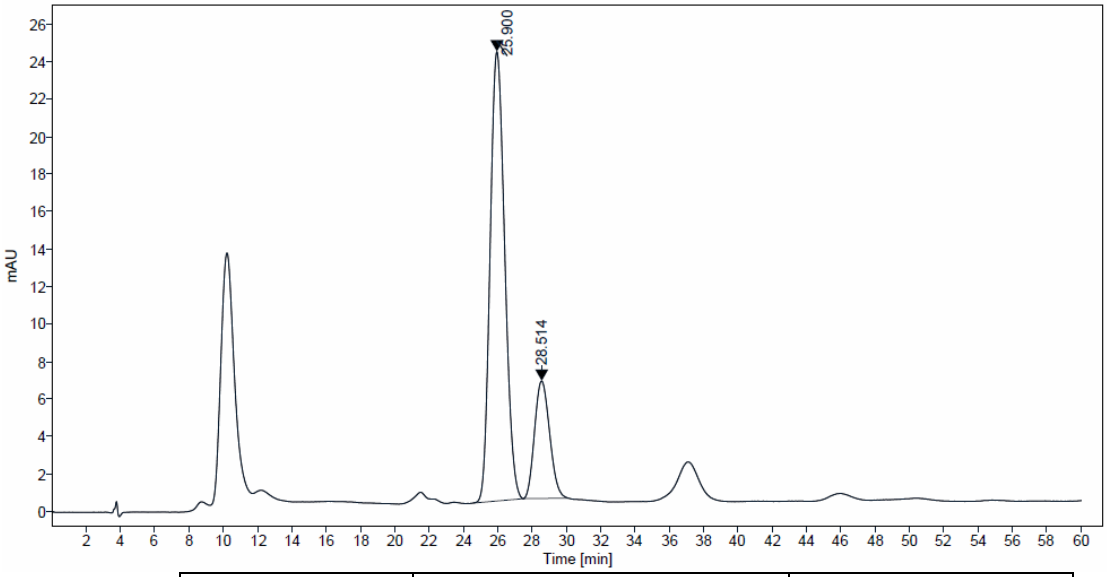


Racemic: Retention time: 26.007 min; 28.572 min

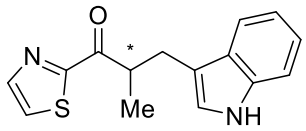


Peak	Retention time (min)	Rel. area (%)
1	26.007	50.3
2	28.572	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**4f** as 2:98 and an enantiomeric excess of 61% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 25.900 min; 28.514 min



Peak	Retention time (min)	Rel. area (%)
1	25.900	80.5
2	28.514	19.5



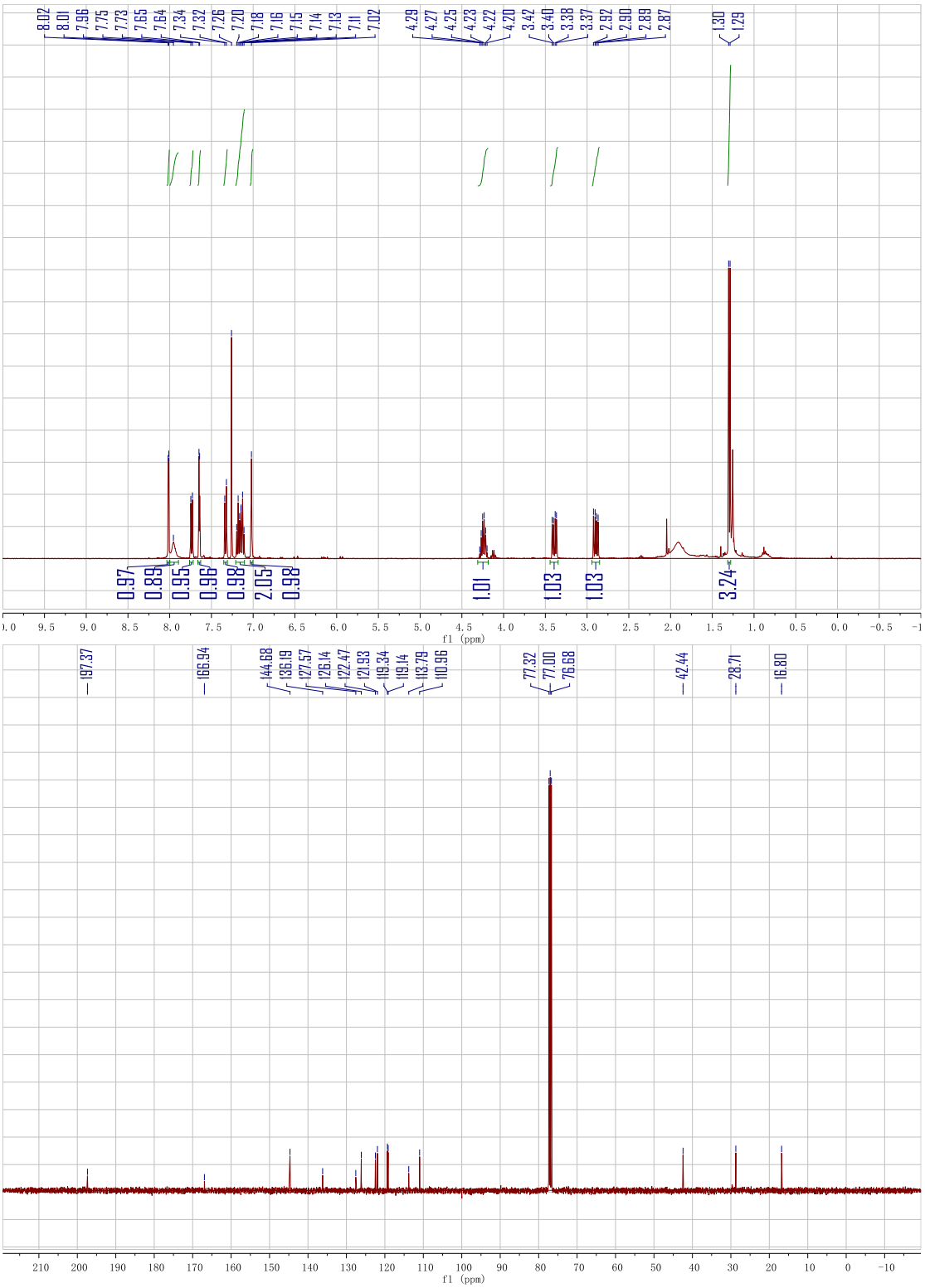
3-(1H-indol-3-yl)-2-methyl-1-(thiazol-2-yl)propan-1-one (6a).

The racemic product was synthesized as described using **5** and Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 3.0 Hz, 1H), 7.96 (s, 1H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 3.0 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.21 – 7.10 (m, 2H), 7.02 (s, 1H), 4.31 – 4.18 (m, 1H), 3.39 (dd, *J* = 14.4, 6.3 Hz, 1H), 2.90 (dd, *J* = 14.4, 7.9 Hz, 1H), 1.30 (d, *J* = 6.9 Hz, 3H).

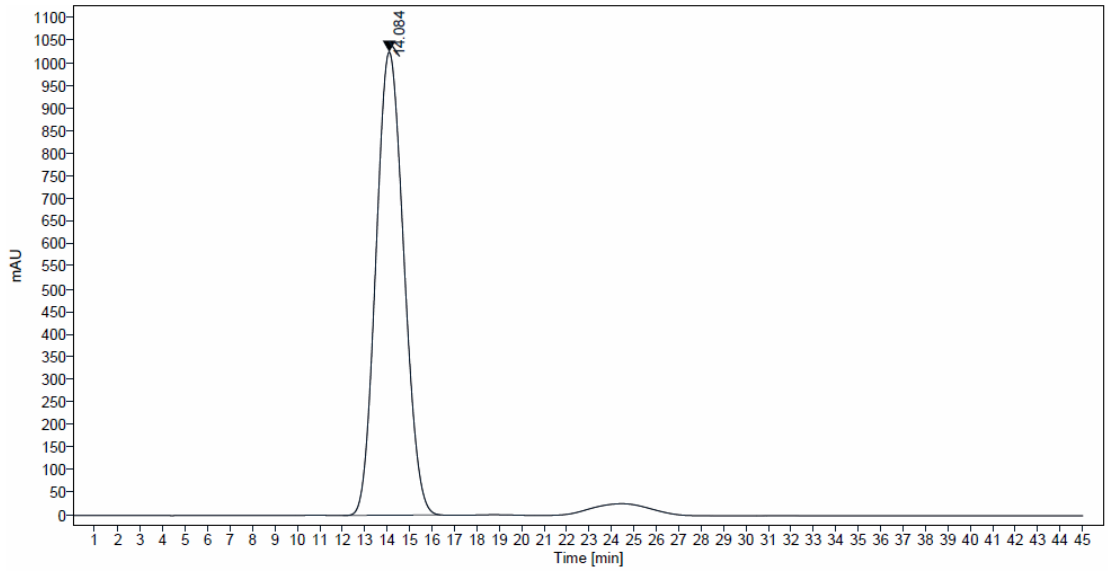
^{13}C NMR (101 MHz, $CDCl_3$) δ 197.37 (s), 166.94 (s), 144.68 (s), 136.19 (s), 127.57 (s), 126.14 (s), 122.47 (s), 121.93 (s), 119.34 (s), 119.14 (s), 113.79 (s), 110.96 (s), 42.44 (s), 28.71 (s), 16.80 (s).

HRMS (ESI) calcd. for $C_{15}H_{14}N_2NaOS$ $[M+Na]^+$: m/z 293.0719, found: 293.0717.

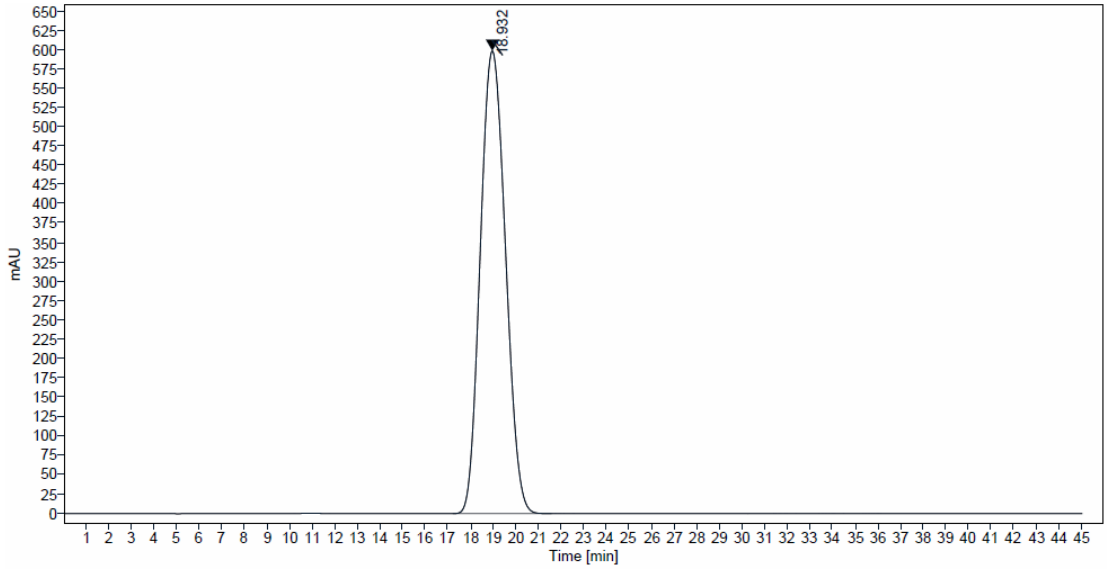


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm

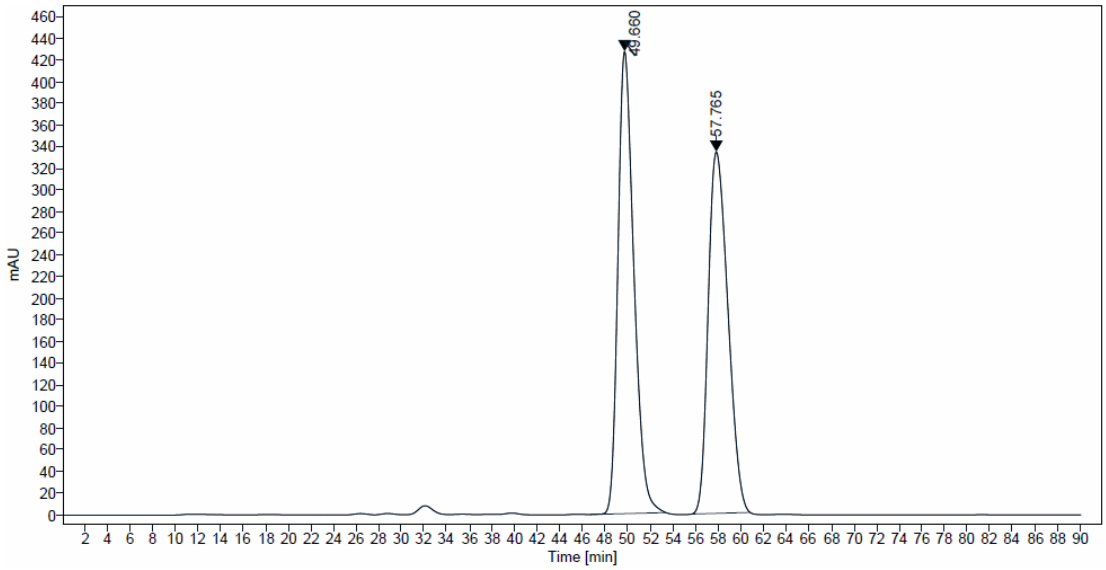
Starting Material (5): Retention time = 14.084 min



Indole: Retention time = 18.932 min

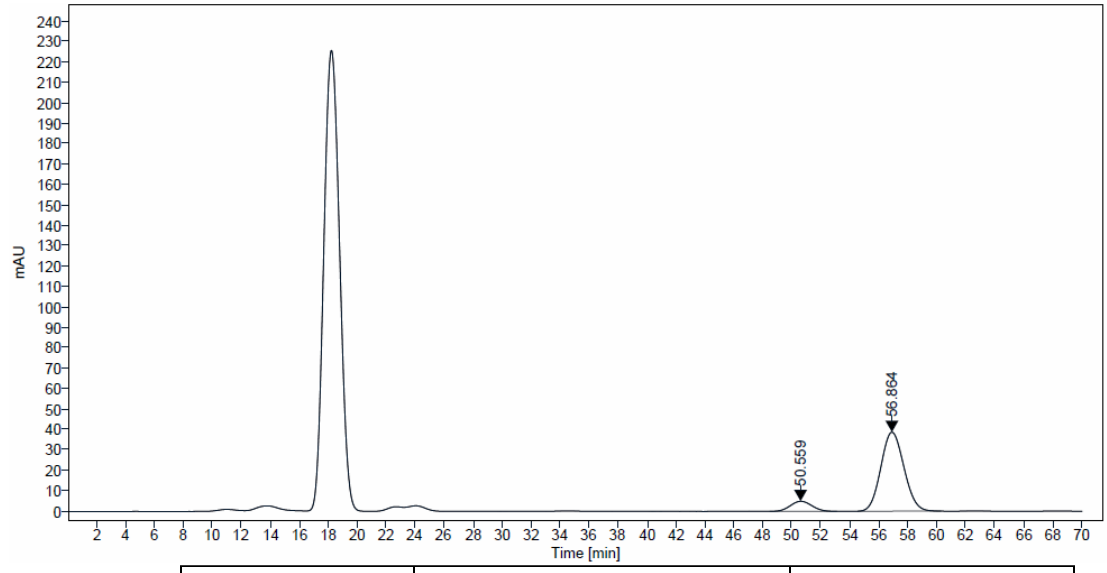


Racemic: Retention time: 49.660 min; 57.765 min

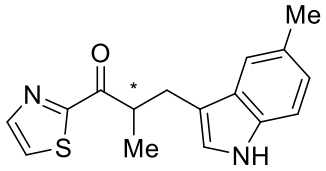


Peak	Retention time (min)	Rel. area (%)
1	49.660	51.0
2	57.765	49.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6a** < 1:99 and an enantiomeric excess of 80% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm]. Retention time: 50.559 min; 56.864 min



Peak	Retention time (min)	Rel. area (%)
1	50.559	10.0
2	56.864	90.0



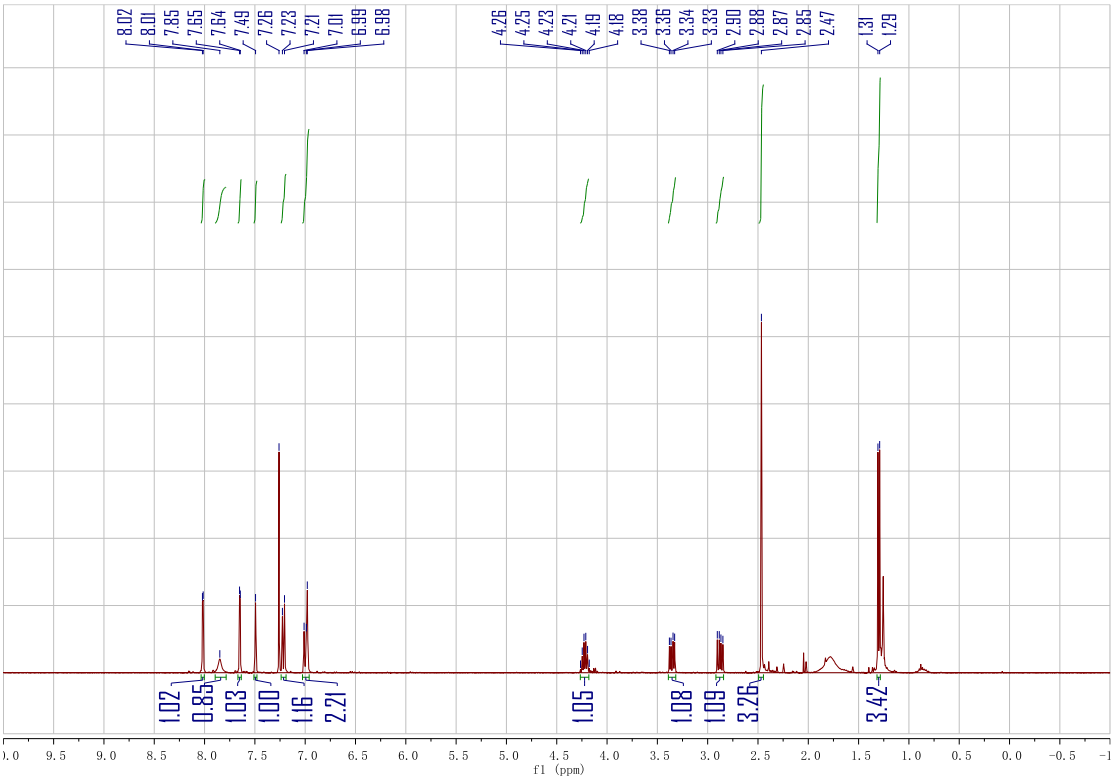
2-methyl-3-(5-methyl-1H-indol-3-yl)-1-(thiazol-2-yl)propan-1-one (6b).

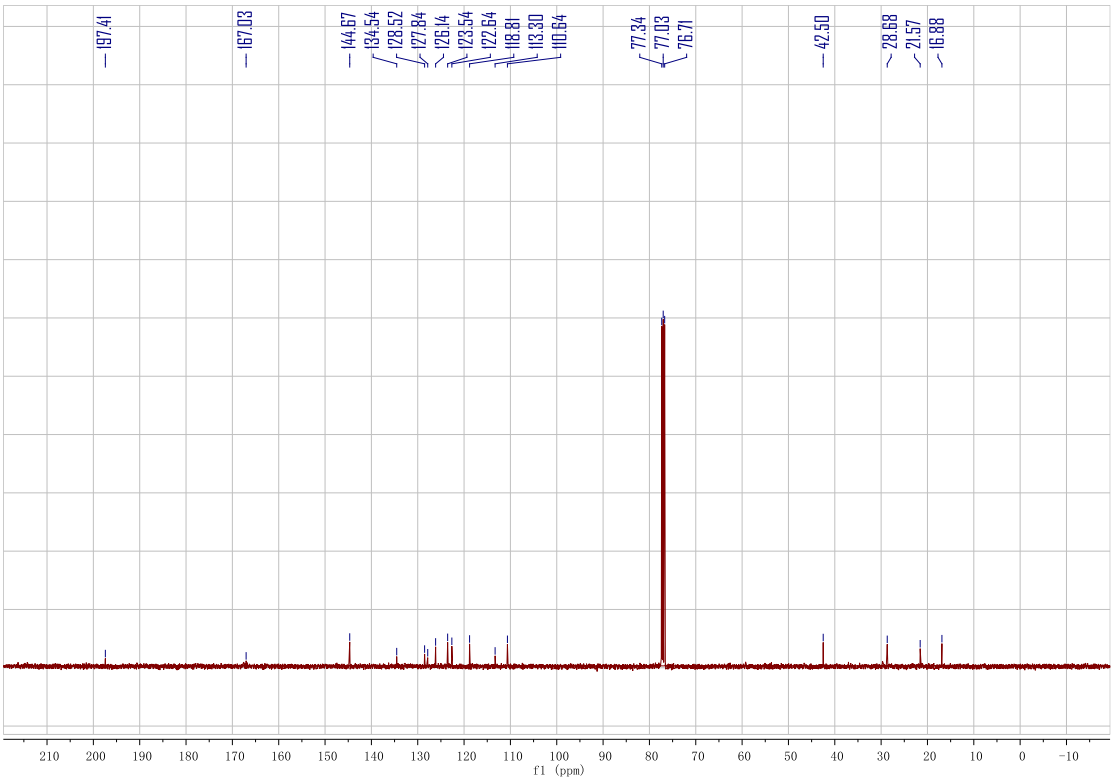
The racemic product was synthesized as described using **5** and 5-Me-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 3.0 Hz, 1H), 7.85 (s, 1H), 7.65 (d, *J* = 3.0 Hz, 1H), 7.49 (s, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.03 – 6.96 (m, 2H), 4.23 (dt, *J* = 14.2, 6.9 Hz, 1H), 3.35 (dd, *J* = 14.4, 6.4 Hz, 1H), 2.88 (dd, *J* = 14.4, 7.8 Hz, 1H), 2.47 (s, 3H), 1.30 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.41 (s), 167.03 (s), 144.67 (s), 134.54 (s), 128.52 (s), 127.84 (s), 126.14 (s), 123.54 (s), 122.64 (s), 118.81 (s), 113.30 (s), 110.64 (s), 42.50 (s), 28.68 (s), 21.57 (s), 16.88 (s).

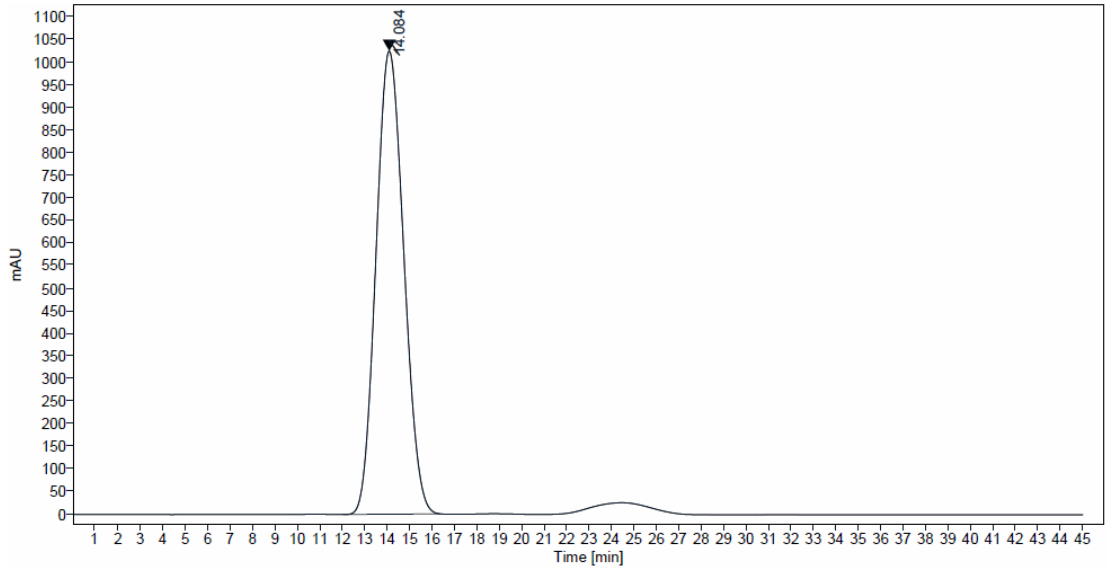
HRMS (ESI) calcd. for $C_{16}H_{16}N_2NaOS$ $[M+Na]^+$: m/z 307.0876, found: 307.0872.



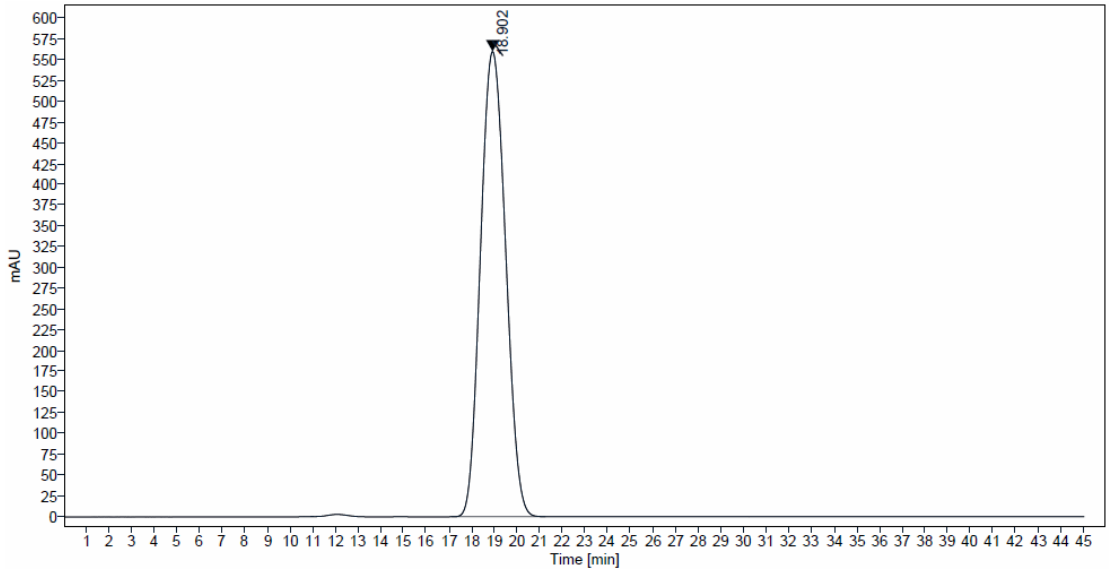


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm

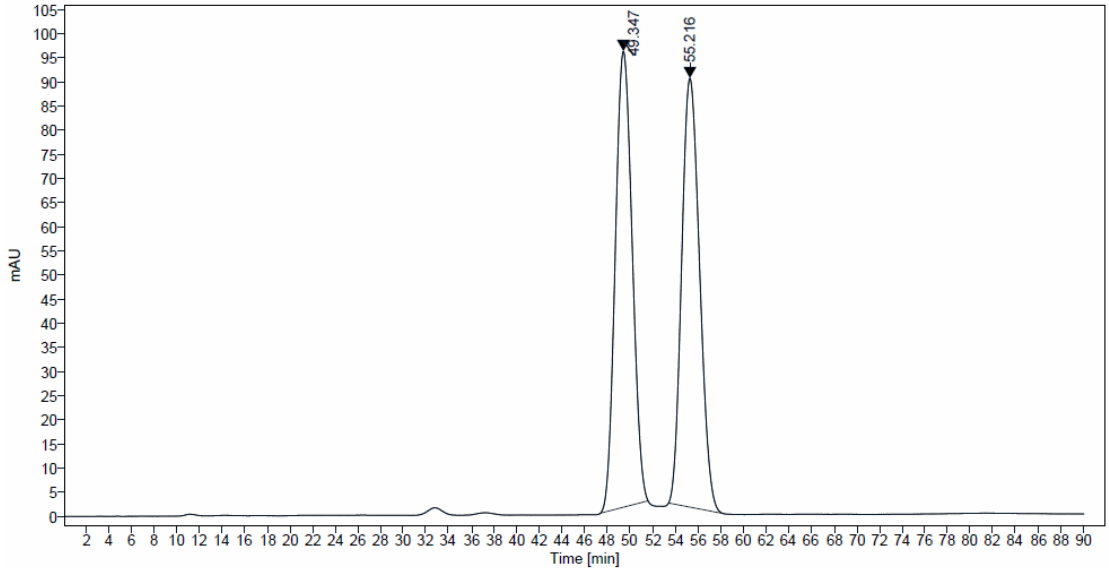
Starting Material (5): Retention time = 14.084 min



5-Me-Indole: Retention time = 18.902 min

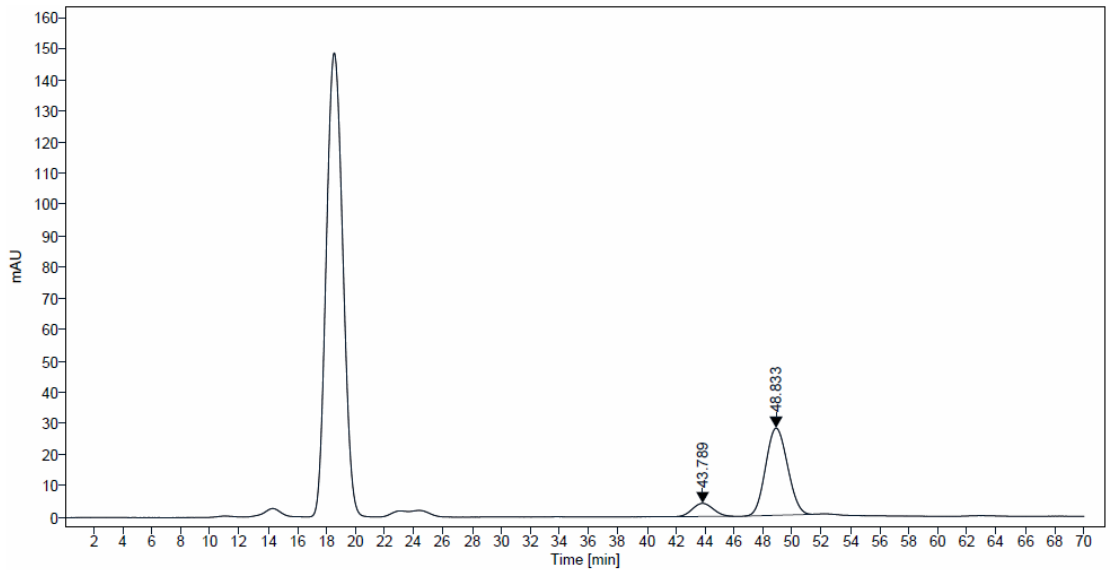


Racemic: Retention time: 49.347 min; 55.216 min

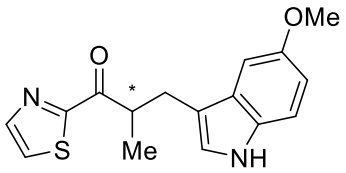


Peak	Retention time (min)	Rel. area (%)
1	49.347	50.0
2	55.216	50.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6b** < 1:99 and an enantiomeric excess of 75% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.4 mL/min, λ = 280 nm]. Retention time: 43.789 min; 48.833 min



Peak	Retention time (min)	Rel. area (%)
1	43.789	12.5
2	48.833	87.5



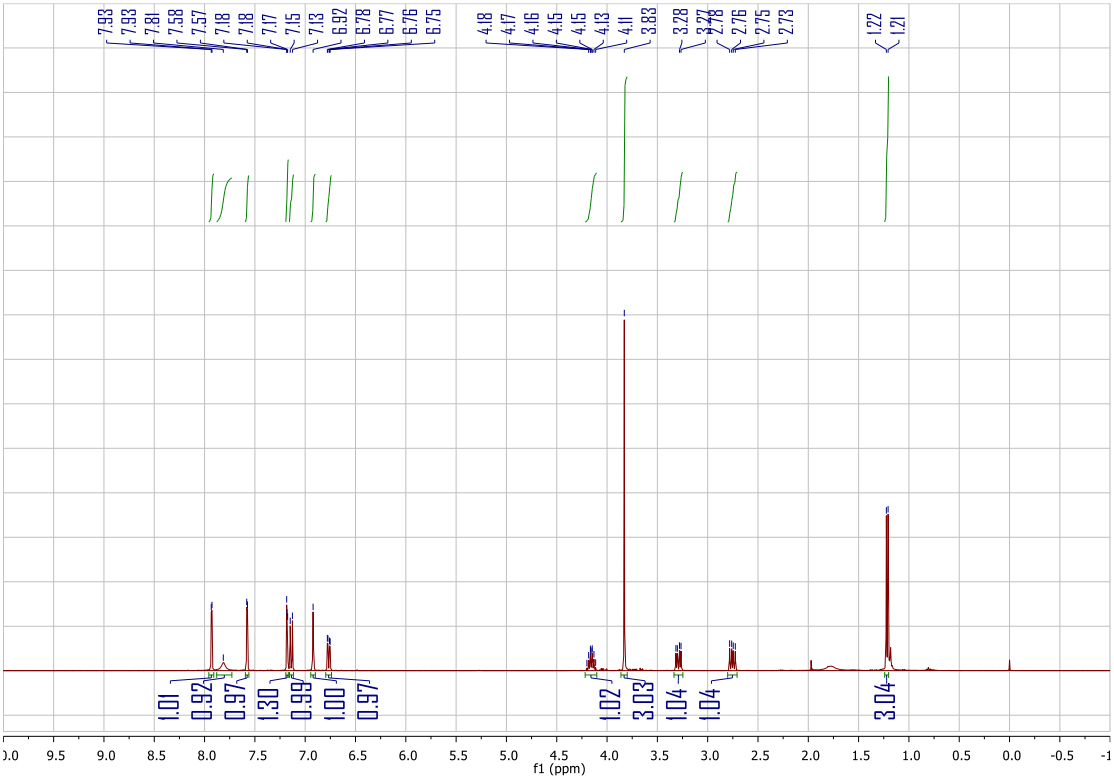
3-(5-methoxy-1H-indol-3-yl)-2-methyl-1-(thiazol-2-yl)propan-1-one (6c).

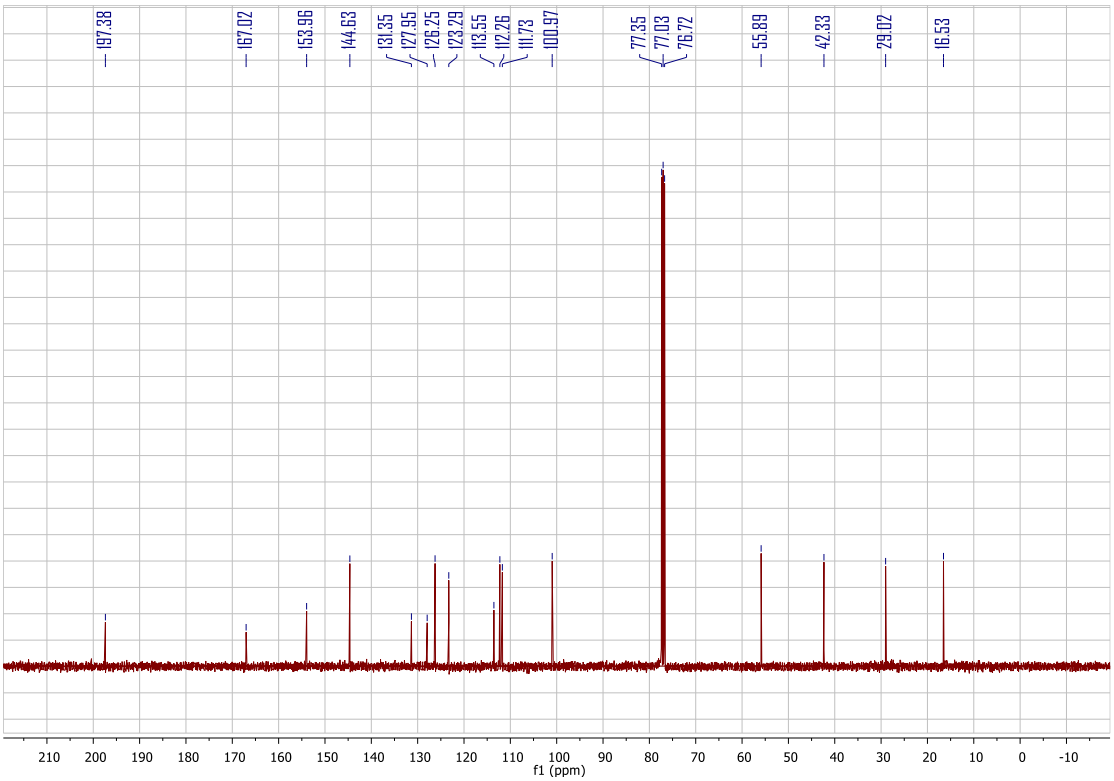
The racemic product was synthesized as described using **5** and 5-OMe-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 3.0 Hz, 1H), 7.81 (s, 1H), 7.58 (d, *J* = 3.0 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 6.92 (s, 1H), 6.77 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.21 – 4.11 (m, 1H), 3.83 (s, 3H), 3.29 (dd, *J* = 14.4, 5.9 Hz, 1H), 2.75 (dd, *J* = 14.4, 8.1 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.38 (s), 153.96 (s), 144.63 (s), 131.35 (s), 127.95 (s), 126.25 (s), 123.29 (s), 113.55 (s), 112.26 (s), 111.73 (s), 100.97 (s), 55.89 (s), 42.33 (s), 29.02 (s), 16.53 (s).

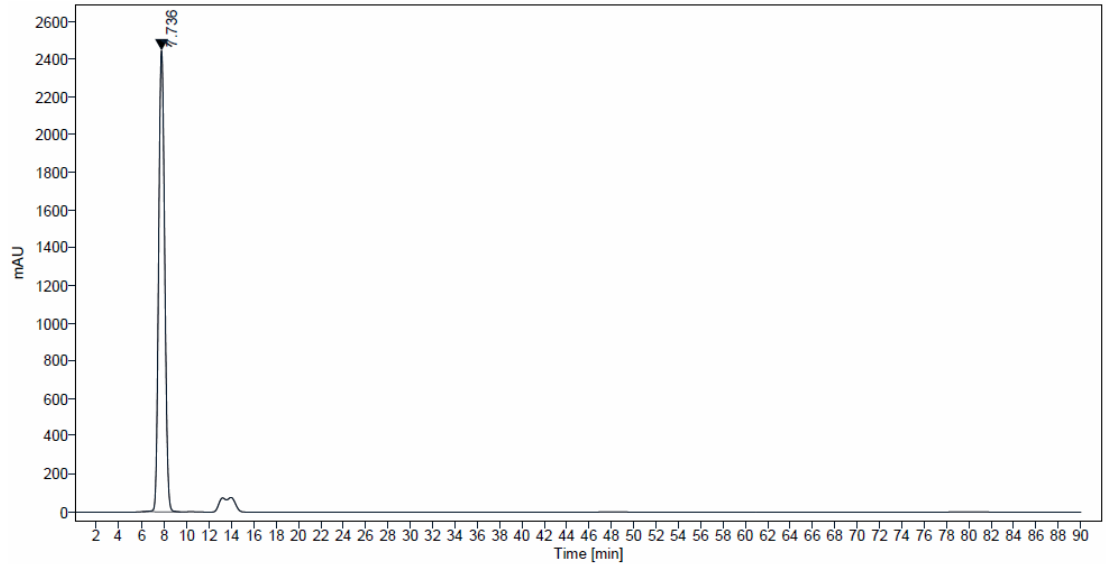
HRMS (ESI) calcd. for $C_{16}H_{16}N_2NaO_2S$ $[M+Na]^+$: m/z 323.0825, found: 323.0824.



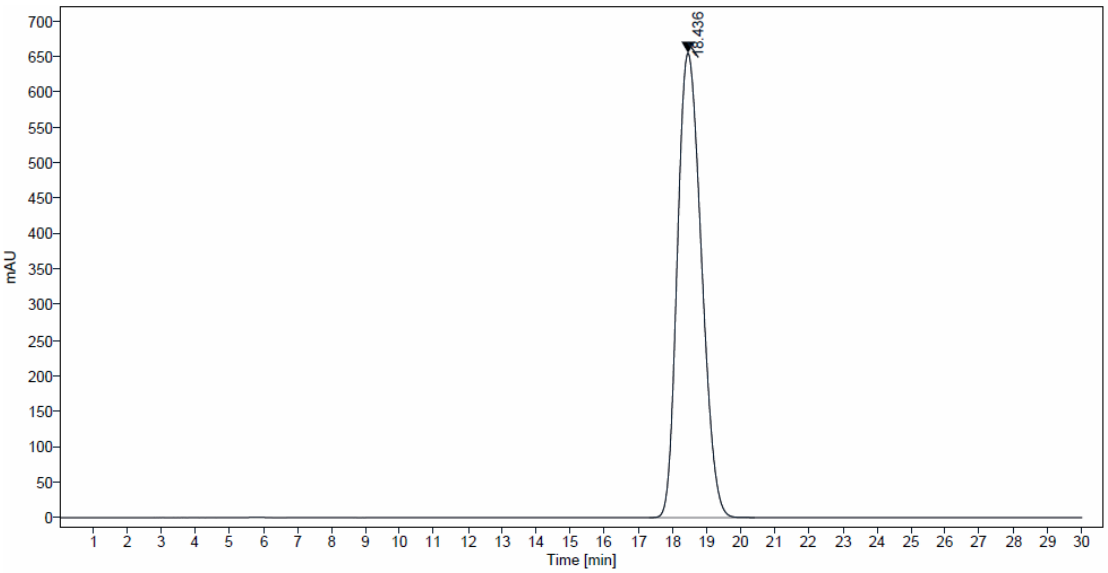


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.75 mL/min, λ = 280 nm

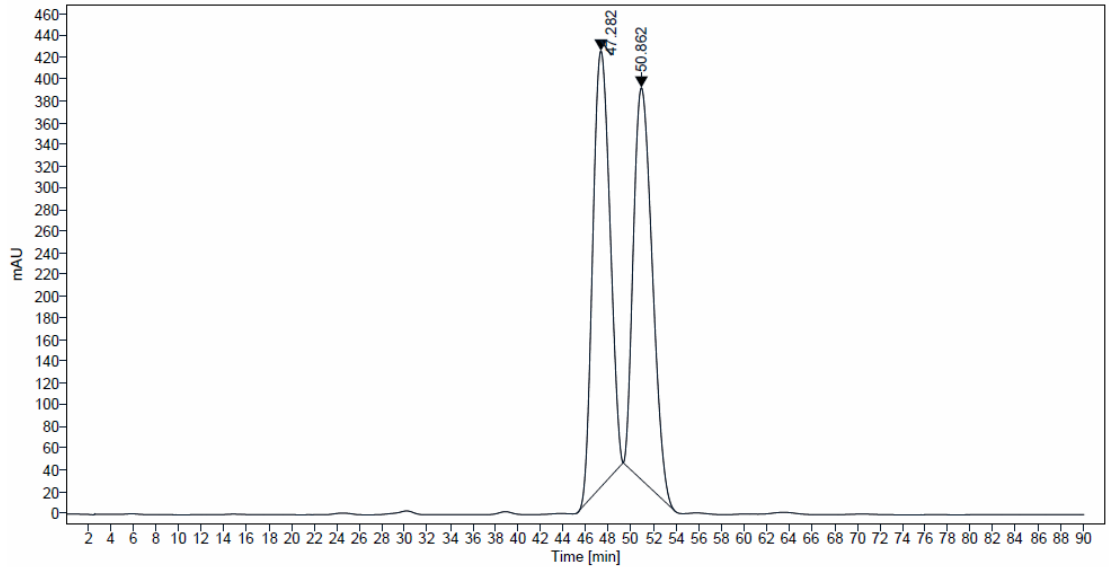
Starting Material (5): Retention time = 7.736 min



5-OMe-Indole: Retention time = 18.436 min

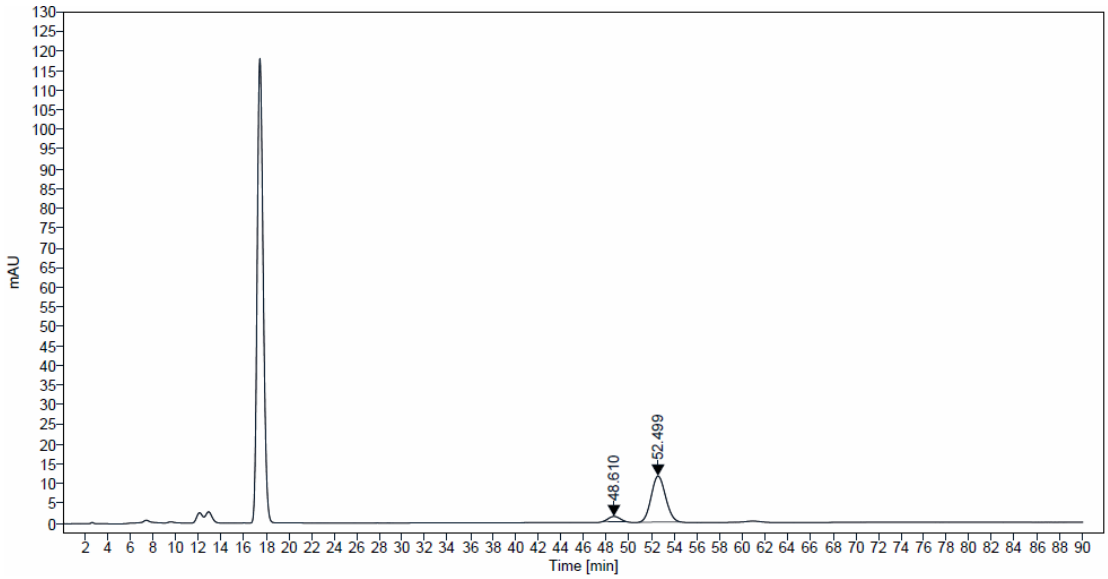


Racemic: Retention time: 47.282 min; 50.862 min

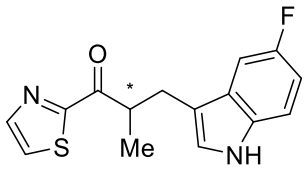


Peak	Retention time (min)	Rel. area (%)
1	47.282	50.5
2	50.862	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6c** < 1:99 and an enantiomeric excess of 91% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 97:03, 0.75 mL/min, λ = 280 nm]. Retention time: 48.610 min; 52.499 min



Peak	Retention time (min)	Rel. area (%)
1	48.610	4.3
2	52.499	95.7



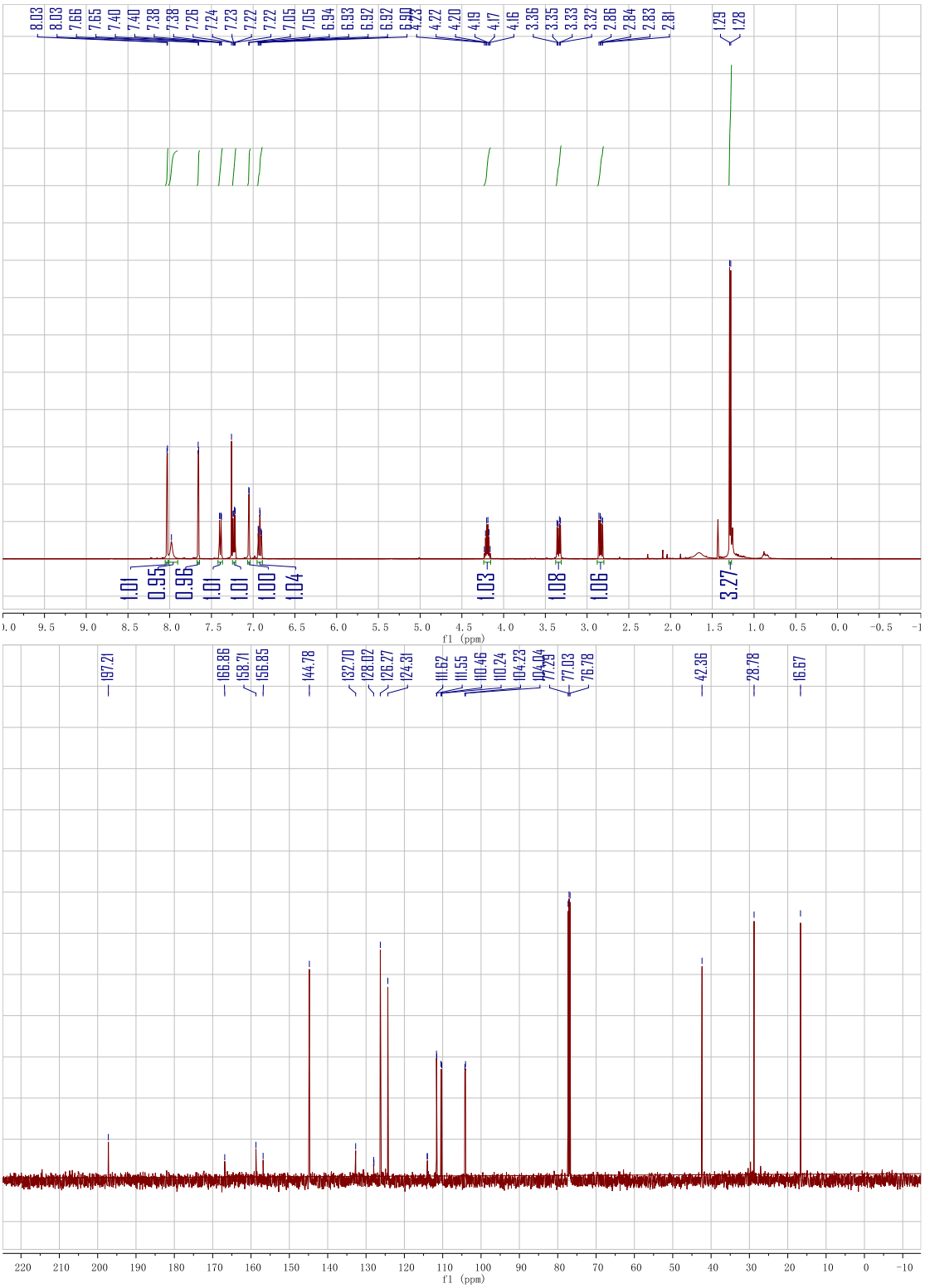
3-(5-fluoro-1H-indol-3-yl)-2-methyl-1-(thiazol-2-yl)propan-1-one (6d).

The racemic product was synthesized as described using **5** and 5-F-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 3.0 Hz, 1H), 7.98 (s, 1H), 7.66 (d, *J* = 3.0 Hz, 1H), 7.39 (dd, *J* = 9.7, 2.4 Hz, 1H), 7.23 (dd, *J* = 8.8, 4.3 Hz, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.92 (td, *J* = 9.0, 2.5 Hz, 1H), 4.24 – 4.15 (m, 1H), 3.34 (dd, *J* = 14.4, 6.2 Hz, 1H), 2.84 (dd, *J* = 14.5, 7.9 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 4H).

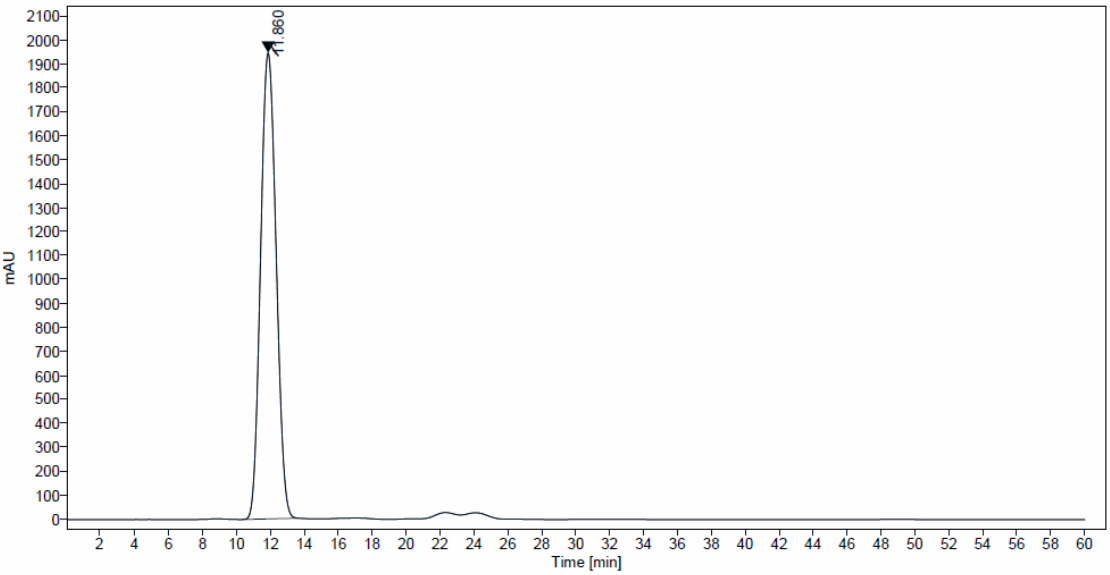
^{13}C NMR (126 MHz, $CDCl_3$) δ 197.21 (s), 166.86 (s), 157.78 (d, *J* = 234.3 Hz), 144.78 (s), 132.70 (s), 127.98 (d, *J* = 9.6 Hz), 126.27 (s), 124.31 (s), 114.02 (d, *J* = 4.7 Hz), 111.58 (d, *J* = 9.7 Hz), 110.35 (d, *J* = 26.5 Hz), 104.14 (d, *J* = 23.5 Hz), 42.36 (s), 28.78 (s), 16.67 (s).

HRMS (ESI) calcd. for $C_{15}H_{13}FN_2NaOS$ $[M+Na]^+$: m/z 311.0625, found: 311.0625.

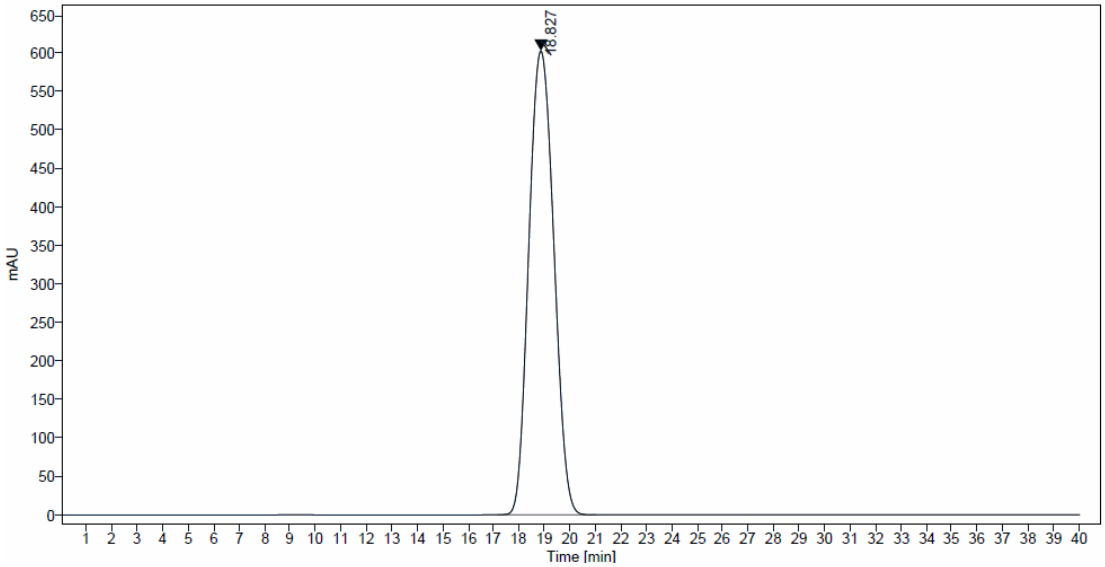


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm

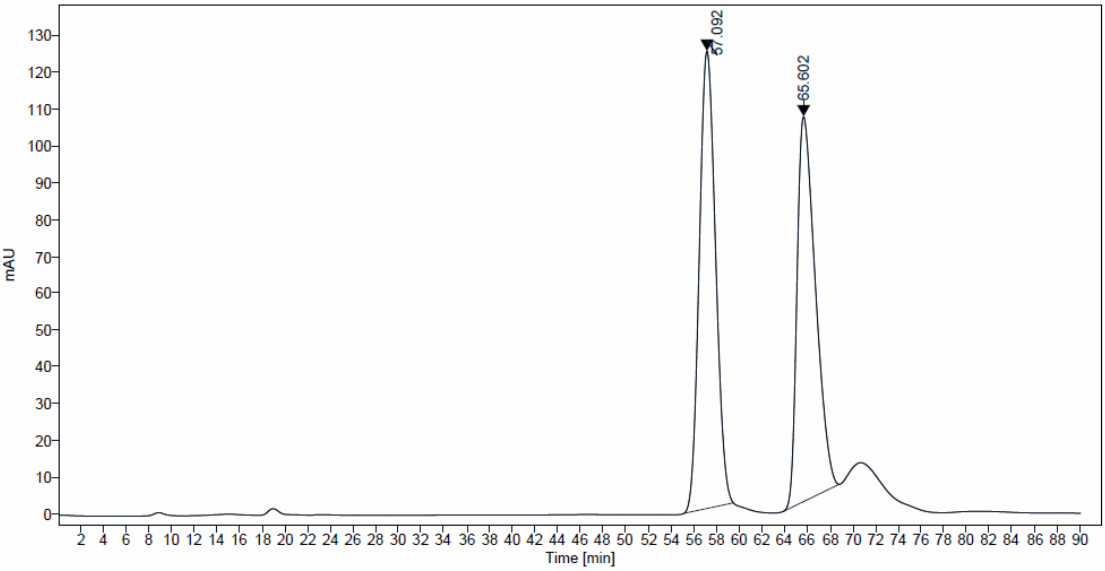
Starting Material (5): Retention time = 11.860 min



5-F-Indole: Retention time = 18.827 min

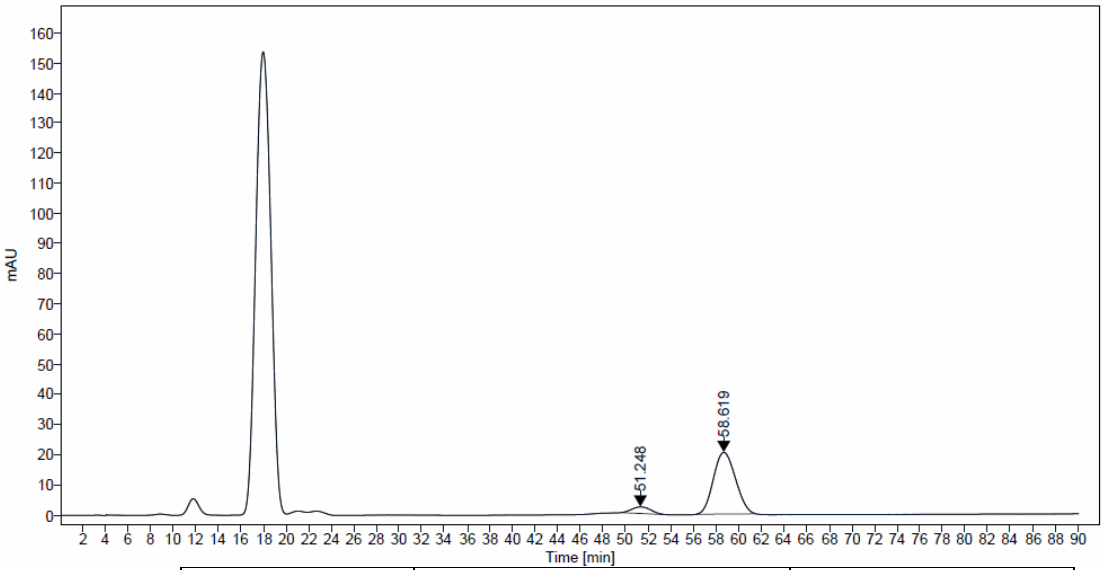


Racemic: Retention time: 57.092 min; 65.602 min

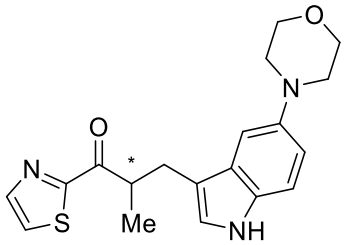


Peak	Retention time (min)	Rel. area (%)
1	57.092	51.3
2	65.602	48.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6d** as 5:95 and an enantiomeric excess of 83% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm]. Retention time: 51.248 min; 58.619 min



Peak	Retention time (min)	Rel. area (%)
1	51.248	8.5
2	58.619	91.5



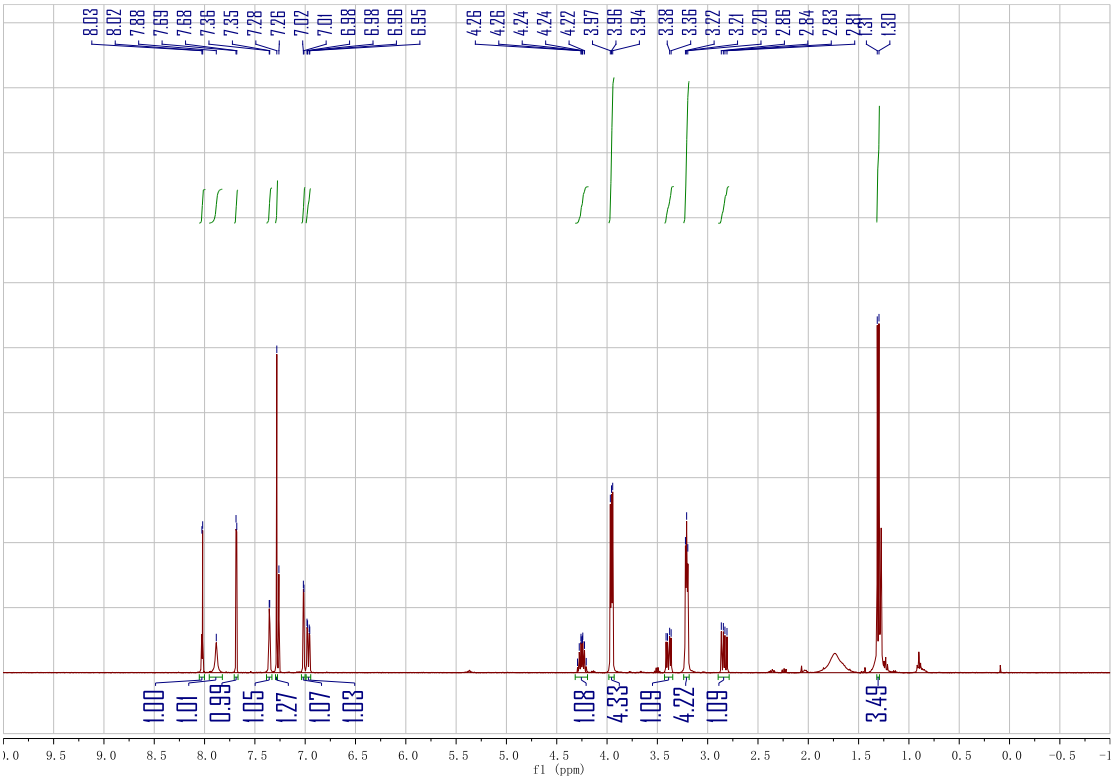
2-methyl-3-(5-morpholino-1H-indol-3-yl)-1-(thiazol-2-yl)propan-1-one (6e).

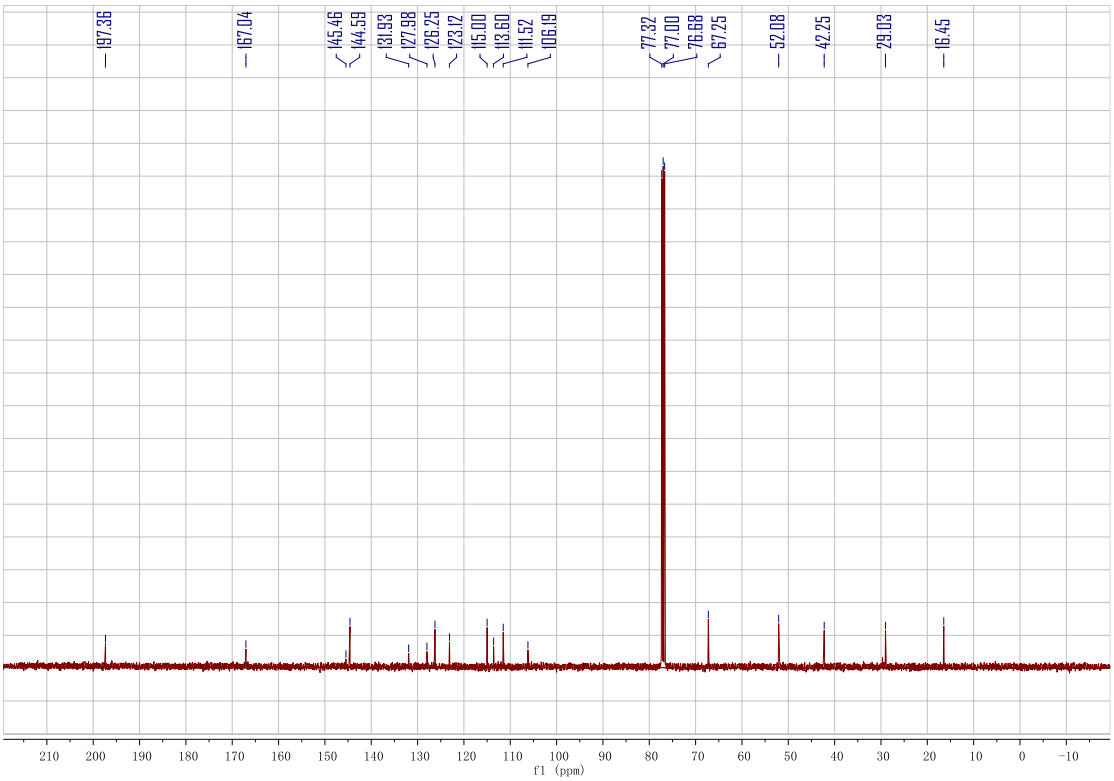
The racemic product was synthesized as described using **5** and 5-Morpholino-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 3.0 Hz, 1H), 7.88 (s, 1H), 7.68 (d, *J* = 3.0 Hz, 1H), 7.36 (d, *J* = 1.8 Hz, 1H), 7.28 (s, 1H), 7.02 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.2 Hz, 1H), 4.31 – 4.20 (m, 1H), 3.98 – 3.93 (m, 4H), 3.39 (dd, *J* = 14.4, 5.8 Hz, 1H), 3.24 – 3.18 (m, 4H), 2.84 (dd, *J* = 14.4, 8.2 Hz, 1H), 1.31 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.36 (s), 167.04 (s), 145.46 (s), 144.59 (s), 131.93 (s), 127.98 (s), 126.25 (s), 123.12 (s), 115.00 (s), 113.60 (s), 111.52 (s), 106.19 (s), 67.25 (s), 52.08 (s), 42.25 (s), 29.03 (s), 16.45 (s).

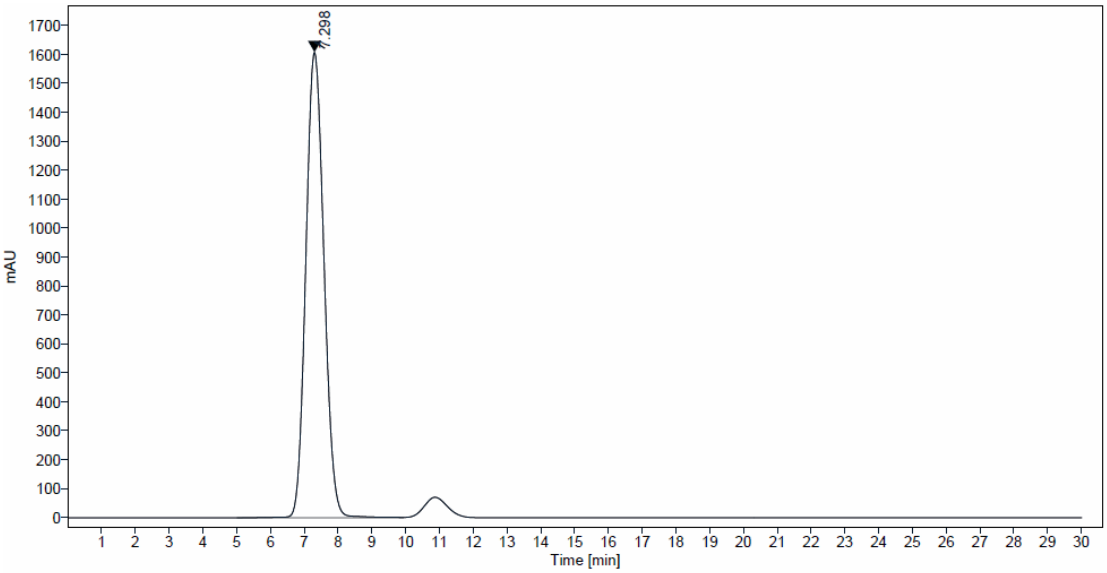
HRMS (ESI) calcd. for $C_{19}H_{22}N_3O_2S$ $[M+H]^+$: m/z 3356.1427, found: 356.1435.



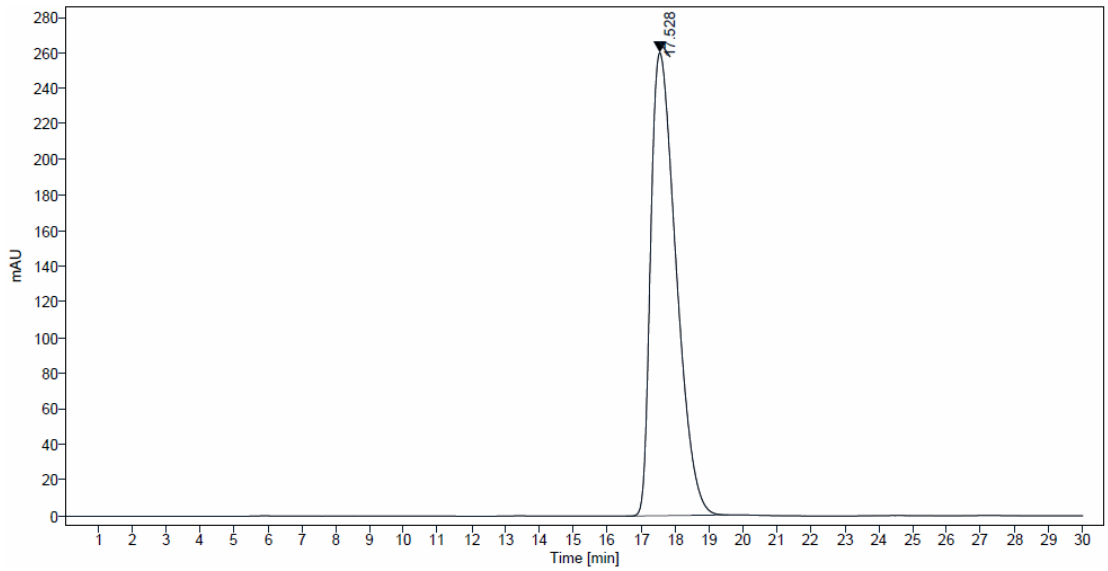


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm

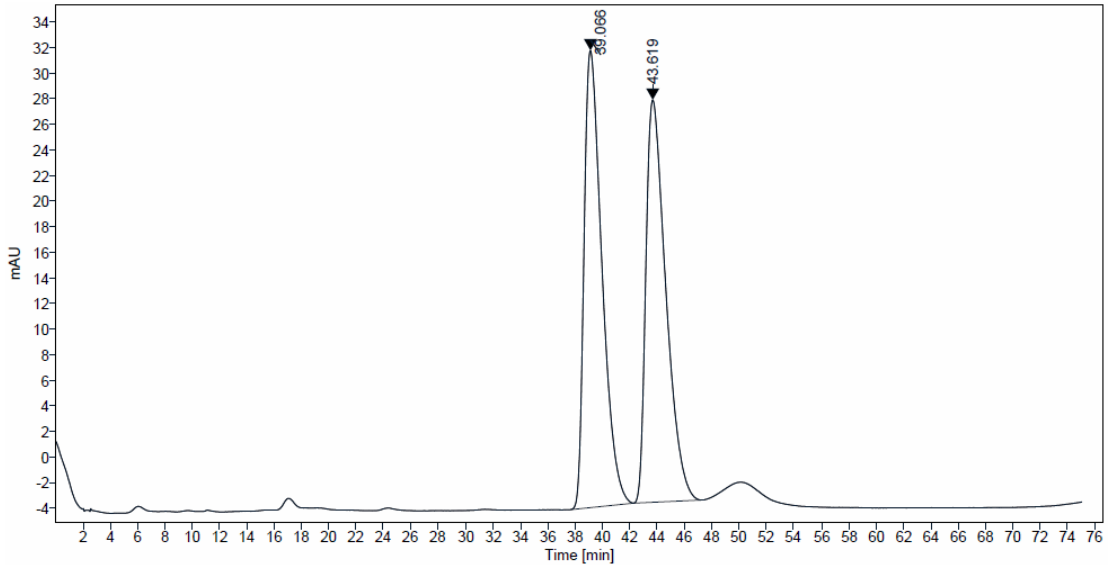
Starting Material (5): Retention time = 7.298min



5-Morpholino-Indole: Retention time = 17.528 min

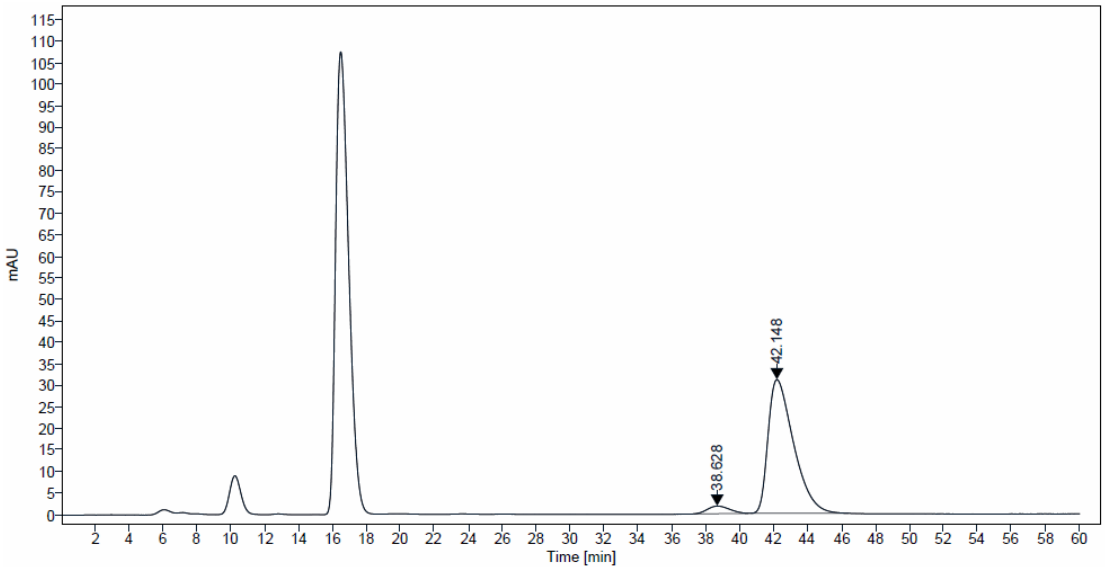


Racemic: Retention time: 39.066 min; 43.619 min

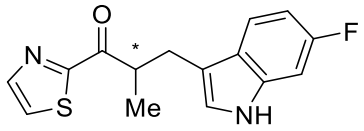


Peak	Retention time (min)	Rel. area (%)
1	39.066	50.5
2	43.619	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6e** as 4:96 and an enantiomeric excess of 92% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 93:07, 0.75 mL/min, λ = 280 nm]. Retention time: 38.628 min; 42.148 min



Peak	Retention time (min)	Rel. area (%)
1	38.628	4.0
2	42.148	96.0



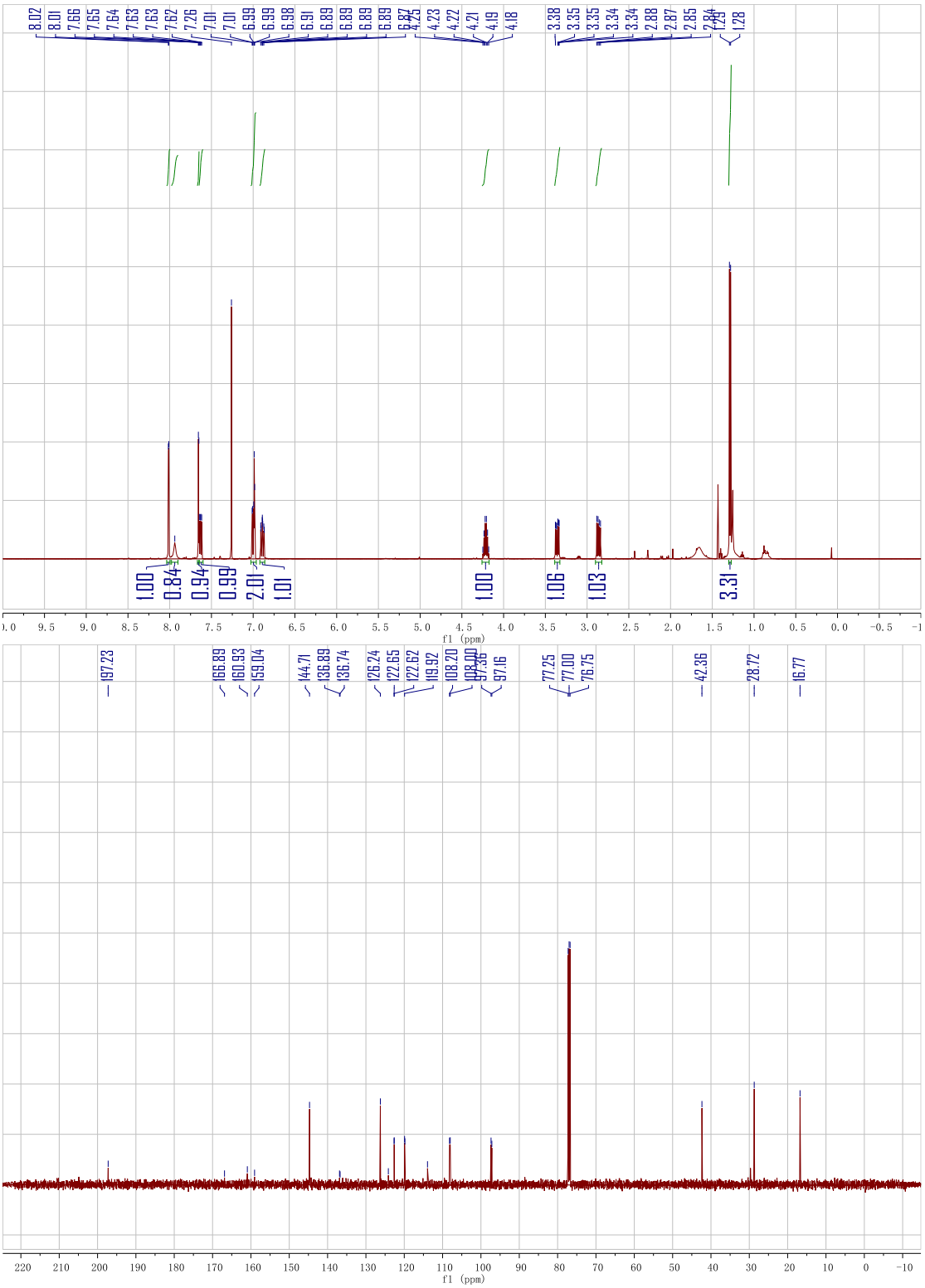
3-(6-fluoro-1H-indol-3-yl)-2-methyl-1-(thiazol-2-yl)propan-1-one (6f).

The racemic product was synthesized as described using **5** and 6-F-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 3.0 Hz, 1H), 7.94 (s, 1H), 7.65 (d, *J* = 3.0 Hz, 1H), 7.63 (dd, *J* = 8.7, 5.3 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.89 (ddd, *J* = 9.6, 8.8, 2.3 Hz, 1H), 4.26 – 4.17 (m, 1H), 3.36 (ddd, *J* = 14.5, 6.5, 0.6 Hz, 1H), 2.86 (dd, *J* = 14.5, 7.8 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 3H).

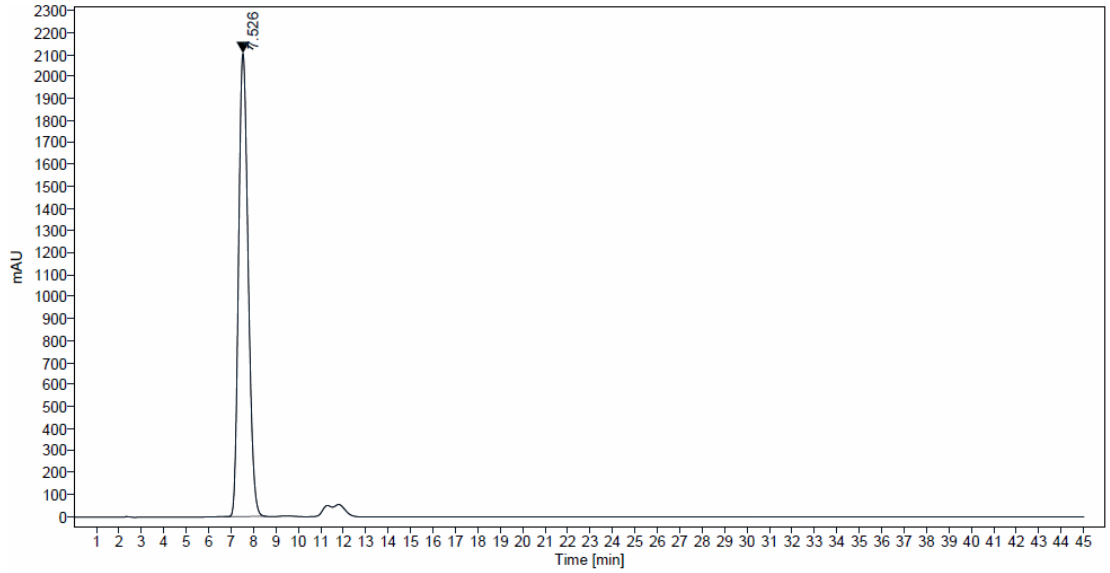
^{13}C NMR (126 MHz, $CDCl_3$) δ 197.23 (s), 166.89 (s), 159.99 (d, *J* = 237.1 Hz), 144.71 (s), 136.81 (d, *J* = 19.2 Hz), 126.24 (s), 124.15 (s), 122.64 (d, *J* = 3.4 Hz), 119.87 (d, *J* = 10.3 Hz), 113.94 (s), 108.10 (d, *J* = 24.5 Hz), 97.26 (d, *J* = 26.1 Hz), 42.36 (s), 28.72 (s), 16.77 (s).

HRMS (ESI) calcd. for $C_{15}H_{14}FN_2OS$ $[M+Na]^+$: m/z 289.0811, found: 289.0808.

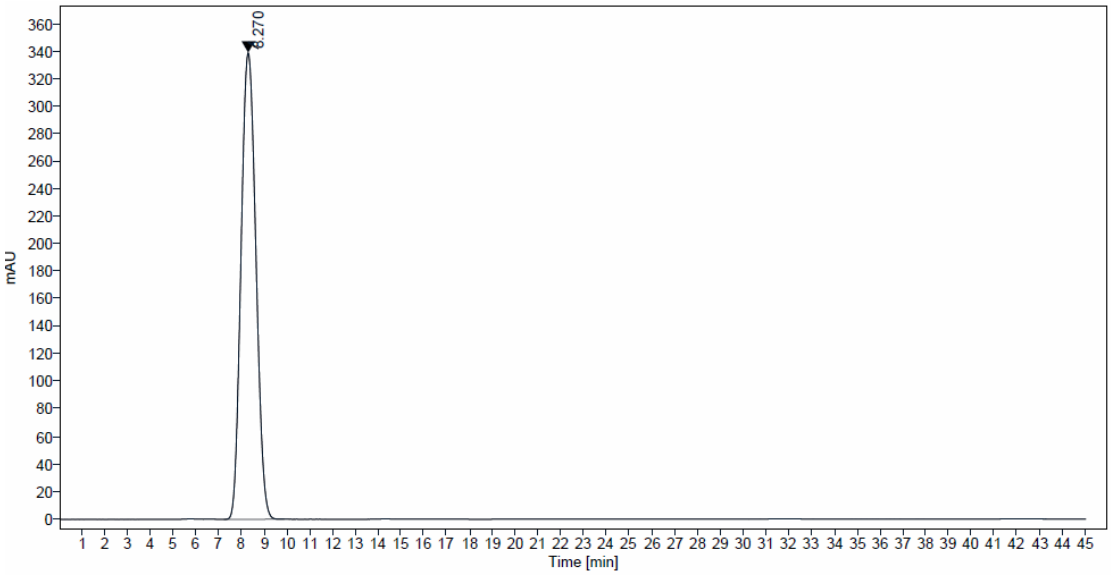


HPLC analysis CHIRALCEL IB column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm

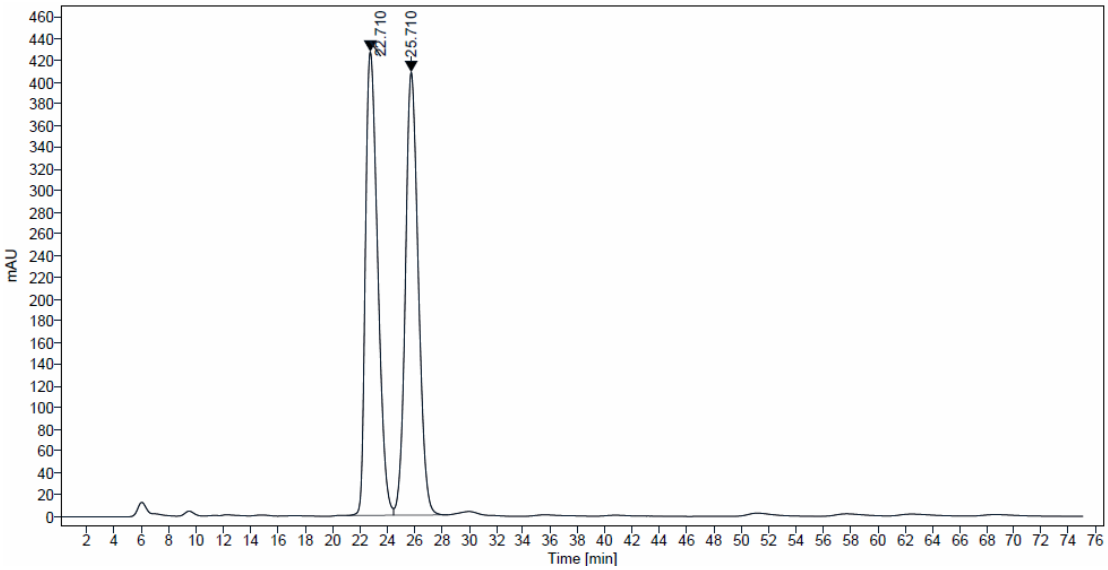
Starting Material (5): Retention time = 7.528 min



6-F-Indole: Retention time = 6.270 min

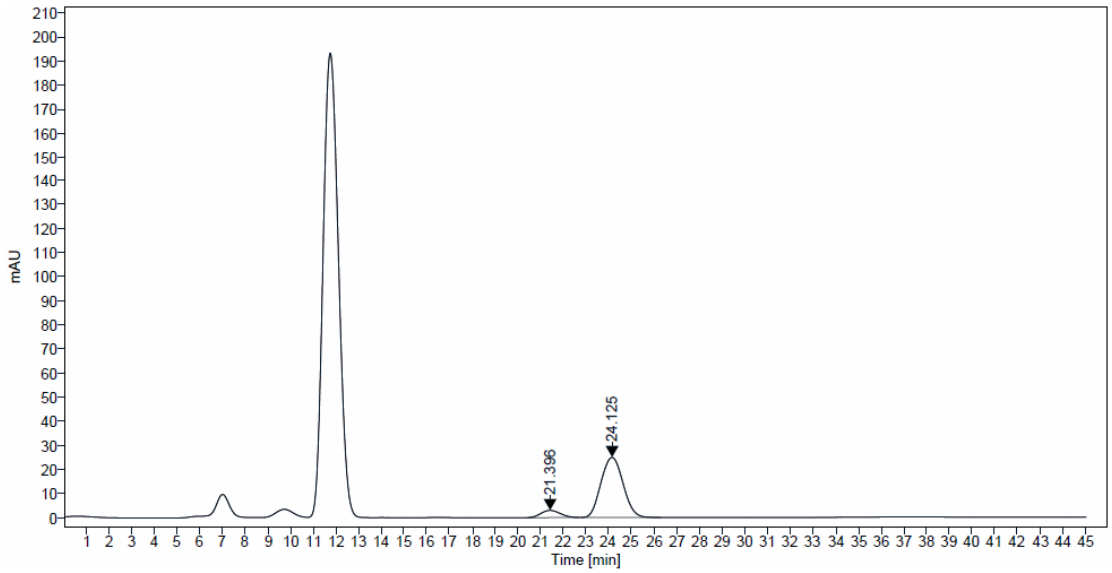


Racemic: Retention time: 22.710 min; 25.710 min

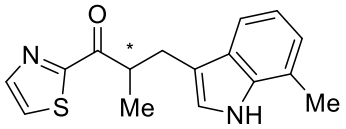


Peak	Retention time (min)	Rel. area (%)
1	22.710	50.3
2	25.710	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6f** as 5:95 and an enantiomeric excess of 91% [**HPLC analysis** CHIRALCEL IB column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm]. Retention time: 21.396 min; 24.125 min



Peak	Retention time (min)	Rel. area (%)
1	21.396	4.5
2	24.125	95.5



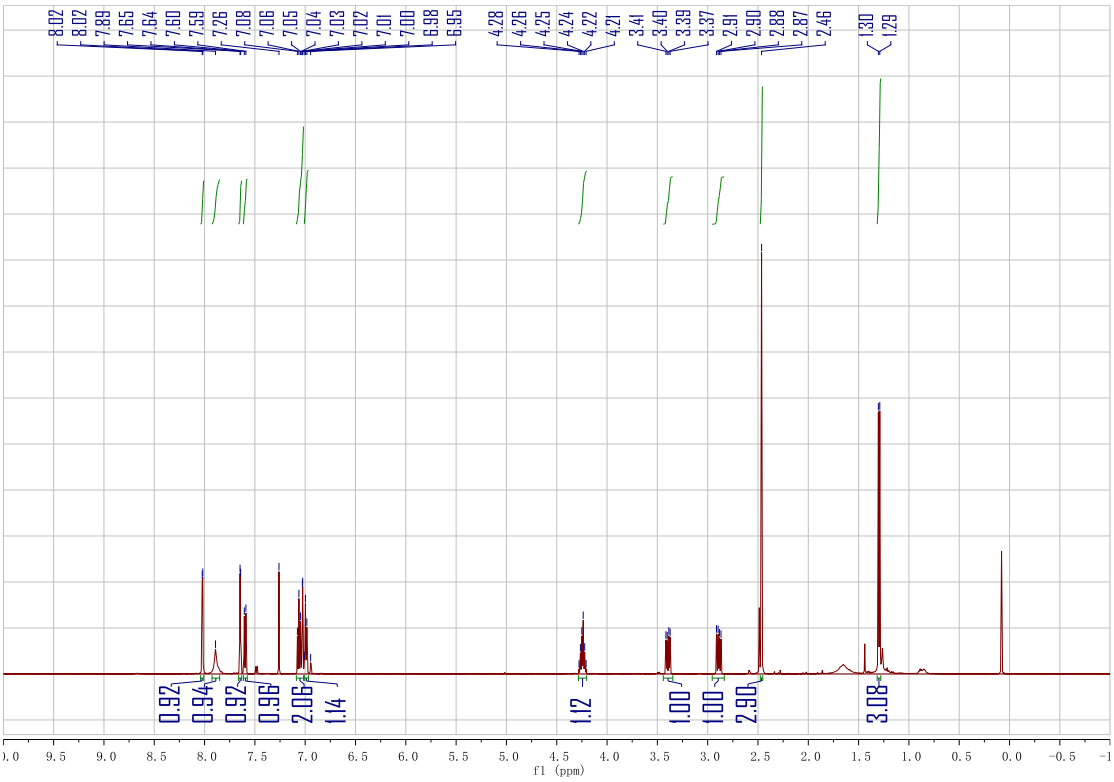
2-methyl-3-(7-methyl-1H-indol-3-yl)-1-(thiazol-2-yl)propan-1-one (6g).

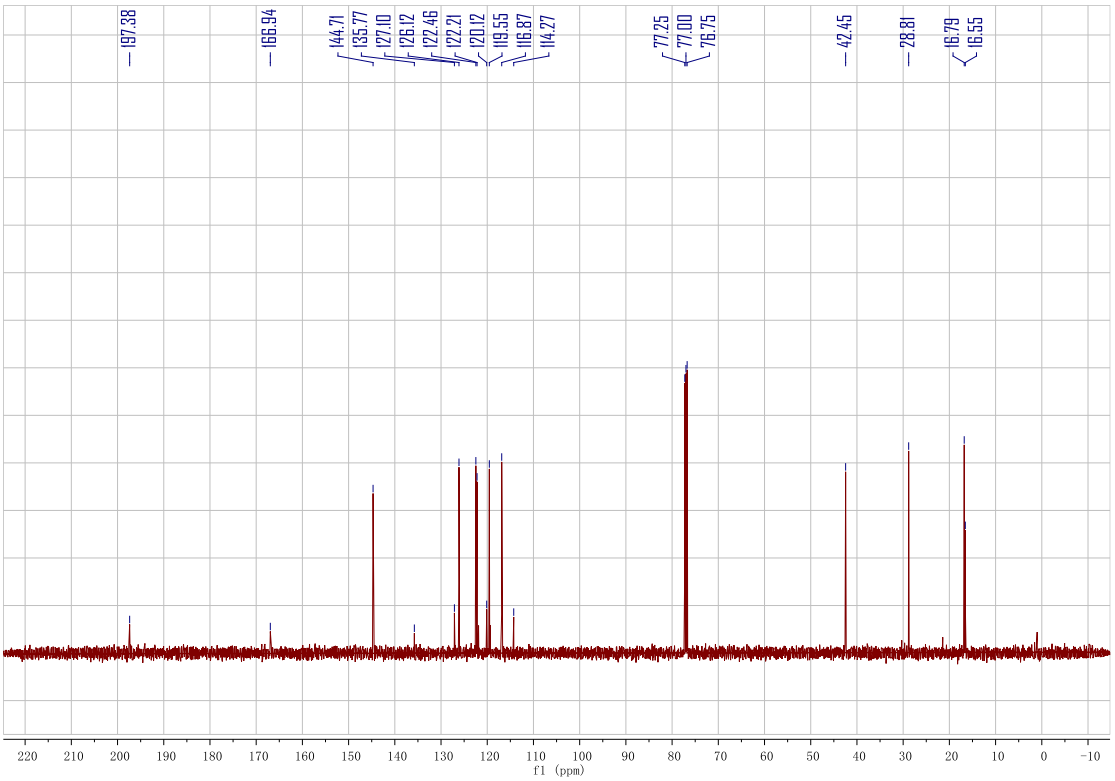
The racemic product was synthesized as described using **5** and 7-Me-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 3.0 Hz, 1H), 7.89 (s, 1H), 7.64 (d, *J* = 3.0 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.09 – 7.02 (m, 2H), 7.01 – 6.94 (m, 1H), 4.24 (h, *J* = 6.9 Hz, 1H), 3.39 (dd, *J* = 14.4, 6.3 Hz, 1H), 2.89 (dd, *J* = 14.4, 7.9 Hz, 1H), 2.46 (s, 3H), 1.30 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.38 (s), 166.94 (s), 144.71 (s), 135.77 (s), 127.10 (s), 126.12 (s), 122.46 (s), 122.21 (s), 120.12 (s), 119.55 (s), 116.87 (s), 114.27 (s), 42.45 (s), 28.81 (s), 16.79 (s), 16.55 (s).

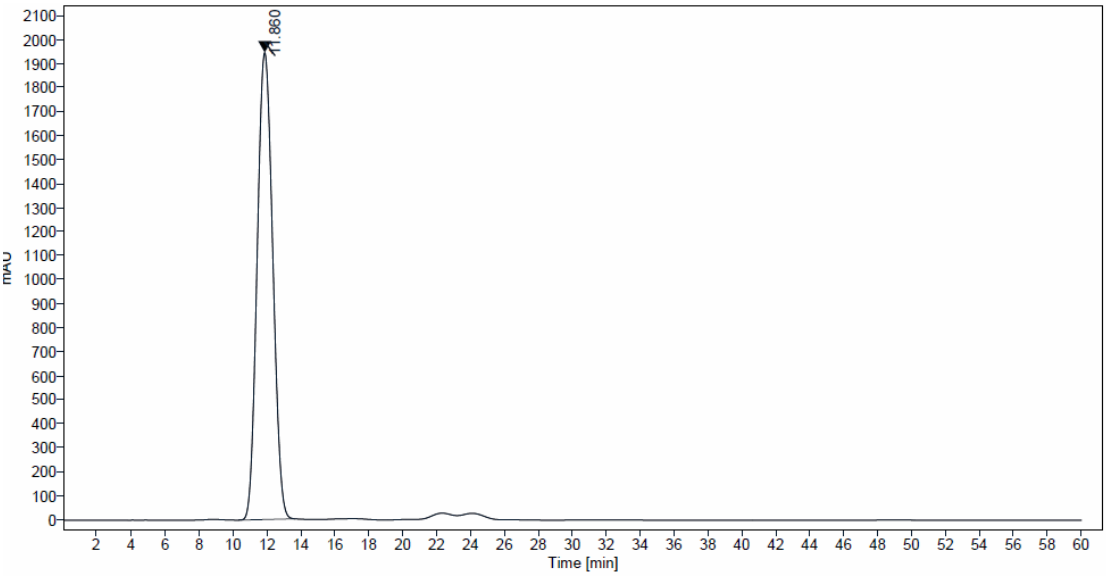
HRMS (ESI) calcd. for $C_{16}H_{17}N_2OS$ $[M+H]^+$: m/z 285.1062, found: 285.1066.



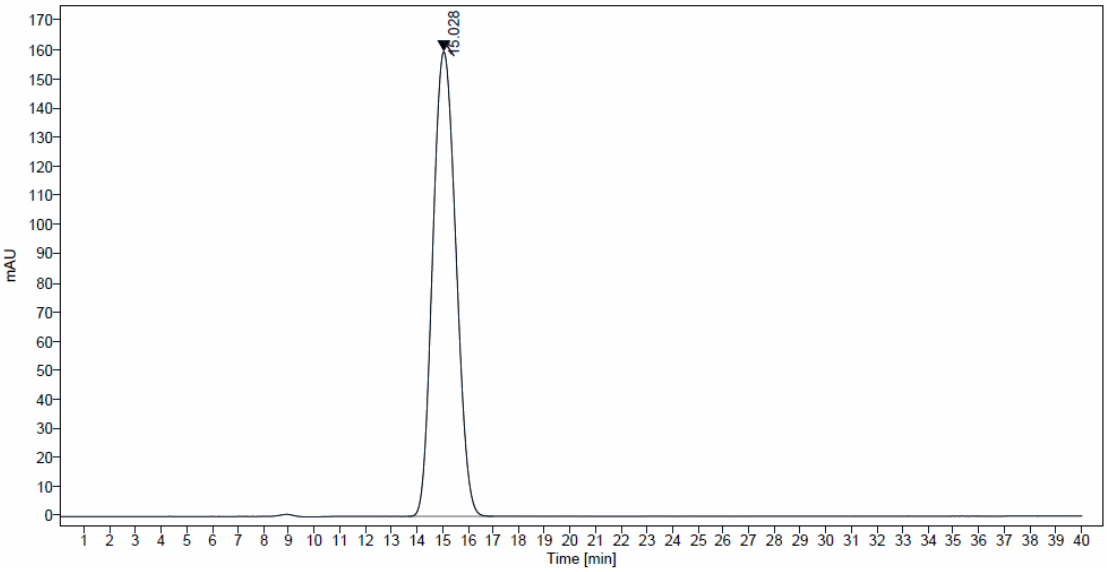


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm

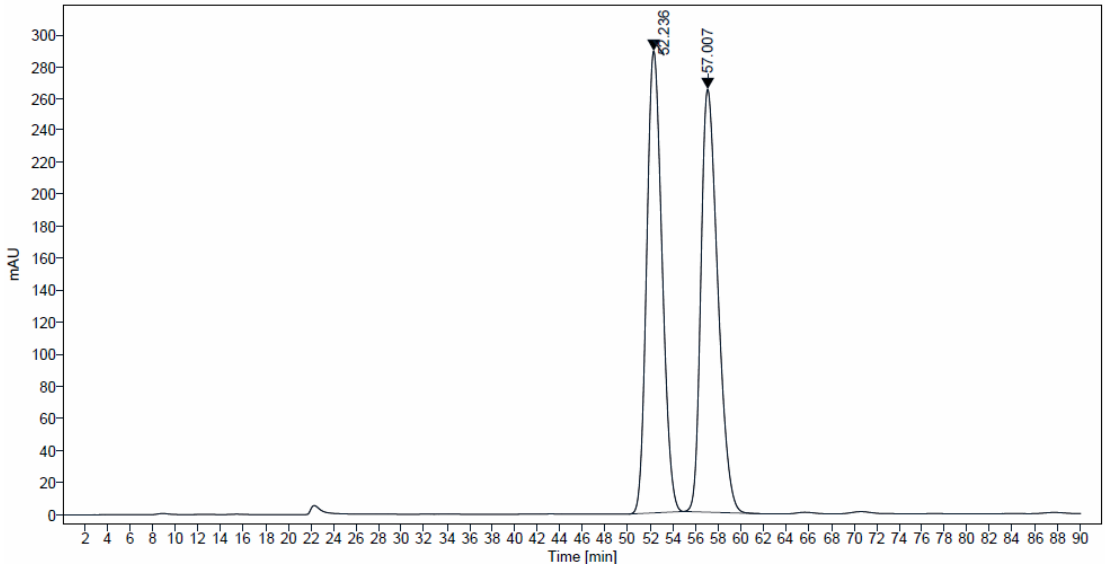
Starting Material (5): Retention time = 11.860 min



7-Me-Indole: Retention time = 15.028 min

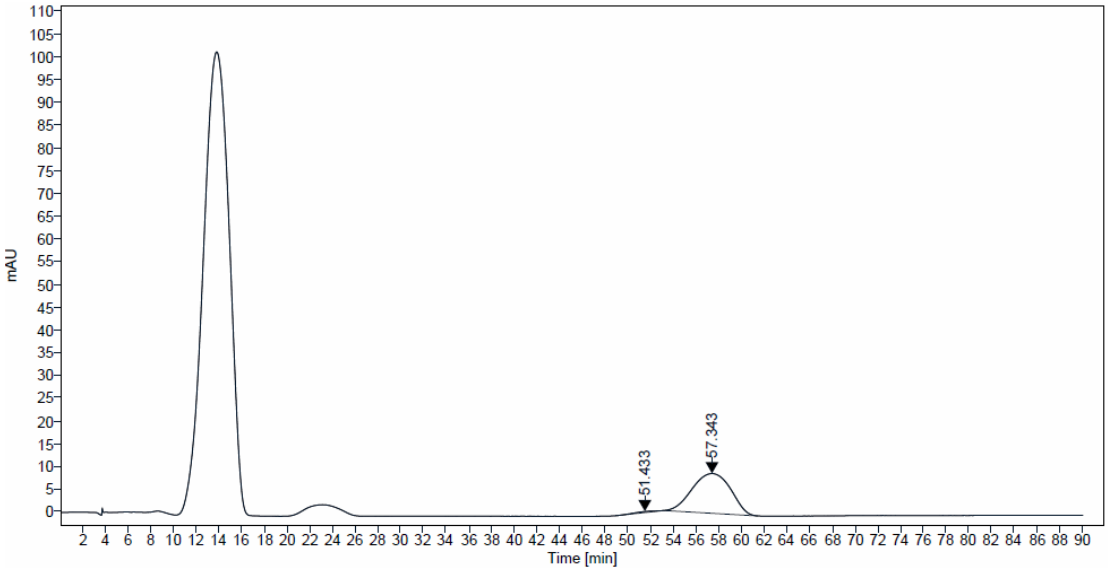


Racemic: Retention time: 52.236 min; 57.007 min

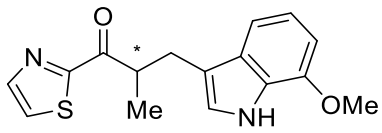


Peak	Retention time (min)	Rel. area (%)
1	52.236	50.1
2	57.007	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6g** < 1:99 and an enantiomeric excess of 97% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm]. Retention time: 51.433 min; 57.343 min



Peak	Retention time (min)	Rel. area (%)
1	51.433	1.5
2	57.343	98.5



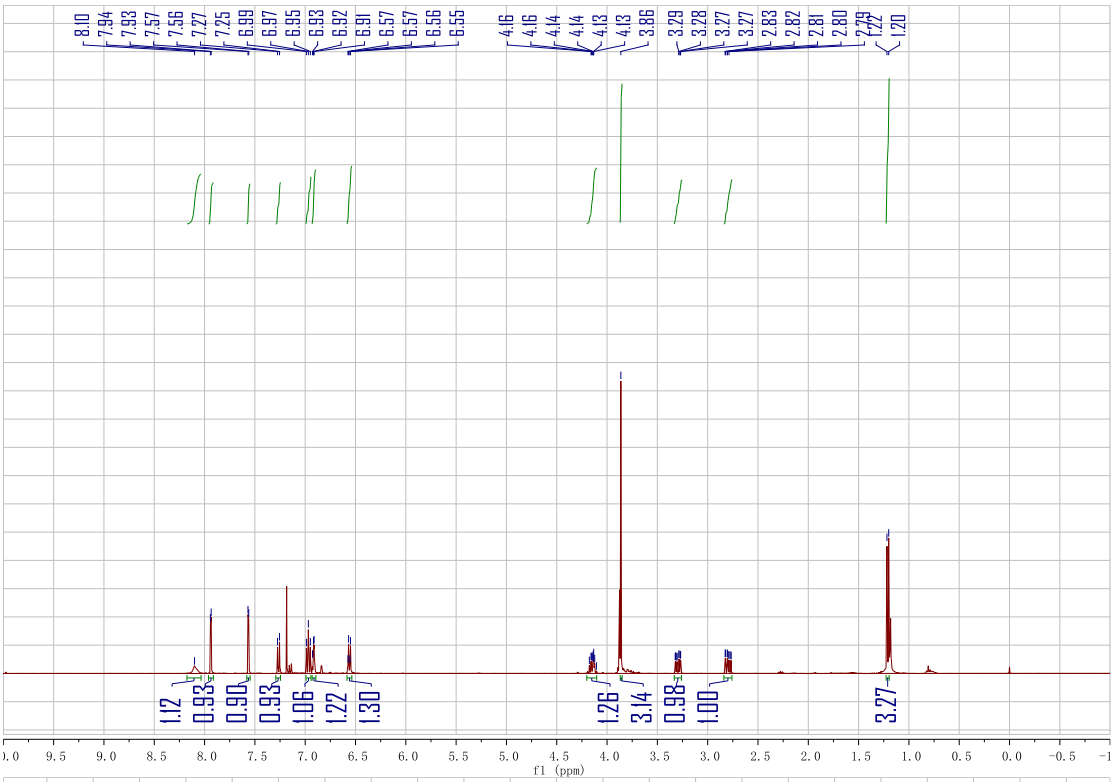
3-(7-methoxy-1H-indol-3-yl)-2-methyl-1-(thiazol-2-yl)propan-1-one (6h).

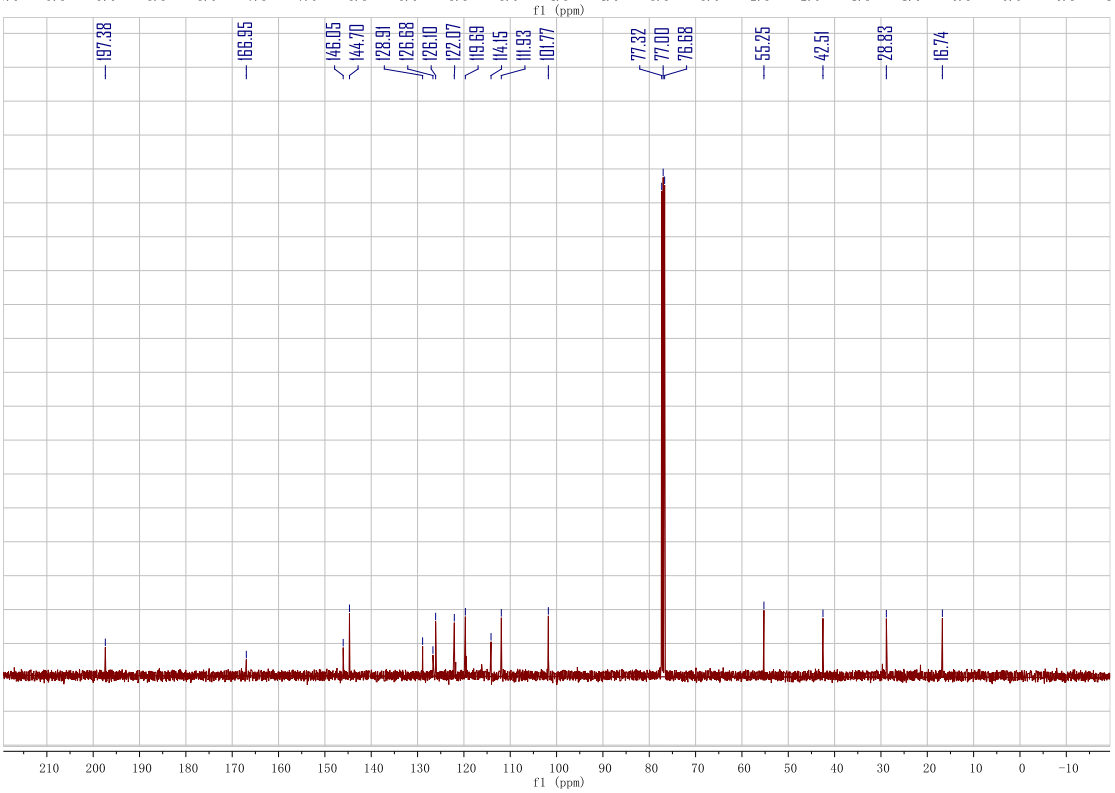
The racemic product was synthesized as described using **5** and 7-OMe-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.94 (d, *J* = 3.0 Hz, 1H), 7.56 (d, *J* = 3.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 6.97 (t, *J* = 7.9 Hz, 1H), 6.93 – 6.90 (m, 1H), 6.56 (dd, *J* = 7.6, 2.4 Hz, 1H), 4.20 – 4.09 (m, 1H), 3.86 (s, 3H), 3.30 (ddd, *J* = 14.4, 6.3, 0.7 Hz, 1H), 2.85 – 2.75 (m, 1H), 1.21 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.38 (s), 166.95 (s), 146.05 (s), 144.70 (s), 128.91 (s), 126.68 (s), 126.10 (s), 122.07 (s), 119.69 (s), 114.15 (s), 111.93 (s), 101.77 (s), 55.25 (s), 42.51 (s), 28.83 (s), 16.74 (s).

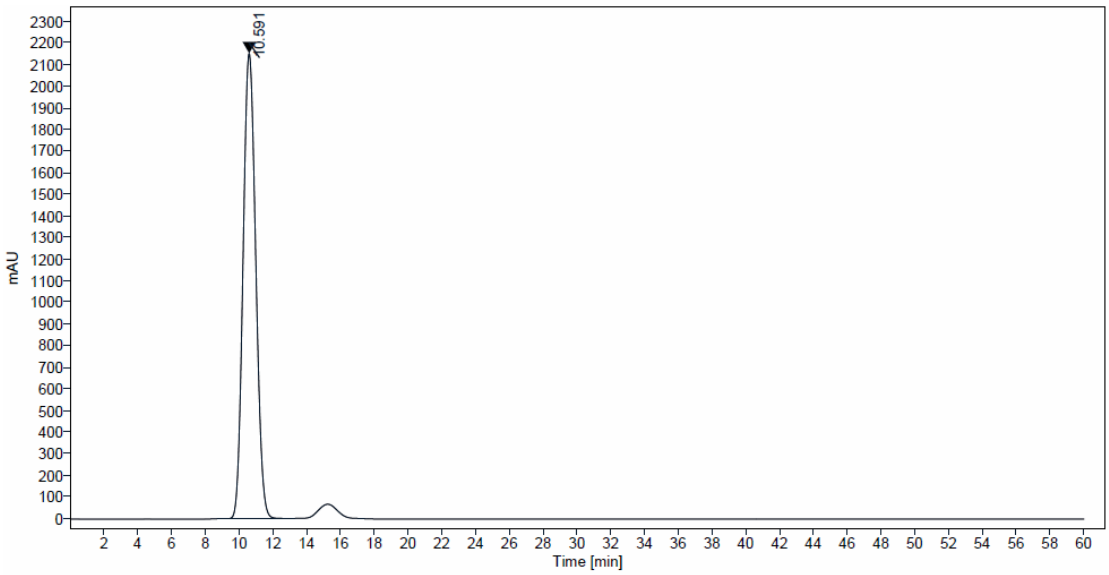
HRMS (ESI) calcd. for $C_{16}H_{16}N_2NaO_2S$ $[M+Na]^+$: m/z 323.0828, found: 323.0825.



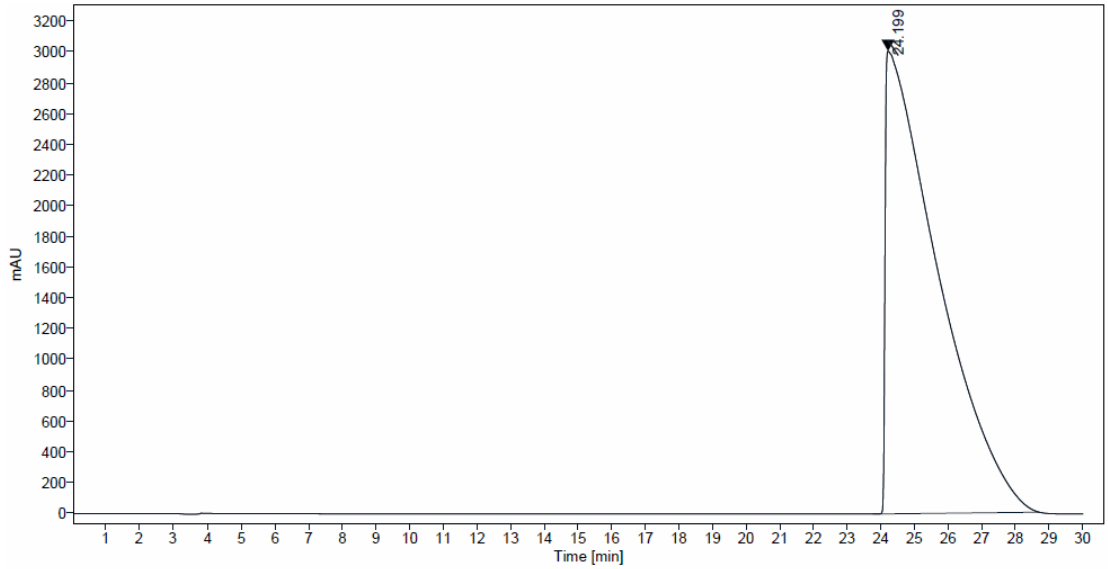


HPLC analysis CHIRALCEL IB column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

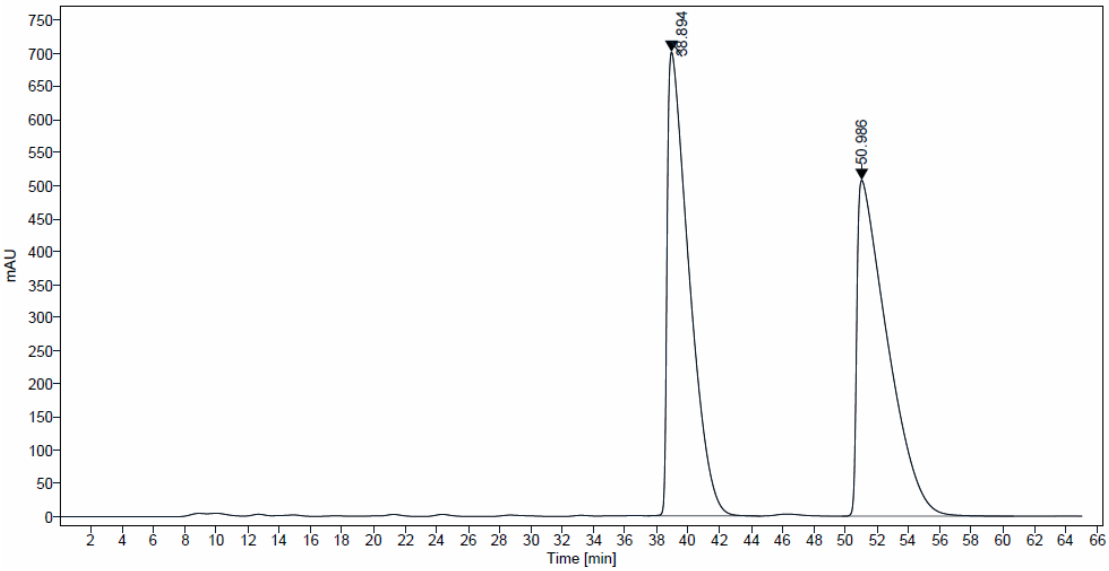
Starting Material (5): Retention time = 10.591 min



7-OMe-Indole: Retention time = 24.199 min

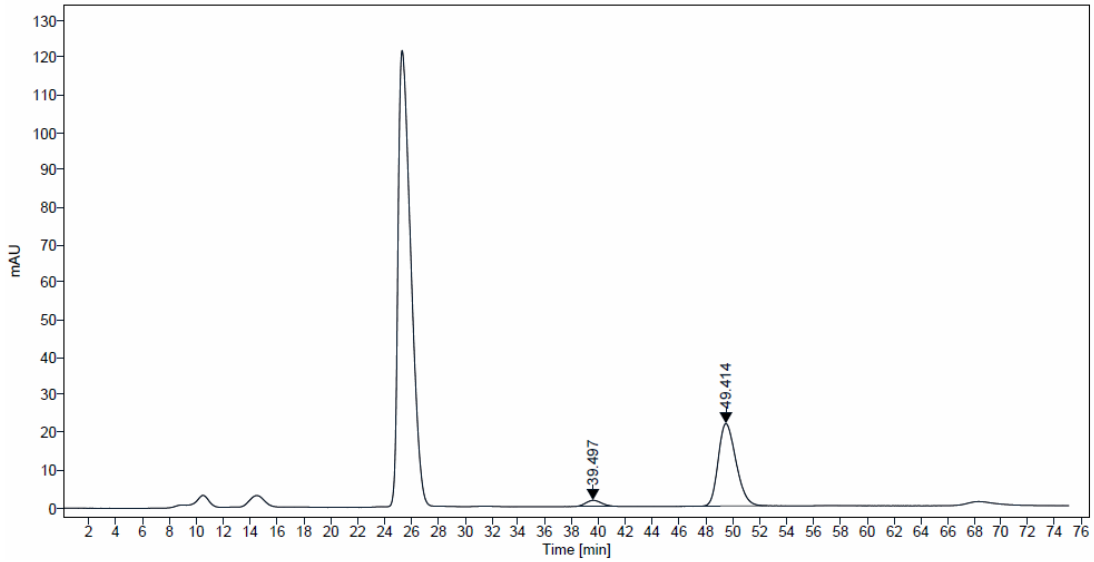


Racemic: Retention time: 38.894 min; 50.986 min

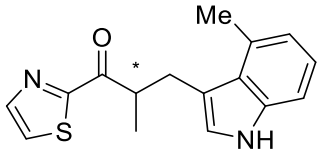


Peak	Retention time (min)	Rel. area (%)
1	38.894	51.0
2	50.986	49.0

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6h** as 4:96 and an enantiomeric excess of 93% [CHIRALCEL IB column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 39.497 min; 49.414 min



Peak	Retention time (min)	Rel. area (%)
1	39.497	3.5
2	49.414	96.5



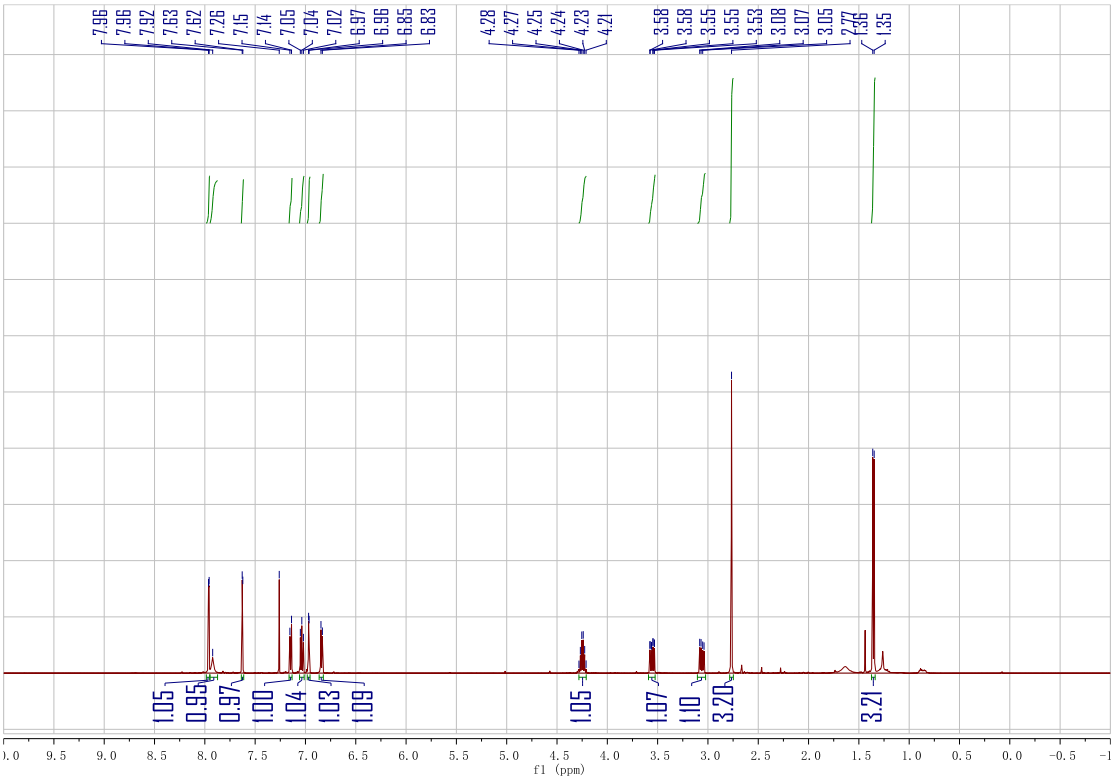
2-methyl-3-(4-methyl-1H-indol-3-yl)-1-(thiazol-2-yl)propan-1-one (6i).

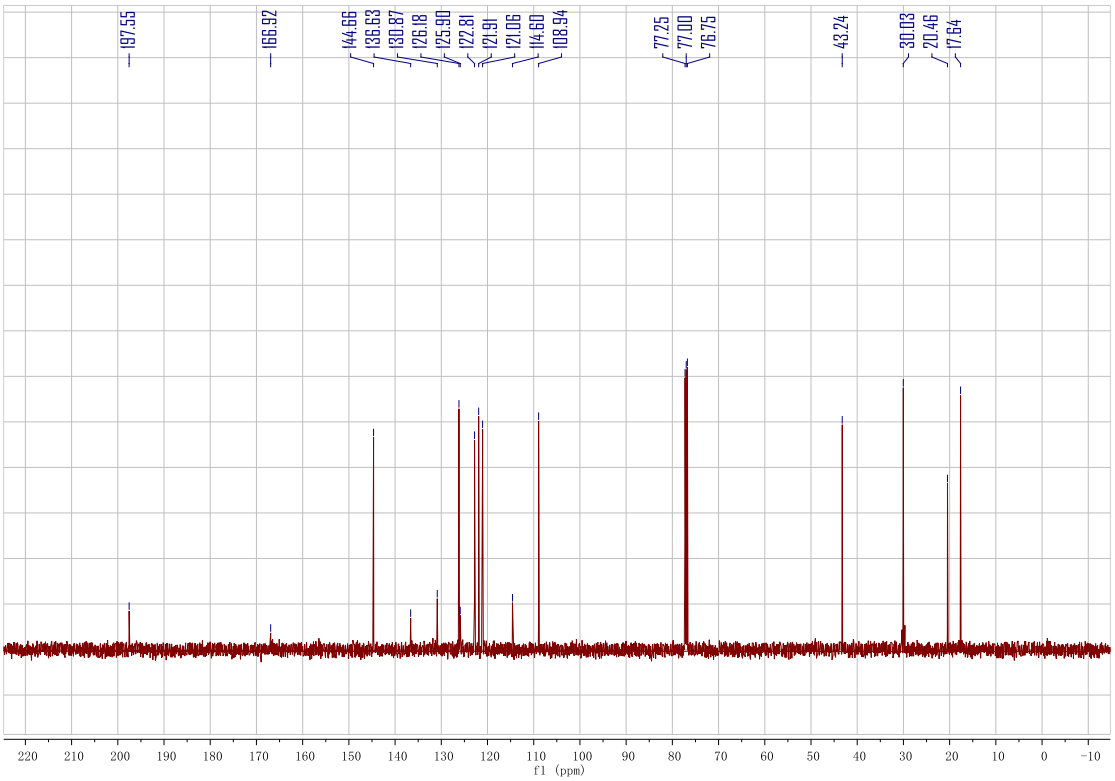
The racemic product was synthesized as described using **5** and 4-Me-Indole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 3.0 Hz, 1H), 7.92 (s, 1H), 7.63 (d, *J* = 3.0 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 7.06 – 7.01 (m, 1H), 6.97 (d, *J* = 2.3 Hz, 1H), 6.84 (d, *J* = 7.1 Hz, 1H), 4.28 – 4.21 (m, 1H), 3.59 – 3.52 (m, 1H), 3.06 (dd, *J* = 14.8, 6.7 Hz, 1H), 2.77 (s, 3H), 1.35 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.55 (s), 166.92 (s), 144.66 (s), 136.63 (s), 130.87 (s), 126.18 (s), 125.90 (s), 122.81 (s), 121.91 (s), 121.06 (s), 114.60 (s), 108.94 (s), 77.25 (s), 77.00 (s), 76.75 (s), 43.24 (s), 30.03 (s), 20.46 (s), 17.64 (s).

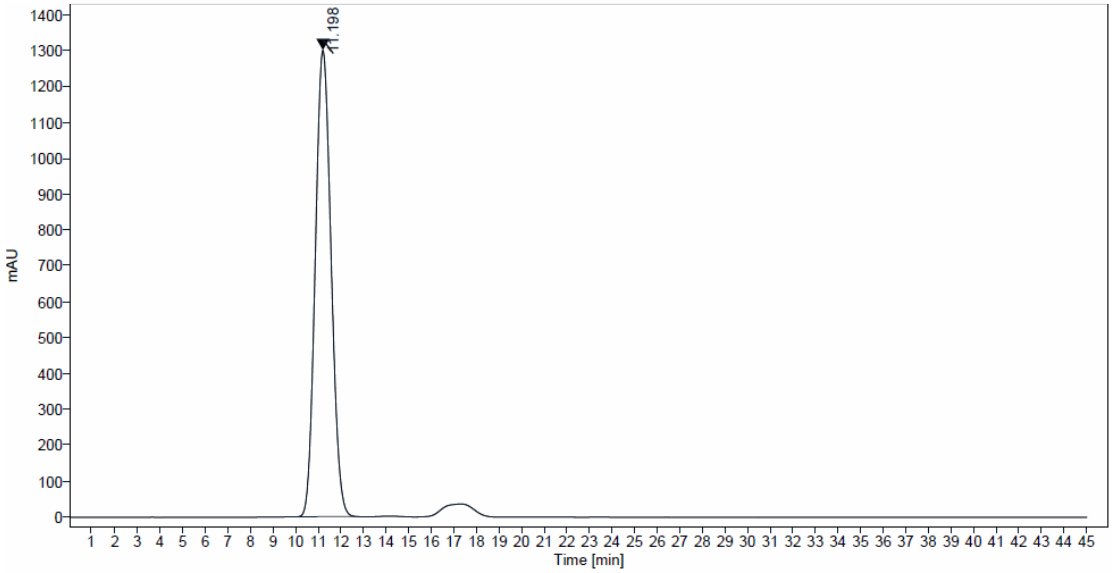
HRMS (ESI) calcd. for $C_{16}H_{16}N_2NaOS$ $[M+Na]^+$: m/z 307.0876, found: 307.0872.



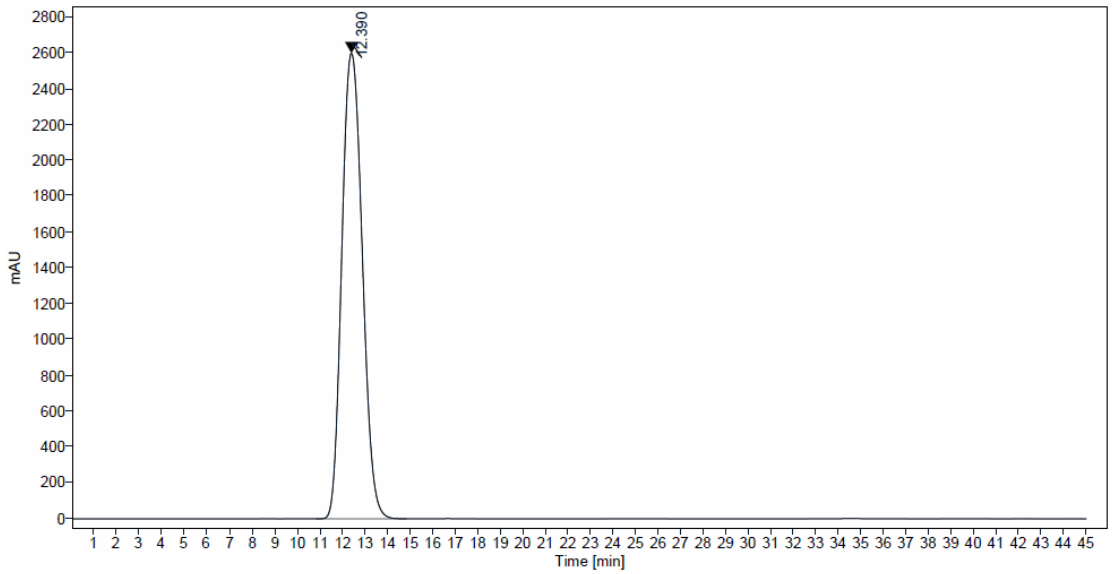


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

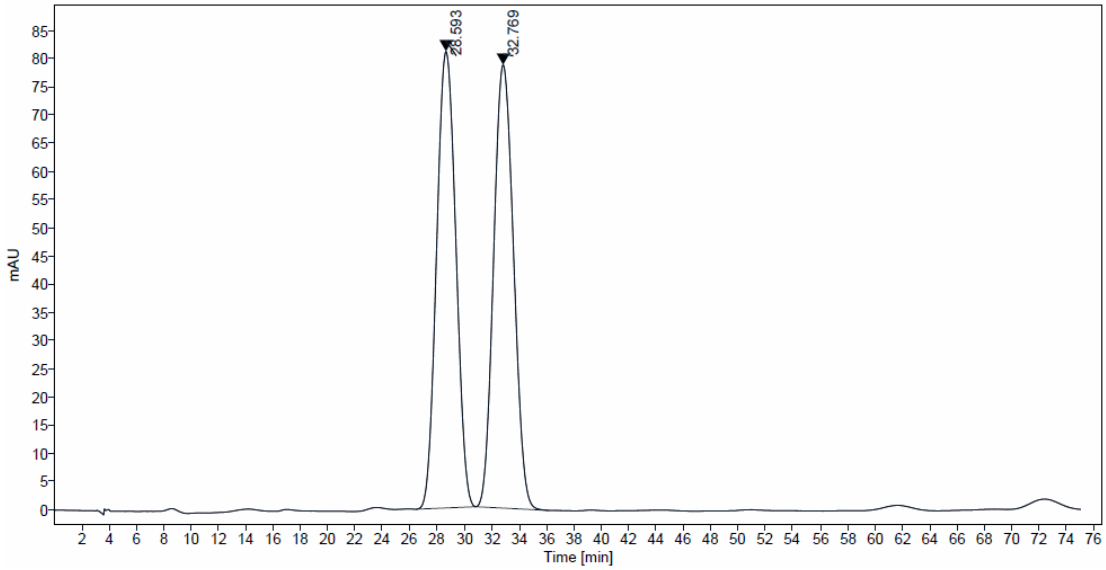
Starting Material (5): Retention time = 11.198 min



4-Me-Indole: Retention time = 12.390 min

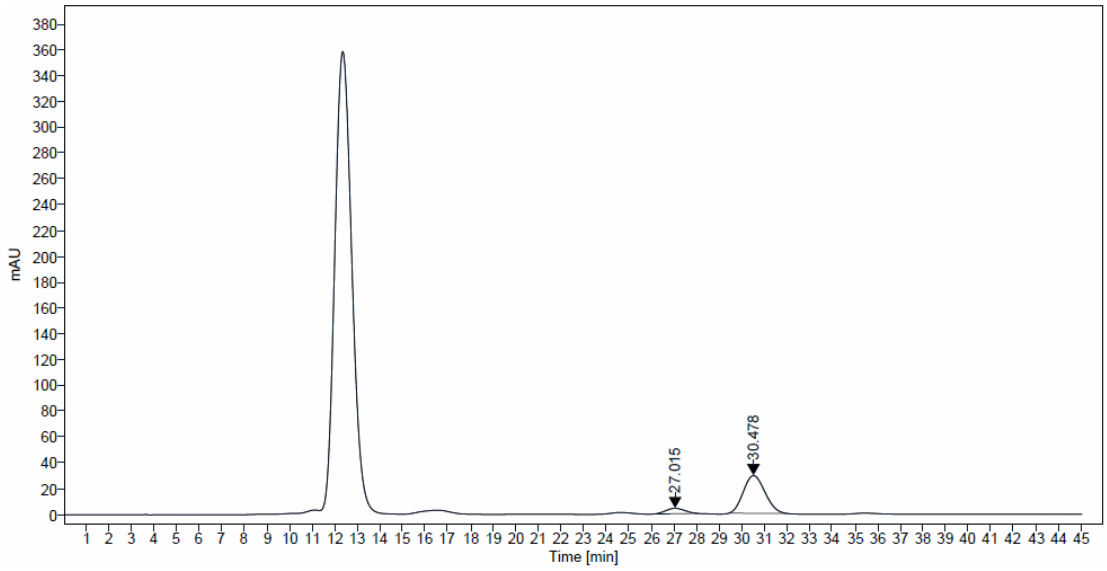


Racemic: Retention time: 28.593 min; 32.769 min

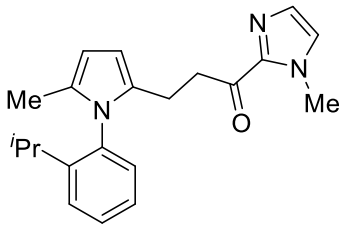


Peak	Retention time (min)	Rel. area (%)
1	28.593	50.3
2	32.769	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**6i** < 1:99 and an enantiomeric excess of 78% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 27.015 min; 30.478 min



Peak	Retention time (min)	Rel. area (%)
1	27.015	11.0
2	30.478	89.0



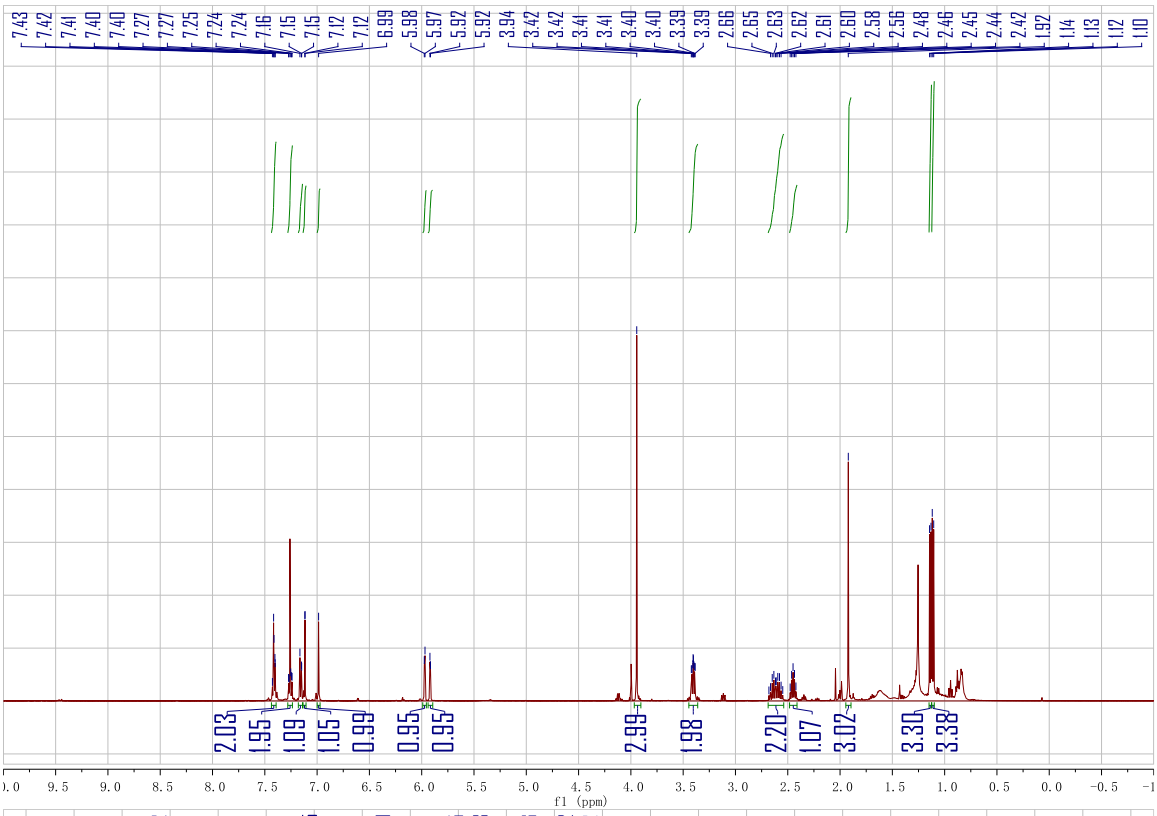
3-(1-(2-isopropylphenyl)-5-methyl-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9a).

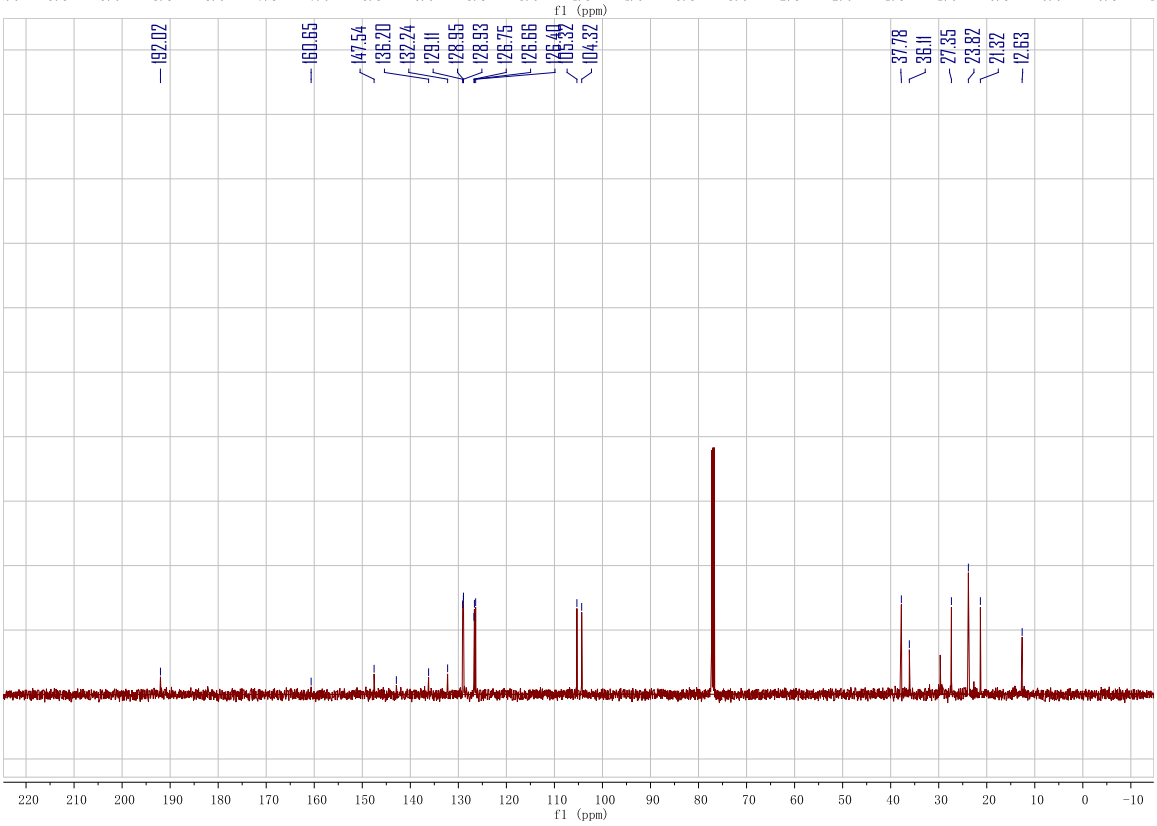
The racemic product was synthesized as described using **7** and 1-(2-isopropylphenyl)-2-methyl-1H-pyrrole. The desired product was obtained as a light-yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 2H), 7.28 – 7.24 (m, 1H), 7.18 – 7.14 (m, 1H), 7.12 (d, *J* = 0.6 Hz, 1H), 6.99 (s, 1H), 5.97 (d, *J* = 3.3 Hz, 1H), 5.92 (d, *J* = 2.7 Hz, 1H), 3.94 (s, 3H), 3.40 (ddd, *J* = 8.4, 6.9, 3.0 Hz, 2H), 2.61 (dtd, *J* = 31.2, 15.7, 7.8 Hz, 2H), 2.45 (dt, *J* = 13.7, 6.9 Hz, 1H), 1.92 (s, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 192.02 (s), 160.65 (s), 147.54 (s), 142.90 (s), 136.20 (s), 132.24 (s), 129.11 (s), 128.95 (s), 128.93 (s), 126.75 (s), 126.66 (s), 126.40 (s), 105.32 (s), 104.32 (s), 37.78 (s), 36.11 (s), 27.35 (s), 23.82 (s), 21.32 (s), 12.63 (s).

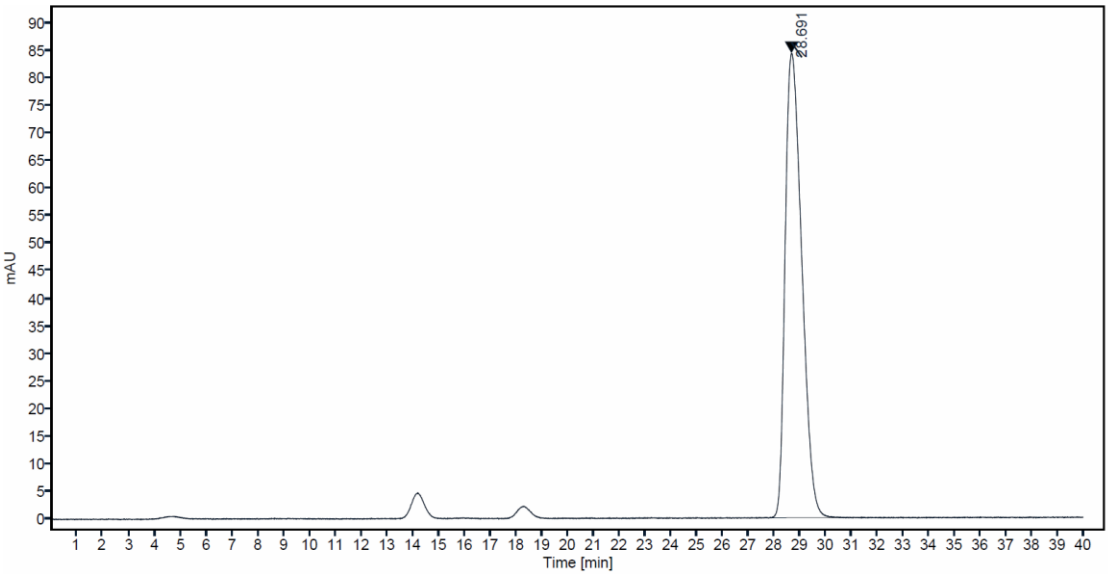
HRMS (ESI) calcd. for $C_{21}H_{26}N_3O$ $[M+H]^+$: m/z 336.2070, found: 336.2074.


7.43
7.42
7.41
7.40
7.40
7.27
7.27
7.25
7.24
7.24
7.16
7.15
7.15
7.12
7.12
6.99
5.98
5.97
5.92
5.92
3.94
3.42
3.42
3.41
3.41
3.40
3.40
3.39
3.39
2.66
2.65
2.63
2.62
2.61
2.60
2.58
2.56
2.48
2.46
2.45
2.44
2.42
1.92
1.14
1.13
1.12
1.10
2.03
1.95
1.09
1.05
0.99
0.95
0.95
2.99
1.98
2.20
1.07
3.02
3.30
3.38
f1 (ppm)

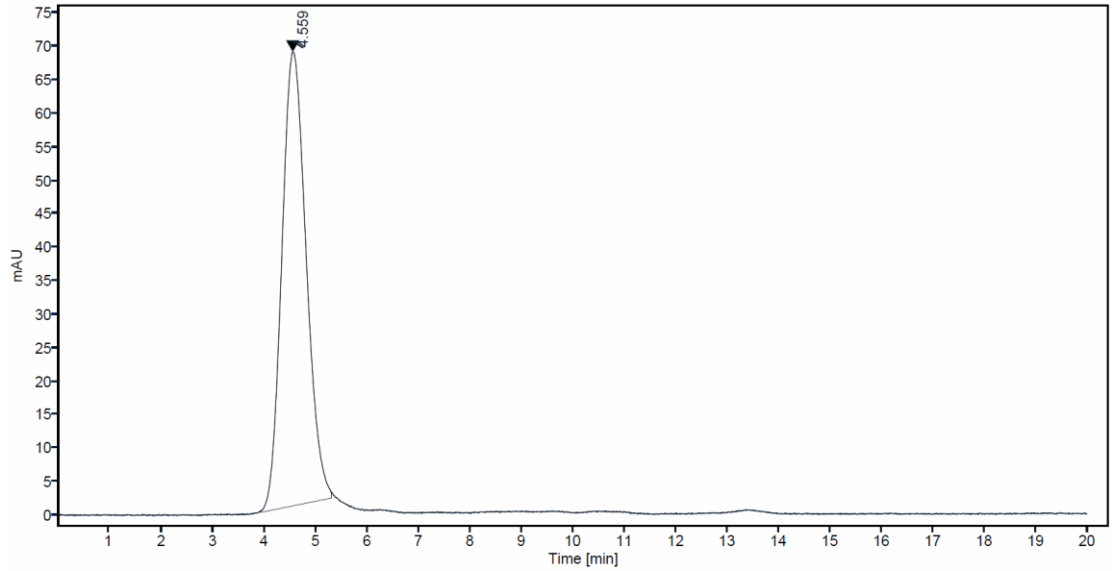

192.02
160.65
147.54
138.20
132.24
129.11
128.95
128.93
126.75
126.66
105.40
104.32
37.78
36.11
27.35
23.82
21.32
12.63
f1 (ppm)

HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 1.0 mL/min, λ = 280 nm

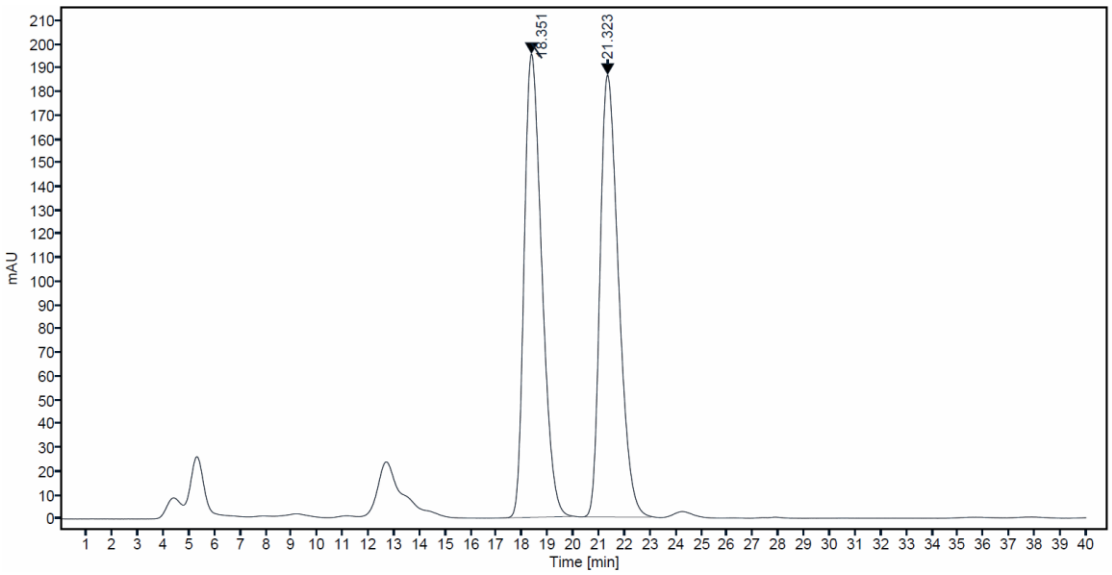
Starting Material (7): Retention time = 28.691 min



1-(2-isopropylphenyl)-2-methyl-1H-pyrrole: Retention time = 4.559 min

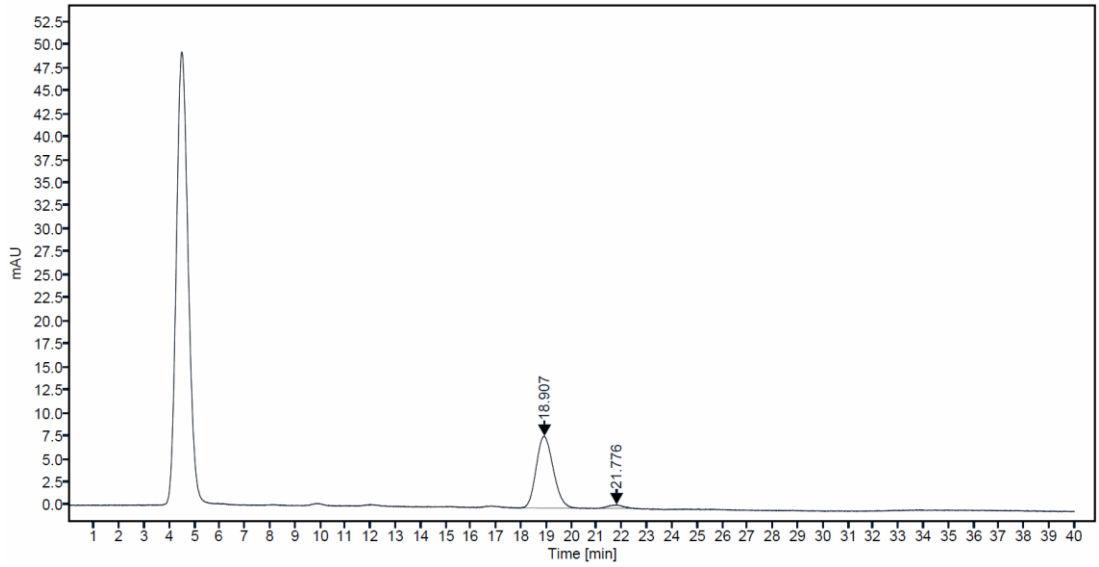


Racemic: Retention time: 18.351 min; 21.323 min

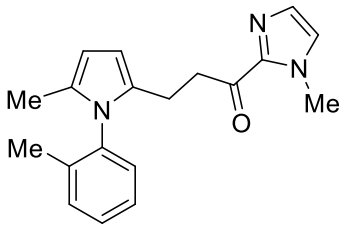


Peak	Retention time (min)	Rel. area (%)
1	18.351	50.1
2	21.323	49.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9a** < 1:99 and an enantiomeric excess of 92% [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 1.0 mL/min, λ = 280 nm]. Retention time: 18.907 min; 21.778 min



Peak	Retention time (min)	Rel. area (%)
1	18.907	95.9
2	21.778	4.1



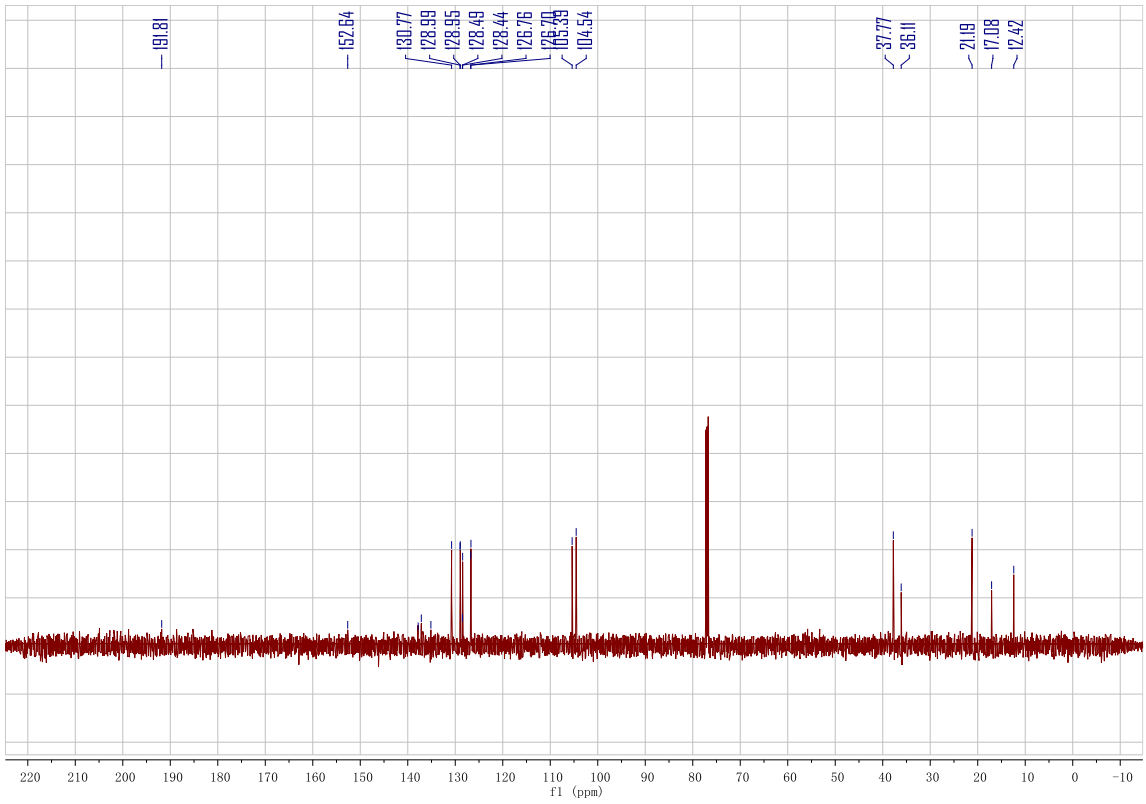
3-(5-methyl-1-(o-tolyl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9b).

The racemic product was synthesized as described using **7** and 2-methyl-1-(o-tolyl)-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.23 (m, 2H), 7.22 – 7.18 (m, 1H), 7.13 (d, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 0.8 Hz, 1H), 6.92 (s, 1H), 5.90 (d, *J* = 3.3 Hz, 1H), 5.85 (d, *J* = 2.6 Hz, 1H), 3.87 (s, 3H), 3.36 – 3.24 (m, 2H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.88 (s, 3H), 1.83 (s, 3H).

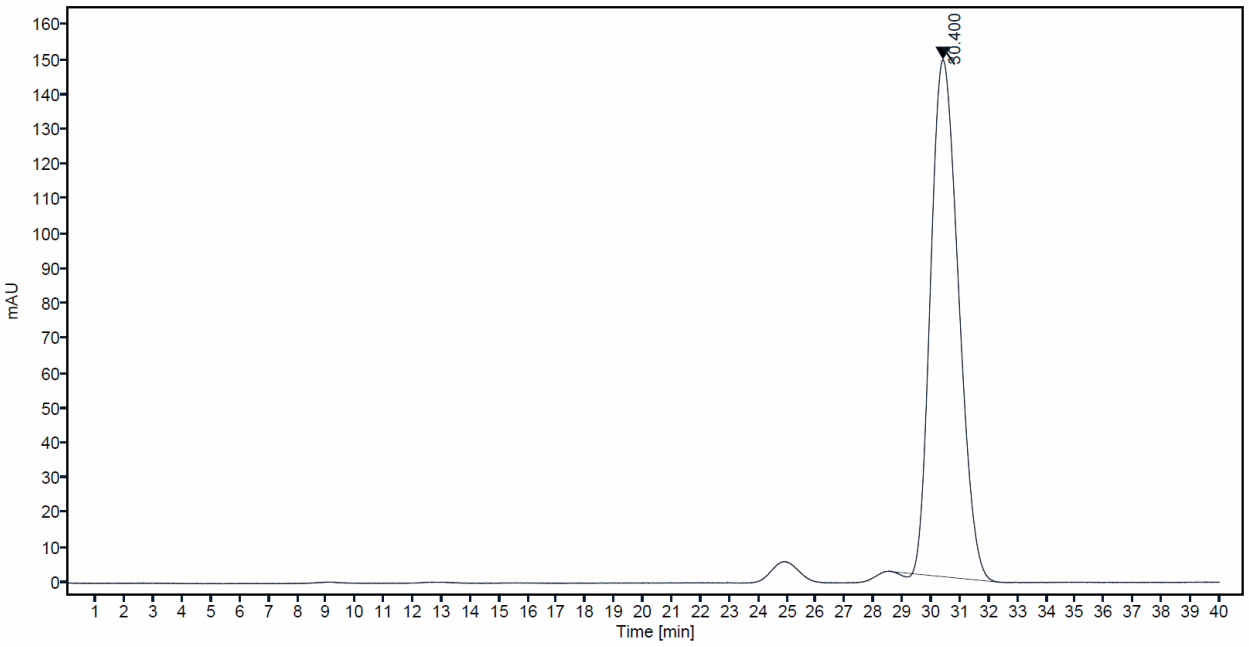
^{13}C NMR (126 MHz, $CDCl_3$) δ 191.81 (s), 152.64 (s), 137.81 (s), 137.15 (s), 135.13 (s), 130.77 (s), 128.99 (s), 128.95 (s), 128.49 (s), 128.44 (s), 126.76 (s), 126.70 (s), 105.39 (s), 104.54 (s), 37.77 (s), 36.11 (s), 21.19 (s), 17.08 (s), 12.42 (s).

HRMS (ESI) calcd. for $C_{19}H_{22}N_3O$ $[M+H]^+$: m/z 308.1757, found: 308.1757.

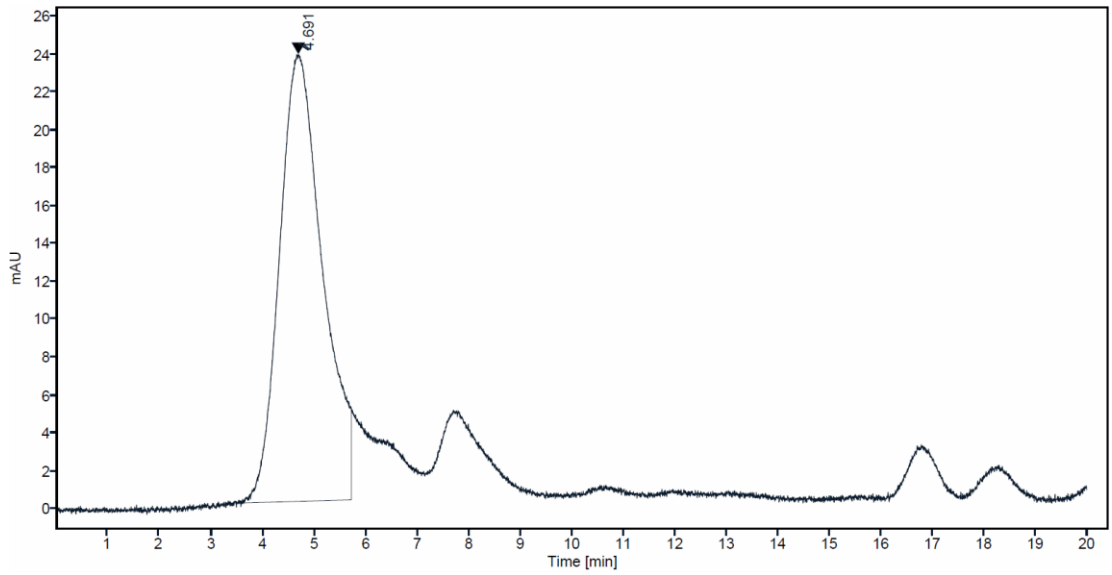


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm

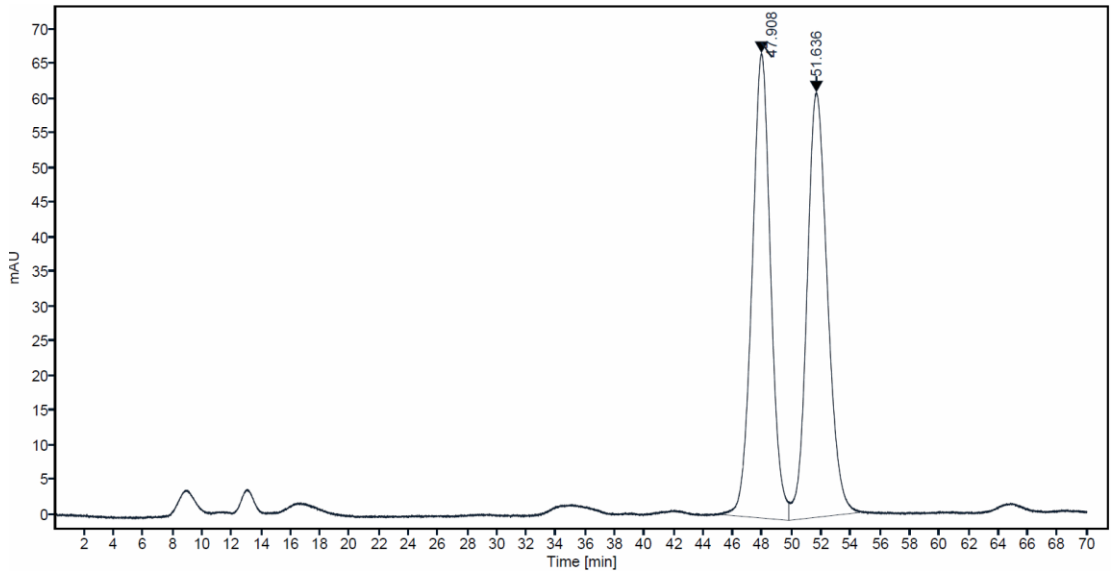
Starting Material (7): Retention time = 30.400 min



2-methyl-1-(o-tolyl)-1H-pyrrole: Retention time = 4.691 min

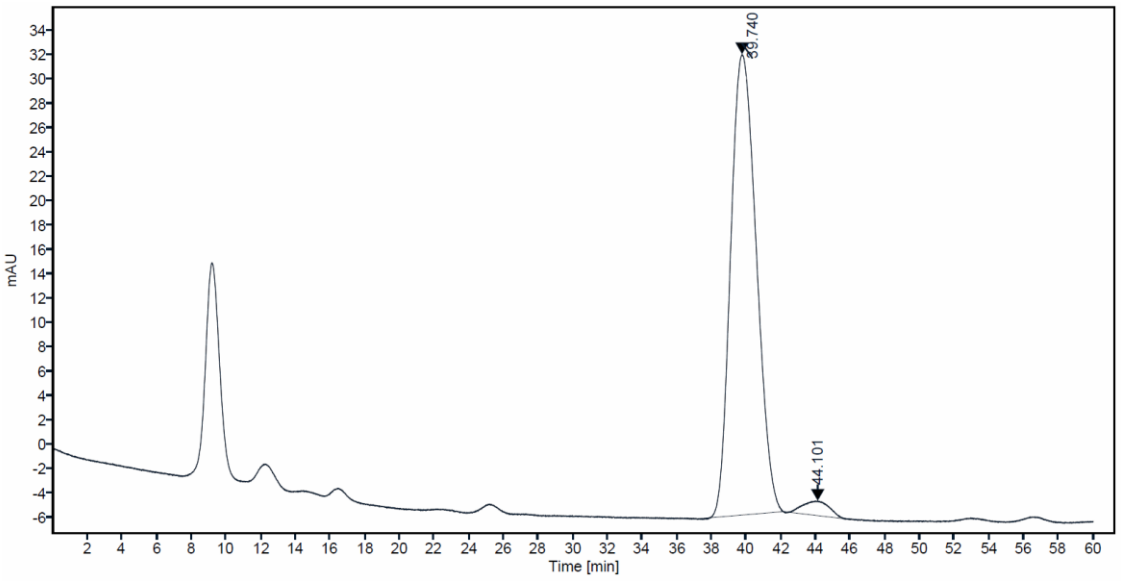


Racemic: Retention time: 47.908 min; 51.636 min

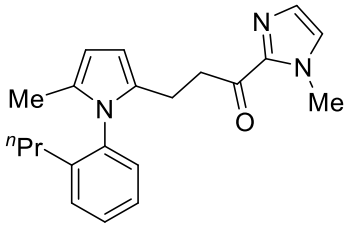


Peak	Retention time (min)	Rel. area (%)
1	47.908	50.3
2	51.636	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9b** as 4:96 and an enantiomeric excess of 94% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 0.5 mL/min, λ = 280 nm]. Retention time: 39.740 min; 40.101 min



Peak	Retention time (min)	Rel. area (%)
1	39.740	97.1
2	44.101	2.9



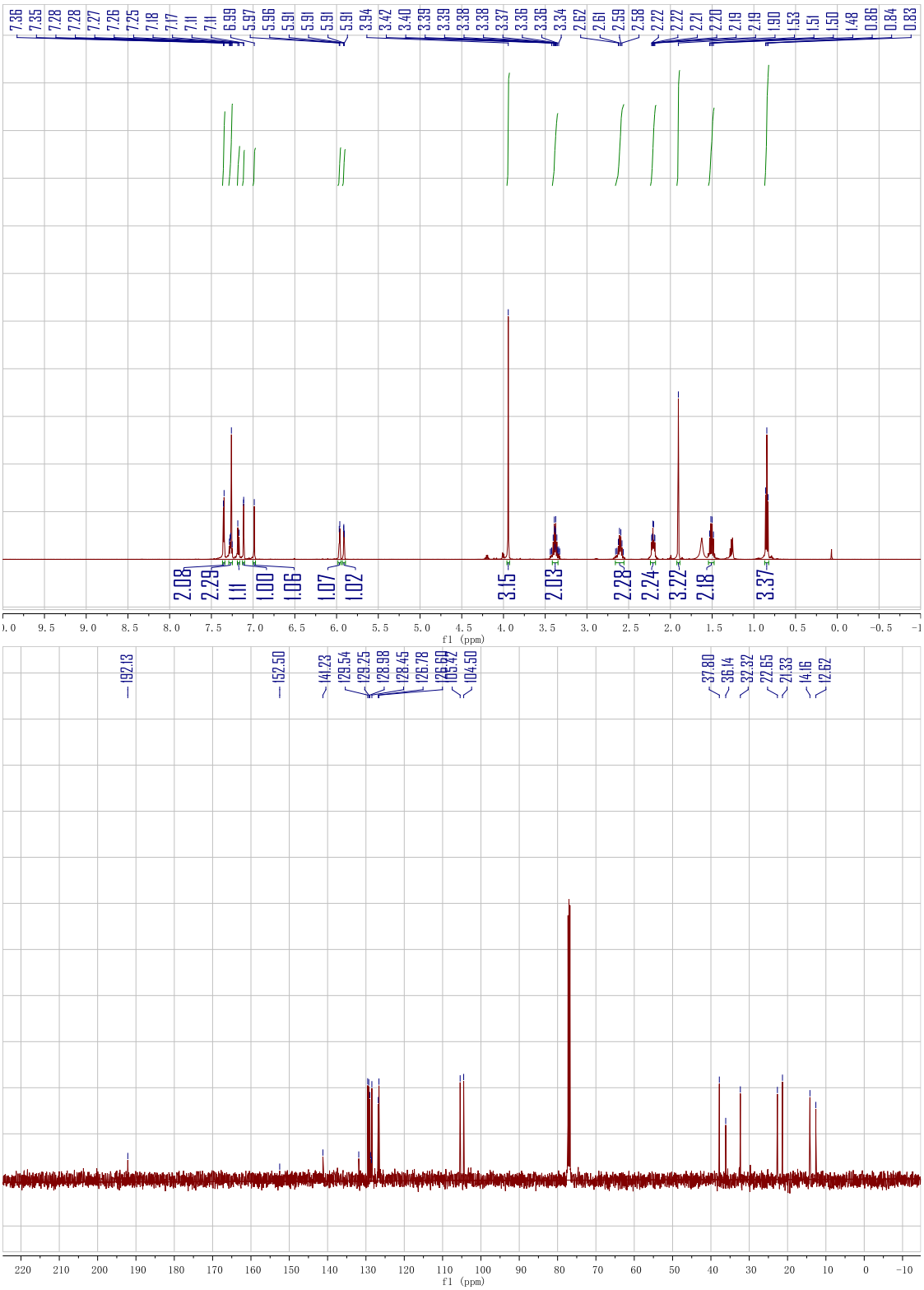
3-(5-methyl-1-(2-propylphenyl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9c).

The racemic product was synthesized as described using **7** and 2-methyl-1-(2-propylphenyl)-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 3.9 Hz, 2H), 7.29 – 7.25 (m, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.11 (d, J = 0.8 Hz, 1H), 6.99 (s, 1H), 5.96 (d, J = 3.3 Hz, 1H), 5.91 (dd, J = 3.3, 0.7 Hz, 1H), 3.94 (s, 3H), 3.41 – 3.35 (m, 2H), 2.66 – 2.56 (m, 2H), 2.21 (td, J = 7.6, 3.5 Hz, 2H), 1.90 (s, 3H), 1.51 (dd, J = 15.4, 7.5 Hz, 2H), 0.84 (t, J = 7.3 Hz, 3H).

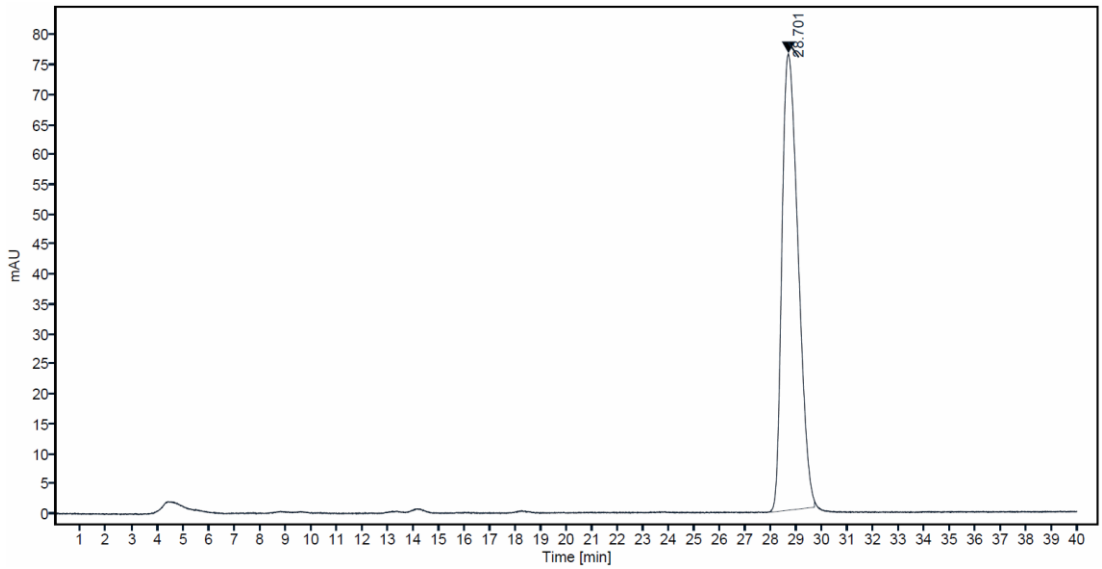
^{13}C NMR (126 MHz, CDCl3) δ 192.13 (s), 152.50 (s), 141.23 (s), 131.87 (s), 129.54 (s), 129.25 (s), 128.98 (s), 128.80 (s), 128.56 (s), 128.45 (s), 126.78 (s), 126.60 (s), 105.42 (s), 104.50 (s), 37.80 (s), 36.14 (s), 32.32 (s), 22.65 (s), 21.33 (s), 14.16 (s), 12.62 (s).

HRMS (ESI) calcd. for $C_{21}H_{26}N_3O$ $[M+H]^+$: m/z 336.2070, found: 336.2062.

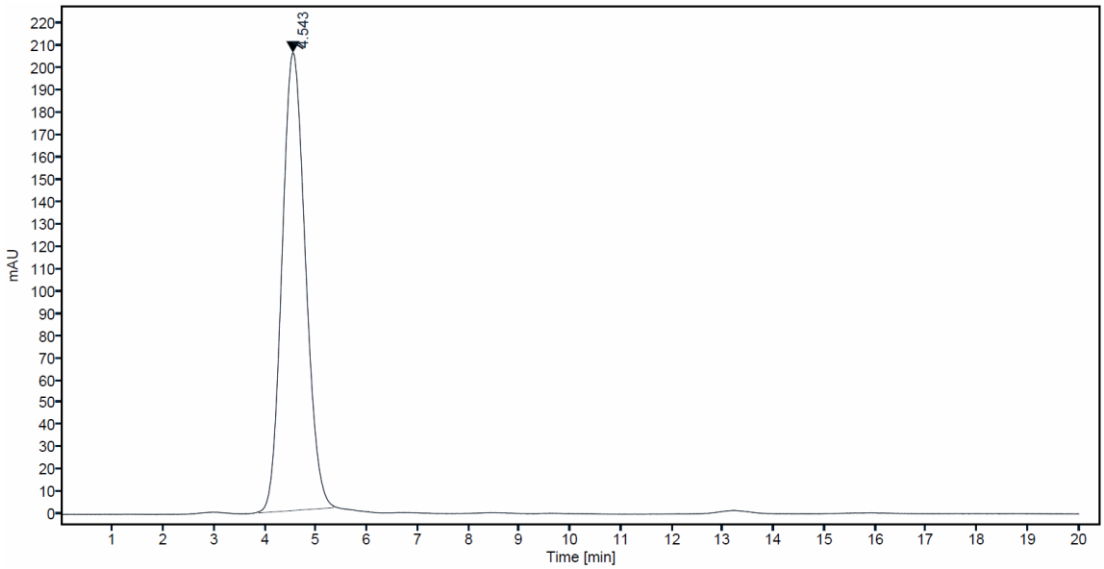


HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 1.0 mL/min, λ = 280 nm

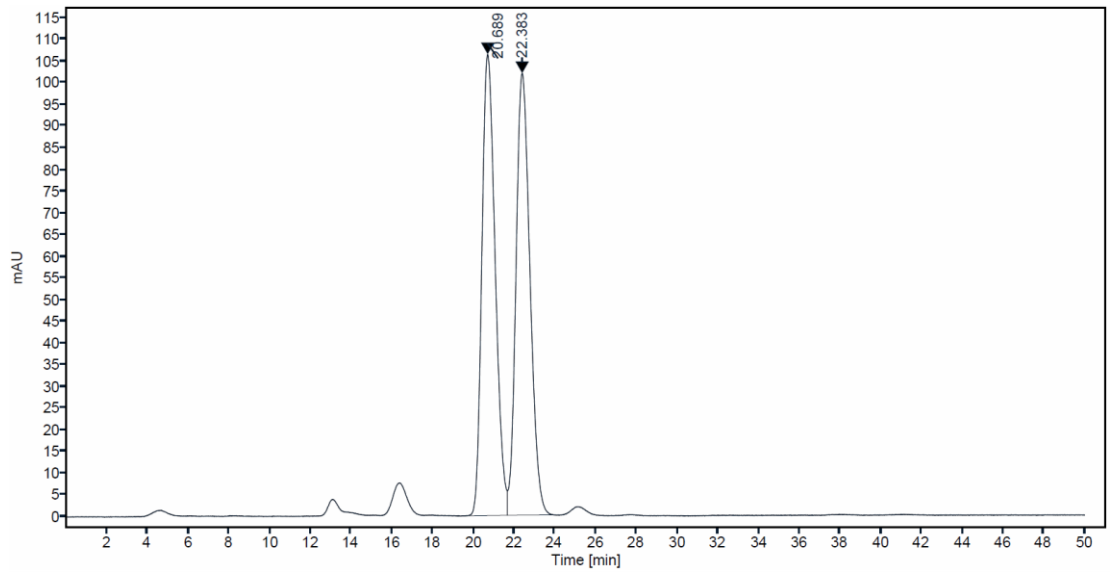
Starting Material (7): Retention time = 28.701 min



2-methyl-1-(2-propylphenyl)-1H-pyrrole: Retention time = 4.543 min

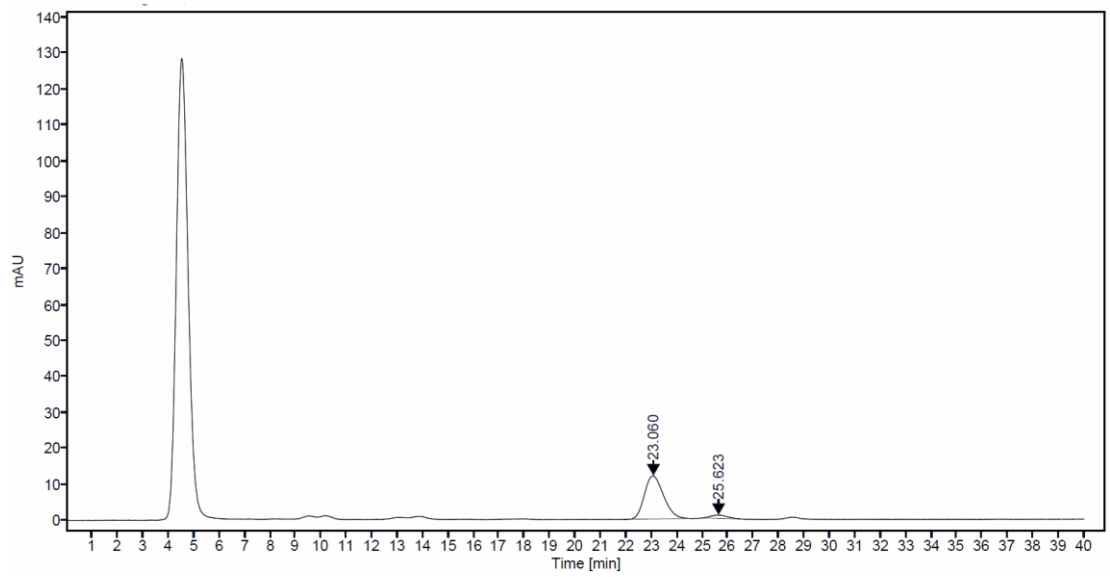


Racemic: Retention time: 20.689 min; 22.383 min

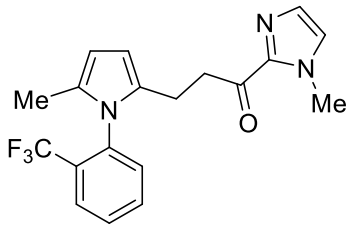


Peak	Retention time (min)	Rel. area (%)
1	20.699	50.3
2	22.383	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9c** as 4:96 and an enantiomeric excess of 88% [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 98:02, 1.0 mL/min, λ = 280 nm]. Retention time: 23.060 min; 25.623 min



Peak	Retention time (min)	Rel. area (%)
1	23.060	94.1
2	25.623	5.9



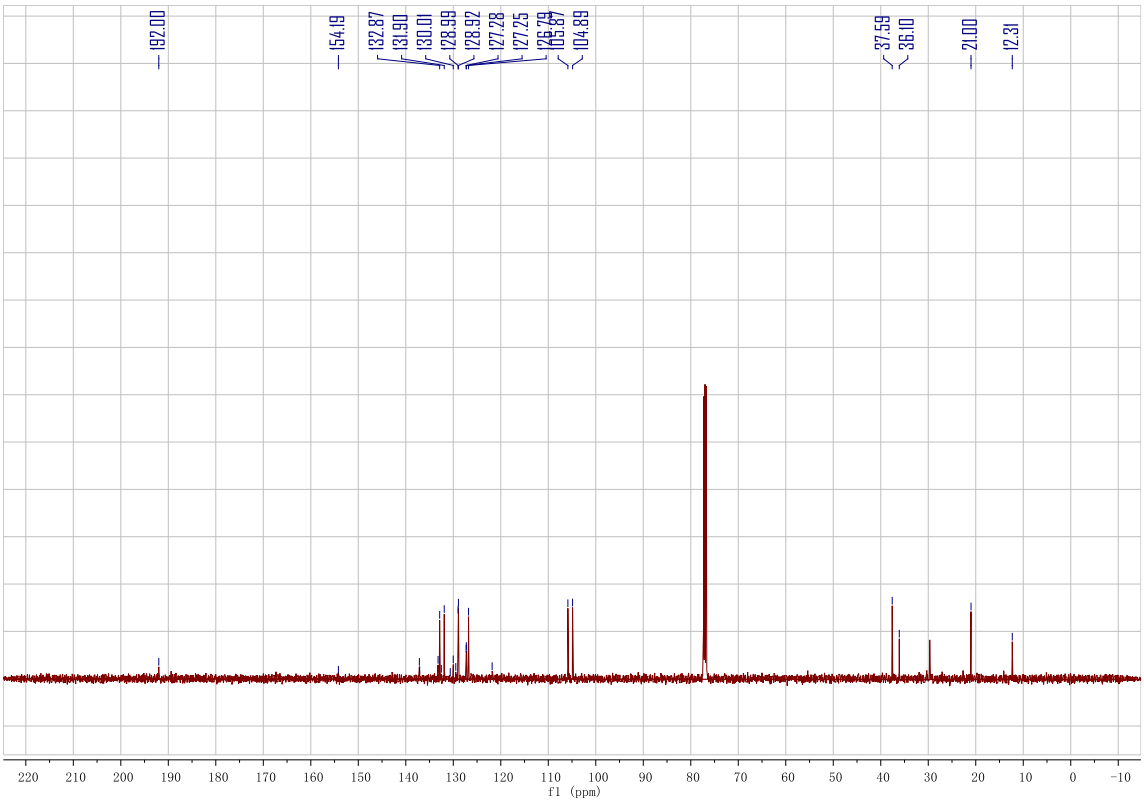
3-(5-methyl-1-(2-(trifluoromethyl)phenyl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9d).

The racemic product was synthesized as described using **7** and 2-methyl-1-(2-(trifluoromethyl) phenyl)-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 40:60).

^{1}H NMR (400 MHz, CDCl3) δ 7.81 (d, J = 7.8 Hz, 1H), 7.67 (t, J = 7.1 Hz, 1H), 7.57 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 7.7 Hz, 1H), 7.12 (d, J = 0.8 Hz, 1H), 6.99 (s, 1H), 5.98 (d, J = 3.4 Hz, 1H), 5.92 (d, J = 2.6 Hz, 1H), 3.94 (s, 3H), 3.41 (dt, J = 8.7, 6.3 Hz, 2H), 2.72 – 2.62 (m, 1H), 2.57 – 2.47 (m, 1H), 1.90 (s, 3H).

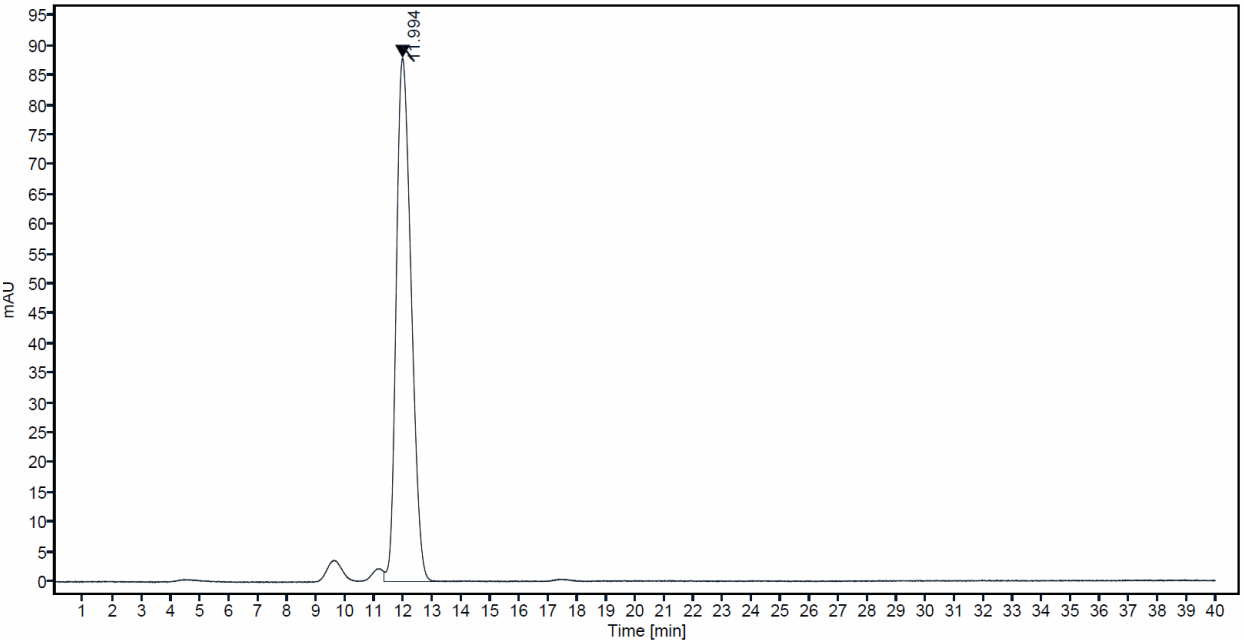
^{13}C NMR (126 MHz, $CDCl_3$) δ 192.00 (s), 154.19 (s), 137.11 (d, J = 8.3 Hz), 133.21 (s), 132.87 (s), 131.90 (s), 131.58 (q, J = 236.3 Hz), 130.01 (s), 128.99 (s), 128.92 (s), 127.27 (d, J = 4.8 Hz), 126.79 (s), 121.82 (s), 105.87 (s), 104.89 (s), 37.59 (s), 36.10 (s), 21.00 (s), 12.31 (s).

HRMS (ESI) calcd. for $C_{19}H_{19}F_3N_3O$ $[M+H]^+$: m/z 362.1475, found: 362.1476.

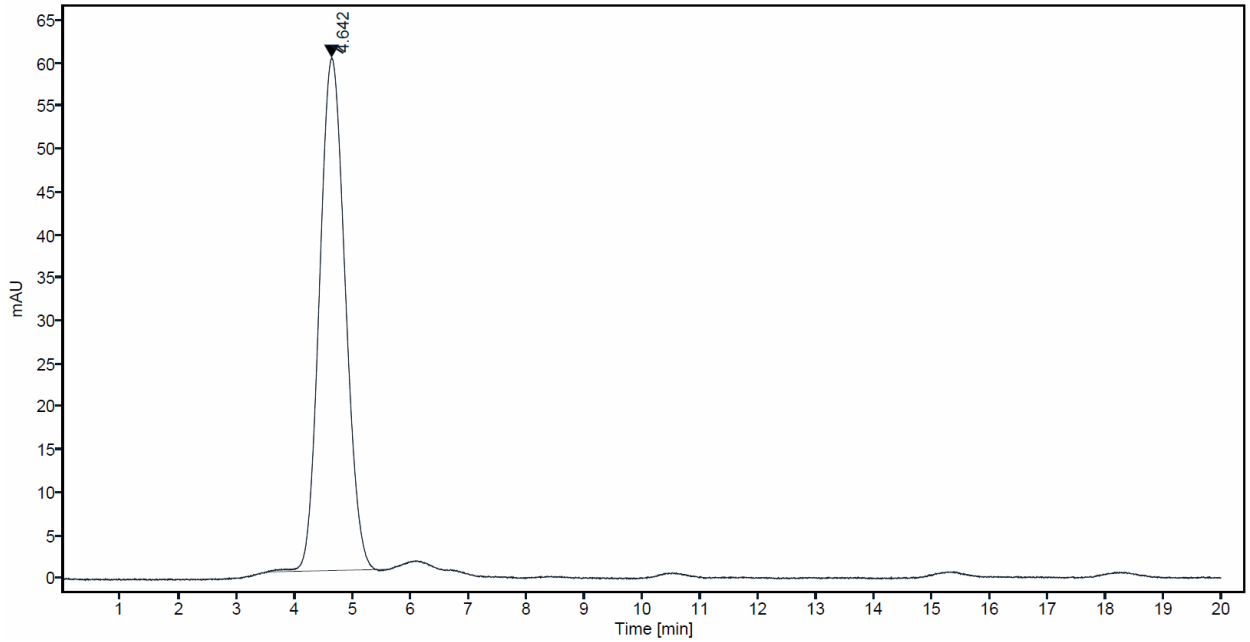


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm

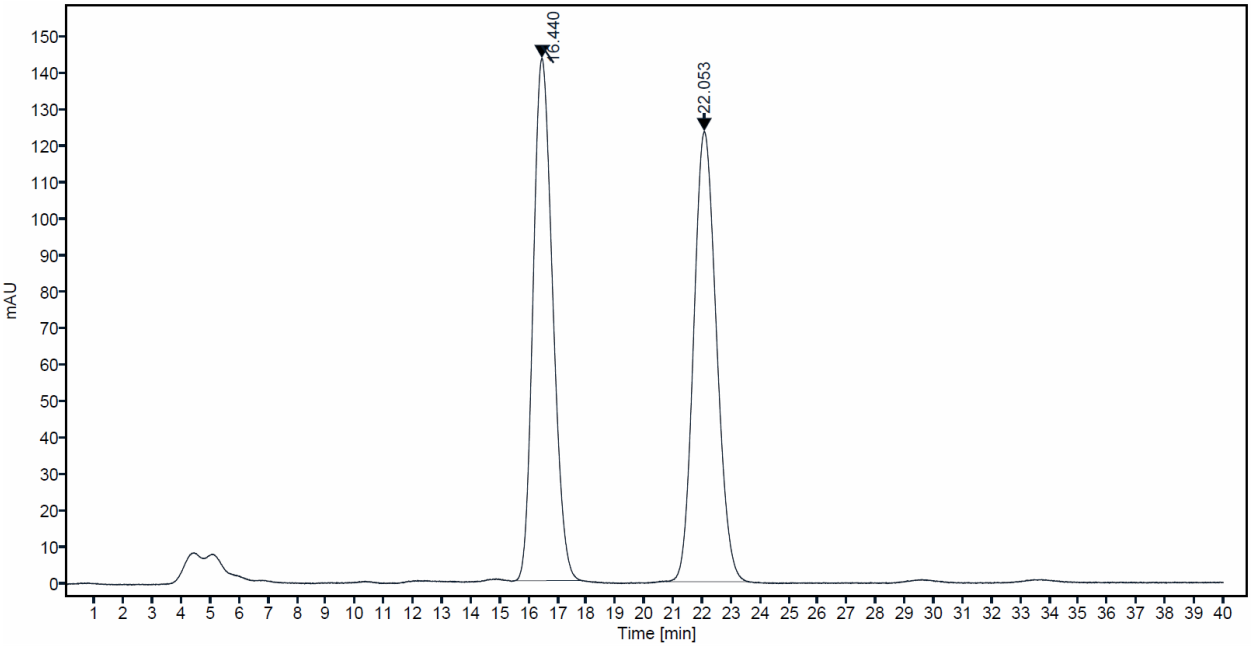
Starting Material (7): Retention time = 11.994 min



2-methyl-1-(2-(trifluoromethyl) phenyl)-1H-pyrrole: Retention time = 4.642 min

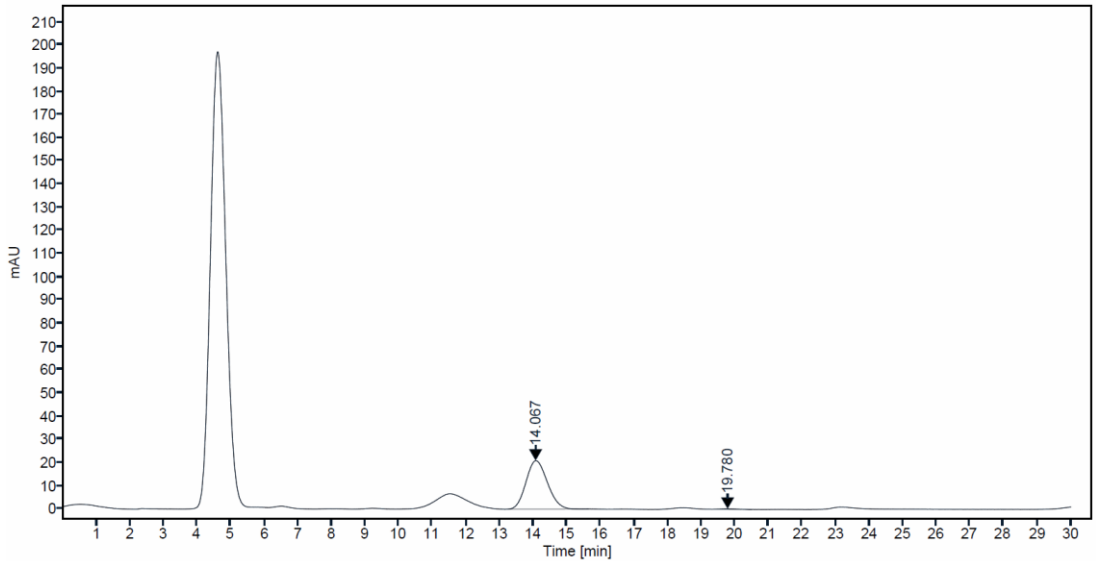


Racemic: Retention time: 16.440 min; 22.053 min

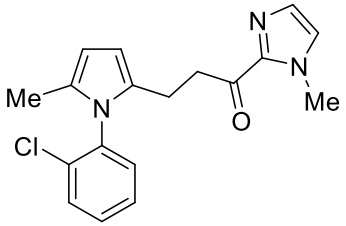


Peak	Retention time (min)	Rel. area (%)
1	16.440	50.5
2	22.053	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9d** as 26:74 and an enantiomeric excess of 97% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm]. Retention time: 14.067 min; 19.780 min



Peak	Retention time (min)	Rel. area (%)
1	14.067	98.5
2	19.780	1.5



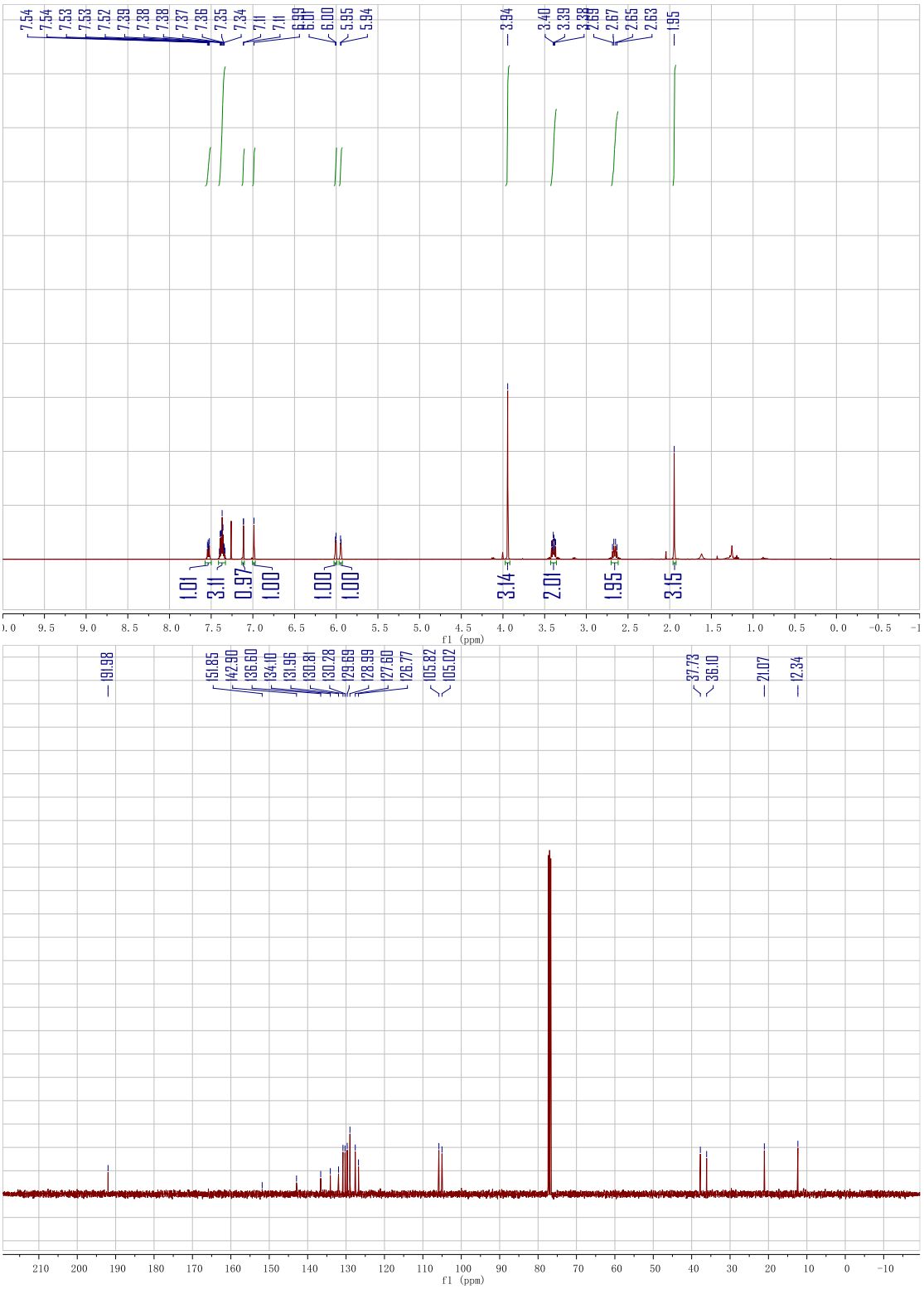
3-(1-(2-chlorophenyl)-5-methyl-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9e).

The racemic product was synthesized as described using **7** and 1-(2-chlorophenyl)-2-methyl-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.50 (m, 1H), 7.41 – 7.33 (m, 3H), 7.11 (d, J = 0.5 Hz, 1H), 6.99 (s, 1H), 6.01 (d, J = 3.3 Hz, 1H), 5.94 (d, J = 2.8 Hz, 1H), 3.94 (s, 3H), 3.39 (ddd, J = 8.1, 5.6, 4.0 Hz, 2H), 2.66 (dd, J = 15.0, 6.7 Hz, 2H), 1.95 (s, 3H).

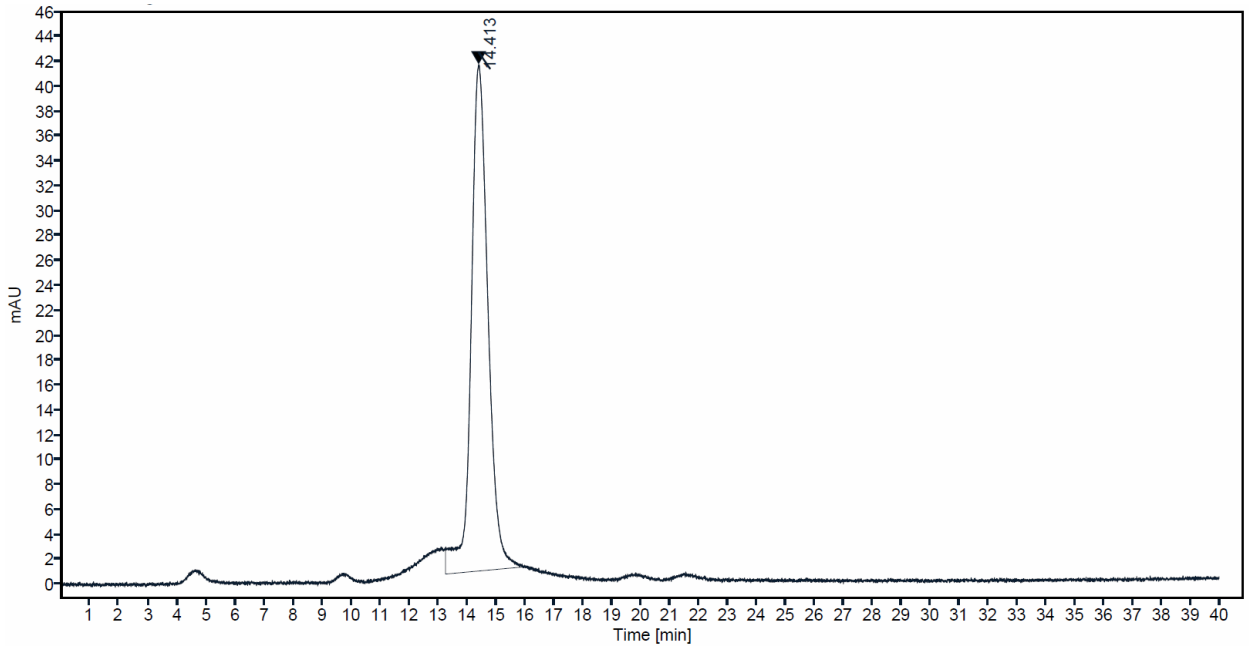
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.98 (s), 151.85 (s), 142.90 (s), 136.60 (s), 134.10 (s), 131.96 (s), 130.81 (s), 130.28 (s), 129.69 (s), 128.99 (s), 127.60 (s), 126.77 (s), 105.82 (s), 105.02 (s), 37.73 (s), 36.10 (s), 21.07 (s), 12.34 (s).

HRMS (ESI) calcd. for $C_{18}H_{19}ClN_3O$ $[M+H]^+$: m/z 328.1211, found: 328.1217.

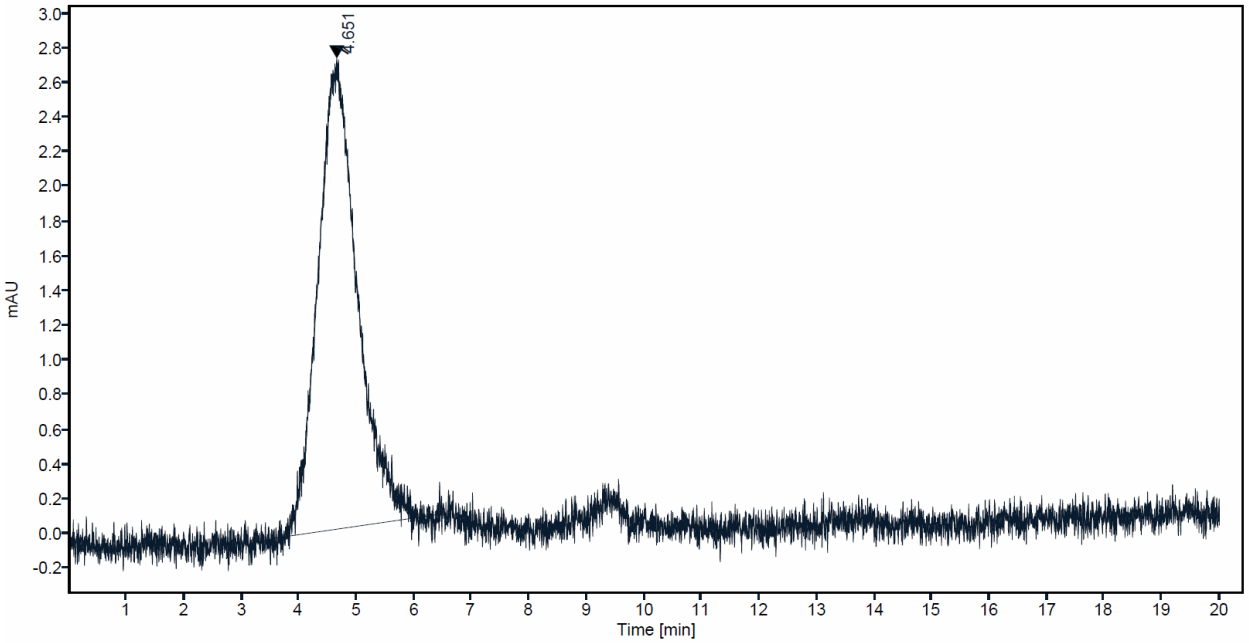


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm

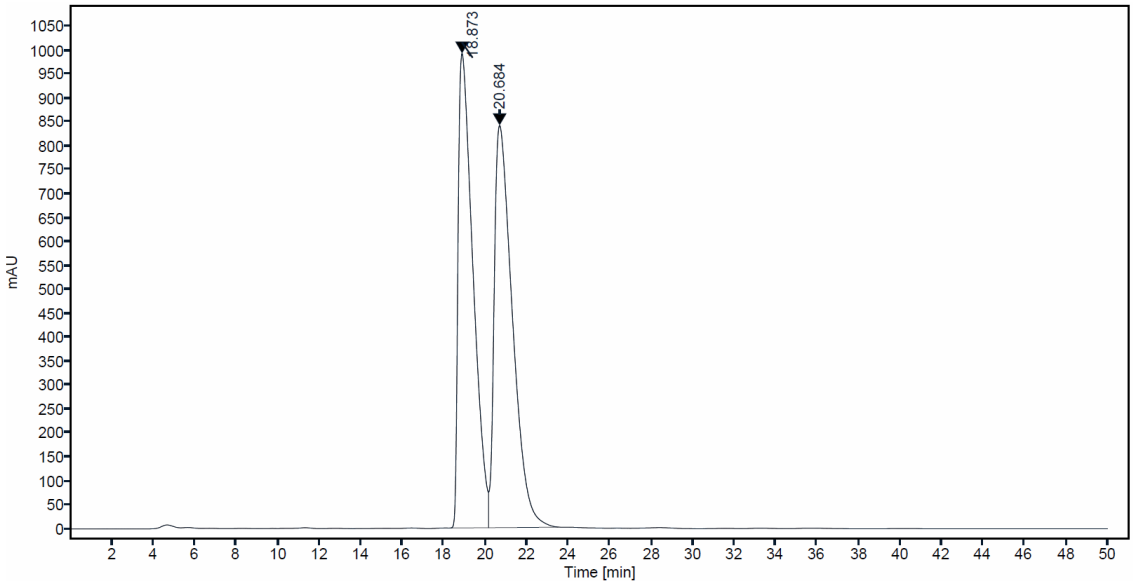
Starting Material (7): Retention time = 14.413 min



1-(2-chlorophenyl)-2-methyl-1H-pyrrole: Retention time = 4.651 min

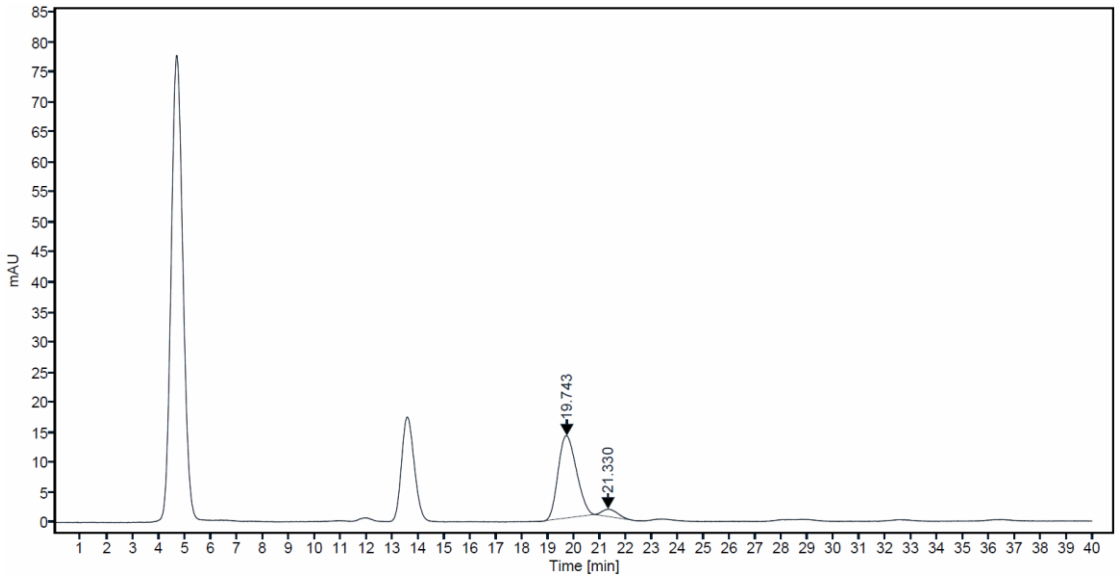


Racemic: Retention time: 18.873 min; 20.684min

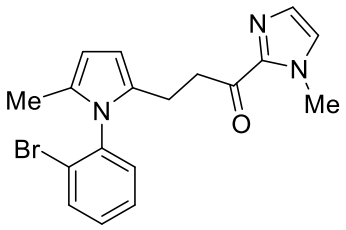


Peak	Retention time (min)	Rel. area (%)
1	18.873	50.5
2	20.684	49.5

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9e** as 32:68 and an enantiomeric excess of 86% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm]. Retention time: 14.067 min; 19.780 min



Peak	Retention time (min)	Rel. area (%)
1	19.743	93.1
2	21.330	6.9



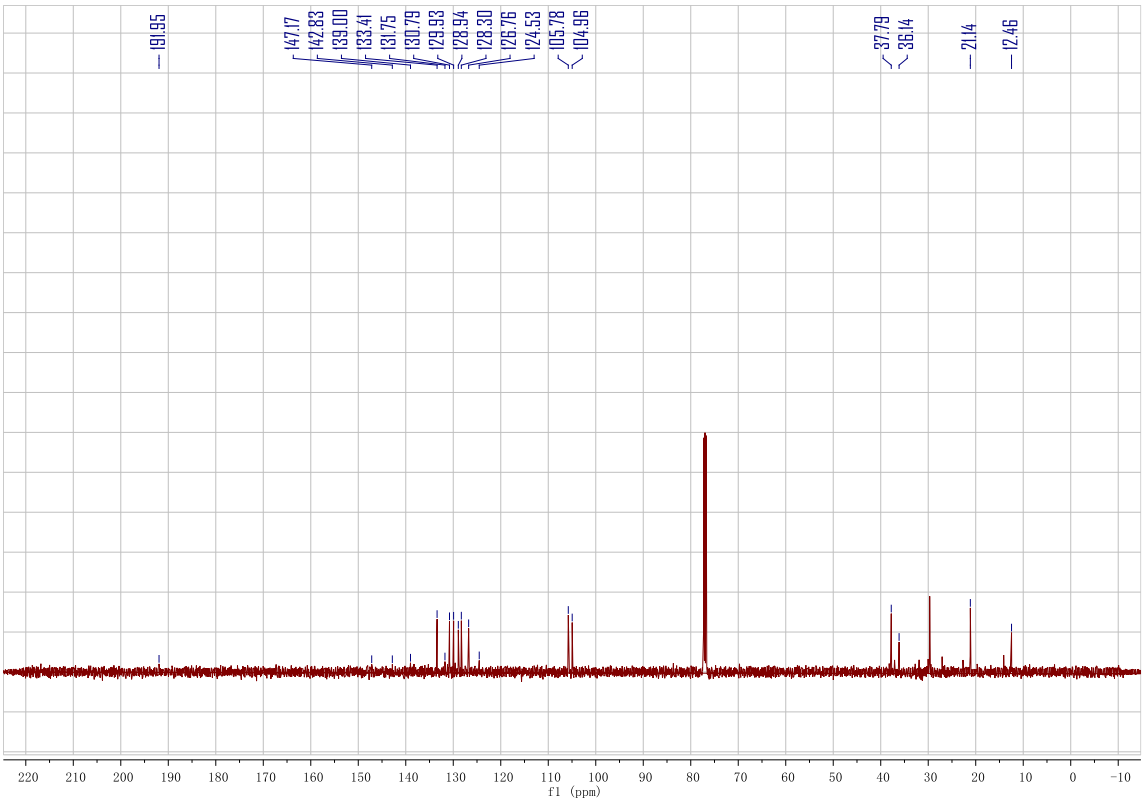
3-(1-(2-bromophenyl)-5-methyl-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9f).

The racemic product was synthesized as described using **7** and 1-(2-bromophenyl)-2-methyl-1H-pyrrole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, CDCl3) δ 7.73 (dd, J = 8.0, 1.2 Hz, 1H), 7.45 (td, J = 7.6, 1.3 Hz, 1H), 7.38 (dd, J = 7.8, 1.6 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.15 (s, 1H), 7.01 (s, 1H), 6.03 (d, J = 3.3 Hz, 1H), 5.97 (d, J = 2.7 Hz, 1H), 3.97 (s, 3H), 3.43 (ddd, J = 8.5, 6.8, 4.7 Hz, 2H), 2.75 – 2.61 (m, 2H), 1.97 (s, 3H).

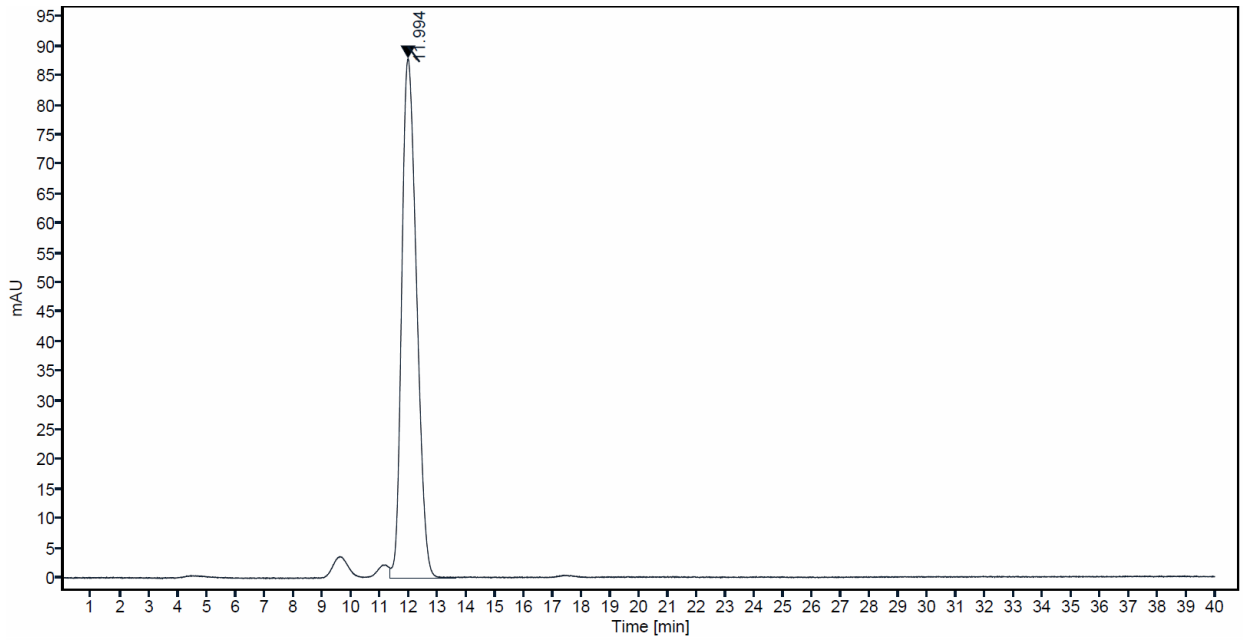
^{13}C NMR (126 MHz, CDCl3) δ 191.95 (s), 147.17 (s), 142.83 (s), 139.00 (s), 133.41 (s), 131.75 (s), 130.79 (s), 129.93 (s), 128.94 (s), 128.30 (s), 126.76 (s), 124.53 (s), 105.78 (s), 104.96 (s), 37.79 (s), 36.14 (s), 21.14 (s), 12.46 (s).

HRMS (ESI) calcd. for $C_{18}H_{17}BrN_3O$ $[M+H]^+$: m/z 370.0550, found: 370.0556.

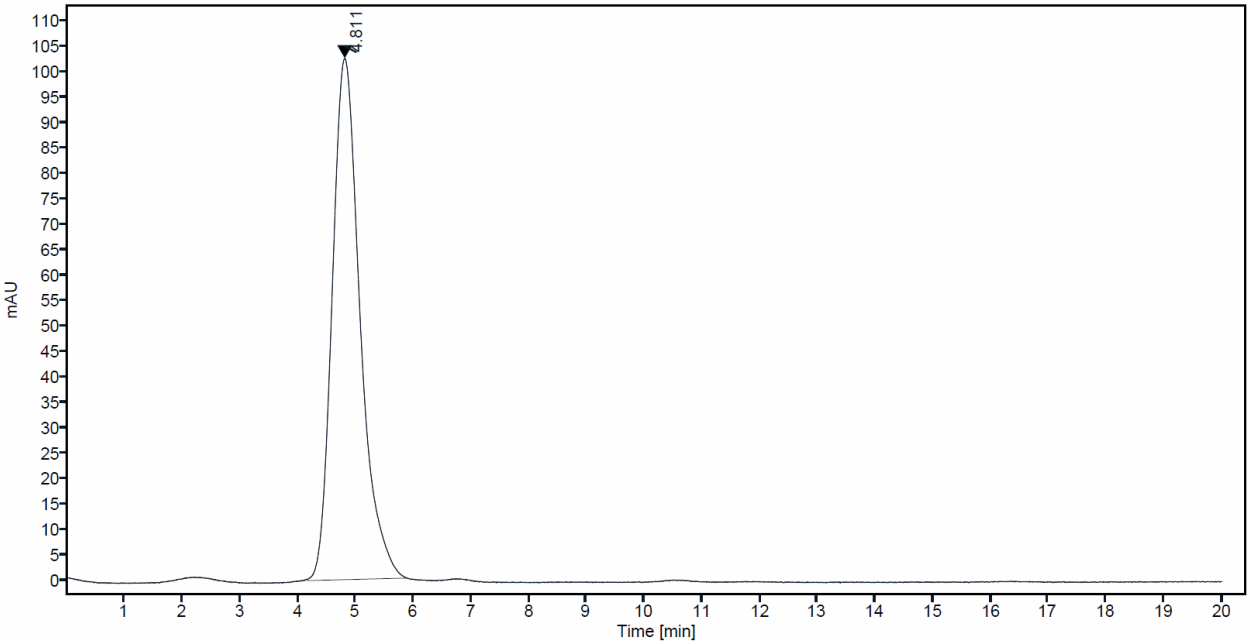


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm

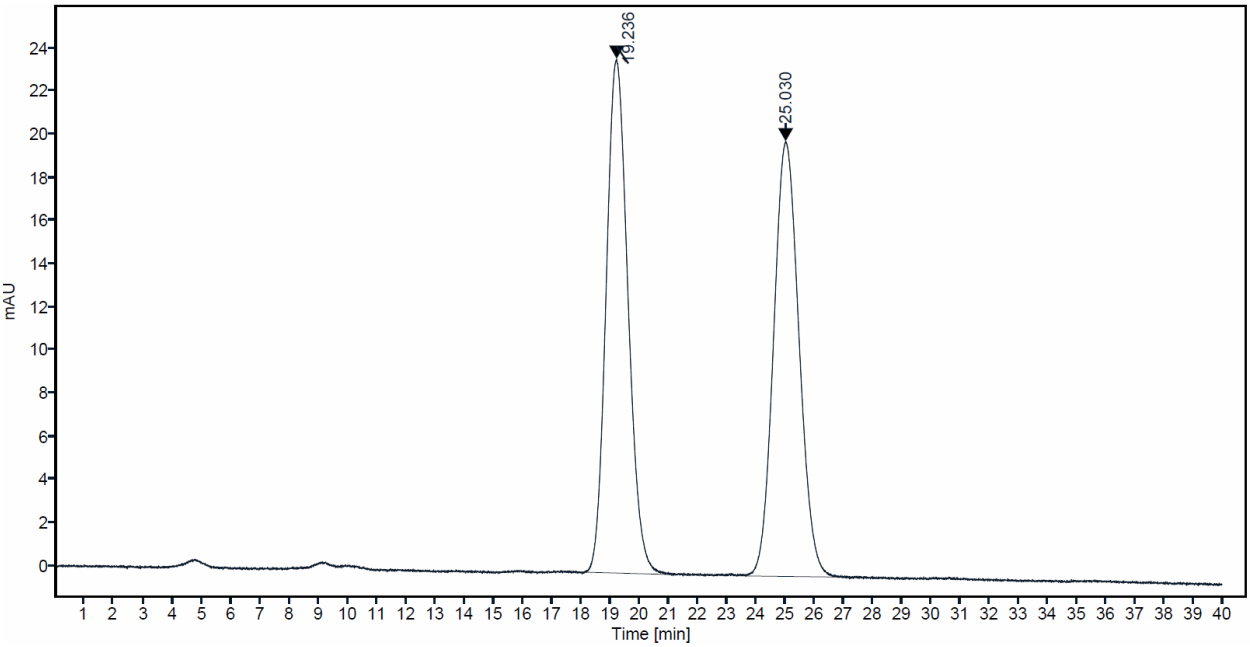
Starting Material (7): Retention time = 11.994 min



1-(2-bromophenyl)-2-methyl-1H-pyrrole: Retention time = 4.811 min

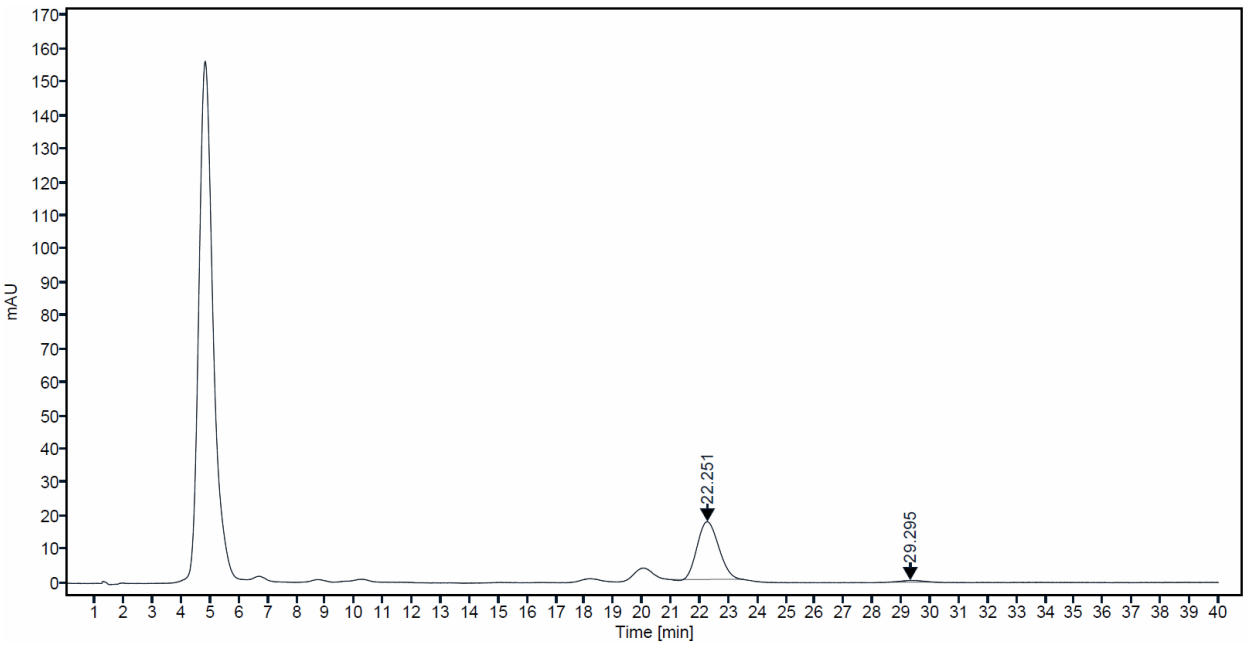


Racemic: Retention time: 19.236 min; 25.030 min

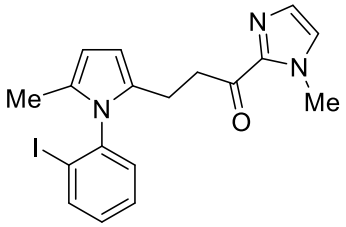


Peak	Retention time (min)	Rel. area (%)
1	19.236	50.3
2	25.030	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9f** as 3:97 and an enantiomeric excess of 90 % [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm]. Retention time: 22.251 min; 29.295 min



Peak	Retention time (min)	Rel. area (%)
1	22.251	94.9
2	29.295	5.1



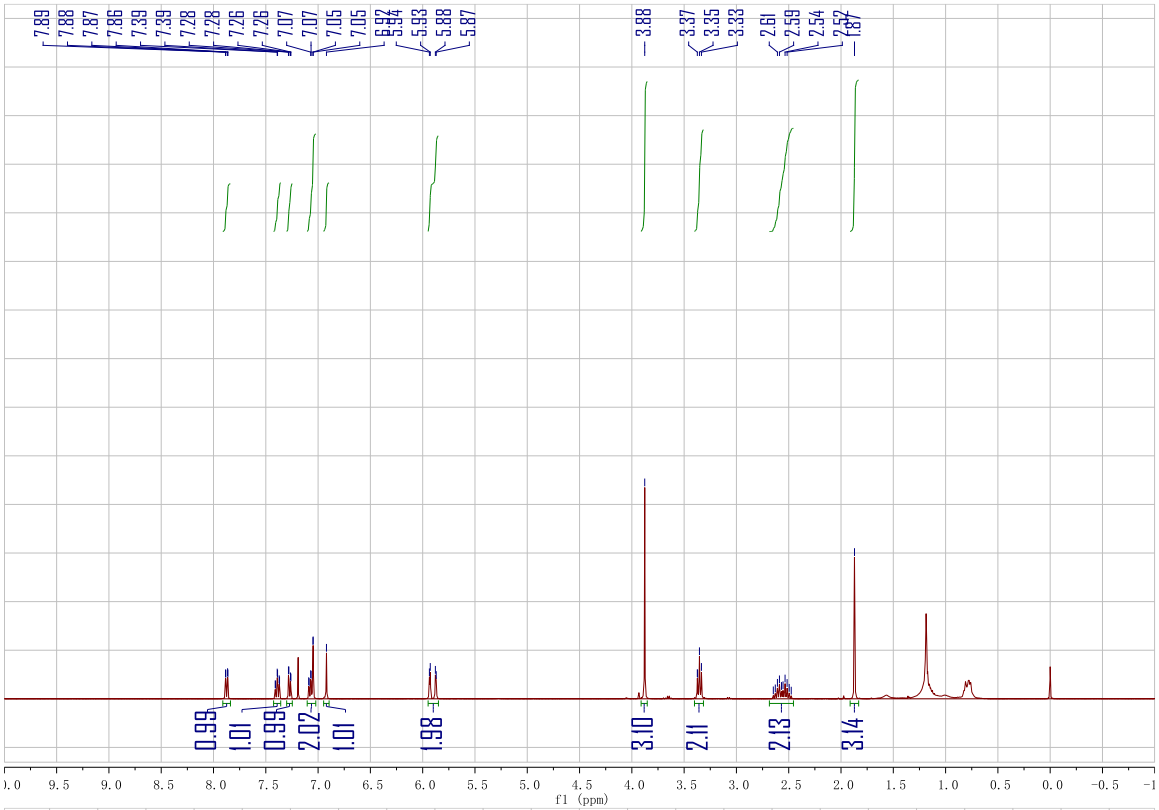
3-(1-(2-iodophenyl)-5-methyl-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9g).

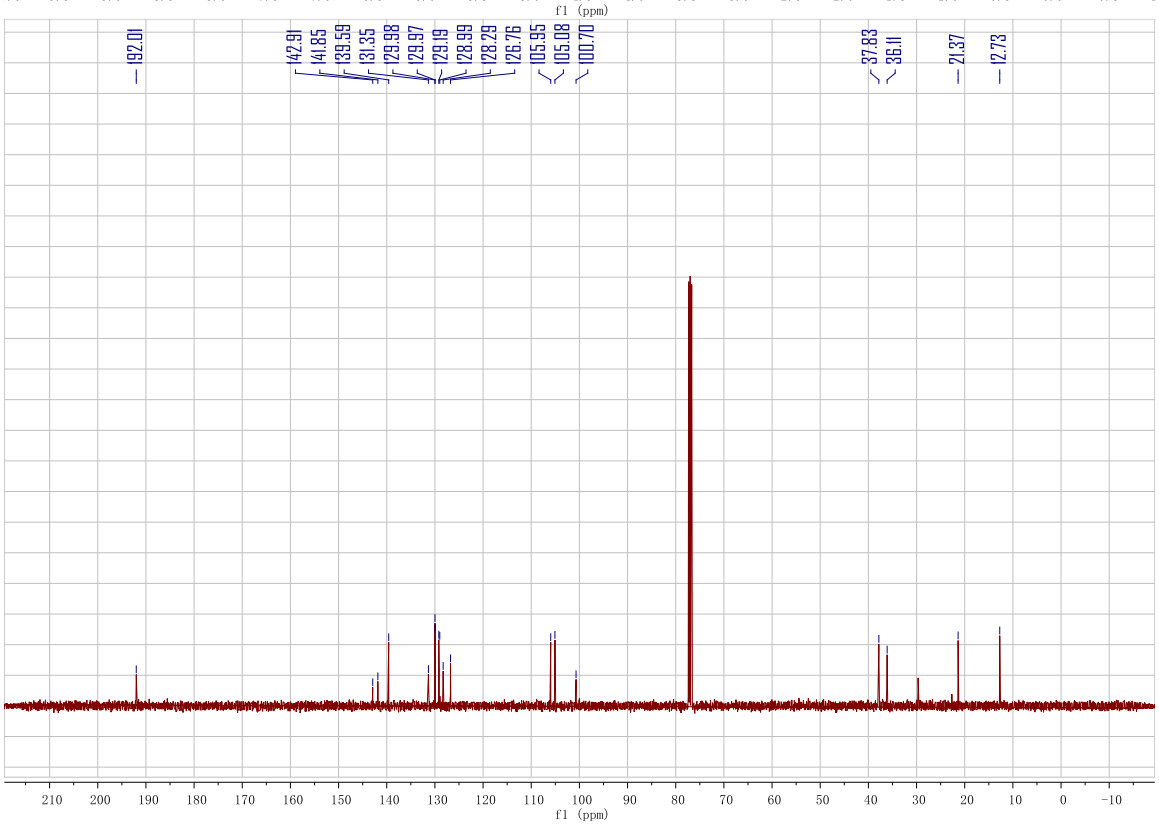
The racemic product was synthesized as described using **7** and 1-(2-iodophenyl)-2-methyl-1H-pyrrole. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, CDCl3) δ 7.87 (dd, J = 7.9, 1.3 Hz, 1H), 7.39 (td, J = 7.6, 1.3 Hz, 1H), 7.27 (dd, J = 7.8, 1.6 Hz, 1H), 7.10 – 7.02 (m, 2H), 6.92 (s, 1H), 5.90 (dd, J = 22.8, 3.3 Hz, 2H), 3.88 (s, 3H), 3.36 (dd, J = 11.5, 4.3 Hz, 2H), 2.68 – 2.45 (m, 2H), 1.87 (s, 3H).

^{13}C NMR (101 MHz, CDCl3) δ 192.01 (s), 142.91 (s), 141.85 (s), 139.59 (s), 131.35 (s), 129.98 (s), 129.97 (s), 129.19 (s), 128.99 (s), 128.29 (s), 126.76 (s), 105.95 (s), 105.08 (s), 100.70 (s), 37.83 (s), 36.11 (s), 21.37 (s), 12.73 (s).

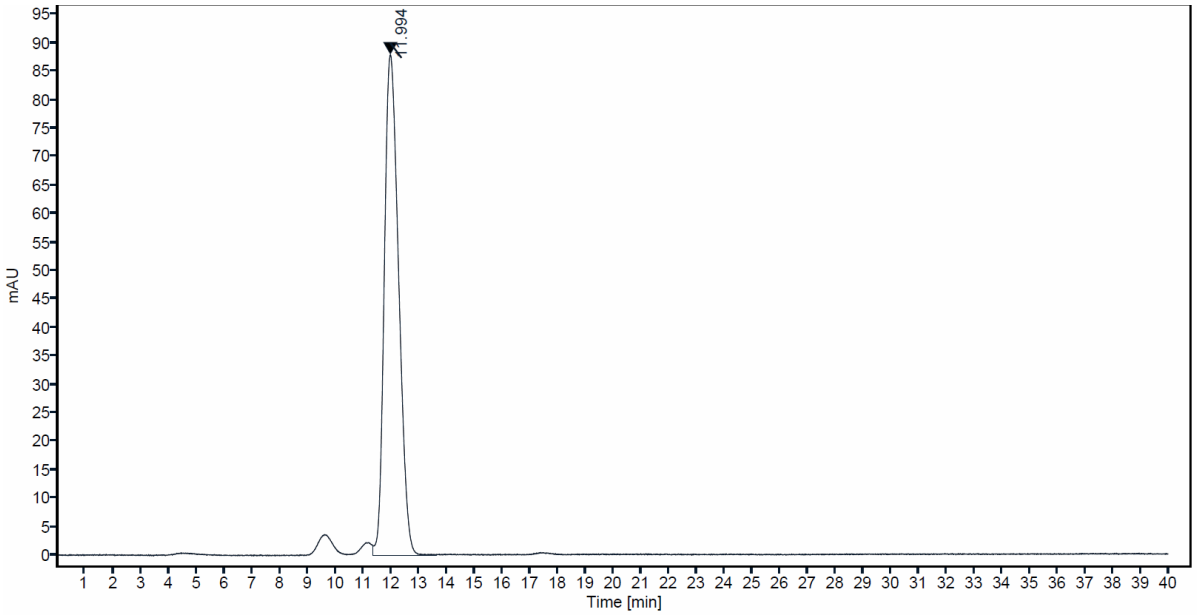
HRMS (ESI) calcd. for $C_{18}H_{19}IN_3O$ $[M+H]^+$: m/z 420.0567, found: 420.0566.


7.89
7.88
7.87
7.86
7.39
7.38
7.28
7.28
7.26
7.26
7.07
7.07
7.05
7.05
6.92
5.94
5.93
5.88
5.87
3.88
3.37
3.35
3.33
2.61
2.59
2.54
2.52
1.57
0.99
1.01
0.99
2.02
1.01
1.98
3.10
2.11
2.13
3.14
f1 (ppm)

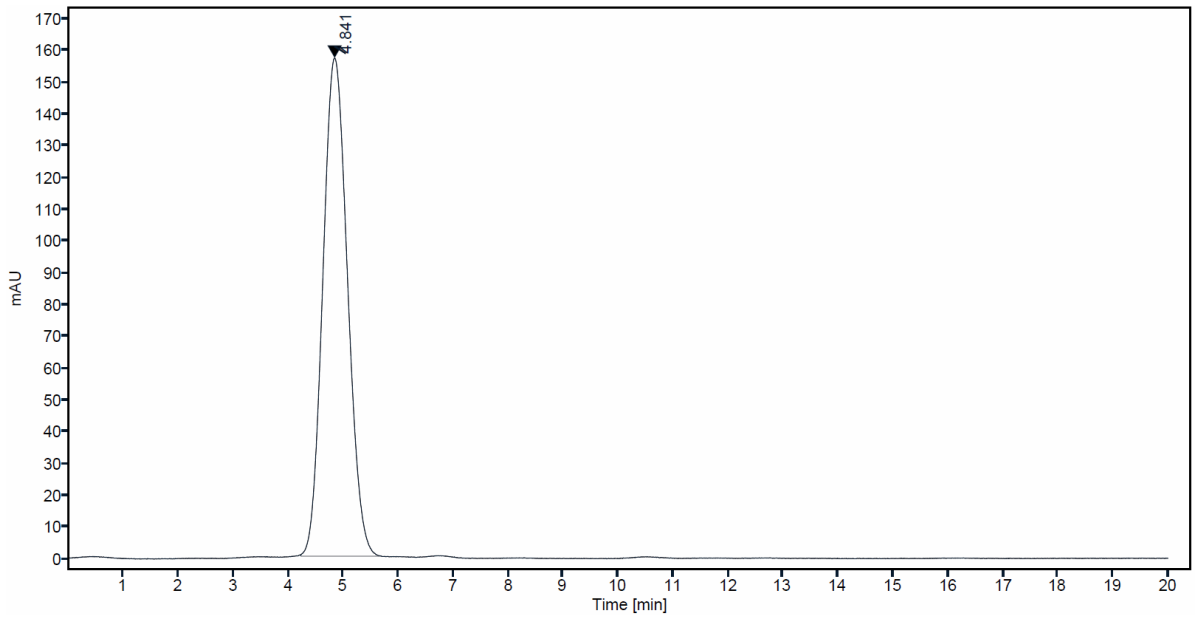

192.01
142.91
141.85
139.59
131.35
129.98
129.97
129.19
128.99
128.29
126.76
105.95
105.08
100.70
37.83
36.11
21.37
12.73
f1 (ppm)

HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm

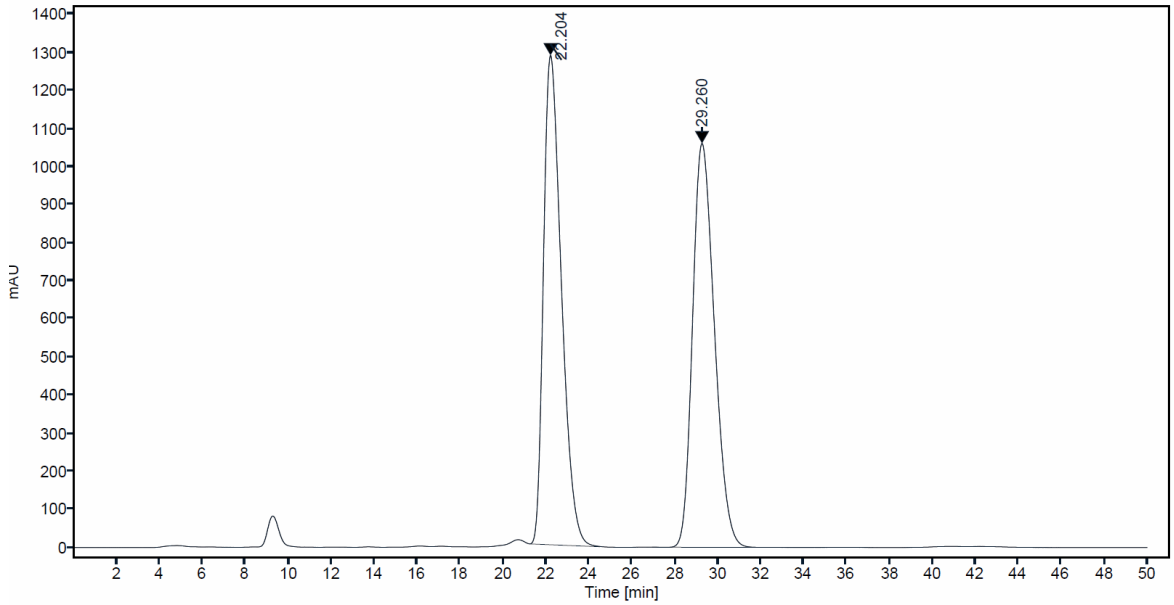
Starting Material (7): Retention time = 11.994 min



1-(2-iodophenyl)-2-methyl-1H-pyrrole: Retention time = 4.841 min

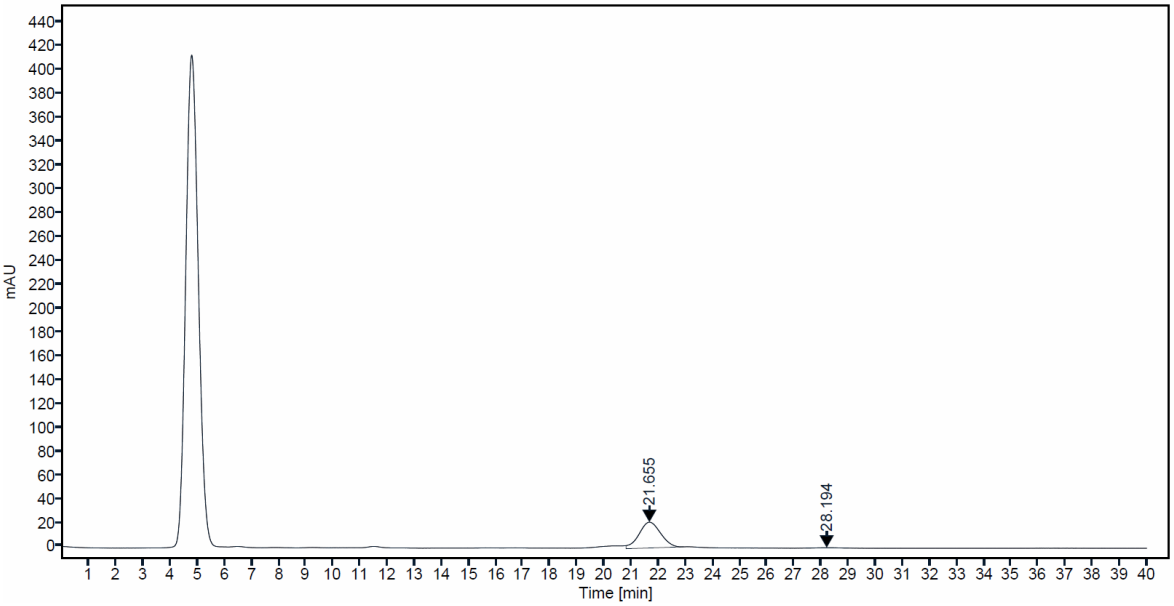


Racemic: Retention time: 22.204 min; 29.260 min

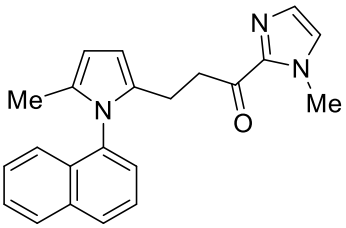


Peak	Retention time (min)	Rel. area (%)
1	22.204	50.9
2	29.260	49.1

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9g** < 1:99 and an enantiomeric excess of 96 % [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm]. Retention time: 21.655 min; 28.194 min



Peak	Retention time (min)	Rel. area (%)
1	21.655	97.9
2	28.194	2.1



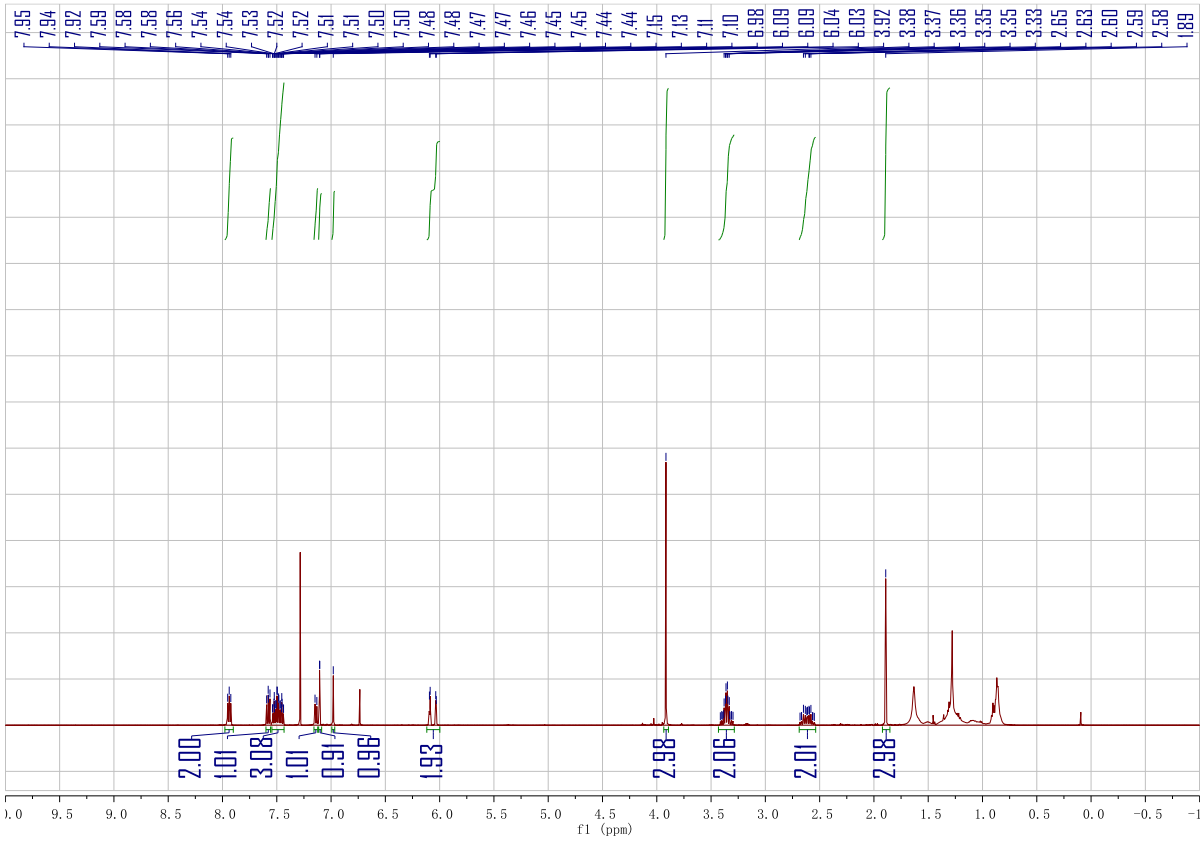
3-(5-methyl-1-(naphthalen-1-yl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9h).

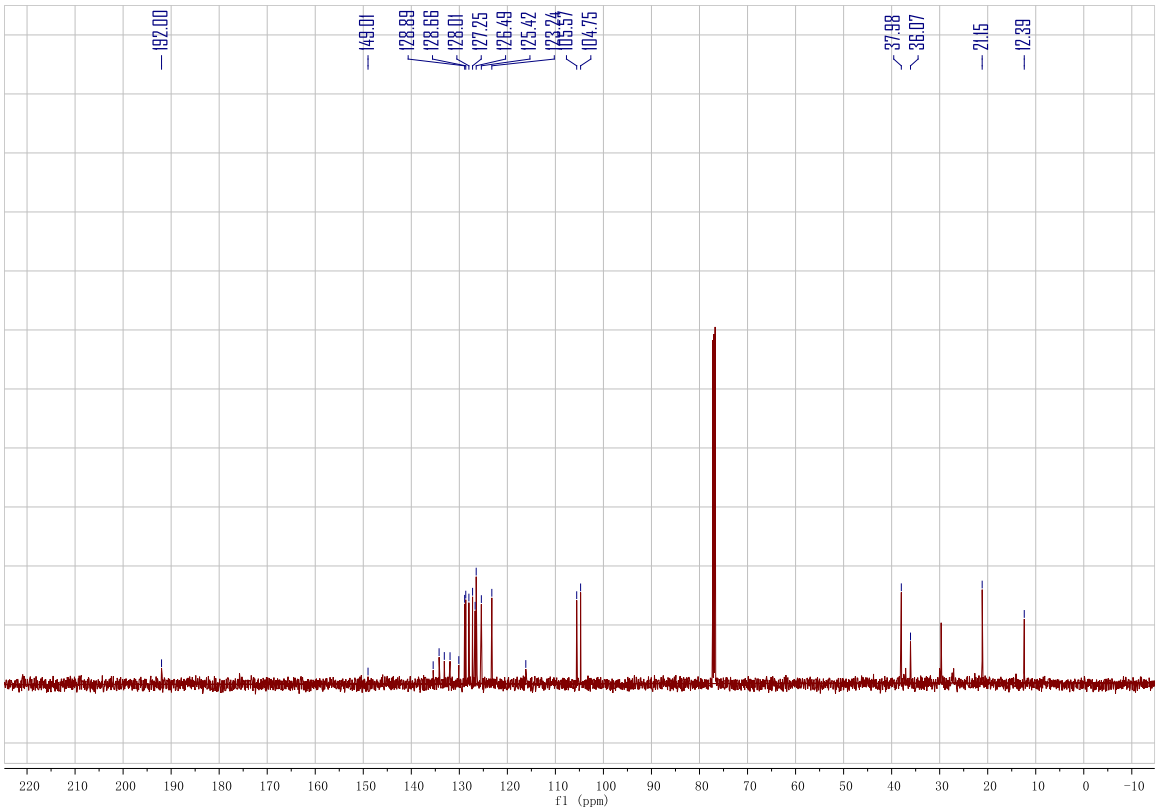
The racemic product was synthesized as described using **7** and 2-methyl-1-(naphthalen-1-yl)-1H-pyrrole. The desired product was obtained as a colorless solid after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, CDCl3) δ 7.98 – 7.90 (m, 2H), 7.58 (dd, J = 8.2, 7.2 Hz, 1H), 7.54 – 7.43 (m, 3H), 7.14 (d, J = 8.4 Hz, 1H), 7.11 (d, J = 0.9 Hz, 1H), 6.98 (s, 1H), 6.06 (dd, J = 28.7, 2.9 Hz, 2H), 3.92 (s, 3H), 3.43 – 3.29 (m, 2H), 2.69 – 2.54 (m, 2H), 1.89 (s, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 192.00 (s), 149.01 (s), 135.45 (s), 134.22 (s), 133.13 (s), 131.94 (s), 130.11 (s), 128.89 (s), 128.66 (s), 128.01 (s), 127.25 (s), 126.72 (s), 126.49 (s), 125.42 (s), 123.24 (s), 116.16 (s), 105.57 (s), 104.75 (s), 37.98 (s), 36.07 (s), 21.15 (s), 12.39 (s).

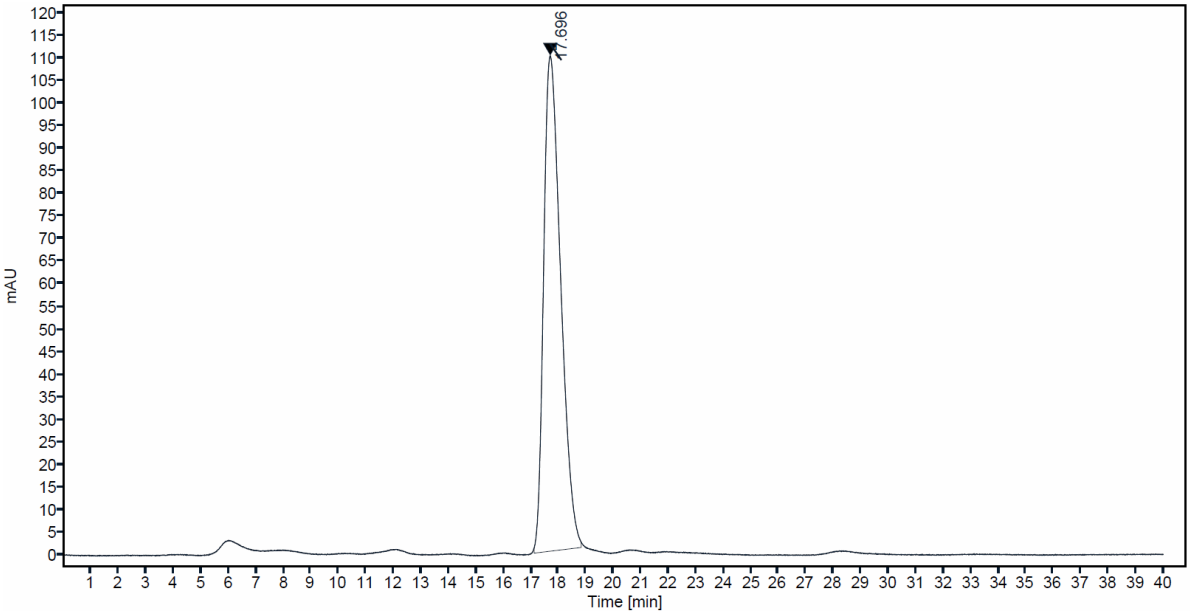
HRMS (ESI) calcd. for $C_{22}H_{22}N_3O$ $[M+H]^+$: m/z 344.1757, found: 344.1762.



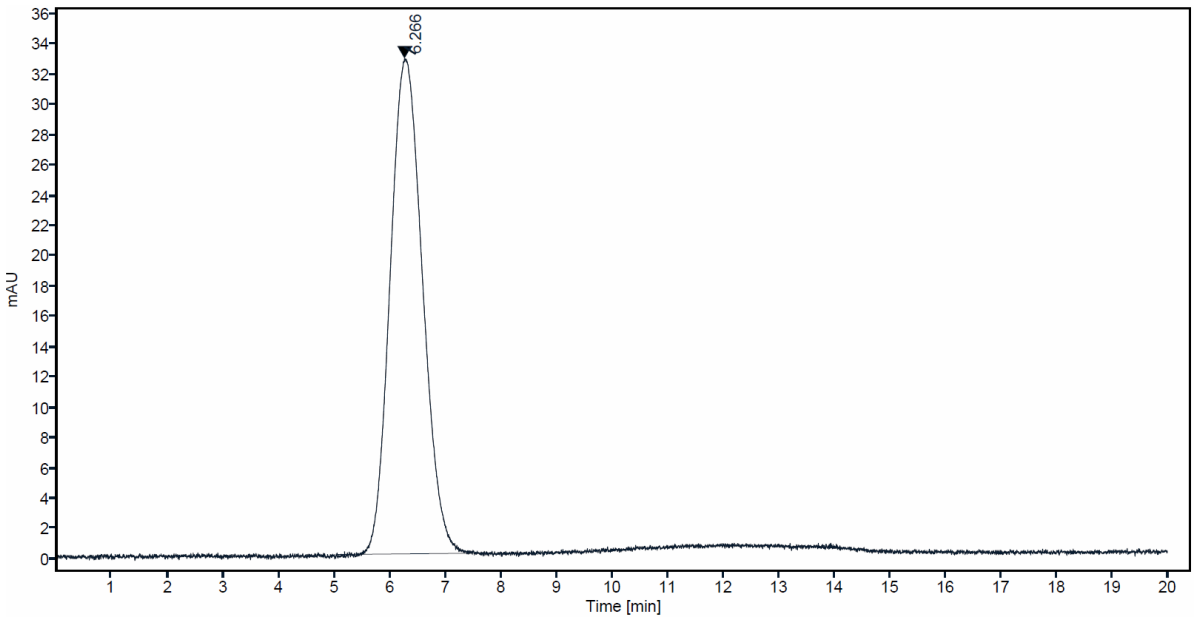


HPLC analysis CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm

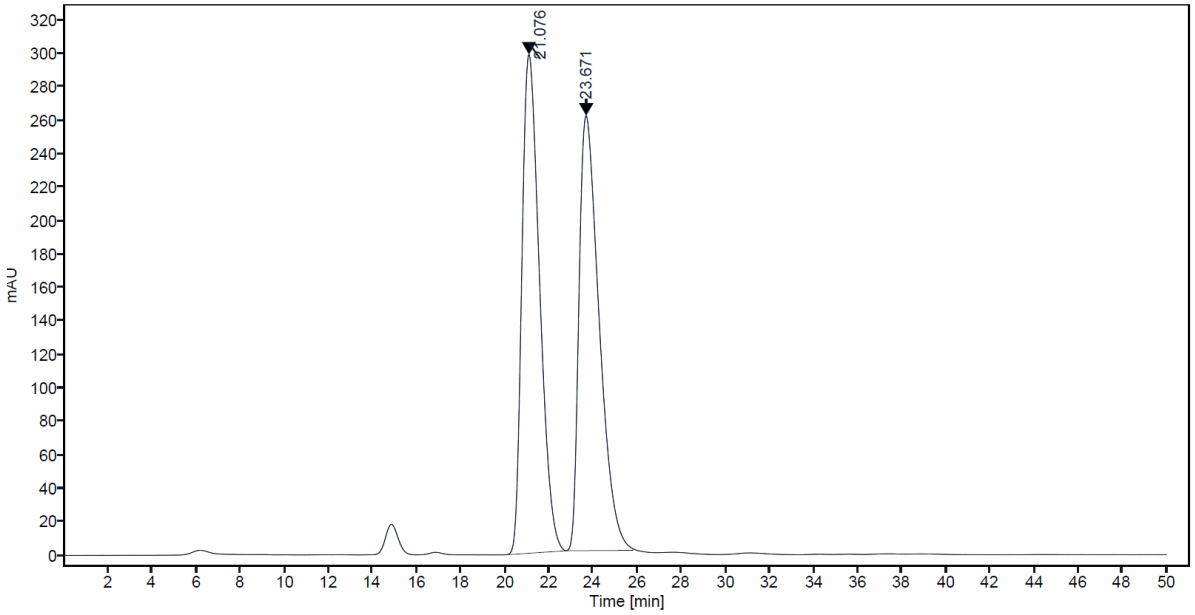
Starting Material (7): Retention time = 17.696 min



2-methyl-1-(naphthalen-1-yl)-1H-pyrrole: Retention time = 6.266 min

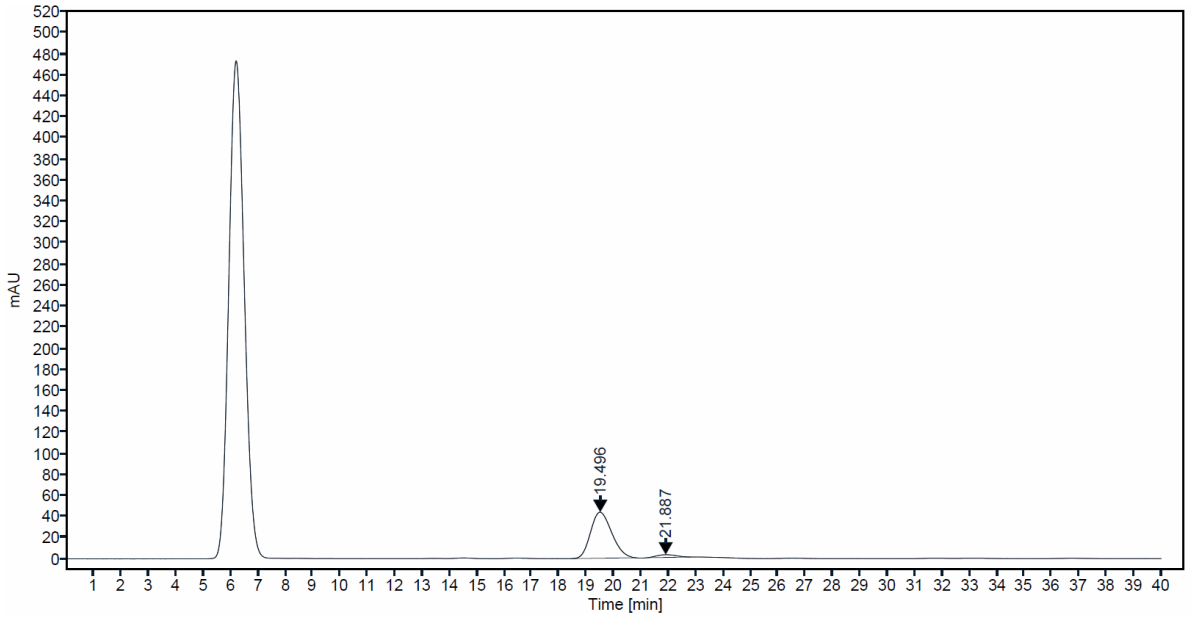


Racemic: Retention time: 21.076min; 23.671 min

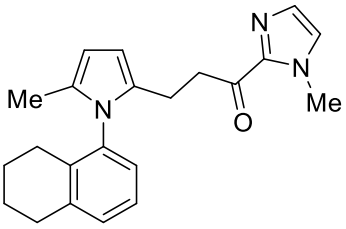


Peak	Retention time (min)	Rel. area (%)
1	21.076	50.4
2	23.671	49.6

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9h** < 1:99 and an enantiomeric excess of 90% [CHIRALCEL ID column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.75 mL/min, λ = 280 nm]. Retention time: 19.496 min; 21.887 min



Peak	Retention time (min)	Rel. area (%)
1	19.496	94.8
2	21.887	5.2



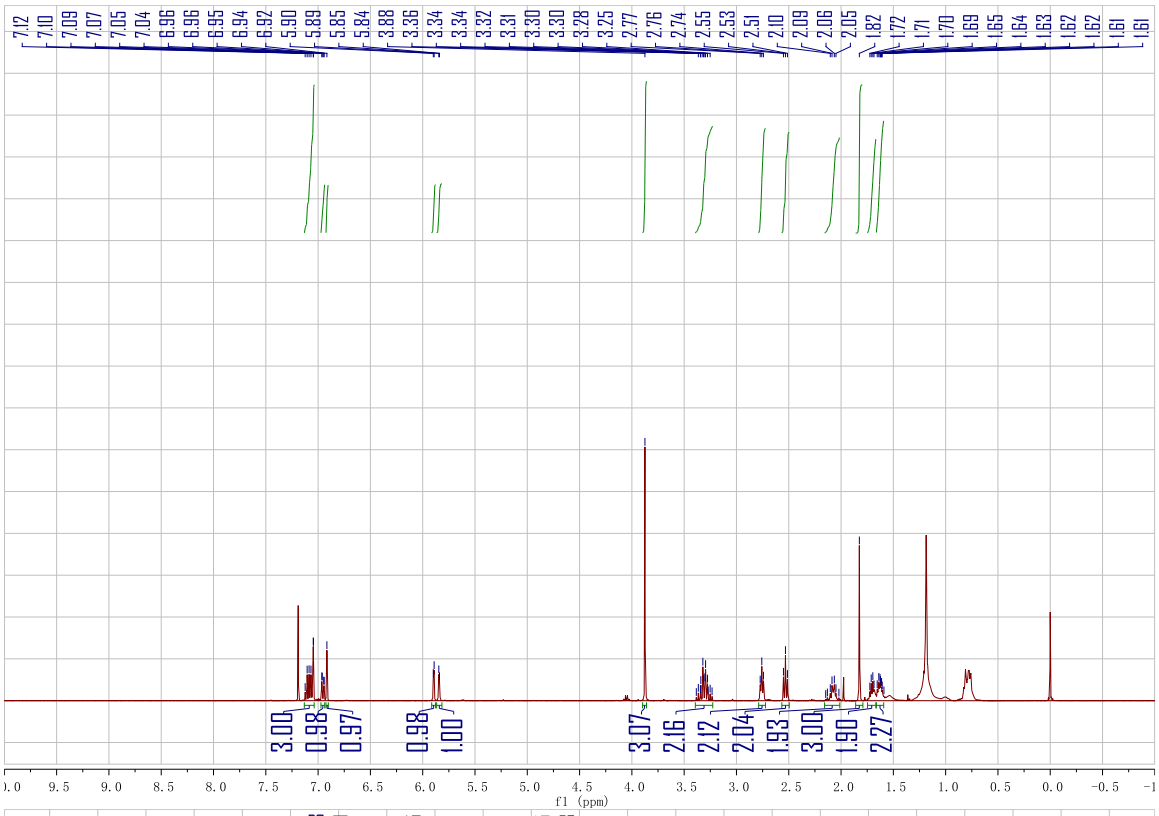
3-(5-methyl-1-(5,6,7,8-tetrahydronaphthalen-1-yl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9i).

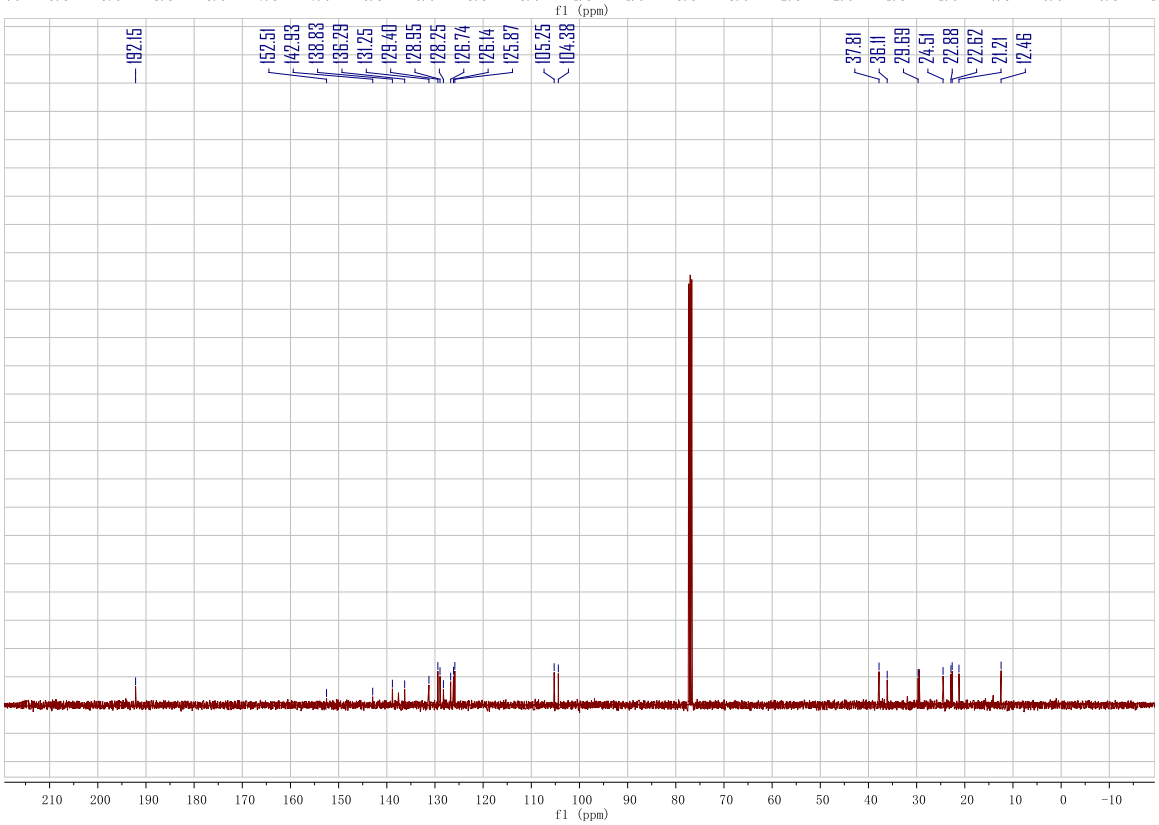
The racemic product was synthesized as described using **7** and 2-methyl-1-(5,6,7,8-tetrahydronaphthalen-1-yl)-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (400 MHz, CDCl3) δ 7.13 – 7.04 (m, 3H), 6.95 (dd, J = 7.3, 1.4 Hz, 1H), 6.92 (s, 1H), 5.89 (d, J = 3.3 Hz, 1H), 5.84 (d, J = 2.7 Hz, 1H), 3.88 (s, 3H), 3.39 – 3.23 (m, 2H), 2.76 (t, J = 6.2 Hz, 2H), 2.53 (t, J = 7.7 Hz, 2H), 2.16 – 2.01 (m, 2H), 1.82 (s, 3H), 1.70 (dd, J = 11.0, 4.8 Hz, 2H), 1.66 – 1.59 (m, 2H).

^{13}C NMR (101 MHz, CDCl3) δ 192.15 (s), 152.51 (s), 142.93 (s), 138.83 (s), 136.29 (s), 131.25 (s), 129.40 (s), 128.95 (s), 128.25 (s), 126.74 (s), 126.14 (s), 125.87 (s), 105.25 (s), 104.38 (s), 37.81 (s), 36.11 (s), 29.69 (s), 24.51 (s), 22.88 (s), 22.62 (s), 21.21 (s), 12.46 (s).

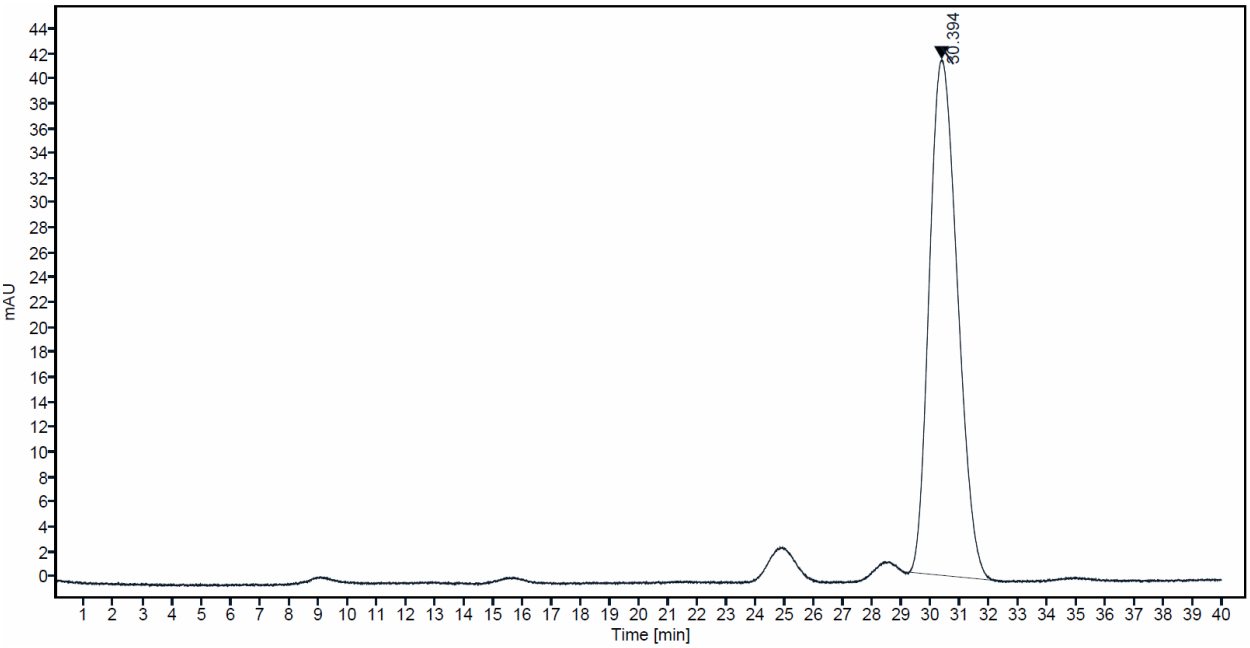
HRMS (ESI) calcd. for $C_{22}H_{26}N_3O$ $[M+H]^+$: m/z 348.2070, found: 348.2075.


7.12 7.10 7.09 7.07 7.05 7.04 6.96 6.96 6.95 6.94 6.92 5.90 5.89 5.85 5.84 3.88 3.36 3.34 3.34 3.32 3.31 3.30 3.30 3.28 3.25 2.77 2.76 2.74 2.55 2.53 2.51 2.10 2.09 2.06 2.05 1.82 1.72 1.71 1.70 1.69 1.65 1.64 1.63 1.62 1.62 1.61 1.61
3.00 0.98 0.97 0.98 1.00 3.07 2.16 2.12 2.04 1.93 3.00 1.90 2.27
f1 (ppm)

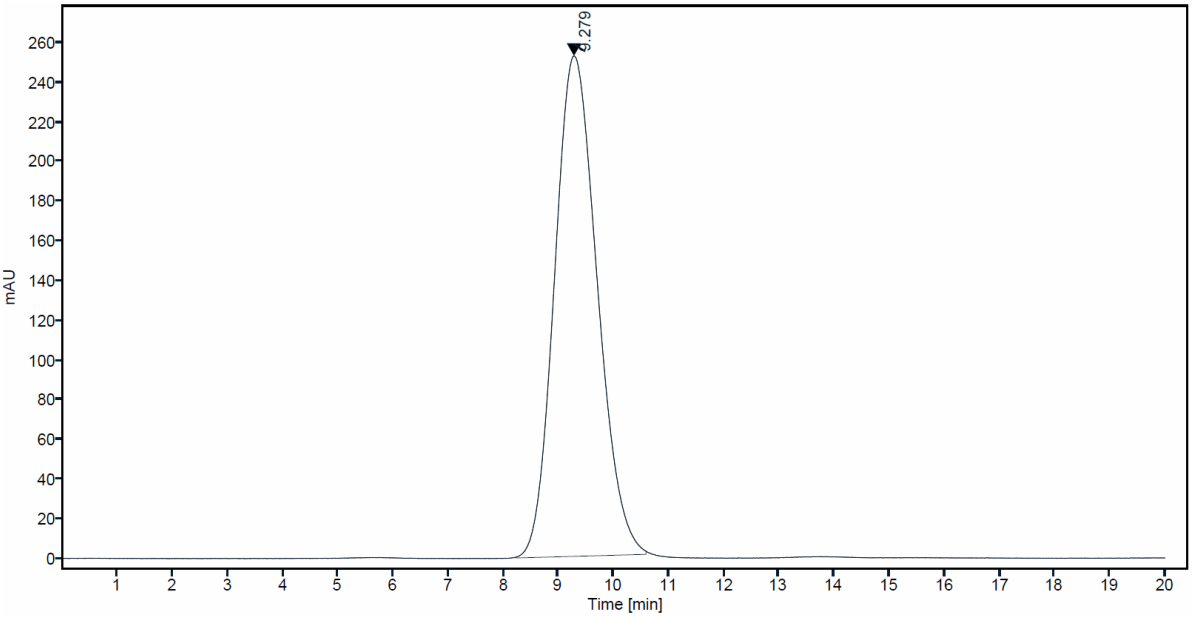

192.15
152.51 142.93 138.83 136.29 131.25 129.40 128.95 128.25 126.74 126.14 125.87 105.25 104.38
37.81 36.11 29.69 24.51 22.88 22.62 21.21 12.46
f1 (ppm)

HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm

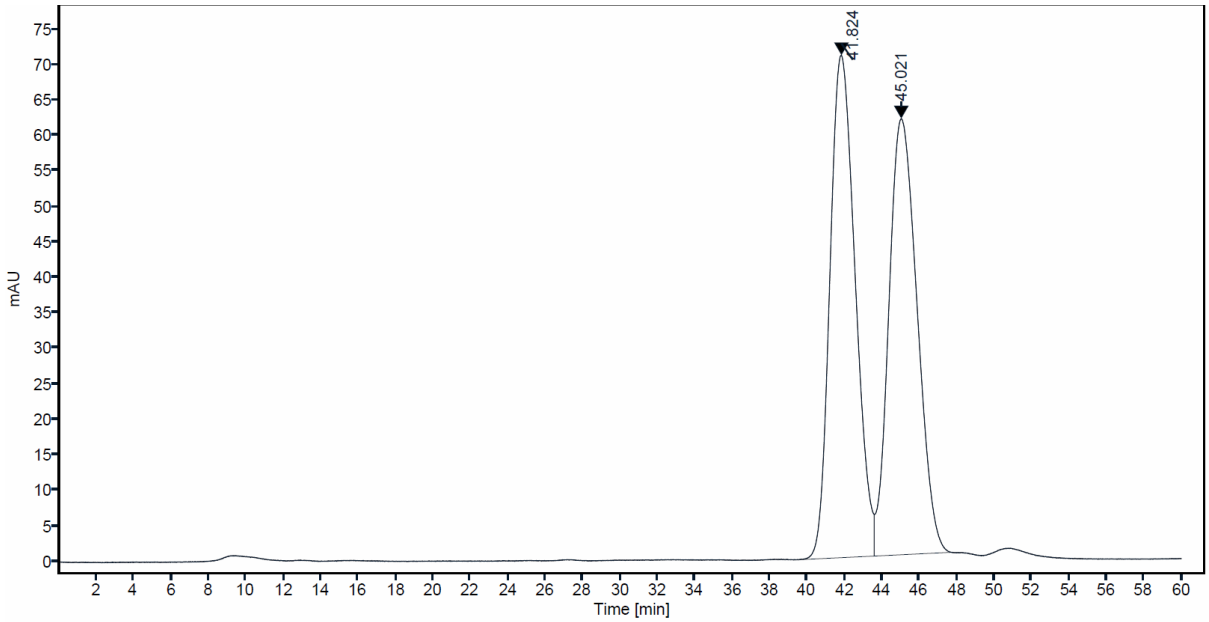
Starting Material (7): Retention time = 30.394 min



2-methyl-1-(5,6,7,8-tetrahydronaphthalen-1-yl)-1H-pyrrole: Retention time = 9.279 min

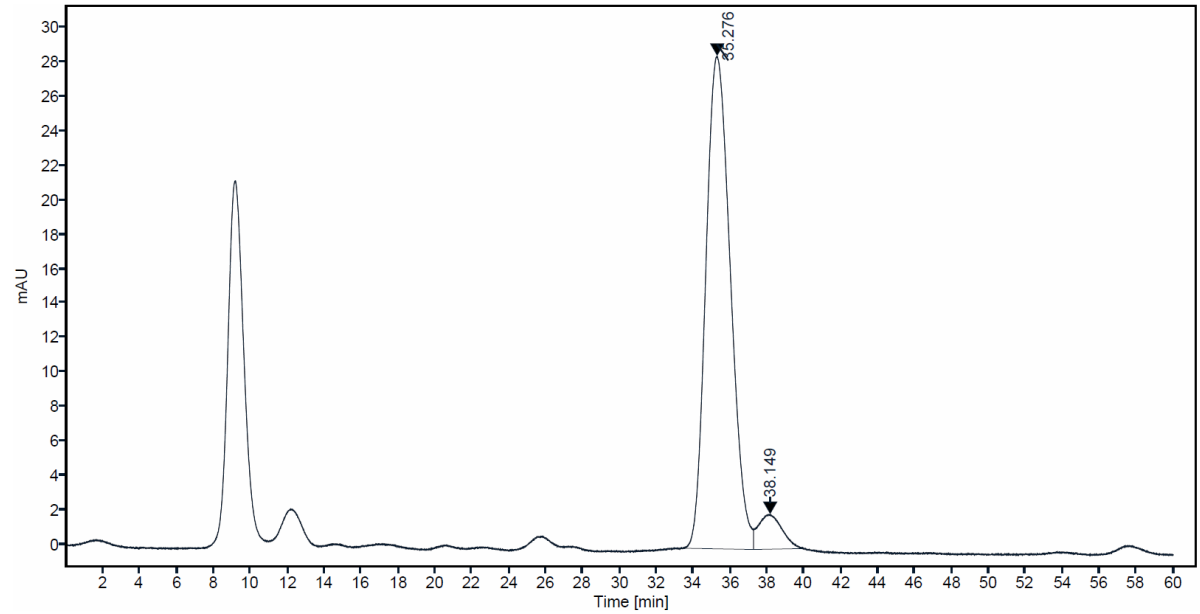


Racemic: Retention time: 41.824 min; 45.021 min

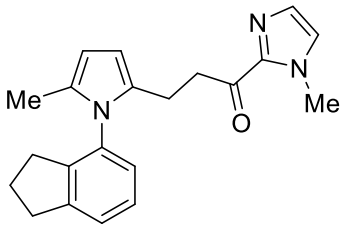


Peak	Retention time (min)	Rel. area (%)
1	41.824	51.1
2	45.021	48.9

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9i** < 1:99 and an enantiomeric excess of 87% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 0.5 mL/min, λ = 280 nm]. Retention time: 35.276 min; 38.149 min



Peak	Retention time (min)	Rel. area (%)
1	35.276	93.6
2	38.149	6.4



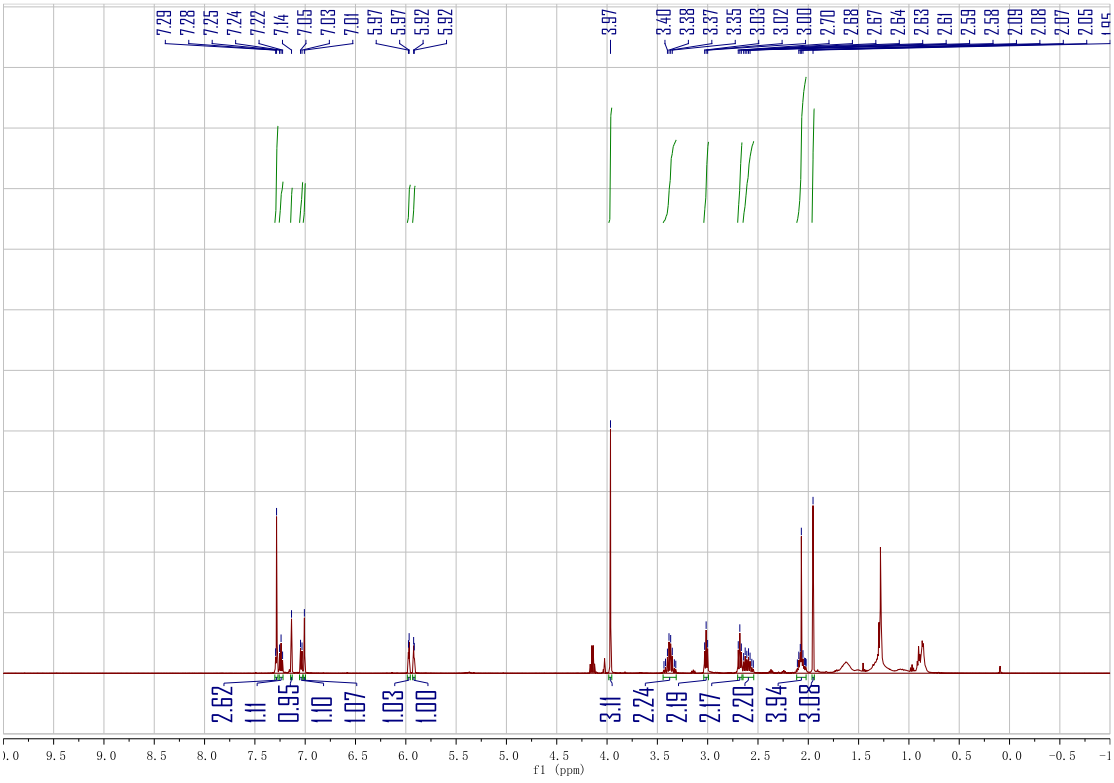
3-(1-(2,3-dihydro-1H-inden-4-yl)-5-methyl-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9j).

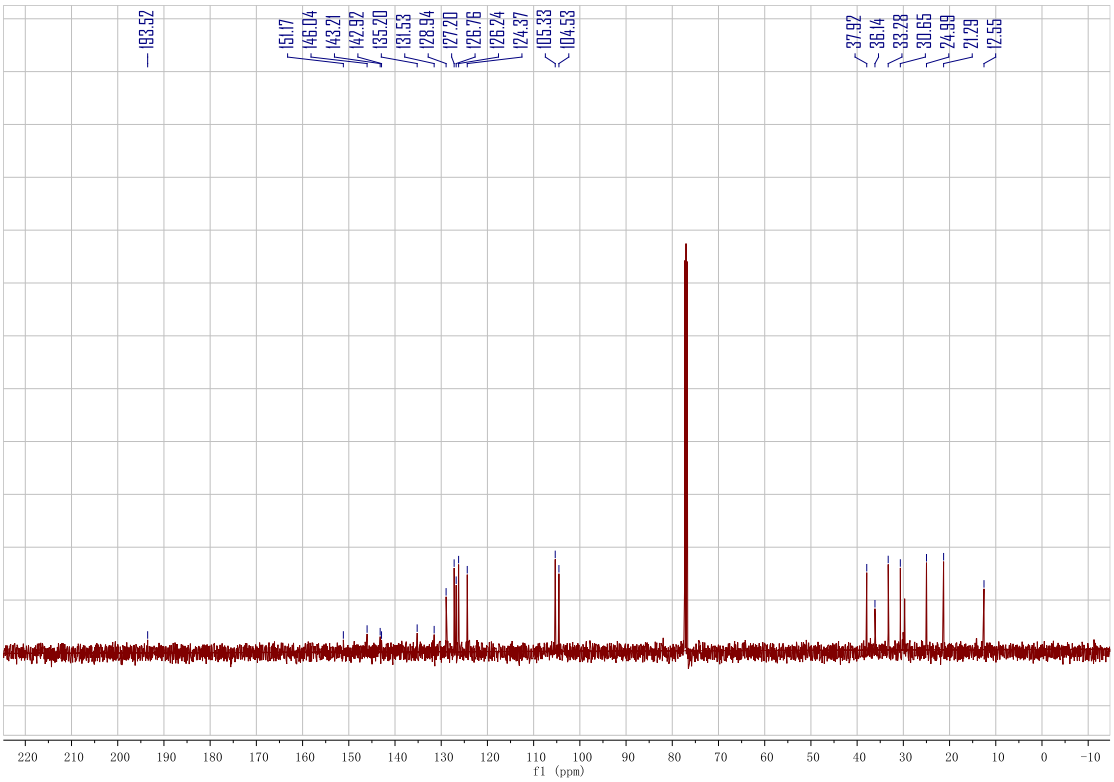
The racemic product was synthesized as described using **7** and 1-(2,3-dihydro-1H-inden-4-yl)-2-methyl-1H-pyrrole. The desired product was obtained as a light yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 4.6 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.14 (s, 1H), 7.04 (d, J = 7.5 Hz, 1H), 7.01 (s, 1H), 5.97 (d, J = 3.3 Hz, 1H), 5.92 (d, J = 3.2 Hz, 1H), 3.97 (s, 3H), 3.44 – 3.31 (m, 2H), 3.02 (t, J = 7.4 Hz, 2H), 2.68 (t, J = 7.7 Hz, 2H), 2.59 (ddd, J = 23.7, 16.0, 7.4 Hz, 2H), 2.12 – 2.02 (m, 2H), 1.95 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.52 (s), 151.17 (s), 146.04 (s), 143.21 (s), 142.92 (s), 135.20 (s), 131.53 (s), 128.94 (s), 127.20 (s), 126.76 (s), 126.24 (s), 124.37 (s), 105.33 (s), 104.53 (s), 37.92 (s), 36.14 (s), 33.28 (s), 30.65 (s), 24.99 (s), 21.29 (s), 12.55 (s).

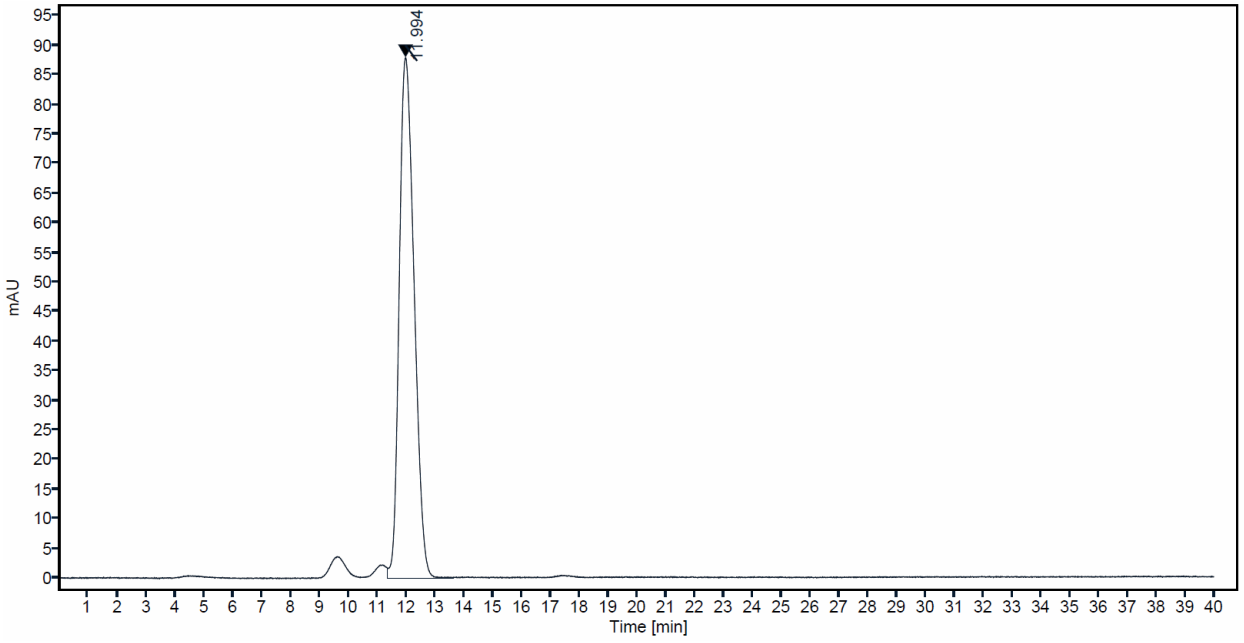
HRMS (ESI) calcd. for $C_{21}H_{24}N_3O$ $[M+H]^+$: m/z 334.1914, found: 334.1918.



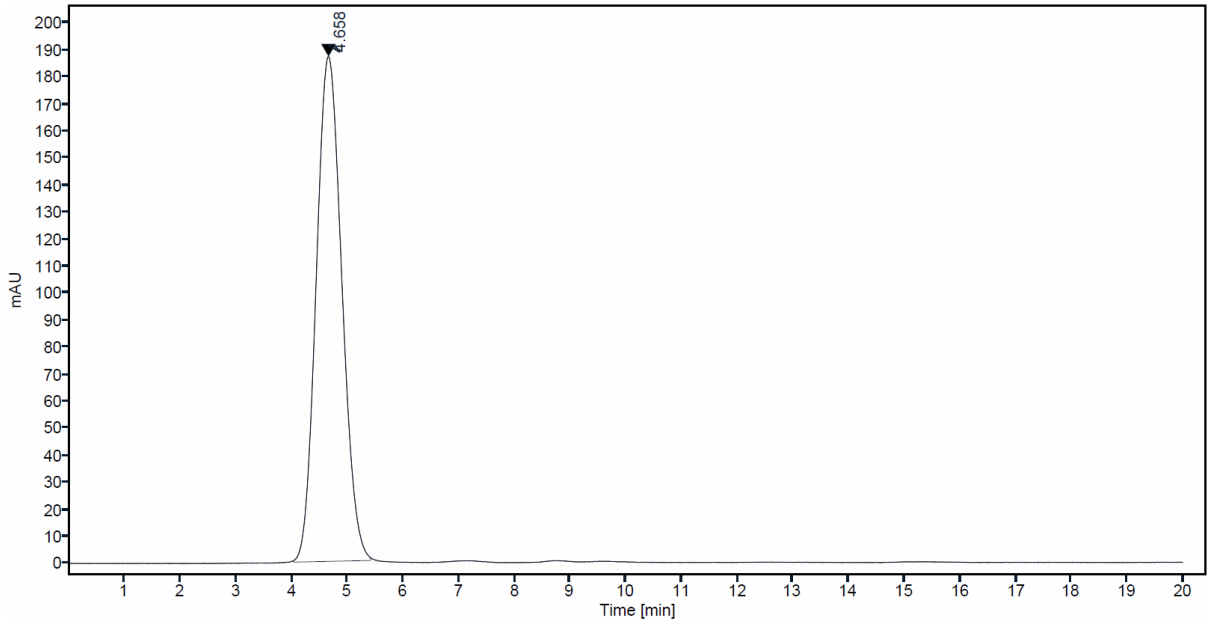


HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm

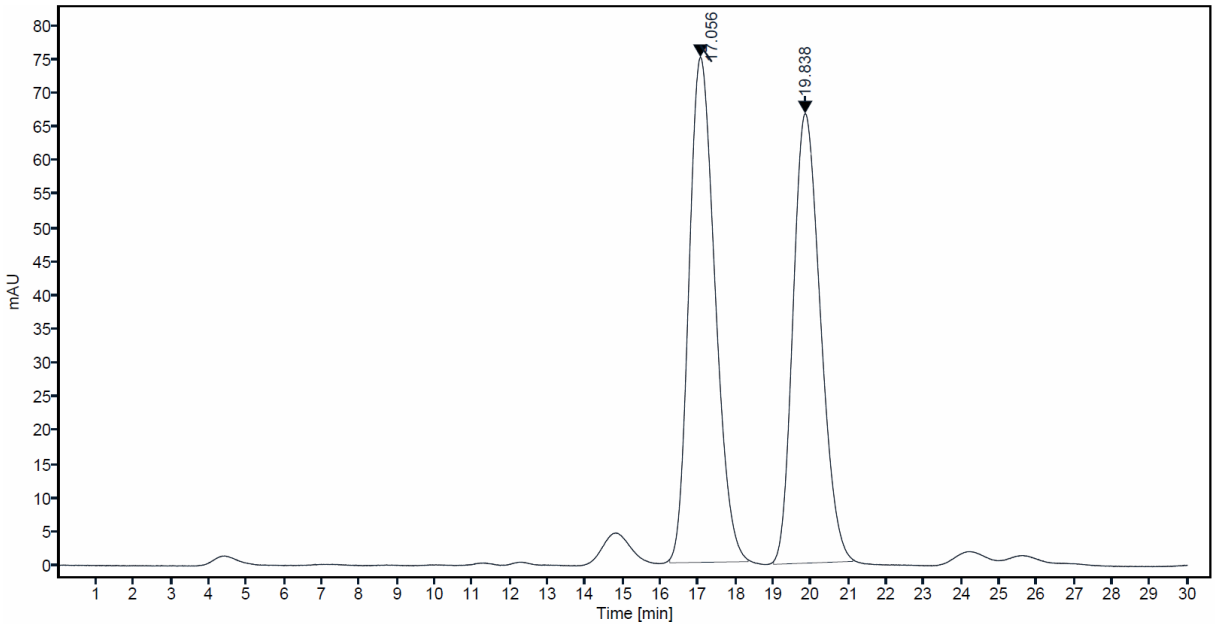
Starting Material (7): Retention time = 11.994 min



1-(2,3-dihydro-1H-inden-4-yl)-2-methyl-1H-pyrrole: Retention time = 4.658 min

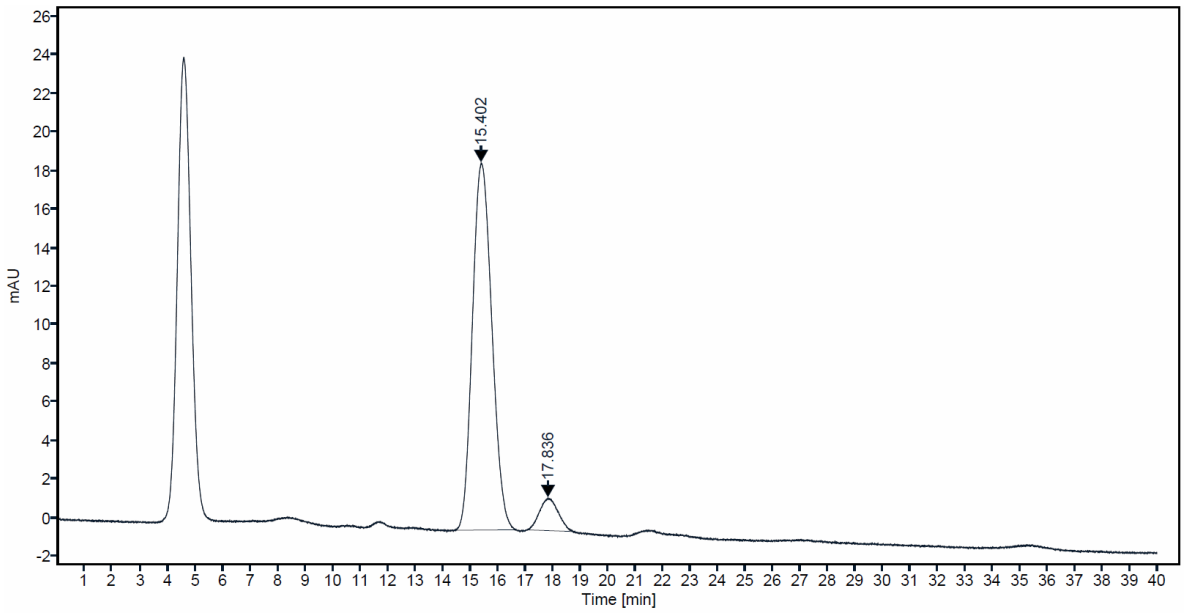


Racemic: Retention time: 17.056 min; 19.839 min

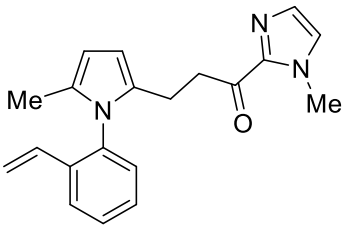


Peak	Retention time (min)	Rel. area (%)
1	17.056	50.2
2	19.838	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9j** as 2:98 and an enantiomeric excess of 84% [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm]. Retention time: 15.402 min; 17.836 min



Peak	Retention time (min)	Rel. area (%)
1	15.402	92.0
2	17.836	8.0



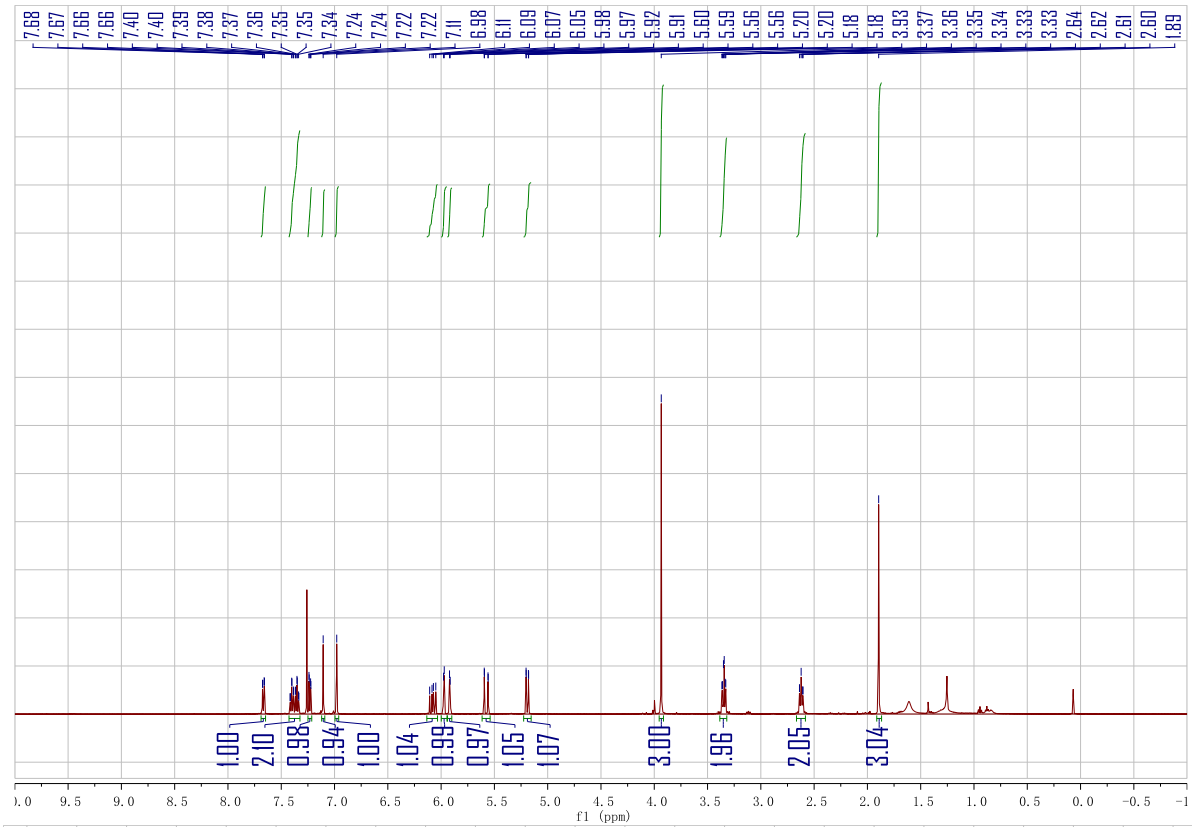
3-(5-methyl-1-(2-vinylphenyl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9k).

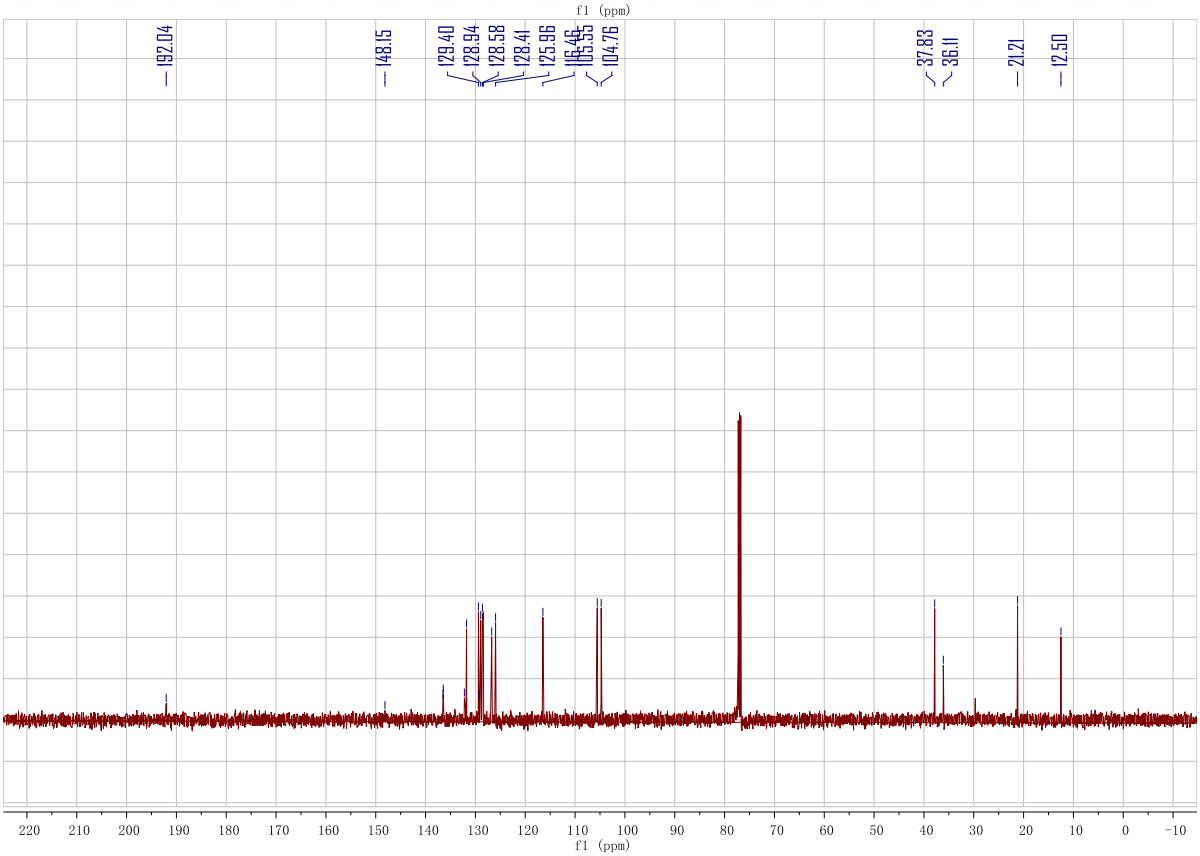
The racemic product was synthesized as described using **7** and 2-methyl-1-(2-vinylphenyl)-1H-pyrrole. The desired product was obtained as a colorless oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 50:50).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.7, 1.4 Hz, 1H), 7.38 (dtd, J = 24.9, 7.4, 1.3 Hz, 2H), 7.23 (dd, J = 7.7, 1.2 Hz, 1H), 7.11 (s, 1H), 6.98 (s, 1H), 6.08 (dd, J = 17.6, 11.1 Hz, 1H), 5.97 (d, J = 3.3 Hz, 1H), 5.92 (d, J = 3.2 Hz, 1H), 5.58 (dd, J = 17.6, 0.8 Hz, 1H), 5.19 (dd, J = 11.1, 0.8 Hz, 1H), 3.93 (s, 3H), 3.35 (td, J = 7.4, 2.9 Hz, 2H), 2.62 (dd, J = 11.8, 4.9 Hz, 2H), 1.89 (s, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 192.04 (s), 148.15 (s), 136.52 (s), 136.44 (s), 132.21 (s), 131.78 (s), 129.33 (d, J = 16.9 Hz), 128.94 (s), 128.58 (s), 128.41 (s), 126.74 (s), 125.96 (s), 116.46 (s), 105.55 (s), 104.76 (s), 37.83 (s), 36.11 (s), 21.21 (s), 12.50 (s).

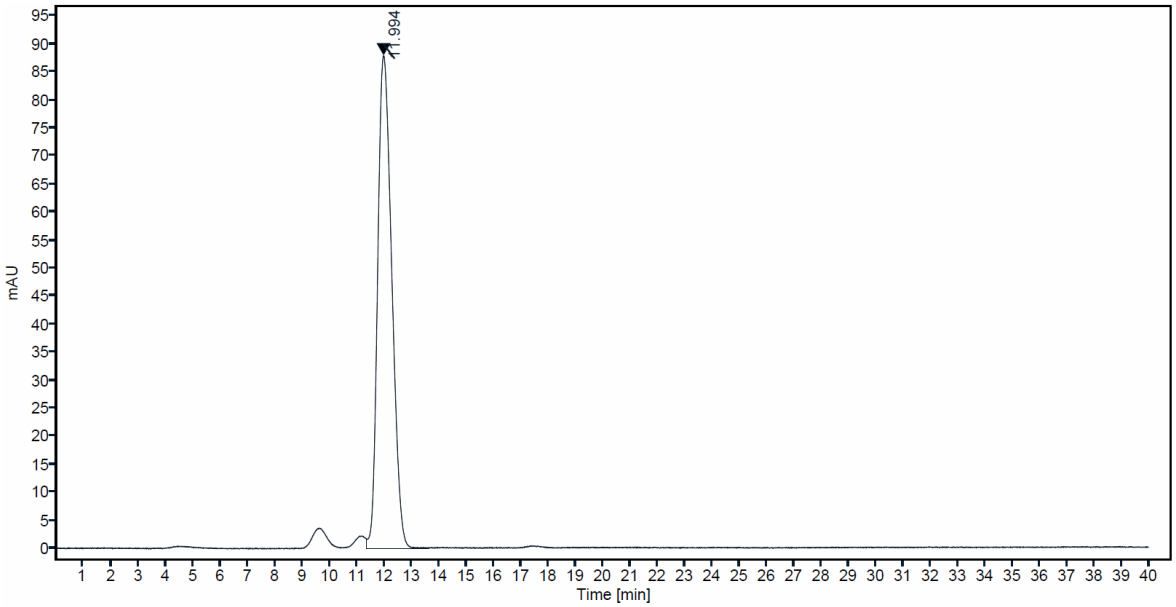
HRMS (ESI) calcd. for $C_{20}H_{22}N_3O$ $[M+H]^+$: m/z 320.1757, found: 320.1762.


7.68 7.67 7.66 7.66 7.40 7.40 7.39 7.38 7.37 7.36 7.35 7.35 7.34 7.24 7.24 7.22 7.22 7.11 6.98 6.11 6.09 6.07 6.05 5.98 5.97 5.92 5.91 5.60 5.59 5.56 5.56 5.20 5.20 5.18 5.18 3.93 3.37 3.36 3.35 3.34 3.33 3.33 2.64 2.62 2.61 2.60 1.89
1.00 2.10 0.98 0.94 1.00 1.04 0.99 0.97 1.05 1.07 3.00 1.96 2.05 3.04
f1 (ppm)

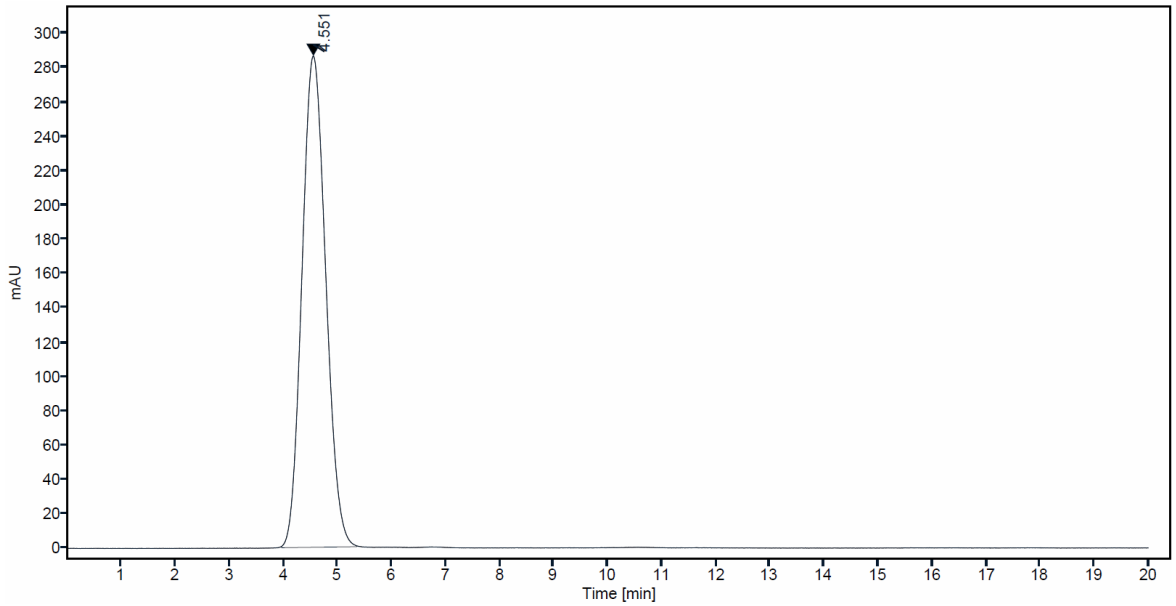

192.04 148.15 129.40 128.94 128.58 128.41 125.96 116.46 105.55 104.76 37.83 36.11 21.21 12.50
f1 (ppm)

HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm

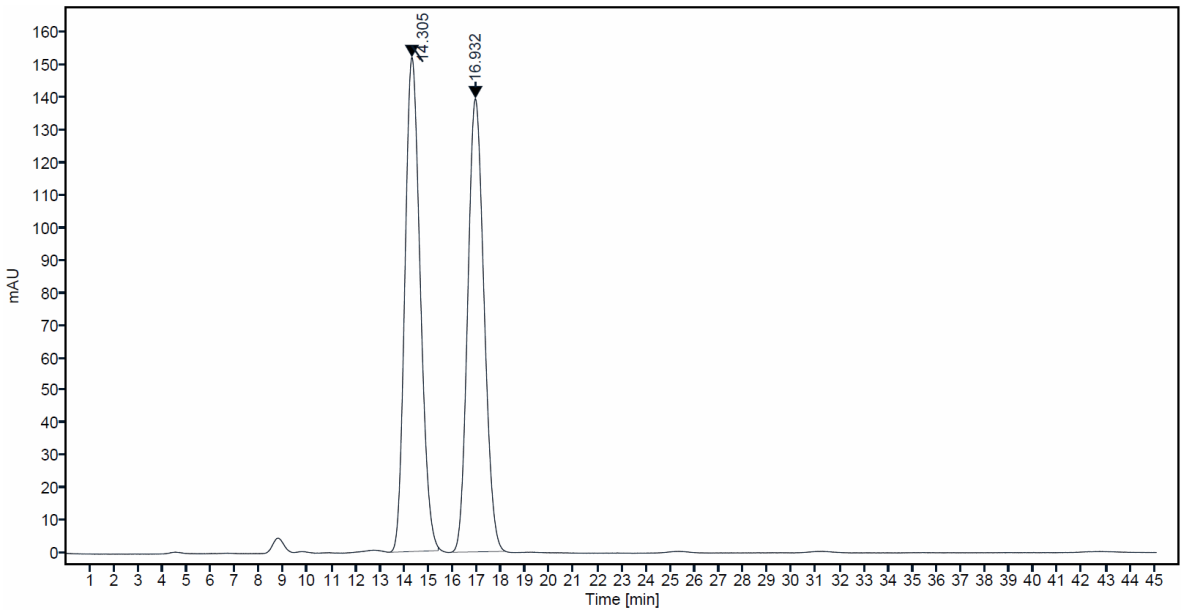
Starting Material (7): Retention time = 11.994 min



2-methyl-1-(2-vinylphenyl)-1H-pyrrole: Retention time = 4.551 min

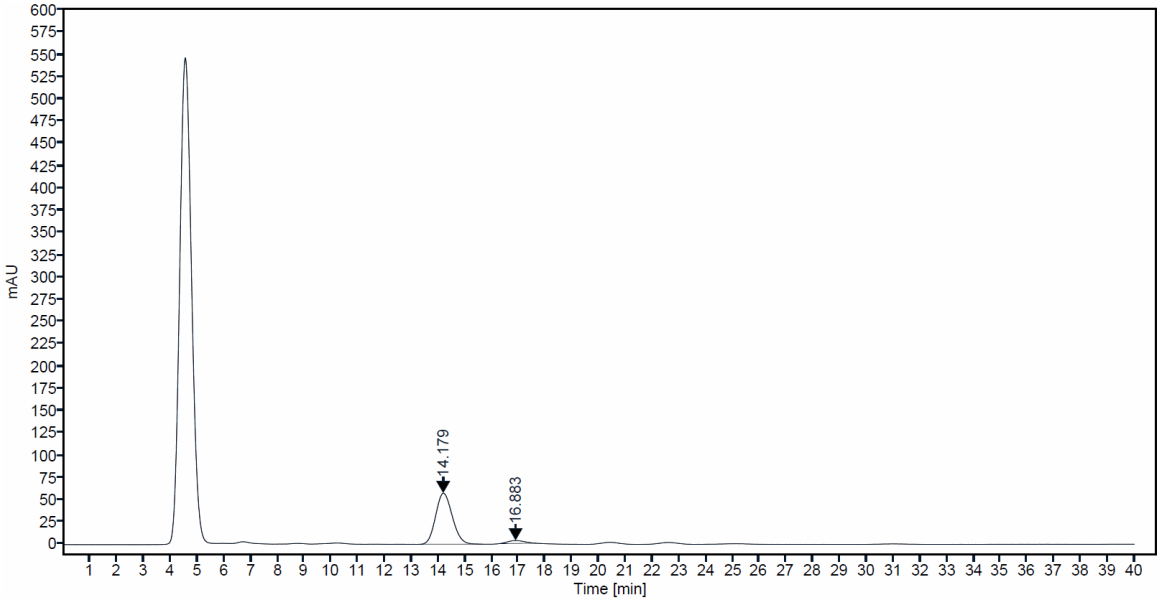


Racemic: Retention time: 14.305 min; 16.932 min

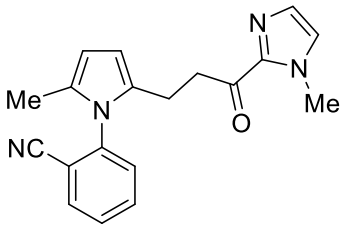


Peak	Retention time (min)	Rel. area (%)
1	14.305	50.3
2	16.932	49.7

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9k** < 1:99 and enantiomeric excess of 89 % [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 95:05, 1.0 mL/min, λ = 280 nm]. Retention time: 14.179 min; 16.883 min



Peak	Retention time (min)	Rel. area (%)
1	14.179	94.6
2	16.883	5.4



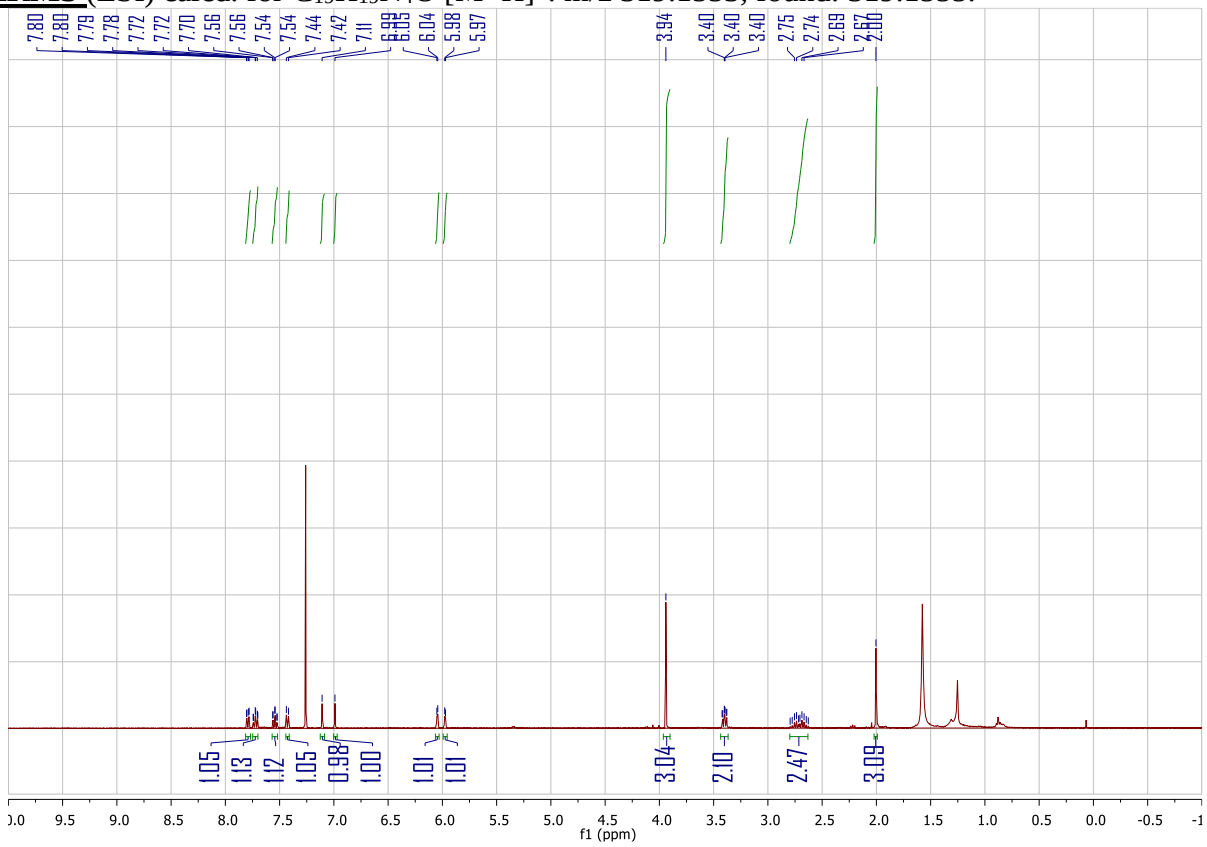
2-(2-methyl-5-(3-(1-methyl-1H-imidazol-2-yl)-3-oxopropyl)-1H-pyrrol-1-yl)benzonitrile (9l).

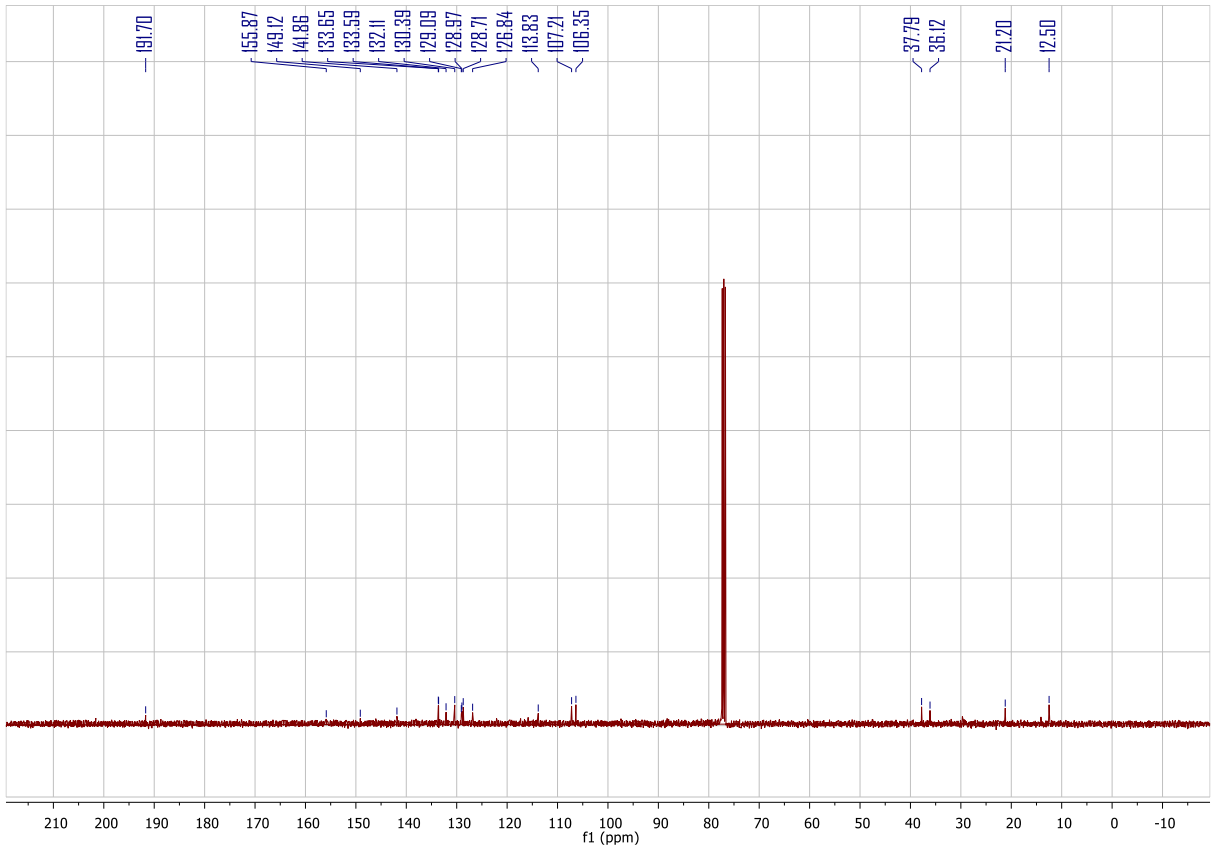
The racemic product was synthesized as described using **7** and 2-(2-methyl-1H-pyrrol-1-yl) benzonitrile. The desired product was obtained as a brown oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 25:75).

^{1}H NMR (400 MHz, CDCl3) δ 7.79 (dd, J = 7.8, 1.4 Hz, 1H), 7.72 (td, J = 7.8, 1.5 Hz, 1H), 7.54 (td, J = 7.7, 1.1 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.11 (s, 1H), 6.99 (s, 1H), 6.05 (d, J = 3.4 Hz, 1H), 5.97 (d, J = 2.9 Hz, 1H), 3.94 (s, 3H), 3.44 – 3.37 (m, 2H), 2.71 (dtd, J = 23.4, 15.8, 7.5 Hz, 2H), 2.00 (s, 3H).

^{13}C NMR (101 MHz, CDCl3) δ 191.70 (s), 155.87 (s), 149.12 (s), 141.86 (s), 133.65 (s), 133.59 (s), 132.11 (s), 130.39 (s), 129.09 (s), 128.97 (s), 128.71 (s), 126.84 (s), 113.83 (s), 107.21 (s), 106.35 (s), 37.79 (s), 36.12 (s), 21.20 (s), 12.50 (s).

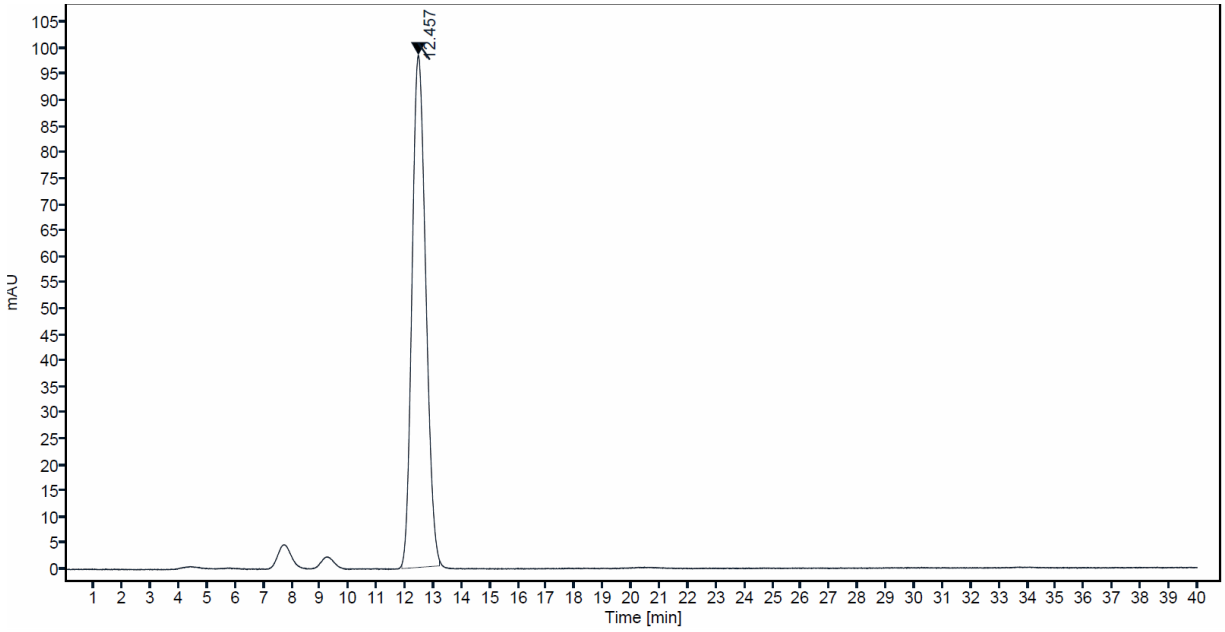
HRMS (ESI) calcd. for $C_{19}H_{19}N_4O$ $[M+H]^+$: m/z 319.1553, found: 319.1555.



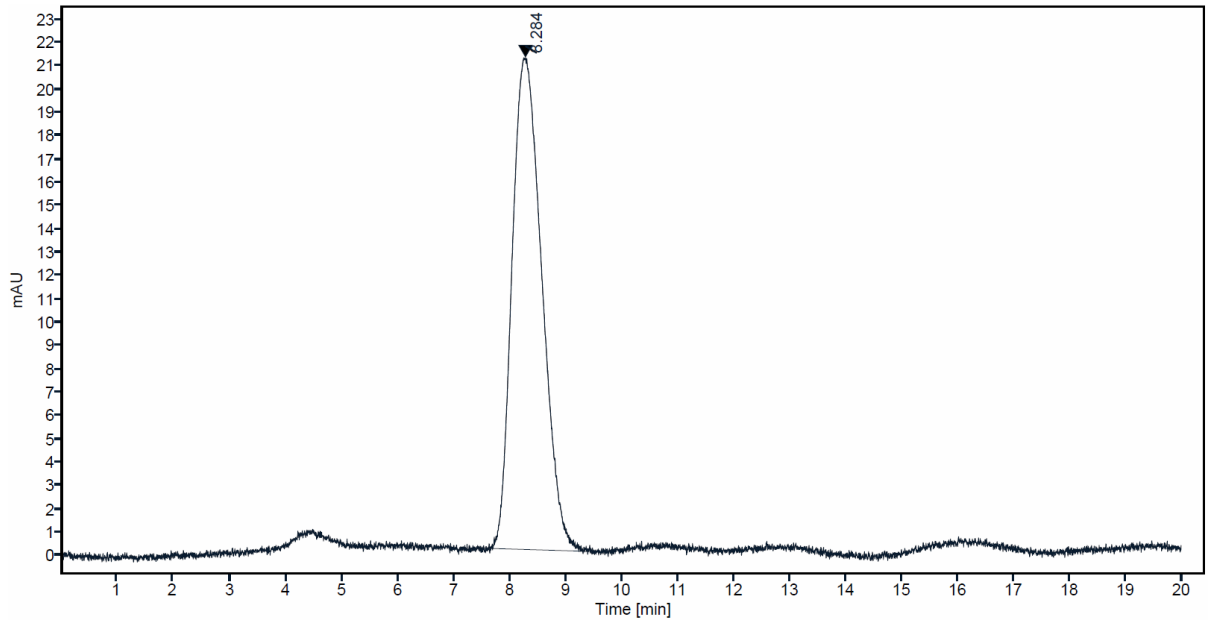


HPLC analysis CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 280 nm

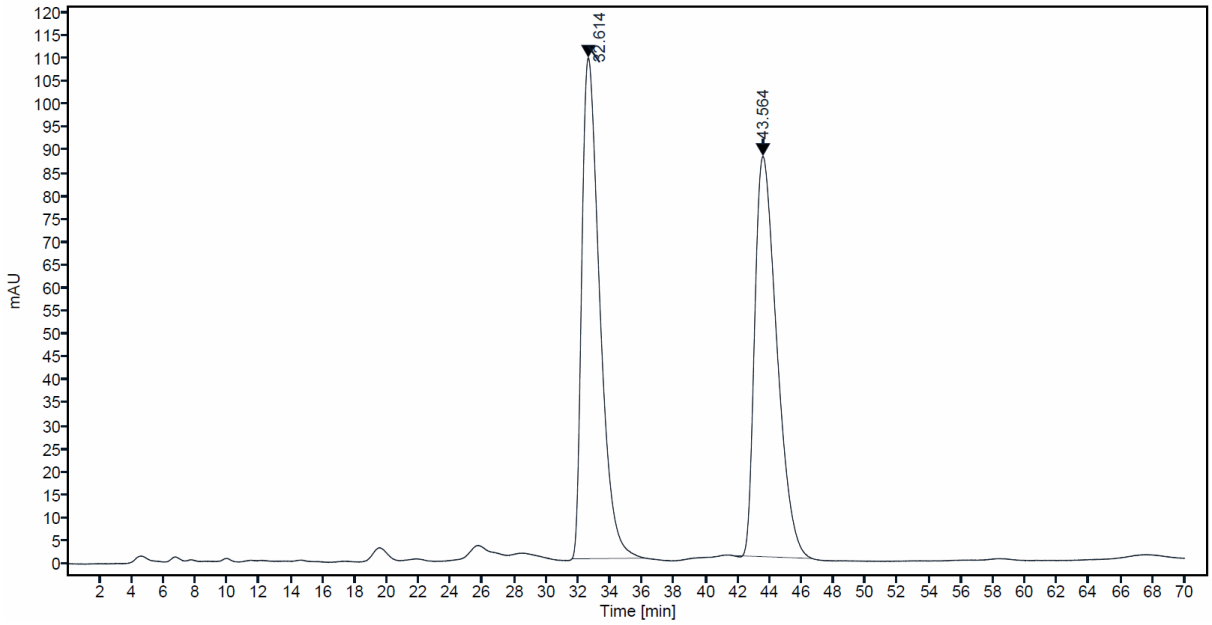
Starting Material (7): Retention time = 12.457 min



2-(2-methyl-1H-pyrrol-1-yl) benzonitrile: Retention time = 6.284 min

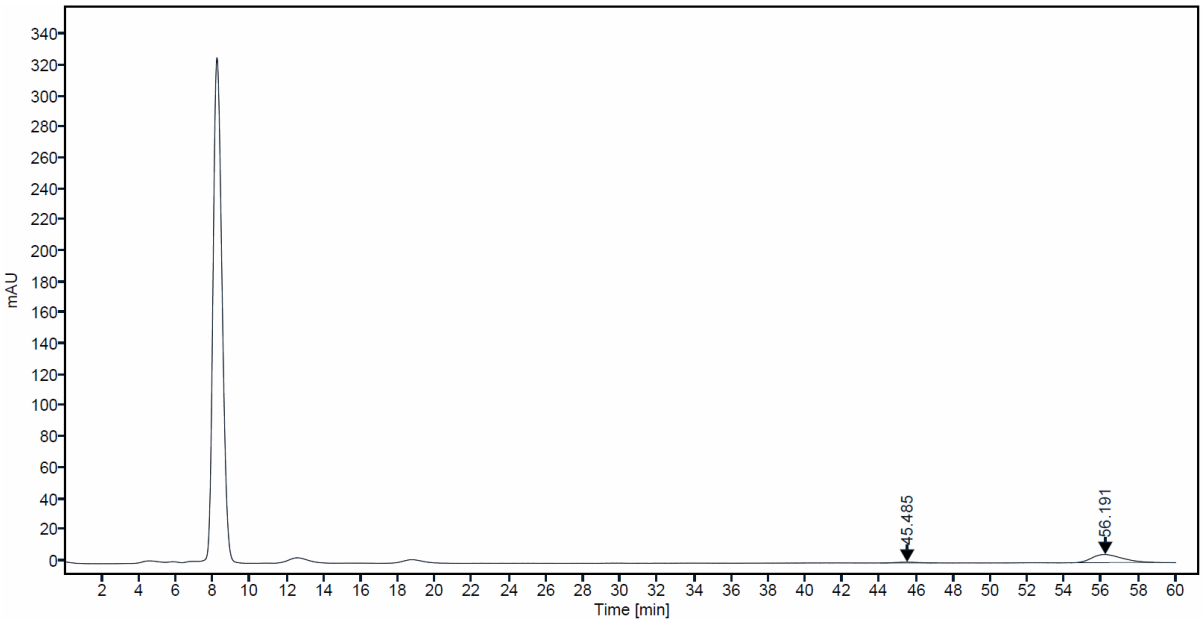


Racemic: Retention time: 32.614 min; 43.564min

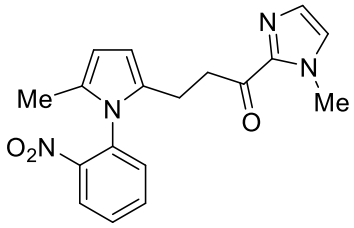


Peak	Retention time (min)	Rel. area (%)
1	32.614	50.9
2	43.564	49.1

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9l** as 10:90 and an enantiomeric excess of 87 % [CHIRALCEL IC column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 280 nm]. Retention time: 45.485 min; 56.191 min



Peak	Retention time (min)	Rel. area (%)
1	45.485	6.5
2	56.191	93.5



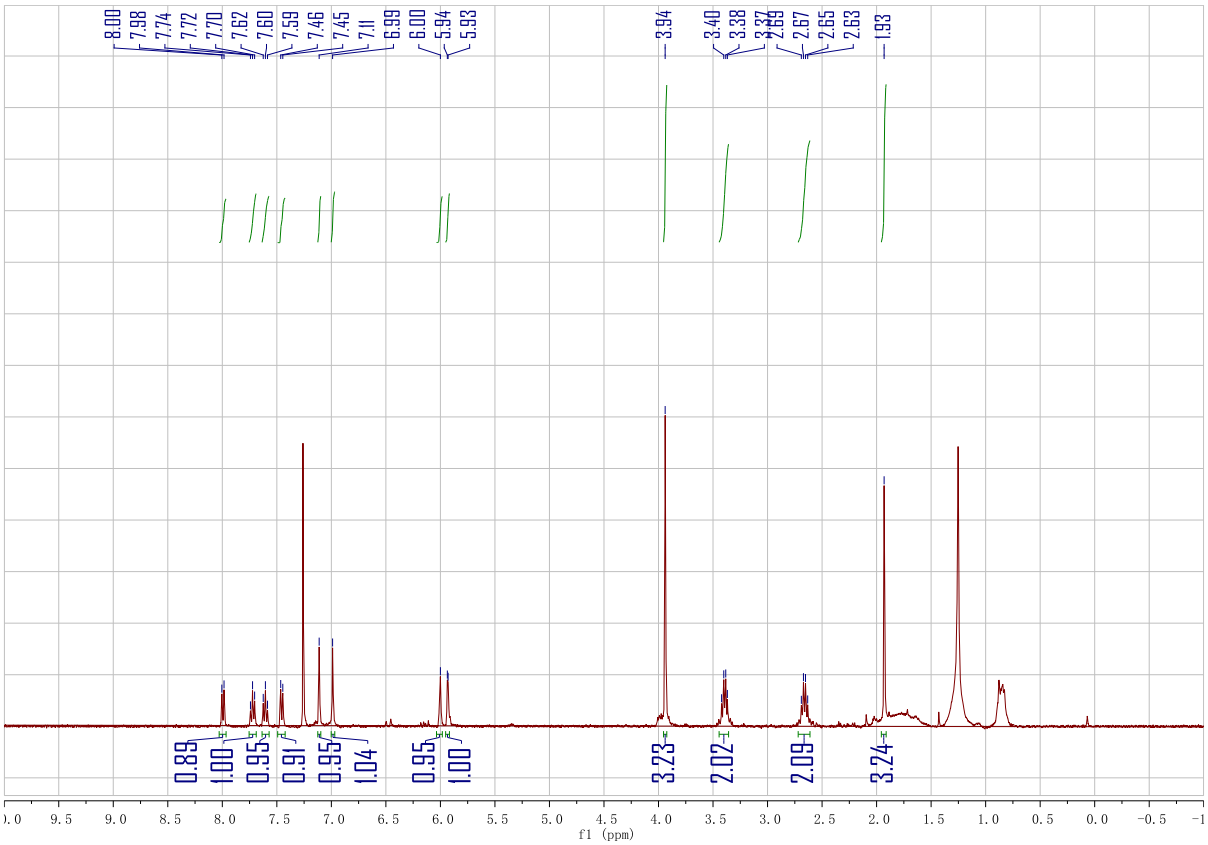
3-(5-methyl-1-(2-nitrophenyl)-1H-pyrrol-2-yl)-1-(1-methyl-1H-imidazol-2-yl)propan-1-one (9m).

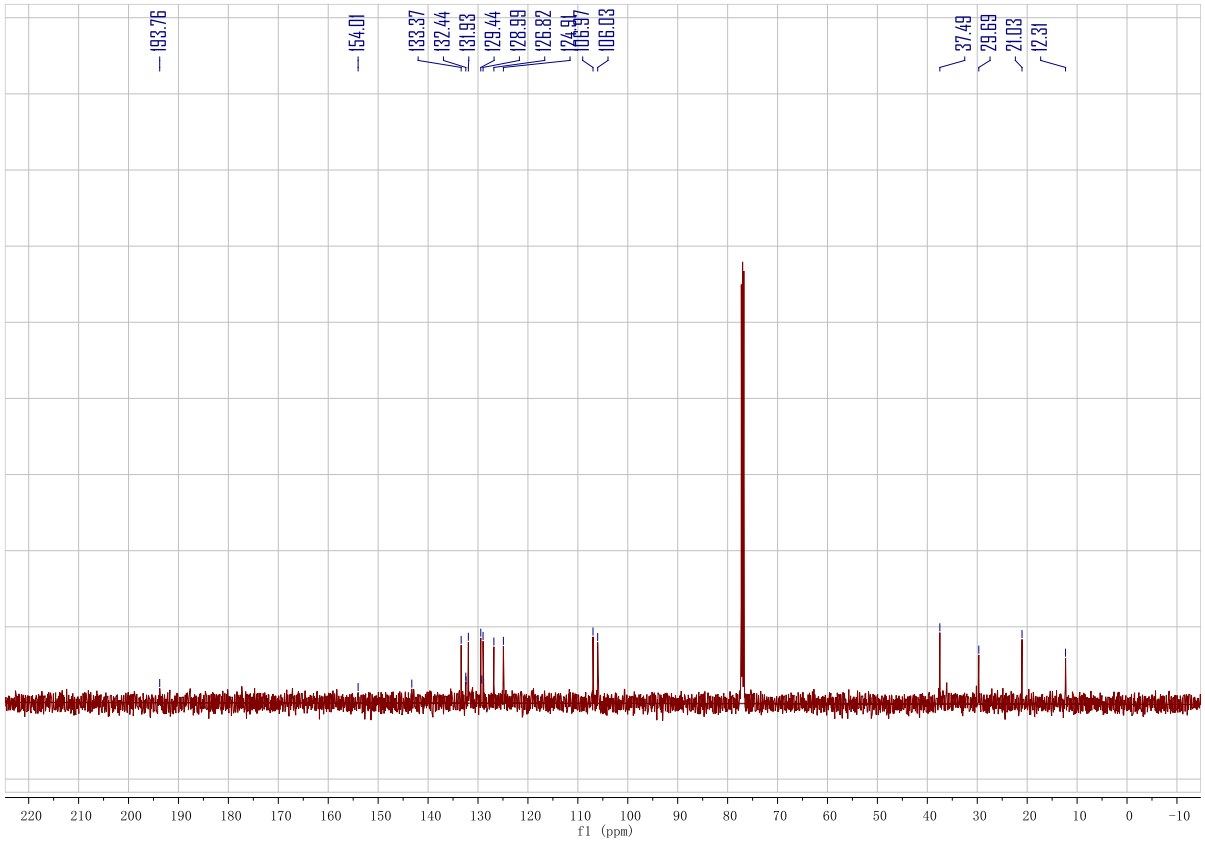
The racemic product was synthesized as described using **7** and 2-methyl-1-(2-nitrophenyl)-1H-pyrrole. The desired product was obtained as a yellow oil after purification by flash column chromatography over silica gel (Hexane: Ethyl acetate, 25:75).

^{1}H NMR (400 MHz, CDCl3) δ 7.99 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.11 (s, 1H), 6.99 (s, 1H), 6.00 (s, 1H), 5.93 (d, J = 2.8 Hz, 1H), 3.94 (s, 3H), 3.39 (dd, J = 14.3, 7.0 Hz, 2H), 2.66 (dd, J = 15.4, 7.9 Hz, 2H), 1.93 (s, 3H).

^{13}C NMR (126 MHz, CDCl3) δ 193.76 (s), 154.01 (s), 143.26 (s), 133.37 (s), 132.44 (s), 132.40 (s), 131.93 (s), 129.44 (s), 129.25 (s), 128.99 (s), 126.82 (s), 124.91 (s), 106.97 (s), 106.03 (s), 37.49 (s), 29.69 (s), 21.03 (s), 12.31 (s).

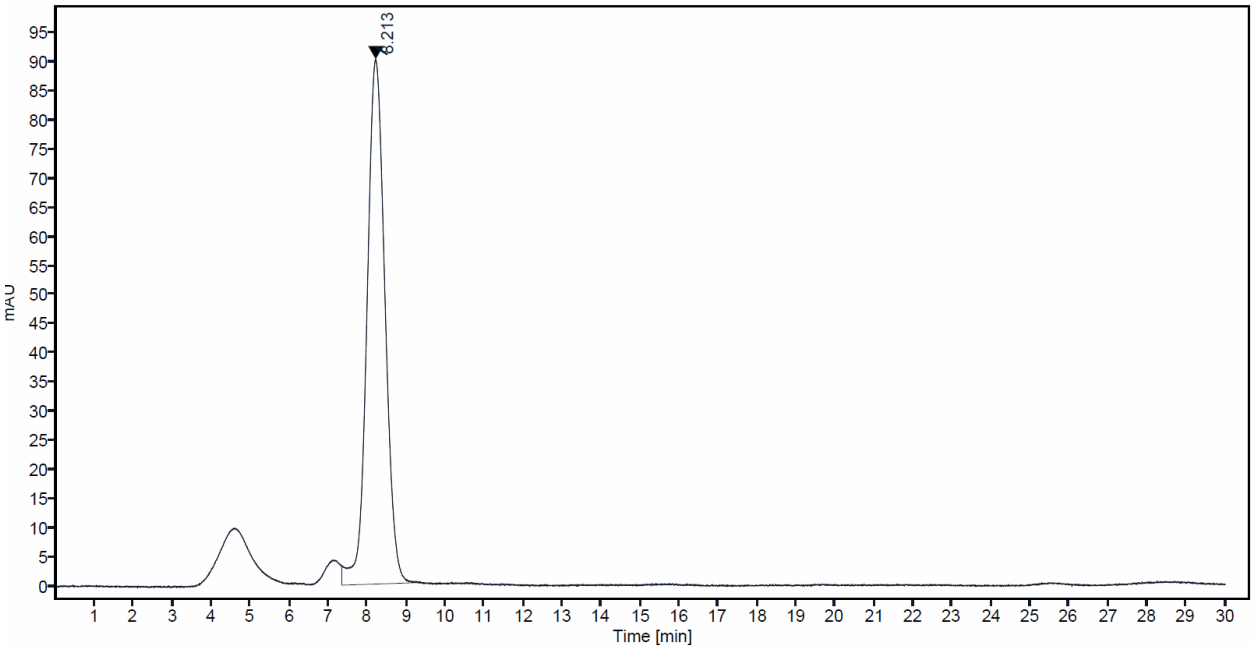
HRMS (ESI) calcd. for $C_{18}H_{19}N_4O_3$ $[M+H]^+$: m/z 339.1452, found: 339.1454.


8.00
7.98
7.74
7.72
7.70
7.62
7.60
7.59
7.46
7.45
7.11
6.99
6.00
5.94
5.93
3.94
3.40
3.38
3.37
2.69
2.67
2.65
2.63
1.93
0.89
1.00
0.95
0.91
0.95
1.04
0.95
1.00
3.23
2.02
2.09
3.24
f1 (ppm)

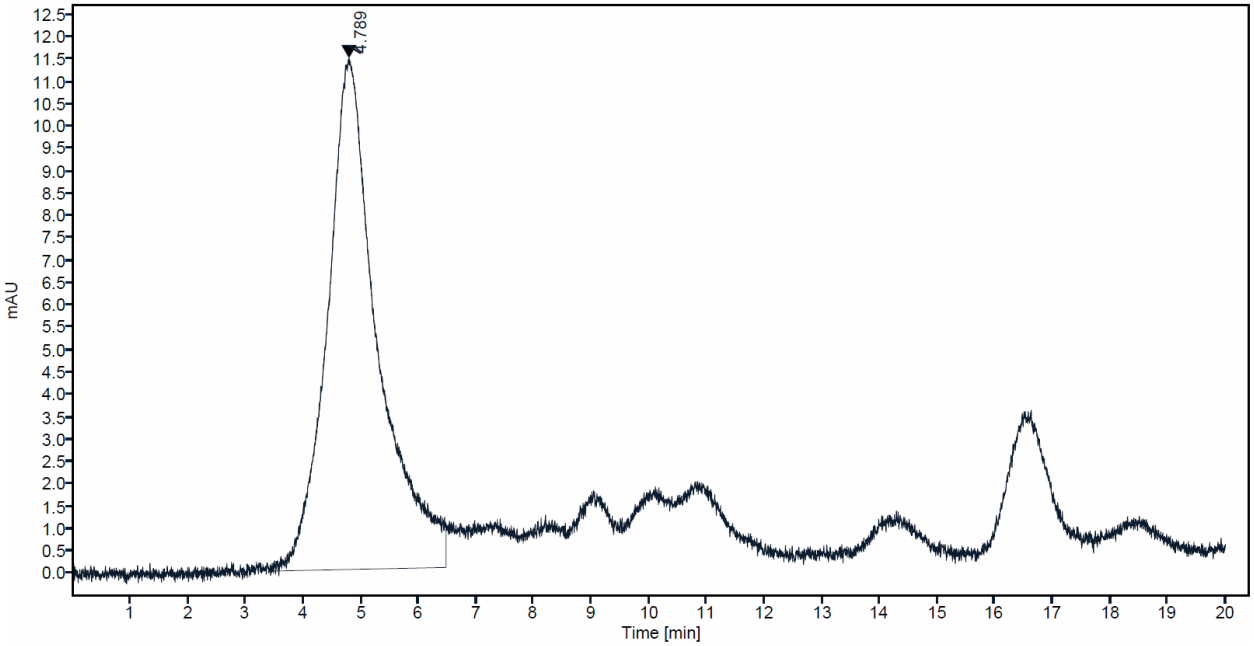

193.76
154.01
133.37
132.44
131.93
129.44
128.99
126.82
124.91
116.97
106.03
37.49
29.69
21.03
12.31
f1 (ppm)

HPLC analysis CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 280 nm

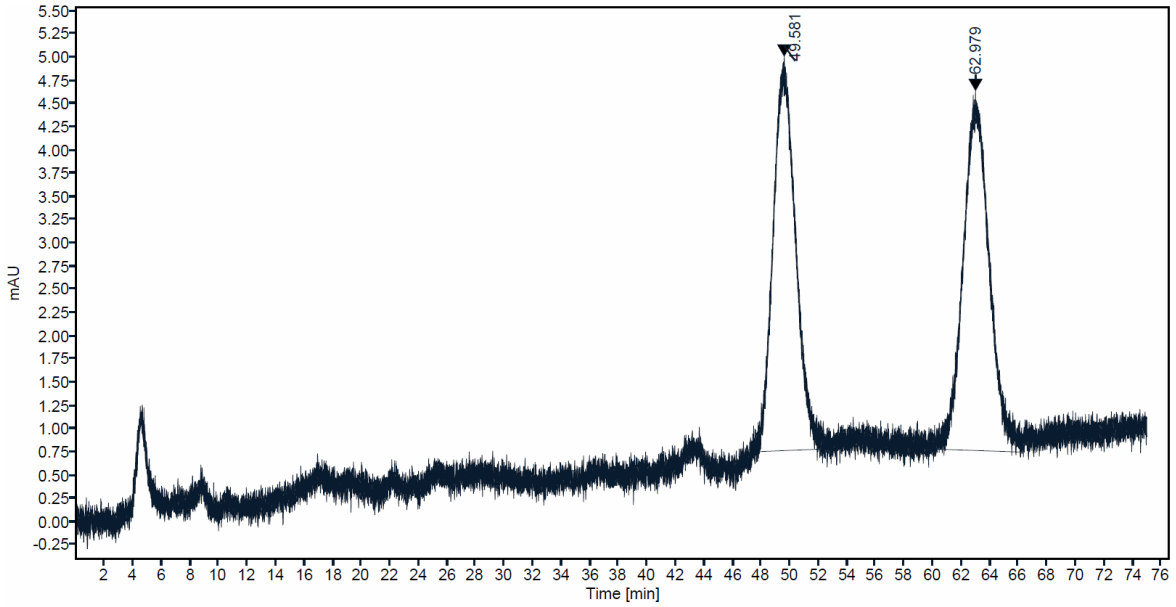
Starting Material (7): Retention time = 6.213 min



2-(2-methyl-1H-pyrrol-1-yl) benzonitrile: Retention time = 4.789 min

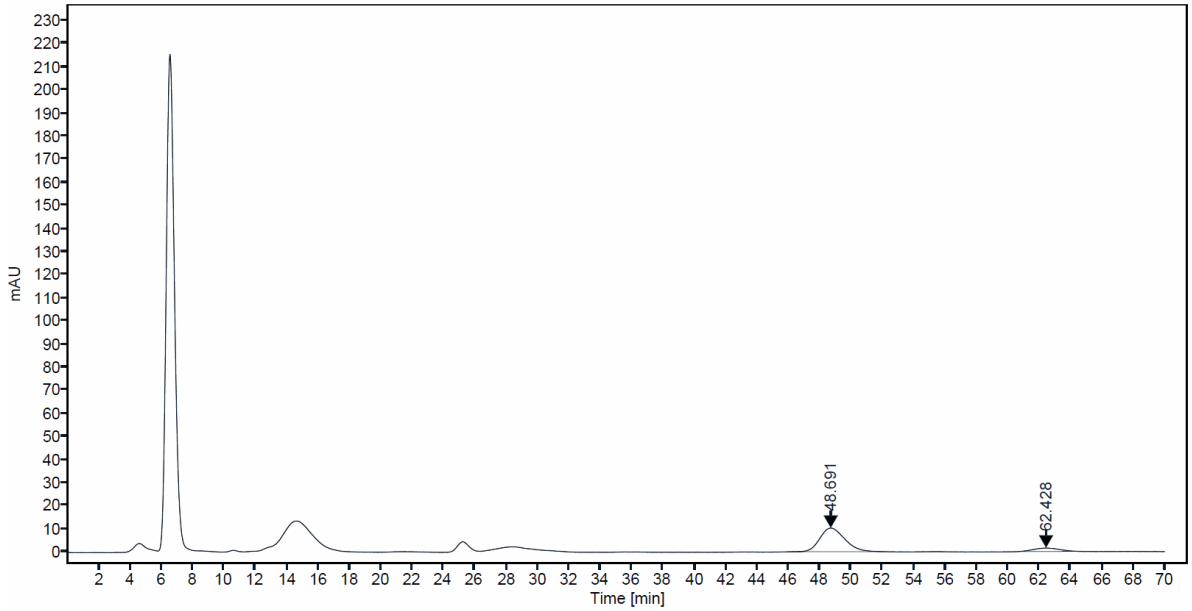


Racemic: Retention time: 49.581 min; 62.979 min



Peak	Retention time (min)	Rel. area (%)
1	49.581	50.2
2	62.979	49.8

DNA Reaction: Following the general procedure. HPLC analysis of the crude residue indicated a ratio of **SM**/**9m** as 1:99 and enantiomeric excess of 75 % [CHIRALCEL IG column, T=25 °C, *n*-Hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 280 nm]. Retention time: 48.691 min; 62.428 min



Peak	Retention time (min)	Rel. area (%)
1	48.691	87.6
2	62.428	12.4

References

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