Highly Enantioselective Synthesis of 1,3-Bis(hydroxymethyl)-2-oxindoles from Unprotected Oxindoles and Formalin Using a Chiral Nd^{III} Complex

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1. General remarks

^{1}H NMR spectra were recorded on commercial instruments (400 MHz and 600 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26 and $(CD_3)_2SO$，δ = 2.54). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR spectra were collected on commercial instruments (100 MHz and 150 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0 and $(CD_3)_2SO$， δ = 40.6). Melting points (m.p.) were measured on electrothermal digital melting point apparatus and were uncorrected. Optical rotations were reported as follows: $[\alpha]^T_D$ (*c* g/100mL, in solvent). Enantiomeric excesses (*ee*) were determined by HPLC using corresponding commercial chiral column as stated in the experimental procedures at 23 °C with UV detector at 254 nm. HRMS was recorded on a commercial apparatus (ESI Source, TOF). Toluene, Et_2O and THF were dried and distilled from sodium benzophenone under nitrogen just before use. Formalin was purchased from Alfa Aesar (37% w/w *aq.* soln., stab. with 7-8% methanol). 3-Substituted-2-oxindoles was prepared in various methods.[1] Racemic samples of **3a-w** were prepared with 5 mol% *N*,*N*,*N*′,*N*′-tetramethylguanidine in CH_2Cl_2.

2. General procedure for chiral *N*,*N*′-dioxides preparation

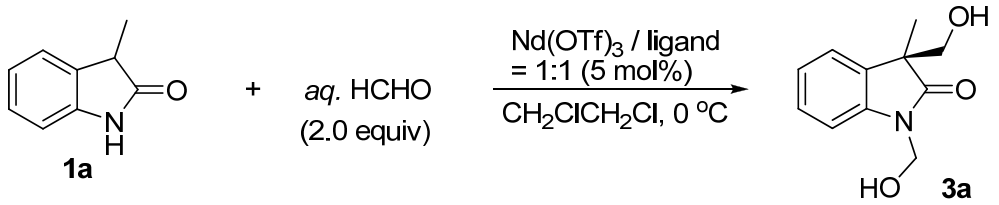
The *N*,*N*′-dioxide ligands **L1-L9** were synthesized by the same procedure in the literature.[2]

3. Typical procedure for the hydroxymethylation reaction of 3-substituted-2-oxindoles with formalin

A mixture of **L3** (5 mol%), $Nd(OTf)_3$ (5 mol%), 3 Å molecular sieves (3 mg) and oxindole **1a** (0.1 mmol) was stirred in CH_2ClCH_2Cl (0.6 mL) at 35 ^{o}C for 1 h. Formalin (2.0 equiv.) was added at 0 ^{o}C. The reaction was stirred at 0 ^{o}C and monitored by TLC. The crude product was directly purified by flash chromatography (petroleum ether/ ethyl acetate, 1:2) to afford a viscous solid. The *ee* value of **3a** was determined by chiral HPLC analysis using a chiralcel AS-H column.

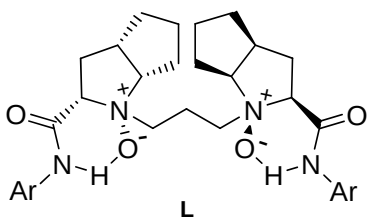
4. Optimization of reaction conditions

Table 1. Ligands evaluated in the hydroxymethylation reaction.[a]

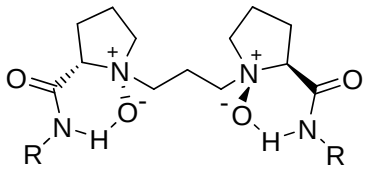


Entry	Ligand	Yield [%][b]	*ee* [%][c]
1	**L1**	33	35
2	**L2**	65	60
3	**L3**	83	87
4	**L4**	18	30
5	**L5**	12	5
6	**L6**	50	40
7	**L7**	88	60
8	**L8**	trace	-
9	**L9**	trace	-

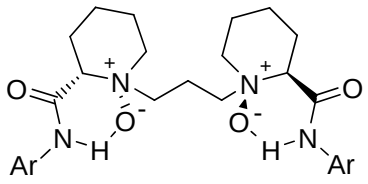
[a] Reaction conditions: **L**-RE(OTf)$_3$ (1:1), **1a** (0.1 mmol) in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2 for 36 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.



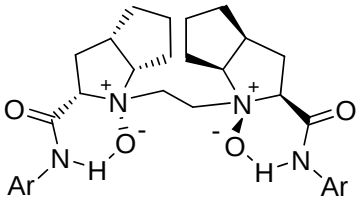
L1: Ar = 2,6-$Me_2C_6H_3$
L2: Ar = 2,6-$Et_2C_6H_3$
L3: Ar = 2,6-*i*$Pr_2C_6H_3$
L4: Ar = 2-*tert*-Bu
L5: Ar = Ph



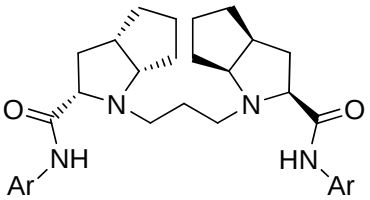
L6: R = 2,6-*i*$Pr_2C_6H_3$



L7: Ar = 2,6-*i*$Pr_2C_6H_3$



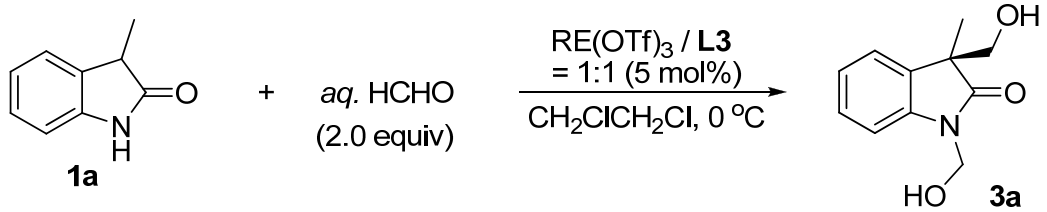
L8: Ar = 2,6-*i*$Pr_2C_6H_3$



L9: Ar = 2,6-*i*$Pr_2C_6H_3$

Figure 1. Ligands evaluated.

Table 2. Screening of RE metals[a]

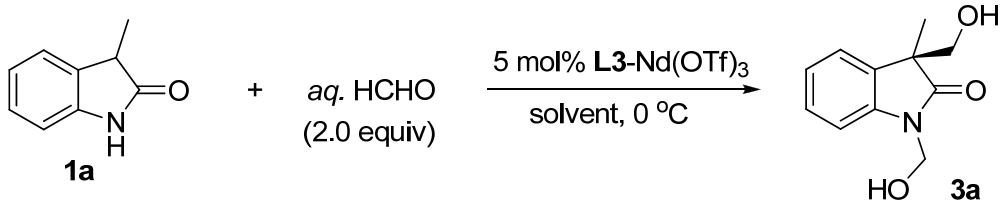


Entry	**RE**	Yield [%][b]	*ee* [%][d]
1	La(OTf)$_3$	90	78
2	Pr(OTf)$_3$	82	84

3	**$Nd(OTf)_3$**	**83**	**87**
4	$Sm(OTf)_3$	88	83
5	$Tb(OTf)_3$	60	70
6	$Dy(OTf)_3$	70	68
7	$Ho(OiPr)_4$	65	70
8	$Yb(OTf)_3$	72	40
9	$Lu(OTf)_3$	50	33
10	$Sc(OTf)_3$	36	55

[a] Unless noted otherwise, the reactions were conducted on a 0.1 mmol scale, 5 mol% catalyst in 0.6 mL CH_2ClCH_2Cl for 36 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

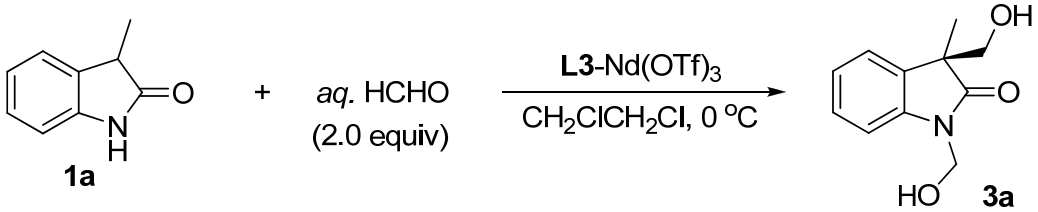
Table 3. Screening of solvents[a]



Entry	Solvent	Yield [%][b]	*ee* [%][c]
1	CH_2Cl_2	75	75
2	$ClCH_2CH_2Cl$	83	87
3[d]	$ClCH_2CH_2Cl$	80	86
4[e]	$ClCH_2CH_2Cl$	84	85
5	$Cl_2CH_2CH_2Cl_2$	80	86
6	Cl_3CCH_3	77	84
7	Et_2O	80	77
8	THF	60	60
9	PhOMe	55	72
10	EtOH	N.R.	-
11	*i*-PrOH	N.R.	-
12	Ethyl acetate	62	65
13	CH_3CN	56	67

[a] Reaction conditions: **L1**-$Nd(OTf)_3$ (1:1), **1a** (0.1 mmol) in CH_2ClCH_2Cl (1.0 mL) at 0 °C under N_2 for 36 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Undistilled CH_2ClCH_2Cl was used. [e] Under aerobic condition. N.R. = no reaction.

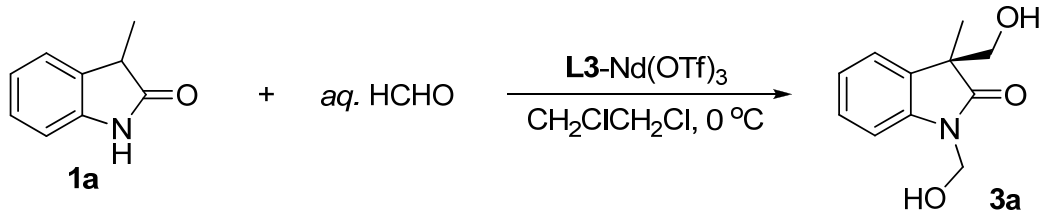
Table 4. Optimization of the ratio between **L3** and $Nd(OTf)_3$[a]



Entry	Ratio of **L3**/$Nd(OTf)_3$	Yield [%][b]	*ee* [%][c]
1	1.5:1	88	85
2	1:1	83	87
3	1:1.5	80	86

[a] Reaction conditions: **1a** (0.1 mmol), 5 mol% catalyst in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2 for 36 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

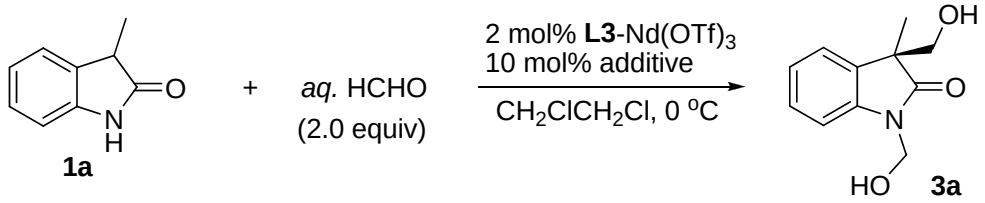
Table 5. Effect of the amount of formalin.[a]



Entry	Amount of formalin (equiv.)	Yield [%][b]	*ee* [%][c]
1	0.8	22	72
2	1.0	35	80
3	1.5	70	88
4	2.0	83	87
5	2.5	88	85
6	3.0	90	84

[a] Reaction conditions: **1a** (0.1 mmol), 5 mol% catalyst in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2 for 36 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

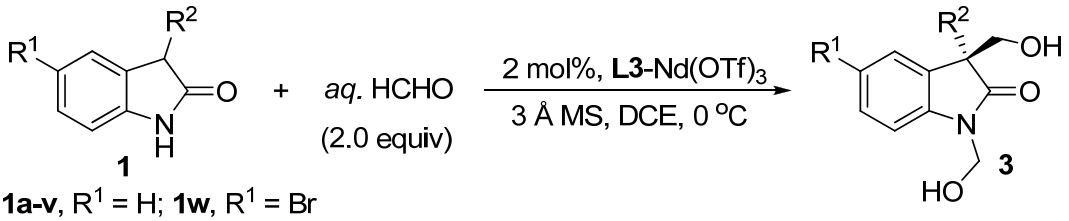
Table 6. Optimization of additives[a]



Entry	Additive	Yield [%][b]	*ee* [%][c]
1	**3 Å MS (3mg)**	**80**	**89**
2	4 Å MS (3mg)	89	86
3	5 Å MS (3mg)	85	82
4	phenol[f]	30	80
5	HCOOH[f]	N.R.	-
6	pyridine[f]	72	84

[a] Reaction conditions: **1a** (0.1 mmol) in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2 for 20 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [f] 1 M in CH_2ClCH_2Cl. N.R. = no reaction.

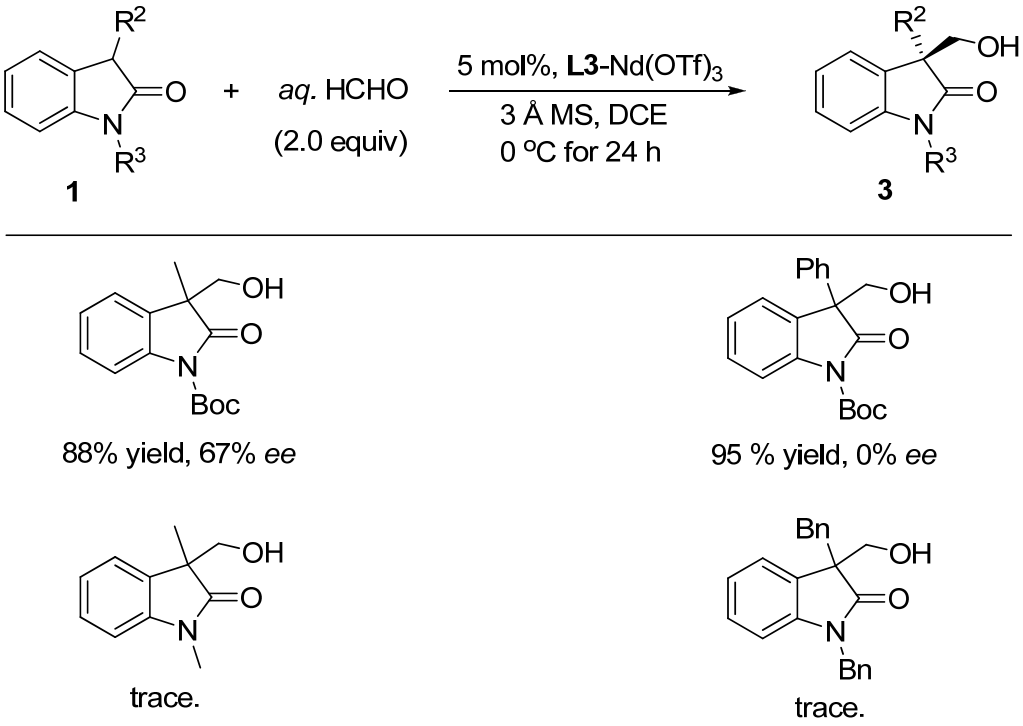
Table 7. Direct catalytic asymmetric hydroxymethylation of oxindoles **1** with formalin.[a]



Entry	R^2	Prod.	*t* [h]	Yield [%][b]	*ee* [%][c]
1	Me	**3a**	20	81	89
2	Et	**3b**	24	82	94
3	*n*-Pr	**3c**	24	77	97
4	*i*-Pr	**3d**	24	60	91
5	*n*-Bu	**3e**	24	83	94
6	Allyl	**3f**	24	87	93
7	Propargyl	**3g**	24	67	96
8	Ph	**3h**	6	91	90
9	Bn	**3i**	24	85	95

10	2-$MeC_6H_4CH_2$	**3j**	24	79	95
11	4-$MeOC_6H_4CH_2$	**3k**	24	81	92
12[d]	Piperonyl	**3l**	36	87	92
13	3-$PhOC_6H_4CH_2$	**3m**	24	91	97
14	4-$PhC_6H_4CH_2$	**3n**	24	87	91
15	2-$ClC_6H_4CH_2$	**3o**	16	90	96
16	4-$ClC_6H_4CH_2$	**3p**	16	79	96
17	2,4-$Cl_2C_6H_3CH_2$	**3q**	16	88	93
18	4-$BrC_6H_4CH_2$	**3r**	16	79	90
19[d]	1-naphthylmethyl	**3s**	16	92	92
20[d]	2-naphthylmethyl	**3t**	16	93	95
21[d]	2-pyridylmethyl	**3u**	36	75	>99
22[d]	2-thienylmethyl	**3v**	24	89	>99
23	Me	**3w**	8	91	89

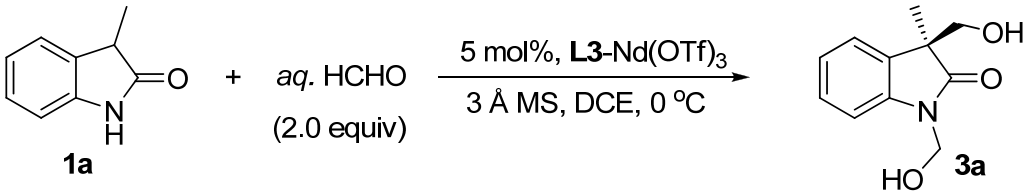
[a] Reaction conditions: **1a** (0.1 mmol), 2 mol% catalyst in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] The reaction was carried out in 0.6 mL of mixed DCE and $CHCl_2CHCl_2$ (v/v, 1:1).



Scheme 1. Investigation of *N*-protected oxindoles.

5. Preliminary mechanism studies.

Table 9. Relationship between reaction time and enantiomeric excess.[a]



Entry	*t* [h]	Yield [%][b]	*ee* [%][c]
1	2	8	86
	4	15	87
2	8	32	87
3	12	51	89
4	16	73	88
5	20	80	89

a] Reaction conditions: **1a** (0.1 mmol) in CH_2ClCH_2Cl (0.6 mL) at 0 °C under N_2 for indicated time. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

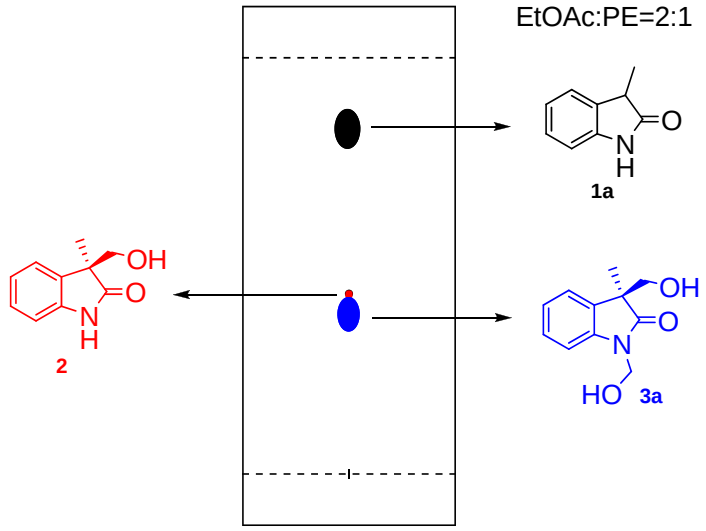
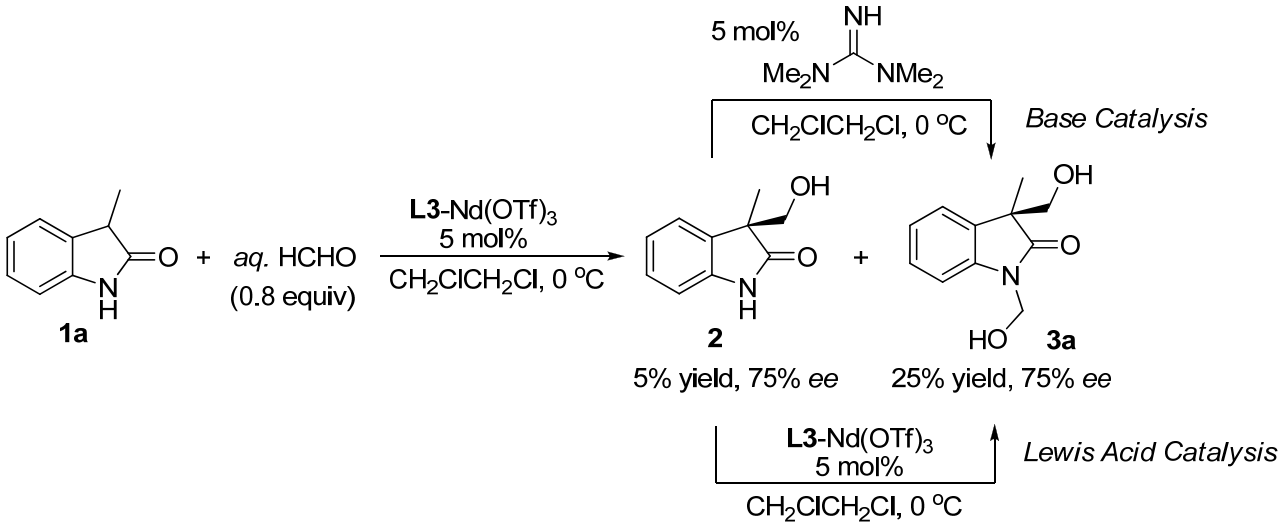


Figure 2. TLC spots of the reaction mixture when 0.8 equiv. formalin was used.



Scheme 2. Transformation of **2** to **3a**. Yield was calculated upon the amount of **1a**.

As shown in Table 7, the enantiomeric excess of **3a** was independent with the reaction time. When the amount of formalin was reduced to 0.8 equiv, **2** was isolated in 5% yield with 75% *ee* (Scheme 2). In this case, the majority product was still **3a** with 75% *ee*. Upon treatment with either 5 mol% 1,1,3,3-tetramethylguanidine or **L3**-Nd(OTf)$_3$, **2** could be converted to **3a** immediately with the maintenance of *ee*. Characterization data of **2**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.25–7.19 (m, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 3.91–3.86 (d, *J* = 12, Hz, 1H), 3.79 (dd, *J* = 10.9, 3.6 Hz, 1H), 1.60 (s, 3H). The *ee* was determined by HPLC analysis using a chiralcel AD column, hexane/2-propanol 80:20, flow rate = 1.0 mL/min 254 nm. *tR* = 7.1 min (major), 14.2 min (minor), 75% *ee*.

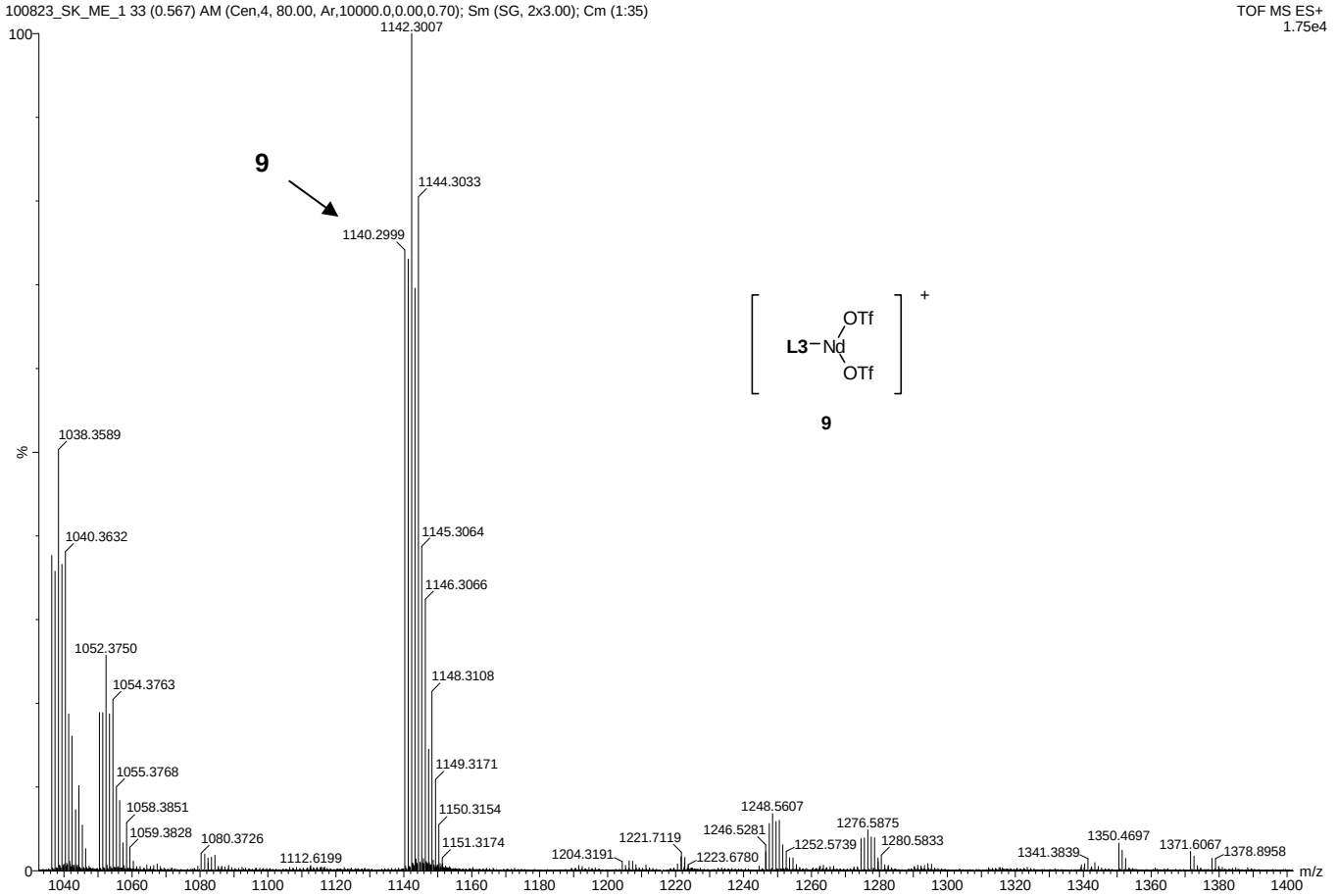


Figure 3. ESIMS spectrum of the hydroxymethylation reaction, 1 h after stirring **L3** and Nd(OTf)$_3$ in DME. HRMS: *m/z* calcd: 1140.3045 [**L3**+Nd(OTf)$_2$]$^+$; found: 1140.3007.

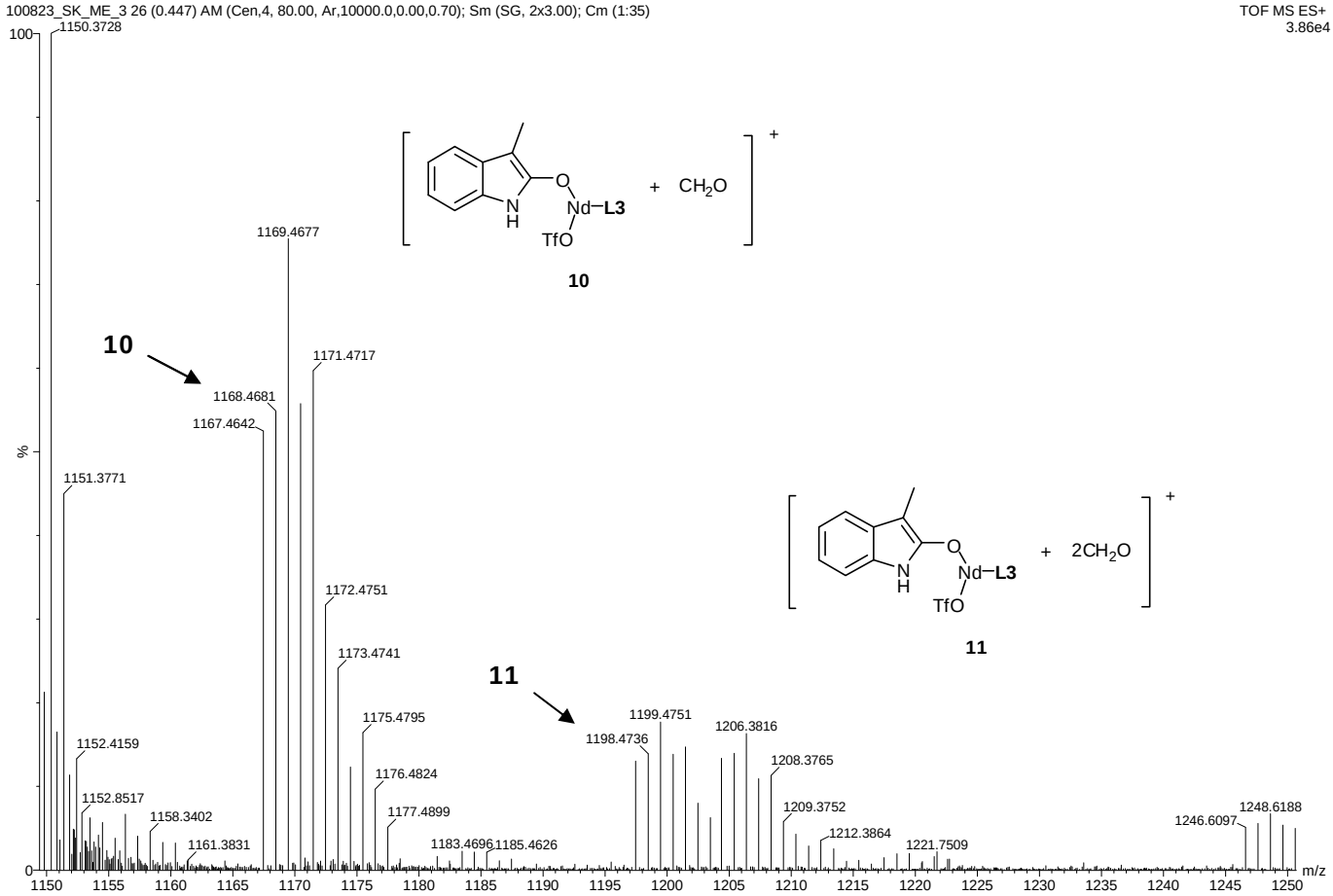
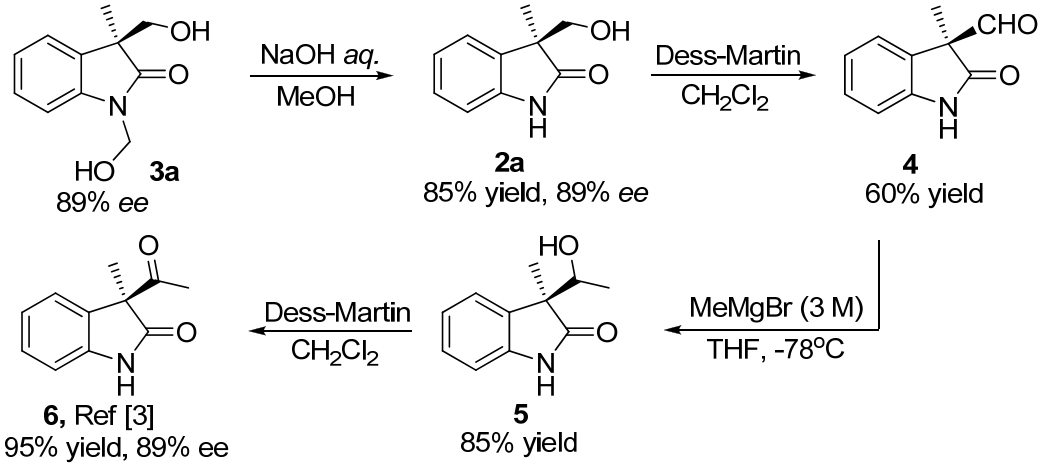


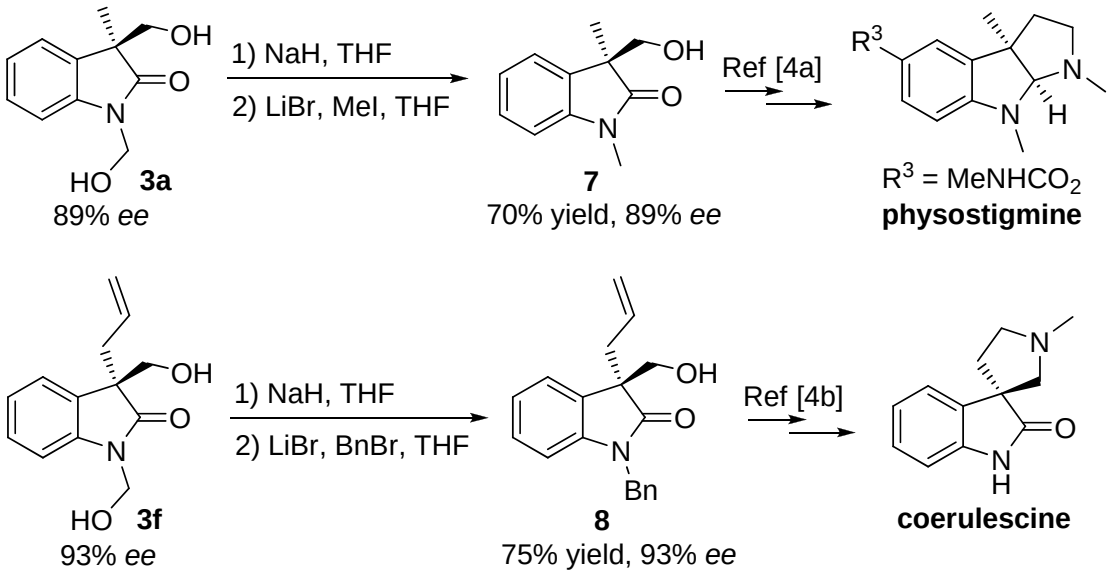
Figure 4. ESIMS spectrum of the hydroxymethylation reaction, 3 h after stirring **2a** with **L5**-$Sc(OTf)_3$ and **1a** in CH_2Cl_2. HRMS: *m/z* calcd: 1168.4315 [**L3**+NdOTf+**1a**+CH_2O]$^+$, 1198.4420 [**L3**+NdOTf+**1a**+$2CH_2O$]$^+$; found: 1168.4681, 1198.4736.

6. Experimental procedure for the structural expansion of 3a and 3f



To a solution of **3a** (41.4 mg, 89% *ee*, 0.2 mmol) in MeOH (2.0 mL) was added *aq.* NaOH (5 M, 0.3 mmol, 1.5 equiv) at 0 ^oC. The mixture was warm to rt and stir for 2 h. Then the mixture was added 2 mL saturated $NaHSO_4$, and was extracted with ethyl acetate. The extraction was concentrated under reduced pressure and purified by flash chromatography (petroleum ether / ethyl acetate = 2/1) afford **2a** (30.2 mg, 85% yield, 89% *ee*). Dess-Martin reagent

(100 mg, 0.24 mmol) was added to a pre-cooled solution of **2a** (30.2 mg, 0.17 mmol) in 3 mL CH_2Cl_2. After stirring for 1 h at ambient temperature, the mixture was filtered though silica gel. The filtrate was purified by flash chromatography (petroleum ether / ethyl acetate = 5/1) afford **4** in 60% yield. Then **4** (17.9 mg, 0.1 mmol) was treated with MeMgBr (3 M, 0.12 mmol) in anhydrous THF at -78 ^{o}C for 2 h. The solution was quenched by saturated *aq.* NH_4Cl at 0 ^{o}C. The organic layer was separated and concentrated. The crude product was purified by flash chromatography (petroleum ether / ethyl acetate = 2/1). To a solution of **5** (16.6 mg, 0.087 mmol) in 3 mL CH_2Cl_2 was added Dess-Martin reagent (50 mg, 0.12 mmol) at rt. After completion of the oxidation, filtration followed by removal of solvent under reduced pressure and silica gel flash column flash to generate 6a in 95% yield with 89% *ee*. Characterization data of **6**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.30 (td, *J* = 7.6, 0.9 Hz, 1H), 7.14 (d, *J* = 7.0 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 2.05 (s, 3H), 1.61 (s, 3H). The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 85:15, flow rate = 1.0 mL/min 254 nm. *tR* = 7.1 min (minor), 14.2 min (major), 89% *ee*.[3]



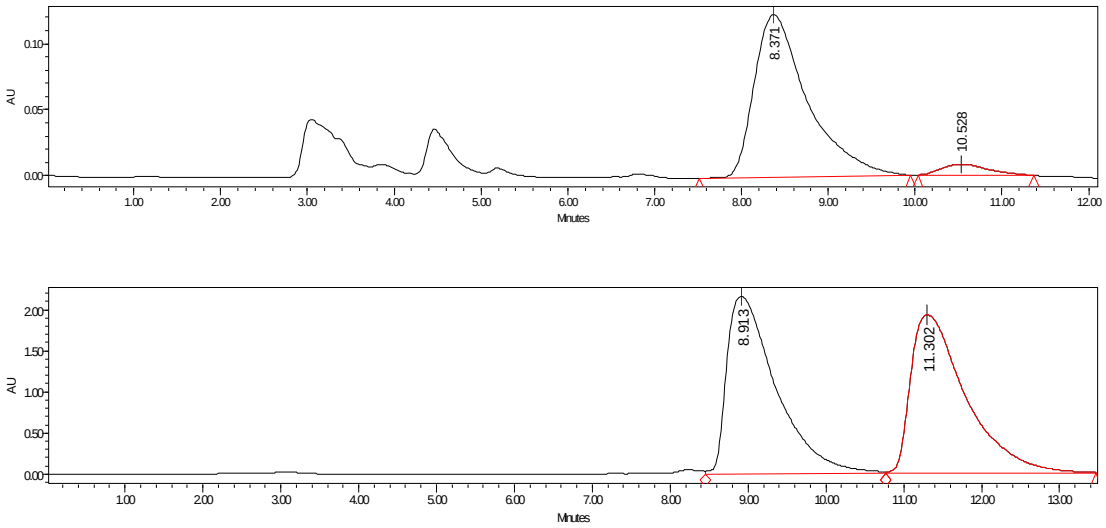
To a solution of **3a** (20.7 mg, 0.1 mmol) in anhydrous THF (3.0 mL) was added NaH (60%, 6 mg, 0.15 mmol, 1.5 equiv) at 0 ^{o}C. The mixture was allowed to warm to ambient temperature for 1h. Then anhydrous LiBr (17.4 mg, 0.2 mmol) and MeI (21.3 mg, 0.15 mmol) was added sequentially to the reaction mixture. The reaction was stirred at rt and monitored by TLC. When **3a** was consumed, water (5 mL) and ethyl acetate (5 mL) were added. The organic phase was saperated and concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether / ethyl acetate = 1/1) afford **7** in 70% yield. For **7**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.31 (t, *J* = 7.7, 1 H), 7.23 (d, *J* = 7.3, 1 H), 7.10 (t, *J* = 7.5, 1 H), 6.88 (d, *J* = 7. 8, 1 H), 3.90–3.80 (m, 1 H), 3.74 (dd, *J* = 10.8, 3.3, 1 H), 3.23 (s, 3 H), 2.29 (s, 1 H), 1.41 (s, 3 H).[4a] Product **8** was synthesized by similar procedure. For **8**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.40 (d, *J* = 7.3 Hz, 2H), 7.33–7.25 (m, 11H), 7.21 (t, *J* = 7.7 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 2H), 6.70 (d, *J* = 7.8 Hz, 2H), 5.65 (ddd, *J* = 16.7, 9.2,

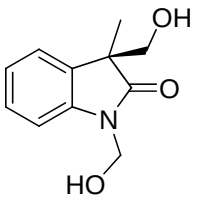
6.3 Hz, 2H), 5.13 (dd, *J* = 18.0, 13.6 Hz, 4H), 5.02 (d, *J* = 15.7 Hz, 2H), 4.74 (d, *J* = 15.7 Hz, 2H), 4.00–3.90 (m, 1 H), 3.84 (dd, *J* = 10.6, 3.2, 1 H), 2.95 (s, 2H), 2.81 (dd, *J* = 13.3, 6.2 Hz, 2H), 2.69 (dd, *J* = 13.3, 8.5 Hz, 2H).[4b]

7. The analytical and spectral characterization data of 3a-w

1,3-bis(hydroxymethyl)-3-methylindolin-2-one (3a):

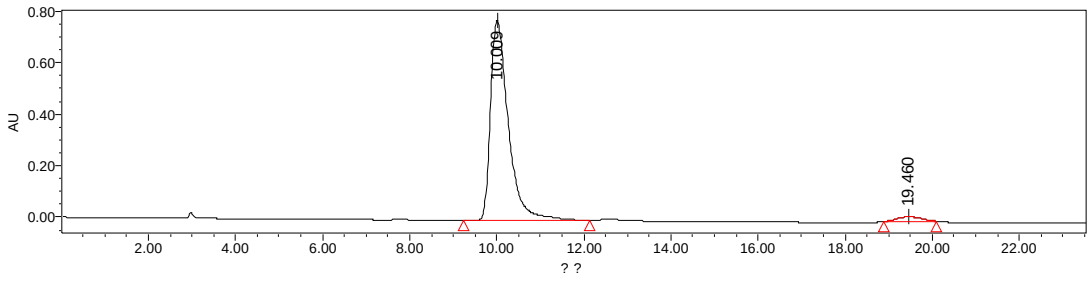
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (80% isolated yield, 89% *ee*). $[\alpha]^{26}_{D}$ = -12.28 (c = 0.08, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.10 (dd, *J* = 17.8, 7.7 Hz, 2H), 5.35 (dd, *J* = 11.1, 5.5 Hz, 1H), 5.12–4.89 (m, 1H), 4.45 (dd, *J* = 8.5, 6.4 Hz, 1H), 3.86 (dd, *J* = 10.5, 6.1 Hz, 1H), 3.71 (d, *J* = 10.8 Hz, 1H), 2.96 (s, 1H), 1.29 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 180.33, 141.90, 131.49, 128.41, 123.26, 122.79, 109.62, 67.62, 63.69, 50.84, 18.90 ppm. HRMS (ESI): calcd for $C_{11}H_{13}NO_3$ [M+H$^+$] 208.0968, found 208.0975. The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 85:15, flow rate = 1.0 mL/min 254 nm. t_R = 8.37 min (major), 10.53 min (minor), 89% *ee*.

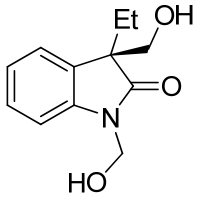


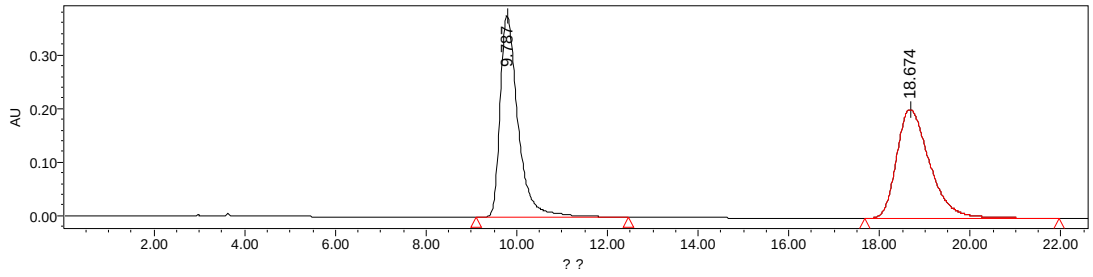


3-ethyl-1,3-bis(hydroxymethyl)indolin-2-one (3b):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to to afford viscous solid (82% isolated yield, 94% *ee*). $[\alpha]^{26}_{D}$ = -4.29 (c = 0.10, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.19 (m, 1H), 7.12 (d, *J* = 7.1 Hz, 1H), 7.07–7.00 (m, 2H), 5.30 (dd, *J* = 11.1, 5.7 Hz, 1H), 4.96–4.87 (m, 1H), 4.57 (dd, *J* = 9.0, 6.1 Hz, 1H), 3.82 (dd, *J* = 10.8, 7.4 Hz, 1H), 3.71–3.65 (m, 1H), 2.98 (dd, *J* = 6.9, 4.9 Hz, 1H), 1.88–1.61 (m, 2H), 0.51 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.82, 142.70, 129.56, 128.41, 123.21, 123.02, 109.46, 67.14, 63.64, 56.18, 26.19, 8.12 ppm. HRMS (ESI): calcd for $C_{12}H_{15}NO_3$ [M+H$^+$] 222.1125, found 222.1133. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90:10, flow rate = 1.0 mL/min 254 nm. t_R = 10.00 min (major), 19.46 min (minor), 94% *ee*.

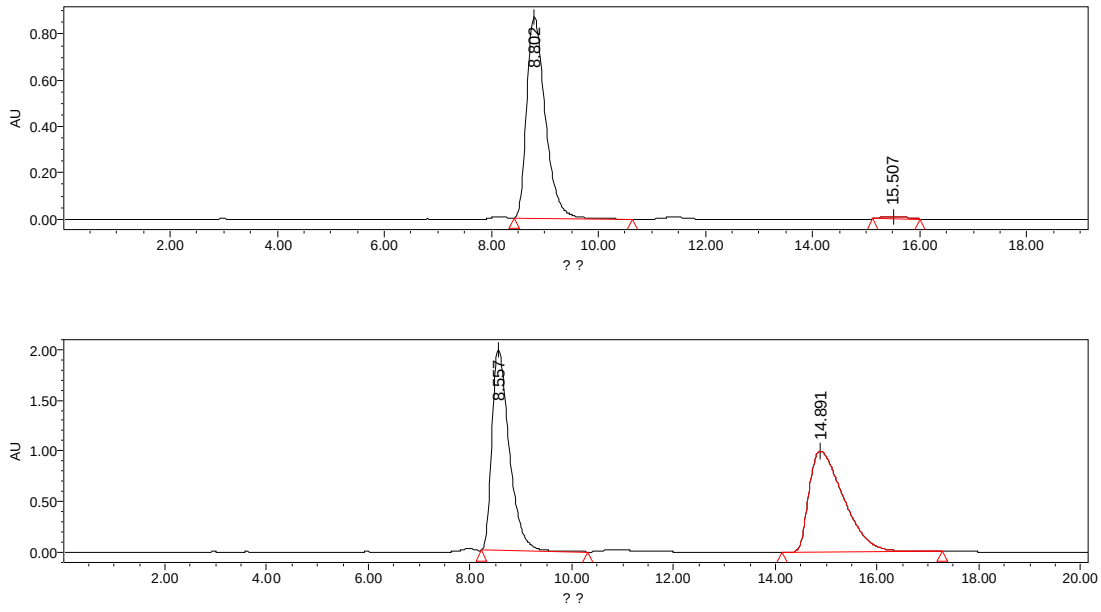


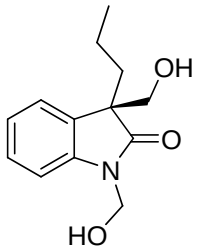




1,3-bis(hydroxymethyl)-3-propylindolin-2-one (3c):

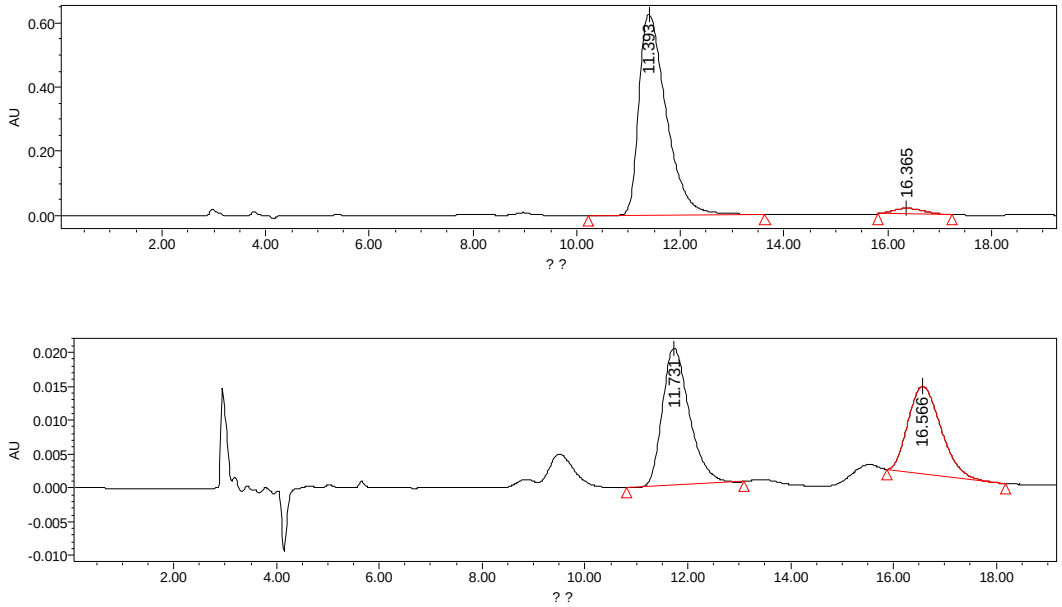
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (77% isolated yield, 97% *ee*). $[\alpha]^{26}_{D}$ = 2.5 (c = 0.11, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 1H), 7.14–7.05 (m, 2H), 5.36 (dd, *J* = 11.1, 5.6 Hz, 1H), 5.03–4.94 (m, 1H), 4.51 (dd, *J* = 8.7, 6.0 Hz, 1H), 3.88 (dd, *J* = 10.8, 7.6 Hz, 1H), 3.74 (dd, *J* = 7.2, 5.1 Hz, 2H), 3.02–2.88 (m, 1H), 2.07 (s, 1H), 1.90–1.80 (m, 2H), 1.65 (td, *J* = 12.7, 4.5 Hz, 1H), 0.76 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.92, 142.54, 129.89, 128.38, 123.21, 122.98, 109.48, 67.39, 63.64, 55.71, 35.28, 17.21, 14.14 ppm. HRMS (ESI): calcd for $C_{13}H_{17}NO_3$ [M+H$^+$] 236.1281, found 236.1284. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90:10, flow rate = 1.0 mL/min 254 nm. t_R = 8.00 min (major), 15.51 min (minor), 97% *ee*.

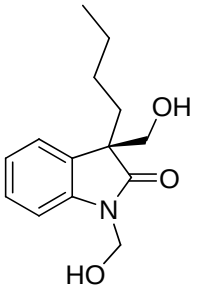




3-butyl-1,3-bis(hydroxymethyl)indolin-2-one (3e):

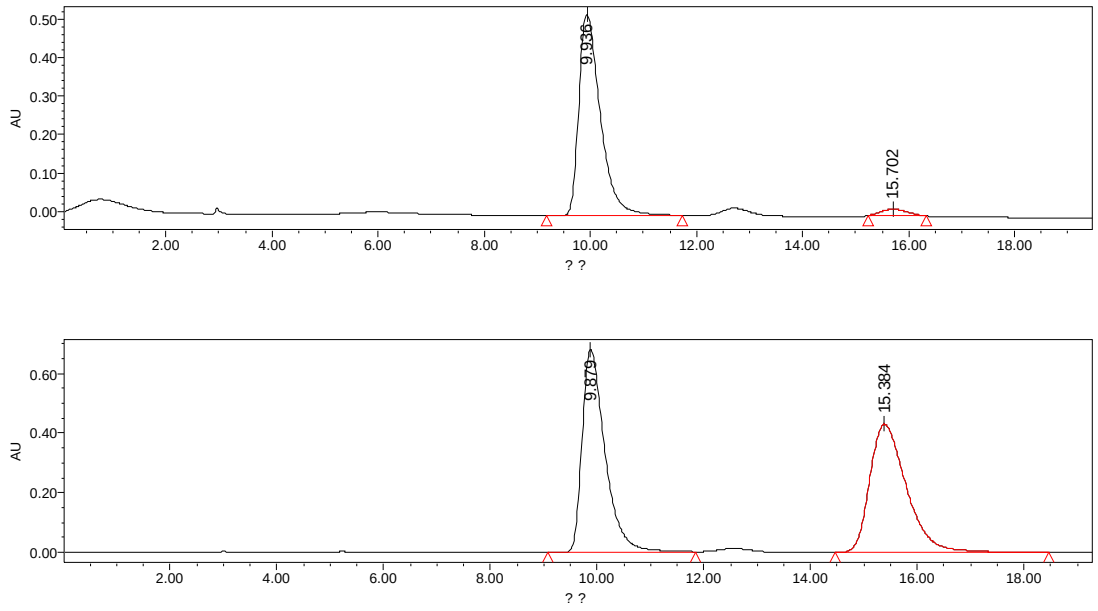
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (83% isolated yield, 94% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$) 7.22 (dd, *J* = 13.5, 5.8, 1 H), 7.12 (d, *J* = 7.3, 1 H), 7.05 (t, *J* = 7.5, 1 H), 7.00 (d, *J* = 7.8, 1 H), 5.30 (dd, *J* = 11.0, 4.0, 1 H), 4.89 (t, *J* = 9.5, 1 H), 4.49 (s, 1 H), 3.80 (d, *J* = 10.0, 1 H), 3.65 (d, *J* = 10.8, 1 H), 2.93 (s, 1 H), 1.78 (td, *J* = 12.8, 4.5, 1 H), 1.59 (td, *J* = 12.8, 4.3, 1 H), 1.09 (tq, *J* = 13.5, 6.8, 2 H), 0.92 – 0.71 (m, 2 H), 0.68 (t, *J* = 7.3, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.91, 142.55, 129.91, 128.36, 123.21, 122.94, 109.52, 67.43, 63.65, 55.64, 32.85, 25.83, 22.78, 13.72 ppm. HRMS (ESI): calcd for $C_{14}H_{19}NO_3$ [M+H$^+$] 250.1438, found 250.1435. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 93:7, flow rate = 1.0 mL/min 254 nm. t_R = 11.39 min (major), 16.37 min (minor), 94% *ee*.

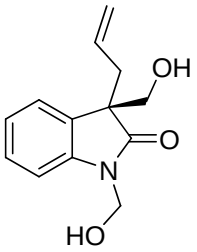




3-allyl-1,3-bis(hydroxymethyl)indolin-2-one (3f):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (87% isolated yield, 93% *ee*). $[\alpha]^{26}_{D}$ = -20.59 (c = 0.15, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (ddd, *J* = 13.9, 11.4, 5.8 Hz, 2H), 7.16–7.05 (m, 2H), 5.34 (dd, *J* = 11.2, 6.0 Hz, 2H), 5.02–4.88 (m, 3H), 4.53 (dd, *J* = 8.5, 6.2 Hz, 1H), 3.99–3.88 (m, 1H), 3.77 (tt, *J* = 8.1, 3.9 Hz, 1H), 3.09 (dd, *J* = 7.5, 4.7 Hz, 1H), 2.59–2.45 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.28, 142.34, 131.30, 129.22, 128.54, 123.38, 123.18, 119.24, 109.55, 66.63, 63.64, 55.09, 37.43 ppm. HRMS (ESI): calcd for $C_{13}H_{15}NO_3$ $[M+H^+]$ 234.1125, found 234.1127. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90:10, flow rate = 1.0 mL/min 254 nm. t_R = 9.94 min (major), 15.70 min (minor), 93% *ee*.

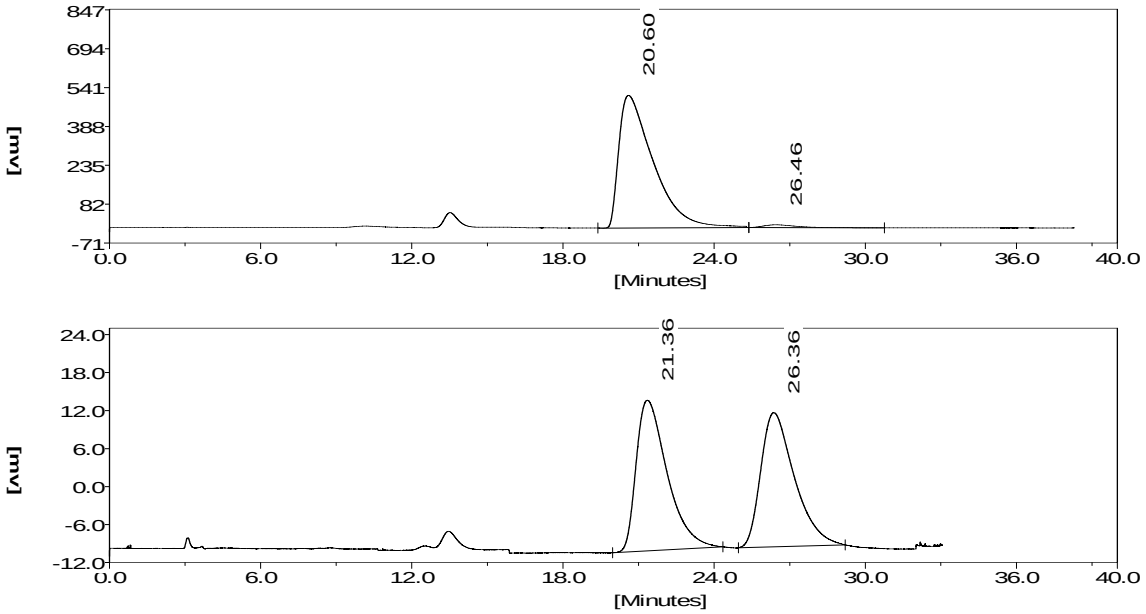


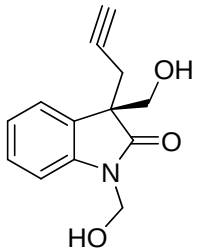


1,3-bis(hydroxymethyl)-3-(prop-2-ynyl)indolin-2-one (3g):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (67% isolated yield, 96% *ee*). $[\alpha]^{26}_{D}$ = 13.88 (c = 0.13, in THF). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.14 (dd, *J* = 19.5, 7.7 Hz, 2H), 5.36–5.28 (m, 3H), 5.17 (dd, *J* = 11.0, 7.9 Hz, 1H), 4.05–3.86 (m, 2H), 3.74 (t, *J* = 6.4 Hz, 1H), 2.82 (dd, *J* = 16.7,

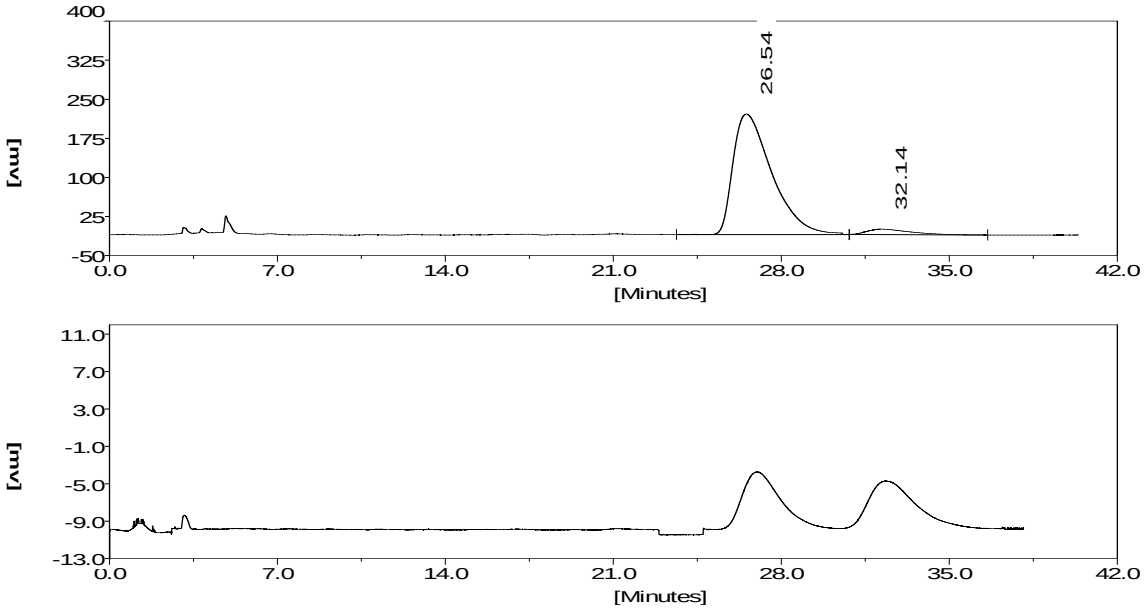
2.6 Hz, 1H), 2.67–2.59 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.52, 142.10, 129.07, 128.59, 123.81, 123.74, 123.41, 109.49, 78.57, 71.31, 67.98, 65.69, 63.91, 23.02 ppm. HRMS (ESI): calcd for $C_{13}H_{13}NO_3$ [M+Na$^+$] 254.0788, found 254.0789. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90: 10, flow rate = 1.0 mL/min 254 nm. t_R = 20.60 min (major), 26.46 min (minor), 96% *ee*.

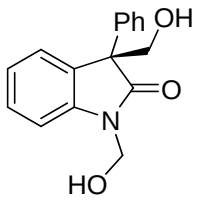




1,3-bis(hydroxymethyl)-3-phenylindolin-2-one (3h):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (91% isolated yield, 90% *ee*). m.p. 124-126 ^{o}C. ^{1}H NMR (600 MHz, d_6-DMSO) 7.36 (d, *J* = 7.4, 1 H), 7.31 (q, *J* = 7.8, 5 H), 7.26 (dd, *J* = 8.8, 3.1, 1 H), 7.16 (d, *J* = 7.8, 1 H), 7.10 (t, *J* = 7.5, 1 H), 6.30–6.26 (m, 1 H), 5.21–5.14 (m, 1 H), 5.05 (dd, *J* = 5.5, 3.4, 1 H), 5.03–4.95 (m, 1 H), 4.20–4.13 (m, 1 H), 4.11–4.04 (m, 1 H) ppm. ^{13}C NMR (151 MHz, d_6-DMSO) δ = 176.99, 143.29, 138.62, 131.39, 128.87, 128.32, 127.66, 127.37, 125.55, 122.65, 109.90, 66.13, 63.15, 59.16 ppm. HRMS (ESI): calcd for $C_{16}H_{15}NO_3$ [M+H$^+$] 270.1125, found 270.1132. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90:10, flow rate = 1.0 mL/min 254 nm. t_R = 26.54 min (major), 32.14 min (minor), 90% *ee*.

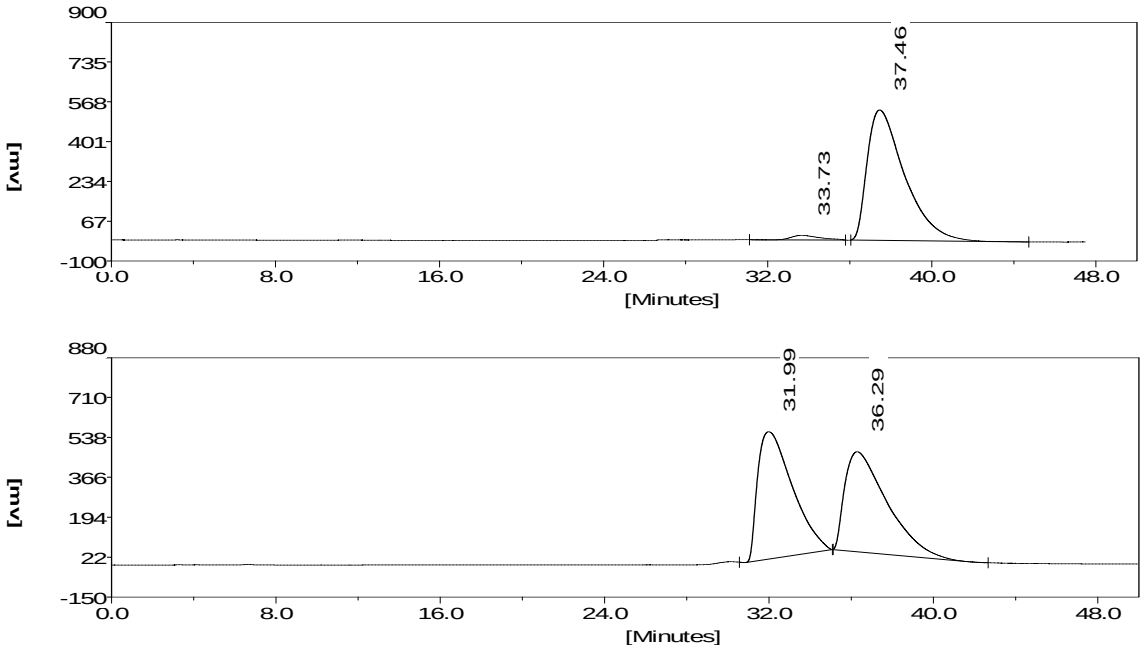


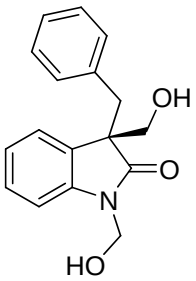


3-benzyl-1,3-bis(hydroxymethyl)indolin-2-one (3i):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (85% isolated yield, 95% *ee*). $[\alpha]^{26}_D$ = -41.53 (c = 0.14, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 13.1, 5.5 Hz, 1H), 7.02 (tt, *J* = 13.7, 6.7 Hz, 5H),

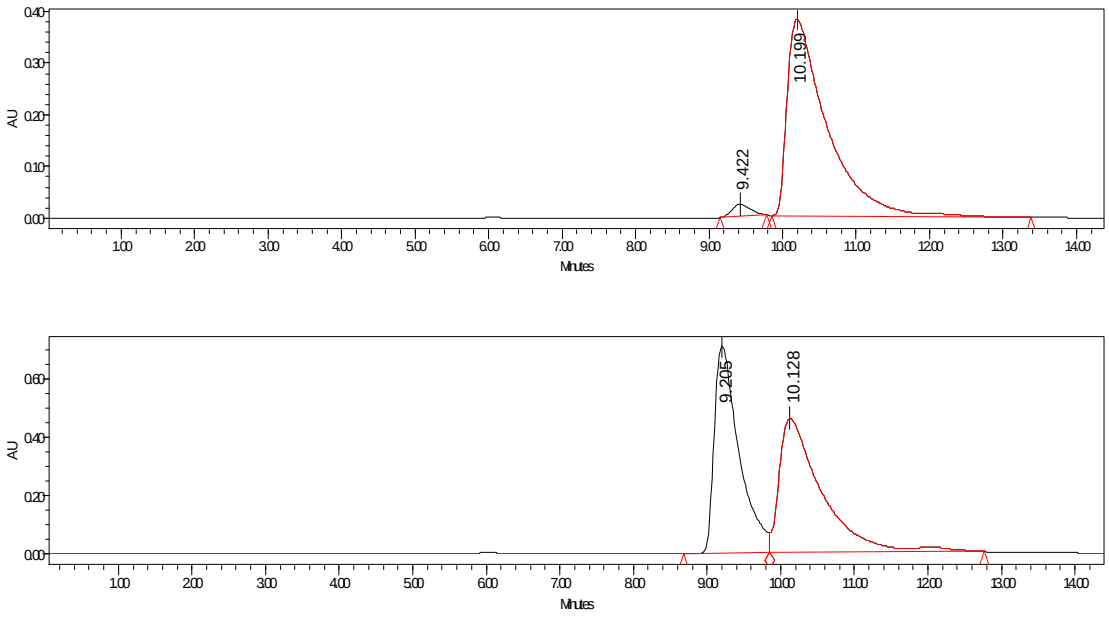
6.79 (dd, *J* = 15.1, 7.5 Hz, 3H), 5.04 (dd, *J* = 11.0, 6.5 Hz, 1H), 4.80–4.70 (m, 1H), 4.00–3.91 (m, 1H), 3.78 (d, *J* = 10.9 Hz, 1H), 3.67 (d, *J* = 6.0 Hz, 1H), 3.05 (d, *J* = 13.1 Hz, 1H), 2.99 (d, *J* = 13.1 Hz, 1H), 2.97 (s, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.23, 142.22, 135.02, 129.94, 128.77, 128.57, 127.74, 126.74, 123.82, 122.94, 109.44, 66.30, 63.46, 56.42, 39.22 ppm. HRMS (ESI): calcd for $C_{17}H_{17}NO_3$ [M+Na$^+$] 306.1101, found 306.1100. The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 95: 5, flow rate = 1.0 mL/min 254 nm. t_R = 33.73 min (minor), 37.46 min (major), 95% *ee*.

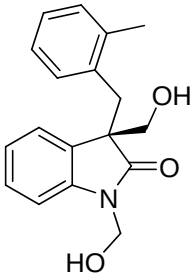




1,3-bis(hydroxymethyl)-3-(2-methylbenzyl)indolin-2-one (3j):

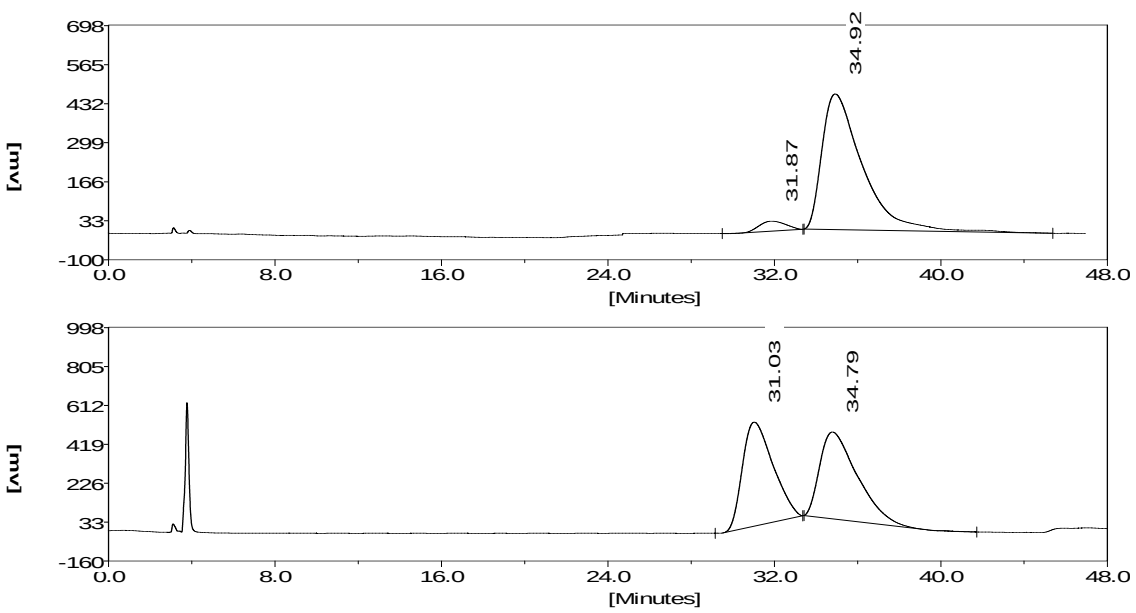
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (79% isolated yield, 95% *ee*). m.p. 104-105 °C. $[\alpha]^{26}_D$ = -14.97 (c = 0.18, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) 7.30–7.26 (m, 1 H), 7.09–6.99 (m, 3 H), 6.96 (d, *J* = 7.8, 2 H), 6.89 (dd, *J* = 7.3, 3.5, 2 H), 5.19–5.00 (m, 2 H), 4.07 (t, *J* = 10.2, 1 H), 3.85 (dd, *J* = 11.1, 2.8, 1 H), 3.20 (s, 2 H), 2.97–2.77 (m, 1 H), 2.67 (d, *J* = 6.8, 1 H), 2.00 (s, 3 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.81, 142.16, 137.24, 133.79, 130.40, 130.34, 128.77, 128.60, 126.87, 125.38, 124.01, 122.86, 109.50, 65.90, 63.55, 55.57, 34.77, 19.89 ppm. HRMS (ESI): calcd for $C_{18}H_{19}NO_3$ [M+H$^+$] 298.1438, found 298.1437. The *ee* was determined by HPLC analysis using a chiralcel IA column, hexane/2-propanol 85:15, flow rate = 1.0 mL/min 254 nm. t_R = 9.42 min (minor), 10.11 min (major), 95% *ee*.

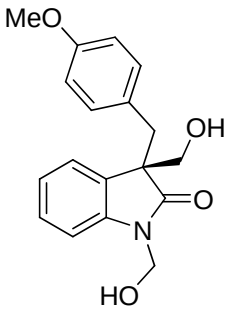




1,3-bis(hydroxymethyl)-3-(4-methoxybenzyl)indolin-2-one (3k)：

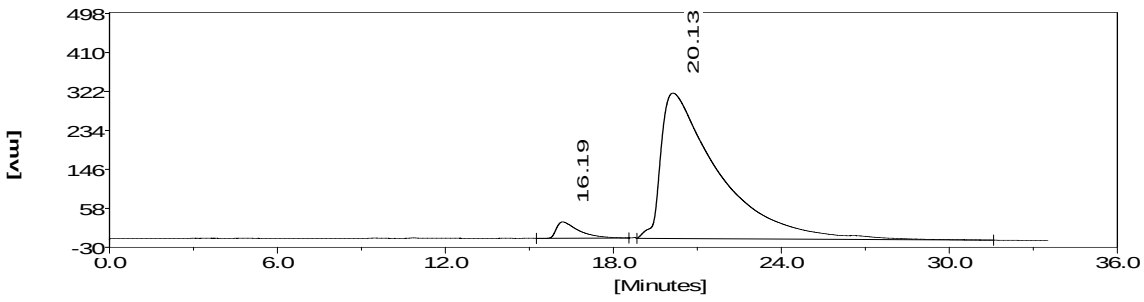
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a colorless needle (81% isolated yield, 92% *ee*). m.p. 92-93 °C. $[\alpha]^{26}_{D}$ = -45.20 (c = 0.17, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) 7.27 (d, *J* = 8.7, 2 H), 7.12 (dt, *J* = 14.7, 7.2, 2 H), 6.90 (d, *J* = 7.8, 1H), 6.79 (d, *J* = 8.0, 2 H), 6.61 (d, *J* = 8.2, 2 H), 5.05 (d, *J* = 7.7, 2 H), 4.03 (t, *J* = 10.1, 1 H), 3.91–3.82 (m, 1 H), 3.70 (3 H, s), 3.15 (d, *J* = 13. 2, 1 H), 3.08 (d, *J* = 13.3, 1 H), 2.46 (dd, *J* = 13.3, 10.2, 2 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.34, 158.32, 142.25, 130.91, 128.91, 128.49, 127.00, 123.78, 122.90, 113.13, 109.51, 66.25, 63.47, 56.61, 55.09, 38.27 ppm. HRMS (ESI): calcd for $C_{18}H_{19}NO_4$ [M+Na^+] 336.1206, found 336.1204. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 95: 5, flow rate = 1.0 mL/min 254 nm. t_R = 31.87 min (minor), 34.92 min (major), 92% *ee*.

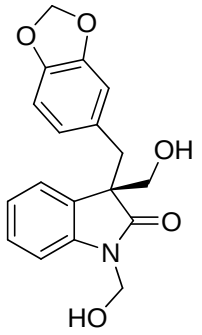


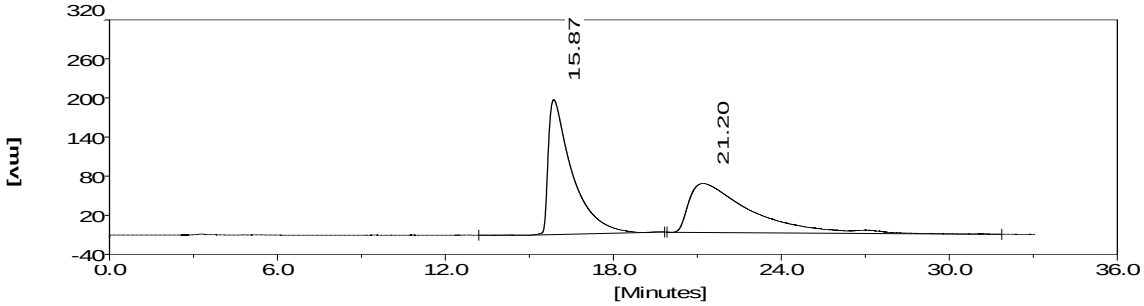


3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-1,3-bis(hydroxymethyl)indolin-2-one (3l)：

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (87% isolated yield, 92% *ee*). $[\alpha]^{26}_{D}$ = -38.86 (c = 0.16, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) 7.24 (d, *J* = 7.61, H), 7.11 (dt, *J* = 14.6, 7.2, 2 H), 6.93 (d, *J* = 7.8, 1 H), 6.51 (d, *J* = 7.7, 1 H), 6.34 (d, *J* = 8.6, 2 H), 5.82 (s, 2 H), 5.18 (dd, *J* = 11.1, 6.3, 1 H), 4.94–4.84 (m, 1 H), 4.04–3.95 (1 H, m), 3.83 (dd, *J* = 12.6, 8.8, 2 H), 3.05 (d, *J* = 13.5, 1 H), 2.99 (d, *J* = 13.5, 1 H), 2.95 (m, 1 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.28, 146.96, 146.23, 142.24, 130.37, 128.75, 128.68, 128.59, 126.86, 126.38, 123.77, 123.15, 123.00, 110.20, 100.75, 66.37, 63.52, 56.50, 38.68 ppm. HRMS (ESI): calcd for $C_{18}H_{17}NO_5$ [M+Na^+] 350.0999, found 350.1002. The *ee* was determined by HPLC analysis using a chiralcel IA column, hexane/2-propanol 85: 15, flow rate = 1.0 mL/min 254 nm. t_R = 16.19 min (minor), 20.13 min (major), 92% *ee*.

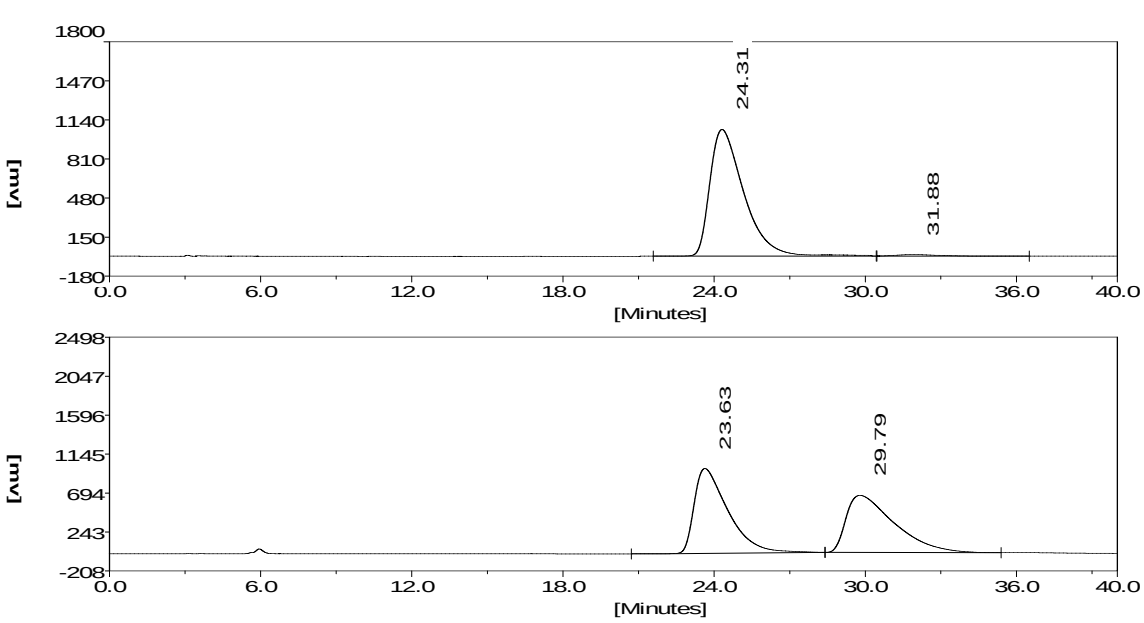


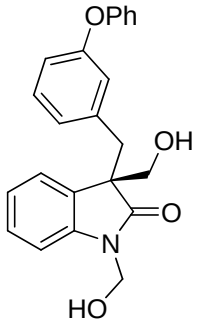




1,3-bis(hydroxymethyl)-3-(3-phenoxybenzyl)indolin-2-one (3m):

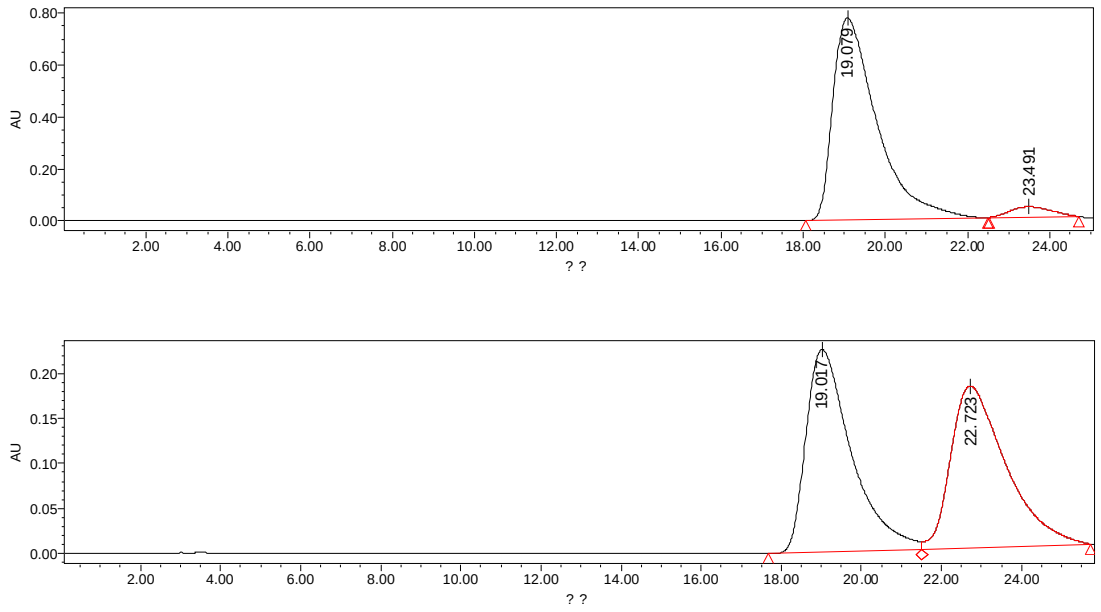
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (91% isolated yield, 97% *ee*). $[\alpha]^{26}_{D}$ = -53.02 (c = 0.10, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dt, *J* = 21.3, 7.7 Hz, 3H), 7.00 (dt, *J* = 16.0, 7.7 Hz, 4H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.70–6.64 (m, 3H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.38 (s, 1H), 5.07 (dd, *J* = 11.0, 6.5 Hz, 1H), 4.80–4.71 (m, 1H), 3.95–3.82 (m, 2H), 3.75 (dd, *J* = 10.8, 2.3 Hz, 1H), 3.06 (d, *J* = 13.2 Hz, 1H), 3.00 (s, 1H), 2.91 (d, *J* = 13.2 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.10, 157.19, 156.41, 142.19, 137.09, 129.66, 129.10, 128.57, 124.94, 123.73, 123.10, 123.01, 120.56, 118.48, 117.71, 109.46, 66.51, 63.51, 56.42, 38.94 ppm. HRMS (ESI): calcd for $C_{23}H_{21}NO_4$ [M+Na$^+$] 398.1363, found 398.1363. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90: 10, flow rate = 1.0 mL/min 254 nm. t_R = 24.31 min (major), 31.88 min (minor), 97% *ee*.





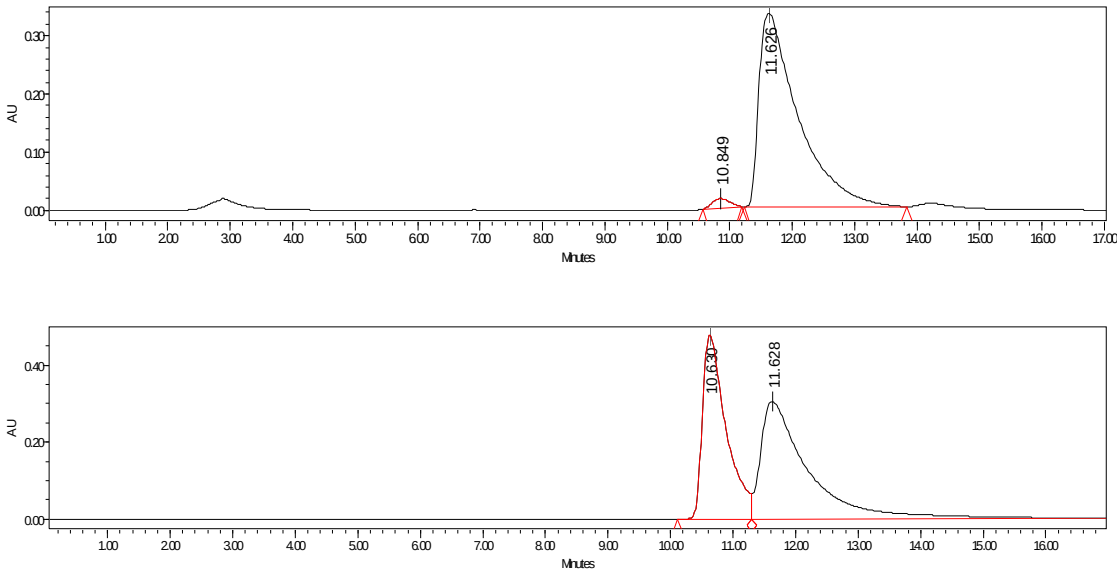
3-(biphenyl-4-ylmethyl)-1,3-bis(hydroxymethyl)indolin-2-one (3n):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (87% isolated yield, 91% *ee*). m.p. 138-140 ^{o}C. $[\alpha]^{26}_{D}$ = -63.05 (c = 0.11, in THF). ^{1}H NMR (400 MHz, $CDCl_3$) 7.49 (d, *J* = 7.8, 2 H), 7.39 (t, *J* = 7.4, 2 H), 7.35–7.26 (m, 6 H), 7.20 (d, *J* = 7.3, 1 H), 7.12 (t, *J* = 7.4, 1 H), 6.95 (d, *J* = 7.7, 2 H), 6.90 (d, *J* = 7.8, 1 H), 5.06 (d, *J* = 7.7, 2 H), 4.07 (t, *J* = 10.3, 1 H), 3.91 (dd, *J* = 11.0, 3.1, 1 H), 3.26 (d, *J* = 13.1, 1 H), 3.19 (d, *J* = 13.1, 1 H), 2.52–2.32 (2 H, m) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.30, 146.98, 146.26, 142.19, 130.39, 128.65, 126.87, 126.38, 123.79, 123.17, 123.03, 110.22, 109.46, 107.63, 100.77, 66.32, 63.58, 56.28, 38.70 ppm. HRMS (ESI): calcd for $C_{23}H_{21}NO_3$ [M+Na$^+$] 382.1414, found 382.1412. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 90: 10, flow rate = 1.0 mL/min 254 nm. t_R = 19.08 min (major), 23.49 min (minor), 91% *ee*.



3-(2-chlorobenzyl)-1,3-bis(hydroxymethyl)indolin-2-one (3o):

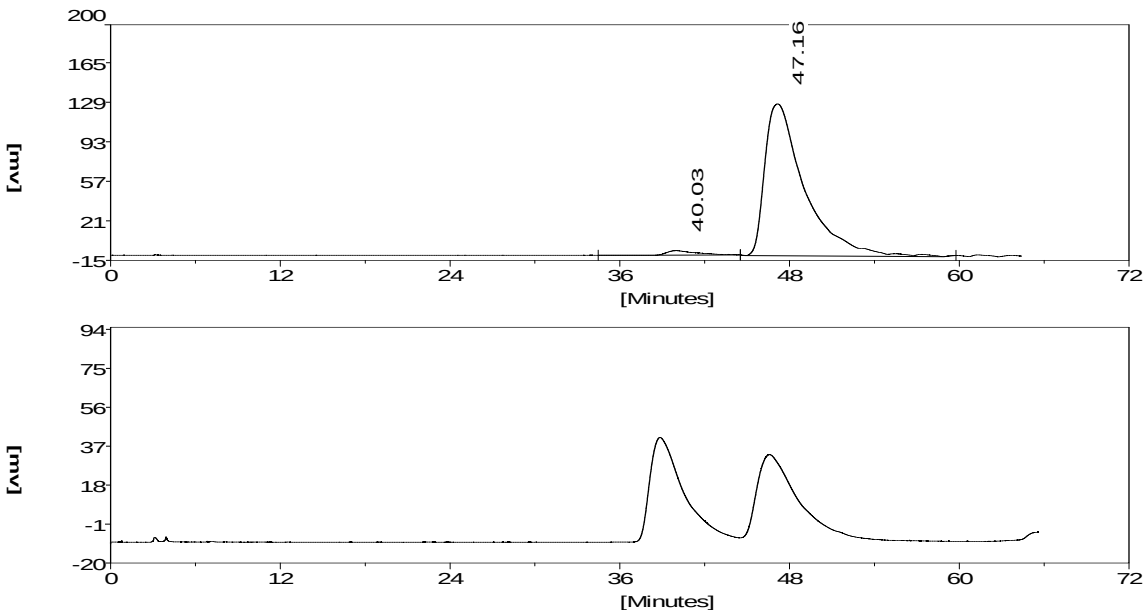
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (90% isolated yield, 96% *ee*). m.p. 116-118 °C. $[\alpha]^{26}_{D}$ = 13.3 (c = 0.15, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) 7.27–7.16 (m, 3 H), 7.14–6.98 (m, 5 H), 6.94 (d, *J* = 7.8, 1 H), 5.26 (dd, *J* = 11.0, 6.9, 1 H), 5.10–4.98 (m, 1 H), 4.09–3.98 (m, 1 H), 3.86 (dd, *J* = 11.1, 3.5, 1 H), 3.44 (d, *J* = 13.8, 1 H), 3.36 (m, 1 H), 3.30 (d, *J* = 13.9, 1 H), 2.68–2.59 (m, 1 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.44, 142.02, 134.71, 133.57, 131.37, 129.49, 128.59, 128.21, 128.17, 126.34, 124.39, 122.84, 109.31, 66.36, 63.64, 55.80, 34.74 ppm. HRMS (ESI): calcd for $C_{17}H_{16}ClNO_3$ $[M+H^+]$ 318.0891, found 318.0896. The *ee* was determined by HPLC analysis using a chiralcel IA column, hexane/2-propanol 95: 5, flow rate = 1.0 mL/min 254 nm. t_R = 10.85 min (minor), 11.63 min (major), 96% *ee*.



3-(4-chlorobenzyl)-1,3-bis(hydroxymethyl)indolin-2-one (3p):

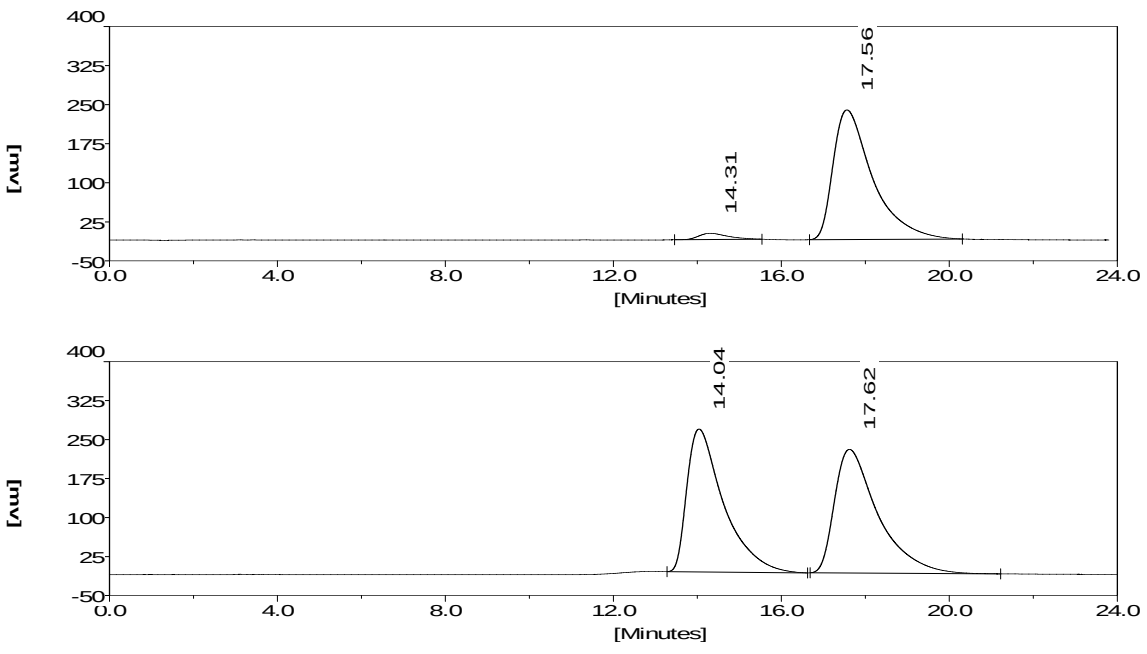
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (87% isolated yield, 91% *ee*). $[\alpha]^{26}_{D}$ = 16.38 (c = 0.10, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 15.6, 8.0 Hz, 2H), 7.08 (d, *J* = 7.3 Hz, 1H), 7.05–6.96 (m, 3H), 6.94 (d, *J* = 7.8 Hz, 1H), 5.28 (dd, *J* = 11.1, 3.6 Hz, 1H), 5.02–4.82 (m, 1H), 4.46 (d, *J* = 4.9 Hz, 1H), 3.98 (d, *J* = 10.4 Hz, 1H), 3.80 (d, *J* = 11.0 Hz, 1H), 3.33 (d, *J* = 13.9 Hz, 1H), 3.23 (s, 1H), 3.17 (d, *J* = 13.9 Hz, 1H) ppm. ^{13}C

NMR (101 MHz, $CDCl_3$) δ = 179.23, 141.99, 135.35, 133.21, 132.27, 132.08, 129.24, 128.78, 127.97, 126.70, 124.32, 122.97, 109.38, 66.38, 63.65, 55.63, 34.17 ppm. HRMS (ESI): calcd for $C_{17}H_{16}ClNO_3$ [M+H^+] 318.0891, found 318.0894. The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 95: 5, flow rate = 1.0 mL/min 254 nm. t_R = 40.03 min (minor), 47.16 min (major), 96% *ee*.



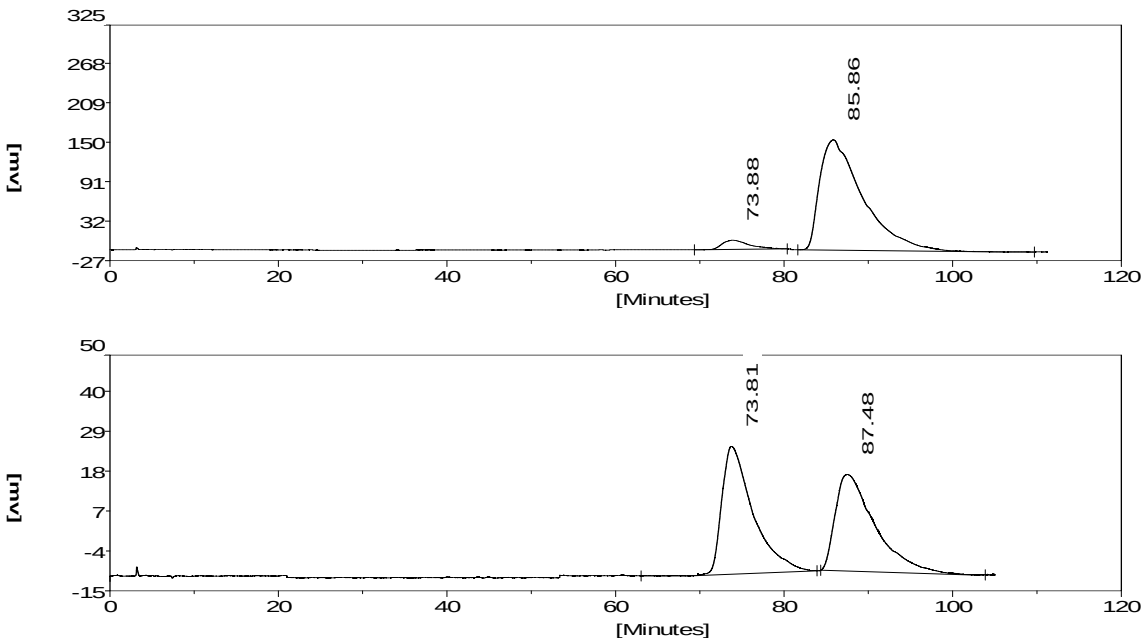
3-(2,4-dichlorobenzyl)-1,3-bis(hydroxymethyl)indolin-2-one (3q)：

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a colorless crystal (88% isolated yield, 93% *ee*). m.p. 69-70 °C. $[\alpha]^{26}_D$ = -40.29 (c = 0.22, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.16 (m, 3H), 7.06 (dd, *J* = 16.1, 7.2 Hz, 4H), 6.95 (t, *J* = 5.4 Hz, 4H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.71 (d, *J* = 8.3 Hz, 4H), 5.09 (dd, *J* = 11.1, 5.8 Hz, 2H), 4.79–4.71 (m, 2H), 3.92 (dd, *J* = 10.3, 6.3 Hz, 2H), 3.78 (dd, *J* = 16.2, 8.8 Hz, 4H), 3.03 (d, *J* = 13.2 Hz, 2H), 2.97 (t, *J* = 10.0 Hz, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.04, 142.16, 133.54, 132.69, 131.33, 131.20, 128.78, 128.41, 127.95, 123.71, 123.09, 109.58, 77.34, 77.23, 77.03, 76.71, 66.35, 63.52, 56.25, 38.29 ppm. HRMS (ESI): calcd for $C_{17}H_{15}C_{l2}NO_3$ [M+Na^+] 374.0321, found 374.0321. The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 90: 10, flow rate = 1.0 mL/min 254 nm. t_R = 14.31 min (minor), 17.56 min (major), 93% *ee*.



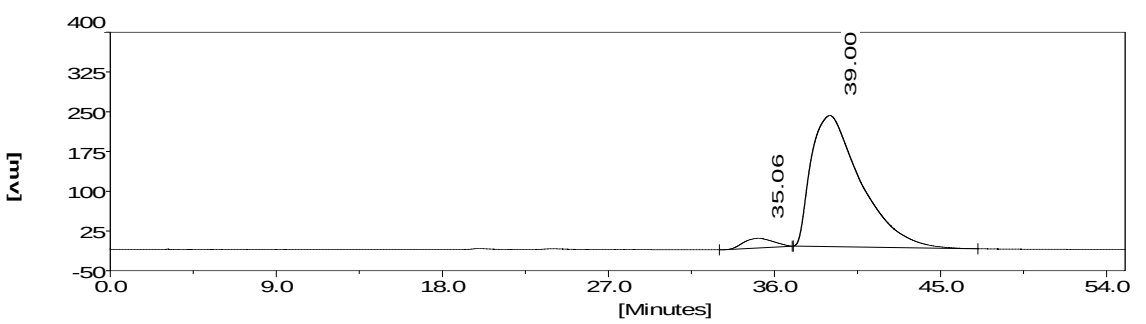
3-(4-bromobenzyl)-1,3-bis(hydroxymethyl)indolin-2-one (3r)：

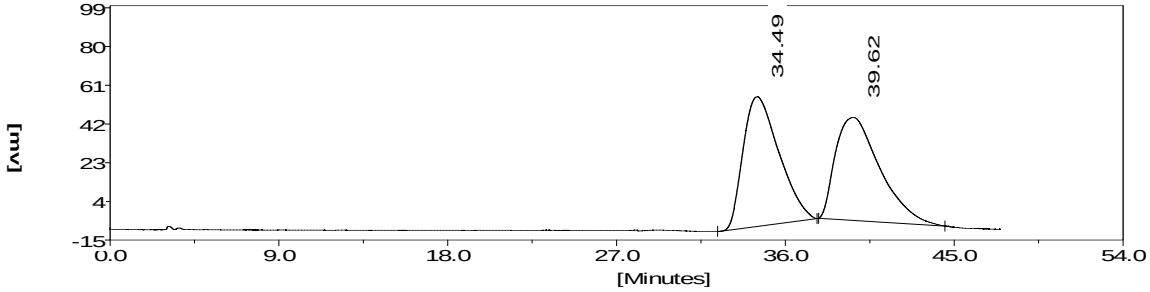
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (79% isolated yield, 90% *ee*). m.p. 138-140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) 7.25 (d, *J* = 7.8, 1 H), 7.18 (d, *J* = 8.3, 2 H), 7.14 (d, *J* = 7.2, 1 H), 7.10 (t, *J* = 7.4, 1 H), 6.91 (d, *J* = 7.8, 1 H), 6.72 (d, *J* = 8.3, 2 H), 5.16 (dd, *J* = 11.1, 6.2, 1 H), 4.83–4.78 (m, 1 H), 3.96 (dt, *J* = 12.8, 9.1, 2 H), 3.84–3.78 (m, 1 H), 3.07 (dd, *J* = 13.1, 3.8, 1 H), 3.06-3.07 (m, 1 H), 2.99 (d, *J* = 13.1, 3.4, 1 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.00, 142.15, 134.04, 131.57, 130.91, 128.79, 128.37, 123.70, 123.10, 120.83, 109.62, 66.37, 63.50, 56.22, 38.31 ppm. HRMS (ESI): calcd for $C_{17}H_{16}BrNO_3$ [M+Na$^+$] 384.0206, found 384.0213. The *ee* was determined by HPLC analysis using a chiralcel AS-H column, hexane/2-propanol 97: 3, flow rate = 1.0 mL/min 254 nm. t_R = 73.88 min (minor), 85.86 min (major), 90% *ee*.



1,3-bis(hydroxymethyl)-3-(naphthalen-1-ylmethyl)indolin-2-one (3s):

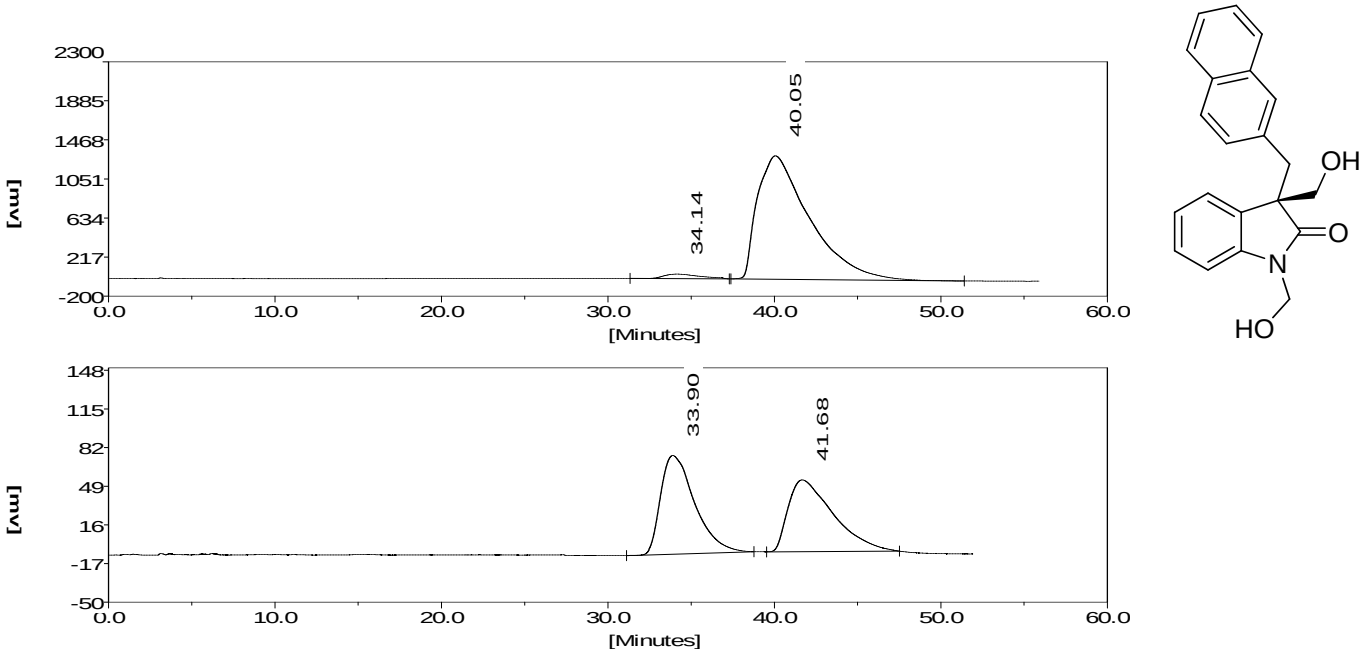
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford viscous solid (92% isolated yield, 92% *ee*). $[\alpha]^{26}_D$ = -14.16 (c = 0.10, in THF). ^{1}H NMR (600 MHz, $CDCl_3$) 7.91 (d, *J* = 8.2, 1 H), 7.73 (d, *J* = 7.7, 1 H), 7.64 (d, *J* = 8.2, 1 H), 7.40–7.32 (m, 2 H), 7.21 (t, *J* = 7.6, 1 H), 7.14 (t, *J* = 7.8, 1 H), 7.06 (d, *J* = 7.1, 1 H), 6.89–6.81 (m, 3 H), 5.06 (dd, *J* = 11.1, 6.2, 1 H), 4.87 (dd, *J* = 10.9, 7.9, 1 H), 4.13 (dd, *J* = 12.3, 5.4, 1 H), 3.86 (d, *J* = 11.1, 1 H), 3.64 (d, *J* = 14.1, 1 H), 3.62–3.59 (m, 1 H), 3.57 (d, *J* = 14.1, 1 H), 3.01 (s, 1 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.79, 142.03, 133.55, 132.41, 131.66, 128.65, 128.49, 128.43, 127.63, 125.42, 125.39, 124.76, 124.51, 124.41, 122.69, 109.29, 66.19, 63.52, 55.74, 34.60 ppm. HRMS (ESI): calcd for $C_{21}H_{19}NO_3$ [M+Na$^+$] 356.1257, found 356.1259. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 95:5, flow rate = 1.0 mL/min 254 nm. t_R = 35.06 min (major), 39.00 min (minor), 92% *ee*.





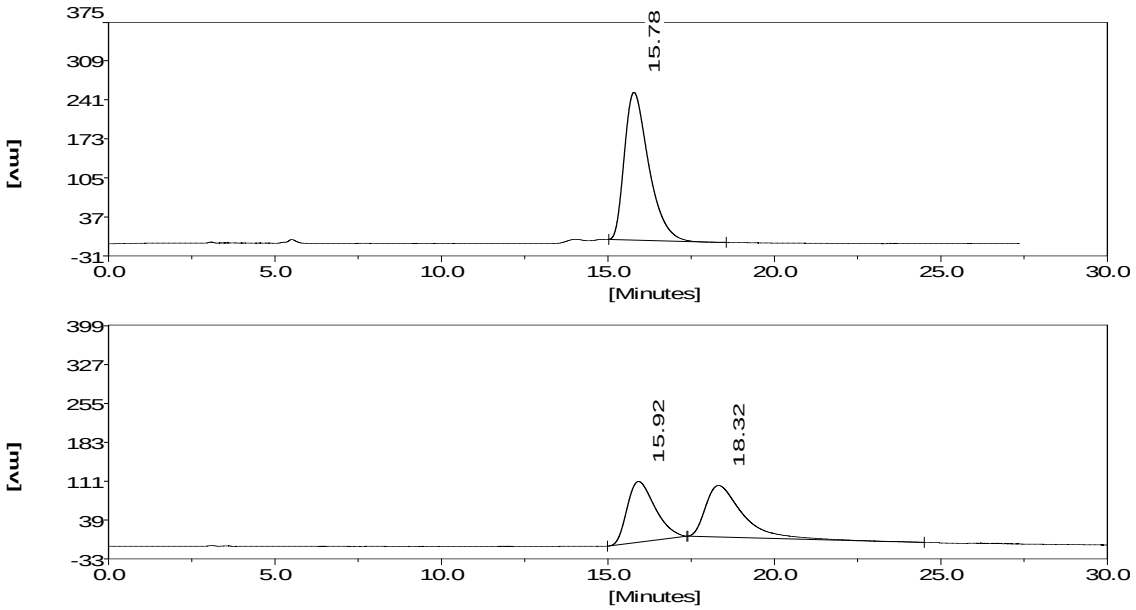
1,3-bis(hydroxymethyl)-3-(naphthalen-2-ylmethyl)indolin-2-one (3t):

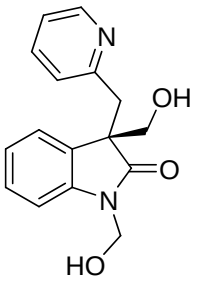
Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (93% isolated yield, 95% *ee*). m.p. 126-128 °C. $[\alpha]^{26}_{D}$ = -46.59 (c = 0.10, in $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) 7.71–7.67 (m, 1 H), 7.63–7.60 (m, 1 H), 7.53–7.51 (m, 1 H), 7.39–7.35 (m, 2 H), 7.34 (s, 1 H), 7.18 (t, *J* = 7.7, 1 H), 7.14 (d, *J* = 7.3, 1 H), 7.06 (t, *J* = 7.5, 1 H), 6.96 (d, *J* = 8.4, 1 H), 6.82 (d, *J* = 7.8, 1 H), 5.12 (dd, *J* = 11.2, 5.7, 1 H), 4.73–4.67 (m, 1 H), 4.09–3.97 (m, 2 H), 3.86 (d, *J* = 11.0, 1 H), 3.25 (d, *J* = 13.3, 1 H), 3.20-3.21 (m, 2 H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = 179.30, 142.19, 132.98, 132.68, 132.16, 128.74, 128.70, 128.58, 128.21, 127.60, 127.45, 127.20, 125.85, 125.57, 123.89, 122.94, 109.52, 66.45, 63.45, 56.47, 39.14 ppm. HRMS (ESI): calcd for $C_{21}H_{19}NO_3$ [M+Na^+] 356.1257, found 356.1252. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 95:5, flow rate = 1.0 mL/min 254 nm. t_R = 34.14 min (minor), 40.05 min (major), 95% *ee*.



1,3-bis(hydroxymethyl)-3-(pyridin-2-ylmethyl)indolin-2-one (3u)：

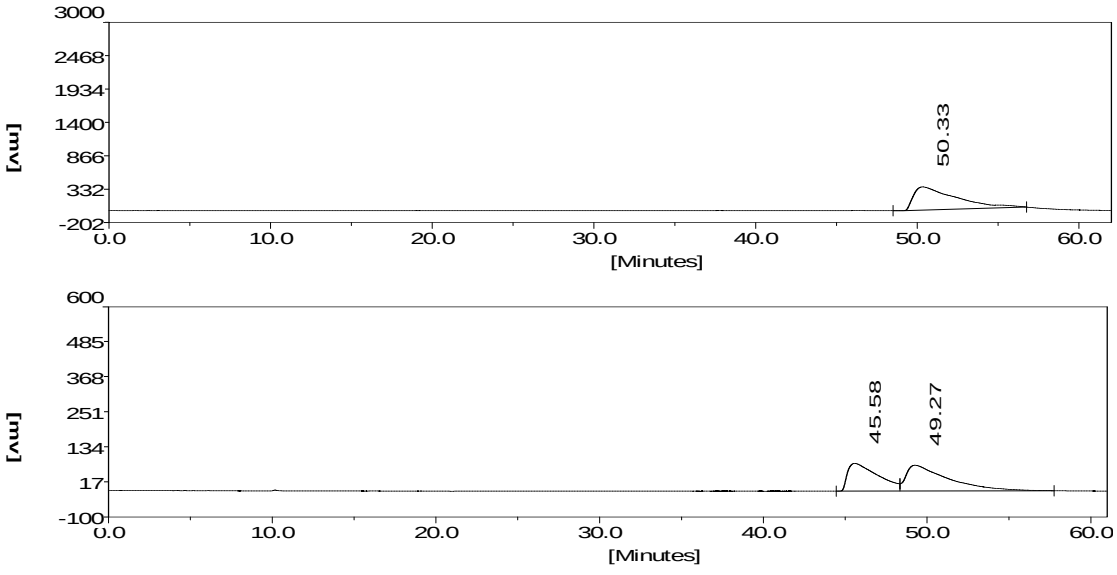
Purified by flash chromatography (EtOAc: MeOH = 20: 1) to afford a white solid (75% isolated yield, >99% *ee*). m.p. 131-132 °C. ^{1}H NMR (400 MHz, DMSO) δ 8.22 (d, *J* = 4.8 Hz, 1H), 7.47 (td, *J* = 7.7, 1.6 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 2H), 7.03 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.96–6.85 (m, 3H), 6.13 (t, *J* = 7.1 Hz, 1H), 5.08–4.90 (m, 3H), 3.79 (dd, *J* = 10.3, 5.1 Hz, 1H), 3.67 (dd, *J* = 10.3, 5.8 Hz, 1H), 3.29 (d, *J* = 13.8 Hz, 1H), 3.16 (d, *J* = 13.8 Hz, 1H) ppm. ^{13}C NMR (101 MHz, DMSO) δ = 177.92, 157.30, 148.87, 143.26, 136.27, 130.38, 127.71, 124.64, 124.02, 121.85, 109.14, 66.65, 62.99, 55.20, 40.93 ppm. HRMS (ESI): calcd for $C_{16}H_{16}N_2O_3$ [M+K^+] 323.0793, found 323.0796. The *ee* was determined by HPLC analysis using a chiralcel OD-H column, hexane/2-propanol 93: 7, flow rate = 1.0 mL/min 254 nm. t_R = 15.78 min (major), >99% *ee*.

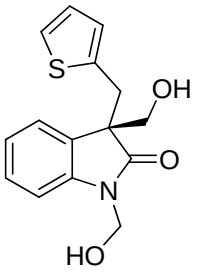




1,3-bis(hydroxymethyl)-3-(thiophen-2-ylmethyl)indolin-2-one (3v):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 3) to afford viscous solid (89% isolated yield, >99% *ee*). $[\alpha]^{26}_{D}$ = -21.70 (c = 0.22, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.92–6.84 (m, 2H), 6.70–6.61 (m, 1H), 6.47 (d, *J* = 3.3 Hz, 1H), 5.09 (dd, *J* = 10.9, 3.7 Hz, 1H), 4.81–4.70 (m, 1H), 4.10 (s, 1H), 3.91 (d, *J* = 10.8 Hz, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 3.33 (d, *J* = 14.4 Hz, 1H), 3.17 (d, *J* = 14.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 178.89, 142.62, 136.73, 128.85, 128.76, 127.07, 126.34, 124.46, 123.69, 123.19, 109.57, 77.38, 77.26, 77.06, 76.74, 66.43, 63.55, 56.38, 33.27 ppm. HRMS (ESI): calcd for $C_{15}H_{15}NO_3S$ [M+H$^+$] 290.0845, found 290.0848. The *ee* was determined by HPLC analysis using a chiralcel IA column, hexane/2-propanol 98: 2, flow rate = 1.0 mL/min 254 nm. t_R = 50.33 min (major), >99% *ee*.

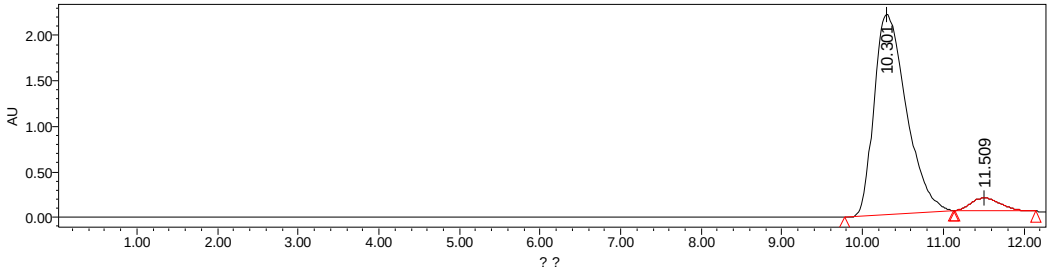


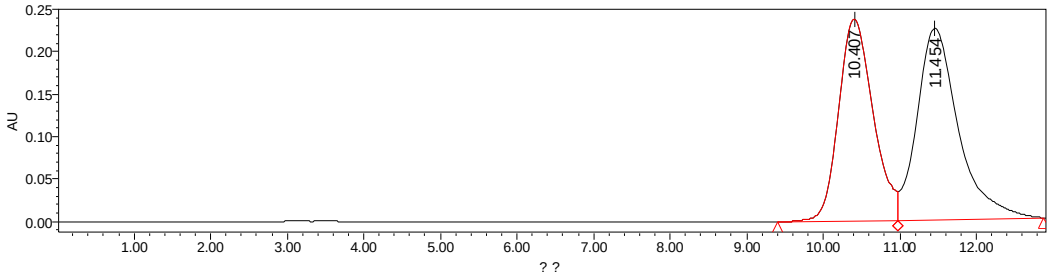


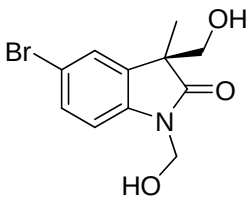
5-bromo-1,3-bis(hydroxymethyl)-3-methylindolin-2-one (3w):

Purified by flash chromatography (petroleum ether: EtOAc = 1: 2) to afford a white solid (91% isolated yield, 89% *ee*). m.p. 145-146 ^{o}C. $[\alpha]^{24}_{D}$ = 4.57 (c = 0.11, in THF). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.3 Hz, 1H), 7.34 (s, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 5.31 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.92 (t, *J* = 10.0 Hz, 1H), 4.49 (d, *J* = 5.8 Hz, 1H), 3.81 (dd, *J* = 10.6, 5.9 Hz, 1H), 3.65 (d, *J* = 10.4 Hz, 1H), 3.13 (s, 1H), 1.26 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 179.61, 140.95, 133.69, 131.28, 126.21, 116.06, 111.13, 77.34, 77.02, 76.70, 67.48, 63.75, 51.13, 18.79 ppm. HRMS (ESI): calcd for $C_{11}H_{12}BrNO_3$ [M+Na$^+$] 307.9893, found 307.9895. The *ee* was determined by HPLC analysis using a chiralcel OD-H column,

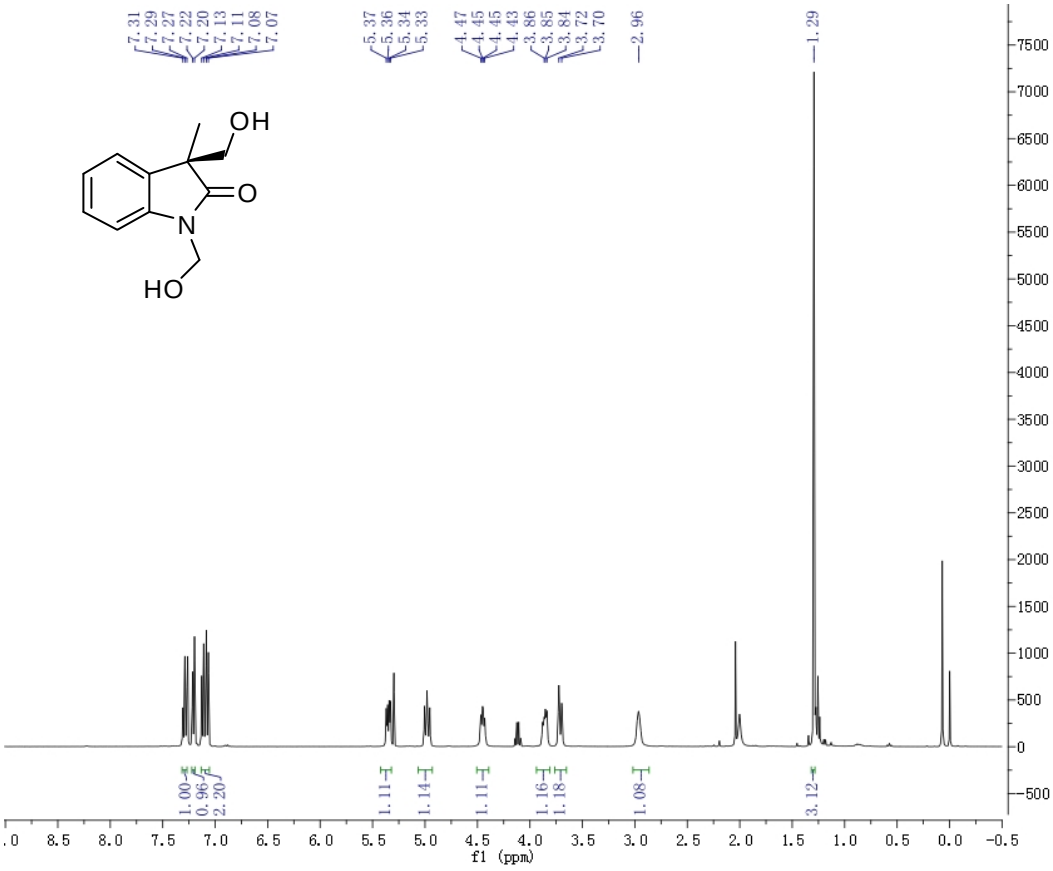
hexane/2-propanol 90:10, flow rate = 1.0 mL/min 254 nm. t_R = 10.30 min (major), 11.51 min (minor), 89% *ee*.







8. Copies of NMR spectra of the products

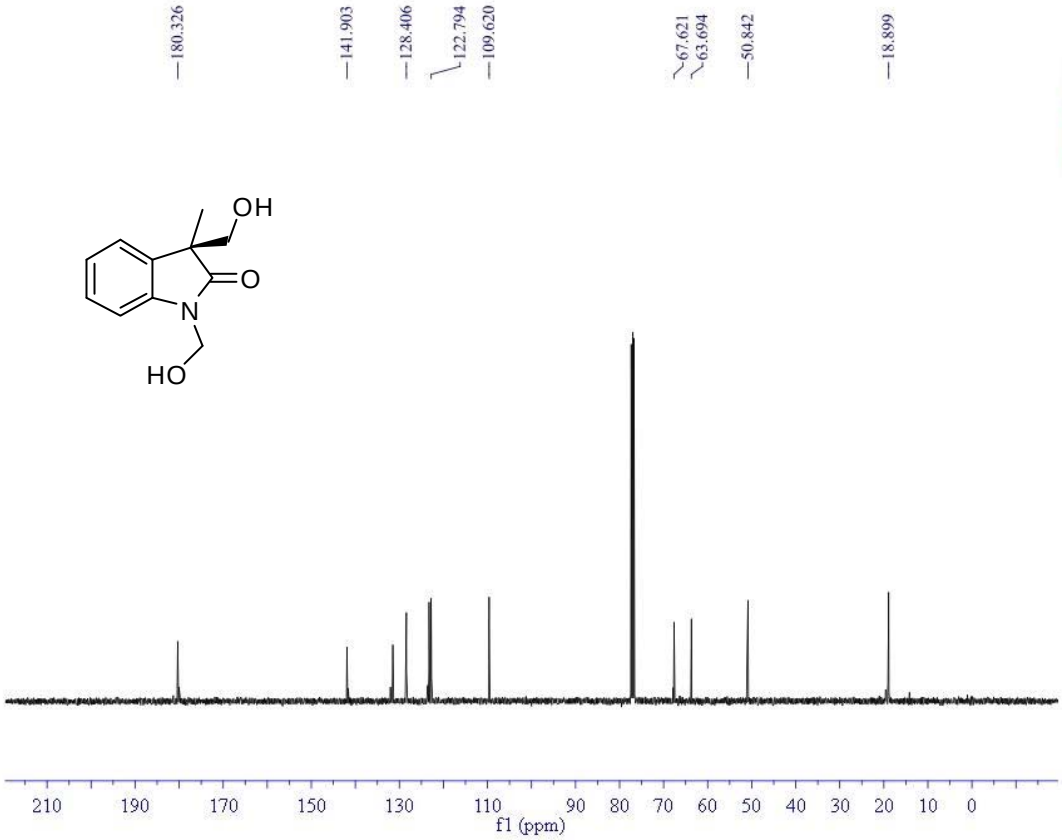


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-19T15:00:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 296 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -11.27
Ph1: 14.53

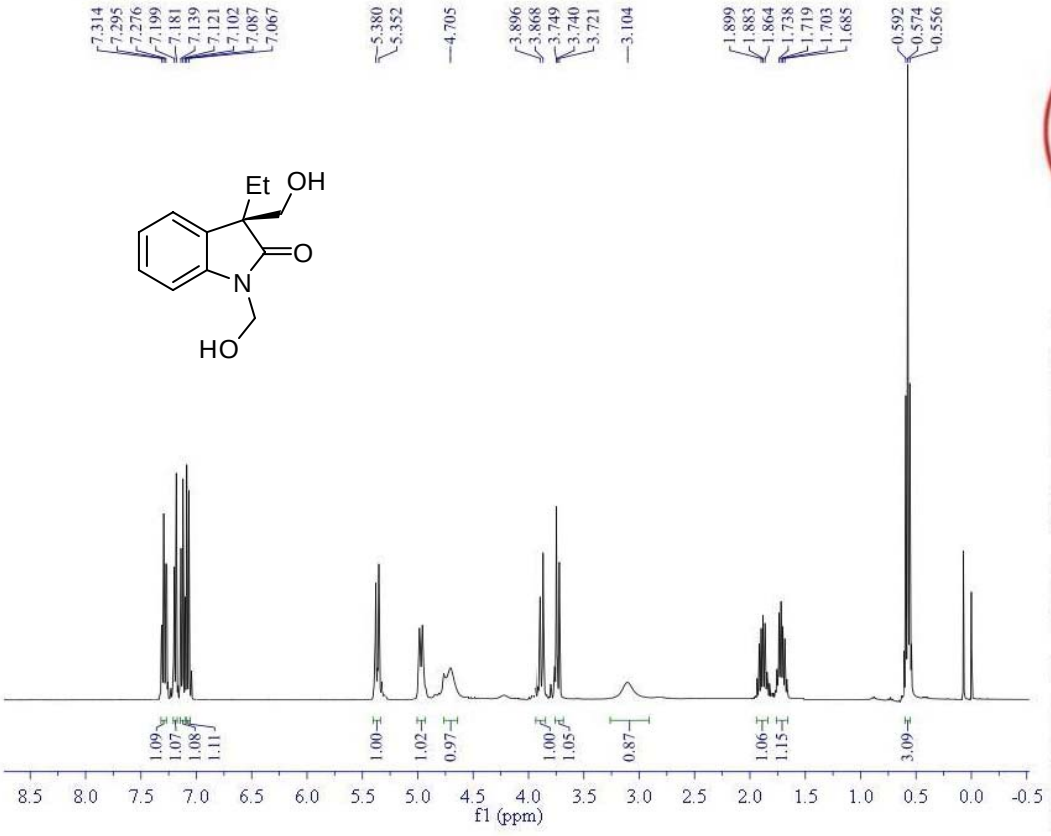


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-26T15:27:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 256
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 299.7 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -106.18
Ph1: 63.21

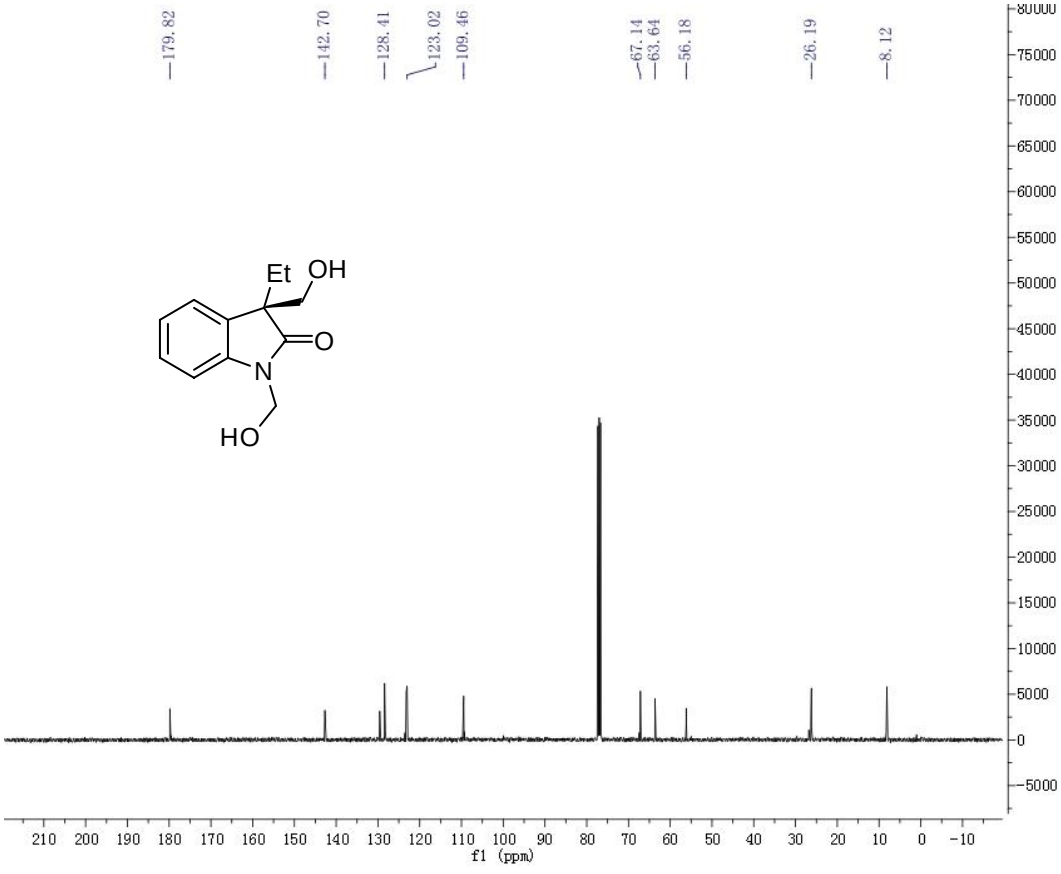


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-08-19T17:48:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 1H
P1: 13.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 2.73
Ph1: 11.51

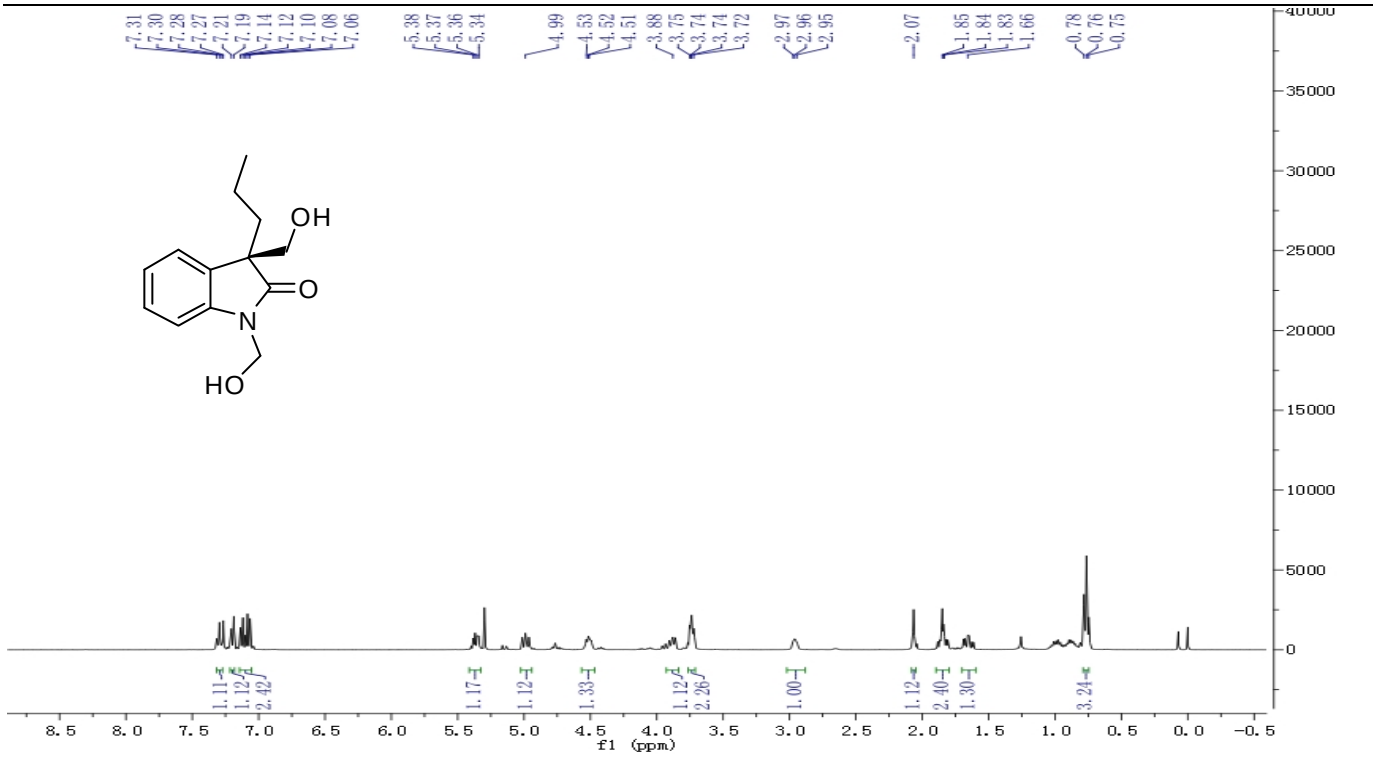


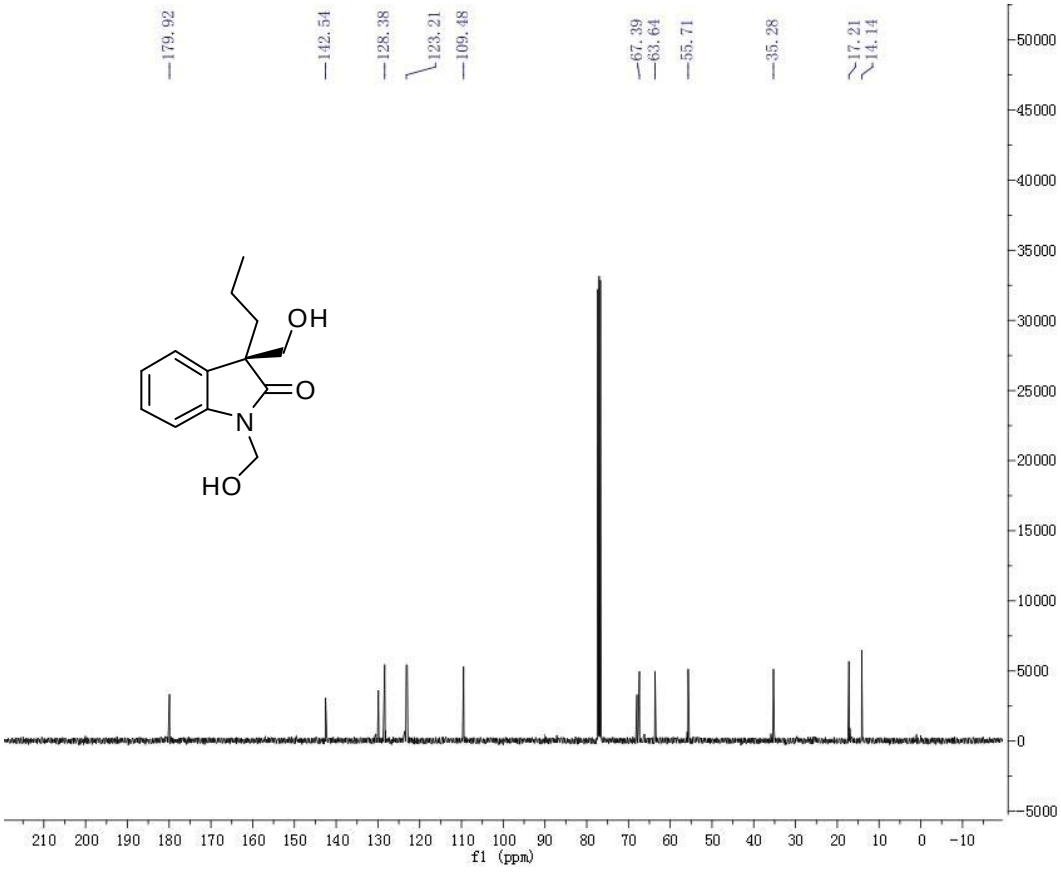
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-26T00:02:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 299.7 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -117.78
Ph1: 89.58





Current Data Parameters

F2 - Acquisition Parameters
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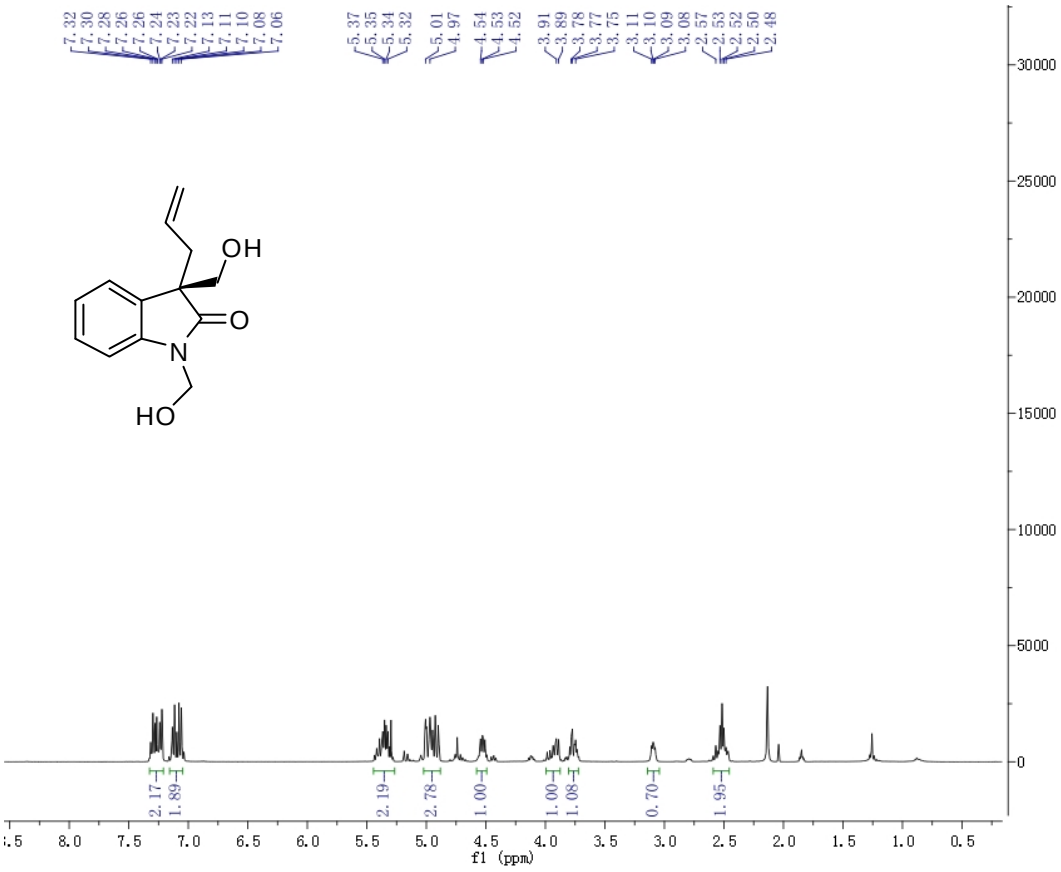
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 296.9 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -92.53
Ph1: 41.99

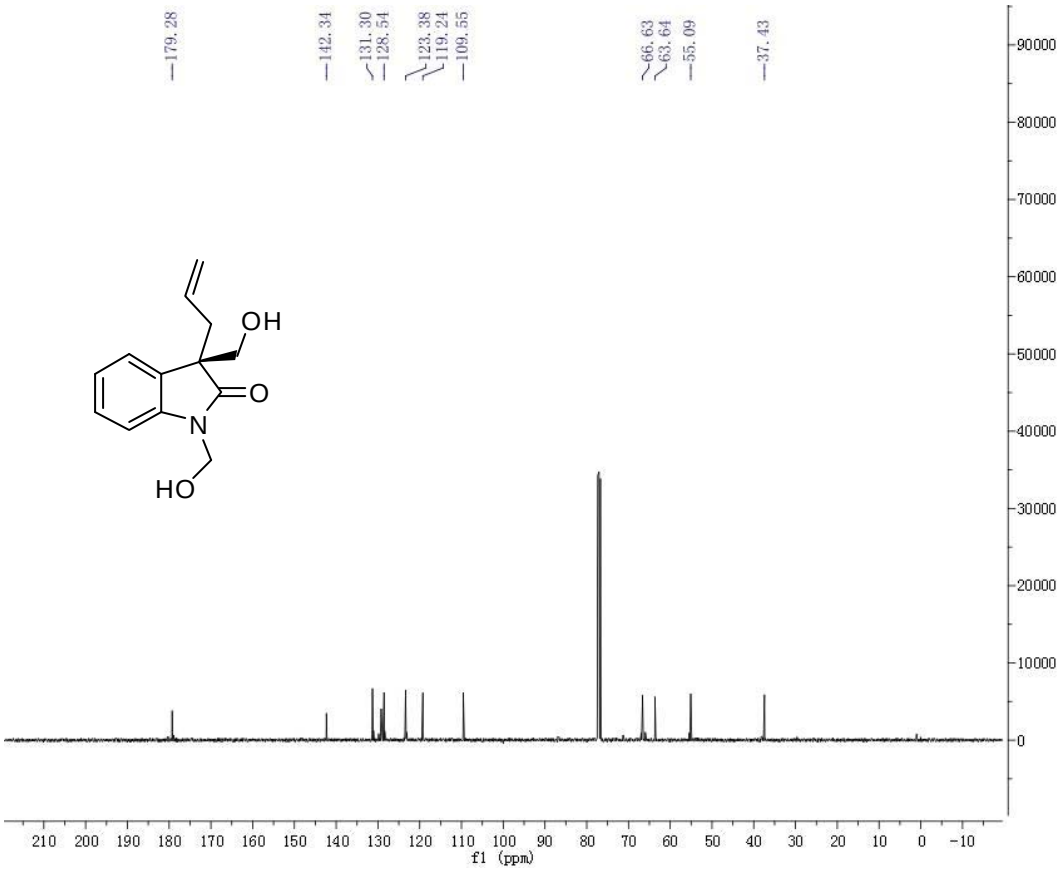


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-26T11:36:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 296.5 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -2.94
Ph1: 31.08

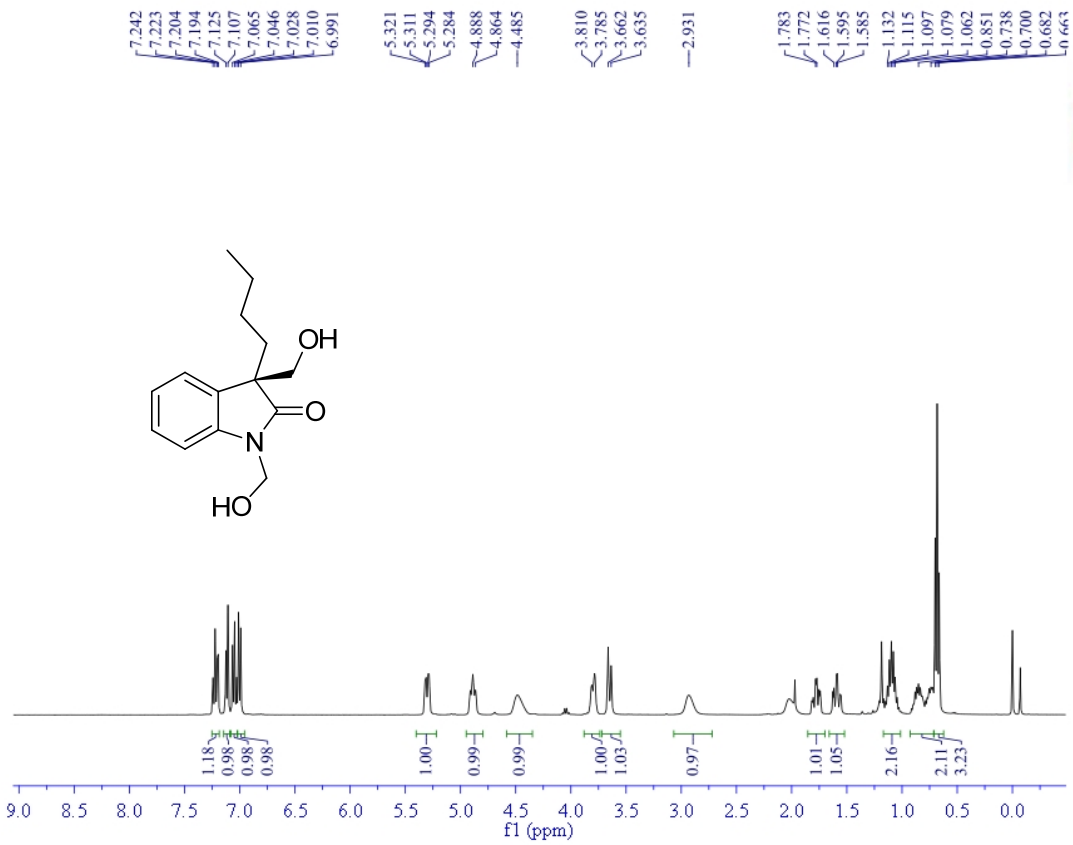


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-26T12:05:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 297.4 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -108.30
Ph1: 76.98

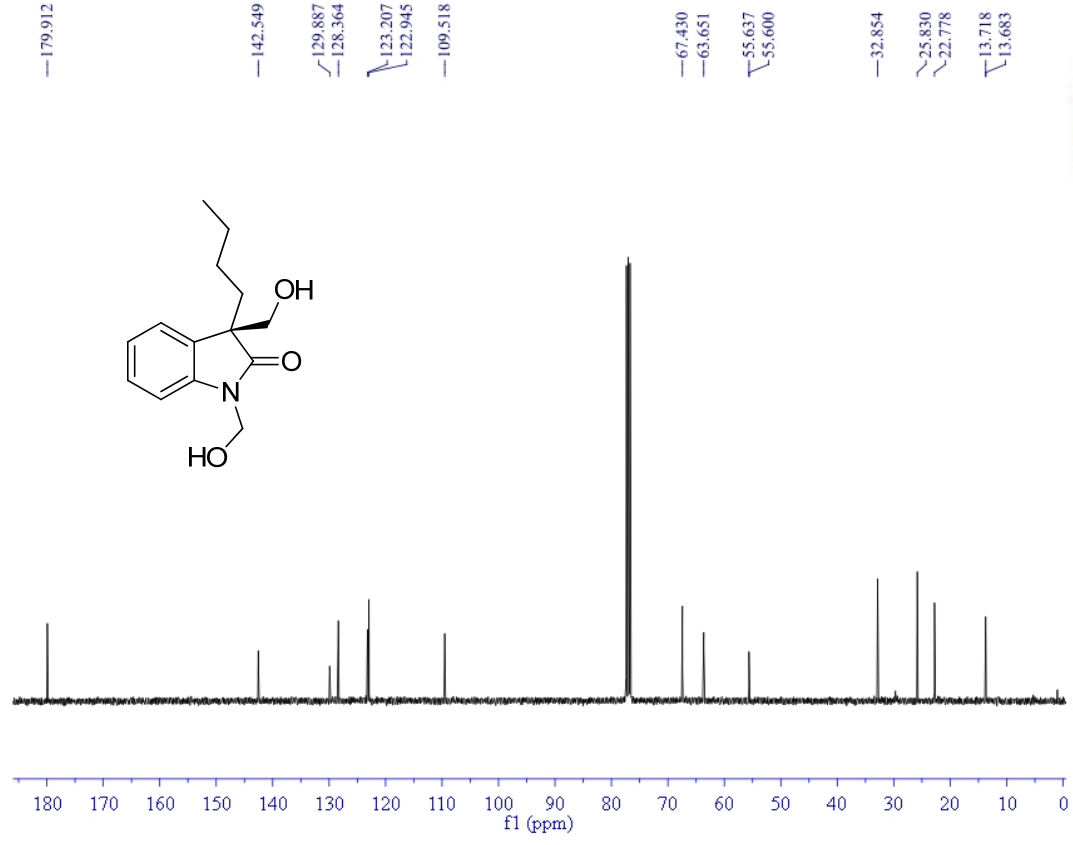


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-06-09T23:17:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 296.2 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 4.78
Ph1: 16.47

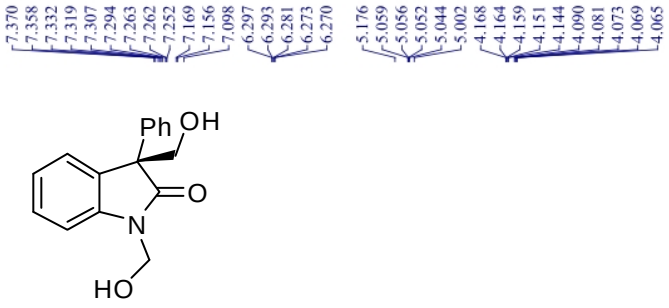


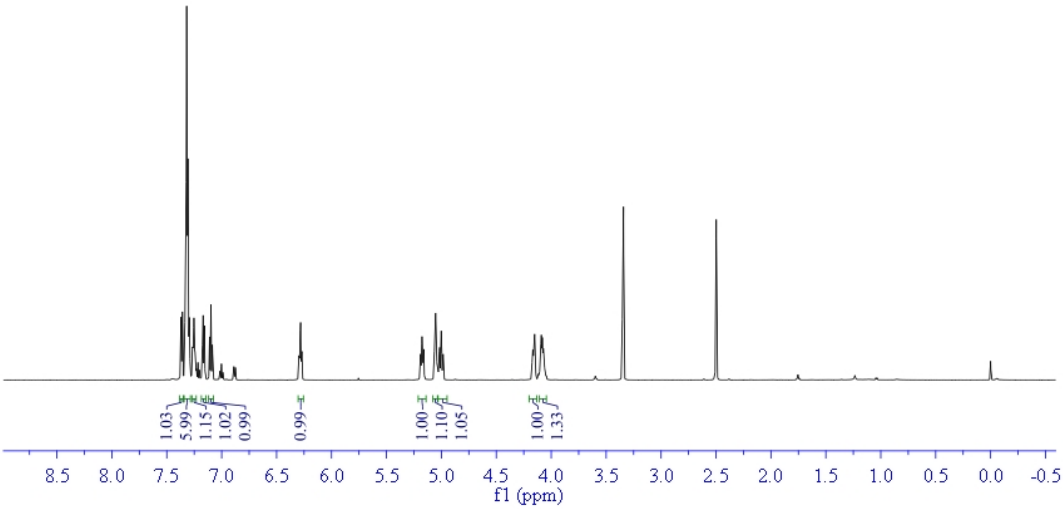
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-06-09T23:46:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 299.5 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -114.27
Ph1: 76.34



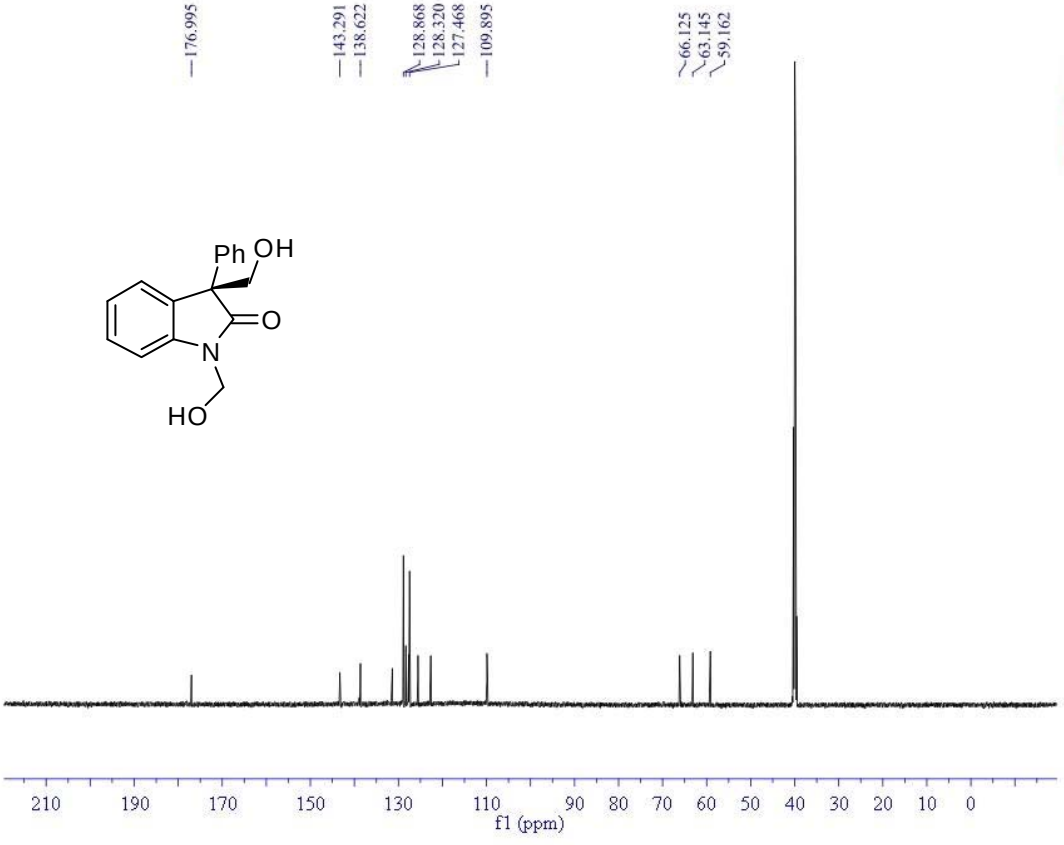


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T12:05:00
PULPROG: zg30
TD: 32768
Solvent: DMSO
NS: 16
DS: undefined
SWH: 12335.5 Hz
AQ: undefined
TE: 295.3 C

CHANNEL f1
NUC1: 1H
P1: 7.2 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 21.27
Ph1: 31.89

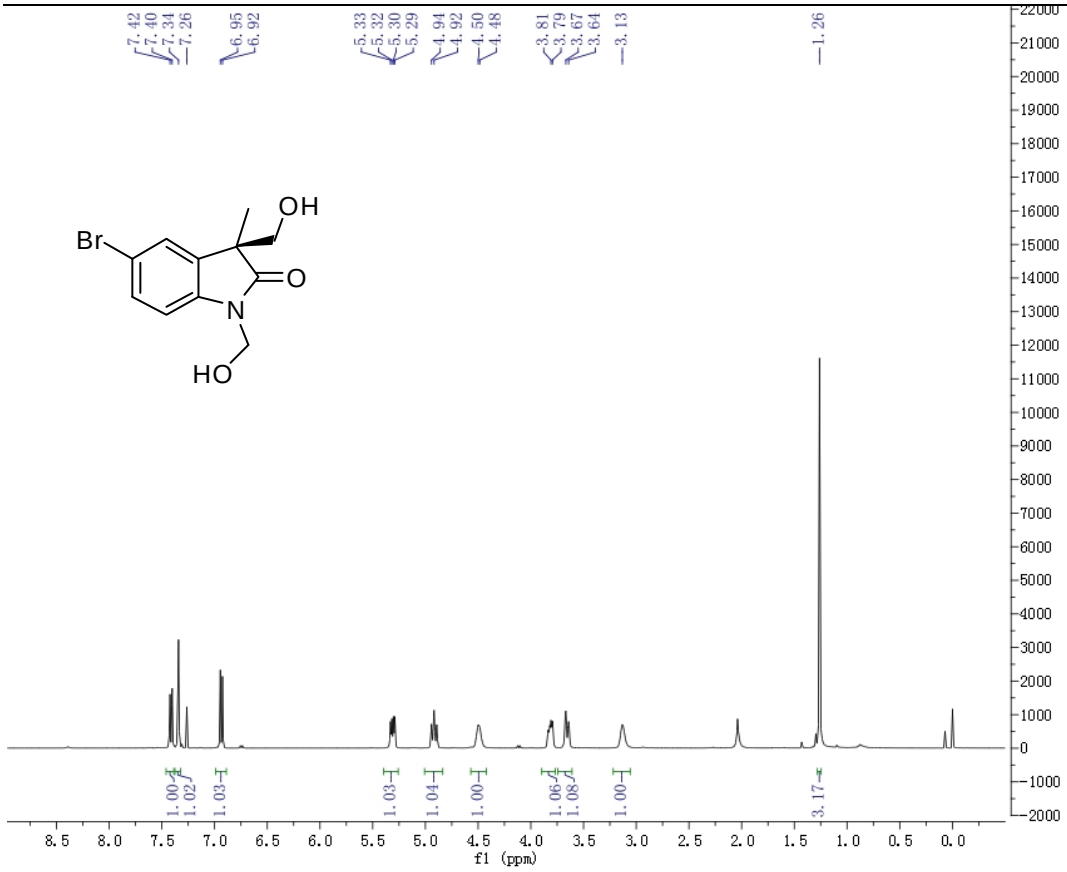


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T12:31:00
PULPROG: zgpg30
TD: 32768
Solvent: DMSO
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 296.3 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 81.44
Ph1: 60.21

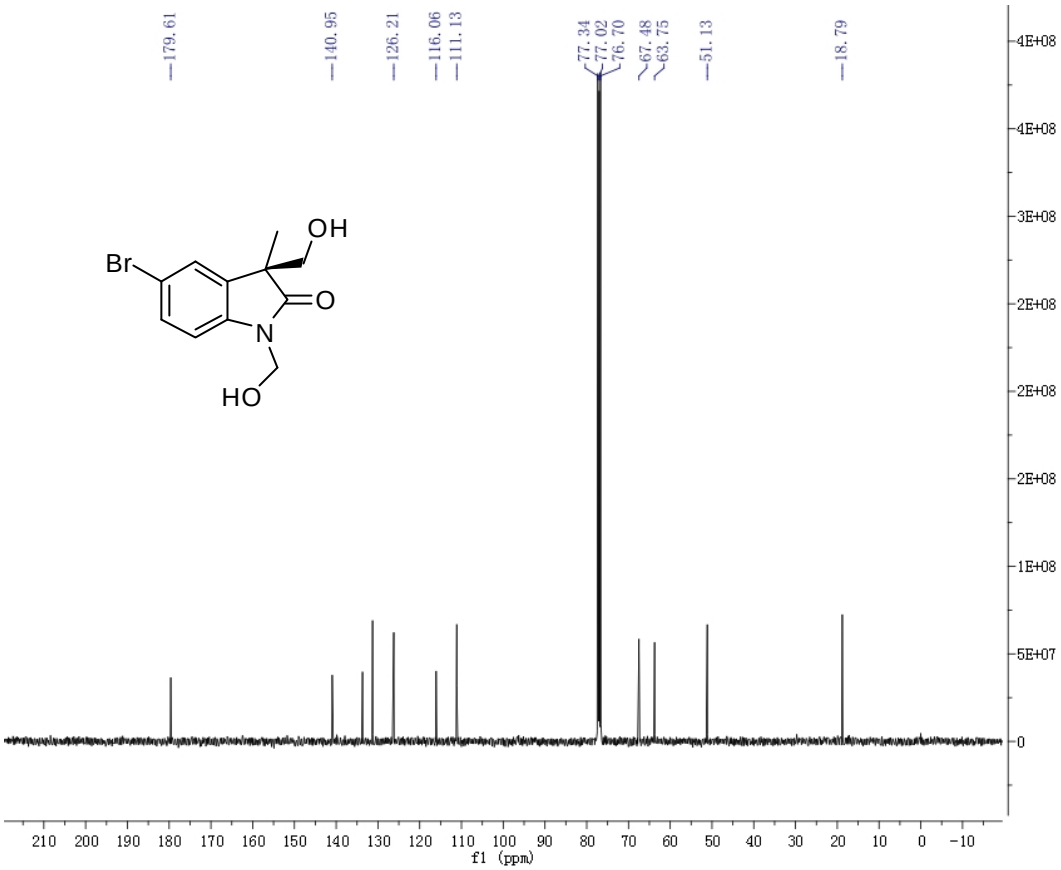


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T13:15:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.1 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 6.69
Ph1: 9.89

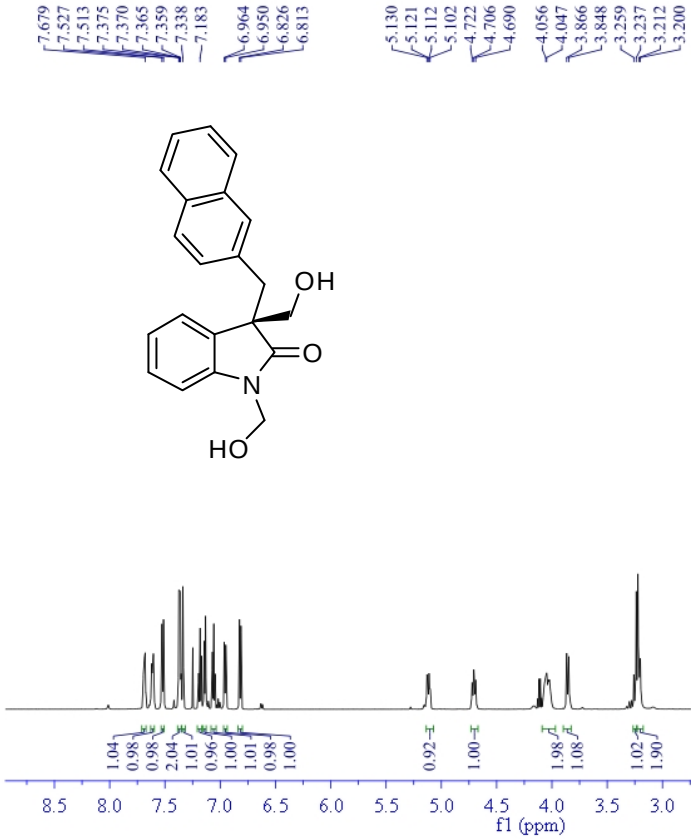


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T13:14:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.9 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 0
FT: Hyper
Phase: NoPC

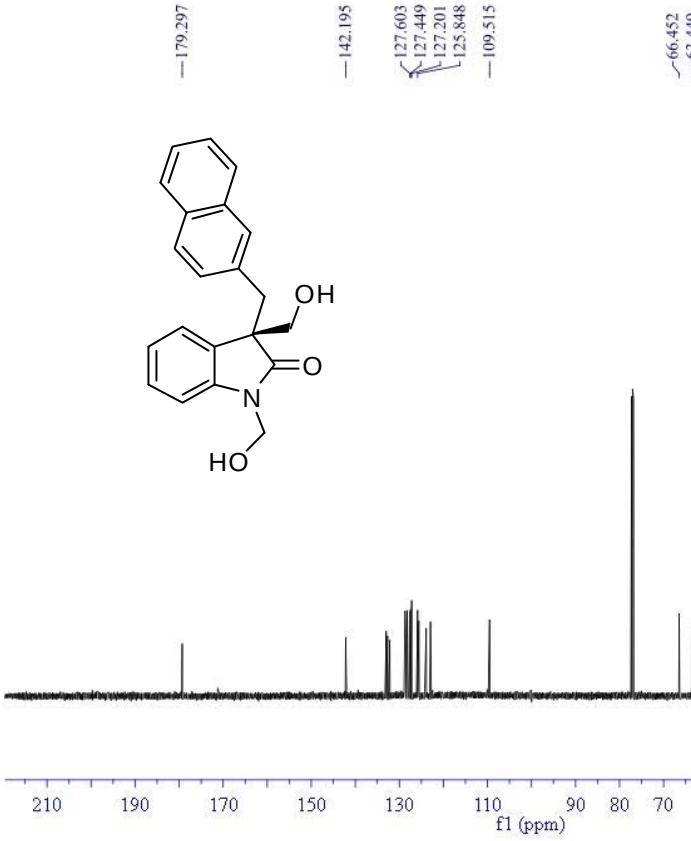


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T10:49:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 12335.5 Hz
AQ: undefined
TE: 295.5 C

CHANNEL f1
NUC1: 1H
P1: 7.2 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 13.57
Ph1: 26.11

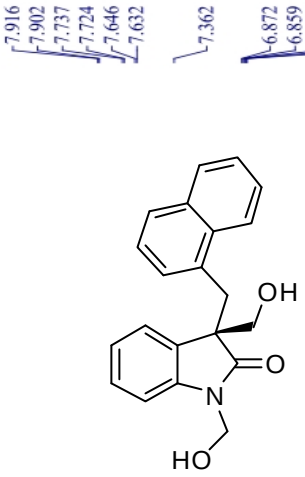


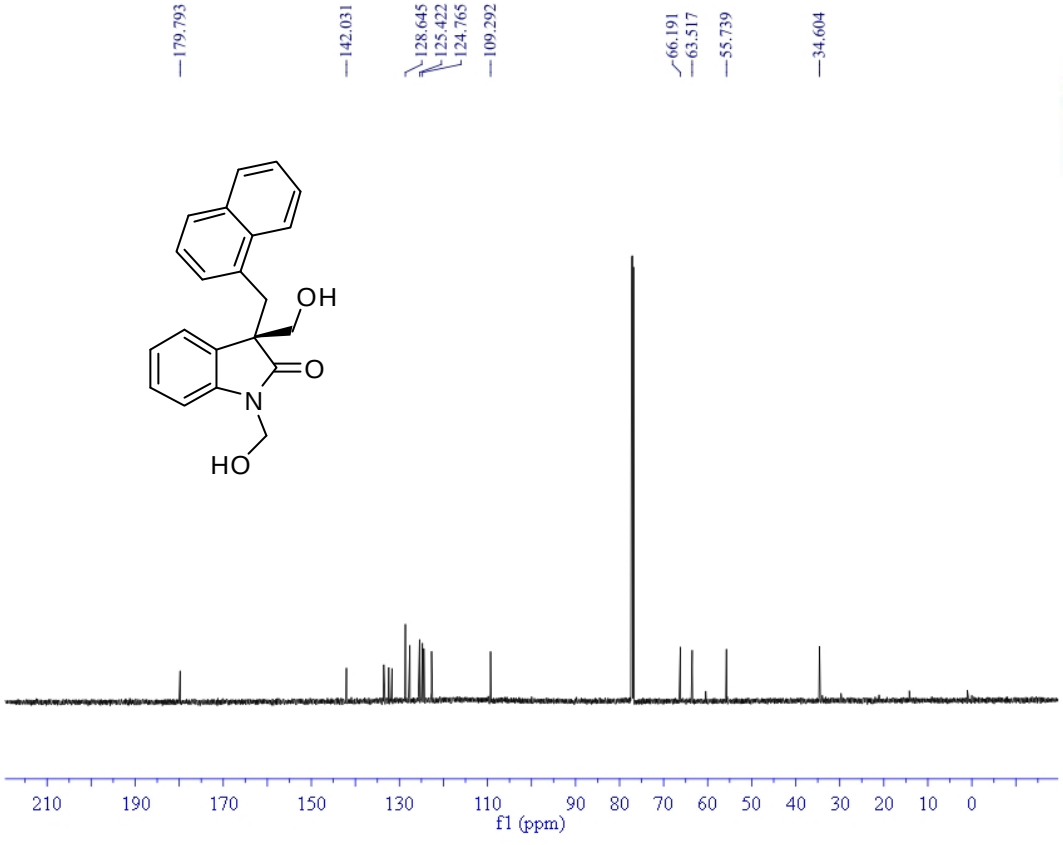
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T17:15:14
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.7 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 72.88
Ph1: 61.13



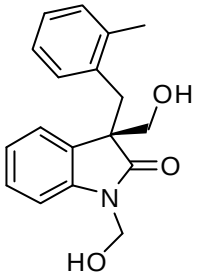


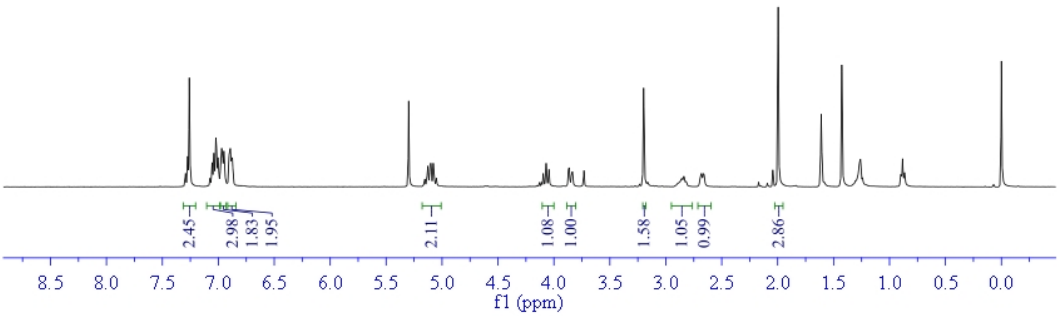
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-24T10:42:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.7 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 72.88
Ph1: 61.13



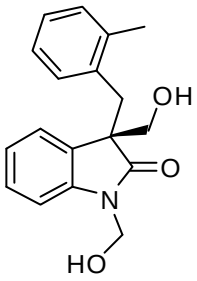


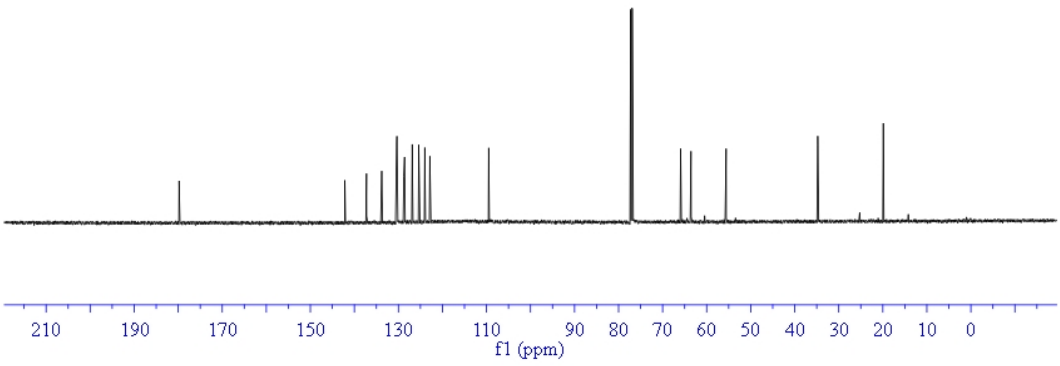
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-04-28T11:04:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.2 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -180.54
Ph1: 13.77



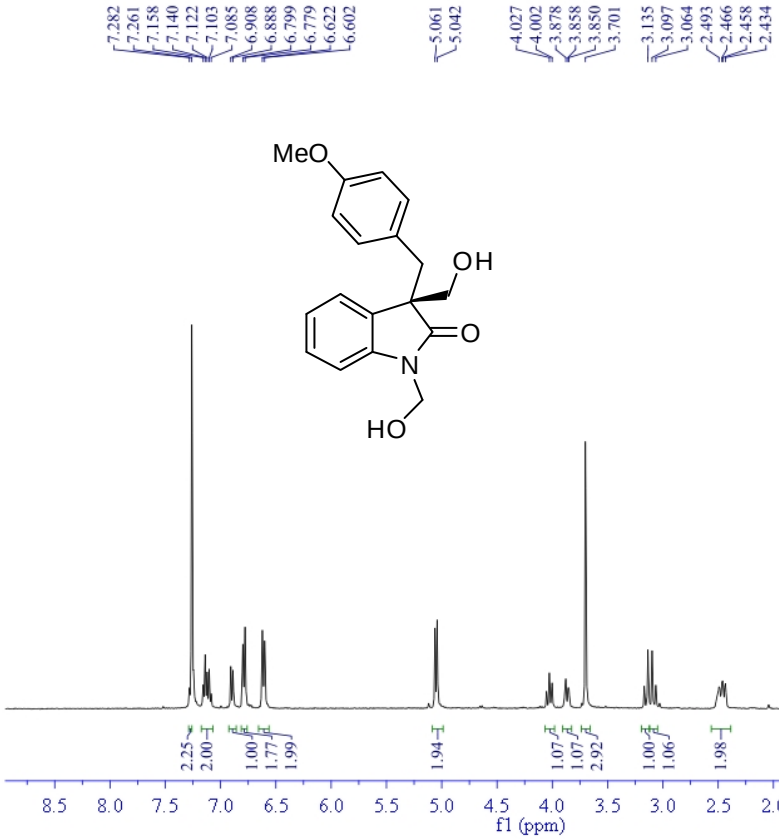


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-10T10:47:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 30.49
Ph1: 113.17

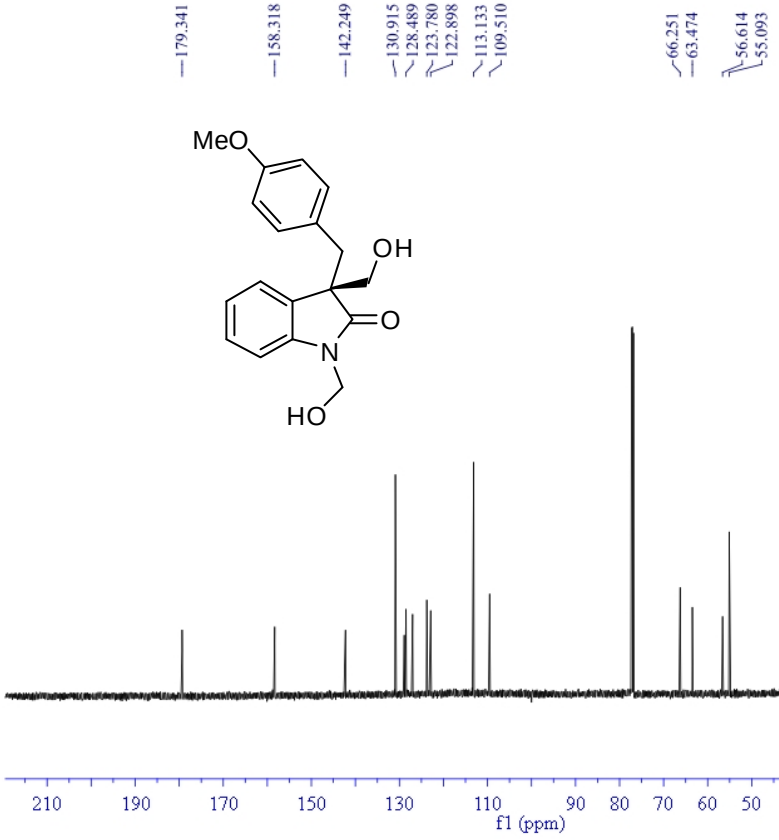


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-04-28T12:05:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -178.90
Ph1: 15.62

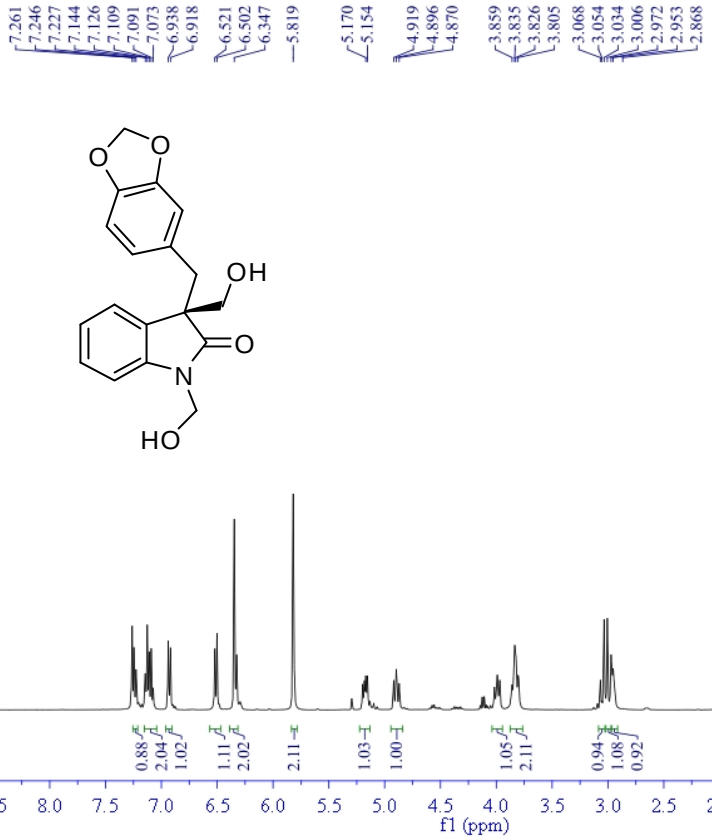


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-10T12:11:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 225
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 49.48
Ph1: 93.75

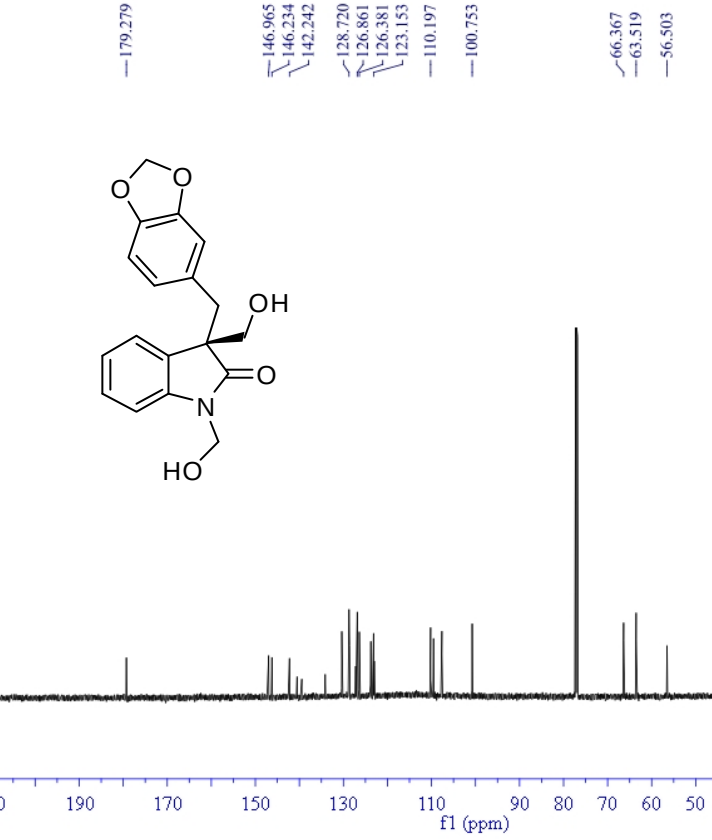


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-04-28T12:44:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -177.39
Ph1: 12.18

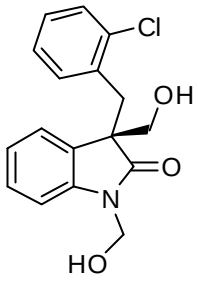


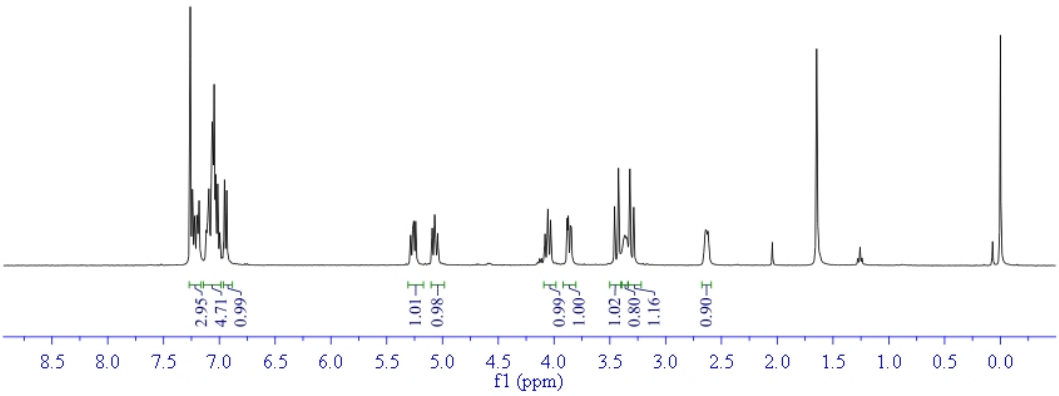
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-10T13:14:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 74.81
Ph1: 51.30



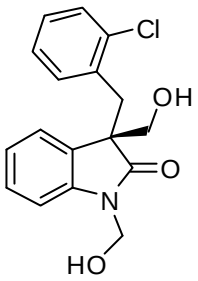


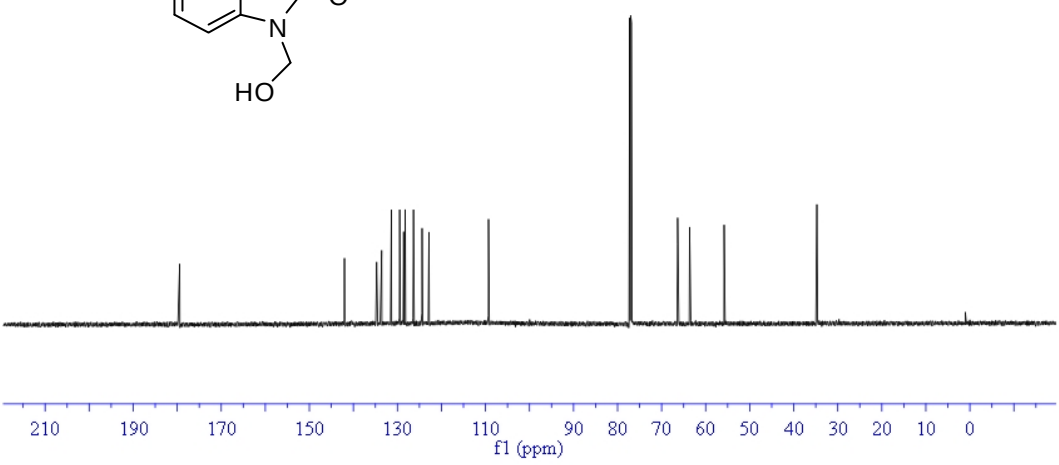
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-04-28T12:39:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298.1 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -183.55
Ph1: 18.96



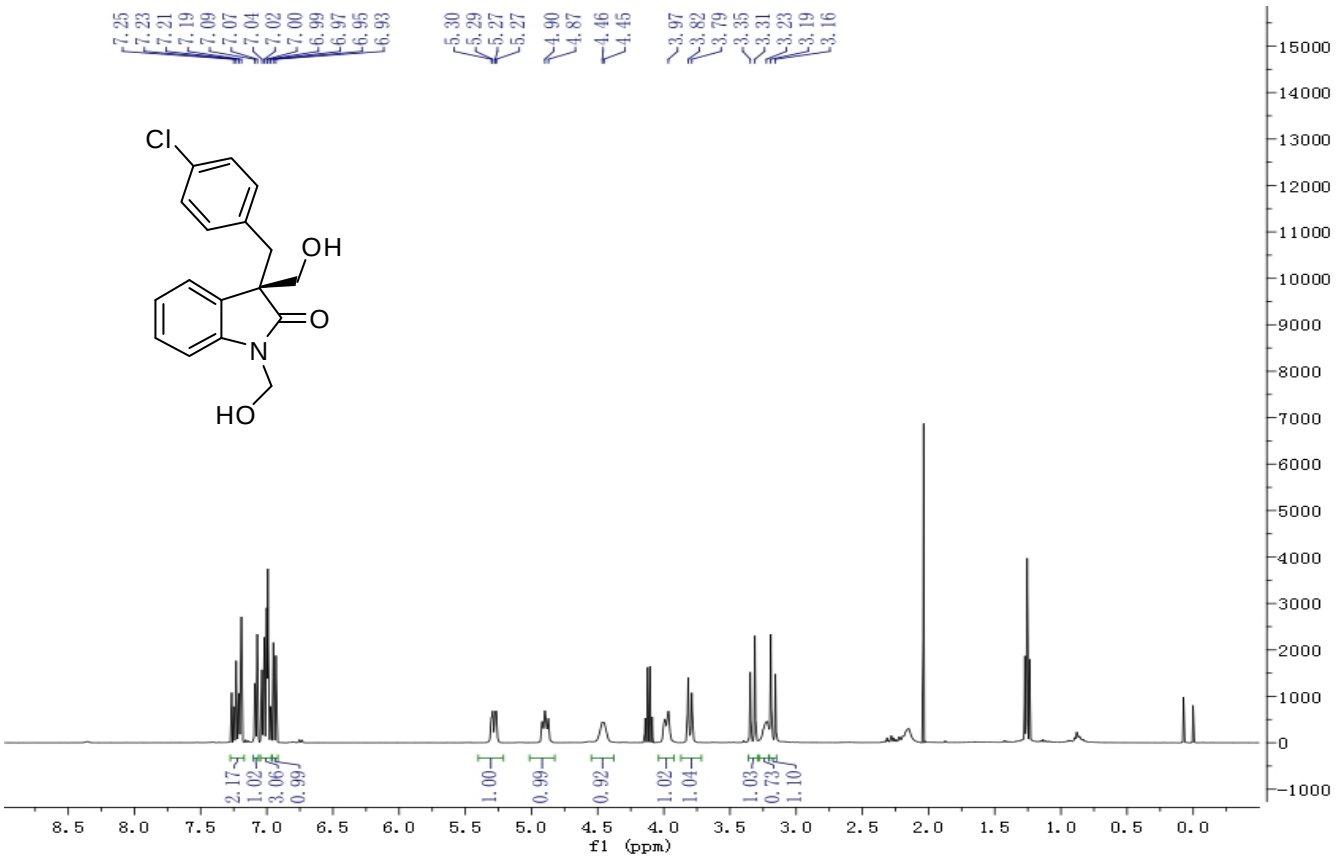


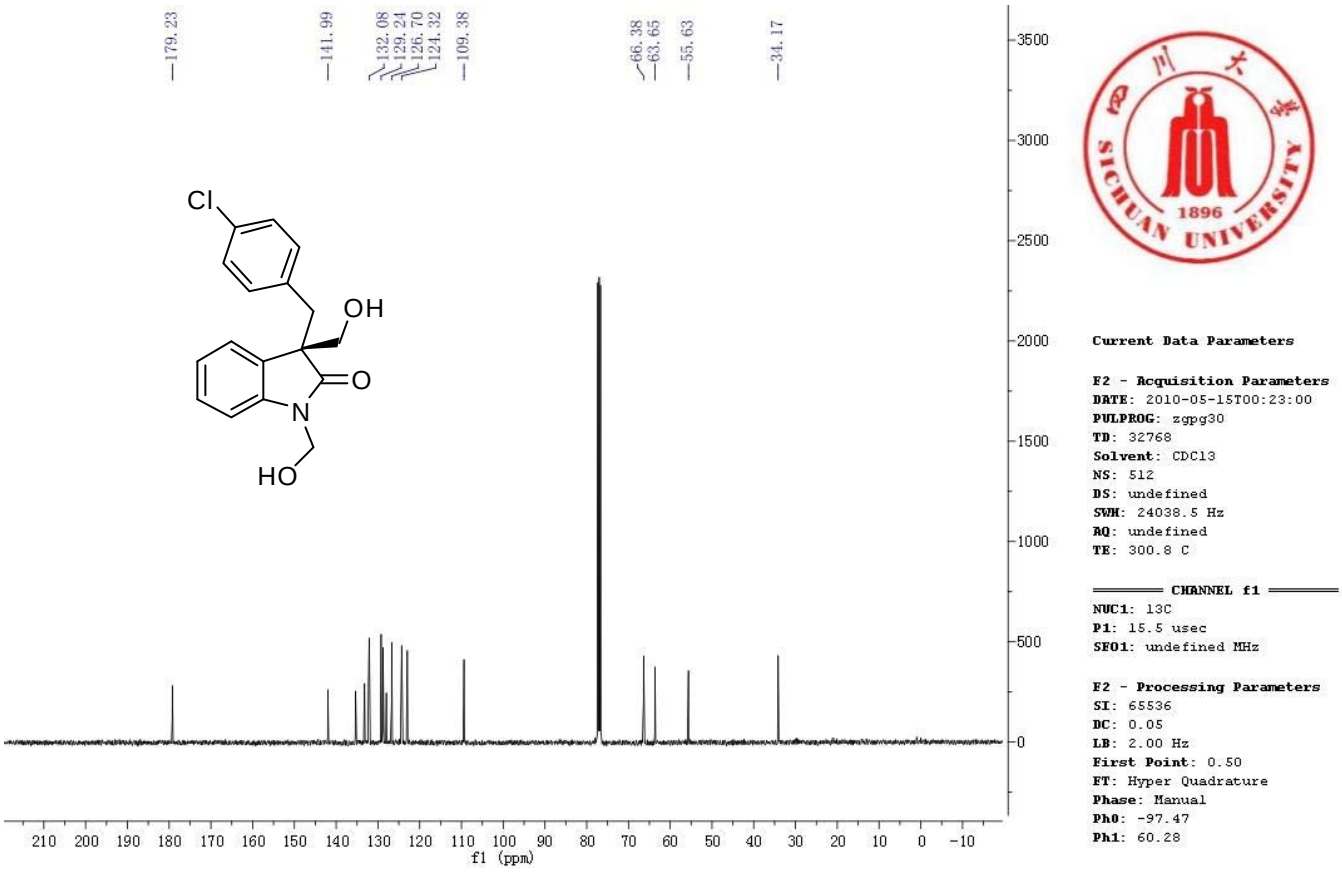
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-10T11:16:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 81.28
Ph1: 30.08



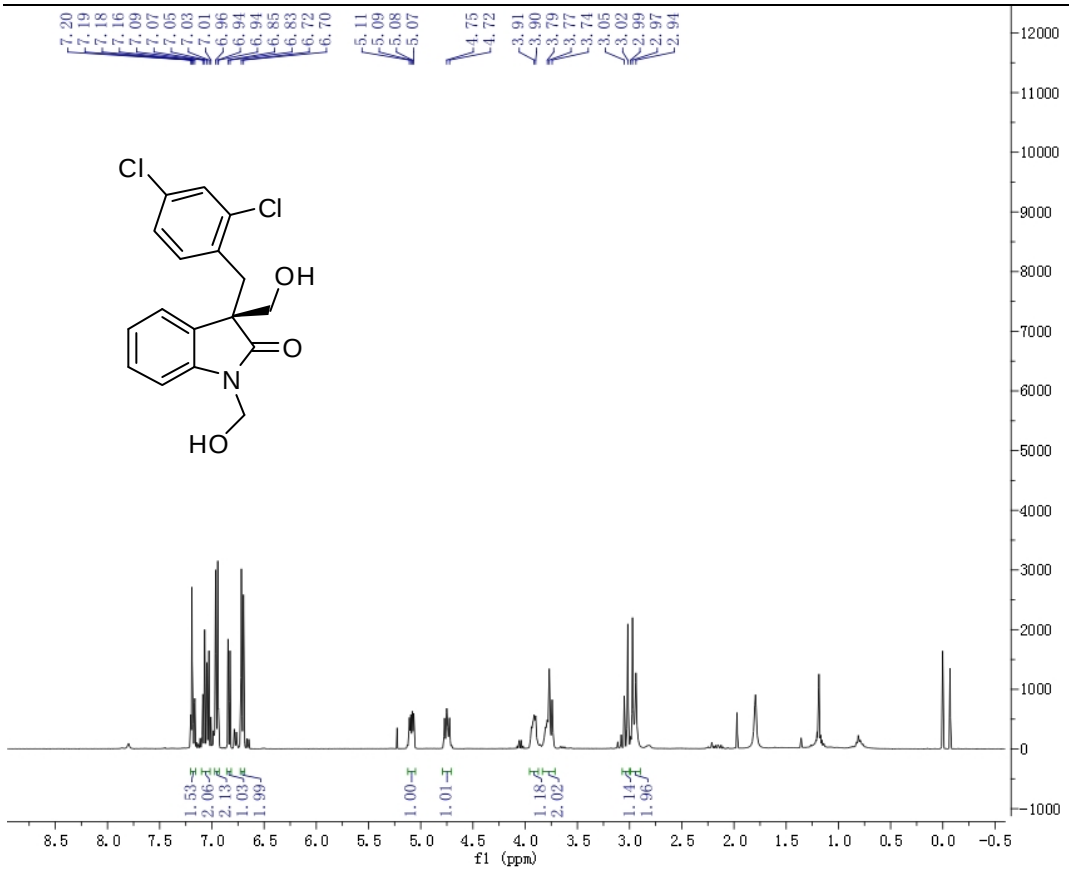


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T00:23:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 300.8 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -97.47
Ph1: 60.28

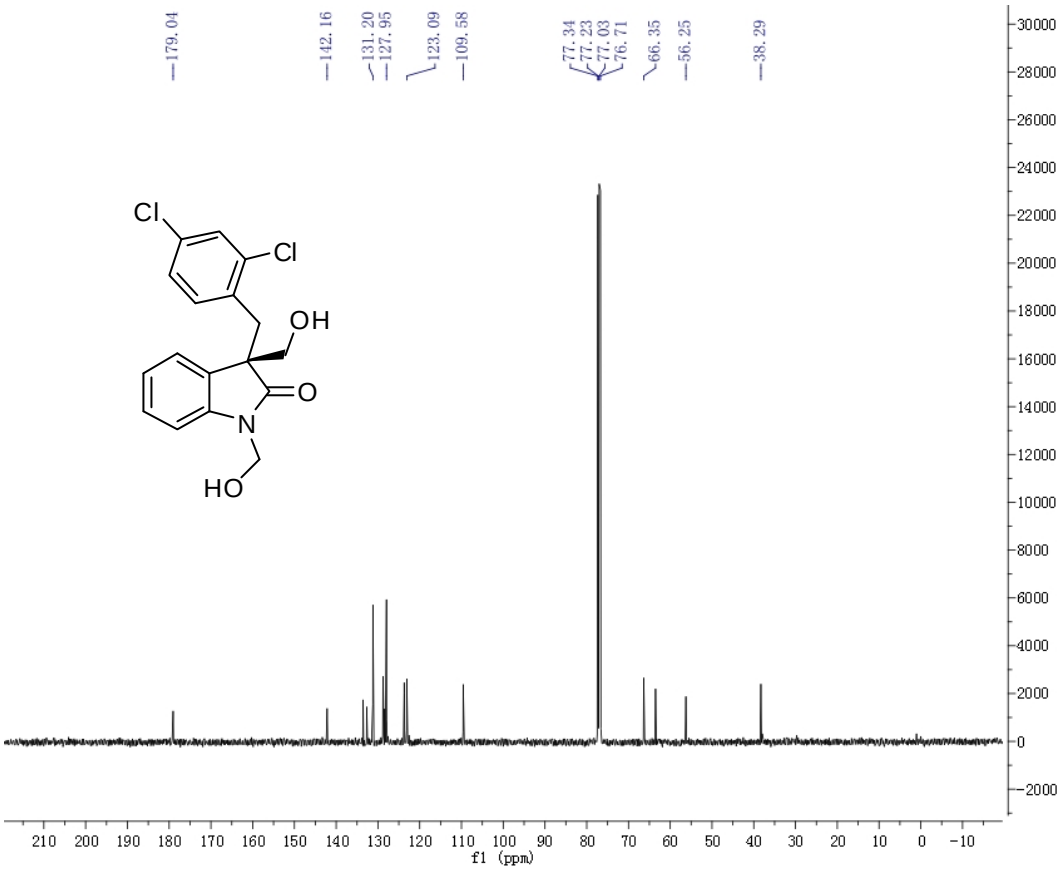


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T10:56:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 297.7 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 0.39
Ph1: 18.44

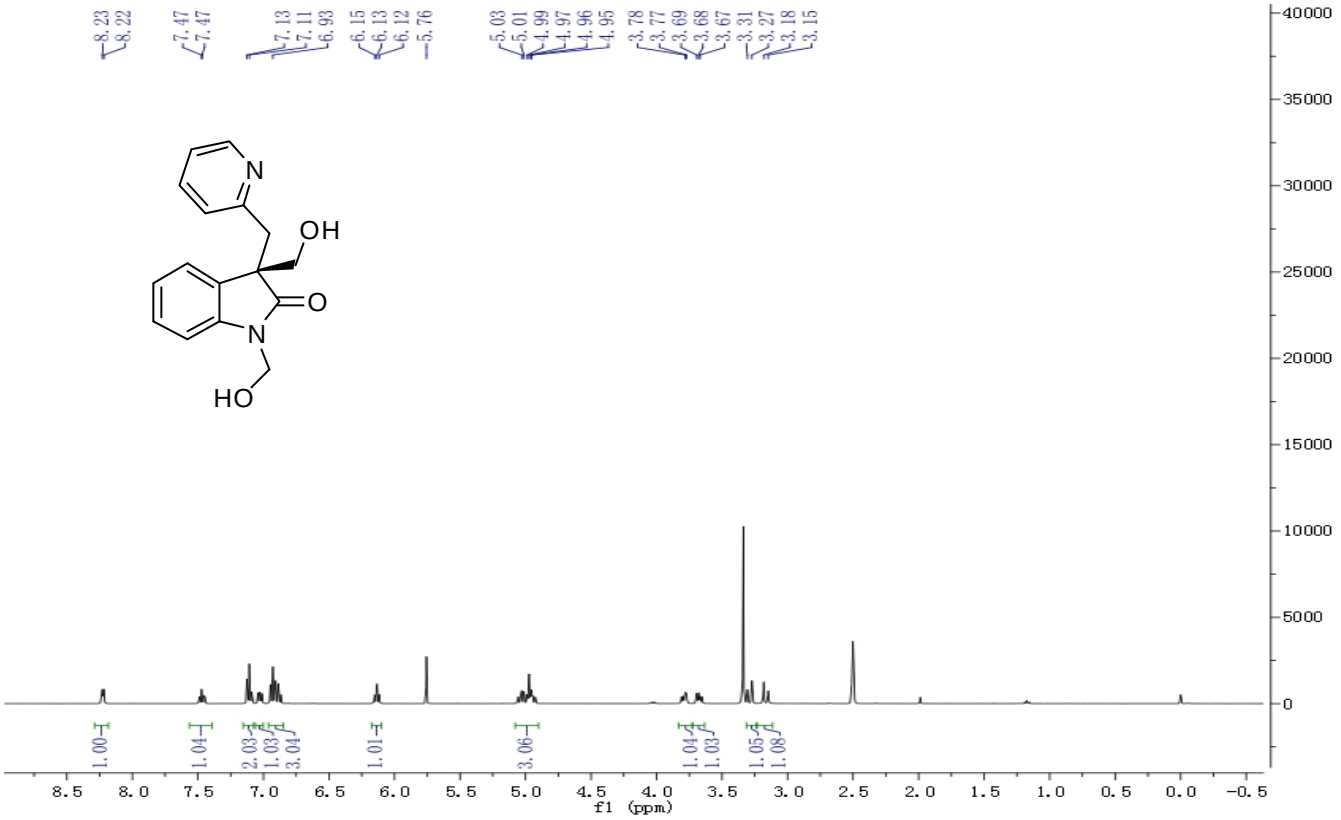


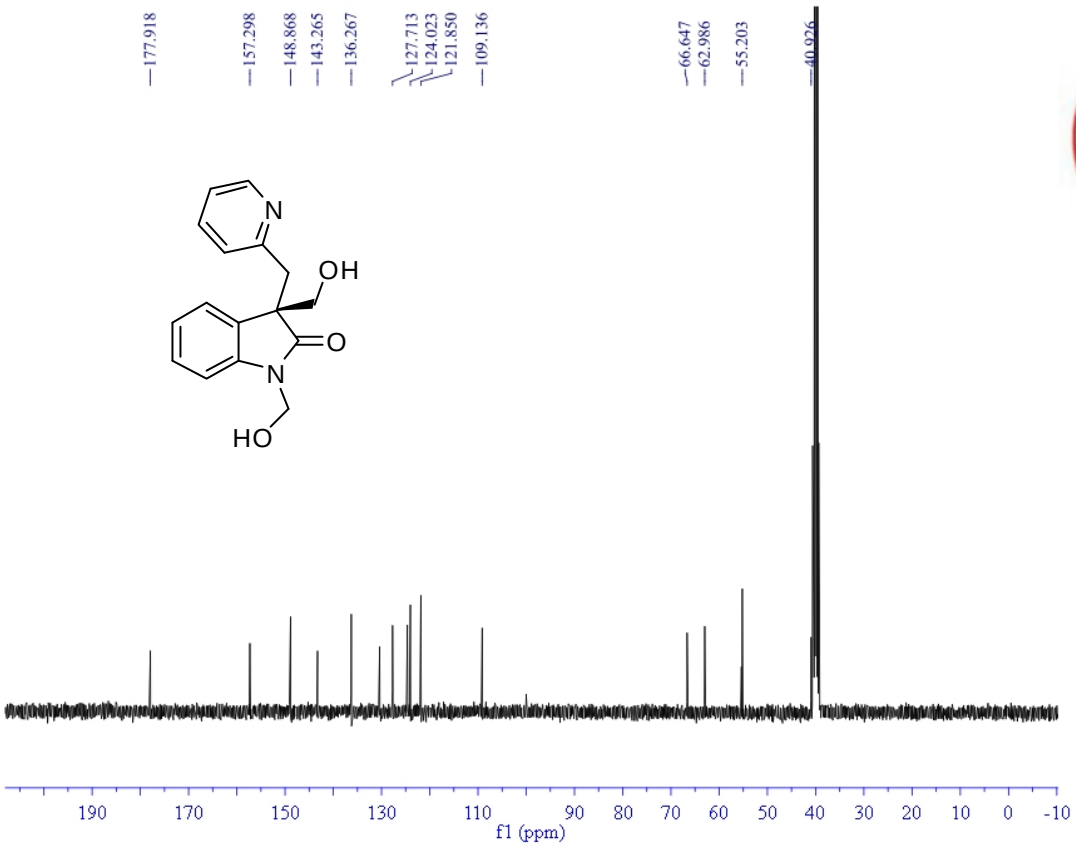
Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T10:50:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.8 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -104.16
Ph1: 72.29



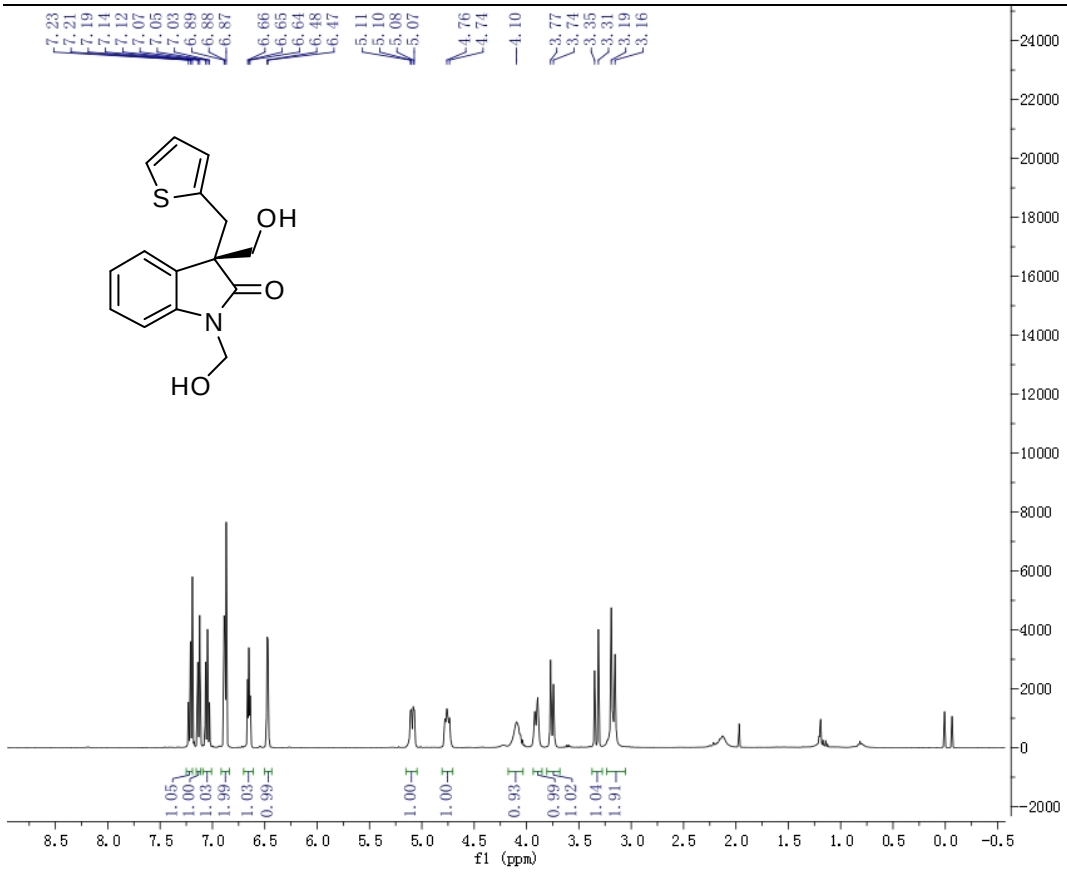


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-26T12:40:00
PULPROG: zgpg30
TD: 32768
Solvent: DMSO
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 297.4 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -43.77
Ph1: -6.69

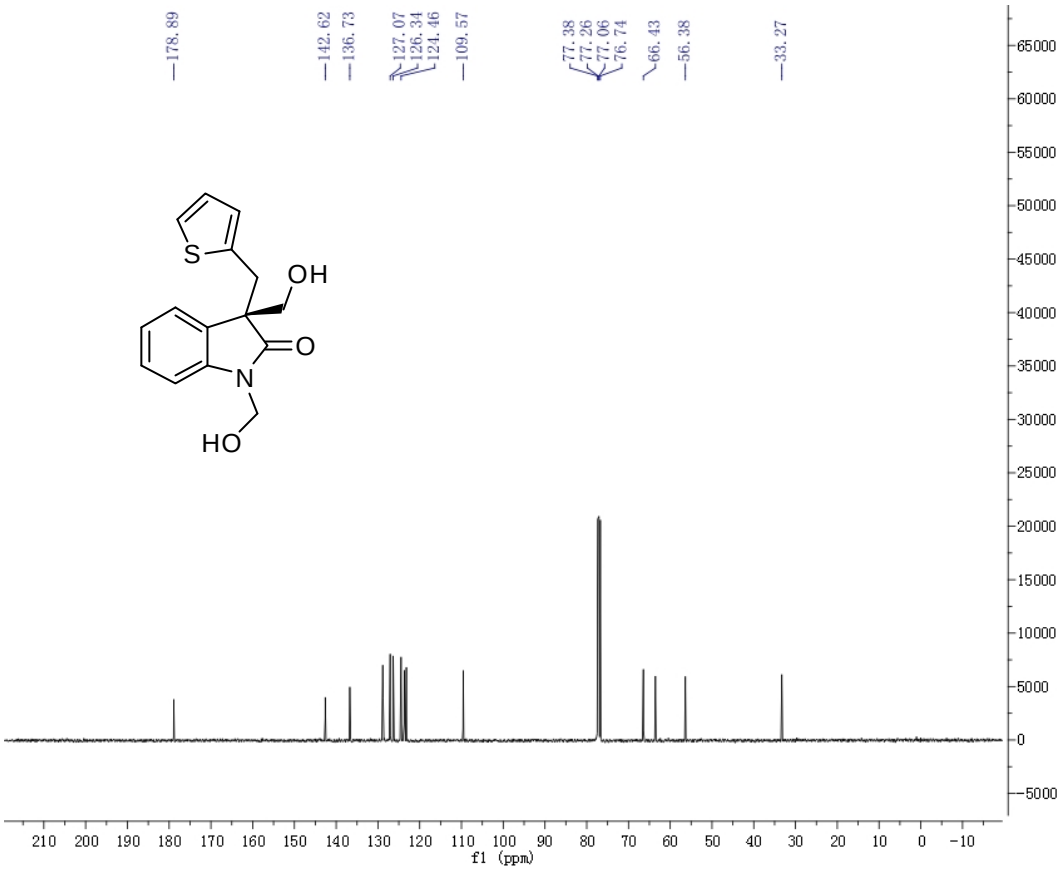


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T11:31:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -1.05
Ph1: 23.18

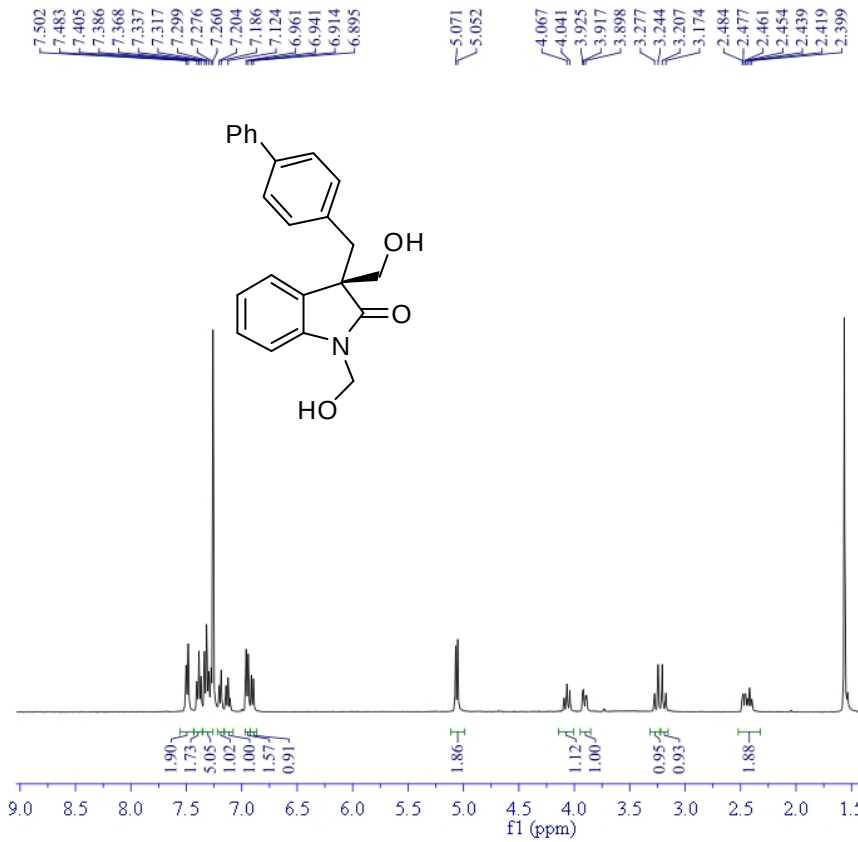


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T11:29:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.9 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -96.49
Ph1: 71.19

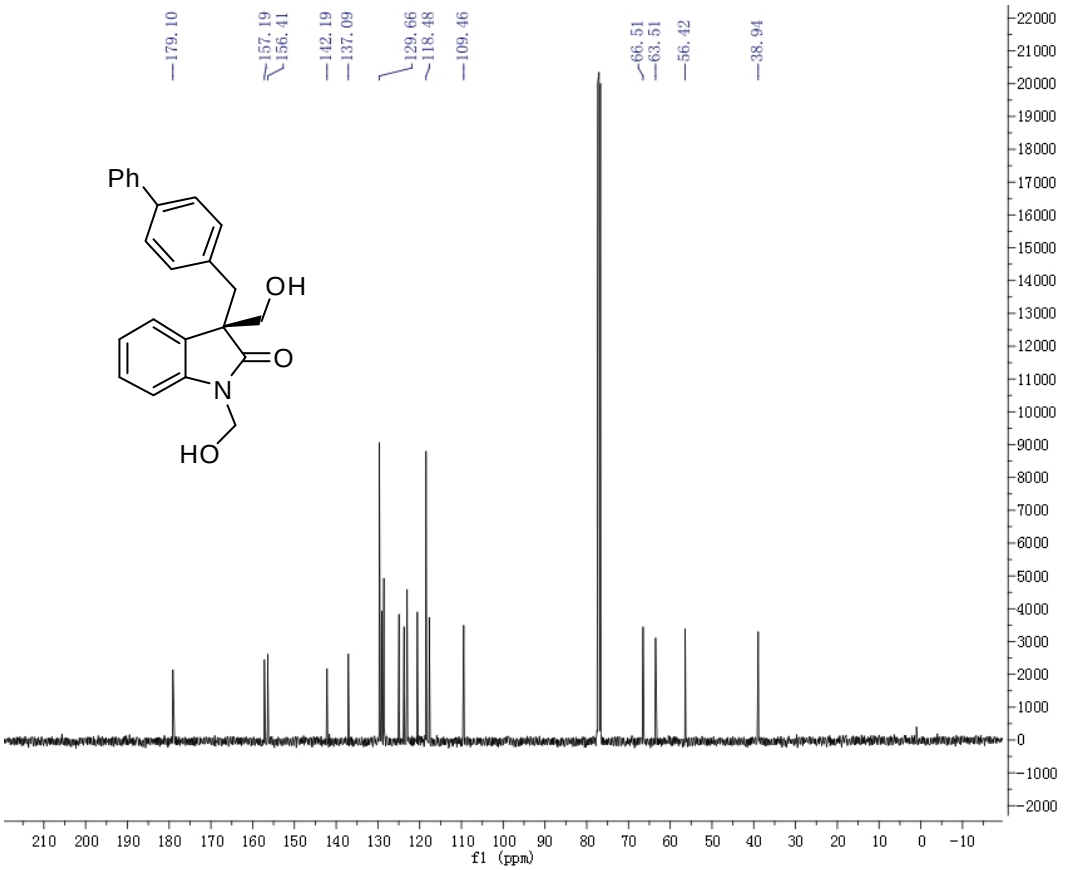


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-04-28T12:23:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -181.20
Ph1: 17.23

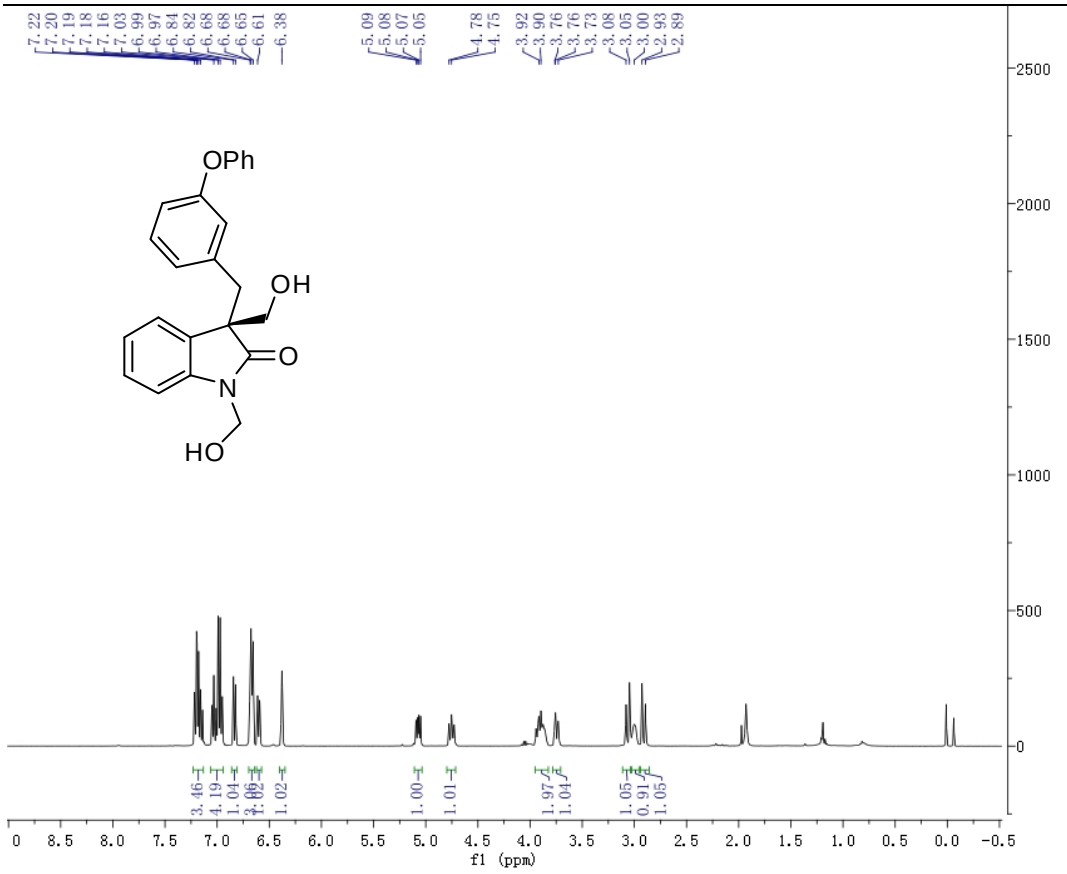


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-15T12:03:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.9 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -110.91
Ph1: 86.31

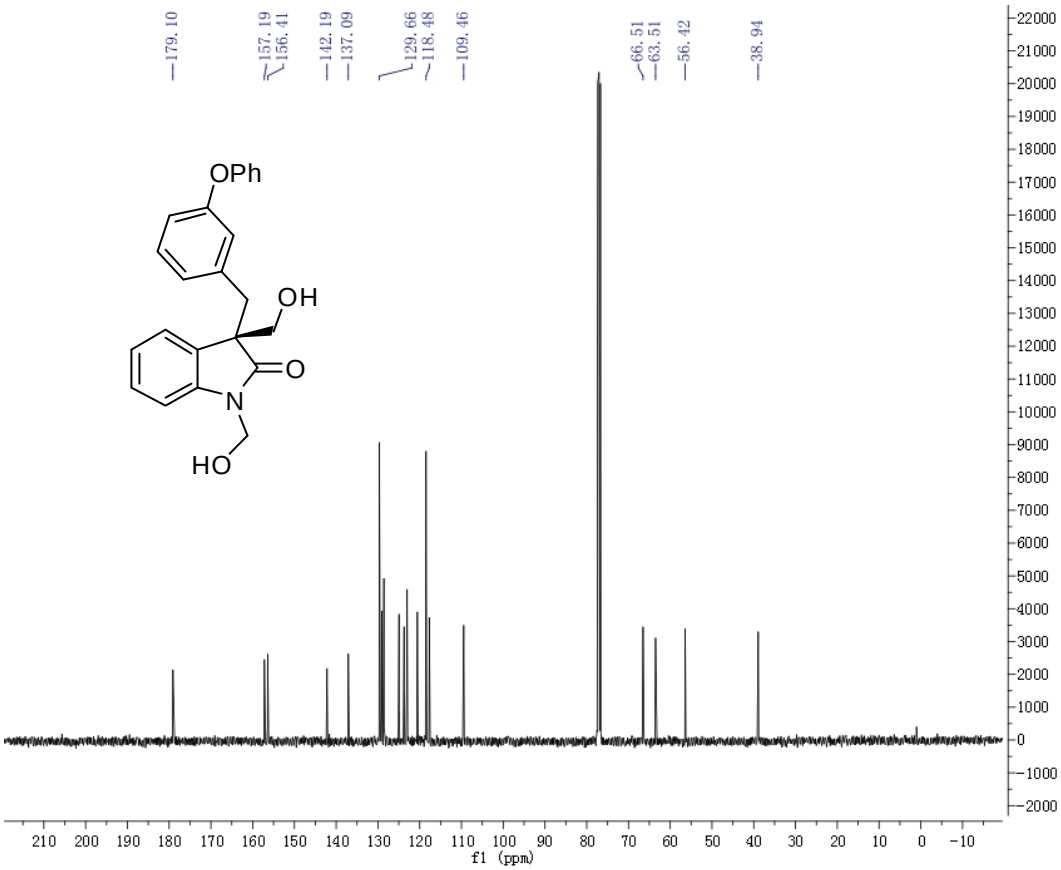


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T12:05:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 298 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -209.97
Ph1: 21.68

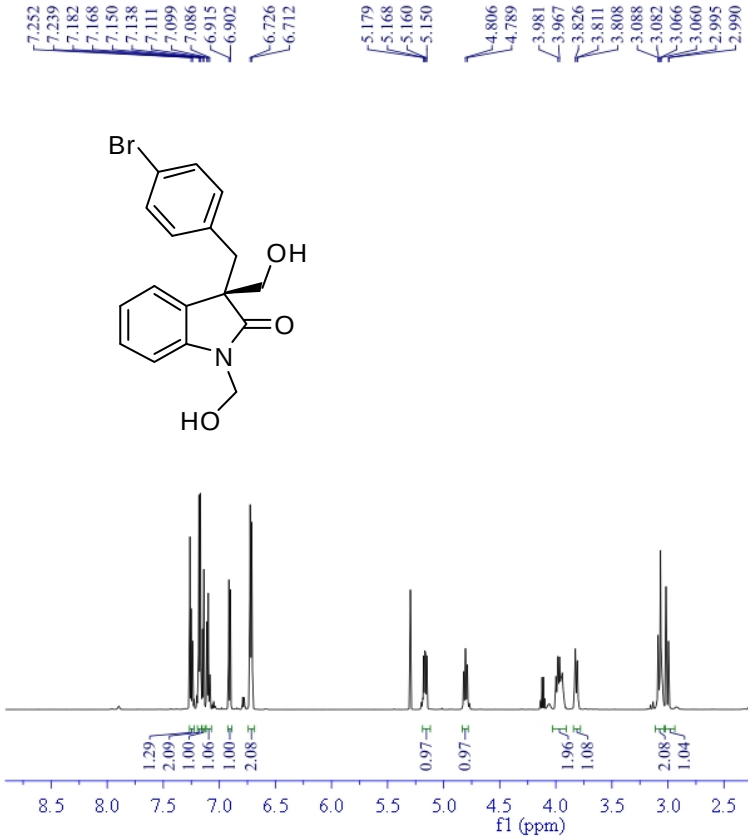


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T12:03:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.9 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -110.91
Ph1: 86.31

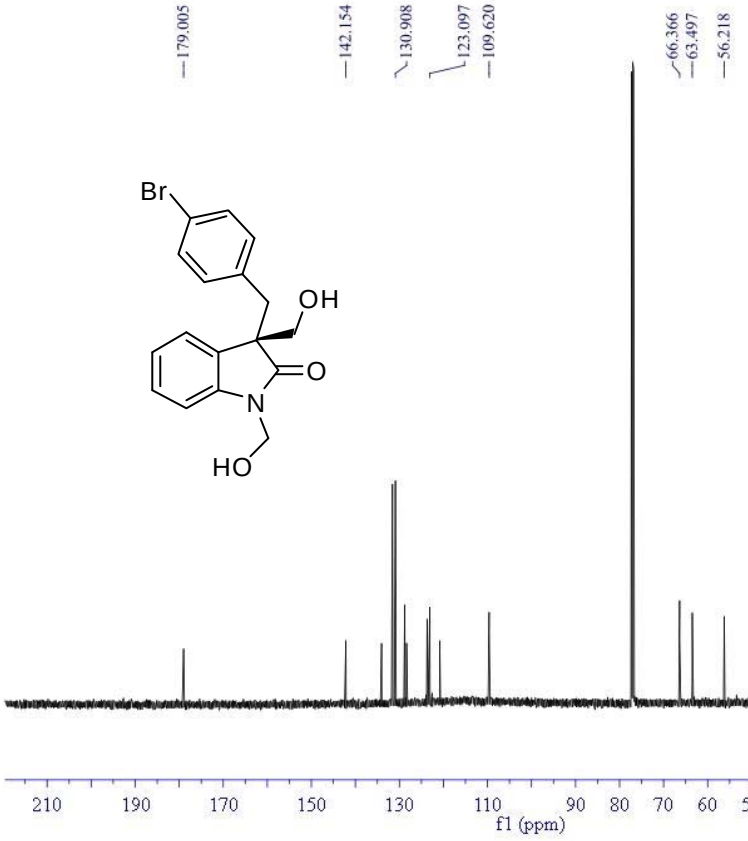


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T11:21:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 12335.5 Hz
AQ: undefined
TE: 295.6 C

CHANNEL f1
NUC1: 1H
P1: 7.2 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 11.28
Ph1: 28.90

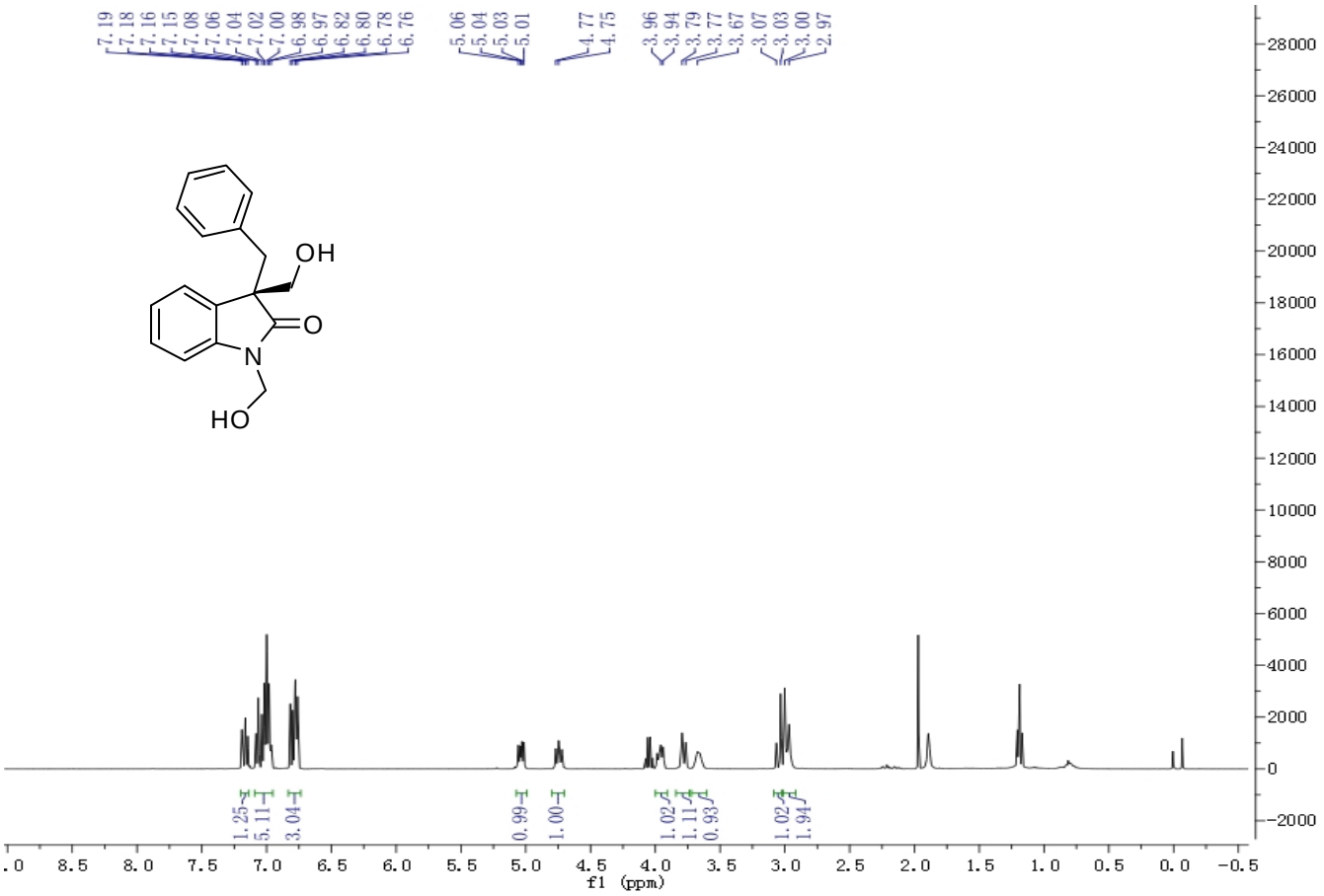


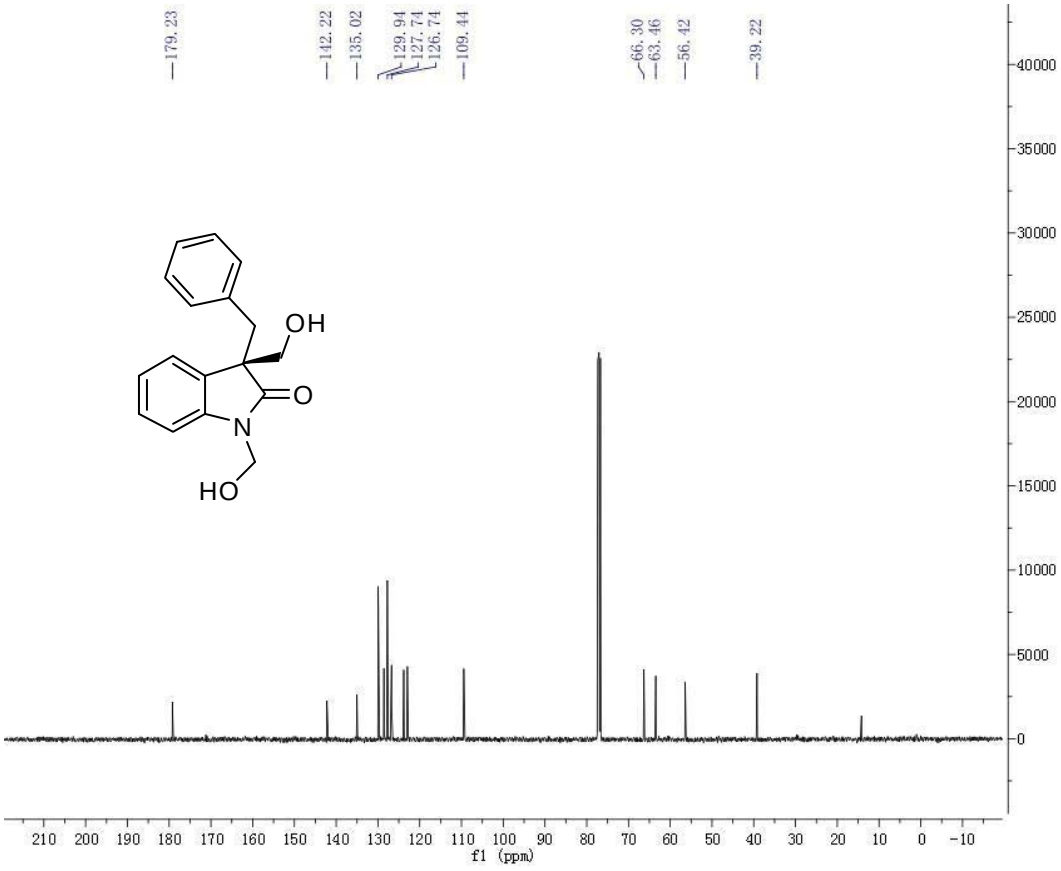
Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-24T11:47:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 36057.7 Hz
AQ: undefined
TE: 295.7 C

CHANNEL f1
NUC1: 13C
P1: 11.5 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 49.45
Ph1: 87.81



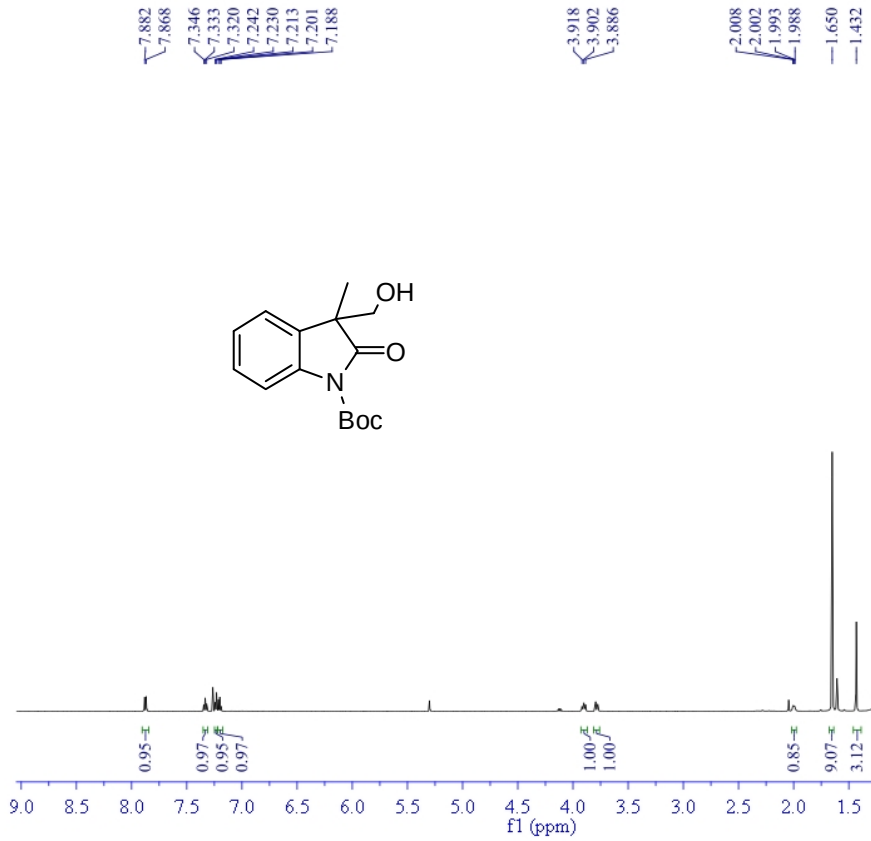


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-15T12:39:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 298.7 C

CHANNEL f1
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -117.51
Ph1: 97.88

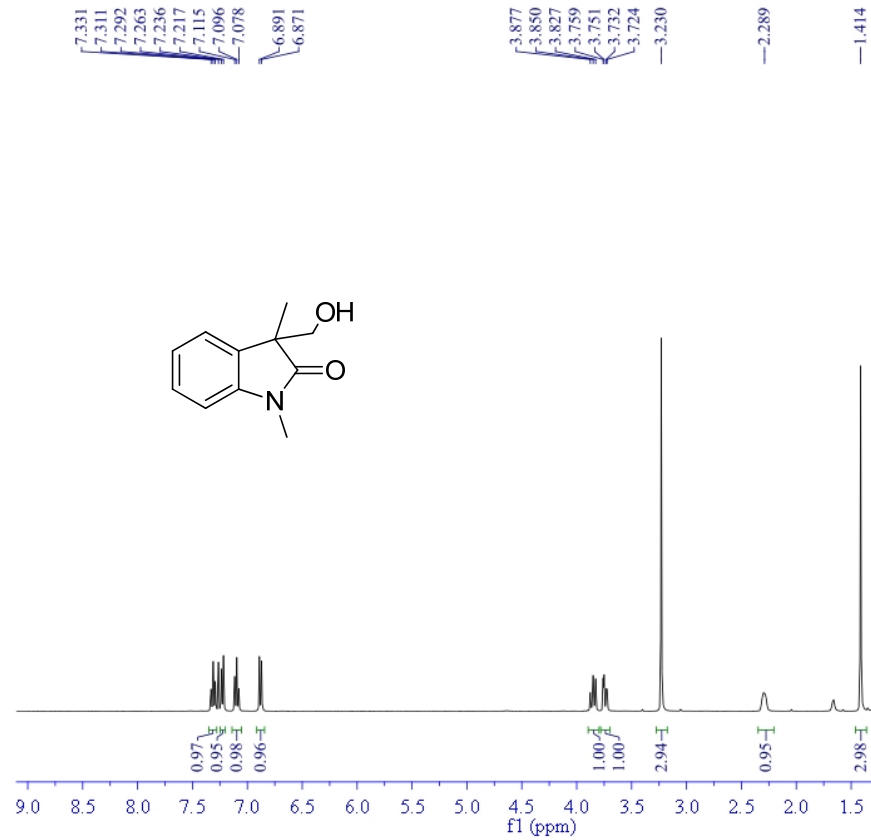


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-24T11:57:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 12335.5 Hz
AQ: undefined
TE: 295.3 C

CHANNEL f1
NUC1: 1H
P1: 7.2 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 9.20
Ph1: 32.04

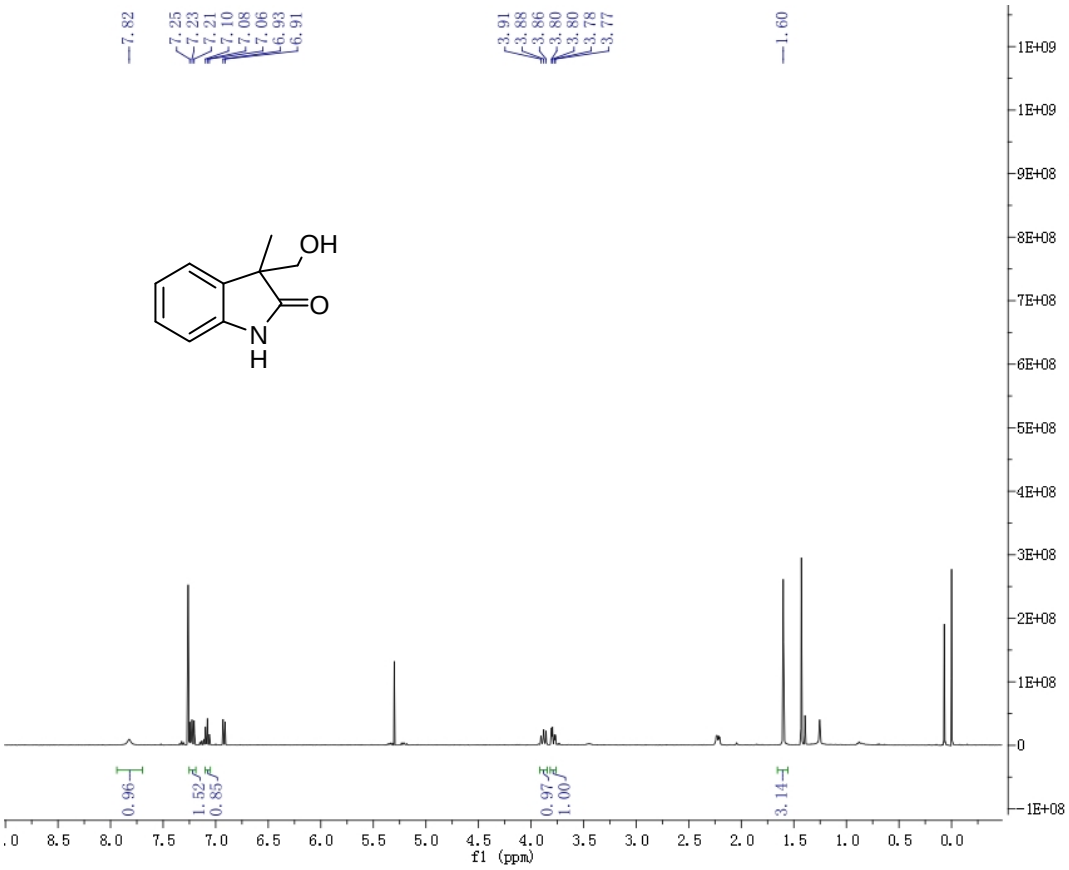


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-06-09T23:11:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 296.1 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.60 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 6.51
Ph1: 16.07

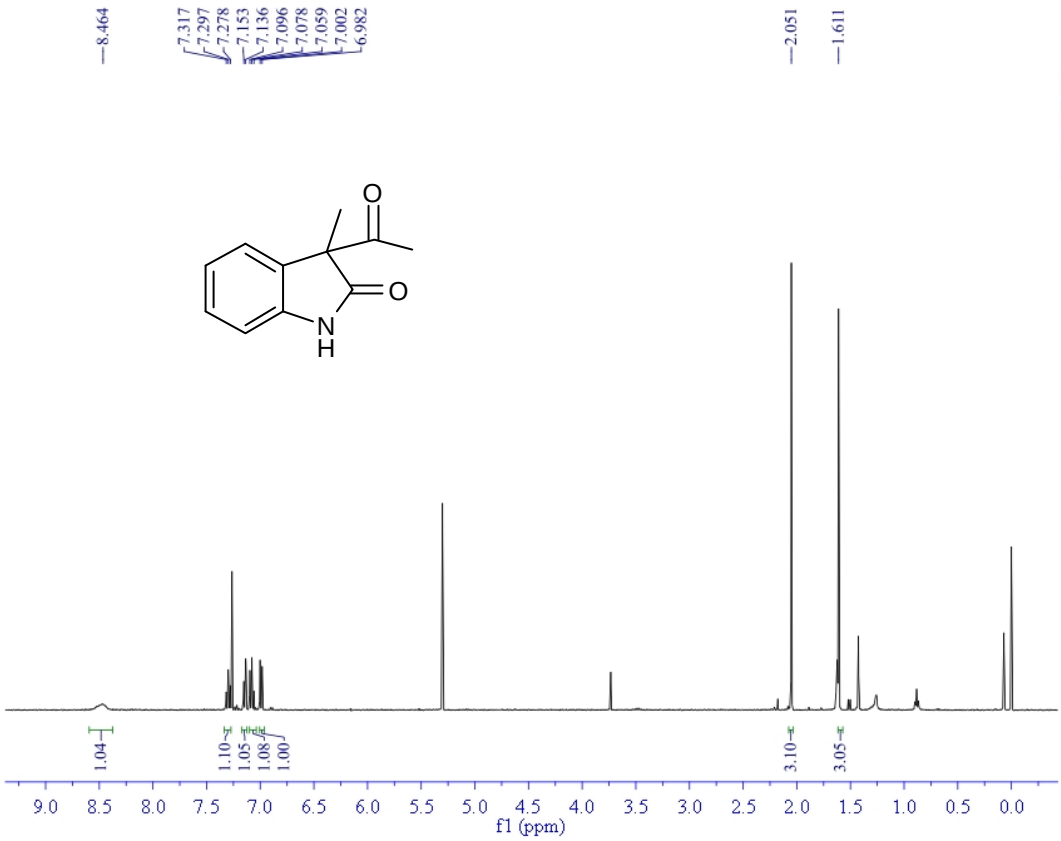


Current Data Parameters

F2 - Acquisition Parameters
DATE: 2010-05-21T23:26:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters
SI: 0
FT: Hyper
Phase: NoPC

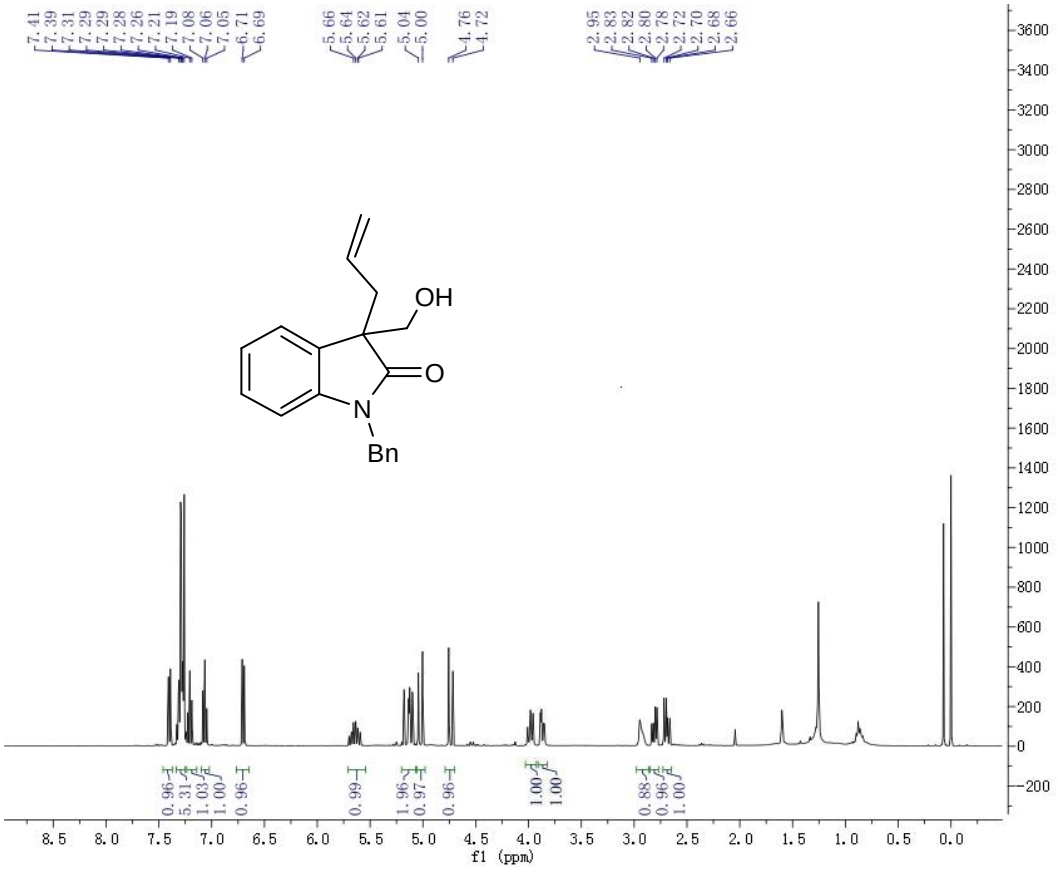


Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-06T10:57:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.1 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 158.14
Ph1: 22.67



Current Data Parameters

E2 - Acquisition Parameters
DATE: 2010-05-25T14:53:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 295.8 C

CHANNEL f1
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

E2 - Processing Parameters
SI: 65536
DC: 0.05
LB: -0.10 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -1.28
Ph1: 21.39

9. References

[1] a) B. M. Trost, Y. Zhang, T. Zhang, *J. Org. Chem.* **2009**, *74*, 5115; b) L. Cheng, L. Liu, D. Wang, Y. J. Chen, *Org. Lett.* **2009**, *11*, 3874 and references therein.

[2] Z. P. Yu, X. H. Liu, Z. H. Dong, M. S. Xie, X. M. Feng, *Angew. Chem. Int. Ed.* **2008**, *47*, 1308.

[3] T. A. Duffey, S. A. Shaw, E. Vedejs, *J. Am. Chem. Soc.* **2009**, *131*, 14.

[4] a) K. Asakawa, N. Noguchi, M. Nakada, *Heterocycles* **2008**, *76*, 183; b) J. E. Thomson, A. F. Kyle, K. B. Ling, S. R. Smith, A. M. Z. Slawin, A. D. Smith, *Tetrahedron* **2010**, *66*, 3801.