Electronic Supplementary Information

Catalytic enantioselective ene-type reactions of vinylogous hydrazone: Construction of α-methylene-γ-butyrolactone derivatives

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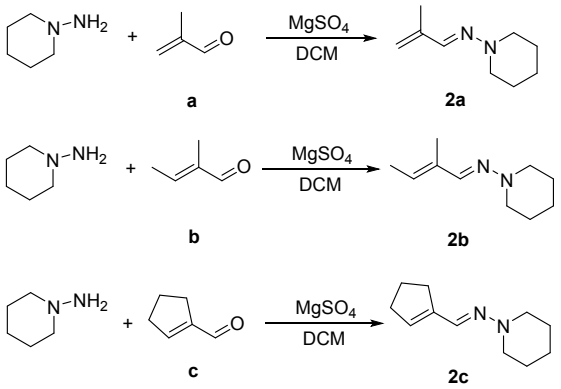
1 General remarks

^{1}H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26, DMSO-d_6, δ = 2.50). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet), coupling constants (Hz), integration. $^{13}C\{^1H\}$ NMR data were collected on commercial instruments (101 MHz) with complete proton decoupling. $^{19}F\{^1H\}$ NMR spectra were collected on commercial instruments (376 MHz) with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.16, DMSO-d_6, δ = 39.52). Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel IA, IB, IC, IE at 23 °C with UV detector at 254 or 210 nm in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]^{20}_{\lambda}$ (λ = 405 nm, *c*: g/100 mL, in CH_2Cl_2). HRMS was recorded on a commercial apparatus (FTMS+c ESI). All the solvents were purified by usual methods before use. Silica gel for Thin-layer chromatography (HG/T2354-92) made in Qingdao Haiyang Chemical Co., Ltd. Chiral *N*,*N*′-dioxide ligands were prepared according to previously reported method.[1]

2 General procedure for the synthesis of the substrates 2a–2c



To a solution of **a–c** (10 mmol) in dry DCM (10 mL) was added $MgSO_4$ (2 equiv.) and piperidin-1-amine(1.3 equiv.). The reaction was stirred at the room temperature for 3 h, concentrated, the residue was purified by flash column chromatography on silica gel with petroleum ether/EtOAc (15:1, v/v) to give the products **2** (oil, 60–70% yield).

2a: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 (s, 1H), 5.15 (d, *J* = 1.6 Hz, 1H), 5.04 (d, *J* = 1.6 Hz, 1H), 3.07 – 2.96 (m, 4H), 1.88 (s, 3H), 1.77 – 1.60 (m, 4H), 1.53 – 1.45 (m, 2H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ = 142.8, 138.4, 116.4, 52.1, 25.3, 24.3, 17.6; **HRMS** (FTMS+c ESI) calcd for $C_9H_{16}N_2H^+$ ([M+H$^+$]) = 153.1392, Found 153.1387.

2b: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (s, 1H), 5.64 (q, *J* = 7.0 Hz, 1H), 3.06 – 2.92 (m, 4H), 1.83 (s, 3H), 1.77 (d, *J* = 6.8 Hz, 3H), 1.73 – 1.69 (m, 4H), 1.52 – 1.40 (m, 2H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ = 141.8, 135.4, 128.3, 52.6, 25.4, 24.3, 13.9, 11.3; **HRMS** (FTMS+c ESI) calcd for $C_{10}H_{18}N_2H^+$ ([M+H$^+$]) = 167.1548, Found 167.1542.

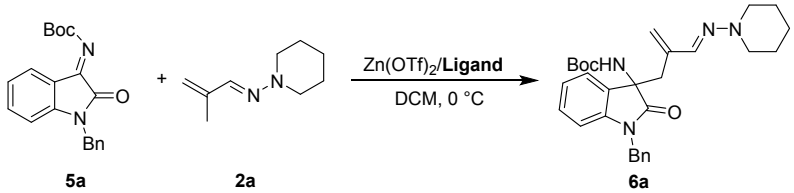
2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 (s, 1H), 5.82 (p, *J* = 2.4 Hz, 1H), 3.04 – 2.93 (m, 4H), 2.57 – 2.51 (m, 2H), 2.50 – 2.38 (m, 2H), 1.93 – 1.85 (m, 2H), 1.72 – 1.64 (m, 4H), 1.52 – 1.43 (m, 2H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ = 143.0, 134.4, 131.8, 131.7, 52.2, 33.0, 31.0, 25.3, 24.3, 23.1; **HRMS** (FTMS+c ESI) calcd for $C_{11}H_{18}N_2H^+$ ([M+H$^+$]) = 179.1548, Found 179.1542.

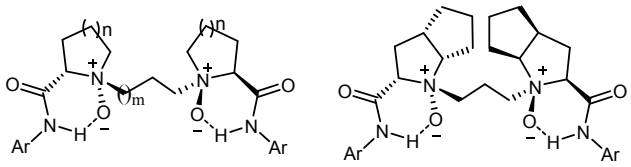
3 General procedures for the preparation of the racemic products

The corresponding racemic products were obtained by using racemic *N*,*N*′-dioxide (±)-**L-PrPr$_2$** as the ligand under the respective catalytic reaction conditions.

4.1. Optimization of the imino-ene reaction conditions

Table S1. Screening of the ligands[a]





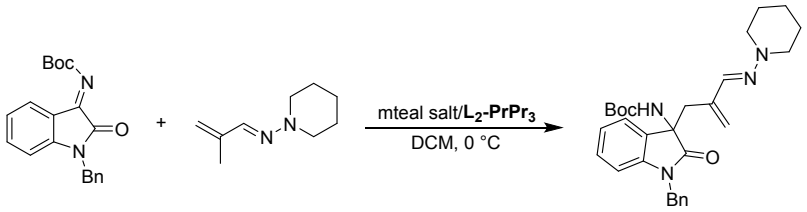
L-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1, m = 1
L-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m = 1
L$_2$-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1, m = 0
L$_4$-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1, m = 2
L$_2$-PrPr$_3$: Ar = 2,4,6-*i*Pr$_3$C$_6$H$_2$, n = 1, m = 0

L-RaPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$

entry	ligand	yield (%)[b]	ee (%)[c]
1	**L-PrPr$_2$**	98	64
2	**L-PiPr$_2$**	99	30
3	**L-RaPr$_2$**	98	74
4	**L$_2$-PrPr$_2$**	98	86
5[d]	**L$_4$-PrPr$_2$**	50	18
6	**L$_2$-PrPr$_3$**	98	88

[a] Unless otherwise noted, all reactions were carried out with ligand/Zn(OTf)$_2$ (1:1, 10 mol%), **5a** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at 0 °C for 15 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] For 24 h.

Table S2. Screening of the metal salts[a]

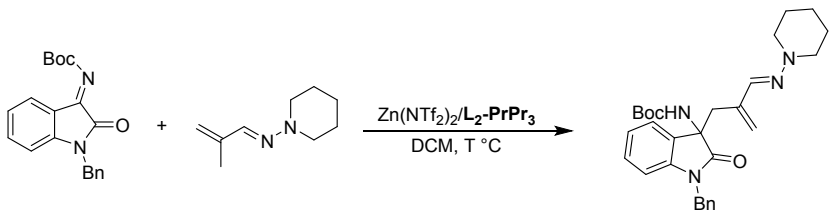


5a **2a** **6a**

entry	metal salt	yield (%)[b]	ee (%)[c]
1	$Zn(NTf_2)_2$	98	91
2	$Ni(OTf)_2$	trace	-
3	$Mg(OTf)_2$	trace	-

[a] Unless otherwise noted, all reactions were carried out with **L$_2$-PrPr$_3$**/metal salt (1:1, 10 mol%), **5a** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at 0 °C for 15 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Table S3. Screening of the reaction temperature[a]



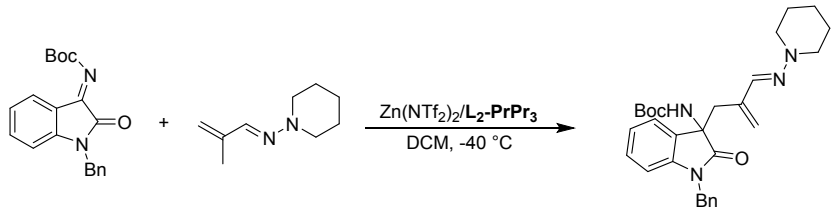
5a **2a** **6a**

entry	T (°C)	yield (%)[b]	ee (%)[c]
1	−10	98	93
2	−20	98	94
3	−30	98	95

4	–40	98	96
5	–50	98	96

[a] Unless otherwise noted, all reactions were carried out with **L_2-PrPr$_3$**/Zn(NTf$_2$)$_2$ (1:1, 10 mol%), **5a** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at T °C for 15 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Table S4. Screening of the molecular sieves[a]

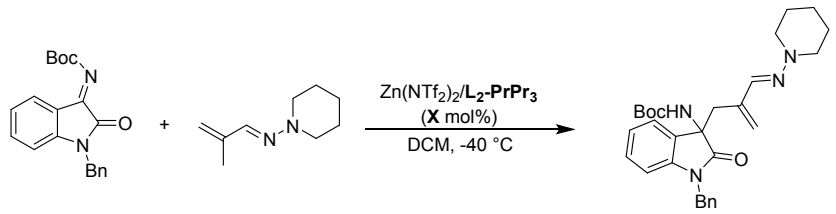


5a **2a** **6a**

entry	additive	yield (%)[b]	ee (%)[c]
1	3 Å MS (20 mg)	97	96
2	3 Å MS (30 mg)	97	95
3	4 Å MS (20 mg)	99	96
4	4 Å MS (30 mg)	99	96
5	5 Å MS (20 mg)	99	96
6	5 Å MS (30 mg)	98	96

[a] Unless otherwise noted, all reactions were carried out with **L_2-PrPr$_3$**/Zn(NTf$_2$)$_2$ (1:1, 10 mol%), **5a** (0.1 mmol), **2a** (0.13 mmol) and additives in DCM (0.5 mL) at –40 °C for 15 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Table S5. Screening of the catalyst loading[a]



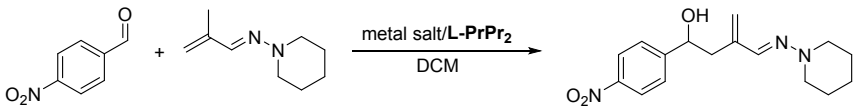
5a **2a** **6a**

entry	**X**	yield (%)[b]	ee (%)[c]
1	10	98	96
2	5	98	96
3[d]	2.5	98	96

[a] Unless otherwise noted, all reactions were carried out with **L_2-PrPr$_3$**/Zn(NTf$_2$)$_2$ (1:1, X mol%), **5a** (0.1 mmol), **2a** (0.13 mmol) and 4 Å MS (20 mg) in DCM (0.5 mL) at –40 °C for 15 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] For 40 h.

4.2 Optimization of the aldehyde-carbonyl-ene reaction conditions

Table S6. Screening of the metal salts[a]

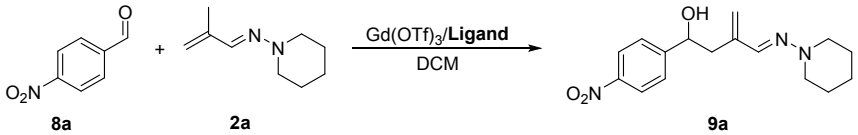


8a **2a** **9a**

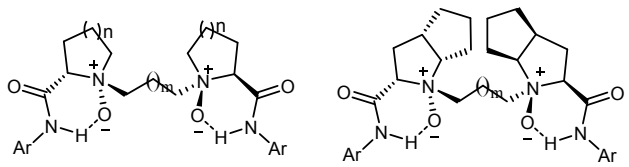
entry	metal salt	yield (%)[b]	ee (%)[c]
1	$Sc(OTf)_3$	43	0
2	$Fe(OTf)_3$	trace	--
3	$Zn(OTf)_2$	89	−5
4	$Ni(OTf)_2$	37	13
5	$Mg(OTf)_2$	19	−17
6	$Dy(OTf)_3$	52	40
7	$Y(OTf)_3$	55	30
8	$Yb(OTf)_3$	64	17
9	$Gd(OTf)_3$	54	53
10	$La(OTf)_3$	23	50

[a] Unless otherwise noted, all reactions were carried out with **L-PrPr$_2$**/metal salt (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at 30 °C for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Table S7. Screening of the ligands[a]



8a **2a** **9a**



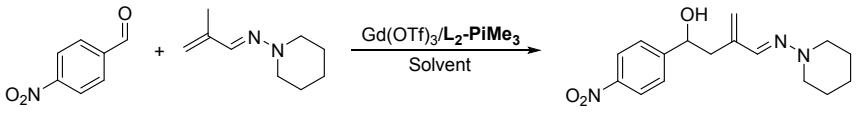
L-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1, m=1
L-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m=1
L-PiEt$_2$: Ar = 2,6-Et$_2$C$_6$H$_3$, n = 2, m=1
L-PiMe$_2$: Ar = 2,6-Me$_2$C$_6$H$_3$, n = 2, m=1
L$_2$-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m=0
L$_4$-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m=2
L-PiPr$_3$: Ar = 2,4,6-*i*Pr$_3$C$_6$H$_2$, n = 2, m=1

L-RaPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$

entry	ligand	yield (%)[b]	ee (%)[c]
1	**L-PrPr$_2$**	54	53
2	**L-PiPr$_2$**	63	60
3	**L-RaPr$_2$**	66	37
4	**L-PiPr$_3$**	78	57
5	**L-PiEt$_2$**	73	62
6	**L-PiMe$_2$**	n. d.[d]	63
7	**L$_2$-PiPr$_2$**	33	−70
8	**L$_4$-PiPr$_2$**	trace	--

[a] Unless otherwise noted, all reactions were carried out with ligand/$Gd(OTf)_3$ (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at 30 °C for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Not determined.

Table S8. Screening of the solvents[a]

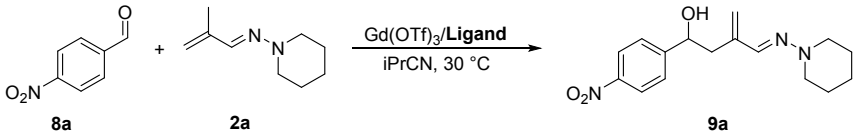


8a **2a** **9a**

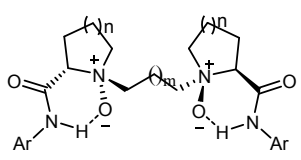
entry	solvent	yield (%)[b]	ee (%)[c]
1	DCM	n. d.[d]	54
2	EtOAc	n. d.[d]	53
3	THF	trace	-
4	CH_3CN	80	44
5	Toluene	n. d.[d]	45
6	MeOH	trace	-
7	iPrCN	36	54
8	PhCN	33	54

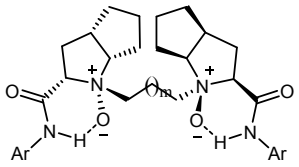
[a] Unless otherwise noted, all reactions were carried out with **L_2-PiMe$_3$**/Gd(OTf)$_3$ (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.13 mmol) in solvent (0.5 mL) at 30 °C for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Not determined.

Table S9. Screening of the ligands[a]



8a **2a** **9a**





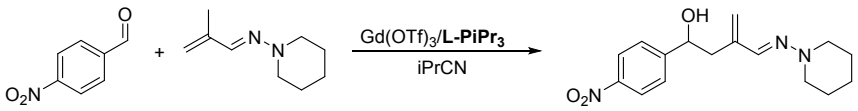
L-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1, m=1
L-PiEt$_2$: Ar = 2,6-Et$_2$C$_6$H$_3$, n = 2, m=1
L-PiPh: Ar = 4-PhC$_6$H$_4$, n = 2, m=1
L_2-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m=0
L_4-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2, m=2
L-PiPr$_3$: Ar = 2,4,6-*i*Pr$_3$C$_6$H$_2$, n = 2, m=1

L-RaPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$

entry	ligand	yield (%)[b]	ee (%)[c]
1	**L-PrPr$_2$**	n. d.[d]	52
2	**L-PiPr$_3$**	48	–77
3	**L-RaPr$_2$**	n. d.[d]	40
4	**L-PiEt$_2$**	48	57
5	**L-PiPh**	trace	--
6	**L_2-PiPr$_2$**	trace	--
7	**L_4-PiPr$_2$**	trace	--

[a] Unless otherwise noted, all reactions were carried out with ligand/Gd(OTf)$_3$ (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.13 mmol) in iPrCN (0.5 mL) at 30 °C for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Not determined.

Table S10. Screening of the additives and other conditions[a]

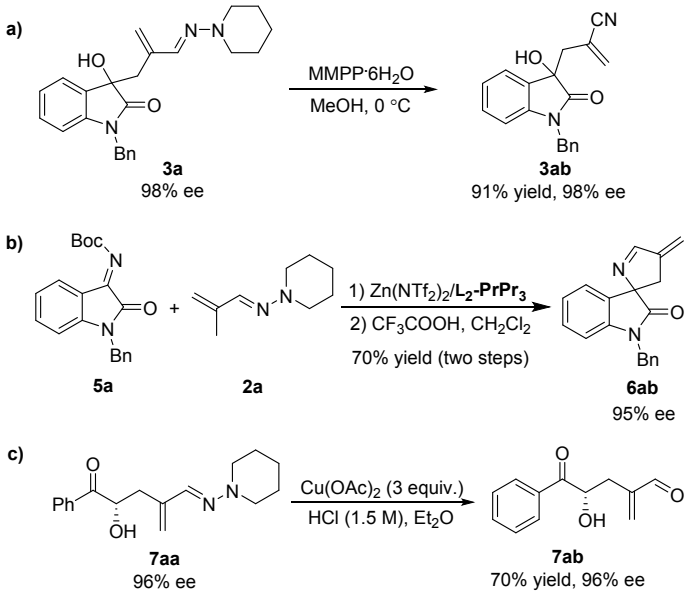


8a **2a** **9a**

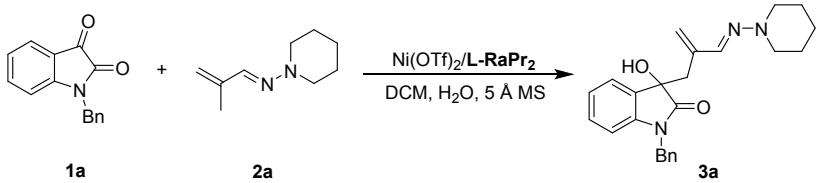
entry	additive	yield (%)[b]	ee (%)[c]
1	3 Å MS (15 mg)	62	–55
2	4 Å MS (15 mg)	45	–60
3	5 Å MS (15 mg)	58	–55
4	$NaBAr^F_4$ (8.9 mg)	64	–81
5	H_2O (5 μL)	41	–80
6	$LiNTf_2$ (0.02 mmol)	n. d.[d]	–74
7	Salicylic acid (10 mg)	n. d.[d]	–35
8[e]	$NaBAr^F_4$ (8.9 mg)	77	–83
9[f]	$NaBAr^F_4$ (8.9 mg)	70	–82
9[e,g]	$NaBAr^F_4$ (8.9 mg)	80	–84

[a] Unless otherwise noted, all reactions were carried out with **L-PiPr$_3$**/Gd(OTf)$_3$ (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.13 mmol) in iPrCN (0.5 mL) at 30 °C for 72 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Not determined. [e] The reaction were carried out with **L-PiPr$_3$**/Gd(OTf)$_3$ (1:1, 10 mol%), **8a** (0.1 mmol), **2a** (0.3 mmol) in iPrCN (0.3 mL) at 30 °C for 72 h. [f] In iPrCN (0.2 mL). [g] At 25 °C.

5.1 Other synthetic utilities



5.2 General procedure for the catalytic Isatin carbonyl-ene reaction

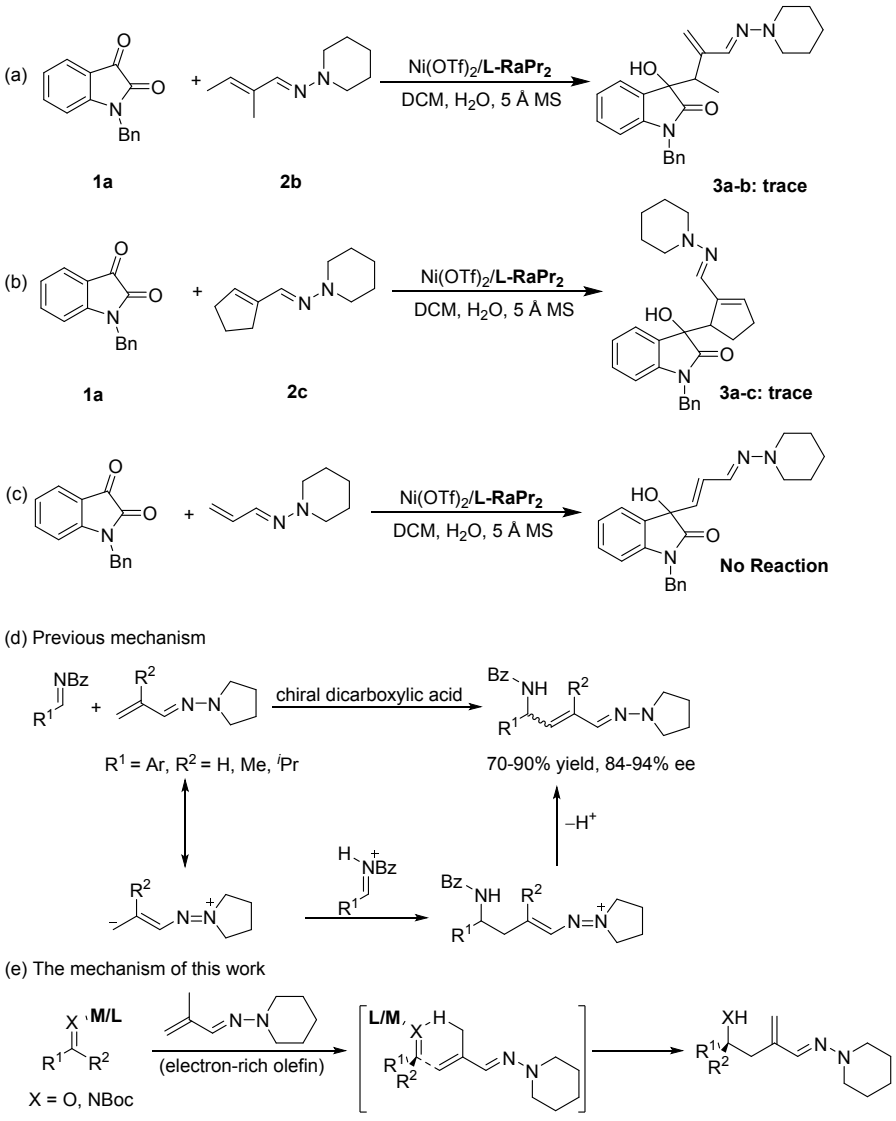


1a **2a** **3a**

An oven-dried test tube was charged with **1a** (0.1 mmol), Ni(OTf)$_2$ (3.6 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol); 5 Å MS (10 mg); H_2O (1 μL); DCM (0.4 mL). This solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone

2a (1.3 equiv.). Then the reaction mixture was stirred at the same temperature for another 36 h. Finally, directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/4, v/v) to afford the desired product **3a**.

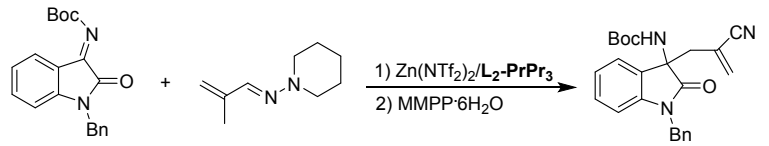
5.3 Some vinylogous hydrazones were unavailable for this reaction and study of reaction mechanism



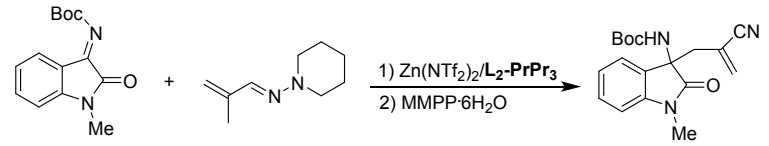
Unless otherwise noted, the reactions were carried out under standard conditions.

As the lager steric hindrance of substituent group of vinylogous hydrazones **2b**–**2c**, trace amount of corresponding products were obtained (a and b). When acroleine hydrazones were performed, the 1,2-addition product was not detected (c), Which indicated that this ene type reaction smoothly proceeded via six-membered cyclic transition state (e) not the previous mechanism[2] (d).

5.4 General procedure for the catalytic Imino-ene reaction



5a **2a** **6aa**



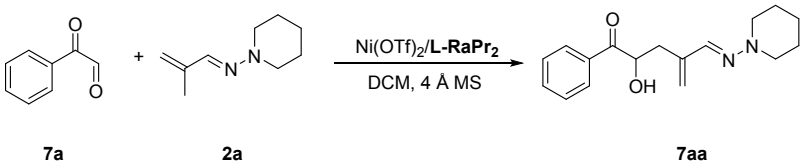
5m **2a** **6mm**

95% yield, <10% ee

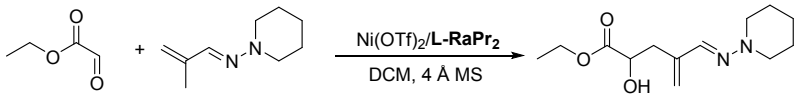
It was noteworthy that a further transformation was performed to give a clear NMR-spectrogram of product 6aa.

1): To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **4a** (0.1 mmol), $Zn(NTf_2)_2$ (3.1 mg, 0.005 mmol) and **L_2-PrPr$_3$** (3.5 mg, 0.005 mmol), 4 Å MS (20 mg), DCM (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at –40 °C. Then the reaction mixture was stirred at the same temperature for 15 h. Directly purified by flash column chromatography (ethyl acetate /petroleum ether = 1/4, v/v) to afford the crude product; 2): To a stirred solution of the crude product in MeOH (1.5 mL) was added magnesium monoperoxyphthalate hydrate (0.15 mmol, 75 mg) at ice-bath and stirred for 20 min at the same temperature. Finally, purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v) to give the product **6aa** (two steps: 96% yield, 96% ee).

5.5 General procedure for the catalytic glyoxal derivative-carbonyl-ene reaction



7a **2a** **7aa**

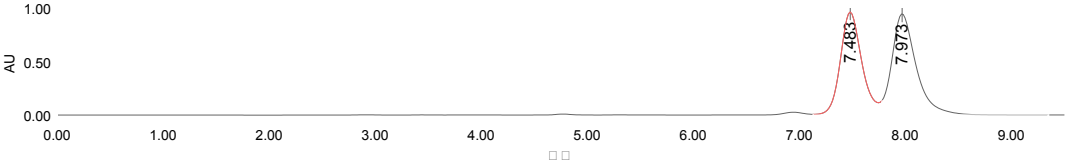


7b **2a** **7bb**

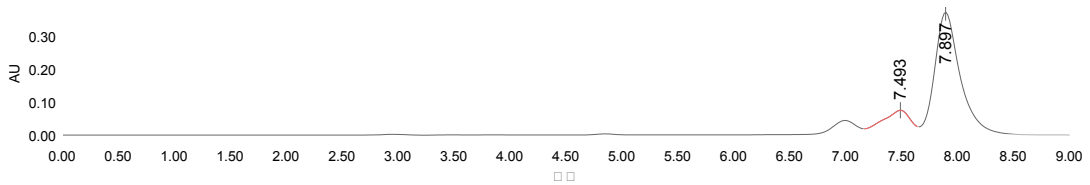
To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **7a** (0.1 mmol, 15.2 mg), $Ni(OTf)_2$ (1.8 mg, 0.005 mmol) and **L-RaPr$_2$** (3.5 mg, 0.005 mmol), 4 Å MS (10 mg), DCM (0.5 mL). The mixture was stirred at 30 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at 30 °C. Then the reaction mixture was stirred at 30 °C for 15 h. Finally, directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/4, v/v) to afford the desired product **7aa** (98% yield, 95% ee).

The experiments with ethyl glyoxalate and its imine derivative as the substrates were investigated.

To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **7b** (0.1 mmol, 50% in toluene), $Ni(OTf)_2$ (3.6 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol), 4 Å MS (30 mg), DCM (0.5 mL). The mixture was stirred at 25 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at 25 °C. Then the reaction mixture was stirred at 25 °C for 15 h. Finally, directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/4, v/v) to afford the desired product **7bb** (30% yield, 63% ee). HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.90 min, t_R (minor) = 7.49 min.

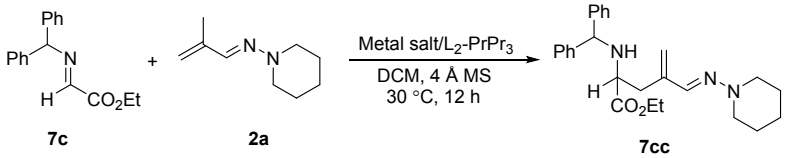


	Retention Time	Area	% Area
1	7.483	14306064	49.80
2	7.973	14422522	50.20



	Retention Time	Area	% Area
1	7.493	1359924	18.67
2	7.897	5924942	81.33

^{1}H NMR (**7bb**, 400 MHz, $CDCl_3$) δ = 7.29 (s, 1H), 5.50 (d, *J* = 6.4 Hz, 1H), 5.28 (d, *J* = 1.3 Hz, 1H), 5.22 (d, *J* = 1.3 Hz, 1H), 4.43 – 4.36 (m, 1H), 4.18 (qq, *J* = 6.8, 3.6 Hz, 2H), 3.11 – 3.04 (m, 4H), 2.92 – 2.84 (m, 1H), 2.88 – 2.72 (m, 1H), 1.73 – 1.65 (m, 4H), 1.52 – 1.45 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 4H); **^{13}C{^{1}H} NMR** (**7bb**, 101 MHz, $CDCl_3$) δ = 174.0, 142.5, 138.3, 120.9, 71.2, 61.1, 51.9, 38.4, 25.0, 24.1, 14.5. **HRMS** (**7bb**, FTMS+c ESI) calcd for $C_{13}H_{23}N_2O_3H^+$ ([M+H$^+$]) = 255.1709, Found 255.1709.

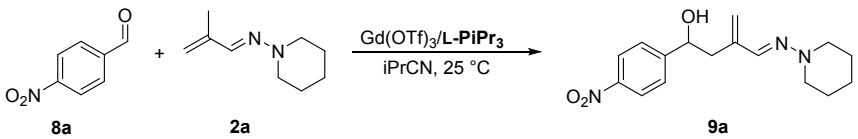


7c **2a** **7cc**

entry	metal salt	yield (%)	ee (%)
1	$Zn(NTf_2)_2$	No reaction	-
2	$Ni(OTf)_2$	No reaction	-
3	$Mg(OTf)_2$	No reaction	-
4	$Gd((OTf)_3$	No reaction	-
5	$Yb(OTf)_3$	No reaction	-
6	$Y(OTf)_3$	No reaction	-

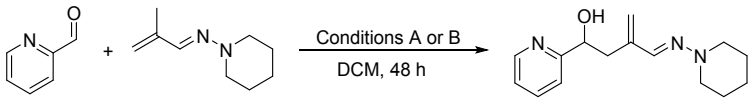
[a] Unless otherwise noted, all reactions were carried out with **L_2-PrPr$_3$**/metal salt (1:1, 5 mol%), **7c** (0.1 mmol), **2a** (0.13 mmol) in DCM (0.5 mL) at 30 °C for 15 h.

5.6 General procedure for the catalytic aldehydes-carbonyl-ene reaction



8a **2a** **9a**

To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **8a** (0.1 mmol, 15.1 mg), $Gd(OTf)_3$ (6.1 mg, 0.01 mmol) and **L-PiPr$_3$** (7.3 mg, 0.01 mmol), $NaBArF_4$ (8.9 mg), iPrCN (0.3 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at 25 °C. Then the reaction mixture was stirred at the same temperature for 72 h. Finally directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/5, v/v) to afford the desired product **9a** (oil, 80% yield, 84% ee).



8h **2a** **9h**

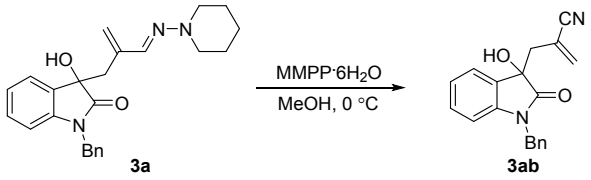
Conditions A: $Mg(OTf)_2$/**L-RaPr$_2$** 35 °C
Conditions B: $Gd(OTf)_3$/**L-RaPr$_2$** 25 °C

Condition A: To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **8h** (0.1 mmol), $Mg(OTf)_2$ (3.2 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol), DCM (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.). Then the reaction mixture was stirred at the same temperature for 72 h. Finally directly

purified by flash column chromatography (ethyl acetate/petroleum ether = 1/2, v/v) to afford the desired product (oil, 38% yield, 99% ee).

Condition B: To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **8h** (0.1 mmol), $Gd(OTf)_3$ (6.1 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol), DCM (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at 25 °C. Then the reaction mixture was stirred at the same temperature for 48 h. Finally, directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/2, v/v) to afford the desired product (oil, 38% yield, –95% ee).

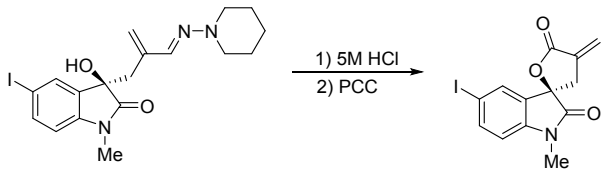
6.1 General procedure for the synthesis of compound 3ab



3a **3ab**

To a stirred solution of **3a** (0.1 mmol) in MeOH (1.5 mL) was added magnesium monoperoxyphthalate hydrate (0.15 mmol, 75 mg) at 0 °C and stirred for another 20 min at the same temperature. Then purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v) to give the product **3ab** (91% yield, 98% ee).

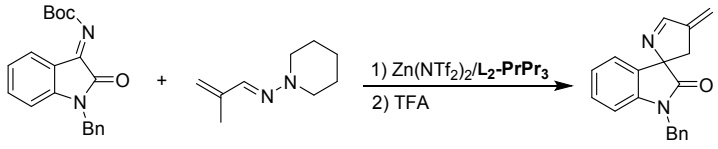
6.2 General procedure for the synthesis of compound 3oa



3o **3oa**

The reaction was carried out with **3o** (0.13 mmol) in 5M HCl (0.3 mL) and Et_2O/DCM (v/v, 6.7:1, 2.3 mL) at rt for 20 min. Next the solution was extracted with Et_2O/DCM (v/v, 6.7:1, 7.7 mL) five times, filtered through a short silicone column, washed with petroleum ether/EtOAc (v/v, 1:1) and concentrated under reduced pressure. Then it was performed with PCC (112 mg.) and 3 Å MS (60 mg) in DCM (2 mL) at rt for 3 h. Finally, the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1:4 v/v) to afford the product **3oa** (two steps: 40% yield, 99% ee).

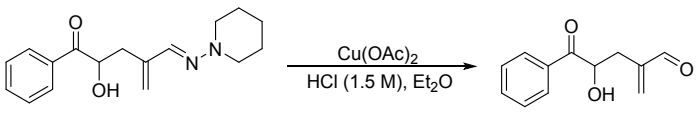
6.3 General procedure for the synthesis of compound 6ab



5a **2a** **6ab**

1): To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **4a** (0.1 mmol), $Zn(NTf_2)_2$ (3.1 mg, 0.005 mmol) and **L$_2$-PrPr$_3$** (3.5 mg, 0.005 mmol), 4 Å MS (20 mg), DCM (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N,N*-dialkylhydrazone **2a** (1.3 equiv.) at –40 °C. Then the reaction mixture was stirred at the same temperature for 15 h. Directly purified by flash column chromatography (ethyl acetate /petroleum ether = 1/4, v/v) to afford the crude product; **2)**: To a stirred solution of the crude product in DCM (1.0 mL) was added TFA (1 mL) at ice-bath and stirred for 2 h at the room temperature. After reaction finished, to the stirred mixture was added K_2CO_3 which had been adjusted to pH ~8. Finally, purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v) to give the product **6ab** (two steps: 70% yield, 95% ee).

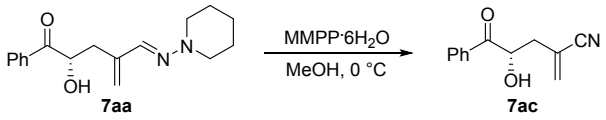
6.4 General procedure for the synthesis of compound 7ab



7aa **7ab**

The reaction were carried out with substrate **7aa** (0.2 mmol), $Cu(OAc)_2$ (3 equiv.) in 1.5M HCl (2 mL) and Et_2O (2 mL) at rt for 24 h. After reaction finished, to the stirred solution was added K_2CO_3 that had been adjusted to pH ~8. The mixture was extracted with DCM, washed with brine, dried over Na_2SO_4, concentrated, the residue was purified by flash chromatography to afford the product **7ab** (70% yield, 96% ee).

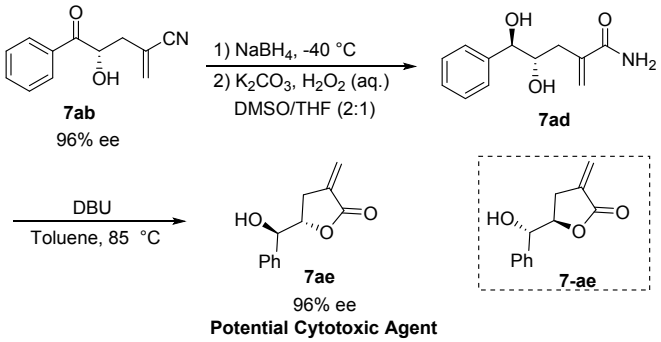
6.5 General procedure for the synthesis of compound 7ac



7aa **7ac**

To a stirred solution of **7aa** (0.1 mmol) in MeOH (1.5 mL) was added magnesium monoperoxyphthalate hydrate (0.15 mmol, 75 mg) at ice-bath and stirred for 20 min at the same temperature. Finally, purified by column chromatography on silica gel (ethyl acetate /petroleum ether = 1/3, v/v) to give the product **7ac** (97% yield, 95% ee).

6.6 General procedure for the synthesis of compound 7ae[3]



7ab
96% ee

7ad

7ae
96% ee
Potential Cytotoxic Agent

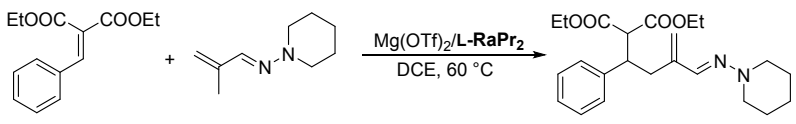
7-ae

Note: The absolute structure of the product **7ae** was thought to be (**1*R***, **5*S***) from the X-ray crystal diffraction analysis of **7aa** and the similar **^{1}H NMR**, **^{13}C{^{1}H} NMR** of the compound **7-ae**.[4]

The reaction were carried out with substrate **7ac** (1.3 mmol), $NaBH_4$ (58.5 mg) in DCM/MeOH (10 mL, 10:1) at –40 °C for 2 h. After reaction finished, to the stirred solution was added saturated ammonium chloride solution (1 mL). The mixture was extracted with DCM, washed with brine, dried over Na_2SO_4, concentrated, the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1/2, v/v) to afford the crude product. Next, the crude product (1.0 mmol) was dissolved in DMSO/THF mixture (3 mL, 2:1) containing K_2CO_3 (43 mg). A solution of 30% aqueous H_2O_2 (1.23 mL) was added dropwise at 0 °C. The reaction mixture was stirred at 30 °C for 1.5 h, then quenched by addition of brine and extracted with EtOAc, dried over Na_2SO_4 and concentrated to give an oil. Finally, the residue was purified by flash chromatography (ethyl acetate) to afford the product **7ad** (two steps: 60% yield).

Compound **7ad** (0.2 mmol) and DBU (60 mg) was dissolved in toluene (3 ml), this reaction mixture was stirred at 85 °C for 8 h, concentrated, the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1/3, v/v) to afford the product **7ae** (60% yield, 96% ee).

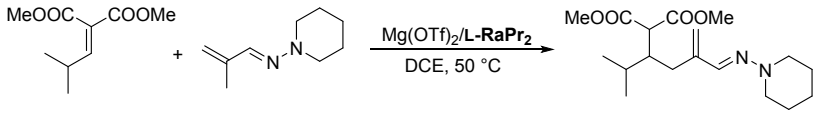
7. General procedure for ene type reaction of C=C bond



10a **2a** **11ab**

To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **10a** (0.1 mmol, 24.8 mg), $Mg(OTf)_2$ (3.2 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol), DCE (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N*,*N*-dialkylhydrazone **2a** (2 equiv.) at 60 °C. Then the reaction mixture was stirred at the same temperature for 24 h. Finally, directly

purified by flash column chromatography (ethyl acetate/petroleum ether = 1/9, v/v) to afford the desired product **11ab** (oil, 50% yield, < 10% ee).



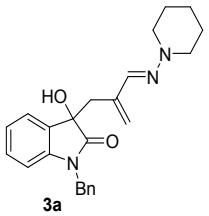
10b **2a** **11bb**

To an oven-dried reaction tube under nitrogen atmosphere was added the substrate **10b** (0.1 mmol, 24.8 mg), $Mg(OTf)_2$ (3.2 mg, 0.01 mmol) and **L-RaPr$_2$** (7.0 mg, 0.01 mmol), DCE (0.5 mL). The solution was stirred at 35 °C for 35 min followed by the addition of aldehyde *N*,*N*-Dialkylhydrazone **2a** (2 equiv.) at 50 °C. Then the reaction mixture was stirred at the same temperature for 12 h. Finally, directly purified by flash column chromatography (ethyl acetate/petroleum ether = 1/9, v/v) to afford the desired product **11bb** (oil, 36% yield, 45% ee).

8 Characterization of the products

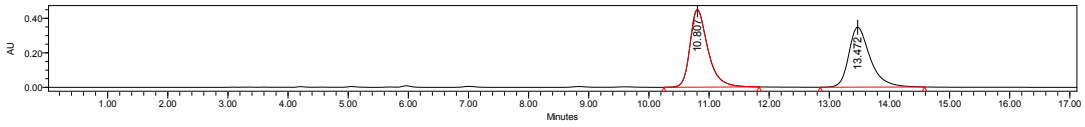
8.1 Characterization of the products of Isatin carbonyl-ene reaction

1-Benzyl-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

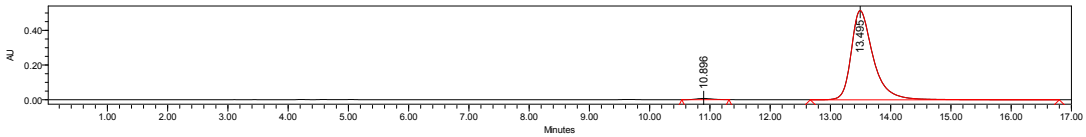


3a

Oil; 90% yield, 98% ee; $[\alpha]^{22}_{\lambda}$ = –61.19 (*c* = 0.67 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 13.50 min, t_R (minor) = 10.90 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.53 (s, 1H), 7.44 (s, 1H), 7.34 – 7.18 (m, 6H), 7.16 – 7.09 (m, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.33 (s, 1H), 5.03 (s, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.79 (d, *J* = 15.6 Hz, 1H), 3.27 – 3.08 (m, 5 (***4+1***) H, -NNC***H***$_2$, C***H***$_2$C=CH_2), 2.61 (d, *J* = 14.0 Hz, 1H), 1.75 – 1.60 (m, 4H), 1.58 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.3, 141.9, 141.1, 138.8, 136.1, 131.5, 128.9, 128.8, 127.6, 127.4, 124.8, 123.1, 122.4, 109.1, 75.8, 51.9, 43.8, 42.5, 24.9, 23.9.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{27}N_3O_2H^+$ ([M+H$^+$]) = 390.2182, Found 390.2184.

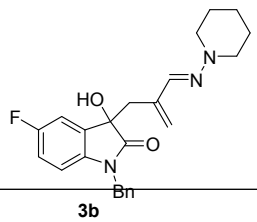


	Retention Time	Area	% Area
1	10.807	9281465	51.91
2	13.472	8597731	48.09



	Retention Time	Area	% Area
1	10.896	136962	1.04
2	13.495	13044113	98.96

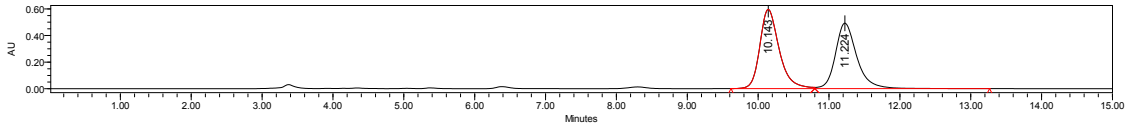
1-Benzyl-5-fluoro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one



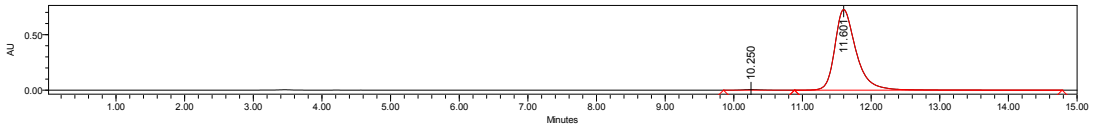
3b

Oil; 98% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = –7.34 (*c* = 0.64 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.60 min, t_R (minor) = 10.25 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.66 (s, 1H), 7.43 (s, 1H), 7.35 – 7.21 (m, 5H), 7.00 – 6.90 (m, 1H), 6.90 – 6.70 (m, 1H), 6.60 – 6.50 (m, 1H), 5.35 (s, 1H), 5.04 (s, 1H), 4.99 – 4.72 (m, 2H), 3.25 (d, *J* = 14.4 Hz, 1H), 3.21 – 3.06 (m, 4H), 2.55 (d, *J* = 14.4 Hz, 1H), 1.80 – 1.70 (m, 4H), 1.58 – 1.50(m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.1, 159.0 (J_{CF} = 242.4 Hz), 140.7, 138.5, 137.7 (J_{CF} = 2.0 Hz), 135.7, 133.0 (J_{CF} = 7.1 Hz), 128.9, 127.7, 127.3, 123.4, 115.1 (J_{CF} = 24.2 Hz), 113.0 (J_{CF} = 24.2 Hz), 109.7 (J_{CF} = 8.1 Hz), 75.91 (J_{CF} = 1.0 Hz), 51.9, 43.9, 42.3, 24.9, 23.9; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −120.8.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}FN_3O_2H^+$ ([M+H$^+$]) = 408.2087, Found 408.2085.

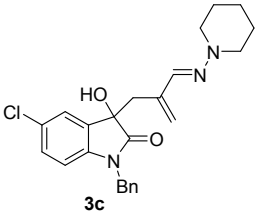


	Retention Time	Area	% Area
1	10.143	11276352	52.24
2	11.224	10310199	47.76



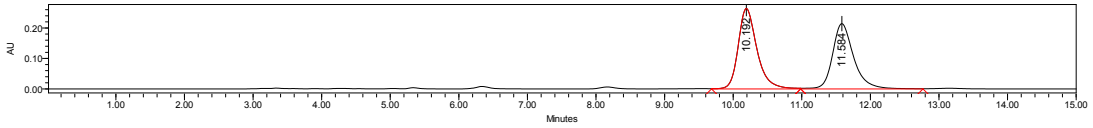
	Retention Time	Area	% Area
1	10.250	107395	0.68
2	11.601	15667788	99.32

1-Benzyl-5-chloro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

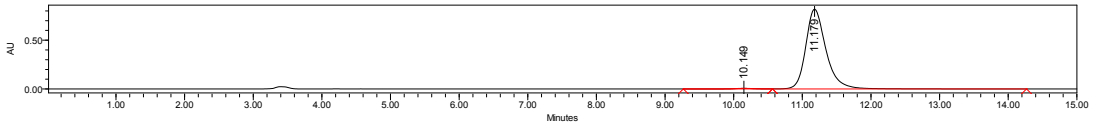


3c

White solid, melting point: 56–59 °C; 98% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = +40.56 (*c* = 0.68 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.18 min, t_R (minor) = 10.15 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (s, 1H), 7.43 (s, 1H), 7.35 – 7.22 (m, 5H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.15 – 7.00 (m, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 5.36 (s, 1H), 5.05 (s, 1H), 4.99 – 4.71 (m, 2H), 3.26 – 3.12 (m, 5 (***4+1***) H, -NNC***H***$_2$, C***H***$_2$C=CH$_2$), 2.57 (d, *J* = 14.0 Hz, 1H), 1.78 – 1.68 (m, 5H), 1.58 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 177.9, 140.6, 140.4, 138.5, 135.6, 133.1, 128.9, 128.8, 127.9, 127.8, 127.3, 125.3, 123.4, 110.2, 75.8, 51.9, 43.9, 42.3, 24.9, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}ClN_3O_2H^+$ ([M+H$^+$]) = 424.1792, 426.1762, Found 424.1789, 426.1758.

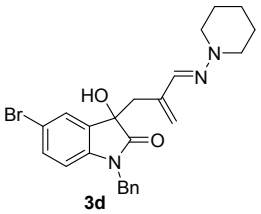


	Retention Time	Area	% Area
1	10.192	5015151	52.19
2	11.584	4593848	47.81



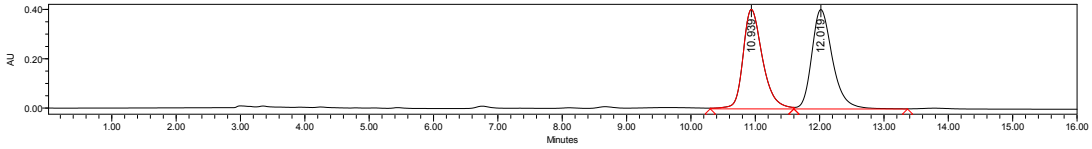
	Retention Time	Area	% Area
1	10.149	128844	0.76
2	11.179	16790963	99.24

1-Benzyl-5-bromo-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

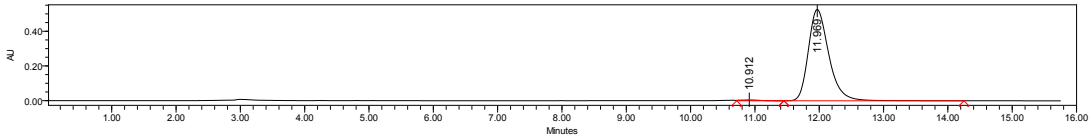


3d

White solid, melting point: 57–59 °C; 98% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = +50.00 (*c* = 0.79 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.97 min, t_R (minor) = 10.91 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63 (s, 1H), 7.42 (s, 1H), 7.35 – 7.17 (m, 7H), 6.54 (m, 1H), 5.36 (s, 1H), 5.05 (s, 1H), 4.98 – 4.72 (m, 2H), 3.27 – 3.08 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.58 (d, *J* = 14.4 Hz, 1H), 1.78 – 1.70 (m, 4H), 1.58 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 177.7, 140.9, 140.6, 138.4, 135.5, 133.4, 131.7, 128.9, 128.0, 127.8, 127.3, 123.3, 115.2, 110.7, 75.7, 51.9, 43.8, 42.3, 24.9, 23.9.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}BrN_3O_2H^+$ ([M+H$^+$]) = 468.1281, 470.1261, Found 468.1286, 470.1265.

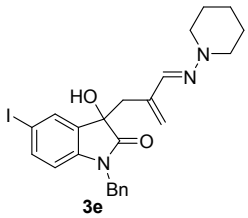


	Retention Time	Area	% Area
1	10.939	8502647	48.45
2	12.019	9045153	51.55



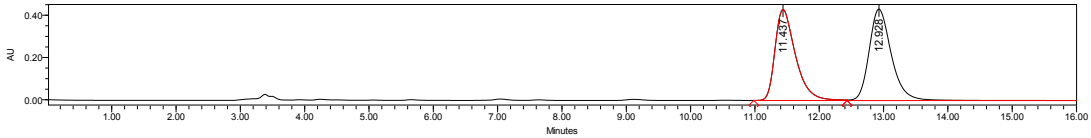
	Retention Time	Area	% Area
1	10.912	81887	0.70
2	11.969	11635838	99.30

1-Benzyl-3-hydroxy-5-iodo-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

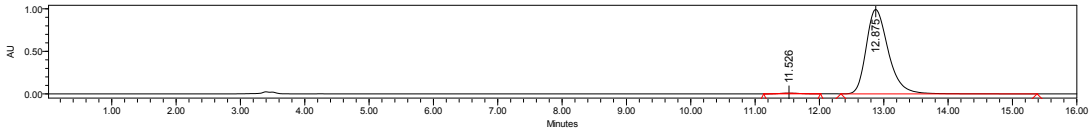


3e

White solid, melting point: 58–60 °C; 98% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = +55.85 (*c* = 0.80 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 12.88 min, t_R (minor) = 11.53 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.59 (s, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.33 – 7.21 (m, 5H), 6.45 (d, *J* = 8.1 Hz, 1H), 5.36 (s, 1H), 5.05 (s, 1H), 4.98 – 4.67 (m, 2H), 3.27 – 3.09 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.58 (d, *J* = 14.2 Hz, 1H), 1.77 – 1.67 (m, 4H), 1.60 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 177.5, 141.6, 140.6, 138.4, 137.7, 135.5, 133.8, 133.6, 128.9, 127.8, 127.3, 123.3, 111.3, 85.2, 75.5, 51.9, 43.8, 42.3, 24.9, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}IN_3O_2H^+$ ([M+H$^+$]) = 516.1142, Found 516.1143.

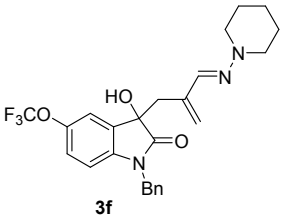


	Retention Time	Area	% Area
1	11.437	9483425	47.78
2	12.928	10366072	52.22



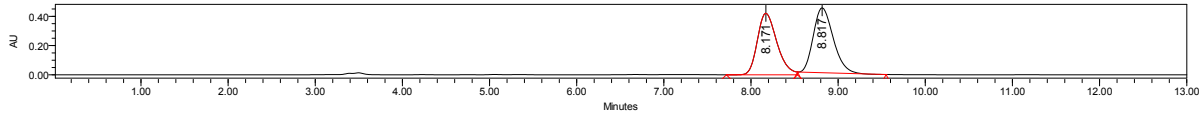
	Retention Time	Area	% Area
1	11.526	173920	0.73
2	12.875	23762924	99.27

1-Benzyl-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)-5-(trifluoromethoxy)indolin-2-one

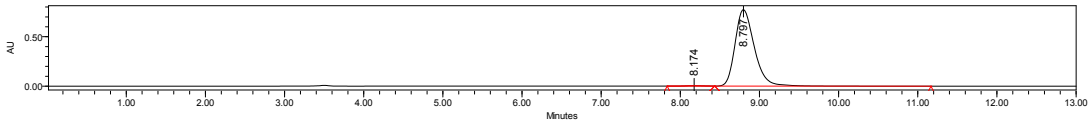


3f

Oil; 99% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = –37.38 (*c* = 0.65 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.80 min, t_R (minor) = 8.17 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 (s, 1H), 7.43 (s, 1H), 7.35 – 7.24 (m, 5H), 7.09 (d, *J* = 2.4 Hz, 1H), 7.00 (m, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 5.36 (s, 1H), 5.01 (s, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.80 (d, *J* = 15.6 Hz, 1H), 3.28 (d, *J* = 14.4 Hz, 1H), 3.23 – 3.10 (m, 4H), 2.52 (d, *J* = 14.3 Hz, 1H), 1.80 – 1.70 (m, 4H), 1.59 – 1.51 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.1, 144.4 (J_{CF} = 3.0 Hz), 140.4, 138.4, 135.4, 132.7, 128.9, 127.8, 127.3, 124.4 (J_{CF} = 257.5 Hz), 123.3, 121.9, 121.8 (J_{CF} = 257.5 Hz), 119.3 (J_{CF} = 257.5 Hz), 116.7 (J_{CF} =257.5 Hz), 118.9, 109.5, 75.6, 51.8, 43.9, 42.2, 24.8, 23.9; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ = –58.3.
HRMS (FTMS+c ESI) calcd for $C_{25}H_{26}F_3N_3O_3H^+$ ([M+H$^+$]) = 474.2005, Found 474.1996.

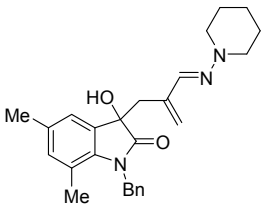


	Retention Time	Area	% Area
1	8.171	6548544	48.07
2	8.817	7074656	51.93



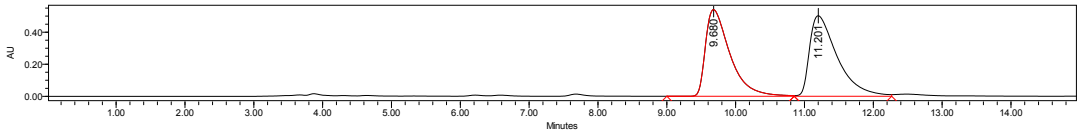
	Retention Time	Area	% Area
1	8.174	57320	0.44
2	8.797	13049754	99.56

1-Benzyl-3-hydroxy-5,7-dimethyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

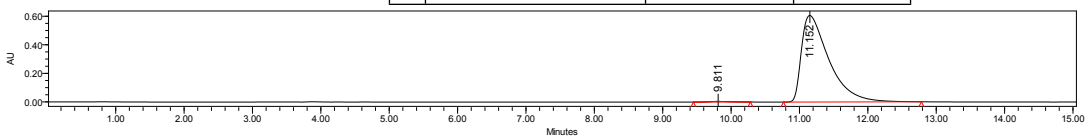


3g

White solid; melting point: 62–67 °C; 86% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = +21.84 (*c* = 0.71 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IB, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.15 min, t_R (minor) = 9.81 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.44 (d, *J* = 6.4 Hz, 2H), 7.32 – 7.11 (m, 5H), 6.96 (s, 1H), 6.72 (s, 1H), 5.33 (s, 1H), 5.19 – 5.00 (m, 3H), 3.23 – 3.05 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.72 (d, *J* = 14.0 Hz, 1H), 2.23 (s, 3H), 2.19 (s, 3H), 1.76 – 1.70 (m, 4H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 179.2, 141.2, 138.9, 137.9, 137.4, 133.3, 132.6, 132.0, 128.8, 127.1, 125.9, 123.3, 122.9, 119.5, 75.2, 51.9, 44.9, 43.0, 25.0, 24.0, 20.9, 18.8.
HRMS (FTMS+c ESI) calcd for $C_{26}H_{31}N_3O_2H^+$ ([M+H$^+$]) = 418.2495, Found 418.2497.



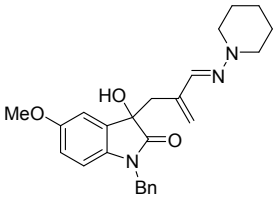
	Retention Time	Area	% Area
1	9.680	13348876	48.68
2	11.201	14071028	51.32



	Retention Time	Area	% Area

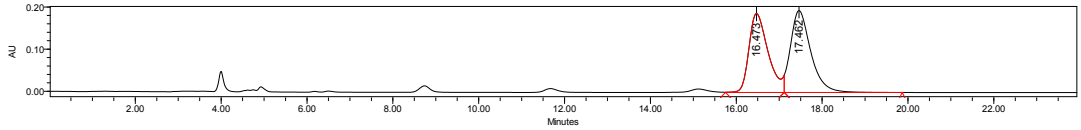
1	9.811	94699	0.56
2	11.152	16916408	99.44

1-Benzyl-3-hydroxy-5-methoxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

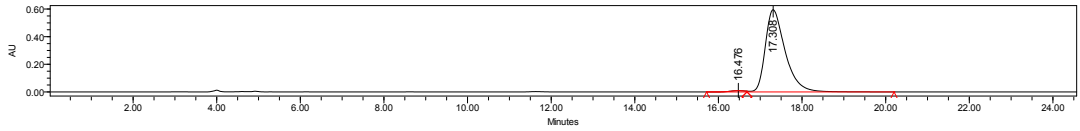


3h

Oil; 88% yield, 98% ee; $[\alpha]^{20}_{\lambda}$ = +8.24 (*c* = 0.74 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 17.31 min, t_R (minor) = 16.48 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 (s, 1H), 7.43 (s, 1H), 7.33 – 7.21 (m, 5H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.68 – 6.50 (m, 2H), 5.35 (s, 1H), 5.06 (s, 1H), 4.99 – 4.70 (m, 2H), 3.72 (s, 3H), 3.25 – 3.08 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.60 (d, *J* = 14.0 Hz, 1H), 1.80 – 1.70 (m, 4H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.1, 155.7, 141.0, 138.7, 136.1, 135.3, 132.7, 128.8, 127.6, 127.4, 123.1, 113.3, 112.2, 109.5, 76.1, 55.9, 51.9, 43.84, 42.5, 24.9, 23.9.
HRMS (FTMS+c ESI) calcd for $C_{25}H_{29}N_3O_3H^+$ ([M+H$^+$]) = 420.2282, Found 420.2279.

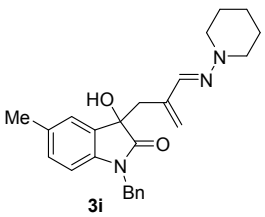


	Retention Time	Area	% Area
1	16.473	5807422	47.78
2	17.462	6347200	52.22



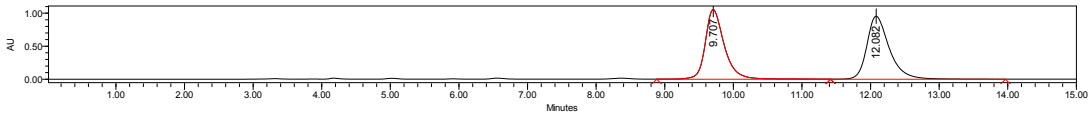
	Retention Time	Area	% Area
1	16.476	229370	1.16
2	17.308	19588693	98.84

1-Benzyl-3-hydroxy-5-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

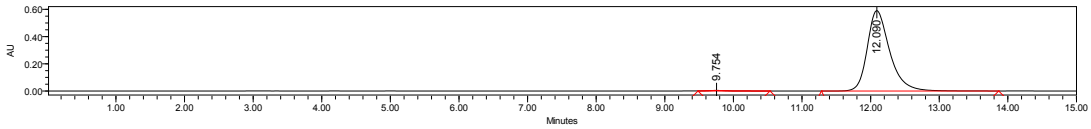


3i

Oil; 92% yield, 98% ee; $[\alpha]^{20}_{\lambda}$ = +5.46 (*c* = 0.68 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 12.09 min, t_R (minor) = 9.75 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (s, 1H),7.44 (s, 1H) 7.31 – 7.20 (m, 5H), 7.06 (d, *J* = 1.6 Hz, 1H), 6.93 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 5.33 (s, 1H), 5.05 (s, 1H), 5.00 – 4.71 (m, 2H), 3.22 – 3.09 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.65 (d, *J* = 14.0 Hz, 1H), 2.25 (s, 3H), 1.77 – 1.70 (m, 4H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.2, 141.1, 139.5, 138.8, 136.2, 131.9, 131.5, 129.1, 128.8, 127.5, 127.4, 125.5, 123.0, 108.9, 75.9, 51.9, 43.8, 42.5, 25.0, 24.0, 21.2.
HRMS (FTMS+c ESI) calcd for $C_{25}H_{26}F_3N_3O_3H^+$ ([M+H$^+$]) = 404.2338, Found 404.2337.

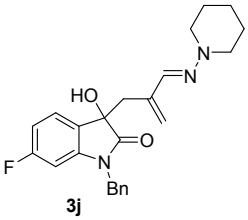


	Retention Time	Area	% Area
1	9.707	20388772	48.34
2	12.082	21790618	51.66



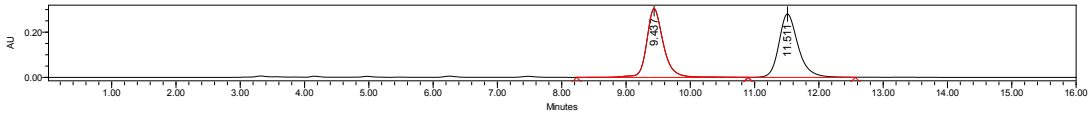
	Retention Time	Area	% Area
1	9.754	98585	0.73
2	12.090	13463245	99.27

1-Benzyl-6-fluoro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

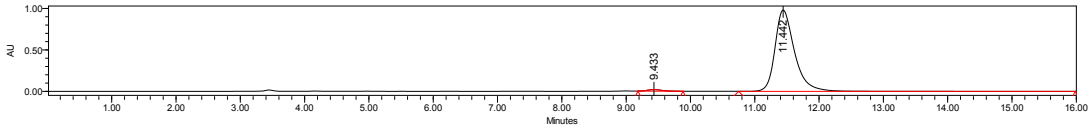


3j

Oil; 84% yield, 97% ee; $[\alpha]^{20}_{\lambda}$ = −54.88 (*c* = 0.68 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.44 min, t_R (minor) = 9.43 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (s, 1H), 7.42 (s, 1H), 7.35 – 7.24 (m, 5H), 7.15 (dd, *J* = 8.2, 5.4 Hz, 1H), 6.65 – 6.59 (m, 1H), 6.41 (dd, *J* = 9.0, 2.3 Hz, 1H), 5.33 (s, 1H), 5.03 (s, 1H), 4.98 – 4.70 (m, 2H), 3.25 – 3.10 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.55 (d, *J* = 14.0 Hz, 1H), 1.75 – 1.70 (m, 4H), 1.58 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.6, 163.5 (J_{CF} = 246.4 Hz), 143.5 (J_{CF} = 12.1 Hz), 140.9, 138.6, 135.5, 129.0, 127.9, 127.4, 126.8 (J_{CF} = 3.0 Hz), 126.0 (J_{CF} = 10.1 Hz), 123.2, 108.4 (J_{CF} = 22.2 Hz), 98.12 (J_{CF} = 27.3 Hz), 75.4, 51.9, 43.9, 42.4, 24.9, 24.0; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −111.2.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}FN_3O_2H^+$ ([M+H$^+$]) = 408.2087, Found 408.2083.

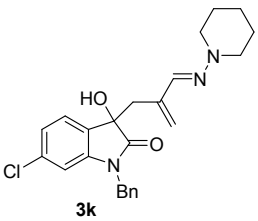


	Retention Time	Area	% Area
1	9.437	5492393	48.44
2	11.511	5845921	51.56



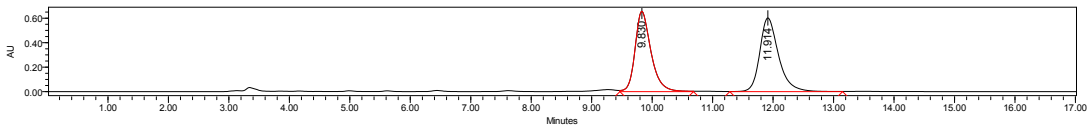
	Retention Time	Area	% Area
1	9.433	290526	1.38
2	11.442	20759224	98.62

1-Benzyl-6-chloro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

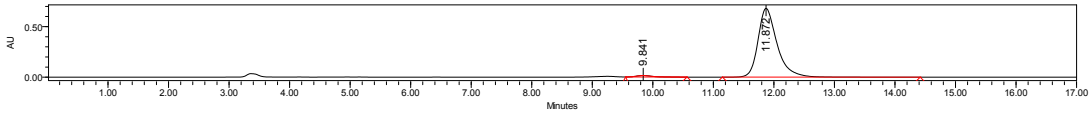


3k

White solid, melting point: 58–62 °C; 93% yield, 96% ee; $[\alpha]^{20}_{\lambda}$ = +10.42 (*c* = 0.67 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.87 min, t_R (minor) = 9.84 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (s, 1H), 7.42 (s, 1H), 7.36 – 7.24 (m, 5H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.0 – 6.9 (m, 1H), 6.67 (d, *J* = 1.6 Hz, 1H), 5.33 (s, 1H), 5.02 (s, 1H), 4.99 – 4.69 (m, 2H), 3.27 – 3.10 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.54 (d, *J* = 14.0 Hz, 1H), 1.78 – 1.65 (m, 4H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.3, 143.2, 140.8, 138.5, 135.5, 134.6, 129.8, 129.0, 127.9, 127.3, 125.8, 123.3, 122.3, 109.7, 75.5, 51.9, 43.9, 42.4, 24.9, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}ClN_3O_2H^+$ ([M+H$^+$]) = 424.1792, 426.1762, Found 424.1786, 426.1757.

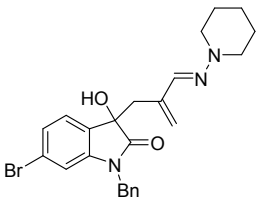


	Retention Time	Area	% Area
1	9.830	11992477	47.98
2	11.914	13001471	52.02



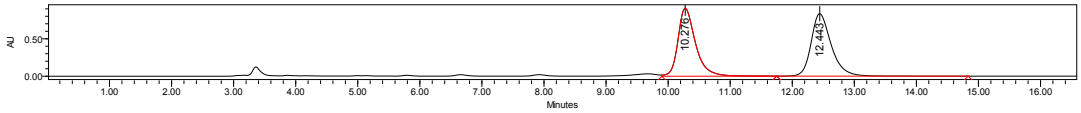
	Retention Time	Area	% Area
1	9.841	265138	1.76
2	11.872	14775367	98.24

1-Benzyl-6-bromo-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

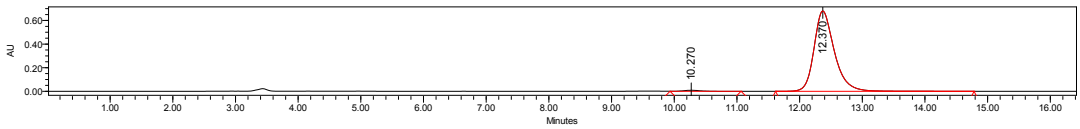


3l

Oil; 93% yield, 98% ee; $[\alpha]^{20}_{\lambda}$ = +28.68 (*c* = 0.77 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 12.37 min, t_R (minor) = 10.27 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 (s, 1H), 7.41 (s, 1H), 7.35 – 7.23 (m, 5H), 7.11 – 7.03 (m, 2H), 6.82 (d, *J* = 1.6 Hz, 1H), 5.33 (s, 1H), 5.01 (s, 1H), 4.98 – 4.67 (m, 2H), 3.25 – 3.08 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.54 (d, *J* = 14.4 Hz, 1H), 1.77 – 1.60 (m, 4H), 1.60 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.1, 143.3, 140.7, 138.5, 135.5, 130.3, 128.9, 127.8, 127.3, 126.1, 125.2, 123.2, 122.5, 112.4, 75.5, 51.9, 43.8, 42.3, 24.9, 24.0
HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}BrN_3O_2H^+$ ([M+H$^+$]) = 468.1287, 470.1266, Found 468.1292, 470.1272.

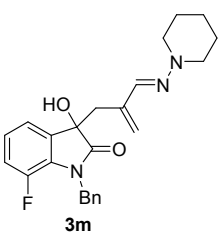


	Retention Time	Area	% Area
1	10.276	17790972	48.48
2	12.443	18905499	51.52



	Retention Time	Area	% Area
1	10.270	175279	1.13
2	12.370	15325797	98.87

1-Benzyl-7-fluoro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

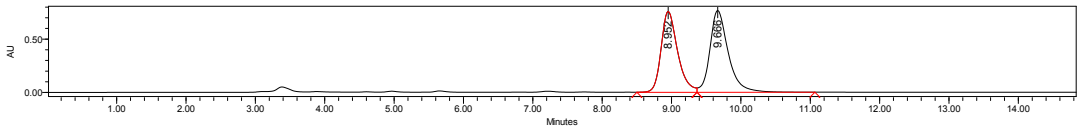


3m

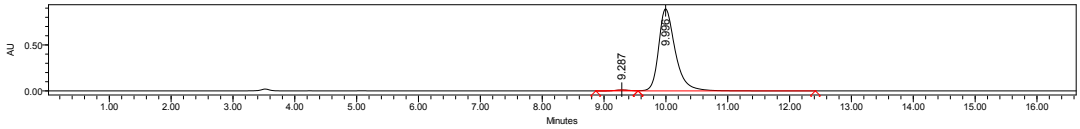
Oil; 98% yield, 98% ee; $[\alpha]^{20}_{\lambda}$ = –38.70 (*c* = 0.71 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 10.00 min, t_R (minor) = 9.29 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 (s, 1H), 7.42 (s, 1H), 7.37 – 7.20 (m, 5H), 7.03 – 6.97 (m, 1H), 6.95 – 6.85 (m, 2H), 5.32 (s, 1H), 5.10 – 4.92 (m, 3H), 3.18 – 3.10 (m, 5 (***4+1***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2), 2.59 (d, *J* = 14.0 Hz, 1H), 1.90 – 1.60 (m, 4H), 1.60 – 1.45 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.0, 147.5 (J_{CF} =

242.4 Hz), 140.7, 138.6, 137.2, 134.5 (J_{CF} = 2.6 Hz), 128.6, 128.3 (J_{CF} = 8.6 Hz), 127.6 (J_{CF} = 1.6 Hz), 127.5, 123.3, 123.1 (J_{CF} = 6.2 Hz), 120.6 (J_{CF} = 3.2 Hz), 117.2 (J_{CF} = 19.5 Hz), 75.9 (J_{CF} = 2.5 Hz), 51.9, 45.3 (J_{CF} = 4.7 Hz), 42.6, 24.9, 24.0; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −133.9.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{26}FN_3O_2H^+$ ([M+H$^+$]) = 408.2087, Found 408.2079.

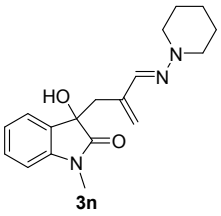


	Retention Time	Area	% Area
1	8.952	12514333	47.01
2	9.666	14108547	52.99



	Retention Time	Area	% Area
1	9.287	170211	1.01
2	9.996	16665114	98.99

3-Hydroxy-1-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one



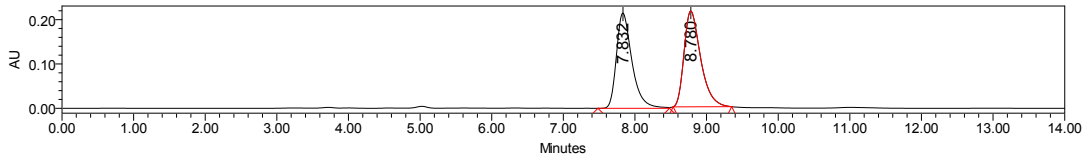
3n

White solid, melting point: 93–95 °C; 80% yield, 98% ee; $[\alpha]^{20}_{\lambda}$ = −173.75 (*c* = 0.48 in CH_2Cl_2).

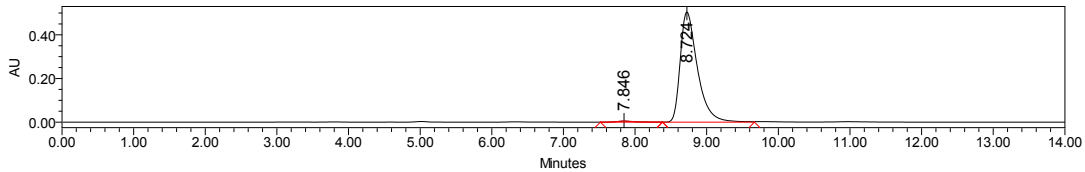
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.72 min, t_R (minor) = 7.85 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (s, 1H), 7.43 (s, 1H), 7.29 – 7.23 (m, 1H), 7.21 – 7.18 (m, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.32 (s, 1H), 5.01 (s, 1H), 3.24 – 3.11 (m, 8 (***4+1+3***) H, -NNC***H***$_2$, -C***H***$_2$C=CH$_2$, -NC***H***$_3$), 2.51 (d, *J* = 14.4 Hz, 1H), 1.76 – 1.69 (m, 4H), 1.58 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 178.2, 142.9, 141.1, 138.8, 131.3, 129.0, 124.8, 123.5, 123.1, 122.3, 108.1, 75.7, 51.9, 42.1, 28.8, 26.3, 24.9, 24.0.

HRMS (FTMS+c ESI) calcd for $C_{18}H_{23}N_3O_2H^+$ ([M+H$^+$]) = 314.1869, Found 314.1862.

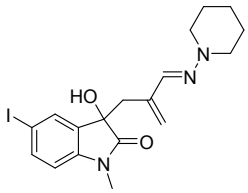


	Retention Time	Area	% Area
1	7.832	3241646	48.27
2	8.780	3474665	51.73



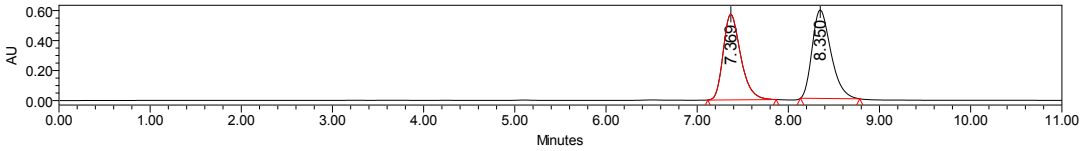
	Retention Time	Area	% Area
1	7.846	81700	0.96
2	8.724	8419161	99.04

3-Hydroxy-5-iodo-1-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

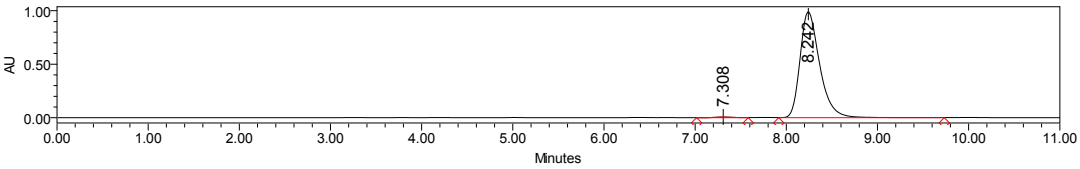


3o

White solid, melting point: 123–125 °C; 99% yield, 99% ee; $[\alpha]^{20}_{\lambda}$ = –53.35 (*c* = 0.75 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.24 min, t_R (minor) = 7.31 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 – 7.55 (m, 1H), 7.52 (s, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.41 (s, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 5.35 (s, 1H), 5.02 (s, 1H), 3.20 – 3.10 (m, 8 (***4+1+3***) H, -NNC***H***$_2$, -C***H***$_2$C=CH_2, -NC***H***$_3$), 2.49 (d, *J* = 14.4 Hz, 1H), 1.80 – 1.70 (m, 4H), 1.56 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 177.5, 142.6, 140.6, 138.5, 137.8, 133.6, 123.2, 110.2, 85.0, 75.4, 51.9, 41.9, 26.3, 24.9, 23.9.
HRMS (FTMS+c ESI) calcd for $C_{18}H_{22}IN_3O_2H^+$ ([M+H$^+$]) = 440.0835, Found 440.0837.

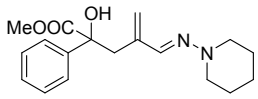


	Retention Time	Area	% Area
1	7.369	7615796	47.49
2	8.350	8421881	52.51



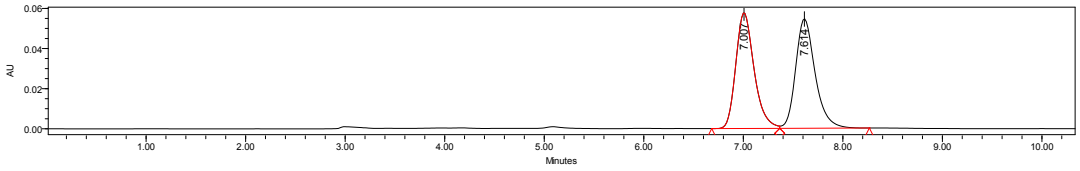
	Retention Time	Area	% Area
1	7.308	90038	0.60
2	8.242	14866088	99.40

3-Hydroxy-5-iodo-1-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one

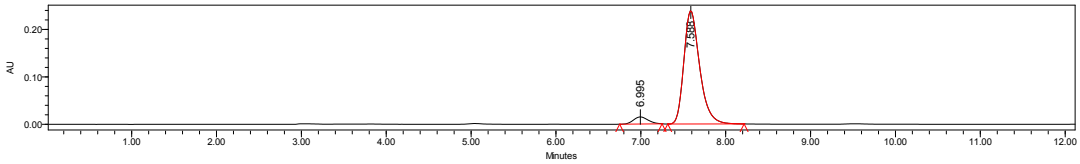


4

Colorless oil; 63% yield, 89% ee; $[\alpha]^{20}_{\lambda}$ = +233.64 (*c* = 0.44 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.59 min, t_R (minor) = 7.00 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 – 7.55 (m, 2H), 7.36 – 7.26 (m, 2H), 7.27 – 7.19 (m, 2H), 7.16 (s, 1H), 5.20 (d, *J* = 1.2 Hz, 1H), 5.17 (d, *J* = 1.6 Hz, 1H), 3.69 (s, 3H), 3.33 – 3.16 (m, 2H), 3.12 – 3.03 (m, 4H), 1.80 – 1.60 (m, 4H), 1.60 – 1.40 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 174.5, 142.3, 141.0, 139.3, 128.0, 127.4, 125.8, 123.7, 79.5, 52.7, 52.0, 44.2, 25.0, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{18}H_{24}N_2O_3H^+$ ([M+H$^+$]) = 317.1865, Found 317.1859.



	Retention Time	Area	% Area
1	7.007	735624	49.84
2	7.614	740336	50.16

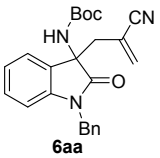


	Retention Time	Area	% Area

1	6.995	179197	5.49
2	7.588	3083751	94.51

8.2 Characterization of the products of imino-ene reaction

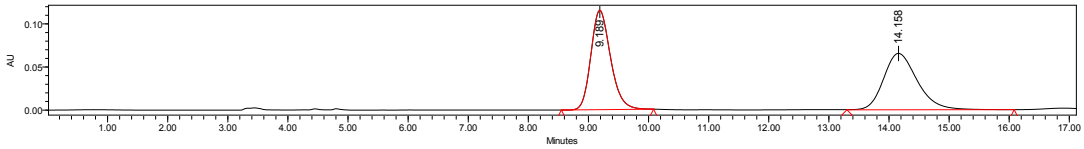
Tert-butyl (1-benzyl-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate



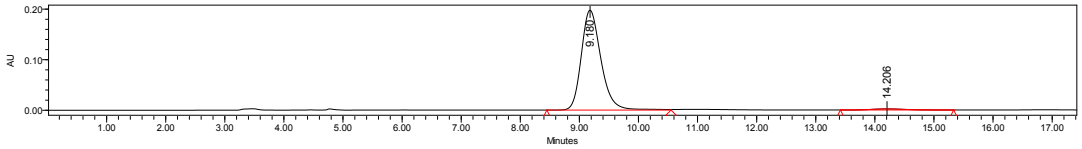
6aa

White solid, melting point: 47–49 °C; 98% yield (two steps), 96% ee; $[\alpha]^{20}_{\lambda}$ = –109.06 (*c* = 0.64 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 9.18 min, t_R (minor) = 14.20 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, *J* = 7.20 Hz, 1H), 7.40 – 7.23 (m, 6H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.72 (s, 1H), 5.65 (s, 1H), 5.38 (s, 1H), 4.90 (m, 2H), 2.87 (q, *J* = 13.2 Hz, 2H), 1.29 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.4, 153.9, 142.7, 137.1, 135.7, 129.8, 128.9, 128.2, 127.9, 127.8, 124.4, 123.3, 117.5, 115.5, 109.6, 80.9, 61.5, 44.4, 41.4, 28.2.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{25}N_3O_3Na^+$ ([M+Na$^+$]) = 426.1794, Found 426.1788.

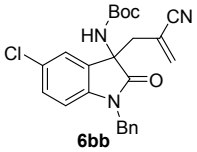


	Retention Time	Area	% Area
1	9.189	2617710	50.76
2	14.158	2538905	49.24



	Retention Time	Area	% Area
1	9.180	4553135	98.14
2	14.206	86212	1.86

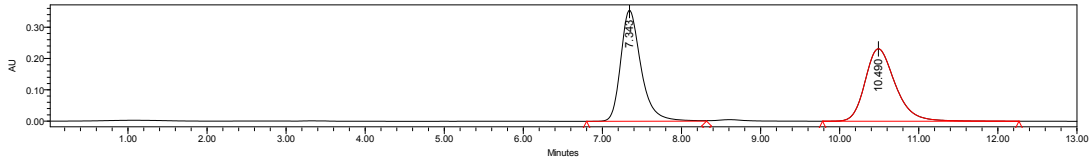
Tert-butyl (1-benzyl-5-chloro-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate



6bb

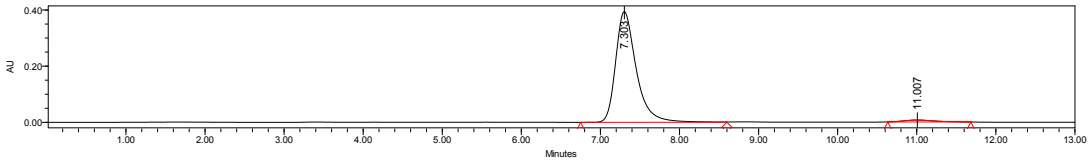
White solid, melting point: 136–138 °C; 98% yield (two steps), 95% ee; $[\alpha]^{22}_{\lambda}$ = –114.50 (*c* = 0.6 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.30 min, t_R (minor) = 11.00 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 2.0 Hz, 1H), 7.38 – 7.18 (m, 6H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.77 (s, 1H), 5.67 (s, 1H), 5.48 (s, 1H), 4.89 (s, 2H), 2.85 (m, 2H), 1.33 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.0, 153.8, 141.3, 137.4, 135.2, 129.9, 129.7, 128.9, 128.8, 128.0, 127.7, 124.7, 117.4, 115.2, 110.6, 81.3, 61.5, 44.5, 41.3, 28.2.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}ClN_3O_3Na^+$ ([M+Na$^+$]) = 460.1398, 4602.1369, Found 460.1387, 462.1359.



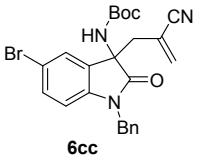
	Retention Time	Area	% Area
1	7.343	6323171	50.74

2	10.490	6138232	49.26



	Retention Time	Area	% Area
1	7.303	7132540	97.42
2	11.007	188789	2.58

Tert-butyl (1-benzyl-5-bromo-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate

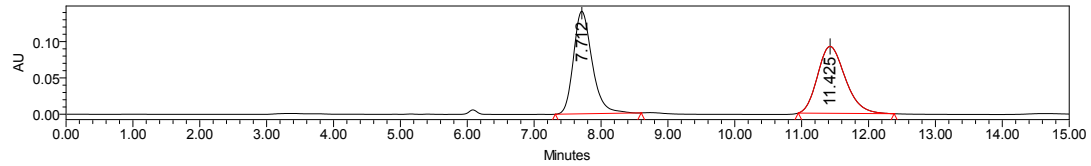


6cc

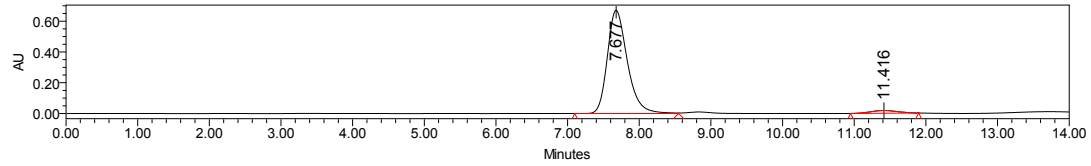
White solid, melting point: 152–155 °C; 94% yield (two steps), 93% ee; $[\alpha]^{20}_{\lambda}$ = –84.65 (*c* = 0.86 in CH_2Cl_2). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.68 min, t_R (minor) = 11.42 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 (s, 1H), 7.39 – 7.27 (m, 6H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.78 (s, 1H), 5.67 (s, 1H), 5.44 (s, 1H), 4.89 (s, 2H), 2.90 – 2.80 (m, 2H), 1.33 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 174.9, 153.8, 141.8, 137.4, 135.2, 132.6, 130.3, 128.9, 128.0, 127.7, 127.4, 117.4, 116.1, 115.2, 111.1, 81.3, 61.4, 44.5, 41.3, 28.3.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}BrN_3O_3Na^+$ ([M+Na$^+$]) = 504.0899, 506.0878, Found 504.0883, 506.0869.

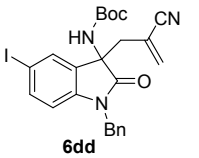


	Retention Time	Area	% Area
1	7.712	2727761	49.69
2	11.425	2761797	50.31



	Retention Time	Area	% Area
1	7.677	13027533	96.59
2	11.416	459335	3.41

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-5-iodo-2-oxoindolin-3-yl)carbamate

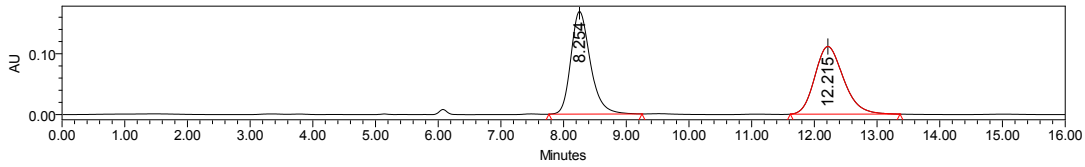


6dd

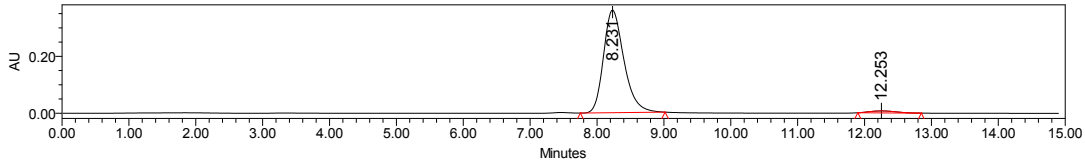
White solid, melting point: 136–139 °C; 96% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = –81.52 (*c* = 0.92 in CH_2Cl_2). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.23 min, t_R (minor) = 12.25 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 1.6 Hz, 1H), 7.56 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.38 – 7.23 (m, 5H), 6.55 (d, *J* = 8.4 Hz, 1H), 5.78 (s, 1H), 5.66 (s, 1H), 5.42 (s, 1H), 4.88 (s, 2H), 2.82 (q, *J* = 13.2 Hz, 2H), 1.33 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 174.7, 153.8,142.4, 138.5, 137.4, 135.2, 132.9, 130.6, 128.9, 127.9, 127.7, 117.4, 115.1, 111.6, 85.8, 81.3, 61.2, 44.4, 41.3, 28.3.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}IN_3O_3Na^+$ ([M+Na$^+$]) = 552.0760, Found 552.0754.

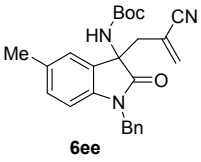


	Retention Time	Area	% Area
1	8.254	3639320	50.74
2	12.215	3533269	49.26



	Retention Time	Area	% Area
1	8.231	7637091	97.58
2	12.253	189650	2.42

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-5-methyl-2-oxoindolin-3-yl)carbamate

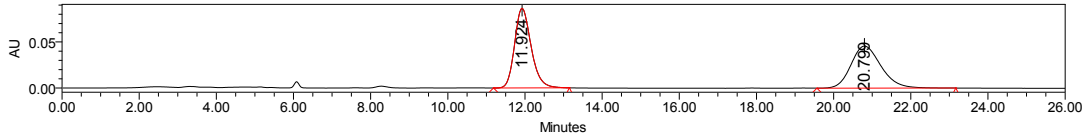


6ee

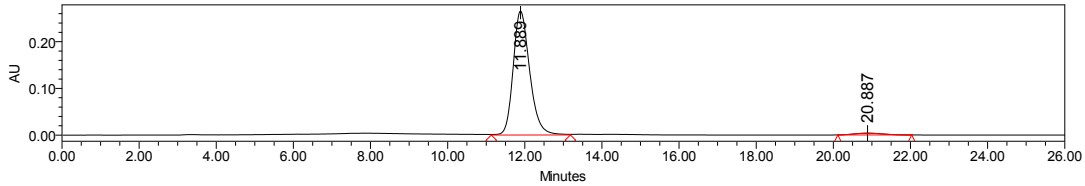
White solid, melting point: 53–55 °C; 96% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = –78.78 (*c* = 0.74 in CH_2Cl_2). HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.89 min, t_R (minor) = 20.89 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 – 7.22 (m, 6H), 7.05 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 5.64 (s, 1H), 5.47 (s, 1H), 4.88 (m, 2H), 2.90 – 2.78 (m, 2H), 2.32 (s, 3H), 1.30 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.3, 153.9, 140.2, 136.9, 135.8, 132.9, 130.0, 128.8, 128.1, 127.8, 125.1, 117.6, 115.6, 109.3, 80.9, 61.6 , 44.4, 41.3, 28.2, 21.3.

HRMS (FTMS+c ESI) calcd for $C_{25}H_{27}N_3O_3Na^+$ ([M+Na$^+$]) = 440.1950, Found 440.1943.

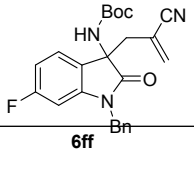


	Retention Time	Area	% Area
1	11.924	2568861	50.99
2	20.799	2469229	49.01



	Retention Time	Area	% Area
1	11.889	7908069	97.64
2	20.887	191006	2.36

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-6-fluoro-2-oxoindolin-3-yl)carbamate



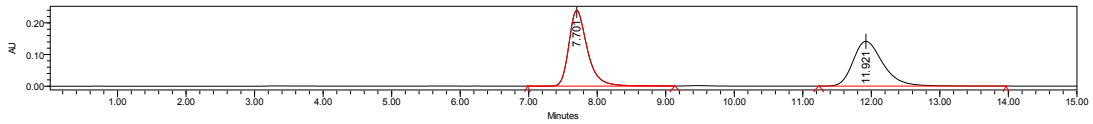
6ff

White solid, melting point: 159–163 °C; 96% yield (two steps), 94% ee; $[\alpha]^{20}_{\lambda}$ = –96.05 (*c* = 0.76 in CH_2Cl_2).

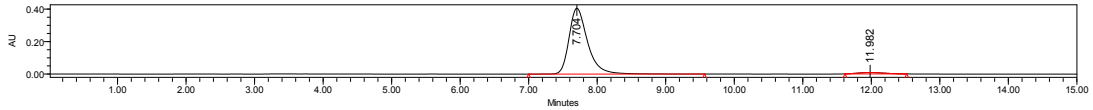
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.70 min, t_R (minor) = 11.98 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 – 7.22 (m, 6H), 6.81-6.70 (m, 1H), 6.57 – 6.46 (m, 1H), 5.75 (s, 1H), 5.66 (s, 1H), 5.39 (s, 1H), 5.00 – 4.80 (m, 2H), 2.86 (q, *J* = 13.2 Hz, 2H), 1.31 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.7, 163.9 (J_{CF} = 247.5 Hz), 153.8, 144.3 (J_{CF} = 12.12 Hz) 137.2, 135.1, 128.9, 128.1, 127.7, 125.6, 123.5, 117.5, 115.4, 109.6 (J_{CF} = 22.2 Hz), 98.5 (J_{CF} = 27.3 Hz), 81.2, 61.1, 44.6, 41.4, 28.2; **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ = −109.4.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}FN_3O_3Na^+$ ([M+Na$^+$]) = 444.1699, Found 444.1693.

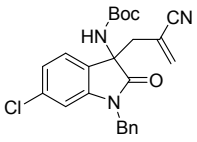


	Retention Time	Area	% Area
1	7.701	4496109	51.14
2	11.921	4296216	48.86



	Retention Time	Area	% Area
1	7.704	7633856	97.14
2	11.982	224579	2.86

Tert-butyl (1-benzyl-6-chloro-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate



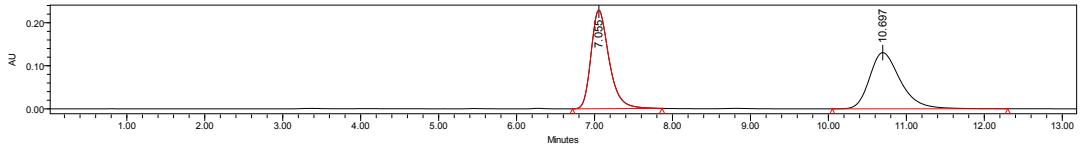
6gg

White solid, melting point: 146–168 °C; 99% yield (two steps), 96% ee; $[\alpha]^{20}_{\lambda}$ = −59.24 (*c* = 0.66 in CH_2Cl_2).

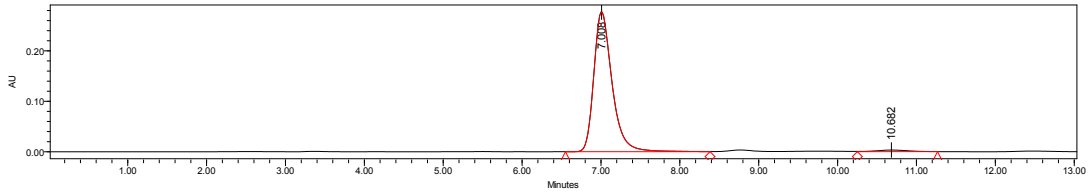
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.00 min, t_R (minor) = 10.68 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 – 7.18 (m, 6H), 7.00 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.71 (s, 1H), 5.68 (s, 1H), 5.57 (s, 1H), 5.42 (s, 1H), 4.81 (s, 2H), 2.75 (t, *J* = 13.2 Hz, 2H), 1.24 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.5, 153.8, 143.9, 137.2, 135.6, 135.1, 128.9, 128.0, 127.7, 126.6, 125.3, 123.2, 117.5, 115.2, 110.2, 81.2, 61.2, 44.5, 41.2, 28.2.

HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}ClN_3O_3Na^+$ ([M+Na$^+$]) = 460.1398, 462.1369, Found 460.1400, 462.1374.

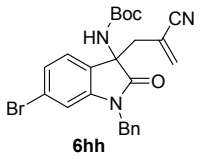


	Retention Time	Area	% Area
1	7.055	3674518	50.65
2	10.697	3580066	49.35



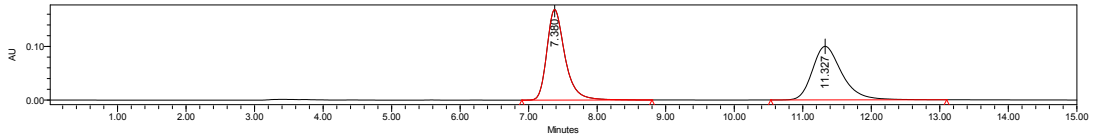
	Retention Time	Area	% Area
1	7.008	4453222	98.10
2	10.682	86439	1.90

Tert-butyl (1-benzyl-6-bromo-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate

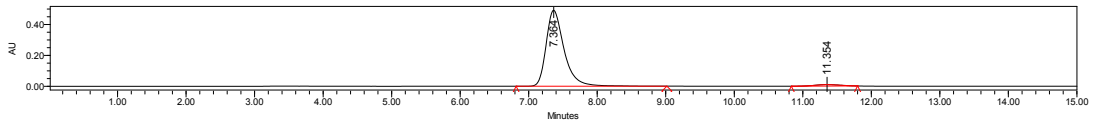


6hh

White solid, melting point: 151–153 °C; 98% yield (two steps), 94% ee; $[\alpha]^{20}_{\lambda}$ = –34.17 (*c* = 0.96 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.36 min, t_R (minor) = 11.35 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 – 7.19 (m, 7H), 6.93 (s, 1H), 5.76 (s, 1H), 5.65 (s, 1H), 5.48 (s, 1H), 4.88 (s, 2H), 2.84 (q, *J* = 13.2 Hz, 2H), 1.31 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 175.4, 153.8, 144.1, 137.3, 135.1, 128.9, 128.1, 127.7, 127.1, 126.2, 125.6, 123.4, 117.6, 115.2, 112.9, 81.3, 61.2, 44.5, 41.1, 28.2.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}BrN_3O_3Na^+$ ([M+Na$^+$]) = 504.0899, 506.0878, Found 504.0885, 506.0867.

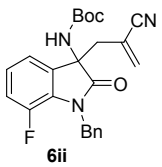


	Retention Time	Area	% Area
1	7.380	3093381	50.87
2	11.327	2988009	49.13



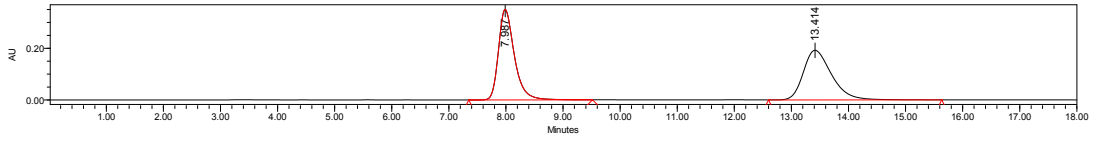
	Retention Time	Area	% Area
1	7.364	8972818	97.29
2	11.354	250139	2.71

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-7-fluoro-2-oxoindolin-3-yl)carbamate

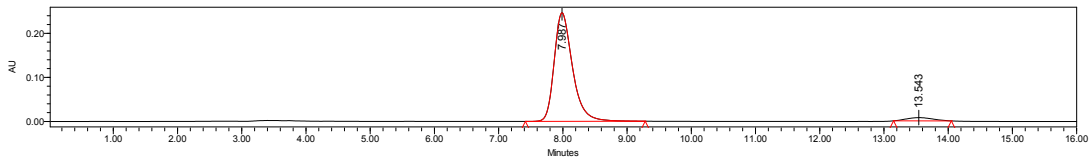


6ii

Oil; 96% yield (two steps), 92% ee; $[\alpha]^{20}_{\lambda}$ = –68.95 (*c* = 0.76 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.99 min, t_R (minor) = 13.54 min.
^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.09 (s, 1H), 7.45 – 6.97 (m, 8H), 5.89 (s, 1H), 5.74 (s, 1H), 5.2 – 4.7 (m, 2H), 2.95 – 2.70 (m, 2H), 1.32 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ = 174.9, 153.8, 146.6 (J_{CF} = 214.0 Hz), 138.3, 137.0, 132.2, 129.1 (J_{CF} = 9.1 Hz), 128.2, 127.0 (J_{CF} = 28.3 Hz), 123.7 (J_{CF} = 6.1 Hz), 119.3 (J_{CF} =2.0 Hz), 117.4, 117.1 (J_{CF} = 20.2 Hz), 114.5, 79.2, 61.3 (J_{CF} = 2.0Hz), 44.9, 40.3, 28.0; **^{19}F{^{1}H} NMR** (376 MHz, Chloroform-*d*) δ = –133.2.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}FN_3O_3Na^+$ ([M+Na$^+$]) = 444.1699, Found 444.1690.

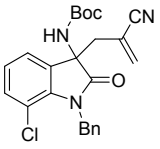


	Retention Time	Area	% Area
1	7.987	6788649	50.77
2	13.414	6582633	49.23



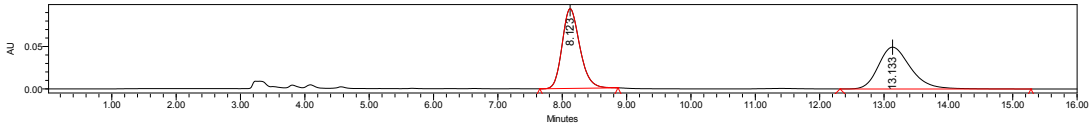
	Retention Time	Area	% Area
1	7.987	4879261	95.91
2	13.543	208254	4.09

Tert-butyl (1-benzyl-7-chloro-3-(2-cyanoallyl)-2-oxoindolin-3-yl)carbamate

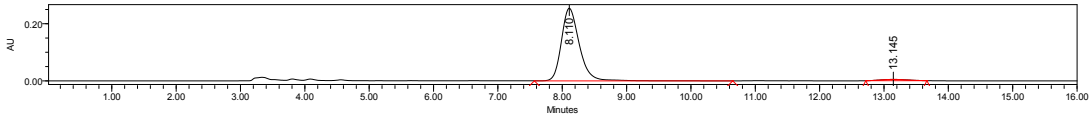


6jj

White solid, melting point: 151–153 °C; 98% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = –56.16 (*c* = 0.86 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.11 min, t_R (minor) = 13.15 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 – 7.21 (m, 7H), 7.07 (t, *J* = 7.8 Hz, 1H), 5.66 (s, 1H), 5.57 (s, 1H), 5.50 – 5.35 (m, 2H), 5.22 (d, *J* = 16.0 Hz, 1H), 2.84 – 2.76 (m, 2H), 1.32 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 176.1, 153.7, 138.9, 137.7, 137.4, 132.5, 131.2, 128.6, 127.4, 127.3, 124.2, 122.7, 117.4, 115.9, 114.7, 81.4, 61.0, 45.5, 41.7, 28.2.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}ClN_3O_3Na^+$ ([M+Na$^+$]) = 460.1398, 462.1369, Found 460.1399, 462.1375.

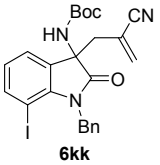


	Retention Time	Area	% Area
1	8.123	1789253	51.15
2	13.133	1708476	48.85



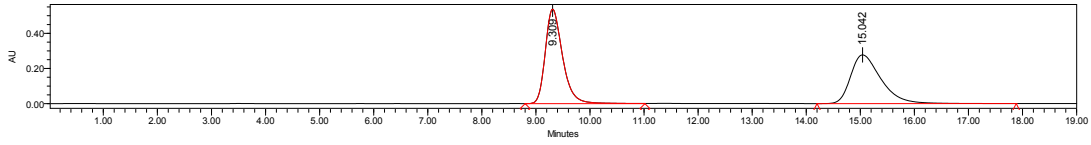
	Retention Time	Area	% Area
1	8.110	4905149	97.40
2	13.145	131071	2.60

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-7-iodo-2-oxoindolin-3-yl)carbamate



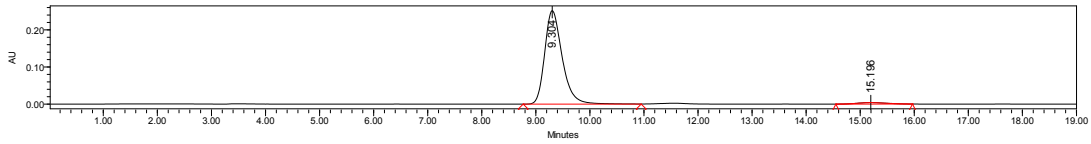
6kk

White solid, melting point: 175–178 °C; 91% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = –20.32 (*c* = 0.97 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 9.30 min, t_R (minor) = 15.20 min.
^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.08 (s, 1H), 7.68 (m, 1H), 7.44 – 7.19 (m, 6H), 6.86 (t, *J* = 7.8 Hz, 1H), 5.95 (s, 1H), 5.70 (s, 1H), 5.26 (s, 2H), 2.92 – 2.70 (m, 2H), 1.33 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ = 176.2, 153.7, 143.0, 141.6, 138.4, 137.6, 132.3, 128.1, 126.6, 126.4, 124.7, 122.9, 117.5, 114.5, 79.2, 72.7, 60.4, 43.7, 40.5, 28.0.
HRMS (FTMS+c ESI) calcd for $C_{24}H_{24}IN_3O_3Na^+$ ([M+Na$^+$]) = 552.0760, Found 552.0763.



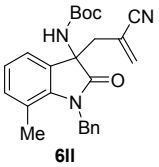
	Retention Time	Area	% Area
1	9.309	11906302	52.42

2	15.042	10807717	47.58



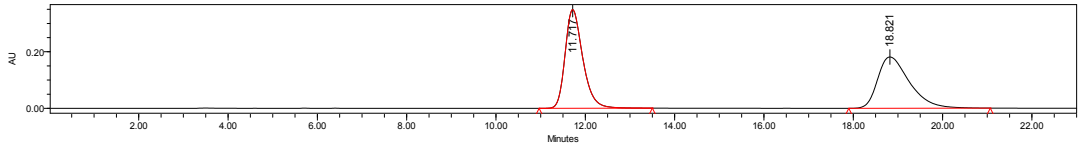
	Retention Time	Area	% Area
1	9.304	5671330	97.42
2	15.196	150234	2.58

Tert-butyl (1-benzyl-3-(2-cyanoallyl)-7-methyl-2-oxoindolin-3-yl)carbamate

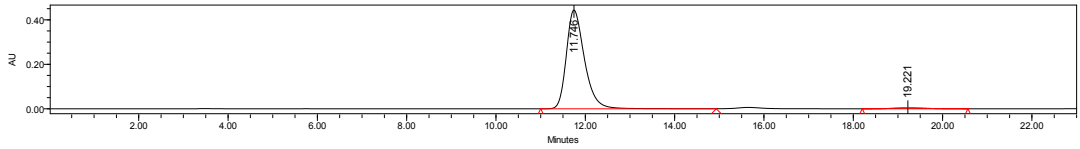


6ll

White solid, melting point: 135–139 °C; 96% yield (two steps), 97% ee; $[\alpha]^{20}_{\lambda}$ = –66.88 (*c* = 0.80 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 11.75 min, t_R (minor) = 19.22 min.
^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.95 (s, 1H), 7.41 – 7.20 (m, 5H), 7.17 – 7.14 (m, 1H), 7.00 – 6.90 (m, 2H), 5.96 (s, 1H), 5.72 (s, 1H), 5.28 – 4.84 (m, 2H), 2.81 (m, 2H), 2.16 (s, 3H), 1.33 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ = 176.0, 153.7, 140.8, 138.3, 137.9, 132.7, 128.4, 126.8, 125.9, 122.6, 120.8, 118.9, 117.6, 115.0, 78.9, 60.6, 44.6, 40.7, 28.0, 18.0.
HRMS (FTMS+c ESI) calcd for $C_{25}H_{27}N_3O_3Na^+$ ([M+Na$^+$]) = 440.1950, Found 444.1945.



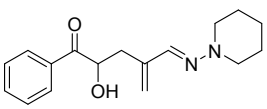
	Retention Time	Area	% Area
1	11.717	9552453	51.64
2	18.821	8947183	48.36



	Retention Time	Area	% Area
1	11.746	12498586	98.59
2	19.221	178471	1.41

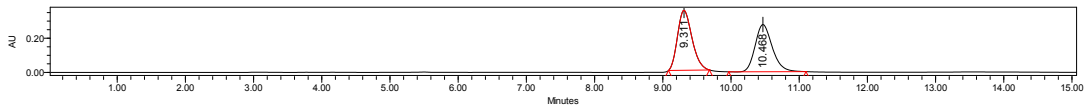
8.3 Characterization of the products of aldehyde-ene reaction

2-Hydroxy-1-phenyl-4-((piperidin-1-ylimino)methyl)pent-4-en-1-one

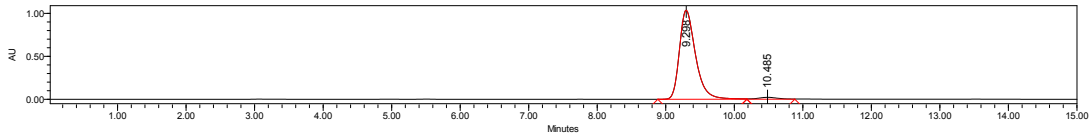


7aa

Solid, melting point: 76–79 °C; 98% yield, 95% ee; $[\alpha]^{20}_{\lambda}$ = –220.5 (*c* = 0.84 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 9.30 min, t_R (minor) = 10. 49 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.22 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H),7.33 (s, 1H) 5.36 (t, *J* = 8.0 Hz, 1H), 5.28 (s, 1H), 5.25 (s, 1H), 4.10 (d, *J* = 6.4 Hz, 1H), 3.19 – 3.02 (m, 5H), 2.22 (dd, *J* = 13.6, 9.9 Hz, 1H), 1.75 – 1.60 (m, 4H), 1.56 – 1.49 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 201.6, 141.9, 137.5, 133.8, 133.7, 129.2, 128.6, 120.2, 72.1, 52.0, 39.6, 25.2, 24.1.
HRMS (FTMS+c ESI) calcd for $C_{17}H_{22}N_2O_2H^+$ ([M+H$^+$]) = 287.1760, Found 287.1752.

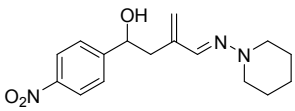


	Retention Time	Area	% Area
1	9.311	5166713	51.68
2	10.468	4830852	48.32



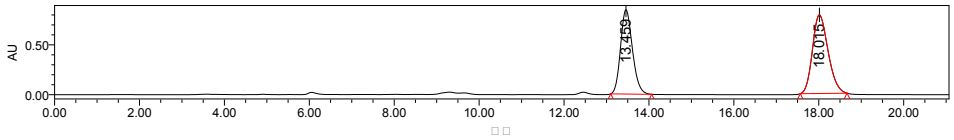
	Retention Time	Area	% Area
1	9.298	16867009	97.40
2	10.485	449895	2.60

1-(4-Nitrophenyl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol

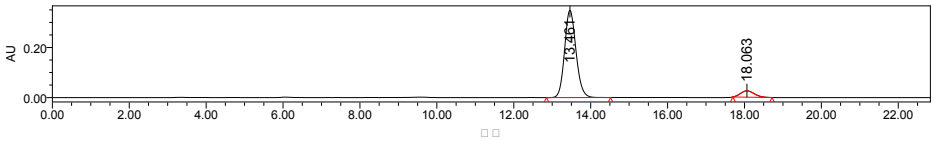


9a

Oil; 80% yield, 84% ee; $[\alpha]^{20}_{\lambda}$ = +253.67 (*c* = 0.46 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 13.46 min, t_R (minor) = 18. 06 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 – 8.12 (m, 2H), 7.55 – 7.48 (m, 2H), 7.30 (s, 1H), 5.92 (d, *J* = 3.6 Hz, 1H), 5.15 (s, 1H), 5.08 (s, 1H), 4.99 (d, *J* = 7.2 Hz, 1H), 3.11 (t, *J* = 5.8 Hz, 4H), 2.88 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.71 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.79 – 1.64 (m, 4H), 1.60 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 152.8, 147.0, 142.6, 138.7, 126.6, 123.5, 121.5, 73.1, 52.1, 43.6, 25.0, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{16}H_{21}N_3O_3H^+$ ([M+H$^+$]) = 304.1656, Found 304.1658.

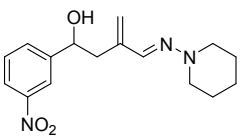


	Retention Time	Area	% Area
1	13.459	16410544	49.00
2	18.015	17078070	51.00



	Retention Time	Area	% Area
1	13.461	7166548	91.97
2	18.063	625991	8.03

1-(3-Nitrophenyl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol

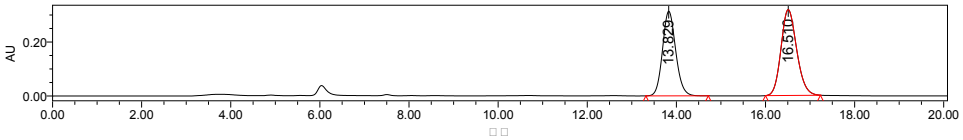


9b

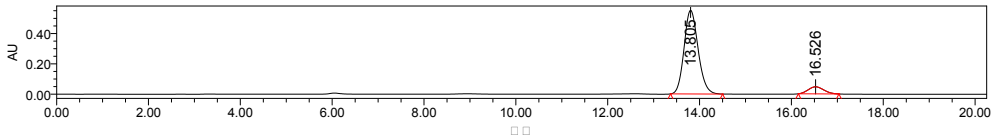
Oil; 80% yield, 83% ee; $[\alpha]^{20}_{\lambda}$ = +343.65 (*c* = 0.39 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 13.81 min, t_R (minor) = 16.53 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (t, *J* = 2.0 Hz, 1H), 8.07 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.30 (s, 1H), 5.91 (d, *J* = 3.6 Hz, 1H), 5.16 (s, 1H), 5.11 (s, 1H), 4.99 (m, 1H), 3.12 (t, *J* = 5.6 Hz, 4H), 2.88 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.74 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.76 – 1.71 (m, 4H), 1.58

– 1.51 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 148.3, 147.5, 142.7, 138.7, 132.1, 129.1, 122.0, 121.4, 121.0, 73.0, 52.1, 43.7, 25.0, 24.0.

HRMS (FTMS+c ESI) calcd for $C_{16}H_{21}N_3O_3H^+$ ([M+H$^+$]) = 304.1656, Found 304.1661.

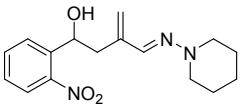


	Retention Time	Area	% Area
1	13.829	6458025	48.72
2	16.510	6798423	51.28



	Retention Time	Area	% Area
1	13.805	11719517	91.45
2	16.526	1096395	8.55

1-(2-Nitrophenyl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol



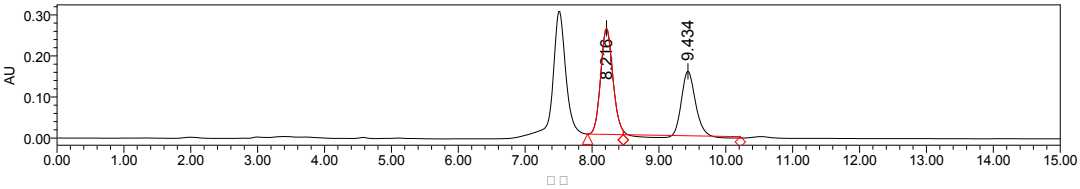
9c

Oil; 82% yield, 70% ee; $[\alpha]^{20}_{\lambda}$ = –337.50 (*c* = 0.45 in CH_2Cl_2).

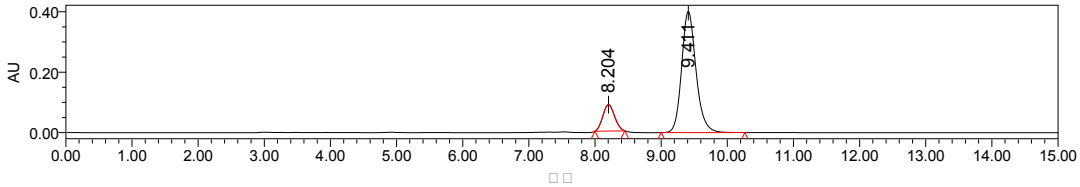
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 9.41 min, t_R (minor) = 8.20 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 – 7.85 (m, 2H), 7.62 – 7.55 (m, 1H), 7.39 – 7.32 (m, 2H), 6.33 (d, *J* = 3.2 Hz, 1H), 5.39 (dt, *J* = 7.6, 2.4 Hz, 1H), 5.26 (s, 1H), 5.20 (s, 1H), 3.11 (t, *J* = 5.6 Hz, 4H), 2.90 (dd, *J* = 14.4, 2.4 Hz, 1H), 2.81 (dd, *J* = 14.0, 7.2 Hz, 1H), 1.78 – 1.67 (m, 4H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 147.7, 143.0, 141.0 , 139.5, 133.2, 128.6, 127.6, 124.2, 121.9, 70.0, 52.1, 42.6, 25.0, 24.0.

HRMS (FTMS+c ESI) calcd for $C_{16}H_{21}N_3O_3H^+$ ([M+H$^+$]) = 304.1656, Found 304.1656.

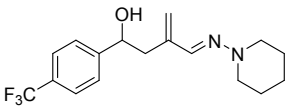


	Retention Time	Area	% Area
1	8.216	3010307	52.02
2	9.434	2776545	47.98



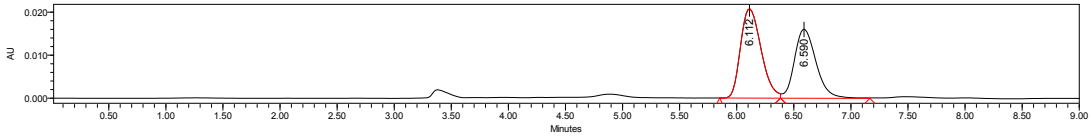
	Retention Time	Area	% Area
1	8.204	1073867	15.06
2	9.411	6059000	84.94

3-((Piperidin-1-ylimino)methyl)-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol

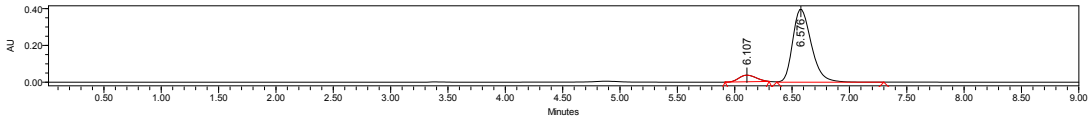


9d

Oil; 70% yield, 84% ee; $[\alpha]^{20}_{\lambda}$ = +184.00 (*c* = 0.40 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IE, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 6.58 min, t_R (minor) = 6.11 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.32 (s, 1H), 5.64 (d, *J* = 3.6 Hz, 1H), 5.16 (s, 1H), 5.12 (s, 1H), 4.96 – 4.90 (m, 1H), 3.15 – 3.07 (m, 4H), 2.84 (dd, *J* = 14.0, 2.8 Hz, 1H), 2.72 (dd, *J* = 14.0, 8.0 Hz, 1H), 1.78 – 1.69 (m, 4H), 1.58 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 149.3, 143.1, 129.6 (J_{CF} = 32.3 Hz), 129.2 (J_{CF} = 32.3 Hz), 128.9 (J_{CF} = 32.3 Hz), 128.6 (J_{CF} = 32.3 Hz), 128.5 (J_{CF} = 272.7 Hz), 138.9, 126.1 ,125.8 (J_{CF} = 272.7 Hz), 125.2 (J_{CF} = 4.0 Hz) 125.15 (J_{CF} = 4.0 Hz), 125.12 (J_{CF} = 4.0 Hz), 125.1 (J_{CF} = 4.0 Hz), 123.1 (J_{CF} = 272.7 Hz) 121.2, 120.4 (J_{CF} = 272.7 Hz), 73.4, 52.1, 43.8, 25.1, 24.1; **^{19}F{^{1}H} NMR** (376 MHz,$CDCl_3$) δ = –62.3.
HRMS (FTMS+c ESI) calcd for $C_{17}H_{21}F_3N_2OH^+$ ([M+H$^+$]) =327.1684, Found 327.1688.

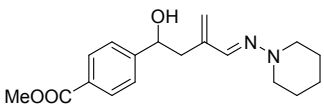


	Retention Time	Area	% Area
1	6.112	250326	53.13
2	6.590	220807	46.87



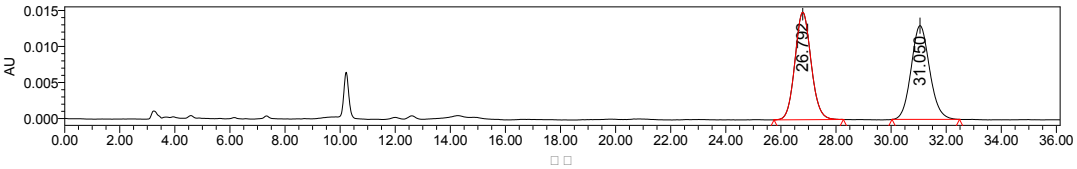
	Retention Time	Area	% Area
1	6.107	372947	7.69
2	6.576	4475236	92.31

Methyl-4-(1-hydroxy-3-((piperidin-1-ylimino)methyl)but-3-en-1-yl)benzoate

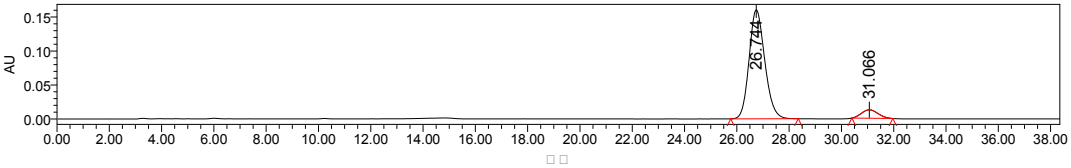


9e

Oil; 57% yield, 85% ee; $[\alpha]^{20}_{\lambda}$ = +255.00 (*c* = 0.26 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 26.74 min, t_R (minor) = 31.07 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 – 7.93 (m, 2H), 7.46 – 7.38 (m, 2H), 7.31 (s, 1H), 5.63 (d, *J* = 3.6 Hz, 1H), 5.14 (d, *J* = 1.2 Hz, 1H), 5.10 (d, *J* = 1.2 Hz, 1H), 4.94 (dt, *J* = 7.6, 3.2 Hz, 1H), 3.89 (s, 3H), 3.14 – 3.04 (m, 4H), 2.88 – 2.80 (m, 1H), 2.72 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.77 – 1.67 (m, 5H), 1.57 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 167.3, 150.6, 143.1, 138.9, 129.6, 128.7, 125.8, 121.1, 73.6, 52.1, 52.1, 43.7, 25.1, 24.1.
HRMS (FTMS+c ESI) calcd for $C_{18}H_{24}N_2O_3H^+$ ([M+H$^+$]) =317.1865, Found 317.1864.



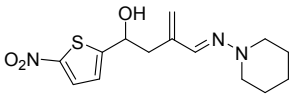
	Retention Time	Area	% Area
1	26.792	606570	50.06
2	31.050	605063	49.94



	Retention Time	Area	% Area
1	26.744	6684101	92.47

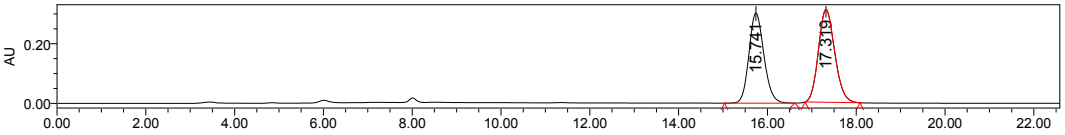
2	31.066	544447	7.53

1-(5-Nitrothiophen-2-yl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol

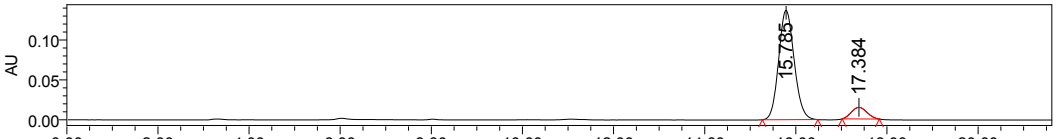


9f

Oil; 87% yield, 81% ee; $[\alpha]^{20}_{\lambda}$ = –410.30 (*c* = 0.47 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 15.79 min, t_R (minor) = 17.38 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 4.4 Hz, 1H), 7.28 (s, 1H), 6.81 (dd, *J* = 4.4, 1.4 Hz, 1H), 6.59 (d, *J* = 4.0 Hz, 1H), 5.22 (s, 1H), 5.19 (s, 1H), 5.10 (d, *J* = 7.2 Hz, 1H), 3.08 (t, *J* = 5.6 Hz, 4H), 2.99 – 2.93 (m, 1H), 2.82 – 2.75 (m, 1H), 1.74 – 1.65 (m, 5H), 1.57 – 1.50 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 160.3, 145.0, 141.8, 138.5, 128.9, 122.2, 121.5, 70.3, 51.9, 43.4, 25.0, 23.9.
HRMS (FTMS+c ESI) calcd for $C_{14}H_{19}N_3O_3SH^+$ ([M+H$^+$]) =310.1225, Found 310.1215.

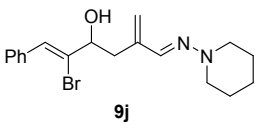


	Retention Time	Area	% Area
1	15.741	7073861	49.15
2	17.319	7319573	50.85



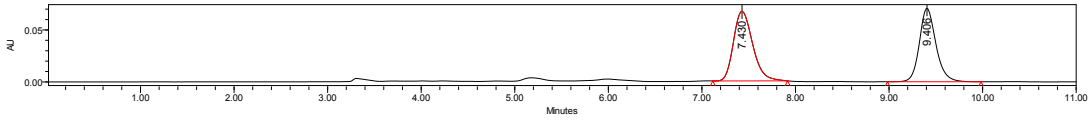
	Retention Time	Area	% Area
1	15.785	3244099	90.41
2	17.384	343983	9.59

(Z)-2-Bromo-1-phenyl-5-(-(piperidin-1-ylimino)methyl)hexa-1,5-dien-3-ol

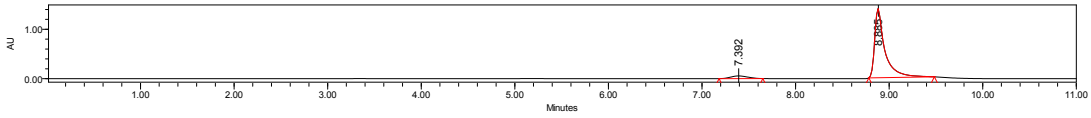


9j

Oil; 47% yield, 88% ee; $[\alpha]^{20}_{\lambda}$ = +268.82 (*c* = 0.36 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 8.89 min, t_R (minor) = 7.39 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58 – 7.52 (m, 2H), 7.36 – 7.30 (m, 3H), 7.28 – 7.23 (m, 1H), 7.15 (s, 1H), 6.15 (d, *J* = 4.8 Hz, 1H), 5.38 (s, 1H), 5.27 (s, 1H), 4.52 – 4.45 (m, 1H), 3.08 (t, *J* = 5.6 Hz, 4H), 2.94 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.86 (dd, *J* = 14.2, 3.0 Hz, 1H), 1.73 – 1.67 (m, 4H), 1.55 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 142.4, 139.4, 136.0, 129.7, 129.2, 128.1, 127.7, 126.6, 121.8, 76.9, 52.1, 39.7, 25.0, 24.0.
HRMS (ESI-TOF) calcd for $C_{18}H_{23}BrN_2OH^+$ ([M+H$^+$]) =363.1072, 365.1052 Found 363.1066, 365.1046.

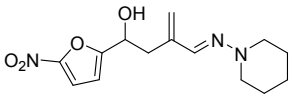


	Retention Time	Area	% Area
1	7.430	954276	52.38
2	9.406	867469	47.62



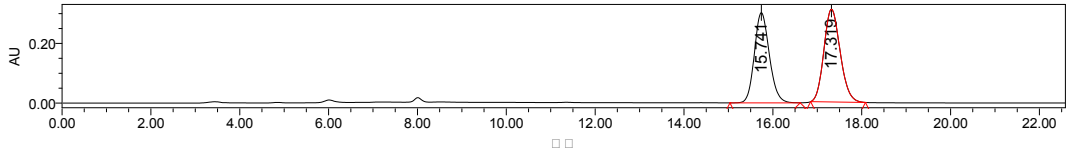
	Retention Time	Area	% Area
1	7.392	675700	6.03
2	8.885	10530836	93.97

1-(5-Nitrofuran-2-yl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol

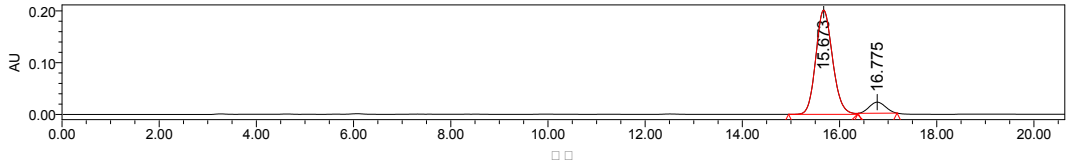


9g

Oil; 80% yield, 81% ee; $[\alpha]^{20}_{\lambda}$ = –666.32 (*c* = 0.38 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 15.67 min, t_R (minor) = 16.78 min.
^{1}H NMR (400 MHz,$CDCl_3$) δ = 7.29 (s, 1H), 7.27 – 7.24 (m, 1H), 6.50 (d, *J* = 3.6 Hz, 1H), 6.38 (s, 1H), 5.26 (s, 1H), 5.20 (s, 1H), 4.93 (d, *J* = 6.8 Hz, 1H), 3.07 (t, *J* = 5.6 Hz, 4H), 2.97 (dd, *J* = 14.4, 2.8 Hz, 1H), 2.89 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.75 – 1.69 (m, 5H), 1.56 – 1.49 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 162.0,151.6, 142.0, 138.9, 122.2, 112.9, 109.2, 68.4, 52.0, 40.3, 24.9, 24.0.
HRMS (FTMS+c ESI) calcd for $C_{14}H_{19}N_3O_4H^+$ ([M+H$^+$]) =294.1454, Found 294.1449.

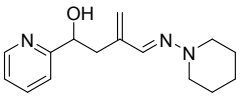


	Retention Time	Area	% Area
1	15.685	2869212	49.84
2	16.775	2887451	50.16



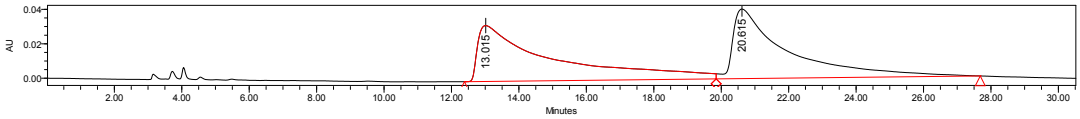
	Retention Time	Area	% Area
1	15.673	4818424	90.72
2	16.775	492845	9.28

3-((Piperidin-1-ylimino)methyl)-1-(pyridin-2-yl)but-3-en-1-ol



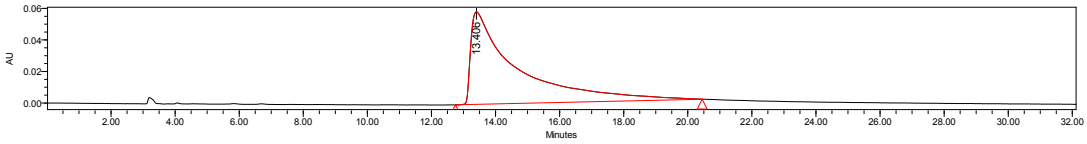
9h

Oil; Conditions A: 38% yield, 99% ee (Condition B: 38% yield, -95% ee); $[\alpha]^{20}_{\lambda}$ = –178.19 (*c* = 0.19 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IB, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 21.25 min, t_R (minor) = 14.05 min. (Conditions B).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.57 – 8.48 (m, 1H), 7.65 (td, *J* = 7.8, 2.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.33 (s, 1H), 7.15 – 7.10 (m, 1H), 5.77 (d, *J* = 4.4 Hz, 1H), 5.20 (s, 1H), 5.15 (s, 1H), 5.02 – 4.93 (m, 1H), 3.14 – 3.05 (t, *J* = 5.6 Hz, 4H), 2.98 (dd, *J* = 14.0, 2.8 Hz, 1H), 2.77 (dd, *J* = 13.6, 8.0 Hz, 1H), 1.74 – 1.66 (m, 4H), 1.57 – 1.48 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz,$CDCl_3$) δ = 163.8, 148.5, 143.2, 139.3, 136.5, 121.9, 121.0, 120.4, 74.2, 52.2, 42.0, 25.1, 24.1.
HRMS (FTMS+c ESI) calcd for $C_{15}H_{21}N_3OH^+$ ([M+H$^+$]) = 260.1763, Found 260.1763.



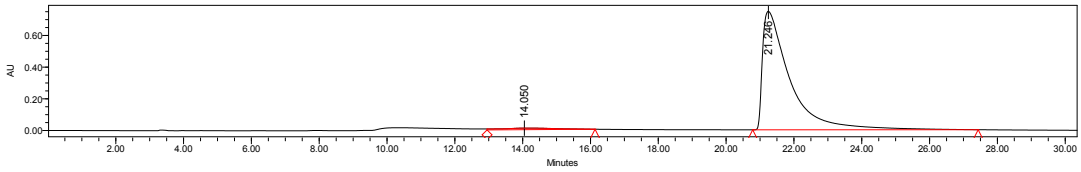
	Retention Time	Area	% Area
1	13.015	4953893	52.20
2	20.615	4536309	47.80

Condition A



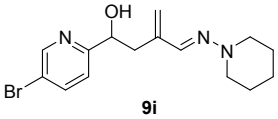
	Retention Time	Area	% Area
1	13.406	5877805	100.00

Condition B



	Retention Time	Area	% Area
1	14.050	1116056	2.59
2	21.246	41968868	97.41

1-(5-bromopyridin-2-yl)-3-((piperidin-1-ylimino)methyl)but-3-en-1-ol



9i

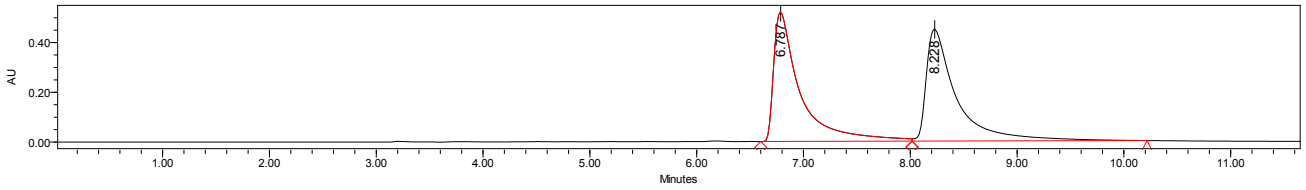
Oil; Conditions A: 75% yield, 97% ee (Condition B: 70% yield, -92% ee); $[\alpha]^{20}_{\lambda}$ = –300.63 (*c* = 0.80 in CH_2Cl_2).

HPLC DAICEL CHIRALCEL IB, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 6.74 min, t_R (minor) = 8.34 min. (Conditions A).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.56 (d, *J* = 2.4 Hz, 1H), 7.75 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 5.90 (d, *J* = 4.4 Hz, 1H), 5.15 (s, 1H), 5.13 (s, 1H), 4.91 (ddd, *J* = 7.4, 4.2, 3.0 Hz, 1H), 3.11 – 3.03 (m, 4H), 2.95 (dd, *J* = 14.0, 2.8 Hz, 1H), 2.77 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.74 – 1.67 (m, 5H), 1.55 – 1.48 (m, 2H).

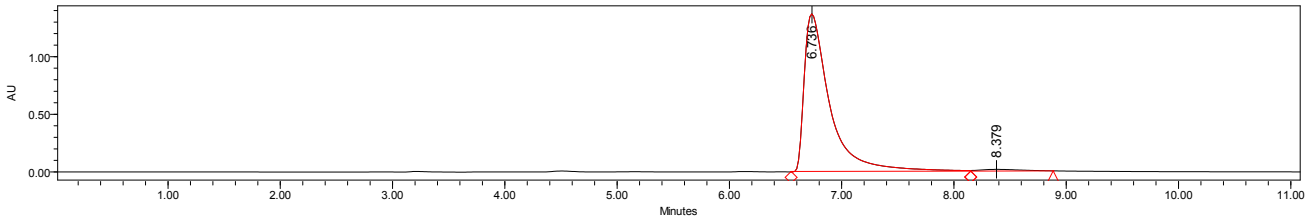
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 162.7, 149.5, 142.9, 139.2, 139.0, 121.9, 121.4, 118.5, 74.0, 52.1, 41.7, 25.0, 24.1.

HRMS (FTMS+c ESI) calcd for $C_{15}H_{20}BrN_3OH^+$ ([M+H$^+$]) = 338.0868, 340.0848, Found 338.0865, 340.0845.



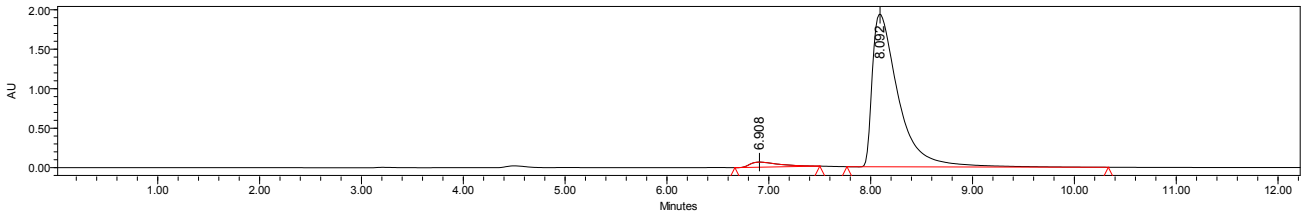
	Retention Time	Area	% Area
1	6.787	8948638	50.35
2	8.228	8825106	49.65

Condition A



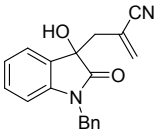
	Retention Time	Area	% Area
1	6.736	21568994	98.44
2	8.379	342520	1.56

Condition B



	Retention Time	Area	% Area
1	6.908	1289380	3.62
2	8.092	34359383	96.38

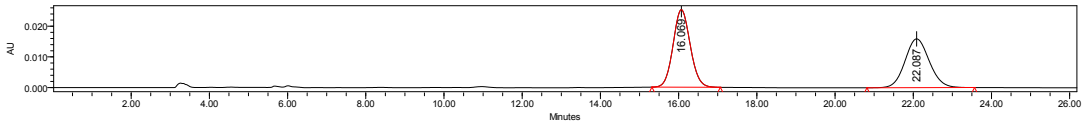
3-Hydroxy-5-iodo-1-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one



3ab

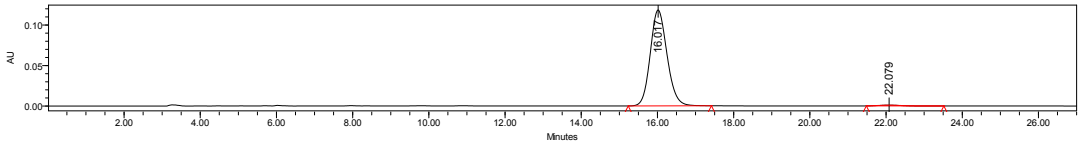
Colorless oil; 82% yield (two steps), 98% ee; $[\alpha]^{20}_{\lambda}$ = +62.50 (*c* = 0.48 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 16.02 min, t_R (minor) = 22.08 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 (d, *J* = 7.2 Hz, 1H), 7.33 – 7.23 (m, 6H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* =8.0 Hz, 1H), 5.84 (s, 1H), 5.74 (s, 1H), 4.94 – 4.71 (m, 2H), 3.89 (s, 1H), 3.01 – 2.84 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 177.0, 142.5, 136.5, 135.2, 130.6, 128.9, 128.0, 127.9, 127.5, 124.9, 123.7, 118.1, 116.2, 110.0, 75.8, 44.1, 42.5.

HRMS (FTMS+c ESI) calcd for $C_{19}H_{16}N_2O_2Na^+$ ([M+Na$^+$]) = 327.1109, Found 327.1098.



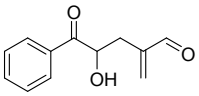
1

	Retention Time	Area	% Area
1	16.069	769411	52.81
2	22.087	687402	47.19



	Retention Time	Area	% Area
1	16.017	3609177	98.98

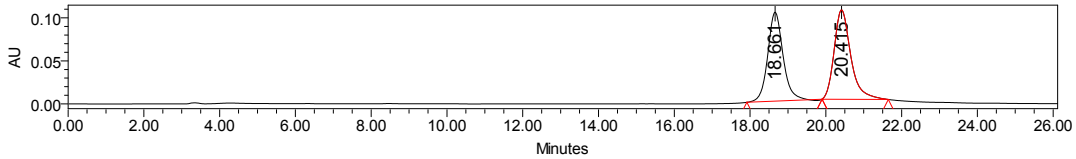
1-Benzyl-5-chloro-3-hydroxy-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one



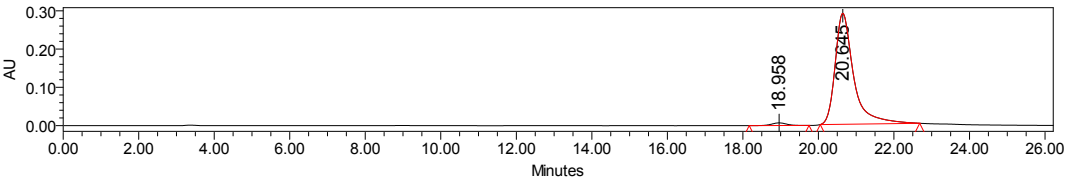
7ab

Oil; 70% yield (two steps), 96% ee; $[\alpha]^{20}_{\lambda}$ = +77.19 (*c* = 0.32 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 20.65 min, t_R (minor) = 18.96 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.60 (s, 1H), 8.21 – 8.03 (m, 2H), 7.67 – 7.60 (m, 1H), 7.57 – 7.50 (m, 2H), 6.47 (s, 1H), 6.20 (s, 1H), 5.22 – 5.15 (m, 1H), 3.73 (d, *J* = 6.7 Hz, 1H), 3.01 (dt, *J* = 13.8, 1.7 Hz, 1H), 2.18 (dd, *J* = 13.9, 9.8 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 201.0, 194.7, 145.2, 137.9, 134.5, 133.1, 129.1, 129.1, 71.0, 36.0.

HRMS (FTMS+c ESI) calcd for $C_{12}H_{12}O_3Na^+$ ([M+Na$^+$]) = 227.0684, Found 227.0676.

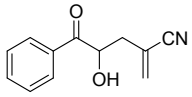


	Retention Time	Area	% Area
1	18.661	3019013	48.27
2	20.415	3235700	51.73



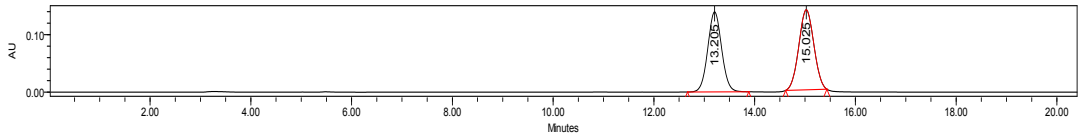
	Retention Time	Area	% Area
1	18.958	194208	1.94
2	20.645	9827034	98.06
2	22.079	37265	1.02

4-Hydroxy-2-methylene-5-oxo-5-phenylpentanenitrile

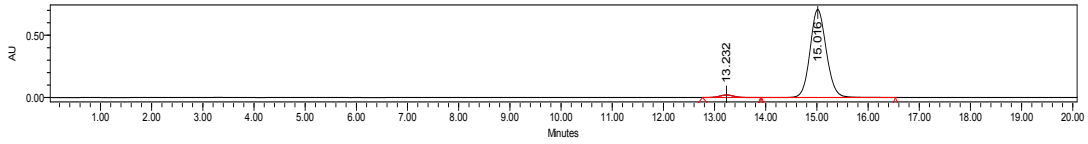


7ac

Oil; 95% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = +46.0 (*c* = 0.50 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IC, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 15.02 min, t_R (minor) = 13.23 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 – 7.90 (m, 2H), 7.68 – 7.63 (m, 1H), 7.56 – 7.50 (m, 2H), 5.99 (s, 1H), 5.80 (s, 1H), 5.30 (m, 1H), 3.86 (d, *J* = 6.5 Hz, 1H), 2.86 – 2.80 (m, 1H), 2.42 – 2.35 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 199.8, 134.7, 134.1, 133.0, 129.3, 128.7, 118.3, 118.2, 70.9, 40.9.
HRMS (FTMS+c ESI) calcd for $C_{12}H_{11}NO_2Na^+$ ([M+Na$^+$]) = 224.0687, Found 224.0680.

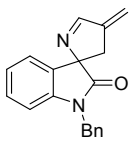


	Retention Time	Area	% Area
1	13.205	2663009	48.07
2	15.025	2876820	51.93



	Retention Time	Area	% Area
1	13.232	389014	2.44
2	15.016	15536716	97.56

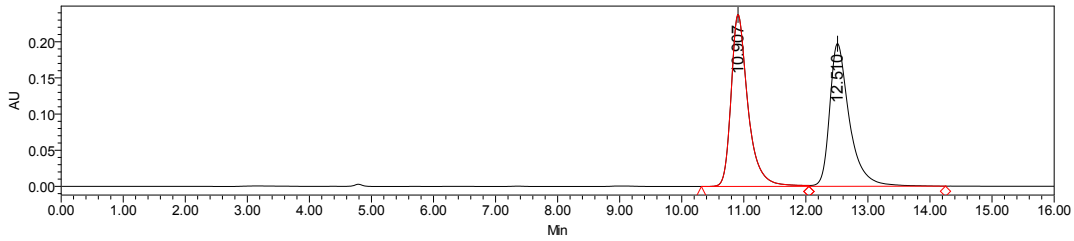
1-Benzyl-4'-methylene-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one



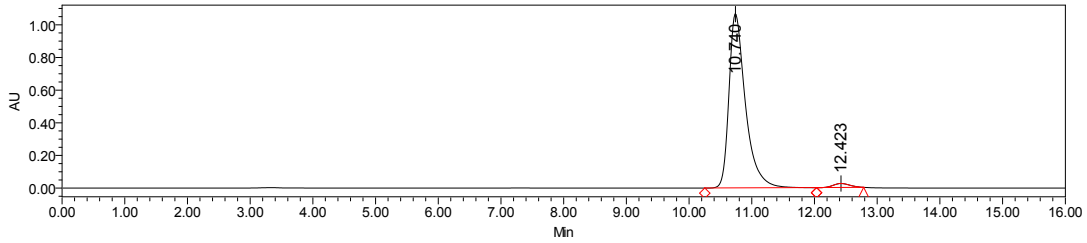
6ab

Colorless Oil; 70% yield (two steps), 95% ee; $[\alpha]^{20}_{\lambda}$ = +197.64 (*c* = 0.72 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 10.74 min, t_R (minor) = 12.42 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 (s, 1H), 7.35 – 7.26 (m, 4H), 7.25 – 7.20 (m, 1H), 7.20 – 7.14 (m, 1H), 7.05 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* =8.0 Hz, 1H), 5.58 (t, *J* = 2.8 Hz, 1H), 5.48 (t, *J* = 2.4

Hz, 1H), 5.00 – 4.83 (m, 2H), 3.13 (dt, *J* = 17.2, 2.4 Hz, 1H), 2.78 (dt, *J* = 17.2, 2.4 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 176.2, 168.5, 150.1, 142.6, 135.5, 131.0, 129.3, 128.8, 127.6, 127.2, 123.5, 123.2, 112.9, 109.4, 80.8, 43.9, 37.1.
HRMS (FTMS+c ESI) calcd for $C_{19}H_{16}N_2OH^+$ ([M+H$^+$]) = 289.1341, Found 289.1335.

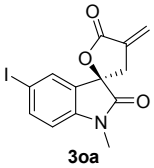


	Retention Time	Area	% Area
1	10.907	4490974	50.73
2	12.510	4361458	49.27

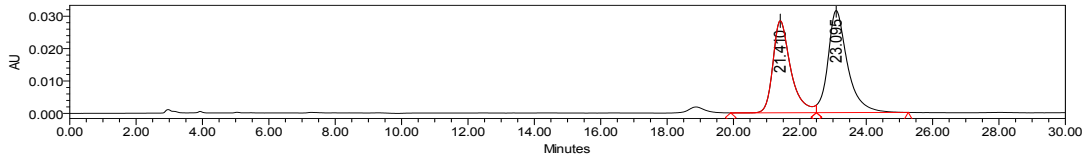


	Retention Time	Area	% Area
1	10.740	19438750	97.75
2	12.423	447361	2.25

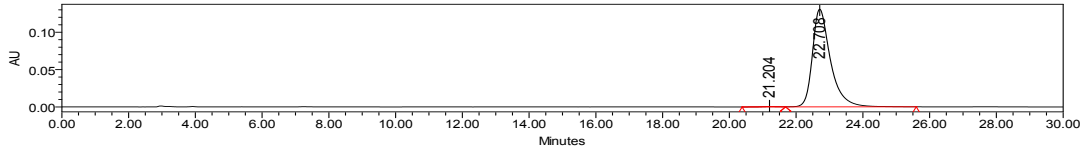
3-Hydroxy-5-iodo-1-methyl-3-(2-((piperidin-1-ylimino)methyl)allyl)indolin-2-one


3oa

Solid, melting point: 165–168 °C; 40% yield (two steps), 99% ee; $[\alpha]^{20}_{\lambda}$ = −167.14 (*c* = 0.42 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 22.71 min, t_R (minor) = 21.20 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.58 (d, *J* = 1.7 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.42 (t, *J* = 2.8 Hz, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 3.29 (dt, *J* = 17.2, 2.5 Hz, 1H), 3.19 (s, 3H), 3.08 (dt, *J* = 17.2, 2.8 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 172.9, 168.7, 143.7, 140.2, 133.1, 132.3, 129.0, 123.9, 111.1, 85.9, 78.8, 36.3 , 26.7.
HRMS (FTMS+c ESI) calcd for $C_{13}H_{10}INO_3Na^+$ ([M+Na$^+$]) = 377.9603, Found 377.9602.



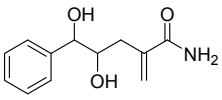
	Retention Time	Area	% Area
1	21.410	1143809	48.72
2	23.095	1203861	51.28



	Retention Time	Area	% Area
1	21.204	14771	0.30

2	22.708	4924663	99.70

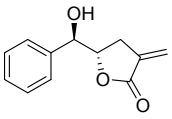
4,5-Dihydroxy-2-methylene-5-phenylpentanamide



7ad

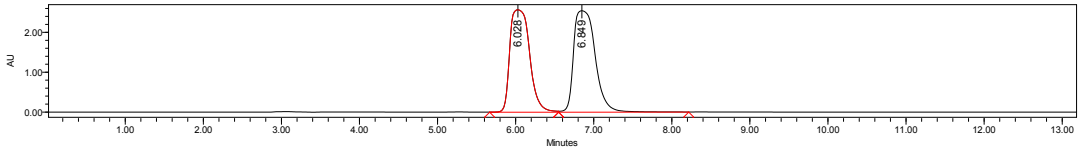
Oil; 60% yield (>99:1 d.r., two steps).
^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.54 (s, 1H), 7.36 – 7.27 (m, 4H), 7.24 – 7.18 (m, 1H), 7.07 (s, 1H), 5.73 (s, 1H), 5.35 (s, 1H), 5.31 (d, *J* = 4.4 Hz, 1H), 4.79 (d, *J* = 5.6 Hz, 1H), 4.36 (t, *J* = 5.2 Hz, 1H), 3.69 – 3.60 (m, 1H), 2.54 – 2.49 (m, 1H), 2.16 (dd, *J* = 14.4, 9.2 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ = 170.7, 143.4, 142.1, 127.5, 127.2, 126.6, 120.4, 76.1, 74.0, 35.5.
HRMS (FTMS+c ESI) calcd for $C_{12}H_{15}NO_3Na^+$ ([M+Na$^+$]) = 244.0950, Found 244.0946.

(1*R*, 5*S*)-5-(Hydroxy(phenyl)methyl)-3-methylenedihydrofuran-2(3H)-one

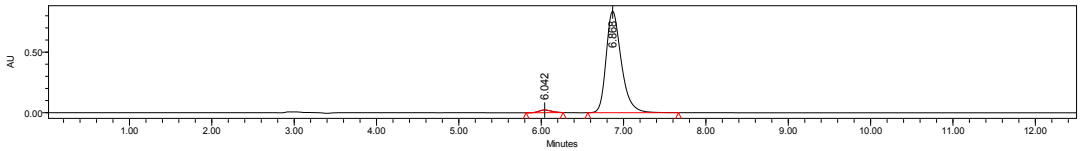


7ae

Oil; 60% yield, >99:1 d.r., 96% ee; $[\alpha]^{20}_{\lambda}$ = –181.67 (*c* = 0.24 in CH_2Cl_2).
HPLC DAICEL CHIRALCEL IA, n-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 210 nm, t_R (major) = 6.89 min, t_R (minor) = 6.04 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 – 7.32 (m, 4H), 7.35 – 7.24 (m, 1H), 6.18 (t, *J* = 3.0 Hz, 1H), 5.58 (t, *J* = 2.6 Hz, 1H), 5.14 (t, *J* = 2.6 Hz, 1H), 4.72 (ddd, *J* = 8.6, 5.6, 3.2 Hz, 1H), 3.08 (d, *J* = 6.4 Hz, 1H), 3.01 (ddt, *J* = 17.5, 5.8, 2.9 Hz, 1H), 2.61 (ddt, *J* = 17.4, 8.2, 2.6 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 170.8, 138.4, 134.6, 128.7, 128.2, 126.1, 122.1, 80.3, 73.0, 26.6.
HRMS (ESI-TOF) calcd for $C_{12}H_{12}O_3Na^+$ ([M+Na$^+$]) = 227.0684, Found 227.0676.

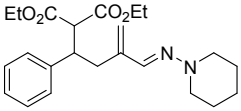


	Retention Time	Area	% Area
1	6.028	45071025	47.98
2	6.849	48874501	52.02



	Retention Time	Area	% Area
1	6.042	232452	2.13
2	6.868	10668928	97.87

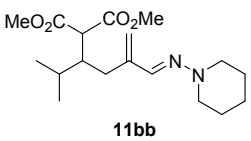
Diethyl-2-(1-phenyl-3-((piperidin-1-ylimino)methyl)but-3-en-1-ylidene)malonate



11ab

Oil; 50% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.25 – 6.88 (m, 6H), 4.92 (d, *J* = 16.8 Hz, 2H), 4.27 – 4.15 (m, 2H), 3.91 – 3.80 (m, 3H), 3.69 (d, *J* = 10.4 Hz, 1H), 3.01 (t, *J* =6.0 Hz, 4H), 2.81 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.68 (dd, *J* = 13.6, 10.4 Hz, 1H), 1.70 – 1.60 (m, 4H), 1.53 – 1.46 (m, 2H), 1.28 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ = 168.5, 168.1, 143.4, 141.1, 137.1, 128.8, 128.0, 126.7, 118.1, 61.5, 61.1, 58.8, 52.2, 44.2, 35.8, 25.2, 24.3, 14.3, 13.8.

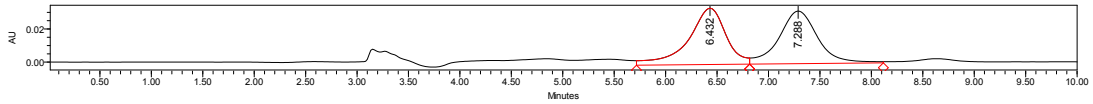
Dimethyl-2-(2-methyl-5-((piperidin-1-ylimino)methyl)hex-5-en-3-yl)malonate



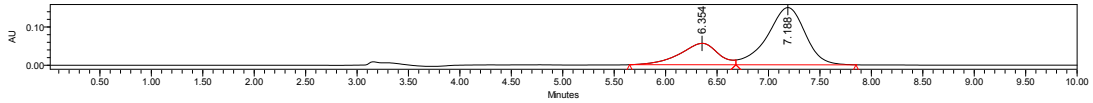
11bb

Oil; 36% yield; 45% ee.
HPLC DAICEL CHIRALCEL ODH, n-hexane/2-propanol = 98/2, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 7.18 min, t_R (minor) = 6.35 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (s, 1H), 5.21 (d, *J* = 1.6 Hz, 1H), 5.11 (d, *J* = 1.6 Hz, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 3.50 (d, *J* = 6.8 Hz, 1H), 3.04 (t, *J* = 5.6 Hz, 4H), 2.75 – 2.68 (m, 1H), 2.65 – 2.55 (m, 1H), 2.16

(dd, *J* = 13.6, 8.5 Hz, 1H), 1.95 – 1.80 (m, 1H), 1.73 – 1.65 (m, 4H), 1.55 – 1.45 (m, 2H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H); **$^{13}C\{^{1}H\}$ NMR** (101 MHz, $CDCl_3$) δ = 170.0, 145.1, 137.0, 117.6, 54.1, 52.3, 52.1, 42.4, 30.5, 29.7, 25.2, 24.4, 20.9, 18.4.
HRMS (FTMS+c ESI) calcd for $C_{18}H_{31}N_2O_4H^+$ ([M+H$^+$]) = 339.2284, Found 339.2276.



	Retention Time	Area	% Area
1	6.432	860719	50.91
2	7.288	830033	49.09

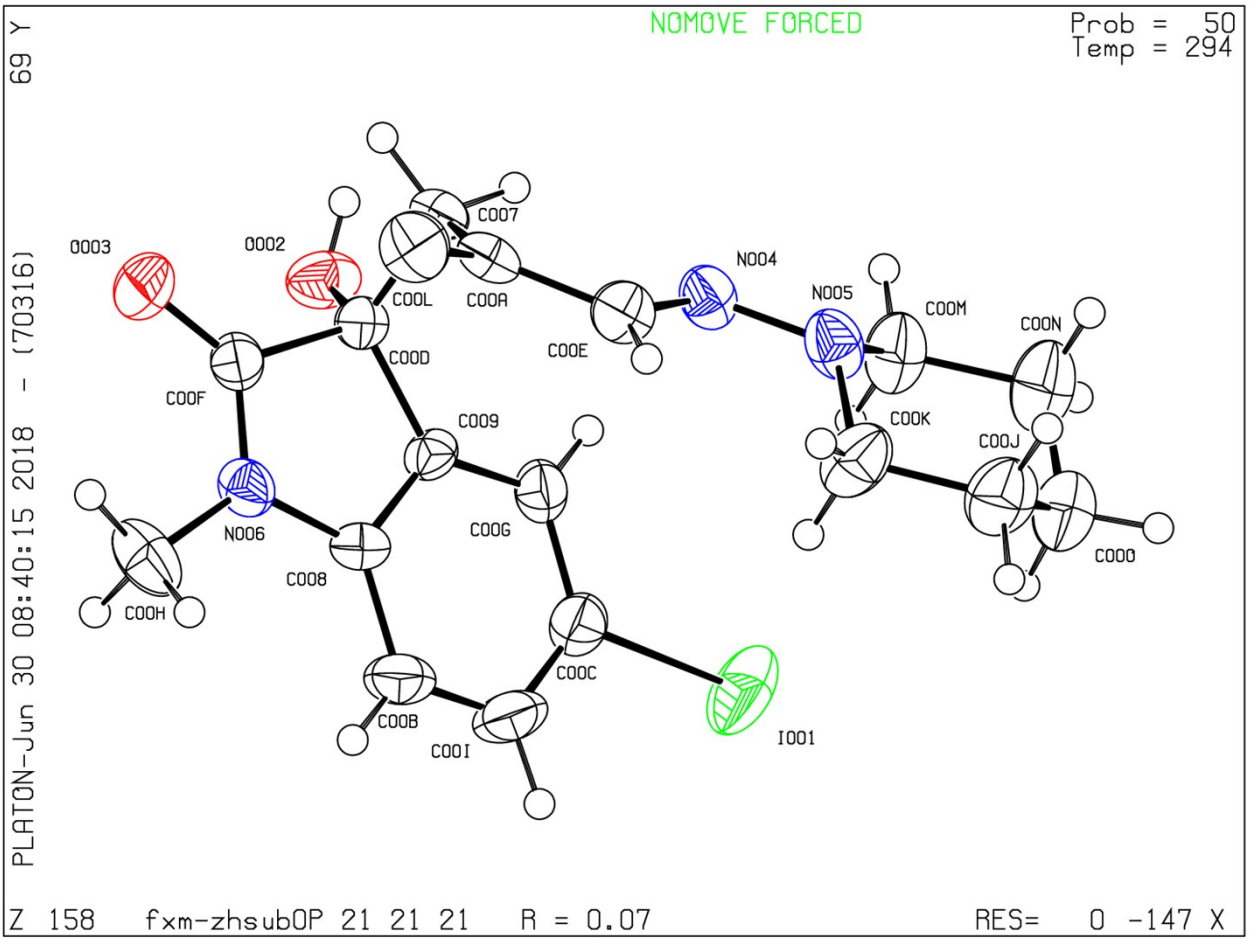


	Retention Time	Area	% Area
1	6.354	1449297	27.44
2	7.188	3832139	72.56

9 Determination of absolute configuration

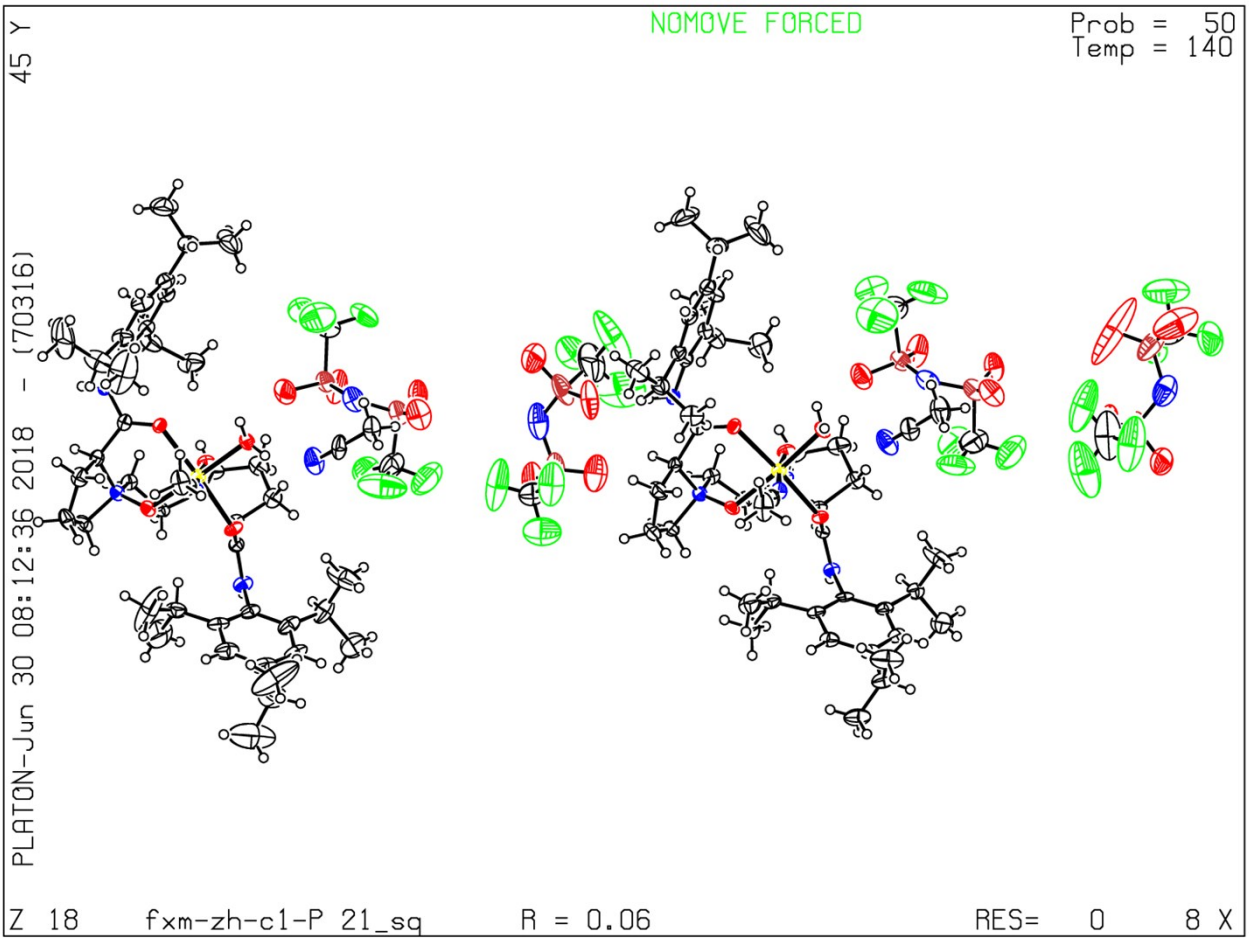
9.1 The X-ray structure of product 3o

The absolute configuration of the product **3o (*R*)** was determined by its X-ray crystal structure.
Single crystal of $C_{18}H_{22}IN_3O_2$ **3o** was recrystallized from mixed solvents of CH_2Cl_2 and petroleum ether. CCDC **1837158** contains the supplementary crystallographic data which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



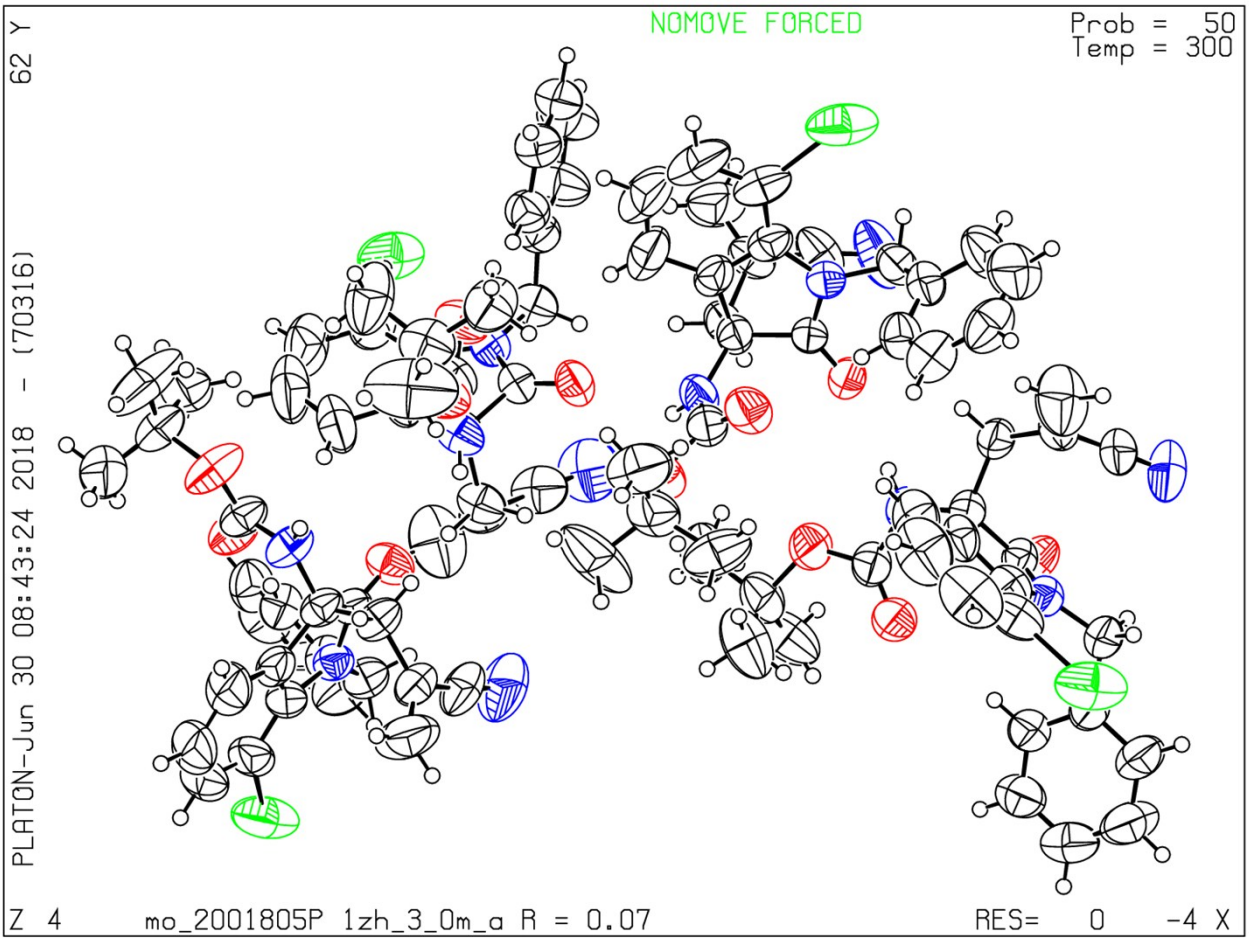
9.2 The X-ray structure of the $Zn(NTf_2)_2/L_2$-$PrPr_3$ complex

The absolute configuration of the complex **$Zn(NTf_2)_2/L_2$-$PrPr_3$** was determined by its X-ray crystal structure. CCDC **1837246** contains the supplementary crystallographic data which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



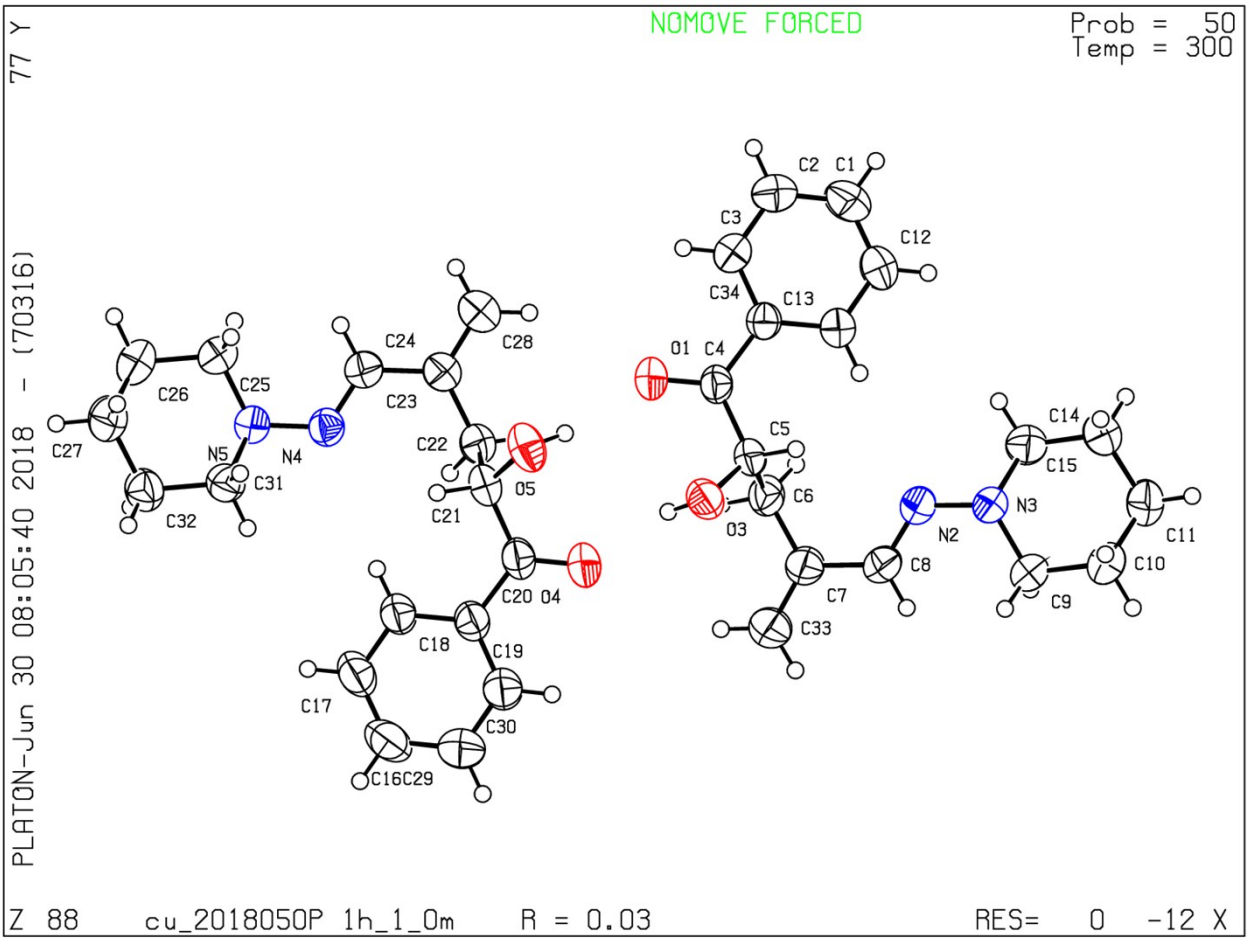
9.3 The X-ray structure of the product 6kk

The absolute configuration of the product **6kk (*S*)** was determined by its X-ray crystal structure. CCDC **1845392** contains the supplementary crystallographic data which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



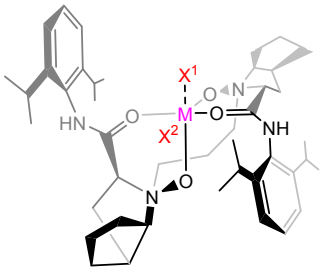
9.4 The X-ray structure of the product 7aa

The absolute configuration of the product **7aa (*S*)** was determined by its X-ray crystal structure. CCDC **1842770** contains the supplementary crystallographic data which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



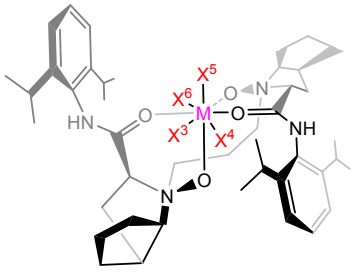
10 The study of mechanism

10.1 The steric conformation of our *N,N′*-dioxide-metal salt complexes



Type A

M = Mg, Ni, Co, Sc...



Type B

M = Gd, (Tm, Dy etc lanthanide metals)

The X-ray structure of chiral Mg^{II}/**L-RaPr$_2$**, Ni^{II}/**L-RaPr$_2$**, Co^{II}/**L-RaPr$_2$**, Sc^{III}/**L-RaPr$_2$**, Gd^{III}/**L-RaPr$_2$** complexes[5] have been obtained and delightly introduced in our precious reviews. (*Acc. Chem. Res.* **2011**, *44*, 574−587; **2017**, *50*, 2621–2631).

Type A

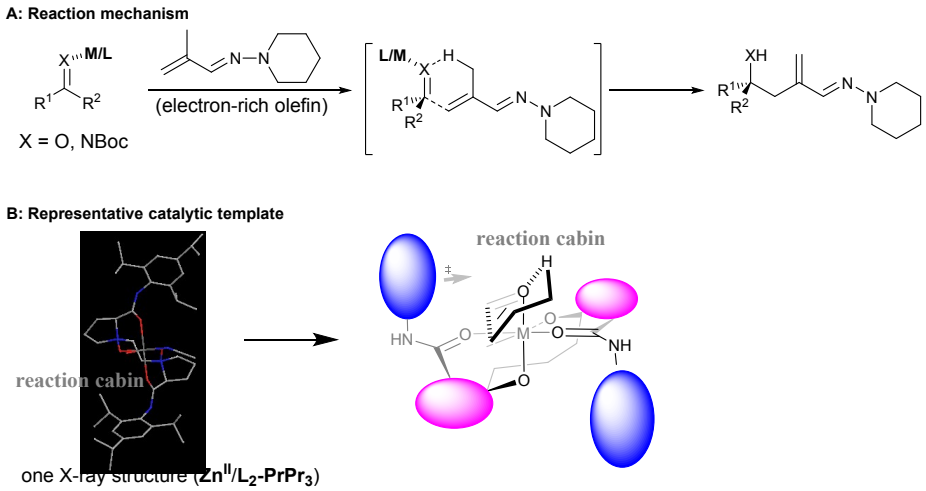
Ni^{II}/L-RaPr$_2$	Mg^{II}/L-RaPr$_2$	Sc^{III}/L-RaPr$_2$
(1)Ni-O (N-O), **2.00** Å;	(1)Mg/O (N-O), **2.01** Å;	(1)Sc-O (N-O), **2.03** Å;
(2) Ni-O (N-O), **2.02** Å;	(2) Mg/O (N-O), **2.02** Å;	(2) Sc-O (N-O), **2.06** Å;
(3) Ni-O (C=O), **2.05** Å;	(3) Mg/O (C=O), **2.04** Å;	(3) Sc-O (C=O), **2.09** Å;
(4) Ni-O (C=O), **2.08** Å;	(4) Mg/O (C=O), **2.06** Å;	(4) Sc-O (C=O), **2.12** Å;
(5) Ni-O (MeOH), 2.12 Å;	(5) Mg/O (OTf), 2.10 Å;	(5) Sc-O (OTf), 2.10 Å;
(6) Ni-O (H_2O), 2.09 Å	(6) Mg/O (H_2O), 2.06 Å	(6) Sc-O (H_2O), 2.13 Å

Type B

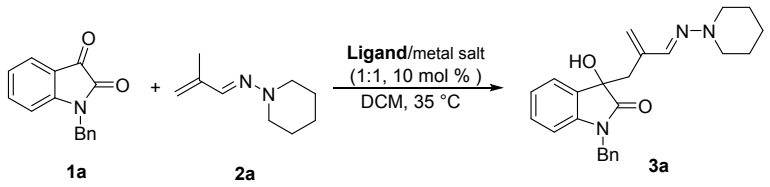
Gd^{III}/L-RaPr$_2$
(1) Gd-O (N-O), **2.27** Å;
(2) Gd-O (N-O), **2.27** Å;
(3) Gd-O (C=O), **2.46** Å;
(4) Gd-O (C=O), **2.40** Å;
(5) Gd-O (MeOH), 2.43 Å;
(6) Gd-O (MeOH), 2.43 Å;
(7) Gd-O (MeOH), 2.45 Å;
(8) Gd-O (OTf), 2.49 Å

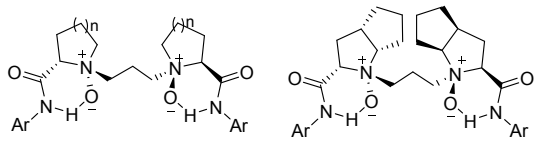
Bond length of the chiral *N,N′*-dioxide-metal salt complexes

10.2 The proposed reaction model



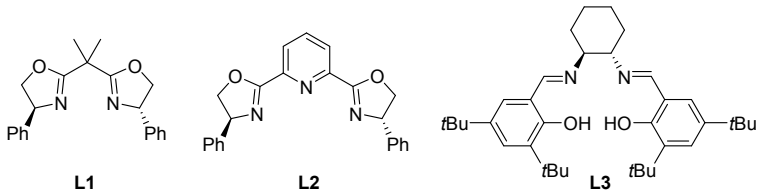
10.3 Control experiments





L-PrPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1
L-PiPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2

L-RaPr$_2$: Ar = 2,6-*i*Pr$_2$C$_6$H$_3$



L1 **L2** **L3**

entry[a]	metal salt	ligand	yield (%)[b]	ee (%)[c]
1	$Ni(OTf)_2$	**L-RaPr$_2$**	90	**98 (high)**
2	$Ni(OTf)_2$	**L1**	82	**–59**
3	$Ni(OTf)_2$	**L2**	59	0
4	$Ni(OTf)_2$	**L3**	60	0

[a] Unless otherwise stated, all reactions were performed with **1a** (0.1 mmol), **2a** (0.13 mmol), 5 Å MS (10 mg), H_2O (1 μL) and ligand/metal salt (1:1, 10 mol %) in CH_2Cl_2 (0.4 mL) at 35 °C for 36 h. [b] Yield of the isolated product. [c] Determined by HPLC.

10.4 Conclusion

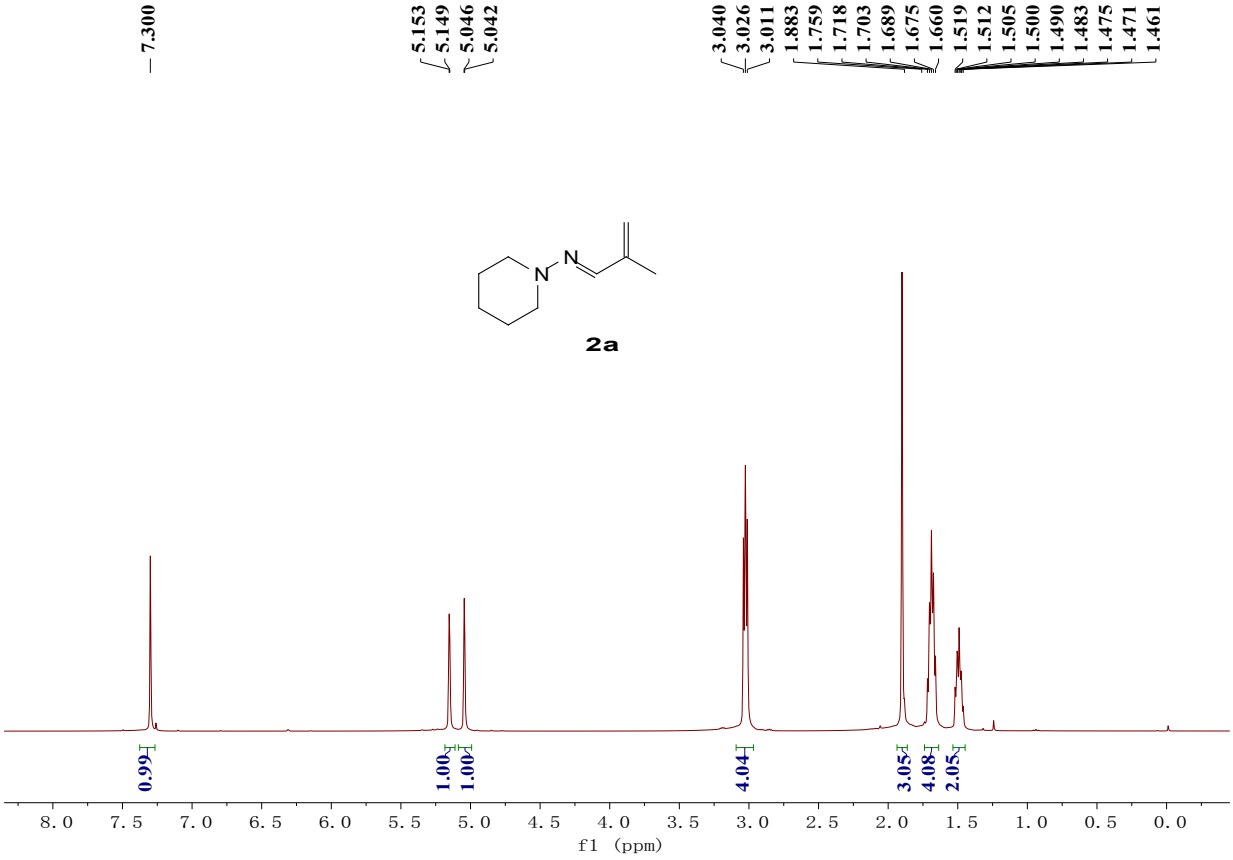
Based on a series of X-ray structure the *N,N′*-dioxide-metal salt complexes, some importand messages of the Lewis acid catalyst are obtained. (1) Firstly, central metal Mg^{II} (Sc^{III}, Ni^{II}, Co^{II}, Zn^{II}) and Gd^{III} (Tm^{III}, Dy^{III}, lanthanide metals) occupied in six- and eight-coordinated manners, respectively (Type **A** and Type **B**, see **10.1**). (2) The comparison of bond lengths between these two type catalysts, suggests the six-coordinated complexes possess more compacted space than eight-coordinated manners, which may result in different steric environment coordinating with substrates and give reciprocal configurations (see **5.5**).(3) The *N,N′*-dioxide ligand combine with Lewis acid metal salt in a quadridentate fashion and form a retractable space (more like a chiral cavity, see **10.2**), which allow to coornate various substrates, providing a good chirality-controlled environment.

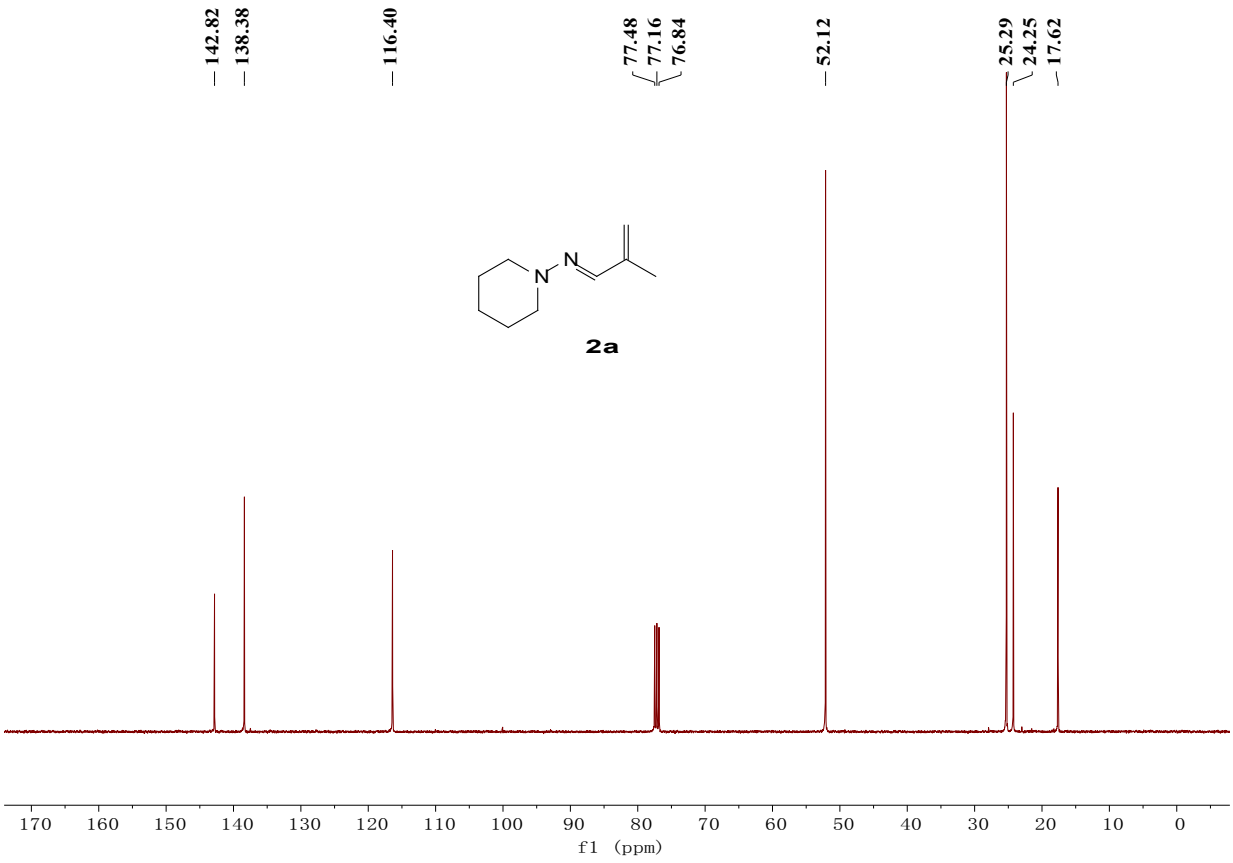
In this ene-type reaction, various electrophiles, like isatins, imines and aldehydes reacted with hydrazone may via a six-membered cyclic transition state in the chiral cavity of *N*,*N′*-dioxide-metal salt complexes with high enantioselectivity. Moreover, we also explored other ligands coordinated with $Ni(OTf)_2$ to catalyze these reactions, such as chiral oxazolin and Salen ligands, no better results were obtained (**10.3**). In compared with them (Ni^{II}/**L1**, Ni^{II}/**L2**, Ni^{II}/**L3**), our catalytic system can provide an adjustable cavity, which can accommodate different six-membered cyclic transition states in the ene-type reaction and achieve high selectivity and generality.

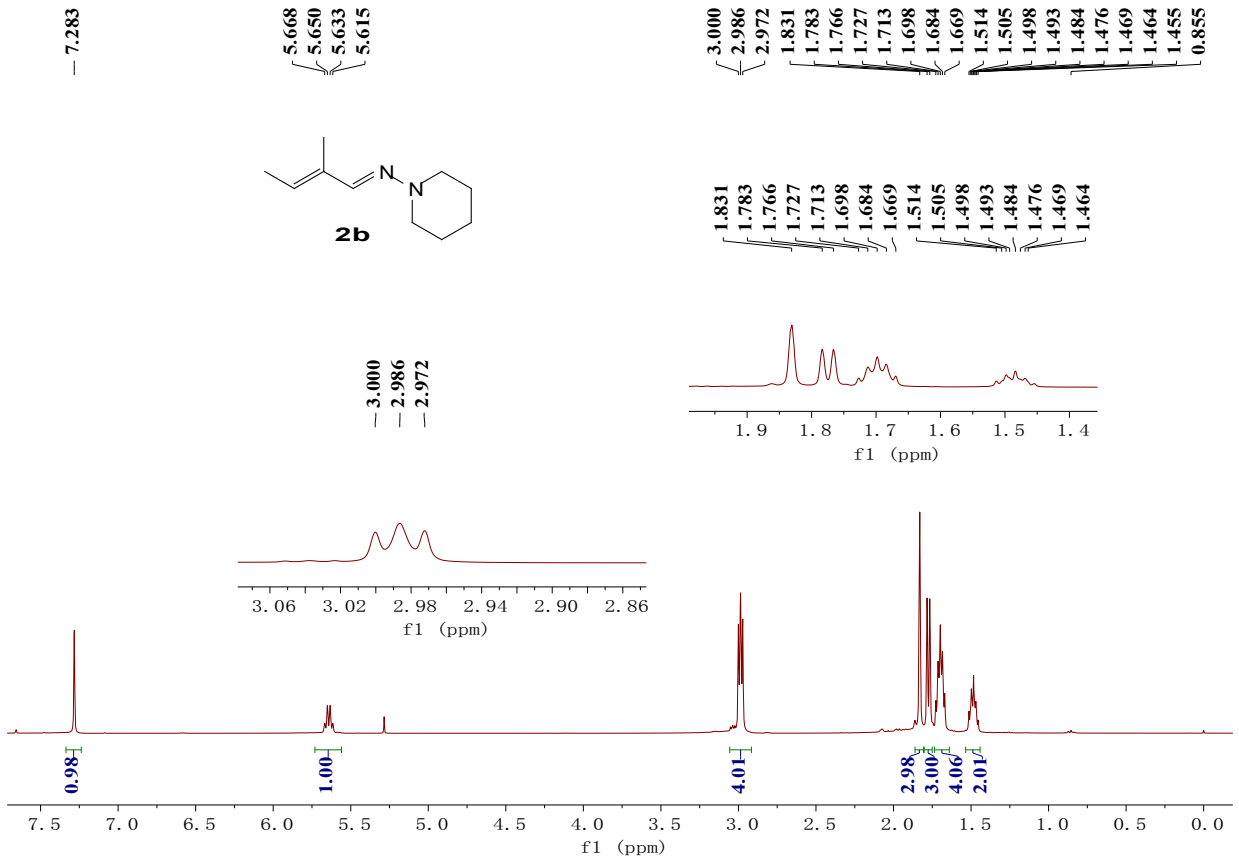
11. References

(1) Wen, Y. H.; Huang, X.; Huang, J. L.; Xiong, Y.; Qin, B.; Feng, X. M. *Synlett* **2005**, 2445.
(2) Hashimoto, T.; Kimura, H.; Maruoka, K. *Angew. Chem. Int. Ed.* **2010**, *49*, 6844–6847.
(3) Long, J.; Zhang, S. F.; Wang, P. P.; Zhang, X. M.; Yang, Z. J.; Zhang, Q.; Chen, Y. *J. Med. Chem.* **2014**, *57*, 7098−7112.
(4) Janecki, T.; Błaszczyk, E.; Studzian, K.; Różalski, M.; Krajewska, U.; Janecka, A. *J. Med. Chem.* **2002**, *45*, 1142−1145.
(5) CCDC:804337 (Mg^{II}/**L-RaPr$_2$**); CCDC:1035849 (Ni^{II}/**L-RaPr$_2$**); CCDC:882608 (Sc^{III}/**L-RaPr$_2$**); CCDC:1838115 (Mg^{II}/**L-PiPr$_2$**); CCDC:739905 (Ni^{II}/**L-PiPr$_2$**); CCDC:704000 (Sc^{III}/**L-PrPr$_2$**); CCDC:1828765 (Gd^{III}/**L-RaPr$_2$**); CCDC:1843378 (Tm^{III}/ent-**L-PiEt$_2$Br**); CCDC: 1861706 (Dy^{III}/**L-PiPr$_2$**).

12. Copies of NMR spectra for substrates and products






7.283
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5.650
5.633
5.615
3.000
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2.972
1.831
1.783
1.766
1.727
1.713
1.698
1.684
1.669
1.514
1.505
1.498
1.493
1.484
1.476
1.469
1.464
1.455
0.855
2b
f1 (ppm)
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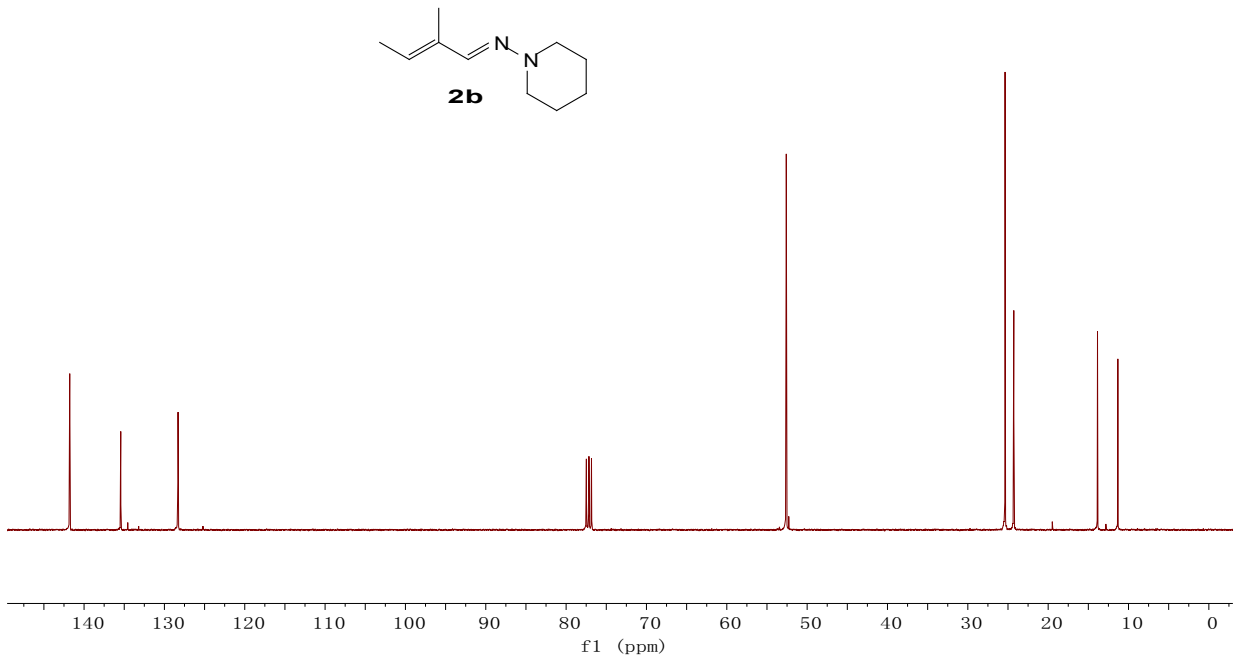
1.00
4.01
2.98
3.00
4.06
2.01


141.78
135.43
128.30
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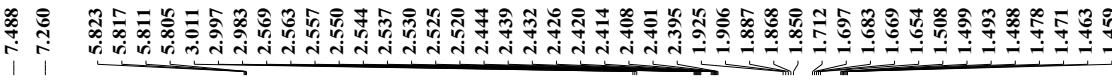
77.16
76.84
52.60
25.36
24.28
13.86
11.33
2b
f1 (ppm)


7.488
7.260
5.823
5.817
5.811
5.805
3.011
2.997
2.983
2.569
2.563
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2.525
2.520
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2.439
2.432
2.426
2.420
2.414
2.408
2.401
2.395
1.925
1.906
1.887
1.868
1.850
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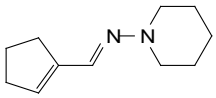
1.471
1.463



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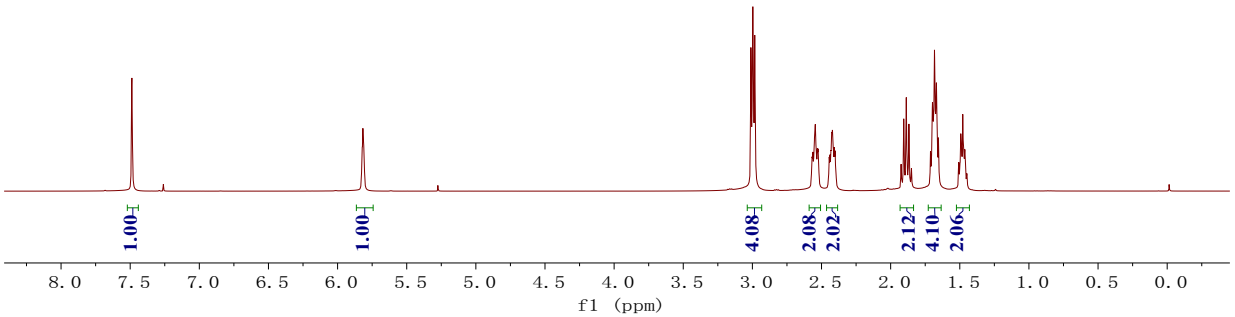
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2.06
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7.0
6.5
6.0
5.5
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4.5
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3.5
3.0
2.5
2.0
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1.0
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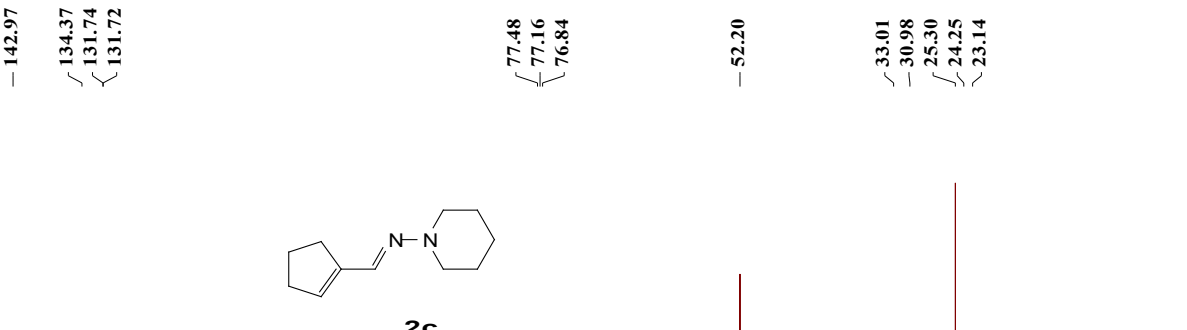
0.0
f1 (ppm)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77.16
76.84
52.20
33.01
30.98
25.30
24.25
23.14

2c

50
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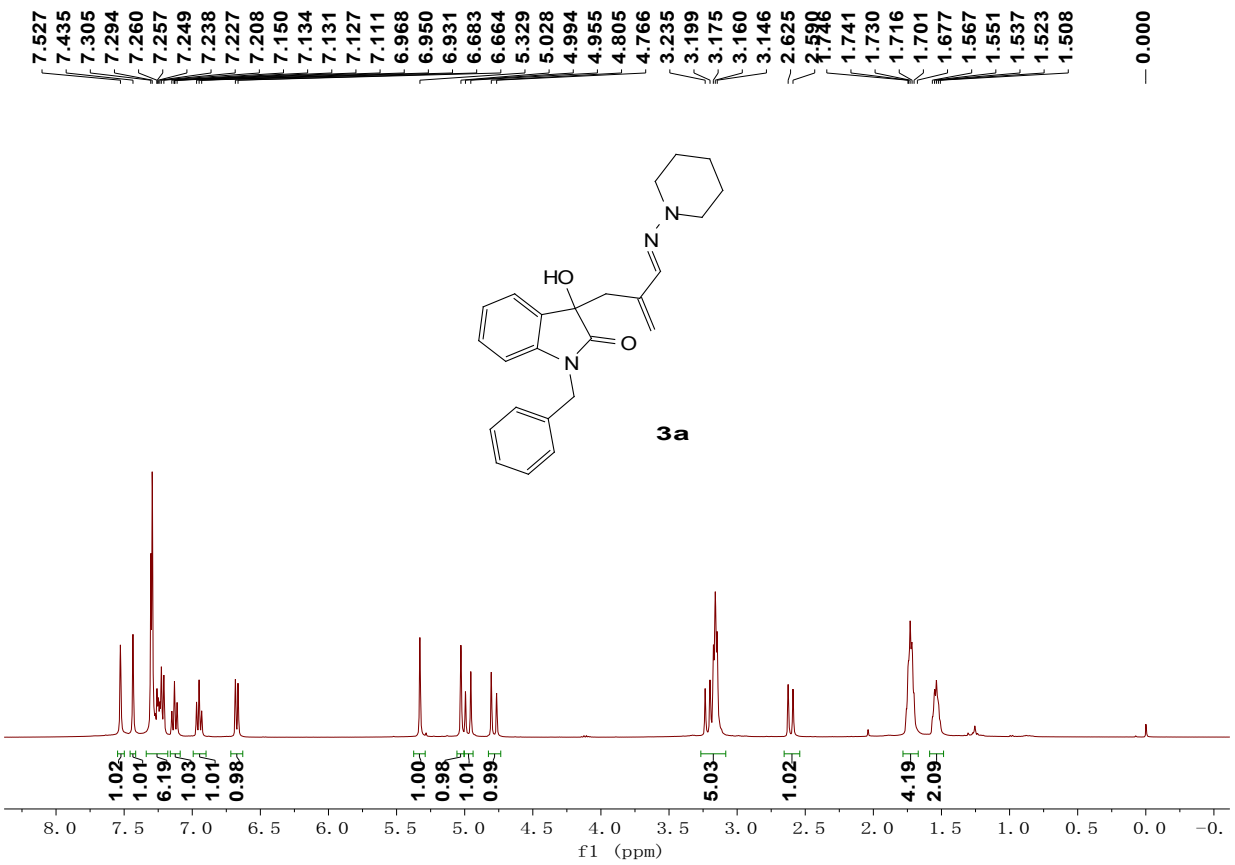
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.131
7.127
7.111
6.968
6.950
6.931
6.683
6.664
5.329
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4.994
4.955
4.805
4.766
3.235
3.199
3.175
3.160
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1.716
1.701
1.677
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1.551
1.537
1.523
1.508
0.000
HO
O
N
3a
1.02
1.01
6.19
1.03
1.01
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1.00
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1.01
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1.02
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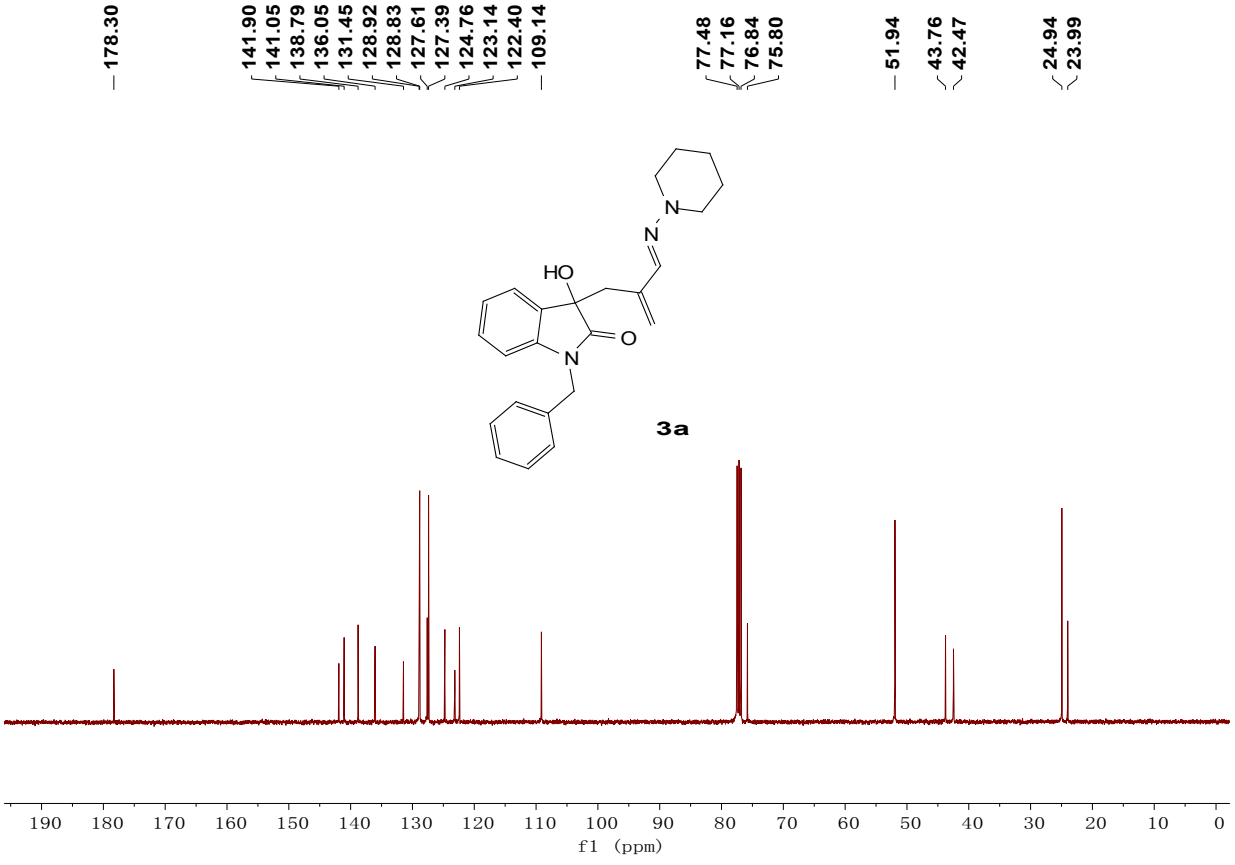
2.09
f1 (ppm)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141.05
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128.83
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123.14
122.40
109.14
77.48
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75.80
51.94
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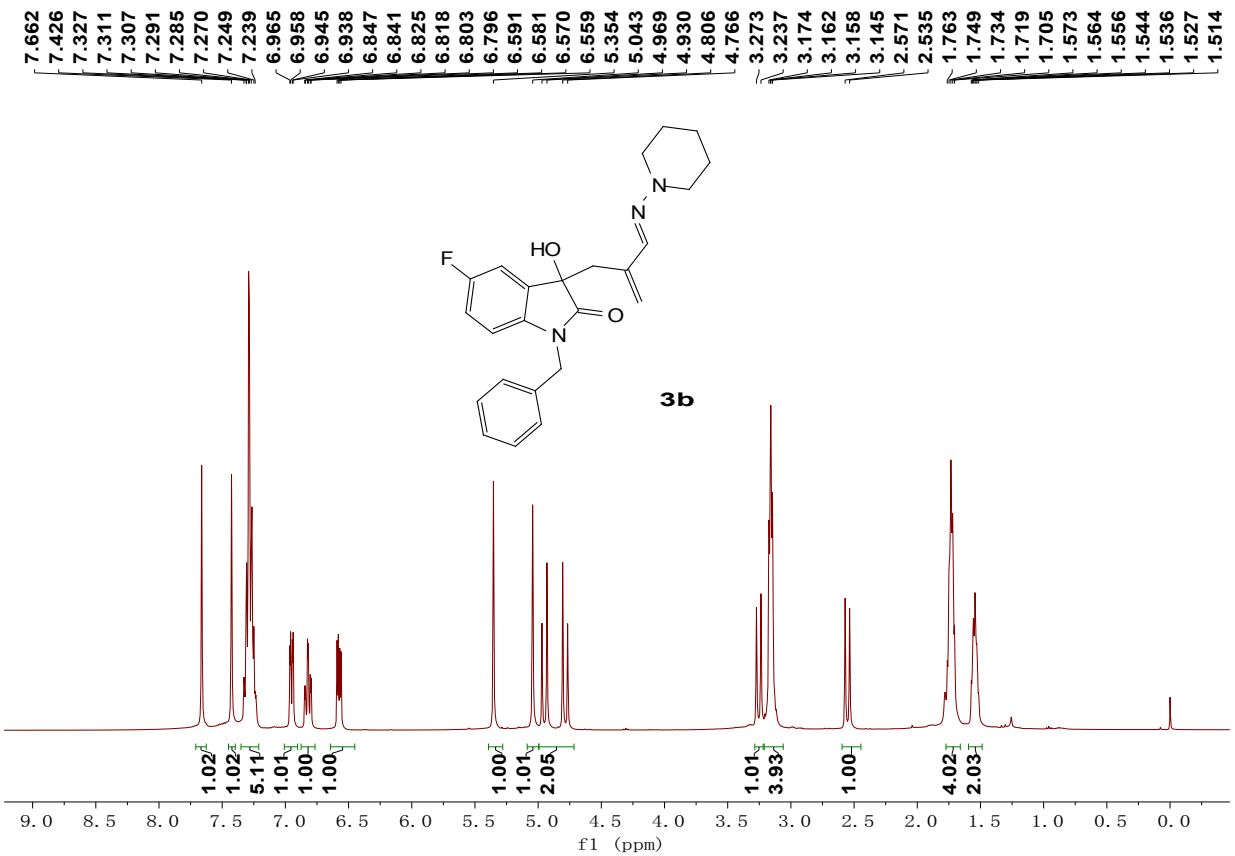
24.94
23.99
HO
O
N
3a
f1 (ppm)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7.285
7.270
7.249
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6.958
6.945
6.938
6.847
6.841
6.825
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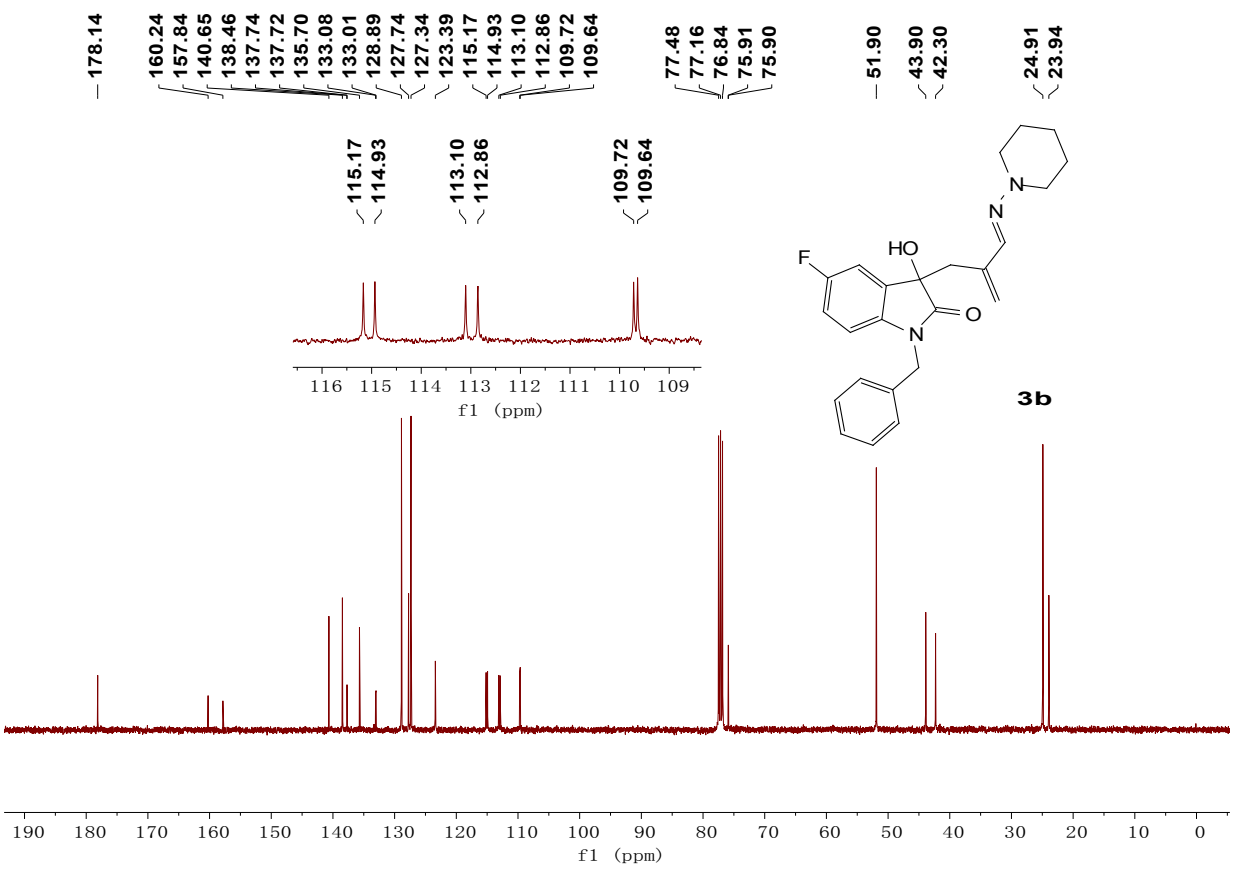
6.803
6.796
6.591
6.581
6.570
6.559
6.354
5.043
4.969
4.930
4.806
4.766
3.273
3.237
3.174
3.162
3.158
3.145
2.571
2.535
1.763
1.749
1.734
1.719
1.705
1.573
1.564
1.556
1.544
1.536
1.527
1.514
F
HO
O
N
N
N
3b
1.02
1.02
5.11
1.01
1.00
1.00
1.00
1.01
2.05
1.01
3.93
1.00
4.02
2.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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135.70
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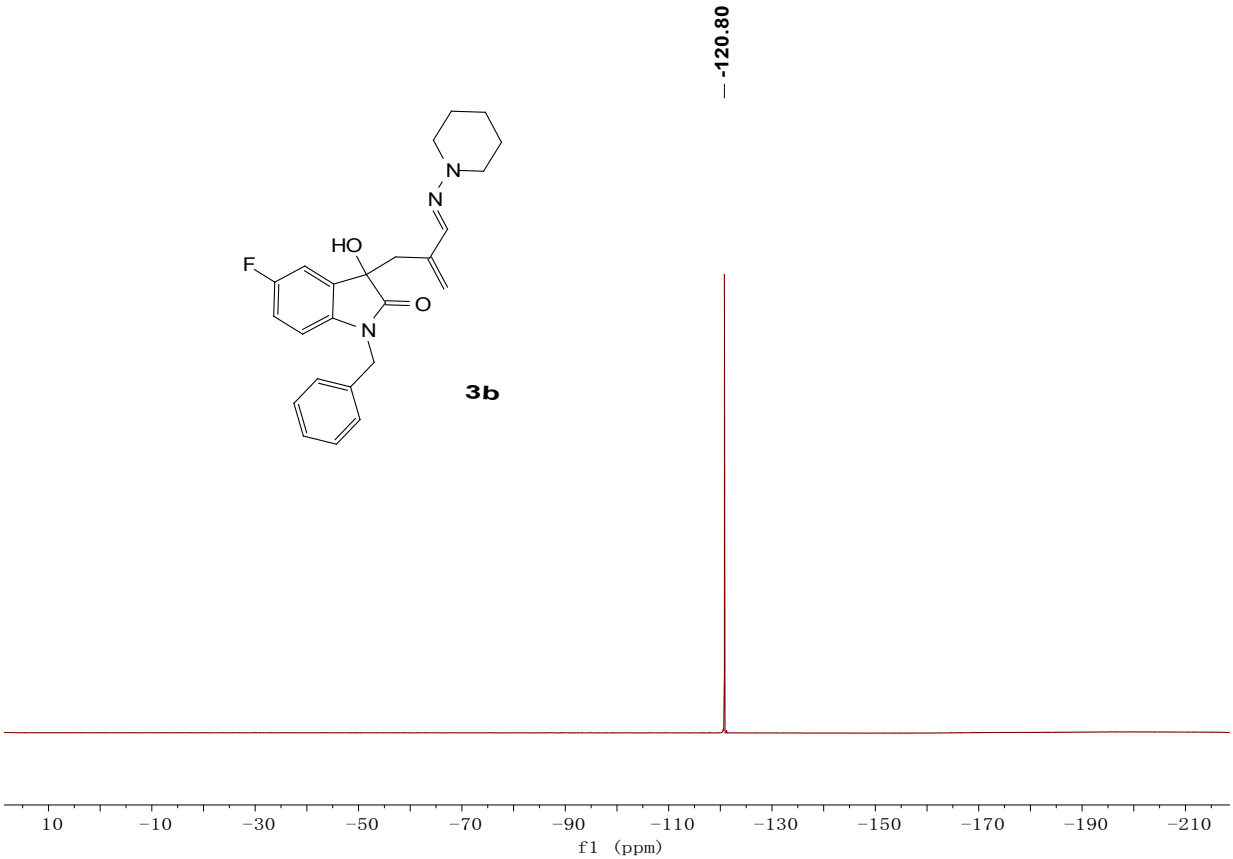
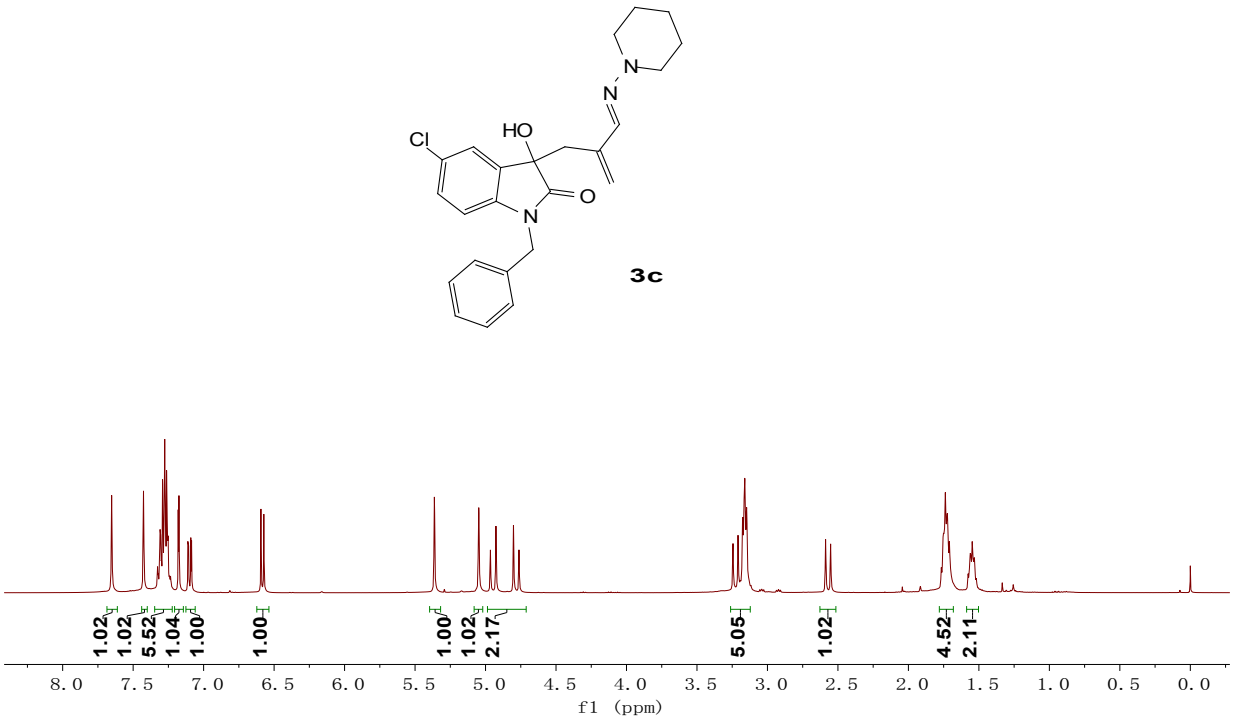
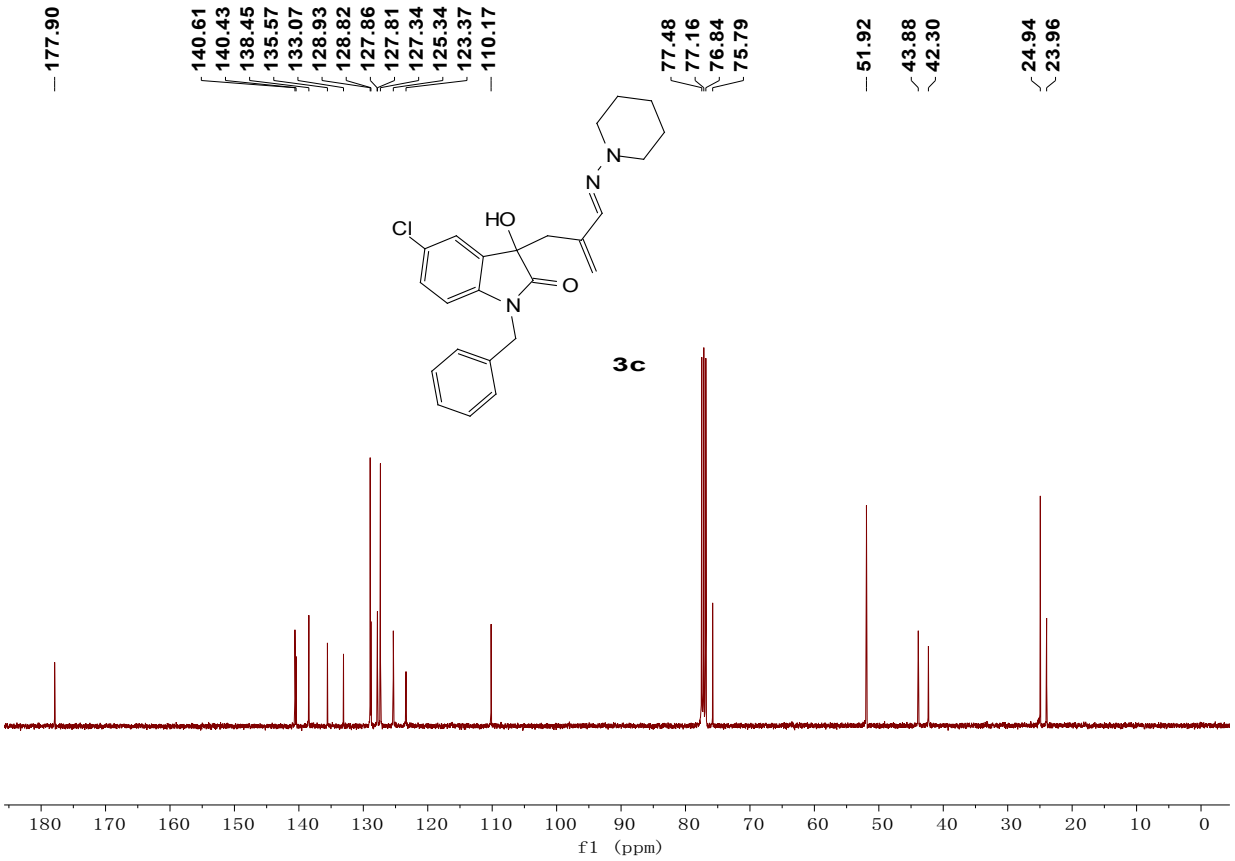
127.74
127.34
123.39
115.17
114.93
113.10
112.86
109.72
109.64
77.48
77.16
76.84
75.91
75.90
51.90
43.90
42.30
24.91
23.94
115.17
114.93
113.10
112.86
109.72
109.64
116 115 114 113 112 111 110 109
f1 (ppm)
F
HO
O
N
N
N
3b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



7.653 7.427 7.327 7.312 7.309 7.305 7.299 7.291 7.276 7.270 7.259 7.252 7.180 7.175 7.112 7.106 7.091 7.086 6.594 6.573 5.364 5.048 4.965 4.926 4.802 4.763 3.244 3.209 3.178 3.175 3.165 3.160 3.150 3.146 2.587 2.552 1.767 1.752 1.738 1.728 1.723 1.719 1.709 1.568 1.562 1.557 1.547 1.540 1.532 -0.000

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140.43
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135.57
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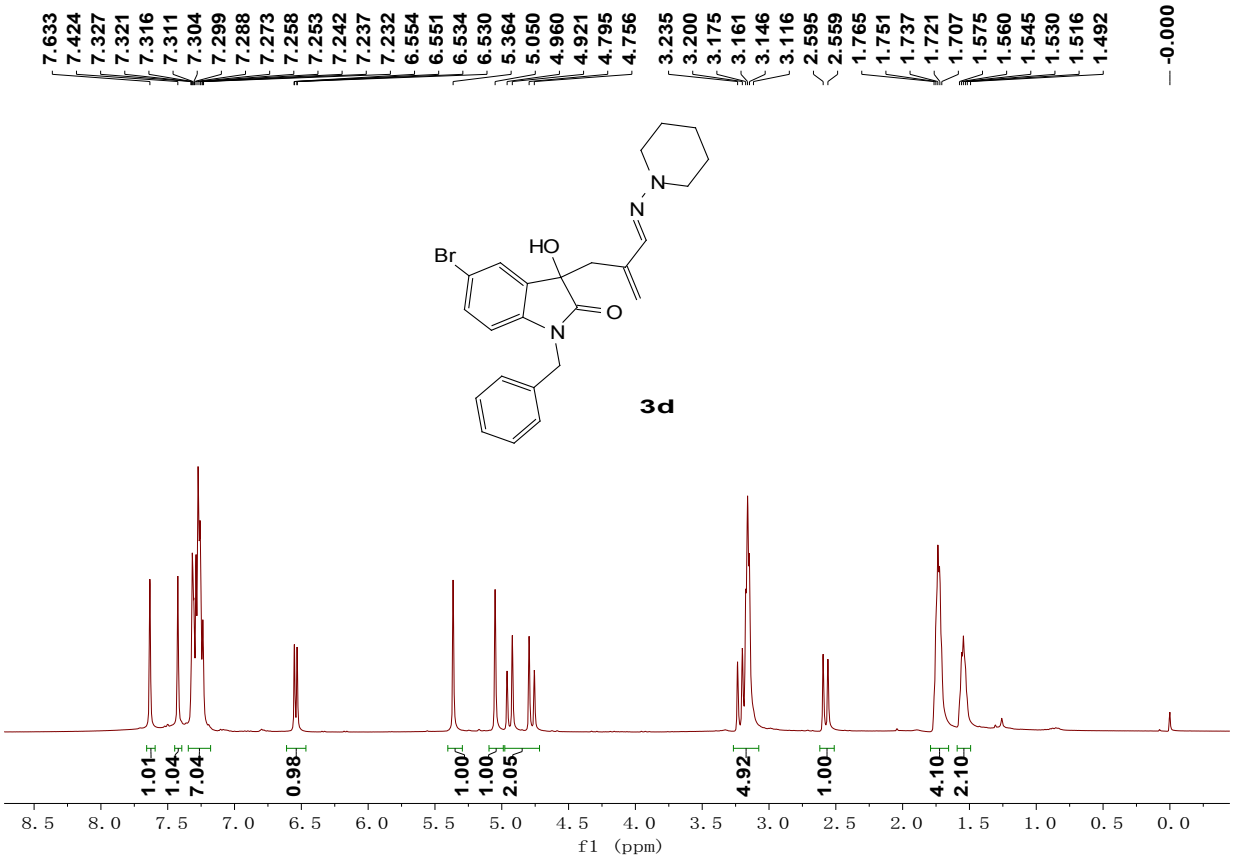
128.93
128.82
127.86
127.81
127.34
125.34
123.37
110.17
77.48
77.16
76.84
75.79
51.92
43.88
42.30
24.94
23.96
Cl
HO
N
N
O
N
3c
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.258
7.253
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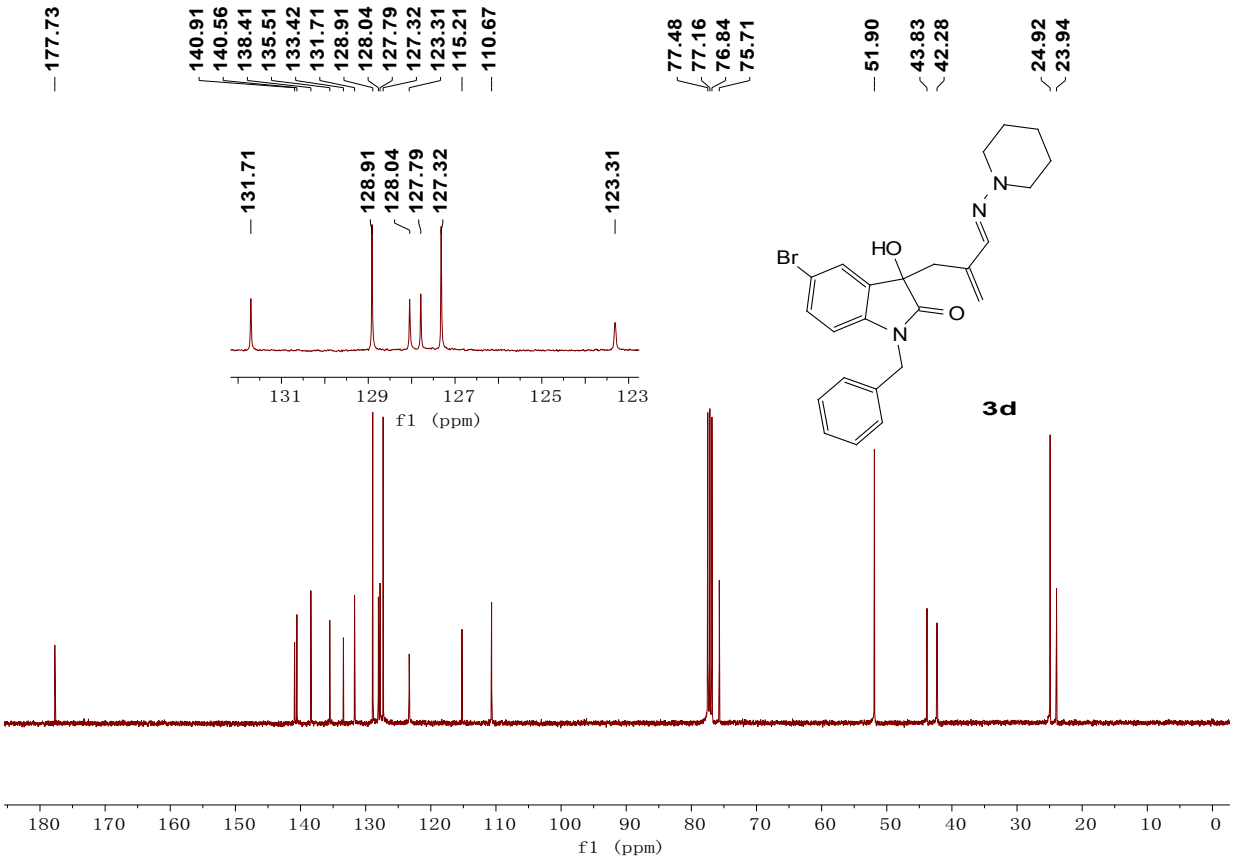
7.237
7.232
6.554
6.551
6.534
6.530
5.364
5.050
4.960
4.921
4.795
4.756
3.235
3.200
3.175
3.161
3.146
3.116
2.595
2.559
1.765
1.751
1.737
1.721
1.707
1.575
1.560
1.545
1.530
1.516
1.492
-0.000
Br
HO
N
N
O
N
3d
1.01
1.04
7.04
0.98
1.00
1.00
2.05
4.92
1.00
4.10
2.10
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.91
128.04
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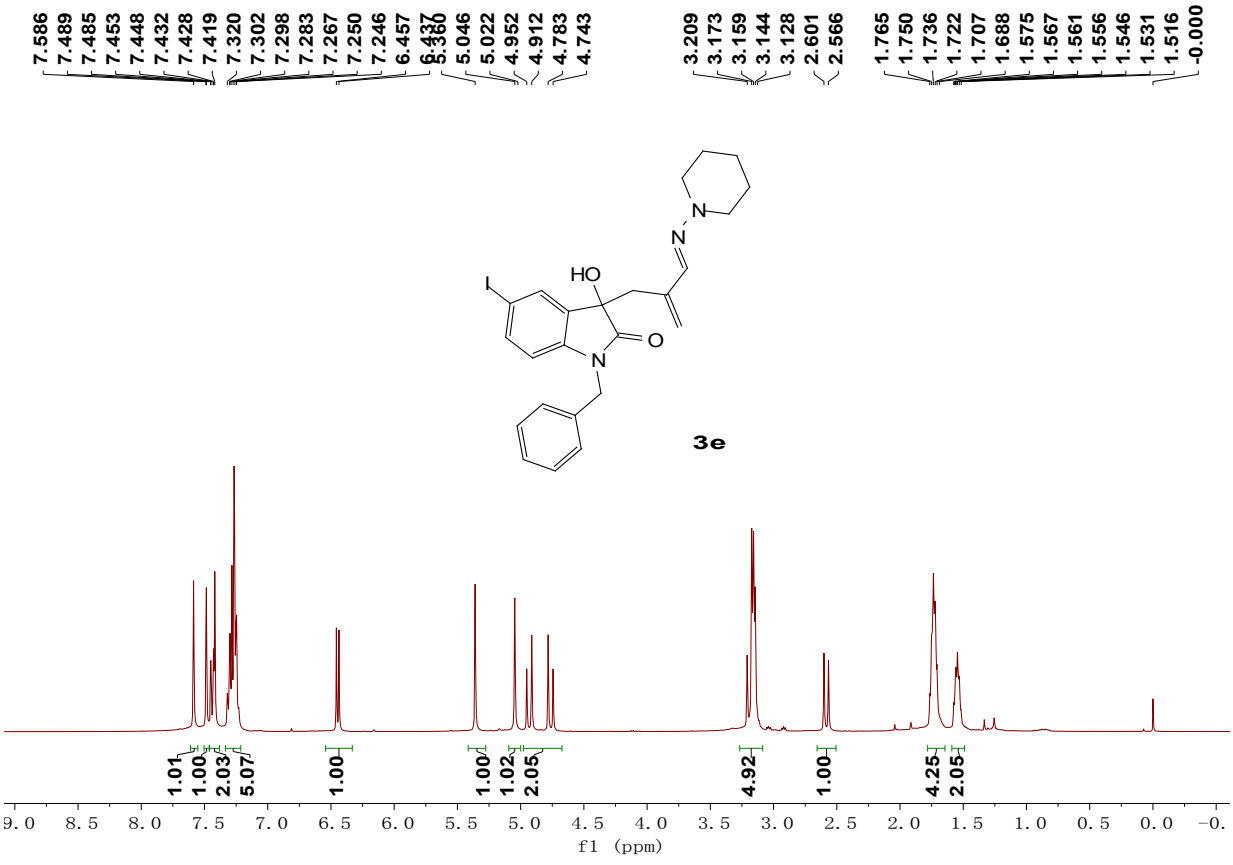
127.32
123.31
115.21
110.67
77.48
77.16
76.84
75.71
51.90
43.83
42.28
24.92
23.94
131.71
128.91
128.04
127.79
127.32
123.31
131
129
127
125
123
f1 (ppm)
Br
HO
O
N
N
3d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.298
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7.267
7.250
7.246
6.457
6.437
6.380
5.046
5.022
4.952
4.912
4.783
4.743
3.209
3.173
3.159
3.144
3.128
2.601
2.566
1.765
1.750
1.736
1.722
1.707
1.688
1.575
1.567
1.561
1.556
1.546
1.531
1.516
-0.000
I
HO
O
N
N
3e
1.01
1.00
2.03
5.07
1.00
1.00
1.02
2.05
4.92
1.00
4.25
2.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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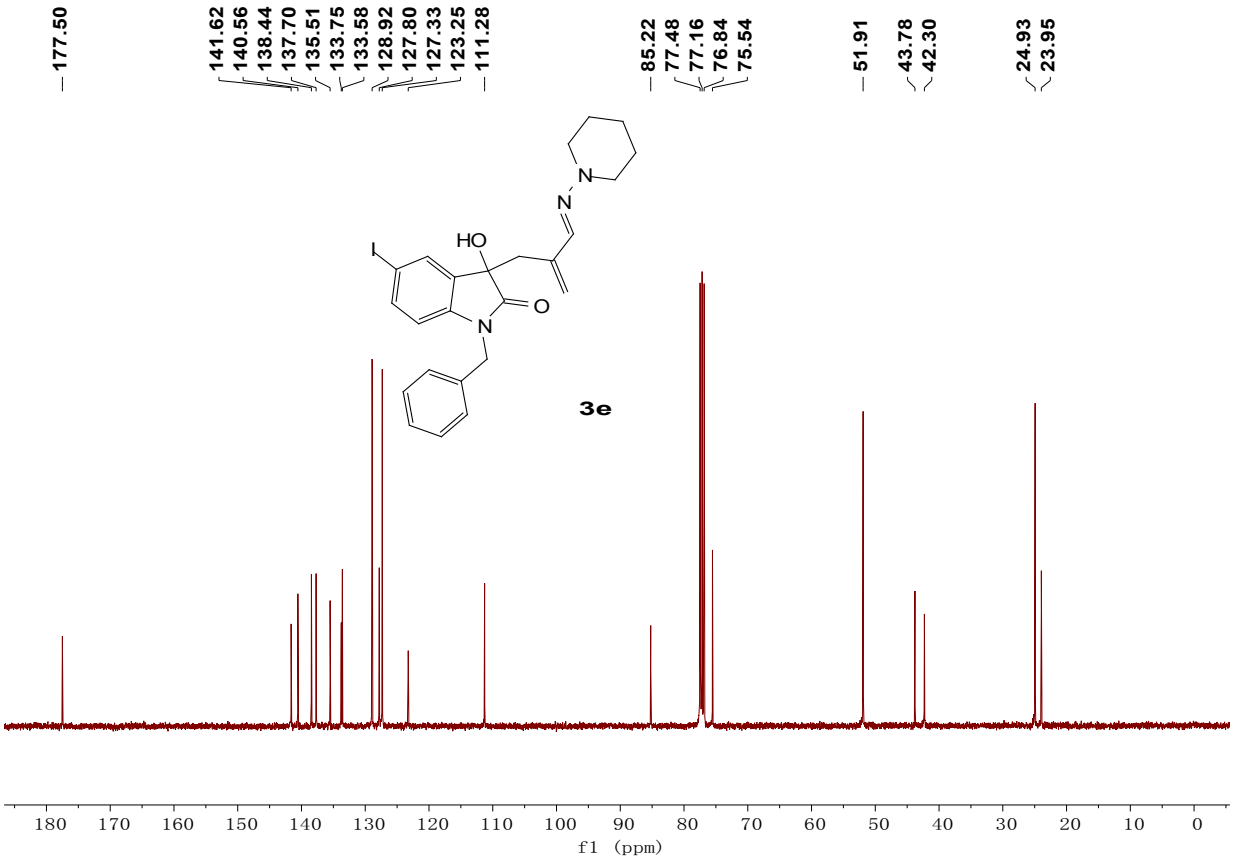
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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133.58
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127.33
123.25
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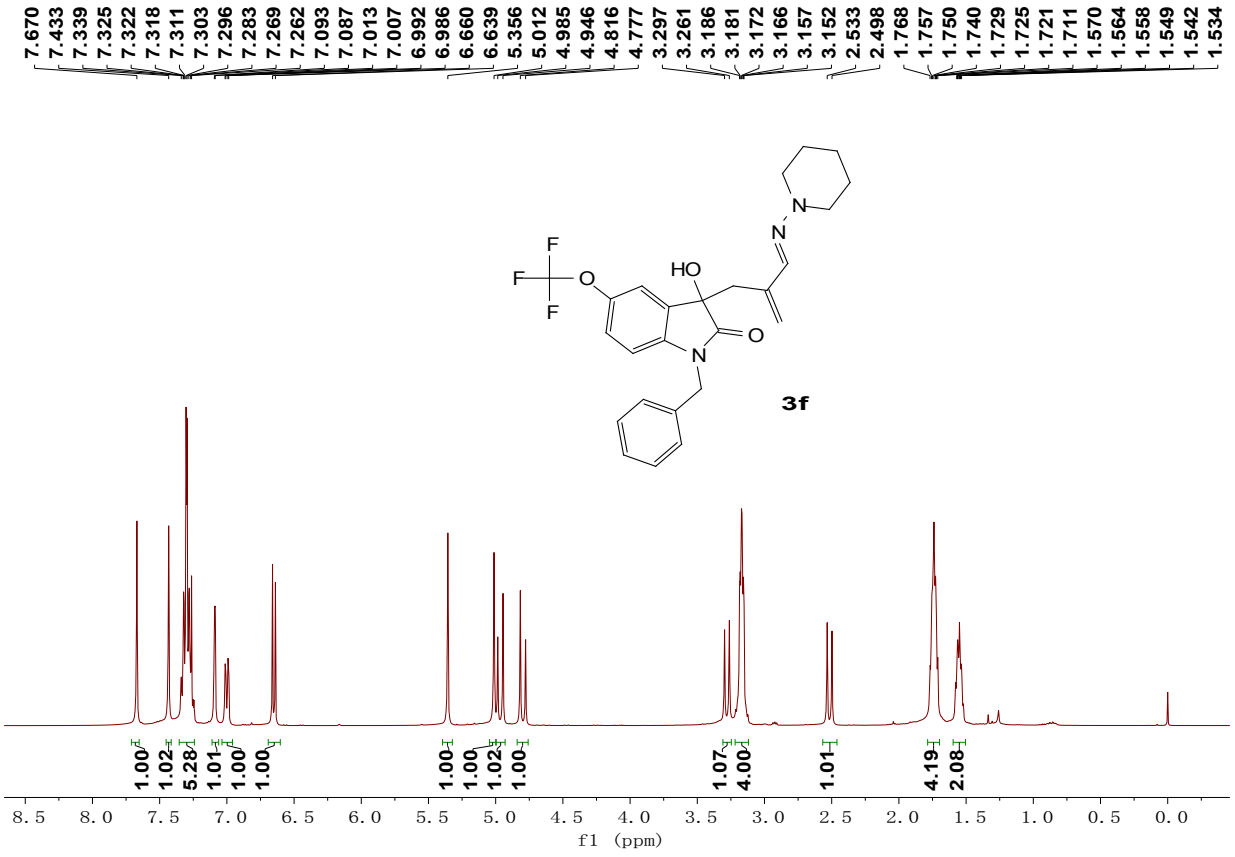
85.22
77.48
77.16
76.84
75.54
51.91
43.78
42.30
24.93
23.95
HO
I
O
N
N
N
3e
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.087
7.013
7.007
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6.660
6.639
5.356
5.012
4.985
4.946
4.816
4.777
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3.261
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3.181
3.172
3.166
3.157
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1.757
1.750
1.740
1.729
1.725
1.721
1.711
1.570
1.564
1.558
1.549
1.542
1.534
F
F
F
O
HO
O
N
N
N
3f
1.00
1.02
5.28
1.01
1.00
1.00
1.00
1.00
1.02
1.00
1.07
4.00
1.01
4.19
2.08
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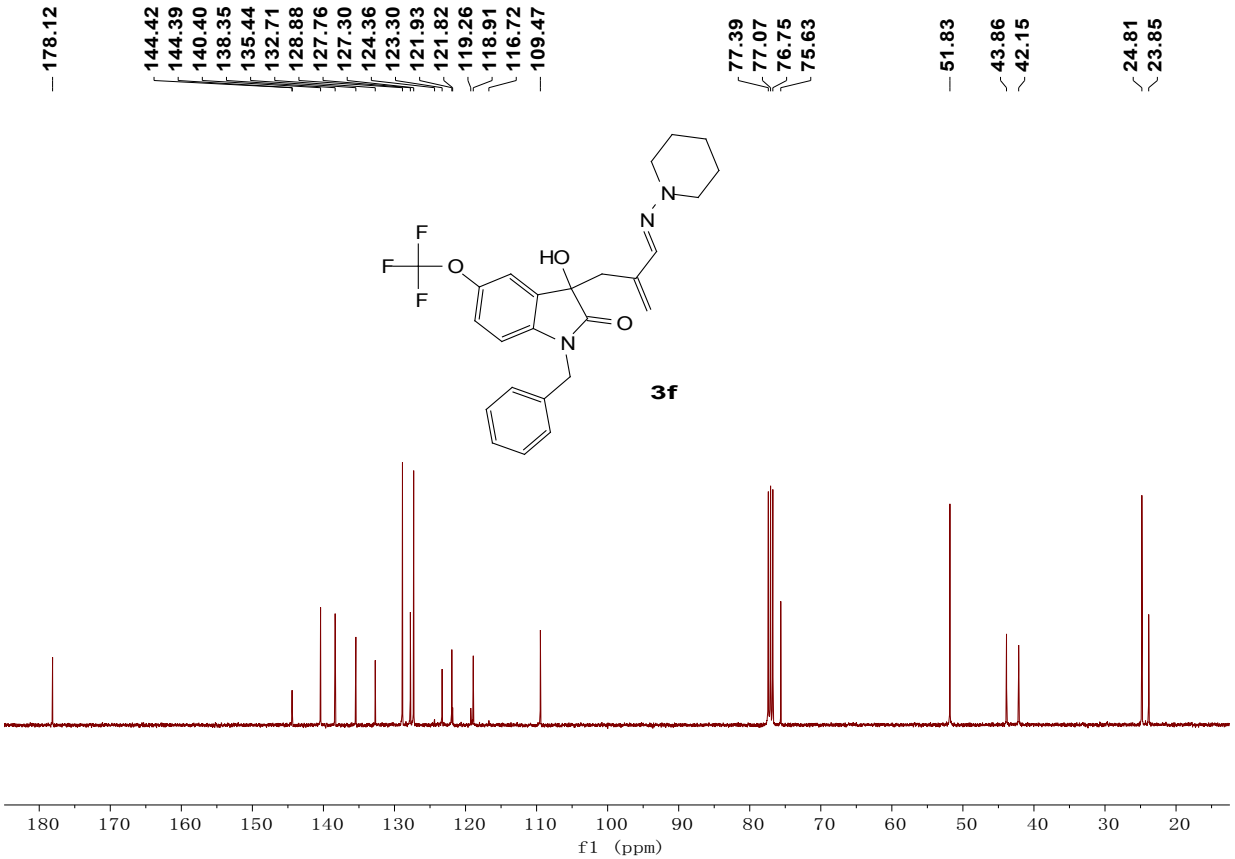
f1 (ppm)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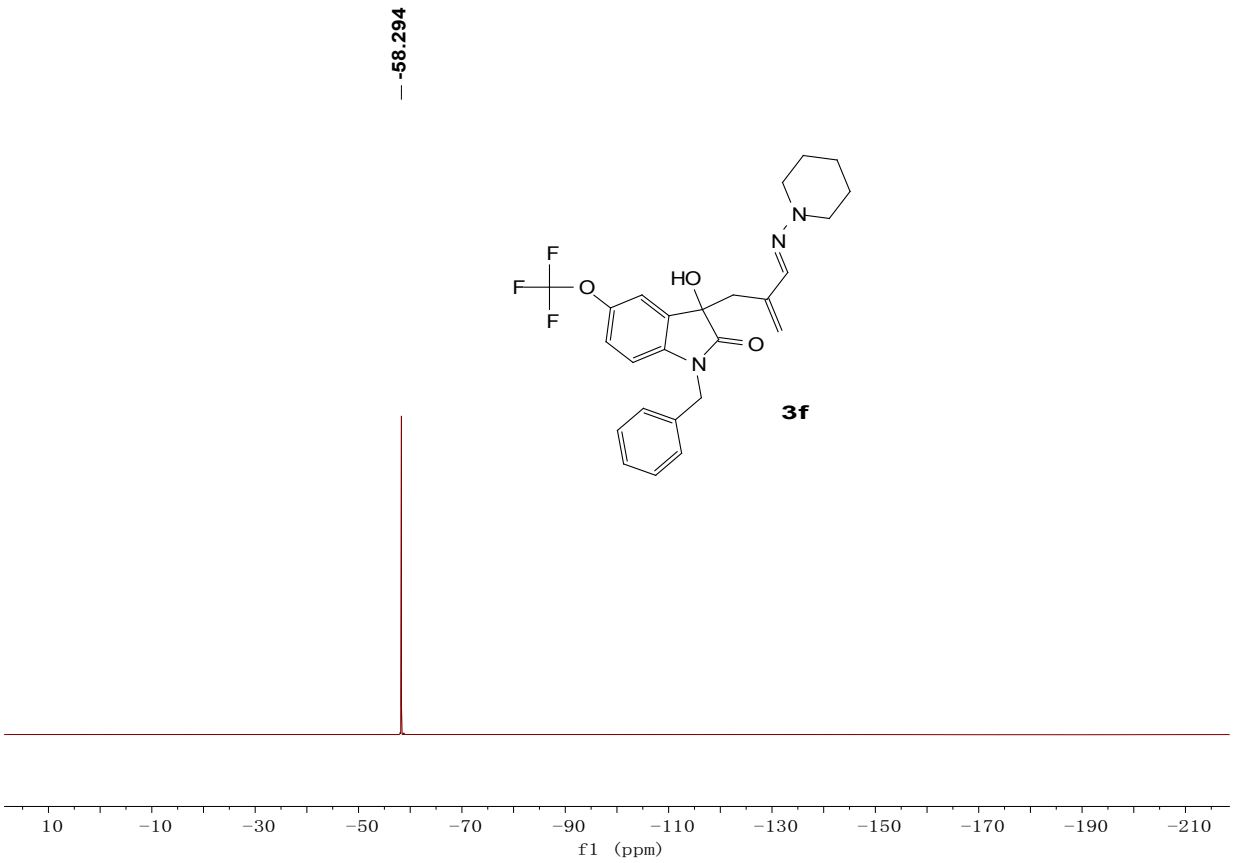
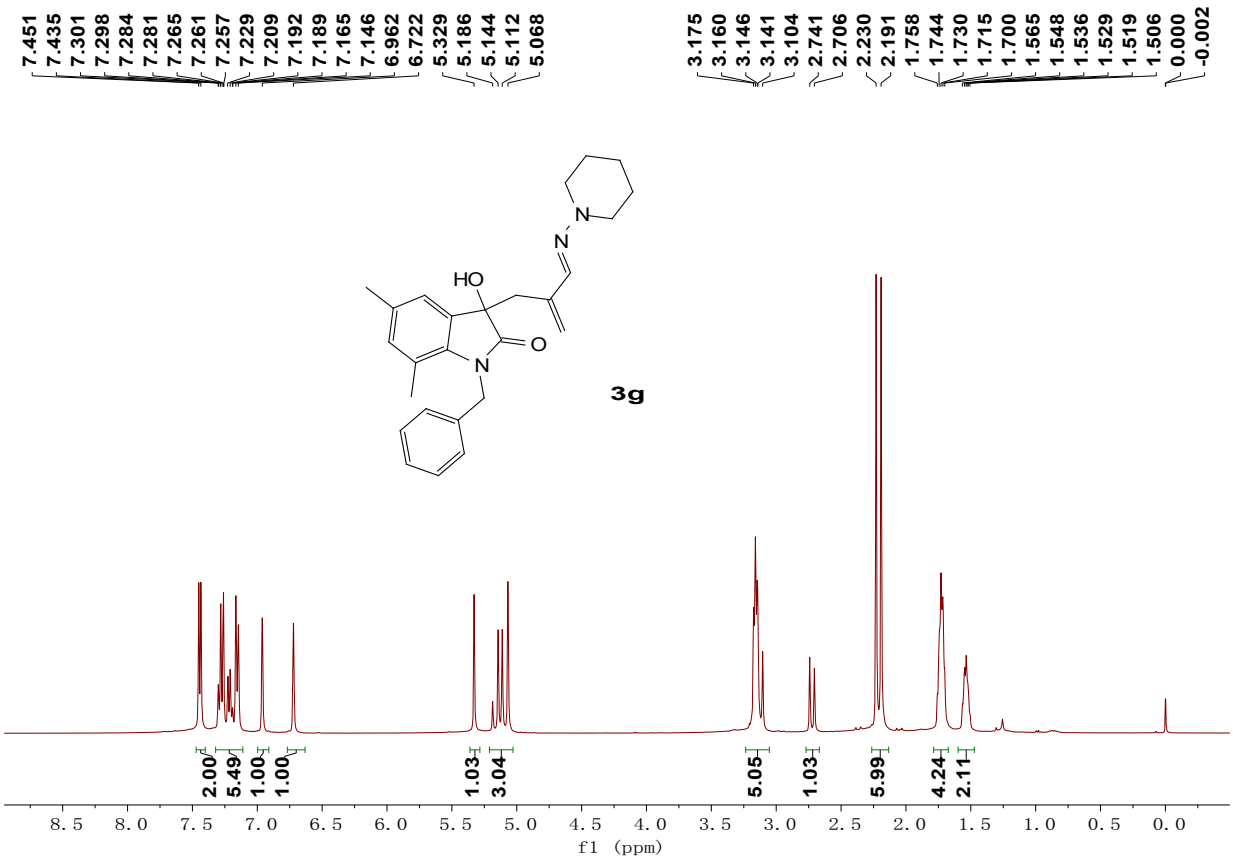
127.30
124.36
123.30
121.93
121.82
119.26
118.91
116.72
109.47
77.39
77.07
76.75
75.63
51.83
43.86
42.15
24.81
23.85
F
F
F
O
HO
N
N
O
N
3f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


-58.294
F
F
F
O
HO
N
N
O
N
3f
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
f1 (ppm)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7.189
7.165
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6.962
6.722
5.329
5.186
5.144
5.112
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3.160
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2.706
2.230
2.191
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1.700
1.565
1.548
1.536
1.529
1.519
1.506
0.000
-0.002
HO
O
N
N
N
3g
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1.00
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1.03
5.99
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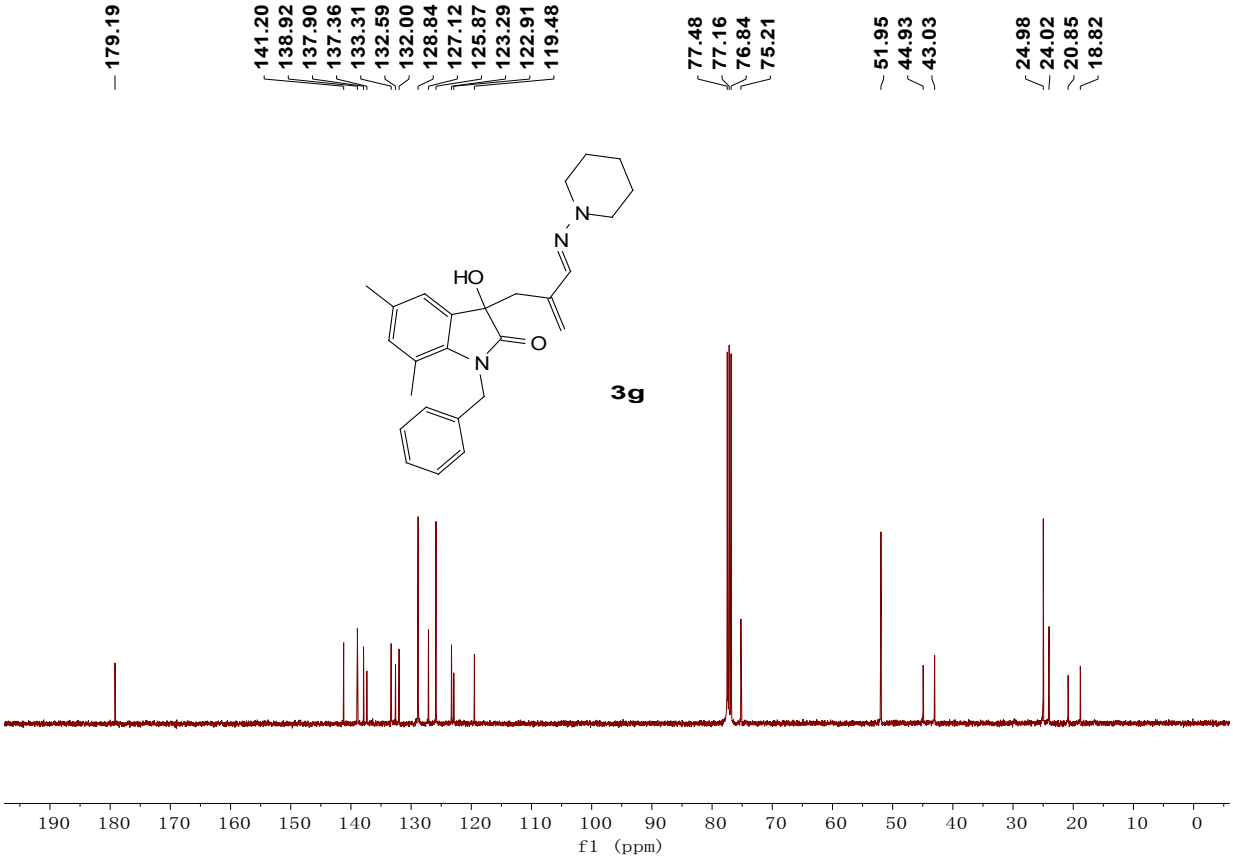
2.11
f1 (ppm)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123.29
122.91
119.48
77.48
77.16
76.84
75.21
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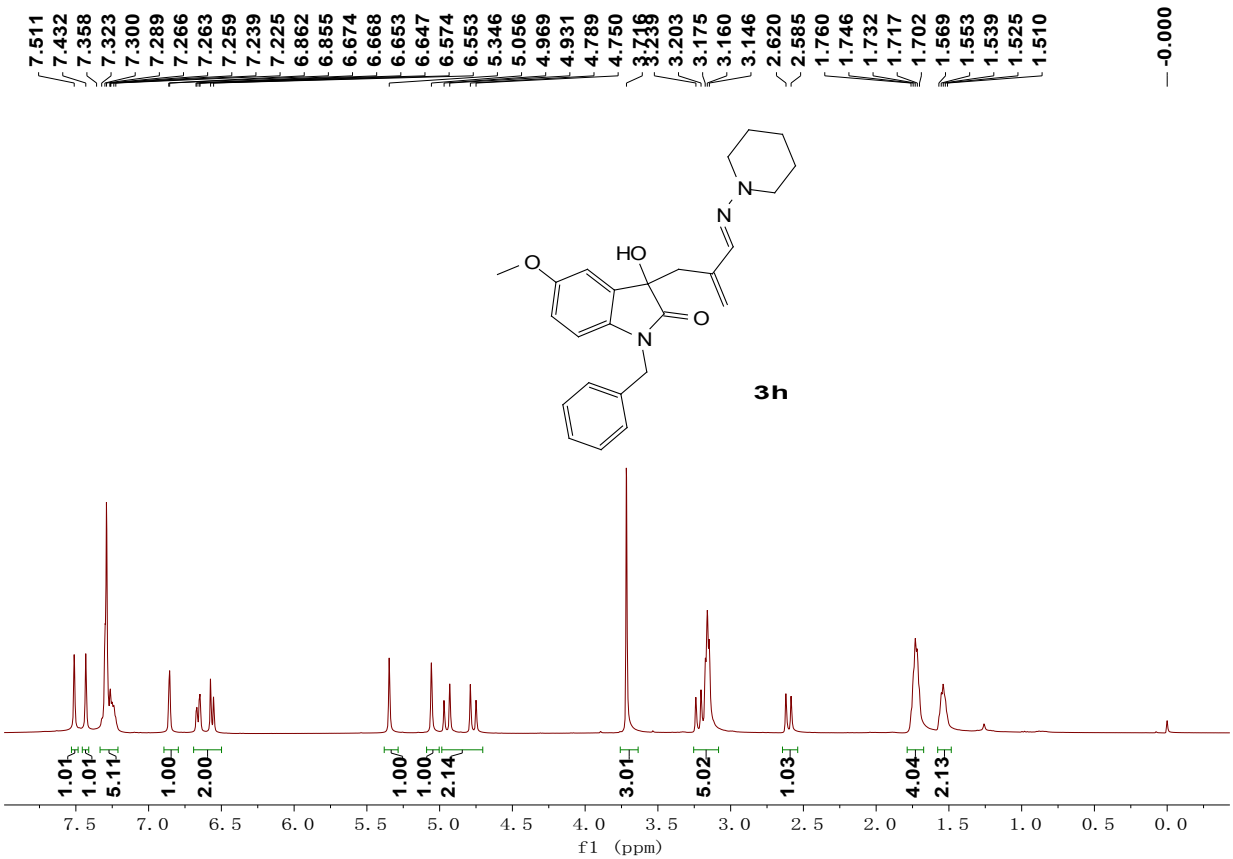
24.02
20.85
18.82
HO
O
N
N
N
3g
f1 (ppm)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6.674
6.668
6.653
6.647
6.574
6.553
5.346
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4.931
4.789
4.750
3.239
3.203
3.175
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1.553
1.539
1.525
1.510
-0.000
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O
N
O
N
3h
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1.01
5.11
1.00
2.00
1.00
1.00
2.14
3.01
5.02
1.03
4.04
2.13
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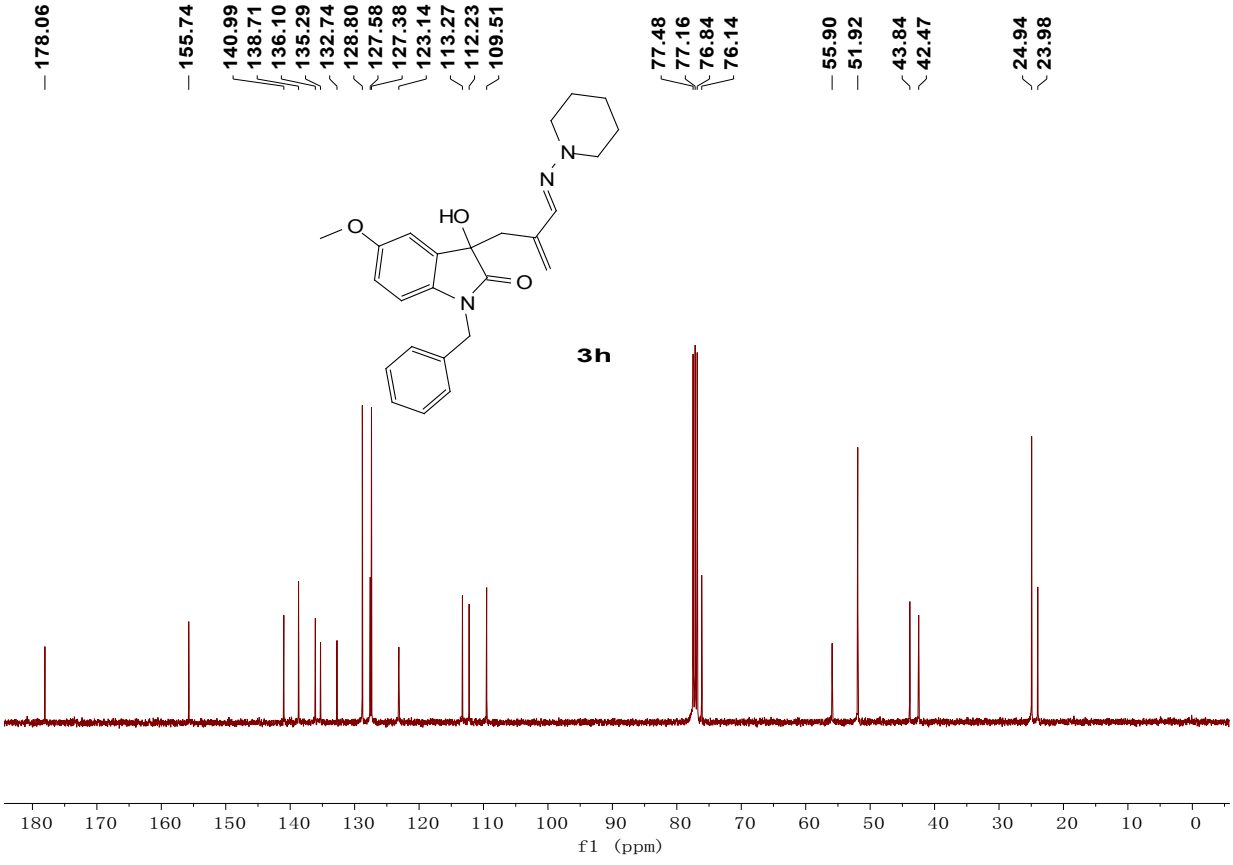
f1 (ppm)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123.14
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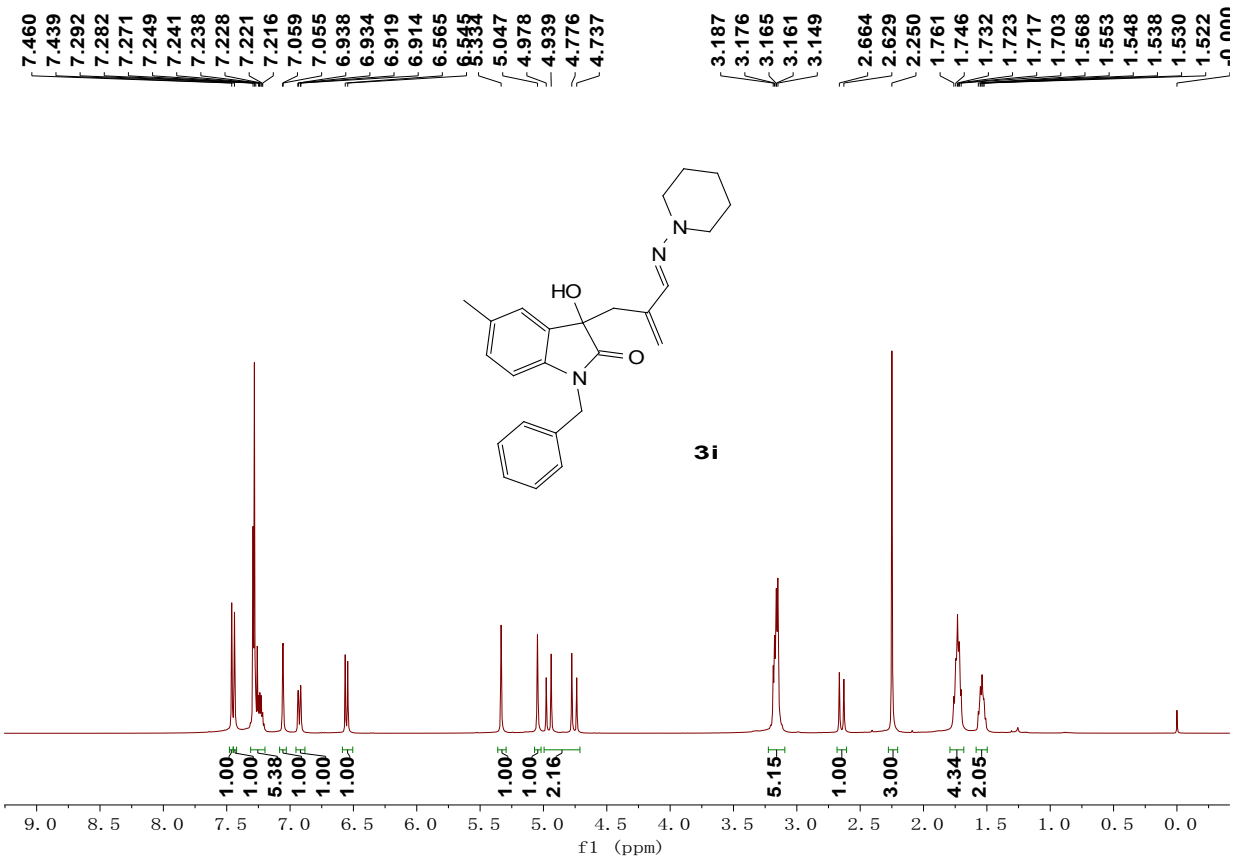
112.23
109.51
77.48
77.16
76.84
76.14
55.90
51.92
43.84
42.47
24.94
23.98
HO
O
N
O
N
3h
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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3.149
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1.732
1.723
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1.548
1.538
1.530
1.522
HO
O
N
3i
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1.00
5.38
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1.00
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4.34
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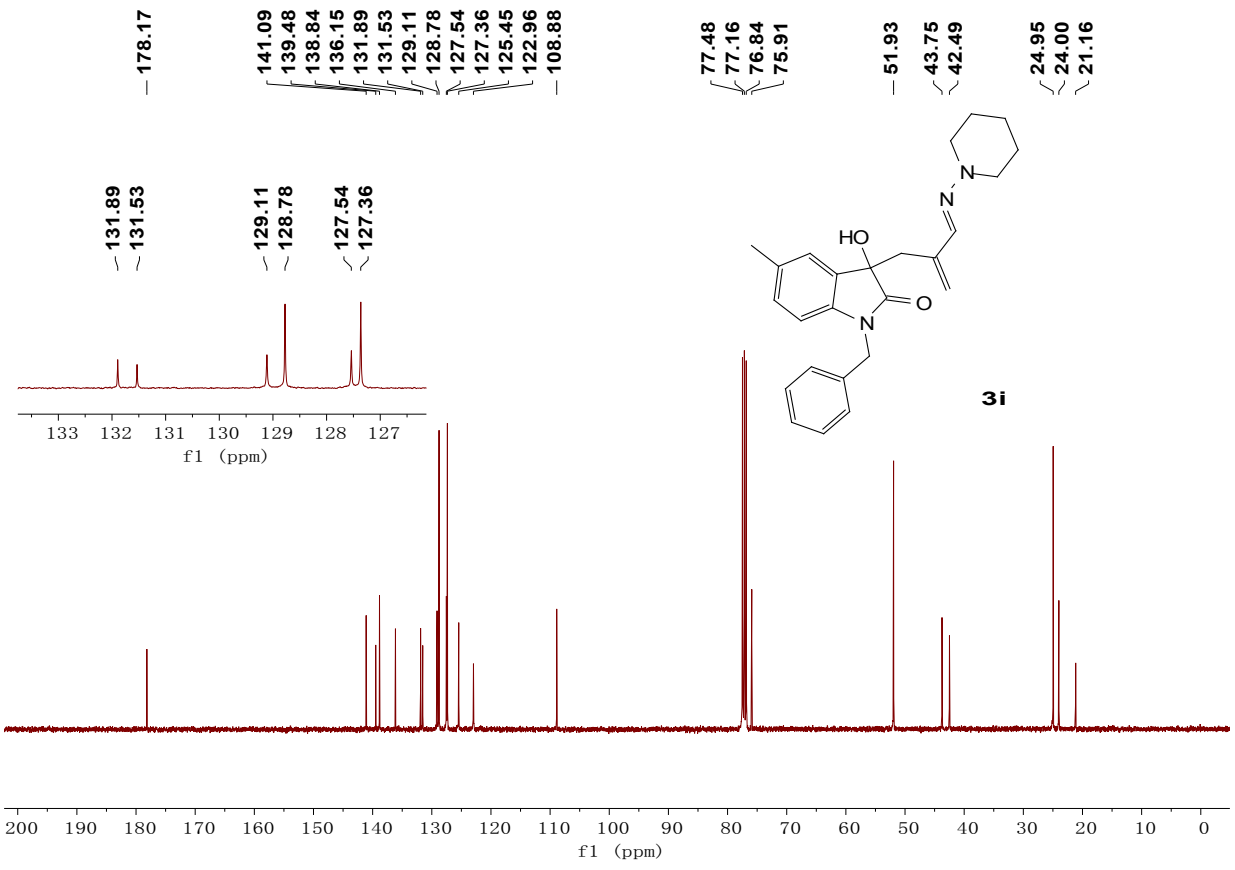
f1 (ppm)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128.78
127.54
127.36
125.45
122.96
108.88
77.48
77.16
76.84
75.91
51.93
43.75
42.49
24.95
24.00
21.16
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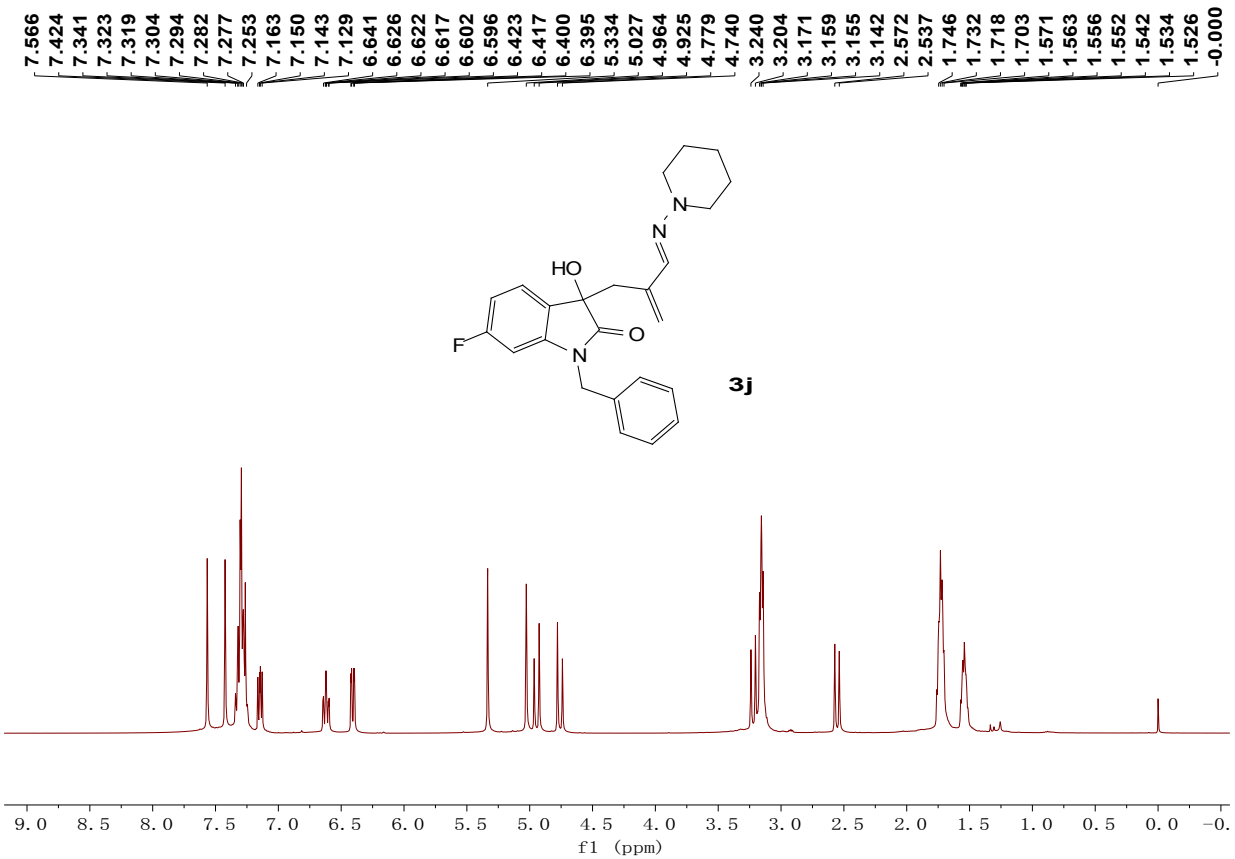
131.53
129.11
128.78
127.54
127.36
HO
O
N
3i
f1 (ppm)
f1 (ppm)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7.323
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7.282
7.277
7.253
7.163
7.150
7.143
7.129
6.641
6.626
6.622
6.617
6.602
6.596
6.423
6.417
6.400
6.395
5.334
5.027
4.964
4.925
4.779
4.740
3.240
3.204
3.171
3.159
3.155
3.142
2.572
2.537
1.746
1.732
1.718
1.703
1.571
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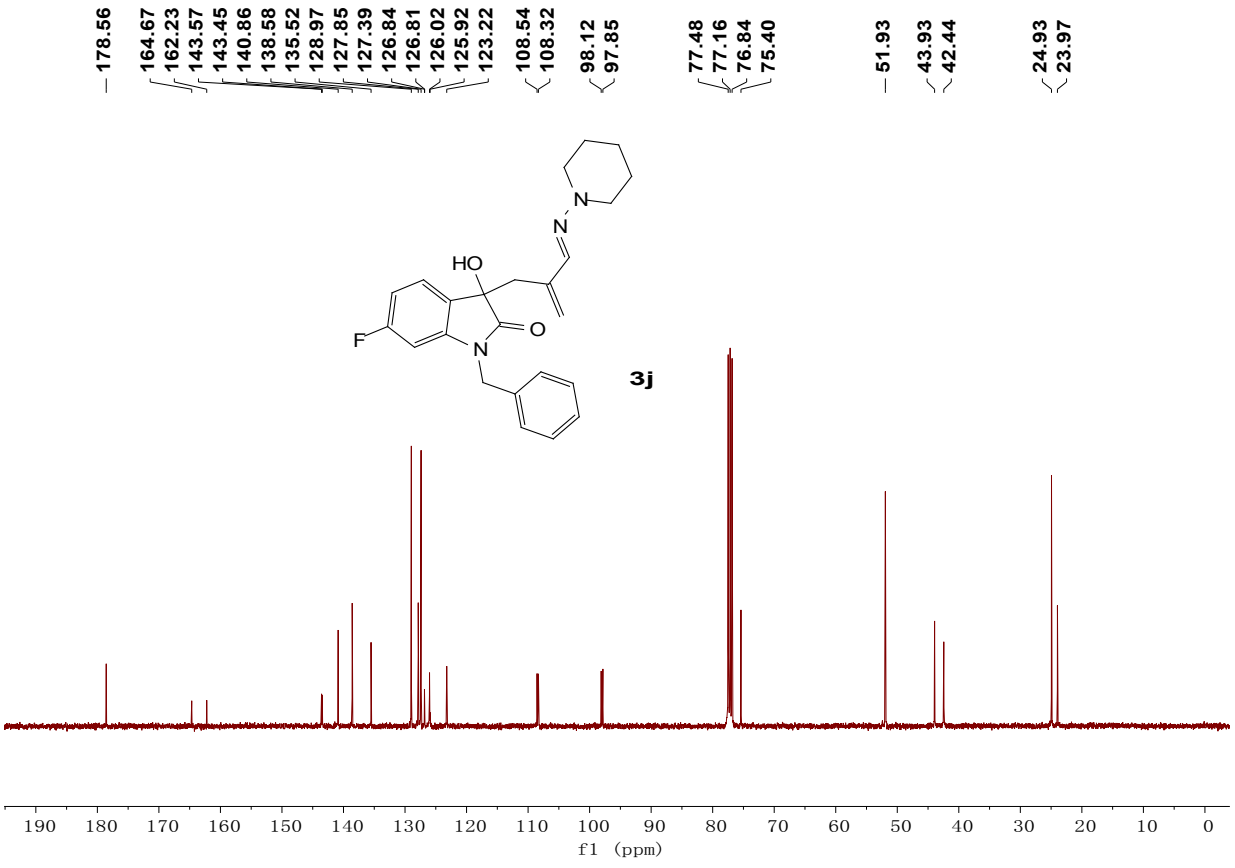
1.552
1.542
1.534
1.526
-0.000
HO
F
O
N
3j
f1 (ppm)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138.58
135.52
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127.85
127.39
126.84
126.81
126.02
125.92
123.22
108.54
108.32
98.12
97.85
77.48
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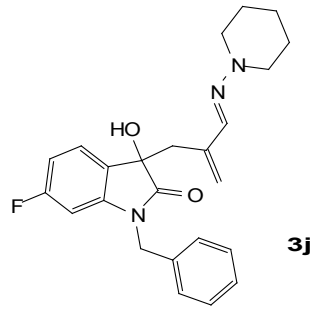
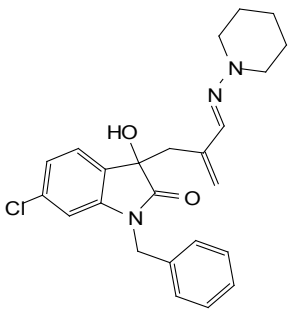
51.93
43.93
42.44
24.93
23.97
HO
F
O
N
3j
f1 (ppm)

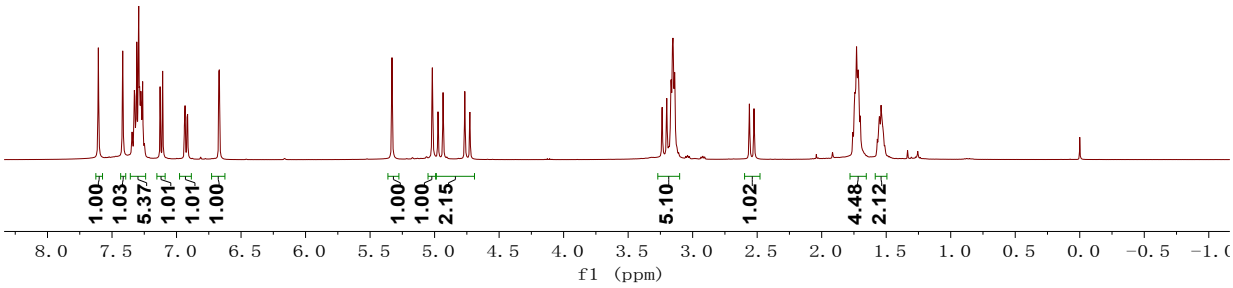


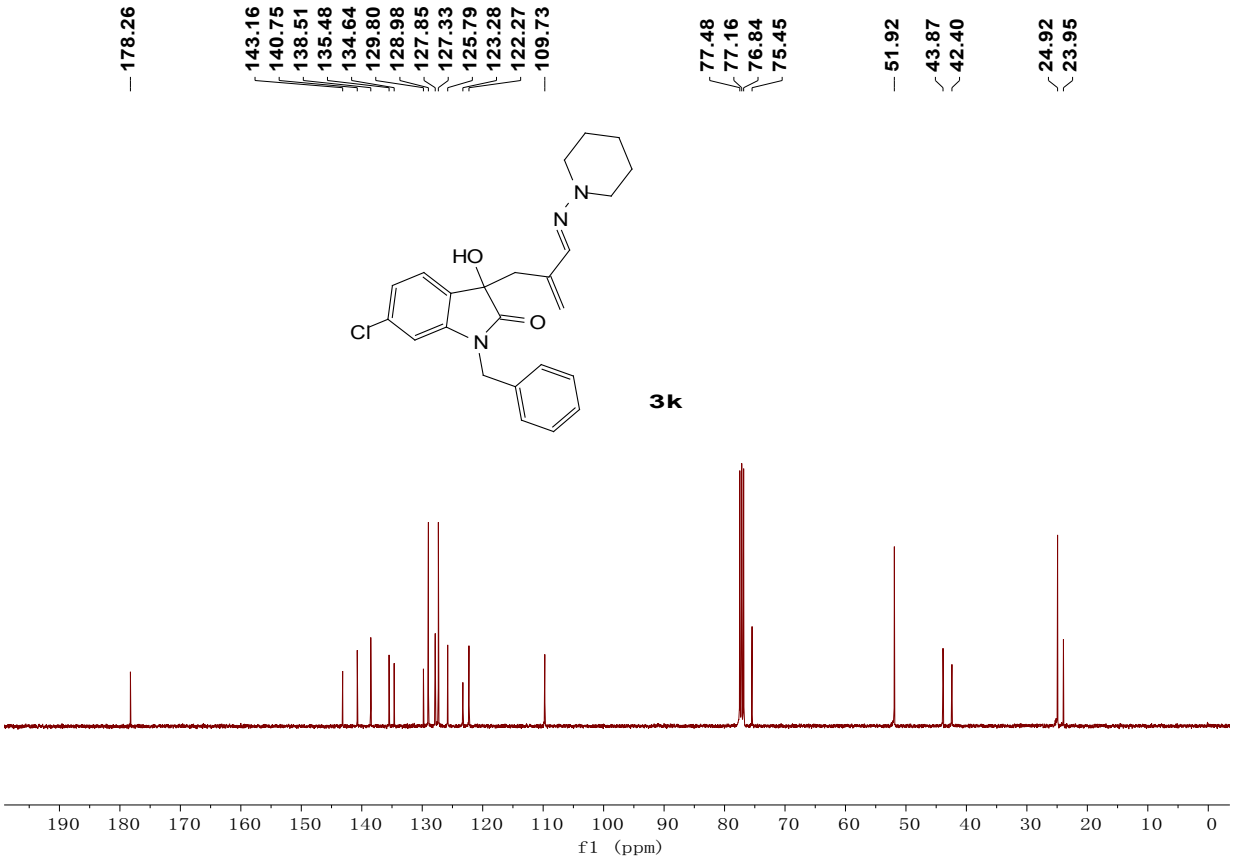
3j

7.606 7.417 7.344 7.330 7.327 7.323 7.316 7.308 7.293 7.285 7.276 7.266 7.127 7.108 6.938 6.934 6.919 6.914 6.672 6.668 5.330 5.017 4.974 4.934 4.766 4.727 3.236 3.201 3.170 3.166 3.156 3.151 3.142 3.138 2.560 2.525 1.744 1.730 1.720 1.715 1.710 1.701 1.569 1.561 1.554 1.550 1.540 1.533 1.524 -0.000



3k

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127.33
125.79
123.28
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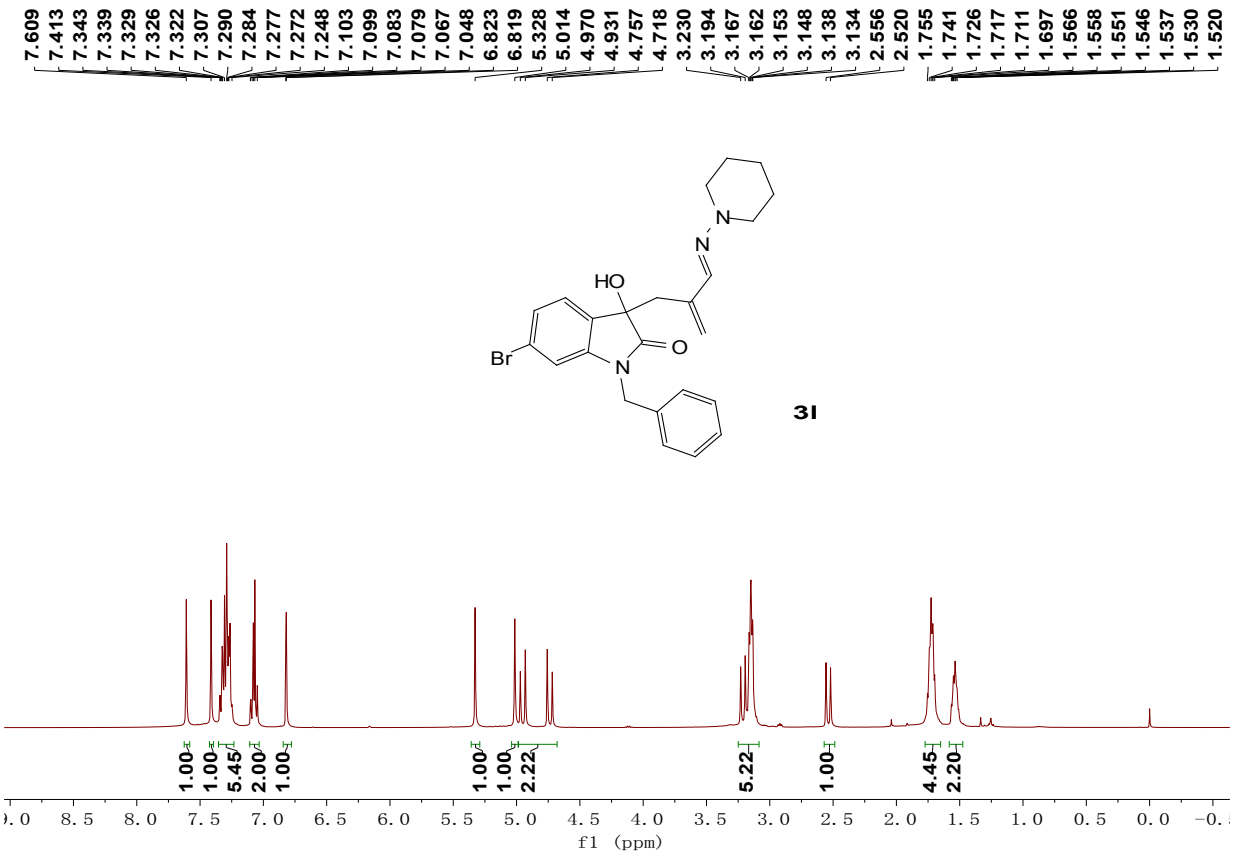
109.73
77.48
77.16
76.84
75.45
51.92
43.87
42.40
24.92
23.95
HO
Cl
O
N
N
N
3k
f1 (ppm)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7.307
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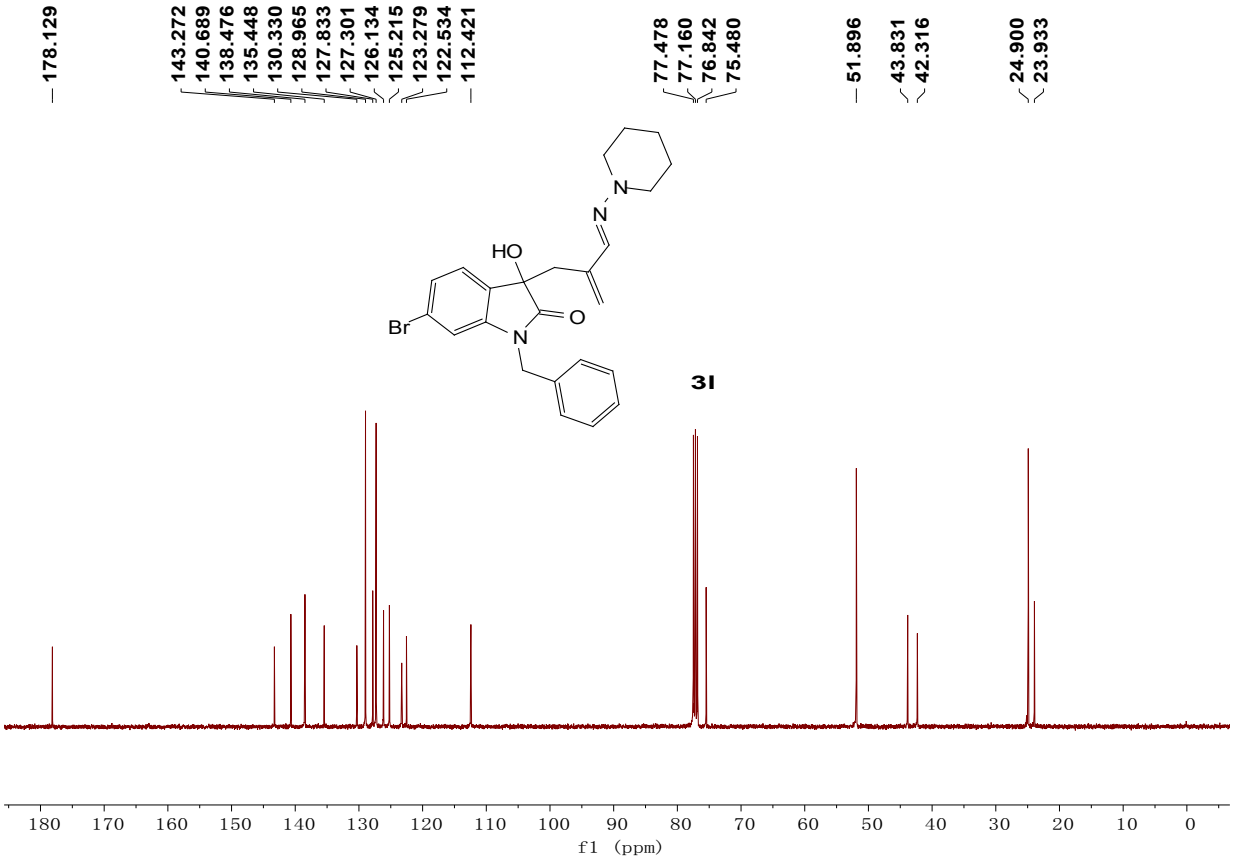
7.284
7.277
7.272
7.248
7.103
7.099
7.083
7.079
7.067
7.048
6.823
6.819
5.328
5.014
4.970
4.931
4.757
4.718
3.230
3.194
3.167
3.162
3.153
3.148
3.138
3.134
2.556
2.520
1.755
1.741
1.726
1.717
1.711
1.697
1.566
1.558
1.551
1.546
1.537
1.530
1.520
HO
Br
O
N
N
N
3l
1.00
1.00
5.45
2.00
1.00
1.00
1.00
2.22
5.22
1.00
4.45
2.20
f1 (ppm)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140.689
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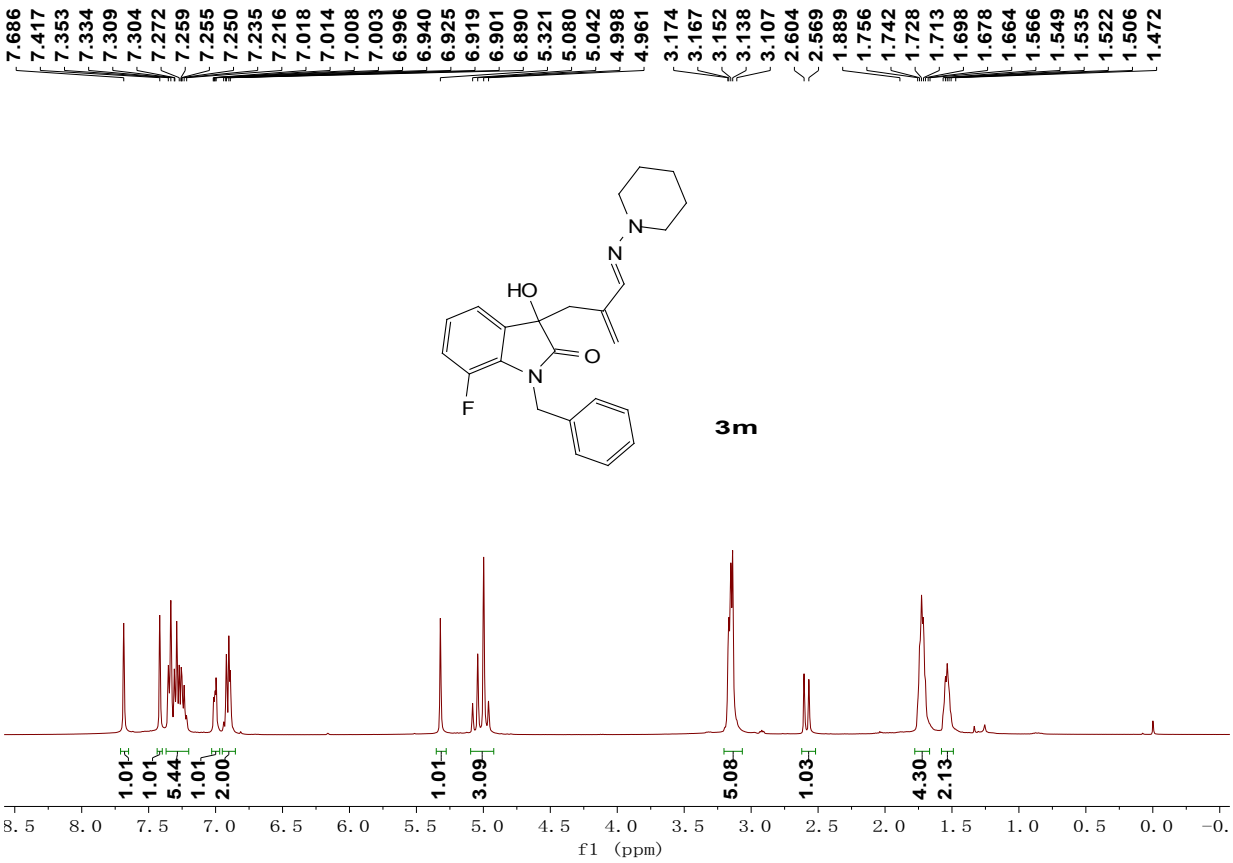
130.330
128.965
127.833
127.301
126.134
125.215
123.279
122.534
112.421
77.478
77.160
76.842
75.480
51.896
43.831
42.316
24.900
23.933
HO
Br
O
N
N
N
3l
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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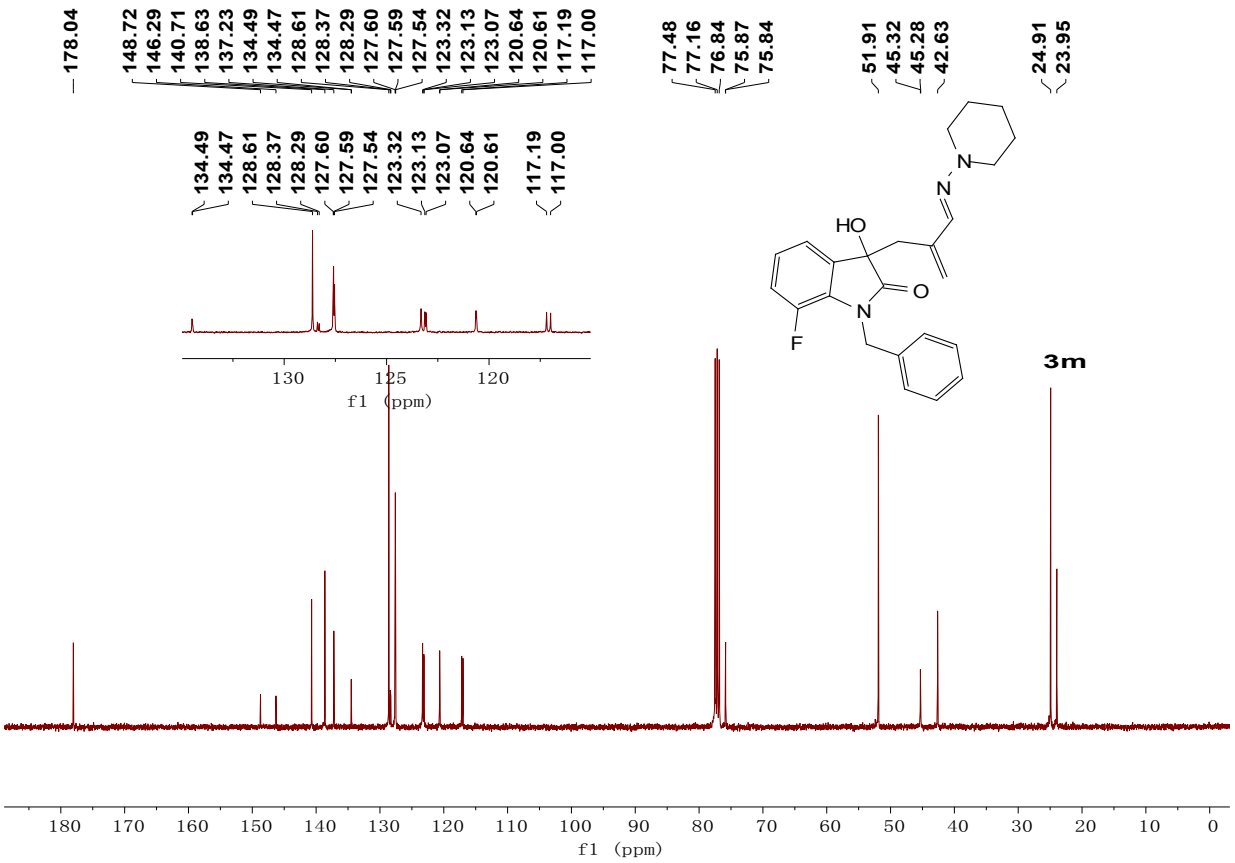
7.309
7.304
7.272
7.259
7.255
7.250
7.235
7.216
7.018
7.014
7.008
7.003
6.996
6.940
6.925
6.919
6.901
6.890
5.321
5.080
5.042
4.998
4.961
3.174
3.167
3.152
3.138
3.107
2.604
2.569
1.889
1.756
1.742
1.728
1.713
1.698
1.678
1.664
1.566
1.549
1.535
1.522
1.506
1.472
HO
O
N
N
F
3m
1.01
1.01
5.44
1.01
2.00
1.01
3.09
5.08
1.03
4.30
2.13
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)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146.29
140.71
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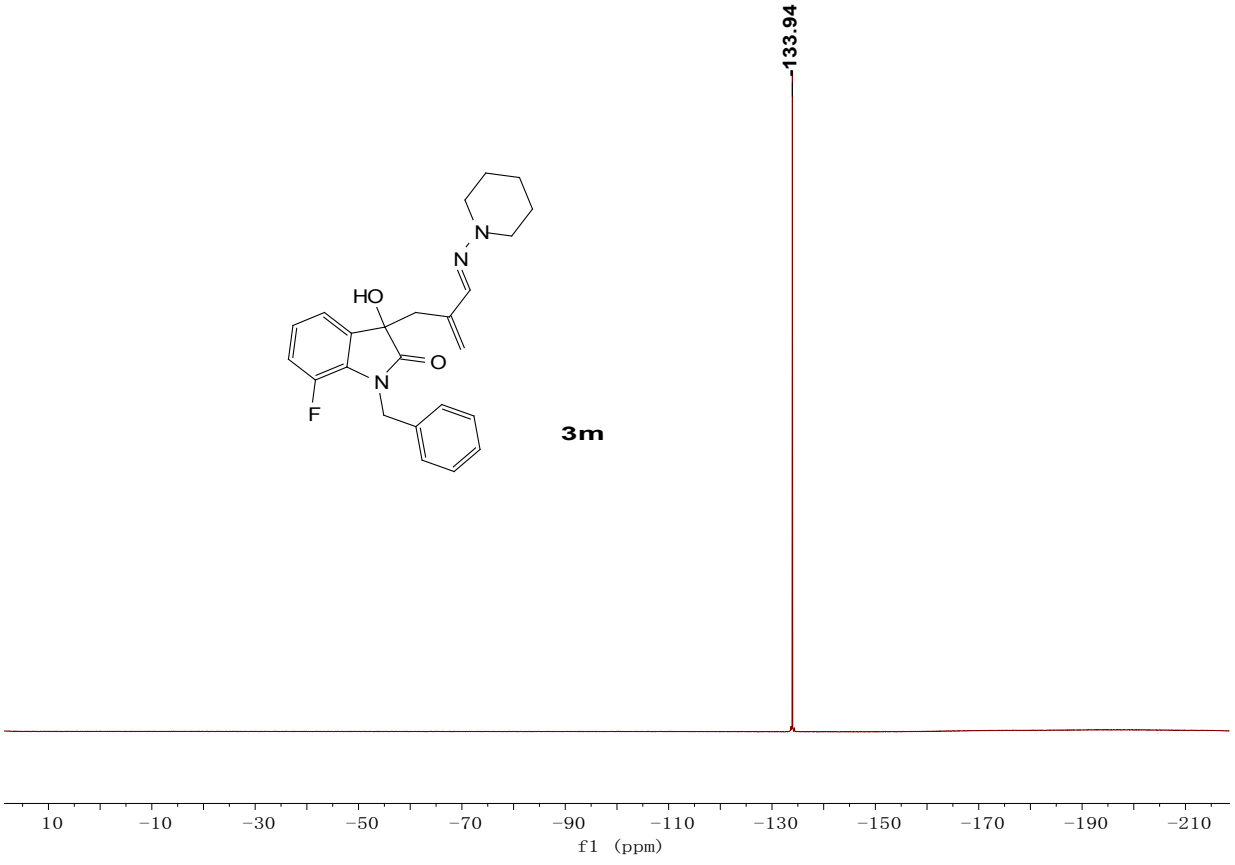
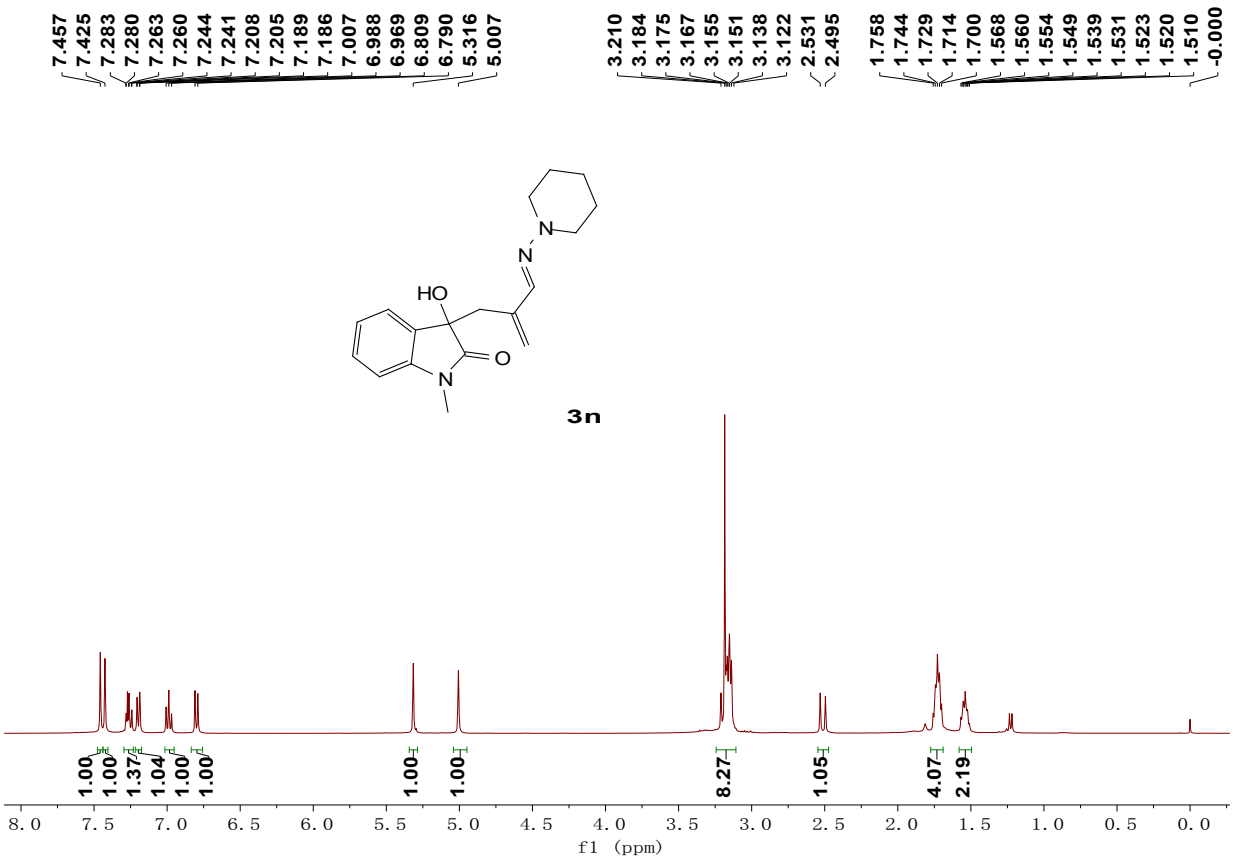
137.23
134.49
134.47
128.61
128.37
128.29
127.60
127.59
127.54
123.32
123.13
123.07
120.64
120.61
117.19
117.00
77.48
77.16
76.84
75.87
75.84
51.91
45.32
45.28
42.63
24.91
23.95
HO
O
N
F
3m
f1 (ppm)


133.94
HO
O
N
F
3m
f1 (ppm)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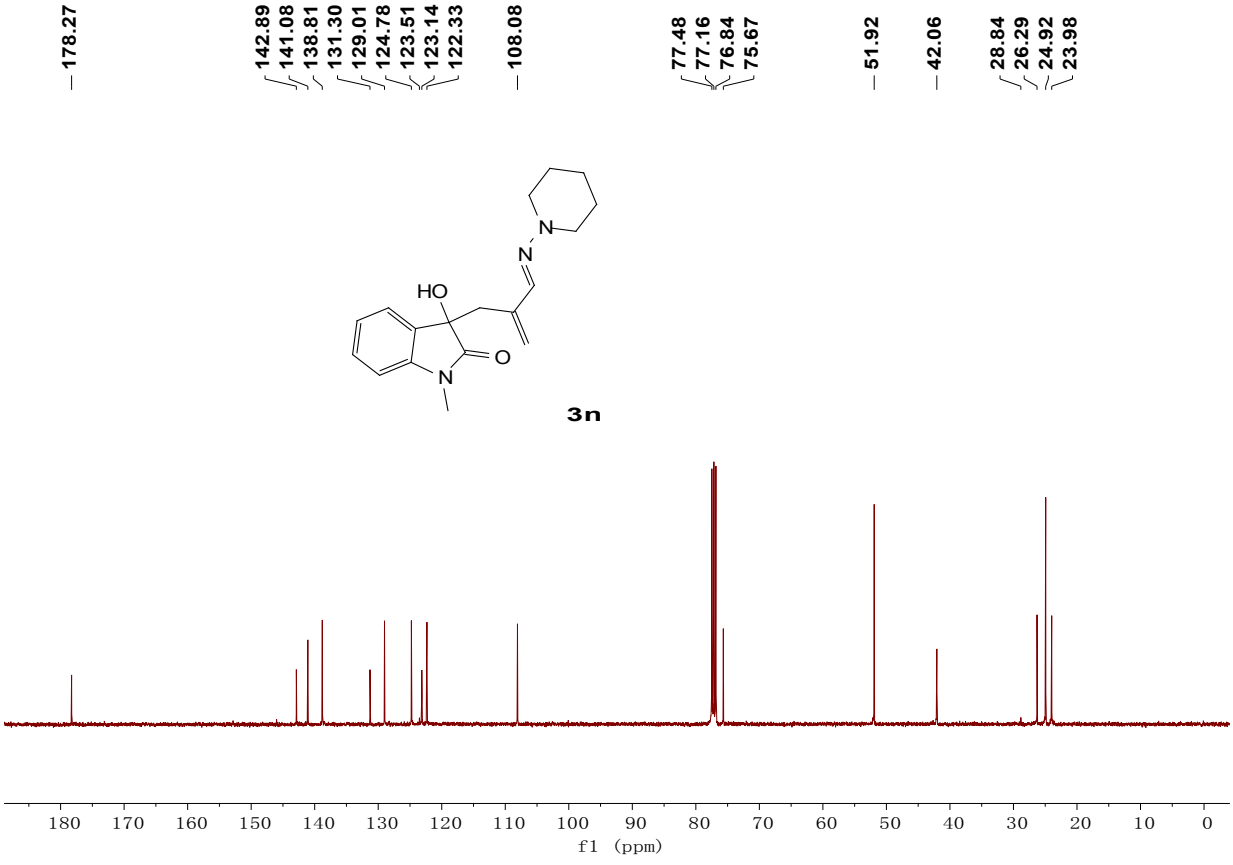
7.263
7.260
7.244
7.241
7.208
7.205
7.189
7.186
7.007
6.988
6.969
6.809
6.790
5.316
5.007
3.210
3.184
3.175
3.167
3.155
3.151
3.138
3.122
2.531
2.495
1.758
1.744
1.729
1.714
1.700
1.568
1.560
1.554
1.549
1.539
1.531
1.523
1.520
1.510
-0.000
HO
O
N
3n
1.00
1.00
1.37
1.04
1.00
1.00
1.00
1.00
8.27
1.05
4.07
2.19
f1 (ppm)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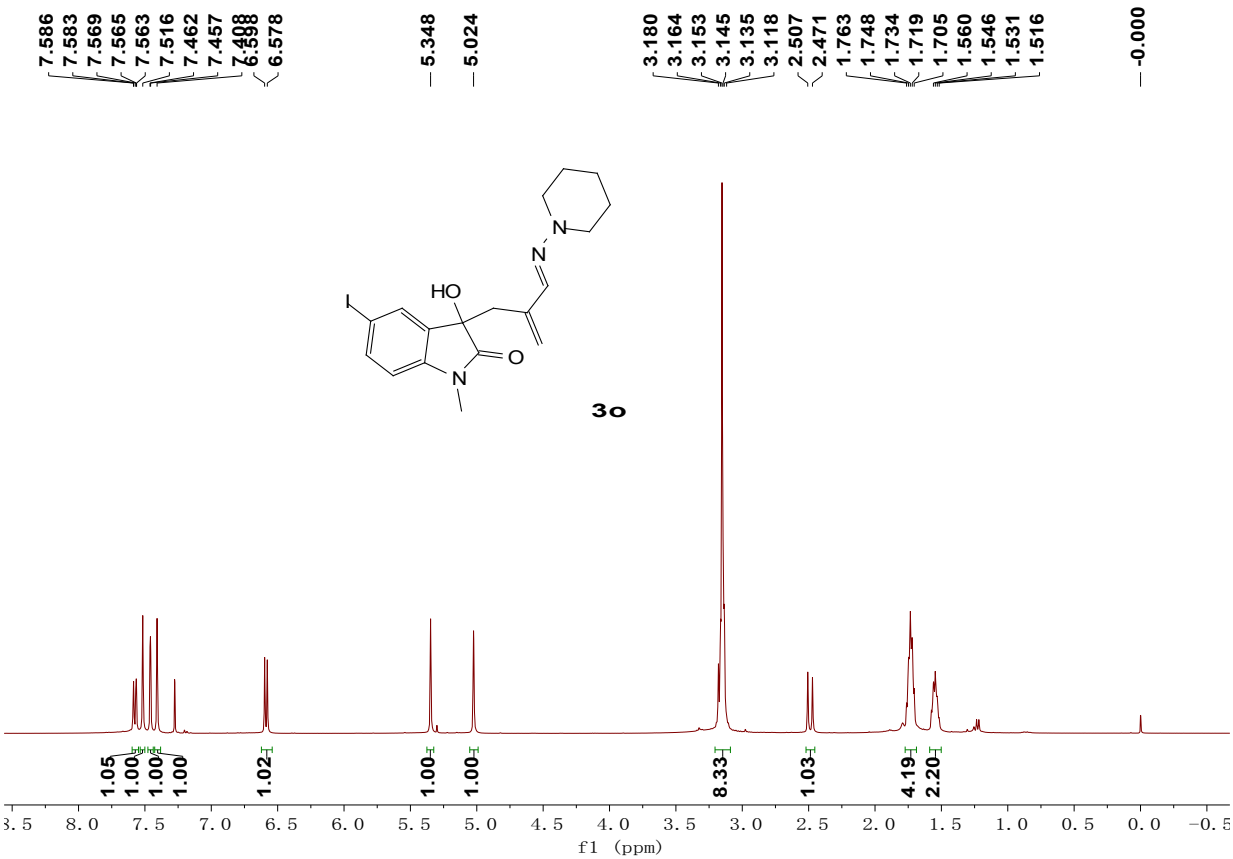
142.89
141.08
138.81
131.30
129.01
124.78
123.51
123.14
122.33
108.08
77.48
77.16
76.84
75.67
51.92
42.06
28.84
26.29
24.92
23.98
HO
O
N
3n
f1 (ppm)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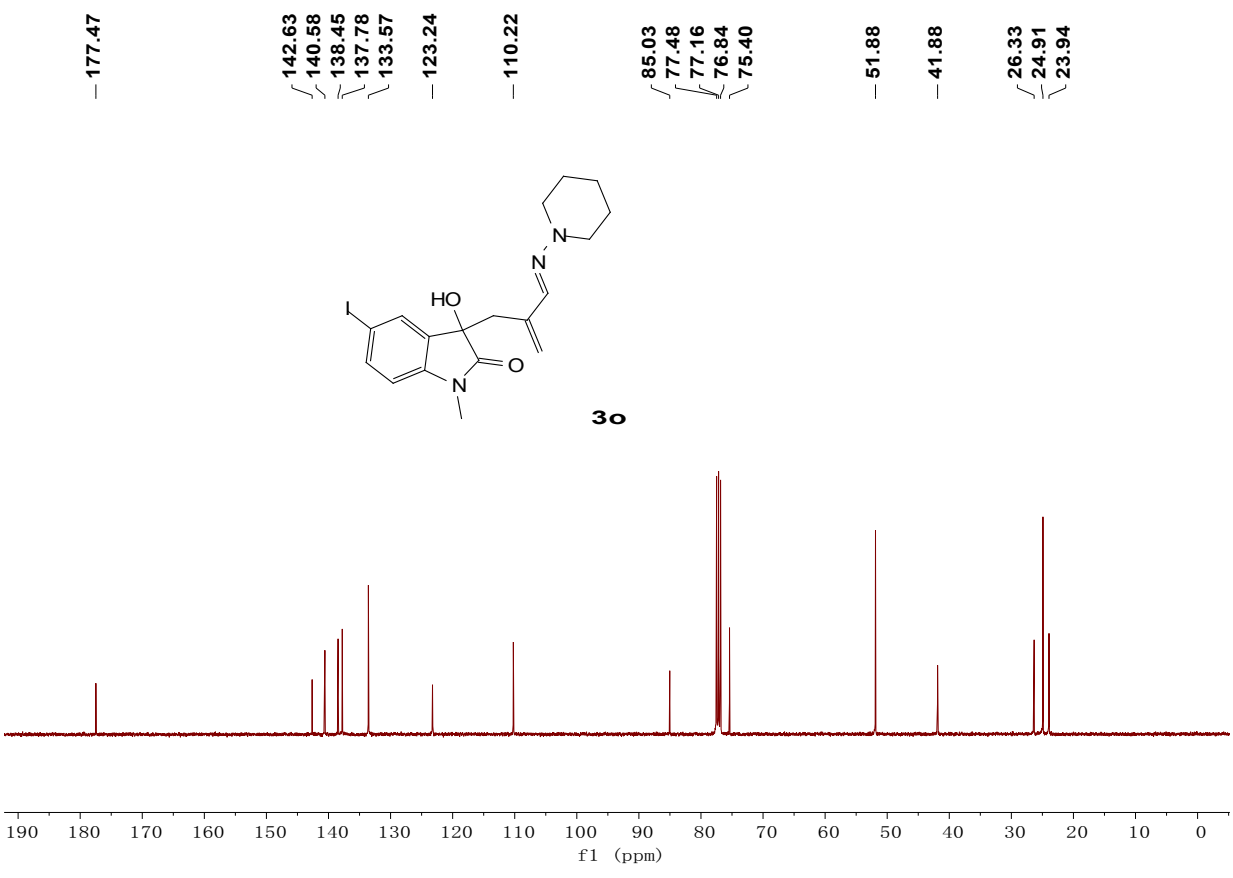
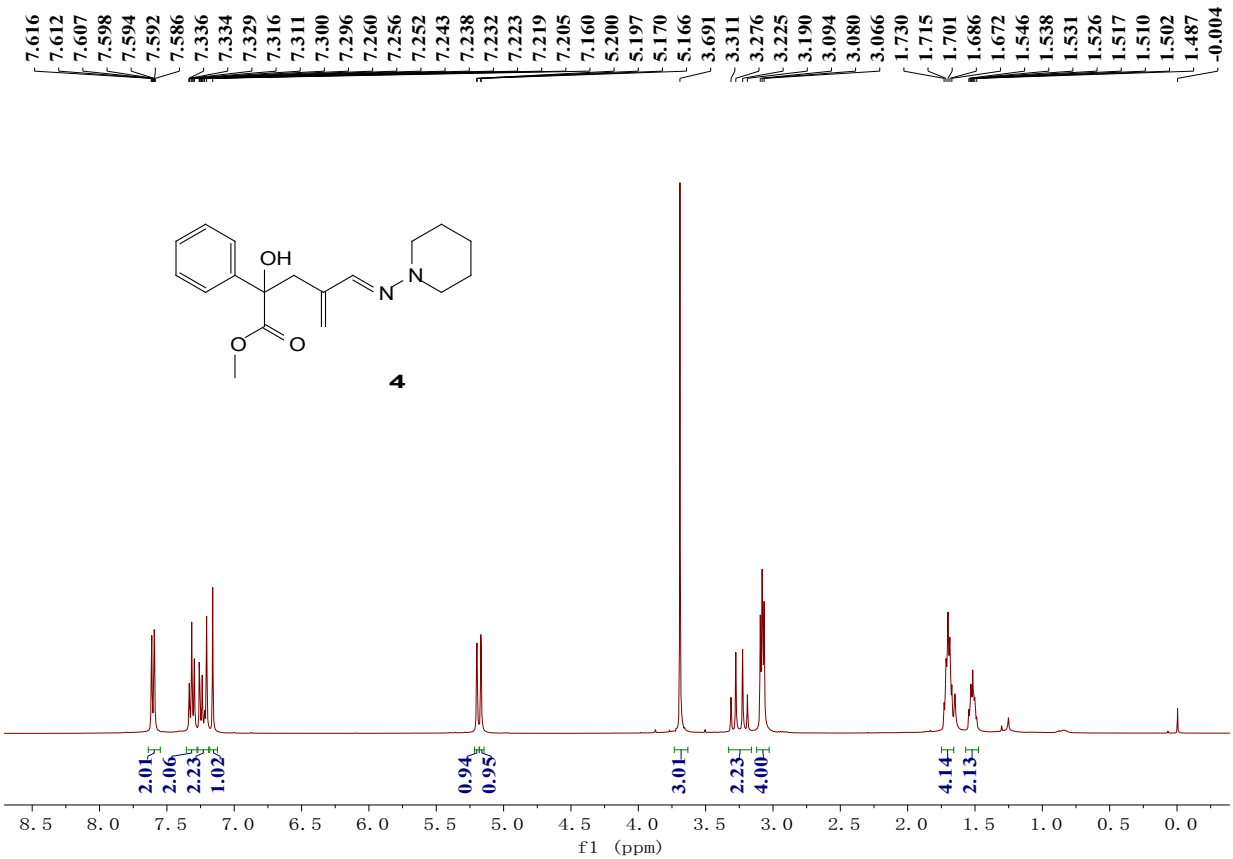
7.569
7.565
7.563
7.516
7.462
7.457
7.408
7.398
6.578
5.348
5.024
3.180
3.164
3.153
3.145
3.135
3.118
2.507
2.471
1.763
1.748
1.734
1.719
1.705
1.560
1.546
1.531
1.516
-0.000
HO
I
O
N
3o
1.05
1.00
1.00
1.00
1.02
1.00
1.00
8.33
1.03
4.19
2.20
f1 (ppm)


177.47
142.63
140.58
138.45
137.78
133.57
123.24
110.22
85.03
77.48
77.16
76.84
75.40
51.88
41.88
26.33
24.91
23.94
HO
I
O
N
3o
f1 (ppm)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7.592
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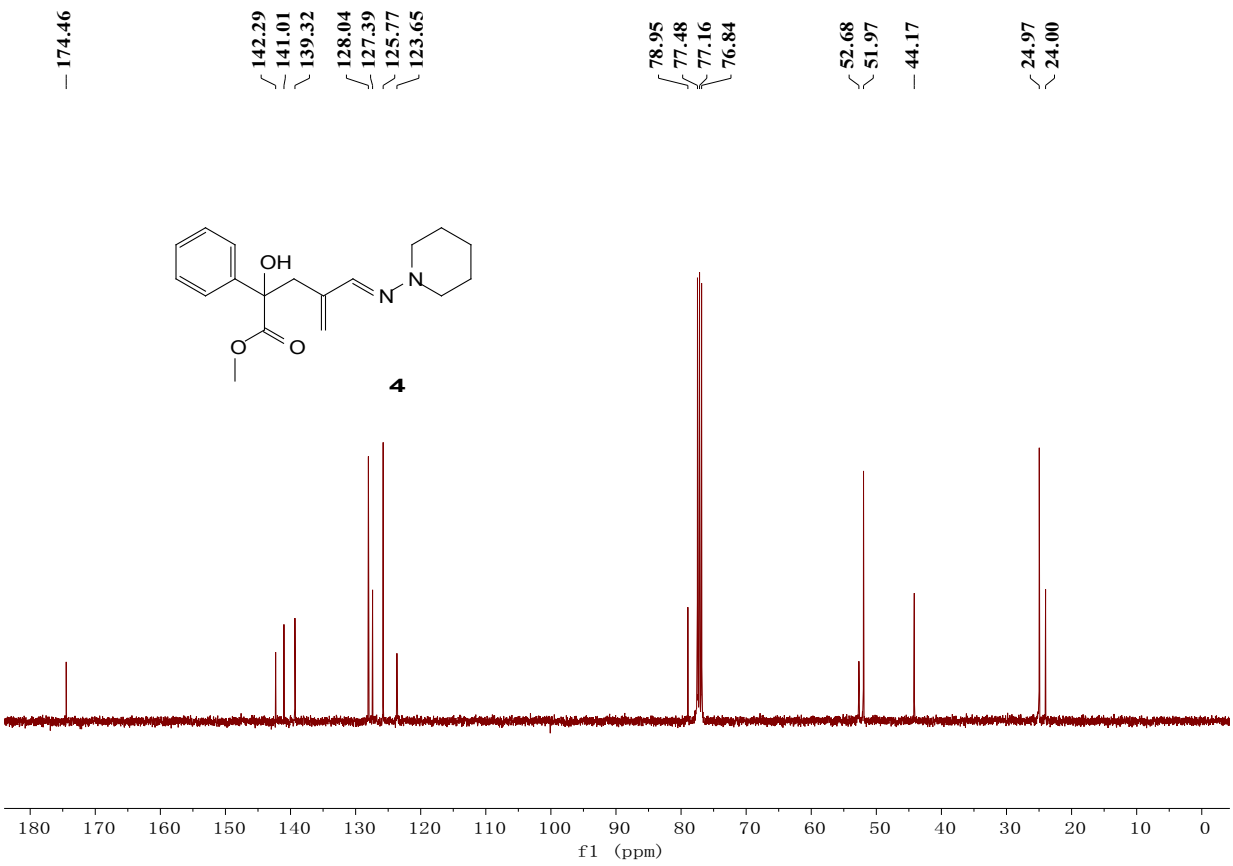
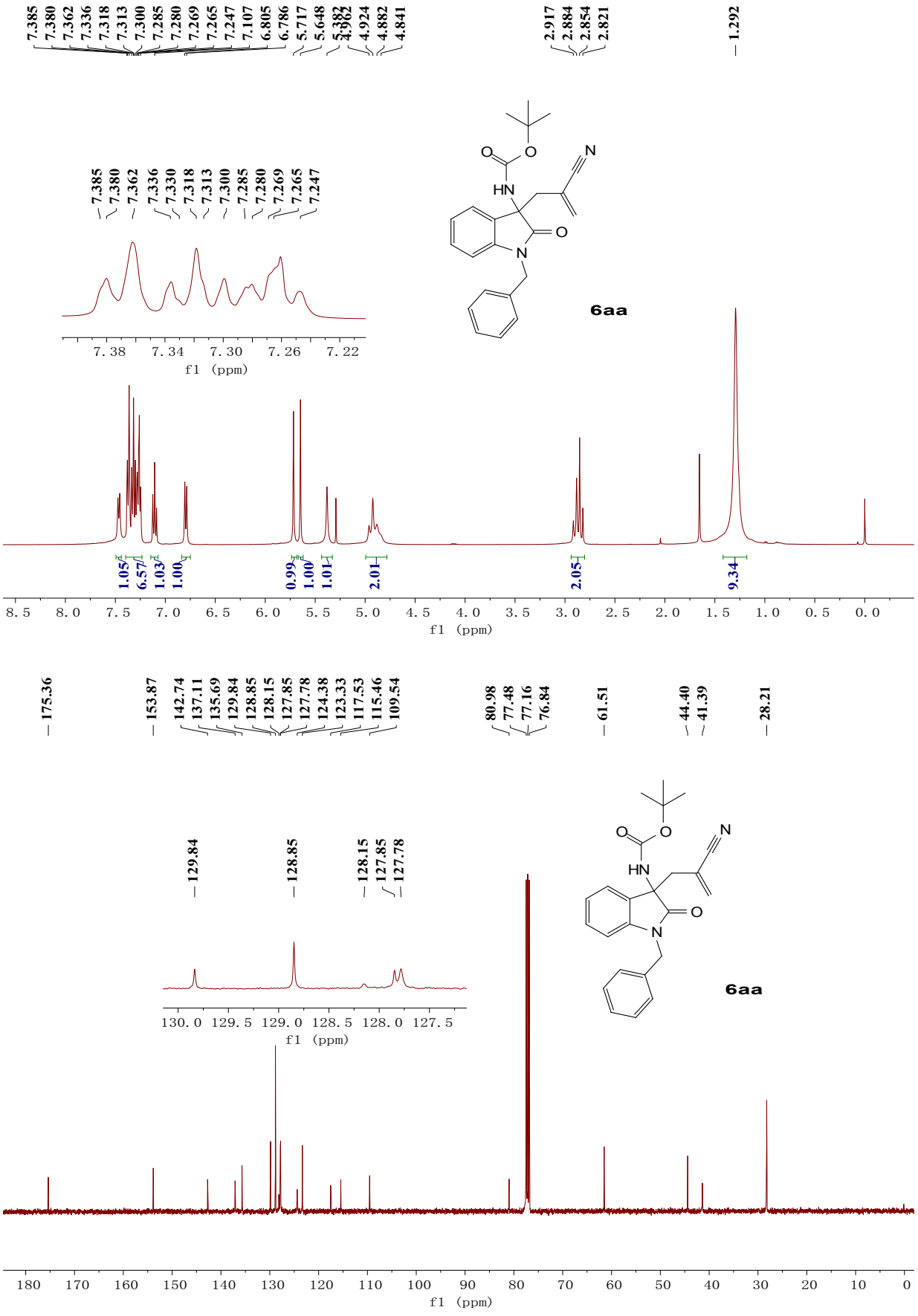
7.336
7.334
7.329
7.316
7.311
7.300
7.296
7.260
7.256
7.252
7.243
7.238
7.232
7.223
7.219
7.205
7.160
5.200
5.197
5.170
5.166
3.691
3.311
3.276
3.225
3.190
3.094
3.080
3.066
1.730
1.715
1.701
1.686
1.672
1.546
1.538
1.531
1.526
1.517
1.510
1.502
1.487
-0.004
OH
N
N
O
O
4
2.01
2.06
2.23
1.02
0.94
0.95
3.01
2.23
4.00
4.14
2.13
f1 (ppm)


174.46
142.29
141.01
139.32
128.04
127.39
125.77
123.65
78.95
77.48
77.16
76.84
52.68
51.97
44.17
24.97
24.00
OH
N
N
O
O
4
f1 (ppm)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7.313
7.300
7.285
7.280
7.269
7.265
7.247
7.107
6.805
6.786
5.717
5.648
4.924
4.882
4.841
2.917
2.884
2.854
2.821
1.292
6aa
1.05
6.57
1.03
1.00
0.99
1.00
1.01
2.01
2.05
9.34
f1 (ppm)
175.36
153.87
142.74
137.11
135.69
129.84
128.85
128.15
127.85
127.78
124.38
123.33
117.53
115.46
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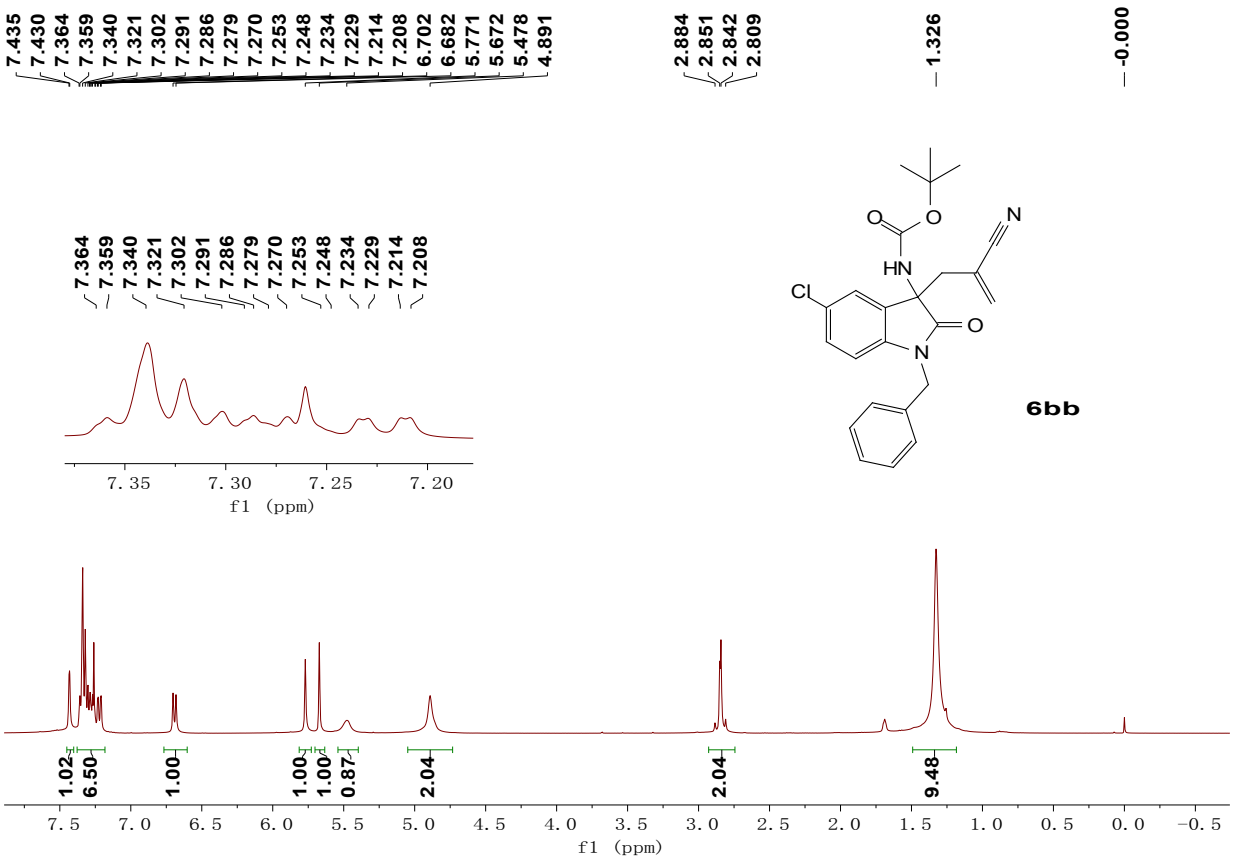
76.84
61.51
44.40
41.39
28.21
6aa
f1 (ppm)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7.359
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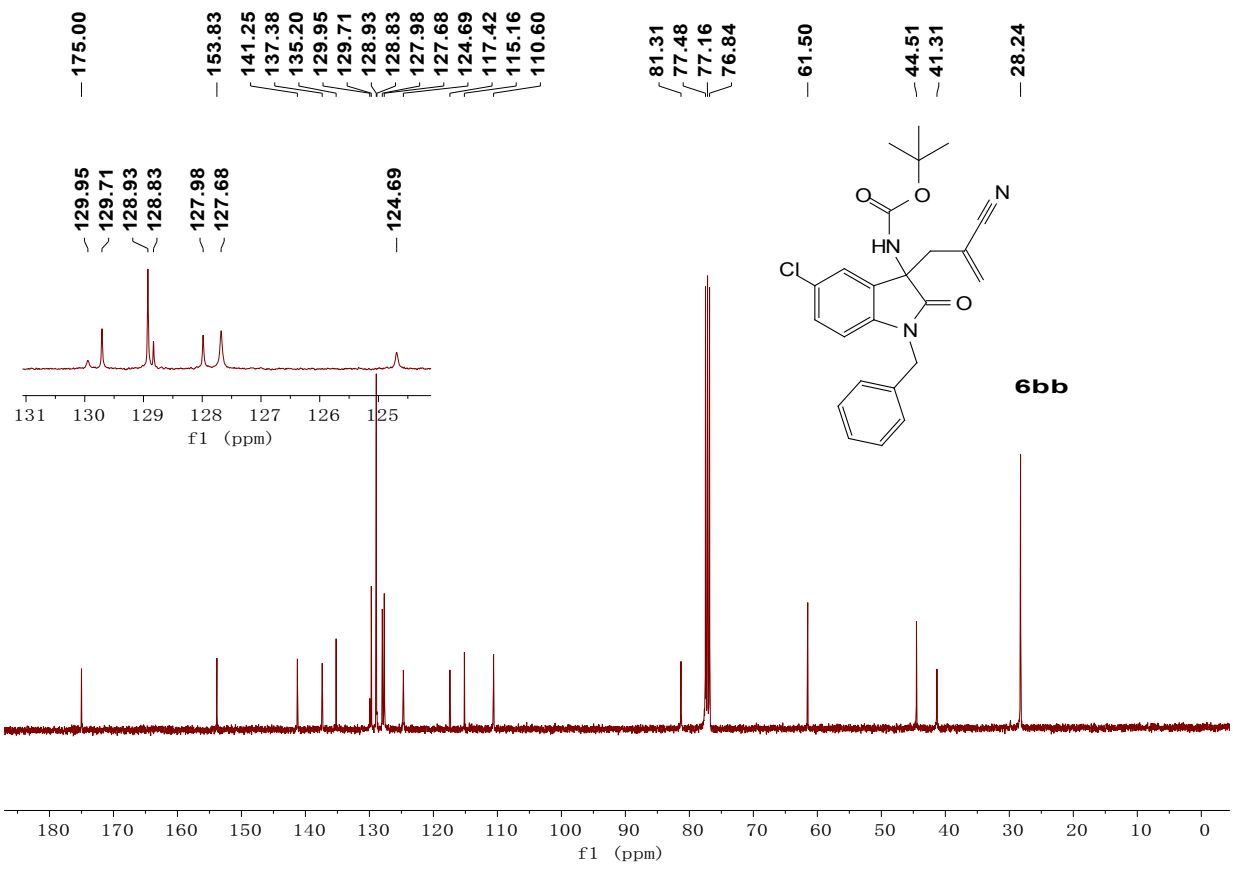
7.321
7.302
7.291
7.286
7.279
7.270
7.253
7.248
7.234
7.229
7.214
7.208
6.702
6.682
5.771
5.672
5.478
4.891
2.884
2.851
2.842
2.809
1.326
-0.000
7.364
7.359
7.340
7.321
7.302
7.291
7.286
7.279
7.270
7.253
7.248
7.234
7.229
7.214
7.208
7.35
7.30
7.25
7.20
f1 (ppm)
HN
Cl
O
N
6bb
1.02
6.50
1.00
1.00
1.00
0.87
2.04
2.04
9.48
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)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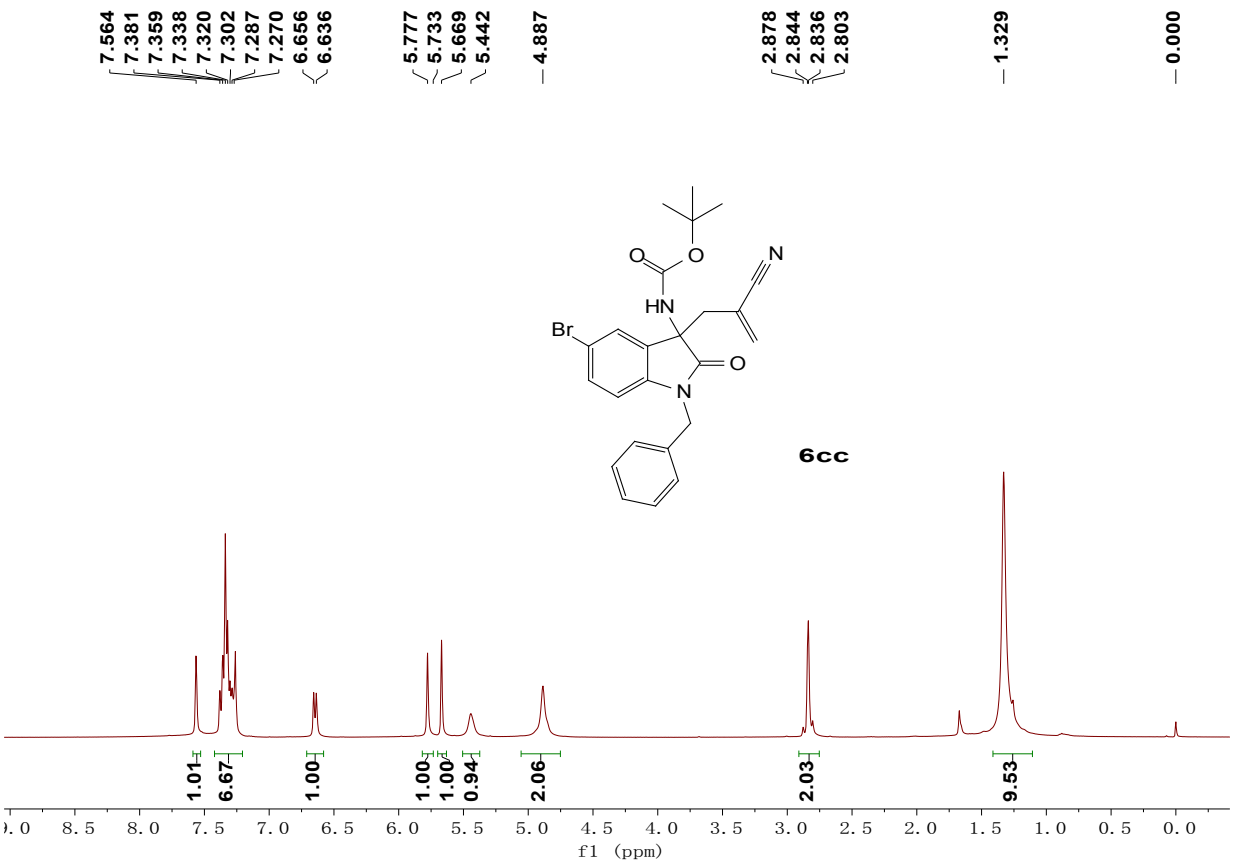
137.38
135.20
129.95
129.71
128.93
128.83
127.98
127.68
124.69
117.42
115.16
110.60
81.31
77.48
77.16
76.84
61.50
44.51
41.31
28.24
129.95
129.71
128.93
128.83
127.98
127.68
124.69
131
130
129
128
127
126
125
f1 (ppm)
HN
Cl
O
N
6bb
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.287
7.270
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6.636
5.777
5.733
5.669
5.442
4.887
2.878
2.844
2.836
2.803
1.329
0.000
Br
HN
O
N
6cc
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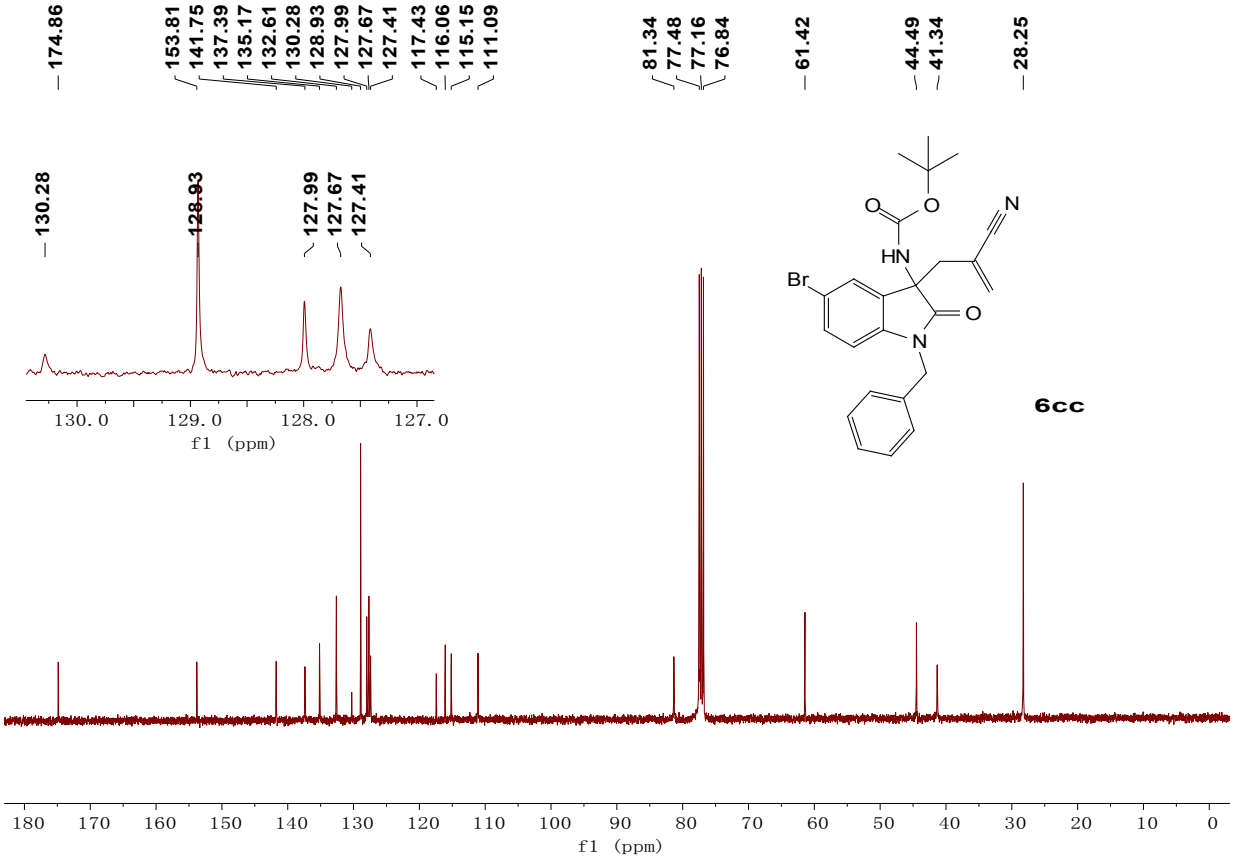
6.67
1.00
1.00
1.00
0.94
2.06
2.03
9.53
f1 (ppm)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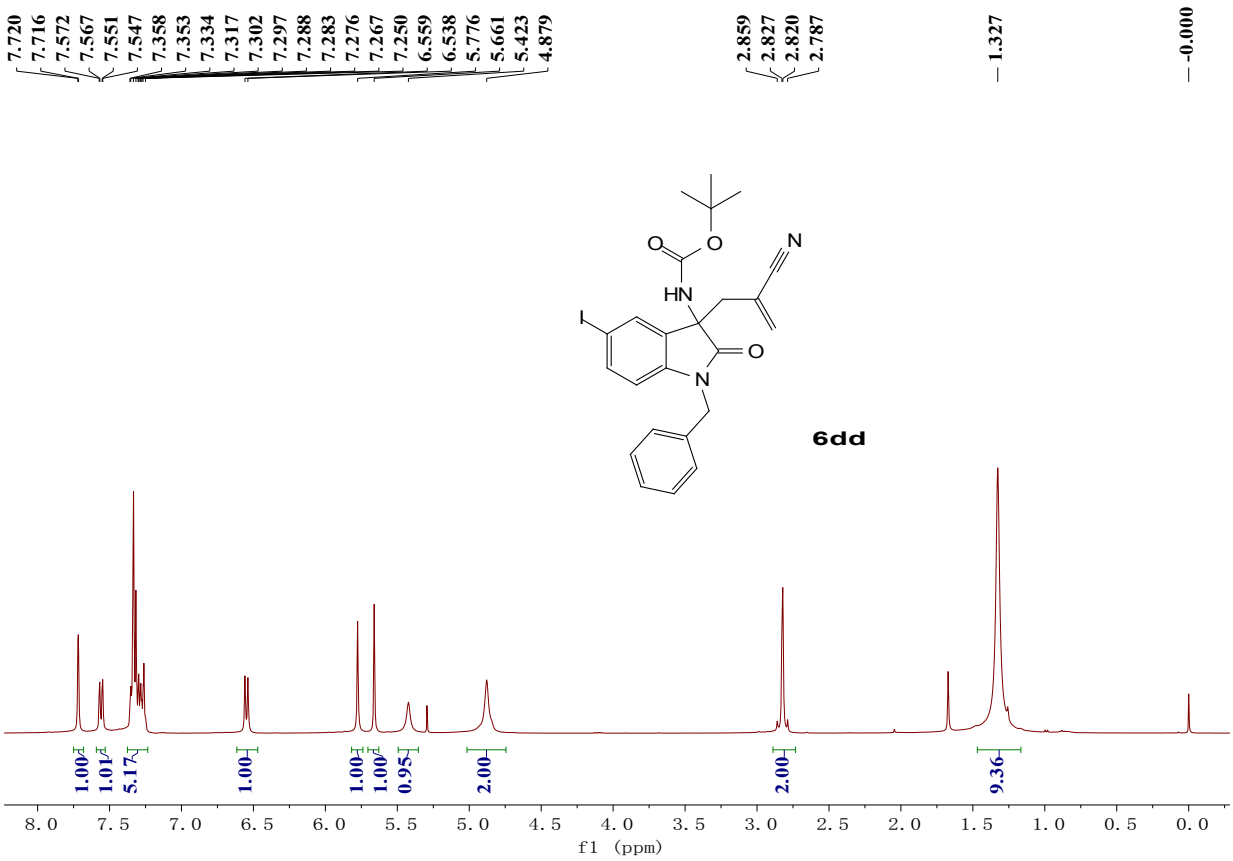
132.61
130.28
128.93
127.99
127.67
127.41
117.43
116.06
115.15
111.09
81.34
77.48
77.16
76.84
61.42
44.49
41.34
28.25
130.28
128.93
127.99
127.67
127.41
Br
HN
O
N
6cc
f1 (ppm)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7.302
7.297
7.288
7.283
7.276
7.267
7.250
6.559
6.538
5.776
5.661
5.423
4.879
2.859
2.827
2.820
2.787
1.327
-0.000
6dd
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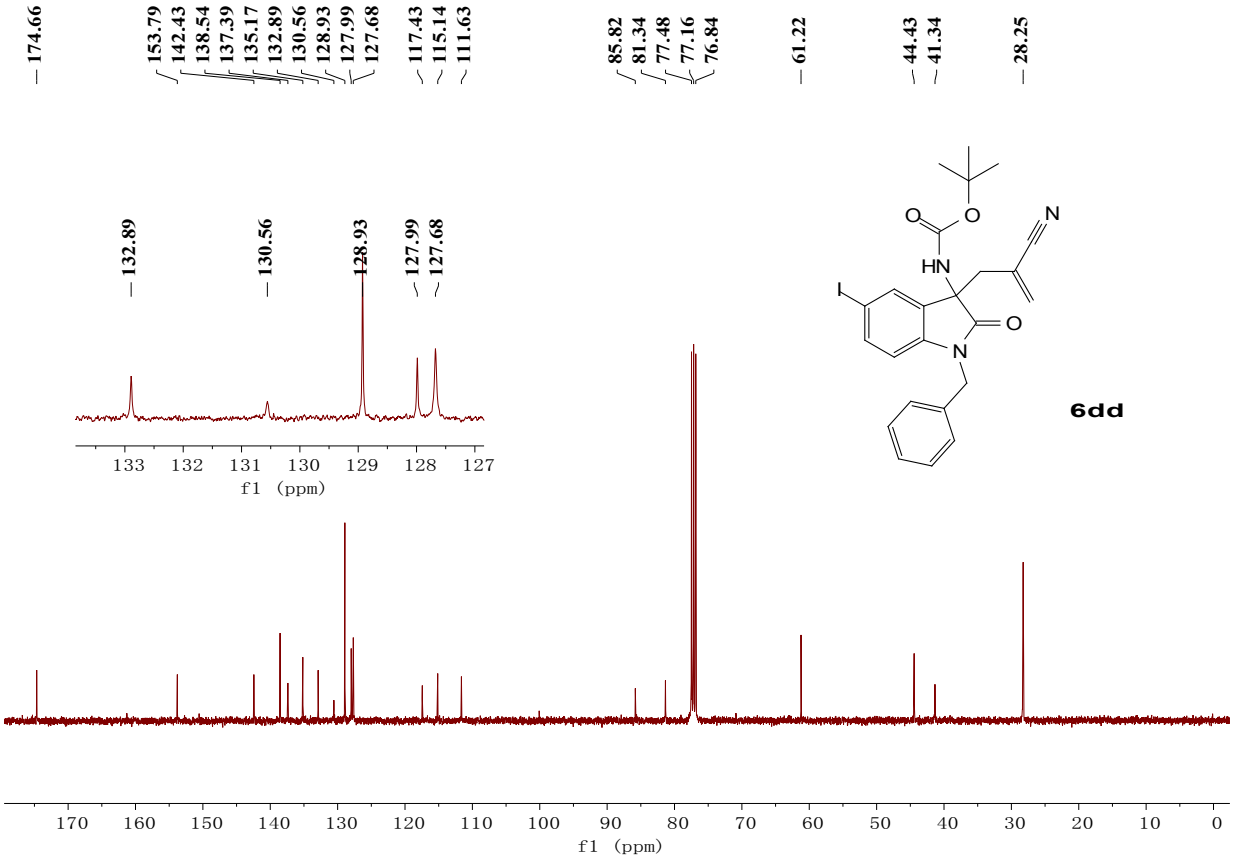
5.17
1.00
1.00
1.00
0.95
2.00
2.00
9.36
f1 (ppm)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77.48
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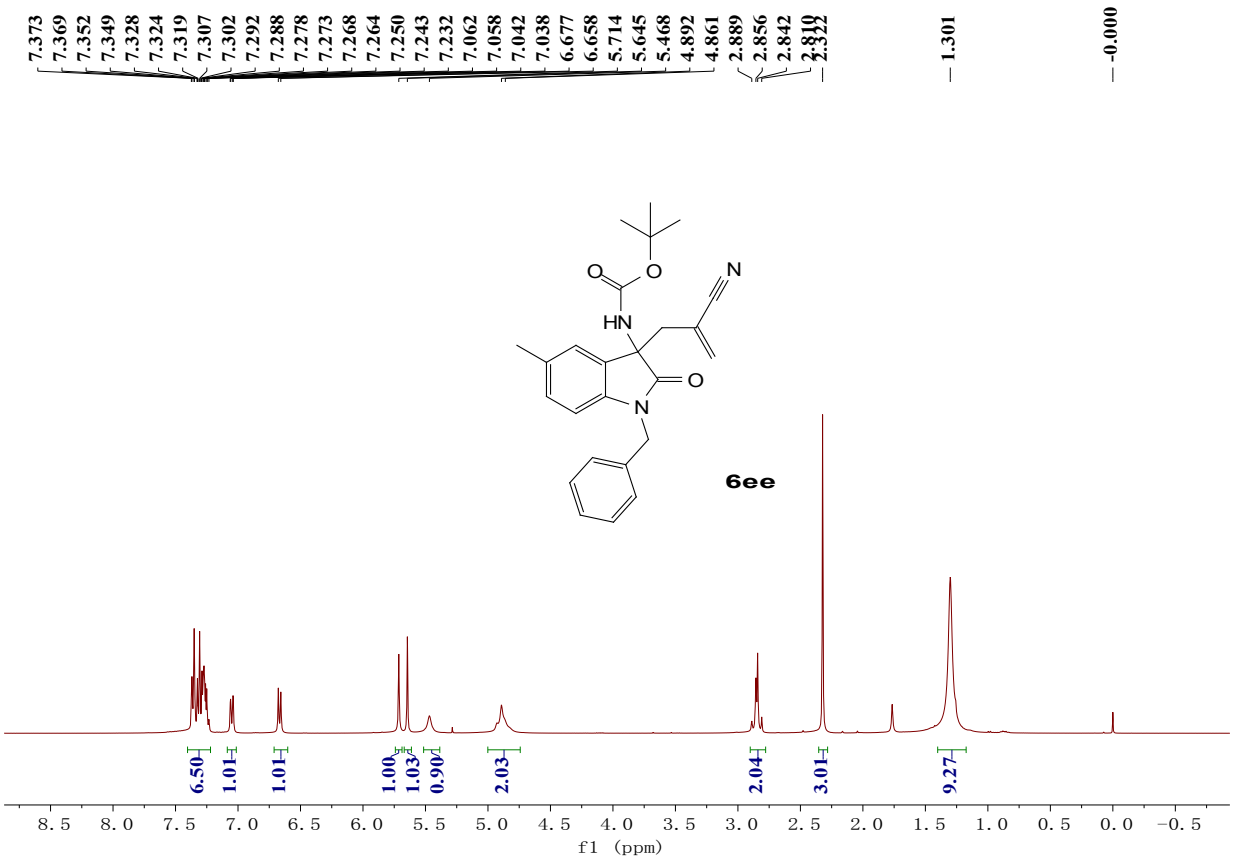
76.84
61.22
44.43
41.34
28.25
6dd
f1 (ppm)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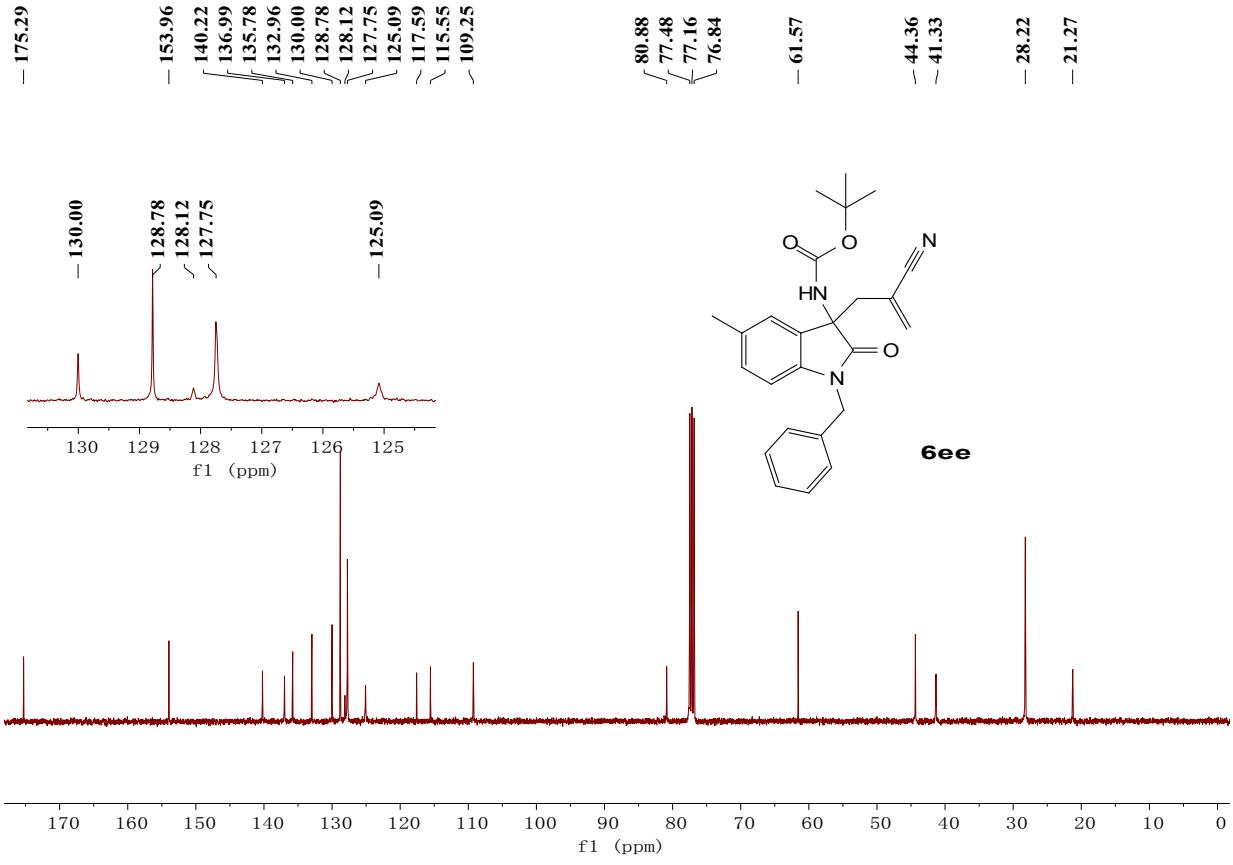
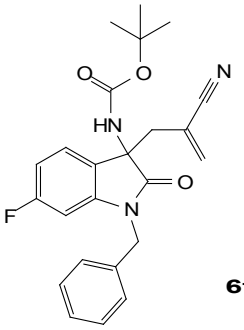
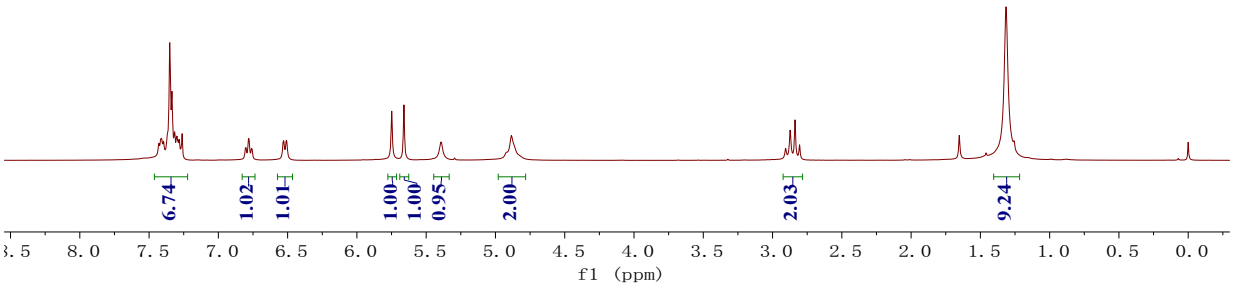
7.268
7.264
7.250
7.243
7.232
7.062
7.058
7.042
7.038
6.677
6.658
5.714
5.645
5.468
4.892
4.861
2.889
2.856
2.842
2.322
1.301
-0.000
O
O
N
HN
O
N
6ee
6.50
1.01
1.01
1.00
1.03
0.90
2.03
2.04
3.01
9.27
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

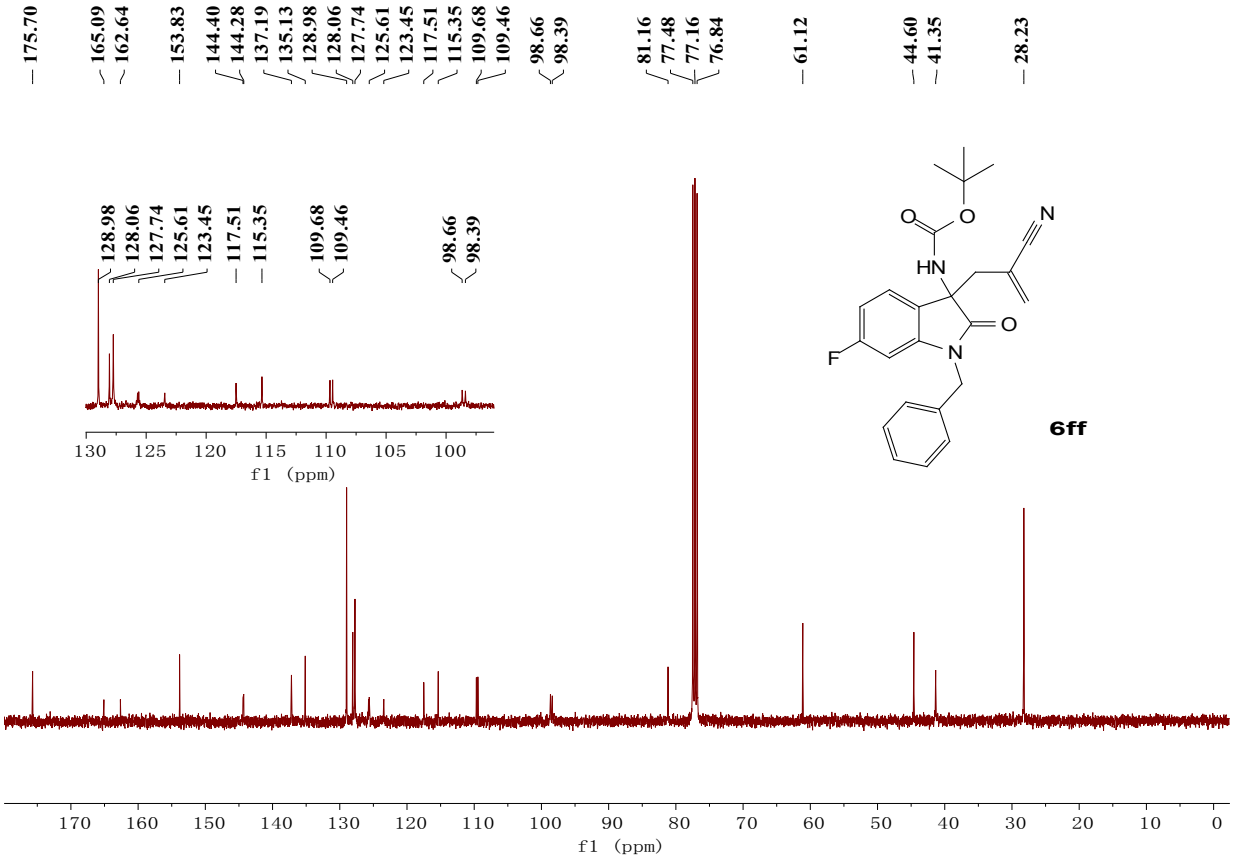

175.29
153.96
140.22
136.99
135.78
132.96
130.00
128.78
128.12
127.75
125.09
117.59
115.55
109.25
80.88
77.48
77.16
76.84
61.57
44.36
41.33
28.22
21.27
130.00
128.78
128.12
127.75
125.09
130 129 128 127 126 125
f1 (ppm)
O
O
N
HN
O
N
6ee
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.409
7.368
7.350
7.334
7.315
7.304
7.299
6.800
6.783
6.778
6.762
6.756
6.533
6.527
6.510
6.505
5.749
5.661
5.392
4.922
4.885
4.862
2.906
2.873
2.838
2.805
1.314
-0.000


O
O
N
HN
O
F
N

6ff

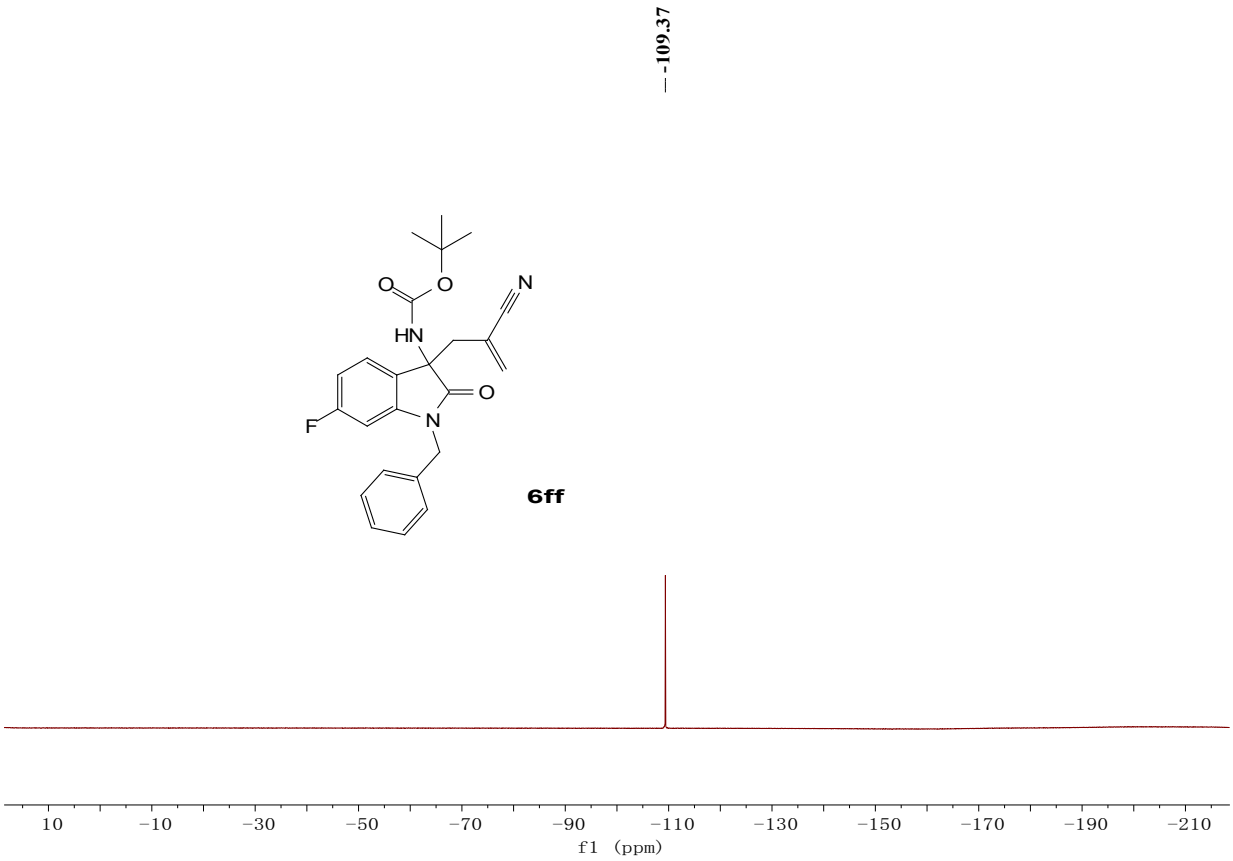

6.74
1.02
1.01
1.00
1.00
0.95
2.00
2.03
9.24
f1 (ppm)


175.70
165.09
162.64
153.83
144.40
144.28
137.19
135.13
128.98
128.06
127.74
125.61
123.45
117.51
115.35
109.68
109.46
98.66
98.39
81.16
77.48
77.16
76.84
61.12
44.60
41.35
28.23
f1 (ppm)

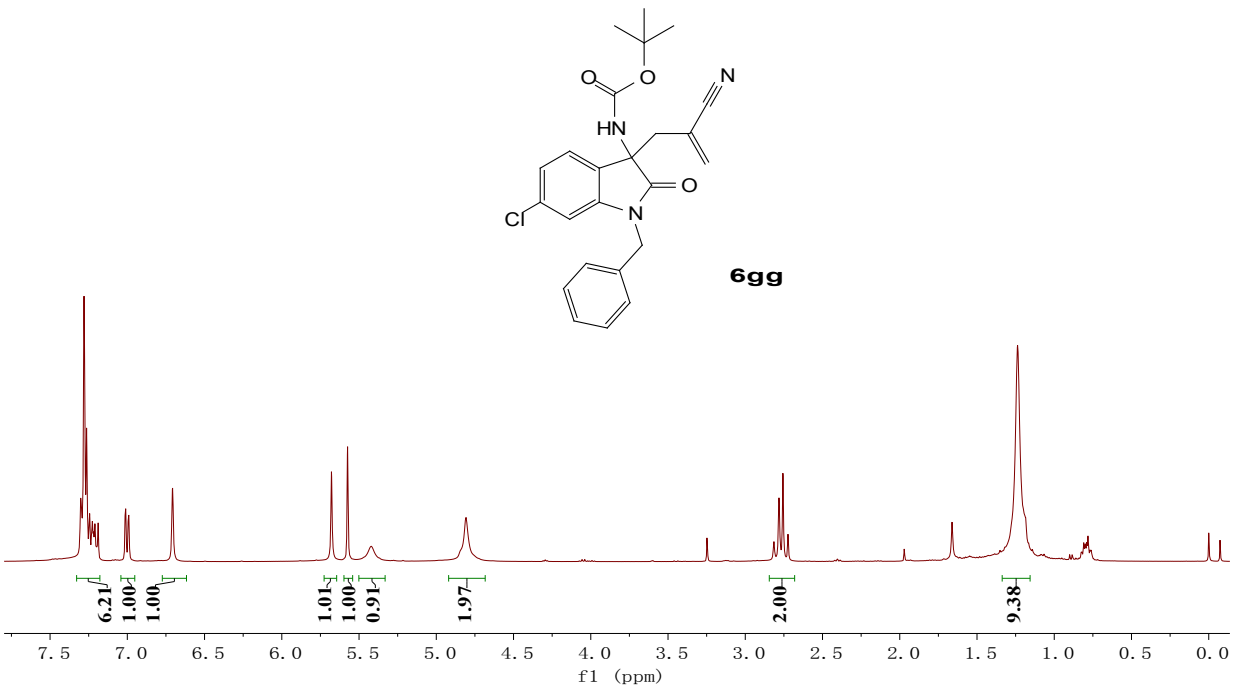
128.98
128.06
127.74
125.61
123.45
117.51
115.35
109.68
109.46
98.66
98.39
f1 (ppm)

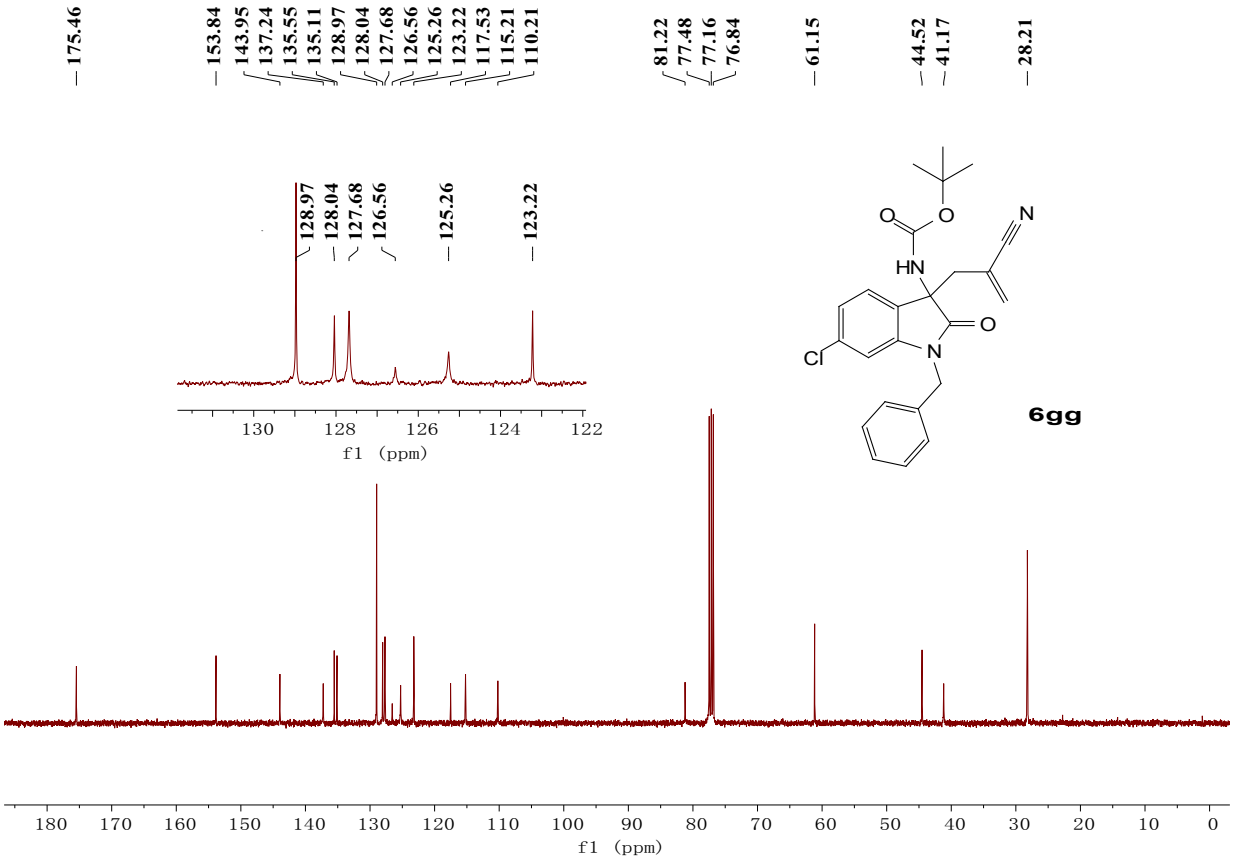
O
O
N
HN
O
F
N

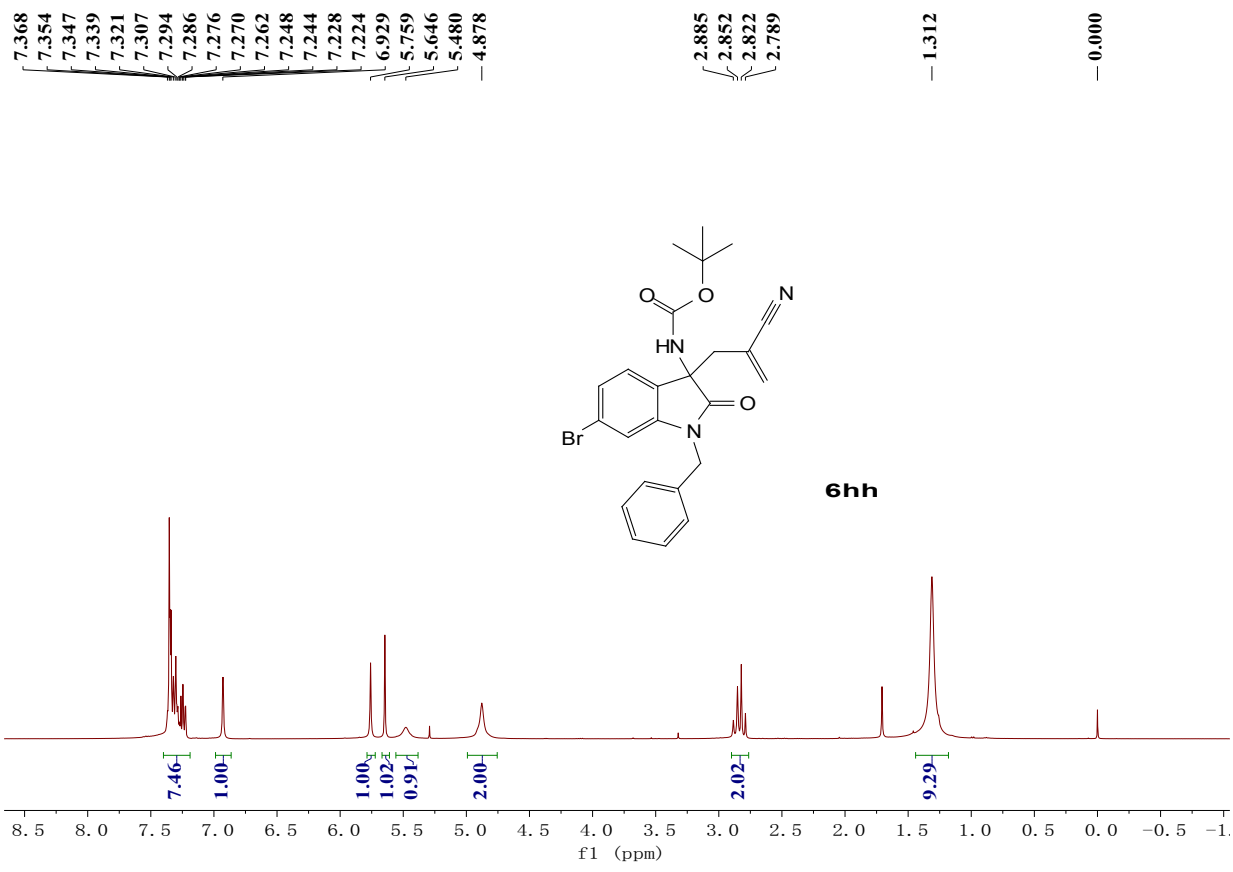
6ff

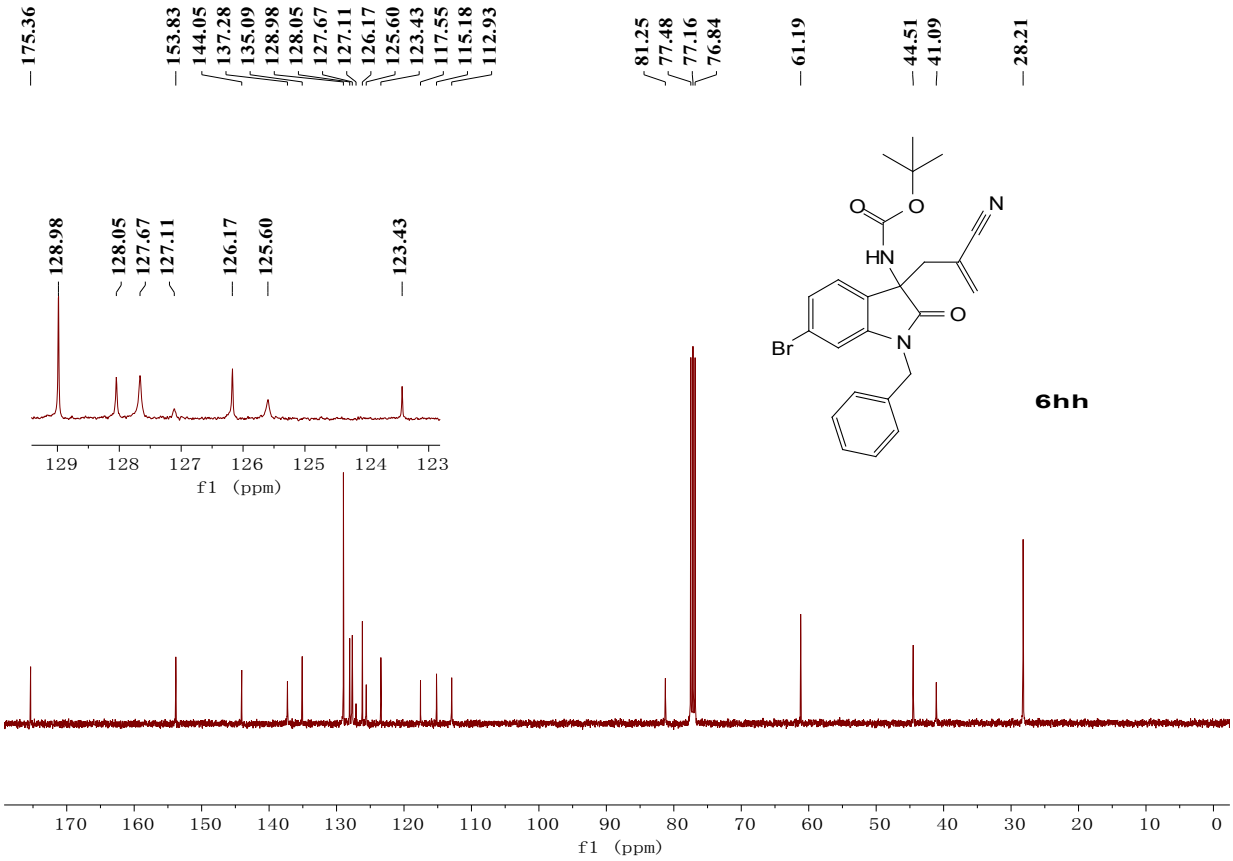

-109.37
O
O
N
HN
O
F
N
6ff
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
f1 (ppm)

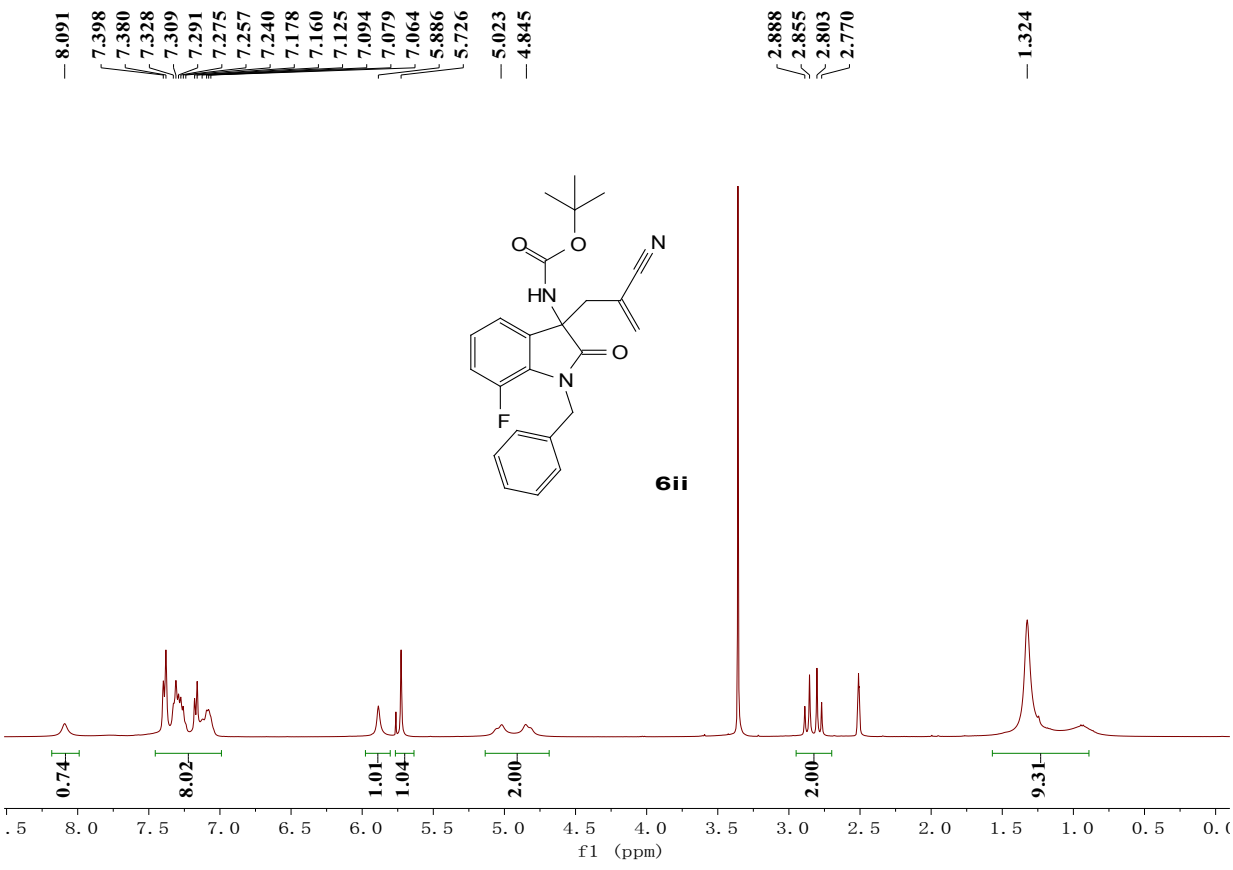

7.302
7.297
7.280
7.264
7.244
7.231
7.219
7.210
7.199
7.189
7.015
7.010
6.995
6.990
6.707
5.678
5.574
5.422
4.807
2.815
2.782
2.756
2.723
1.237
0.000

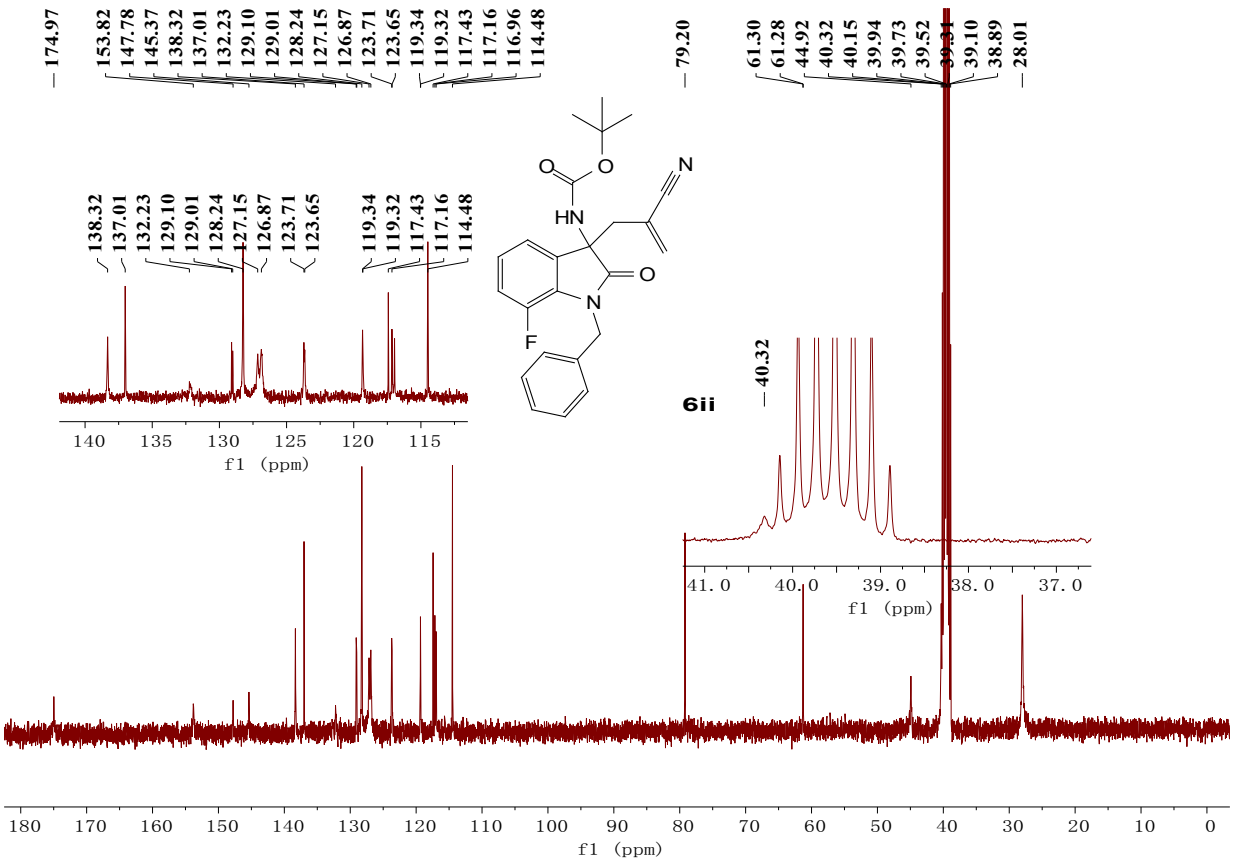

O
O
N
HN
O
Cl
N
6gg
6.21
1.00
1.00
1.01
1.00
0.91
1.97
2.00
9.38
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

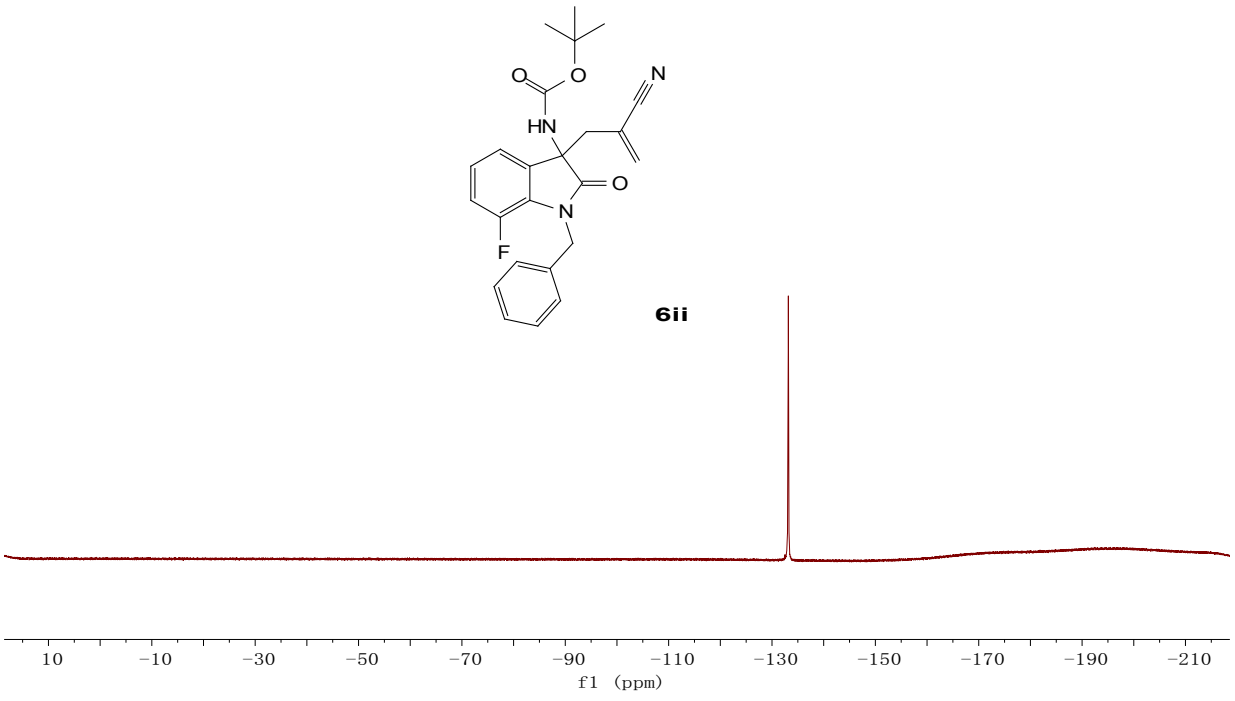

175.46
153.84
143.95
137.24
135.55
135.11
128.97
128.04
127.68
126.56
125.26
123.22
117.53
115.21
110.21
81.22
77.48
77.16
76.84
61.15
44.52
41.17
28.21
128.97
128.04
127.68
126.56
125.26
123.22
130
128
126
124
122
f1 (ppm)
O
O
HN
N
O
N
Cl
6gg
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

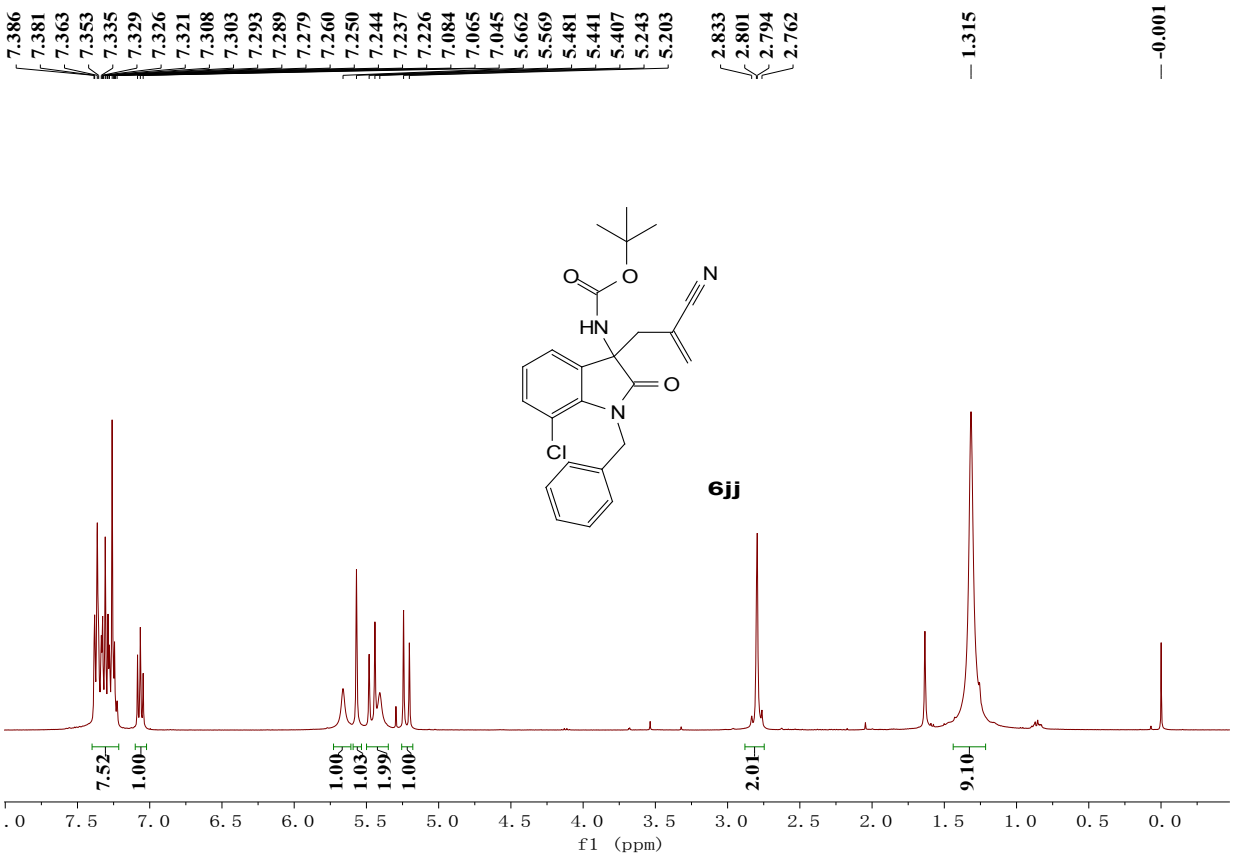

7.368
7.354
7.347
7.339
7.321
7.307
7.294
7.286
7.276
7.270
7.262
7.248
7.244
7.228
7.224
6.929
5.759
5.646
5.480
4.878
2.885
2.852
2.822
2.789
1.312
0.000
O
O
HN
N
O
N
Br
6hh
7.46
1.00
1.00
1.02
0.91
2.00
2.02
9.29
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

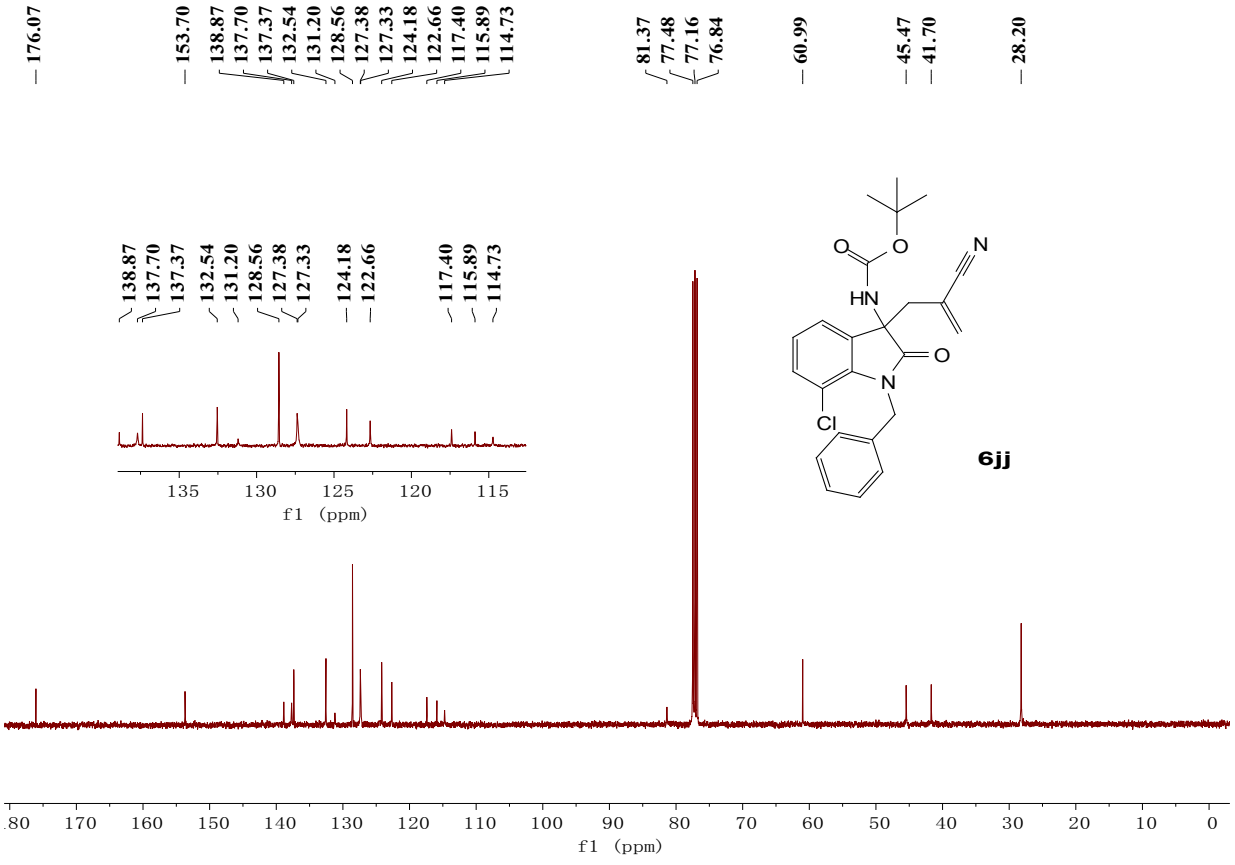

175.36
153.83
144.05
137.28
135.09
128.98
128.05
127.67
127.11
126.17
125.60
123.43
117.55
115.18
112.93
81.25
77.48
77.16
76.84
61.19
44.51
41.09
28.21
f1 (ppm)
6hh

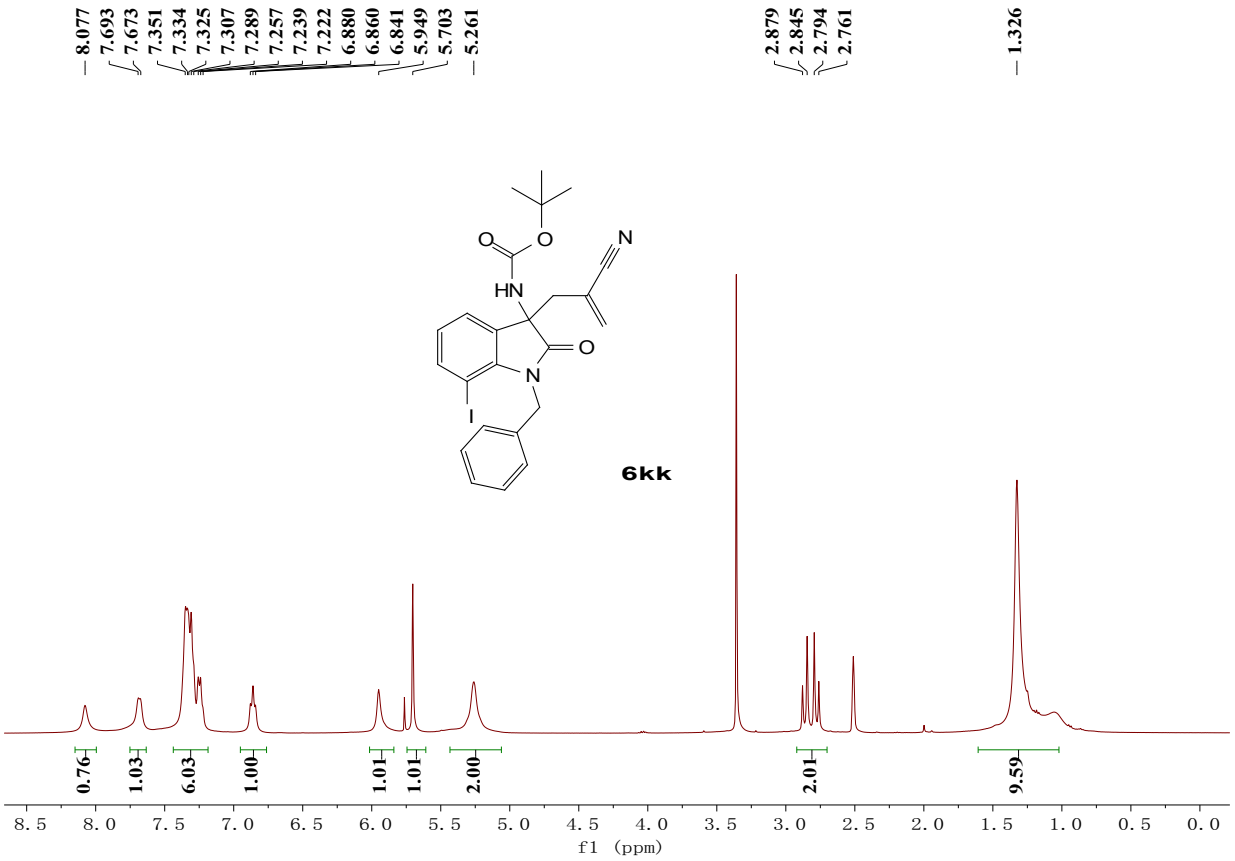

8.091
7.398
7.380
7.328
7.309
7.291
7.275
7.257
7.240
7.178
7.160
7.125
7.094
7.079
7.064
5.886
5.726
5.023
4.845
2.888
2.855
2.803
2.770
1.324
0.74
8.02
1.01
1.04
2.00
2.00
9.31
f1 (ppm)
6ii

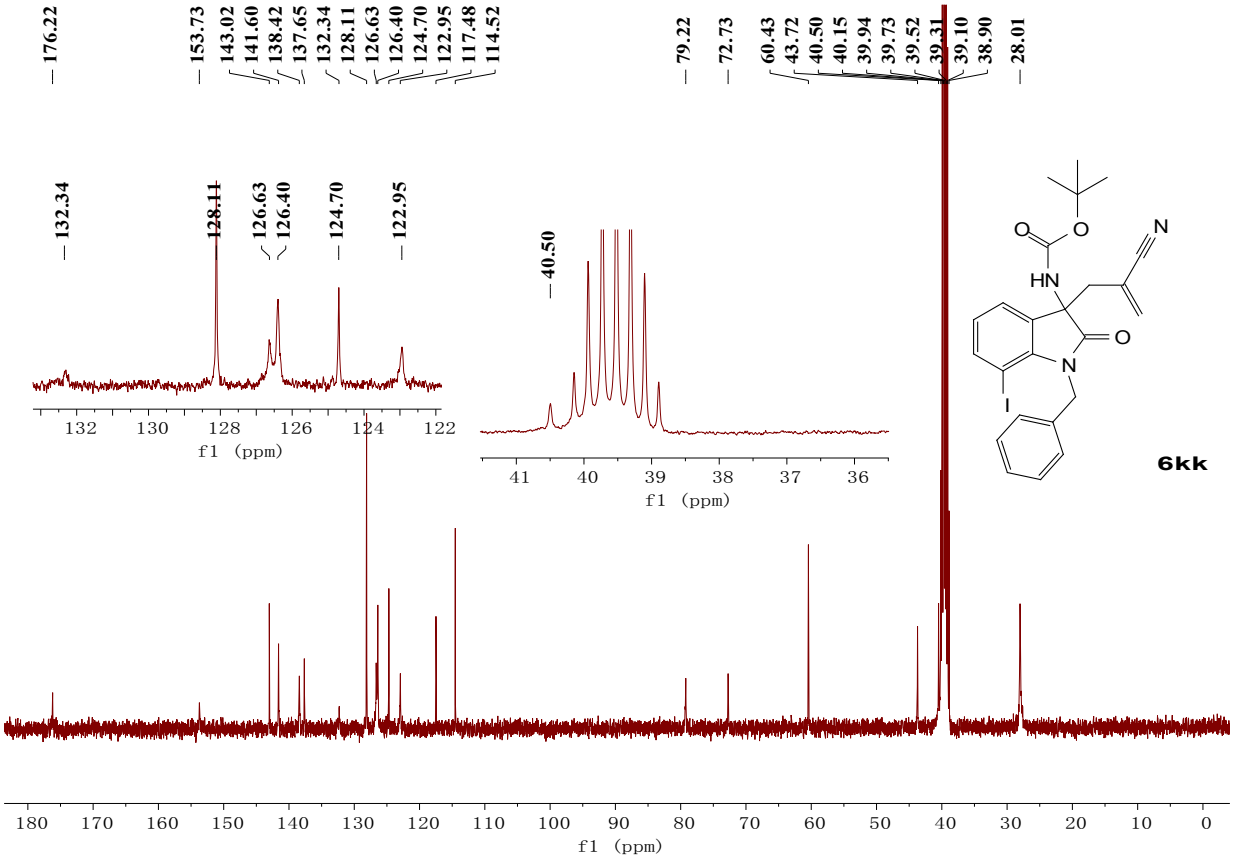

174.97
153.82
147.78
145.37
138.32
137.01
132.23
129.10
129.01
128.24
127.15
126.87
123.71
123.65
119.34
119.32
117.43
117.16
116.96
114.48
79.20
61.30
61.28
44.92
40.32
40.15
39.94
39.73
39.52
39.31
39.10
38.89
28.01
O
O
HN
N
O
N
F
6ii
f1 (ppm)
f1 (ppm)
f1 (ppm)

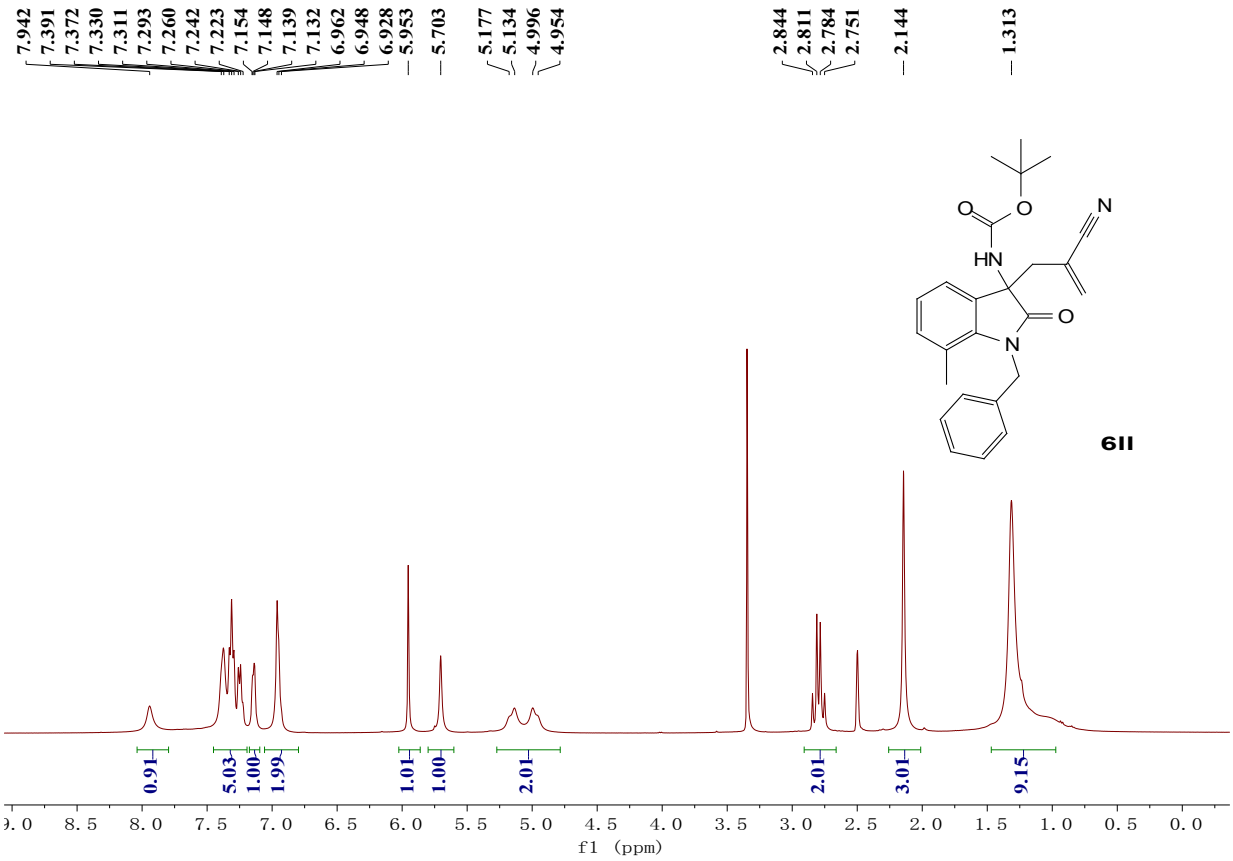

O
O
HN
N
O
N
F
6ii
f1 (ppm)


7.386
7.381
7.363
7.353
7.335
7.329
7.326
7.321
7.308
7.303
7.293
7.289
7.279
7.260
7.250
7.244
7.237
7.226
7.084
7.065
7.045
5.662
5.569
5.481
5.441
5.407
5.243
5.203
2.833
2.801
2.794
2.762
1.315
-0.001
O
O
HN
N
O
N
Cl
6jj
7.52
1.00
1.00
1.03
1.99
1.00
2.01
9.10
f1 (ppm)


176.07
153.70
138.87
137.70
137.37
132.54
131.20
128.56
127.38
127.33
124.18
122.66
117.40
115.89
114.73
81.37
77.48
77.16
76.84
60.99
45.47
41.70
28.20
O
O
HN
N
O
N
Cl
6jj
f1 (ppm)


8.077
7.693
7.673
7.351
7.334
7.325
7.307
7.289
7.257
7.239
7.222
6.880
6.860
6.841
5.949
5.703
5.261
2.879
2.845
2.794
2.761
1.326
6kk
0.76
1.03
6.03
1.00
1.01
1.01
2.00
2.01
9.59
f1 (ppm)


176.22
153.73
143.02
141.60
138.42
137.65
132.34
128.11
126.63
126.40
124.70
122.95
117.48
114.52
79.22
72.73
60.43
43.72
40.50
40.15
39.94
39.73
39.52
39.31
39.10
38.90
28.01
6kk
f1 (ppm)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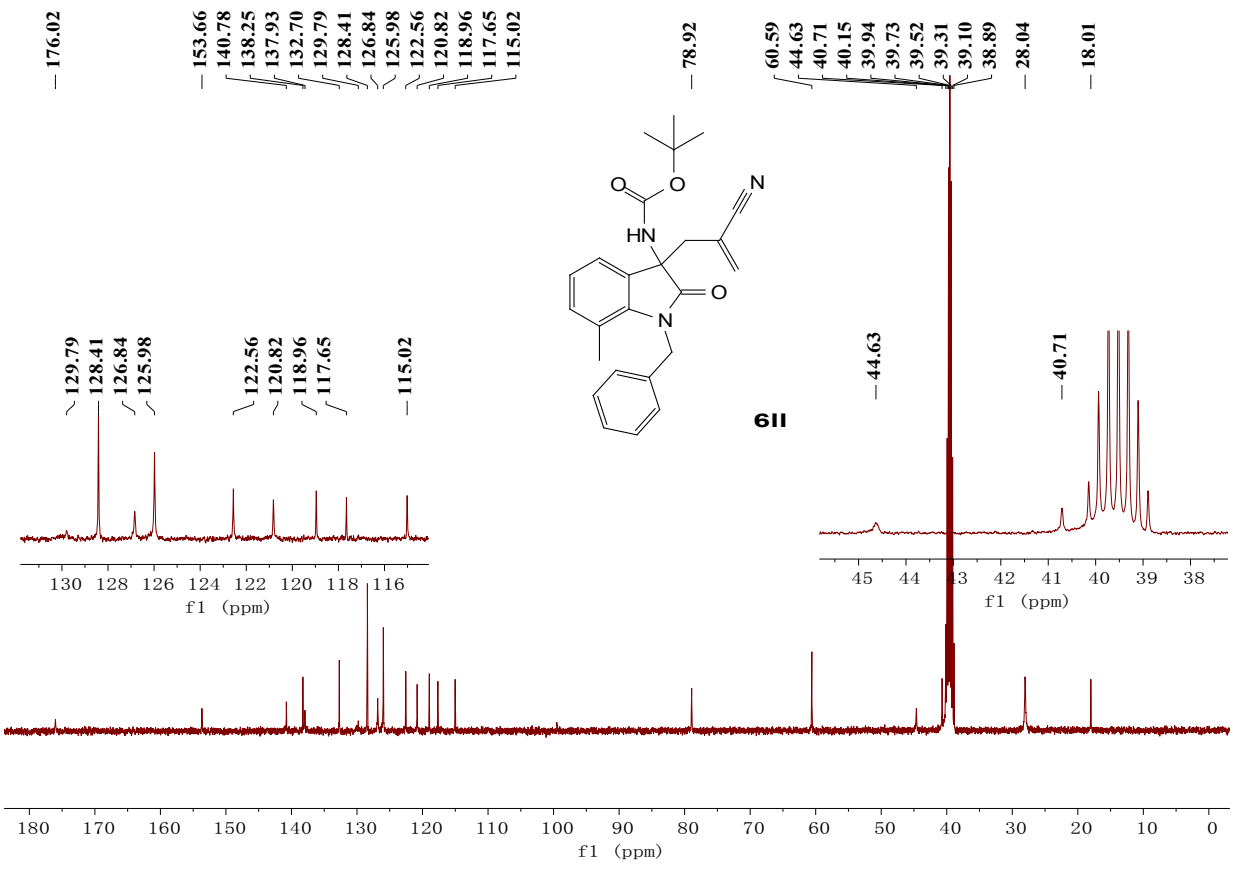
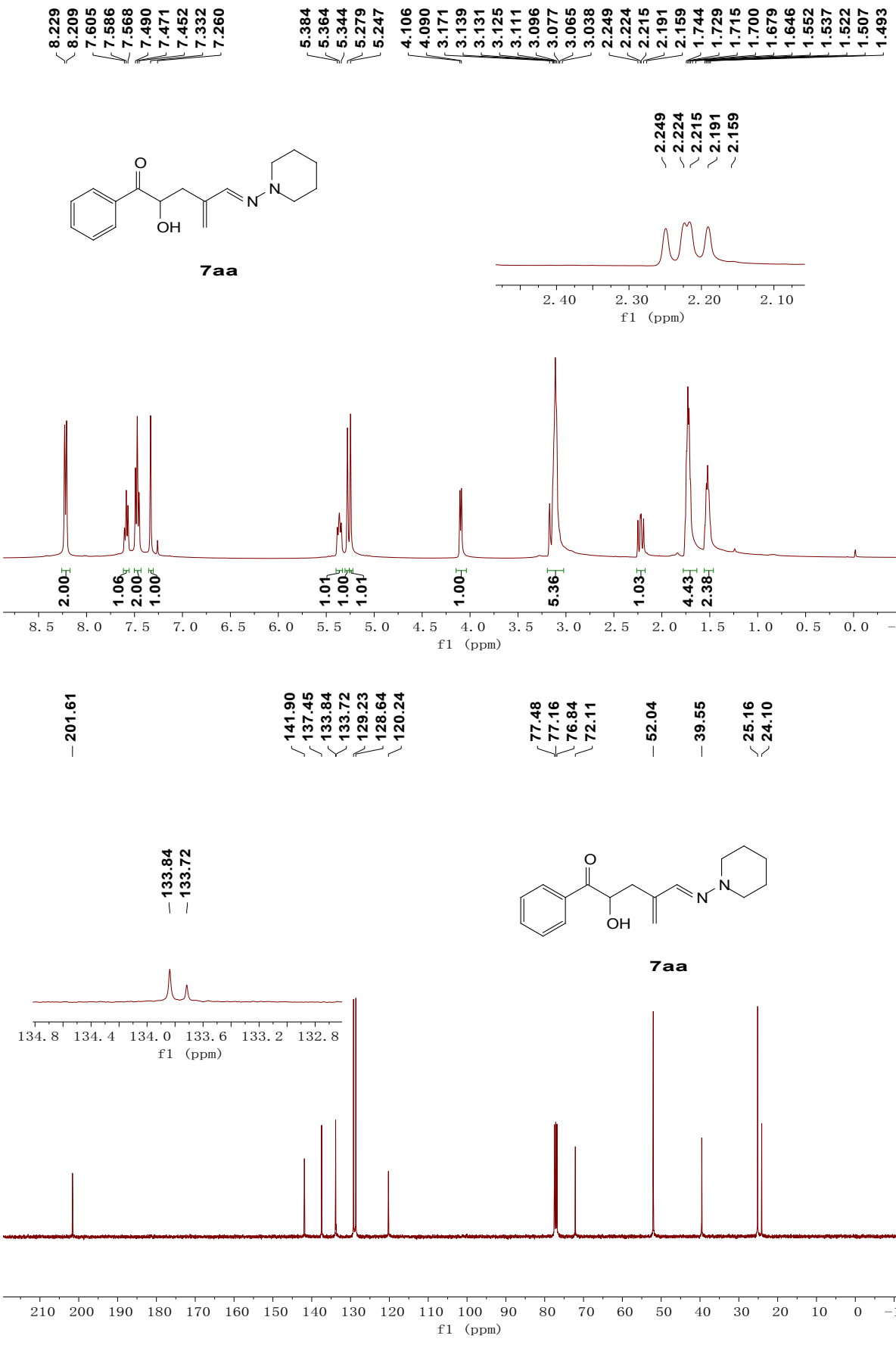
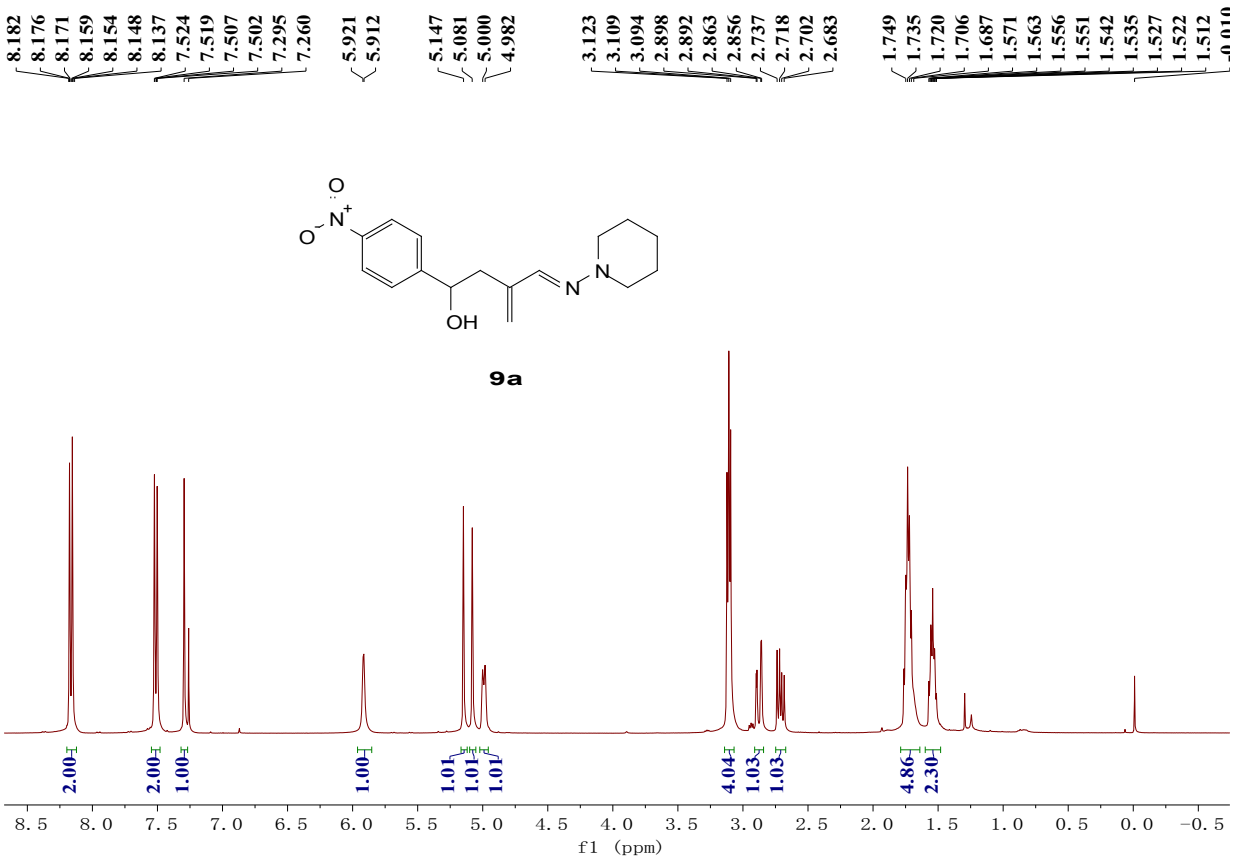
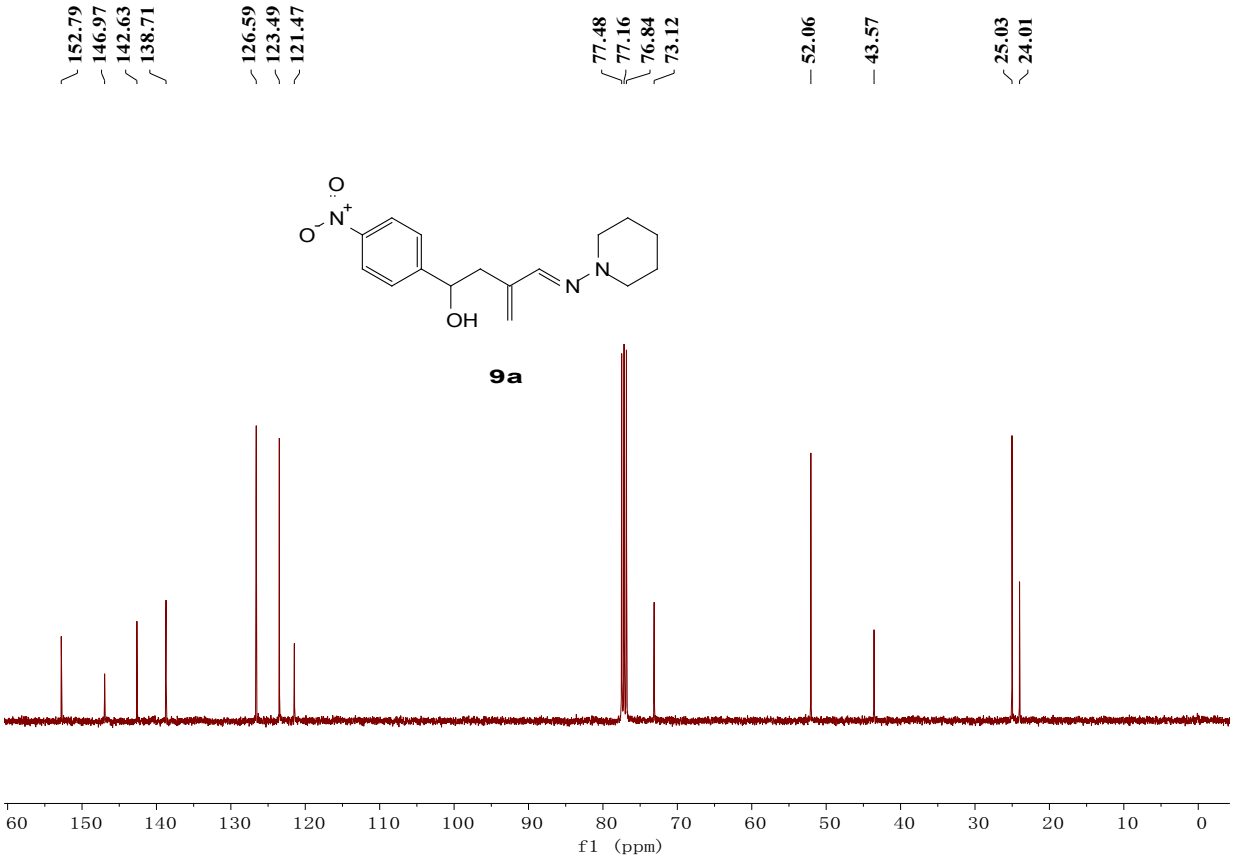
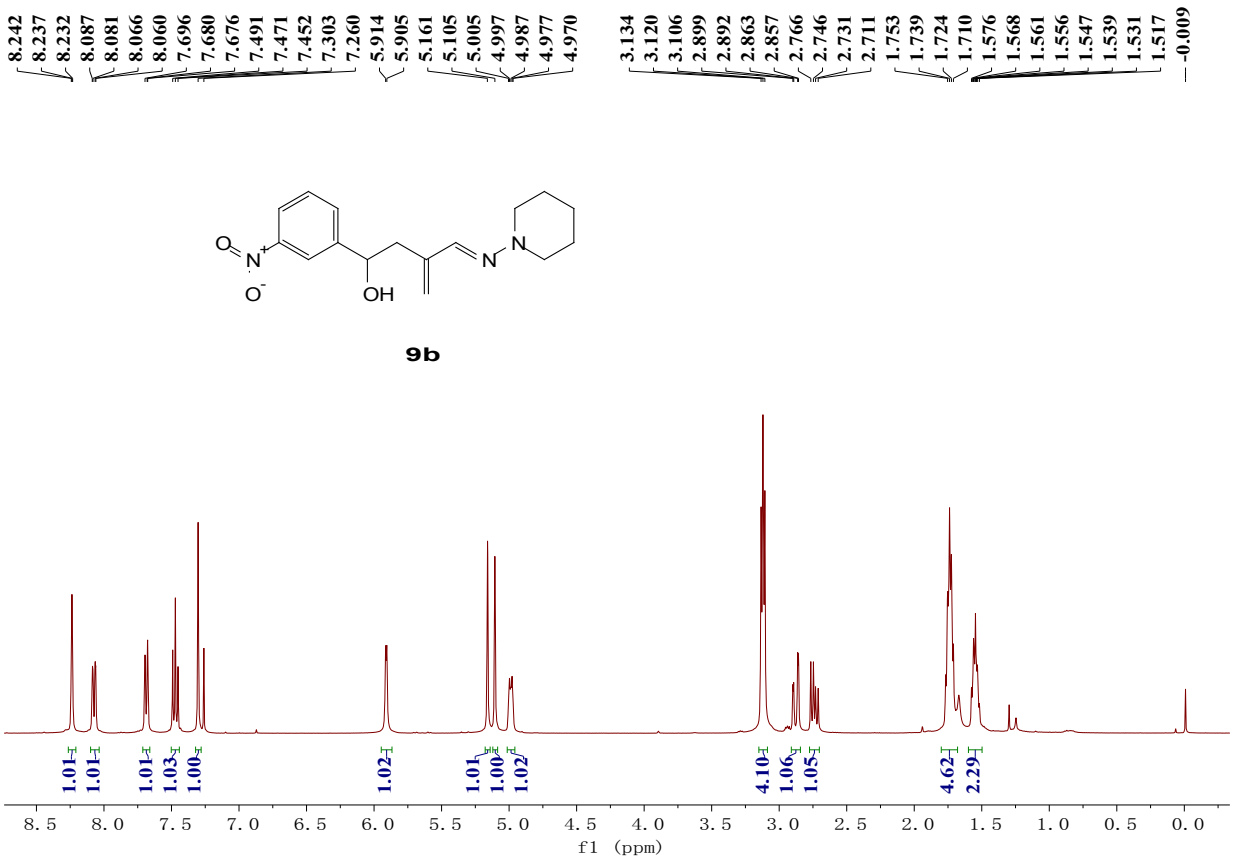
7.391
7.372
7.330
7.311
7.293
7.260
7.242
7.223
7.154
7.148
7.139
7.132
6.962
6.948
6.928
5.953
5.703
5.177
5.134
4.996
4.954
2.844
2.811
2.784
2.751
2.144
1.313
6ll
0.91
5.03
1.00
1.99
1.01
1.00
2.01
2.01
3.01
9.15
f1 (ppm)

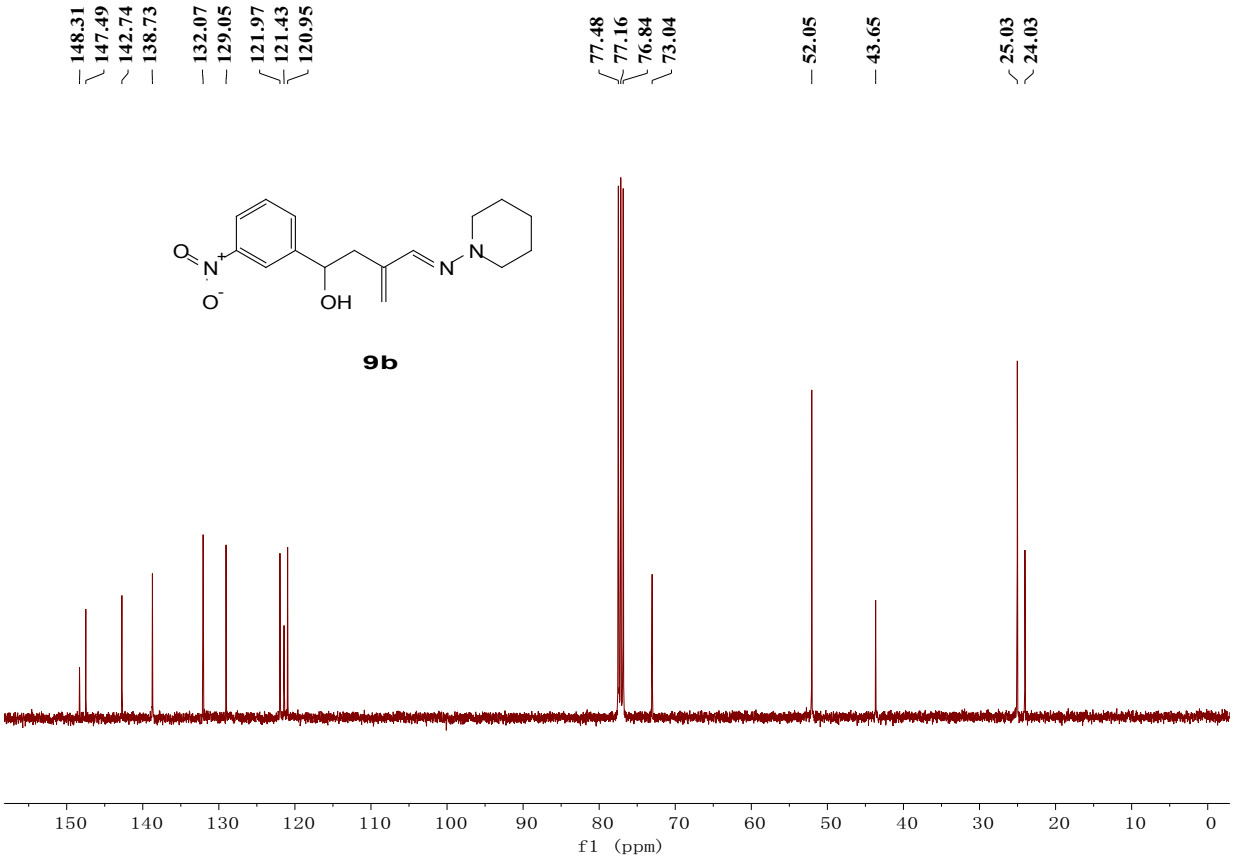

176.02
153.66
140.78
138.25
137.93
132.70
129.79
128.41
126.84
125.98
122.56
120.82
118.96
117.65
115.02
78.92
60.59
44.63
40.71
40.15
39.94
39.73
39.52
39.31
39.10
38.89
28.04
18.01
6ll
f1 (ppm)


8.229
8.209
7.605
7.586
7.568
7.490
7.471
7.452
7.332
7.260
5.384
5.364
5.344
5.279
5.247
4.106
4.090
3.171
3.139
3.131
3.125
3.111
3.096
3.077
3.065
3.038
2.249
2.224
2.215
2.191
2.159
1.744
1.729
1.715
1.700
1.679
1.646
1.552
1.537
1.522
1.507
1.493
O
N
N
OH
7aa
f1 (ppm)
2.00
1.06
2.00
1.00
1.01
1.00
1.01
1.00
5.36
1.03
4.43
2.38
201.61
141.90
137.45
133.84
133.72
129.23
128.64
120.24
77.48
77.16
76.84
72.11
52.04
39.55
25.16
24.10

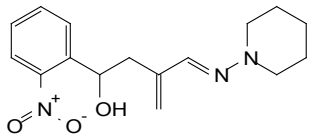

8.182
8.176
8.171
8.159
8.154
8.148
8.137
7.524
7.519
7.507
7.502
7.295
7.260
5.921
5.912
5.147
5.081
5.000
4.982
3.123
3.109
3.094
2.898
2.892
2.863
2.856
2.737
2.718
2.702
2.683
1.749
1.735
1.720
1.706
1.687
1.571
1.563
1.556
1.551
1.542
1.535
1.527
1.522
1.512
O
N+
O
N
N
OH
9a
2.00
2.00
1.00
1.00
1.01
1.01
1.01
4.04
1.03
1.03
4.86
2.30
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


152.79
146.97
142.63
138.71
126.59
123.49
121.47
77.48
77.16
76.84
73.12
52.06
43.57
25.03
24.01
O
N+
O
N
N
OH
9a
60 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

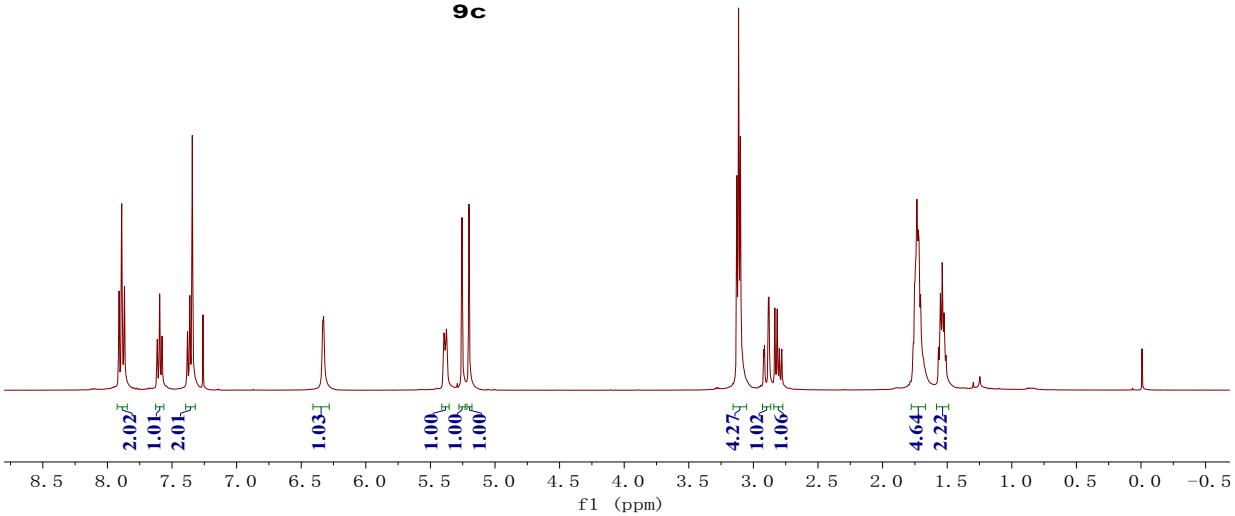

8.242
8.237
8.232
8.087
8.081
8.066
8.060
7.696
7.680
7.676
7.491
7.471
7.452
7.303
7.260
5.914
5.905
5.161
5.105
5.005
4.997
4.987
4.977
4.970
3.134
3.120
3.106
2.899
2.892
2.863
2.857
2.766
2.746
2.731
2.711
1.753
1.739
1.724
1.710
1.576
1.568
1.561
1.556
1.547
1.539
1.531
1.517
-0.009
O
N+
O-
OH
N
N
9b
1.01
1.01
1.01
1.03
1.00
1.02
1.01
1.00
1.02
4.10
1.06
1.05
4.62
2.29
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


148.31
147.49
142.74
138.73
132.07
129.05
121.97
121.43
120.95
77.48
77.16
76.84
73.04
52.05
43.65
25.03
24.03
O
N+
O-
OH
N
N
9b
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

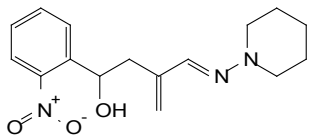
7.913 7.910 7.892 7.889 7.871 7.867 7.617 7.614 7.598 7.595 7.579 7.575 7.383 7.380 7.364 7.362 7.360 7.343 7.260 6.334 6.326 5.395 5.389 5.382 5.376 5.256 5.200 3.129 3.115 3.101 2.914 2.884 2.878 2.834 2.816 2.799 2.780 1.762 1.753 1.746 1.734 1.724 1.718 1.706 1.568 1.553 1.538 1.532 1.523 -0.008



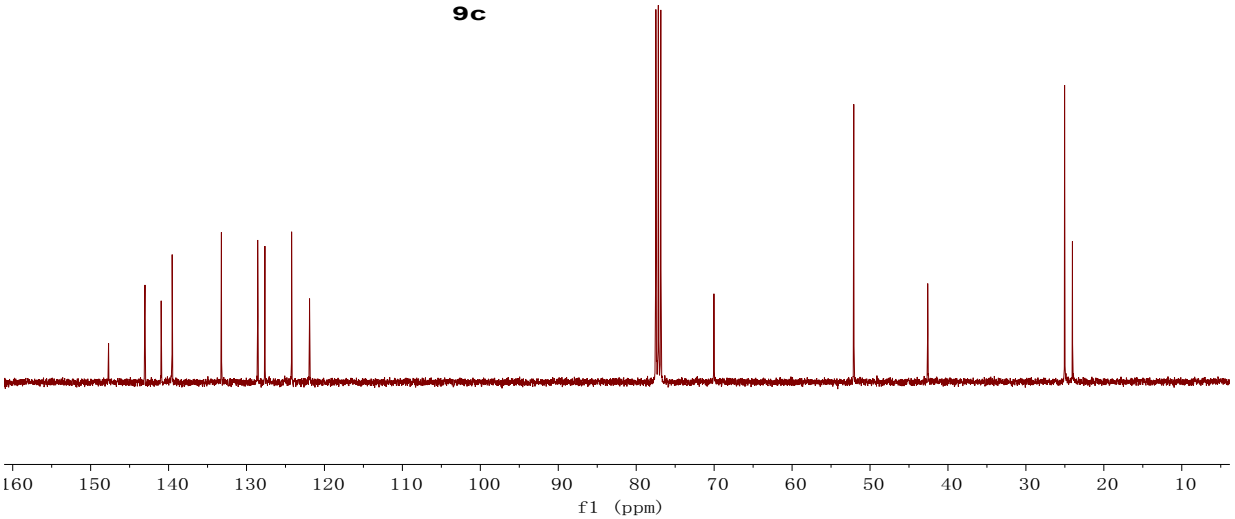
9c

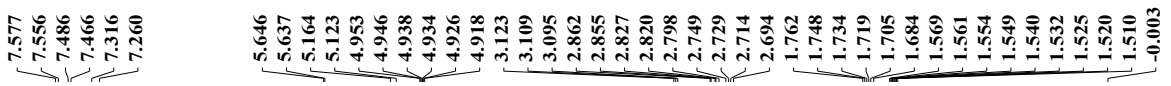


147.70 143.03 140.95 139.54 133.22 128.57 127.64 124.21 121.91 77.48 77.16 76.84 70.03 52.09 42.60 25.03 24.03



9c

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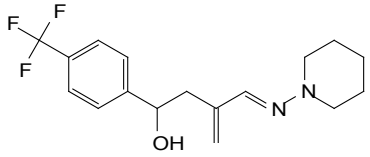
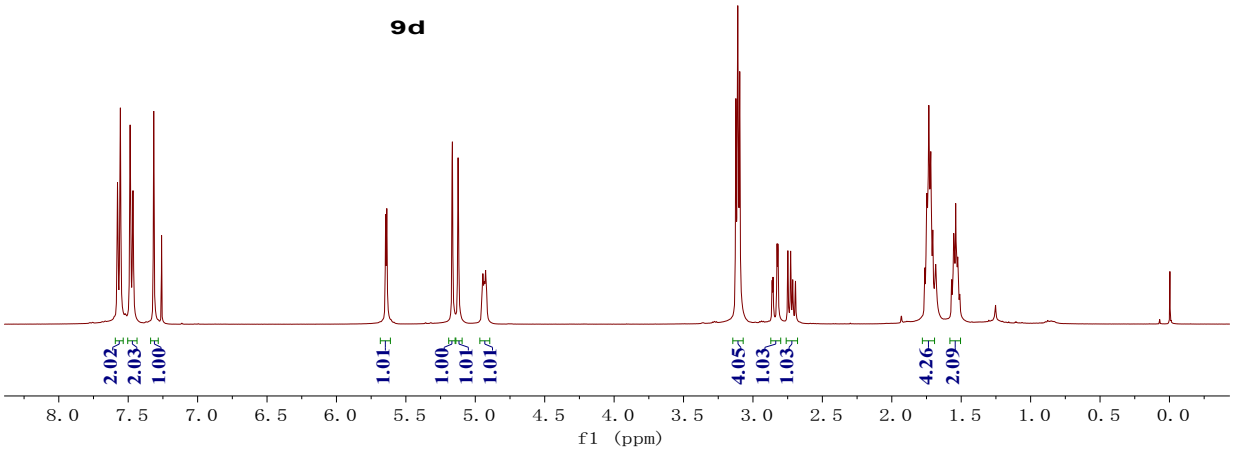
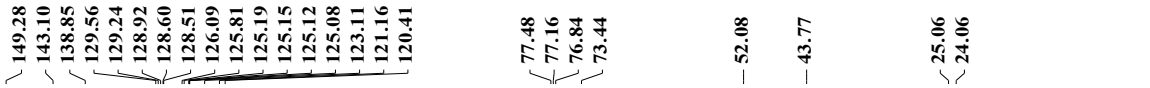
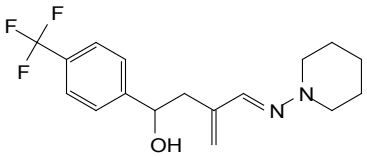
7.556
7.486
7.466
7.316
7.260
5.646
5.637
5.164
5.123
4.953
4.946
4.938
4.934
4.926
4.918
3.123
3.109
3.095
2.862
2.855
2.827
2.820
2.798
2.749
2.729
2.714
2.694
1.762
1.748
1.734
1.719
1.705
1.684
1.569
1.561
1.554
1.549
1.540
1.532
1.525
1.520
1.510
-0.003


F
F
F
N
N
OH

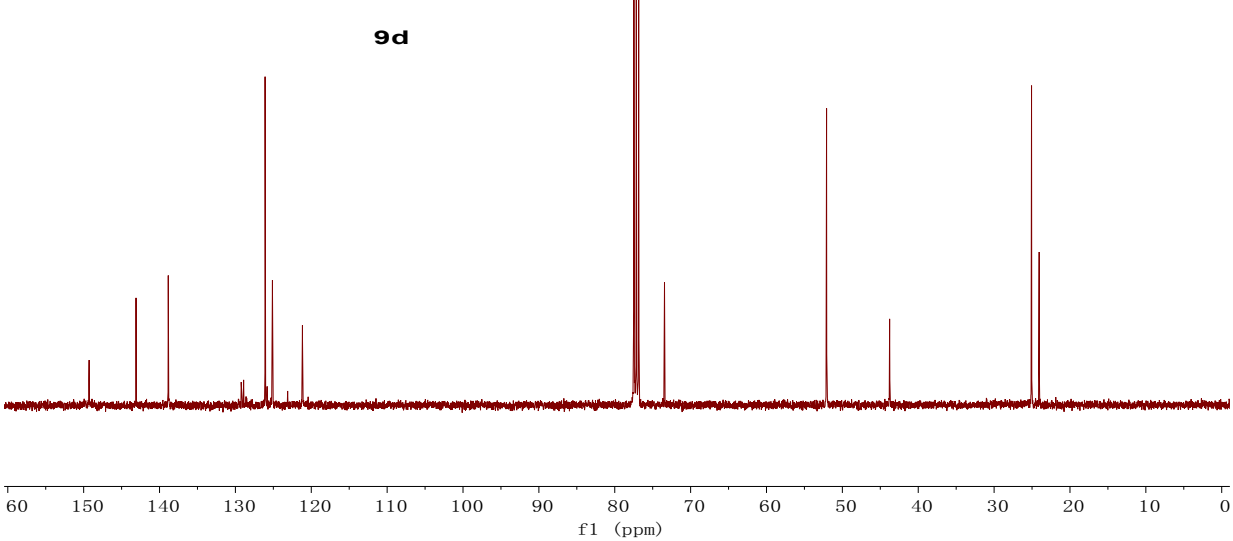
9d

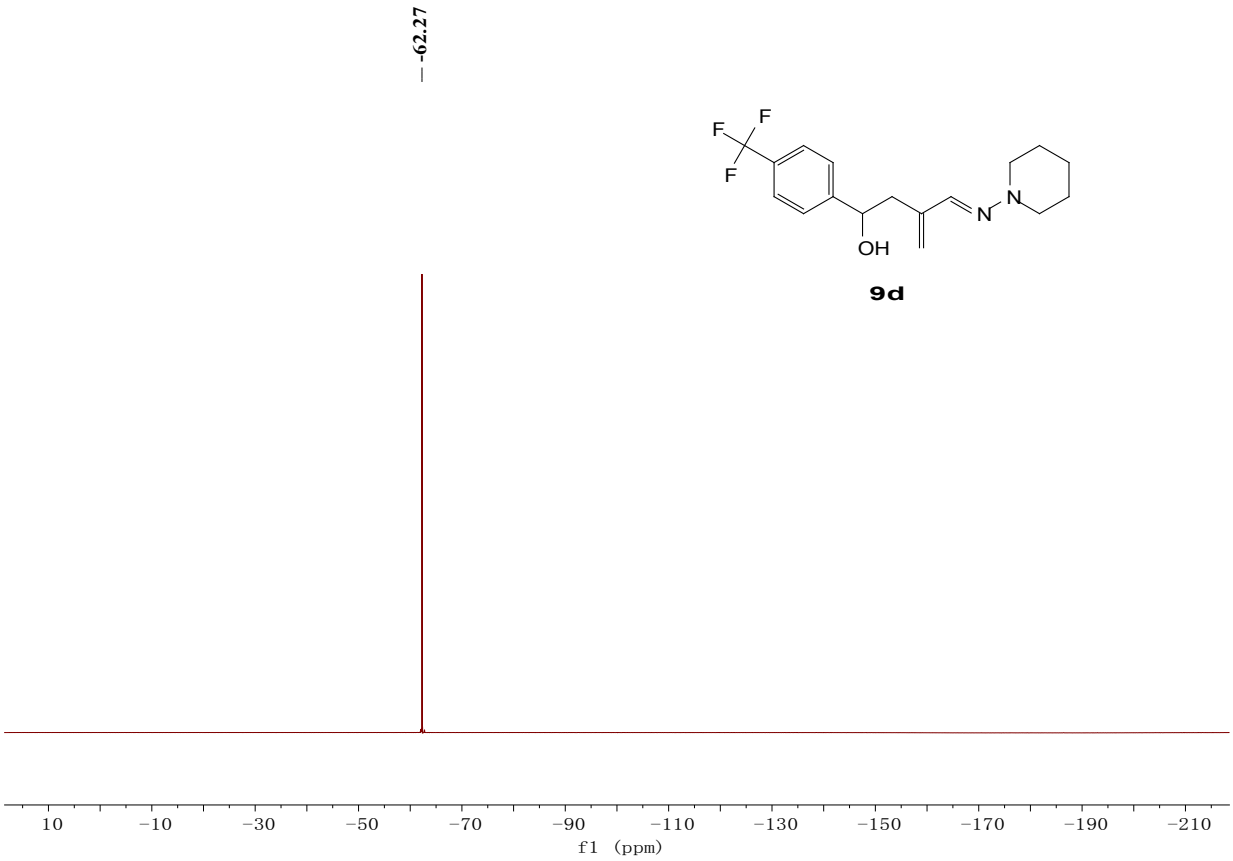

2.02
2.03
1.00
1.01
1.00
1.01
1.01
4.05
1.03
1.03
4.26
2.09
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


149.28
143.10
138.85
129.56
129.24
128.92
128.60
128.51
126.09
125.81
125.19
125.15
125.12
125.08
123.11
121.16
120.41
77.48
77.16
76.84
73.44
52.08
43.77
25.06
24.06


F
F
F
N
N
OH

9d


60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



7.999
7.994
7.990
7.978
7.973
7.968
7.437
7.432
7.421
7.416
7.305
7.260
5.637
5.628
5.143
5.140
5.102
5.099
4.949
4.941
4.937
4.929
3.895
3.120
3.106
3.092
2.867
2.865
2.860
2.858
2.832
2.830
2.824
2.745
2.726
2.710
2.691
1.757
1.742
1.729
1.714
1.700
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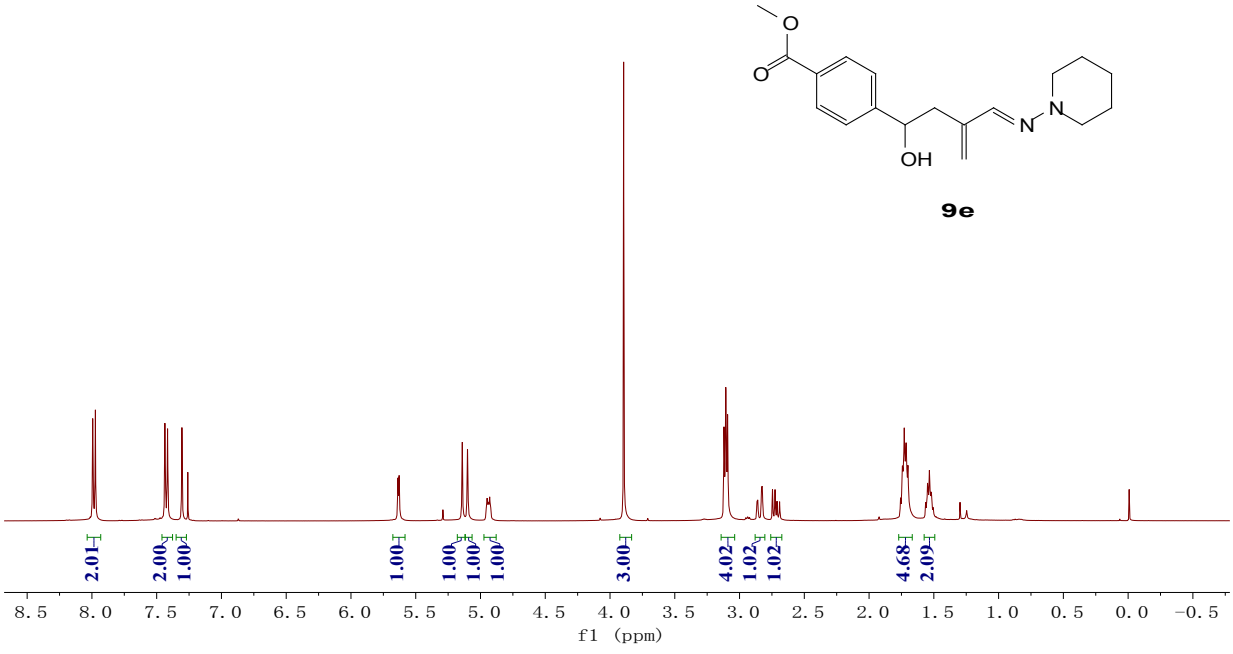
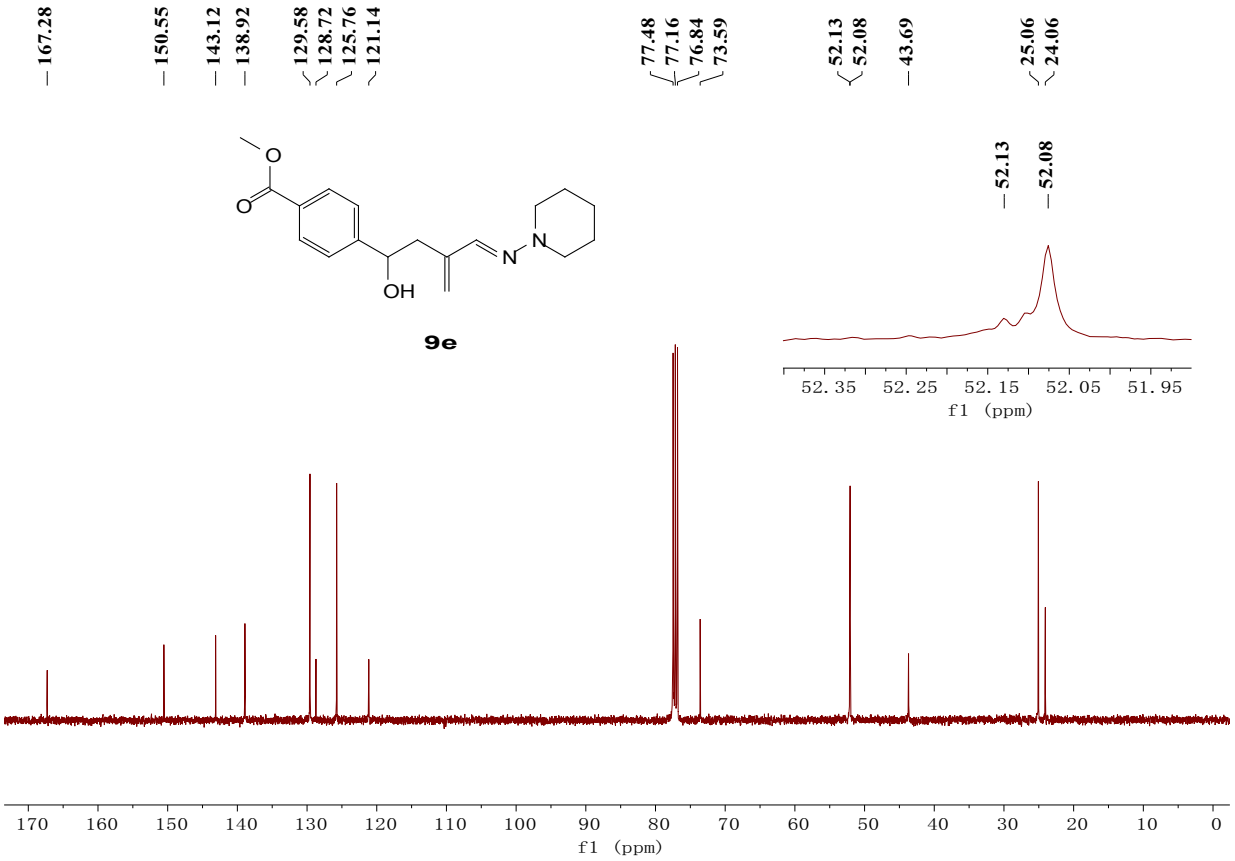
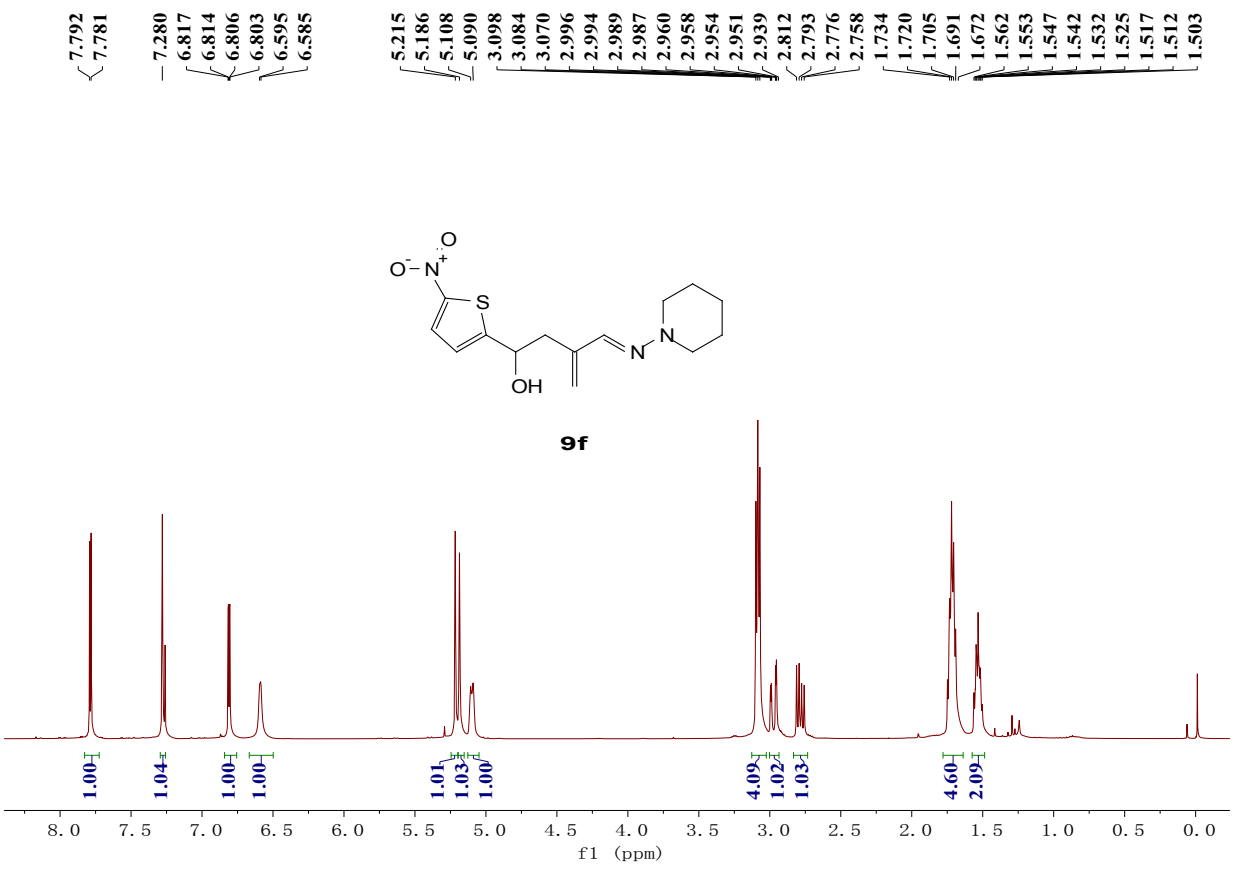
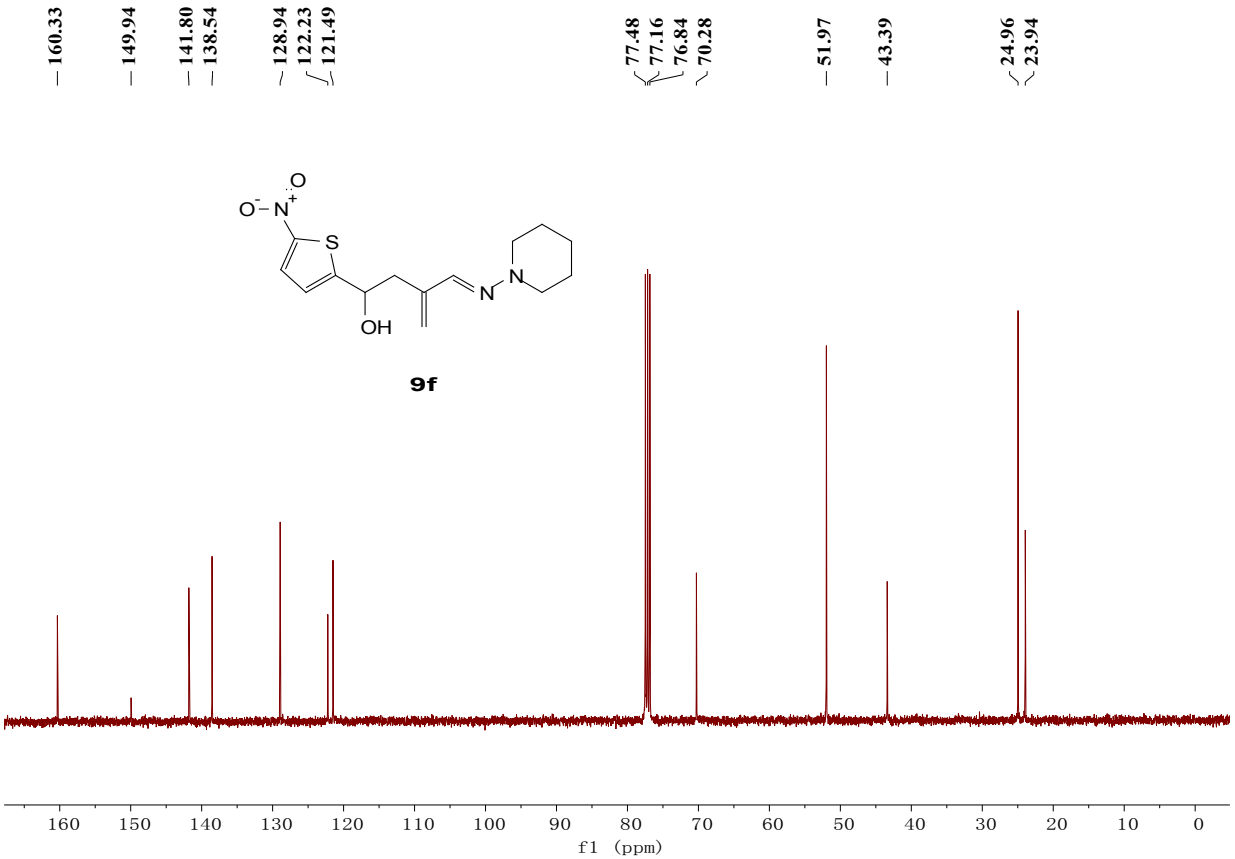
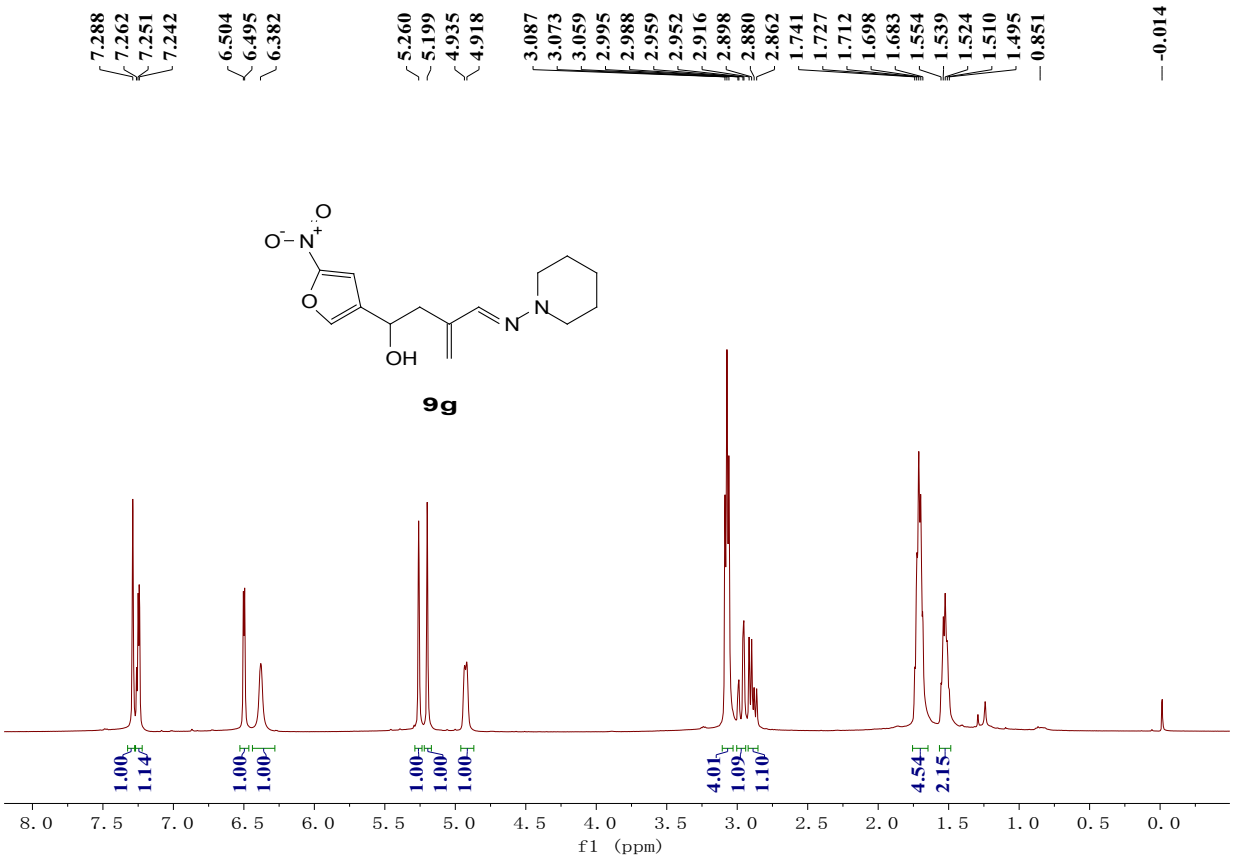
1.556
1.549
1.543
1.534
1.528
1.519
-0.008

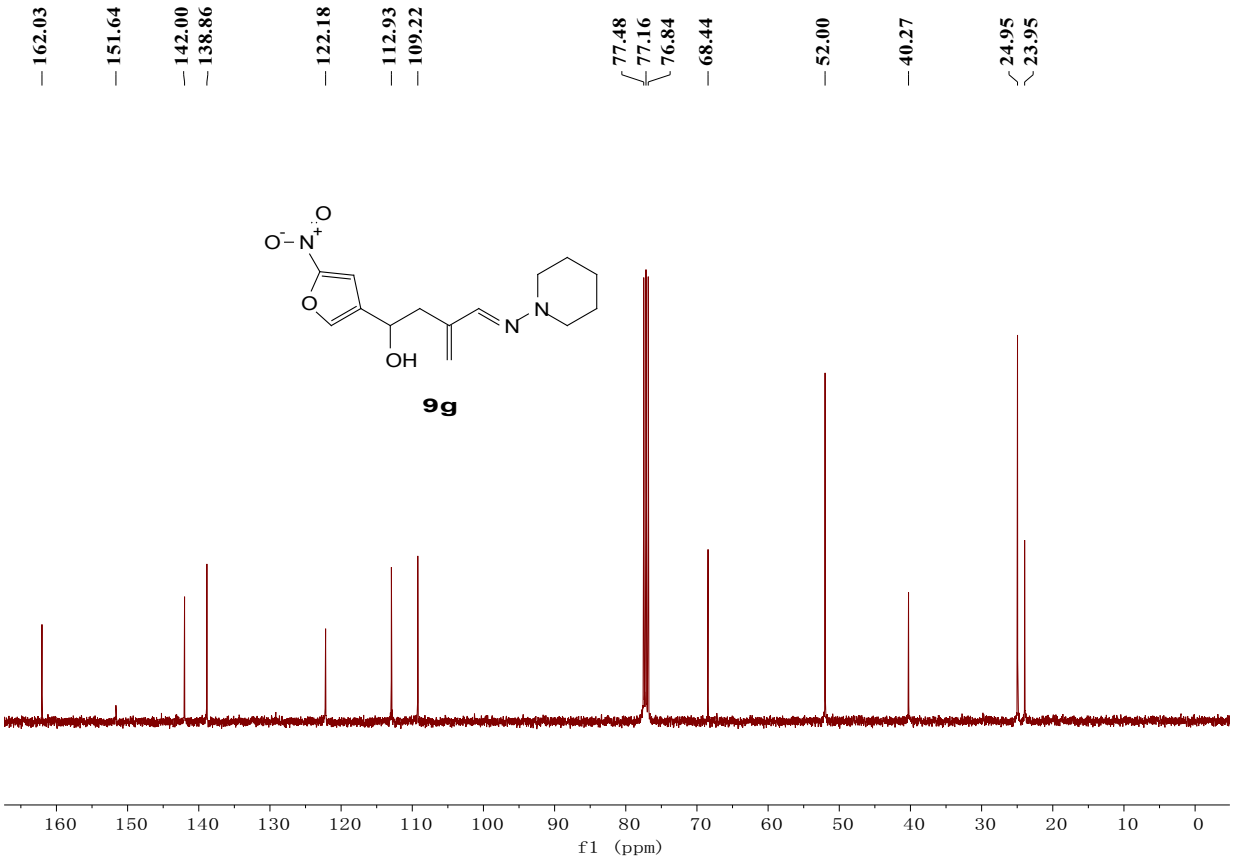



167.28
150.55
143.12
138.92
129.58
128.72
125.76
121.14
77.48
77.16
76.84
73.59
52.13
52.08
43.69
25.06
24.06
O
O
N
N
OH
9e
52.13
52.08
52.35 52.25 52.15 52.05 51.95
f1 (ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

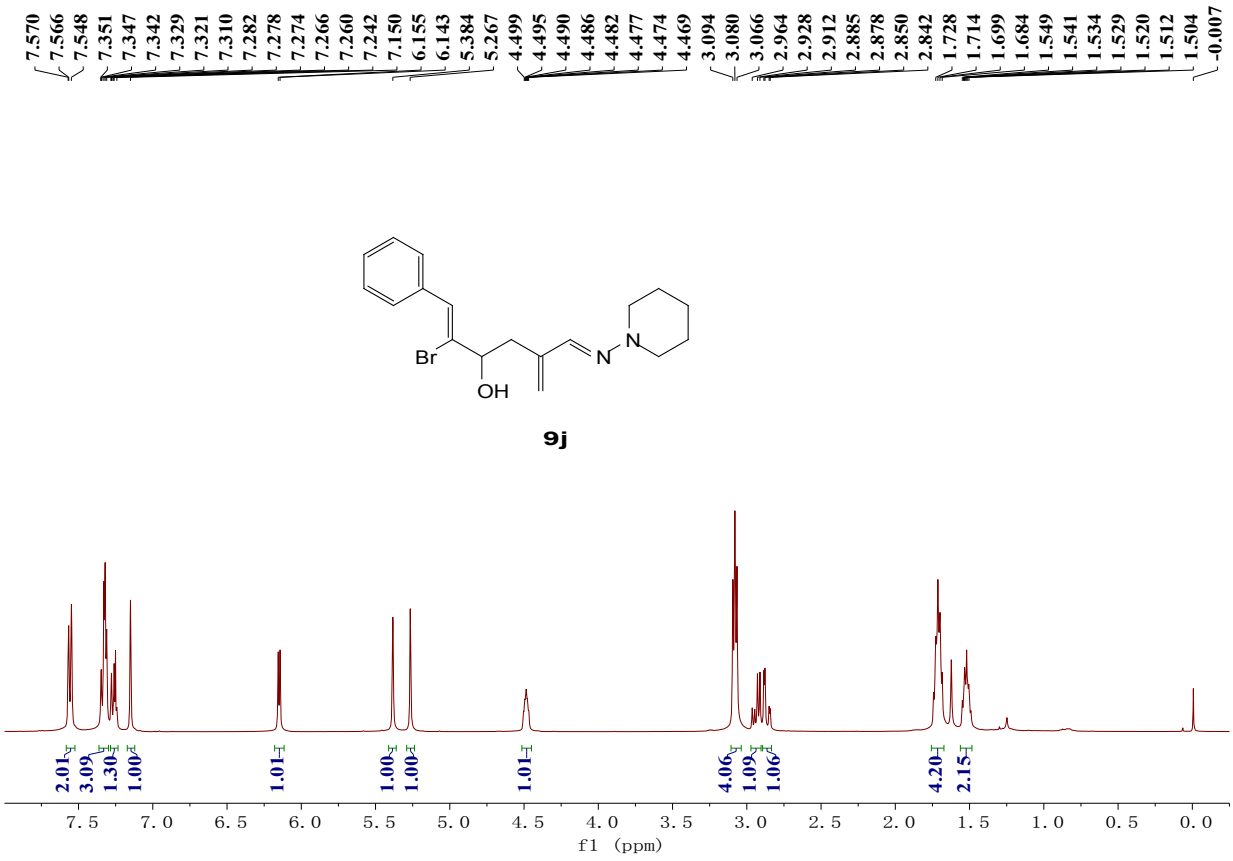

7.792
7.781
7.280
6.817
6.814
6.806
6.803
6.595
6.585
5.215
5.186
5.108
5.090
3.098
3.084
3.070
2.996
2.994
2.989
2.987
2.960
2.958
2.954
2.951
2.939
2.812
2.793
2.776
2.758
1.734
1.720
1.705
1.691
1.672
1.562
1.553
1.547
1.542
1.532
1.525
1.517
1.512
1.503
O
O
N
S
N
OH
9f
1.00
1.04
1.00
1.00
1.01
1.03
1.00
4.09
1.02
1.03
4.60
2.09
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


160.33
149.94
141.80
138.54
128.94
122.23
121.49
77.48
77.16
76.84
70.28
51.97
43.39
24.96
23.94
9f
f1 (ppm)

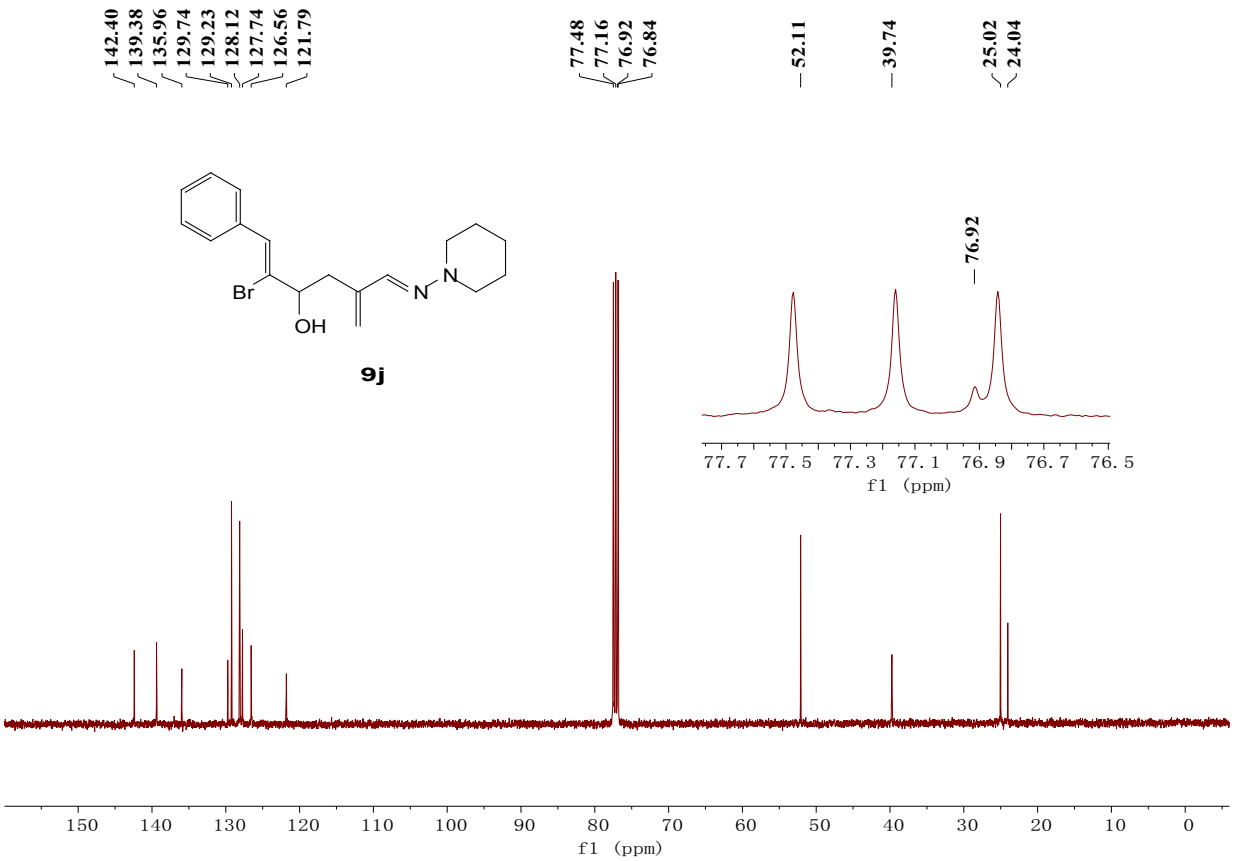

7.288
7.262
7.251
7.242
6.504
6.495
6.382
5.260
5.199
4.935
4.918
3.087
3.073
3.059
2.995
2.988
2.959
2.952
2.916
2.898
2.880
2.862
1.741
1.727
1.712
1.698
1.683
1.554
1.539
1.524
1.510
1.495
0.851
-0.014
9g
1.00
1.14
1.00
1.00
1.00
1.00
1.00
4.01
1.09
1.10
4.54
2.15
f1 (ppm)

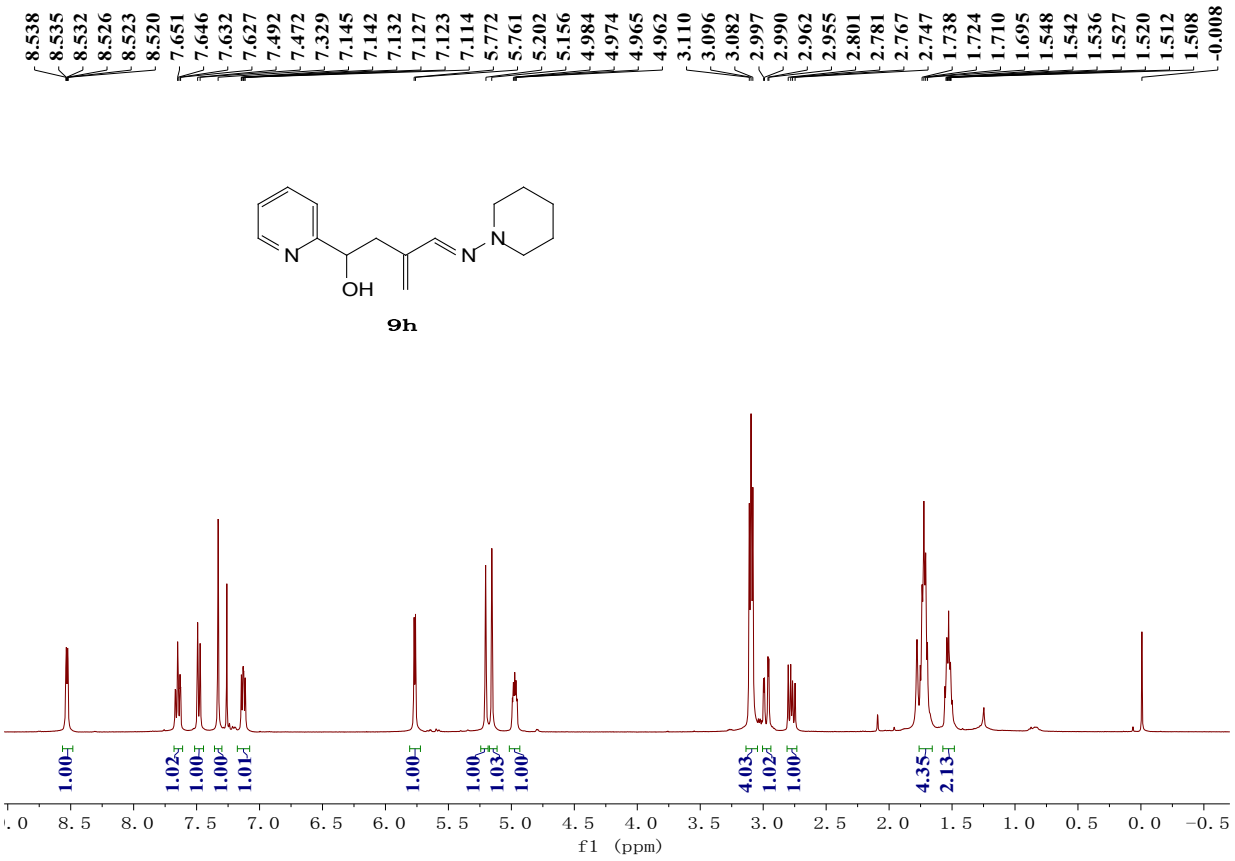

162.03
151.64
142.00
138.86
122.18
112.93
109.22
77.48
77.16
76.84
68.44
52.00
40.27
24.95
23.95
O
O
N
O
N
OH
f1 (ppm)

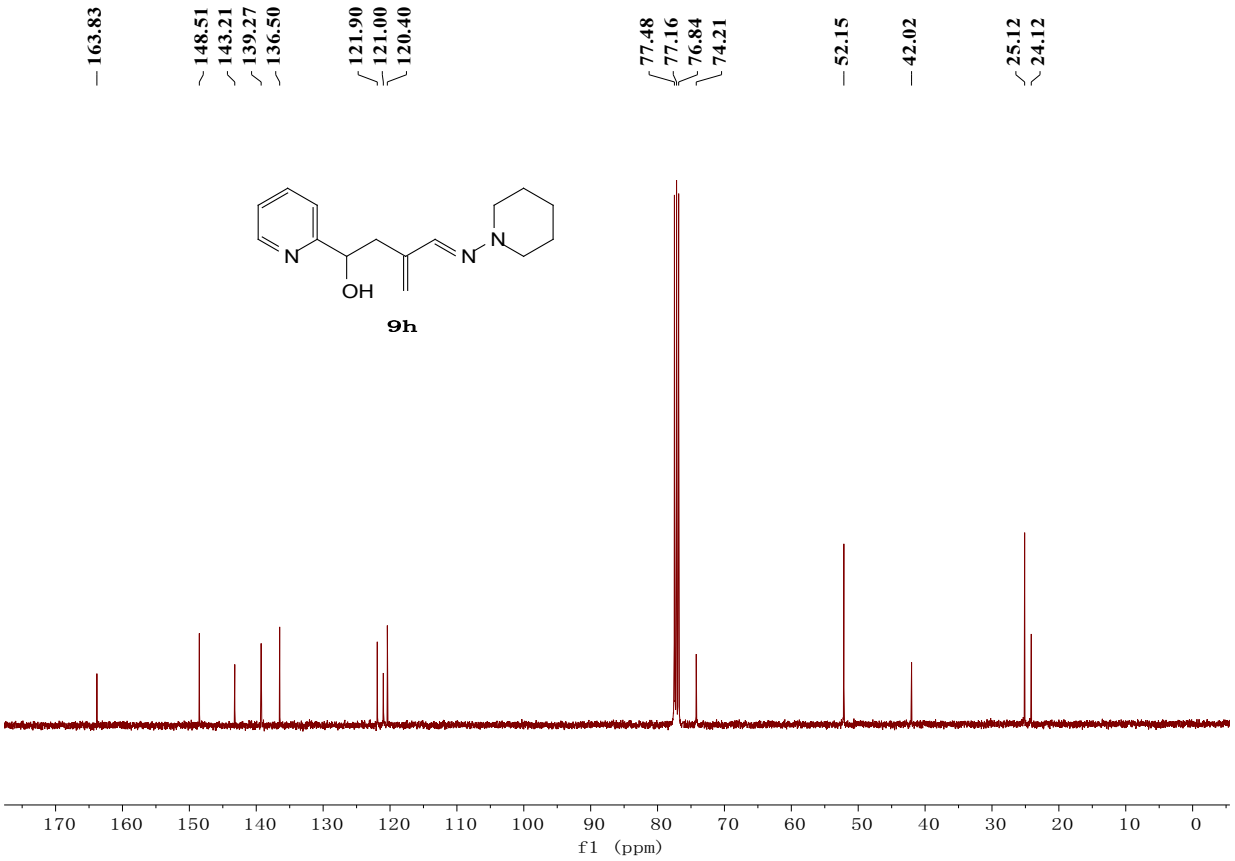
9g

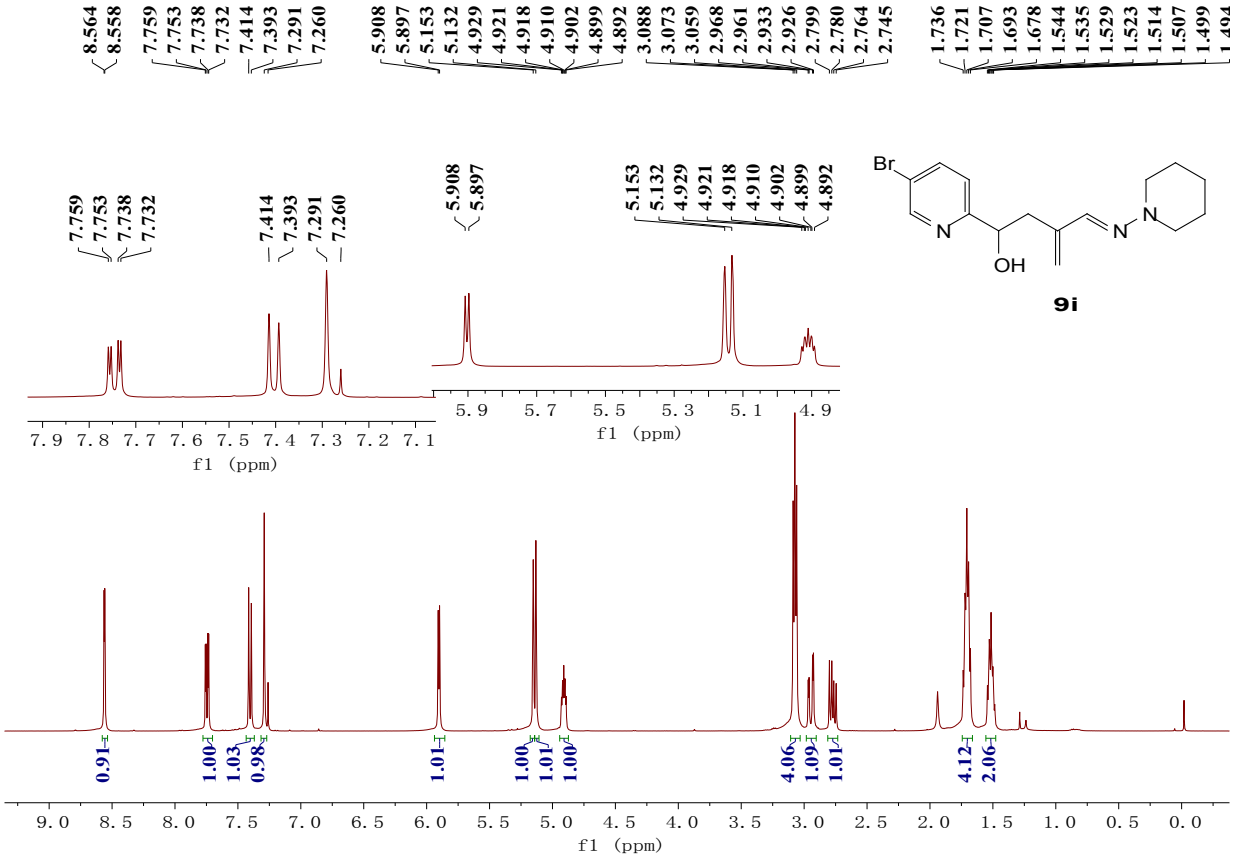

7.570
7.566
7.548
7.351
7.347
7.342
7.329
7.321
7.310
7.282
7.278
7.274
7.266
7.260
7.242
7.150
6.155
6.143
5.384
5.267
4.499
4.495
4.490
4.486
4.482
4.477
4.474
4.469
3.094
3.080
3.066
2.964
2.928
2.912
2.885
2.878
2.850
2.842
1.728
1.714
1.699
1.684
1.549
1.541
1.534
1.529
1.520
1.512
1.504
-0.007
Br
N
OH
2.01
3.09
1.30
1.00
1.01
1.00
1.00
1.01
4.06
1.09
1.06
4.20
2.15
f1 (ppm)

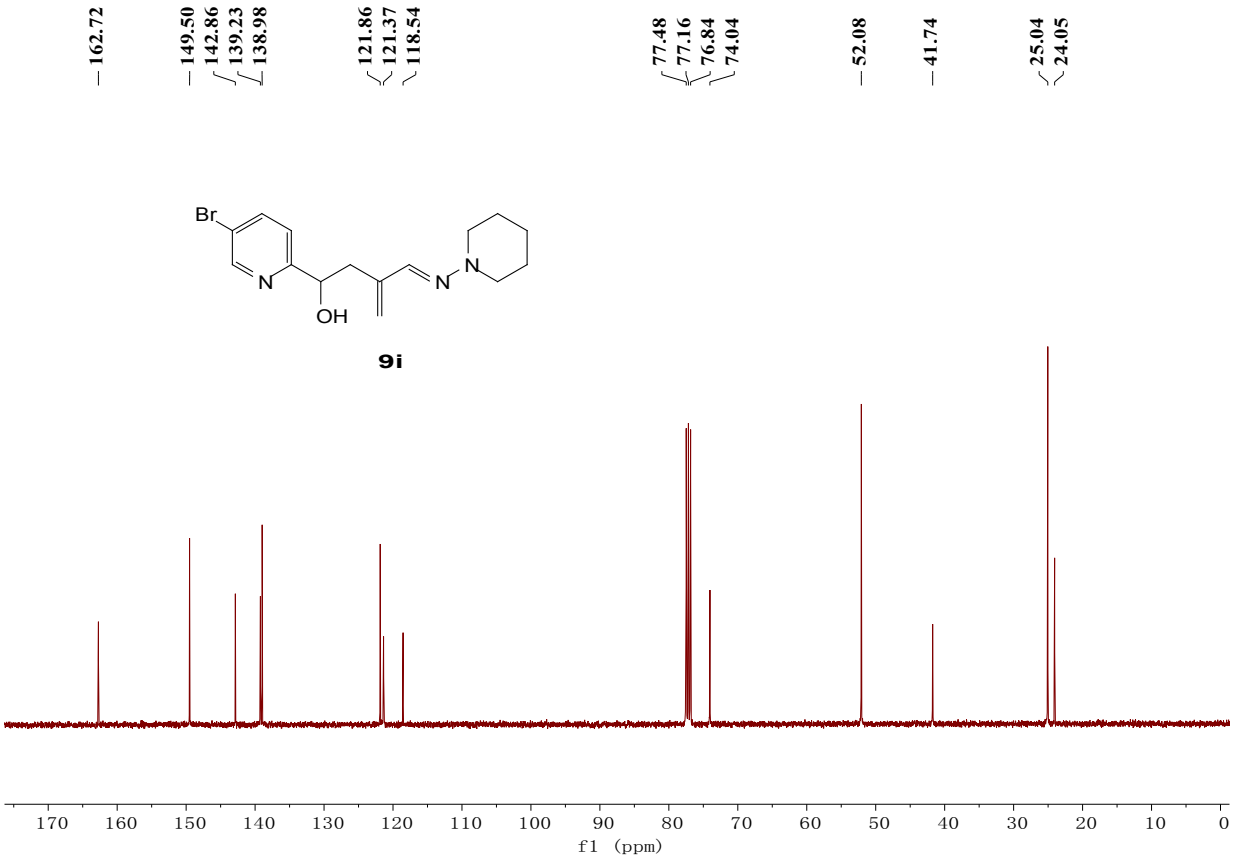
9j

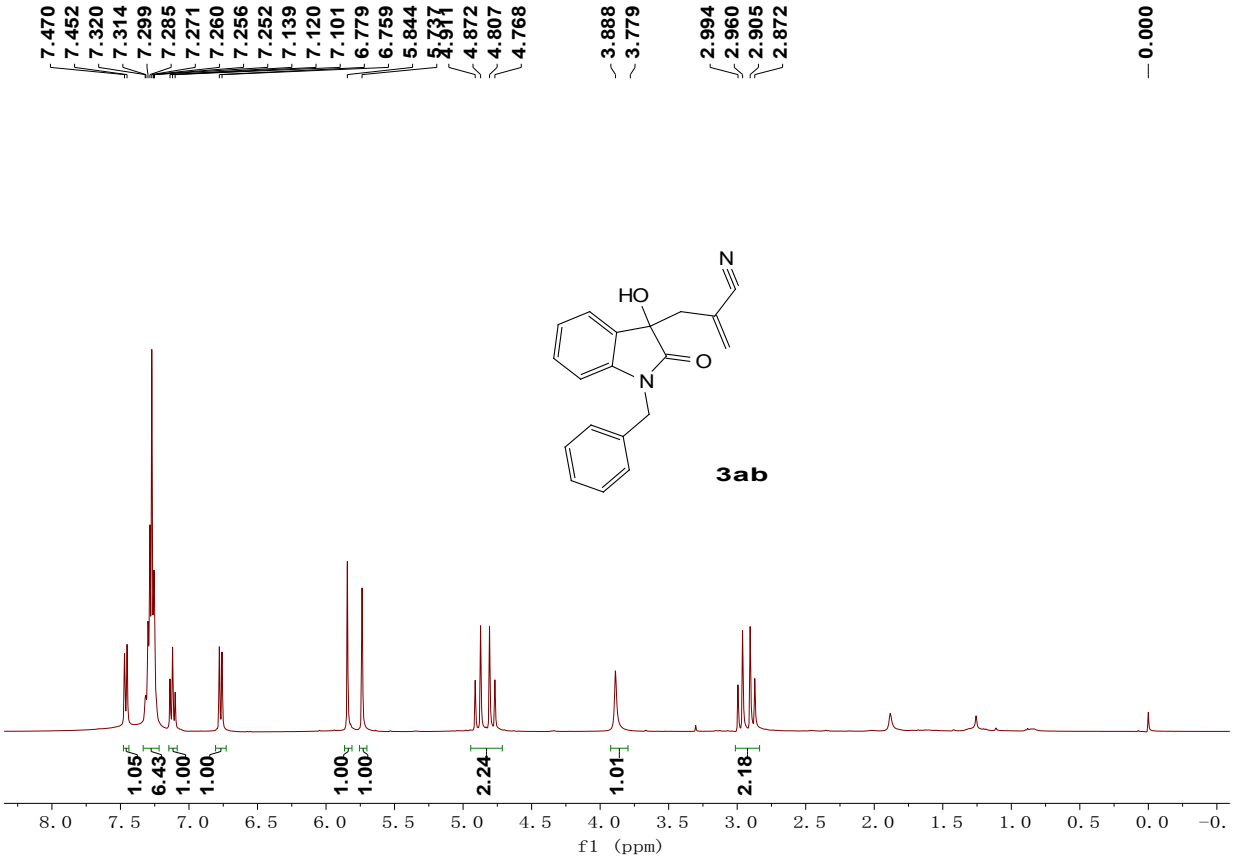

142.40
139.38
135.96
129.74
129.23
128.12
127.74
126.56
121.79
77.48
77.16
76.92
76.84
52.11
39.74
25.02
24.04
Br
OH
N
N
9j
76.92
77.7 77.5 77.3 77.1 76.9 76.7 76.5
f1 (ppm)
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

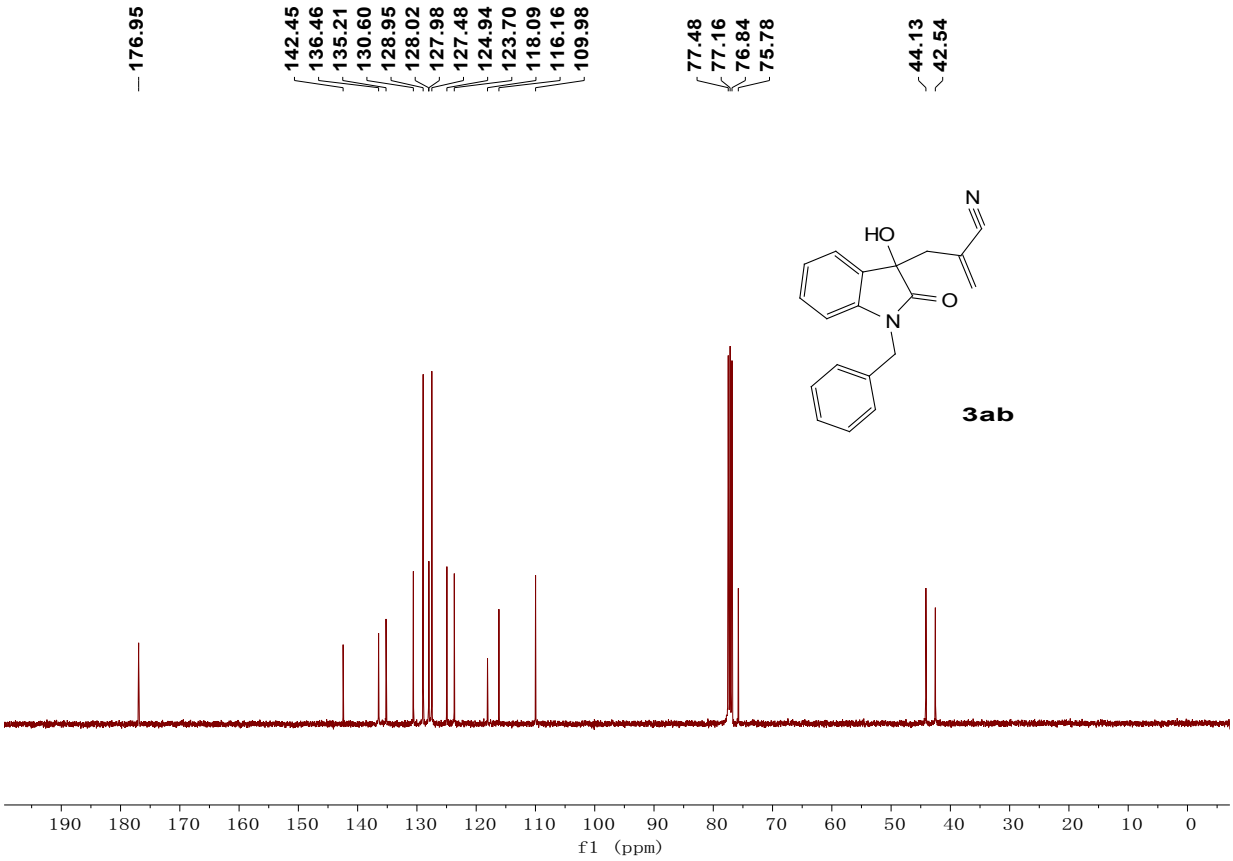

8.538
8.535
8.532
8.526
8.523
8.520
7.651
7.646
7.632
7.627
7.492
7.472
7.329
7.145
7.142
7.132
7.127
7.123
7.114
5.772
5.761
5.202
5.156
4.984
4.974
4.965
4.962
3.110
3.096
3.082
2.997
2.990
2.962
2.955
2.801
2.781
2.767
2.747
1.738
1.724
1.710
1.695
1.548
1.542
1.536
1.527
1.520
1.512
1.508
-0.008
N
N
OH
N
9h
1.00
1.02
1.00
1.00
1.01
1.00
1.00
1.03
1.00
4.03
1.02
1.00
4.35
2.13
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

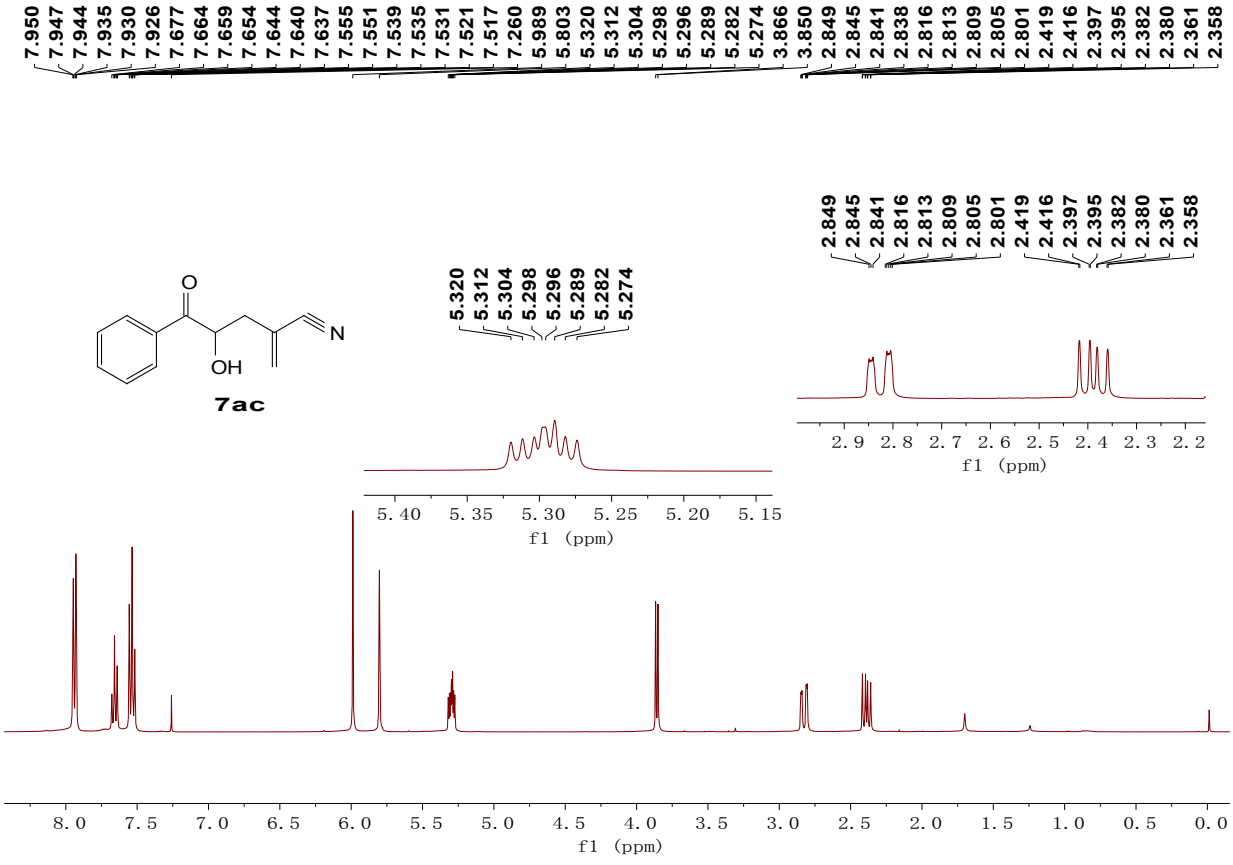

163.83
148.51
143.21
139.27
136.50
121.90
121.00
120.40
77.48
77.16
76.84
74.21
52.15
42.02
25.12
24.12
N
N
N
OH
9h
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

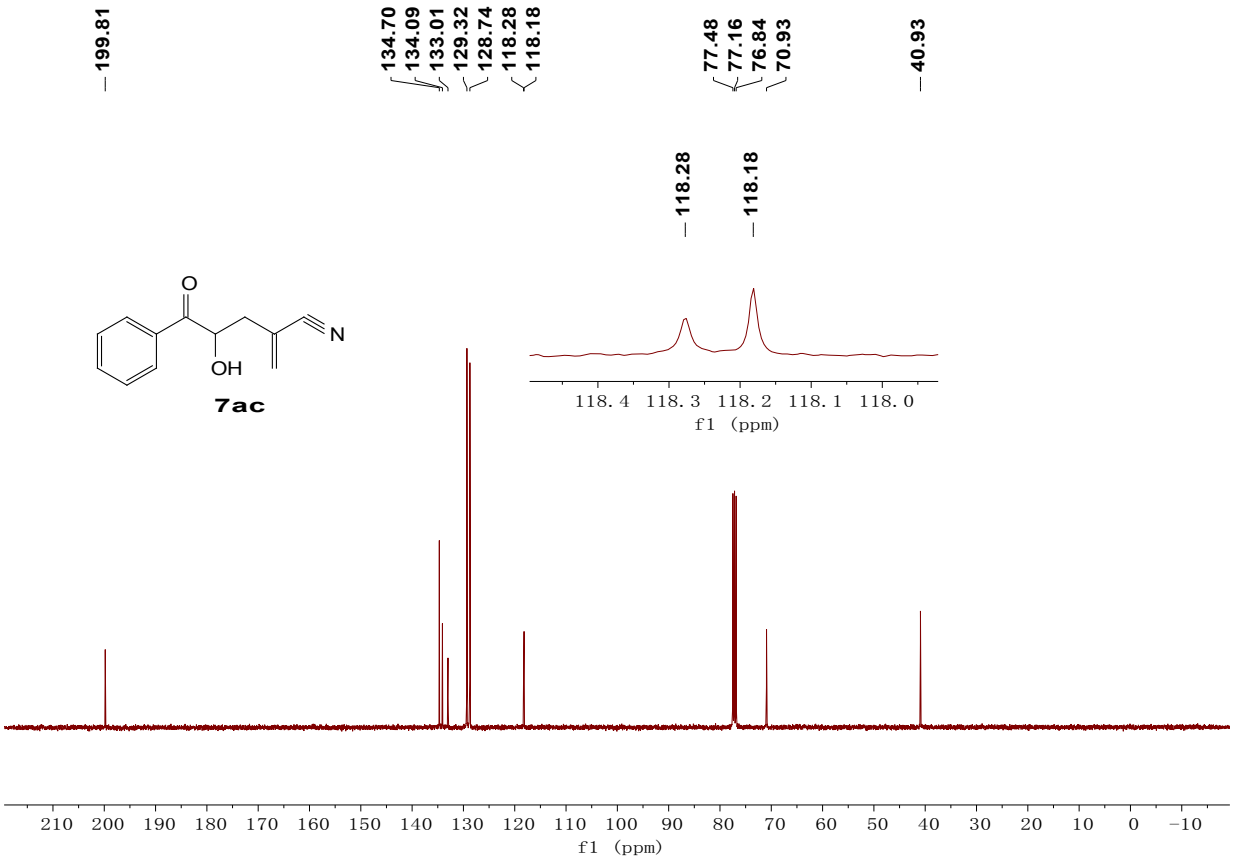

8.564
8.558
7.759
7.753
7.738
7.732
7.414
7.393
7.291
7.260
5.908
5.897
5.153
5.132
4.929
4.921
4.918
4.910
4.902
4.899
4.892
3.088
3.073
3.059
2.968
2.961
2.933
2.926
2.799
2.780
2.764
2.745
1.736
1.721
1.707
1.693
1.678
1.544
1.535
1.529
1.523
1.514
1.507
1.499
1.494
Br
N
N
N
OH
9i
0.91
1.00
1.03
0.98
1.01
1.00
1.01
1.00
4.06
1.09
1.01
4.12
2.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

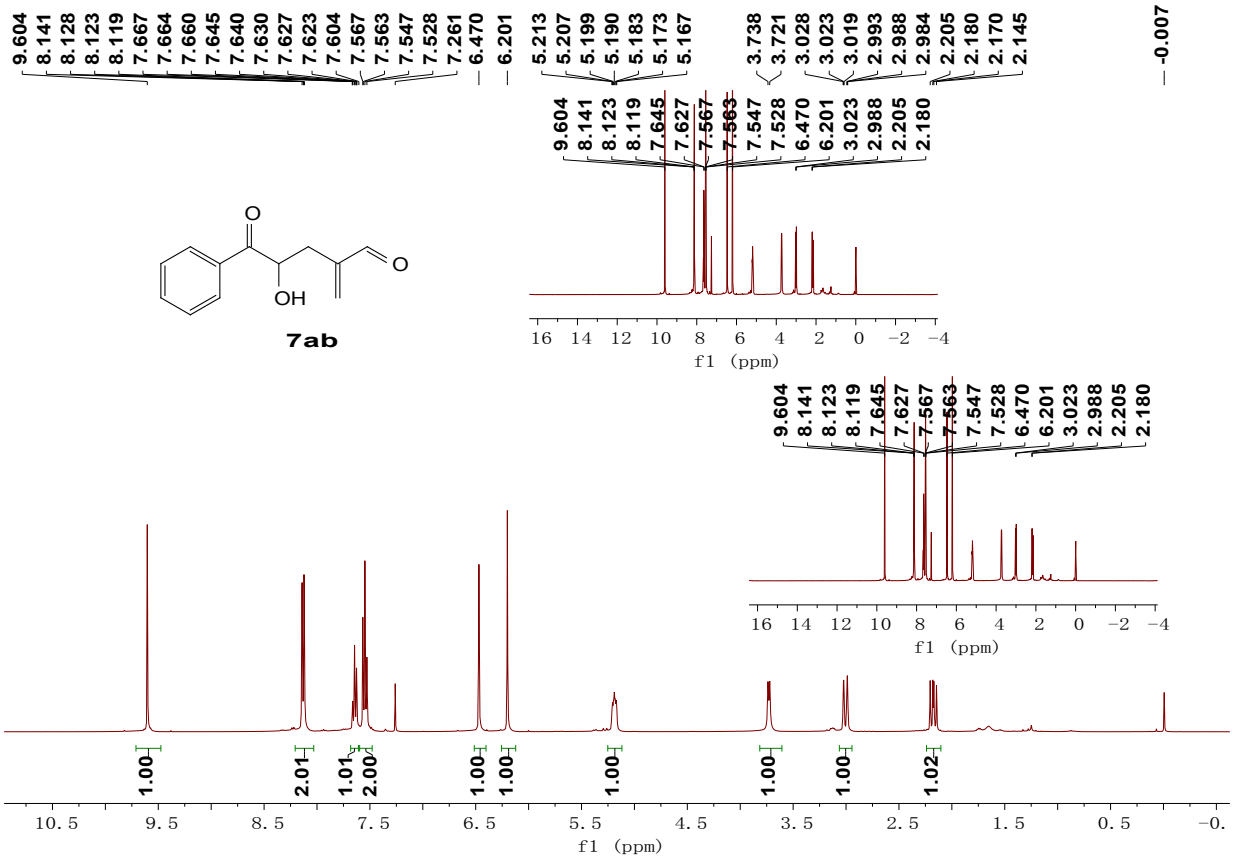

162.72
149.50
142.86
139.23
138.98
121.86
121.37
118.54
77.48
77.16
76.84
74.04
52.08
41.74
25.04
24.05
Br
N
N
N
OH
9i
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

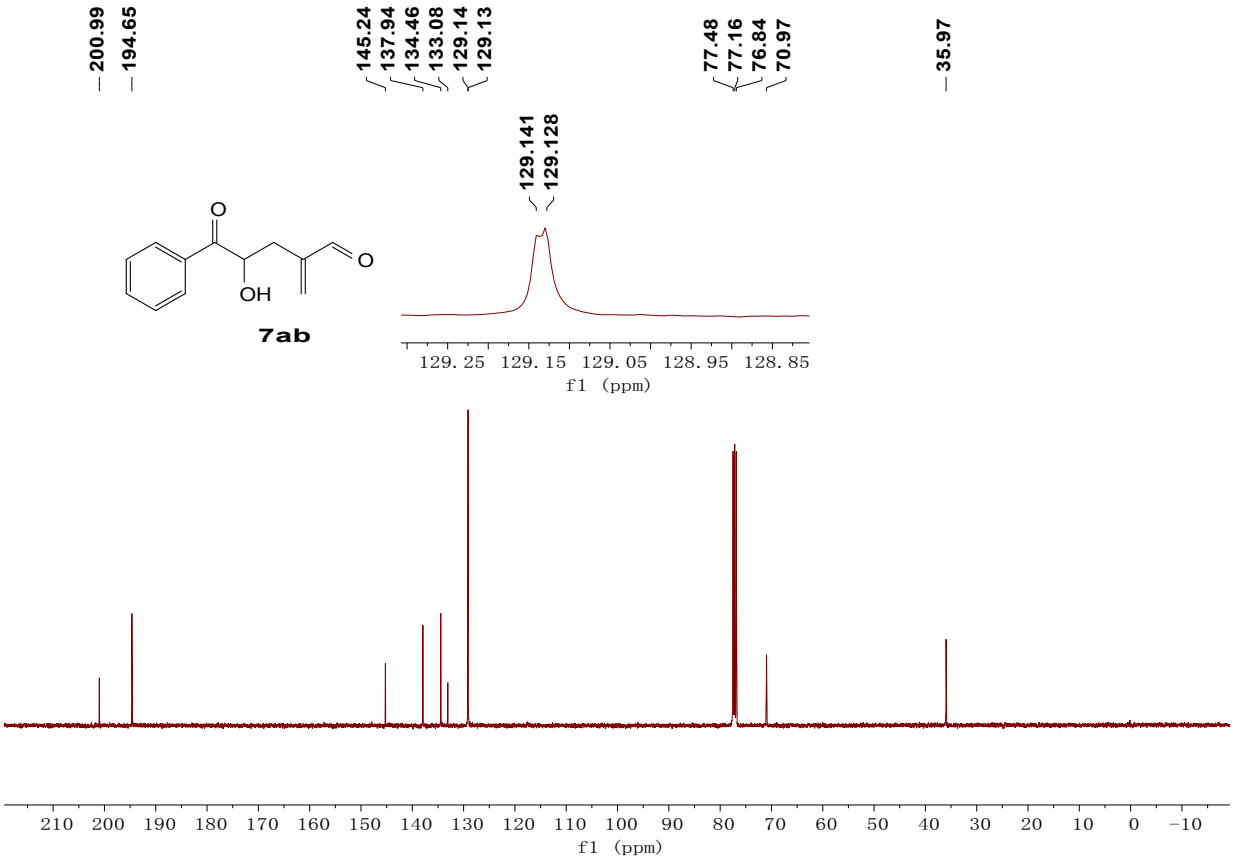

7.470
7.452
7.320
7.314
7.299
7.285
7.271
7.260
7.256
7.252
7.139
7.120
7.101
6.779
6.759
5.844
4.872
4.807
4.768
3.888
3.779
2.994
2.960
2.905
2.872
0.000
N
HO
O
N
3ab
1.05
6.43
1.00
1.00
1.00
1.00
2.24
1.01
2.18
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

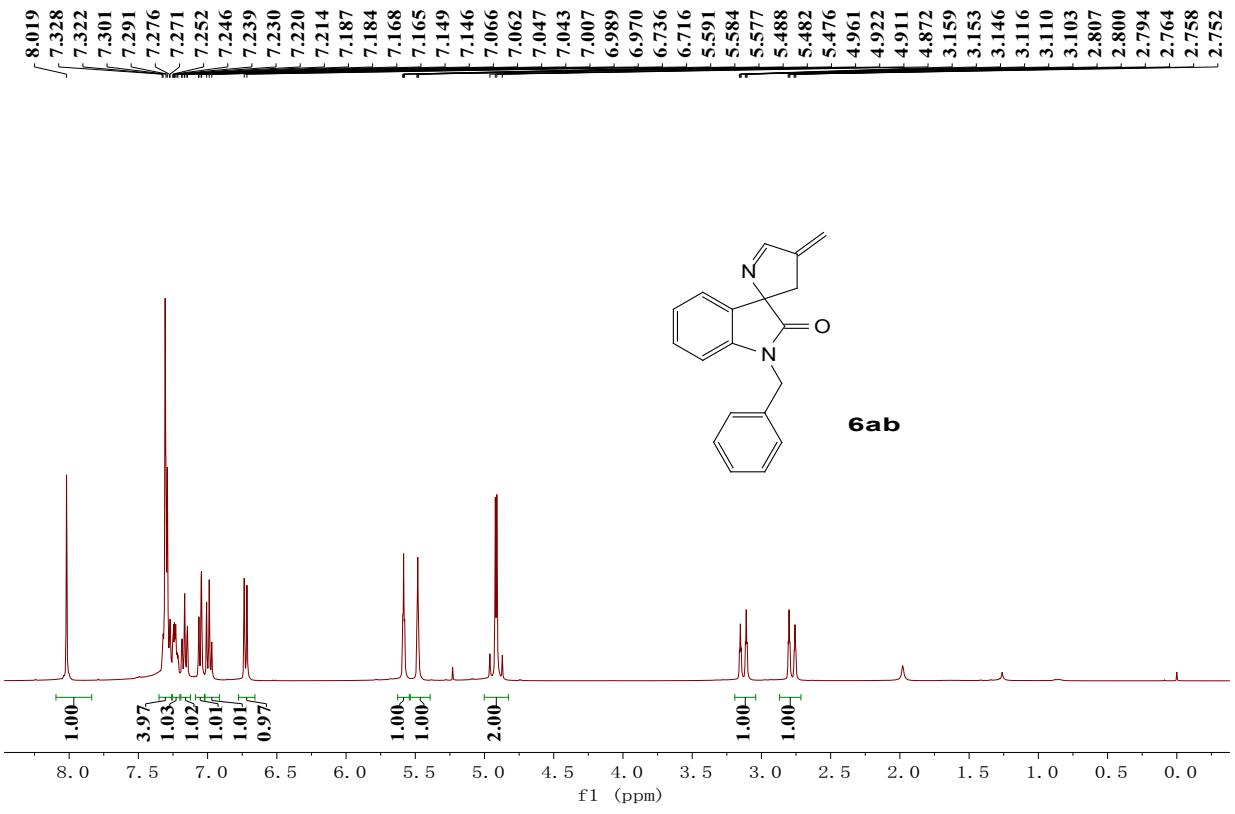

176.95
142.45
136.46
135.21
130.60
128.95
128.02
127.98
127.48
124.94
123.70
118.09
116.16
109.98
77.48
77.16
76.84
75.78
44.13
42.54
HO
N
O
N
3ab
f1 (ppm)

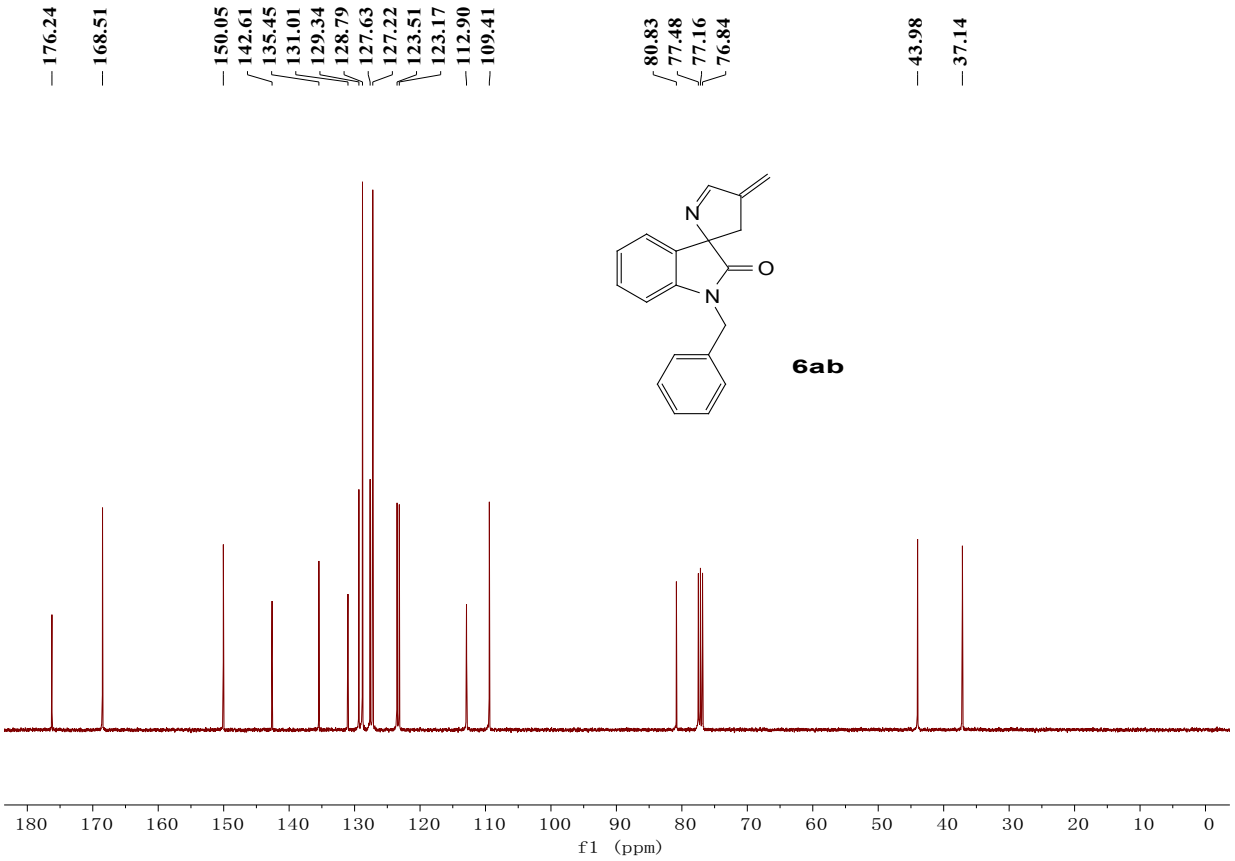

7.950
7.947
7.944
7.935
7.930
7.926
7.677
7.664
7.659
7.654
7.644
7.640
7.637
7.555
7.551
7.539
7.535
7.531
7.521
7.517
7.260
5.989
5.803
5.320
5.312
5.304
5.298
5.296
5.289
5.282
5.274
3.866
3.850
2.849
2.845
2.841
2.838
2.816
2.813
2.809
2.805
2.801
2.419
2.416
2.397
2.395
2.382
2.380
2.361
2.358
O
OH
N
7ac
f1 (ppm)
f1 (ppm)
f1 (ppm)

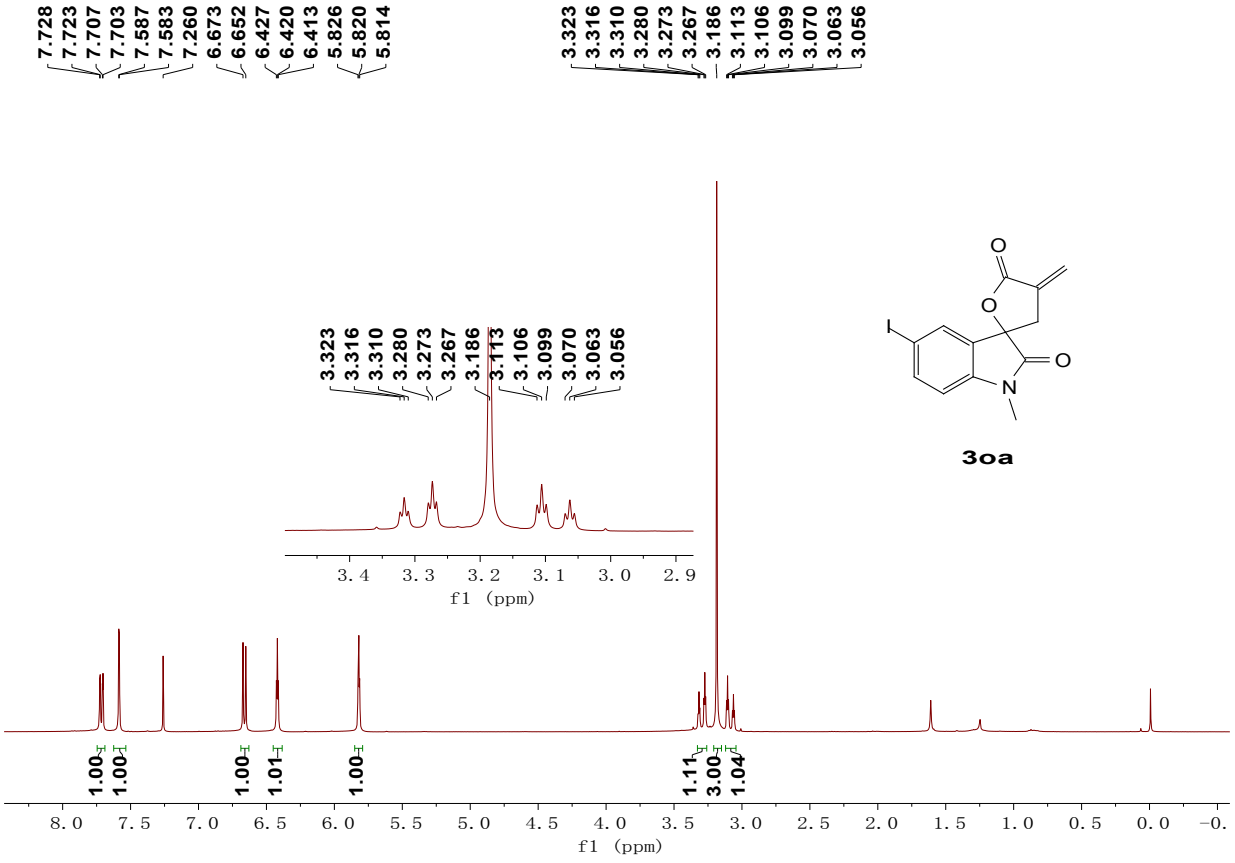

199.81
134.70
134.09
133.01
129.32
128.74
118.28
118.18
77.48
77.16
76.84
70.93
40.93
118.28
118.18
O
OH
N
7ac
118.4 118.3 118.2 118.1 118.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

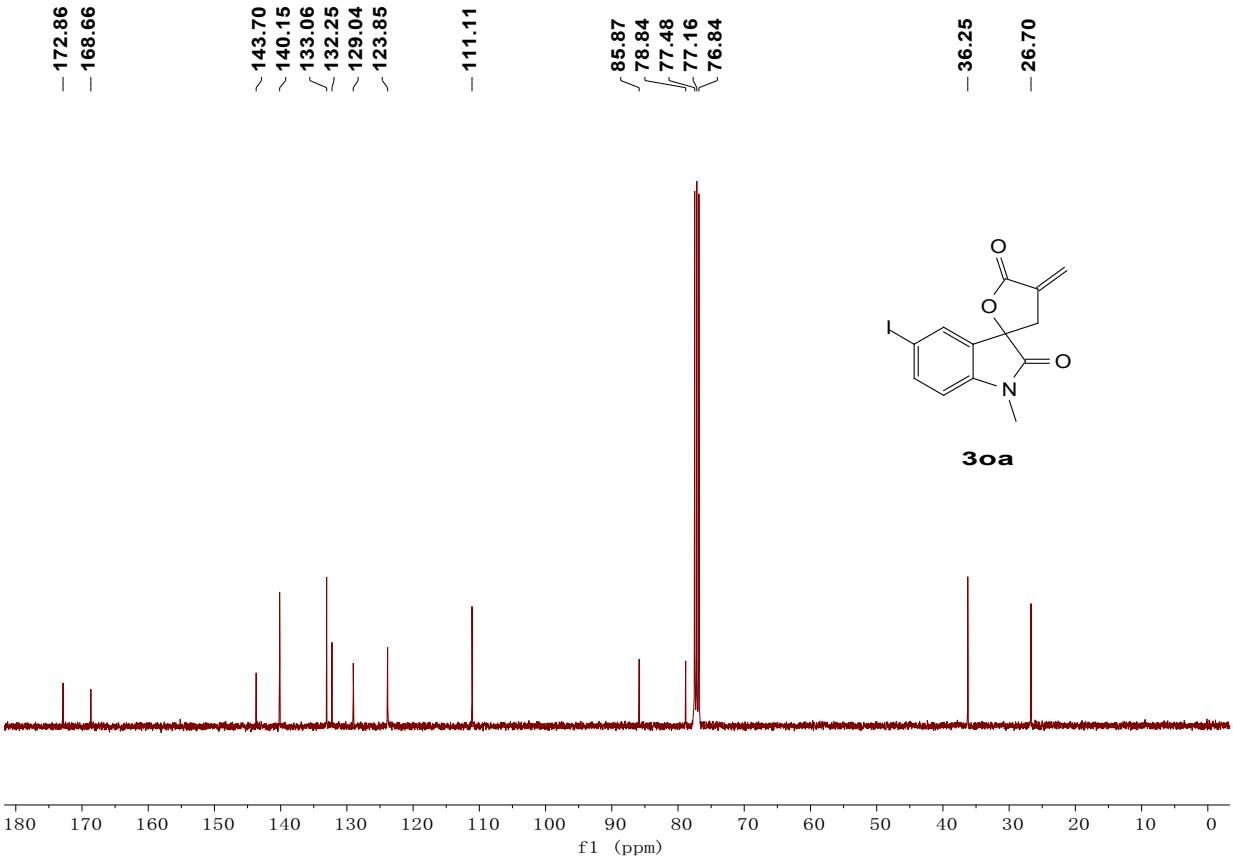

9.604
8.141
8.128
8.123
8.119
7.667
7.664
7.660
7.645
7.640
7.630
7.627
7.623
7.604
7.567
7.563
7.547
7.528
7.261
6.470
6.201
5.213
5.207
5.199
5.190
5.183
5.173
5.167
3.738
3.721
3.028
3.023
3.019
2.993
2.988
2.984
2.205
2.180
2.170
2.145
-0.007
O
OH
O
7ab
16 14 12 10 8 6 4 2 0 −2 −4
f1 (ppm)
1.00
2.01
1.01
2.00
1.00
1.00
1.00
1.00
1.00
1.02
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 −0.
f1 (ppm)

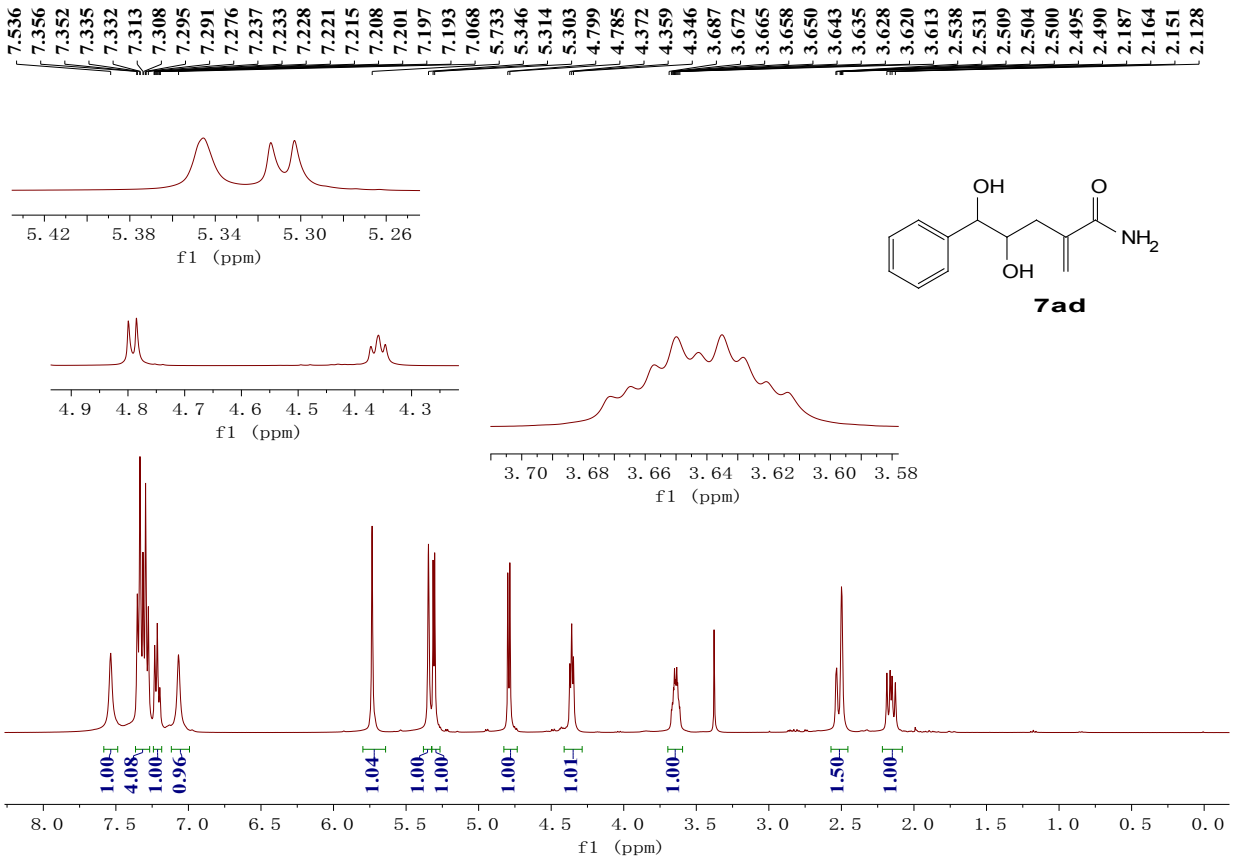

200.99
194.65
145.24
137.94
134.46
133.08
129.14
129.13
77.48
77.16
76.84
70.97
35.97
129.141
129.128
O
O
OH
7ab
129.25 129.15 129.05 128.95 128.85
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

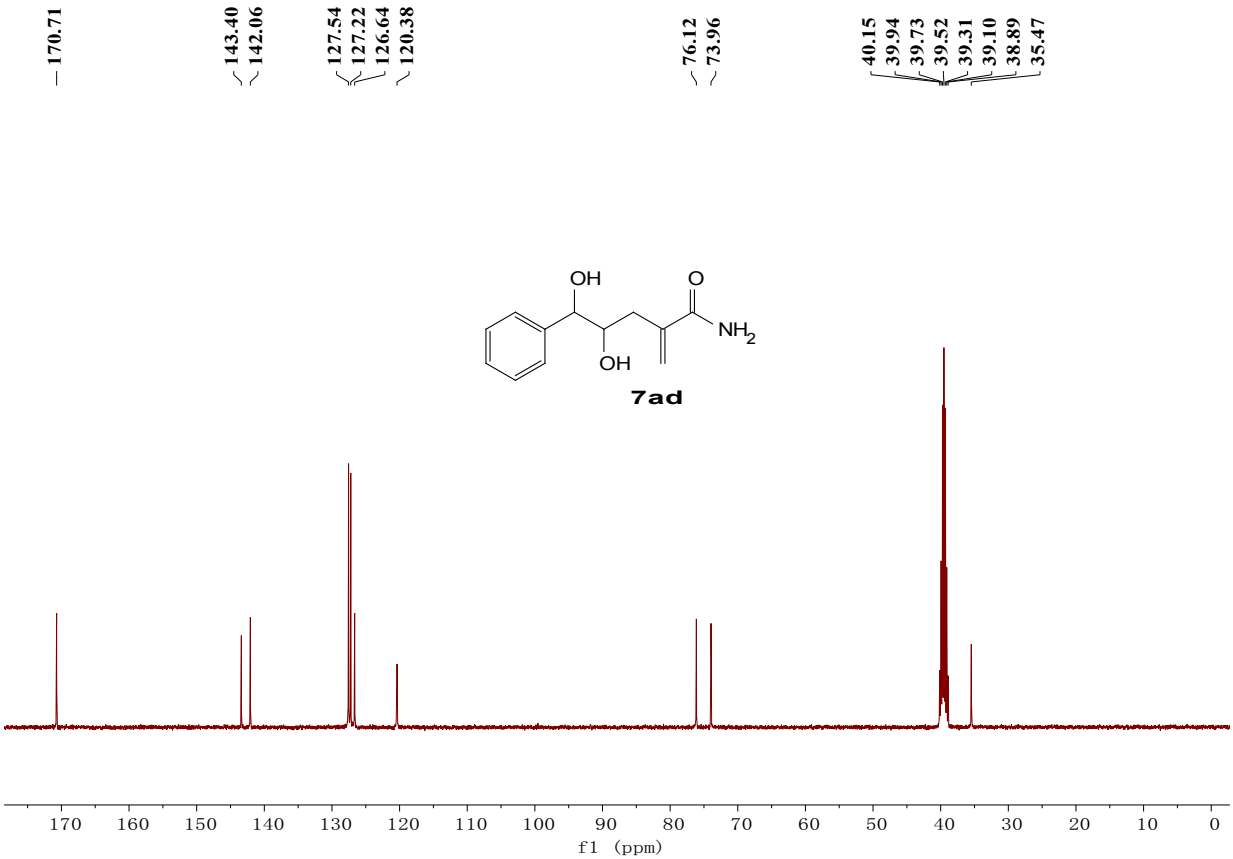

8.019
7.328
7.322
7.301
7.291
7.276
7.271
7.252
7.246
7.239
7.230
7.220
7.214
7.187
7.184
7.168
7.165
7.149
7.146
7.066
7.062
7.047
7.043
7.007
6.989
6.970
6.736
6.716
5.591
5.584
5.577
5.488
5.482
5.476
4.961
4.922
4.911
4.872
3.159
3.153
3.146
3.116
3.110
3.103
2.807
2.800
2.794
2.764
2.758
2.752
N
O
N
6ab
1.00
3.97
1.03
1.02
1.01
1.01
0.97
1.00
1.00
2.00
1.00
1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

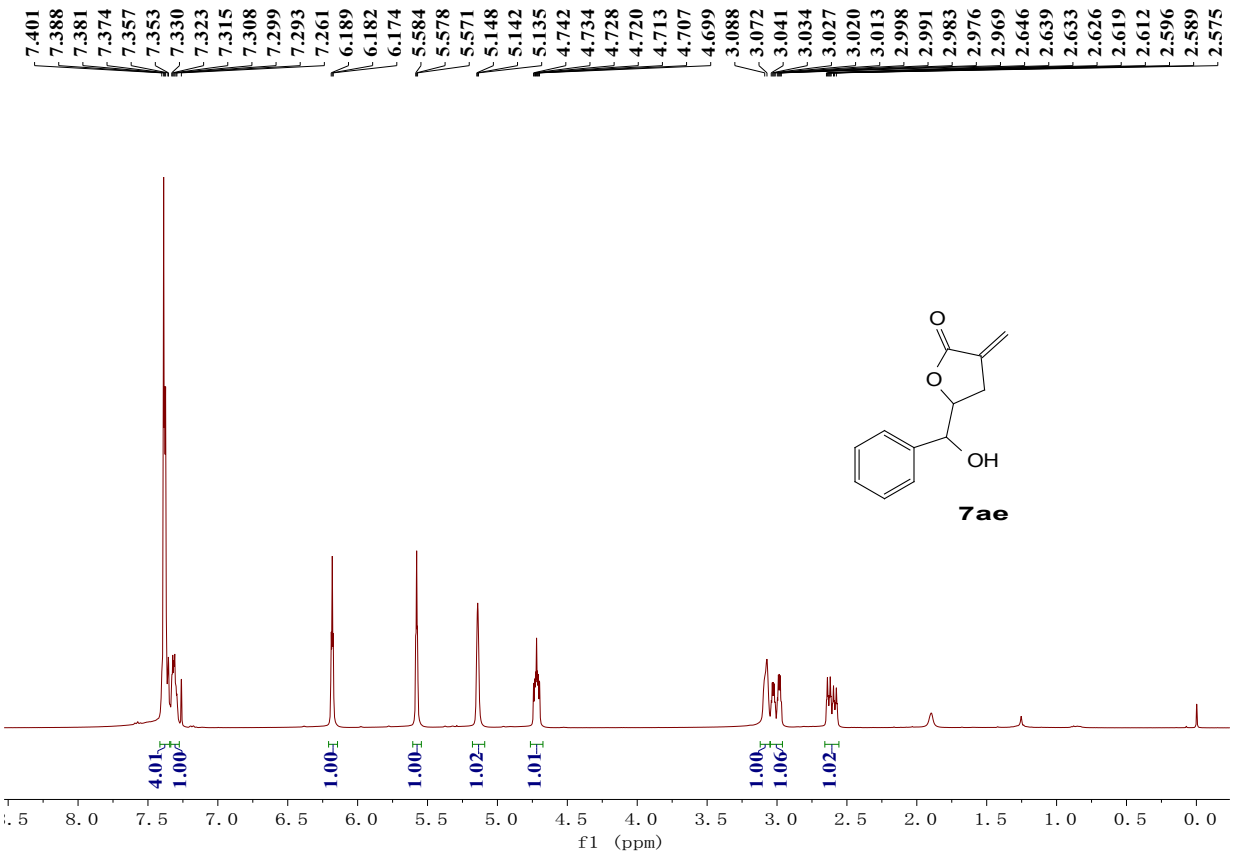

176.24
168.51
150.05
142.61
135.45
131.01
129.34
128.79
127.63
127.22
123.51
123.17
112.90
109.41
80.83
77.48
77.16
76.84
43.98
37.14
6ab
f1 (ppm)

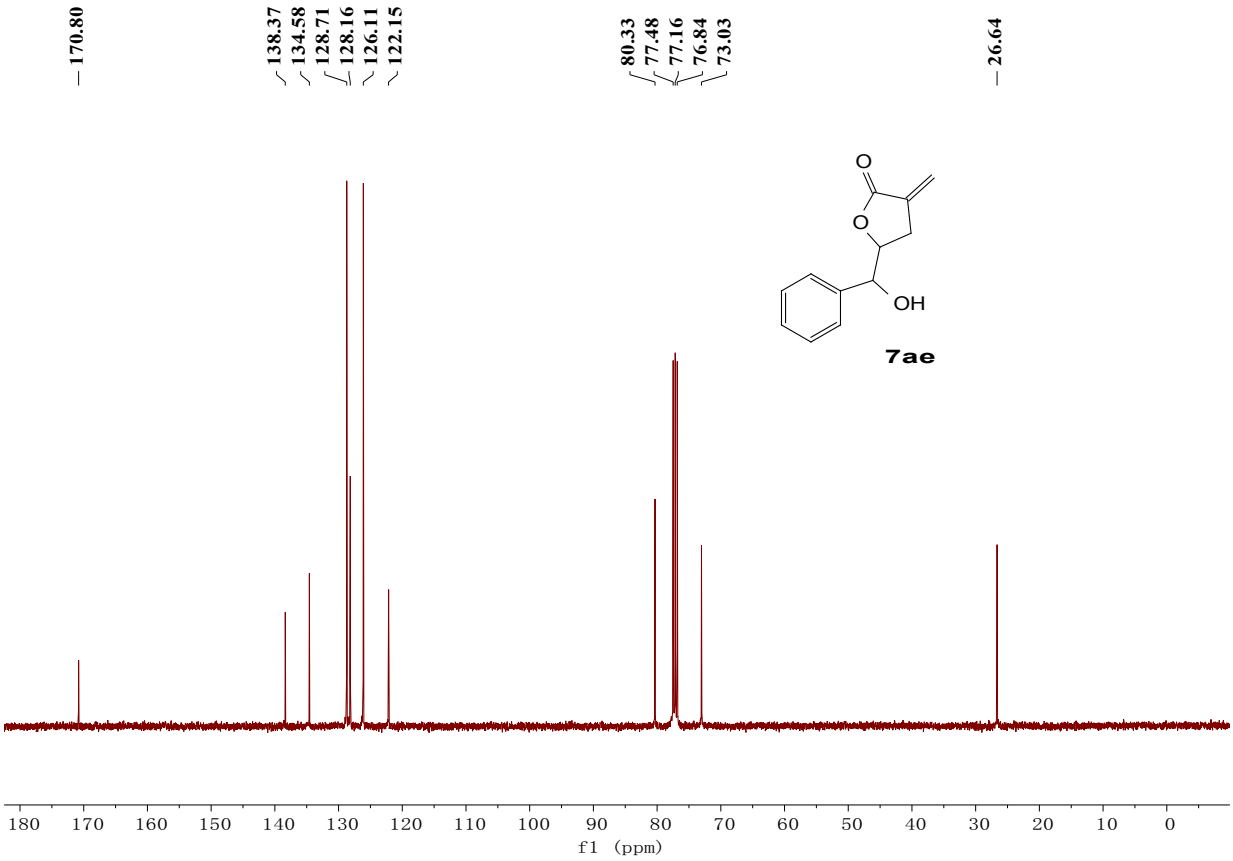

7.728
7.723
7.707
7.703
7.587
7.583
7.260
6.673
6.652
6.427
6.420
6.413
5.826
5.820
5.814
3.323
3.316
3.310
3.280
3.273
3.267
3.186
3.113
3.106
3.099
3.070
3.063
3.056
3oa
1.00
1.00
1.00
1.01
1.00
1.11
3.00
1.04
f1 (ppm)

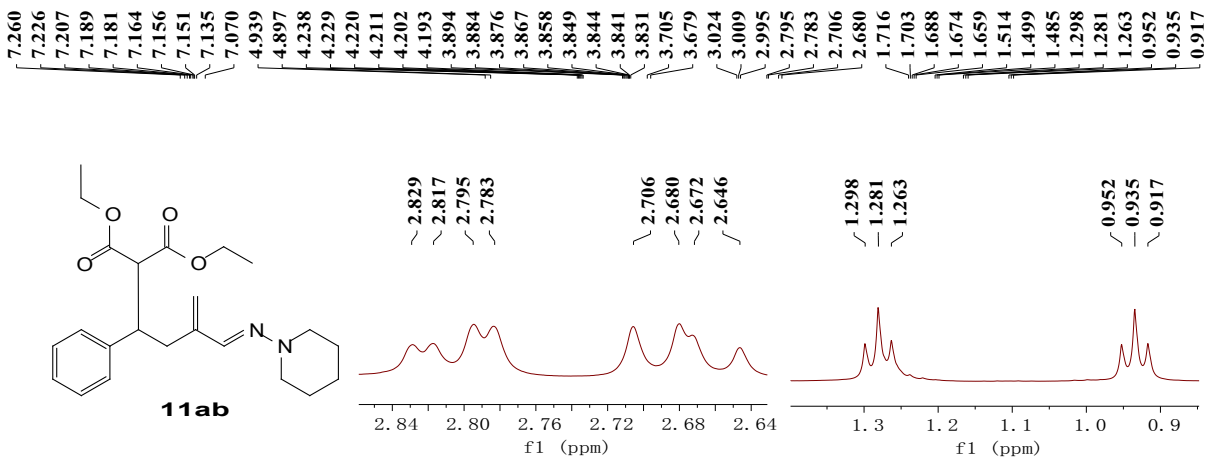

172.86
168.66
143.70
140.15
133.06
132.25
129.04
123.85
111.11
85.87
78.84
77.48
77.16
76.84
36.25
26.70
O
O
I
O
N
3oa
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

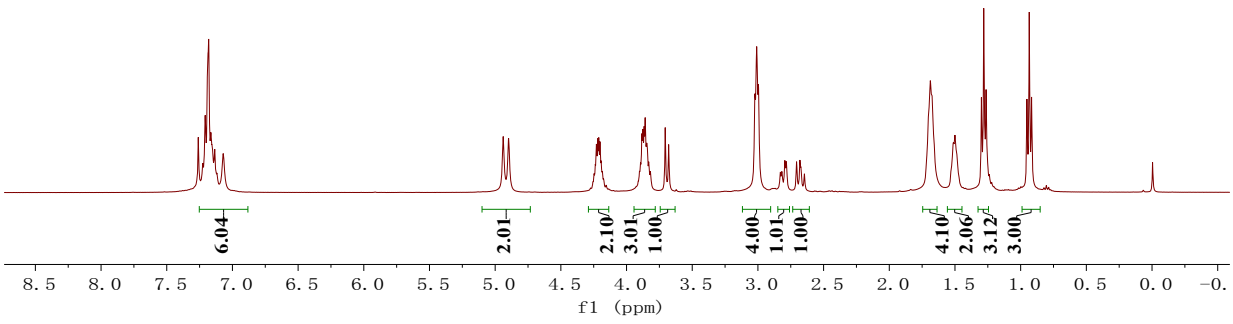

7.536
7.356
7.352
7.335
7.332
7.313
7.308
7.295
7.291
7.276
7.237
7.233
7.228
7.221
7.215
7.208
7.201
7.197
7.193
7.068
5.733
5.346
5.314
5.303
4.799
4.785
4.372
4.359
4.346
3.687
3.672
3.665
3.658
3.650
3.643
3.635
3.628
3.620
3.613
2.538
2.531
2.509
2.504
2.500
2.495
2.490
2.187
2.164
2.151
2.128
OH
O
NH2
OH
7ad
5.42 5.38 5.34 5.30 5.26
f1 (ppm)
4.9 4.8 4.7 4.6 4.5 4.4 4.3
f1 (ppm)
3.70 3.68 3.66 3.64 3.62 3.60 3.58
f1 (ppm)
1.00
4.08
1.00
0.96
1.04
1.00
1.00
1.00
1.01
1.00
1.50
1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

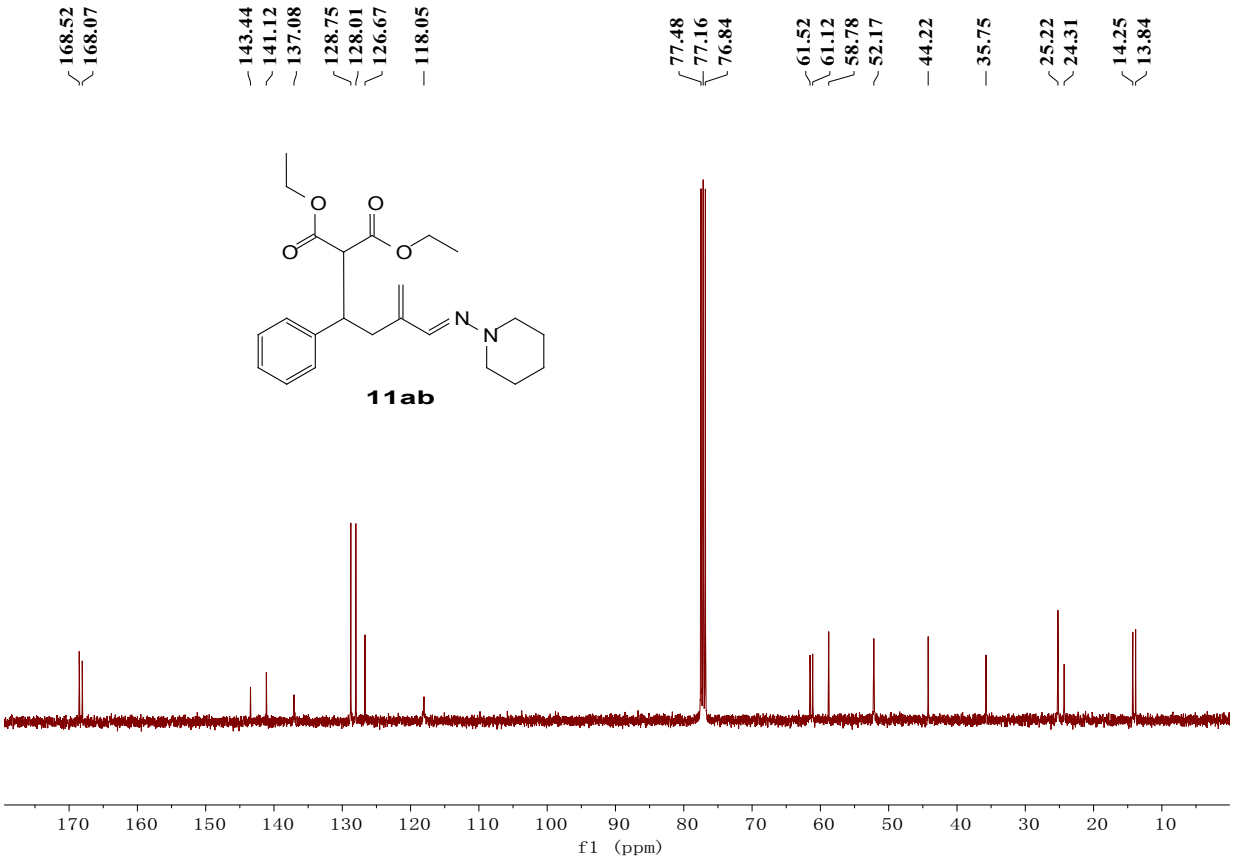

170.71
143.40
142.06
127.54
127.22
126.64
120.38
76.12
73.96
40.15
39.94
39.73
39.52
39.31
39.10
38.89
35.47
OH
O
NH2
OH
7ad
f1 (ppm)

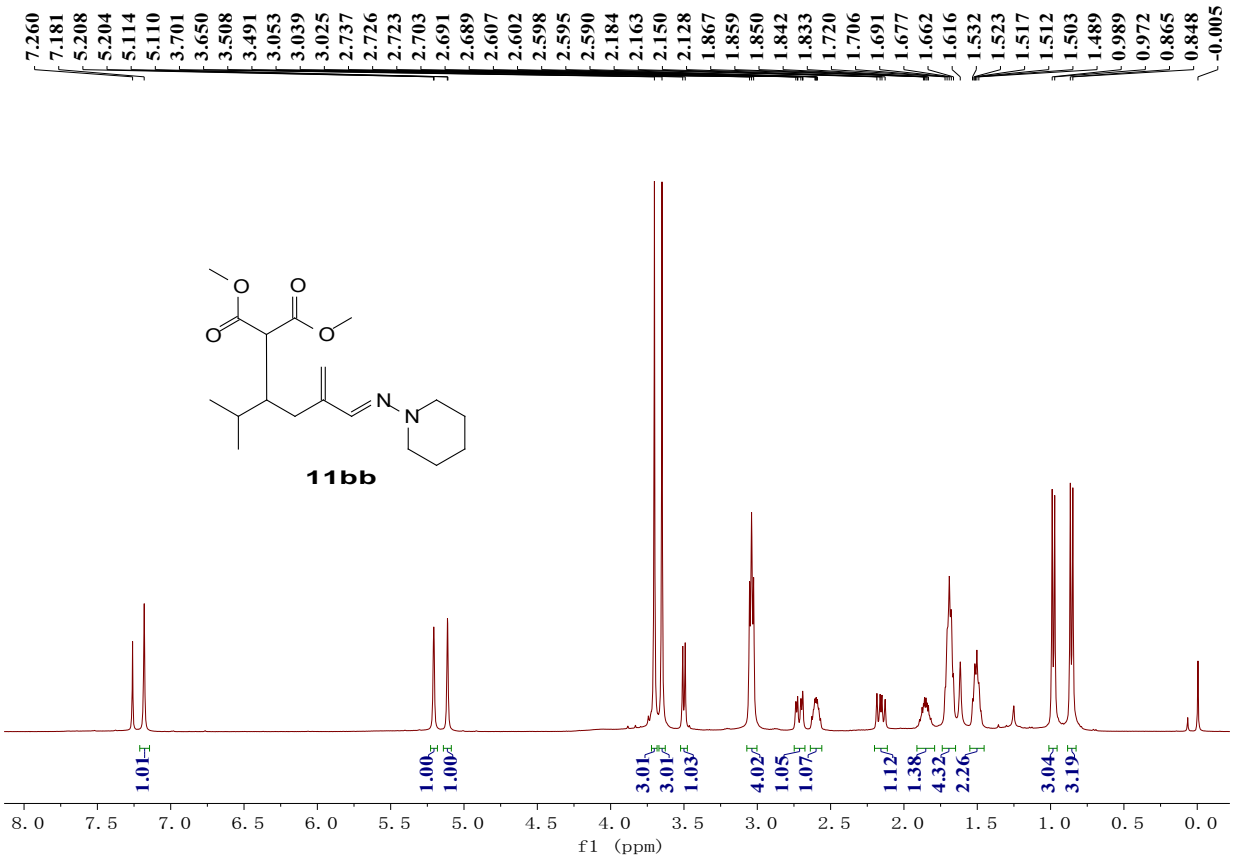

7.401
7.388
7.381
7.374
7.357
7.353
7.330
7.323
7.315
7.308
7.299
7.293
7.261
6.189
6.182
6.174
5.584
5.578
5.571
5.148
5.142
5.135
4.742
4.734
4.728
4.720
4.713
4.707
4.699
3.088
3.072
3.041
3.034
3.027
3.020
3.013
2.998
2.991
2.983
2.976
2.969
2.646
2.639
2.633
2.626
2.619
2.612
2.596
2.589
2.575
O
O
OH
7ae
4.01
1.00
1.00
1.00
1.02
1.01
1.00
1.06
1.02
f1 (ppm)

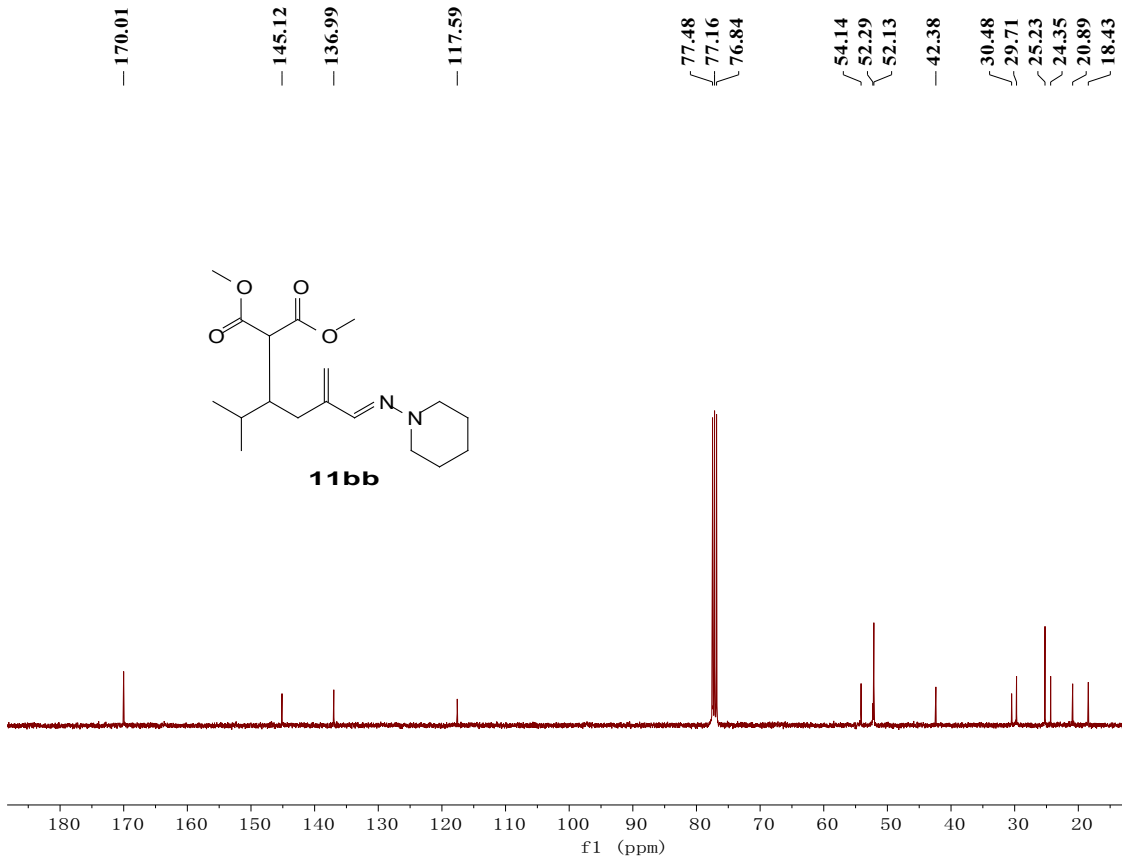

170.80
138.37
134.58
128.71
128.16
126.11
122.15
80.33
77.48
77.16
76.84
73.03
26.64
O
O
OH
7ae
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

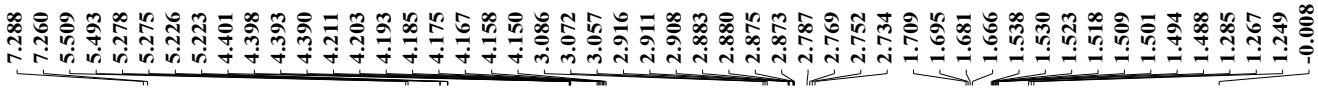

7.260
7.226
7.207
7.189
7.181
7.164
7.156
7.151
7.135
7.070
4.939
4.897
4.238
4.229
4.220
4.211
4.202
4.193
3.894
3.884
3.876
3.867
3.858
3.849
3.844
3.841
3.831
3.705
3.679
3.024
3.009
2.995
2.795
2.783
2.706
2.680
1.716
1.703
1.688
1.674
1.659
1.514
1.499
1.485
1.298
1.281
1.263
0.952
0.935
0.917
O
O
O
O
N
N
11ab
2.829
2.817
2.795
2.783
2.706
2.680
2.672
2.646
1.298
1.281
1.263
0.952
0.935
0.917
2.84 2.80 2.76 2.72 2.68 2.64
f1 (ppm)
1.3 1.2 1.1 1.0 0.9
f1 (ppm)


6.04
2.01
2.10
3.01
1.00
4.00
1.01
1.00
4.10
2.06
3.12
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


168.52
168.07
143.44
141.12
137.08
128.75
128.01
126.67
118.05
77.48
77.16
76.84
61.52
61.12
58.78
52.17
44.22
35.75
25.22
24.31
14.25
13.84
11ab
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.260
7.181
5.208
5.204
5.114
5.110
3.701
3.650
3.508
3.491
3.053
3.039
3.025
2.737
2.726
2.723
2.703
2.691
2.689
2.607
2.602
2.598
2.595
2.590
2.184
2.163
2.150
2.128
1.867
1.859
1.850
1.842
1.833
1.720
1.706
1.691
1.677
1.662
1.616
1.532
1.523
1.517
1.512
1.503
1.489
0.989
0.972
0.865
0.848
-0.005
11bb
1.01
1.00
1.00
3.01
3.01
1.03
4.02
1.05
1.07
1.12
1.38
4.32
2.26
3.04
3.19
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.01
145.12
136.99
117.59
77.48
77.16
76.84
54.14
52.29
52.13
42.38
30.48
29.71
25.23
24.35
20.89
18.43
11bb
f1 (ppm)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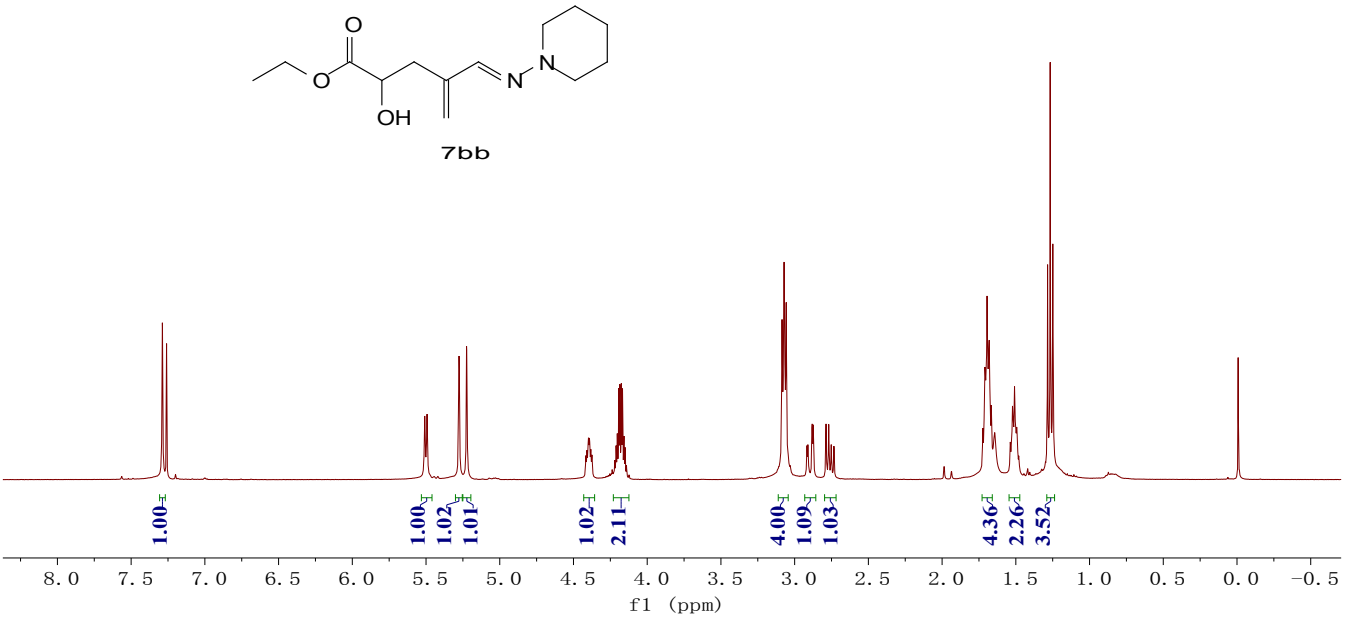
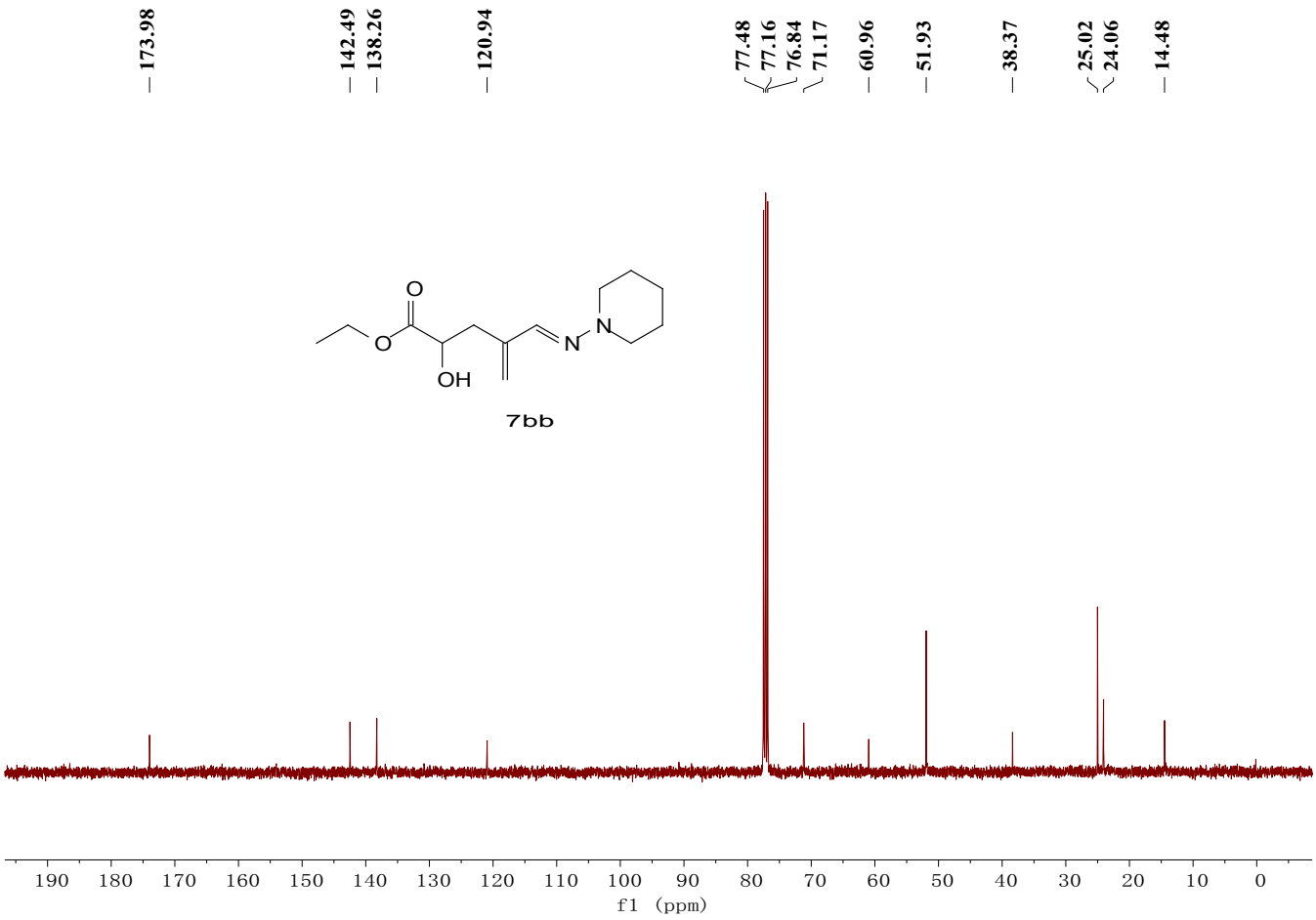
5.278
5.275
5.226
5.223
4.401
4.398
4.393
4.390
4.211
4.203
4.193
4.185
4.175
4.167
4.158
4.150
3.086
3.072
3.057
2.916
2.911
2.908
2.883
2.880
2.875
2.873
2.787
2.769
2.752
2.734
1.709
1.695
1.681
1.666
1.538
1.530
1.523
1.518
1.509
1.501
1.494
1.488
1.285
1.267
1.249
-0.008


7bb
1.00
1.00
1.02
1.01
1.02
2.11
4.00
1.09
1.03
4.36
2.26
3.52
f1 (ppm)


173.98
142.49
138.26
120.94
77.48
77.16
76.84
71.17
60.96
51.93
38.37
25.02
24.06
14.48
O
O
OH
N
N
7bb
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)