Binaphthyl-Prolinol chiral ligands: Design and Their Application in Enantioselective Arylation of Aromatic Aldehydes

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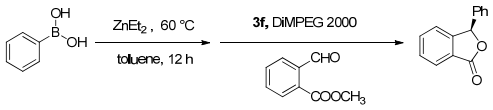
Contents

1. Optimization of Reaction Conditions for Enantioselective Arylation-Lactonization of Methyl 2-Formylbenzoate

The general procedure for aryl transfer was adopted. Further study showed that the reaction temperature played a crucial role on the enantioselectivity and reactivity (Table S1, entries 1-2). The yield could be improved when the reaction time was prolonged from 24 h to 36 h. (Table S1, entries 2-3). Further increasing the reaction time didn't improve the yield of the reaction (Table S1, entries 3-4). The amount of chiral ligand was also studied, and 10 mol% of the chiral ligand was still the best choice (Table S1, entries 3, 5 and 6). Therefore, the final reaction condition was fixed as follows: reactions were performed on 0.25 mmol scale with $PhB(OH)_2$ (2.4 equiv), Et_2Zn (7.2 equiv) in toluene (stirring at 60 °C for 12 h), then addition of **3f** (10 mol%), DiMPEG 2000 (10 mol%) and aldehyde at 0 °C. The reaction mixture was stirred at 0 °C for 36 h under in an argon atmosphere.

Table **S1**. Optimization of enantioselective arylation-lactonization of methyl 2-formylbenzoate[a]



entry	Ligand (mol%)	T(°C)	t(h)	yield (%)[b]	ee (%)[c]	config.[d]
1	10	25	24	83	89	R
2	10	0	24	67	94	R
3	10	0	36	76	95	R
4	10	0	48	75	95	R
5	5	0	36	73	93	R
6	20	0	36	71	90	R

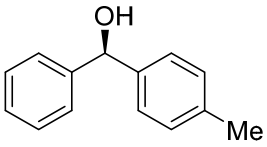
[a] Reactions were performed on a 0.25 mmol scale with $PhB(OH)_2$ (2.4 equiv), Et_2Zn (7.2 equiv)

in toluene (stirring at 60 °C for 12 h), then addition of **3f** (10 mol%), DiMPEG 2000 (10 mol%) and aldehyde at 0 °C, with stirring for 36 h under an atmosphere of argon. [b] Isolated yields. [c] The ee values were determined by HPLC (chiralcel OD-H column). [d] Absolute configuration was assigned by comparison to reported value and sign of specific rotation of the product.[1]

2. Preparation and Characterization of Chiral Ligands

The method for preparation of intermediate **4**, ligands **1** and **2** can be found in our previously report.[2]

3. Characterization and Enantiomeric Excesses of Products



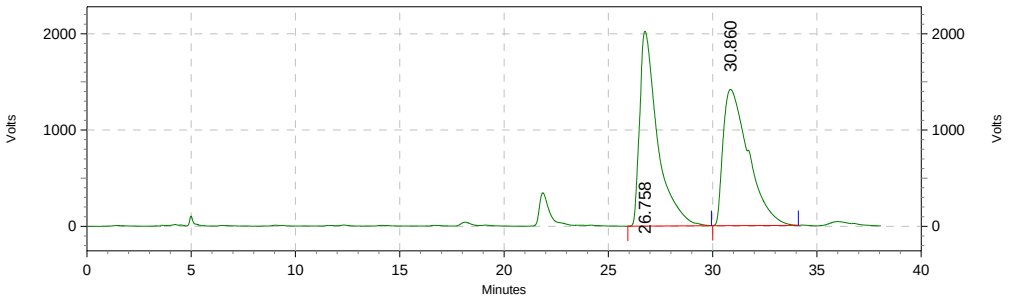
(*R*)-phenyl(p-tolyl)methanol (**15a**)[3]

90% yield, 98% ee, Colorless oil; HPLC (Chiralcel OD-H, 2% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 27.3 min for enantiomer (S), t_R = 30.7 min for enantiomer (R). $[\alpha]_D^{20}$ = +17.8 (*c* = 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 4H), 7.24 – 7.15 (m, 3H), 7.09 (d, *J* = 7.9 Hz, 2H), 5.69 (s, 1H), 2.62 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 141.0, 137.3, 129.6, 129.2, 128.5, 127.5, 126.7, 126.6, 120.4, 115.5, 76.1, 21.2.

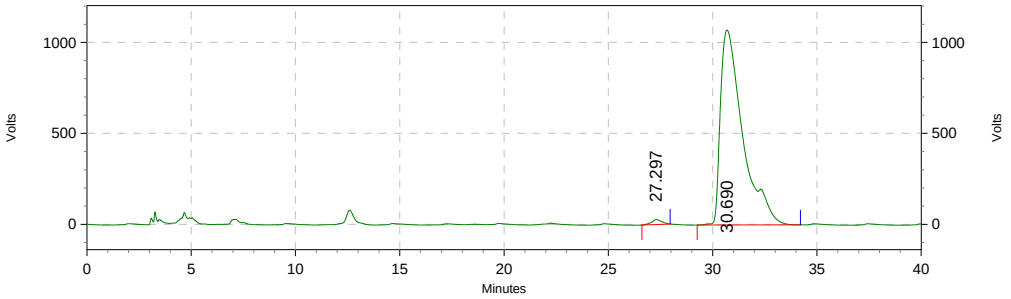
(*S*)-phenyl (p-tolyl) methanol

93% yield, 88% ee, Colorless oil; HPLC (Chiralcel OD-H, 2% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 28.0 min for enantiomer (S), t_R = 32.3 min for enantiomer (R). $[\alpha]_D^{20}$ = -8.9 (c = 0.60, $CHCl_3$)

HPLC Chromatograms - Enantiomer *R*

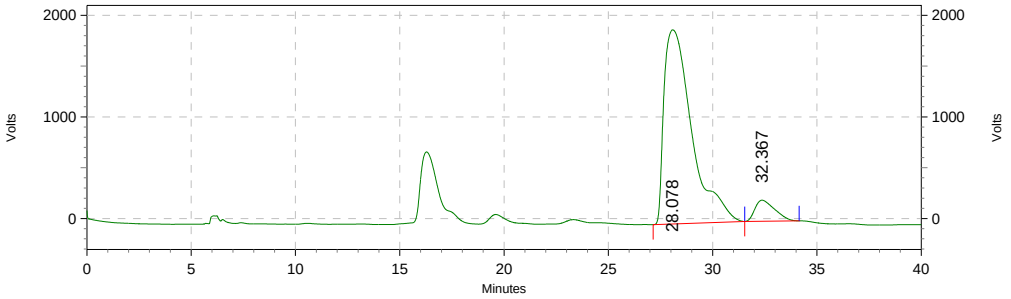


Peak	Ret. Time.	Area	Area%
1	26.758	120170246	50.059
2	30.860	119885244	49.941

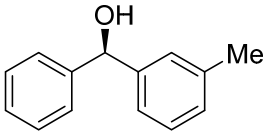


Peak	Ret. Time.	Area	Area%
1	27.297	906169	1.129
2	30.690	79369129	98.871

HPLC Chromatograms - Enantiomer *S*



Peak	Ret. Time.	Area	Area%
1	28.078	57253350	94.127
2	32.367	3572003	5.873



(*R*)-phenyl(m-tolyl)methanol (**15b**)[4]

89% yield, 95% ee, Colorless oil; HPLC (Chiralcel OB-H, 25% IPA in

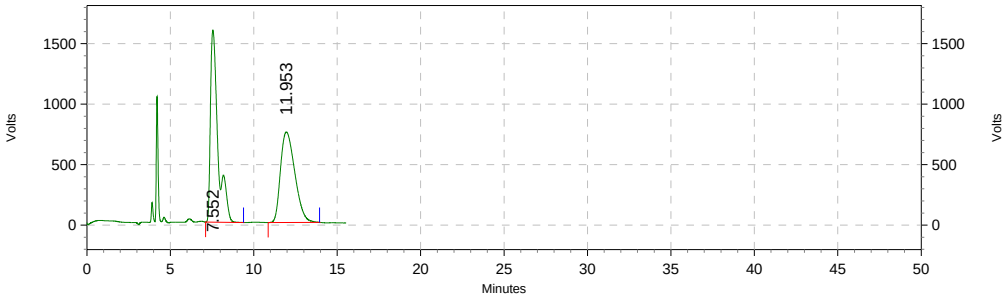
hexane, 1.0 mL/min, UV 220 nm): t_R = 7.4 min for enantiomer (R), t_R = 12.2 min for enantiomer (S). $[\alpha]_D^{20}$ = +4.8 (c = 0.40, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 4H), 7.22 – 7.09 (m, 4H), 7.06 – 6.99 (m, 1H), 5.67 (s, 1H), 2.67 (s, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 143.8, 138.2, 128.5, 127.5, 127.3, 126.6, 123.8, 120.4, 115.5, 76.3, 21.5.

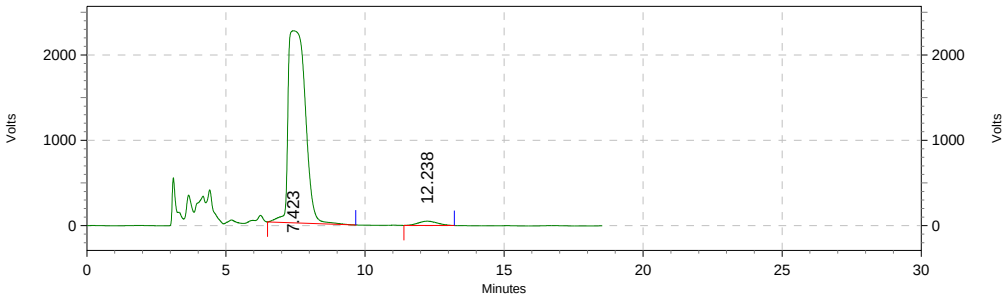
(*S*)-phenyl(m-tolyl)methanol[4]

78% yield, 81% ee, Colorless oil; HPLC (Chiralcel OB-H, 25% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 7.8 min for enantiomer (R), t_R = 12.0 min for enantiomer (S). $[\alpha]_D^{20}$ = -2.6 (c = 0.40, $CHCl_3$).

HPLC Chromatograms - Enantiomer *R*

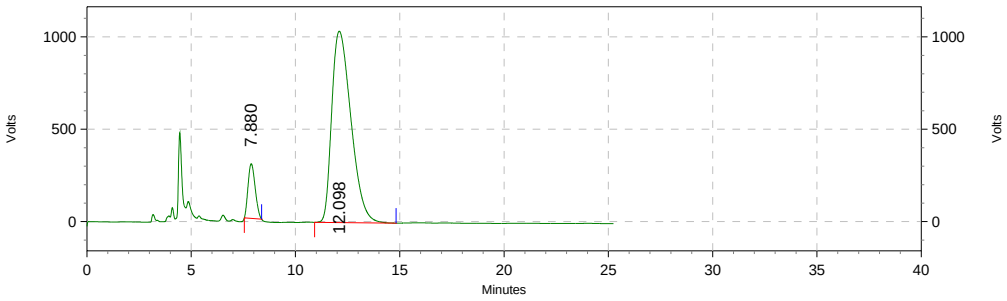


Peak	Ret. Time.	Area	Area%
1	7.552	49602752	52.616
2	11.953	44670188	47.384

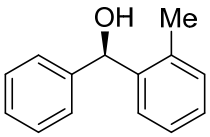


Peak	Ret. Time.	Area	Area%
1	7.423	96757278	97.604
2	12.238	2374724	2.396

HPLC Chromatograms - Enantiomer *S*



Peak	Ret. Time.	Area	Area%
1	7.880	7004516	9.570
2	12.098	66190294	90.430



(*R*)-phenyl(o-tolyl)methanol (**15c**)[5]

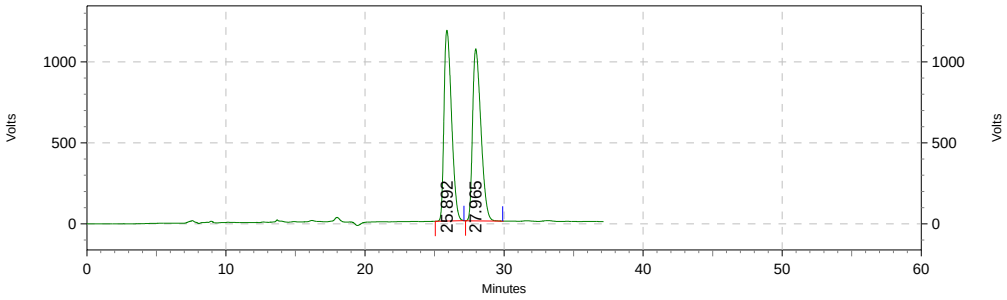
88% yield, 98% ee, Colorless oil; HPLC (Chiralcel OJ-H, 10% IPA in hexane, 0.4 mL/min, UV 210 nm): t_R = 25.4 min for enantiomer (R), t_R = 27.9 min for enantiomer (S). $[\alpha]_D^{20}$ = -7.8 (*c* = 1.25, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 - 7.49 (m, 1H), 7.34 - 7.28 (m, 4H), 7.27 – 7.19 (m, 3H), 7.14 - 7.12 (m, 1H), 5.99 (s, 1H), 2.24 (s, 3H), 1.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 141.6, 135.5, 130.7, 128.6, 127.7, 127.7, 127.2, 126.5, 126.3, 73.6, 19.5.

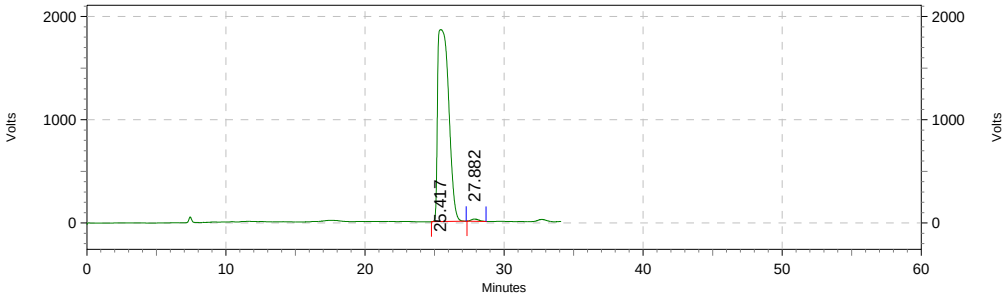
(*S*)-phenyl(o-tolyl)methanol[5]

81% yield, 92% ee, Colorless oil; HPLC (Chiralcel OJ-H, 10% IPA in hexane, 0.4 mL/min, UV 210 nm): t_R = 29.9 min for enantiomer (R), t_R = 31.7 min for enantiomer (S). $[\alpha]_D^{20}$ = +11.8 (*c* = 0.70, $CHCl_3$)

HPLC Chromatograms - Enantiomer *R*

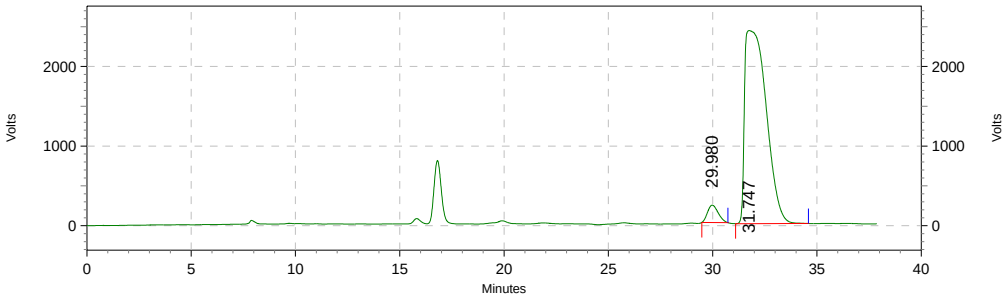


Peak	Ret. Time.	Area	Area%
1	25.892	44361361	50.075
2	27.965	44228030	49.925

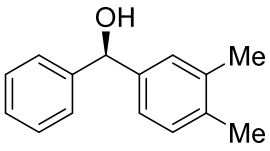


Peak	Ret. Time.	Area	Area%
1	25.417	103590074	99.233
2	27.882	800625	0.767

HPLC Chromatograms - Enantiomer *S*



Peak	Ret. Time.	Area	Area%
1	29.980	7756623	4.055
2	31.747	174536197	95.945

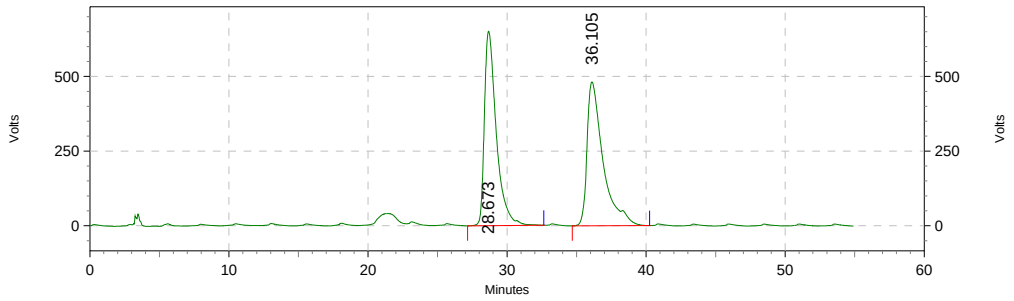


(*R*)-(3,4-dimethylphenyl)(phenyl)methanol (**15d**)[6]

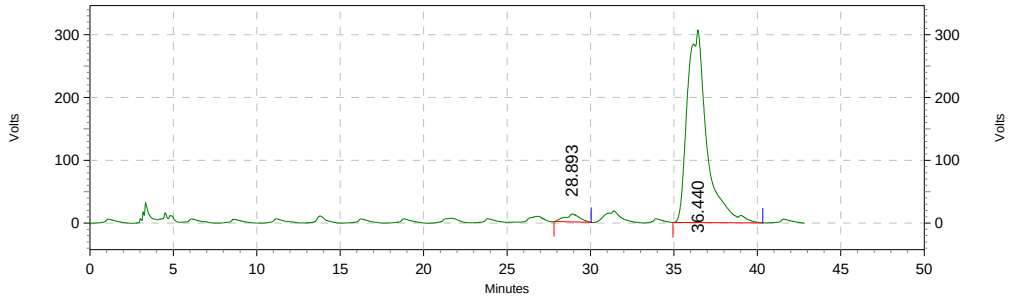
95% yield, 94% ee, Colorless oil; HPLC (Chiralcel OD-H, 2% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 28.9 min for enantiomer (S), t_R = 36.4 min for enantiomer (R). $[\alpha]_D^{20}$ = -7.7 (*c* = 0.30, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.35 (m, 2H), 7.23 (d, *J* = 2.4 Hz, 2H), 7.16-7.13 (m, 1H), 7.08 (d, *J* = 1.3 Hz, 3H), 5.77 (s, 1H), 2.23 (s, 6H), 2.21 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 141.6, 136.9, 136.1, 129.9, 128.6, 128.0, 127.5, 127.3, 126.6, 124.2, 76.3, 19.9, 19.5.

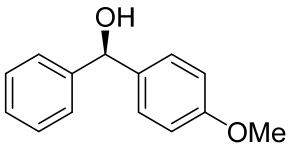
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	28.673	38684604	50.048
2	36.105	38610304	49.952



Peak	Ret. Time.	Area	Area%
1	28.893	774994	3.017
2	36.440	24915255	96.983

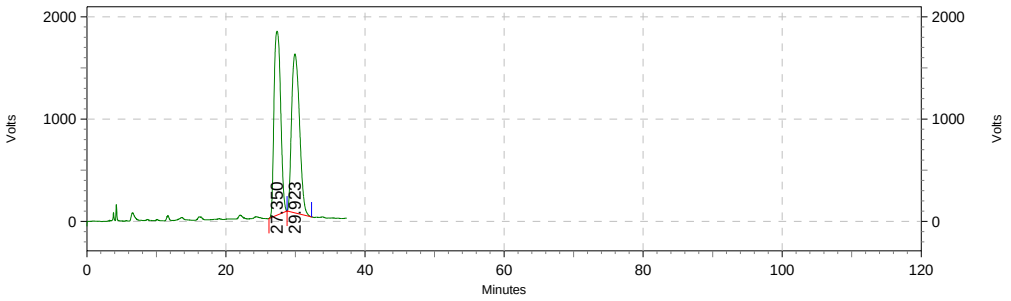


(*R*)-(4-methoxyphenyl)(phenyl)methanol (**15e**)[4]

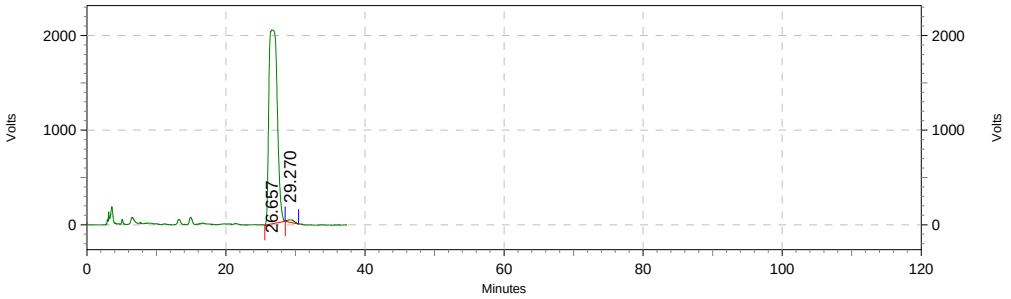
91% yield, 98% ee, Colorless oil; HPLC (Chiralcel AD-H, 3% IPA in hexane, 1.0 mL/min, UV 215 nm): t_R = 26.6 min for enantiomer (R), t_R = 29.2 min for enantiomer (S). $[\alpha]_D^{20}$ = +19.8 (*c* = 0.60, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 4H), 7.27 – 7.20 (m, 3H), 6.87 – 6.75 (m, 2H), 5.75 (s, 1H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 144.2, 136.4, 128.5, 128.0, 127.5, 126.5, 114.0, 75.9, 55.4.

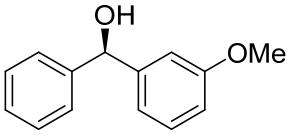
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	27.350	118799455	49.091
2	29.923	123200964	50.909



Peak	Ret. Time.	Area	Area%
1	26.657	171868688	98.954
2	29.270	1816911	1.046



(*R*)-(3-methoxyphenyl)(phenyl)methanol (**15f**)[7]

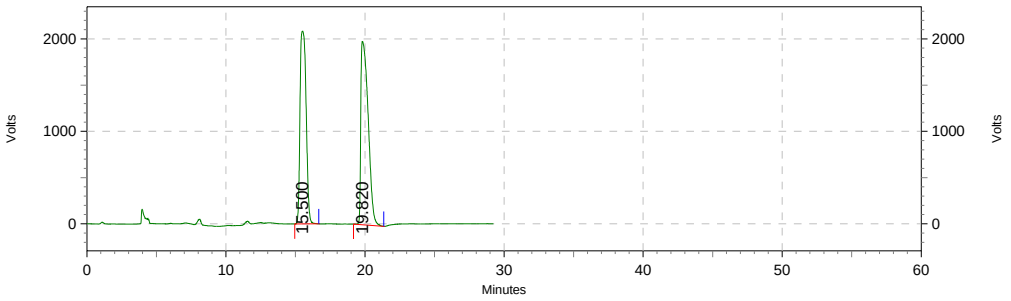
96% yield, 99% ee, Colorless oil; HPLC (Chiralcel IB, 5% IPA in hexane, 0.8 mL/min, UV 220 nm): t_R = 14.8 min for enantiomer (R), t_R = 19.0 min for enantiomer (S). $[\alpha]_D^{20}$ = -24.6 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 4H), 7.19 – 7.13 (m, 3H), 6.83 – 6.71 (m, 2H), 5.68 (s, 1H), 3.68 (s, 3H), 2.29 (d, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 144.2, 136.3, 128.5, 128.5, 128.0, 127.5, 126.5, 114.0, 75.9, 55.4.

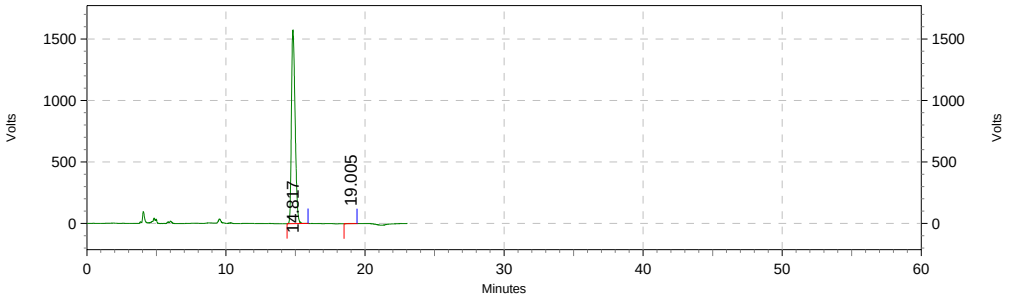
(*S*)-(3-methoxyphenyl)(phenyl)methanol

90% yield, 99% ee, Colorless oil; HPLC (Chiralcel IB, 5% IPA in hexane, 0.8 mL/min, UV 220 nm): t_R = 14.7 min for enantiomer (R), t_R = 18.8 min for enantiomer (S). $[\alpha]_D^{20}$ = +22.9 (*c* = 1.00, $CHCl_3$).

HPLC Chromatograms - Enantiomer *R*

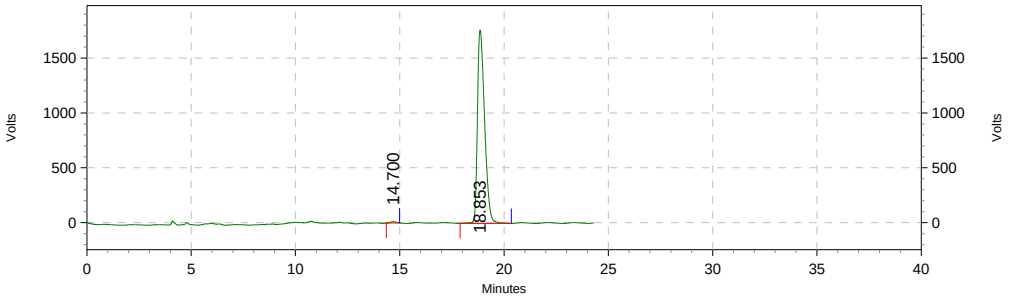


Peak	Ret. Time.	Area	Area%
1	15.500	63501739	46.587
2	19.820	72804990	53.413

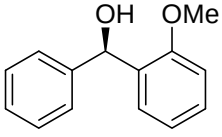


Peak	Ret. Time.	Area	Area%
1	14.817	28987365	99.824
2	19.005	51073	0.176

HPLC Chromatograms - Enantiomer *S*



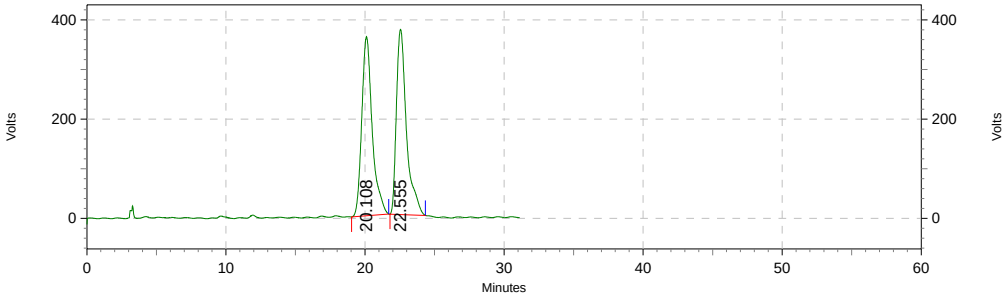
Peak	Ret. Time.	Area	Area%
1	14.700	237547	0.562
2	18.853	42034180	99.438



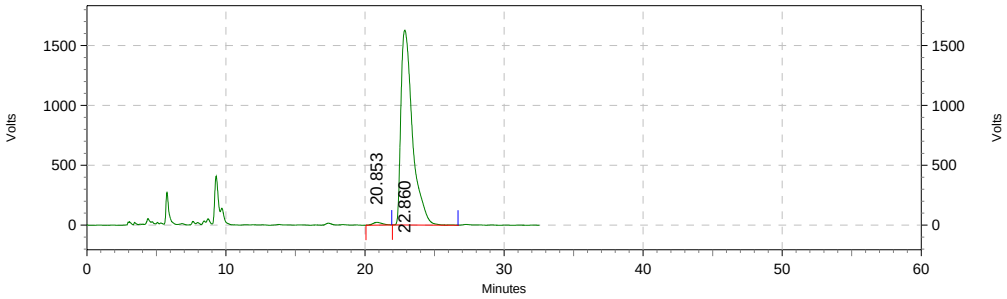
(*R*)-(2-methoxyphenyl)(phenyl)methanol (**15g**)[8]

92% yield, 94% ee, Colorless oil; HPLC (Chiralcel OD-H, 2% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 20.8 min for enantiomer (S), t_R = 22.8 min for enantiomer (R). $[\alpha]_D^{20}$ = +22.9 (c =0.60, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 2H), 7.33 – 7.28 (m, 2H), 7.26 – 7.19 (m, 3H), 6.99 – 6.82 (m, 2H), 6.05 (d, J = 4.8 Hz, 1H), 3.79 (s, 3H), 3.01 (d, J = 5.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 143.5, 132.2, 128.8, 128.3, 128.0, 127.3, 126.7, 121.0, 110.9, 72.4, 55.5.

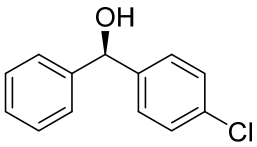
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	20.108	18857569	50.126
2	22.555	18762604	49.874



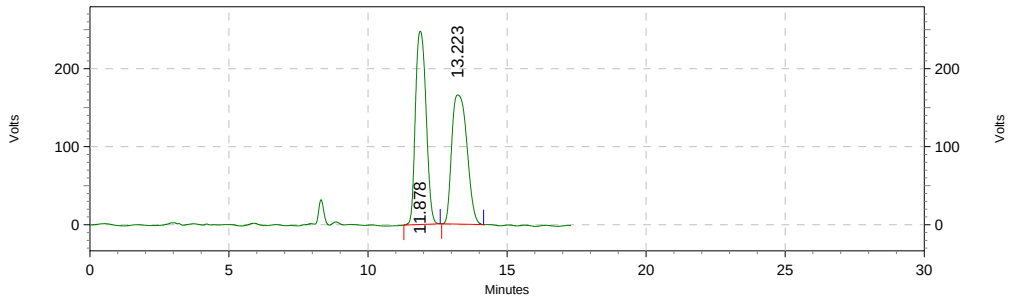
Peak	Ret. Time.	Area	Area%
1	20.853	1064825	1.121
2	22.860	93923608	98.879



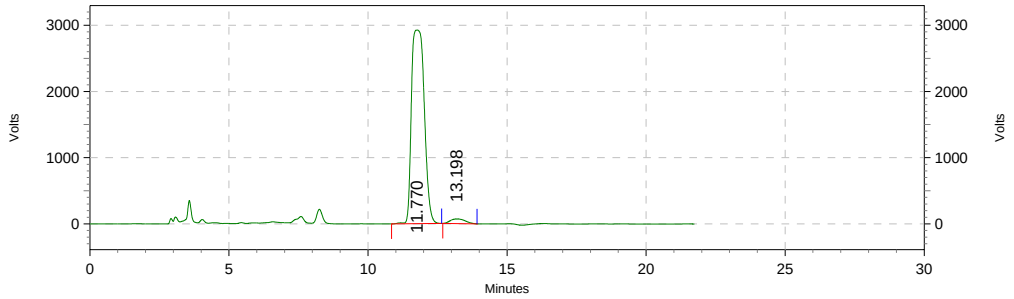
(*R*)-(4-chlorophenyl)(phenyl)methanol (**15h**)[4]

93% yield, 94% ee, Colorless oil; HPLC (Chiralcel AD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 11.7 min for enantiomer (R), t_R = 13.2 min for enantiomer (S). $[\alpha]_D^{20}$ = -12.7 (c = 0.80, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 6.90 (m, 9H), 5.59 (d, J = 1.9 Hz, 1H), 2.62 (d, J = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 142.3, 133.3, 128.7, 128.7, 128.0, 127.9, 127.9, 126.6, 75.6.

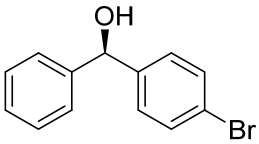
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	11.878	6591379	51.075
2	13.223	6314025	48.925



Peak	Ret. Time.	Area	Area%
1	11.770	93957177	97.292
2	13.198	2615648	2.708



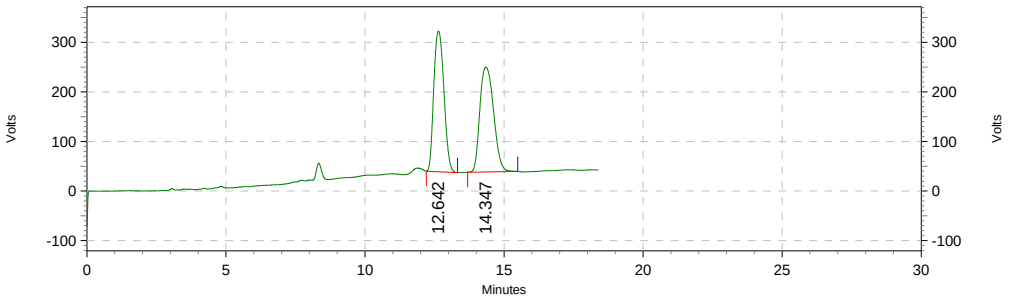
(*R*)-(4-bromophenyl)(phenyl)methanol (**15i**)[7]

92% yield, 94% ee, Colorless oil; HPLC (Chiralcel AD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 12.5 min for enantiomer (R), t_R = 14.2 min for enantiomer (S). $[\alpha]_D^{20}$ = -10.8 (*c* = 0.50, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 2H), 7.26 – 7.06 (m, 7H), 5.61 (s, 1H), 2.50 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 142.8, 131.6, 131.6, 128.7, 128.3, 127.9, 126.6, 121.5, 75.7.

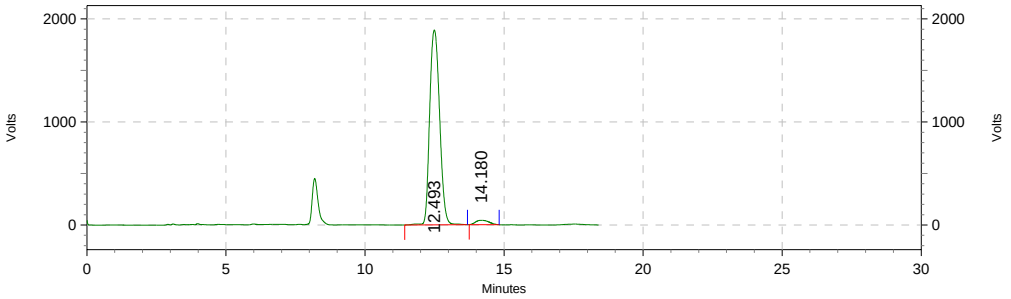
(*S*)-(4-bromophenyl)(phenyl)methanol

93% yield, 88% ee, Colorless oil; HPLC (Chiralcel AD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 14.1 min for enantiomer (R), t_R = 15.7 min for enantiomer (S). $[\alpha]_D^{20}$ = +15.6 (*c* = 0.50, $CHCl_3$)

HPLC Chromatograms - Enantiomer *R*

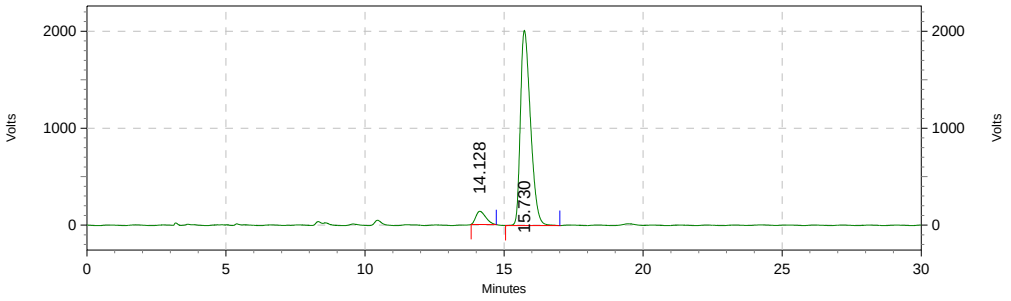


Peak	Ret. Time.	Area	Area%
1	12.642	7188278	49.750
2	14.347	7260504	50.250

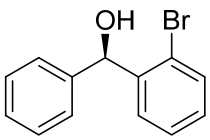


Peak	Ret. Time.	Area	Area%
1	12.493	46967534	97.075
2	14.180	1415322	2.925

HPLC Chromatograms - Enantiomer *S*



Peak	Ret. Time.	Area	Area%
1	14.128	3359104	6.009
2	15.730	50738521	93.991

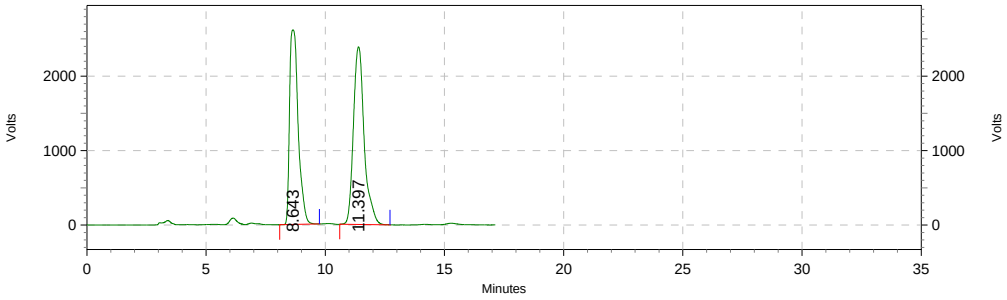


(*R*)-(2-bromophenyl)(phenyl)methanol (**15j**)[9]

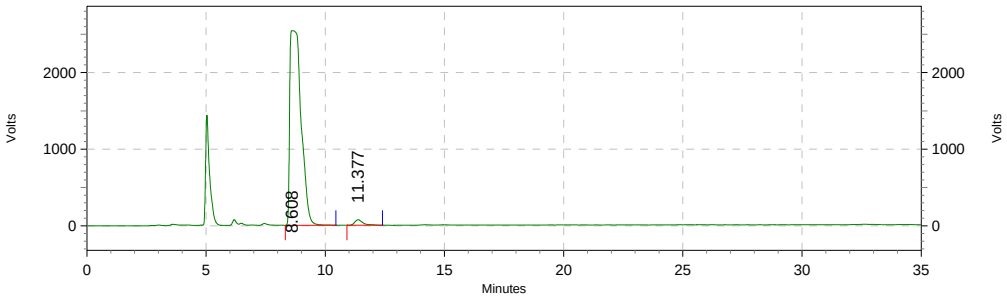
95% yield, 96% ee, Colorless oil; HPLC (Chiralcel OD-H, 10% IPA in hexane, 1.0 mL/min, UV 210 nm): t_R = 8.6 min for enantiomer (R), t_R = 11.3 min for

enantiomer (S). $[\alpha]_D^{20}$ = +37.8 (*c* = 1.50, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.35 (m, 2H), 7.26 – 7.22 (m, 2H), 7.21 – 7.09 (m, 4H), 7.03 – 6.90 (m, 1H), 6.00 (s, 1H), 2.68 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 142.2, 132.9, 129.1, 128.5, 128.5, 127.8, 127.8, 127.1, 122.8, 74.8.

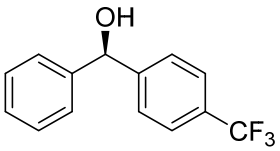
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	8.643	65928972	46.774
2	11.397	75021949	53.226



Peak	Ret. Time.	Area	Area%
1	8.608	83996801	97.977
2	11.377	1734080	2.023

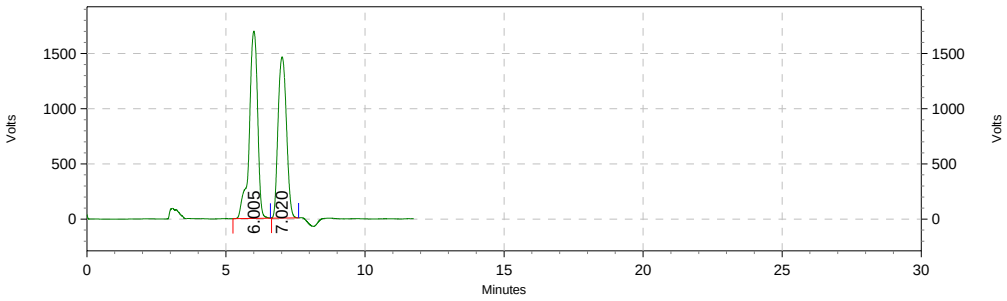


(*R*)-phenyl(4-(trifluoromethyl)phenyl)methanol (**15k**)[4]

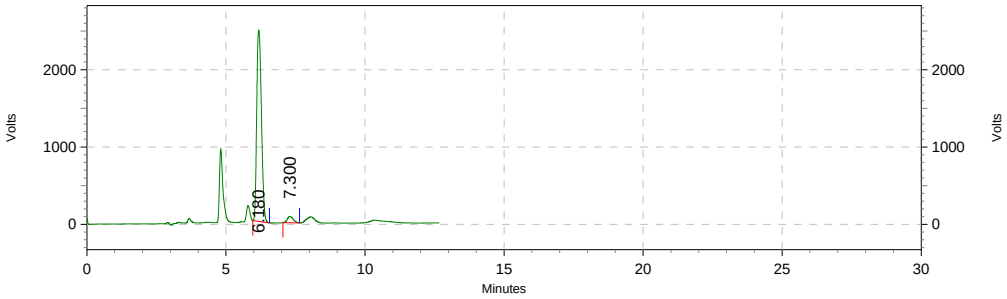
74% yield, 92% ee, Colorless oil; HPLC (Chiralcel AD-H, 10% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 6.2 min for enantiomer (R), t_R = 7.3 min for enantiomer (S). $[\alpha]_D^{20}$ = -27.8 (*c* = 1.30, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.12 (m, 5H), 5.67 (s, 1H), 2.70 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 143.2, 129.8 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 128.9, 128.2, 126.8, 126.8, 125.5 (q, $^3J_{C\text{-}F}$ = 3.9 Hz), 124.29 (q, $^1J_{C\text{-}F}$ = 271.9 Hz).75.8.

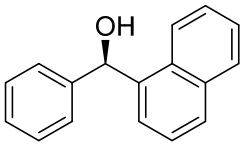
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	6.005	35284157	53.459
2	7.020	30717661	46.541



Peak	Ret. Time.	Area	Area%
1	6.180	29151506	96.088
2	7.300	1186863	3.912

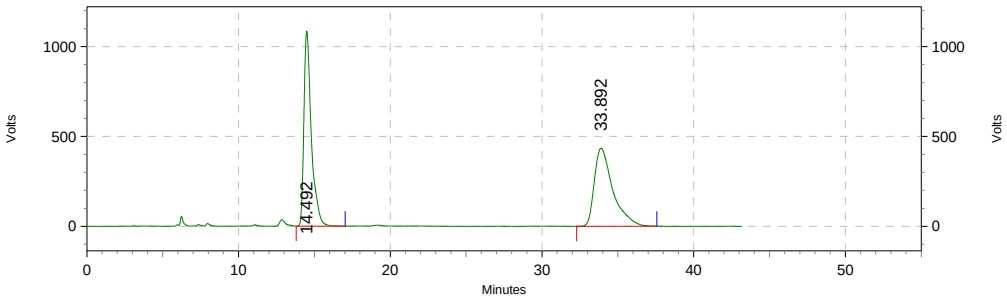


(*R*)-naphthalen-1-yl(phenyl)methanol (**15l**)[4]

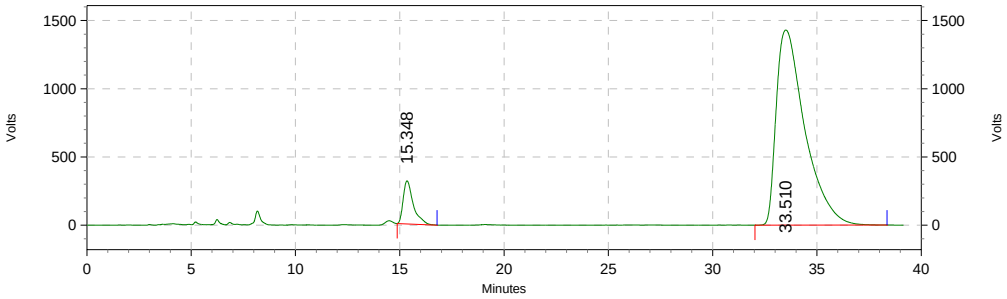
90% yield, 86% ee, Colorless oil; HPLC (Chiralcel OD-H, 10% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 15.3 min for enantiomer (S), t_R = 33.5min for enantiomer (R). $[\alpha]_D^{20}$ = +67.8 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 1H), 7.79 – 7.66 (m, 2H), 7.55 – 7.47 (m, 1H), 7.41 – 7.25 (m, 5H), 7.25 – 7.11 (m, 3H), 6.38 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 138.9, 134.1, 130.8, 128.9, 128.6, 128.6, 127.8, 127.2, 126.3, 125.7, 125.4, 124.7, 124.1, 73.7.

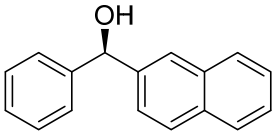
HPLC Chromatograms - Enantiomer *S*



Peak	Ret. Time.	Area	Area%
1	14.492	36936567	50.147
2	33.892	36720704	49.853



Peak	Ret. Time.	Area	Area%
1	15.348	10593701	7.216
2	33.510	136218117	92.784

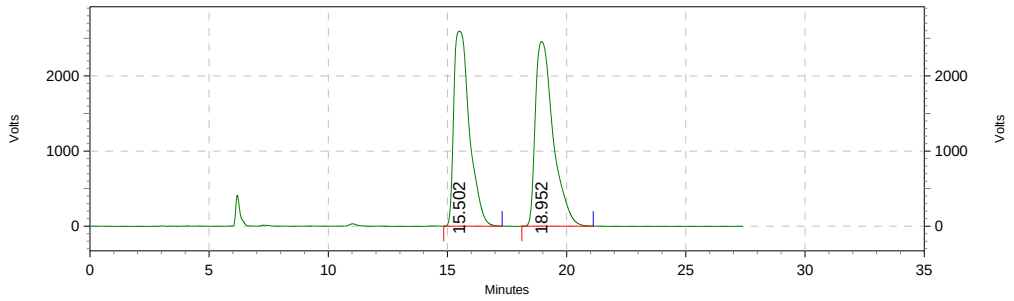


(*R*)-naphthalen-2-yl(phenyl)methanol (**15m**)[4]

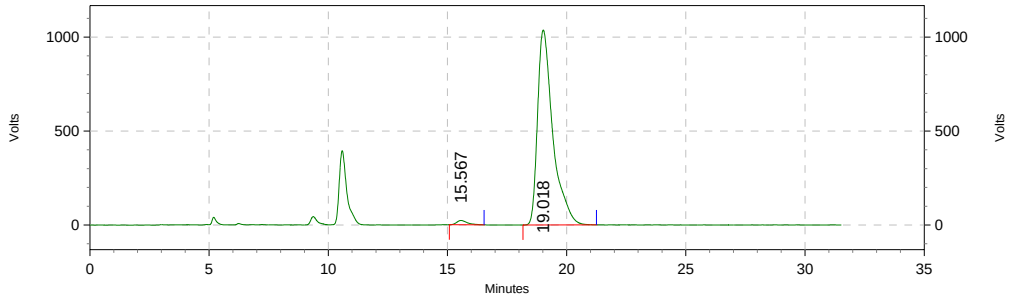
86% yield, 97% ee, Colorless oil; HPLC (Chiralcel OD-H, 10% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 15.5 min for enantiomer (R), t_R = 19.0 min for enantiomer (S). $[\alpha]_D^{20}$ = +22.6 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.55 (m, 4H), 7.38 – 7.29 (m, 2H), 7.29 – 7.22 (m, 3H), 7.22 – 7.09 (m, 3H), 5.92 – 5.68 (s, 1H), 2.55 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 141.2, 133.3, 133.0, 129.7, 128.6, 128.4, 128.2, 127.8, 127.7, 126.8, 126.3, 126.1, 125.1, 124.9, 120.5, 115.4, 76.4.

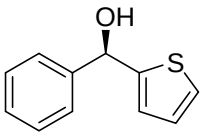
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	15.502	118481630	48.114
2	18.952	127769174	51.886



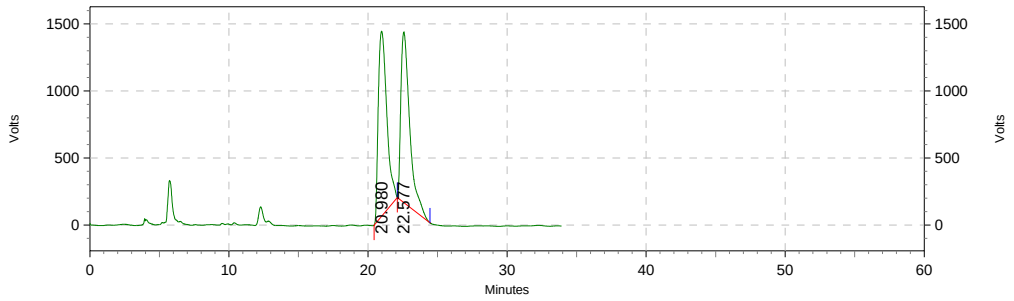
Peak	Ret. Time.	Area	Area%
1	15.567	711889	1.517
2	19.018	46216489	98.483



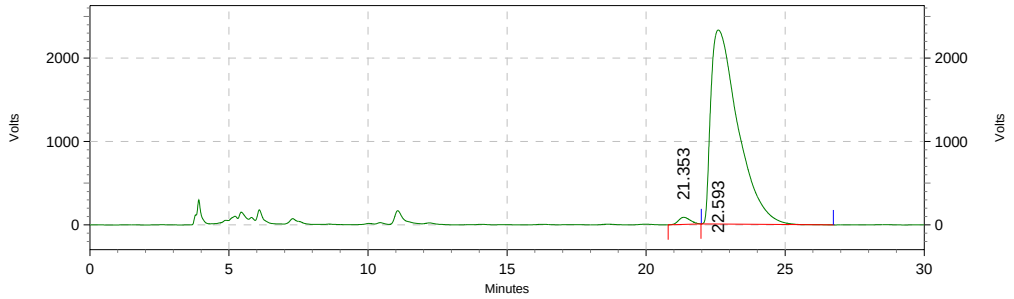
(*R*)-phenyl(thiophen-2-yl)methanol (**15n**)[7]

92% yield, 97% ee, Colorless oil; HPLC (Chiralcel OD-H, 5% IPA in hexane, 0.8 mL/min, UV 220 nm): t_R = 21.3 min for enantiomer (S), t_R = 22.5 min for enantiomer (R). $[\alpha]_D^{20}$ = -15.7 (*c* = 1.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.31 – 7.21 (m, 3H), 7.19 – 7.15 (m, 1H), 6.90 – 6.82 (m, 1H), 6.82 – 6.73 (m, 1H), 5.95 (d, *J* = 2.8 Hz, 1H), 2.43 (d, *J* = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 143.3, 128.7, 128.1, 126.8, 126.4, 125.5, 125.0, 72.5.

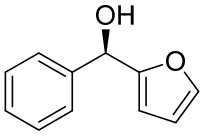
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	20.980	58768574	51.140
2	22.577	56149423	48.860



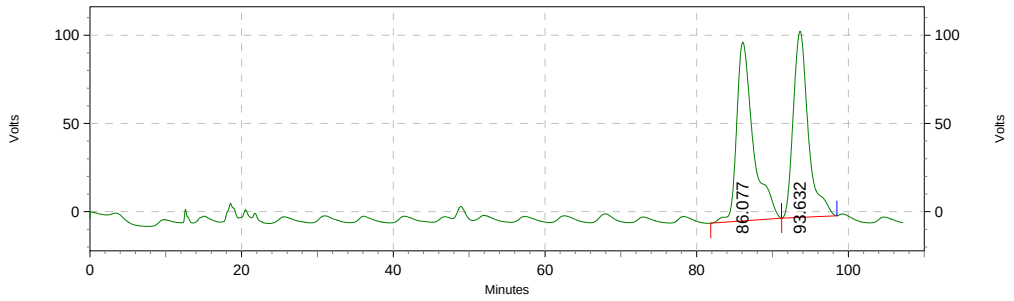
Peak	Ret. Time.	Area	Area%
1	21.353	2452525	1.533
2	22.593	157543653	98.467



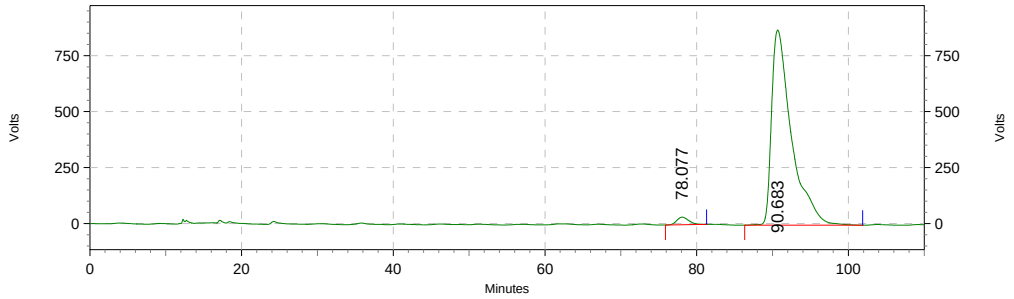
(*R*)-furan-2-yl(phenyl)methanol (**15o**)[7]

96% yield, 95% ee, Yellow oil; HPLC (Chiralcel OD-H, 3% IPA in hexane, 0.25 mL/min, UV 220 nm): t_R = 78.0 min for enantiomer (S), t_R = 90.7 min for enantiomer (R). $[\alpha]_D^{20}$ = +19.1(*c* = 1.30, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.35 – 7.23 (m, 4H), 6.34 – 6.19 (m, 1H), 6.06 (d, *J* = 3.2 Hz, 1H), 5.72 (s, 1H), 2.86 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 142.5, 141.0, 128.5, 128.0, 126.7, 110.3, 107.4, 70.1.

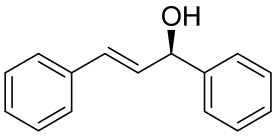
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	86.077	15468682	51.652
2	93.632	14479476	48.348



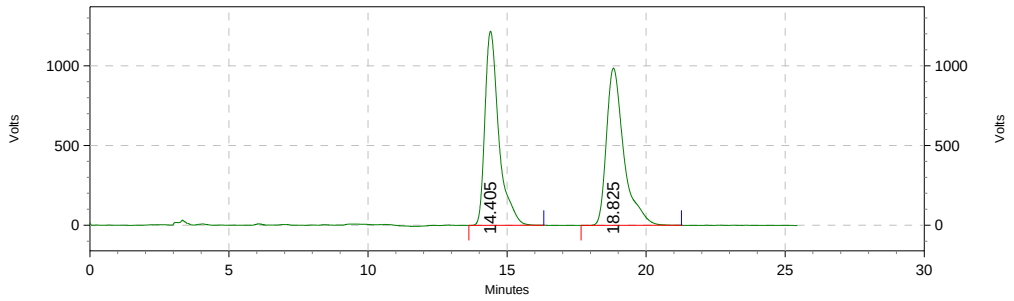
Peak	Ret. Time.	Area	Area%
1	78.077	3787377	2.334
2	90.683	158517144	97.666



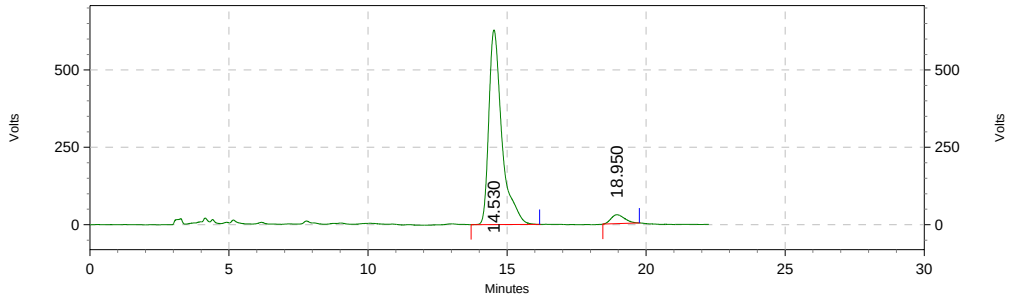
(*R*,*E*)-1,3-diphenylprop-2-en-1-ol (**15p**)[10]

78% yield, 91% ee, Colorless oil; HPLC (Chiralcel OD-H, 10% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 14.5 min for enantiomer (R), t_R = 18.9 min for enantiomer (S). $[\alpha]_D^{20}$ = +29.8 (*c* = 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 2H), 7.29 – 7.23 (m, 4H), 7.22 – 7.17 (m, 3H), 7.15 – 7.11 (m, 1H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.38 – 6.09 (m, 1H), 5.24 (d, *J* = 6.5 Hz, 1H), 2.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 136.7, 131.7, 130.6, 128.7, 128.7, 128.6, 127.9, 127.2, 126.7, 126.5, 75.2.

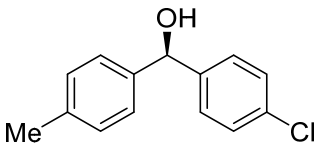
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	14.405	42340091	49.681
2	18.825	42883813	50.319



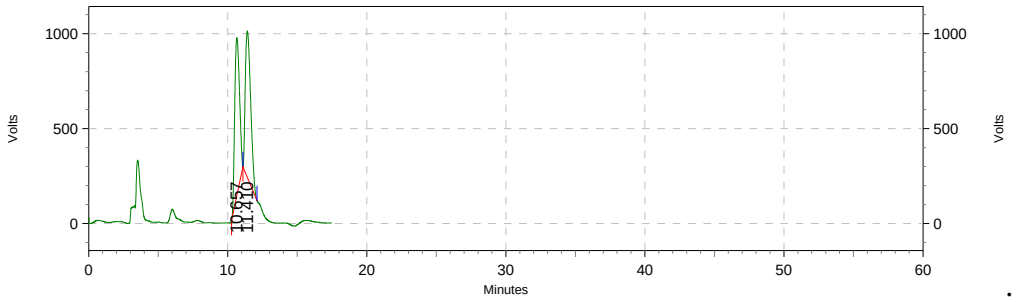
Peak	Ret. Time.	Area	Area%
1	14.530	20471426	95.434
2	18.950	979428	4.566



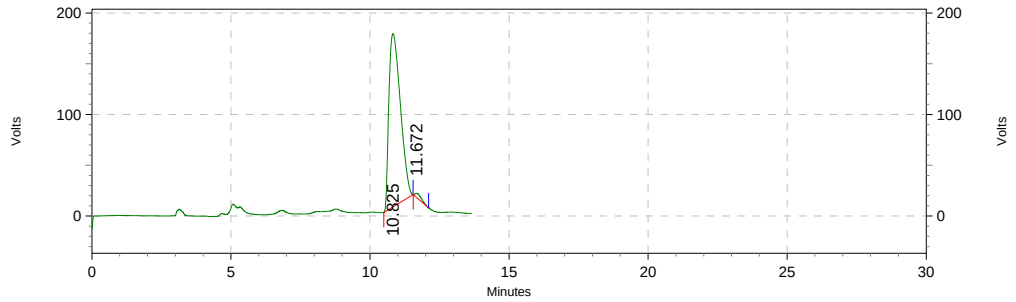
(*R*)-(4-chlorophenyl)(p-tolyl)methanol (**15q**)[8]

83% yield, 97% ee, Colorless oil; HPLC (Chiralcel OD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 10.8 min for enantiomer (R), t_R = 11.6 min for enantiomer (S). $[\alpha]_D^{20}$ = +8.9 (*c* = 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 4H), 7.23 – 7.18 (m, 2H), 7.17 – 7.10 (m, 2H), 5.76 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 140.7, 137.8, 133.3, 129.5, 128.7, 127.9, 126.6, 75.6, 21.2

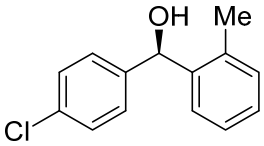
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	10.657	19815421	48.627
2	11.410	20934242	51.373



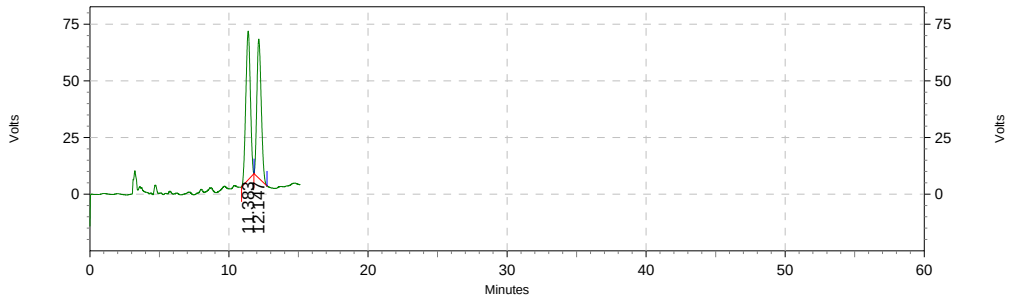
Peak	Ret. Time.	Area	Area%
1	10.825	4893634	98.561
2	11.672	71452	1.439



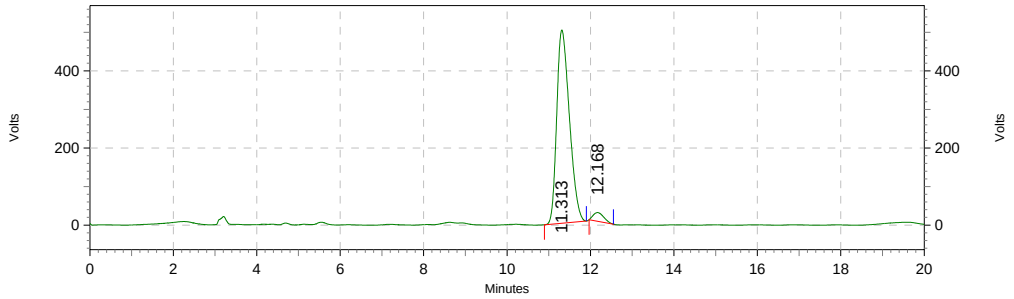
(*R*)-(4-chlorophenyl)(o-tolyl)methanol (**15r**)[8]

89% yield, 93% ee, Colorless oil; HPLC (Chiralcel AD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm): t_R = 11.3 min for enantiomer (R), t_R = 12.1 min for enantiomer (S). $[\alpha]_D^{20}$ = +49.8 (*c* = 1.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 1H), 7.30 – 7.19 (m, 6H), 7.16 – 7.11 (m, 1H), 5.95 (s, 1H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 141.2, 135.5, 133.4, 130.8, 128.7, 128.6, 127.9, 126.5, 126.4, 72.9, 19.5.

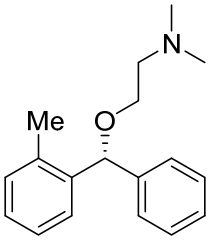
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	11.383	1486412	52.608
2	12.147	1339029	47.392

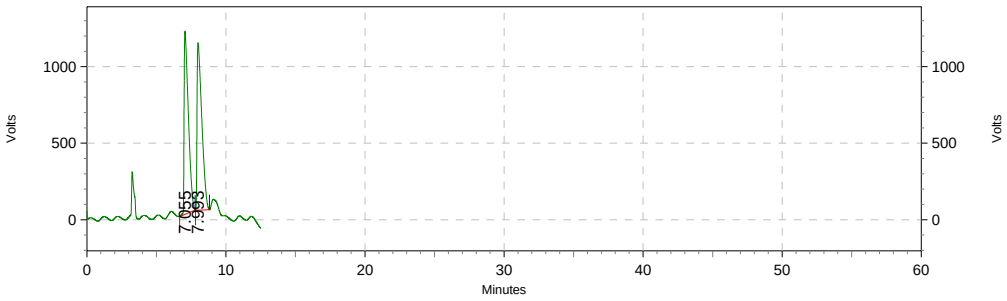


Peak	Ret. Time.	Area	Area%
1	11.313	10559687	96.307
2	12.168	404898	3.693

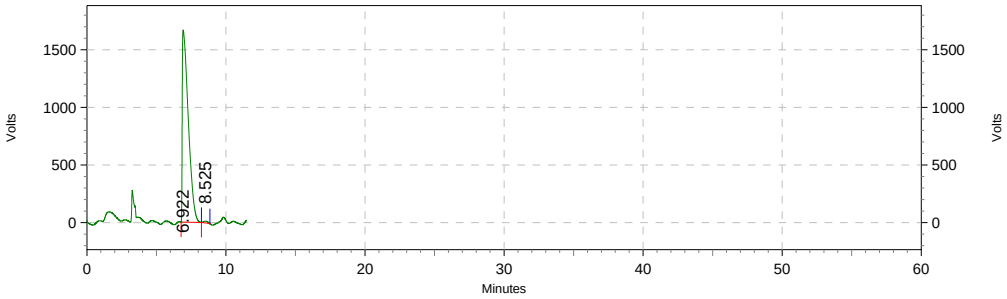


(*R*)-N,N-dimethyl-2-(phenyl(o-tolyl)methoxy)ethan-1-amine-Orphenadrine[11] 71% yield, 98% ee, Colorless oil; HPLC (Chiralcel IB, 95:5 *n*-Heptane / (Ethanol / *iso*-propanol 50:50 + 0.5% diethylamine), 1.0 mL/min, UV 220 nm): t_R = 6.9 min for enantiomer (R), t_R = 8.5 min for enantiomer (S). $[\alpha]_D^{20}$ = +4.8 (*c* = 0.90, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 1H), 7.32 – 7.25 (m, 4H), 7.24 – 7.13 (m, 3H), 7.13 – 7.08 (m, 1H), 5.53 (s, 1H), 3.64 – 3.49 (m, 2H), 2.69 – 2.55 (m, 2H), 2.28 (s, 6H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 139.8, 135.9, 130.6, 128.3, 127.6, 127.4, 127.1, 126.0, 81.4, 67.3, 58.9, 45.8, 19.5.

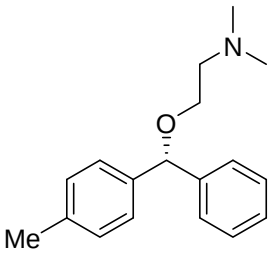
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	7.055	25309097	49.370
2	7.993	25954793	50.630



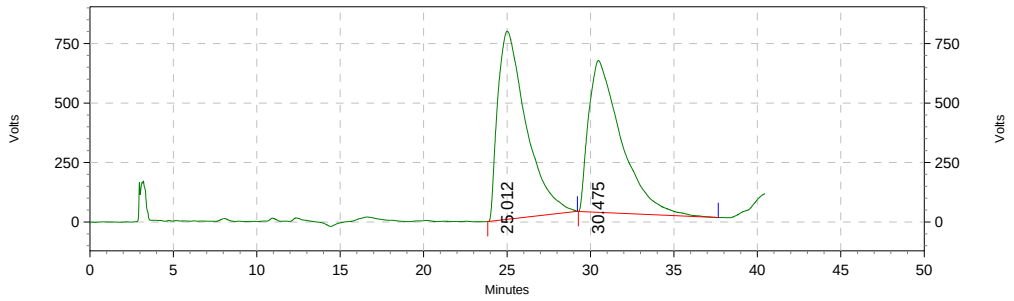
Peak	Ret. Time.	Area	Area%
1	6.922	50102519	99.332
2	8.525	337147	0.668



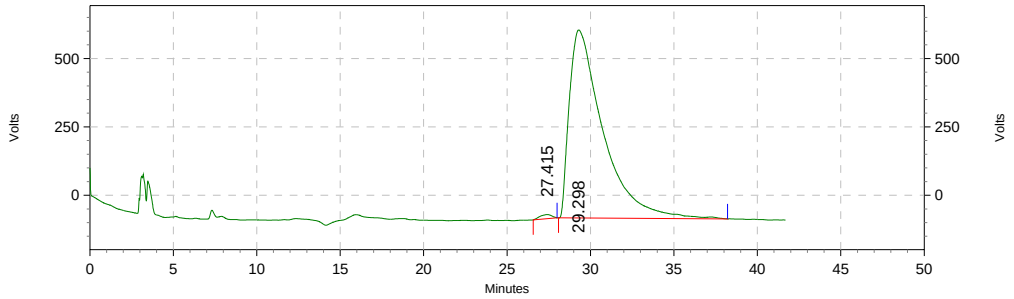
(*R*)-N,N-dimethyl-2-(phenyl(p-tolyl)methoxy)ethan-1-amine-Neobenodine[12]

76% yield, 98% ee, Colorless oil; HPLC (Chiralcel OD-H, 5% IPA in hexane, 1.0 mL/min, UV 220 nm, 1.0 mL/min, UV 220 nm): t_R = 27.4 min for enantiomer (S), t_R = 29.2 min for enantiomer (R). $[\alpha]_D^{20}$ = -6.6 (*c* = 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 4H), 7.25 – 7.16 (m, 3H), 7.10 (d, *J* = 7.9 Hz, 2H), 5.33 (s, 1H), 3.57 (t, *J* = 5.9 Hz, 2H), 2.64 (t, *J* = 5.9 Hz, 2H), 2.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 139.3, 137.1, 129.1, 128.4, 127.4, 127.0, 126.9, 83.9, 67.2, 58.8, 45.8, 21.2.

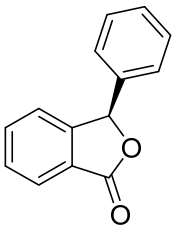
HPLC Chromatograms - Enantiomer *R*



Peak	Ret. Time.	Area	Area%
1	25.012	93411299	51.754
2	30.475	87078272	48.246

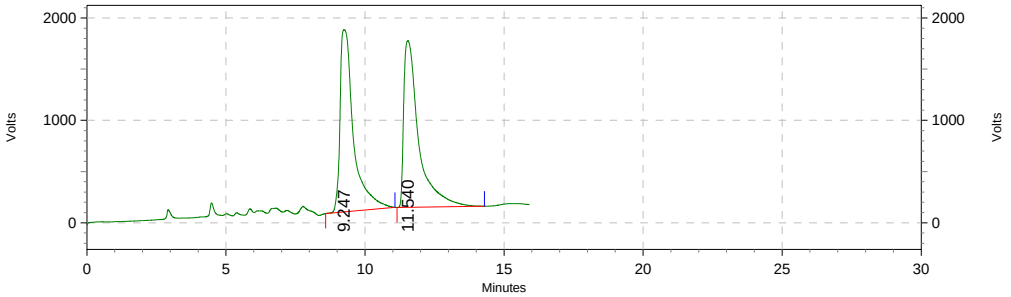


Peak	Ret. Time.	Area	Area%
1	27.415	738046	0.759
2	29.298	96456969	99.241

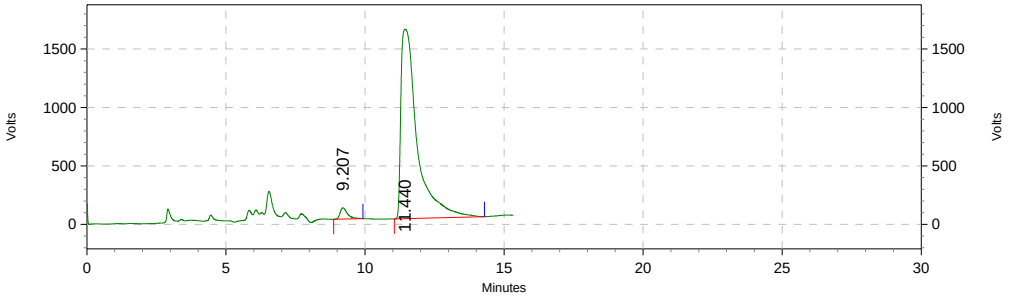


(R)-3-phenylisobenzofuran-1(3H)-one (**16a**)[13]

83% yield, 95% ee; after recrystallization: 98.5% ee; White solid. $[\alpha]_D^{20}$ = -52.98 (*c* = 1.20 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 9.2 min for enantiomer (S), t_R = 11.5 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.85 (m, 1H), 7.62 – 7.52 (m, 1H), 7.51 – 7.43 (m, 1H), 7.31 – 7.23 (m, 4H), 7.22 – 7.17 (m, 2H), 6.33 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 149.8, 136.5, 134.4, 129.5, 129.4, 129.1, 127.1, 125.8, 125.7, 123.0, 82.8.

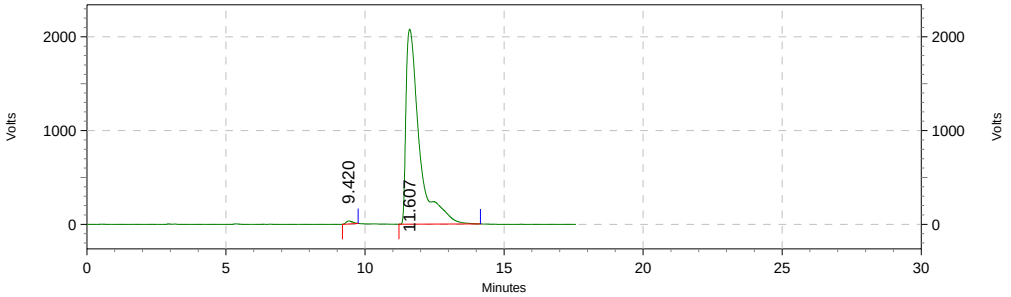


Peak	Ret. Time.	Area	Area%
1	9.247	59793930	49.774
2	11.540	60337557	50.226

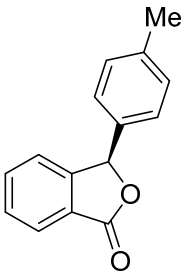


Peak	Ret. Time.	Area	Area%
1	9.207	1778848	2.646
2	11.440	65455979	97.354

After recrystallization

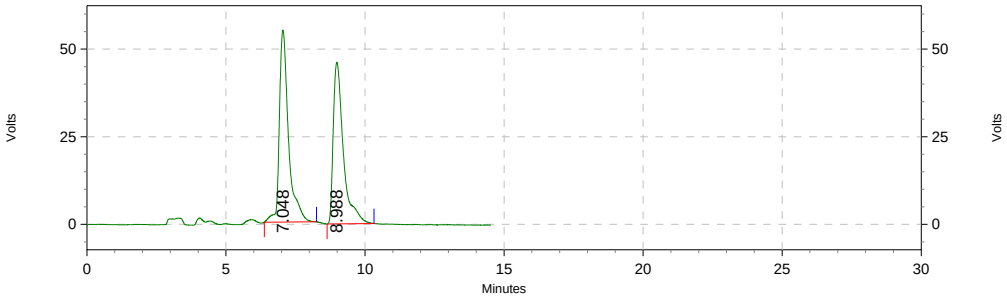


Peak	Ret. Time.	Area	Area%
1	9.420	504926	0.319
2	11.607	69727990	99.681

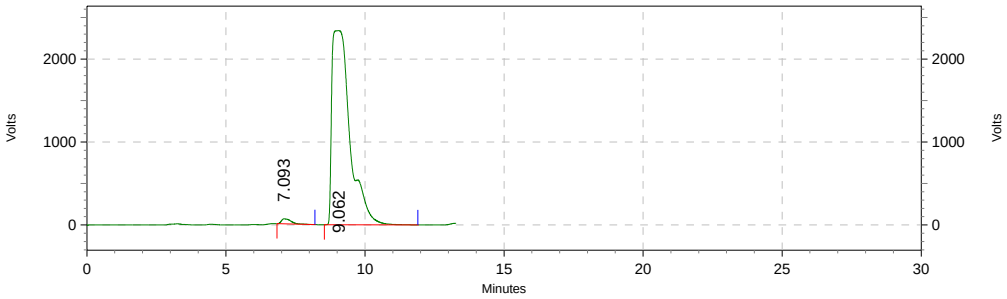


(R)-3-(p-tolyl)isobenzofuran-1(3H)-one (**16b**)[13]

88% yield, 97% ee; after recrystallization: 99.1% ee; White solid. $[\alpha]_D^{20}$ = -23.88 (*c* = 1.00 in $CHCl_3$). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 7.0 min for enantiomer (S), t_R = 8.9 min for enantiomer (R). ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 1H), 7.68 – 7.61 (m, 1H), 7.58 – 7.52 (m, 1H), 7.34 – 7.29 (m, 1H), 7.20 – 7.13 (m, 4H), 6.38 (s, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 150.0, 139.5, 134.4, 133.5, 129.8, 129.7, 129.4, 127.2, 125.8, 125.7, 123.0, 82.9, 21.4.

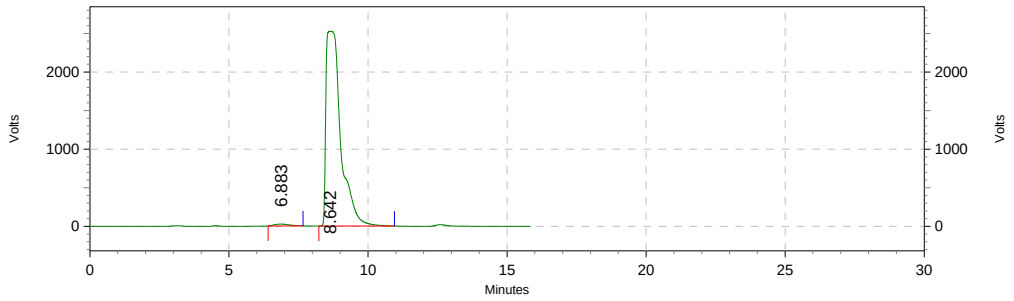


Peak	Ret. Time.	Area	Area%
1	7.048	1255438	51.892
2	8.988	1163880	48.108

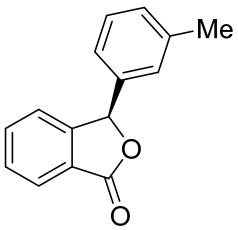


Peak	Ret. Time.	Area	Area%
1	7.093	1483756	1.383
2	9.062	105786162	98.617

After recrystallization

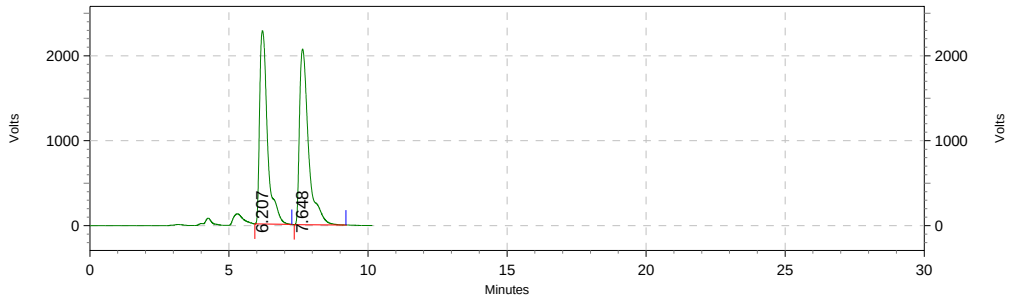


Peak	Ret. Time.	Area	Area%
1	6.883	911820	0.467
2	8.642	93412417	99.533

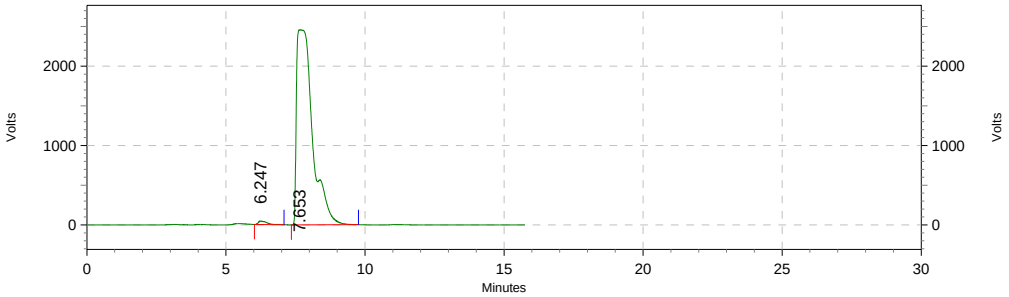


(R)-3-(m-tolyl)isobenzofuran-1(3H)-one (**16c**)[14]

90% yield, 98% ee; after recrystallization: 99.9% ee; White solid. $[\alpha]_D^{20}$ = -2.60 (*c* = 0.15 in $CHCl_3$). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 6.2 min for enantiomer (S), t_R = 7.6 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 7.6, 1.0 Hz, 1H), 7.65 (td, J = 7.5, 1.2 Hz, 1H), 7.55 (tt, J = 7.5, 0.8 Hz, 1H), 7.35-7.32 (m, 1H), 7.28 – 7.23 (m, 1H), 7.22 – 7.14 (m, 1H), 7.08 (dd, J = 9.3, 1.9 Hz, 2H), 6.37 (s, 1H), 2.33 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 149.9, 139.0, 136.4, 134.4, 130.2, 129.4, 129.0, 127.6, 125.7, 125.7, 124.2, 123.0, 82.9, 21.5.

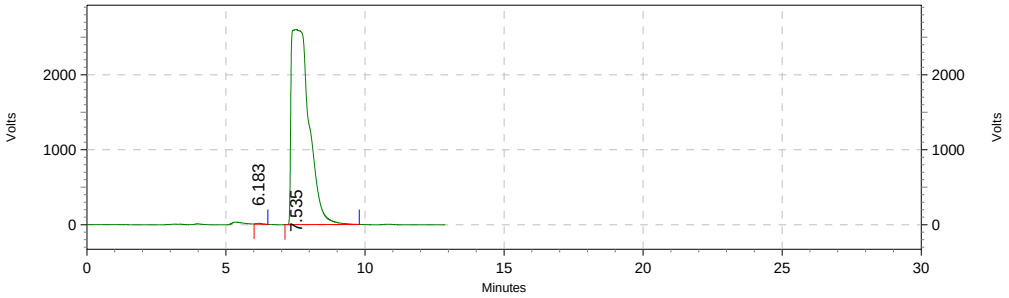


Peak	Ret. Time.	Area	Area%
1	6.207	44792535	48.970
2	7.648	46675932	51.030

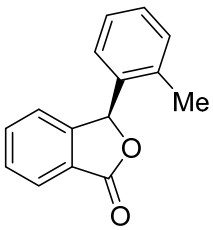


Peak	Ret. Time.	Area	Area%
1	6.247	915960	0.926
2	7.653	98003911	99.074

After recrystallization

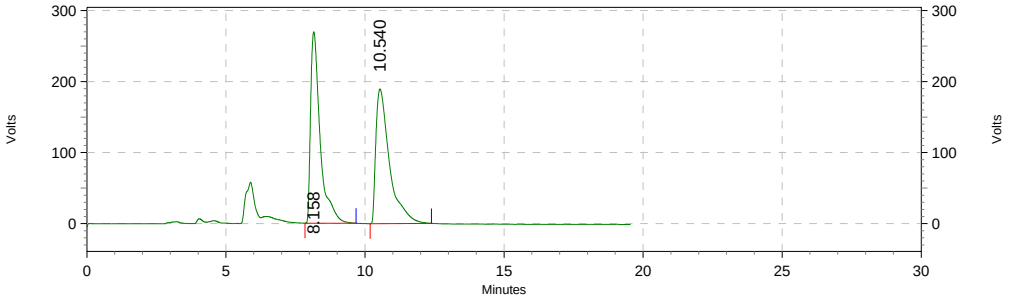


Peak	Ret. Time.	Area	Area%
1	6.183	153973	0.032
2	7.535	116736694	99.968

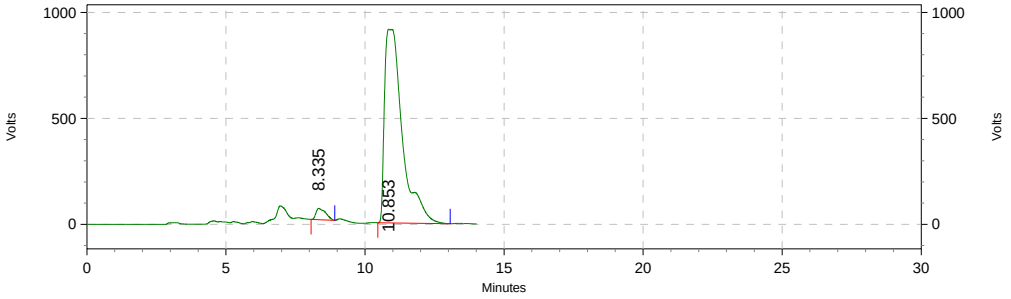


(R)-3-(o-tolyl)isobenzofuran-1(3H)-one (**16d**)[13]

84% yield, 94% ee; after recrystallization: 99.9% ee; White solid. $[\alpha]_D^{20}$ = + 13.78 (c = 0.50 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 8.1 min for enantiomer (S), t_R = 10.5 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dt, J = 7.6, 1.0 Hz, 1H), 7.67 (td, J = 7.5, 1.2 Hz, 1H), 7.59-7.55 (m, 1H), 7.36-7.33 (m, 1H), 7.28 – 7.25 (m, 2H), 7.15-7.11 (m, 1H), 6.97 – 6.88 (m, 1H), 6.68 (s, 1H), 2.50 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 149.4, 137.3, 134.3, 134.2, 131.3, 129.5, 129.4, 127.4, 126.5, 125.9, 123.1, 80.7, 19.5.

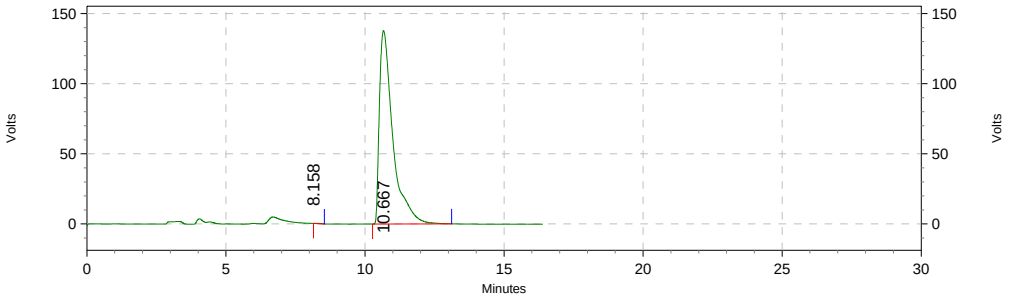


Peak	Ret. Time.	Area	Area%
1	8.158	6441968	49.980
2	10.540	6447196	50.020

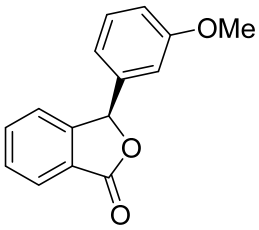


Peak	Ret. Time.	Area	Area%
1	8.335	1289157	3.077
2	10.853	40609420	96.923

After recrystallization

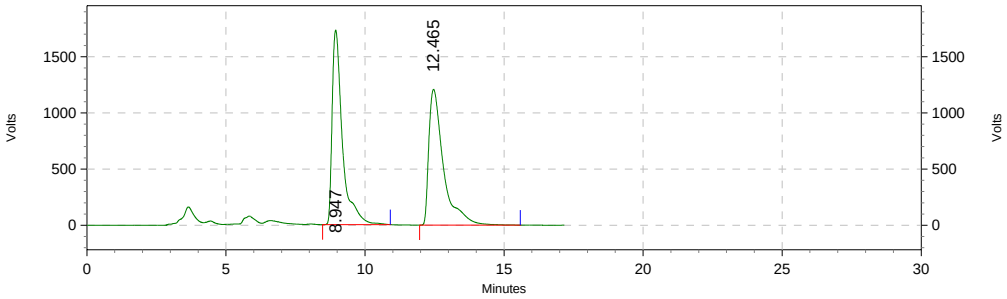


Peak	Ret. Time.	Area	Area%
1	8.158	2163	0.047
2	10.667	4631087	99.953

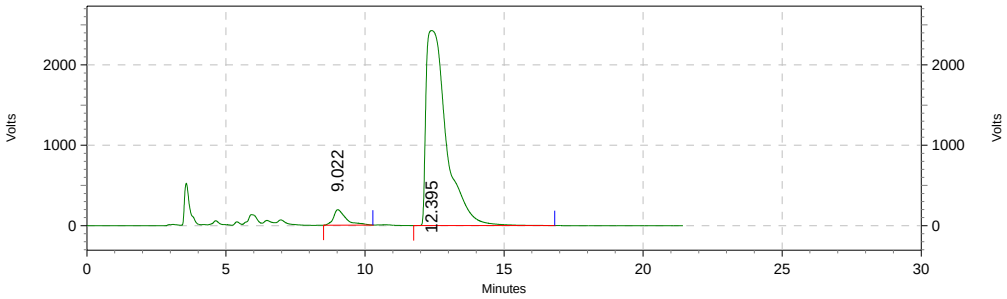


(R)-3-(3-methoxyphenyl)isobenzofuran-1(3H)-one (**16e**)[13]

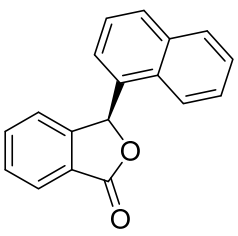
84% yield, 90% ee; yellow oil. $[\alpha]_D^{20}$ = -33.42 (c = 0.70 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 8.9 min for enantiomer (S), t_R = 12.4 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 7.8, 1.0 Hz, 1H), 7.56 (td, J = 7.5, 1.1 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.24 – 7.18 (m, 1H), 6.85 – 6.76 (m, 2H), 6.71 (t, J = 2.1 Hz, 1H), 6.29 (s, 1H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 160.1, 149.7, 138.0, 134.5, 130.2, 129.5, 125.7, 125.5, 122.9, 119.2, 114.7, 112.5, 82.6, 55.4.



Peak	Ret. Time.	Area	Area%
1	8.947	44520482	50.202
2	12.465	44161586	49.798



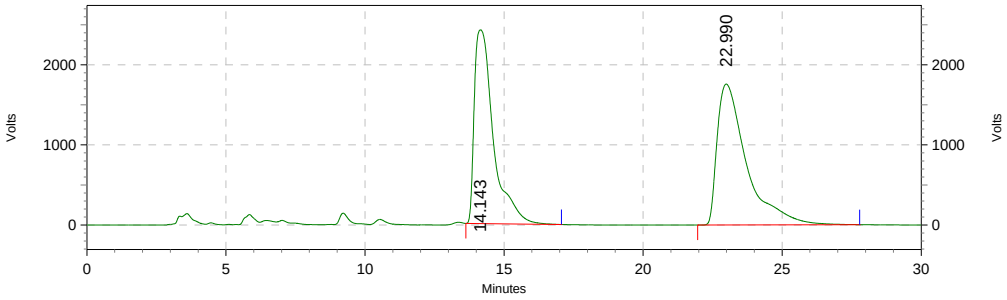
Peak	Ret. Time.	Area	Area%
1	9.022	6022110	4.659
2	12.395	123225536	95.341



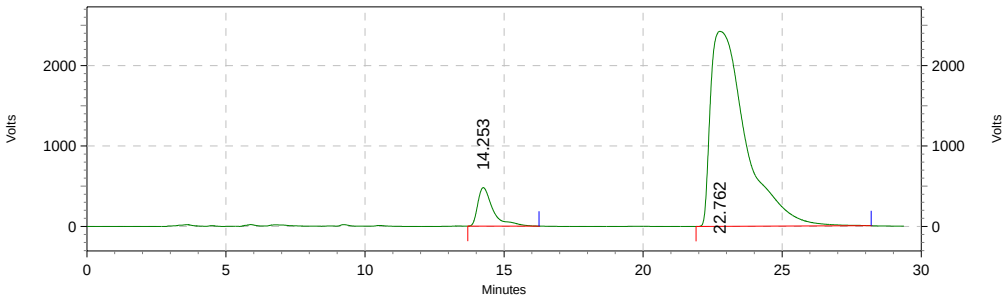
(R)-3-(naphthalen-1-yl)isobenzofuran-1(3H)-one (**16f**)[13]

65% yield, 86% ee; after recrystallization: 99.9% ee; White solid. $[\alpha]_D^{20}$ = + 9.81 (c = 0.90 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1

mL/min, UV 215 nm): t_R = 14.1 min for enantiomer (S), t_R = 22.9 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.22 (m, 1H), 8.02 (dt, J = 7.4, 1.1 Hz, 1H), 7.98 – 7.91 (m, 1H), 7.91 – 7.84 (m, 1H), 7.72 – 7.52 (m, 4H), 7.48 – 7.35 (m, 2H), 7.28 – 7.25 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 149.5, 134.3, 134.2, 132.1, 131.5, 130.1, 129.6, 129.2, 127.2, 126.4, 126.3, 126.2, 125.4, 124.7, 123.4, 123.1, 79.8.

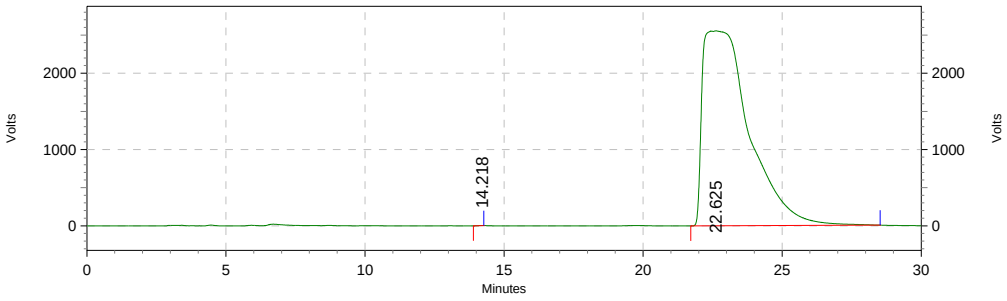


Peak	Ret. Time.	Area	Area%
1	14.143	115248549	47.223
2	22.990	128802311	52.777

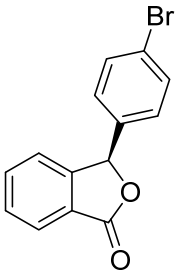


Peak	Ret. Time.	Area	Area%
1	14.253	18293680	7.898
2	22.762	213336186	92.102

After recrystallization

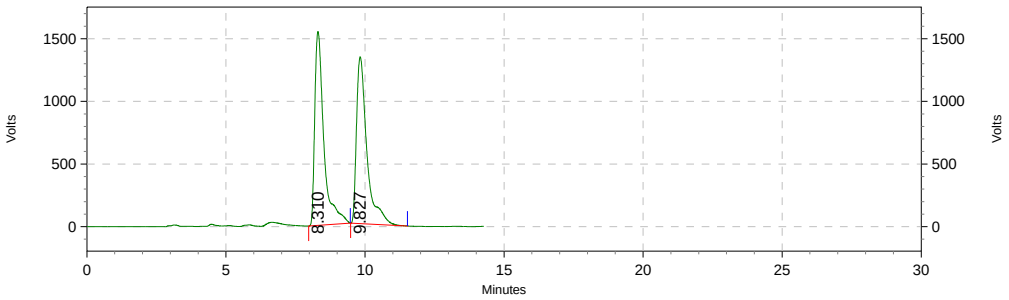


Peak	Ret. Time.	Area	Area%
1	14.218	8740	0.003
2	22.625	299472667	99.997

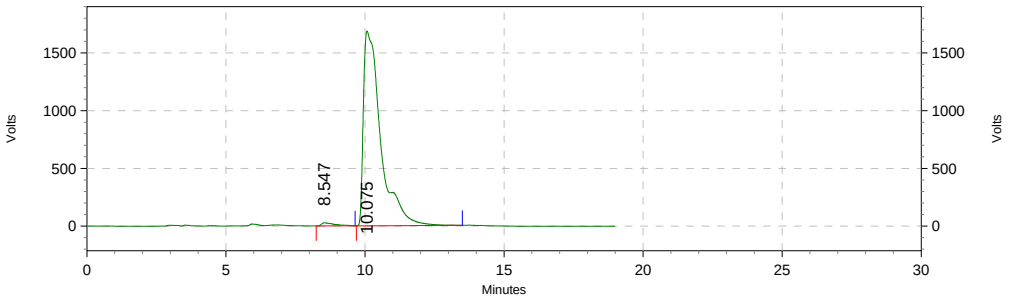


(R)-3-(4-bromophenyl)isobenzofuran-1(3H)-one (**16g**)[13]

91% yield, 97% ee; after recrystallization: 99.5% ee; White solid. $[\alpha]_D^{20}$ = - 18.77 (c = 1.00 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 8.3 min for enantiomer (S), t_R = 9.8 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 7.6, 1.0 Hz, 1H), 7.67 (td, J = 7.5, 1.2 Hz, 1H), 7.57 (tt, J = 7.6, 0.8 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.32 (dq, J = 7.8, 0.9 Hz, 1H), 7.20 – 7.12 (m, 2H), 6.36 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 149.3, 135.6, 134.6, 132.3, 129.7, 128.7, 125.9, 125.6, 123.6, 122.9, 82.0.

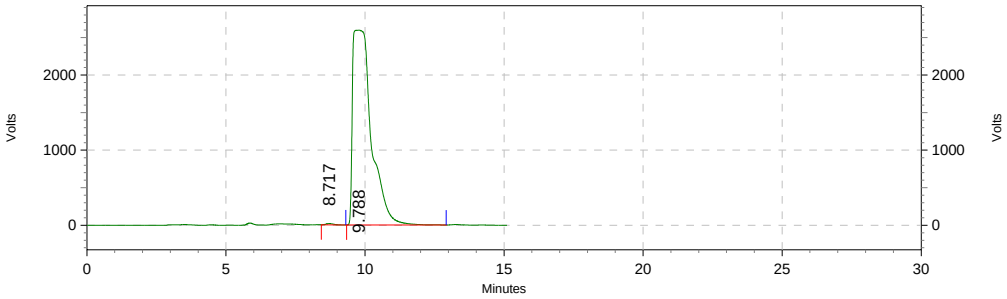


Peak	Ret. Time.	Area	Area%
1	8.310	35128708	50.439
2	9.827	34516912	49.561

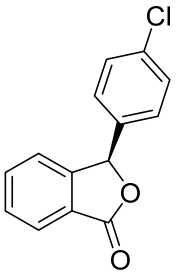


Peak	Ret. Time.	Area	Area%
1	8.547	901606	1.225
2	10.075	72701751	98.775

After recrystallization

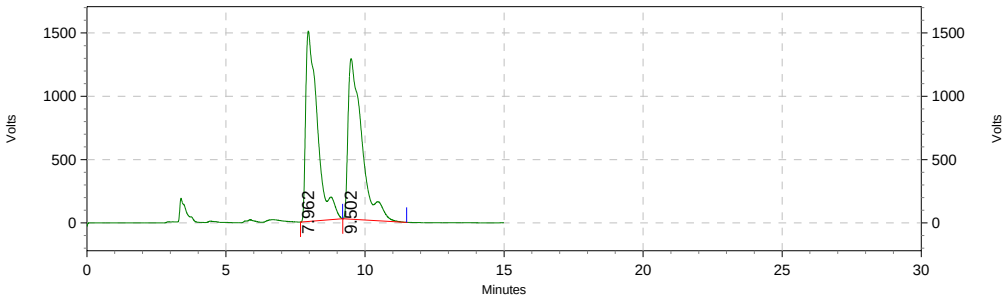


Peak	Ret. Time.	Area	Area%
1	8.717	289757	0.037
2	9.788	121910097	99.963

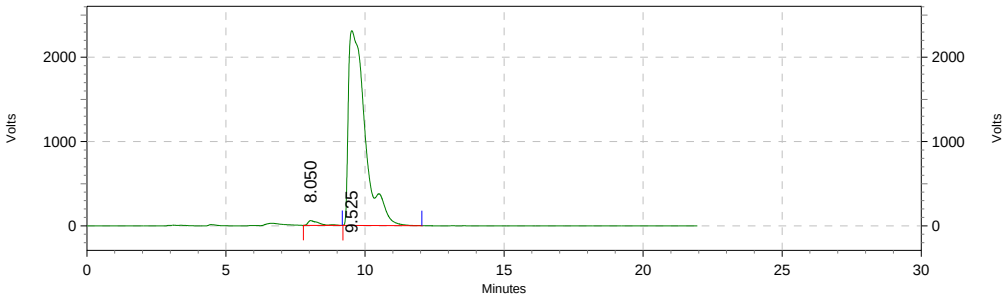


(R)-3-(4-chlorophenyl)isobenzofuran-1(3H)-one (**16h**)[13]

91% yield, 97% ee; after recrystallization: 99.9% ee; White solid. $[\alpha]_D^{20}$ = - 29.88 (*c* = 0.98 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 7.9 min for enantiomer (S), t_R = 9.5 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.67 (td, *J* = 7.5, 1.2 Hz, 1H), 7.57 (tt, *J* = 7.5, 0.8 Hz, 1H), 7.40 – 7.29 (m, 3H), 7.25 – 7.19 (m, 2H), 6.38 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 149.4, 135.5, 135.1, 134.6, 129.7, 129.4, 128.5, 126.0, 125.7, 122.9, 82.0.

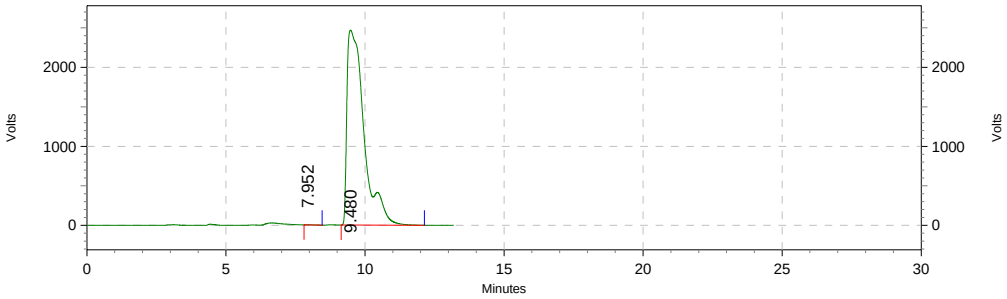


Peak	Ret. Time.	Area	Area%
1	7.962	44001896	50.064
2	9.502	43889065	49.936

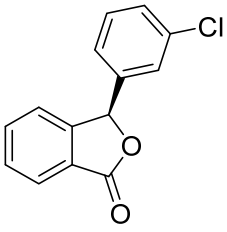


Peak	Ret. Time.	Area	Area%
1	8.050	1516271	1.541
2	9.525	96855673	98.459

After recrystallization



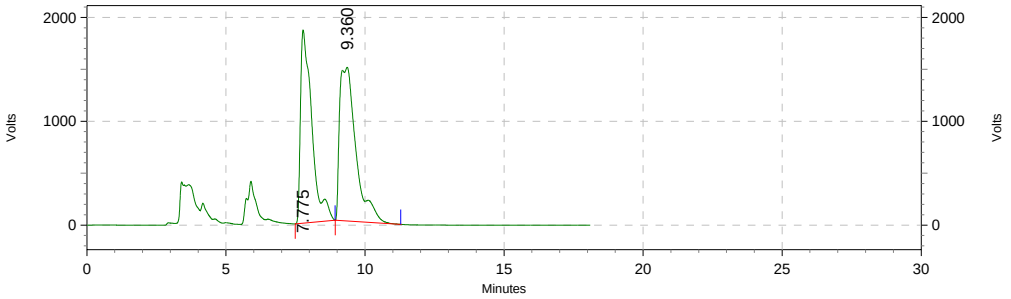
Peak	Ret. Time.	Area	Area%
1	7.952	26740	0.025
2	9.480	104974303	99.975



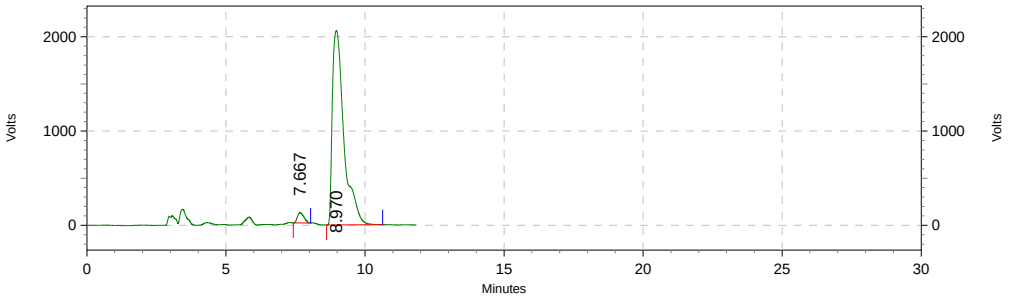
(R)-3-(3-chlorophenyl)isobenzofuran-1(3H)-one (**16i**)[15]

93% yield, 94% ee; after recrystallization: 99.9% ee; White solid. $[\alpha]_D^{20}$ = -46.31 (*c* = 1.20 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 7.9 min for enantiomer (S), t_R = 9.5 min for enantiomer (R).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.60 (td, *J* = 7.5, 1.2

Hz, 1H), 7.52-7.48 (m, 1H), 7.31 – 7.21 (m, 3H), 7.19 (d, J = 1.8 Hz, 1H), 7.12 (dt, J = 6.8, 1.9 Hz, 1H), 6.29 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 149.2, 138.6, 135.1, 134.7, 130.4, 129.8, 129.6, 127.1, 126.0, 125.5, 125.2, 122.9, 81.8.

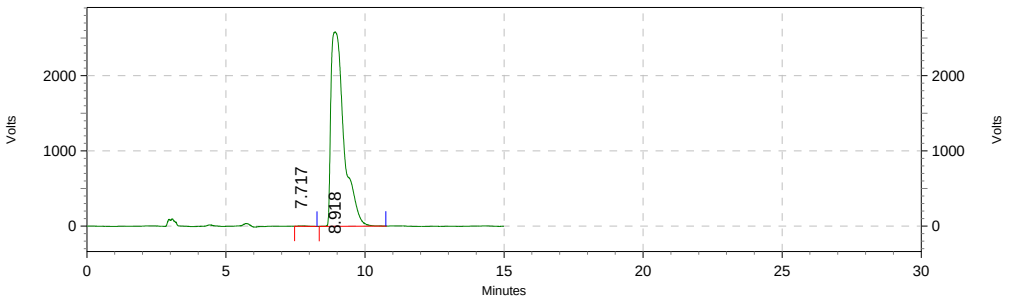


Peak	Ret. Time.	Area	Area%
1	7.775	52634918	48.596
2	9.360	60325962	51.404

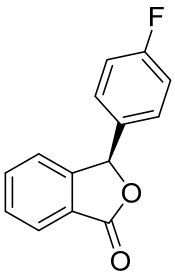


Peak	Ret. Time.	Area	Area%
1	7.667	1776023	2.894
2	8.970	59585285	97.106

After recrystallization

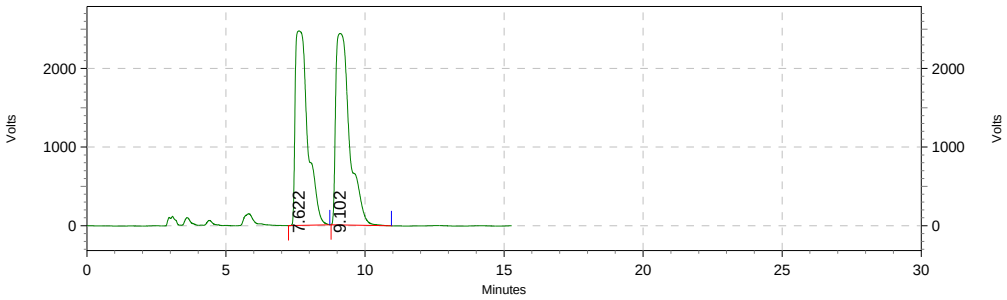


Peak	Ret. Time.	Area	Area%
1	7.717	90132	0.007
2	8.918	84246720	99.993

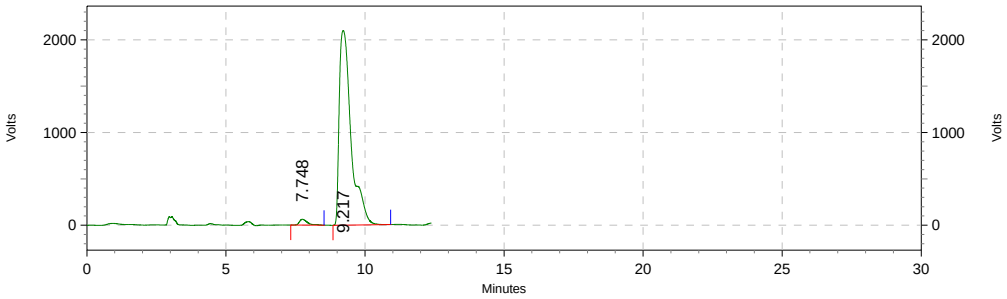


(R)-3-(4-fluorophenyl)isobenzofuran-1(3H)-one (**16j**)[15]

95% yield, 96% ee; after recrystallization: 99.5% ee; White solid. $[\alpha]_D^{20}$ = +23.28 (*c* = 1.00 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 7.6 min for enantiomer (S), t_R = 9.1 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.67 (td, *J* = 7.5, 1.2 Hz, 1H), 7.57 (tt, *J* = 7.5, 0.9 Hz, 1H), 7.32 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.07 (ddt, *J* = 8.6, 6.5, 2.5 Hz, 2H), 6.40 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 164.5, 162.1, 149.5, 134.6, 132.4, 132.4, 129.6, 129.2, 129.1, 125.8, 125.7, 123.0, 116.2, 116.0, 82.1.

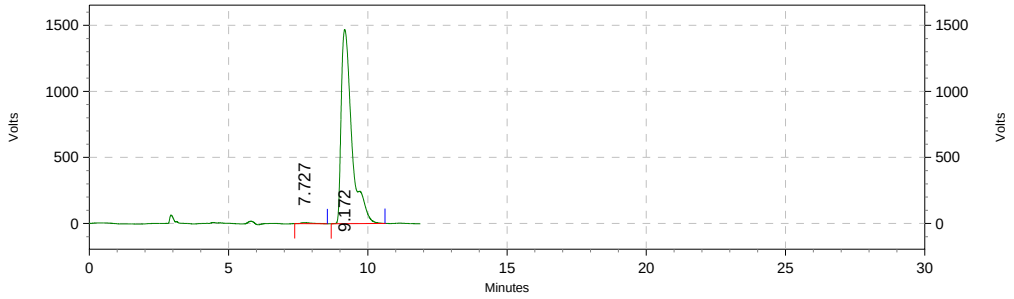


Peak	Ret. Time.	Area	Area%
1	7.622	77246767	48.789
2	9.102	84393644	51.211

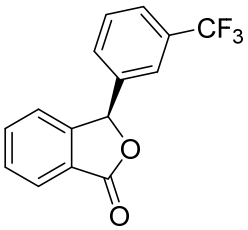


Peak	Ret. Time.	Area	Area%
1	7.748	1247790	1.969
2	9.217	62139491	98.031

After recrystallization

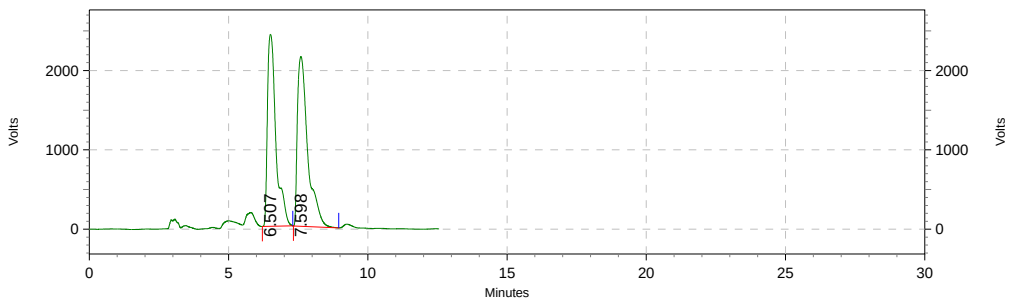


Peak	Ret. Time.	Area	Area%
1	7.727	214008	0.246
2	9.172	38963331	99.754

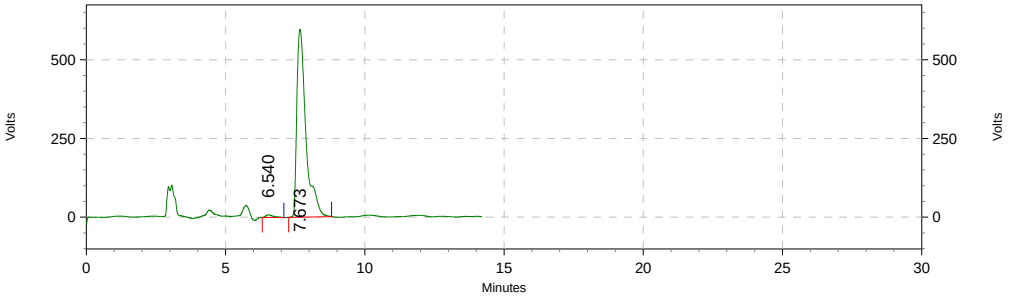


(R)-3-(3-(trifluoromethyl)phenyl)isobenzofuran-1(3H)-one (**16k**)[15]

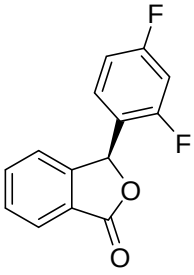
84% yield, 98% ee; White solid. $[\alpha]_D^{20}$ = - 53.21 (*c* = 1.10 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 6.5 min for enantiomer (S), t_R = 7.5 min for enantiomer (R).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.63 – 7.56 (m, 2H), 7.55 – 7.47 (m, 2H), 7.35 (dq, *J* = 7.7, 0.9 Hz, 1H), 6.46 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 149.0, 137.7, 134.8, 131.60 (q, $^2J_{C\text{-}F}$ = 32.7 Hz), 130.3, 129.9, 129.8, 126.3 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 126.1, 125.5, 123.84 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 123.82 (q, $^1J_{C\text{-}F}$ = 272.4 Hz), 122.9, 81.8.



Peak	Ret. Time.	Area	Area%
1	6.507	51209460	48.133
2	7.598	55182670	51.867

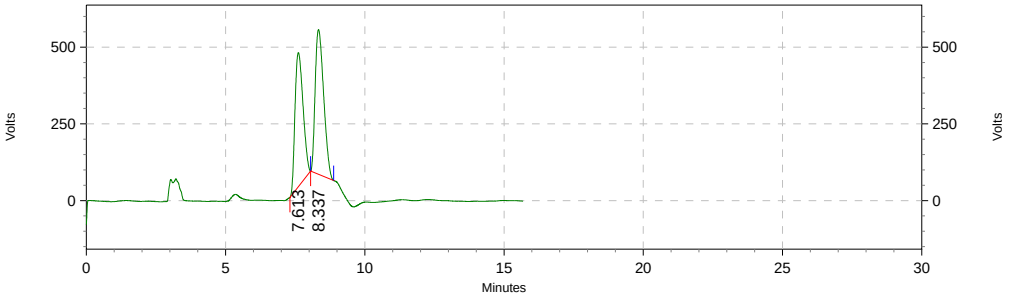


Peak	Ret. Time.	Area	Area%
1	6.540	163911	1.195
2	7.673	13553325	98.805

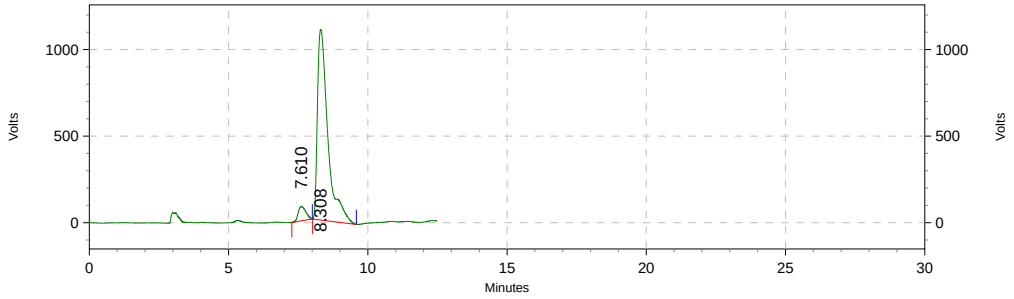


(S)-3-(2,4-difluorophenyl)isobenzofuran-1(3H)-one (**16l**)[13]

89% yield, 91% ee; after recrystallization: ee 99.5%; White solid. $[\alpha]_D^{20}$ = - 14.88 (*c* = 1.00 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 7.6 min for enantiomer (S), t_R = 8.3 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.68 (td, *J* = 7.5, 1.1 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.26 (s, 1H), 7.11 (td, *J* = 8.5, 6.1 Hz, 1H), 6.95 – 6.82 (m, 2H), 6.70 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 163.6 (dd, $^1J_{C-F}$ = 254.0 Hz, $^3J_{C-F}$ =12.5 Hz), 160.94 (dd, $^1J_{C-F}$ = 251.5 Hz, $^3J_{C-F}$ = 11.5 Hz), 149.0, 134.7, 129.8, 129.2 (dd, $^3J_{C-F}$ = 10.1 Hz, $^4J_{C-F}$ = 4.9 Hz), 126.0, 125.7, 122.9 (d, J_{C-F} = 1.9 Hz), 120.3 (d, $^3J_{C-F}$ = 12.7 Hz), 112.2 (dd, $^2J_{C-F}$ = 21.5 Hz, $^1J_{C-F}$ = 3.6 Hz), 104.7 (t, *J* = 25.4 Hz), 76.4 (d, $^4J_{C-F}$ = 3.9 Hz).

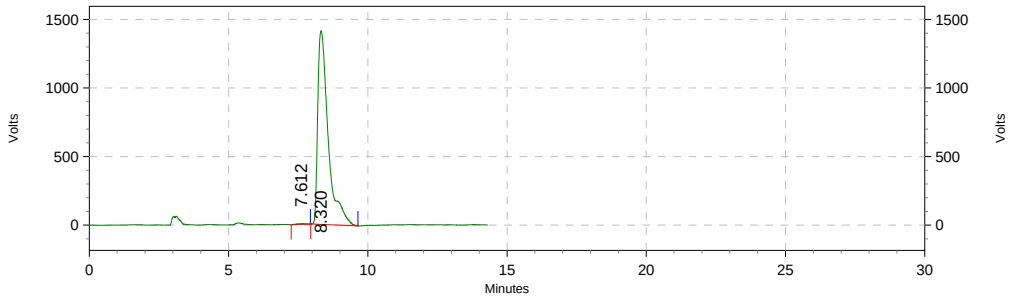


Peak	Ret. Time.	Area	Area%
1	7.613	8722581	46.575
2	8.337	10005485	53.425

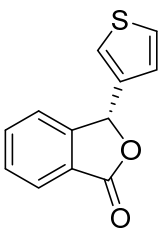


Peak	Ret. Time.	Area	Area%
1	7.610	1582081	4.273
2	8.308	28420515	95.727

After recrystallization



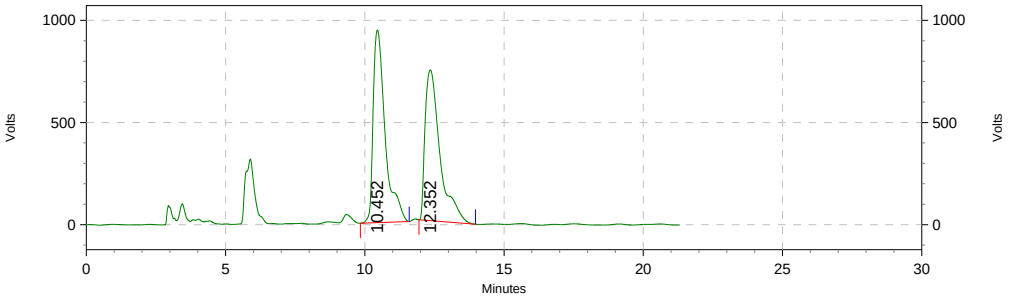
Peak	Ret. Time.	Area	Area%
1	7.612	99183	0.269
2	8.320	36770352	99.731



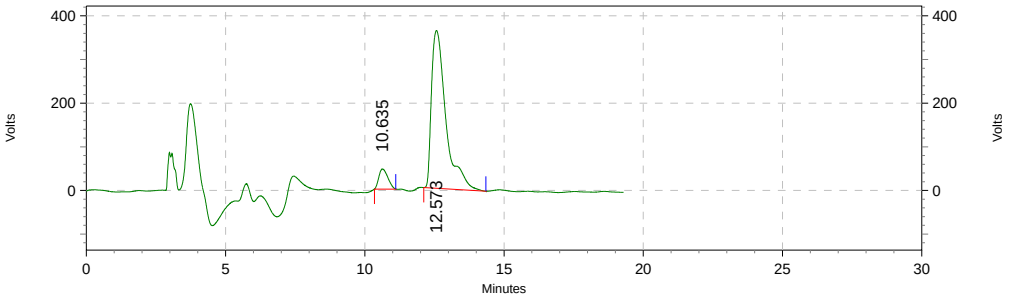
(R)-3-(thiophen-3-yl)isobenzofuran-1(3H)-one (**16m**)[15]

77% yield, 87% ee; White solid. $[\alpha]_D^{20}$ = +18.19 (*c* = 0.50 in DCM). HPLC (Chiralcel OD-H, 85% IPA in hexane, 1 mL/min, UV 215 nm): t_R = 10.4 min for enantiomer (S), t_R = 12.3 min for enantiomer (R). ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.89 (d, J = 7.6 Hz, 1H), 7.62 (td, J = 7.5, 1.1 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.31 – 7.22 (m, 2H), 6.88 (dd, J = 4.5, 1.9 Hz, 1H), 6.44 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 149.2, 137.4, 134.4, 129.6, 127.4, 126.1, 126.0, 125.9, 124.6, 123.0, 78.6.

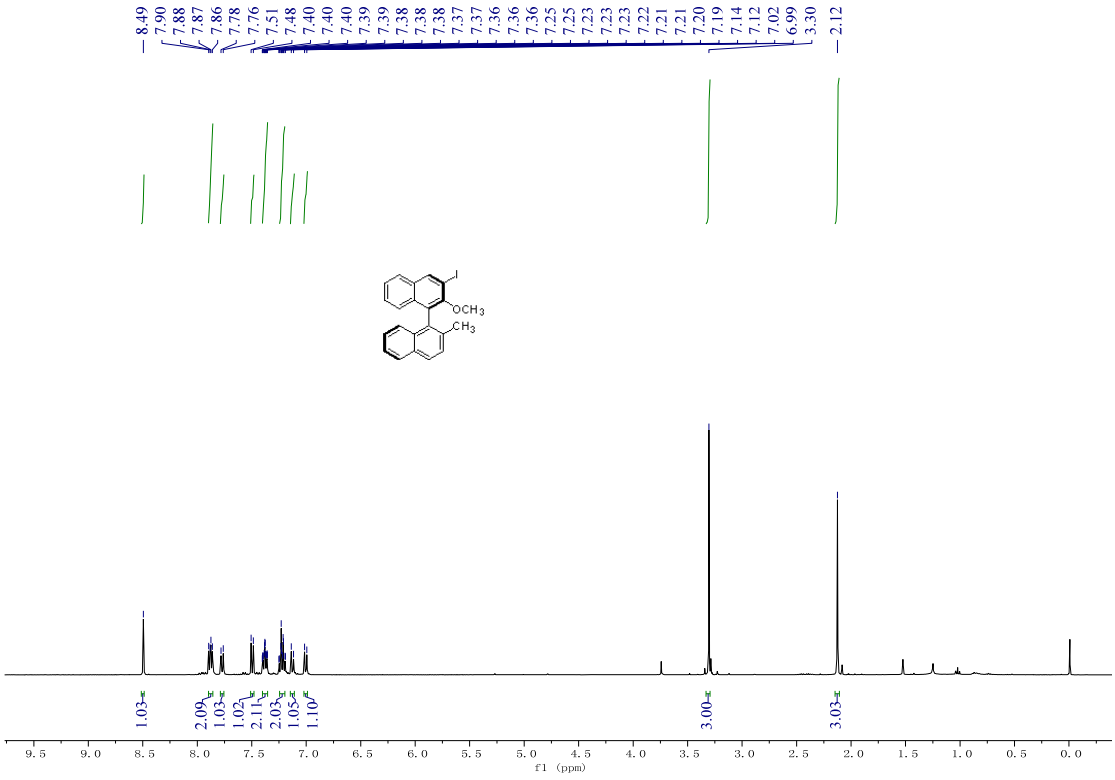


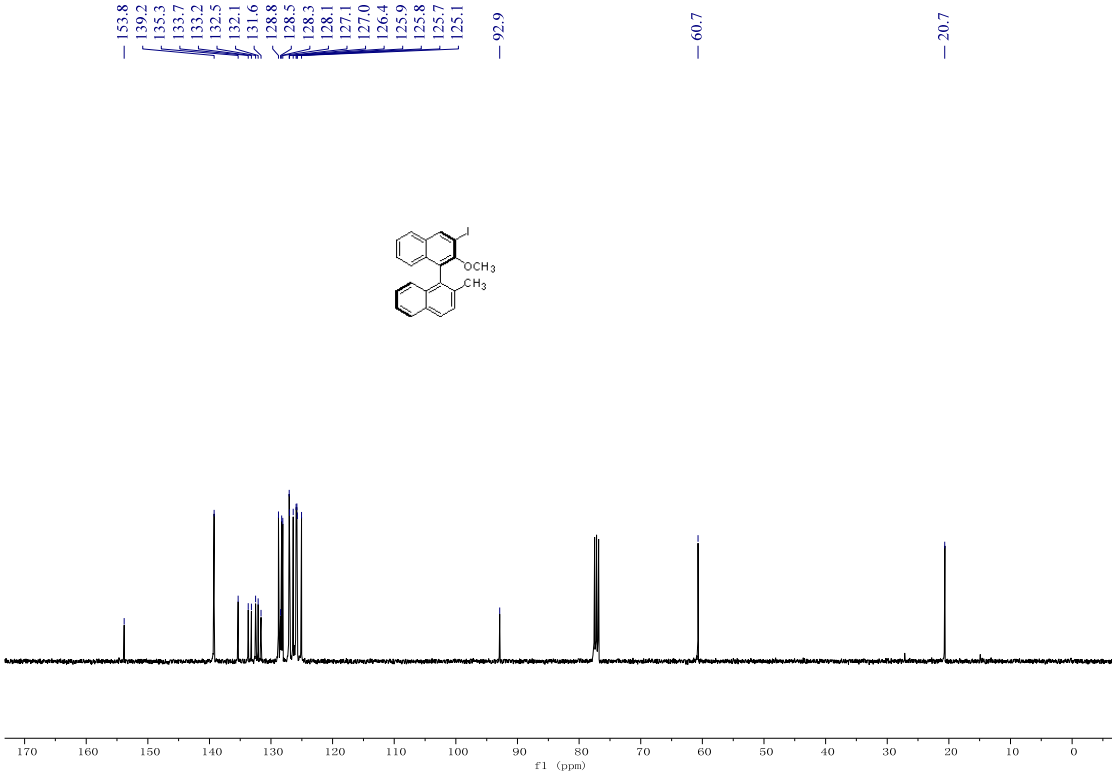
Peak	Ret. Time.	Area	Area%
1	10.452	28318483	50.786
2	12.352	27442384	49.214

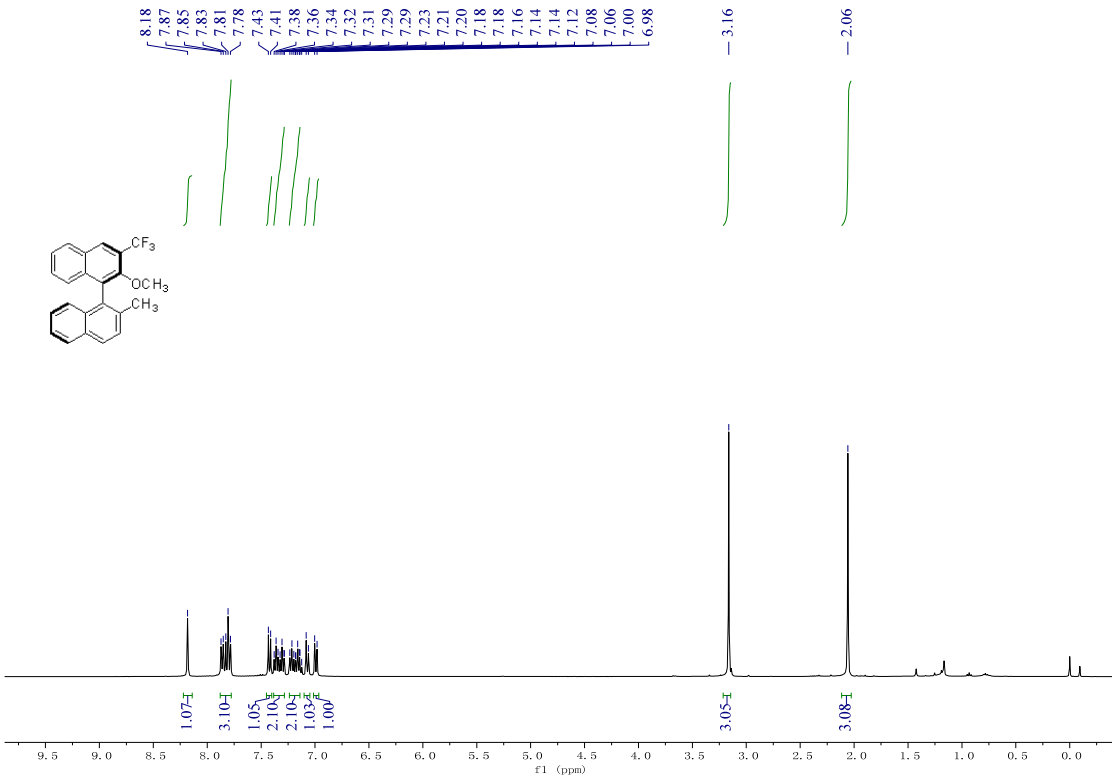


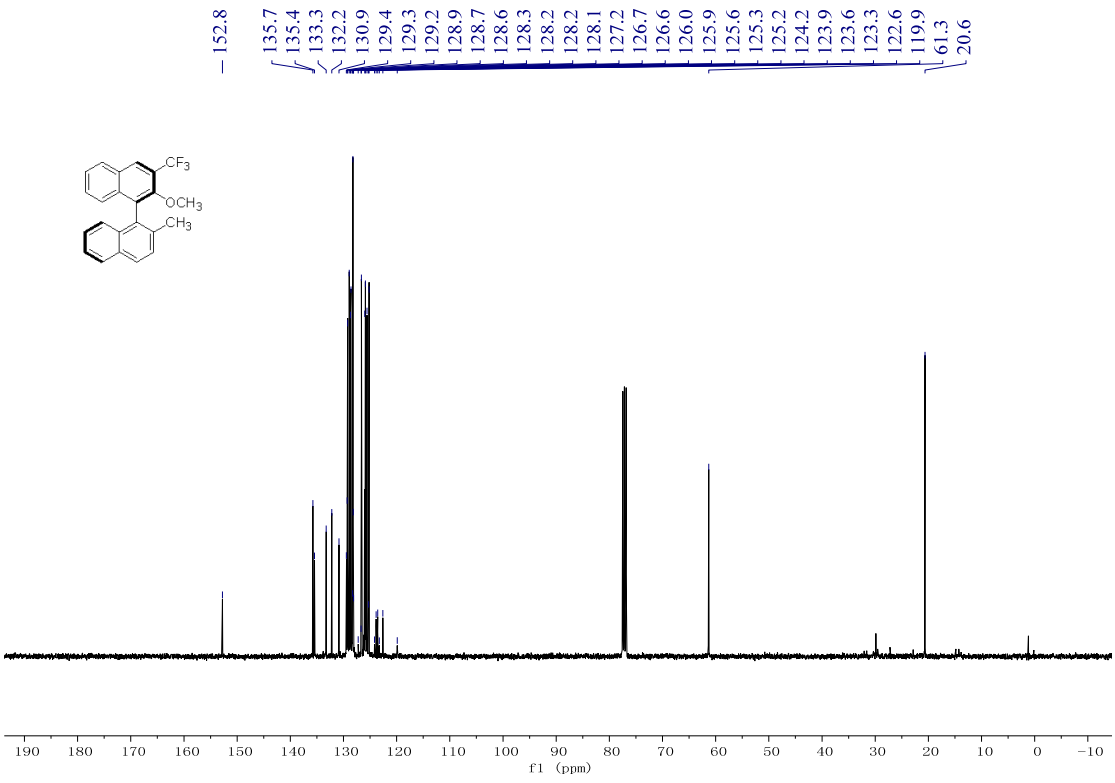
Peak	Ret. Time.	Area	Area%
1	10.635	1034863	6.386
2	12.573	12976737	93.614

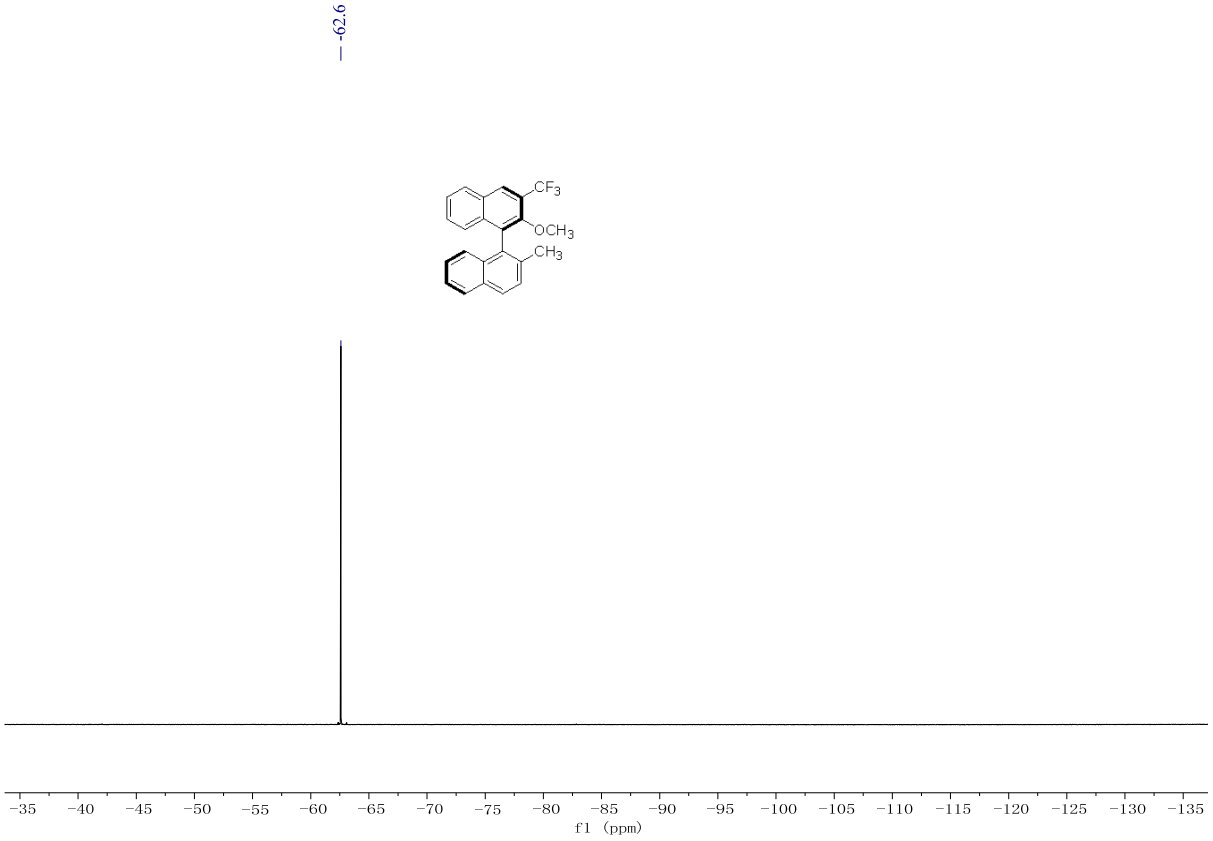
4. Copies of NMR Spectra of Chiral Ligands.

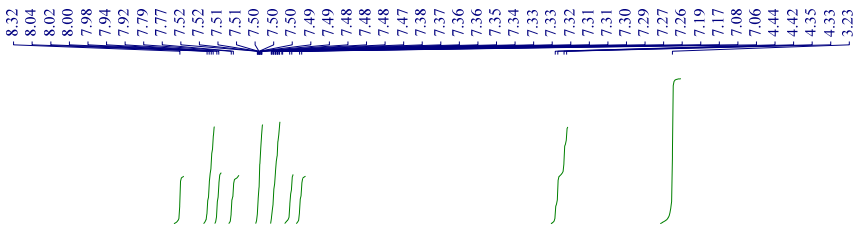


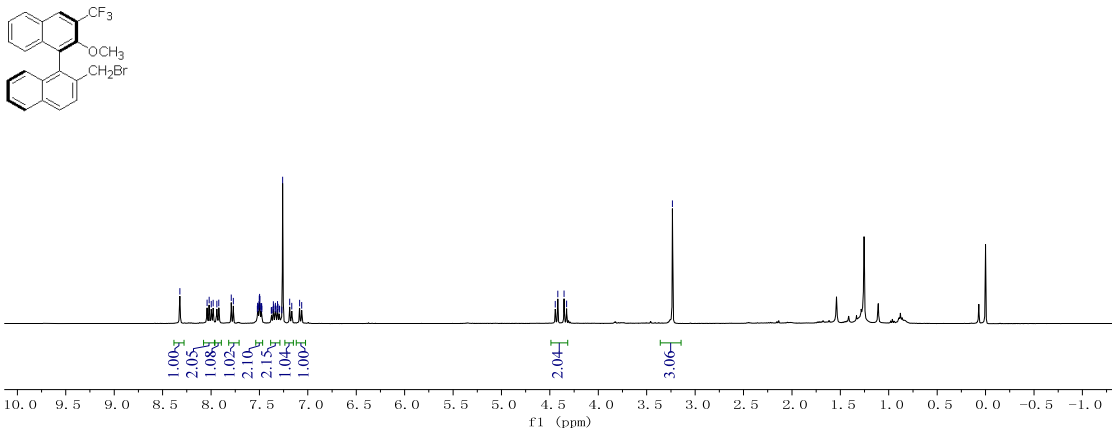


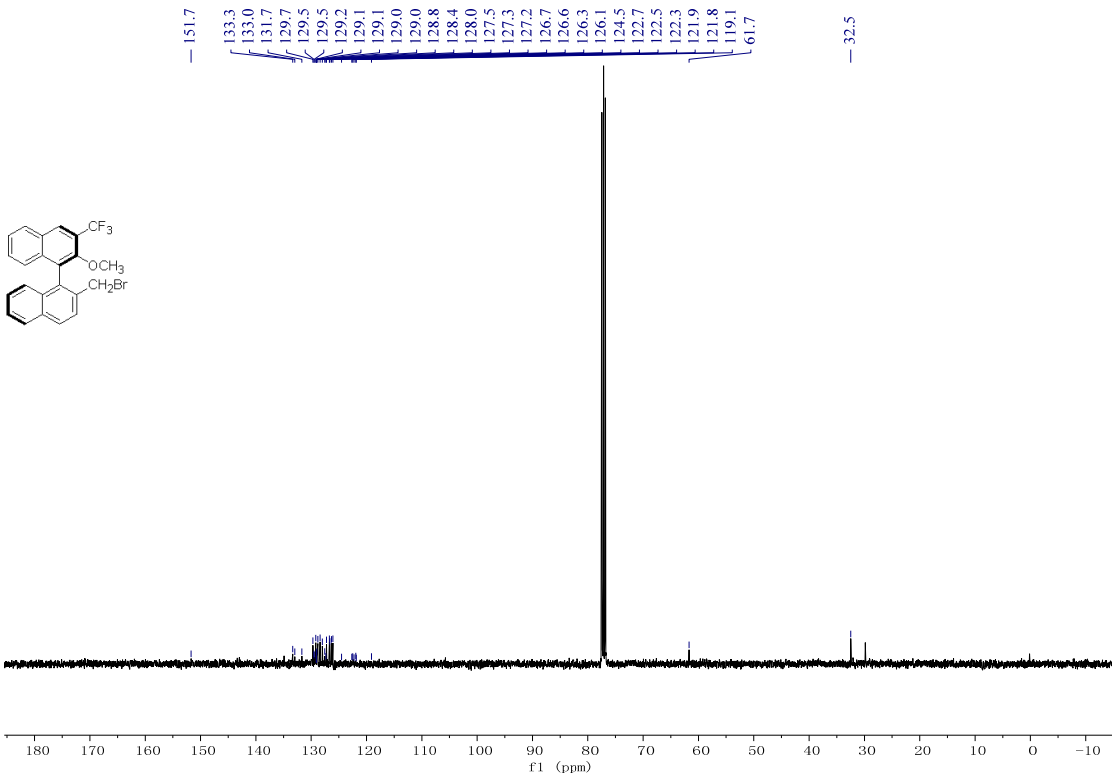

8.18
7.87
7.85
7.83
7.81
7.78
7.43
7.41
7.38
7.36
7.34
7.32
7.31
7.29
7.29
7.23
7.21
7.20
7.18
7.18
7.16
7.14
7.14
7.12
7.08
7.06
7.00
6.98
3.16
2.06
CF3
OCH3
CH3
1.07
3.10
1.05
2.10
2.10
1.03
1.00
3.05
3.08
f1 (ppm)


152.8
135.7
135.4
133.3
132.2
130.9
129.4
129.3
129.2
128.9
128.7
128.6
128.3
128.2
128.2
128.1
127.2
126.7
126.6
126.0
125.9
125.6
125.3
125.2
124.2
123.9
123.6
123.3
122.6
119.9
61.3
20.6
CF3
OCH3
CH3
f1 (ppm)


-62.6
CF3
OCH3
CH3
−35 −40 −45 −50 −55 −60 −65 −70 −75 −80 −85 −90 −95 −100 −105 −110 −115 −120 −125 −130 −135
f1 (ppm)


8.32 8.04 8.02 8.00 7.98 7.94 7.92 7.79 7.77 7.52 7.52 7.51 7.51 7.50 7.50 7.50 7.49 7.49 7.48 7.48 7.48 7.47 7.38 7.37 7.36 7.36 7.35 7.34 7.33 7.33 7.32 7.31 7.31 7.30 7.29 7.27 7.26 7.19 7.17 7.08 7.06 4.44 4.42 4.35 4.33 3.23


CF3
OCH3
CH2Br
1.00 2.05 1.08 1.02 2.10 2.15 1.04 1.00 2.04 3.06
10.0 9.5 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 −0.5 −1.0
f1 (ppm)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133.3
133.0
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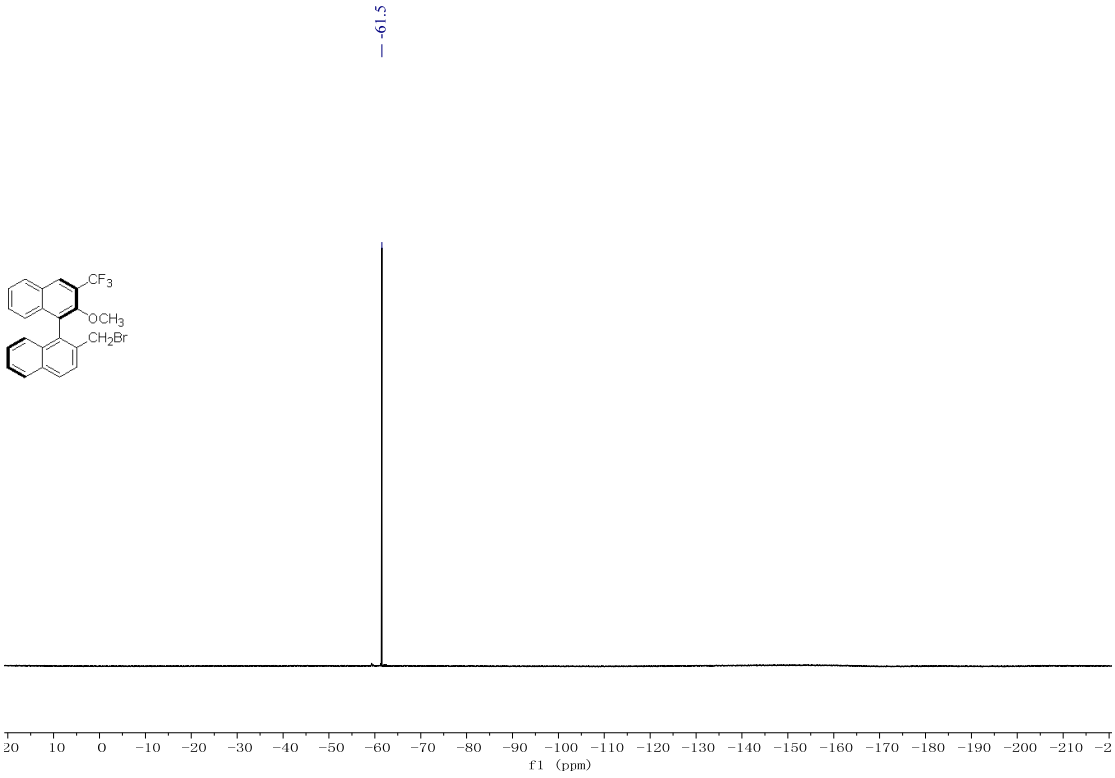
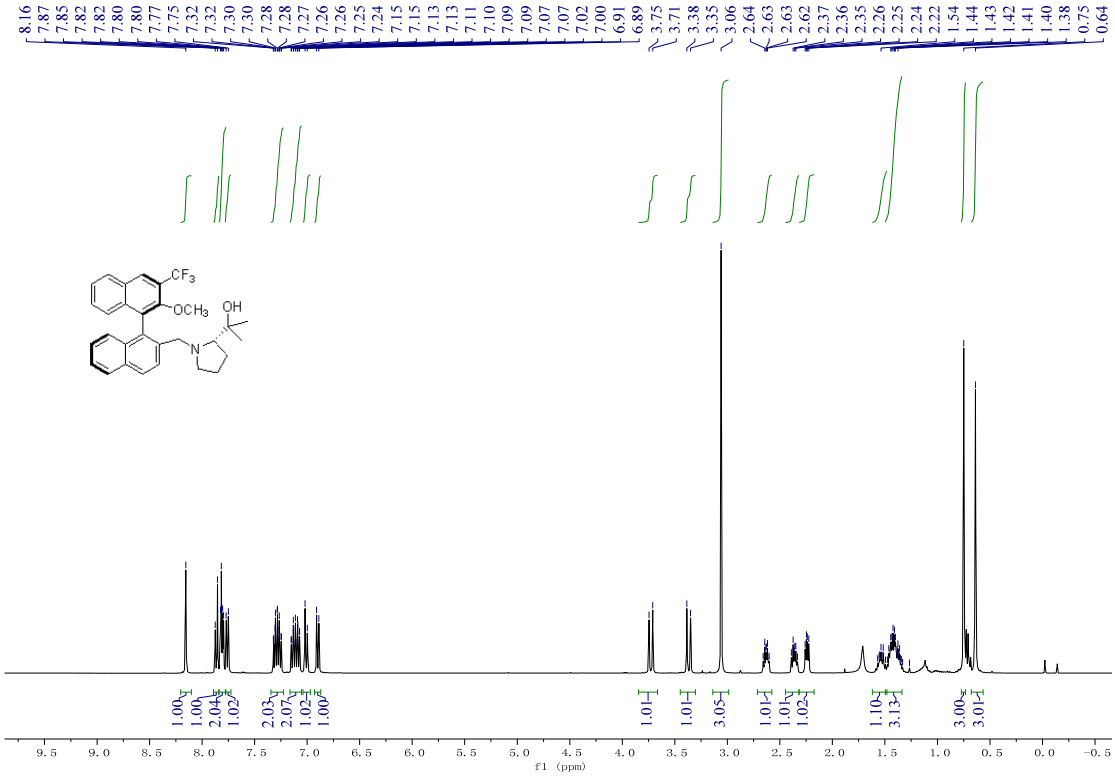
129.5
129.2
129.1
129.1
129.0
129.0
128.8
128.4
128.0
127.5
127.3
127.2
126.7
126.6
126.3
126.1
124.5
122.7
122.5
122.3
121.9
121.8
119.1
61.7
32.5
CF3
OCH3
CH2Br
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


-61.5
CF3
OCH3
CH2Br
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)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7.77
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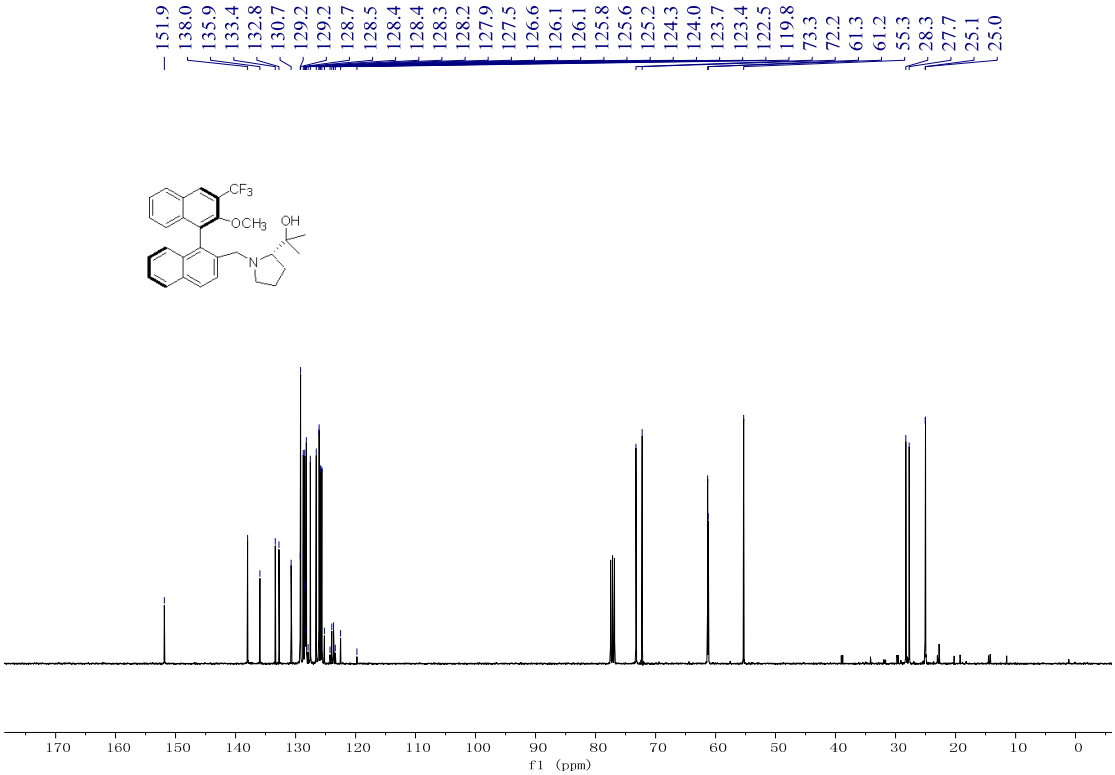
7.30
7.28
7.28
7.27
7.26
7.26
7.25
7.24
7.15
7.13
7.13
7.11
7.10
7.09
7.09
7.07
7.07
7.02
7.00
6.91
6.89
3.75
3.71
3.38
3.35
3.06
2.64
2.63
2.63
2.62
2.37
2.36
2.35
2.26
2.25
2.24
2.22
1.54
1.44
1.43
1.42
1.41
1.40
1.38
0.75
0.64
CF3
OCH3
OH
N
1.00
1.00
2.04
1.02
2.03
2.07
1.02
1.00
1.01
1.01
3.05
1.01
1.01
1.02
1.10
3.13
3.00
3.01
f1 (ppm)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129.2
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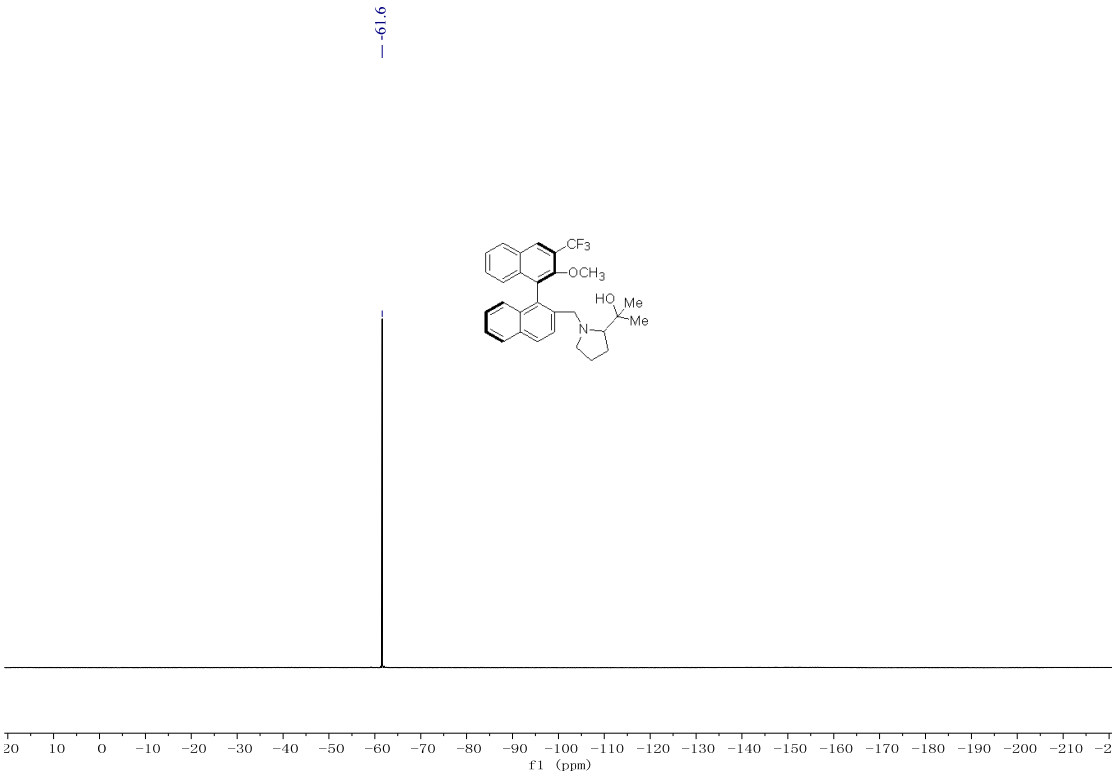
128.4
128.4
128.3
128.2
127.9
127.5
126.6
126.1
126.1
125.8
125.6
125.2
124.3
124.0
123.7
123.4
122.5
119.8
73.3
72.2
61.3
61.2
55.3
28.3
27.7
25.1
25.0
CF3
OCH3
OH
N
f1 (ppm)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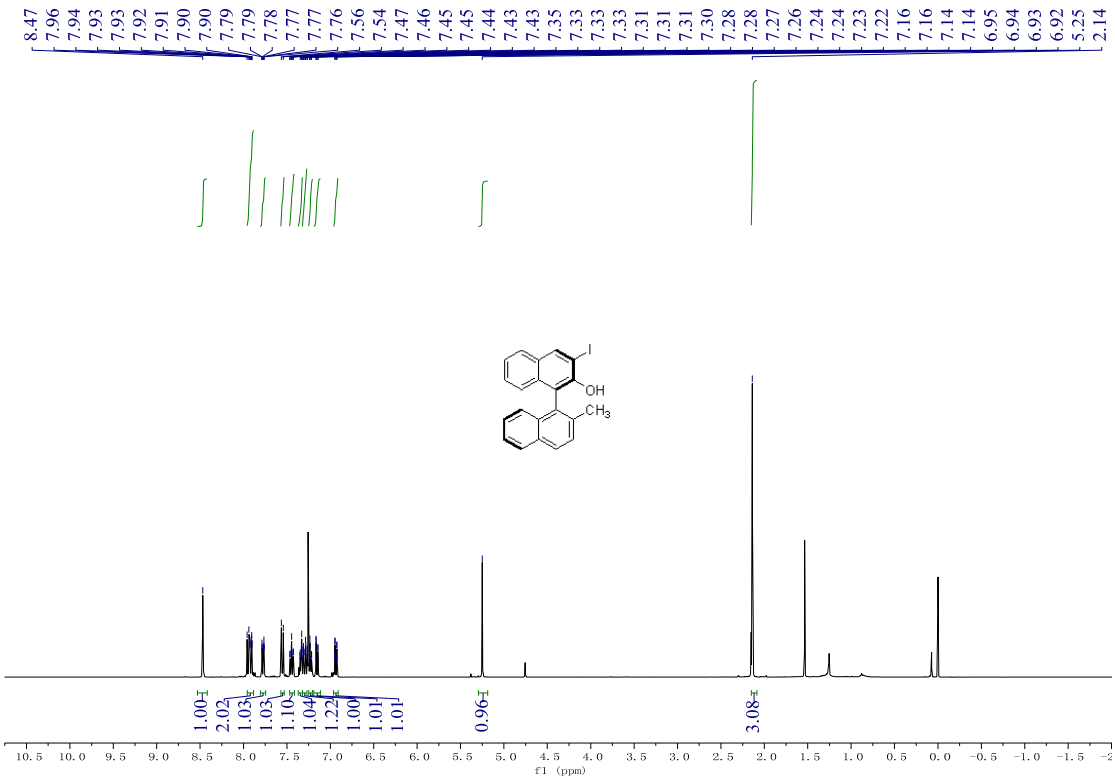
CF3
OCH3
HO
Me
Me
N
f1 (ppm)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7.94
7.93
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7.92
7.91
7.90
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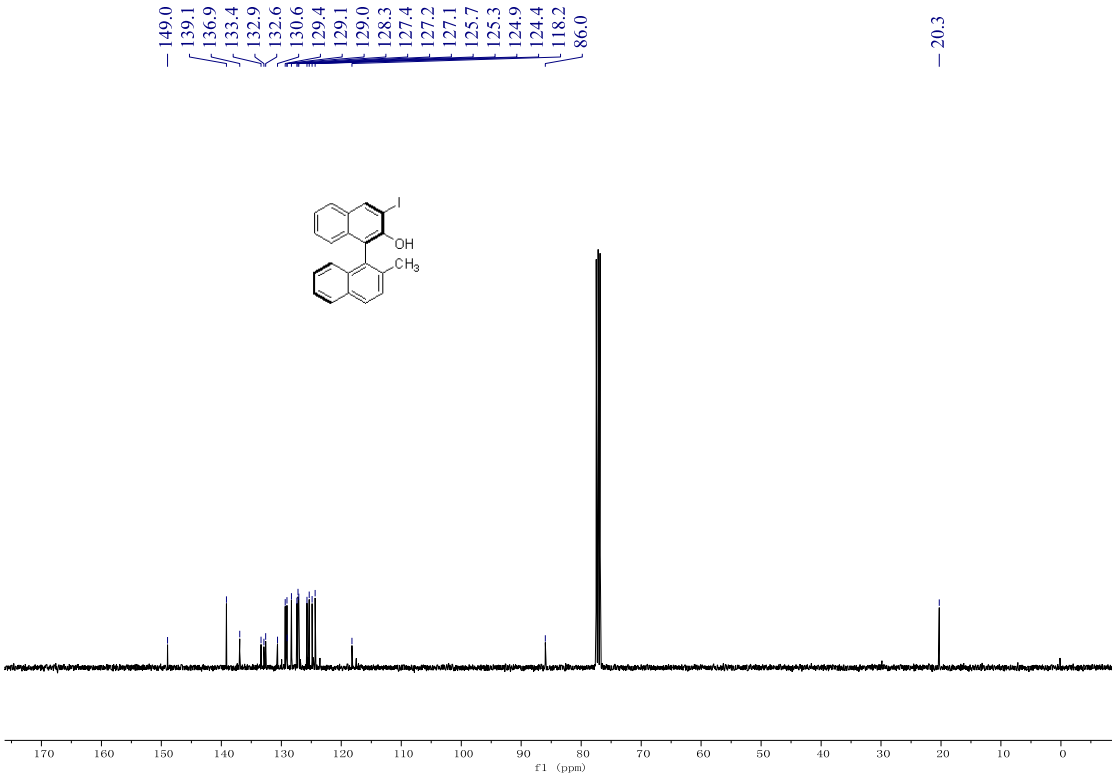
7.79
7.79
7.78
7.77
7.77
7.76
7.56
7.54
7.47
7.46
7.45
7.45
7.44
7.43
7.43
7.35
7.33
7.33
7.33
7.31
7.31
7.31
7.30
7.28
7.28
7.27
7.26
7.24
7.24
7.23
7.22
7.16
7.16
7.14
7.14
6.95
6.94
6.93
6.92
5.25
2.14
I
OH
CH3
1.00
2.02
1.03
1.03
1.10
1.04
1.22
1.00
1.01
1.01
0.96
3.08
f1 (ppm)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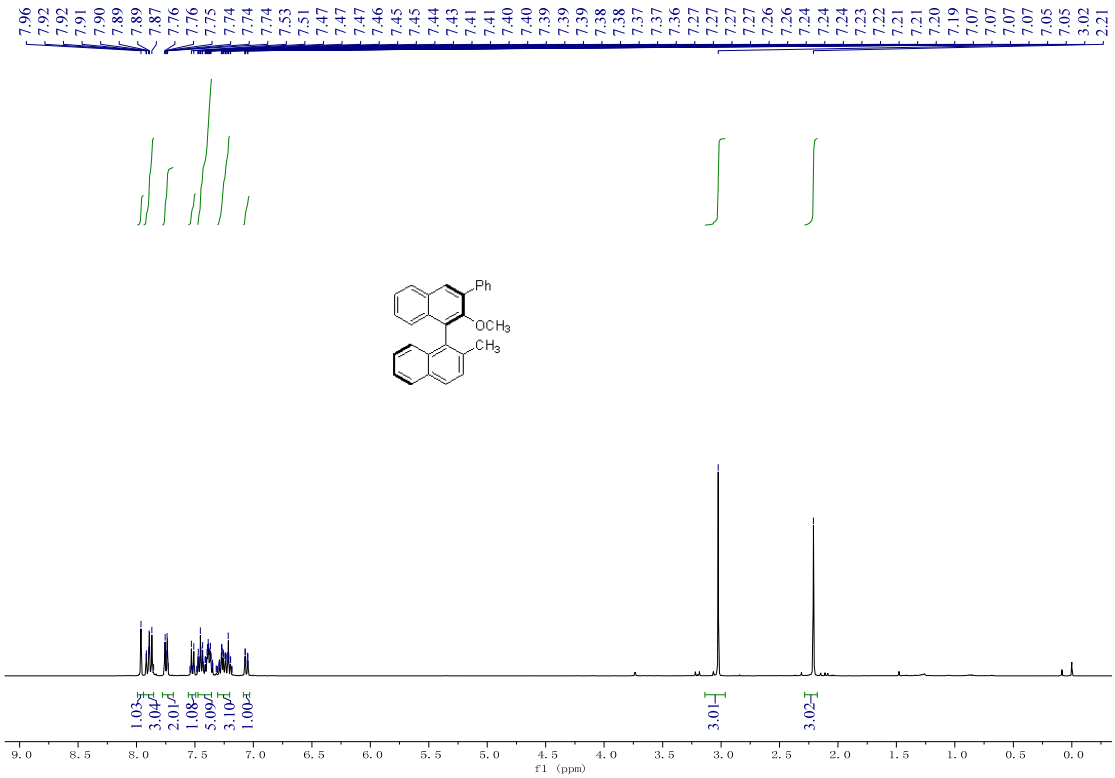
139.1
136.9
133.4
132.9
132.6
130.6
129.4
129.1
129.0
128.3
127.4
127.2
127.1
125.7
125.3
124.9
124.4
118.2
86.0
20.3
I
OH
CH3
f1 (ppm)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7.75
7.74
7.74
7.74
7.53
7.51
7.47
7.47
7.47
7.46
7.45
7.45
7.44
7.43
7.41
7.41
7.40
7.40
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7.37
7.37
7.36
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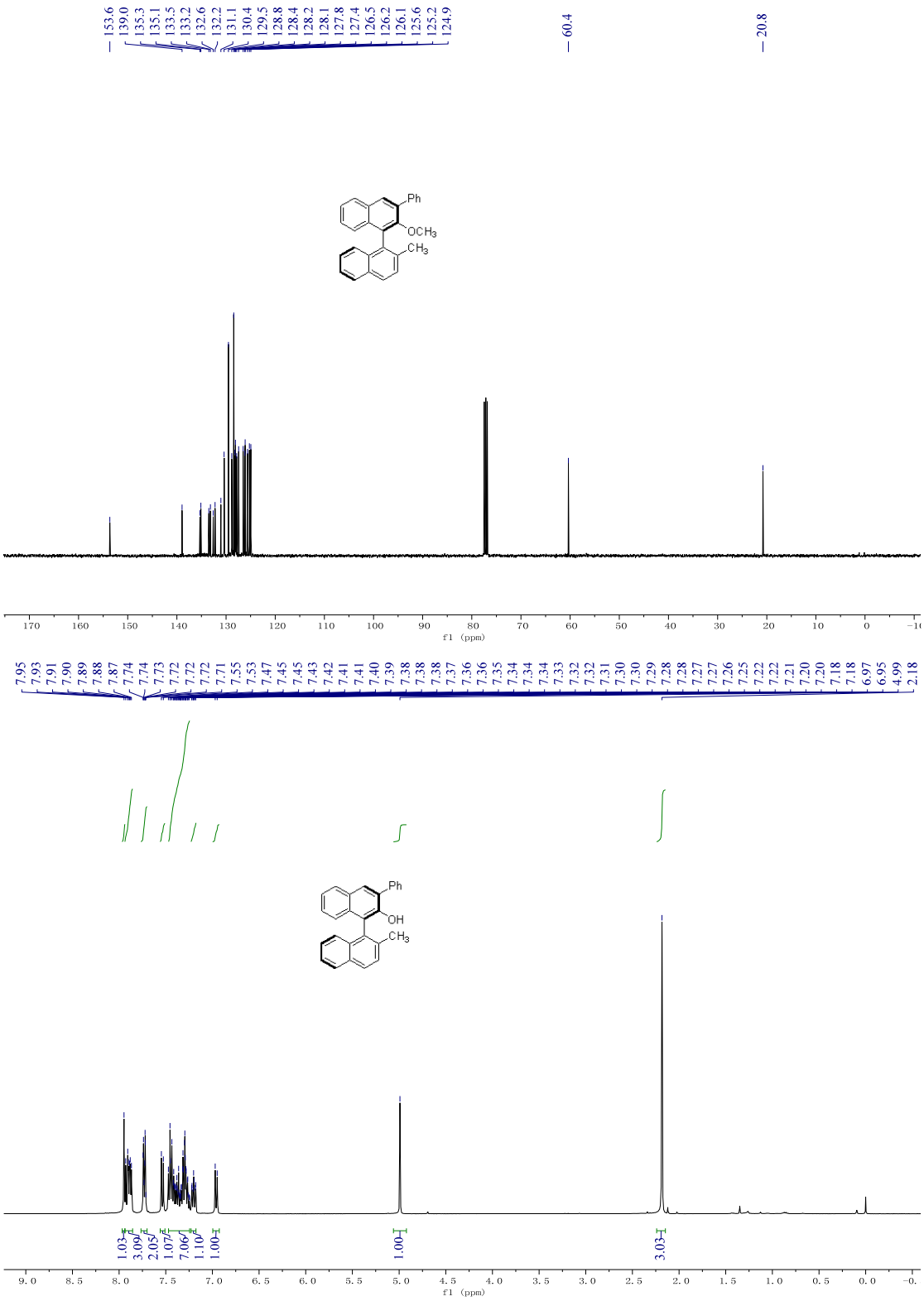
7.27
7.27
7.27
7.26
7.26
7.24
7.24
7.24
7.23
7.22
7.21
7.21
7.20
7.19
7.07
7.07
7.07
7.07
7.05
7.05
3.02
2.21
Ph
OCH3
CH3
1.03
3.04
2.01
1.08
5.09
3.10
1.00
3.01
3.02
f1 (ppm)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133.2
132.6
132.2
131.1
130.4
129.5
128.8
128.4
128.2
128.1
127.8
127.4
126.5
126.2
126.1
125.6
125.2
124.9
60.4
20.8
Ph
OCH3
CH3
f1 (ppm)
7.95
7.93
7.91
7.90
7.89
7.88
7.87
7.74
7.74
7.73
7.72
7.72
7.72
7.71
7.55
7.53
7.47
7.45
7.45
7.43
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.38
7.37
7.36
7.36
7.35
7.34
7.34
7.34
7.33
7.32
7.32
7.31
7.30
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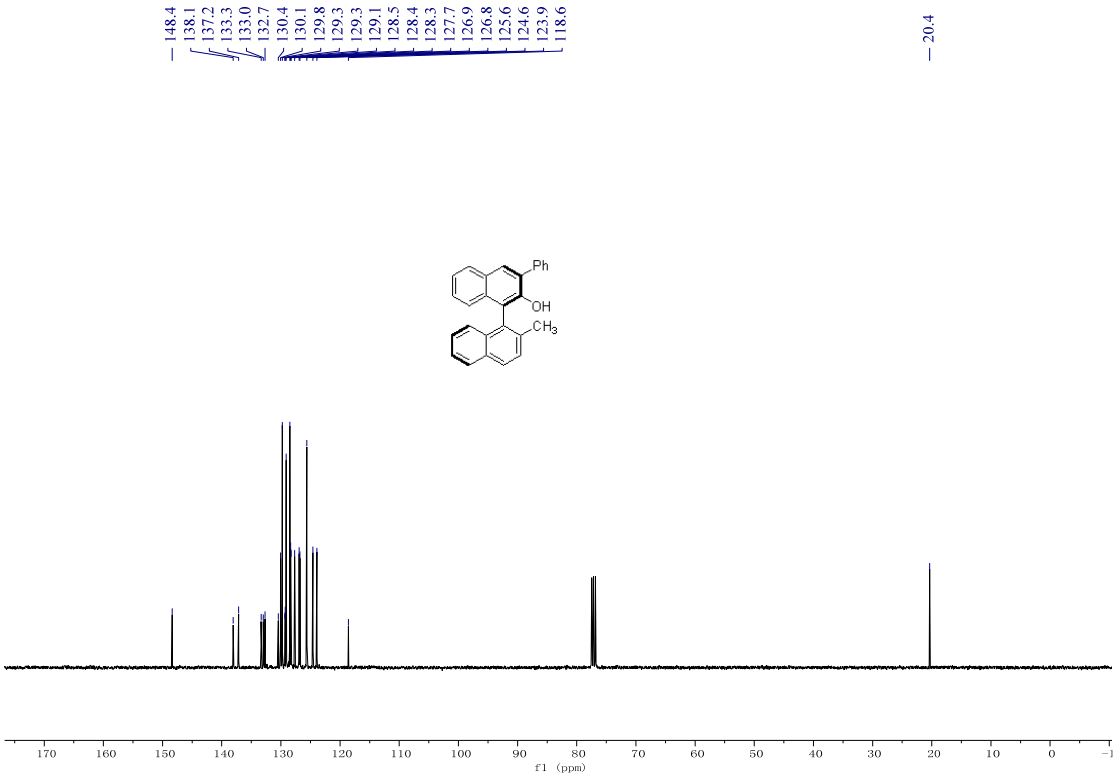
7.27
7.27
7.26
7.25
7.22
7.22
7.21
7.20
7.20
7.18
7.18
6.97
6.95
4.99
2.18
Ph
OH
CH3
1.03
3.09
2.05
1.07
7.06
1.10
1.00
1.00
3.03
f1 (ppm)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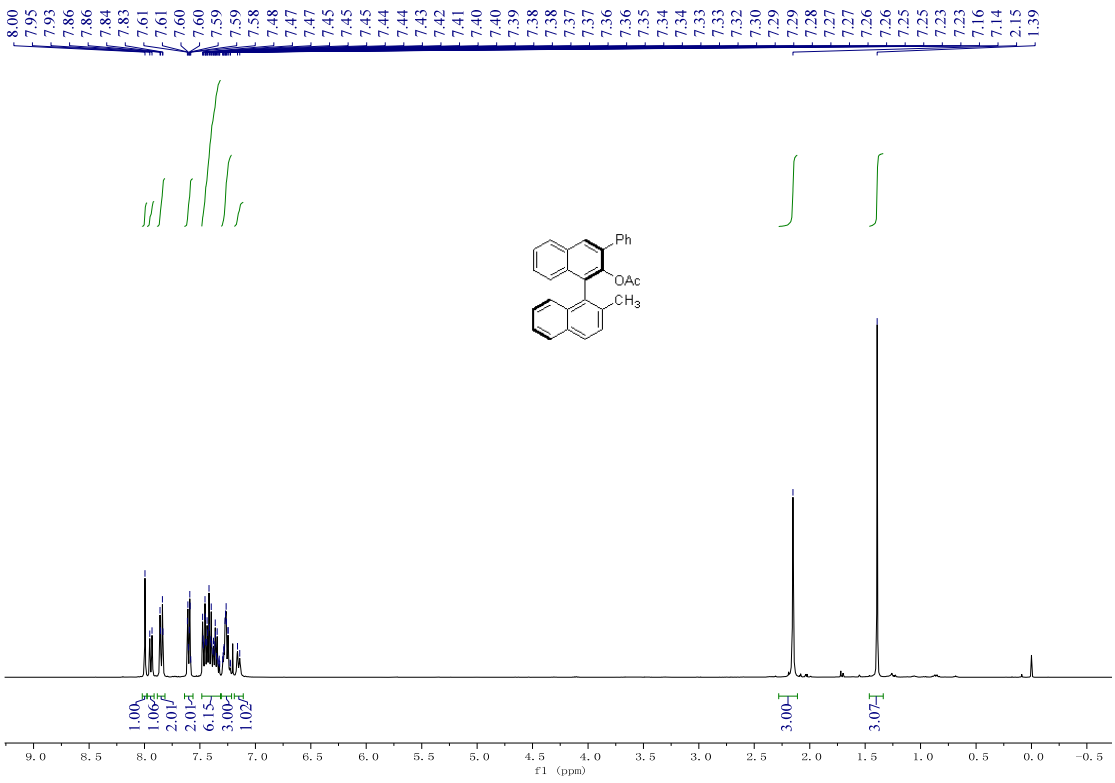
137.2
133.3
133.0
132.7
130.4
130.1
129.8
129.3
129.3
129.1
128.5
128.4
128.3
127.7
126.9
126.8
125.6
124.6
123.9
118.6
20.4
Ph
OH
CH3
f1 (ppm)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7.60
7.59
7.59
7.58
7.48
7.47
7.47
7.45
7.45
7.45
7.44
7.44
7.43
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.37
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7.36
7.35
7.34
7.34
7.33
7.33
7.32
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7.29
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7.27
7.26
7.26
7.25
7.25
7.23
7.23
7.16
7.14
2.15
1.39
Ph
OAc
CH3
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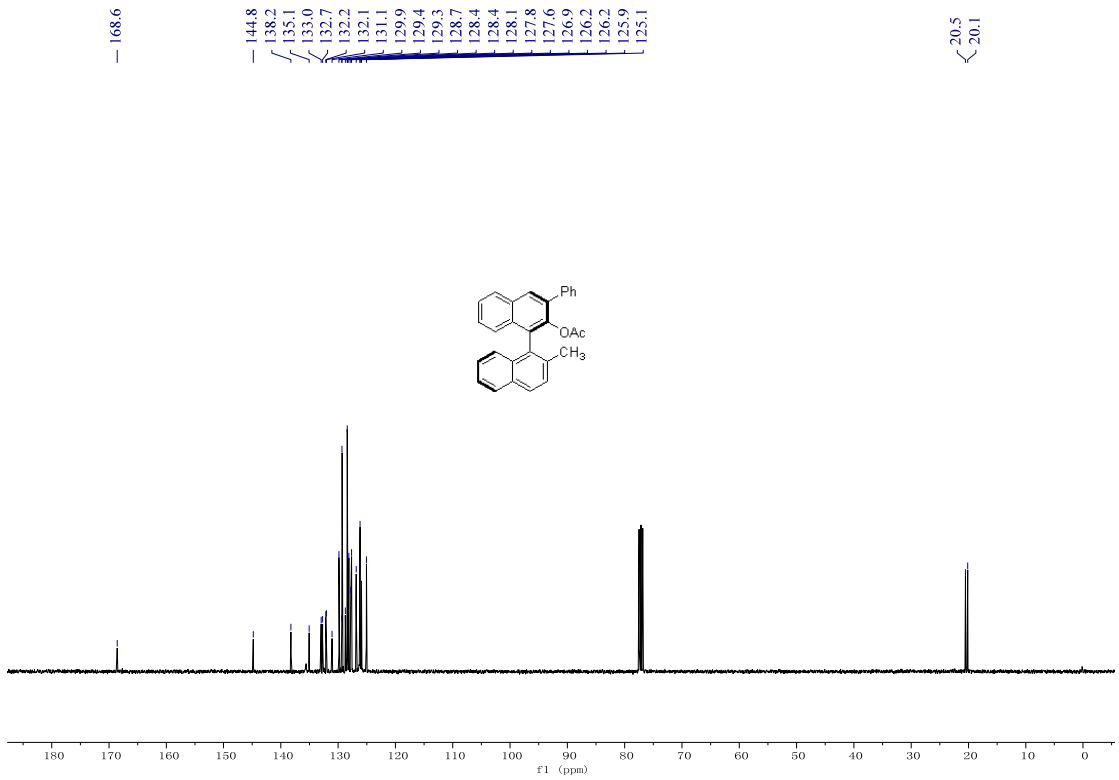
1.06
2.01
2.01
6.15
3.00
1.02
3.00
3.07
f1 (ppm)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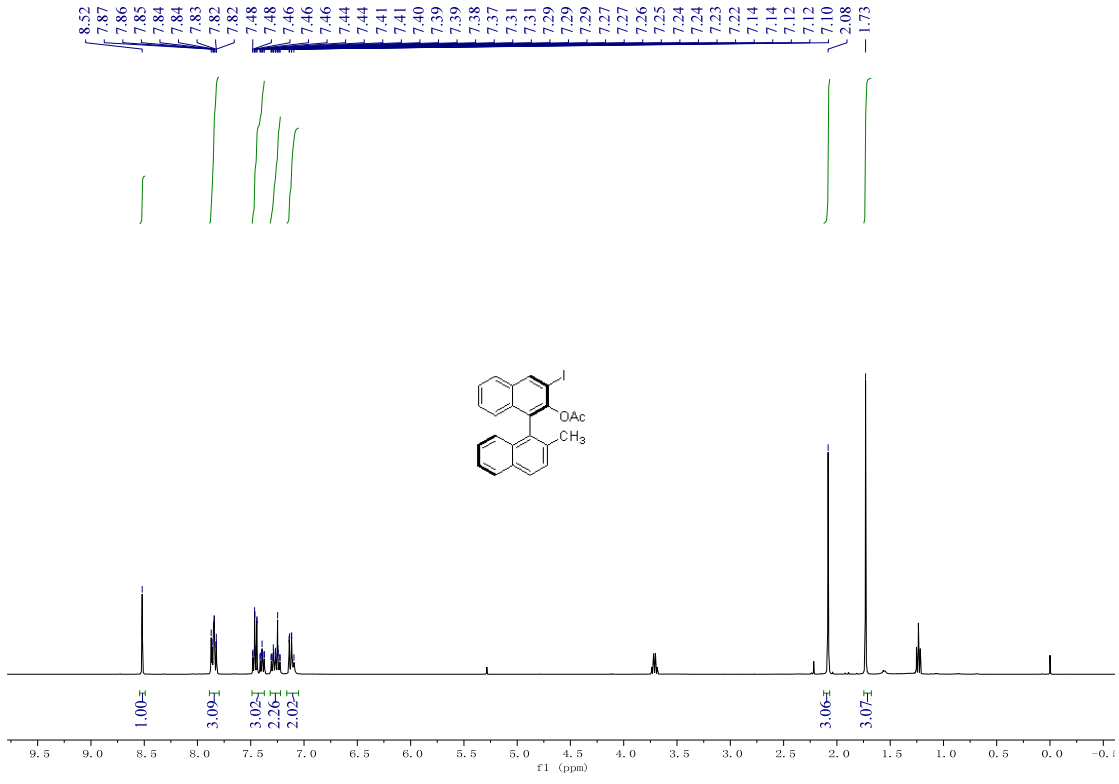
138.2
135.1
133.0
132.7
132.2
132.1
131.1
129.9
129.4
129.3
128.7
128.4
128.4
128.1
127.8
127.6
126.9
126.2
126.2
125.9
125.1
20.5
20.1
Ph
OAc
CH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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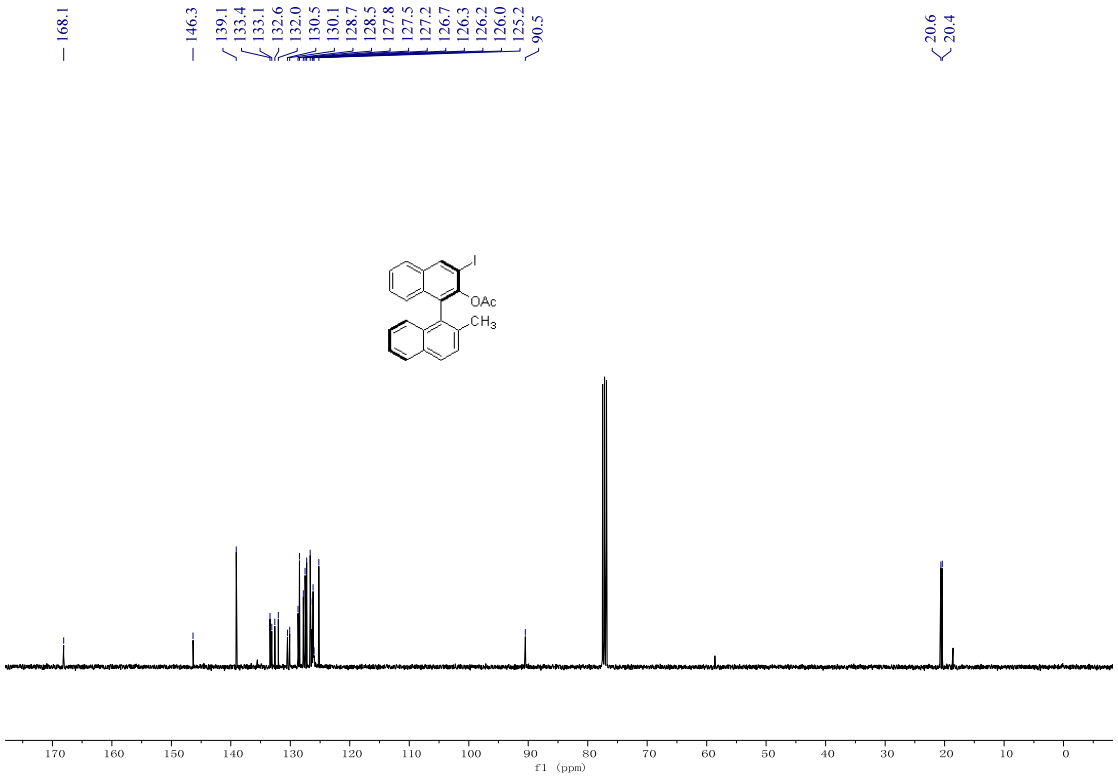
7.46
7.46
7.44
7.44
7.41
7.41
7.40
7.39
7.39
7.38
7.37
7.31
7.31
7.29
7.29
7.29
7.27
7.27
7.26
7.25
7.24
7.24
7.23
7.22
7.14
7.14
7.12
7.12
7.10
2.08
1.73
I
OAc
CH3
1.00
3.09
3.02
2.26
2.02
3.06
3.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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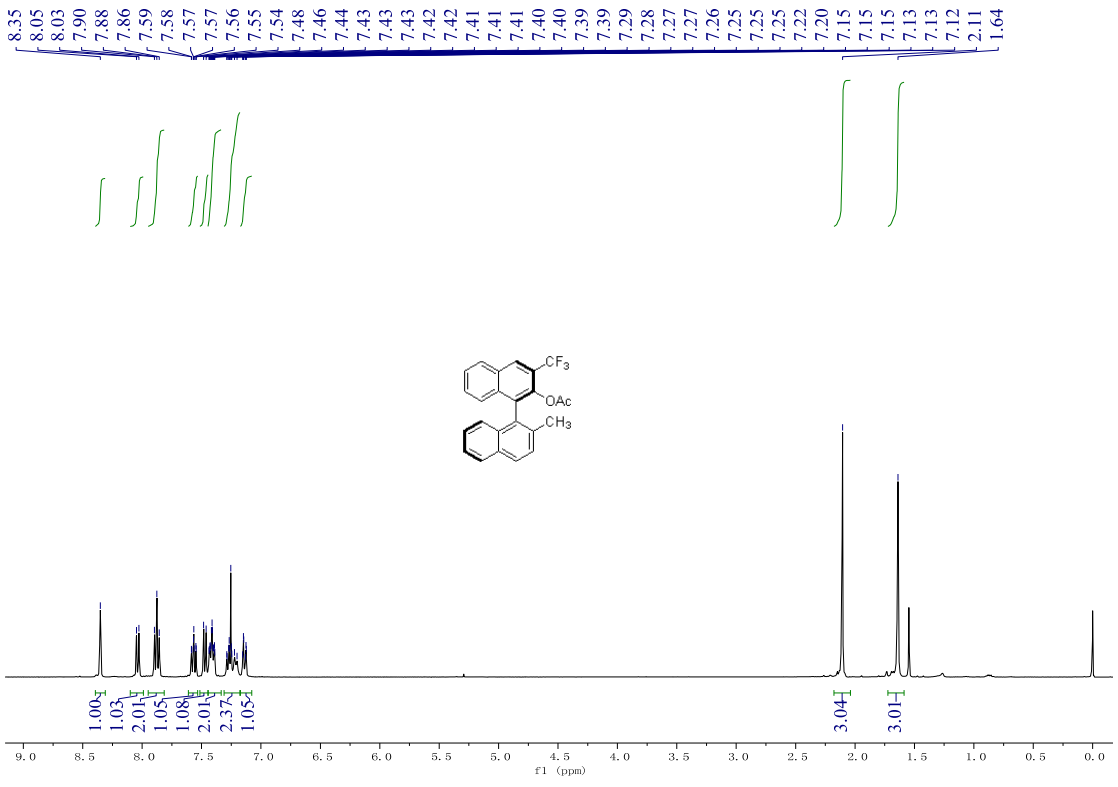
139.1
133.4
133.1
132.6
132.0
130.5
130.1
128.7
128.5
127.8
127.5
127.2
126.7
126.3
126.2
126.0
125.2
90.5
20.6
20.4
I
OAc
CH3
f1 (ppm)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8.03
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7.88
7.86
7.59
7.58
7.57
7.57
7.56
7.55
7.54
7.48
7.46
7.44
7.43
7.43
7.43
7.42
7.42
7.41
7.41
7.41
7.40
7.40
7.39
7.39
7.29
7.28
7.27
7.27
7.26
7.25
7.25
7.25
7.22
7.20
7.15
7.15
7.15
7.13
7.12
2.11
1.64
CF3
OAc
CH3
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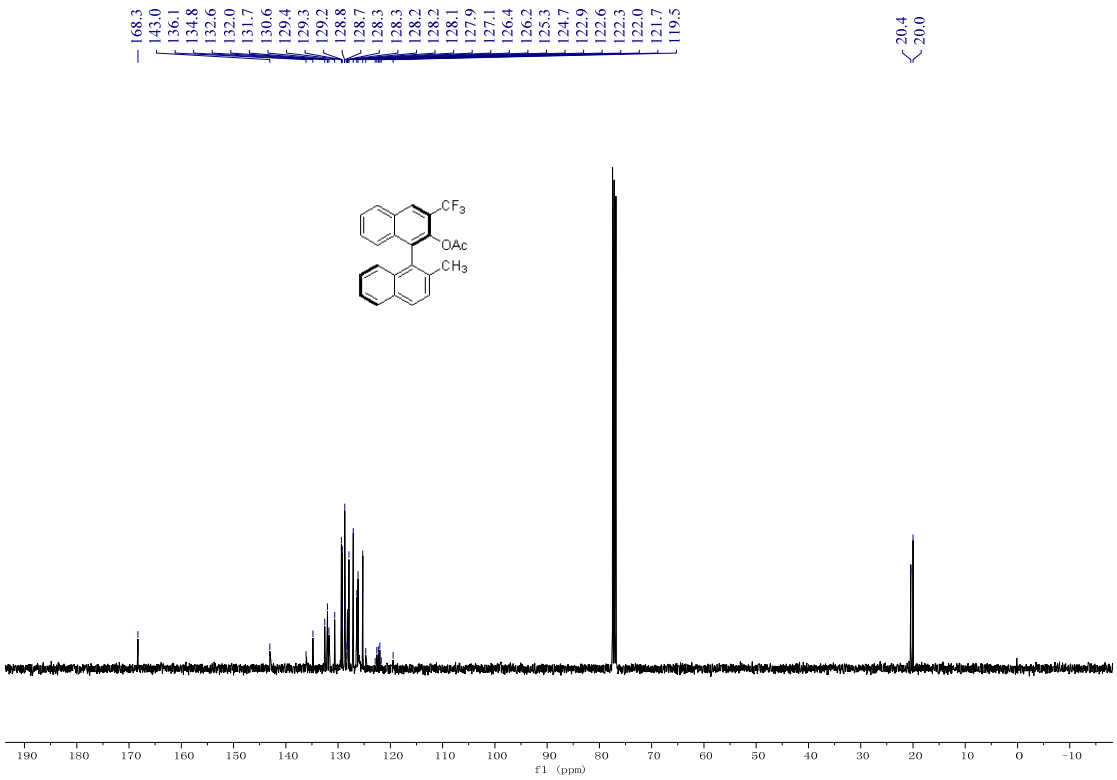
2.01
1.05
1.08
2.01
2.37
1.05
3.04
3.01
f1 (ppm)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132.0
131.7
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129.4
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129.2
128.8
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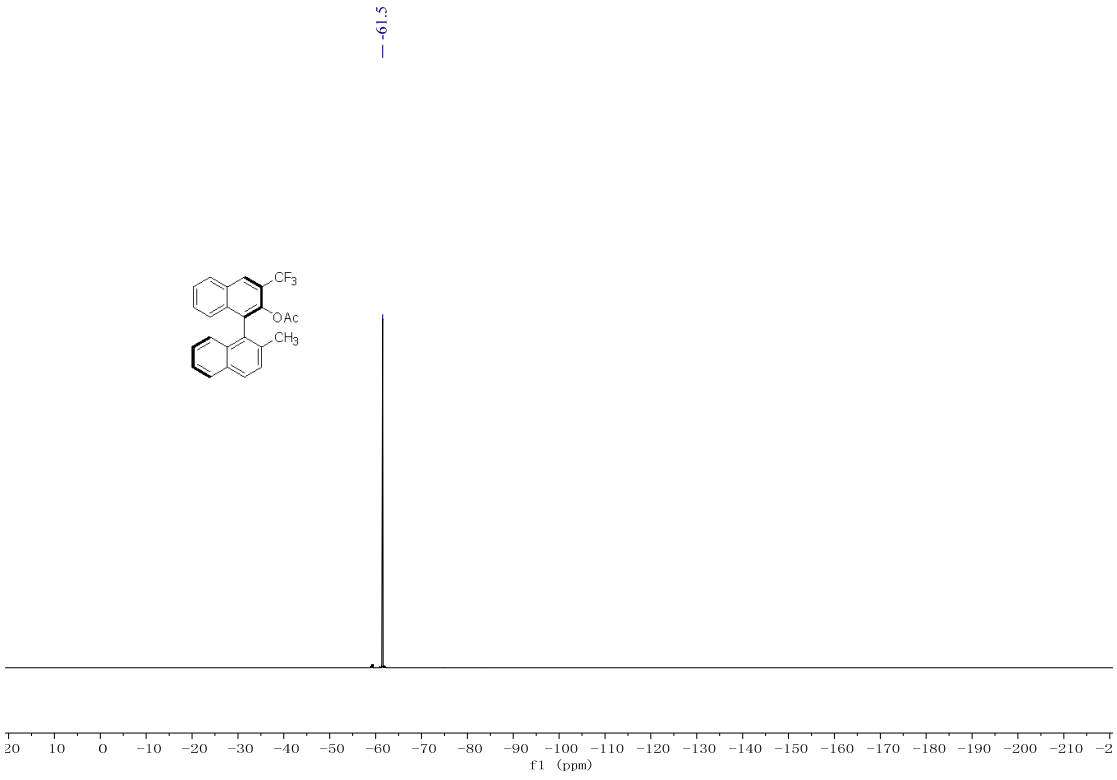
128.3
128.3
128.2
128.2
128.1
127.9
127.1
126.4
126.2
125.3
124.7
122.9
122.6
122.3
122.0
121.7
119.5
20.4
20.0
CF3
OAc
CH3
f1 (ppm)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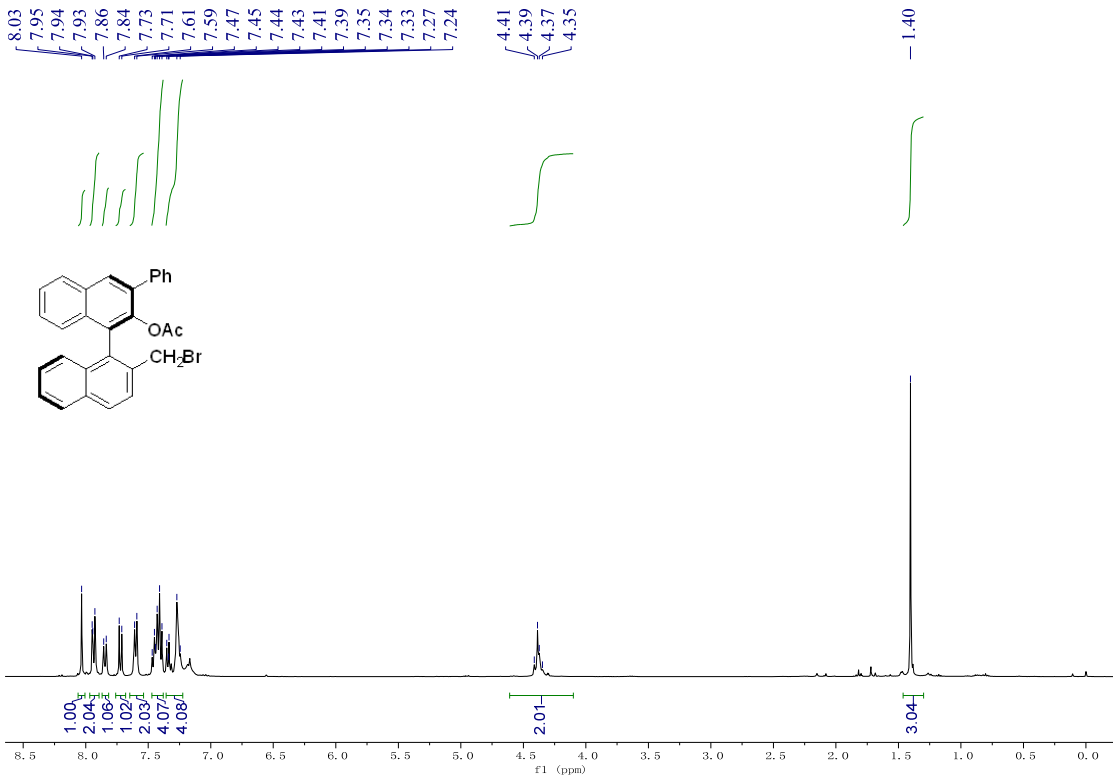
CF3
OAc
CH3
f1 (ppm)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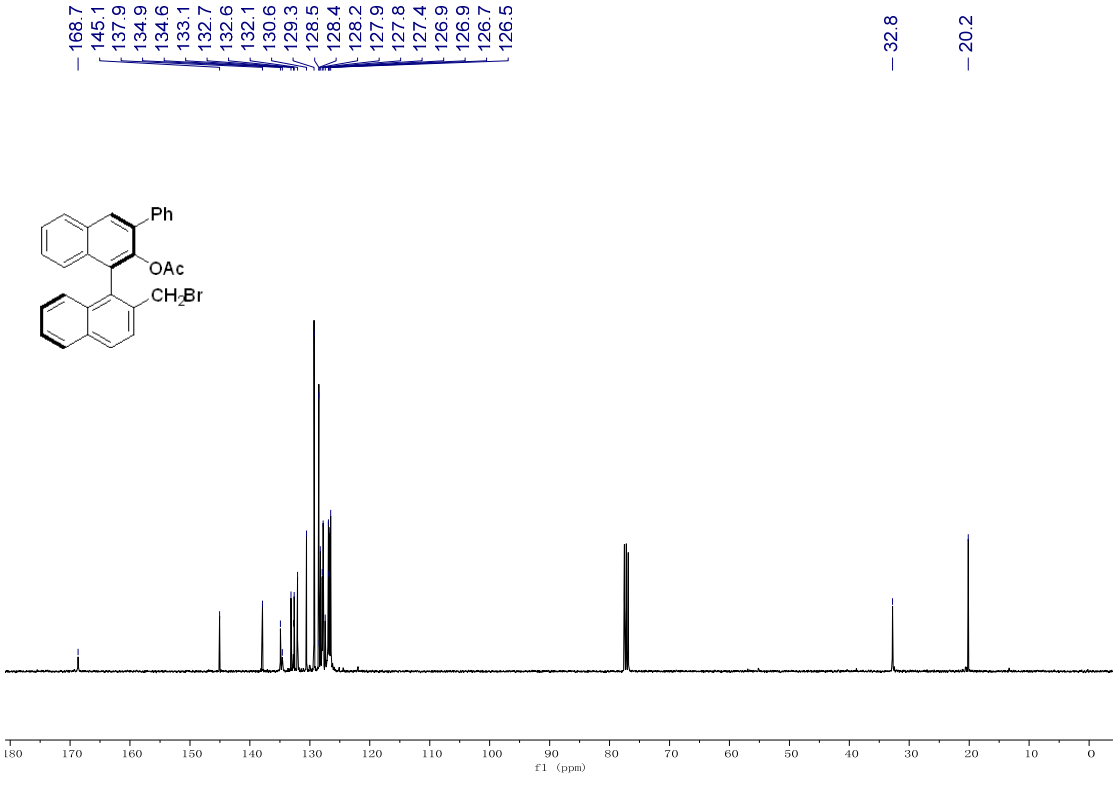
7.43
7.41
7.39
7.35
7.34
7.33
7.27
7.24
4.41
4.39
4.37
4.35
1.40
Ph
OAc
CH2Br
1.00
2.04
1.06
1.02
2.03
4.07
4.08
2.01
3.04
f1 (ppm)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145.1
137.9
134.9
134.6
133.1
132.7
132.6
132.1
130.6
129.3
128.5
128.4
128.2
127.9
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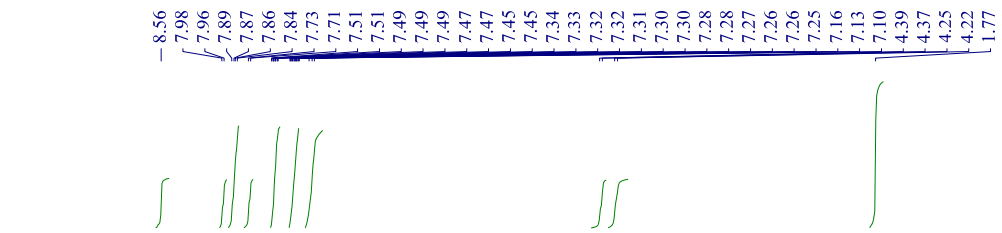
126.9
126.7
126.5
32.8
20.2
Ph
OAc
CH2Br
f1 (ppm)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7.98
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7.89
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7.86
7.84
7.73
7.71
7.51
7.51
7.49
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7.49
7.47
7.47
7.45
7.45
7.34
7.33
7.32
7.32
7.31
7.30
7.30
7.28
7.28
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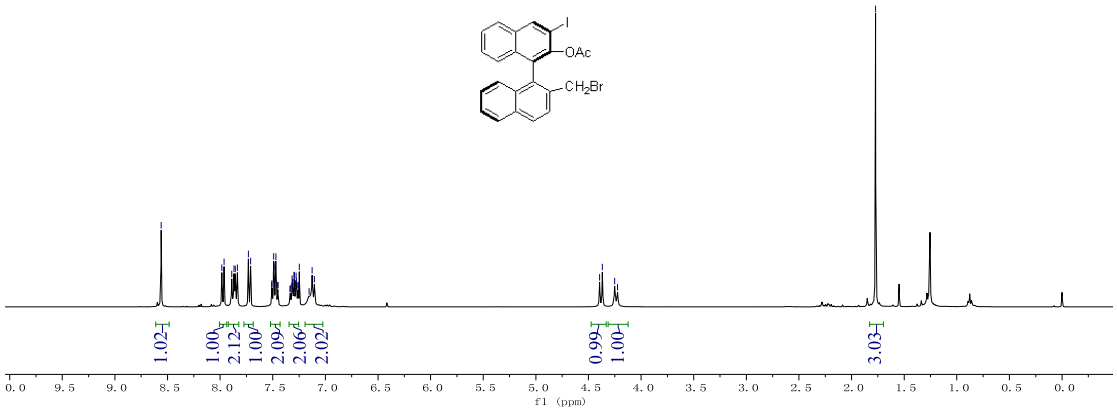
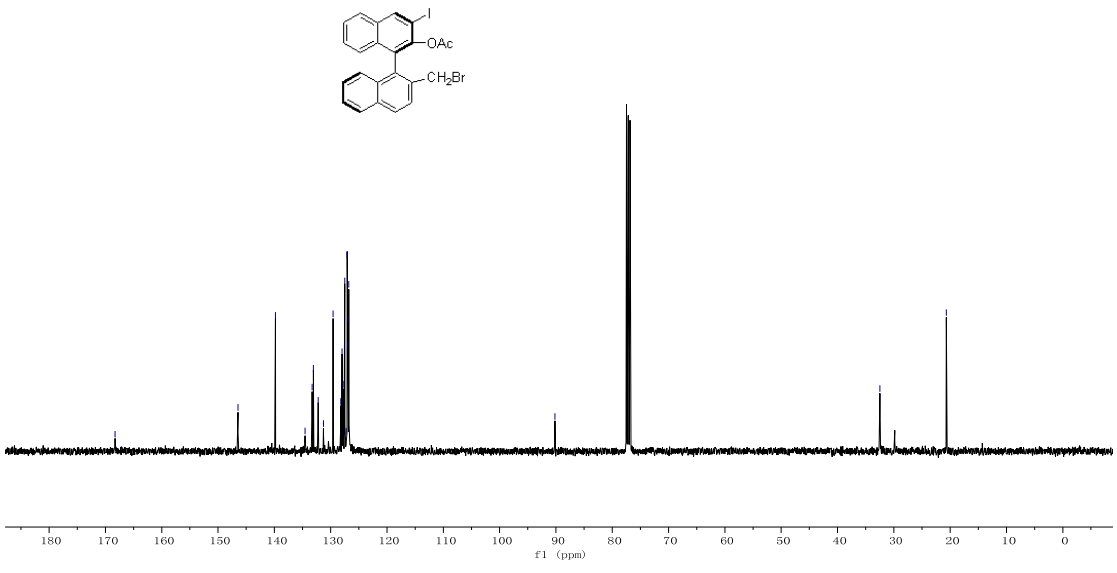
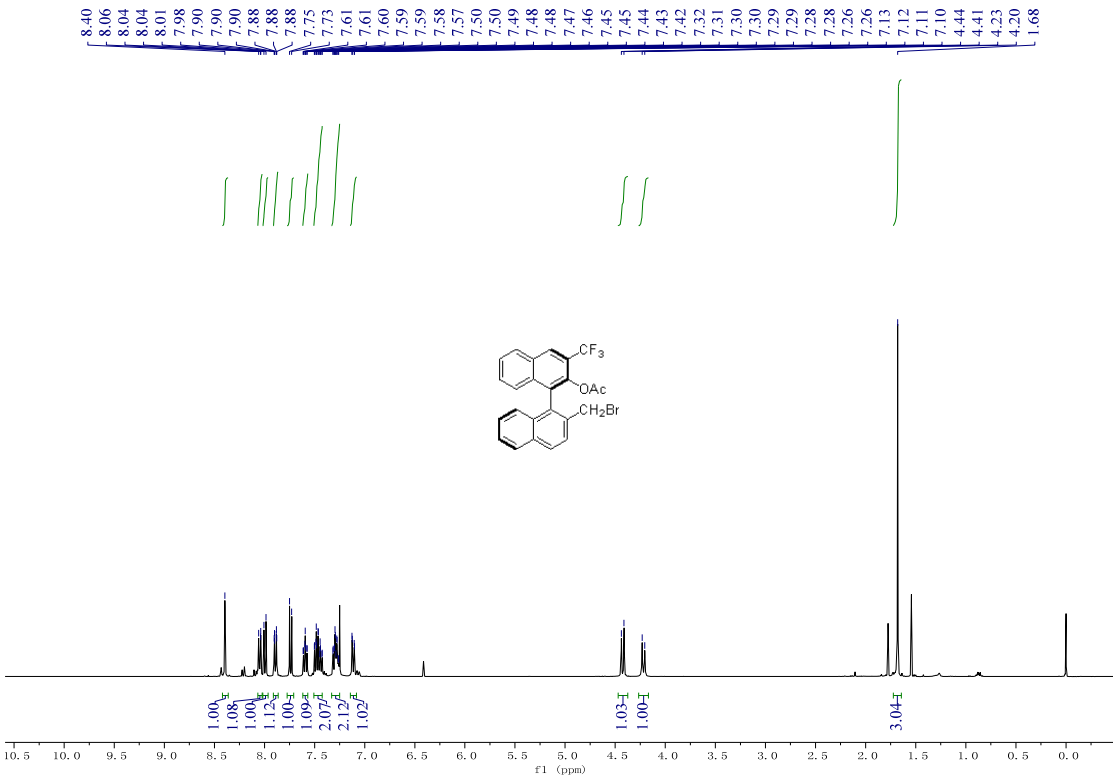
4.25
4.22
1.77


I
OAc
CH2Br
1.02
1.00
2.12
1.00
2.09
2.06
2.02
0.99
1.00
3.03
f1 (ppm)


168.3
146.5
139.8
134.6
133.3
133.1
132.2
131.3
129.6
128.2
128.0
127.8
127.5
127.2
127.1
127.0
126.9
126.8
90.2
32.5
20.7


I
OAc
CH2Br
f1 (ppm)


8.40
8.06
8.04
8.04
8.01
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7.90
7.90
7.90
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7.88
7.88
7.75
7.73
7.61
7.61
7.60
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7.59
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7.57
7.50
7.50
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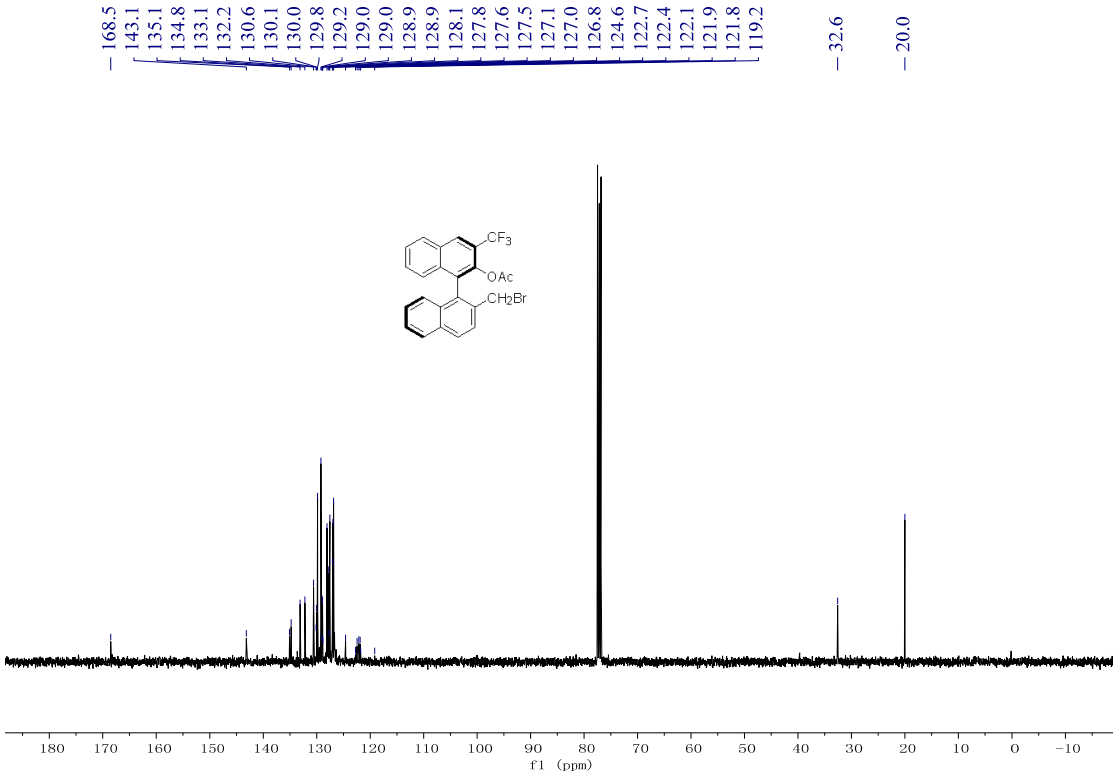
7.48
7.48
7.47
7.46
7.45
7.45
7.44
7.43
7.42
7.32
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.26
7.26
7.13
7.12
7.11
7.10
4.44
4.41
4.23
4.20
1.68
CF3
OAc
CH2Br
1.00
1.08
1.00
1.12
1.00
1.09
2.07
2.12
1.02
1.03
1.00
3.04
f1 (ppm)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135.1
134.8
133.1
132.2
130.6
130.1
130.0
129.8
129.2
129.0
129.0
128.9
128.9
128.1
127.8
127.6
127.5
127.1
127.0
126.8
124.6
122.7
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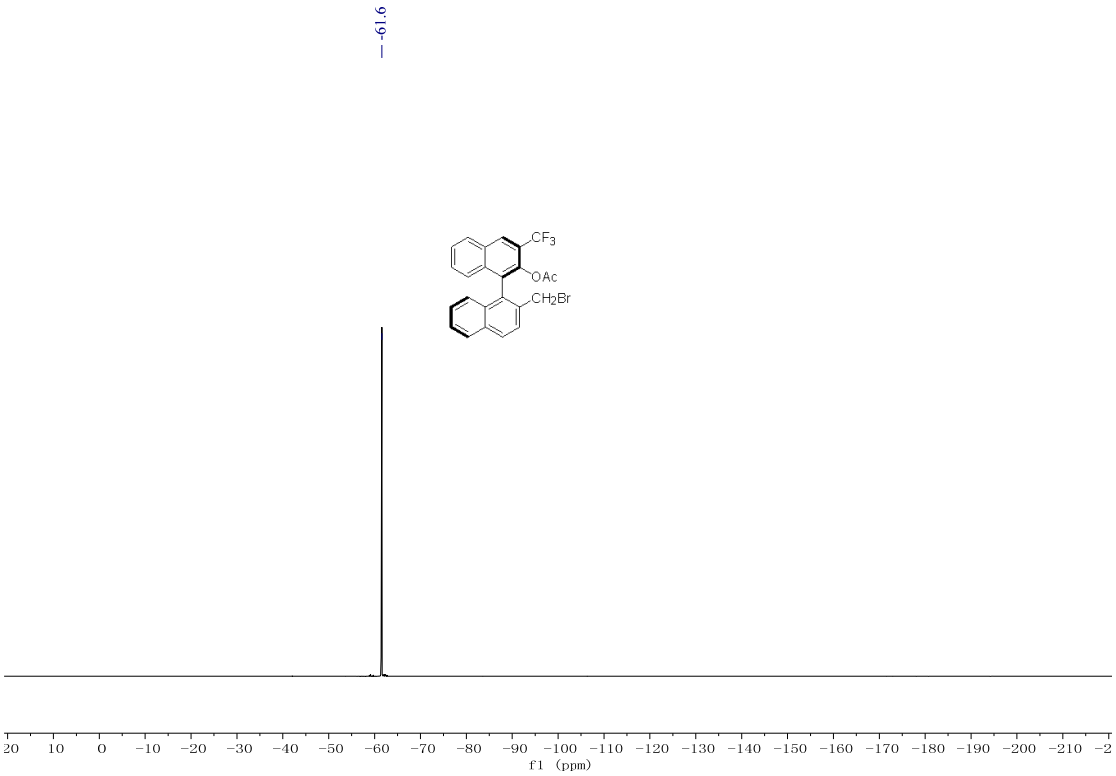
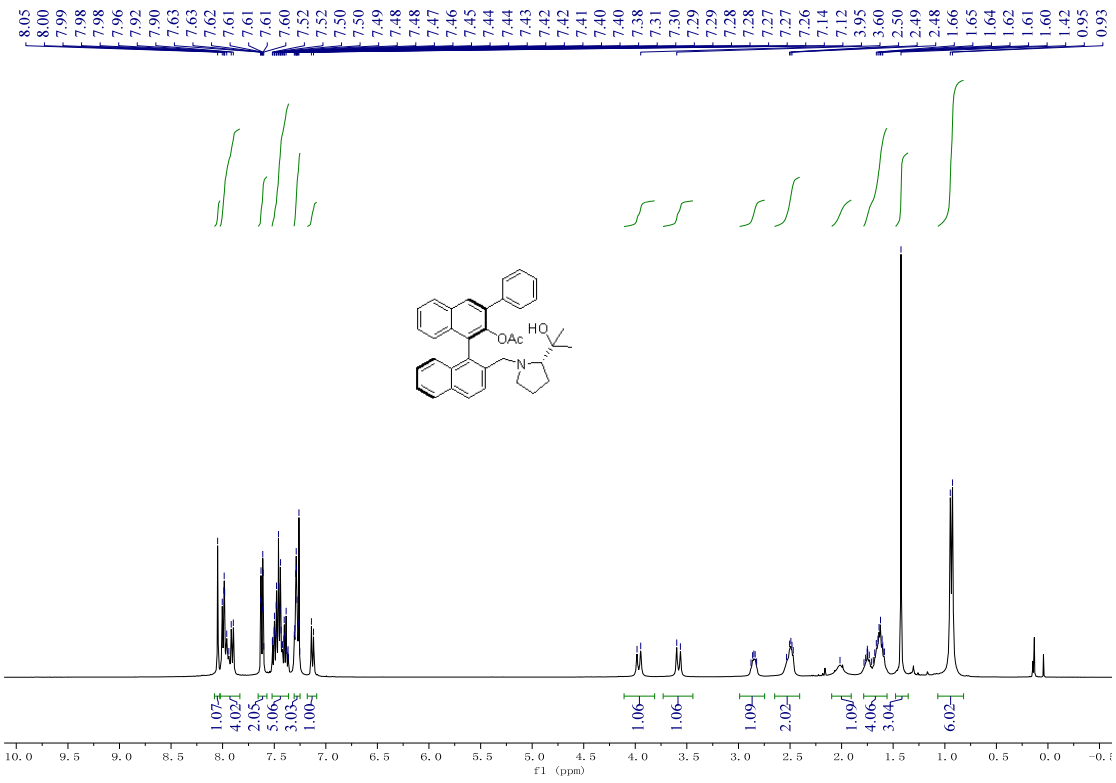
122.1
121.9
121.8
119.2
32.6
20.0
CF3
OAc
CH2Br
f1 (ppm)


-61.6
CF3
OAc
CH2Br
f1 (ppm)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8.00
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7.90
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7.63
7.62
7.61
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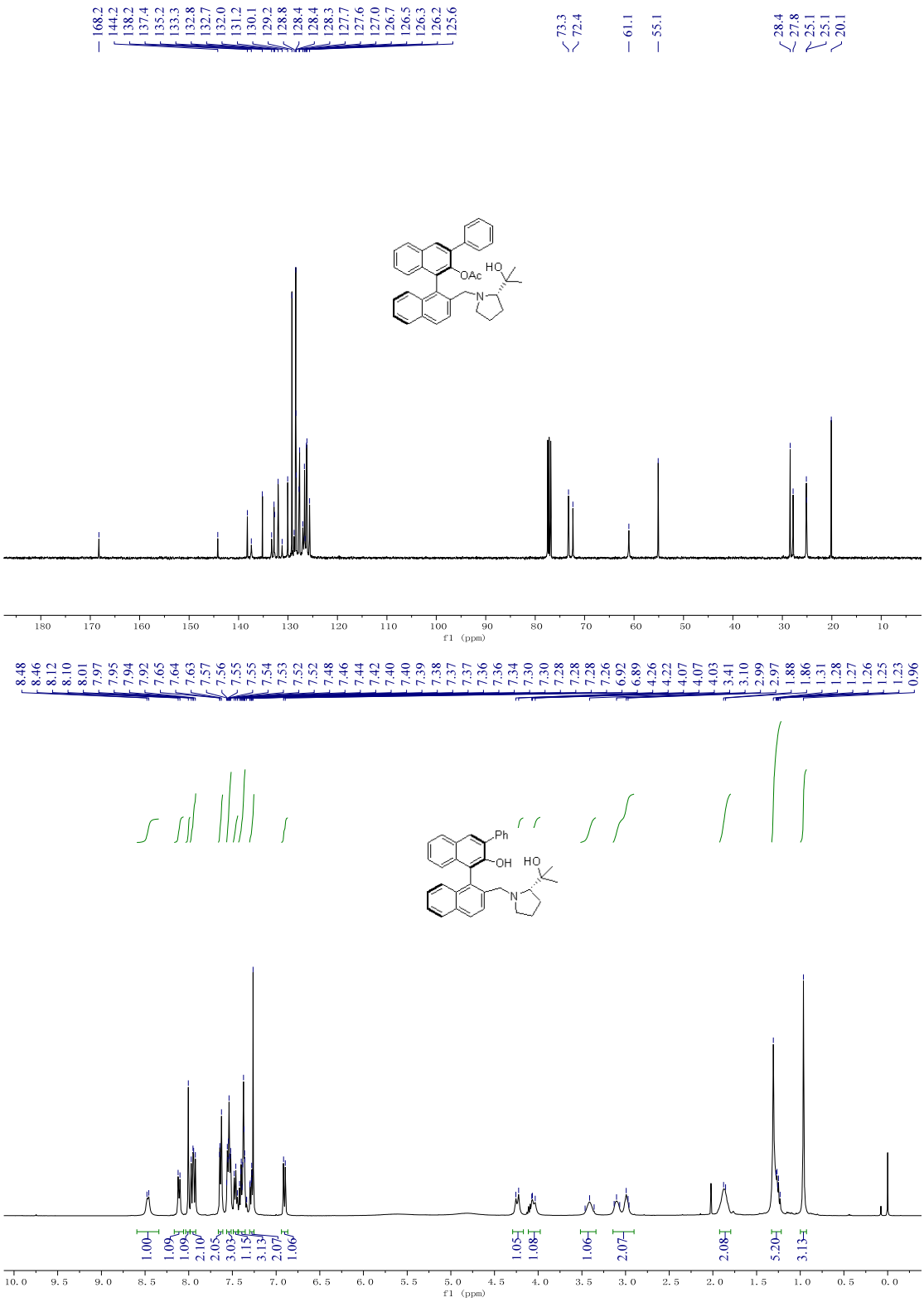
7.61
7.60
7.52
7.52
7.50
7.50
7.49
7.48
7.48
7.47
7.46
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.38
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.14
7.12
3.95
3.60
2.50
2.49
2.48
1.66
1.65
1.64
1.62
1.61
1.60
1.42
0.95
0.93
OAc
HO
N
1.07
4.02
2.05
5.06
3.03
1.00
1.06
1.06
1.09
2.02
1.09
4.06
3.04
6.02
f1 (ppm)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138.2
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132.8
132.7
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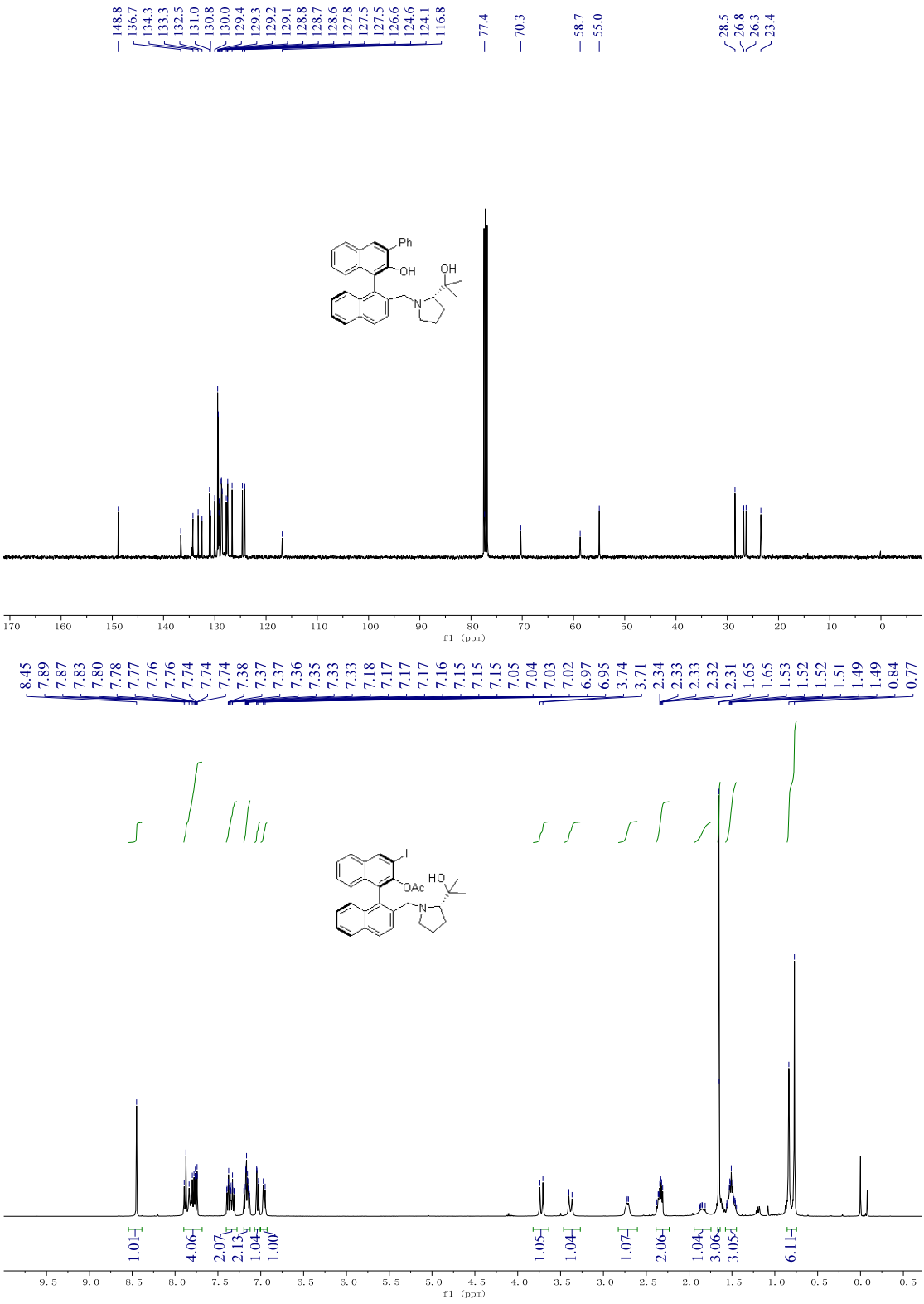
131.2
130.1
129.2
128.8
128.4
128.4
128.3
127.7
127.6
127.0
126.7
126.5
126.3
126.2
125.6
73.3
72.4
61.1
55.1
28.4
27.8
25.1
25.1
20.1
OAc
HO
N
f1 (ppm)
8.48
8.46
8.12
8.10
8.01
7.97
7.95
7.94
7.92
7.65
7.64
7.63
7.57
7.56
7.55
7.55
7.54
7.53
7.52
7.52
7.48
7.46
7.44
7.42
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.36
7.34
7.30
7.30
7.28
7.28
7.28
7.26
6.92
6.89
4.26
4.22
4.07
4.07
4.03
3.41
3.10
2.99
2.97
1.88
1.86
1.31
1.28
1.27
1.26
1.25
1.23
0.96
Ph
OH
HO
N
1.00
1.09
1.09
2.10
2.05
3.03
1.15
3.13
2.07
1.06
1.05
1.08
1.06
2.07
2.08
5.20
3.13
f1 (ppm)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134.3
133.3
132.5
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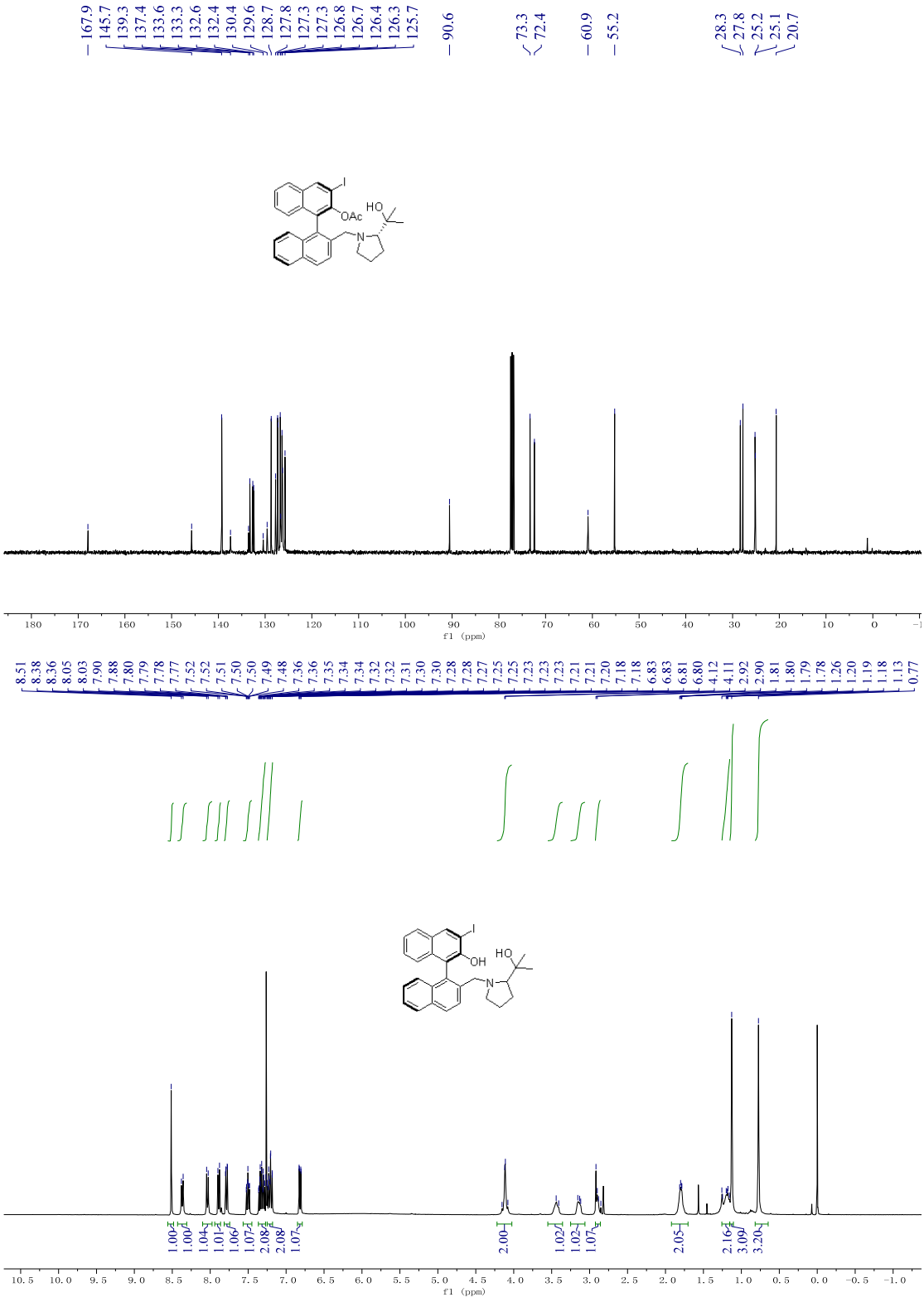
130.8
130.0
129.4
129.3
129.2
129.1
128.8
128.7
128.6
127.8
127.5
127.5
126.6
124.6
124.1
116.8
77.4
70.3
58.7
55.0
28.5
26.8
26.3
23.4
Ph
OH
OH
N
f1 (ppm)
8.45
7.89
7.87
7.83
7.80
7.78
7.77
7.76
7.76
7.74
7.74
7.74
7.38
7.37
7.37
7.36
7.35
7.33
7.33
7.18
7.17
7.17
7.17
7.16
7.15
7.15
7.15
7.05
7.04
7.03
7.02
6.97
6.95
3.74
3.71
2.34
2.33
2.33
2.32
2.31
1.65
1.65
1.53
1.52
1.52
1.51
1.49
1.49
0.84
0.77
I
OAc
HO
N
1.01
4.06
2.07
2.13
1.04
1.00
1.05
1.04
1.07
2.06
1.04
3.06
3.05
6.11
f1 (ppm)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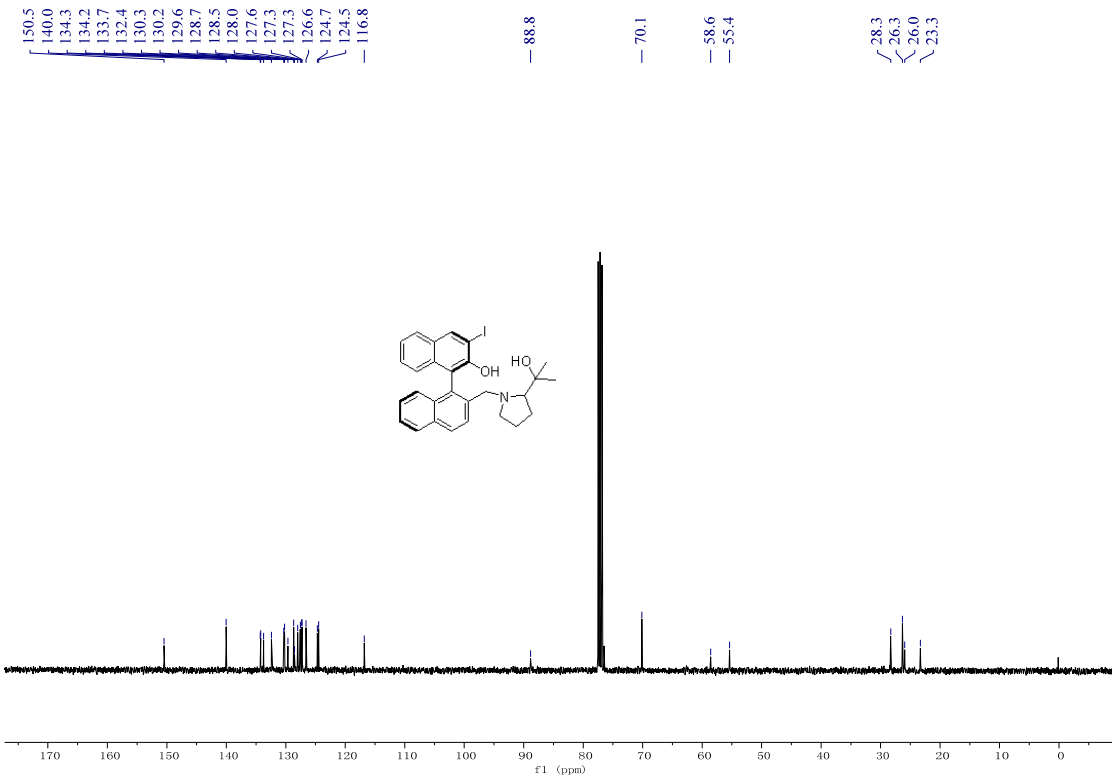
145.7
139.3
137.4
133.6
133.3
132.6
132.4
130.4
129.6
128.7
127.8
127.3
127.3
126.8
126.7
126.4
126.3
125.7
90.6
73.3
72.4
60.9
55.2
28.3
27.8
25.2
25.1
20.7
I
OAc
HO
N
f1 (ppm)
8.51
8.38
8.36
8.05
8.03
7.90
7.88
7.80
7.79
7.78
7.77
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.36
7.36
7.35
7.34
7.34
7.32
7.32
7.31
7.30
7.30
7.28
7.28
7.27
7.25
7.25
7.23
7.23
7.23
7.21
7.21
7.20
7.18
7.18
6.83
6.81
6.80
4.12
4.11
2.92
2.90
1.81
1.80
1.79
1.78
1.26
1.20
1.19
1.18
1.13
0.77
I
OH
HO
N
1.00
1.00
1.04
1.01
1.06
1.07
2.08
2.08
1.07
2.00
1.02
1.02
1.07
2.05
2.16
3.09
3.20
f1 (ppm)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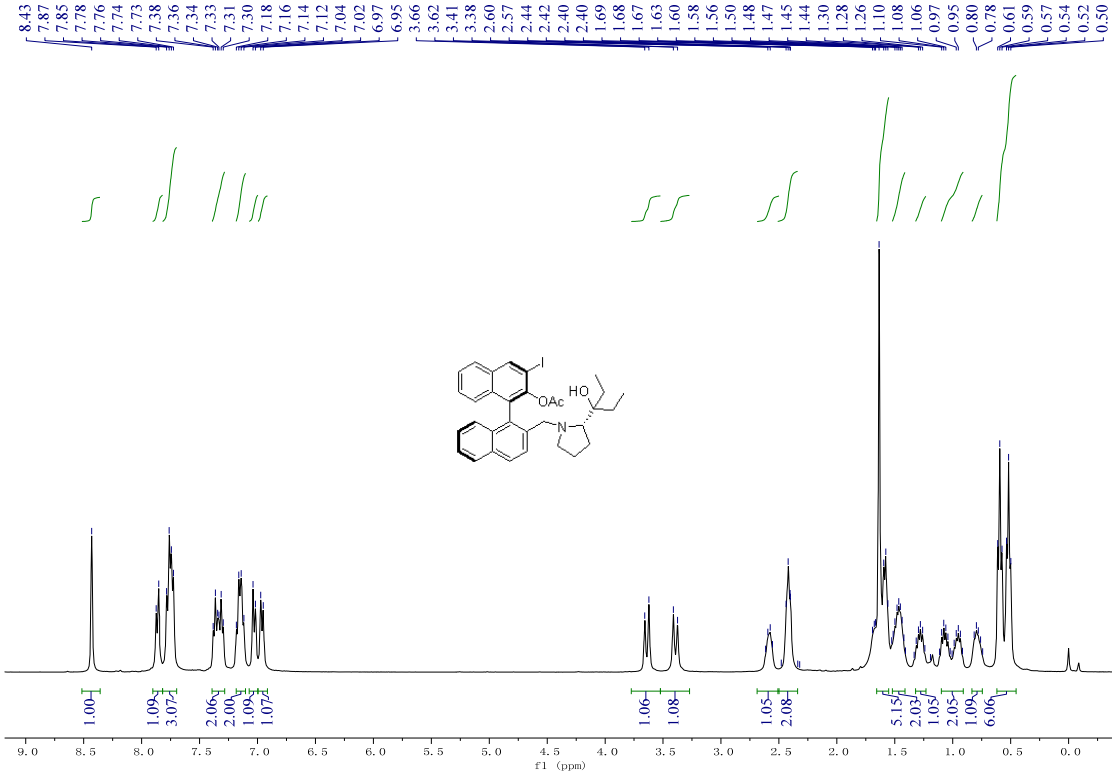
133.7
132.4
130.3
130.2
129.6
128.7
128.5
128.0
127.6
127.3
127.3
126.6
124.7
124.5
116.8
88.8
70.1
58.6
55.4
28.3
26.3
26.0
23.3
I
OH
HO
N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.78
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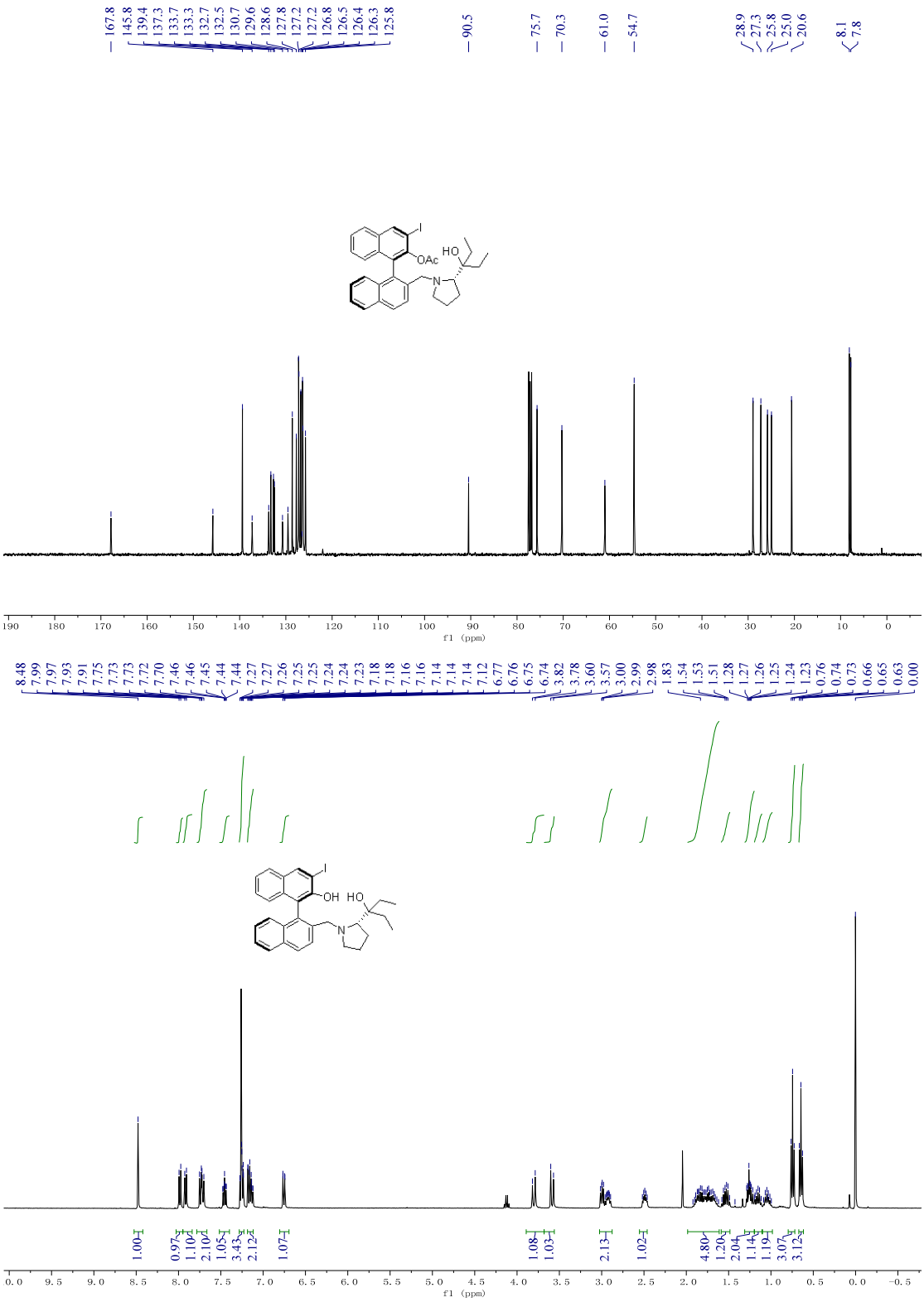
7.74
7.73
7.38
7.36
7.34
7.33
7.31
7.30
7.18
7.16
7.14
7.12
7.04
7.02
6.97
6.95
3.66
3.62
3.41
3.38
2.60
2.57
2.44
2.42
2.40
2.40
1.69
1.68
1.67
1.63
1.60
1.58
1.56
1.50
1.48
1.47
1.45
1.44
1.30
1.28
1.26
1.10
1.08
1.06
0.97
0.95
0.80
0.78
0.61
0.59
0.57
0.54
0.52
0.50
I
OAc
HO
N
1.00
1.09
3.07
2.06
2.00
1.09
1.07
1.06
1.08
1.05
2.08
5.15
2.03
1.05
2.05
1.09
6.06
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)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133.7
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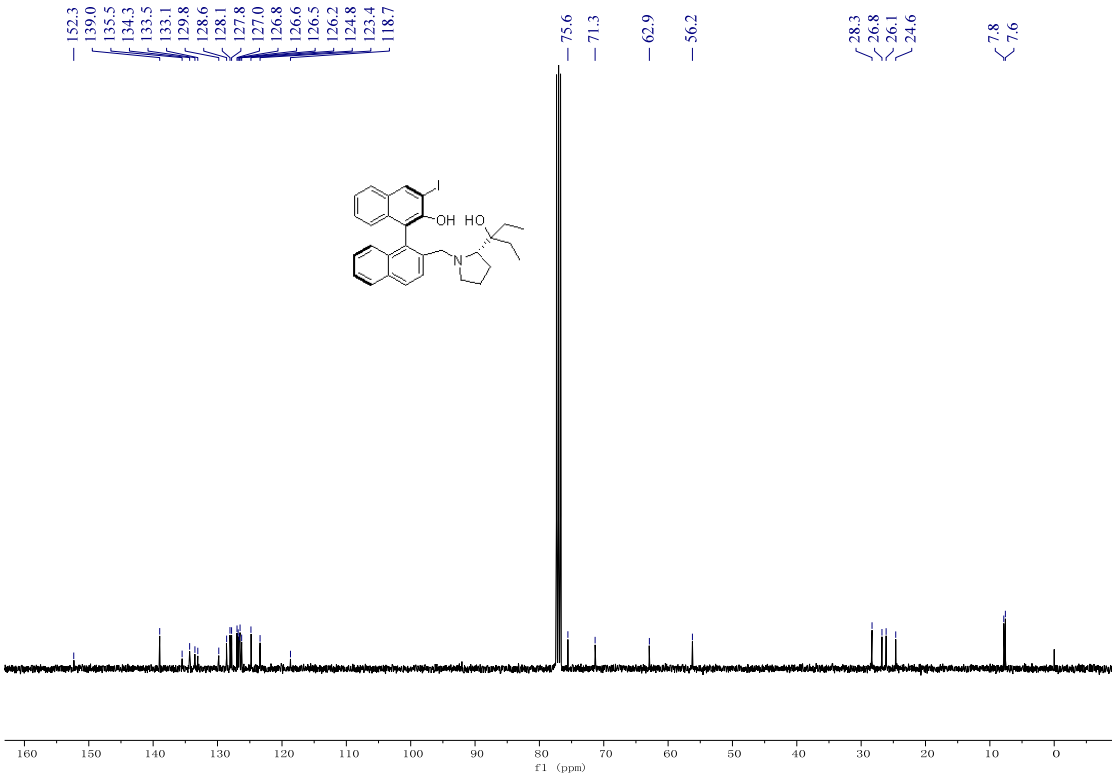
132.7
132.5
130.7
129.6
128.6
127.8
127.2
127.2
126.8
126.5
126.4
126.3
125.8
90.5
75.7
70.3
61.0
54.7
28.9
27.3
25.8
25.0
20.6
8.1
7.8
I
OAc
HO
N
f1 (ppm)
8.48
7.99
7.97
7.93
7.91
7.75
7.73
7.73
7.72
7.70
7.46
7.46
7.45
7.44
7.44
7.27
7.27
7.26
7.25
7.25
7.24
7.24
7.23
7.18
7.18
7.16
7.16
7.14
7.14
7.14
7.12
6.77
6.76
6.75
6.74
3.82
3.78
3.60
3.57
3.00
2.99
2.98
1.83
1.54
1.53
1.51
1.28
1.27
1.26
1.25
1.24
1.23
0.76
0.74
0.73
0.66
0.65
0.63
0.00
I
OH
HO
N
1.00
0.97
1.10
2.10
1.05
3.43
2.12
1.07
1.08
1.03
2.13
1.02
4.80
1.20
2.04
1.14
1.19
3.07
3.12
f1 (ppm)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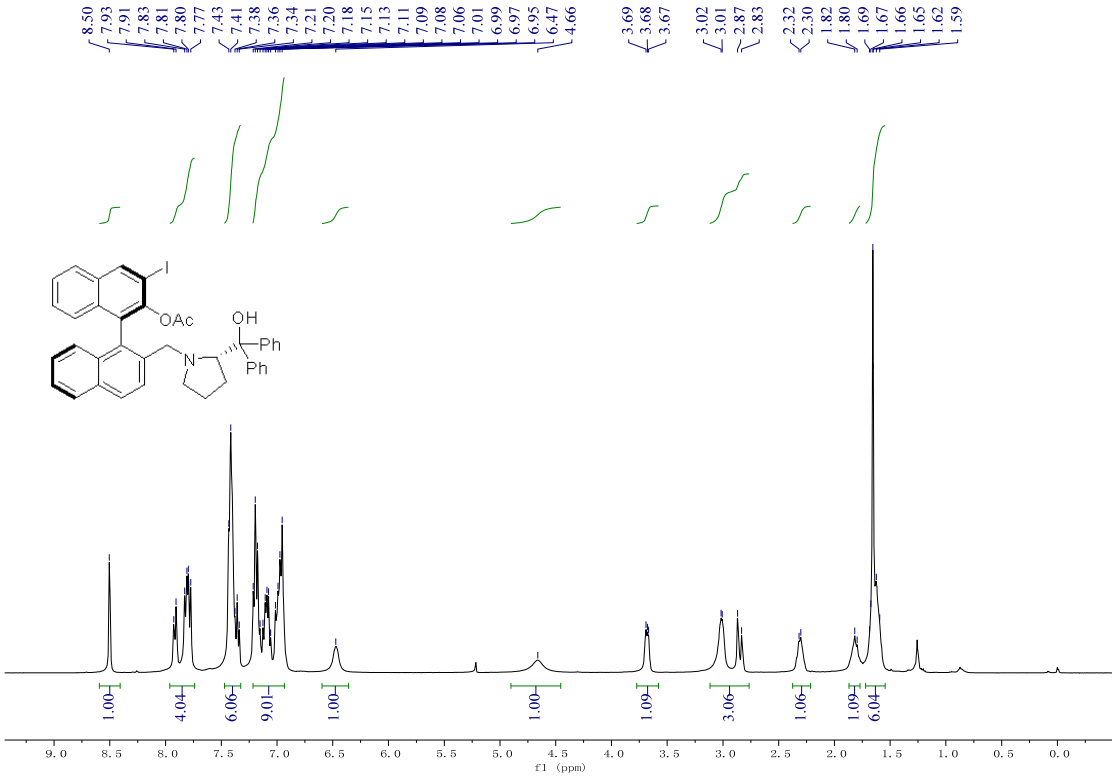
128.1
127.8
127.0
126.8
126.6
126.5
126.2
124.8
123.4
118.7
75.6
71.3
62.9
56.2
28.3
26.8
26.1
24.6
7.8
7.6
I
OH
HO
N
f1 (ppm)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7.80
7.77
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7.41
7.38
7.36
7.34
7.21
7.20
7.18
7.15
7.13
7.11
7.09
7.08
7.06
7.01
6.99
6.97
6.95
6.47
4.66
3.69
3.68
3.67
3.02
3.01
2.87
2.83
2.32
2.30
1.82
1.80
1.69
1.67
1.66
1.65
1.62
1.59
I
OAc
OH
Ph
Ph
N
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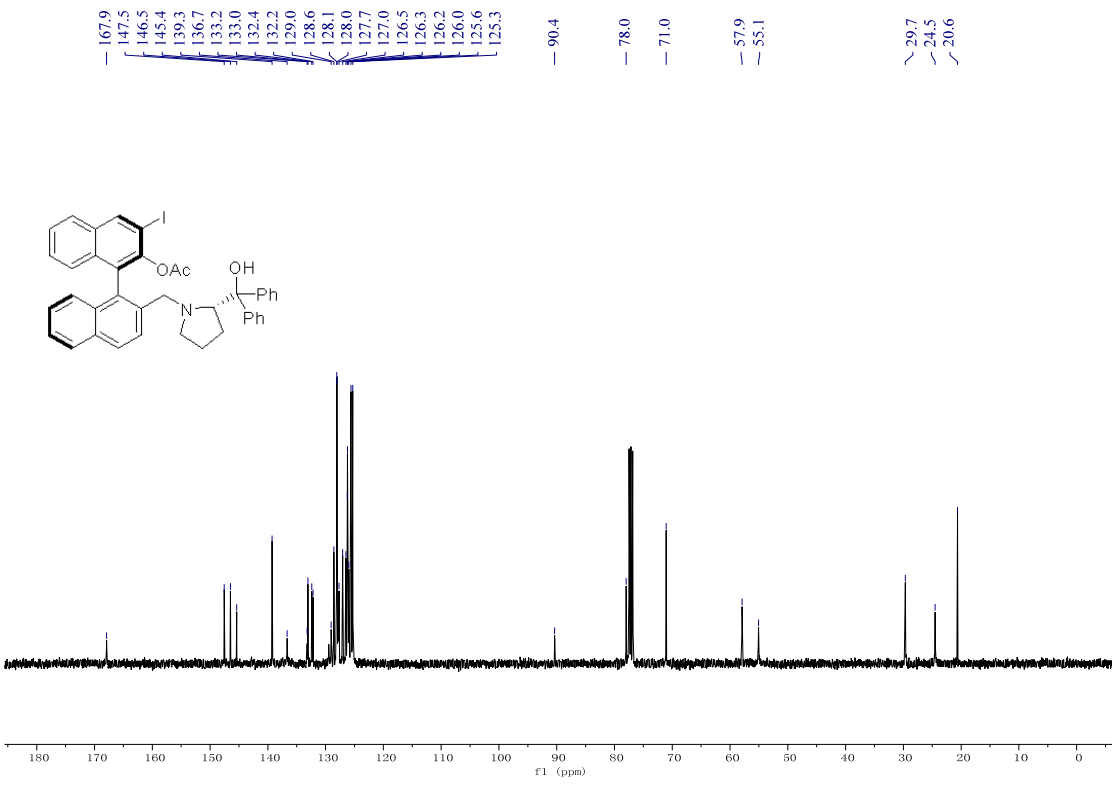
4.04
6.06
9.01
1.00
1.00
1.09
3.06
1.06
1.09
6.04
f1 (ppm)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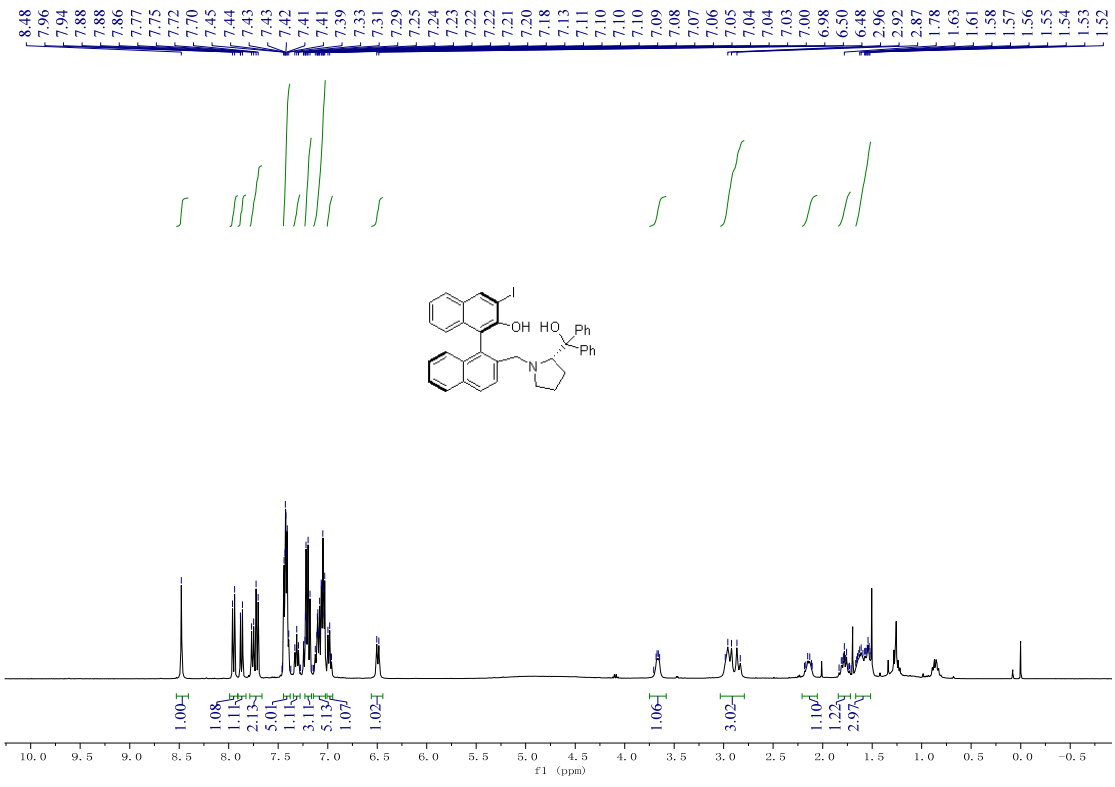
146.5
145.4
139.3
136.7
133.2
133.0
132.4
132.2
129.0
128.6
128.1
128.0
127.7
127.0
126.5
126.3
126.2
126.0
125.6
125.3
90.4
78.0
71.0
57.9
55.1
29.7
24.5
20.6
I
OAc
OH
Ph
Ph
N
f1 (ppm)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7.88
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7.70
7.45
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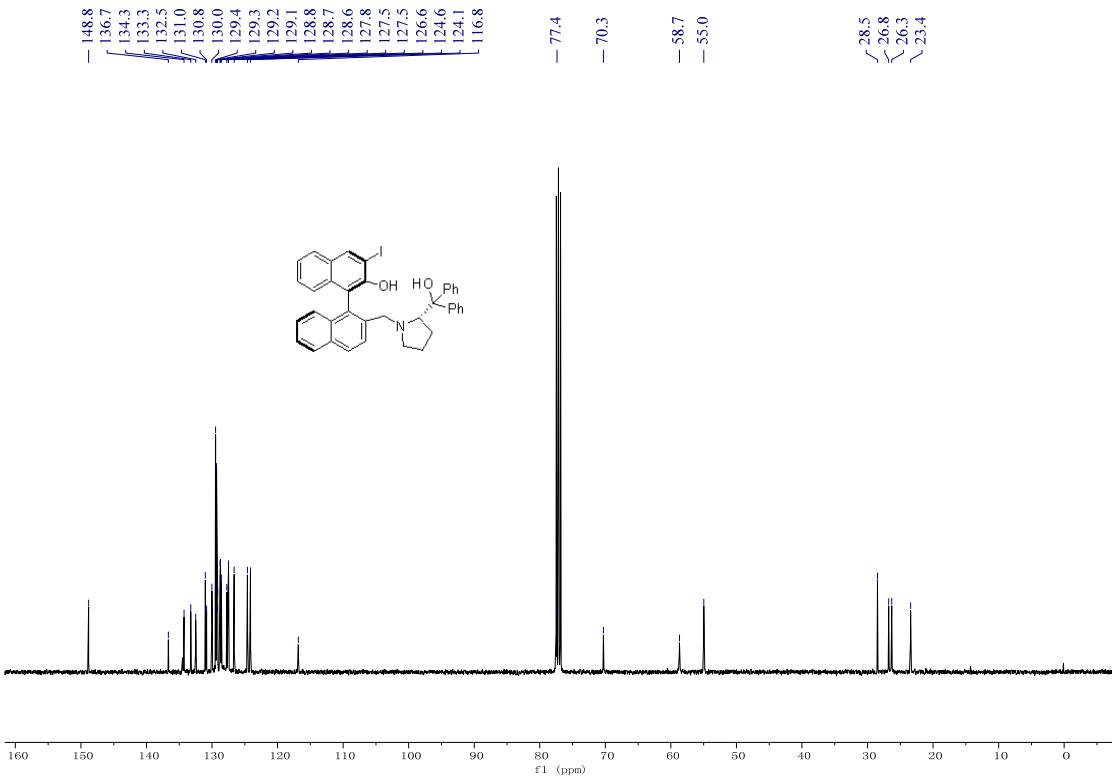
7.43
7.43
7.42
7.41
7.41
7.39
7.33
7.31
7.29
7.25
7.24
7.23
7.22
7.22
7.21
7.20
7.18
7.13
7.11
7.10
7.10
7.10
7.09
7.08
7.07
7.06
7.05
7.04
7.04
7.03
7.00
6.98
6.50
6.48
2.96
2.92
2.87
1.78
1.63
1.61
1.58
1.57
1.56
1.55
1.54
1.53
1.52
I
OH
HO
Ph
Ph
N
1.00
1.08
1.11
2.13
5.01
1.11
3.11
5.13
1.07
1.02
1.06
3.02
1.10
1.22
2.97
f1 (ppm)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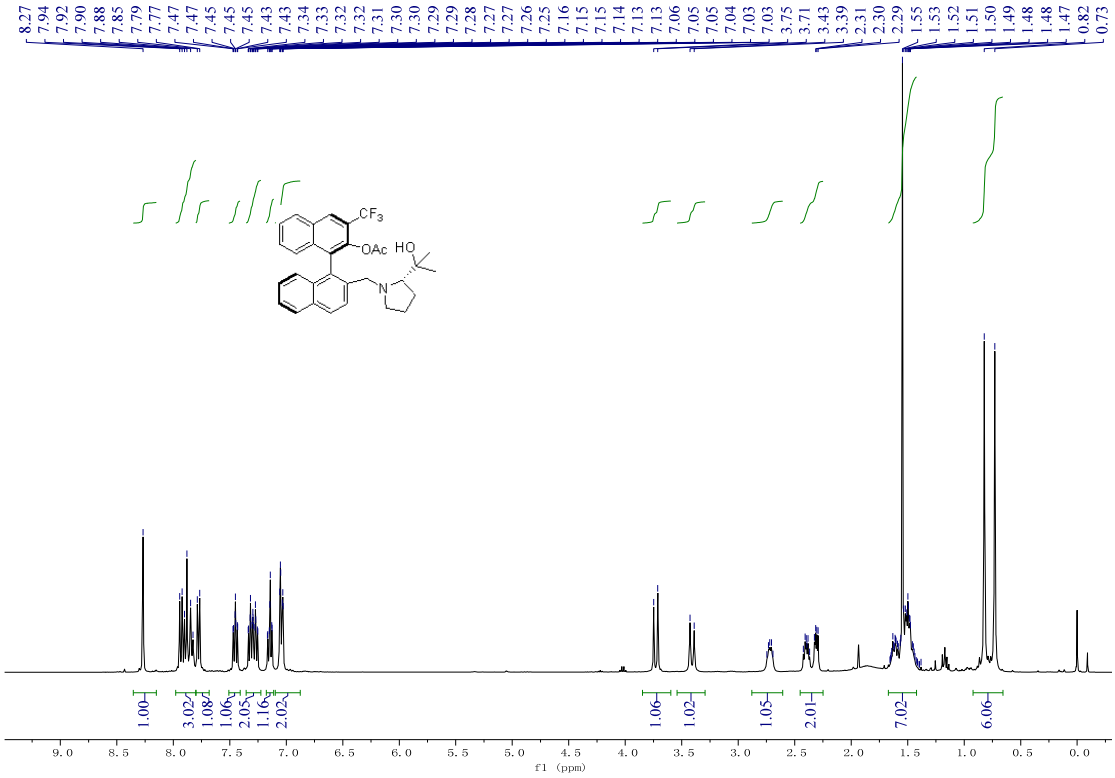
130.8
130.0
129.4
129.3
129.2
129.1
128.8
128.7
128.6
127.8
127.5
127.5
126.6
124.6
124.1
116.8
77.4
70.3
58.7
55.0
28.5
26.8
26.3
23.4
I
OH
HO
Ph
Ph
N
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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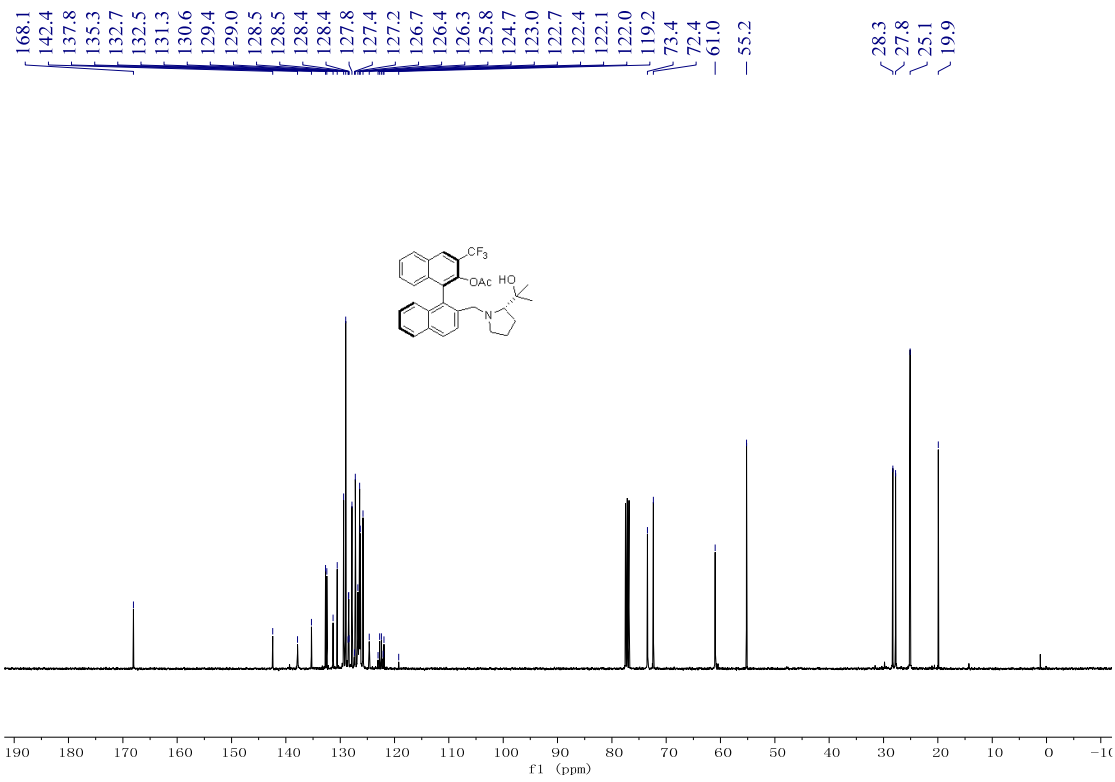
7.45
7.43
7.43
7.34
7.33
7.32
7.32
7.31
7.30
7.30
7.29
7.29
7.28
7.27
7.27
7.26
7.25
7.16
7.15
7.15
7.14
7.13
7.13
7.06
7.05
7.05
7.04
7.03
7.03
3.75
3.71
3.43
3.39
2.31
2.30
2.29
1.55
1.53
1.52
1.51
1.50
1.49
1.48
1.48
1.47
0.82
0.73
CF3
OAc
HO
N
1.00
3.02
1.08
1.06
2.05
1.16
2.02
1.06
1.02
1.05
2.01
7.02
6.06
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)


168.1
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137.8
135.3
132.7
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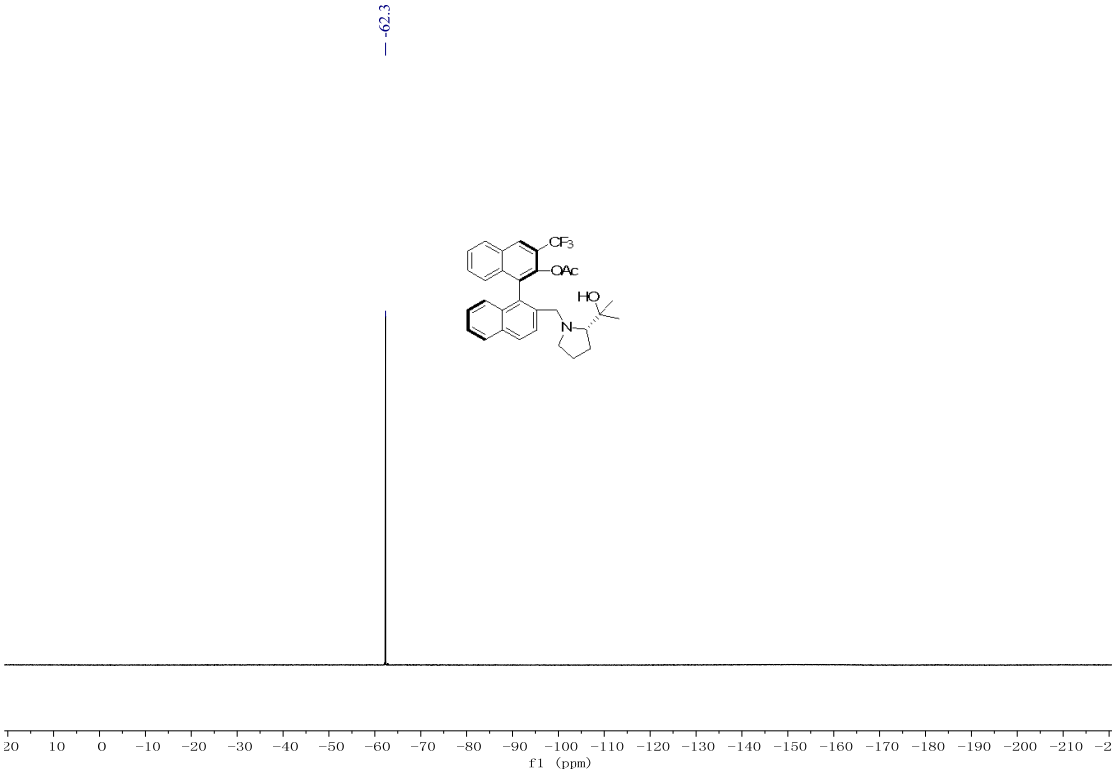
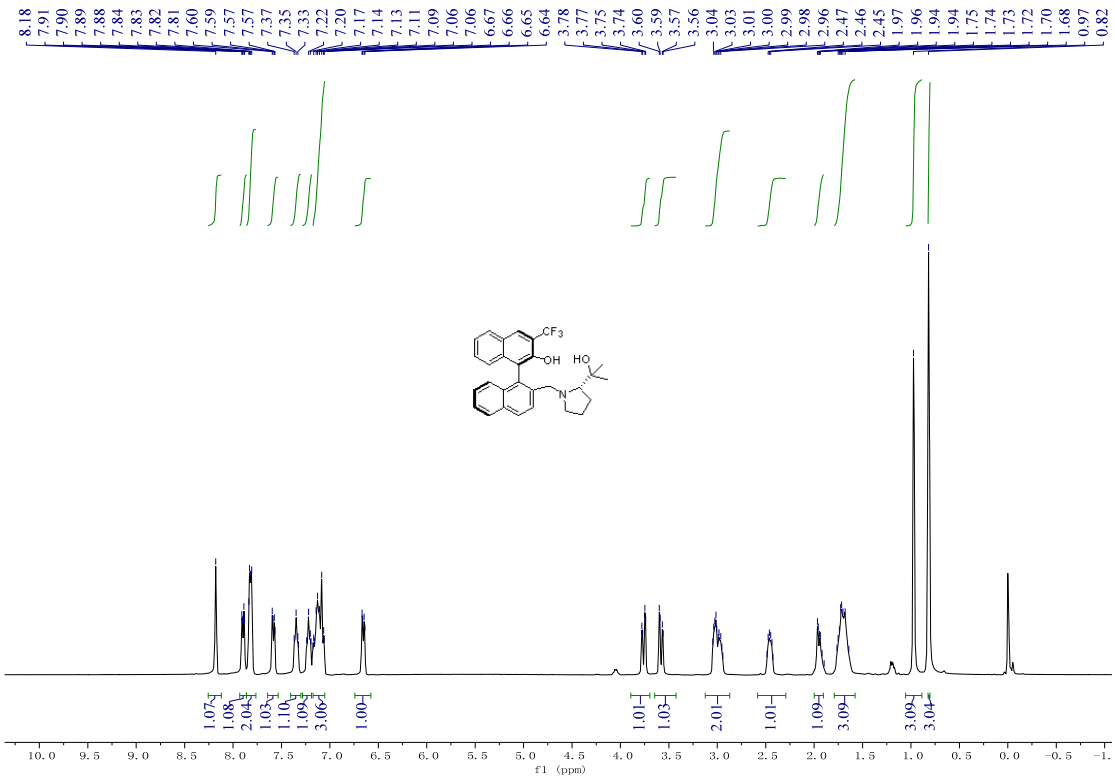
131.3
130.6
129.4
129.0
128.5
128.5
128.4
128.4
127.8
127.4
127.2
126.7
126.4
126.3
125.8
124.7
123.0
122.7
122.4
122.1
122.0
119.2
73.4
72.4
61.0
55.2
28.3
27.8
25.1
19.9
CF3
OAc
HO
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-62.3
CF3
OAc
HO
N
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2
f1 (ppm)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7.33
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7.09
7.06
7.06
6.67
6.66
6.65
6.64
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3.77
3.75
3.74
3.60
3.59
3.57
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3.04
3.03
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3.00
2.99
2.98
2.96
2.47
2.46
2.45
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1.96
1.94
1.94
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1.73
1.72
1.70
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0.82
CF3
OH
HO
N
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1.08
2.04
1.03
1.10
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3.09
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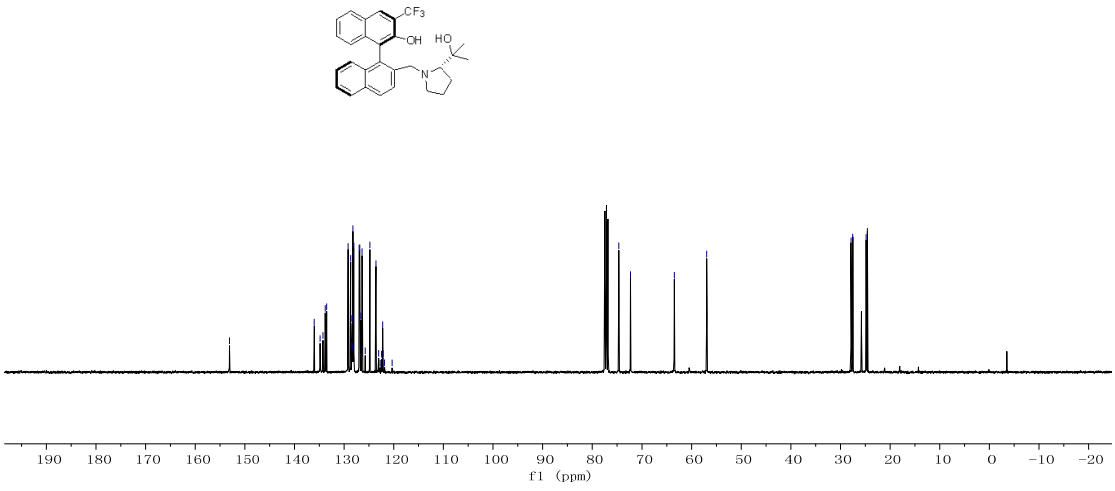
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126.4
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124.8
123.6
123.0
122.7
122.5
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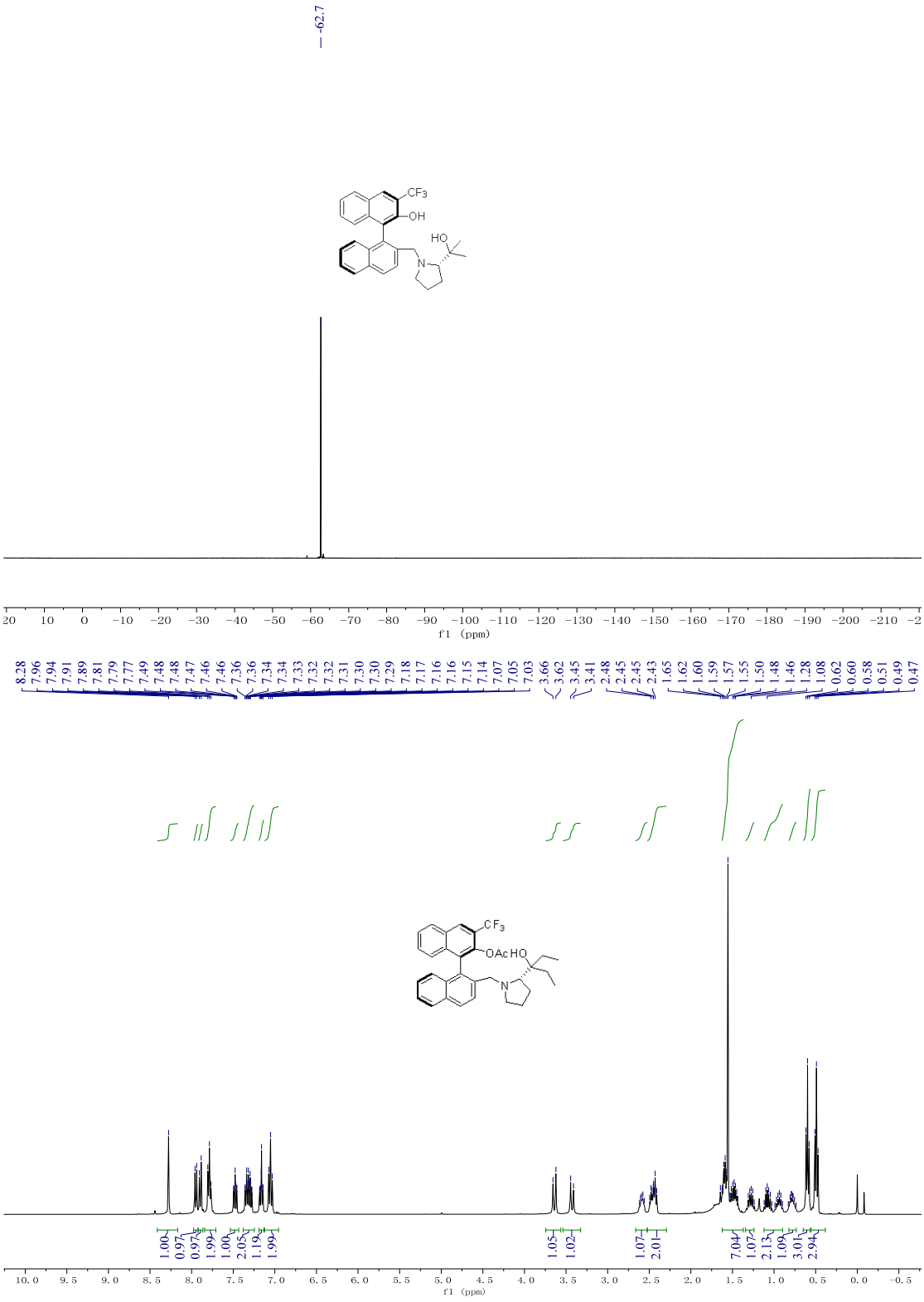
f1 (ppm)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HO
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7.34
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2.45
2.45
2.43
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1.62
1.60
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1.57
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1.50
1.48
1.46
1.28
1.08
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0.60
0.58
0.51
0.49
0.47
CF3
OAc HO
N
1.00
0.97
0.97
1.99
1.00
2.05
1.19
1.99
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1.07
2.01
7.04
1.07
2.13
1.09
3.01
2.94
f1 (ppm)


168.1
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139.4
137.8
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124.7
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122.7
122.4
122.1
122.0
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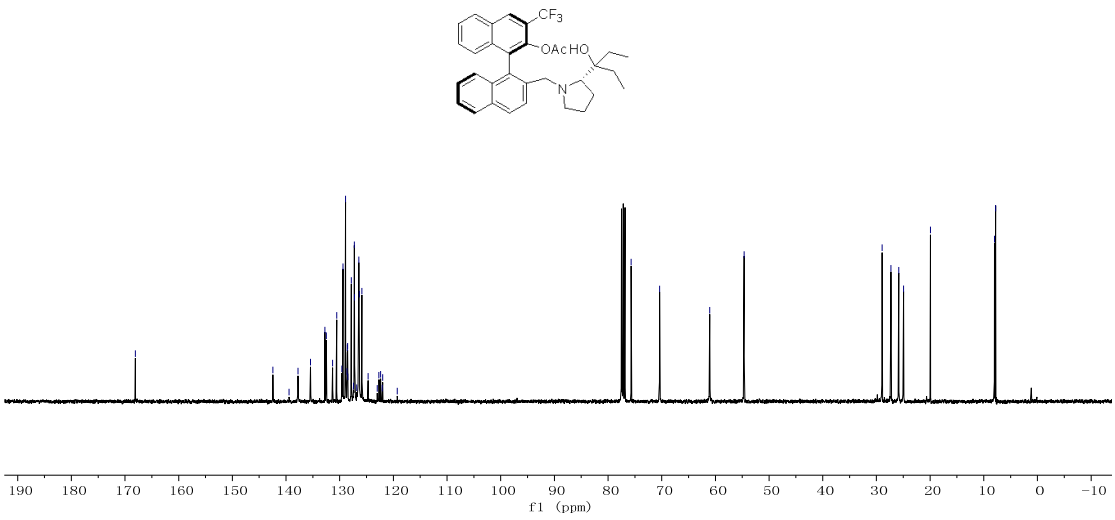
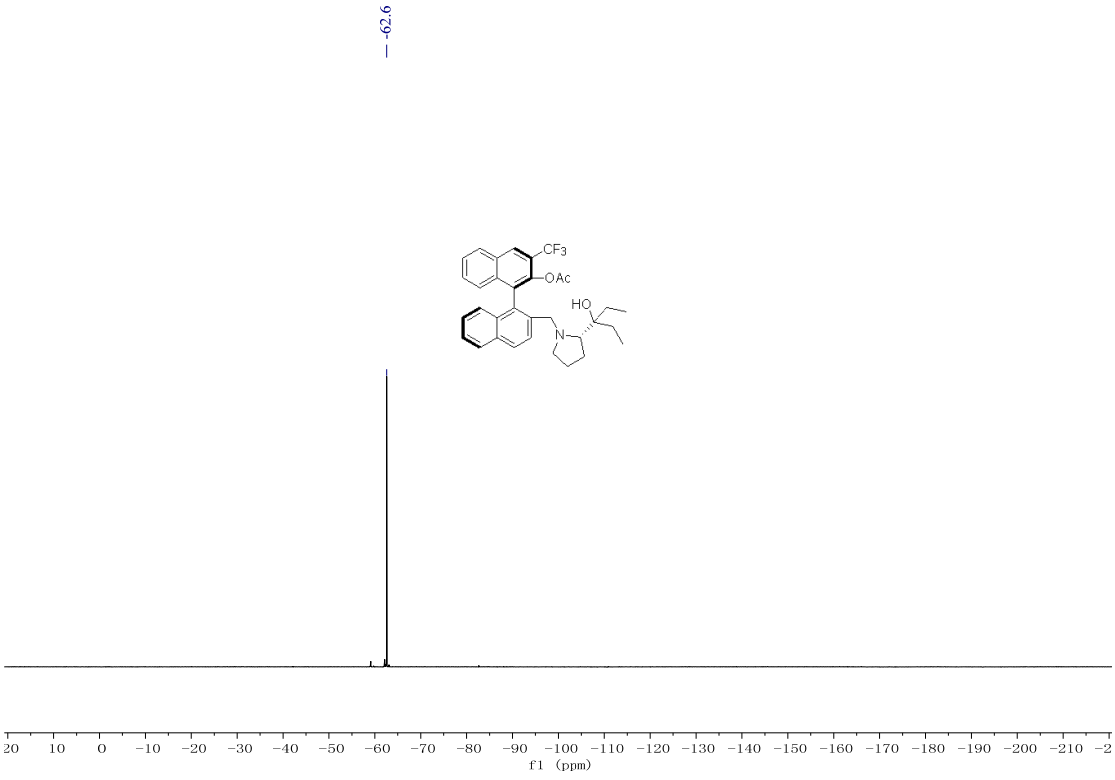
7.8


CF3
OAc
HO
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)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CF3
OAc
HO
N
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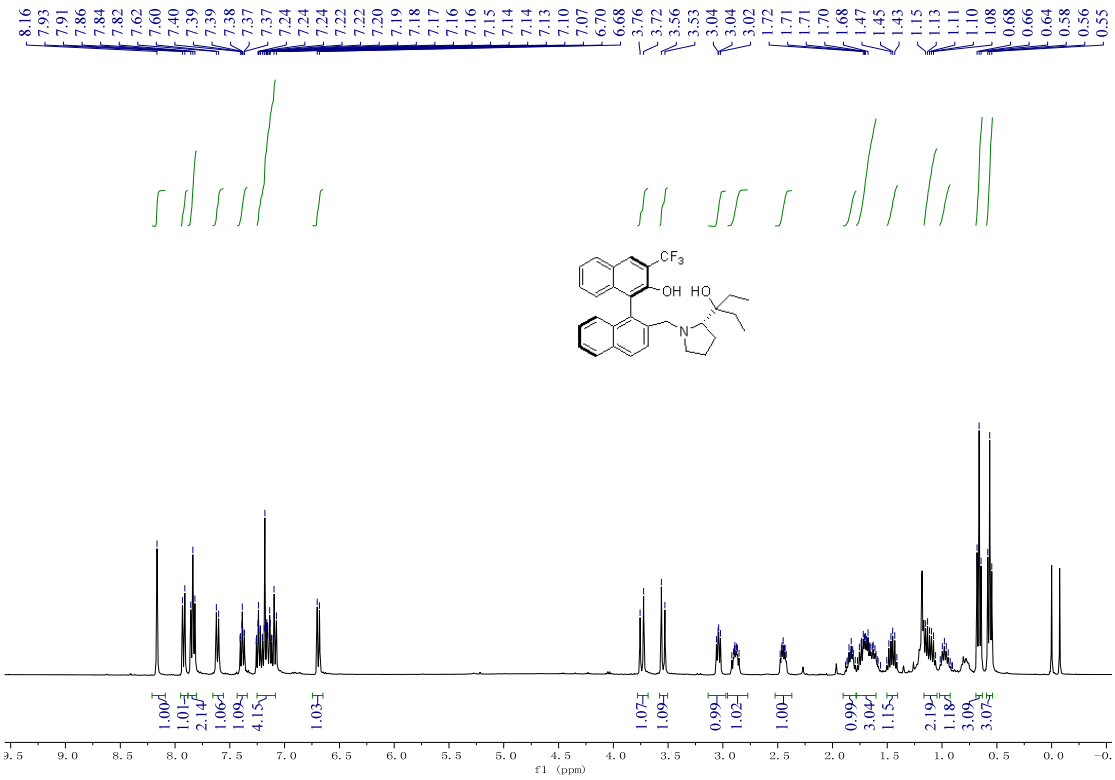
f1 (ppm)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7.24
7.24
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7.22
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7.19
7.18
7.17
7.16
7.16
7.15
7.14
7.14
7.13
7.10
7.07
6.70
6.68
3.76
3.72
3.56
3.53
3.04
3.04
3.02
1.72
1.71
1.71
1.70
1.68
1.47
1.45
1.43
1.15
1.13
1.11
1.10
1.08
0.68
0.66
0.64
0.58
0.56
0.55
CF3
OH HO
N
1.00
1.01
2.14
1.06
1.09
4.15
1.03
1.07
1.09
0.99
1.02
1.00
0.99
3.04
1.15
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1.18
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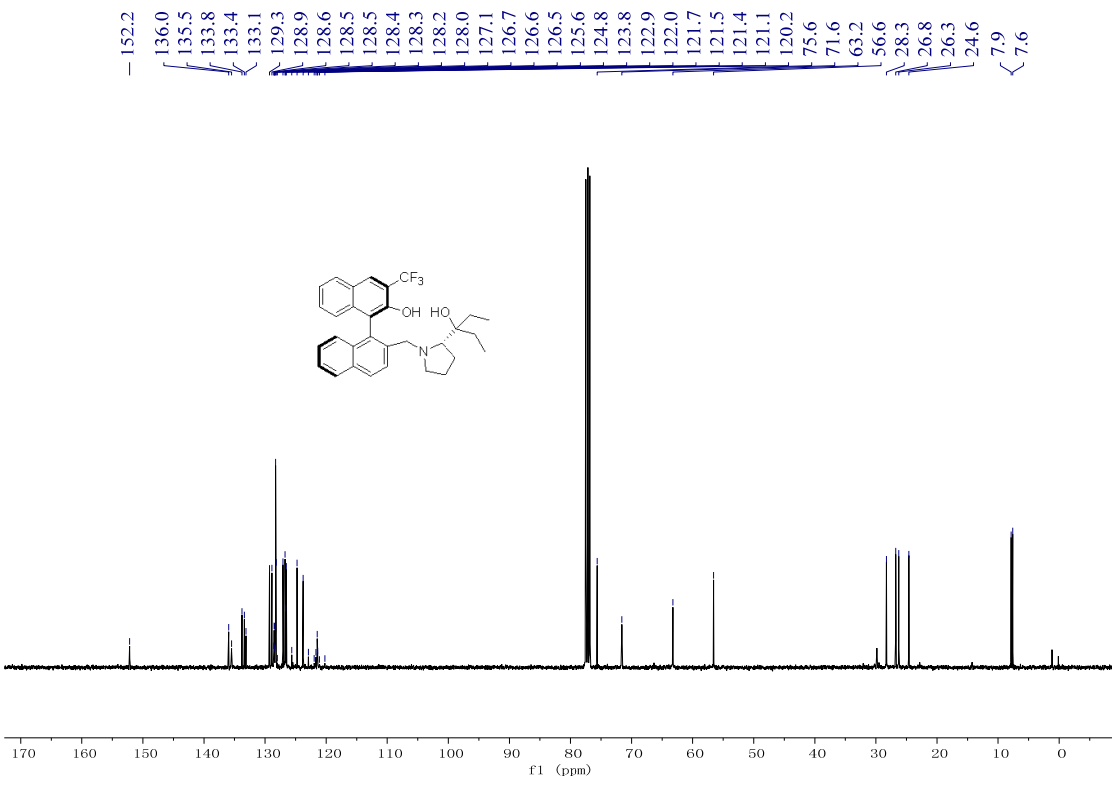
3.07
f1 (ppm)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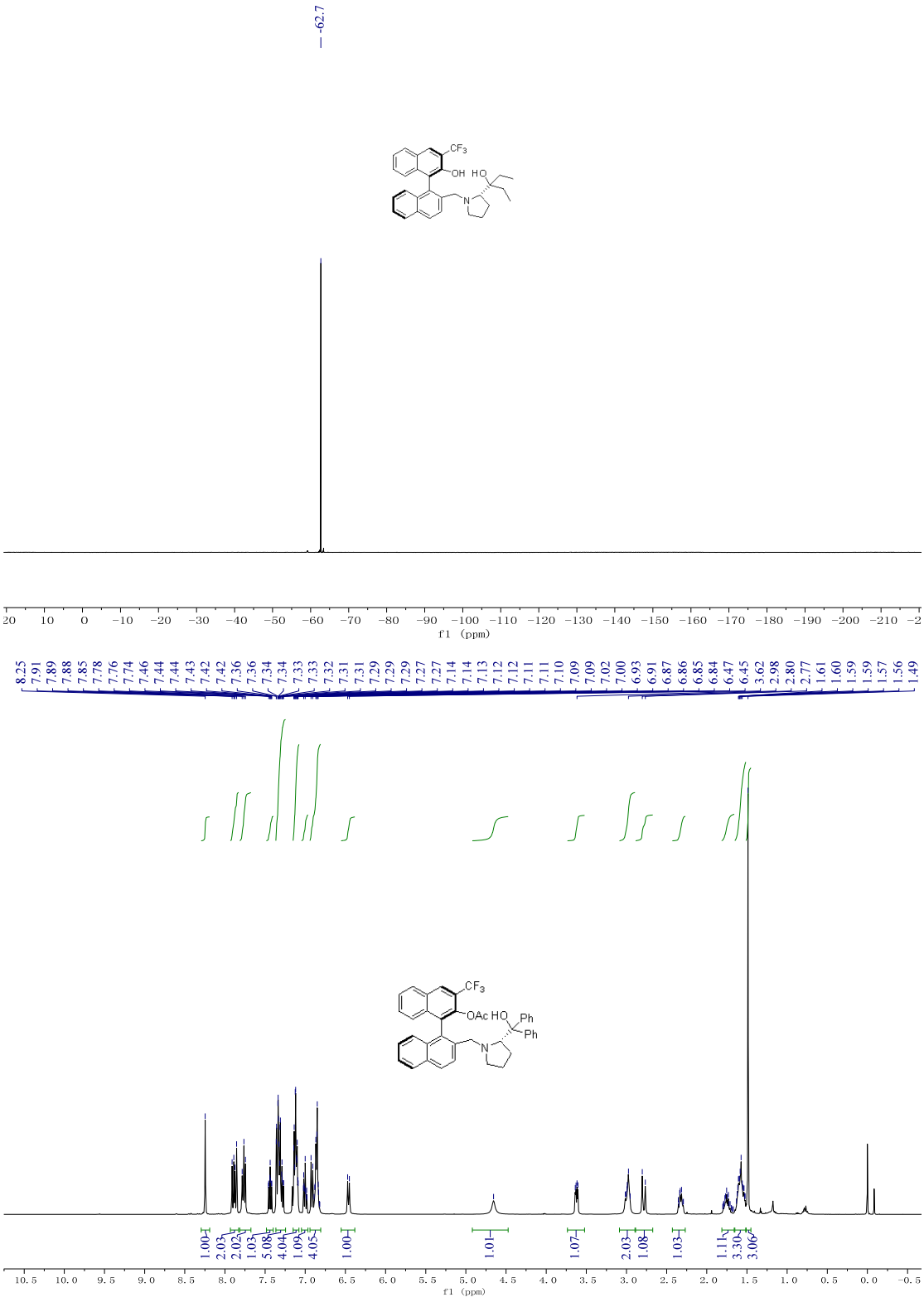
128.3
128.2
128.0
127.1
126.7
126.6
126.5
125.6
124.8
123.8
122.9
122.0
121.7
121.5
121.4
121.1
120.2
75.6
71.6
63.2
56.6
28.3
26.8
26.3
24.6
7.9
7.6
CF3
OH HO
N
f1 (ppm)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CF3
OH HO
N
f1 (ppm)
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7.11
7.10
7.09
7.09
7.02
7.00
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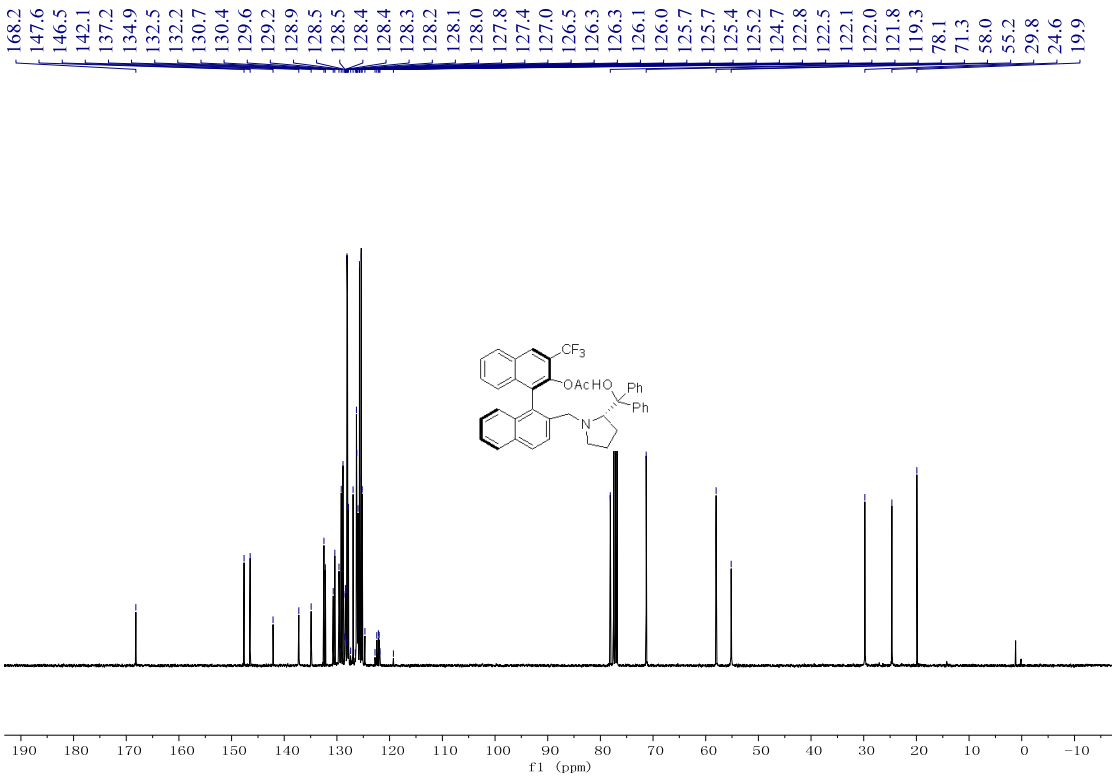
6.91
6.87
6.86
6.85
6.84
6.47
6.45
3.62
2.98
2.80
2.77
1.61
1.60
1.59
1.59
1.57
1.56
1.49
CF3
OAc HO
Ph
Ph
N
1.00
2.03
2.02
1.03
5.08
4.04
1.09
4.05
1.00
1.01
1.07
2.03
1.08
1.03
1.11
3.30
3.06
f1 (ppm)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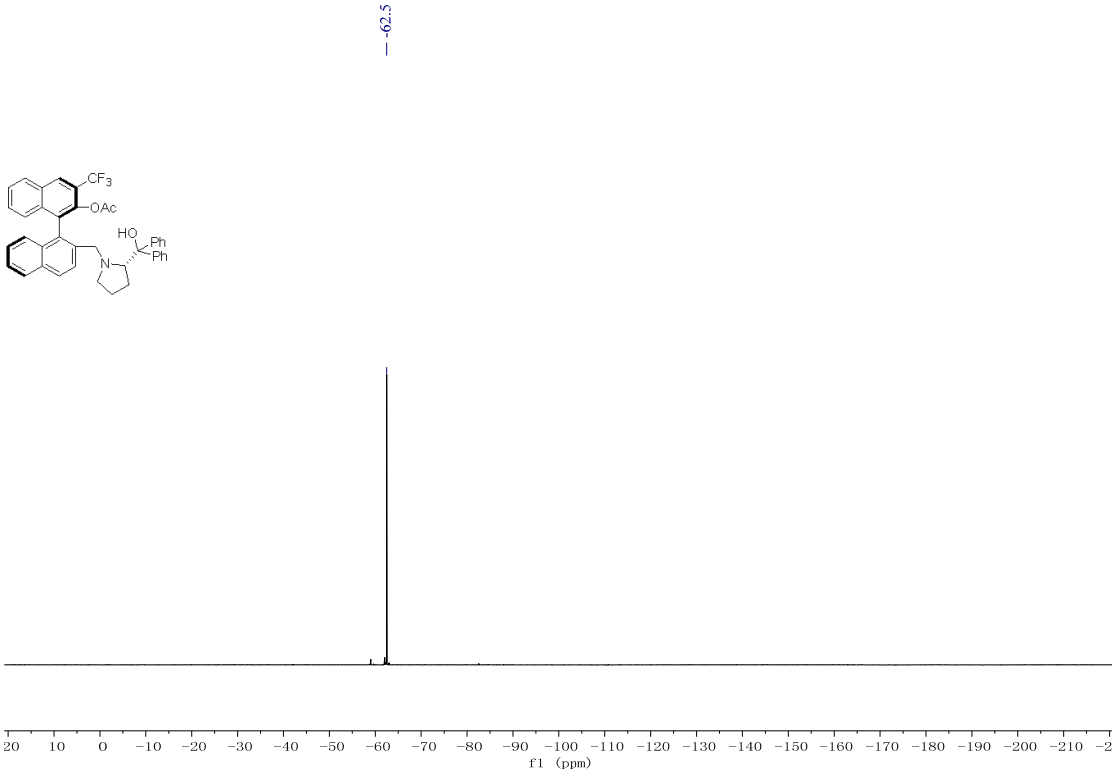
128.5
128.4
128.4
128.3
128.2
128.1
128.0
127.8
127.4
127.0
126.5
126.3
126.3
126.1
126.0
125.7
125.7
125.4
125.2
124.7
122.8
122.5
122.1
122.0
121.8
119.3
78.1
71.3
58.0
55.2
29.8
24.6
19.9
CF3
OAc
HO
Ph
Ph
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)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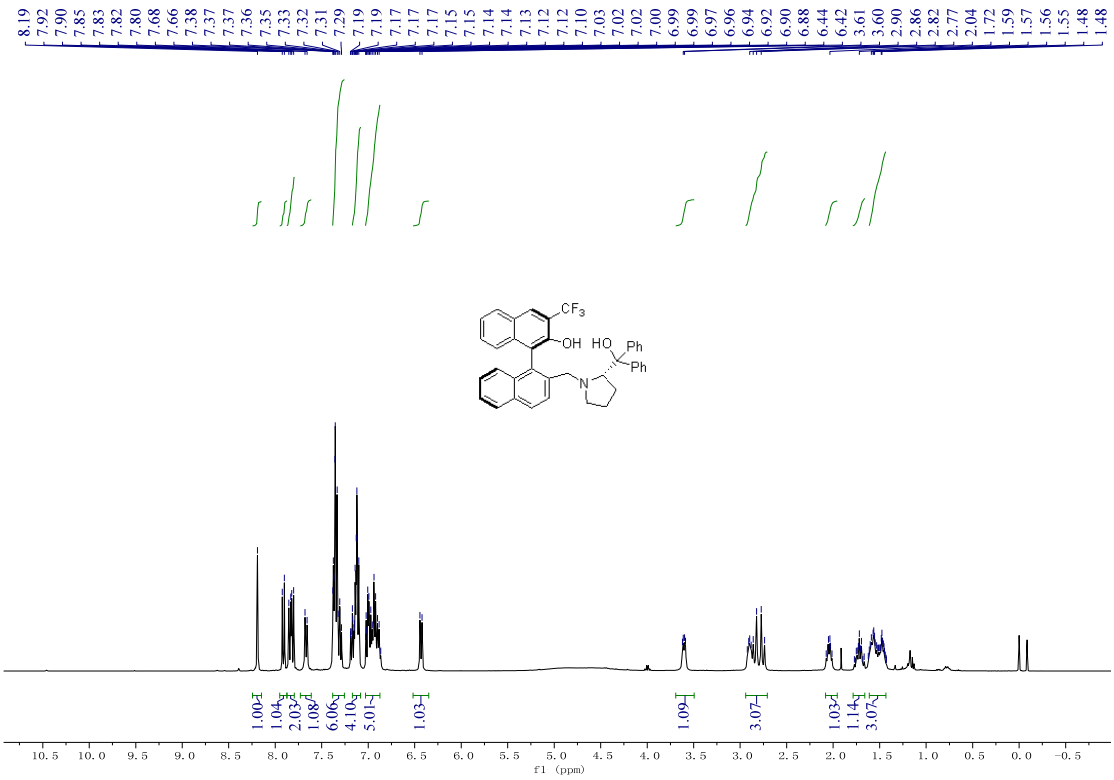
CF3
OAc
HO
Ph
Ph
N
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210 −2
f1 (ppm)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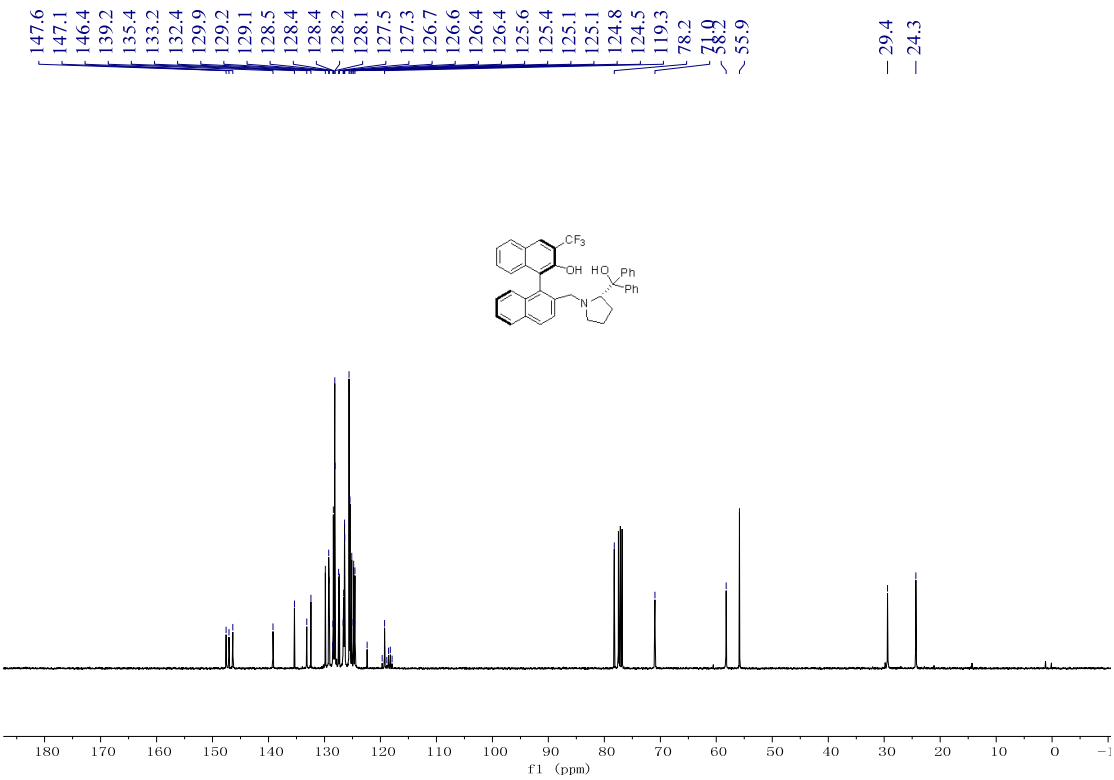
CF3
OH
HO
Ph
Ph
N
1.00 1.04 2.03 1.08 6.06 4.10 5.01 1.03 1.09 3.07 1.03 1.14 3.07
f1 (ppm)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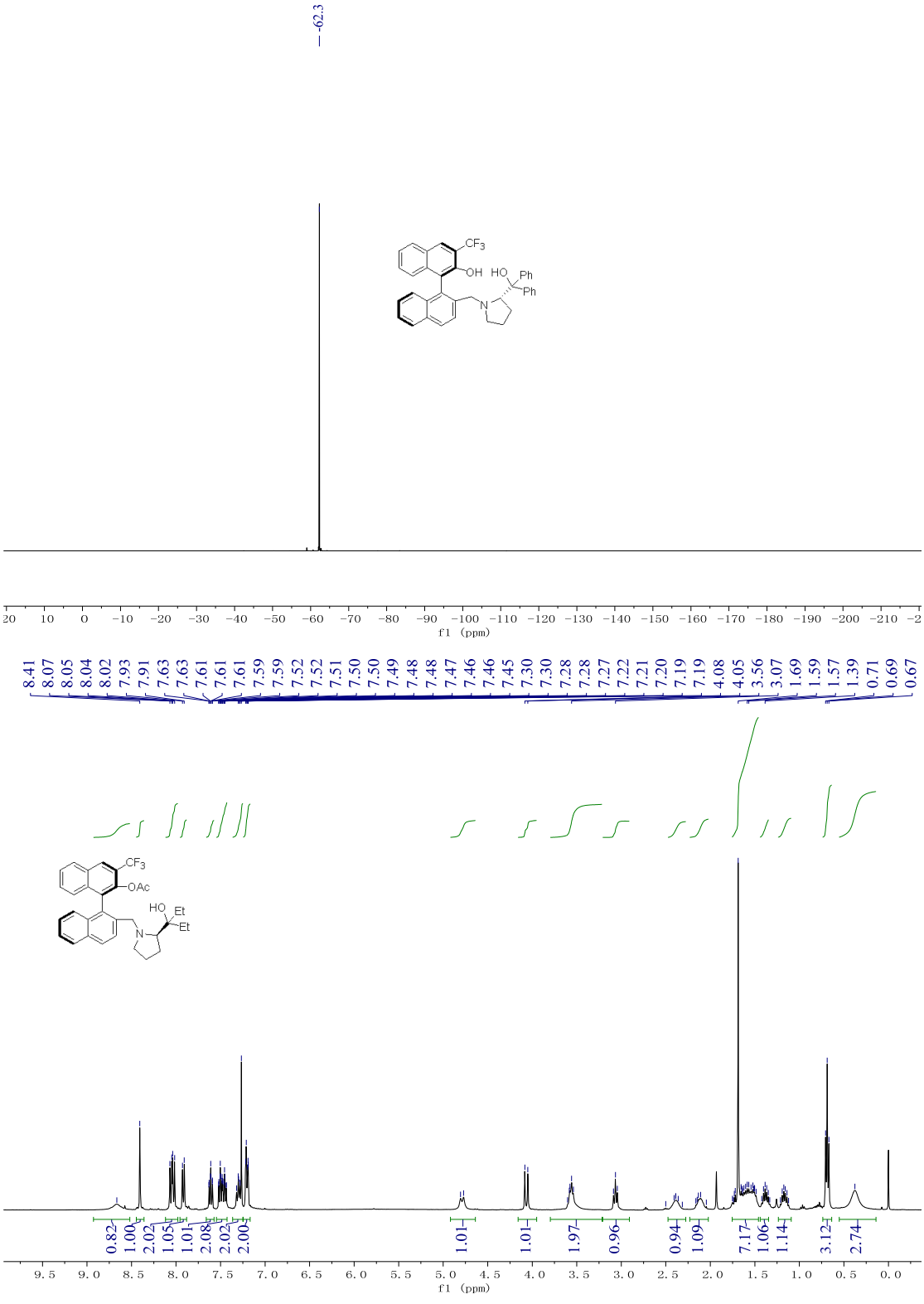
CF3
OH
HO
Ph
Ph
N
f1 (ppm)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CF3
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HO
Ph
Ph
N
f1 (ppm)
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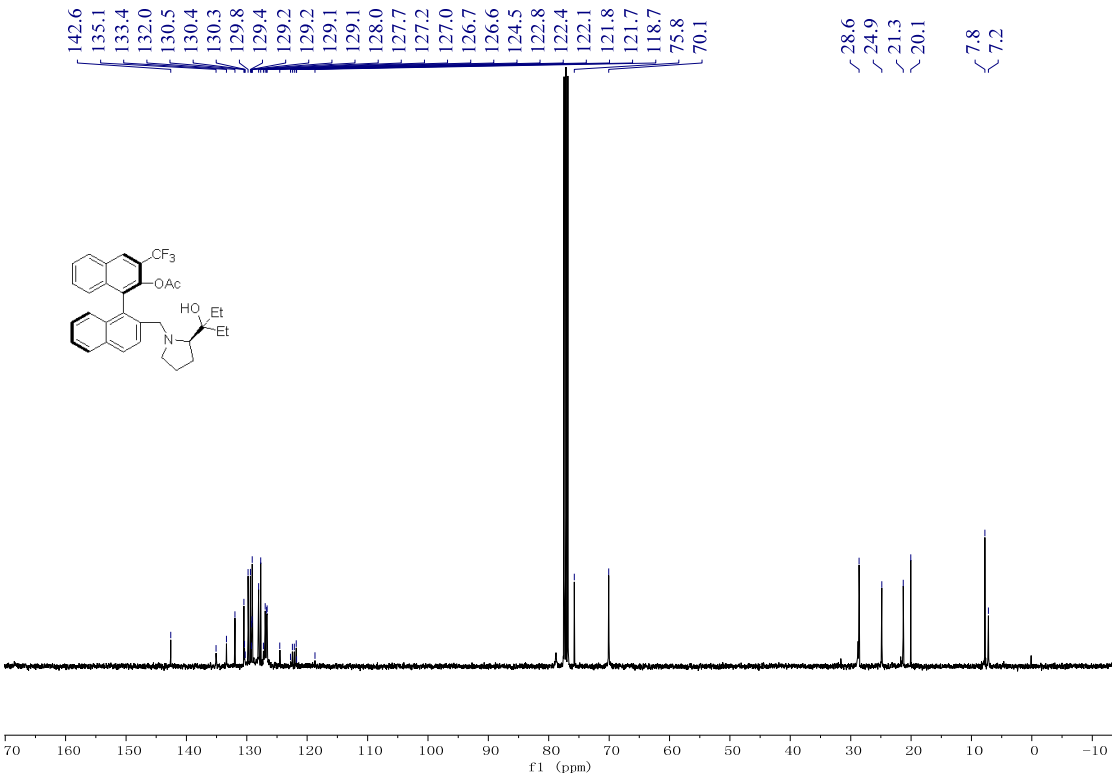
CF3
OAc
HO
Et
Et
N
0.82 1.00 2.02 1.05 1.01 2.08 2.02 2.00 1.01 1.01 1.97 0.96 0.94 1.09 7.17 1.06 1.14 3.12 2.74
f1 (ppm)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129.2
129.2
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128.0
127.7
127.2
127.0
126.7
126.6
124.5
122.8
122.4
122.1
121.8
121.7
118.7
75.8
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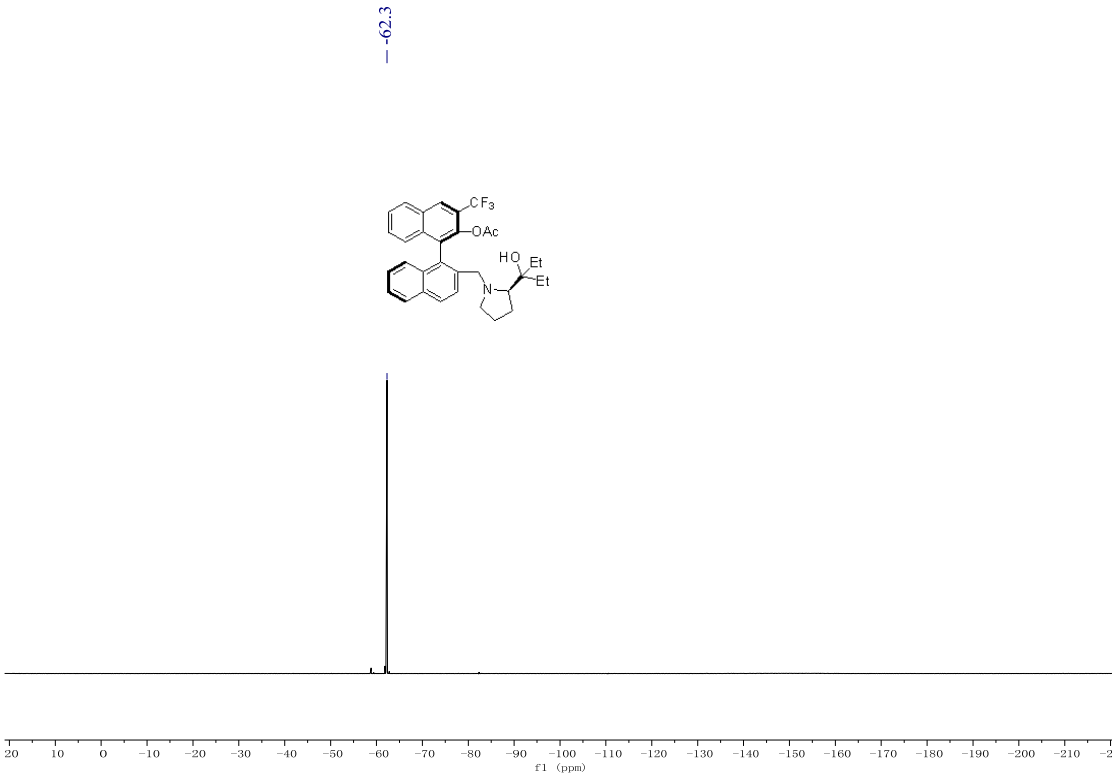
21.3
20.1
7.8
7.2
CF3
OAc
HO
Et
Et
N
f1 (ppm)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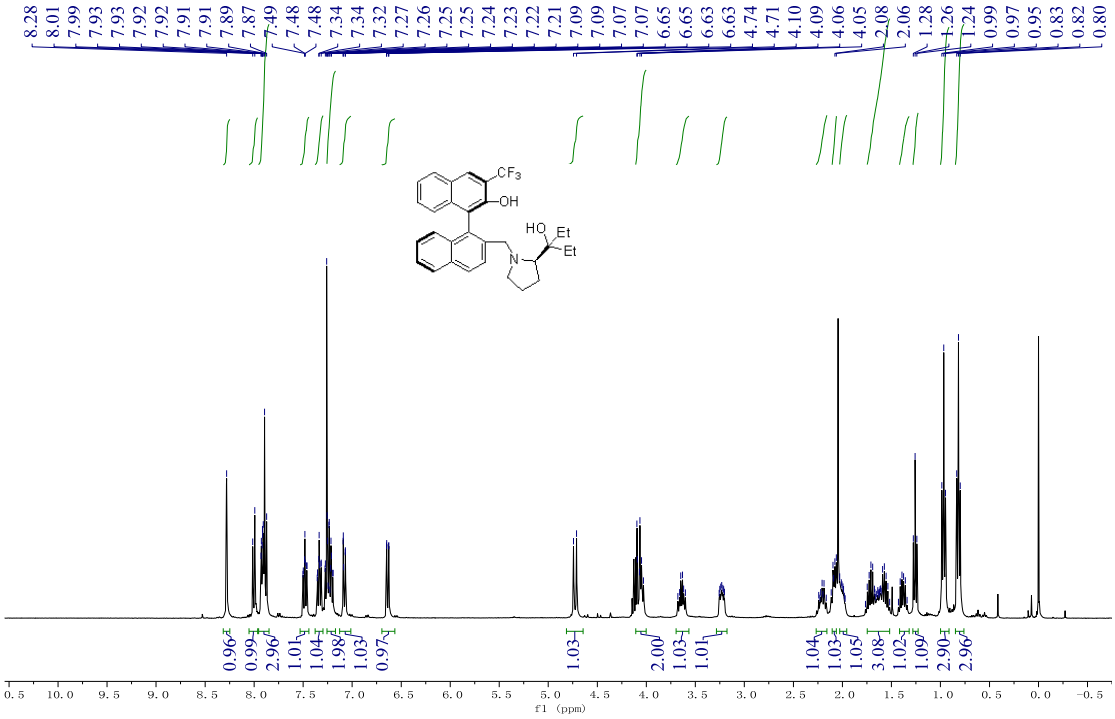
Et
Et
N
f1 (ppm)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7.32
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7.25
7.24
7.23
7.22
7.21
7.09
7.09
7.07
7.07
6.65
6.65
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6.63
4.74
4.71
4.10
4.09
4.06
4.05
2.08
2.06
1.28
1.26
1.24
0.99
0.97
0.95
0.83
0.82
0.80
CF3
OH
HO
Et
Et
N
0.96
0.99
2.96
1.01
1.04
1.98
1.03
0.97
1.03
2.00
1.03
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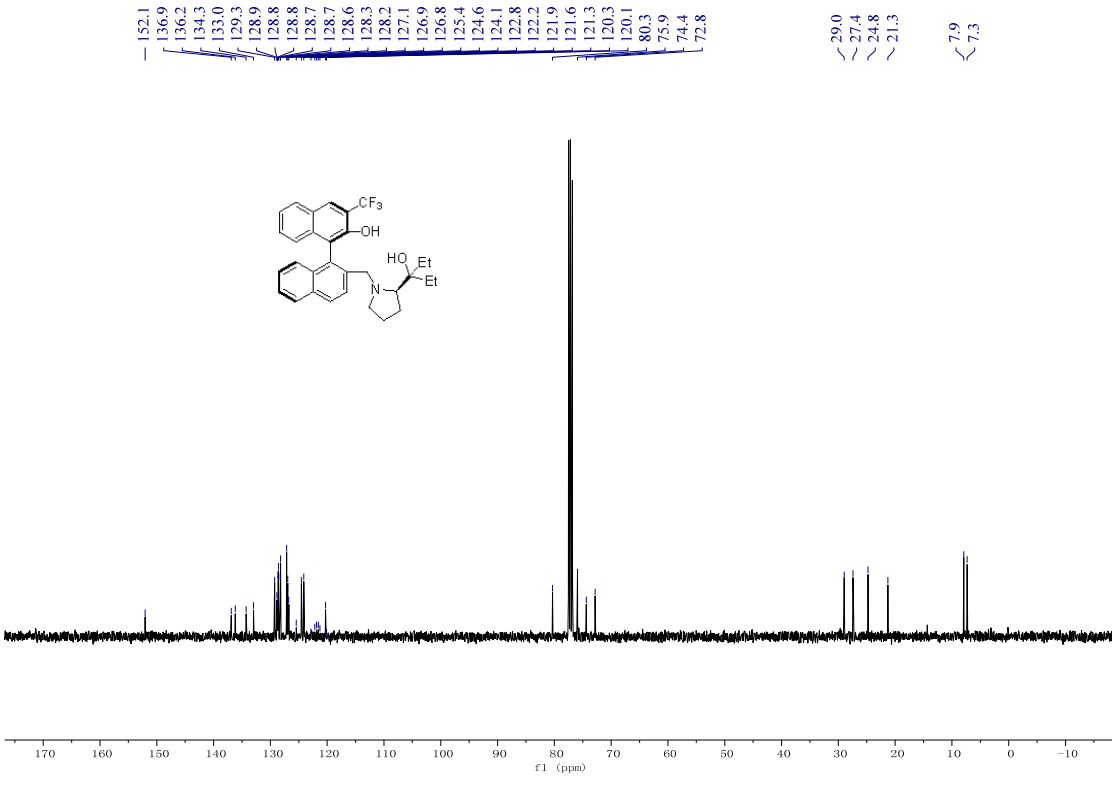
1.04
1.03
1.05
3.08
1.02
1.09
2.90
2.96
f1 (ppm)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128.3
128.2
127.1
126.9
126.8
125.4
124.6
124.1
122.8
122.2
121.9
121.6
121.3
120.3
120.1
80.3
75.9
74.4
72.8
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24.8
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7.9
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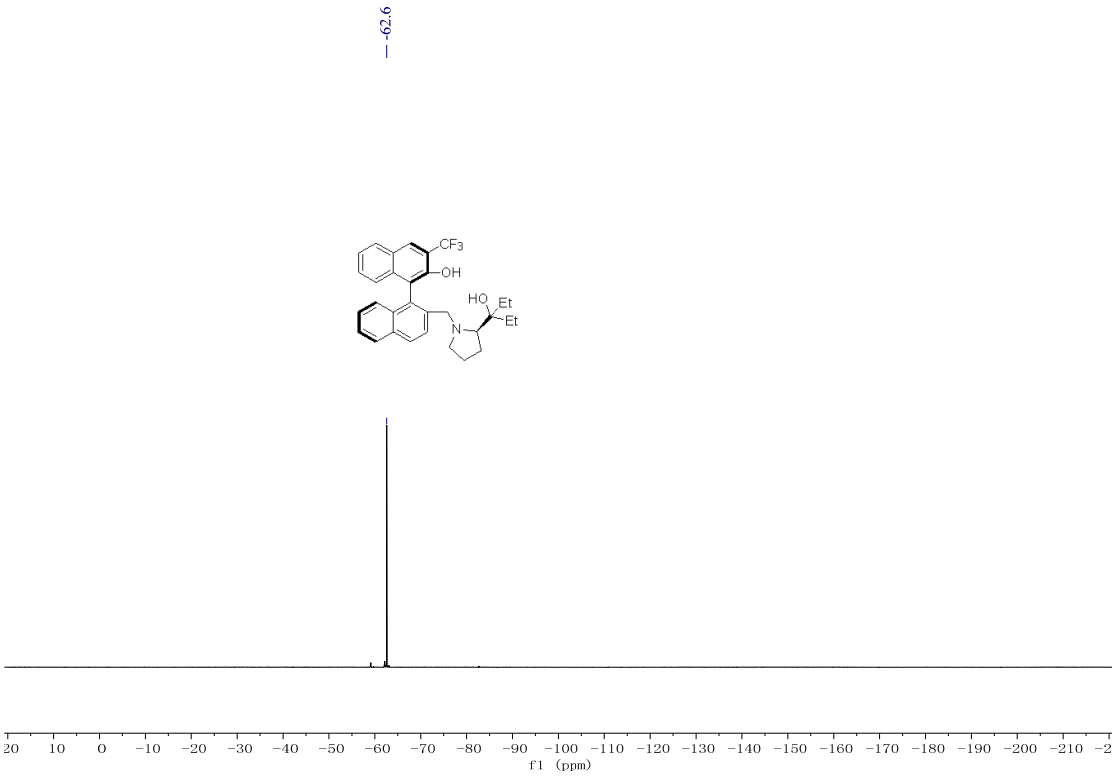
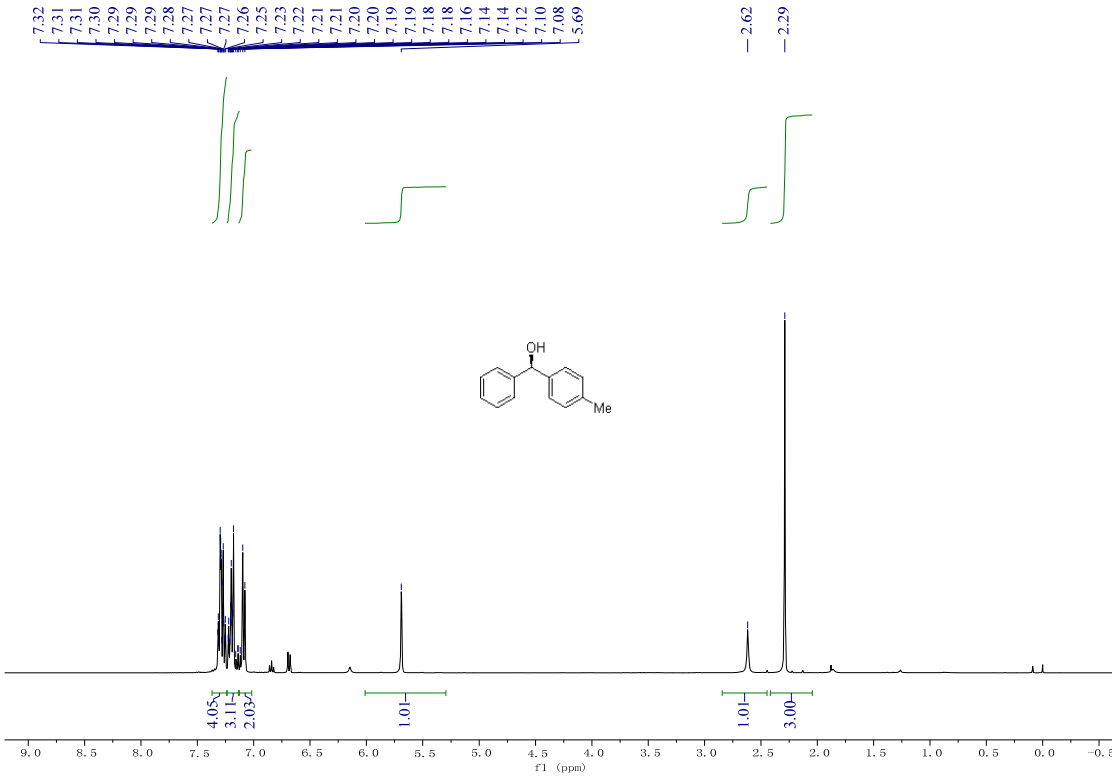
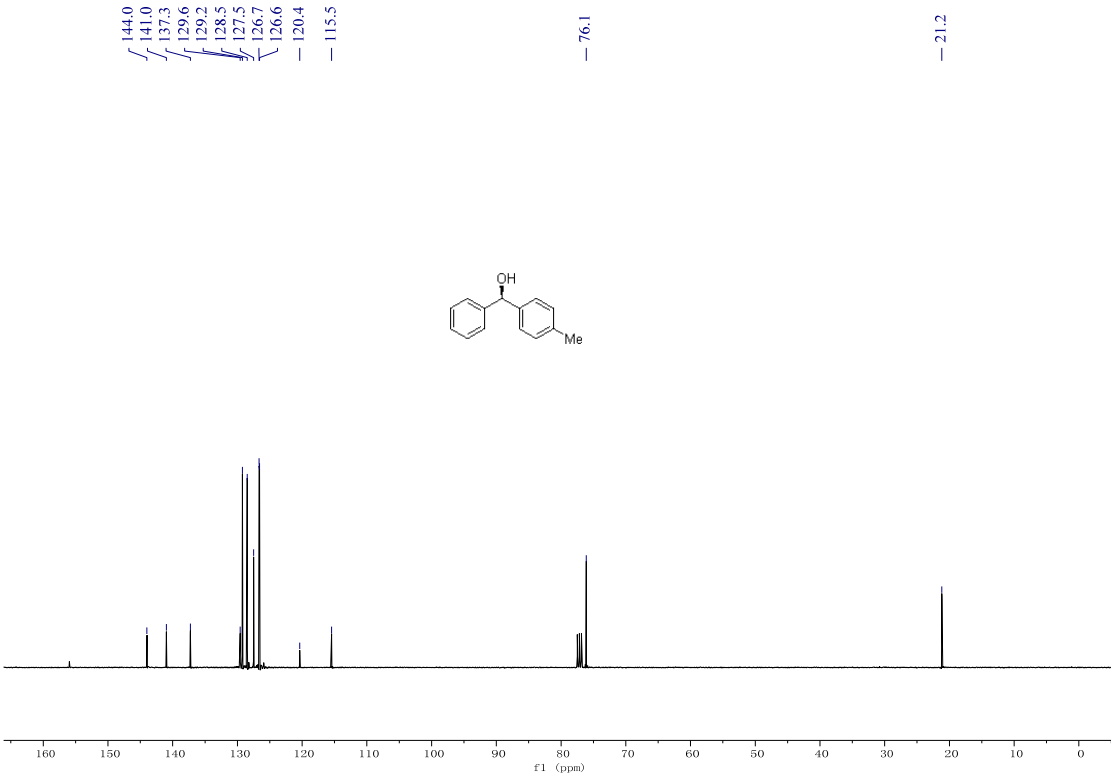
CF3
OH
HO
Et
Et
N
f1 (ppm)



5. Copies of NMR Spectra of Products

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115.5
76.1
21.2
OH
Me
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150
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130
120
110
100
90
80
70
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50
40
30
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10
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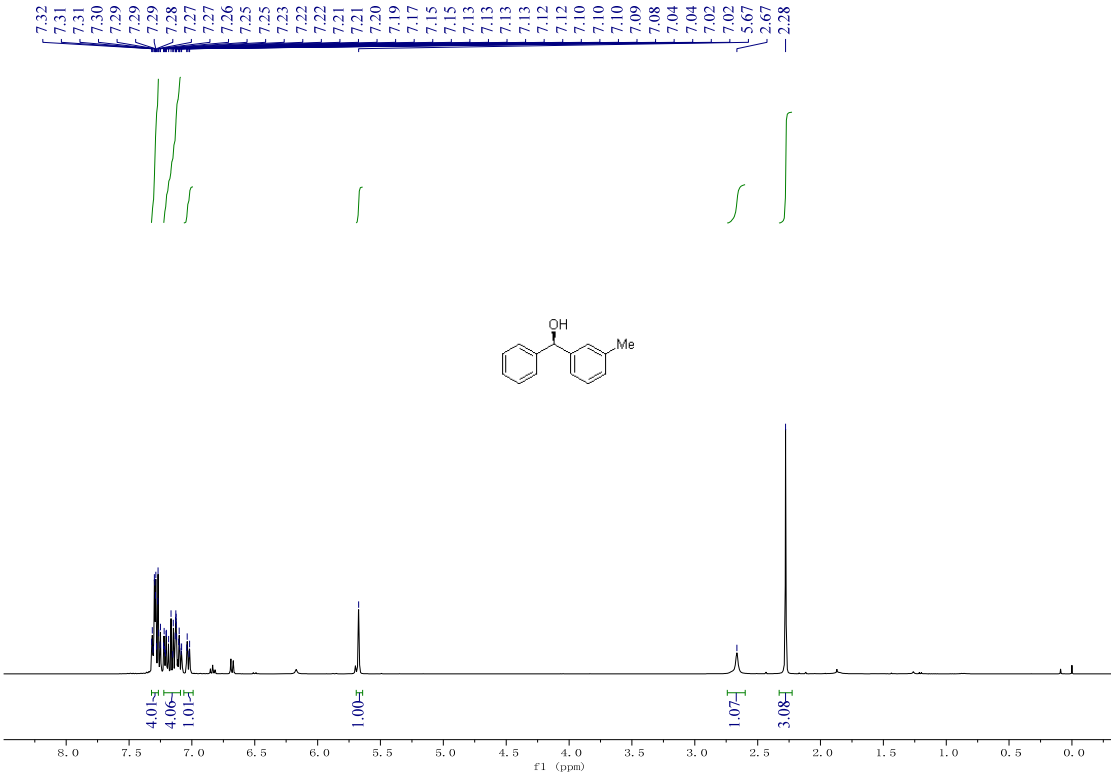
f1 (ppm)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7.22
7.21
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7.20
7.19
7.17
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7.15
7.13
7.13
7.13
7.12
7.12
7.10
7.10
7.10
7.09
7.08
7.04
7.04
7.02
7.02
5.67
2.67
2.28
OH
Me
4.01
4.06
1.01
1.00
1.07
3.08
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
1.5
1.0
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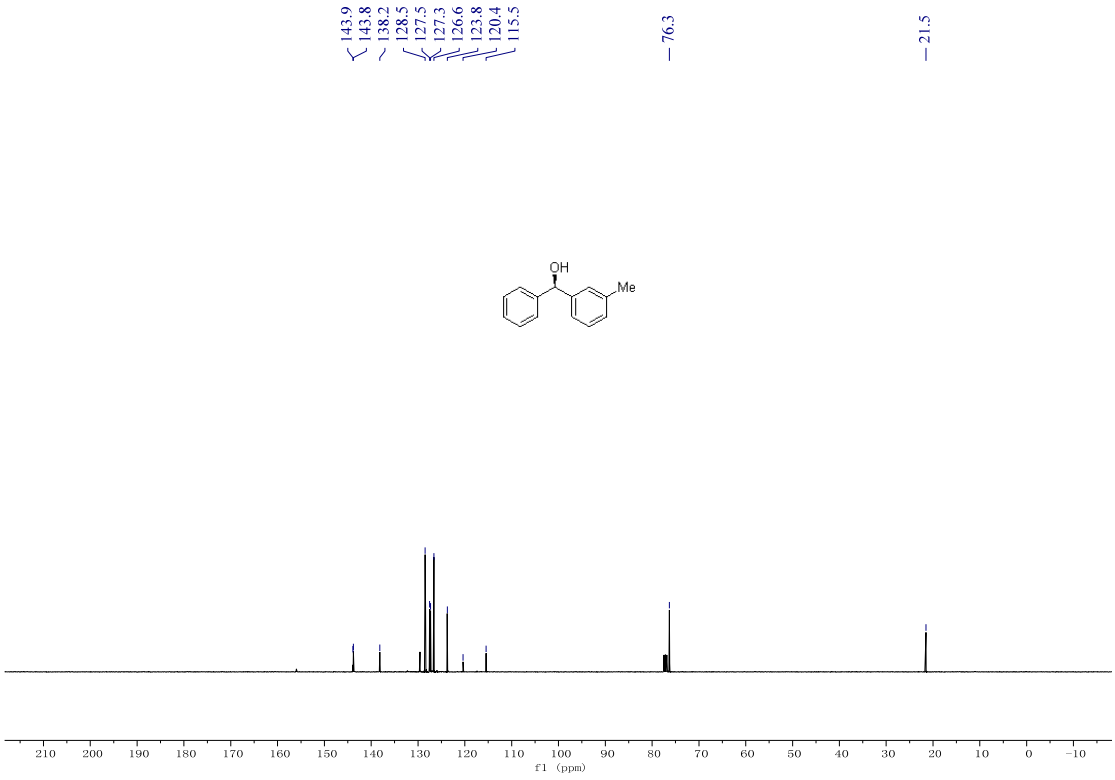
0.0
f1 (ppm)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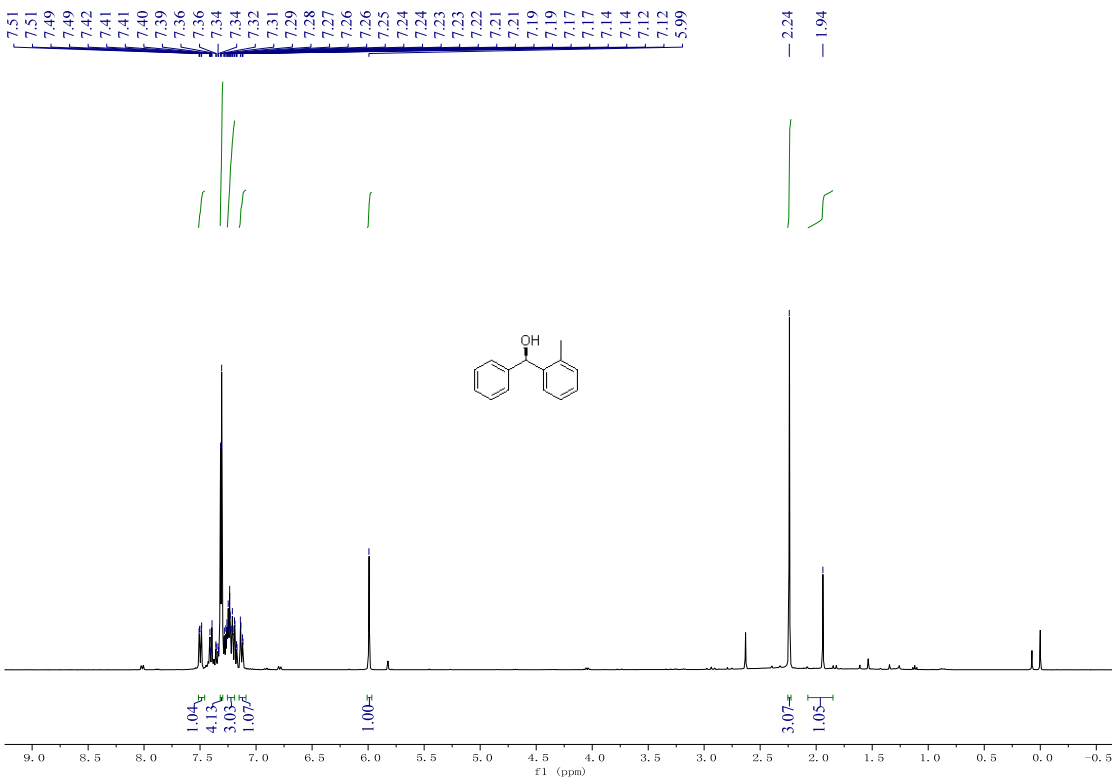
127.3
126.6
123.8
120.4
115.5
76.3
21.5
OH
Me
f1 (ppm)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7.19
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7.14
7.14
7.12
7.12
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OH
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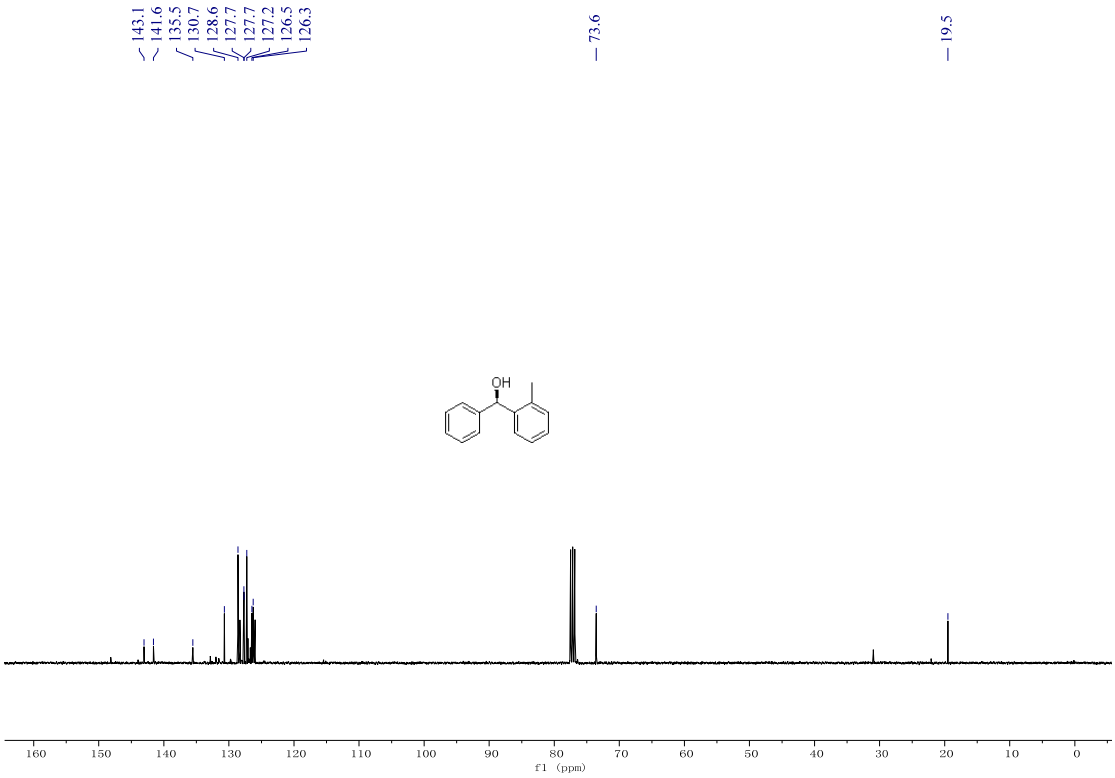
1.00
3.07
1.05
f1 (ppm)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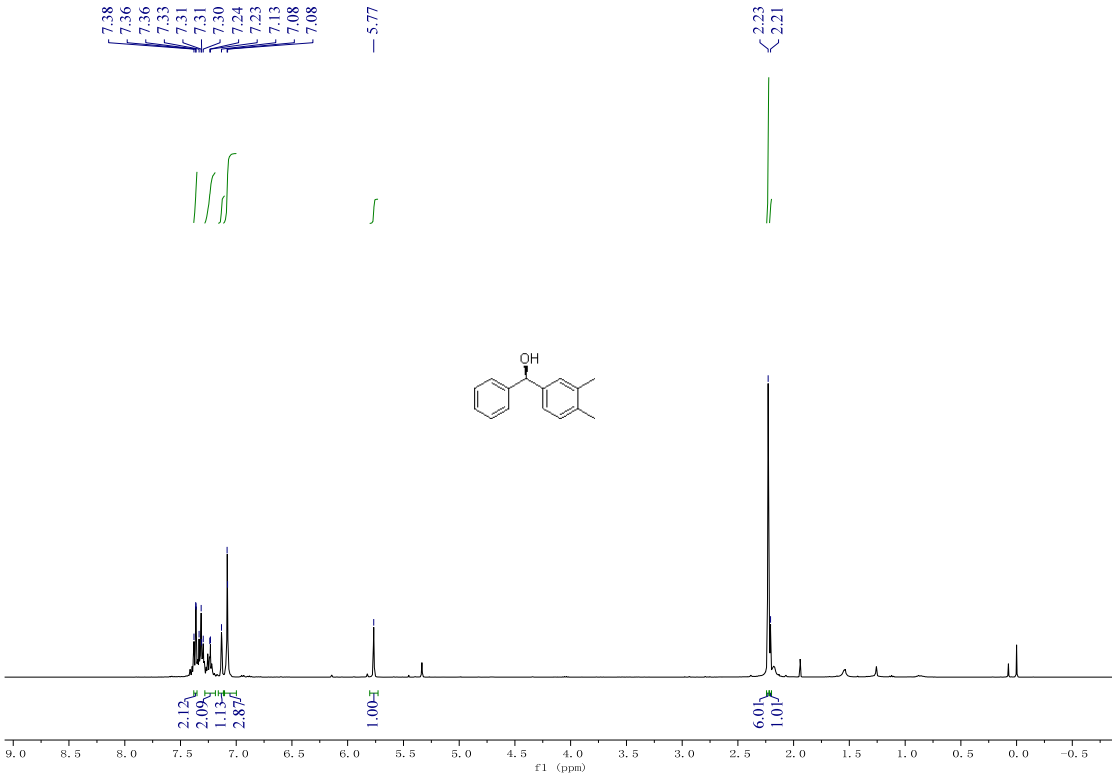
130.7
128.6
127.7
127.7
127.2
126.5
126.3
73.6
19.5
OH
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.08
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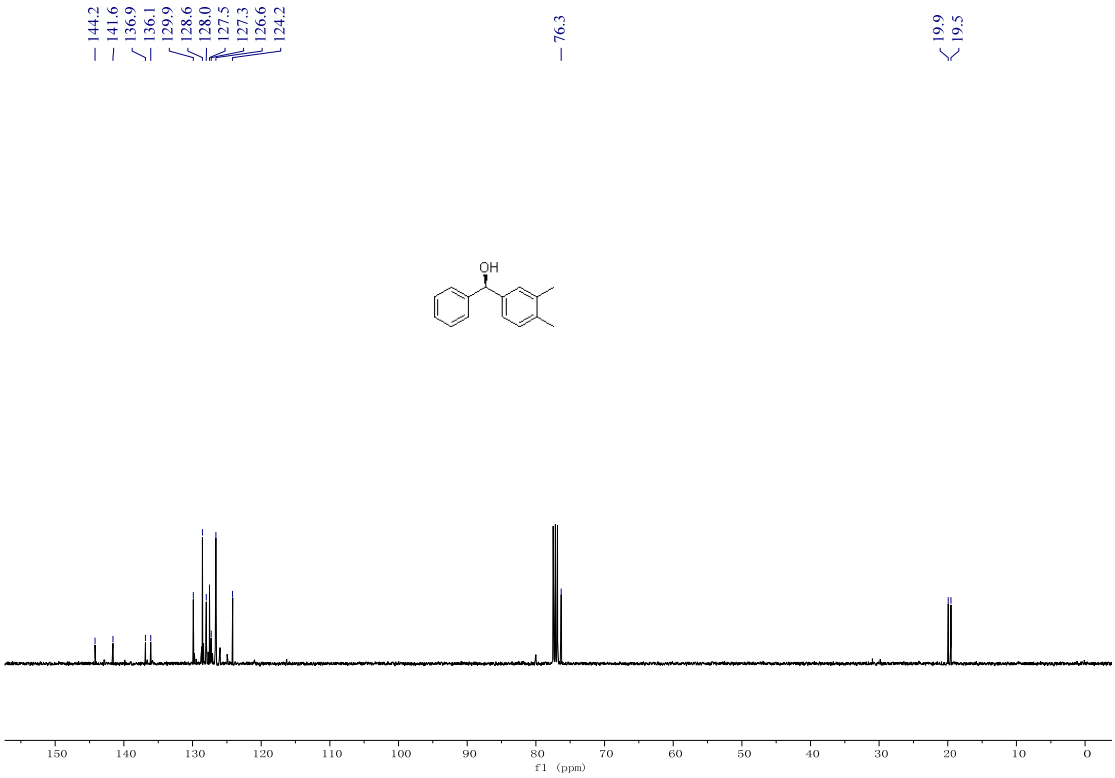
2.23
2.21
OH
2.12
2.09
1.13
2.87
1.00
6.01
1.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.6
128.0
127.5
127.3
126.6
124.2
76.3
19.9
19.5
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130
120
110
100
90
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70
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50
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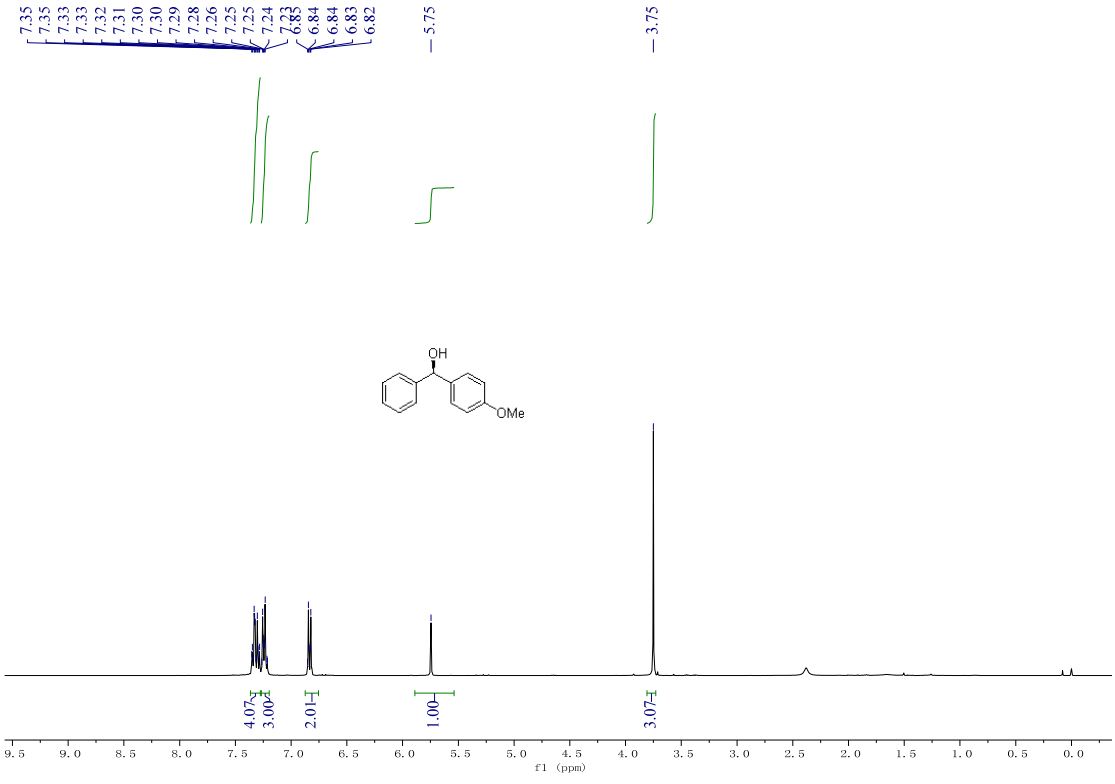
0
f1 (ppm)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6.84
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3.75
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2.01
1.00
3.07
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6.5
6.0
5.5
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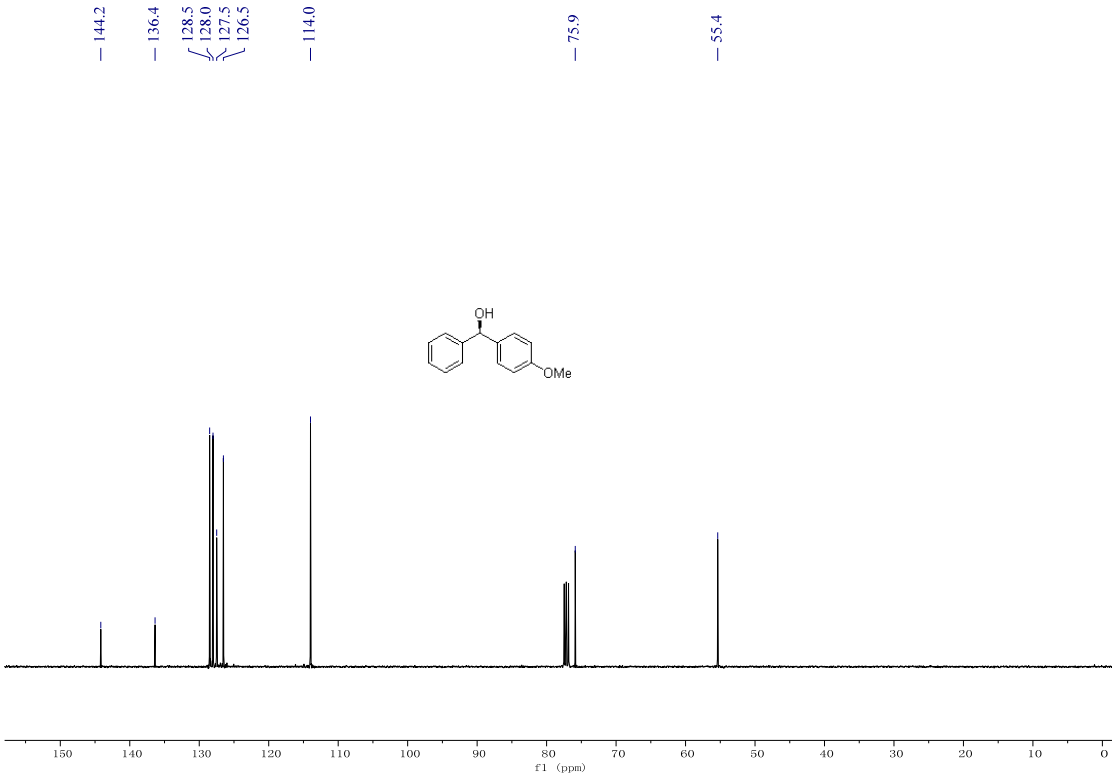
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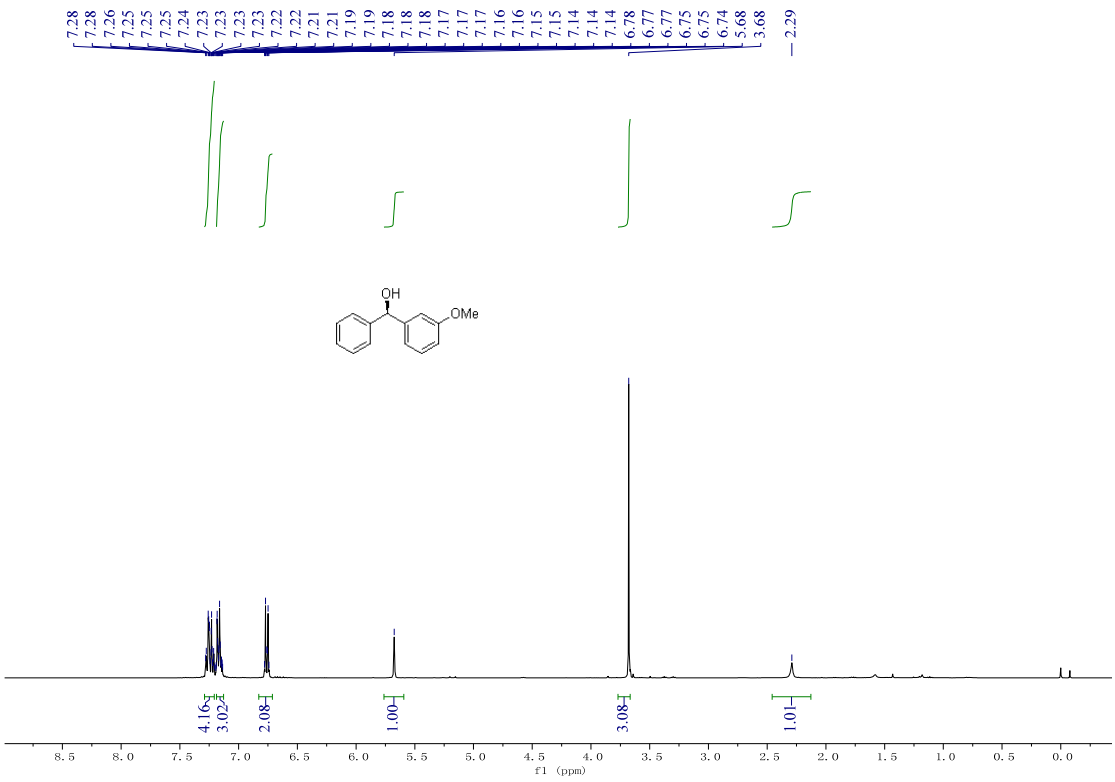
OH
OMe
f1 (ppm)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7.14
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6.75
6.75
6.74
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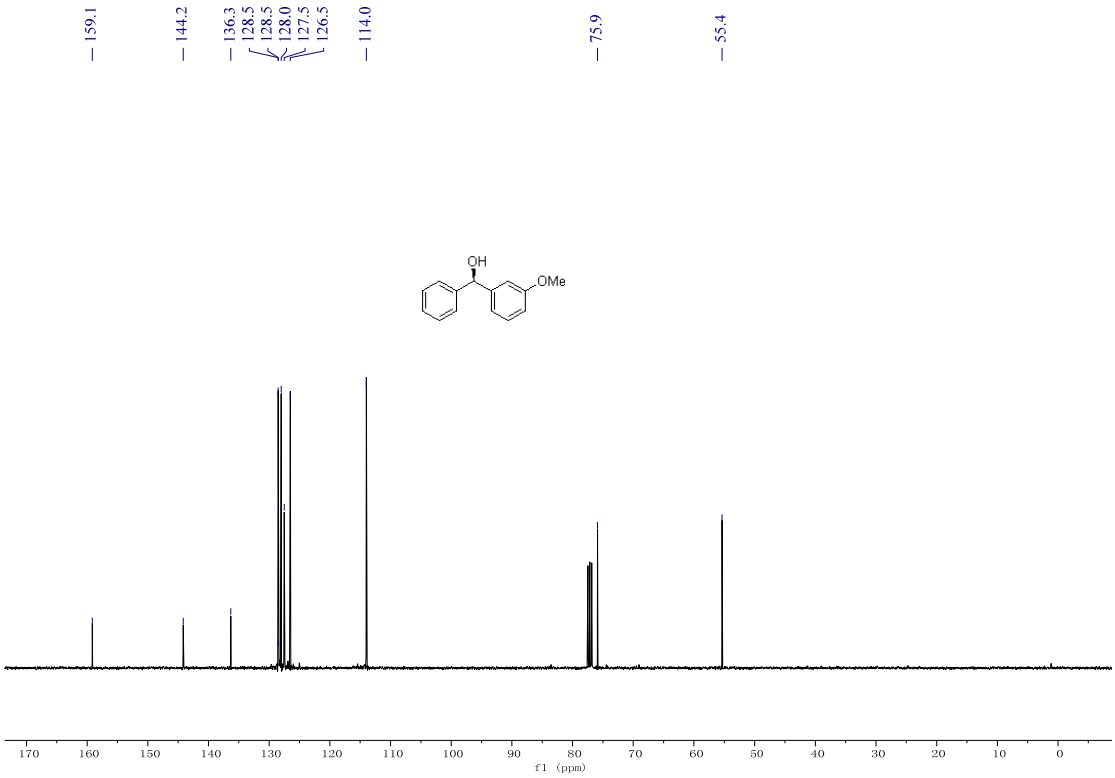
2.08
1.00
3.08
1.01
f1 (ppm)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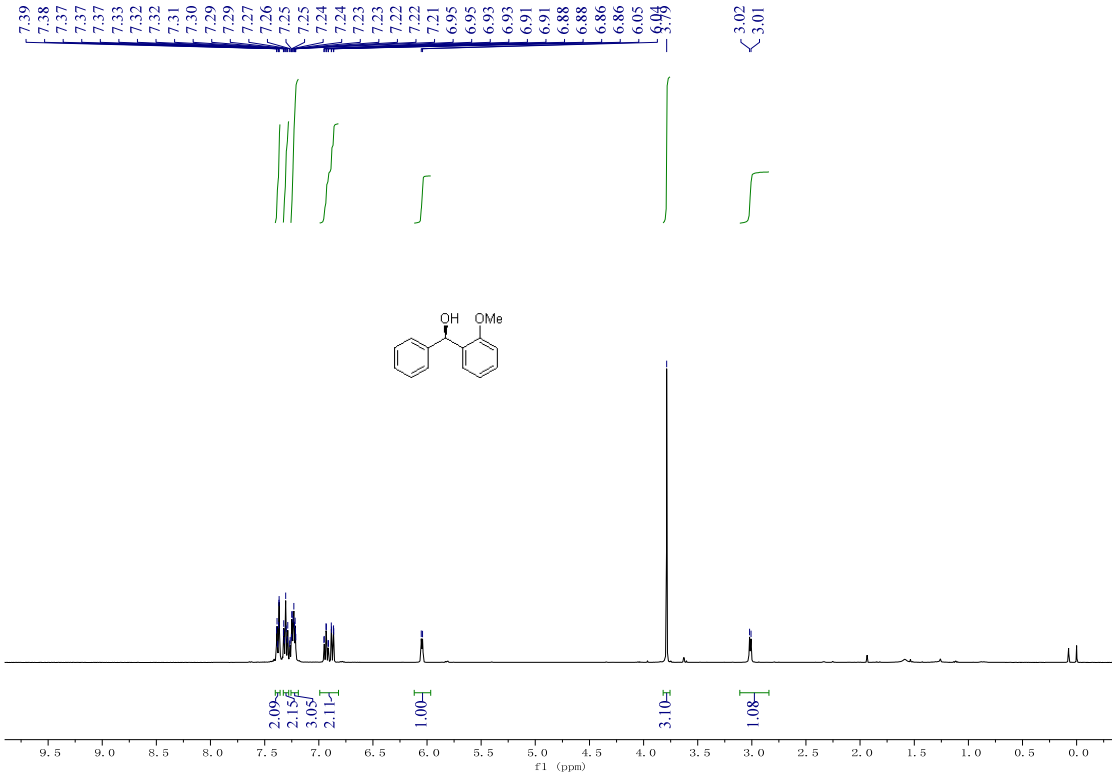
OH
OMe
f1 (ppm)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6.04
3.79
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OH
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3.05
2.11
1.00
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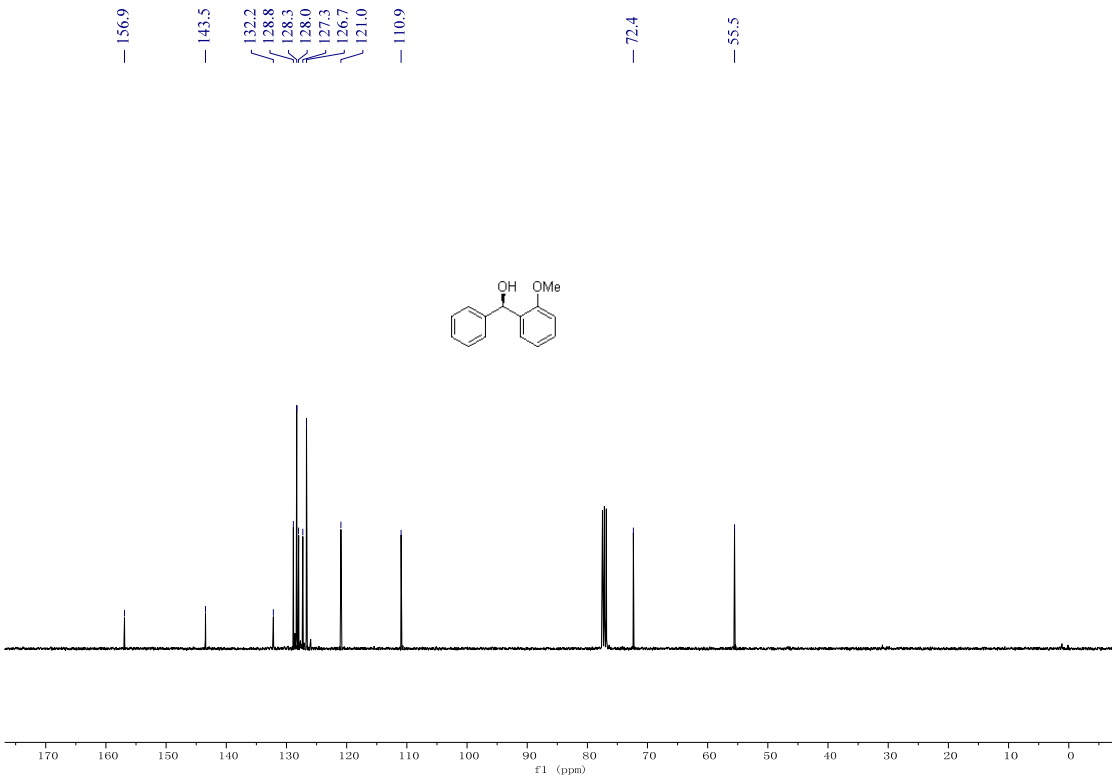
1.08
f1 (ppm)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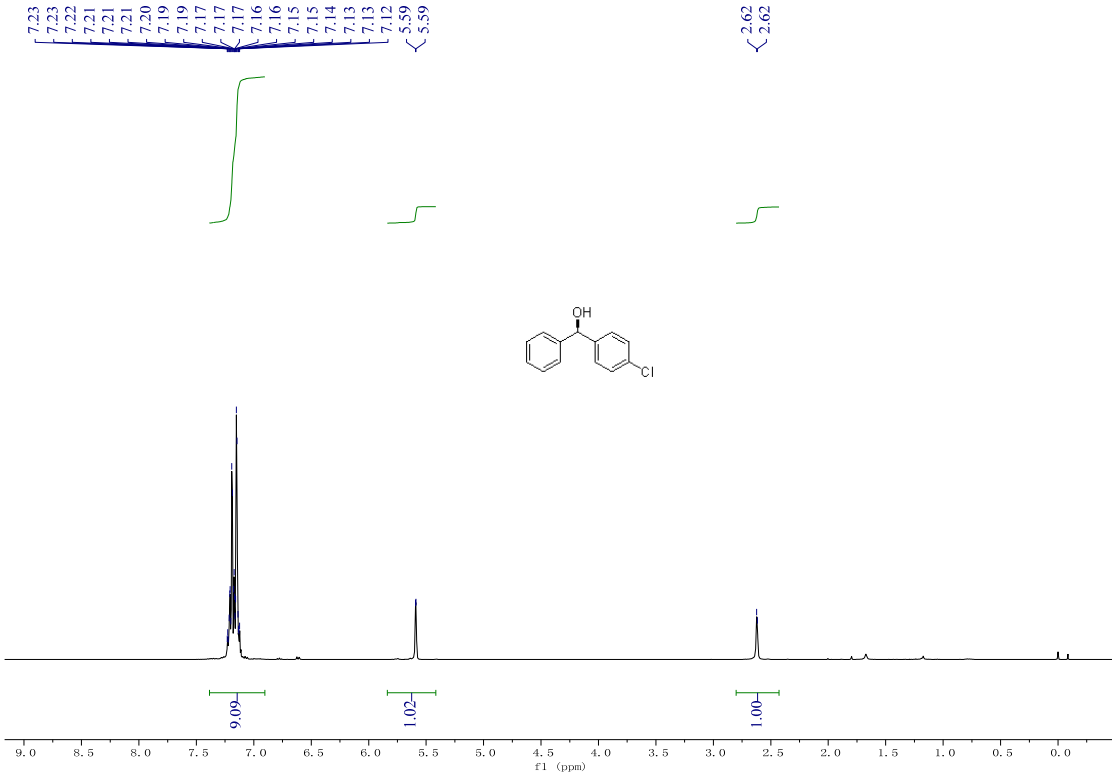
127.3
126.7
121.0
110.9
72.4
55.5
OH
OMe
f1 (ppm)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7.15
7.15
7.14
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5.59
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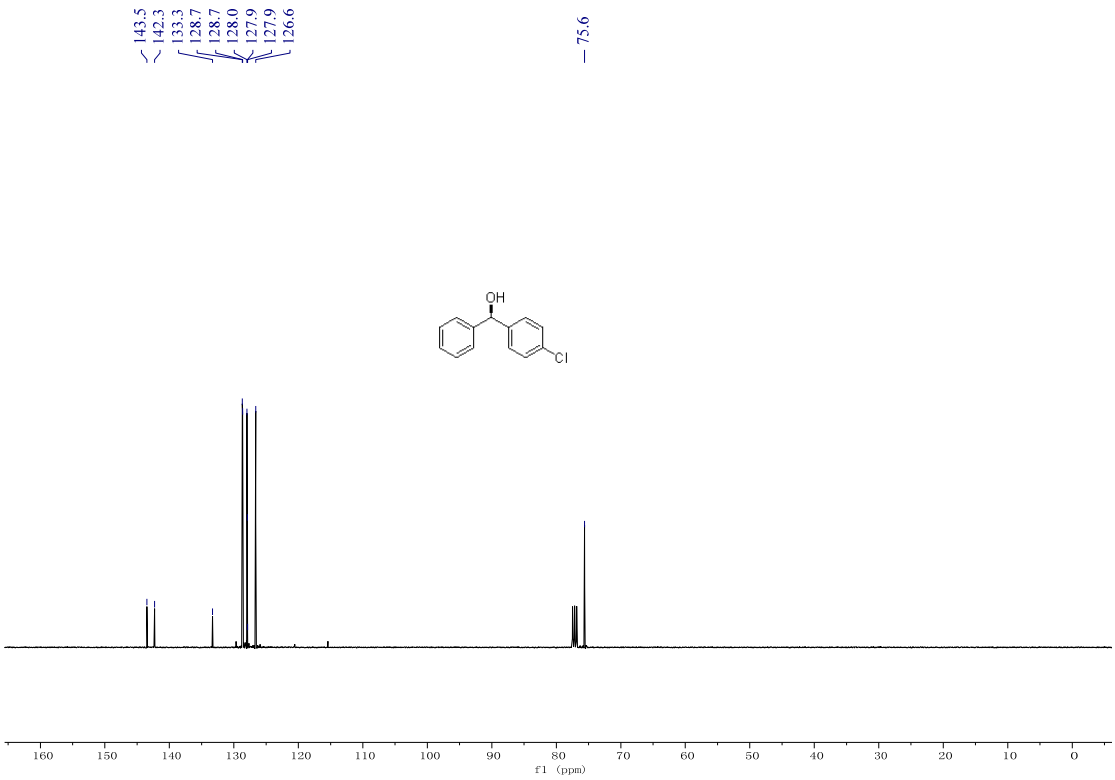
2.62
OH
Cl
9.09
1.02
1.00
f1 (ppm)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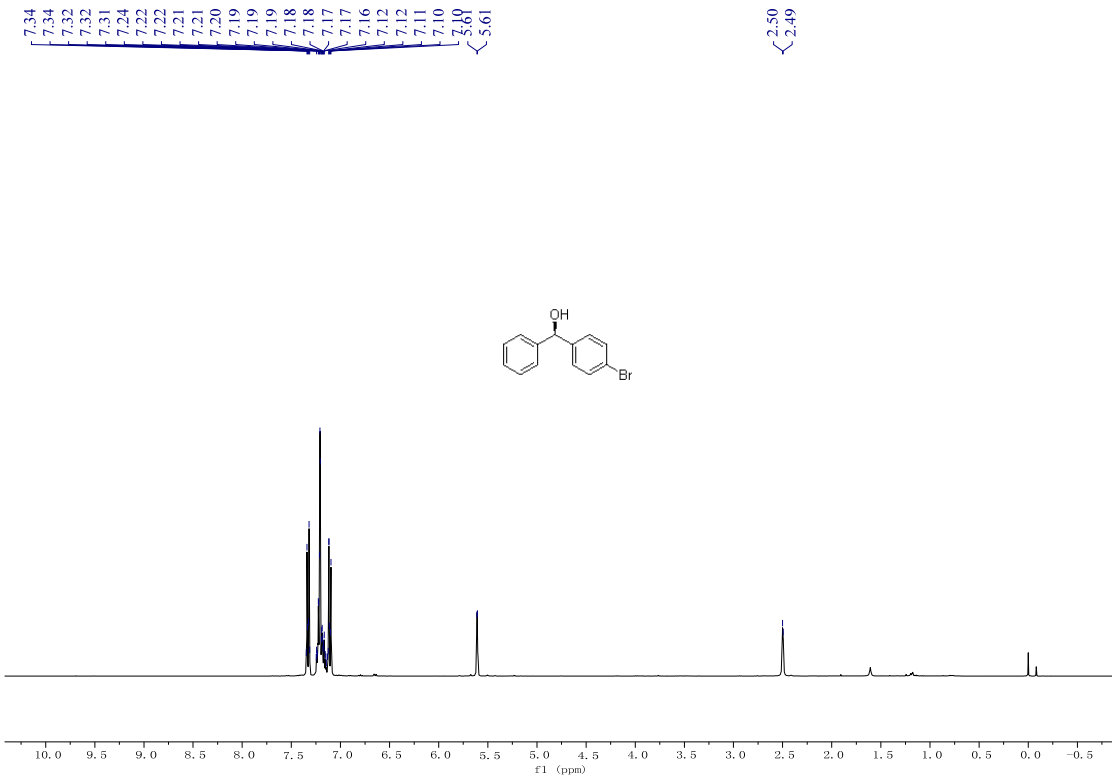
126.6
75.6
OH
Cl
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.16
7.12
7.12
7.11
7.10
7.10
5.61
5.61
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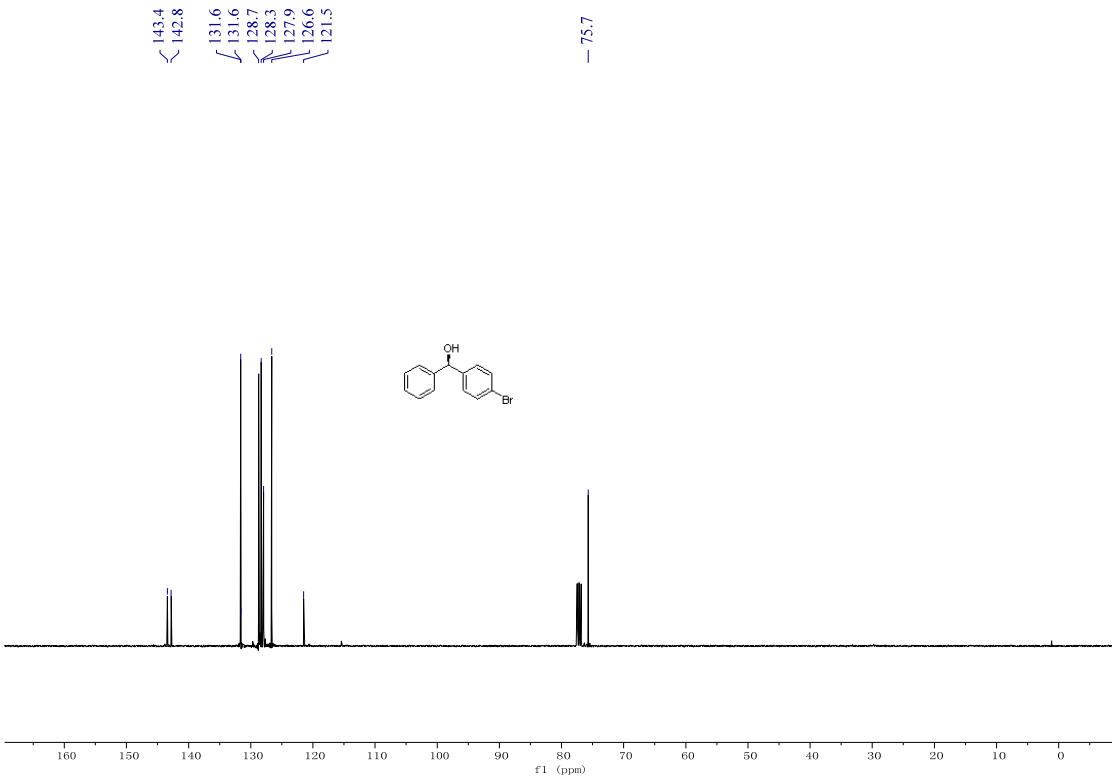
2.49
OH
Br
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.3
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126.6
121.5
75.7
OH
Br
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150
140
130
120
110
100
90
80
70
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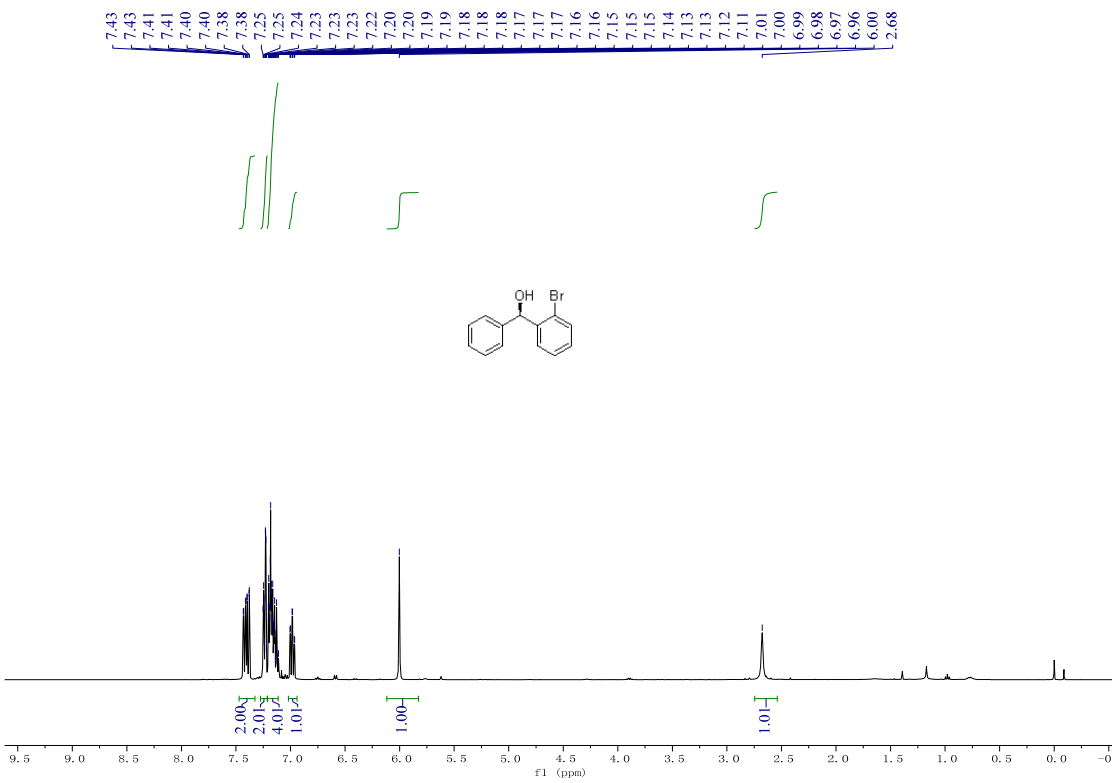
50
40
30
20
10
0
f1 (ppm)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7.14
7.13
7.13
7.12
7.11
7.01
7.00
6.99
6.98
6.97
6.96
6.00
2.68
OH
Br
2.00
2.01
4.01
1.01
1.00
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
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2.0
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1.0
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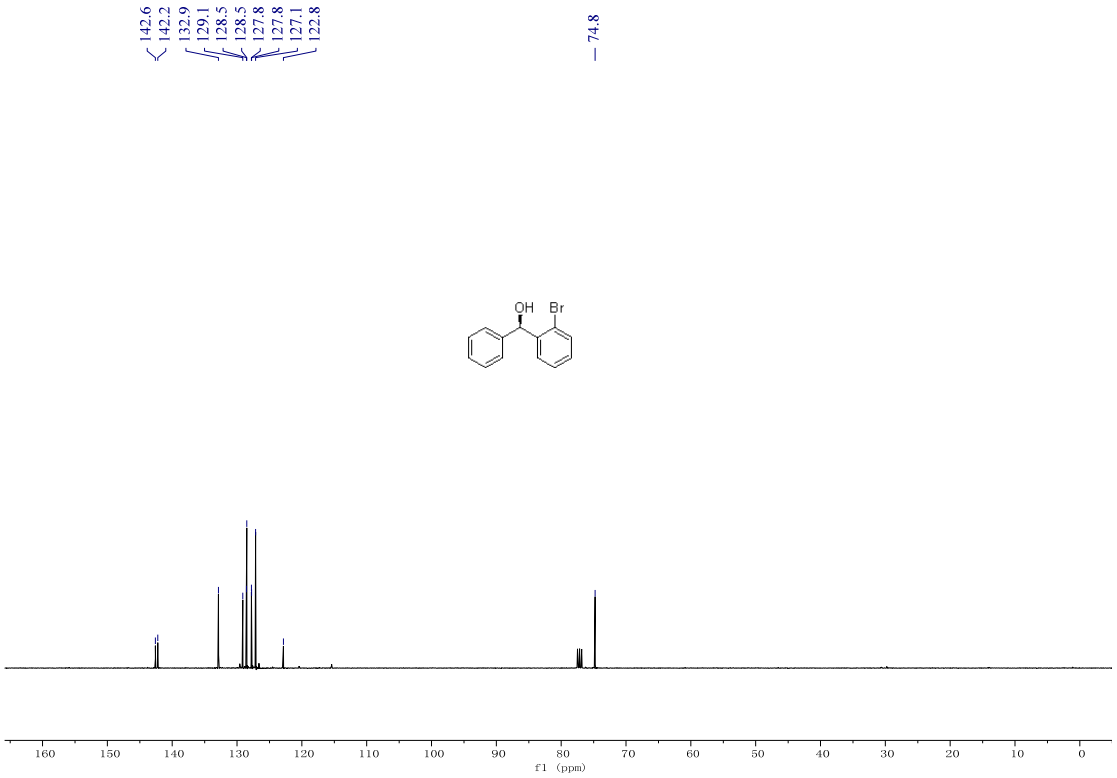
f1 (ppm)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74.8
OH
Br
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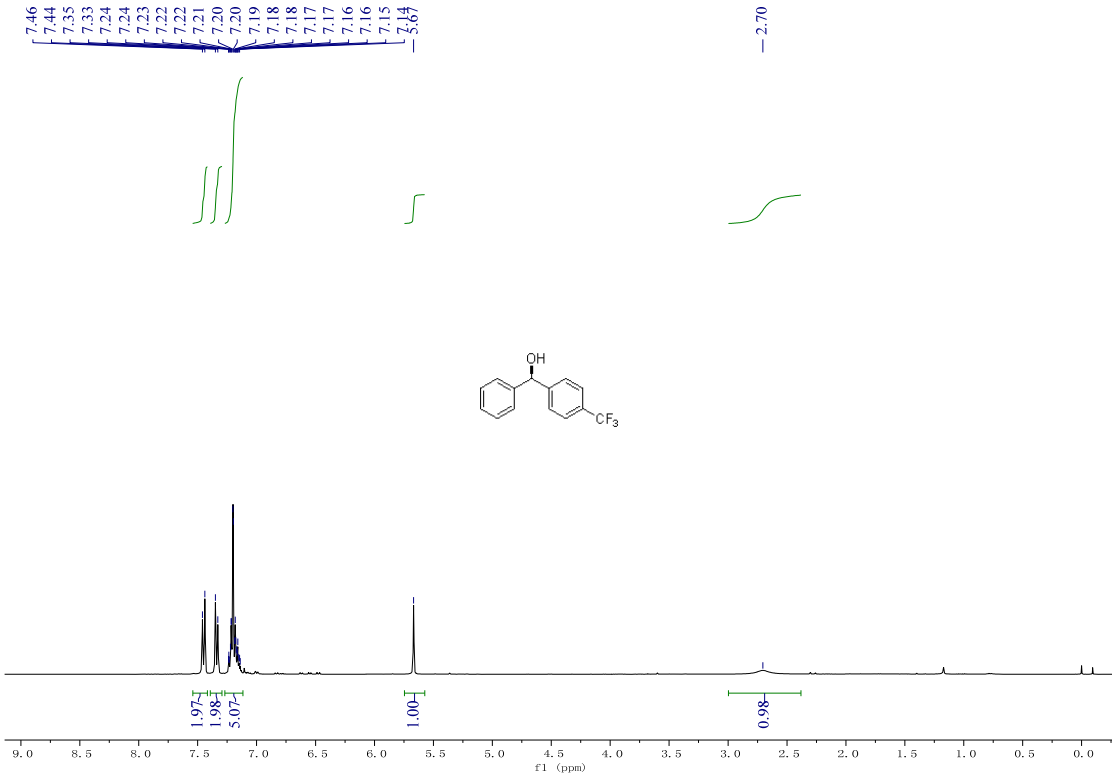
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.16
7.15
7.14
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2.70
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CF3
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1.98
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1.00
0.98
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
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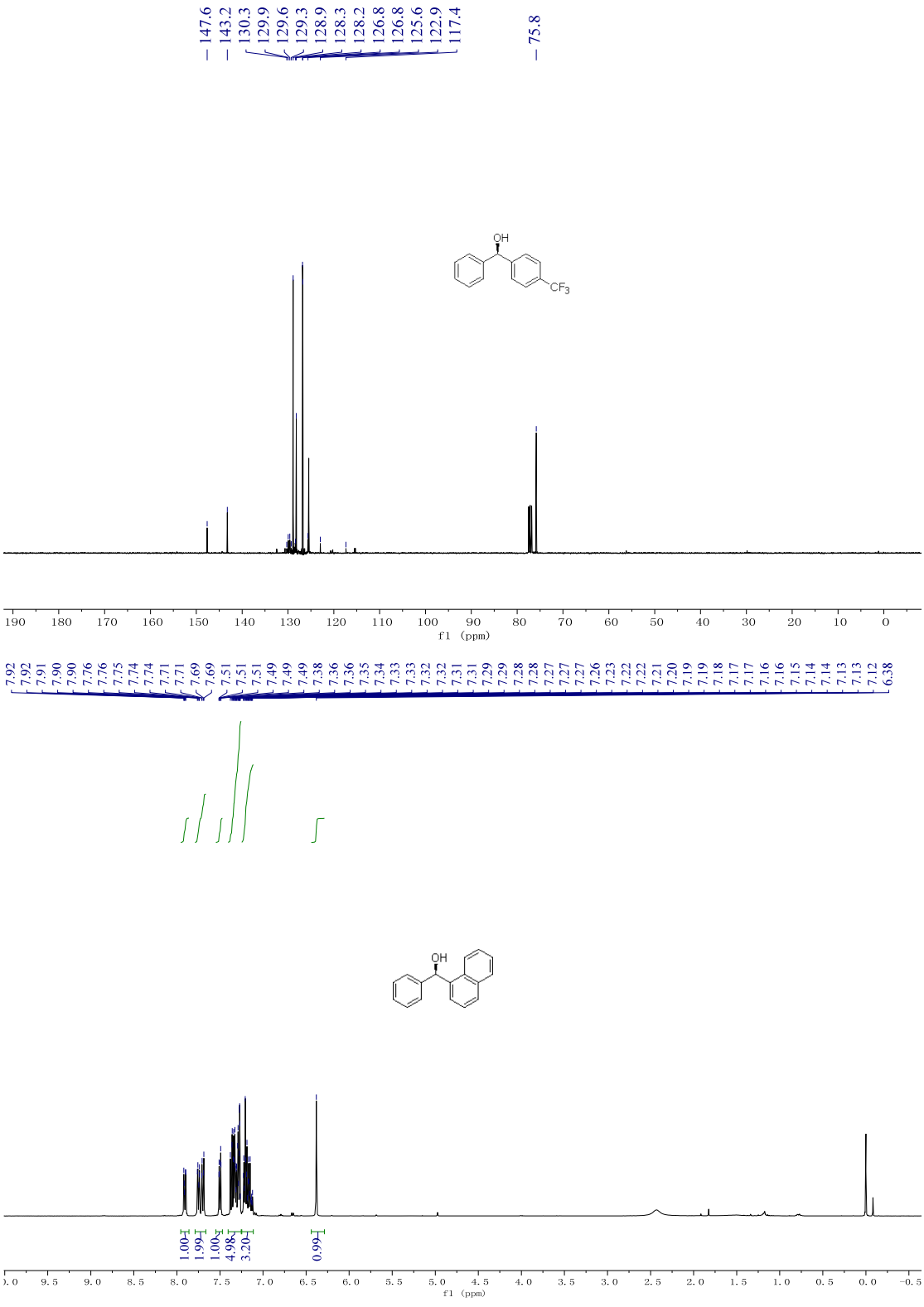
1.0
0.5
0.0
f1 (ppm)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128.3
128.2
126.8
126.8
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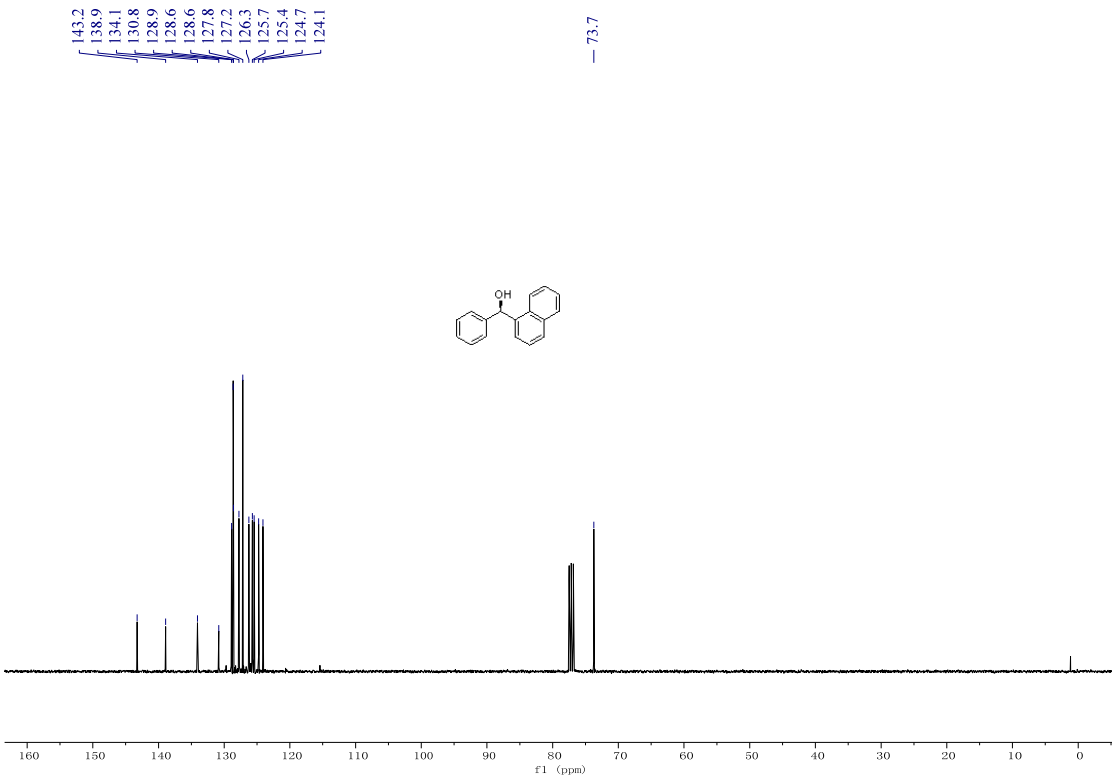
122.9
117.4
75.8
OH
CF3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
7.92 7.92 7.91 7.90 7.90 7.76 7.76 7.75 7.74 7.74 7.71 7.71 7.69 7.69 7.51 7.51 7.51 7.49 7.49 7.49 7.38 7.36 7.36 7.35 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.29 7.29 7.28 7.28 7.27 7.27 7.27 7.26 7.23 7.22 7.22 7.21 7.20 7.19 7.19 7.18 7.17 7.17 7.16 7.16 7.15 7.14 7.14 7.13 7.13 7.12 6.38
OH
1.00 1.99 1.00 4.98 3.20 0.99
9.5 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 -0.5
f1 (ppm)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124.7
124.1
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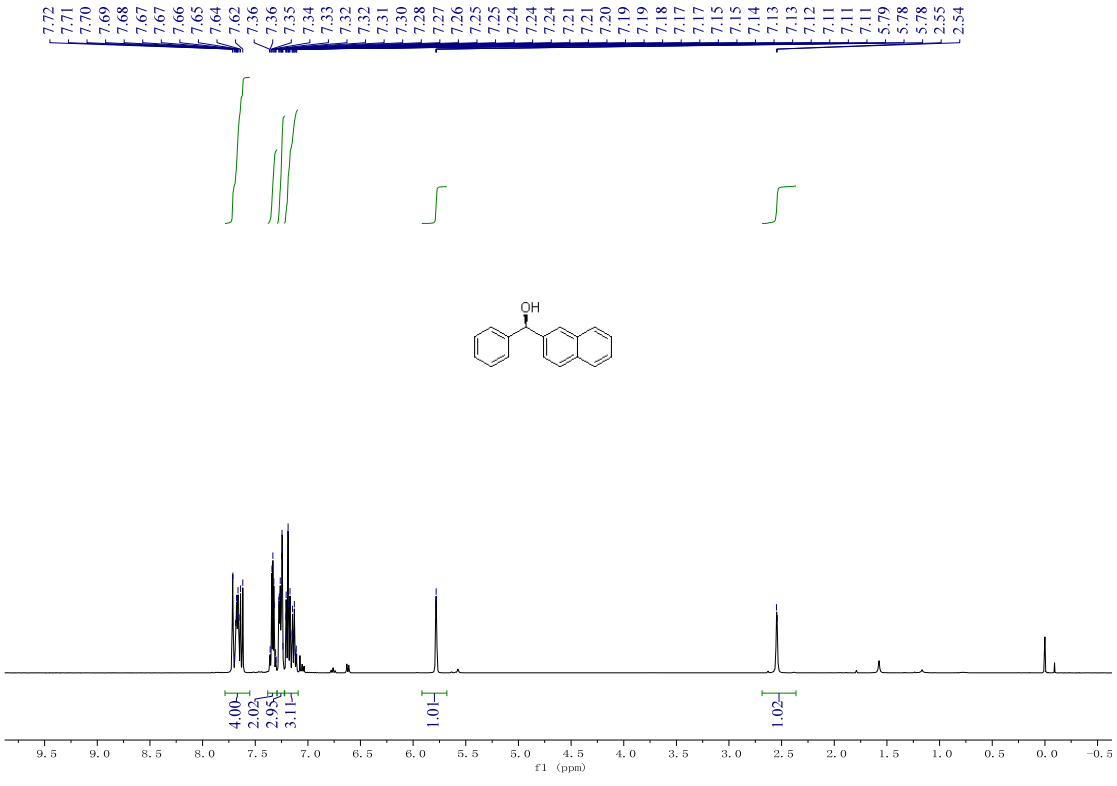
OH
f1 (ppm)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7.13
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7.11
5.79
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2.02
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3.11
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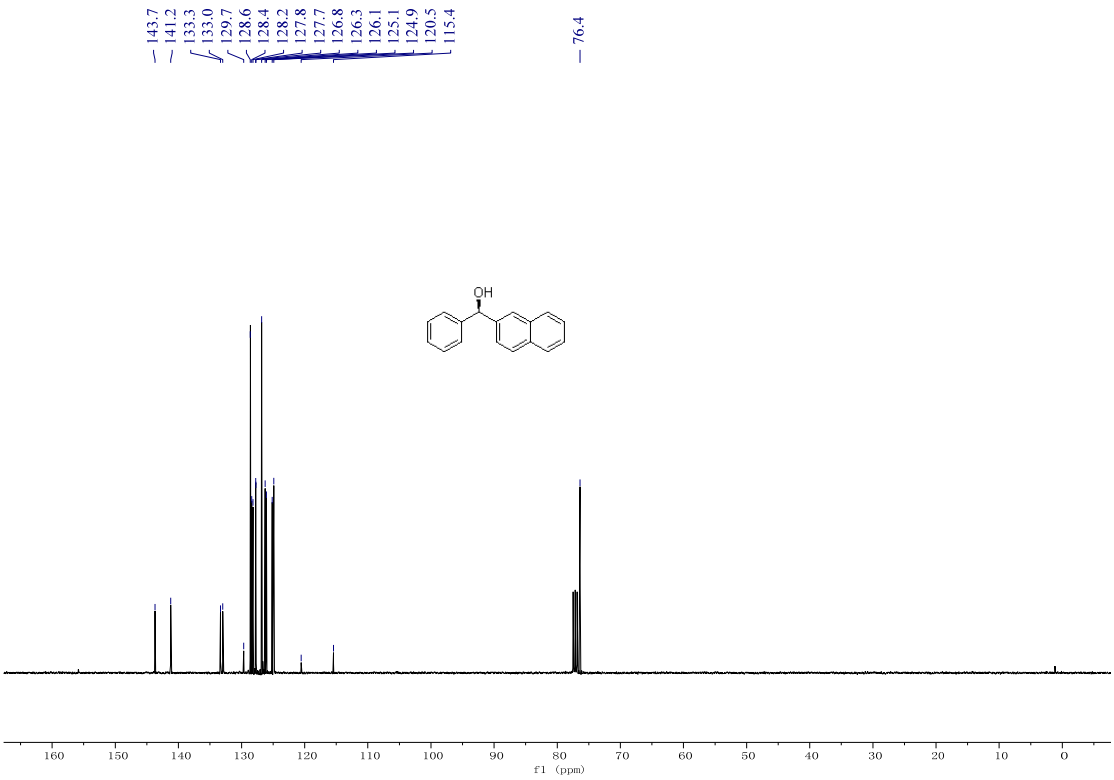
1.02
f1 (ppm)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125.1
124.9
120.5
115.4
76.4
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120
110
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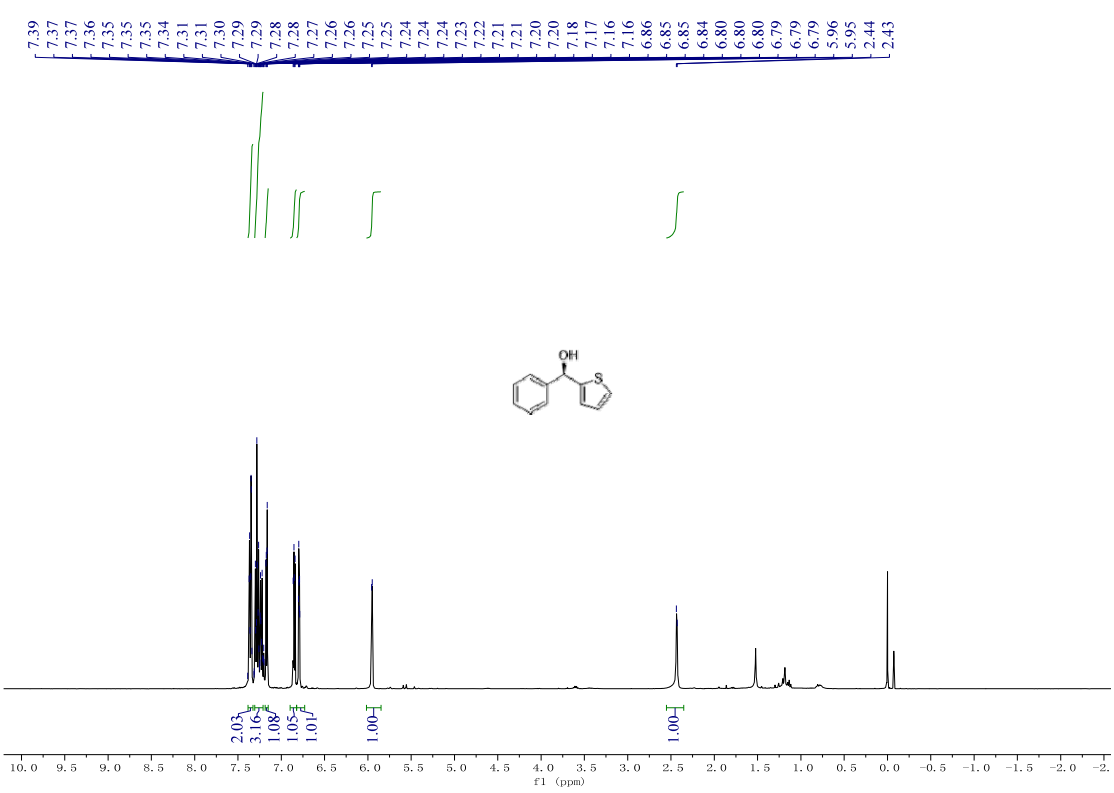
80
70
60
50
40
30
20
10
0
f1 (ppm)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S
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1.00
1.00
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4.0
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3.0
2.5
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-1.5
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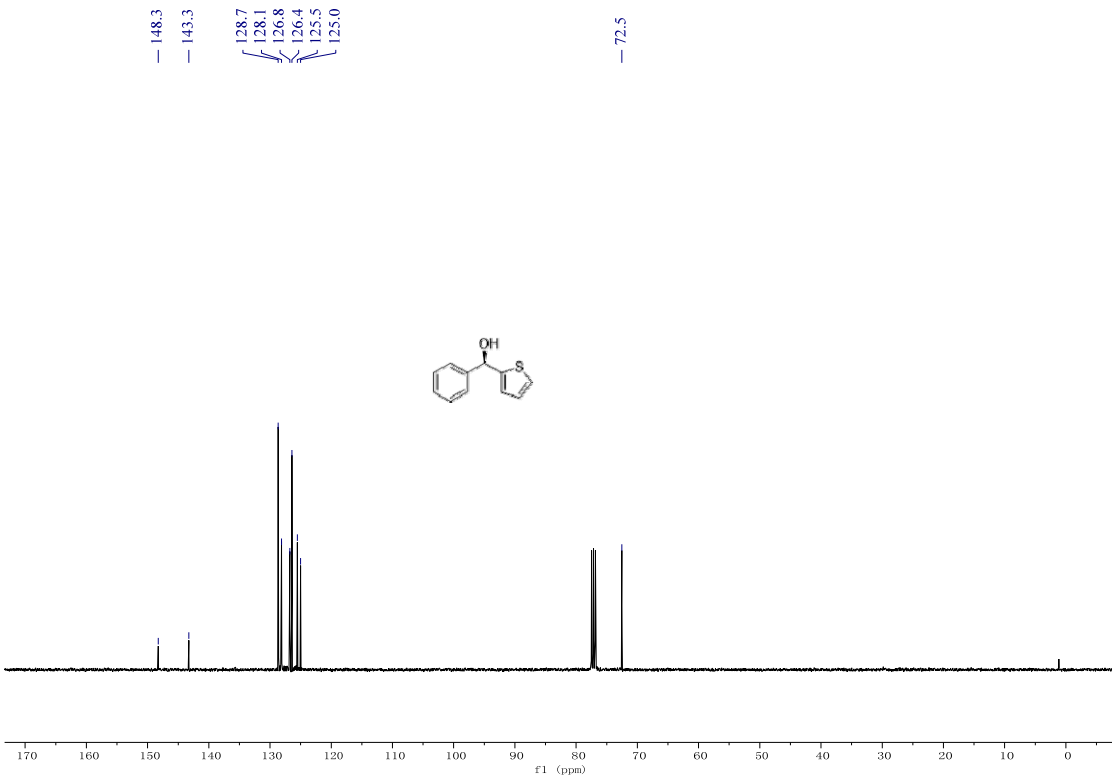
-2.
f1 (ppm)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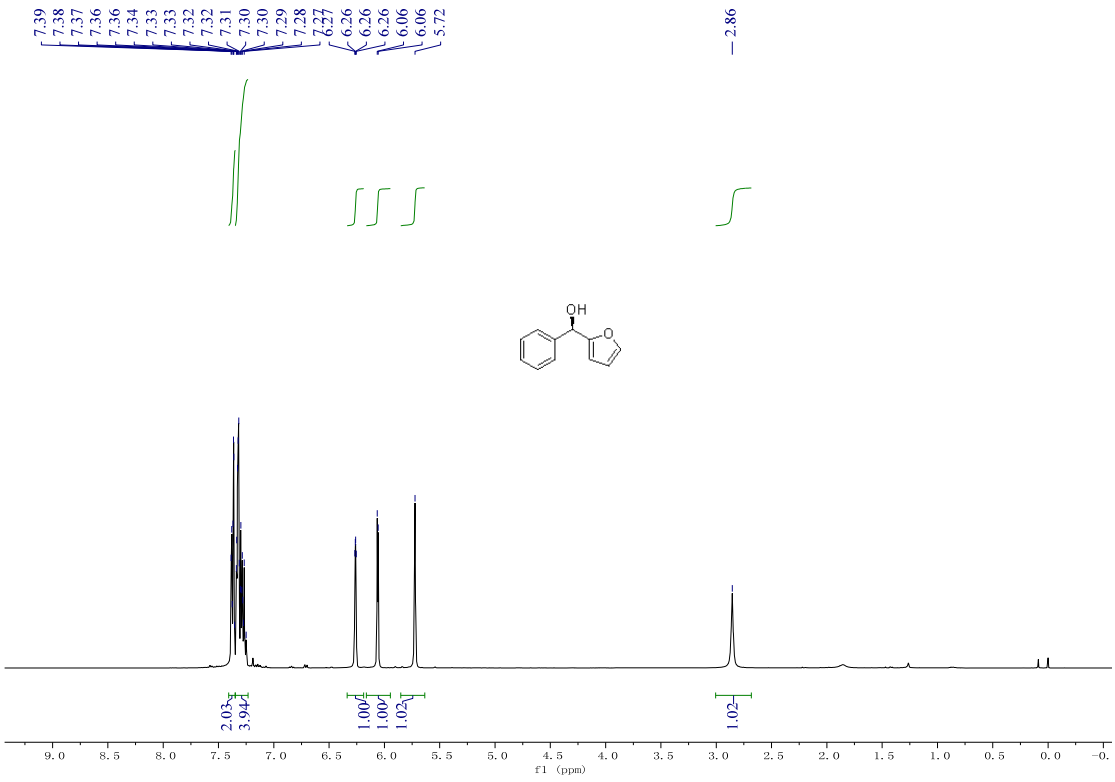
72.5
OH
S
f1 (ppm)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6.26
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OH
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1.00
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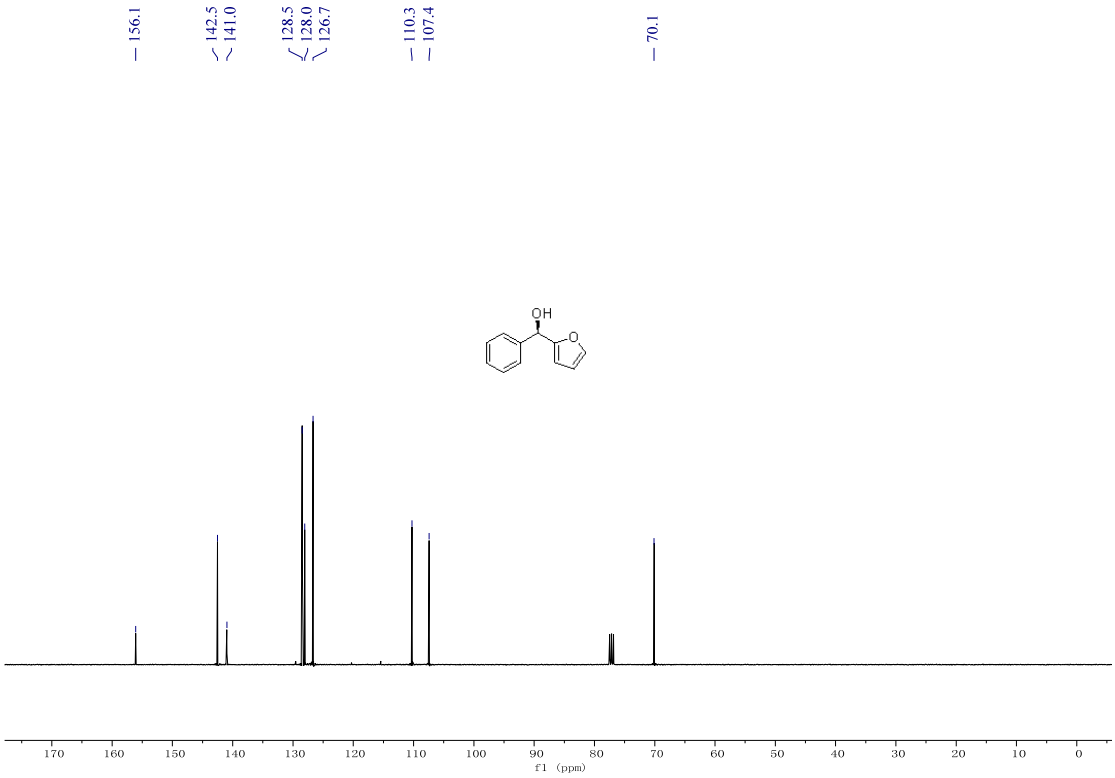
1.02
f1 (ppm)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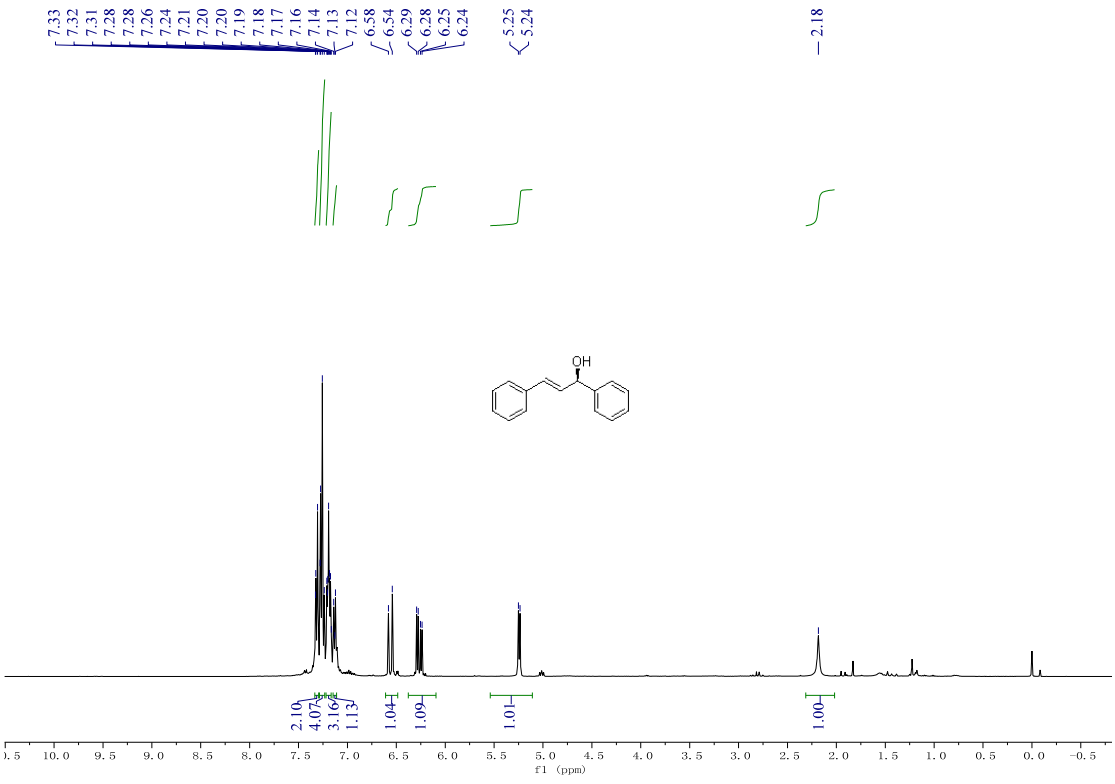
128.0
126.7
110.3
107.4
70.1
OH
O
f1 (ppm)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7.13
7.12
6.58
6.54
6.29
6.28
6.25
6.24
5.25
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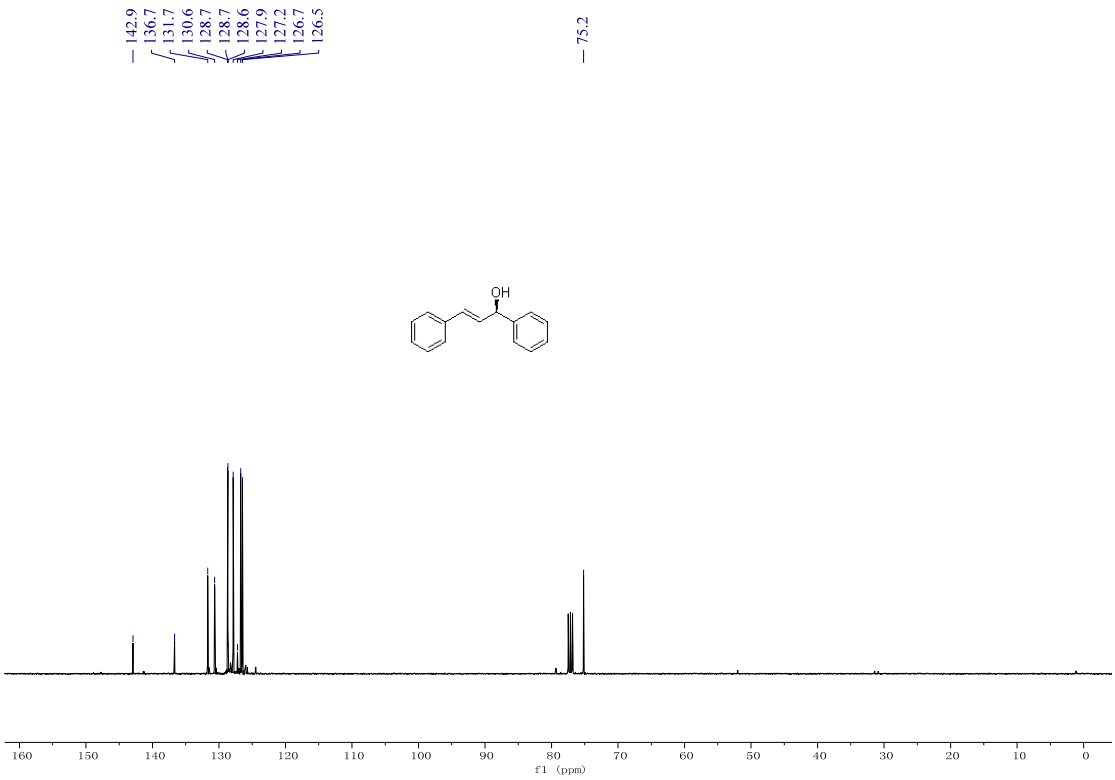
4.07
3.16
1.13
1.04
1.09
1.01
1.00
f1 (ppm)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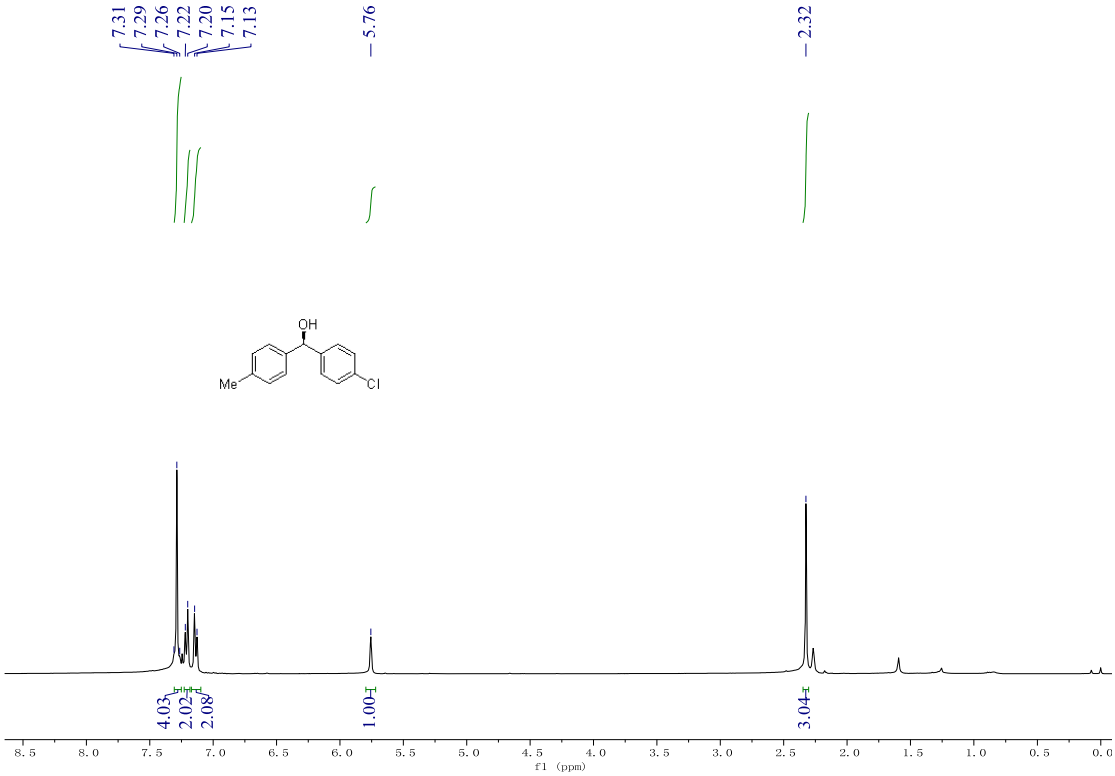
128.6
127.9
127.2
126.7
126.5
75.2
OH
f1 (ppm)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Me
Cl
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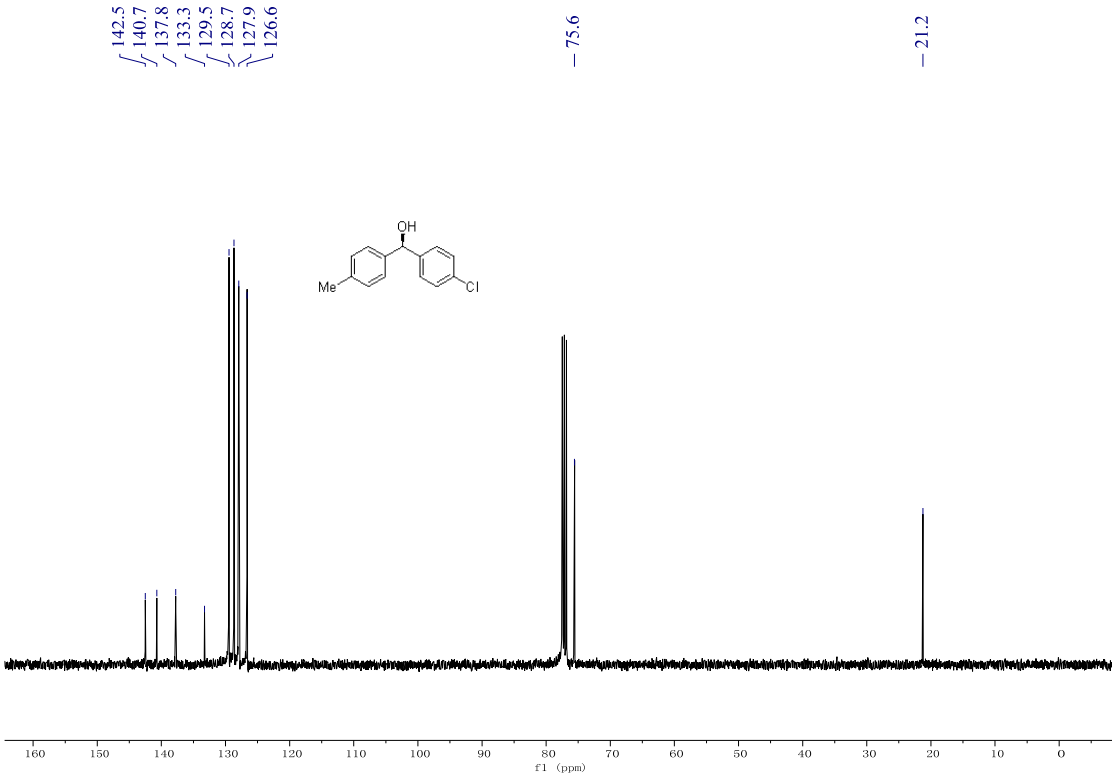
2.02
2.08
1.00
3.04
f1 (ppm)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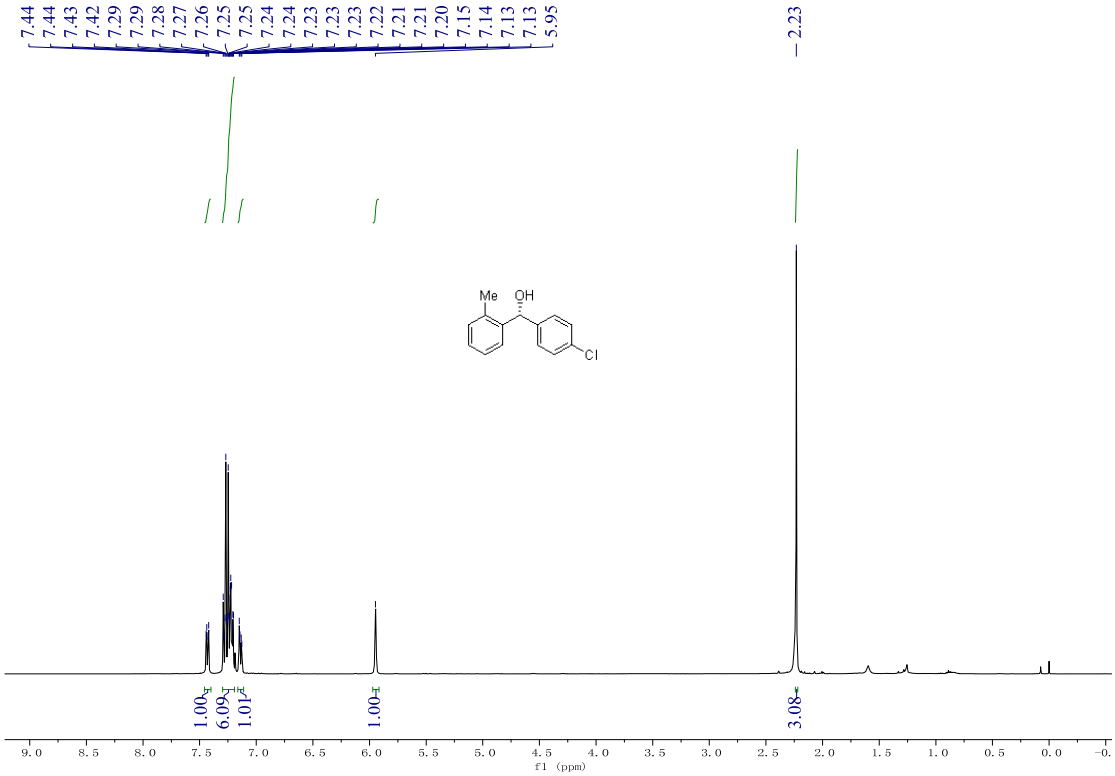
129.5
128.7
127.9
126.6
75.6
21.2
OH
Me
Cl
f1 (ppm)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7.23
7.23
7.23
7.22
7.21
7.21
7.20
7.15
7.14
7.13
7.13
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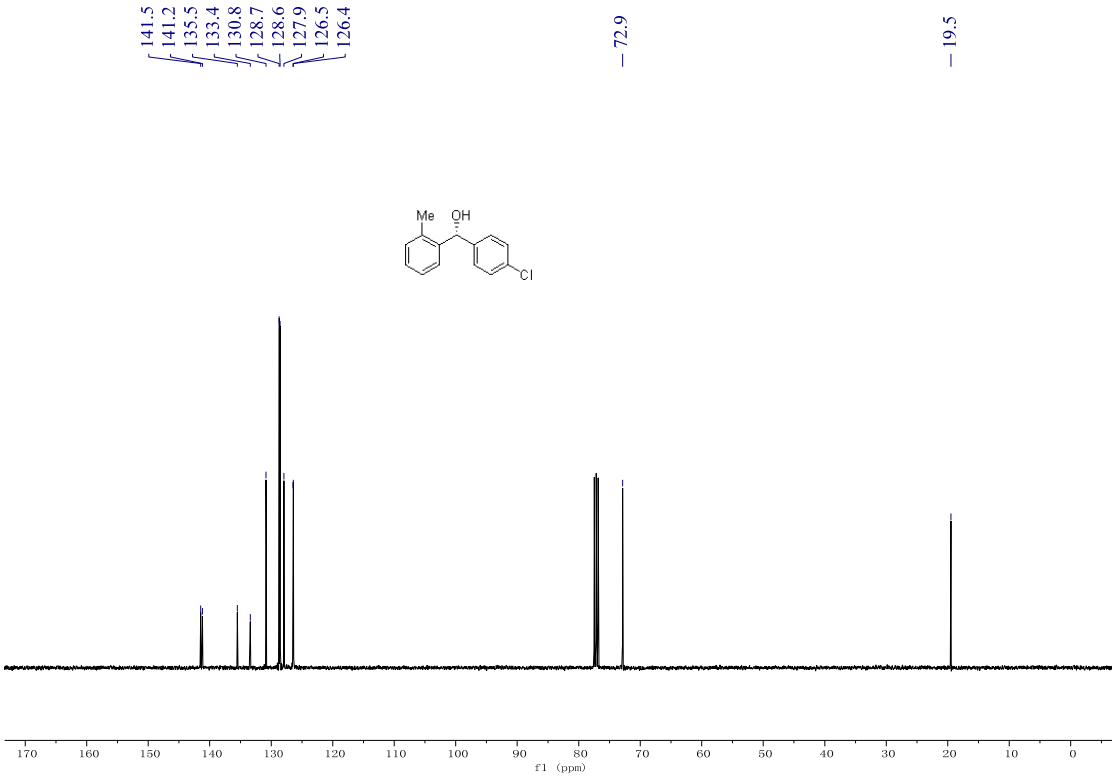
2.23
Me
OH
Cl
1.00
6.09
1.01
1.00
3.08
f1 (ppm)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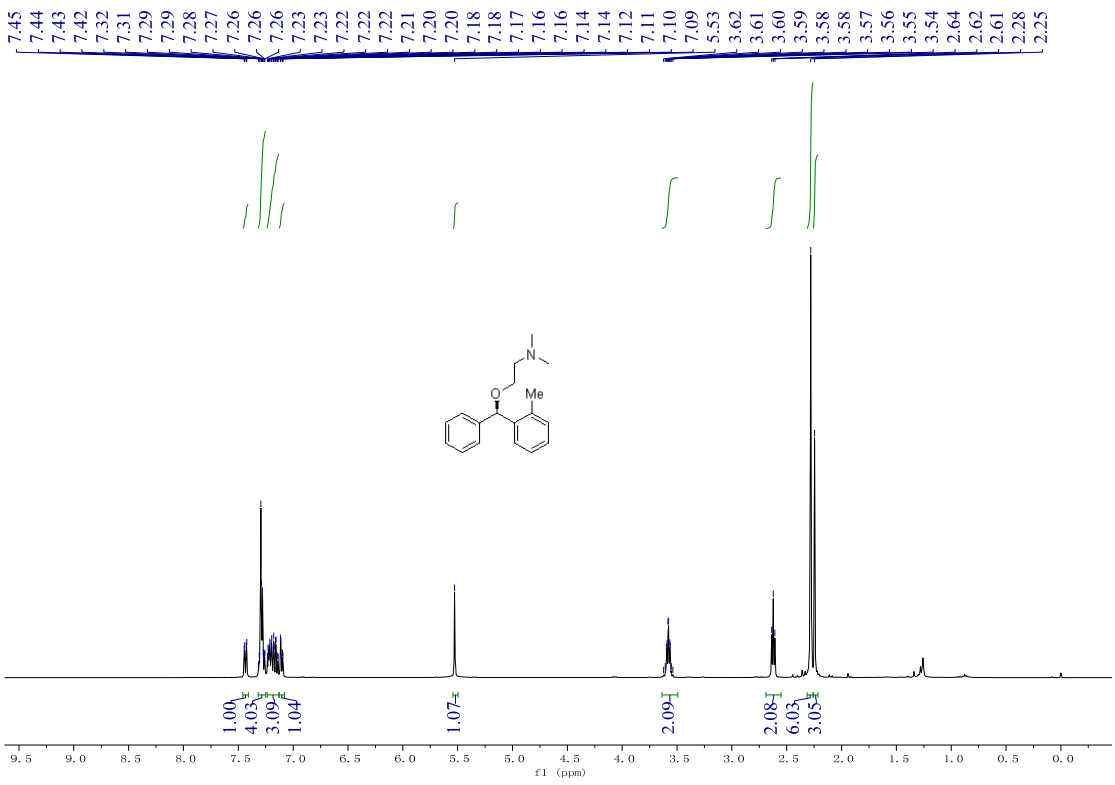
127.9
126.5
126.4
72.9
19.5
Me
OH
Cl
f1 (ppm)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7.20
7.20
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7.16
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7.14
7.12
7.11
7.10
7.09
5.53
3.62
3.61
3.60
3.59
3.58
3.58
3.57
3.56
3.55
3.54
2.64
2.62
2.61
2.28
2.25
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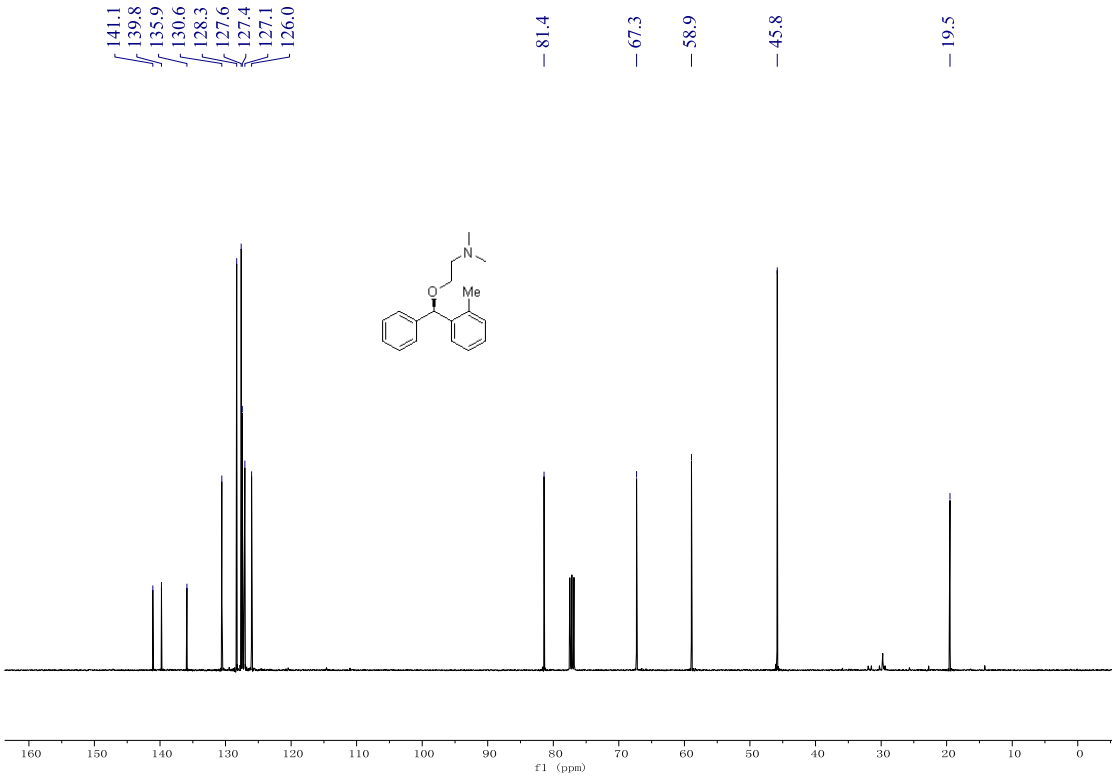
1.04
1.07
2.09
2.08
6.03
3.05
f1 (ppm)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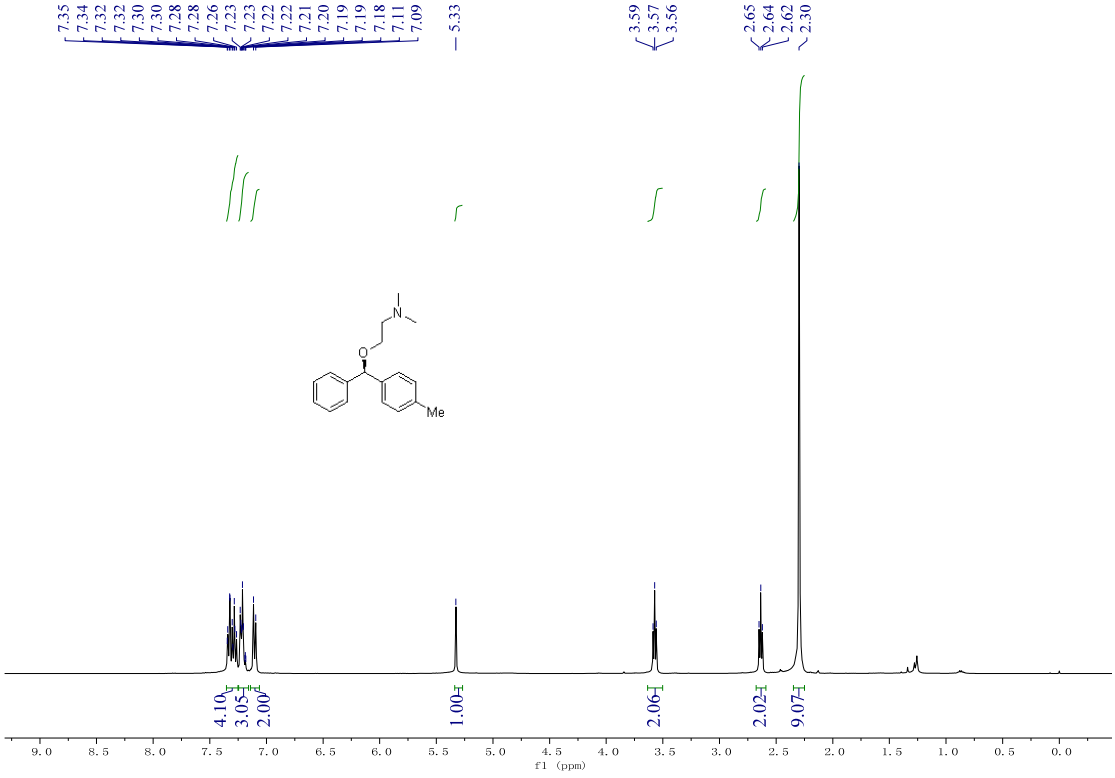
67.3
58.9
45.8
19.5
N
O
Me
f1 (ppm)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7.20
7.19
7.19
7.18
7.11
7.09
5.33
3.59
3.57
3.56
2.65
2.64
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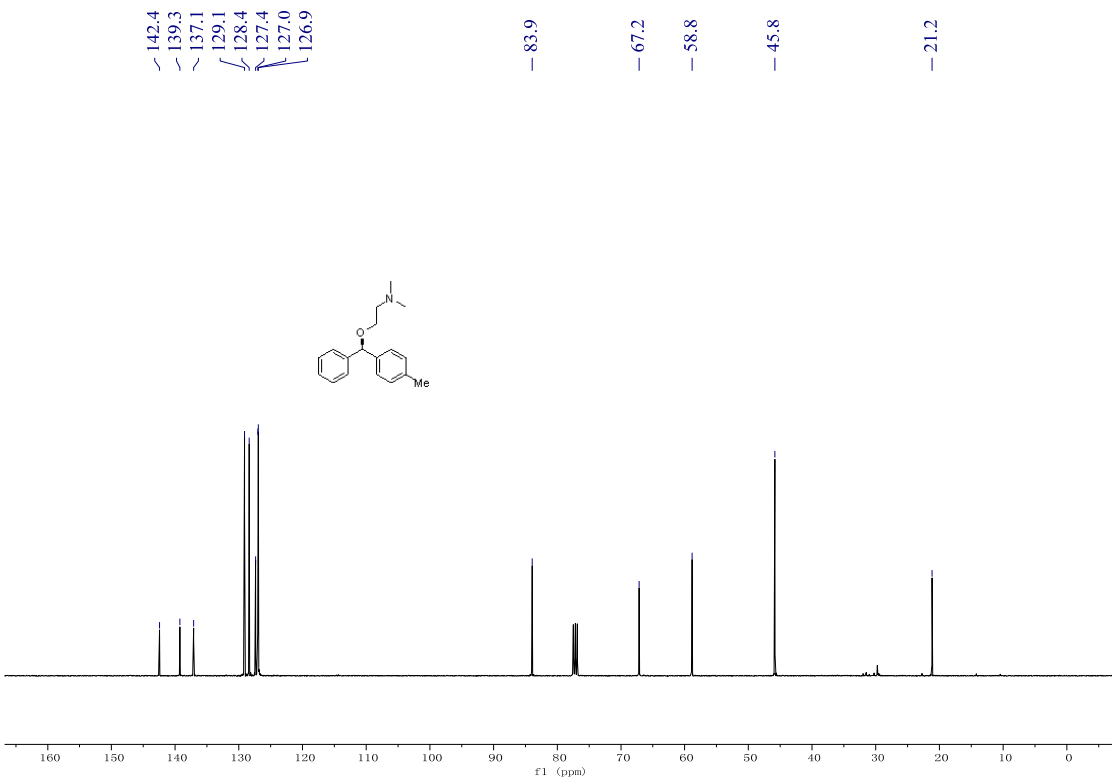
Me
4.10
3.05
2.00
1.00
2.06
2.02
9.07
f1 (ppm)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58.8
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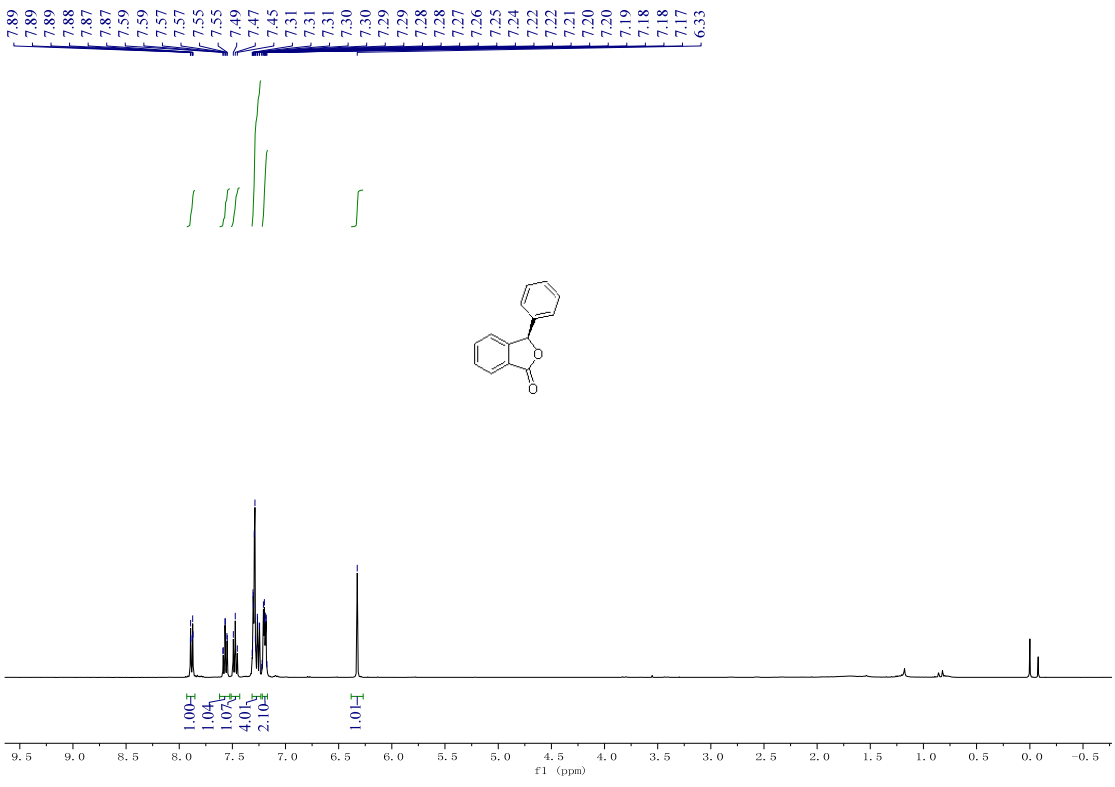
21.2
Me
f1 (ppm)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7.24
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7.22
7.21
7.20
7.20
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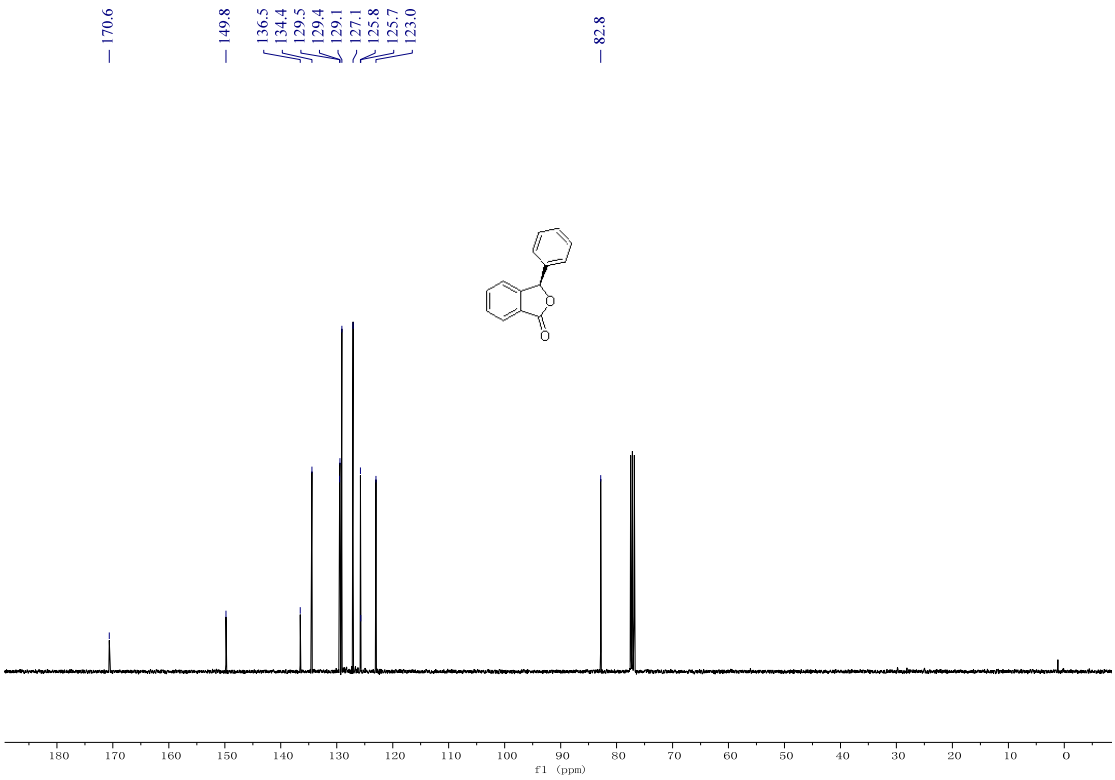
O
O
1.00
1.04
1.07
4.01
2.10
1.01
f1 (ppm)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125.7
123.0
82.8
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O
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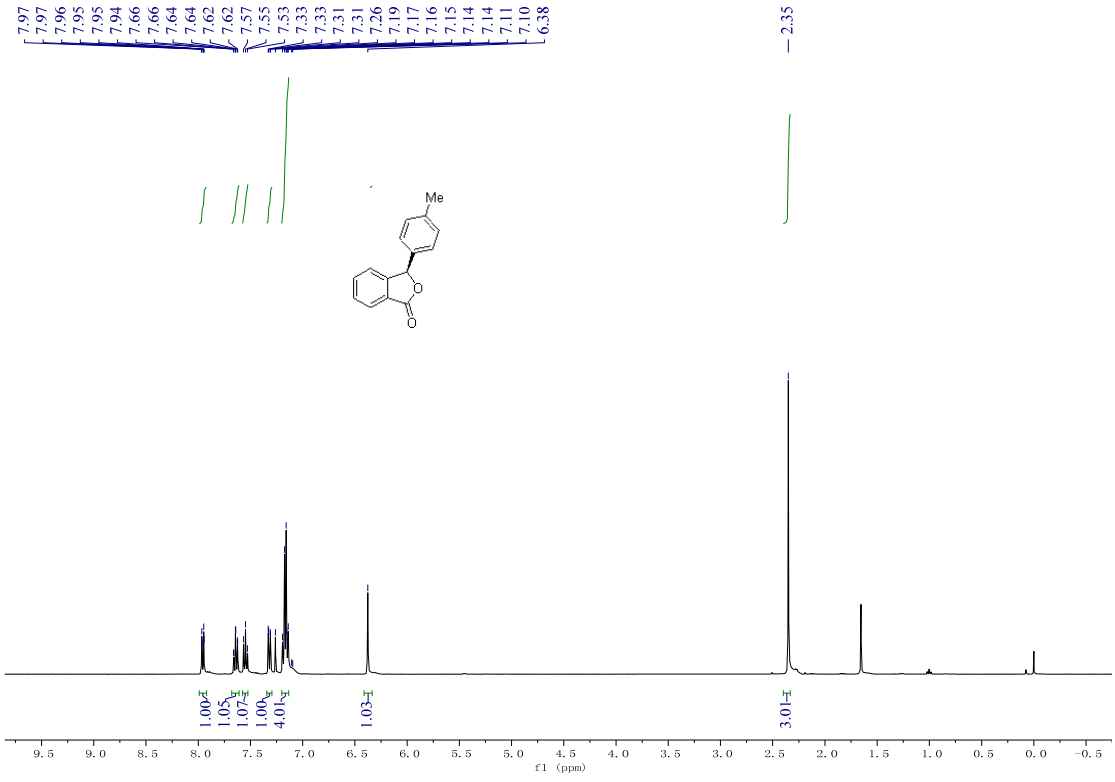
f1 (ppm)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7.31
7.26
7.19
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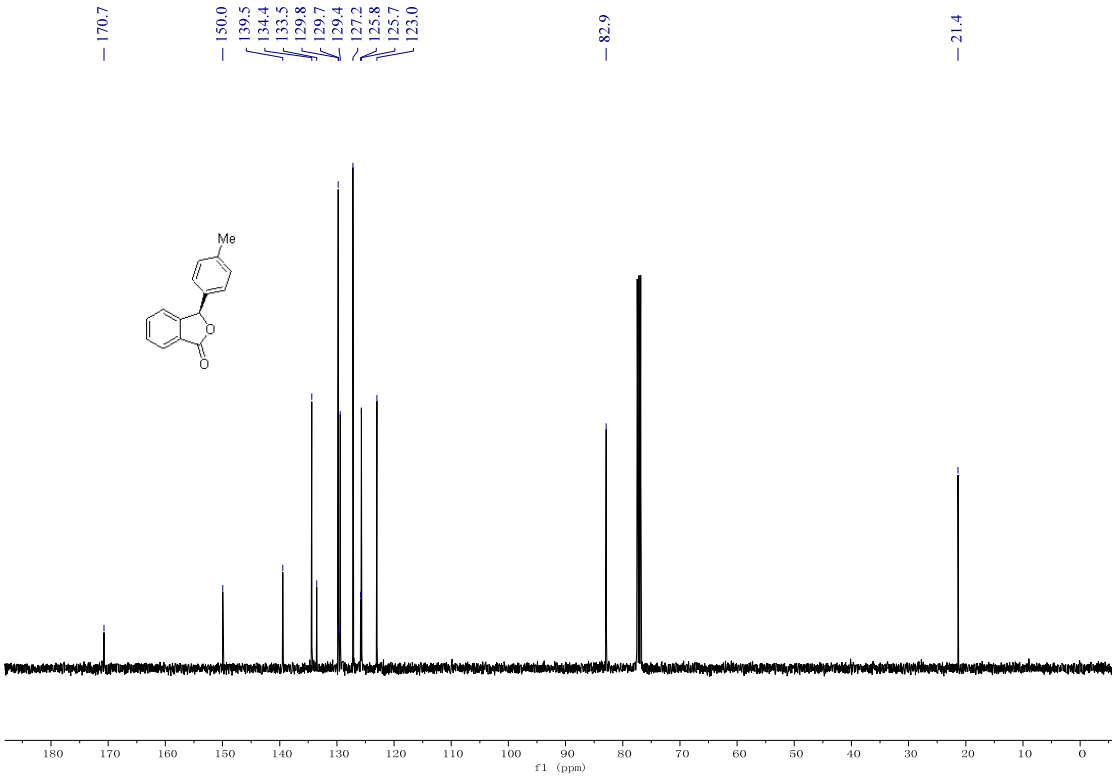
7.16
7.15
7.14
7.14
7.11
7.10
6.38
2.35
Me
O
O
1.00
1.05
1.07
1.00
4.01
1.03
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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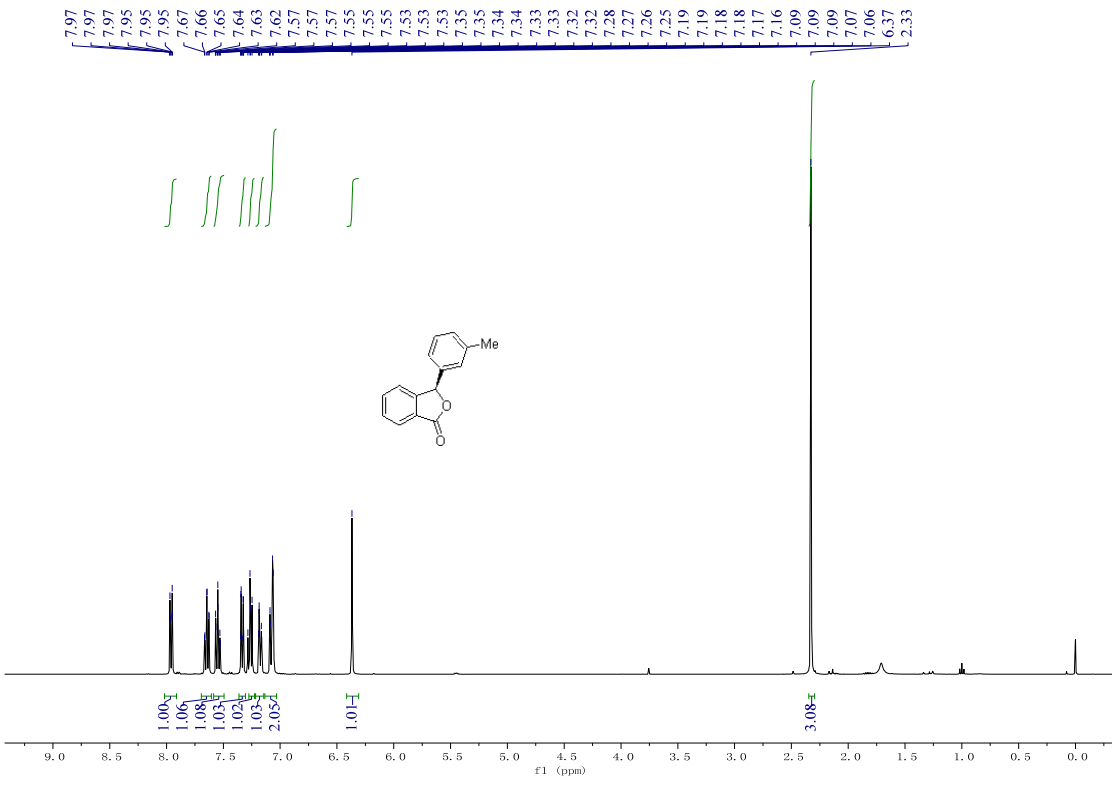
125.7
123.0
82.9
21.4
Me
O
O
f1 (ppm)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7.17
7.16
7.09
7.09
7.09
7.07
7.06
6.37
2.33
Me
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1.06
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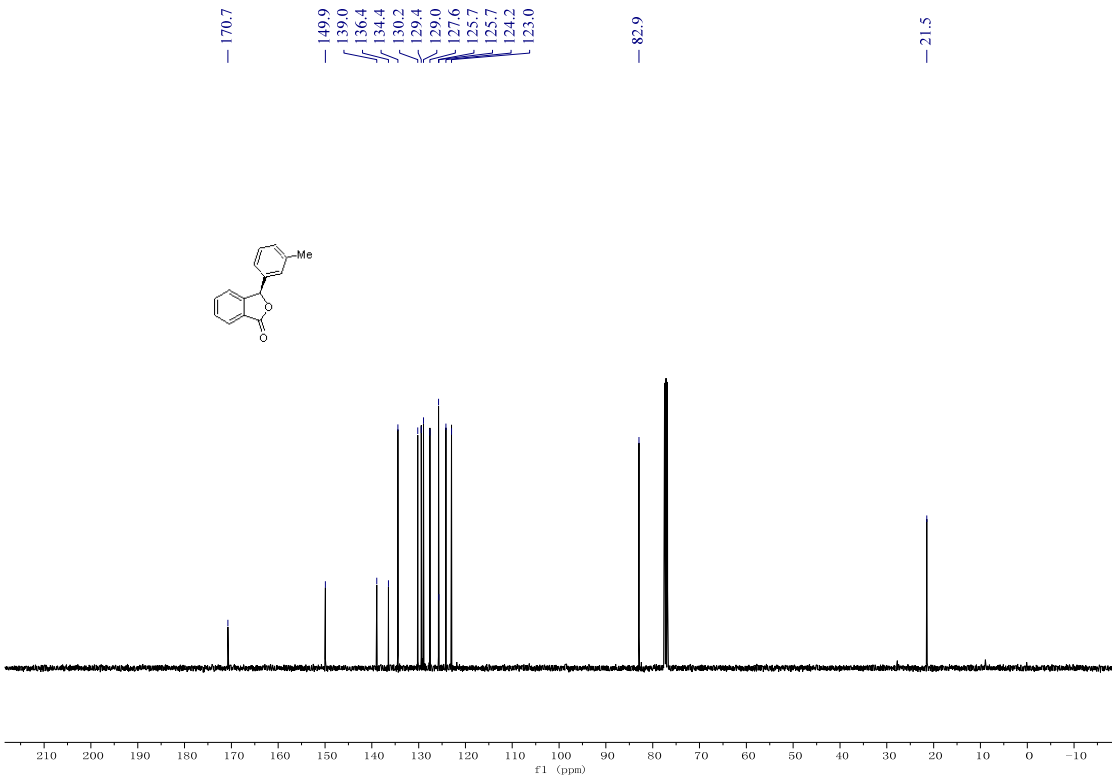
1.03
1.02
1.03
2.05
1.01
3.08
f1 (ppm)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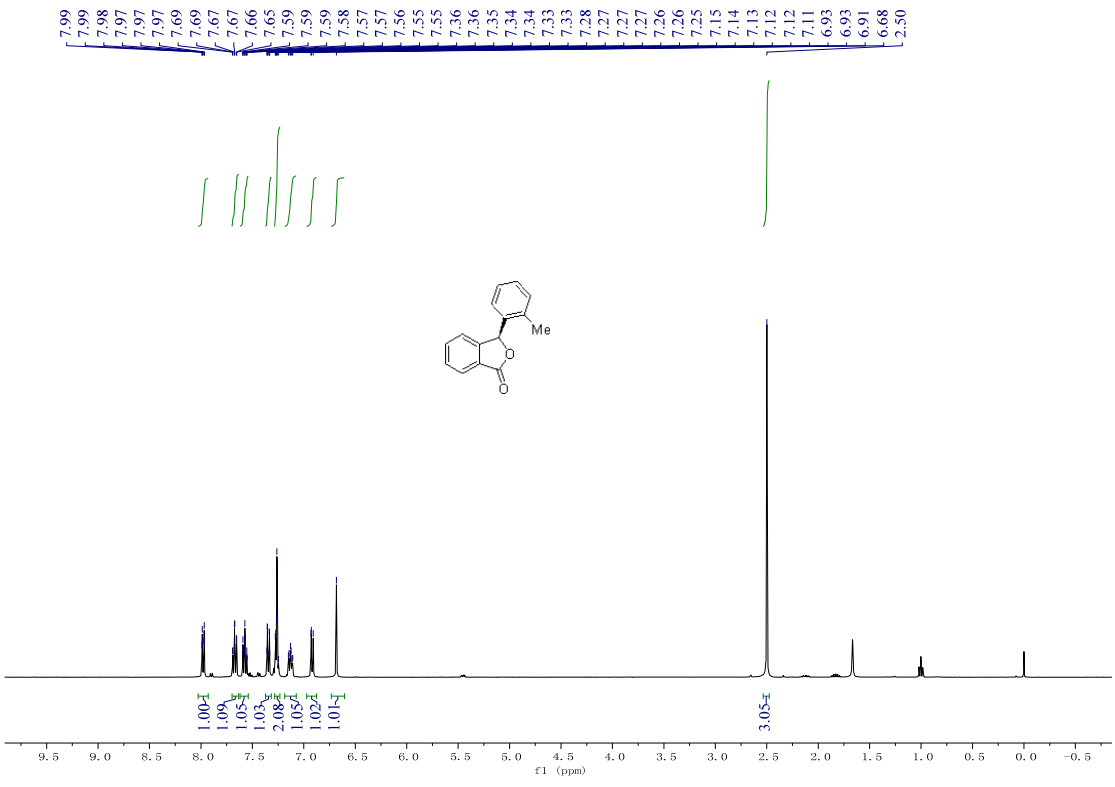
124.2
123.0
82.9
21.5
Me
O
O
f1 (ppm)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7.12
7.11
6.93
6.93
6.91
6.68
2.50
Me
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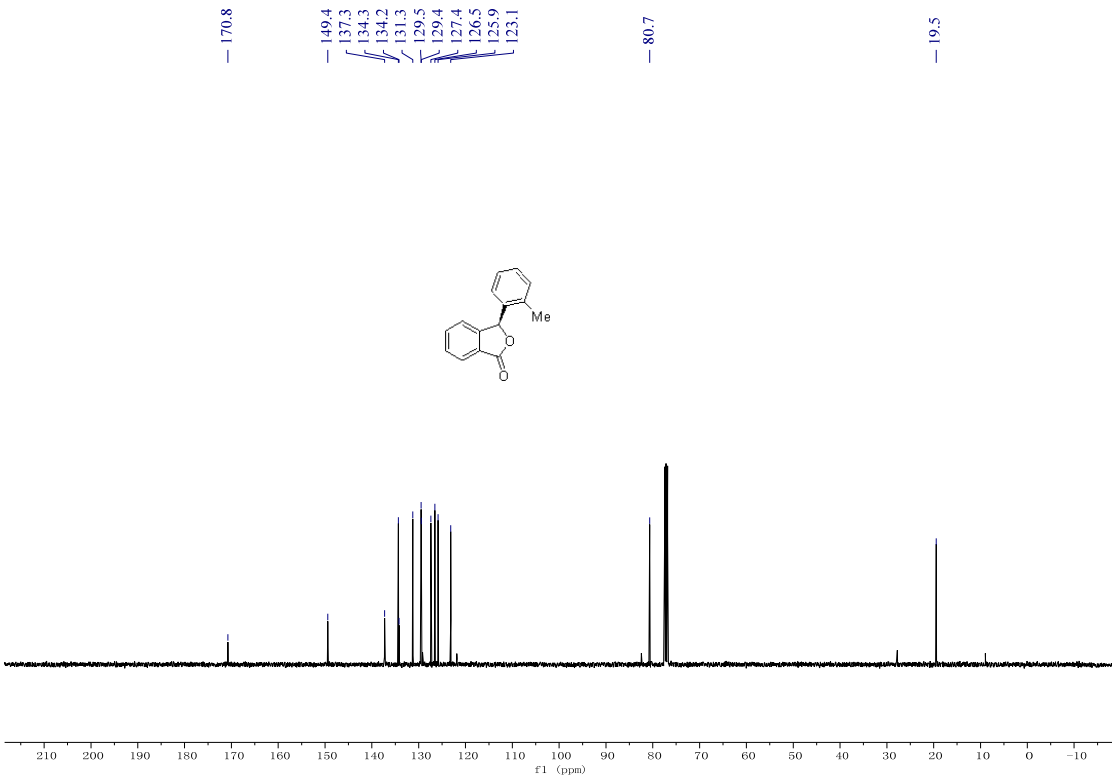
1.05
1.03
2.08
1.05
1.02
1.01
3.05
f1 (ppm)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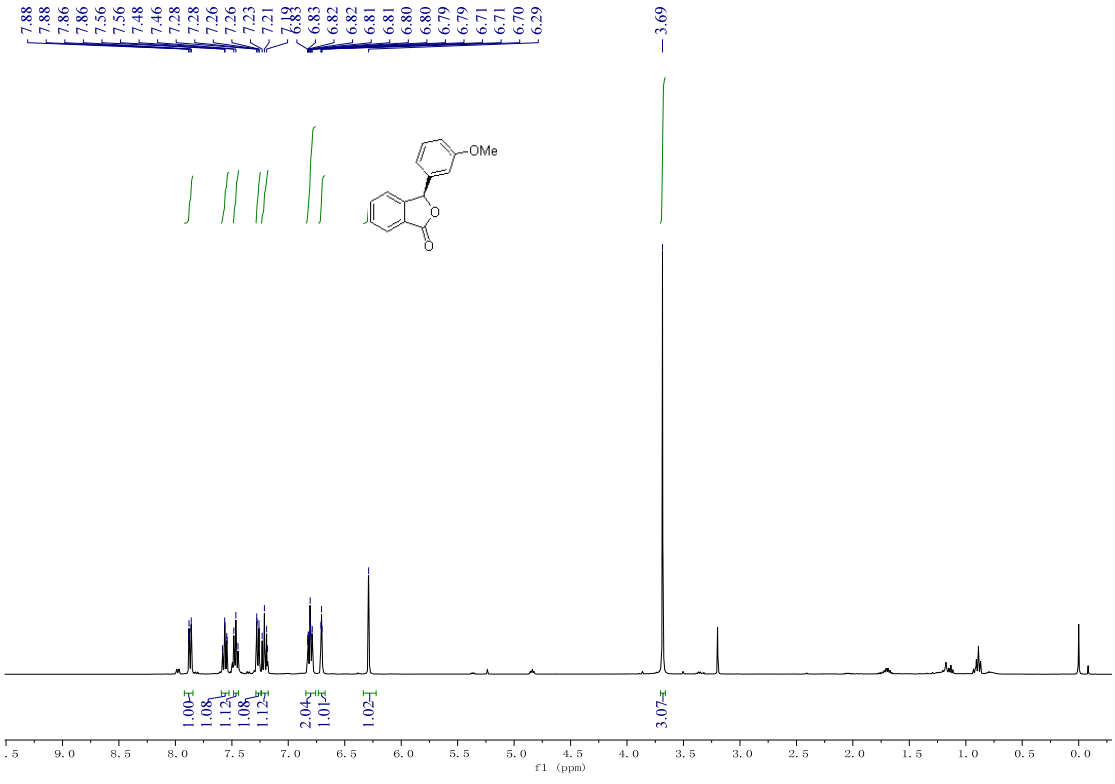
123.1
80.7
19.5
Me
O
O
f1 (ppm)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6.82
6.82
6.81
6.81
6.80
6.80
6.79
6.79
6.71
6.71
6.70
6.29
3.69
OMe
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O
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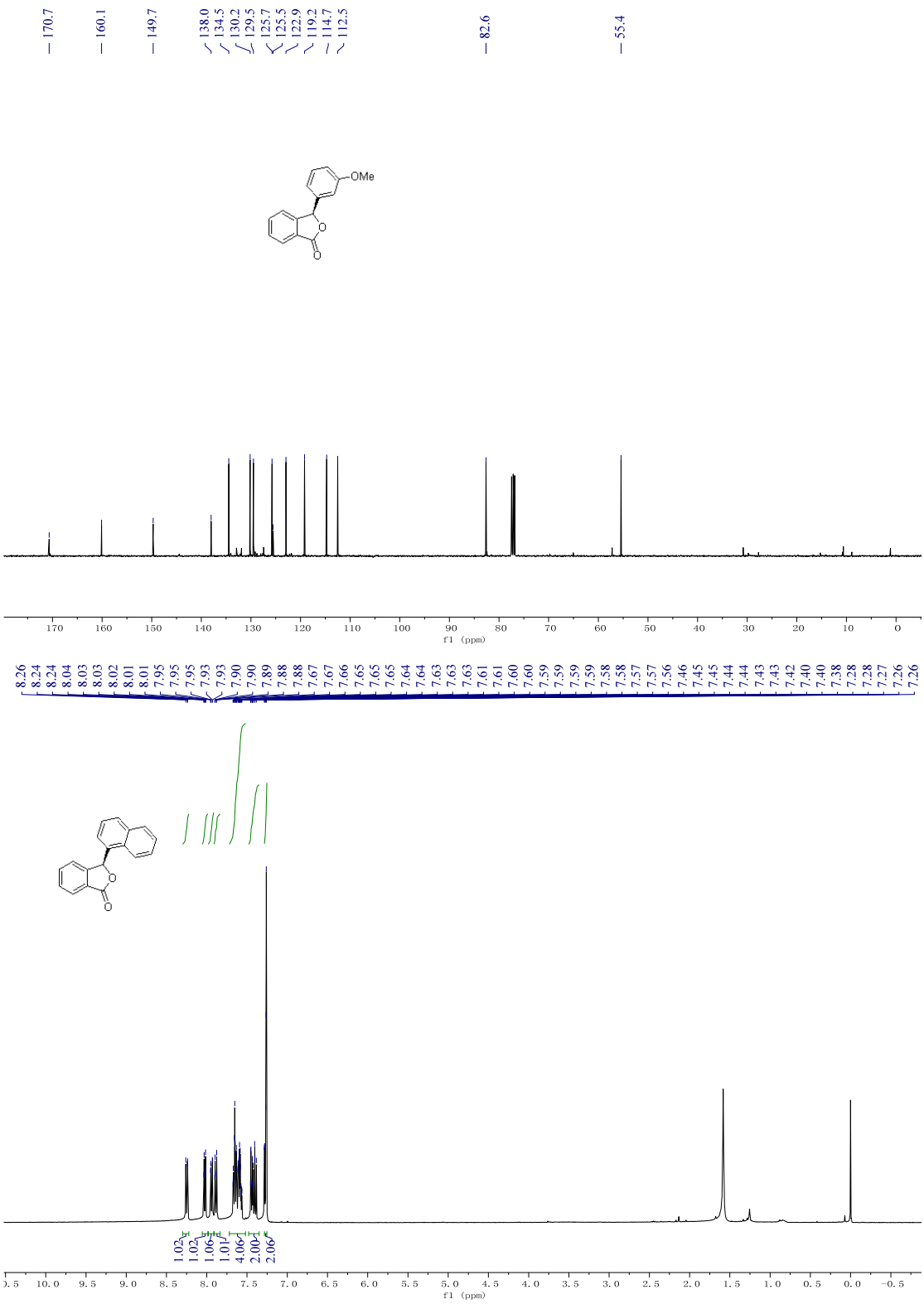
1.08
1.12
1.08
1.12
2.04
1.01
1.02
3.07
f1 (ppm)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122.9
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114.7
112.5
82.6
55.4
OMe
O
O
f1 (ppm)
8.26
8.24
8.24
8.04
8.03
8.03
8.02
8.01
8.01
7.95
7.95
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7.43
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7.28
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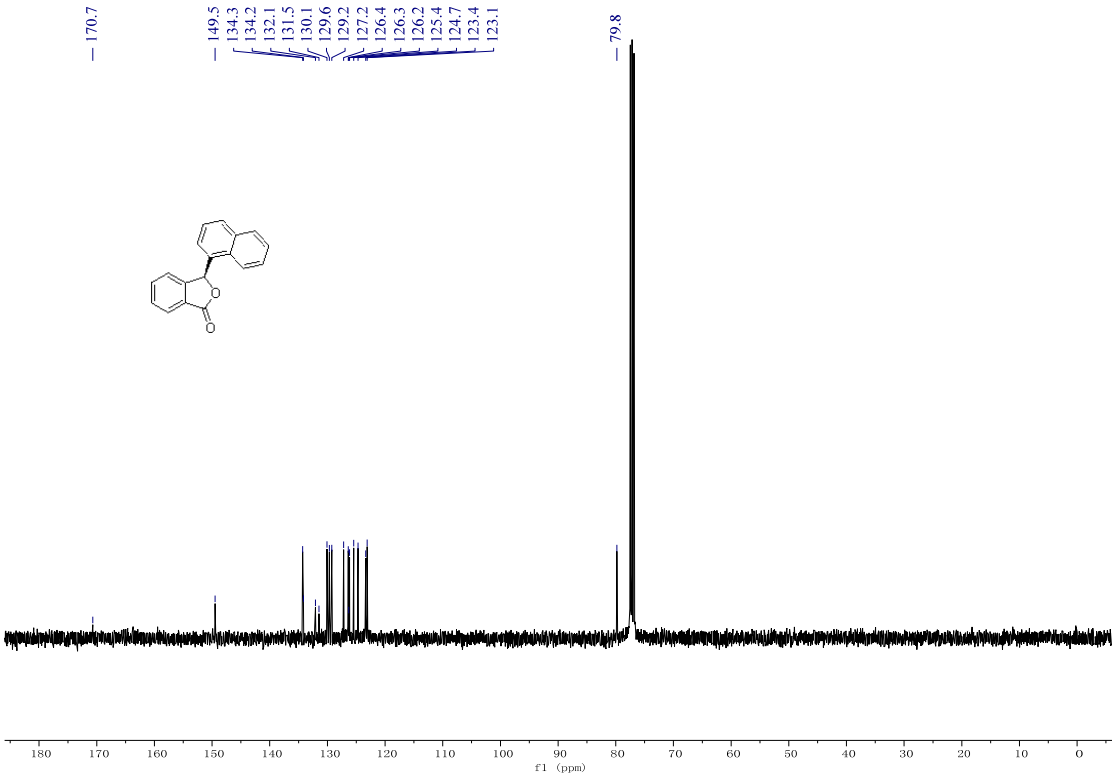
7.26
1.02
1.02
1.06
1.01
4.06
2.00
2.06
f1 (ppm)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126.3
126.2
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124.7
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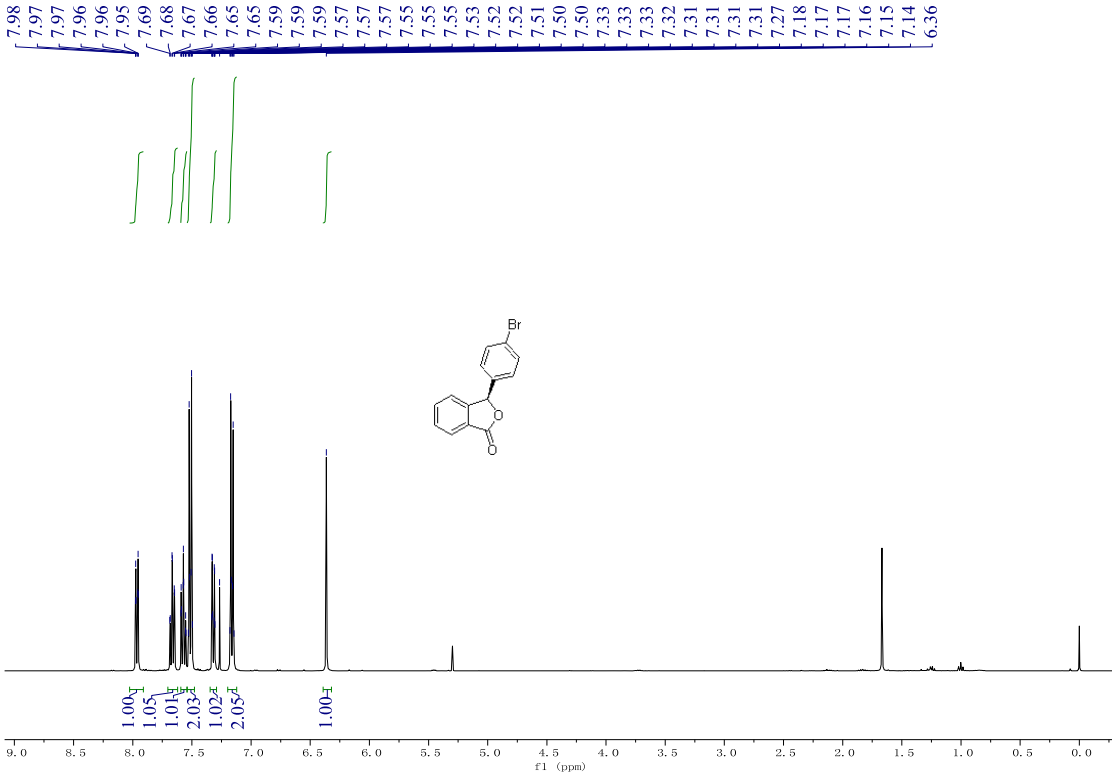
123.1
79.8
O
O
f1 (ppm)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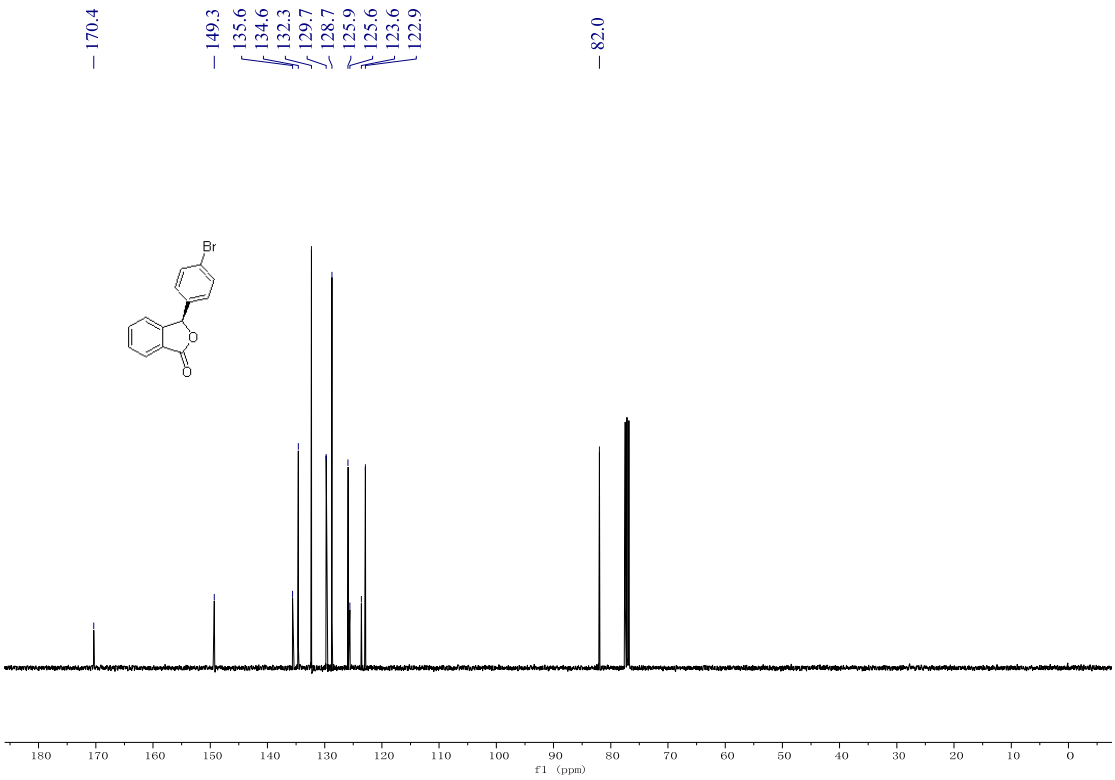
7.32
7.31
7.31
7.31
7.31
7.27
7.18
7.17
7.17
7.16
7.15
7.14
6.36
Br
O
O
1.00
1.05
1.01
2.03
1.02
2.05
1.00
f1 (ppm)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135.6
134.6
132.3
129.7
128.7
125.9
125.6
123.6
122.9
82.0
Br
O
O
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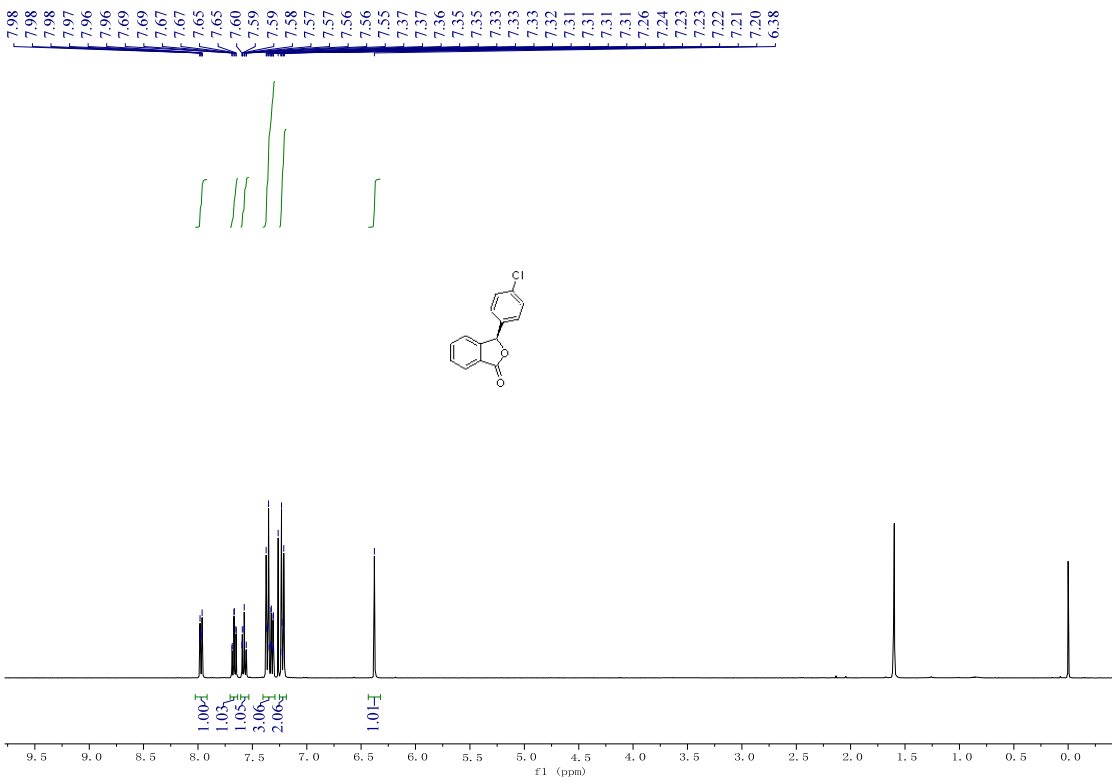
f1 (ppm)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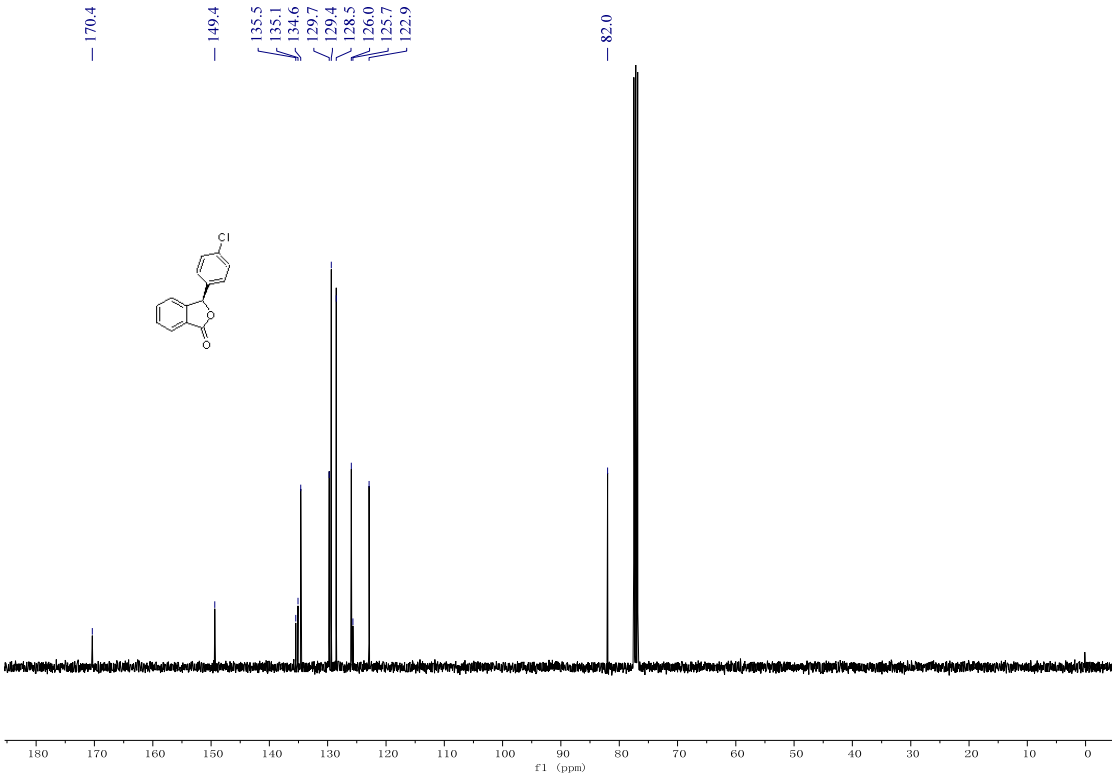
Cl
O
O
1.00
1.03
1.05
3.06
2.06
1.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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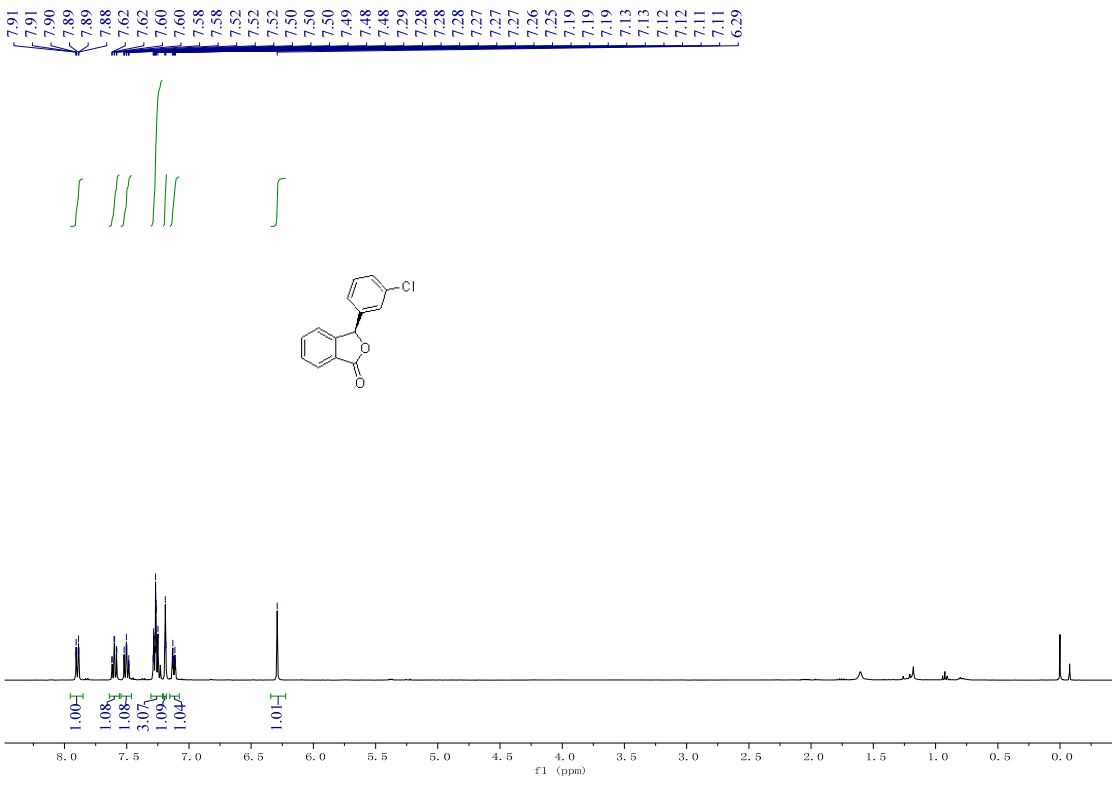
128.5
126.0
125.7
122.9
82.0
Cl
O
O
f1 (ppm)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7.26
7.25
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7.19
7.19
7.13
7.13
7.12
7.12
7.11
7.11
6.29
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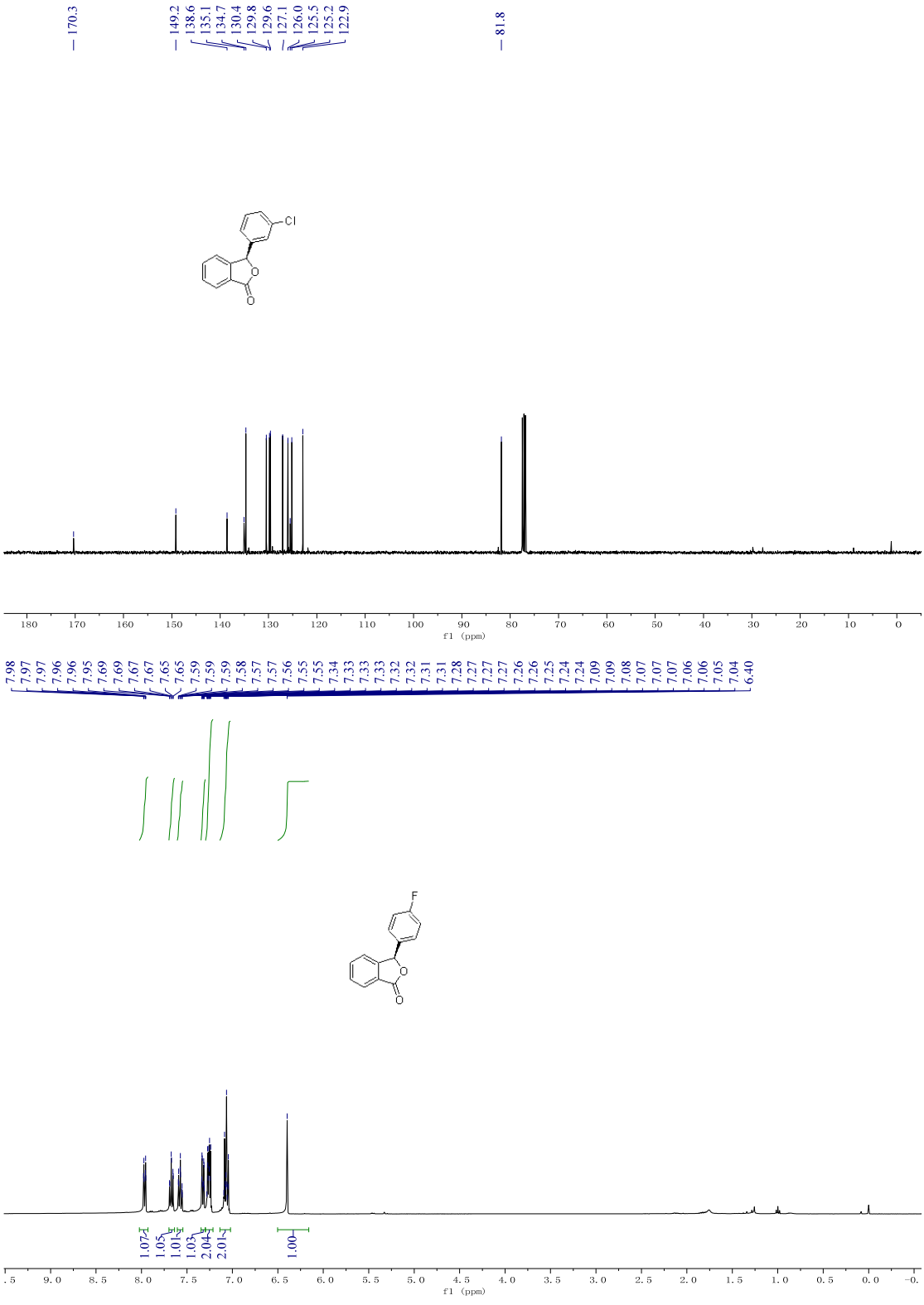
O
O
1.00
1.08
1.08
3.07
1.09
1.04
1.01
f1 (ppm)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135.1
134.7
130.4
129.8
129.6
127.1
126.0
125.5
125.2
122.9
81.8
Cl
O
O
f1 (ppm)
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7.97
7.97
7.96
7.96
7.95
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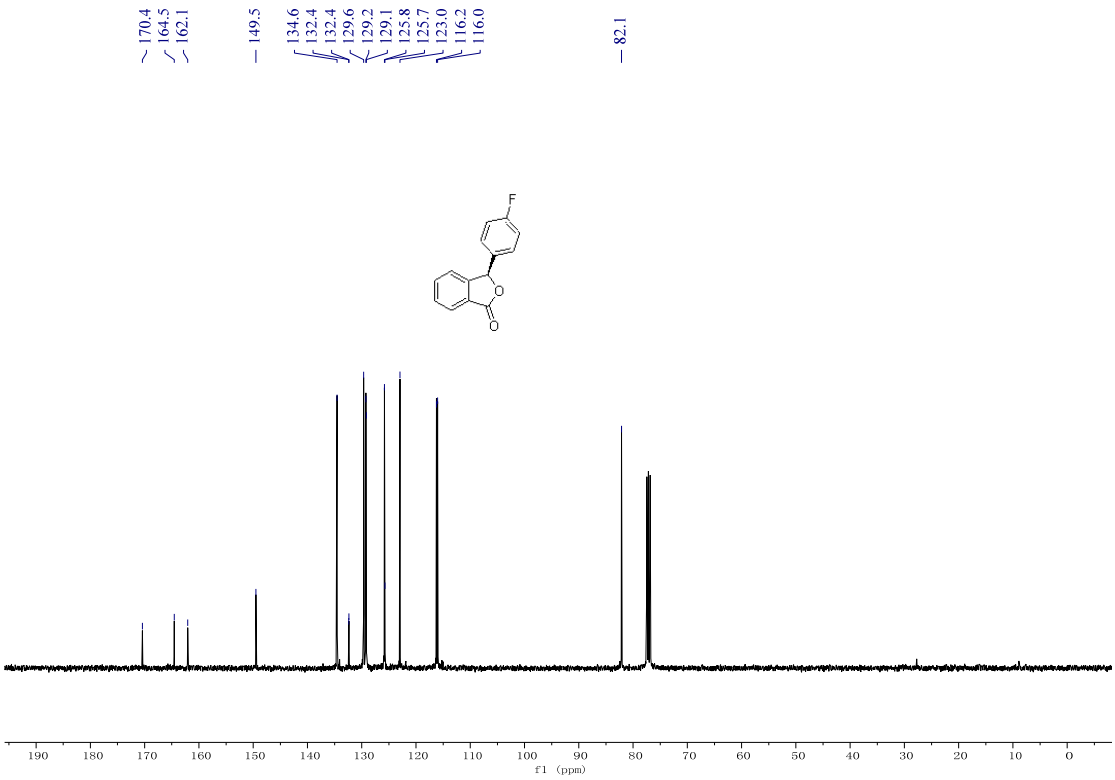
7.24
7.09
7.09
7.08
7.07
7.07
7.07
7.06
7.06
7.05
7.04
6.40
F
O
O
1.07
1.05
1.01
1.03
2.04
2.01
1.00
f1 (ppm)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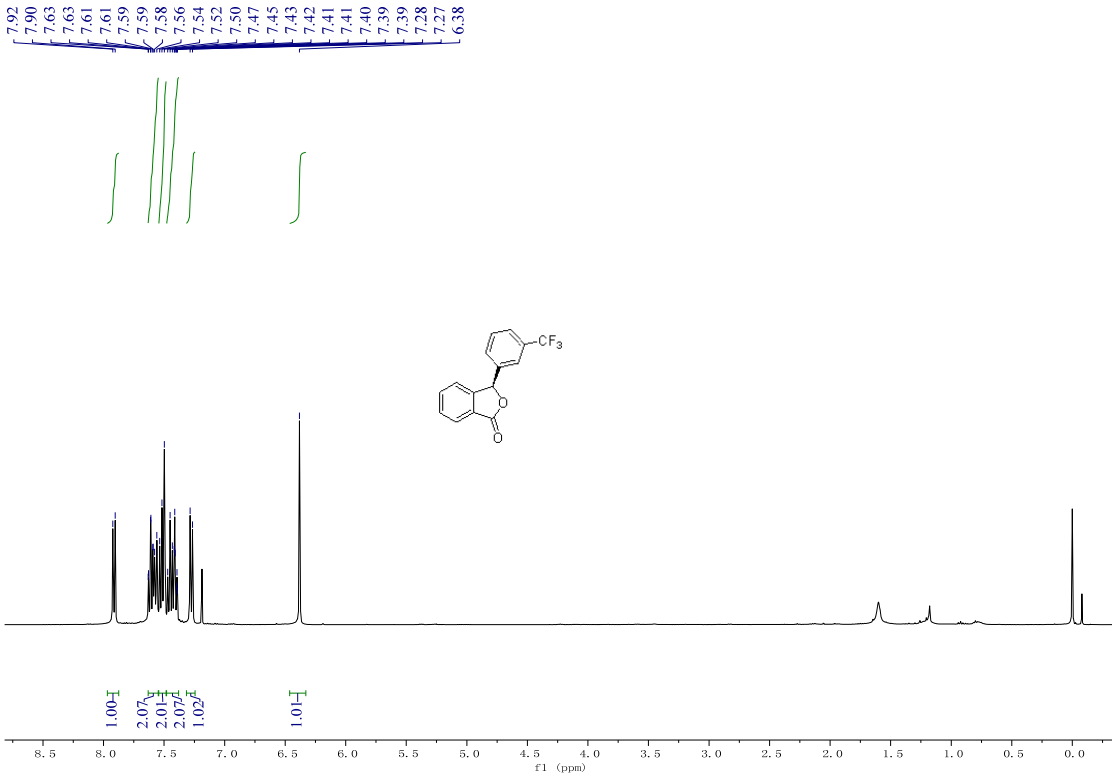
132.4
129.6
129.2
129.1
125.8
125.7
123.0
116.2
116.0
82.1
F
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.41
7.40
7.39
7.39
7.28
7.27
6.38
CF3
O
O
1.00
2.07
2.01
2.07
1.02
1.01
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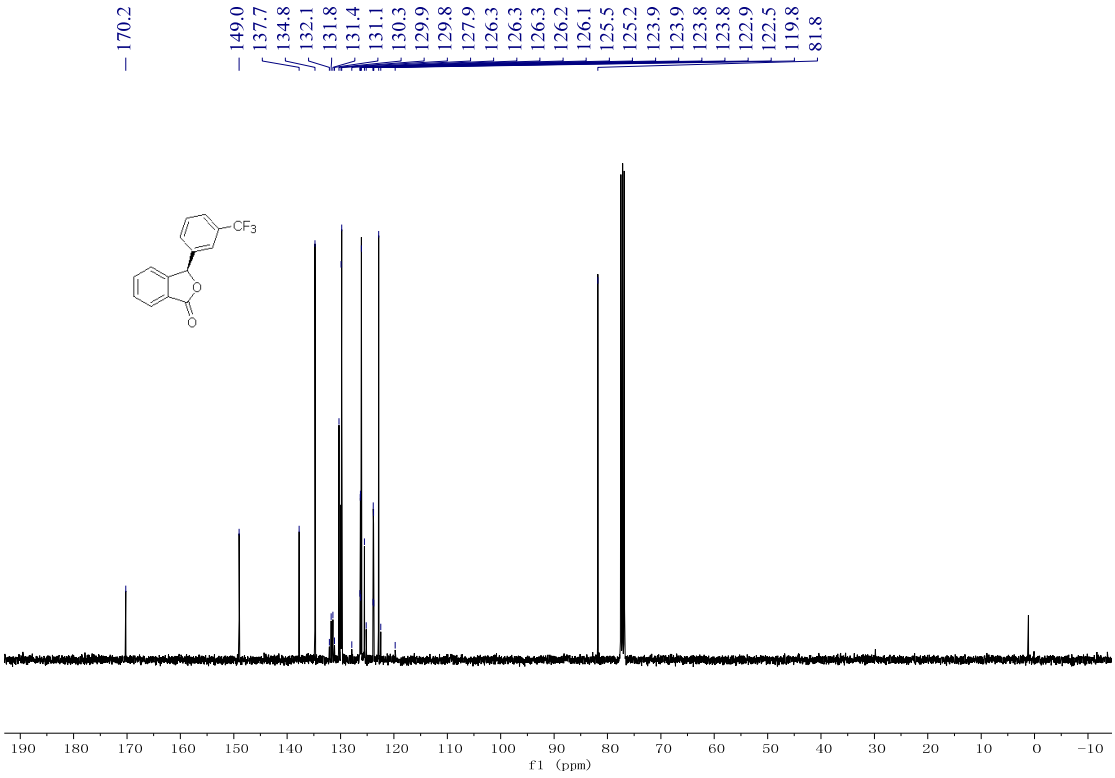
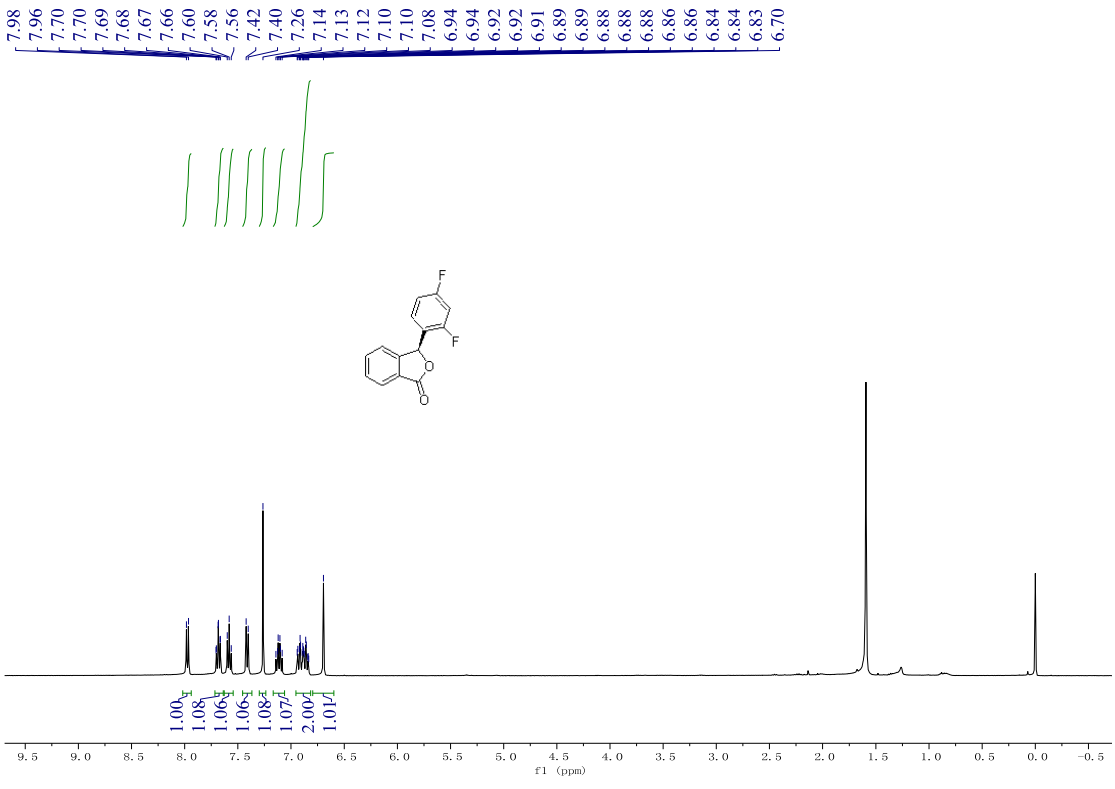
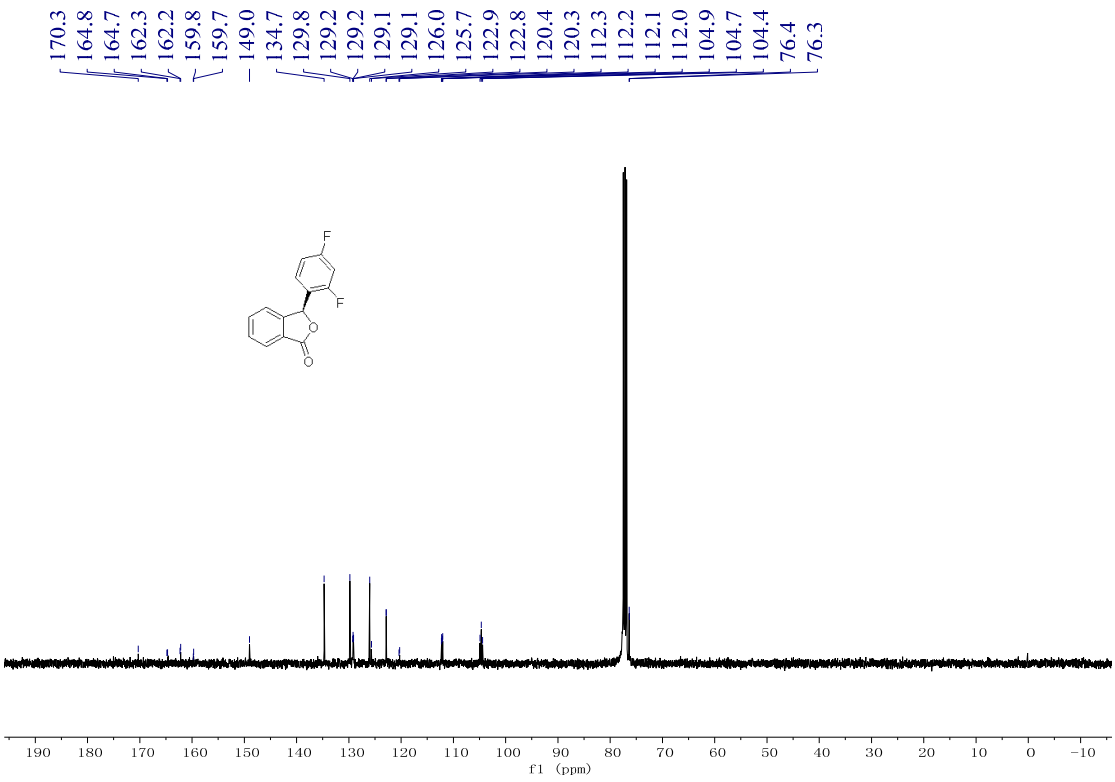
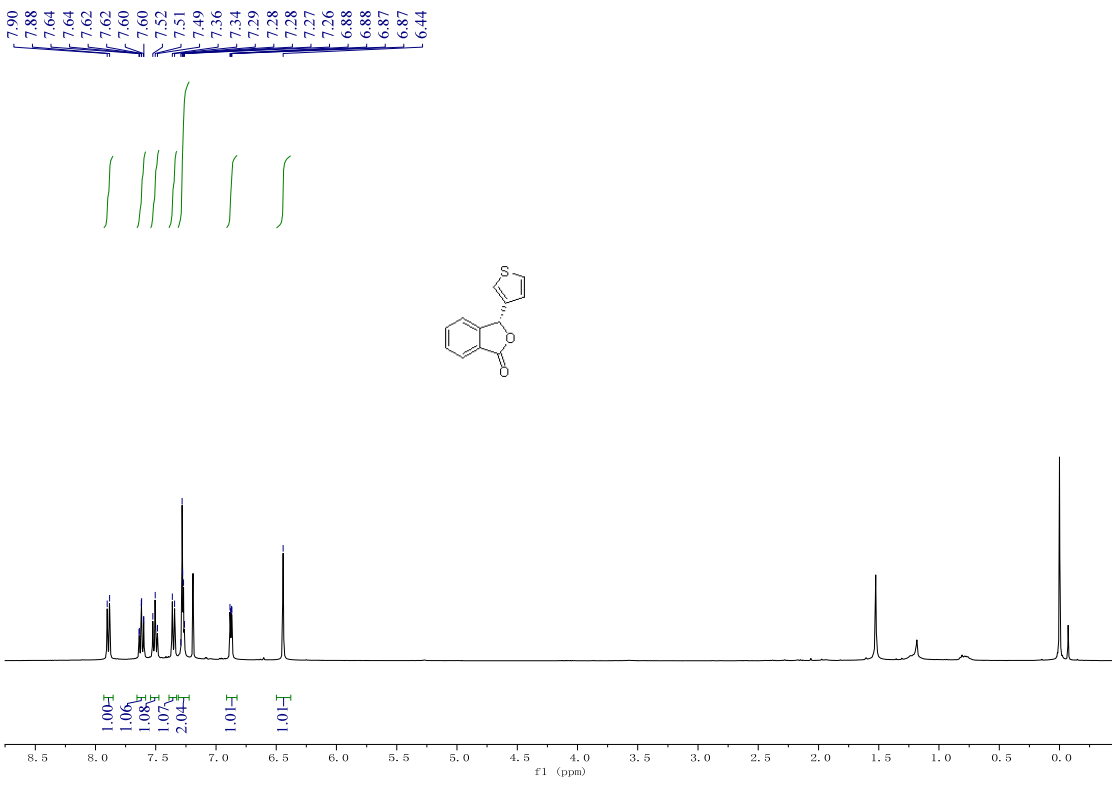
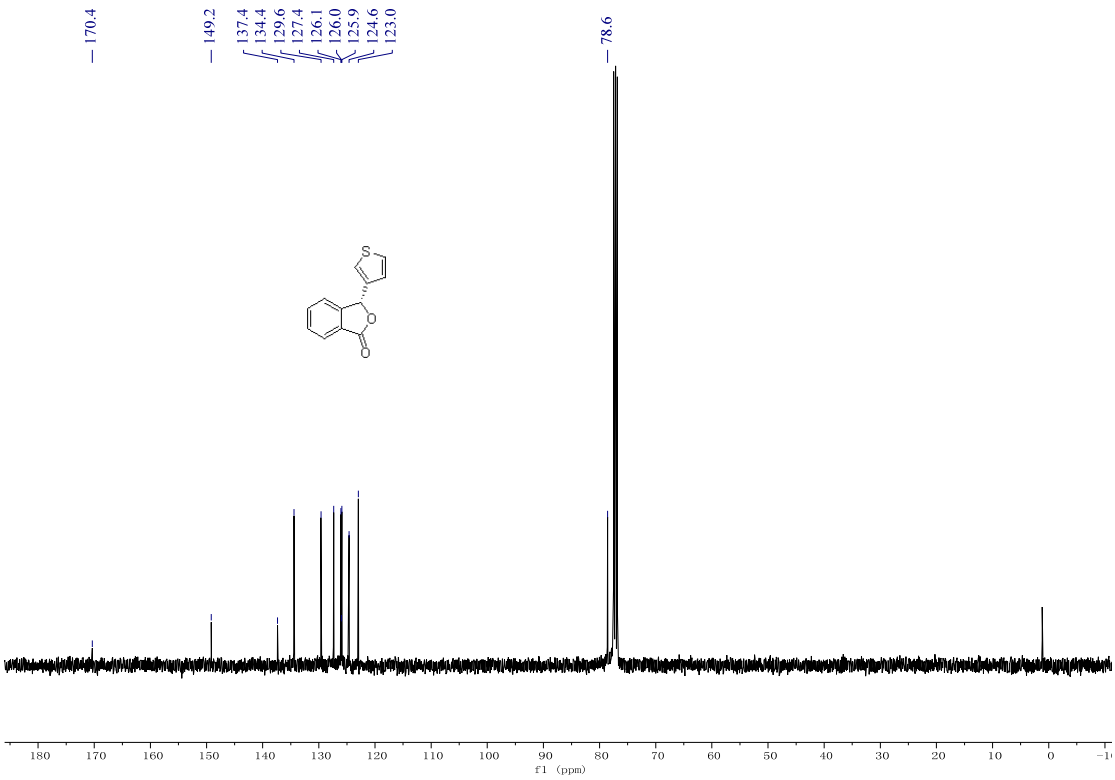
f1 (ppm)


170.2
149.0
137.7
134.8
132.1
131.8
131.4
131.1
130.3
129.9
129.8
127.9
126.3
126.3
126.3
126.2
126.1
125.5
125.2
123.9
123.9
123.8
123.8
122.9
122.5
119.8
81.8
CF3
O
O
f1 (ppm)


7.98
7.96
7.70
7.70
7.69
7.68
7.67
7.66
7.60
7.58
7.56
7.42
7.40
7.26
7.14
7.13
7.12
7.10
7.10
7.08
6.94
6.94
6.92
6.92
6.91
6.89
6.89
6.88
6.88
6.88
6.86
6.86
6.84
6.84
6.83
6.70
F
F
O
O
1.00
1.08
1.06
1.06
1.08
1.07
2.00
1.01
f1 (ppm)


170.3
164.8
164.7
162.3
162.2
159.8
159.7
149.0
134.7
129.8
129.2
129.2
129.1
129.1
126.0
125.7
122.9
122.8
120.4
120.3
112.3
112.2
112.1
112.0
104.9
104.7
104.4
76.4
76.3
F
F
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.90
7.88
7.64
7.64
7.62
7.62
7.60
7.60
7.52
7.51
7.49
7.36
7.34
7.29
7.28
7.28
7.27
7.26
6.88
6.88
6.87
6.87
6.44
S
O
O
1.00
1.06
1.08
1.07
2.04
1.01
1.01
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)


170.4
149.2
137.4
134.4
129.6
127.4
126.1
126.0
125.9
124.6
123.0
78.6
S
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

6. References

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