Surfactant-aided chiral palladium(II) catalysis exerted exclusively in water for the C–H functionalization of indoles

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Supporting Information

Total number of pages: 37 (S1-S37)
Total number of figures: 29 (Figure S1-Figure S29)
Total number of schemes and tables: 0

Contents

Experimental

General

Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECX-500 or 600 spectrometer, operating at 500 or 600 MHz for ^{1}H and 125 or 150 MHz for ^{13}C NMR in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) served as the internal standard ($\delta = 0$) for ^{1}H NMR and $CDCl_3$ was used as the internal standard ($\delta = 77.0$) for ^{13}C NMR. Infrared (IR) spectra were obtained using a JASCO FT/IR-4200 spectrometer. Data are represented as frequency of absorption (cm^{-1}). High-performance liquid chromatography was carried out using following apparatuses; SHIMADZU LC-10ATvp (liquid chromatograph), SHIMADZU SPD-10A (UV detector) and SHIMADZU C-R8A (Chromatopac) using Daicel chiralpak® or chiralcel® columns. Preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F from Wako Pure Chemical Industries, Ltd. High Resolution Mass Spectra (HRMS) were recorded using a JEOL JMS-T100TD (DART) spectrometer. Optical rotations were measured on a JASCO P1010 polarimeter using a 2 mL cell with 1 dm path length. Data are reported as follows: $[\alpha]_D^T$ (*c* in g/100 mL, solvent). Deionized water from a MILLIPORE MilliQ machine (Gradient A 10) was used as solvent without further treatment. All organic solvents used were commercially available dry solvents, which were distilled appropriately under an argon atmosphere or were stored over molecular sieves prior to use. All reagents used as additives were either distilled or recrystallized before use.

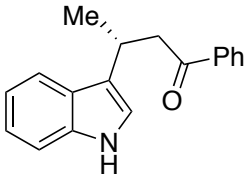
<Reagents>

Unless stated otherwise, commercially available reagents were used as received with the exception of the following substrates, which were prepared through reported methods. Analytical data for these compounds are in full agreement with reported data. Chiral 2,2'-bipyridine **L1** was synthesized using protocols described in literatures.[1,2]

Typical Experimental Procedure for $PdCl_2$-Catalyzed Asymmetric 1,4-Addition of Indoles to α,β-Unsaturated Carbonyl Compounds in Water (Table 3, entry 7):

To degassed water (0.6 mL) were added $PdCl_2$ (2.7 mg, 0.015 mmol), sodium dodecylsulfate (SDS, 8.7 mg, 0.030 mmol), **L1** (6.0 mg, 0.018 mmol), and $PhNMe_2$ (4.4 mg, 0.036 mmol). After vigorous stirring for 1 h at room temperature, 1-phenyl-2-buten-1-one **1a** (43.9 mg, 0.30 mmol) and indole **2a** (42.2 mg, 0.36 mmol) were added to the resultant mixture. After stirring for 24 h, the reaction mixture was quenched with saturated $NaHCO_3$ aqueous solution (1 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. After concentrated under reduced pressure, the crude mixture was purified by preparative TLC (^{n}hexane/AcOEt = 3/1) to afford the desired product **3aa** (62.2 mg, 79% yield) as a white solid. The obtained analytical data for the compound is in full agreement with reported data. The absolute configuration was determined by comparison of the order of retention time in the chiral HPLC analyses. The absolute configurations of optically active compounds were determined in the same way.

(*R*)-3-(1*H*-indol-3-yl)-1-phenylbutan-1-one (**3aa**)[3]



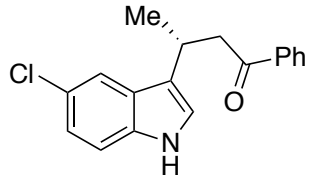
White solid; mp 100-101 °C.

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.45 (d, *J* = 6.9 Hz, 3H), 3.23 (dd, *J* = 9.1, 16.4 Hz, 1H), 3.47 (dd, *J* = 4.9, 16.3 Hz, 1H), 3.86-3.79 (m, 1H), 7.00 (s, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.55-7.51 (m, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.98-7.93 (m, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ: 21.0, 27.1, 46.4, 111.3, 119.2 (2C), 120.2, 121.4, 121.9, 126.3, 128.1, 128.5, 132.9, 136.5, 137.2, 199.8.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 90/10, flow rate 1.0 mL/min); t_R = 19.9 min (*S*, minor), t_R = 29.8 min (*R*, major).

(*R*)-3-(5-chloro-1*H*-indol-3-yl)-1-phenylbutan-1-one (**3ab**)[4]



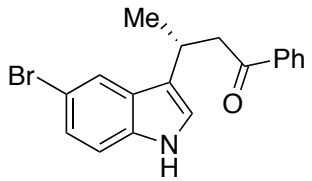
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.43 (d, *J* = 6.9 Hz, 3H), 3.21-3.26 (dd, *J* = 8.0, 16.6 Hz, 1H), 3.39-3.44 (dd, *J* = 5.2, 16.6 Hz, 1H), 3.73-3.80 (m, 1H), 7.03 (s, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.62 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 8.02 (br, 1H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 21.1, 27.0, 46.3, 112.2, 118.7, 121.3, 121.6, 122.3, 125.0, 127.4, 128.1, 128.6, 133.0, 134.8, 137.2, 199.5.

HPLC (Dialcel Chiralcel OD-H, *n*hexane/ *i*PrOH = 90/10, flow rate 1.0 mL/min); t_R = 14.9 min (*S*, minor), t_R = 20.6 min (*R*, major).

(*R*)-3-(5-bromo-1*H*-indol-3-yl)-1-phenylbutan-1-one (**3ac**)[5]



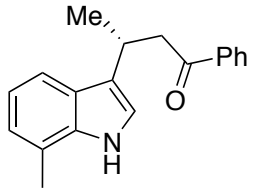
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.46 (d, *J* = 7.4 Hz, 3H), 3.24-3.29 (dd, *J* = 8.6, 16.6 Hz, 1H), 3.42-3.46 (dd, *J* = 5.8, 16.7 Hz, 1H), 3.76-3.83 (m, 1H), 7.04 (s, 1H), 7.22-7.29 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.80 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 2H), 8.08 (br, 1H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 21.1, 27.0, 46.3, 112.5, 112.6, 121.2, 121.5, 121.8, 124.8, 128.1 (2C), 128.6, 133.0, 135.1, 137.2, 199.4.

HPLC (Dialcel Chiralcel OD-H, *n*hexane/ *i*PrOH = 90/10, flow rate 1.0 mL/min); t_R = 15.2 min (*S*, minor), t_R = 19.0 min (*R*, major).

(*R*)-3-(7-methyl-1*H*-indol-3-yl)-1-phenylbutan-1-one (**3ad**)[6]



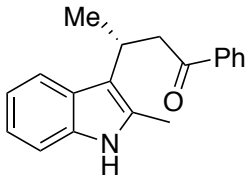
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.44 (d, *J* = 6.9 Hz, 3H), 2.46 (s, 3H), 3.23 (dd, *J* = 8.8, 16.1 Hz, 1H), 3.47 (dd, *J* = 4.6, 16.4 Hz, 1H), 3.79-3.84 (m, 1H), 6.98-7.06 (m, 3H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.51-7.53 (m, 2H), 7.94 (d, *J* = 7.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 16.6, 21.0, 27.3, 46.5, 117.0, 119.5, 120.0, 120.5, 122.0, 122.6, 125.8, 128.1, 128.5, 132.9, 136. 137.3, 199.8.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 49/1, flow rate 1.0 mL/min); t_R = 49.9 min (*S*, minor), t_R = 54.8 min (*R*, major).

(*R*)-3-(2-methyl-1*H*-indol-3-yl)-1-phenylbutan-1-one (**3ae**)[6]



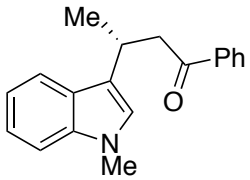
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.50 (dd, *J* = 3.4, 7.4 Hz, 3H), 2.38 (d, *J* = 3.5 Hz, 3H), 3.35-3.41 (m, 1H), 3.50-3.56 (m, 1H), 3.72-3.78 (m, 1H), 7.05-7.09 (m, 2H), 7.23-7.25 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.4Hz, 1H), 7.67-7.69 (m, 2H), 7.88 (d, *J* = 6.9 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 12.0, 21.0, 27.3, 45.6, 110.5, 115.5, 118.9, 119.0, 120.6, 127.1, 128.0, 128.4, 130.3, 132.8, 135.5, 137.3, 200.0.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 90/10, flow rate 1.0 mL/min); t_R = 20.9 min (*S*), t_R = 23.2 min (*R*).

(*R*)-3-(1-methyl-1*H*-indol-3-yl)-1-phenylbutan-1-one (**3af**)[6]



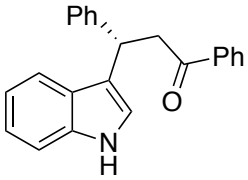
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.44 (d, *J* = 6.9 Hz, 3H), 3.20-3.25 (dd, *J* = 9.2, 16.4 Hz, 1H), 3.44-3.48 (dd, *J* = 4.9, 16.3 Hz, 1H), 3.73 (s, 3H), 3.79-3.83 (m, 1H), 6.88 (s, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 21.1, 27.1, 32.6, 46.7, 109.3, 118.7, 119.3, 120.0, 121.6, 125.0, 126.7, 128.1, 128.5, 132.9, 137.2, 137.3, 199.7.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 90/10, flow rate 1.0 mL/min); t_R = 19.1 min (*R*, major), t_R = 22.2 min (*S*, minor).

(*S*)-3-(1H-indol-3-yl)-1,3-diphenylpropan-1-one (**3ba**)[4]



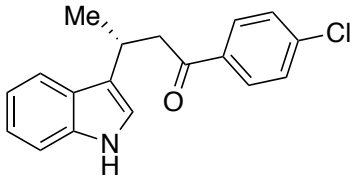
White solid; mp 128-130 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$); δ = 3.72 (dd, *J* = 7.6, 16.5 Hz, 1H), 3.81 (dd, *J* = 6.9, 18.4 Hz, 1H), 5.07 (t, *J* = 6.9 Hz, 1H), 6.96 (s, 1H), 7.01 (t, *J* = 6.3 Hz, 1H), 7.12-7.16 (m, 2H), 7.24-7.26 (m, 2H), 7.29 (d, *J* = 6.3 Hz, 1H), 7.34 (d, *J* = 5.8 Hz, 2H), 7.40-7.44 (m, 2H), 7.52-7.54 (m, 1H), 7.92 (d, *J* = 6.3 Hz, 2H), 7.97 (br, s, 1H).

^{13}C NMR (150 MHz, $CDCl_3$); δ = 38.2, 45.2, 111.1, 119.3, 119.4, 119.5, 121.4, 122.1, 126.3, 126.6, 127.8, 128.1, 128.4, 128.6, 133.0, 136.6, 137.1, 144.2, 198.5.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 90/10, flow rate 1.0 mL/min); t_R = 28.6 min (*S*, minor), t_R = 40.1 min (*R*, major).

(*R*)-3-(1*H*-indol-3-yl)-1-(4-chlorophenyl)-butan-1-one (**3ca**)



Colorless oil

IR(neat) ν = 1587, 1679, 3410 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$); δ = 1.44 (d, *J* = 6.8 Hz, 3H), 3.16-3.20 (dd, *J* = 8.9, 16.8 Hz, 1H), 3.40-3.43 (dd, *J* = 5.2, 16.9 Hz, 1H), 3.77-3.81 (m, 1H), 6.96 (s, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.9 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.99 (br, 1H).

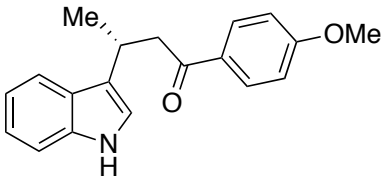
^{13}C NMR (150 MHz, $CDCl_3$); δ = 20.9, 27.2, 46.4, 111.3, 119.1, 119.2, 120.2, 121.1, 122.0, 126.2, 128.8, 129.5, 135.5, 136.5, 139.3, 198.6.

HPLC (Dialcel Chiralcel OD-H, ^{n}hexane/ ^{i}PrOH = 90/10, flow rate 1.0 mL/min); t_R = 23.5 min (*S*, minor), t_R = 57.1 min (*R*, major).

DART-HRMS: Calcd for $C_{18}H_{17}NOCl$ $[M+H]^+$ 298.0999, Found 298.0994.

$[\alpha]_D^{25}$ = +18.8 (*c* = 0.61, $CHCl_3$).

(*R*)-3-(1*H*-indol-3-yl)-1-(4-methoxyphenyl)-butan-1-one (**3da**)[4]



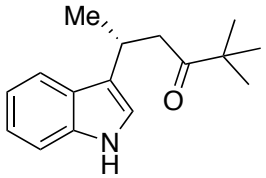
Colorless oil

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.43 (d, *J* = 6.9 Hz, 3H), 3.15-3.20 (dd, *J* = 9.2, 16.1 Hz, 1H), 3.39-3.43 (dd, *J* = 4.6, 16.0 Hz, 1H), 3.80-3.84 (m, 4H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.99 (s, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.6 Hz, 2H), 8.01 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 21.0, 27.3, 46.1, 55.4, 111.2, 113.6, 119.2 (2C), 120.2, 121.6, 121.9, 126.3, 130.4 (2C), 136.5, 163.3, 198.4.

HPLC (Dialcel Chiralcel OD-H, *n*hexane/ *i*PrOH = 90/10, flow rate 1.0 mL/min); t_R = 25.0 min (*S*, minor), t_R = 61.3 min (*R*, major).

(*R*)-5-(1H-indol-3-yl)-2,2-dimethylhexan-3-one (**3ea**)



Colorless oil

IR(neat) ν = 738, 1459, 1697, 2968, 3398 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$); δ = 1.09 (s, 9H), 1.34 (d, *J* = 6.8 Hz, 3H), 2.79 (dd, *J* = 8.7, 17.3 Hz, 1H), 2.92 (dd, *J* = 4.8, 17.3 Hz, 1H), 3.68-3.72 (m, 1H), 6.96 (s, 1H), 7.09-7.12 (m, 1H), 7.16-7.19 (m, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.97 (br, s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$); δ = 20.6, 26.2, 26.3, 44.2, 44.6, 111.2, 119.1, 119.3, 120.1, 121.7, 121.9, 126.3, 136.5, 215.1.

HPLC (Dialcel Chiralcel OD-H, *n*hexane/ *i*PrOH = 90/10, flow rate 1.0 mL/min); t_R = 8.5 min (*S*, minor), t_R = 10.0 min (*R*, major).

DART-HRMS: Calcd for $C_{16}H_{21}NO$ $[M+H]^+$ 244.1701, Found 244.1712.

$[\alpha]_D^{30}$ = +1.36 (*c* = 0.38, $CHCl_3$).

References

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Figure S1. ^{1}H NMR spectrum of **3aa**.

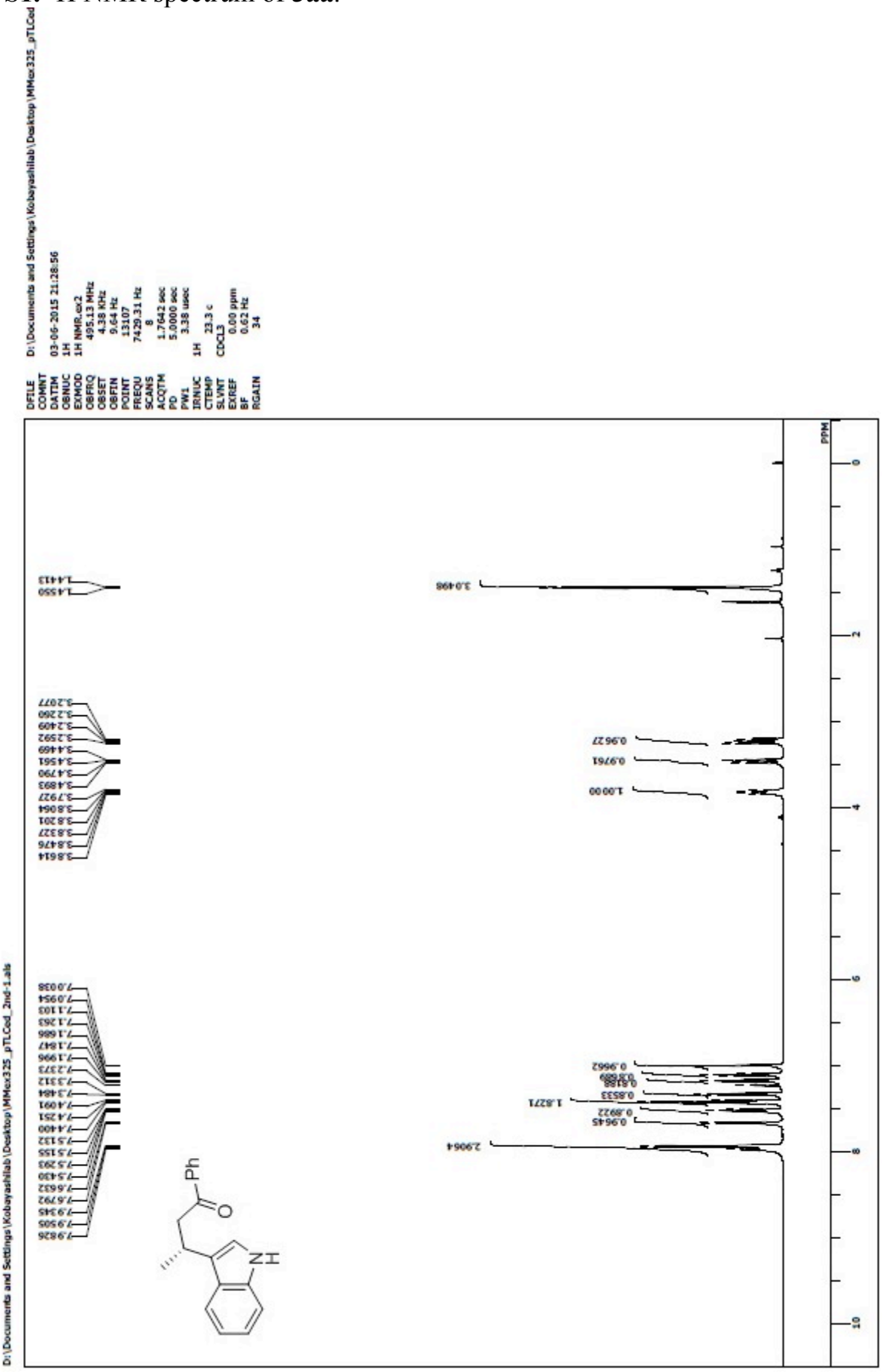


Figure S2. ^{13}C NMR spectrum of **3aa**.

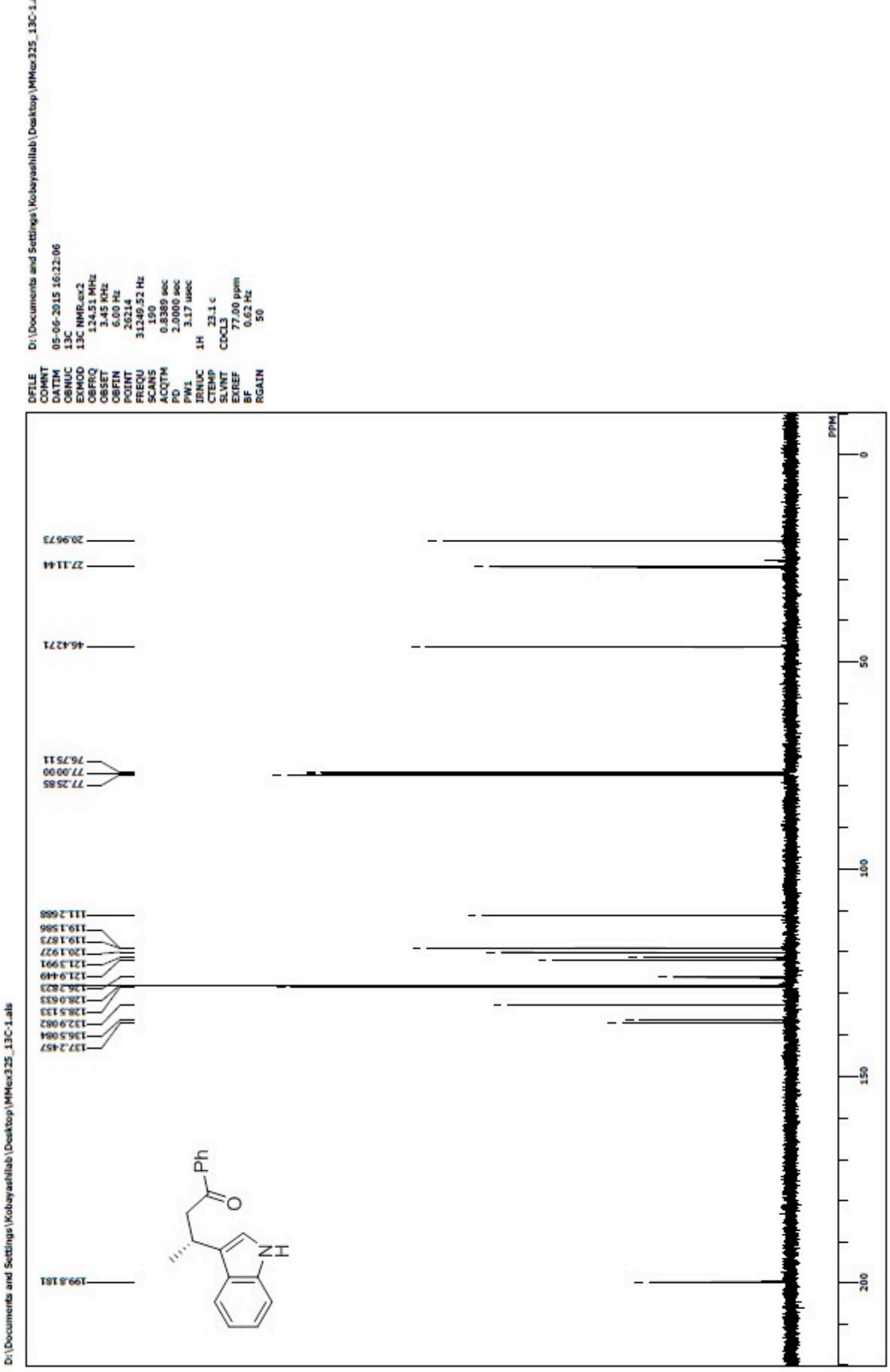
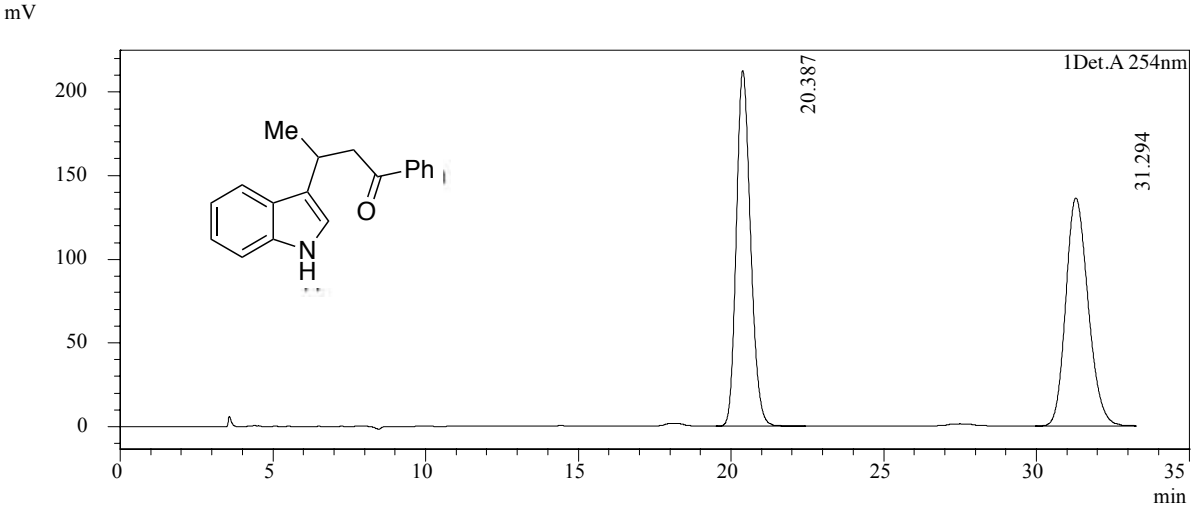


Figure S3. HPLC spectrum of racemic and chiral **3aa**.



Det.A 254nm

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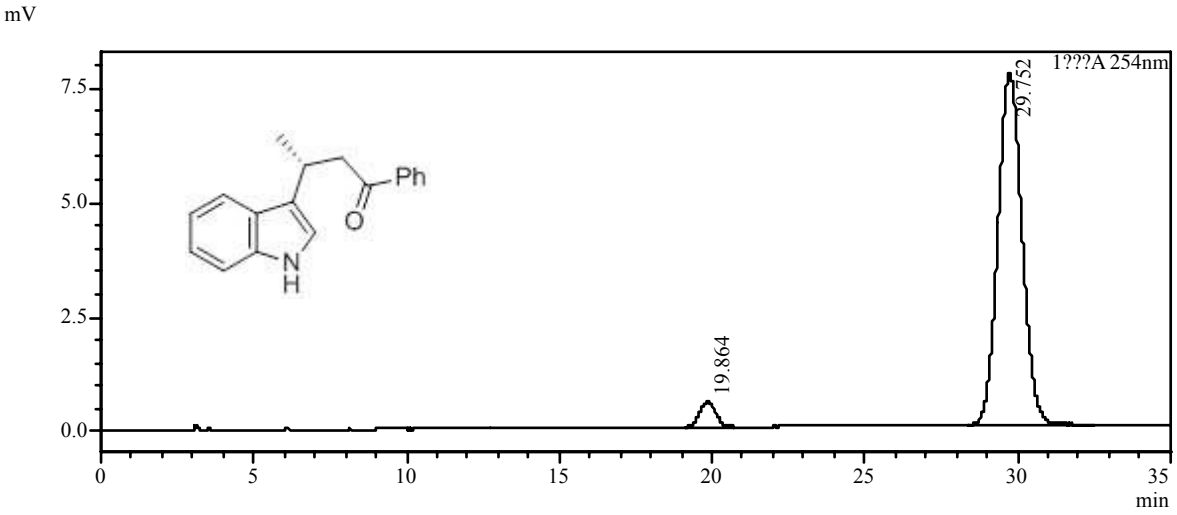
2	31.294	6933822	136246	50.164



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	19.864	19954	555	4.533
2	29.752	420187	7679	95.467

Figure S4. ^{1}H NMR spectrum of **3ab**.

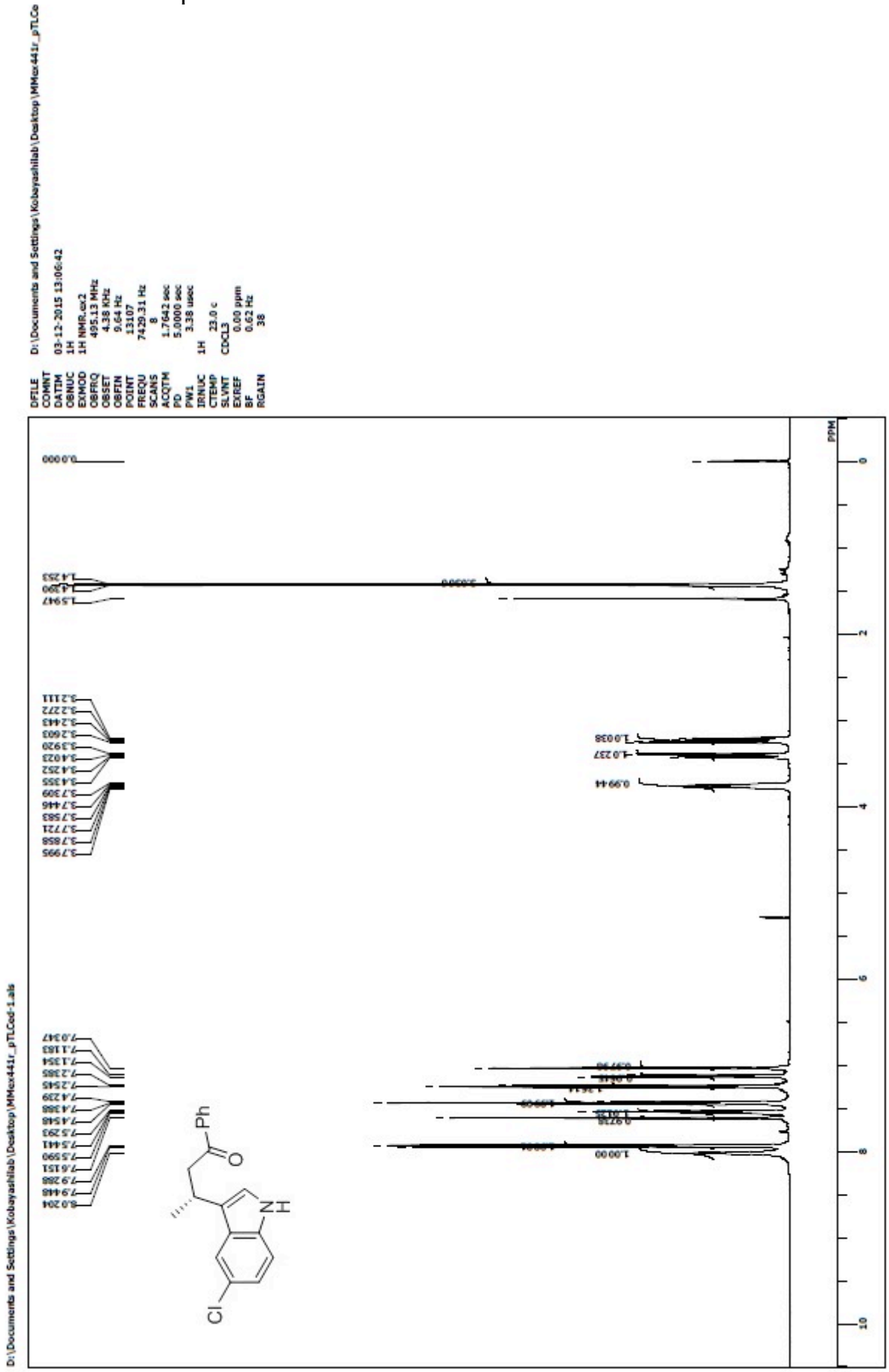


Figure S5. ^{13}C NMR spectrum of **3ab**.

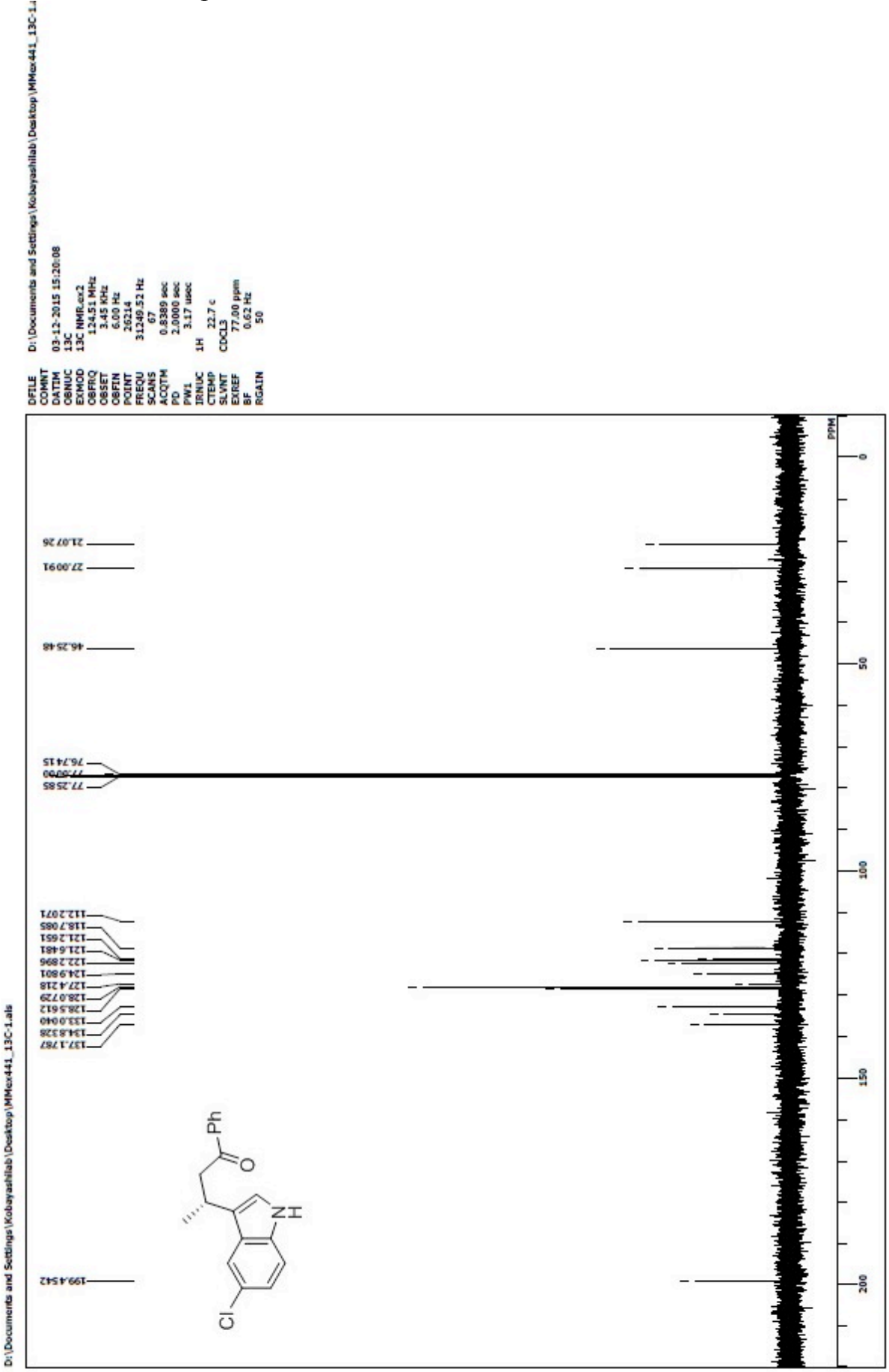
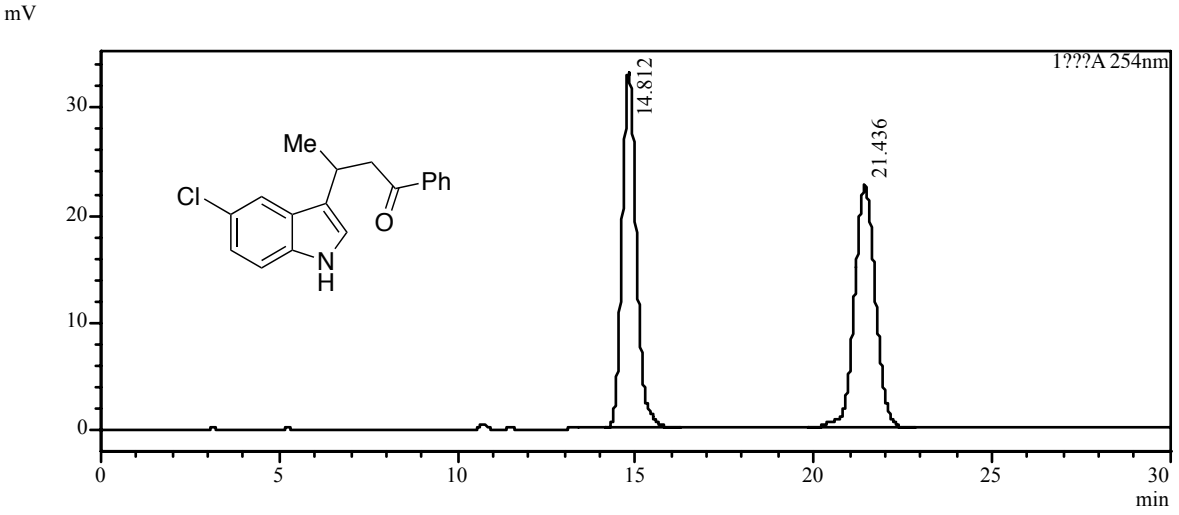
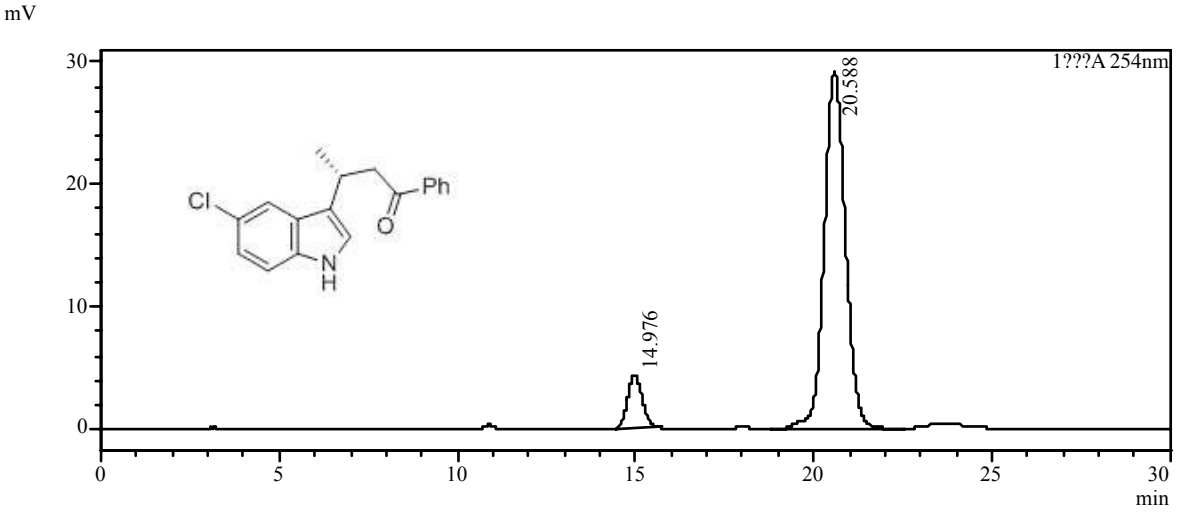


Figure S6. HPLC spectrum of racemic and chiral **3ab**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.812	931763	33154	49.990
2	21.436	932153	22529	50.010



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.976	125113	4360	9.341
2	20.588	1214348	29214	90.659

Figure S7. ^{1}H NMR spectrum of **3ac**.

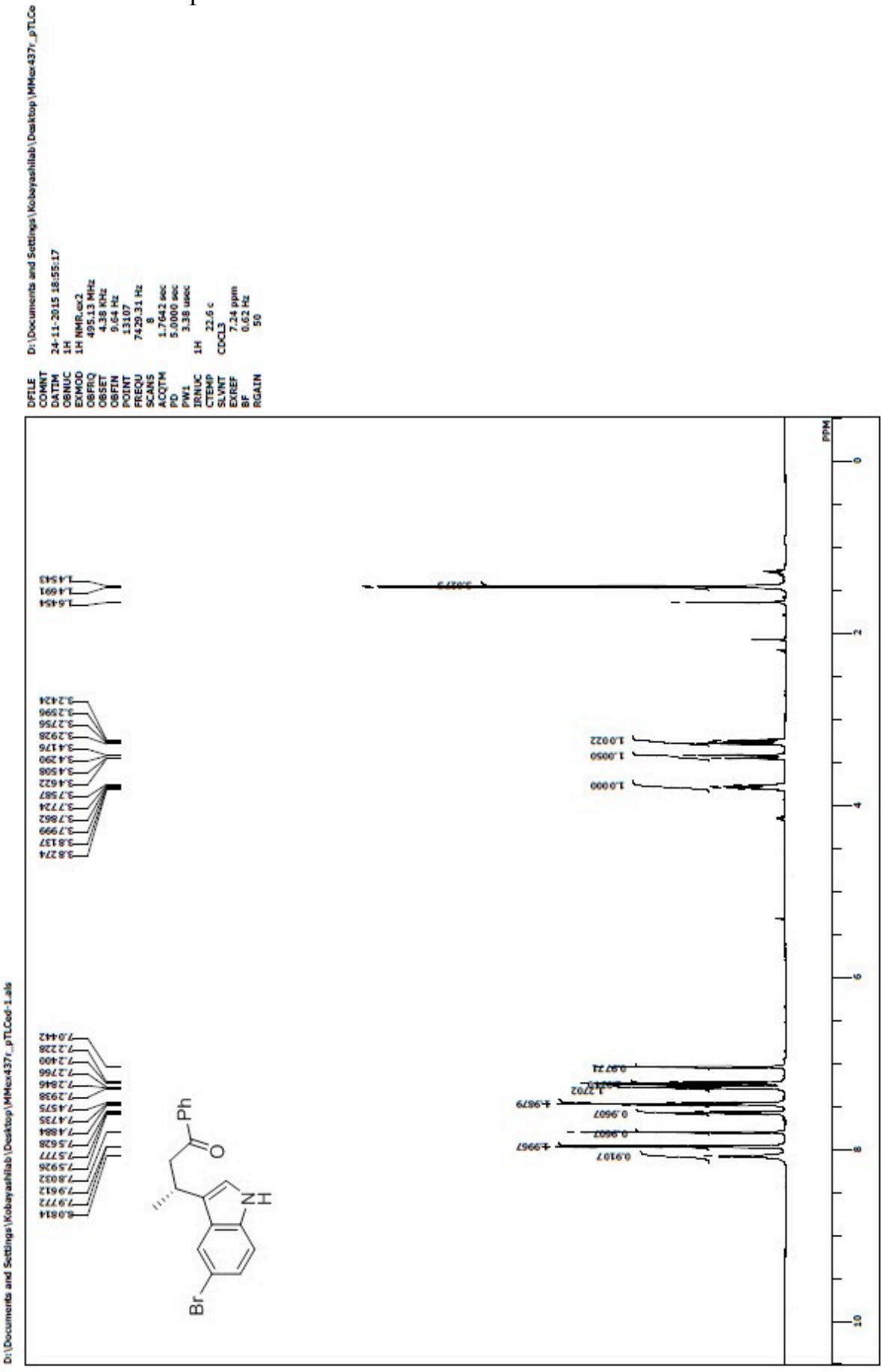


Figure S8. ^{13}C NMR spectrum of **3ac**.

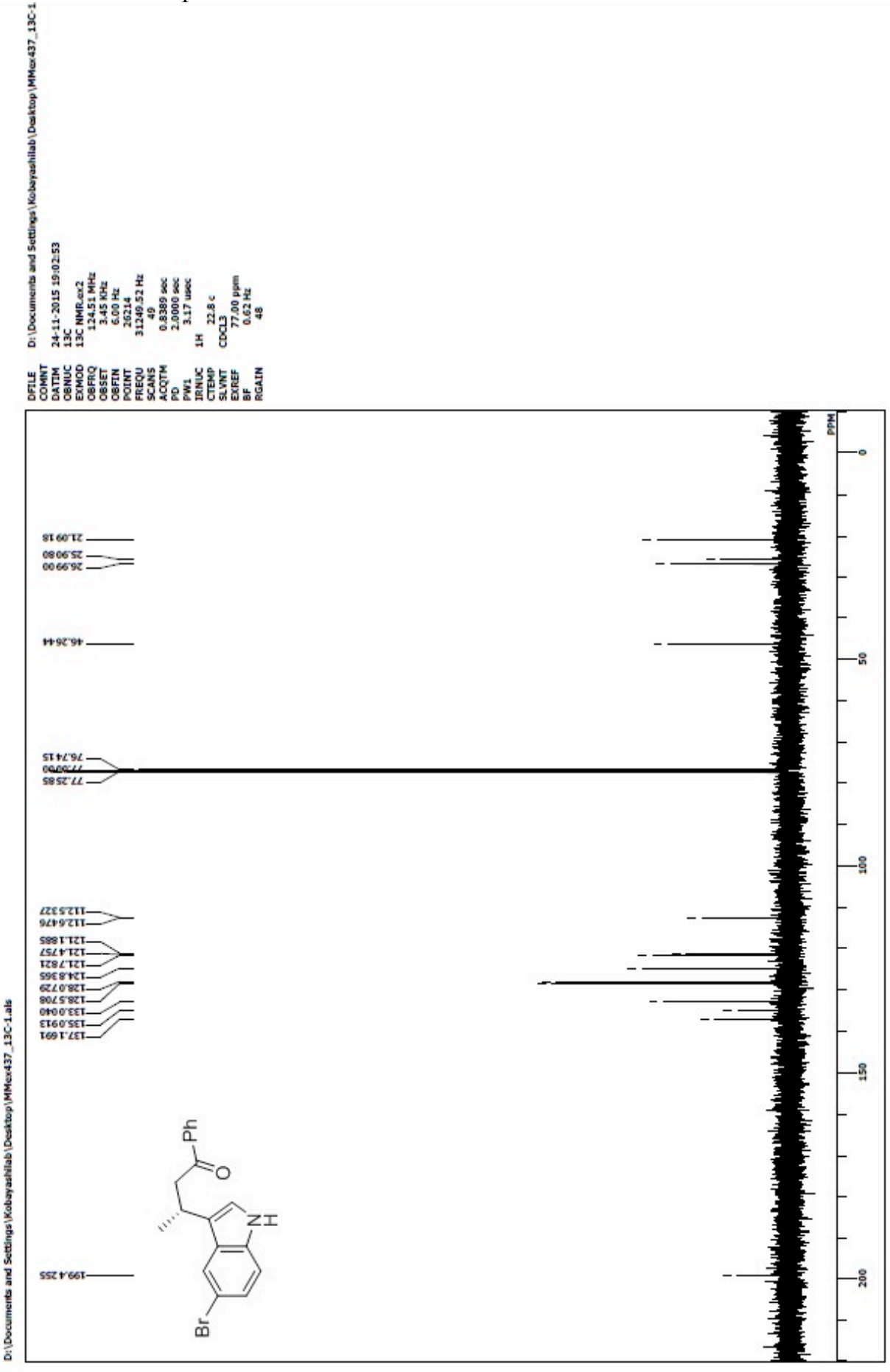
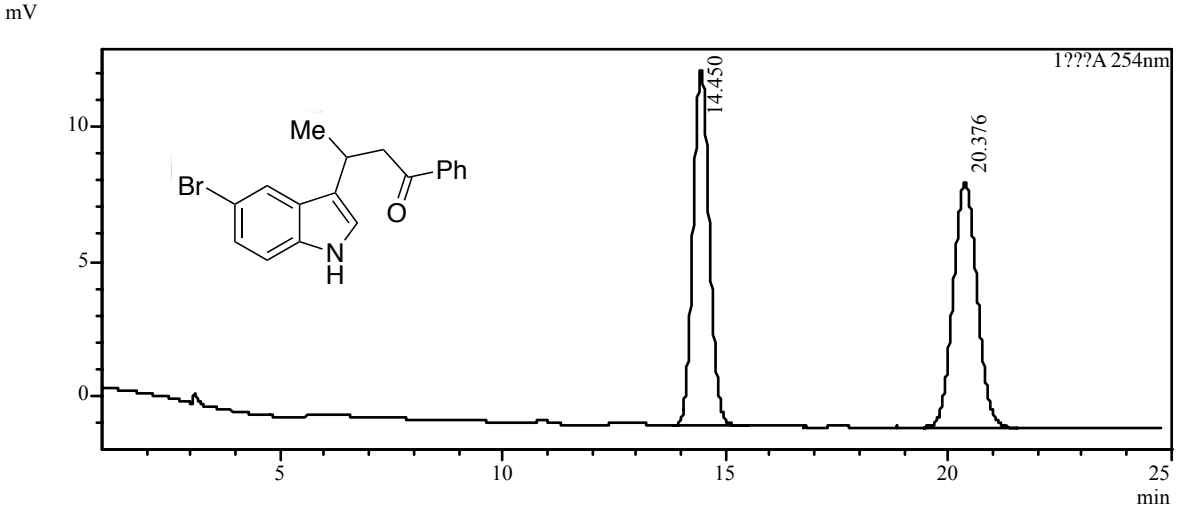
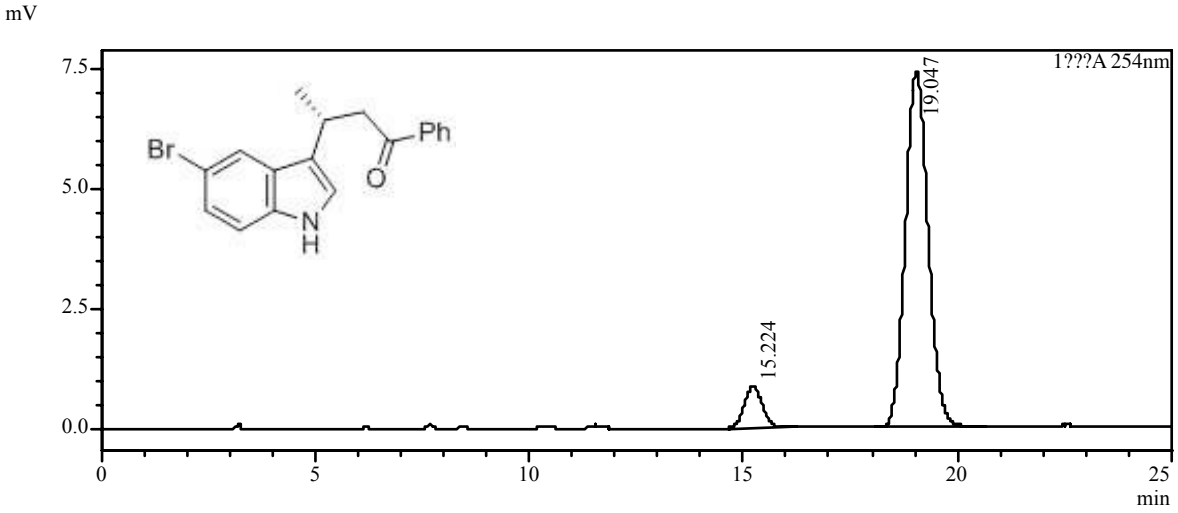


Figure S9. HPLC spectrum of racemic and chiral **3ac**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.450	336466	13147	49.848
2	20.376	338522	9093	50.152



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.224	24978	866	8.329
2	19.047	274924	7395	91.671

Figure S10. ^{1}H NMR spectrum of **3ad**.

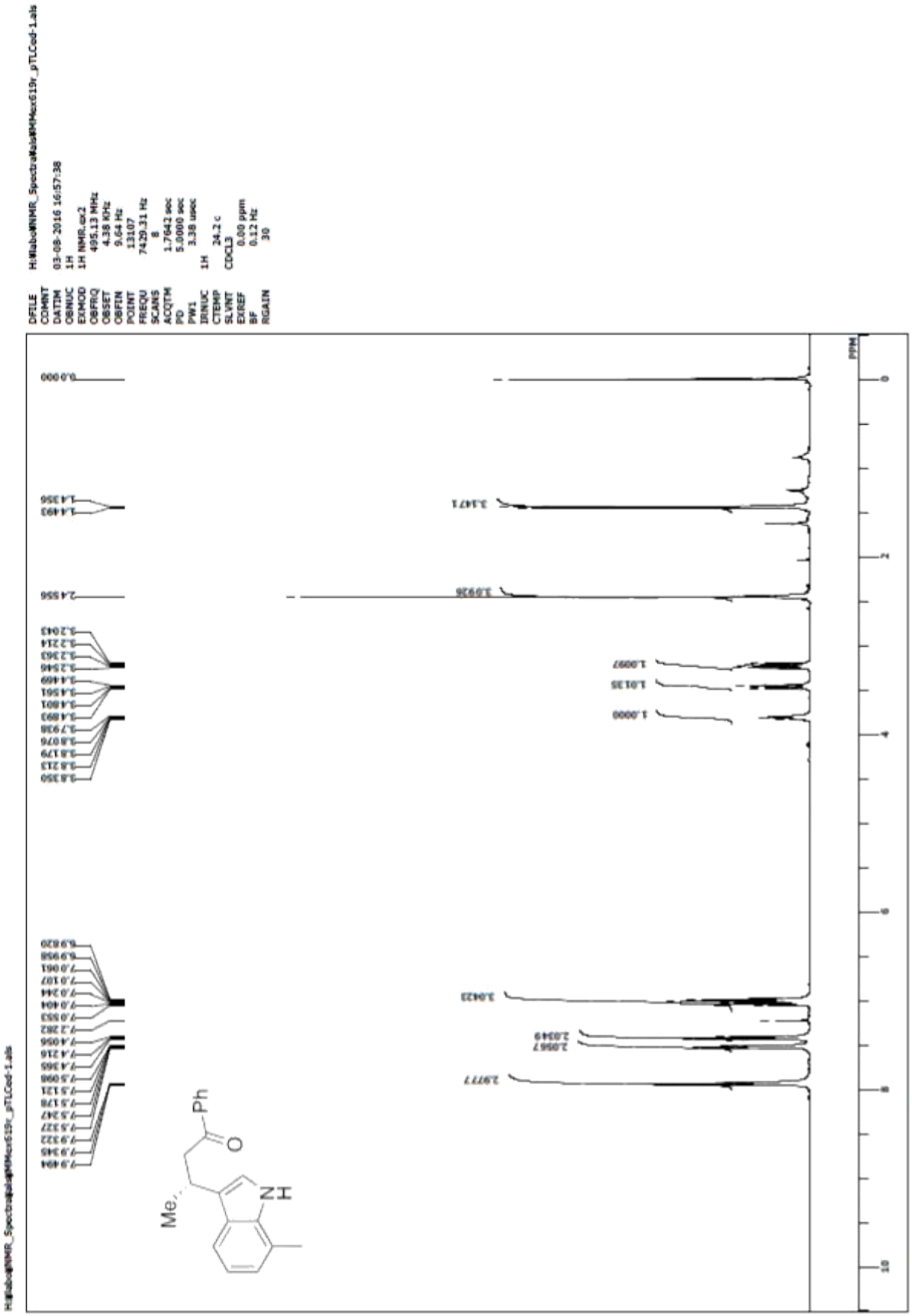


Figure S11. ^{13}C NMR spectrum of **3ad**.

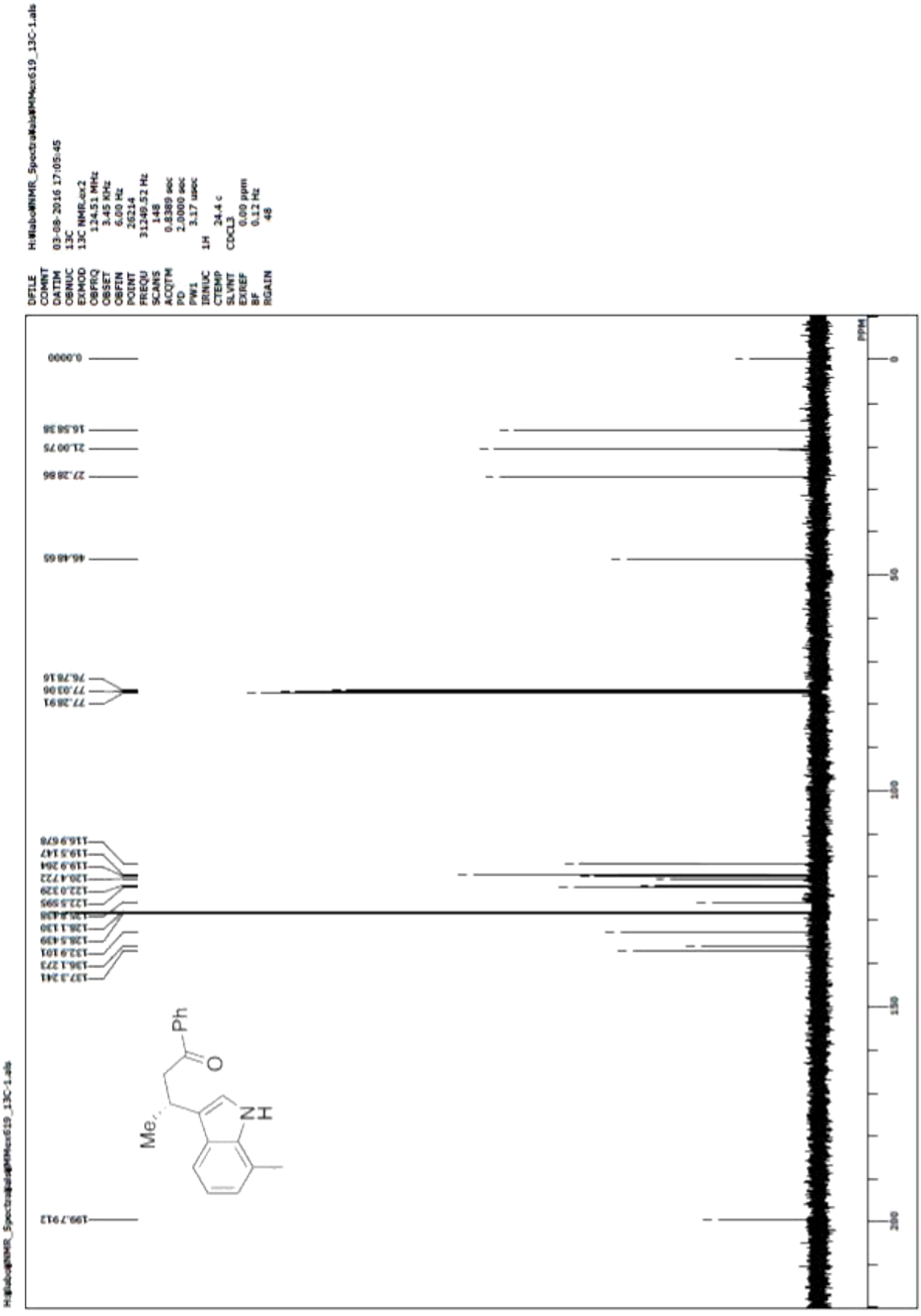
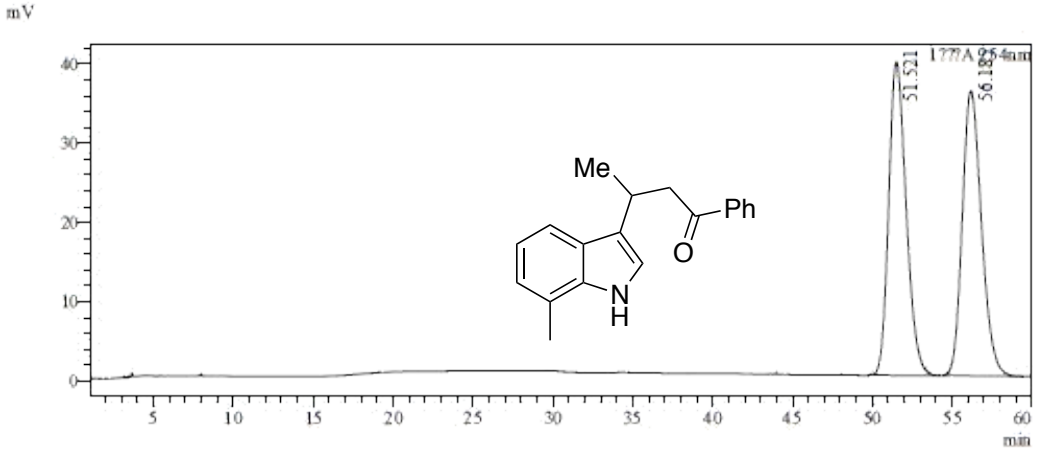
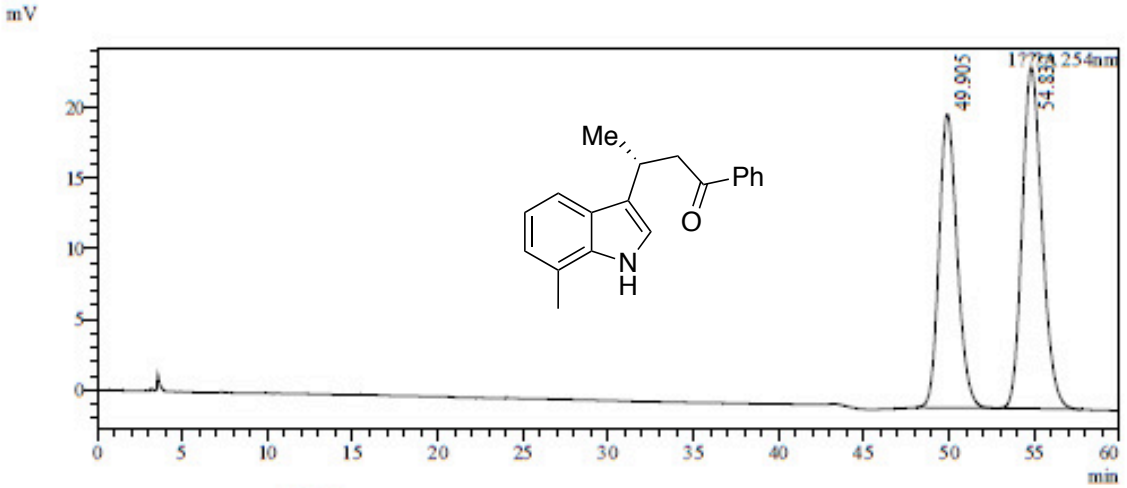


Figure S12. HPLC spectrum of racemic and chiral **3ad**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	51.521	3012526	39584	50.007
2	56.185	3011626	36000	49.993



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	49.905	1545226	20837	43.928
2	54.832	1972406	24196	56.072

Figure S13. ^{1}H NMR spectrum of **3ae**.

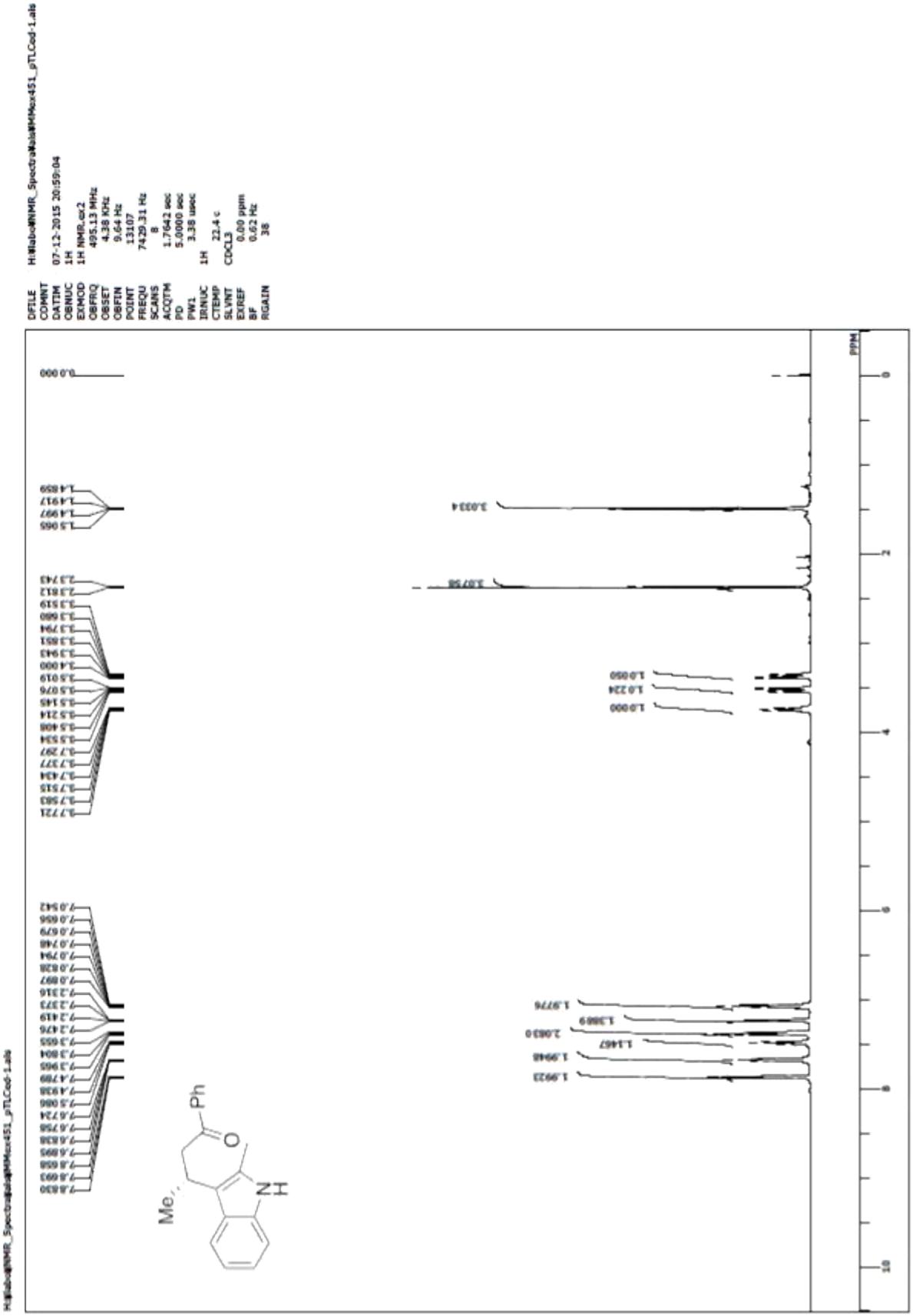


Figure S14. ^{13}C NMR spectrum of **3ae**.

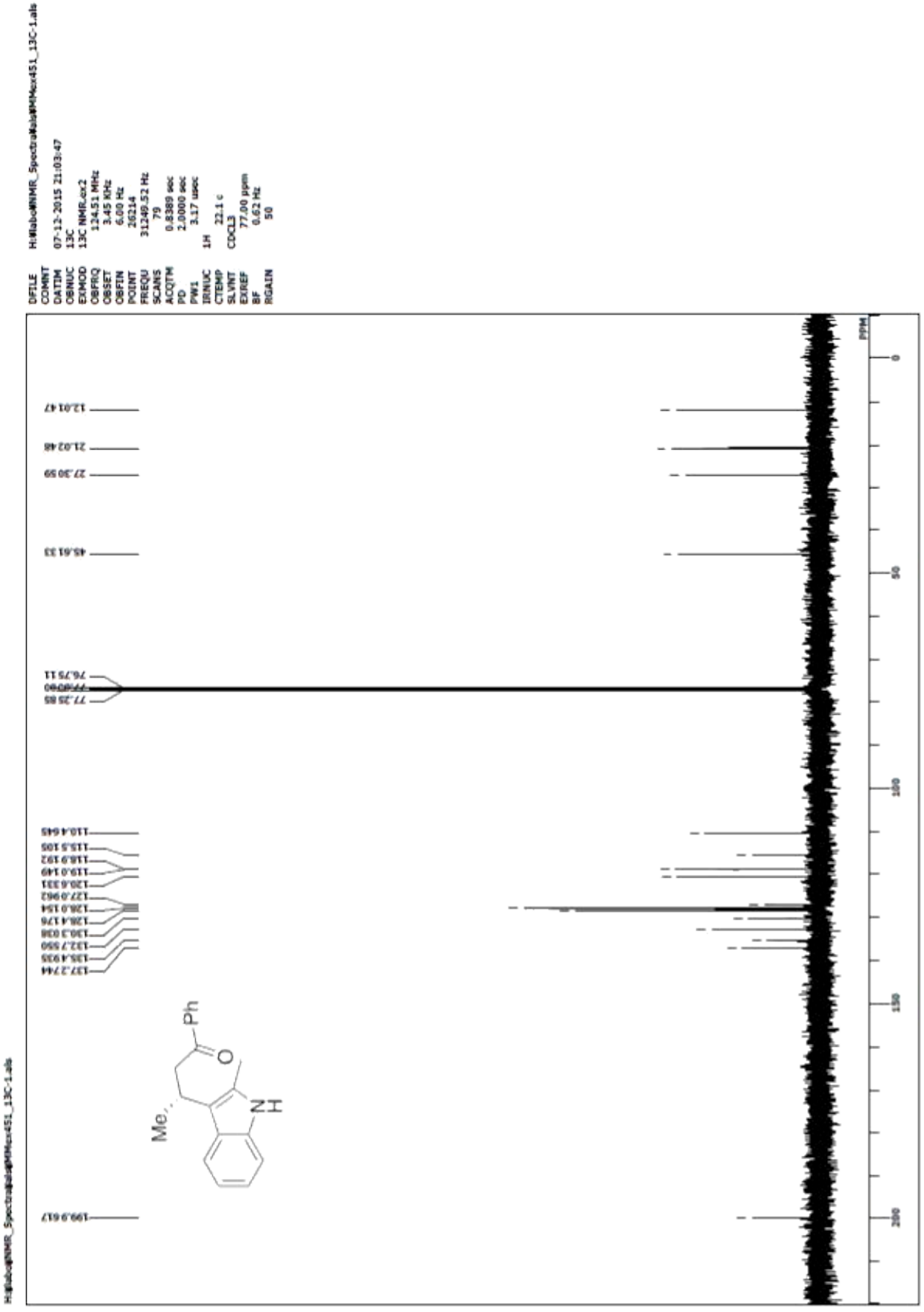


Figure S15. ^{1}H NMR spectrum of **3af**.

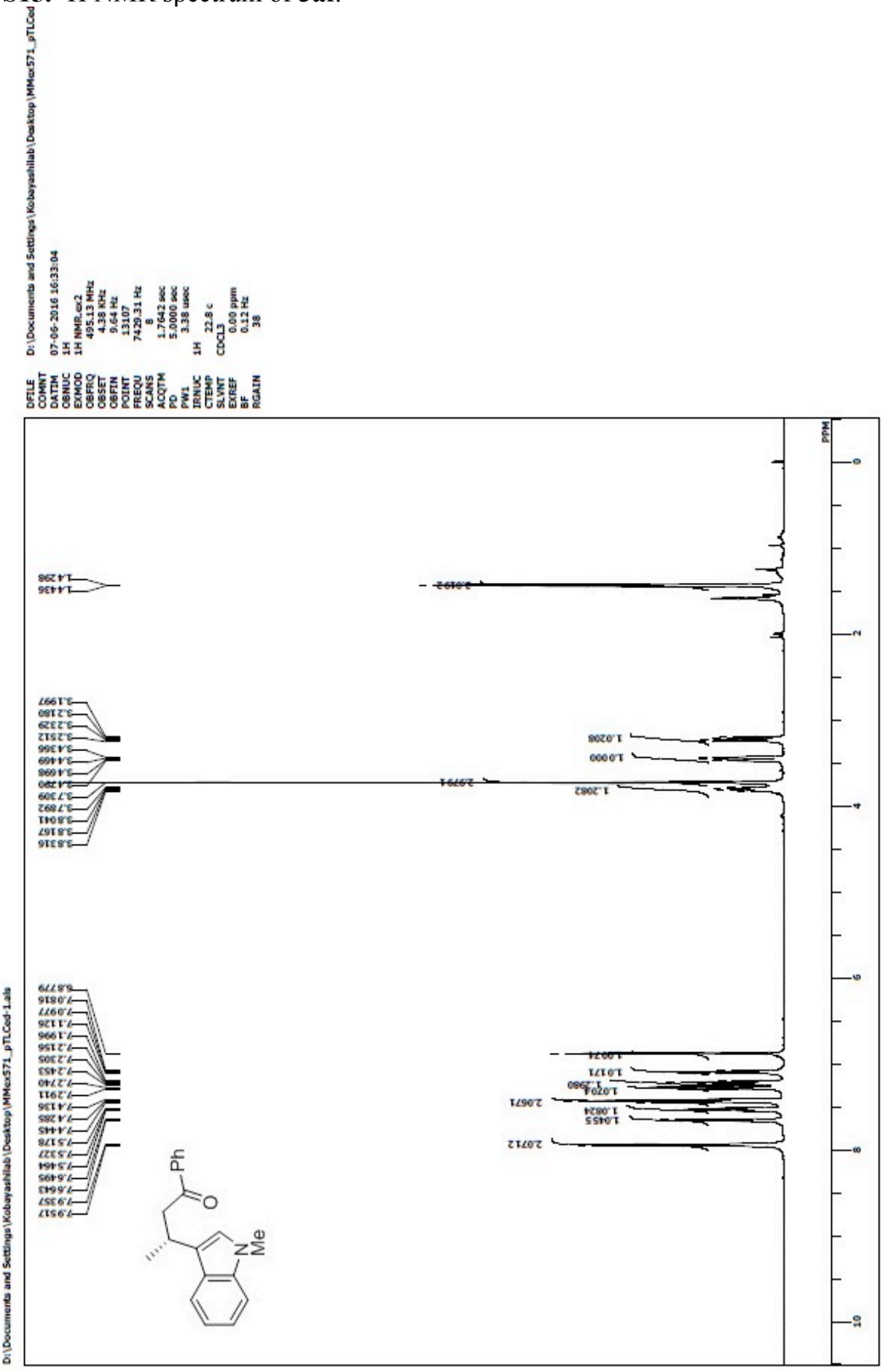


Figure S16. ^{13}C NMR spectrum of **3af**.

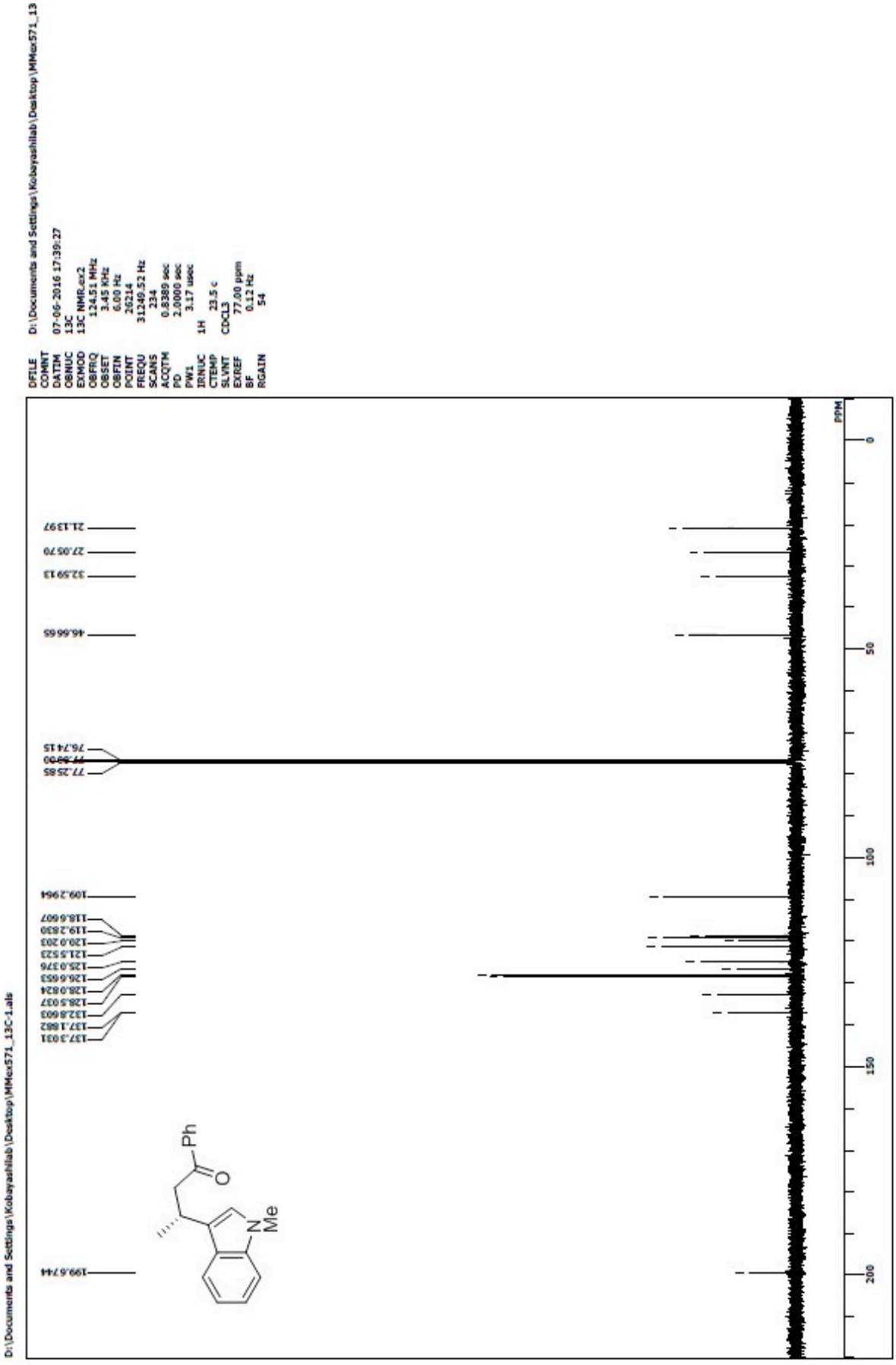
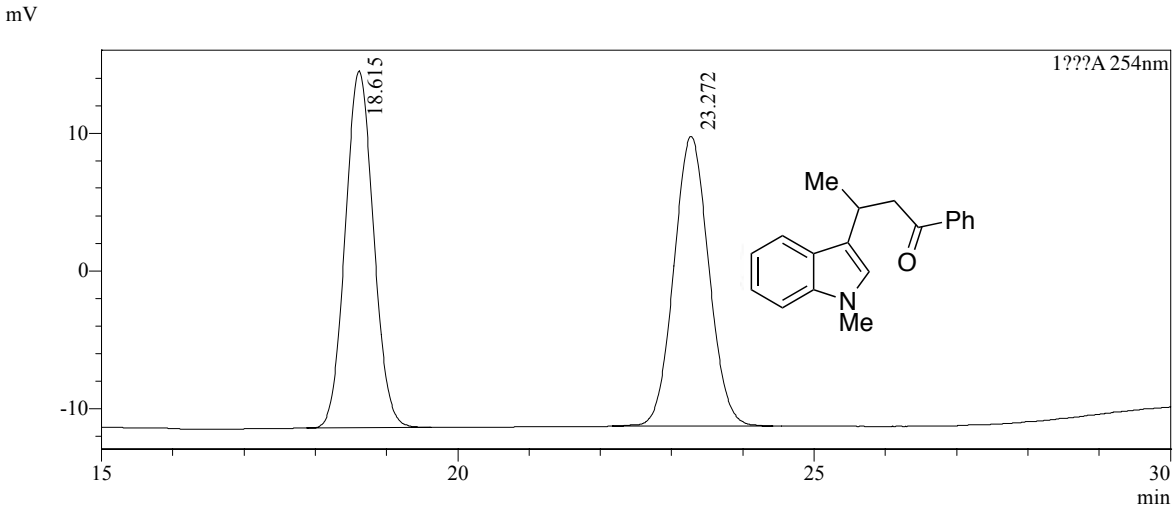
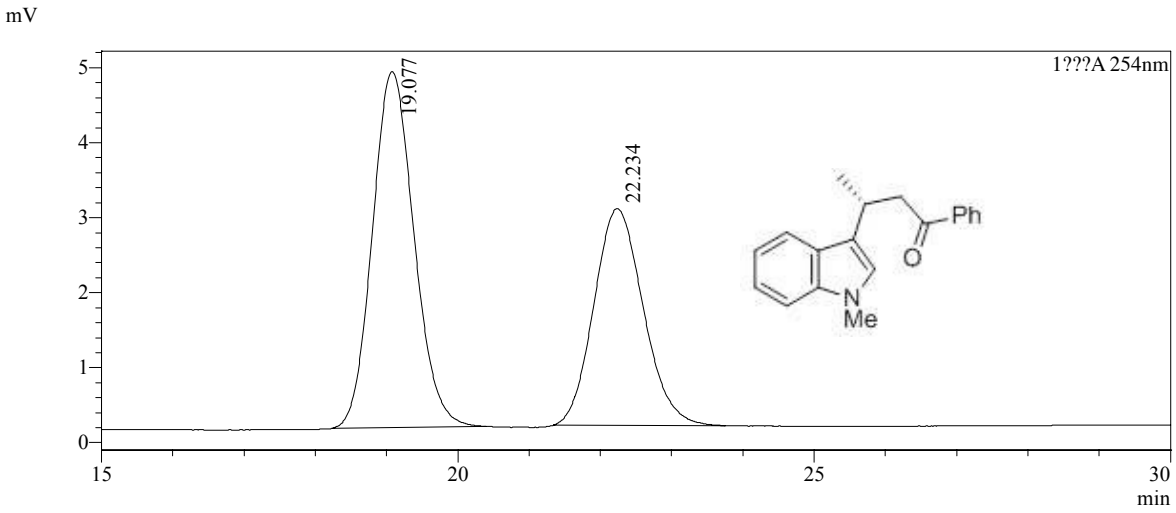


Figure S17. HPLC spectrum of racemic and chiral **3af**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	18.615	714274	25932	49.956
2	23.272	715524	21014	50.044



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	19.077	192232	4748	57.986
2	22.234	139281	2890	42.014

Figure S18. ^{1}H NMR spectrum of **3ba**.

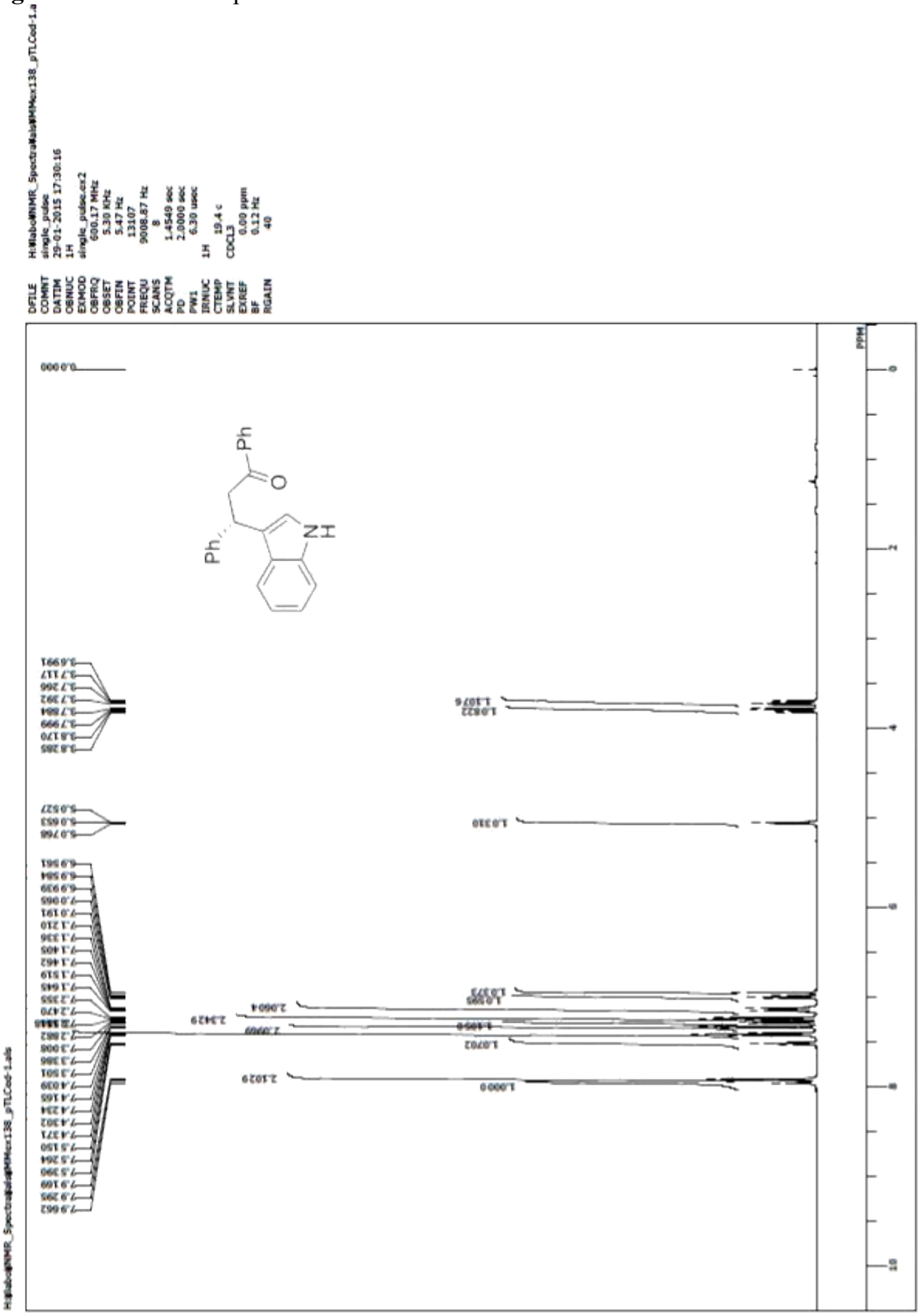


Figure S19. ^{13}C NMR spectrum of **3ba**.

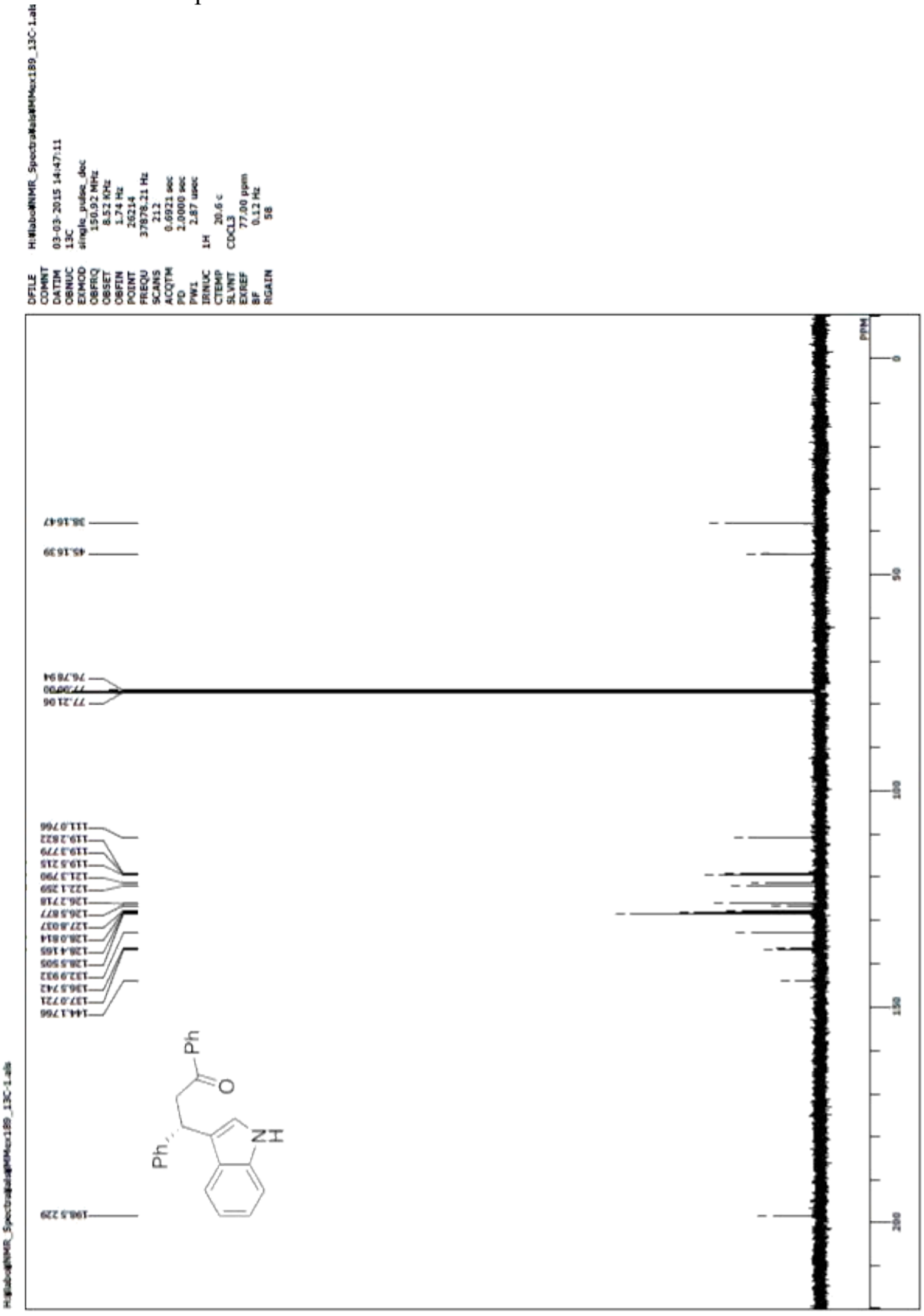
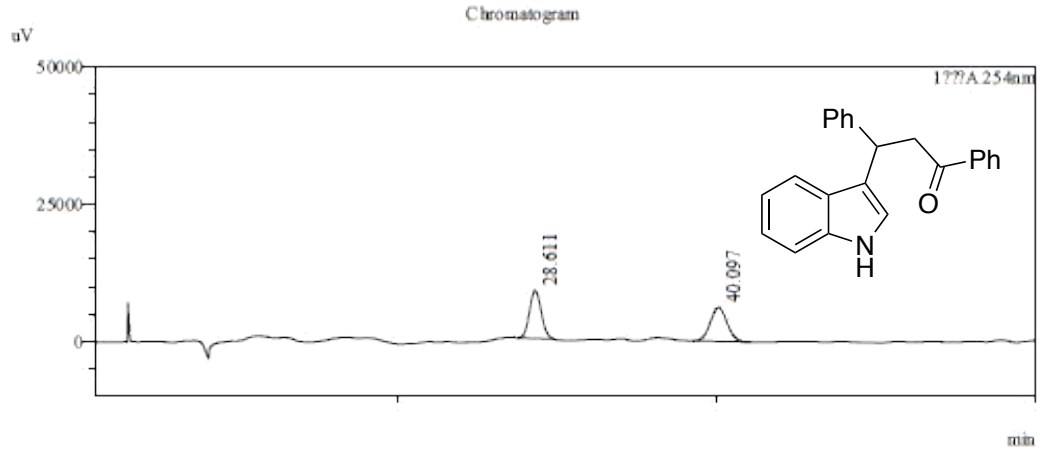
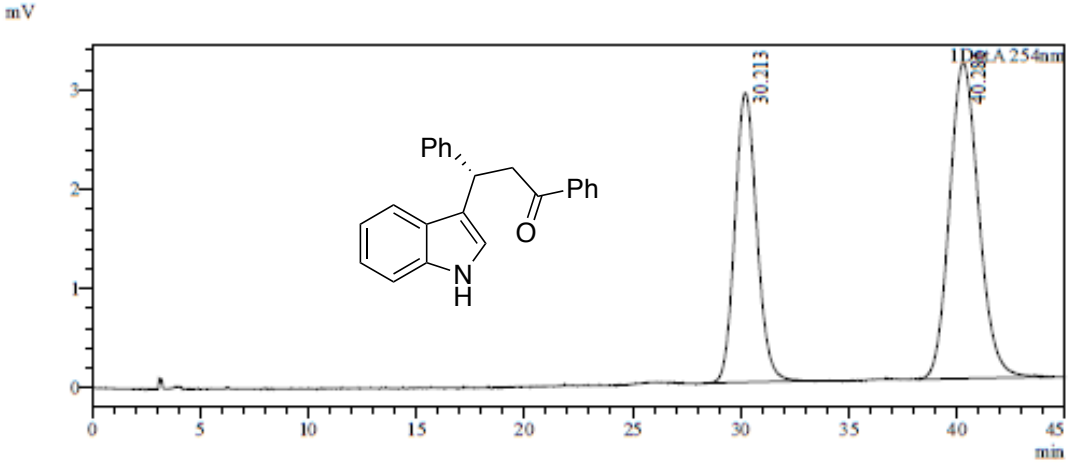


Figure S20. HPLC spectrum of racemic and chiral **3ba**.



???A,254nm

Peak#	Ret. Time	Area	Height	Area%
1	28.611	450976	8776	50.011
2	40.097	450783	6173	49.989



Det.A,254nm

Peak#	Ret. Time	Area	Height	Area%
1	30.213	205268	2917	40.665
2	40.286	299503	3179	59.335

Figure S21. ^{1}H NMR spectrum of **3ca**.

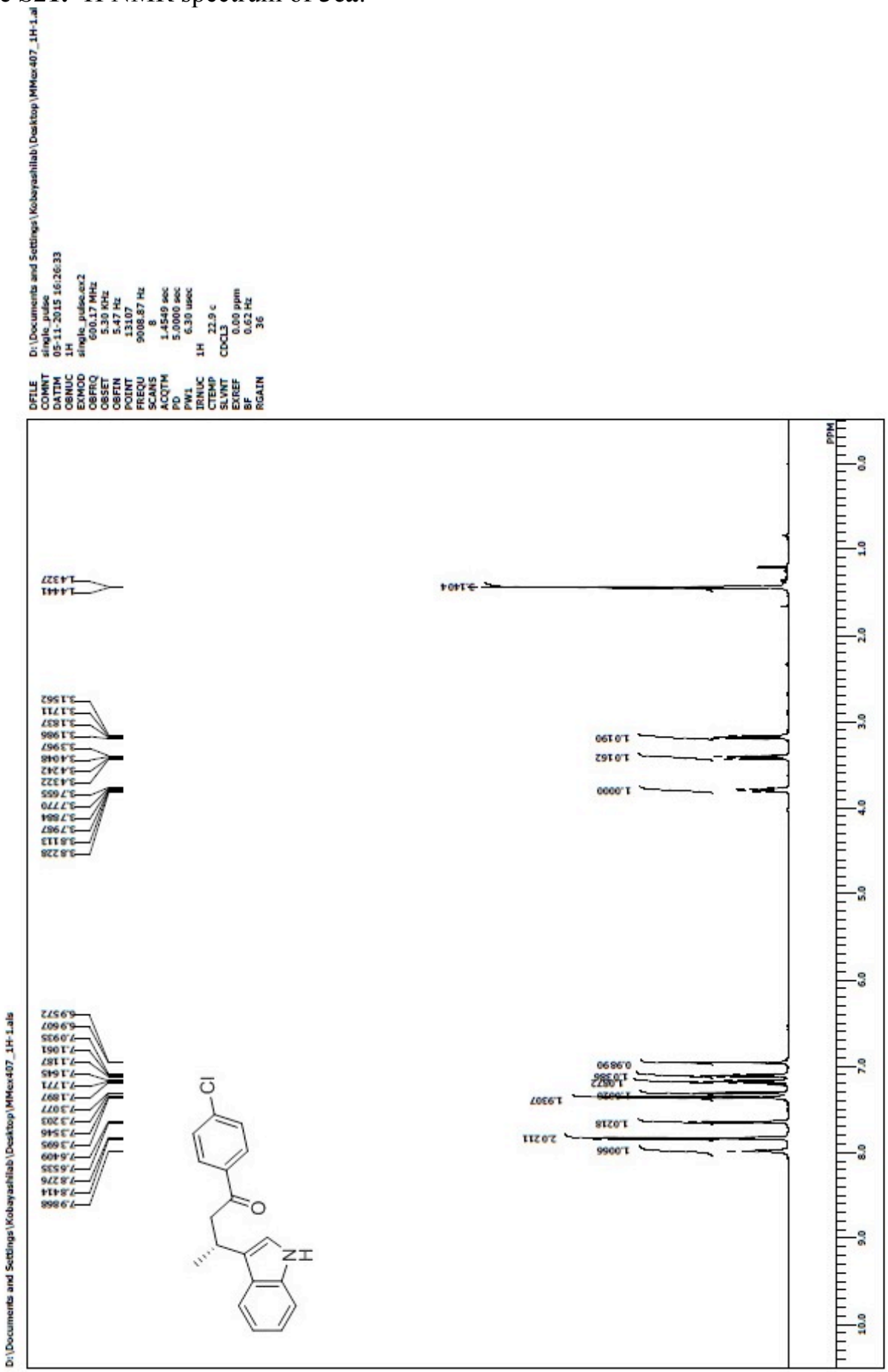


Figure S22. ^{13}C NMR spectrum of **3ca**.

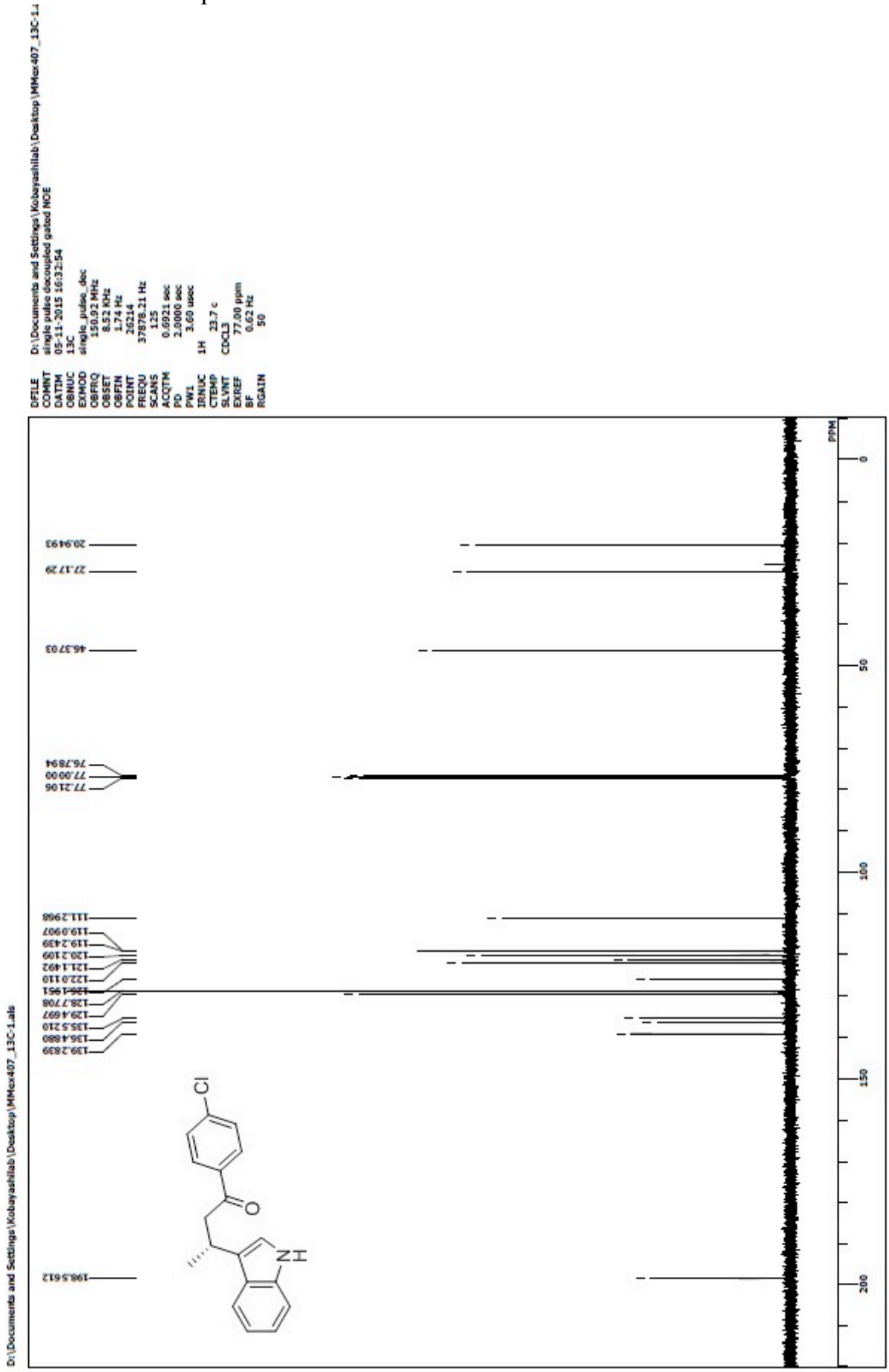
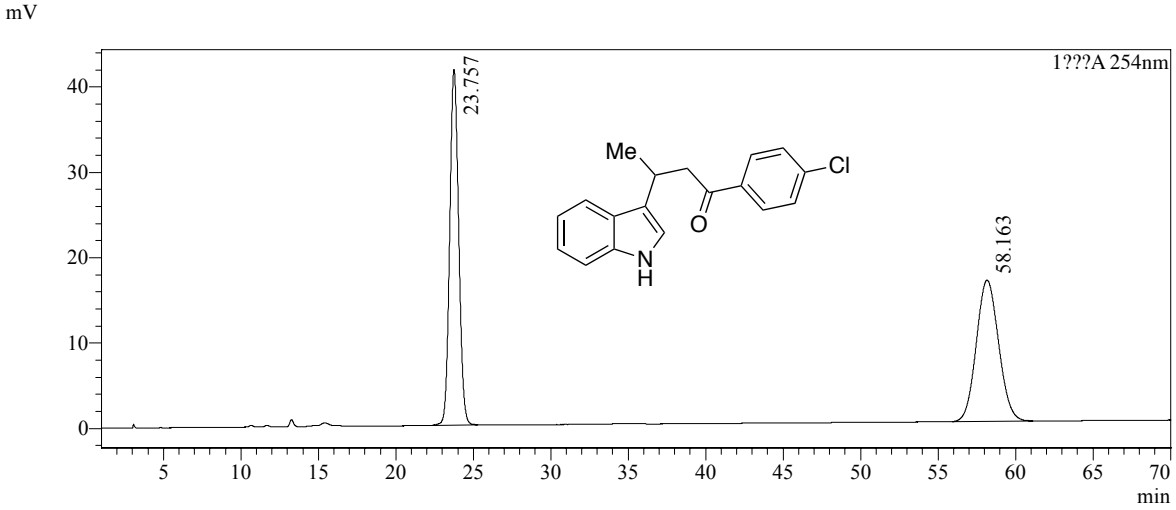
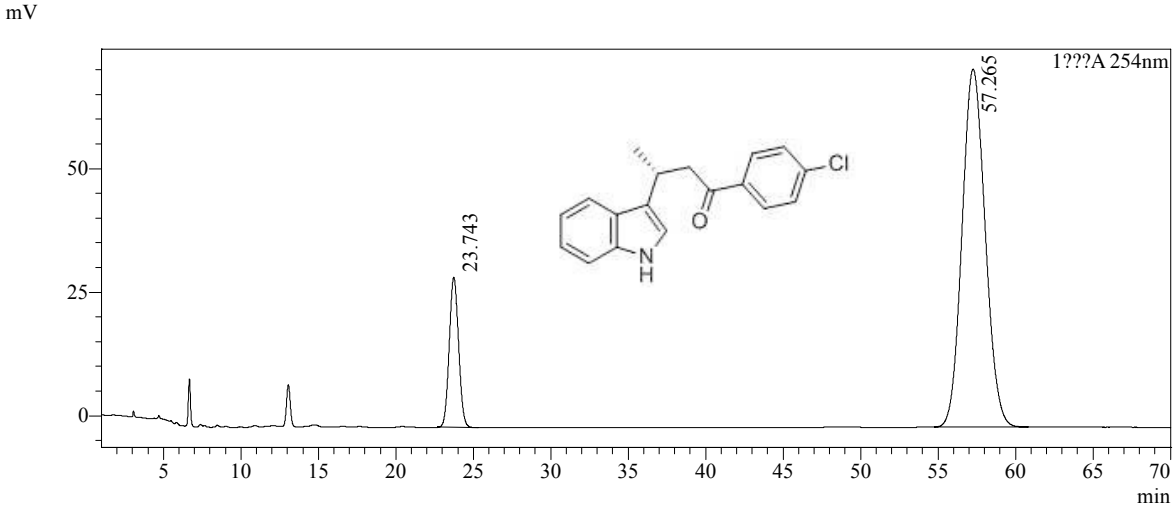


Figure S23. HPLC spectrum of racemic and chiral **3ca**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	23.757	1672112	41629	50.320
2	58.163	1650840	16533	49.680



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	23.743	1275646	30368	14.513
2	57.265	7514116	72426	85.487

Figure S24. ^{1}H NMR spectrum of **3da**.

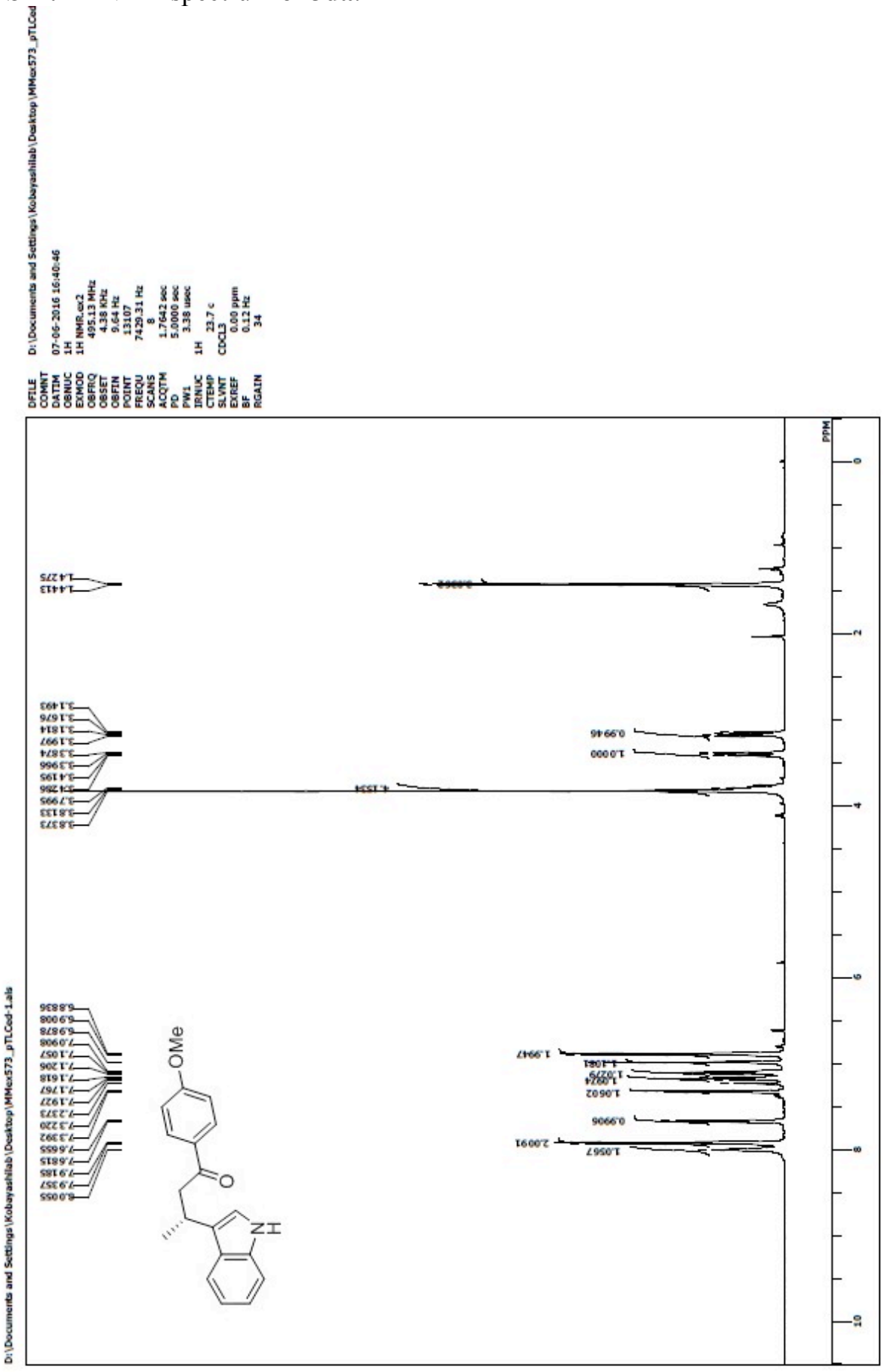


Figure S25. ^{13}C NMR spectrum of **3da**.

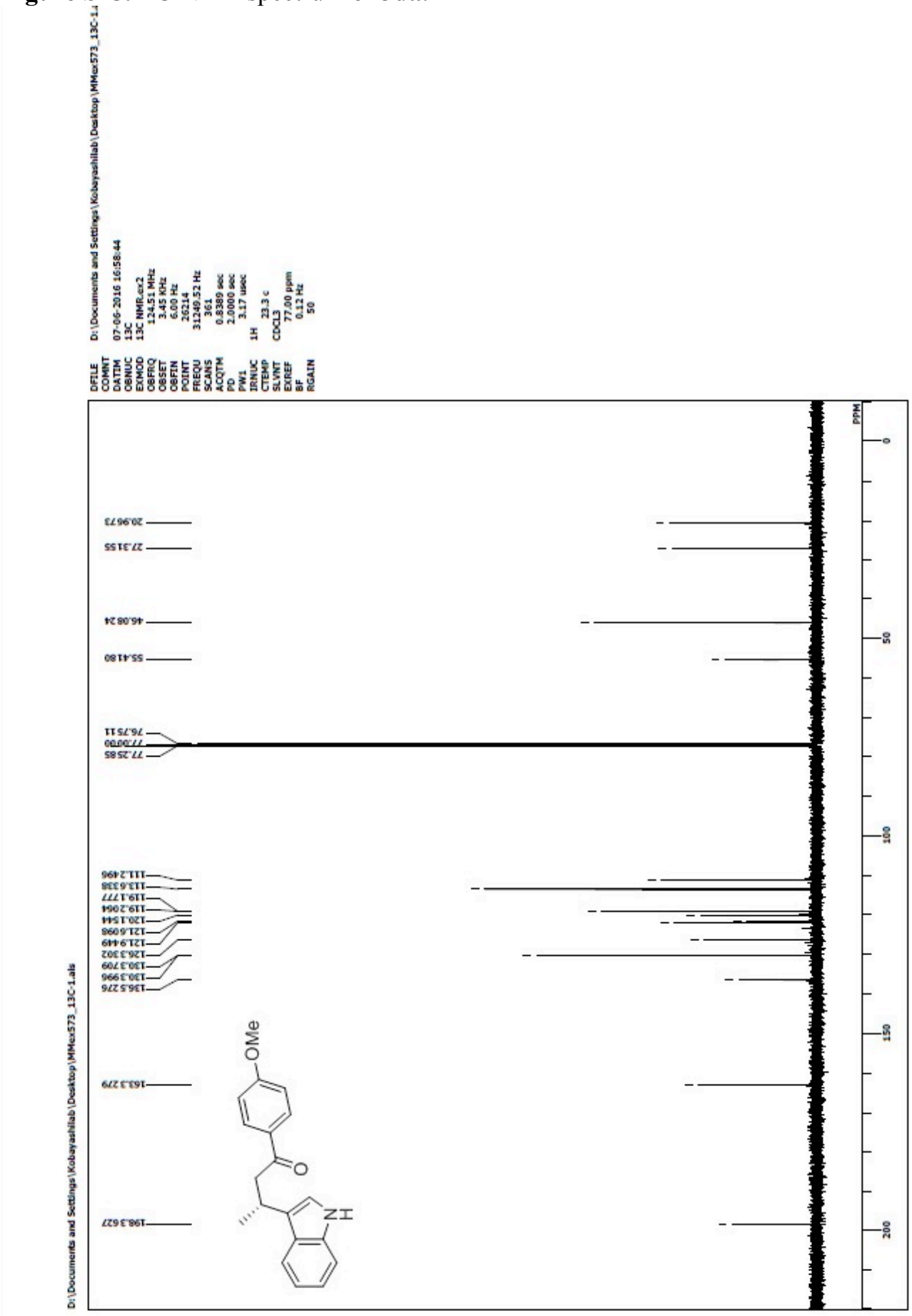
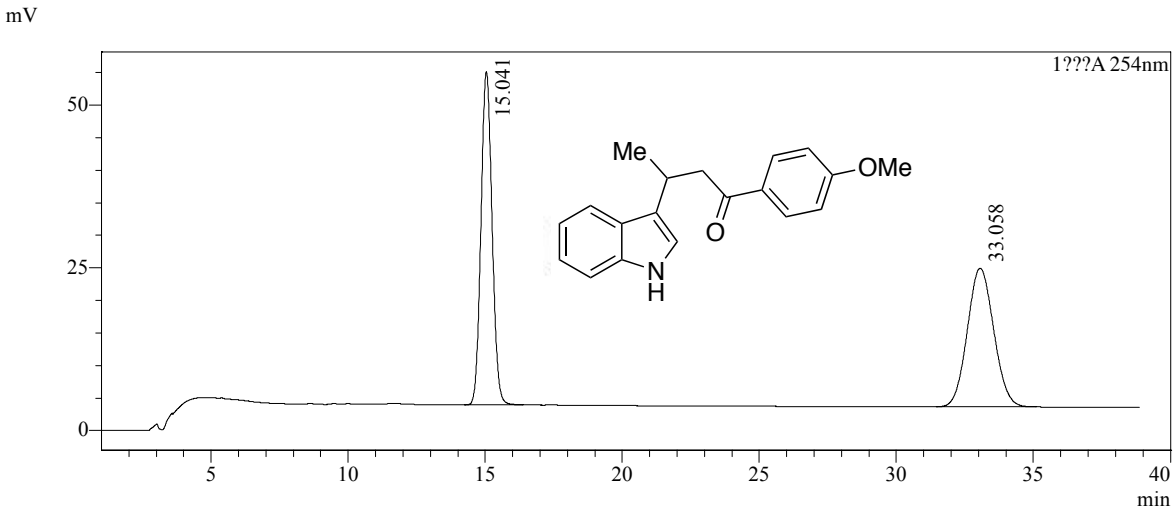
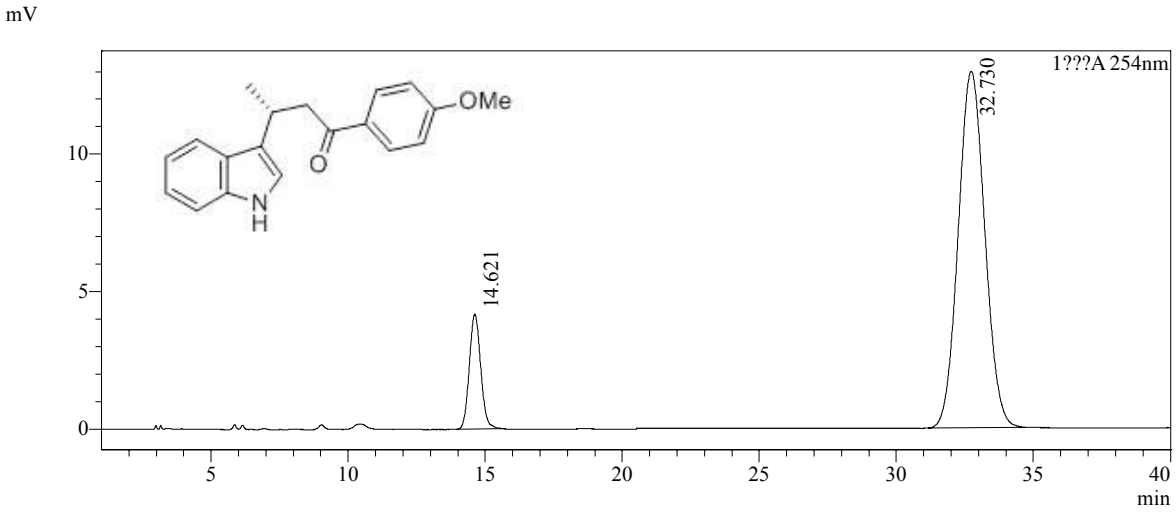


Figure S26. HPLC spectrum of racemic and chiral **3da**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.041	1443024	51169	50.241
2	33.058	1429184	21310	49.759



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	14.621	121592	4179	12.254
2	32.730	870692	12950	87.746

Figure S27. ^{1}H NMR spectrum of **3ea**.

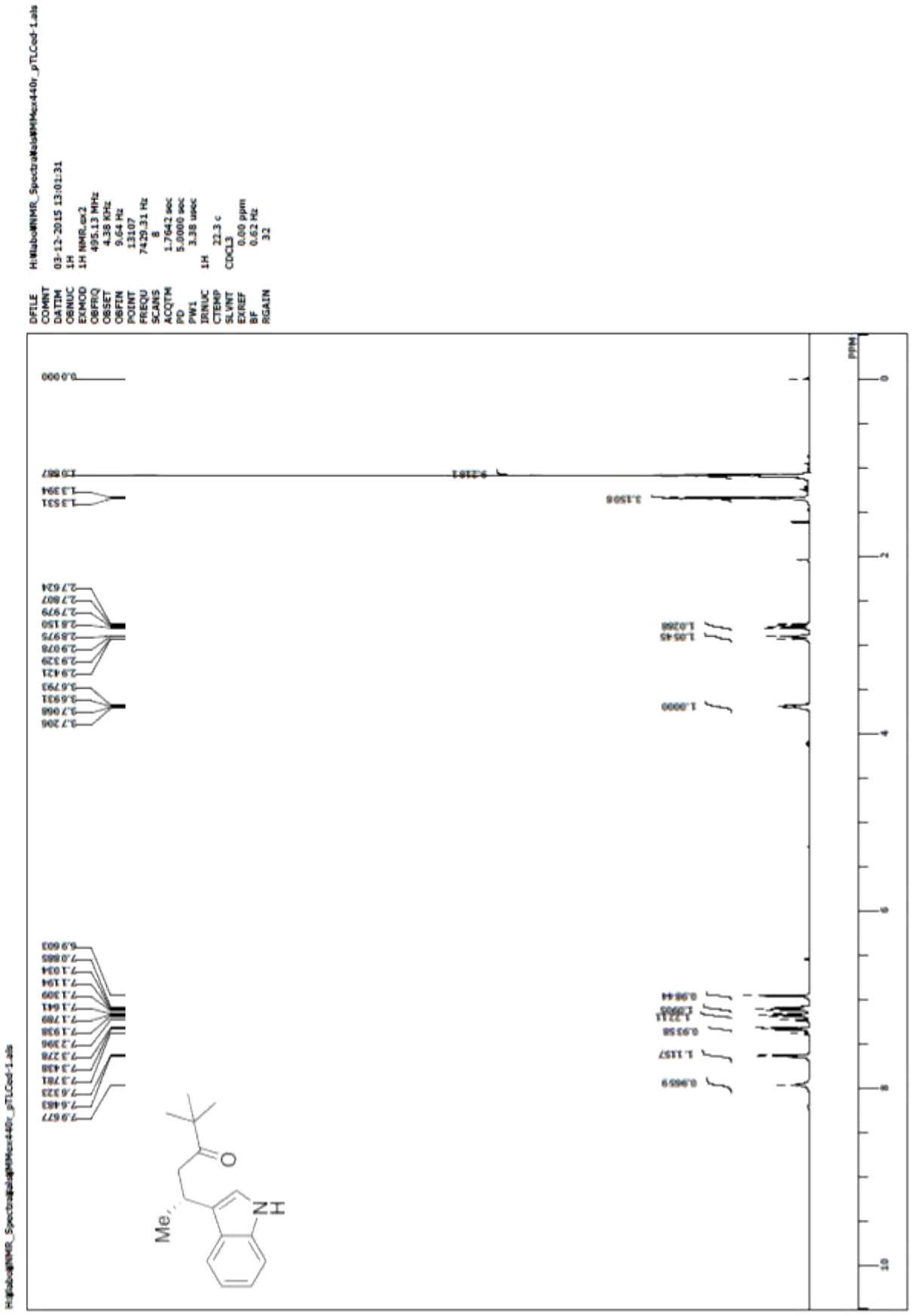


Figure S28. ^{13}C NMR spectrum of **3ea**.

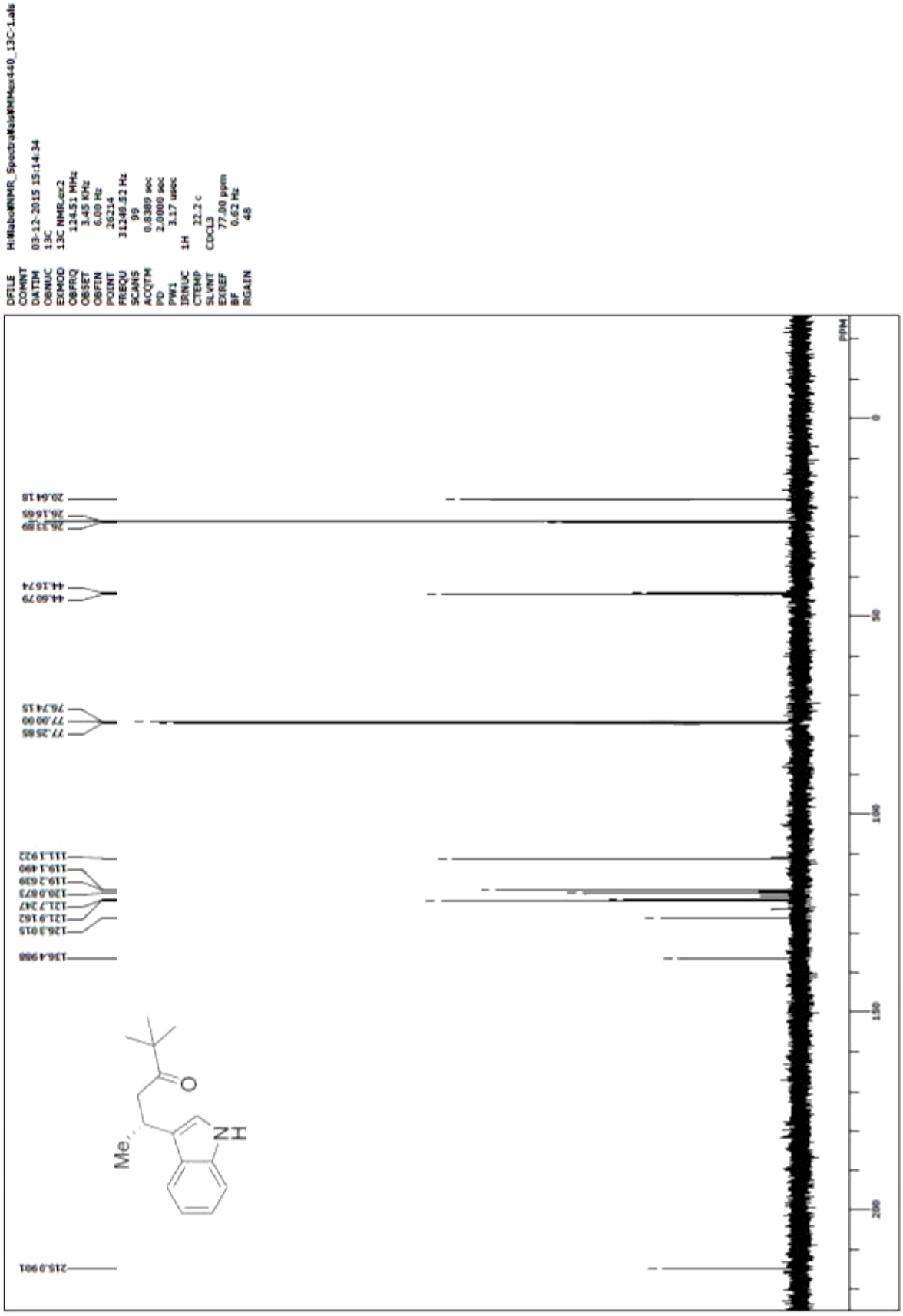
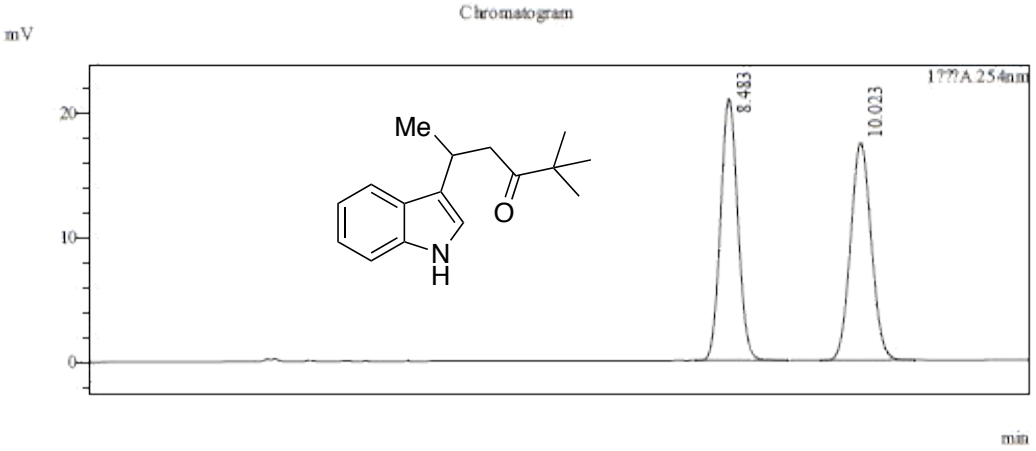
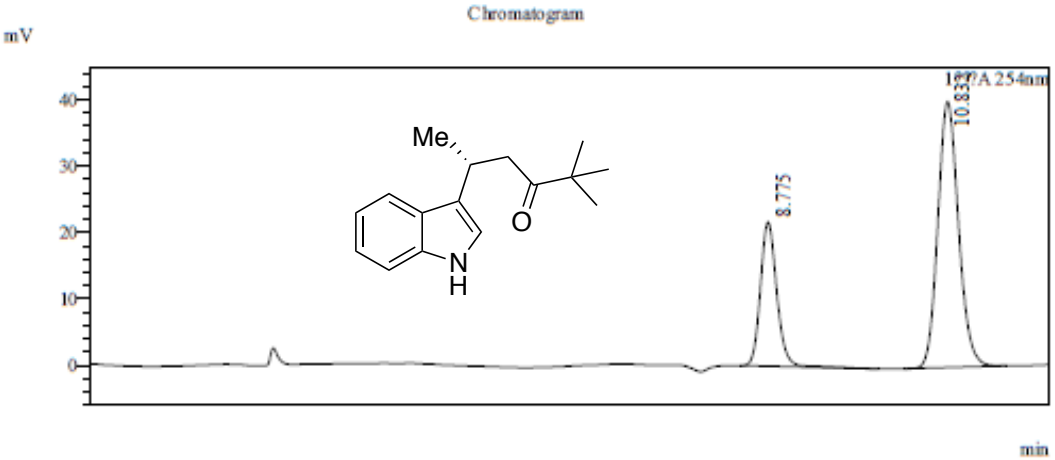


Figure S29. HPLC spectrum of racemic and chiral **3ea**.



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.483	294113	20986	50.013
2	10.023	293955	17432	49.987



???A 254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.775	283664	21693	30.049
2	10.832	660334	40027	69.951