Supporting information

for

Organocatalytic Asymmetric Reaction of Indol-2-yl Carbinols with Enamides: Synthesis of Chiral 2-Indole-Substituted 1,1-Diarylalkanes

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Table of contents

General Information

All reactions were carried out under nitrogen atmosphere in oven-dried glassware. Unless otherwise noted, all commercial materials were used without further purification. Anhydrous solvents were prepared by distillation according to standard methods. The ^{1}H NMR spectra were recorded at 300 MHz or 600 MHz (Bruker AV) and the ^{13}C NMR spectra were recorded at 101 MHz or 151 MHz with TMS as internal standard. All chemical shifts are given in ppm. All coupling constants (*J* values) were reported in Hertz (Hz). X-ray crystallographic analysis was performed on a Bruker SMART APEX Ⅱ CCD diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å) operated at 2.0 kW (50 kV, 40 mA). The structures were solved by direct methods using the program SHELXL-97 and refined anisotropically by full matrix least squares on F^2 values with SHELXL-97. Hydrogen atoms were located from the expected geometry and were refined only isotropically. Optical rotations were determined with Polarimeter 341LC (Pekin Elmer) at 589 nm and 25 °C. Data are reported as follows: $[\alpha]_{\lambda}^{temp}$, concentration (c in g/100 mL), and solvent. High resolution mass was measured by using Autoflex III Smartbeam MALDI-TOF, Bruker. HPLC analysis was performed on LC-6AD Shimadzu. Chiralcel AD-H and OJ-H columns were purchased from Daicel Chemical Industries, LTD. Column chromatography was performed on silica gel with 230–400 mesh.

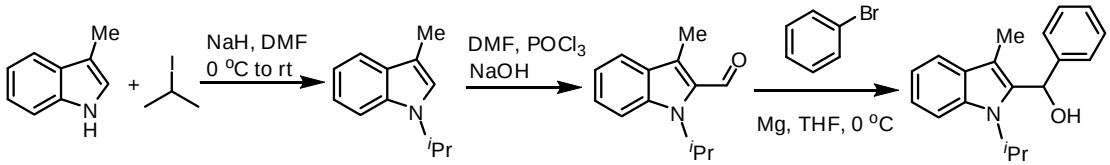
Experimental Procedures and Characterization

Preparation of catalysts

All catalysts were synthesized according to the literature[1-3] and acidified with 4 N HCl before use.

Preparation of substrates

The 3-methyl indoles[4] and enamides[5-6] were prepared according to the known procedures. The general procedure for the preparation of indol-2-yl carbinol substrates[3] was represented by the synthesis of **1a**.

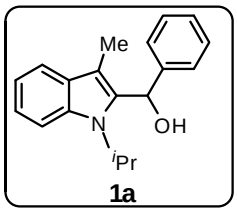


1a

To a DMF solution (40 mL) of NaH (60% in mineral oil, 0.80 g, 20 mmol) was added 3-methylindole (1.31 g, 10 mmol) at 0 °C. The slurry thus formed was gradually warmed to room temperature over a 30 min period. Isopropyl iodide (0.26 g, 15 mmol) was added to the reaction mixture at room temperature and the mixture was stirred for an additional 12 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layer was washed with H_2O (3 × 30 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 50/1) to provide *N*-isopropyl-3-methylindole as a colorless oil (1.56 g, 90% yield).

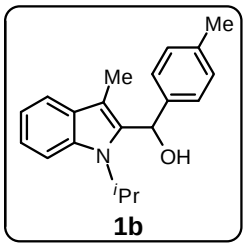
A three-necked flask was charged with *N*-isopropyl-3-methylindole (1.04 g, 4 mmol) and DMF (20 mL). The mixture was stirred and cooled to 0 °C, then freshly distilled $POCl_3$ (3.07 g, 20 mmol) was added dropwise. The solution was heated at 55 °C for 5 h. Then 2 M NaOH aqueous solution (35 mL) was added slowly and the reaction mixture was stirred at room temperature for 1 h. The mixture was extracted with ethyl acetate (3 × 30 mL). The combined organic layer was washed with H_2O (3 × 30 mL) and brine, dried over Na_2SO_4, separated, evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30/1) to provide the *N*-isopropyl-3-methylindole-2-carbaldehyde as a white solid (0.52 g, 65% yield).

A solution of phenylmagnesium bromide [prepared from magnesium turnings (0.11 g, 4.4 mmol), bromobenzene (0.63 g, 4 mmol), and a catalytic amount of I_2 in dry THF] was added dropwise to a THF solution of *N*-isopropyl-3-methylindole-2-carbaldehyde (0.40 g, 2 mmol) at 0 °C. The reaction mixture was stirred for 15 min at room temperature, then quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to provide the indol-2-yl carbinol **1a** as a white solid (0.54 g, 97% yield).



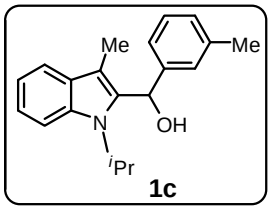
1a

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.52 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.34–7.19 (m, 5H), 7.07–6.96 (m, 2H), 6.22 (d, J = 3.9 Hz, 1H), 6.19 (d, J = 3.9 Hz, 1H), 4.80–4.71 (m, 1H), 2.34 (s, 3H), 1.44 (d, J = 6.9 Hz, 3H), 0.88 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 143.31, 137.11, 134.08, 128.83, 128.00, 126.45, 125.43, 120.90, 118.91, 117.93, 111.90, 106.90, 65.38, 47.09, 20.71, 19.71, 8.73. HRMS (MALDI-TOF) m/z Calcd for $C_{19}H_{21}NO$ $[M]^+$: 279.1623, found: 279.1614.



1b

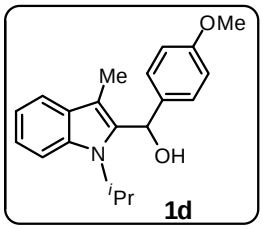
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.51 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.13–6.95 (m, 6H), 6.15 (s, 2H), 4.82–4.72 (m, 1H), 2.32 (s, 3H), 2.26 (s, 3H), 1.43 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 140.55, 137.43, 135.61, 134.33, 129.09, 128.81, 125.63, 121.09, 119.13, 118.15, 112.15, 107.01, 65.55, 47.33, 20.96, 20.06, 8.98. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO$ $[M]^+$: 293.1780, found: 293.1773.



1c

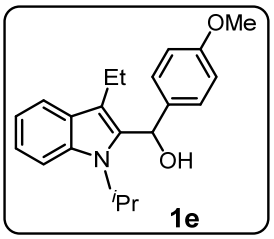
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.52 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.06–6.96 (m, 5H), 6.17 (d, J = 3.9 Hz, 2H), 4.80–4.71 (m, 1H), 2.33 (s, 3H), 2.25 (s, 3H), 1.44 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 143.27, 137.12, 136.99, 134.07, 128.83, 127.92, 127.11, 125.95, 122.61, 120.85, 118.90, 117.90, 111.91, 106.82, 65.36, 47.08, 21.20, 20.69, 19.75, 8.74. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO$ $[M]^+$: 293.1780,

found: 293.1774.



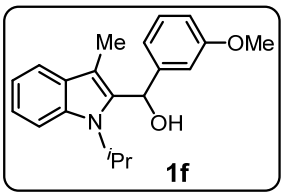
1d

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.51 (d, J = 6.9 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 8.7 Hz, 2H), 7.07–6.96 (m, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.15 (s, 2H), 4.84–4.75 (m, 1H), 3.71 (s, 3H), 2.33 (s, 3H), 1.44 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.92, 137.22, 135.20, 134.10, 128.84, 126.59, 120.82, 118.86, 117.89, 113.41, 111.89, 106.69, 65.13, 55.05, 47.06, 20.71, 19.88, 8.72. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO_2$ $[M]^+$: 309.1729, found: 309.1721.



1e

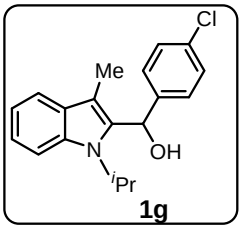
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.56 (d, J = 7.2 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.07－6.95 (m, 2H), 6.89 (d, J = 8.7 Hz, 2H), 6.18 (d, J = 3.9 Hz, 2H), 6.13 (s, 1H), 4.78－4.67 (m, 1H), 3.71 (s, 3H), 2.81 (q, J = 15.0, 7.2, 7.8 Hz, 2H), 1.43 (d, J = 6.9 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H), 0.94 (d, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.19, 136.72, 135.45, 134.46, 128.09, 126.88, 121.01, 119.11, 118.18, 114.10, 113.66, 112.30, 65.12, 55.30, 47.34, 20.92, 20.01, 17.34, 16.86. HRMS (MALDI-TOF) m/z Calcd for $C_{21}H_{25}NO_2$ $[M]^+$: 323.1885, found: 323.1874.



1f

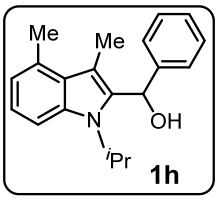
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.52 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.21 (t, J = 8.1 Hz, 1H), 7.08–6.98 (m, 2H), 6.89–6.73 (m, 3H), 6.24 (d, J = 3.9 Hz, 1H), 6.15 (d, J = 3.6 Hz, 1H), 4.82–4.73 (m, 1H), 3.70 (s, 3H), 2.33 (s, 3H), 1.45 (d, J = 6.6 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.31,

145.08, 136.98, 134.09, 129.10, 128.82, 120.90, 118.92, 117.93, 117.89, 111.91, 111.48, 111.45, 106.89, 65.33, 55.01, 47.13, 20.72, 19.80, 8.71. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO_2$ $[M]^+$: 309.1729, found: 309.1717.



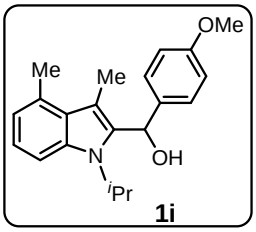
1g

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.52 (d, J = 7.5 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.38 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.08–6.96 (m, 2H), 6.34 (d, J = 3.9 Hz, 1H), 6.17 (d, J = 3.6 Hz, 1H), 4.75–4.65 (m, 1H), 2.33 (s, 3H), 1.44 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 142.40, 136.50, 134.13, 131.07, 128.77, 128.00, 127.40, 121.06, 118.98, 118.02, 111.95, 107.19, 64.98, 47.13, 20.69, 19.81, 8.69. HRMS (MALDI-TOF) m/z Calcd for $C_{19}H_{20}ClNO$ $[M]^+$: 313.1233, found: 313.1225.



1h

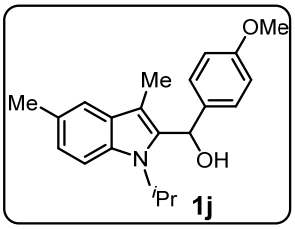
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.35–7.21 (m, 6H), 6.89 (t, J = 7.5 Hz, 1H), 6.69 (d, J = 6.9 Hz, 1H), 6.22 (s, 2H), 4.83–4.74 (m, 1H), 2.70 (s, 3H), 2.57 (s, 3H), 1.43 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 143.52, 136.83, 134.40, 130.65, 127.97, 127.12, 126.35, 125.37, 120.71, 119.78, 109.96, 107.82, 64.85, 46.97, 20.60, 20.54, 19.44, 11.78. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO$ $[M]^+$: 293.1780, found: 293.1773.



1i

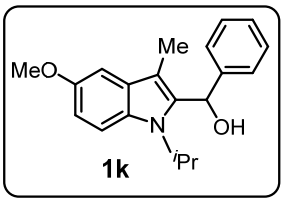
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 1H), 7.24–7.21 (m, 2H), 7.01 (t, J = 7.2 Hz, 1H), 6.85–6.78 (m, 3H), 6.34 (s, 1H), 4.78–4.68 (m, 1H), 3.78 (s, 3H), 2.76 (s, 3H), 2.58 (s, 3H), 2.26 (d, J = 2.7 Hz, 1H), 1.50 (d, J = 7.2 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.86, 136.90, 135.38, 134.40,

130.59, 127.10, 126.50, 120.63, 119.74, 113.39, 109.96, 107.61, 64.55, 55.06, 46.92, 20.59, 20.55, 19.61, 11.74. HRMS (MALDI-TOF) m/z Calcd for $C_{21}H_{25}NO_2$ $[M]^+$: 323.1885, found: 323.1876.



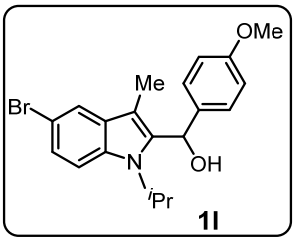
1j

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.34–7.28 (m, 2H), 7.14 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 3H), 6.11 (s, 2H), 4.79–4.70 (m, 1H), 3.71 (s, 3H), 2.37 (s, 3H), 2.29 (s, 3H), 1.41 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.89, 137.24, 135.27, 132.46, 129.06, 126.56, 126.30, 122.37, 118.50, 113.38, 111.62, 106.12, 65.12, 55.05, 46.94, 21.10, 20.77, 19.91, 8.72. HRMS (MALDI-TOF) m/z Calcd for $C_{21}H_{25}NO_2$ $[M]^+$: 323.1885, found: 323.1879.



1k

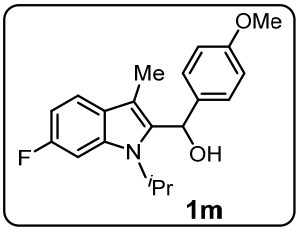
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.36–7.18 (m, 6H), 7.00 (d, J = 2.4 Hz, 1H), 6.69 (dd, J = 9.0, 2.4 Hz, 1H), 6.19–6.16 (m, 2H), 4.76–4.67 (m, 1H), 3.77 (s, 3H), 2.31 (s, 3H), 1.41 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 152.76, 143.35, 137.73, 129.21, 129.19, 127.97, 126.41, 125.40, 112.54, 110.79, 106.53, 100.97, 65.41, 55.45, 46.96, 20.88, 19.86, 8.83. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{23}NO_2$ $[M]^+$: 309.1729, found: 309.1720.



1l

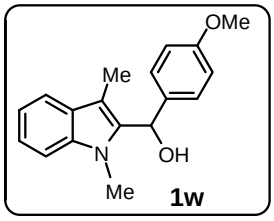
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.70 (d, J = 1.8 Hz, 1H), 7.44 (d, J = 8.7 Hz, 1H), 7.15 (d, J = 8.7 Hz, 3H), 6.88 (d, J = 8.7 Hz, 2H), 6.23 (d, J = 3.9 Hz, 1H), 6.14 (d, J = 3.9 Hz, 1H), 4.84–4.75 (m, 1H), 3.71 (s, 3H), 2.31 (s, 3H), 1.42 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.99, 138.89, 134.79, 132.75, 130.76, 126.55, 123.16, 121.12, 113.82, 113.48, 110.74, 106.66, 65.03, 55.06,

47.30, 20.66, 19.82, 8.58. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{22}BrNO_2$ $[M]^+$: 387.0834, found: 387.0822.



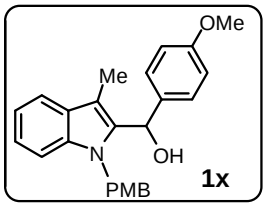
1m

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.50 (dd, J = 8.7, 5.7 Hz, 1H), 7.25 (dd, J = 11.1, 1.8 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 6.89–6.81 (m, 3H), 6.15 (d, J = 3.9 Hz, 1H), 6.10 (d, J = 3.3 Hz, 1H), 4.80–4.71 (m, 1H), 3.71 (s, 3H), 2.31 (s, 3H), 1.41 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 159.21, 157.95, 157.66, 137.88, 135.03, 133.80, 133.72, 126.57, 125.60, 119.75, 119.68, 113.44, 107.02, 106.32, 106.16, 98.15, 97.97, 65.12, 55.04, 47.18, 20.36, 19.55, 8.64. HRMS (MALDI-TOF) m/z Calcd for $C_{20}H_{22}FNO_2$ $[M]^+$: 327.1635, found: 327.1628.



1w

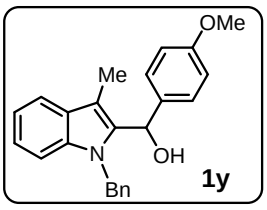
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.49 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.10 (t, J = 7.2 Hz, 1H), 7.00 (t, J = 7.2 Hz, 1H), 6.88 (d, J = 8.4 Hz, 2H), 6.14 (d, J = 3.6 Hz, 1H), 6.05 (d, J = 3.9 Hz, 1H), 3.71 (s, 3H), 3.49 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 158.02, 137.55, 136.84, 135.20, 127.65, 126.82, 121.25, 118.39, 113.53, 108.93, 106.98, 65.45, 55.04, 30.63, 8.74. HRMS (MALDI-TOF) m/z Calcd for $C_{18}H_{19}NO_2$ $[M]^+$: 281.1416, found: 281.1408.



1x

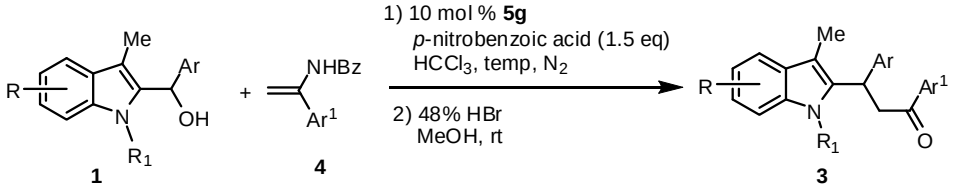
^{1}H NMR (300 MHz, DMSO-d_6) δ 7.51–7.48 (m, 1H), 7.16 (d, J = 8.4 Hz, 2H), 7.06–6.96 (m, 3H), 6.84–6.79 (m, 4H), 6.70 (d, J = 8.7 Hz, 2H), 6.15 (d, J = 4.2 Hz, 1H), 6.11 (d, J = 4.5 Hz, 1H), 5.29–5.15 (m, 2H), 3.69 (s, 3H), 3.66 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 158.06, 137.88, 136.30, 135.25, 130.59, 128.25, 127.67, 126.85, 121.32, 118.58, 118.47, 113.50, 110.02, 107.24, 65.78, 55.02,

54.97, 46.64, 8.92. HRMS (MALDI-TOF) m/z Calcd for $C_{25}H_{25}NO_3$ $[M]^+$: 387.1834, found: 387.1824.



^{1}H NMR (300 MHz, DMSO-d_6) δ 7.53–7.50 (m, 1H), 7.18–7.12 (m, 5H), 7.04–6.96 (m, 3H), 6.88–6.86 (m, 2H), 6.79 (d, J = 8.7 Hz, 2H), 6.16–6.12 (m, 2H), 5.37–5.25 (m, 2H), 3.66 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 158.04, 138.70, 137.90, 136.31, 135.15, 128.20, 128.03, 126.81, 126.56, 126.32, 121.36, 118.63, 118.49, 113.51, 109.91, 107.28, 65.74, 55.05, 47.11, 8.90. HRMS (MALDI-TOF) m/z Calcd for $C_{24}H_{23}NO_2$ $[M]^+$: 357.1729, found: 357.1717.

General procedure and product characterization of the asymmetric reaction

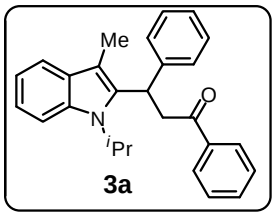


To a 20 mL dried Schlenck tube equipped with a magnetic bar was charged with alcohol **1** (0.1 mmol), enamide **4** (0.2 mmol, 2.0 equiv), *p*-nitrobenzoic acid (0.15 mmol, 250.7 mg, 1.5 equiv) and catalyst **5g** (8.3 mg, 0.01 mmol, 0.1 equiv), the pre-cooled solvent $CHCl_3$ (2 mL, freshly distilled) was added and the solution was stirred at a scheduled temperature under nitrogen for 3–12 h. Upon completion of the reaction (monitored by TLC), five drops of Et_3N was added to quench the reaction. The reaction mixture was purified by flash column chromatography. The product was dissolved in methanol (2 mL) and aqueous HBr (48%, 0.8 mL) and was stirred at room temperature for 12 h. The reaction mixture was then quenched by saturated aqueous $NaHCO_3$ at 0 ^{o}C. The reaction mixture was extracted four times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, concentrated. The residue was purified by flash chromatography on silica gel to give the product **3**.

Table S1. Optimization of temperature, additives, and concetration.[a]

entry	additive (equiv)	Temperature (°C)	time (h)	yield (%)[b]	ee (%)[c]
1	–	10	7	50	89
2	–	0	12	32	91
3	–	-10	48	29	94
4	3 Å MS (20 mg)	-10	48	48	87
5	4 Å MS (20 mg)	-10	48	47	85
6	5 Å MS (20 mg)	-10	48	53	87
7	$PhCO_2H$ (1.0)	0	12	39	91
8	*p*-$NO_2C_6H_4CO_2H$ (1.0)	0	6	67	91
9	*m*-$NO_2C_6H_4CO_2H$ (1.0)	0	6	53	91
10	*o*-$NO_2C_6H_4CO_2H$ (1.0)	0	6	47	91
11	AcOH (1.0)	0	12	trace[d]	–
12	CSA (1.0)	0	6	trace[d]	–
13	*p*-$NO_2C_6H_4CO_2H$ (1.5)	0	6	78	91
14	*p*-$NO_2C_6H_4CO_2H$ (2.0)	0	6	80	91
15	*p*-$NO_2C_6H_4CO_2H$ (1.5)	-5	12	74	93
16[e]	*p*-$NO_2C_6H_4CO_2H$ (1.5)	0	12	77	91
17[f]	*p*-$NO_2C_6H_4CO_2H$ (1.5)	0	12	67	92
18[g]	*p*-$NO_2C_6H_4CO_2H$ (1.5)	0	12	60	92
19[h]	*p*-$NO_2C_6H_4CO_2H$ (1.5)	0	12	n.r.	–

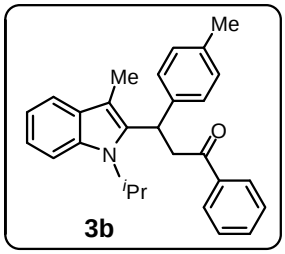
[a] Unless otherwise noted, the reaction conditions are: **1a** (0.1 mmol), **4d** (0.2 mmol, 2.0 equiv), catalyst **5g** (10 mol%) in $CHCl_3$ (2 mL); [b] isolated yield; [c] the ee values were determined by chiral HPLC on a AD-H column; [d] **4d** was decomposed; [e] Run in 1 mL $CHCl_3$; [f] Run in 3 mL $CHCl_3$; [g] Run in 4 mL $CHCl_3$; [i] catalyst **5g** was absent.



3a

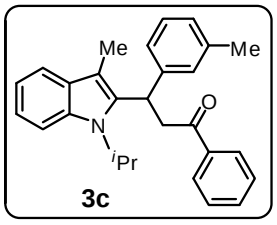
74% yield; 93% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +55 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.12–8.09 (m, 2H), 7.66–7.61 (m, 1H), 7.56–7.46 (m, 4H), 7.32–7.17 (m, 5H), 7.06–6.95 (m, 2H), 5.43 (t, *J* = 6.9 Hz, 1H), 4.67–4.62 (m, 1H), 4.24 (dd, *J* = 17.4, 7.5 Hz, 1H), 3.85 (dd, *J* = 17.4, 6.9 Hz, 1H), 2.25 (s, 3H), 1.57 (d, *J* = 6.9 Hz,

3H), 1.18 (d, J = 6.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.30, 141.45, 136.78, 136.30, 133.84, 132.91, 129.16, 128.36, 128.08, 127.74, 126.84, 125.91, 120.25, 118.26, 117.91, 111.41, 107.22, 47.19, 42.50, 35.65, 20.95, 20.15, 9.11. HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{27}NO$ $[M]^+$: 381.2093, found: 381.2088; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 17.054 min (minor), 21.015 min (major); 93% ee.



3b

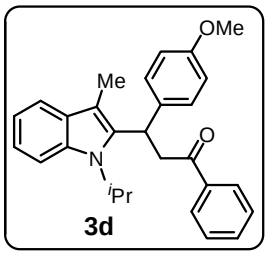
82% yield; 93% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +66 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J = 7.2 Hz, 2H), 7.59–7.52 (m, 2H), 7.46 (t, J = 7.5 Hz , 3H), 7.13–7.04 (m, 6H), 5.36 (t, J = 6.6 Hz, 1H), 4.56–4.52 (m, 1H), 3.98 (dd, J = 17.1, 7.5 Hz, 1H), 3.71 (dd, J = 17.1, 6.0 Hz, 1H), 2.27 (d, J = 3.9 Hz, 6H), 1.54 (d, J = 7.2 Hz, 3H), 1.29 (d, J = 6.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.42, 138.37, 136.90, 136.35, 135.42, 133.84, 132.87, 129.19, 128.75, 128.34, 127.74, 126.69, 120.17, 118.21, 117.86, 111.42, 107.11, 47.12, 42.69, 35.33, 20.98, 20.54, 20.26, 9.13. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}NO_2$ $[M]^+$: 395.2249, found: 395.2241; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 19.950 min (minor), 23.435 min (major); 93% ee.



3c

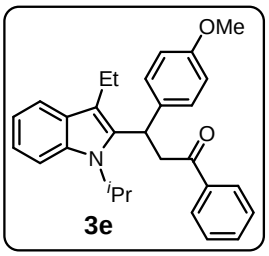
57% yield; 89% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +57 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98–7.95 (m, 2H), 7.60–7.44 (m, 5H), 7.17–6.95 (m, 6H), 5.38 (t, J = 6.3 Hz, 1H), 4.54–4.50 (m, 1H), 3.99 (dd, J = 17.1, 7.5 Hz, 1H), 3.71 (dd, J = 17.1, 6.0 Hz, 1H), 2.26 (d, J = 7.5 Hz, 6H), 1.55 (d, J = 6.9 Hz, 3H), 1.27 (d, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.75, 141.79, 138.07, 137.23, 136.74, 134.25, 133.26, 129.61, 128.74, 128.36, 128.13, 128.08, 127.10, 124.07, 120.57, 118.65,

118.26, 111.81, 107.57, 47.57, 43.03, 35.96, 21.53, 21.36, 20.58, 9.52. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}NO$ $[M]^+$: 395.2249, found: 395.2240; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5, flow rate 0.5 mL/min), t_r: 10.235 min (minor), 11.608 min (major); 89% ee.



3d

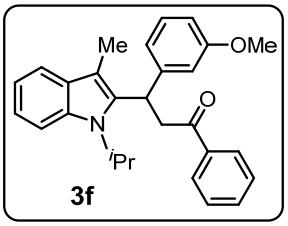
94% yield; 96% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +51 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.2 Hz, 2H), 7.59–7.52 (m, 2H), 7.46 (t, *J* = 7.8 Hz , 3H), 7.14–7.05 (m, 4H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.34 (t, *J* = 6.3 Hz, 1H), 4.56–4.53 (m, 1H), 3.98 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75–3.66 (m, 4H), 2.28 (s, 3H), 1.53 (d, *J* = 6.9 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.45, 157.62, 136.93, 136.32, 133.83, 133.48, 132.88, 129.16, 128.34, 127.84, 127.74, 120.19, 118.21, 117.87, 113.44, 111.40, 107.00, 54.85, 47.12, 42.80, 35.02, 20.95, 20.27, 9.12. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}NO_2$ $[M]^+$: 411.2198, found: 411.2190; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 15.806 min (minor), 17.771 min (major); 96% ee.



3e

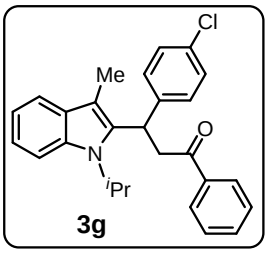
yield: 90%; ee: 91%; (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 35/1); $[\alpha]_D^{25}$ = +95 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01–7.98 (m, 2H), 7.62–7.56 (m, 2H), 7.51–7.44 (m, 3H), 7.15–7.02 (m, 4H), 6.79–6.76 (m, 2H), 5.42–5.37 (m, 1H), 4.44 (brs, 1H), 4.06 (dd, *J* = 17.1, 8.4 Hz, 1H), 3.75 (s, 3H), 3.57 (dd, *J* = 17.4, 4.8 Hz, 1H), 2.79 (q, 15.0, 7.5, 7.5Hz, 2H), 1.59 (d, *J* = 6.9 Hz, 3H), 1.20 (t, *J* = 14.7, 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.51, 157.86, 137.01, 136.57, 134.33, 133.63, 133.24, 128.66, 128.50,

128.01, 120.43, 118.78, 118.15, 114.32, 113.68, 111.82, 55.13, 47.61, 42.89, 34.48, 21.22, 20.26, 17.80, 15.90. HRMS (MALDI-TOF) *m/z* Calcd for $C_{29}H_{31}NO_2$ $[M]^+$: 425.2355, found: 425.2344; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 12.794 min (major), 14.988 min (minor); 91% ee.



3f

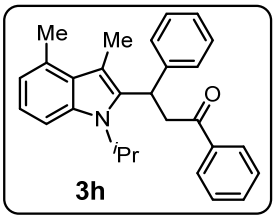
71% yield; 91% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +34 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.59–7.52 (m, 2H), 7.46 (t, *J* = 7.5 Hz, 3H), 7.19–7.04 (m, 3H), 6.75–6.71 (m, 3H), 5.38 (t, *J* = 6.0 Hz, 1H), 4.56–4.52 (m, 1H), 3.99 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.73–3.66 (m, 4H), 2.28 (s, 3H), 1.55 (d, *J* = 7.2 Hz, 3H), 1.30 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.25, 159.44, 143.25, 136.62, 136.35, 133.91, 132.88, 129.22, 129.05, 128.35, 127.73, 120.24, 119.34, 118.28, 117.88, 113.31, 111.38, 110.73, 107.26, 54.78, 47.16, 42.58, 35.68, 21.00, 20.26, 9.11. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}NO_2$ $[M]^+$: 411.2198, found: 411.2189; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 21.397 min (minor), 26.035 min (major); 91% ee.



3g

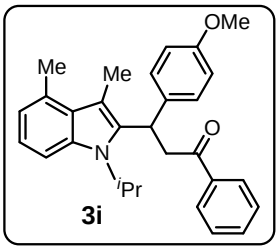
67% yield; 88% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +50 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98–7.95 (m, 2H), 7.58–7.44 (m, 5H), 7.23–7.06 (m, 6H), 5.37 (t, *J* = 6.6 Hz, 1H), 4.49 (br, 1H), 3.97 (dd, *J* = 17.4, 8.1 Hz, 1H), 3.72 (dd, *J* = 17.4, 5.4 Hz, 1H), 2.28 (s, 3H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.31 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.01, 140.11, 136.22, 136.11, 133.84, 133.06, 131.74, 129.07, 128.40, 128.25, 128.17, 127.72, 120.47, 118.29, 118.06, 111.43, 107.34, 47.16, 42.59,

35.09, 21.01, 20.33, 9.16. HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{26}ClNO$ $[M]^+$: 415.1703, found: 415.1694 ; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 22.227 min (minor), 25.790 min (major); 88% ee.



3h

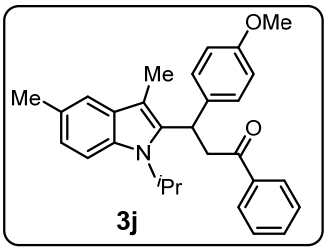
71% yield; 92% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +69 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.13–8.10 (m, 2H), 7.67–7.62 (m,1H), 7.56–7.51 (m, 2H), 7.32–7.16 (m, 6H), 6.90–6.85 (m, 1H), 6.68 (d, *J* = 6.9 Hz, 1H), 5.48 (t, *J* = 6.6 Hz, 1H), 4.57 (br, 1H), 4.32 (dd, *J* = 17.4, 7.8 Hz, 1H), 3.73 (dd, *J* = 17.1, 6.0 Hz, 1H), 2.67 (s, 3H), 2.46 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H), 1.05 (br, 3H); ^{13}C NMR (101 MHz, Acetone-d_6) δ 197.42, 142.08, 137.24, 136.90, 134.68, 133.07, 130.38, 128.65, 128.21, 128.13, 127.81, 127.06, 125.91, 120.27, 120.08, 109.85, 107.98, 47.53, 41.59, 34.81, 20.42, 20.23, 19.21, 11.68 . HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}NO_2$ $[M]^+$: 395.2249, found: 395.2240; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 99/1, flow rate 0.5 mL/min), t_r: 27.337 min (major), 34.703 min (major); 92% ee.



3i

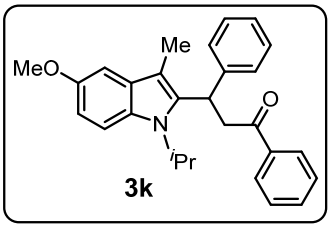
92% yield; 96% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +97 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.05–6.94 (m, 3H), 6.80–6.76 (m, 3H), 5.41 (t, *J* = 6.3 Hz, 1H), 4.48 (br, 1H), 4.02 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.76 (s, 3H), 3.59 (dd, *J* = 17.1, 5.1 Hz, 1H), 2.73 (s, 3H), 2.47 (s, 3H), 1.60 (d, *J* = 6.9 Hz, 3H), 1.18 (brs, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.83, 157.90, 137.43, 136.66, 134.53, 133.76, 133.27, 131.09, 128.72, 128.14, 127.98, 127.67, 120.49, 120.33, 113.76, 109.87, 108.52, 55.23, 47.63, 42.81, 34.15, 21.24, 20.95, 20.18, 12.40. HRMS (MALDI-TOF)

m/z Calcd for $C_{29}H_{31}NO_2$ $[M]^+$: 425.2355, found: 425.2345; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 26.143 min (major), 40.395 min (minor); 96% ee.



3j

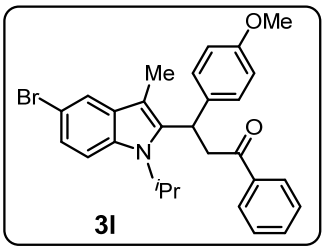
99% yield; 99% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +46 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.8 Hz , 2H), 7.34 (d, *J* = 9.0 Hz, 2H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 5.31 (t, *J* = 6.6 Hz, 1H), 4.53–4.48 (m, 1H), 3.96 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75 (s, 3H), 3.69 (dd, *J* = 17.1, 6.0 Hz, 1H), 2.44 (s, 3H), 2.25 (s, 3H), 1.51 (d, *J* = 7.2 Hz, 3H), 1.27 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.52, 157.61, 137.07, 136.37, 133.58, 132.87, 132.10, 129.39, 128.35, 127.84, 127.76, 127.13, 121.75, 117.98, 113.43, 111.13, 106.49, 54.86, 47.08, 42.81, 35.03, 21.01, 20.94, 20.34, 9.11. HRMS (MALDI-TOF) *m/z* Calcd for $C_{29}H_{31}NO_2$ $[M]^+$: 425.2355, found: 425.2347; The ee was determined by HPLC with a Daicel Chiralcel OJ-H column (hexane/isopropanol = 70/30, flow rate 1.0 mL/min), t_r: 7.868 min (major), 12.631 min (minor); 99% ee.



3k

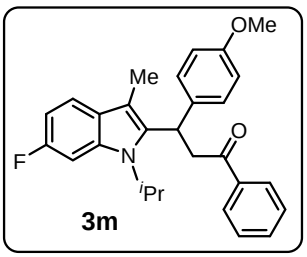
71% yield; 91% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +52 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.10 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.38–7.17 (m, 6H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.70 (dd, *J* = 9.0, 2.4 Hz, 1H), 5.39 (t, *J* = 6.9 Hz, 1H), 4.63–4.58 (m, 1H), 4.22 (dd, *J* = 17.4, 7.2 Hz, 1H), 3.88–3.80 (m, 4H), 2.22 (s, 3H), 1.55 (d, *J* = 6.9 Hz, 3H), 1.16 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, Acetone-d_6) δ 197.36, 153.42, 142.16, 137.87, 136.92, 133.04, 130.09, 129.39, 128.64, 128.23, 128.08, 127.23, 126.00, 112.26, 110.29, 106.55, 100.45, 54.92, 47.32, 41.85, 35.99, 20.71, 19.83, 8.69. HRMS (MALDI-TOF) *m/z*

Calcd for $C_{28}H_{29}NO_2$ $[M]^+$: 411.2198, found: 411.2185; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 17.947 min (minor), 25.007 min (major); 91% ee.



3l

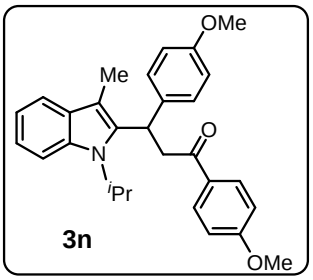
98% yield; 97% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +45 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97–7.94 (m, 2H), 7.63–7.55 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 1H), 7.17 (dd, *J* = 8.7, 2.1Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 5.30 (t, *J* = 6.6 Hz, 1H), 4.57–4.52 (m, 1H), 3.96 (dd, *J* = 16.8, 7.5 Hz, 1H), 3.76–3.66 (m, 4H), 2.21 (s, 3H), 1.50 (d, *J* = 7.2 Hz, 3H), 1.28 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.26, 157.73, 138.23, 136.23, 133.05, 132.97, 132.45, 131.00, 128.38, 127.76, 127.71, 122.86, 120.78, 113.56, 112.67, 111.36, 106.77, 54.86, 47.25, 42.57, 35.11, 20.92, 20.29, 9.05. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{28}BrNO_2$ $[M]^+$: 489.1303, found: 489.1296; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 18.156 min (major), 19.976 min (minor); 97% ee.



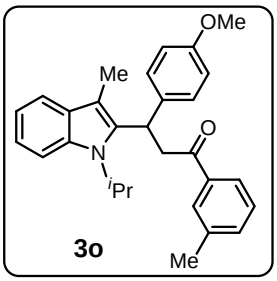
3m

99% yield; 97% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +42 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.10–8.07 (m, 2H), 7.67–7.62 (m, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.43 (dd, *J* = 8.4, 5.4 Hz, 1H), 7.23–7.14 (m, 3H), 6.88–6.76 (m, 3H), 5.32 (t, *J* = 7.2 Hz, 1H), 4.69–4.64 (m, 1H), 4.18 (dd, *J* = 17.1, 7.2 Hz, 1H), 3.83 (dd, *J* = 17.4, 7.2 Hz, 1H), 3.75 (s, 3H), 2.23 (s, 3H), 1.55 (d, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.37, 159.35, 157.78, 157.69, 137.15, 136.29, 133.59, 133.32, 132.93, 128.36, 127.79, 127.72, 125.69, 118.69, 118.62, 113.52, 107.10, 106.40, 106.23, 97.68, 54.85, 47.14, 42.71, 35.13, 20.65, 20.01, 9.10. HRMS

(MALDI-TOF) *m/z* Calcd for $C_{28}H_{28}FNO_2$ $[M]^+$: 429.2104, found: 429.2096; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 15.539 min (minor), 17.779 min (major); 97 % ee.

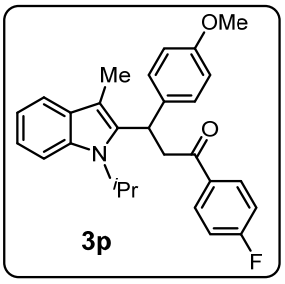


70% yield; 82% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2/1); $[\alpha]_D^{25}$ = +51 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.7 Hz, 2H), 7.55–7.52 (m, 1H), 7.44 (d, *J* = 7.5Hz , 1H), 7.11–7.04 (m, 4H), 6.93 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 5.33 (t, *J* = 6.9 Hz, 1H), 4.57–4.53 (m, 1H), 3.92 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.64 (dd, *J* = 16.8, 5.7 Hz, 1H), 2.28 (s, 3H), 1.53 (d, *J* = 7.2 Hz, 3H), 1.30 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.93, 163.25, 157.58, 137.18, 133.82, 133.66, 130.04, 129.38, 129.19, 127.87, 120.15, 118.20, 117.85, 113.49, 113.42, 111.40, 106.95, 55.10, 54.85, 47.11, 42.41, 35.10, 20.97, 20.29, 9.15. HRMS (MALDI-TOF) *m/z* Calcd for $C_{29}H_{31}NO_3$ $[M]^+$: 441.2304, found: 441.2291; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5, flow rate 1.0 mL/min), t_r: 20.476 min (minor), 25.723 min (major); 82% ee.

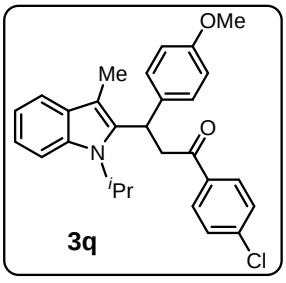


99% yield; 96% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +19 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.37–7.32 (m, 2H), 7.13–7.05 (m, 4H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.33 (t, *J* = 6.6 Hz, 1H), 4.57–4.53 (m, 1H), 3.94 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.75–3.65 (m, 4H), 2.39 (s, 3H), 2.28 (s, 3H), 1.53 (d, *J* = 7.2 Hz, 3H), 1.29 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.72, 157.60, 138.15, 137.01, 136.37, 133.83, 133.63, 133.53, 129.17, 128.28, 128.18, 127.86, 124.93, 120.17, 118.20, 117.85, 113.43, 111.41,

106.98, 54.85, 47.11, 42.87, 35.09, 29.31, 20.96, 20.29, 9.12. HRMS (MALDI-TOF) *m/z* Calcd for $C_{29}H_{31}NO_2$ $[M]^+$: 425.2355, found: 425.2347; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 25.606 min (major), 27.476 min (minor); 96% ee.

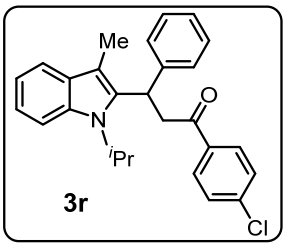


93% yield; 97% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +44 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01–7.96 (m, 2H), 7.55–7.52 (m, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.16–7.04 (m, 6H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.31 (t, *J* = 6.6 Hz, 1H), 4.56–4.52 (m, 1H), 3.93 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75–3.65 (m, 4H), 2.28 (s, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 195.87, 166.29, 164.60, 157.68, 136.75, 133.85, 133.38, 132.77, 130.42, 130.36, 129.16, 127.83, 120.27, 118.23, 117.93, 115.54, 115.39, 113.49, 111.41, 107.01, 54.86, 47.13, 42.73 , 35.13, 20.97, 20.30, 9.18. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{28}FNO_2$ $[M]^+$: 429.2104, found: 429.2095; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 16.544 min (minor), 20.555 min (major); 97% ee.



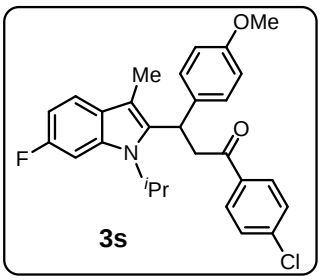
94% yield; 97% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.5/1); $[\alpha]_D^{25}$ = +47 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.54–7.52 (m, 1H), 7.46–7.42 (m, 3H), 7.14–7.04 (m, 4H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.30 (t, *J* = 6.6 Hz, 1H), 4.56–4.51 (m, 1H), 3.91 (dd, *J* = 16.8, 7.5 Hz, 1H), 3.75 (s, 3H), 3.69 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.27 (s, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.27, 157.68, 139.36, 136.63, 134.62, 133.83, 133.29, 129.14, 128.66, 127.80,

120.28, 118.22, 117.92, 113.49, 111.42, 107.01, 54.86, 47.11, 42.76, 35.13, 20.96, 20.30, 9.18. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{28}ClNO_2$ $[M]^+$: 445.1809, found: 445.1797; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 18.763 min (minor), 23.221 min (major); 97% ee.



3r

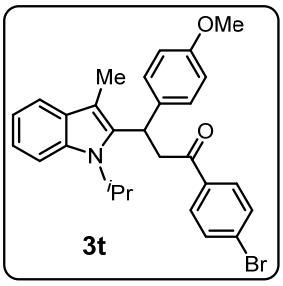
66% yield; 93% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +69 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 8.12 (d, *J* = 8.7 Hz, 2H), 7.58–7.56 (m, 2H), 7.47 (d, *J* = 9.0 Hz, 2H), 7.32–7.17 (m, 5H), 7.07–6.95 (m, 2H), 5.40 (t, *J* = 7.2 Hz, 1H), 4.66–4.61 (m, 1H), 4.25 (dd, *J* = 17.4, 7.2 Hz, 1H), 3.87 (dd, *J* = 17.4, 6.9 Hz, 1H), 2.25 (s, 3H), 1.56 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.48, 141.64, 139.76, 136.84, 134.97, 134.21, 129.51, 129.05, 128.50, 127.16, 126.38, 120.71, 118.64, 118.34, 111.77, 107.60, 47.55, 42.85, 36.11, 21.33, 20.56, 9.54. HRMS (MALDI-TOF) *m/z* Calcd for $C_{27}H_{26}ClNO$ $[M]^+$: 415.1703, found: 415.1696; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 19.439 min (minor), 25.237 min (major); 93% ee.



3s

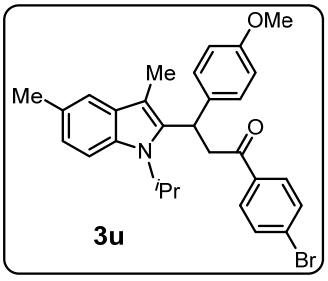
95% yield; 98% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.5/1); $[\alpha]_D^{25}$ = +43 (c = 1.0, DCM);^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.45–7.38 (m, 3H), 7.11 (dd, *J* = 10.8, 2.1 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.86–6.78 (m, 3H), 5.26 (t, *J* = 6.9 Hz, 1H), 4.52–4.47 (m, 1H), 3.90 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75 (s, 3H), 3.67 (dd, *J* = 16.8, 6.3 Hz, 1H), 2.24 (s, 3H), 1.48 (d, *J* = 7.2 Hz, 3H), 1.26 (d, *J* = 5.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.17, 159.36, 157.80, 157.73, 139.40, 136.85, 134.57, 133.51, 133.11,

129.11, 128.67, 127.74, 125.63, 118.69, 118.62, 113.55, 107.08, 106.45, 106.29, 97.67, 54.85, 47.12, 42.68, 35.20, 20.65, 20.03, 9.15. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{27}ClFNO_2$ $[M]^+$: 463.1714, found: 463.1704; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 19.171 min (minor), 24.578 min (major); 98% ee.



3t

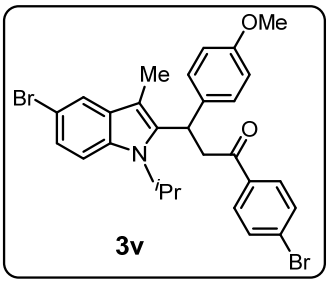
96% yield; 98% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +44 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.54–7.51 (m, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.12–7.03 (m, 4H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.29 (t, *J* = 6.9 Hz, 1H), 4.56–4.51 (m, 1H), 3.91 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75 (s, 3H), 3.68 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.27 (s, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.46, 157.68, 136.60, 135.02, 133.83, 133.27, 131.66, 129.23, 129.12, 128.08, 127.80, 120.28, 118.21, 117.92, 113.49, 111.41, 107.01, 54.86, 47.10, 42.74, 35.12, 20.95, 20.32, 9.19. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{28}BrNO_2$ $[M]^+$: 489.1303, found: 489.1295; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 21.736 min (minor), 26.237min (major); 98% ee.



3u

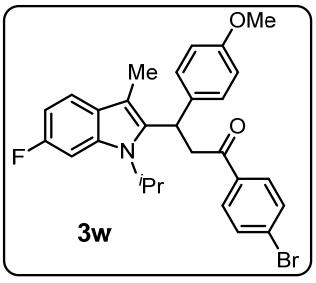
99% yield; 97% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.5/1); $[\alpha]_D^{25}$ = +41 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.35–7.32 (m, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.94 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 5.27 (t, *J* = 6.9 Hz, 1H), 4.52–4.47 (m, 1H), 3.89 (dd, *J* = 17.1, 7.8 Hz, 1H), 3.75 (s, 3H), 3.67 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.44 (s, 3H), 2.24 (s, 3H), 1.50 (d, *J* = 6.9 Hz, 3H), 1.28 (d,

J = 6.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.53, 157.67, 136.72, 135.07, 133.36, 132.10, 131.66, 129.35, 129.26, 128.06, 127.80, 127.19, 121.84, 117.98, 113.48, 111.13, 106.49, 54.87, 47.06, 42.76, 35.14, 21.01, 20.94, 20.37, 9.18. HRMS (MALDI-TOF) *m/z* Calcd for $C_{29}H_{30}BrNO_2$ $[M]^+$: 503.1460, found: 503.1448; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 1.0 mL/min), t_r: 17.976 min (minor), 20.169 min (major); 97% ee.



3v

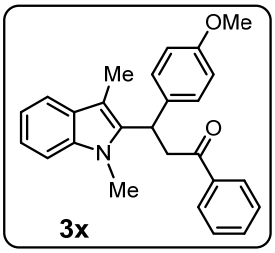
99% yield; 98% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 35/1–25/1); $[\alpha]_D^{25}$ = +33 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.63–7.59 (m, 3H), 7.30 (d, *J* = 8.7 Hz, 1H), 7.17 (dd, *J* = 9.0, 2.1Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 5.27 (t, *J* = 6.9 Hz, 1H), 4.55–4.51 (m, 1H), 3.89 (dd, *J* = 16.8, 7.5 Hz, 1H), 3.76 (s, 3H), 3.68 (dd, *J* = 17.1, 6.6 Hz, 1H), 2.21 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.28 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.26, 157.79, 137.91, 134.92, 132.84, 132.45, 131.69, 130.95, 129.20, 128.18, 127.72, 122.95, 120.78, 113.60, 112.66, 111.41, 106.75, 54.87, 47.23, 42.54, 35.18, 20.92, 20.31, 9.13. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{27}Br_2NO_2$ $[M]^+$: 567.0409; found: 567.0396; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 98/2, flow rate 0.5 mL/min), t_r: 52.297 min (major), 56.511 min (minor); 98% ee.



3w

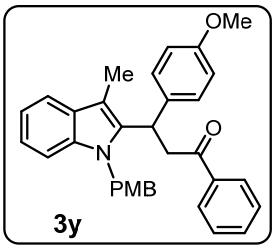
96% yield; 98% ee (purified by flash column chromatography with petroleum ether and DCM eluents, v/v = 2.3/1); $[\alpha]_D^{25}$ = +39 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.40 (dd, *J* = 8.7, 5.7 Hz, 1H), 7.11 (dd, *J* = 11.1, 2.1Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.86–6.78 (m, 3H), 5.25 (t, *J* = 6.9 Hz, 1H), 4.52–4.47 (m, 1H), 3.90 (dd, *J* = 16.8, 7.5 Hz, 1H), 3.76 (s, 3H),

3.67 (dd, J = 16.8, 6.3 Hz, 1H), 2.24 (s, 3H), 1.48 (d, J = 6.9 Hz, 3H), 1.26 (d, J = 6.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.38, 159.37, 157.81, 157.75, 136.84, 134.98, 133.52, 133.10, 131.67, 129.22, 128.12, 127.75, 125.65, 118.71, 118.64, 113.56, 107.11, 106.47, 106.31, 97.69, 54.86, 47.13, 42.67, 35.21, 20.66, 20.04, 9.16. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{27}BrFNO_2$ $[M]^+$: 507.1209, found: 507.1197; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5 , flow rate 1.0 mL/min), t_r: 11.321 min (minor), 14.041 min (major); 98% ee.



3x

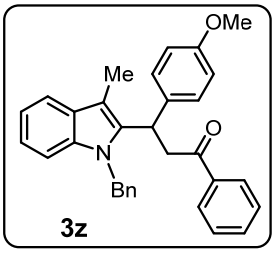
98% yield; 81% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +13 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95–7.92 (m, 2H), 7.57–7.41 (m, 4H), 7.20–7.05 (m, 5H), 6.79 (d, J = 8.7 Hz, 2H), 5.26 (t, J = 6.9 Hz, 1H), 3.89–3.84 (m, 2H), 3.75 (s, 3H), 3.59 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.56, 157.72, 137.09, 136.39, 136.35, 133.43, 132.83, 128.29, 128.18, 128.02, 127.67, 120.72, 118.26, 117.80, 113.57, 108.34, 106.95, 54.85, 43.08, 35.27, 29.94, 9.24. HRMS (MALDI-TOF) *m/z* Calcd for $C_{26}H_{25}NO_2$ $[M]^+$: 383.1885, found: 383.1878; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5, flow rate 1.0 mL/min), t_r: 17.407 min (major), 21.004 min (minor); 81% ee.



3y

87% yield; 50% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +16 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 7.2 Hz, 2H), 7.58–7.49 (m, 2H), 7.37 (t, J = 7.8 Hz, 2H), 7.19–7.08 (m, 3H), 6.97 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 6.72 (t, J = 8.4 Hz, 4H), 5.24–5.09 (m, 3H), 3.74–3.64 (m, 7H), 3.51 (dd, J = 18.0, 6.0 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.44, 158.66, 158.01, 137.66, 136.82,

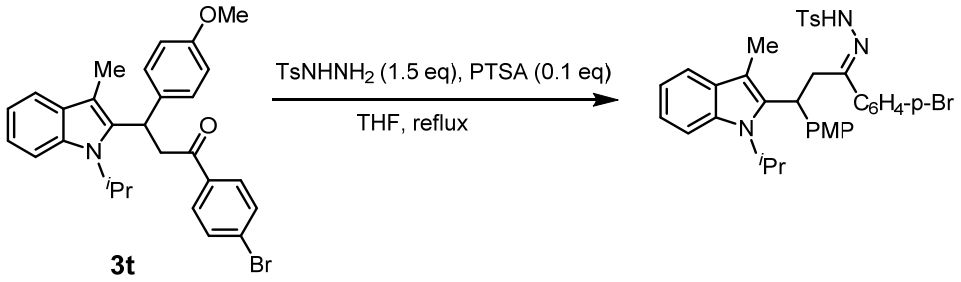
136.55, 133.52, 133.05, 130.43, 128.69, 128.48, 128.36, 127.96, 127.29, 121.46, 118.95, 118.27, 114.04, 113.83, 109.20, 108.25, 55.18, 46.35, 43.20, 35.19, 9.65. HRMS (MALDI-TOF) *m/z* Calcd for $C_{33}H_{31}NO_3$ $[M]^+$: 489.2304, found: 489.2289; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5, flow rate 1.0 mL/min), t_r: 16.289 min (major), 27.461 min (minor); 50% ee.



3z

yield: 88%; ee: 38%; (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 30/1); $[\alpha]_D^{25}$ = +22 (c = 1.0, DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.2 Hz, 2H), 7.59–7.48 (m, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.21–7.11 (m, 6H), 6.98–6.93 (m, 4H), 6.73 (d, *J* = 8.7 Hz, 2H), 5.30–5.15 (m, 3H), 3.74–3.65 (m, 4H), 3.51 (dd, *J* = 17.7, 6.0 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.42, 158.06, 138.45, 137.73, 136.91, 136.55, 133.49, 133.10, 128.71, 128.53, 128.38, 127.98, 127.04, 126.12, 121.55, 119.07, 118.34, 113.88, 109.24, 108.30, 55.22, 46.93, 43.32, 35.21, 9.70. HRMS (MALDI-TOF) *m/z* Calcd for $C_{32}H_{29}NO_2$ $[M]^+$: 459.2198, found: 459.2182; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5 , flow rate 1mL/min), t_r: 10.995 min (major), 13.731 min (minor); 38% ee.

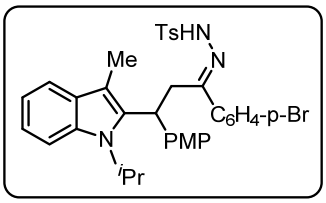
Determination of the Absolute Configuration of Products (a derivative from 3t)



3t

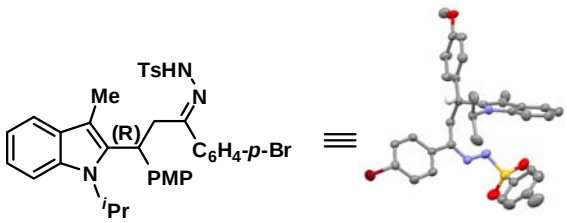
A suspension of ketone **3t** (196.2 mg, 0.4 mmol, 97% ee), *p*-toluenesulfonyl hydrazide (111.7 mg, 0.6 mmol, 1.5 equiv), and *p*-toluenesulfonic acid (7.6 mg, 0.04

mmol, 0.1 equiv) in THF (20 mL) was refluxed for 12 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 12/1) to afford the product as a white solid.



90% yield; 97% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 12/1); $[\alpha]_D^{25}$ = -124 (c = 1.0, DCM); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.88 (s, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.35 (t, J = 7.8 Hz, 5H), 7.24 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 7.8 Hz, 2H), 6.97 (t, J = 7.2 Hz , 1H), 6.92 (t, J = 7.8 Hz, 5H), 6.84 (d, J = 8.4 Hz, 2H), 4.81 (brs, 1H), 4.38–4.35 (m, 1H), 3.70 (s, 4H), 3.60–3.56 (m, 1H), 2.36 (s, 3H), 1.99 (s, 3H), 1.34 (d, J = 5.4 Hz, 3H), 0.89 (brs, 3H), ^{13}C NMR (151 MHz, DMSO-d_6) δ 157.72, 154.54, 143.47, 136.64, 136.20, 136.02, 133.65, 133.45, 130.92, 129.54, 128.94, 128.46, 128.38, 127.53, 122.32, 120.50, 118.28, 117.95, 113.67, 111.73, 107.13, 55.13, 46.82, 35.78, 30.68, 21.06, 20.98, 20.11, 8.89. The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 95/5, flow rate 1.0 mL/min), t_r: 11.414 min (minor), 15.212 min (major); 97% ee.

Crystal structure of hydrozone derivative

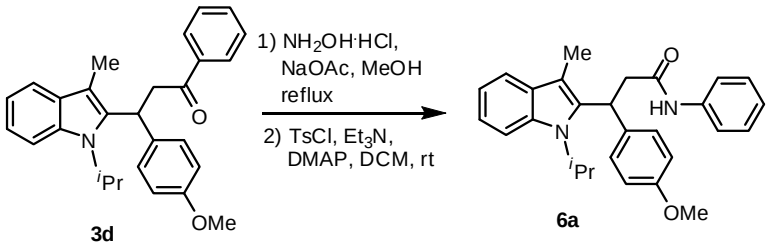


Crystal data and structure refinement:

Empirical formula	C_{35} H_{36} Br N_3 O_3 S
Formula weight	658.64
Temperature	296(2) K
Wavelength	0.71073 Å

Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 9.4805(11) Å alpha = 90°. b = 15.3417(19) Å beta = 111.930(2)°. c = 11.8162(14) Å gamma = 90 °.
Volume	1594.3(3) $Å^3$
Z, Calculated density	2, 1.372 Mg/m^3
Absorption coefficient	1.394 mm^{-1}
F(000)	684
Crystal size	0.20 x 0.18 x 0.15 mm
Theta range for data collection	1.86 to 26.05°
Limiting indices	-11<=h<=11, -18<=k<=18, -11<=l<=14
Reflections collected / unique	10385 / 6126 [R(int) = 0.0448]
Completeness to theta = 26.05	99.2 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8181 and 0.7679
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6126 / 1 / 393
Goodness-of-fit on F^2	1.002
Final R indices [I>2sigma(I)]	R1 = 0.0450, wR2 = 0.1073
R indices (all data)	R1 = 0.0557, wR2 = 0.1363
Absolute structure parameter	-0.008(9)
Largest diff. peak and hole	0.780 and -0.412 $e.A^{-3}$

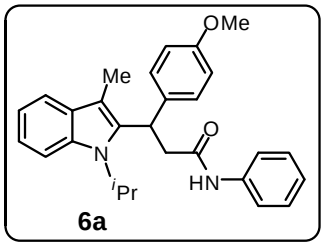
Conversion of 3 into amides [7]



A suspension of ketone **3d** (197.5 mg, 0.48 mmol, 96% ee), hydroxylamine hydrocholoride (98.6 mg, 1.44 mmol, 3 equiv), and NaOAc (43.5 mg, 0.53 mmol, 1.1 equiv) in MeOH (20 mL) was refluxed for 12 h. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10/1) to afford the oxime product as a white solid.

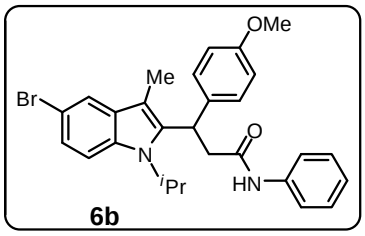
To a mixture of *p*-toluenesulfonyl choride (124.7 mg, 0.654 mmol, 1.5 equiv), triethylamine (91μL, 0.654 mmol, 1.5 equiv), and DMAP (10.7 mg, 0.087 mmol, 0.2 equiv) in DCM (20 mL) was added the oxime (186.0 mg, 0.436 mmol). The mixture was stirred for 12 h at room temperature and concentrated under reduced pressure, and purified by flash column chromatography (petroleum ether/ethyl acetate = 8/1) to afford the amide product (160.0 mg, 75% yield for two steps) as a white solid.

The amide **6b** was synthesized from **3l** in 80% yield over two steps according to the same procedure as **6a**.



75% yield for two steps; 95% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 8/1); $[\alpha]_D^{25}$ = +48 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 9.35 (s, 1H), 7.62 (d, *J*= 7.8 Hz, 2H), 7.49–7.46 (m, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.05–6.95 (m, 3H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.27 (t, *J* = 7.2 Hz, 1H), 4.62 (brs, 1H), 3.74 (s, 3H), 3.51 (dd, *J* = 15.0, 8.1 Hz, 1H), 3.12 (dd, *J* = 15.0, 6.6 Hz, 1H), 2.33 (s, 3H), 1.53 (d, *J* = 7.2 Hz, 3H), 1.23 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (101 MHz, Acetone-d_6) δ 169.11, 158.05, 139.27, 137.36, 134.21, 133.95, 129.63, 128.50, 128.05, 123.14, 120.22, 119.09, 119.01,

118.21, 117.90, 113.56, 111.54, 106.71, 54.44, 47.13, 40.82, 36.23, 20.41, 19.81, 8.62 . HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{30}N_2O_2$ $[M]^+$: 426.2307, found: 426.2297; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 85/15, flow rate 1.0 mL/min), t_r: 8.275 min (major),17.030 min (minor); 95% ee.



6b

80% yield for two steps; 96% ee (purified by flash column chromatography with petroleum ether and ethyl acetate eluents, v/v = 8/1); $[\alpha]_D^{25}$ = +41 (c = 1.0, DCM); ^{1}H NMR (300 MHz, Acetone-d_6) δ 9.34 (s, 1H), 7.61 (d, *J*= 8.1 Hz, 3H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.19–7.12 (m, 3H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.26 (t, *J* = 7.2 Hz, 1H), 4.67–4.63 (m, 1H), 3.74 (s, 3H), 3.51 (dd, *J* = 15.0, 8.1 Hz, 1H), 3.13 (dd, *J* = 15.0, 6.9 Hz, 1H), 2.30 (s, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 5.7 Hz, 3H). ^{13}C NMR (101 MHz, Acetone-d_6) δ 168.91, 158.13, 139.19, 133.48, 132.82, 131.48, 128.50, 128.02, 123.18, 122.67, 120.62, 119.09, 113.63, 113.23, 111.02, 106.68, 54.45, 47.37, 40.59, 36.24, 20.36, 19.77, 8.50. HRMS (MALDI-TOF) *m/z* Calcd for $C_{28}H_{29}BrN_2O_2$ $[M]^+$: 504.1412, found: 504.1400; The ee was determined by HPLC with a Daicel Chiralcel AD-H column (hexane/isopropanol = 85/15, flow rate 1.0 mL/min), t_r: 8.410 min (major),14.621 min (minor); 96% ee.

References

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(2) D. Nakashima, H. Yamamoto, *J. Am. Chem. Soc*. **2006**, *128*, 9626.

(3) S. Qi, C.-Y. Liu, J.-Y. Ding, F.-S. Han, *Chem. Commun.*, **2014**, *50*, 8605.

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(6) Y.-X. Jia, J. Zhong, S.-F. Zhu, C.-M. Zhang, Q.-L. Zhou, *Angew. Chem. Int. Ed*. **2007**, *46*, 5565.

(7) J.-W. Zhang, Q. Cai, X.-X. Shi, W. Zhang, S.-L. You, *Synlett.* **2011**, *9*, 1239.

Copies of ^{1}H- and ^{13}C-NMR spectra of products

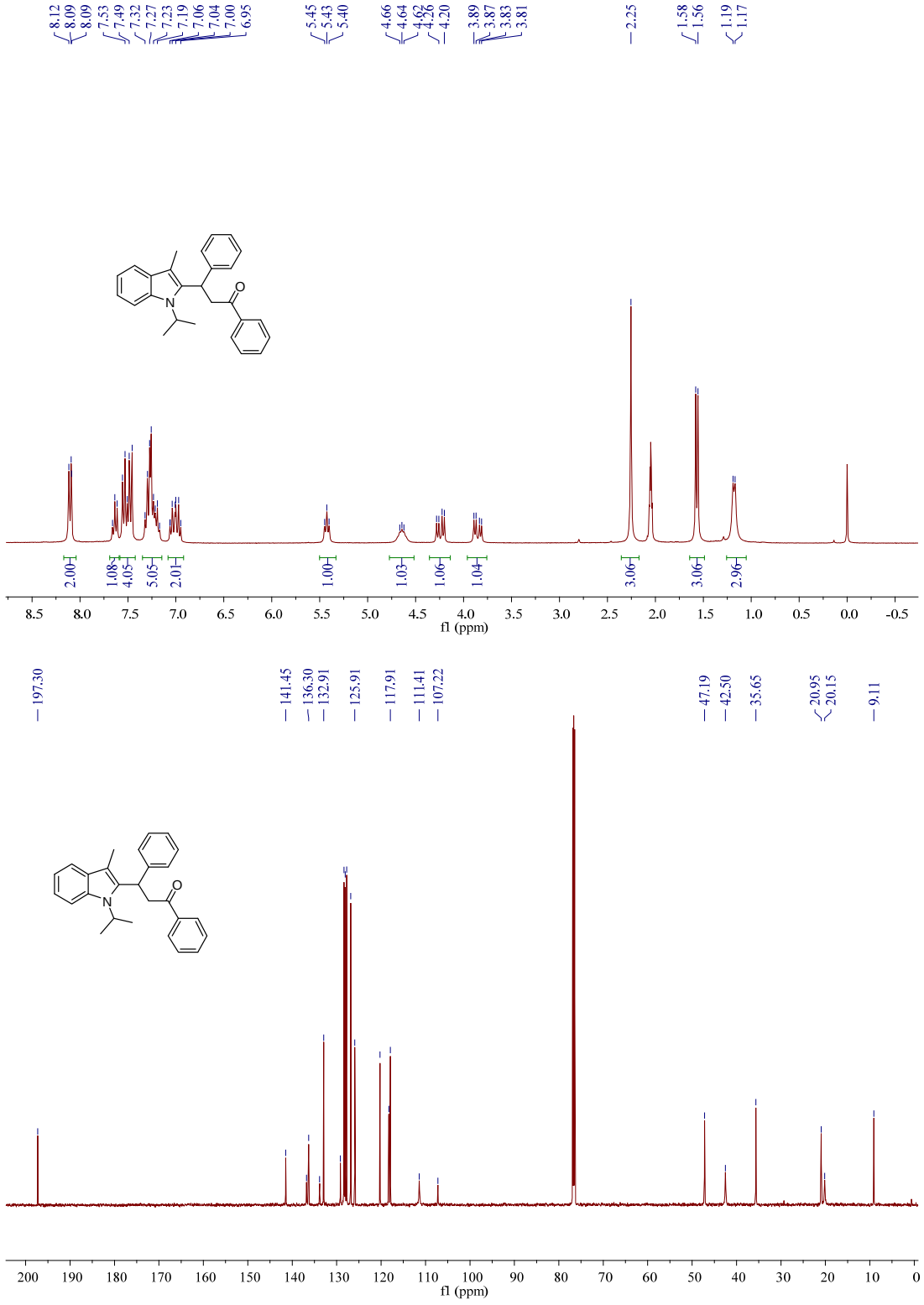


Figure S1. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3a**

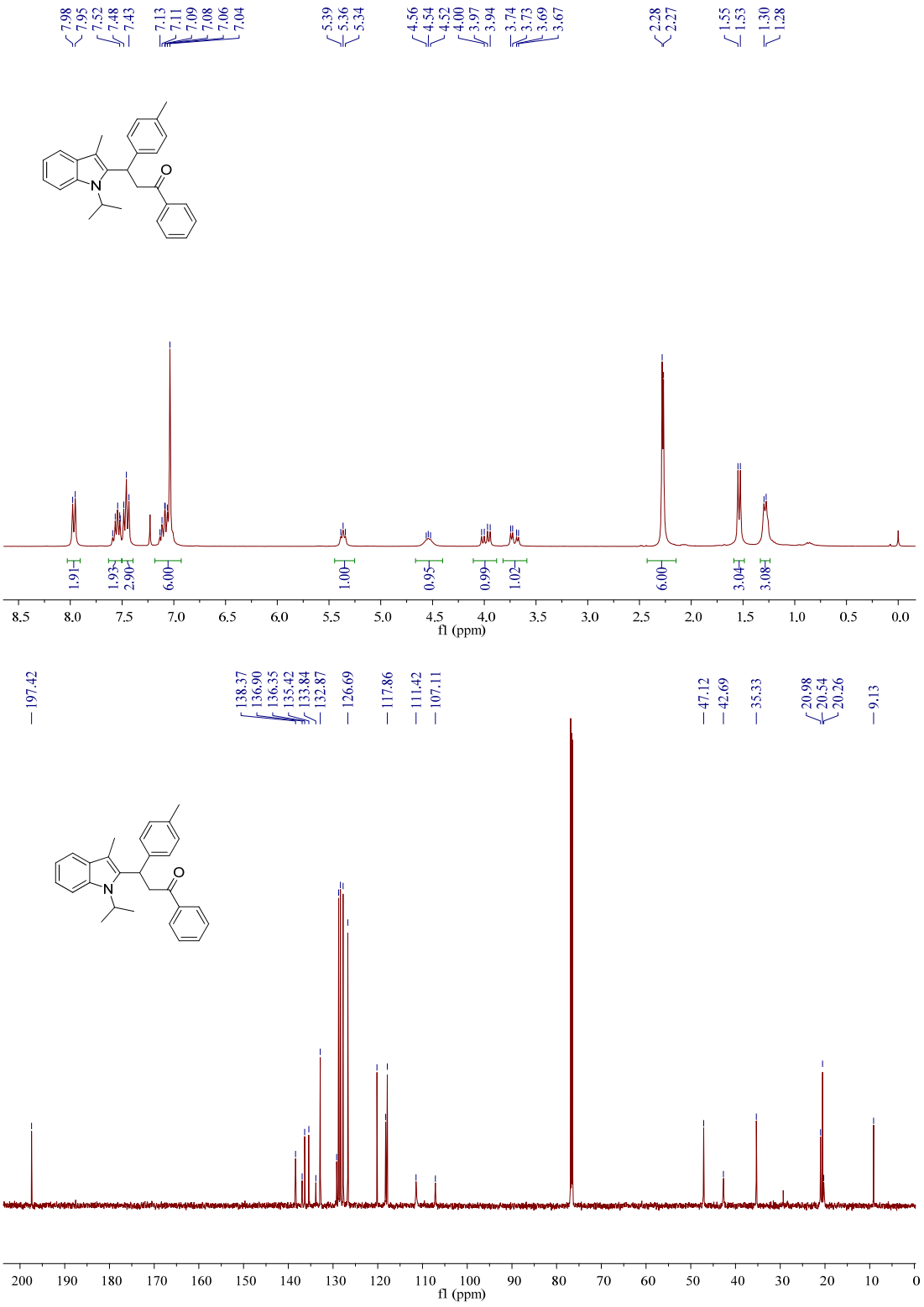


Figure S2. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3b**

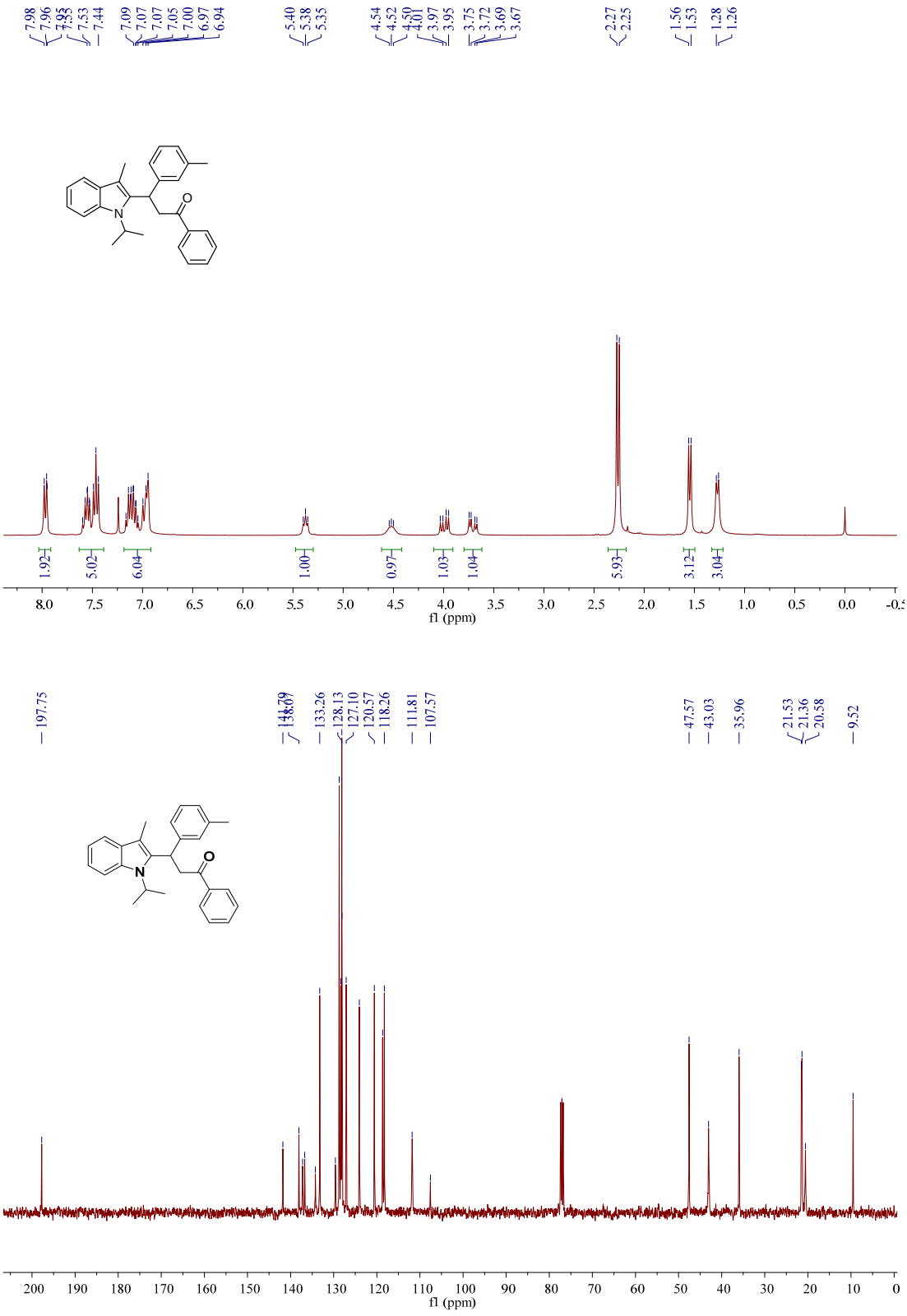


Figure S3. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3c**

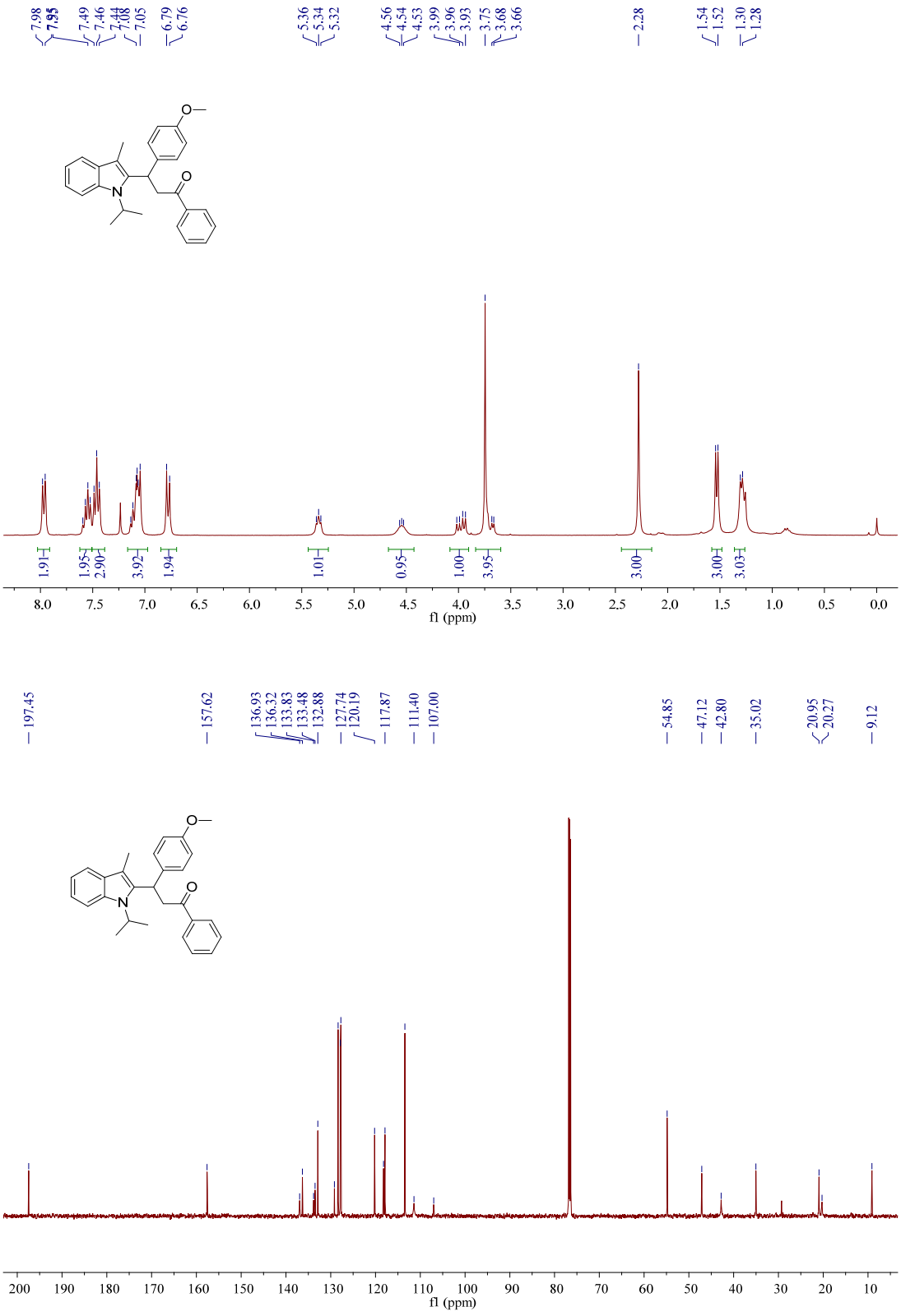


Figure S4. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3d**

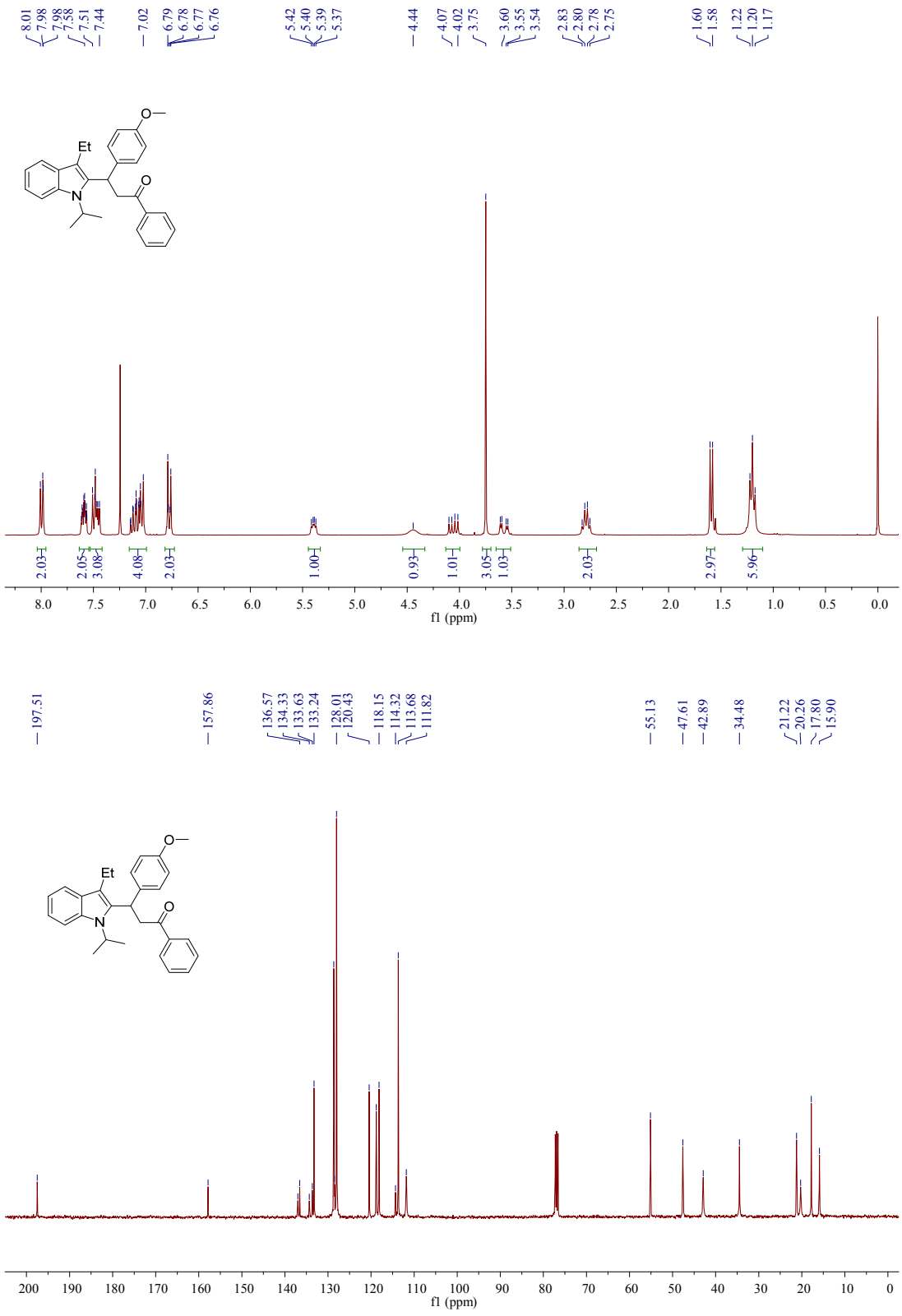


Figure S5. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3e**

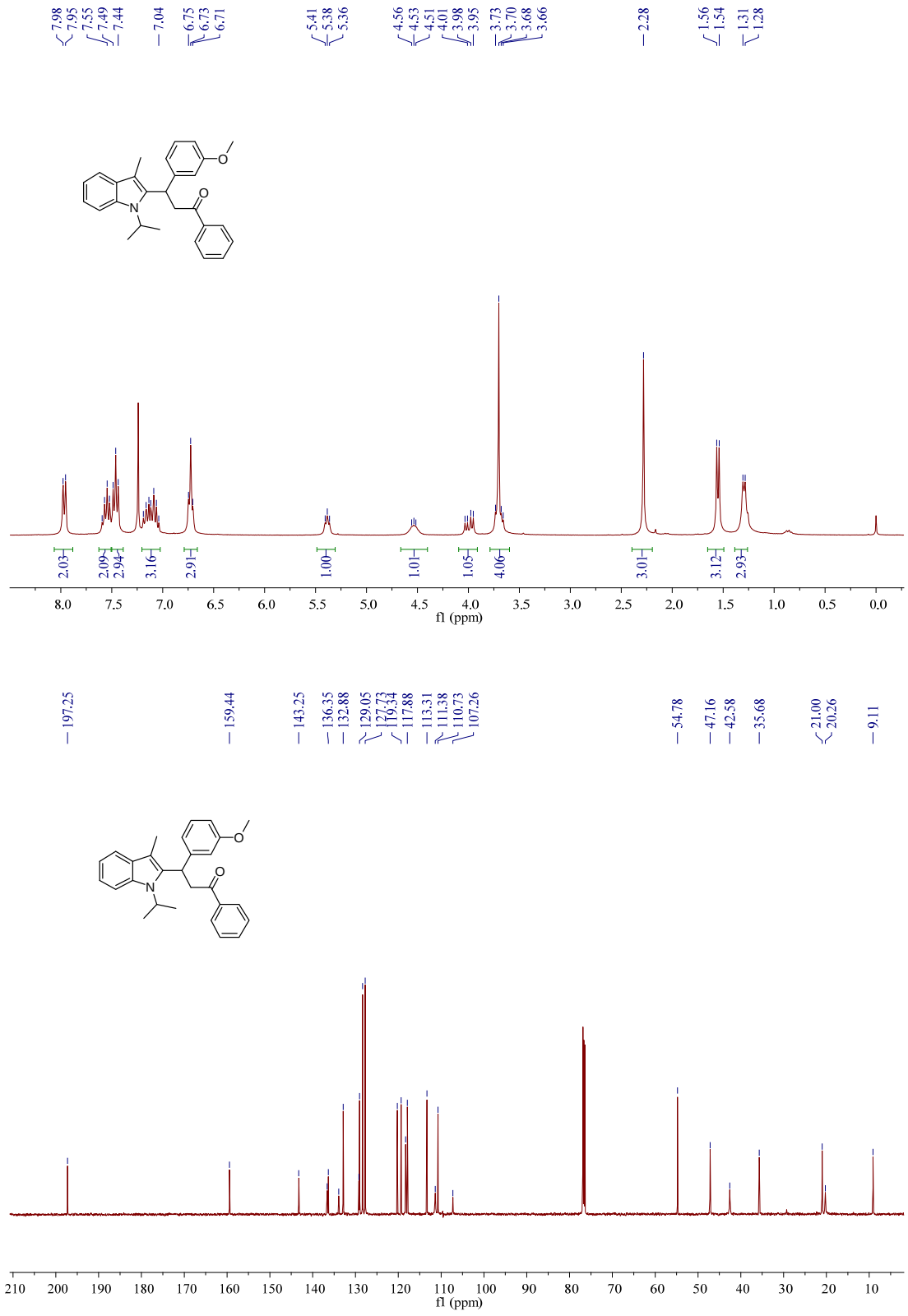


Figure S6. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3f**

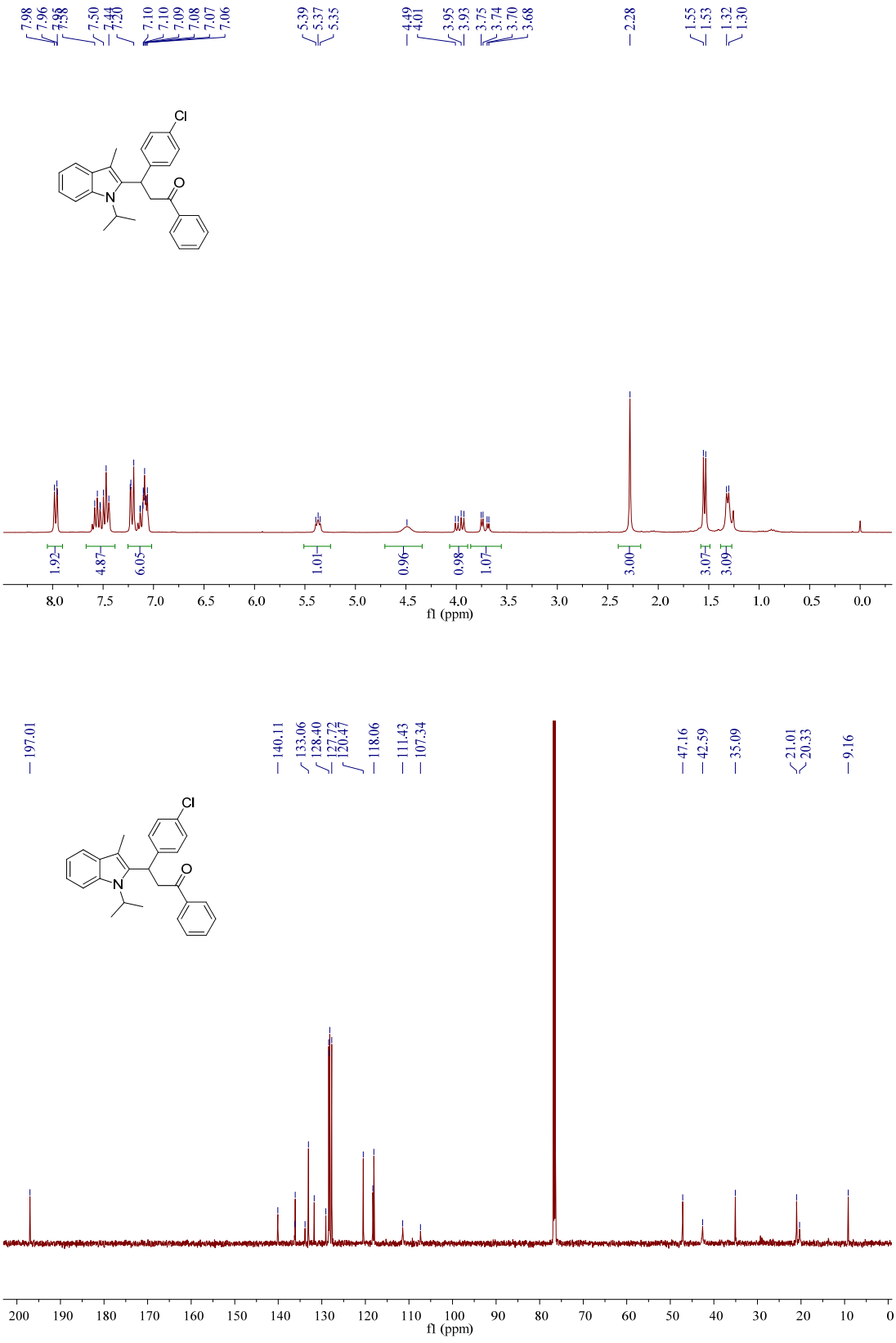


Figure S7. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3g**

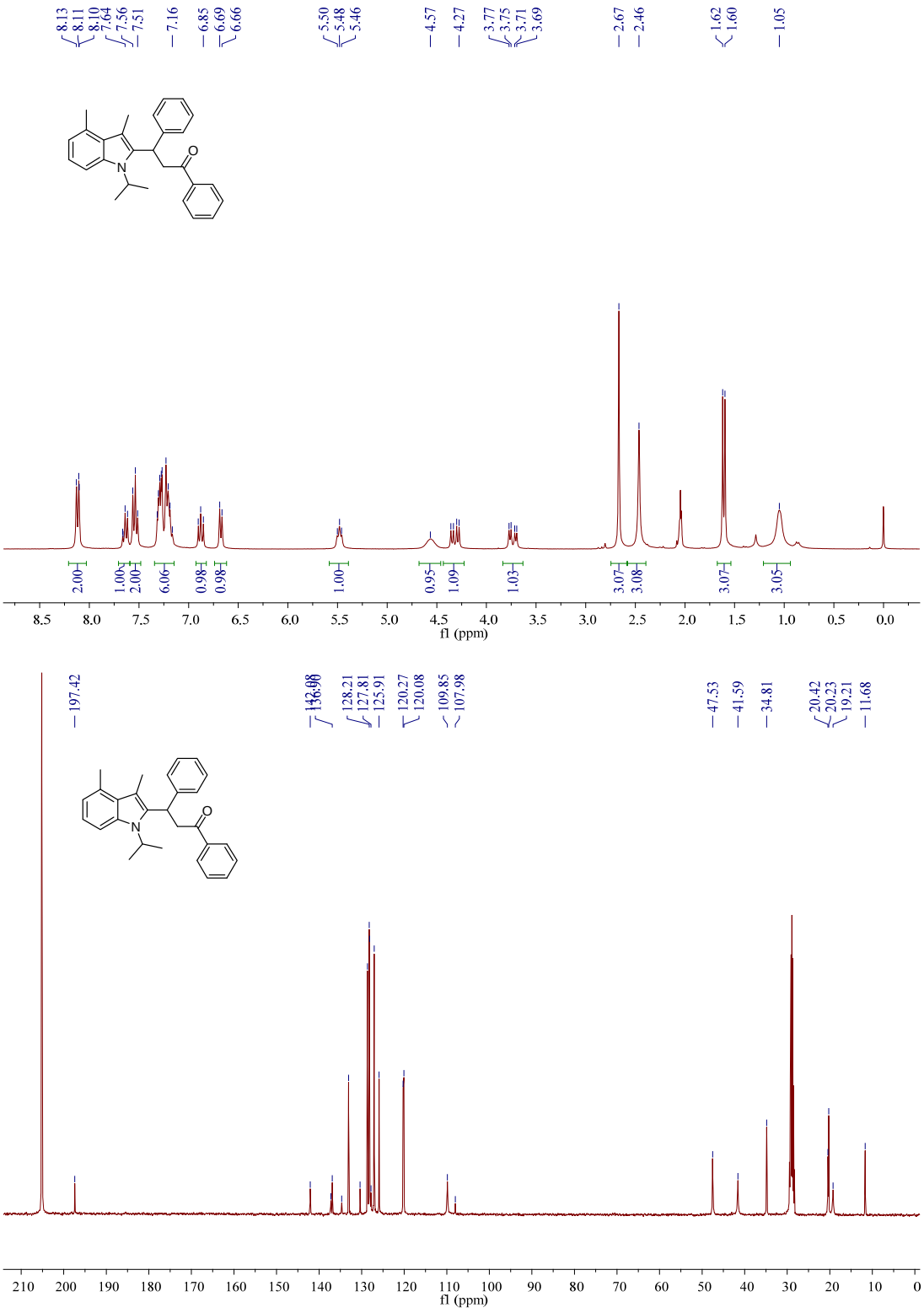


Figure S8. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3h**

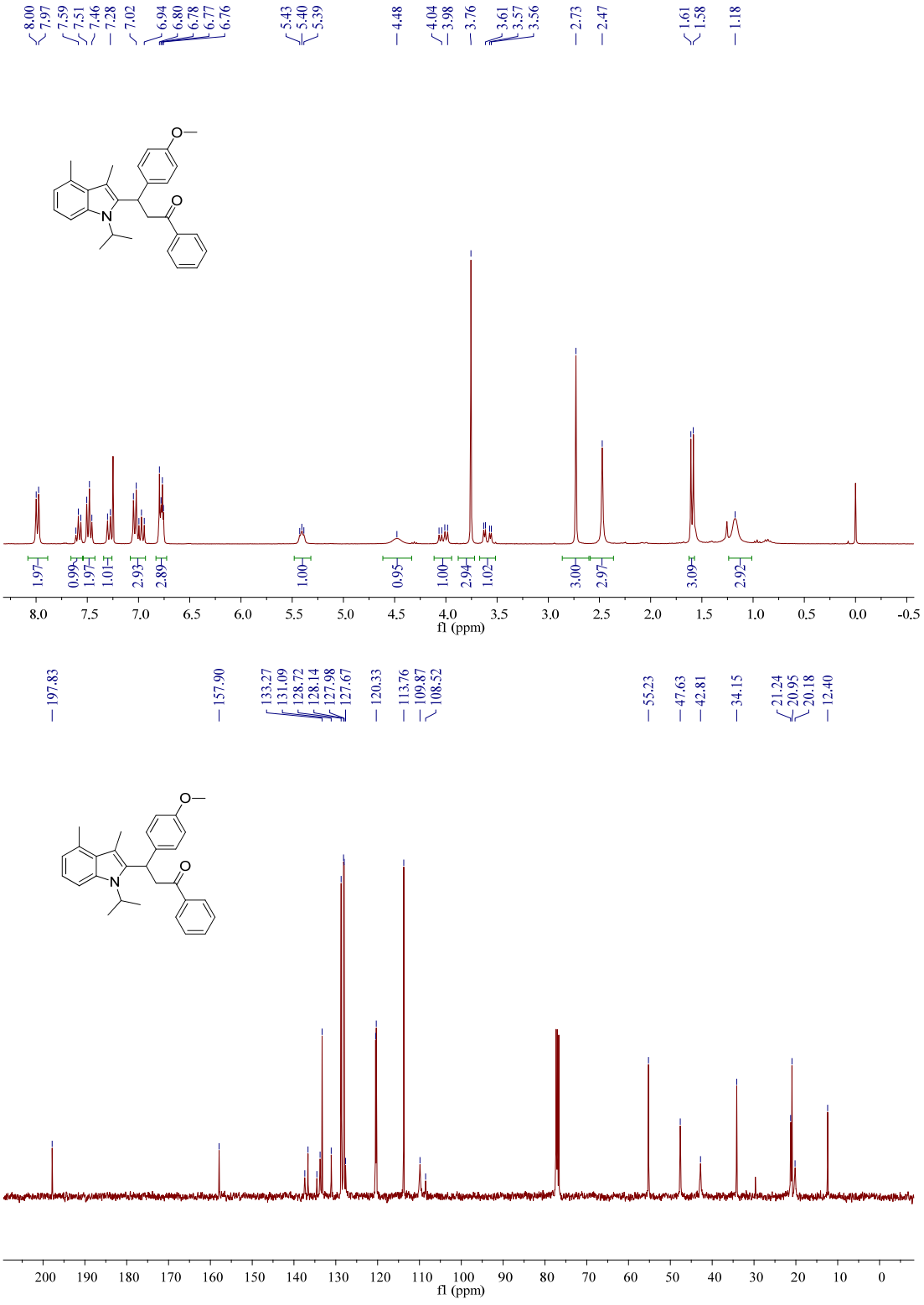


Figure S9. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3i**

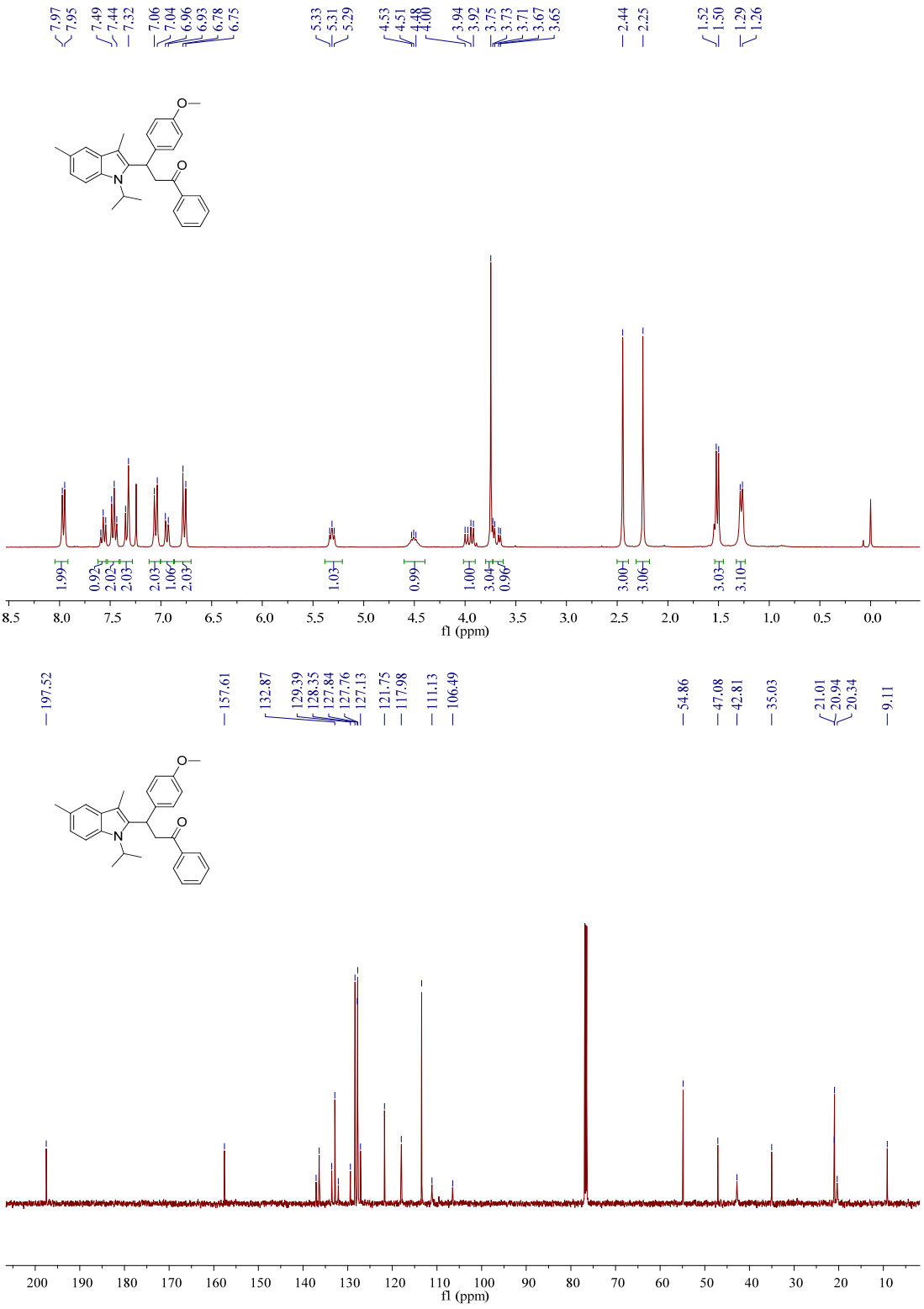


Figure S10. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3j**

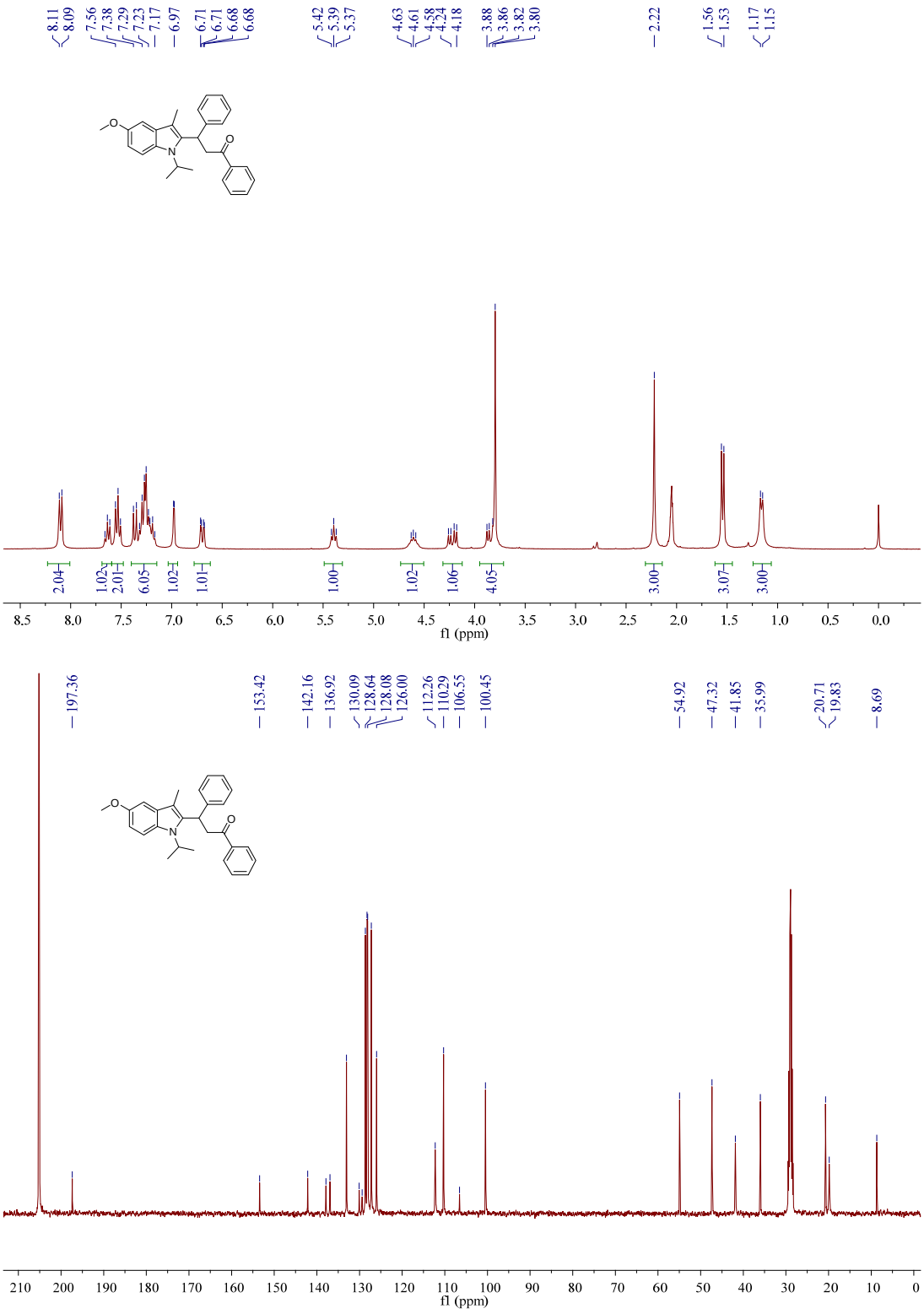


Figure S11. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3k**

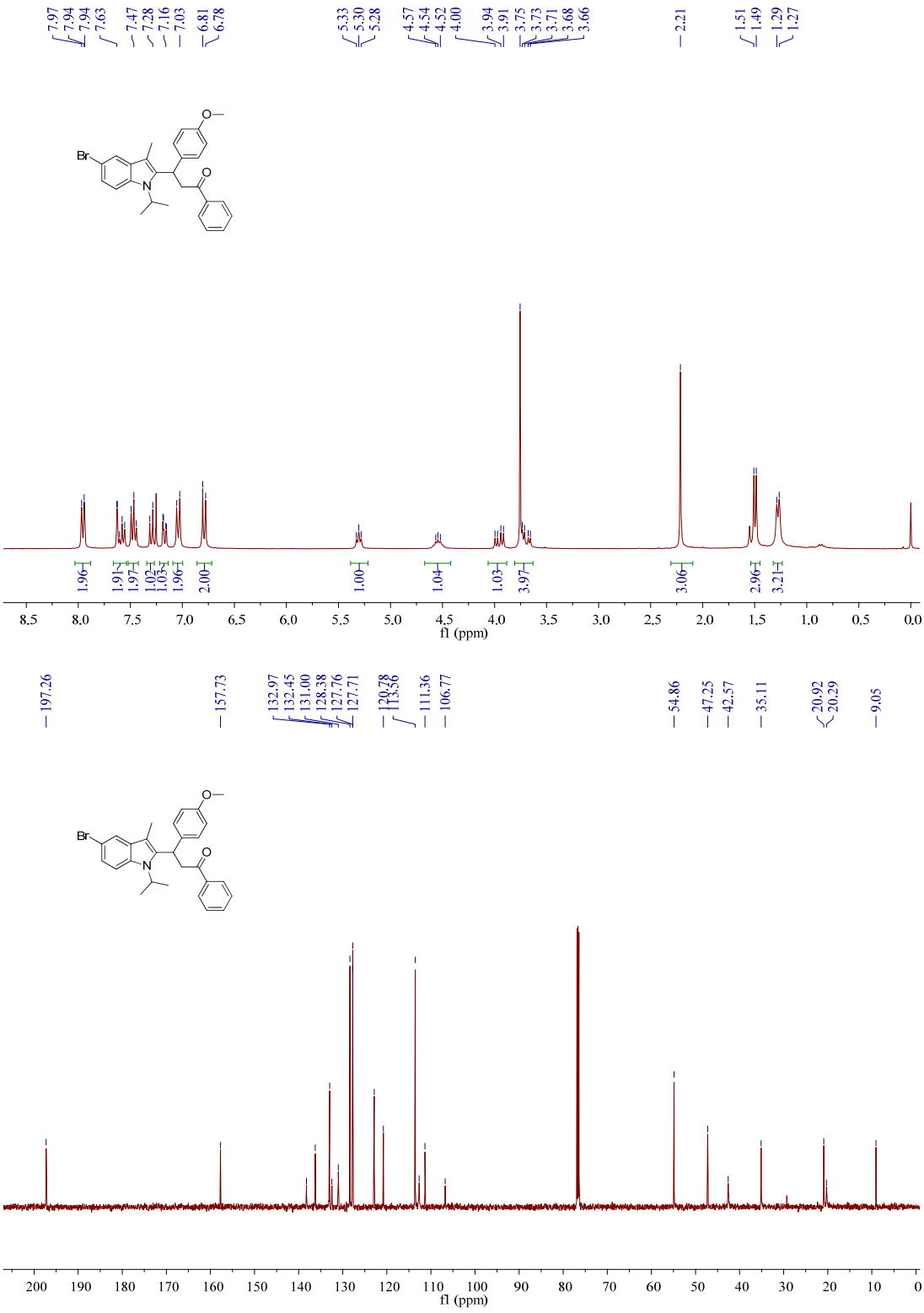


Figure S12. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3l**

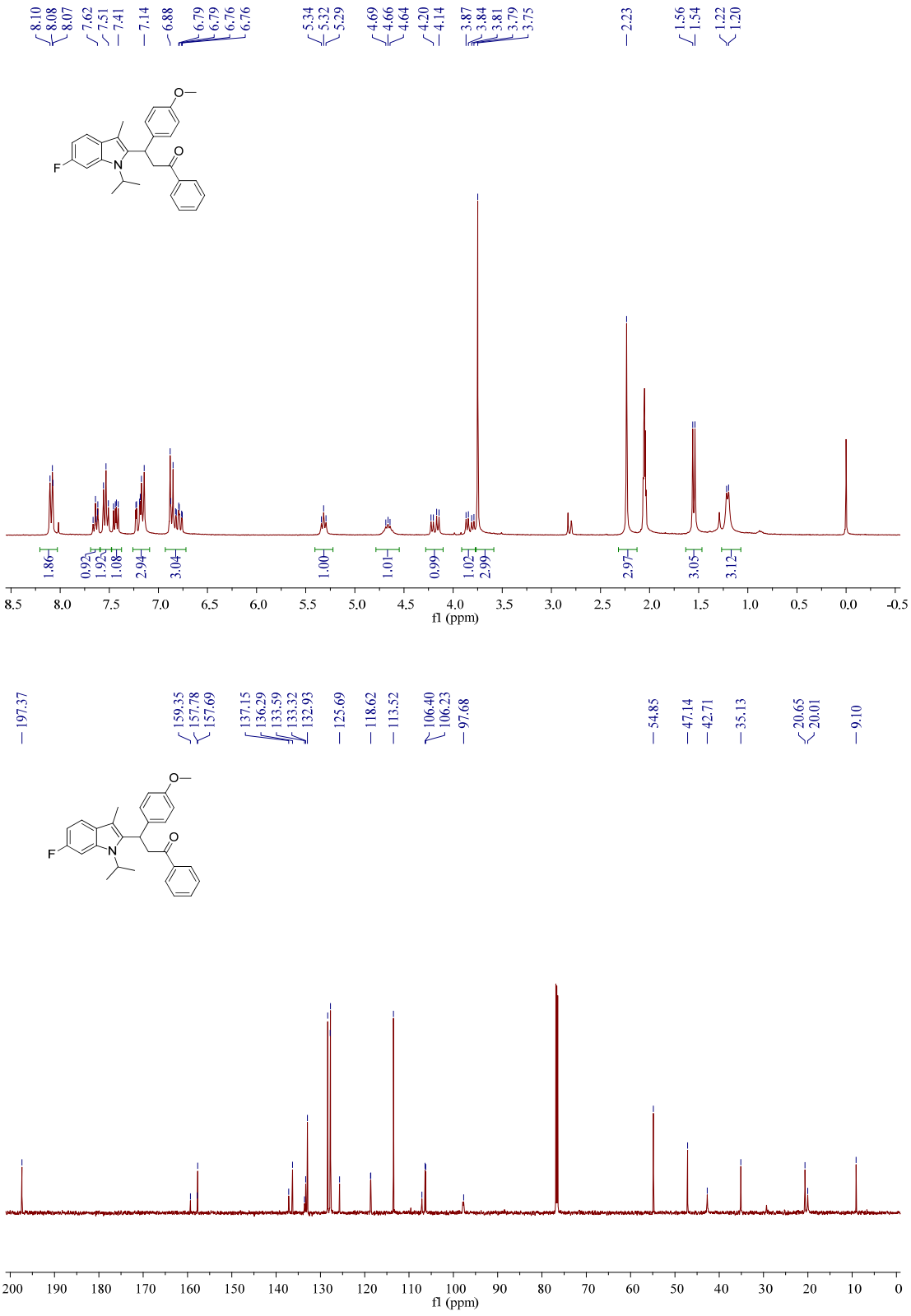


Figure S13. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3m**

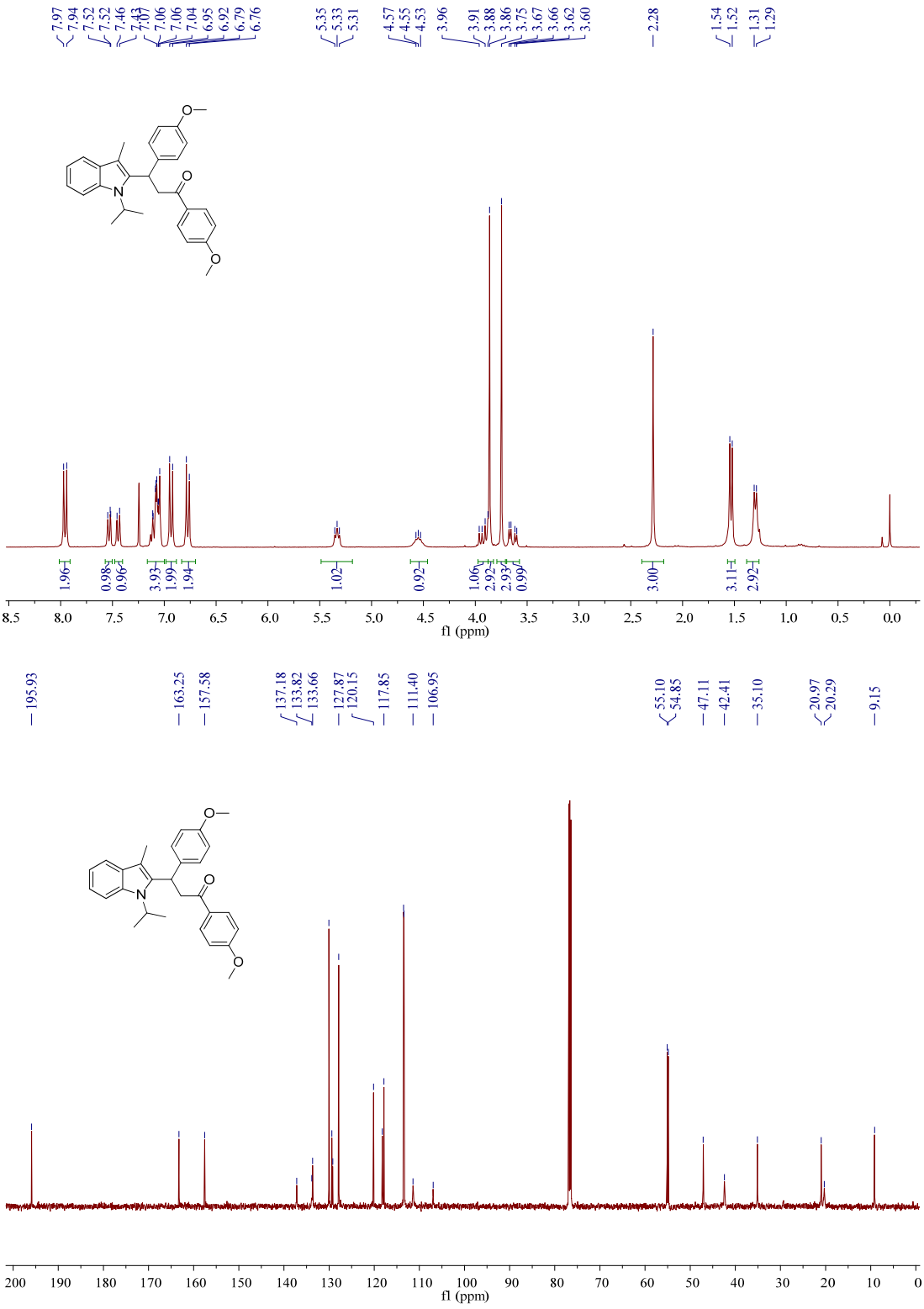


Figure S14. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3n**

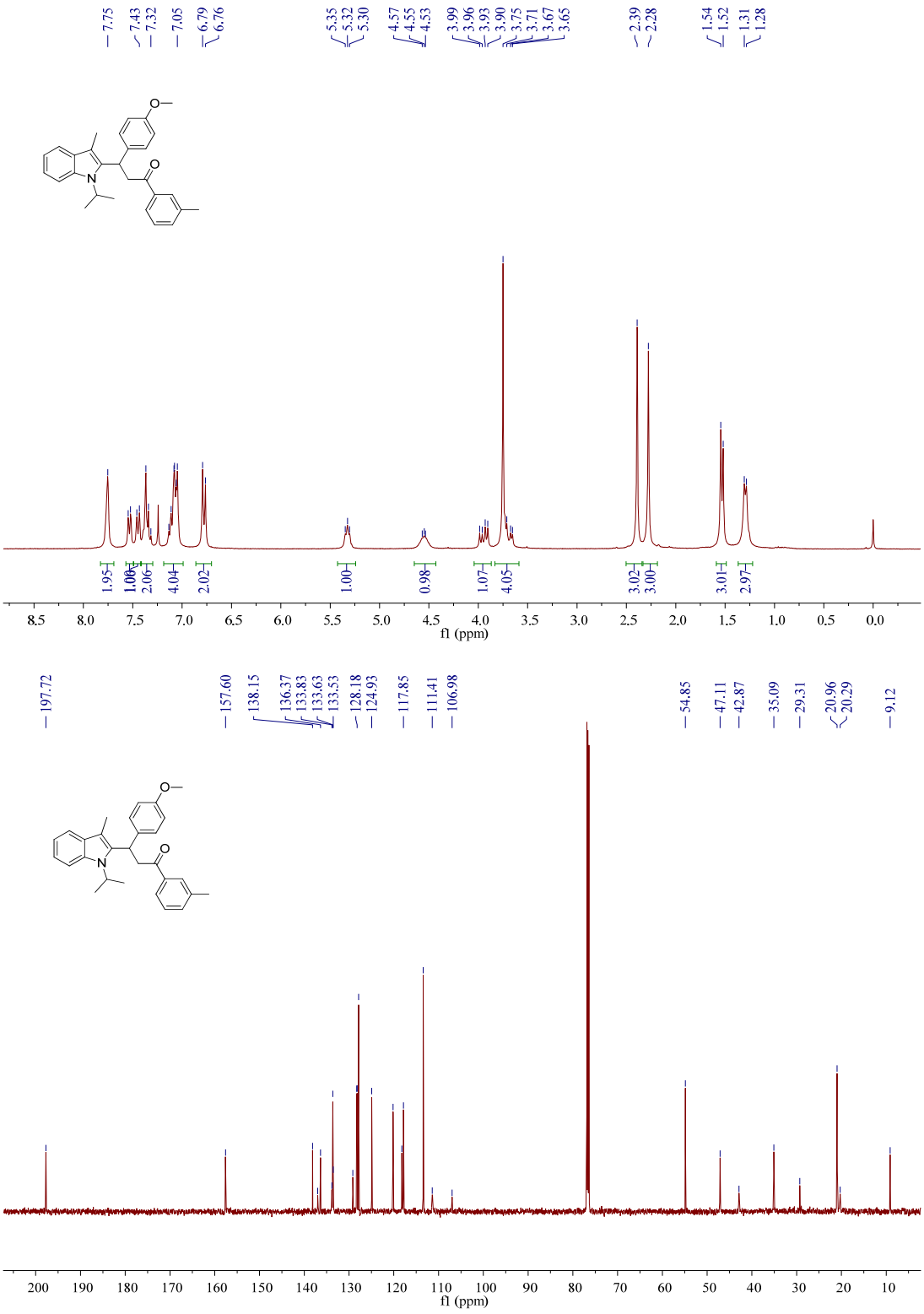


Figure S15. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3o**

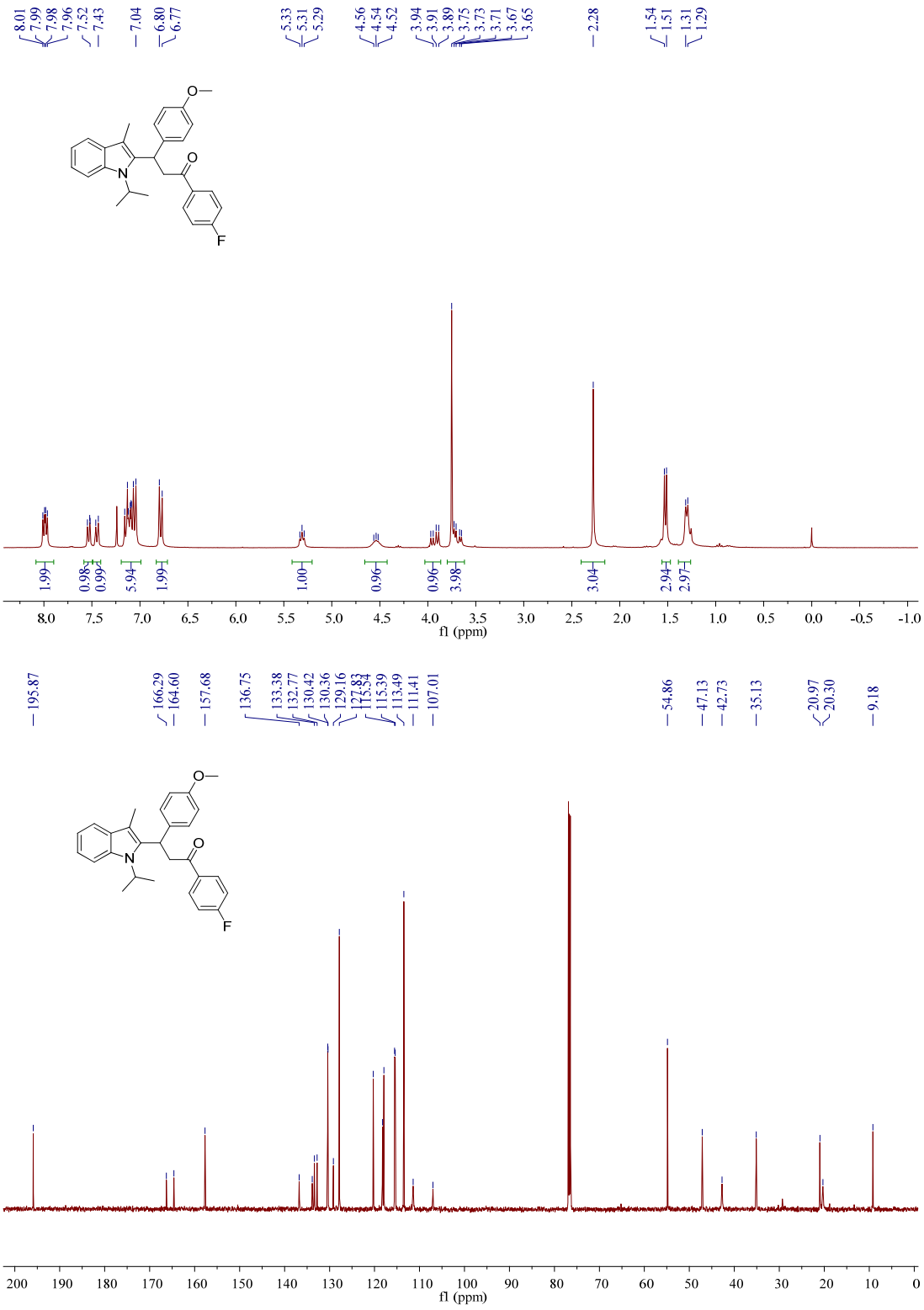


Figure S16. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3p**

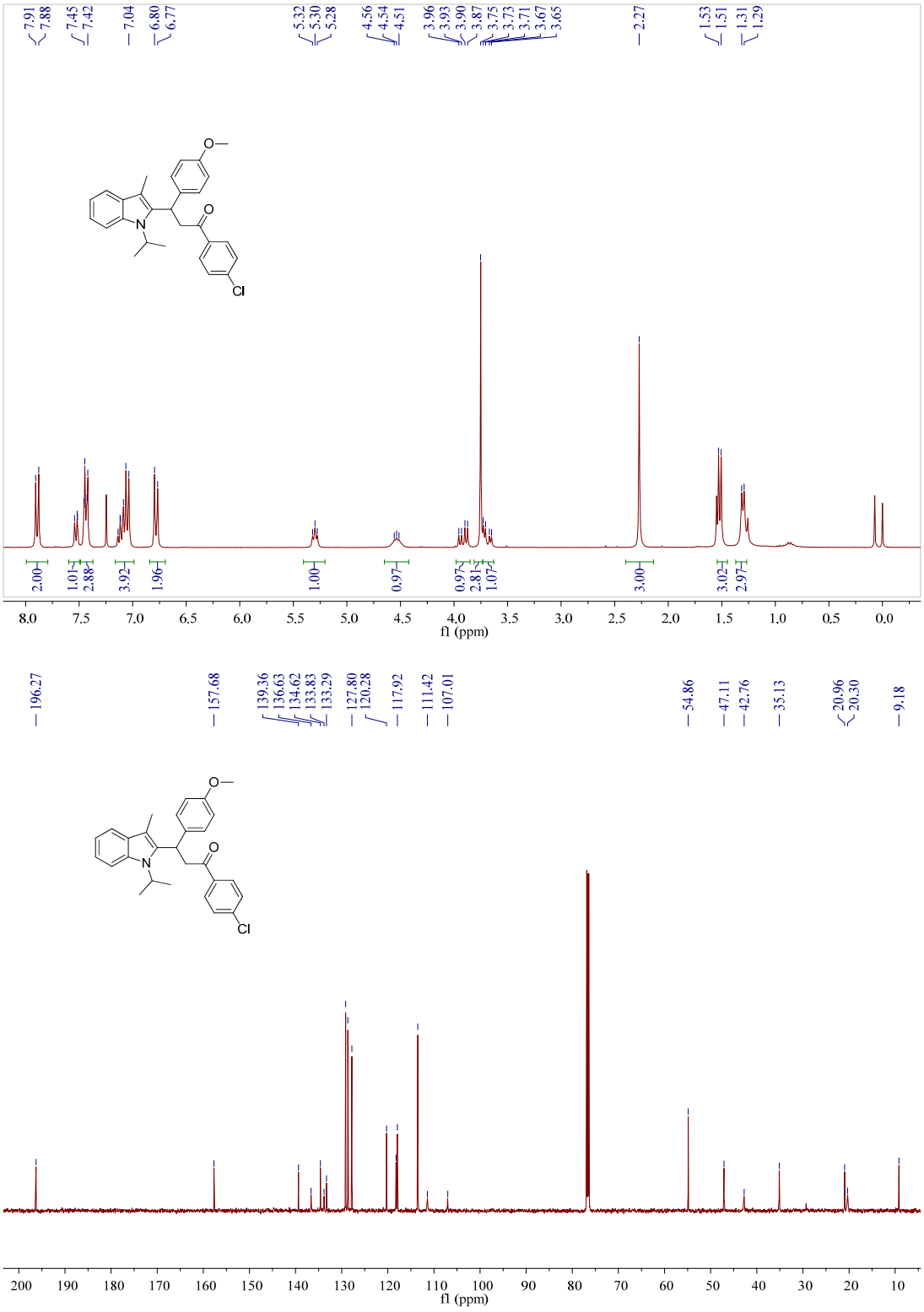


Figure S17. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3q**

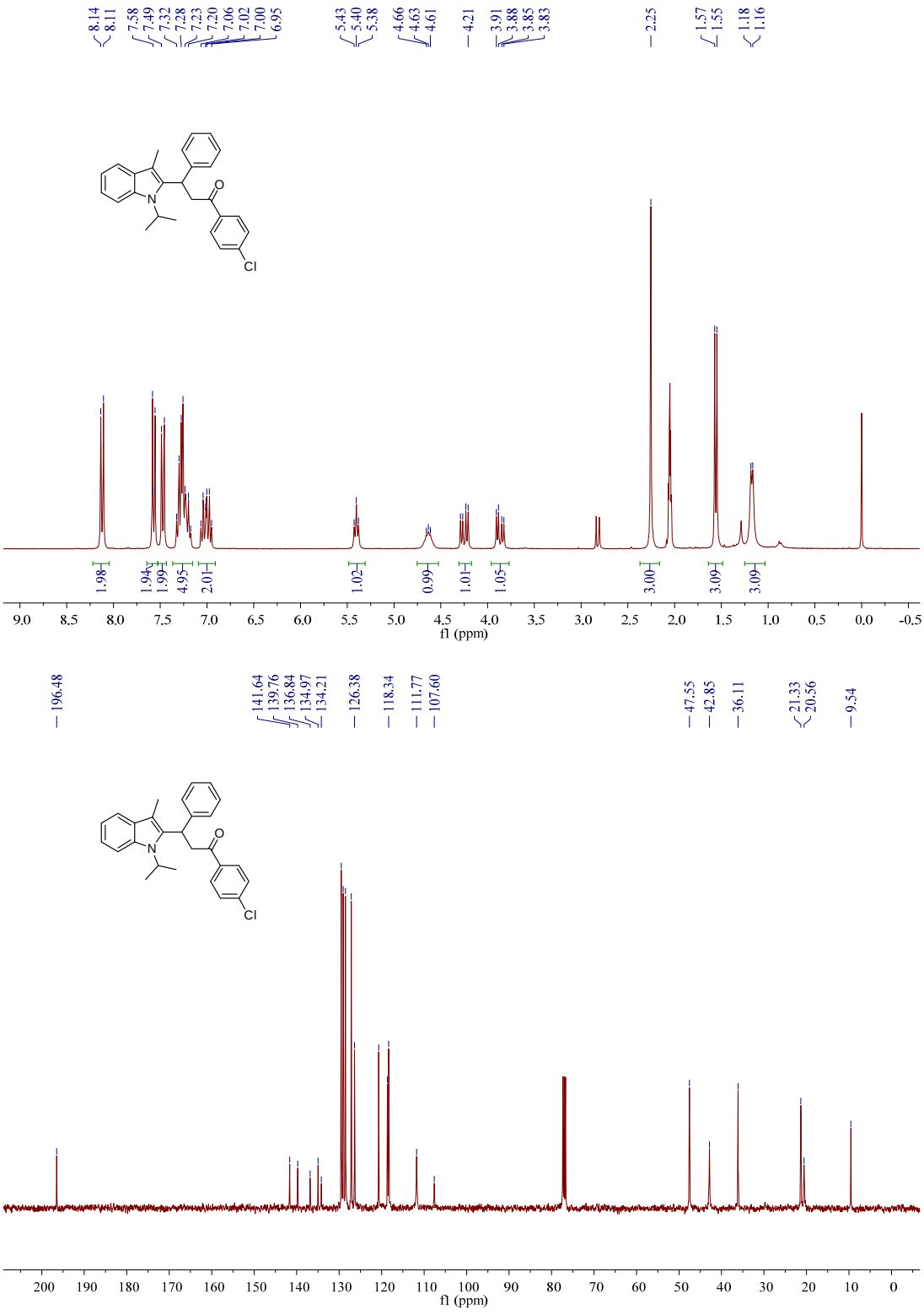


Figure S18. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3r**

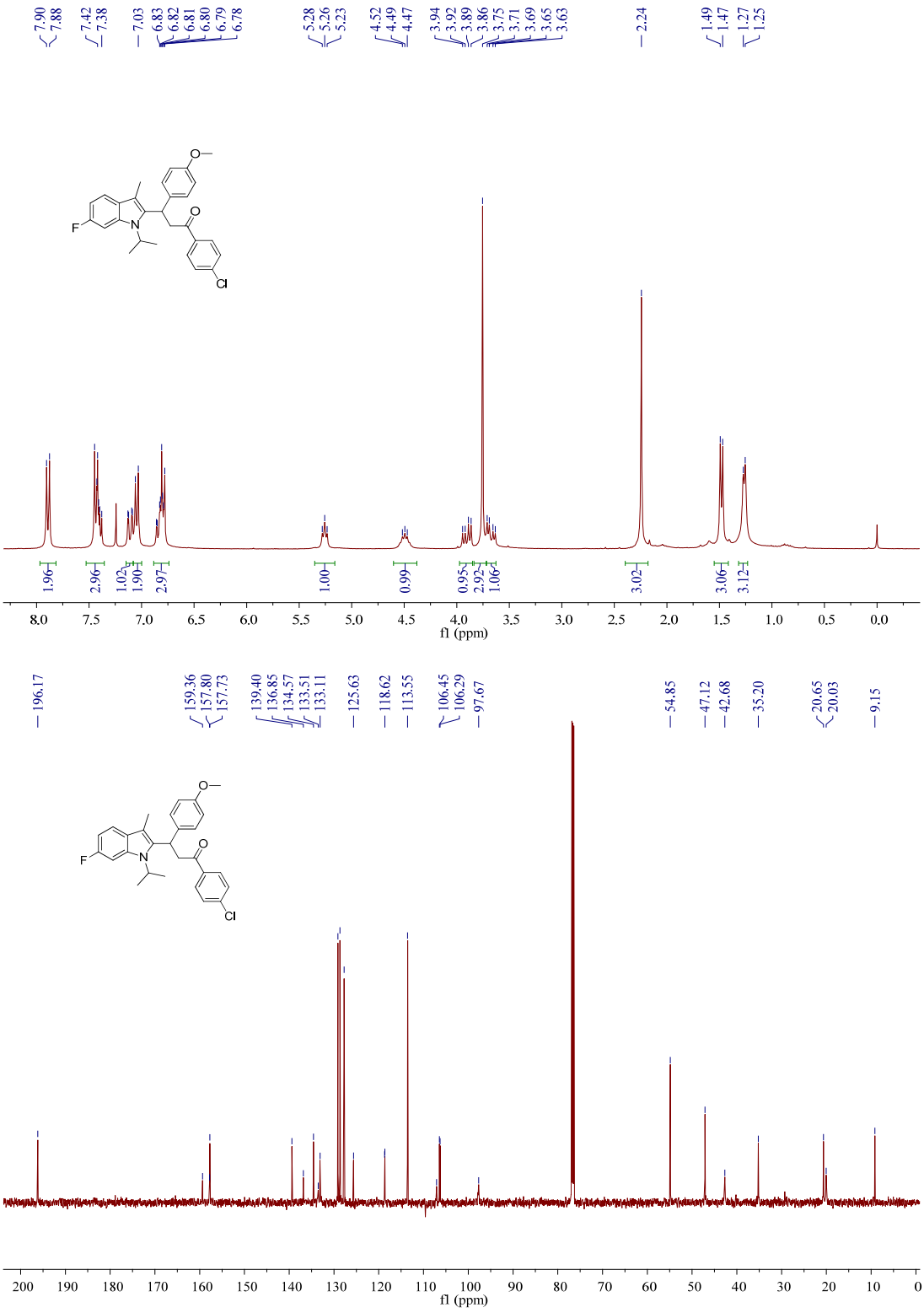


Figure S19. ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3s**

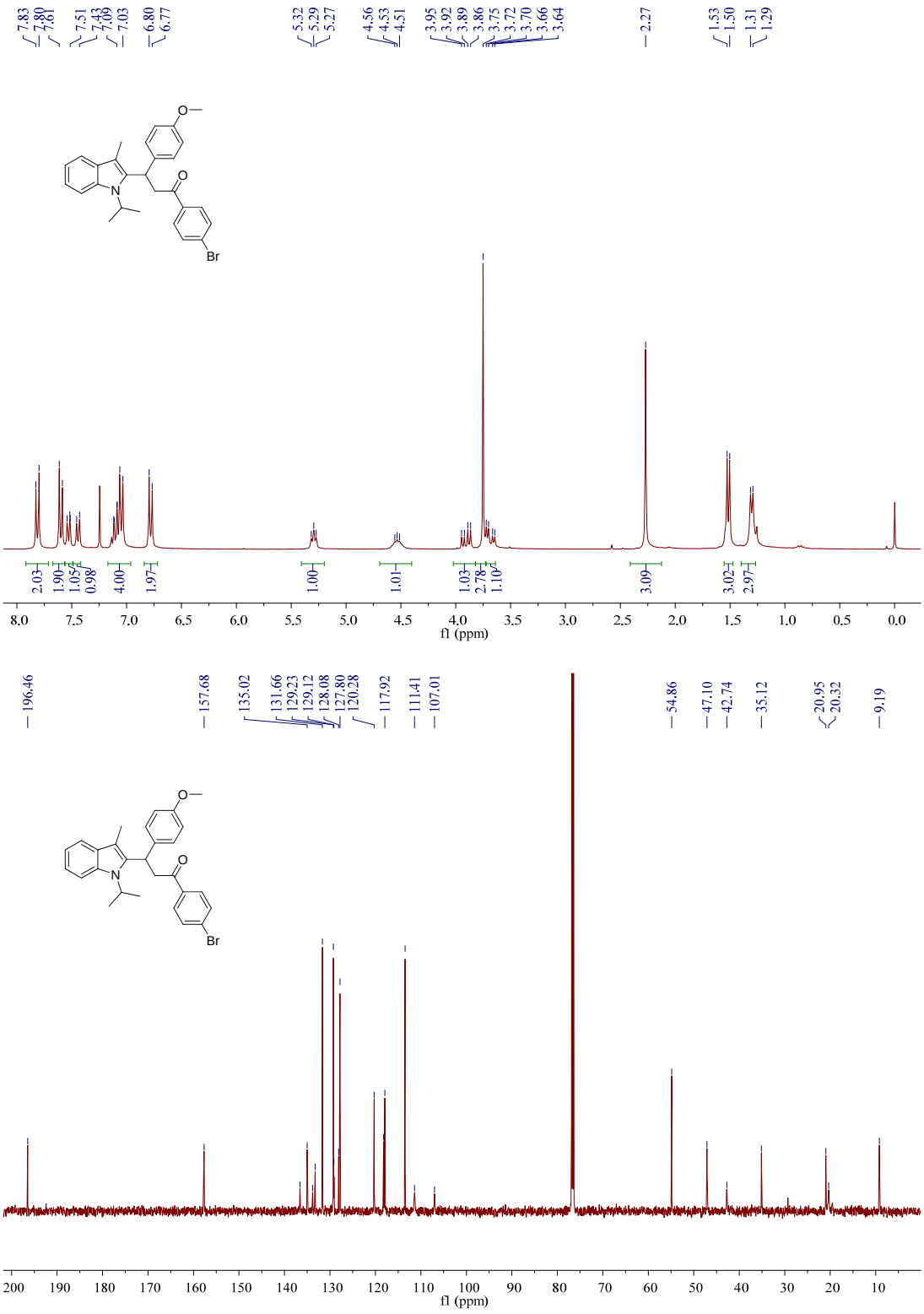


Figure S20 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3t**

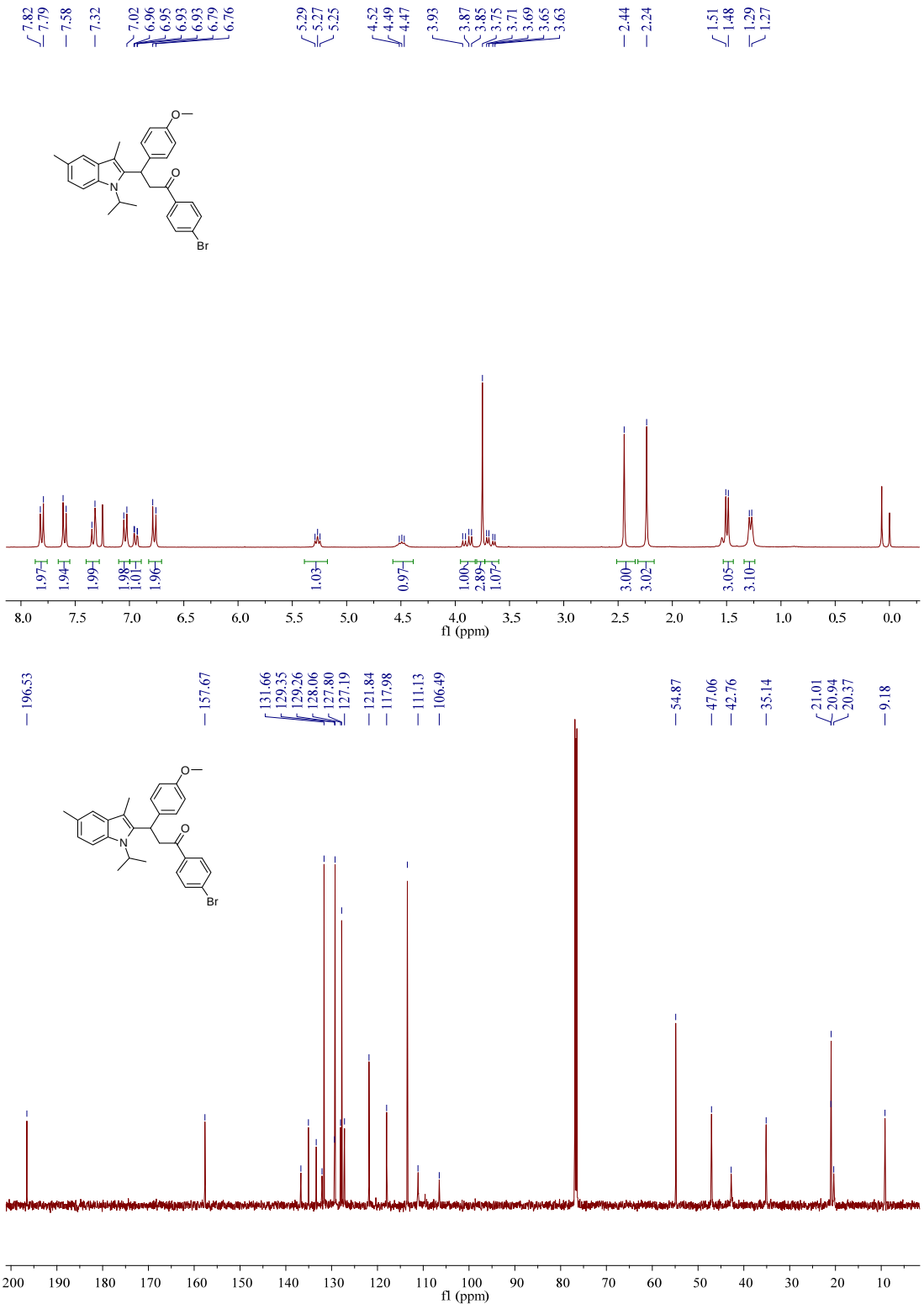


Figure S21 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3u**

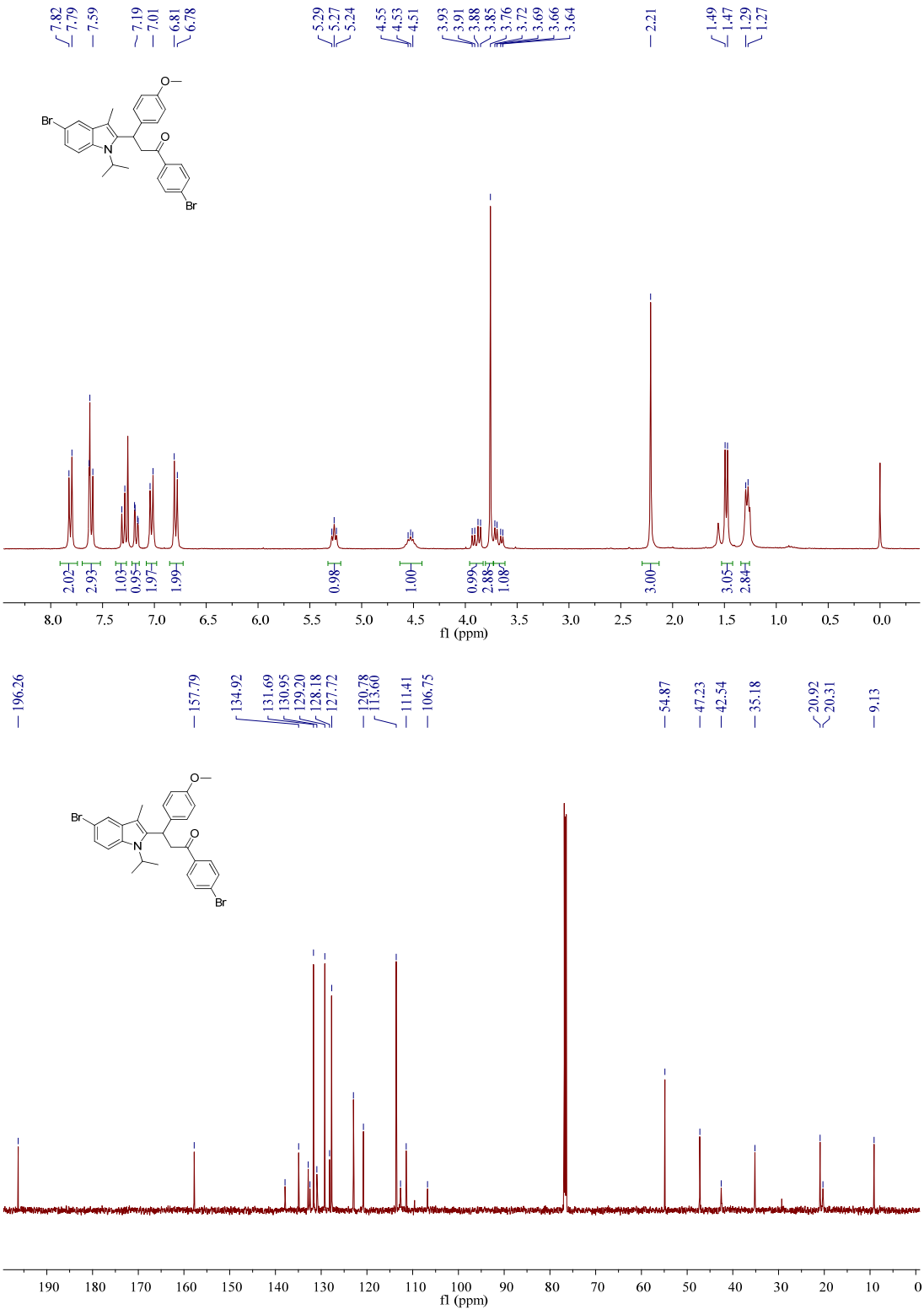


Figure S22 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3v**

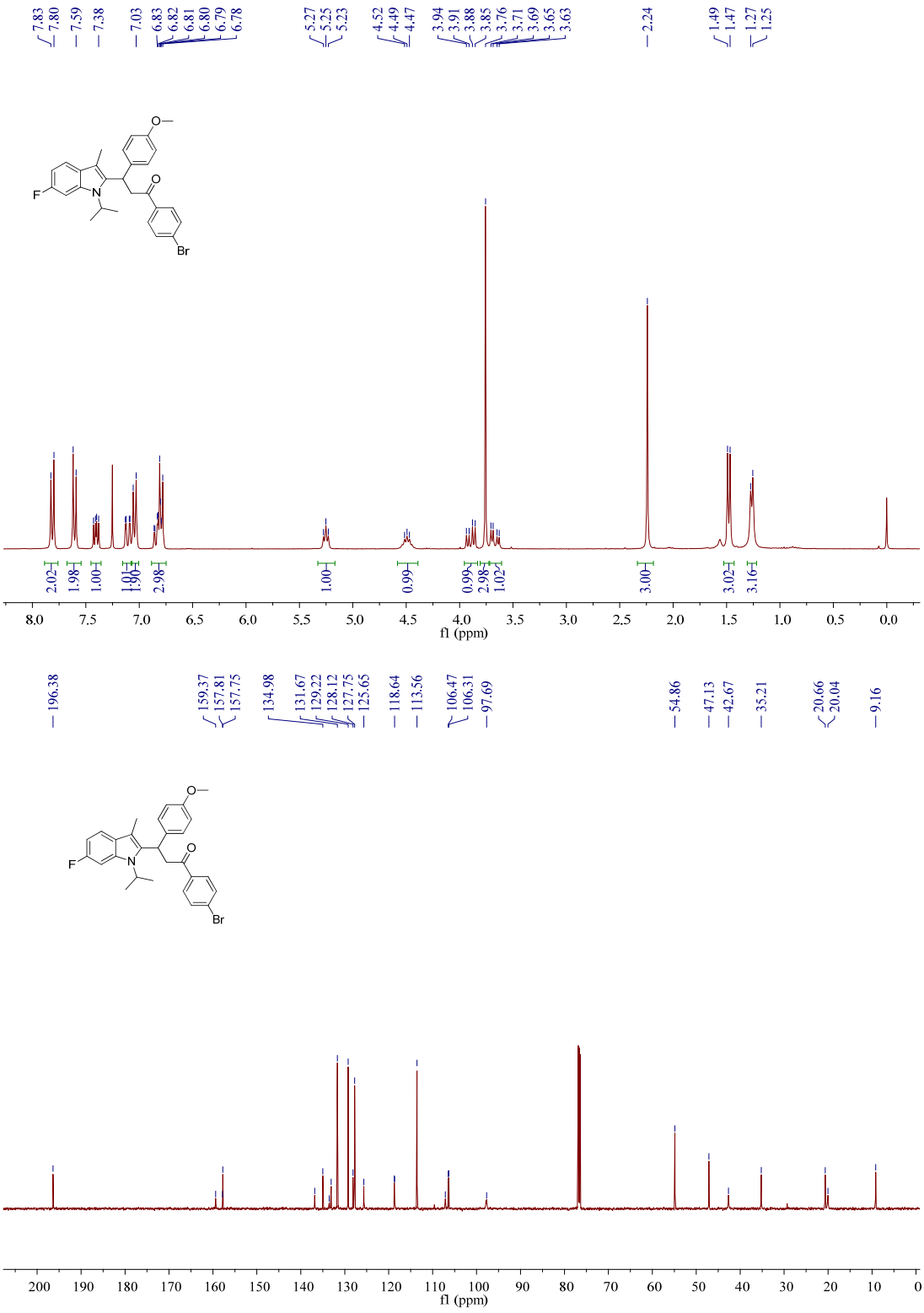


Figure S23 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3w**

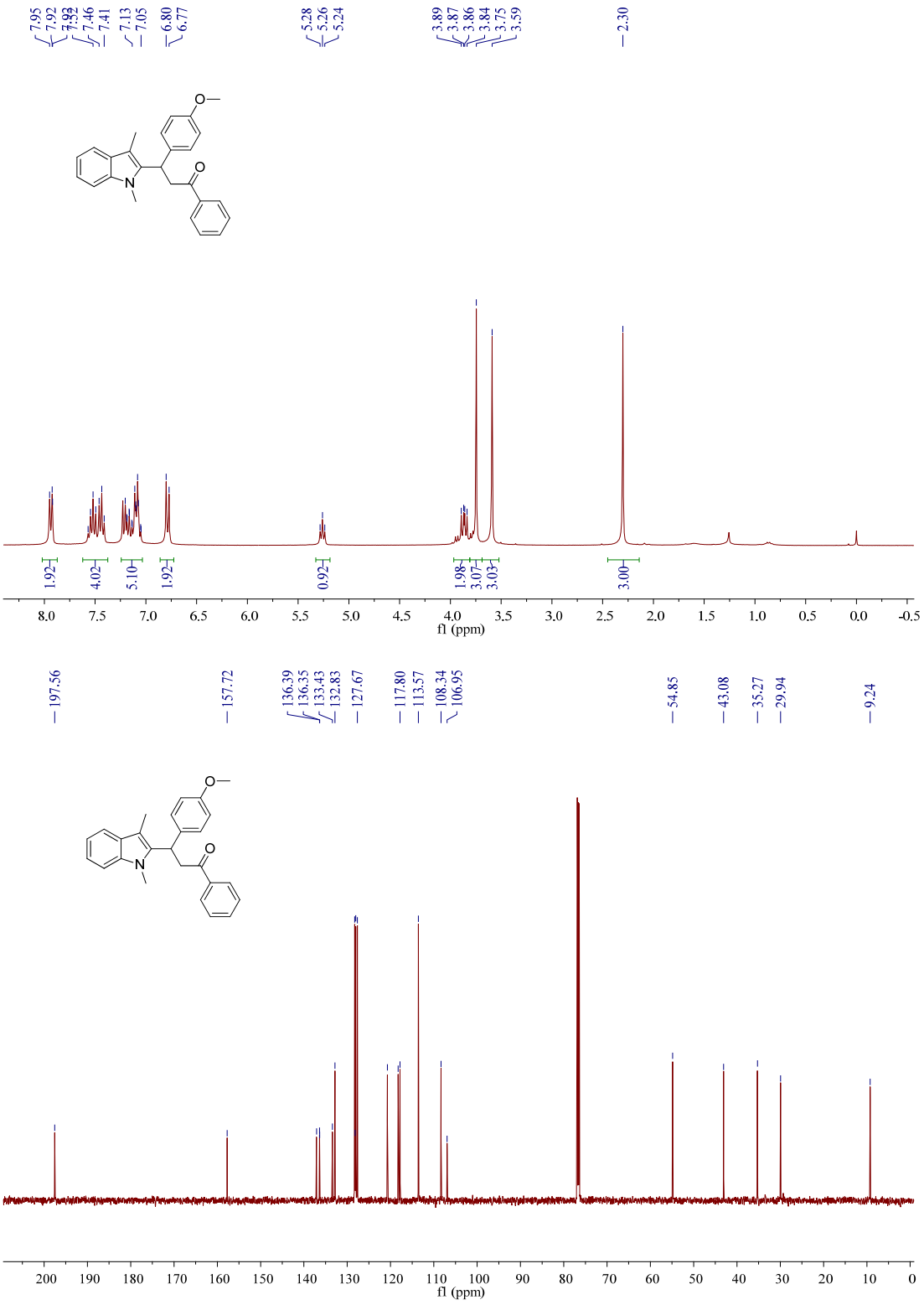


Figure S24 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3x**

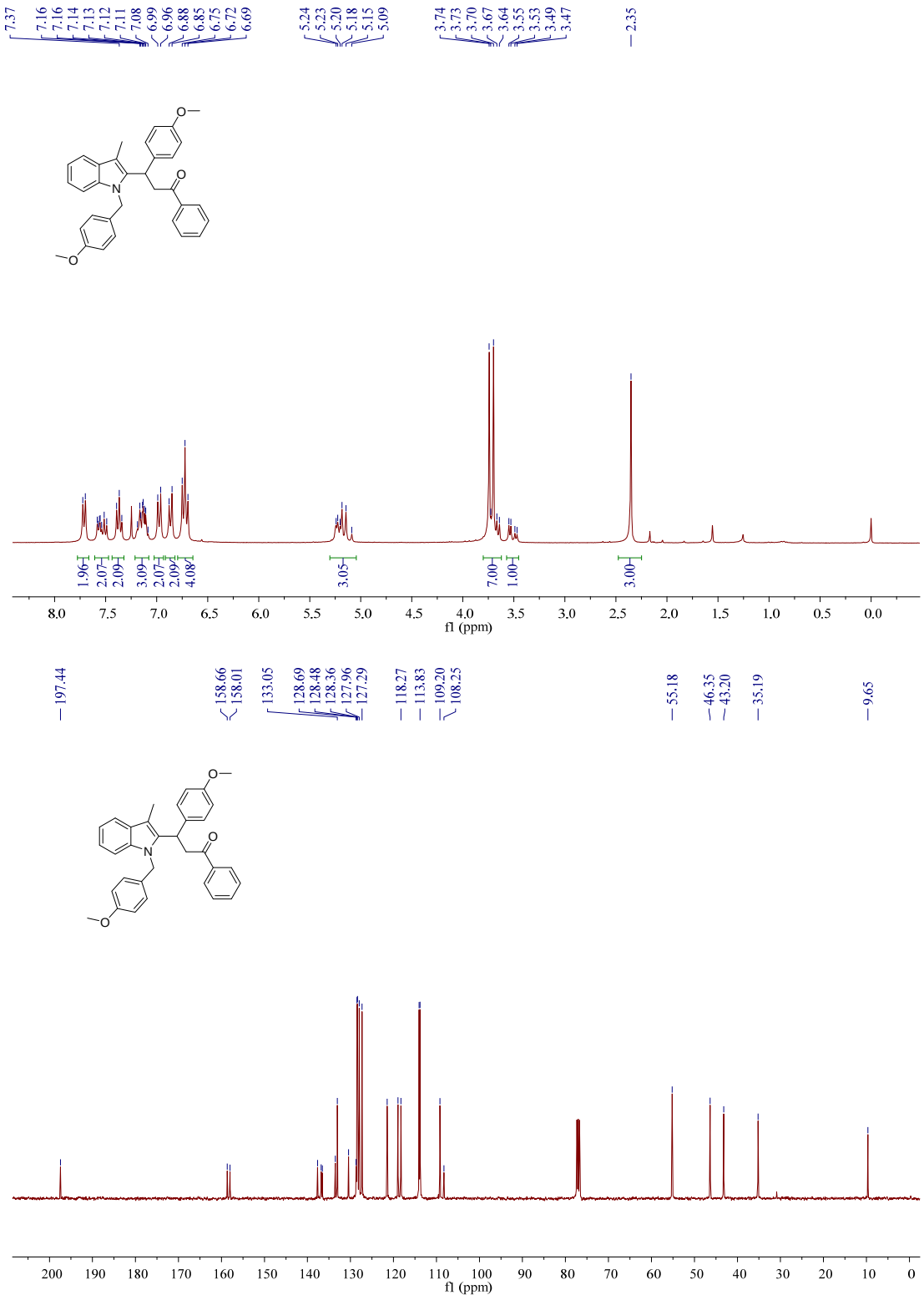


Figure S25 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3y**

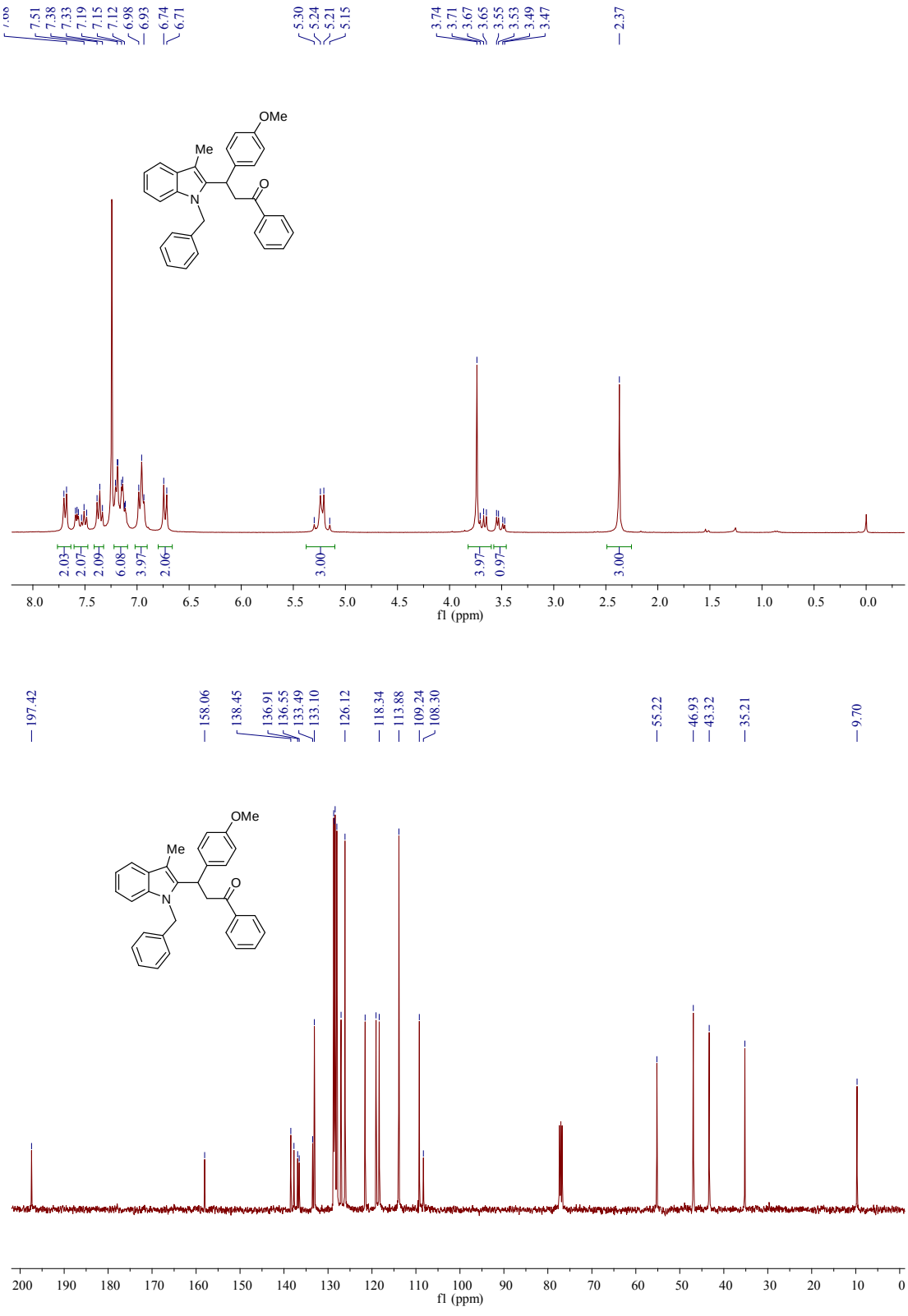


Figure S26 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **3z**

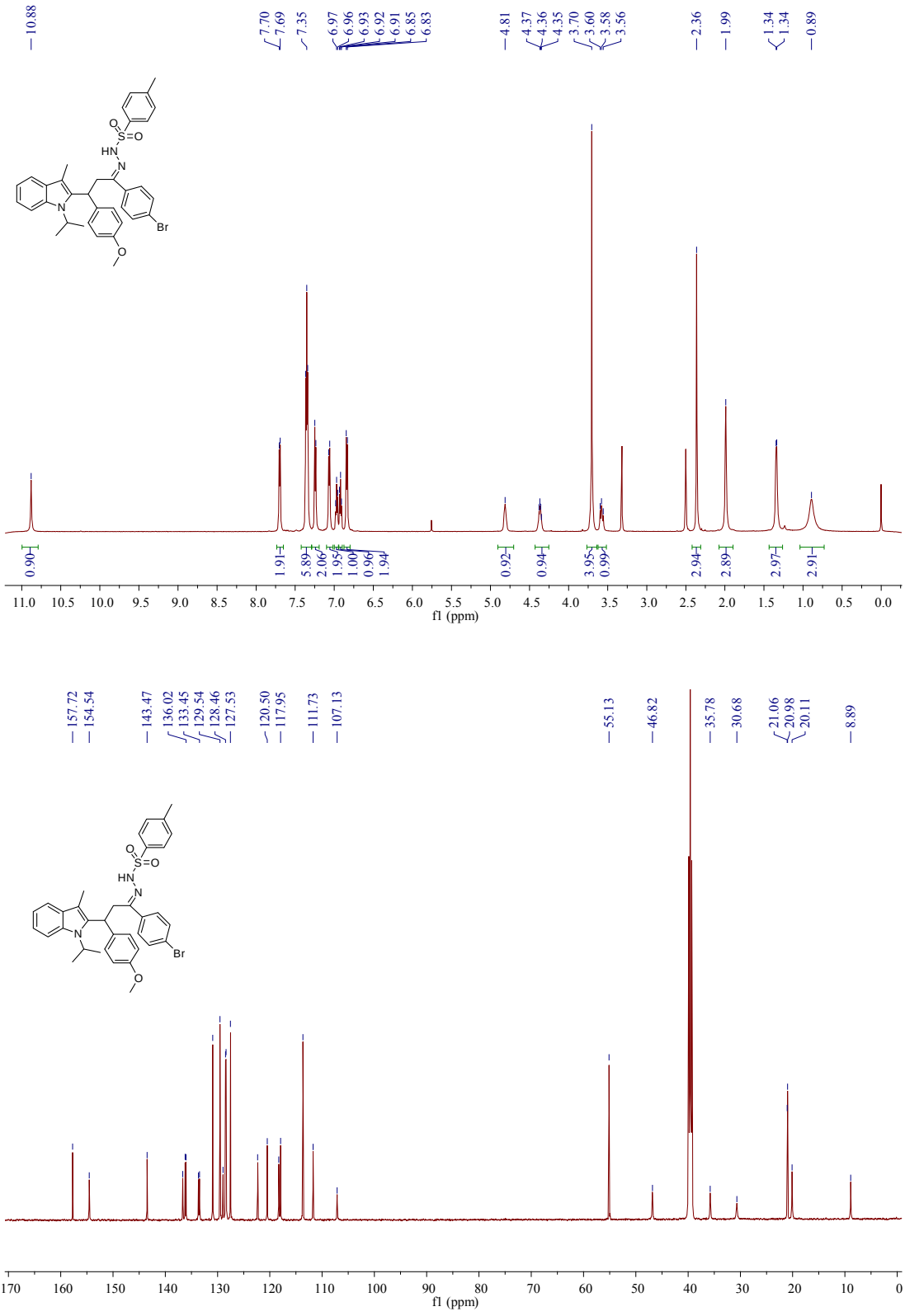


Figure S27 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **hydrozone derivative**

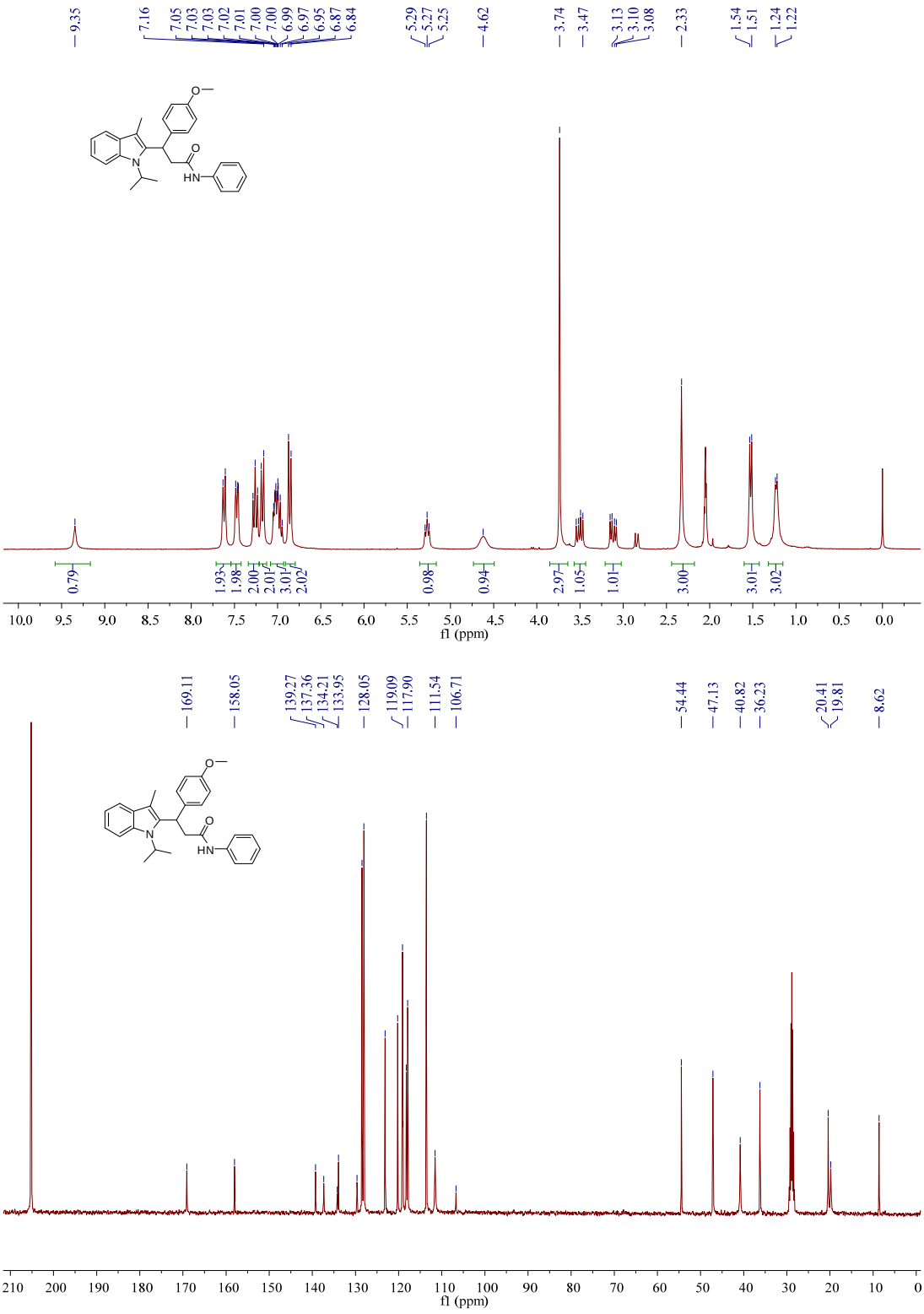


Figure S28 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **6a**

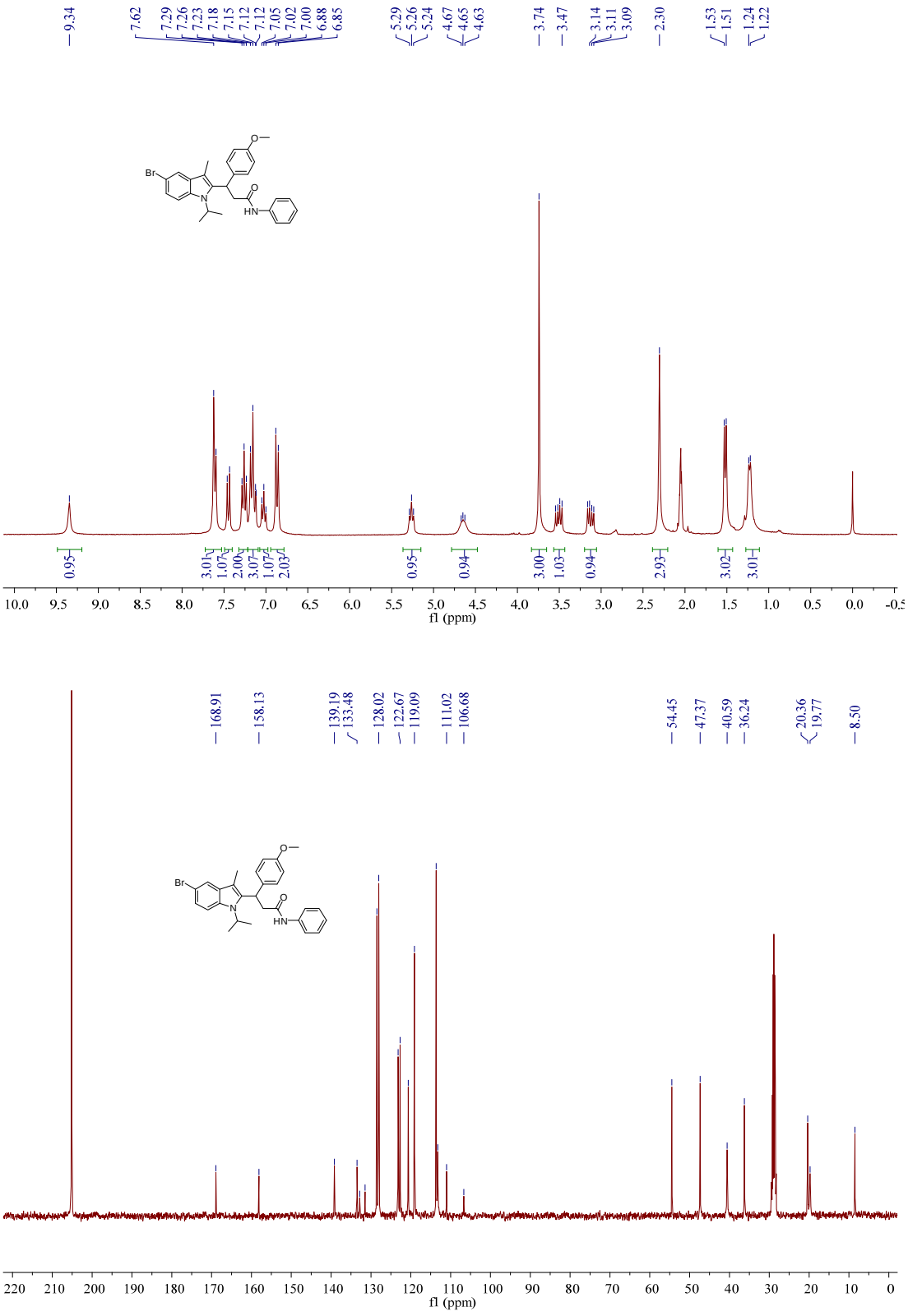
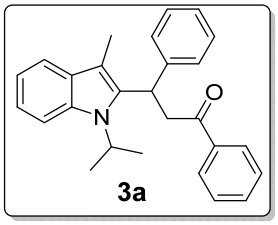
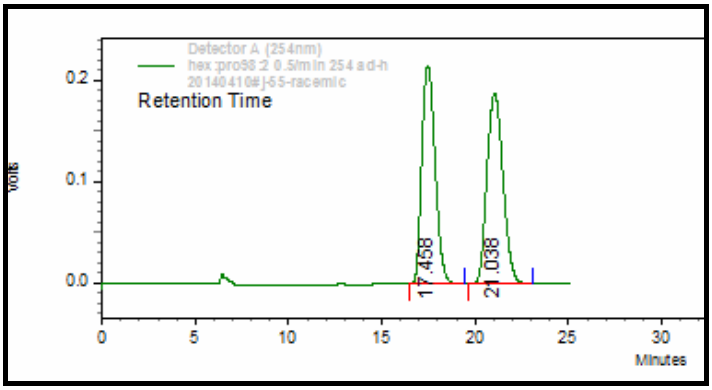


Figure S29 ^{1}H- (upper) and ^{13}C-NMR (bottom) of **6b**

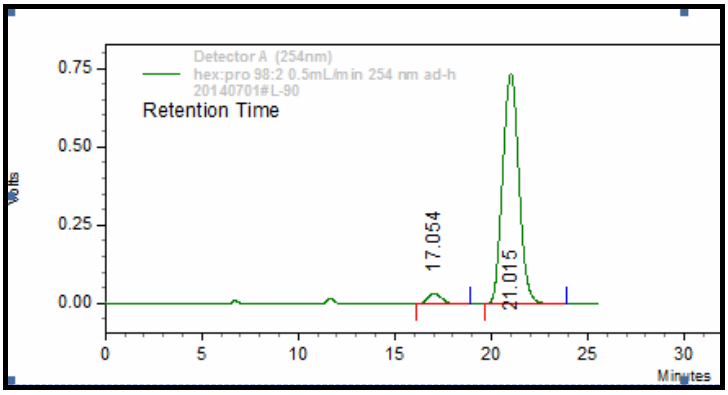
Copies of HPLC Charts





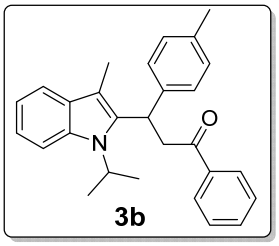
Detector A (254nm)

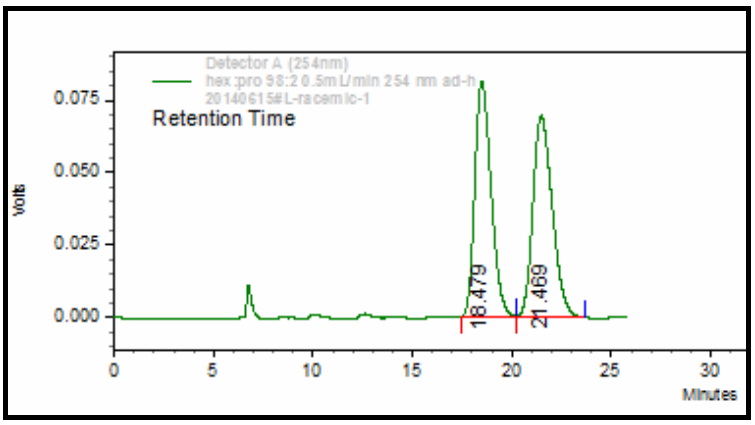
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.458	10707412	48.613	215143	53.361
2	21.038	11318487	51.387	188038	46.639
Total		22025899	100.000	403182	100.000



Detector A (254nm)

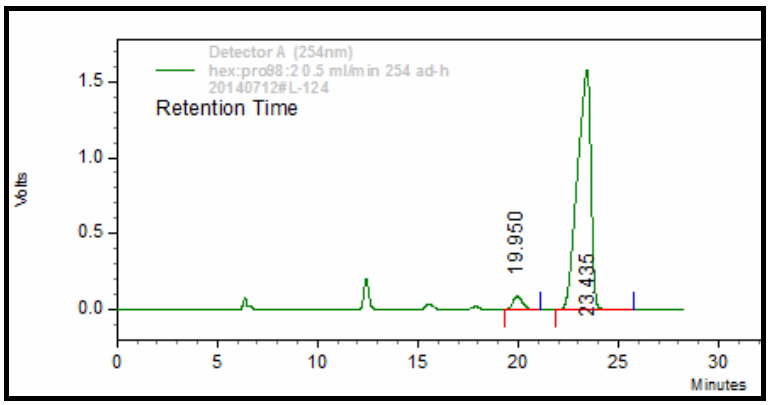
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.054	1600023	3.594	32772	4.264
2	21.015	42922645	96.406	735771	95.736
Total		44522668	100.000	768543	100.000





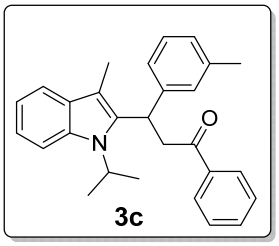
Detector A (254nm)

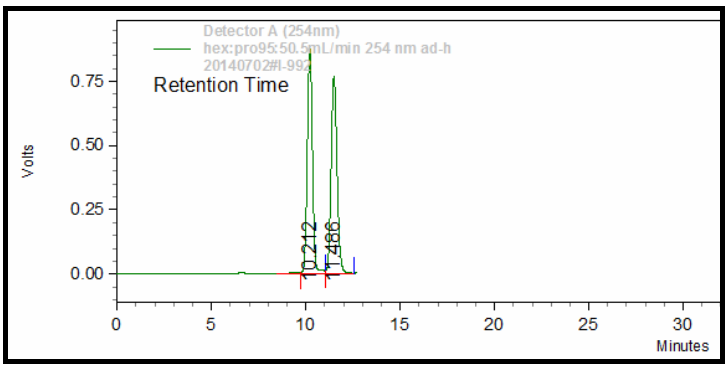
Pk #	Retention Time	Area	Area %	Height	Height %
1	18.479	4628577	49.494	81287	53.904
2	21.469	4723263	50.506	69511	46.096
Total		9351840	100.000	150798	100.000



Detector A (254nm)

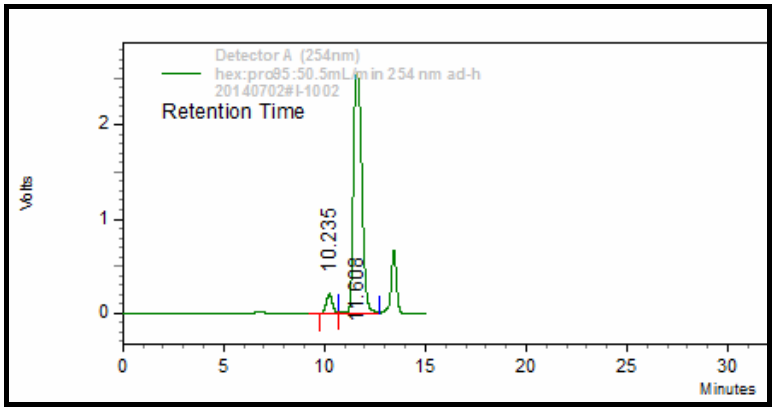
Pk #	Retention Time	Area	Area %	Height	Height %
1	19.950	2723218	3.566	85450	5.132
2	23.435	73634942	96.434	1579662	94.868
Total		76358161	100.000	1665112	100.000





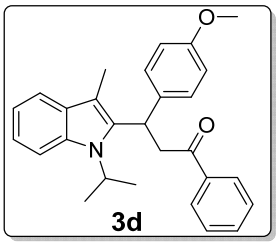
Detector A (254nm)

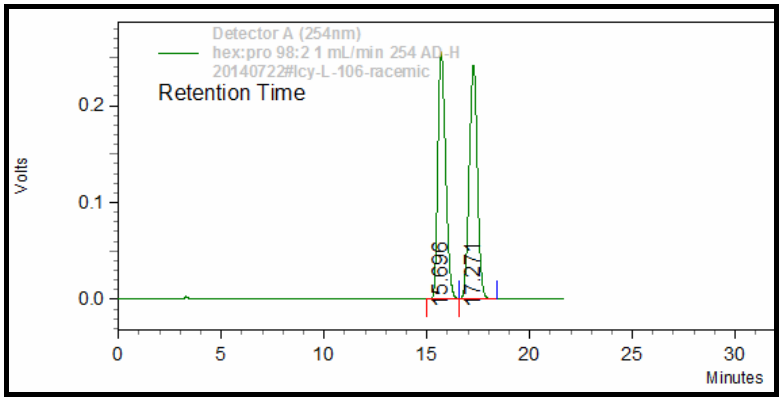
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.212	16954533	50.259	877157	53.382
2	11.486	16779752	49.741	766002	46.618
Total		33734285	100.000	1643160	100.000



Detector A (254nm)

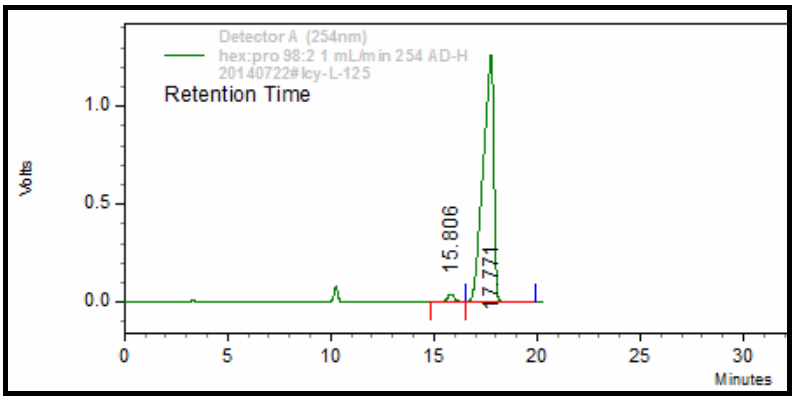
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.235	4365608	5.566	207594	7.514
2	11.608	74062870	94.434	2555174	92.486
Total		78428478	100.000	2762768	100.000





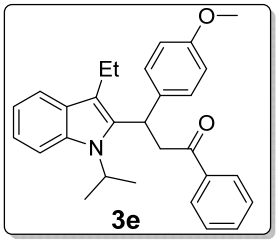
Detector A (254nm)

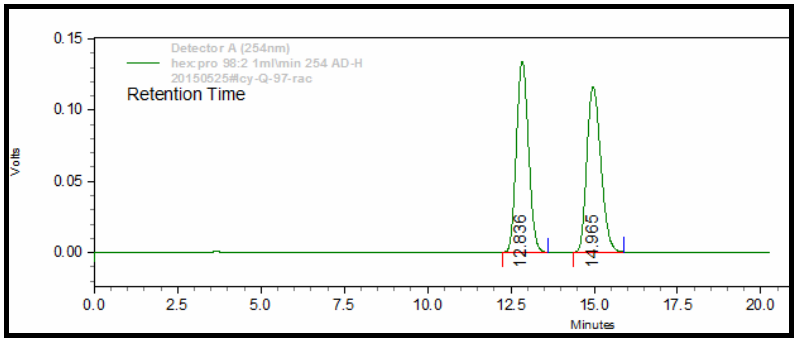
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.696	6711162	49.909	255114	51.341
2	17.271	6735530	50.091	241791	48.659
Total		13446692	100.000	496905	100.000



Detector A (254nm)

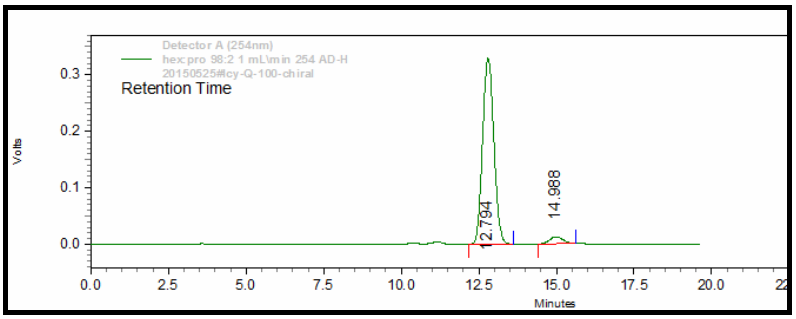
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.806	957316	2.069	37079	2.851
2	17.771	45322148	97.931	1263722	97.149
Total		46279464	100.000	1300802	100.000





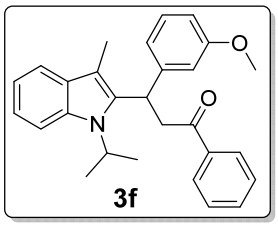
Detector A (254nm)

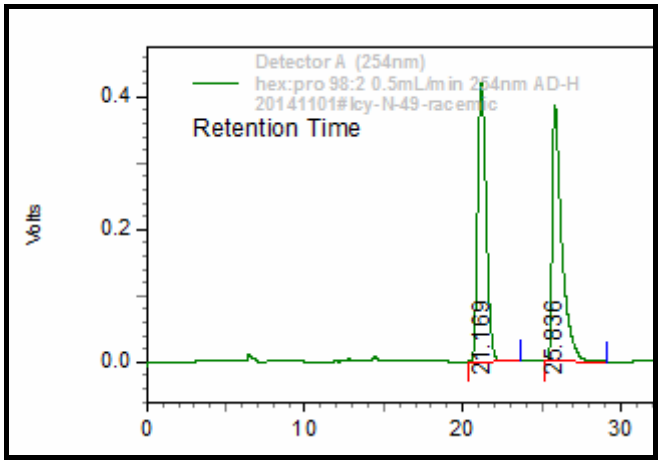
Pk #	Retention Time	Area	Area %	Height	Height %
1	12.836	3392088	49.953	133622	53.534
2	14.965	3398415	50.047	115982	46.466
Total		6790503	100.000	249604	100.000



Detector A (254nm)

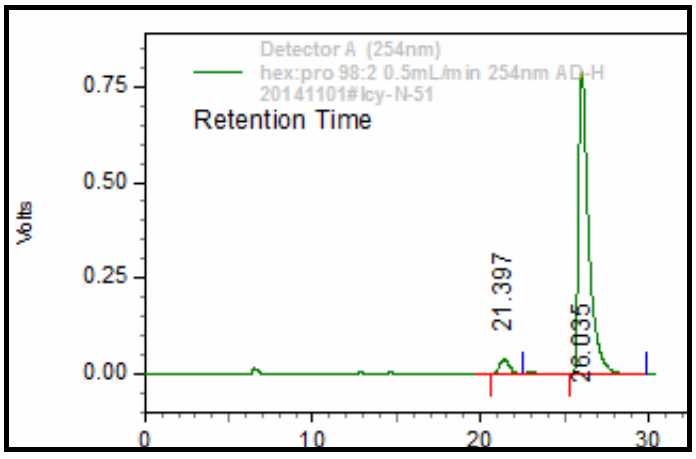
Pk #	Retention Time	Area	Area %	Height	Height %
1	12.794	8321061	95.776	328979	96.400
2	14.988	366960	4.224	12286	3.600
Total		8688021	100.000	341265	100.000





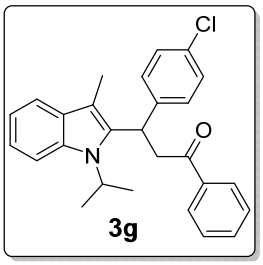
Detector A (254nm)

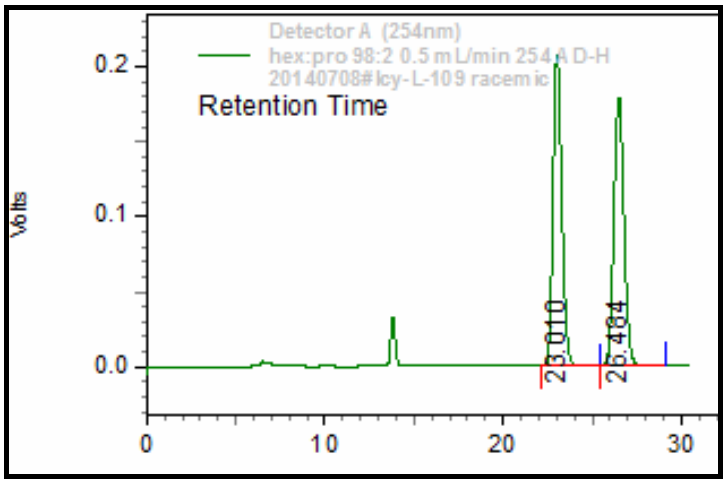
Pk #	Retention Time	Area	Area %	Height	Height %
1	21.169	15766690	49.401	420803	52.171
2	25.836	16148809	50.599	385776	47.829
Total		31915499	100.000	806579	100.000



Detector A (254nm)

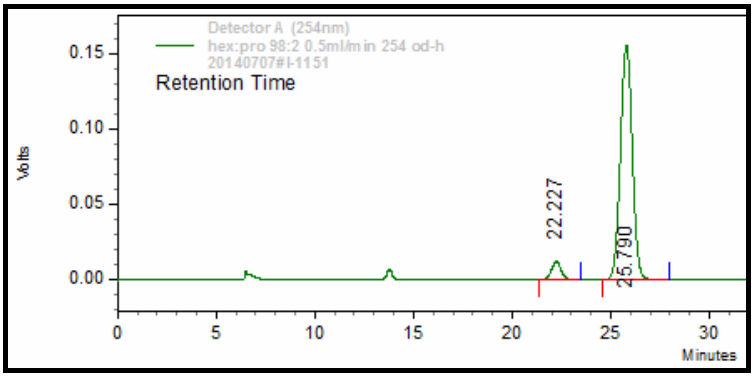
Pk #	Retention Time	Area	Area %	Height	Height %
1	21.397	1537869	4.405	37937	4.575
2	26.035	33377567	95.595	791326	95.425
Total		34915436	100.000	829263	100.000





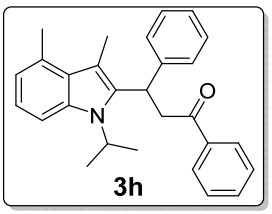
Detector A (254nm)

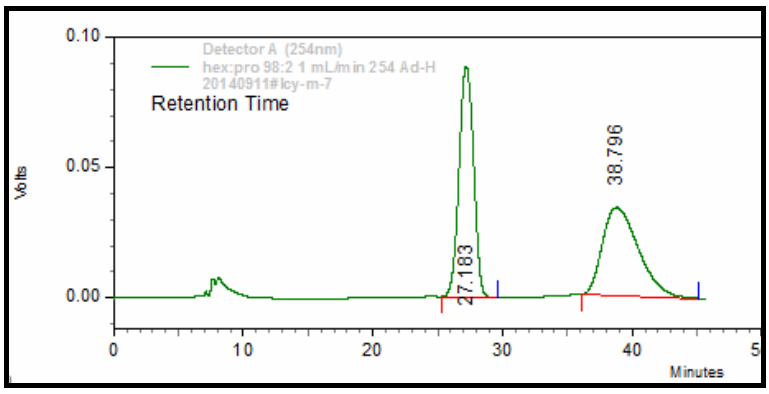
Pk #	Retention Time	Area	Area %	Height	Height %
1	23.010	7094547	49.991	207725	53.749
2	26.484	7097186	50.009	178744	46.251
Total		14191733	100.000	386469	100.000



Detector A (254nm)

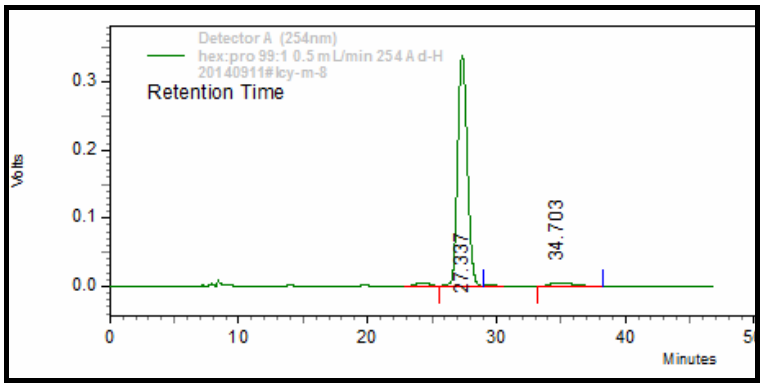
Pk #	Retention Time	Area	Area %	Height	Height %
1	22.227	405865	5.828	11868	7.062
2	25.790	6557639	94.172	156195	92.938
Total		6963504	100.000	168063	100.000





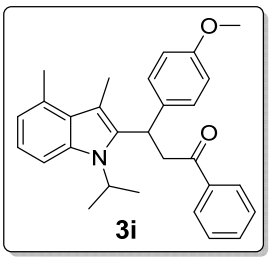
Detector A (254nm)

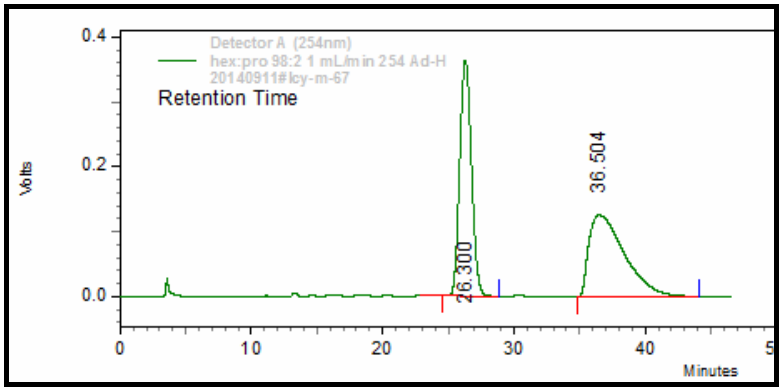
Pk #	Retention Time	Area	Area %	Height	Height %
1	27.183	6926994	51.580	88771	72.429
2	38.796	6502703	48.420	33793	27.571
Total		13429697	100.000	122564	100.000



Detector A (254nm)

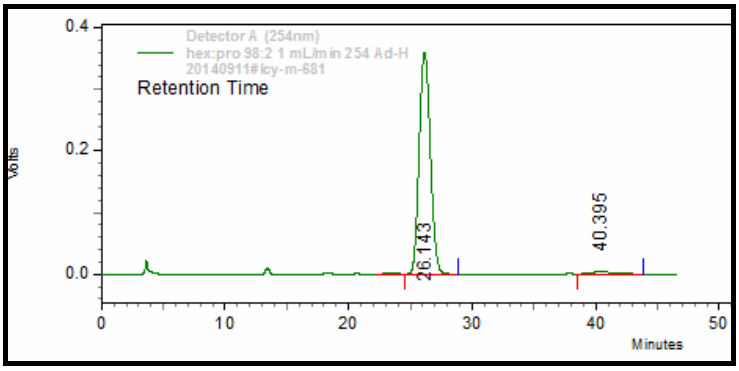
Pk #	Retention Time	Area	Area %	Height	Height %
1	27.337	17860145	96.134	340095	98.467
2	34.703	718173	3.866	5295	1.533
Total		18578318	100.000	345390	100.000





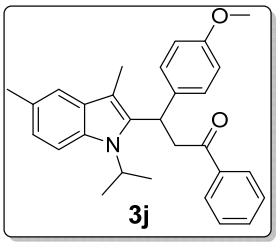
Detector A (254nm)

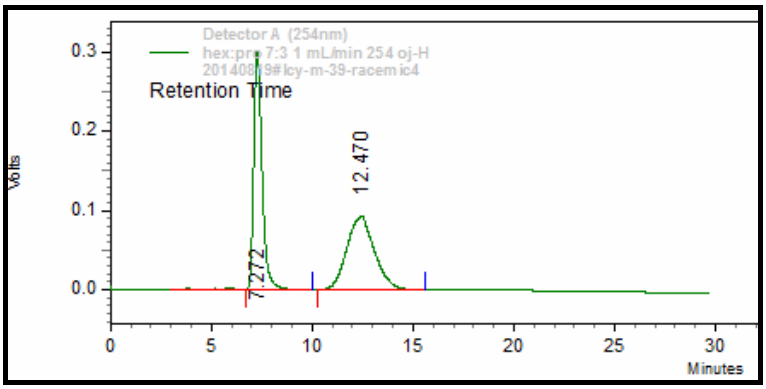
Pk #	Retention Time	Area	Area %	Height	Height %
1	26.300	22714346	49.227	363922	74.356
2	36.504	23427373	50.773	125511	25.644
Total		46141718	100.000	489433	100.000



Detector A (254nm)

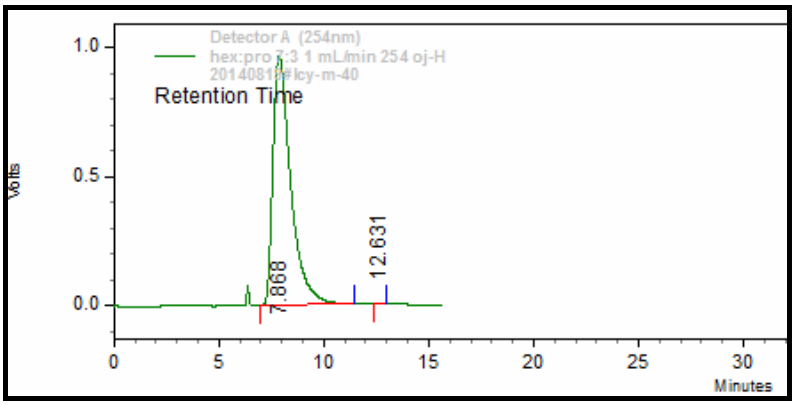
Pk #	Retention Time	Area	Area %	Height	Height %
1	26.143	22681073	98.091	359982	99.093
2	40.395	441358	1.909	3293	0.907
Total		23122431	100.000	363275	100.000





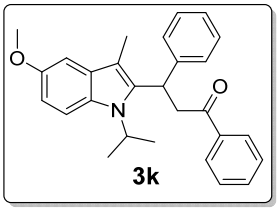
Detector A (254nm)

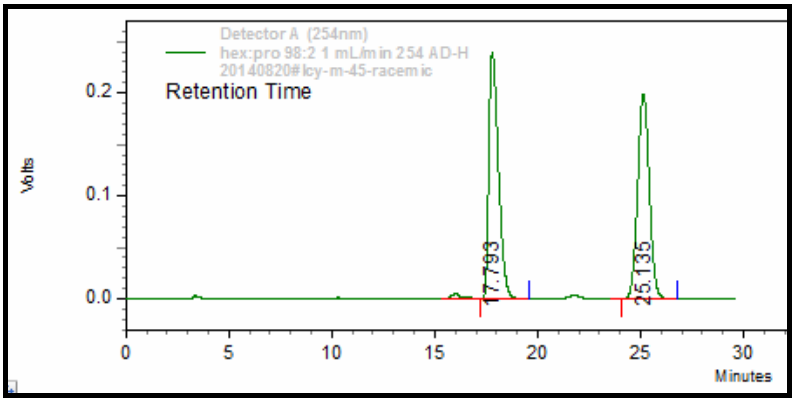
Pk #	Retention Time	Area	Area %	Height	Height %
1	7.272	8754580	49.804	300519	76.470
2	12.470	8823627	50.196	92469	23.530
Total		17578207	100.000	392987	100.000



Detector A (254nm)

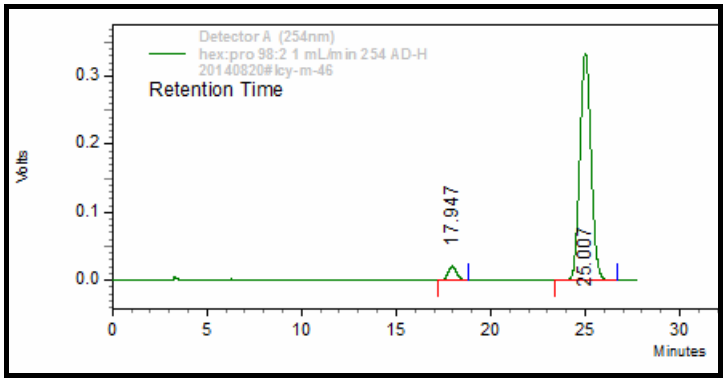
Pk #	Retention Time	Area	Area %	Height	Height %
1	7.868	57447131	99.939	966141	99.748
2	12.631	35128	0.061	2439	0.252
Total		57482259	100.000	968581	100.000





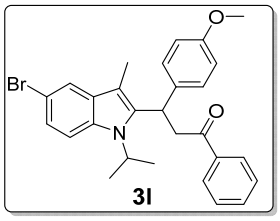
Detector A (254nm)

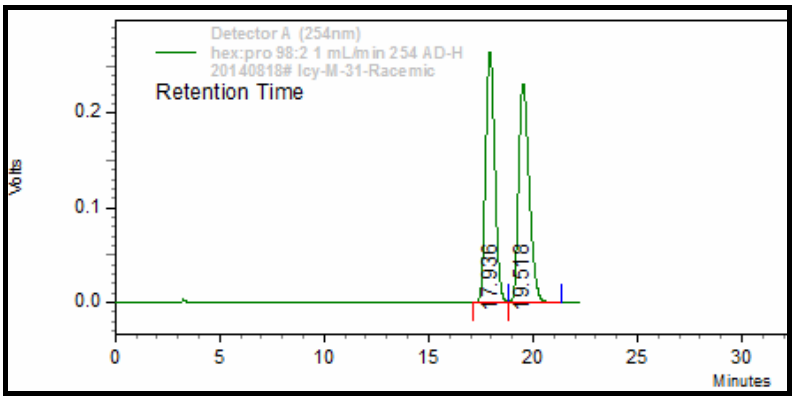
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.793	7802282	49.946	239883	54.616
2	25.135	7819168	50.054	199337	45.384
Total		15621450	100.000	439219	100.000



Detector A (254nm)

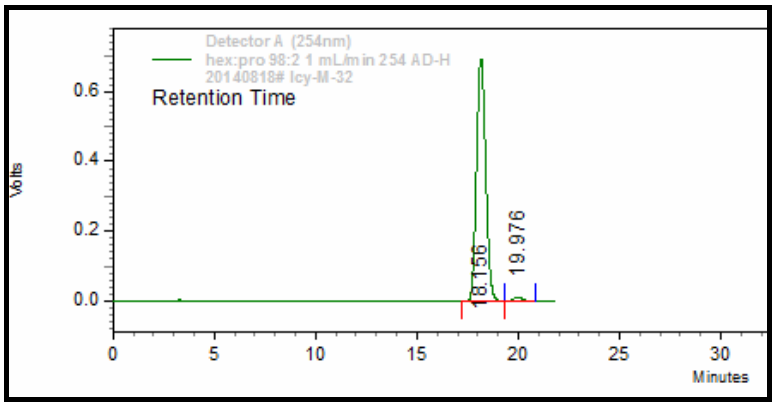
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.947	630132	4.382	20197	5.697
2	25.007	13748808	95.618	334297	94.303
Total		14378939	100.000	354493	100.000





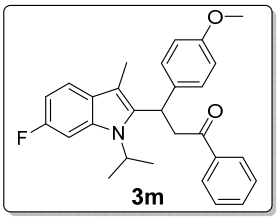
Detector A (254nm)

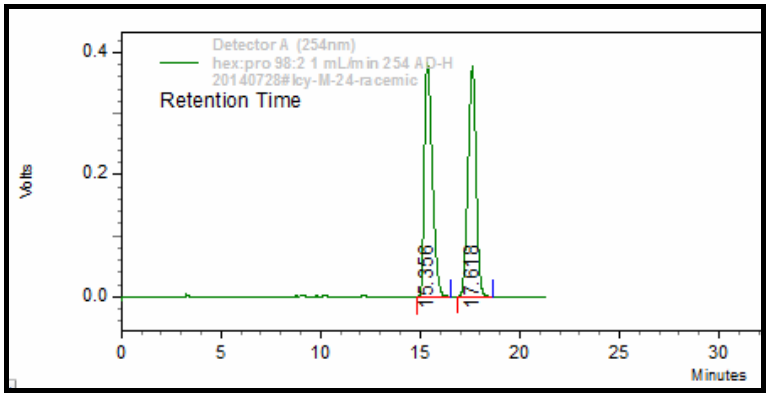
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.936	8131773	49.913	265078	53.479
2	19.518	8160004	50.087	230587	46.521
Total		16291777	100.000	495664	100.000



Detector A (254nm)

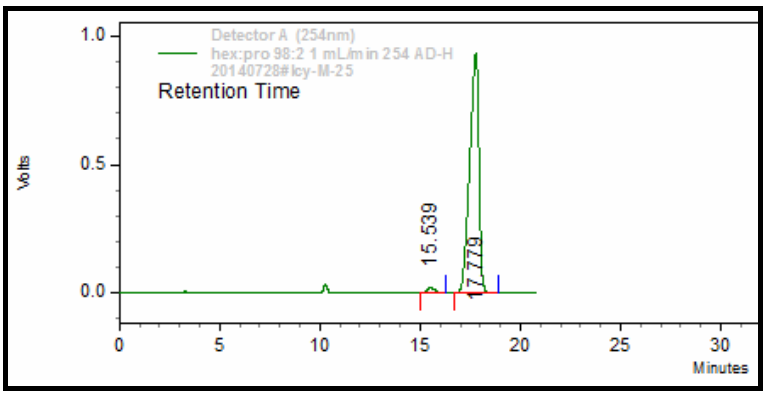
Pk #	Retention Time	Area	Area %	Height	Height %
1	18.156	21953457	98.372	694501	98.502
2	19.976	363272	1.628	10560	1.498
Total		22316729	100.000	705061	100.000





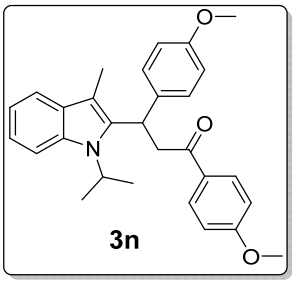
Detector A (254nm)

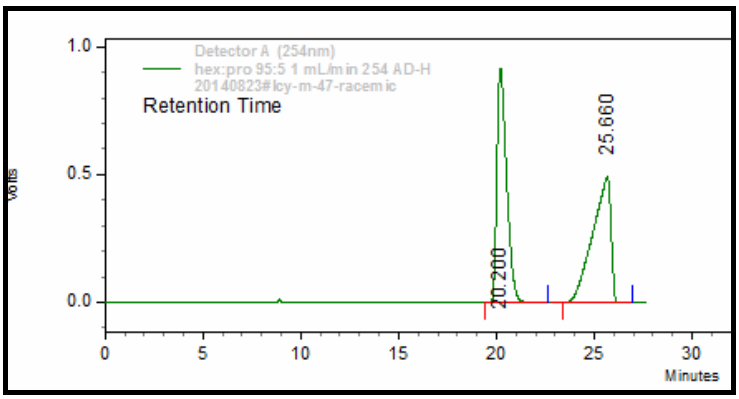
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.356	10630845	49.872	383888	50.487
2	17.618	10685495	50.128	376481	49.513
Total		21316340	100.000	760368	100.000



Detector A (254nm)

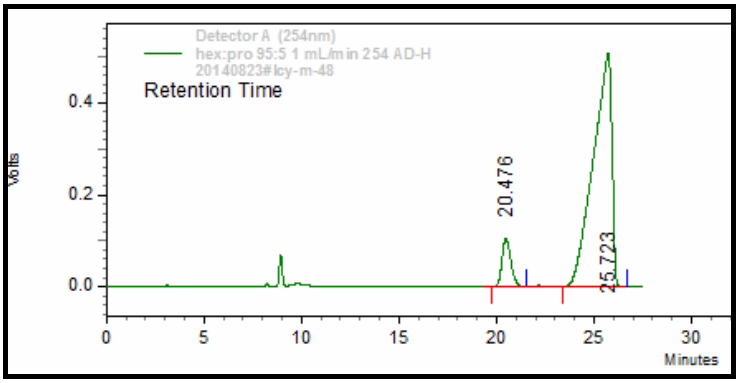
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.539	515938	1.699	19703	2.061
2	17.779	29855696	98.301	936395	97.939
Total		30371633	100.000	956098	100.000





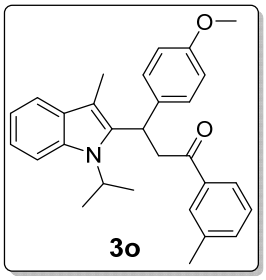
Detector A (254nm)

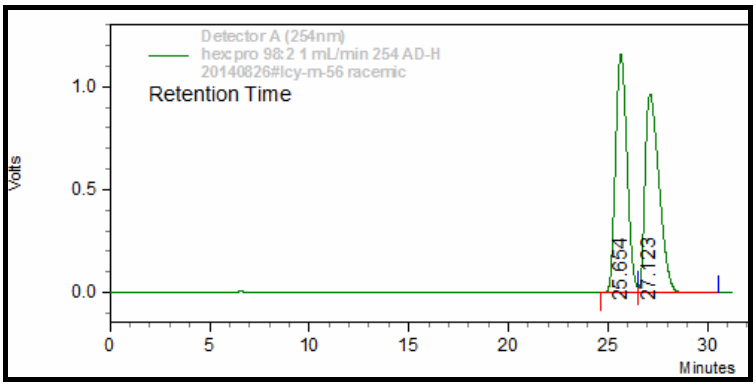
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.200	31576803	49.756	915829	65.116
2	25.660	31887005	50.244	490637	34.884
Total		63463807	100.000	1406466	100.000



Detector A (254nm)

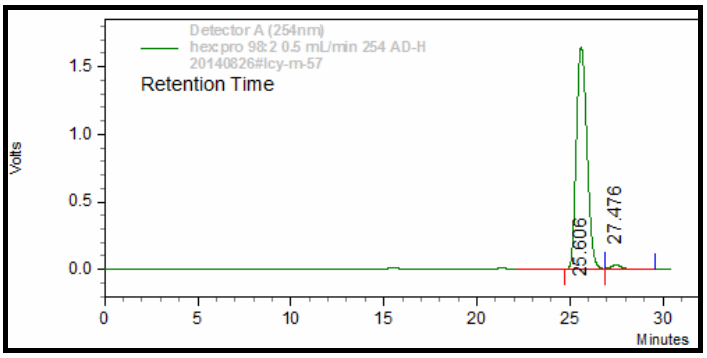
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.476	3309272	8.923	103884	16.953
2	25.723	33777252	91.077	508909	83.047
Total		37086524	100.000	612793	100.000





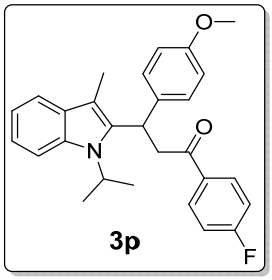
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	25.654	46574637	49.482	1160681	54.578
2	27.123	47549807	50.518	965951	45.422
Total		94124444	100.000	2126632	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	25.606	65276355	97.965	1646008	98.069
2	27.476	1356231	2.035	32409	1.931
Total		66632587	100.000	1678417	100.000



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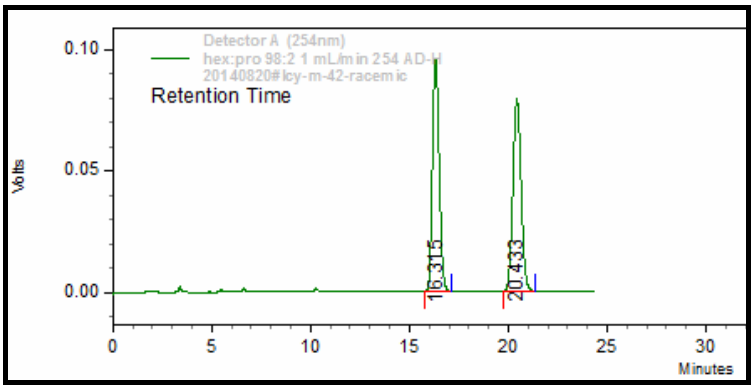
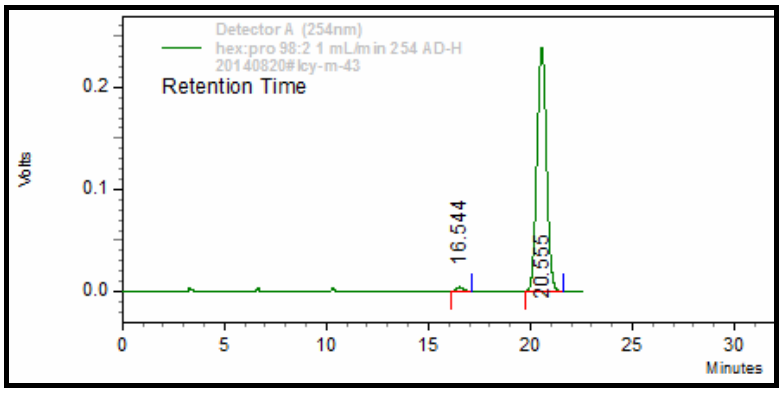


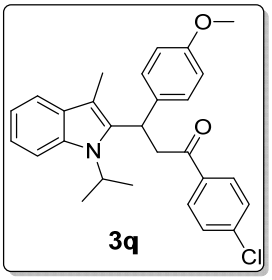
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.315	2285602	49.659	96390	54.861
2	20.433	2316989	50.341	79309	45.139
Total		4602591	100.000	175699	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	16.544	107508	1.361	4222	1.736
2	20.555	7793395	98.639	239041	98.264
Total		7900903	100.000	243263	100.000



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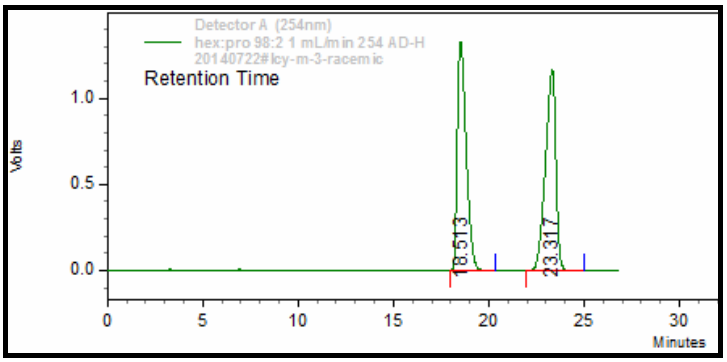
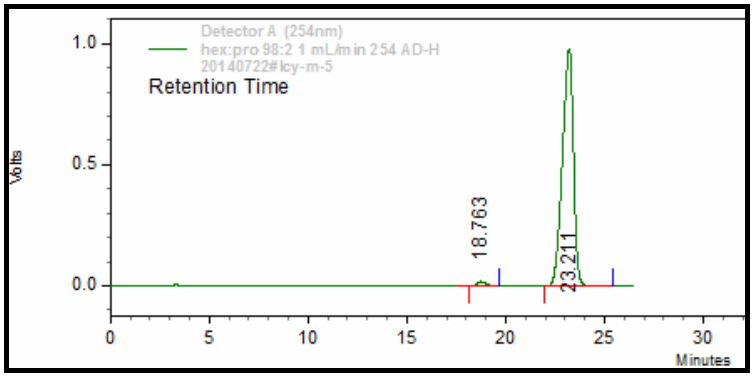


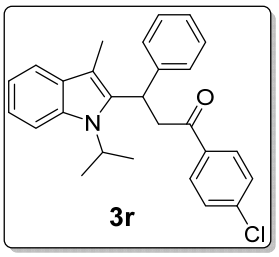
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.513	42814534	49.265	1328825	53.204
2	23.317	44091310	50.735	1168775	46.796
Total		86905844	100.000	2497599	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.763	541035	1.410	17857	1.790
2	23.211	37841152	98.590	979960	98.210
Total		38382187	100.000	997817	100.000



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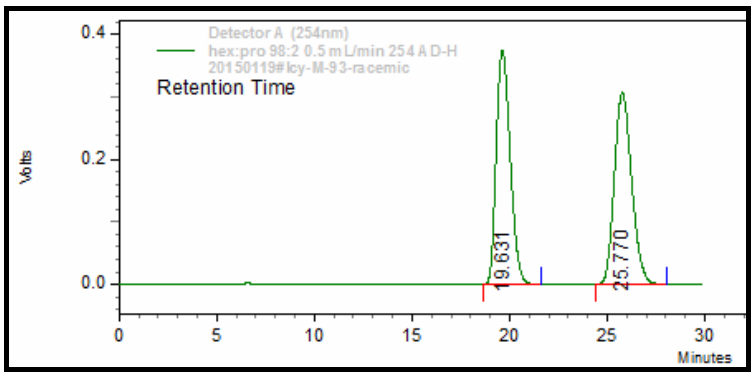
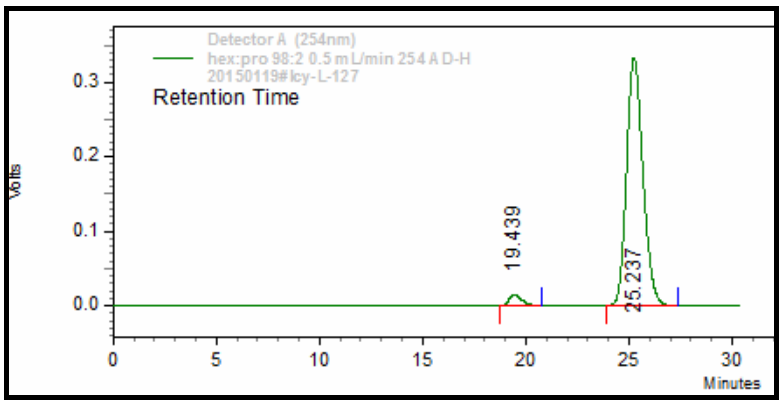


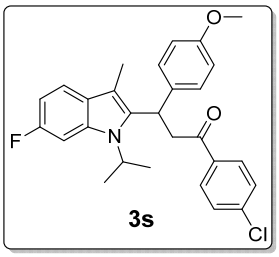
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.631	18598671	49.584	375022	55.028
2	25.770	18911112	50.416	306486	44.972
Total		37509783	100.000	681508	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.439	624389	3.296	14820	4.260
2	25.237	18322229	96.704	333076	95.740
Total		18946618	100.000	347896	100.000



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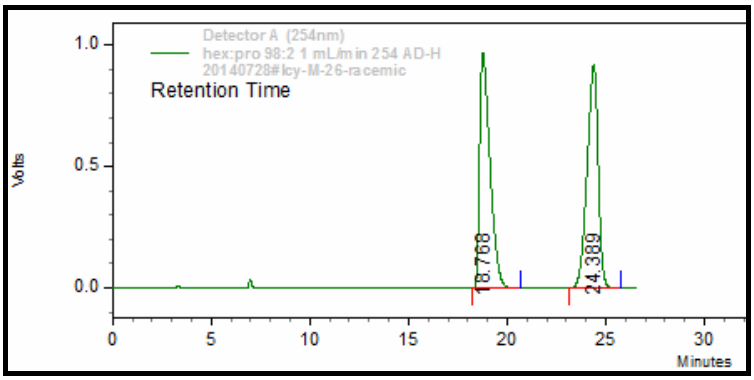
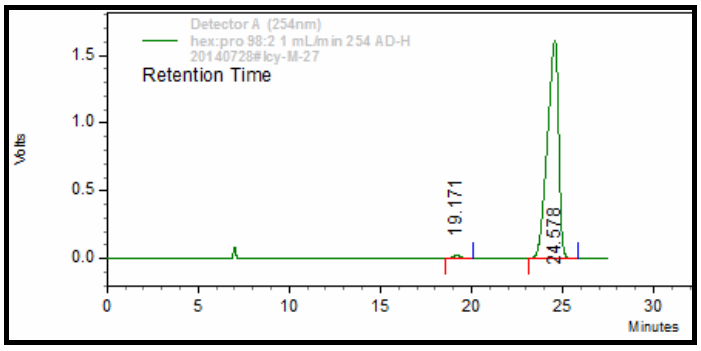


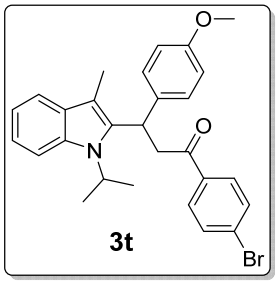
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.768	35503714	49.699	970486	51.340
2	24.389	35933136	50.301	919842	48.660
Total		71436850	100.000	1890328	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.171	677795	0.971	21932	1.340
2	24.578	69161113	99.029	1614520	98.660
Total		69838908	100.000	1636452	100.000



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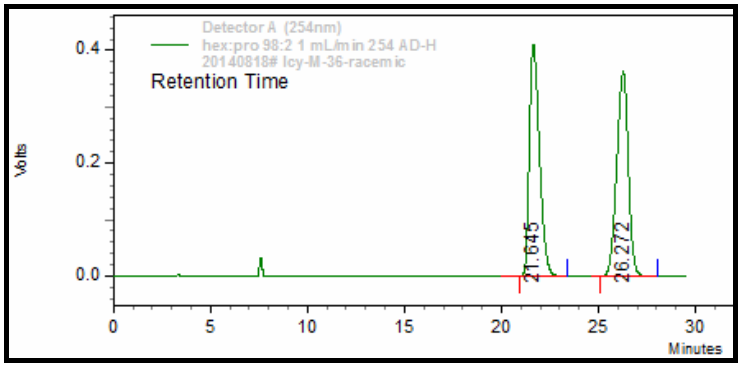
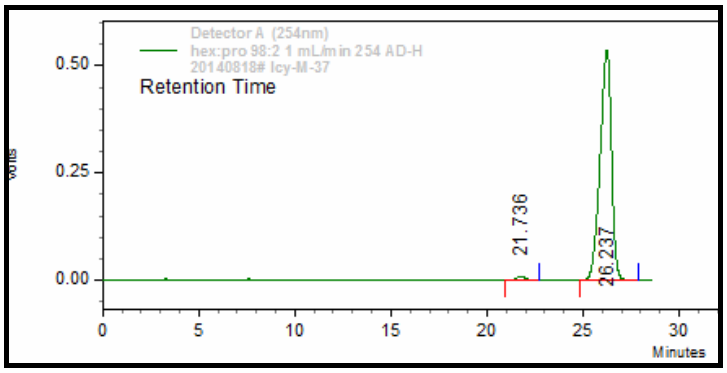


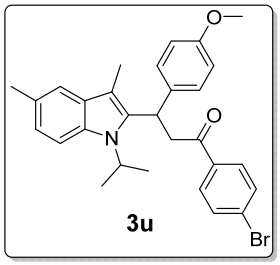
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	21.645	14867837	49.818	411271	53.172
2	26.272	14976594	50.182	362196	46.828
Total		29844432	100.000	773467	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	21.736	278949	1.246	8286	1.519
2	26.237	22114380	98.754	537280	98.481
Total		22393329	100.000	545566	100.000



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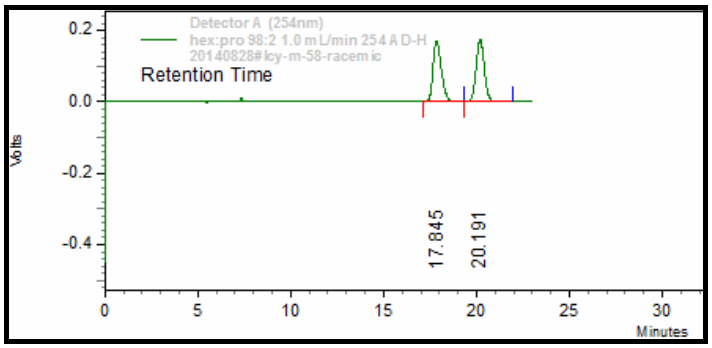
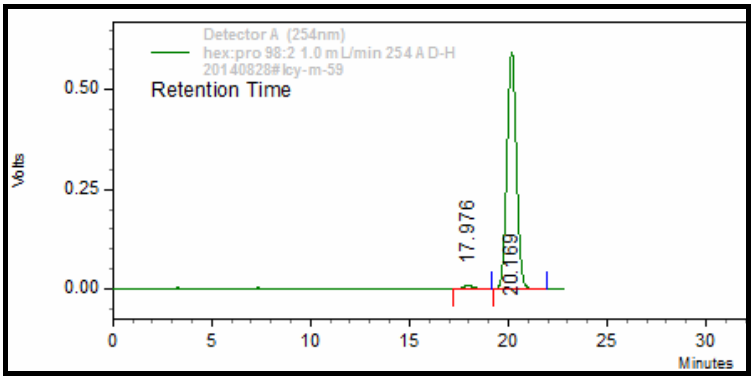


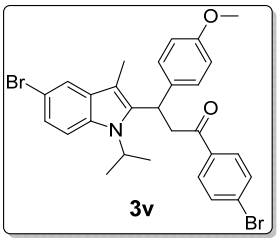
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.845	5338750	49.676	170580	49.191
2	20.191	5408427	50.324	176191	50.809
Total		10747176	100.000	346771	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.976	305520	1.520	9129	1.510
2	20.169	19792889	98.480	595435	98.490
Total		20098409	100.000	604564	100.000



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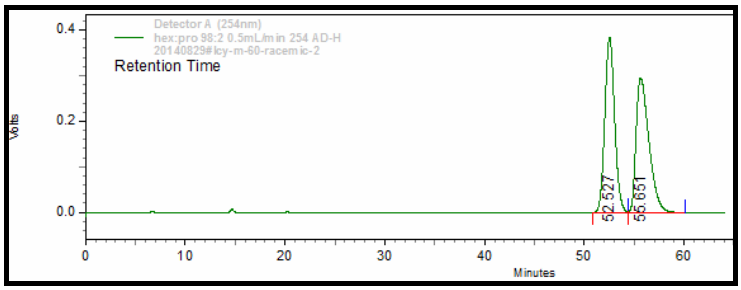
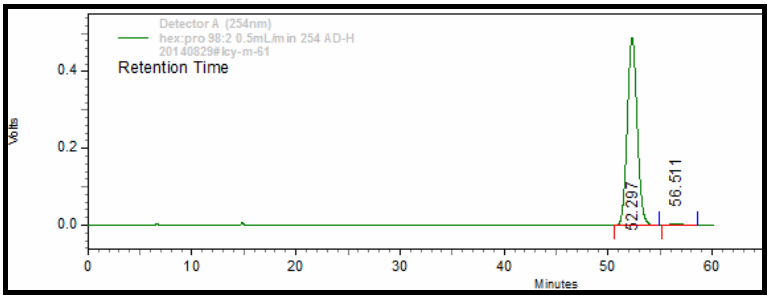


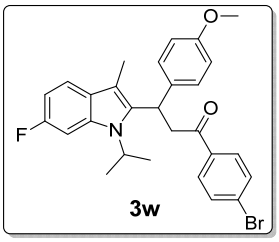
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	52.527	26209301	49.765	384541	56.605
2	55.651	26456372	50.235	294801	43.395
Total		52665673	100.000	679342	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	52.297	32160137	99.063	488928	99.346
2	56.511	304354	0.937	3220	0.654
Total		32464491	100.000	492148	100.000



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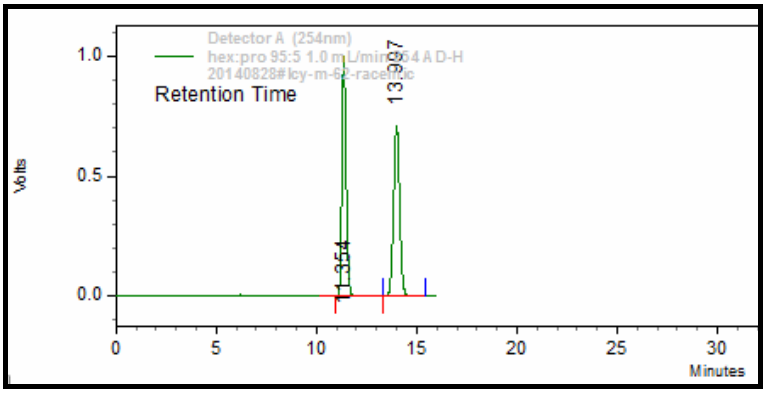
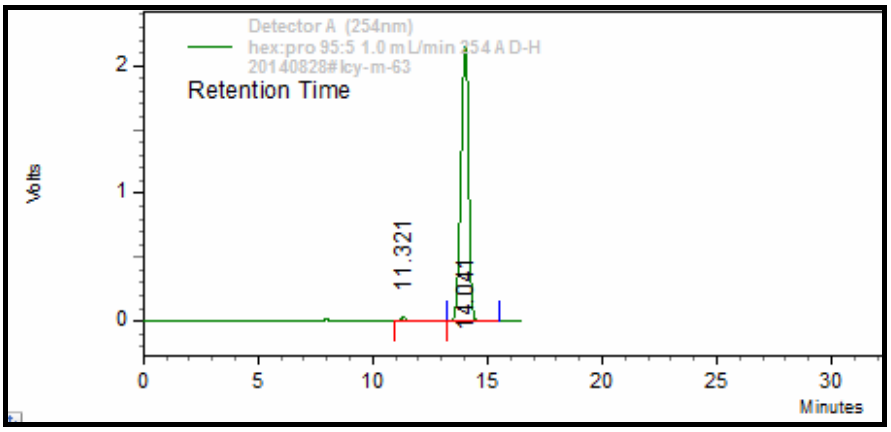


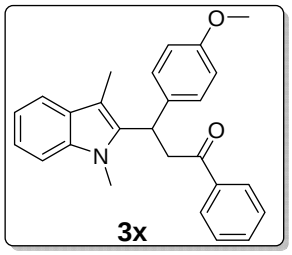
Detector A (254nm)

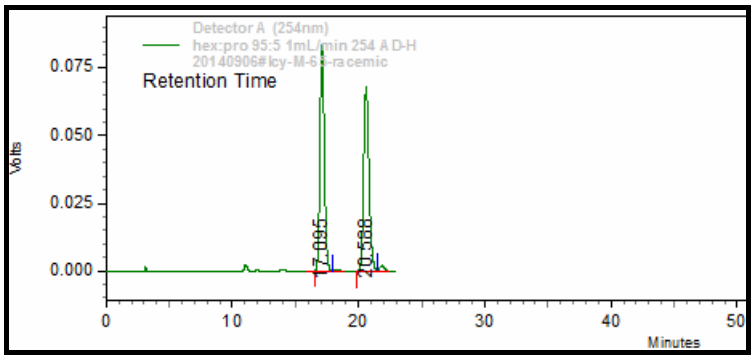
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.354	14895496	49.767	1003227	58.558
2	13.997	15034901	50.233	709989	41.442
Total		29930397	100.000	1713217	100.000



Detector A (254nm)

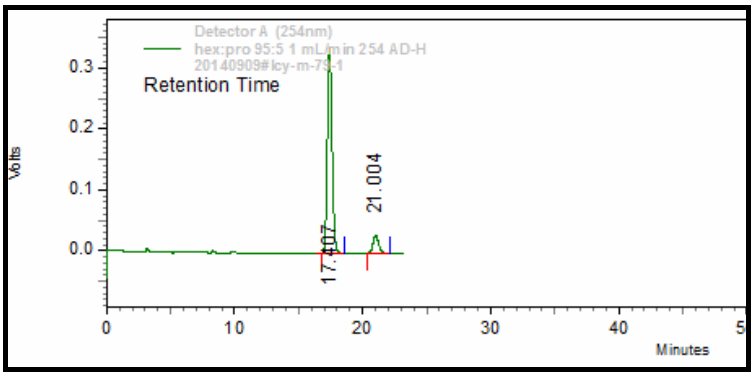
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.321	523806	1.030	36593	1.671
2	14.041	50336722	98.970	2153637	98.329
Total		50860528	100.000	2190230	100.000





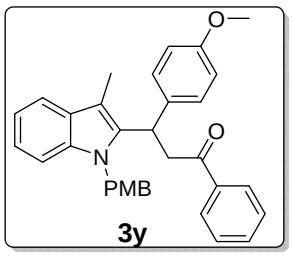
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.095	2036621	50.016	83888	55.087
2	20.588	2035358	49.984	68395	44.913
Total		4071979	100.000	152283	100.000

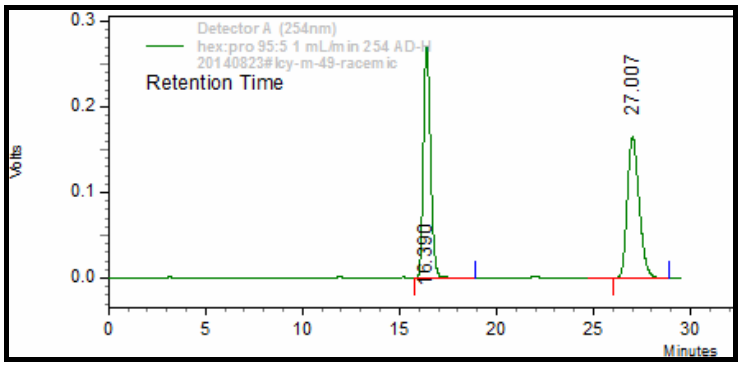


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	17.407	8615113	90.562	335899	92.015
2	21.004	897884	9.438	29149	7.985
Total		9512997	100.000	365049	100.000

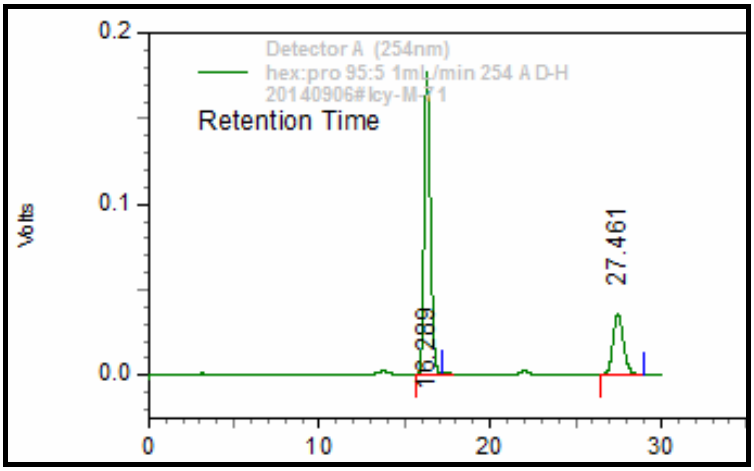


3y



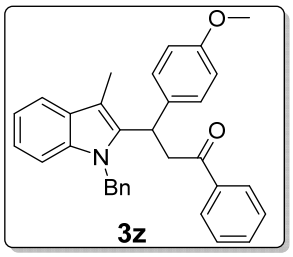
Detector A (254nm)

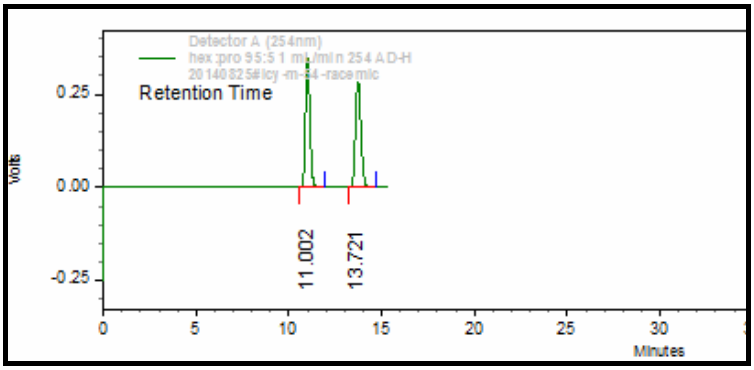
Pk #	Retention Time	Area	Area %	Height	Height %
1	16.390	6937713	49.879	271932	62.279
2	27.007	6971329	50.121	164700	37.721
Total		13909041	100.000	436632	100.000



Detector A (254nm)

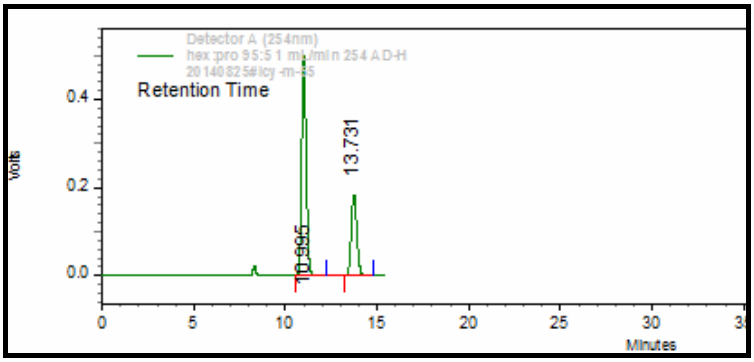
Pk #	Retention Time	Area	Area %	Height	Height %
1	16.289	4492062	75.100	177249	83.490
2	27.461	1489347	24.900	35049	16.510
Total		5981410	100.000	212299	100.000





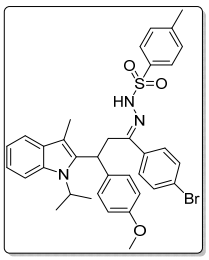
Detector A (254nm)

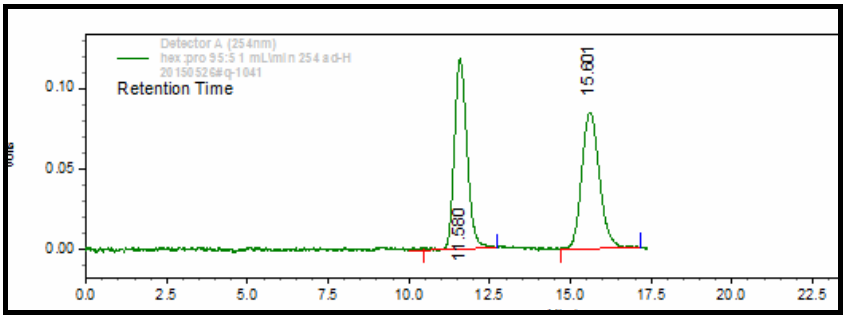
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.002	5784218	49.857	346729	55.050
2	13.721	5817328	50.143	283113	44.950
Total		11601546	100.000	629842	100.000



Detector A (254nm)

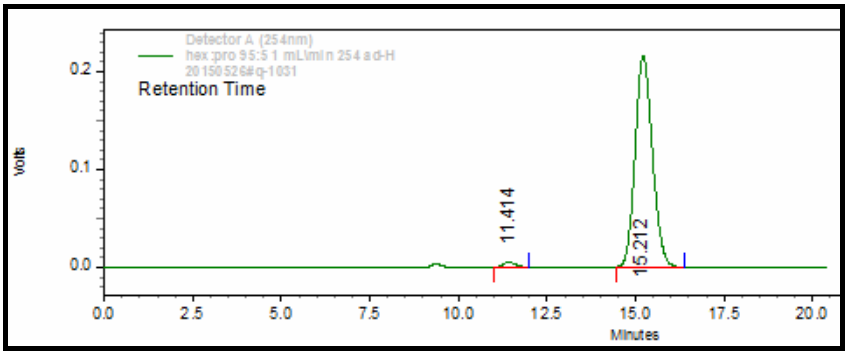
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.995	8505632	68.831	499217	73.085
2	13.731	3851695	31.169	183846	26.915
Total		12357327	100.000	683064	100.000





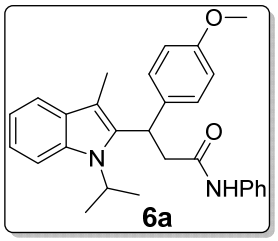
Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.580	3209309	49.783	118135	58.293
2	15.601	3237238	50.217	84521	41.707
Total		6446546	100.000	202656	100.000

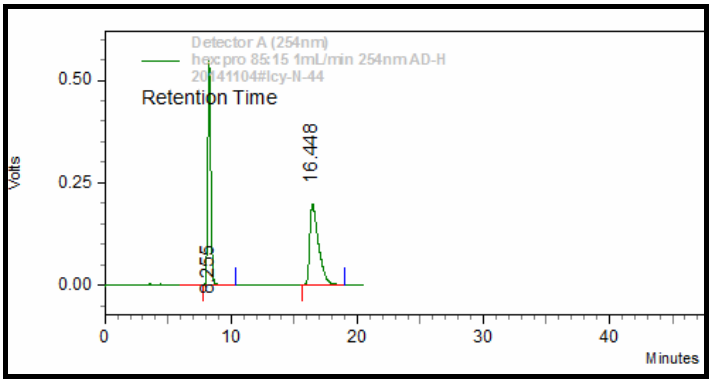


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.414	124387	1.657	5081	2.300
2	15.212	7381321	98.343	215863	97.700
Total		7505708	100.000	220944	100.000

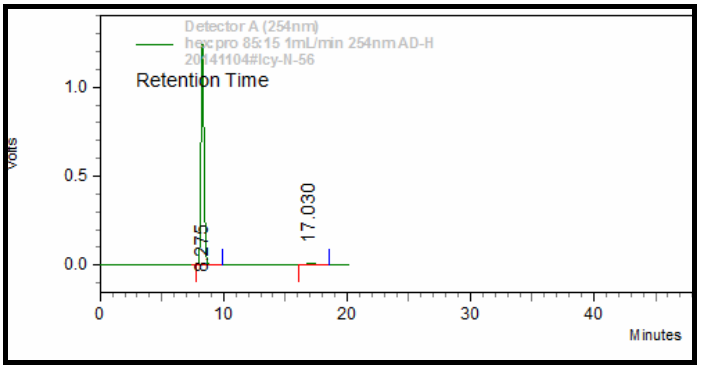


6a



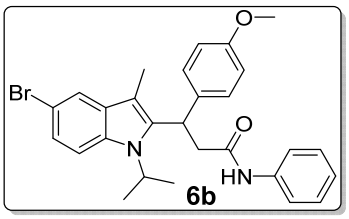
Detector A (254nm)

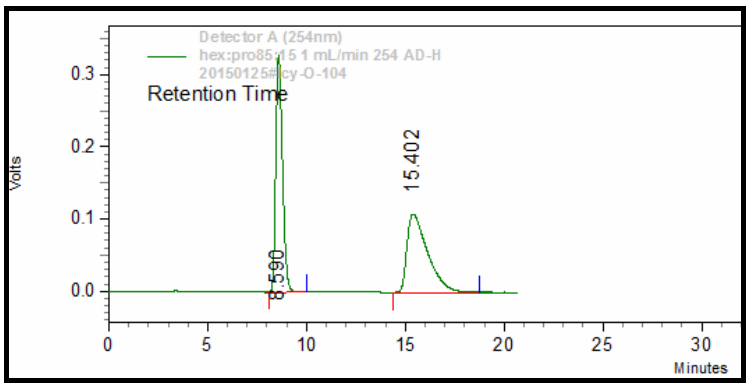
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.255	9269344	49.796	548871	73.739
2	16.448	9345273	50.204	195469	26.261
Total		18614617	100.000	744340	100.000



Detector A (254nm)

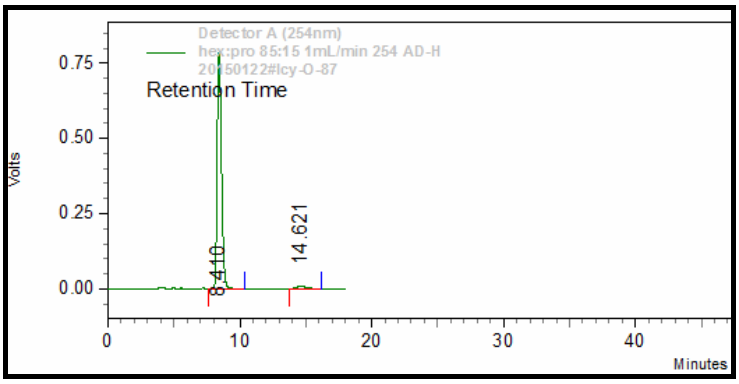
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.275	21398563	97.299	1246346	99.014
2	17.030	594028	2.701	12409	0.986
Total		21992592	100.000	1258755	100.000





Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.590	7771482	49.706	328244	75.167
2	15.402	7863468	50.294	108440	24.833
Total		15634950	100.000	436684	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	8.410	17971220	97.728	789255	98.980
2	14.621	417867	2.272	8136	1.020
Total		18389087	100.000	797391	100.000